Merging Nucleophilic and Hydrogen Bonding Catalysis: An anion Binding Approach to the Kinetic Resolution of Propargylic Amines

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Supporting Information

General Information: Reagents and solvents were purchased from commercial sources and were used as received. Toluene was freshly distilled from sodium under nitrogen prior to use. Reactions were run under a nitrogen atmosphere. Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F_{254} plates. Visualization was accomplished with UV light and anisaldehyde stain, followed by heating. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on a Varian VNMRS-500 MHz instrument and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm, $(CD_3)_2CO$ at 2.05 ppm, $(CD_3)_2SO$ at 2.50 ppm, CD_2Cl_2 at 5.32 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex; br = broad; integration; coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C-NMR) spectra were recorded on a Varian VNMRS-500 MHz instrument or Varian VNMRS-400 MHz instrument and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm, $(CD_3)_2CO$ at 29.8 ppm, $(CD_3)_2SO$ at 39.5 ppm, CD_2Cl_2 at 53.8 ppm). Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer or on a Finnigan 2001 Fourier Transform Ion Cyclotron Resonance Mass Spectrometer. HPLC analysis was carried out on an Agilent 1100 series instrument with auto sampler and multiple wavelength detectors. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Perkin Elmer 343 polarimeter at 589 nm at 20 °C. Conversions and s-factors were calculated in accord with standard procedures.[1] Propargyl amines were prepared according to literature methods.[2,3]

General Procedure for Kinetic Resolutions:

A flame dried round bottom flask was charged with benzoic anhydride (34.0 mg, 0.150 mmol, 0.6 equiv.) and 4Å MS (100 mg). DMAP (1.52 mg, 0.0125 mmol, 0.05 equiv.) in 1 mL of toluene was added. Freshly distilled toluene (21.0 mL, 0.01M) was added and the reaction mixture was cooled to –78 ºC over 15 min and a solution of catalyst (7.82 mg, 0.0125 mmol, 0.05 equiv.) in 2 mL of toluene was added. After 15 min, a solution of amine (0.25 mmol) in 1 mL of toluene was added and the reaction mixture was stirred at –78 ºC for 3 hours. The reaction was quenched by adding 3.0M MeMgCl in THF (0.500 mmol, 0.167 mL) at –78 ºC and stirring was continued for another 10 minutes. Excess Grignard reagent was quenched with 1M aq HCl (5 mL) solution. The reaction mixture was allowed to warm to room temperature and was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with 5 mL of 1M HCl, then brine. The combined organic extracts were then dried with anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure and the crude product was purified by flash chromatography.

The unreacted amine was isolated by basifying the aqueous layer with 15% NaOH (pH 10) and subsequent extraction with diethyl ether (5 x 50 mL). The combined organic layers were washed with brine, and then dried with anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure. The crude material was benzoylated following a standard procedure.

The second runs were conducted using the general procedure without any modifications.

The conversion, $\mathbf{C_{HPLC}}$, for each catalytic reaction was calculated[1] using the following equation:

$\boldsymbol{C_{HPLC}} = \frac{ee_{SM}}{ee_P + ee_{SM}}$, where $\mathbf{ee_p}$ is the enantiomeric excess of the amide product and $\mathbf{ee_{SM}}$ is the enantiomeric excess of the recovered amine.

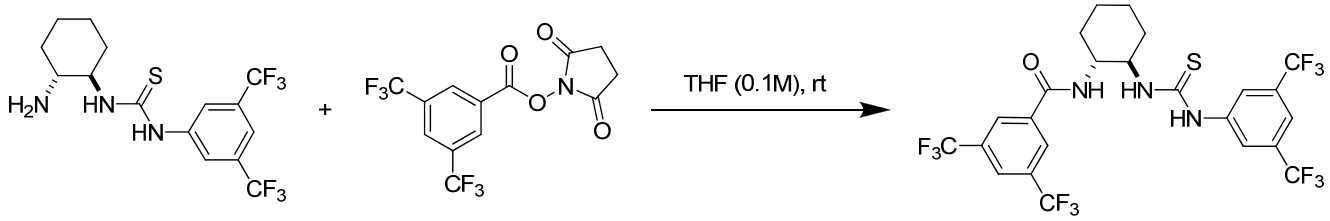
The s-factor was calculated using the calculated conversion and ee from either the product, $\mathbf{ee_p}$, or recovered starting material, $\mathbf{ee_{SM}}$, following the equation:

$$\boldsymbol{s} = \frac{\boldsymbol{ln}\big((\mathbf{1}-\boldsymbol{C_{HPLC}})(\mathbf{1}-\boldsymbol{ee_P})\big)}{\boldsymbol{ln}\big((\mathbf{1}-\boldsymbol{C_{HPLC}})(\mathbf{1}+\boldsymbol{ee_P})\big)}$$

$$\boldsymbol{s} = \frac{\boldsymbol{ln}\big((\mathbf{1}-\boldsymbol{C_{HPLC}})(\mathbf{1}-\boldsymbol{ee_{SM}})\big)}{\boldsymbol{ln}\big((\mathbf{1}-\boldsymbol{C_{HPLC}})(\mathbf{1}+\boldsymbol{ee_{SM}})\big)}$$

General Procedure for Preparation of Catalysts

Catalysts were prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(3,5-bis(trifluoromethyl)phenyl)-thiourea[4] and N-hydroxysuccinimide (NHS) esters.[6,7] As an alternative to the use of activated esters, the corresponding acid chlorides can also be employed. However, in our hands, this resulted in lower overall catalyst yields.



In a flamed dried round bottom flask, NHS ester (1.5 equiv.) was added to a solution of aminothiourea (0.26 mmol, 100 mg, 1.0 equiv.) in THF (2.6 ml, 0.1M). The reaction mixture was stirred at rt and monitored by TLC (1:1 Hex/EtOAc). After full conversion of the aminothiourea, the reaction mixture was concentrated under reduced pressure and the crude material was purified by flash chromatography on silica gel.

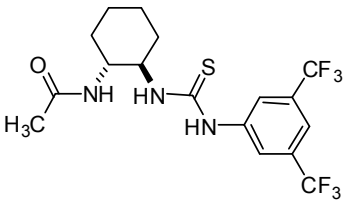
Preparation and Characterization Data of Catalysts

***N*,*N*'-((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(3,5-bis(trifluoromethyl)benzamide) (2):** In a flamed dried round bottom flask was added NHS ester (2.5 equiv.) to a solution of diaminocyclohexane (0.26 mmol, 100 mg, 1.0 equiv.) in THF (2.6 ml, 0.1M). The reaction mixture was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure. The product was precipitated by addition of 5 ml of ether. The product was filtered and washed with ether to yield pure catalyst as a white solid in 93% yield (242 mg). mp > 250 ºC; Rf = 0.50 (Hexanes/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ –93.3 (c 1.0, acetone); IR (KBr) 3266, 2951, 1638, 1544, 1281, 1129, 908, 682 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 8.38 (s, 4H), 8.25 (m, 2H), 8.15 (s, 2H), 4.08 (m, 2H), 2.16 (m, 2H), 1.85 (m, 2H), 1.63 (m, 2H), 1.43 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 164.3, 137.4, 131.3 (q, J_{C-F} = 33.8 Hz,), 128.1, 124.8 (m), 123.5 (q, J_{C-F} = 271.3 Hz), 54.8, 31.8, 24.9.; *m/z* (ESI-MS) 595.0 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)formamide (3a):** Acetic formic anhydride (prepared by stirring 1.0 equiv. of acetic anhydride and 1.1 equiv. of formic acid for 2 h at 55 °C) (2.6 mmol, 229 mg, 10 equiv.) was added dropwise at 0 °C to a stirred solution of the aminothiourea (0.26 mmol, 100 mg, 1.0 equiv.) and triethylamine (0.52 mmol, 0.073 ml, 2.0 equiv.) in THF (2.6 ml, 0.1M). The reaction mixture was warmed to rt and monitored by TLC (1:1 Hex/EtOAc). After full conversion of the aminothiourea, the reaction mixture was concentrated under reduced pressure and the crude material was purified by flash chromatography on silica gel. The pure product was obtained as a white solid in 81% yield (87 mg). mp = 136–138 ºC; Rf = 0.21 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ +93.6 (c 1.0, $CHCl_3$); IR (KBr) 3298, 2931, 1664, 1560, 1474, 1387, 1275, 1133, 882, 679 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.10 (s, 1H), 8.02 (s, 2H), 7.60 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 6.73 (d,

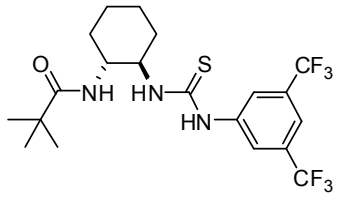
J = 7.9 Hz, 1H), 4.55 (m, 1H), 3.85 (m, 1H), 2.27 (m, 1H), 2.08 (m, 1H), 1.88 (comp, 2H), 1.47–1.33 (comp, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.6, 162.5, 140.5, 132.1 (q, $J_{C\text{-}F}$ = 33.8 Hz), 123.4, 123.3 (q, $J_{C\text{-}F}$ = 271.3 Hz), 118.4, 56.9, 53.9, 32.6 (2), 25.1, 24.8.; *m/z* (ESI-MS) 414.0 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)acetamide (3b):**



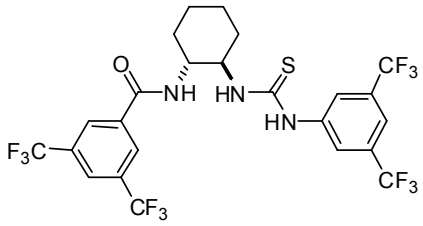
The general procedure was followed to yield a white solid in 78% yield (87 mg). mp = 195–197 ºC; Rf = 0.21 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ +66.4 (c 1.0, $CHCl_3$); IR (KBr) 3301, 3108, 2927, 1629. 1551, 1474, 1390, 1316, 1183, 881, 678 cm^{-1}; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 9.65 (s, 1H), 8.35 (s, 2H), 7.69 (comp, 2H), 7.42 (s, 1H), 4.23 (m, 1H), 3.83 (m, 1H), 2.34 (m, 1H), 2.06 (m, 1H), 1.97 (s, 3H), 1.77 (comp, 2H), 1.46–1.36 (comp, 5H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 181.2, 171.4, 142.4, 131.2 (q, $J_{C\text{-}F}$ = 33.8 Hz), 123.7 (q, $J_{C\text{-}F}$ = 270.0 Hz), 122.2, 116.5, 58.5, 53.0, 32.1, 31.9, 25.1, 24.6, 22.5.; *m/z* (ESI-MS) 428.0 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)pivalamide (3c):**



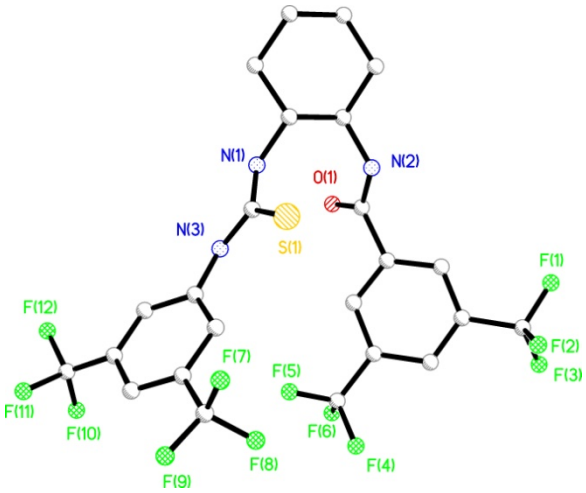
The general procedure was followed to yield a white solid in 72% yield (88 mg). mp = 158–160 ºC; Rf = 0.42 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ +112.2 (c 1.0, $CHCl_3$); IR (KBr) 3314, 2938, 1620, 1536, 1385, 1276, 1132, 969, 880, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 1H), 8.00–7.95 (comp, 3H), 7.60 (s, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 4.73 (m, 1H), 3.79 (m, 1H), 2.27 (m, 1H), 2.03 (m, 1H), 1.90 (comp, 2H), 1.47 (comp, 4H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 180.6, 140.9, 131.8 (q, $J_{C\text{-}F}$ = 32.5 Hz), 124.7, 123.3 (q, $J_{C\text{-}F}$ = 271.3 Hz), 118.4, 56.6, 55.4, 39.1, 32.9, 32.8, 27.5, 25.3, 25.0.; *m/z* (ESI-MS) 469.9 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-3,5-bis(trifluoromethyl)-benzamide (4a):**



The general procedure was followed to yield a white solid in 92% yield (149 mg). mp = 162–164 ºC; Rf = 0.38 (Hexanes/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ +16.7 (c 1.0, $CHCl_3$); IR (KBr) 3311, 2942, 1647, 1548, 1384, 1278, 1128, 885, 681 cm^{-1}; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.68 (s, 1H), 8.26 (s, 2H), 7.99 (s, 1H), 7.71 (comp, 3H), 7.61 (s, 1H), 7.44 (m, 1H), 4.75 (m, 1H), 4.04 (m, 1H), 2.29 (comp, 2H), 1.94 (comp, 2H), 1.52 (comp, 4H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 181.9, 166.1, 139.8, 136.3, 132.3 (q, $J_{C\text{-}F}$ = 33.8 Hz), 132.1 (q, $J_{C\text{-}F}$ = 33.8 Hz), 127.7, 125.6, 123.9, 123.1 (q, $J_{C\text{-}F}$ = 271.3 Hz,), 123.0 (q, $J_{C\text{-}F}$ = 271.3 Hz), 119.0, 57.33, 57.0, 32.4, 32.2, 24.9 (2).; *m/z* (ESI-MS) 625.8 $[M+H]^+$.

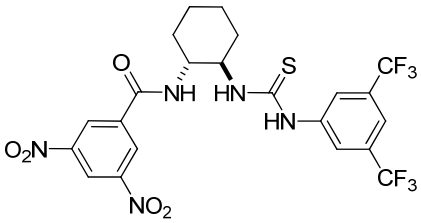
The title compound was further characterized by X-ray crystallography:



The enantiopure catalyst **4a** was crystallized from hexanes/ethyl acetate through slow diffusion at room temperature.

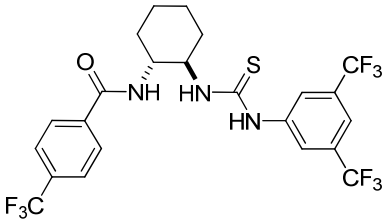
The requisite CIF file has been submitted to the journal.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-3,5-dinitrobenzamide**

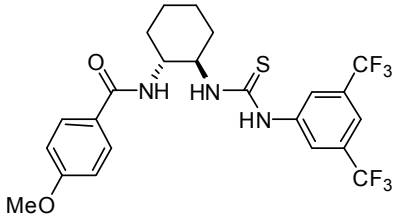


(4b): The general procedure was followed to yield a white solid in 78% yield (117 mg). mp > 250 ºC; Rf = 0.17 (Hexanes/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ –67.0 (c 1.0, acetone); IR (KBr) 3303, 2939, 1654, 1544, 1343, 1279, 1133, 729, 682 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 9.38 (s, 1H), 9.10 (comp, 2H), 9.05 (m, 1H), 8.60 (d, J = 8.0 Hz, 1H), 8.14 (s, 2H), 7.68 (comp, 2H), 4.59 (m, 1H), 4.12 (m, 1H), 2.30 (m, 1H), 2.17 (m, 1H), 1.83 (comp, 2H), 1.64 (m, 1H), 1.51–1.41 (comp, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 181.6, 162.9, 148.8, 141.8, 138.1, 131.3 (q, $J_{C\text{-}F}$ = 33.8 Hz), 127.7, 123.6 (q, $J_{C\text{-}F}$ = 270.0 Hz), 123.2, 120.9, 117.2 (m), 58.1, 54.9, 31.9, 31.7, 24.8, 24.8.; *m/z* (ESI-MS) 579.9 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-4-(trifluoromethyl) benzamide (4c):** The general procedure was followed to yield a white solid in 95% yield (137 mg). mp > 250 ºC; Rf = 0.42 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ –30.9 (c 1.0, acetone); IR (KBr) 3266, 2943, 1639, 1545, 1327, 1278, 1128, 680 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 9.44 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 8.12 (s, 2H), 8.08 (d, J = 8.1 Hz, 2H), 7.78–7.74 (comp, 3H), 7.67 (s, 1H), 4.58 (m, 1H), 4.07 (m, 1H), 2.28 (m, 1H), 2.16 (m, 1H), 1.83 (comp, 2H), 1.63–1.41 (comp, 4H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 181.6, 166.6, 132.6 (q, $J_{C\text{-}F}$ = 32.0 Hz), 131.2 (q, $J_{C\text{-}F}$ = 33.0 Hz), 128.4, 125.5 (m), 123.6, 123.2 (q, $J_{C\text{-}F}$ = 271.6 Hz), 117.1, 58.0, 54.8, 32.0, 31.9, 24.9, 24.9.; *m/z* (ESI-MS) 557.9 $[M+H]^+$.

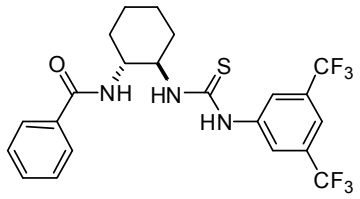


***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-4-methoxybenzamide**



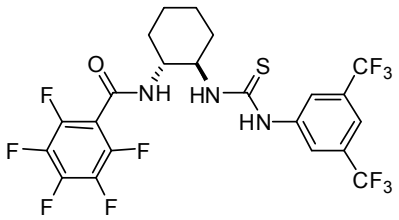
(4d): The general procedure was followed to yield a white solid in 89% yield (120 mg). mp = 154–156 ºC; Rf = 0.29 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ –55.2 (c 1.0, acetone); IR (KBr) 3289, 3065, 2944, 1628, 1540, 1504, 1384, 1277, 1179, 1131, 844, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 7.74–7.70 (comp, 4H), 7.53 (s, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 4.85 (m, 1H), 3.95 (m, 1H), 3.75, (s, 3H), 2.30 (comp, 2H), 1.98 (comp, 2H), 1.63–1.46 (comp, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 169.3, 163.1, 140.7, 131.6 (q, J_{C-F} = 33.8 Hz), 124.41 (m), 123.2 (q, J_{C-F} = 271.3 Hz), 114.4, 57.3, 56.1, 55.5, 32.9 (2), 25.3, 25.1.; *m/z* (ESI-MS) 519.8 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)benzamide (4e):** The



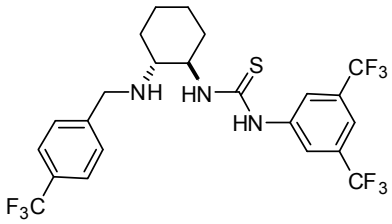
general procedure was followed to yield a white solid in 92% yield (117 mg). mp = 83–85 ºC; Rf = 0.42 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ –27.0 (c 1.0, acetone); IR (KBr) 3301, 2939, 1637, 1544, 1384, 1277, 1179, 1132, 969, 885, 681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.20 (d, *J* = 9.0 Hz, 1H), 7.75 (comp, 4H), 7.51 (comp, 2H), 7.44 (app t, *J* = 7.4 Hz, 1H), 7.30 (app t, *J* = 7.1 Hz, 1H), 4.88 (m, 1H), 4.20 (m, 1H), 2.38–2.27 (comp, 2H), 1.98 (comp, 2H), 1.63–1.44 (comp, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.2, 169.8, 140.6, 133.8, 132.6, 131.6 (q, J_{C-F} = 33.8 Hz), 129.0, 124.1, 123.2 (q, J_{C-F} = 272.5 Hz), 118.3 (m), 57.2, 56.2, 32.9, 32.8, 25.3, 25.1.; *m/z* (ESI-MS) 489.9 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-2,3,4,5,6-pentafluoro-**



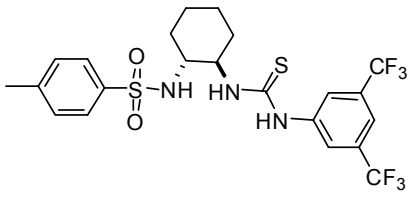
benzamide (4f): The general procedure was followed to yield a white solid in 87% yield (131 mg). mp = 153–155 ºC; Rf = 0.33 (Hexanes/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ –11.5 (c 1.0, acetone); IR (KBr) 3282, 2943, 1655, 1518, 1384, 1278, 1181, 1135, 994, 971, 886, 681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.73 (s, 2H), 7.61 (s, 1H), 7.49 (m, 1H), 7.37 (m, 1H), 4.69 (m, 1H), 3.98 (m, 1H), 2.31–2.26 (comp, 2H), 1.99–1.94 (comp, 2H), 1.59–1.42 (comp, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.0, 159.3, 144.7 (m), 142.7 (m), 141.9 (m), 138.9 (m), 139.9, 136.9, 132.3 (q, J_{C-F} = 33.8 Hz), 123.8, 123.1 (q, J_{C-F} = 271.3 Hz), 111.0 (m), 57.4, 56.8, 32.6, 32.3, 25.1, 24.9.; *m/z* (ESI-MS) 579.9 $[M+H]^+$.

1-(3,5-bis(trifluoromethyl)phenyl)-3-((1*R*,2*R*)-2((4(trifluoromethyl)benzyl)amino) cyclohexyl)-

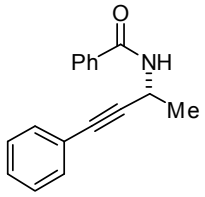


thiourea (5): The catalyst was prepared according to the literature procedure.[4] Aminothiorea (100 mg, 0.26 mmol, 1.0 equiv.) and $NaBH_4$ (11 mg, 0.28 mmol, 1.1 equiv.) were stirred in anhydrous MeOH (0.74 ml, 0.35M) at rt. 4-(trifluoromethyl)benzaldehyde (47 mg, 0.27 mmol, 1.05 equiv.) was added slowly. After 20 min, the reaction was quenched by adding saturated aq. NH_4Cl followed by conc. NH_4OH. The reaction mixture was stirred for an additional 20 min, then extracted with DCM (5 x 20 ml). The extracts were dried over Na_2SO_4, evaporated under reduced pressure. The crude reaction mixture was purified by flash chromatography on silica gel (hexanes, EtOAc, MeOH, NH_4OH (400:100:5:1) to yield a white solid in 89% yield (130 mg). mp = 113–115 ºC; Rf = 0.17 (Hexanes/EtOAc 1:1 v/v); $[\alpha]_D^{20}$ +67.8 (c 1.0, $CHCl_3$); IR (KBr) 3312, 2947,

1560, 1390, 1278, 1068, 881, 681 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2SO$, 80 ºC) δ 8.22 (s, 2H), 7.61–7.56 (comp, 5H), 4.12 (app s, 1H), 3.93 (app d, J = 14.2 Hz, 1H), 3.81 (app d, J = 14.2 Hz, 1H), 2.56 (m, 1H), 2.07–1.99 (comp, 2H), 1.67 (comp, 2H), 1.30–1.26 (comp, 4H); ^{13}C NMR (125 MHz, $(CD_3)_2SO$, 80 ºC) δ 181.4, 142.1, 143.0, 130.9 (q, J_{C-F} = 32.5 Hz), 129.1, 125.4 (q, J_{C-F} = 3.8 Hz), 125.0, 122.8, 116.4, 60.8, 57.9, 50.5, 32.0, 31.5, 24.8, 26.9.; m/*z* (ESI-MS) 540.0 $[M+H]^+$.

***N*-((1*R*,2*R*)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)-4-methylbenzenesulfonamide (6):** 
Tosyl chloride (0.28 mmol, 54 mg, 1.1 equiv.) was added to a stirred solution of the aminothiourea (0.26 mmol, 100 mg, 1.0 equiv.) and triethylamine (0.31 mmol, 0.044 ml, 1.2 equiv.) in THF (2.6 ml, 0.1M). The reaction mixture was stirred at rt and monitored by TLC (1:1 Hex/EtOAc). After full conversion of the aminothiourea, the reaction mixture was concentrated under reduced pressure and the crude material was purified by flash chromatography on silica gel. The pure product was obtained as a white solid in 75% yield (106 mg). mp = 173–175 ºC; Rf = 0.21 (Hexanes/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ +40.0 (c 1.0, $CHCl_3$); IR (KBr) 3349, 2939, 1544, 1475,1386, 1277, 1134, 980, 883, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.91 (s, 2H), 7.72 (d, J = 6.7 Hz, 2H), 7.56 (s, 1H), 7.20 (d, J = 7.2 Hz, 2H), 6.78 (d, J = 7.7 Hz, 1H), 6.55 (m, 1H), 4.36 (m, 1H), 3.20 (m, 1H), 2.31 (s, 3H), 2.11 (m, 1H), 1.81–1.69 (comp, 4H), 1.36–1.15 (comp, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.4, 144.0, 139.9, 138.0, 137.1 (q, J_{C-F} = 33.8 Hz), 130.0, 126.7, 123.5, 123.2 (q, J_{C-F} = 271.3 Hz), 59.5, 57.2, 34.1, 32.2, 24.7, 24.6, 21.6.; *m/z* (ESI-MS) 539.9 $[M+H]^+$.

Characterization Data of Products

(*R*)-*N*-(4-phenylbut-3-yn-2-yl)benzamide (8a): 
Following the general procedure, compound **8a** was obtained as a white solid in 43% yield (27.4 mg). mp = 124–126 ºC; Rf = 0.33 (Hexanes/EtOAc 8:2 v/v); $[\alpha]_D^{20}$ +45.8 (c 1.0, $CHCl_3$, 87.8% *ee*); IR (KBr) 3279, 2977, 1633, 1529, 1487, 1278, 758, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (comp, 2H), 7.50–7.36 (comp, 5H), 7.24–7.16 (comp, 2H), 6.79 (d, J = 7.7 Hz, 1H), 5.31 (m, 1H), 1.61 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 134.4, 131.8, 128.8, 128.6, 128.5, 127.4, 122.8, 89.8, 82.7, 38.4, 22.8.; *m/z* (ESI-MS) 250.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 10.9 min (major) and t_R = 13.7 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (81.2% *ee*, *S*-enantiomer). Calculated conversion = 48; **s = 39**.

Second run: conversion = 48; **s = 39** (benzoylated product: 27.2 mg, 44% yield, 87.8% *ee*; benzoylated starting material: 81.6% *ee*, *S*-enantiomer).

The absolute configuration of the recovered amine **7a** ($[\alpha]_D^{20}$ –34 (c 0.9, $CHCl_3$, 81.2% *ee*) was assigned by comparison with the compound reported in the literature[7] ($[\alpha]_D^{20}$ –27.5 (c 0.8, $CHCl_3$, >98% *ee*).

(*R*)-*N*-(4-(*p*-tolyl)but-3-yn-2-yl)benzamide (8b): Following the general procedure, compound **8b** was obtained as a white solid in 42% yield (27.8 mg). mp = 152–154 ºC; Rf = 0.29 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +49.7 (c 1.0, $CHCl_3$, 89.3% *ee*); IR (KBr) 3276, 2978, 1629, 1525, 1488, 1277, 824, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.51 (m, 1H), 7.43 (comp, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.51 (d, *J* = 67.7 Hz, 1H), 5.26 (m, 1H), 2.34 (s, 3H), 1.59 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 138.7, 134.4, 131.9, 131.8, 129.3, 128.8, 127.3, 119.7, 88.9, 82.9, 38.5, 23.0, 21.7.; *m/z* (ESI-MS) 264.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 98/2, Flow rate = 1 mL/min, UV = 254 nm, t_R = 31.8 min (major) and t_R = 36.8 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (70.0% *ee*, *S*-enantiomer). Calculated conversion = 44; **s = 37**.

Second run: conversion = 42; **s = 33** (benzoylated product: 26.5mg, 40% yield, 89.0% *ee*; benzoylated starting material: 64.2% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-*N*-(4-(*m*-tolyl)but-3-yn-2-yl)benzamide (8c): Following the general procedure, compound **8c** was obtained as a white solid in 42% yield (28.0 mg). mp = 91–93 ºC; Rf = 0.29 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +52.8 (c 1.0, $CHCl_3$, 89.0% *ee*); IR (KBr) 3282, 2978, 1632, 1536, 1487, 1280, 783, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 2H), 7.51 (m, 1H), 7.44 (comp, 2H), 7.26–7.18 (comp, 3H), 7.13 (m, 1H), 6.43 (d, *J* = 7.3 Hz, 1H), 5.27 (m, 1H), 2.32 (s, 3H), 1.60 (d, *J* = 6.8, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 138.2, 134.4, 132.6, 131.9, 129.5, 129.0, 128.8, 128.4, 127.2, 122.6, 89.2, 83.0, 38.5, 23.0, 21.4.; *m/z* (ESI-MS) 264.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 10.6 min (major) and t_R = 12.4 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (84.0% *ee*, *S*-enantiomer). Calculated conversion = 48; **s = 45**.

Second run: conversion = 48; **s = 43** (benzoylated product: 28.0mg, 42% yield, 89.0% *ee*; benzoylated starting material: 81.0% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

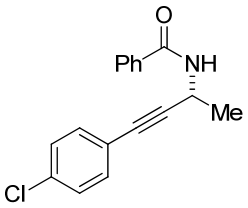
(*R*)-*N*-(4-(*o*-tolyl)but-3-yn-2-yl)benzamide (8d): Following the general procedure, compound **8d** was obtained as a white solid in 43% yield (28.3 mg). mp = 93–95 ºC; Rf = 0.29 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +50.0 (c 1.0, $CHCl_3$, 82.0% *ee*); IR (KBr) 3273, 2978, 1634, 1531, 1488, 1273, 761, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.7 Hz, 2H), 7.48 (m, 1H), 7.40–7.37 (comp, 3H), 7.22–7.10 (comp, 3H), 6.88 (d, *J* = 7.7 Hz, 1H), 5.33 (m, 1H), 2.42 (s, 3H), 1.61 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 140.5, 132.2, 131.8, 129.7, 128.8, 128.6, 127.4, 125.7, 122.6, 105.0, 93.8, 81.6, 38.6, 23.0, 20.9.; *m/z* (ESI-MS) 264.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-

hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 9.5 min (major) and t_R = 13.3 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (66.2% *ee*, *S*-enantiomer). Calculated conversion = 45; **s = 20**.

Second run: conversion = 42; **s = 17** (benzoylated product: 27.0 mg, 41% yield, 81.3% *ee*; benzoylated starting material: 58.2% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

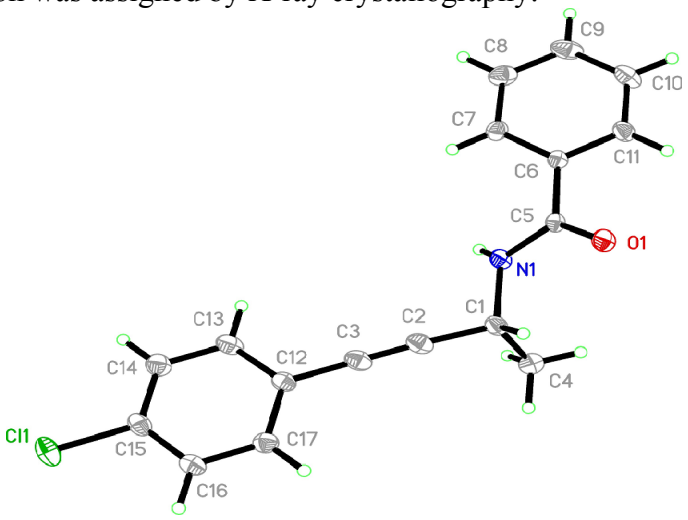
(*R*)-*N*-(4-(4-chlorophenyl)but-3-yn-2-yl)benzamide (8e): 

Following the general procedure, compound **8e** was obtained as a white solid in 36% yield (25.6 mg). mp = 152–154 ºC; Rf = 0.30 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +53.1 (c 1.0, $CHCl_3$, 88.0% *ee*); IR (KBr) 3263, 2989, 1637, 1527, 1490, 1273, 761, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.52 (m, 1H), 7.44 (comp, 2H), 7.35 (comp, 2H), 7.27 (comp, 2H), 6.44 (d, *J* = 7.6 Hz, 1H), 5.26 (m, 1H), 1.59 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 134.7, 134.3, 133.2, 131.9, 128.9, 128.8, 127.3, 121.3, 90.6, 81.7, 38.4, 22.8.; *m/z* (ESI-MS) 284.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 11.3 min and t_R = 14.2 min (major).

The recovered starting material was benzoylated and the *ee* was determined by HPLC (75.4% *ee*, *S*-enantiomer). Calculated conversion = 46; **s = 36**.

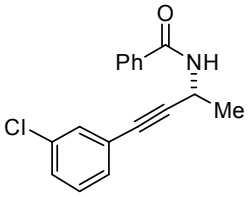
Second run: conversion = 46; **s = 40** (benzoylated product: 27.2 mg, 38% yield, 89.2% *ee*; benzoylated starting material: 75.6% *ee*, *S*-enantiomer).

The absolute configuration was assigned by X-ray crystallography:



The enantioenriched amide **8e** (89% ee) was recrystallized from hexanes/ether and was recovered in >99% ee. The highly enantioenriched **8e** was crystallized from hexanes/ether through slow diffusion at room temperature to yield x-ray quality crystals. The requisite CIF file has been submitted to the journal.

(*R*)-*N*-(4-(3-chlorophenyl)but-3-yn-2-yl)benzamide (8f): Following the general procedure, compound **8f** was obtained as a white solid in 40% yield (28.6 mg). mp = 95–97 ºC; Rf = 0.30 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +43.7 (c 1.0, $CHCl_3$, 91.8% *ee*); IR (KBr) 3287, 2979, 1629, 1528, 1122, 786, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz , 2H), 7.51 (m, 1H), 7.44–7.40 (comp, 3H), 7.30–7.20 (comp, 3H), 6.48 (d, *J* = 7.6 Hz, 1H), 5.26 (m, 1H), 1.59 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 134.3, 134.2, 131.8, 130.1, 129.7, 128.4, 128.8, 128.8, 127.3, 124.3, 90.9, 81.4, 38.3, 22.7.; *m/z* (ESI-MS) 284.1 $[M+H]^+$; HPLC: Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm, t_R = 11.1 min (major) and t_R = 16.8 min.

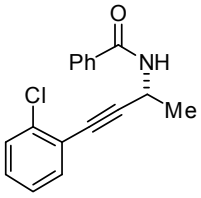


The recovered starting material was benzoylated and the *ee* was determined by HPLC (80.0% *ee*, *S*-enantiomer). Calculated conversion = 47; **s = 57**.

Second run: conversion = 47; **s = 55** (benzoylated product: 27.6 mg, 39% yield, 91.4% *ee*; benzoylated starting material: 80.2% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-*N*-(4-(2-chlorophenyl)but-3-yn-2-yl)benzamide (8g): Following the general procedure, compound **8g** was obtained as a white solid in 42% yield (30.2 mg). mp = 98–100 ºC; Rf = 0.30 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ –16.1 (c 1.0, $CHCl_3$, 82.2% *ee*); IR (KBr) 3278, 2979, 1628, 1529, 1117, 754, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.50–7.35 (comp, 5H), 7.24–7.15 (comp, 2H), 6.69 (d, *J* = 7.7 Hz, 1H), 5.31 (m, 1H), 1.61 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 136.3, 134.3, 133.6, 131.9, 129.6, 129.4, 128.8, 127.3, 126.6, 122.7, 95.0, 79.6, 38.6, 22.7.; *m/z* (ESI-MS) 284.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 10.5 min (major) and t_R = 12.9 min.

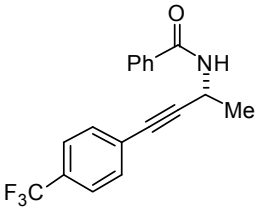


The recovered starting material was benzoylated and the *ee* was determined by HPLC (67.4% *ee*, *S*-enantiomer). Calculated conversion = 45; **s = 21**.

Second run: conversion = 45; **s = 21** (benzoylated product: 31.5 mg, 44% yield, 82.3% *ee*; benzoylated starting material: 68.0% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-*N*-(4-(4-(trifluoromethyl)phenyl)but-3-yn-2-yl)benzamide (8h): Following the general procedure, compound **8h** was obtained as a white solid in 41% yield (32.7 mg). mp = 137–139 ºC; Rf = 0.28 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +35.8 (c 1.0, $CHCl_3$, 86.8% *ee*); IR (KBr) 3290, 1636, 1531, 1329, 1117, 1068, 843, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.6 Hz, 2H), 7.54–7.48 (comp, 5H), 7.42 (comp, 2H), 6.69 (d, *J* = 7.5 Hz, 1H), 5.30 (m, 1H), 1.60 (d, *J* = 6.9 Hz, 3H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 134.2, 132.2, 131.9, 130.4, 130.2, 128.8, 127.3, 126.7, 125.4 (q, J_{C-F} = 3.7 Hz, 1C), 125.2, 123.0, 92.2, 81.4, 38.3, 22.6.; *m/z* (ESI-MS) 318.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 10.3 min and t_R = 16.8 min (major).

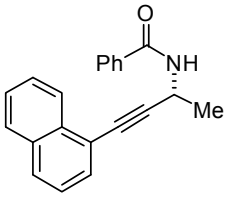


The recovered starting material was benzoylated and the *ee* was determined by HPLC (67.2% *ee*, *S*-enantiomer). Calculated conversion = 44; **s = 28**.

Second run: conversion = 45; **s = 29** (benzoylated product: 33.4 mg, 42% yield, 86.6% *ee*; benzoylated starting material: 70.8% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-*N*-(4-(naphthalen-1-yl)but-3-yn-2-yl)benzamide (8i): Following the general procedure, compound **8i** was obtained as a white solid in 41% yield (30.8 mg). mp = 129–131 ºC; Rf = 0.40 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +42.6 (c 1.0, $CHCl_3$, 79.9% *ee*); IR (KBr) 3283, 2979, 1626, 1529, 1342, 1280, 800, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.3 Hz, 1H), 7.85–7.82 (comp, 4H), 7.67 (d, *J* = 7.1 Hz, 1H), 7.58–7.50 (comp, 2H), 7.46–7.40 (comp, 3H), 6.58 (d, *J* = 7.5 Hz, 1H), 5.45 (m, 1H), 1.72 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 134.4, 133.6, 133.4, 131.9, 130.9, 129.2, 128.8, 128.5, 127.3, 127.1, 126.7, 126.2, 125.4, 120.4, 94.5, 80.9, 38.7, 23.1.; *m/z* (ESI-MS) 300.1 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 14.6 min (major) and t_R = 18.0 min.

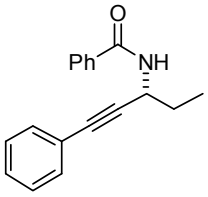


The recovered starting material was benzoylated and the *ee* was determined by HPLC (72.4% *ee*, *S*-enantiomer). Calculated conversion = 48; **s = 19**.

Second run: conversion = 48; **s = 18** (benzoylated product: 31.2 mg, 42% yield, 78.8% *ee*; benzoylated starting material: 72.4% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-*N*-(1-phenylpent-1-yn-3-yl)benzamide (8j): Following the general procedure, compound **8j** was obtained as a white solid in 45% yield (29.3 mg). mp = 108–110 ºC; Rf = 0.35 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +47.2 (c 1.0, $CHCl_3$, 89.5% *ee*); IR (KBr) 3278, 2964, 1628, 1529, 1489, 1276, 758, 690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (comp, 2H), 7.53 (m, 1H), 7.47–7.44 (comp, 4H), 7.32–7.30 (comp, 3H),6.40 (d, *J* = 7.9 Hz, 1H), 5.17 (m, 1H), 1.96–1.85 (m, 2H), 1.14 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 134.4, 131.9, 131.8, 128.7, 128.5, 128.4, 127.2, 122.8, 88.4, 83.6, 44.0, 29.5, 10.3.; *m/z* (ESI-MS) 264.1 $[M+H]^+$; HPLC: Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm, t_R = 10.5 min (major) and t_R = 14.3 min.

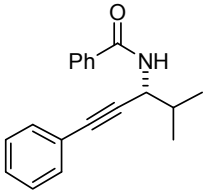


The recovered starting material was benzoylated and the *ee* was determined by HPLC (81.1% *ee*, *S*-enantiomer). Calculated conversion = 48; **s = 45**.

Second run: conversion = 48; **s = 46** (benzoylated product: 28.4 mg, 43% yield, 88.6% *ee*; benzoylated starting material: 86.2% *ee*, *S*-enantiomer).

The absolute configuration of the recovered amine **7j** ($[\alpha]_D^{20}$ +6.3 (c 0.9, $CHCl_3$, 81.1% *ee*) was assigned by comparison with the compound reported in the literature[7] ($[\alpha]_D^{20}$ +12 (c 1.2, $CHCl_3$, >98% *ee*).

(*R*)-*N*-(4-methyl-1-phenylpent-1-yn-3-yl)benzamide (8k): Following the general procedure, compound **8k** was obtained as a white solid in 40% yield (28.2 mg). mp = 90–93 ºC; Rf = 0.41 (Hexanes/EtOAC 8:2 v/v); $[\alpha]_D^{20}$ +48.2 (c 1.0, $CHCl_3$, 90.8% *ee*); IR (KBr) 3319, 2961, 1633, 1521, 1489, 1306, 1265, 754, 690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (comp, 2H), 7.52 (m, 1H), 7.45–7.42 (comp, 4H), 7.32–7.29 (comp, 3H), 6.51 (d, *J* = 8.5 Hz, 1H), 5.13 (dd, *J* = 5.6, 3.1 Hz, 1H), 2.16 (m, 1H), 1.12 (comp, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 132.0, 131.9, 128.8, 128.9, 128.5, 127.3, 123.0, 87.2, 84.4, 48.5, 33.5, 19.3, 18.1.; *m/z* (ESI-MS) 278.1 $[M+H]^+$; HPLC: Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 9.1 min (major) and t_R = 11.6 min.

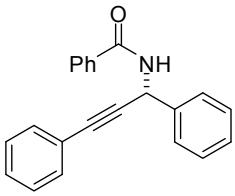


The recovered starting material was benzoylated and the *ee* was determined by HPLC (84.0% *ee*, *S*-enantiomer). Calculated conversion = 48; **s = 55**.

Second run: conversion = 47; **s = 57** (benzoylated product: 29.8 mg, 43% yield, 91.6% *ee*; benzoylated starting material: 81.4% *ee*, *S*-enantiomer).

The absolute configuration of the recovered amine **7k** ($[\alpha]_D^{20}$ –2.0 (c 0.9, $CHCl_3$, 84.0% *ee*) was assigned by comparison with the compound reported in the literature[8] ($[\alpha]_D^{20}$ –2.8 (c 0.8, $CHCl_3$, 85% *ee*).

(*R*)-N-(1,3-diphenylprop-2-ynyl)benzamide (8l): Following the general procedure (but run for 8 hours prior to quench), compound **8l** was obtained as a white solid in 29% yield (23.1 mg). $[\alpha]_D^{20}$ –5.0 (c 1.0, $CHCl_3$, 78.6% *ee*); The spectral data were consistent with the reported literature values.[9] HPLC Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm, t_R = 11.2 min and t_R = 14.4 min (major).



The recovered starting material was benzoylated and the *ee* was determined by HPLC (41.2% *ee*, *S*-enantiomer). Calculated conversion = 34; **s = 12**.

Second run: conversion = 35; **s = 11** (benzoylated product: 23.0 mg, 29% yield, 76.2% *ee*; benzoylated starting material: 40.6% *ee*, *S*-enantiomer).

The absolute configuration of **8l** ($[\alpha]_D^{20}$ –5.3 (c 1.0, $CHCl_3$, 78.6% *ee*) was assigned by comparison with the compound reported in the literature[9] ($[\alpha]_D^{23}$ –5.7 (c 0.8, $CHCl_3$, 92% *ee*).

(*R*)-*N*-(1-phenylnon-4-yn-3-yl)benzamide (8m): The catalytic reaction was run following the general procedure. After three hours the reaction was quenched by adding 3.0 M MeMgCl in THF (0.500 mmol, 0.167 mL) at –78 ºC and stirring was continued for another 10 minutes. Excess Grignard reagent was quenched with saturated aq. NH_4Cl (5 mL) solution. The reaction mixture was allowed to warm to room temperature and was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The unreacted amine was separated from the product by flash chromatography (Hexanes/EtOAc 80:20 → EtOAc). The product was obtained as a white solid in 41% yield (30.8 mg). mp = 53–55 ºC; Rf = 0.25 (Hexanes/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ +18.3 (c 1.0, $CHCl_3$, 76.2% *ee*); IR (KBr) 3280, 2925, 1630, 1525, 1283, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 2H), 7.50 (m, 1H), 7.42 (comp, 2H), 7.31–7.18 (comp, 5H), 6.17 (d, *J* = 7.9 Hz, 1H), 5.00 (m, 1H), 2.91–2.78 (comp, 2H), 2.23 (app d of t, *J* = 7.0 Hz, *J* = 2.1 Hz, 2H), 2.14–2.00 (comp, 2H), 1.56–1.40 (comp, 5H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 141.6, 134.4, 131.8, 128.7, 128.7, 127.1, 126.2, 84.8, 79.0, 42.5, 37.9, 32.3, 31.0, 22.2, 18.6, 13.8.; *m/z* (ESI-MS) 216.1 $[M+H]^+$; HPLC: Daicel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm, t_R = 13.1 min (major) and t_R = 15.2 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (66.0% *ee*, *S*-enantiomer). Calculated conversion = 46; **s = 15**.

Second run: conversion = 46; **s = 15** (benzoylated product: 31.2 mg, 42% yield, 76.4% *ee*; benzoylated starting material: 65.8% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-N-(dodec-3-yn-2-yl)benzamide (8n): The catalytic reaction was run following the general procedure. After three hours the reaction was quenched by adding 3.0 M MeMgCl in THF (0.500 mmol, 0.167 mL) at –78 ºC and stirring was continued for another 10 minutes. Excess Grignard reagent was quenched with saturated aq. NH_4Cl (5 mL) solution. The reaction mixture was allowed to warm to room temperature and was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The unreacted amine was separated from the product by flash chromatography (Hexanes/EtOAc 90:10 → 50:50 Hexanes/EtOAc). The product was obtained as a clear oil in 38% yield (27.0 mg). Rf = 0.23 (Hexanes/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ +18.5 (c 1.0, $CHCl_3$, 69.0% *ee*); IR (KBr) 3301, 2926, 1640, 1531, 1269, 1173, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (comp, 2H), 7.50 (app tt, *J* = 7.5 Hz, *J* = 1.0 Hz 1H), 7.38 (comp, 2H), 6.51 (d, *J* = 7.5 Hz, 1H), 4.98 (m, 1H), 2.15 (app dt, *J* = 7.0 Hz, *J* = 2.0 Hz, 2H), 1.50–1.44 (comp, 5H), 1.37–1.32 (m, 2H), 1.30–1.22 (comp, 8H), 0.86 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 134.2, 131.3, 128.4, 126.9, 83.0, 80.2, 37.8, 31.7, 29.1, 29.0, 28.8, 28.6, 22.8, 22.5, 22.8, 22.5, 18.5, 14.0.; *m/z* (ESI-MS) 286.2 $[M+H]^+$; HPLC: Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, t_R = 8.5 min and t_R = 10.2 min (major).

The recovered starting material was benzoylated and the *ee* was determined by HPLC (72.2% *ee*, *S*-enantiomer). Calculated conversion = 51; **s = 12**.

Second run: conversion = 53; **s = 11** (benzoylated product: 27.6 mg, 39% yield, 67.4% *ee*; benzoylated starting material: 74.6% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

(*R*)-N-(tetradec-5-yn-7-yl)benzamide (8o): The catalytic reaction was run following the general procedure. After three hours the reaction was quenched by adding 3.0 M MeMgCl in THF (0.500 mmol, 0.167 mL) at –78 ºC and stirring was continued for another 10 minutes. Excess Grignard reagent was quenched with saturated aq. NH_4Cl (5 mL) solution. The reaction mixture was allowed to warm to room temperature and was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The unreacted amine was separated from the product by flash chromatography (Hexanes/EtOAc 90:10 → 50:50 Hexanes/EtOAc). The product was obtained as a white solid in 45% yield (35.1 mg). mp = 38–40ºC; Rf = 0.38 (Hexanes/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ +15.3 (c 1.0, $CHCl_3$, 72.2% *ee*); IR (KBr) 3288, 2926, 1639, 1524, 1277, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (app d, *J* = 7.0 Hz, 2H), 7.44 (app t, *J* = 7.5 Hz, 1H), 7.36 (app t, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 4.90 (m, 1H), 2.15 (dt, *J* = 7.0 Hz, *J* = 2.0 Hz, 2H), 1.77–1.64 (comp, 2H), 1.48–1.41 (comp, 4H), 1.40–1.34 (m, 2H), 1.31–1.25 (comp, 8H), 0.89–0.86 (comp, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 134.2, 131.2, 128.2, 126.9, 83.4, 79.3, 42.2, 36.2, 31.6, 30.6, 29.1, 29.0, 25.6, 22.5, 21.8, 18.2, 13.9, 13.4.; *m/z* (ESI-MS) 314.1 $[M+H]^+$; HPLC: Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 98/2, Flow rate = 1 mL/min, UV = 230 nm, t_R = 11.7 min (major) and t_R = 14.1 min.

The recovered starting material was benzoylated and the *ee* was determined by HPLC (73.3% *ee*, *S*-enantiomer). Calculated conversion = 50; **s = 13**.

Second run: conversion = 50; **s = 14** (benzoylated product: 34.2 mg, 44% yield, 73.0% *ee*; benzoylated starting material: 73.5% *ee*, *S*-enantiomer).

The absolute configuration was assigned by analogy.

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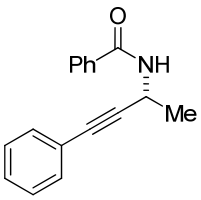
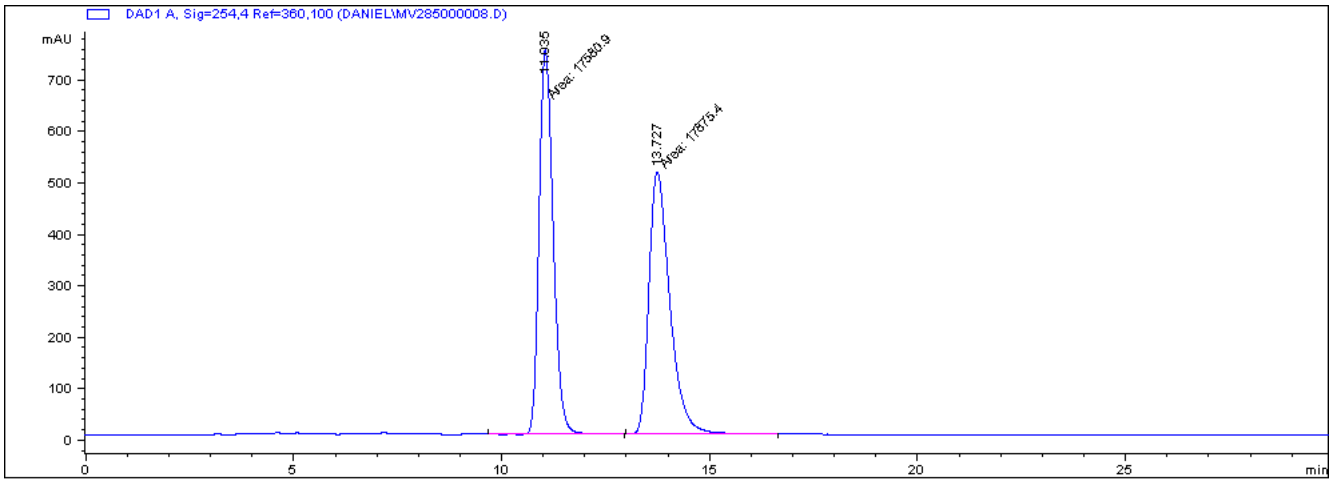
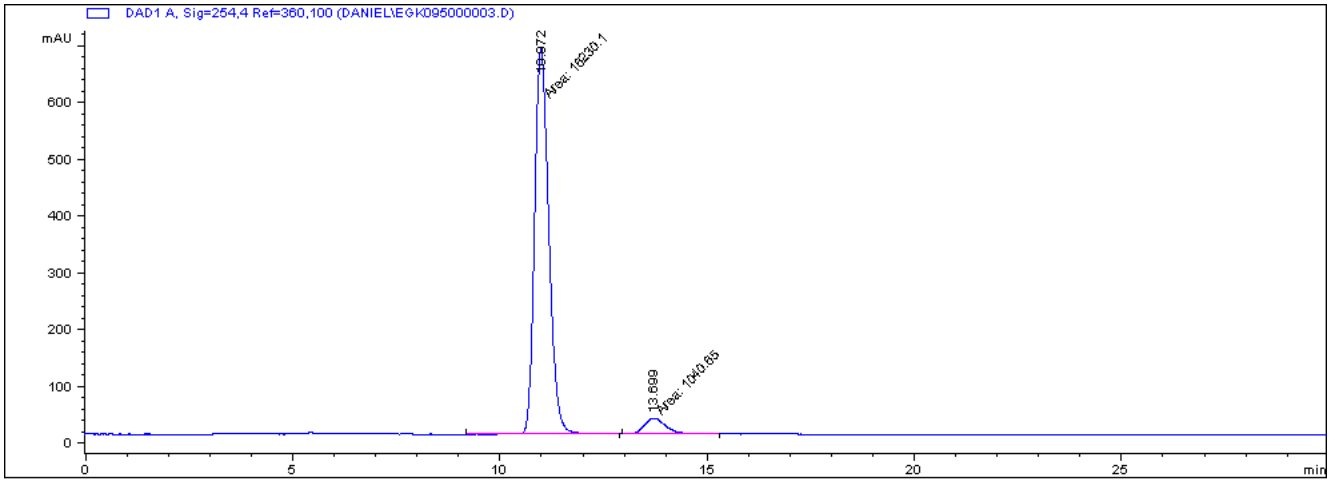
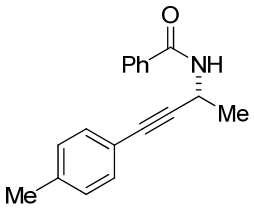


HPLC profile of **8a**

Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm

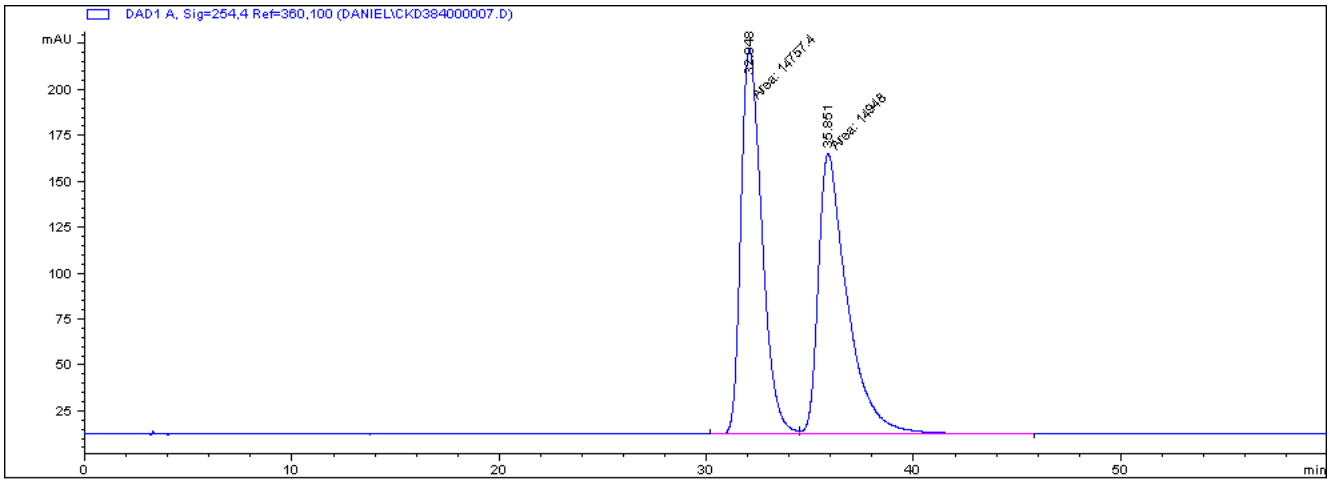


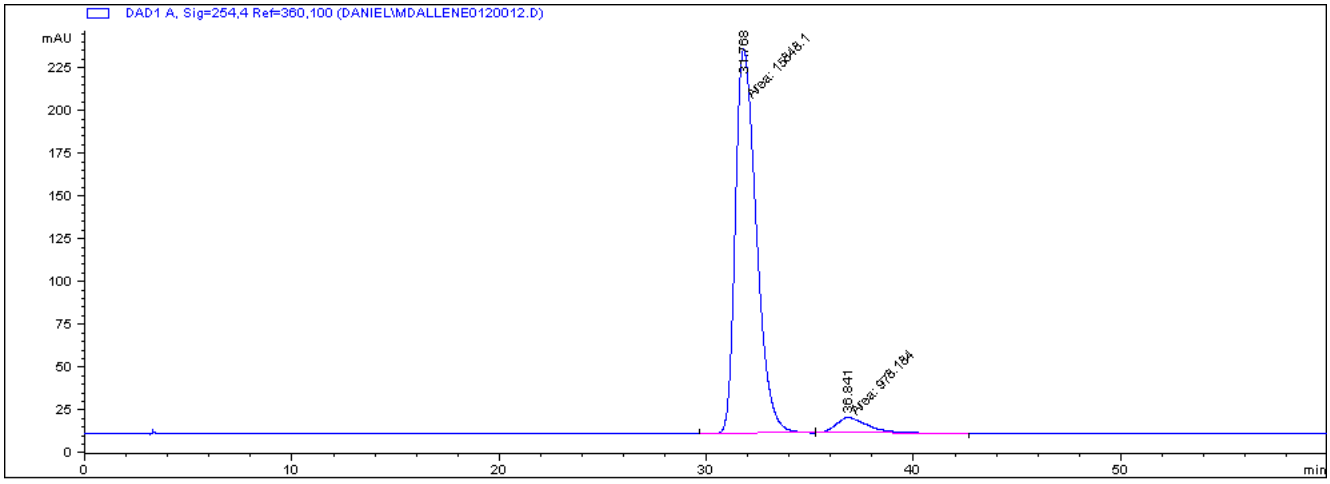


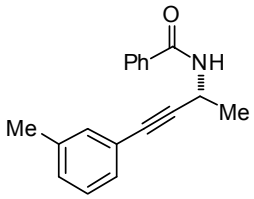


HPLC profile of **8b**

Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 98/2, Flow rate = 1 mL/min, UV = 254 nm

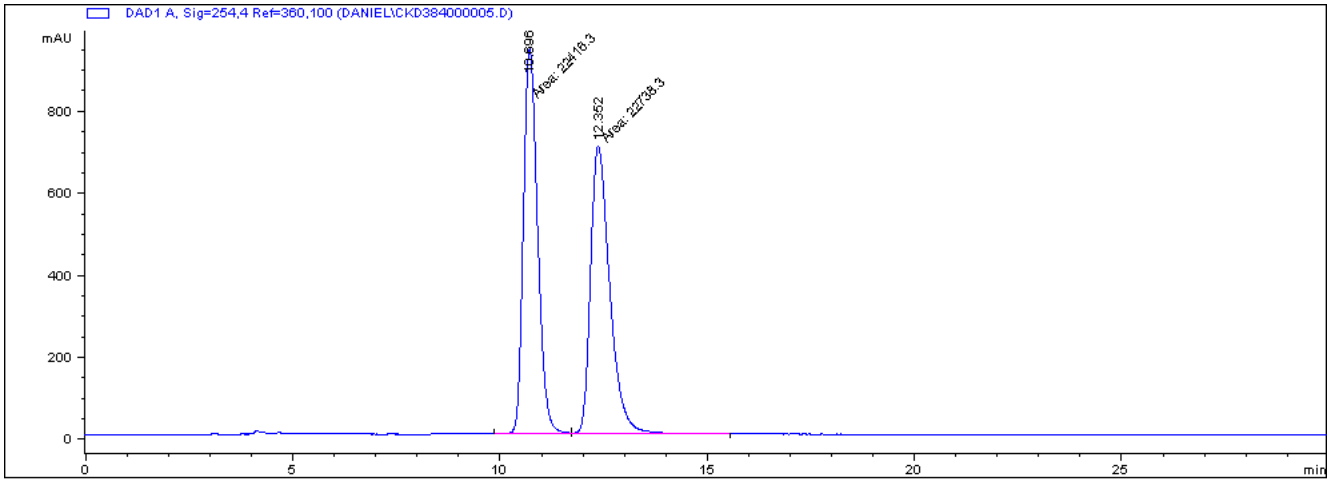


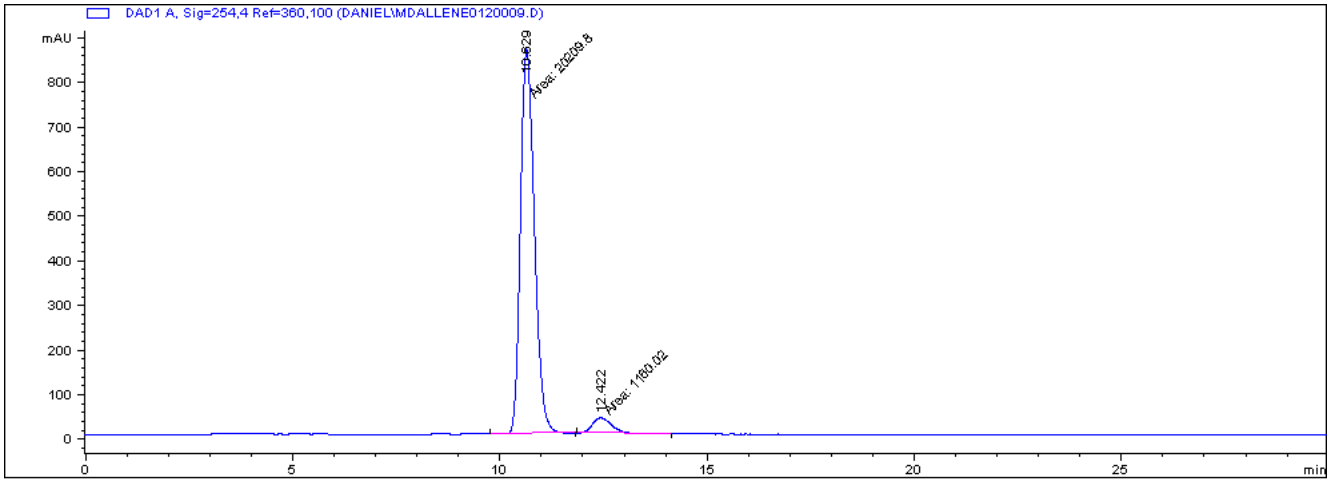


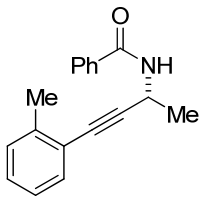


HPLC profile of **8c**

Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm







HPLC profile of **8d**

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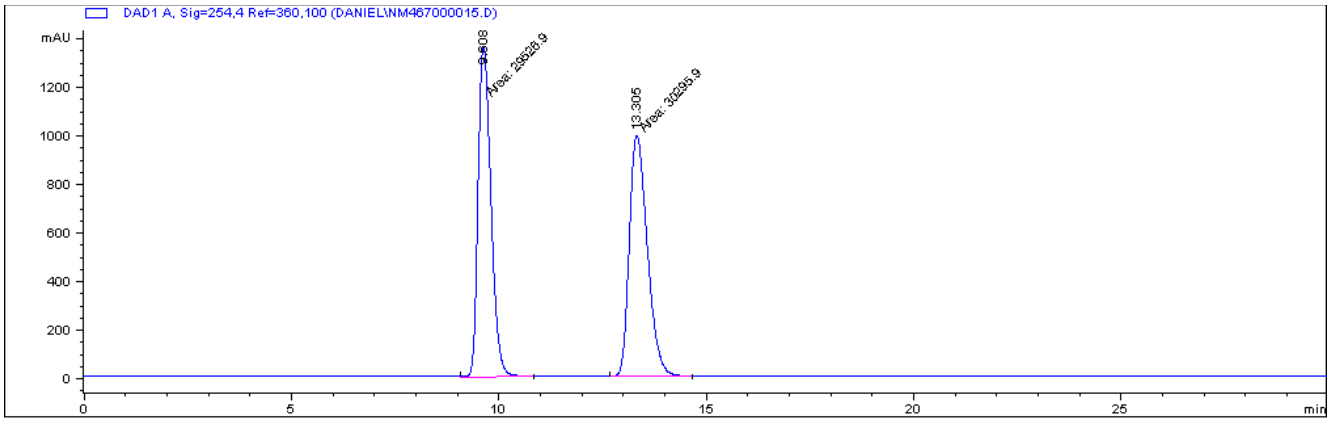

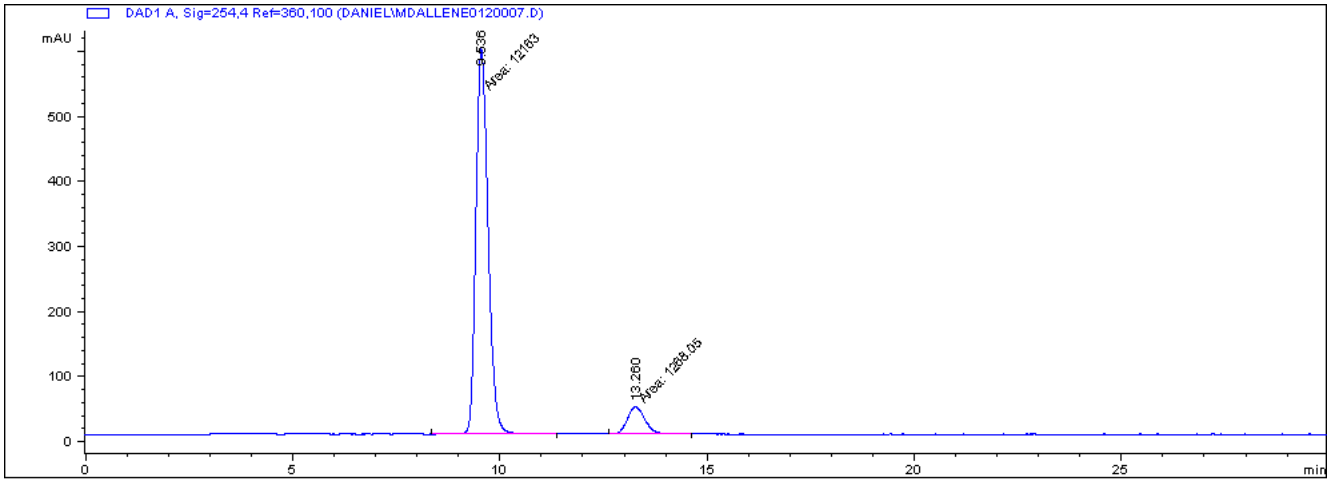

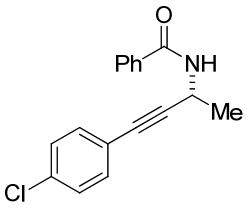

HPLC profile of **8e**

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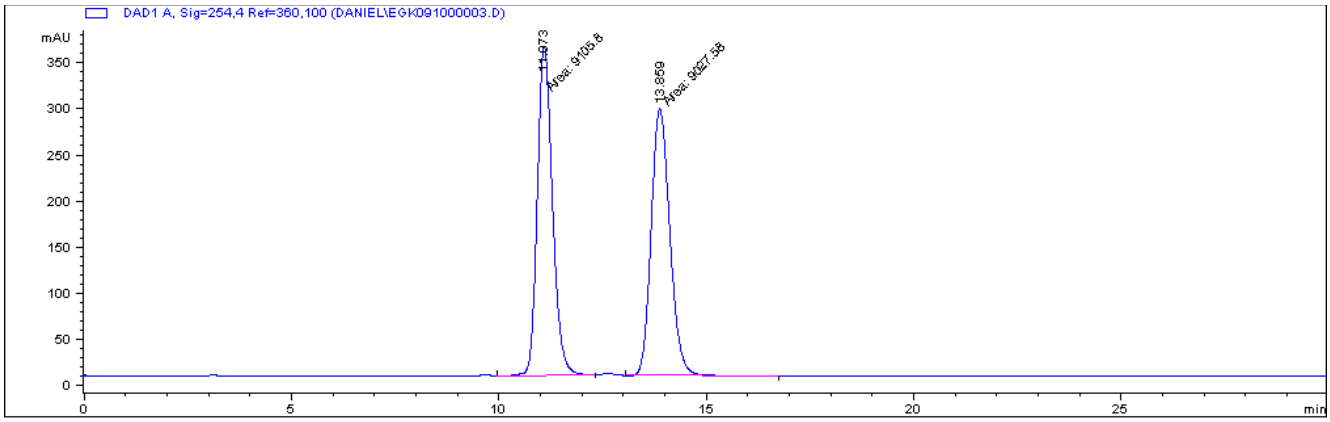
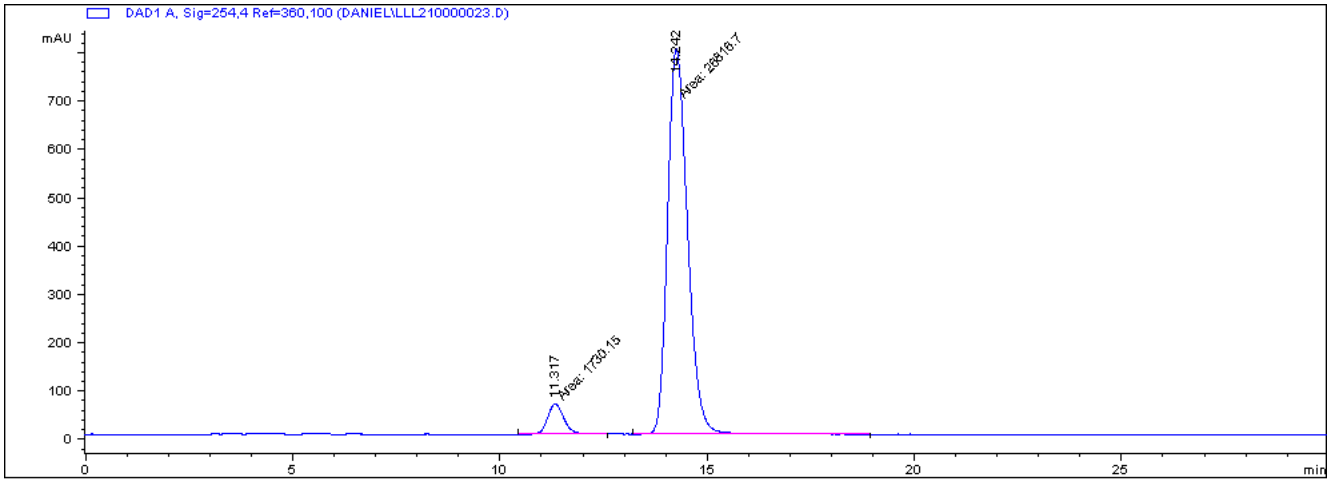
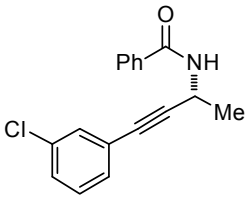
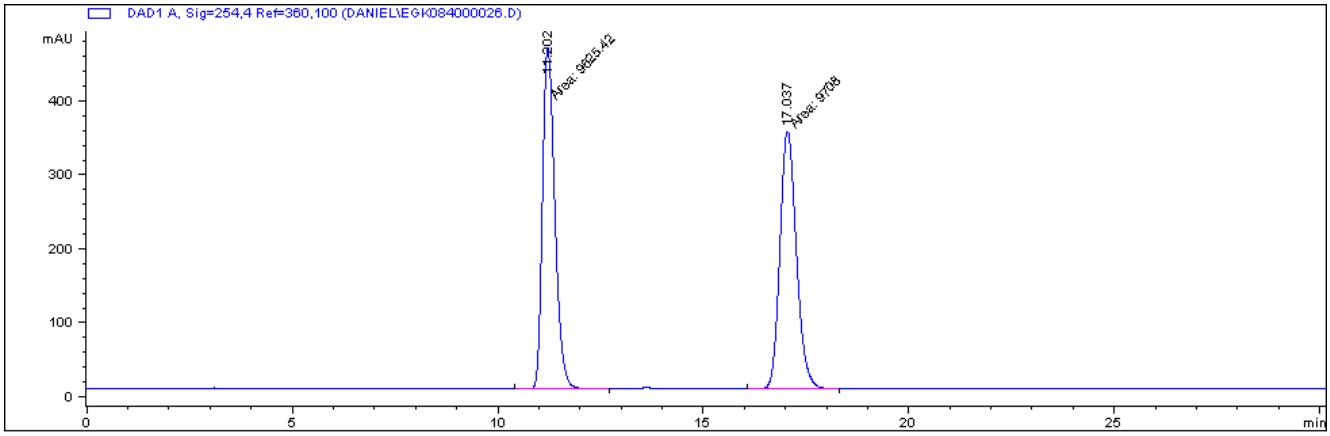


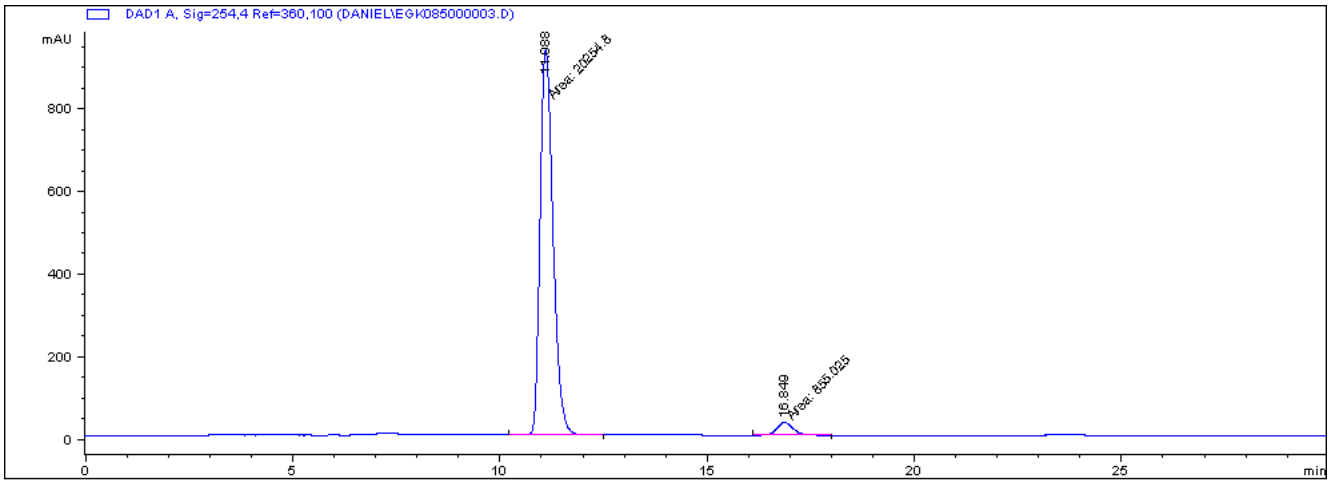


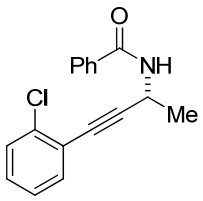


HPLC profile of **8f**

Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm







HPLC profile of **8g**

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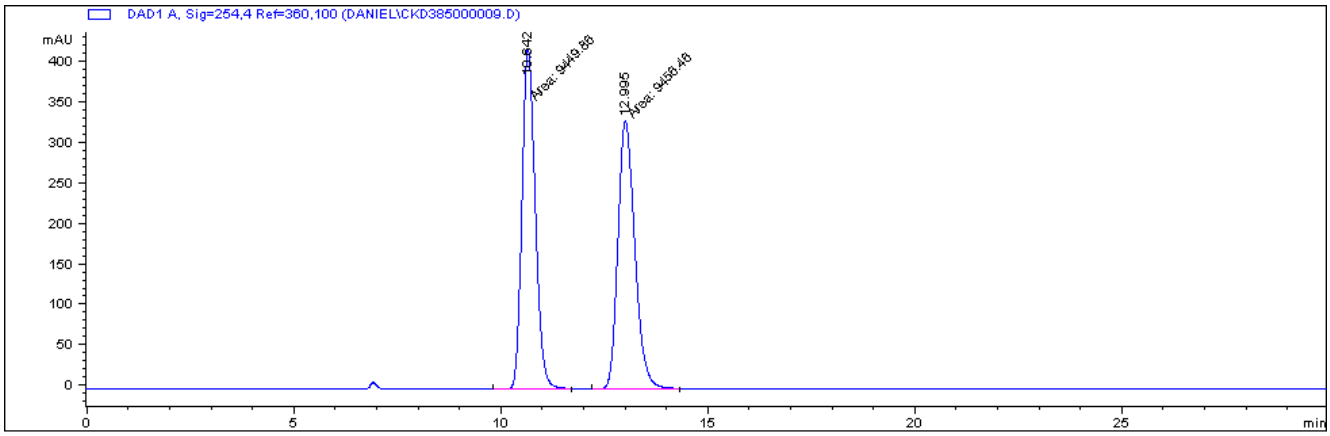
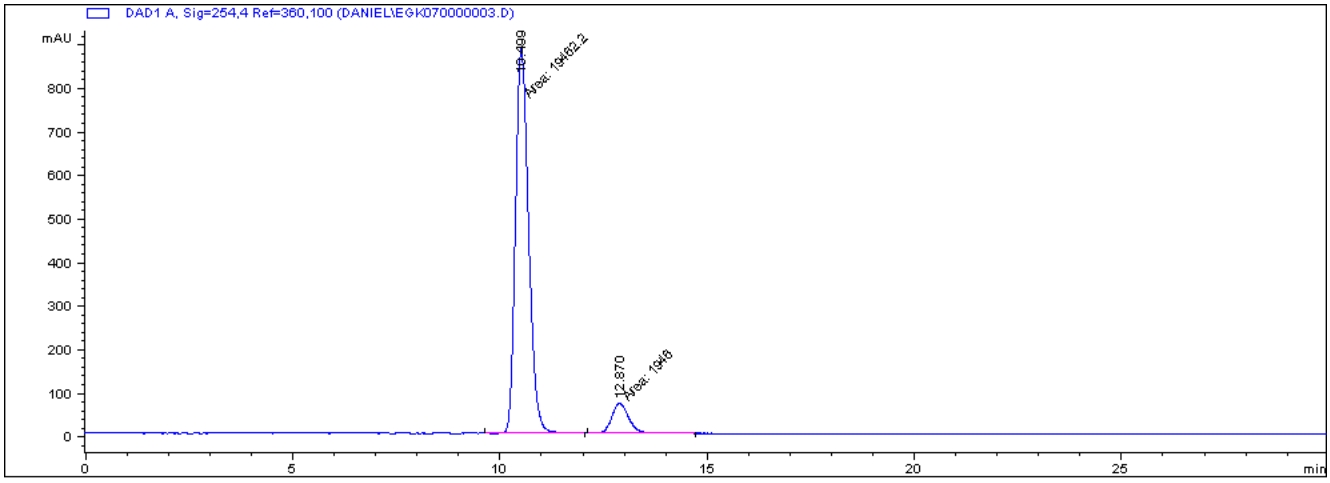
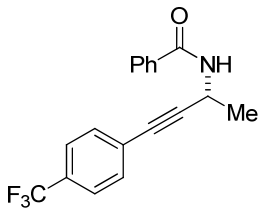
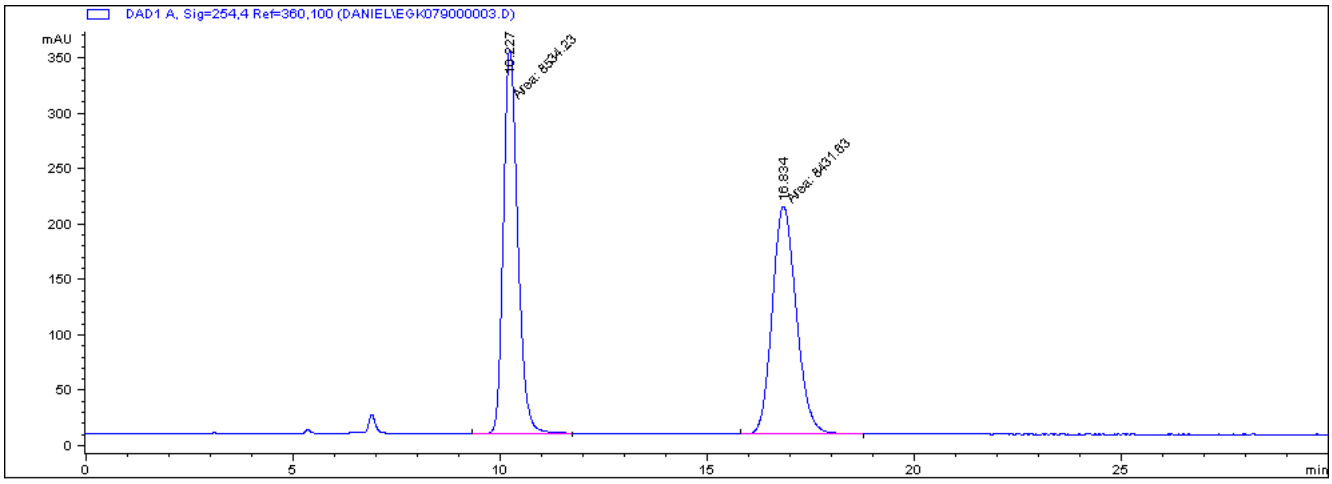


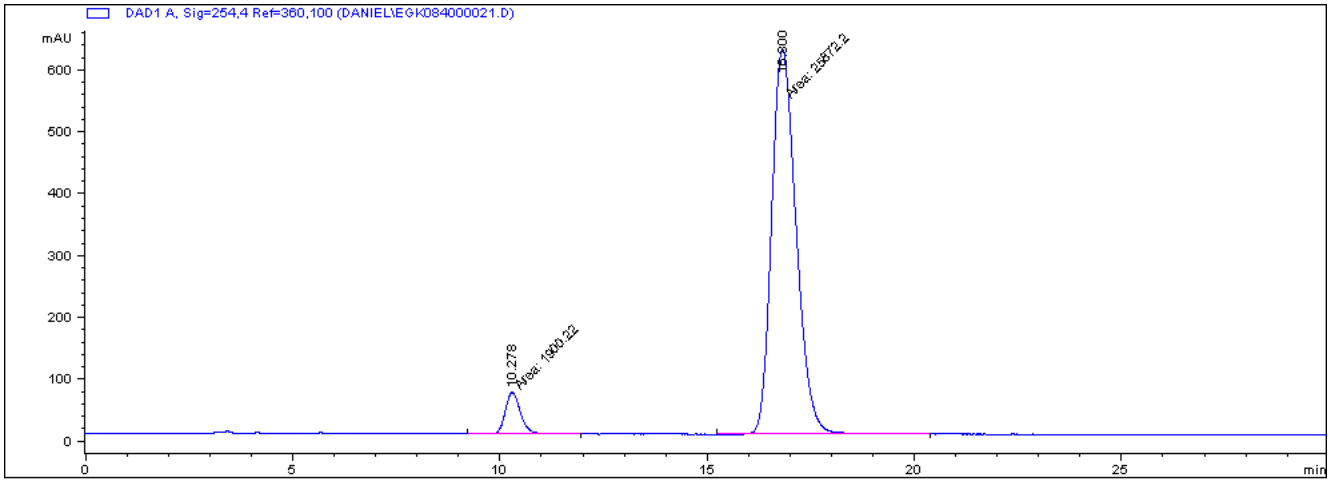


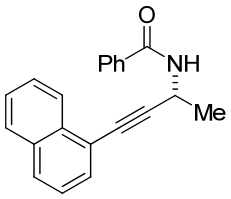


HPLC profile of **8h**

Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm







HPLC profile of **8i**

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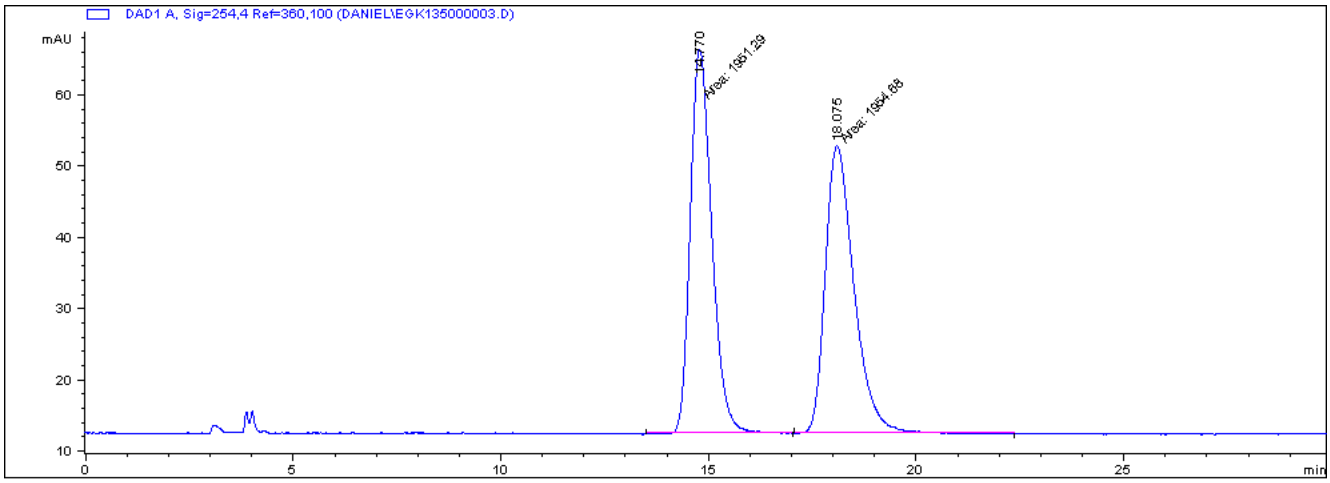
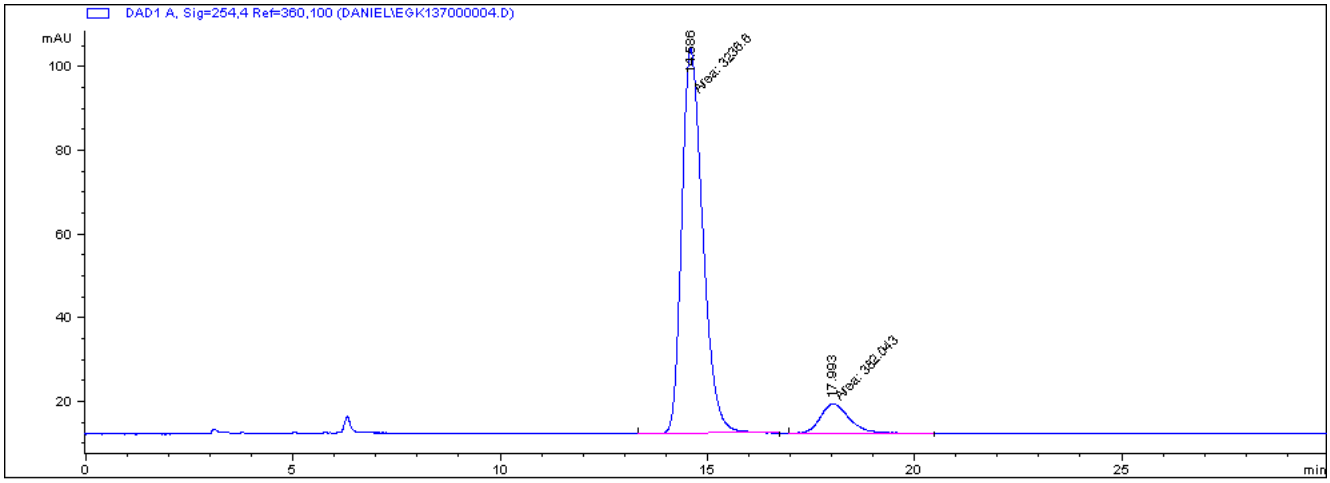
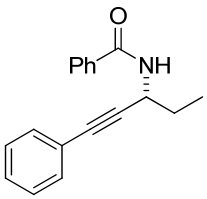
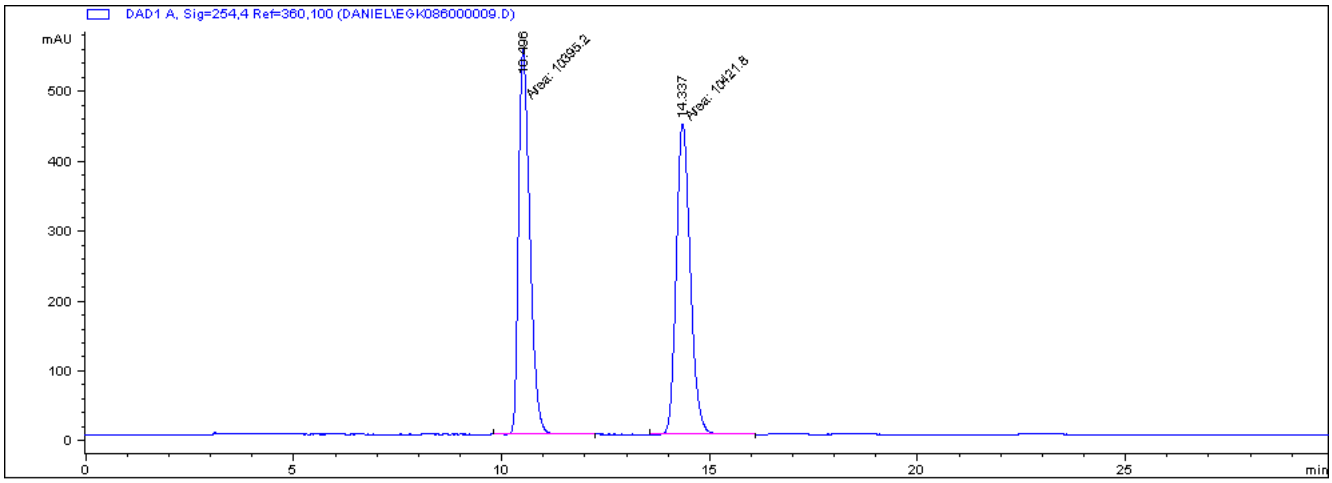


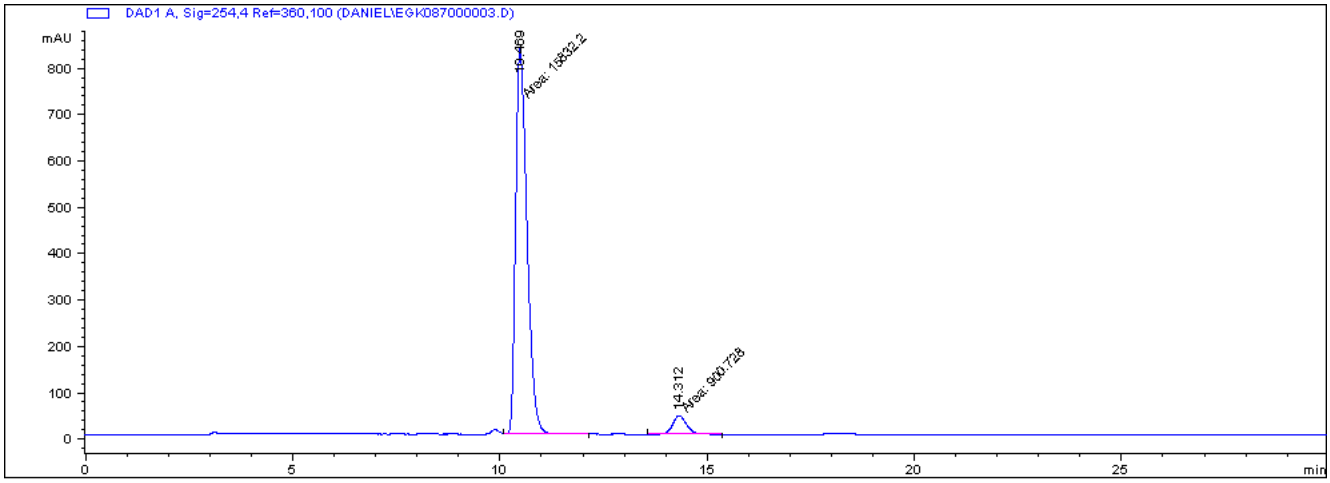


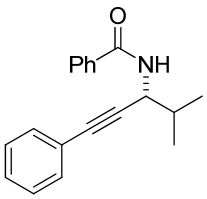


HPLC profile of 8j

Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm

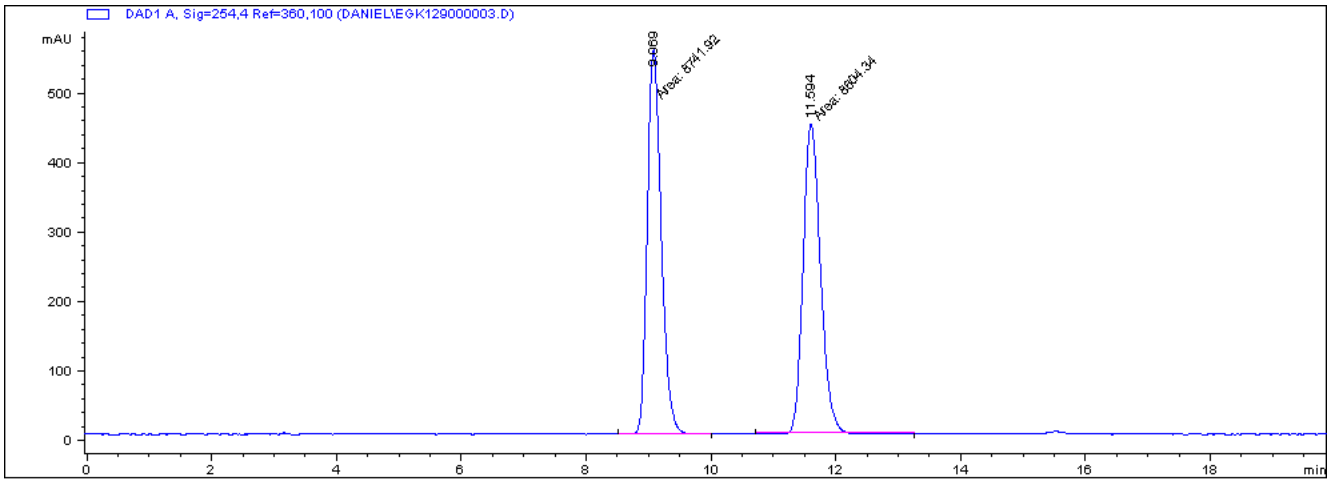


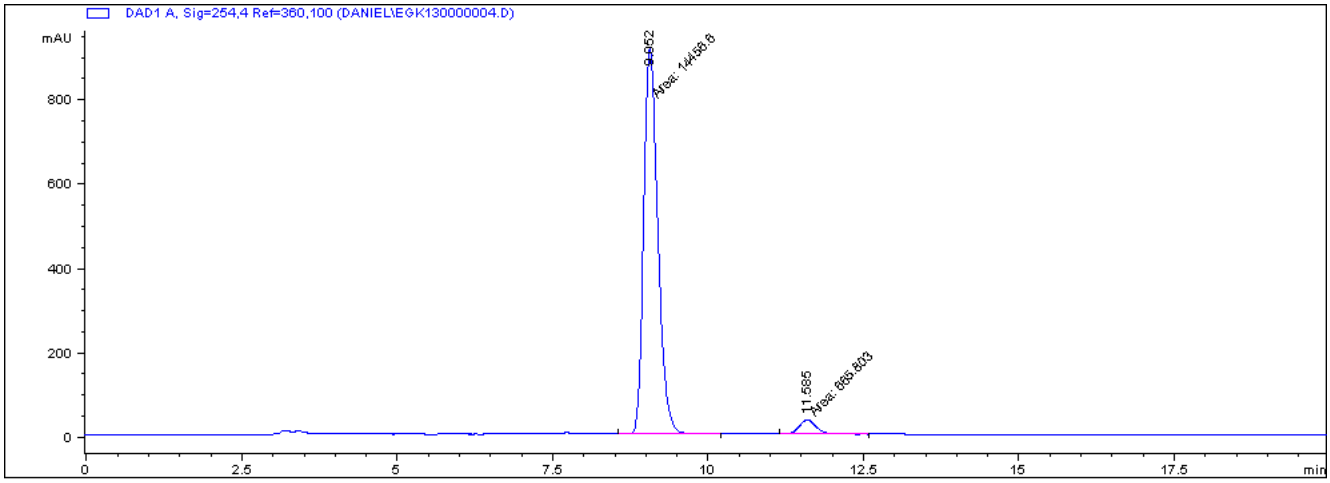


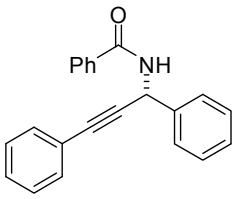


HPLC profile of **8k**

Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm

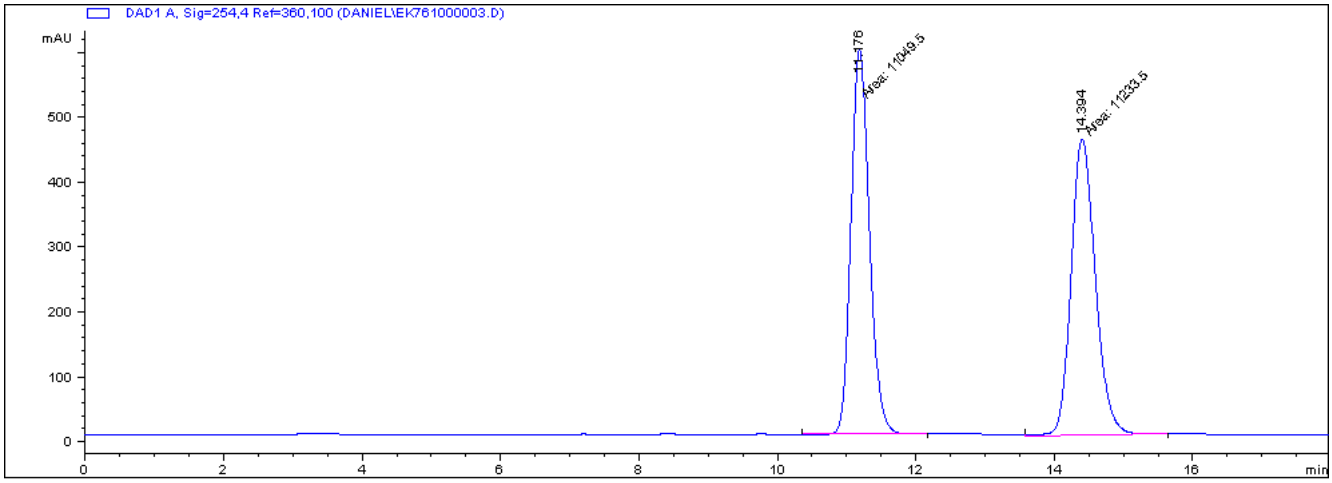


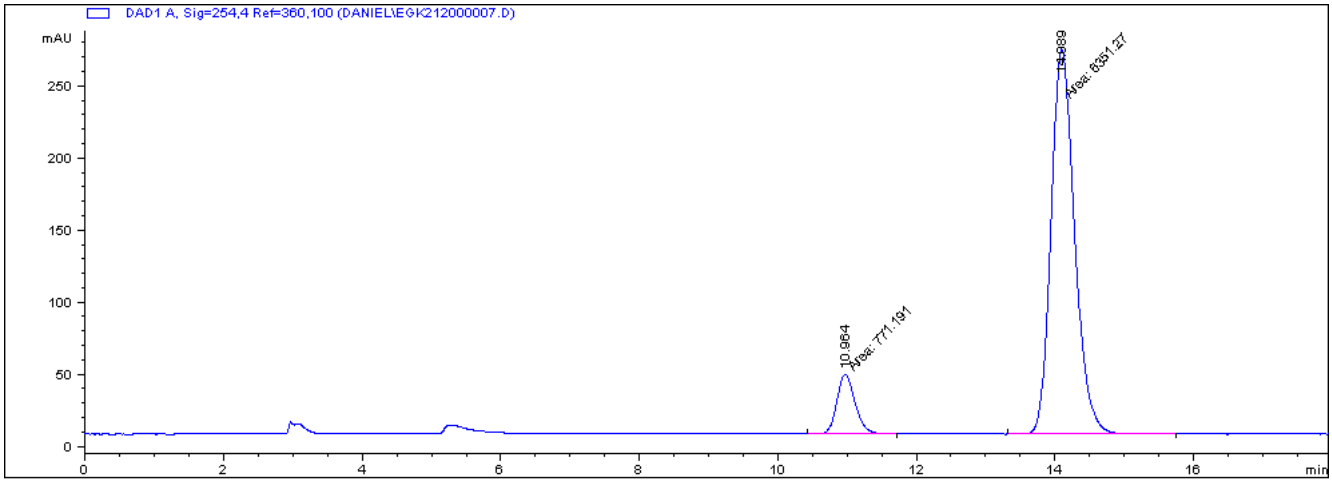


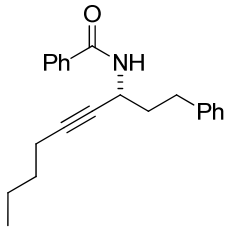


HPLC profile of **8l**

Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, Flow rate = 1 mL/min, UV = 254 nm

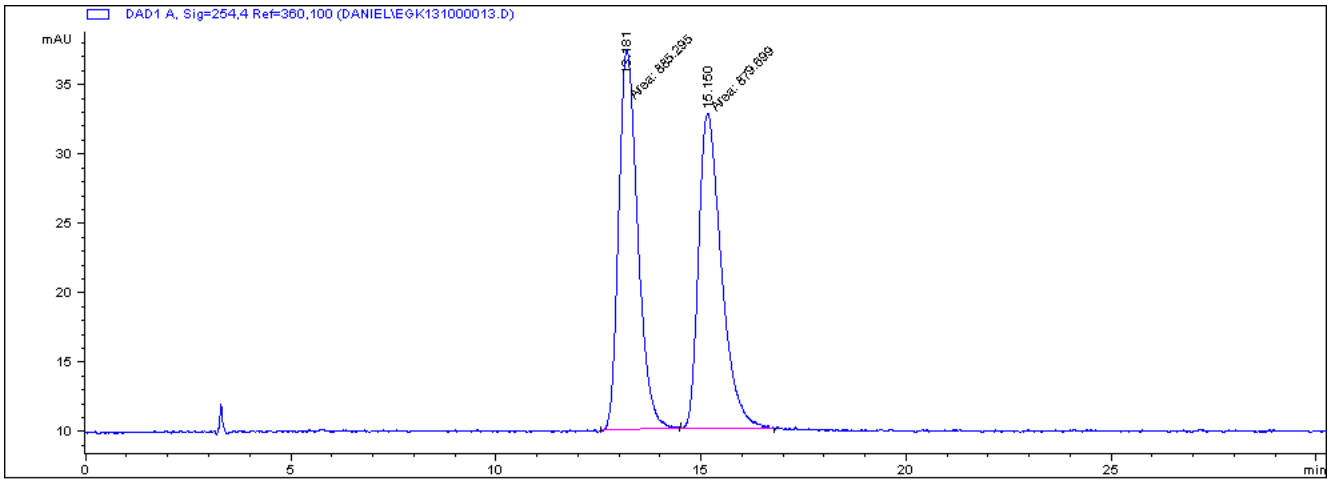


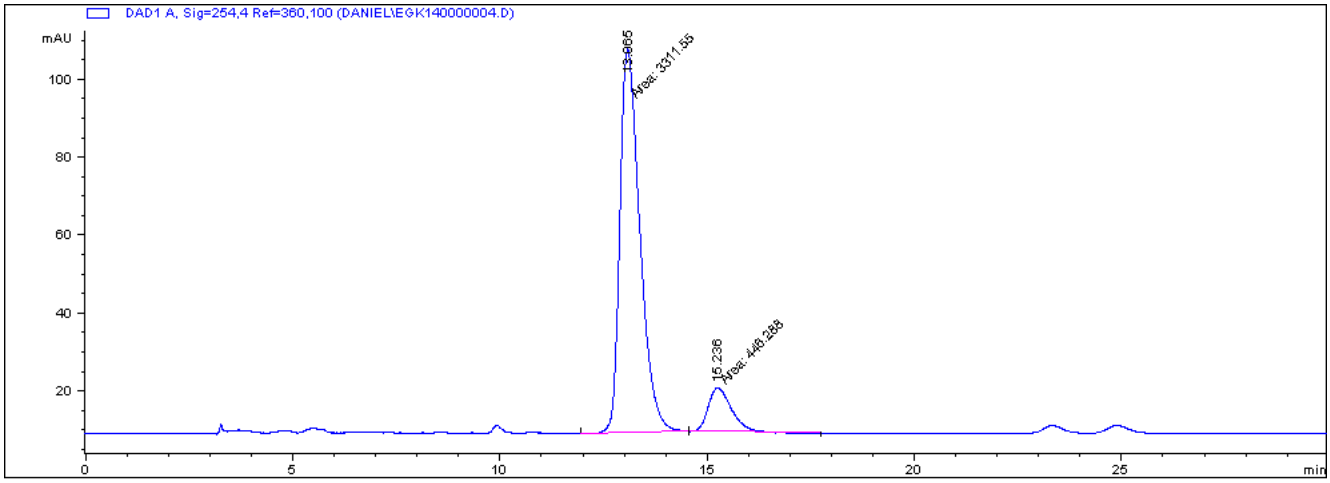


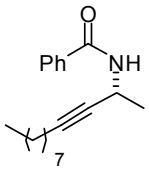


HPLC profile of **8m**

Daicel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 254 nm

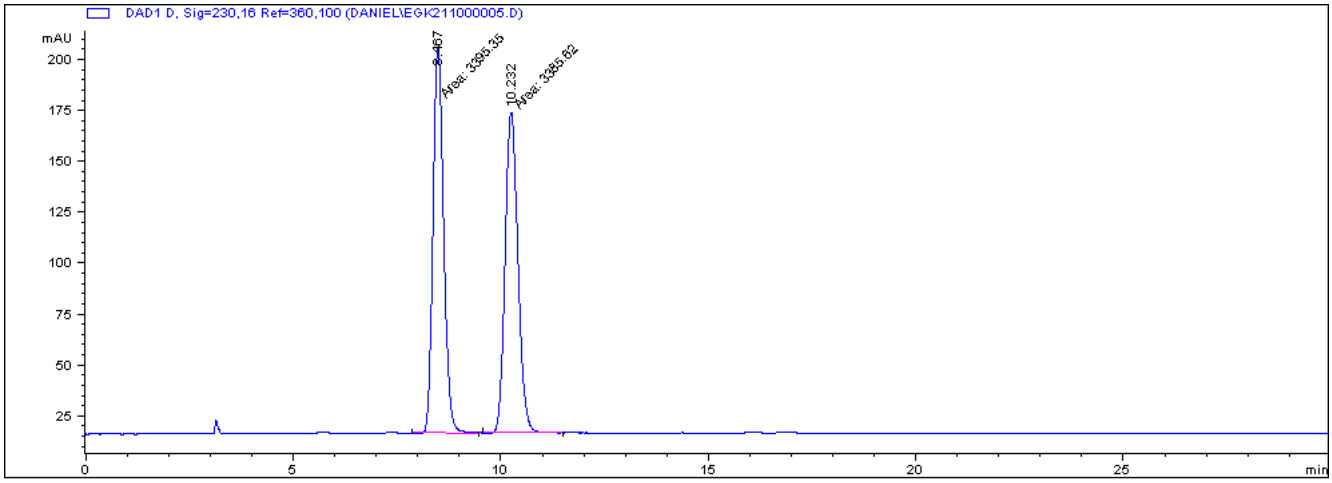


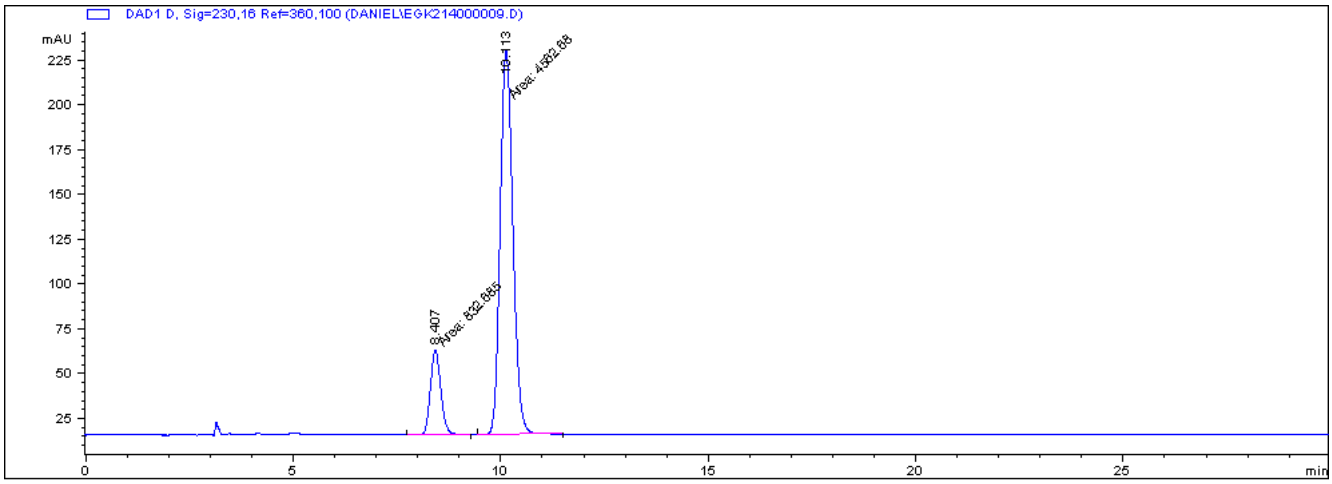


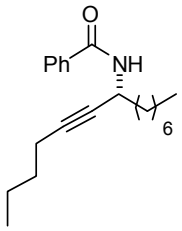


HPLC profile of **8n**

Daicel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm

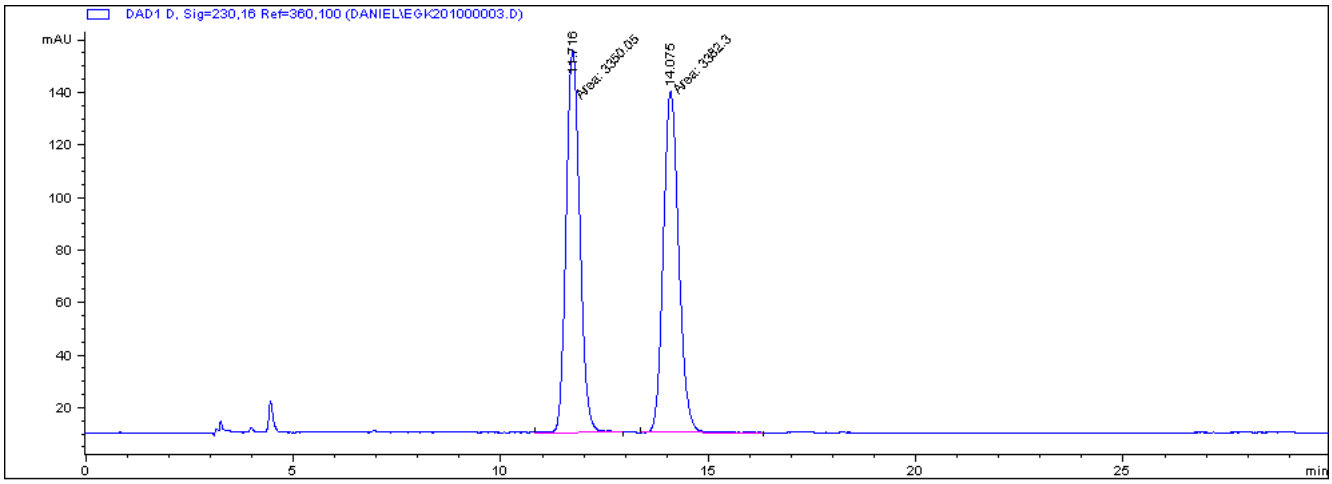


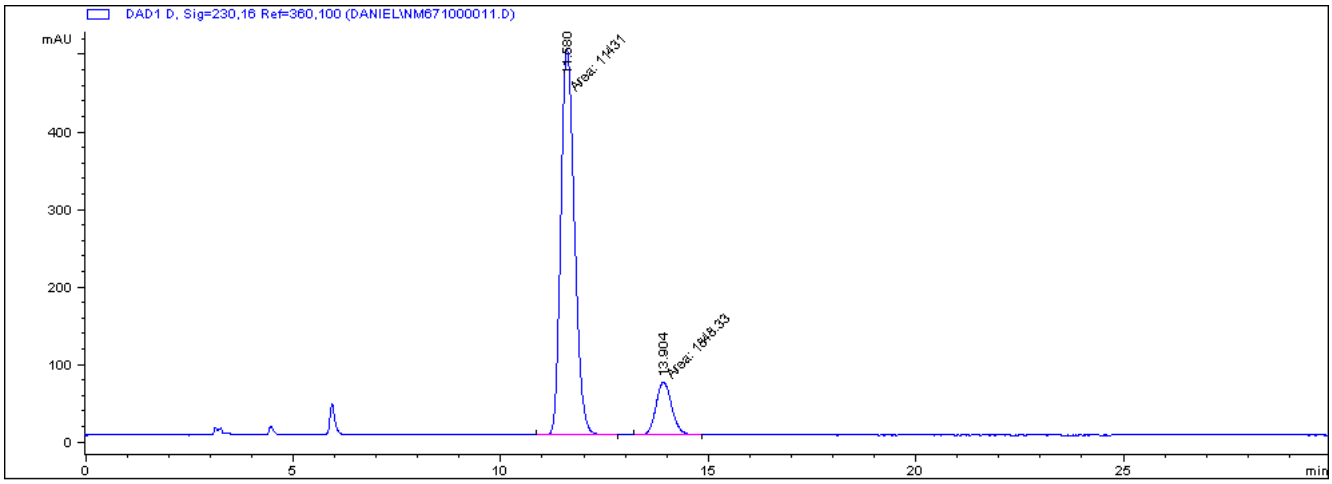


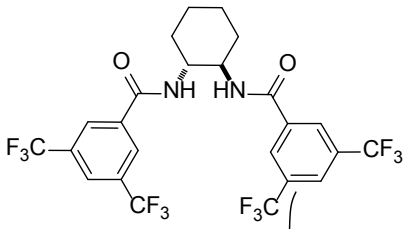


HPLC profile of **8o**

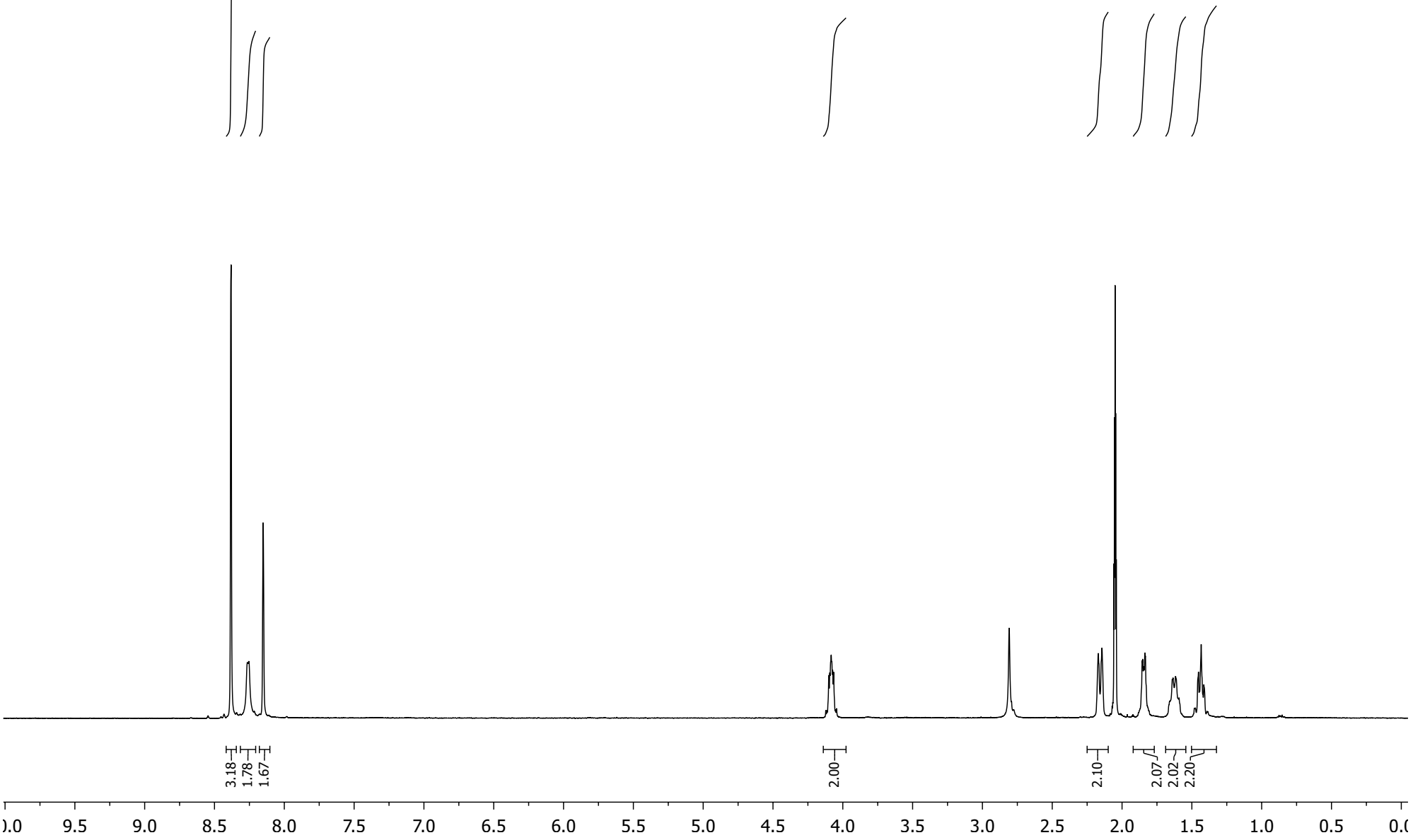
Daicel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 98/2, Flow rate = 1 mL/min, UV = 230 nm

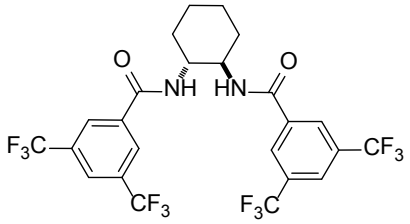




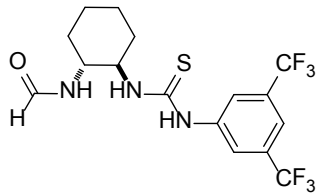

O
NH
HN
O
F3C
CF3
CF3
F3C

^{1}H NMR of **2**

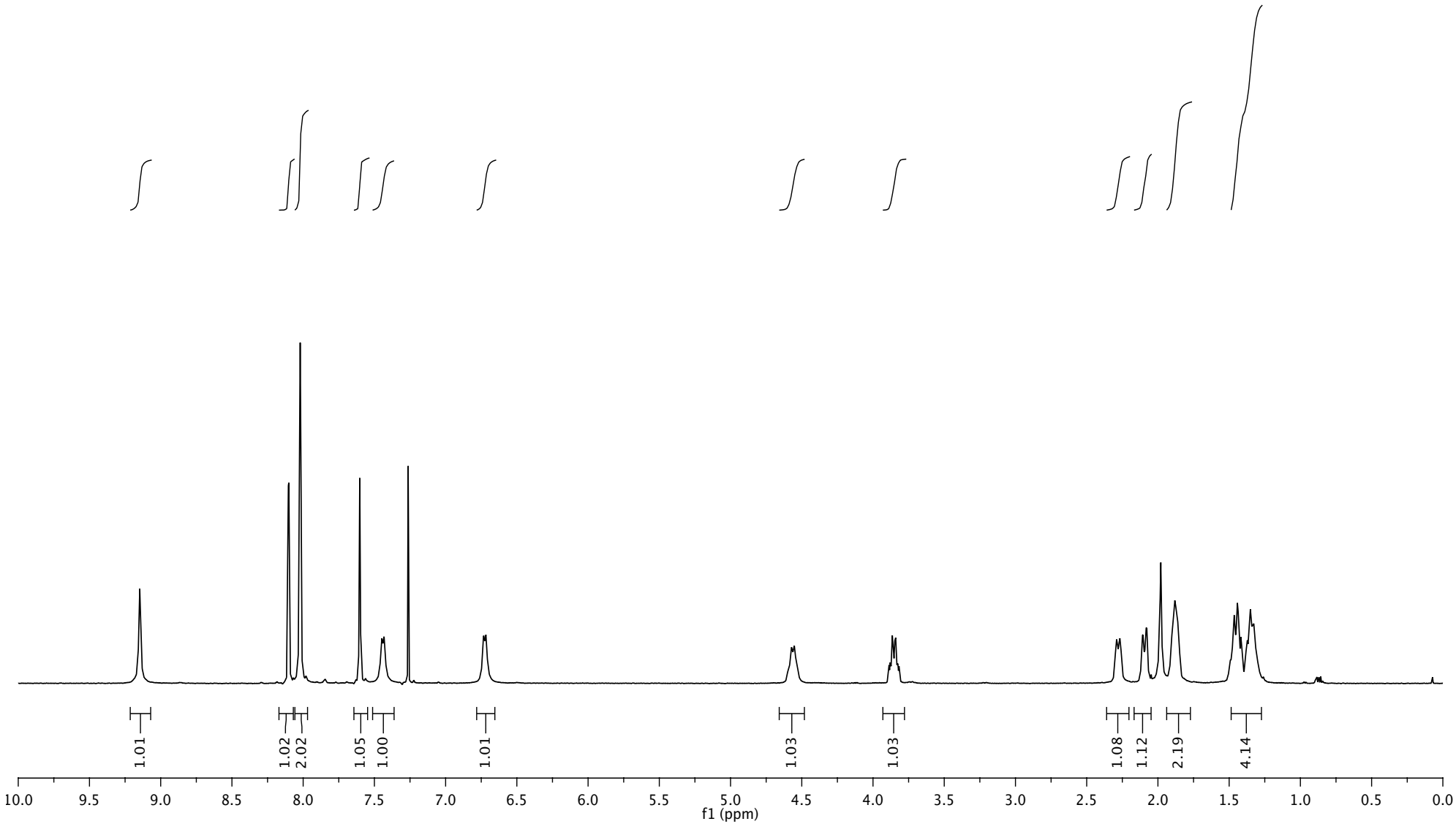

3.18
1.78
1.67
2.00
2.10
2.07
2.02
2.20
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

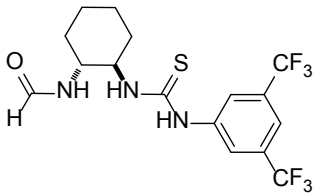


^{13}C NMR of **2**


O
NH
HN
S
HN
CF3
CF3
H

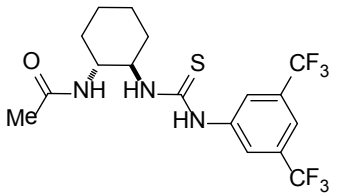
^{1}H NMR of **3a**


1.01
1.02
2.02
1.05
1.00
1.01
1.03
1.03
1.08
1.12
2.19
4.14
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
f1 (ppm)

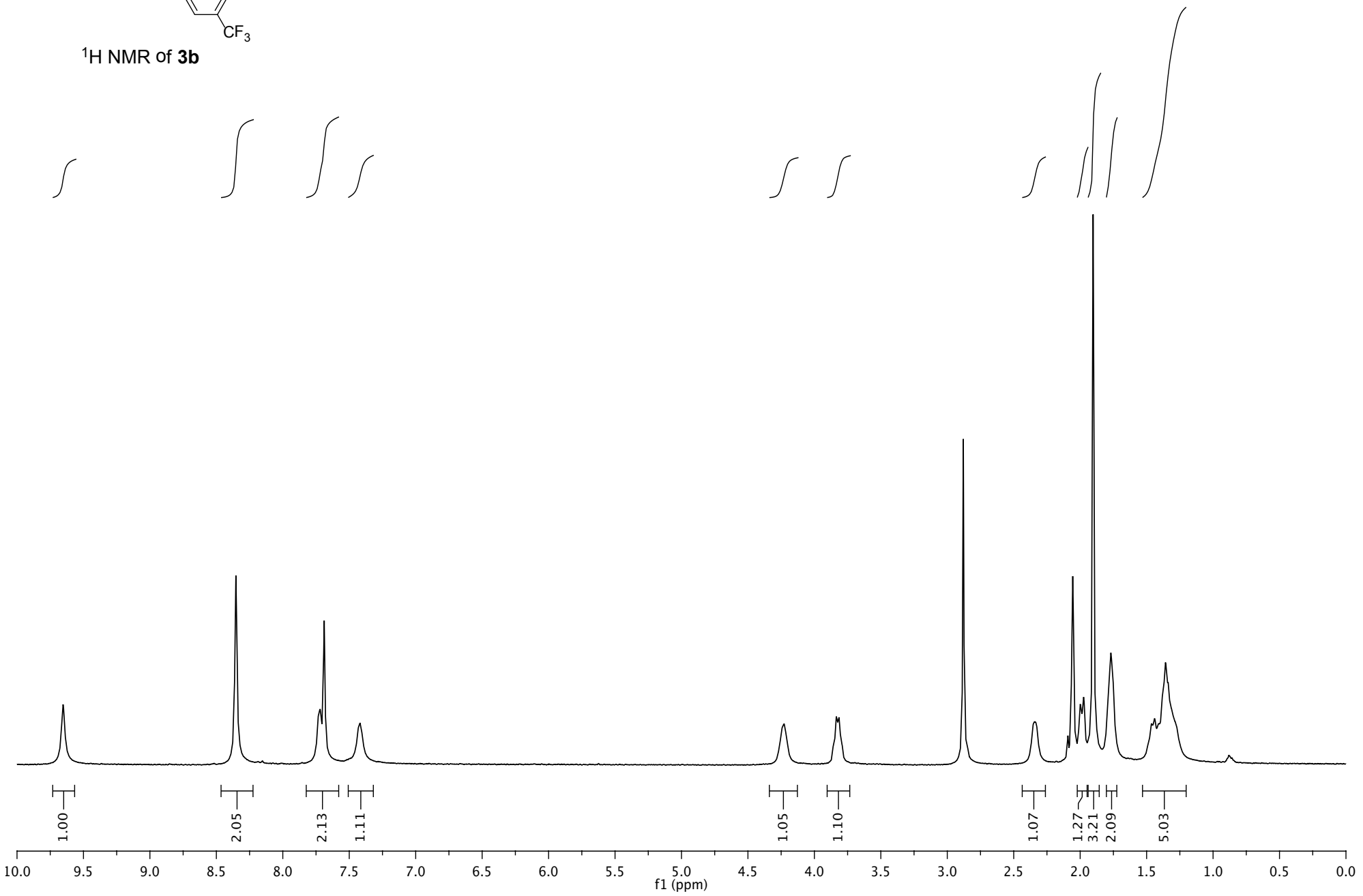

O
S
CF3
NH
HN
HN
H
CF3

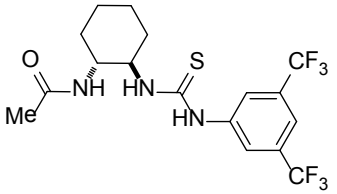
^{13}C NMR of **3a**

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
NH
HN
S
HN
CF3
CF3
Me

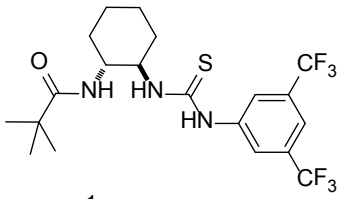
^{1}H NMR of **3b**


1.00
2.05
2.13
1.11
1.05
1.10
1.07
1.27
3.21
2.09
5.03
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
f1 (ppm)


O
NH
HN
S
CF3
Me
HN
CF3

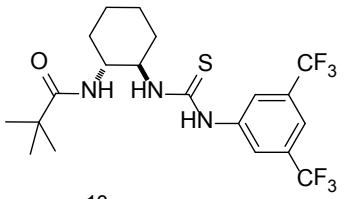
^{13}C NMR of **3b**

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
NH
HN
S
HN
CF3
CF3

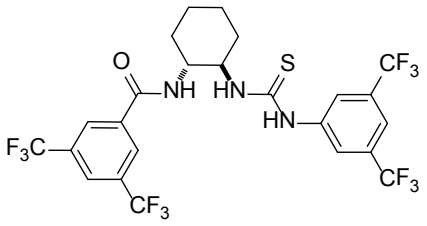
^{1}H NMR of **3c**

1.00
3.13
1.02
1.00
1.00
1.00
1.04
1.14
2.24
4.38
9.39
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
f1 (ppm)

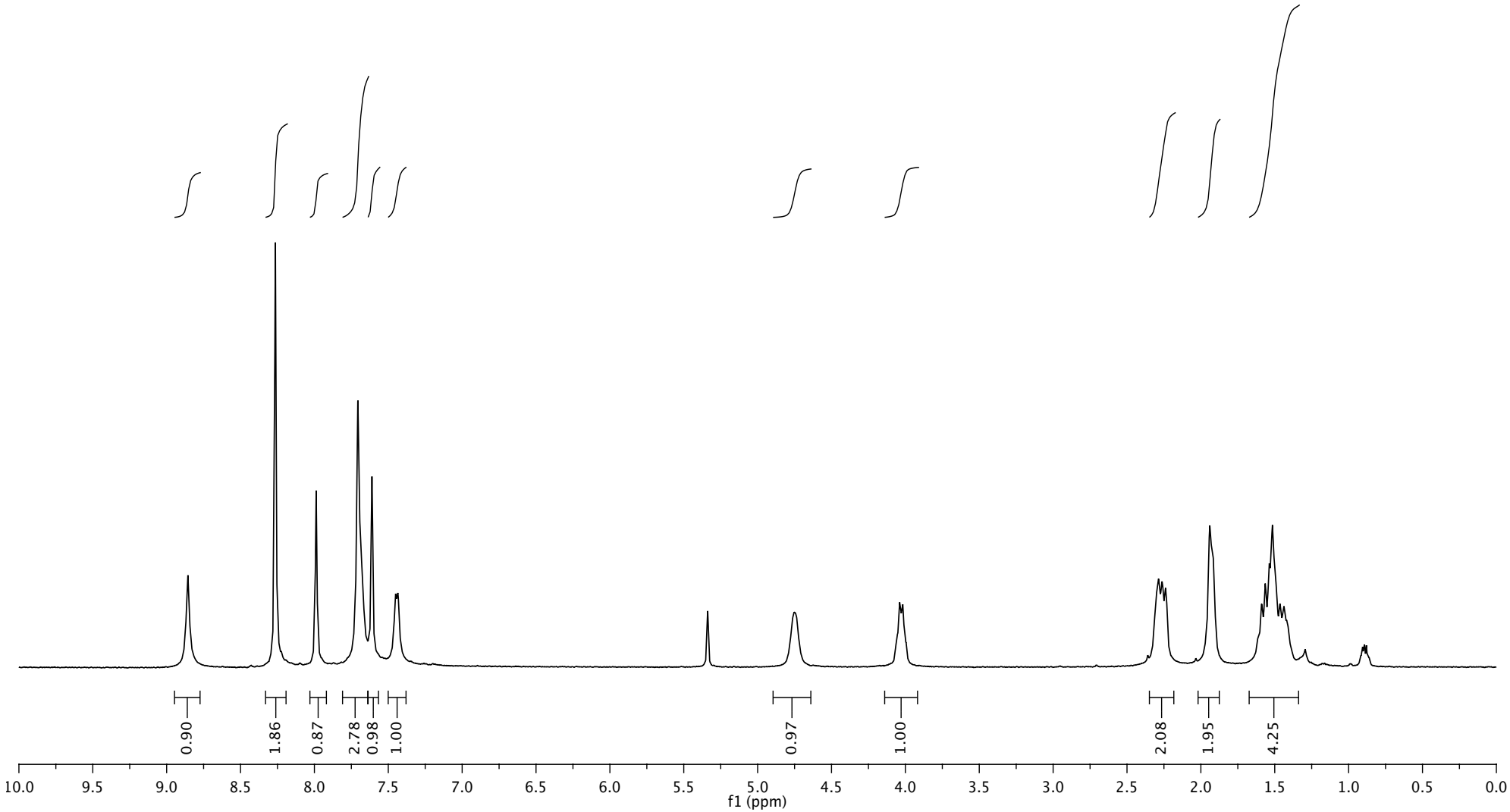

O
NH
HN
S
HN
CF3
CF3

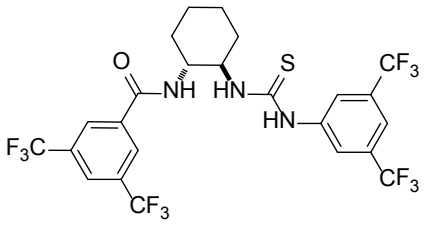
^{13}C NMR of **3c**

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

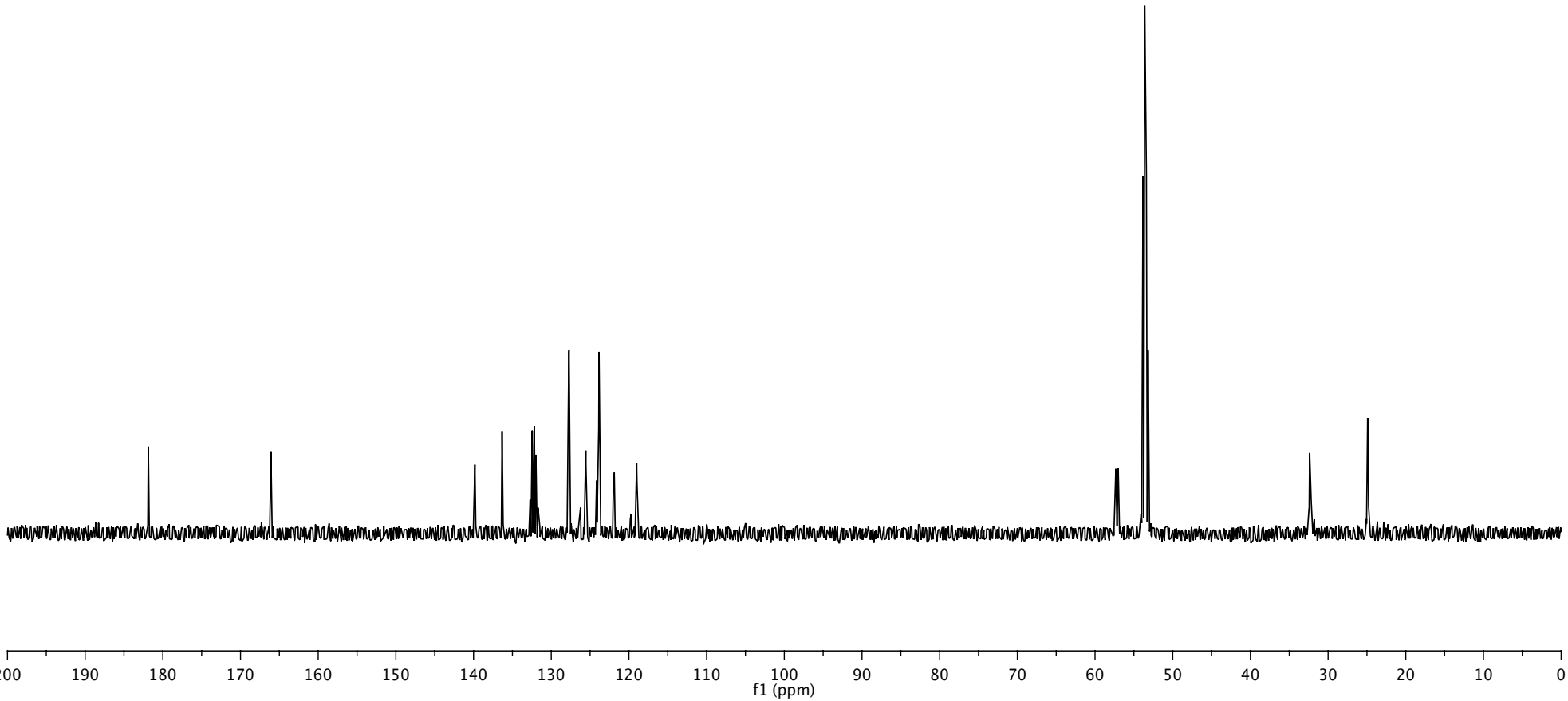

O
NH
HN
S
HN
CF3
CF3
F3C
CF3

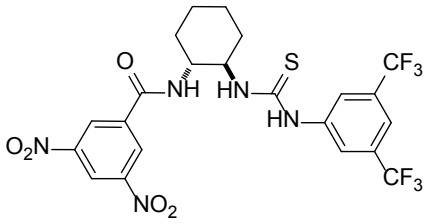
^{1}H NMR of **4a**


0.90
1.86
0.87
2.78
0.98
1.00
0.97
1.00
2.08
1.95
4.25
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
f1 (ppm)

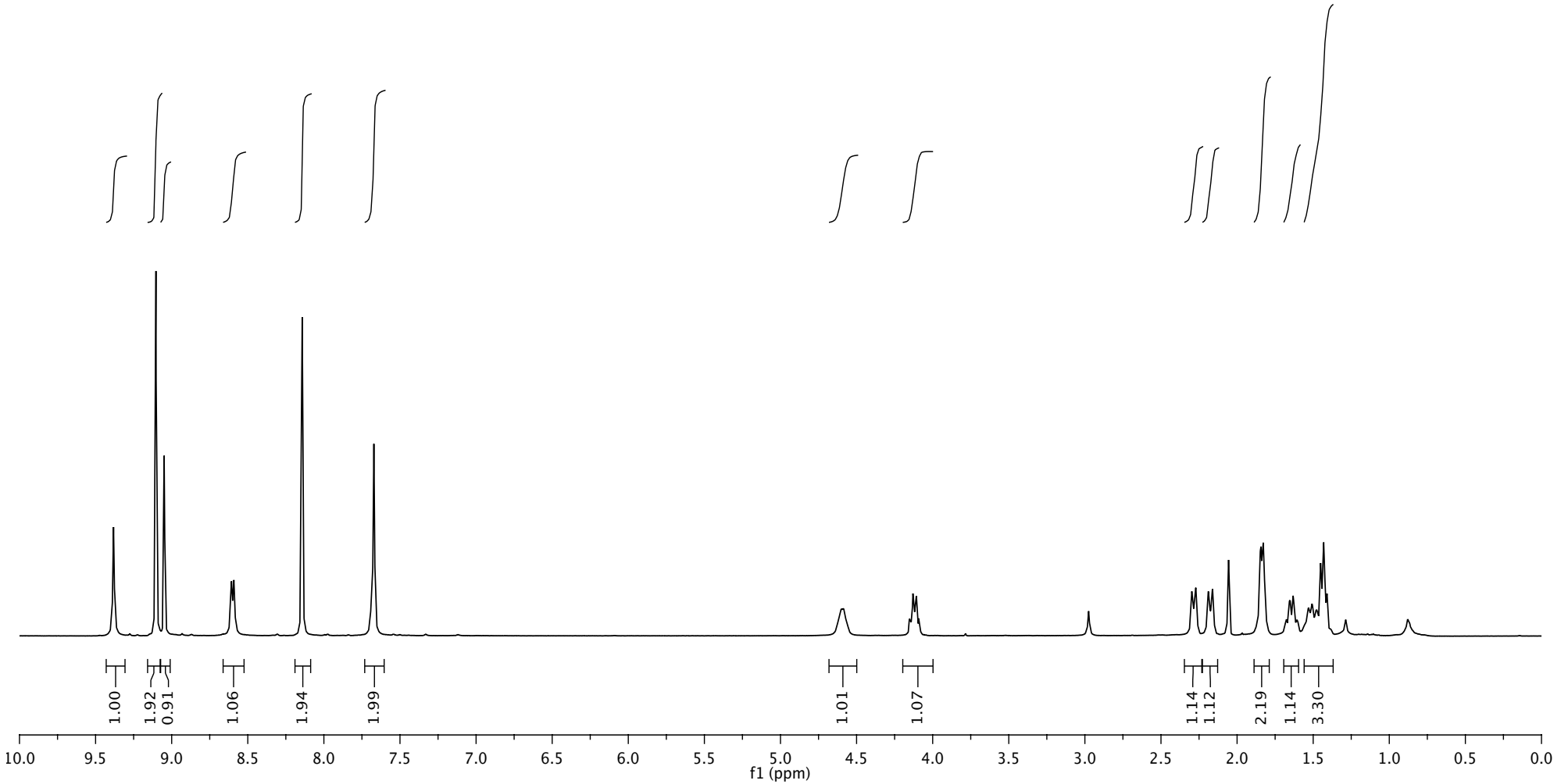

O
NH
HN
S
HN
CF3
CF3
F3C
CF3

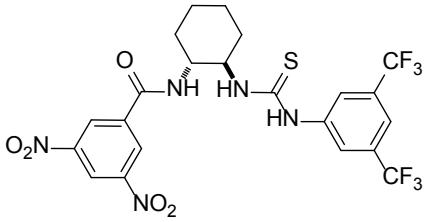
^{13}C NMR of **4a**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

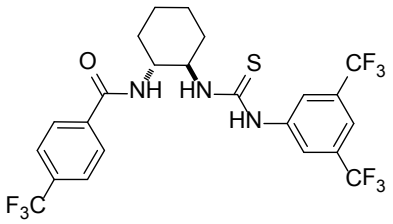

O
NH
HN
S
HN
CF3
CF3
O2N
NO2

^{1}H NMR of **4b**

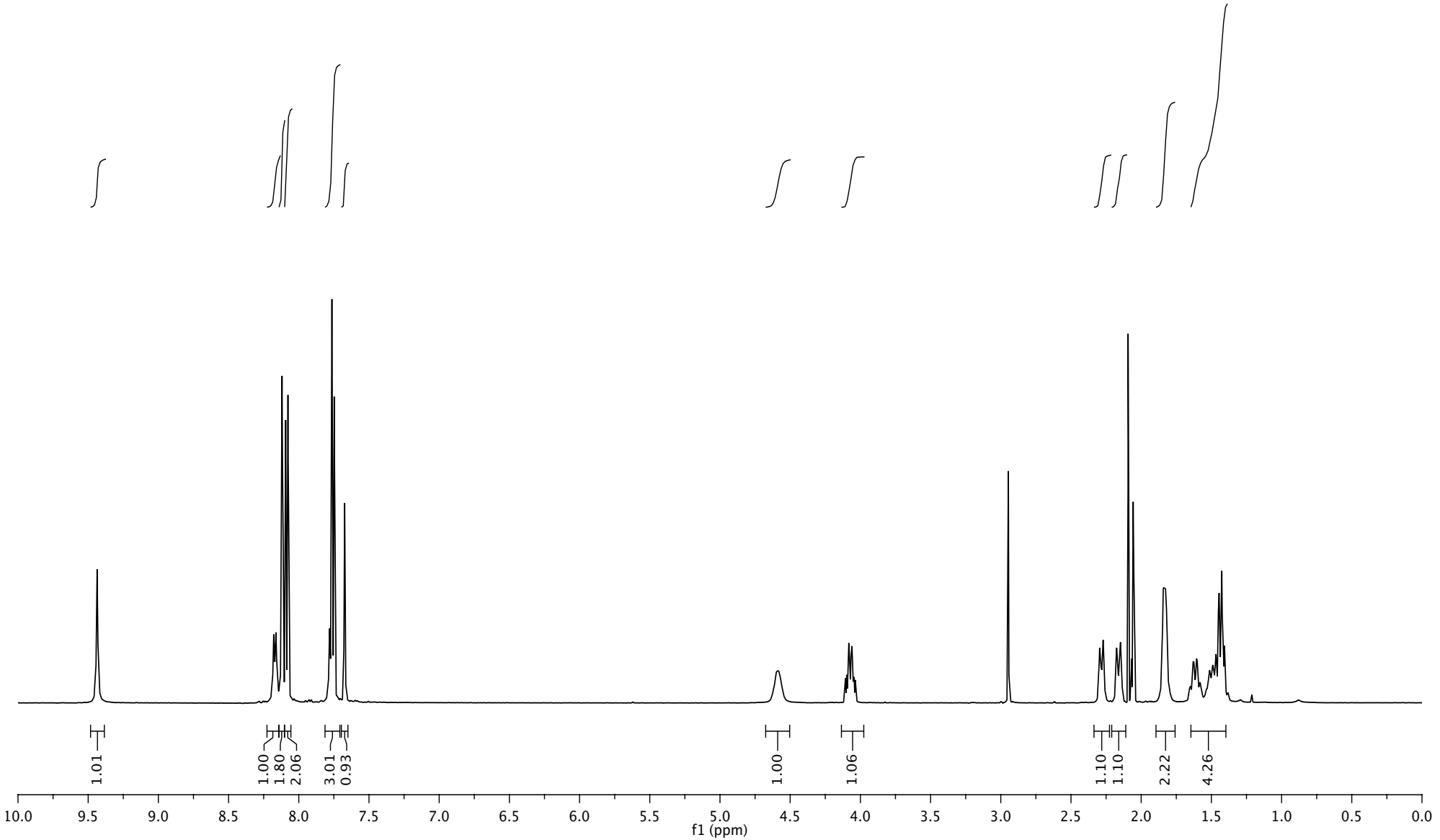

1.00
1.92
0.91
1.06
1.94
1.99
1.01
1.07
1.14
1.12
2.19
1.14
3.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

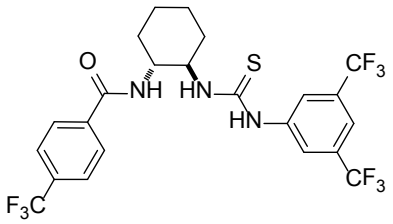


^{13}C NMR of **4b**

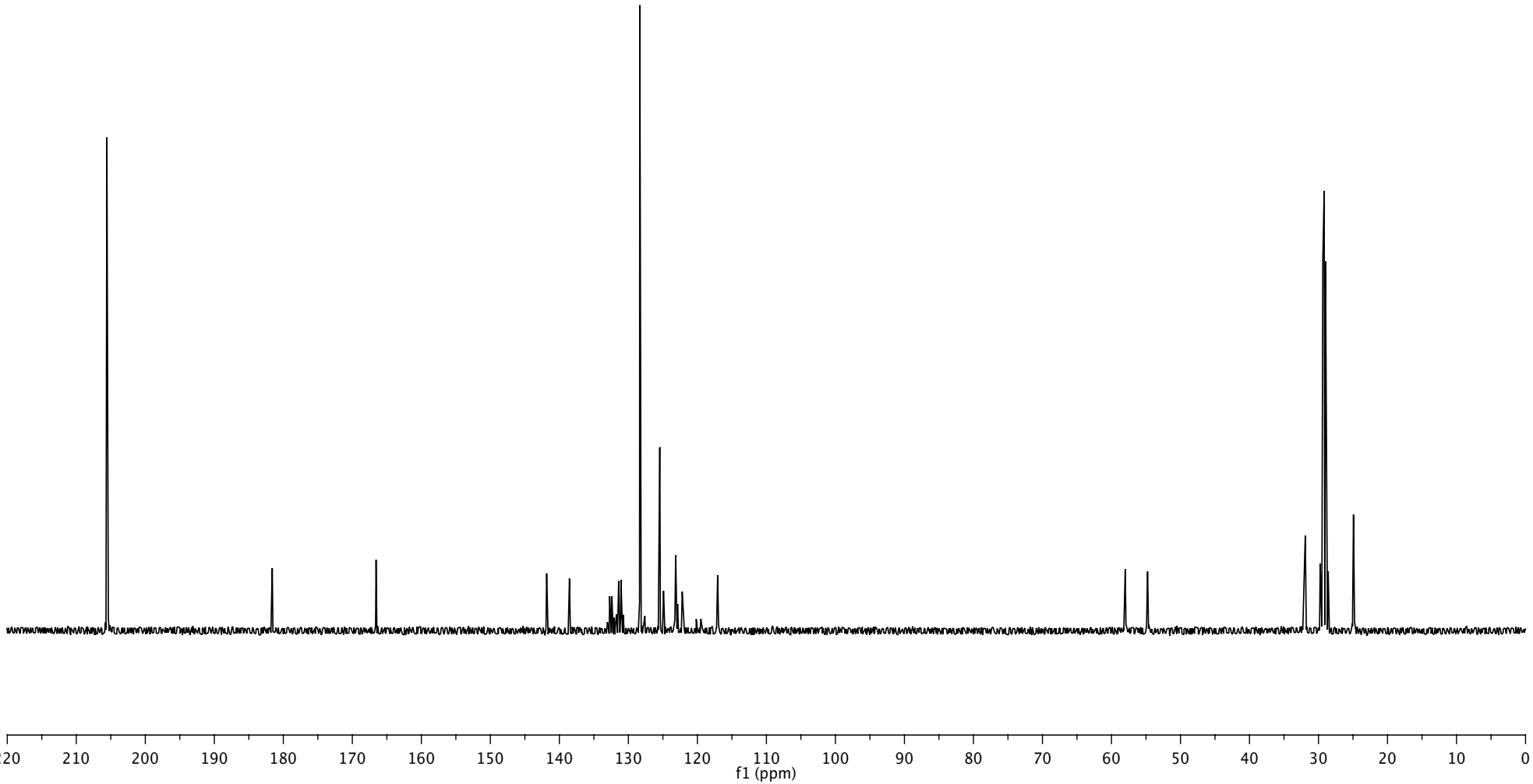

O
NH
HN
S
HN
CF3
CF3
F3C

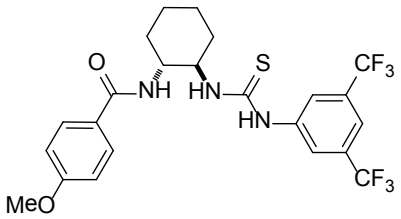
^{1}H NMR of **4c**


1.01
1.00
1.80
2.06
3.01
0.93
1.00
1.06
1.10
1.10
2.22
4.26
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
f1 (ppm)

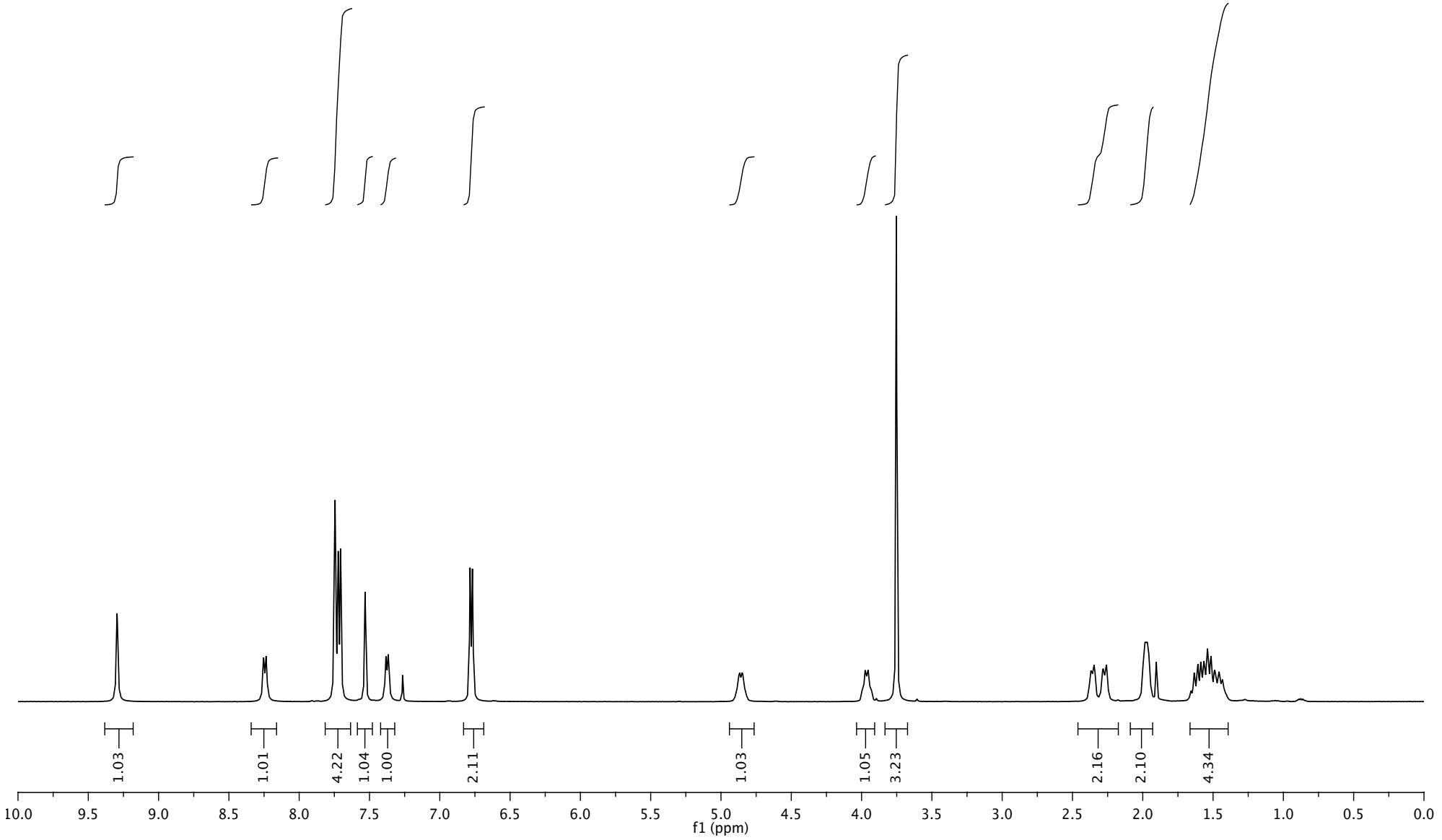

O
NH
HN
S
HN
CF3
CF3
F3C

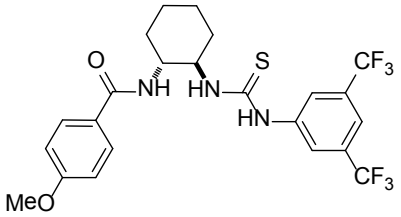
^{13}C NMR of **4c**


220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

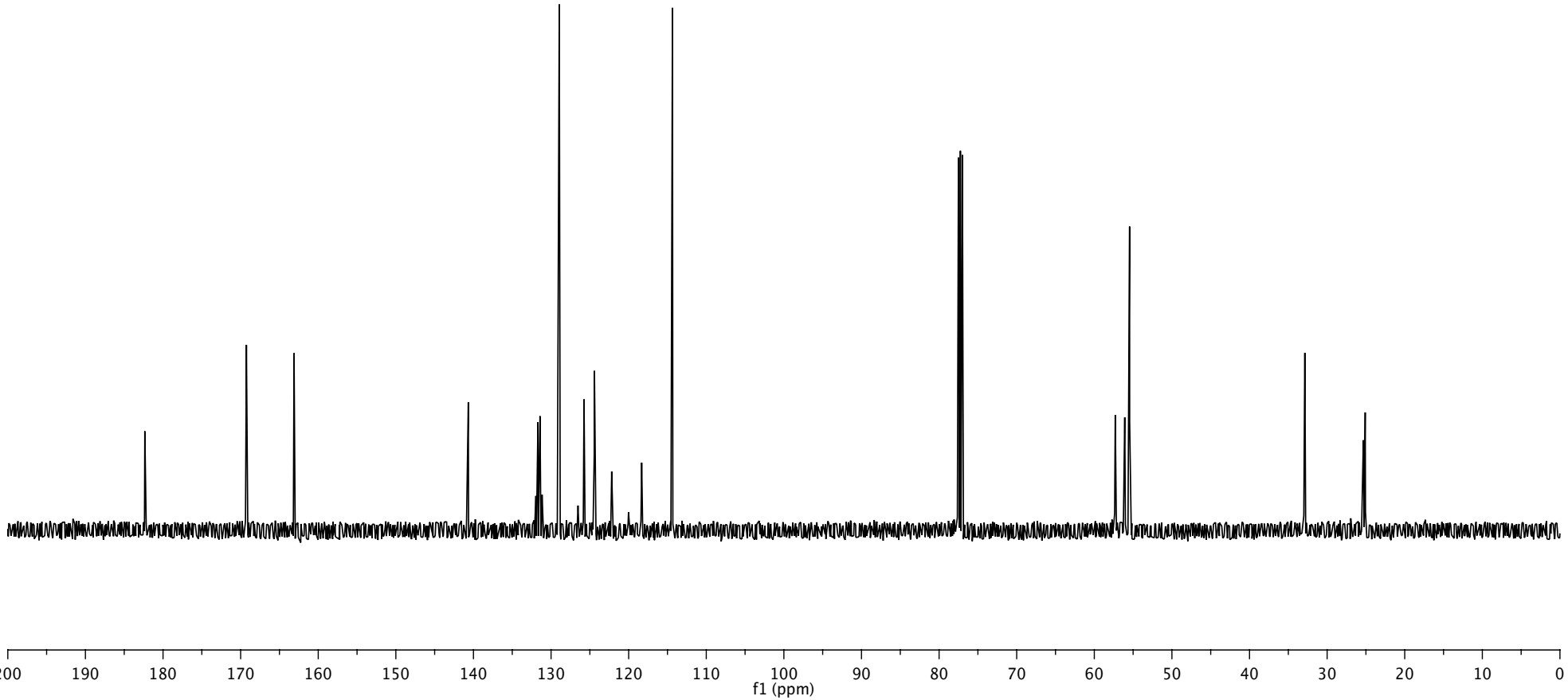

O
NH
HN
S
HN
CF3
CF3
MeO

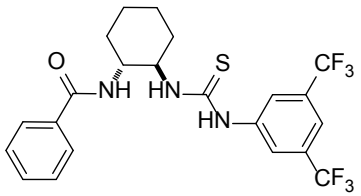
^{1}H NMR of **4d**


1.03
1.01
4.22
1.04
1.00
2.11
1.03
1.05
3.23
2.16
2.10
4.34
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
f1 (ppm)

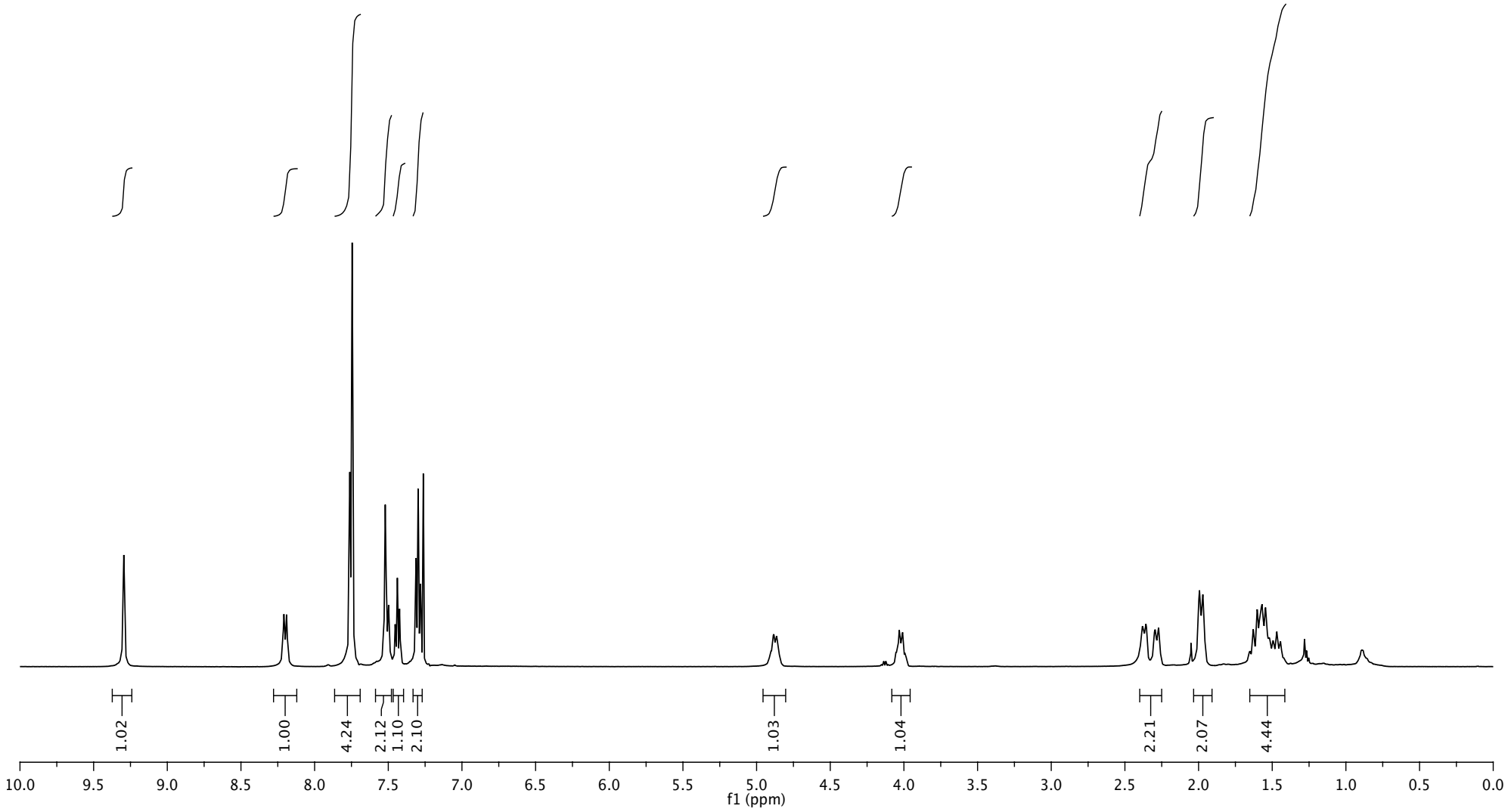

O
NH
HN
S
HN
CF3
CF3
MeO

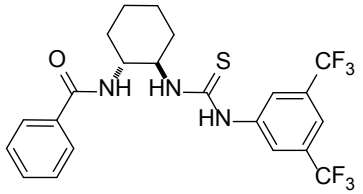
^{13}C NMR of **4d**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

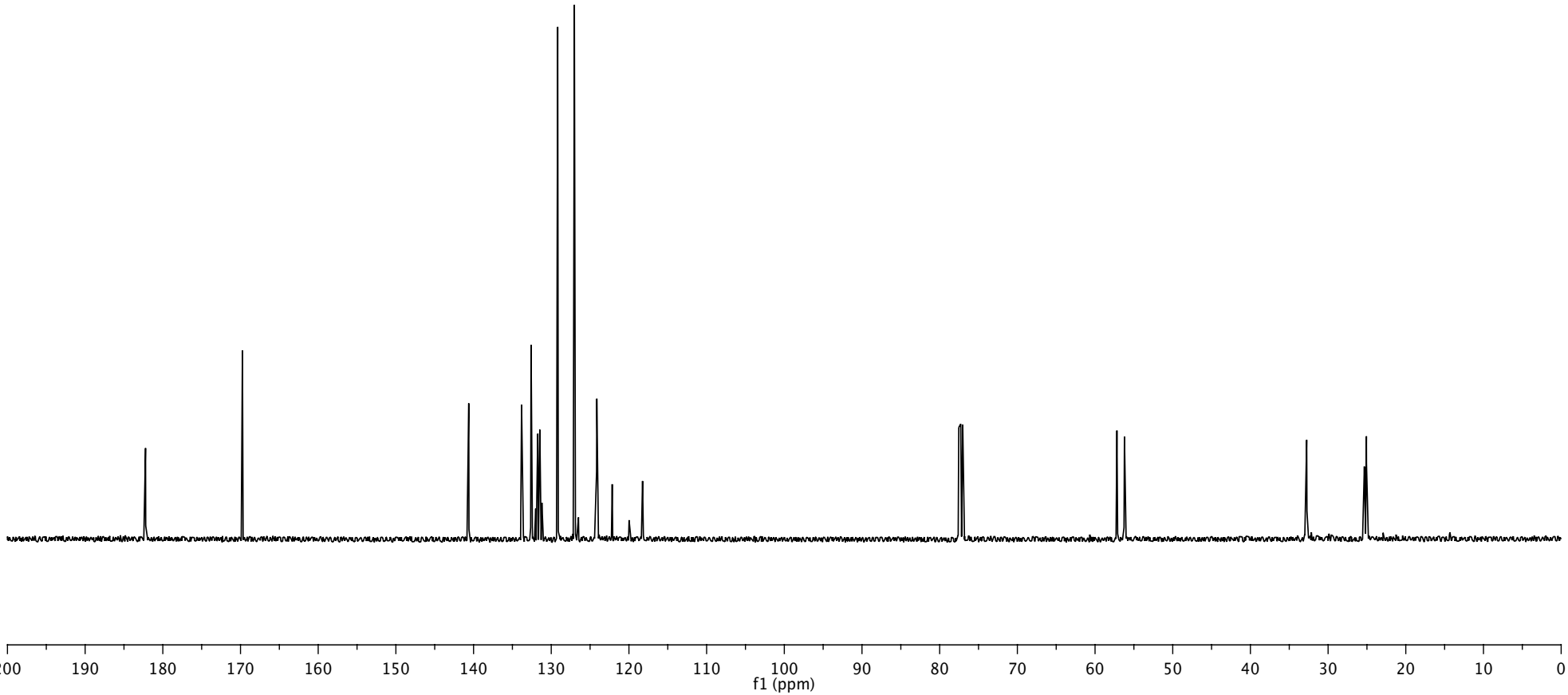

O
NH
HN
S
HN
CF3
CF3

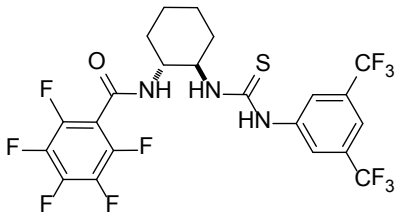
^{1}H NMR of **4e**


1.02
1.00
4.24
2.12
1.10
2.10
1.03
1.04
2.21
2.07
4.44
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
f1 (ppm)

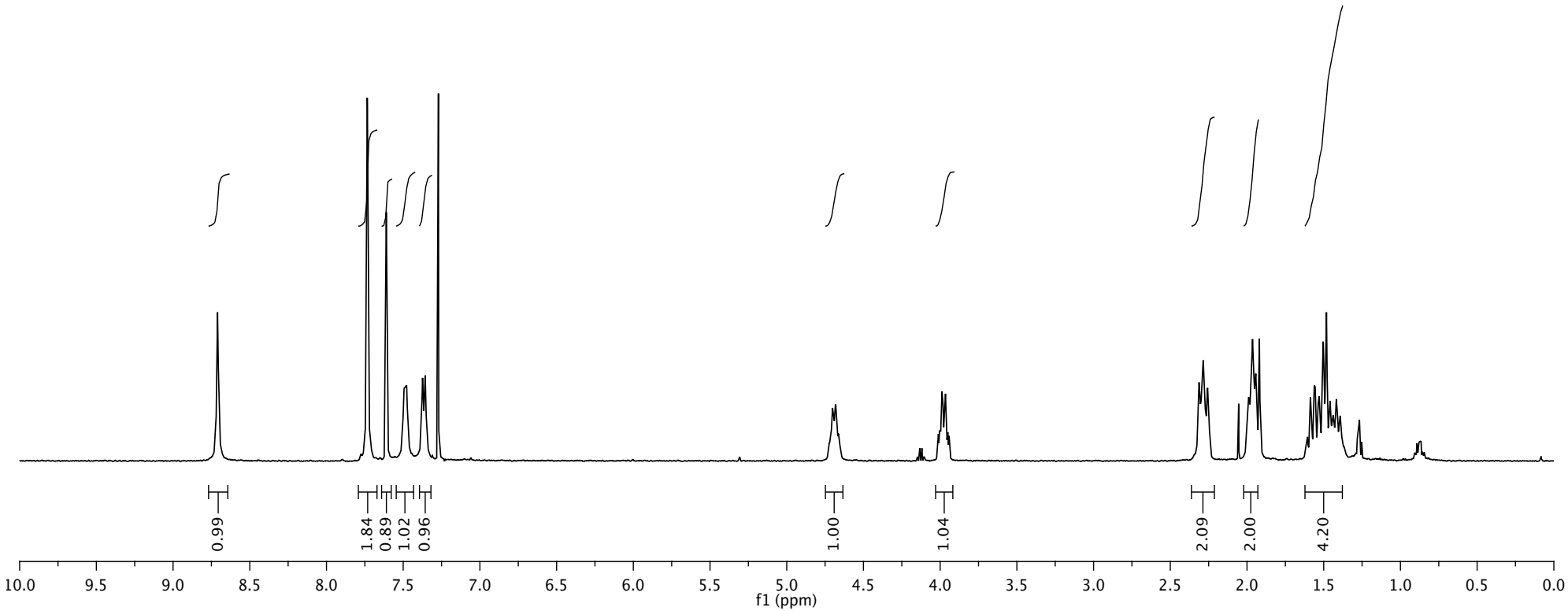

O
NH
HN
S
HN
CF3
CF3

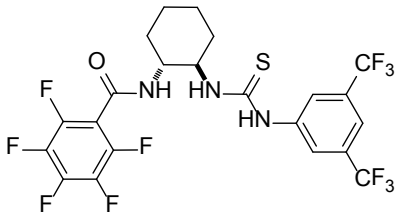
^{13}C NMR of **4e**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
NH
HN
S
HN
CF3
CF3
F
F
F
F
F

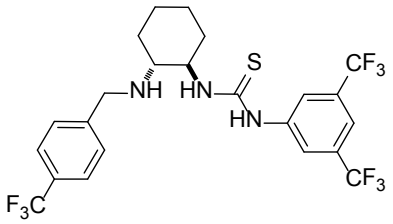
^{1}H NMR of **4f**


0.99
1.84
0.89
1.02
0.96
1.00
1.04
2.09
2.00
4.20
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
f1 (ppm)

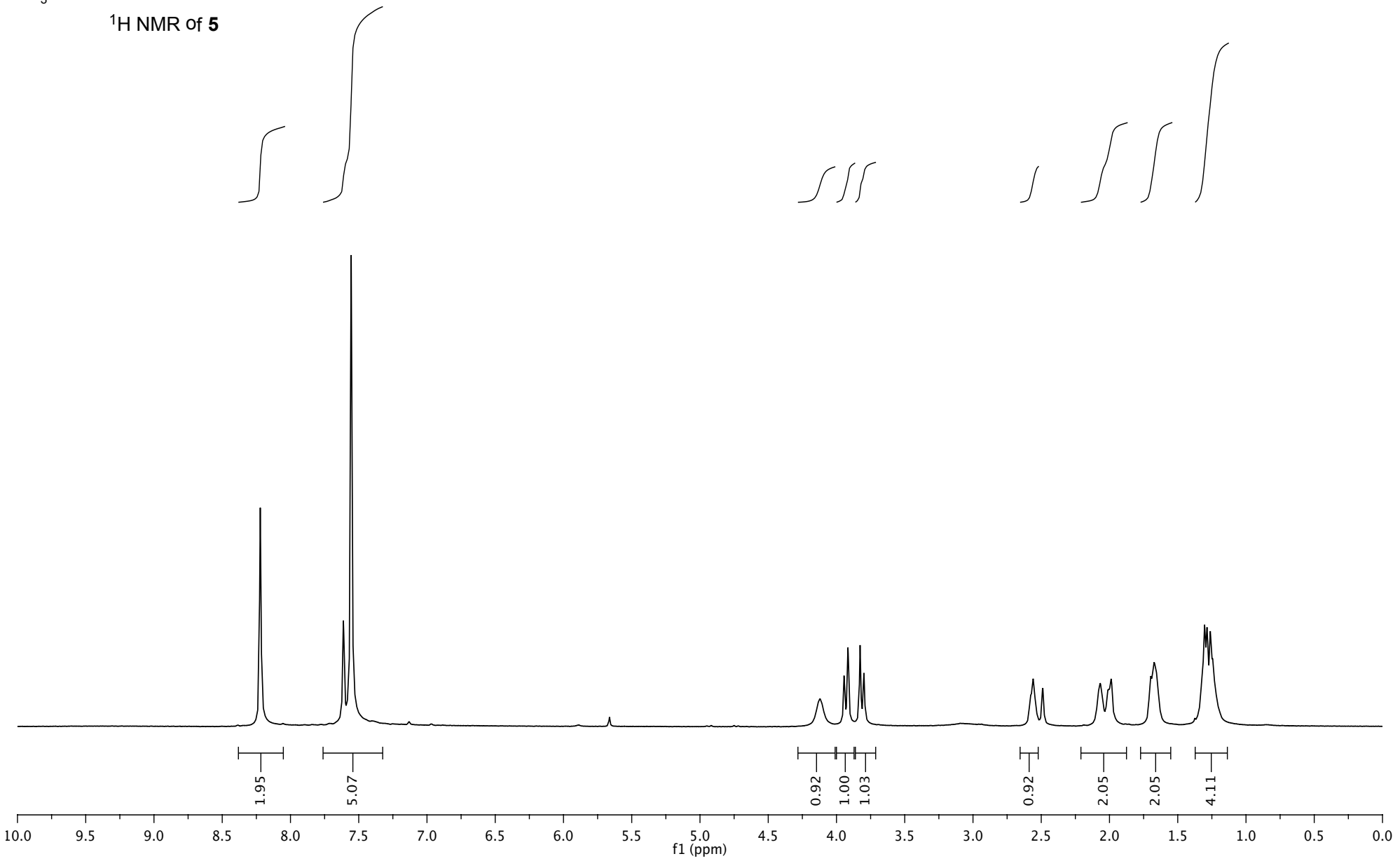

O
S
NH
HN
HN
F
F
F
F
F
CF3
CF3

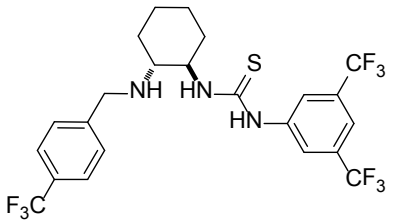
^{13}C NMR of **4f**

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

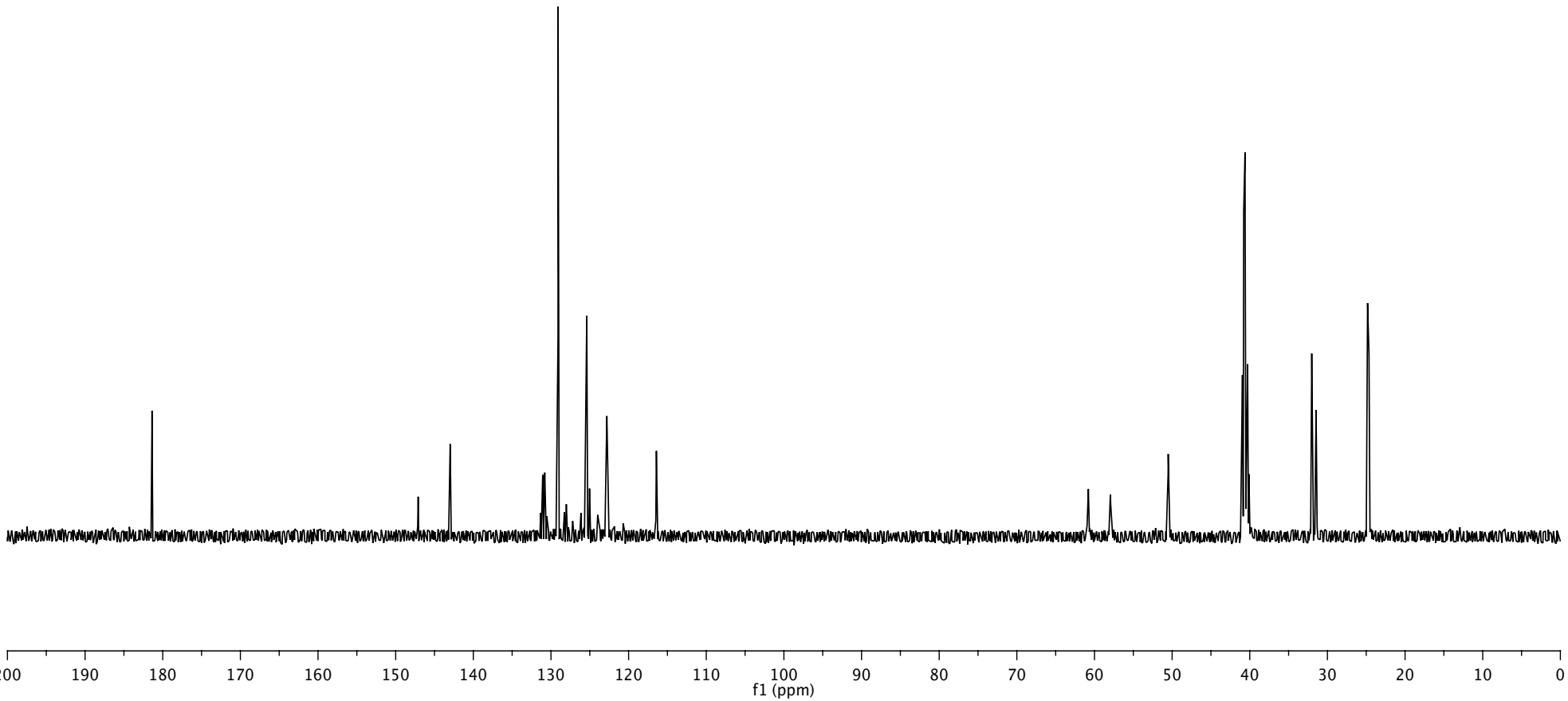

S
CF3
NH
HN
HN
CF3
F3C

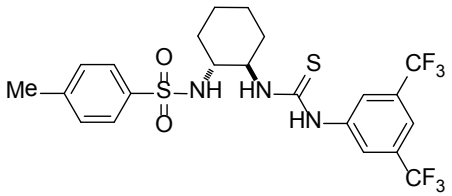
^{1}H NMR of **5**


1.95
5.07
0.92
1.00
1.03
0.92
2.05
2.05
4.11
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
f1 (ppm)

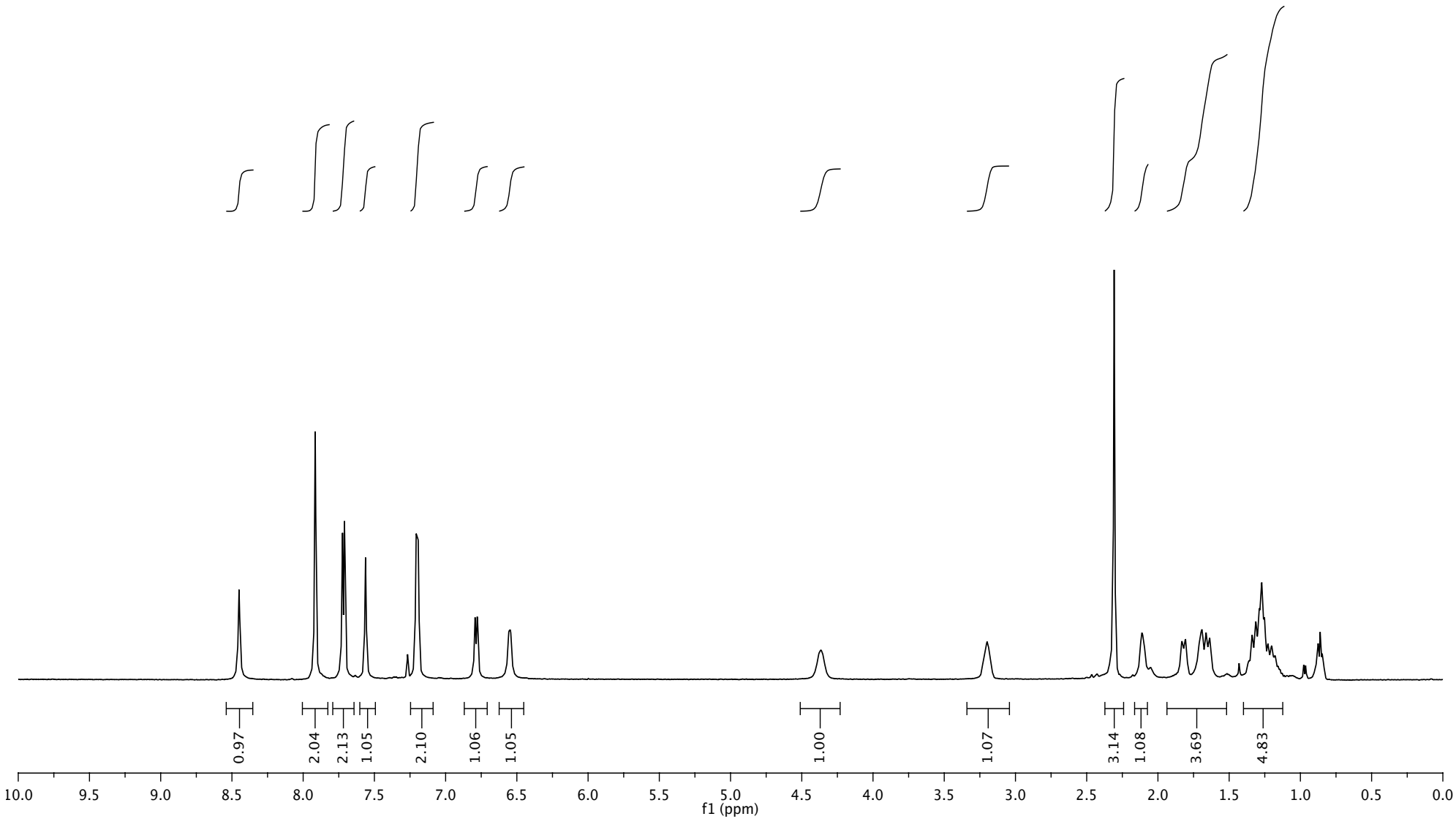

S
CF3
NH
HN
HN
CF3
F3C

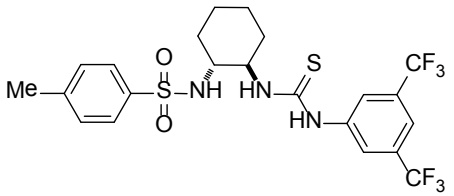
^{13}C NMR of **5**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

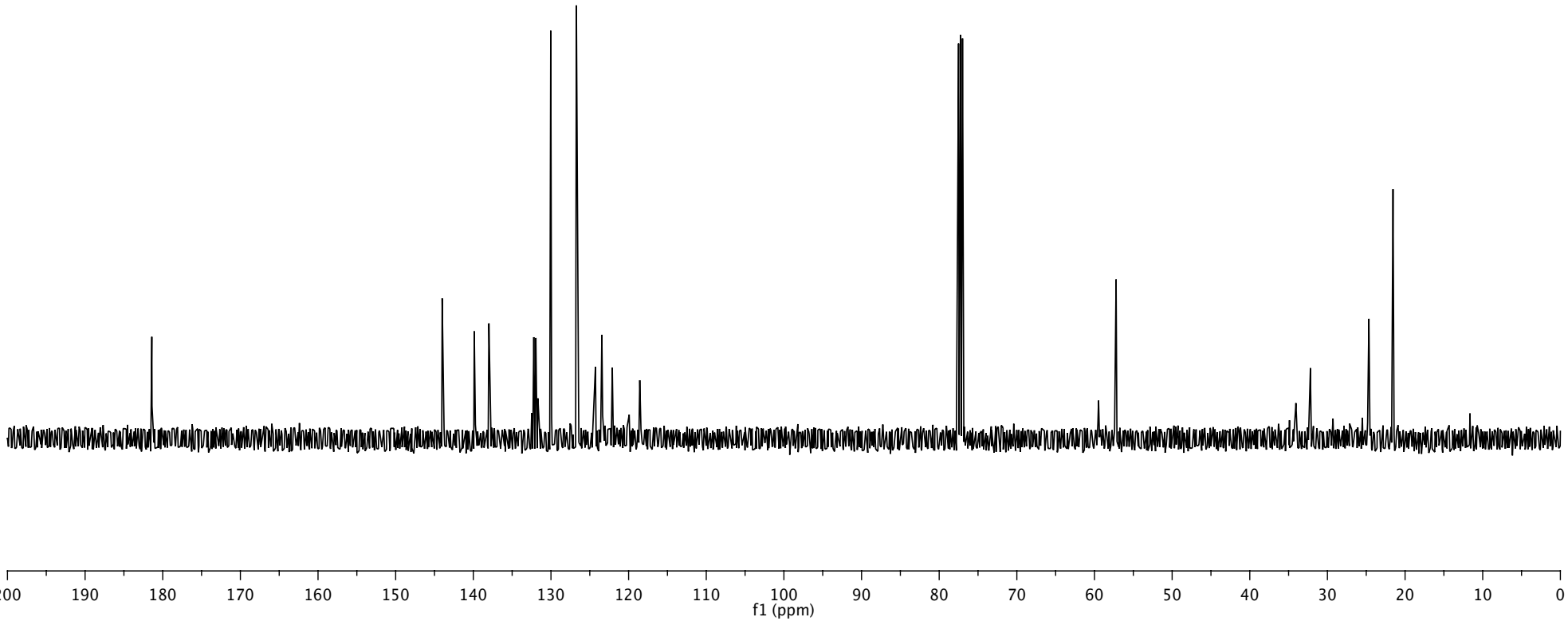

Me
O
S
O
NH
HN
S
HN
CF3
CF3

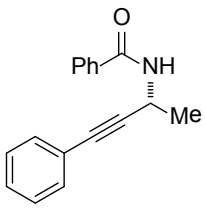
^{1}H NMR of **6**


0.97
2.04
2.13
1.05
2.10
1.06
1.05
1.00
1.07
3.14
1.08
3.69
4.83
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
f1 (ppm)

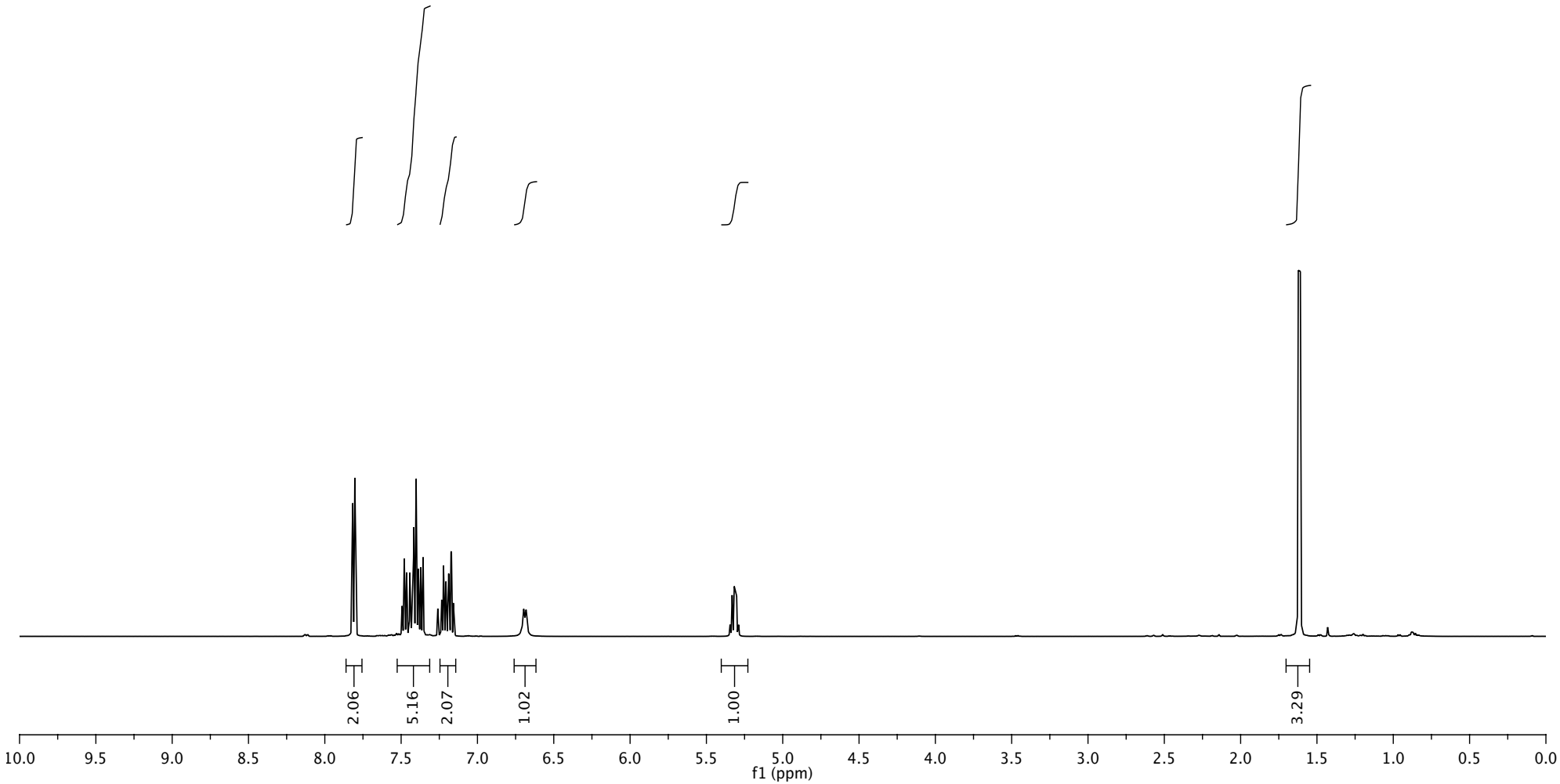

Me
O
S
NH
HN
S
HN
CF3
CF3

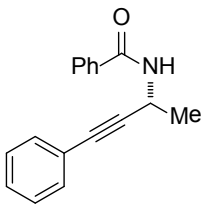
^{13}C NMR of **6**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

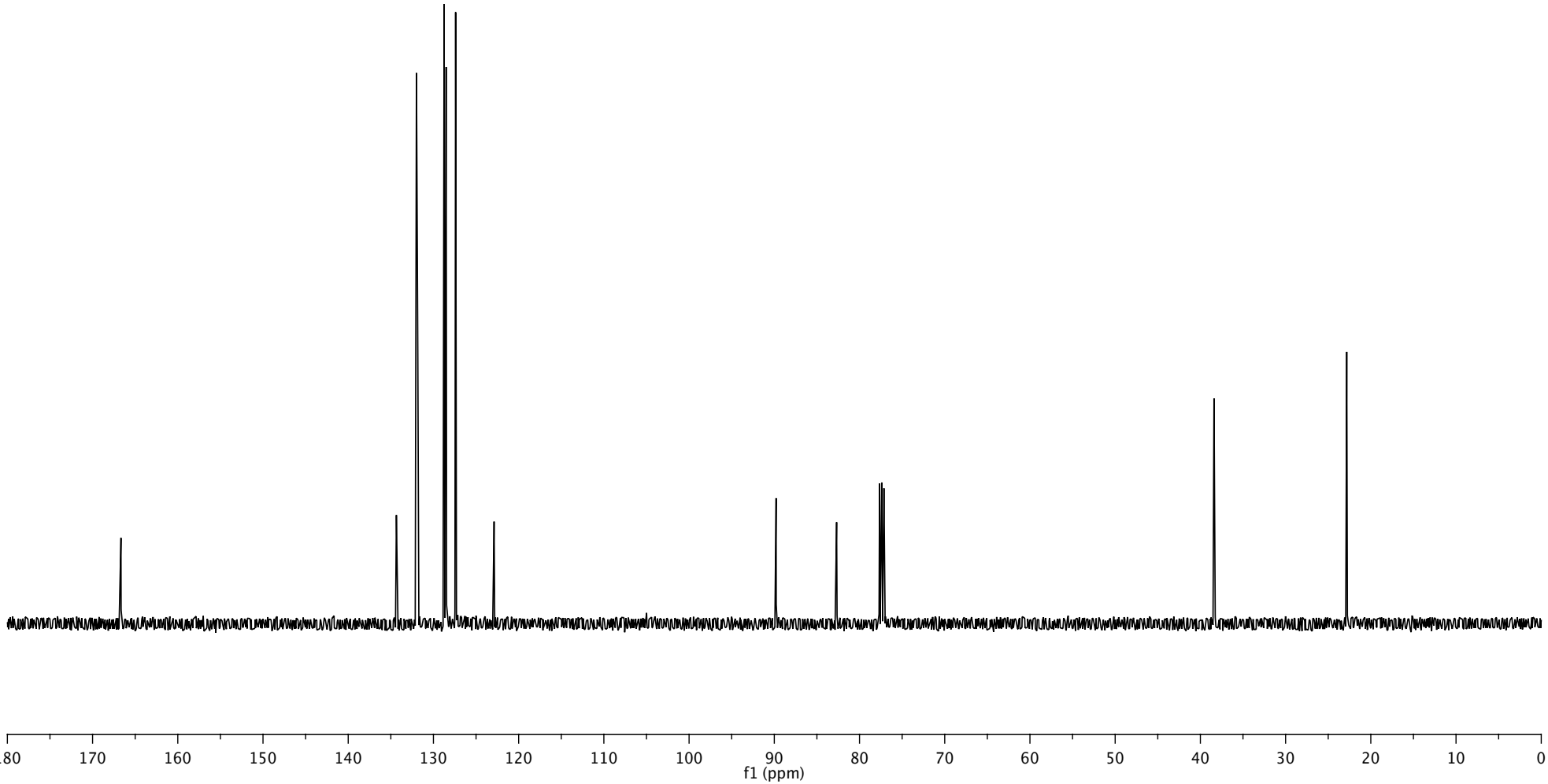

O
Ph
NH
Me

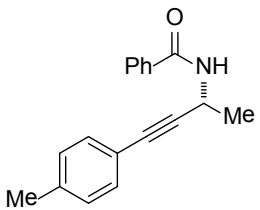
^{1}H NMR of **8a**


2.06
5.16
2.07
1.02
1.00
3.29
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
f1 (ppm)

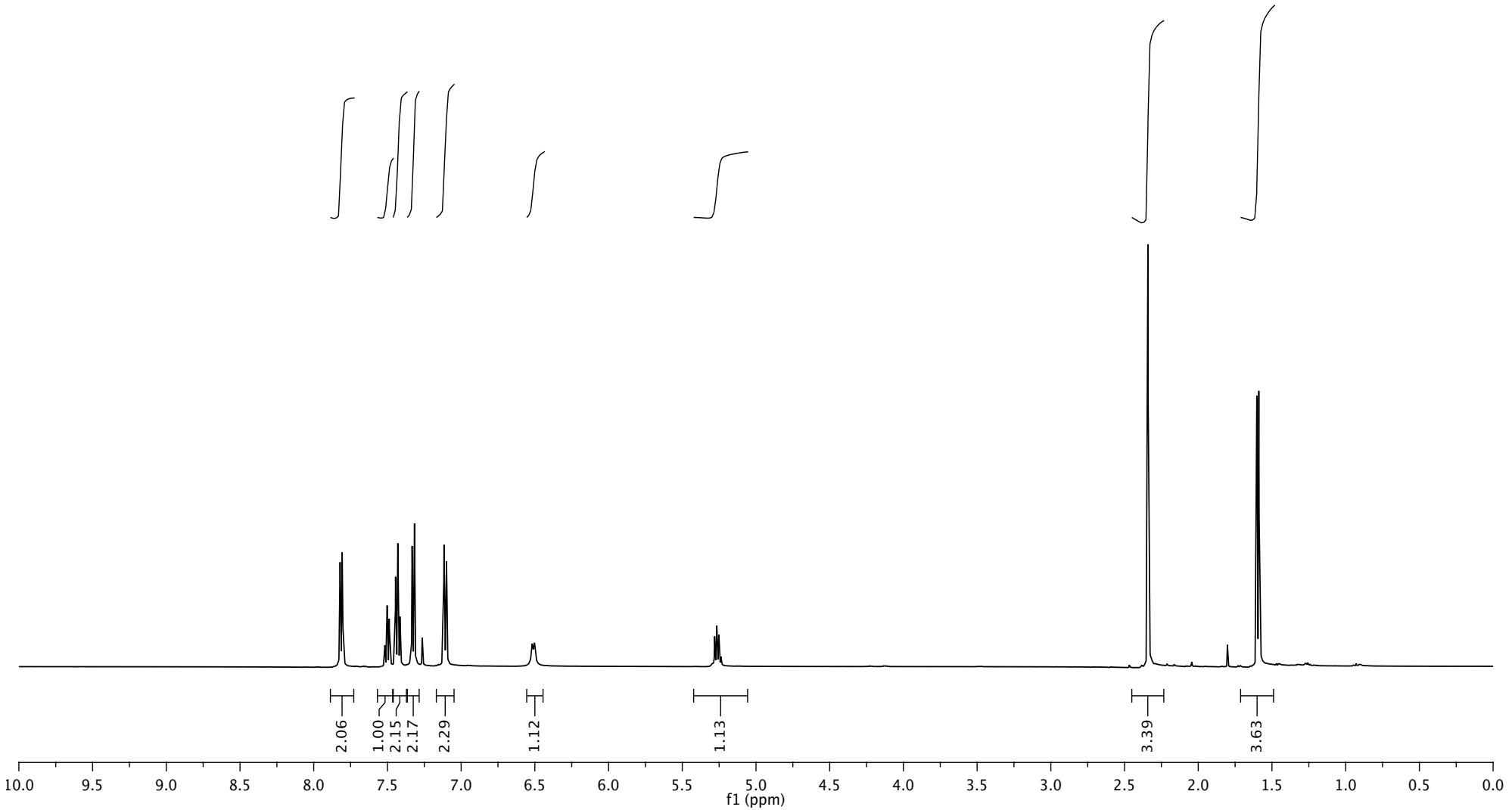

O
Ph
NH
Me

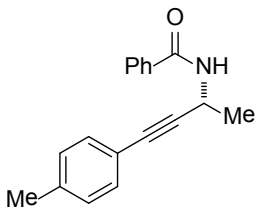
^{13}C NMR of **8a**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

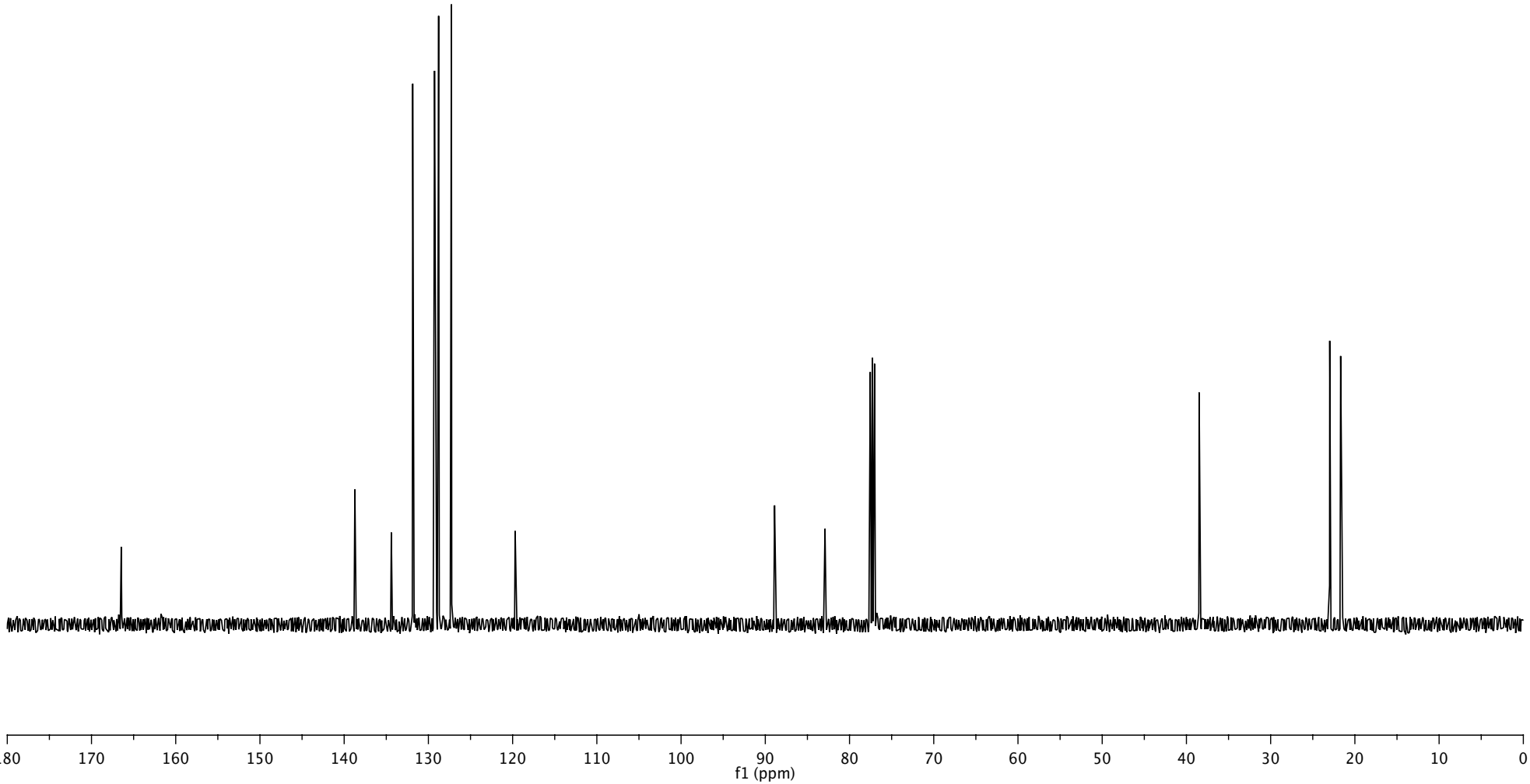

O
Ph
NH
Me
Me

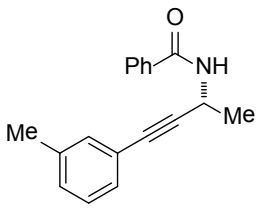
^{1}H NMR of **8b**


2.06
1.00
2.15
2.17
2.29
1.12
1.13
3.39
3.63
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
f1 (ppm)

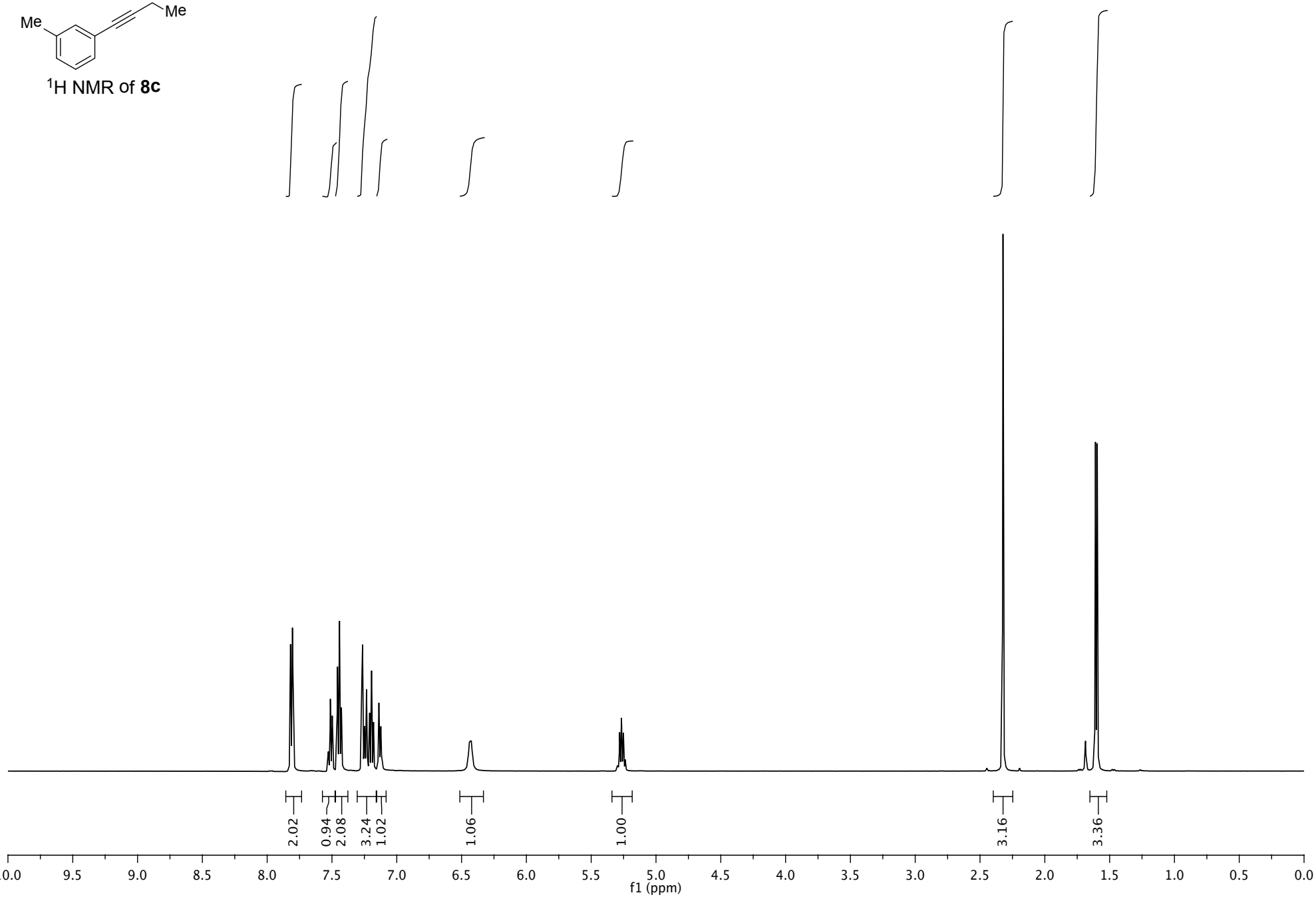

O
Ph
NH
Me
Me

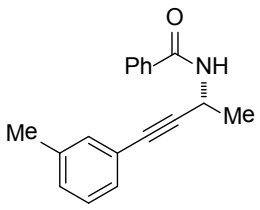
^{13}C NMR of **8b**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

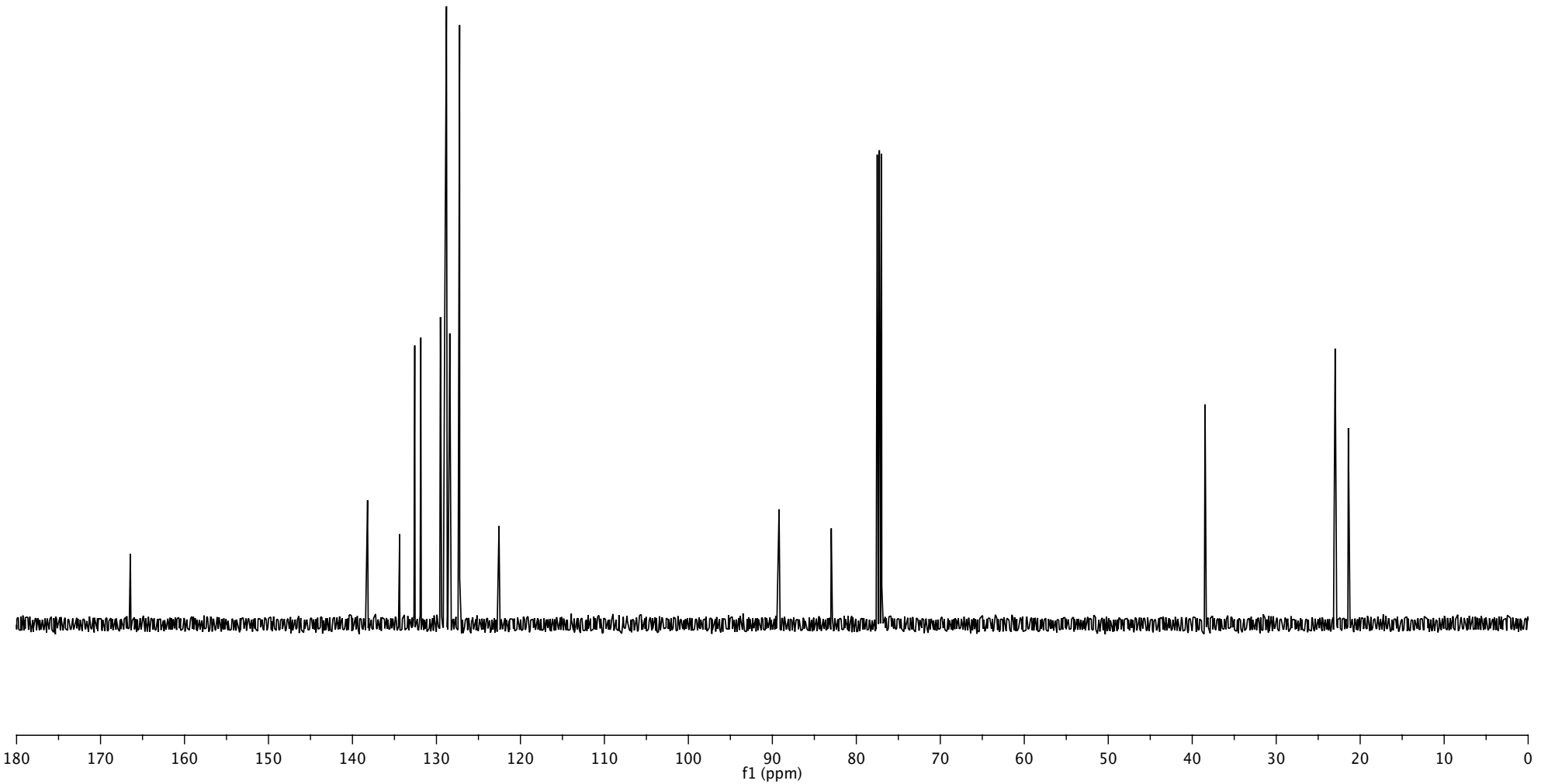

O
Ph
NH
Me
Me

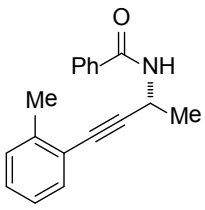
^{1}H NMR of **8c**


2.02
0.94
2.08
3.24
1.02
1.06
1.00
3.16
3.36
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
f1 (ppm)

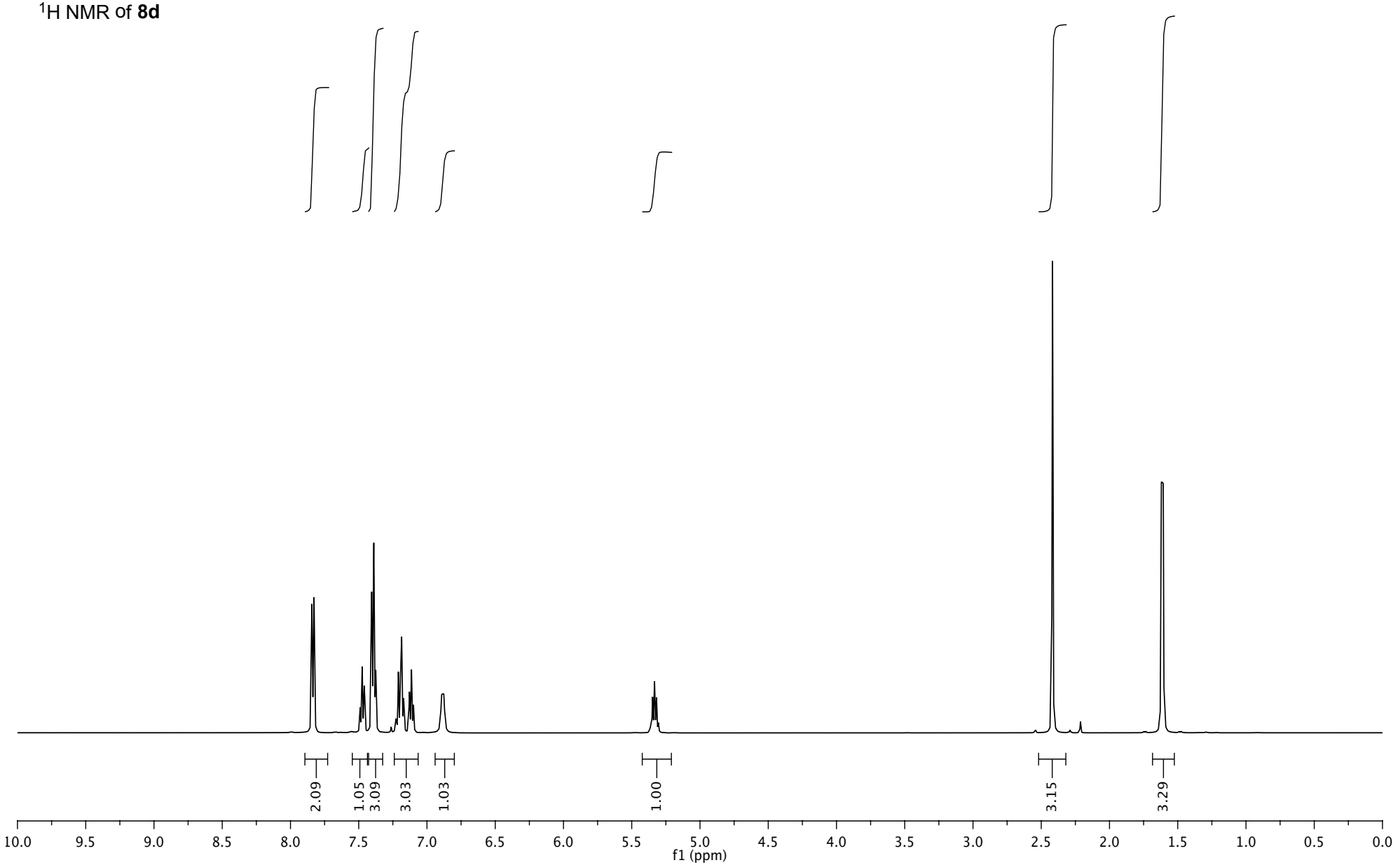

O
Ph
NH
Me
Me

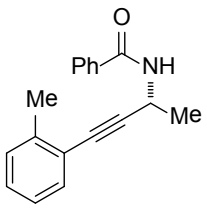
^{13}C NMR of **8c**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

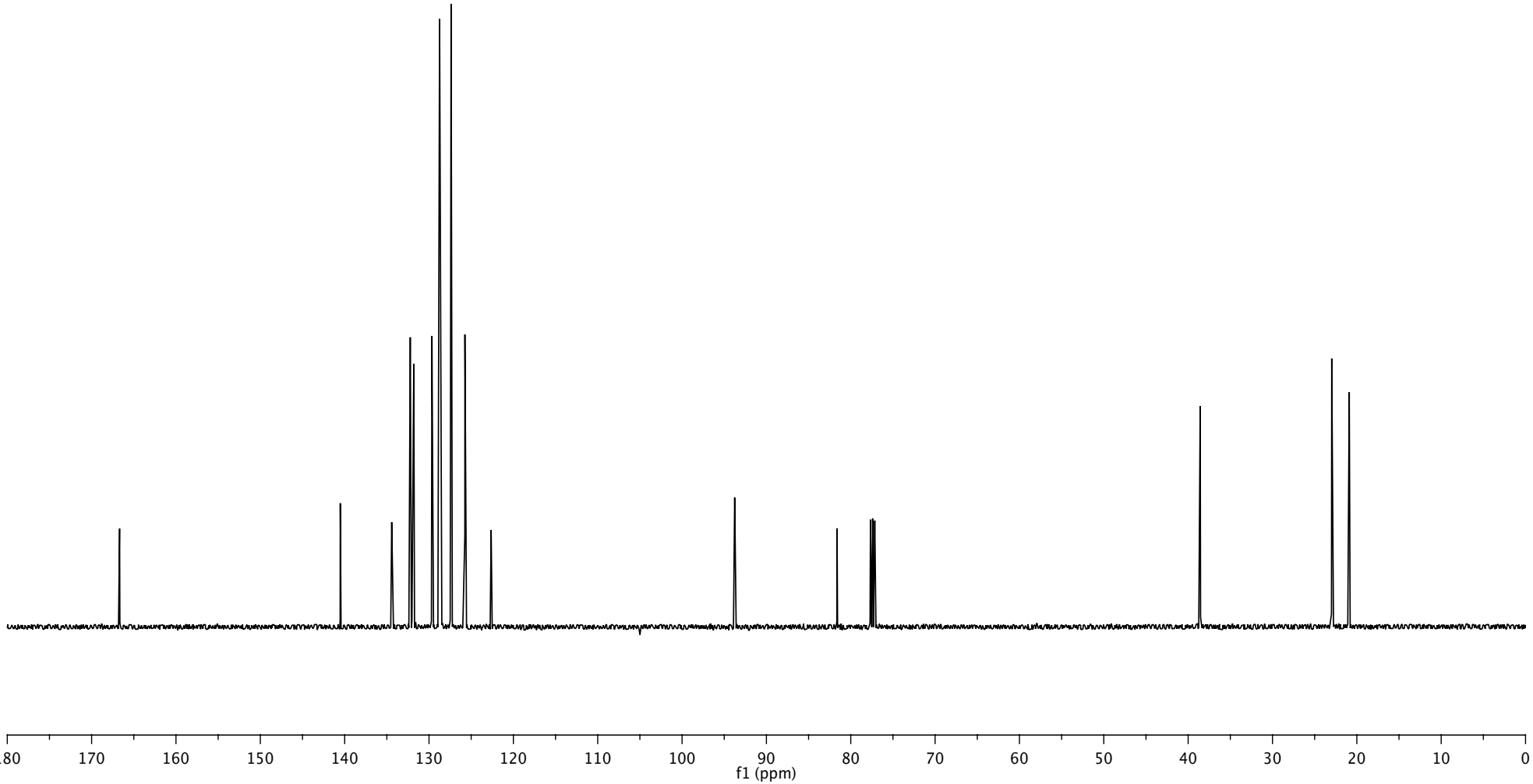

O
Ph
NH
Me
Me

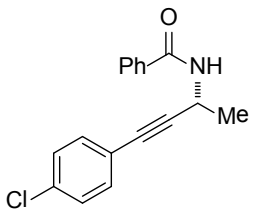
^{1}H NMR of **8d**


2.09
1.05
3.09
3.03
1.03
1.00
3.15
3.29
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
f1 (ppm)

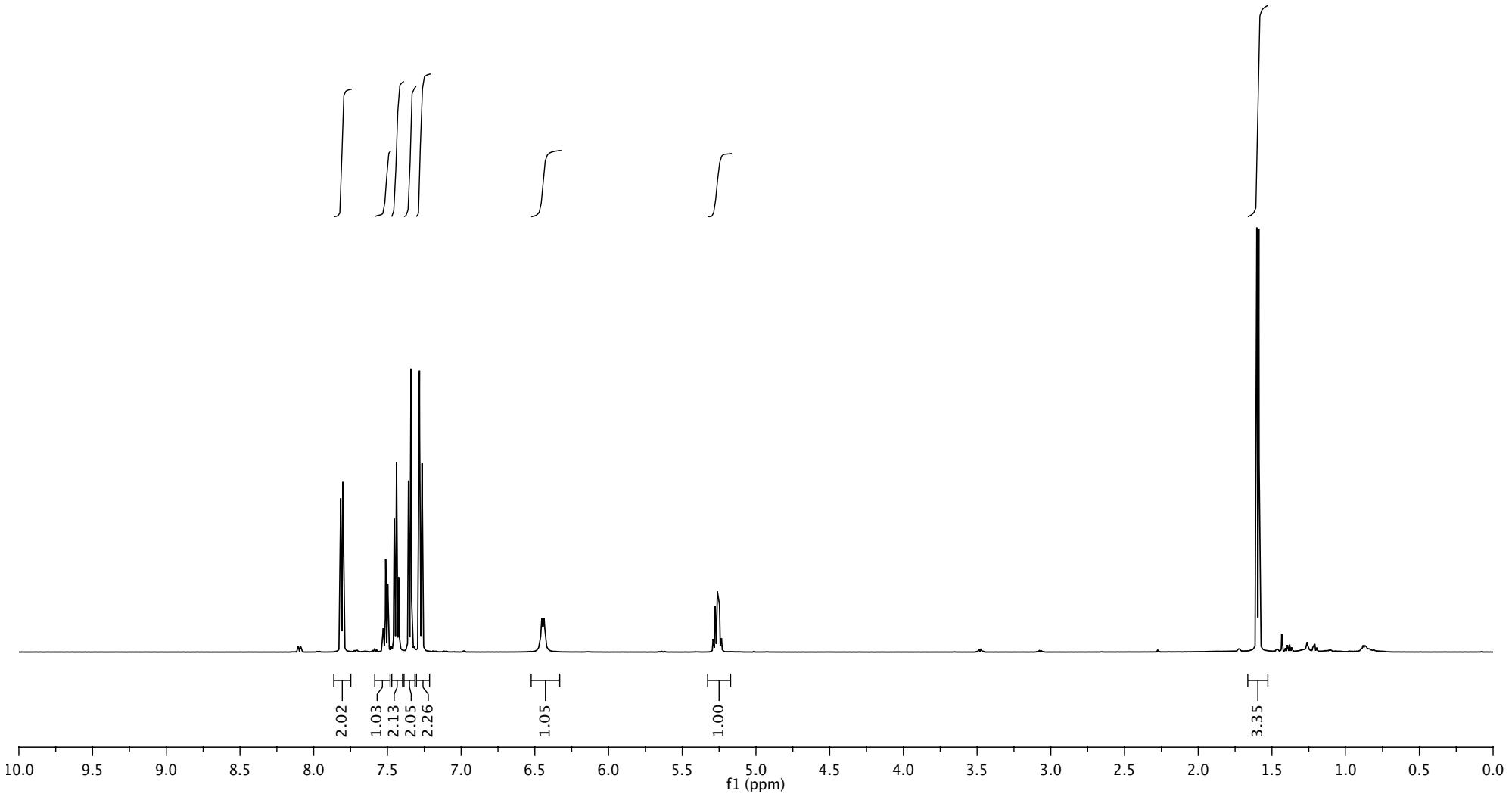

O
Ph
NH
Me
Me

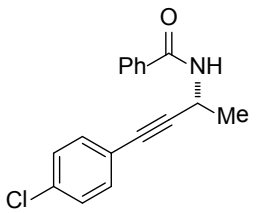
^{13}C NMR of **8d**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

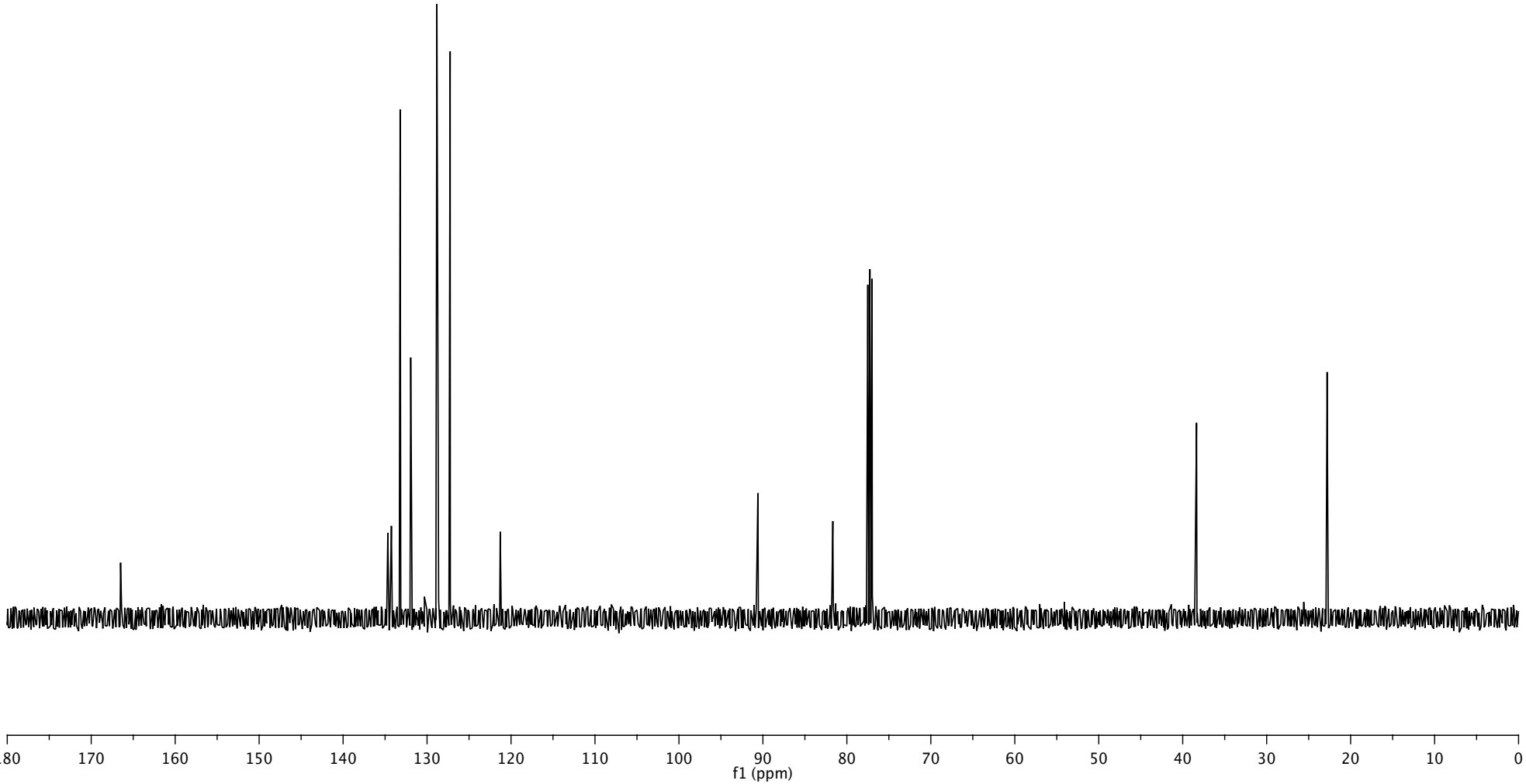

O
Ph
NH
Me
Cl

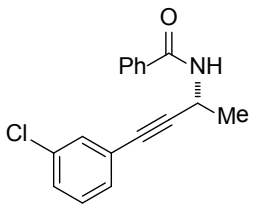
^{1}H NMR of **8e**


2.02
1.03
2.13
2.05
2.26
1.05
1.00
3.35
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
f1 (ppm)

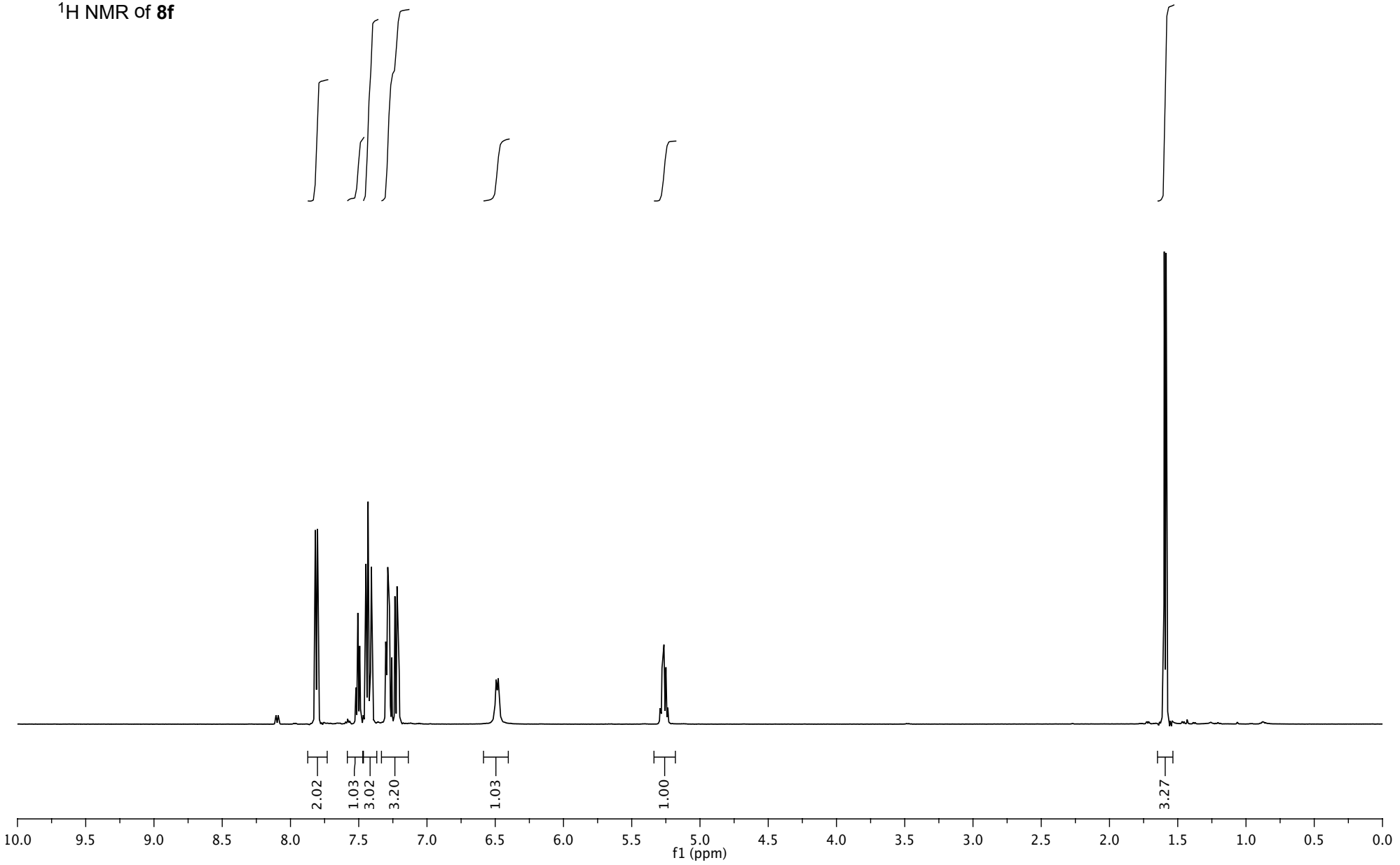

O
Ph
NH
Me
Cl

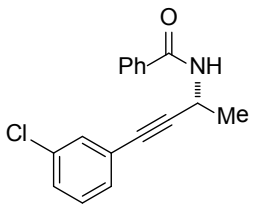
^{13}C NMR of **8e**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

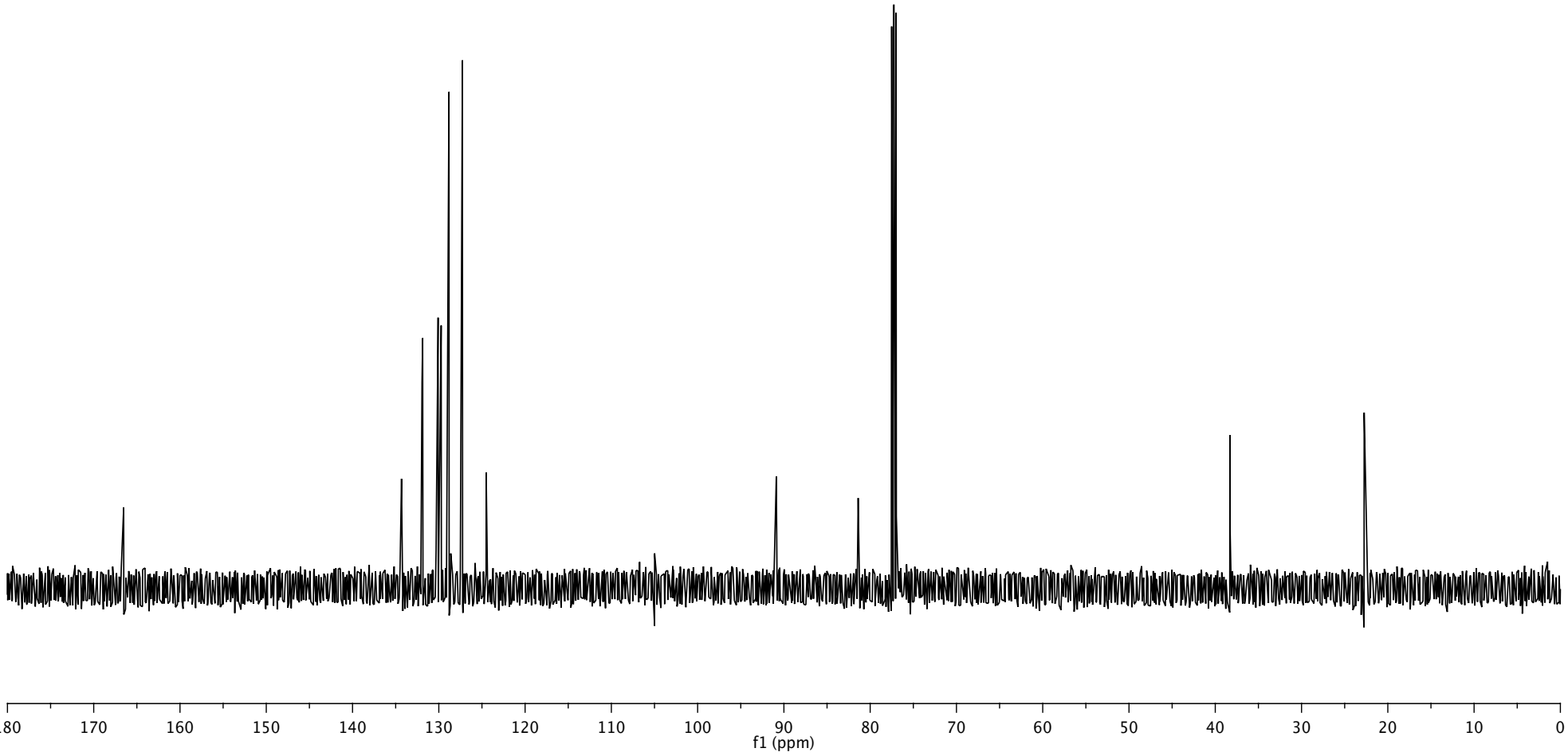

O
Ph
NH
Me
Cl

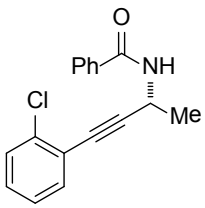
^{1}H NMR of **8f**


2.02
1.03
3.02
3.20
1.03
1.00
3.27
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
f1 (ppm)

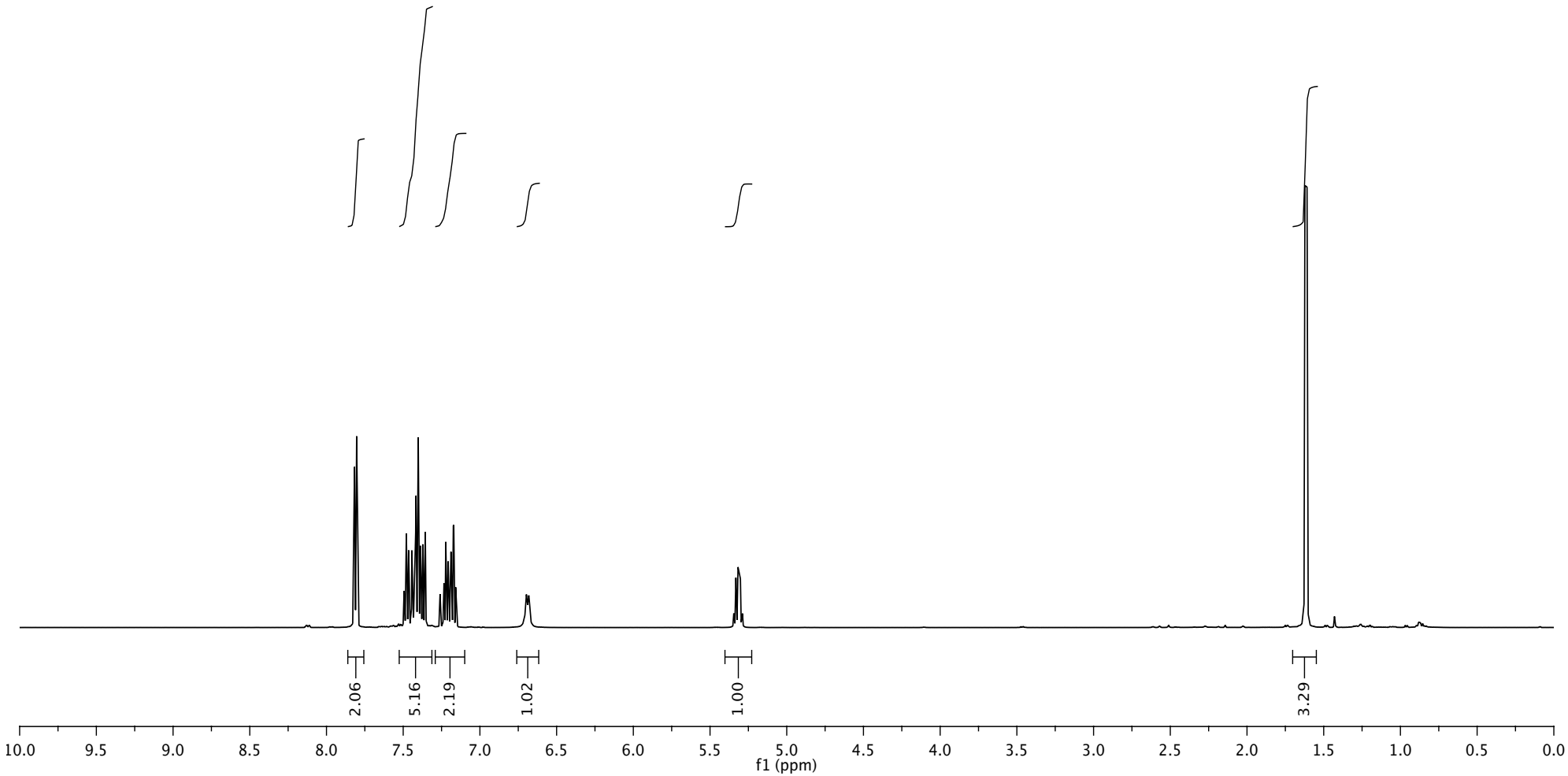

O
Ph
NH
Me
Cl

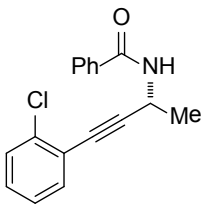
^{13}C NMR of **8f**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

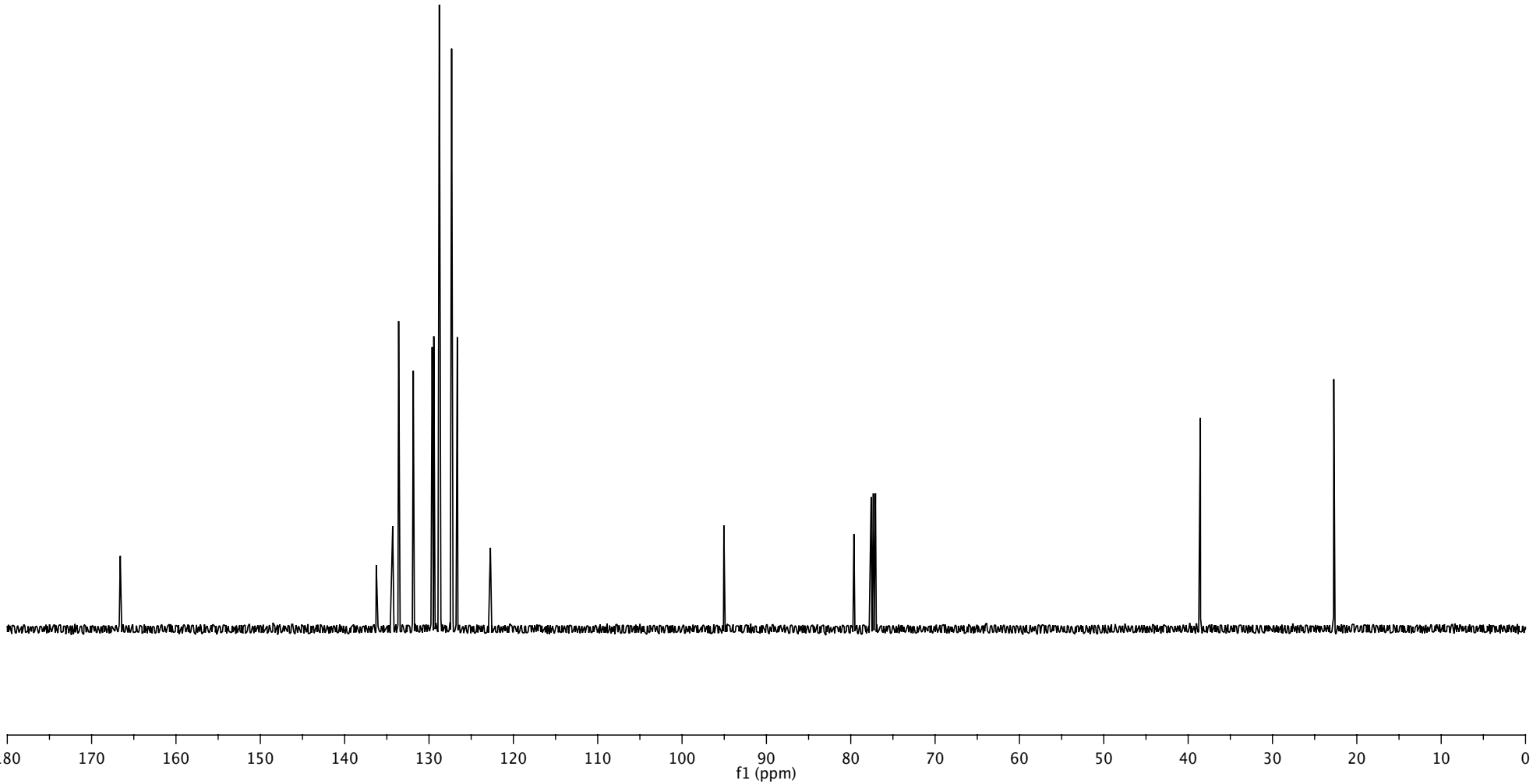

O
Ph
NH
Cl
Me

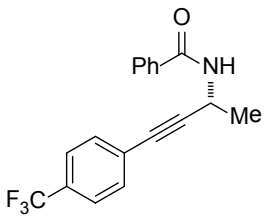
^{1}H NMR of **8g**


2.06
5.16
2.19
1.02
1.00
3.29
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
f1 (ppm)

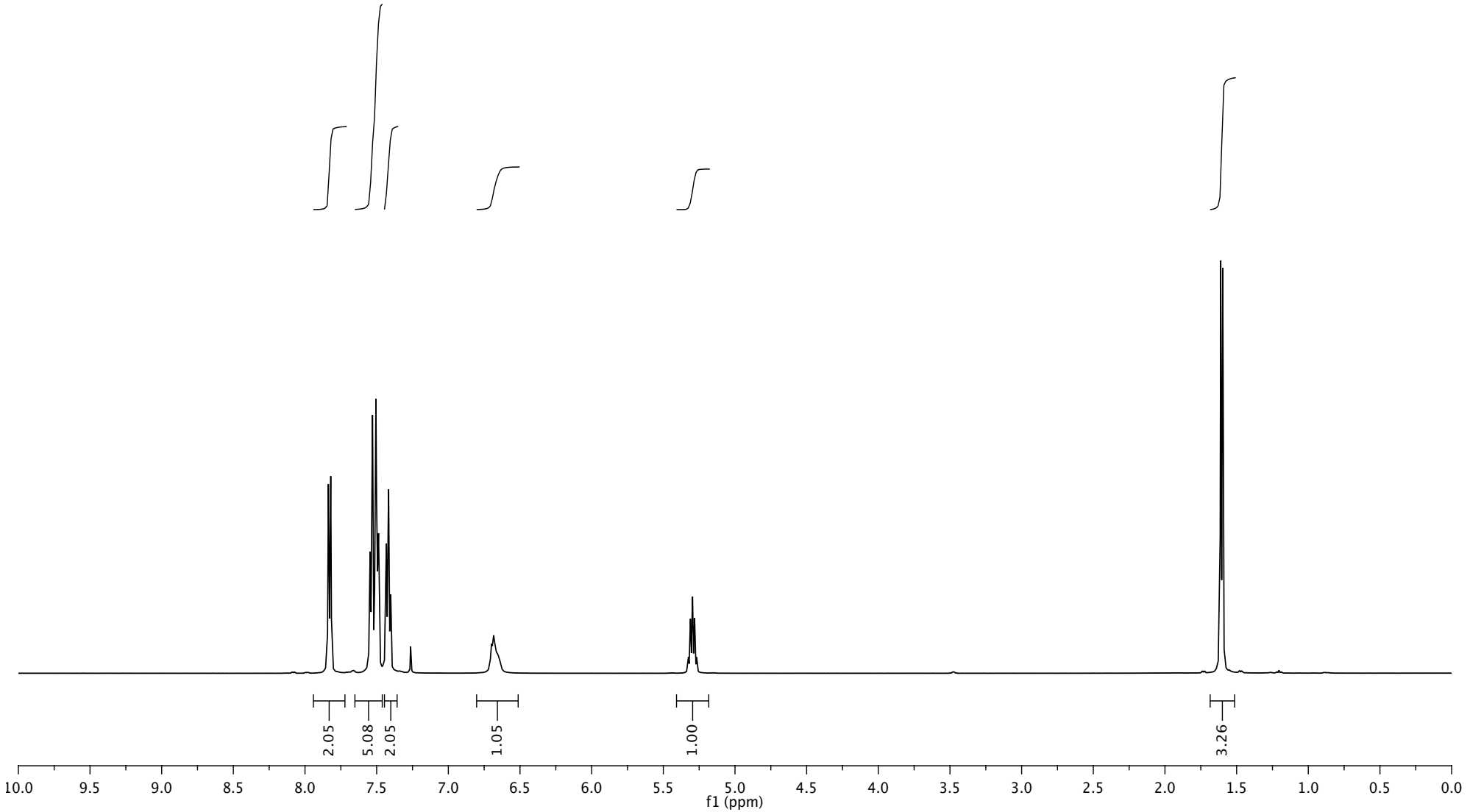

O
Ph
NH
Cl
Me

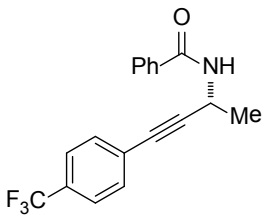
^{13}C NMR of **8g**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

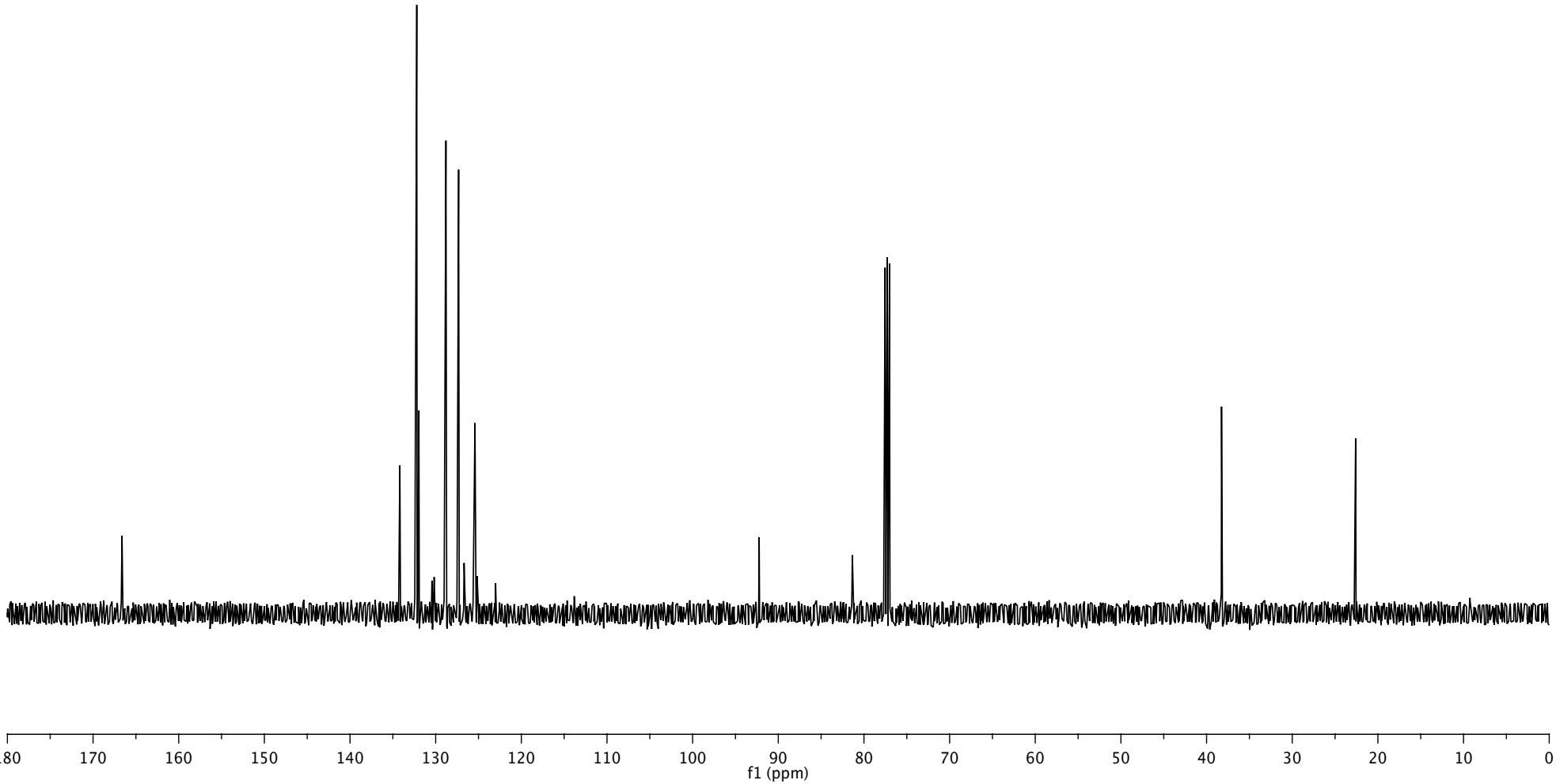

O
Ph
NH
Me
F3C

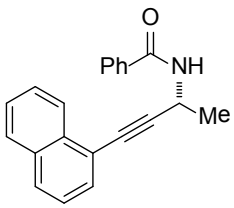
^{1}H NMR of **8h**


2.05
5.08
2.05
1.05
1.00
3.26
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
f1 (ppm)

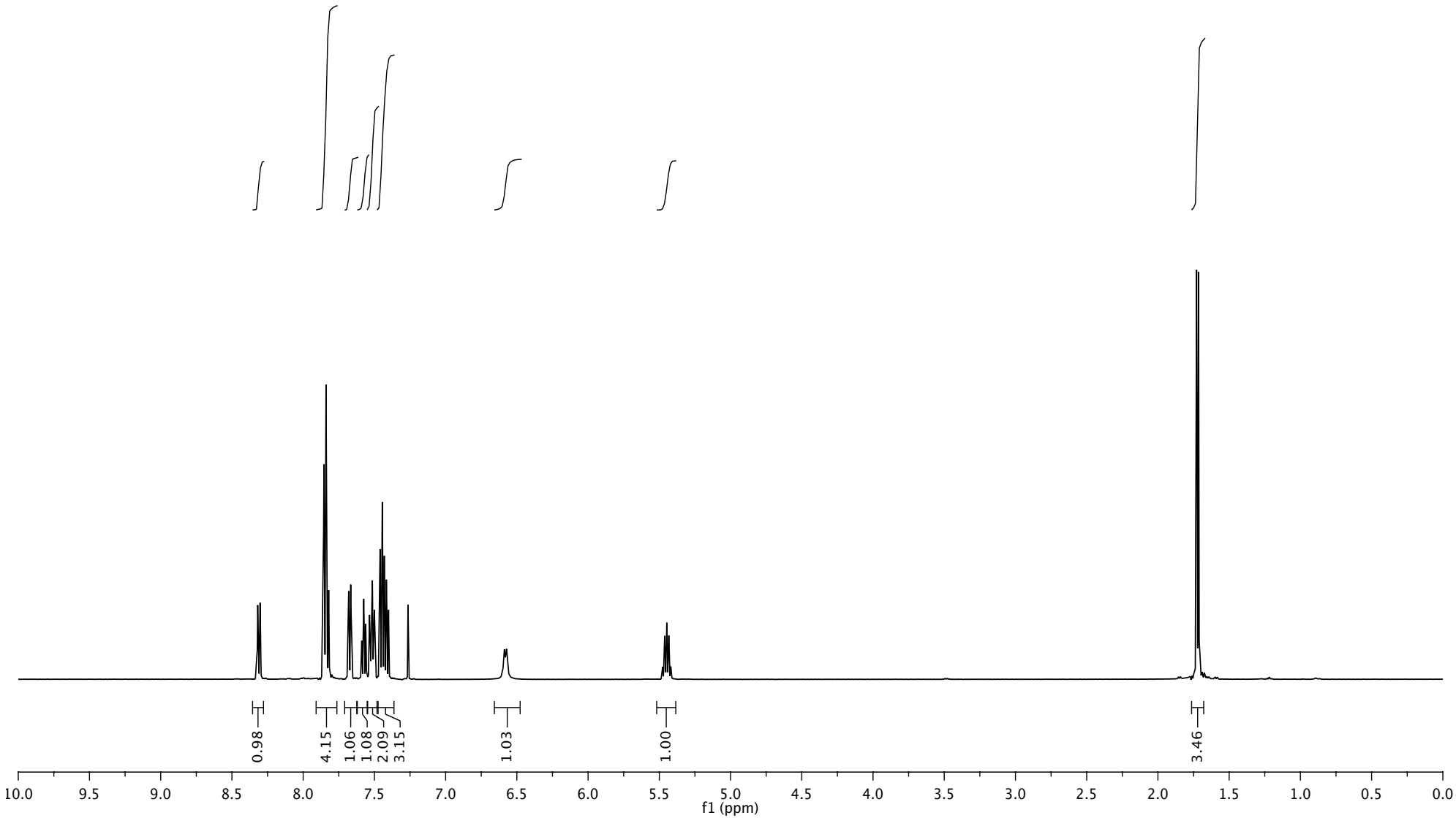

O
Ph
NH
Me
F3C

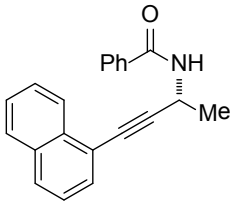
^{13}C NMR of **8h**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

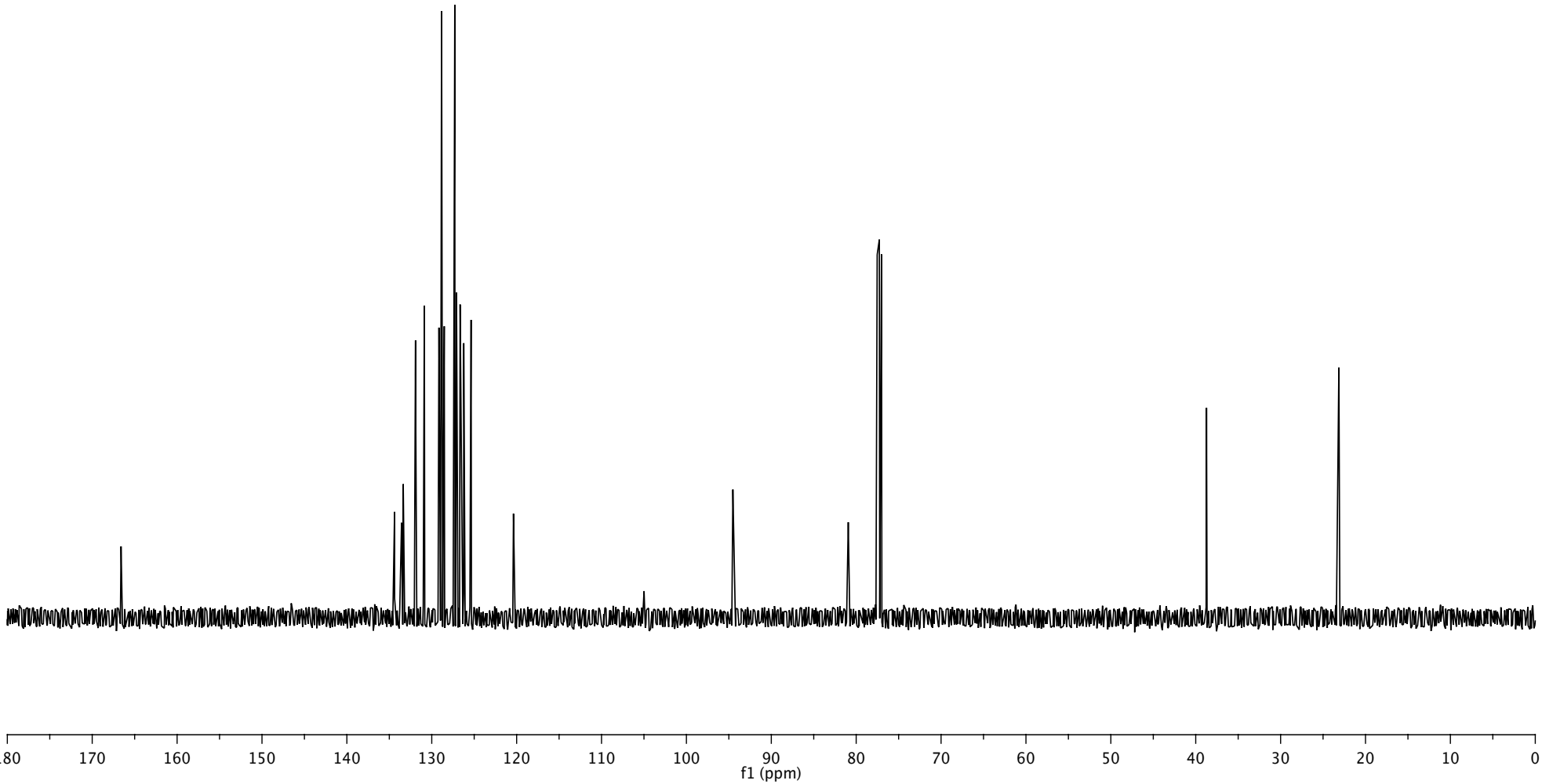

O
Ph
NH
Me

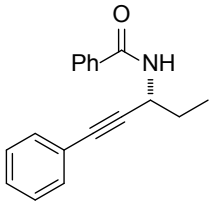
^{1}H NMR of **8i**


0.98
4.15
1.06
1.08
2.09
3.15
1.03
1.00
3.46
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
f1 (ppm)

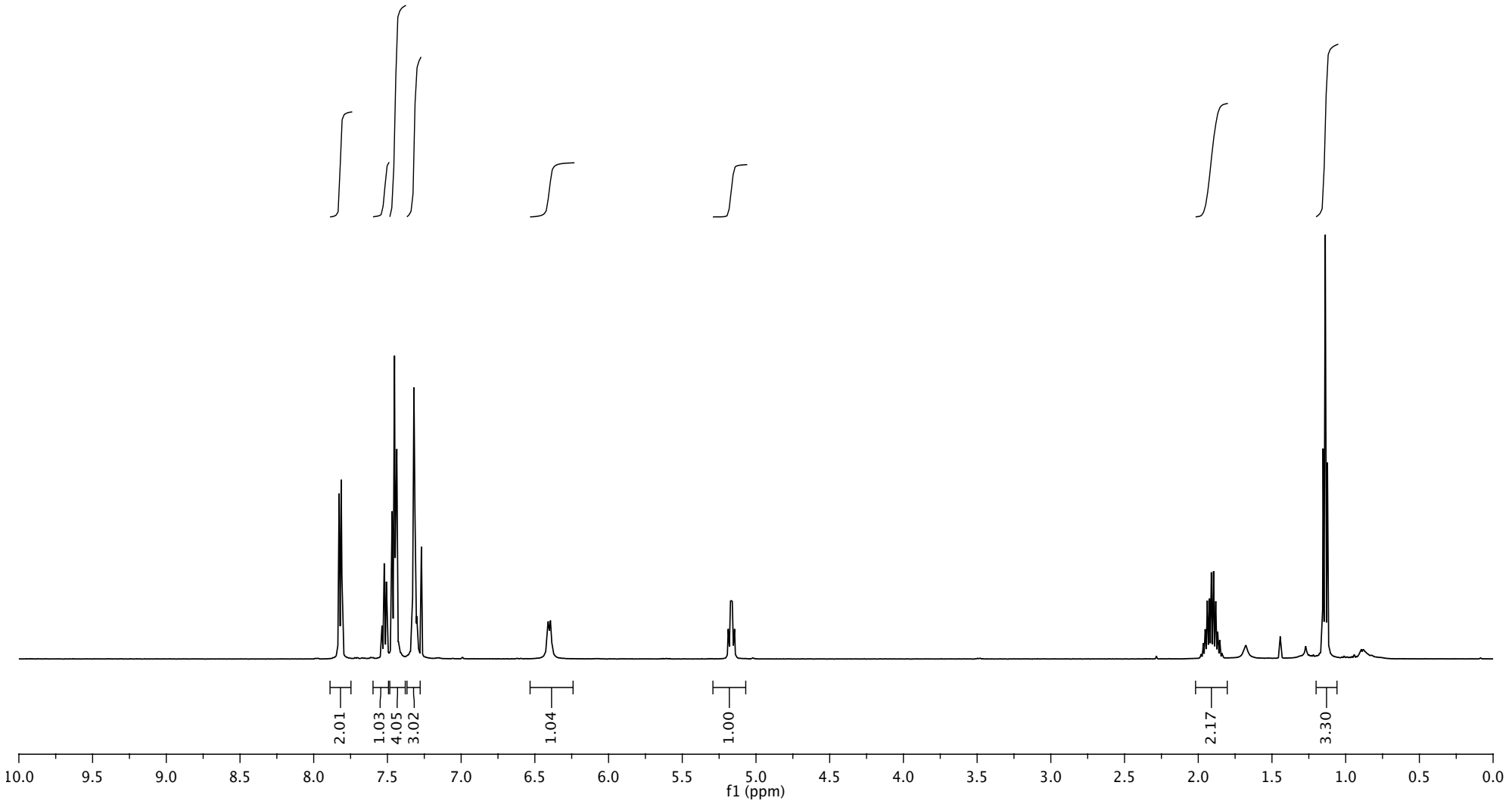

O
Ph
NH
Me

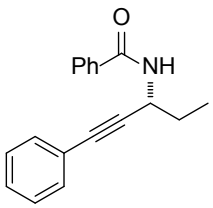
^{13}C NMR of **8i**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

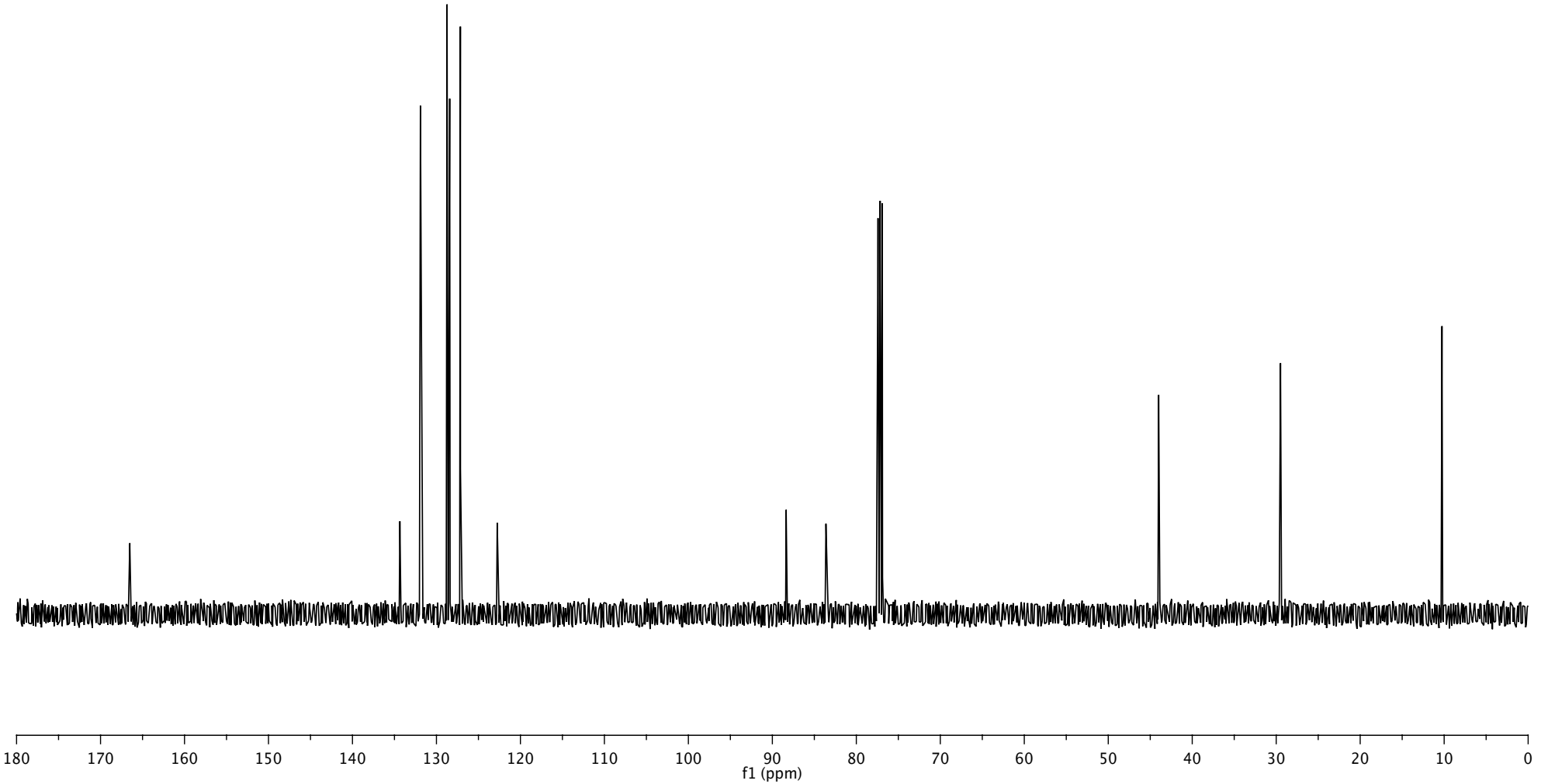

O
Ph
NH

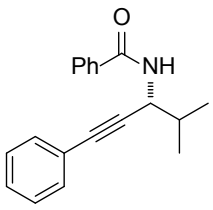
^{1}H NMR of **8j**


2.01
1.03
4.05
3.02
1.04
1.00
2.17
3.30
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
f1 (ppm)

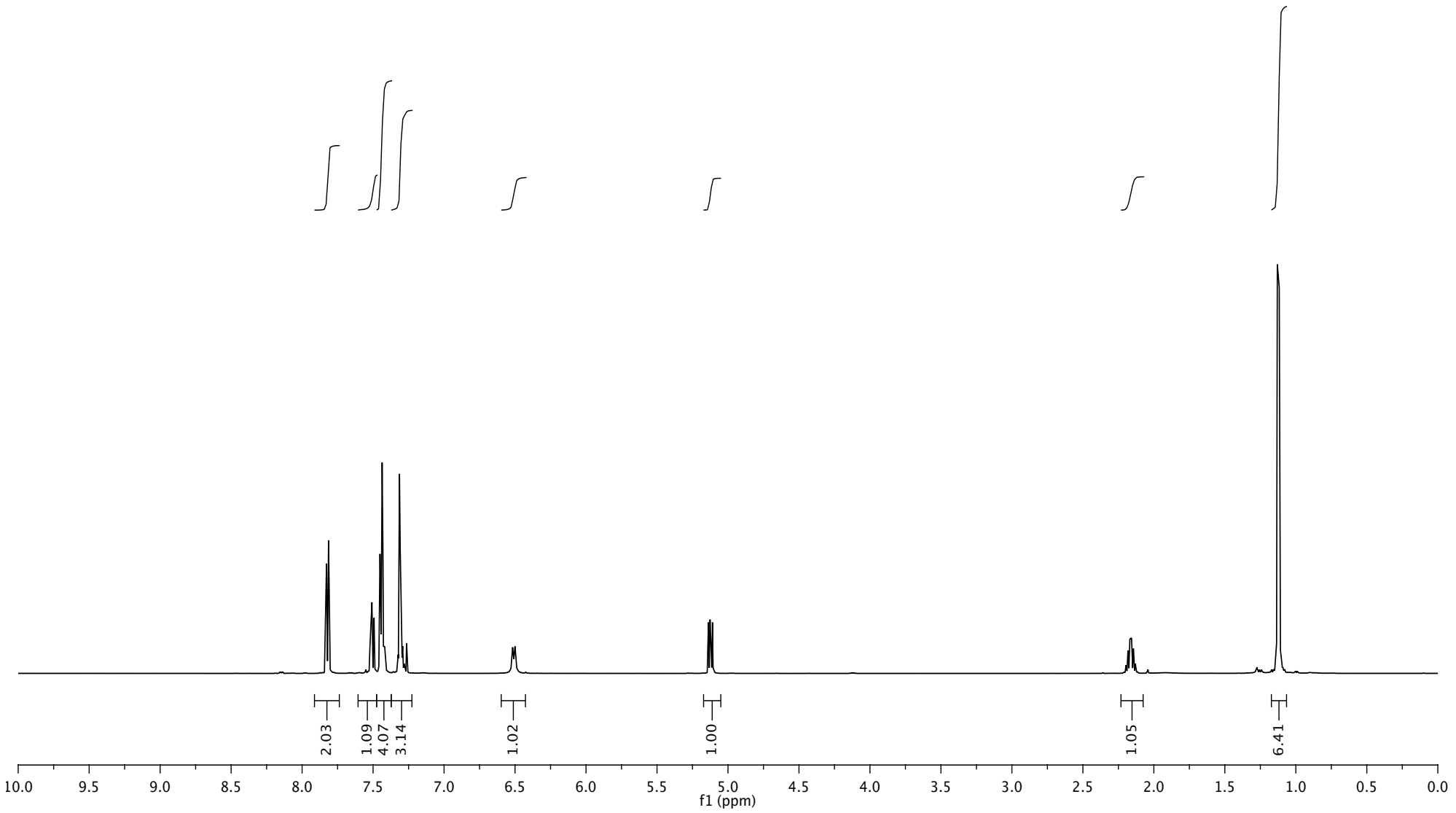

O
Ph
NH

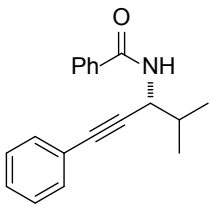
^{13}C NMR of **8j**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

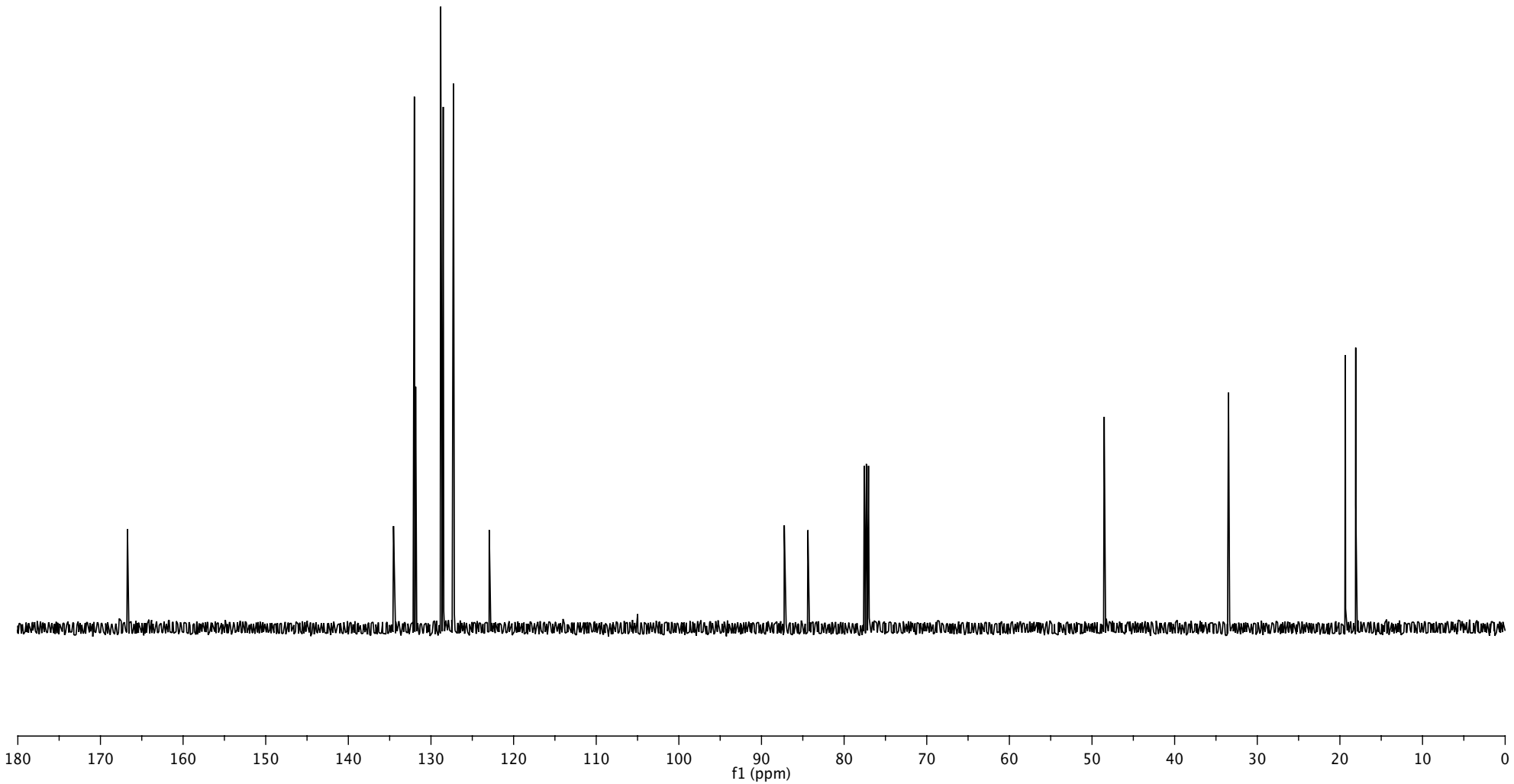

O
Ph
NH

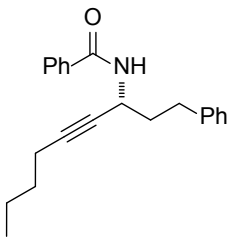
^{1}H NMR of **8k**


2.03
1.09
4.07
3.14
1.02
1.00
1.05
6.41
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
f1 (ppm)

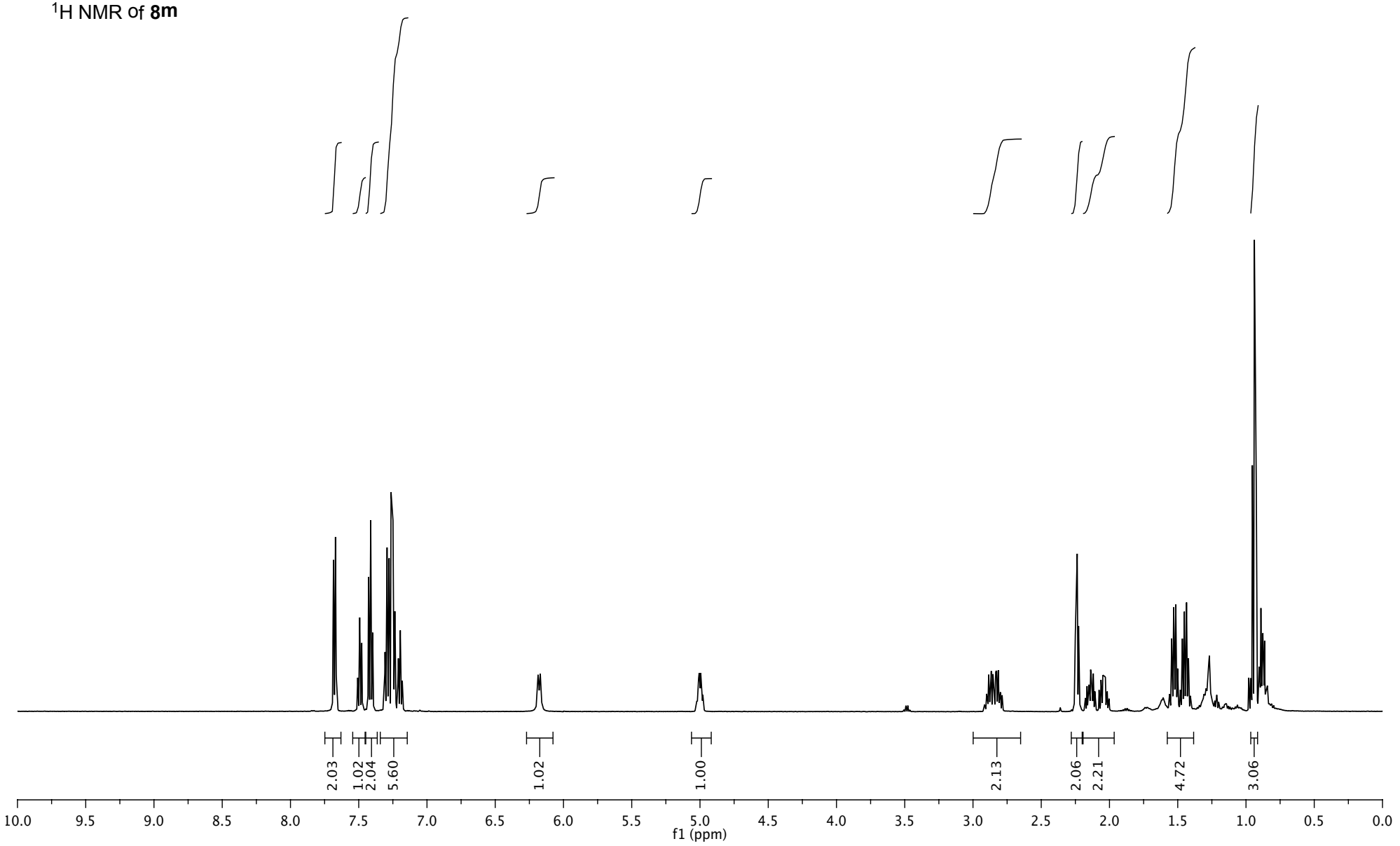

O
Ph
NH

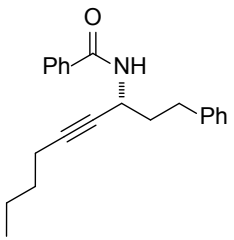
^{13}C NMR of **8k**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

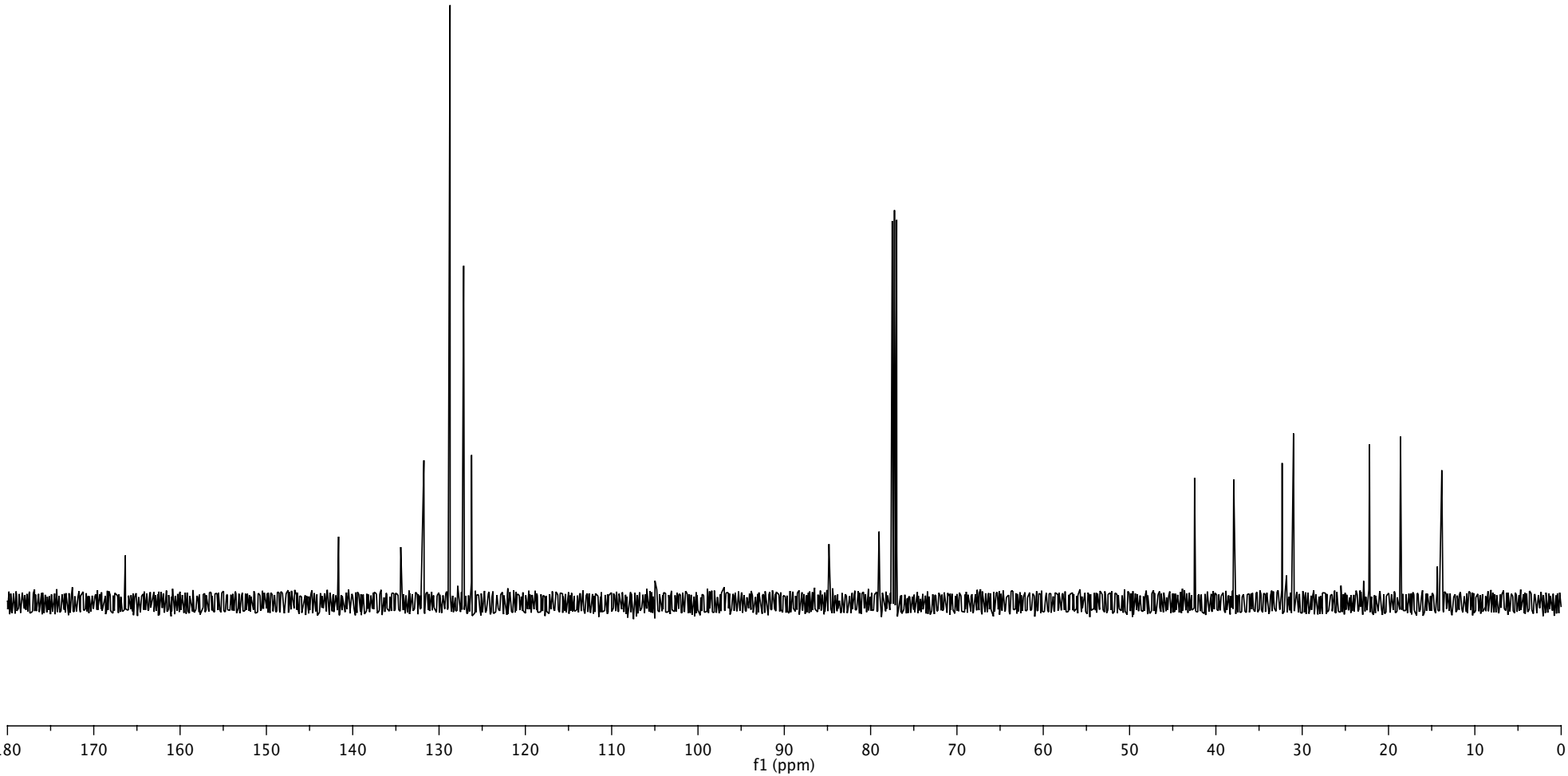

O
Ph
NH
Ph

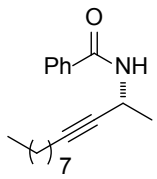
^{1}H NMR of **8m**


2.03
1.02
2.04
5.60
1.02
1.00
2.13
2.06
2.21
4.72
3.06
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
f1 (ppm)

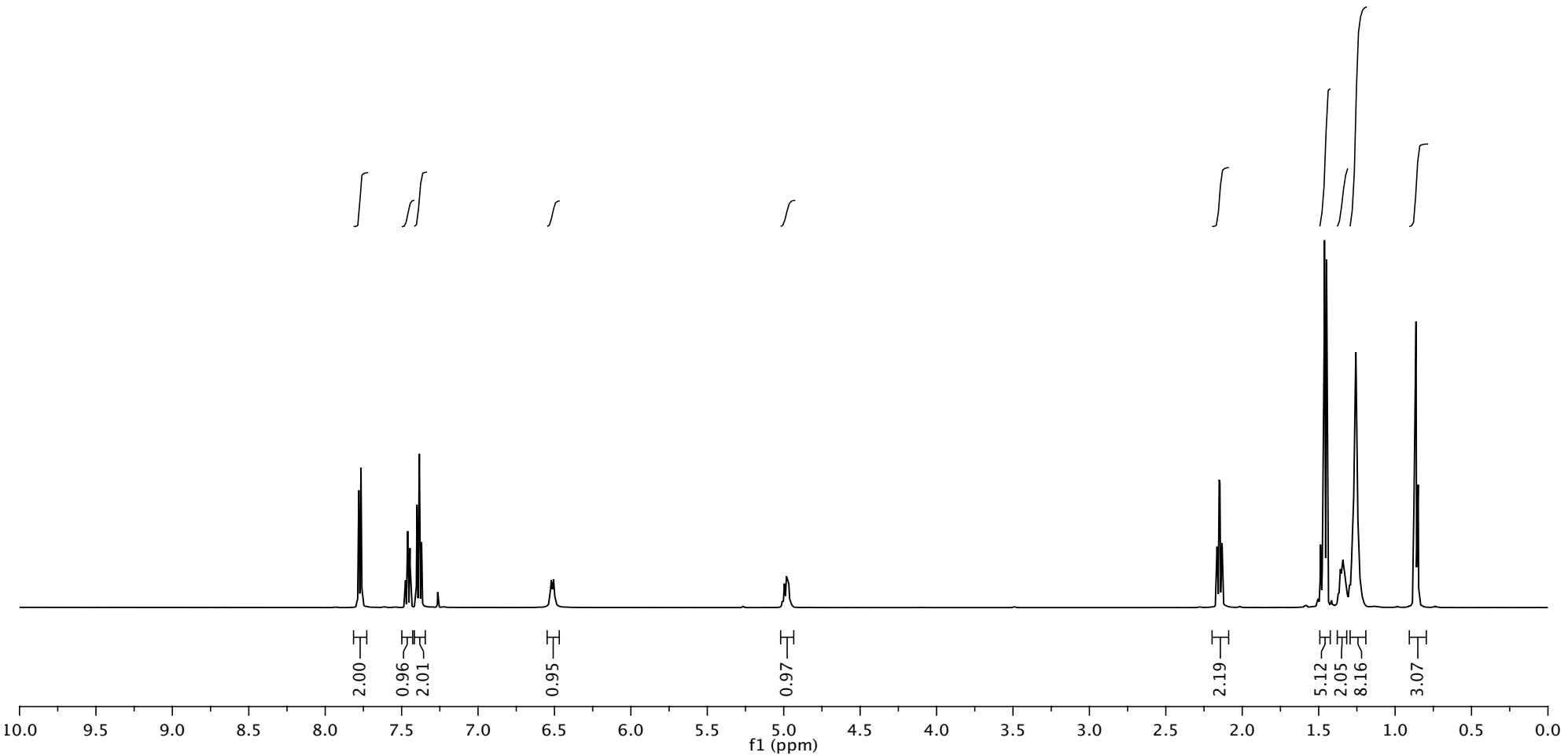

O
Ph
NH
Ph

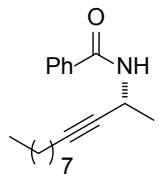
^{13}C NMR of **8m**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

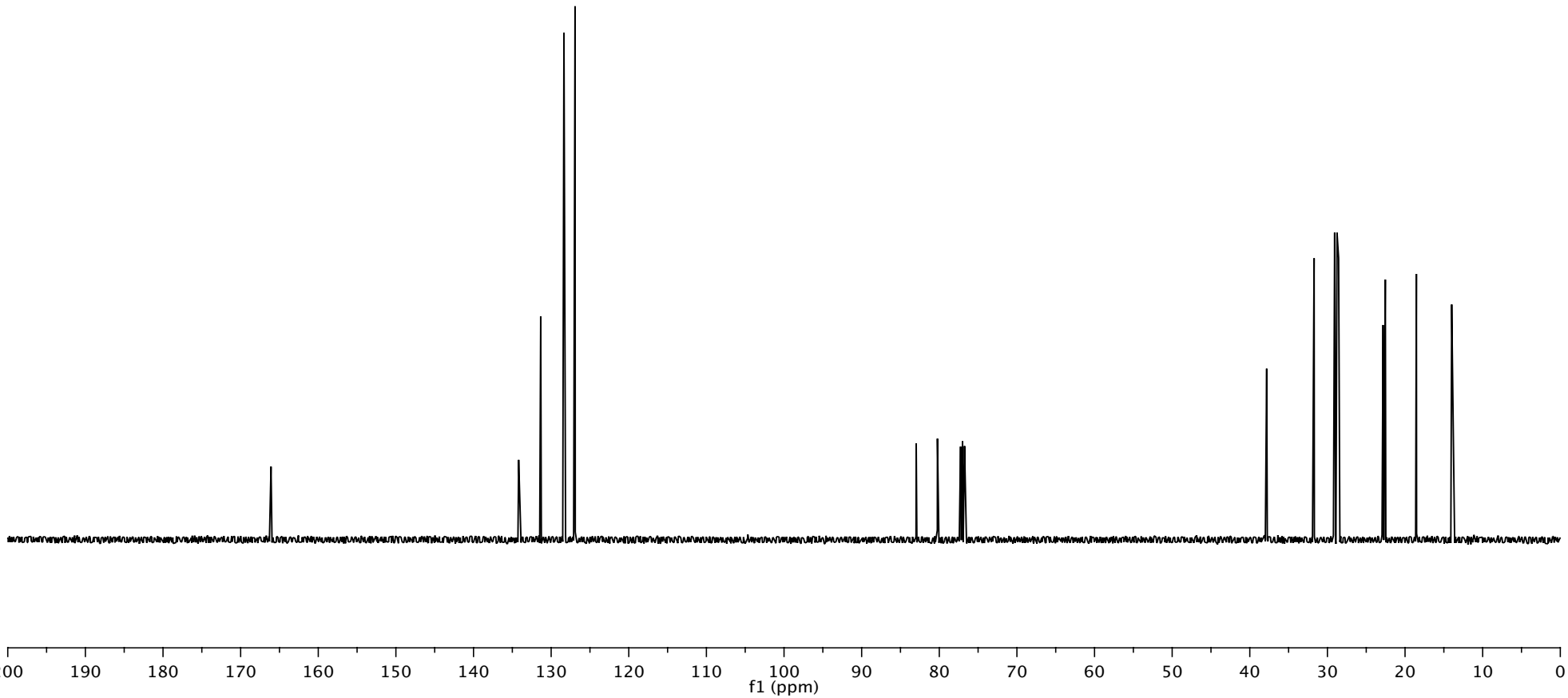

O
Ph
NH
7

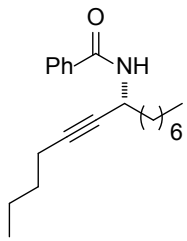
^{1}H NMR of **8n**


2.00
0.96
2.01
0.95
0.97
2.19
5.12
2.05
8.16
3.07
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
f1 (ppm)

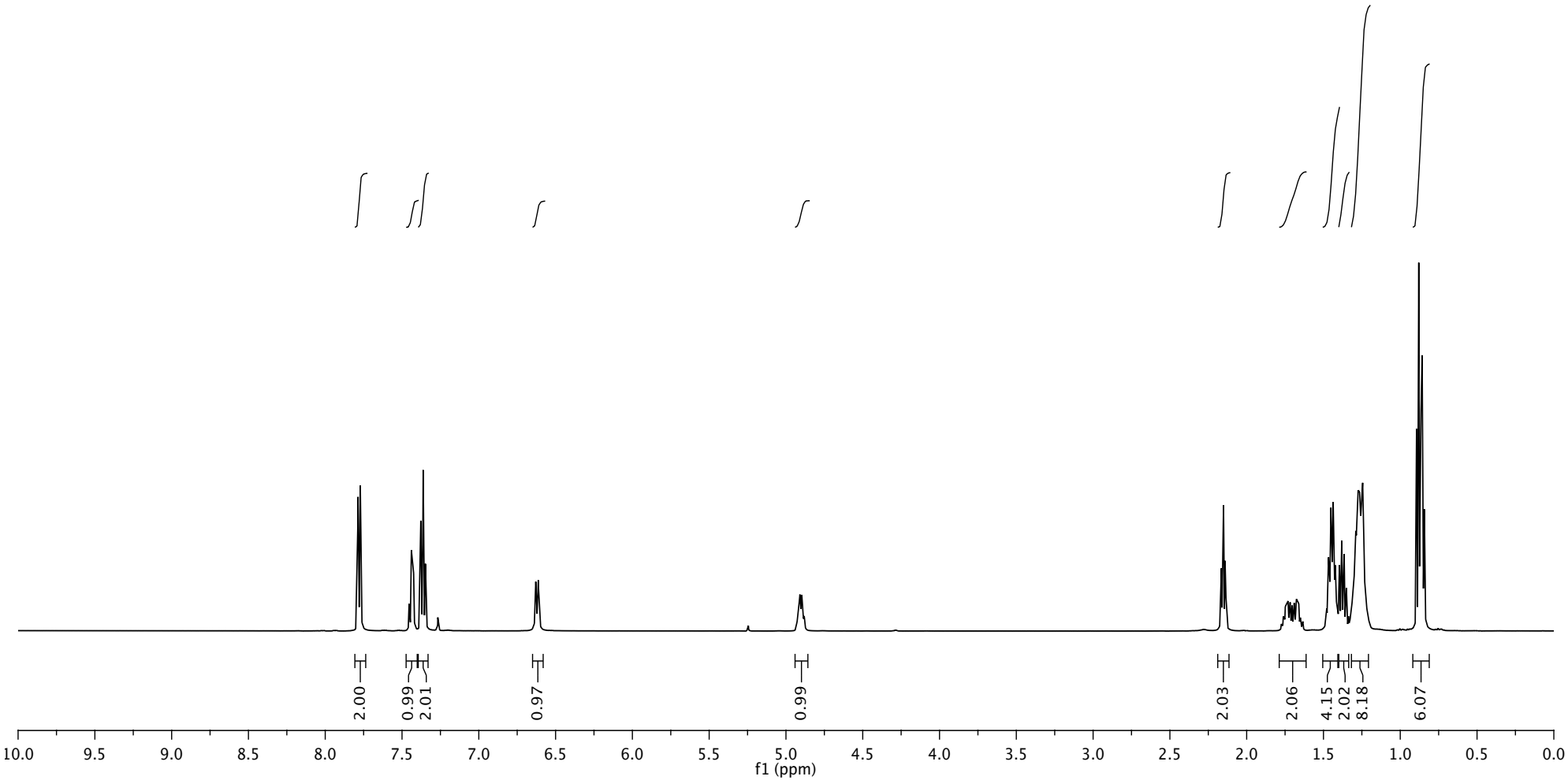

O
Ph
NH
7

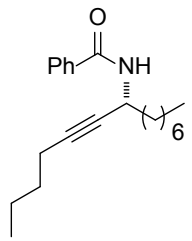
^{13}C NMR of **8n**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

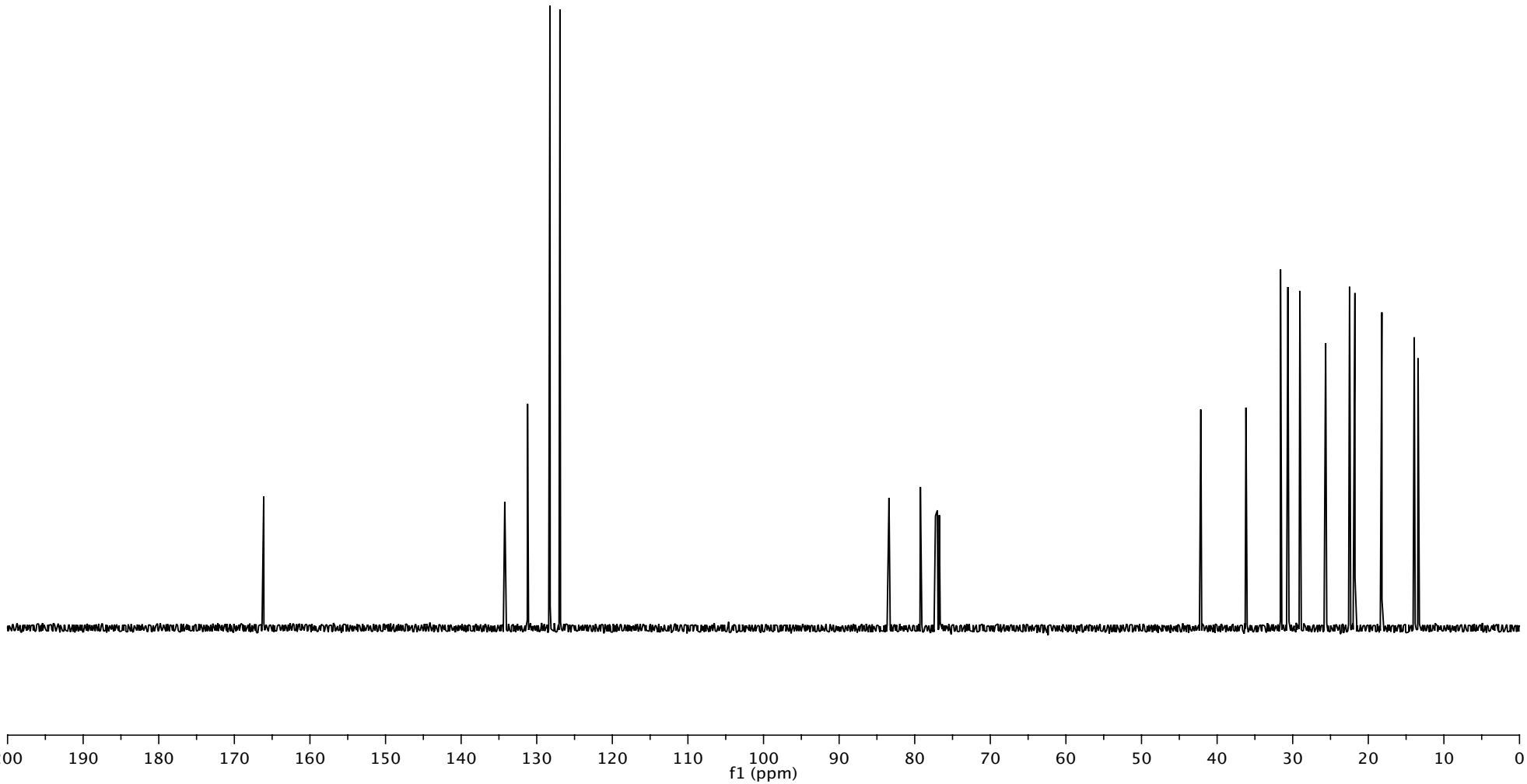

O
Ph
NH
6

^{1}H NMR of **8o**


2.00
0.99
2.01
0.97
0.99
2.03
2.06
4.15
2.02
8.18
6.07
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
f1 (ppm)


O
Ph
NH
6

^{13}C NMR of **8o**


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)