# Ethyl lactate as a renewable carbonyl source for the synthesis of diynones

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# Electronic Supplementary Information

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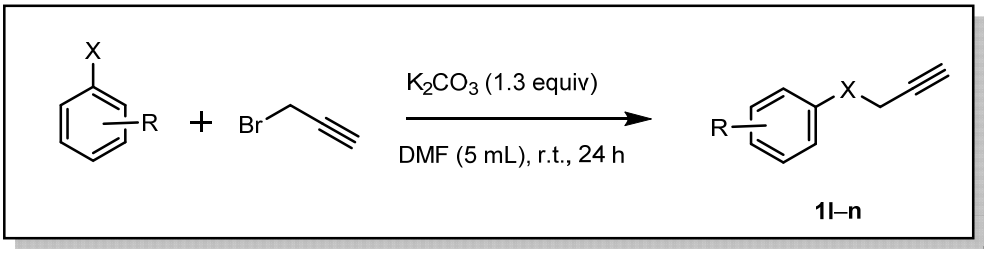
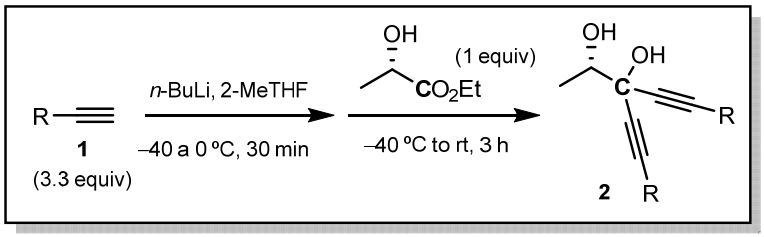
**General methods:** All common reagents and solvents were obtained from commercial suppliers and used without any further purification. TLC was performed on aluminum-backed plates coated with silica gel 60 with $F_{254}$ indicator; the chromatograms were visualized under ultraviolet light and/or by staining with a Ce/Mo reagent and subsequent heating. NMR spectra were measured on Varian Mercury-Plus 300 MHz, Bruker Avance 300 MHz and Varian Inova-400 MHz spectrometers. $^{1}$H NMR: splitting pattern abbreviations are: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; ddd, doublets of doublets of doublets; ddt, double doublet of triplets; dt, doublet of triplets; dq, doublet of quartets; td, triplet of doublets; qd, quartet of doublets; quin, quintuplet; sext, sextet; hept, heptet; ad, apparent doublet; at, apparent triplet; aq, apparent quartet; m, multiplet; the chemical shifts are reported in ppm using residual solvent peak as reference. $^{13}$C NMR spectra were recorded at 75.4 MHz or 100.6 MHz using broadband proton decoupling and chemical shifts are reported in ppm using residual solvent peaks as reference ($CDCl_3$: δ 77.16) and the multiplicities were determined by DEPT experiments. Products were characterized by NMR spectroscopy and capillary gas chromatography (GC). The microwave heating was performed in a microwave reactor (CEM Discover S-Class) with a single-mode microwave cavity producing continuous irradiation (temperature measurements were conducted using an IR sensor located below the microwave cavity floor, and reaction times refer to the total hold time at the indicated temperature; the maximum wattage supplied was 300 W). High resolution mass spectra (HRMS) were recorded on a LC-MS instrument (1260 Infinity, Agilent) equipped with a QTOF analyzer using ESI (+). Low resolution mass spectra (LRMS) measurements were recorded on an Agilent 6890N/5973 Network GC System, equipped with a HP-5MS column. Melting points were measured on a Gallenkamp apparatus using open capillary tubes and are uncorrected.

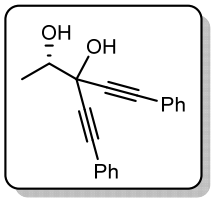



**General procedure for the synthesis of alkynes 1l-n:** Propargyl bromide (20 mmol, 2.03 mL) was added to a stirred solution of the corresponding phenol or aniline derivative (20 mmol) and $K_2CO_3$ (26 mmol, 3.59 g) in anhydrous DMF (5 mL) under $N_2$. The resulting mixture was stirred at rt until the corresponding phenol or aniline derivative was consumed as determined by GC-MS. NaOH (0.5 M, 10 mL) was added and the resulting solution was

extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with $H_2O$ (3 x 5 mL), dried over anhydrous $Na_2SO_4$ and the solvents were removed under reduced pressure. The obtained alkynes **1** were not further purified. The spectroscopic data of alkynes **1l-n** match with those reported in the literature. **1l**: N.-H. Nguyen, N. Bogliotti, R. Chennoufi, E. Henry, P. Tauc, E. Salas, L. J. Roman, A. Slama-Schwok, E. Deprezb and J. Xie, *Org. Biomol. Chem.,* 2016, **14**, 9519. **1m**: I. Volchkov and D. Lee, *J. Am. Chem. Soc.*, 2013, **135**, 5324. **1n**: J. M. Schulman, A. A. Friedman, J. Panteleev and M. Lautens, *Chem. Commun*., 2012, **48**, 55.




**General procedure for the synthesis of bispropargyl diols 2 and characterization data:** *n*-BuLi (3.3 mmol, 1.32 mL of a 2.5 M solution in hexane) was added to a solution of the appropriate alkyne **1** (3.4 mmol) in 2-MeTHF (4 mL) at –40 °C. The resulting solution was stirred for 30 min at 0 °C to obtain the corresponding lithium acetylide. Ethyl (*S*)-(–)-lactate (1 mmol, 121 mg) in 2-MeTHF (2 mL) was added dropwise with an addition funnel to the acetylide solution at –40 °C. The resulting mixture was stirred for 20 min at the same temperature and, after removal of the cooling bath, it was further stirred at rt until ethyl lactate was consumed as determined by GC–MS. For the synthesis of **2m** and **2n**, EtMgBr (4 mmol, 1.33 mL of a 3 M solution in diethyl ether) and the corresponding alkyne (3.6 mmol) were used for the generation of the magnesium acetylide instead of the lithium acetylide. Following the previously described addition, ethyl lactate was reacted overnight at rt and then, the mixture was refluxed for 2 h. For the synthesis of **2q**, ethynyl magnesium bromide (5 mmol, 10 mL of a 0.5 M solution in THF) was directly used and the reaction mixture was refluxed overnight. In all the cases, aqueous $NH_4Cl$ (10 mL) was added and the resulting solution was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography using mixtures of hexane and EtOAc as eluents to obtain the corresponding diol **2**. Alternatively, methyl lactate could be used instead of ethyl lactate, as shown with the preparation of **2b** and **2f**.

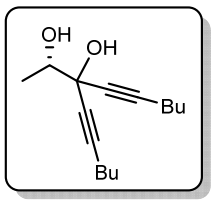



**(*S*)-5-Phenyl-3-(phenylethynyl)pent-4-yne-2,3-diol (2a):**[1] Yellow solid. Yield = 84%. $R_f$ = 0.16 (hexane/EtOAc, 3:1), m.p. 116–118 °C (lit.[1] 113–114 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.60–7.50 (m, 4H), 7.42–7.33 (m, 6H), 4.14 (q, *J* = 6.3 Hz, 1H), 3.37 (br s, 1H), 2.60 (br s, 1H), 1.57 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 132.1 (2 x CH), 132.0 (2 x CH), 129.00 (CH), 128.98 (CH), 128.4 (4 x CH), 121.9 (C), 121.8 (C), 87.1 (C), 86.1 (C), 85.6 (C), 85.1 (C), 74.6 (CH), 68.8 (C), 17.88 ($CH_3$)

**EI-LRMS:** *m/z* (%) 258 ($M^+$–$H_2O$, 13), 231 (100), 214 (86), 129 (90), 102 (35)

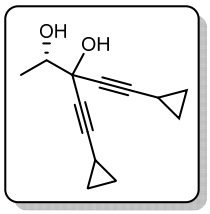



**(*S*)-3-(Hex-1-yn-1-yl)non-4-yne-2,3-diol (2b):**[1] Orange oil. Yield = 89%. $R_f$ = 0.23 (hexane/EtOAc, 3:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.80 (q, *J* = 6.3 Hz, 1H), 2.87 (br s, 2H), 2.26–2.17 (m, 4H), 1.56–1.35 (m, 8H), 1.33 (d, *J* = 6.3 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 6H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 85.5 (C), 84.9 (C), 79.0 (C), 77.7 (C), 74.2 (CH), 67.7 (C), 30.3 ($CH_2$), 30.2 ($CH_2$), 21.78 ($CH_2$), 21.76 ($CH_2$), 18.23 ($CH_2$), 18.19 ($CH_2$), 17.3 ($CH_3$), 13.4 (2 x $CH_3$)

**EI-LRMS:** *m/z* (%) 218 ($M^+$–$H_2O$, 9), 191 (100), 121 (67), 108 (82), 91 (71), 79 (55)

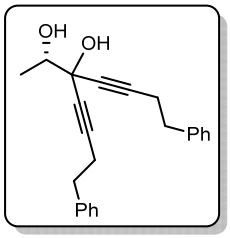



**(*S*)-5-Cyclopropyl-3-(cyclopropylethynyl)pent-4-yne-2,3-diol (2c):**[1] Yellow solid. Yield = 83%. $R_f$ = 0.19 (hexane/EtOAc, 3:1), m.p. 59–61 °C (lit.[1] 55–56 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.79–3.69 (m, 1H), 3.19 (d, *J* = 6.7 Hz, 1H), 2.57 (br s, 1H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.26–1.18 (m, 2H), 0.79–0.63 (m, 8H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 88.4 (C), 87.8 (C), 74.1 (CH), 74.0 (C), 72.7 (C), 67.5 (C), 17.3 ($CH_3$), 8.1 (2 x $CH_2$), 8.0 (2 x $CH_2$), -0.7 (CH), –0.8 (CH)

**EI-LRMS:** *m/z* (%) 204 ($M^+$, 1), 159 (100), 142 (52), 115 (82), 93 (50)




**(*S*)-7-Phenyl-3-(4-phenylbut-1-yn-1-yl)hept-4-yne-2,3-diol (2d):** White solid. Yield = 74%. $R_f$ = 0.14 (hexane/EtOAc, 3:1), m.p. 57–59 °C

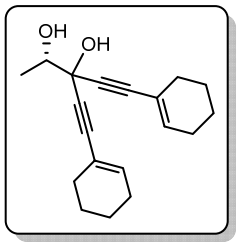
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.34–7.27 (m, 4H), 7.26–7.18 (m, 6H), 3.71 (q, *J* = 6.3 Hz, 1H), 2.90–2.81 (m, 4H), 2.60–2.51 (m, 4H), 1.94 (br s, 1H), 1.19 (d, *J* = 6.3 Hz, 3H). One OH signal does not appear

[1] B. Zhang, T. Wang and Z. Zhang, *J. Org. Chem.*, 2017, **82**, 11644.

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 140.14 (C), 140.07 (C), 128.22 (2 x CH), 128.19 (2 x CH), 128.13 (2 x CH), 128.12 (2 x CH), 126.1 (2 x CH), 84.6 (C), 84.2 (C), 79.7 (C), 78.4 (C), 74.1 (CH), 67.6 (C), 34.4 ($CH_2$), 34.3 ($CH_2$), 20.62 ($CH_2$), 20.60 ($CH_2$), 17.3 ($CH_3$)

**EI-LRMS:** *m/z* (%) 314 ($M^+$–$H_2O$, 7), 223 (28), 91 (100)

**HRMS** (ESI-TOF): calculated for $C_{23}H_{24}O_2Na$ $[M+Na]^+$ 355.1669; found 355.1672



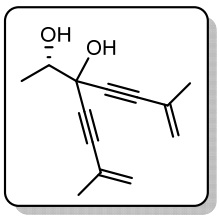
**(*S*)-5-(Cyclohex-1-en-1-yl)-3-(cyclohex-1-en-1-ylethynyl)pent-4-yne-2,3-diol (2e):** Orange oil. Yield = 75%. $R_f$ = 0.29 (hexane/EtOAc, 3:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.18–6.14 (m, 2H), 3.89 (q, *J* = 6.3 Hz, 1H), 3.13 (br s, 1H), 2.46 (br s, 1H), 2.17–2.03 (m, 8H), 1.67–1.52 (m, 8H), 1.37 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 136.5 (2 x CH), 119.70 (C), 119.67 (C), 87.0 (C), 86.5 (C), 84.7 (C), 83.5 (C), 74.5 (CH), 68.6 (C), 29.0 ($CH_2$), 28.9 ($CH_2$), 25.7 (3 x $CH_2$), 22.22 ($CH_2$), 22.21 ($CH_2$), 21.4 ($CH_2$), 17.7 ($CH_3$)

**EI-LRMS:** *m/z* (%) 284 ($M^+$, 3), 266 (28), 239 (100), 222 (42)

**HRMS** (ESI-TOF): calculated for $C_{19}H_{24}O_2Na$ $[M+Na]^+$ 307.1669; found 307.1674



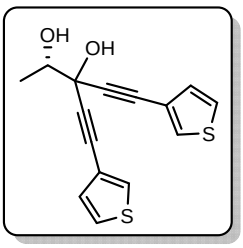
**(*S*)-6-Methyl-3-(3-methylbut-3-en-1-yn-1-yl)hept-6-en-4-yne-2,3-diol (2f):** White solid. Yield = 74%. $R_f$ = 0.22 (hexane/EtOAc, 3:1), m.p. 79–81 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 5.38–5.35 (m, 2H), 5.31–5.27 (m, 2H), 3.92 (q, *J* = 6.3 Hz, 1H), 3.18 (br s, 1H), 2.46 (br s, 1H), 1.91–1.88 (m, 6H), 1.39 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 125.81 (C), 125.77 (C), 123.6 (2 x $CH_2$), 86.6 (C), 86.1 (C), 86.0 (C), 84.9 (C), 74.4 (CH), 68.6 (C), 23.3 ($CH_3$), 23.2 ($CH_3$), 17.7 ($CH_3$)

**EI-LRMS:** *m/z* (%) 186 ($M^+$–$H_2O$, 3), 160 (100), 142 (71), 115 (77), 93 (58)

**HRMS** (ESI-TOF): calculated for $C_{13}H_{16}O_2Na$ $[M+Na]^+$ 227.1043; found 227.1042

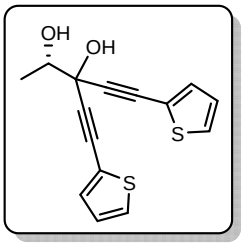


**(*S*)-5-(Thiophen-3-yl)-3-(thiophen-3-ylethynyl)pent-4-yne-2,3-diol (2g):**[1] Brown oil. Yield = 70%. $R_f$ = 0.20 (hexane/EtOAc, 3:1)

**$^1$H NMR** (300 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.82–7.79 (m, 2H), 7.61 (dd, *J* = 5.0, 3.0 Hz, 2H), 7.17 (dd, *J* = 5.0, 0.4 Hz, 2H), 6.47 (br s, 1H), 5.12 (d, *J* = 5.1 Hz, 1H), 3.81–3.73 (m, 1H), 1.29 (d, *J* = 6.2 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, DMSO-$d_6$) $\delta$ (ppm): 130.1 (CH), 130.0 (CH), 129.7 (CH), 129.6 (CH), 126.84 (CH), 126.78 (CH), 121.0 (C), 120.8 (C), 89.2 (C), 89.0 (C), 78.4 (C), 78.2 (C), 73.1 (CH), 67.8 (C), 18.3 ($CH_3$)

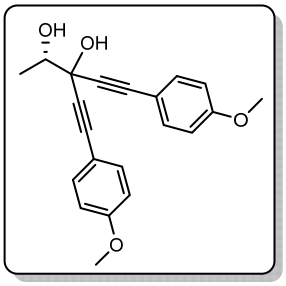
**EI-LRMS:** *m/z* (%) 270 ($M^+$–$H_2O$, 40), 269 (35), 241 (36), 227 (42), 226 (100), 225 (39), 182 (31)



**(*S*)-5-(Thiophen-2-yl)-3-(thiophen-2-ylethynyl)pent-4-yne-2,3-diol (2h):**[1] Brown solid. Yield = 75%. $R_f$ = 0.19 (hexane/EtOAc, 3:1), m.p. 133–135 °C (lit.[1] 138–139 °C)

**$^1$H NMR** (300 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.65–7.61 (m, 2H), 7.37–7.34 (m, 2H), 7.09 (dd, *J* = 5.2, 3.6 Hz, 2H), 6.66 (br s, 1H), 5.26 (d, *J* = 5.5 Hz, 1H), 3.86–3.72 (m, 1H), 1.27 (d, J = 6.2 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, DMSO-$d_6$) $\delta$ (ppm): 132.84 (CH), 132.77 (CH), 128.8 (CH), 128.7 (CH), 127.7 (CH), 127.6 (CH), 121.5 (C), 121.3 (C), 93.5 (C), 93.0 (C), 76.6 (C), 76.3 (C), 72.9 (CH), 68.1 (C), 18.2 ($CH_3$)

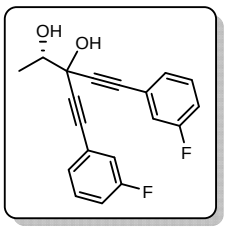


**(*S*)-5-(4-Methoxyphenyl)-3-((4-methoxyphenyl)ethynyl)pent-4-yne-2,3-diol (2i):**[1] Yellow solid. Yield = 74%. $R_f$ = 0.10 (hexane/EtOAc, 2:1), m.p. 116–118 °C (lit.[1] 107–108 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.46–7.39 (m, 4H), 6.86–6.81 (m, 4H), 4.11-4.03 (m, 1H), 3.80 (s, 6H), 3.32 (d, *J* = 8.5 Hz, 1H), 2.57 (br s, 1H), 1.51 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 159.92 (C), 159.90 (C), 133.5 (2 x CH), 133.4 (2 x CH), 114.0 (2 x C), 113.93 (2 x CH), 113.92 (2 x CH), 86.1 (C), 85.3 (C), 85.0 (C), 84.8 (C), 74.6 (CH), 68.8 (C), 55.3 (2 x $CH_3$), 17.8 ($CH_3$)

**EI-LRMS:** *m/z* (%) 318 ($M^+$–$H_2O$, 99), 291 (100), 274 (43), 273 (41), 159 (73)



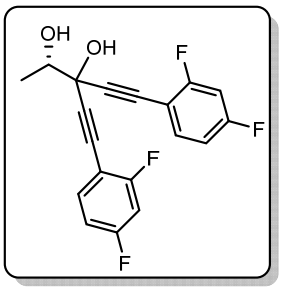
**(*S*)-5-(3-Fluorophenyl)-3-((3-fluorophenyl)ethynyl)pent-4-yne-2,3-diol (2j):** Yellow solid. Yield = 72%. $R_f$ = 0.24 (hexane/EtOAc, 3:1), m.p. 94–96 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.32–7.24 (m, 4H), 7.22–7.14 (m, 2H), 7.10–7.00 (m, 2H), 4.11 (q, *J* = 6.3 Hz, 1H), 3.74 (br s, 1H), 2.81 (br s, 1H), 1.52 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 162.3 (d, *J* = 246.9 Hz, 2 x C), 130.1 (d, *J* = 1.6 Hz, CH), 130.0 (d, *J* = 1.6 Hz, CH), 128.0 (d, *J* = 3.1 Hz, CH), 127.9 (d, *J* = 3.1 Hz, CH), 123.6 (d, *J* = 5.5 Hz, C), 123.5 (d, *J* = 5.5 Hz, C), 119.0 (d, *J* = 6.3 Hz, CH), 118.7 (d, *J* = 6.3 Hz, CH), 116.6 (d, *J* = 2.3 Hz, CH), 116.3 (d, *J* = 2.3 Hz, CH), 87.8 (C), 86.7 (C), 84.4 (d, *J* = 3.4 Hz, C), 83.9 (d, *J* = 3.4 Hz, C), 74.5 (CH), 68.7 (C), 17.9 ($CH_3$)

**EI-LRMS:** *m/z* (%) 312 ($M^+$, 1), 267 (83), 250 (100), 240 (48), 147 (86)

**HRMS** (ESI-TOF): calculated for $C_{19}H_{15}F_2O_2$ $[M+H]^+$ 313.1035; found 313.1040

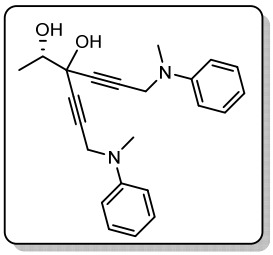


**(*S*)-5-(2,4-Difluorophenyl)-3-((2,4-difluorophenyl)ethynyl)pent-4-yne-2,3-diol (2k):** Brown solid. Yield = 73%. $R_f$ = 0.13 (hexane/EtOAc, 3:1), m.p. 102–104 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.56–7.40 (m, 2H), 6.91–6.79 (m, 4H), 4.11 (q, *J* = 6.3 Hz, 1H), 3.38 (br s, 1H), 2.50 (br s, 1H), 1.53 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 163.7 (d, *J* = 254.6 Hz, C), 163.5 (d, *J* = 254.5 Hz, C), 163.4 (d, *J* = 253.2 Hz, C), 163.2 (d, *J* = 253.0 Hz, C), 134.8 (dd, *J* = 5.1, 2.6 Hz, CH), 134.7 (dd, *J* = 5.2, 2.5 Hz, CH), 111.9 (d, *J* = 3.8 Hz, CH), 111.6 (d, *J* = 3.8 Hz, CH), 107.0 (C), 106.8 (C), 104.46 (t, *J* = 25.2 Hz, CH), 104.45 (t, *J* = 25.3 Hz, CH), 91.7 (dd, *J* = 3.5, 1.8 Hz, C), 90.8 (dd, *J* = 3.6, 2.0 Hz, C), 78.3 (C), 77.9 (C), 74.6 (CH), 69.0 (C), 17.8 ($CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{19}H_{12}F_4O_2Na$ $[M+Na]^+$ 371.0666; found 371.0672

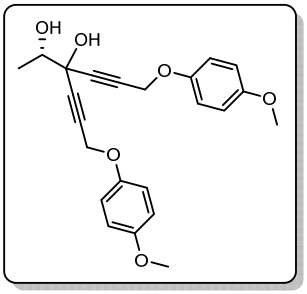


**(*S*)-6-(Methyl(phenyl)amino)-3-(3-(methyl(phenyl)amino)prop-1-yn-1-yl)hex-4-yne-2,3-diol (2l):** Brown solid. Yield = 71%. $R_f$ = 0.23 (hexane/EtOAc, 2:1), m.p. 75–77 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.33–7.28 (m, 4H), 6.92–6.82 (m, 6H), 4.10 (s, 2H), 4.08 (s, 2H), 3.69 (q, *J* = 6.3 Hz, 1H), 3.42 (br s, 1H), 2.94 (s, 3H), 2.93 (s, 3H), 2.20 (br s, 1H), 1.13 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 149.0 (C), 148.9 (C), 129.0 (4 x CH), 118.7 (CH), 118.6 (CH), 114.8 (2 x CH), 114.7 (2 x CH), 82.6 (C), 81.5 (C), 80.6 (C), 80.3 (C), 74.0 (CH), 67.4 (C), 43.0 ($CH_2$), 42.8 ($CH_2$), 38.7 ($CH_3$), 38.6 ($CH_3$), 17.2 ($CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{23}H_{26}N_2O_2Na$ $[M+Na]^+$ 385.1886; found 385.1890

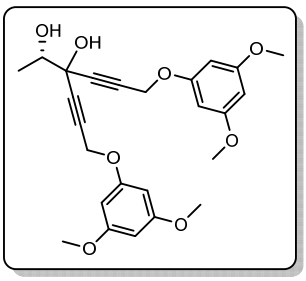


**(*S*)-6-(4-Methoxyphenoxy)-3-(3-(4-methoxyphenoxy)prop-1-yn-1-yl)hex-4-yne-2,3-diol (2m):** Brown solid. Yield = 66%. $R_f$ = 0.26 (hexane/EtOAc, 2:1), m.p. 74–76 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.93–6.86 (m, 4H), 6.86–6.79 (m, 4H), 4.67 (s, 2H), 4.65 (s, 2H), 3.82 (q, *J* = 6.3 Hz, 1H), 3.76 (s, 6H), 3.35 (br s, 1H), 2.33 (br s, 1H), 1.24 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 154.5 (2 x C), 151.6 (2 x C), 116.4 (2 x CH), 116.3 (2 x CH), 114.6 (4 x CH), 85.0 (C), 84.1 (C), 80.8 (C), 80.4 (C), 74.0 (CH), 67.7 (C), 57.0 ($CH_2$), 56.9 ($CH_2$), 55.7 (2 x $CH_3$), 17.4 ($CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{23}H_{24}O_6Na$ $[M+Na]^+$ 419.1465; found 419.1470

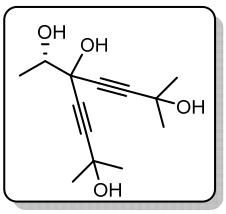


**(*S*)-6-(3,5-Dimethoxyphenoxy)-3-(3-(3,5-dimethoxyphenoxy)prop-1-yn-1-yl)hex-4-yne-2,3-diol (2n):** Yellow solid. Yield = 70%. $R_f$ = 0.27 (hexane/EtOAc, 1:1), m.p. 77–79 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.15–6.09 (m, 6H), 4.68 (s, 2H), 4.66 (s, 2H), 3.90–3.80 (m, 2H), 3.75 (s, 12H), 2.42 (br s, 1H), 1.29 (d, *J* = 6.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.4 (4 x C), 159.4 (2 x C), 93.9 (2 x CH), 93.8 (4 x CH), 85.2 (C), 84.2 (C), 80.4 (C), 80.0 (C), 74.0 (CH), 67.7 (C), 56.1 ($CH_2$), 56.0 ($CH_2$), 55.4 (4 x $CH_3$), 17.4 ($CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{25}H_{29}O_8$ $[M+H]^+$ 457.1857; found 457.1862

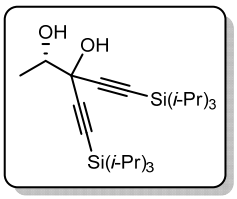


**(*S*)-5-(1-hydroxyethyl)-2,8-dimethylnona-3,6-diyne-2,5,8-triol (2o):** Orange oil. Yield = 62%. $R_f$ = 0.35 (EtOAc)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 5.29 (br s, 1H), 4.45 (br s, 1H), 3.88 (q, *J* = 6.1 Hz, 1H), 2.96 (br s, 2H), 1.54–1.47 (m, 12H), 1.34 (d, *J* = 6.1 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 90.0 (C), 89.6 (C), 80.4 (C), 79.4 (C), 74.5 (CH), 67.7 (C), 65.02 (C), 64.98 (C), 31.12 ($CH_3$), 31.10 ($CH_3$), 31.05 ($CH_3$), 30.9 ($CH_3$), 17.9 ($CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{13}H_{20}O_4Na$ $[M+Na]^+$ 263.1254; found 263.1260



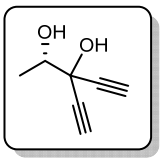
**(*S*)-5-(Triisopropylsilyl)-3-((triisopropylsilyl)ethynyl)pent-4-yne-2,3-diol (2p):** Yellow oil. Yield = 80%. $R_f$ = 0.55 (hexane/EtOAc, 4:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.89 (q, *J* = 6.3 Hz, 1H), 2.94 (br s, 1H), 2.29 (br s, 1H), 1.42 (d, *J* = 6.3 Hz, 3H), 1.08 (s, 42H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 105.3 (C), 104.1 (C), 87.0 (C), 86.6 (C), 74.4 (CH), 68.6 (C), 18.70 (4 x $CH_3$), 18.69 (4 x $CH_3$), 18.67 (4 x $CH_3$), 17.8 ($CH_3$), 11.24 (3 x CH), 11.22 (3 x CH)

**EI-LRMS:** *m/z* (%) 418 ($M^+$–$H_2O$, 1), 375 (50), 350 (100), 349 (58), 115 (95), 75 (58)

**HRMS** (ESI-TOF): calculated for $C_{25}H_{48}O_2Si_2Na$ $[M+Na]^+$ 459.3085; found 459.3091



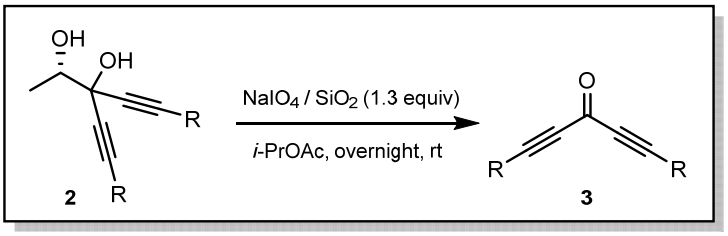
**(*S*)-3-Ethynylpent-4-yne-2,3-diol (2q):** Orange oil. Yield = 84%. $R_f$ = 0.37 (hexane/EtOAc, 2:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.93 (q, *J* = 6.3 Hz, 1H), 3.68 (br s, 1H), 2.85 (br s, 1H), 2.63 (s, 1H), 2.61 (s, 1H), 1.39 (d, *J* = 6.3 Hz, 3H)

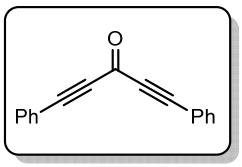
**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 81.7 (C), 80.6 (C), 74.2 (CH), 73.9 (CH), 73.7 (CH), 67.3 (C), 17.4 ($CH_3$)

**EI-LRMS:** *m/z* (%) 80 ($M^+$–$C_2H_4O$, 100), 62 (29), 54 (81), 53 (50), 45 (85)

**HRMS** (ESI-TOF): calculated for $C_7H_8O_2Na$ $[M+Na]^+$ 147.0417; found 147.0414




**General procedure for the synthesis of skipped diynones 3 and characterization data:** A solution of the corresponding bispropargyl diol **2** (0.5 mmol) in *i*-PrOAc (2 mL) was added to a vigorously stirred suspension of silica gel–supported $NaIO_4$ reagent[2] (952 mg) in *i*-PrOAc (3 mL). The reaction was monitored by TLC until disappearance of the starting material. The mixture was filtered through a celite pad in a sintered glass filter funnel and the silica gel was washed with *i*-PrOAc (5 mL). Removal of solvents from the filtrate under reduced pressure afforded the corresponding skipped diynone **3** that was obtained in pure form without further purification.

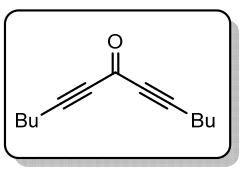



**1,5-Diphenylpenta-1,4-diyn-3-one (3a):**[3] Orange solid. Yield = 95%. $R_f$ = 0.59 (hexane/EtOAc, 10:1), m.p. 59–61 °C (lit.[4] 60 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.67 (d, *J* = 8.2 Hz, 4H), 7.57–7.48 (m, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 4H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 160.8 (C), 133.3 (4 x CH), 131.3 (2 x CH), 128.7 (4 x CH), 119.4 (2 x C), 91.7 (2 x C), 89.4 (2 x C)

**EI-LRMS:** *m/z* (%) 230 ($M^+$, 31), 202 (100), 200 (36)



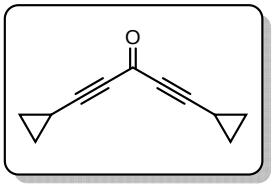

**Trideca-5,8-diyn-7-one (3b):**[5] Yellow oil. Yield = 98%. $R_f$ = 0.36 (hexane/EtOAc, 10:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 2.41 (t, *J* = 7.0 Hz, 4H), 1.65–1.53 (m, 4H), 1.51–1.38 (m, 4H), 0.94 (t, *J* = 7.3 Hz, 6H)

[2] Y.–L. Zhong and T. K. M. Shing, *J. Org. Chem.*, 1997, **62**, 2622.
[3] Y.-F. Qiu, F. Yang, Z.-H. Qiu, M.-J Zhong, L.-J. Wang, Y.-Y. Ye, B. Song and Y.-M. Liang, *J. Org. Chem.,* 2013, **78**, 12018.
[4] J. Chauvelier, *Ann. Chim. (Paris),* 1948, **12**, 410.
[5] R. K. Shiroodi, M. Soltani and V. Gevorgyan, *J. Am. Chem. Soc.,* 2014, **136**, 9882.

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.4 (C), 94.6 (2 x C), 82.3 (2 x C), 29.5 (2 x $CH_2$), 22.0 (2 x $CH_2$), 18.8 (2 x $CH_2$), 13.5 (2 x $CH_3$)

**EI-LRMS:** *m/z* (%) 190 ($M^+$, 1), 148 (83), 109 (100), 91 (49), 79 (55)

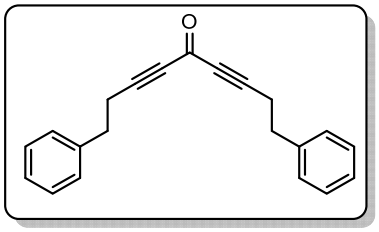


**1,5-Dicyclopropylpenta-1,4-diyn-3-one (3c):**[3] Yellow oil. Yield = 91%. $R_f$ = 0.49 (hexane/EtOAc, 10:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.50–1.40 (m, 2H), 1.07–0.92 (m, 8H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 160.5 (C), 98.8 (2 x C), 77.9 (2 x C), 9.9 (4 x $CH_2$), -0.2 (2 x CH)

**EI-LRMS:** *m/z* (%) 158 ($M^+$, 42), 129 (39), 128 (100), 127 (40), 115 (81)



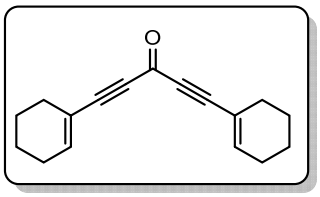
**1,9-Diphenylnona-3,6-diyn-5-one (3d):** Yellow oil. Yield = 93%. $R_f$ = 0.38 (hexane/EtOAc, 10:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.42–7.34 (m, 4H), 7.34–7.26 (m, 6H), 2.97 (t, *J* = 7.4 Hz, 4H), 2.74 (t, *J* = 7.4 Hz, 4H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.0 (C), 139.5 (2 x C), 128.6 (4 x CH), 128.4 (4 x CH), 126.7 (2 x CH), 93.7 (2 x C), 82.7 (2 x C), 33.8 (2 x $CH_2$), 21.3 (2 x $CH_2$)

**EI-LRMS:** *m/z* (%) 286 ($M^+$, 9), 285 (10), 195 (27), 91 (100)

**HRMS** (ESI-TOF): calculated for $C_{21}H_{18}ONa$ $[M+Na]^+$ 309.125; found 309.1254

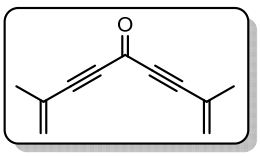


**1,5-Di(cyclohex-1-en-1-yl)penta-1,4-diyn-3-one (3e):**[6] Brown oil. Yield = 96%. $R_f$ = 0.5 (hexane/EtOAc, 10:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.58–6.51 (m, 2H), 2.23–2.15 (m, 8H), 1.72–1.58 (m, 8H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.3 (C), 143.7 (2 x CH), 118.9 (2 x C), 93.5 (2 x C), 88.0 (2 x C), 28.1 (2 x $CH_2$), 26.3 (2 x $CH_2$), 21.9 (2 x $CH_2$), 21.1 (2 x $CH_2$)

**EI-LRMS:** *m/z* (%) 238 ($M^+$, 100), 210 (40), 167 (59), 165 (52), 153 (40), 77 (36)



**2,8-Dimethylnona-1,8-dien-3,6-diyn-5-one (3f):** Brown oil. Yield = 97%. $R_f$ = 0.72 (hexane/EtOAc, 2:1)

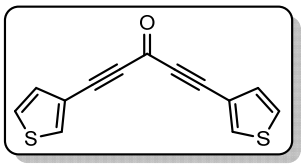
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 5.68–5.66 (m, 2H), 5.60–5.57 (m, 2H), 1.98 (dd, *J* = 1.6, 1.1 Hz, 6H)

[6] A. Dermenci, R. E. Whittaker and G. Dong, *Org. Lett.*, 2013, **15**, 2242.

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.0 (C), 128.9 (2 x $CH_2$), 124.6 (2 x C), 92.3 (2 x C), 88.0 (2 x C), 22.4 (2 x $CH_3$)

**EI-LRMS:** *m/z* (%) 158 ($M^+$, 75), 130 (79), 128 (93), 115 (100)

**HRMS** (ESI-TOF): calculated for $C_{11}H_{11}O$ $[M+H]^+$ 159.0804; found 159.0805



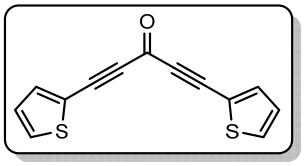
**2,8-Dimethylnona-1,8-dien-3,6-diyn-5-one (3g):** Brown solid. Yield = 92%. $R_f$ = 0.65 (hexane/EtOAc, 3:1), m.p. 95–97 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.85 (dd, *J* = 3.0, 1.2 Hz, 2H), 7.36 (dd, *J* = 5.0, 3.0 Hz, 2H), 7.29 (dd, *J* = 5.0, 1.2 Hz, 2H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 160.8 (C), 135.0 (2 x CH), 130.4 (2 x CH), 126.5 (2 x CH), 118.9 (2 x C), 89.8 (2 x C), 87.2 (2 x C)

**EI-LRMS:** *m/z* (%) 242 ($M^+$, 47), 214 (100), 169 (19)

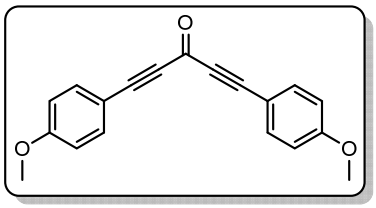
**HRMS** (ESI-TOF): calculated for $C_{13}H_6OS_2Na$ $[M+Na]^+$ 264.9752; found 264.9756



**1,5-Di(thiophen-2-yl)penta-1,4-diyn-3-one (3h):**[7] Brown solid. Yield = 94%. $R_f$ = 0.18 (hexane/EtOAc, 40:1), m.p. 115–117 °C

**$^1$H NMR** (300 MHz, DMSO-$D_6$) $\delta$ (ppm): 8.02 (dd, *J* = 5.1, 1.2 Hz, 2H), 7.83 (dd, *J* = 3.8, 1.2 Hz, 2H), 7.26 (dd, *J* = 5.1, 3.8 Hz, 2H)

**$^{13}$C NMR** (75.4 MHz, DMSO-$D_6$) $\delta$ (ppm): 158.4 (C), 139.0 (2 x CH), 135.1 (2 x CH), 128.8 (2 x CH), 117.5 (2 x C), 93.5 (2 x C), 86.1 (2 x C)

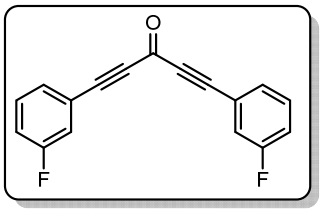


**1,5-Bis(4-methoxyphenyl)penta-1,4-diyn-3-one (3i):**[3] Red solid. Yield = 88%. $R_f$ = 0.38 (hexane/EtOAc, 3:1), m.p. 125–127 °C (lit.[8] 117–119 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.64–7.58 (m, 4H), 6.95–6.89 (m, 4H), 3.86 (s, 6H)

**$^{13}$C NMR** (75.4 MHz, $C_6D_6$) $\delta$ (ppm): 162.1 (2 x C), 160.5 (C), 135.6 (4 x CH), 114.6 (4 x CH), 111.8 (2 x C), 91.7 (2 x C), 90.6 (2 x C), 54.8 (2 x $CH_3$)

**EI-LRMS:** *m/z* (%) 290 ($M^+$, 71), 262 (100), 247 (96)



**1,5-Bis(3-fluorophenyl)penta-1,4-diyn-3-one (3j):**[3] Orange solid. Yield = 96%. $R_f$ = 0.67 (hexane/EtOAc, 3:1), m.p. 105–107 °C

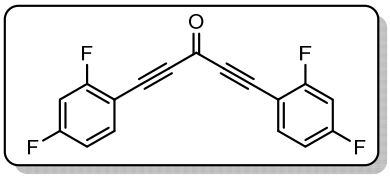
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.50–7.30 (m, 6H), 7.27–7.15 (m, 2H)

[7] S. Eisler, N. Chahal, R. McDonald, R. R. Tykwinski, *Chem. Eur. J.,* 2003, **9**, 2542.

[8] A. Auffrant, F. Diederich, C. Boudon, J.-P. Gisselbrecht and M. Gross, *Helvetica Chim. Acta*, 2004, **87**, 3085.

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 162.3 (d, *J* = 248.6 Hz, 2 x C), 160.3 (C), 130.6 (d, *J* = 8.5 Hz, 2 x CH), 129.3 (d, *J* = 3.2 Hz, 2 x CH), 121.2 (d, *J* = 9.4 Hz, 2 x C), 120.0 (d, *J* = 23.3 Hz, 2 x CH), 118.9 (d, *J* = 21.2 Hz, 2 x CH), 90.0 (d, *J* = 3.6 Hz, 2 x C), 89.4 (2 x C)

**EI-LRMS:** *m/z* (%) 266 ($M^+$, 27), 238 (100), 147 (9)

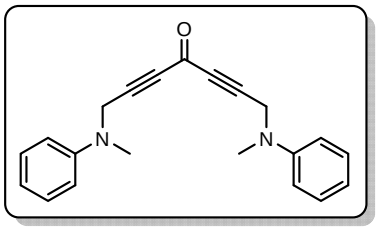



**1,5-bis(2,4-difluorophenyl)penta-1,4-diyn-3-one (3k):** Yellow solid. Yield = 93%. $R_f$ = 0.28 (hexane/EtOAc, 40:1), m.p. 119–121 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.67–7.56 (m, 2H), 7.00–6.88 (m, 4H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 165.1 (d, *J* = 257.1 Hz, C), 165.0 (d, *J* = 257.0 Hz, C), 164.9 (d, *J* = 259.6 Hz, C), 164.7 (d, *J* = 259.4 Hz, C), 159.9 (C), 136.3 (dd, *J* = 10.3, 1.1 Hz, 2 x CH), 112.6 (dd, *J* = 22.2, 3.7 Hz, 2 x CH), 105.1 (dd, *J* = 25.8, 24.3 Hz, 2 x CH), 104.91 (C), 104.85 (C), 93.4 (2 x C), 84.6 (2 x C)

**HRMS** (ESI-TOF): calculated for $C_{17}H_6F_4ONa$ $[M+Na]^+$ 325.0247; found 325.0247



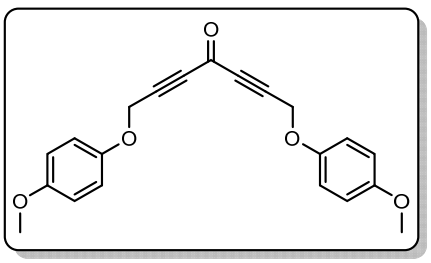

**1,7-Bis(methyl(phenyl)amino)hepta-2,5-diyn-4-one (3l):** Brown oil. Yield = 82%. $R_f$ = 0.27 (hexane/EtOAc, 1:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 7.35–7.28 (m, 4H), 6.93–6.82 (m, 6H), 4.25 (s, 4H), 2.98 (s, 6H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 160.0 (C), 148.6 (2 x C), 129.3 (4 x CH), 118.9 (2 x CH), 114.4 (4 x CH), 89.5 (2 x C), 84.4 (2 x C), 42.9 (2 x $CH_3$), 38.8 (2 x $CH_2$)

**EI-LRMS:** GS-MS could not be recorded due to decomposition

**HRMS** (ESI-TOF): calculated for $C_{21}H_{21}N_2O$ $[M+H]^+$ 317.1648; found 317.1653



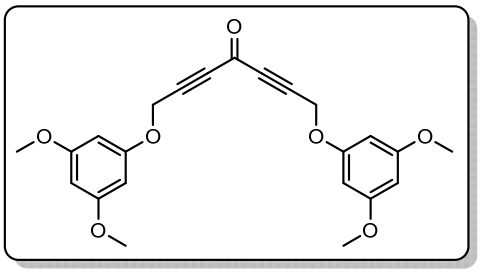

**1,7-Bis(4-methoxyphenoxy)hepta-2,5-diyn-4-one (3m):** Brown solid. Yield = 93%. $R_f$ = 0.33 (hexane/EtOAc, 1:1), m.p. 65–67 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.94–6.81 (m, 8H), 4.79 (s, 4H), 3.77 (s, 6H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 159.3 (C), 154.9 (2 x C), 151.4 (2 x C), 116.5 (4 x CH), 114.8 (4 x CH), 88.3 (2 x C), 86.0 (2 x C), 56.8 (2 x $CH_2$), 55.7 (2 x $CH_3$)

**EI-LRMS:** GS-MS could not be recorded due to decomposition

**HRMS** (ESI-TOF): calculated for $C_{21}H_{18}O_5Na$ $[M+Na]^+$ 373.1046; found 373.1049



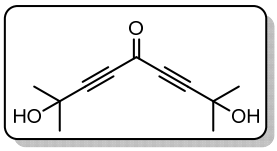
**1,7-Bis(3,5-dimethoxyphenoxy)hepta-2,5-diyn-4-one (3n):** Brown solid. Yield = 95%. $R_f$ = 0.8 (hexane/EtOAc, 1:1), mp 121−123 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 6.16–6.14 (m, 2H), 6.12 (d, $J$ = 2.1 Hz, 4H), 4.81 (s, 4H), 3.77 (s, 12H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.6 (4 x C), 159.2 (3 x C), 94.2 (2 x CH), 93.8 (4 x CH), 87.8 (2 x C), 86.0 (2 x C), 55.8 (2 x $CH_2$), 55.5 (4 x $CH_3$)

**EI-LRMS:** GS-MS could not be recorded due to decomposition

**HRMS** (ESI-TOF): calculated for $C_{23}H_{23}O_7$ $[M+H]^+$ 411.1438; found 411.1442

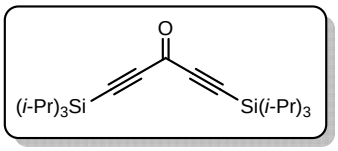


**2,8-dihydroxy-2,8-dimethylnona-3,6-diyn-5-one (3o):** Brown oil. Yield = 93%. $R_f$ = 0.12 (hexane/EtOAc, 3:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.06 (br s, 2H ), 1.57 (s, 12H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 161.3 (C), 97.3 (2 x C), 82.06 (2 x C), 65.1 (2 x C), 30.4 (4 x $CH_3$)

**HRMS** (ESI-TOF): calculated for $C_{11}H_{14}O_3Na$ $[M+Ma]^+$ 217.0835; found 217.0836

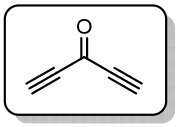


**1,5-Bis(triisopropylsilyl)penta-1,4-diyn-3-one (3p):**[9] Yellow oil. Yield = 96%. $R_f$ = 0.25 (hexane/EtOAc, 5:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.19–1.07 (m, 42H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 160.0 (C), 105.4 (2 x C), 97.7 (2 x C), 18.5 (12 x $CH_3$), 11.1 (6 x CH)

**EI-LRMS** *m/z* (%) 390 ($M^+$, 4), 347 (100), 305 (55), 277 (37), 96 (24)

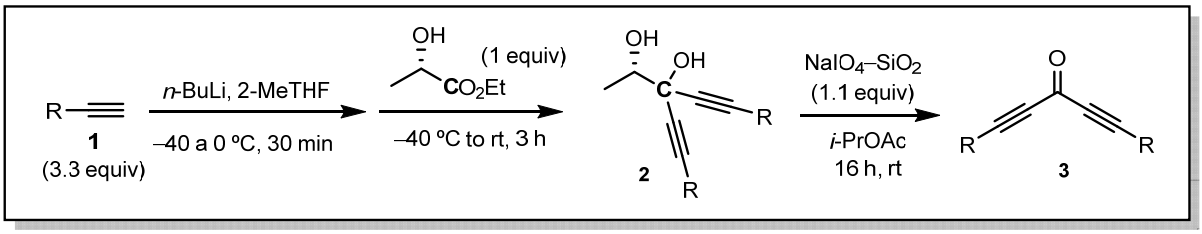


**Penta-1,4-diyn-3-one (3q):**[10] Brown oil. Yield = 85% (the reaction was carried out in $CDCl_3$ and the yield was determined by $^1$H-NMR)

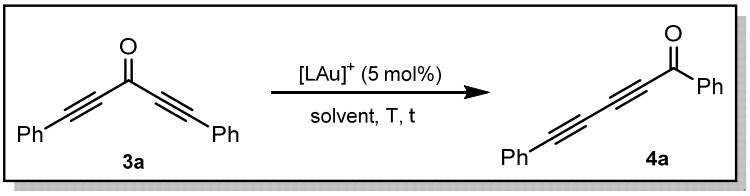
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.39 (s, 2H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 159.7 (C), 81.8 (2 x C), 80.1 (2 x CH)

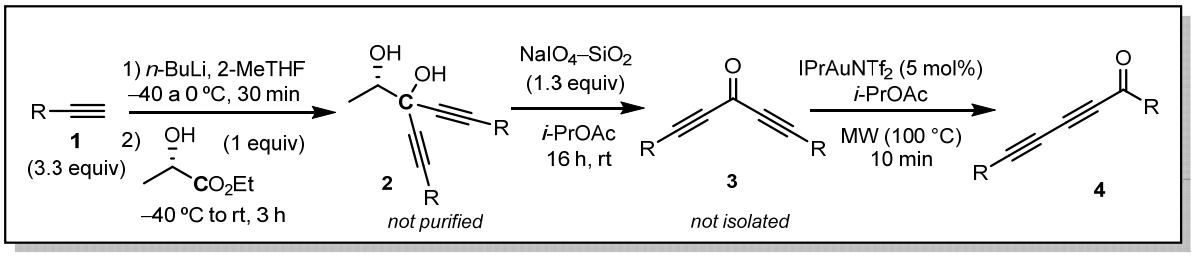
[9] D. R. Kohn, P. Gawel, Y. Xiong, K. E. Christensen and H. L. Anderson, *J. Org. Chem.*, 2018, **83**, 2077.
[10] W. Thong, Q.-Y. Li, Y.-L. Xu, H.-S. Wang, Y.-Y. Chen and Y.-M. Pan, *Adv. Synth. Catal.*, 2017, **359**, 4025.




**Gram-scale preparation of selected skipped diynones 3:** *n*-BuLi (19.8 mmol, 7.92 mL of a 2.5 M solution in hexane) was added to a solution of the appropriate alkyne **1** (20.4 mmol) in 2-MeTHF (10 mL) at –40 °C. The resulting solution was stirred for 30 min at 0 °C to obtain the corresponding lithium acetylide. Ethyl (*S*)-(–)-lactate (6 mmol, 709 mg) in 2-MeTHF (4 mL) was added dropwise with an addition funnel to the acetylide solution at –40 °C. The solution was firstly stirred for 20 min at the same temperature and, after the removal of the cooling bath, it was further stirred at rt until ethyl lactate was consumed as determined by GC–MS. Aqueous $NH_4Cl$ (30 mL) was added and the resulting solution was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvents were removed under reduced pressure to obtain the corresponding diol **2**. Without further purification, the residue was dissolved in *i*-PrOAc (8 mL) and the resulting solution was added to a vigorously stirred suspension of silica gel–supported $NaIO_4$ reagent (9.67 g) in *i*-PrOAc (10 mL). The reaction was monitored by TLC until disappearance of the starting diol **2**. The mixture was filtered through a celite pad in a sintered glass filter funnel and the silica gel was washed with *i*-PrOAc (10 mL). Removal of the solvent under reduced pressure from the filtrate afforded the corresponding skipped diynone **3** in pure form (see the crude NMR spectra for the gram-scale synthesis of diynones **3**, p. 94).



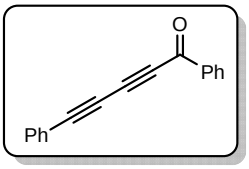

**General procedure for the optimization of the Au-catalyzed 1,3-transposition of 3a:** The corresponding gold catalyst (or the mixture of a silver salt and a gold chloride complex) (0.01 mmol, 5 mol%) was dissolved in the corresponding solvent (1 mL), and the resulting solution was stirred for 5 minutes. A solution of the skipped diynone **3a** (0.2 mmol, 0.046 g) in the same solvent (1 mL) was added, and the reaction mixture was stirred at the given temperature (see Table 4) until complete disappearance of the starting skipped diynone. The mixture was filtered through a short pad of silica gel and celite using a mixture of hexane/EtOAc (1:1), and the solvents were removed under reduced pressure.




**General procedure for the synthesis of conjugated diynones 4 from ethyl lactate and characterization data:** *n*-BuLi (1.65 mmol, 0.66 mL of a 2.5 M solution in hexane) was added to a solution of the appropriate alkyne **1** (1.7 mmol) in 2-MeTHF (4 mL) at –40 °C. The resulting solution was stirred for 30 min at 0 °C to obtain the corresponding lithium acetylide. Ethyl (*S*)-(–)-lactate (0.5 mmol, 60 mg) in 2-MeTHF (2 mL) was added dropwise with an addition funnel to the acetylide solution at –40 °C. The resulting mixture was stirred for 20 min at the same temperature and, after removal of the cooling bath, it was further stirred at r.t. until ethyl lactate was consumed as determined by GC–MS. Aqueous $NH_4Cl$ (5 mL) was added and the resulting solution was extracted with EtOAc (3 x 5 mL) The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvents were removed under reduced pressure to afford the corresponding isolated diol **2**.

Then, a solution of the corresponding crude diol **2** in *i*-PrOAc (2 mL) was added to a vigorously stirred suspension of silica gel–supported $NaIO_4$ reagent (952 mg) in *i*-PrOAc (3 mL). The reaction was monitored by TLC until disappearance of the starting material. The mixture was filtered through a celite pad in a sintered glass filter funnel and the silica gel was washed with *i*-PrOAc (5 mL). The resulting filtrate was partially evaporated to remove the co-generated acetaldehyde, obtaining a solution of the corresponding skipped diynone **3** in *i*-PrOAc (~1 mL).

Finally, $IPrAuNTf_2$ (5 mol %, 22 mg) was dissolved in *i*-PrOAc (1 mL) and the resulting solution was stirred for 5 minutes. The solution of the corresponding crude skipped diynone **3** (0.5 mmol) in *i*-PrOAc (1 mL) was added and the reaction mixture was stirred for 10 minutes at 100 °C under microwave irradiation until complete consumption of the diynone **3**. The mixture was filtered through a short pad of silica gel and celite using a mixture of hexane/EtOAc (1:1) and the solvents were removed under reduced pressure. The crude product was almost pure (see crude NMR spectra for the synthesis of conjugated diynones **4** from ethyl lactate, p. 112), but for characterization purpose was further purified by flash column chromatography on silica gel using mixtures of hexane and EtOAc as eluents to obtain the corresponding conjugated diynones **4**.

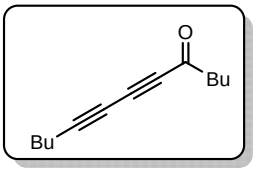



**1,5-Diphenylpenta-2,4-diyn-1-one (4a):**[11] Brown solid. Yield = 55%. $R_f$ = 0.49 (hexane/EtOAc, 20:1), m.p. 36–38 °C (lit.[12] 38–39 °C)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 8.20–8.14 (m, 2H), 7.68–7.57 (m, 3H), 7.55–7.35 (m, 5H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 177.0 (C), 136.7 (C), 134.6 (CH), 133.2 (2 x CH), 130.7 (CH), 129.7 (2 x CH), 128.81 (2 x CH), 128.77 (2 x CH), 120.3 (C), 86.5 (C), 78.0 (C), 77.6 (C), 72.6 (C)

**EI-LRMS:** *m/z* (%) 230 ($M^+$, 35), 202 (100), 153 (21)

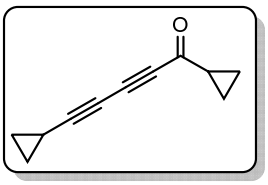



**Trideca-6,8-diyn-5-one (4b):**[8] Orange oil. Yield = 70%. $R_f$ = 0.46 (hexane/EtOAc, 20:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 2.53 (t, *J* = 6.8 Hz, 2H), 2.35 (t, *J* = 6.9 Hz, 2H), 1.67–1.25 (m, 8H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 187.4 (C), 90.7 (C), 76.2 (C), 72.3 (C), 63.9 (C), 45.3 ($CH_2$), 29.9 ($CH_2$), 26.1 ($CH_2$), 22.2 ($CH_2$), 22.0 ($CH_2$), 19.4 ($CH_2$), 13.8 ($CH_3$), 13.5 ($CH_3$)

**EI-LRMS:** *m/z* (%) 190 ($M^+$, 1), 133 (100), 105 (20), 91 (35), 79 (19), 77 (36)



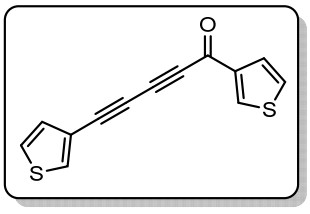

**1,5-Dicyclopropylpenta-2,4-diyn-1-one (4c):** Red oil. Yield = 71%. $R_f$ = 0.38 (hexane/EtOAc, 30:1)

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 2.07–1.96 (m, 1H), 1.44–1.32 (m, 1H), 1.24–1.14 (m, 2H), 1.05–0.96 (m, 2H), 0.95–0.82 (m, 4H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 187.5 (C), 93.4 (C), 76.4 (C), 70.4 (C), 59.3 (C), 24.8 (CH), 11.2 (2 x $CH_2$), 9.7 (2 x $CH_2$), 0.5 (CH)

**EI-LRMS:** *m/z* (%) 158 ($M^+$, 62), 128 (50), 117 (100), 115 (46), 89 (43)

**HRMS** (ESI-TOF): calculated for $C_{11}H_{11}O$ $[M+H]^+$ 159.0804; found 159.0806




**1,5-Di(thiophen-3-yl)penta-2,4-diyn-1-one (4g):** Brown solid. Yield = 60%. $R_f$ = 0.40 (hexane/EtOAc, 30:1), m.p. 89–91 °C

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ (ppm): 8.32 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.74 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.63 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.37–7.31 (m, 2H), 7.22 (dd, *J* = 5.1, 1.2 Hz, 1H)

**$^{13}$C NMR** (75.4 MHz, $CDCl_3$) $\delta$ (ppm): 170.2 (C), 142.8 (C), 136.1 (CH), 133.9 (CH), 130.3 (CH), 127.1 (CH), 126.7 (CH), 126.3 (CH), 119.5 (C), 81.5 (C), 78.3 (C), 76.0 (C), 72.5 (C)

**HRMS** (ESI-TOF): calculated for $C_{13}H_7OS_2$ $[M+H]^+$ 242.9933; found 242.9934

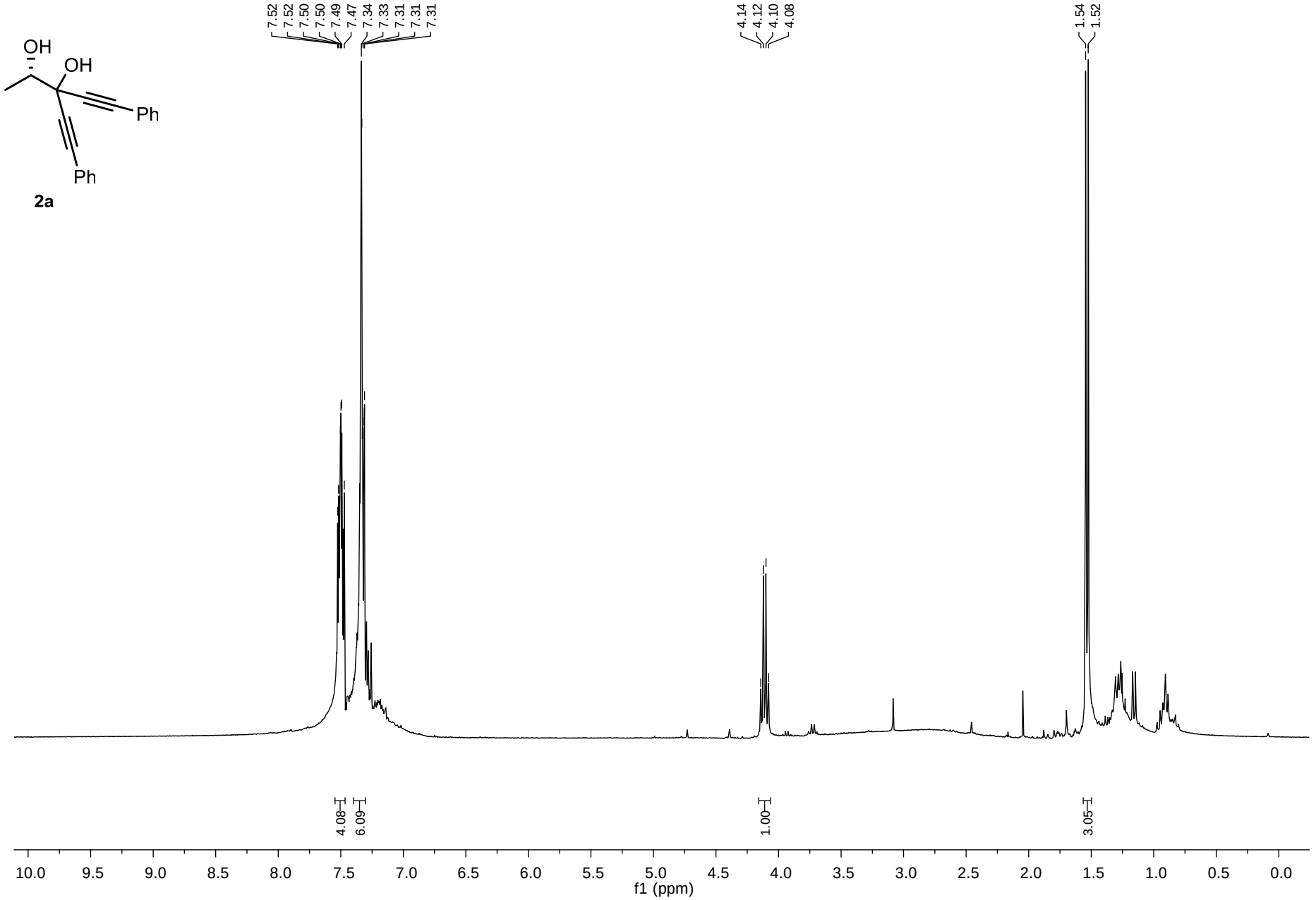
[11] R. K. Shiroodi, M. Soltani and V. Gevorgyan, *J. Am. Chem. Soc.,* 2014, **136**, 9882.
[12] B. W. Nash, D. A. Thomas, W. K. Warburton and T. D. Williams, *J. Chem. Soc.,* 1965, 2983.

# NMR spectra of crude reaction mixtures and pure compounds

# NMR spectra of crude selected glycols 2 in Table 1

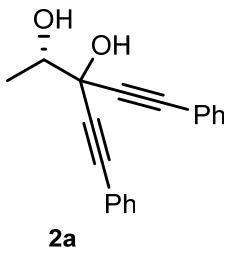
$^{1}$H-NMR ($CDCl_3$, 300 MHz)

Crude NMR for the synthesis of **2a**



$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

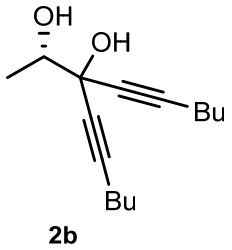
Crude NMR for the synthesis of **2a**




**2a**

$^{1}$H-NMR ($CDCl_3$, 300 MHz)

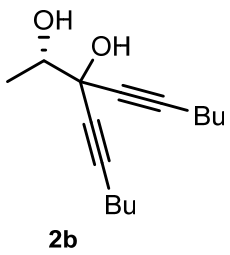
Crude NMR for the synthesis of **2b**




**2b**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

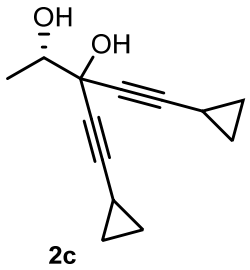
Crude NMR for the synthesis of **2b**




**2b**

$^{1}$H-NMR ($CDCl_3$, 300 MHz)

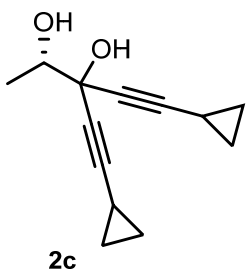
Crude NMR for the synthesis of **2c**




**2c**

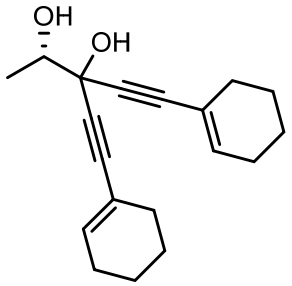
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **2c**



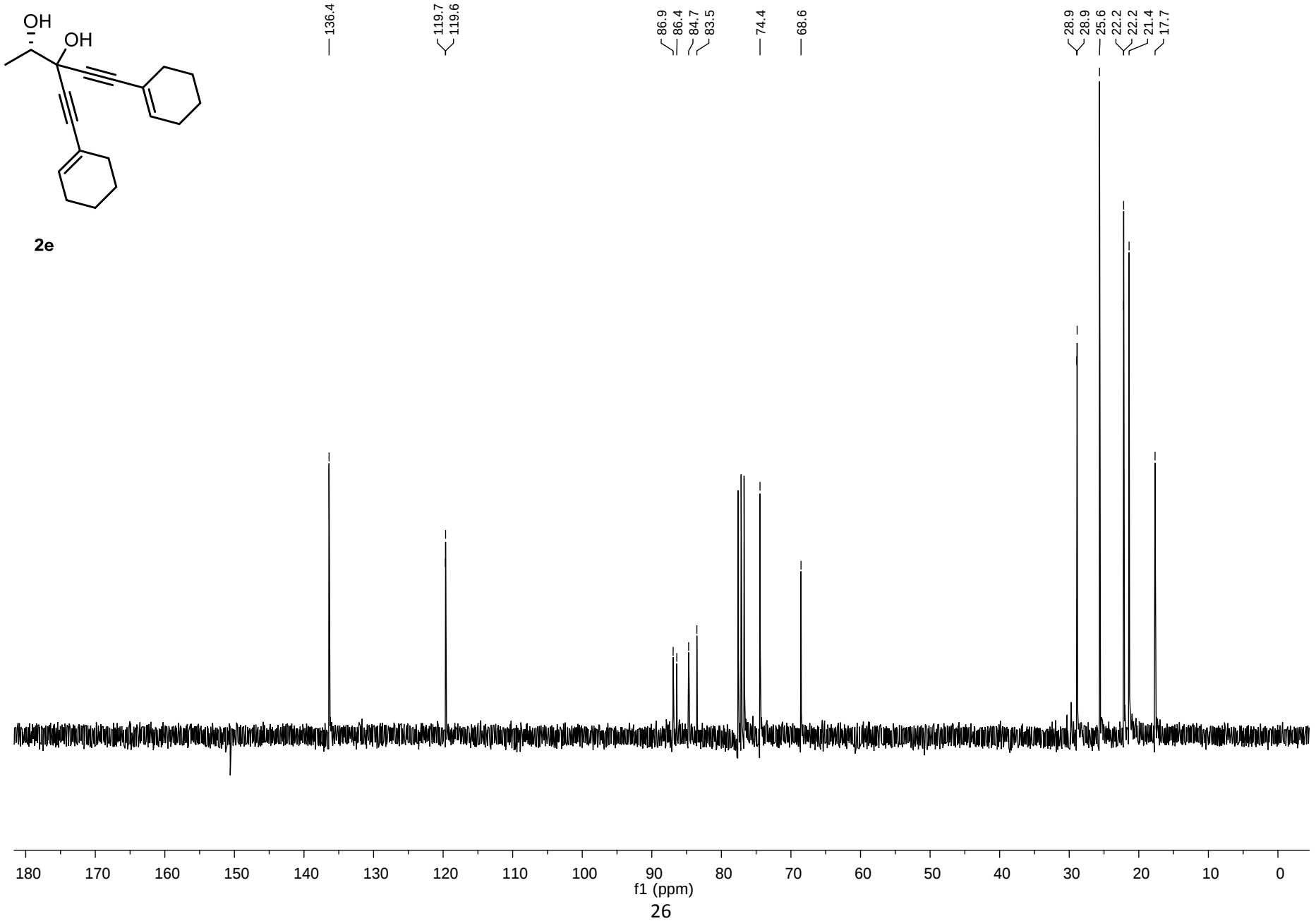

**2c**

$^{1}$H-NMR ($CDCl_3$, 300 MHz) Crude NMR for the synthesis of **2e**



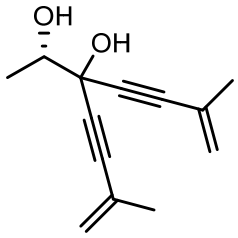

**2e**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz) Crude NMR for the synthesis of **2e**



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

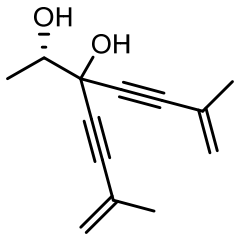
Crude NMR for the synthesis of **2f**




**2f**

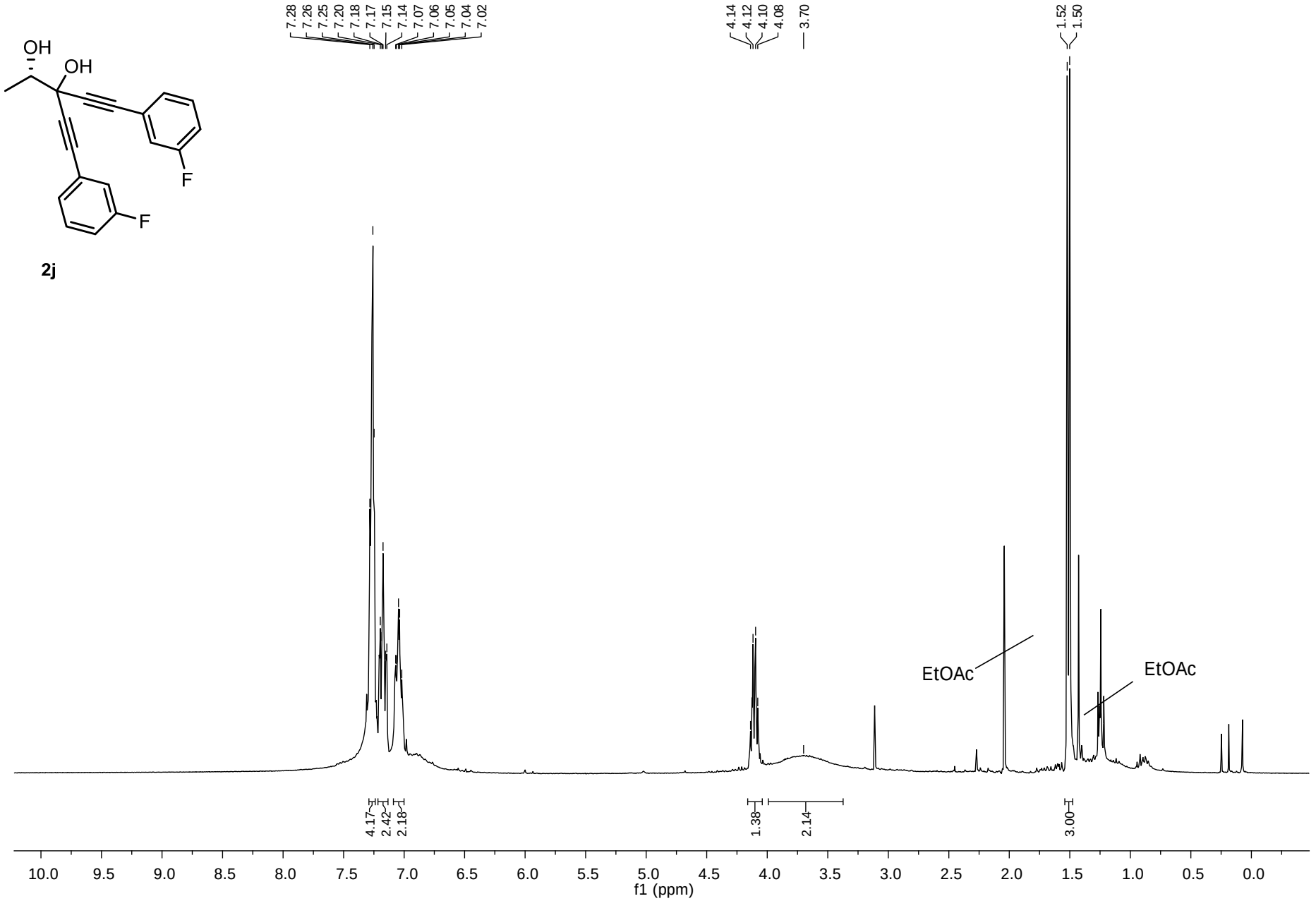
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **2f**

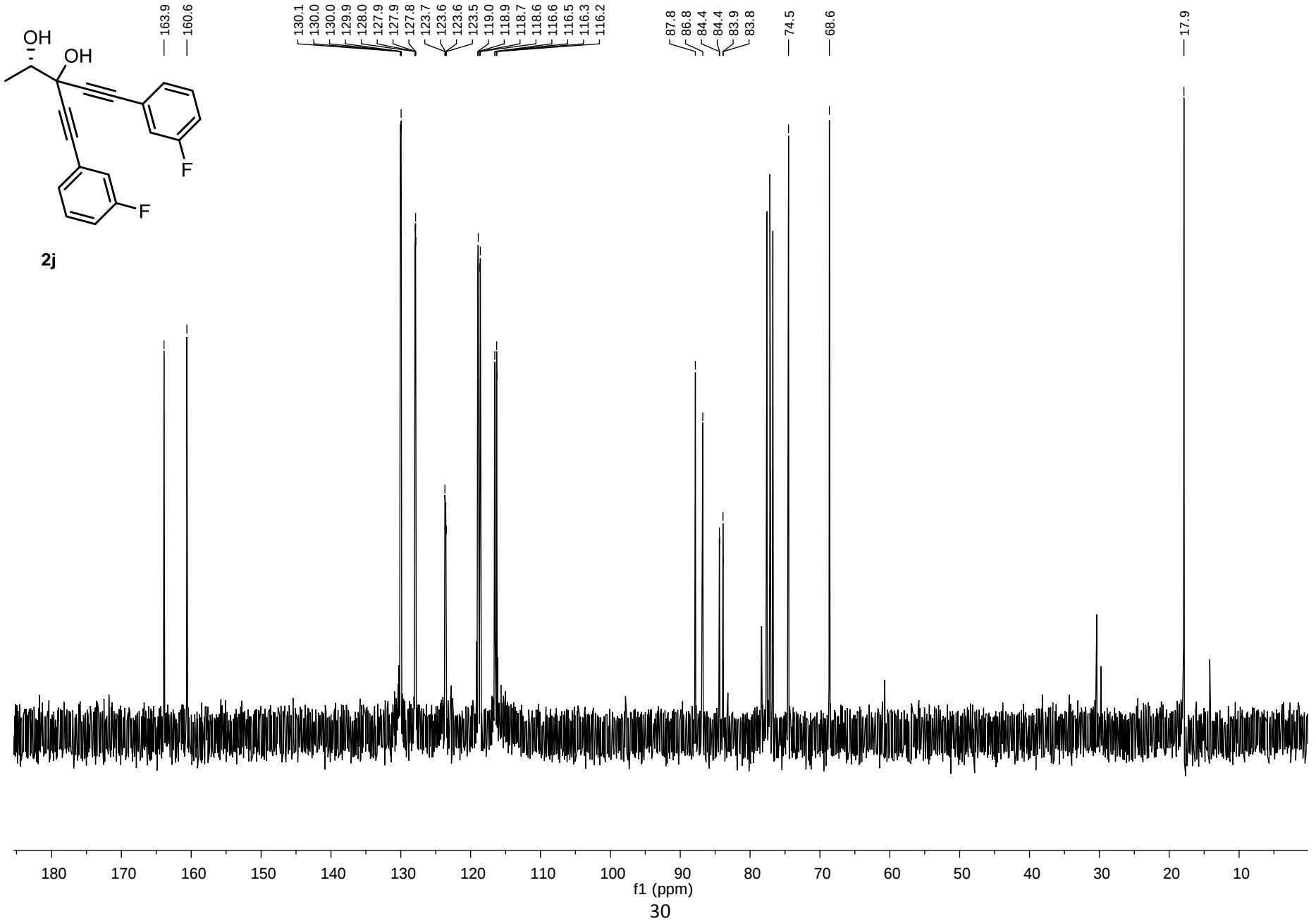



**2f**

$^{1}$H-NMR ($CDCl_3$, 300 MHz) Crude NMR for the synthesis of **2j**

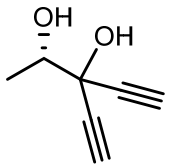


$^{13}$C-NMR ($CDCl_3$, 75.4 MHz) Crude NMR for the synthesis of **2j**



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

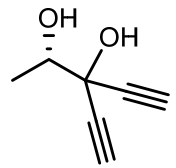
Crude NMR for the synthesis of **2q**




**2q**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

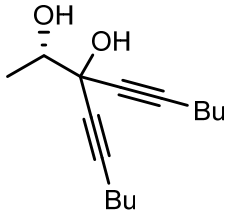
Crude NMR for the synthesis of **2q**




**2q**

$^{1}$H-NMR ($CDCl_3$, 300 MHz)

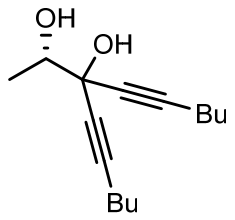
Crude NMR for the synthesis of **2b** from methyl lactate




**2b**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

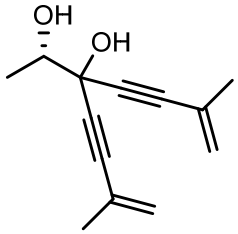
Crude NMR for the synthesis of **2b** from methyl lactate




**2b**

$^{1}$H-NMR ($CDCl_3$, 300 MHz)

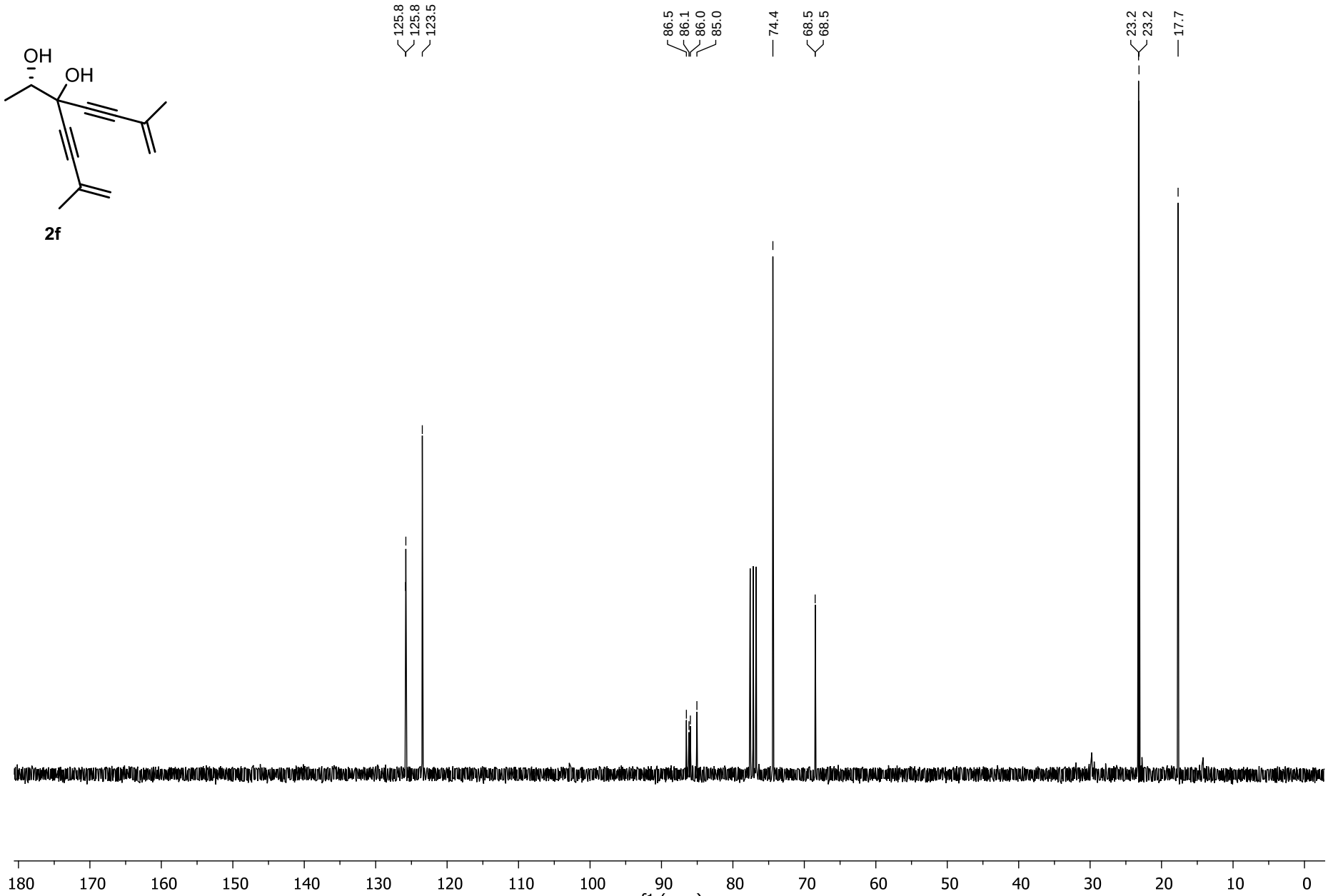
Crude NMR for the synthesis of **2f** from methyl lactate




**2f**

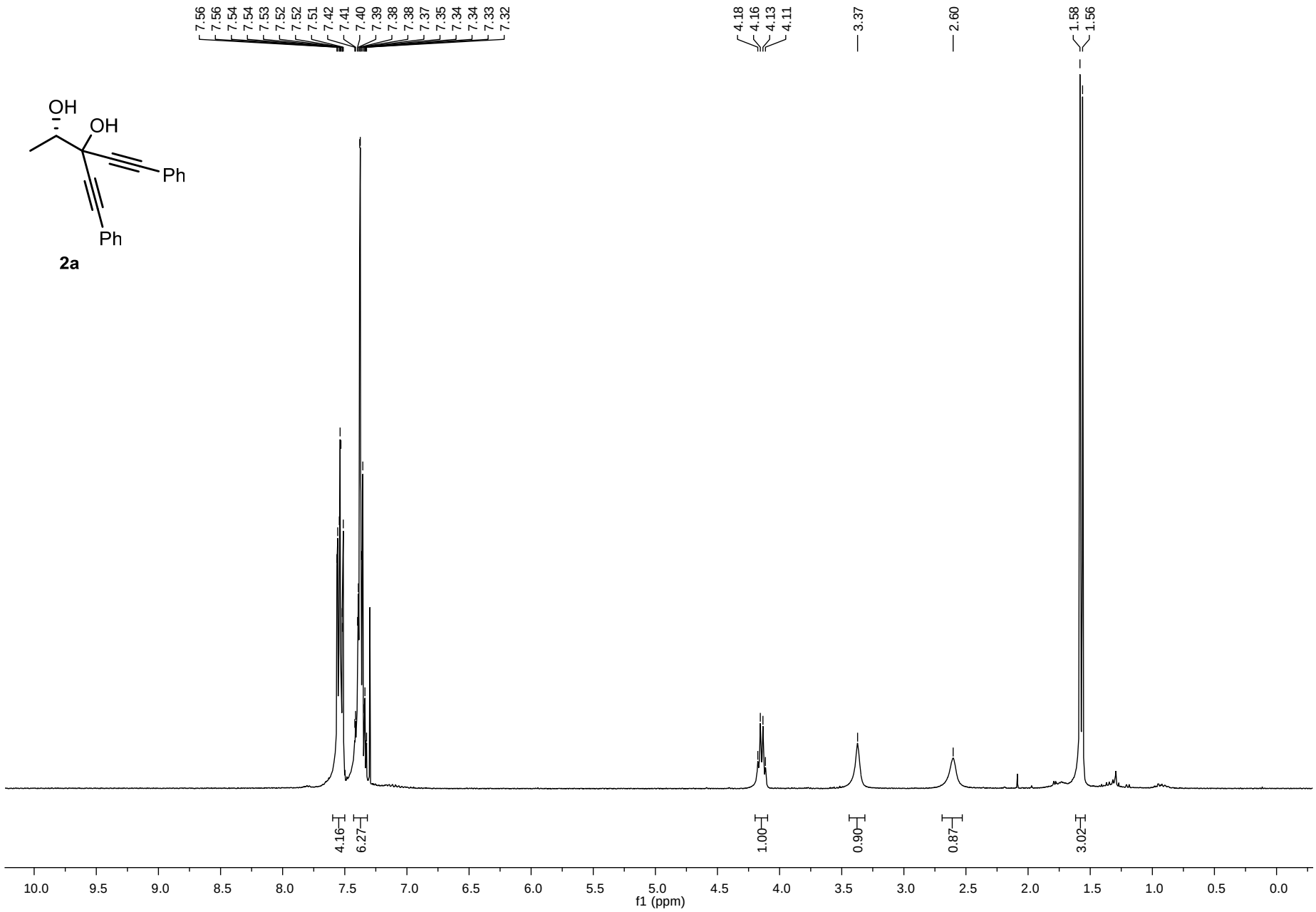
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **2f** from methyl lactate

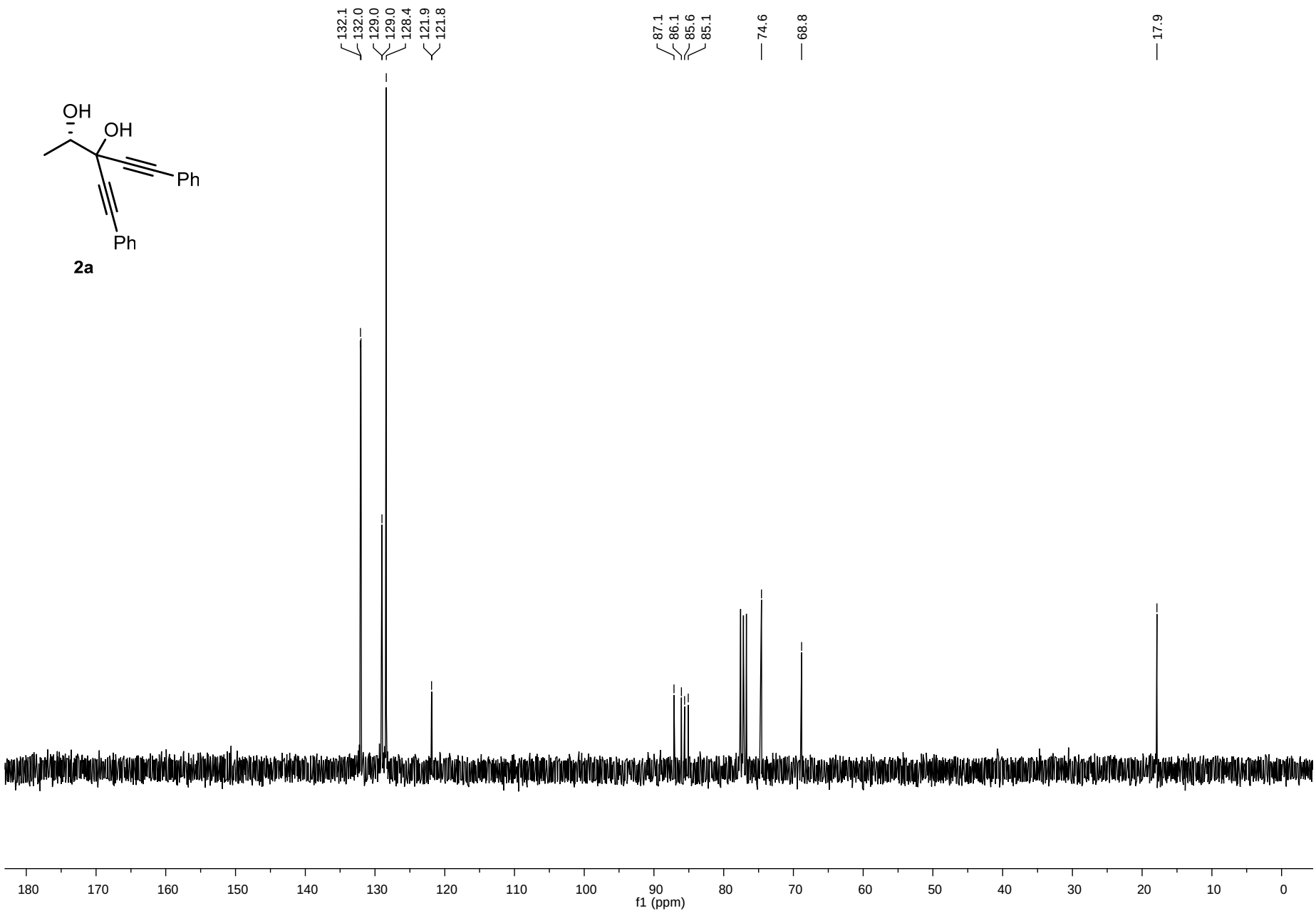


# NMR spectra of bispropargyl diols 2

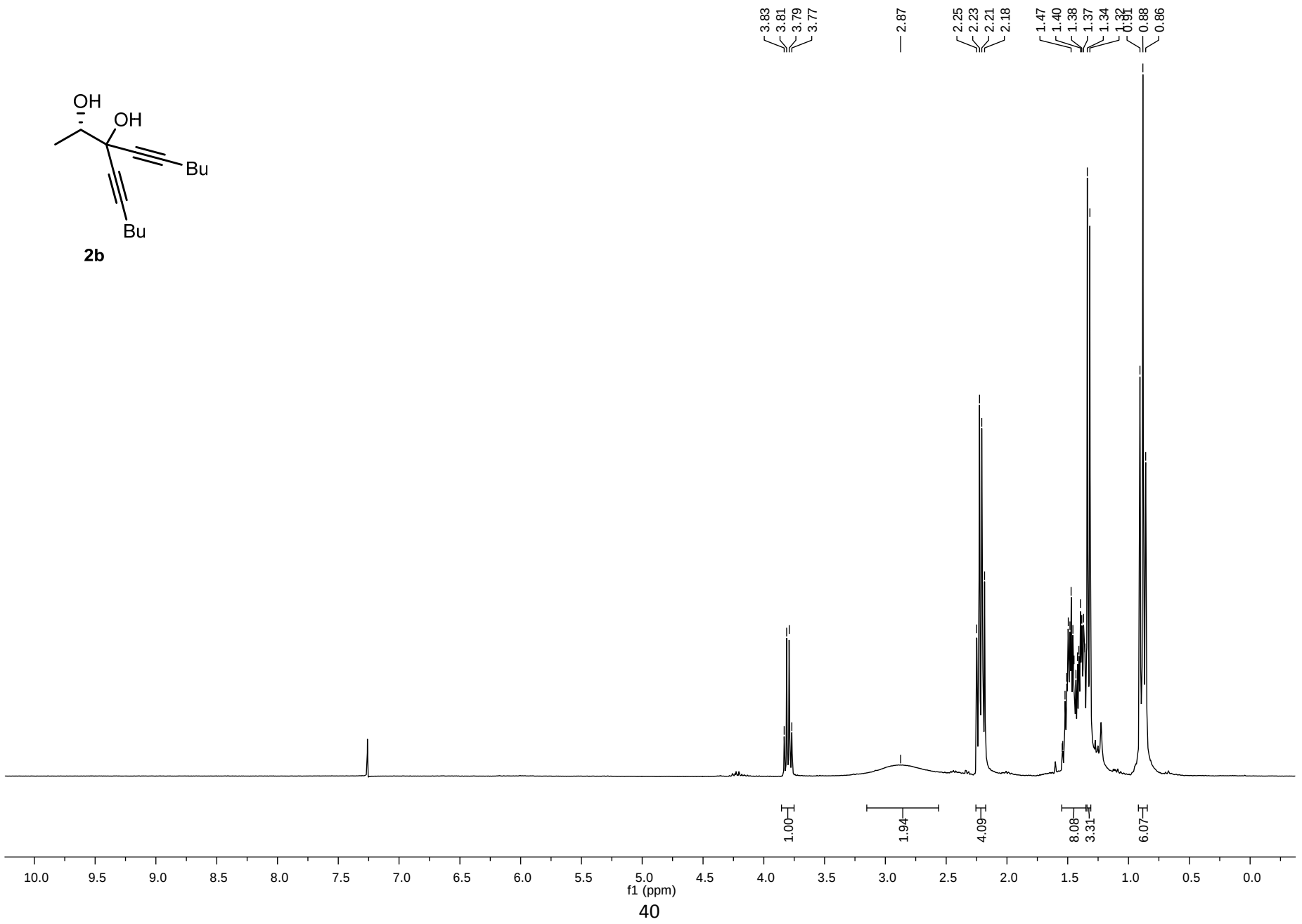
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



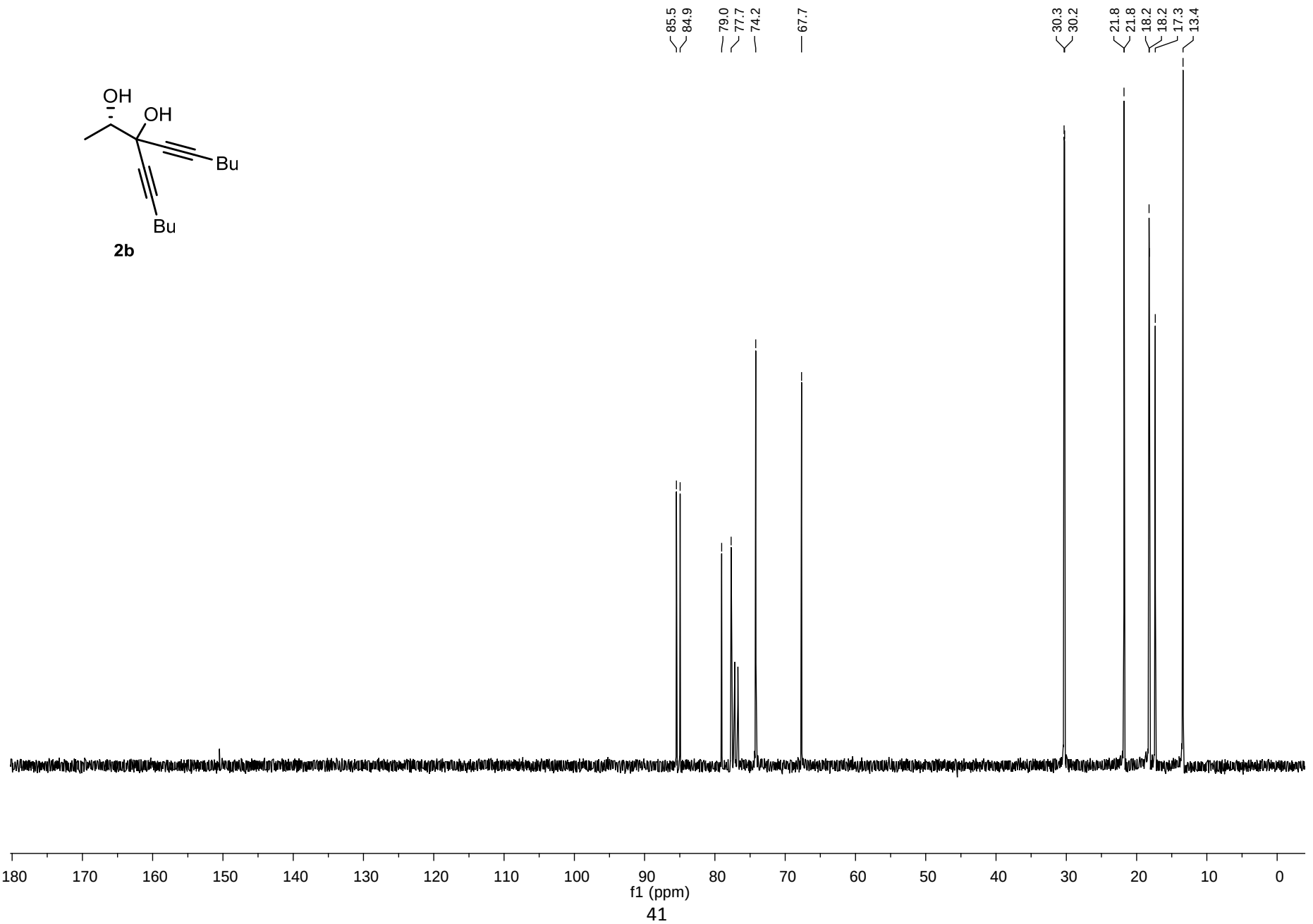
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



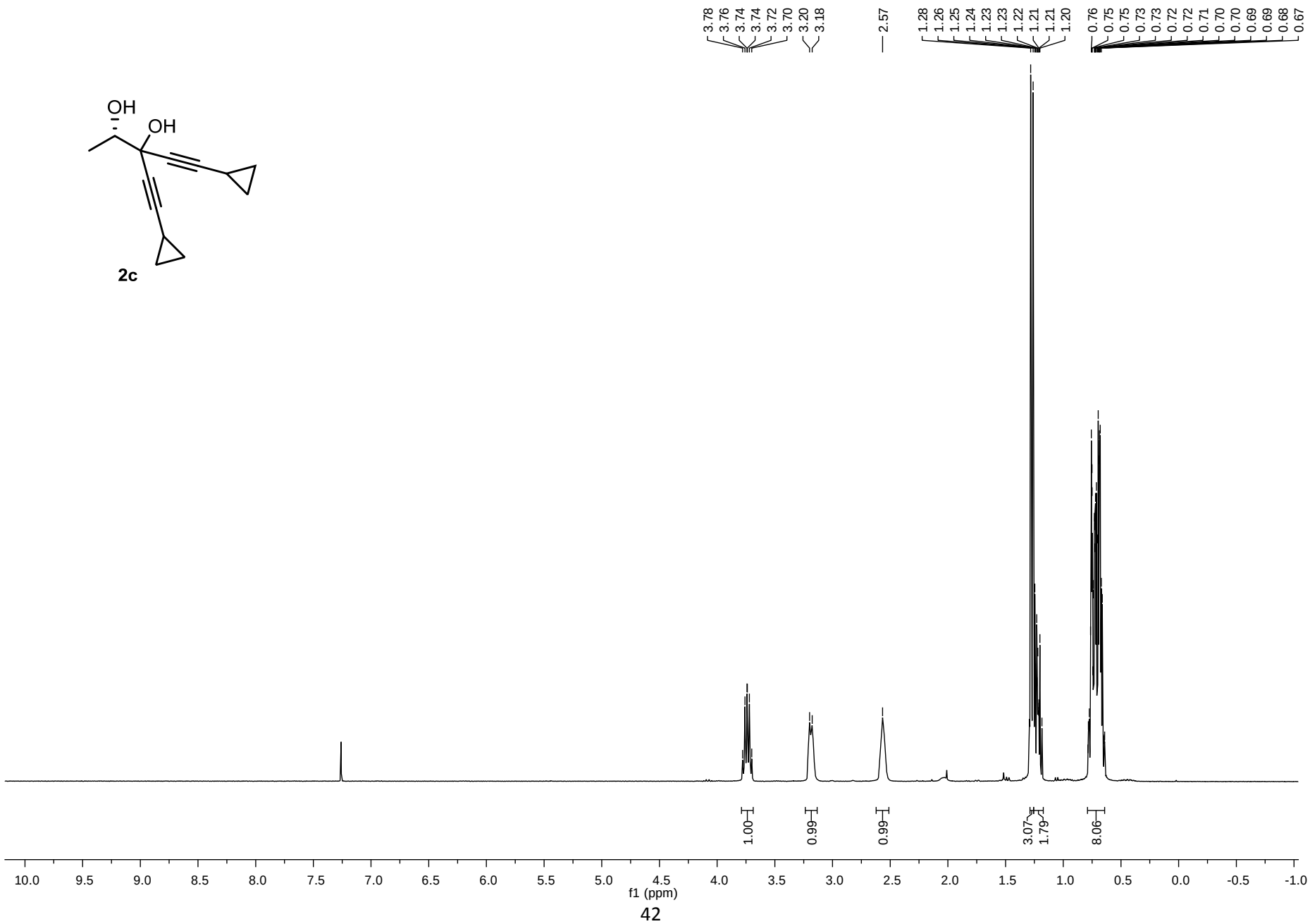
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



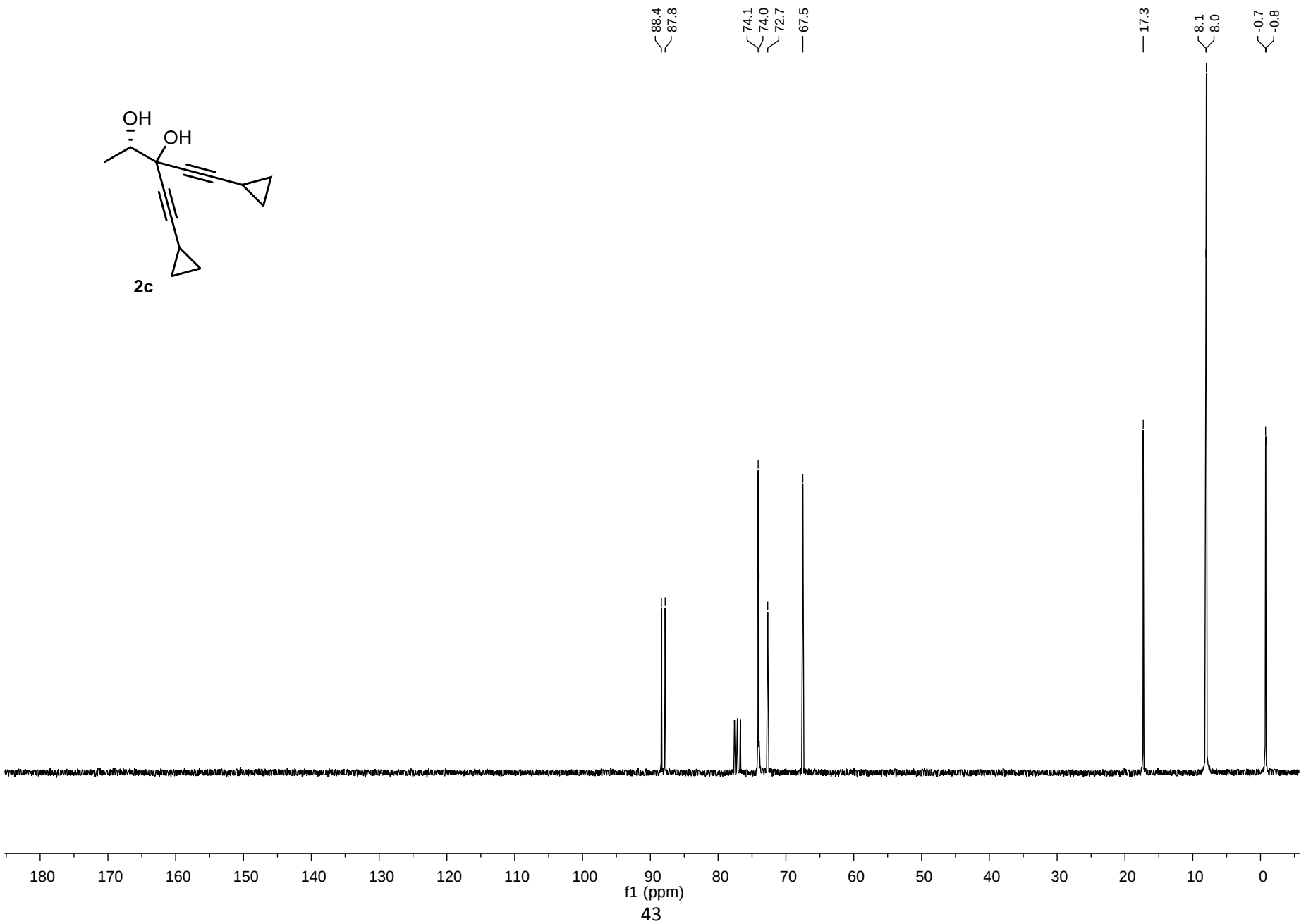
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



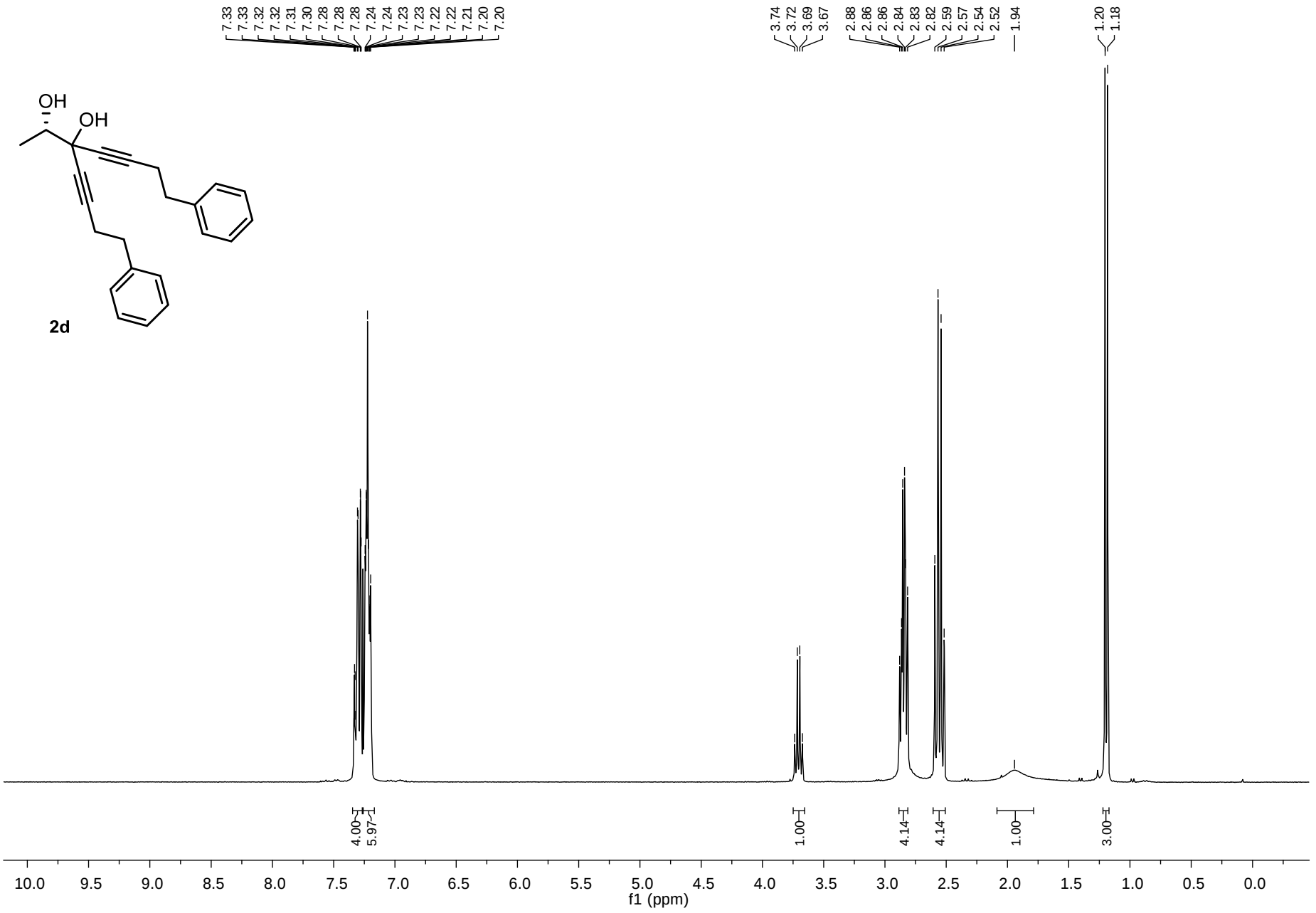
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



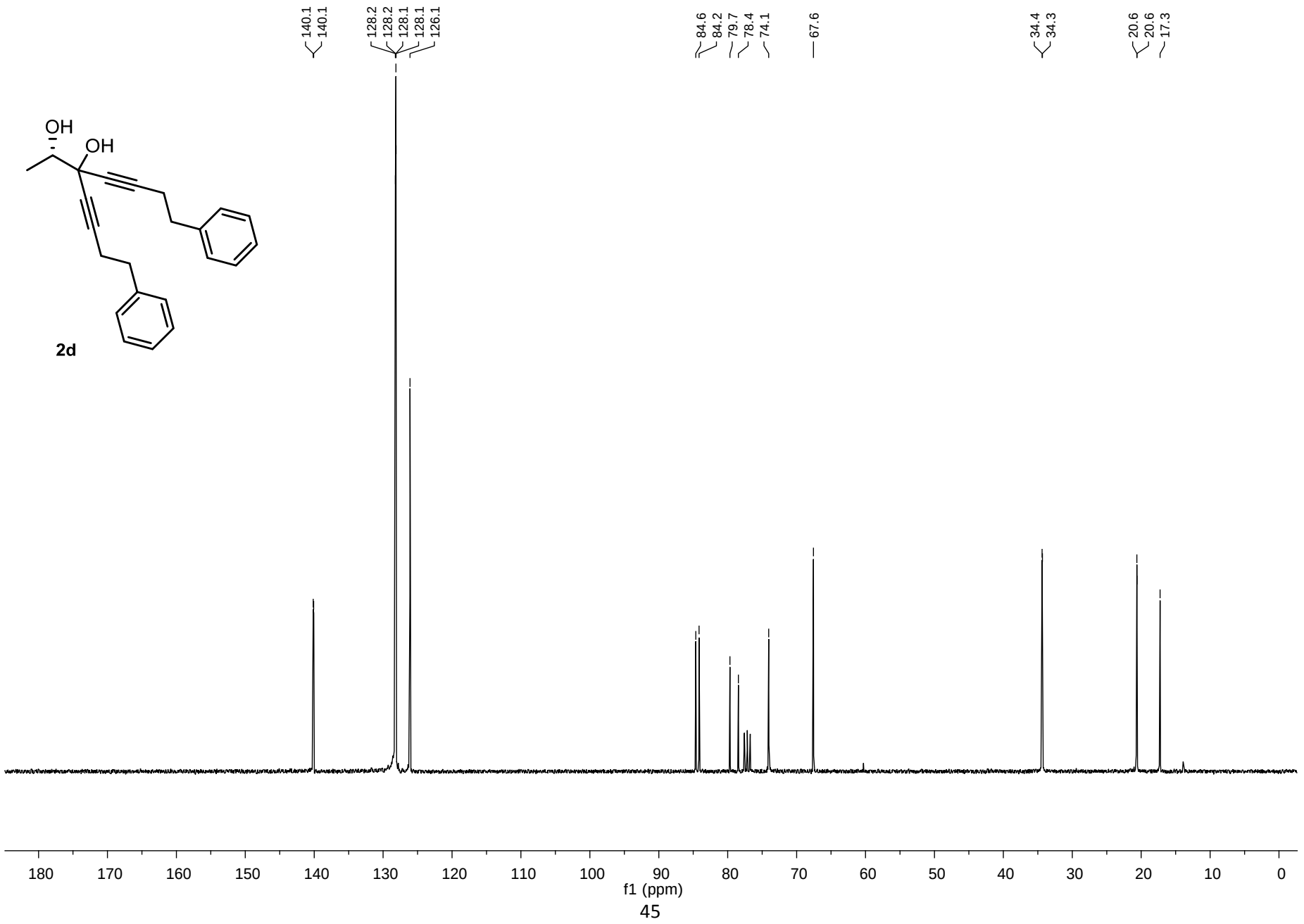
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



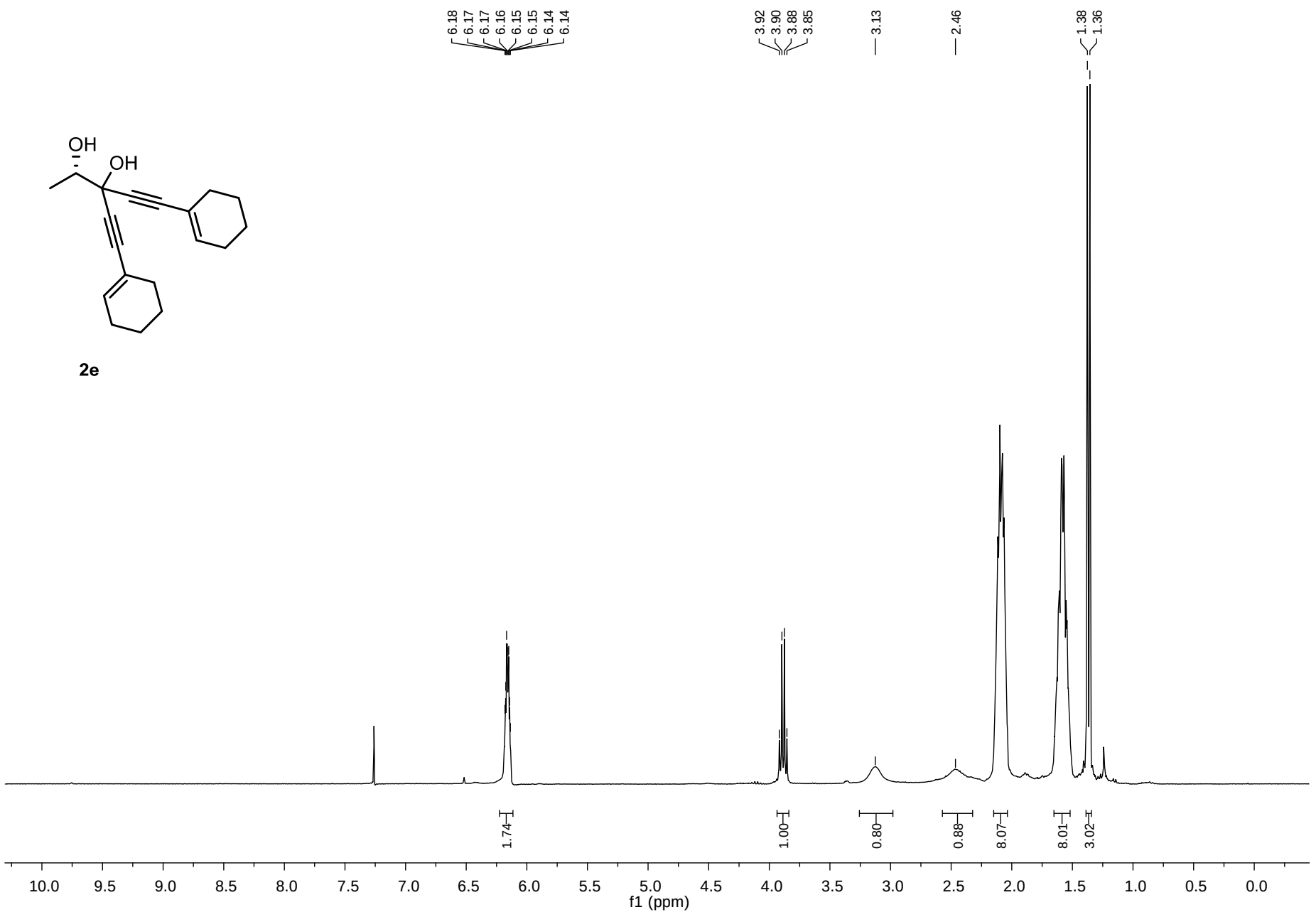
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



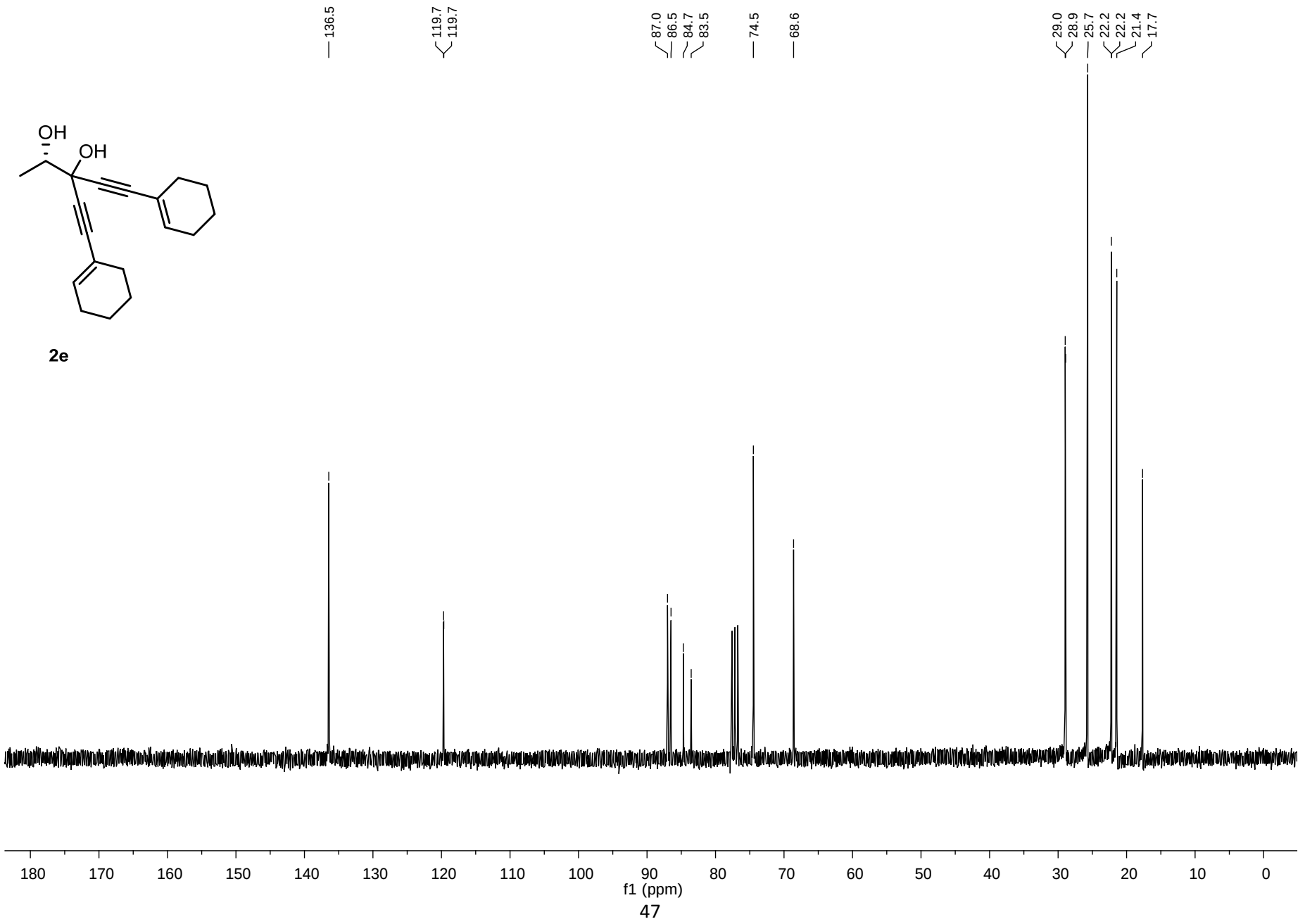
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



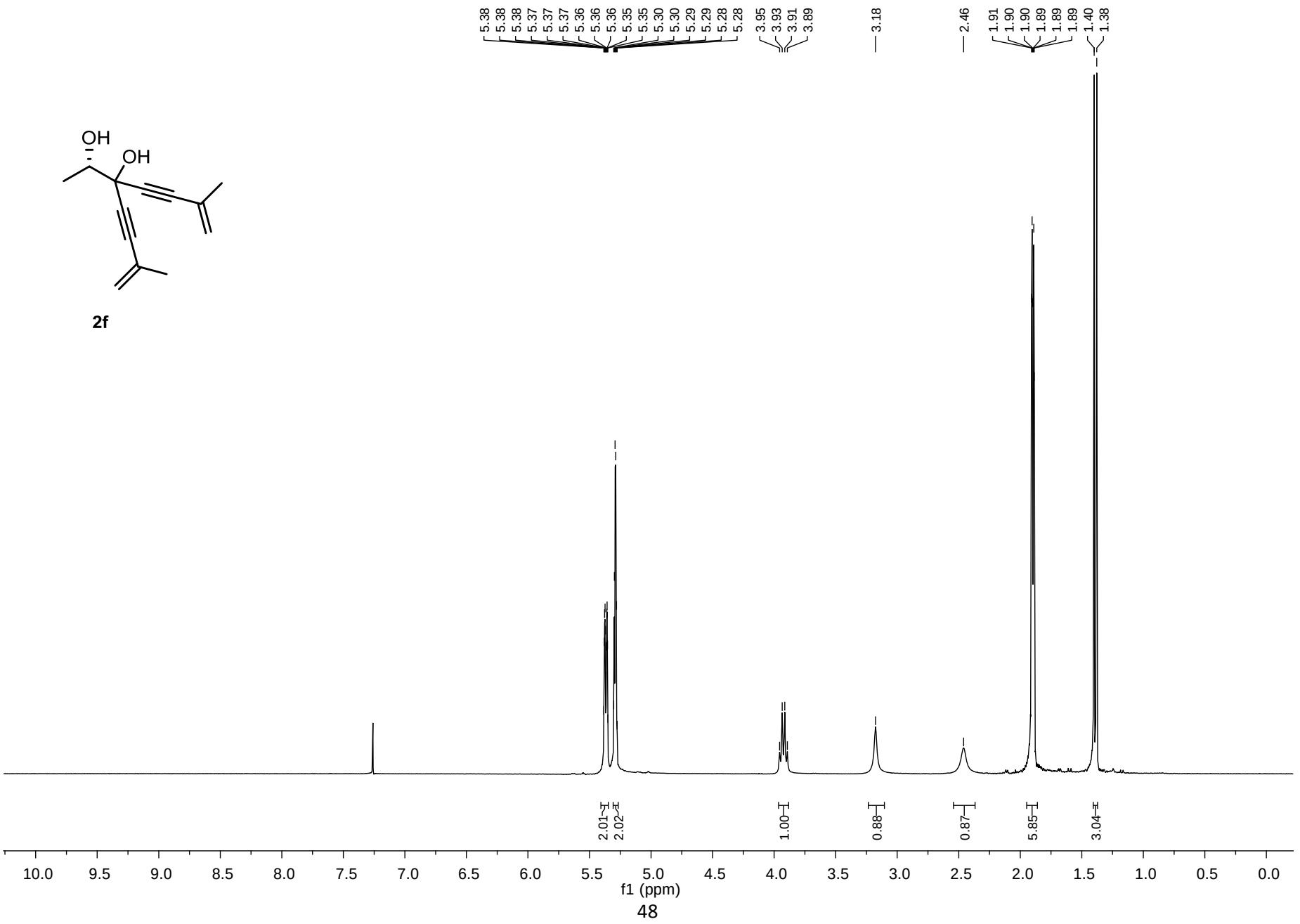
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



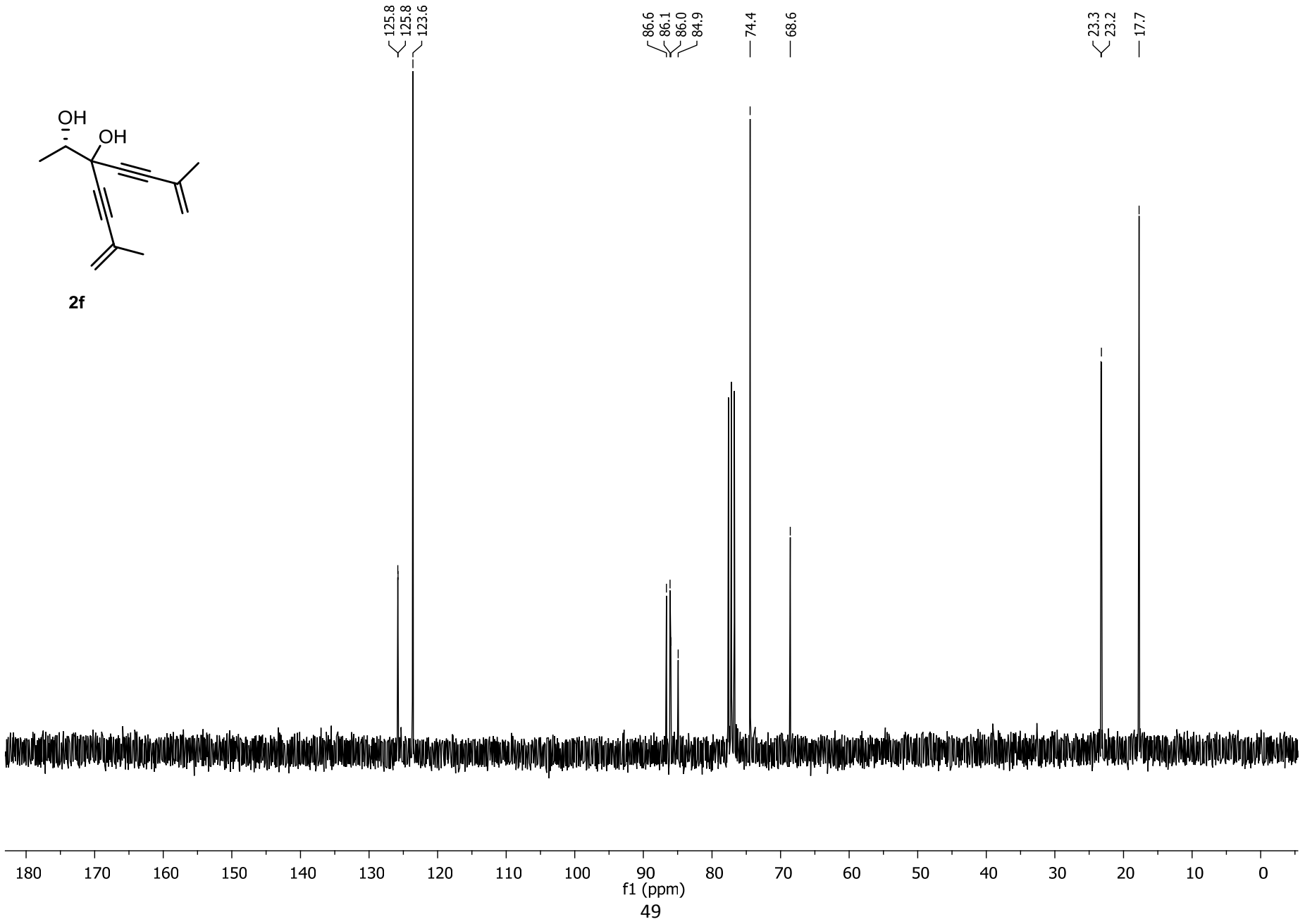
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



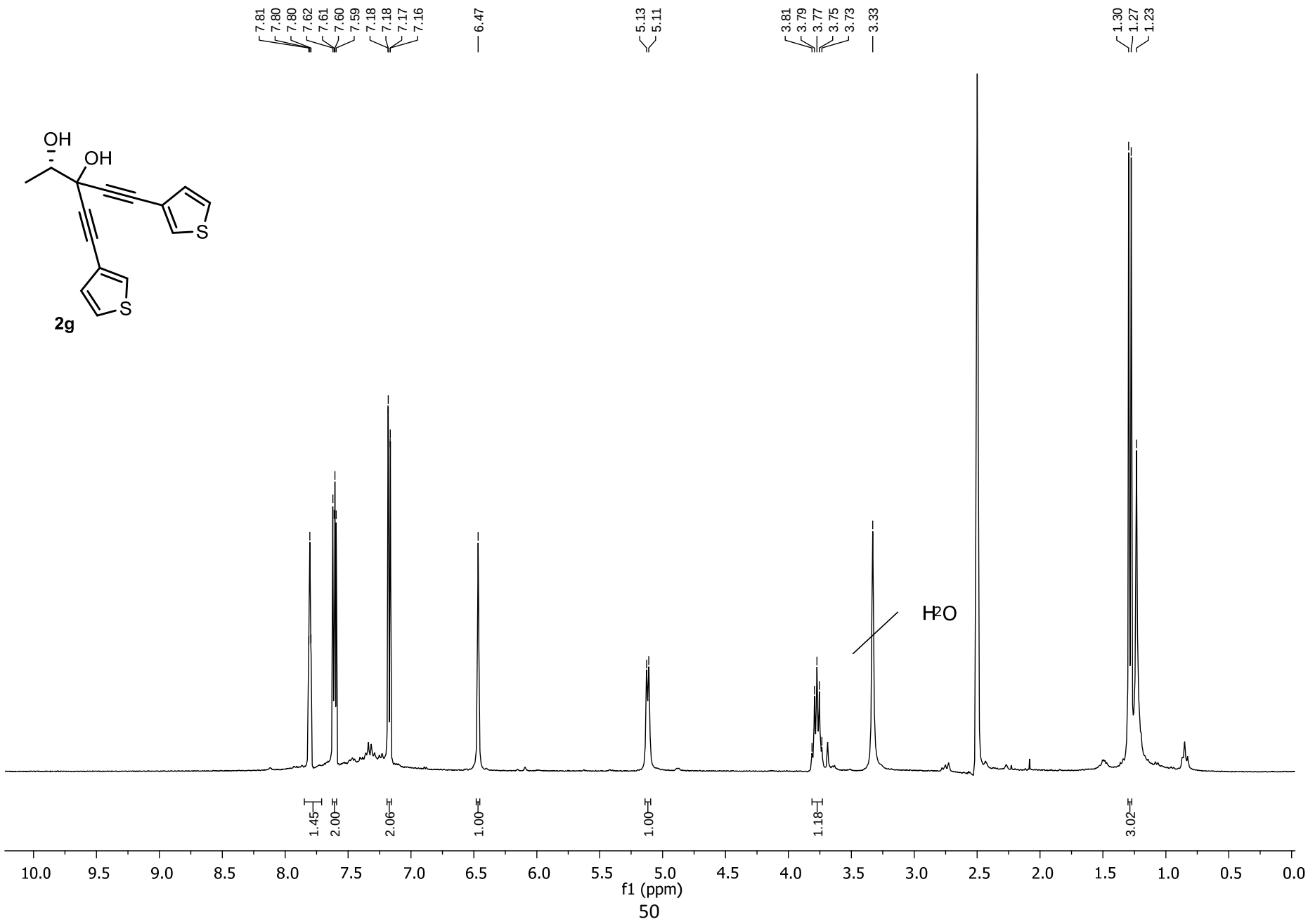
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



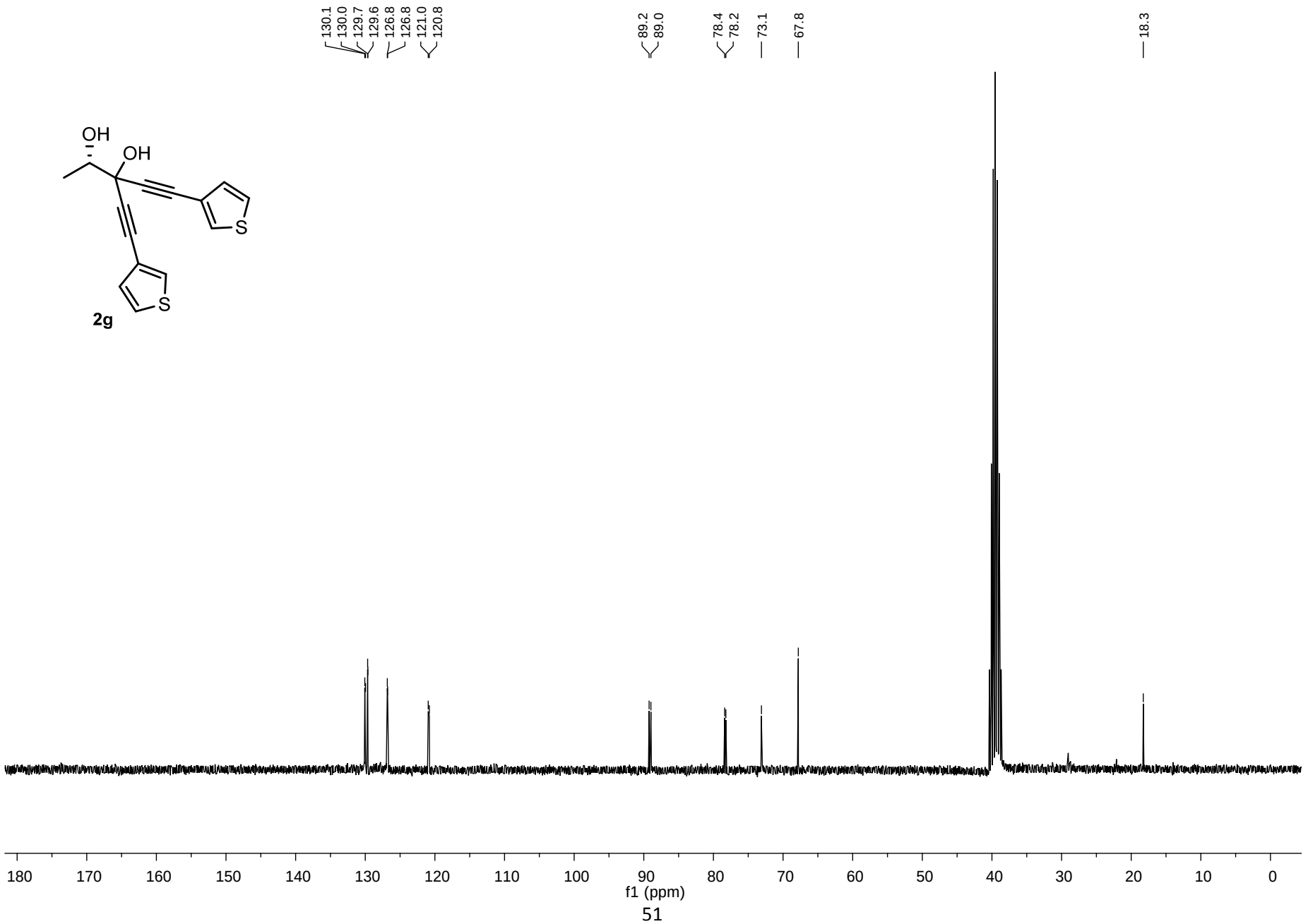
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



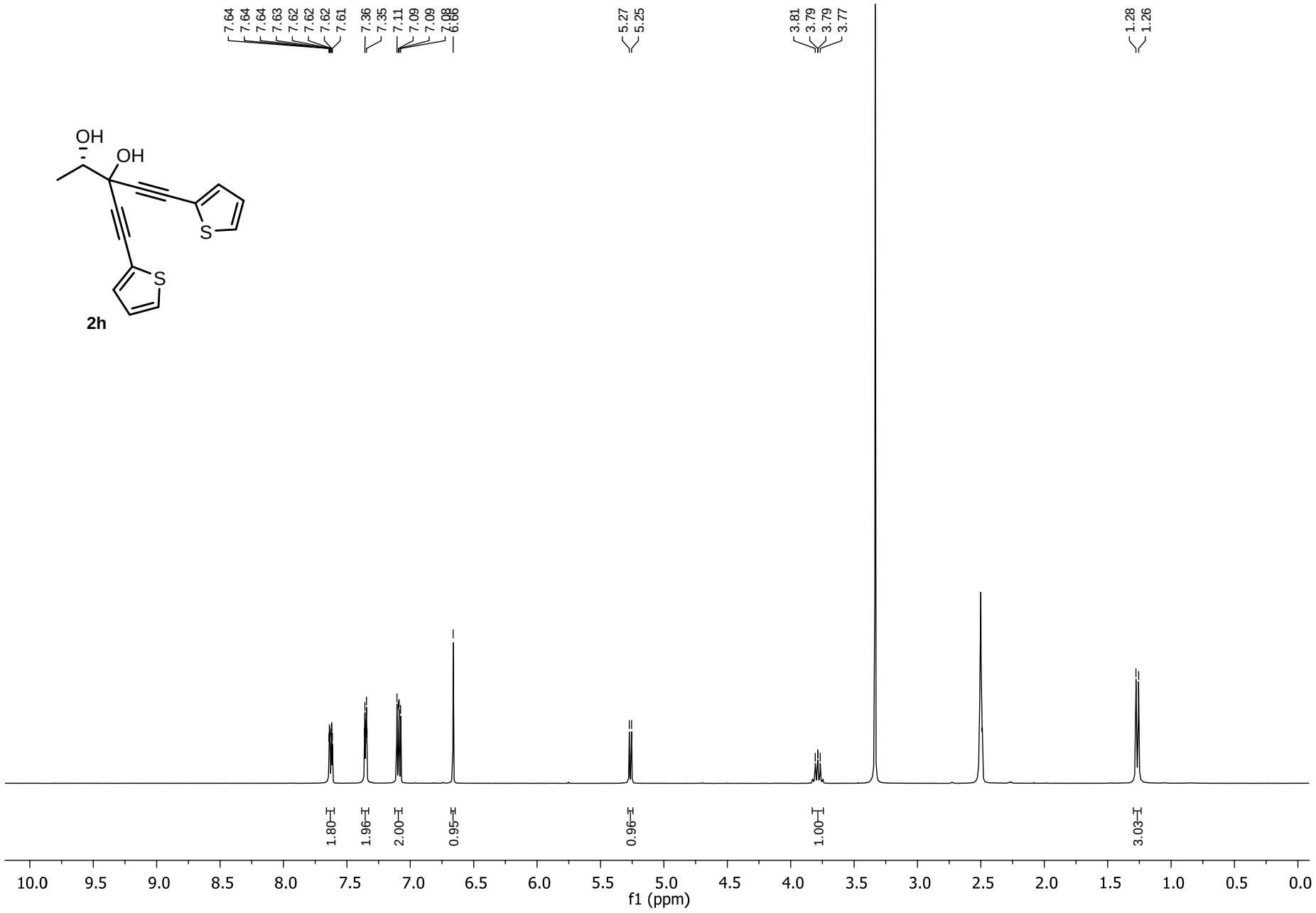
$^{1}$H-NMR (DMSO-$d_6$, 300 MHz)



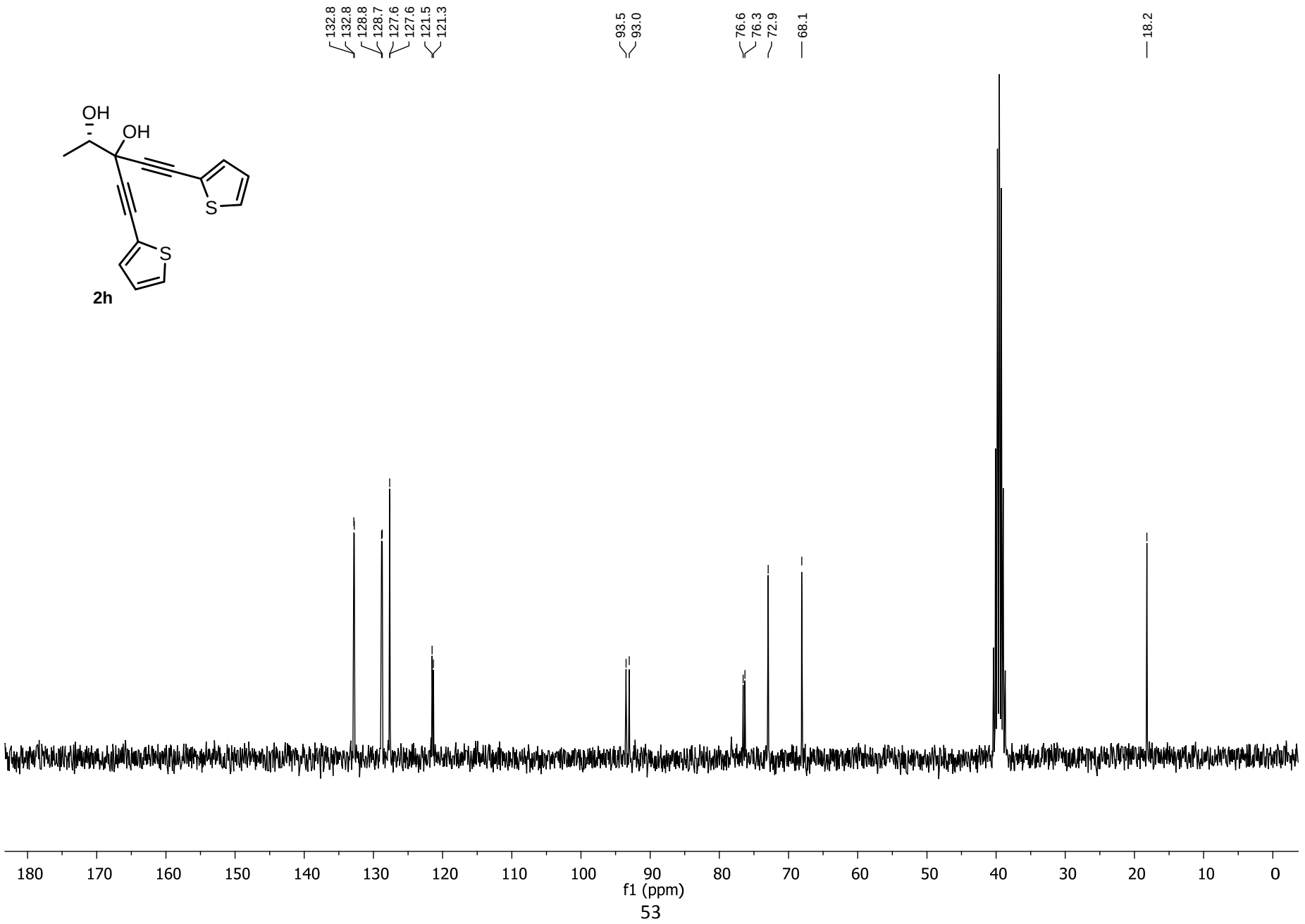
$^{13}$C-NMR (DMSO-$d_6$, 75.4 MHz)



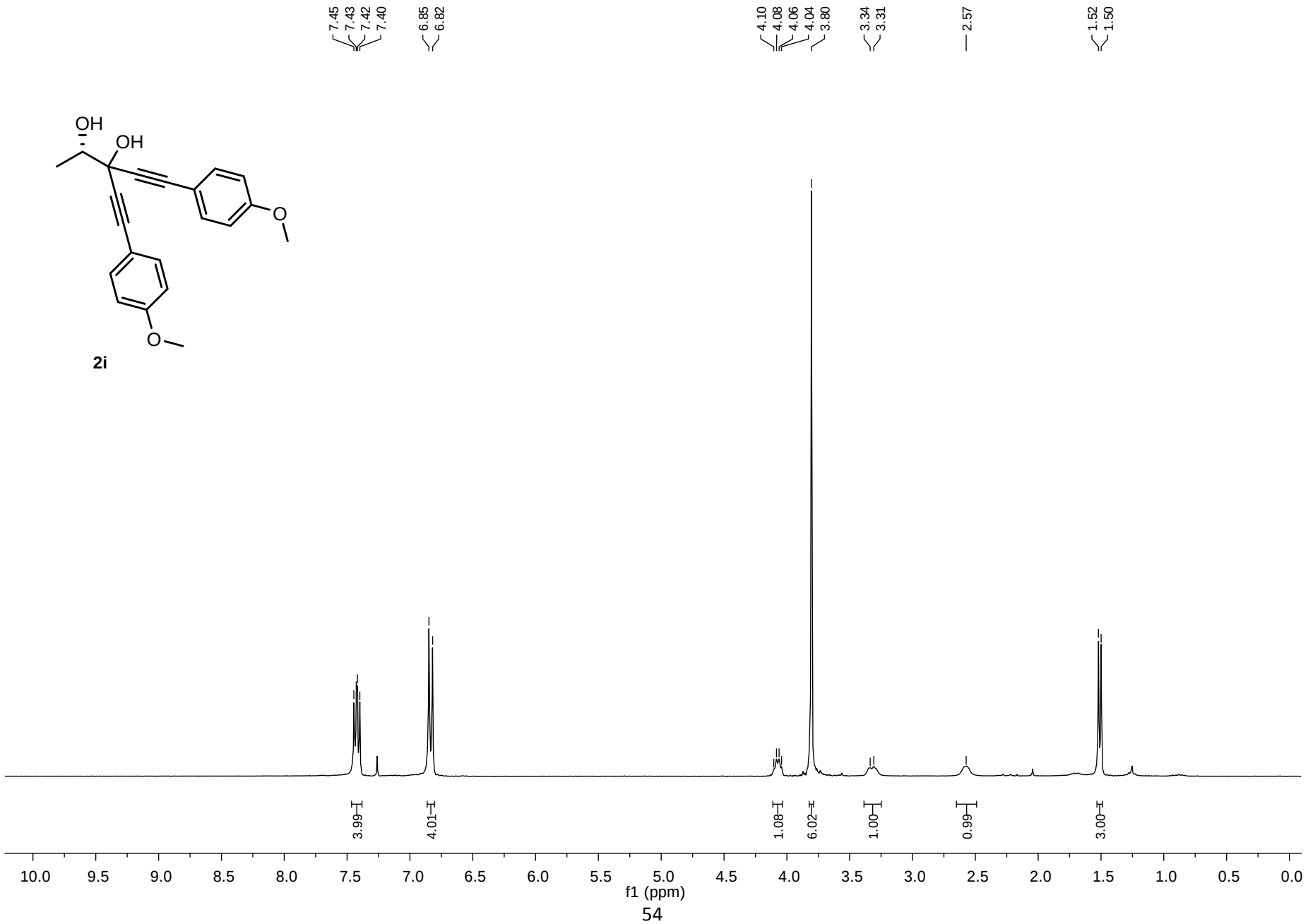
$^{1}$H-NMR (DMSO-$d_6$, 300 MHz)



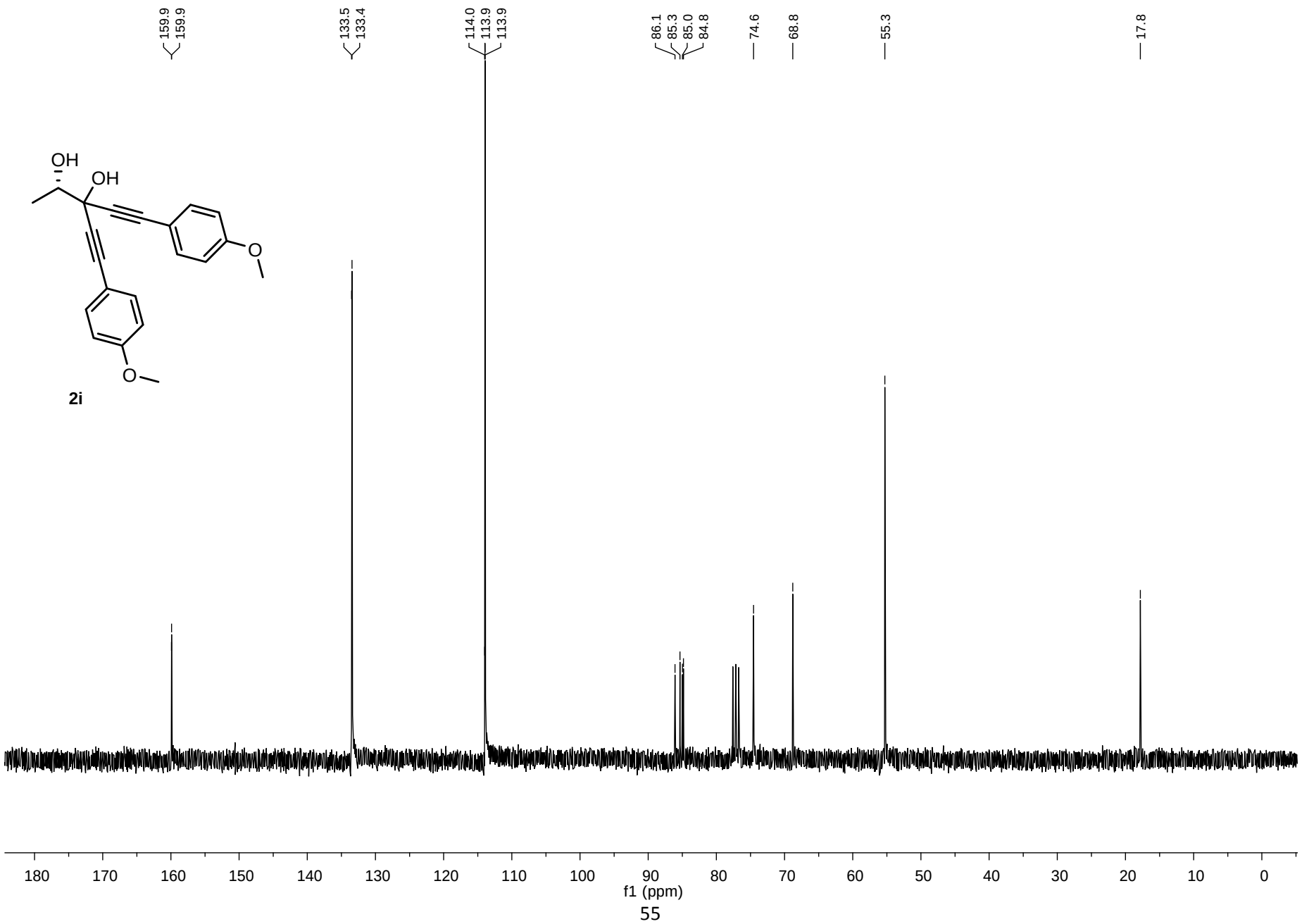
$^{13}$C-NMR (DMSO-$d_6$, 75.4 MHz)



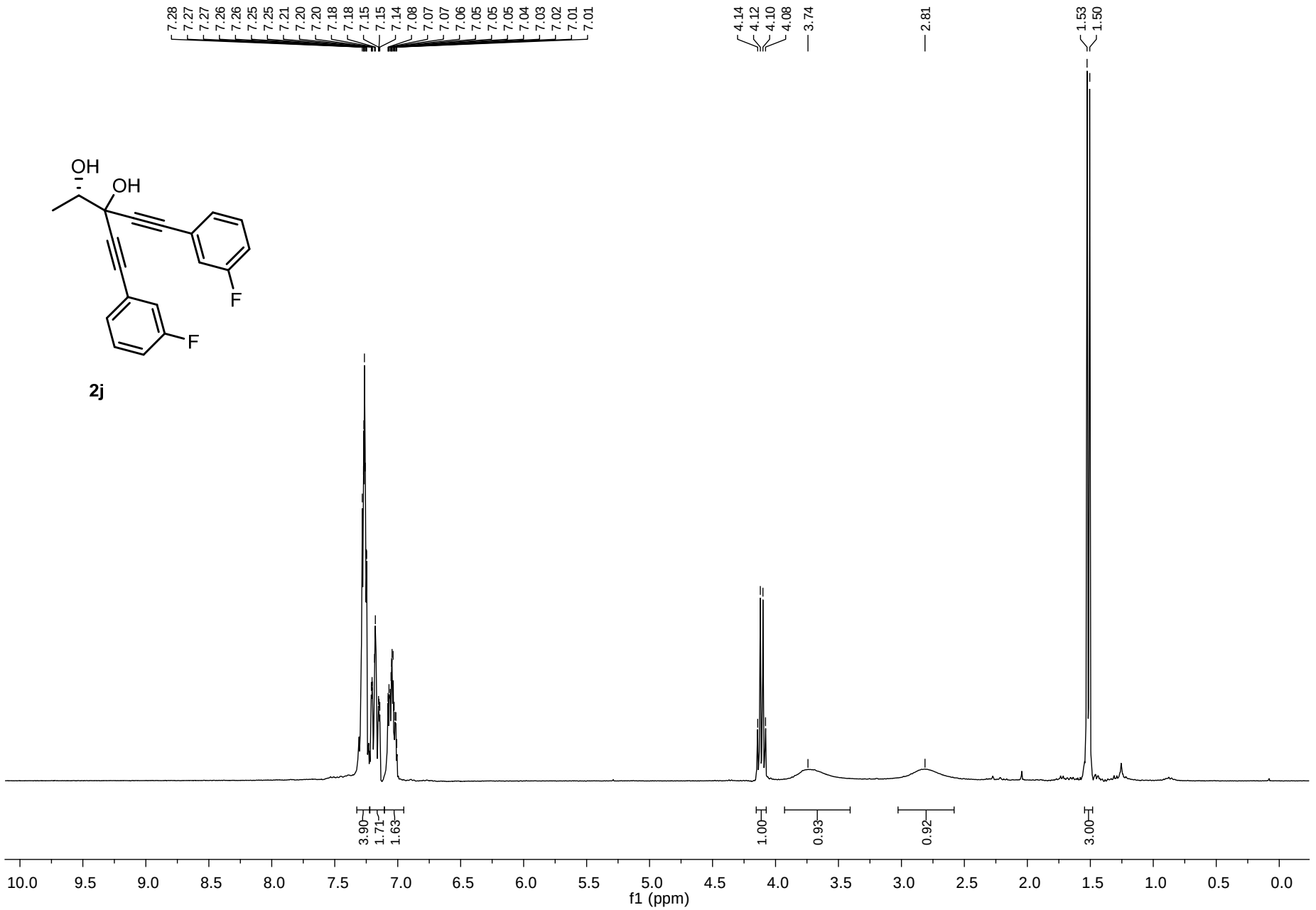
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



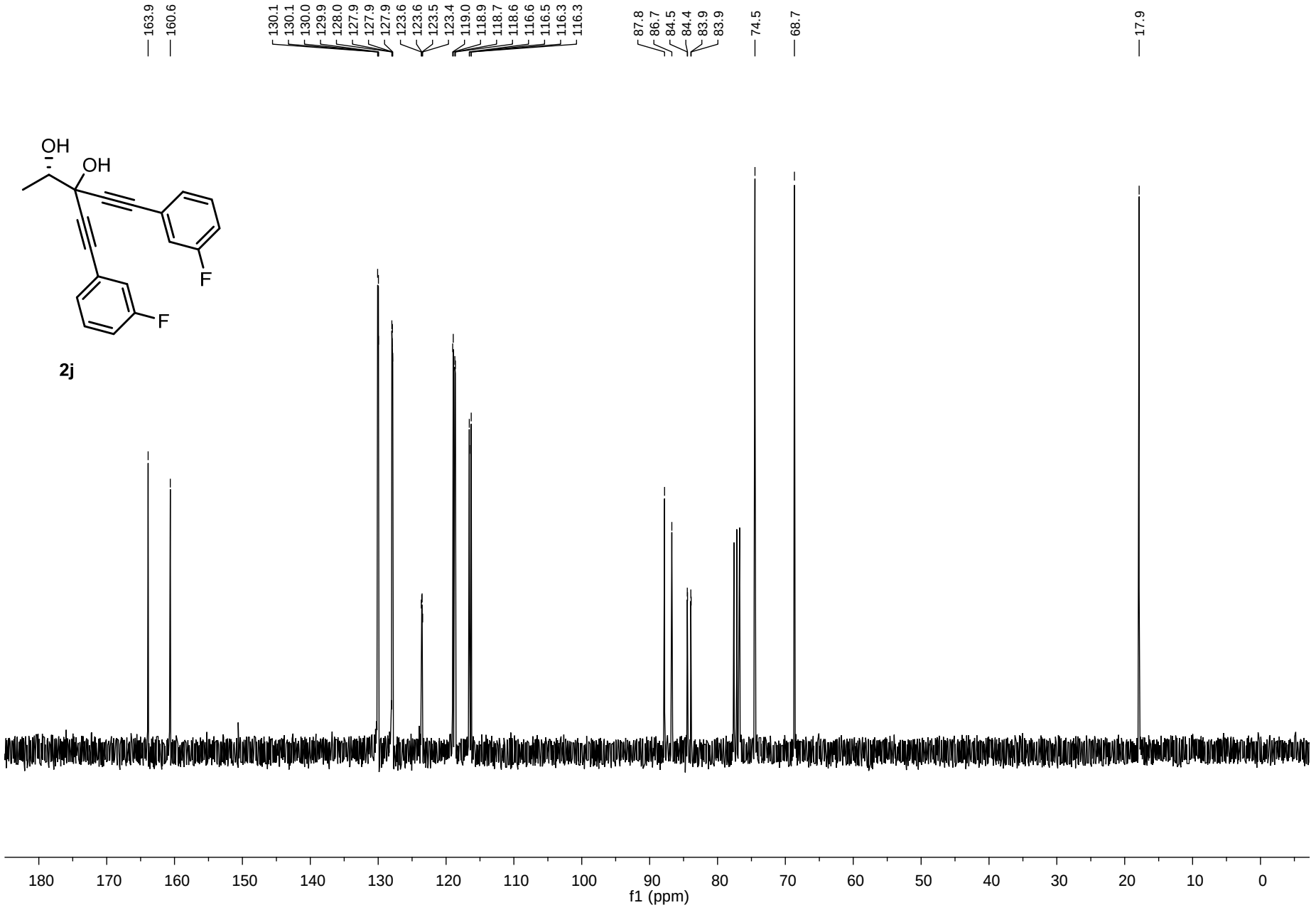
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



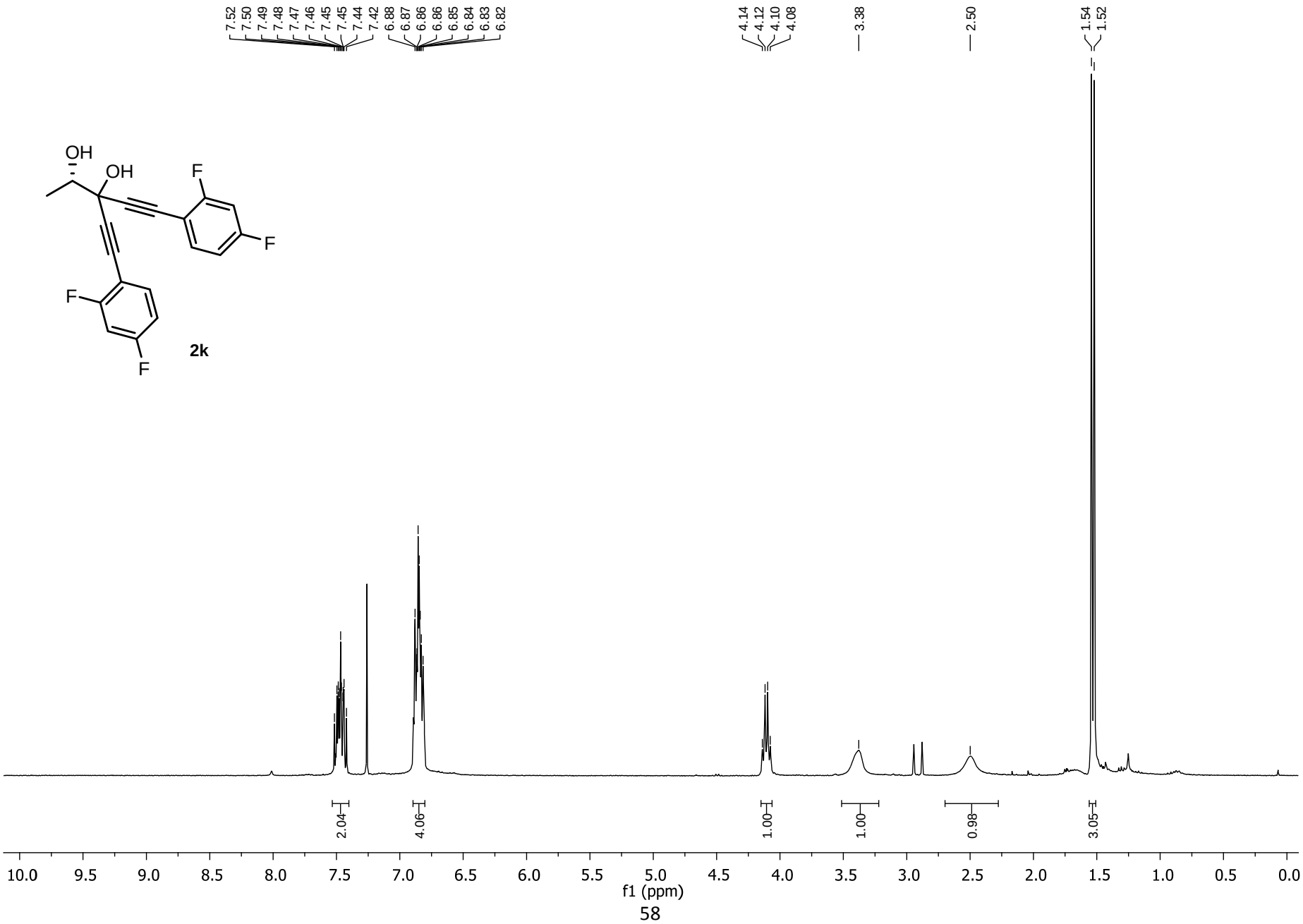
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



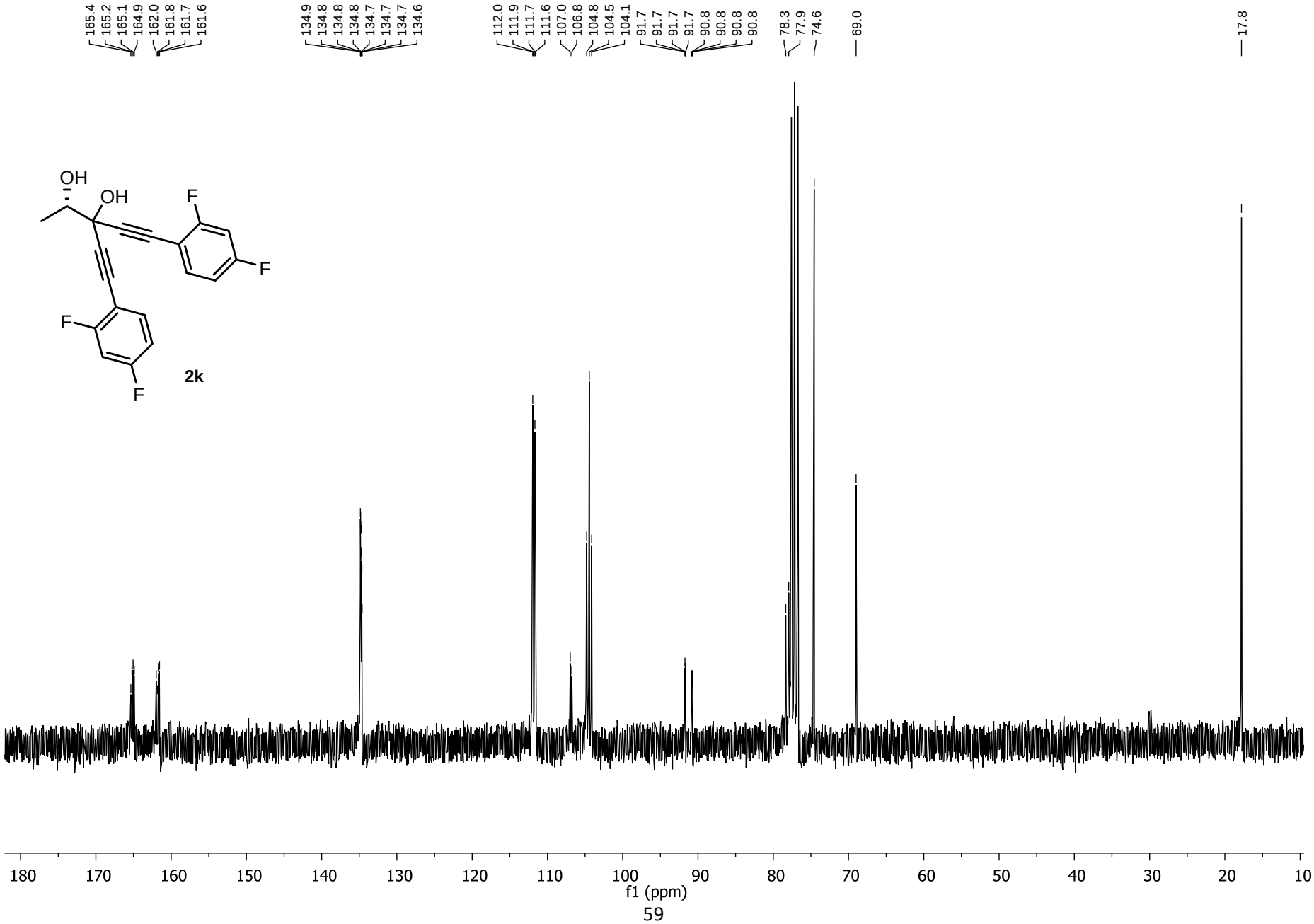
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



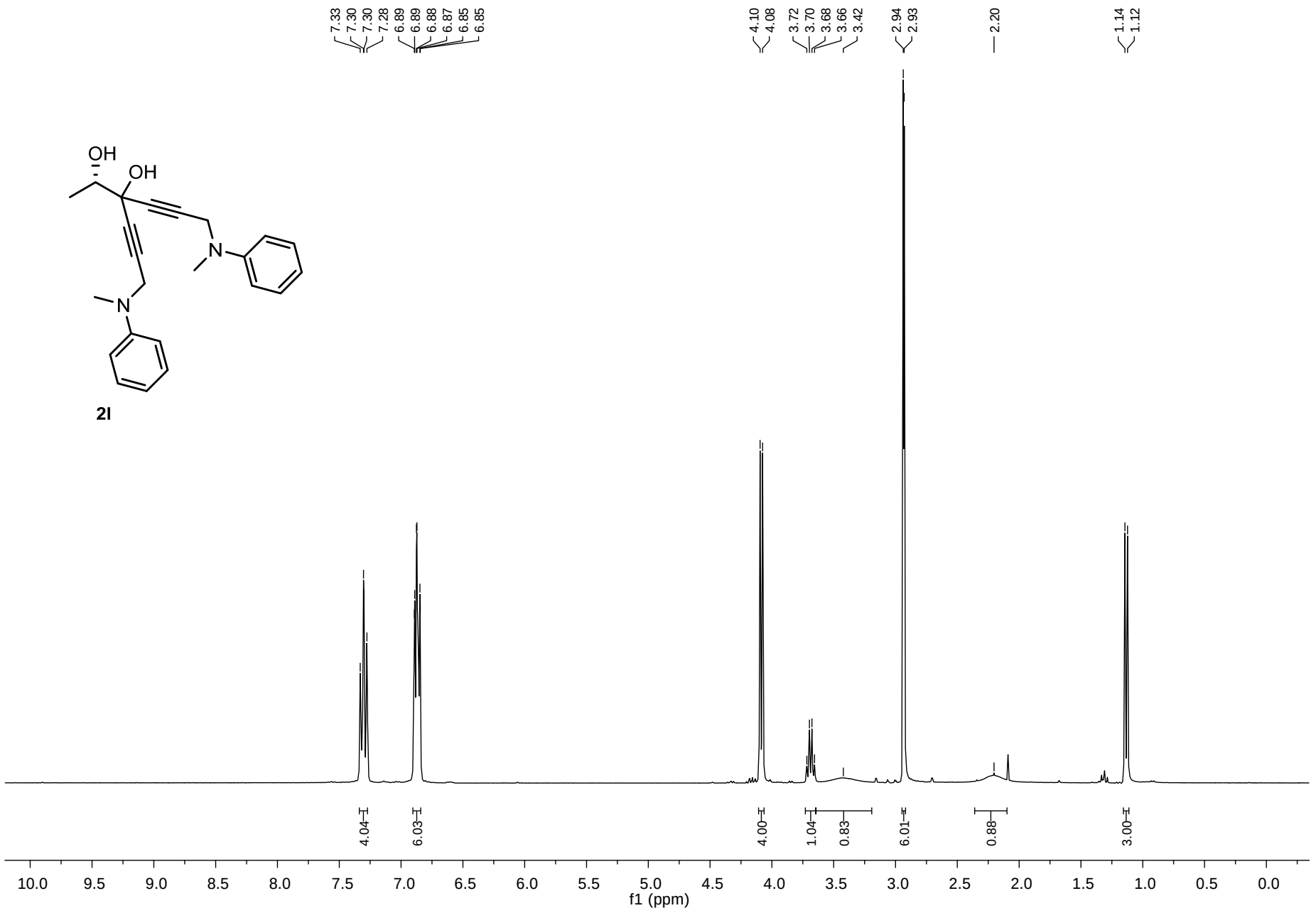
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



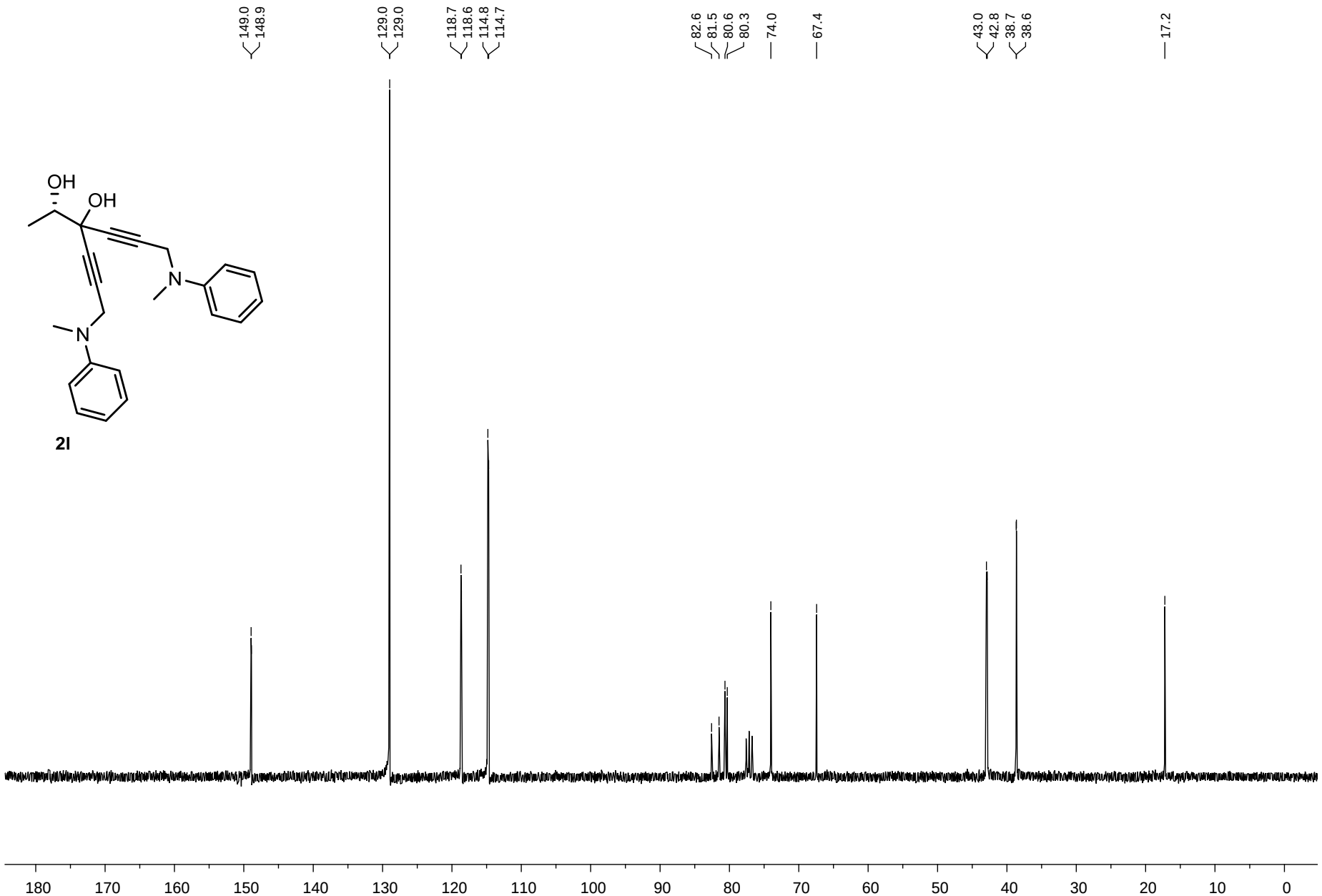
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



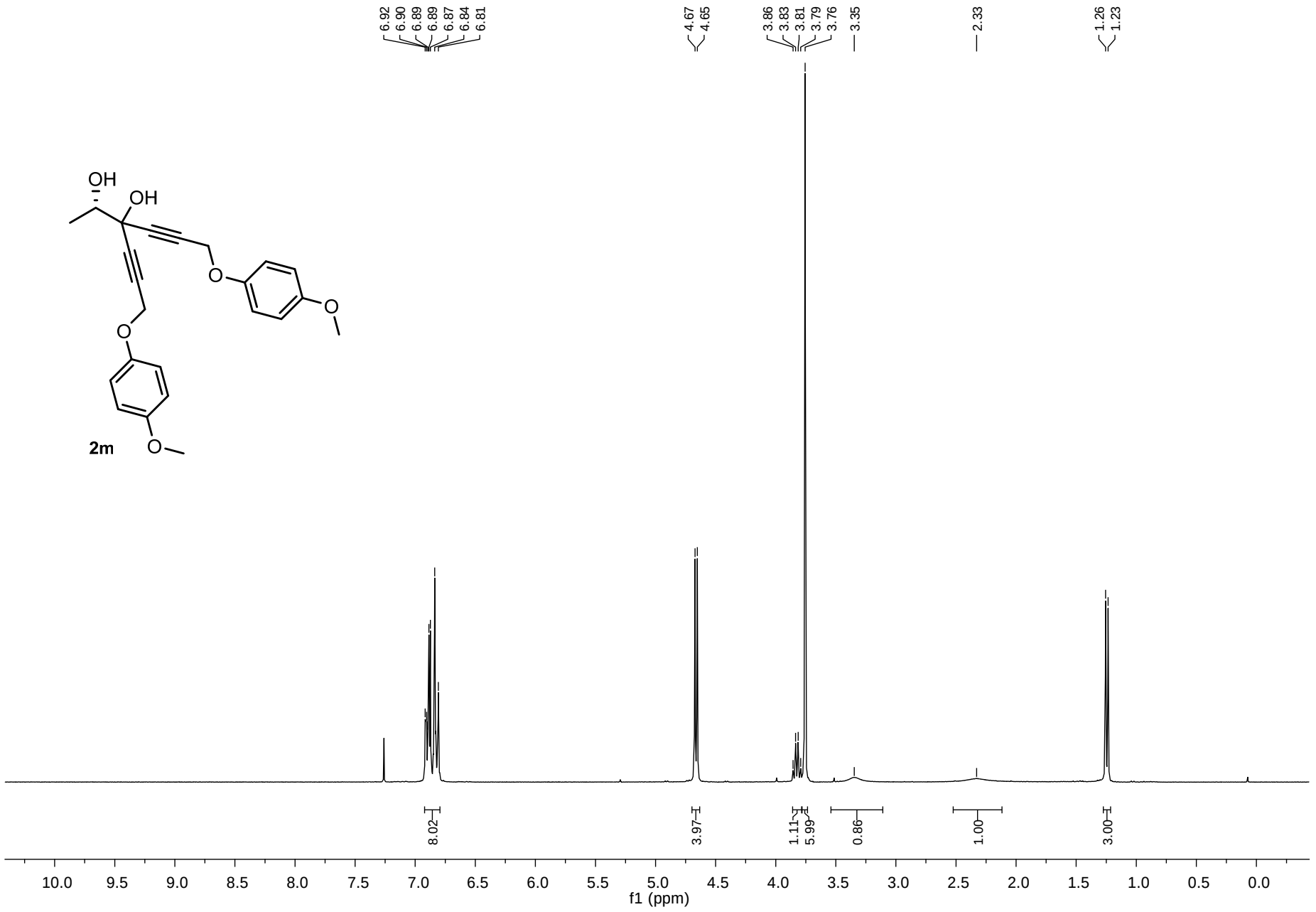
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



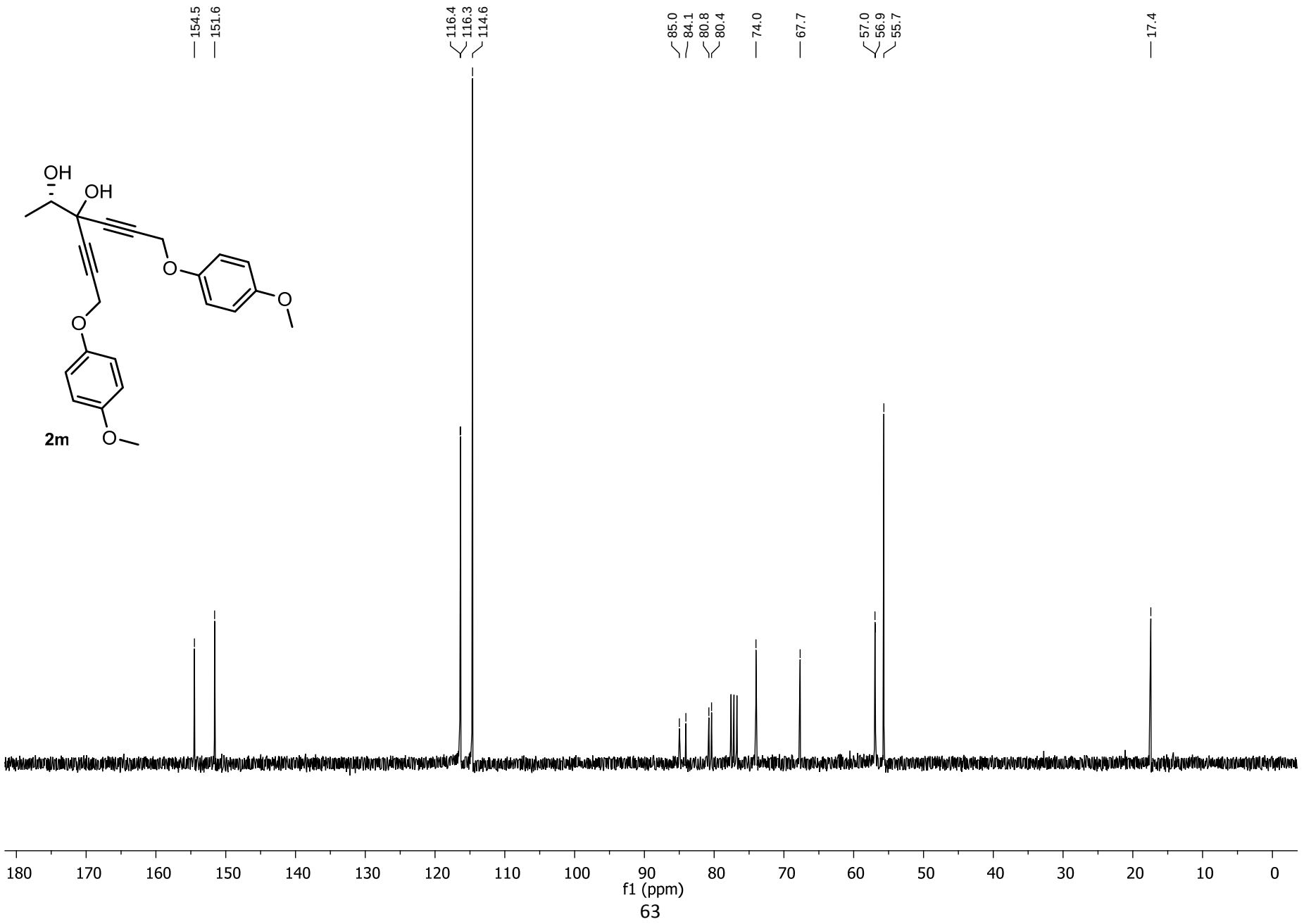
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



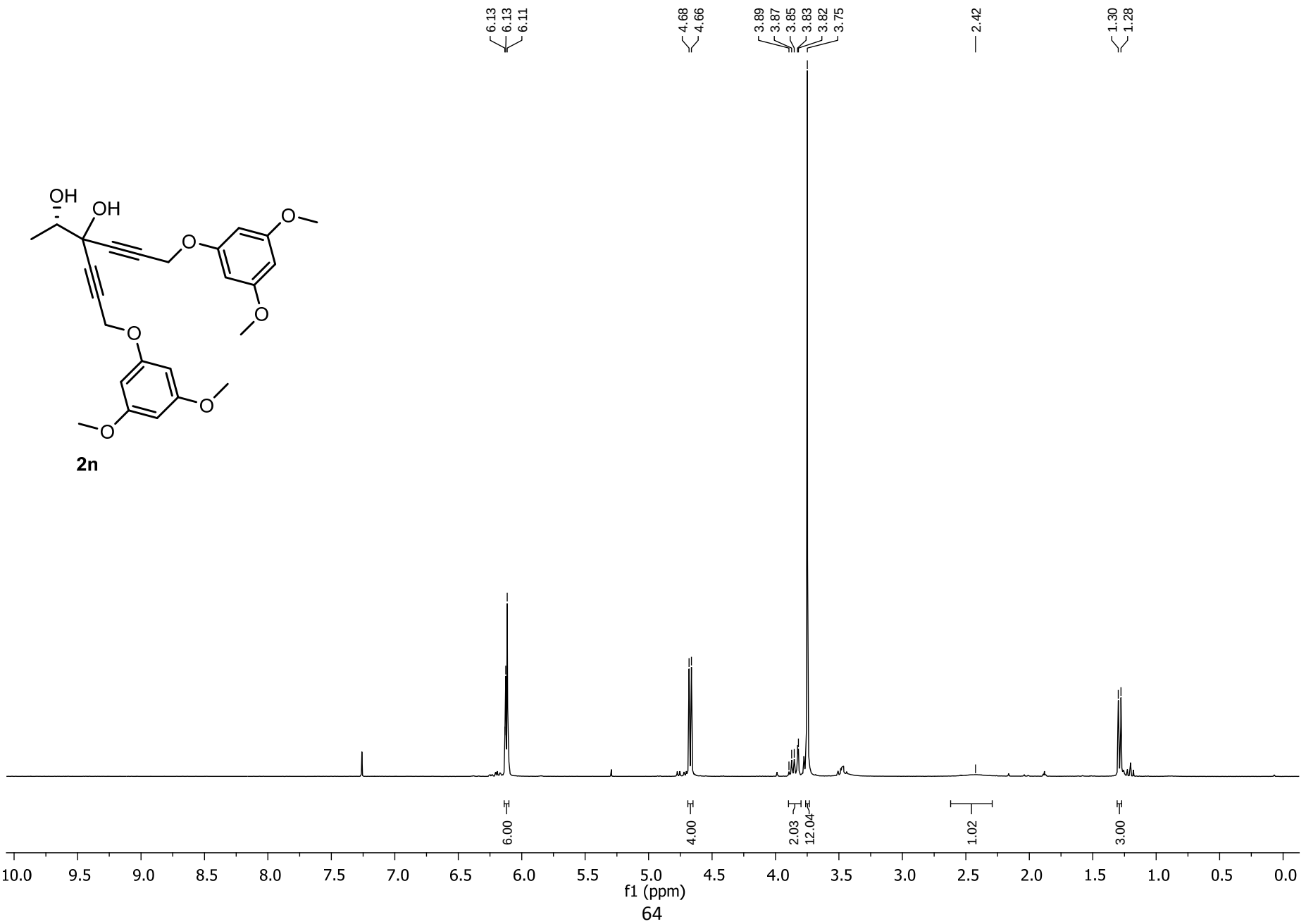
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

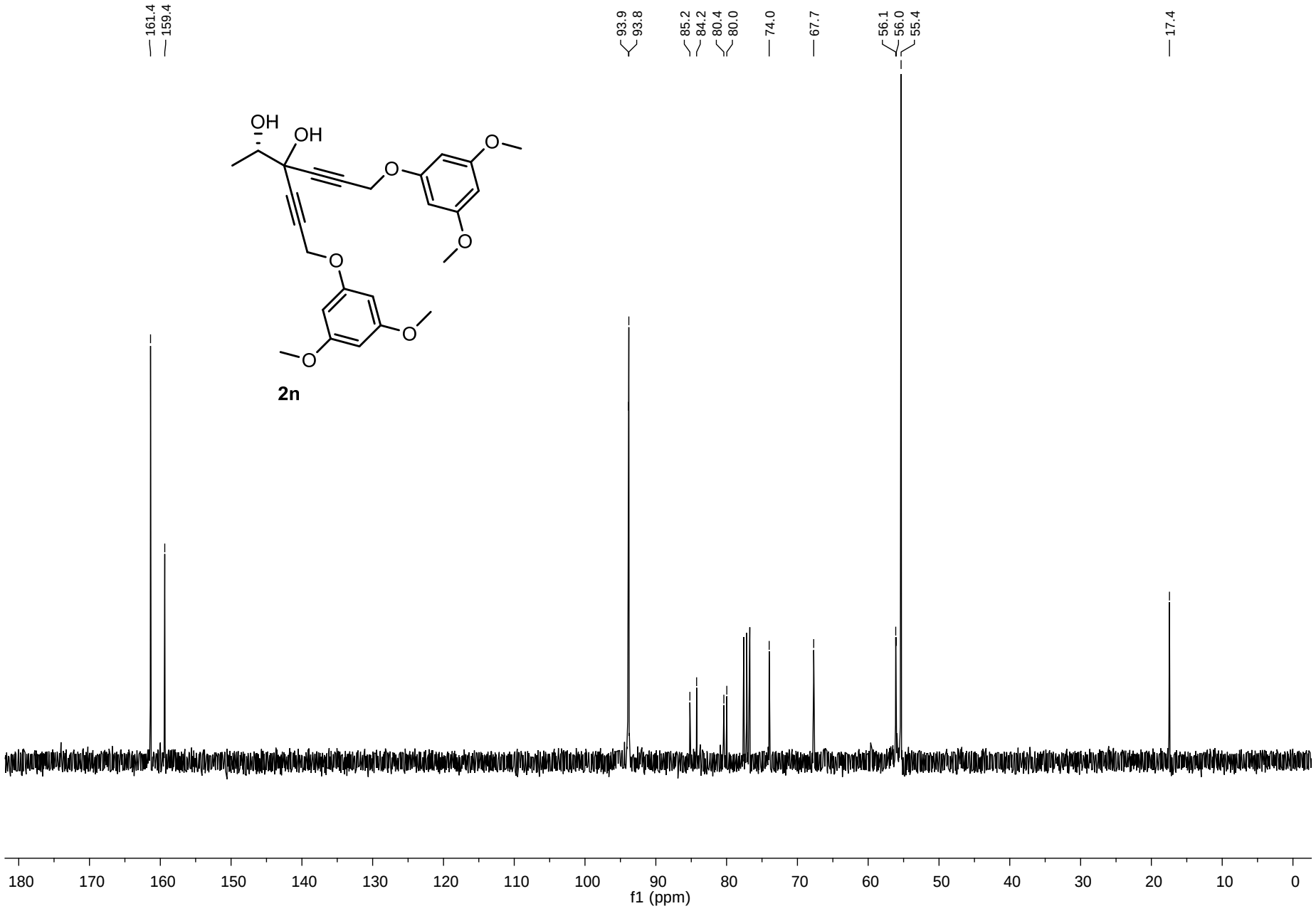


$^{1}$H-NMR ($CDCl_3$, 300 MHz)

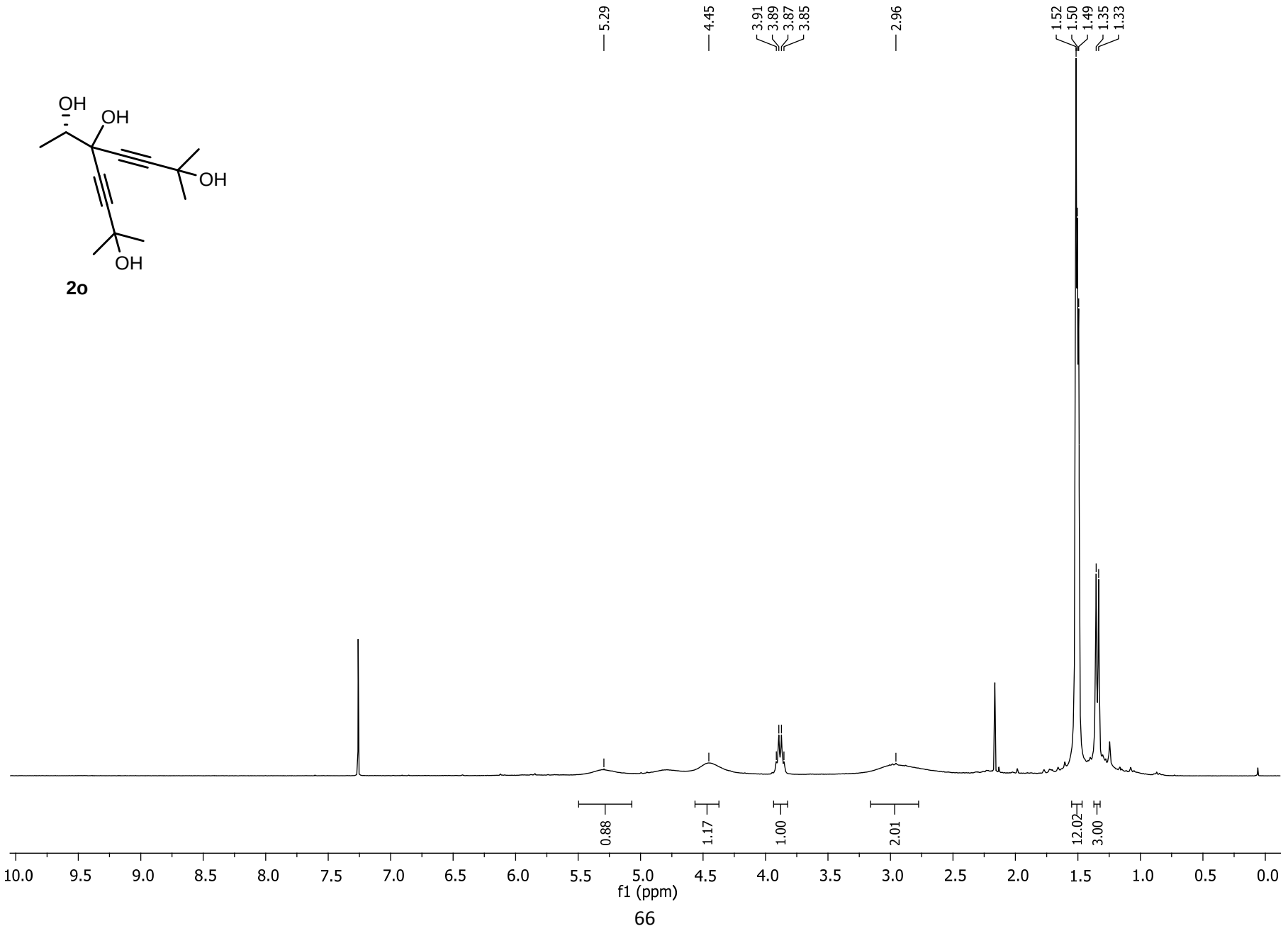



**2n**

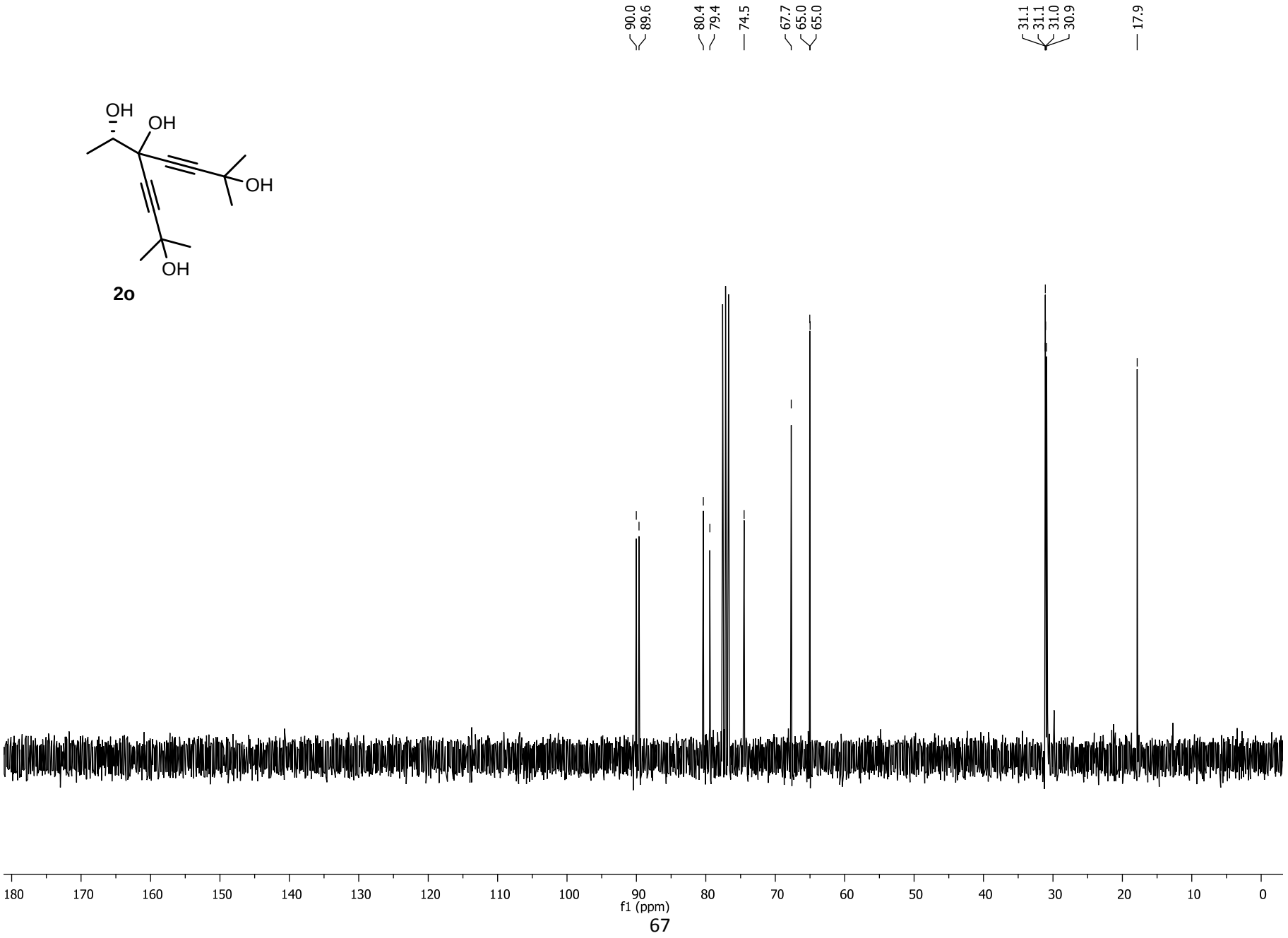
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



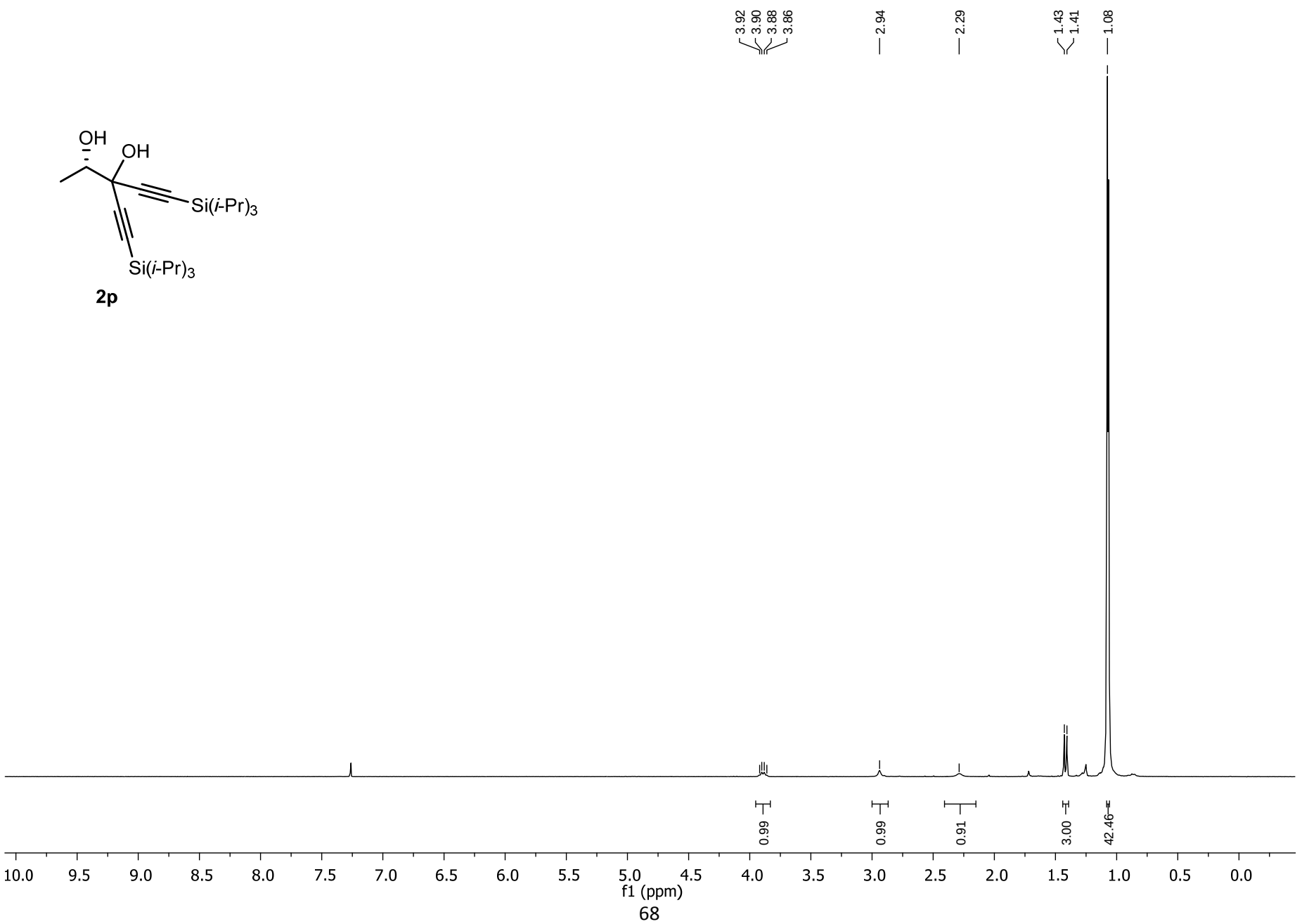
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



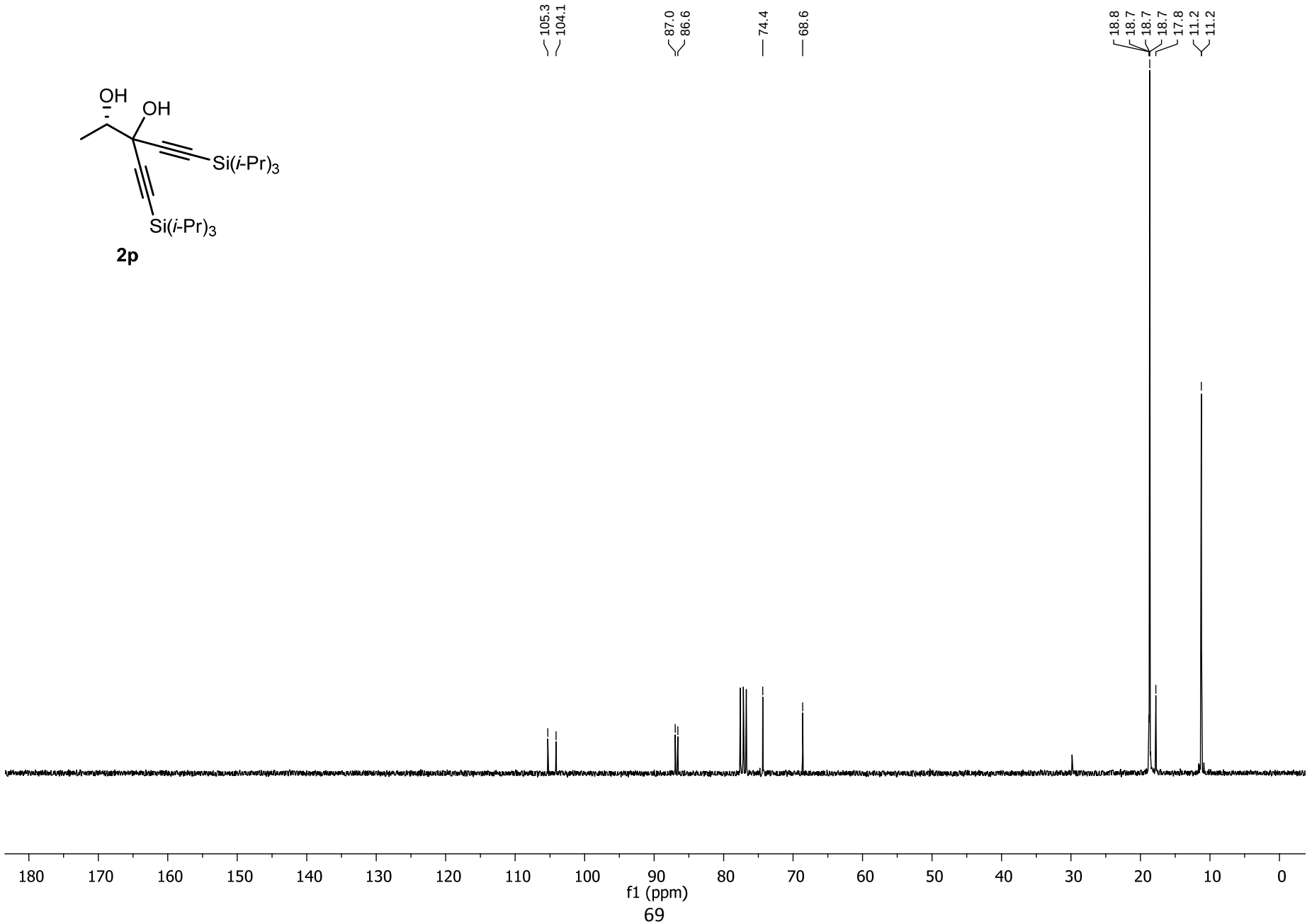
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



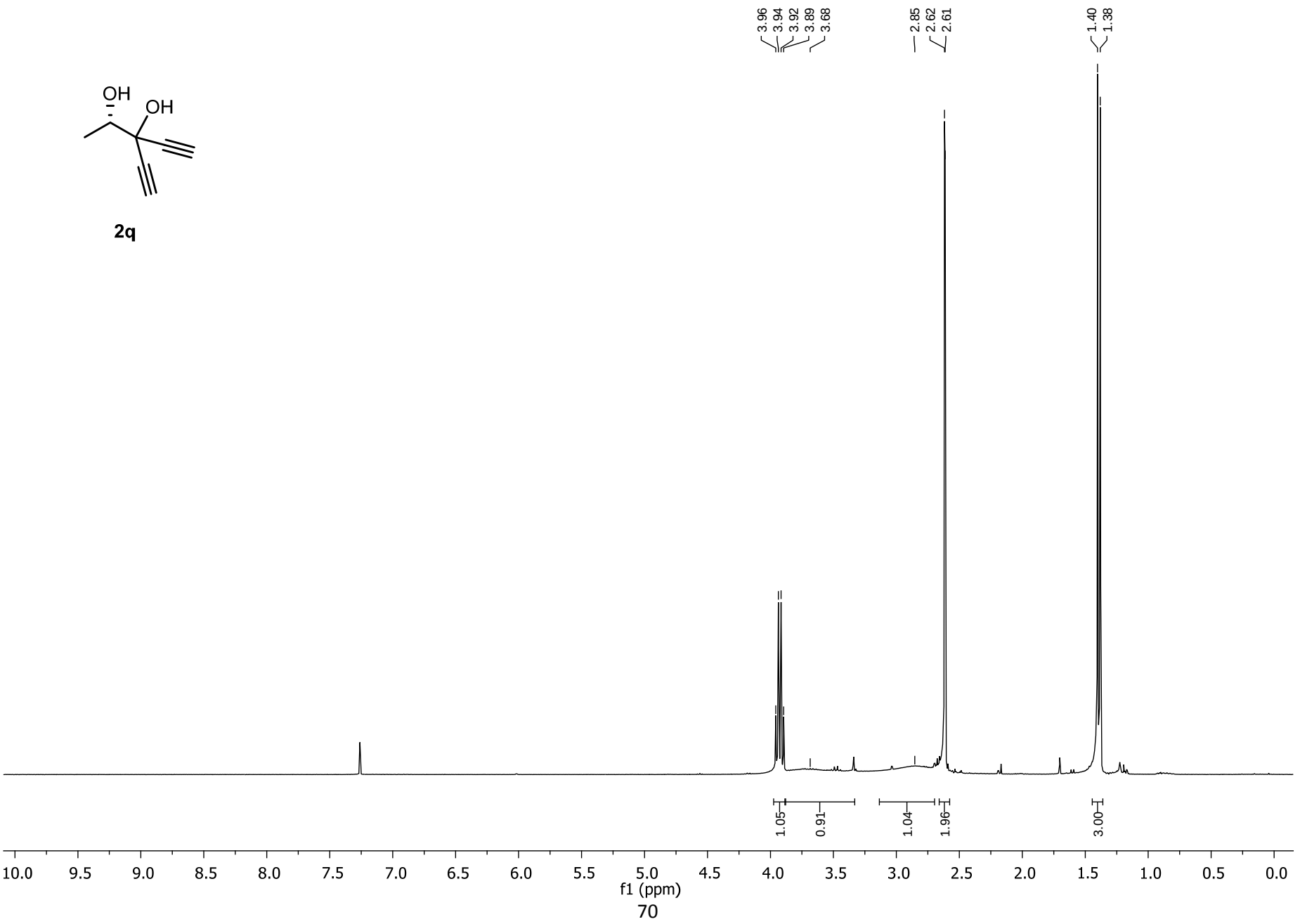
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



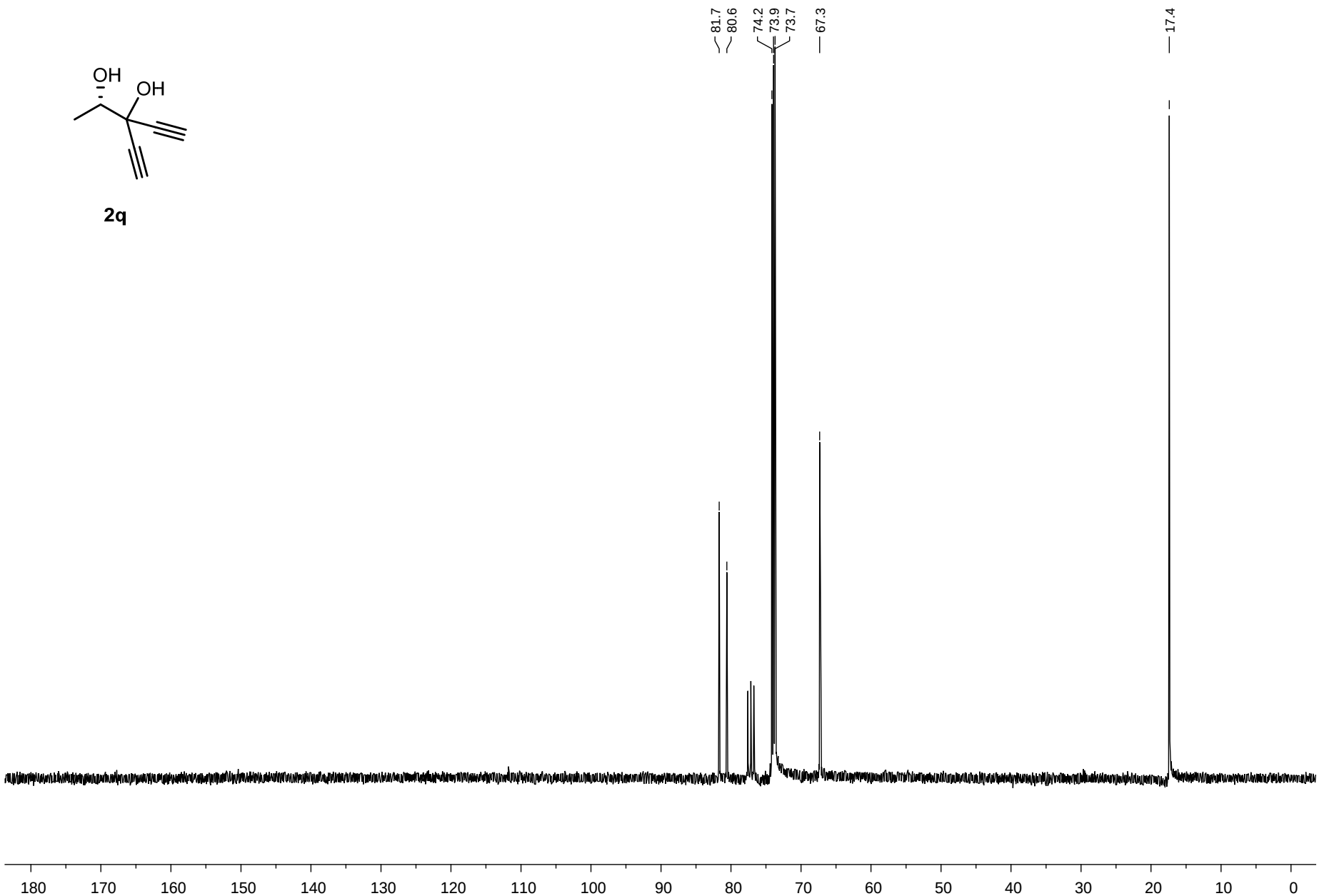
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

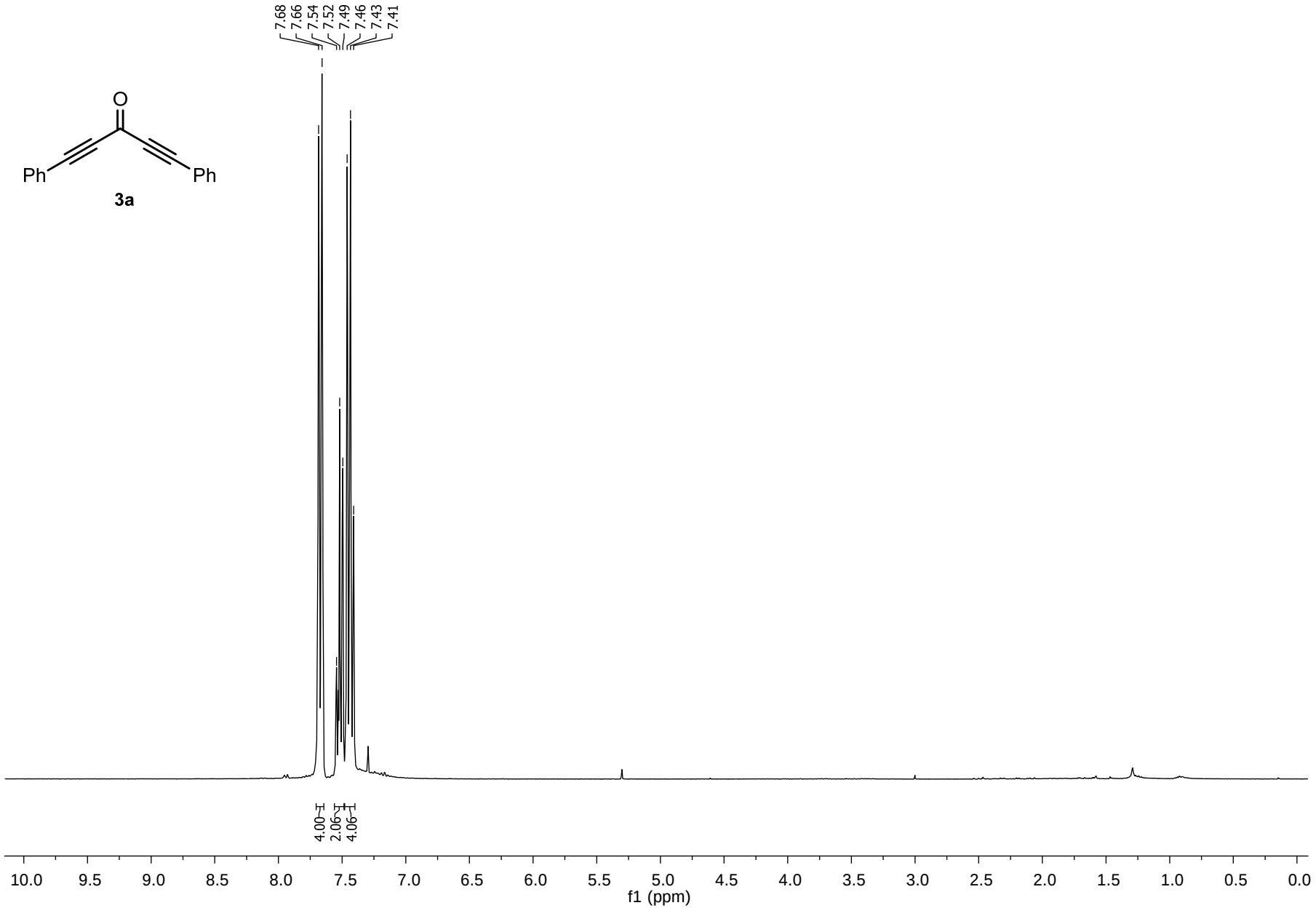


$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

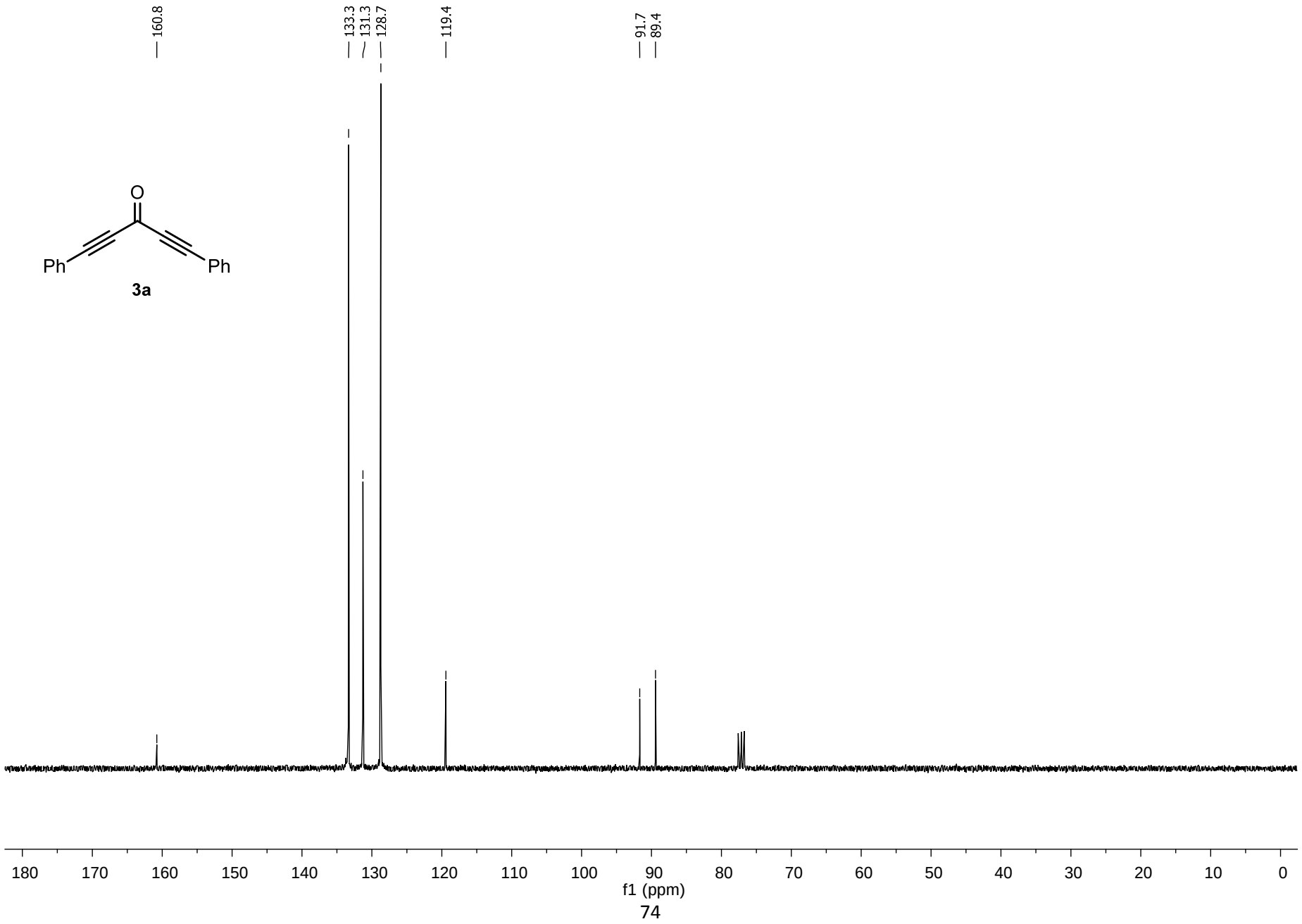


# NMR spectra of skipped diynones 3

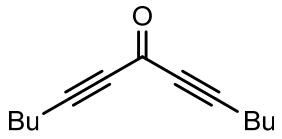
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

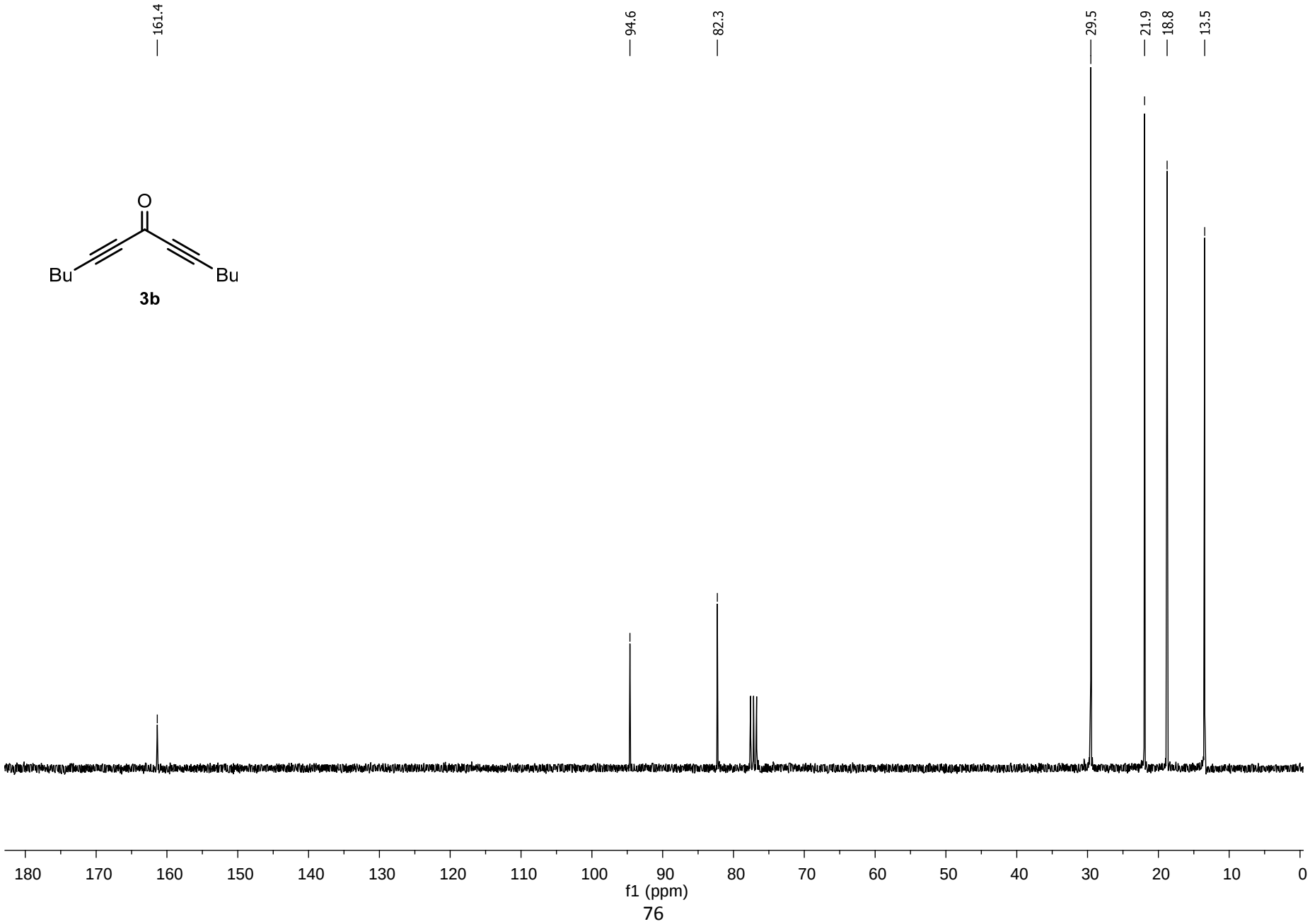


$^{1}$H-NMR ($CDCl_3$, 300 MHz)

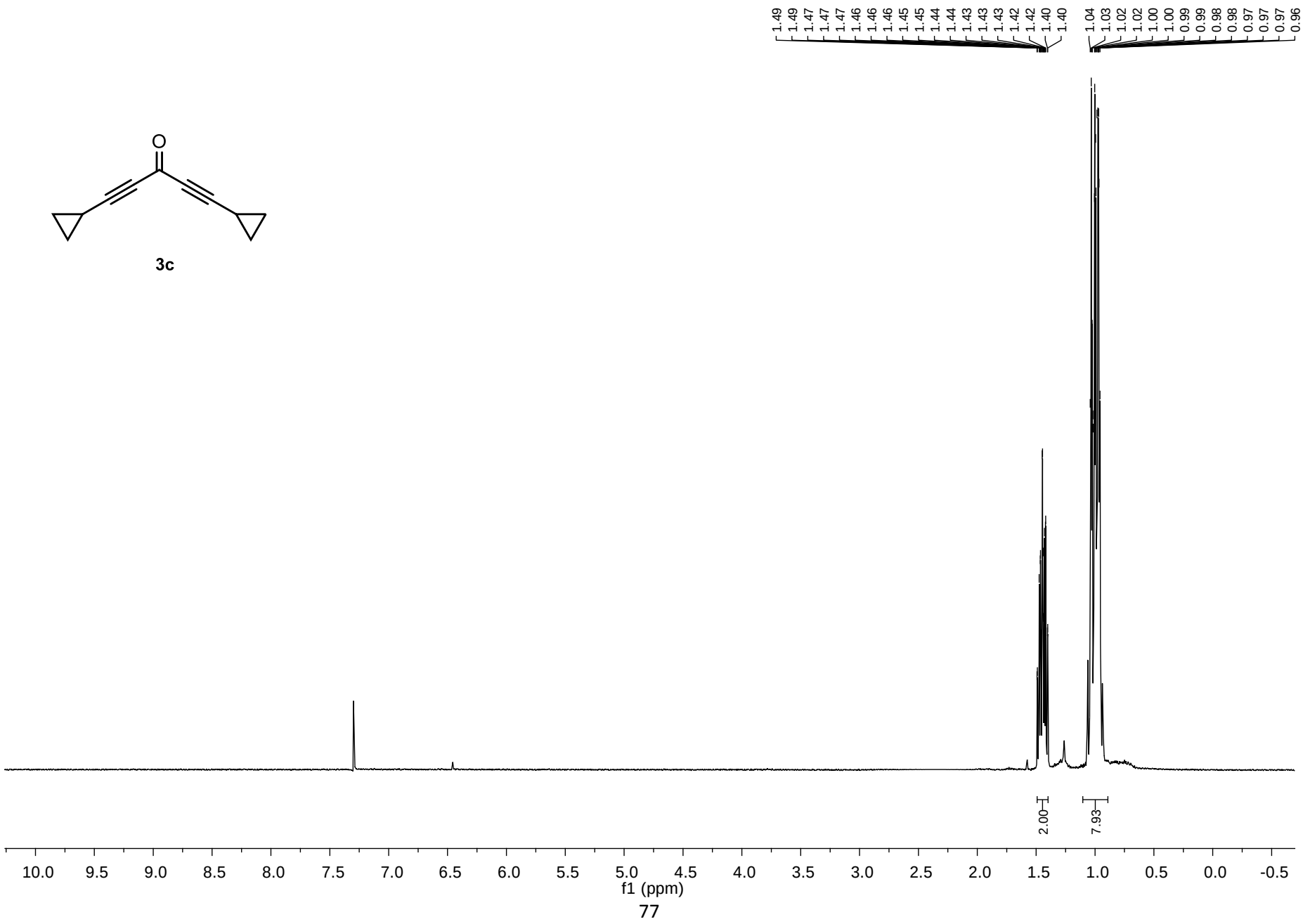



**3b**

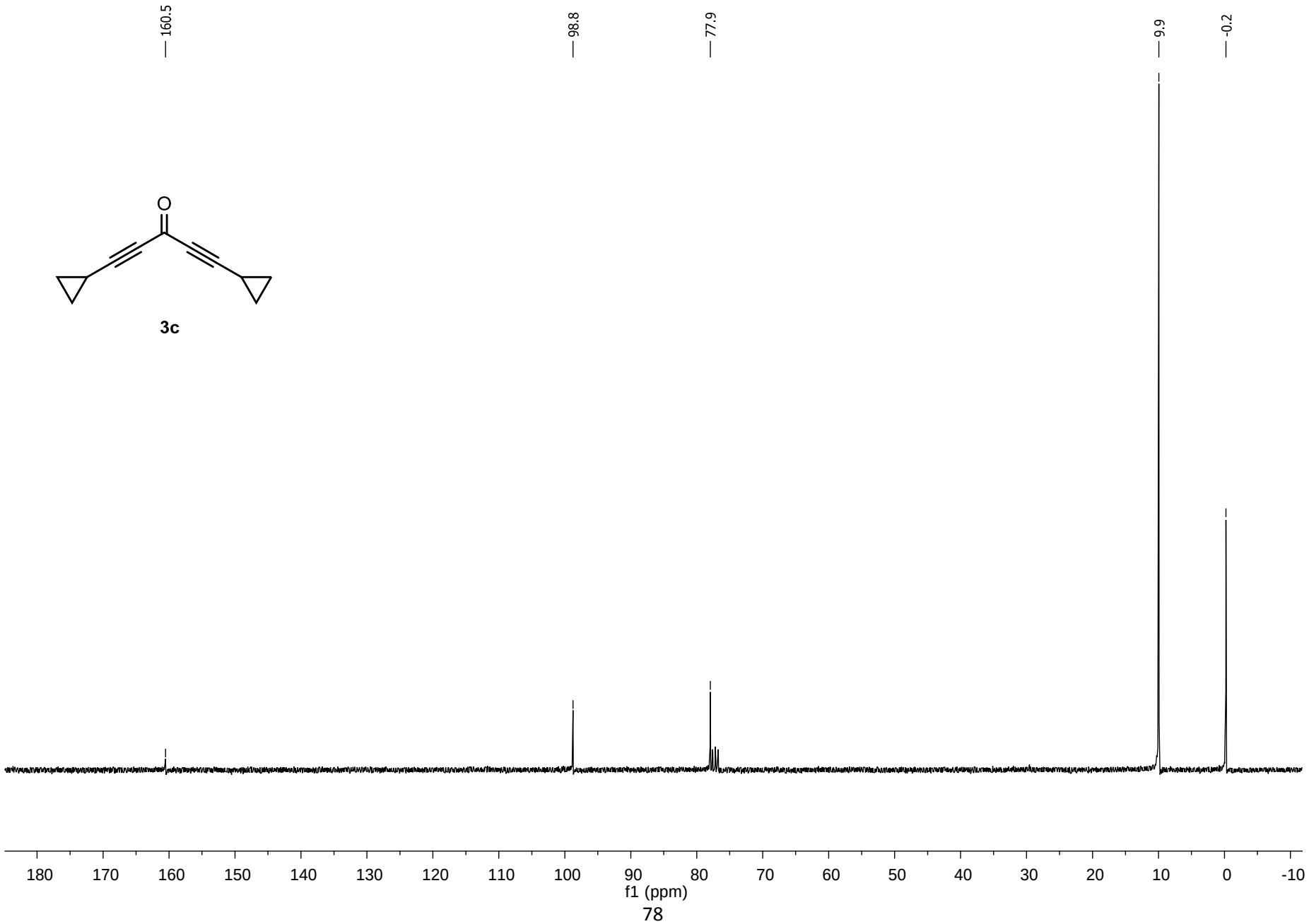
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



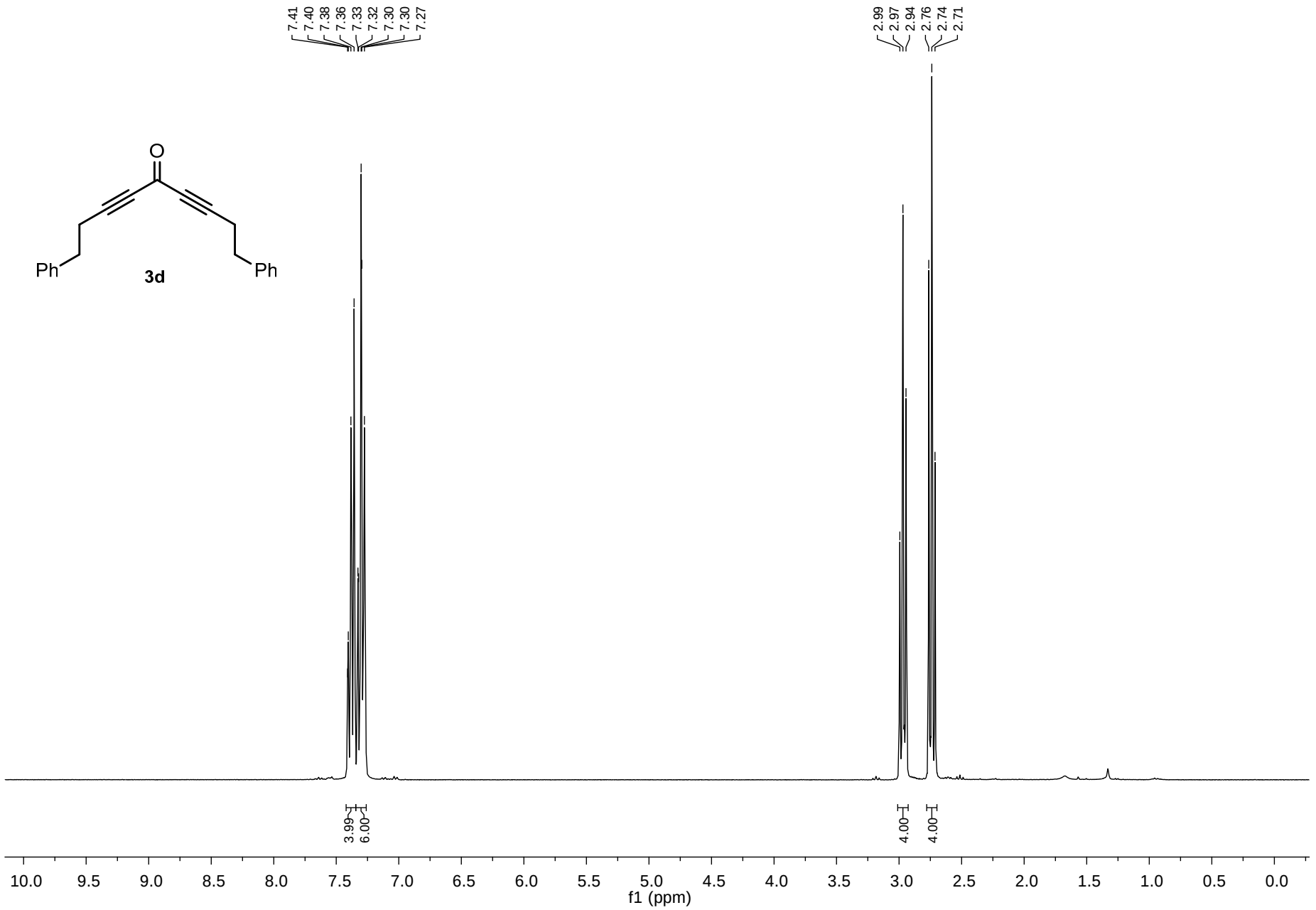
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



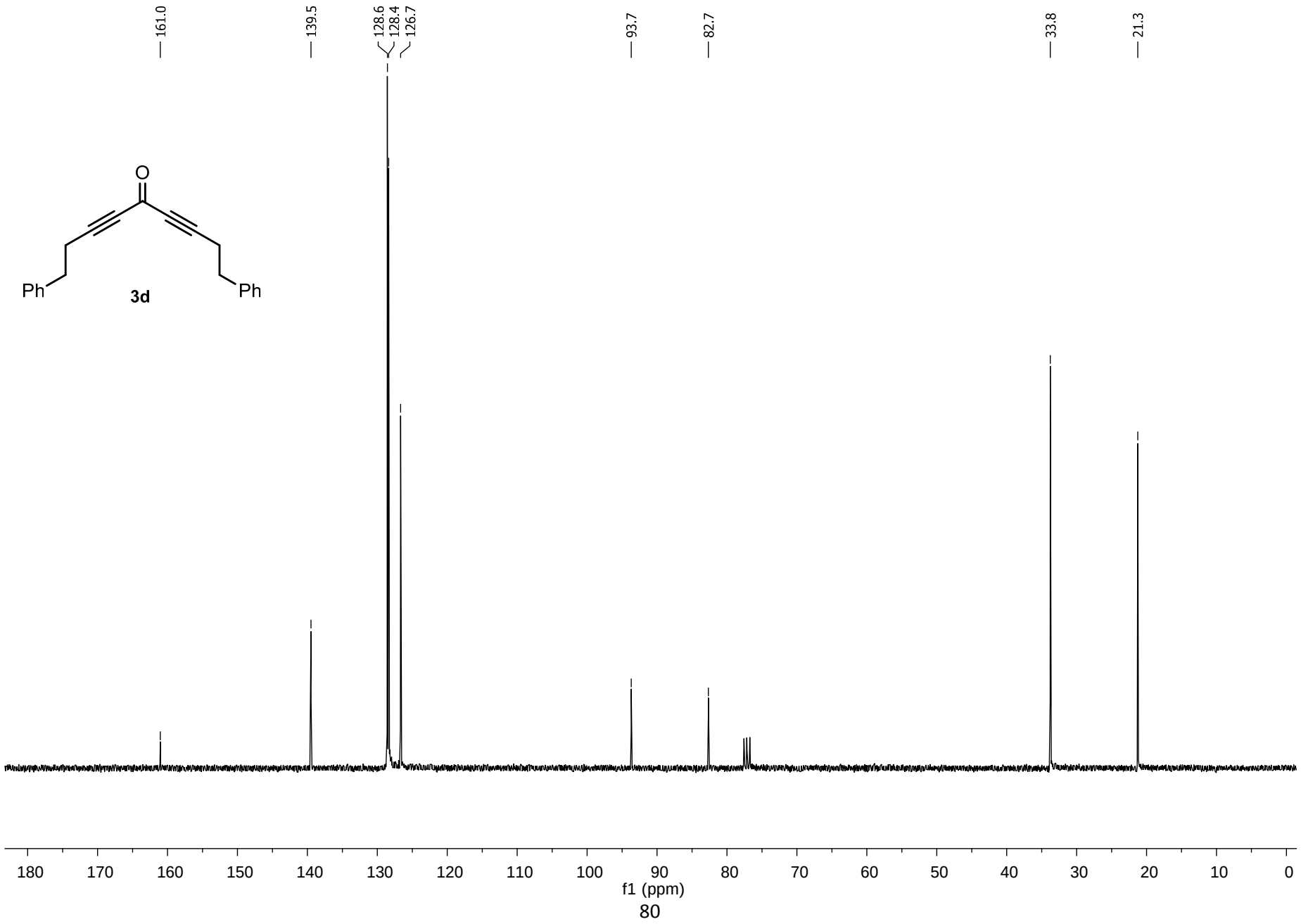
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



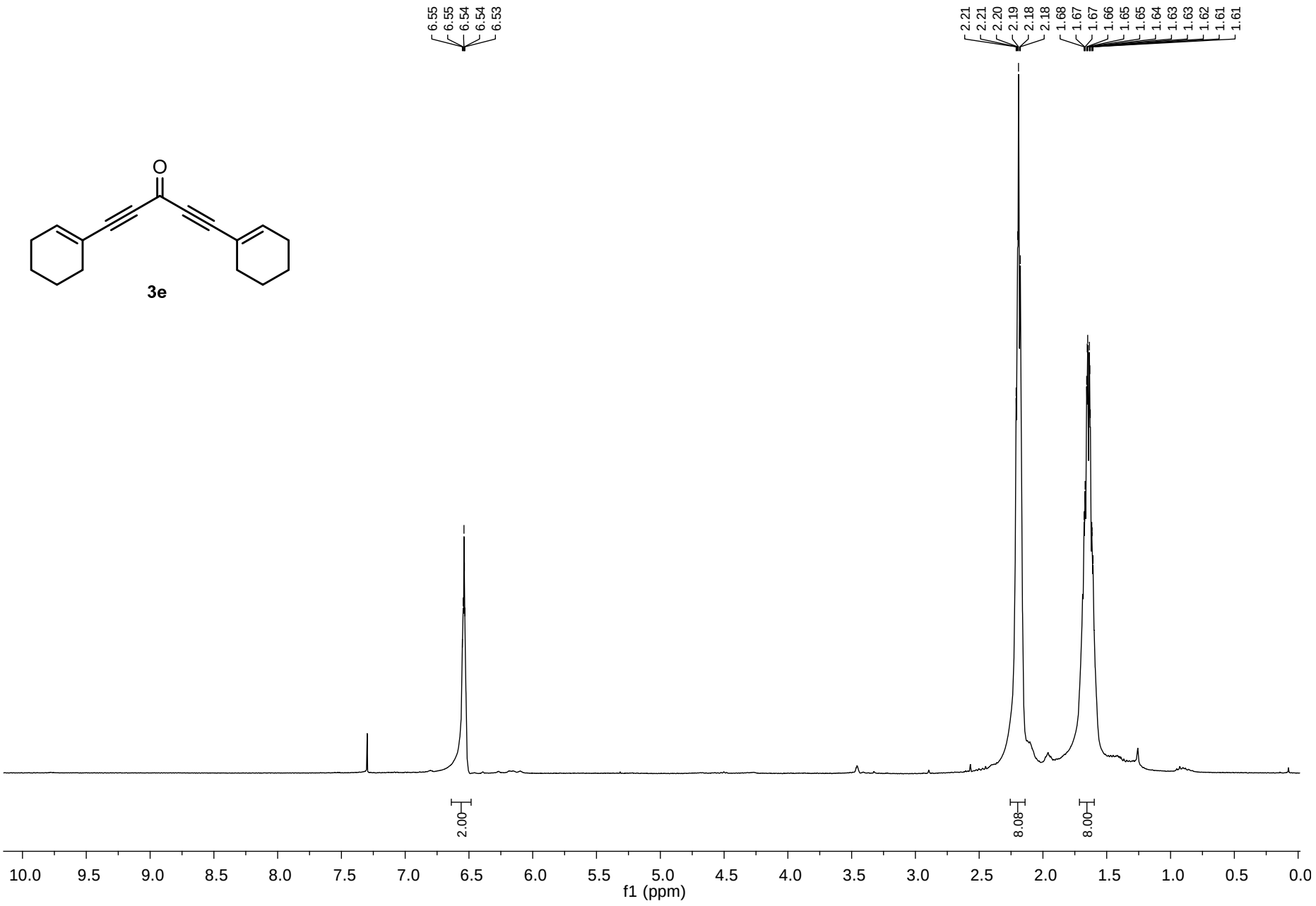
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



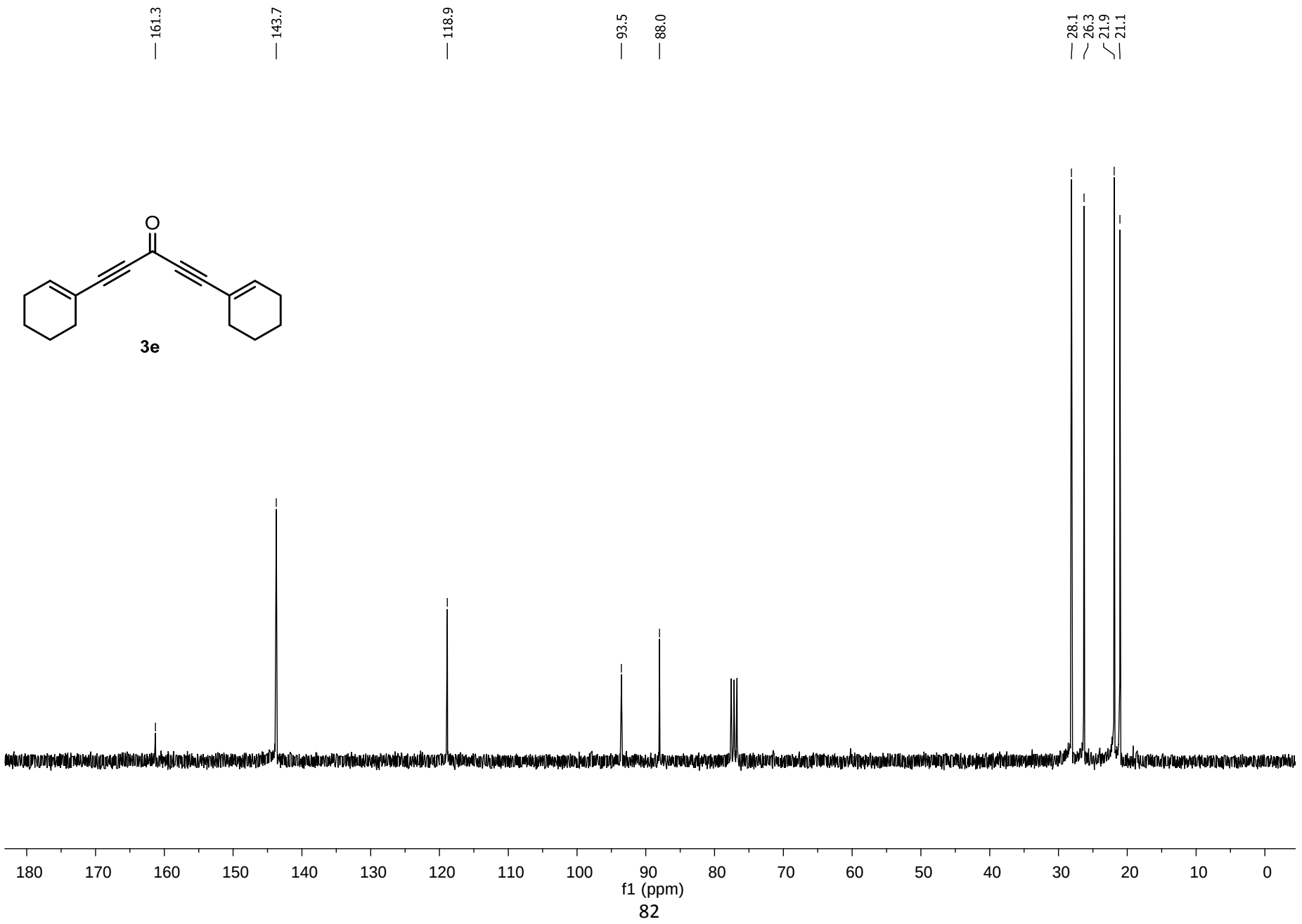
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



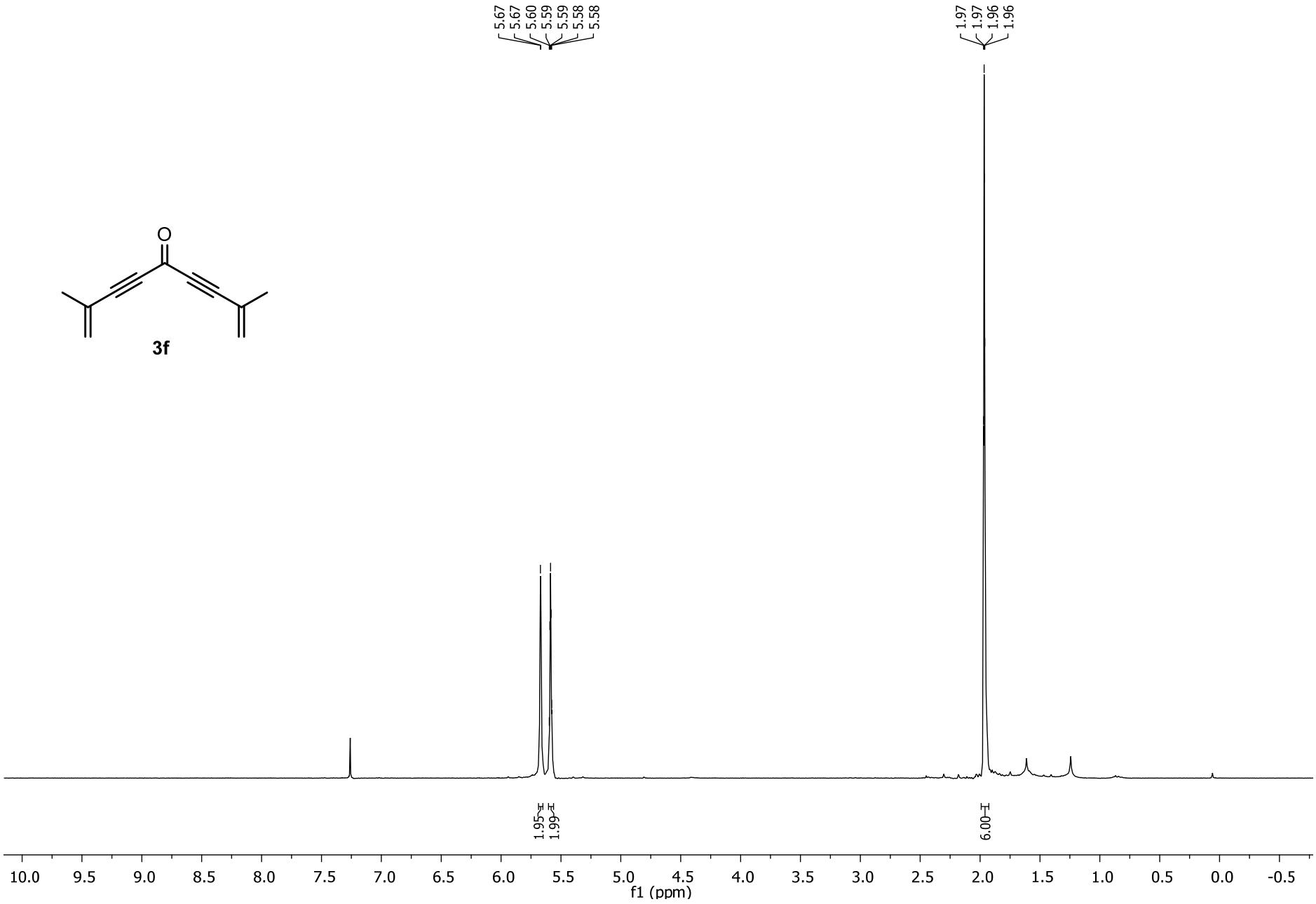
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



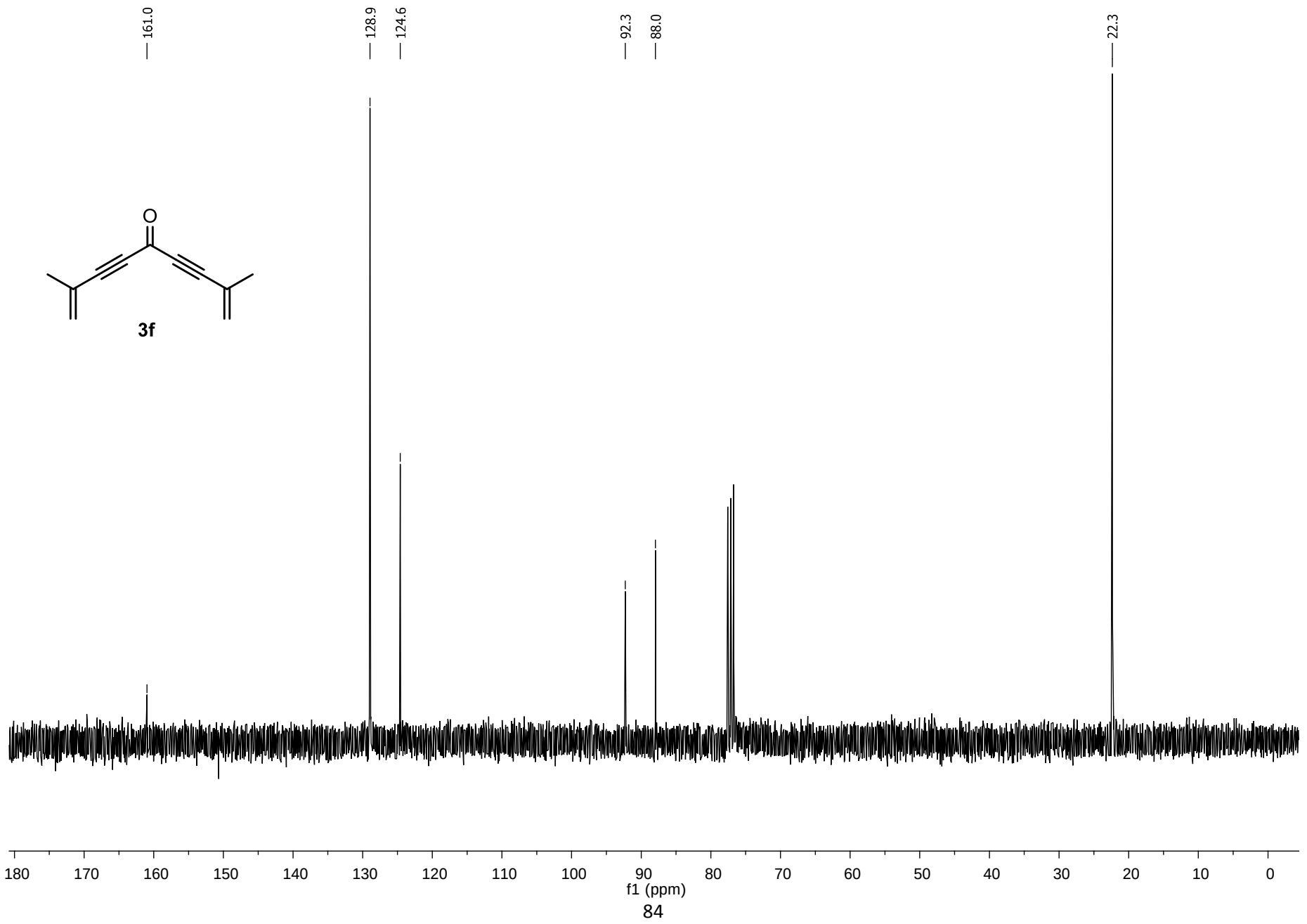
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



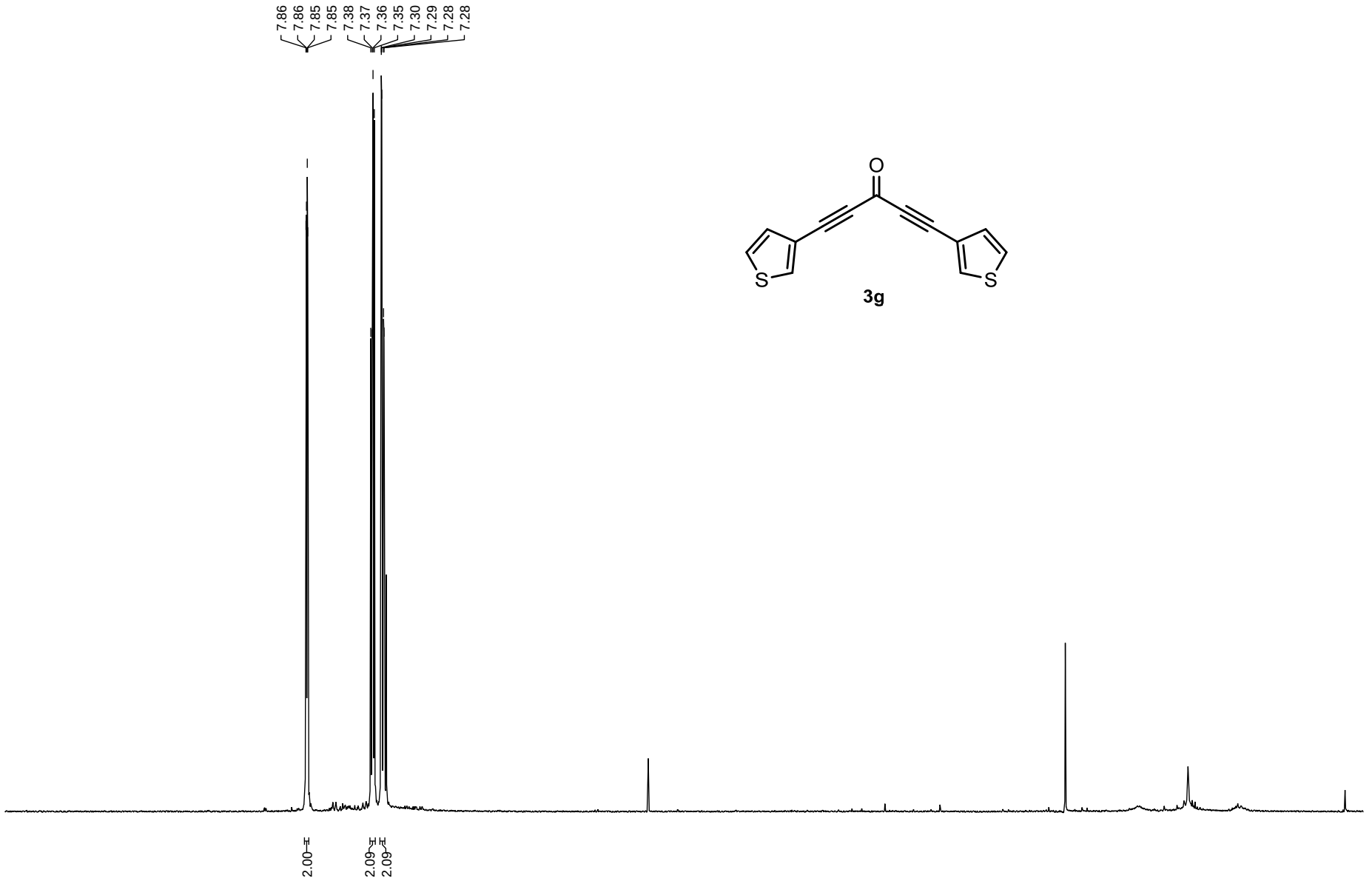
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



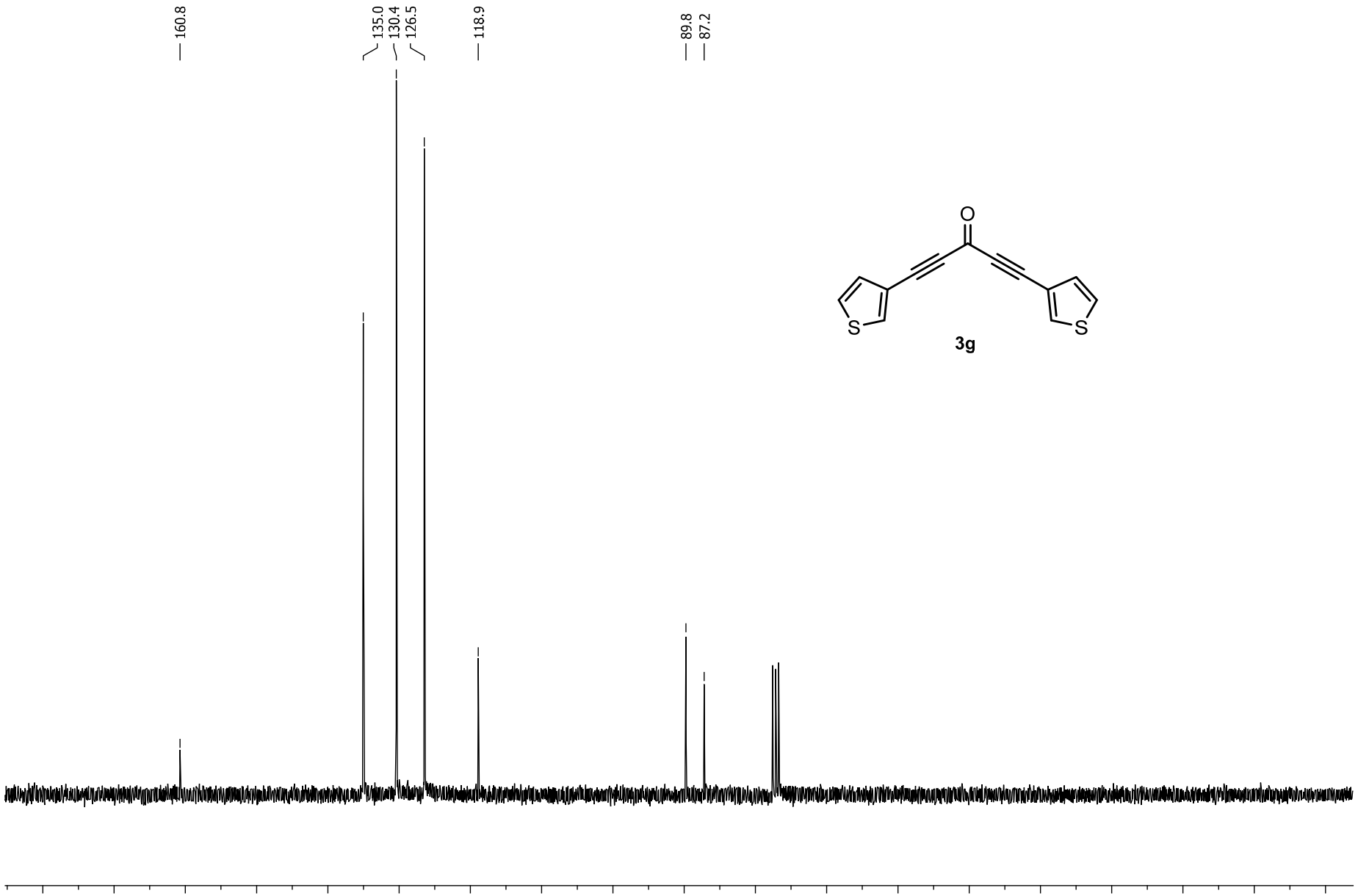
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



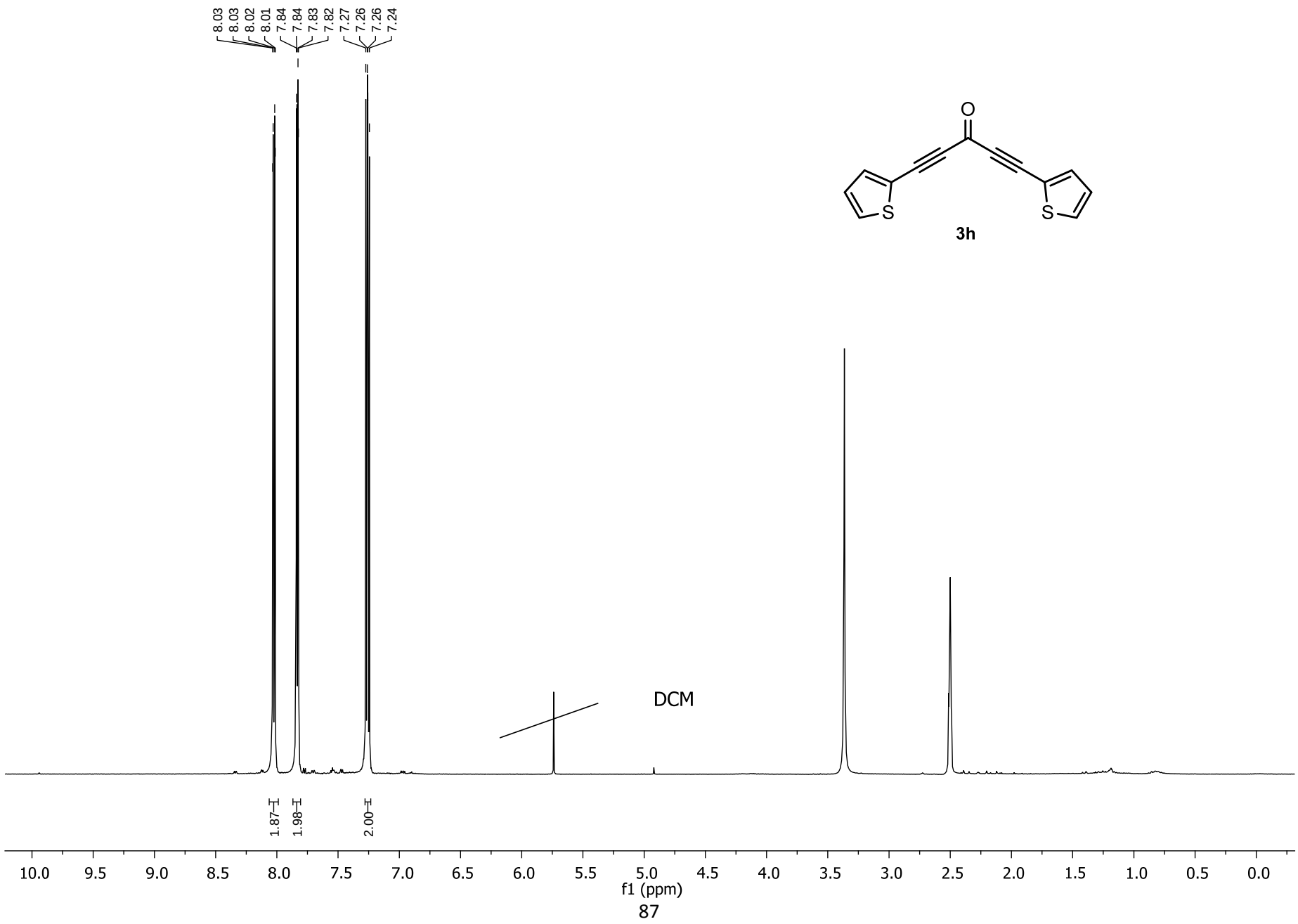
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



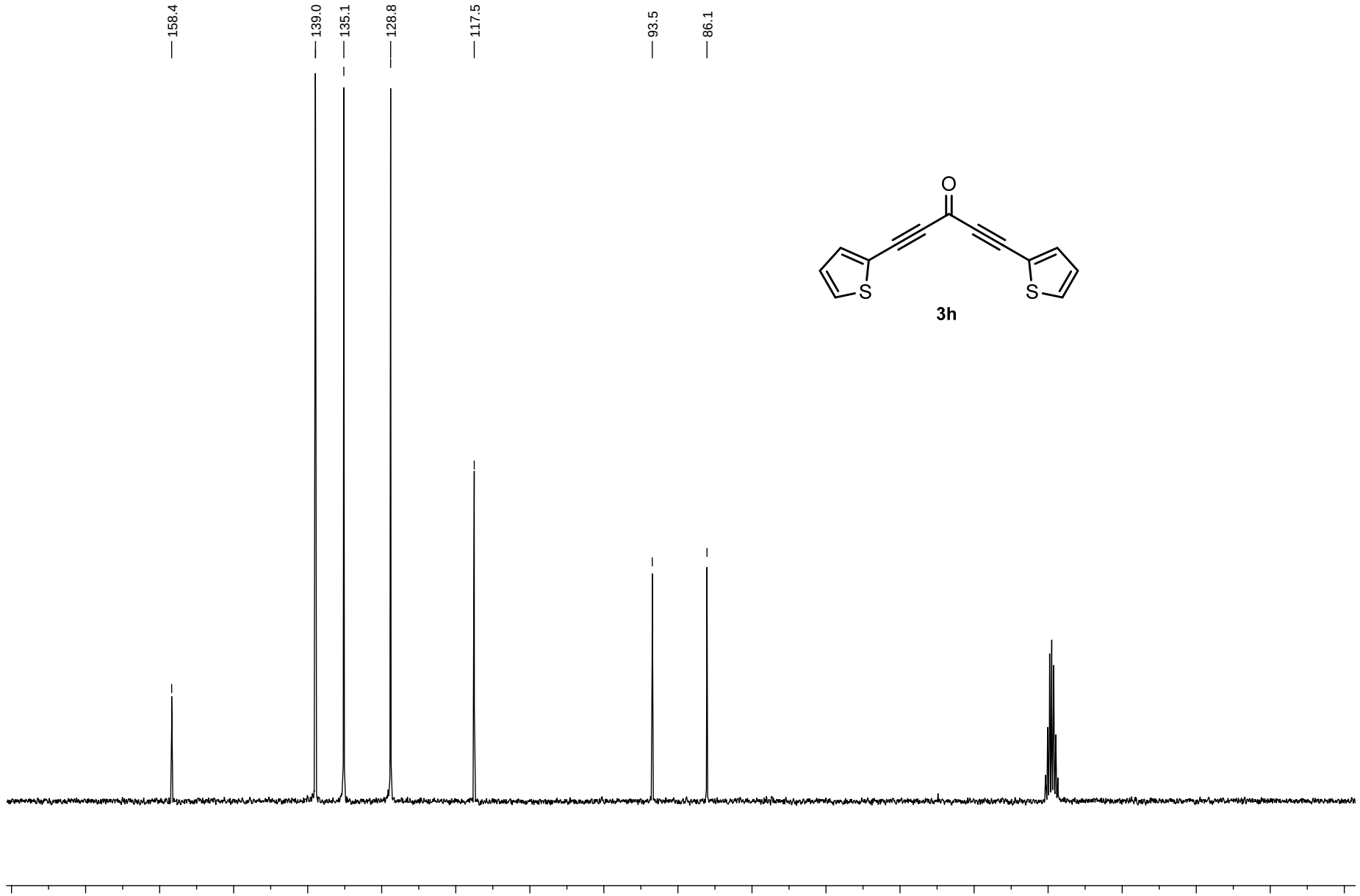
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



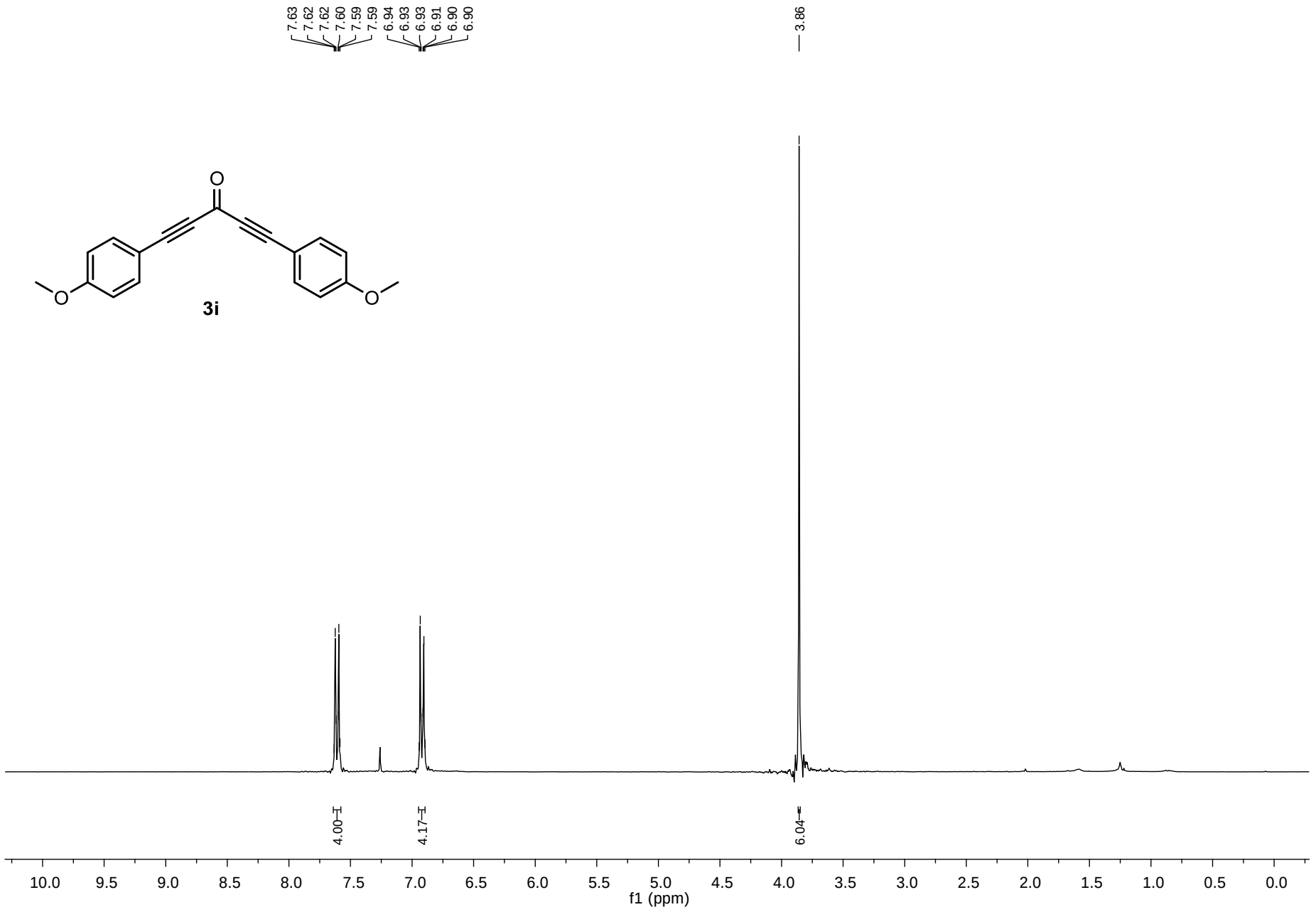
$^{1}$H-NMR (dmso-$d_6$, 300 MHz)



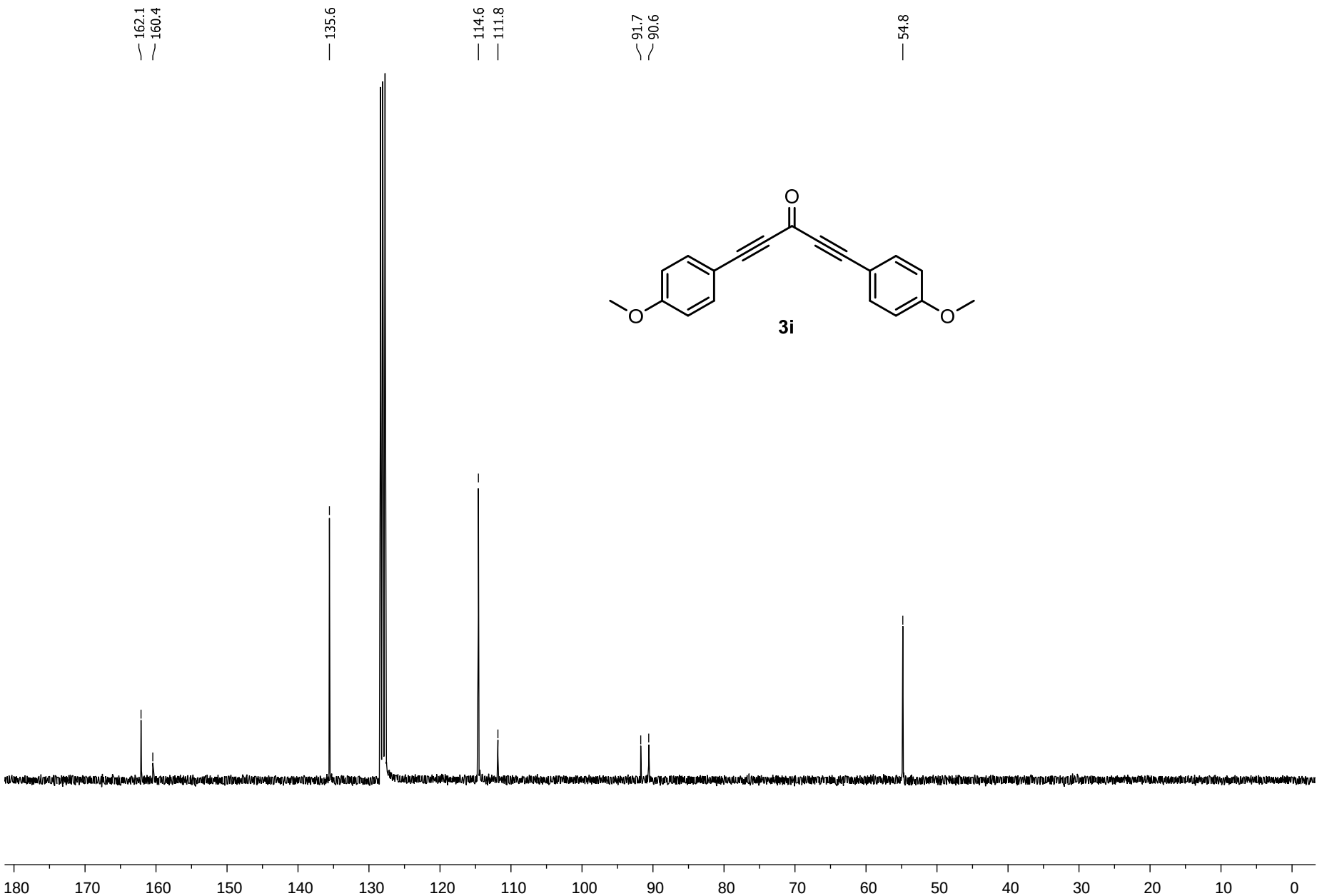
$^{13}$C-NMR (dmso-$d_6$, 75.4 MHz)



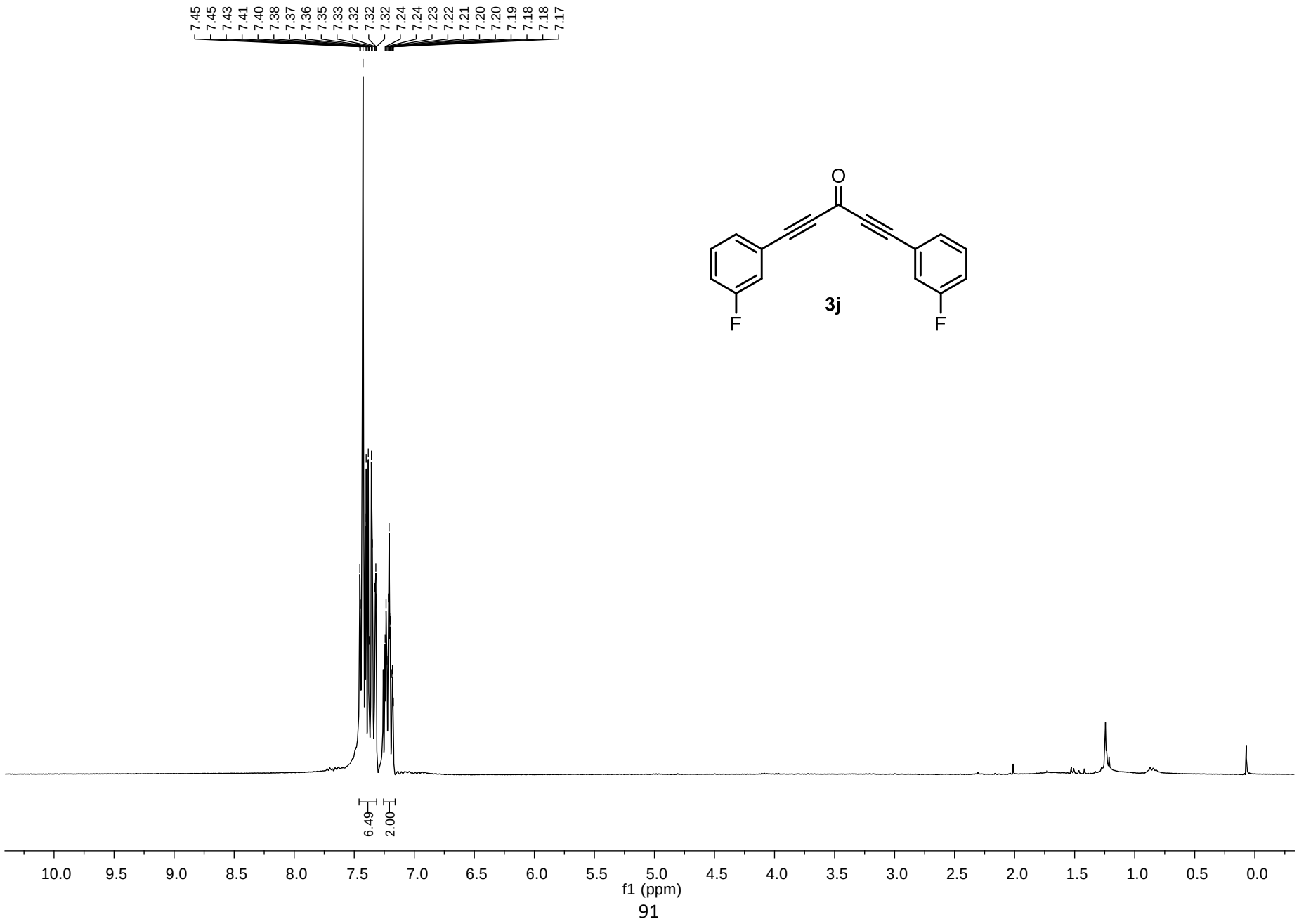
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



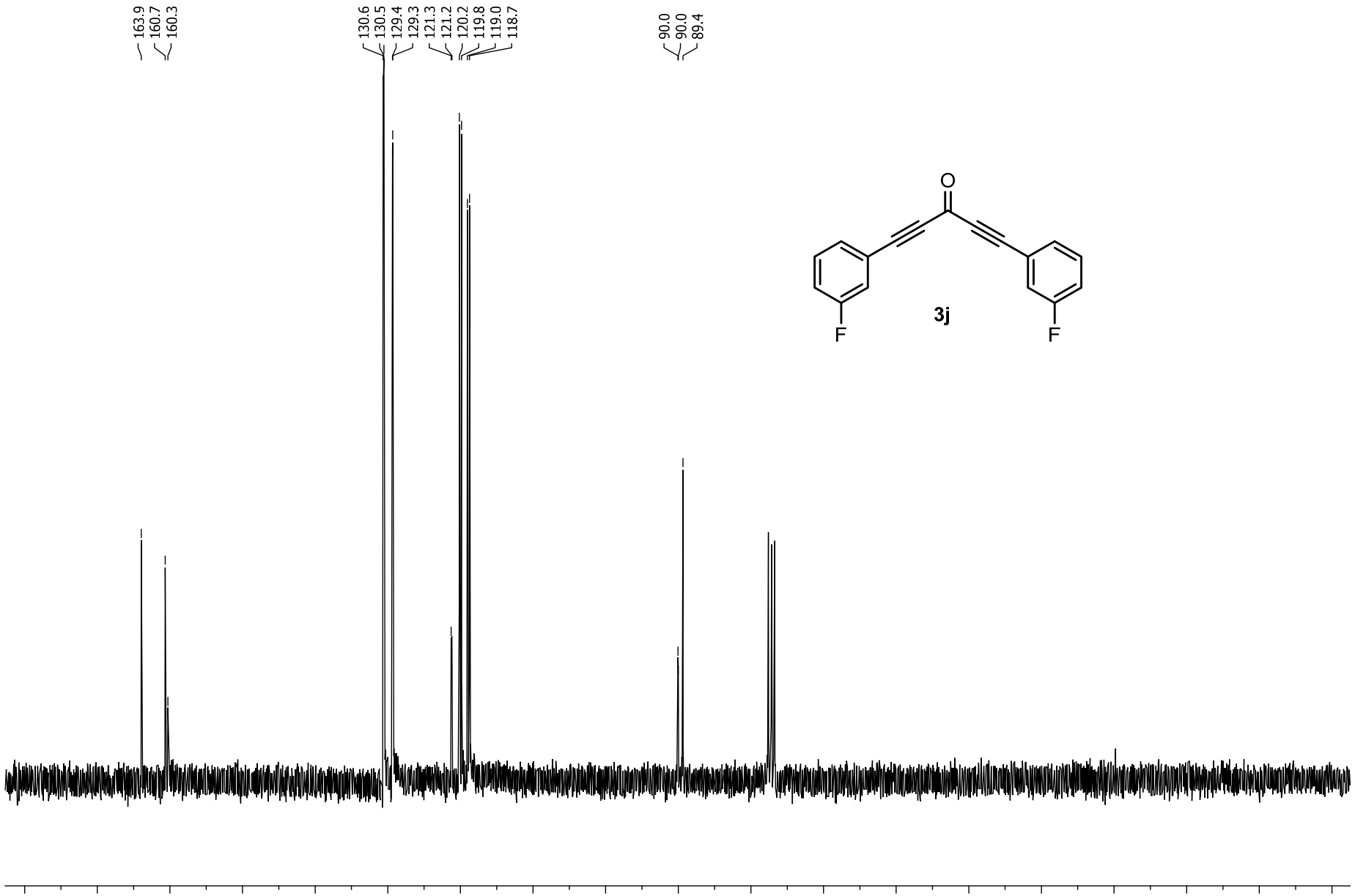
$^{13}$C-NMR ($C_6D_6$, 75.4 MHz)



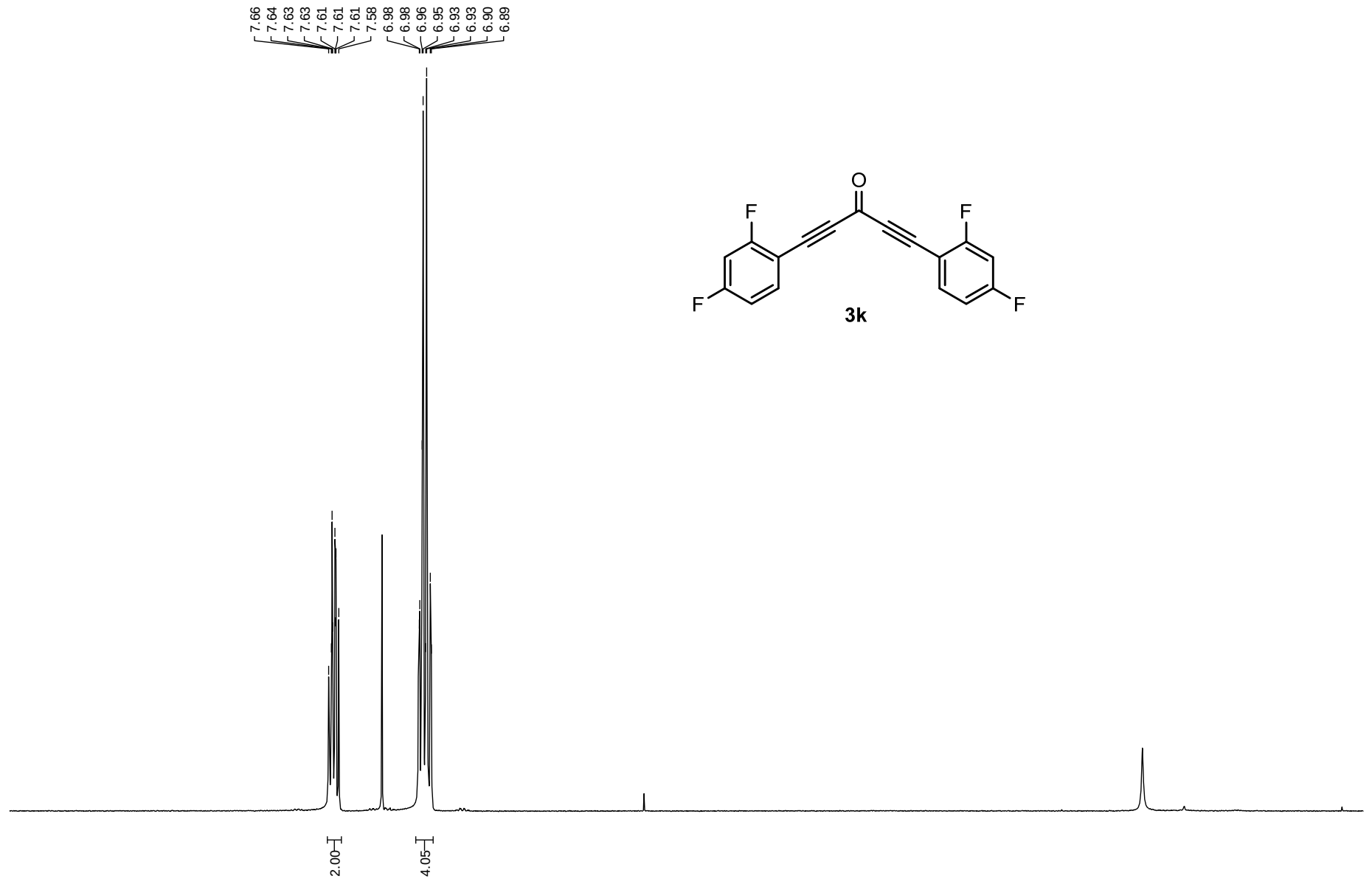
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



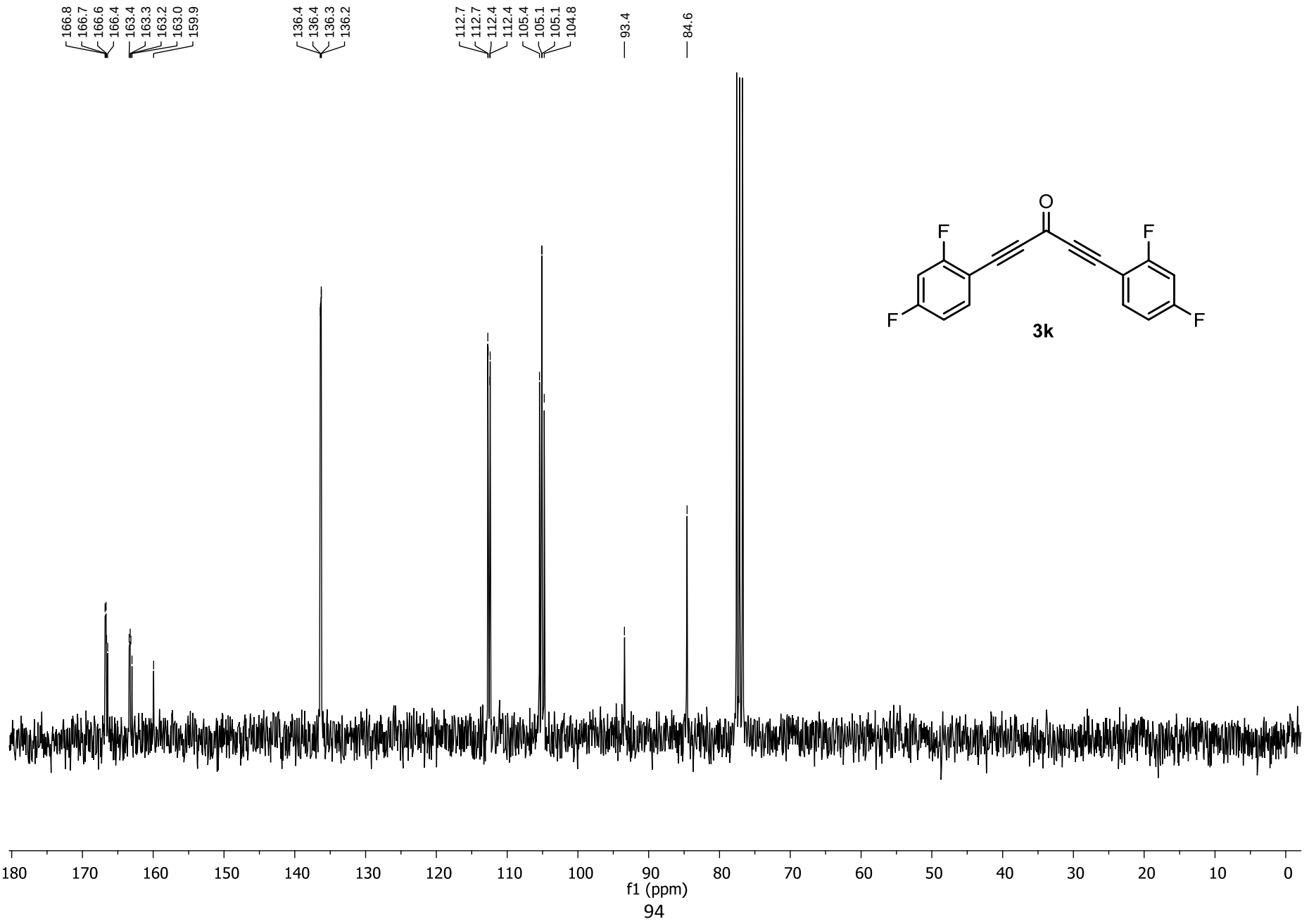
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



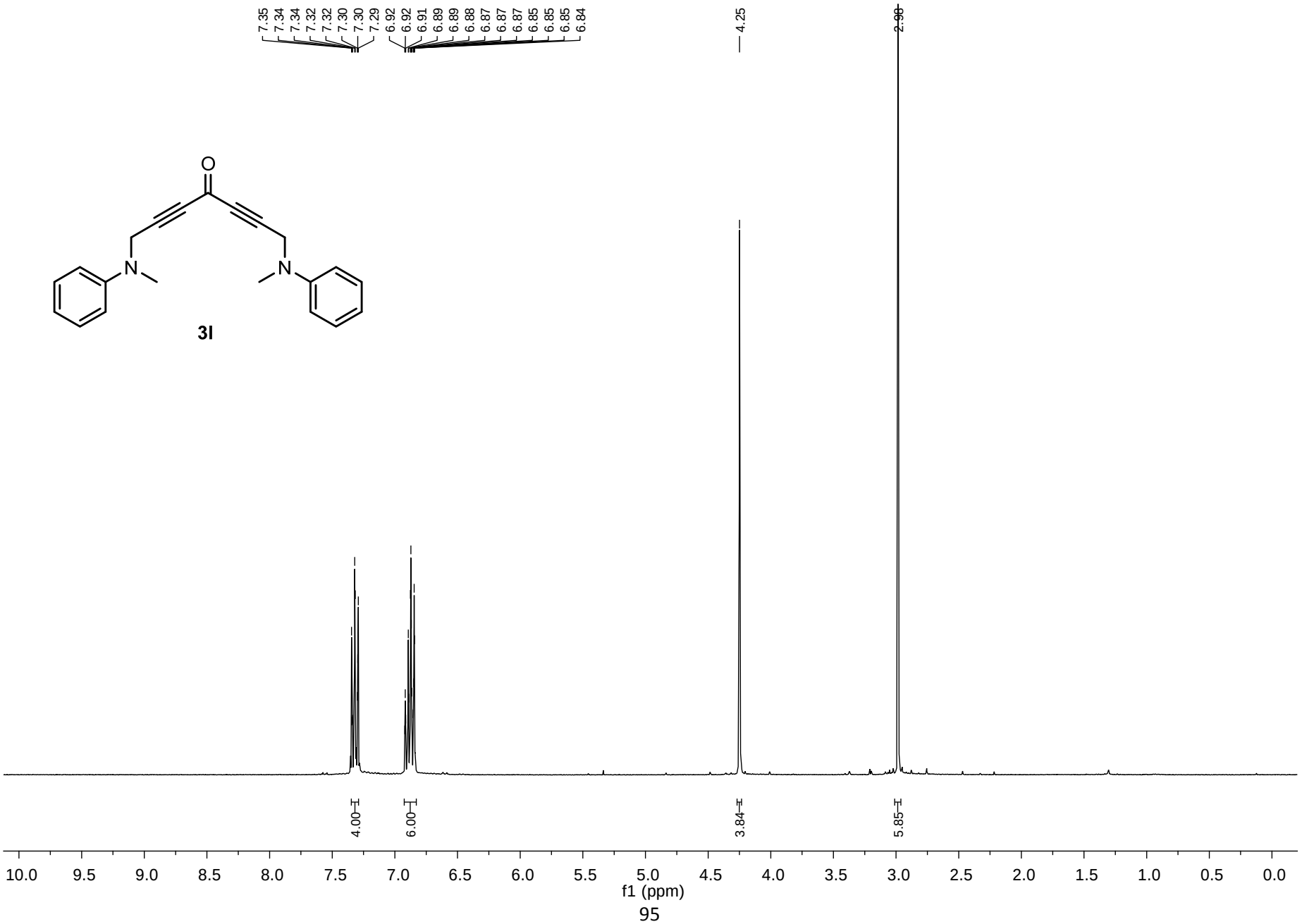
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



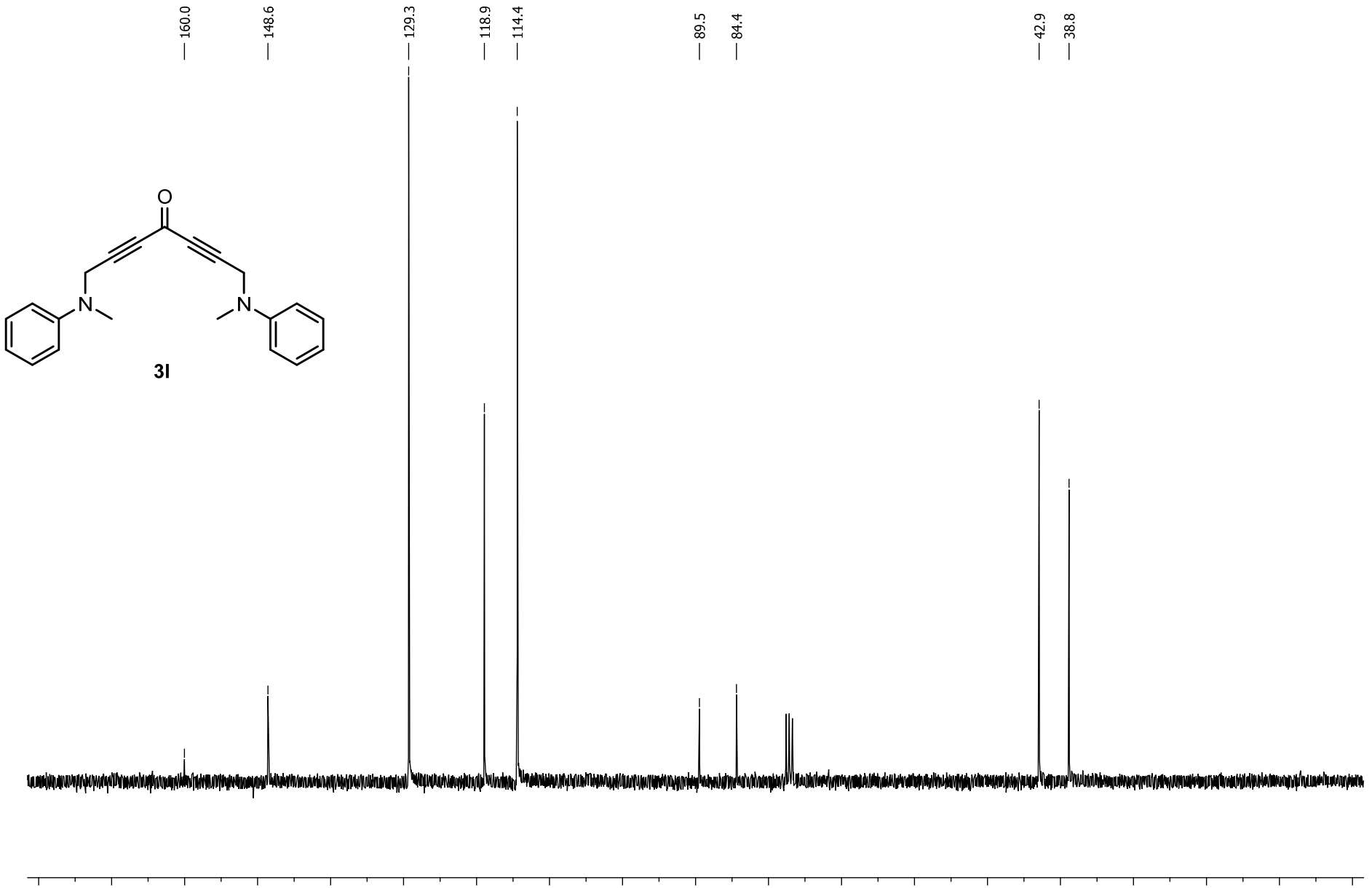
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



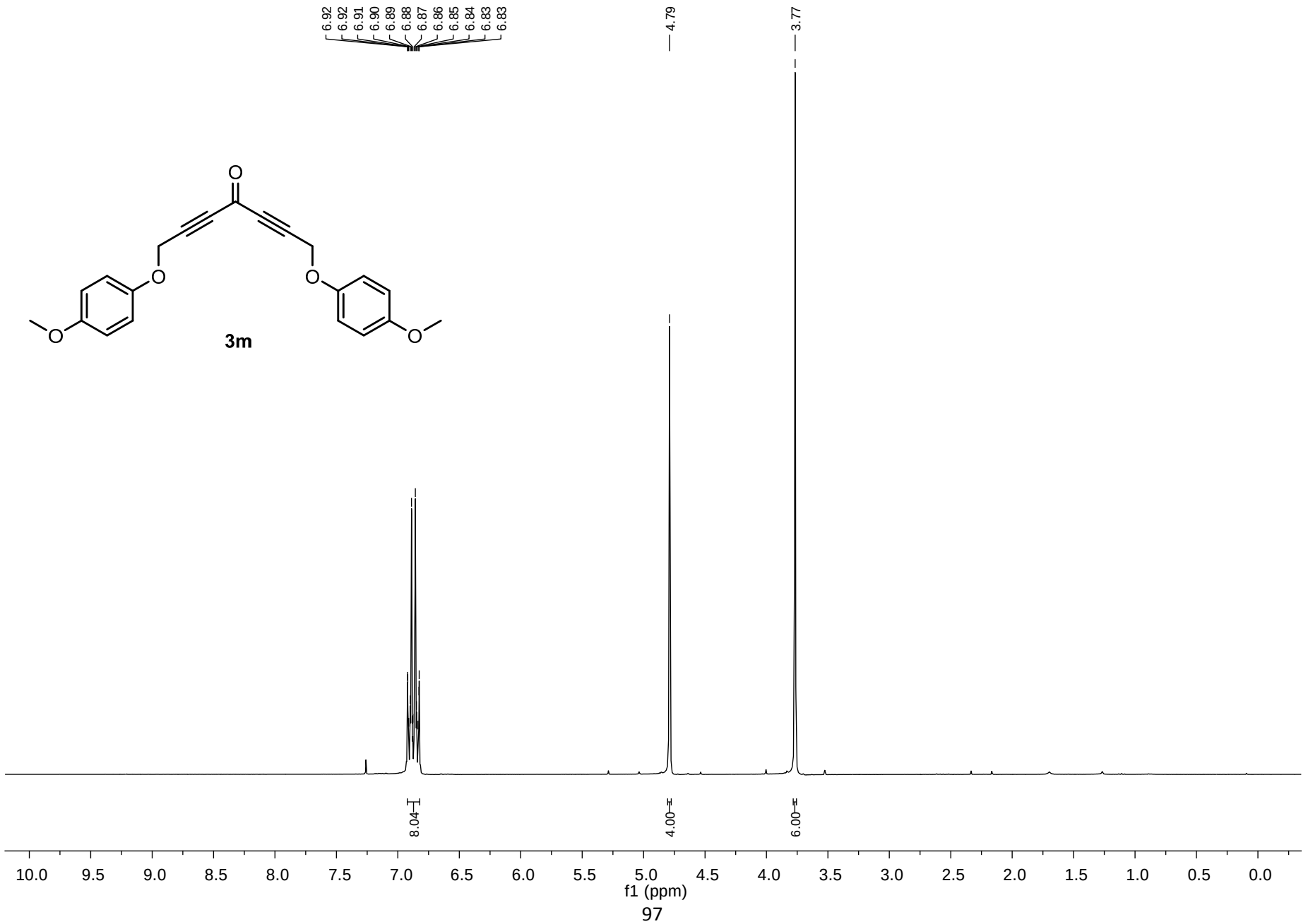
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



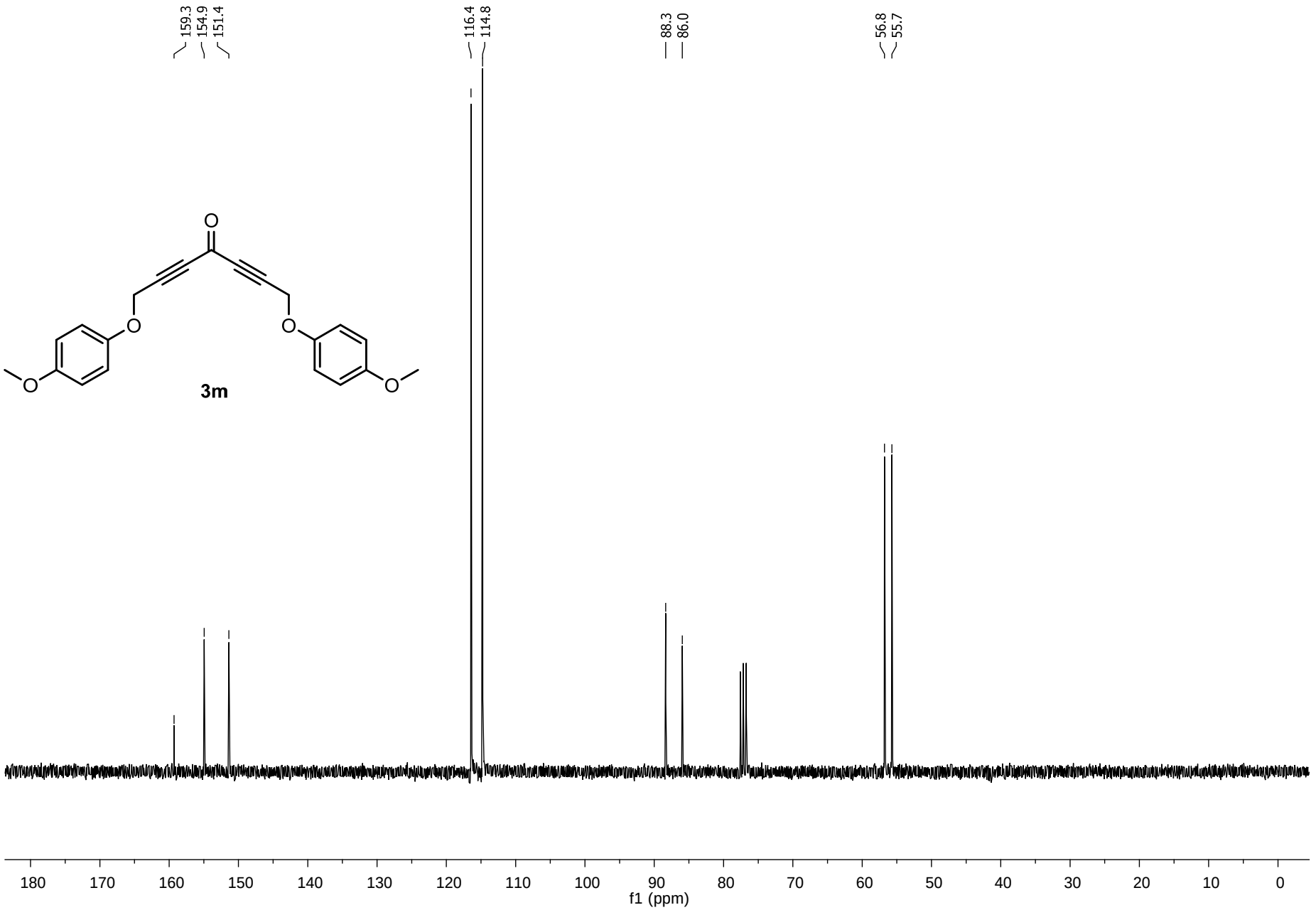
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



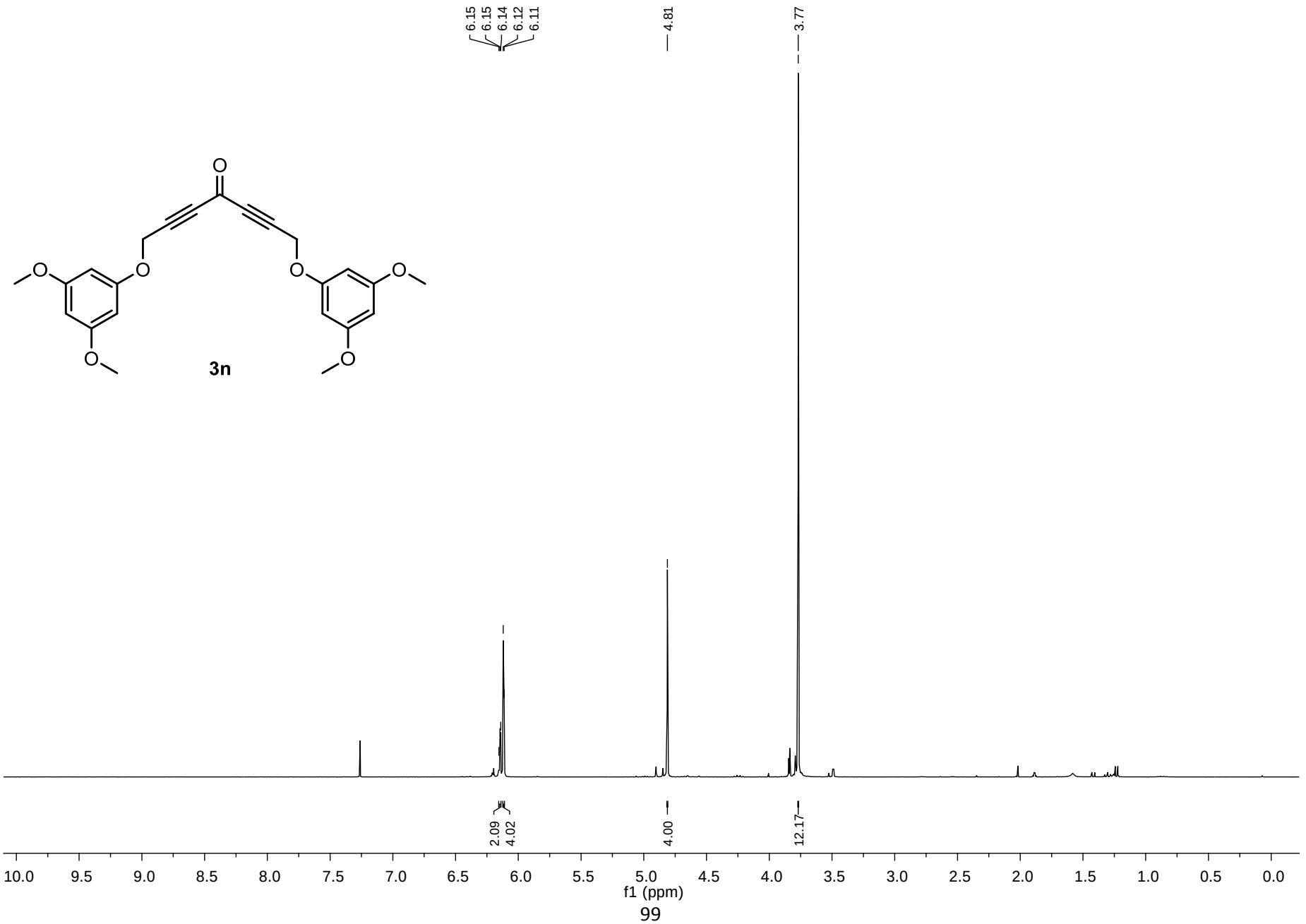
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



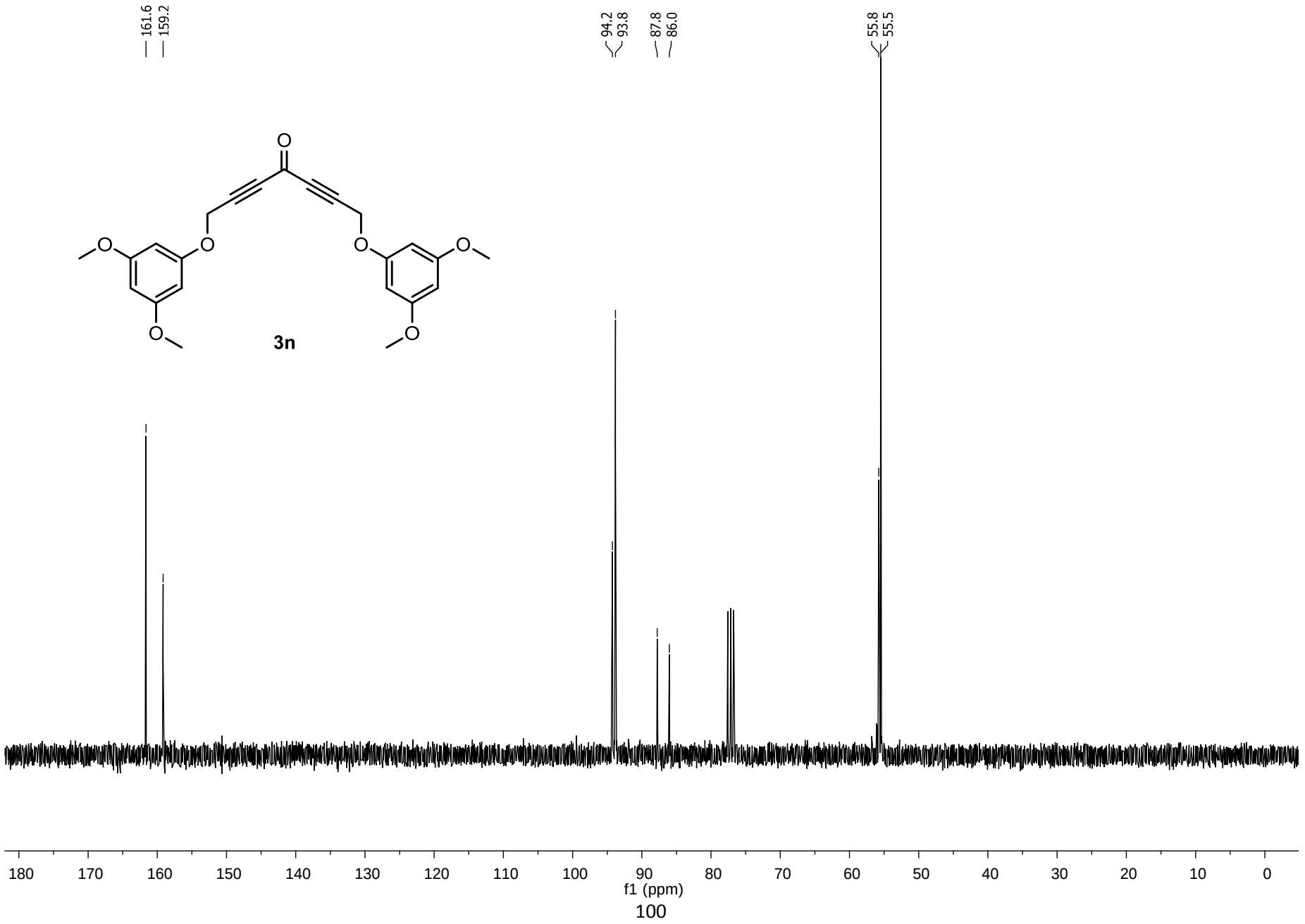
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



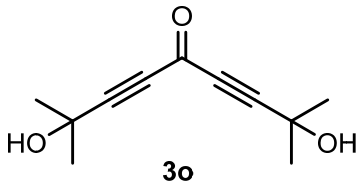
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

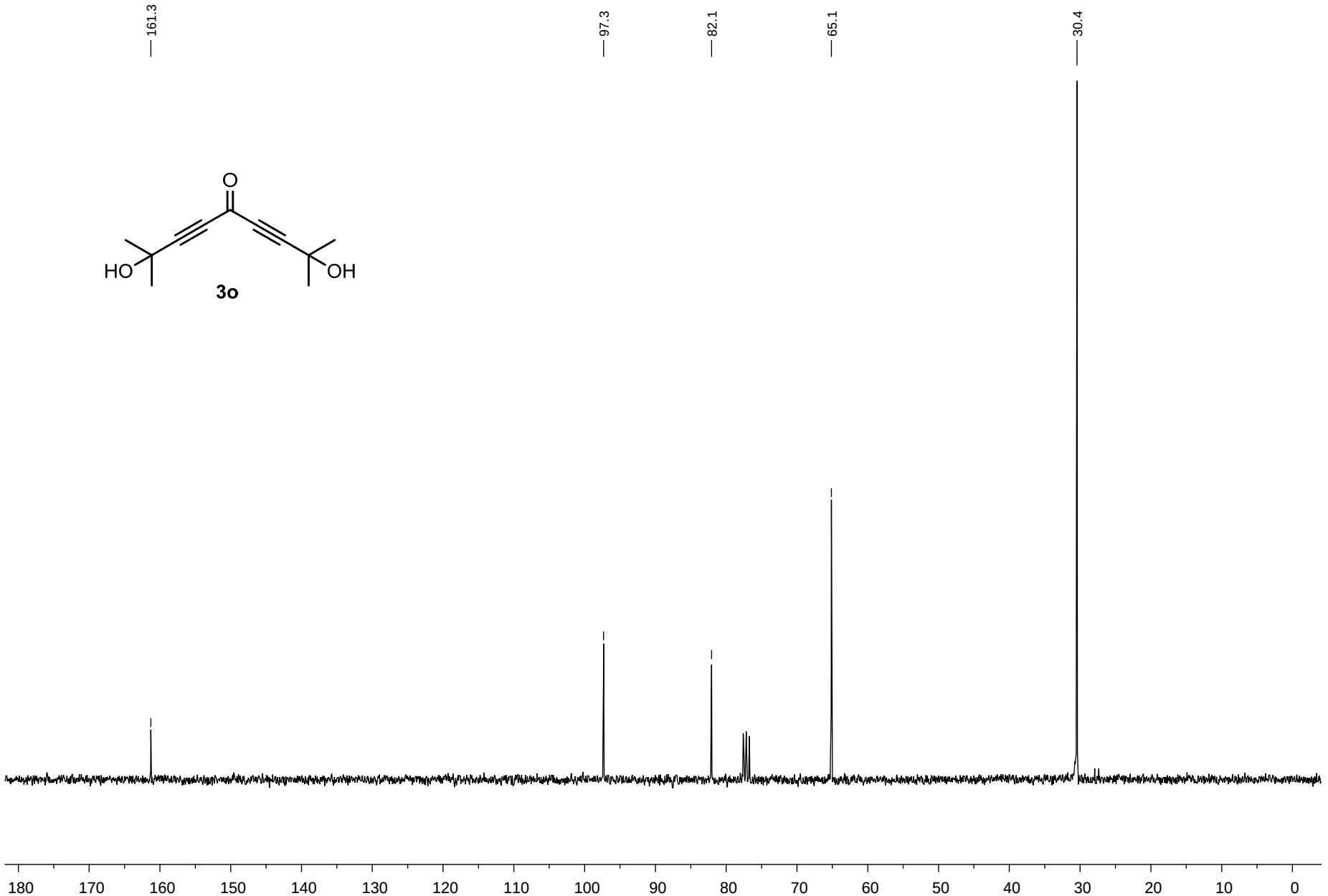


$^{1}$H-NMR ($CDCl_3$, 300 MHz)

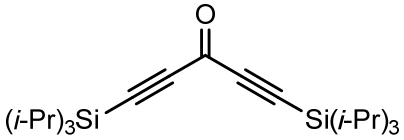



**3o**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

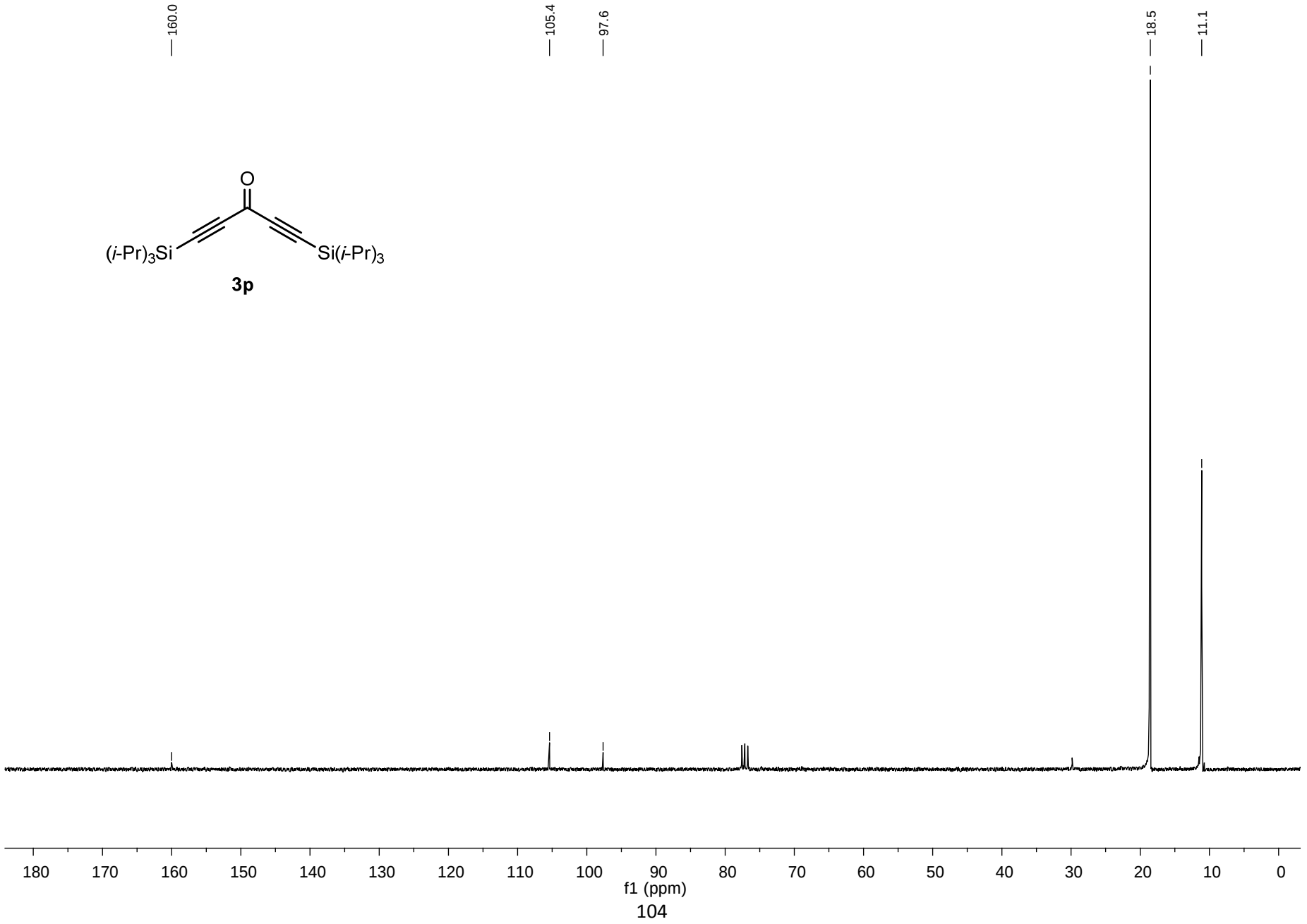


$^{1}$H-NMR ($CDCl_3$, 300 MHz)

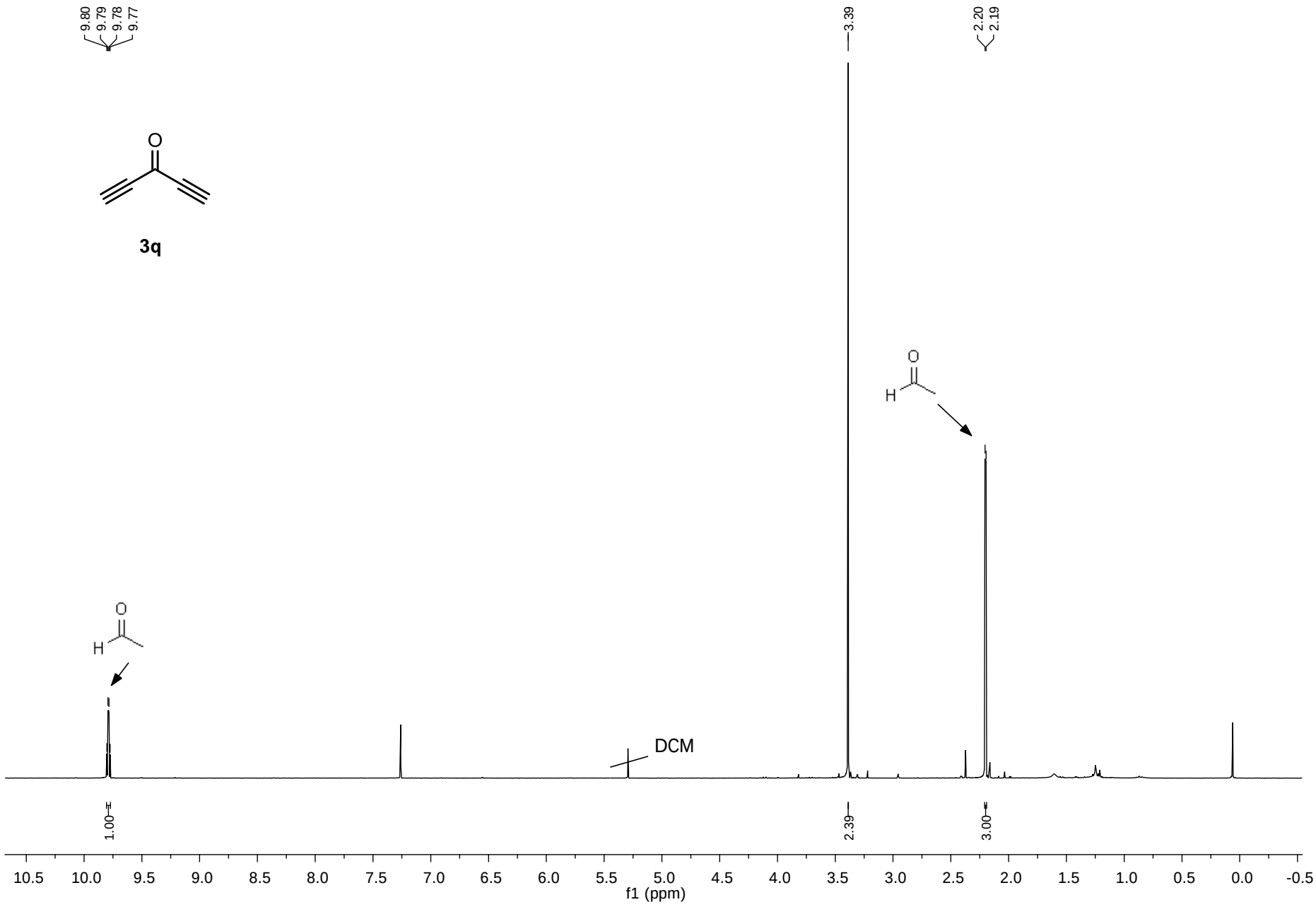



**3p**

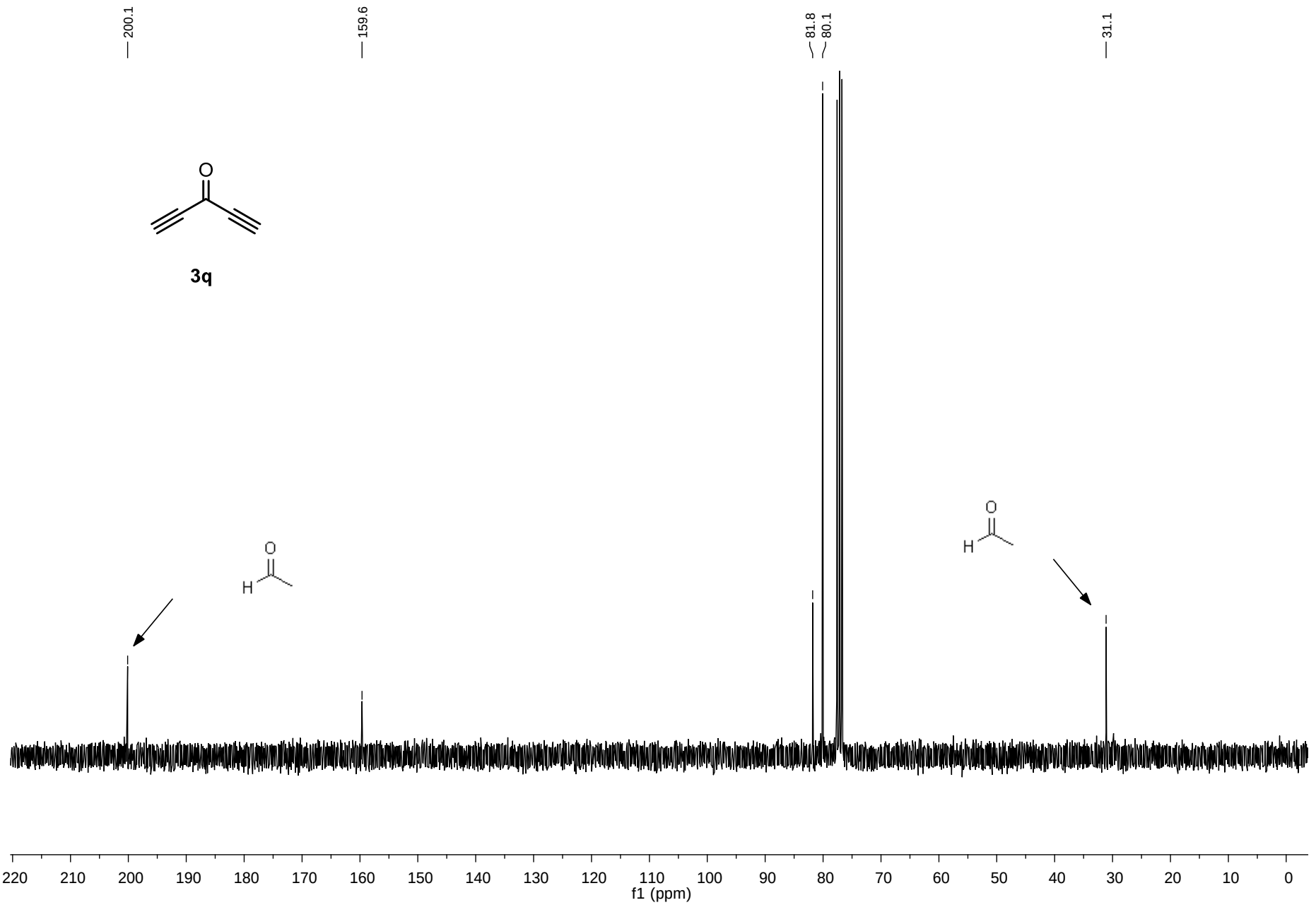
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



$^{1}$H-NMR ($CDCl_3$, 300 MHz)



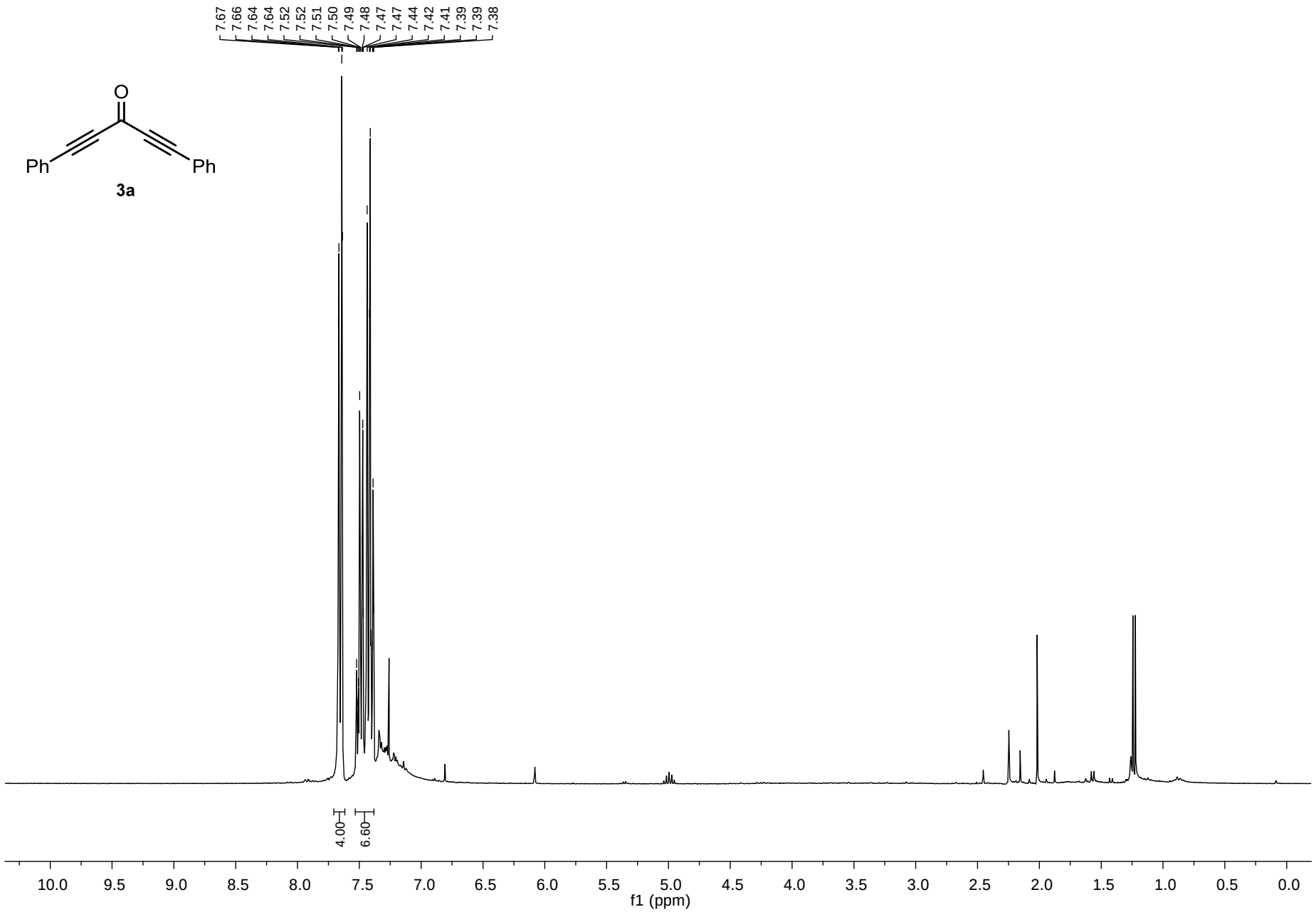
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



# NMR spectra of crude diynones 3 (gram-scale synthesis in Scheme3)

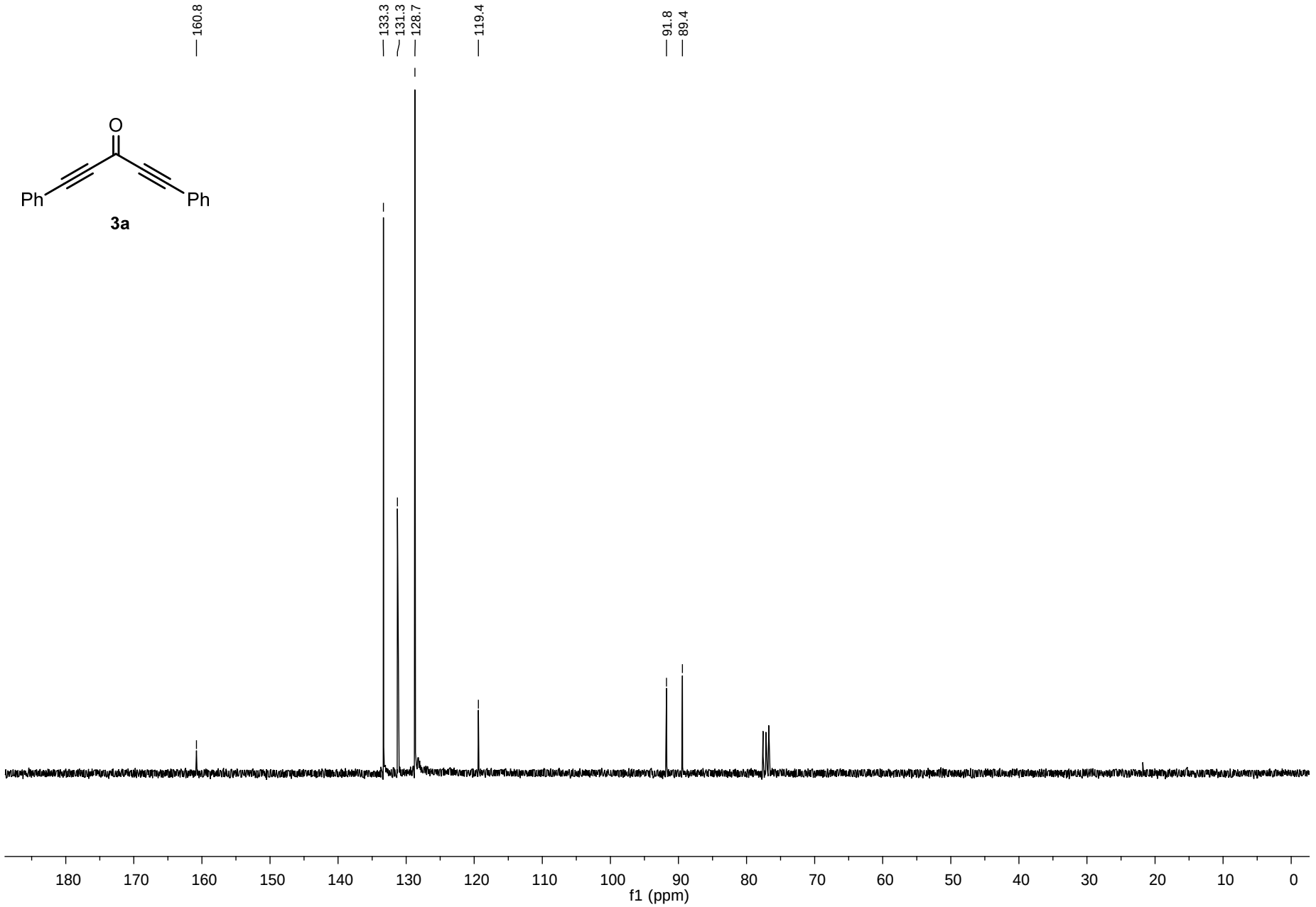
$^{1}$H-NMR ($CDCl_3$, 300 MHz)

Crude NMR for the gram-scale synthesis of **3a** from EL



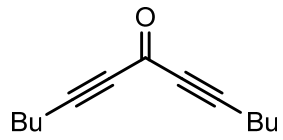
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the gram-scale synthesis of **3a** from EL



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

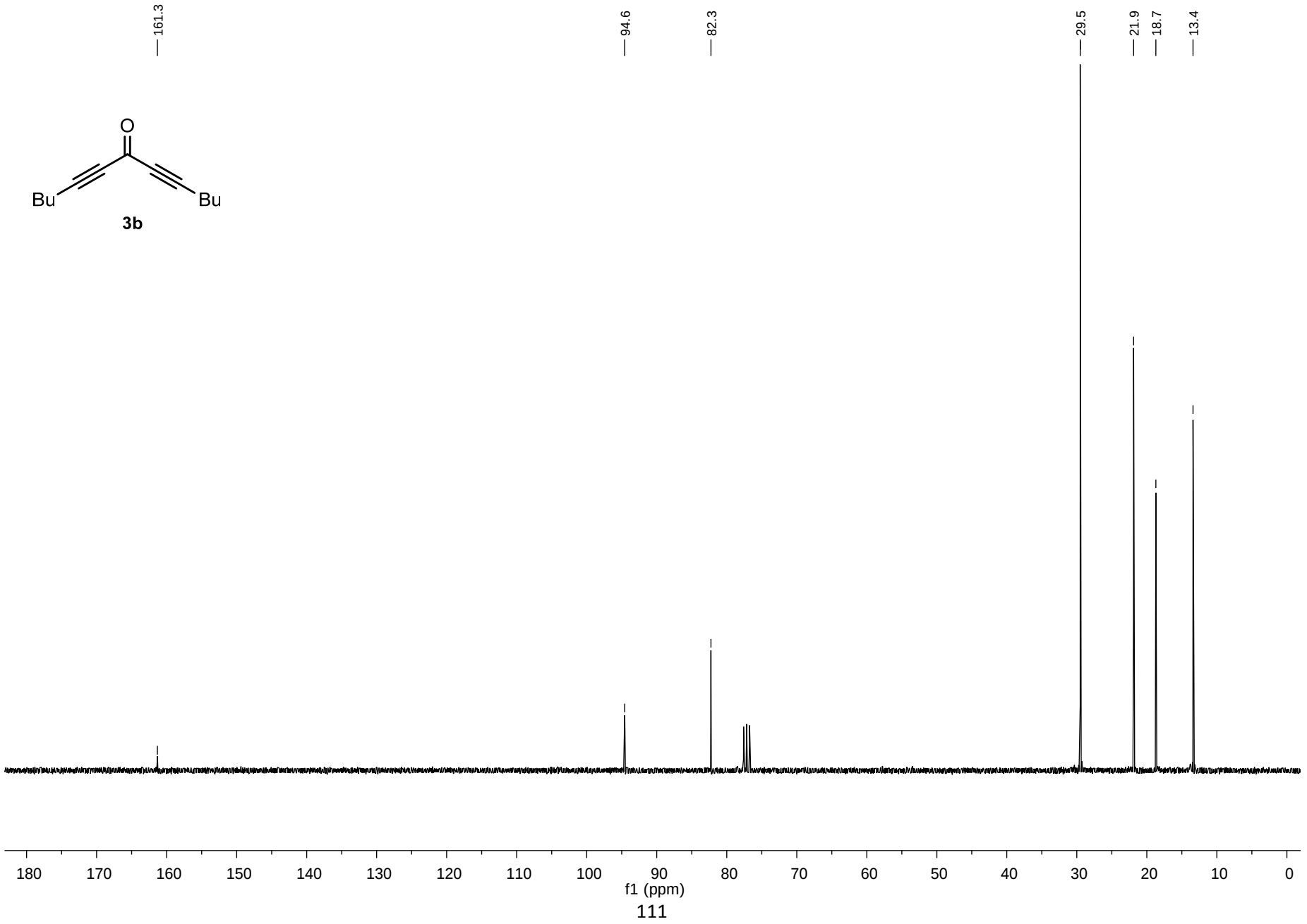
Crude NMR for the gram-scale synthesis of **3b** from EL




**3b**

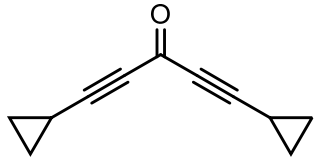
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the gram-scale synthesis of **3b** from EL



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

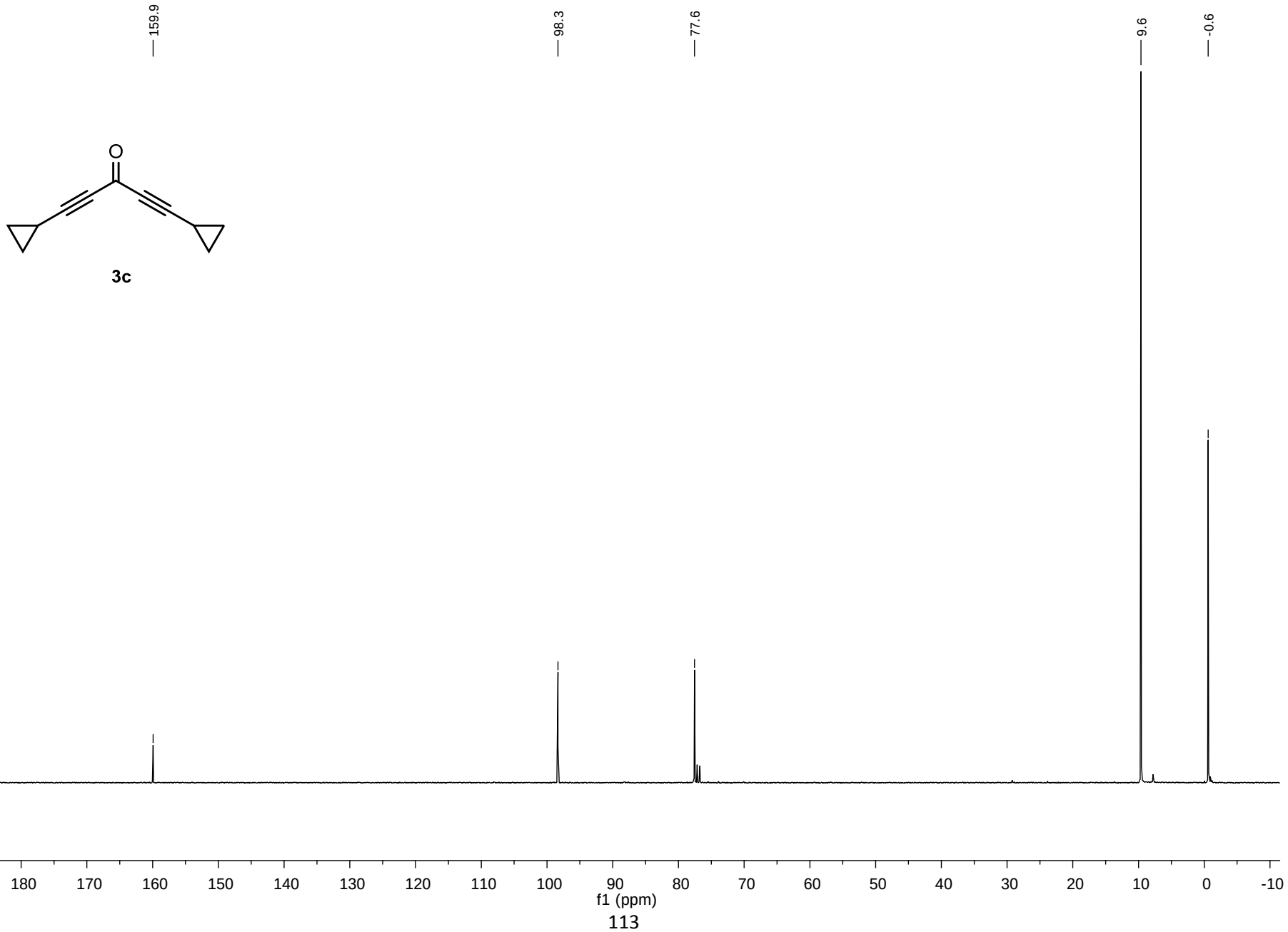
Crude NMR for the gram-scale synthesis of **3c** from EL



**3c**

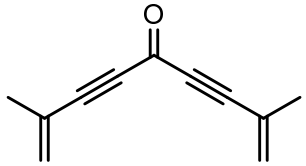
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the gram-scale synthesis of **3c** from EL



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

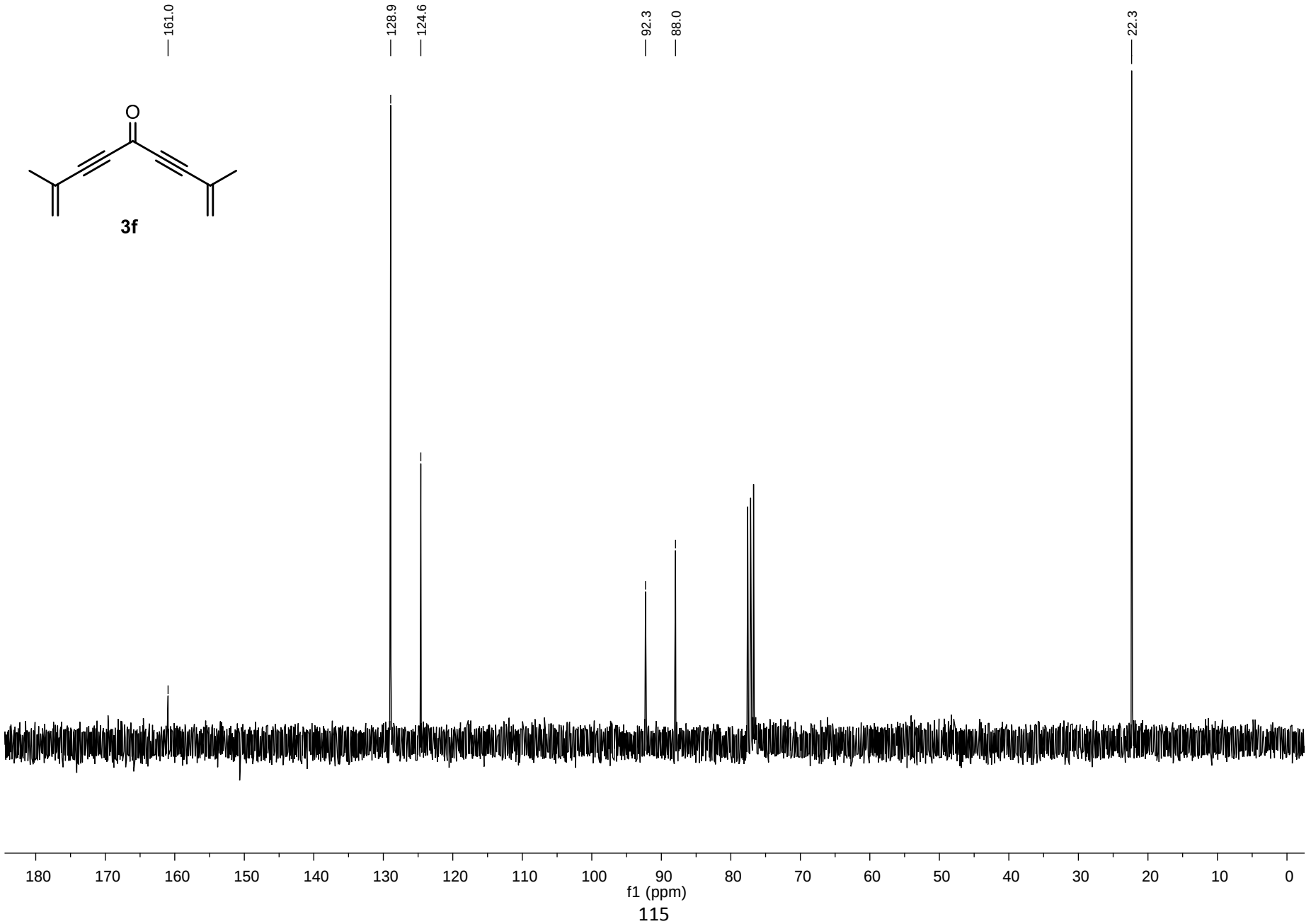
Crude NMR for the gram-scale synthesis of **3f** from EL



**3f**

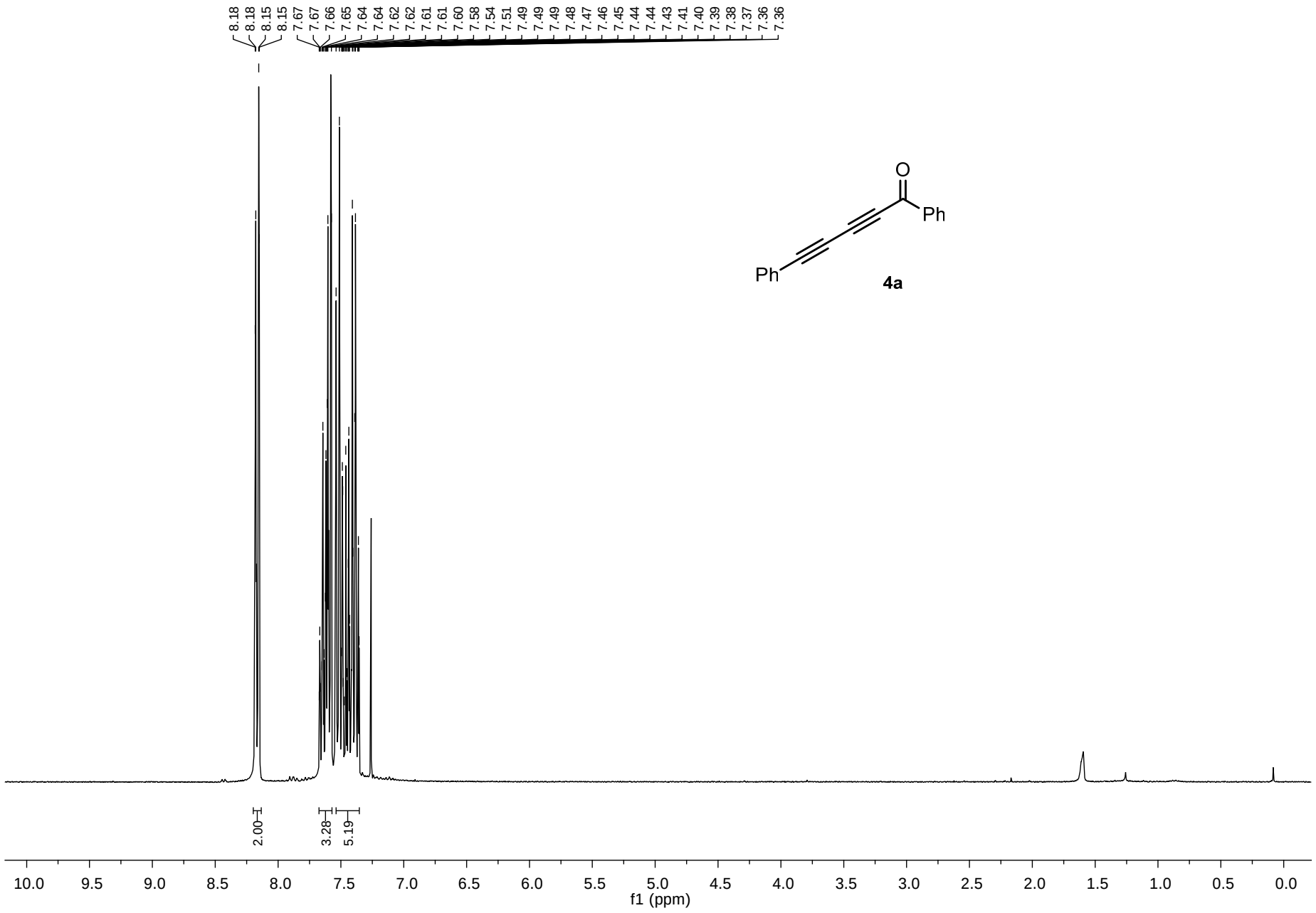
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the gram-scale synthesis of **3f** from EL

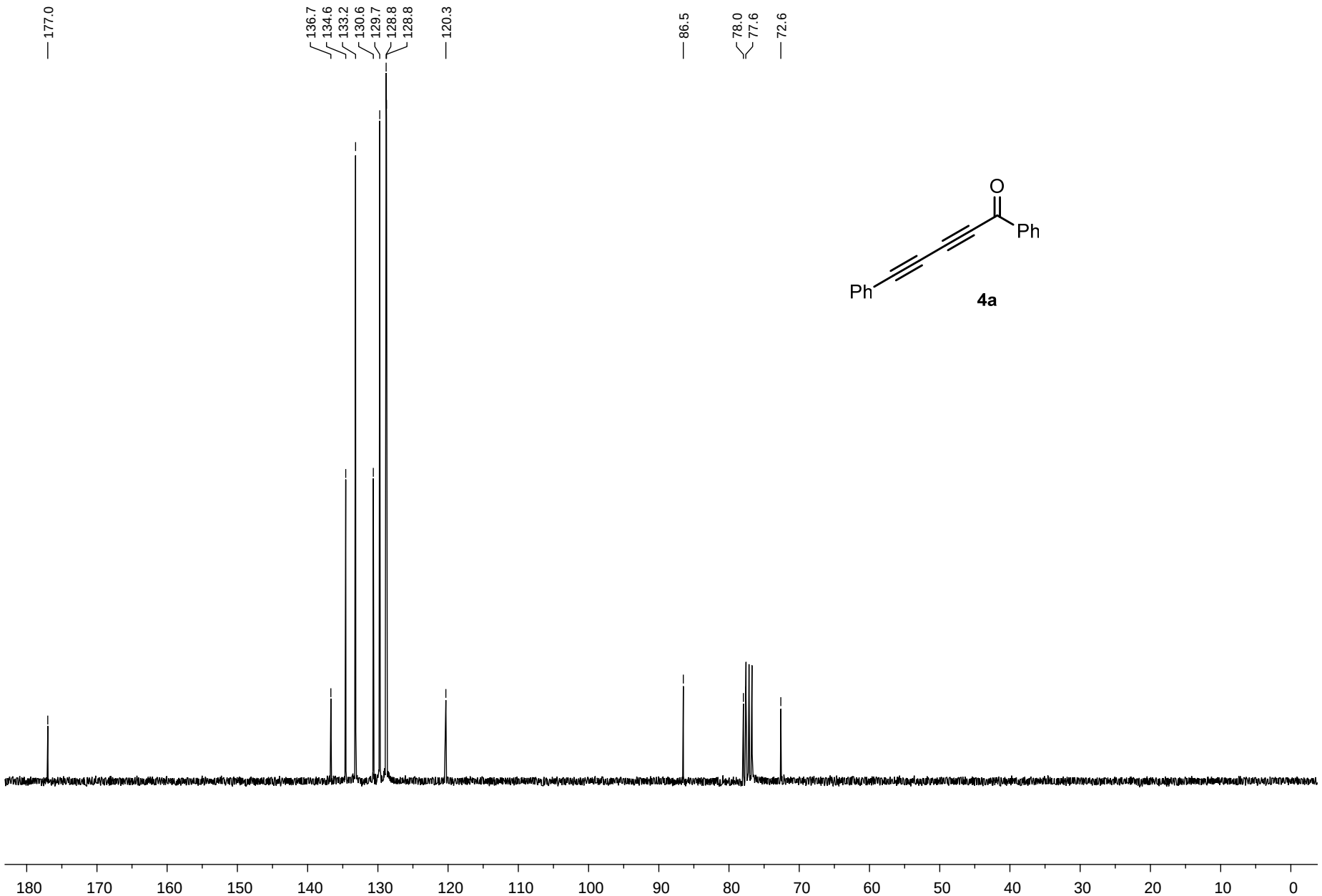


# NMR spectra of conjugated diynones 4

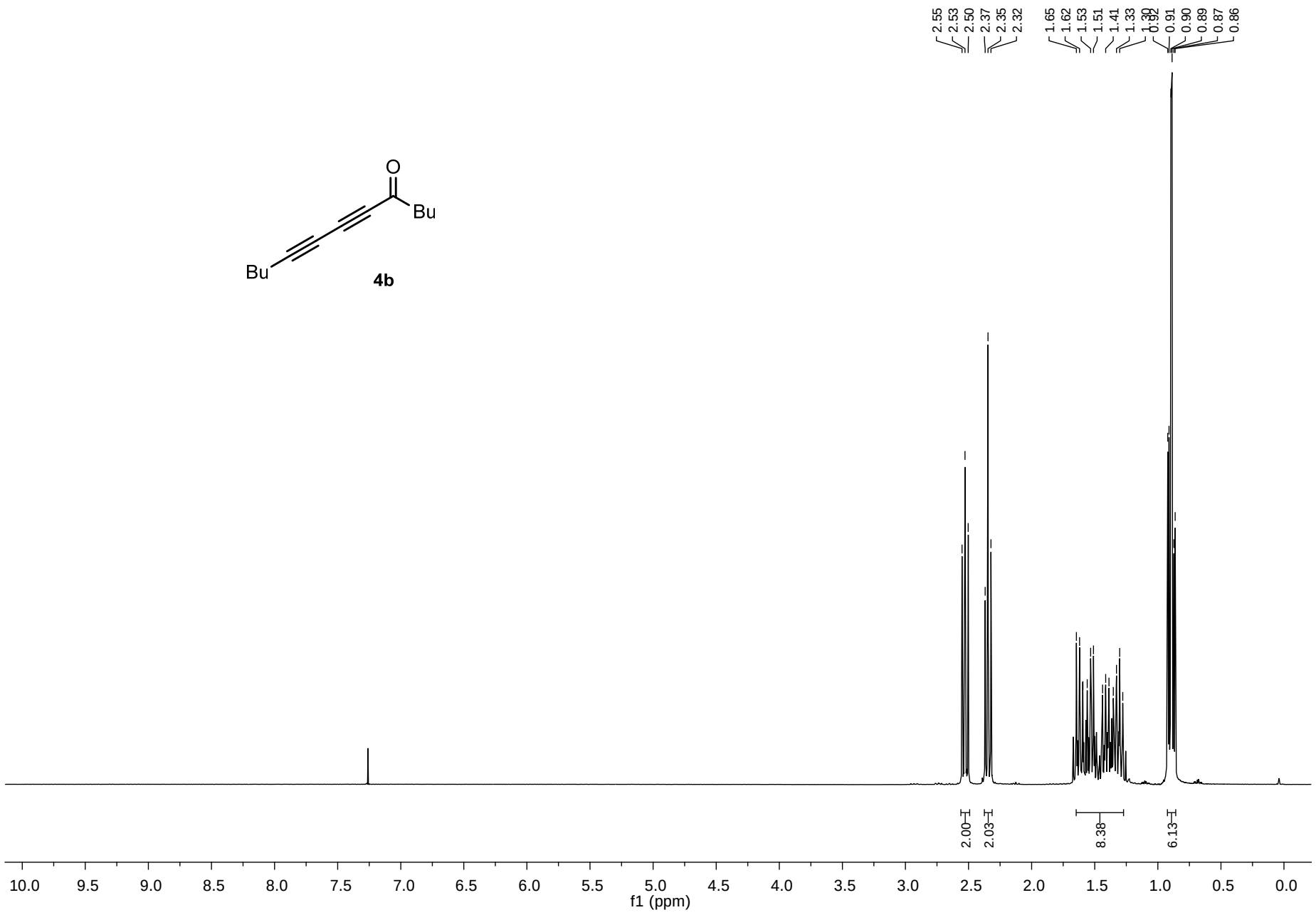
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



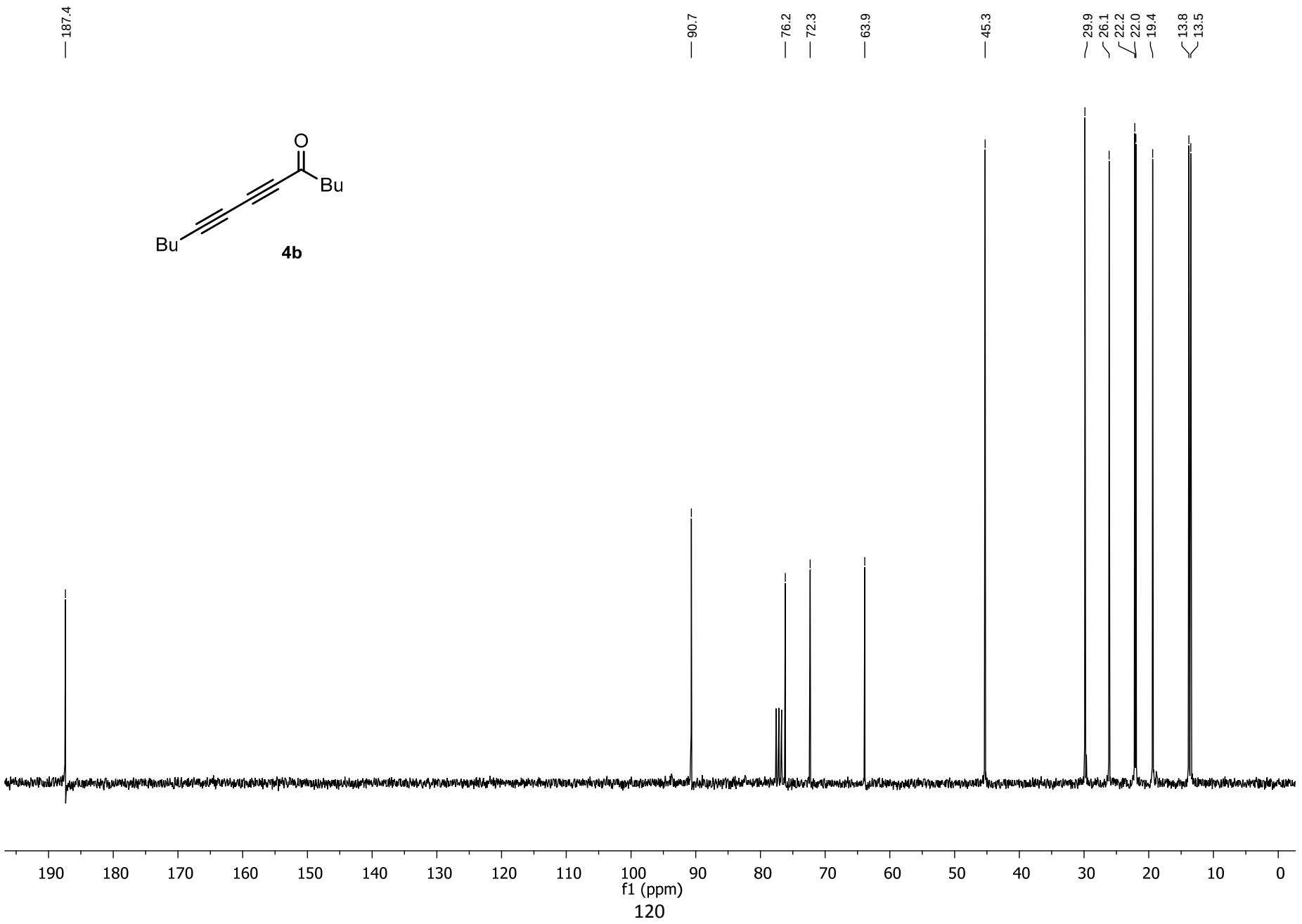
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



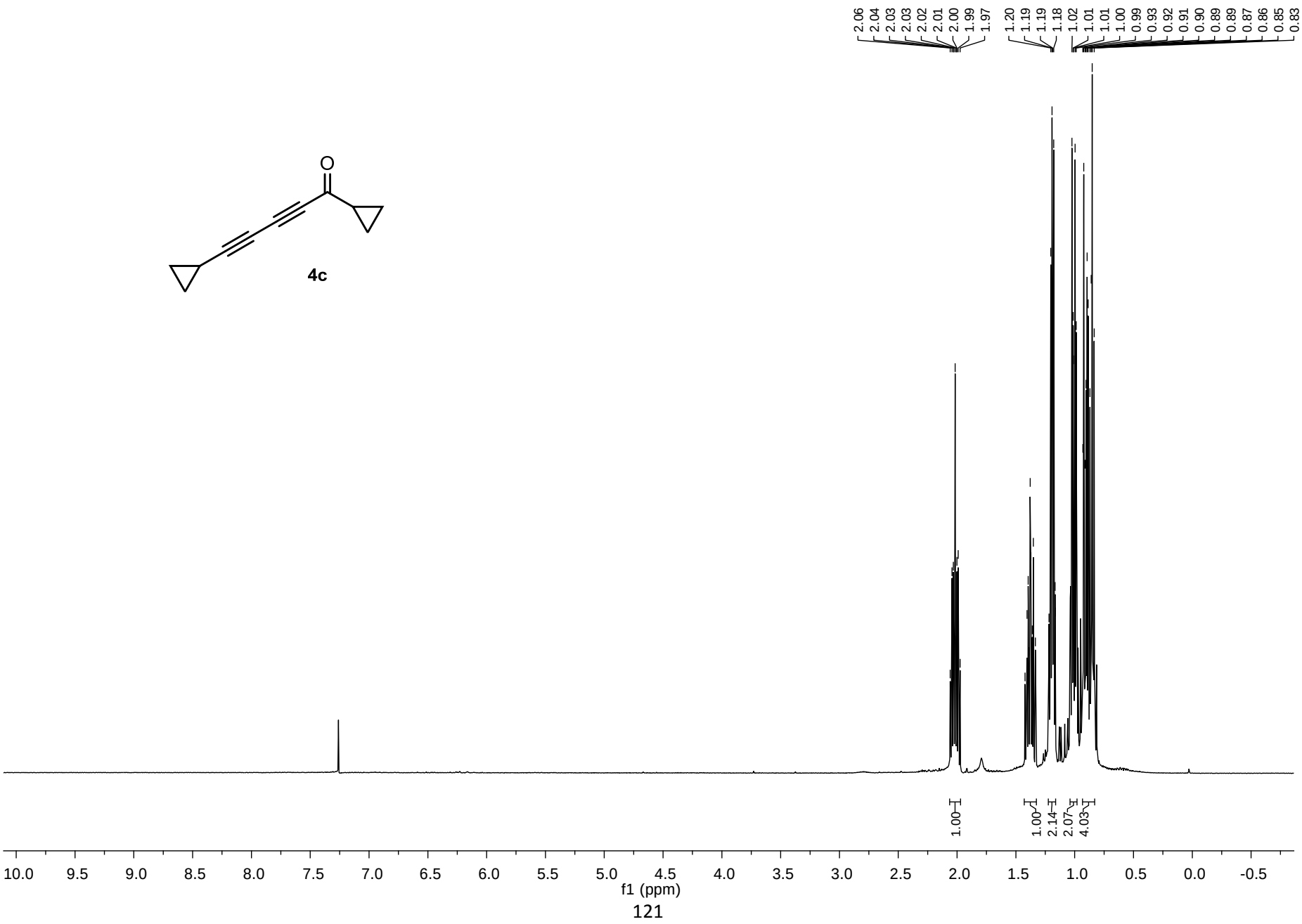
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



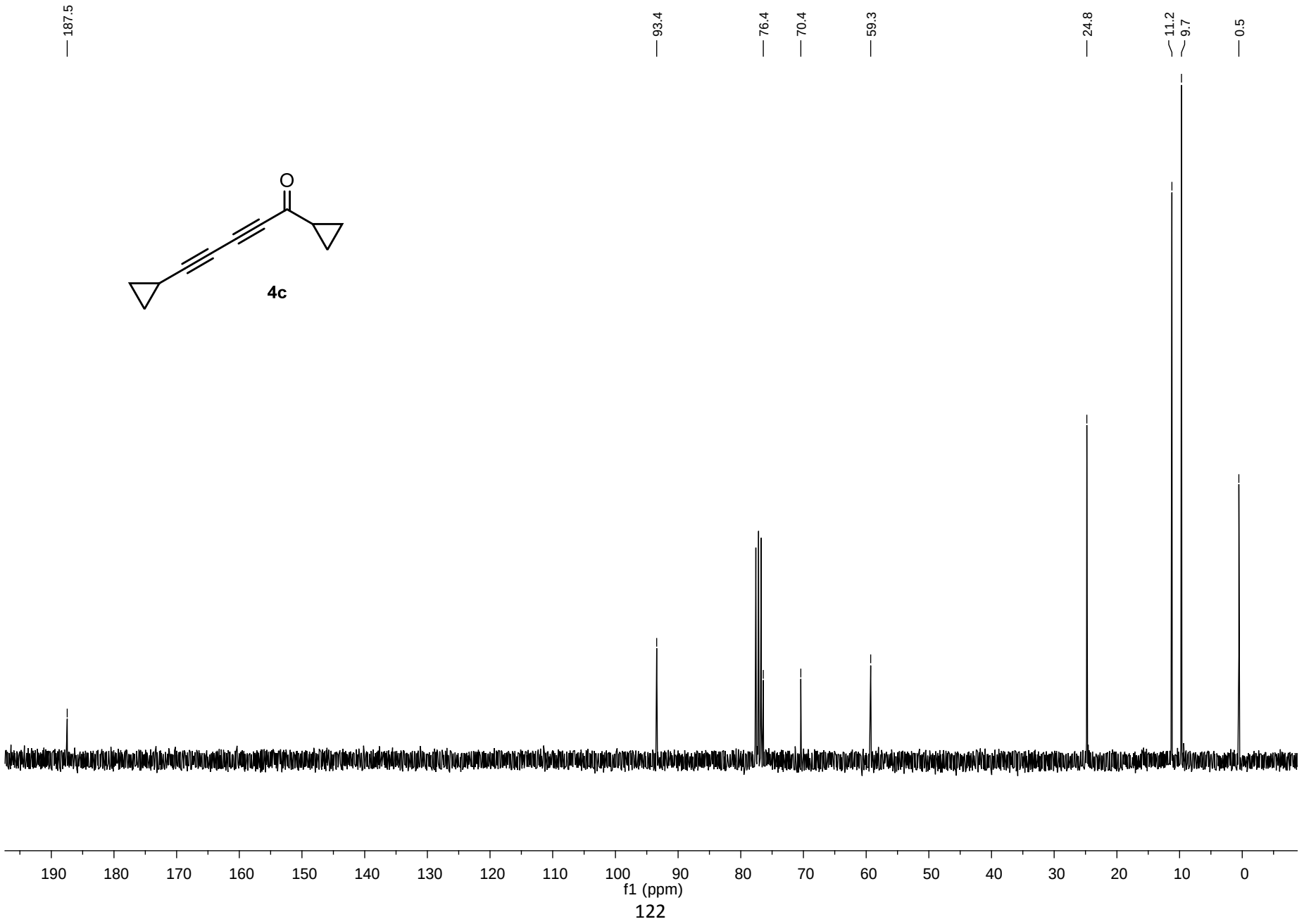
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



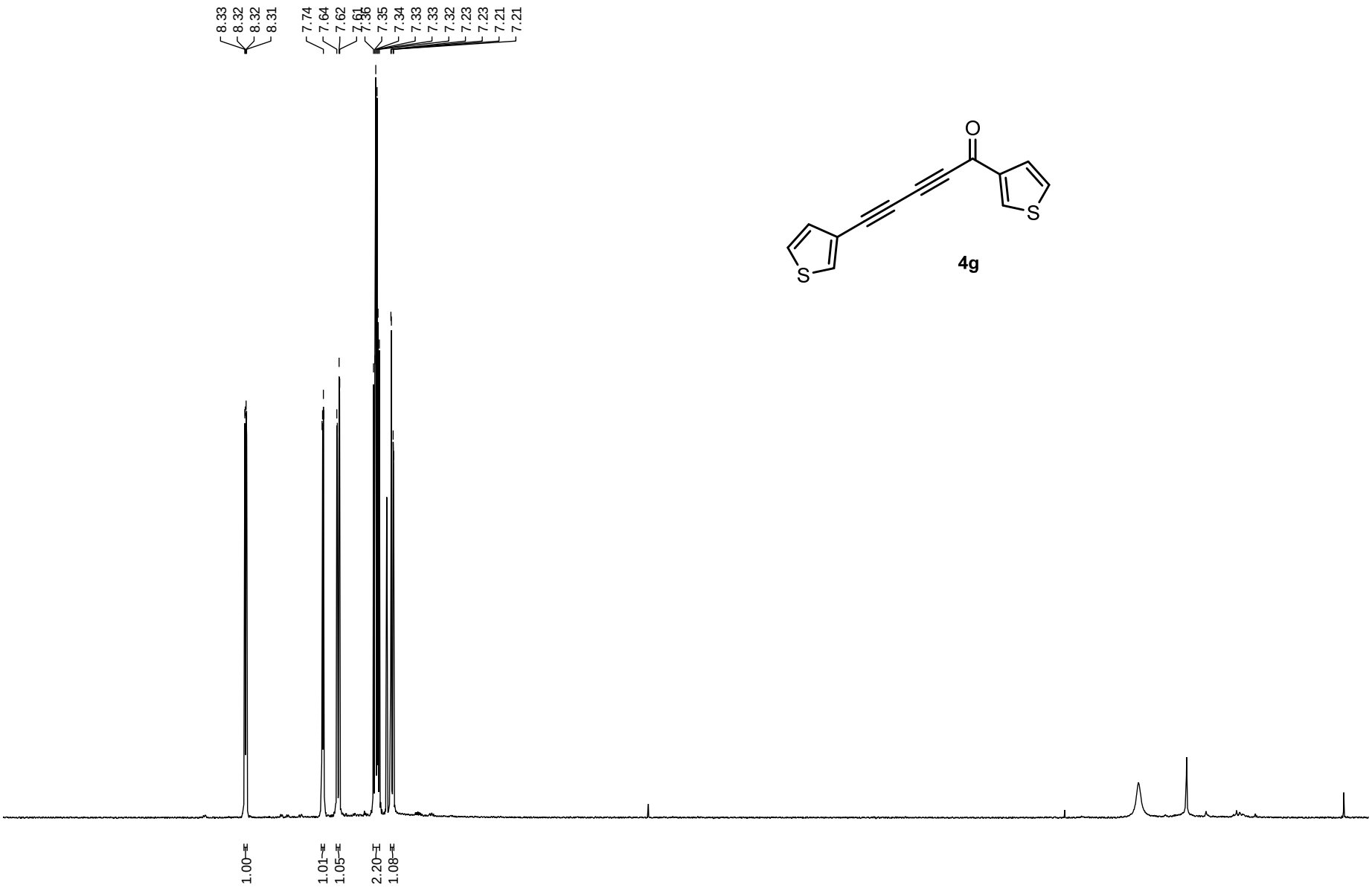
$^{1}$H-NMR ($CDCl_3$, 300 MHz)



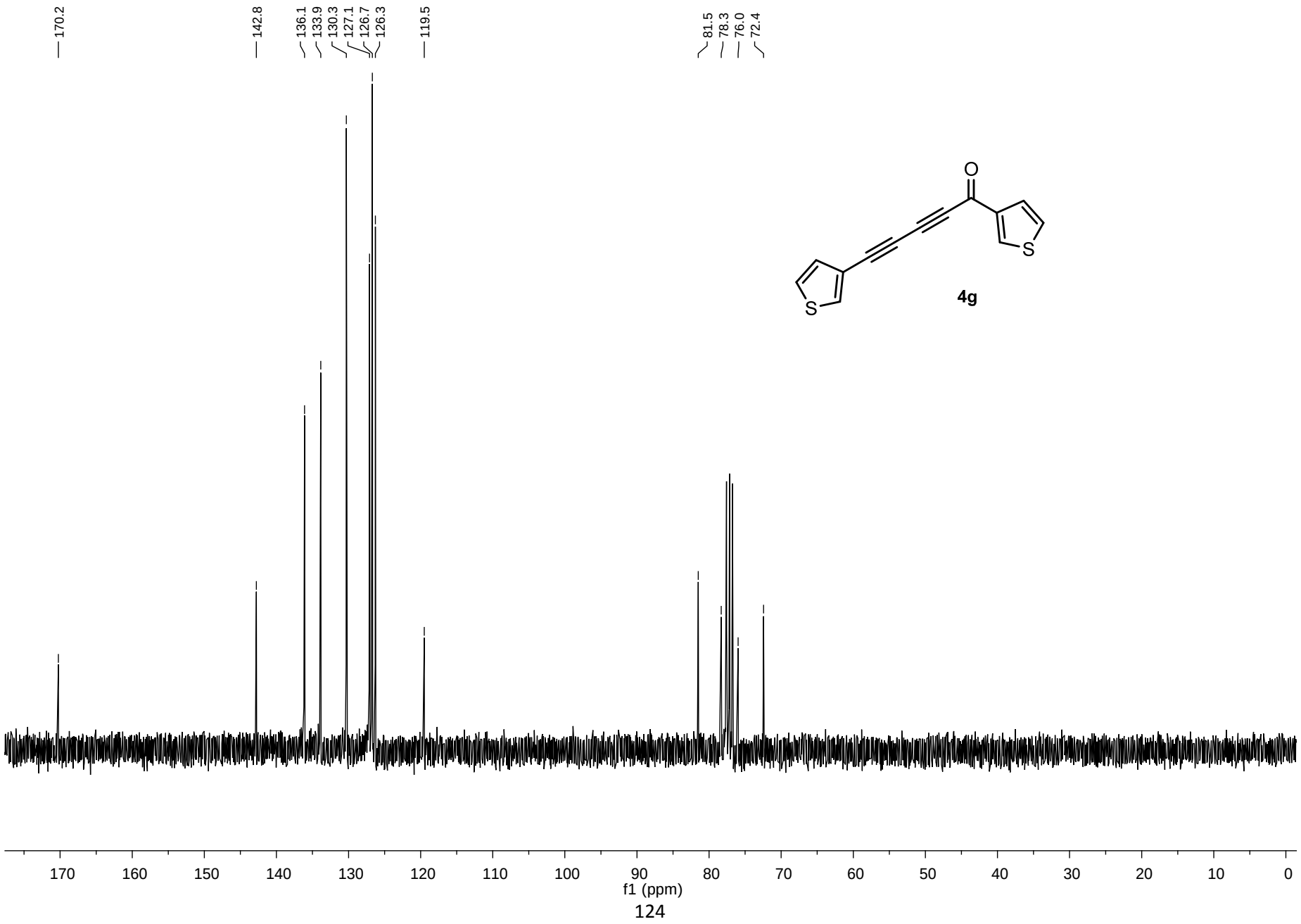
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

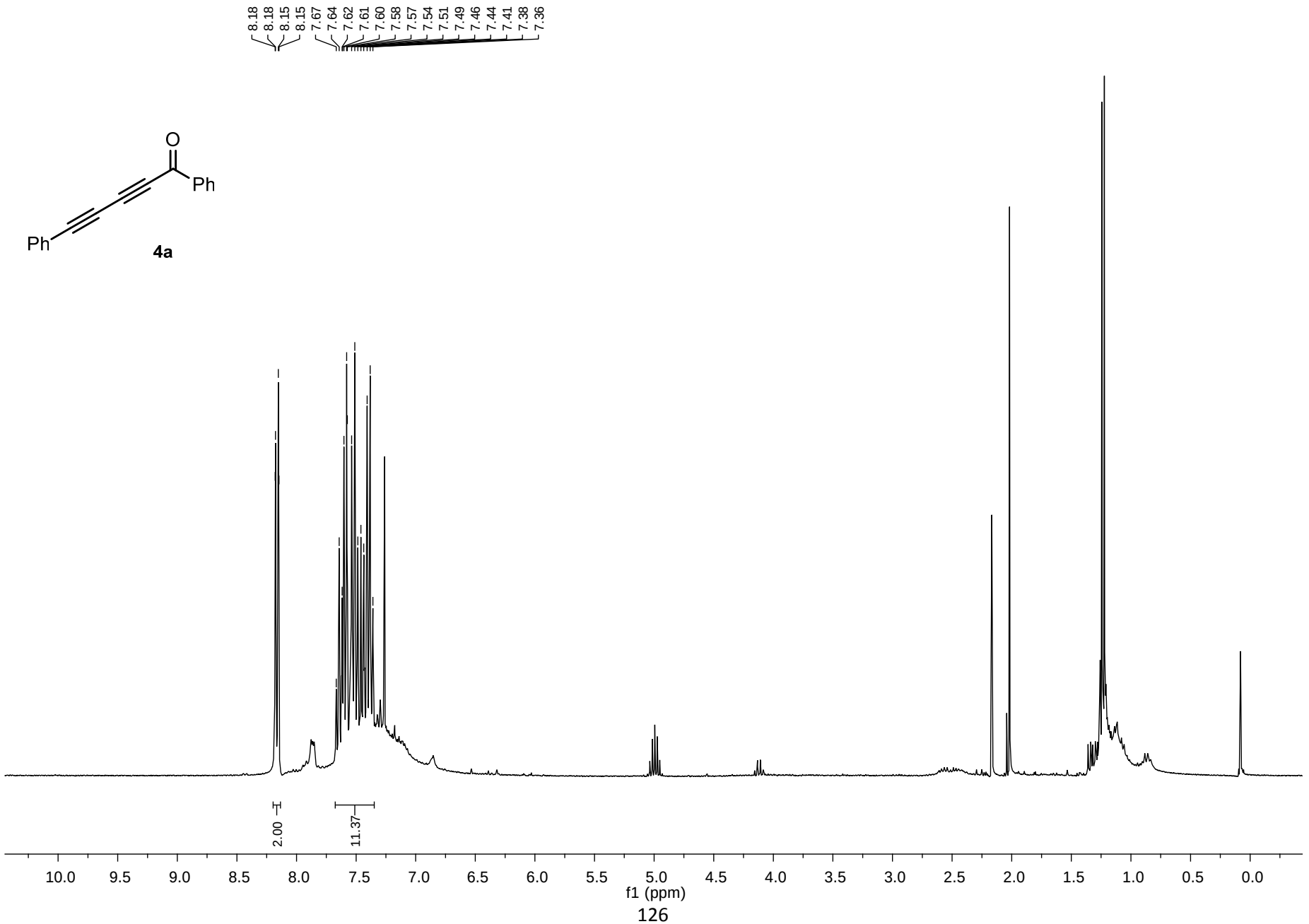


$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)



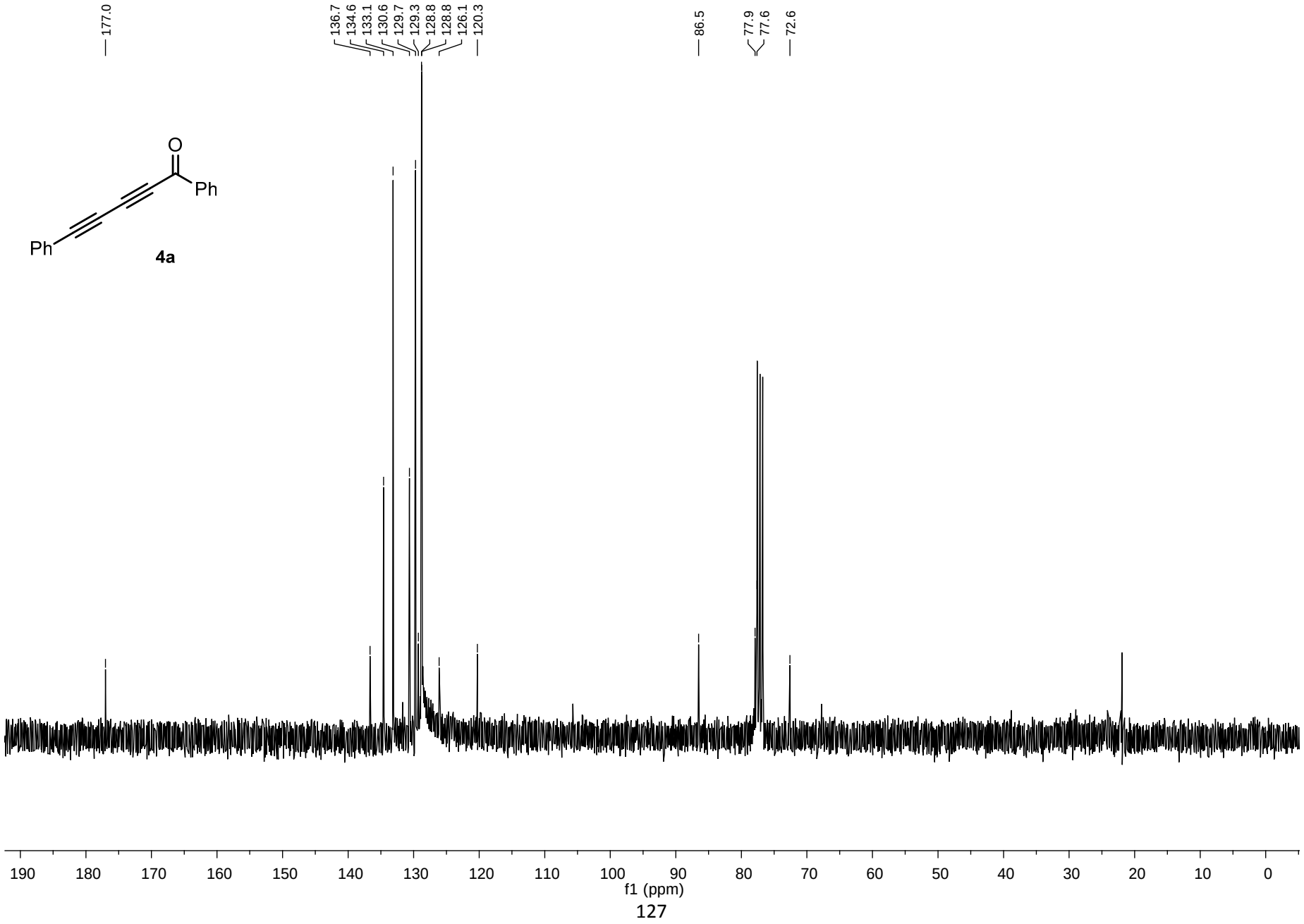
# NMR spectra of the crude conjugated diynones 4 from ethyl lactate

$^{1}$H-NMR ($CDCl_3$, 300 MHz) Crude NMR for the synthesis of **4a**



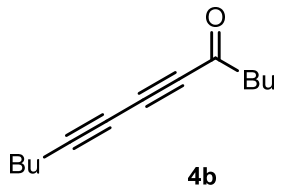
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **4a**



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

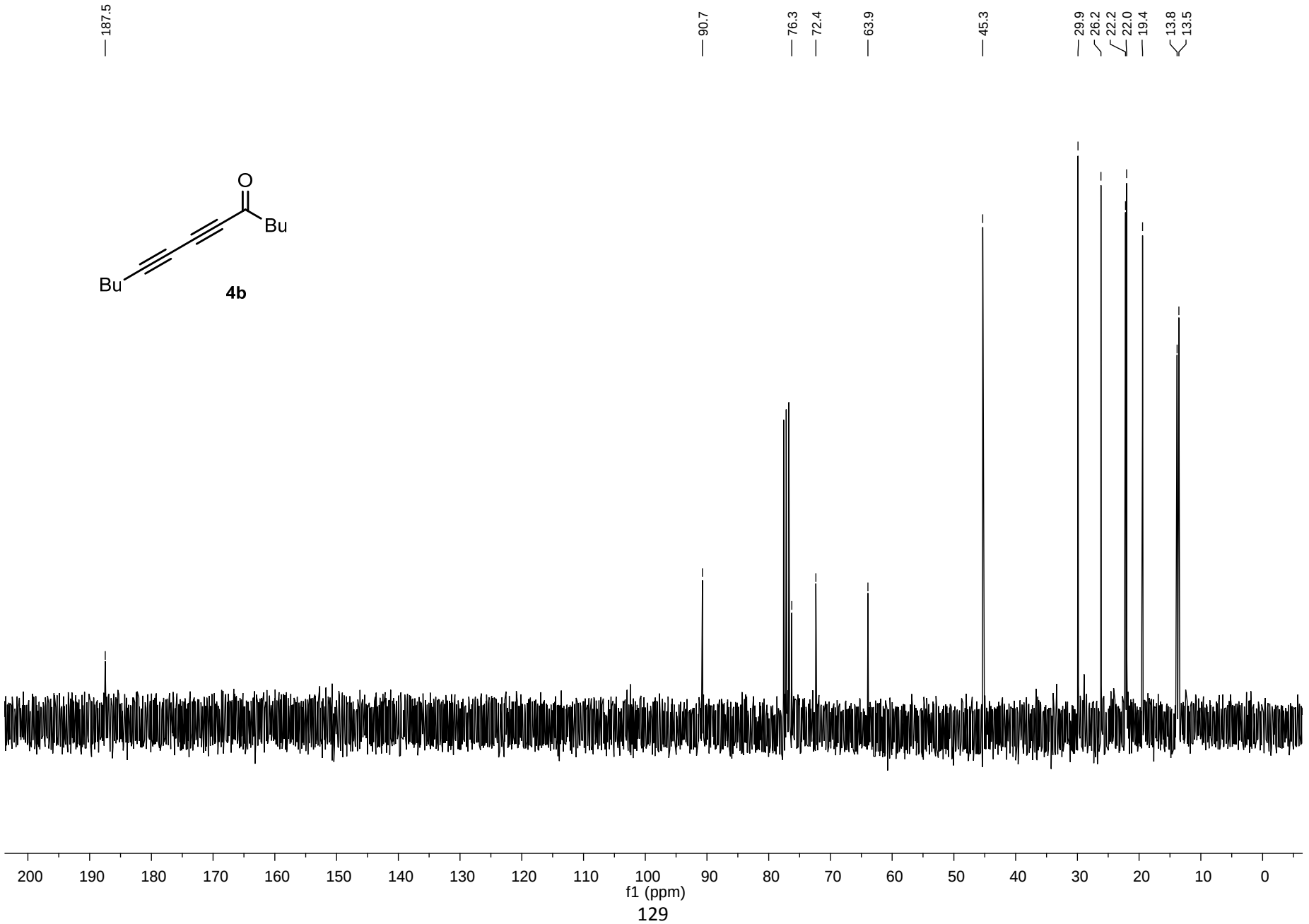
Crude NMR for the synthesis of **4b**




**4b**

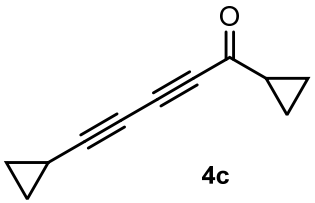
$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **4b**



$^{1}$H-NMR ($CDCl_3$, 300 MHz)

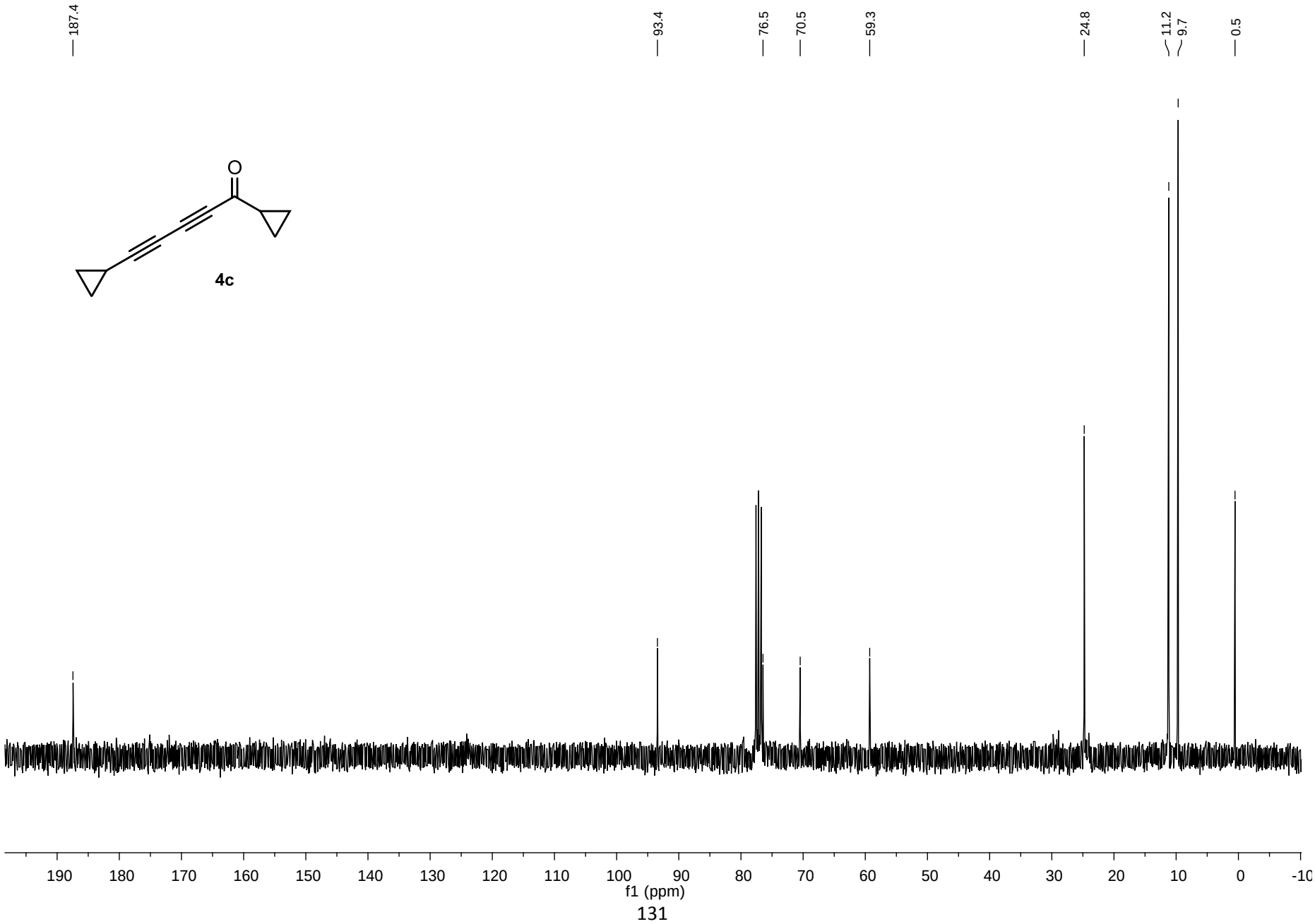
Crude NMR for the synthesis of **4c**



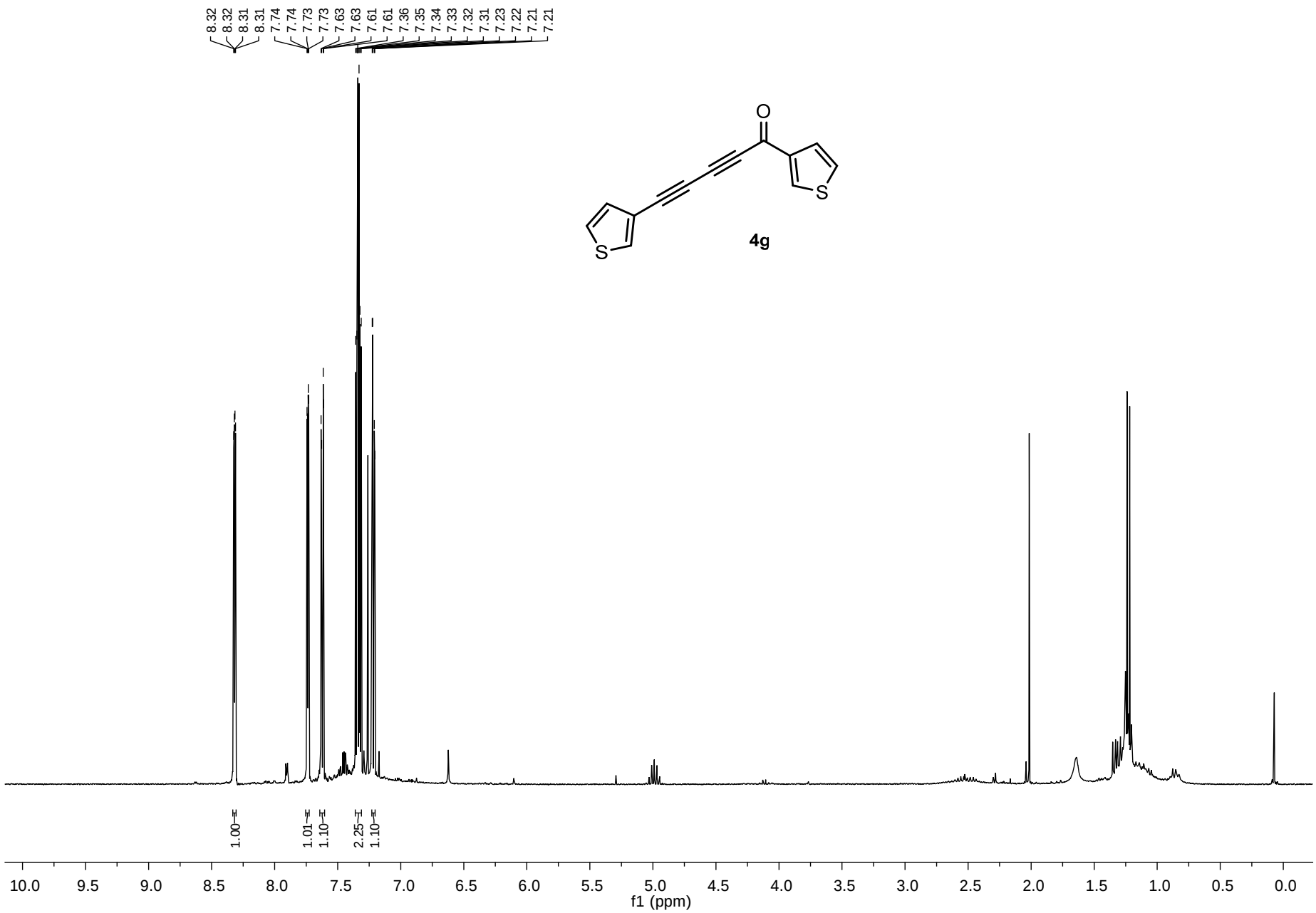
**4c**

$^{13}$C-NMR ($CDCl_3$, 75.4 MHz)

Crude NMR for the synthesis of **4c**



$^{1}$H-NMR ($CDCl_3$, 300 MHz) Crude NMR for the synthesis of **4g**



$^{13}$C-NMR ($CDCl_3$, 75.4 MHz) Crude NMR for the synthesis of **4g**