Electronic Supplementary Material (ESI) for ChemComm.

Electronic Supplementary Information

A new method for peptide synthesis in the N→C direction: amide assembly through silver-promoted reaction of thioamides

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General Information

^{1}H NMR spectra were recorded using a Varian Unity Inova 500 (500 MHz), a Varian Unity Inova 400 (400 MHz) or a Bruker AVANCE2 500 MHz spectrometer with TXI cryoprobe. Spectra were recorded at 298 K. Spectra were obtained in deuterated chloroform, unless otherwise stated, utilising the residual solvent peak as the internal reference. The spectra are reported as: parts per million (ppm) downfield shift, relative to the residual solvent peak; relative integral, multiplicity (s = singlet, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq doublet of quartets, m = multiplet) and coupling constant (*J* in Hz). ^{13}C NMR spectra were recorded using a Varian Unity Inova 500 (125 MHz) or a Varian Unity Inova 400 (100 MHz) and spectra were obtained at 298 K unless stated otherwise. Chemical shifts (δ) are reported in parts per million (ppm) relative to the internal standard of the solvent peak; $CHCl_3$ (77). IR spectra were recorded on a Perkin Elmer FT-IR spectrometer and were obtained from a thin film of the neat product. Absorption maxima are expressed in wavenumbers (cm^{-1}). All mass spectra were recorded on an Agilent 6220 ESI-TOF Mass Spectrometer coupled to an Agillent 1100 LC System (Agilent, Palo Alto, CA). All data were acquired and reference mass corrected via a dual spray electrospray ionisation (ESI) source. Acquisition was performed using the Agilent Mass Hunter software version B.02.01 and analysis was performed using the Agilent Mass Hunter software version B.04.00. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-1000 polarimeter at 589 nm with a cell path length of 10 cm; solution concentrations are reported in grams per 100 ml using the indicated spectroscopic grade solvents.

Most reagents were commercially available reagent grade chemicals and were used without further purification. Toluene was distilled over sodium. Anhydrous THF, Et_2O and CH_2Cl_2 were obtained from solvent drying and dispensing system where the solvent was dried by passage through two packed columns of neutral alumina. Methanol and triethylamine were distilled from calcium hydride. Powdered molecular sieves were activated with a microwave and allowed to cool under vacuum. DMSO and DMF were dried over activated sieves (4 Å) for 16 h before use.

Analytical thin layer chromatography was performed with aluminium backed plates precoated with silica gel 60 F254 (0.2 mm), and visualisation was achieved by inspection under short-wave UV light followed by staining with phosphomolybdic acid dip

[polyphosphomolybdic acid (12 g), ethanol (250mL)]. Flash chromatography was performed using silica gel (230-400 mesh); eluting solvents reported as % v/v mixtures Analytical, preparative and semi-preparative reverse phase HPLC (RP-HPLC) were performed using an Agilent 1200 series LC System. Analytical HPLC employed a SGE Protecol-P C18 HPH 125 column (4.6 × 150 mm column, 5 μm particle size, flow rate of 1 mL min^{-1}). Preparative RP-HPLC employed a Phenomenex C18 column (21.2 × 150 mm, 5 μm particle size, flow rate 8 mL min^{-1}). Semi-preparative RP-HPLC employed a Phenomenex Synergy Hydro-RP column (50 × 21.2 mm, 4 μm particle size, flow rate 5 mL min^{-1}). Chiral HPLC was perfromed using a Phenomenex Lux 5μ Cellulose-3 LC column (250 x 10.00 mm, flow rate of 2 mL min^{-1}). The mobile phase consisted of eluents A (0.1% TFA in water) and B (0.1% TFA in acetonitrile). The results were analysed on Agilent ChemStation version B.01.03 software.

General Procedures

General Procedure A: Formation of thioacetamides using Lawesson's reagent. Acetic anhydride (2.2 mL, 23 mmol) was added dropwise to a cooled solution (0 °C) of the amine (20 mmol) and triethylamine (5.4 mL, 40 mmol) in CH_2Cl_2 (4 mL) and the solution was stirred for 18 h. The solution was diluted with CH_2Cl_2 (100 mL) and partitioned with 1 M HCl (100 ml). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic fractions were washed with 5% $NaHCO_3$ (100 mL), brine (100 mL) and dried ($MgSO_4$). The solvent was evaporated to provide the crude amide. The amide was dissolved in toluene (100 mL) and Lawesson's reagent (4.4 g, 11 mmol) was added. The solution was stirred at room temperature for 16 h. The solvent was evaporated and the residue was purified by flash chromatography (SiO_2) eluting with 2:1 hexanes: EtOAc to afford the desired thioacetamide.

General Procedure B: Formation of thioacetamides using ethyl dithioacetate. Ethyl dithioacetate (0.14 mL, 1.4 mmol) and triethylamine (0.27 mL, 2.0 mmol) were added to a solution of the amine (1.0 mmol) in CH_2Cl_2 (12 mL). The solution was stirred for 16 h before the solvent was removed and the residue partitioned between EtOAc (100 ml) and 1 M HCl (100 mL). The aqueous fraction was extracted with EtOAc (3 × 100 mL).The combined organic fractions were washed with 5% $NaHCO_3$ (100 mL), brine (100 mL) and dried ($MgSO_4$). The

solvent was evaporated and the residue was purified by flash chromatography (SiO_2), eluting with 2:1 hexanes: EtOAc to afford the desired thioacetamide.

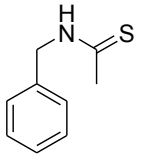
General procedure C: Imide synthesis at room temperature. Silver carbonate (0.15 mmol) was added to a vigorously stirred solution of acid (0.1 mmol) and thioamide (0.15 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred for 2 h, then the solvent was evaporated and the residue purified by flash chromatography (SiO_2) eluting with 1:1 hexanes:EtOAc to afford the imide.

General procedure D: Imide synthesis at 40 °C. Silver carbonate (0.15 mmol) was added to a vigorously stirred solution of acid (0.10 mmol) and thioamide (0.15 mmol) in CH_2Cl_2 (5 mL). The mixture was heated at reflux for 16 h, then the solvent was evaporated and the residue purified by flash chromatography (SiO_2) eluting with 1:1 hexanes:EtOAc to afford the imide.

General Procedure E: Imide methanolysis. $NaHCO_3$ (1.0 mmol) was added to a solution of the imide (0.10 mmol) in dry methanol (2 mL) and the solution was stirred for 2 h. The solvent was evaporated, the residue redissolved in EtOAc and filtered to remove $NaHCO_3$. The solvent was evaporated to yield the crude amide.

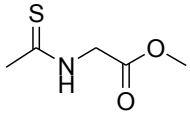
General Procedure F: Concomitant imide and methyl ester hydrolysis. A solution of NaOH (0.30 mmol) in H_2O (1 mL) was added to a solution of the imide ester (0.10 mmol) in dioxane (1 mL) and the solution was stirred for 2 h. Citric acid (0.15 mmol) was added adjust the solution to pH 5–6, then the solution was partitioned between EtOAc (50 mL) and H_2O (50 mL). The aqueous phase was extracted with EtOAc (2 × 50 mL). The organic fractions were combined, washed with brine (50 mL) and dried ($MgSO_4$). The solvent was evaporated and the residue purified by flash chromatography (SiO_2) eluting with 14:2:1 EtOAc: MeOH: H_2O to afford the desired acid.

N-Benzylthioacetamide 9



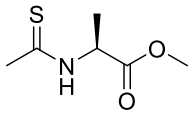
Compound **9** was prepared from benzylamine (2.2 mL, 22 mmol) according to General Procedure A. After recrystallization (ether/hexanes) the title compound **9** was isolated as colourless crystals (3.4 g, 92%): **MP.** 67–70 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40–7.32 (5 H, m, ArH), 7.30 (1 H, brs, NH), 4.82 (2 H, d, *J* = 5.0 Hz, CH_2Ar), 2.59 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.9, 136.0, 129.0, 128.4, 128.2, 50.6, 34.1; **IR (thin film)**: 3210, 1553, 1454,1291,1341,1164, 939, 736, 693 cm^{-1}. Characterisation data consistent with that reported.[1]

N-Thioacetylglycine methyl ester 12G



Compound **12G** was prepared from glycine methyl ester hydrochloride (2.5 g, 20 mmol) according to General Procedure A. The title product was isolated as a pale yellow oil (2.7 g, 92%): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.02 (1 H, br s, NH), 4.30 (2 H, m, *J* = 4.2 Hz, CH_2CO), 3.75 (3 H, s, OMe), 2.56 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 201.5, 168.9, 52.5, 47.0, 33.2; **MS (ESI)** *m/z* 148 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_5H_9NO_2S$ 148.0427, found 148.0395**; IR (thin film)**: 3309, 3042, 1736,1532, 1355, 1208, 1174 cm^{-1}.Characterisation data consistent with that reported for the ethyl ester.[2]

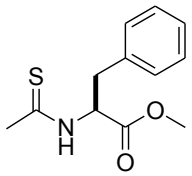
N-Thioacetyl-L-alanine methyl ester 12A



Compound **12A** was prepared from alanine methyl ester (2.0 g, 14 mmol) according to General Procedure A. The title compound **12A** was isolated as a pale yellow oil (2.0 g, 89%). **$[\alpha]^{24}_D$** –6.7 (*c* 1.7, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (1 H, br s, NH), 5.11 (1 H, m, NHC*H*), 3.79(3 H, s, OMe), 2.57 (3 H, s, Me), 1.53 (3 H, d, *J* = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.8, 172.9, 63.6, 62.7, 34.2, 17.1; **MS** (ESI) *m/z* 162 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$)

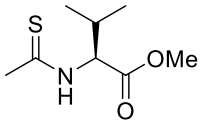
calcd. $C_6H_{11}NO_2S$ 162.0583, found 162.0584; **IR (thin film)**: 3308, 3031, 1738, 1534, 1453, 1375, 1206, 1132 cm^{-1}.

N-Thioacetyl-L-phenylalanine methyl ester 12F



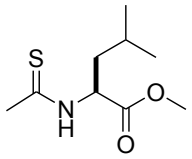
Compound **12F** was prepared from phenylalanine methyl ester hydrochloride (2.2 g, 10 mmol) according to General Procedure A. The title product was isolated as a pale yellow crystals (1.8 g, 72%): **MP.** 105–108 °C; $[\alpha]^{24}_D$ +237 (*c* 0.8, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 (1 H, s, NH), 7.32–7.24 (3 H, m, ArH), 7.07 (2 H, m, ArH), 5.40 (1 H, m, CH_2CH), 3.77 (3 H, s, OMe), 3.44 (1 H, dd, *J* = 6.0, 14.0 Hz, CHHAr), 3.21 (1 H, dd, *J* = 4.6, 14.0 Hz, CHHAr), 2.56 (3 H, s, Me). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.8, 171.1, 135.3, 129.2, 128.6, 127.3, 58.5, 52.5, 36.1, 34.2; **MS** (ESI) m/z 238 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{12}H_{15}NO_2S$ 238.0896, found 238.0896; **IR (thin film)**: 3313, 3029, 2952, 1737, 1524, 1438, 1370, 1203 cm^{-1}.

N-Thioacetyl-L-valine methyl ester 12V



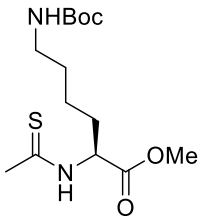
Compound **12V** was prepared from valine methyl ester hydrochloride (2.0 g, 12 mmol) according to General Procedure A. The title compound was isolated as a pale yellow oil (1.8 g, 79%): $[\alpha]^{24}_D$ +9.2 (*c* 1.7, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (1 H, br s, NH), 5.14 (1 H, dd, *J* = 4.9, 8.4 Hz, NHC*H*CH), 3.77 (3 H, s, OMe),2.39 (3 H, s, Me), 2.15 (1 H, m, NHCHC*H*), 1.02 (3 H, d, *J* = 7.0 Hz), 0.95 (3 H, d, *J* = 7.0 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 201.6, 171.7, 62.9, 62.3, 34.3, 31.0, 18.7, 18.3; **MS** (ESI) *m/z* 190 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_8H_{15}NO_2S$ 190.0896, found 190.0893; **IR (thin film)**: 3313, 2966, 1729, 1527, 1372, 1180 cm^{-1}.

N-Thioacetyl-L-leucine methyl ester 12L



Compound **12L** was prepared from leucine methyl ester hydrochloride (1.8 g, 10 mmol) according to General Procedure A. The title compound was isolated as a pale yellow oil (1.6 g, 70%). $[\alpha]^{24}_{D}$ +8.4 (*c* 0.6, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (1 H, brd, *J* = 8.05 Hz, NH), 5.07 (1 H, m, C*H*NH), 3.66 (3 H, s, OMe), 2.47 (3 H, s, Me), 1.66–1.55 (3 H, m, C*H*CH_2), 0.85 (6 H, m, CH(*Me*)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 172.6, 56.6, 52.2, 40.2, 33.3, 24.6, 22.3, 21.7; **MS** (ESI) *m/z* 204 [$(M+H)^+$, 100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_9H_{17}NO_2S$ 204.1053, found 204.1054; **IR (thin film)**: 3308, 2957, 1739, 1537, 1438, 1371, 1207 cm^{-1}.

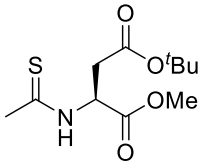
N$^{\varepsilon}$-Boc-N$^{\alpha}$-thioacetyl-L-lysine methyl ester 12K



Method A: Compound **12K** was prepared from H-Lys(Boc)OMe (2.0 g, 6.8 mmol) according to General Procedure A. The title compound was isolated as a pale yellow oil (1.6 g, 75%): $[\alpha]^{24}_{D}$ +24 (*c* 1.3, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (1 H, br s, NH), 5.08 (1 H, m, NH), 4.61 (1 H, br s, C*H*CH_2), 3.77 (3 H, s, OMe), 3.10 (2 H, m, CH_2NH), 2.59 (3 H, s, Me), 2.02–1.84 (2 H, m, CHCH_2), 1.51–1.27 (4 H, m, CH_2CH_2), 1.43 (9 H, s, tBu); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 201.6, 171.9, 156.3, 79.3, 58.0, 52.5, 39.6, 34.0, 30.5, 29.8, 28.4, 22.1; **MS** (ESI) *m/z* 319 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{14}H_{26}N_2O_4S$ 319.1686, found 319.1686; **IR (thin film)**: 3255, 2935, 1744, 1686, 1524, 1366, 1252, 1171 cm^{-1}.

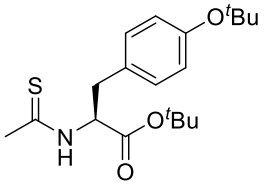
Method B: Compound **12K** was prepared from H-Lys(Boc)OMe (100 mg, 0.34 mmol) according to General Procedure B. The title compound was isolated as a colourless oil (68 mg, 63%). Characterisation identical to that above.

N-Thioacetyl-L-aspartate α-methyl β-t-butyl diester 12D



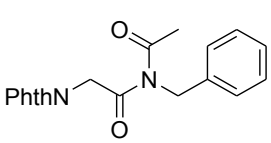
Compound **12D** was prepared from H-Asp(O^{t}Bu) methyl ester hydrochloride (2.0 g, 8.4 mmol) according to General Procedure A. The title compound was isolated as a colourless oil (1.6 g, 73%): **[α]$^{24}_D$** +126 (*c* 0.28, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (1 H, d, *J* = 7.0 Hz, NH), 5.35 (1 H, dt, *J* = 4.4, 7.0 Hz, NHC*H*CH_2), 3.72 (3 H, s, OMe), 2.94 (2 H, m, CHCH_2), 2.53 (3 H, s, Me), 1.37 (9 H, s, tBu); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 201.0, 170.4, 170.0, 81.8, 54.1,52.6, 35.8, 33.8, 27.8; **MS** (ESI) *m/z* 262 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{11}H_{19}NO_4S$ 262.1108, found 262.1098; **IR (thin film)**: 3334, 1725, 1365, 1224, 1143 cm^{-1}.

N-Thioacetyl-O-t-butyl-L-tyrosine t-butyl ester 12Y



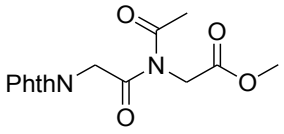
Compound **12Y** was prepared from H-Tyr(O^{t}Bu) methyl ester hydrochloride (2.0 g, 6.1 mmol) according to General Procedure A. The title compound was isolated as a colourless oil (1.6 g, 75%): **[α]$^{24}_D$** +128 (*c* 0.32, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (1 H, d, *J* = 6.6 Hz, NH), 7.04 (2 H, d, *J* = 8.7 Hz, ArH), 6.89 (2 H, d, *J* = 8.7 Hz, ArH), 5.17 (1 H, m, NHC*H*CH_2), 3.21 (2 H, m, CHCH_2), 2.54 (3 H, s, Me), 1.38 (9 H, s, tBu), 1.31 (9 H, s, tBu); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.3, 170.1, 154.3, 130.6, 129.8, 124.0, 83.0, 78.3, 59.1, 35.6, 34.1, 28.7, 27.9; **MS** (ESI) *m/z* 352 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{19}H_{29}NO_3S$ 352.1941, found 352.1943; **IR (thin film)**: 3294, 2977, 1725, 1506, 1366, 1159 cm^{-1}.

N′-Acetyl-N′-benzyl N-phthaloylglycinamide 10



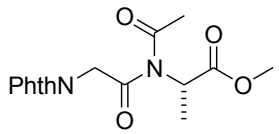
The title compound was prepared from N-phthaloylglycine **11G** (0.24 mmol, 51 mg) and N-benzylthioacetamide **9** (0.24 mmol, 41 mg) with silver (I) carbonate (0.24 mmol, 68 mg) according to general procedure C. The title compound was isolated as a white solid (55 mg, 66%). **^{1}HNMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.71 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.37–7.13 (5 H, m, ArH), 5.00 (2 H, s, CH_2), 4.98 (2 H, s, CH_2), 32.31 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.5, 170.1, 167.8, 135.9, 134.1, 132.2, 129.0, 127.6, 126.1, 123.5, 48.0, 44.2, 25.5;; **MS** (ESI) m/z 359 [$(M+Na)^+$, 100%], **HRMS** (ESI, MNa^+) Calcd. for $C_{19}H_{16}N_2O_4Na$ 359.100 found 359.090.

N-Phthaloylglycinyl-N-acetylglycine methyl ester 10GG



The title compound was prepared from N-phthaloylglycine **11G** (0.33 mmol, 68 mg) and N-thioacetylglycine methyl ester **12G** (0.49 mmol, 73 mg) with silver (I) carbonate (0.49 mmol, 0.14 g) according to general procedure C. The title compound was isolated as white solid (80 mg, 76%). **MP.** 130–134 °C; **^{1}HNMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.72 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.96 (2 H, s, CH_2), 4.46 (2 H, s, CH_2), 3.75 (3 H, s,OMe), 2.33 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.3, 169.6, 168.2, 167.5, 134.1, 132.1, 123.5, 52.7, 46.1, 43.9, 24.9;; **MS** (ESI) m/z 319 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{15}H_{14}N_2O_6$ 319.0925 found 319.0929; **IR** ($CHCl_3$): 2956, 1775, 1749, 1711, 1615, 1468, 1405, 1371, 1192, 980, 953, 715 cm^{-1}.

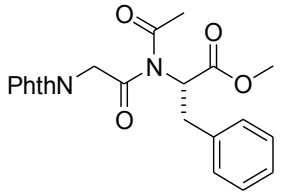
N-Phthaloylglycinyl-N-acetyl-L-alanine methyl ester 10GA



The title compound was prepared from N-phthaloylglycine **11G** (0.15 mmol, 33 mg) and N-thioacetyl-L-alanine methyl ester **12A** (0.24 mmol, 38.3 mg) with silver (I) carbonate (0.24 mmol, 66 mg) according to general procedure C. The title compound **10GA** was isolated as white solid (52 mg, 99%); **MP.** 113–115 °C; **$[\alpha]^{22}_D$** –18 (*c* 0.97, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.85 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.72 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.93 (1 H, d,

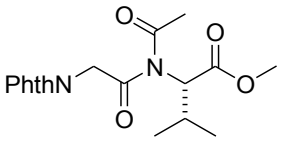
J = 17.7 Hz, C*H*H), 4.84 (1 H, d, *J* = 17.9 Hz, CH*H*), 4.54 (1 H, q, *J* = 6.8 Hz, C*H*Me), 3.68 (3 H, s, OMe), 2.39 (3 H, s, Me), 1.57 (3 H, d, *J* = 6.8 Hz, Me). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.3, 169.9, 169.6, 167.7, 134.1, 132.1, 123.4, 54.9, 52.6, 44.1, 24.8, 15.2; **MS** (ESI) m/z 333 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{16}H_{16}N_2O_6$ 333.1081 found 333.1090; **IR** ($CHCl_3$): 3460, 3016, 2970, 1740, 1715, 1615, 1468, 1406, 1376, 1313, 1274, 1217, 1109, 1068, 954, 755, 717 cm^{-1}.

N-Phthaloylglycinyl-N-acetyl-L-phenylalanine methyl ester 10GF



The title compound was prepared from N-phthaloylglycine **11G** (0.12 mmol, 26 mg) and N-thioacetyl-L-phenylalanine methyl ester **12F** (0.19 mmol, 44 mg) with silver (I) carbonate (0.19 mmol, 52 mg) according to general procedure C. The title compound was isolated as colorless crystals (48 mg, 94%): **MP**. 135–140 °C; **$[\alpha]^{22}_{D}$** –281 (c 0.84, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.88 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.74 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.37 (2 H, m, ArH), 7.31–7.23 (3 H, m, ArH), 4.98 (1 H, d, *J* = 18.0 Hz, C*H*CH), 4.8 (1 H, d, *J* = 18.0 Hz, CHC*H*), 4.43 (1 H, dd, *J* = 3.7, 10.7 Hz, CH), 3.72 (3 H, s, OMe), 3.49 (1 H, dd, *J* = 3.8, 14.3 Hz, C*H*H), 3.22 (1 H, dd, *J* = 10.4, 14.0 Hz, CH*H*), 1.83 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.8, 170.1, 169.1, 167.8, 137.2, 134.1, 132.1, 129.5, 129.0, 127.2, 123.5, 61.9, 52.7, 44.4, 34.5, 24.5; **IR** ($CHCl_3$): 3028, 2954, 1775, 1746, 1712, 1615, 1496, 1468, 1454, 1403, 1378, 1246, 1211, 1169, 953, 751, 715, 705 cm^{-1}; **MS** (ESI) m/z 409 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{22}H_{20}N_2O_6$ 409.1394 found 409.1410.

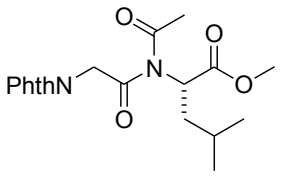
N-Phthaloylglycinyl-N-acetyl-L-valine methyl ester 10GV



The title compound was prepared from N-phthaloylglycine **11G** (0.18 mmol, 38 mg) and N-thioacetyl-L-valine methyl ester **12V** (0.28 mol, 52 mg) with silver (I) carbonate (0.28 mmol, 77

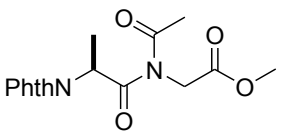
mg) according to general procedure C. The title compound was isolated as colorless oil (66 mg, 99%); **[α]$^{22}_{D}$** –56 (c 0.86, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.85 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.72 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.94 (1 H, d, *J* = 18.0 Hz, C*H*H), 4.87 (1 H, d, *J* = 18.2 Hz, CH*H*), 4.07 (1 H, d, *J* = 9.5 Hz, CH), 3.68 (3 H, s, OMe), 2.61 (1 H, m, C*H*$(Me)_2$), 2.39 (3 H, s, Me), 1.18 (3 H, d, *J* = 6.5 Hz, Me), 0.90 (3 H, d, *J* = 6.9 Hz, Me); **^{13}C NMR** (100 MHZ, $CDCl_3$), δ 173.1, 170.0, 169.5, 167.6, 134.1, 132.1, 123.5, 64.8, 52.5, 43.9, 27.6, 25.4, 22.4, 19.3; **MS** (ESI) m/z 361 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{18}H_{20}N_2O_6$ 361.1394 found 361.1401; **IR** ($CHCl_3$): 2966, 1775, 1717, 1469, 1405, 1381, 1267, 1215, 1115, 1076, 1018, 954, 730, 716 cm^{-1}.

N-Phthaloylglycinyl-N-acetyl-L-leucine methyl ester 10GL



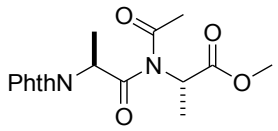
The title compound was prepared from N-phthaloylglycine **11G** (0.14 mmol, 29 mg) and N-thioacetyl-L-leucine methyl ester **12L** (0.21 mmol, 44 mg) with silver (I) carbonate (0.21 mmol, 59 mg) according to general procedure C. The title compound was isolated as colorless crystals (52 mg, 97%); **MP.** 84–88 °C; **[α]$^{22}_{D}$** +326 (c 0.20, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.72 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.95 (1 H, d, *J* = 18.1 Hz, C*H*CH), 4.83 (1 H, d, *J* = 18.1 Hz, CHC*H*), 4.56 (1 H, m, CH), 3.70 (3 H, s, OMe), 2.40 (3 H, s, Me), 2.14 (1 H, m, CH), 1.71 (2 H, m, C*HH*CH), 0.97 (3 H, d, *J* = 6.5 Hz, Me), 0.96 (3 H, d, *J* = 6.5 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.9, 170.1, 170.0, 167.7, 134.1, 132.1, 123.5, 57.4, 52.7, 44.1, 38.5, 25.4, 25.2, 22.8, 22.3; **MS** (ESI) m/z 375 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{19}H_{22}N_2O_6$ 375.1551 found 375.1554; **IR** ($CHCl_3$): 3459, 2970, 1719, 1468, 1406, 1375, 1216, 1090, 954, 716 cm^{-1}.

N-Phthaloyl-L-alaninyl-N-acetylglycine methyl ester 10AG



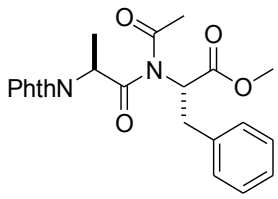
The title compound was prepared from (*S*)-N-phthaloylalanine **11A** (0.20 mmol, 44 mg) and N-thioacetyl-glycine methyl ester **12G** (0.30 mmol, 44 mg) with silver (I) carbonate (0.30 mmol, 83 mg) according to general procedure C. The title compound was isolated as white solid (56 mg, 84%): **MP**. 117–119 °C; **[α]$^{25}_{D}$** –87 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.84 (2 H, m, ArH), 7.73 (2 H, m, ArH), 5.48 (1 H, q, *J* = 6.8 Hz, C*H*Me), 4.30 (2 H, s, CH_2), 3.52 (3 H, s, OMe), 2.35 (3 H, s, MeCO), 1.65 (3 H, d, *J* = 6.8 Hz, CH(*Me*)). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.8, 172.5, 168.3, 167.2, 134.2, 131.7, 123.5, 52.4, 49.9, 46.1, 25.1, 15.4; **MS** (ESI) m/z 333 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{16}H_{16}N_2O_6$ 333.1081 found 333.1077; **IR** ($CHCl_3$): 2957, 1780, 1750, 1713, 1438, 1385, 1272, 1197, 1073, 990, 884, 753, 721 cm^{-1}.

N-Phthaloyl-L-alaninyl-N-acetyl-L-alanine methyl ester 10AA



The title compound was prepared from (*S*)-N-phthaloylalanine (0.15 mmol, 34 mg) and N-thioacetyl-L-alanine methyl ester (0.23 mmol, 38 mg) with silver (I) carbonate (0.23 mmol, 65 mg) according to general procedure C. The title compound was isolated as colorless crystals (51 mg, 95%); **MP**. 124–126 °C; **[α]$^{22}_{D}$** –180 (*c* 0.58, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.87 (2 H, dd, *J* =3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.36 (1 H, q, *J* = 6.9 Hz, C*H*Me), 4.20 (1 H, q, *J* = 6.9 Hz, C*H*Me), 3.13 (3 H, s, OMe), 2.38 (3 H, s, Me), 1.66 (3 H, d, *J* = 7.0 Hz, CH*Me*), 1.52 (3 H, d, *J* = 7.0 Hz, CH*Me*).**^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.4, 172.6, 169.7, 167.5, 134.5, 131.6, 123.7, 53.8, 52.0, 48.9, 25.0, 16.0, 15.5; **MS** (ESI) m/z 347 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{17}H_{18}N_2O_6$ 347.1238 found 347.1235; **IR** ($CHCl_3$): 2950, 1713, 1435, 1384, 1269, 1230, 1087, 878, 770, 722 cm^{-1}.

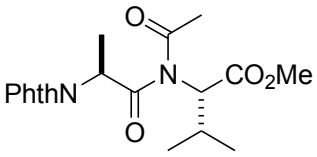
N-Phthaloyl-L-alaninyl-N-acetyl-L-phenylalanine methyl ester 10AF



The title compound was prepared from (*S*)-N-phthaloylalanine (0.14 mmol, 31 mg) and N-thioacetyl-L-phenylalanine methyl ester (0.21 mmol, 51 mg) with silver (I) carbonate (0.21

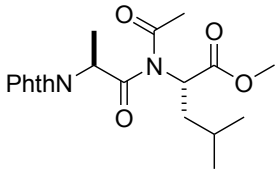
mmol, 59 mg) according to general procedure C. The title compound was isolated as white solid (50 mg, 83%); **MP**. 76–78 °C; **[α]$^{22}_{D}$** –217 (*c* 0.50, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.85 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.31 (3 H, m, ArH), 7.18 (2 H, m, ArH), 4.66 (1 H, m, C*H*Me), 4.13 (1 H, dd, *J* = 3.5, 10.5 Hz, C*H*CH_2), 3.45 (1 H, dd, *J* = 3.5, 14.1 Hz, CHC*H*H), 3.23 (1 H, dd, *J* = 10.8, 14.0 Hz, CHCH*H*), 3.05 (3 H, s, OMe), 2.33 (3 H, s, Me), 1.27 (3 H, d, *J* = 6.9 Hz, CH*Me*); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.3, 172.7, 168.8, 167.1, 137.0, 134.3, 131.8, 129.8, 128.9, 127.3, 123.5, 60.4, 51.9, 47.6, 35.7, 25.3, 15.1; **MS** (ESI) m/z 423 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{23}H_{22}N_2O_6$ 423.1551 found 423.1550; **IR** ($CHCl_3$): 2970, 1715, 1384, 1217, 1074, 764, 722 cm^{-1}.

N-Phthaloyl-L-alaninyl-N-acetyl-L-valine methyl ester 10AV



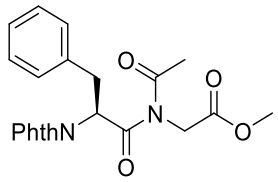
The title compound was prepared from (*S*)-N-phthaloylalanine (0.10 mmol, 22 mg) and N-thioacetyl-L-valine methyl ester (0.15 mmol, 28 mg) with silver (I) carbonate (0.15 mmol, 41 mg) according to general procedure C. The title compound was isolated as white crystals (36 mg, 95%); **MP.** 165–170 °C; **[α]$^{22}_{D}$** –265 (c 0.95, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.87 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.33 (1 H, q, *J* = 7.0 Hz, C*H*Me), 3.61 (1 H, d, *J* = 8.9 Hz, CH), 2.98 (3 H, s, OMe), 2.64 (1 H, m, C*H*$(Me)_2$), 2.39 (3 H, s, CH*Me*), 1.66 (3 H, d, *J* = 7.0 Hz, CH*Me*), 1.14 (3 H, d, *J* = 6.5 Hz, CH*Me*), 0.82 (3 H, d, *J* = 7.0 Hz, CH*Me*); **^{13}CNMR** (100 MHz, $CDCl_3$), δ174.0, 173.1, 168.8, 167.3, 134.2, 131.8, 123.5, 63.5, 51.6, 48.2, 29.1, 24.8, 22.1, 19.5, 15.6; **MS** (ESI) m/z 375 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{19}H_{22}N_2O_6$ 375.1551 found 375.1535; **IR** ($CHCl_3$): 2970, 1752, 1715, 1468, 1385, 1277, 1227, 1071, 1019, 991, 878, 743, 722 cm^{-1}.

N-Phthaloyl-L-alaninyl-N-acetyl-L-leucine methyl ester 10AL



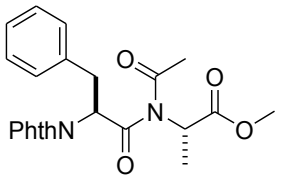
The title compound was prepared from (*S*)-N-phthaloylalanine (0.18 mmol, 39 mg) and N-thioacetyl-L-leucine methyl ester (0.27 mmol, 55 mg) with silver (I) carbonate (0.27 mmol, 74 mg) according to general procedure C. The title compound was isolated as white solid (69 mg, 99%); **MP**. 73–75 °C; **[α]$^{22}_{D}$** –185 (*c* 0.77, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.74 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.38 (1 H, q, *J* = 6.9 Hz, C*H*Me), 4.08 (1 H, dd, *J* = 4.9, 8.4 Hz, C*H*CH_2), 3.07 (3 H, s, OMe), 2.38 (3 H, s, Me), 2.05 (1 H, ddd, *J* = 5.0, 8.9, 14.4 Hz, CHC*H*H), 1.76 (1 H, ddd, *J* = 5.0, 8.3, 14.4 Hz, CHCH*H*), 1.67 (3 H, d, *J* = 6.8 Hz, CH*Me*), 1.57 (1 H, m, CH), 0.97 (3 H, d, *J* = 6.6 Hz, CH*Me*), 0.96 (3 H, d, *J* = 6.6 Hz, CH*Me*); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.9, 172.3, 169.3, 166.9, 134.2, 131.5, 123.4, 56.7, 51.8, 48.7, 39.0, 25.1, 24.8, 22.9, 22.0, 15.6; **MS** (ESI) m/z 389 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{20}H_{24}N_2O_6$ 389.1707 found 389.1717; **IR** ($CHCl_3$): 2970, 1716, 1435, 1384, 1266, 1217, 880, 721 cm^{-1}.

N-Phthaloyl-L-phenylalaninyl-N-acetylglycine methyl ester 10FG



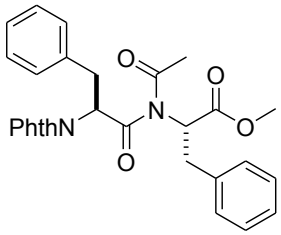
The title compound was prepared from (*S*)-N-phthaloylphenylalanine (0.17 mmol, 50 mg) and N-thioacetyl-glycine methyl ester (0.25 mmol, 38 mg) with silver (I) carbonate (0.25 mmol, 70 mg) according to general procedure C. The title compound was isolated as white solid (51 mg, 74%); **MP**. 82–87 °C; **[α]$^{25}_{D}$** +87 (*c* 0.92, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.76 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.68 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.23–7.11 (5 H, m, ArH), 5.77 (1 H, dd, *J* = 4.5, 10.3 Hz, C*H*CH_2), 4.35 (2 H, s, CH_2CO), 3.57 (1 H, dd, *J* = 10.4, 14.1 Hz, C*H*H), 3.54 (3 H, s, OMe), 3.48 (1 H, dd, *J* = 4.6, 14.2 Hz, CH*H*), 2.41 (3 H, s, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.5, 172.1, 168.3, 167.4, 136.4, 134.1, 131.3, 129.0, 128.5, 126.9, 123.4, 56.2, 52.5, 46.2, 34.5, 25.2; **MS** (ESI) m/z 409 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{22}H_{20}N_2O_6$ 409.1394 found 409.1405; **IR** ($CHCl_3$): 3028, 1775, 1750, 1714, 1383, 1214, 1191, 979, 927, 875, 752, 720, 701 cm^{-1}.

N-Phthaloyl-L-phenylalaninyl-N-acetyl-L-alanine methyl ester 10FA



The title compound was prepared from (*S*)-N-phthaloylphenylalanine (0.13 mmol, 41 mg) and N-thioacetyl-L-alanine methyl ester (0.21 mmol, 33 mg) with silver (I) carbonate (0.21 mmol, 57 mg) according to general procedure C. The title compound was isolated as white solid (50 mg, 86%); **MP**. 53–56 °C; **[α]$^{22}_{D}$** –237 (c 0.87, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.77 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.69 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.15 (5 H, m, ArH), 5.57 (1 H, t, *J* = 8.0 Hz, C*H*CH_2), 4.25 (1 H, q, *J* = 7.0 Hz, C*H*Me), 3.50 (2 H, d, *J* = 8.0 Hz, CH_2CH), 3.15 (3 H, s, OMe), 2.42 (3 H, s, Me), 1.55 (3 H, d, *J* = 6.8 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.7, 172.5, 169.7, 167.4, 136.3, 134.2, 131.4, 129.0, 128.6, 127.0, 123.4, 55.2, 54.0, 52.1, 34.8, 25.0, 16.1; **MS** (ESI) m/z 423 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{23}H_{22}N_2O_6$ 423.1551 found 423.1555; **IR** ($CHCl_3$): 3026, 2952, 1776, 1713, 1606, 1497, 1468, 1455, 1435, 1383, 1266, 1233, 1101, 1032, 979, 878, 753, 720 cm^{-1}.

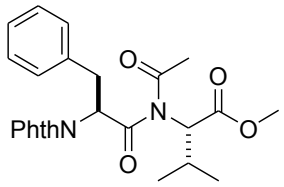
N-Phthaloyl-L-phenylalaninyl-N-acetyl-L-phenylalanine methyl ester 10FF



The title compound was prepared from (*S*)-N-phthaloylphenylalanine (0.12 mmol, 36 mg) and N-thioacetyl-L-phenylalanine methyl ester (0.18 mmol, 42 mg) with silver (I) carbonate (0.18 mmol, 50 mg) according to general procedure C. The title compound was isolated as colorless crystals (49 mg, 79%); **MP.** 137–139 °C; **[α]$^{22}_{D}$** –271 (*c* 0.94, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.76 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.70 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 6.87–7.41 (10 H, m, ArH), 4.76 (1 H, m, C*H*CH_2), 4.16 (1 H, m, C*H*CH_2), 3.46 (1 H, dd, *J* = 3.56, 13.96 Hz, C*H*H), 3.23 (1 H, dd, *J* = 10.9, 13.9 Hz, CH*H*), 3.10 (1 H, m, C*H*H), 3.04 (3 H, brs, OMe), 2.96 (1 H, dd, *J* = 4.4, 13.9 Hz, CH*H*), 2.36 (3 H, s, Me). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.3, 171.9, 168.7, 167.1, 137.2, 136.2, 134.2, 131.3, 129.8, 128.9, 128.9, 128.4, 127.3, 126.8, 123.4,

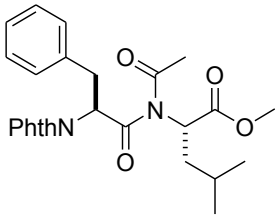
60.4, 53.9, 51.9, 35.7, 35.0, 25.3. **IR** ($CHCl_3$): 3028. 2952. 1775. 1748. 1713. 1605. 1496. 1435. 1381. 1262. 1243. 1215. 1100. 1085. 978. 749. 719. 700 cm^{-1}. **MS** (ESI) m/z 499 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{29}H_{26}N_2O_6$ 499.1864 found 499.1785.

N-Phthaloyl-L-phenylalaninyl-N-acetyl-L-valine methyl ester 10FV



The title compound was prepared from (*S*)-N-phthaloylphenylalanine (0.16 mmol, 48 mg) and N-thioacetyl-L-valine methyl ester (0.24 mmol, 46 mg) with silver (I) carbonate (0.24 mmol, 67 mg) according to general procedure C. The title compound was isolated as white solid (72 mg, 99%); **MP**. 67–69 °C; **$[\alpha]^{22}_D$** –279 (c 0.93, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.78 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.70 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.16 (5 H, m, ArH), 5.51 (1 H, m, C*H*CH_2), 3.67 (1 H, d, *J* = 8.9 Hz, C*H*CH), 3.55 (1 H, dd, *J* = 5.5, 13.9 Hz, C*H*HCH), 3.48 (1 H, dd, *J* = 9.7, 13.9 Hz, CH*H*CH), 3.02 (3 H, s, OMe), 2.65 (1 H, m, C*H*$(Me)_2$), 2.43 (3 H, s, Me), 1.15 (3 H, d, *J* = 6.4 Hz, Me), 0.84 (3 H, d, *J* = 6.9 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.2, 173.1, 168.9, 167.3, 136.3, 134.2, 131.5, 129.0, 128.5, 126.9, 123.5, 63.8, 54.8, 51.6, 35.1, 28.9, 25.0, 22.1, 19.7 (2 C overlapping or obscured); **MS** (ESI) m/z 451 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{25}H_{26}N_2O_6$ 451.1864 found 451.1864; **IR** ($CHCl_3$): 2959, 1753, 1716, 1468, 1384, 1271, 1229, 1204, 1104, 877, 722 cm^{-1}.

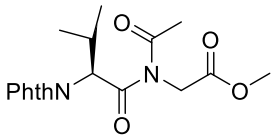
N-Phthaloyl-L-phenylalaninyl-N-acetyl-L-leucine methyl ester 10FL



The title compound was prepared from (*S*)-N-phthaloylphenylalanine (0.16 mmol, 48 mg) and N-thioacetyl-L-luecine methyl ester (0.24 mmol, 50 mg) with silver (I) carbonate (0.24 mmol, 67 mg) according to general procedure C. The title compound was isolated as white solid (61 mg, 81%); **MP**. 63–65 °C; **$[\alpha]^{25}_D$** –284 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ7.77

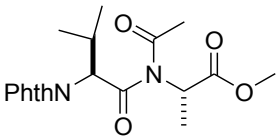
(2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.69 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.20–7.11 (5 H, m, ArH), 5.60 (1 H, m , CH), 4.15 (1 H, dd, *J*= 4.5, 8.5 Hz, CH), 3.54 (1 H, dd, *J* = 5.1, 13.9 Hz, C*H*H), 3.45 (1 H, dd, *J* = 10.1, 13.9 Hz, CH*H*), 3.12 (3 H, s, OMe), 2.42 (3 H, s, Me), 2.04 (1 H, ddd, *J* = 4.6, 8.8, 14.1 Hz, C*H*H), 1.82 (1 H, ddd, *J* = 4.6, 8.5, 13.1 Hz, CH*H*), 1.58 (1 H, m, CH), 0.97 (6 H, d, *J* = 6.7 Hz, CH(*Me*)$_2$); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.0, 172.7, 169.7, 167.3, 136.3, 134.1, 131.4, 129.0, 128.6, 127.0, 123.4, 56.9, 55.2, 52.0, 38.9, 35.0, 25.2, 25.0, 23.1, 22.0; **MS** (ESI) m/z 465 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{26}H_{28}N_2O_6$ 465.2020 found 465.2004; **IR** ($CHCl_3$): 3030, 2956, 2872, 1776, 1713, 1606, 1382, 1264, 1200, 1102, 1084, 992, 977, 879, 752, 719, 701 cm^{-1}.

N-Phthaloyl-L-valinyl-N-acetylglycine methyl ester 10VG



The title compound was prepared from (*S*)-N-phthaloylvaline (0.14 mmol, 35 mg) and N-thioacetyl-glycine methyl ester (0.21 mmol, 32 mg) with silver (I) carbonate (0.21 mmol, 59 mg) according to general procedure C. The title compound was isolated as white solid (39 mg, 76%); **MP**. 76–78 °C; **[α]$^{22}_{D}$** –200 (c 0.36, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.76 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.83 (1 H, d, *J* = 8.5 Hz, C*H*CH), 4.28 (2 H, m, CH_2), 3.47 (3 H, s, OMe), 2.85 (1 H, m, C*H*$(Me)_2$), 2.40 (3 H, s, Me), 1.12 (3 H, d, *J* = 6.5 Hz, Me), 0.86 (3 H, d, *J* = 6.6 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.2, 171.3, 168.2, 167.0, 134.2, 131.6, 123.5, 58.3, 52.3, 45.6, 28.6, 25.5, 20.8, 18.7; **MS** (ESI) m/z 361 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{18}H_{20}N_2O_6$ 361.1394 found 361.1395; **IR** ($CHCl_3$): 2964, 1719, 1383, 1193, 720 cm^{-1}.

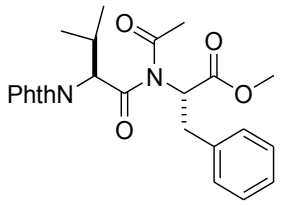
N-Phthaloyl-L-valinyl-N-acetyl-L-alanine methyl ester 10VA



The title compound was prepared from (*S*)-N-phthaloylvaline (0.13 mmol, 33.4 mg) and N-thioacetyl-L-alanine methyl ester (0.20 mmol, 32.6 mg) with silver (I) carbonate (0.20 mmol,

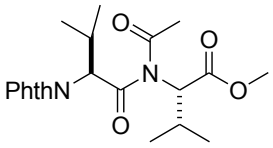
55.8 mg) according to general procedure C. The title compound was isolated as colorless crystals (35.8 mg, 71%); **MP**. 124–128 °C; **[α]$^{22}_{D}$** –274 (*c* 0.61, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.87 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.77 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.73 (1 H, d, *J* = 8.4 Hz, CH), 4.16 (1 H, q, *J* = 6.8 Hz, C*H*Me), 2.96 (3 H, s, OMe), 2.84 (1 H, m, C*H*$(Me)_2$), 2.38 (3 H, s, Me), 1.51 (3 H, d, *J* = 6.2 Hz, Me), 1.15 (3 H, d, *J* = 5.8 Hz, Me), 0.89 (3 H, d, *J* = 6.7 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.9, 171.8, 169.4, 167.6, 134.4, 131.5, 123.6, 57.4, 53.5, 51.8, 28.8, 25.1, 21.1, 18.8, 16.4; **MS** (ESI) m/z 375 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{19}H_{22}N_2O_6$ 375.1551 found 375.1545; **IR** ($CHCl_3$): 2967, 1771, 1749, 1713, 1613, 1468, 1435, 1380, 1260, 1219, 1100, 1070, 975, 791, 761, 720 cm^{-1}.

N-Phthaloyl-L-valinyl-N-acetyl-L-phenylalanine methyl ester 10VF



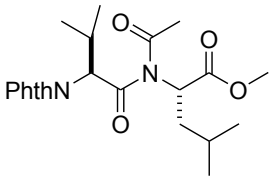
The title compound was prepared from (*S*)-N-phthaloylvaline (0.12 mmol, 31 mg) and N-thioacetyl-L-phenylalanine methyl ester (0.19 mmol, 45 mg) with silver (I) carbonate (0.19 mmol, 52 mg) according to general procedure C. The title compound was isolated as white solid (40 mg, 71%); **MP**. 105–107 °C; **[α]$^{25}_{D}$** –188 (*c* 0.66, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$),δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.76 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.34 (2 H, m, ArH), 7.25 (1 H, m, ArH), 7.17 (2 H, m, ArH), 4.14 (1 H, dd, *J* = 3.2, 11.0 Hz, CH), 4.01 (1 H, d, *J* = 9.0 Hz, CH), 3.43 (1 H, dd, *J* = 3.2, 14.1 Hz, C*H*H), 3.23 (1 H, dd, *J* = 11.1, 14.1 Hz, CH*H*), 2.90 (3 H, s, OMe), 2.43 (1 H, m, C*H*$(Me)_2$), 2.39 (3 H, s, Me), 0.65 (3 H, d, *J* = 6.8 Hz, Me), 0.54 (3 H, d, *J* = 6.8 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.7, 171.4, 168.8, 167.4, 137.0, 134.3, 131.4, 129.7, 129.1, 127.2, 123.5, 60.0, 56.5, 51.6, 35.9, 27.9, 25.6, 20.6, 18.5; **MS** (ESI) m/z 451 [$(M+H)^+$, 100%]; **HRMS** (EST, MH^+) Calcd. for $C_{25}H_{26}N_2O_6$ 451.1864 found 451.1859; **IR** ($CHCl_3$): 2966, 1752, 1715, 1468, 1435, 1383, 1336, 1288, 1264, 1216, 1168, 1084, 971, 896, 753, 721 cm^{-1}.

N-Phthaloyl-L-valinyl-N-acetyl-L-valine methyl ester 10VV



The title compound was prepared from (*S*)-N-phthaloylvaline (0.16 mmol, 40 mg) and N-thioacetyl-L-valine methyl ester (0.24, 46 mg) with silver (I) carbonate (0.24 mmol, 67 mg) according to general procedure C. The title compound was isolated as white solid (62 mg, 94%); **MP**. 86–88 °C; $[\alpha]^{22}_{D}$ –242 (*c* 0.83, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.88 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.77 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.71 (1 H, d, *J* = 9.0 Hz, CH), 3.62 (1 H, d, *J* = 8.9 Hz, CH), 2.84 (1 H, m, CH), 2.80 (3 H, s, OMe), 2.65 (1 H, m, CH), 2.39 (3 H, s, Me), 1.16 (3 H, d, *J* = 6.4 Hz, CH*Me*), 1.16 (3 H, d, *J* = 6.6 Hz, CH*Me*), 0.87 (3 H, d, *J* = 6.9 Hz, CH*Me*), 0.81 (3 H, d, *J* = 7.1 Hz, CH*Me*); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.5, 172.4, 168.7, 167.4, 134.5, 131.5, 123.6, 63.0, 56.9, 51.4, 29.4, 28.6, 25.2, 22.0, 21.0, 19.8, 18.7; **MS** (ESI) m/z 403 [$(M+H)^+$, 100%]; **HRMS** (EST, MH^+) Calcd. for $C_{21}H_{26}N_2O_6$ 403.1864 found 403.1831; **IR** ($CHCl_3$): 2966, 2874, 1754, 1715, 1613, 1468, 1435, 1382, 1218, 1085, 1019, 896, 792, 732, 718 cm^{-1}.

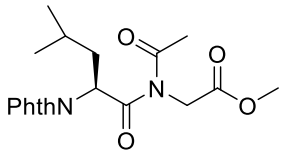
N-Phthaloylvalinyl-N-acetylleucine methyl ester 10VL



The title compound was prepared from (*S*)-N-phthaloylvaline (0.14 mmol, 34.3 mg) and N-thioacetyl-L-leucine methyl ester (0.21mmol, 42.3 mg) with silver (I) carbonate (0.21 mmol, 57.4 mg) according to general procedure C. The title compound was isolated as white solid (57.0 mg, 99%); **MP**. 77–79 °C; $[\alpha]^{22}_{D}$ –244 (*c* 1.0, $CHCl_3$); **^{1}HNMR** (400 MHz, $CDCl_3$), δ 7.87 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.77 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 4.75 (1 H, d, *J* = 8.9 Hz, CH), 4.05 (1 H, dd, *J* = 4.7, 8.8 Hz, C*H*CH_2), 2.87 (3 H, s, OMe), 2.84 (1 H, m, CH), 2.38 (3 H, s, Me), 2.03 (1 H, ddd, *J* = 4.6, 9.3, 14.0 Hz, C*H*HCH), 1.82 (1 H, ddd, *J* = 4.6, 9.0, 14.5 Hz, CH*H*CH), 1.53 (1 H, m, CH), 1.15 (3 H, d, *J* = 6.5 Hz, CH*Me*), 1.00 (3 H, d, *J* = 6.3 Hz, CH*Me*), 0.95 (3 H, d, *J* = 6.8 Hz, CH*Me*), 0.87 (3 H, d, *J* = 6.8 Hz, CH*Me*); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.1, 172.4, 169.6, 167.6, 134.3, 131.6, 123.6, 57.2, 56.2, 51.7, 39.5, 28.5, 25.3, 25.1,

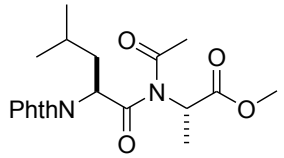
23.2, 22.2, 21.1, 18.8; **MS** (ESI) m/z 417 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{22}H_{28}N_2O_6$ 417.2020 found 417.2075; **IR** ($CHCl_3$): 2960, 2873, 1770, 1749, 1715, 1613, 1468, 1435, 1382, 1266, 1212, 1085, 972, 790, 759, 720 cm^{-1}.

N-Phthaloyl-L-leucinyl-N-acetylglycine methyl ester 10LG



The title compound was prepared from N-phthaloylglycine (0.10 mmol, 22 mg) and N-thioacetyl-glycine methyl ester (0.13 mmol, 19 mg) with silver (I) carbonate (0.13 mmol, 35 mg) according to general procedure C. The title compound was isolated as colorless oil (22 mg, 70%); $[\alpha]^{22}_D$ 50 (c 0.37, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.85 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.74 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.56 (1 H, dd, *J* = 4.3, 10.8 Hz, C*H*CH_2), 4.35 (2 H, s, CH_2), 3.57 (3 H, s, OMe), 2.37 (3 H, s, Me), 2.33 (1 H, ddd, *J* = 4.3, 10.5, 14.3 Hz, C*H*HCH), 1.87 (1 H, ddd, *J* = 4.3, 10.1, 14.3 Hz, CH*H*CH), 1.52 (1 H, m, CH), 0.98 (3 H, d, *J* = 6.6 Hz, Me), 0.93 (3 H, d, *J* = 6.6 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.9, 172.5, 168.3, 167.7, 134.2, 131.8, 123.6, 53.3, 52.5, 46.2, 37.2, 25.2, 25.1, 23.1, 21.0; **MS** (ESI) m/z 375 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{19}H_{22}N_2O_6$ 375.1551 found 375.1554; **IR** ($CHCl_3$): 2958, 1751, 1715, 1382, 1196, 1071, 980, 914, 720 cm^{-1}.

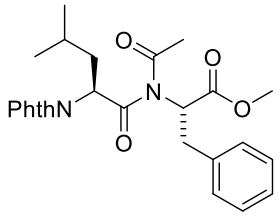
N-Phthaloyl-L-leucinyl-N-acetyl-L-alanine methyl ester 10LA



The title compound was prepared from (*S*)-N-phthaloylleucine (0.14 mmol, 38 mg) and N-thioacetyl-L-alanine methyl ester (0.22 mmol, 35.0 mg) with silver (I) carbonate (0.22 mmol, 60 mg) according to general procedure C. The title compound was isolated as white solid (52 mg, 92%); **MP**. 80–82 °C; $[\alpha]^{22}_D$ –132 (*c* 0.80, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.40 (1 H, dd, *J* = 3.9, 6.9 Hz, C*H*CH_2), 4.28 (1 H, q, *J* = 6.7 Hz, C*H*Me), 3.18 (3 H, s, OMe), 2.36 (3 H, s, Me), 2.29 (1 H, ddd, *J* = 4.0, 10.6, 14.3 Hz, C*H*HCH), 1.85 (1 H, ddd, *J* = 4.2, 10.3, 14.2 Hz, CH*H*CH), 1.53 (3 H, d,

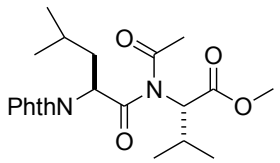
J = 6.8 Hz, Me), 1.47 (1 H, m, CH), 0.98 (3 H, d, *J* = 6.8 Hz, Me), 0.93 (3H, d, *J* = 6.8 Hz, Me). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.7, 172.3, 169.8, 167.7, 134.1, 131.7, 123.5, 54.0, 52.4, 52.0, 37.5, 25.0, 25.0, 23.3, 21.1, 15.8; **MS** (ESI) m/z 389 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{20}H_{24}N_2O_6$ 389.1707 found 389.1672; **IR** ($CHCl_3$): 2956, 2873, 1774, 1748, 1710, 1613, 1468, 1435, 1380, 1244, 1212, 1104, 944, 878, 857, 755, 720 cm^{-1}.

N-Phthaloyl-L-leucinyl-N-acetyl-L-phenylalanine methyl ester 10LF



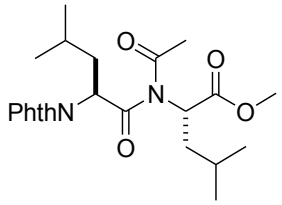
The title compound was prepared from (*S*)-N-phthaloylleucine (0.10 mmol, 26 mg) and N-thioacetyl-L-phenylalanine methyl ester (0.15 mmol, 36 mg) with silver (I) carbonate (0.15 mmol, 41 mg) according to general procedure C. The title compound was isolated as white solid (35 mg, 75%); **MP**. 55–57 °C; **$[\alpha]^{22}_D$** –210 (*c* 0.57, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.85 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.33 (2 H, m, ArH), 7.28 (1 H, m, ArH), 7.21(2 H, m, ArH), 4.57 (1 H, m, CH), 4.20 (1 H, dd, *J* = 3.1, 11.0 Hz, CH), 3.46 (1 H, dd, *J* = 3.3, 14.1 Hz, C*H*H), 3.22 (1 H, dd, *J* = 11.0, 14.3 Hz, CH*H*), 3.01 (3 H, s, OMe), 2.33 (3 H, s, Me), 1.78 (1 H, m, CH), 1.49 (1 H, ddd, *J* = 4.5, 9.9, 14.4 Hz, CH), 1.17 (1 H, m, CH), 0.78 (3 H, d, *J* = 6.3 Hz, Me), 0.76 (3 H, d, *J* = 6.5 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 172.7, 168.9, 167.5, 167.4, 137.2, 134.3, 131.6, 129.7, 129.0, 127.2, 123.4, 60.3, 51.8, 50.4, 38.0, 35.7, 25.3, 24.4, 23.2, 21.3; **MS** (ESI) m/z 423 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{26}H_{28}N_2O_6$ 465.2020 found 465.2016; **IR** ($CHCl_3$): 2956, 1714, 1435, 1382, 1251, 1216, 1166, 1084, 754, 721, 702 cm^{-1}.

N-Phthaloyl-L-leucinyl-N-acetyl-L-valine methyl ester 10LV



The title compound was prepared from (*S*)-N-phthaloylleucine (0.10 mmol, 24 mg) and N-thioacetyl-L-valine methyl ester (0.14 mmol, 26 mg) with silver (I) carbonate (0.14 mmol, 38 mg) according to general procedure C. The title compound was isolated as white solid (34 mg, 90%); **MP.** 100–103 °C; $[\alpha]^{22}_{D}$ –189 (*c* 0.63, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.87 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.76 (2 H, dd, *J* = 3.0,5.0 Hz, ArH), 5.33 (1 H, dd, *J* = 4.5, 9.8 Hz, C*H*CH_2), 3.71 (1 H, d, *J* = 9.9 Hz, C*H*CH), 3.01 (3 H, s, OMe), 2.65 (1 H, m, C*H*$(Me)_2$), 2.39 (3 H, s, Me), 2.17 (1 H, ddd, *J* = 4.4, 9.6, 14.4 Hz, C*H*HCH), 2.00 (1 H, ddd, *J* = 4.4, 9.6, 14.4 Hz, CH*H*CH), 1.52 (1 H, m, C*H*$(Me)_2$), 1.16 (3 H, d, *J* = 6.55 Hz, Me), 0.99 (3 H, d, *J* = 6.6 Hz, Me), 0.94 (3 H, d, *J* = 6.6 Hz, Me), 0.84 (3 H, d, *J* = 6.9 Hz, Me); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.0, 173.1, 169.0, 167.6, 134.3, 131.8, 123.5, 63.5, 51.6, 51.5, 38.0, 28.9, 25.0, 24.9, 23.1, 22.2, 21.4, 19.7; **MS** (ESI) m/z 417 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{22}H_{28}N_2O_6$ 417.2020 found 417.2029; **IR** ($CHCl_3$): 2961, 1753, 1716, 1468, 1383, 1214, 1058, 878, 722 cm^{-1}.

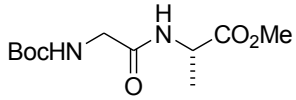
N-Phthaloyl-L-leucinyl-N-acetyl-L-leucine methyl ester 10LL



The title compound was prepared from (*S*)-N-phthaloylleucine (0.17 mmol, 46 mg) and N-thioacetyl-L-leucine methyl ester (0.26 mmol, 53 mg) with silver (I) carbonate (0.26 mmol, 73 mg) according to general procedure C. The title compound was isolated as white solid (63 mg, 84%);. **MP**. 97–99 °C; $[\alpha]^{22}_{D}$ –162 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.86 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.75 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 5.38 (1 H, dd, *J* = 4.5, 9.4 Hz, CH), 4.15 (1 H, dd, *J* = 4.9, 8.6 Hz, CH), 3.08 (3 H, s, OMe), 2.37 (3 H, s, Me), 2.17 (1 H, ddd, *J* = 4.7, 11.4, 14.8 Hz, C*H*HCH), 2.06 (1 H, ddd, *J* = 4.7, 9.1, 14.1 Hz, CH*H*CH), 1.95 (1 H, ddd, *J* = 4.7, 9.8, 14.1 Hz, C*H*HCH), 1.77 (1 H, ddd, *J* = 5.1, 8.8, 13.9 Hz, CH*H*CH), 1.57 (1 H, m, C*H*CH_2), 1.49 (1 H, m, C*H*CH_2), 0.99 (3 H, d, *J* = 6.54 Hz, CH*Me*), 0.98 (3 H, d, *J* = 6.5 Hz, CH*Me*), 0.97 (3 H, d, *J* = 4.7 Hz, CH*Me*), 0.93 (3 H, d, *J* = 6.1 Hz, CH*Me*). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.9, 172.7, 169.8, 167.6, 134.2, 131.7, 123.5, 56.7, 51.9, 51.8, 39.1, 37.8, 25.1, 25.0, 24.9, 23.1, 23.1, 22.0, 21.2; **MS** (ESI) m/z 431 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+)

Calcd. for $C_{23}H_{30}N_2O_6$ 431.2177 found 431.2181; **IR** ($CHCl_3$): 2958, 2873, 1775, 1748, 1713, 1613, 1468, 1435, 1382, 1265, 1207, 1057, 993, 760, 720 cm^{-1}.

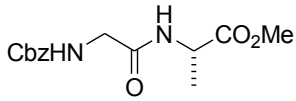
N-Boc-glycinyl-L-alanine methyl ester 13



N-Boc-glycinyl-N-acetyl-L-alanine methyl ester was prepared from N-Boc-glycine (0.57 mmol, 0.10 g), N-thioacetyl-L-alanine methyl ester (0.85 mmol, 136.0 mg) and silver (I) carbonate (0.85 mmol, 0.24 g) according to general procedure C. A mixture of imides **14a** and **14b** was isolated as a colorless oil (0.17 g, 98%); **Major isomer:** ^{1}H NMR (400 MHz, $CDCl_3$), δ 6.23 (1H, d, *J* = 8.0 Hz, N*H*CH), 4.57 (1H, p, *J* = 6.9 Hz, C*H*NHMe), 4.39 (1H, d, *J* = 14.7 Hz, C*H*HCO), 4.33 (1H, d, *J* = 14.7 Hz, CH*H*CO), 3.73 (3H, s, OMe), 2.53 (3H, s, MeCO), 1.49 (9H, s, $C(Me)_3$), 1.39 (3H, d, *J* = 7.0 Hz, CH*Me*); **Minor isomer:** ^{1}H NMR (400 MHz, $CDCl_3$), δ 5.23 (1H, brs, N*H*CH_2), 4.49 (1H, q, *J* = 7.0 Hz, C*H*Me), 4.28 (2H, d, *J* = 4.9 Hz, NHC*H*$_2$), 3.69 (3H, s, OMe), 2.37 (3H, s, OMe), 1.55 (3H, d, *J* = 6.7 Hz, CH*Me*), 1.43 (9H, s, $C(Me)_3$); **MS** (ESI) m/z 325 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{13}H_{22}N_2O_6$ 325.1370 found 325.1390.

The mixture of imides **14a/b** (0.21 mmol, 64 mg) was treated with $NaHCO_3$ (2.11 mmol, 176.4 mg) in methanol according to general procedure E to give the title compound as colorless oil (41 mg, 75%); $[\alpha]^{24}_D$ –6.4 (c 1.6, AcOEt); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 6.60 (1 H, brs, NH), 5.11 (1 H, brs, NH), 4.60 (1 H, m, C*H*NHMe), 3.81 (2 H, m, C*H*$_2$NH), 3.75 (3 H, s, OMe), 1.46 (9 H, s, $C(Me)_3$), 1.41 (3 H, d, *J* = 7.0 Hz, CH*Me*); **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.1, 168.9, 155.9, 58.4, 52.4, 48.0, 44.3, 28.4, 18.3. **MS** (ESI) m/z 261 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{11}H_{20}N_2O_5$ 261.1445 found 261.1426; **IR** ($CHCl_3$): 3308, 2979, 1743, 1668, 1525, 1454, 1367, 1279, 1248, 1214, 1165, 1052, 1030, 985, 941, 865, 783 cm^{-1}.

N-Cbz-glycinyl-L-alanine methyl ester 16

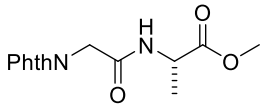


N-Cbz-glycinyl-N-acetyl-L-alanine methyl ester was prepared from N-Cbz-glycine (0.71 mmol, 0.15 g), N-thioacetyl-L-alanine methyl ester (1.07 mmol, 0.17 g) and silver(I) carbonate (1.07 mmol, 0.30 g) according to general procedure C. A mixture of imides **17a/b** was isolated as

colorless oil. **Major isomer:** ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.40–7.28 (5H, m, ArH), 6.13 (1H, m, NH), 5.22 (2H, brs, C*H*$_2$ArH), 4.55 (1H, m, CH*H*NH), 4.44 (1H, m, CH*H*CO), 4.09 (1H, m, CH*Me*), 3.74 (3H, s, OMe), 2.58 (3H, s, MeCO), 1.57 (3H, d, *J* = 6.7 Hz, CH*Me*); **Minor isomer:** ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.40–7.28 (5H, m, ArH), 5.46 (1H, brs, NH), 5.12 (2 H, m, C*H*$_2$ArH), 4.49 (1H, m, C*H*HNH), 4.39 (1H, m, C*H*HCO), 3.94 (1H, m, C*H*Me), 3.71 (3H, s, OMe), 2.37 (3H, s, MeCO), 1.35 (3H, d, *J* = 7.8 Hz, CH*Me*); **MS** (ESI) m/z 337 [$(M+H)^+$, 100%]; **HRMS** (ESI, MH^+) Calcd. for $C_{16}H_{20}N_2O_6$ 337.1394 found 337.1395.

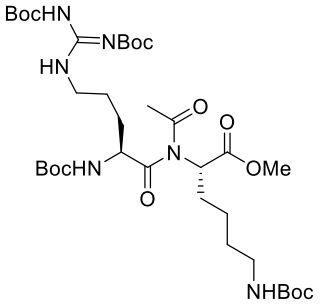
The mixture of imides **17a/b** was treated with $NaHCO_3$ according to general procedure E to give the title compound as a colorless oil (0.16 g, 74%); **[α]$^{24}_D$** –5.6 (*c* 1.08, AcOEt, lit.[4] –6.0); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.29 (1H, d, *J* = 7.2 Hz, NH), 7.42 (1H, dd, *J* = 6.2, 12.7 Hz, NH), 7.39–7.28 (5H, m, ArH), 5.03 (2H, brs, C*H*$_2$ArH), 4.29 (1H, dq, *J* = 7.4, 7.2 Hz, C*H*Me), 3.67 (1H, dd, *J* = 6.1, 16.5 Hz, CH*H*NH), 3.62 (3H, s, OMe), 3.61 (1H, m, C*H*HNH), 1.27 (3H, d, *J* = 7.4 Hz, CH*Me*); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 173.1, 168.8, 156.3, 136.8, 128.3, 127.8, 127.7, 65.3, 51.9, 47.5, 43.0, 17.0. **MS** (ESI) m/z 317 [$(M+Na)^+$, 100%]; **HRMS** (ESI, MNa^+) Calcd. for $C_{14}H_{18}N_2O_5$ 317.1108 found 317.1102. Characterisation data consistent with that reported.[4,5]

N-Phthaloyl-glycinyl-L-alanine methyl ester 19



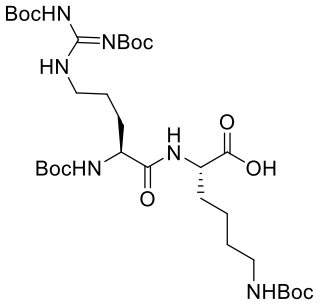
N-Phthaloylglycine-N-acetylalanine methyl ester **10GA** (0.45 mmol, 0.15 g) was treated with $NaHCO_3$ (4.5 mmol, 0.38 g) according to general procedure E. The title compound was isolated as colorless solid (81 mg, 62%); **MP.** 194–196 °C; **[α]$^{25}_D$** –28 (*c* 0.81, AcOEt); **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.88 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 7.73 (2 H, dd, *J* = 3.0, 5.0 Hz, ArH), 6.44 (1 H, d, *J* = 7.0 Hz NH), 4.60 (1 H, m, C*H*NHMe), 4.41 (1 H, d, *J* = 15.7 Hz, CH*H*CO), 4.35 (1 H, d, *J* = 16.0 Hz, C*H*HCO), 3.75 (3 H, s, OMe), 1.42 (3 H, d, *J* = 7.1 Hz, CH*Me*). **^{13}C NMR** (100 MHz, $CDCl_3$), δ 173.1, 167.8, 165.4, 134.2, 131.8, 123.6, 52.6, 48.4, 40.6, 18.5; **MS** (ESI) m/z 291 [$(M+H)^+$, 100%], **HRMS** (ESI, MH^+) Calcd. for $C_{14}H_{14}N_2O_5$ 291.0975 found 291.0994; **IR** (AcOEt): 3296, 3091, 2182, 1777, 1727, 1666, 1563, 1419, 1320, 1227, 1118, 952, 742, 715 cm^{-1}.

$Boc_3Arg\text{-}Lys^{Ac}(Boc)\text{-}OMe$ 21



Compound **21** was prepared from $(Boc)_3$Arg-OH (0.23 g, 0.49 mmol) according to general procedure D for imide synthesis. The residue was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes: EtOAc to afford the title compound as a colourless oil (0.31 g, 83%); $[\alpha]^{24}_D$ –4.0 (*c* 0.16, $CHCl_3$): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.30 (2 H, br s, NHs), 6.18 (1 H, d, *J* = 7.5 Hz, NH), 5.14 (1 H, dd, *J* = 5.3, 9.7 Hz, NH), 4.66 (1 H, br s), 4.53 (1 H, m), 3.90 (2 H, m), 3.72 (3 H, s, OMe), 3.08 (2 H, m), 2.52 (3 H, s, Me), 2.10–1.55 (6 H, m), 1.50 (9 H, s, tBu), 1.49 (9 H, s, tBu), 1.46 (9 H, s, tBu), 1.42 (9 H, s, tBu), 1.35–1.22 (4 H, m); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.3, 172.7, 169.7, 163.8, 160.5, 155.9, 155.0, 152.5, 84.4, 83.9, 79.1, 78.6, 56.8, 52.4, 52.2, 44.1, 40.1, 32.1, 29.5, 28.4,28.3, 28.0, 27.9, 26.5, 26.1,25.7, 22.4; **MS** (ESI) *m/z* 759 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{35}H_{62}N_6O_{12}$ 759.4498 found. 759.4490; **IR** (thin film): 3379, 2777, 2932 ,1712, 1609, 1513, 1368,1275, 1250,1149 cm^{-1}.

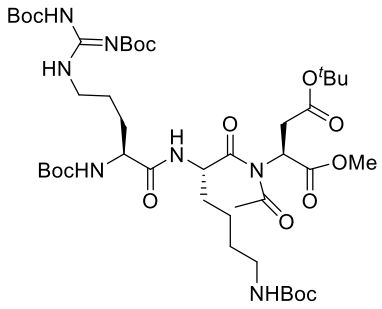
$Boc_3Arg\text{-}Lys(Boc)\text{-}OH$ 22



Method A: Compound **22** was prepared according to general procedure F from imide **21** (0.40 g, 0.53 mmol). The title compound was isolated as a colourless oil (0.26 g, 71%); $[\alpha]^{24}_D$ +7.4 (*c* 0.18, $CHCl_3$); **^{1}H NMR** (500 MHz, CD_3OD) δ 4.26 (1 H, m), 4.04 (1 H, m), 3.87 (2 H, m), 3.00 (2 H, t, *J* = 7.0 Hz), 1.88–1.57 (6 H, m), 1.54 (9 H, s, tBu), 1.48 (9 H, s, tBu), 1.45 (9 H, s, tBu), 1.42 (9 H, s, tBu), 1.39–1.22 (4 H, m); **^{13}C NMR** (125 MHz, CD_3OD) δ 174.0, 173.6, 164.4,

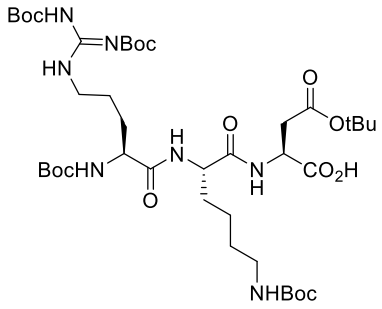
161.8, 158.4, 157.8, 156.1, 85.2, 80.6, 80.0, 79.7, 56.2, 45.8, 41.3, 33.5, 30.7(5), 30.7(0), 30.3, 28.8(5), 28.8(0), 28.6, 28.3, 26.6, 23.8; **MS** (ESI) *m/z* 703 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{32}H_{58}N_6O_{11}$ 703.4236, found 703.4236; **IR** (thin film): 3380, 2778, 2932, 1712, 1609, 1513, 1392, 1367, 1273, 1252, 1149, 774 cm^{-1}.

Boc$_3$Arg-Lys(Boc)-Asp^{Ac}(tBu)-OMe 23



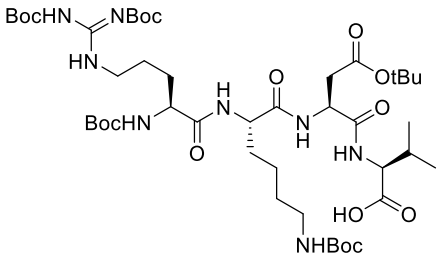
Compound **23** was prepared according to general procedure D from Compound **22** (0.23 g, 0.33 mmol). The title compound was isolated as a colourless oil (0.25 g, 80%); $[\alpha]^{24}_D$ –31 (*c* 0.40, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.27 (2 H, br s, NHs), 6.99 (1 H, d, *J* = 9.0 Hz), 5.98 (1 H, br s, NH), 5.50 (1 H, m), 4.93 (1 H, m), 4.77 (1 H, br s), 4.19 (1 H, m), 3.80 (2 H, m), 3.67 (3 H, s), 3.21 (1 H, dd, *J* = 4.6, 17.4 Hz), 3.04 (2 H, m), 2.73 (1 H, dd, *J* = 8.4, 17.4 Hz), 2.45 (3 H, s), 1.87–1.61 (6 H, m), 1.50–1.33 (4 H, m), 1.50 (18 H, s), 1.44 (9 H, s), 1.43 (9 H, s), 1.42. (9 H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.3, 172.8, 172.0, 170.3, 169.1,163.4, 160.7, 155.9, 154.8, 84.0, 81.7, 79.9, 79.2, 78.9, 55.7, 54.4, 53.2, 52.8, 44.0, 40.2, 35.8, 32.8, 28.9, 28.4(5), 28.4(0), 28.3, 28.2, 28.0, 27.9(9), 27.4, 25.5, 24.8, 22.7; **MS** (ESI) *m/z* 930 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{43}H_{75}N_7O_{15}$ 930.5394, found 930.5394; **IR** (thin film): 3381, 2777, 2932, 1714, 1610, 1513, 1368, 1272, 1252, 1150 cm^{-1}.

Boc$_3$Arg-Lys(Boc)-Asp(tBu)-OH 25



Compound **25** was prepared from imide **23** (0.19 g, 0.21 mmol) according to general procedure E for imide methanolysis, which afforded the corresponding amide as a colourless oil (quantitative, NMR), followed by general procedure for ester hydrolysis. The title compound **25** was isolated as a colourless oil (0.13 g, 70%); $[\alpha]^{24}_{D}$ –1.0 (*c* 0.50, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3OD) δ 4.64 (1 H, m), 4.38 (1 H, dd, *J* = 5.7, 8.7 Hz), 4.05 (1 H, br s), 3.87 (2 H, t, *J* = 6.8 Hz), 3.01 (2 H, t, *J* = 6.8 Hz), 2.77 (1 H, dd, *J* = 5.5, 15.4 Hz), 2.68 (1 H, dd, *J* = 6.2, 15.4 Hz), 1.87–1.58 (8 H, m), 1.56 –1.29 (2 H, m), 1.55 (9 H, s), 1.48 (9 H, s), 1.44(5) (9 H, s), 1.44(0) (9 H, s), 1.43 (9 H, s); **^{13}C NMR** (125 MHz, CD_3OD) δ 174.7, 173.4, 171.5, 164.2, 161.7, 158.5, 157.9, 157.7, 156.0, 85.2, 82.3, 80.6, 80.2, 79.8, 55.9, 54.3, 45.6, 41.2, 38.8, 33.1, 30.7, 30.5, 30.3, 28.8 (2 C), 28.6, 28.4, 28.3, 26.5, 23.9; **MS** (ESI) *m/z* 874 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{40}H_{71}N_7O_{14}$ 874.5132, found 874.5135; **IR** (thin film): 3382, 2978, 2935, 1713, 1512, 1367, 1275, 1252, 1150 cm^{-1}.

Boc$_3$Arg-Lys(Boc)-Asp(tBu)-Val-OH 26

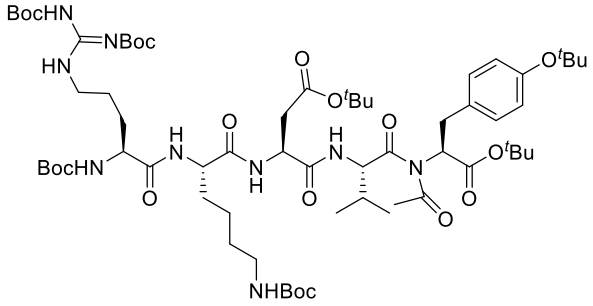


The tetrapeptide imide was prepared from compound **25** (84 mg, 0.096 mmol) according to general procedure C for imide synthesis. The title compound was isolated as a colourless oil (61 mg, 65%, 73% BRSM); $[\alpha]^{24}_{D}$ –46 (*c* 0.30, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.29 (2 H, br s, NHs), 7.18 (1 H, d, *J* = 8.6 Hz, NH), 7.00 (1 H, d, *J* = 8.5 Hz, NH), 6.01 (1 H, br s, NH), 5.37 (1 H, m), 4.78 (1 H, br s, NH), 4.35 (1 H , m), 4.20 (1 H, m), 4.17 (1 H, d, *J* = 8.9 Hz), 3.79 (2 H, m), 3.66 (3 H, s, OMe), 3.04 (2 H, m), 2.83 (1 H, dd, *J* = 6.2, 15.4 Hz), 2.67–2.58 (1 H, m), 2.62 (1 H, dd, *J* = 5.0, 15.4), 2.39 (3 H, s, Me), 1.83 (6 H, m), 1.69–1.52 (2 H, m), 1.51 (9 H, s), 1.50 (9 H, s), 1.44 (9 H, s), 1.42 (18 H, s), 1.40–1.24 (2 H, m), 1.18 (3 H, d, *J* = 6.7 Hz, Me), 0.82 (3 H, d, *J* = 7.0 Hz, Me); **^{13}C NMR** (125 MHz, CDCl3) δ 174.2, 173.5, 172.5, 170.7, 170.1, 169.6, 163.3, 160.7, 156.0 (2 C), 154.8, 84.1, 81.6, 80.6, 79.3, 79.0, 64.0, 54.4, 52.9, 52.4, 50.3, 44.0, 40.1, 37.4, 31.4, 29.4, 28.4(2), 28.4(0), 28.3, 28.2, 28.0(1), 28.(0), 27.3, 25.7, 24.8, 22.7, 22.3, 19.5; **MS** (ESI) *m/z* 1029 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{48}H_{84}N_8O_{16}$

1029.6078, found 1029.6084; **IR** (thin film); 3380, 2779, 1716, 1515, 1368, 1275, 1252, 1151cm^{-1}.

The tetrapeptide imide (43 mg, 0.042 mmol) was then treated according to general procedure E for imide methanolysis. This afforded the crude amide as a colourless oil (quantitative, NMR), which was subjected to general procedure F for ester hydrolysis. The title compound **26** was isolated as a colourless oil (30 mg, 74%); **[α]$^{24}_{D}$** +14.6 (*c* 0.10, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3OD) δ 4.73 (1 H, t, *J* = 7.0 Hz), 4.35 (1 H, dd, *J* = 5.2, 8.4 Hz), 4.30 (1 H, d, *J* = 4.3 Hz), 4.04 (1 H, dd, *J* = 5.2, 9.0 Hz), 3.87 (2 H, t, *J* = 7.0 Hz), 3.01 (2 H, t, *J* = 7.0 Hz), 2.81 (1 H, dd, *J* = 6.1, 16.4 Hz), 2.62 (1 H, dd, 7.2, 16.4 Hz), 2.18 (3 H, m), 1,87–1.56 (6 H, m), 1.54–1.22 (2 H, m), 1.55 (9 H, s), 1.49 (9 H, s), 1.45 (9 H, s), 1.44 (9 H, s), 1.43 (9 H,s), 0.96 (3 H, d, *J* = 7.1 Hz), 0.95 (3 H, d, *J* = 7.1 Hz); **^{13}C NMR** (100 MHz, CD_3OD) δ 174.9 (2 C), 173.9, 172.5, 171.3, 164.3, 161.7, 158.5, 158.0, 156.0, 85.2, 82.5, 80.7, 80.1, 79.8, 59.4, 56.0, 54.5, 51.2, 45.5, 41.1, 38.1, 33.1, 32.0, 30.7, 30.5, 30.1, 28.8, 28.6, 28.4. 28.3, 26.5, 24.0, 19.7, 18.3; **MS** (ESI) *m/z* 973 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{45}H_{80}N_8O_{15}$ 973.5816, found 973.5822; IR (thin film) : 3370, 2977, 1714, 1514, 1392, 1368, 1272, 1251, 1150 cm^{-1}.

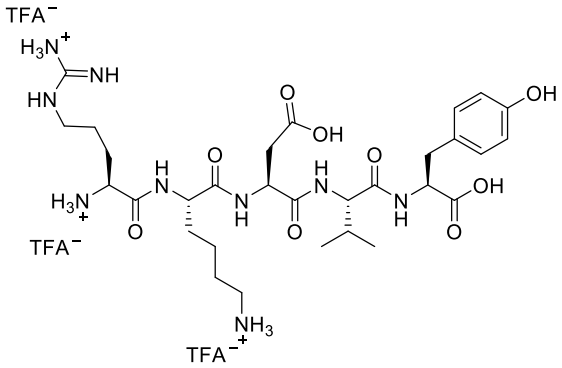
Boc$_3$Arg-Lys(Boc)-Asp(tBu)-Val-Tyr^{Ac}(tBu)-OtBu 27



Compound **27** was prepared from compound **26** (20 mg, 0.021 mmol) according to general procedure D for imide synthesis. The title compound was isolated as a colourless oil (24 mg, 89%); **[α]$^{24}_{D}$** –7.1 (*c* 0.20, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.29 (2 H, br s, NHs), 7.35 (1 H, br s), 7.15 (1 H, d, *J* = 9.0 Hz, NH), 7.04 (3 H, m), 6.92 (2 H, d, *J* = 8.30 Hz), 5.98 (1 H, d, *J* = 6.0 Hz), 4.87 (1 H, br s), 4.74 (2 H, m), 4.60 (1 H, m), 4.35 (1 H, m), 4.20 (1 H, m), 3.81 (2 H, m), 3.44 (1 H, dd, *J* = 4.3, 14.6), 3.06 (4 H, m), 2.86 (1 H, dd, *J* = 4.0, 17.5 Hz), 2.58 (1 H, m), 2.12 (3 H,s), 1.99–1.78 (4 H, m), 1.64 (6 H, m), 1.52 (18 H, s), 1.45 (9 H, s), 1.44 (9 H, s), 1.43 (9 H,s), 1.42 (9 H, s), 1.32 (9 H, s), 0.80 (3 H, d, 6.60 Hz), 0.72 (3 H, m); **^{13}C NMR** (125 MHz,

$CDCl_3$) δ 174.9, 173.2, 172.6, 171.4, 170.9, 170.1, 168.2, 163.4, 160.7, 156.0, 154.8, 154.3,132.8, 129.9, 124.4, 124.1, 84.0, 82.2, 81.2, 80.1, 79.2, 79.0, 78.4, 61.3, 57.7, 54.6, 53.6, 49.2, 44.0, 40.1, 37.5, 36.9, 33.9, 31.8, 30.2, 29.5, 28.8, 28.4, 28.3, 28.0 (2 C), 27.9, 27.8, 25.9, 24.9, 22.8, 19.7, 16.5; MS (ESI) *m/z* 1290 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{64}H_{107}N_9O_{18}$ 1290.7807, found 1290.7804; **IR** (thin film): 3354, 2977, 1714, 1508, 1367, 1251, 1157 cm^{-1}

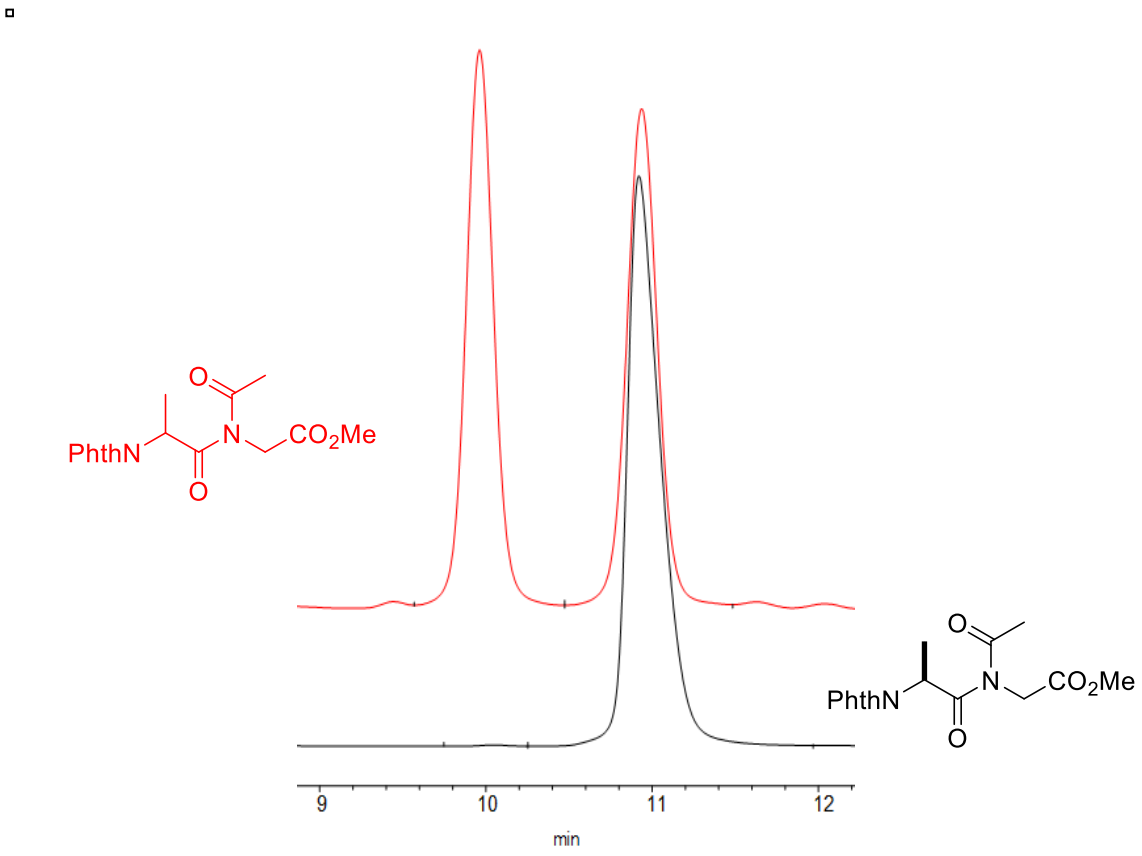
Thymopentin 28



Compound **28** was prepared from imide **27** (6.0 mg, 0.0047 mmol) according to general procedure E for imide methanolysis. This afforded the crude amide as a colourless oil (5.2 mg, 90%), which was used without further purification. The amide was dissolved in 1:1:0.1:0.1 CH_2Cl_2:TFA:H_2O:TIPS (3 mL) and stirred for 2 h. The solvent was evaporated and the residue was triturated with ether (3 × 5 mL). The residue was then puried by RP-HPLC (0–50% B over 60 min). Thymopentin **15** was obtained as a lyophilised white solid (2.0 mg, 63%): **^{1}H NMR** (500 MHz, D_2O) δ 7.14 (2 H, d, J = 8.1 Hz), 6.84 (2 H, d, *J* = 8.2 Hz), 4.67 (1 H, dd, *J* = 5.6, 8.2 Hz), 4.56 (1 H, d, *J* = 5.2, 9.0 Hz), 4.39 (1 H, t, *J* = 7.3 Hz), 4.08 (2 H, m), 3.24 (2 H, t, *J* = 6.7 Hz), 3.16 (1 H, dd, *J* = 5.2, 14.2 Hz), 3.0 (2 H, t, *J* = 7.5 Hz), 2.93 (1 H, dd, *J* = 9.2, 14.2 Hz), 2.82 (1 H, dd, *J* = 5.5, 16.8 Hz), 2.76 (1 H, dd, *J* = 8.1, 16.8 Hz), 2.02–1.92 (3 H, m), 1.86–1.61 (6 H, m), 1.44 (2 H, m), 0.86 (3 H, d, *J* = 6.0 Hz), 0.85 (3 H, d, *J* = 6.0 Hz); **^{13}C NMR** (125 MHz, D_2O) δ 175.7, 174.9, 172.9, 172.3, 171.9, 169.2, 156.7, 154.2, 130.5, 128.8, 115.3, 59.3, 53.5, 52.5, 50.6 (2 C), 40.4, 39.1, 36.1(2 C), 30.4,30.2, 28.0, 26.3, 23.3, 22.0, 18.3, 17.4; **MS** (ESI) *m/z* 680 [$(M+H)^+$, 100%]; **HRMS** (ESI, $[M+H]^+$) calcd. for $C_{30}H_{49}N_9O_9$ 680.3726 found 680.3726; Characterisation data consistent with an authetic sample purchased from BACHEM by HPLC co-injection and co-NMR (See later sections).

Chiral HPLC analysis of 10AG

Chiral HPLC was performed using a Phenomenex Lux 5µ Cellulose-3 LC column (250 x 10.00 mm, flow rate of 2 mL min^{-1}). Elution was performed using an isocratic solution of 1:1 CH_3CN: H_2O. The peaks were visualised at 280 nm.



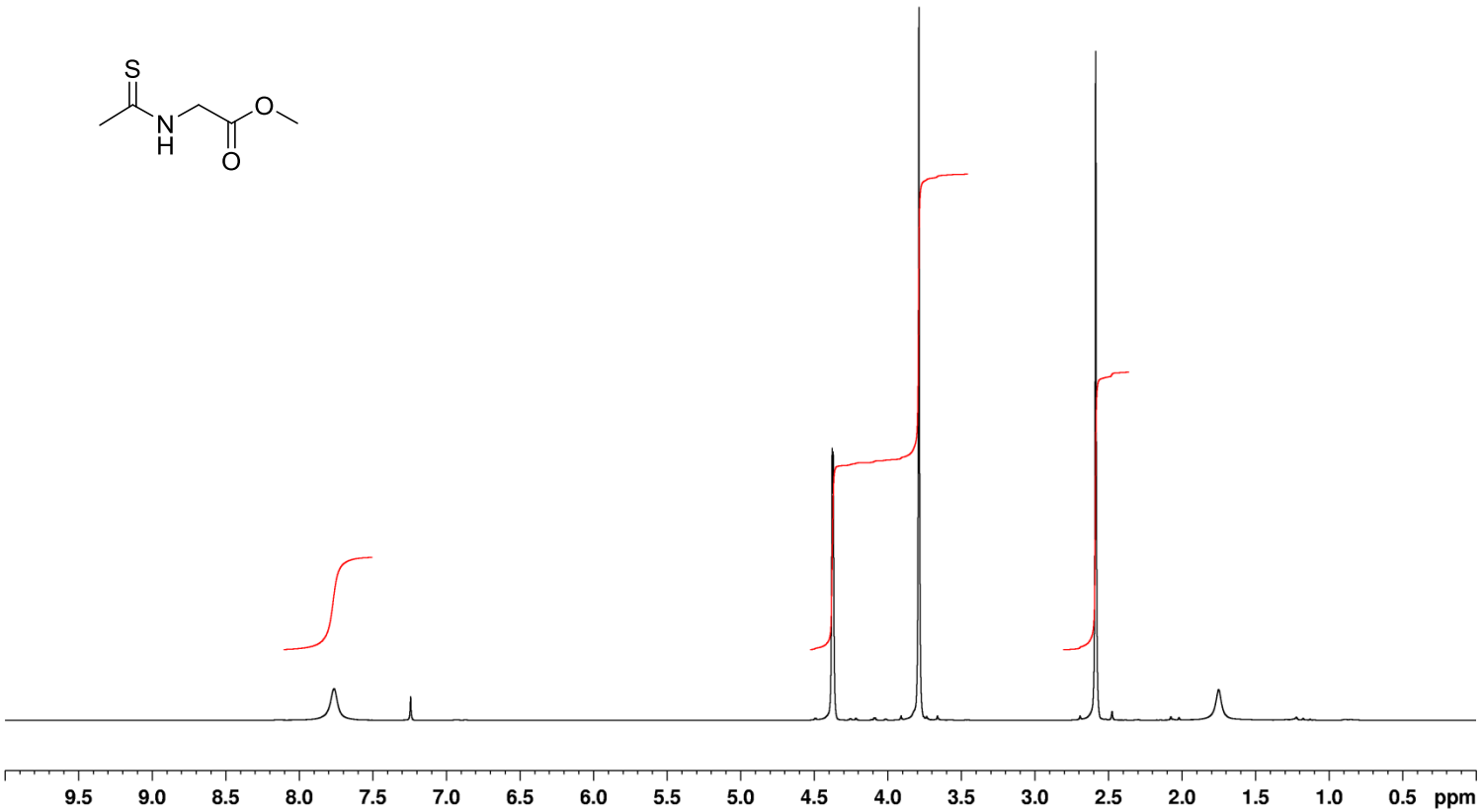
Integration results

Sample: (-)3AG

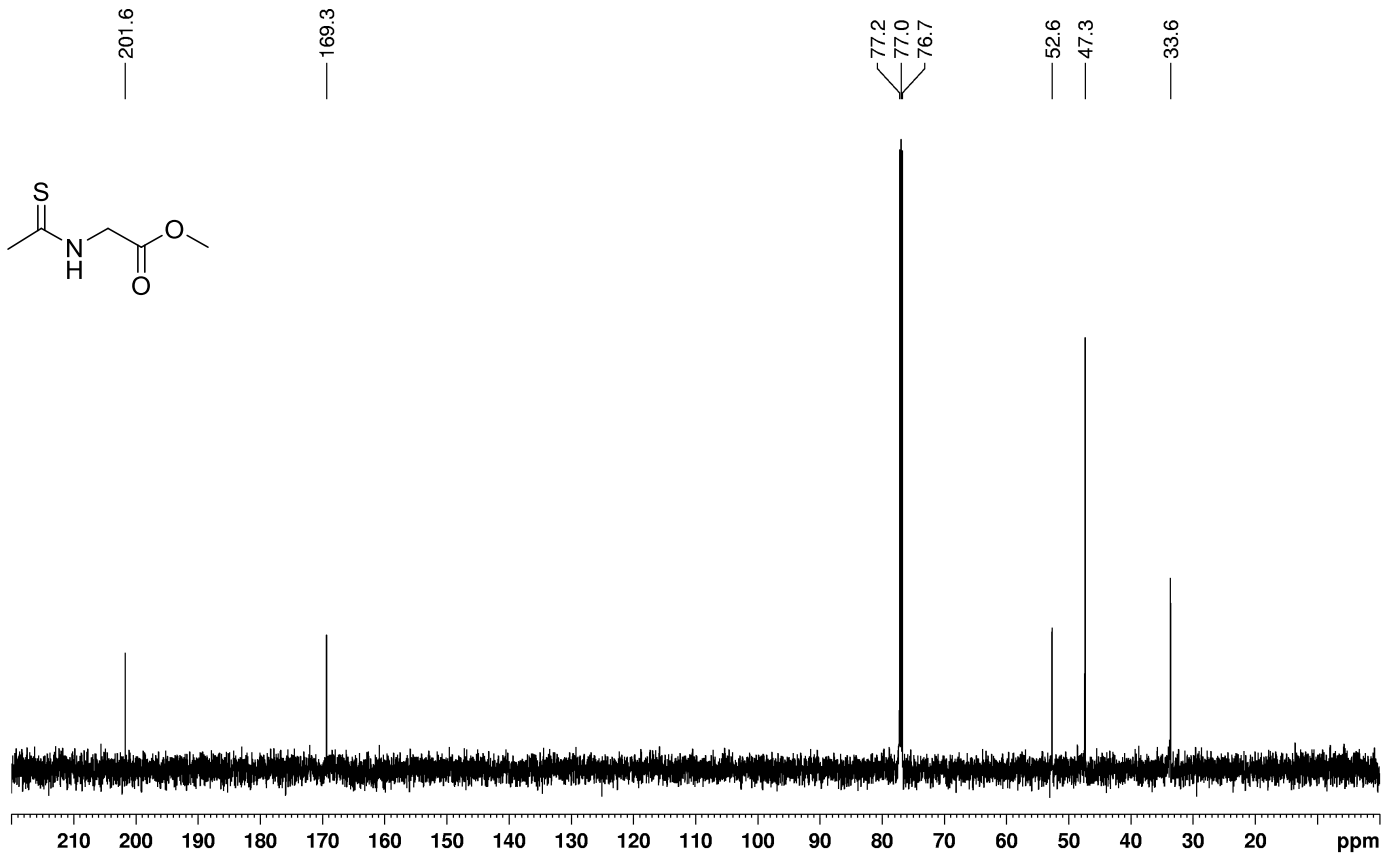
Signal 1: MWD1 E, Sig=280, 16 Ref = 600, 100

Peak #	Time [min]	Type	Area [mAu*s]	Height [mAU]	Width [min]	Start [min]	End[min]
1	10.199	MM	12.07127	1.49660	0.1344	10.078	10.308
2	11.11	MM	1.55E+04	1056.73535	0.2446	10.622	12.003

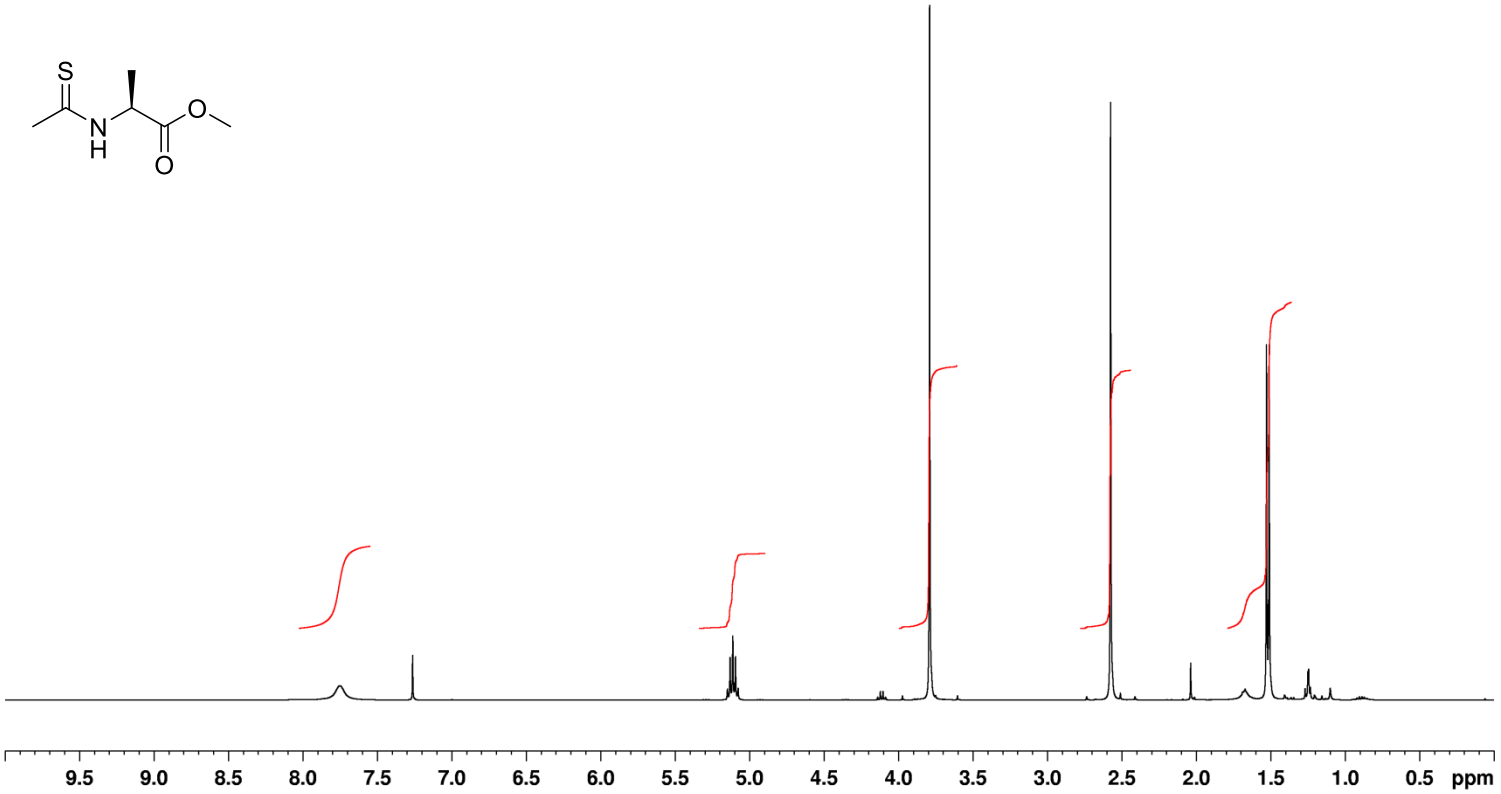
Compound 12G (600 MHz, $CDCl_3$)



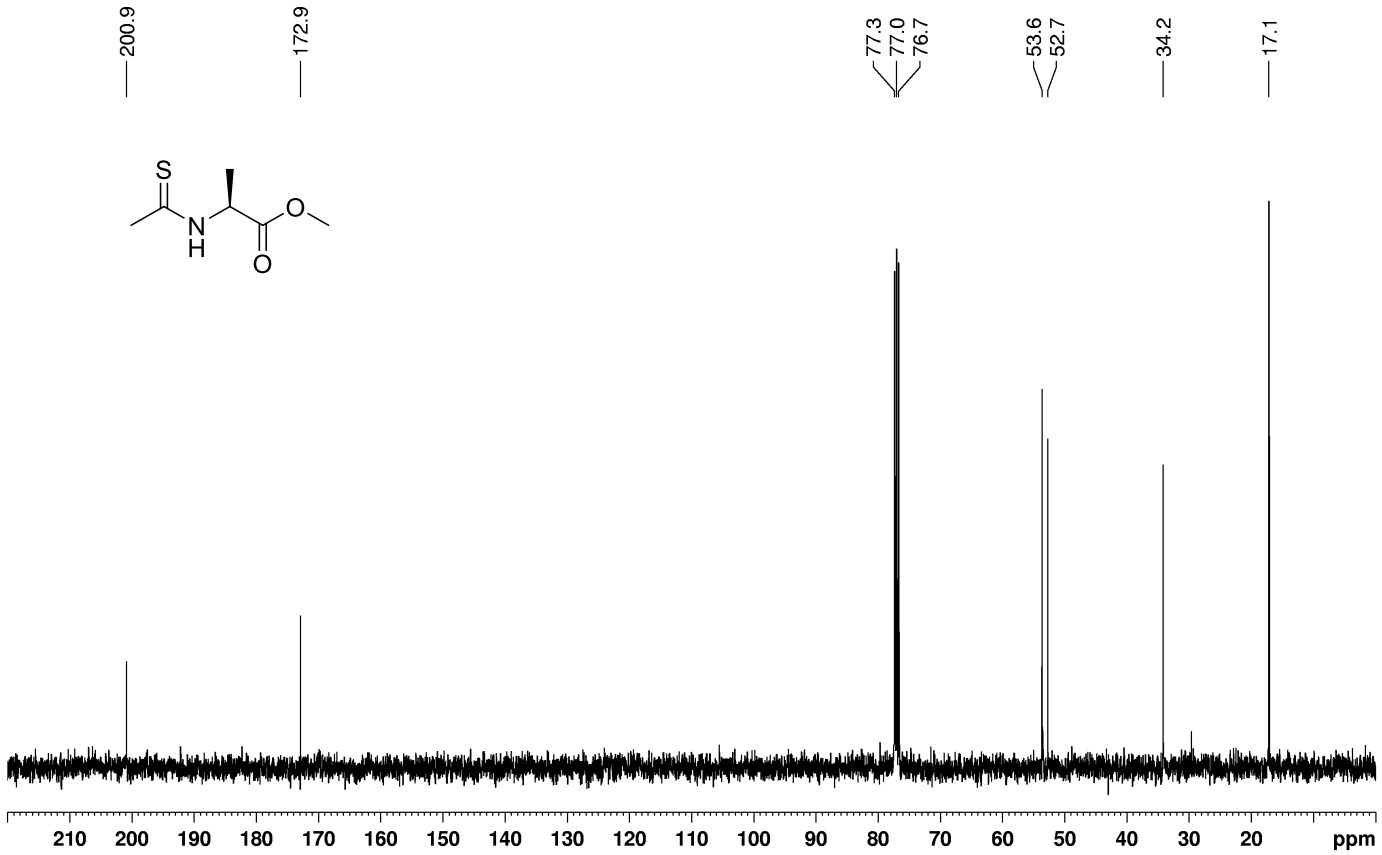
Compound 12G (150 MHz, CDCl3)



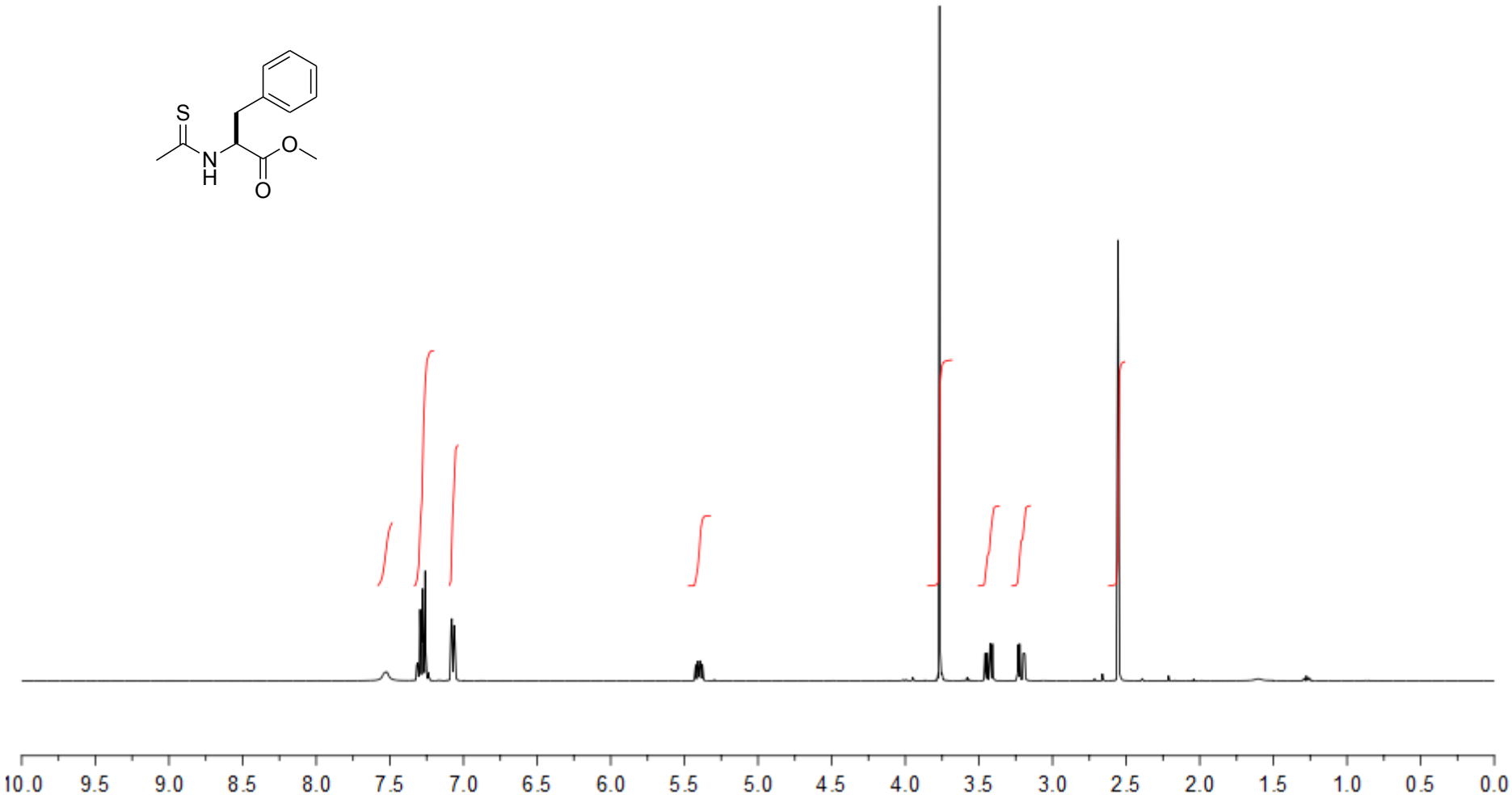
Compound 12A (400 MHz, CDCl3)



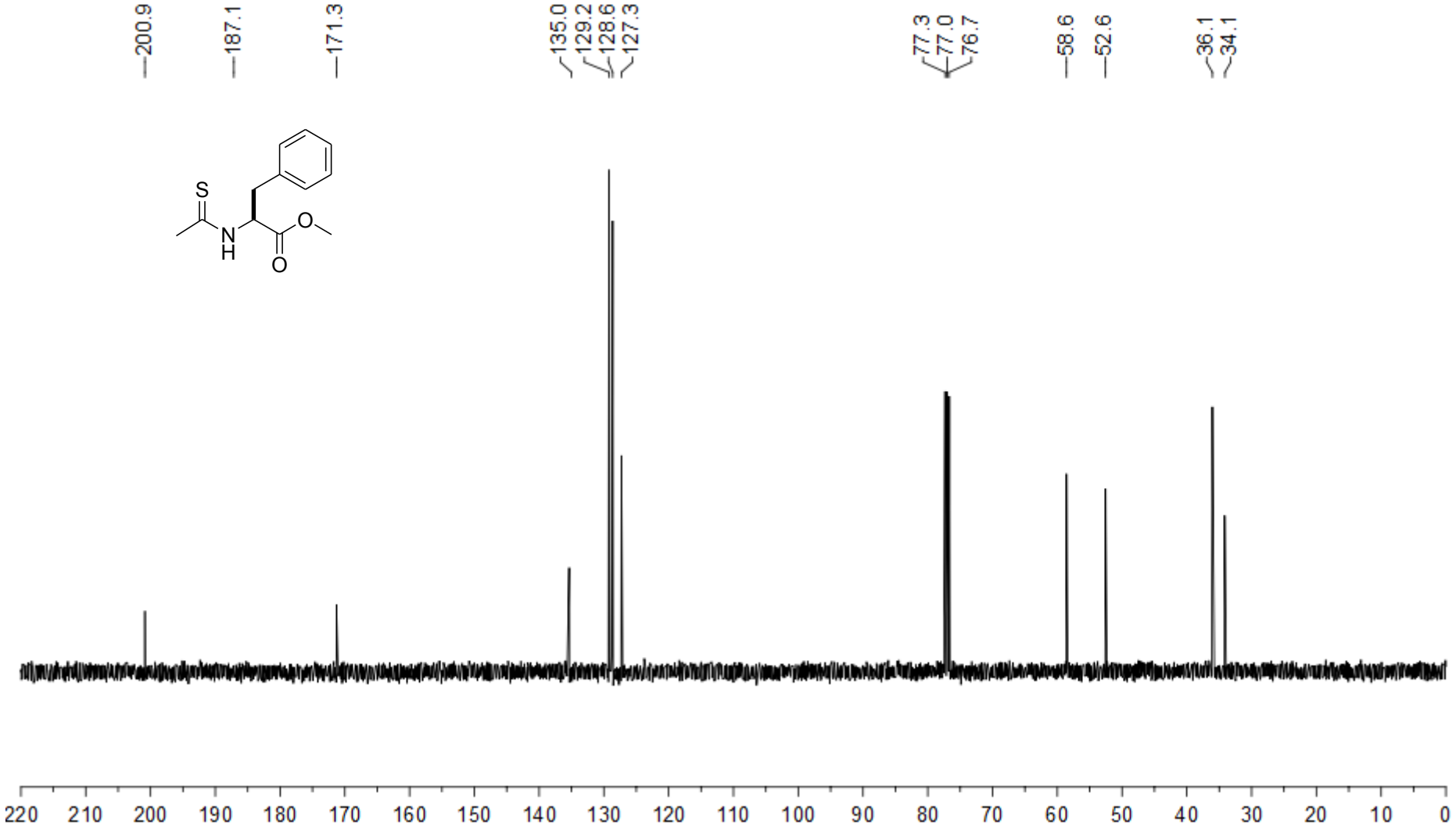
Compound 12A (100 MHz, CDCl3)



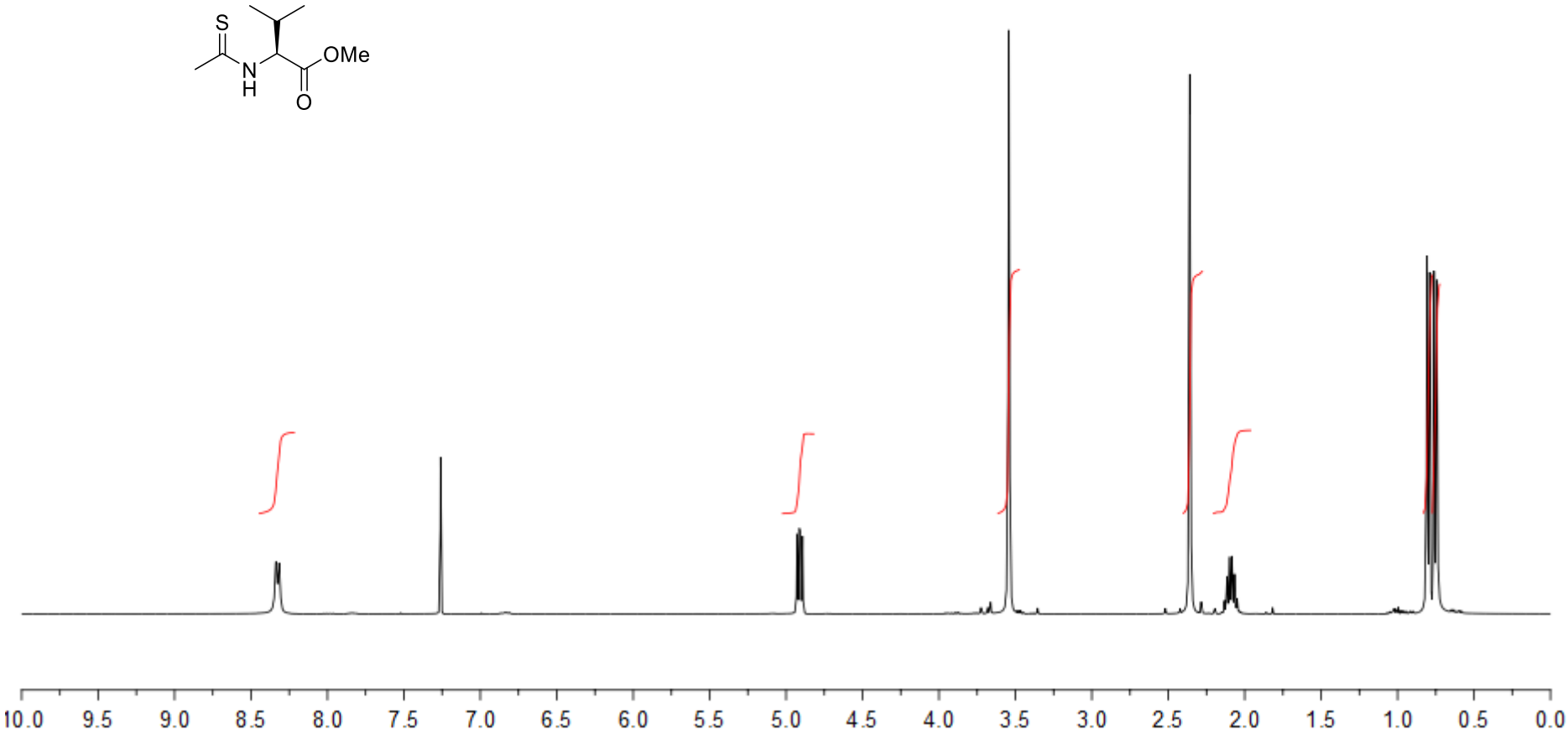
Compound 12F (400 MHz, $CDCl_3$)



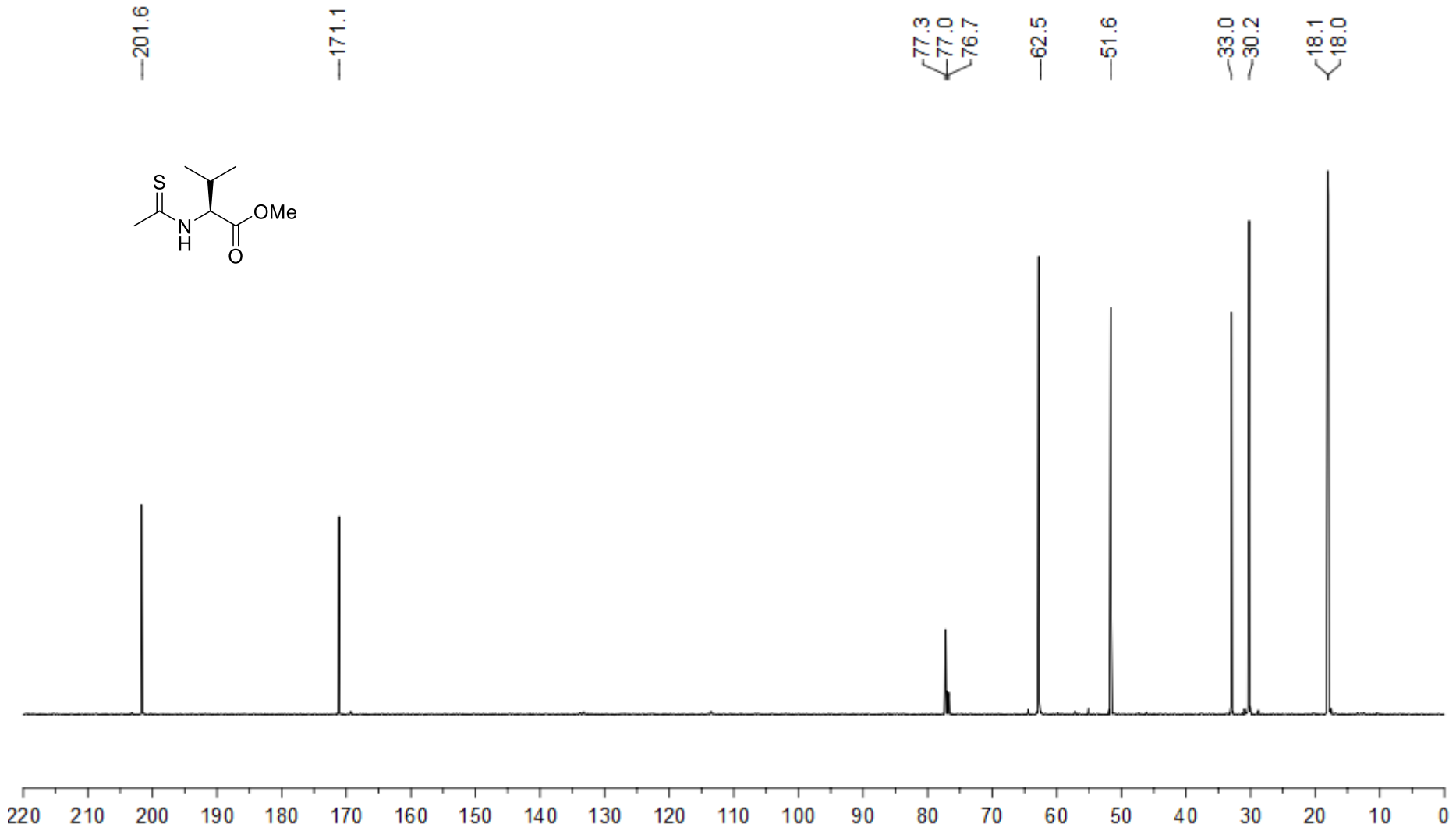
Compound 12F (100 MHz, $CDCl_3$)



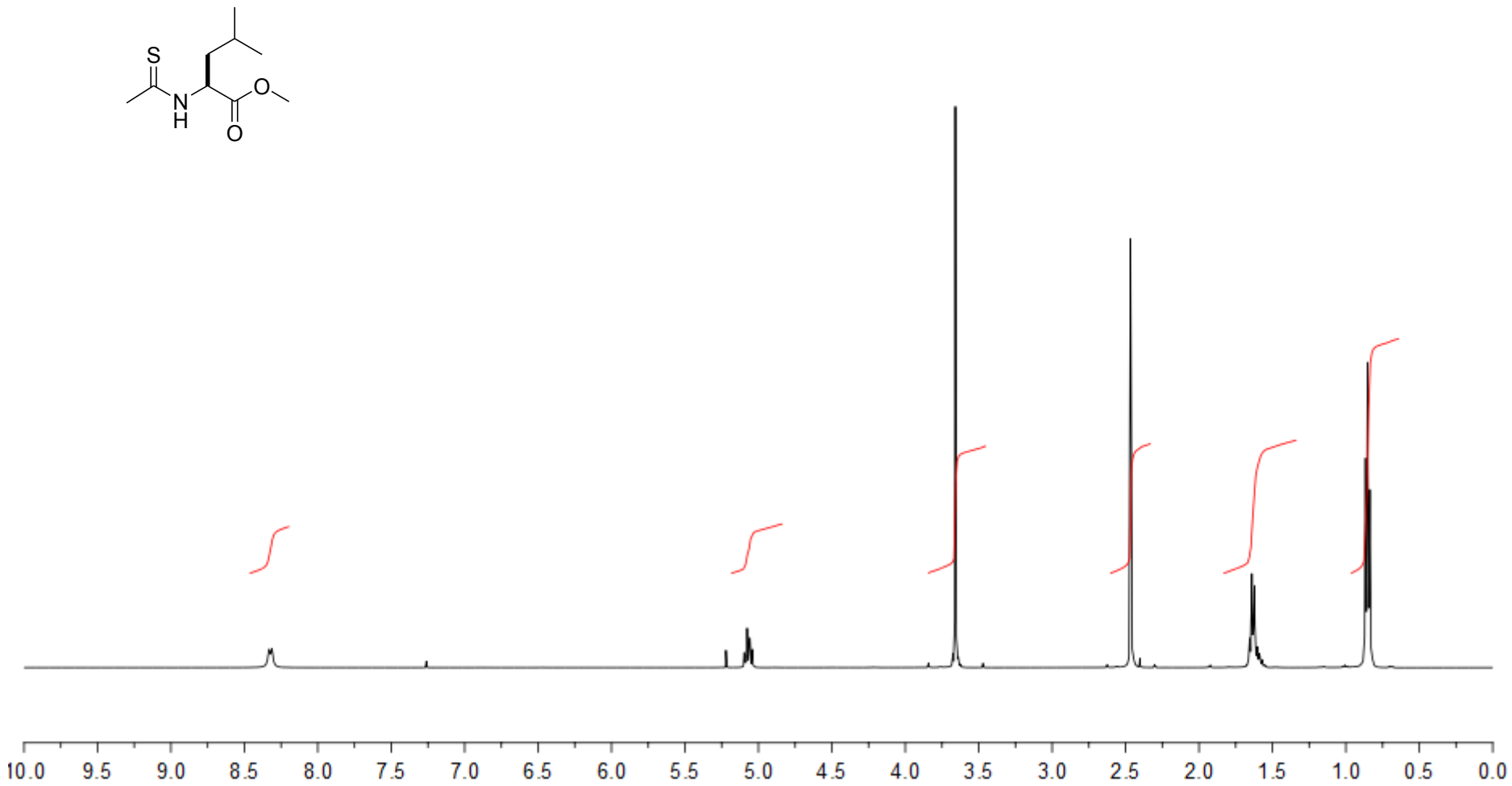
Compound 12V (400 MHz, CDCl3)



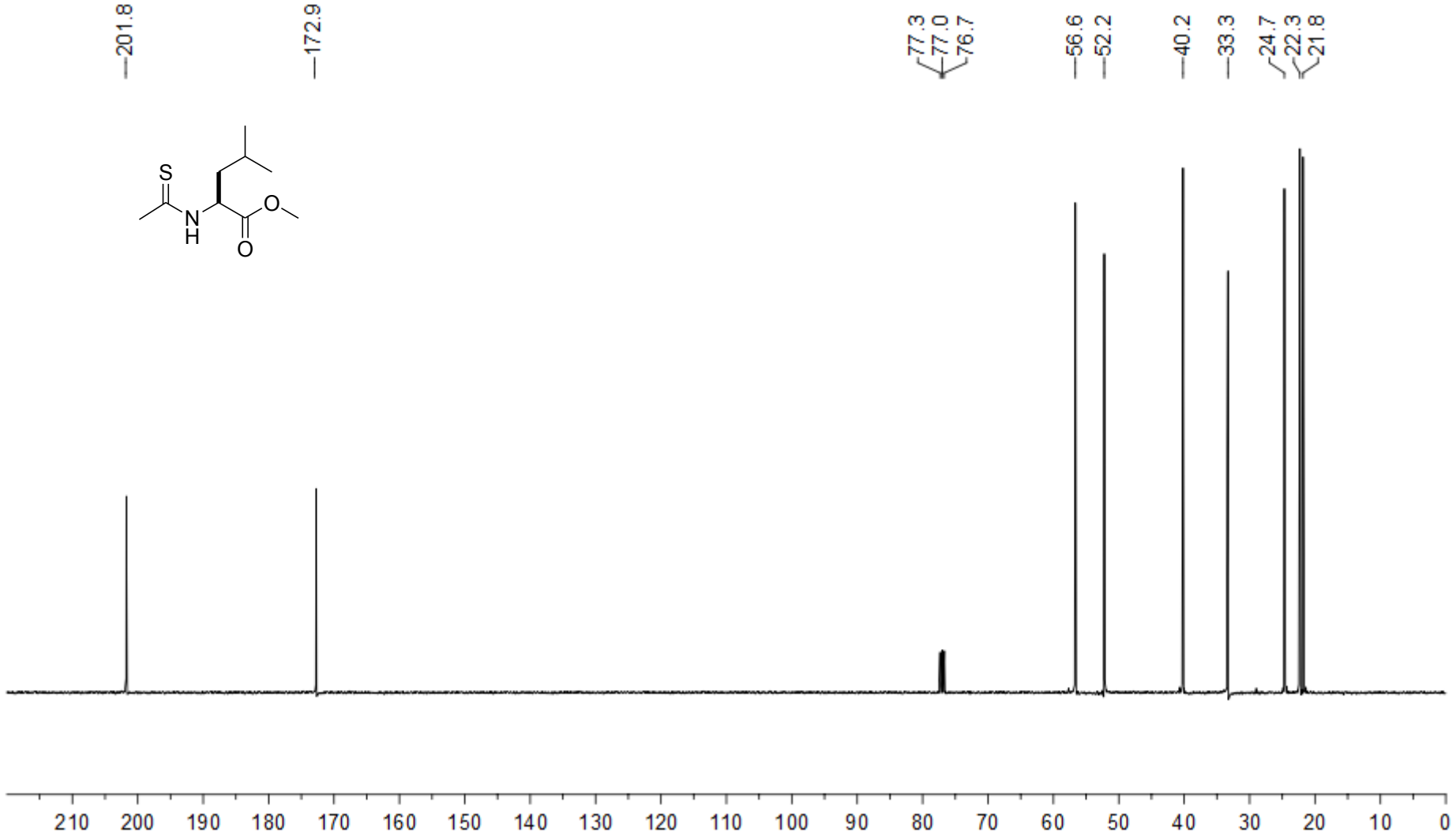
Compound 12V (100 MHz, CDCl3)



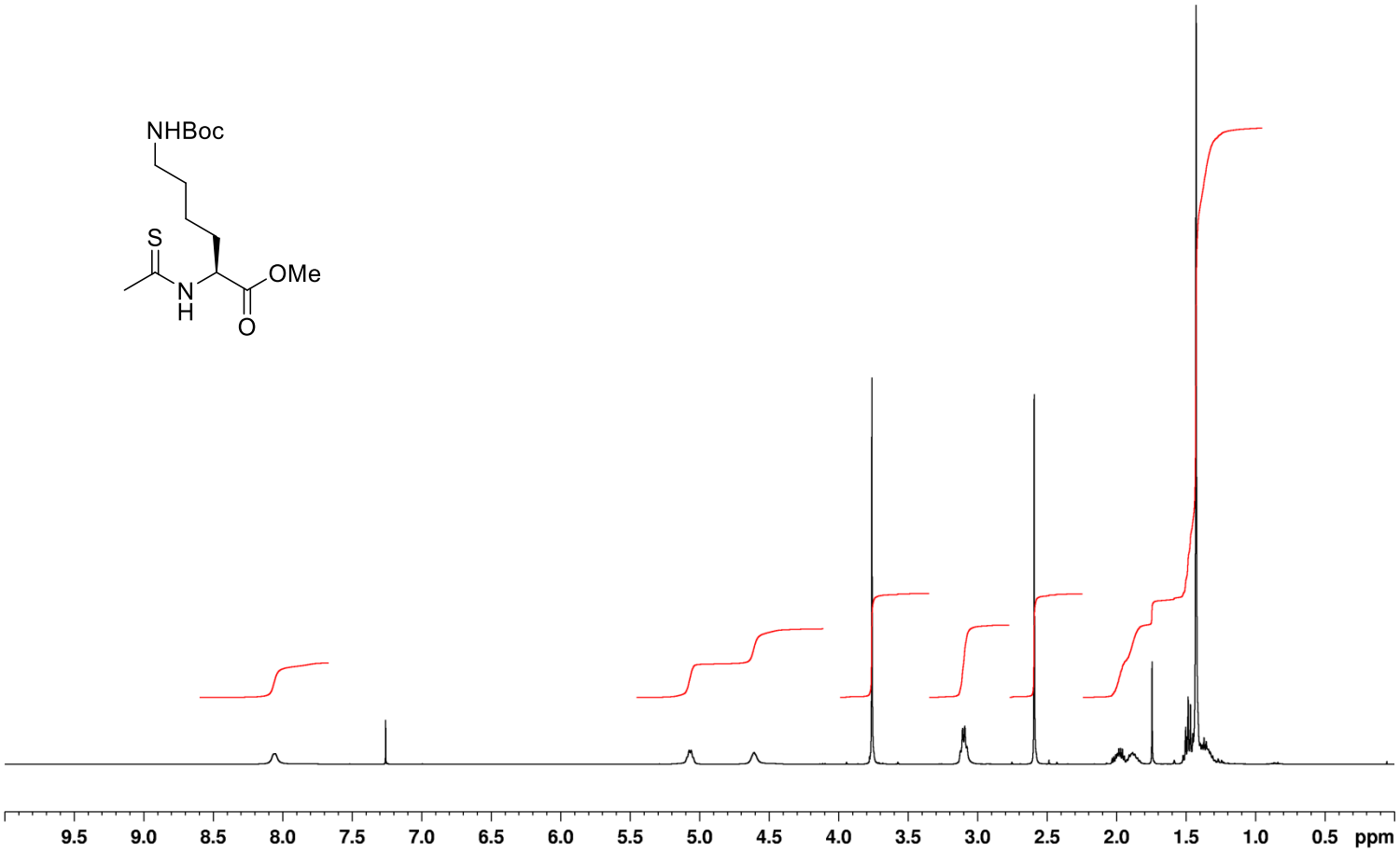
Compound 12L (400 MHz, $CDCl_3$)



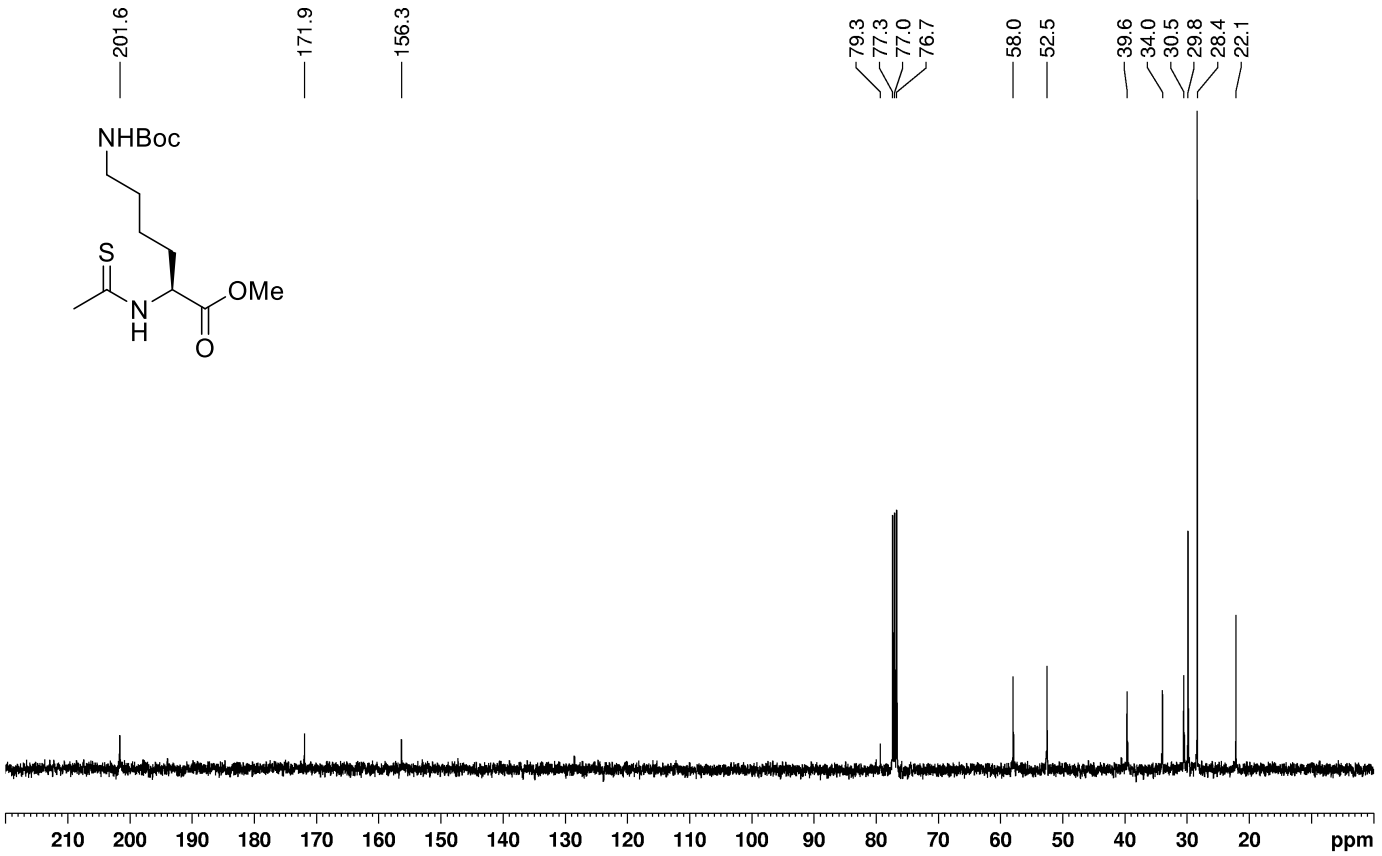
Compound 12L (100 MHz, CDCl3)



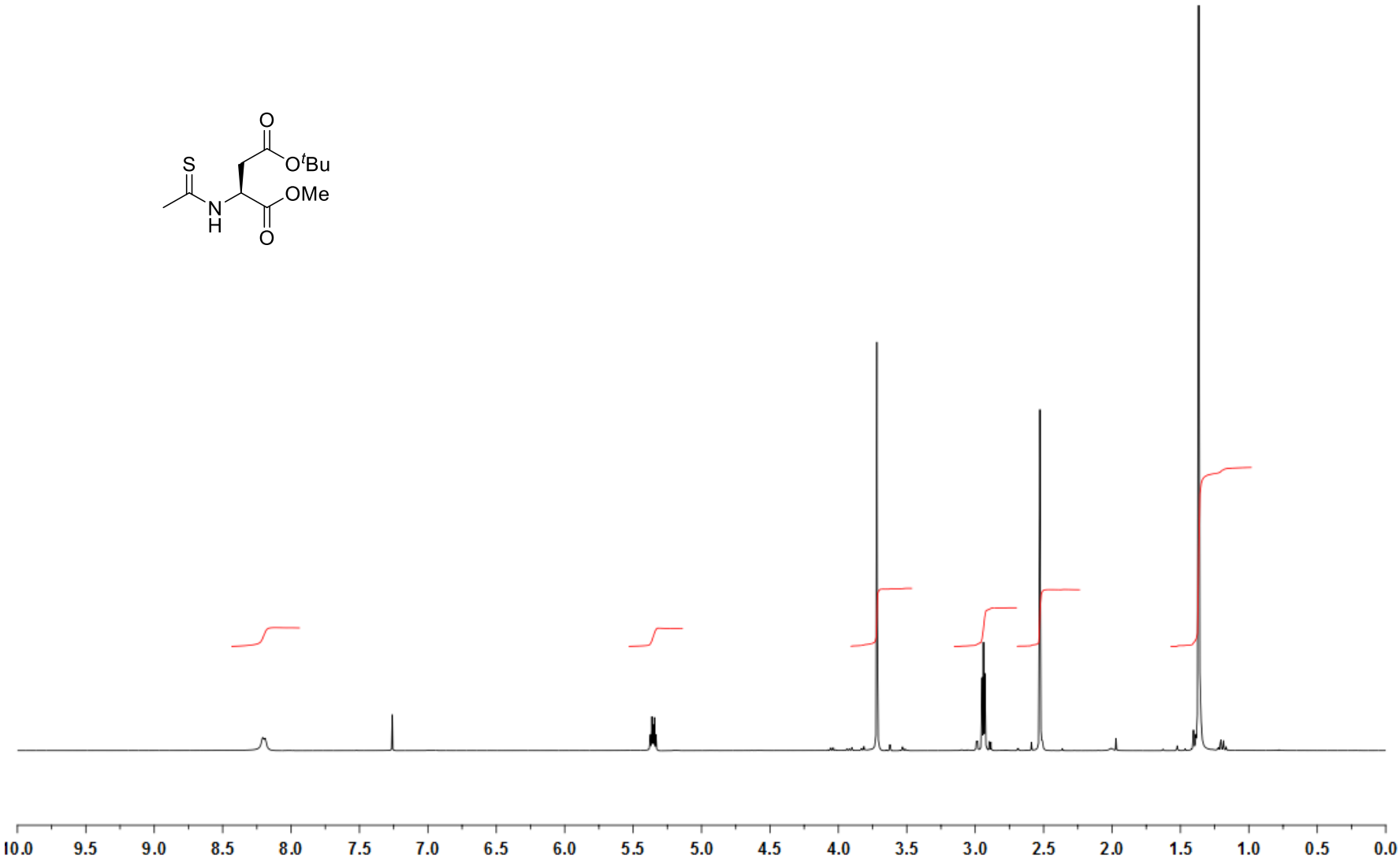
Compound 12K (400 MHz, $CDCl_3$)



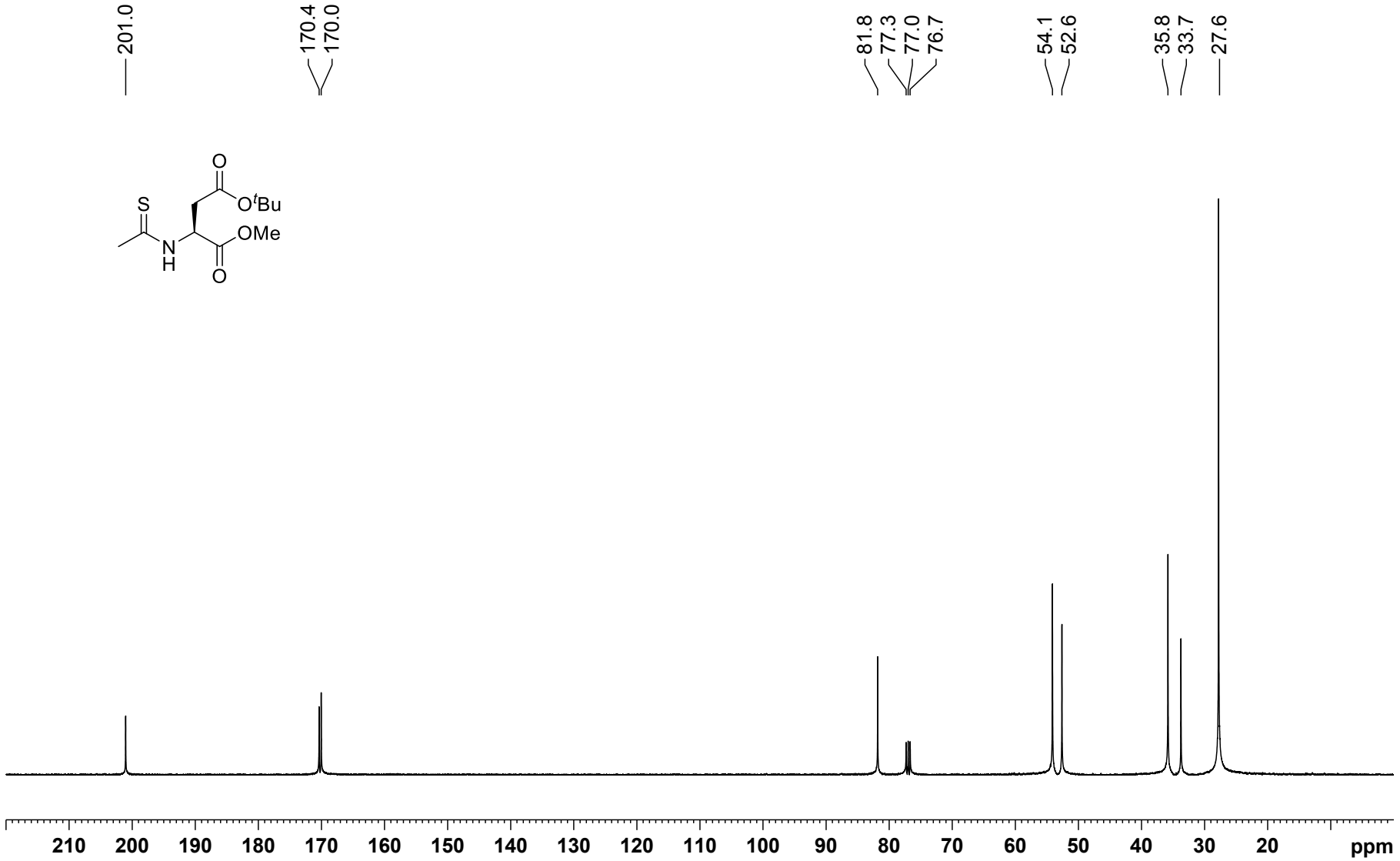
Compound 12K (100 MHz, $CDCl_3$)



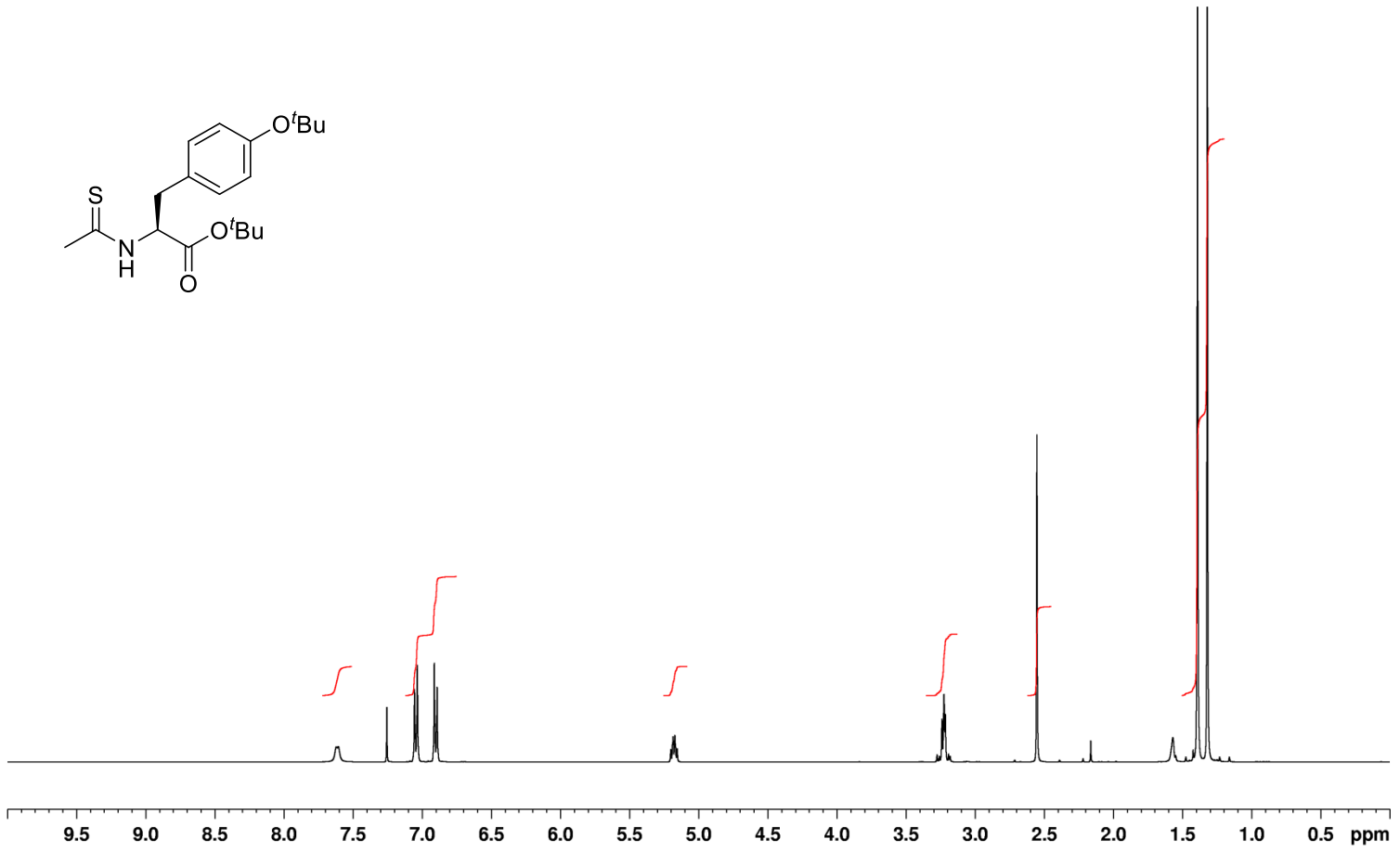
Compound 12D (400 MHz, $CDCl_3$)



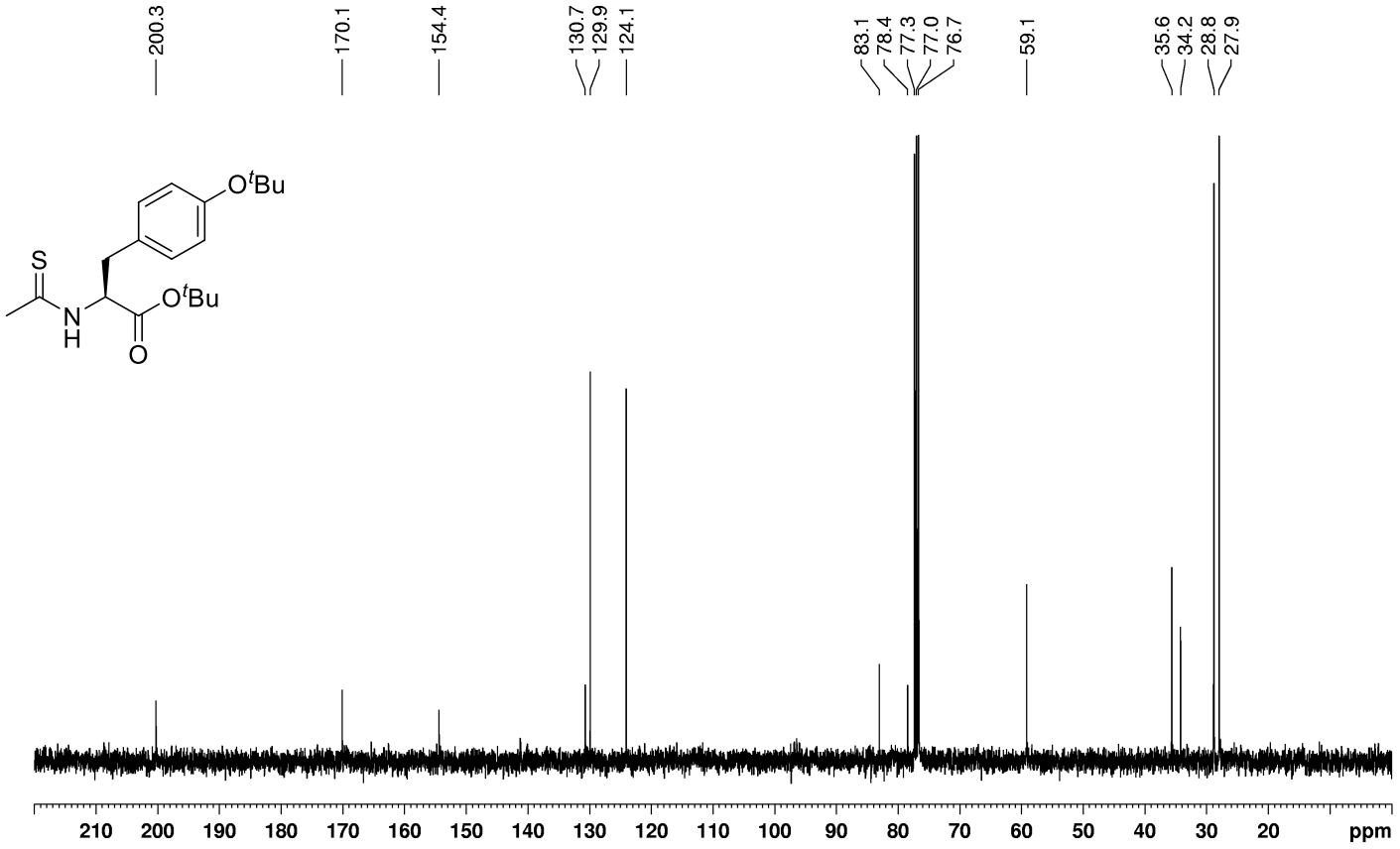
Compound 12D (100 MHz, $CDCl_3$)



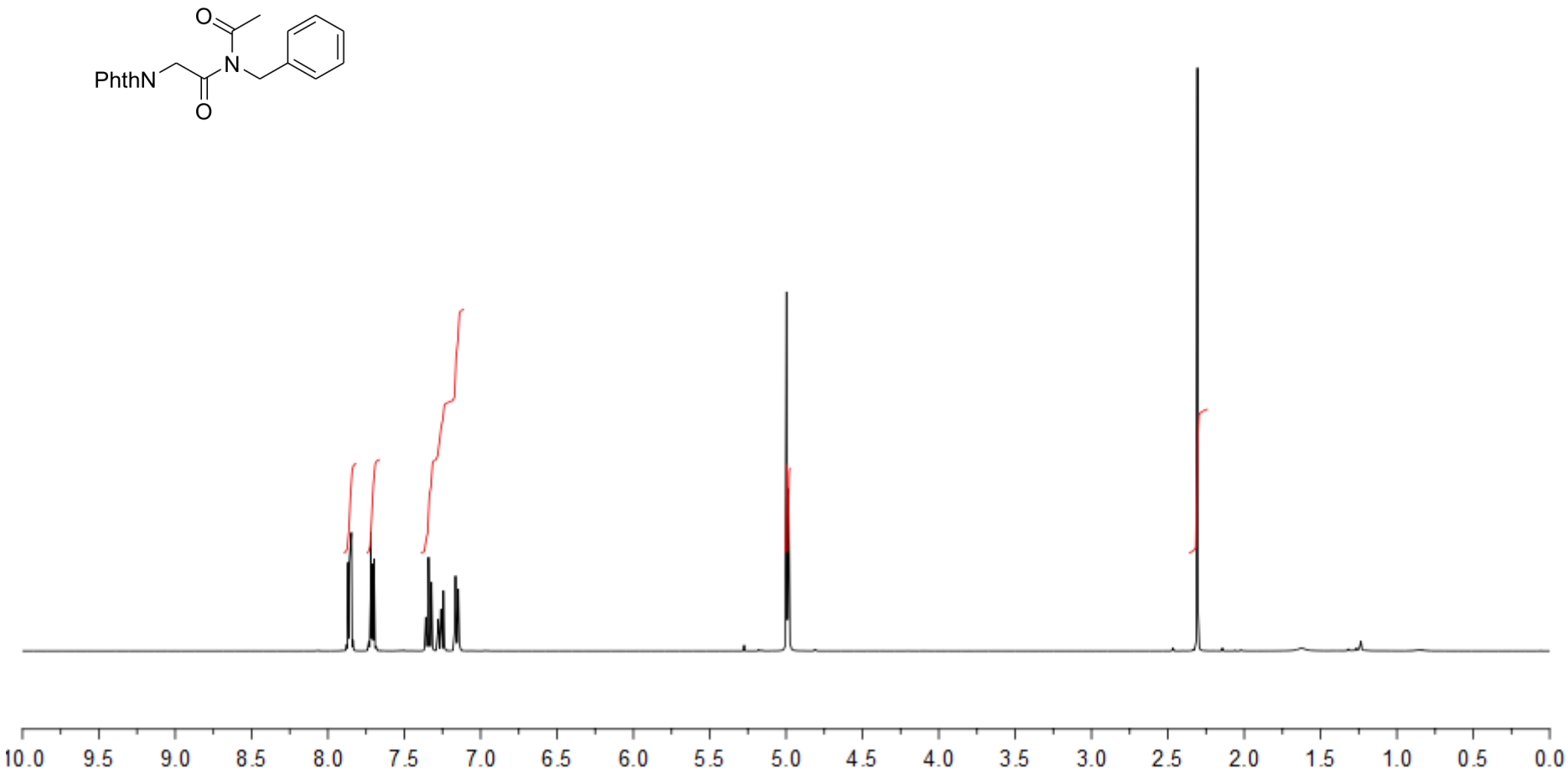
Compound 12Y (400 MHz, $CDCl_3$)



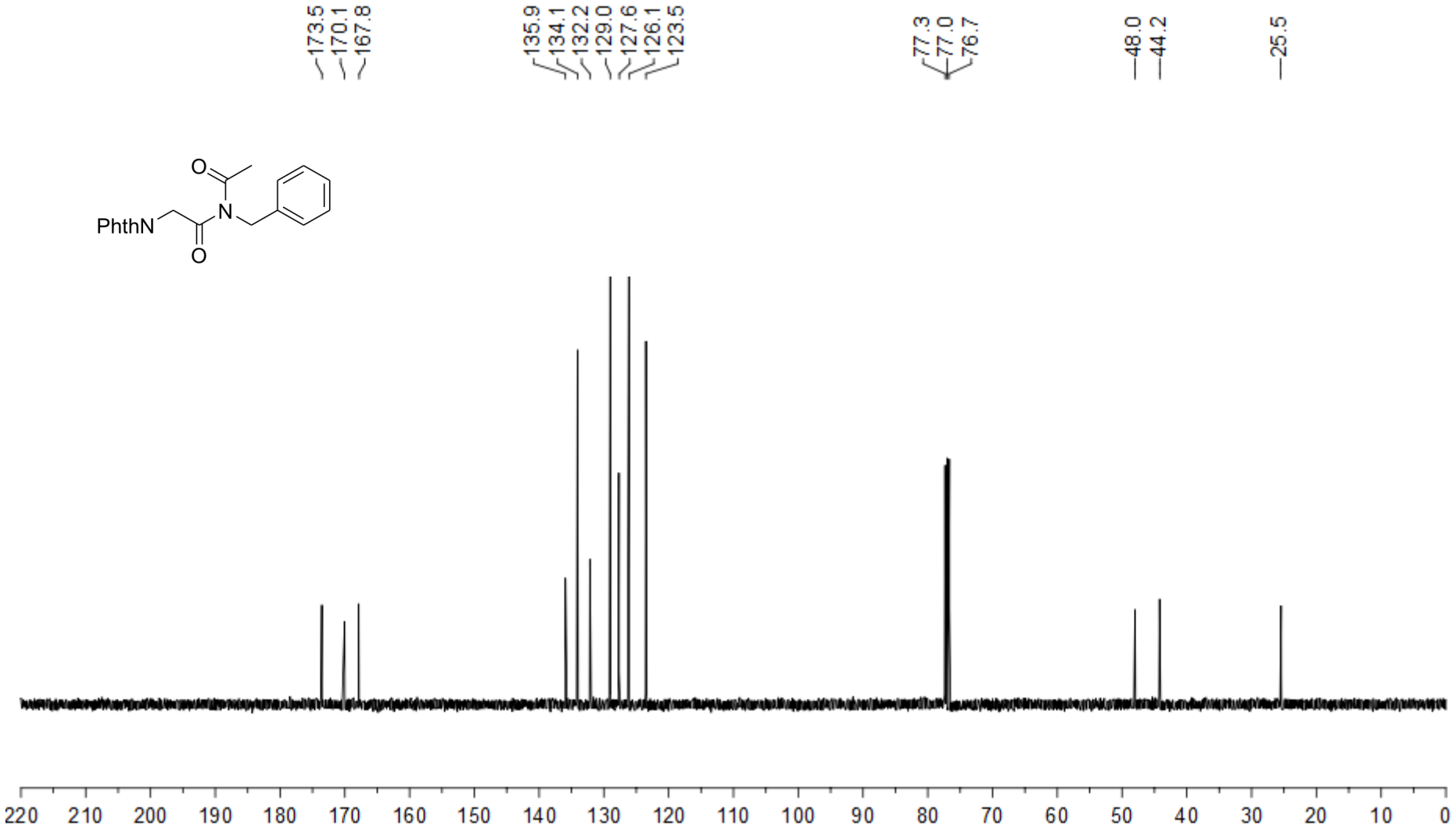
Compound 12Y (100 MHz, $CDCl_3$)



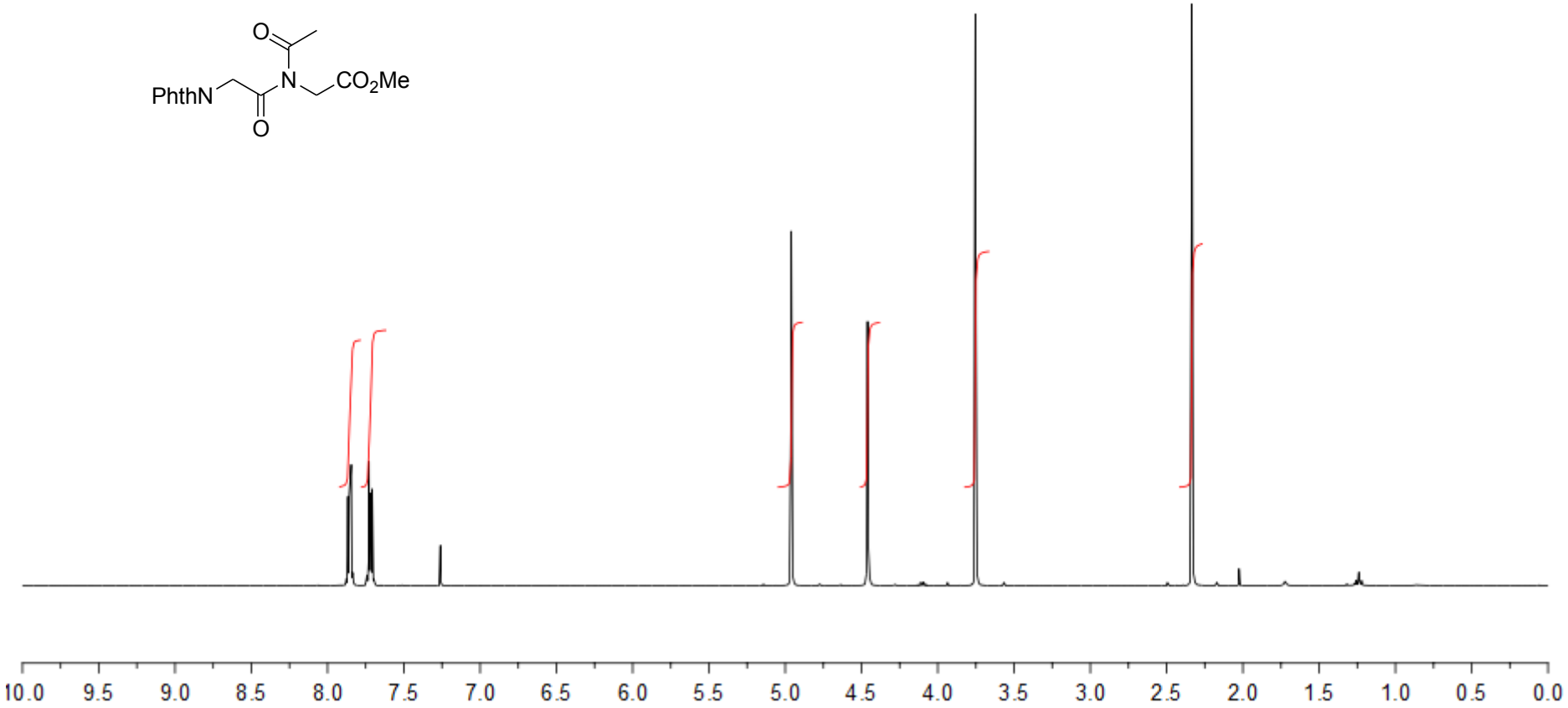
Compound 10 (400 MHz, $CDCl_3$)



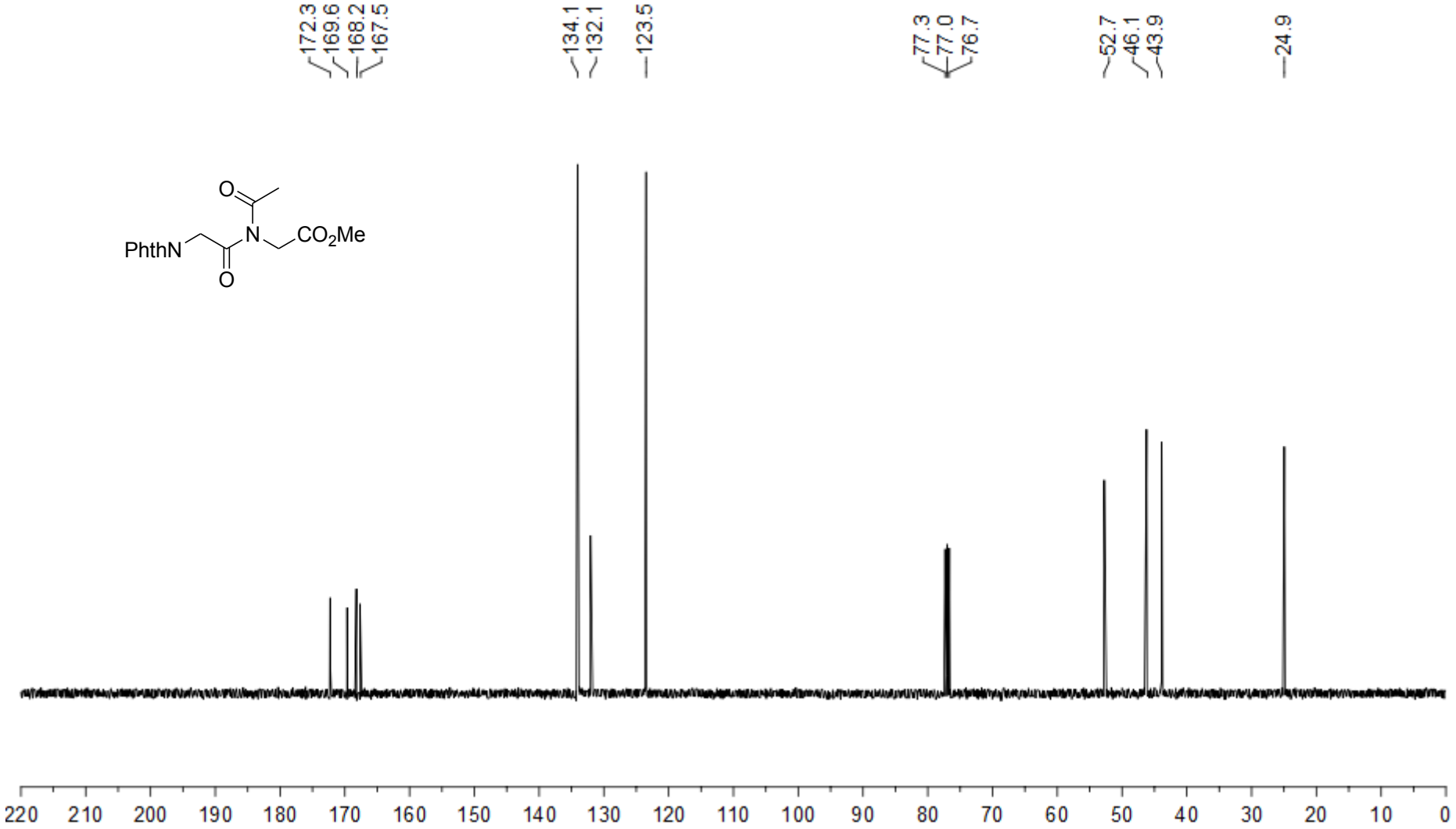
Compound 10 (100 MHz, $CDCl_3$)



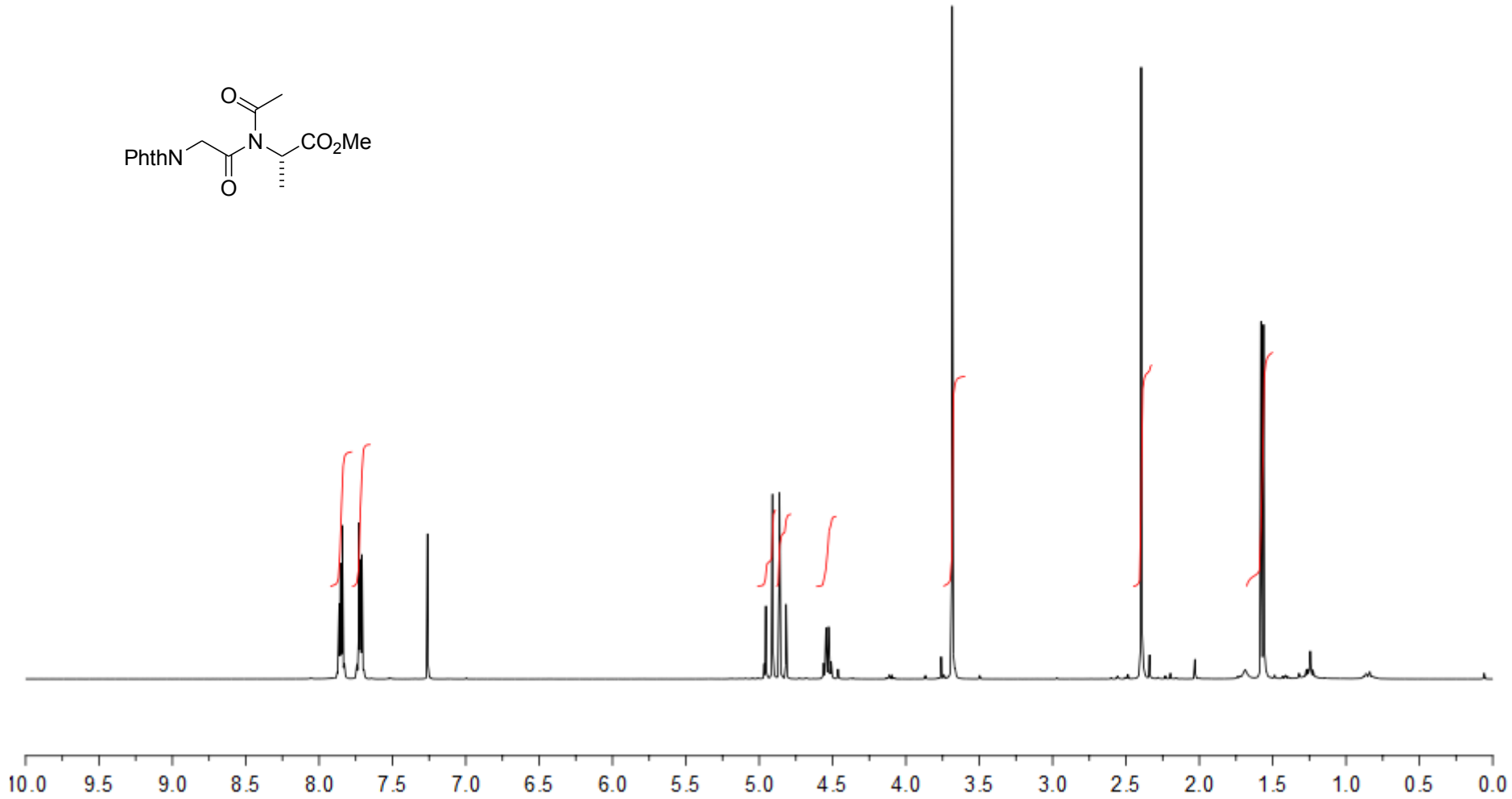
Compound 10GG (400 MHz, $CDCl_3$)



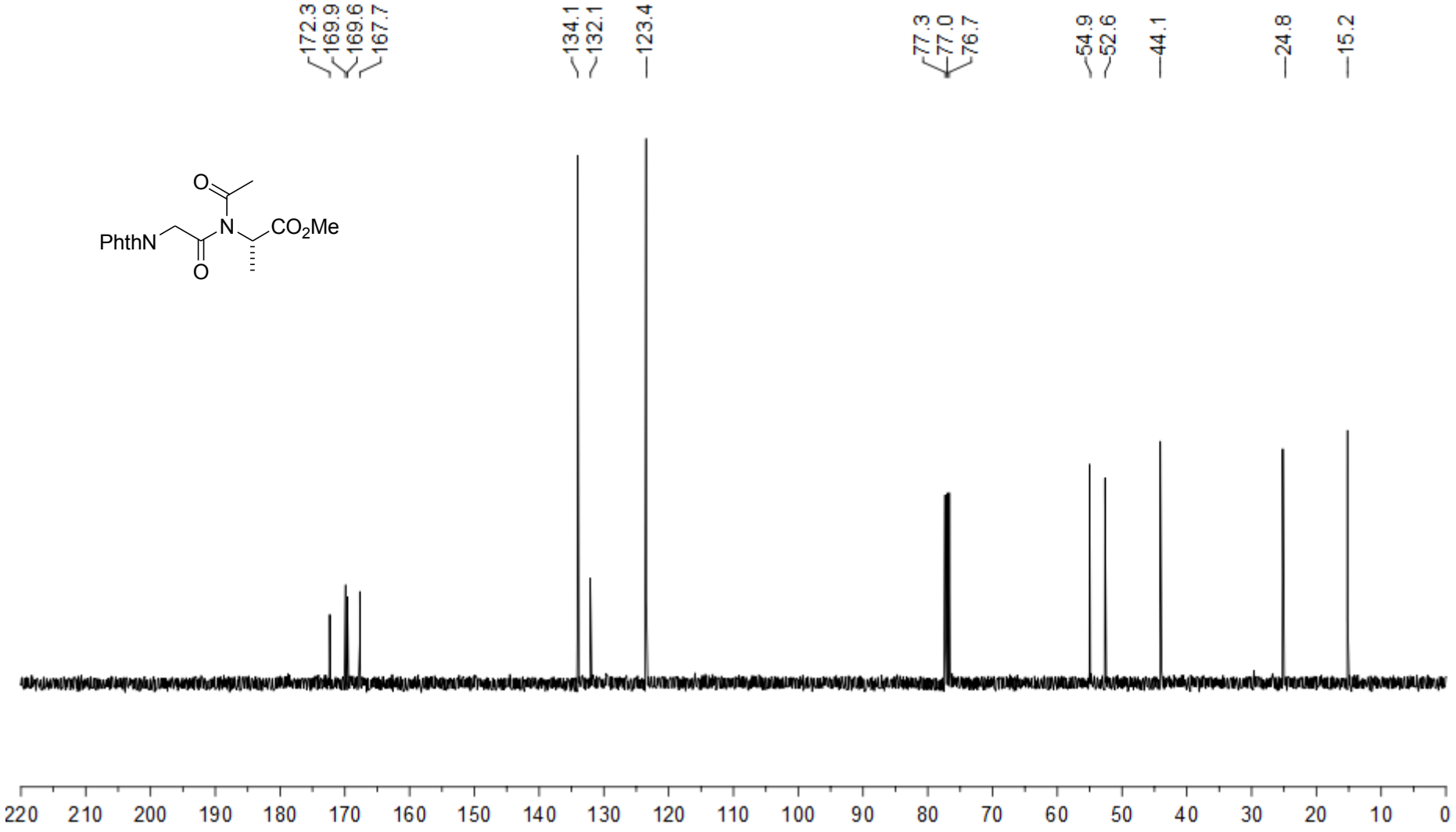
Compound 10GG (100 MHz, $CDCl_3$)



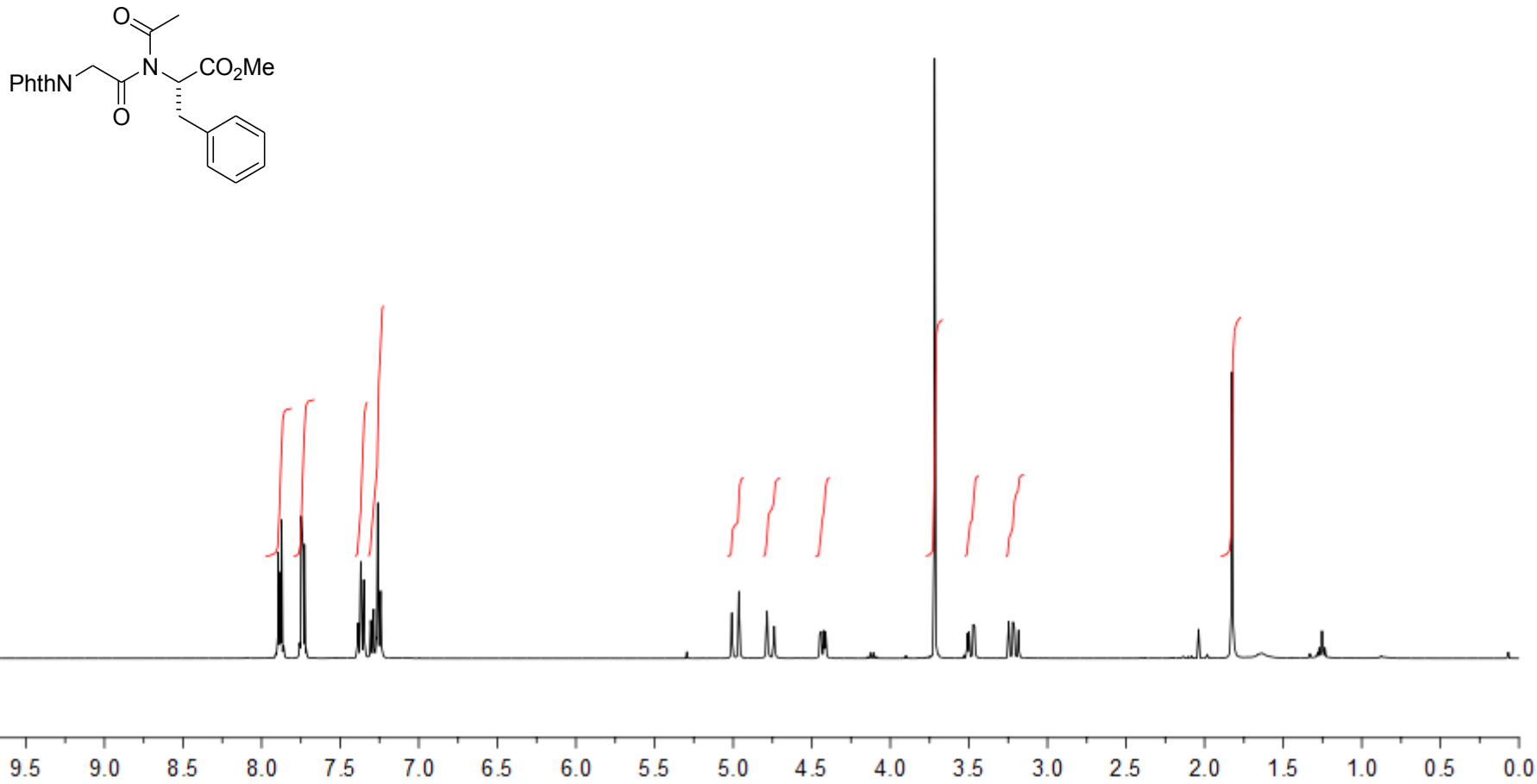
Compound 10GA (400 MHz, $CDCl_3$)



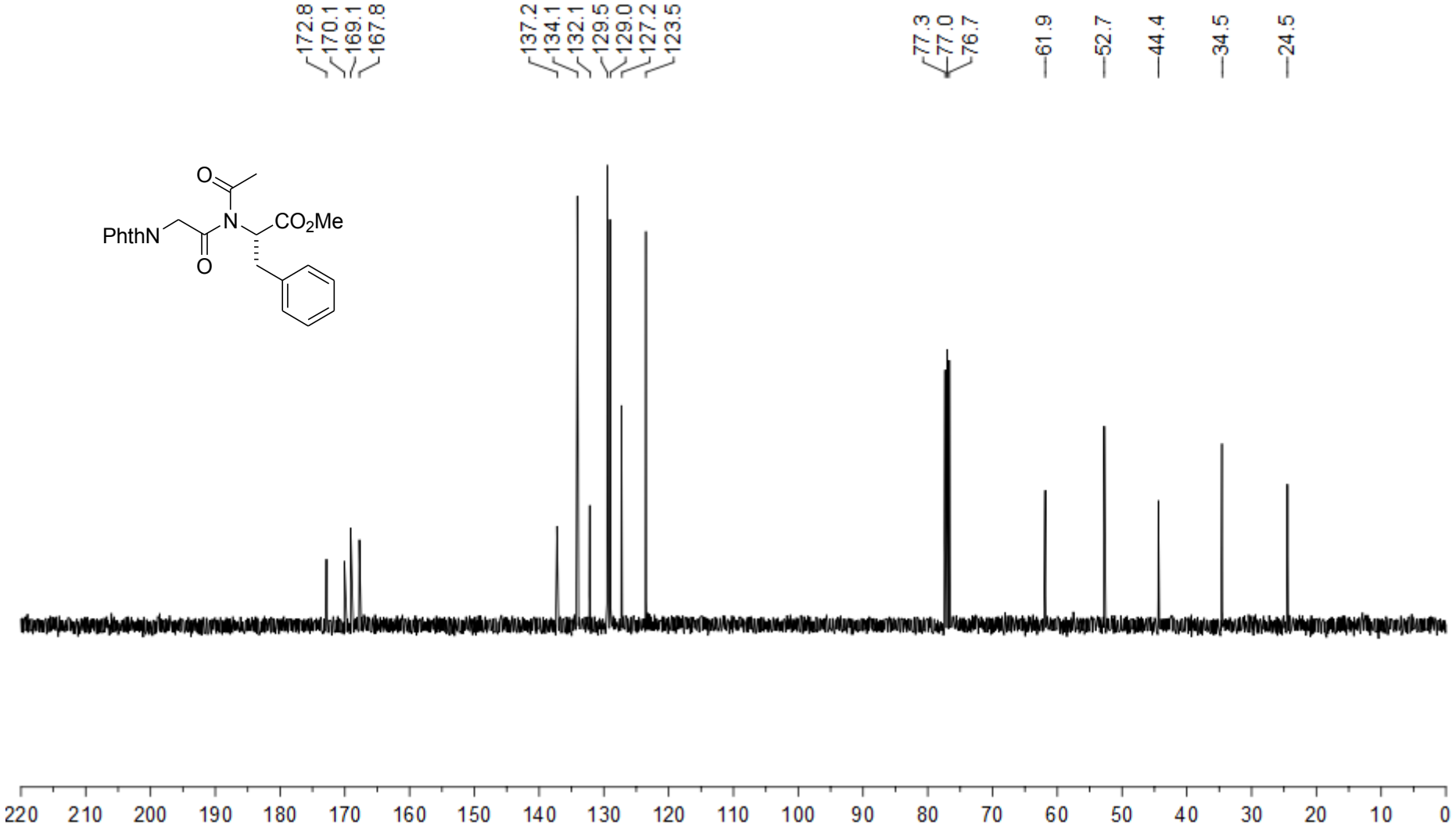
Compound 10GA (100 MHz, $CDCl_3$)



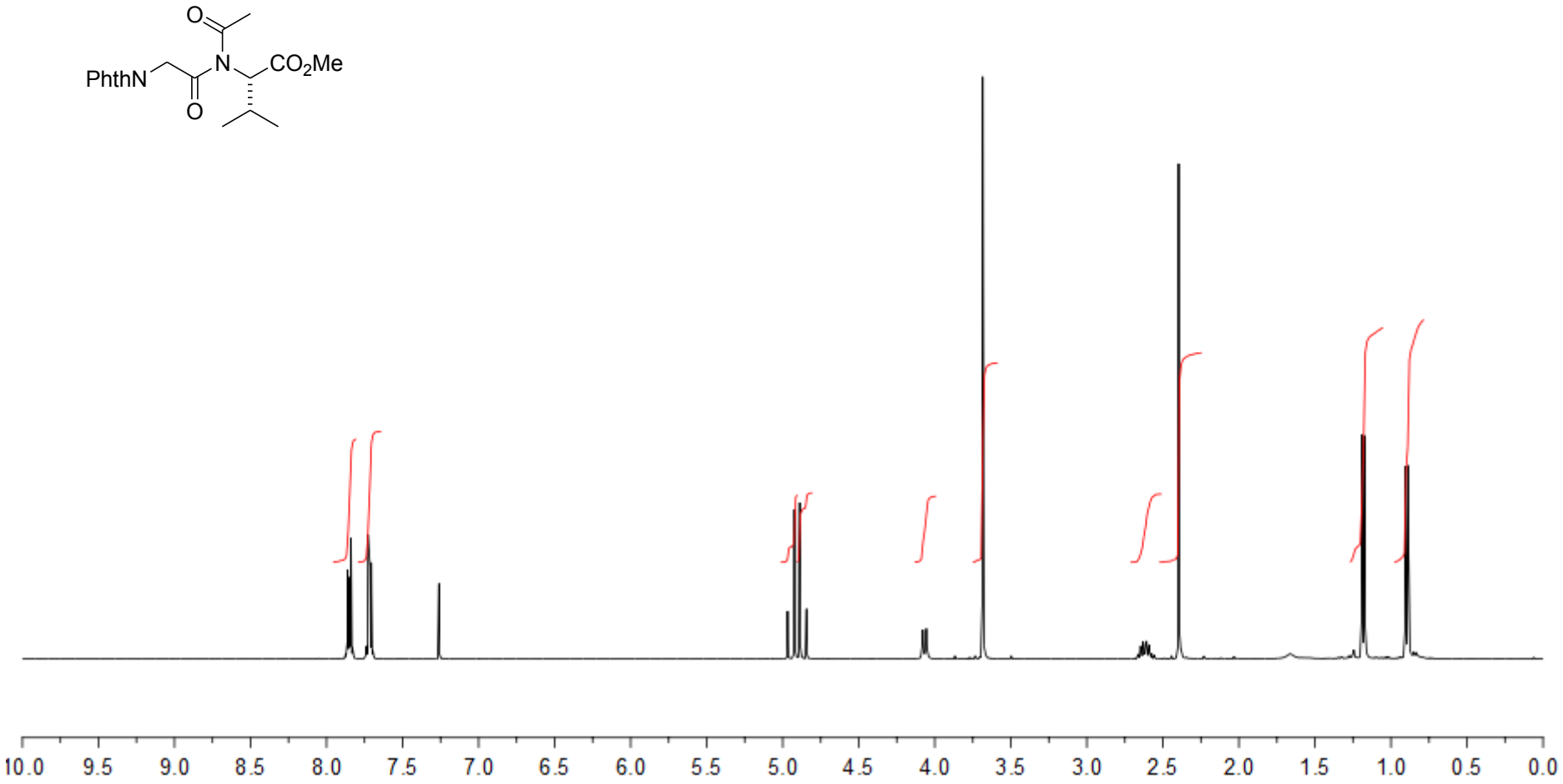
Compound 10GF (400 MHz, $CDCl_3$)



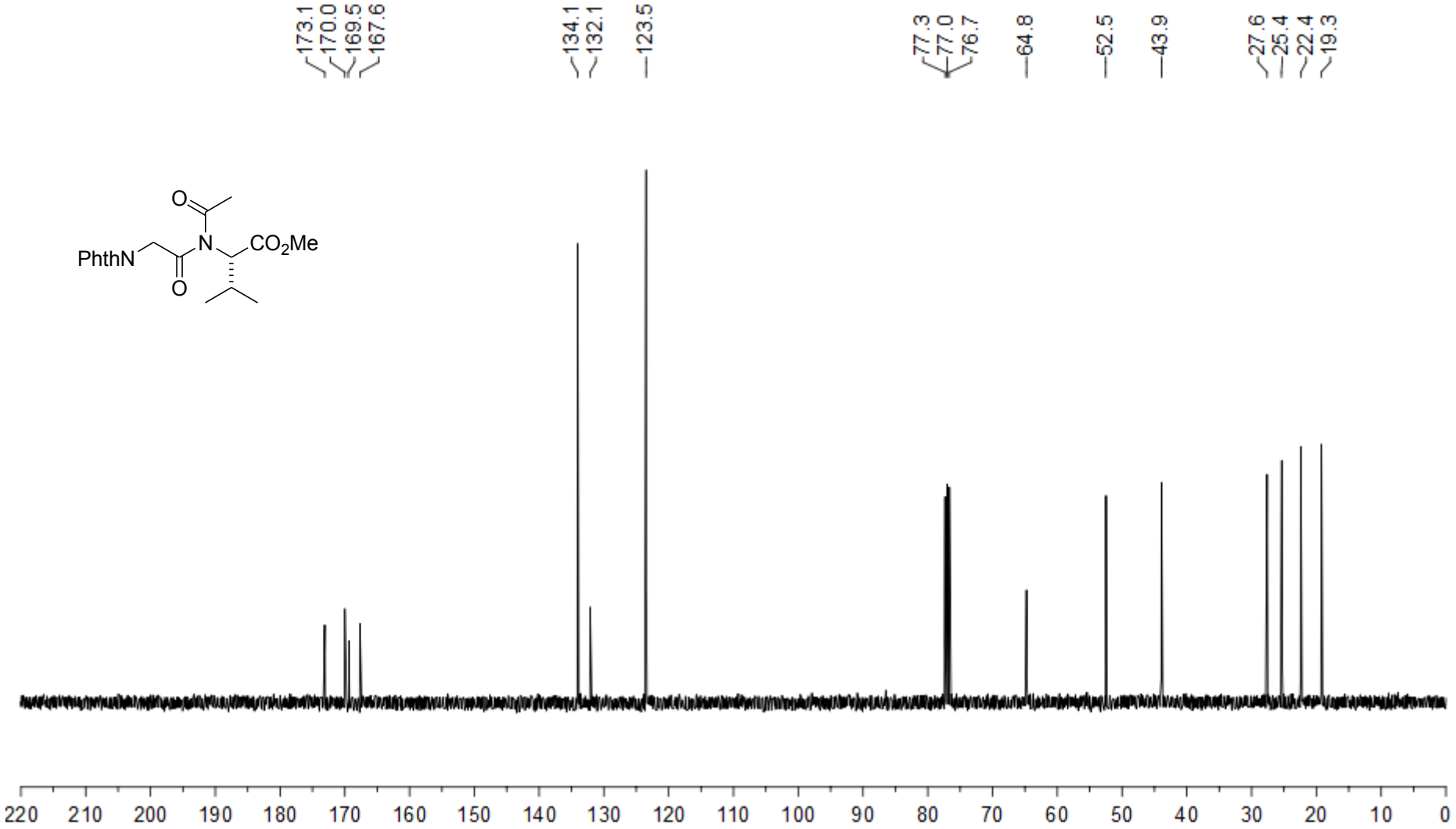
Compound 10GF (100 MHz, $CDCl_3$)



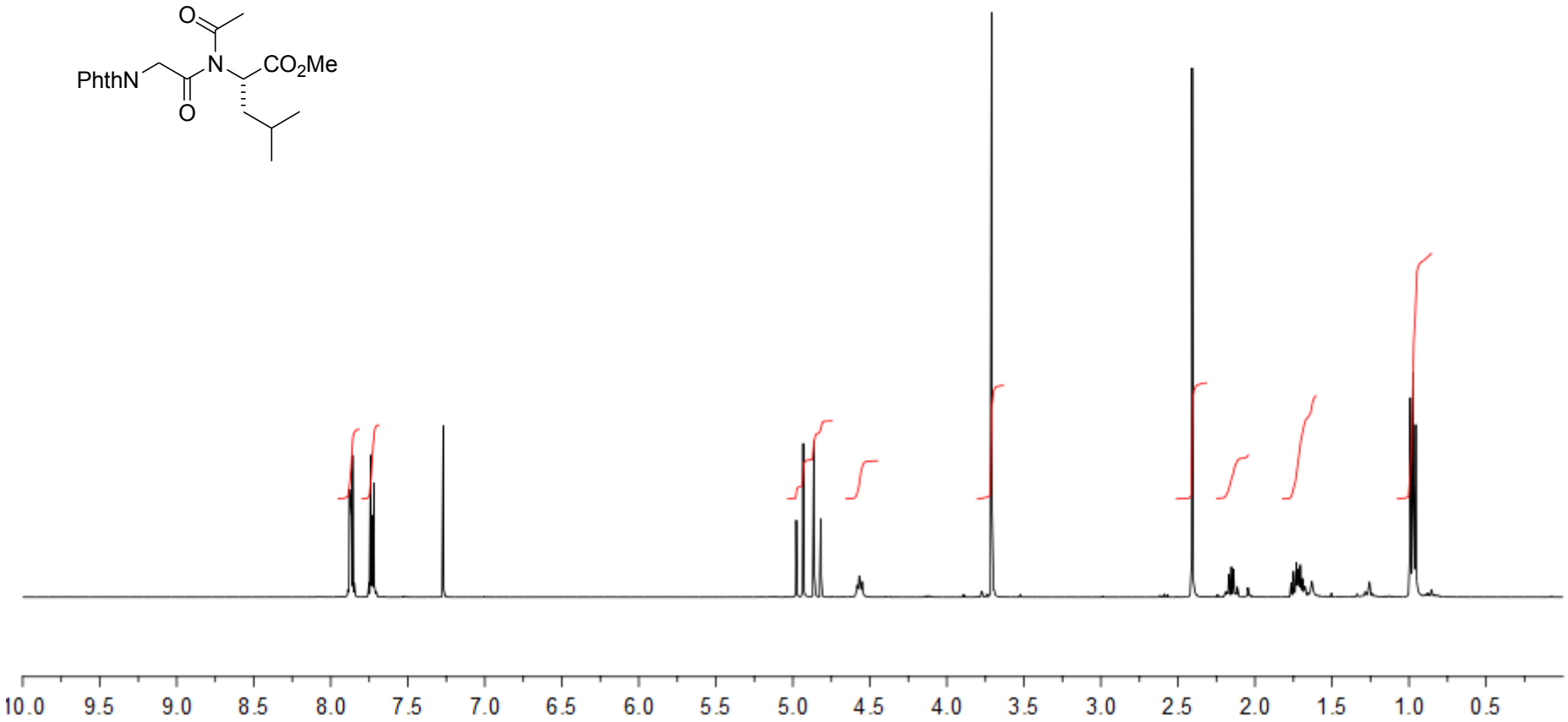
Compound 10GV (400 MHz, $CDCl_3$)



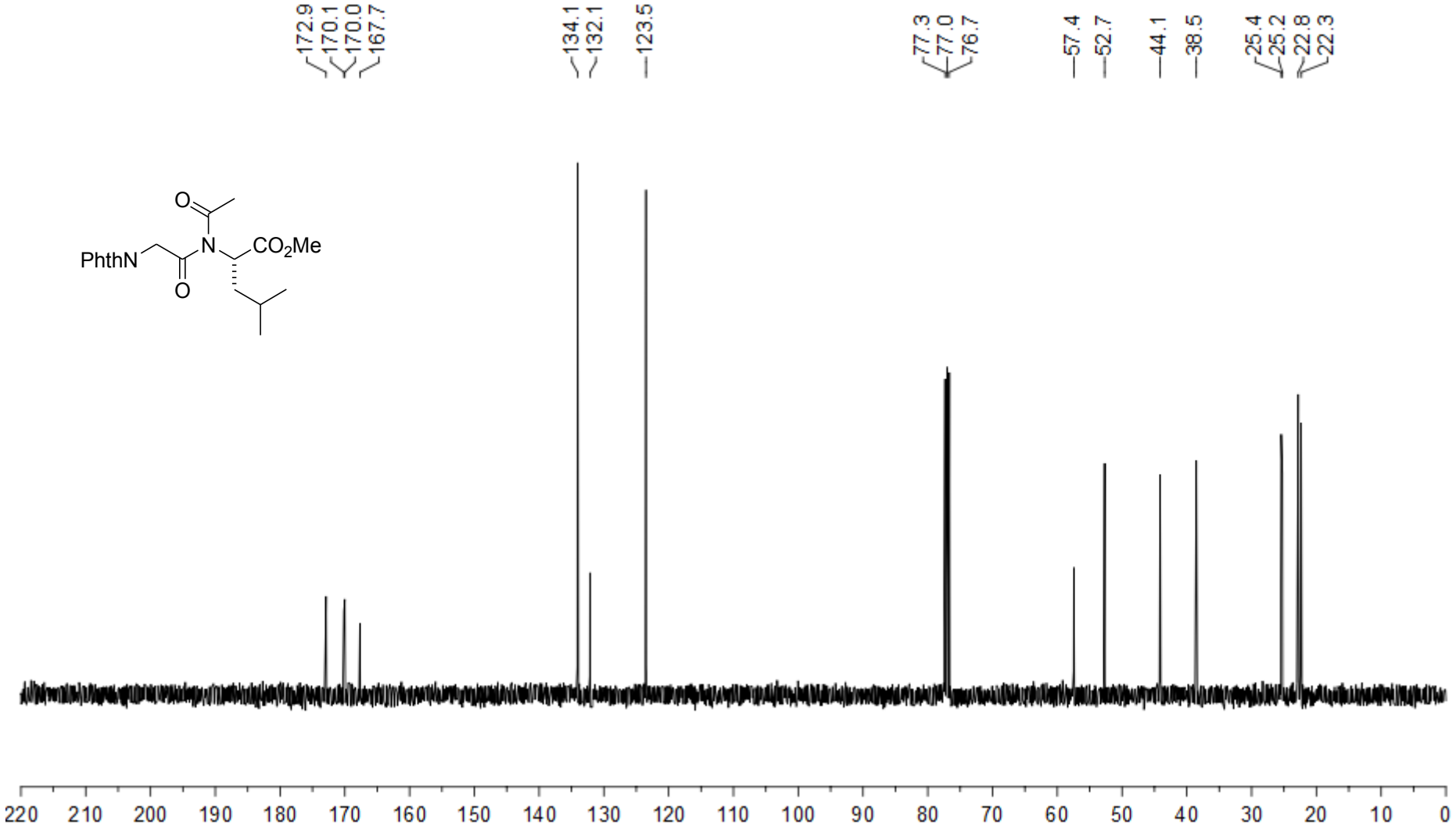
Compound 10GV (100 MHz, $CDCl_3$)



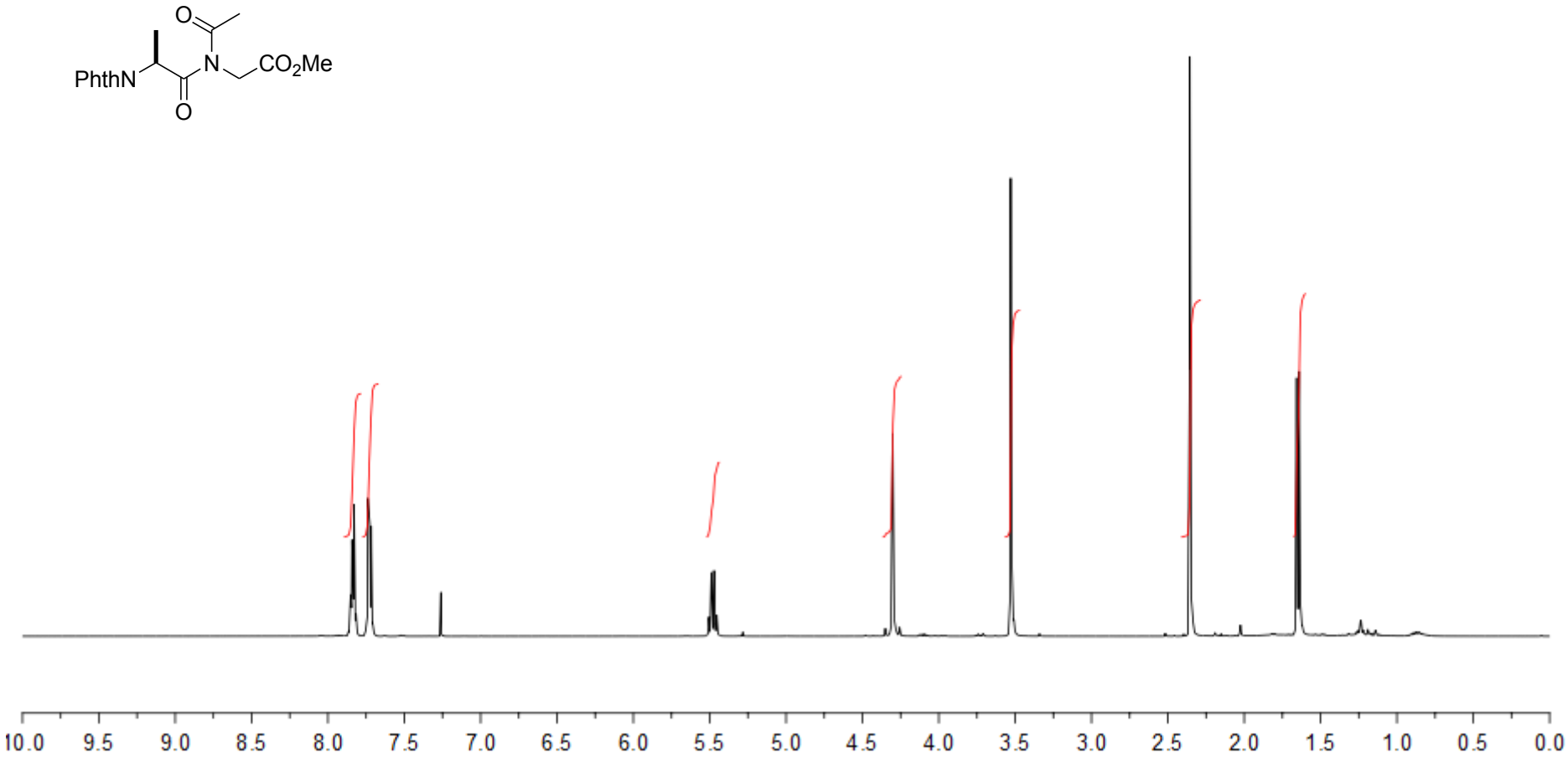
Compound 10GL (400 MHz, $CDCl_3$)



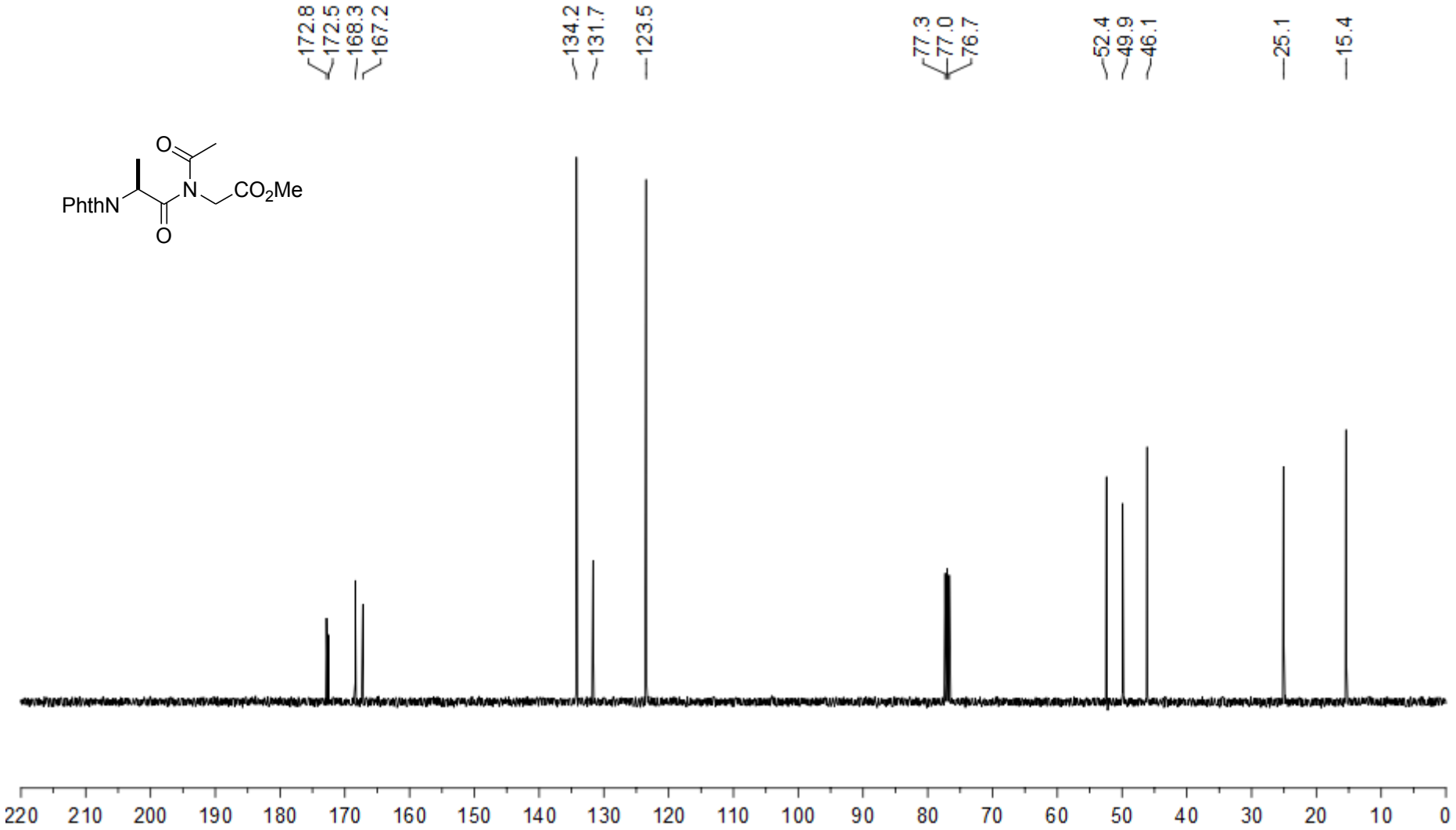
Compound 10GL (100 MHz, $CDCl_3$)



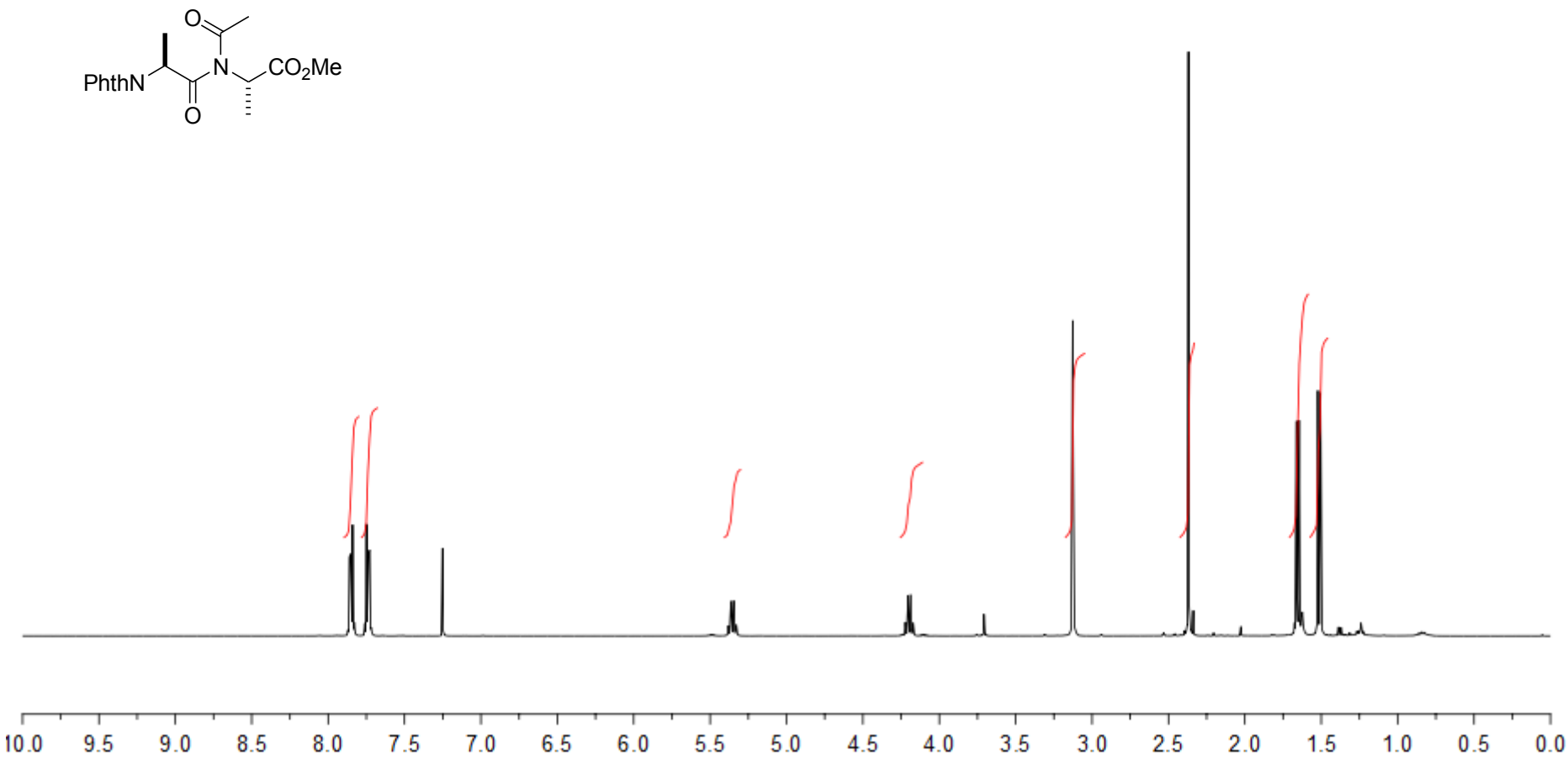
Compound AG (400 MHz, $CDCl_3$)



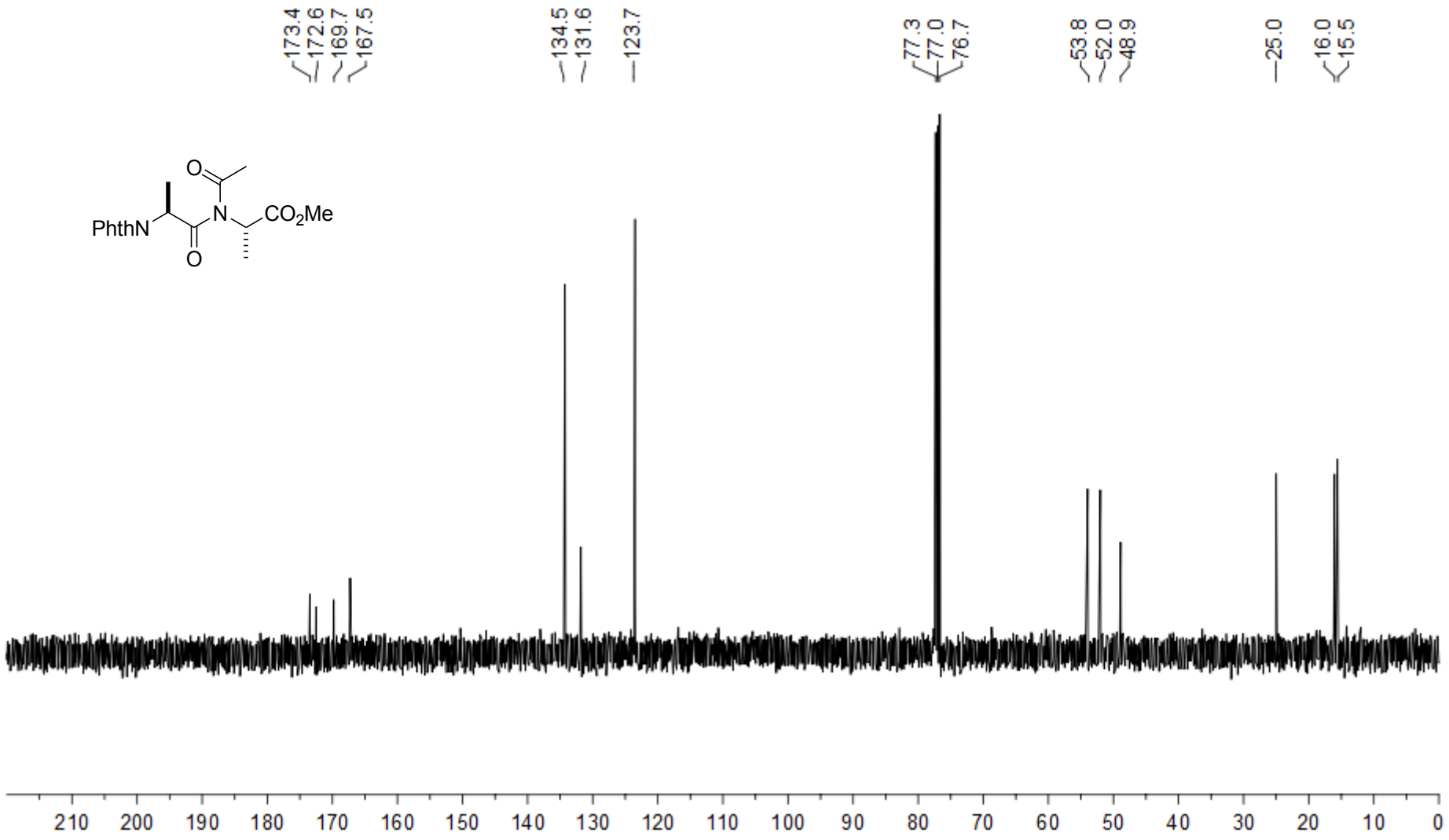
Compound AG (100 MHz, $CDCl_3$)



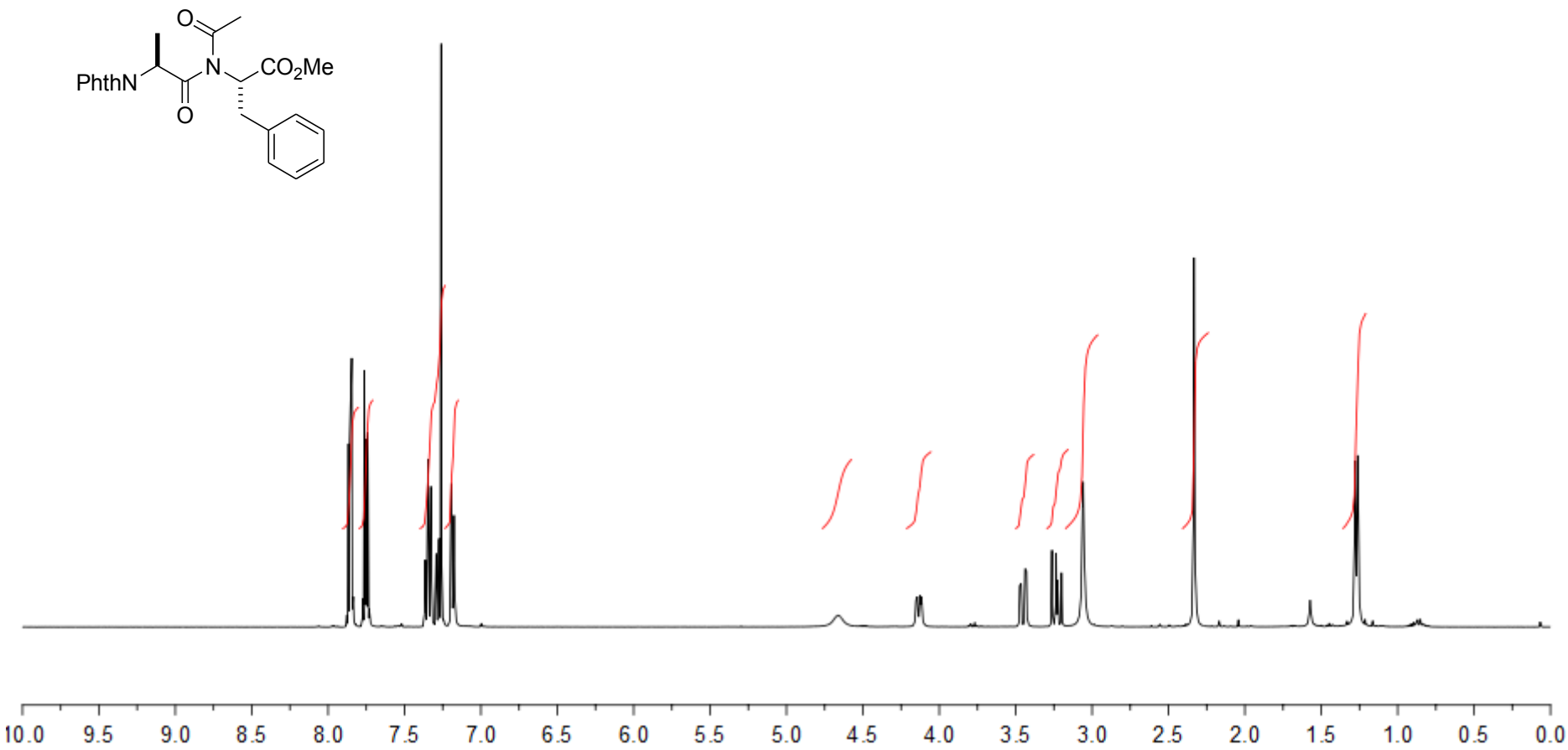
Compound AA (400 MHz, $CDCl_3$)



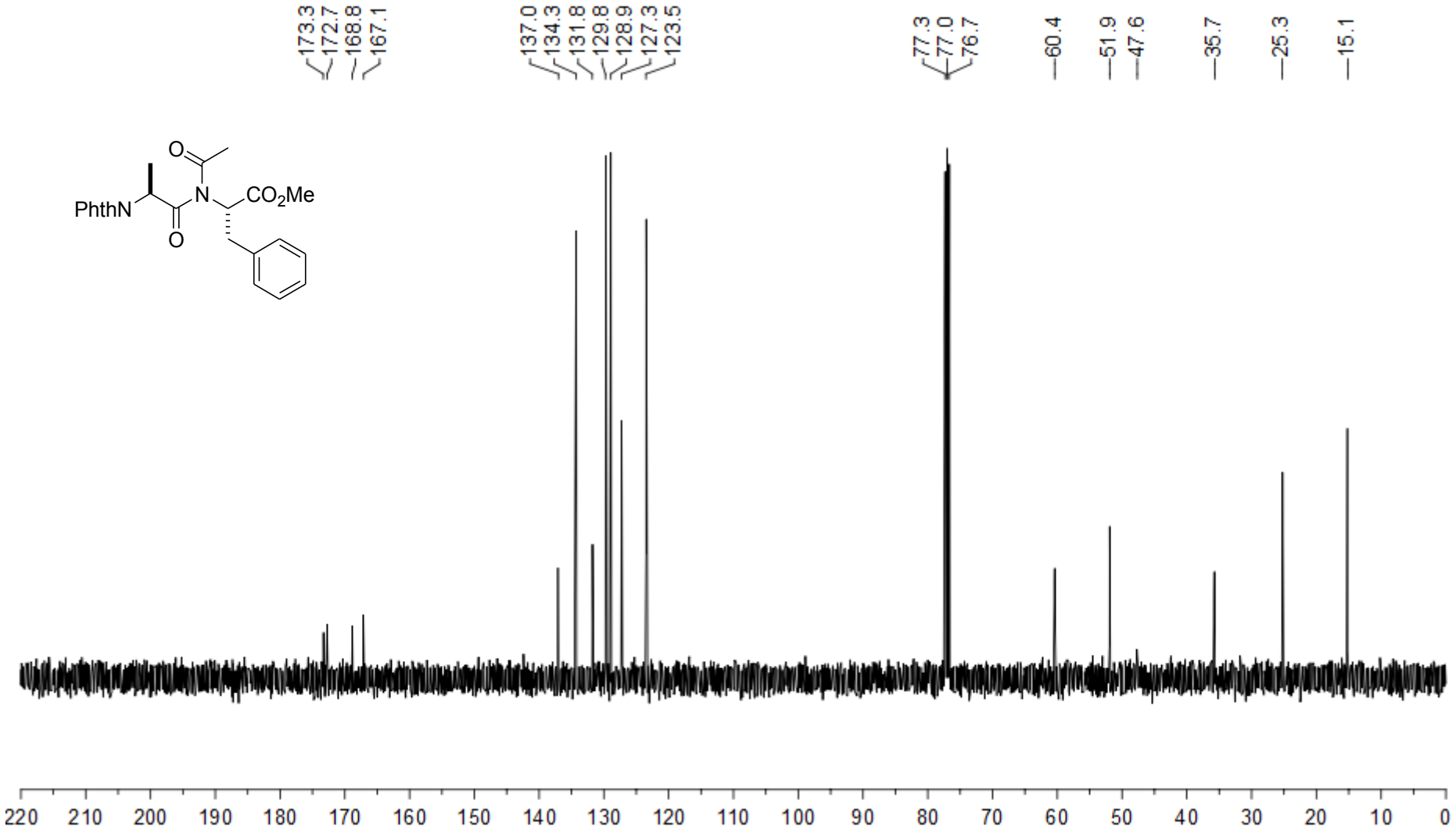
Compound AA (100 MHz, $CDCl_3$)



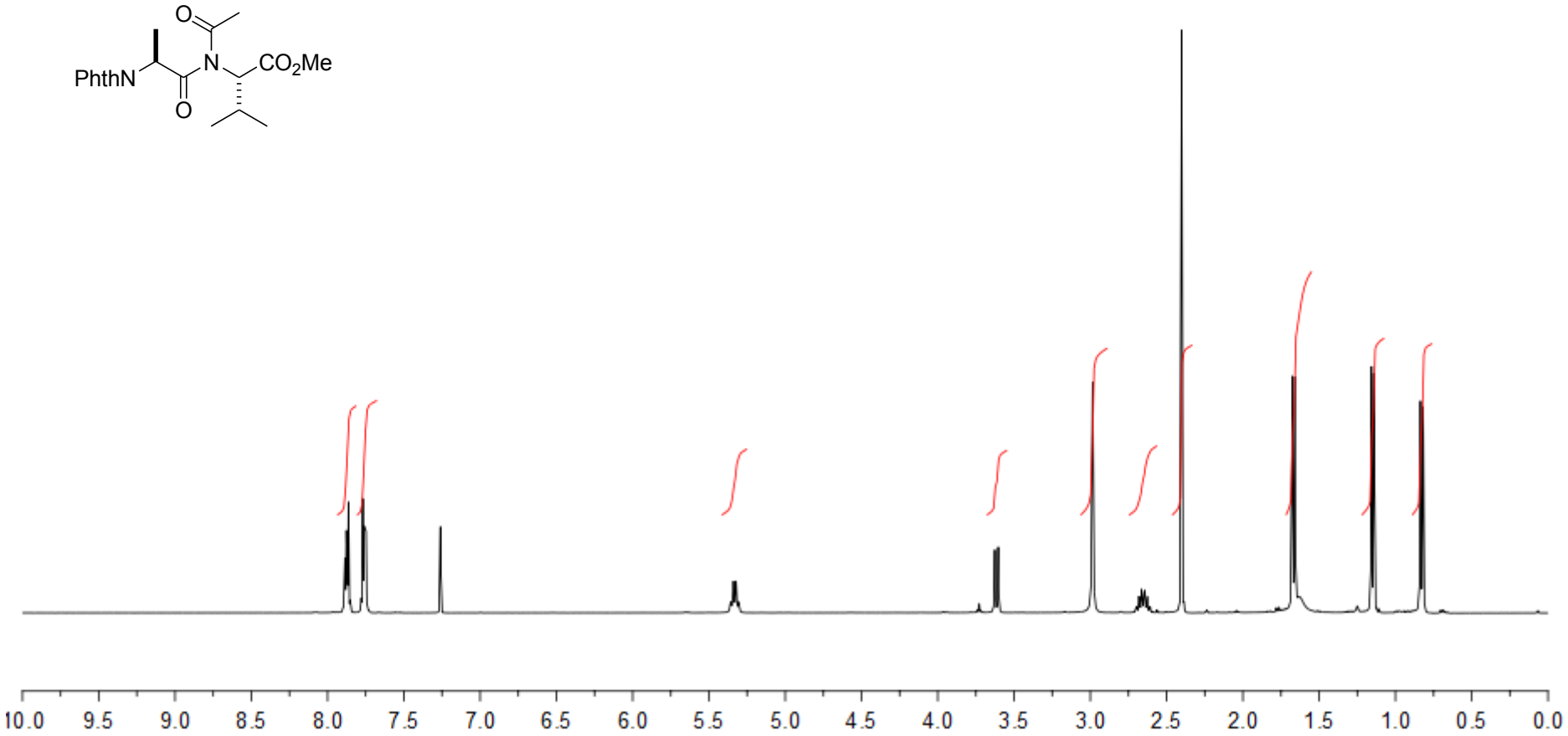
Compound AF (400 MHz, $CDCl_3$)



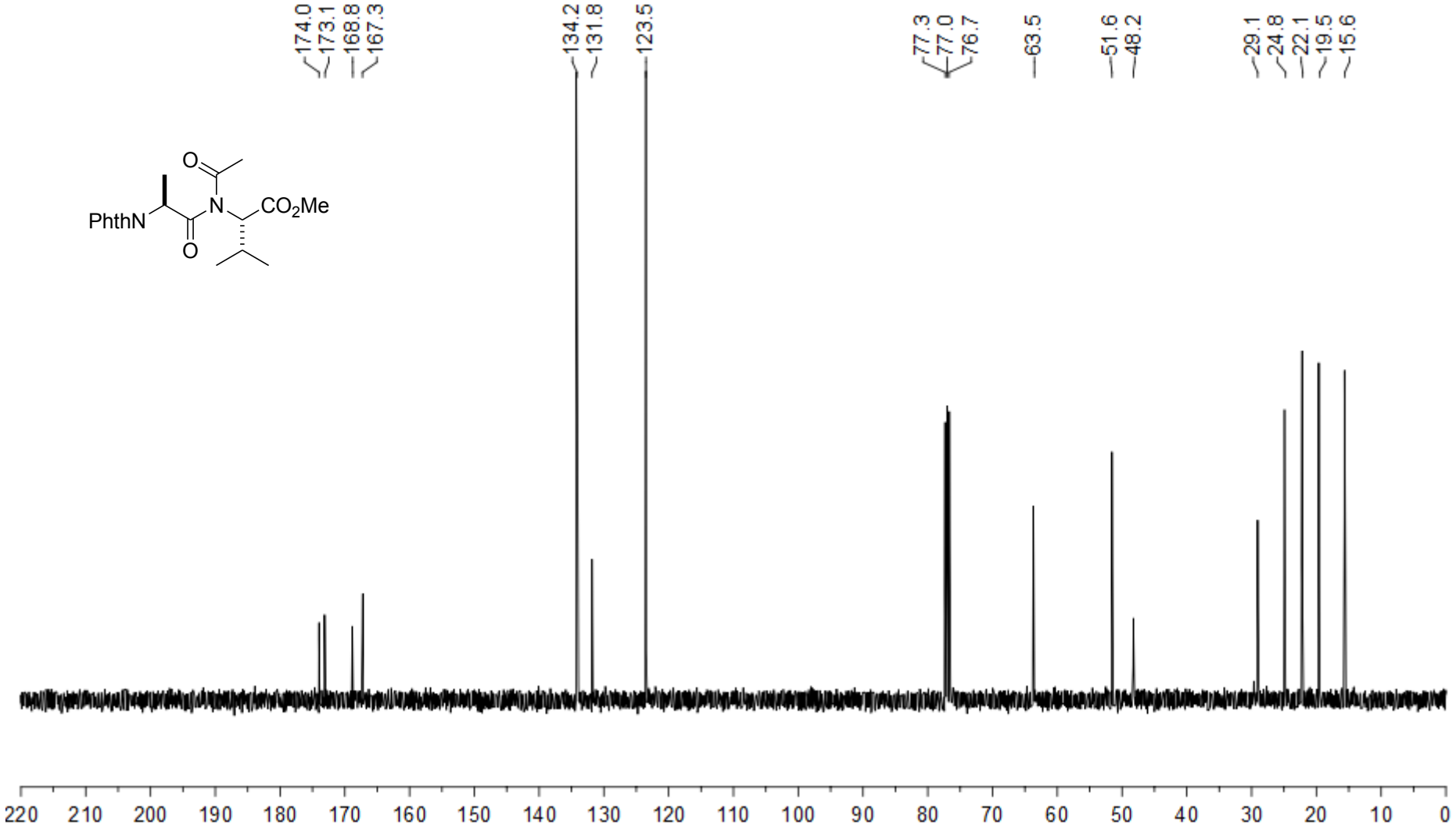
Compound AF (100 MHz, $CDCl_3$)



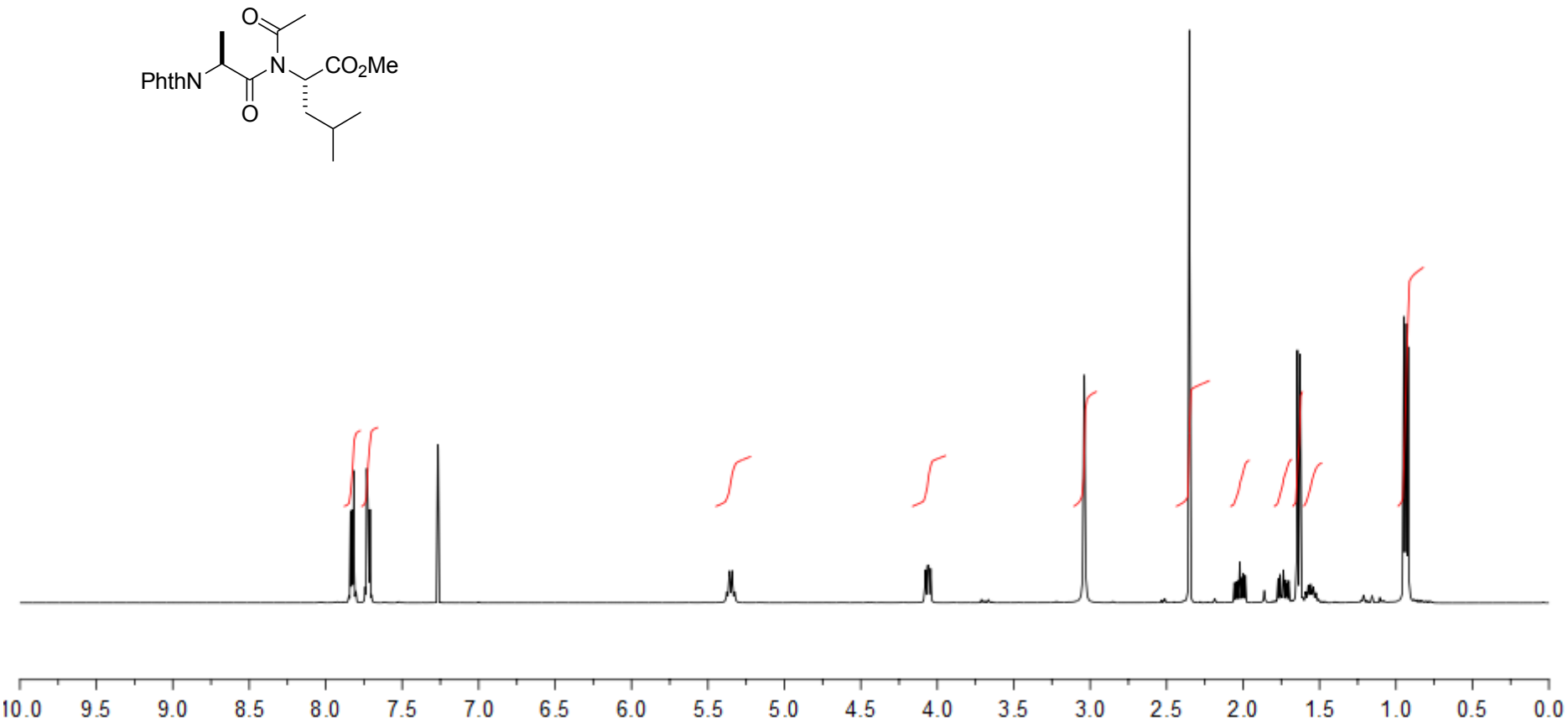
Compound AV (400 MHz, $CDCl_3$)



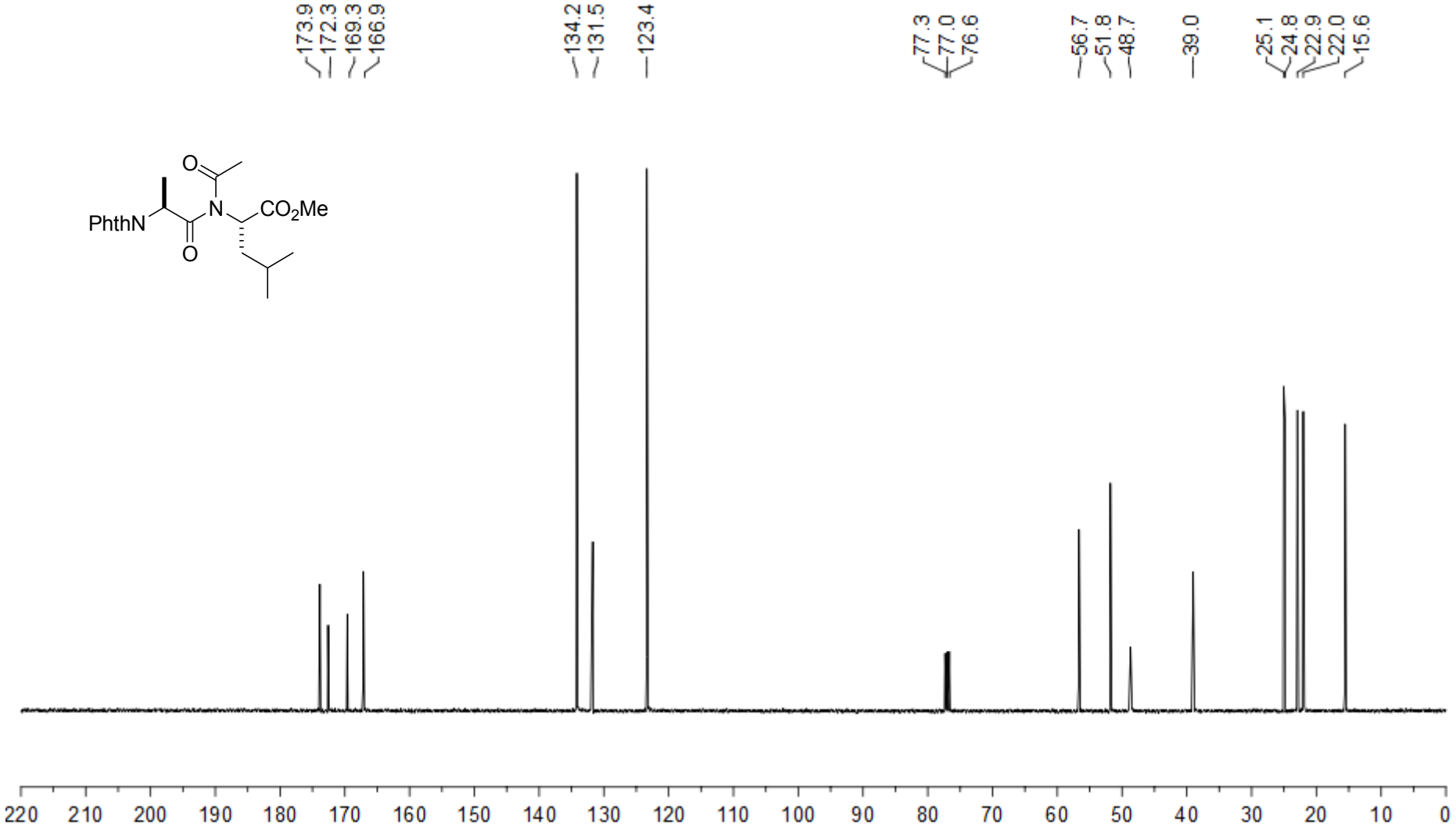
Compound AV (100 MHz, $CDCl_3$)



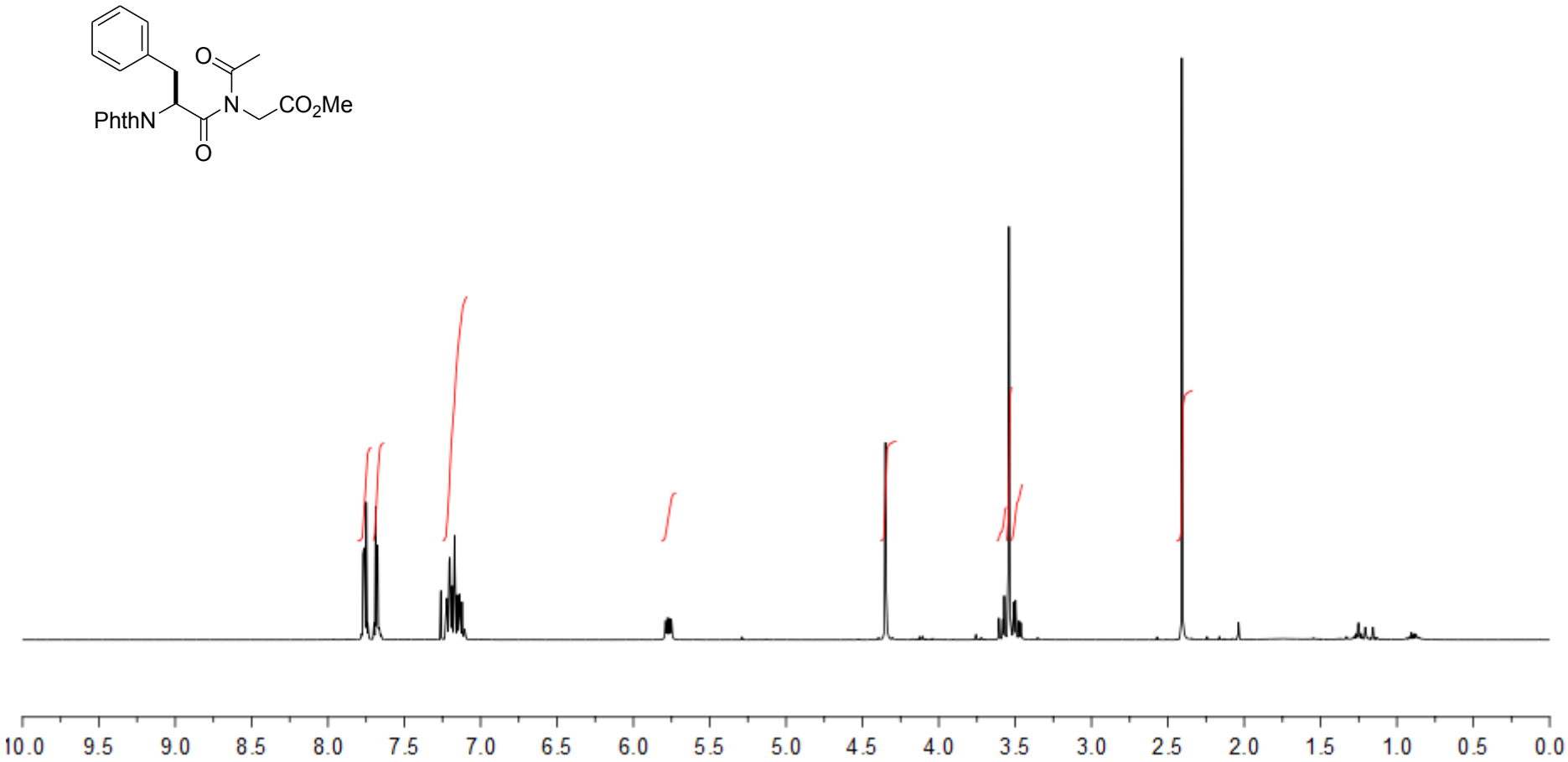
Compound AL (400 MHz, $CDCl_3$)



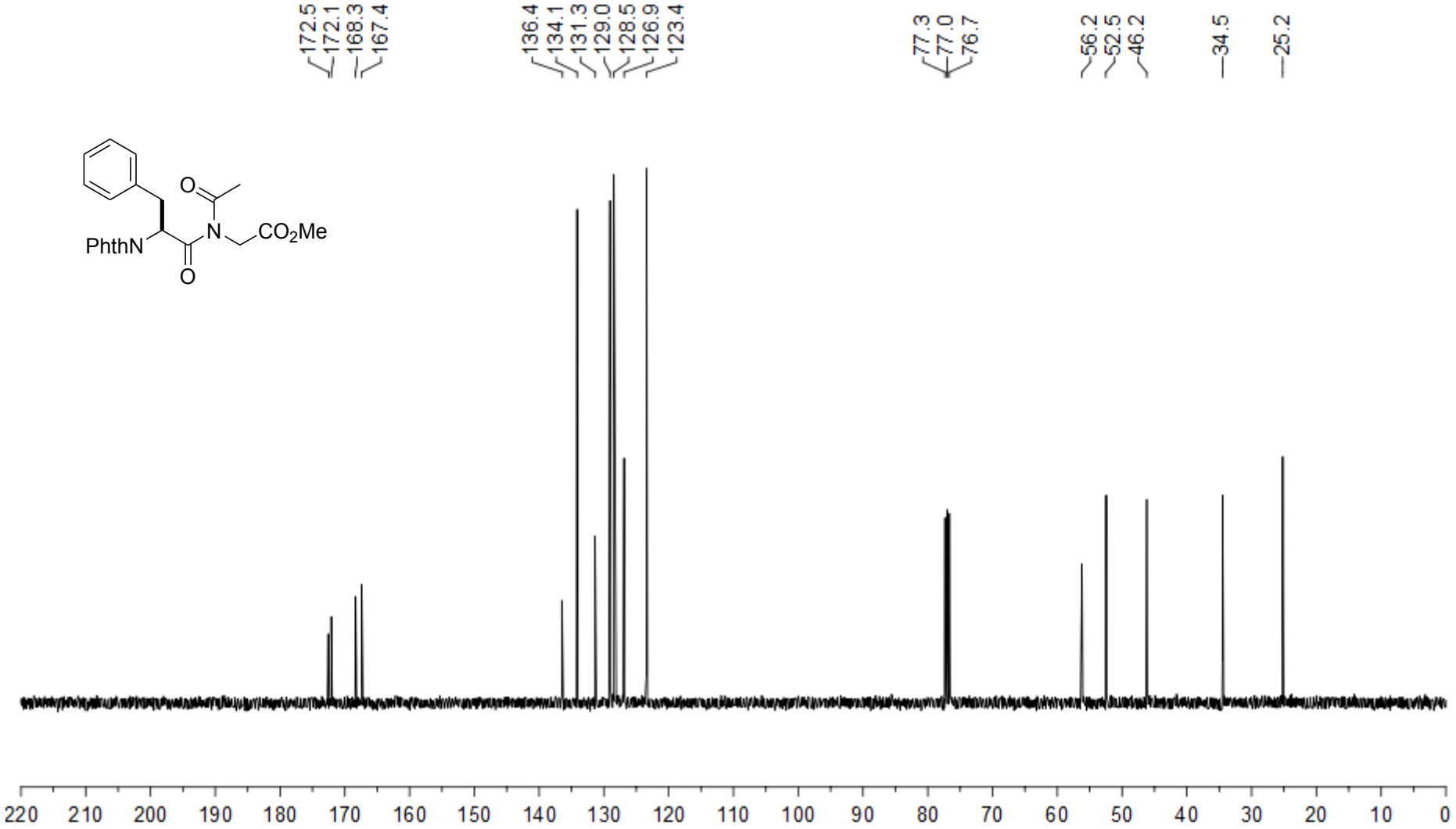
Compound AL (100 MHz, $CDCl_3$)



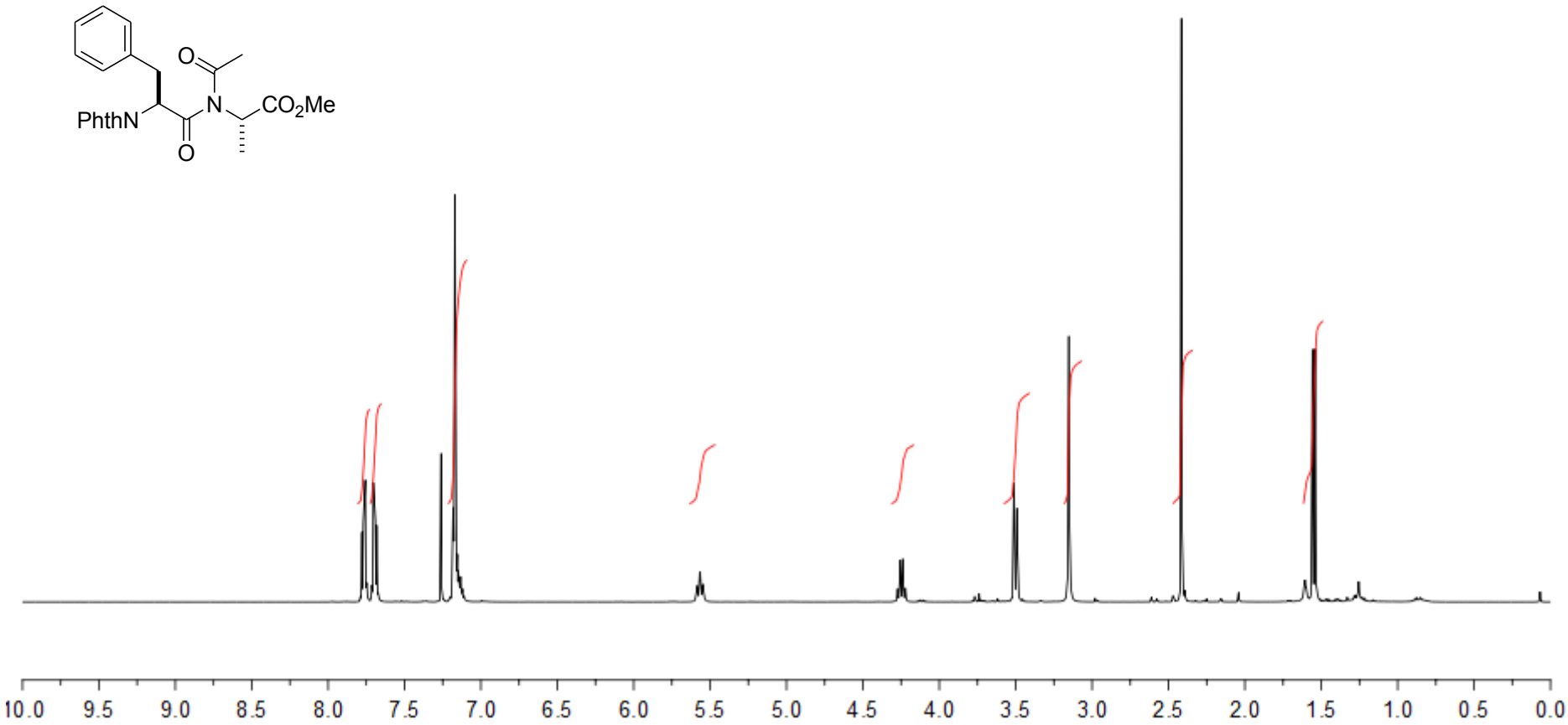
Compound 10FG (400 MHz, $CDCl_3$)



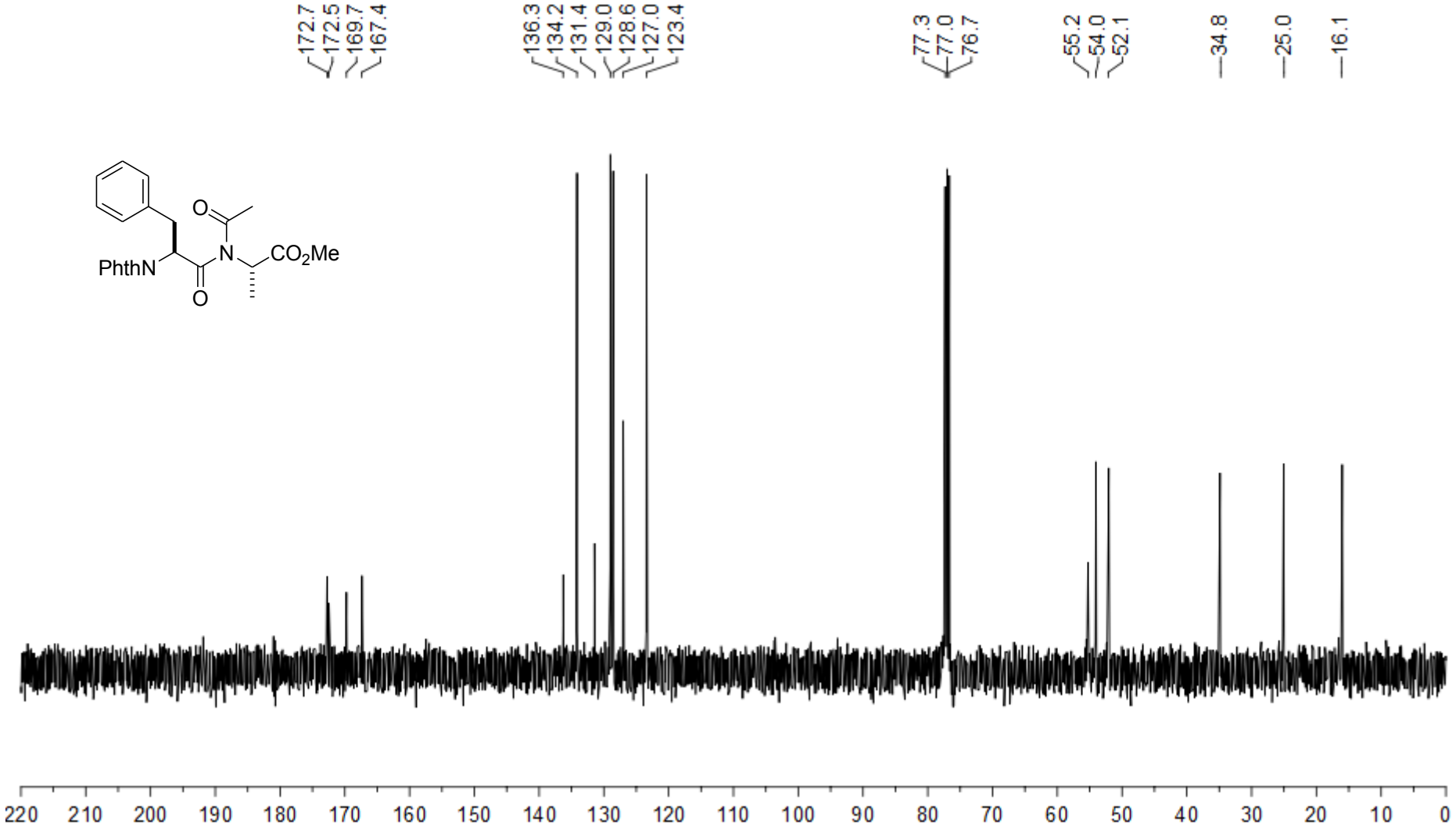
Compound 10FG (100 MHz, $CDCl_3$)



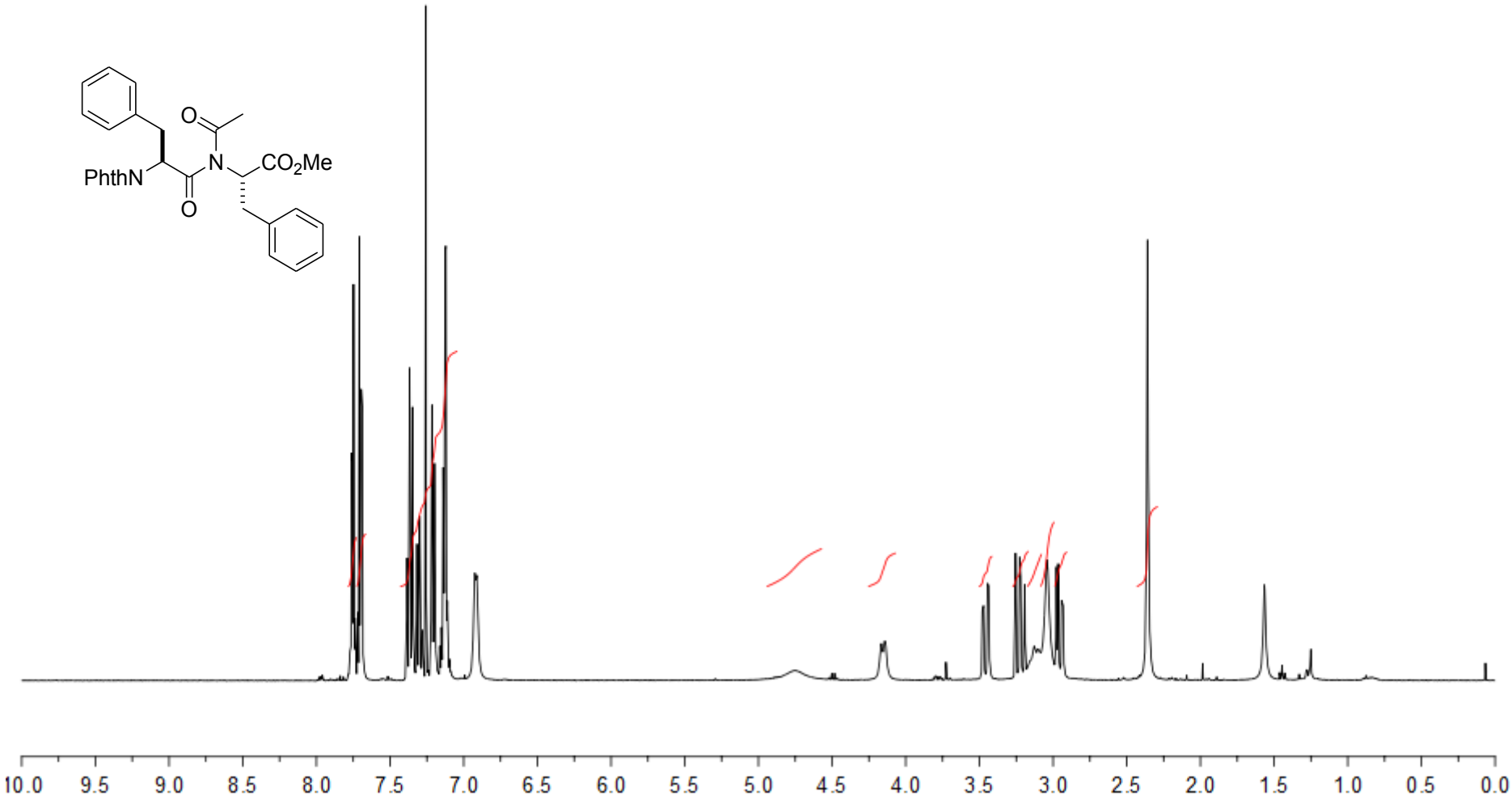
Compound 10FA (400 MHz, $CDCl_3$)



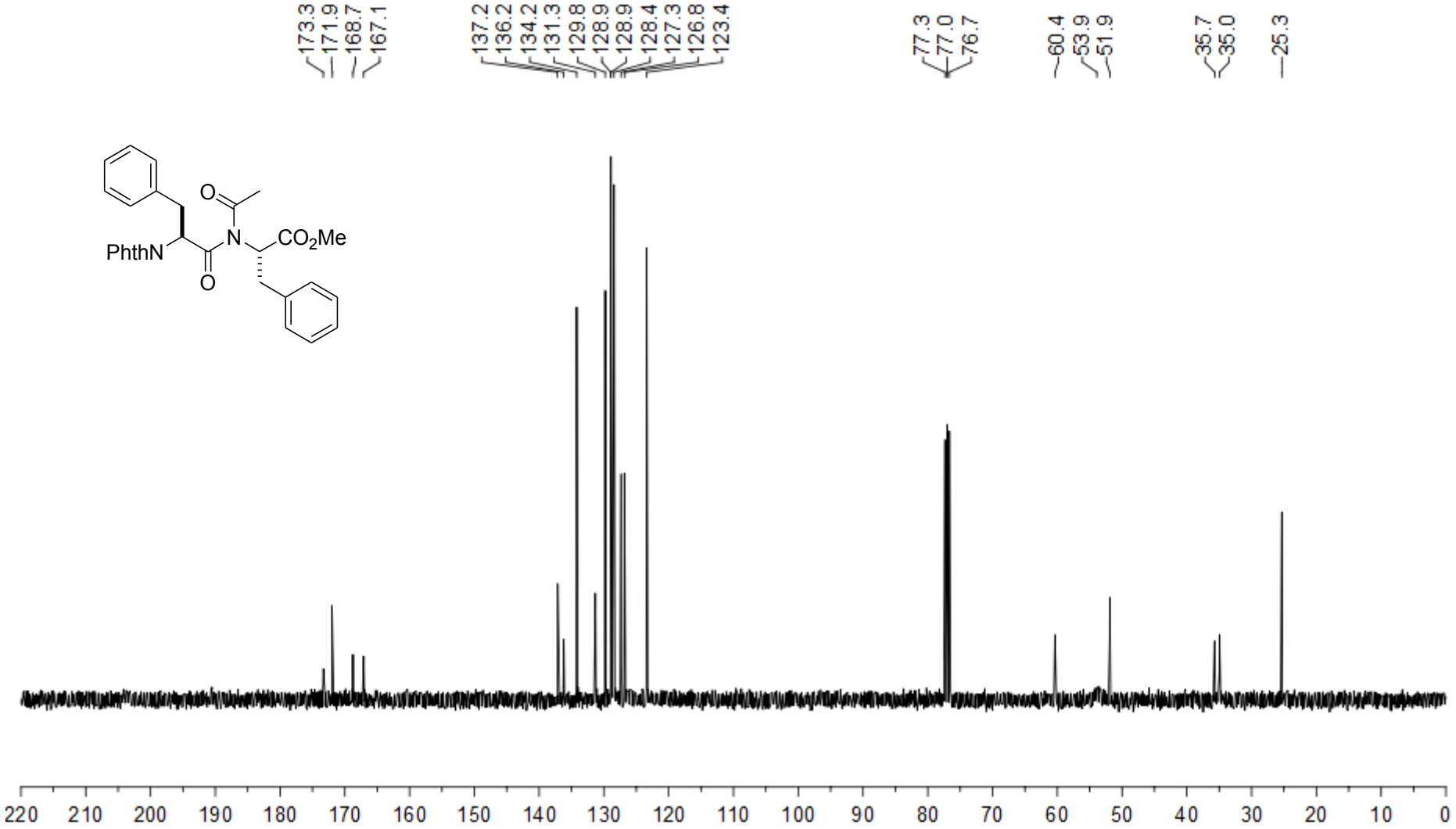
Compound 10FA (100 MHz, $CDCl_3$)



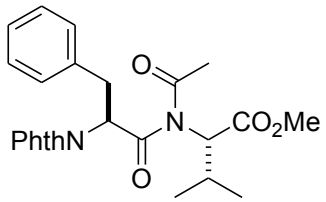
Compound 10FF (400 MHz, $CDCl_3$)

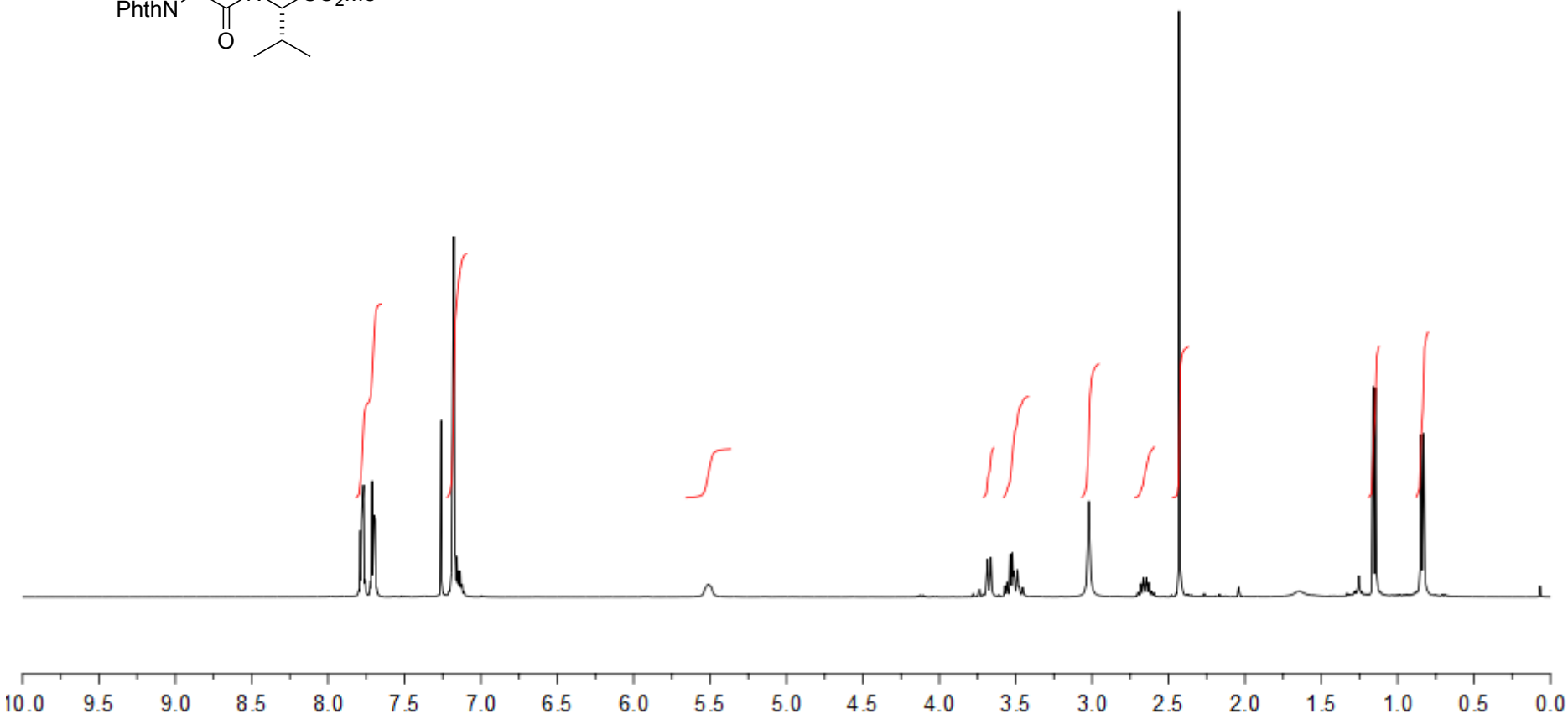


Compound 10FF (100 MHz, $CDCl_3$)

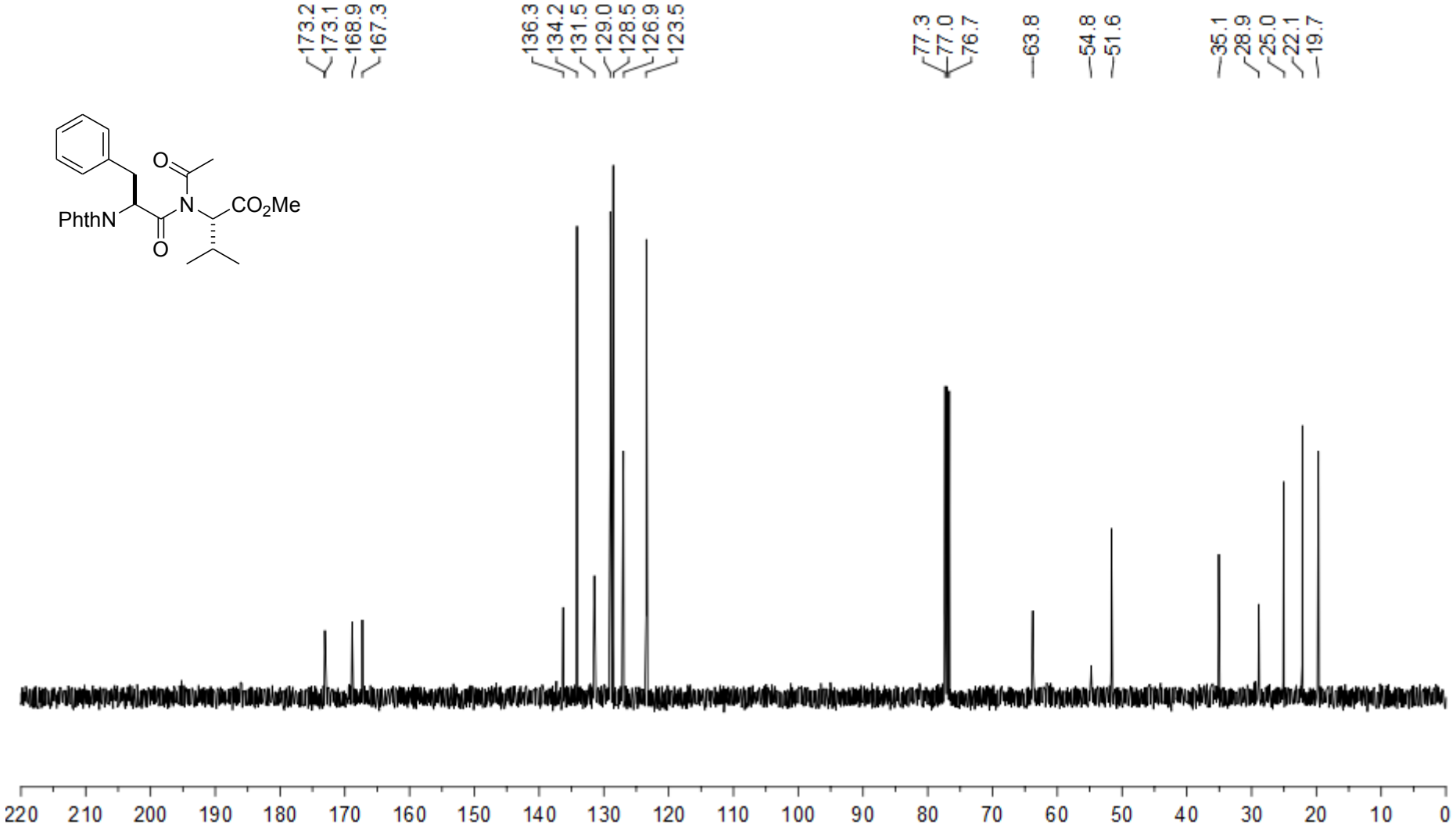


Compound 10FV (400 MHz, $CDCl_3$)

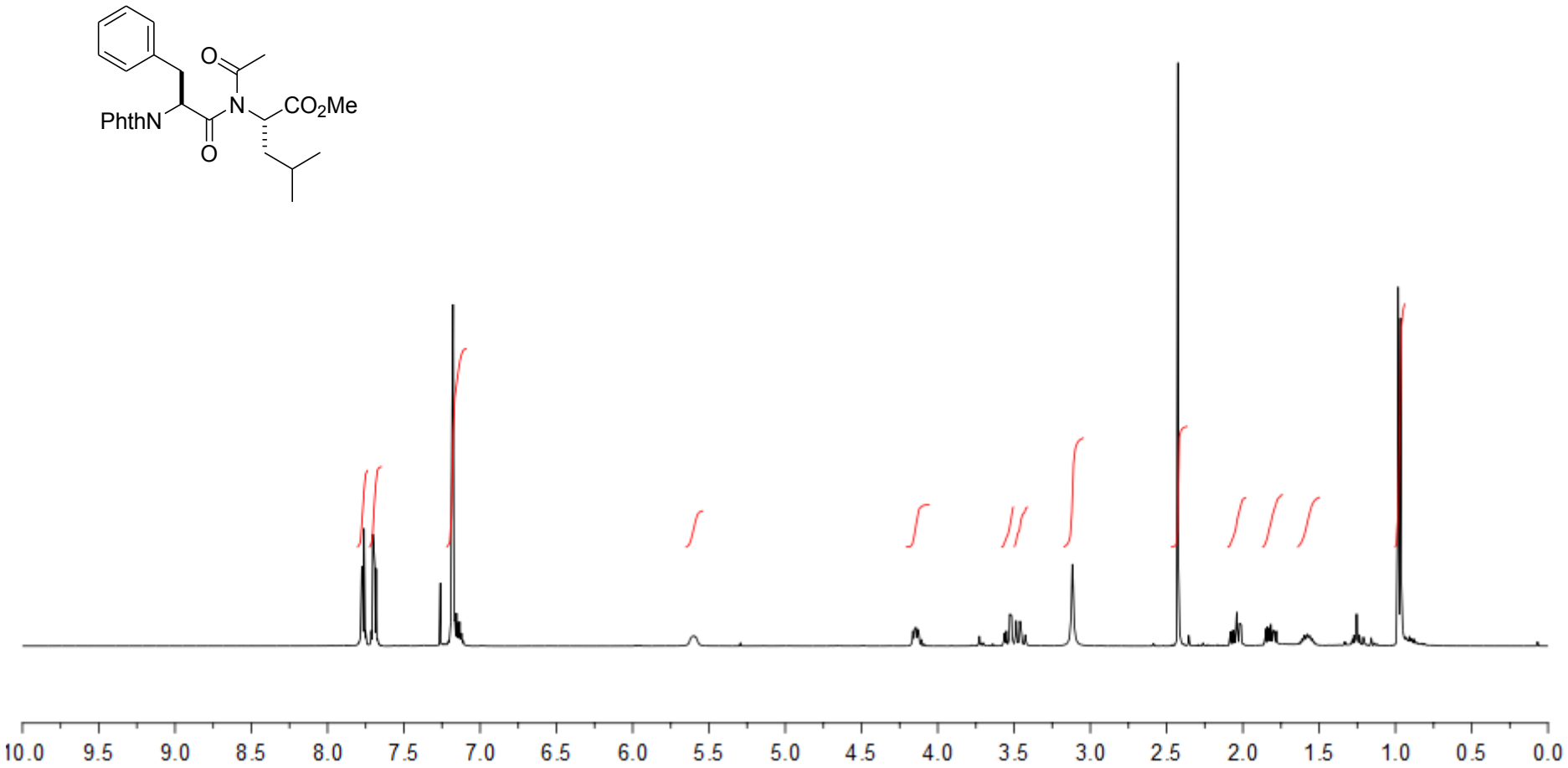




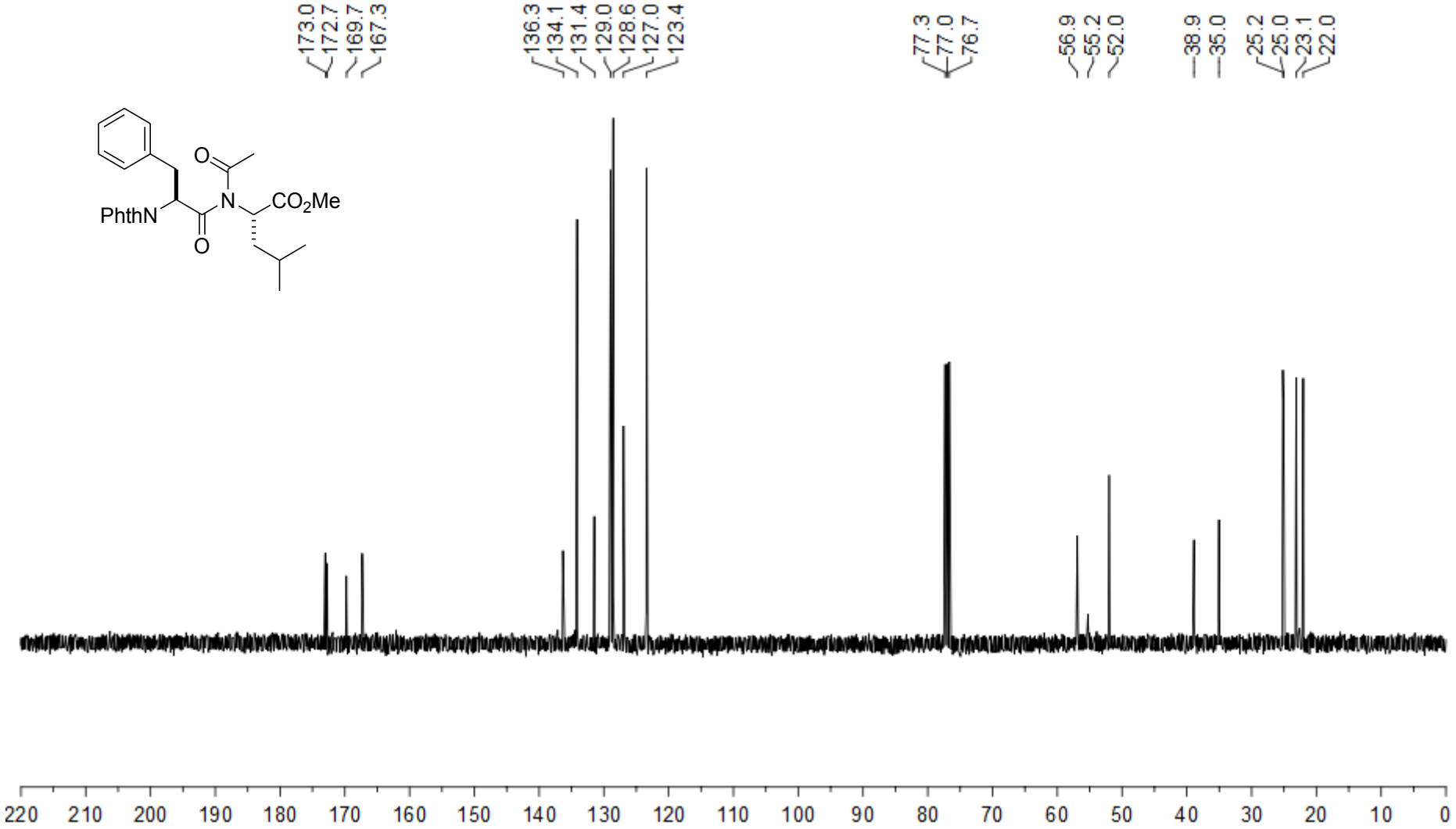
Compound 10FV (100 MHz, $CDCl_3$)



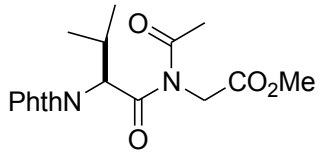
Compound 10FL (400 MHz, $CDCl_3$)

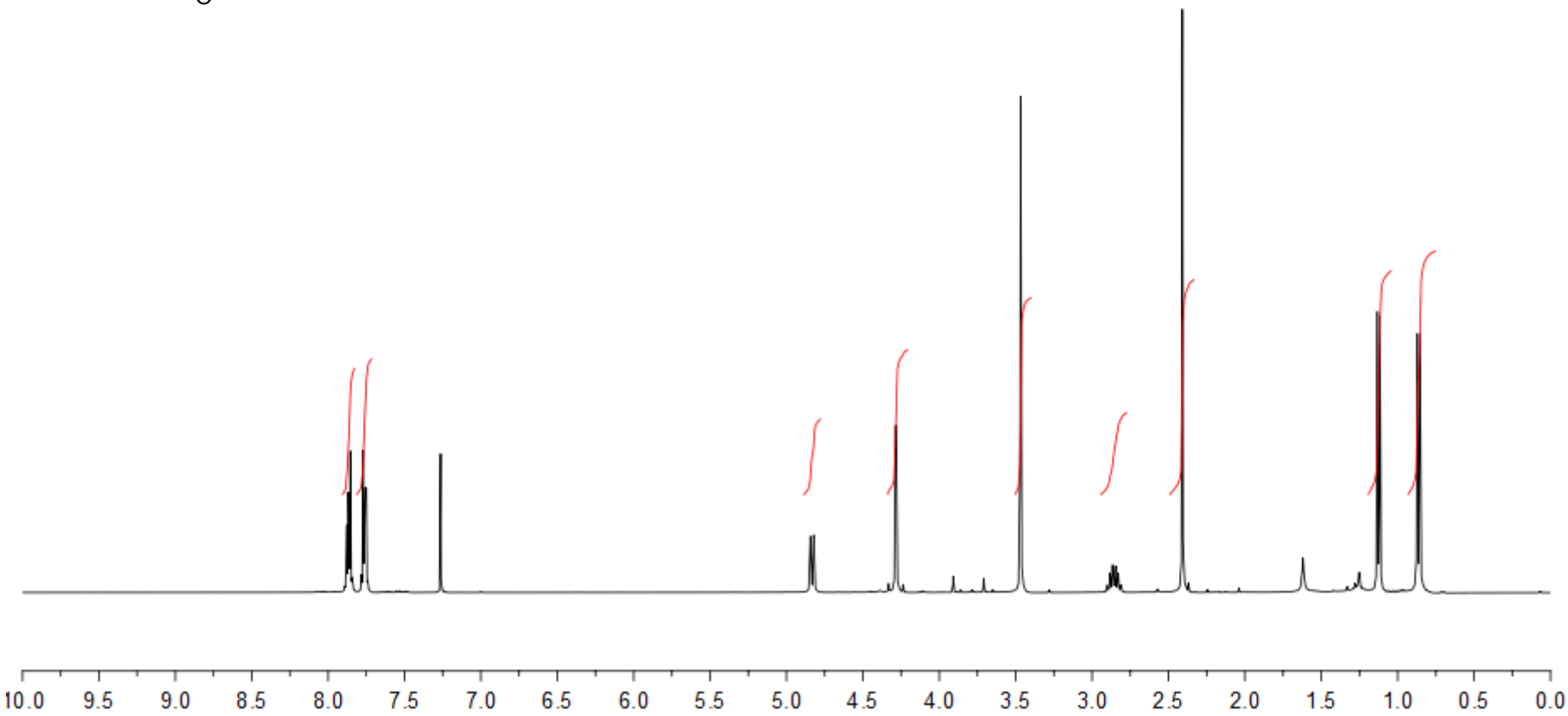


Compound 10FL (100 MHz, $CDCl_3$)

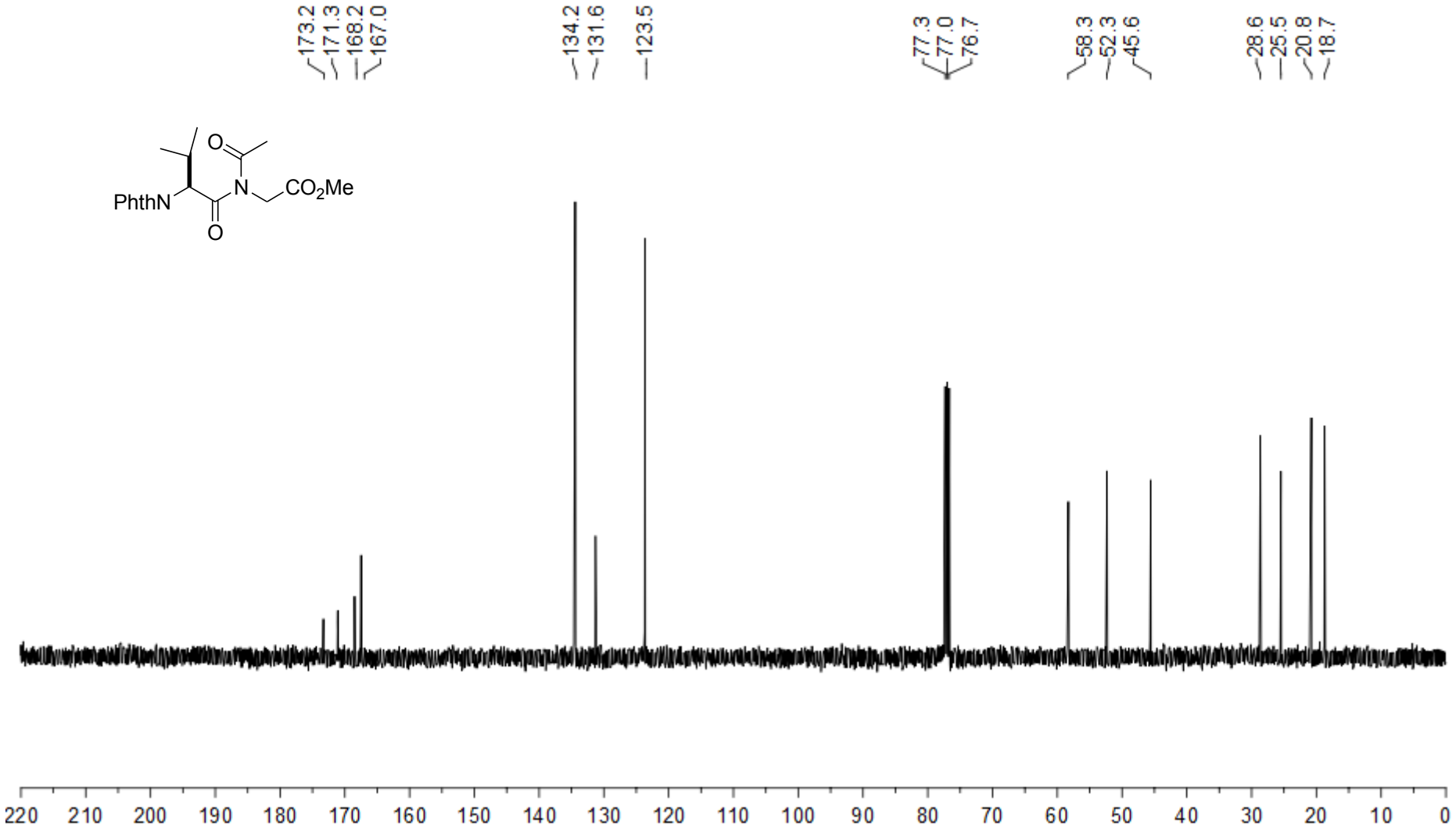


Compound 10VG (400 MHz, $CDCl_3$)

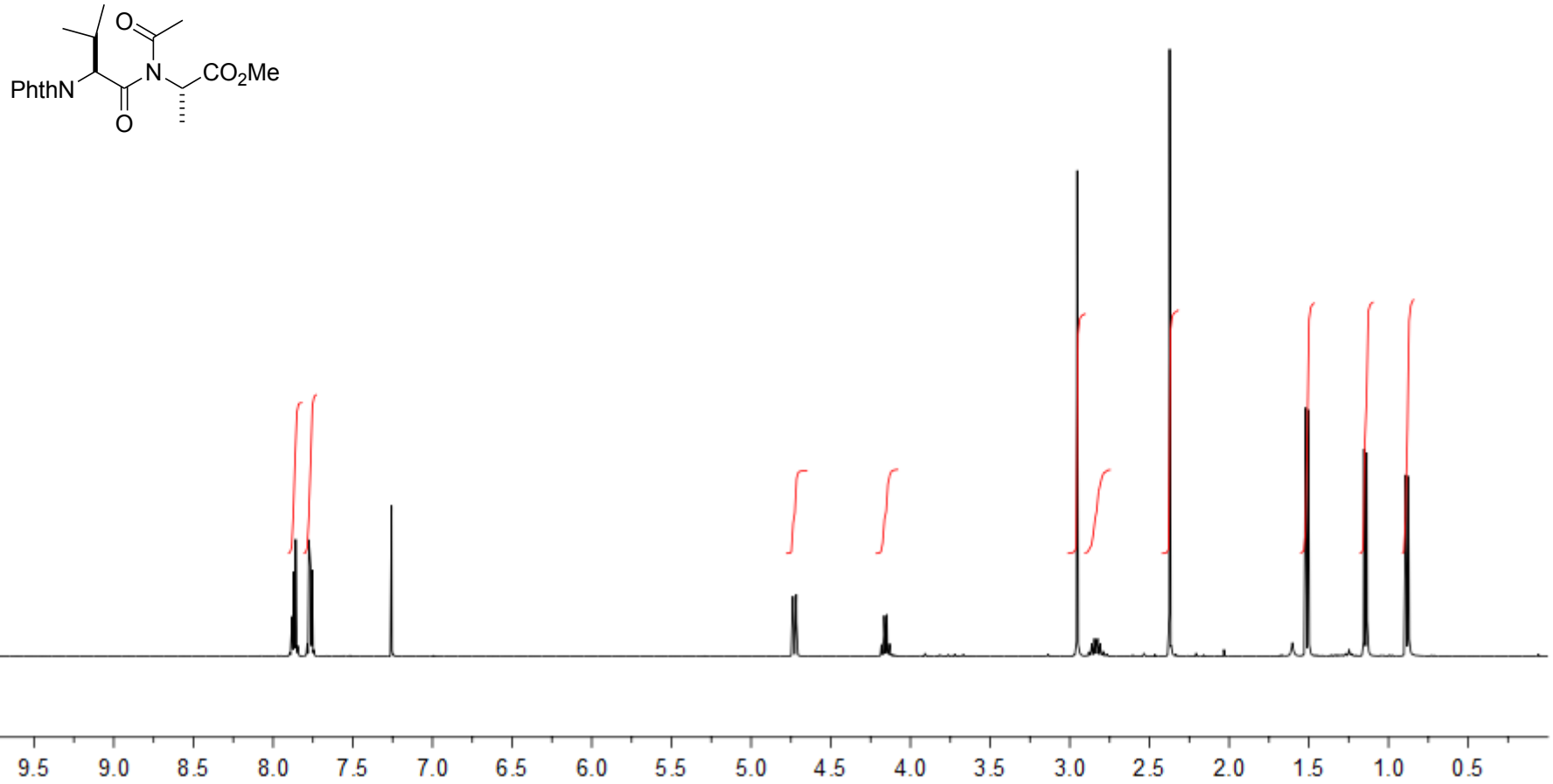




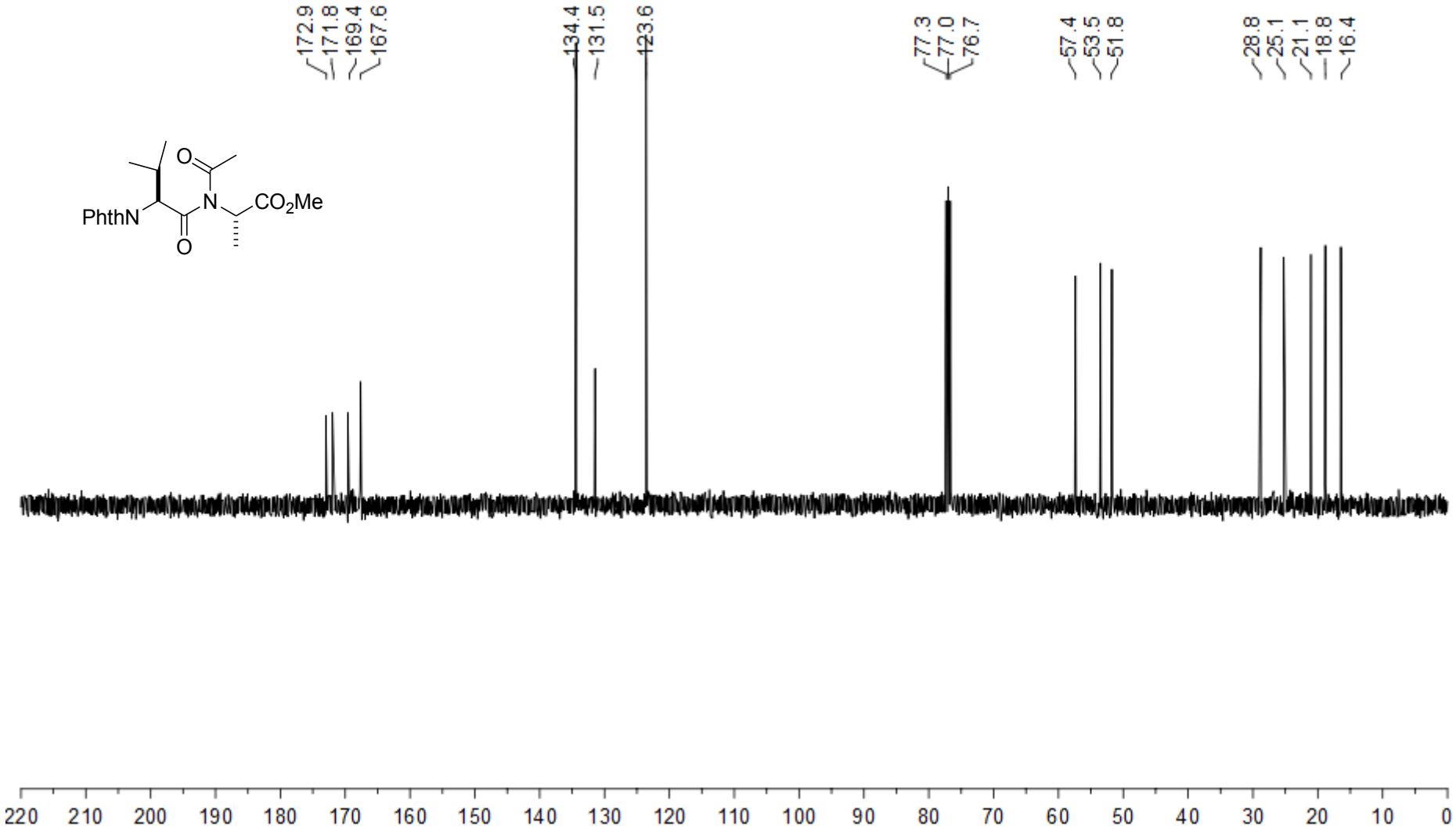
Compound 10VG (100 MHz, $CDCl_3$)



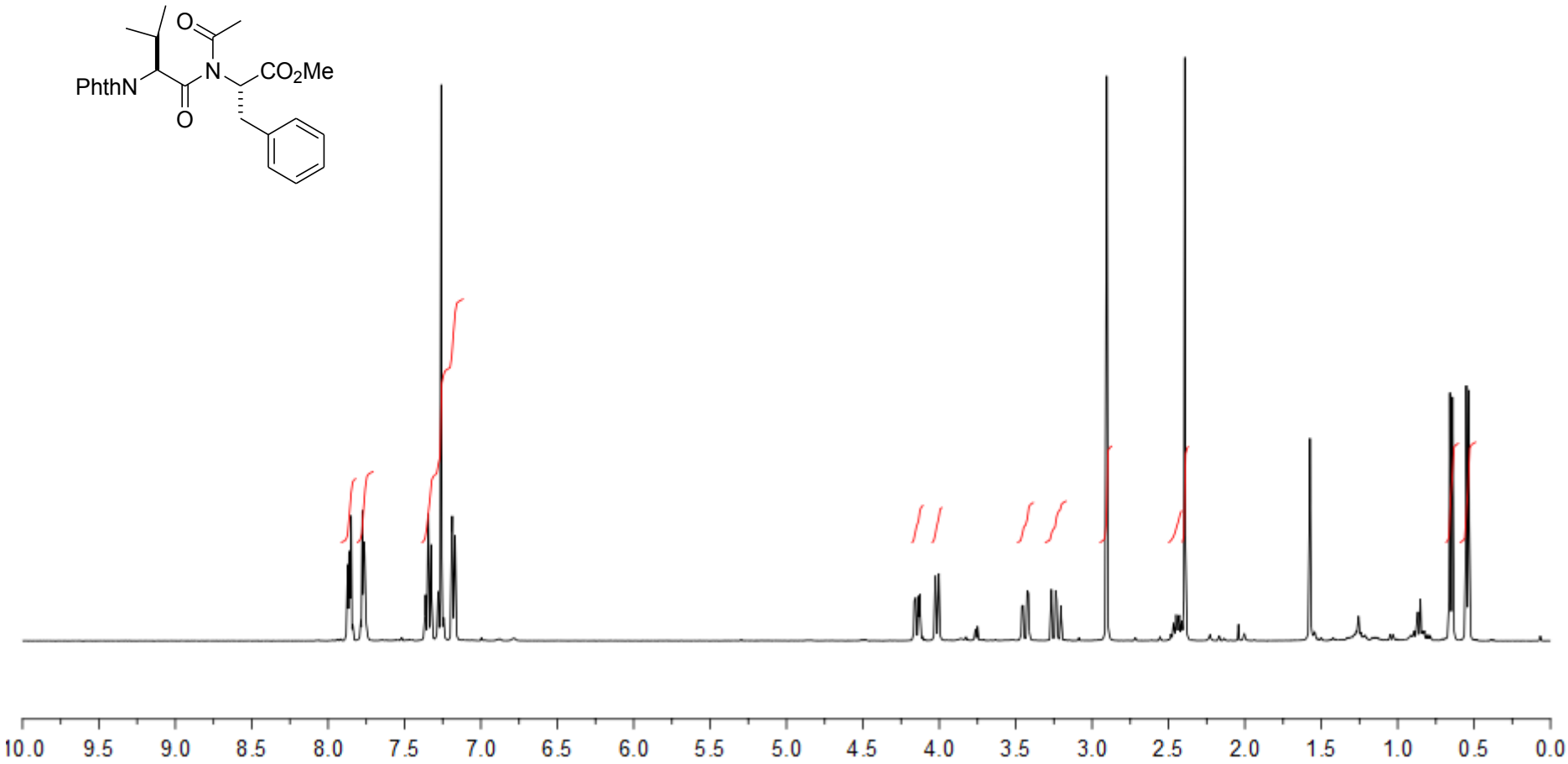
Compound 10VA (400 MHz, $CDCl_3$)



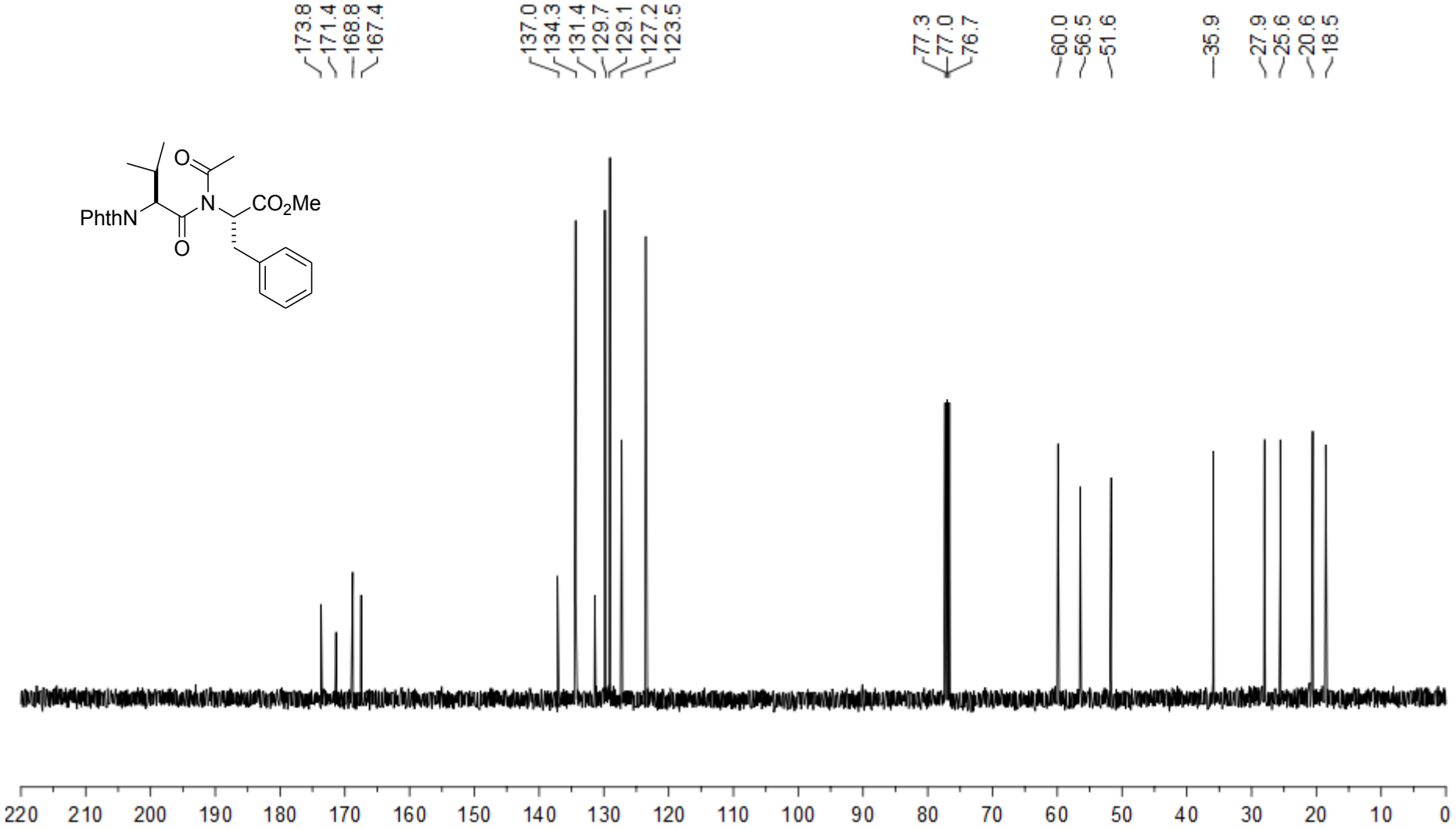
Compound 10VA (100 MHz, $CDCl_3$)



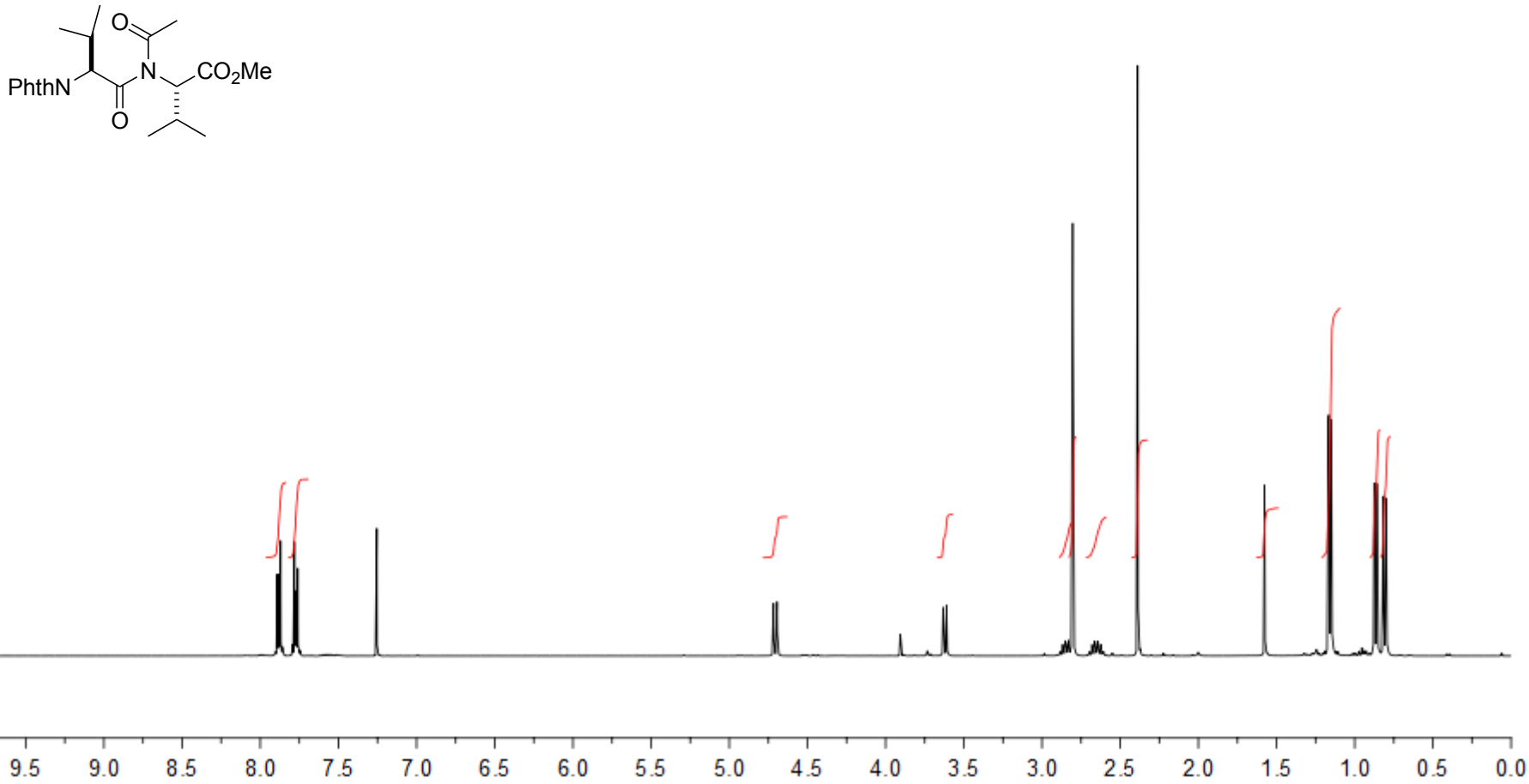
Compound 10VF (400 MHz, $CDCl_3$)



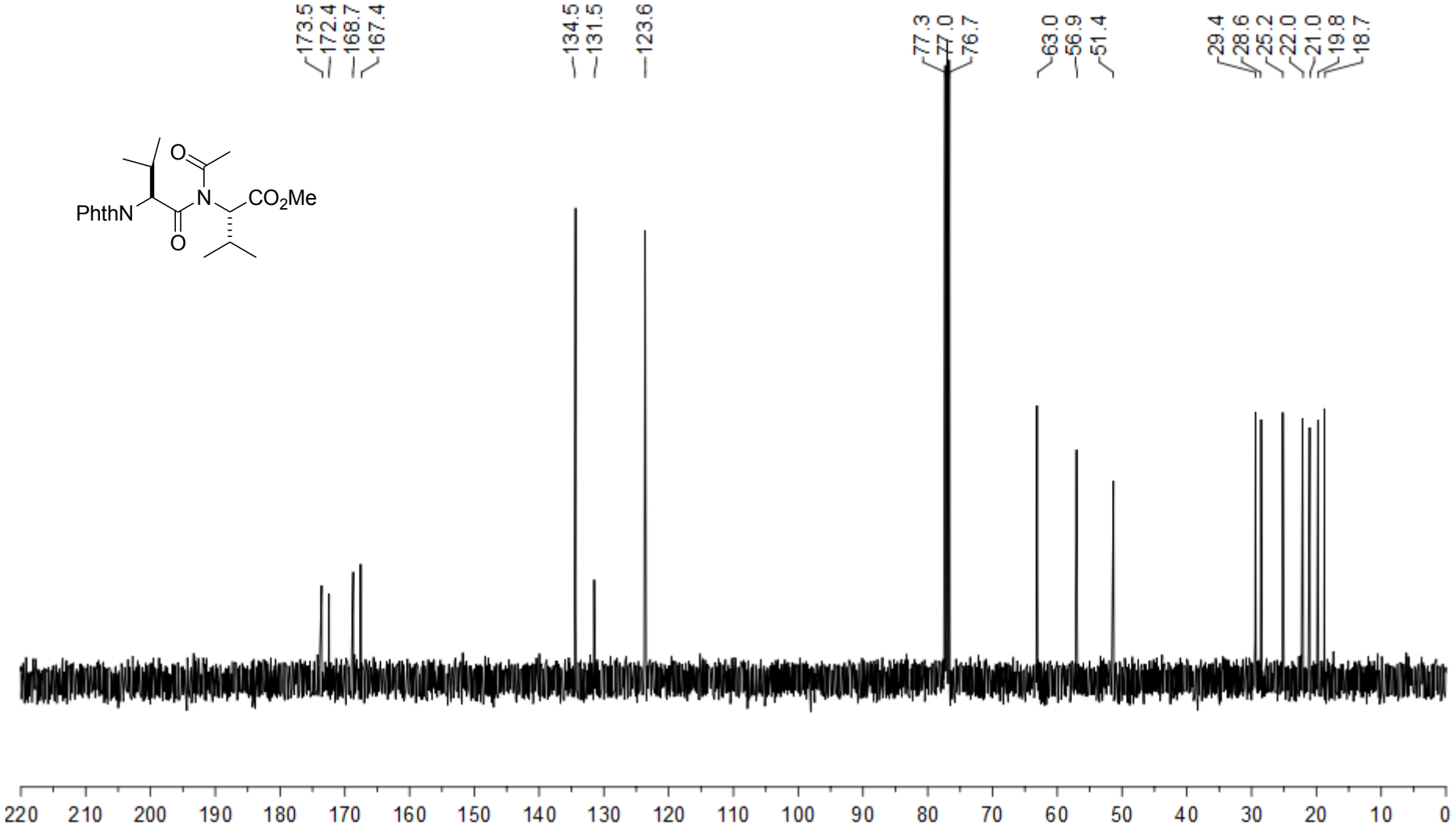
Compound 10VF (100 MHz, $CDCl_3$)



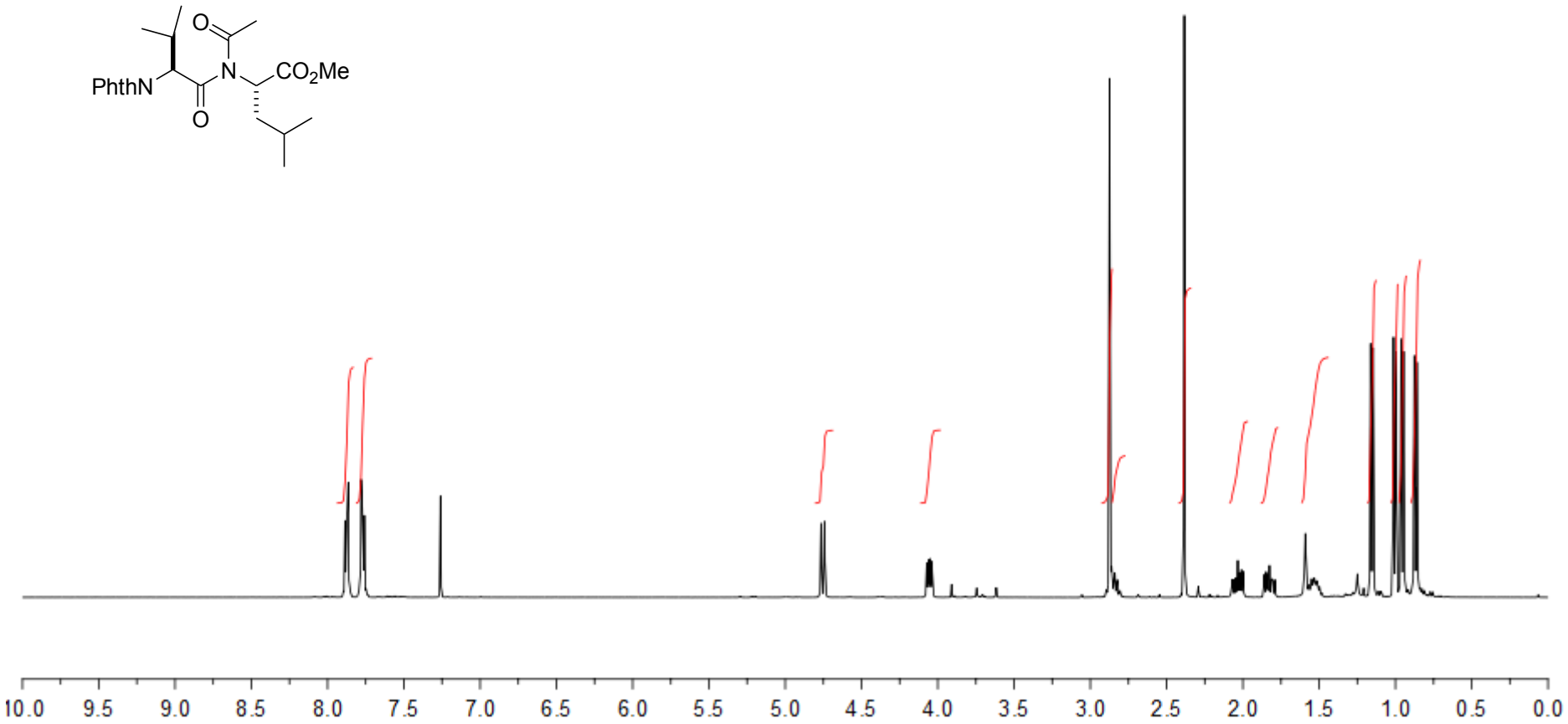
Compound 10VV (400 MHz, $CDCl_3$)



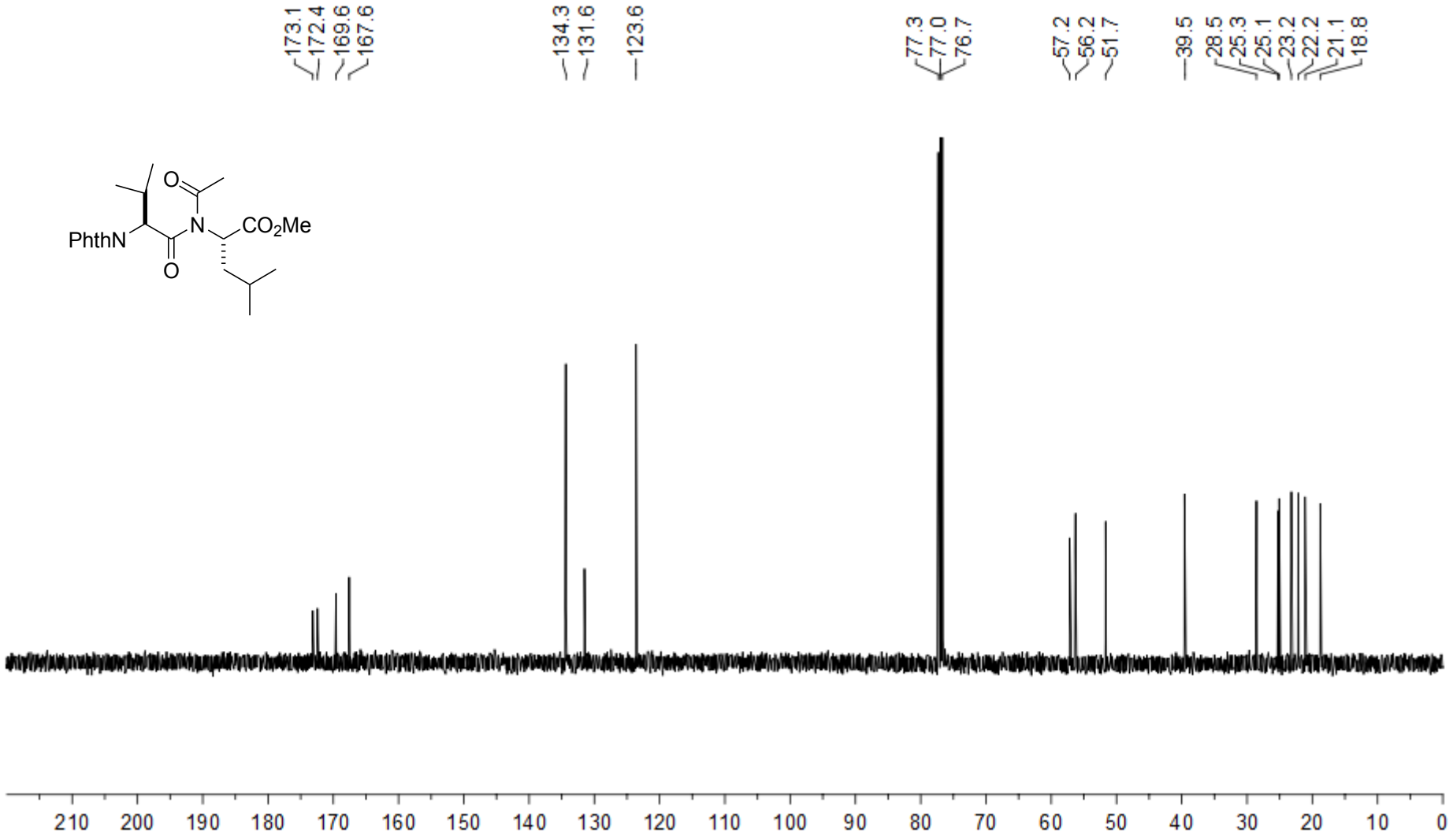
Compound 10VV (100 MHz, $CDCl_3$)



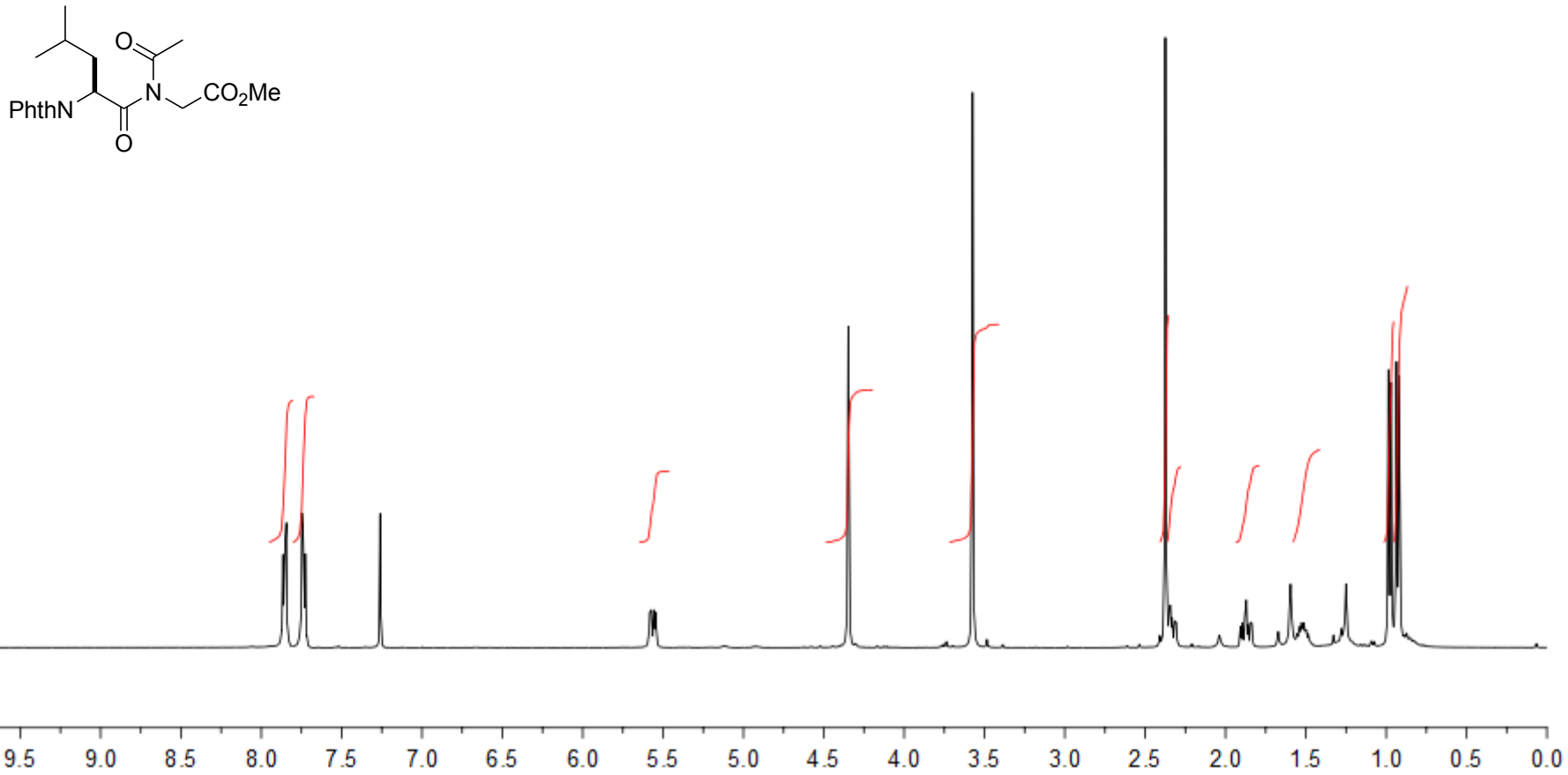
Compound 10VL (400 MHz, $CDCl_3$)



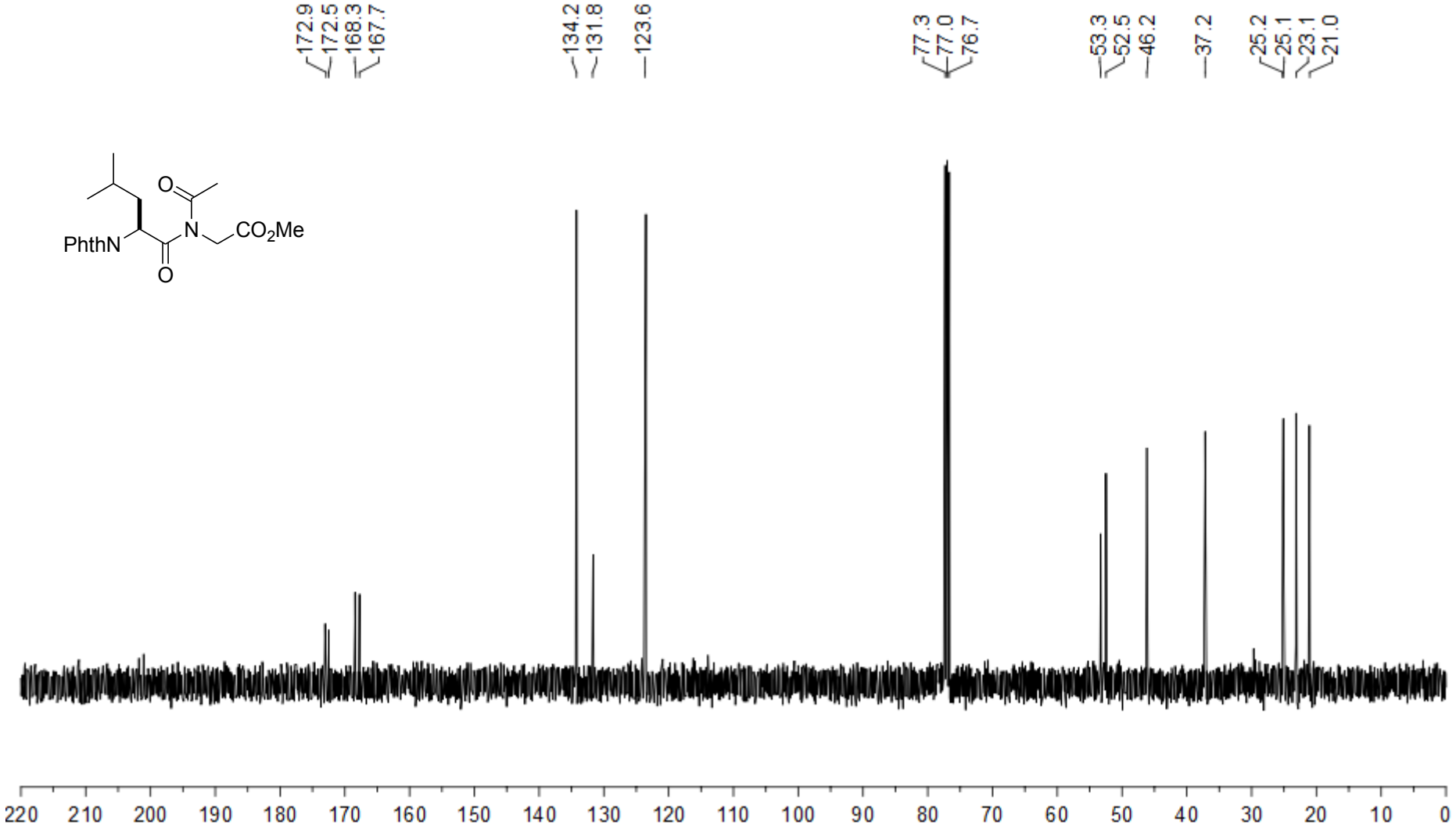
Compound 10VL (100 MHz, $CDCl_3$)



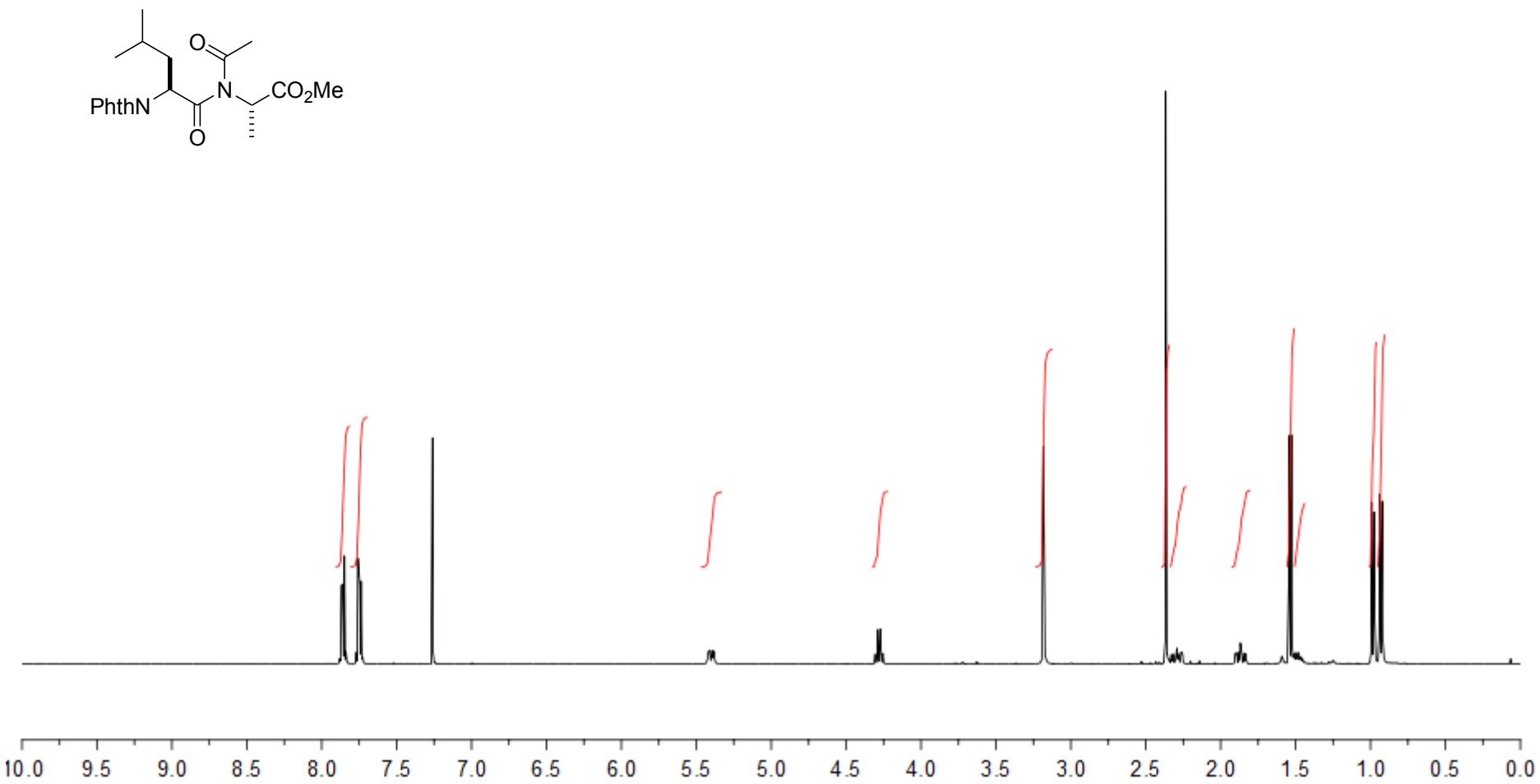
Compound 10LG (400 MHz, $CDCl_3$)



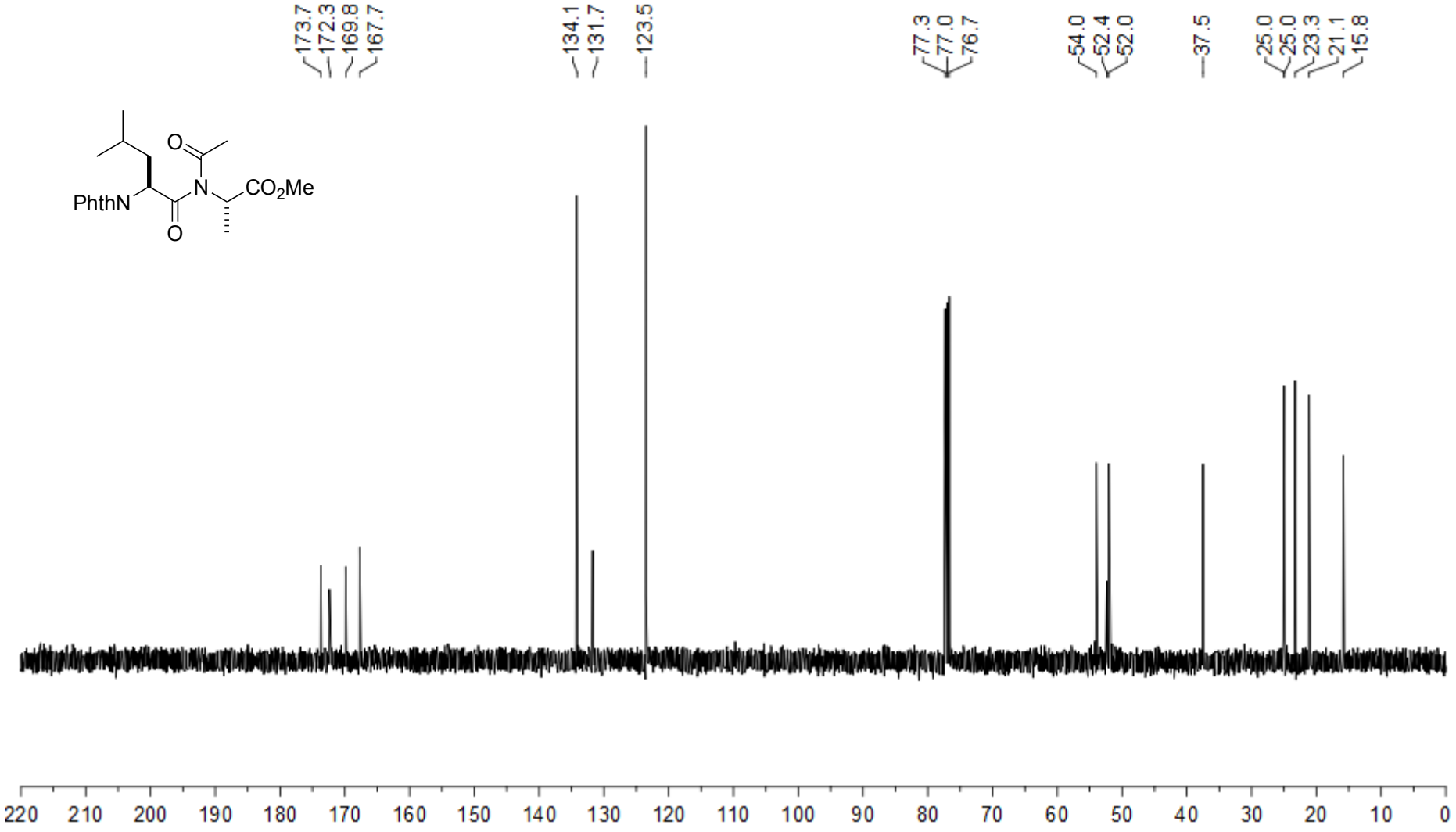
Compound 10LG (100 MHz, $CDCl_3$)



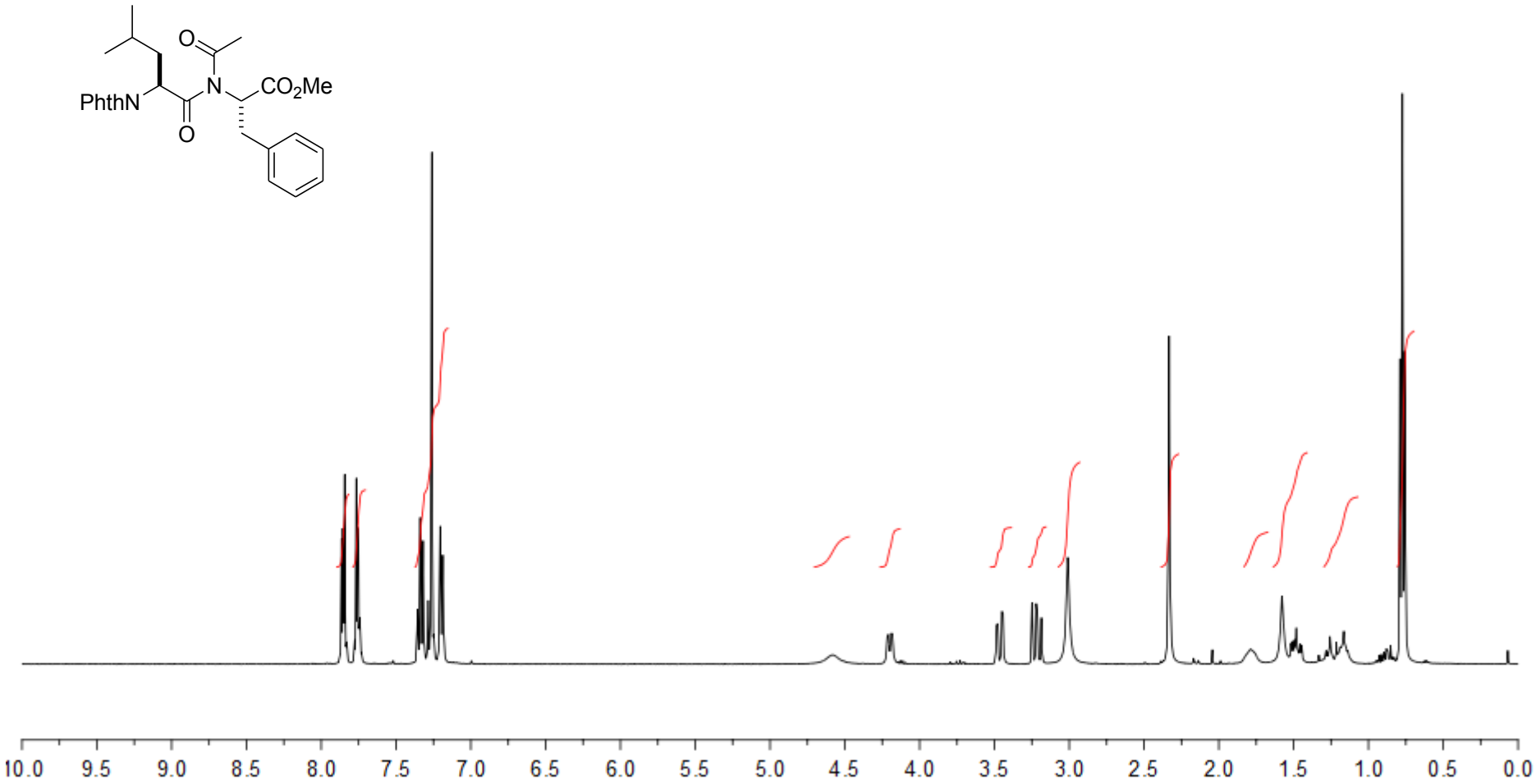
Compound 10LA (400 MHz, $CDCl_3$)



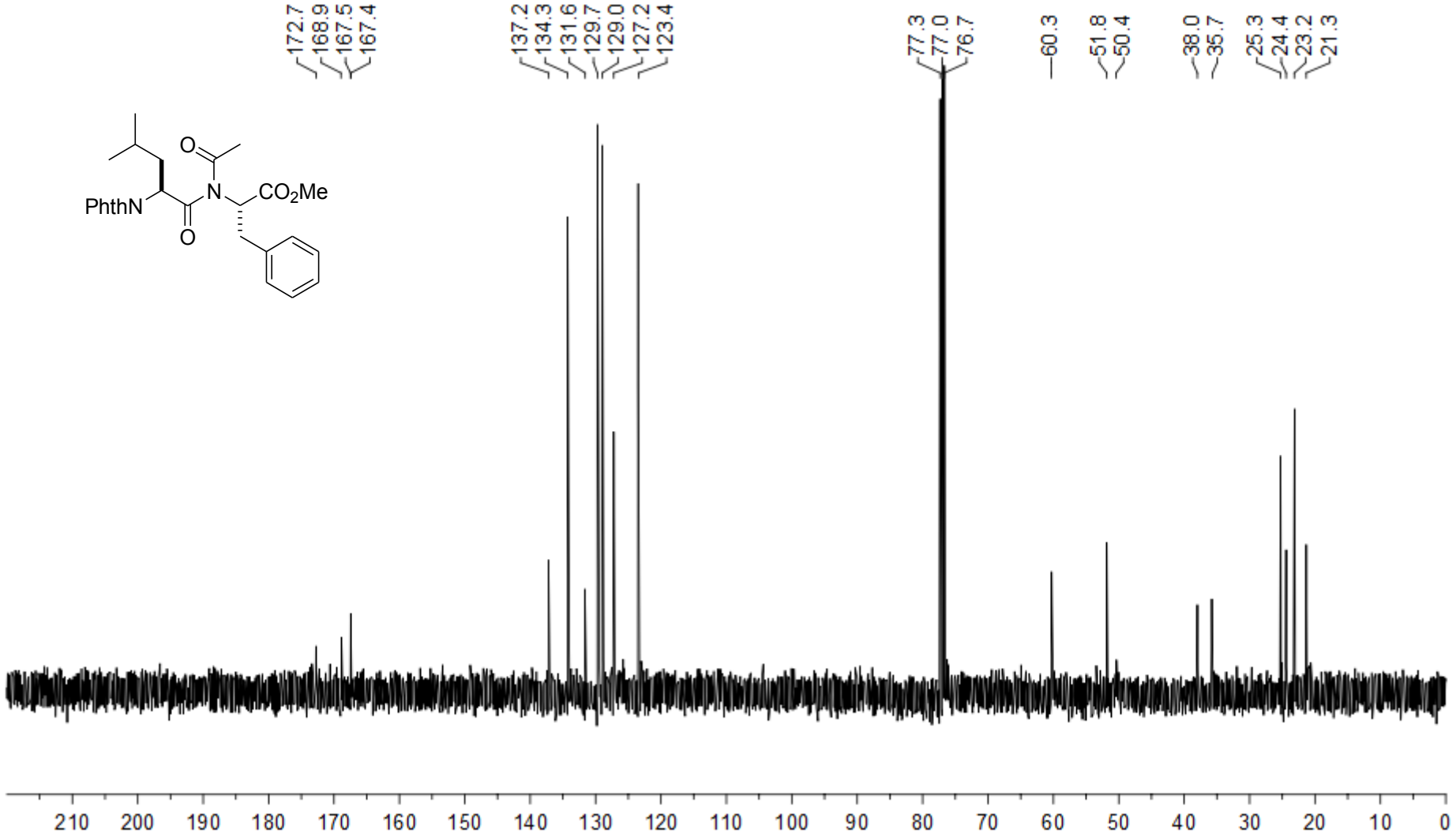
Compound 10LA (100 MHz, $CDCl_3$)



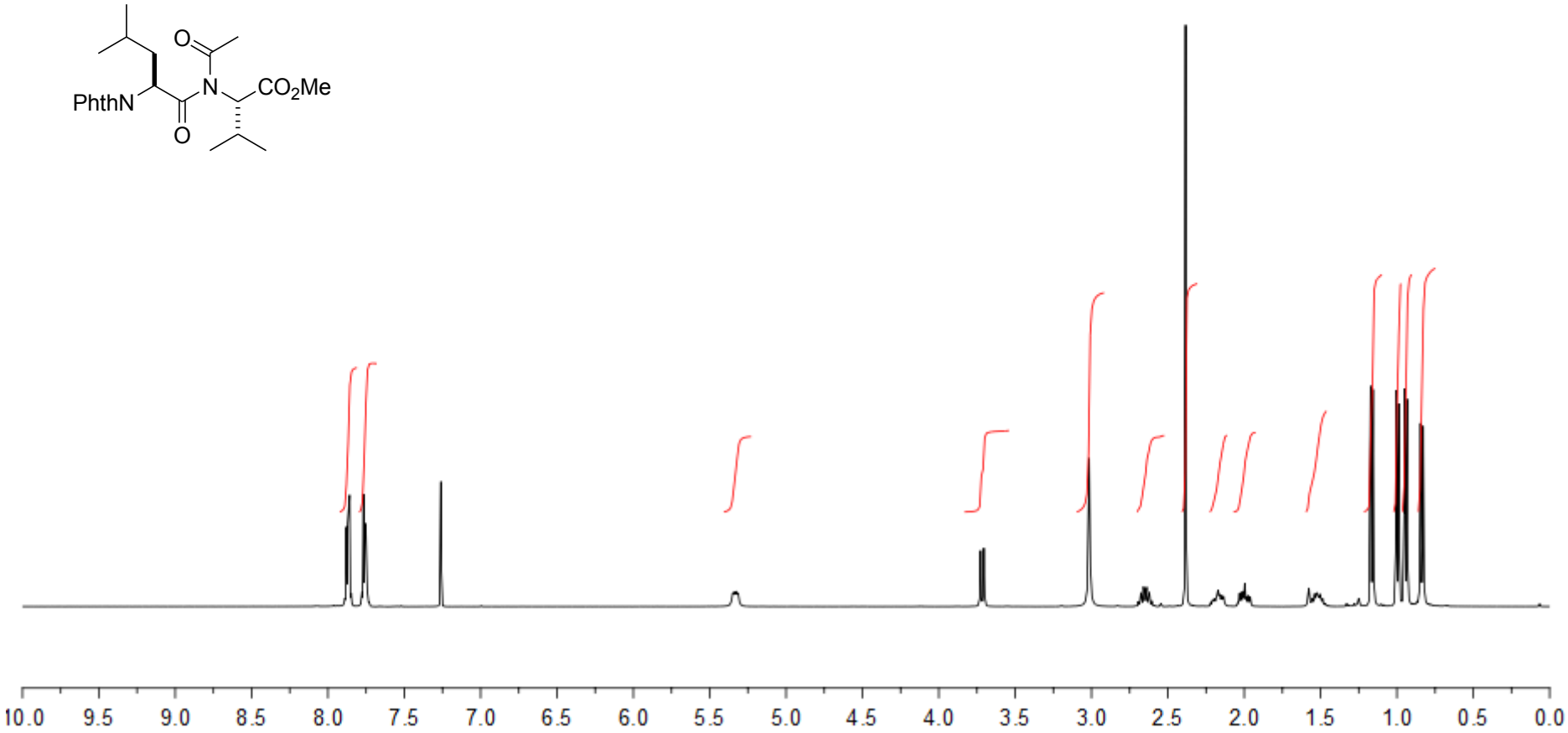
Compound 10LF (400 MHz, $CDCl_3$)



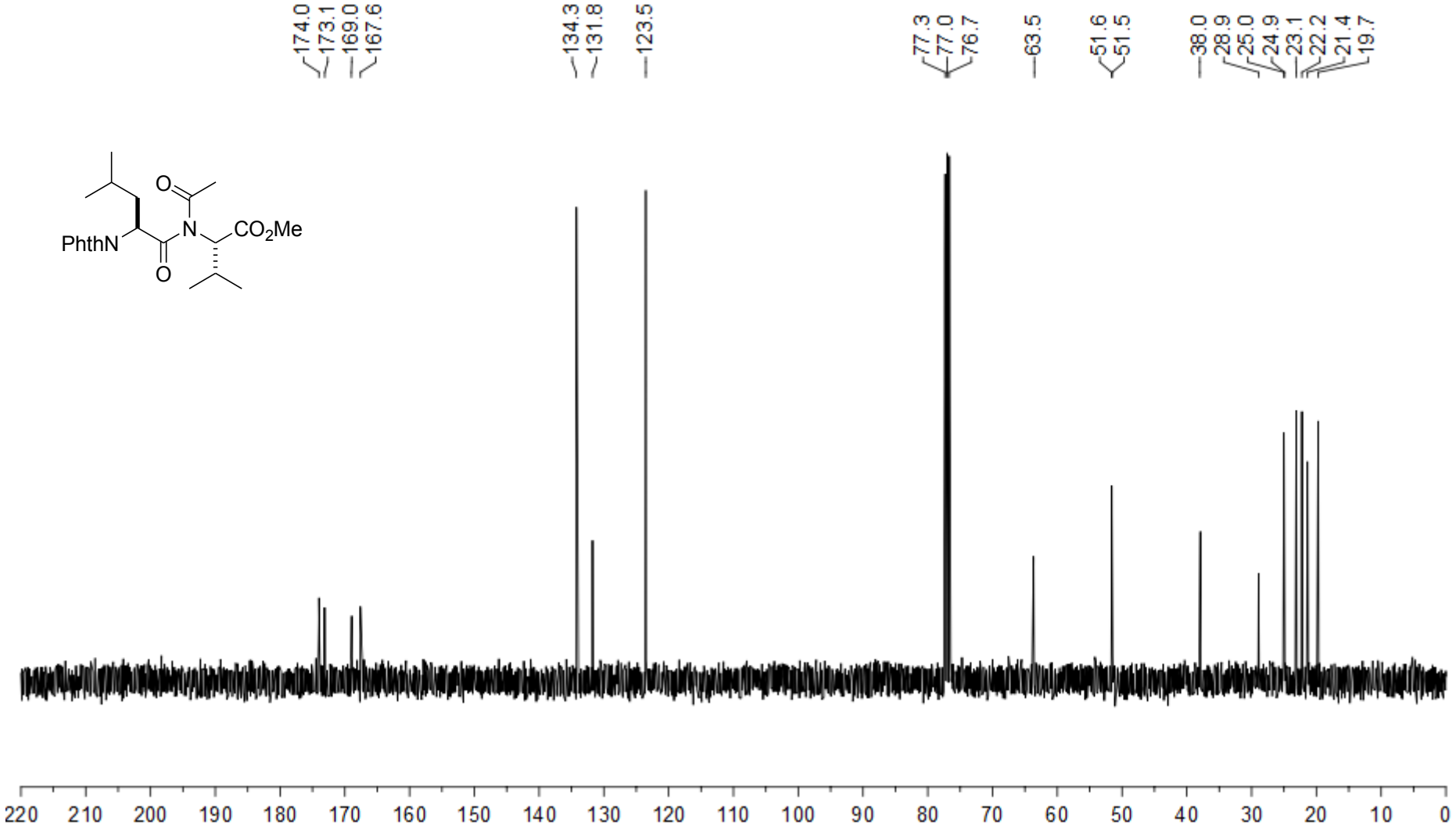
Compound 10LF (100 MHz, $CDCl_3$)



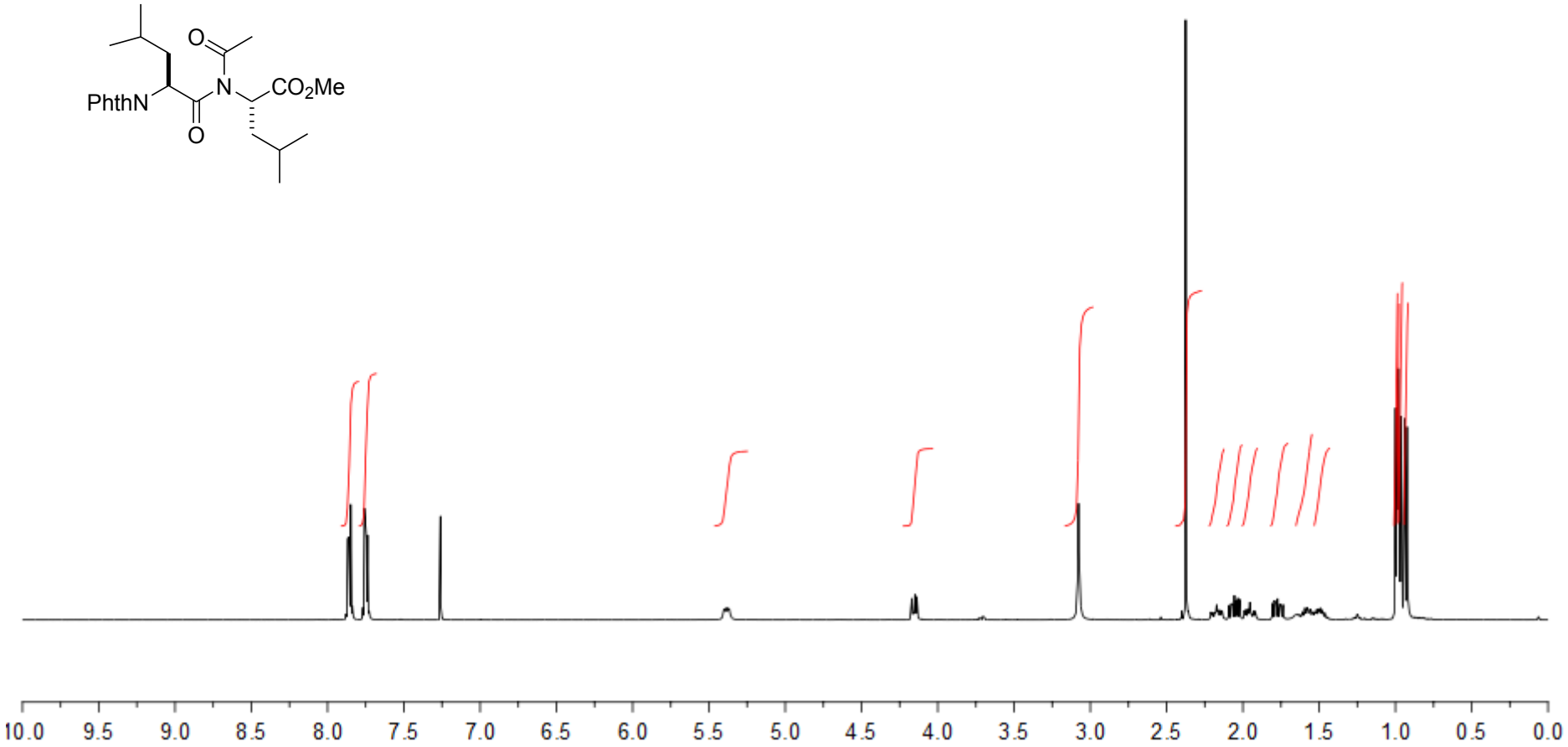
Compound 10LV (400 MHz, $CDCl_3$)



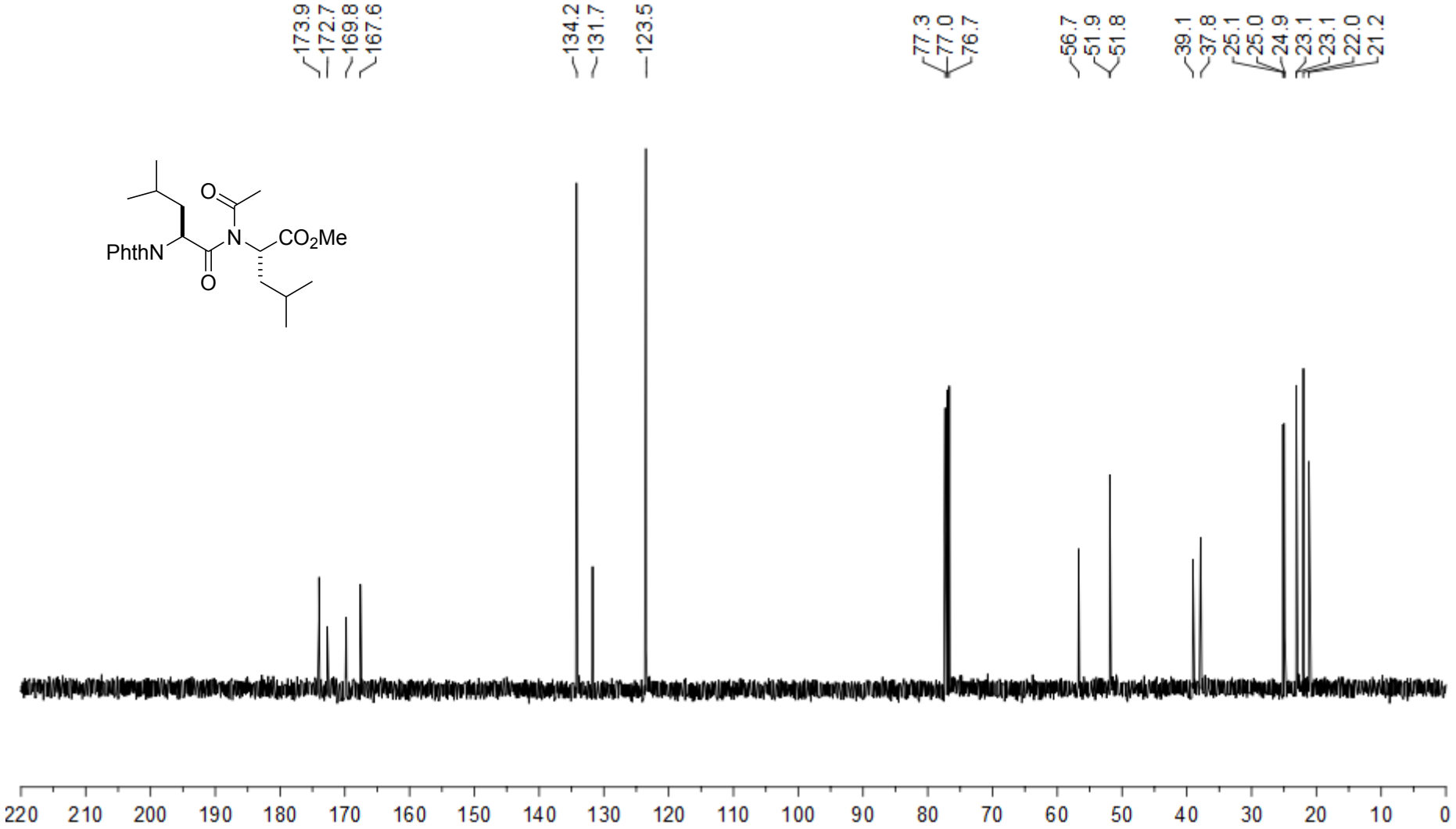
Compound 10LV (100 MHz, $CDCl_3$)



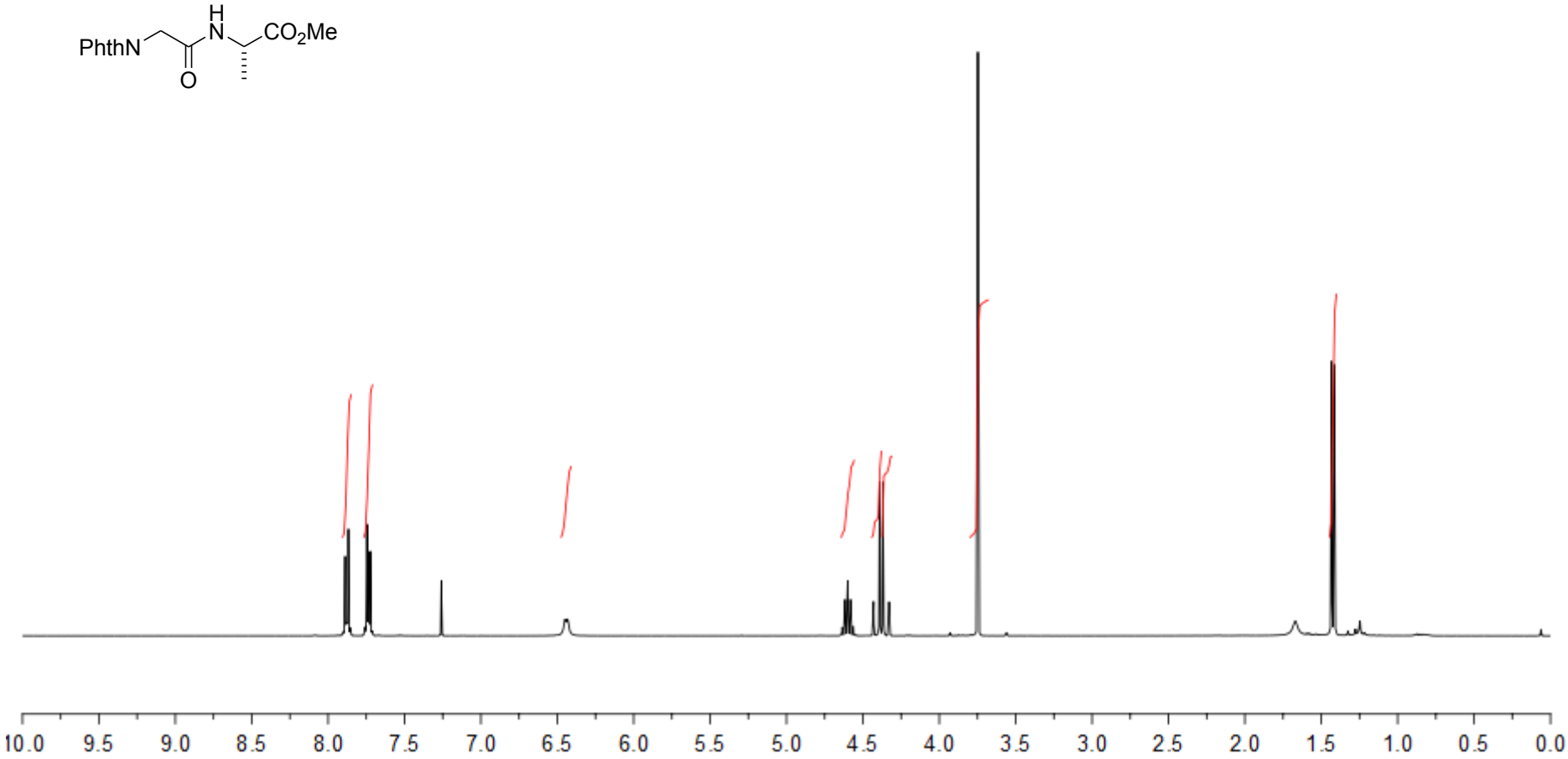
Compound 10LL (400 MHz, $CDCl_3$)



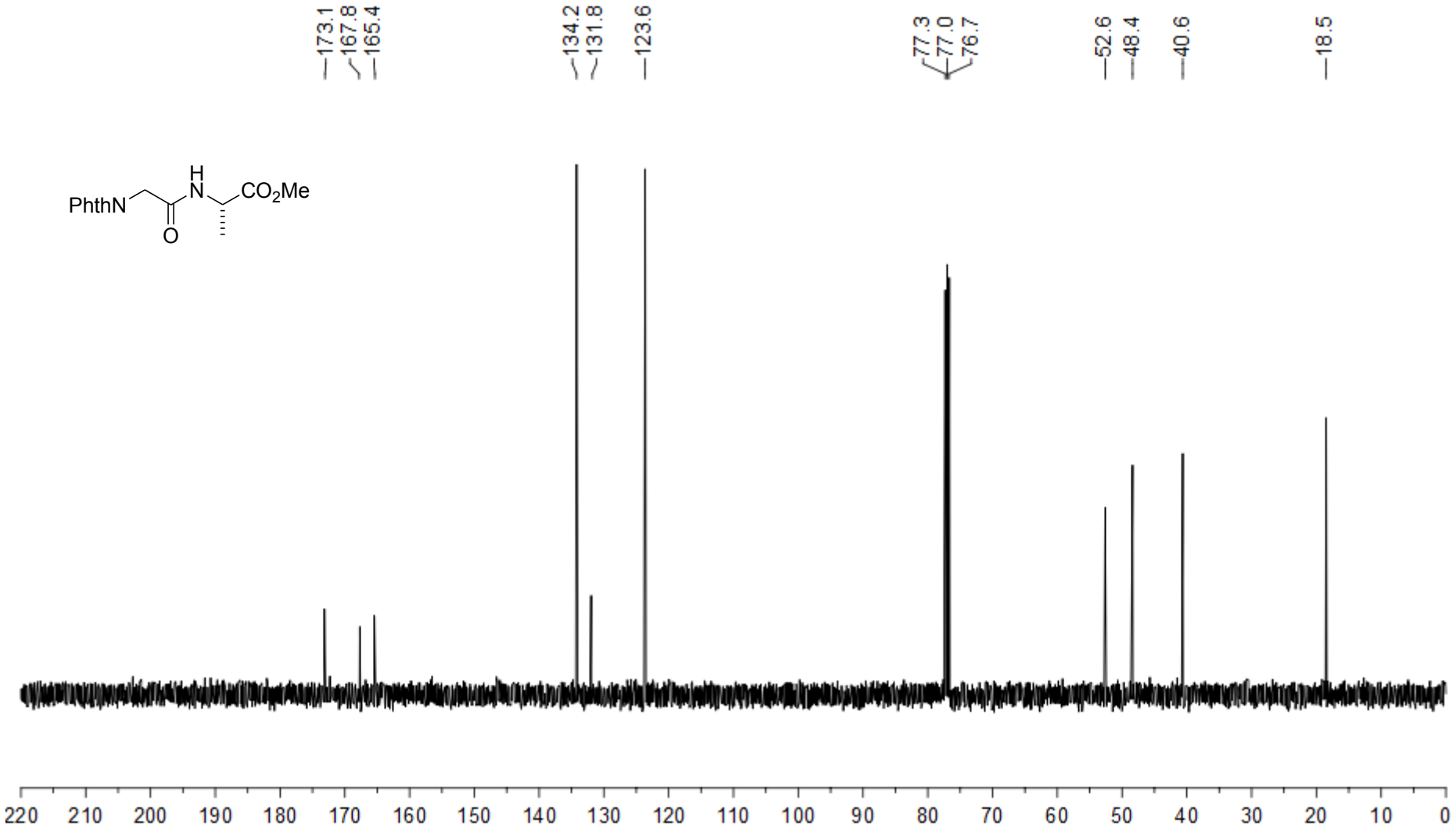
Compound 10LL (100 MHz, $CDCl_3$)



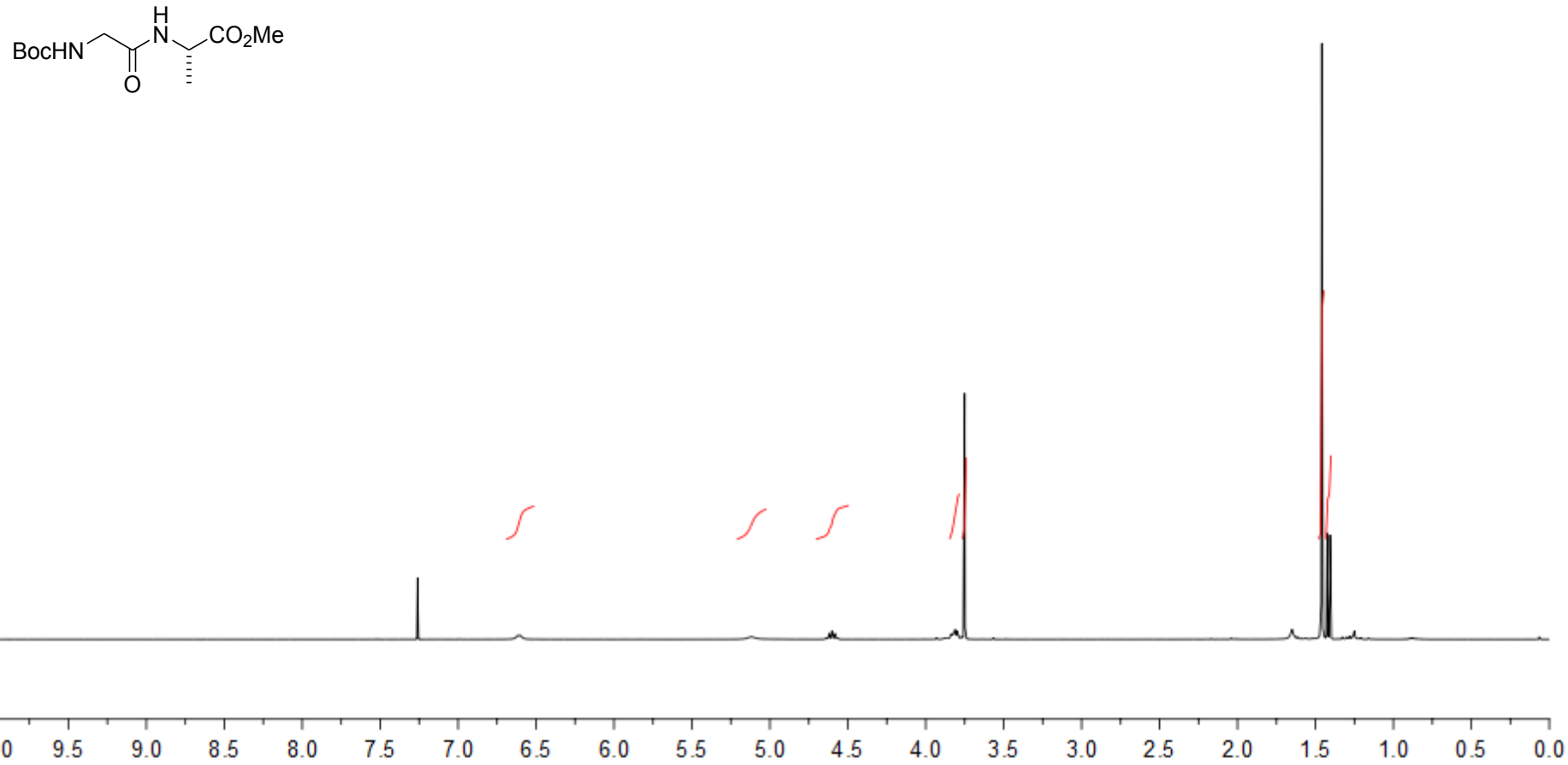
Dipeptide 19 (400 MHz, $CDCl_3$)



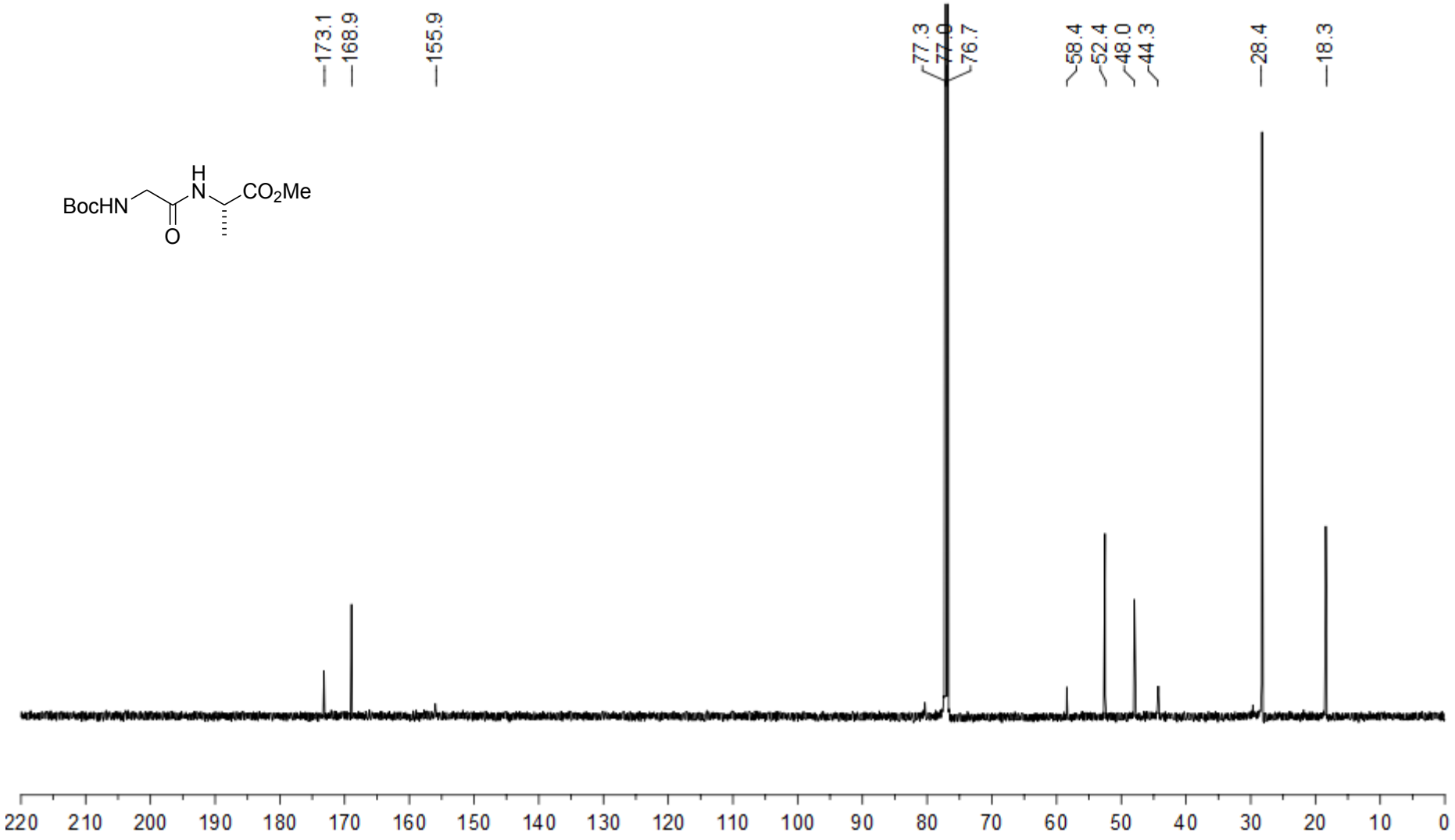
Dipeptide 19 (400 MHz, $CDCl_3$)



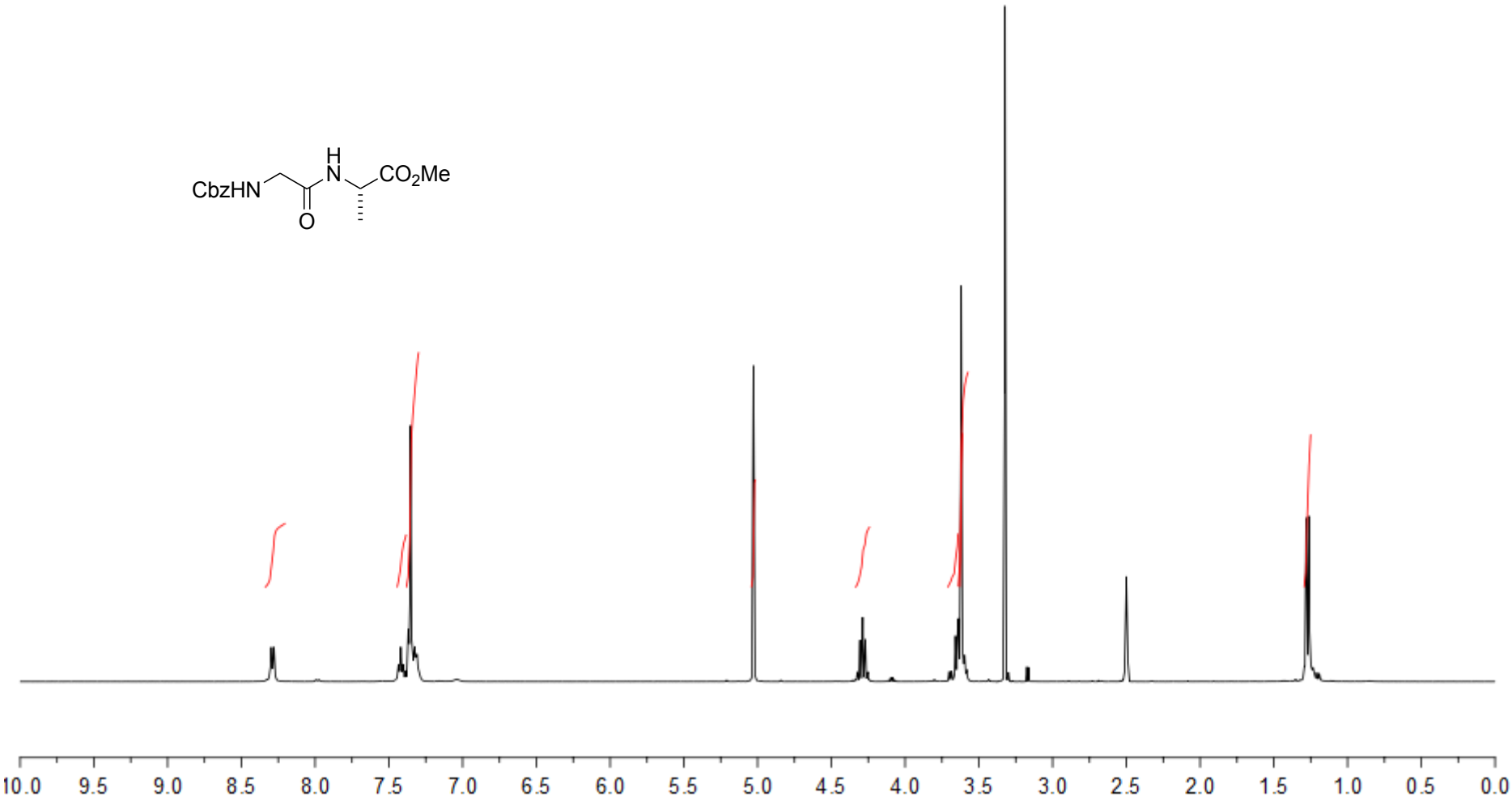
Compound 15 (400 MHz, $CDCl_3$)



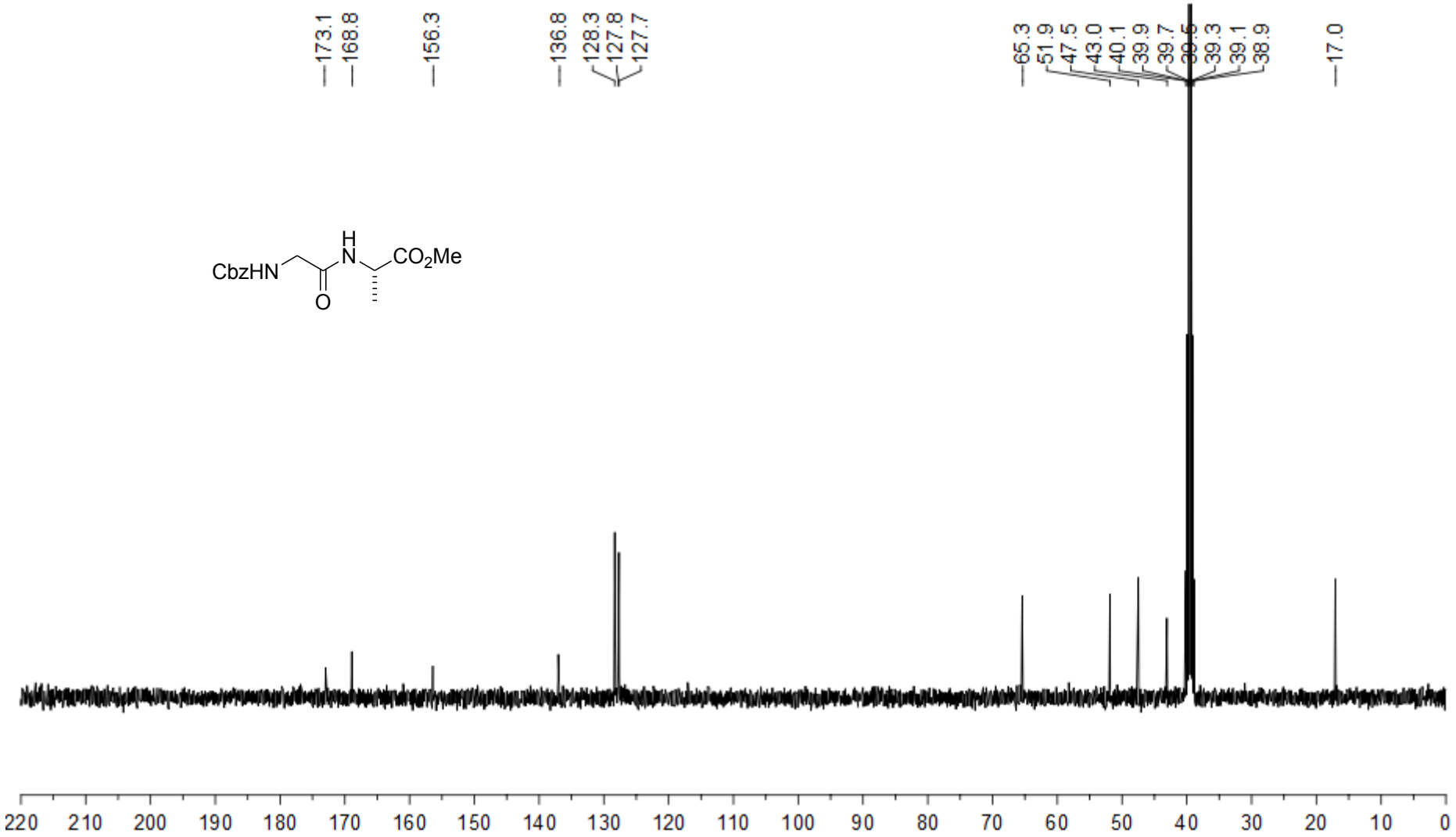
Compound 15 (100 MHz, $CDCl_3$)



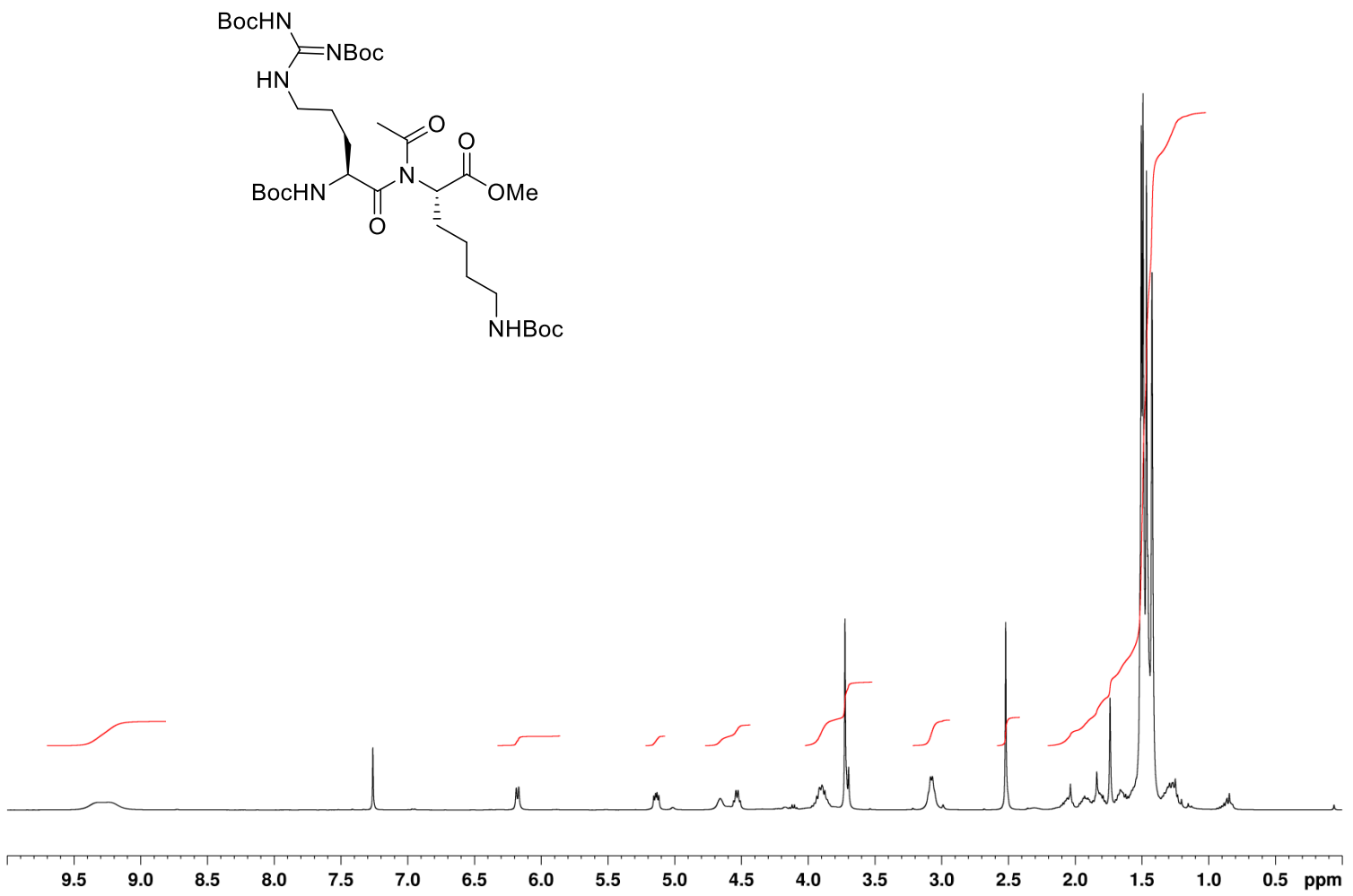
Compound 18 (400 MHz, DMSO-d_6)



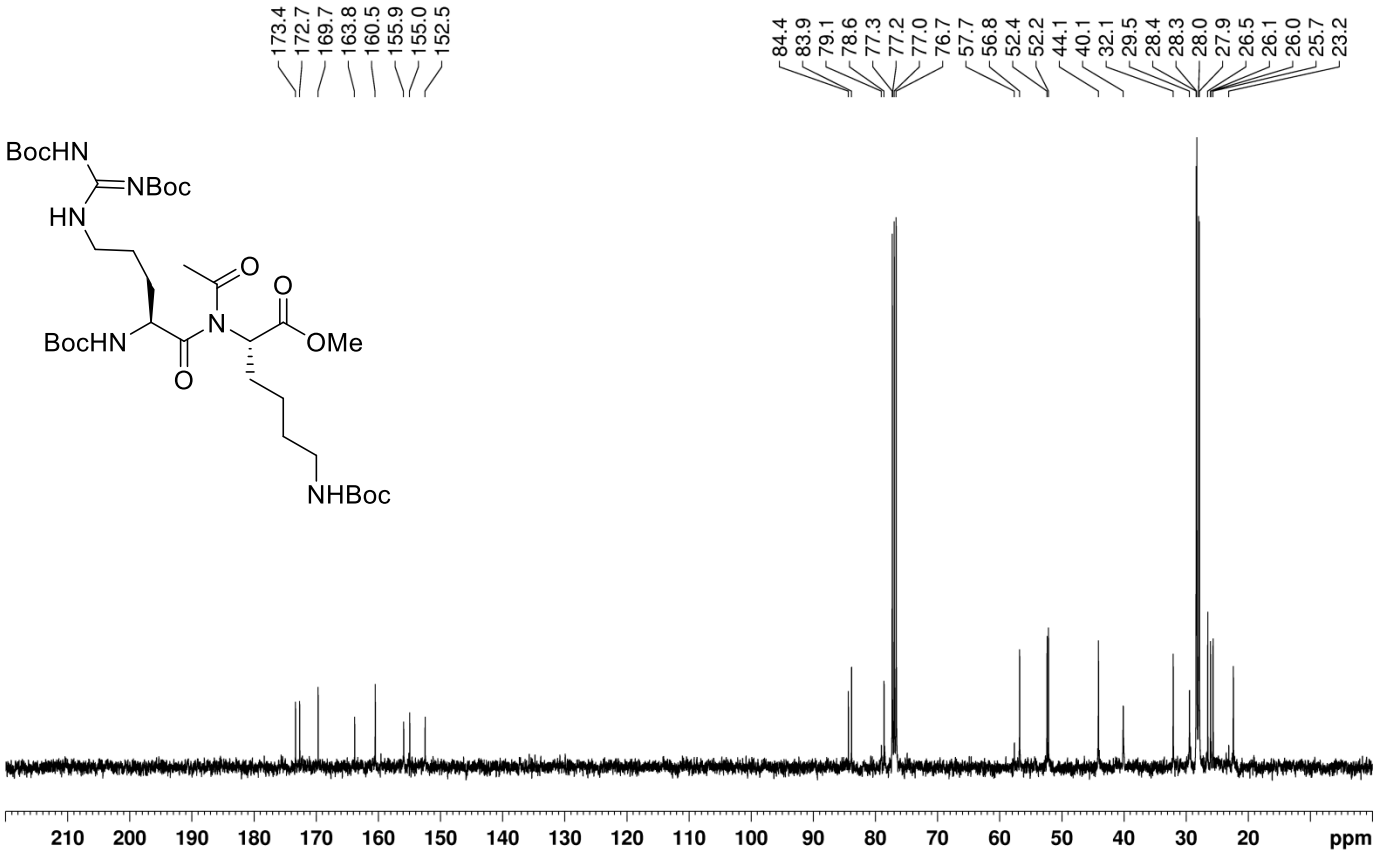
Compound 18 (100 MHz, DMSO-d_6)



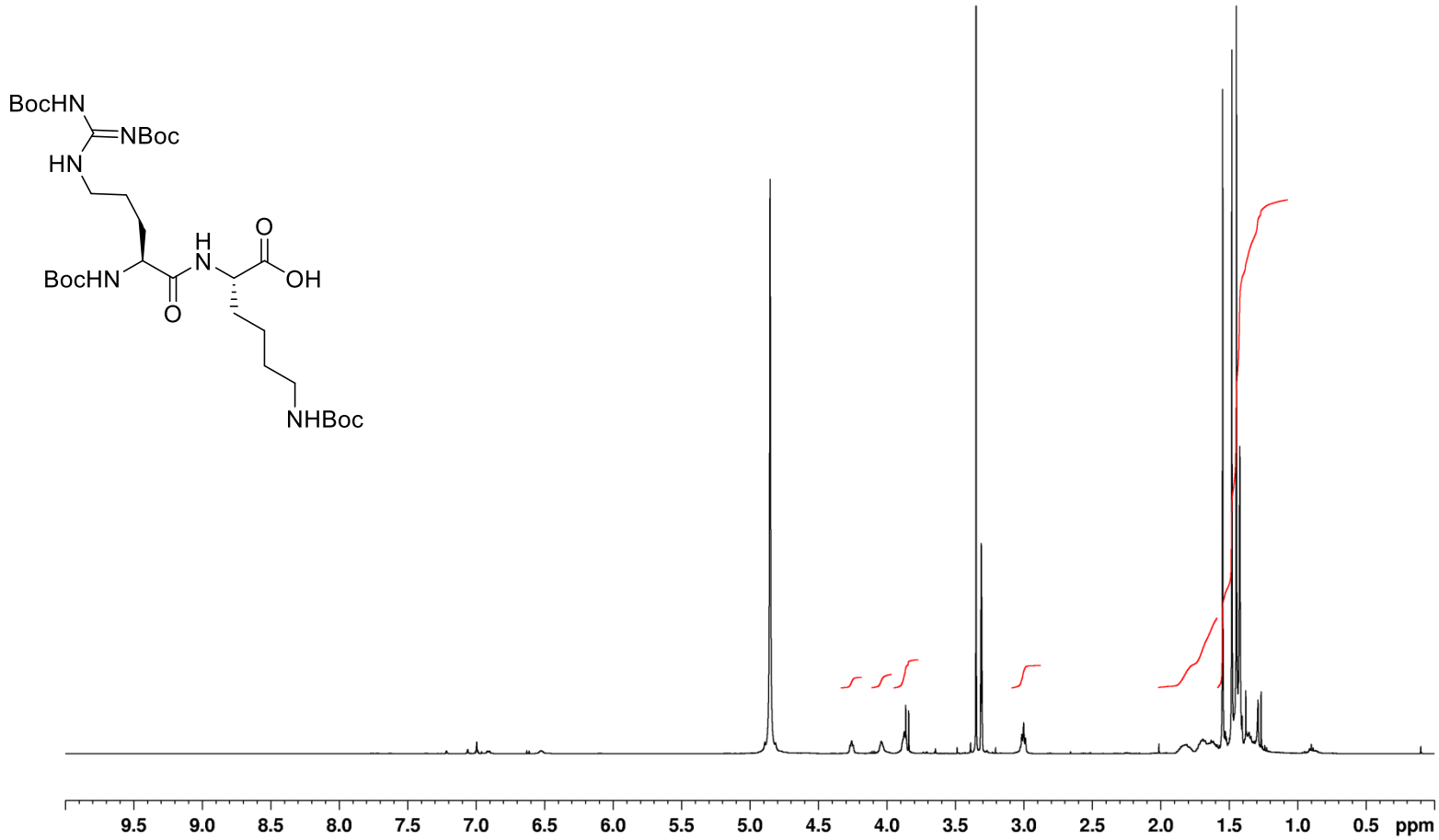
Compound 21 (400 MHz $CDCl_3$)



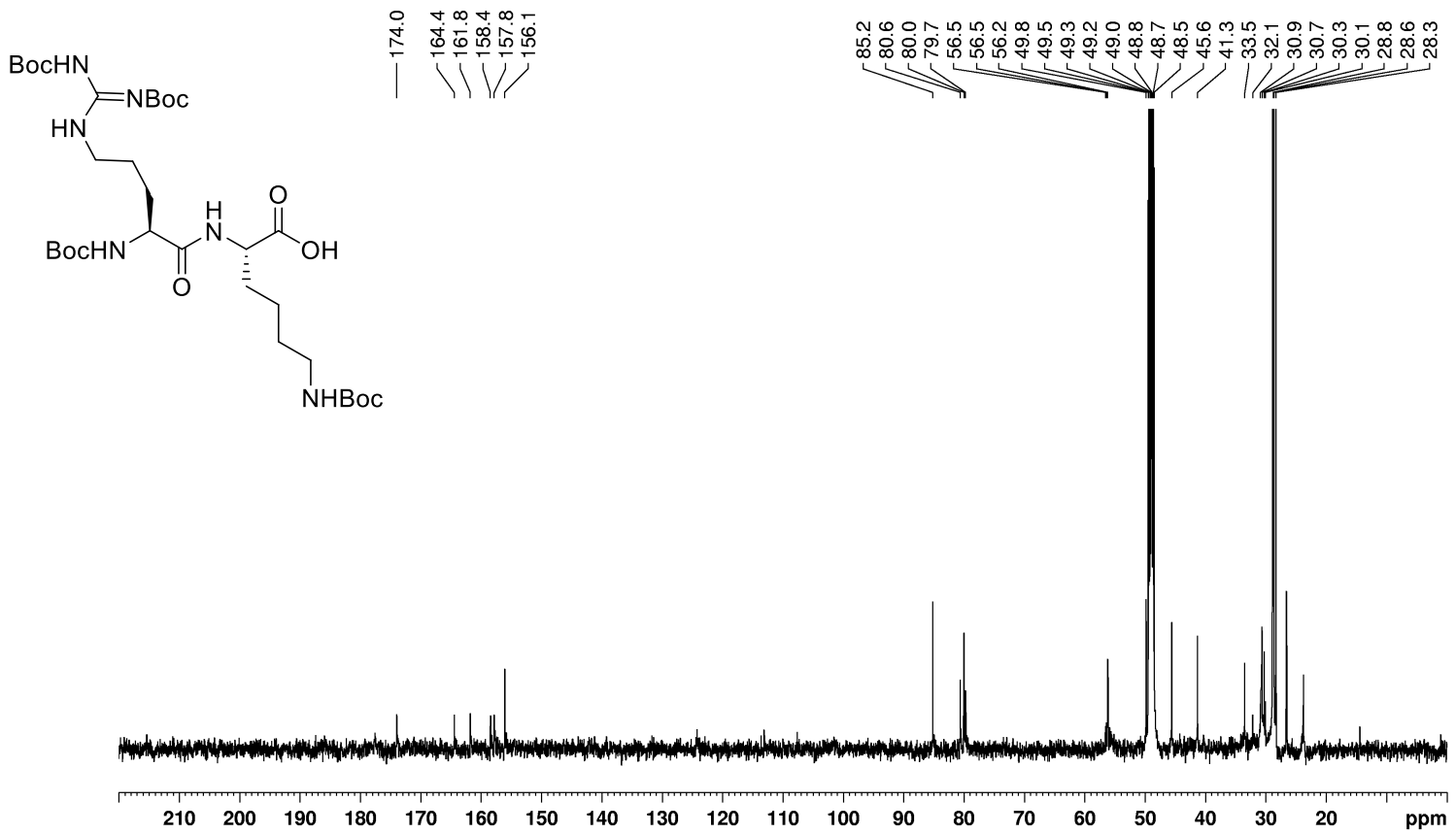
Compound 21 (100 MHz, $CDCl_3$)



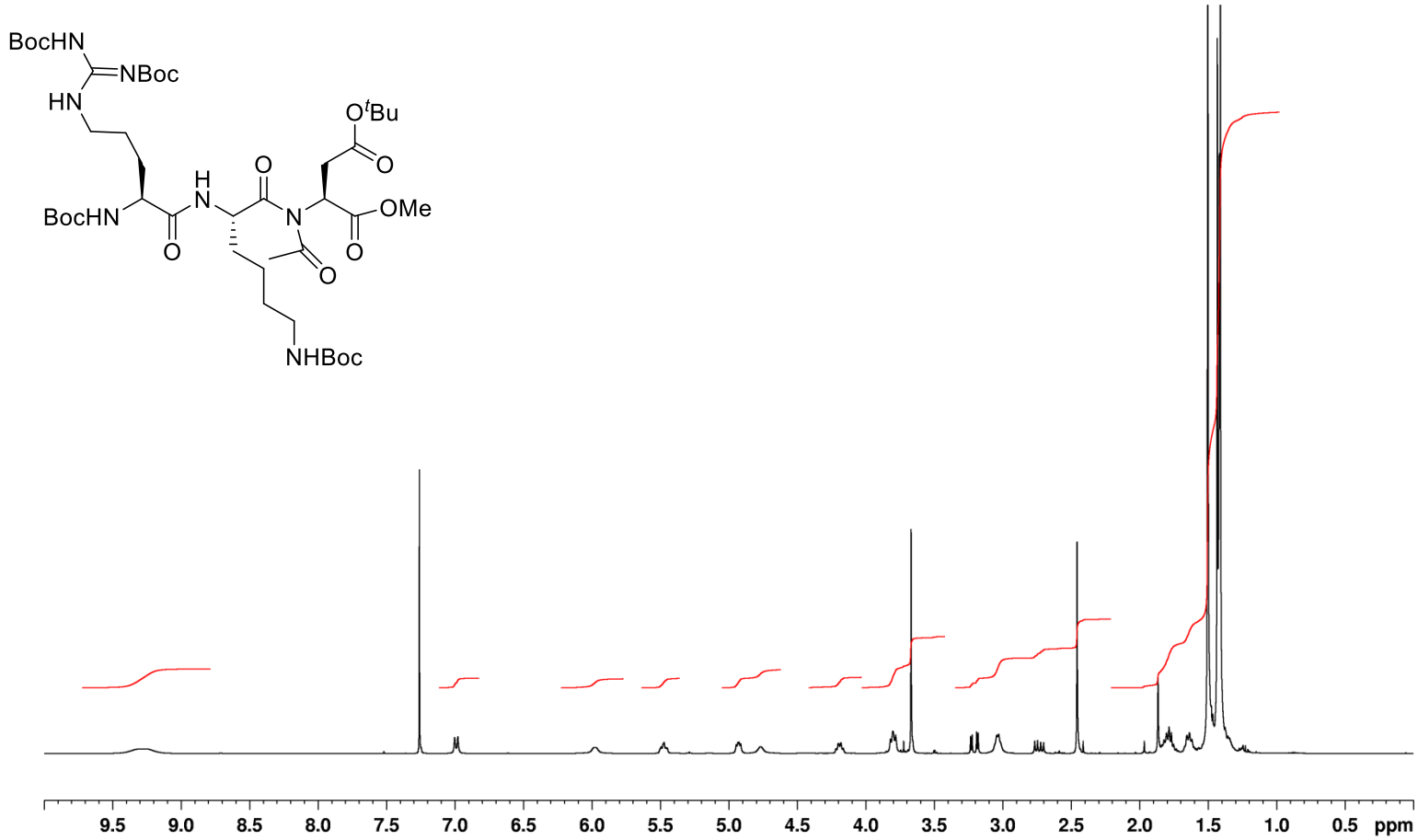
Compound 22 (500 MHz, CD_3OD)



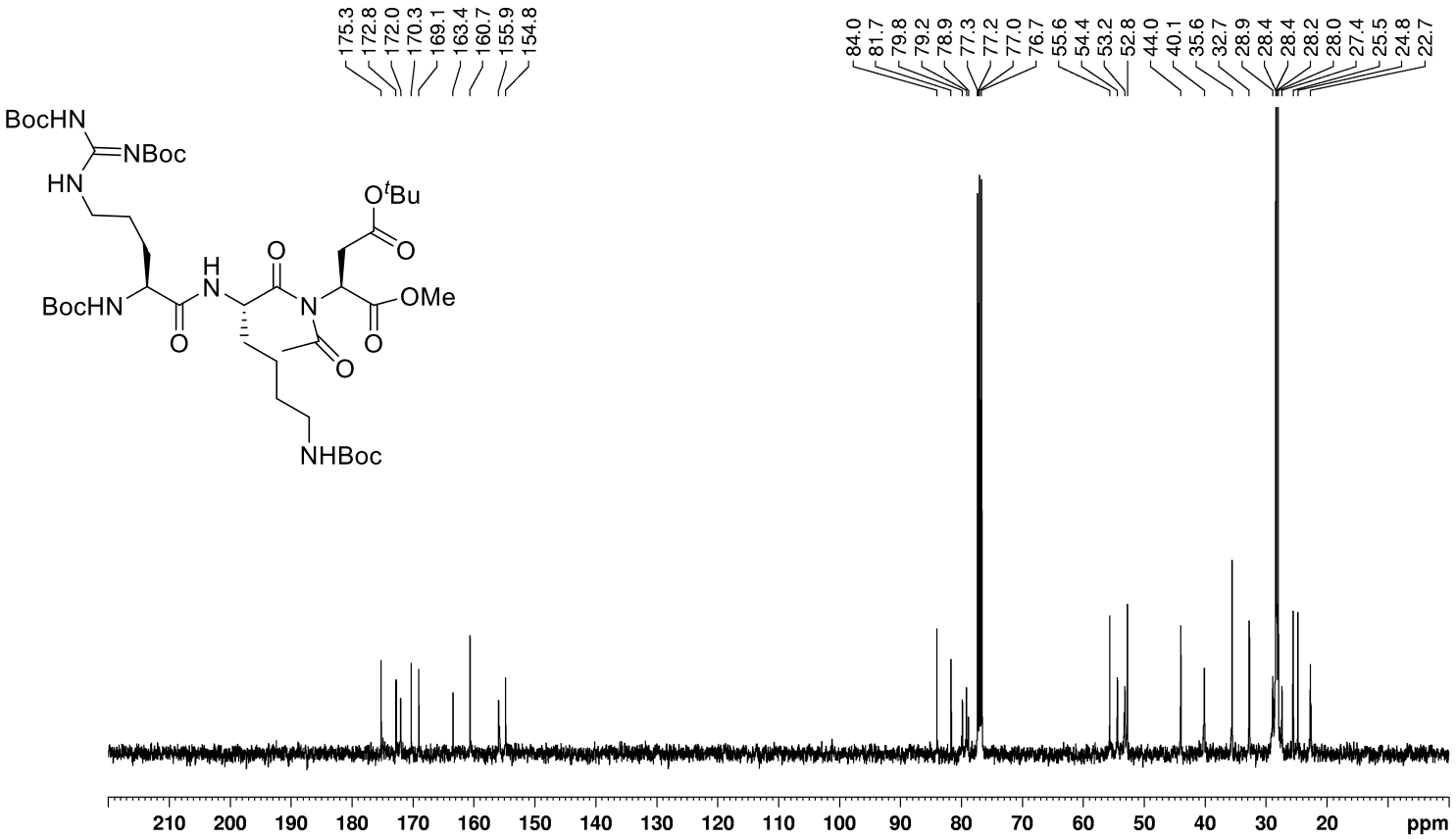
Compound 22 (125 MHz, CD_3OD)



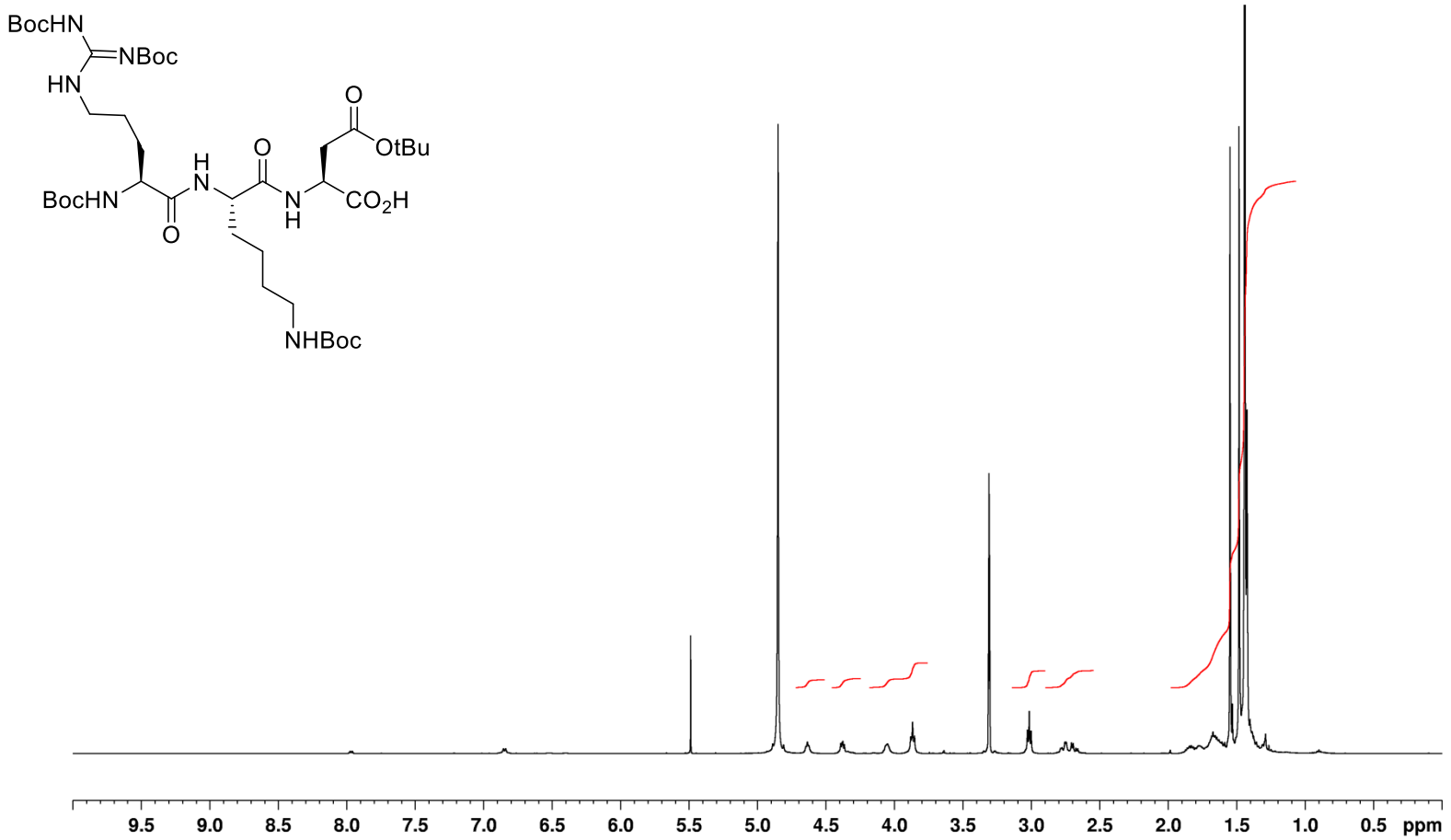
Compound 23 (400 MHz, $CDCl_3$)



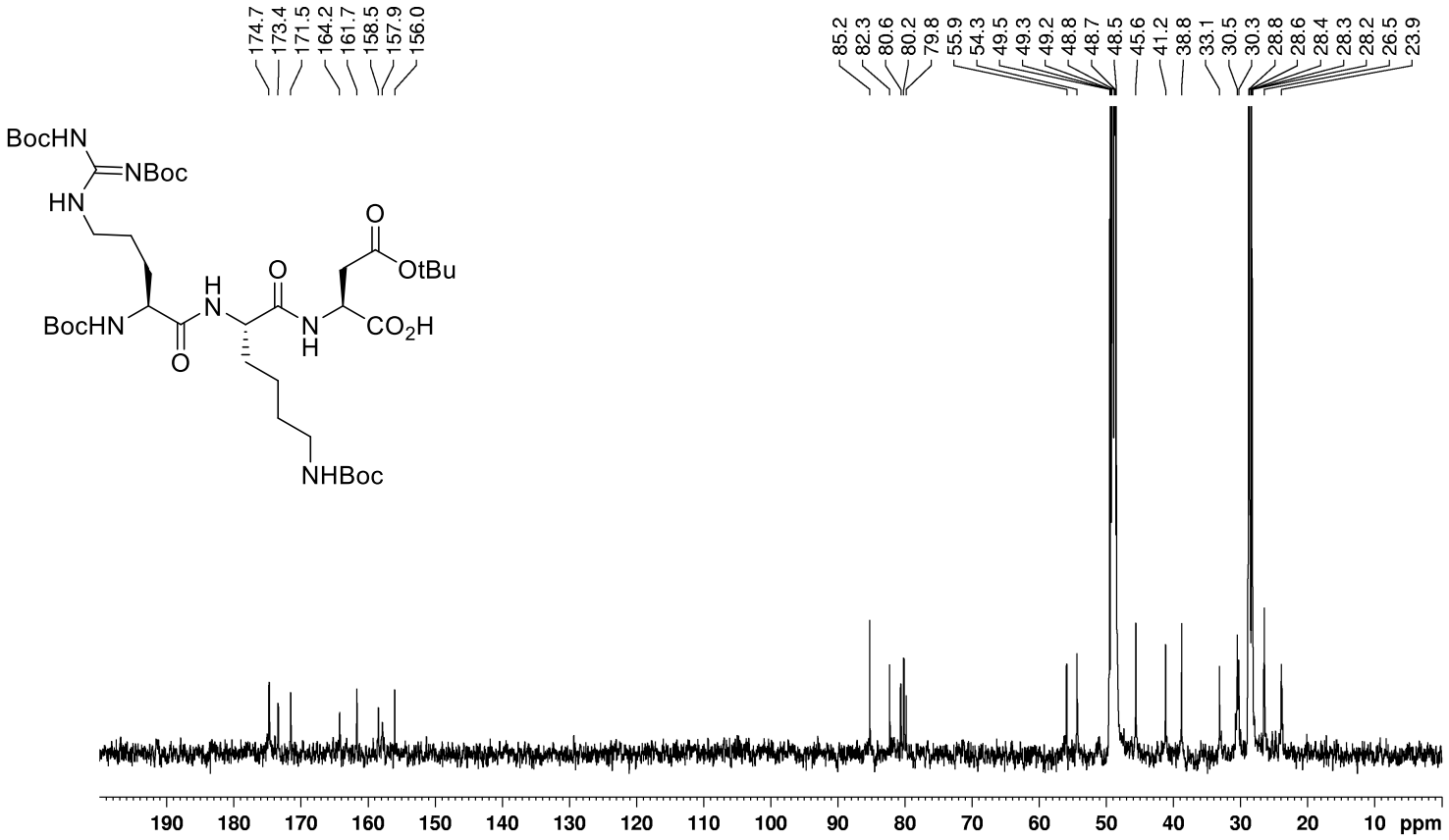
Compound 23 (100 MHz, $CDCl_3$)



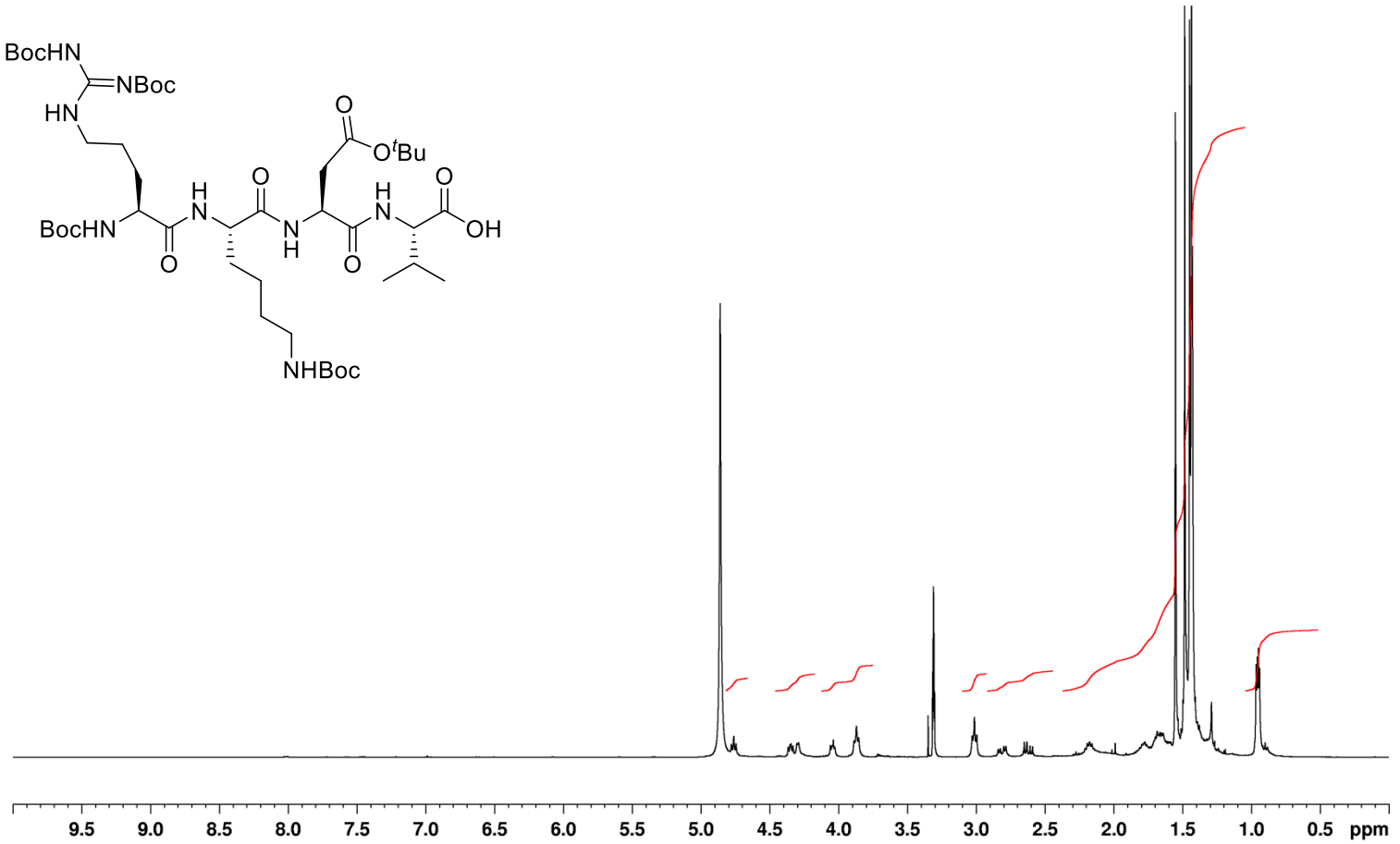
Compound 25 (500 MHz, CD_3OD)



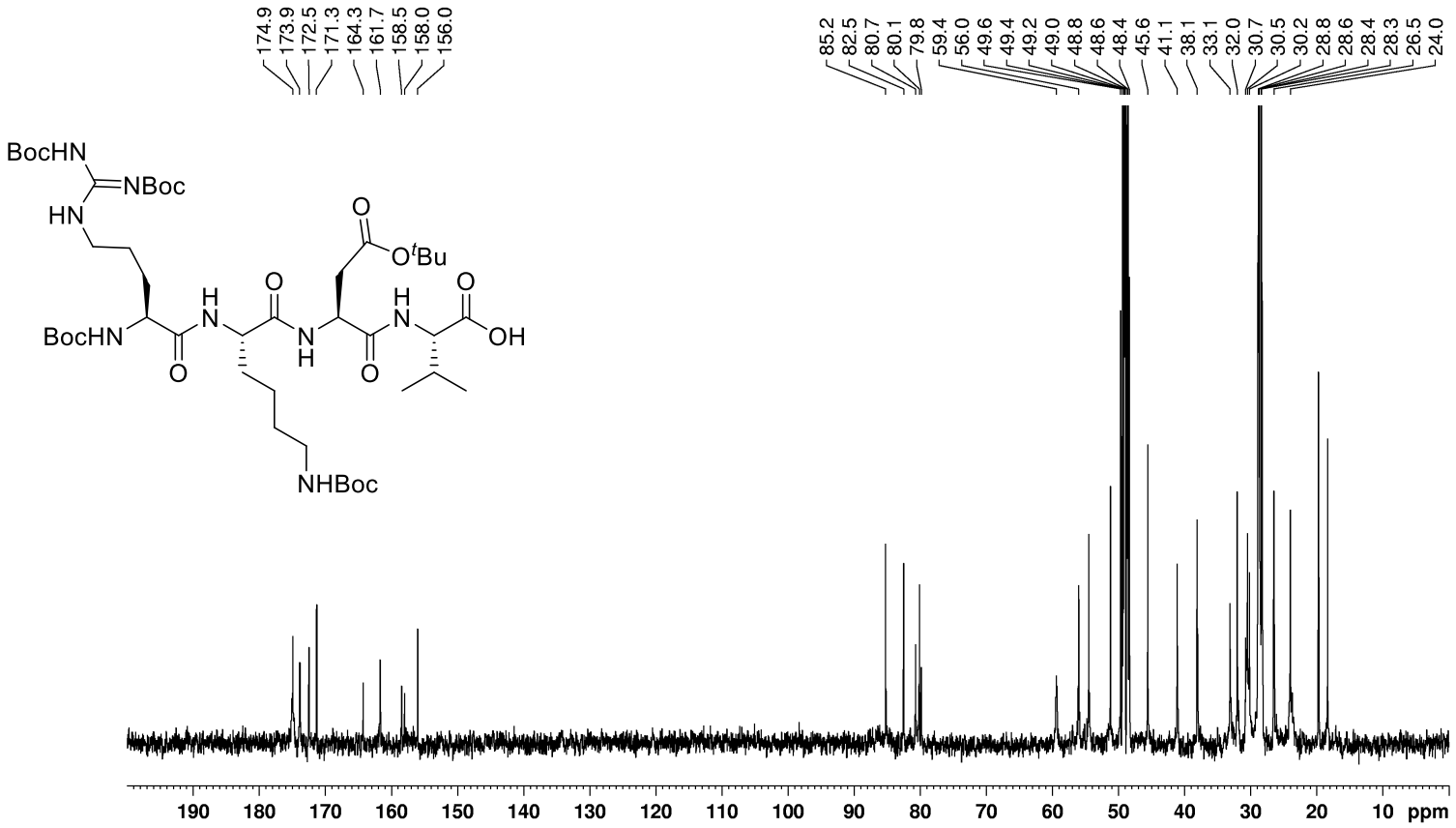
Compound 25 (125 MHz, CD_3OD)



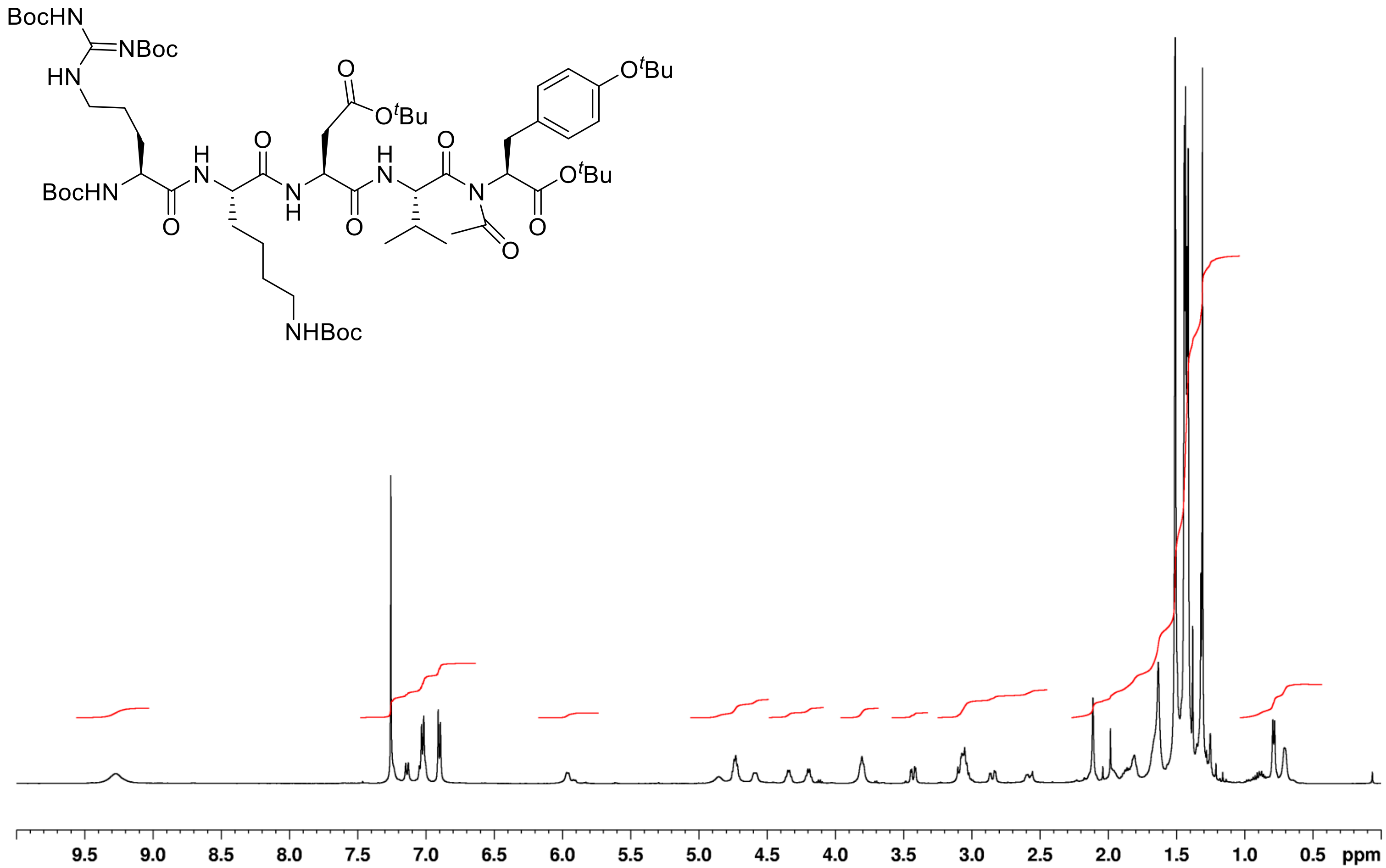
Compound 26 (500 MHz, CD_3OD)



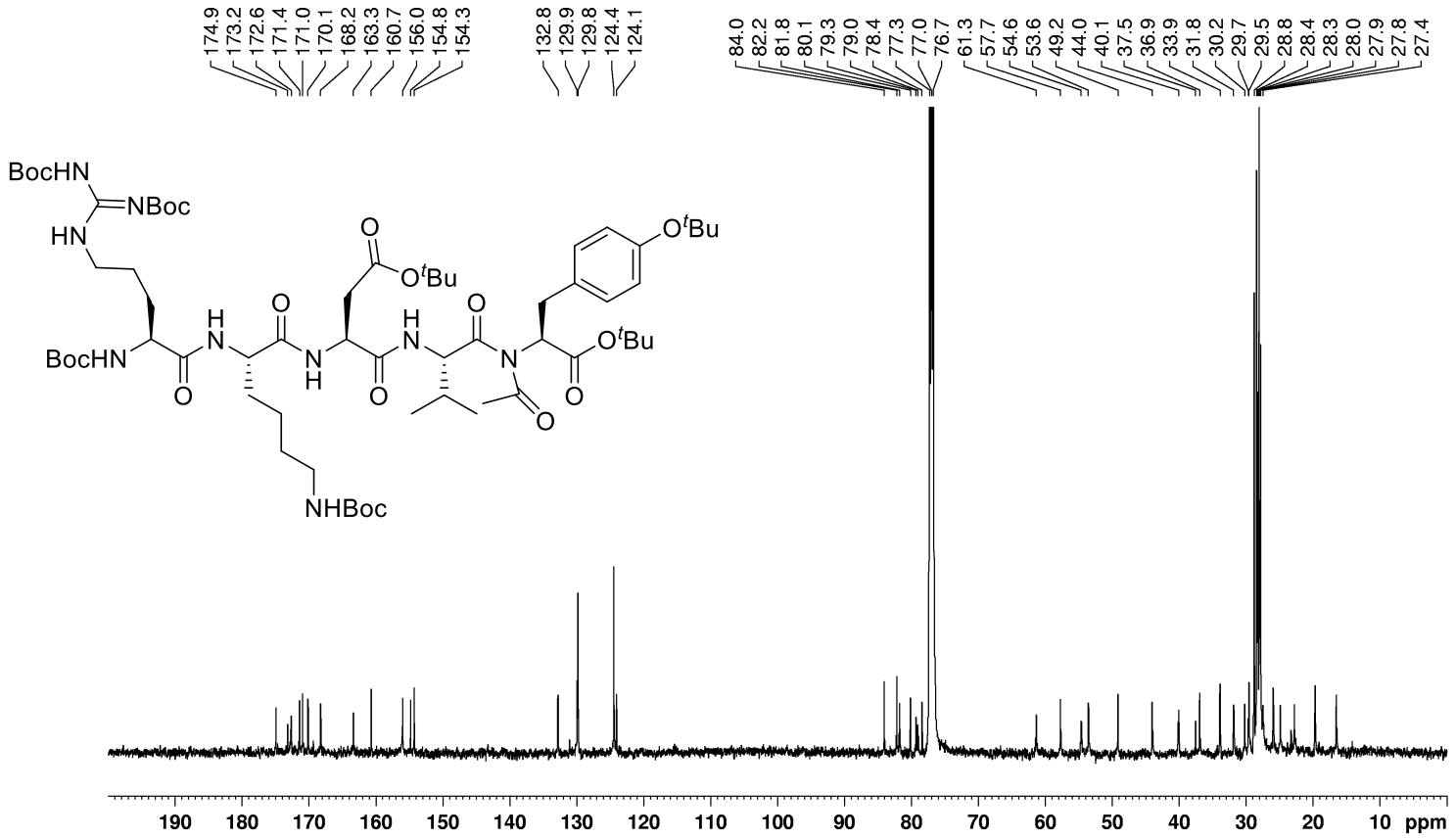
Compound 26 (125 MHz, CD_3OD)



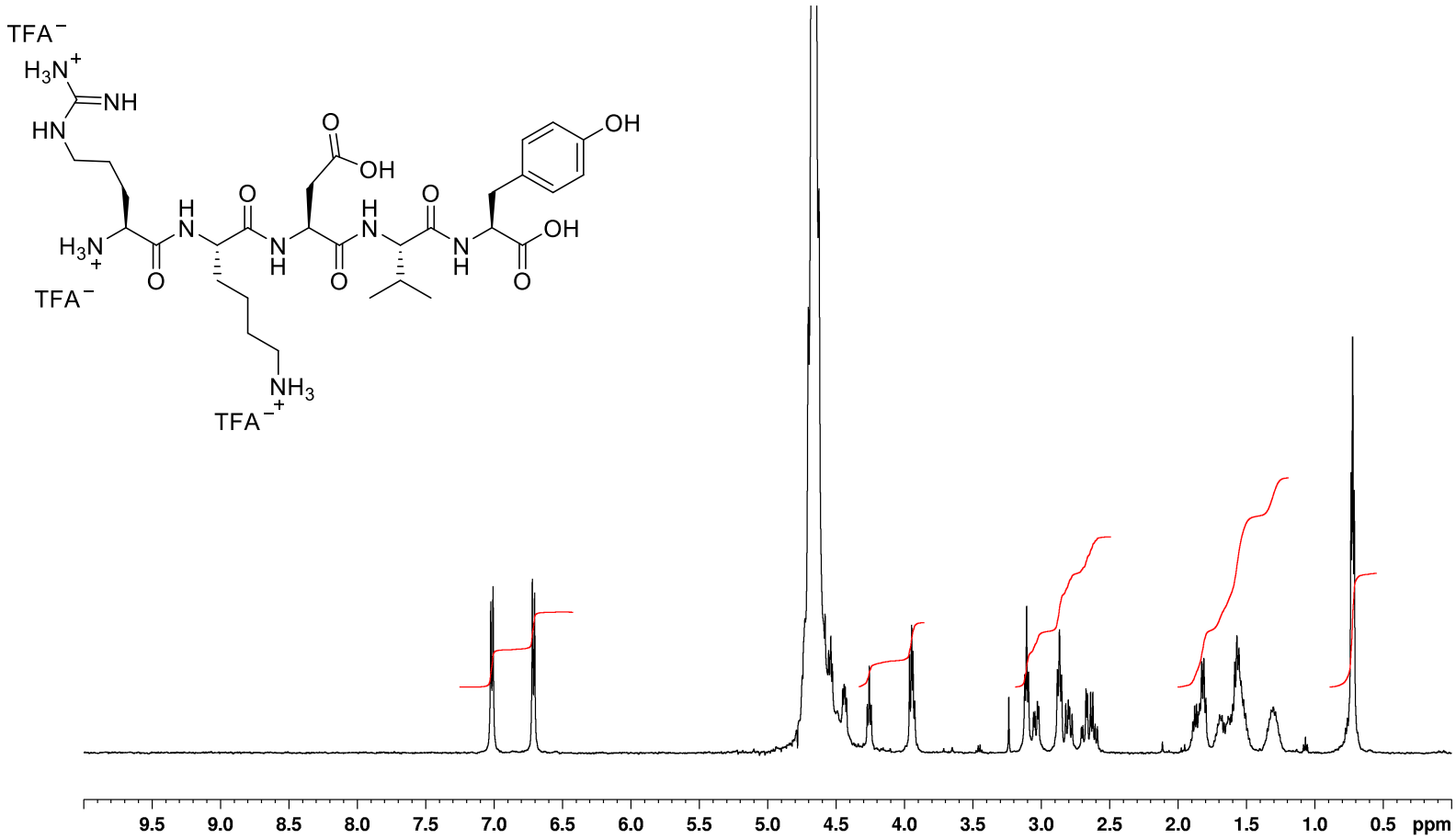
Compound 27 (500 MHz, $CDCl_3$)



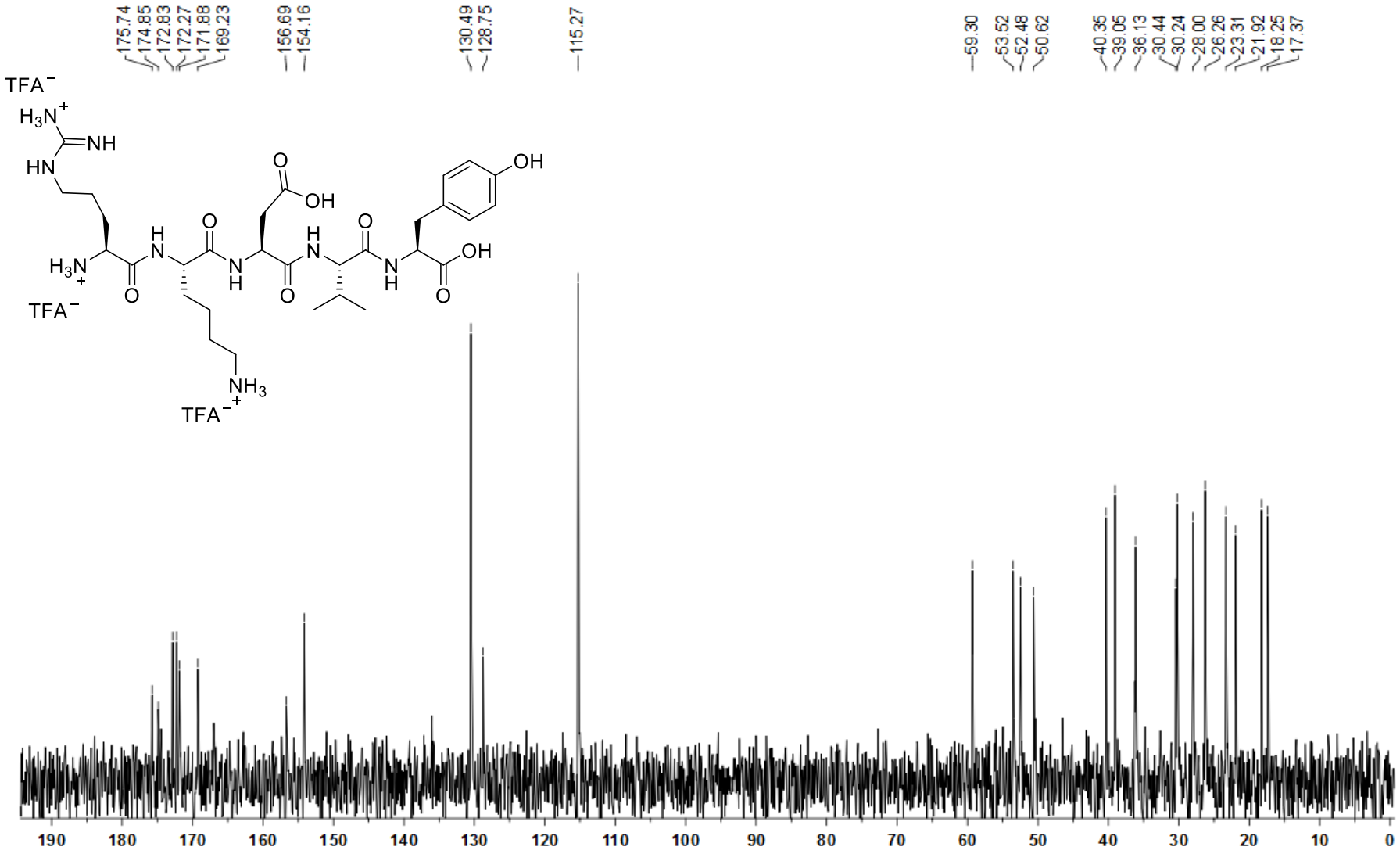
Compound 27 (125 MHz, $CDCl_3$)



Compound 28 (500 MHz, D_2O)

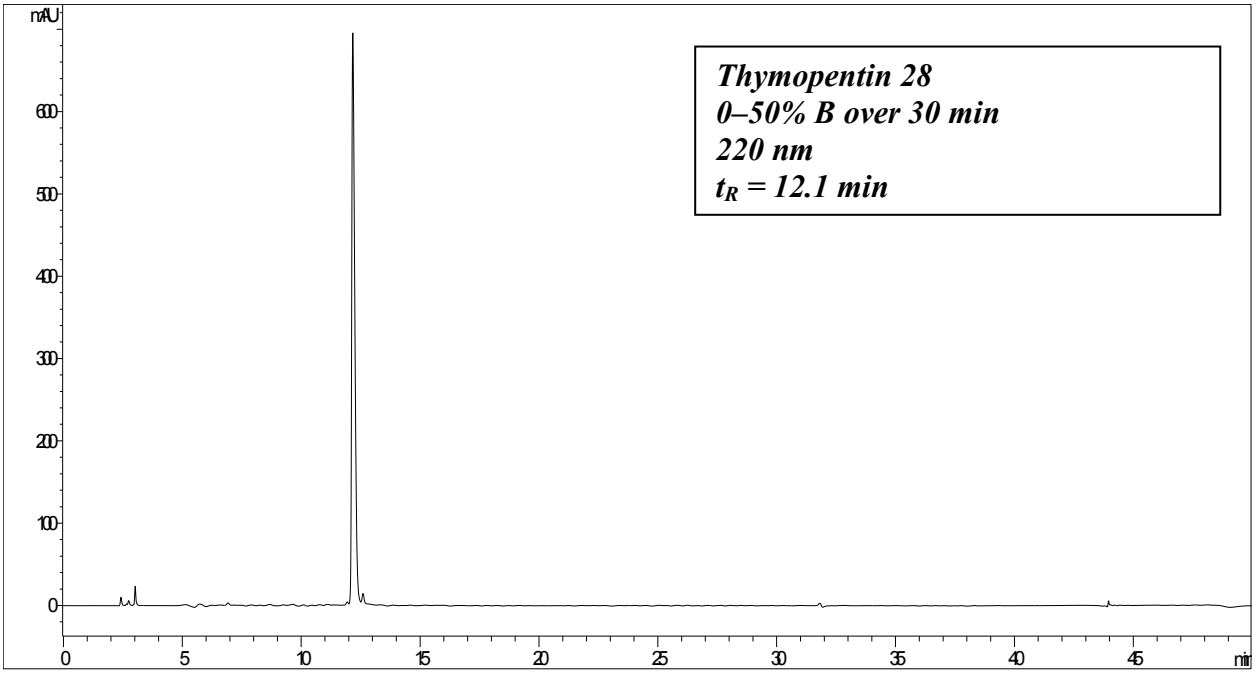


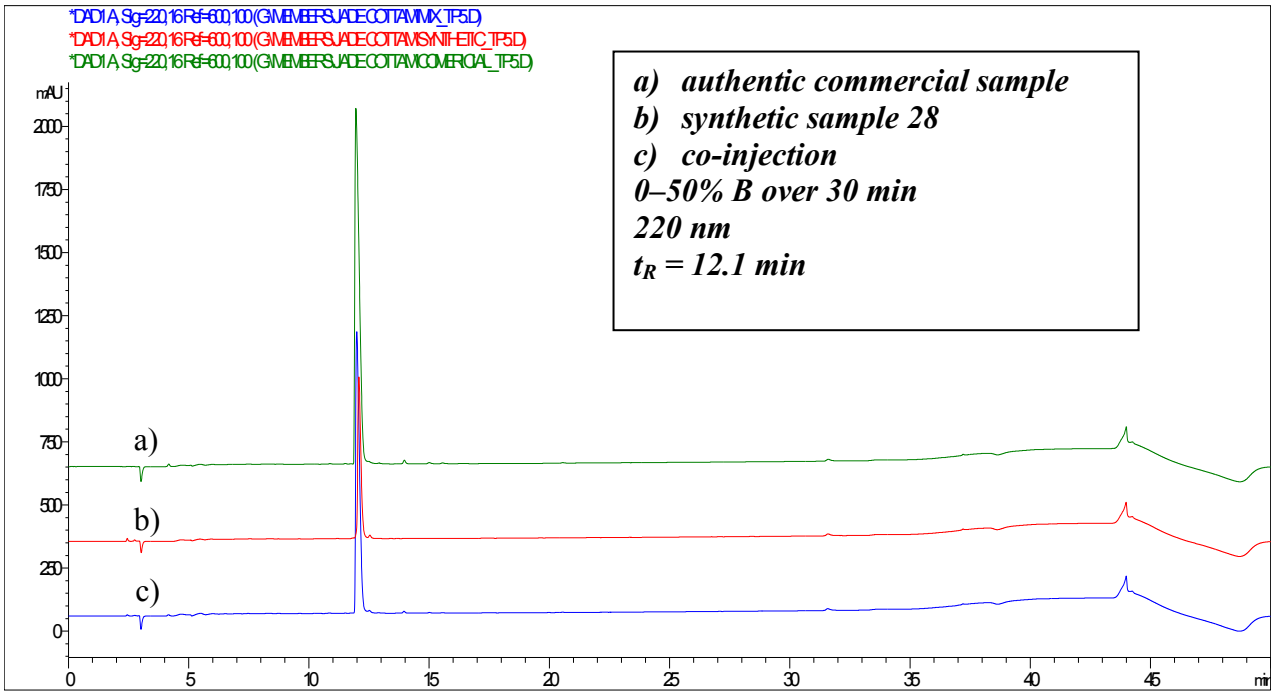
Compound 28 (125 MHz, D_2O)



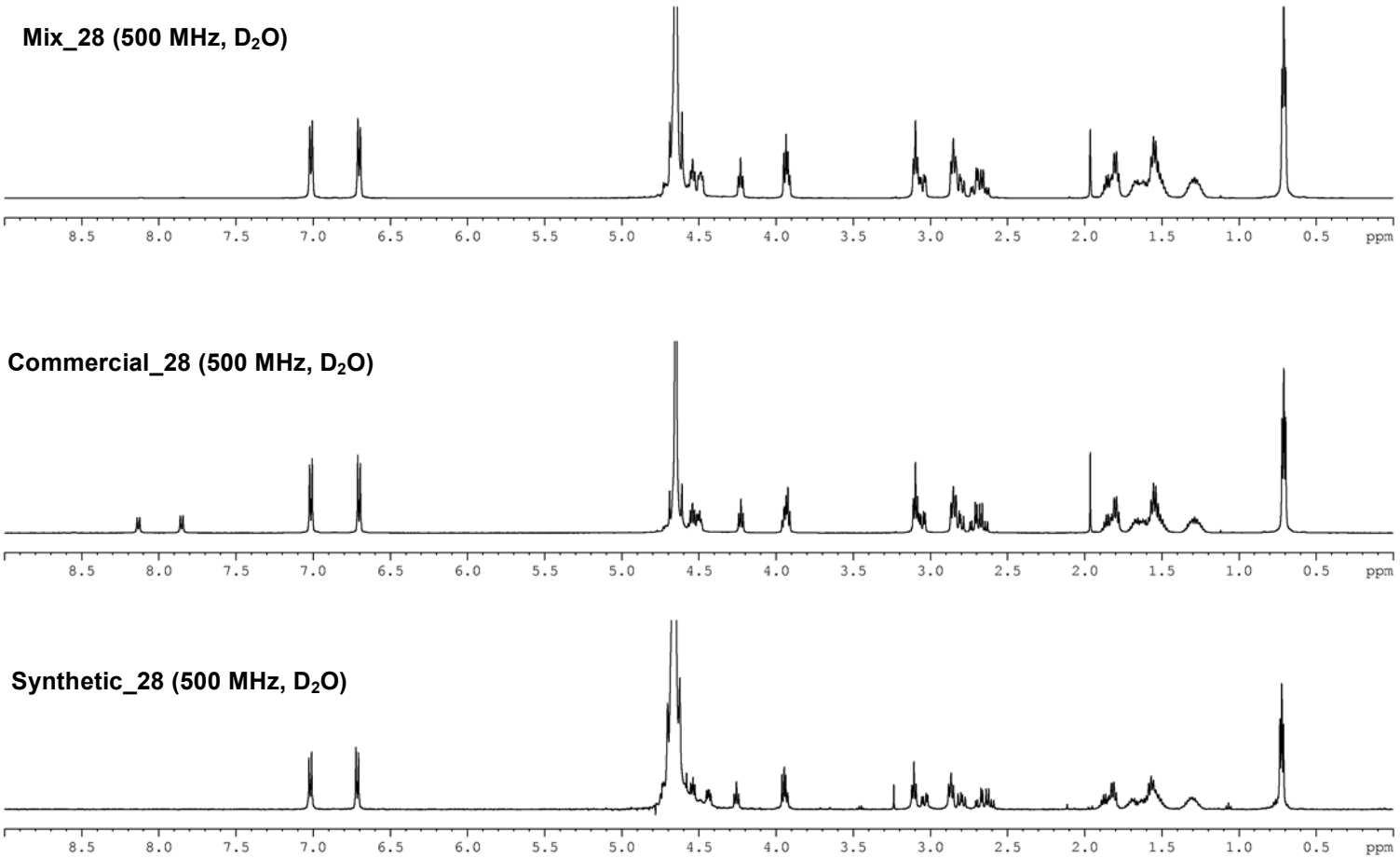
HPLC analysis of thymopentin 28

Analytical HPLC was performed using a SGE Protecol-P C18 HPH 125 column (4.6 × 150 mm column, 5 μm particle size, flow rate of 1 mL min^{-1}).





^{1}H NMR comparison of synthetic and commercial thymopentin 28



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