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SUPPLEMENTARY INFORMATION

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Asymmetric formation of γ-lactams via C–H amidation enabled by chiral hydrogen-bond-donor catalysts

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Supplementary Information

Asymmetric Formation of γ-Lactams via C−H Amidation Enabled by Chiral Hydrogen-Bond-Donor Catalysts

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Supplementary Methods

General Considerations

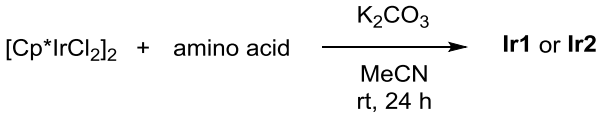
Unless otherwise stated, all commercial reagents and solvents were used without additional purification. 1,1,2,2-Tetrachloroethane, dichloromethane, and tetrahydrofuran were degassed and dried over activated 4 Å molecular sieve. ^{1}H NMR spectra were recorded on Agilent Technologies DD2 (600 MHz) or Bruker AVHD-400 (400 MHz) at the room temperature, unless otherwise noted. Chemical shifts were quoted in parts per million (ppm) referenced to the residual solvent peak. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, t = triplet, appt = apparent triplet, q = quartet, p = pentet, hept = heptet, m = multiplet, br = broad. Coupling constants, *J*, were reported in hertz (Hz). ^{13}C NMR spectra were obtained on Agilent Technologies DD2 (150 MHz), Bruker AVHD-400 (100 MHz) and was fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the residual solvent peak. ^{19}F NMR spectra were recorded on Agilent Technologies DD2 (564 MHz), and chemical shifts were reported in ppm referenced to external α,α,α-trifluorotoluene as -63.72 ppm. Infrared (IR) spectra were recorded on Bruker Alpha FT-IR Spectrometer. Frequencies are given in reciprocal centimeters (cm^{-1}) and only selected absorbance is reported. Frequencies are given in wave numbers (cm^{-1}) and only selected peaks were reported. High resolution mass spectra were obtained from the Korea Basic Science Institute (Daegu) by using EI or FAB method and from the KAIST Research Analysis Center by using ESI method. X-ray diffraction data was collected on a Bruker SMART APEX III coated with Paraton-*N* oil under a stream of N_2 (g) at 133 K. Melting point was measured with Buchi Melting Point M-565. High pressure liquid chromatography (HPLC) analysis was performed at 32 ^{o}C with Shimadzu Prominence HPLC system composed of LC20A pump, and SPD-M20A photodiode array detector. Optical rotations were recorded with Jasco P-2000 Polarimeter equipped with temperature controller.

Procedures for the Preparation of Iridium Catalysts

D-Proline, D-*tert*-leucine, (1*S*,2*S*)-2-amino-1,2-diphenylethan-1-ol, D-prolinamide, (1*S*,2*S*)-cyclohexane-1,2-diamine, (1*S*,2*S*)-1,2-diphenylethane-1,2-diamine, *N*-{(1*S*,2*S*)-2-amino-1,2-diphenylethyl}-4-methylbenzenesulfonamide, (1*S*,2*S*)-1,2-dimesitylethane-1,2-diamine were purchased from Sigma-Aldrich, TCI chemical company, and Strem, and used without further purification.

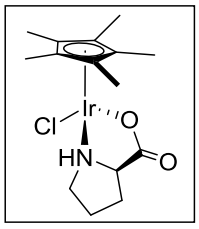
N-{(1*S*,2*S*)-2-Aminocyclohexyl}-4-methylbenzenesulfonamide,[1] *N*-{(1*S*,2*S*)-2-amino-1,2-diphenylethyl}-4-methoxybenzenesulfonamide,[2] *N*-{(1*S*,2*S*)-2-amino-1,2-diphenylethyl}-4-fluorobenzenesulfonamide,[2] and *N*-{(1*S*,2*S*)-2-amino-1,2-dimesitylethyl}-4-methylbenzenesulfonamide[3] were synthesized according to previously reported methods.

Preparation of Ir1 and Ir2



$[Cp^*IrCl_2]_2$ (200 mg, 0.25 mmol), amino acid (0.50 mmol) and K_2CO_3 (80 mg, 0.58 mmol) in acetonitrile (5 mL) were stirred for 24 h at room temperature. After completion, solvent was removed under reduced pressure, and the residue was suspended in dichloromethane (10 mL). The suspension was filtered through a pad of Celite, and further rinsed with additional dichloromethane (40 mL). The combined yellow filtrates were concentrated to 5.0 mL and layered with a large excess of dry pentane (30 mL). The precipitate was collected and was dried under reduced pressure to afford the desired complexes.

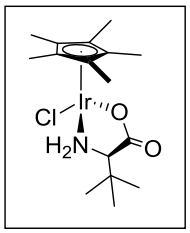
Ir1[4]



Yellow solid (155 mg, 65%); **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 4.53 – 4. 30 (m, 1H) 3.98 – 3.85 (m, 1H), 3.65 – 3.52 (m, 1H), 3.01 – 2.84 (m, 1H), 2.28 – 2.14 (m, 1H), 2.01 – 1.86 (m, 2H), 1.65 (s, 15H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 184.52, 84.62, 62.84, 55.40, 29.47, 27.55, 9.46.

NMR spectroscopic signatures were matched with previously reported ones.[5]

Ir2

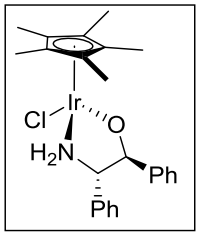


Yellow solid (227 mg, 92%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 5.33 (appt, J = 8.4 Hz, 1H), 3.78 (appt, J = 10.8 Hz, 1H), 2.97 (dd, J = 11.3, 6.7 Hz, 1H), 1.70 (s, 15H), 1.10 (s, 9H). Minor isomer: 4.36 – 4.25 (m, 1H), 4.00 – 3.87 (m, 1H), 3.18 – 3.08 (m, 1H), 1.69 (s, 15H), 1.09 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.94, 84.27, 65.45, 35.33, 27.07, 9.32, Minor isomer: 83.98, 61.99, 34.64, 27.03, 9.19.

NMR spectroscopic signatures were matched with previously reported ones.[5]

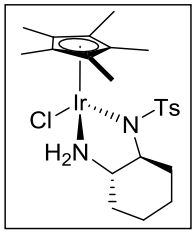
Preparation of Ir3 and Ir5 to Ir10

Ir3



Orange solid (201 mg, 70%); **m.p.** 164–166 °C (decomp.); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 3H), 7.07 – 6.97 (m, 7H), 4.85 (d, J = 9.8 Hz, 1H), 4.41 (appt, J = 11.3 Hz, 1H), 4.30 (d, J = 10.0 Hz, 1H), 3.21 – 3.04 (m, 1H), 1.78 (s, 15H); **^{13}C NMR** (151 MHz, $CDCl_3$, *one carbon merged to others*) δ 143.27, 139.13, 128.72, 128.21, 127.54, 127.41, 126.70, 85.10, 83.05, 73.72, 9.10. **IR** (cm^{-1}) 3203, 3025, 2914, 1492, 1376, 1023, 698, 579; **HRMS** (EI) m/z calcd. for $C_{24}H_{29}ClIrNO$ $[M+H]^+$: 576.1645, found: 576.1644.

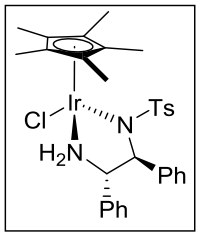
Ir5



Orange solid (100 mg, 62%, 0.13 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.83 (d, J = 7.9 Hz, 2H), 7.18 (d, J = 7.9 Hz, 2H), 4.05 (d, J = 10.3 Hz, 1H), 3.63 – 3.42 (m, 1H), 2.63 – 2.53 (m, 1H), 2.36 (s, 3H), 2.37 – 2.27 (m, 1H), 2.27 – 2.14 (m, 1H), 2.02 (d, J = 11.8 Hz, 1H), 1.67 (s, 15H), 1.50 (d, J = 13.4 Hz, 1H), 1.37 (d, J = 13.3 Hz, 1H), 1.29 – 1.15 (m, 1H), 1.12 – 1.04 (m, 1H), 0.97 – 0.81 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.07, 141.95, 130.32, 129.33, 87.11, 68.01, 65.77, 37.66, 35.45, 26.77, 26.74, 22.90, 11.08.

NMR spectroscopic signatures were matched with previously reported ones.[6]

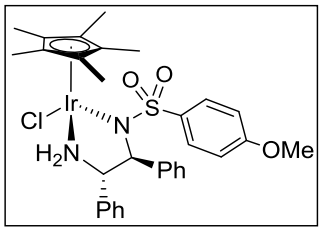
Ir6



Orange solid (290 mg, 80%); **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 7.33 (d, J = 8.0 Hz, 2H), 7.23 – 7.10 (m, 3H), 6.94 – 6.77 (m, 7H), 6.66 (d, J = 7.1 Hz, 2H), 4.42 (appt, J = 12.0 Hz, 1H), 4.28 (d, J = 10.9 Hz, 1H), 4.20 (d, J = 10.4 Hz, 1H), 3.68 (ddd, J = 13.8, 10.9, 3.0 Hz, 1H), 2.24 (s, 3H), 1.80 (s, 15H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 141.81, 140.11, 139.53, 139.29, 129.44, 129.13, 129.04, 128.65, 128.36, 127.63, 127.61, 127.01, 86.08, 74.41, 69.92, 21.44, 9.85.

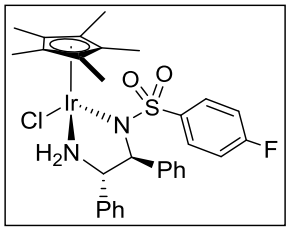
NMR spectroscopic signatures were matched with previously reported ones.[6]

Ir7



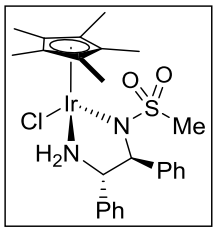
Orange solid (77 mg, 80%, 0.13 mmol scale); **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 7.37 (d, *J* = 8.9 Hz, 2H), 7.18 – 7.11 (m, 3H), 6.91 – 6.80 (m, 5H), 6.65 (d, *J* = 6.9 Hz, 2H), 6.54 (d, *J* = 8.9 Hz, 2H), 4.39 (appt, *J* = 12.1 Hz, 1H), 4.31 – 4.21 (m, 2H), 3.72 (s, 3H), 3.69 – 3.63 (m, 1H), 1.79 (s, 15H); **^{13}C NMR** (151 MHz, CD_2Cl_2) δ 160.96, 139.62, 139.31, 136.75, 130.51, 129.42, 129.11, 129.00, 127.63, 127.12, 112.96, 86.08, 74.41, 70.04, 55.80, 9.84; **HRMS** (ESI) m/z calcd. for $C_{31}H_{36}ClIrN_2O_3S$ $[M\text{-}Cl]^+$: 709.2076, found: 709.2096.

Ir8



Orange solid (221 mg, 85%); **m.p.** 239–241 °C (decomp.); **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 7.43 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.22 – 7.12 (m, 3H), 6.94 – 6.86 (m, 3H), 6.83 (appt, *J* = 7.5 Hz, 2H), 6.71 (appt, *J* = 8.6 Hz, 2H), 6.65 (d, *J* = 7.5 Hz, 2H), 4.39 (appt, *J* = 12.1 Hz, 1H), 4.35 – 4.25 (m, 2H), 3.70 (appt, *J* = 11.1, 1H), 1.80 (s, 15H); **^{13}C NMR** (150 MHz, CD_2Cl_2) δ 163.56 (d, *J* = 248.8 Hz), 141.08 (d, *J* = 3.1 Hz), 139.18, 139.13, 130.96 (d, *J* = 8.8 Hz), 129.44, 129.12, 129.04, 127.72, 127.60, 127.25, 114.46 (d, *J* = 114.5 Hz), 86.11 (C_5Me_5), 74.19, 69.93, 9.83 ($C_5\mathit{Me}_5$); **^{19}F NMR** (564 MHz, CD_2Cl_2) δ -112.4; **IR** (cm^{-1}) 1739, 1579, 1489, 1147, 908, 649, 552; **HRMS** (EI) m/z calcd. for $C_{30}H_{33}ClFIrN_2O_2S$ $[M]^+$: 732.1565, found: 732.1562.

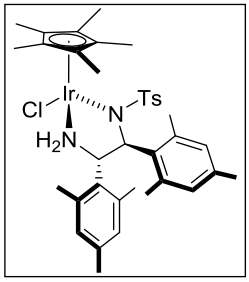
Ir9



Orange solid（290 g, 89%);**^{1}H NMR** (400 MHz, CD_2Cl_2) δ 7.27 – 7.17 (m, 3H), 7.17 – 7.09 (m, 3H), 7.08 – 7.03 (m, 2H), 7.02 – 6.96 (m, 2H), 4.52 – 4.36 (m, 2H), 4.34 – 4.16 (m, 1H), 3.85 – 3.71 (m, 1H), 2.28 (s, 3H), 1.72 (s, 15H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 141.32, 139.18, 129.26, 129.20, 129.17, 128.46, 127.80, 127.71, 86.02 (C_5Me_5), 73.93, 69.79, 44.16, 9.68 ($C_5\mathit{Me}_5$).

NMR spectroscopic signatures are matched with previously reported ones.[7]

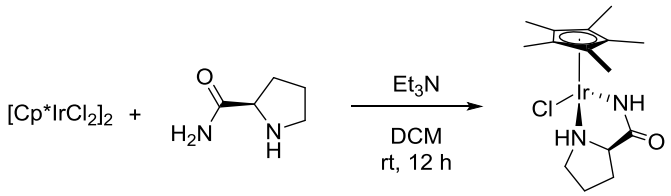
Ir10



Orange solid (218 mg, 93%, 0.289 mmol scale); **m.p.** 176–178 °C (decomp.); **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 7.25 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 6.1 Hz, 2H), 6.77 (s, 1H), 6.53 (s, 1H), 6.28 (s, 1H), 6.15 (s, 1H), 5.35 – 5.33 (m, 1H), 5.19 (appt, J = 12.2 Hz, 1H), 4.57 – 4.47 (m, 1H), 3.99 (d, J = 10.2 Hz, 1H), 2.74 (s, 3H), 2.50 (s, 3H), 2.23 (s, 3H), 2.13 (s, 3H), 2.01 (s, 3H), 1.77 (s, 15H), 1.69 (s, 3H), 1.56 (s, 3H); **^{13}C NMR** (101 MHz, CD_2Cl_2, *one carbon merged to others*) δ 141.64, 139.77, 138.92, 138.34, 138.27, 136.64, 136.31, 132.20, 131.92, 131.65, 130.57,

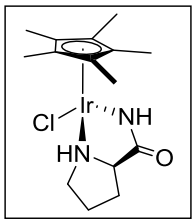
129.82, 128.81, 127.99, 127.89, 86.18 (C_5Me_5), 64.90, 61.72, 22.70, 22.00, 21.41, 21.03, 20.90, 20.80, 20.42, 10.06 ($C_5\mathit{Me}_5$); **IR** (cm^{-1}) 2956, 2916, 2852, 1739, 1611, 1454, 1376, 1129, 1084, 896, 666, 571, 549; **HRMS** (EI) m/z calcd. for $C_{37}H_{48}ClIrN_2O_2S$ $[M]^+$: 812.2754, found: 812.2752.
Solid-state structure was characterized by X-ray diffraction analysis (CCDC 1884674).

Preparation of Ir4[8]



$[Cp^*IrCl_2]_2$ (350 mg, 0.44 mmol), D-prolinamide (100 mg, 0.88 mmol), and triethylamine (93 mg, 0.92 mmol) in dichloromethane (8 mL) were stirred for 12 h at room temperature. To the reaction was added 20% NaCl (aq), and the mixture was extracted with dichloromethane (10 mL x 2), dried under Na_2SO_4, and solvent was removed under reduced pressure. The resulting solid was re-dissolved in 5 mL of THF/diisopropyl ether (1/1) solution, and stirred for 1 h at room temperature. Orange precipitate was collected and dried under reduced pressure to afford the desired complex.

Ir4

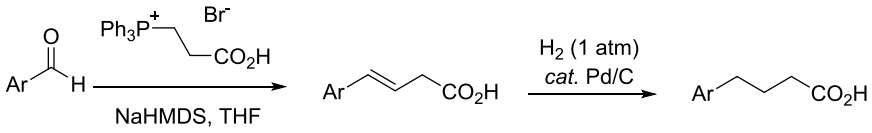


Orange solid (301 mg, 72%); **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 4.96 (br, 1H), 4.86 (br, 1H), 3.83 (q, J = 8.0 Hz, 1H), 3.58 – 3.45 (m, 1H), 3.00 – 2.64 (m, 1H), 2.45 – 2.22 (m, 1H), 2.22 – 2.08 (m, 1H), 1.98 – 1.85 (m, 2H), 1.71 (s, 15H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 184.03, 84.92, 63.26, 55.04, 29.00, 27.61, 9.45; **IR** (cm^{-1}) 3119, 2967, 291, 1740, 1583, 1446, 1378, 1032, 923; **HRMS** (EI) m/z calcd. for $C_{15}H_{24}ClIrN_2O$ $[M+H]^+$: 477.1285, found: 477.1281.
NMR spectroscopic signatures are matched with previously reported ones.[8]

Procedures for the Preparation of Starting Materials

4-(4-Chlorophenyl)butanoic acid, 4-(*p*-tolyl)butanoic acid, 4-{4-(*tert*-butyl)phenyl}butanoic acid, 4-{4-(trifluoromethyl)phenyl}butanoic acid, 4-(naphthalen-2-yl)butanoic acid, 5-cyclohexylpentanoic acid, 6-phenylhexanoic acid, 6-aminohexanoic acid, 5-phenylpentanoic acid, 5-methylhexanoic acid, myristic acid, oleic acid, elaidic acid, and 2-{1-(aminomethyl)cyclopentyl}acetic acid were purchased from Sigma-Aldrich, Alfa, Enamine, or TCI chemical company, and used without further purification. 4-(4-Iodophenyl)butanoic acid was synthesized according to previously reported methods.[9]

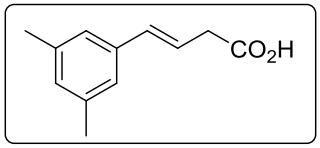
Preparation of carboxylic acids from aldehyde precursors[10]



A 100 mL round-bottom flask were added (2-carboxyethyl)triphenylphosphonium bromide (2.41 g, 6 mmol) and dry THF (18 mL) under Ar atmosphere. The reaction mixture was cooled to 0 ℃, then NaHMDS (2.29 g, 12.5 mmol) was added to the mixture. The solution was stirred at 0 ℃ for 15 min, and substituted benzaldehyde (5 mmol) was directly added. The solution was stirred at room temperature for overnight. The resulting reaction mixture was concentrated under reduced pressure, and the residue was treated with aqueous NaOH (2 N). The mixture was washed with CH_2Cl_2 for three times. 3N HCl was added to aqueous NaOH at 0 ℃, and the solution was stirred at 0 ℃. After 1 h, dichloromethane was added to the aqueous solution, and the organic phase was washed with H_2O, and dried over anhydrous $MgSO_4$. The filtrate was concentrated under reduced pressure, and purified by flash chromatography (*n*-hexane/EtOAc) to afford the olefin products.

A solution of the olefin, 10 mol % Pd/C and ethanol (0.1 M) were purged with hydrogen gas (1 atm) and stirred for overnight. The reaction was then filtered through a pad of Celite, and solvent was removed under reduced pressure to afford the desired carboxylic acid.

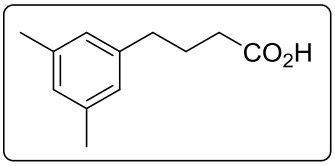
(*E*)-4-(3,5-Dimethylphenyl)but-3-enoic acid



Yellow oil (290 mg, 30%, 5 mmol scale); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (s, 2H), 6.89 (s, 1H), 6.46 (d, J = 15.9 Hz, 1H), 6.26 (dt, J = 15.9, 7.1 Hz, 1H), 3.29 (dd, J = 7.1, 1.4 Hz, 2H), 2.30 (s, 6H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 177.99, 138.15, 136.66, 134.26, 129.56, 124.35, 120.48, 77.48, 77.16, 76.84, 38.16, 21.38.

NMR spectroscopic signatures are matched with previously reported ones.[11]

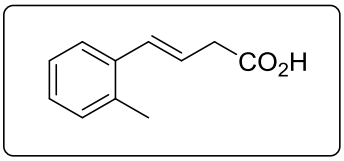
4-(3,5-Dimethylphenyl)butanoic acid



Colorless oil (285 mg, 99%, 1.47 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 12.5 – 10.6 (br, 1H), 6.84 (s, 1H), 6.81 (s, 2H), 2.60 (t, J = 7.6 Hz, 2H), 2.38 (t, J = 7.5 Hz, 2H), 2.29 (s, 6H), 1.95 (p, J = 7.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.67, 141.26, 138.04, 127.82, 126.46, 35.00, 33.49, 26.37, 21.39

NMR spectroscopic signatures are matched with previously reported ones.[11]

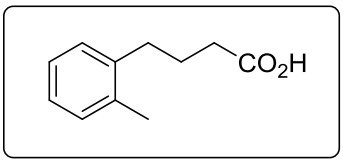
(*E*)-4-(*o*-Tolyl)but-3-enoic acid



White solid (500 mg, 28%, 10 mmol scale);**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.51 (m, 1H), 7.19 – 7.13 (m, 3H), 6.74 (d, J = 15.7 Hz, 1H), 6.18 (dt, J = 15.7, 7.1 Hz, 1H), 3.34 (dd, J = 7.1, 1.6 Hz, 2H), 2.35 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.23, 135.92, 135.42, 132.04, 130.38, 127.74, 126.24, 125.88, 122.24, 38.46, 19.91.

NMR spectroscopic signatures are matched with previously reported ones.[12]

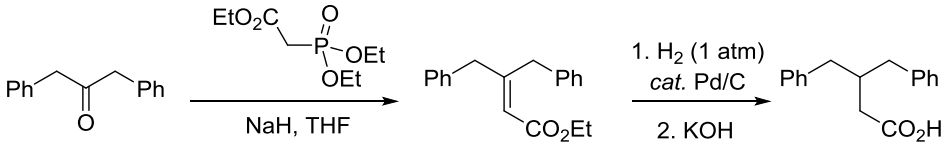
4-(*o*-Tolyl)butanoic acid



White solid (400 mg, 87%);**^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.20 – 7.02 (m, 4H), 2.66 (t, J = 7.4 Hz, 2H), 2.43 (t, J = 7.3 Hz, 2H), 2.31 (s, 3H), 1.93 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.73, 139.55, 136.10, 130.43, 129.09, 126.34, 126.12, 33.71, 32.56, 25.14, 19.35.

NMR spectroscopic signatures are matched with previously reported ones.[13]

Preparation of 3-benzyl-4-phenylbutanoic acid[14]

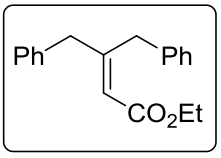


To a round bottom flask containing 60% dispersion NaH (600 mg, 1.5 equiv) and anhydrous THF (25 mL) at 0° C. was added triethylphosphonoacetate (3.70 g, 1.65 equiv). The reaction mixture was warmed to room temperature, followed by dropwise addition of diphenyl acetone (2.10 g, 10 mmol). The reaction mixture was stirred for 12 h, poured in water and extracted with DCM. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. This was purified by flash chromatograph (*n*-hexane/EtOAc) to give the olefin product.

A solution of the olefin (720 mg, 2.57 mmol), Pd/C (270mg, 10 mol %) and ethanol (0.1 M) were purged with hydrogen gas (1 atm) and stirred for overnight. The reaction was then filtered through a pad of Celite, and solvent was removed under reduced pressure to afford the desired ester. To the ester was added potassium hydroxide (413 mg, 4 equiv) in ethanol (6 mL) and H_2O (4 mL). The reaction

mixture was heated to 70 °C for 4 h, and 1N HCl was slowly added until pH of 2 under room temperature. Ethanol was removed under reduced pressure, and the aqueous solution was extracted with EtOAc (3 times). After washed with brine, organic phase was separated and dried over $MgSO_4$, followed by removal of solvent gave the afford carboxylic acid.

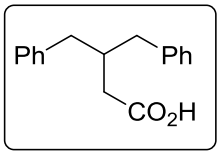
Ethyl 3-benzyl-4-phenylbut-2-enoate



Colorless oil (720 mg, 25%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 4H), 7.22 – 7.15 (m, 4H), 7.06 (d, J = 7.2 Hz, 1H), 5.70 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.95 (s, 2H), 3.30 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) 166.70, 159.95, 138.88, 137.85, 129.49, 129.21, 128.72, 128.65, 126.81, 126.47, 118.54, 60.05, 43.55, 36.88, 14.44.

NMR spectroscopic signatures are matched with previously reported ones.[14]

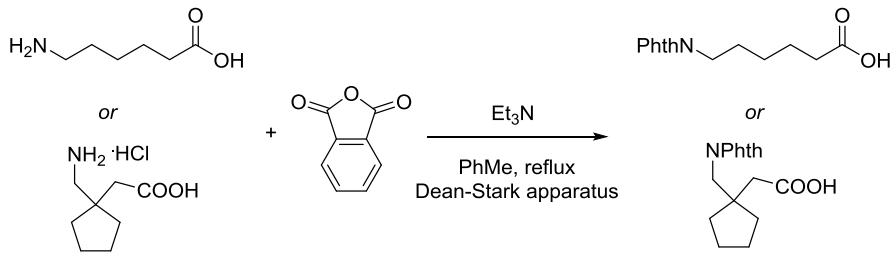
3-Benzyl-4-phenylbutanoic acid



White solid (653 mg, 99% combined yield for two steps); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.29 (appt, J = 7.5 Hz, 4H), 7.35 – 7.23 (m, 6H), 2.72 – 2.66 (m, 2H), 2.66 – 2.59 (m, 2H), 2.49 (hept, J = 7.0 Hz, 1H), 2.27 (d, J = 6.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.87, 139.98, 129.42, 128.53, 126.35, 40.18, 39.00, 37.49.

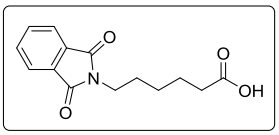
NMR spectroscopic signatures are matched with previously reported ones. [14]

Preparation of *N*-protected carboxylic acids



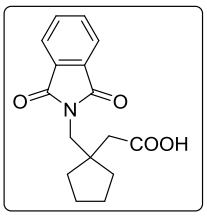
A suspension of substrate (20 mmol), phthalic anhydride (3.0 g, 20 mmol) and triethylamine (0.28 mL, 2.0 mmol) in toluene (20 mL) was stirred at 130 °C for 4 h, equipped with Dean-Stark apparatus. After completion, solvent was removed under reduced pressure. The crude product was dissolved in dichloromethane (150 mL), and washed with aqueous HCl (0.5-1.0 M, 100 mL x2) and brine (100 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and filtered through a pad of Celite and washed with DCM (30 mL) to afford the corresponding products.

6-(1,3-Dioxoisoindolin-2-yl)hexanoic acid



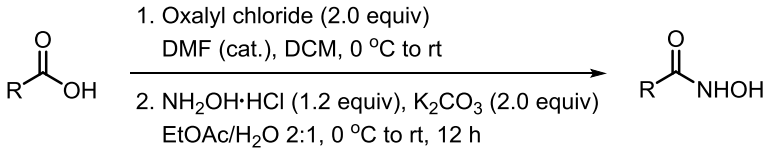
White solid (4.96 g, 95%); **^{1}H NMR** (599 MHz, DMSO-d_6) δ 11.98 (s, 1H), 8.02 – 7.64 (m, 4H), 3.55 (t, J = 7.1 Hz, 2H), 2.18 (t, J = 7.4 Hz, 2H), 1.58 (p, J = 7.4 Hz, 2H), 1.50 (p, J = 7.5 Hz, 2H), 1.27 (p, J = 8.0 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 174.37, 167.93, 134.36, 131.60, 122.99, 37.26, 33.44, 27.68, 25.77, 24.04. NMR spectroscopic signatures are matched with previously reported ones.[15]

2-[1-{(1,3-Dioxoisoindolin-2-yl)methyl}cyclopentyl]acetic acid



White solid (650 mg, 88%, 2.58 mmol scale); **m.p.** 101–103 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.78 – 7.70 (m, 2H), 3.81 (s, 2H), 2.45 (s, 2H), 1.85 – 1.75 (m, 2H), 1.75 – 1.65 (m, 4H), 1.62 – 1.52 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.26, 169.66, 134.29, 132.03, 123.57, 46.65, 44.69, 42.10, 35.91, 24.11; **IR** (cm^{-1}) 2945, 2870, 1768, 1701, 1616, 1421, 1336, 875, 712; **HRMS** (EI) m/z calcd. for $C_{16}H_{17}NO_4$ $[M]^+$: 287.1158, found: 287.1160.

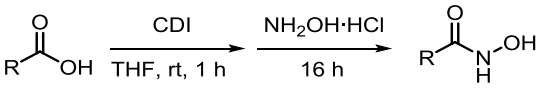
Preparation of Hydroxamic Acids



Procedure A[16] Carboxylic acids, oxalyl chloride (2.0 equiv.), DMF (2 drops), and dichloromethane (0.33 M) were added at 0 ºC. The mixture was allowed to stir at room temperature for 2 h, then the reaction mixture was concentrated to afford the acid chloride that was directly used in the next reaction.

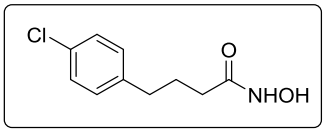
Hydroxylamine hydrochloride (1.2 equiv) was added to a biphasic mixture of K_2CO_3 (2.0 equiv) in a 2:1 mixture of EtOAc (0.5 M) and H_2O (0.25 M). The resulting solution was cooled to 0 °C, followed by dropwise addition of the unpurified acid chloride dissolved in a minimum amount of EtOAc under air. The flask containing the acid chloride was then rinsed with additional EtOAc. The reaction was warmed to room temperature for stirring additional 12 h. After completion, the phases were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by recrystallization (DCM+few drops of methanol/*n*-pentane) or silica chromatography (eluent: DCM/methanol = 30:1 ~ 10:1) to afford the desired hydroxamic acid.

Note: Procedure A was generally utilized for the synthesis, unless otherwise stated.



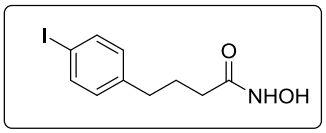
Procedure B[16] To a stirred solution of carboxylic acid in dry tetrahydrofuran (THF, 0.33 M) was added 1,1´-carbonyldiimidazole (CDI, 1.5 equiv) in one portion. The reaction mixture was stirred at room temperature for 1 h. Powdered hydroxylamine hydrochloride (2 equiv) was added, and the resulting mixture was stirred for overnight. The mixture was diluted with 5% aq. $KHSO_4$ (30 ml) and extracted with EtOAc. The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude mixture, which was further purified by silica gel column chromatography (eluent: DCM/methanol = 30:1 ~ 10:1) to obtain the hydroxamic acids.

4-(4-Chlorophenyl)-*N*-hydroxybutanamide



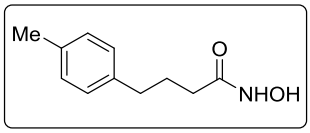
White solid (550 mg, 86%, 3 mmol scale); **m.p.** 81–83 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.36 (br, 1H), 8.70 (br, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 2.55 (t, J =7.5 Hz, 2H), 1.96 (t, J = 7.4 Hz, 2H), 1.77 (p, J = 7.4 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.76, 140.67, 130.39, 130.20, 128.22, 33.79, 31.60, 26.77; **IR** (cm^{-1}) 3198, 3036, 2899, 1621, 1491, 1078, 798, 592; **HRMS** (EI) m/z calcd. for $C_{10}H_{12}ClNO_2$ $[M]^+$: 213.0557, found: 213.0559.

***N*-Hydroxy-4-(4-iodophenyl)butanamide**



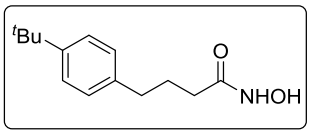
White solid (380 mg, 84%, 1.48 mmol scale); **m.p.** 144–146 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.35 (br, 1H), 8.69 (br, 1H), 7.62 (d, J = 7.8 Hz, 2H), 7.01 (d, J = 7.8 Hz, 2H), 2.52 – 2.50 (m, 2H), 1.94 (t, J = 7.5 Hz, 2H), 1.75 (p, J = 7.6 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 168.72, 141.44, 136.97, 130.83, 91.28, 33.93, 31.57, 26.63. **IR** (cm^{-1}) 3025, 3033, 2898, 1620, 1483, 1081, 1005, 817, 478; **HRMS** (EI) m/z calcd. for $C_{10}H_{12}INO_2$ $[M]^+$: 304.9913, found: 304.9915.

***N*-Hydroxy-4-(*p*-tolyl)butanamide**



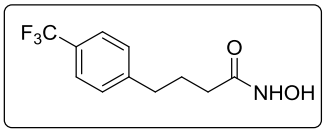
White solid (690 mg, 89%, 4 mmol scale); **m.p.** 100–102 °C; **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 10.34 (br, 1H), 8.68 (br, 1H), 7.14 – 6.99 (m, 4H), 2.52 – 2.49 (m, 2H), 2.25 (s, 3H), 1.95 (t, J = 7.4 Hz, 1H), 1.75 (p, J = 7.4 Hz, 1H); **^{13}C NMR** (101 MHz, DMSO-d$_6$) δ 168.90, 138.52, 134.63, 128.87, 128.18, 34.18, 31.76, 27.06, 20.62. **IR** (cm^{-1}) 3197, 3026, 2908, 2855, 1622, 1074, 806, 482; **HRMS** (EI) m/z calcd. for $C_{11}H_{15}NO_2$ $[M]^+$: 193.1103, found: 119.1105.

4-{4-(*tert*-Butyl)phenyl}-*N*-hydroxybutanamide



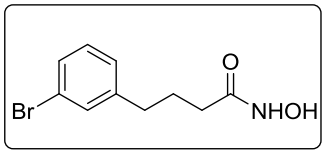
White solid (386 mg, 82%, 2 mmol scale); **m.p.** 78–80 °C; **^{1}H NMR** (400 MHz, DMSO-d_6, *two protons merged to the solvent residual peaks*) δ 10.35 (br, 1H), 8.68 (br, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.3 Hz, 2H), 1.96 (t, J = 7.4 Hz, 2H), 1.76 (p, J = 7.5 Hz, 2H), 1.26 (s, 9H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.89, 147.98, 138.54, 127.94, 125.00, 34.08, 34.05, 31.84, 31.22, 26.96; **IR** (cm^{-1}) 3234, 3143, 3061, 3019, 2958, 1898, 2862, 1619, 1078, 563; **HRMS** (EI) m/z calcd. for $C_{14}H_{21}NO_2$ $[M]^+$: 235.1572, found: 235.1573.

_N_-Hydroxy-4-{4-(trifluoromethyl)phenyl}butanamide



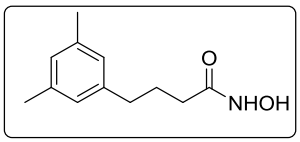
White solid (400 mg, 81%, 2 mmol scale); **m.p.** 92–94 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.35 (br, 1H), 8.68 (br, 1H), 7.61 (d, J = 7.9 Hz, 2H), 7.39 (d, J = 7.9 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.94 (t, J = 7.4 Hz, 2H), 1.79 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 168.66, 146.63, 129.12, 126.63 (q, J = 31.9 Hz), 125.10 (q, J = 3.9 Hz), 124.44 (q, J = 271.8 Hz), 34.25, 31.57, 26.50; **^{19}F NMR** (564 MHz, DMSO-d_6) δ -60.75; **IR** (cm^{-1}) 3214, 3040, 2929, 2871, 1626, 1322, 1109, 1065, 805, 586; **HRMS** (EI) m/z calcd. for $C_{11}H_{12}F_3NO_2$ $[M]^+$: 247.0820, found: 247.0823.

4-(3-Bromophenyl)-_N_-hydroxybutanamide



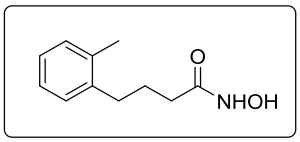
White solid (402 mg, 78%, 2 mmol scale); **m.p.** 98–100 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 8.70 (s, 1H), 7.44 – 7.35 (m, 2H), 7.30 – 7.10 (m, 2H), 2.55 (t, J = 7.6 Hz, 2H), 1.95 (t, J = 7.4 Hz, 2H), 1.77 (p, J = 7.8 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.75, 144.61, 131.06, 130.47, 128.73, 127.49, 121.66, 34.07, 31.61, 26.70; **IR** (cm^{-1}) 3170, 3056, 2925, 1627, 1555, 971, 767, 665; **HRMS** (EI) m/z calcd. for $C_{10}H_{12}BrNO_2$ $[M]^+$: 257.0051, found: 257.0054.

4-(3,5-Dimethylphenyl)-_N_-hydroxybutanamide



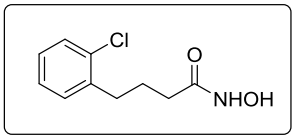
White solid (240 mg, 79%, 1.46 mmol scale); **m.p.** 94–96 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.34 (br, 1H), 8.67 (br, 1H), 6.79 (s, 1H), 6.77 (s, 2H), 2.46 (t, J = 7.7 Hz, 2H), 1.95 (t, J = 7.4 Hz, 2H), 1.75 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.90, 141.46, 137.11, 127.21, 126.10, 34.49, 31.84, 26.98, 20.92; **IR** (cm^{-1}) 3251, 3011, 2952, 2911, 2858, 1617, 1458, 1077, 1052, 954, 840, 702, 528; **HRMS** (EI) m/z calcd. for $C_{12}H_{17}NO_2$ $[M]^+$: 207.1259, found: 207.1261.

_N_-Hydroxy-4-(_o_-tolyl)butanamide



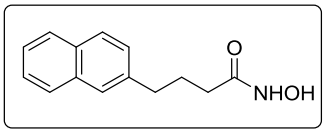
White solid (330 mg, 85%); **m.p.** 78–80 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.63 (br, 1H), 8.95 (br, 1H), 7.41 – 7.30 (m, 4H), 3.60 (s, 3H), 2.78 (t, J = 7.4 Hz), 2.27 (t, J = 7.3 Hz, 1H), 1.98 (p, J = 7.5 Hz, 1H).; **^{13}C NMR** (151 MHz, DMSO-d_6, *two carbons merged to others*) δ 168.89, 139.83, 135.44, 129.95, 128.63, 125.83, 2.01, 25.74, 18.79; **IR** (cm^{-1}) 3232, 3020, 2954, 2923, 2864, 1620, 1455, 1071, 939, 737, 545; **HRMS** (EI) m/z calcd. for $C_{12}H_{17}NO_2$ $[M]^+$: 207.1259, found: 207.1261.

4-(2-Chlorophenyl)-*N*-hydroxybutanamide



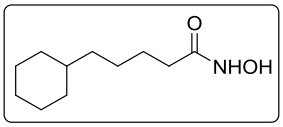
White solid (307 mg, 72%, 2 mmol scale); **m.p.** 86–88 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.39 (br, 1H), 8.71 (br, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.36 – 7.14 (m, 3H), 2.67 (t, J = 7.8 Hz, 2H), 2.00 (t, J = 7.5 Hz, 2H), 1.78 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.68, 138.97, 132.86, 130.67, 129.23, 127.88, 127.29, 32.30, 31.82, 25.31. **IR** (cm^{-1}) 3166, 3036, 2973, 2868, 1654, 1428, 1069, 744, 594; **HRMS** (EI) m/z calcd. for $C_{10}H_{12}ClNO_2$ $[M]^+$: 213.0557, found: 213.0560.

***N*-Hydroxy-4-(naphthalen-2-yl)butanamide**



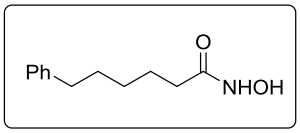
White solid (219 mg, 75%, 1.11 mmol scale); **m.p.** 126–128 °C;**^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.36 (br, 1H), 8.69 (br, 1H), 7.89 – 7.80 (m, 3H), 7.68 (s, 1H), 7.52 – 7.42 (m, 2H), 7.37 (dd, J = 8.4, 1.7 Hz, 1H), 2.73 (t, J = 7.6 Hz, 2H), 2.01 (t, J = 7.4 Hz, 2H), 1.89 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 168.84, 139.26, 133.15, 131.58, 127.72, 127.42, 127.28, 126.11, 125.91, 125.16, 34.68, 31.75, 26.74; **IR** (cm^{-1}) 3167, 3017, 2915, 2853, 1651, 1548, 1361, 1070, 823, 741, 472; **HRMS** (EI) m/z calcd. for $C_{14}H_{15}NO_2$ $[M]^+$: 229.1103, found: 229.1107.

5-Cyclohexyl-*N*-hydroxypentanamide



White solid (917 mg, 92%, 5 mmol scale); **m.p.** 56–58 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.64 (s, 1H), 1.92 (t, J = 7.4 Hz, 2H), 1.68 – 1.57 (m, 5H), 1.44 (p, J = 7.4 Hz, 2H), 1.27 – 1.04 (m, 8H), 0.88 – 0.77 (m, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6, one carbon merged to others) δ 169.08, 36.92, 36.57, 32.83, 32.28, 26.19, 25.82, 25.39; **IR** (cm^{-1}) 3258, 2918, 2848, 1620, 1542, 1445, 540, 483; **HRMS** (FAB) m/z calcd. for $C_{11}H_{21}NO_2$ $[M+H]^+$: 200.1651, found: 200.1647.

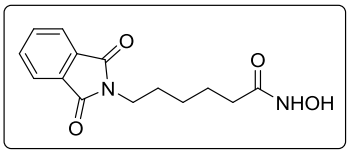
***N*-Hydroxy-6-phenylhexanamide**



White solid (922 mg, 89%, 5 mmol scale);**^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.33 (br, 1H), 8.66 (br, 1H), 7.26 (appt, J = 7.5 Hz, 2H), 7.20 – 7.14 (m, 3H), 2.55 (t, J = 7.7 Hz, 2H), 1.93 (t, J = 7.4 Hz, 2H), 1.59 – 1.46 (m, 4H), 1.25 (p, J = 7.7 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 169.04, 142.21, 128.24, 128.20, 125.59, 35.04, 32.18, 30.70, 28.22, 24.94.

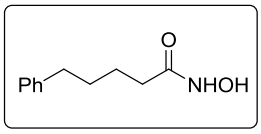
NMR spectroscopic signatures are matched with previously reported ones.[17]

6-(1,3-Dioxoisoindolin-2-yl)-*N*-hydroxyhexanamide



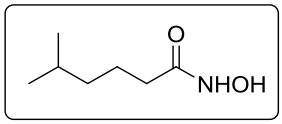
Procedure B was utilized. White solid (1.28 g, 93%, 5 mmol scale); **m.p.** 123–125 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.32 (br, 1H), 8.66 (br, 1H), 7.93 – 7.75 (m, 4H), 3.54 (t, *J* = 7.1 Hz, 2H), 1.92 (t, *J* = 7.4 Hz, 2H), 1.57 (p, *J* = 7.4 Hz, 2H), 1.50 (p, *J* = 7.5 Hz, 2H), 1.23 (p, *J* = 7.8 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 168.95, 167.91, 134.36, 131.58, 122.98, 37.29, 32.04, 27.71, 25.85, 24.67; **IR** (cm^{-1}) 3248, 2929, 2861, 1711, 1614, 1395, 1047, 720, 530; **HRMS** (EI) m/z calcd. for $C_{14}H_{16}N_2O_4$ $[M]^+$: 276.1110, found: 276.1112.

***N*-Hydroxy-5-phenylpentanamide**



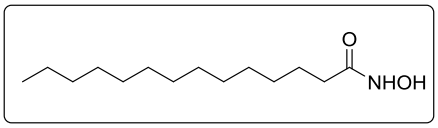
White solid (889 mg, 92%, 5 mmol scale); **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.72 (s, 1H), 7.27 (appt, J = 7.5 Hz, 2H), 7.17 (d, J = 7.6 Hz, 3H), 2.55 (t, J = 7.1 Hz, 2H), 1.97 (t, J = 6.8 Hz, 2H), 1.58 – 1.46 (m, 4H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 169.00, 142.06, 128.26, 128.22, 125.63, 34.82, 32.11, 30.56, 24.78.
NMR spectroscopic signatures are matched with previously reported ones.[18]

***N*-Hydroxy-5-methylhexanamide**



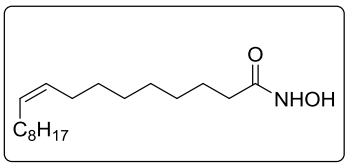
White solid (603 mg, 83%, 5 mmol scale); **m.p.** 74–76 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.31 (br, 1H), 8.64 (br, 1H), 1.91 (t, *J* = 7.4 Hz, 2H), 1.54 – 1.44 (m, 3H), 1.11 (q, *J* = 7.1 Hz, 2H), 0.84 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 169.07, 37.86, 32.45, 27.17, 22.94, 22.39; **IR** (cm^{-1}) 3197, 2965, 2936, 2868, 1624, 1544, 1121, 1063, 657, 607; **HRMS** (FAB) m/z calcd. for $C_7H_{15}NO_2$ $[M+H]^+$: 146.1181, found: 146.1183.

***N*-Hydroxytetradecanamide**



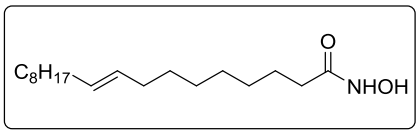
White solid (1.13 g, 93%, 5.0 mmol scale); **m.p.** 88–90 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.31 (br, 1H), 8.64 (br, 0H), 1.92 (t, *J* = 7.3 Hz, 2H), 1.54 – 1.41 (m, 2H), 1.33 – 1.12 (m, 20H), 0.85 (t, J = 6.6 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6, *three carbons merged to others*) δ 169.11, 32.26, 31.31, 29.07, 29.04, 28.97, 28.77, 28.73, 28.61, 25.13, 22.11; **IR** (cm^{-1}) 3249, 3063, 2954, 2846, 1660, 1620, 1470, 717, 511.

***N*-Hydroxyoleamide**



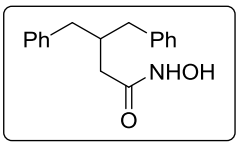
White solid (1.27 g, 86%, 5.0 mmol scale); **m.p.** 66–68 °C; **^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.31 (br, 1H), 8.64 (br, 1H), 5.38 – 5.26 (m, 2H), 1.98 (q, J = 6.5 Hz, 4H), 1.92 (t, J = 7.4 Hz, 2H), 1.46 (p, J = 7.3 Hz, 2H), 1.31 – 1.20 (m, 20H), 0.85 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, DMSO-d_6, *one carbon merged to others*) δ 169.04, 129.60, 129.58, 32.23, 31.25, 29.10, 29.07, 28.80, 28.65, 28.60, 28.57, 28.53, 26.59, 26.55, 25.09, 22.06, 13.90; **IR** (cm^{-1}) 3280, 2916, 2848, 1664, 1462, 1067, 978, 726; **HRMS** (EI) m/z calcd. for $C_{18}H_{35}NO_2$ $[M]^+$: 297.2668, found: 297.2664.

(*E*)-*N*-Hydroxyoctadec-9-enamide



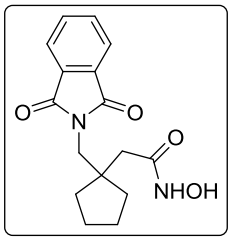
White solid (1.27 g, 86%, 5.0 mmol scale); **m.p.** 90–92 °C;**^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.32 (br, 1H), 8.64 (br, 1H), 5.43 – 5.29 (m, 2H), 2.03 – 1.81 (m, 6H), 1.46 (p, *J* = 7.2 Hz, 2H), 1.33 – 1.17 (m, 20H), 0.85 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR** (101 MHz, DMSO-d_6, *three carbons merged to others*) δ 169.08, 130.07, 130.05, 32.25, 31.96, 31.28, 29.01, 28.82, 28.70, 28.59, 28.50, 28.43, 25.12, 22.10, 13.95; **IR** (cm^{-1}) 3249, 2913, 2847, 1659, 1468, 1065, 963, 718; **HRMS** (FAB) m/z calcd. for $C_{18}H_{35}NO_2$ $[M+H]^+$: 298.2746, found: 298.2748.

3-Benzyl-*N*-hydroxy-4-phenylbutanamide



White solid (550 mg, 84%, 2.4 mmol scale); **m.p.** 89–91 °C;**^{1}H NMR** (599 MHz, DMSO-d_6) δ 10.41 (br, 1H), 8.74 (br, 1H), 7.29 (appt, *J* = 7.6 Hz, 4H), 7.19 (appt, J = 7.4 Hz, 2H), 7.13 (d, *J* = 7.5 Hz, 4H), 2.54 – 2.43 (m, 4H), 2.37 (hept, *J* = 6.6 Hz, 1H), 1.84 (d, *J* = 6.8 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 168.27, 140.10, 128.98, 128.25, 125.89, 38.83, 38.43, 35.79; **IR** (cm^{-1}) 3220, 3026, 2912, 1626, 747, 738, 504; **HRMS** (EI) m/z calcd. for $C_{17}H_{19}NO_2$ $[M]^+$: 269.1416, found: 269.1419.

2-[1-{(1,3-Dioxoisoindolin-2-yl)methyl}cyclopentyl]-*N*-hydroxyacetamide

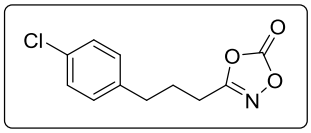


Procedure B was utilized. White solid (455 mg, 72%, 0.21 mmol scale); **^{1}H NMR** (599 MHz, CD_3OD) δ 7.91 – 7.84 (m, 2H), 7.84 – 7.79 (m, 2H), 3.73 (s, 2H), 2.20 (s, 2H), 1.76 – 1.59 (m, 8H); **^{13}C NMR** (151 MHz, CD_3OD, *one carbonyl missing*) δ 170.91, 135.46, 133.30, 124.19, 48.45, 46.57, 41.39, 35.88, 25.01.

Preparation of 3-substituted-1,4,2-dioxazol-5-ones[19]

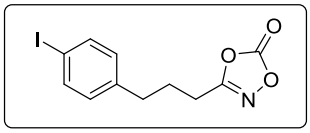
3-(3-Phenylpropyl)-1,4,2-dioxazol-5-one, 3-{3-(4-fluorophenyl)propyl}-1,4,2-dioxazol-5-one, 3-{3-(4-nitrophenyl)propyl}-1,4,2-dioxazol-5-one, 3-[{(3r,5r,7r)-adamantan-1-yl}methyl]-1,4,2-dioxazol-5-one, 3-(5-phenylpent-4-yn-1-yl)-1,4,2-dioxazol-5-one (*E*)-3-(6-phenylhex-5-en-1-yl)-1,4,2-dioxazol-5-one, 3-{(2,3-dihydro-1*H*-inden-2-yl)methyl}-1,4,2-dioxazol-5-one, and 3-(cyclohexylmethyl)-1,4,2-dioxazol-5-one were synthesized according to previously reported methods.[19]

3-{3-(4-Chlorophenyl)propyl}-1,4,2-dioxazol-5-one



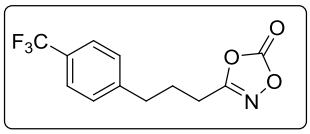
White solid (516 mg, 94%, 2.3 mmol scale); **m.p.** 37–39 °C;**^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.28 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 2.71 (t, J = 7.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.04 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.38, 154.14, 138.37, 132.51, 129.91, 128.95, 34.01, 25.92, 24.08; **IR** (cm^{-1}) 2926, 1899, 1866, 1828, 1788, 1633, 1492, 1392, 1353, 1217, 1094, 991, 801, 757, 516; **HRMS** (EI) m/z calcd. for $C_{11}H_{10}ClNO_3$ $[M]^+$: 239.0349, found: 239.0352.

3-{3-(4-Iodophenyl)propyl}-1,4,2-dioxazol-5-one



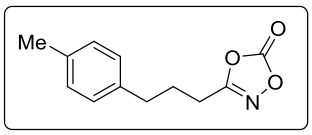
White solid (350 mg, 78%, 1.5 mmol scale); **m.p.** 57–59 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 2.69 (t, J = 7.5 Hz, 1H), 2.61 (t, J = 7.5 Hz, 1H), 2.04 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.36, 154.14, 139.55, 137.89, 130.63, 91.83, 34.16, 25.82, 24.09; **IR** (cm^{-1}) 2923, 1897, 1828, 1631, 1152, 989, 793, 758, 503; **HRMS** (EI) m/z calcd. for $C_{11}H_{10}INO_3$ $[M]^+$: 330.9705, found: 330.9707.

3-[3-{4-(Trifluoromethyl)phenyl}propyl]-1,4,2-dioxazol-5-one



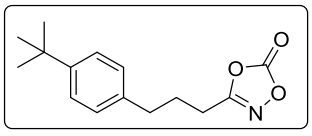
Colorless liquid (401 mg, 92%, 1.6 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.57 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 2.81 (t, J = 7.6 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H), 2.08 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.36, 154.14, 144.25, 128.89, 128.89 (q, J = 32.2 Hz), 125.63 (q, J = 3.7 Hz), 124.33 (q, J = 271.8 Hz). 34.36, 25.61, 24.03; **^{19}F NMR** (564 MHz, $CDCl_3$) δ -62.45; **IR** (cm^{-1}) 1871, 1827, 1322, 1156, 1108, 1066, 980, 761; **HRMS** (EI) m/z calcd. for $C_{12}H_{10}F_3NO_3$ $[M]^+$: 273.0613, found: 273.0610.

3-{3-(*p*-Tolyl)propyl}-1,4,2-dioxazol-5-one



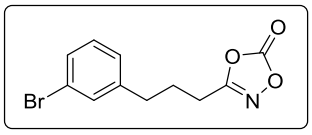
White solid (720 mg, 96%, 3.4 mmol scale); **m.p.** 42–44 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (d, J = 7.9 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H), 2.61 (t, J = 7.5 Hz, 2H), 2.33 (s, 3H), 2.04 (p, J = 7.4 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.63, 154.25, 136.80, 136.24, 129.47, 128.47, 34.24, 26.11, 24.13, 21.14; **IR** (cm^{-1}) 2921, 1898, 1866, 1829, 1630, 1515, 1393, 1153, 990, 802, 750, 530; **HRMS** (EI) m/z calcd. for $C_{12}H_{13}NO_3$ $[M]^+$: 219.0895, found: 219.0898.

3-[3-{4-(*tert*-Butyl)phenyl}propyl]-1,4,2-dioxazol-5-one



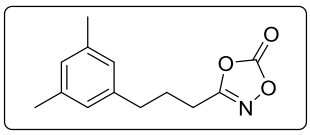
White solid (237 mg, 91%, 1.0 mmol scale); **m.p.** 47–49 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 2.72 (t, J = 7.3 Hz, 2H), 2.63 (t, J = 7.5 Hz, 2H), 2.07 (p, J = 7.4 Hz, 2H), 1.32 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.64, 154.23, 149.58, 136.78, 128.28, 125.68, 34.55, 34.15, 31.49, 25.97, 24.21; **IR** (cm^{-1}) 2957, 2864, 1882, 1867, 1821, 1761, 1653, 1163, 1149, 1000, 752, 543; **HRMS** (EI) m/z calcd. for $C_{15}H_{19}NO_3$ $[M]^+$: 261.1365, found: 261.1362.

3-{3-(3-Bromophenyl)propyl}-1,4,2-dioxazol-5-one



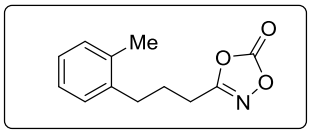
Colorless liquid (498 mg, 88%, 2 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.36 (d, J = 8.0 Hz, 1H), 7.34 (s, 1H), 7.18 (appt, J = 7.8 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 2.71 (t, J = 7.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.05 (p, J = 7.5 Hz, 2H); **IR** (cm^{-1}) 1870, 1823, 1146, 978, 778, 760, 693; **HRMS** (EI) m/z calcd. for $C_{11}H_{10}BrNO_3$ $[M]^+$: 282.9844, found: 282.9844.

3-{3-(3,5-Dimethylphenyl)propyl}-1,4,2-dioxazol-5-one



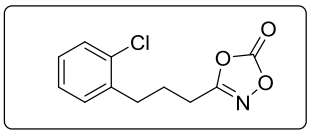
White solid (221 mg, 94%, 1.0 mmol scale); **m.p.** 34–36 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.79 (s, 2H), 2.66 (t, J = 7.4 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.04 (p, J = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.67, 154.27, 139.82, 138.34, 128.27, 126.42, 34.55, 26.03, 24.23, 21.38.; **IR** (cm^{-1}) 2919, 1869, 1825, 1635, 1606, 1146, 978, 760, 701; **HRMS** (EI) m/z calcd. for $C_{13}H_{15}NO_3$ $[M]^+$: 233.1052, found: 233.1049.

3-{3-(*o*-Tolyl)propyl}-1,4,2-dioxazol-5-one



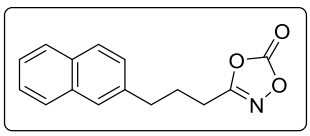
White solid (260 mg, 84%, 1.4 mmol scale); **m.p.** 44–46 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.05 (m, 4H), 2.74 (t, J = 7.5 Hz, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.32 (s, 3H), 2.03 (p, J = 7.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.58, 154.22, 138.15, 136.03, 130.69, 129.06, 126.81, 126.31, 32.14, 24.74, 24.49, 19.38; **IR** (cm^{-1}) 2955, 1880, 1818, 1750, 1631, 1160, 986, 757, 456; **HRMS** (EI) m/z calcd. for $C_{12}H_{13}NO_3$ $[M]^+$: 219.0895, found: 219.0896.

3-{3-(2-Chlorophenyl)propyl}-1,4,2-dioxazol-5-one



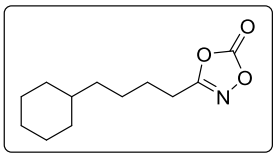
Yellow oil (208 mg, 87%, 1.0 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 1H), 7.25 – 7.12 (m, 3H), 2.87 (t, J = 7.5 Hz, 2H), 2.72 – 2.60 (m, 2H), 2.08 (p, J = 7.5, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.46, 154.19, 137.68, 134.10, 130.64, 129.95, 128.26, 127.19, 32.50, 24.47, 24.31; **IR** (cm^{-1}) 1870, 1825, 1146, 979, 751; **HRMS** (EI) m/z calcd. for $C_{11}H_{10}ClNO_3$ $[M]^+$: 239.0349, found: 239.0347.

3-{3-(Naphthalen-2-yl)propyl}-1,4,2-dioxazol-5-one



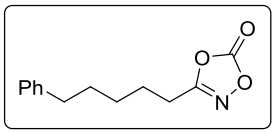
White solid (157 mg, 96%, 0.64 mmol scale); **m.p.** 46–48 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.86 – 7.77 (m, 3H), 7.63 (s, 1H), 7.52 – 7.42 (m, 2H), 7.32 (d, J = 8.4 Hz, 1H), 2.91 (t, J = 7.4 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H), 2.16 (p, J = 7.4 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.57, 154.22, 137.36, 133.70, 132.41, 128.58, 127.82, 127.60, 126.98, 126.92, 126.40, 125.76, 34.83, 25.91, 24.17; **IR** (cm^{-1}) 1870, 1819, 1629, 1155, 1134, 986, 935, 820, 754, 473; **HRMS** (EI) m/z calcd. for $C_{15}H_{13}NO_3$ $[M]^+$: 255.0895, found: 255.0897.

3-(4-Cyclohexylbutyl)-1,4,2-dioxazol-5-one



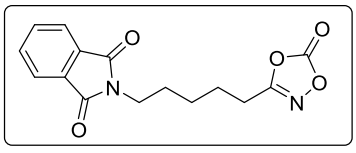
Colorless liquid (419 mg, 93%, 2.0 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 2.62 (t, J = 7.6 Hz, 2H), 1.75 – 1.61 (m, 7H), 1.40 (p, J = 7.9 Hz, 2H), 1.27 – 1.09 (m, 6H), 0.86 (q, J = 10.4 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.88, 154.36, 37.52, 36.84, 33.43, 26.76, 26.46, 26.14, 24.96, 24.90; **IR** (cm^{-1}) 2920, 2849, 1867, 1826, 1636, 1448, 1146, 978, 978, 761; **HRMS** (FAB) m/z calcd. for $C_{12}H_{19}NO_3$ $[M+H]^+$: 226.1443, found: 226.1444.

3-(5-Phenylpentyl)-1,4,2-dioxazol-5-one



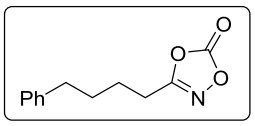
Colorless liquid (720 mg, 91%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.29 (t, J = 7.7 Hz, 1H), 7.23 – 7.14 (m, 3H), 2.66 – 2.59 (m, 4H), 1.75 (p, J = 7.6 Hz, 2H), 1.68 (p, J = 7.7 Hz, 2H), 1.45 (p, J = 7.7 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.72, 154.30, 142.06, 128.52, 128.48, 126.03, 35.64, 30.81, 28.36, 24.82, 24.52; **IR** (cm^{-1}) 2934, 2858, 1862, 1825, 1635, 1149, 980, 747, 698; **HRMS** (EI) m/z calcd. for $C_{13}H_{15}NO_3$ $[M]^+$: 233.1052, found: 233.1056.

2-{5-(5-Oxo-1,4,2-dioxazol-3-yl)pentyl}isoindoline-1,3-dione



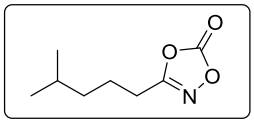
White solid (670 mg, 95%, 3.0 mmol scale); **m.p.** 83–85 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.4, 3.0 Hz, 1H), 7.72 (dd, J = 5.4, 3.0 Hz, 1H), 3.70 (t, J = 7.1 Hz, 2H), 2.63 (t, J = 7.5 Hz, 2H), 1.79 (p, J = 7.4 Hz, 2H), 1.74 (p, J = 7.4 Hz, 2H), 1.51 – 1.42 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.57, 166.49, 154.27, 134.16, 132.19, 123.42, 37.42, 28.04, 25.93, 24.78, 24.07; **IR** (cm^{-1}) 2930, 1892, 1860, 1771, 1714, 1393, 1372, 982, 721, 712; **HRMS** (EI) m/z calcd. for $C_{15}H_{14}N_2O_5$ $[M]^+$: 302.0903, found: 302.0906.

3-(4-Phenylbutyl)-1,4,2-dioxazol-5-one



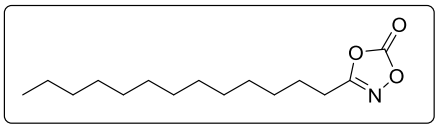
Colorless liquid (604 mg, 92%, 3.0 mmol scale);**^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.30 (appt, *J* = 7.5 Hz, 2H), 7.21 (appt, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 7.4 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H), 2.64 (t, *J* = 7.0 Hz, 2H), 1.81 – 1.71 (m, 4H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.61, 154.26, 141.31, 128.60, 128.45, 126.22, 35.26, 30.46, 24.76, 24.10; **IR** (cm^{-1}) 1870, 1825, 1149, 980, 759, 748, 699; **HRMS** (EI) m/z calcd. for $C_{12}H_{13}NO_3$ $[M]^+$: 219.0895, found: 219.0895.

3-(4-Methylpentyl)-1,4,2-dioxazol-5-one



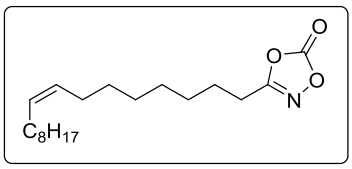
Colorless liquid (630 mg, 89%, 4.1 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 2.60 (t, J = 7.6 Hz, 2H), 1.72 (p, J = 7.7 Hz, 2H), 1.63 – 1.55 (m, 1H), 1.32 – 1.22 (m, 2H), 0.90 (d, J = 6.7 Hz, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.85, 154.35, 37.99, 27.71, 25.13, 22.60, 22.44; **IR** (cm^{-1}) 2957, 1867, 1827, 1636, 1366, 1148, 980, 761; **HRMS** (FAB) m/z calcd. for $C_8H_{13}NO_3$ $[M+H]^+$: 172.0974, found: 172.0973.

3-Tridecyl-1,4,2-dioxazol-5-one



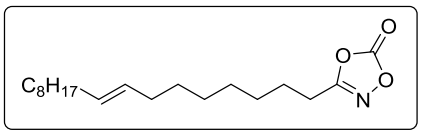
Colorless resin (792 mg, 98%, 3.0 mmol scale); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.62 (t, J = 7.5 Hz, 2H), 1.72 (p, J = 7.5 Hz, 2H), 1.44 – 1.36 (m, 2H), 1.33 – 1.21 (m, 18H), 0.88 (t, J = 6.7 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, *one carbon merged to others*) δ 166.88, 154.38, 32.06, 29.78, 29.73, 29.65, 29.49, 29.44, 29.07, 28.85, 24.90, 24.67, 22.84, 14.26; **IR** (cm^{-1}) 2922, 2853, 1869, 1820, 1146, 979, 762; **HRMS** (FAB) m/z calcd. for $C_{15}H_{27}NO_3$ $[M+H]^+$: 270.2069, found: 270.2067.

(*Z*)-3-(Heptadec-8-en-1-yl)-1,4,2-dioxazol-5-one



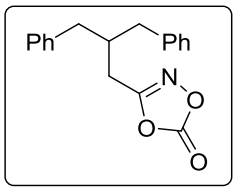
Colorless liquid (901 mg, 93%, 3.0 mmol scale); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 5.45 – 5.30 (m, 2H), 2.61 (t, J = 7.5 Hz, 2H), 2.06 – 1.96 (m, 4H), 1.71 (p, J = 7.6 Hz, 2H), 1.44 – 1.36 (m, 2H), 1.37 – 1.21 (m, 18H), 0.87 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$, *one carbon merged to others*) δ 166.84, 154.35, 130.33, 129.68, 32.05, 29.90, 29.73, 29.66, 29.47, 29.05, 28.98, 28.83, 27.38, 27.23, 24.89, 24.65, 22.82, 14.24; **IR** (cm^{-1}) 3004, 2923, 2853, 1870, 1820, 1146, 979, 761; **HRMS** (EI) m/z calcd. for $C_{19}H_{33}NO_3$ $[M]^+$: 323.2460, found: 323.2458.

(*E*)-3-(Heptadec-8-en-1-yl)-1,4,2-dioxazol-5-one



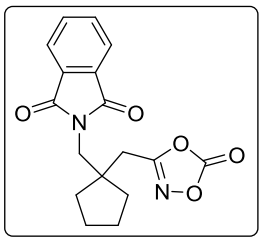
Colorless resin (267 mg, 91%, 0.91 mmol scale); **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 5.47 – 5.32 (m, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.05 – 1.91 (m, 4H), 1.70 (p, J = 7.4 Hz, 2H), 1.41 – 1.23 (m, 20H), 0.88 (t, J = 6.8, 3H); **^{13}C NMR** (101 MHz, CD_2Cl_2, *two carbons merged to others*) δ 167.60, 154.93, 131.12, 130.68, 33.16, 33.05, 32.48, 30.24, 30.06, 29.90, 29.74, 29.35, 29.22, 25.28, 25.05, 23.26, 14.46; **IR** (cm^{-1}) 2922, 2853, 1869, 1820, 1464, 1146, 977, 762; **HRMS** (EI) m/z calcd. for $C_{19}H_{33}NO_3$ $[M]^+$: 323.2460, found: 323.2463.

3-(2-Benzyl-3-phenylpropyl)-1,4,2-dioxazol-5-one



Colorless oil (480 mg, 94%, 1.7 mmol scale); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (appt, J = 7.4 Hz, 4H), 7.29 (d, J = 7.3 Hz, 2H), 7.21 (d, J = 7.7 Hz, 4H), 2.92 – 2.81 (m, 2H), 2.70 – 2.62 (m, 2H), 2.61 – 2.51 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.92, 154.01, 138.73, 129.24, 128.80, 126.88, 40.40, 39.00, 28.45. **IR** (cm^{-1}) 1872, 1825, 1143, 980, 751, 739, 698; **HRMS** (EI) m/z calcd. for $C_{18}H_{17}NO_3$ $[M]^+$: 295.1208, found: 295.1205.

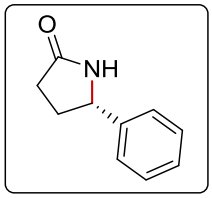
2-[[1-{(5-Oxo-1,4,2-dioxazol-3-yl)methyl}cyclopentyl]methyl]isoindoline-1,3-dione



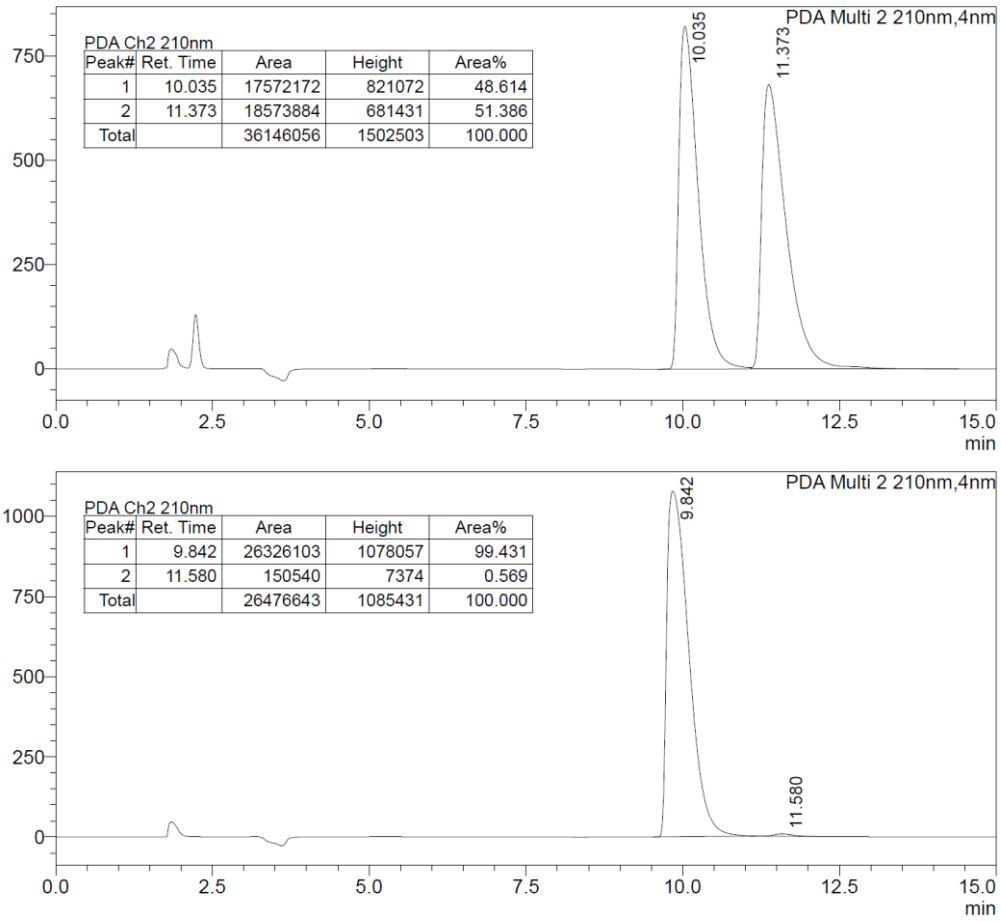
White solid (50 mg, 90%, 0.17 mmol scale); **m.p.** 105–107 °C; **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 7.92 – 7.81 (m, 2H), 7.79 – 7.68 (m, 2H), 3.75 (s, 2H), 2.75 (s, 2H), 1.92 – 1.74 (m, 4H), 1.73 – 1.65 (m, 2H), 1.61 – 1.51 (m, 2H); **^{13}C NMR** (151 MHz, CD_2Cl_2) δ 169.76, 166.15, 154.74, 134.84, 132.47, 123.87, 47.30, 44.96, 36.15, 33.91, 24.61; **IR** (cm^{-1}) 1836, 1773, 1708, 1631, 1390, 1341, 1155, 991, 918, 712, 529; **HRMS** (EI) m/z calcd. for $C_{17}H_{16}N_2O_5$ $[M]^+$: 328.1059, found: 328.1057.

Characterization of Chiral Lactam Products

5-Phenylpyrrolidin-2-one (2)

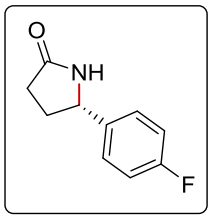


White solid (31 mg, 96%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 2H), 7.34 – 7.27 (m, 3H), 6.20 (br, 1H), 4.75 (t, *J* = 7.1 Hz, 1H), 2.63 – 2.52 (m, 1H), 2.52 – 2.35 (m, 2H), 2.04 – 1.92 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.59, 142.59, 129.06, 128.08, 125.77, 58.22, 31.54, 30.41; **Specific Rotation** $[\alpha]_D^{25}$ – 58.2 ± 0.2 (*c* 1.0, $CHCl_3$), lit.[20] –51 (*c* 0.97, CH_2Cl_2); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 210 nm, t_{R1} (major) = 9.84 min, t_{R2} (minor) =11.58 min, >99:1 er. NMR spectroscopic signatures are matched with previously reported ones.[16].



Supplementary Figure 1. HPLC traces of racemic and scalemic compounds of **2**.

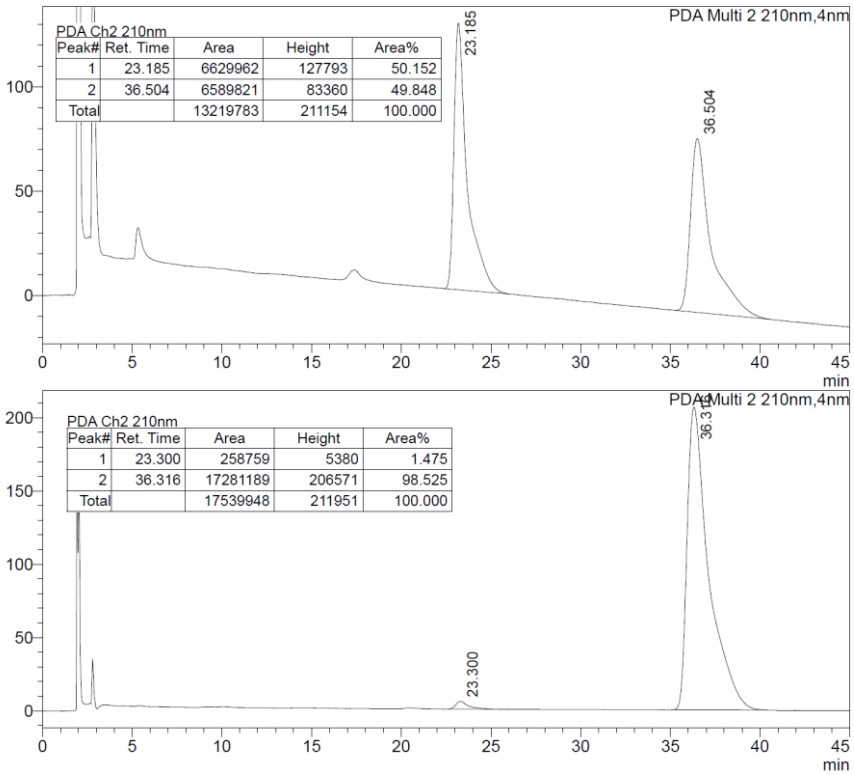
5-(4-Fluorophenyl)pyrrolidin-2-one (4)



White solid (30 mg, 85%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.14 – 7.00 (m, 2H), 6.17 (br, 1H), 4.74 (t, *J* = 7.1 Hz, 1H), 2.64 – 2.51 (m, 1H), 2.50 – 2.36 (m, 1H), 2.01 – 1.87 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.5, 162.5 (d, *J* = 246.3 Hz), 138.3 (d, *J* = 3.2 Hz), 127.5 (d, *J* = 8.1 Hz), 116.0 (d, *J* = 21.6 Hz), 57.6, 31.7, 30.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.3; **Specific Rotation** $[\alpha]_D^{25}$ –66.2 ±1.7 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 23.30 min, t_{R2} (major) = 36.31 min, 99:1 er.

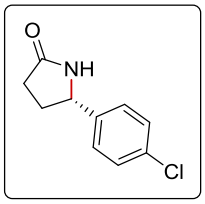
NMR spectroscopic signatures are matched with previously reported ones.[16]

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



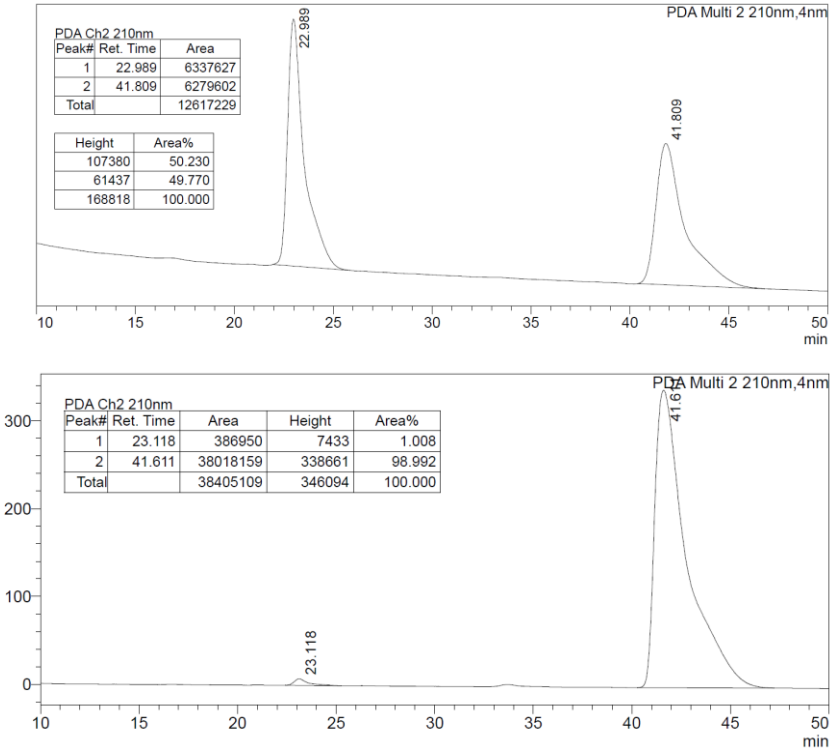
Supplementary Figure 2. HPLC traces of racemic and scalemic compounds of **4**.

5-(4-Chlorophenyl)pyrrolidin-2-one (5)



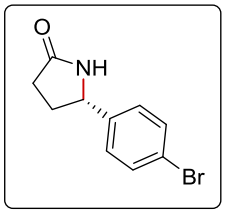
White solid (37 mg, 95%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.32 (d, J = 7.9 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.97 (br, 1H), 4.72 (t, J = 7.2 Hz, 1H), 2.62 – 2.50 (m, 1H), 2.49 – 2.33 (m, 2H), 1.95 – 1.84 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.90, 141.19, 133.69, 129.15, 127.11, 57.65, 31.32, 30.39; **Specific Rotation** $[\alpha]_D^{25}$ – 52.6 ±1.2 (*c* 0.5, $CHCl_3$), lit.[21] +46.0 for the (*R*) isomer (*c* 0.6, CH_2Cl_2, 97% ee); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 23.12 min, t_{R2} (major) =41.61 min, 99:1 er.

NMR spectroscopic signatures are matched with previously reported ones.[21]



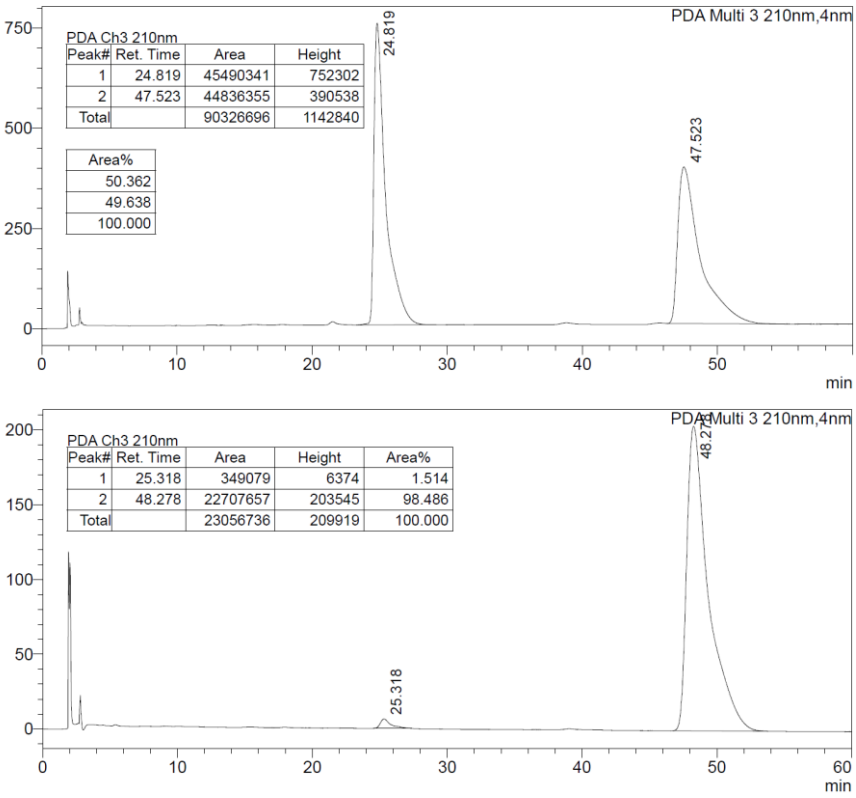
Supplementary Figure 3. HPLC traces of racemic and scalemic compounds of **5**.

5-(4-Bromophenyl)pyrrolidin-2-one (6)



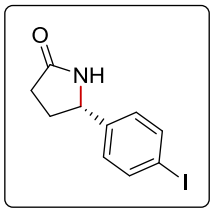
White solid (47 mg, 98%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.31 (br, 1H), 4.72 (t, *J* = 7.1 Hz, 1H), 2.63 – 2.52 (m, 1H), 2.52 – 2.36 (m, 2H), 1.99 – 1.89 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.53, 141.68, 132.21, 127.50, 121.91, 57.67, 31.43, 30.28; **Specific Rotation** $[\alpha]_D^{25}$ –48.5 ±1.2 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 25.32 min, t_{R2} (minor) = 48.27 min, 98:2 er. NMR spectroscopic signatures are matched with previously reported ones.[16]

Solid-state structure and its absolute configuration was characterized by X-ray diffraction analysis (Absolute structure parameter: 0.04(3), CCDC 1873623).



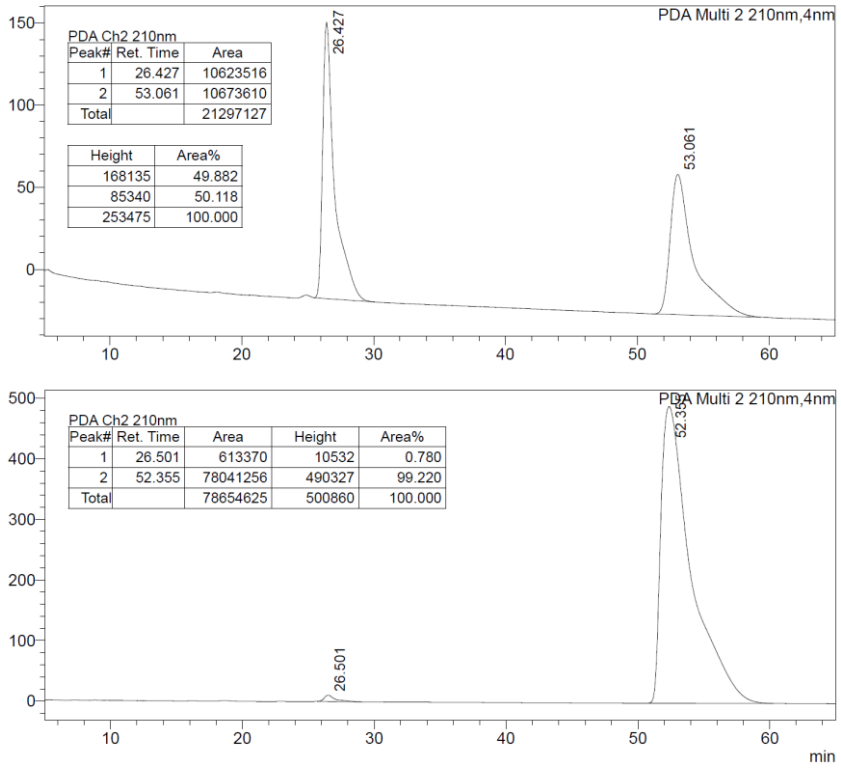
Supplementary Figure 4. HPLC traces of racemic and scalemic compounds of **6**.

5-(4-Iodophenyl)pyrrolidin-2-one (7)



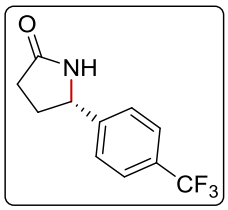
White solid (53 mg, 92%); **m.p.** 187–189 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.67 (d, J = 7.9 Hz, 2H), 7.05 (br, 1H), 7.03 (d, J = 7.9 Hz, 2H), 4.68 (t, J = 7.2 Hz, 1H), 2.59 – 2.49 (m, 1H), 2.47 – 2.33 (m, 2H), 1.94 – 1.82 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.94, 142.41, 138.03, 127.68, 93.24, 57.77, 31.23, 30.38; **IR** (cm^{-1}) 3022, 3085, 2877, 1709, 1664, 1291, 1254, 1002, 803, 480; **HRMS** (EI) m/z calcd. $C_{10}H_{10}INO$ $[M]^+$: 286.9807, found: 286.9809.; **Specific Rotation** $[\alpha]_D^{25}$ -33.6 ±0.9 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 26.50 min, t_{R2} (major) = 52.36 min, 99:1 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



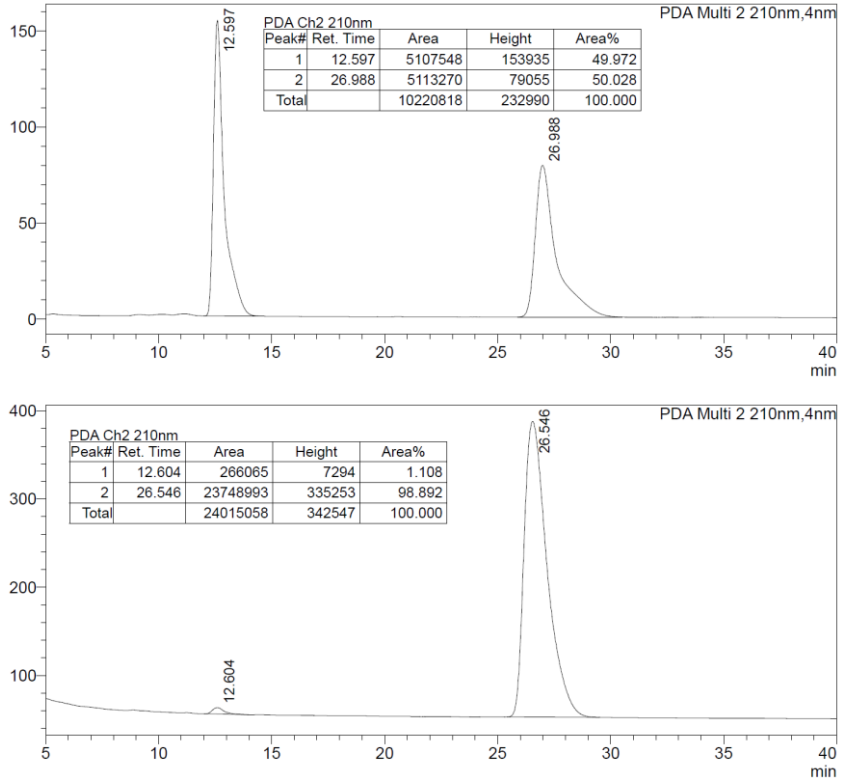
Supplementary Figure 5. HPLC traces of racemic and scalemic compounds of **7**.

5-{4-(Trifluoromethyl)phenyl}pyrrolidin-2-one (8)



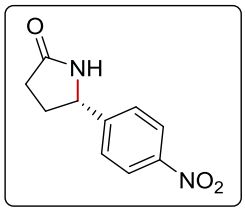
White solid (38 mg, 83%); **m.p.** 139–141 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.63 (d, J = 7.9 Hz, 2H), 7.42 (d, J = 7.9 Hz, 2H), 7.01 (br, 1H), 4.83 (t, J = 7.1 Hz, 1H), 2.67 – 2.55 (m, 1H), 2.53 – 2.36 (m, 2H), 1.99 – 1.91 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.91, 146.75, 130.36 (q, J = 32.4 Hz), 126.11, 126.08 (q, J = 3.7 Hz), 124.10 (q, J = 272.0 Hz), 57.81, 31.27, 30.49; **^{19}F NMR** (564 MHz, $CDCl_3$) δ -62.61; **IR** (cm^{-1}) 3198, 3099, 2946, 2882, 1703, 1119, 1013, 739, 489; **HRMS** (EI) m/z calcd. for $C_{11}H_{10}F_3NO$ $[M]^+$: 229.0714, found: 229.0711; **Specific Rotation** $[\alpha]_D^{25}$ –56.2 ±0.4 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 12.60 min, t_{R2} (major) = 26.55 min, 99:1 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



Supplementary Figure 6. HPLC traces of racemic and scalemic compounds of **8**.

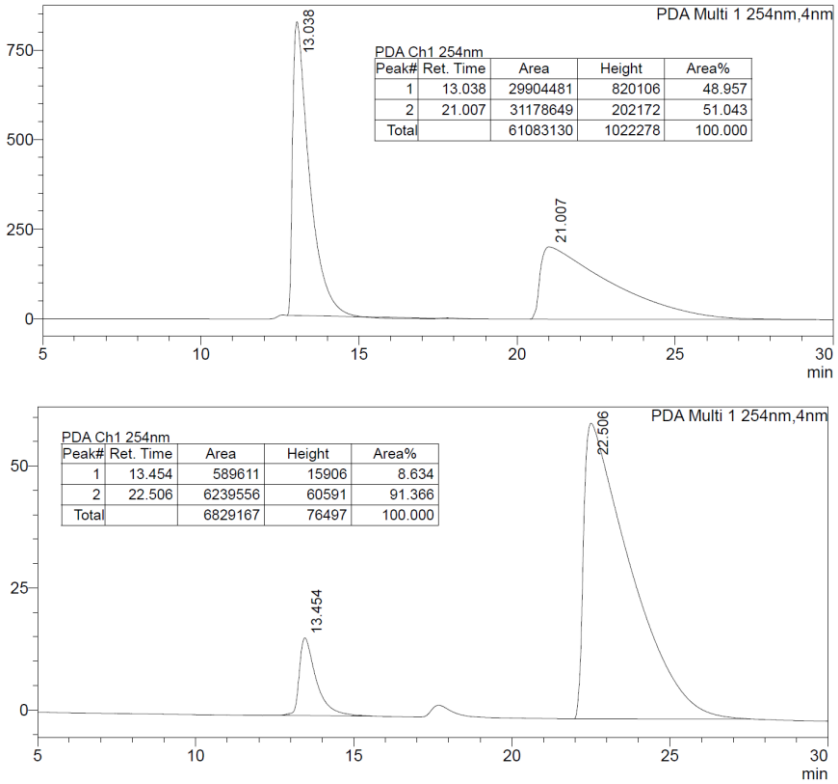
5-(4-Nitrophenyl)pyrrolidin-2-one (9)



10 mol % of catalyst and $NaBAr^F_4$ used at 50 °C; White solid (21 mg, 51%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 8.25 (d, J = 8.9 Hz, 1H), 7.49 (d, J = 8.7 Hz, 1H), 6.02 (s, 1H), 4.87 (t, J = 7.2 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.57 – 2.40 (m, 1H), 2.01 – 1.91 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.74, 150.01, 147.79, 126.58, 124.42, 57.58, 31.20, 30.17; **Specific Rotation** $[\alpha]_D^{25}$ –38.3 ±0.3 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 254 nm, t_{R1} (minor) = 13.45 min, t_{R2} (major) = 22.5 min, 91:9 er.

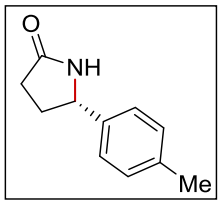
NMR spectroscopic signatures are matched with previously reported ones.[16]

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



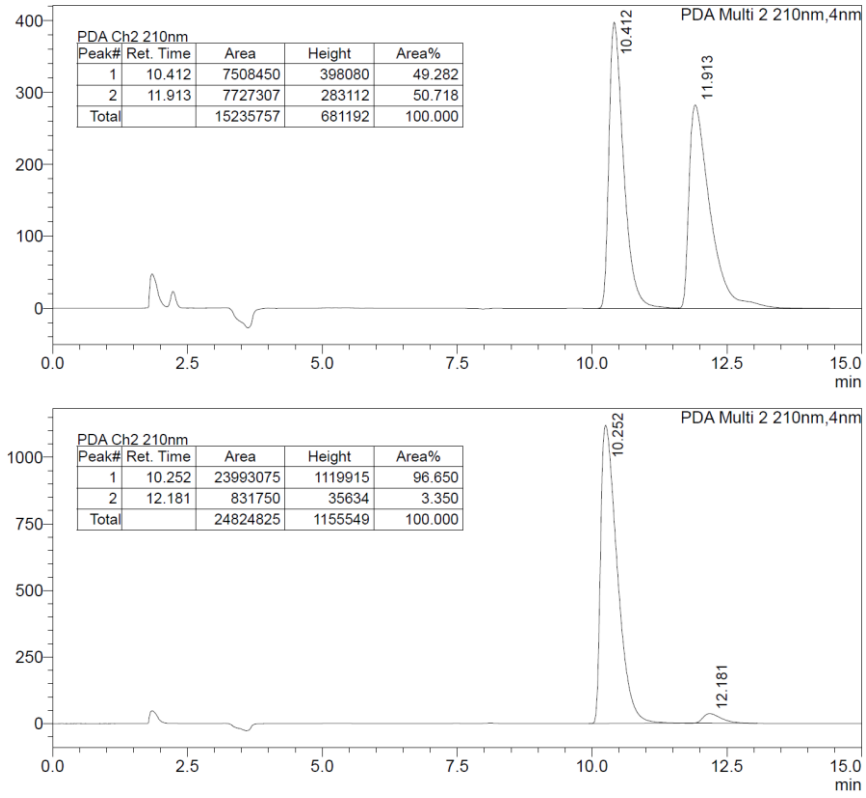
Supplementary Figure 7. HPLC traces of racemic and scalemic compounds of **9**.

5-(*p*-Tolyl)pyrrolidin-2-one (10)



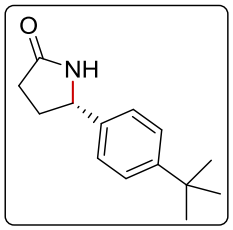
White solid (28 mg, 80%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.09 (m, 4H), 6.27 (br, 1H), 4.71 (t, *J* = 7.1 Hz, 1H), 2.63 – 2.49 (m, 1H), 2.49 – 2.38 (m, 2H), 2.34 (s, 3H), 2.03 – 1.87 (m, 1H).; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.60, 139.58, 137.81, 129.67, 125.72, 58.03, 31.58, 30.51, 21.18.; **Specific Rotation** $[\alpha]_D^{25}$ – 43.0 ± 0.2 (*c* 1.30, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 210 nm, t_{R1} (major) = 10.25 min, t_{R2} (minor) = 12.18 min, 97:3 er. NMR spectroscopic signatures are matched with previously reported ones.[22]

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



Supplementary Figure 8. HPLC traces of racemic and scalemic compounds of 10.

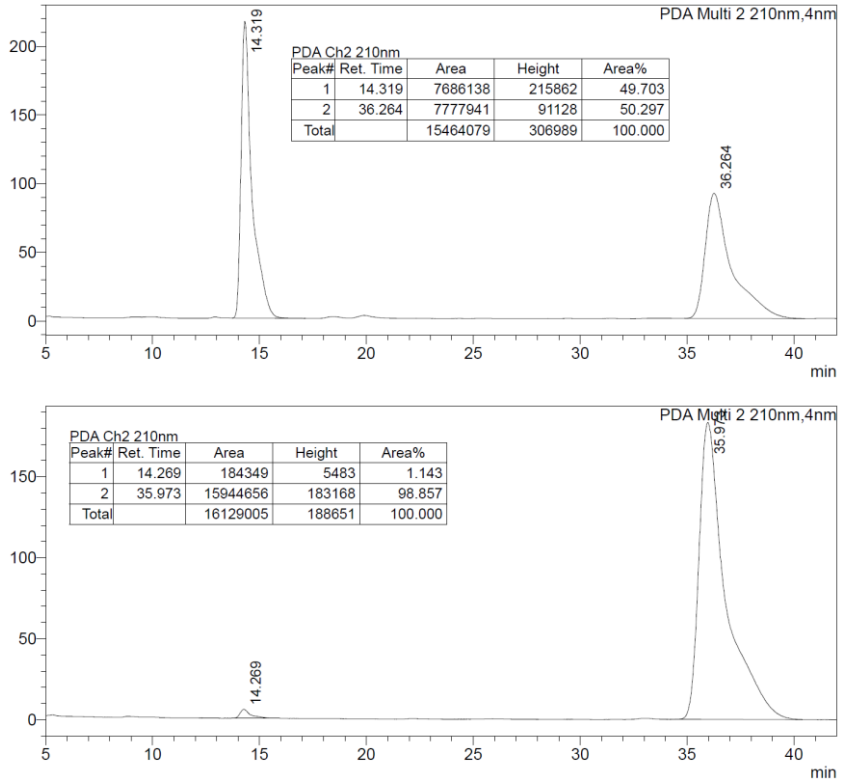
5-{4-(*tert*-Butyl)phenyl}pyrrolidin-2-one (11)



White solid (42 mg, 97%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 6.69 (br, 1H), 4.72 (t, J = 7.1 Hz, 1H), 2.59 – 2.46 (m, 1H), 2.46 – 2.32 (m, 2H), 2.04 – 1.91 (m, 1H), 1.31 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.79, 150.95, 139.52, 125.85, 125.48, 57.96, 34.62, 31.40, 30.56; **Specific Rotation** $[\alpha]_D^{25}$ –43.8 ±0.1 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 14.27 min, t_{R2} (major) = 35.97 min, 99:1 er.

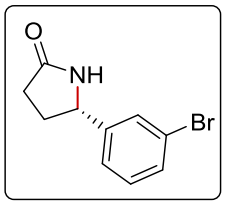
NMR spectroscopic signatures are matched with previously reported ones.[23]

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



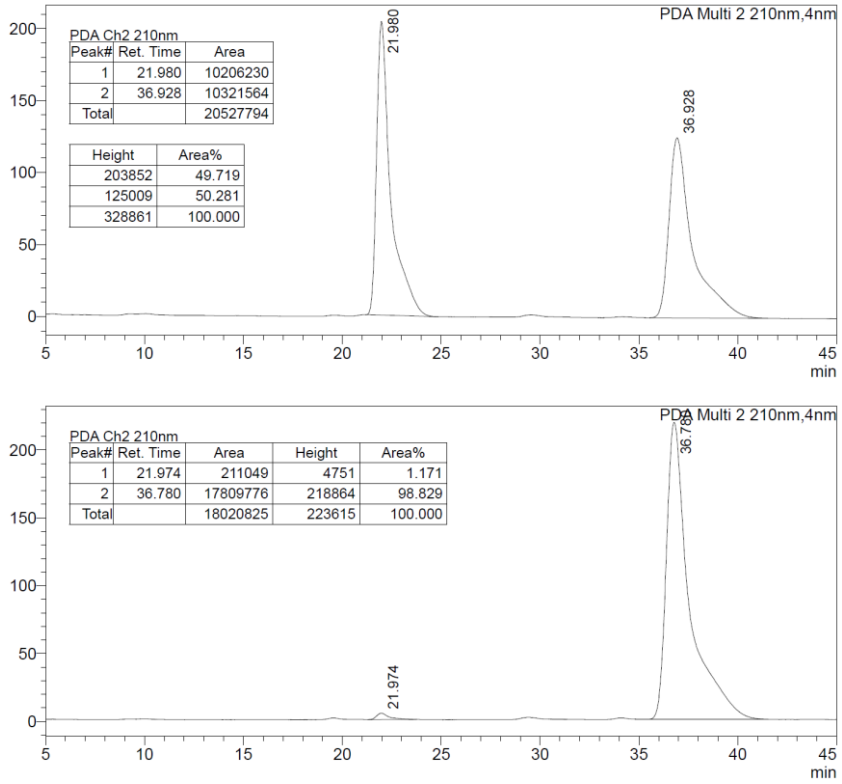
Supplementary Figure 9. HPLC traces of racemic and scalemic compounds of **11**.

5-(3-Bromophenyl)pyrrolidin-2-one (12)



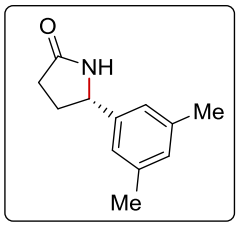
White solid (45 mg, 94%); **m.p.** 165–167 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.51 – 7.39 (m, 2H), 7.21 – 7.19 (m, 2H), 6.40 (br, 1H), 4.83 – 4.65 (m, 1H), 2.66 – 2.54 (m, 1H), 2.54 – 2.36 (m, 2H), 2.02 – 1.89 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.64, 145.07, 131.20, 130.69, 128.97, 124.41, 123.19, 57.66, 31.37, 29.82; **IR** (cm^{-1}) 3178, 3086, 1682, 1650, 1262, 786, 764, 694, 486, 432; **HRMS** (EI) m/z calcd. for $C_{10}H_{10}BrNO$ $[M]^+$: 238.9946, found: 238.9941; **Specific Rotation** $[\alpha]_D^{25}$ –43.9 ±1.4 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 21.97 min, t_{R2} (major) = 36.78 min, 99:1 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



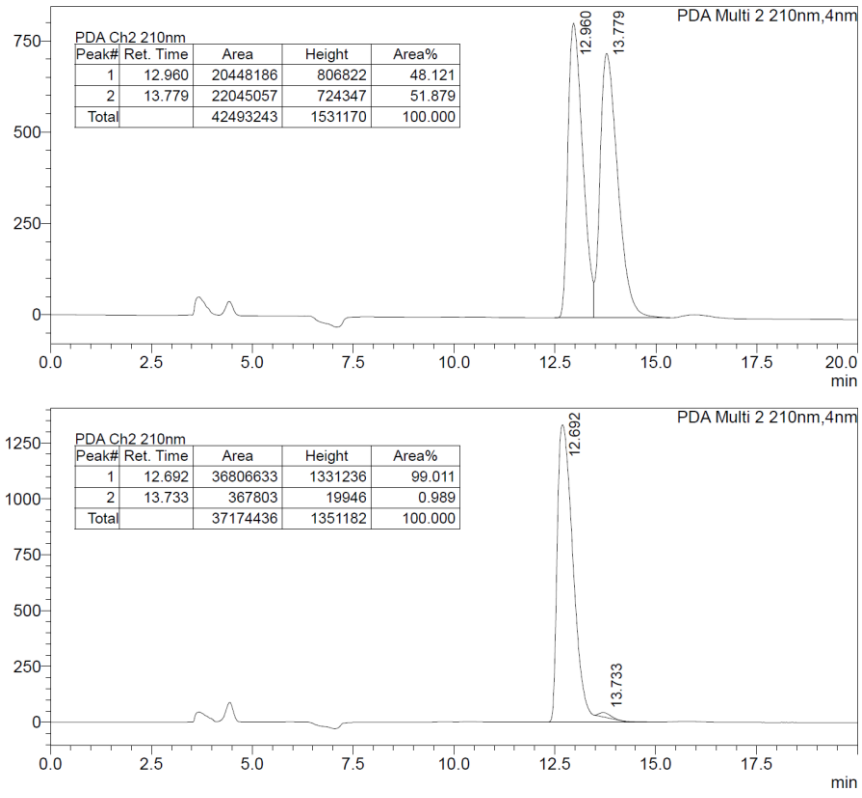
Supplementary Figure 10. HPLC traces of racemic and scalemic compounds of **12**.

5-(3,5-Dimethylphenyl)pyrrolidin-2-one (13)



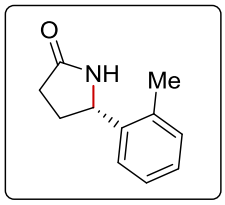
White solid (31 mg, 82%); **m.p.** 177–179 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.93 (s, 1H), 6.90 (s, 2H), 6.10 (br, 1H), 4.67 (t, J = 7.1 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.51 – 2.44 (m, 1H), 2.44 – 2.36 (m, 1H), 2.31 (s, 6H) 2.00 – 1.91 (m, 1H).; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.5, 142.6, 138.7, 129.6, 123.5, 58. 1, 31.5, 30.4, 21.4; **IR** (cm^{-1}) 3167, 2945, 2885, 1685, 1656, 1334, 1261, 852, 791, 702, 485; **HRMS** (EI) m/z calcd. for $C_{12}H_{15}NO$ $[M]^+$: 189.1154, found: 189.1155.; **Specific Rotation** $[\alpha]_D^{25}$ – 48.0 (*c* 1.0, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 0.5 mL/min, 210 nm, t_{R1} (major) = 12.69 min, t_{R2} (minor) =13.73 min, 99:1 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



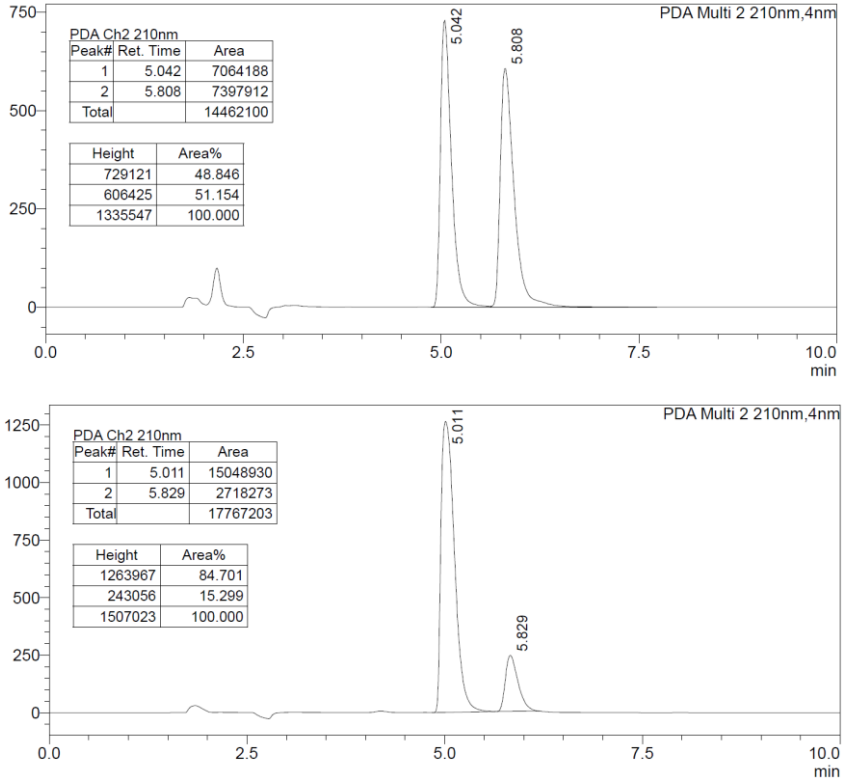
Supplementary Figure 11. HPLC traces of racemic and scalemic mixtures of **13**.

5-(*o*-Tolyl)pyrrolidin-2-one (14)



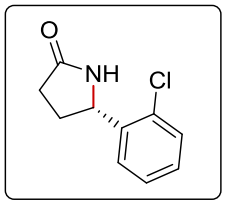
10 mol % of catalyst and $NaBAr^F_4$ used at 50 °C; White solid (17 mg, 49%); **m.p.** 93–95 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.34 (d, J = 7.6 Hz, 1H), 7.23 (appt, J = 7.2 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.21 (br, 1H), 4.99 (t, J = 6.8 Hz, 1H), 2.68 – 2.57 (m, 1H), 2.49 – 2.36 (m, 2H), 2.34 (s, 3H), 1.91 – 1.84 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.74, 140.60, 134.57, 130.92, 127.63, 126.75, 124.13, 54.69, 29.99, 29.72, 19.10; **IR** (cm^{-1}) 3428, 3181, 1660, 1347, 1085, 791, 751, 448; **HRMS** (EI) m/z calcd. for $C_{11}H_{13}NO$ $[M]^+$: 175.0997, found: 175.0996; **Specific Rotation** $[\alpha]_D^{25}$ –72.4 ±2.4 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (major) = 5.01 min, t_{R2} (minor) = 5.83 min, 85:15 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



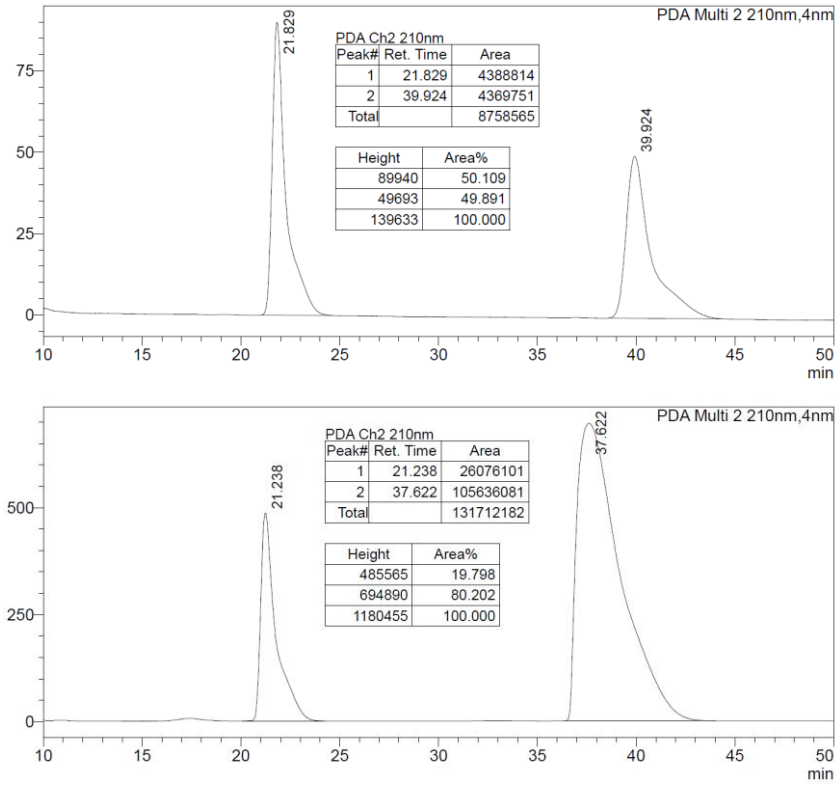
Supplementary Figure 12. HPLC traces of racemic and scalemic compounds of **14**.

5-(2-Chlorophenyl)pyrrolidin-2-one (15)



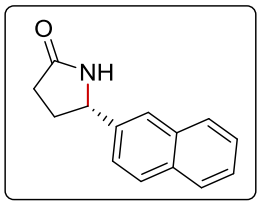
10 mol % of catalyst and $NaBAr^F_4$ used at 50 °C; White solid (16 mg, 41%); **m.p.** 99 – 101 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.39 (appt, J = 7.7 Hz, 2H), 7.30 (appt, J = 7.5 Hz, 1H), 7.28 – 7.21 (m, 1H), 6.13 (br, 1H), 5.21 – 5.13 (m, 1H), 2.77 – 2.68 (m, 1H), 2.50 – 2.35 (m, 2H), 2.01 – 1.89 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.78, 139.98, 132.43, 130.13, 129.04, 127.52, 125.90, 54.83, 29.74, 29.27; **HRMS** (EI) m/z calcd. for $C_{10}H_{10}ClNO$ $[M]^+$: 195.0451, found: 195.04514; **Specific Rotation** $[\alpha]_D^{25}$ –37.4 ±2.0 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 21.24 min, t_{R2} (major) = 37.62 min, 80:20 er.

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



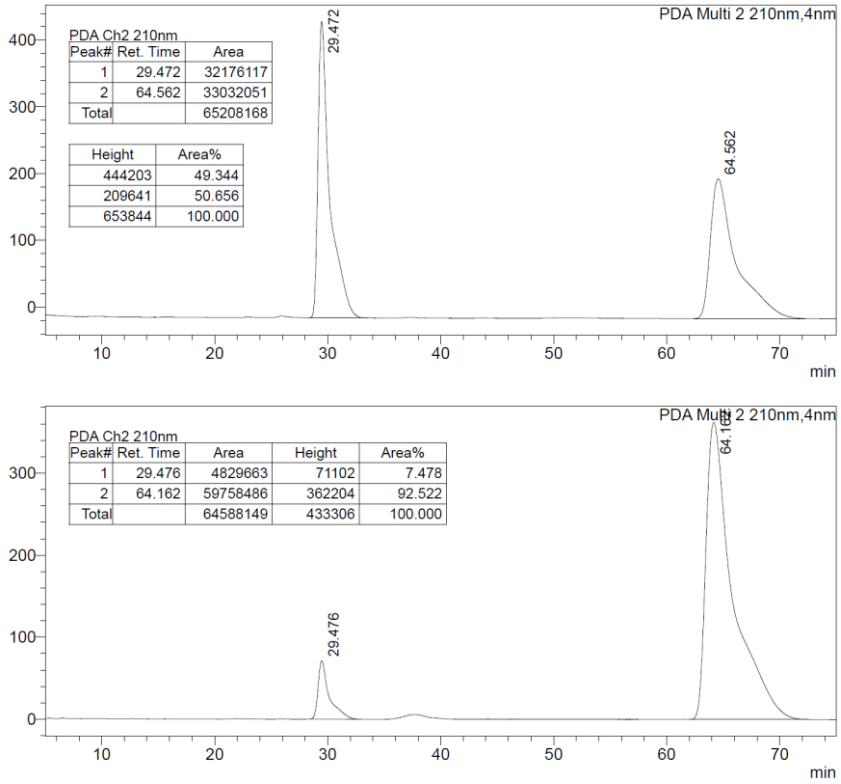
Supplementary Figure 13. HPLC traces of racemic and scalemic compounds of **15**.

5-(Naphthalen-2-yl)pyrrolidin-2-one (16)



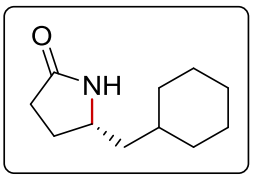
White solid (32 mg, 76%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 3H), 7.73 (s, 1H), 7.53 – 7.45 (m, 2H), 7.40 (dd, J = 8.5, 1.8 Hz, 1H), 6.51 (br, 1H), 4.90 (t, J = 7.1 Hz, 1H), 2.71 – 2.57 (m, 1H), 2.55 – 2.39 (m, 2H), 2.12 – 1.98 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.74, 139.93, 133.39, 133.14, 129.10, 127.95, 127.83, 126.65, 126.27, 124.42, 123.72, 58.28, 31.24, 30.35; **Specific Rotation** $[\alpha]_D^{25}$ –28.5 ±1.8 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 7.48 min, t_{R2} (major) = 64.16 min, 93:7 er. NMR spectroscopic signatures are matched with previously reported ones.[24]

The absolute stereochemistry was assigned by analogy to compound **2**, **5** and **6**.



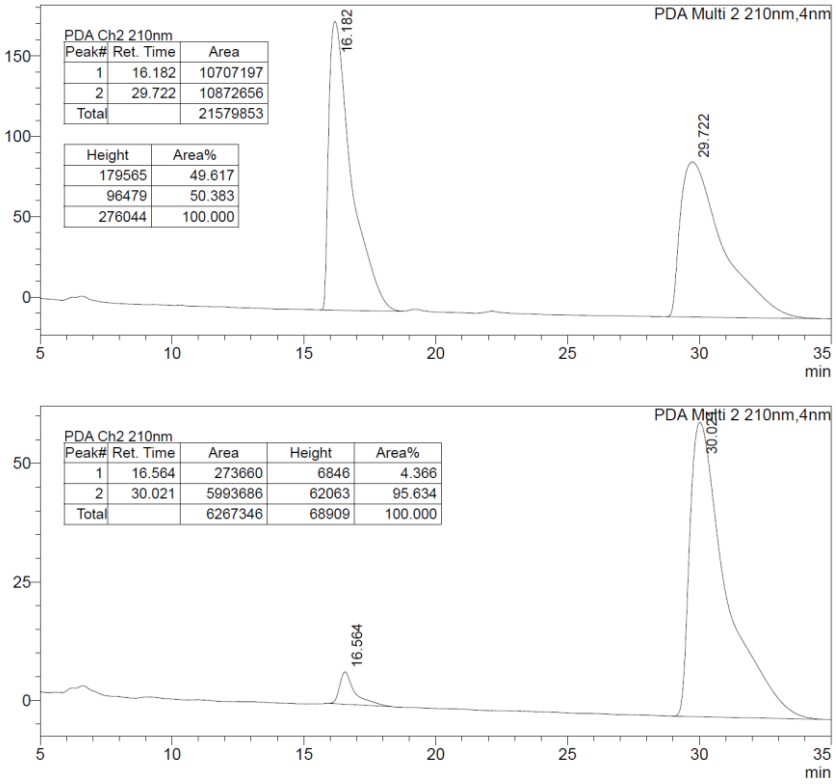
Supplementary Figure 14. HPLC traces of racemic and scalemic compounds of **16**.

5-(Cyclohexylmethyl)pyrrolidin-2-one (17)



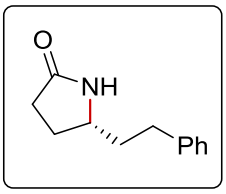
White solid (22 mg, 61%); **m.p.** 97–99 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.14 (br, 1H), 3.73 (p, J = 6.7 Hz, 1H), 2.39 – 2.19 (m, 3H), 1.74 – 1.61 (m, 6H), 1.46 – 1.40 (m, 1H), 1.36 – 1.10 (m, 5H), 0.96 – 0.86 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.21, 52.15, 44.68, 34.98, 33.73, 33.31, 30.27, 28.04, 26.52, 26.28, 26.25; **IR** (cm^{-1}) 3348, 3174, 3089, 2973, 2849, 1686, 1461, 1288, 797, 652, 523; **HRMS** (EI) m/z calcd. for $C_{11}H_{19}NO$ $[M]^+$: 181.1467, found: 181.1464; **Specific Rotation** $[\alpha]_D^{25}$ +10.7 ±1.1 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 85:15, 1.0 mL/min, 210 nm, t_{R1} (minor) = 16.56 min, t_{R2} (major) = 30.02 min, 96:4 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



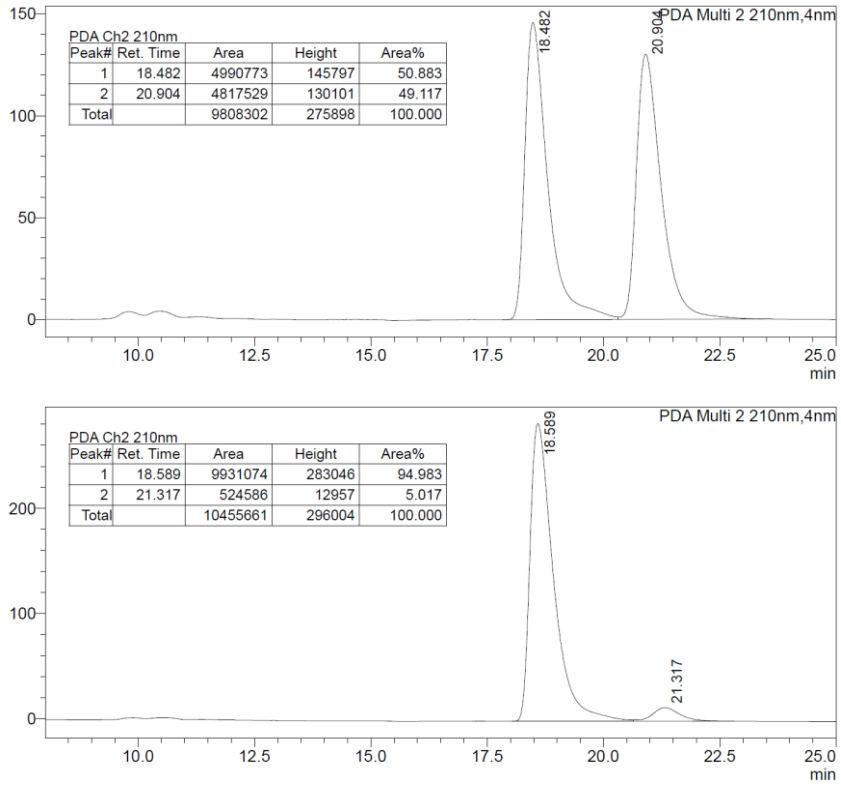
Supplementary Figure 15. HPLC traces of racemic and scalemic compounds of **17**.

5-Phenethylpyrrolidin-2-one (18)



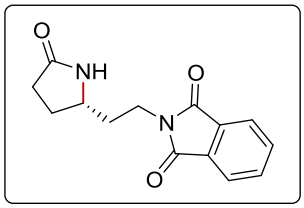
White solid (28 mg, 73%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (appt, J = 7.3 Hz, 2H), 7.23 – 7.11 (m, 3H), 6.84 (br, 1H), 3.86 – 3.54 (m, 1H), 2.67 (t, J = 7.6 Hz, 2H), 2.40 – 2.22 (m, 3H), 1.94 – 1.70 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.65, 141.10, 128.69, 128.45, 126.29, 54.17, 38.57, 32.47, 30.64, 27.46**;** **Specific Rotation** $[\alpha]_D^{25}$ +20.5 ±1.2 (*c* 1.0, $CHCl_3$), lit.[23] –22.2 for the (*S*) isomer (*c* 1.35, $CHCl_3$, 82% ee); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 0.5 mL/min, 210 nm, t_{R1} (major) = 18.59 min, t_{R2} (minor) = 21.32 min, 95:5 er.

NMR spectroscopic signatures are matched with previously reported ones.[23]



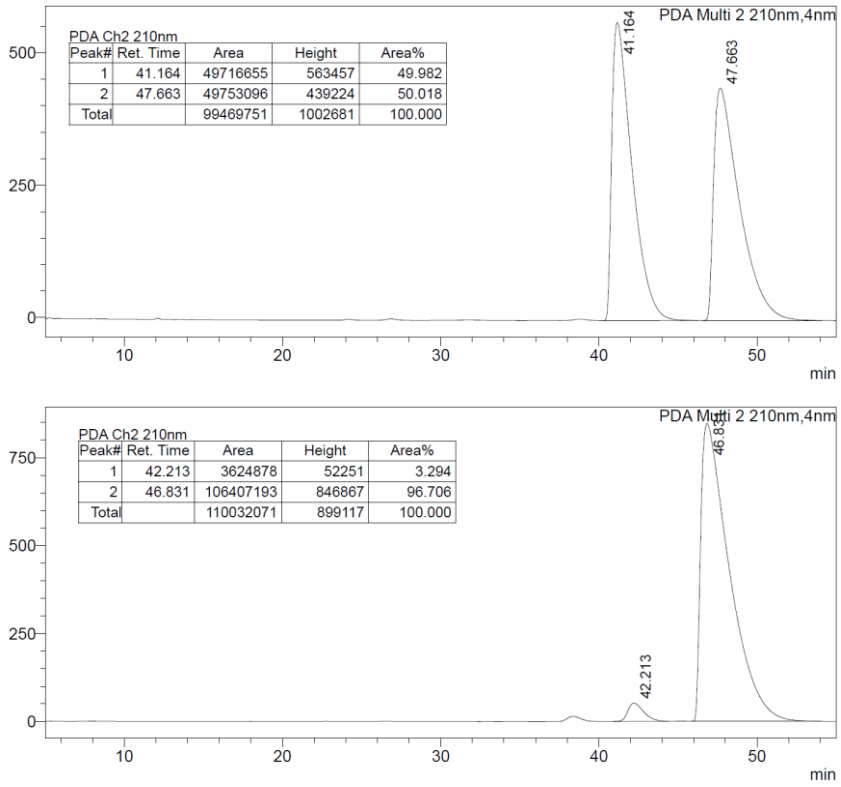
Supplementary Figure 16. HPLC traces of racemic and scalemic compounds of **18**.

2-{2-(5-Oxopyrrolidin-2-yl)ethyl}isoindoline-1,3-dione (19)



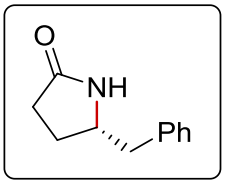
10 mol % of catalyst used; White solid (39 mg, 75%); **m.p.** 119–121 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 2H), 7.74 – 7.70 (m, 2H), 6.58 (br, 1H), 3.82 – 3.70 (m, 2H), 3.58 (p, J = 5.7 Hz, 1H), 2.42 – 2.34 (m, 1H), 2.34 – 2.24 (m, 2H), 1.93 – 1.85 (m, 1H), 1.85 – 1.70 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.09, 168.56, 134.30, 132.00, 123.53, 51.54, 35.66, 34.81, 29.88, 27.12; **IR** (cm^{-1}) 3197, 3090, 2919, 2851, 1707, 1685, 1438, 1257, 1071, 797, 721; **HRMS** (EI) m/z calcd. for $C_{14}H_{14}N_2O_3$ $[M]^+$: 258.1004, found: 258.1006; **Specific Rotation** $[\alpha]_D^{25}$ +71.4 ±0.4 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALCEL OJ-H, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 42.21 min, t_{R2} (major) = 46.83 min, 97:3 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



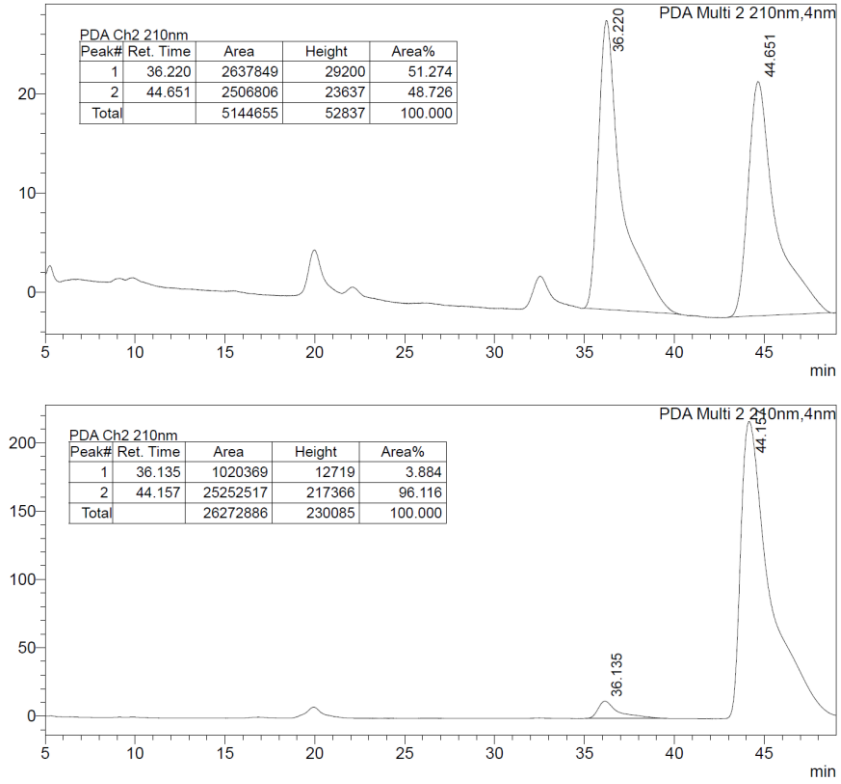
Supplementary Figure 17. HPLC traces of racemic and scalemic compounds of **19**.

5-Benzylpyrrolidin-2-one (20)



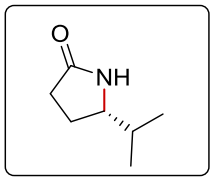
10 mol % of catalyst used; Cololess resin (30 mg, 86%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.31 (t, J = 7.5 Hz, 2H), 7.24 (appt, J = 7.4 Hz, 1H), 7.17 (d, J = 7.3 Hz, 2H), 6.02 (br, 1H), 3.88 (p, J = 6.5 Hz, 1H), 2.83 (dd, J = 13.4, 5.7 Hz, 1H), 2.73 (dd, J = 13.5, 8.0 Hz, 1H), 2.36 – 2.27 (m, 2H), 2.29 – 2.20 (m, 1H), 1.89 – 1.79 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.99, 137.63, 129.13, 128.90, 126.96, 55.79, 43.11, 30.19, 27.03; **IR** (cm^{-1}) 3219, 2925, 1681, 1603, 1261, 699; **HRMS** (EI) m/z calcd. for $C_{11}H_{13}NO$ $[M]^+$: 175.0997, found: 175.0999; **Specific Rotation** $[\alpha]_D^{25}$ +60.9 ±0.6 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 36.14 min, t_{R2} (major) = 44.16 min, 96:4 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



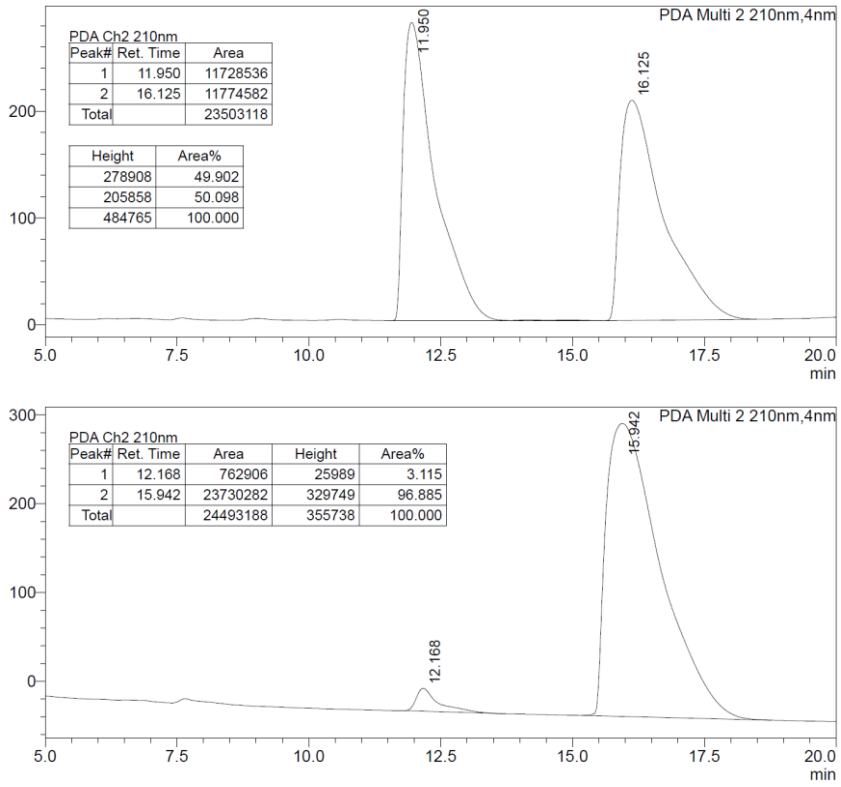
Supplementary Figure 18. HPLC traces of racemic and scalemic compounds of **20**.

5-Isopropylpyrrolidin-2-one (21)



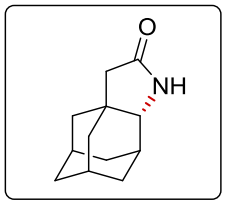
10 mol % of catalyst used; White solid (20 mg, 79%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.38 (br, 1H), 3.38 (q, J = 6.9 Hz, 1H), 2.37 – 2.26 (m, 2H), 2.22 – 2.13 (m, 1H), 1.81 – 1.72 (m, 1H), 1.69 – 1.58 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.61, 60.66, 33.65, 30.66, 24.86, 18.90, 18.20; **Specific Rotation** $[\alpha]_D^{25}$ –11.7 ±0.8 (*c* 0.5, $CHCl_3$) lit.[25] –16.5 (*c* 2.0, CH_2Cl_2); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 85:15, 1.0 mL/min, 210 nm, t_{R1} (minor) = 12.17 min, t_{R2} (major) = 15.94 min, 97:3 er.

NMR spectroscopic signatures are matched with previously reported ones. [25]



Supplementary Figure 19. HPLC traces of racemic and scalemic compounds of **21**.

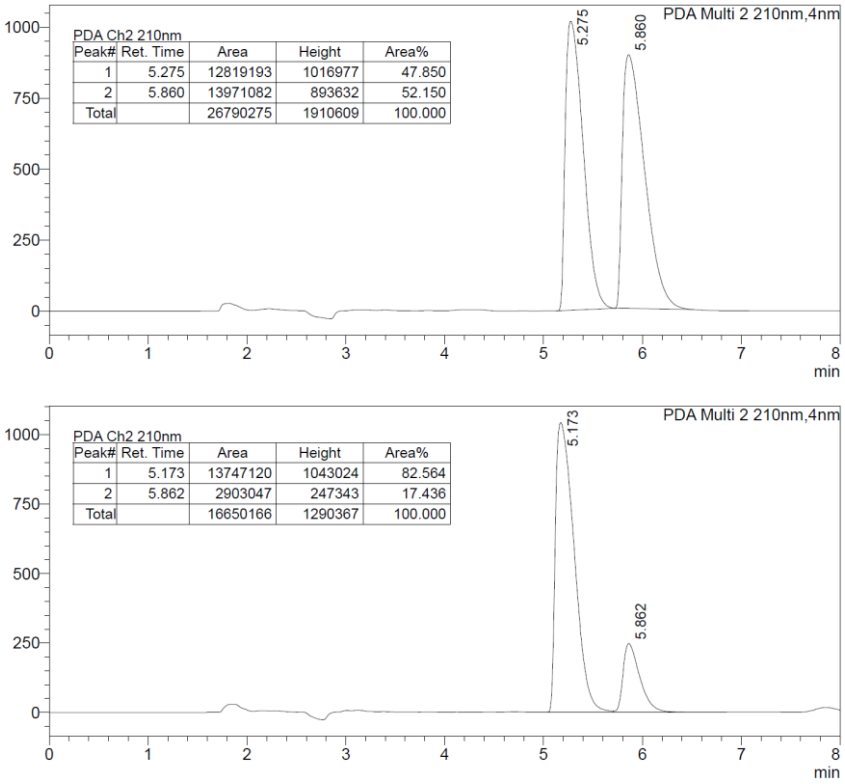
Octahydro-3a,7:5,9-dimethanocycloocta[b]pyrrol-2(*3H*)-one (22)



White solid (20 mg, 52%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.21 (br, 1H), 3.45 (s, 1H), 2.10 – 1.98 (m, 3H), 1.92 – 1.76 (m, 6H), 1.75 – 1.67 (m, 3H), 1.65 (d, J = 12.0 Hz, 1H), 1.58 (d, J = 12.8 Hz, 1H), 1.39 (d, J = 11.9 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.38, 64.17, 46.44, 40.15, 38.69, 37.28, 37.17, 37.06, 36.86, 29.61, 29.09, 27.46; **Specific Rotation** $[\alpha]_D^{25}$ +4.1 ±0.4 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (major) = 5.17 min, t_{R2} (minor) = 5.86 min, 83:17 er.

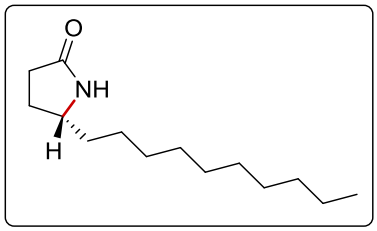
NMR spectroscopic signatures are matched with previously reported ones.[16]

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



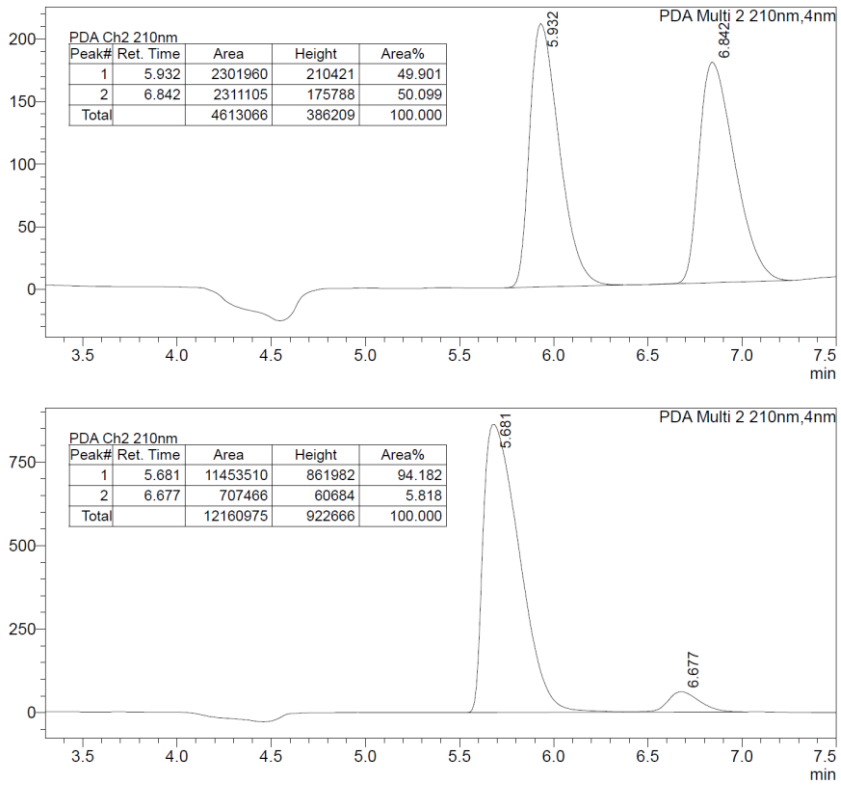
Supplementary Figure 20. HPLC traces of racemic and scalemic compounds of **22**.

5-Decylpyrrolidin-2-one (23)



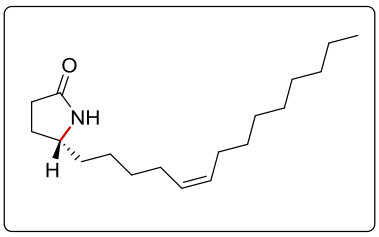
White solid (28 mg, 62%); **m.p.** 65–67 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.20 (br, 1H), 3.62 (p, J = 6.6 Hz, 1H), 2.39 – 2.27 (m, 2H), 2.27 – 2.19 (m, 1H), 1.74 – 1.66 (m, 1H), 1.56 – 1.48 (m, 1H), 1.49 – 1.40 (m, 1H), 1.32 – 1.21 (m, 16H), 0.87 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$, *one carbon merged to others*) δ 178.43, 54.80, 36.89, 32.01, 30.51, 29.68, 29.66, 29.61, 29.42, 27.44, 25.97, 22.78, 14.21; **IR** (cm^{-1}) 3176, 3089, 2955, 2916, 2850, 1704, 1654, 1469, 798, 455; **HRMS** (EI) m/z calcd. for $C_{14}H_{27}NO$ $[M]^+$: 225.2093, found: 225.2094; **Specific Rotation** $[\alpha]_D^{25}$ -6.9 ±0.3 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (major) = 5.68 min, t_{R2} (minor) = 6.68 min, 94:6 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



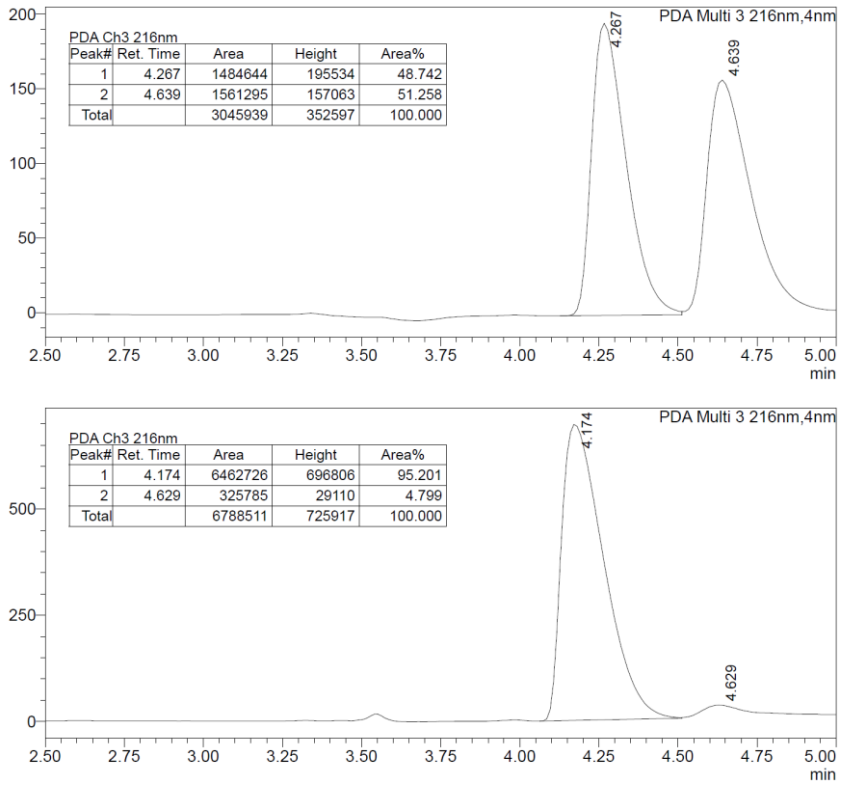
Supplementary Figure 21. HPLC traces of racemic and scalemic compounds of **23**.

(*Z*)-5-(Tetradec-5-en-1-yl)pyrrolidin-2-one (24)



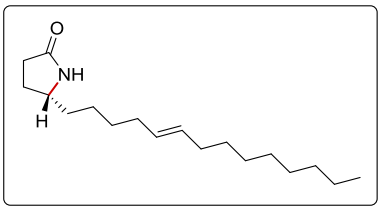
10 mol % of catalyst used at 50 °C; Colorless liquid (39 mg, 70%);**^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.59 (br, 1H), 5.39 – 5.27 (m, 2H), 3.61 (p, J = 6.6 Hz, 1H), 2.41 – 2.27 (m, 2H), 2.27 – 2.18 (m, 1H), 2.08 – 1.94 (m, 4H), 1.73 – 1.63 (m, 1H), 1.59 – 1.48 (m, 1H), 1.49 – 1.40 (m, 1H), 1.35 – 1.22 (m, 16H), 0.86 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.41, 130.53, 129.29, 54.72, 36.76, 32.01, 30.38, 29.85, 29.67, 29.63, 29.44, 29.42, 27.40, 27.36, 27.10, 25.56, 22.78, 14.21; **IR** (cm^{-1}) 3198, 3003, 2921, 2852, 1693, 1460, 722; **HRMS** (EI) m/z calcd. for $C_{18}H_{33}NO$ $[M]^+$: 279.2562, found: 279.2561; **Specific Rotation** $[\alpha]_D^{25}$ +6.1 ±0.3 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 216 nm, t_{R1} (major) = 4.17 min, t_{R2} (minor) = 4.63 min, 95:5 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



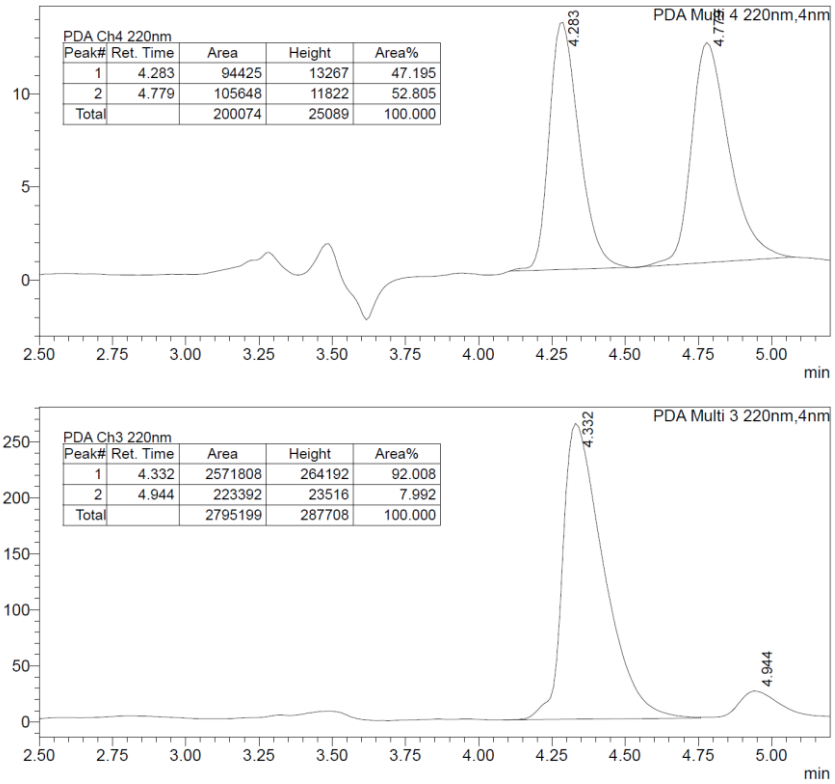
Supplementary Figure 22. HPLC traces of racemic and scalemic compounds of **24**.

(*E*)-5-(Tetradec-5-en-1-yl)pyrrolidin-2-one (25)



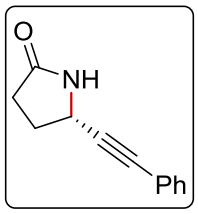
10 mol % of catalyst used at 50 °C; Colorless resin (31 mg, 55%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 6.12 (s, 1H), 5.47 – 5.27 (m, 2H), 3.61 (p, J = 6.6 Hz, 1H), 2.38 – 2.27 (m, 2H), 2.28 – 2.18 (m, 1H), 2.01 – 1.93 (m, 4H), 1.74 – 1.65 (m, 1H), 1.57 – 1.48 (m, 1H), 1.50 – 1.41 (m, 1H), 1.37 – 1.23 (m, 16H), 0.87 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.25, 131.12, 129.75, 54.67, 36.73, 32.72, 32.48, 32.03, 30.31, 29.75, 29.61, 29.53, 29.45, 29.32, 27.46, 25.42, 22.81, 14.24; **IR** (cm^{-1}) 3445, 3185, 3089, 2957, 2918, 2849, 1677, 1463, 963, 777, 656; **HRMS** (EI) m/z calcd. for $C_{18}H_{33}NO$ $[M]^+$: 279.2562, found: 279.2565; **Specific Rotation** $[\alpha]_D^{25}$ –9.3 ±0.7 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 220 nm, t_{R1} (major) = 4.33 min, t_{R2} (minor) = 4.94 min, 92:8 er.

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



Supplementary Figure 23 HPLC traces of racemic and scalemic compounds of **25**.

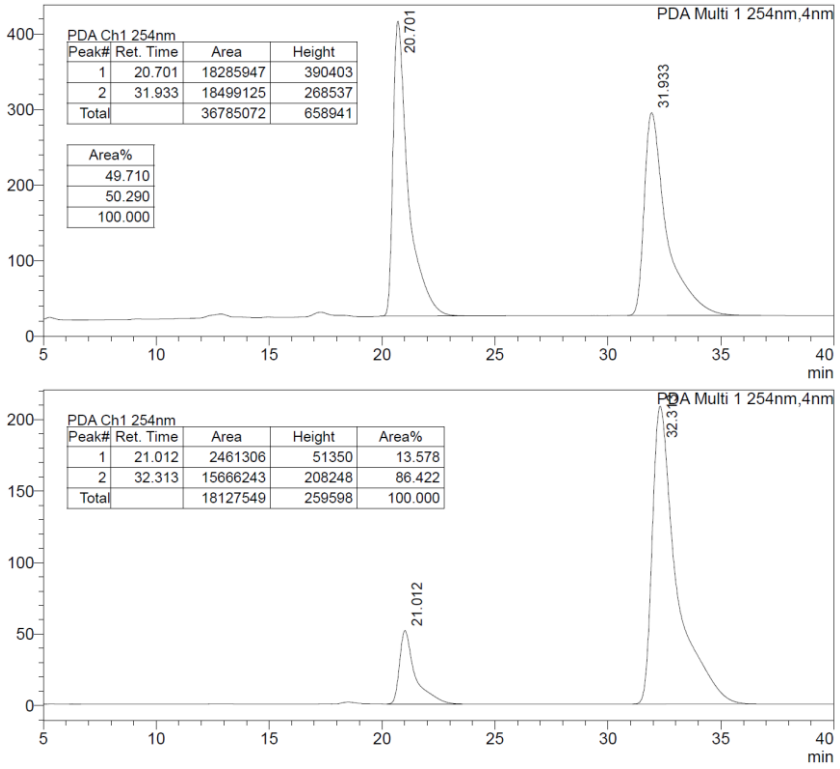
5-(Phenylethynyl)pyrrolidin-2-one (26)



White solid (25 mg, 67%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 2H), 7.37 – 7.27 (m, 3H), 6.39 (br, 1H), 4.62 (s, 1H), 2.58 – 2.44 (m, 2H), 2.41 – 2.23 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.00, 131.79, 128.72, 128.45, 122.31, 88.08, 84.11, 45.47, 30.04, 29.29; **Specific Rotation** $[\alpha]_D^{25}$ +10.4 ±0.1 (*c* 0.1, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 21.01 min, t_{R2} (major) = 32.31 min, 86:14 er.

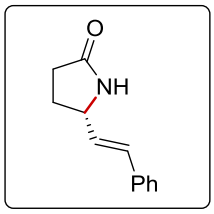
NMR spectroscopic signatures are matched with previously reported ones.[16]

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.



Supplementary Figure 24. HPLC traces of racemic and scalemic compounds of **26**.

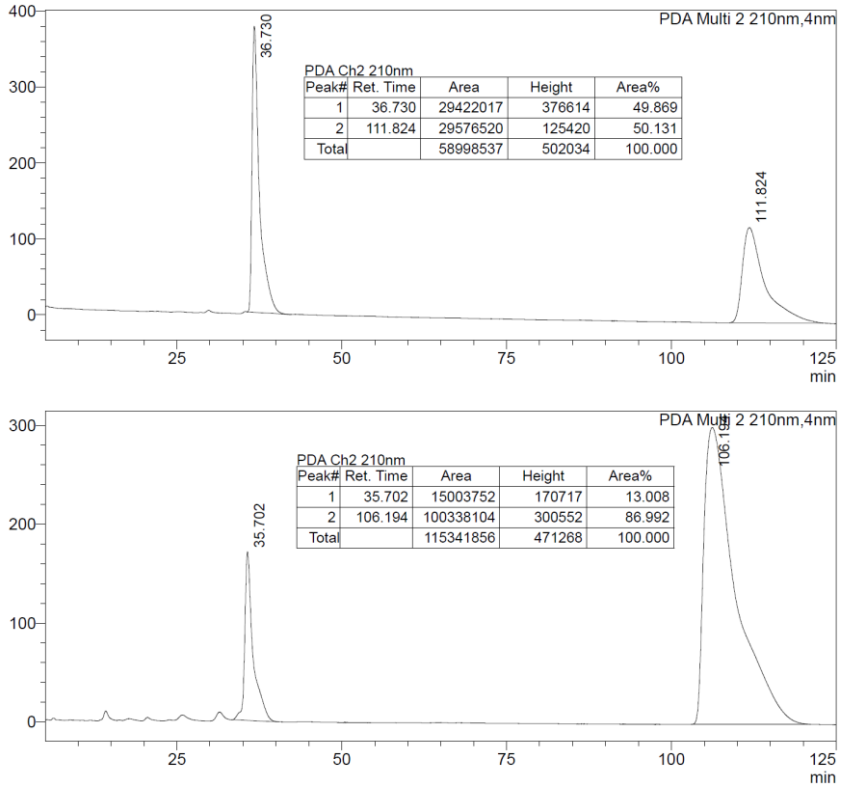
(*E*)-5-Styrylpyrrolidin-2-one (27)



10 mol % of catalyst and $NaBAr^{F}_{4}$ used at 50 ºC; White solid (15 mg, 40%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.37 (d, J = 7.7 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.29 – 7.26 (m, 1H), 6.55 (d, J = 15.8 Hz, 1H), 6.13 (dd, J = 15.8, 7.4 Hz, 1H), 5.63 (br, 1H), 4.34 (q, J = 7.4, 1H), 2.50 – 2.33 (m, 3H), 2.01 – 1.90 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.11, 136.09, 131.44, 129.93, 128.86, 128.25, 126.65, 56.56, 30.01, 28.70; **Specific Rotation** $[\alpha]_D^{25}$ +3.1 ±5.0 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 35.7 min, t_{R2} (major) = 106.19 min, 87:13 er.

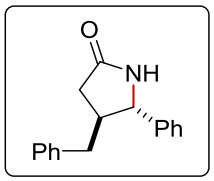
NMR spectroscopic signatures are matched with previously reported ones.[16]

The absolute stereochemistry was assigned by analogy to compound **18** and **21**.

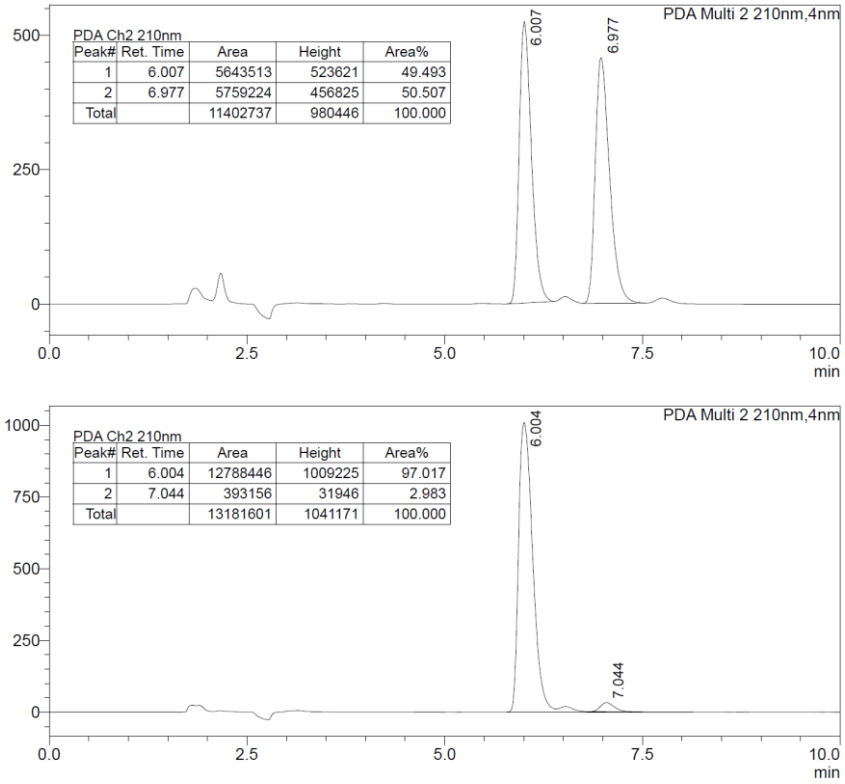


Supplementary Figure 25. HPLC traces of racemic and scalemic compounds of **27**.

***anti*-4-Benzyl-5-phenylpyrrolidin-2-one (28)**

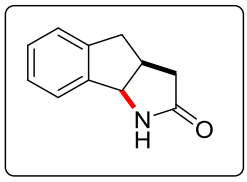


White solid (45 mg, 90%); **m.p.** 114–116 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.15 (m, 5H), 7.16 – 7.06 (m, 3H), 7.01 (d, J = 7.0 Hz, 2H), 6.63 (s, 1H), 4.31 (d, J = 5.3 Hz, 1H), 2.82 (dd, J = 13.6, 6.0 Hz, 1H), 2.63 (dd, J = 13.6, 8.2 Hz, 1H), 2.51 – 2.34 (m, 2H), 2.07 (dd, J = 16.2, 6.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.59, 141.54, 138.98, 128.98, 128.89, 128.63, 128.01, 126.59, 126.09, 63.31, 46.55, 39.56, 36.31; **IR** (cm^{-1}) 3248, 2955, 2913, 1691, 1285, 1023, 698, 475; **HRMS** (EI) m/z calcd. for $C_{17}H_{17}NO$ $[M]^+$: 251.1310, found: 251.1313.; **Specific Rotation** $[\alpha]_D^{25}$ -4.0 ±0.5 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (major) = 6.01 min, t_{R2} (minor) = 7.04 min, 97:3 er.



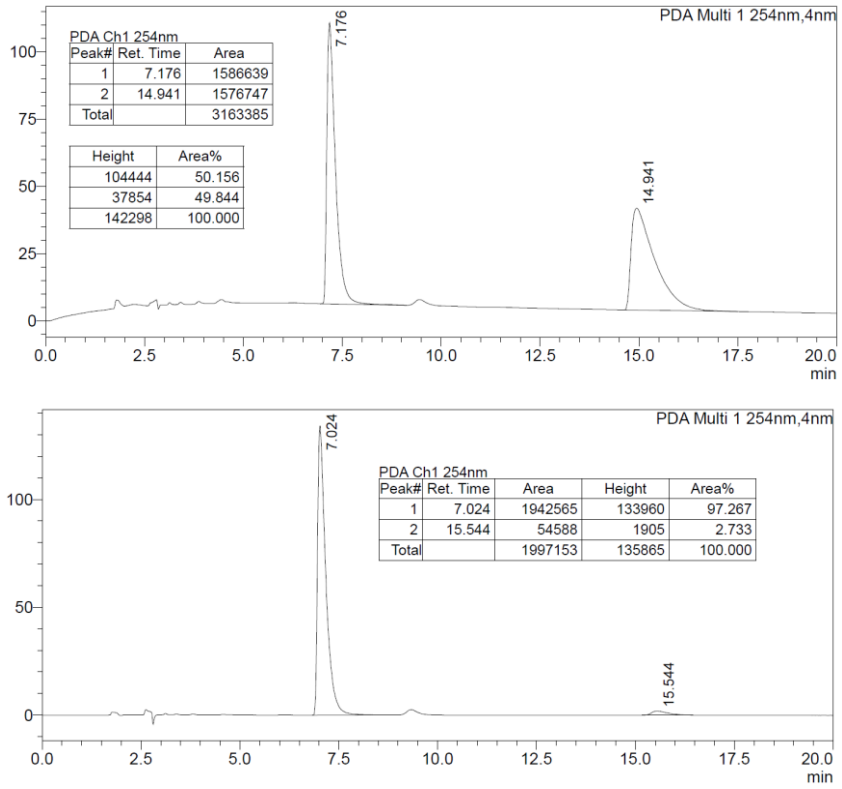
Supplementary Figure 26 HPLC traces of racemic and scalemic compounds of **28**.

***syn*-3,3a,4,8b-Tetrahydroindeno[1,2-b]pyrrol-2(*1H*)-one (29)**



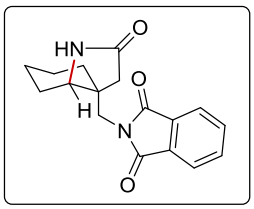
White solid (34 mg, 98%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.40 (br, 1H), 7.30 – 7.17 (m, 4H), 5.02 (d, J = 6.7 Hz, 1H), 3.32 – 3.24 (m, 2H), 2.82 (q, J = 8.1 Hz, 1H), 2.70 (dd, J = 17.3, 8.8 Hz, 1H), 2.19 (dd, J = 17.5, 4.4 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.00, 142.49, 141.72, 128.68, 127.34, 125.38, 124.94, 63.62, 38.60, 37.77, 37.52; **Specific Rotation** $[\alpha]_D^{25}$ +55.1 ±0.3 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (major) = 7.02 min, t_{R2} (minor) = 15.54 min, 97:3 er.

NMR spectroscopic signatures are matched with previously reported ones.[16]



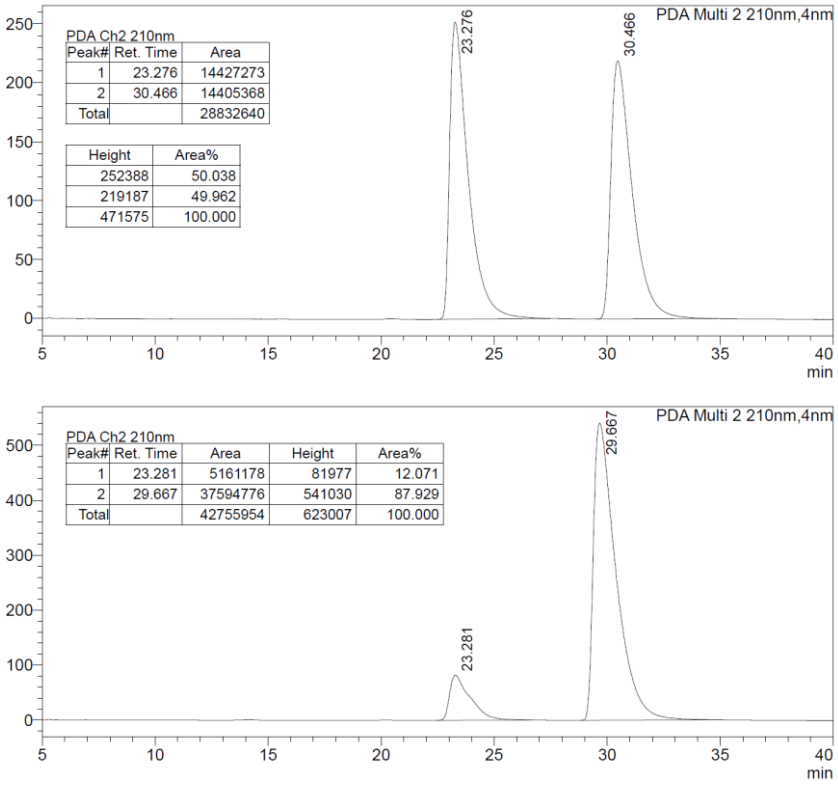
Supplementary Figure 27. HPLC traces of racemic and scalemic compounds of **29**.

2-{(2-Oxooctahydro-3aH-indol-3a-yl)methyl}isoindoline-1,3-dione (30)



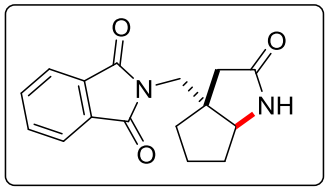
White solid (59 mg, 99%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.1 Hz, 2H), 6.29 (br, 1H), 3.76 (s, 2H), 3.55 (s, 1H), 2.46 (d, *J* = 16.4 Hz, 1H), 1.98 (d, *J* = 16.4 Hz, 1H), 1.92 – 1.80 (m, 1H), 1.77 – 1.65 (m, 1H), 1.61 – 1.37 (m, 6H).; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.04, 168.94, 134.34, 131.87, 123.58, 55.53, 43.45, 43.00, 42.48, 30.72, 26.30, 21.19, 19.91; **Specific Rotation** $[\alpha]_D^{25}$ –19.9 ±0.6 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 210 nm, t_{R1} (minor) = 23.28 min, t_{R2} (major) = 29.67 min, 88:12 er.

NMR spectroscopic signatures are matched with previously reported ones.[16]



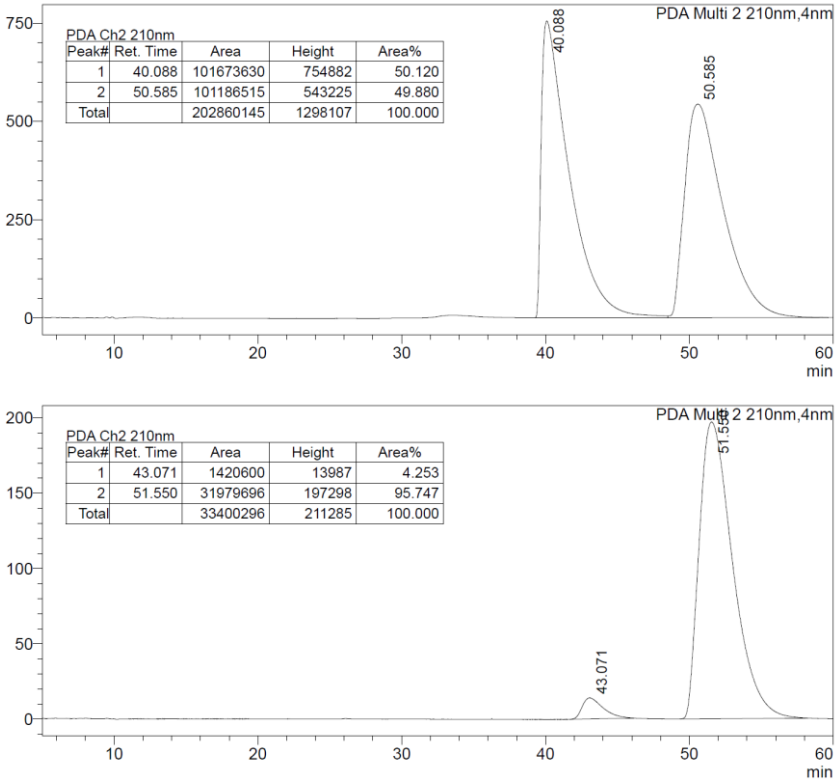
Supplementary Figure 28. HPLC traces of racemic and scalemic compounds of **30**.

2-[{*syn*-2-Oxohexahydrocyclopenta[b]pyrrol-3a(*1H*)-yl}methyl]isoindoline-1,3-dione (31)



White solid (25 mg, 88%, 0.1 mmol scale); **m.p.** 192–194 °C; **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 2H), 7.79 – 7.69 (m, 2H), 6.28 (s, 1H), 4.05 (d, J = 5.0 Hz, 1H), 3.81 (d, J = 14.0 Hz, 1H), 3.75 (d, J = 14.0 Hz, 1H), 2.69 (d, J = 17.8 Hz, 1H), 2.22 (d, J = 17.8 Hz, 1H), 1.79 – 1.64 (m, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.79, 169.17, 134.40, 131.83, 123.64, 62.53, 51.43, 45.15, 41.72, 38.39, 34.06, 23.85; **IR** (cm^{-1}) 3293, 2967, 2931, 1772, 1706, 1695, 1651, 1420, 1338, 1262, 975, 713, 530; **HRMS** (EI) m/z calcd. for $C_{16}H_{16}N_2O_3$ $[M]^+$: 284.1161, found: 284.1159; **Specific Rotation** $[\alpha]_D^{25}$ –15.1 ±1.1 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALCEL OJ-H, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 210 nm, t_{R1} (minor) = 43.07 min, t_{R2} major) 51.55 min, 96:4 er.

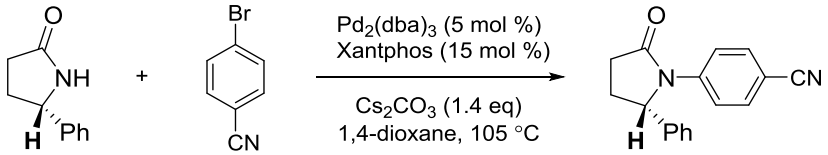
Solid-state structure was characterized by X-ray diffraction analysis (CCDC 1873624).



Supplementary Figure 29 HPLC traces of racemic and scalemic compounds of **31**.

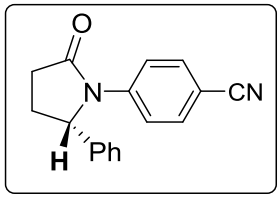
Procedures for Further Derivatization

Access to *N*-arylated product[26]

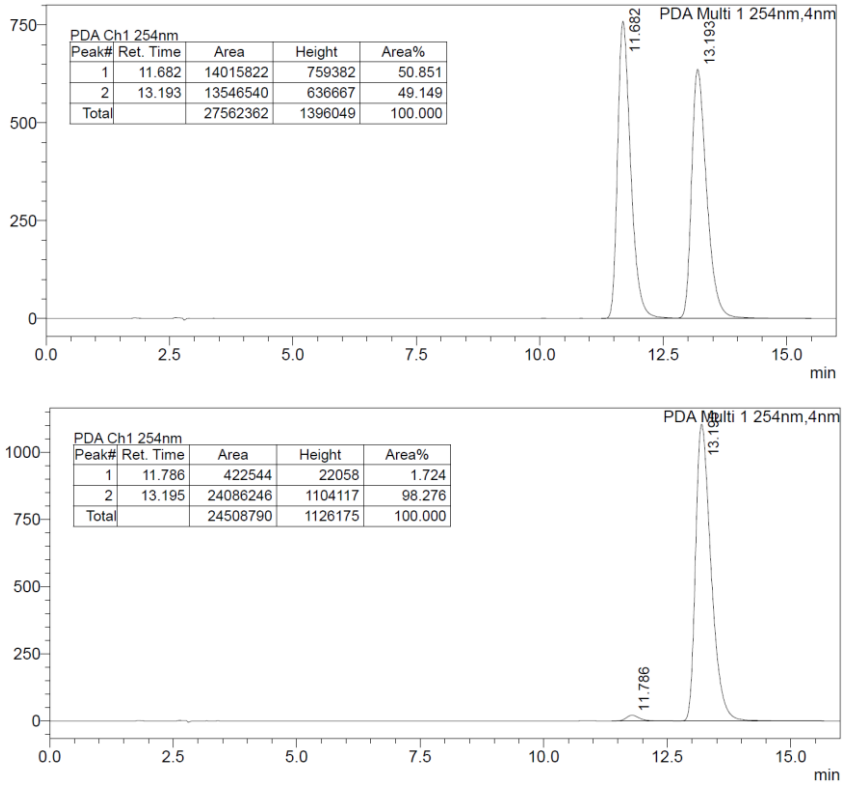


To a reaction vial were added $Pd_2(dba)_3$ (5.8 mg, 0.01 mmol), Xantphos (17.3 mg, 0.03 mmol), **2** (39 mg, 0.24 mmol) and 4-bromobenzonitrile (36 mg, 0.2 mmol) under air. Subsequently, cesium carbonate (91 mg, 0.28 mmol) and 1,4-dioxane (0.6 mL) were added to the reaction under Ar atmosphere. The reaction was heated to 105 °C for 12 h. After completion, the resulting mixture was filtered through a pad of Celite with CH_2Cl_2 washing (~10 mL). The crude material was purified by flash chromatography (*n*-hexane/EtOAc) to afford the desired product.

4-(2-Oxo-5-phenylpyrrolidin-1-yl)benzonitrile (32)

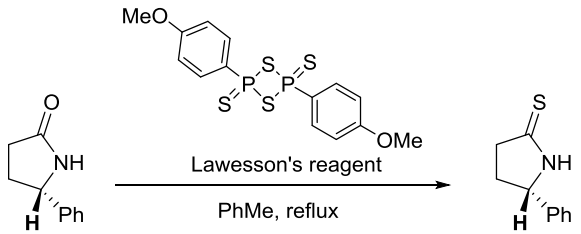


Colorless resin (52 mg, 99%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.60 (d, J = 8.9 Hz, 2H), 7.48 (d, J = 8.9 Hz, 2H), 7.31 (t, J = 7.5 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.16 (d, J = 7.3 Hz, 2H), 5.33 – 5.20 (m, 1H), 2.79 – 2.71 (m, 1H), 2.70 – 2.56 (m, 2H), 2.06 – 1.98 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.33, 142.26, 140.28, 132.75, 129.33, 128.17, 125.58, 121.20, 118.78, 107.36, 63.33, 31.20, 29.09. **IR (cm^{-1})** 2223, 1700, 1601, 1506, 1370, 1298, 1281, 836, 700, 543, 493; **HRMS** (EI) m/z calcd. for $C_{17}H_{14}N_2O$ $[M]^+$: 262.1106, found: 262.1107; **Specific Rotation** $[\alpha]_D^{25}$ –7.4 ±0.3 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALPAK IA-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 254 nm, t_{R1} (minor) = 11.79 min, t_{R2} (major) =13.20 min, 98:2 er.



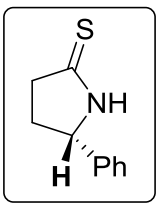
Supplementary Figure 30. HPLC traces of racemic and scalemic compounds of **32**.

Access to thioamide[27]



To a reaction vial was added **2** (16 mg, 0.1 mmol) under air. Subsequently, Lawesson's reagent (20 mg, 0.05 mmol) and anhydrous toluene (0.5 mL) was added under Ar atmosphere, and the reaction was stirred at 80 ˚C for 6 h. The crude material was poured into deionized water, extracted with EtOAc for three times, and dried under reduced pressure. The residue was purified by flash chromatography (*n*-hexane /EtOAc) to afford the desired product

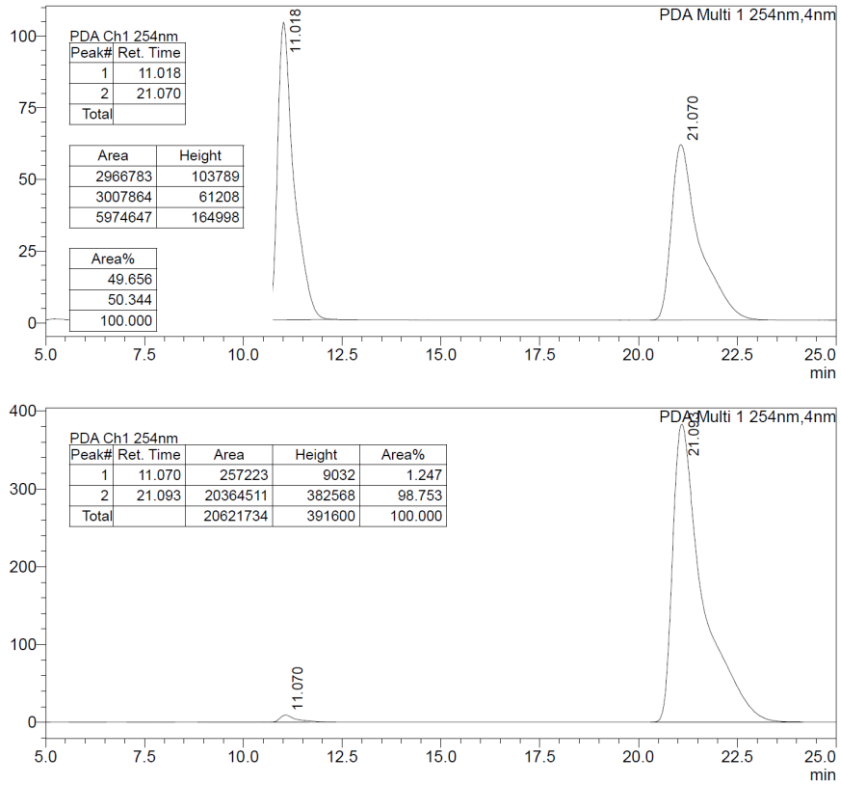
5-Phenylpyrrolidine-2-thione (33)



White solid (17 mg, 96%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.37 (t, J = 7.4 Hz, 2H), 7.34 – 7.30 (m, 1H), 7.25 (d, J = 7.0 Hz, 2H), 4.99 (t, J = 7.4 Hz, 1H), 3.12 – 3.03 (m, 1H), 3.01 – 2.89 (m, 1H), 2.70 – 2.60 (m, 1H), 2.16 – 2.02 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 206.35, 140.33, 129.22, 128.59, 126.05, 65.85, 43.27, 33.57; **Specific Rotation** $[\alpha]_D^{25}$ –90.9 ±0.5 (*c* 0.5, $CHCl_3$), lit.[27] –25.2° (*c* 0.25, CH_2Cl_2, 80%

ee); **HPLC Analysis**. CHIRALPAK IC-3, 32 °C, hexane:^{i}PrOH = 90:10, 1.0 mL/min, 254 nm, t_{R1} (minor) = 11.07 min, t_{R2} (major) = 21.09 min, 99:1 er.

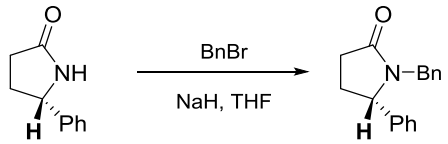
NMR spectroscopic signatures are matched with previously reported ones.[27]



Supplementary Figure 31. HPLC traces of racemic and scalemic compounds of **33**.

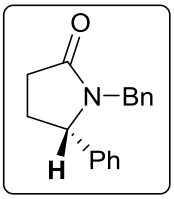
Access to chiral pyrroridine

N-Benzyl protection



To a reaction vial was added **2** (16 mg, 0.1 mmol) under air. Subsequently, anhydrous THF (0.5 mL) was added under Ar atmosphere, and the reaction was cooled to -30 ºC. To the reaction was added NaH (4 mg, 0.15 mmol), and cooled to -30 ºC. Then, benzyl bromide (21 mg, 0.12 mmol) in 0.5 mL THF was transferred to the reaction, and the resulting mixture was stirred at rt for 24 h. The crude material was poured into saturated $NaHCO_3$ (aq), extracted with Et_2O for three times, and the organic layer was dried under reduced pressure. The residue was purified by flash chromatography (*n*-hexane/EtOAc) to afford the desired product.

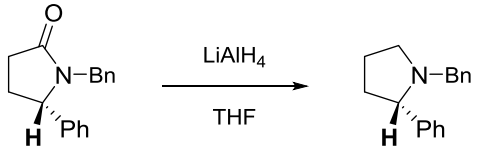
***N*-Benzyl-5-phenylpyrrolidin-2-one**



White solid (25 mg, 99%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.37 (t, J = 7.4 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.13 (d, J = 7.4 Hz, 2H), 7.07 (d, J = 6.9 Hz, 2H), 5.11 (d, J = 14.6 Hz, 1H), 4.40 (dd, J = 8.2, 5.5 Hz, 1H), 3.47 (d, J = 14.6 Hz, 1H), 2.64 (ddd, J = 16.3, 9.8, 6.0 Hz, 1H), 2.49 (ddd, J = 16.9, 9.9, 6.6 Hz, 1H), 2.45 – 2.34 (m, 1H), 1.94 – 1.84 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.55, 140.93, 136.47, 129.15, 128.68, 128.65, 128.24, 127.64, 126.86, 61.43, 44.47, 30.42, 28.37; **Specific Rotation** $[\alpha]_D^{25}$ +37.2 ±0.8 (*c* 0.5, $CHCl_3$).

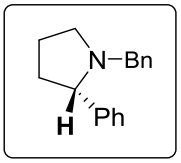
NMR spectroscopic signatures are matched with previously reported ones.[28]

*Access to chiral pyrolidine (***34***)*[29]



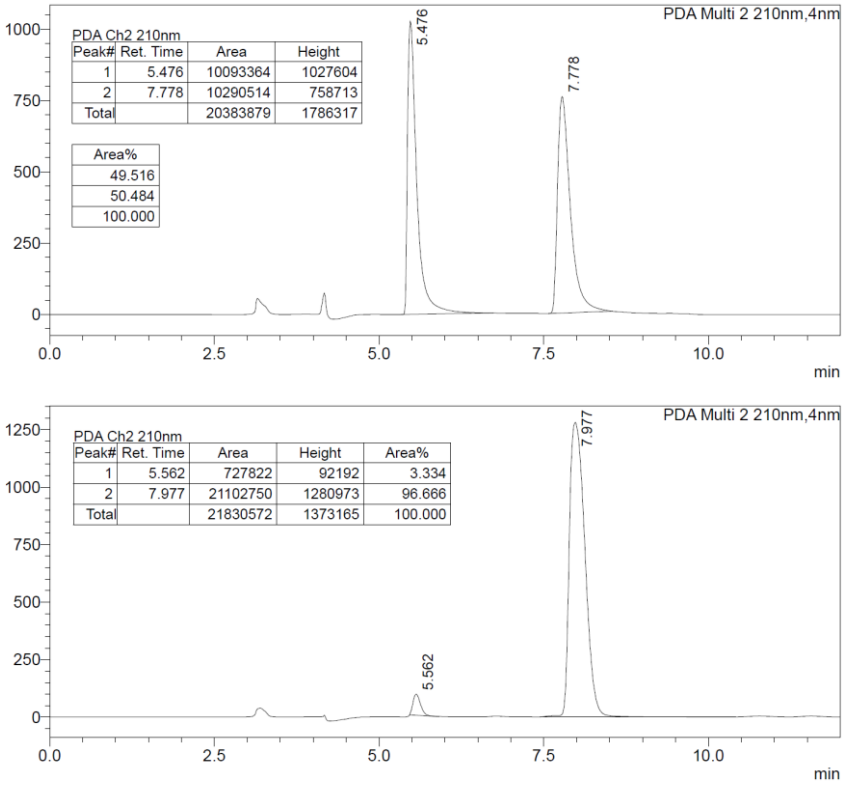
To a reaction vial was added **2** (25 mg, 0.1 mmol) under air. Subsequently, lithium aluminum hydride (16 mg, 0.5 mmol) and anhydrous THF (0.5 mL) was added under Ar atmosphere, and the reaction was stirred at rt for 6 h. After completion, the crude material was transferred to 20 mL vial. The reaction vial was washed with EtOAc, and three drops of deionized water was added for quenching. Water was removed by $MgSO_4$, and the resulting mixture was filtered through a pad of Celite. Solvent was removed under reduced pressure to afford the desired product.

***N*-Benzyl-2-phenylpyrrolidine (34)**



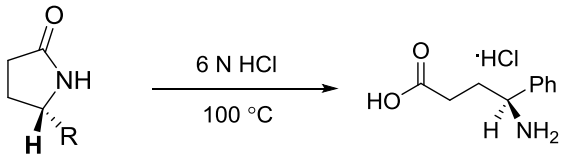
White solid (24 mg, 99%); **^{1}H NMR** (599 MHz, $CDCl_3$) δ 7.49 (d, J = 7.4 Hz, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.34 – 7.20 (m, 6H), 3.87 (d, J = 13.1 Hz, 1H), 3.38 (t, J = 8.2 Hz, 1H), 3.11 (t, J = 8.7 Hz, 1H), 3.05 (d, J = 13.1 Hz, 1H), 2.27 – 2.16 (m, 2H), 1.95 – 1.84 (m, 1H), 1.84 – 1.71 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.03, 139.89, 128.81, 128.55, 128.21, 127.69, 127.11, 126.79, 69.76, 58.25, 53.47, 35.36, 22.46. **Specific Rotation** $[\alpha]_D^{25}$ –96.9 ±0.7 (*c* 0.5, $CHCl_3$); **HPLC Analysis**. CHIRALCEL OJ-H, 32 °C, hexane:^{i}PrOH = 95:5, 1.0 mL/min, 210 nm, t_{R1} (minor) = 5.56 min, t_{R2} (major) = 7.98 min, 97:3 er.

NMR spectroscopic signatures are matched with previously reported ones.[30]



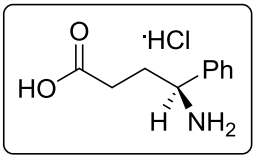
Supplementary Figure 32. HPLC traces of racemic and scalemic compounds of **34**

Access to γ-amino acid derivative[31]



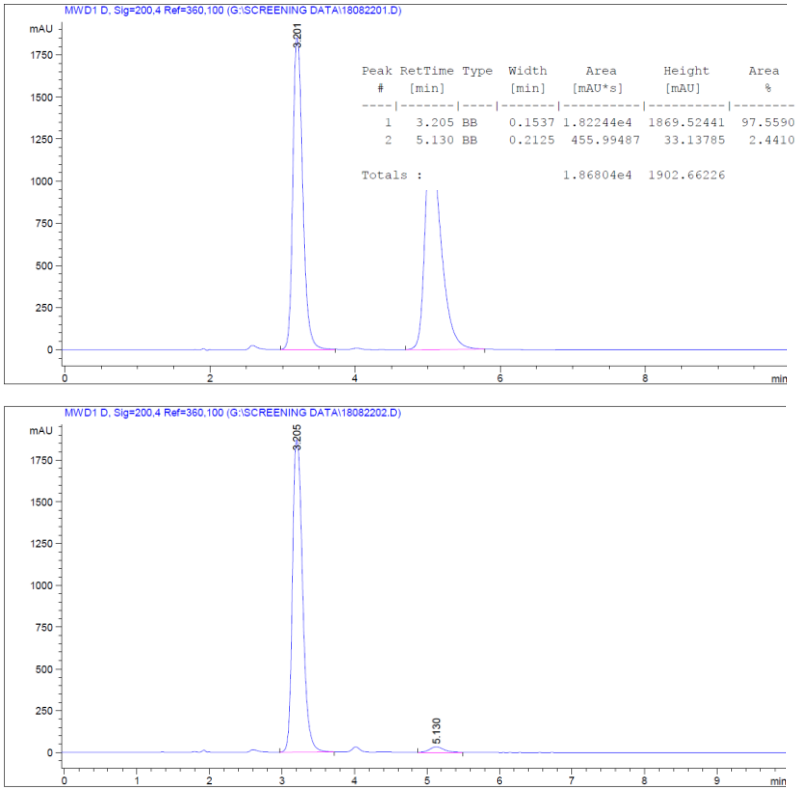
A solution of **2** (16 mg, 0.1 mmol) in 0.6 mL of 6 N hydrochloric acid was heated to 100 ºC for 12 h. After cooled to rt, the solvent was removed under reduced pressure. Ethyl acetate (1 mL) was added, then the mixture was suspended by sonication and stirred at rt for 1 h. The solid product was obtained by filtration with MeOH washing.

4-Amino-4-phenylbutanoic acid hydrochloride (35)



White solid (21 mg, 97 %), **^{1}H NMR** (599 MHz, CD_3OD) δ 7.49 – 7.41 (m, 5H), 4.35 (dd, J = 9.4, 5.4 Hz, 1H), 2.36 – 2.29 (m, 1H), 2.24 – 2.13 (m, 3H); **^{13}C NMR** (151 MHz, CD_3OD) δ 175.56, 137.45, 130.58, 130.49, 128.46, 56.11, 30.84, 30.55. **Specific Rotation** $[\alpha]_D^{25}$ +21.3 ±0.2 (*c* 0.5, H_2O), lit.[32] –39.4 for the (*R*) isomer (*c* 0.2, CD_3OD); **HPLC Analysis**. CROWNPAK CR-I(+), $HClO_4$ (aq, pH =1.5):MeCN = 80:20, 0.5 mL/min, 210 nm, t_{R1} (major) = 3.21 min, t_{R2} (minor) = 5.13 min, 98:2 er.

NMR spectroscopic signatures are matched with previously reported ones.[32]



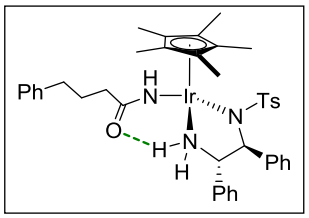
Supplementary Figure 33. HPLC traces of racemic and scalemic compounds of **35**.

Procedures for Experimental Mechanistic Studies

Benzamide and 4-phenylbutanamide were purchased from Sigma-Aldrich and Oakwood Chemical, respectively, and used without further purification. 4-Methyl-*N*-{(1*S*,2*S*)-2-(methylamino)-1,2-diphenylethyl}benzenesulfonamide,[41] *N*-{(1*S*,2*S*)-2-(dimethylamino)-1,2-diphenylethyl}-4-methylbenzenesulfonamide,[42] and **Ir11**[43-44] were synthesized according to previously reported methods.

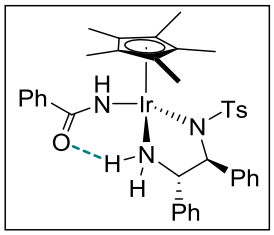
Synthesis of Ir-amido complexes (Fig. 4b)[3,45-46]

Ir12



Orange solid (57 mg, 92%); **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 11.22 (t, J = 11.8 Hz, 1H), 7.32 – 7.26 (m, 4H), 7.21 – 7.17 (m, 1H), 7.15 – 7.10 (m, 5H), 7.02 – 6.95 (m, 2H), 6.82 – 6.73 (m, 1H), 6.72 (d, J = 7.9 Hz, 2H), 6.67 (t, J = 7.5 Hz, 2H), 6.61 – 6.54 (m, 2H), 5.25 (br, 1H), 4.33 (d, J = 10.8 Hz, 1H), 3.66– 3.50 (m, 2H), 2.83 – 2.67 (m, 2H), 2.41 – 2.35 (m, 2H), 2.18 (s, 3H), 2.02 (p, J = 7.7 Hz, 2H), 1.75 (s, 15H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 182.97, 143.38, 142.74, 140.88, 139.73, 139.68, 129.37, 129.12, 128.81, 128.76, 128.36, 128.29, 127.92, 127.77, 127.50, 126.49, 126.13, 85.37, 75.44, 70.78, 42.18, 36.33, 29.55, 21.33, 9.44.

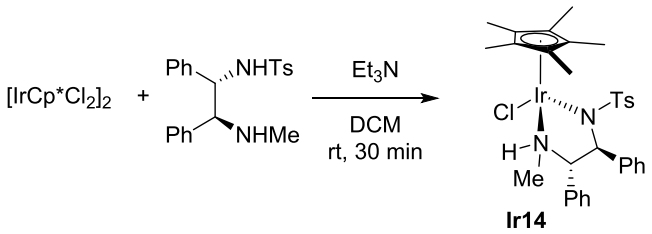
Ir13



Yellow solid (56 mg, 95%); **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 10.85 (t, J = 11.5 Hz, 1H), 7.93 (d, J = 6.3 Hz, 2H), 7.43 (d, J = 7.7 Hz, 3H), 7.16 (d, J = 4.5 Hz, 3H), 7.12 (d, J = 8.1 Hz, 2H), 7.06 – 6.99 (m, 2H), 6.79 (t, J = 7.3 Hz, 1H), 6.69 (t, J = 8.1 Hz, 4H), 6.60 (d, J = 7.6 Hz, 2H), 6.13 (br, 1H), 4.41 (d, J = 11.0 Hz, 1H), 3.85 – 3.73 (m, 1H), 3.71 – 3.59 (m, 1H), 2.17 (s, 3H), 1.81 (s, 15H); **^{13}C NMR** (151 MHz, CD_2Cl_2) δ 177.50, 142.56, 141.88, 140.69, 139.78, 139.54, 129.70, 129.38, 128.86, 128.49, 128.46, 128.27, 127.93, 127.78, 127.53, 127.46, 126.54, 85.68, 75.44, 70.81, 21.32, 9.49.

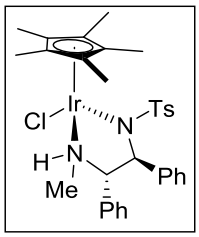
Solid-state structure was characterized by X-ray diffraction analysis (CCDC 1873622).

Preparation of Ir14



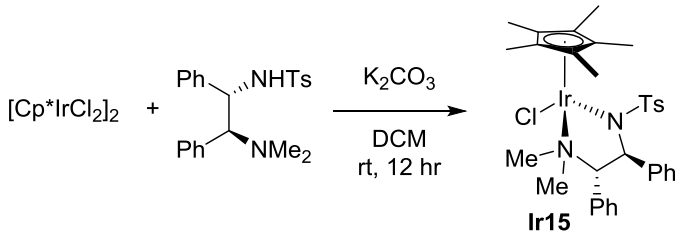
A solution of $[Cp^*IrCl_2]_2$ (100 mg, 0.13 mmol), 4-Methyl-*N*-{(1*S*,2*S*)-2-(methylamino)-1,2-diphenylethyl}benzenesulfonamide (96 mg, 0.25 mmol), and triethylamine (50 mg, 0.5 mmol) in dichloromethane (5 mL) were stirred for 30 min at room temperature. After completion, the crude mixture was purified by flash chromatography (eluent: DCM/MeOH= 20:1), followed by recrystallization from dichloromethane/pentane to afford the desired complexes.

Ir14



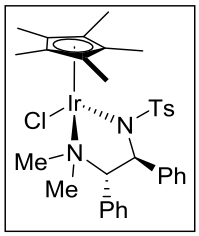
Orange solid (150 mg, 85%); **m.p.** 219–221 °C; **^{1}H NMR** (599 MHz, CD_2Cl_2) δ 7.53 (d, J = 7.9 Hz, 2H), 7.24 – 7.14 (m, 3H), 7.01 – 6.91 (m, 5H), 6.83 – 6.73 (m, 2H), 6.70 (d, J = 7.5 Hz, 2H), 4.41 – 4.30 (m, 2H), 3.60 (appt, J = 11.4 Hz, 1H), 2.62 (d, J = 6.2 Hz, 3H), 2.29 (s, 3H), 1.74 (s, 15H); **^{13}C NMR** (151 MHz, CD_2Cl_2) δ 141.61, 140.71, 136.62, 129.29, 129.12, 128.82, 128.77, 128.59, 128.52, 128.12, 127.73, 126.97, 86.78, 82.62, 70.37, 41.28, 21.54, 10.17; **IR** (cm^{-1}) 3029, 3031, 2918, 2856, 1739, 1454, 1271, 1135, 928, 699, 580, 546; **HRMS** (EI) m/z calcd. for $C_{32}H_{38}ClIrN_2O_2S$ $[M]^+$: 742.1972, found: 742.1969.

Preparation of Ir 15[47]



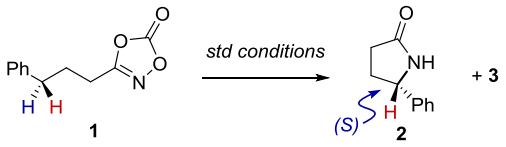
A solution of $[Cp^*IrCl_2]_2$ (76 mg, 0.095 mmol), *N*-{(1*S*,2*S*)-2-(dimethylamino)-1,2-diphenylethyl}-4-methylbenzenesulfonamide (75 mg, 0.19 mmol), and K_2CO_3 (43 mg, 0.31 mmol) in dichloromethane (5 mL) were stirred for 30 min at 25 °C for overnight. After completion, the crude mixture was purified by flash chromatography (eluent: DCM/MeOH= 1:20), followed by recrystallization from chloroform/pentane to afford the desired complexes.

Ir15

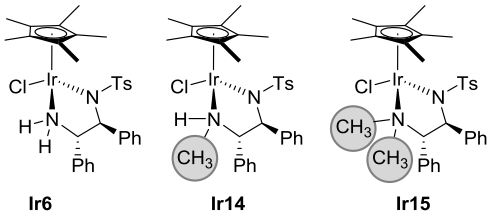


Orange solid (86 mg, 60%); **m.p.** 135–137 °C (decomp.); **^{1}H NMR** (400 MHz, $CDCl_3$, –10 °C) δ 7.66 (d, J = 8.1 Hz, 2H), 7.47 – 7.35 (m, 2H), 7.34 – 7.26 (m, 1H), 7.19 (appt, J = 7.4 Hz, 1H), 7.13 – 7.05 (m, 1H), 7.03 – 6.88 (m, 3H), 6.86 – 6.70 (m, 4H), 5.36 (d, J = 10.9 Hz, 1H), 5.29 (d, J = 11.1 Hz, 1H), 3.21 (s, 3H), 2.77 (s, 3H), 2.24 (s, 3H), 1.47 (s, 15H); **^{13}C NMR** (101 MHz, $CDCl_3$, –10 °C) δ 142.73, 140.25, 139.87, 134.68, 130.39, 130.11, 129.80, 128.84, 128.33, 127.57, 126.70, 125.72, 86.86 (C_5Me_5), 78.09, 67.36, 48.91, 47.70, 21.47, 9.74 ($C_5\mathit{Me}_5$). **IR** (cm^{-1}) 3028, 2913, 1739, 1453, 1375, 1262, 1135, 942, 698, 548; **HRMS** (ESI) m/z calcd. for $C_{33}H_{40}IrN_2O_2S$ $[M\text{-}Cl]^+$: 721.2440, found: 721.2463.

Effects of *N*-methylated catalysts on enantioselective C−H amidation (Fig. 4f)



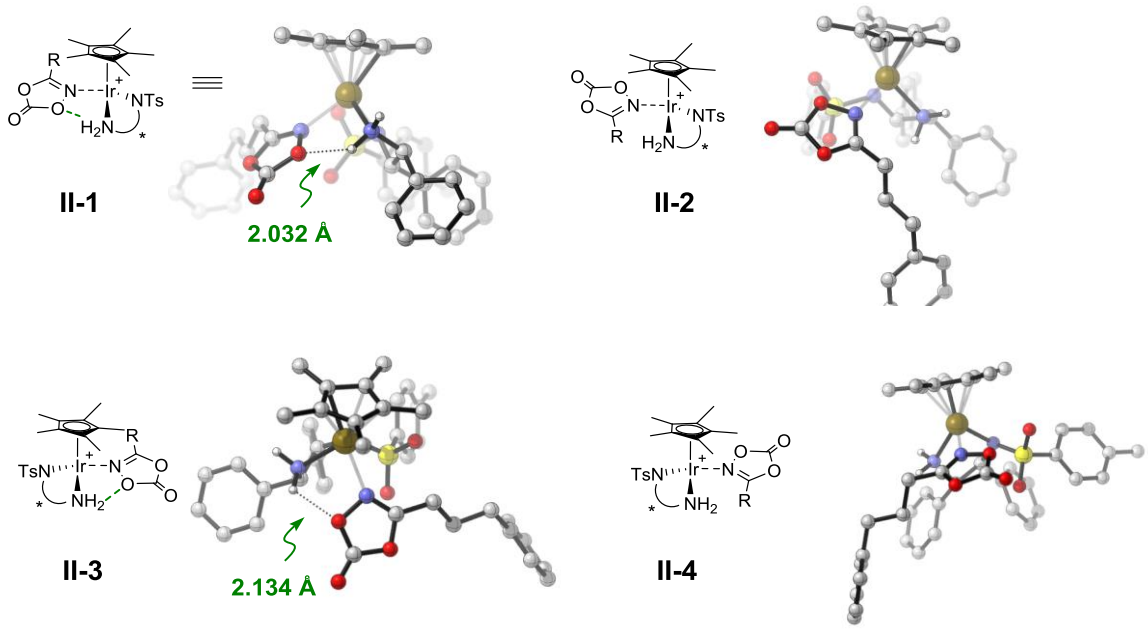
catalyst	Ir6	Ir14	Ir15
yield of **2**	31%, 98:2 e.r.	12%, 81:19 e.r.	12%, 40:60 e.r.
yield of **3**	<5%	15%	50%



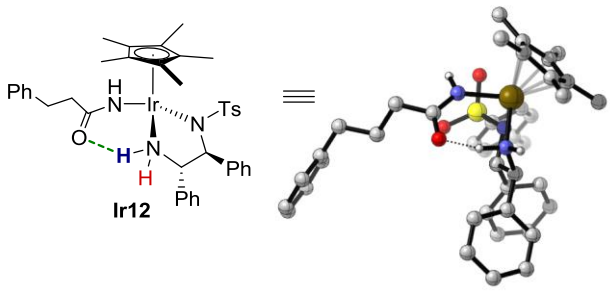
To a 4 mL vial were added **1** (20.6 mg, 0.1 mmol) and anhydrous 1,1,2,2-tetrachloroethane-d_2 (0.5 mL) under Ar atmosphere. Subsequently, iridium catalyst (4 mol %), sodium tetrakis{3,5-bis(trifluoromethyl)phenyl}borate (3.5 mg, 4 mol %) were directly added. The reaction mixture was vigorously stirred in a pre-heated aluminum block at 50 °C for 12 h. The crude yields with respect to **2** and **3** were measured by using ^{1}H NMR spectroscopy using 1,1,2-trichloroethane as an internal standard. Enantiomeric ratio was measured after purification by preparative thin-layer chromatography.

DFT Calculations

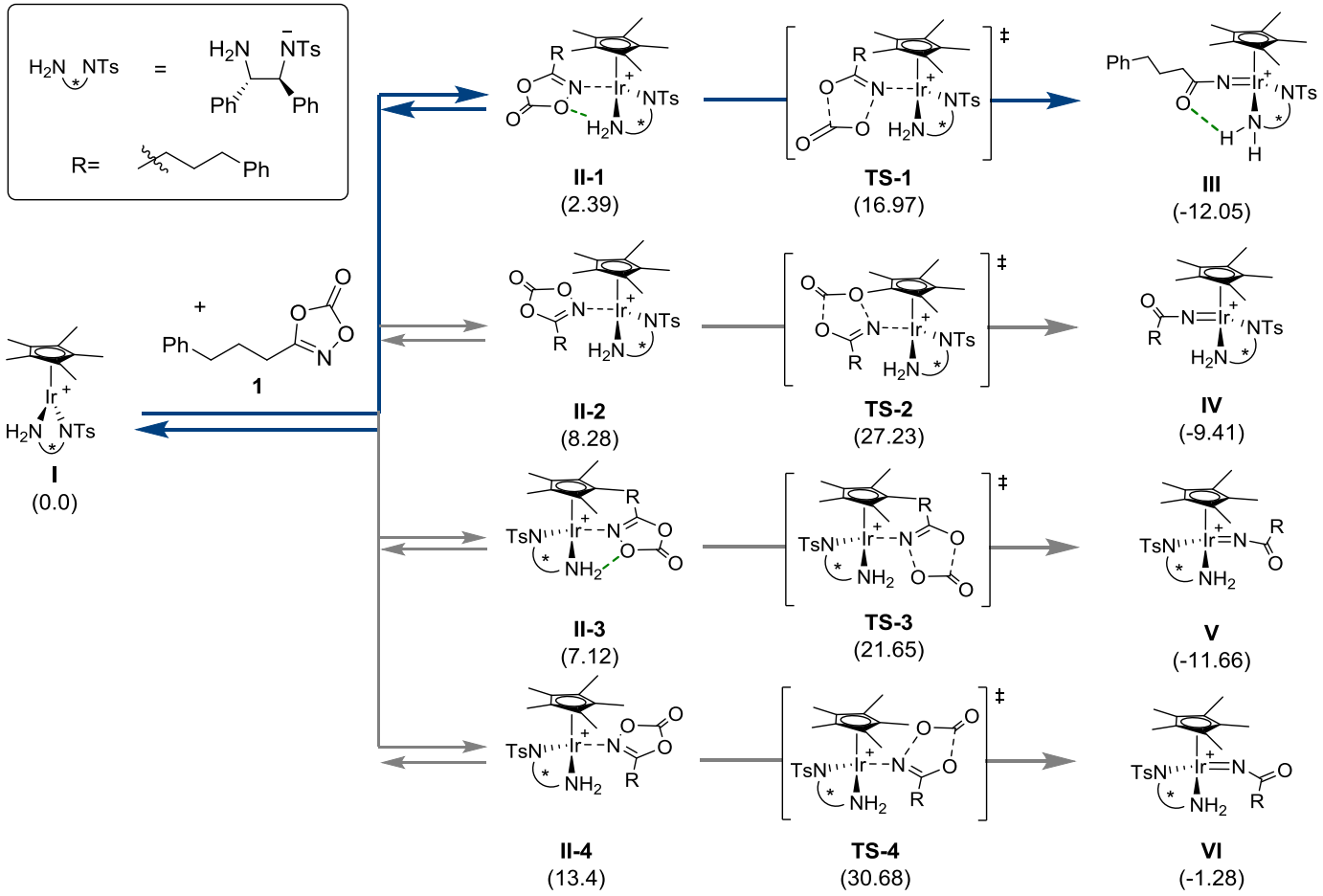
All DFT calculations were carried out with Gaussian09 quantum chemical package.[33] Geometry optimizations were performed with B3LYP functional[34-38] and the 6-31G** basis set. Iridium atom was represented using the Los Alamos LANL2DZ basis set,[39] which includes relativistic effective core potentials. For those structures having various conformations, the most stable conformer was searched and utilized. Vibrational frequency calculations were carried out at the same level of theory as the geometry optimizations. The single-point calculations of the optimized geometries were performed with M06 functional and the basis sets including the Stuttgart/Dresden basis set (SDD) for iridium and 6-311+G** basis set for other atoms. Solvation calculations were carried out with the same level of the single-point calculations via PCM model employing the dielectric constants of ε = 10.125 for dichloroethane. Graphical structures are visualized with CYLview.[40]



Supplementary Figure 34. Optimized structures of the adduct species



Supplementary Figure 35. Optimized structure of **Ir12**

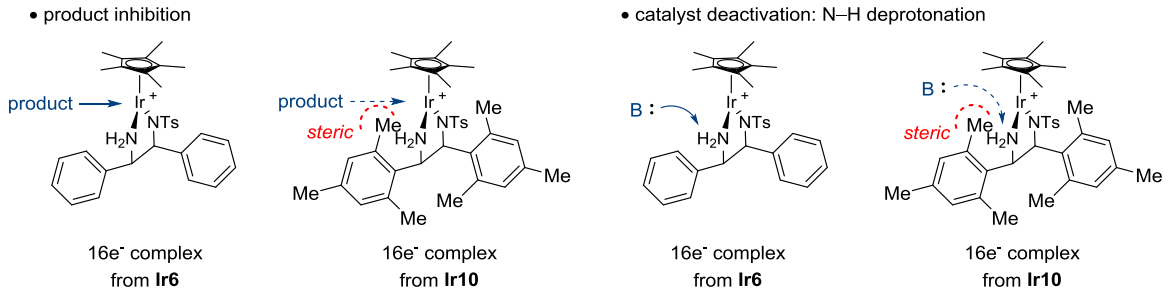


Supplementary Figure 36. Full energy profile of diastereoselective decarboxylation step

Supplementary Discussion

Rationalization of reactivity difference between Ir6 and Ir10. Structures of **Ir6** and **Ir10** are almost identical, and provided essentially same stereochemical outcomes. Thus, we assume that the same stereochemical model for enantioselectivity might be operative for both systems. One significant difference, on the other hand, is on catalytic turnover, which would be largely affected by catalyst stability and/or degree of product inhibition. In current stage, we believe that dimesityl groups in **Ir10** provide beneficial effects on catalysis when it compared with **Ir6** because additional methyl groups on the mesityl moiety can prevent a product approach to the catalyst presumably due to the steric repulsion.

As displayed in the left side of Supplementary Figure 37, generated chiral lactam product can coordinate to a catalytically active 16-electron complex when effective concentration of the product increases. Catalyst-product binding might result in the formation of dead-end adduct species. Dimethyl group on the *ortho*-positions might retard the process owing to their steric influence. Similarly, as illustrated in the right side of Supplementary Figure 37, catalyst deactivation could be prevented with the aid of the dimesityl substituents. Potential deactivation pathway includes deprotonation of N−H group of the catalyst because iridium-coordinated amine moiety is expected to be more acidic, and proximal methyl moiety could also inhibit such side reaction pathway.

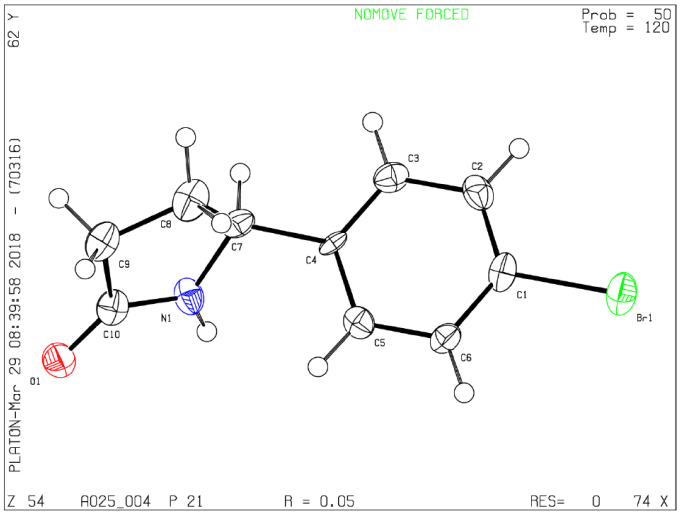


Supplementary Figure 37. Potential product inhibition and catalyst deactivation.

Supplementary Table

Crystallographic data

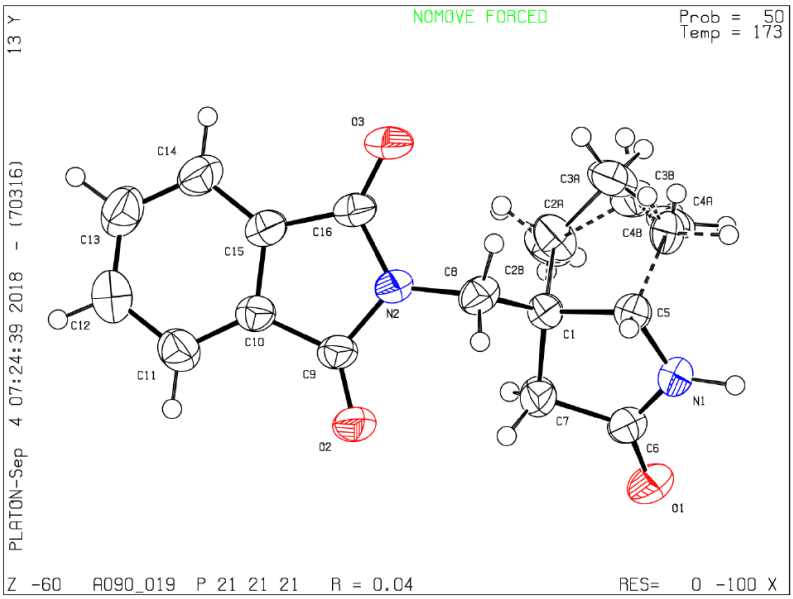
Crystallographic data for **6** (CCDC 1873623)



Supplementary Table 1. Crystal data and structure refinement for **6**

Empirical formula	$C_{10}H_{10}NOBr$	
Formula weight	240.10	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 4.8042(6) Å	α = 90°
	b = 7.0307(8) Å	β = 96.748(9)°
	c = 14.4135(17) Å	γ = 90°
Volume	483.47(10) $Å^3$	
Z	2	
Density (calculated)	1.649 Mg/m^3	
Absorption coefficient	4.208 mm^{-1}	
F(000)	240	
Crystal size	0.178 x 0.084 x 0.034 mm^3	
Theta range for data collection	4.063 to 25.994°.	
Index ranges	–5<=h<=5, –8<=k<=8, –17<=l<=17	
Reflections collected	3128	
Independent reflections	1653 [R(int) = 0.0652]	
Completeness to theta = 25.242°	96.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.5489	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1653 / 14 / 126	
Goodness-of-fit on F^2	0.963	
Final R indices [I>2sigma(I)]	R1 = 0.0476, wR2 = 0.0898	
R indices (all data)	R1 = 0.0775, wR2 = 0.0982	
Absolute structure parameter	0.04(3)	
Largest diff. peak and hole	1.227 and –0.621 $e \cdot Å^{-3}$	

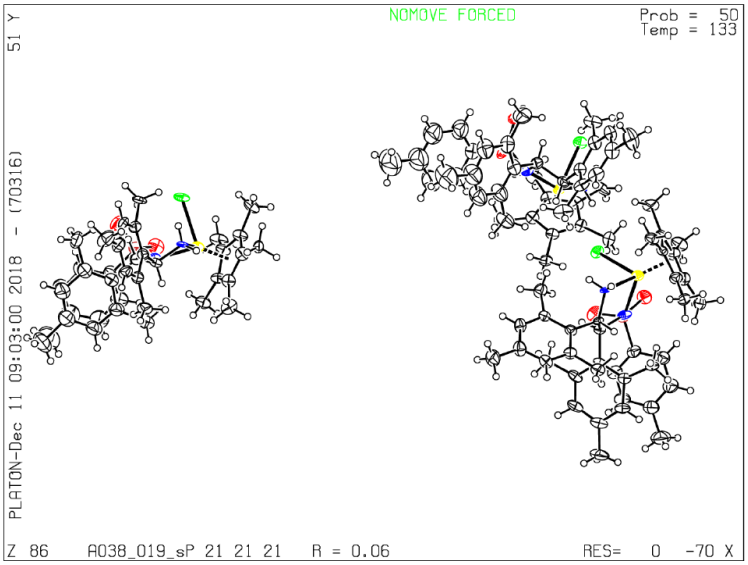
Crystallographic data for **31** (CCDC 1873624)



Supplementary Table 2. Crystal data and structure refinement for **31**

Empirical formula	$C_{16}H_{16}N_2O_3$	
Formula weight	284.31	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.4526(4) Å	α = 90°
	b = 8.6247(5) Å	β = 90°
	c = 21.8258(13) Å	γ = 90°
Volume	1402.88(14) $Å^3$	
Z	4	
Density (calculated)	1.346 Mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	600	
Crystal size	0.220 x 0.205 x 0.097 mm^3	
Theta range for data collection	2.888 to 28.304°.	
Index ranges	–9<=h<=9, –11<=k<=11, –29<=l<=29	
Reflections collected	39079	
Independent reflections	3478 [R(int) = 0.0815]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7312 and 0.7014	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3478 / 36 / 224	
Goodness-of-fit on F^2	1.036	
Final R indices [I>2sigma(I)]	R1 = 0.0432, wR2 = 0.0968	
R indices (all data)	R1 = 0.0624, wR2 = 0.1054	
Absolute structure parameter	-0.2(5)	
Largest diff. peak and hole	0.180 and –0.198 $e·Å^{-3}$	

Crystallographic data for **Ir10** (CCDC 1884674)



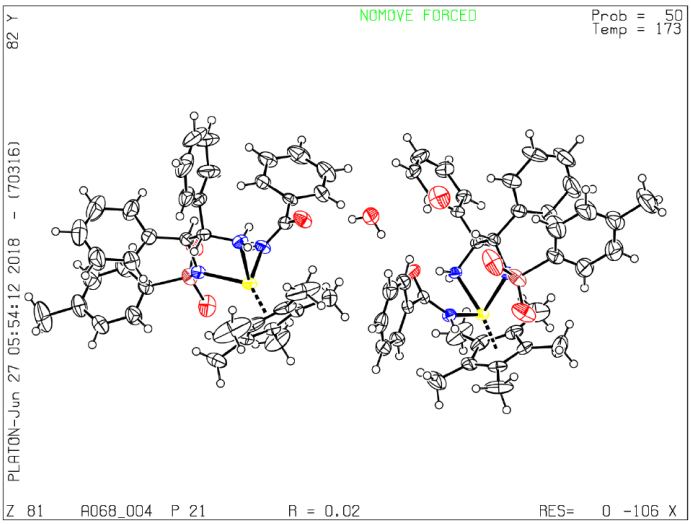
Supplementary Table 3. Crystal data and structure refinement for **Ir10**

Empirical formula	$C_{37}H_{48}N_2O_2SClIr$	
Formula weight	812.48	
Temperature	133(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 17.3773(18) Å	α = 90°
	b = 26.096(3) Å	β = 90°
	c = 30.877(3) Å	γ = 90°
Volume	14002(3) $Å^3$	
Z	12	
Density (calculated)	1.156 Mg/m^3	
Absorption coefficient	2.988 mm^{-1}	
F(000)	4920	
Crystal size	0.402 x 0.085 x 0.082 mm^3	
Theta range for data collection	2.893 to 24.498°.	
Index ranges	–20<=h<=20, –30<=k<=30, –36<=l<=36	
Reflections collected	291468	
Independent reflections	23261 [R(int) = 0.1732]	
Completeness to theta = 24.498°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7454 and 0.5375	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	23261 / 1448 / 1200	
Goodness-of-fit on F^2	1.068	
Final R indices [I>2sigma(I)]	R1 = 0.0565, wR2 = 0.1121	
R indices (all data)	R1 = 0.0872, wR2 = 0.1252	
Absolute structure parameter	0.057(11)	
Largest diff. peak and hole	1.802 and –1.417 $e·Å^{-3}$	

Supplementary Note 1

Alert level B (PLAT342) is due to relatively low quality of diffraction data, mainly based on instability of obtained single crystal. Nevertheless, obtained data strongly support our experimental finding.

Crystallographic data for **Ir13** (CCDC 1873622)



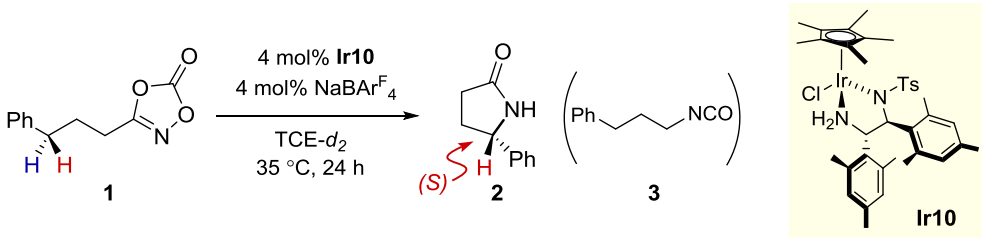
Supplementary Table 4. Crystal data and structure refinement for **Ir13**

Empirical formula	$C_{76}H_{86.50}N_6O_{7.25}S_2Ir_2$	
Formula weight	1648.53	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 16.5121(13) Å	α = 90°
	b = 11.2176(10) Å	β = 106.100(3)°
	c = 20.2408(19) Å	γ = 90°
Volume	3602.1(5) $Å^3$	
Z	2	
Density (calculated)	1.520 Mg/m^3	
Absorption coefficient	3.806 mm^{-1}	
F(000)	1657	
Crystal size	0.256 x 0.254 x 0.205 mm^3	
Theta range for data collection	3.082 to 29.239°.	
Index ranges	–22<=h<=22, –15<=k<=15, –27<=l<=27	
Reflections collected	126288	
Independent reflections	19508 [R(int) = 0.0496]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7458 and 0.5851	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	19508 / 1 / 884	
Goodness-of-fit on F^2	1.047	
Final R indices [I>2sigma(I)]	R1 = 0.0237, wR2 = 0.0412	
R indices (all data)	R1 = 0.0299, wR2 = 0.0425	
Absolute structure parameter	0.002(2)	
Extinction coefficient	0.00083(6)	
Largest diff. peak and hole	0.907 and –0.927 $e·Å^{-3}$	

Supplementary Note 2

Alert level B (PLAT910) of this data is due to systematic limitation of the instrument caused by shading of diffraction by beam stopper.

Supplementary Table 5. Additional control experiments and effects of other reaction parameters



entry	changes from the above condition	yield of **2** (%)	e.r. of **2**	yield of **3** (%)
1	none	>95	>99:1	<5
2	in the absence of **Ir10**	<5	-	<5
3	in the absence of $NaBAr^F_4$	<5	-	73
4	$AgNTf_2$ instead of $NaBAr^F_4$	90	99:1	<5
5	exposed to air	>95	99:1	<5
6	1,2-dichloroethane-d_4 as solvent	78	97:3	5
7	dichloromethane-d_2 as solvent	64	97:3	13
8	TCE as solvent (non-deuterated form)	>95	99:1	<5
9	TCE : Ethanol = 0.4 mL : 0.1 mL as solvent	57	83:17	42
10	Ethanol as solvent	57	63:37	40
11	2,2,2-Trifluoroethanol as solvent	32	56:44	62
12	Hexafluoroisopropanol as solvent	37	55:45	23
13	***ent*-Ir10** instead of **Ir10**	>95	1:99	<5

Yields were determined by ^{1}H NMR analysis using 1,1,2-trichloroethane as an internal standard. Enantiomeric ratios (e.r.) were determined by HPLC analysis.

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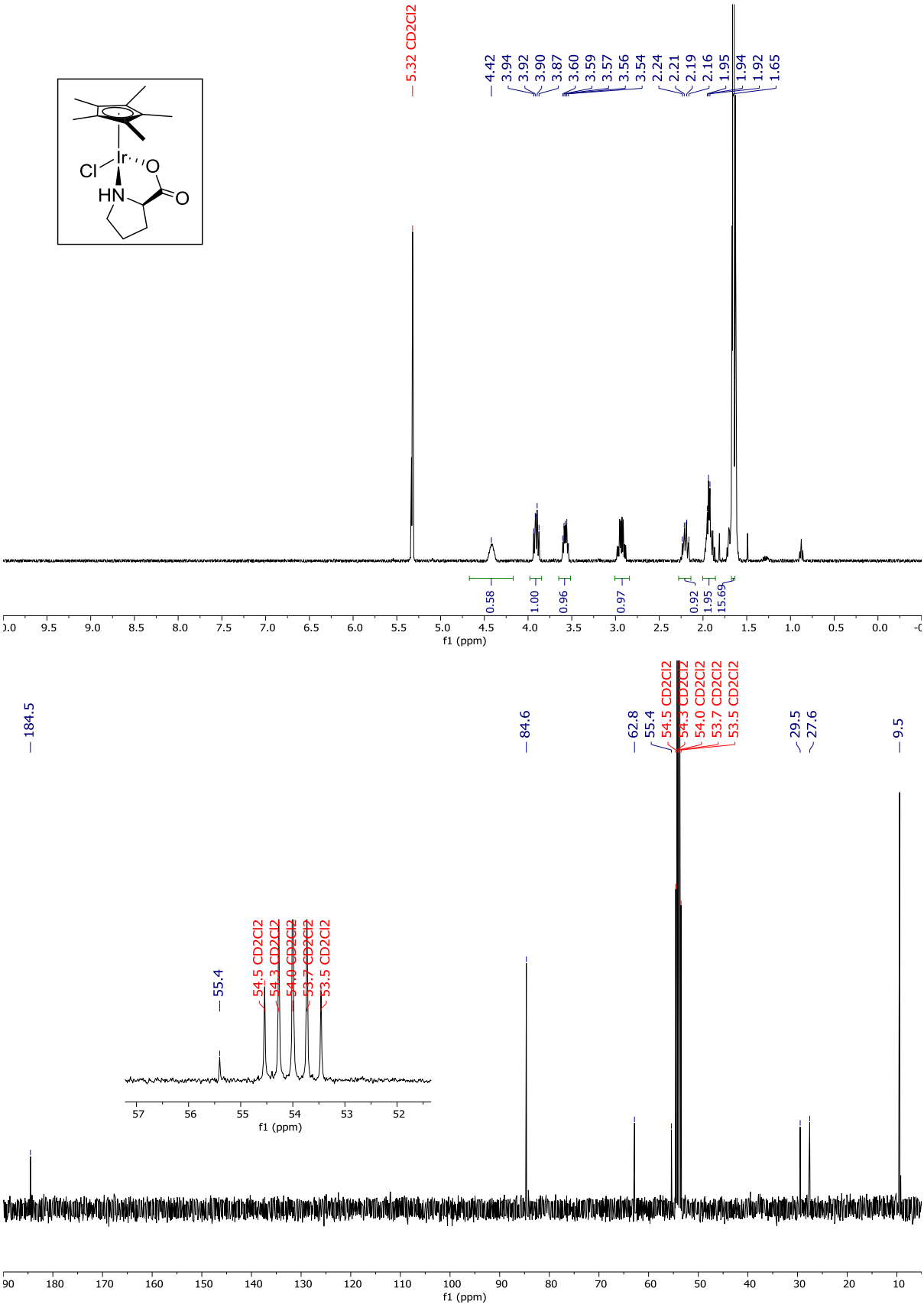
Spectral Copies of ^{1}H, ^{13}C and ^{19}F NMR of Compounds

Ir1



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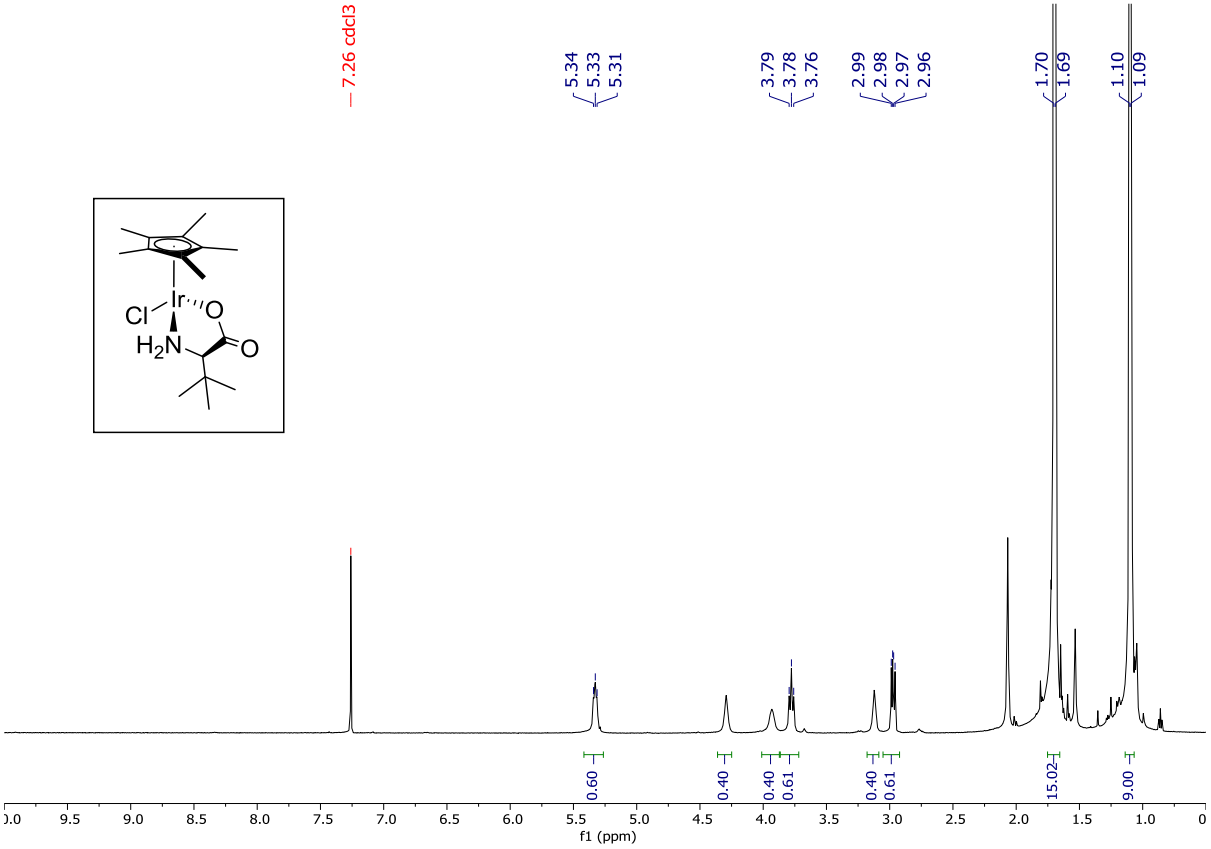
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3.79
3.78
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2.98
2.97
2.96
1.70
1.69
1.10
1.09
Cl
Ir
O
H2N
O
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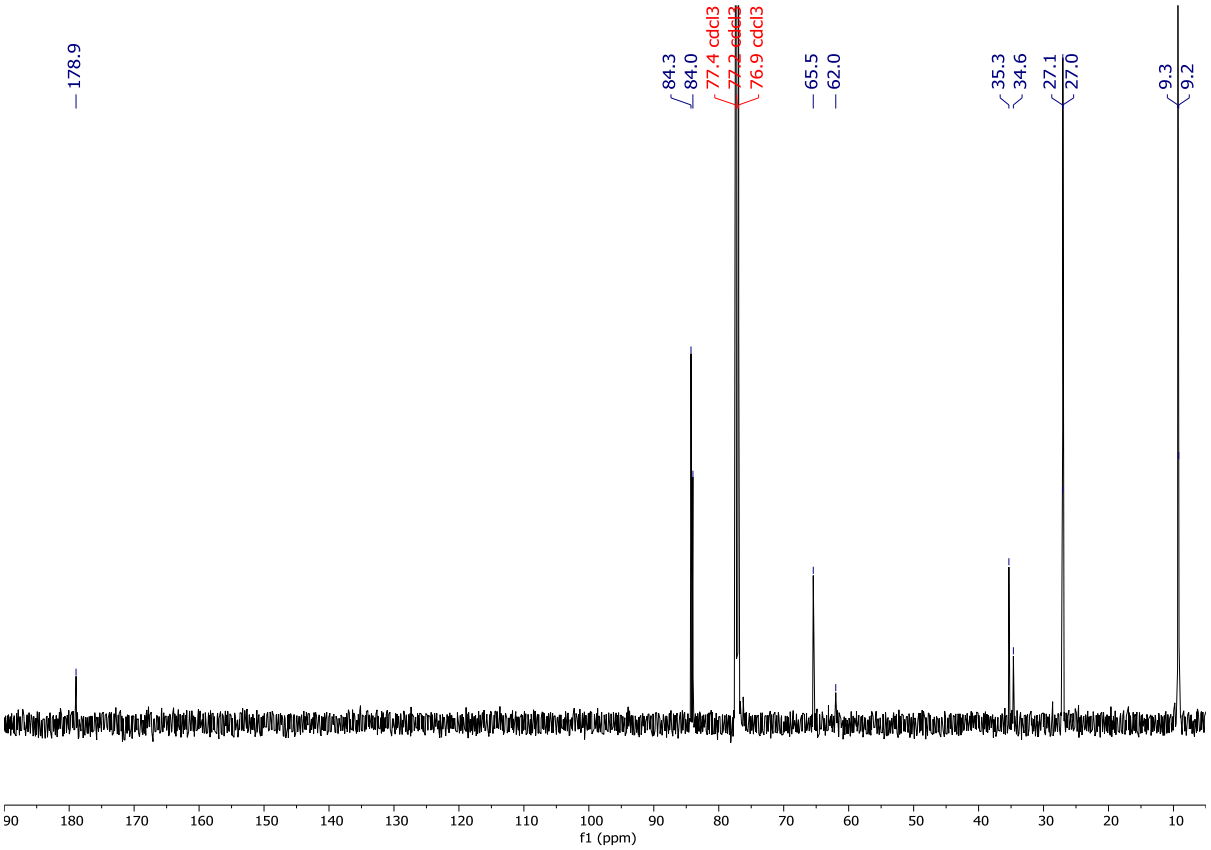
0.40
0.40
0.61
0.40
0.61
15.02
9.00
f1 (ppm)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84.3
84.0
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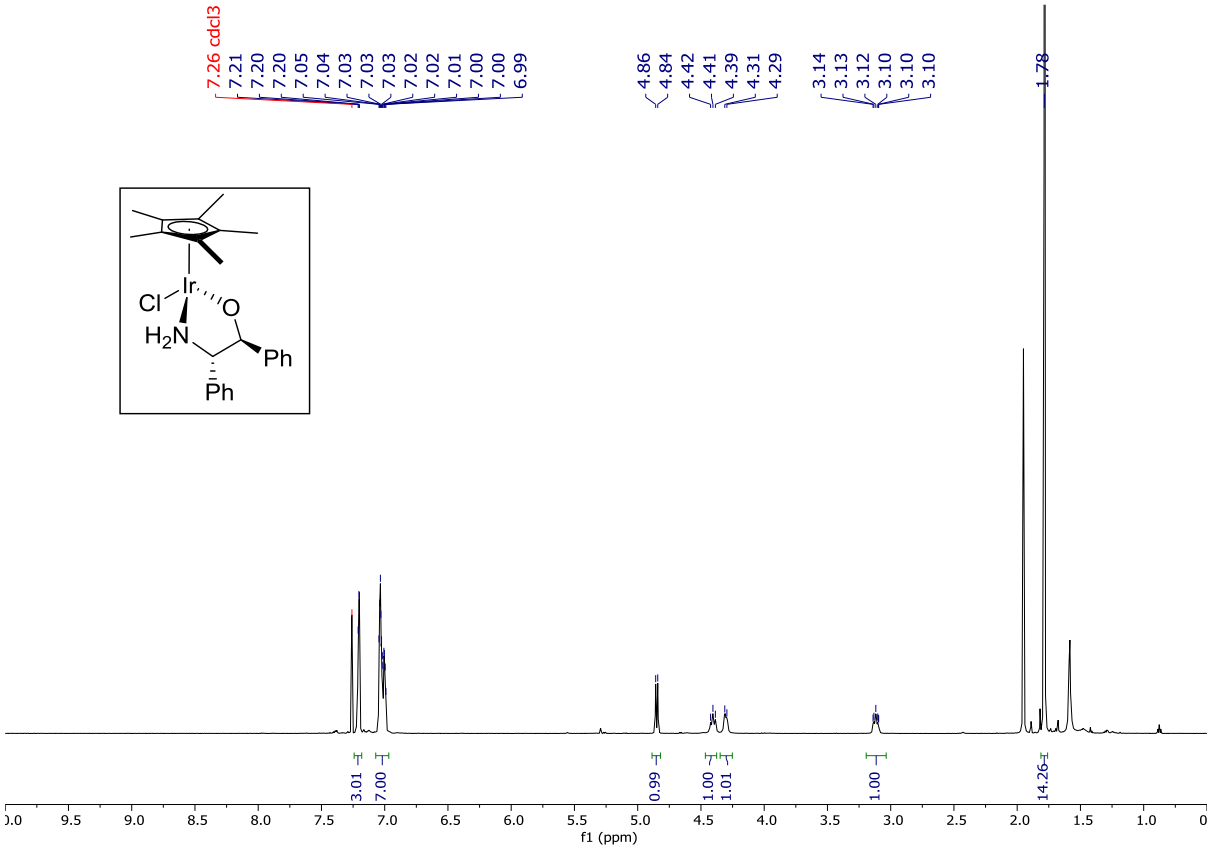
77.2 cdcl3
76.9 cdcl3
65.5
62.0
35.3
34.6
27.1
27.0
9.3
9.2
f1 (ppm)

Ir3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7.20
7.20
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7.04
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7.03
7.03
7.02
7.02
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7.00
7.00
6.99
4.86
4.84
4.42
4.41
4.39
4.31
4.29
3.14
3.13
3.12
3.10
3.10
3.10
1.78
Cl
Ir
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Ph
Ph
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1.00
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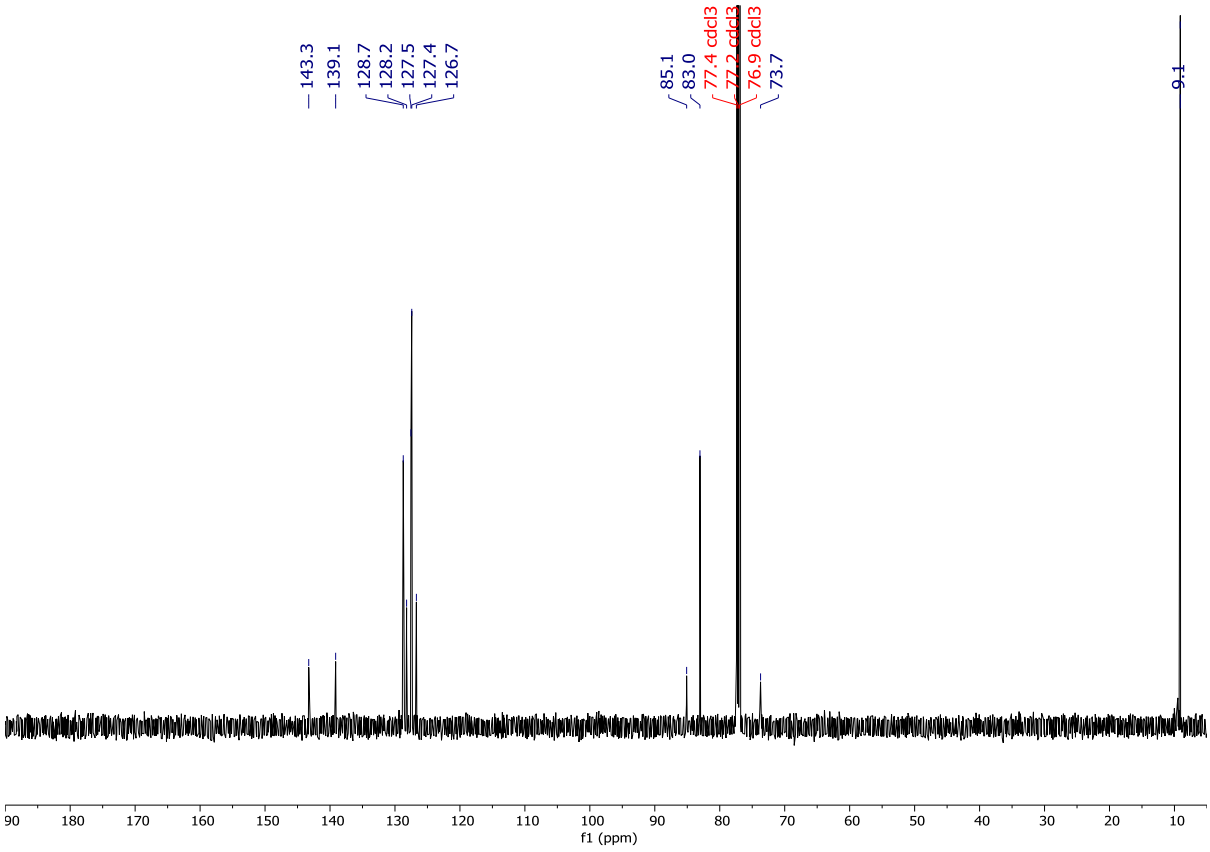
1.00
14.26
f1 (ppm)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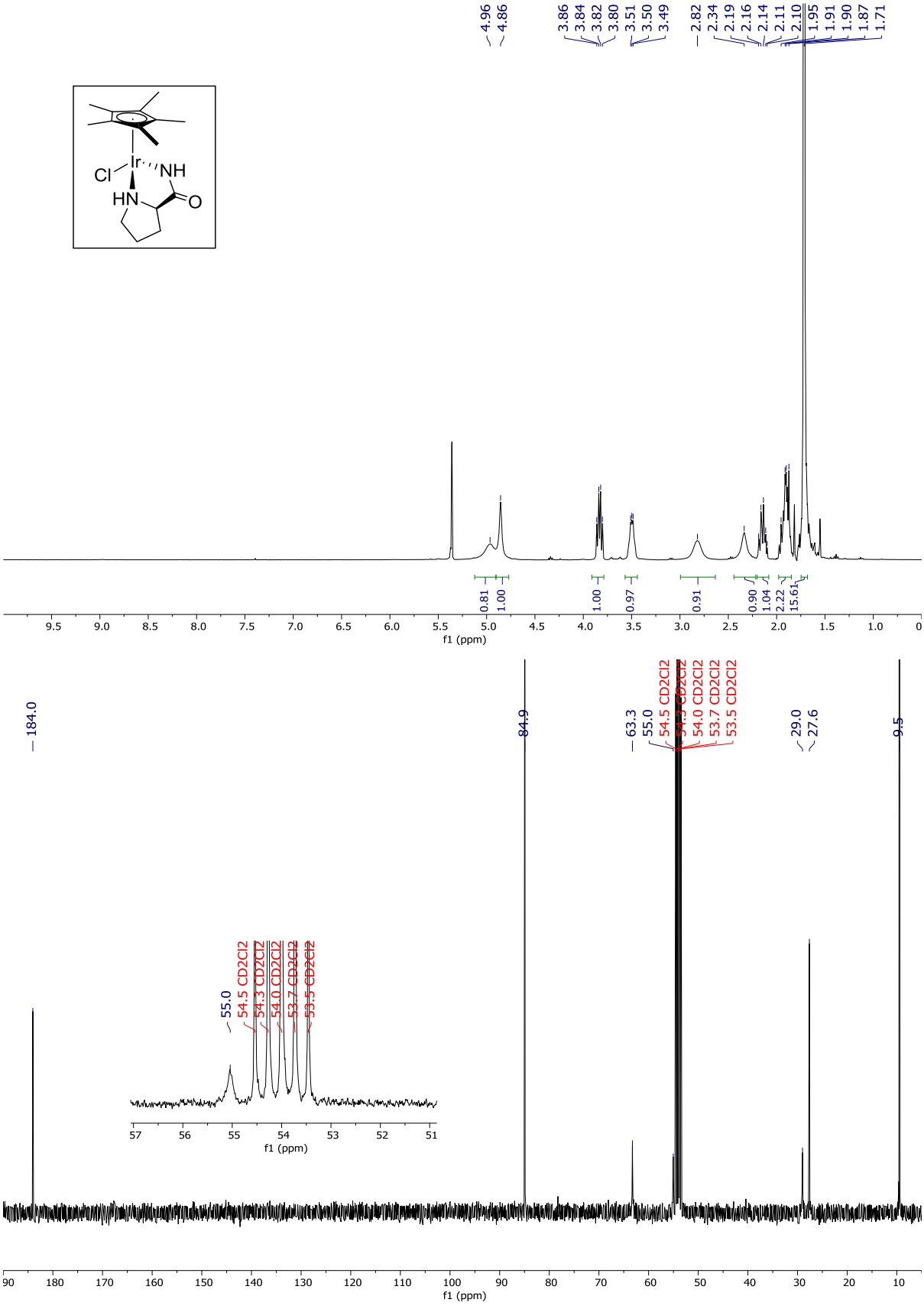
139.1
128.7
128.2
127.5
127.4
126.7
85.1
83.0
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.7
9.1
f1 (ppm)

Ir4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Ir
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HN
O
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3.51
3.50
3.49
2.82
2.34
2.19
2.16
2.14
2.11
2.10
1.95
1.91
1.90
1.87
1.71
0.81
1.00
1.00
0.97
0.91
0.90
1.04
2.22
15.61
f1 (ppm)
184.0
84.9
63.3
55.0
54.5 CD2Cl2
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53.7 CD2Cl2
53.5 CD2Cl2
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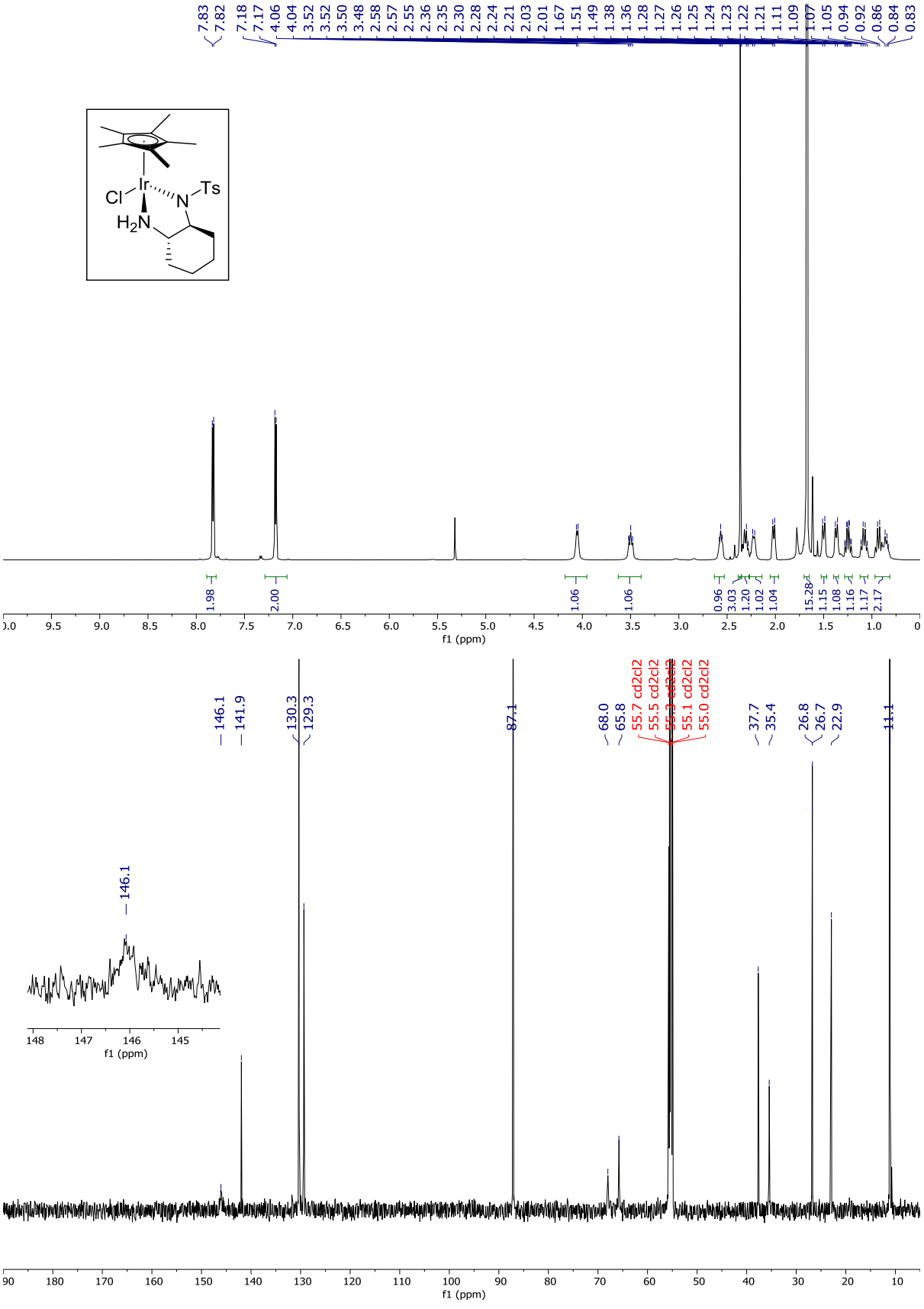
27.6
9.5
f1 (ppm)

Ir5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2.57
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2.35
2.30
2.28
2.24
2.21
2.03
2.01
1.67
1.51
1.49
1.38
1.36
1.28
1.27
1.26
1.25
1.24
1.23
1.22
1.21
1.11
1.09
1.07
1.05
0.94
0.92
0.86
0.84
0.83
Cl
Ir
N
Ts
H2N
1.98
2.00
1.06
1.06
0.96
3.03
1.20
1.02
1.04
15.28
1.15
1.08
1.16
1.17
2.17
f1 (ppm)
146.1
141.9
130.3
129.3
87.1
68.0
65.8
55.7 cd2cl2
55.5 cd2cl2
55.1 cd2cl2
55.0 cd2cl2
37.7
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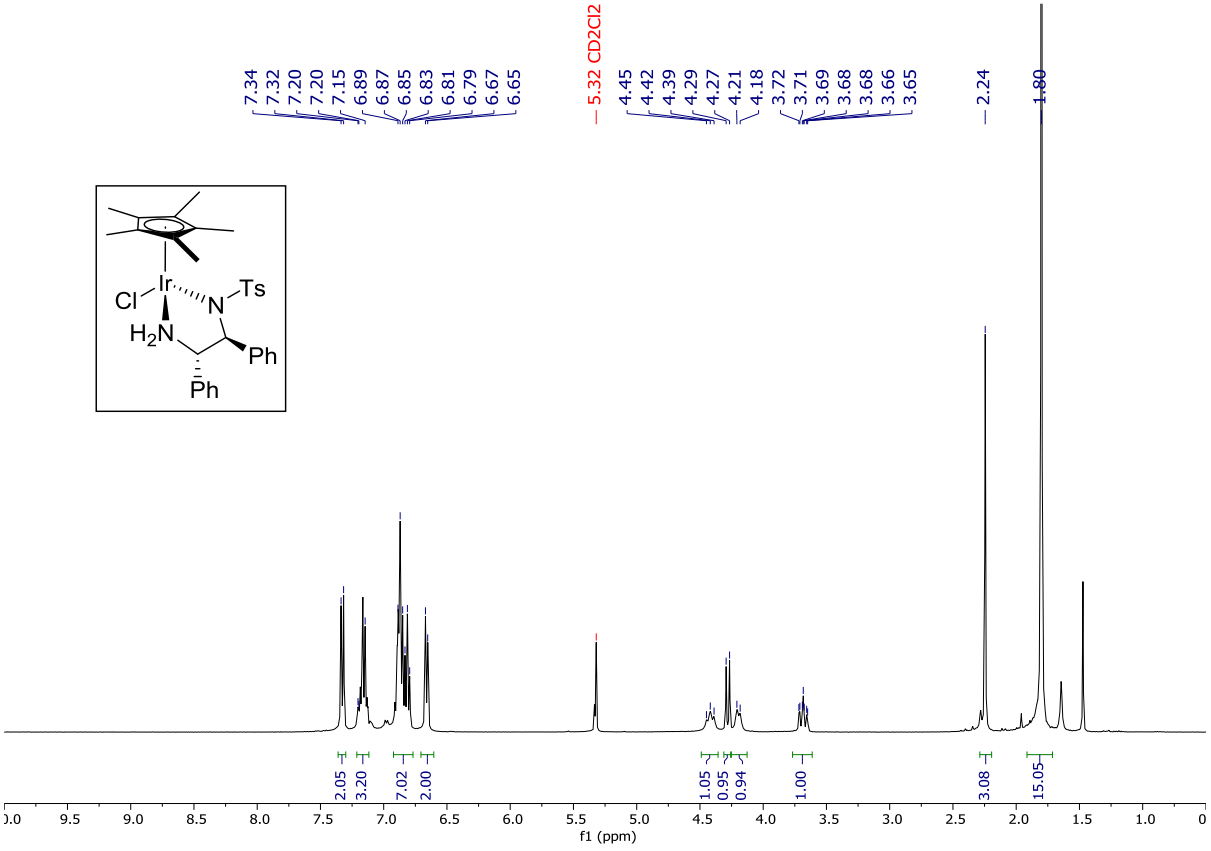
26.7
22.9
11.1
146.1
148
147
146
145
f1 (ppm)
f1 (ppm)

Ir6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6.81
6.79
6.67
6.65
5.32 CD2Cl2
4.45
4.42
4.39
4.29
4.27
4.21
4.18
3.72
3.71
3.69
3.68
3.68
3.66
3.65
2.24
1.80
Ir
Cl
N
Ts
H2N
Ph
Ph
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1.05
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1.00
3.08
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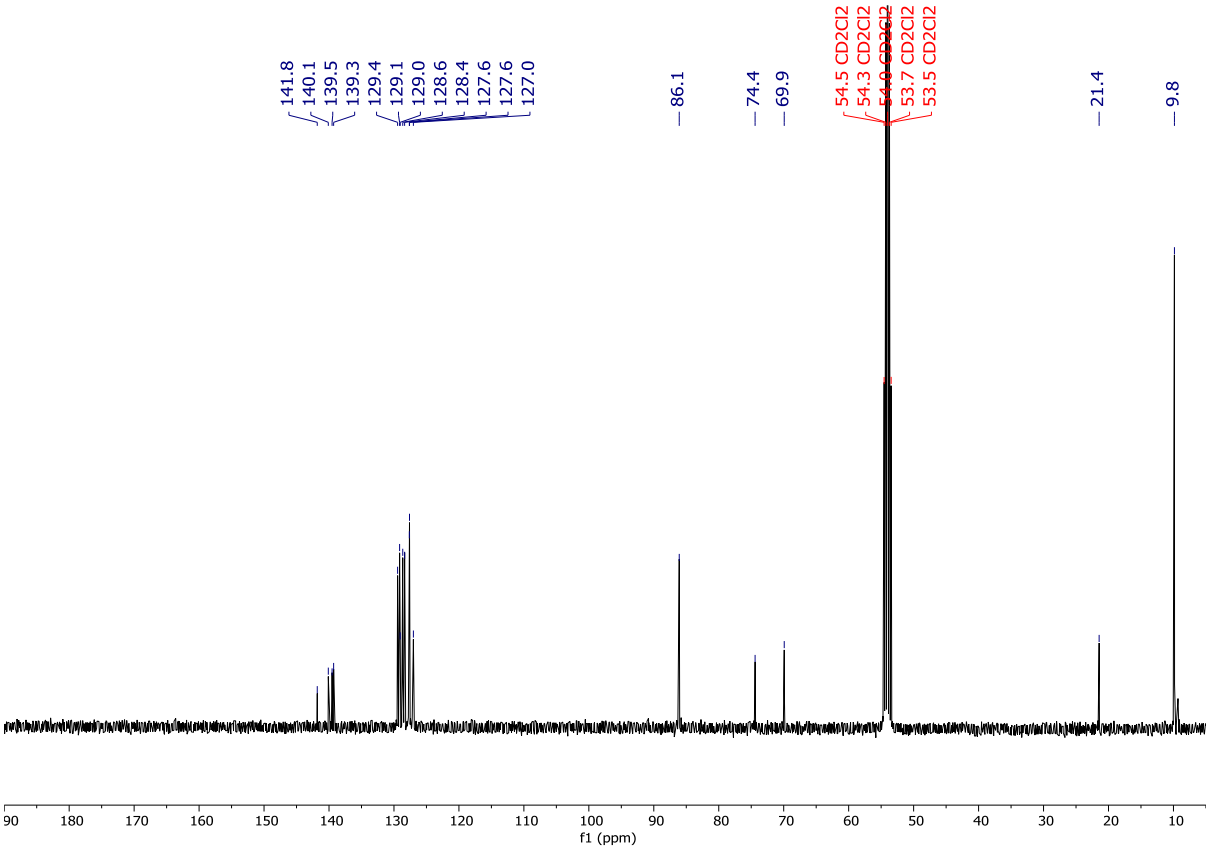
f1 (ppm)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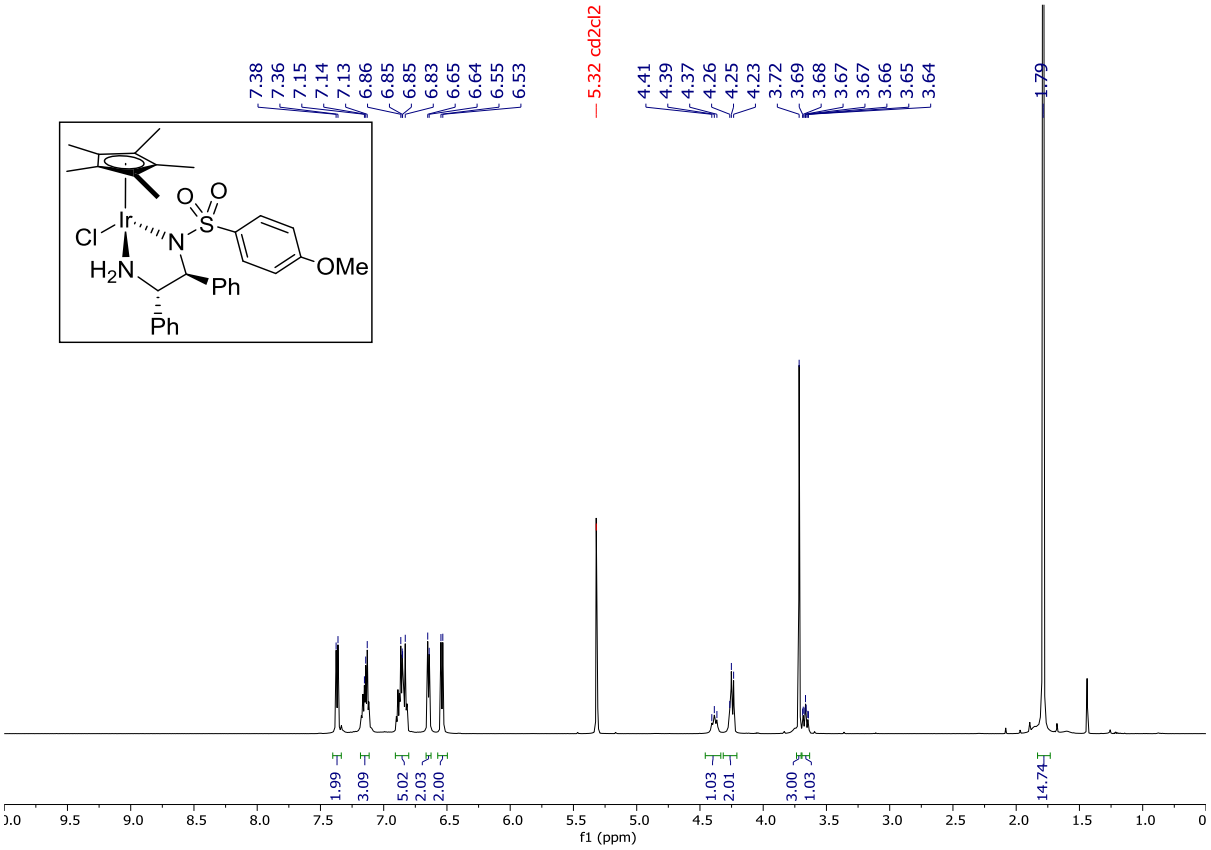
128.4
127.6
127.6
127.0
86.1
74.4
69.9
54.5 CD2Cl2
54.3 CD2Cl2
54.0 CD2Cl2
53.7 CD2Cl2
53.5 CD2Cl2
21.4
9.8
f1 (ppm)

Ir7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6.85
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6.65
6.64
6.55
6.53
5.32 cd2cl2
4.41
4.39
4.37
4.26
4.25
4.23
3.72
3.69
3.68
3.67
3.67
3.66
3.65
3.64
1.79
Cl
Ir
N
O
O
S
H2N
Ph
Ph
OMe
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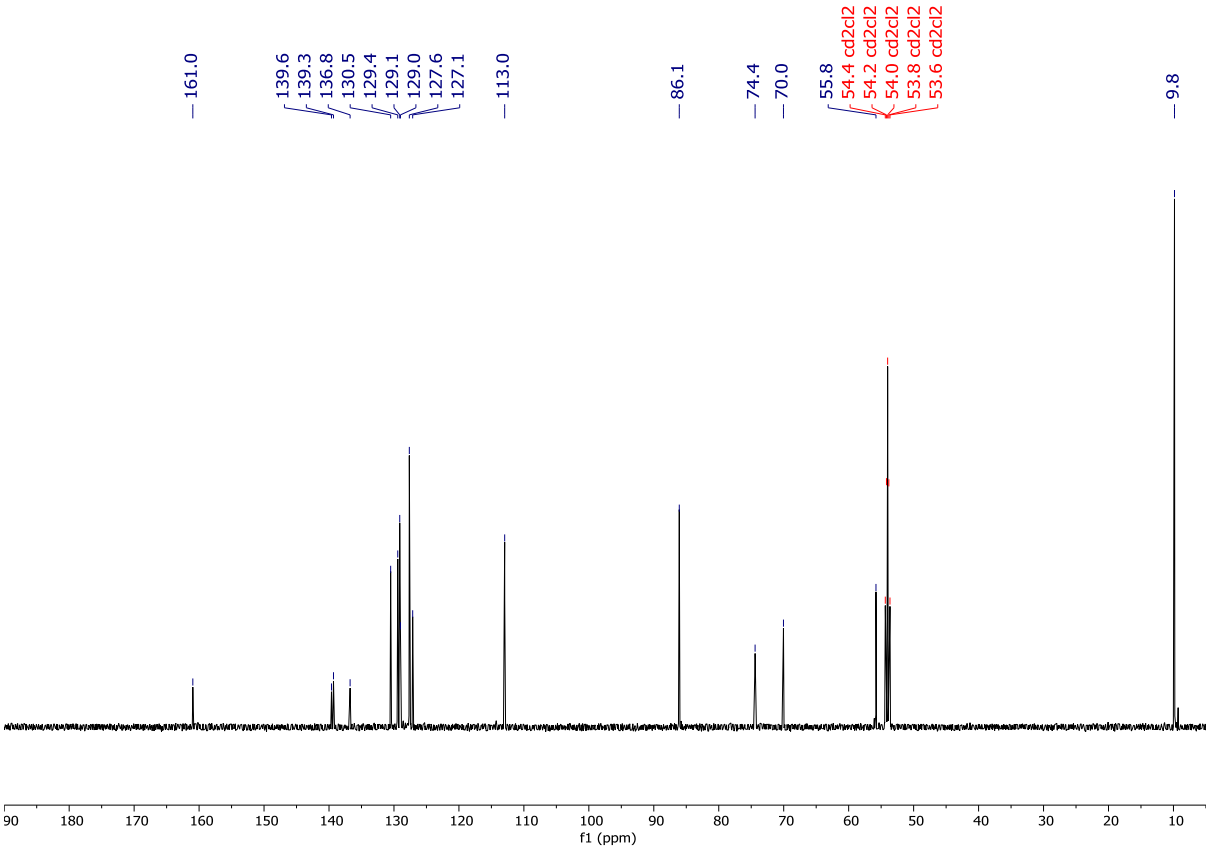
3.09
5.02
2.03
2.00
1.03
2.01
3.00
1.03
14.74
f1 (ppm)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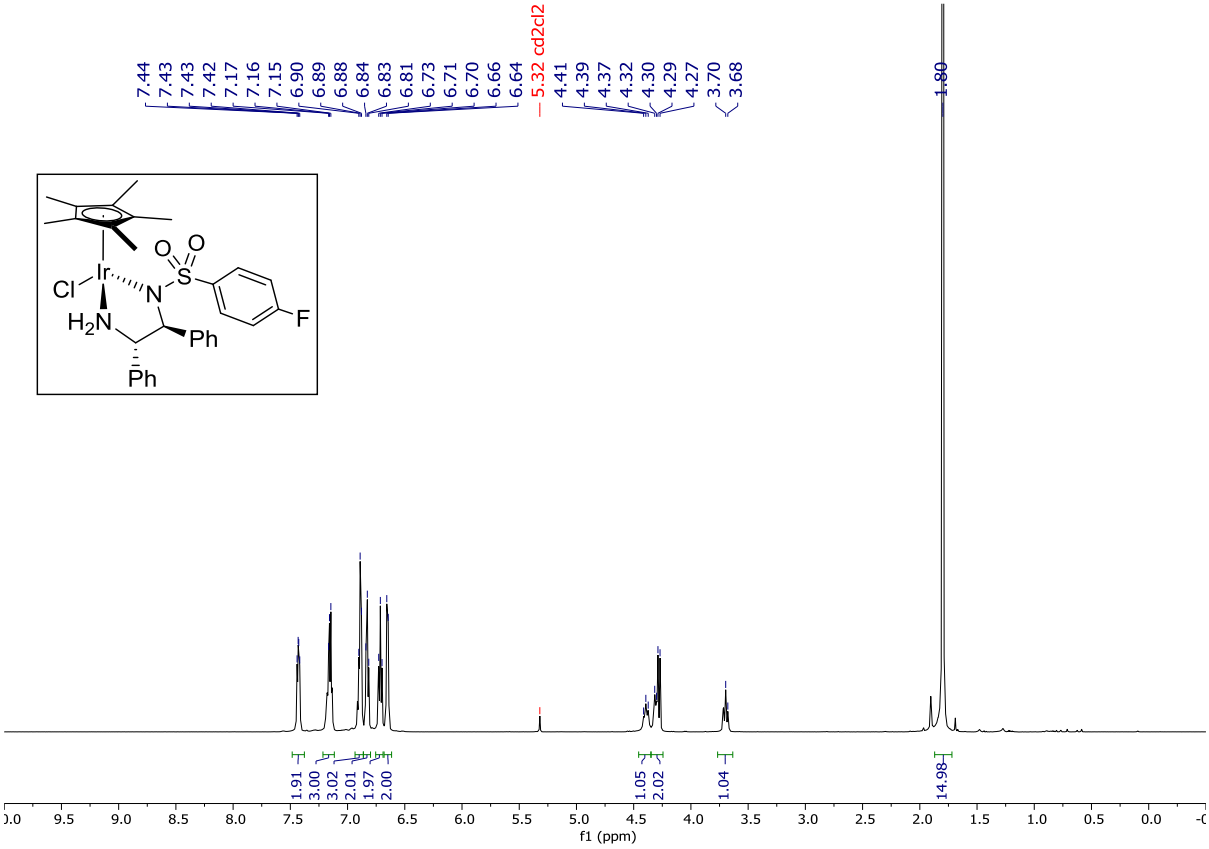
139.3
136.8
130.5
129.4
129.1
129.0
127.6
127.1
113.0
86.1
74.4
70.0
55.8
54.4 cd2cl2
54.2 cd2cl2
54.0 cd2cl2
53.8 cd2cl2
53.6 cd2cl2
9.8
f1 (ppm)

Ir8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6.81
6.73
6.71
6.70
6.66
6.64
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4.37
4.32
4.30
4.29
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3.68
1.80
Cl
Ir
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F
H2N
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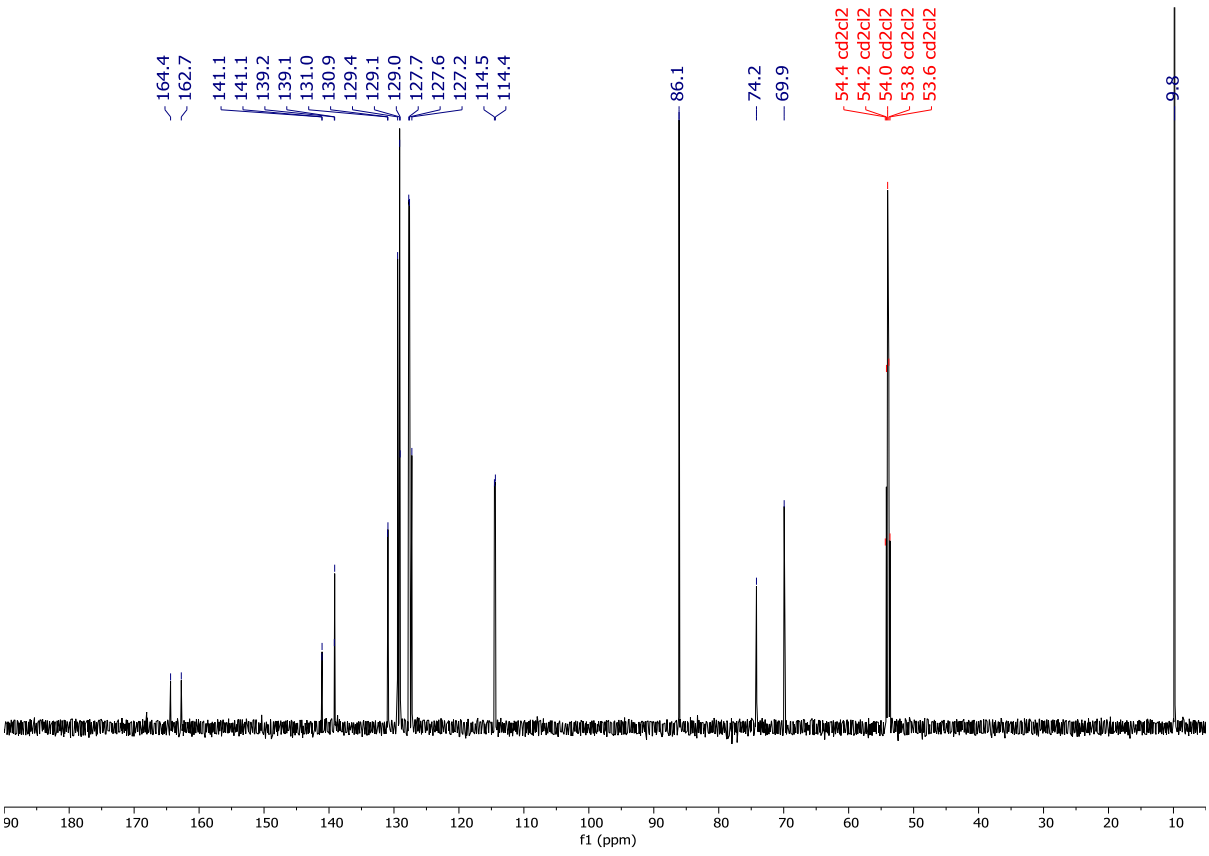
2.02
1.04
14.98
f1 (ppm)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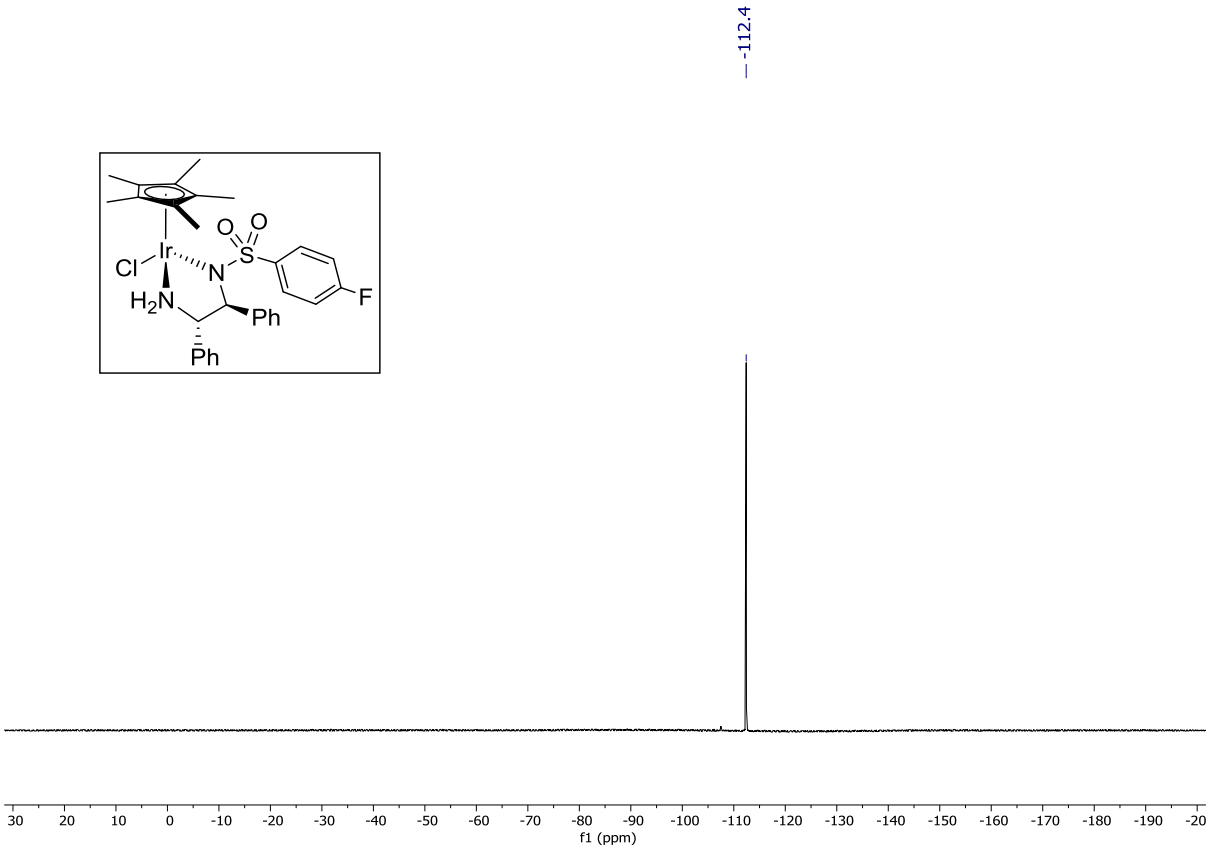
131.0
130.9
129.4
129.1
129.0
127.7
127.6
127.2
114.5
114.4
86.1
74.2
69.9
54.4 cd2cl2
54.2 cd2cl2
54.0 cd2cl2
53.8 cd2cl2
53.6 cd2cl2
9.8
f1 (ppm)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Ir
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O
S
N
F
H2N
Ph
Ph
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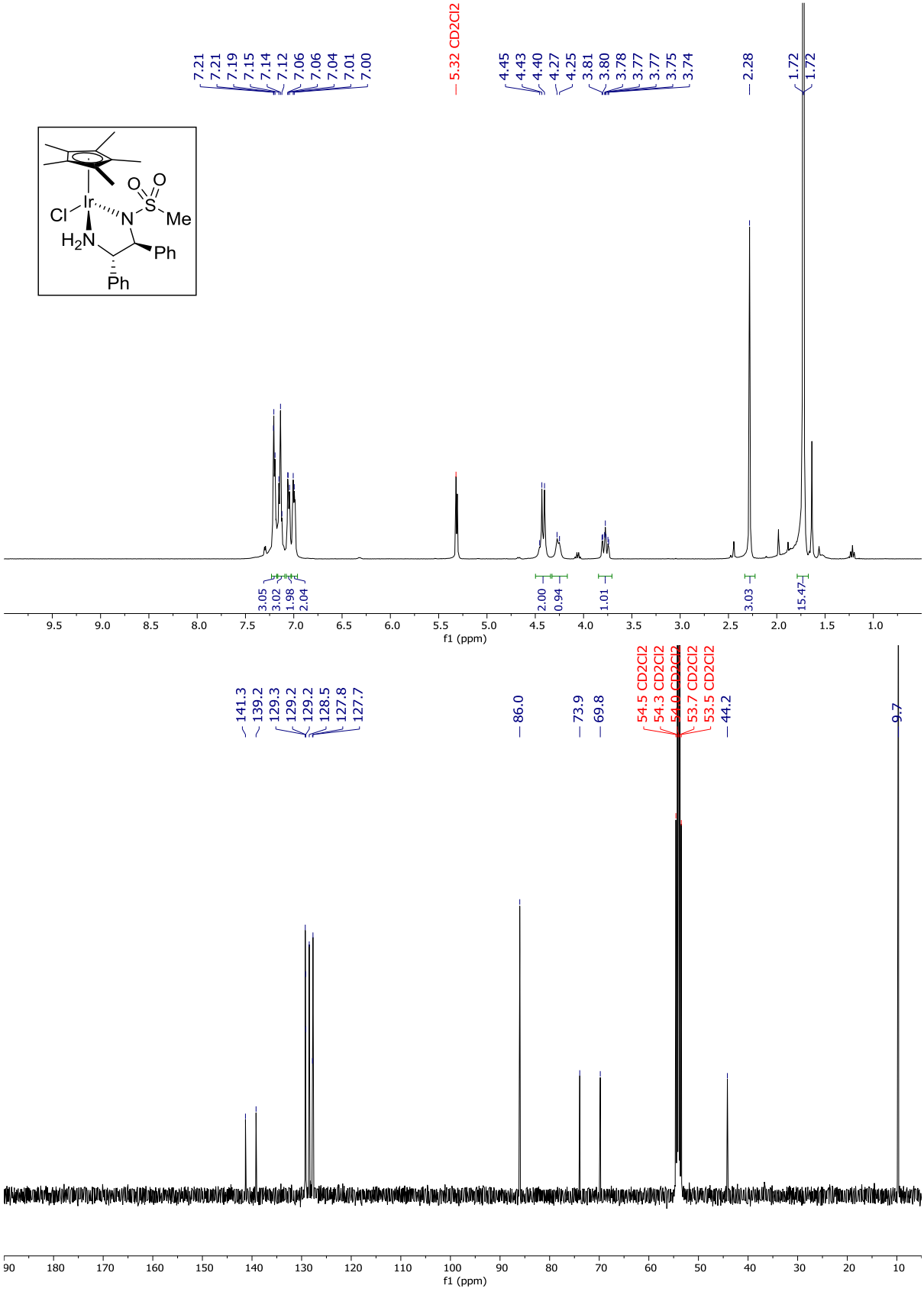
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)

Ir9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7.14
7.12
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7.06
7.04
7.01
7.00
5.32 CD2Cl2
4.45
4.43
4.40
4.27
4.25
3.81
3.80
3.78
3.77
3.77
3.75
3.74
2.28
1.72
1.72
Cl
Ir
O
O
S
N
Me
H2N
Ph
Ph
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3.02
1.98
2.04
2.00
0.94
1.01
3.03
15.47
f1 (ppm)
141.3
139.2
129.3
129.2
129.2
128.5
127.8
127.7
86.0
73.9
69.8
54.5 CD2Cl2
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54.0 CD2Cl2
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53.5 CD2Cl2
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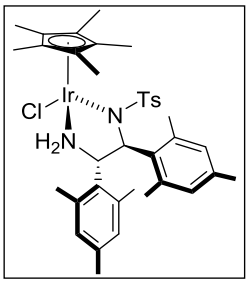
9.7
f1 (ppm)

Ir10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Ir
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Ts
H2N

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6.28
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5.33
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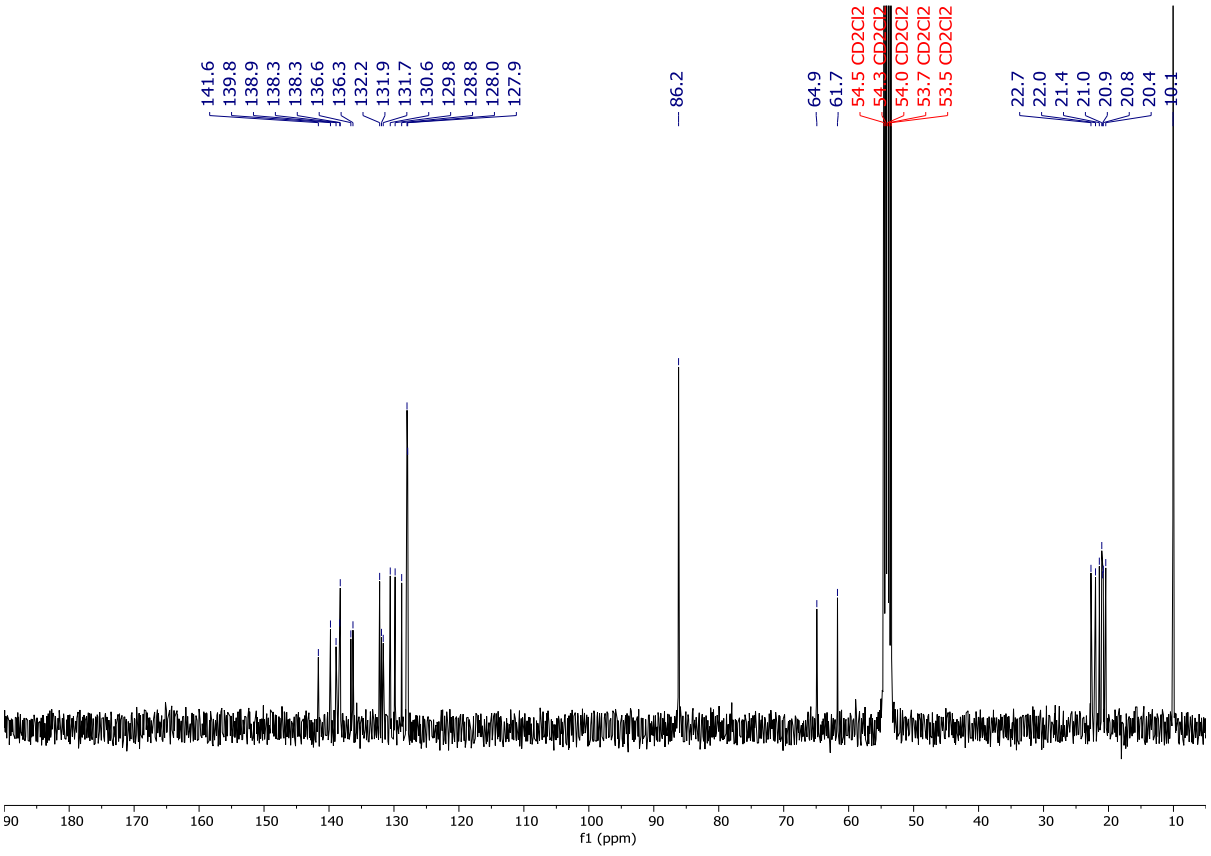
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128.8
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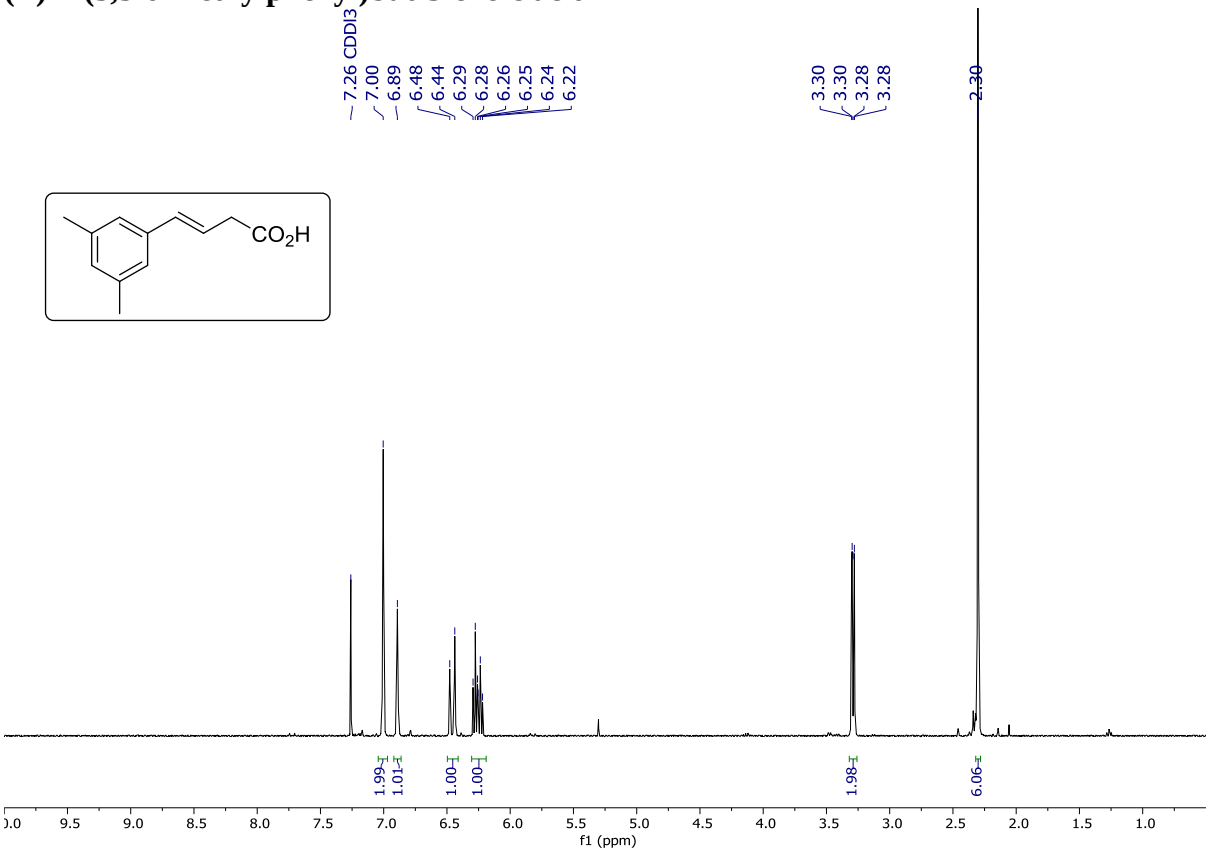
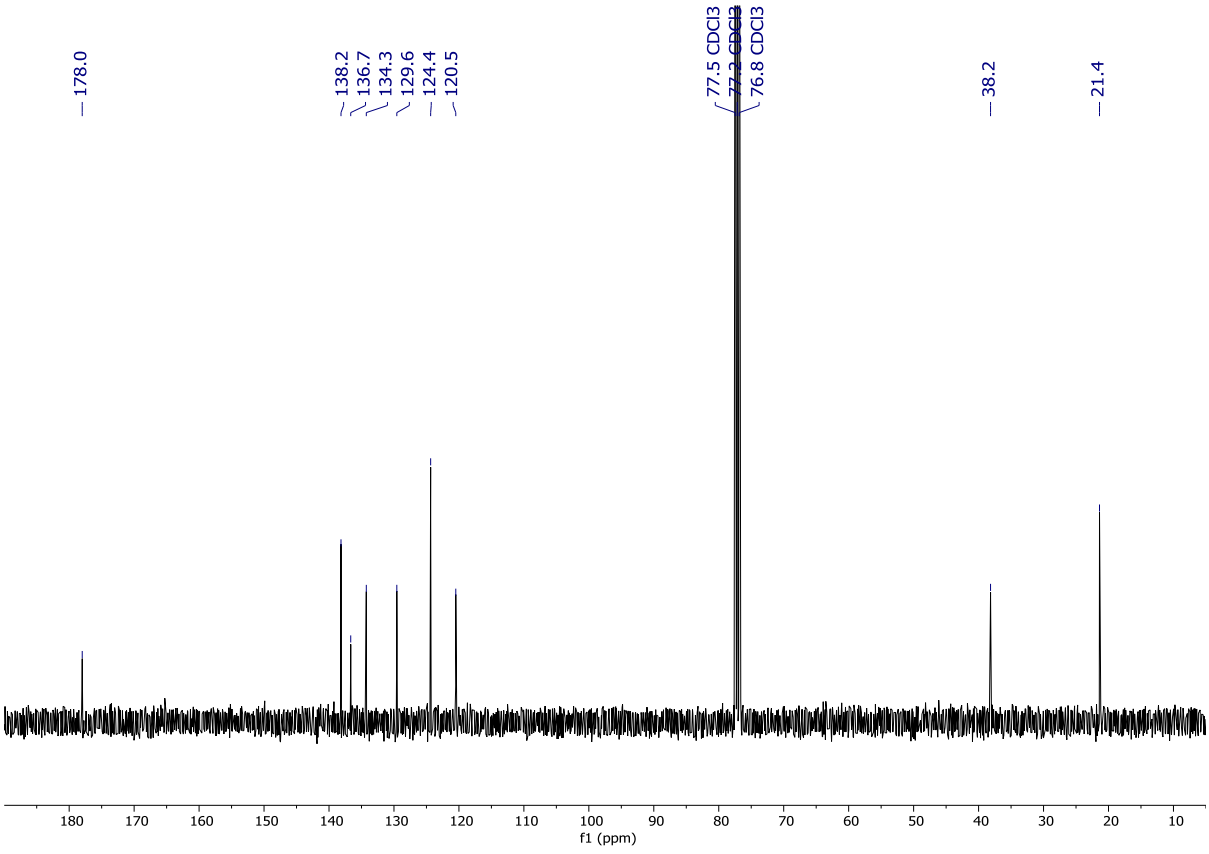
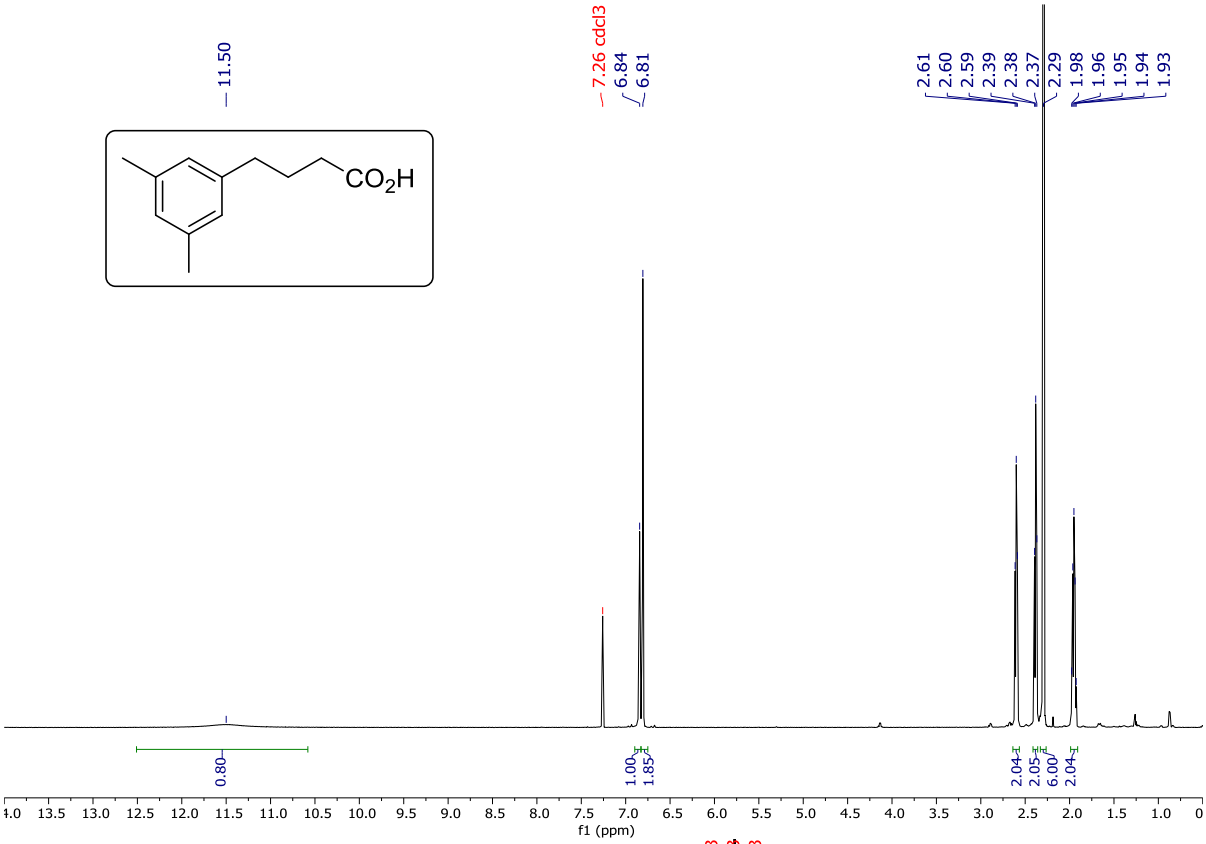
127.9
86.2
64.9
61.7
54.5 CD2Cl2
54.3 CD2Cl2
54.0 CD2Cl2
53.7 CD2Cl2
53.5 CD2Cl2
22.7
22.0
21.4
21.0
20.9
20.8
20.4
10.1
f1 (ppm)

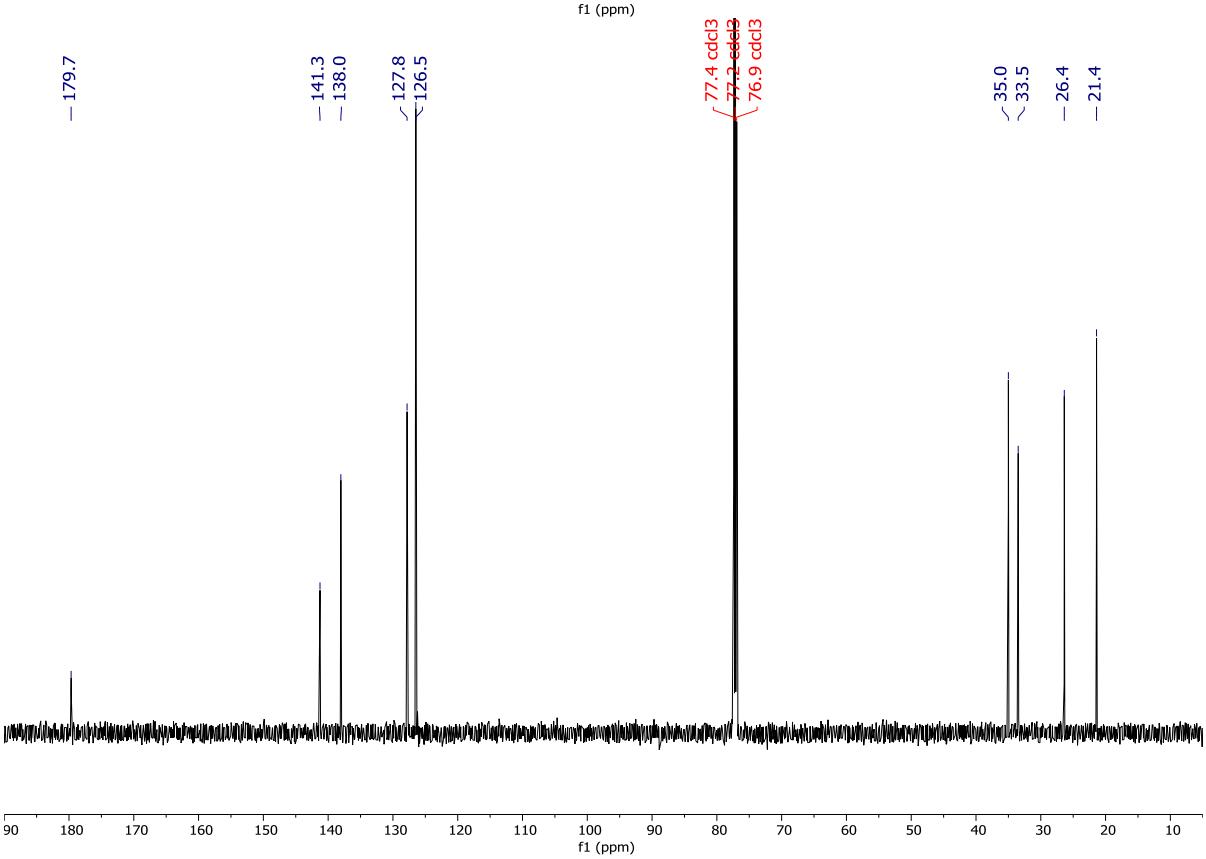
(*E*)-4-(3,5-dimethylphenyl)but-3-enoic acid



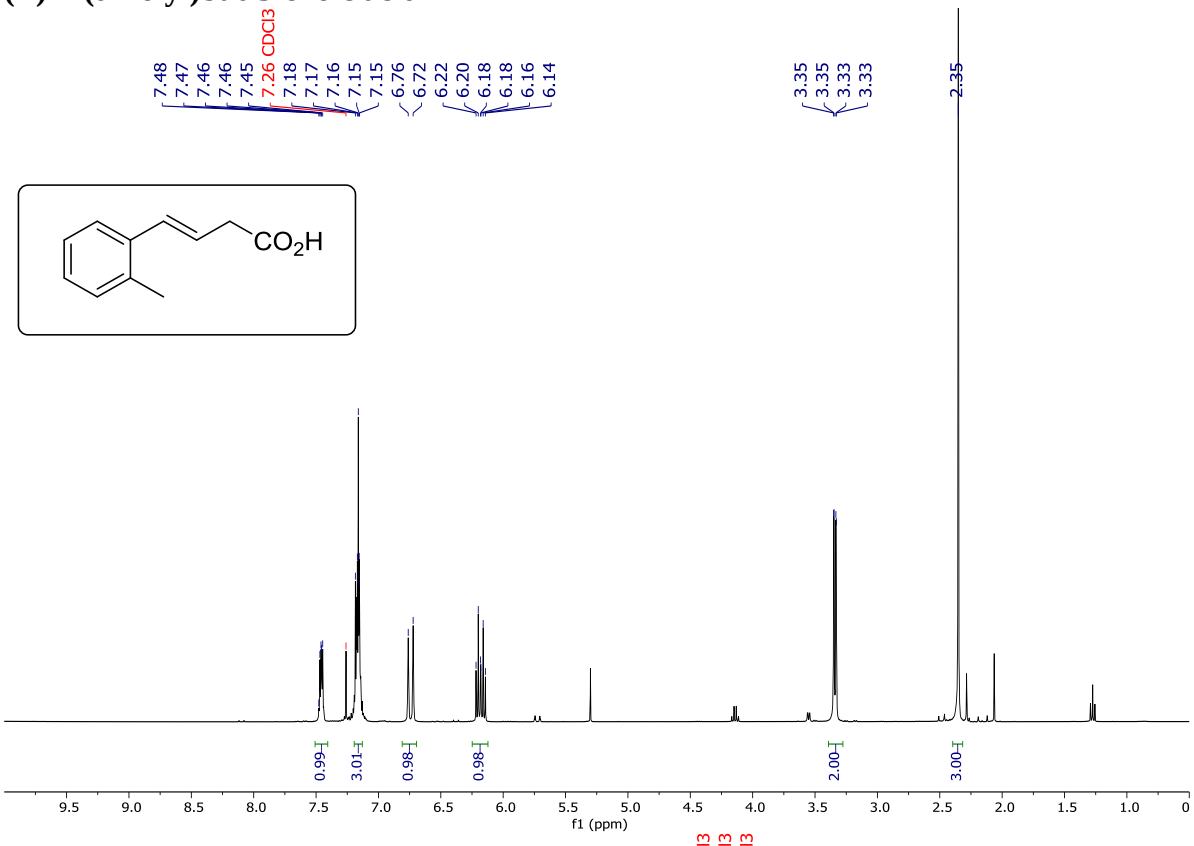


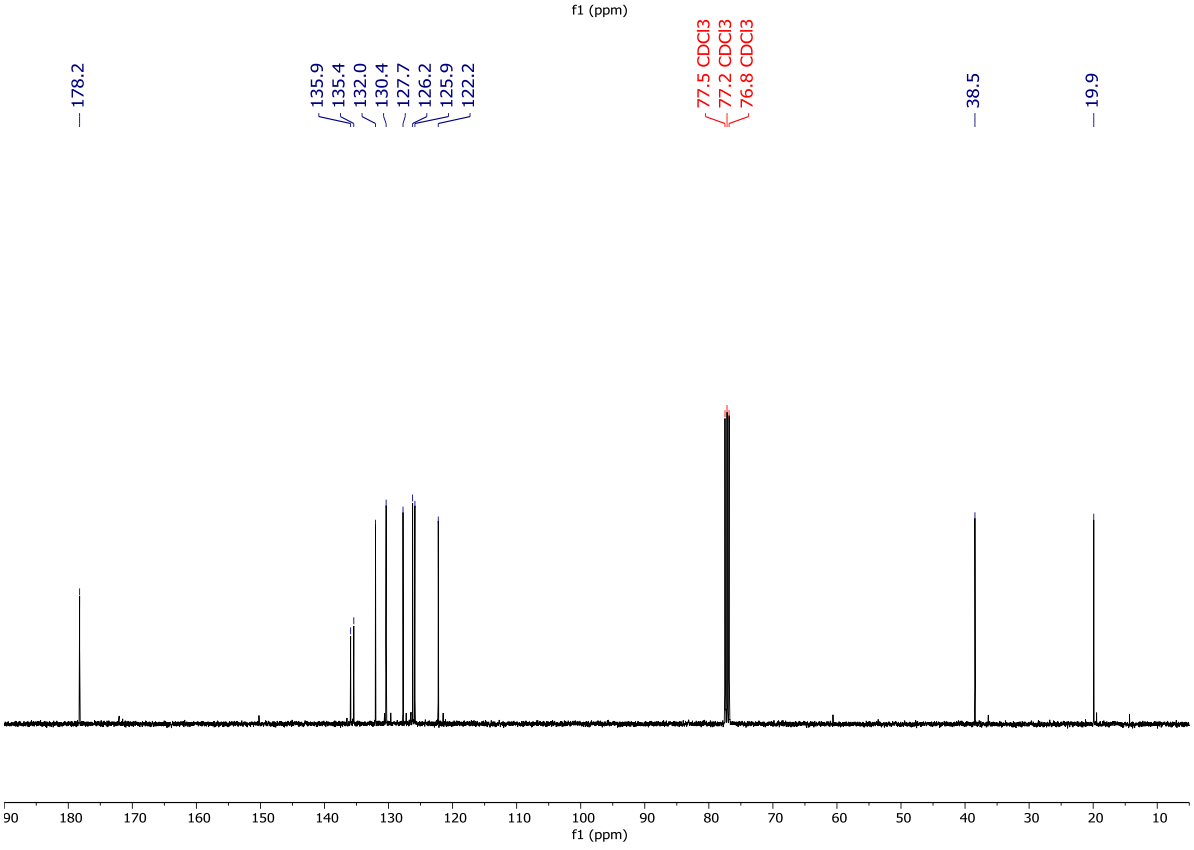
4-(3,5-Dimethylphenyl)butanoic acid



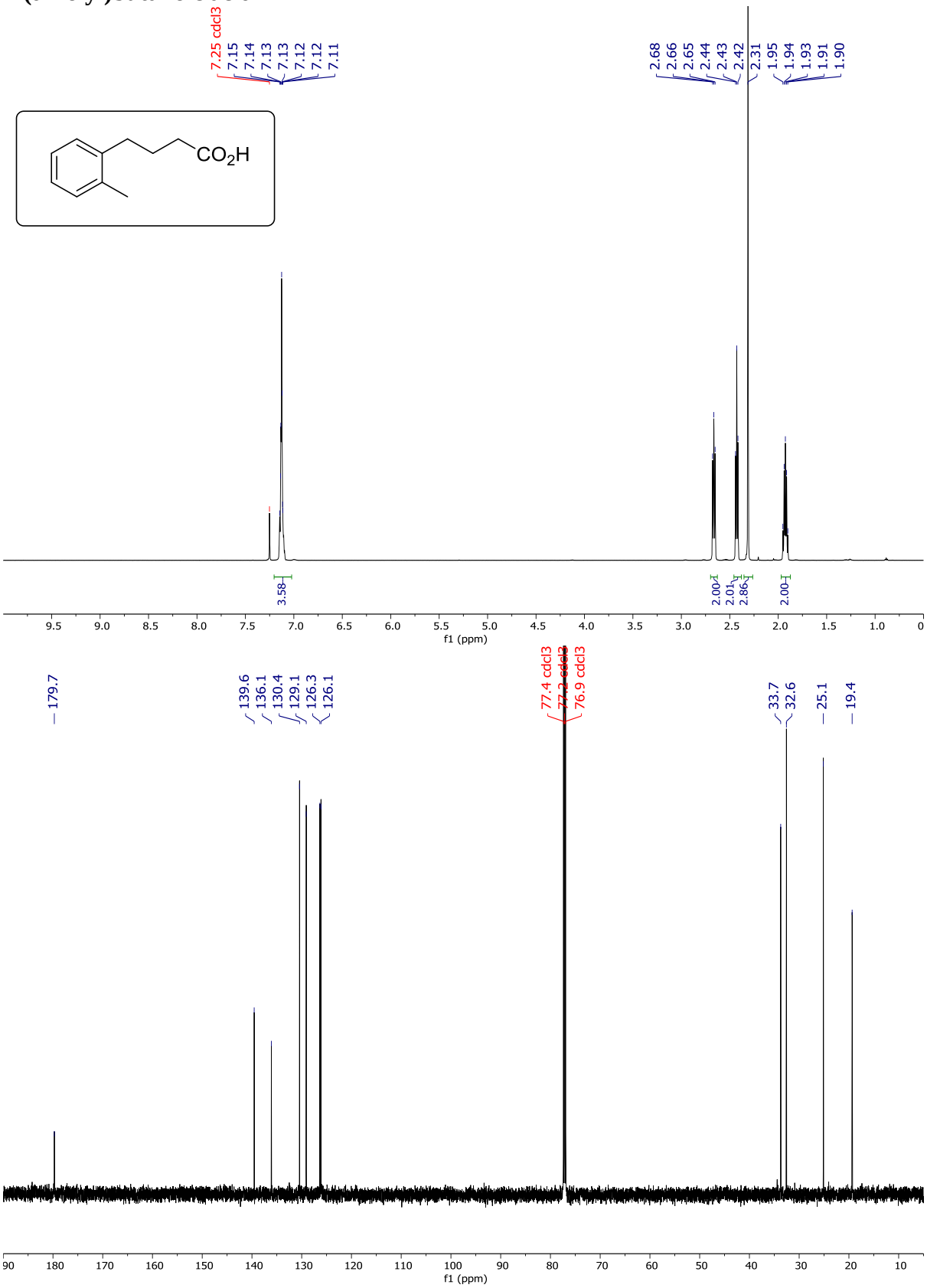


(*E*)-4-(*o*-Tolyl)but-3-enoic acid

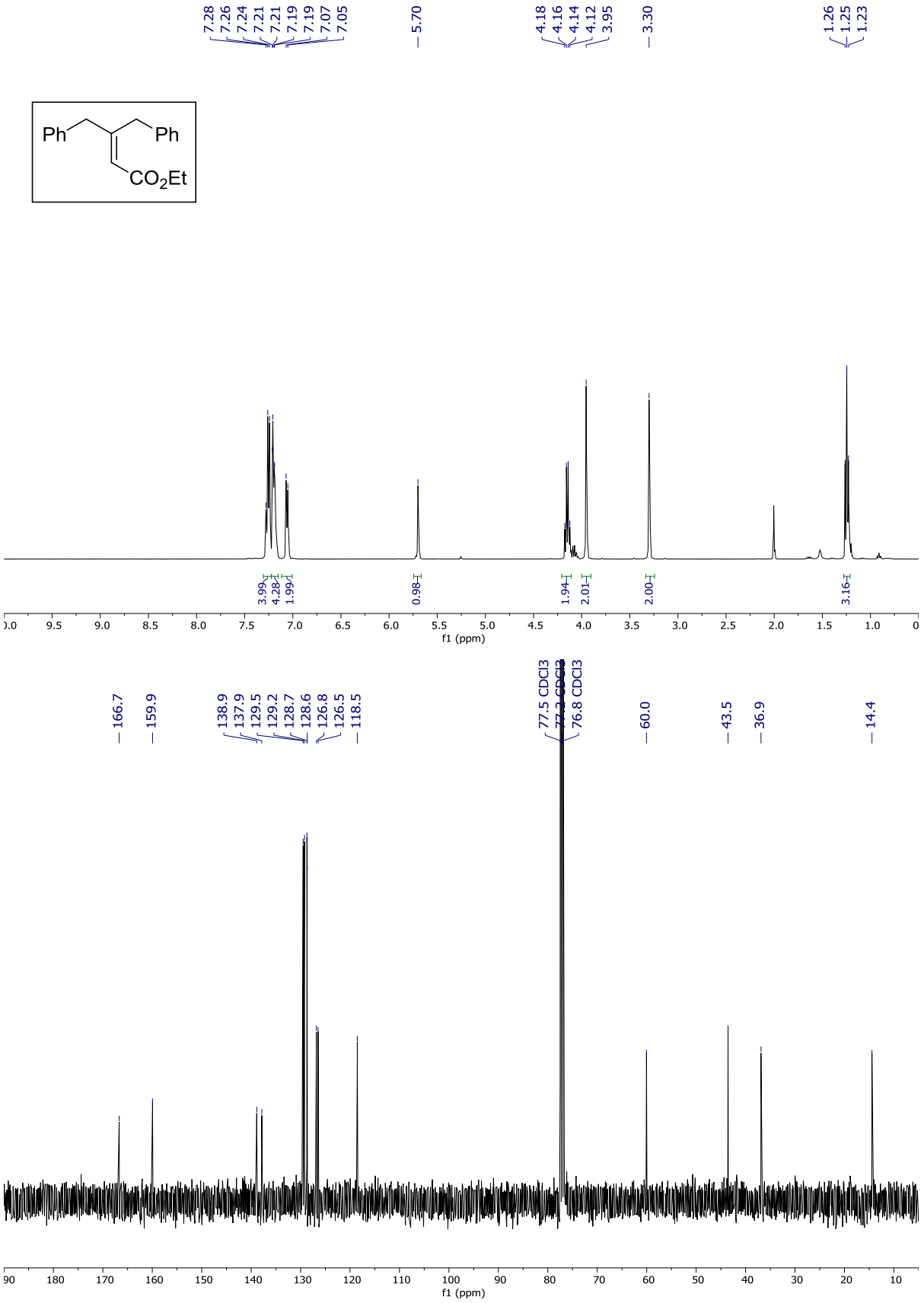




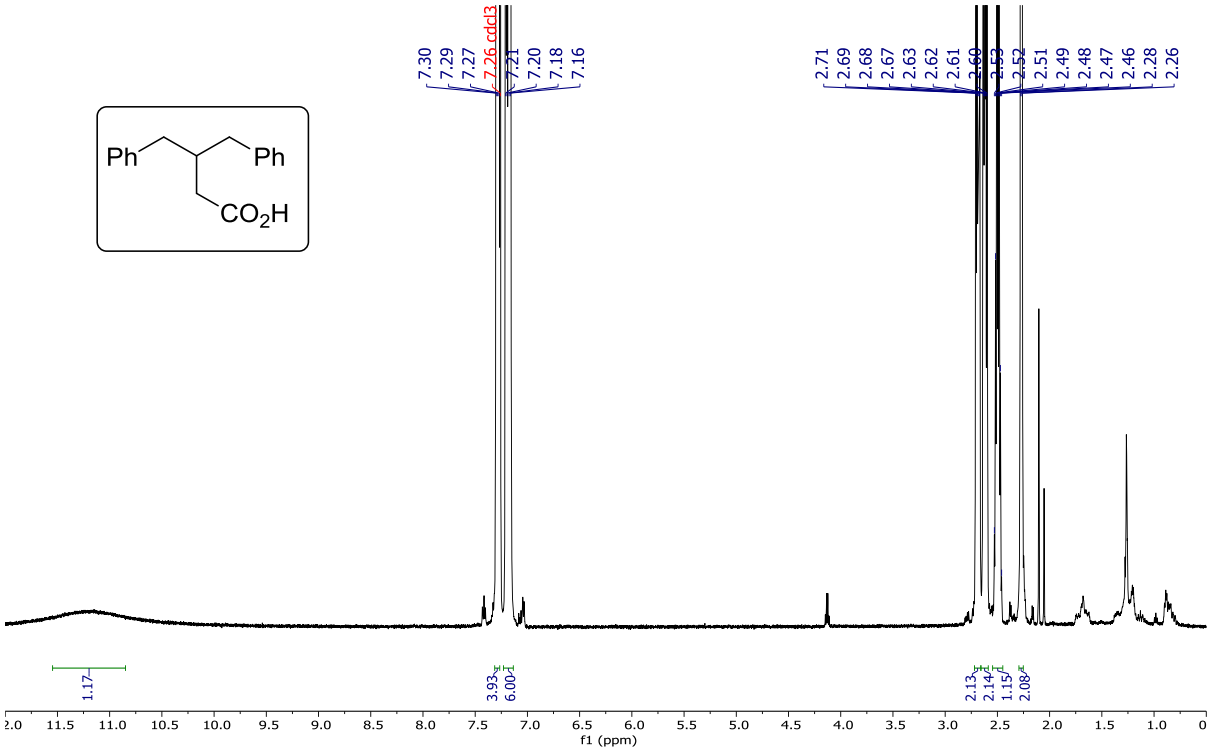
4-(*o*-Tolyl)butanoic acid

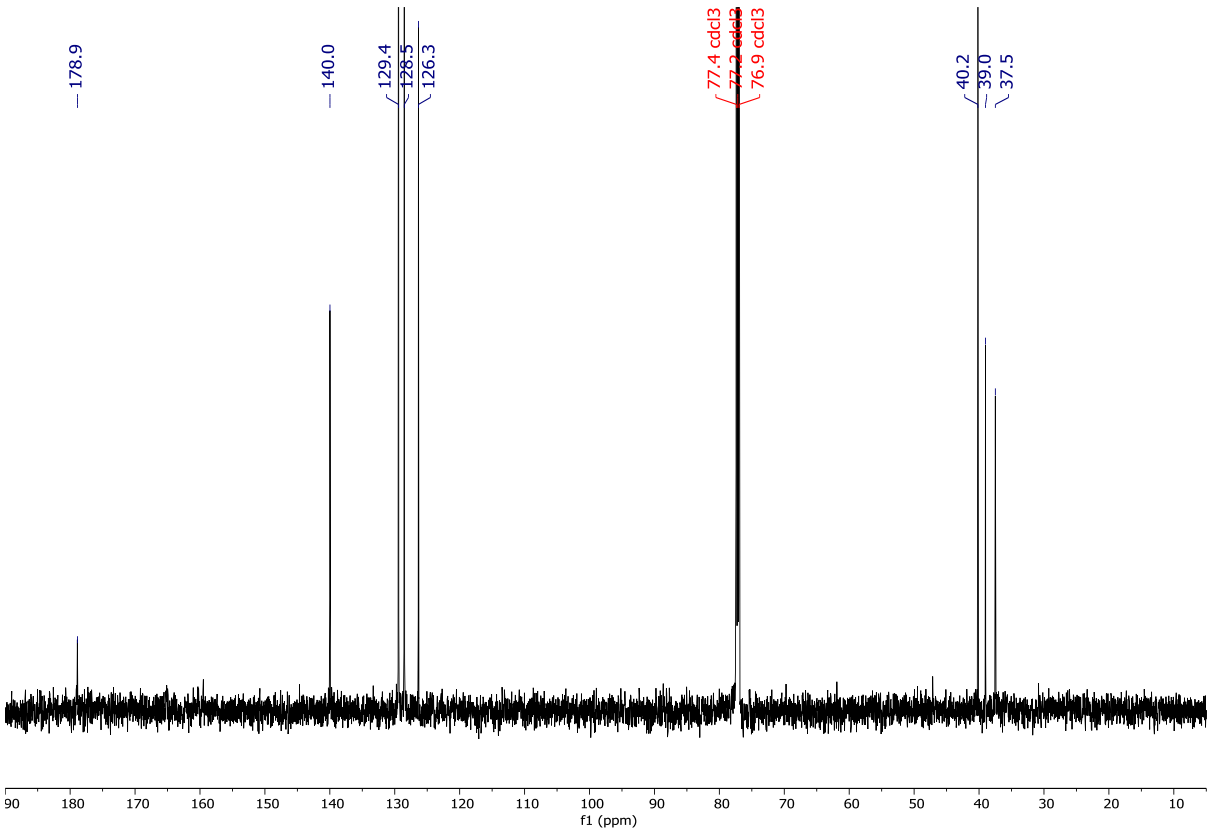


Ethyl 3-benzyl-4-phenylbut-2-enoate

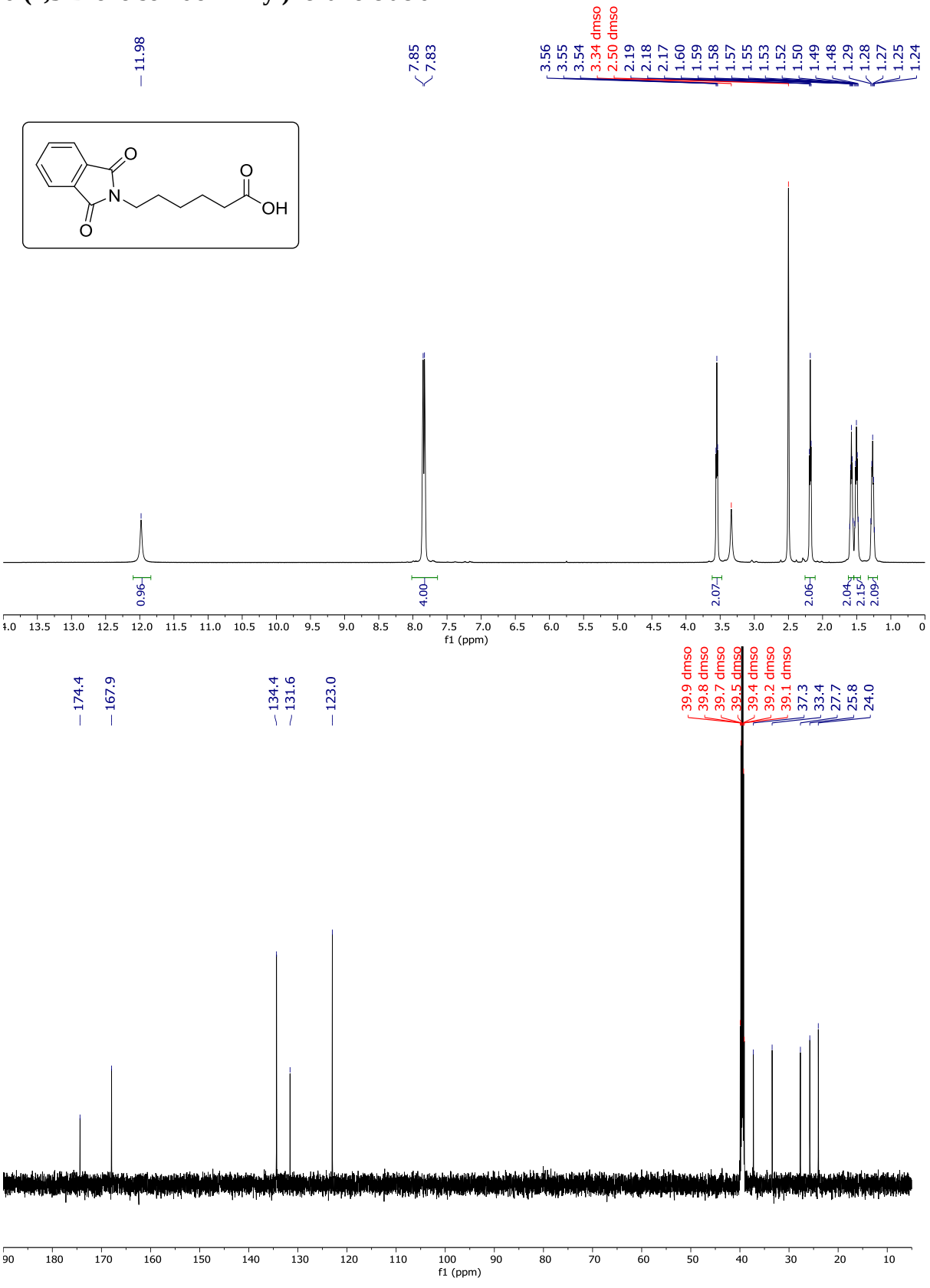


3-Benzyl-4-phenylbutanoic acid

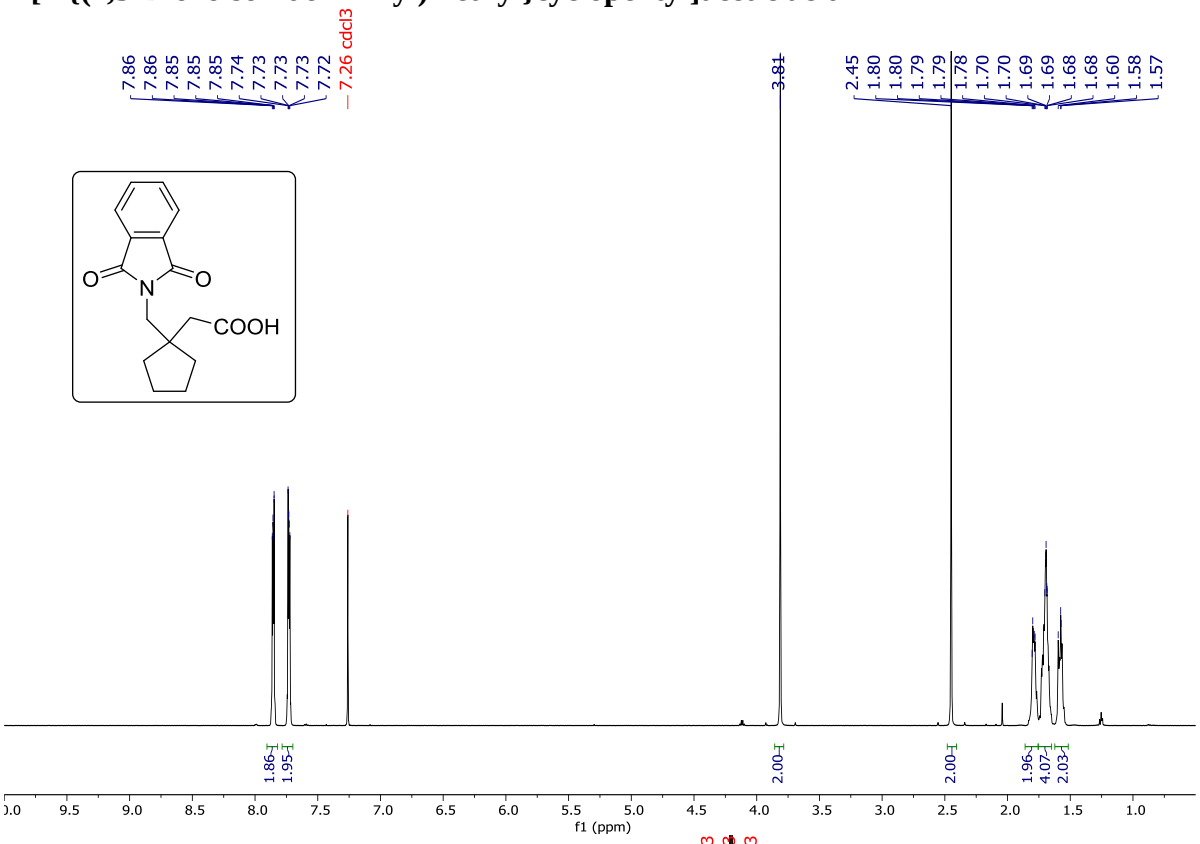


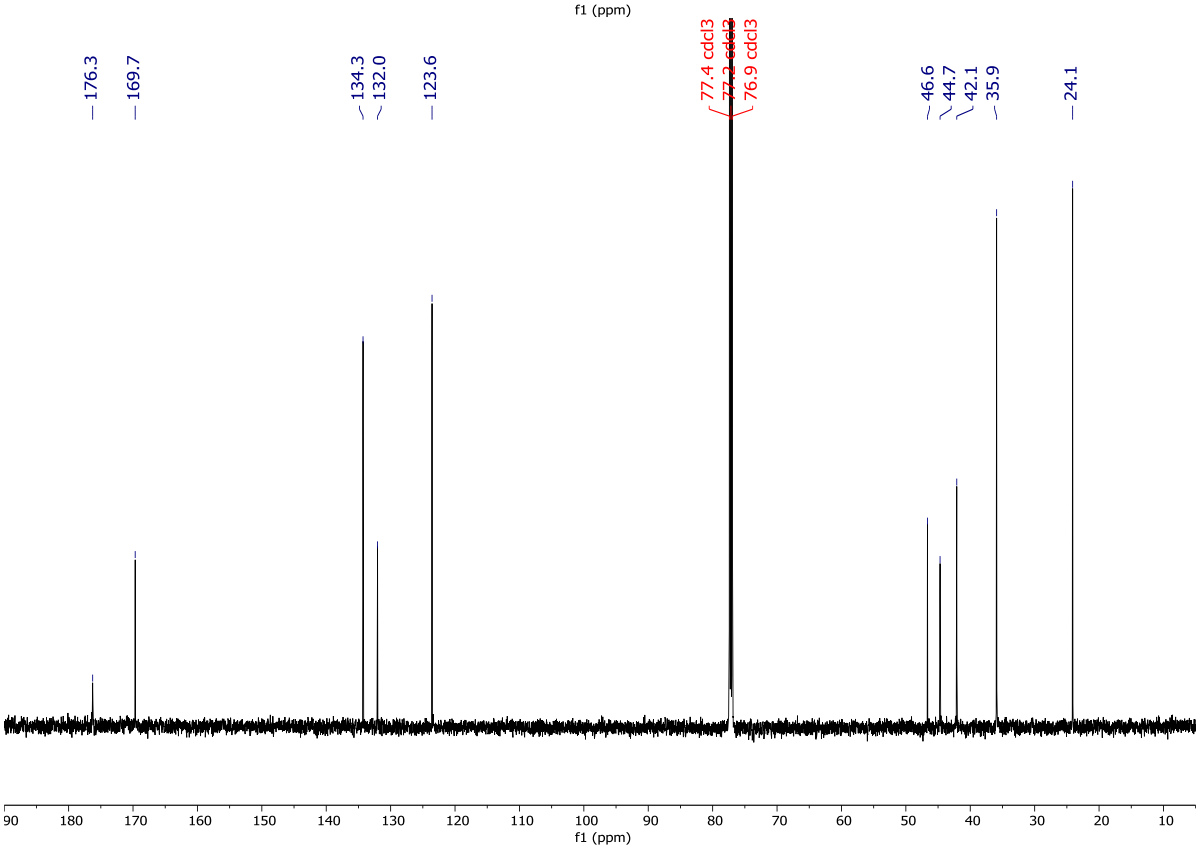


6-(1,3-Dioxoisoindolin-2-yl)hexanoic acid

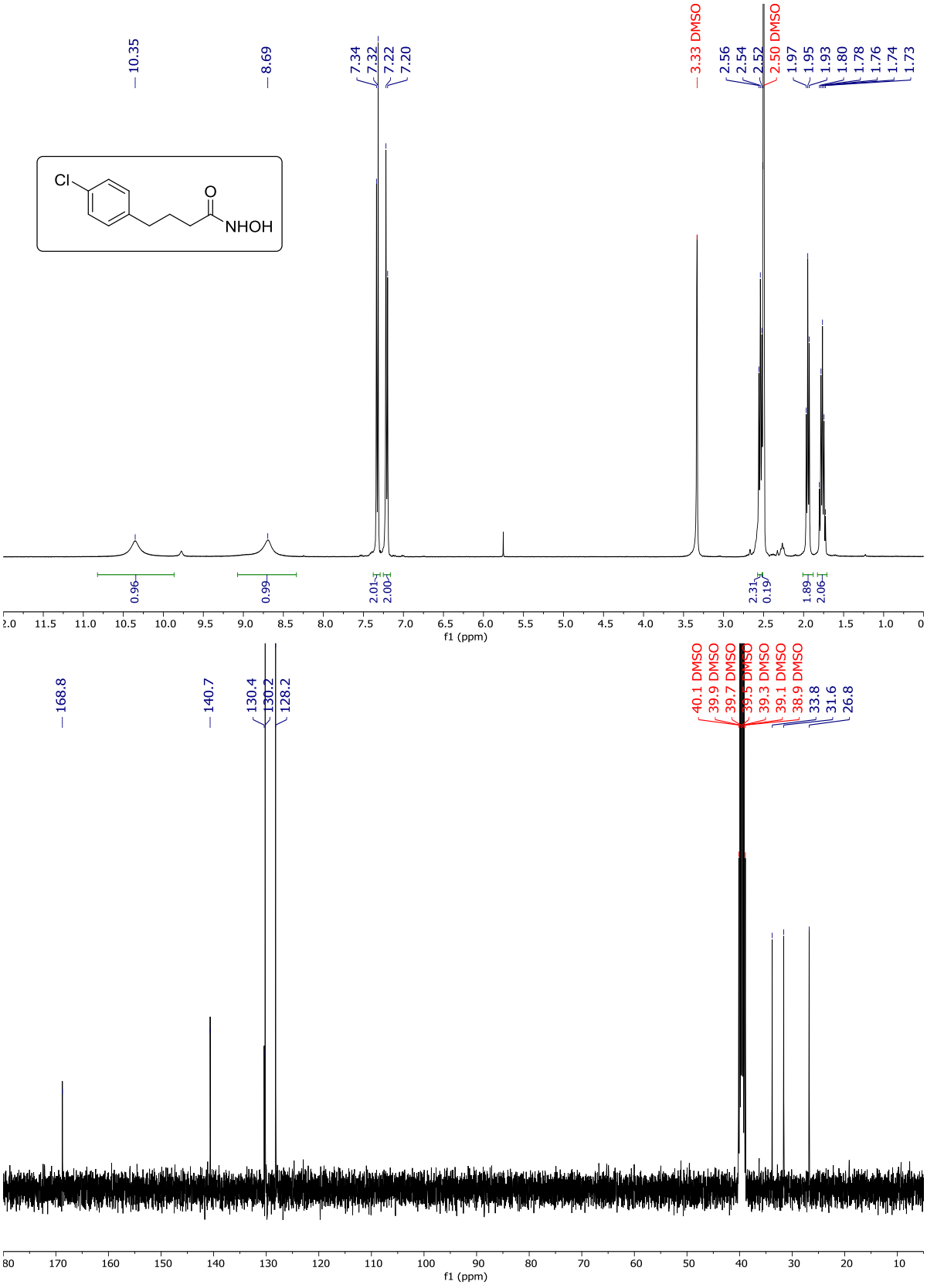


2-[1-{(1,3-Dioxoisoindolin-2-yl)methyl}cyclopentyl]acetic acid

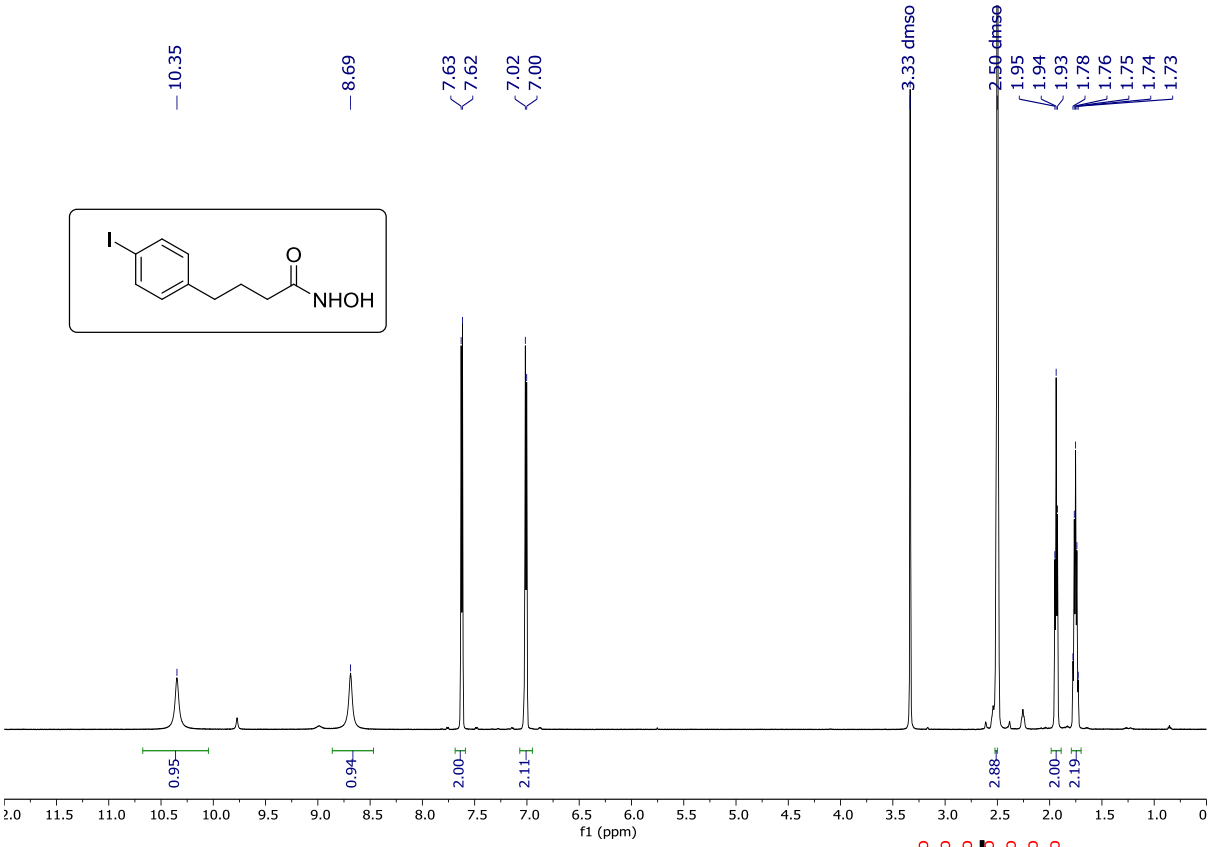


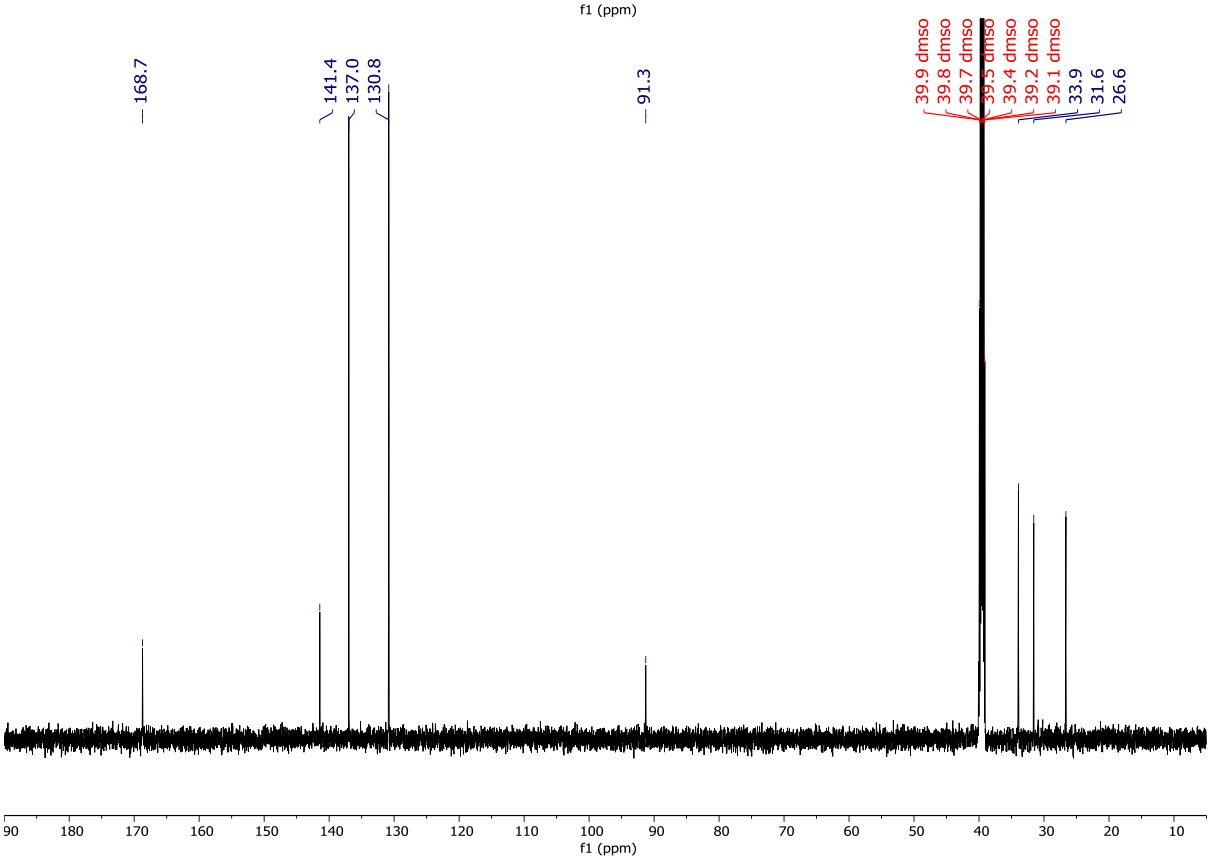


4-(4-Chlorophenyl)-*N*-hydroxybutanamide

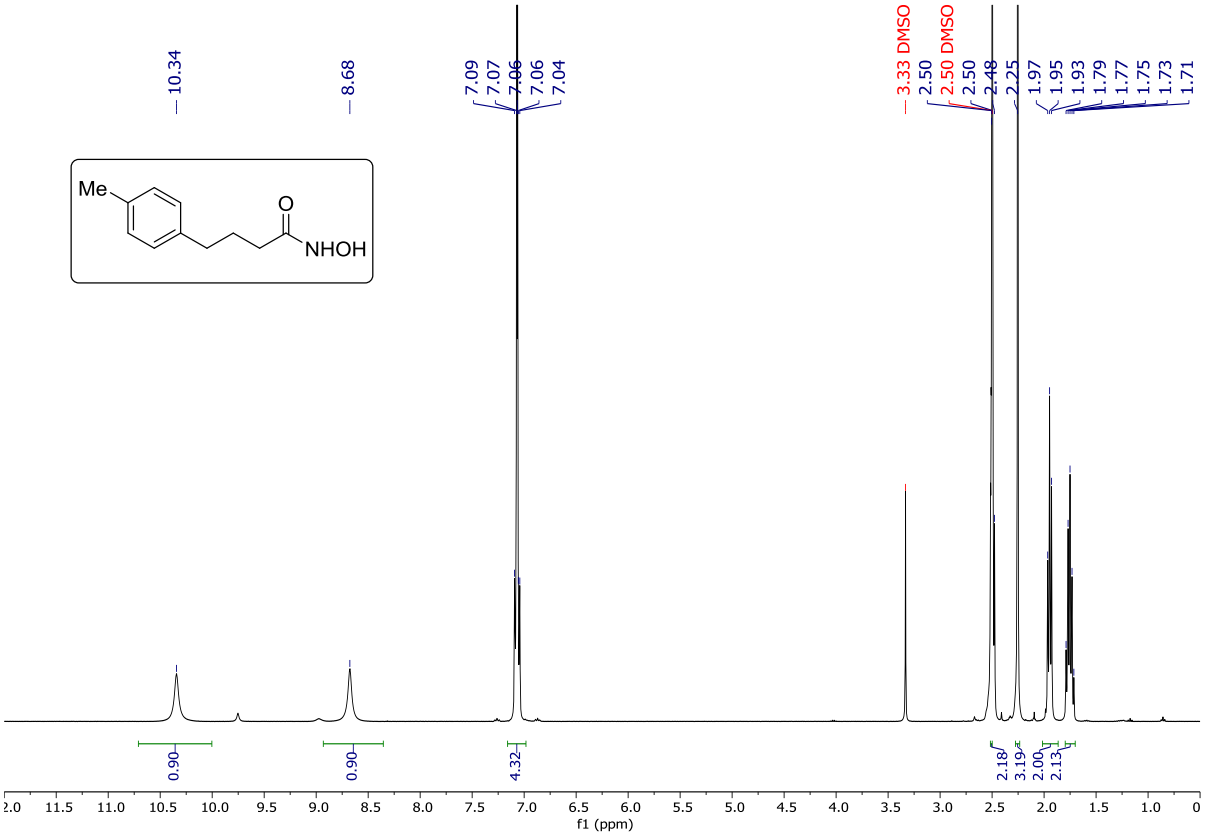


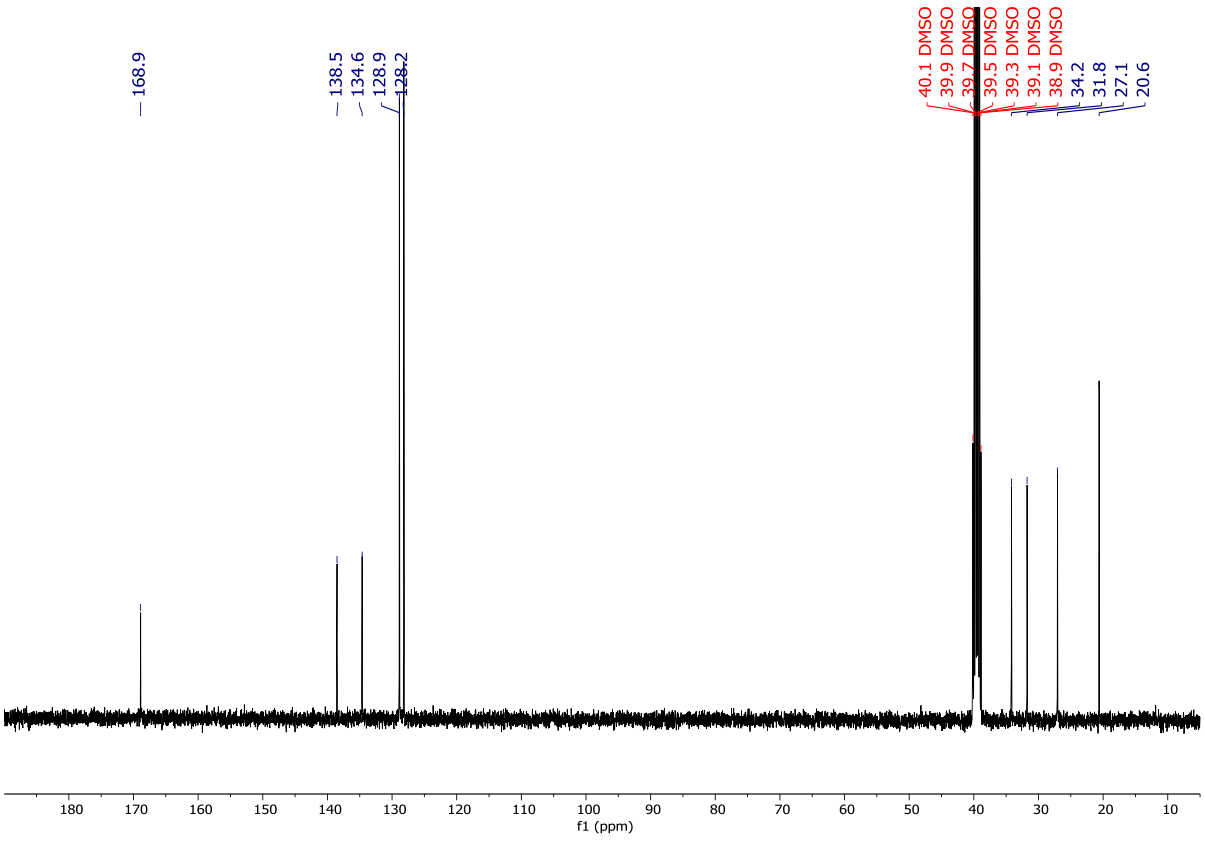
N-hydroxy-4-(4-iodophenyl)butanamide



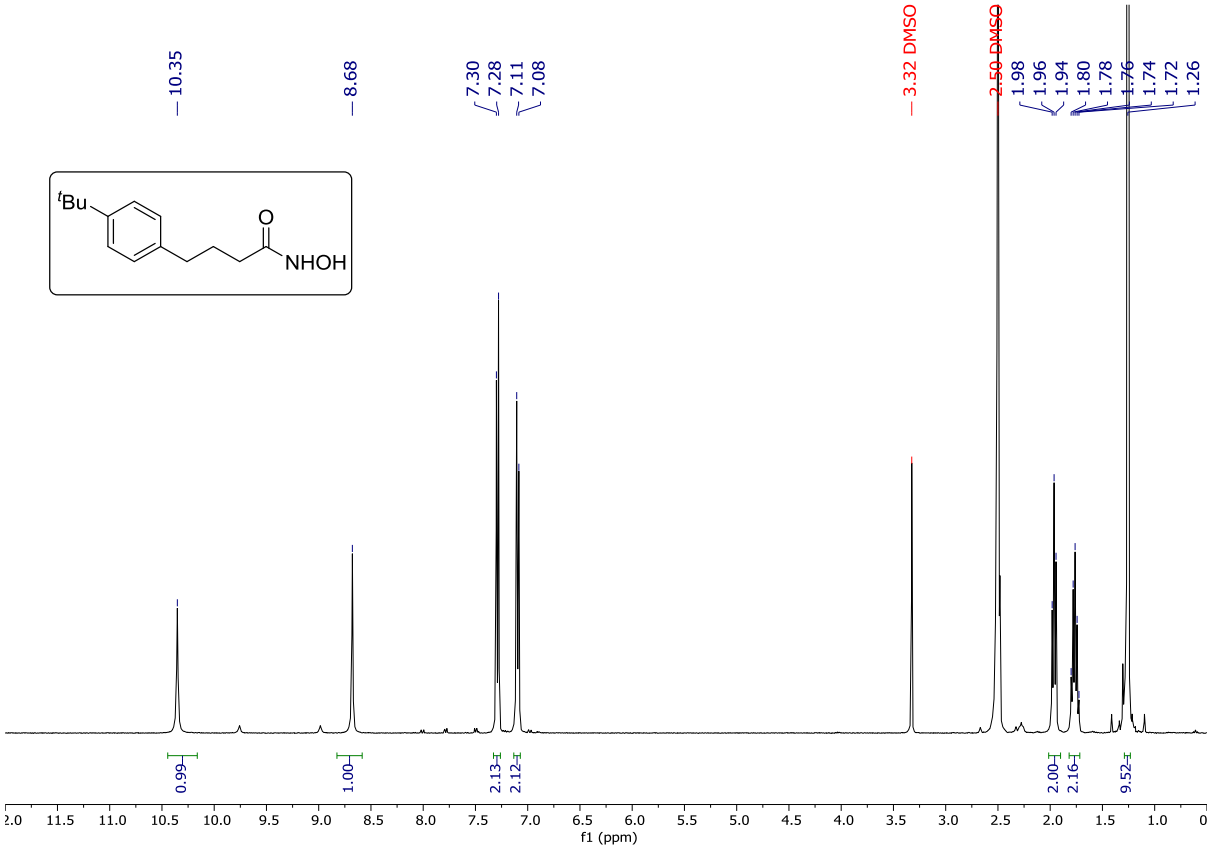


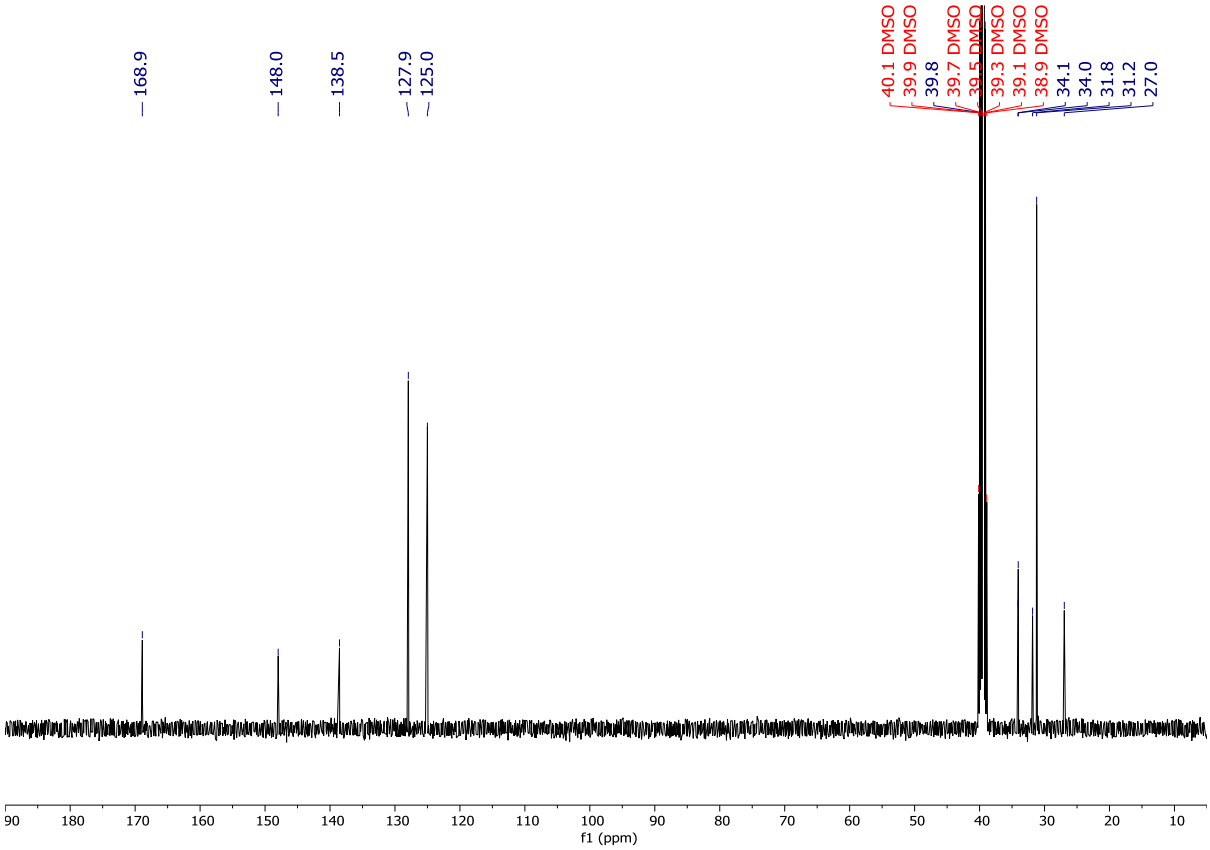
N-Hydroxy-4-(*p*-tolyl)butanamide



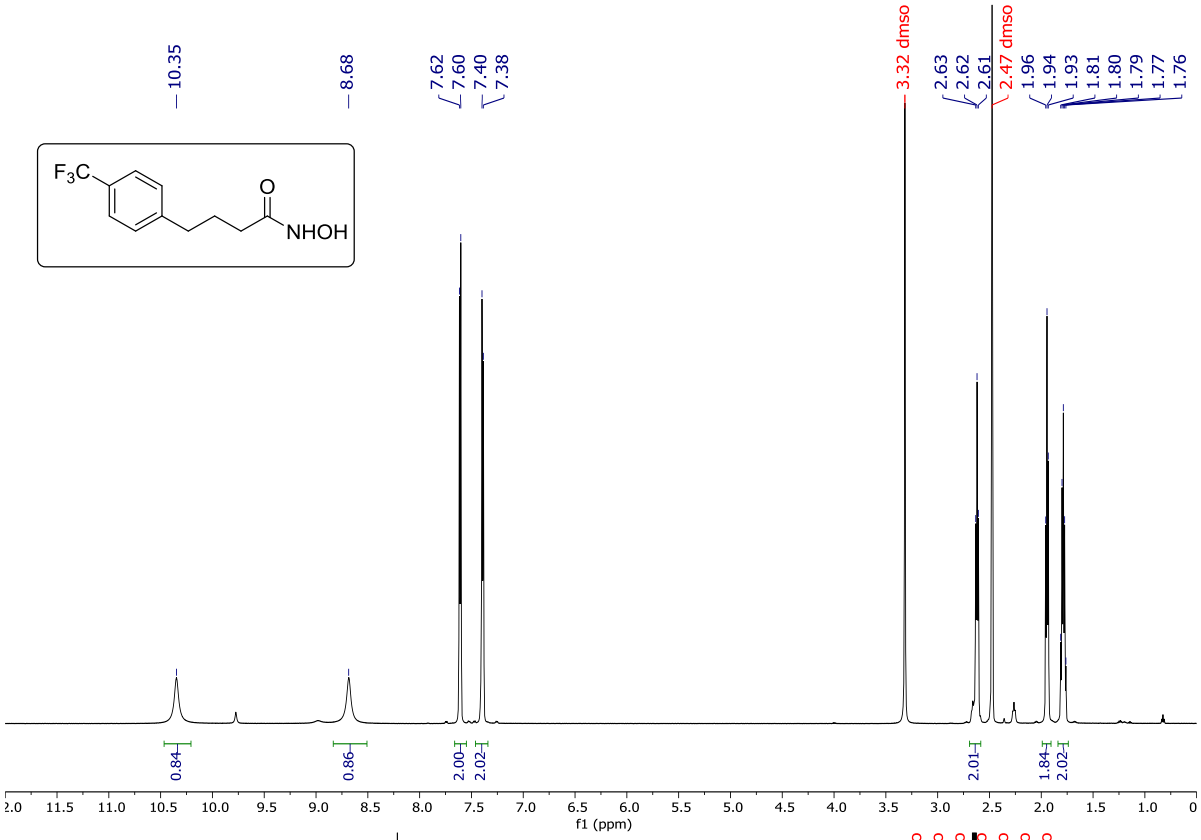


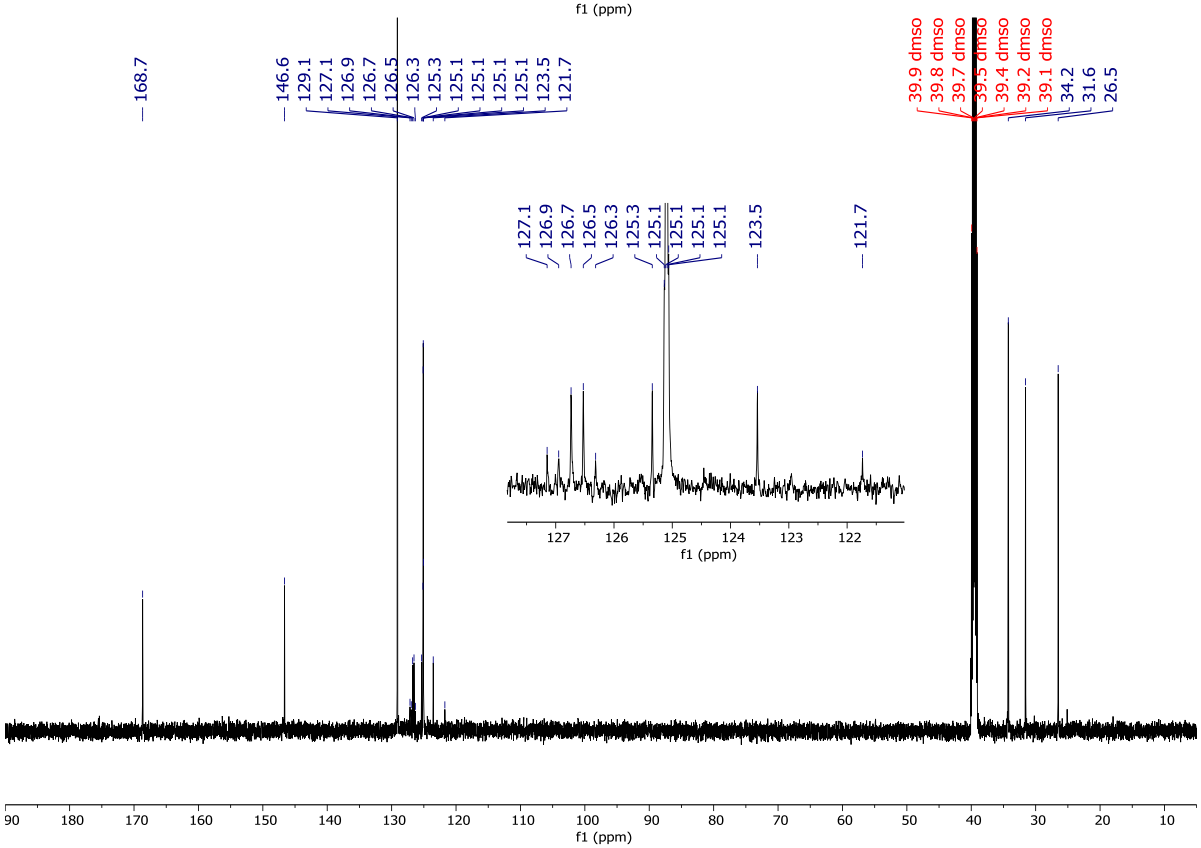
4-{4-(*tert*-Butyl)phenyl}-*N*-hydroxybutanamide

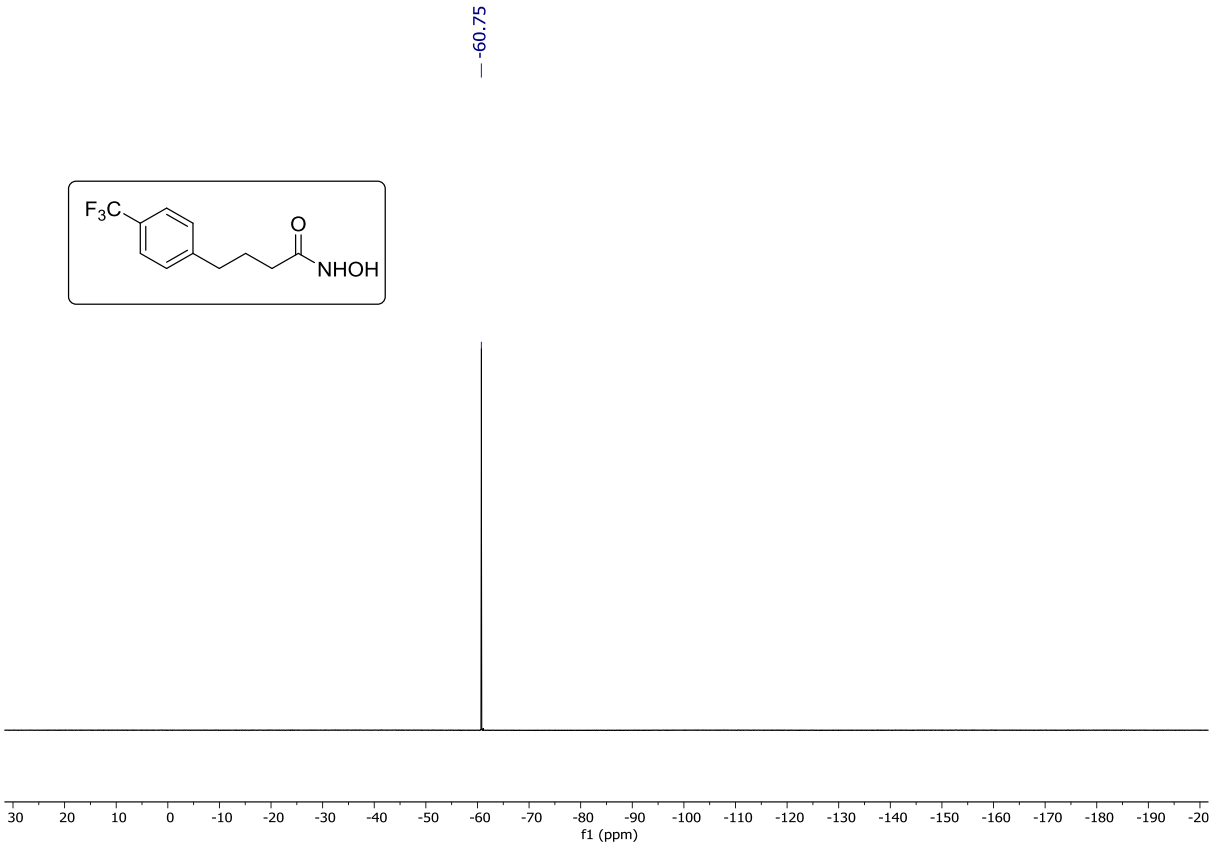




N-hydroxy-4-(4-(trifluoromethyl)phenyl)butanamide



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F3C
O
NHOH
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
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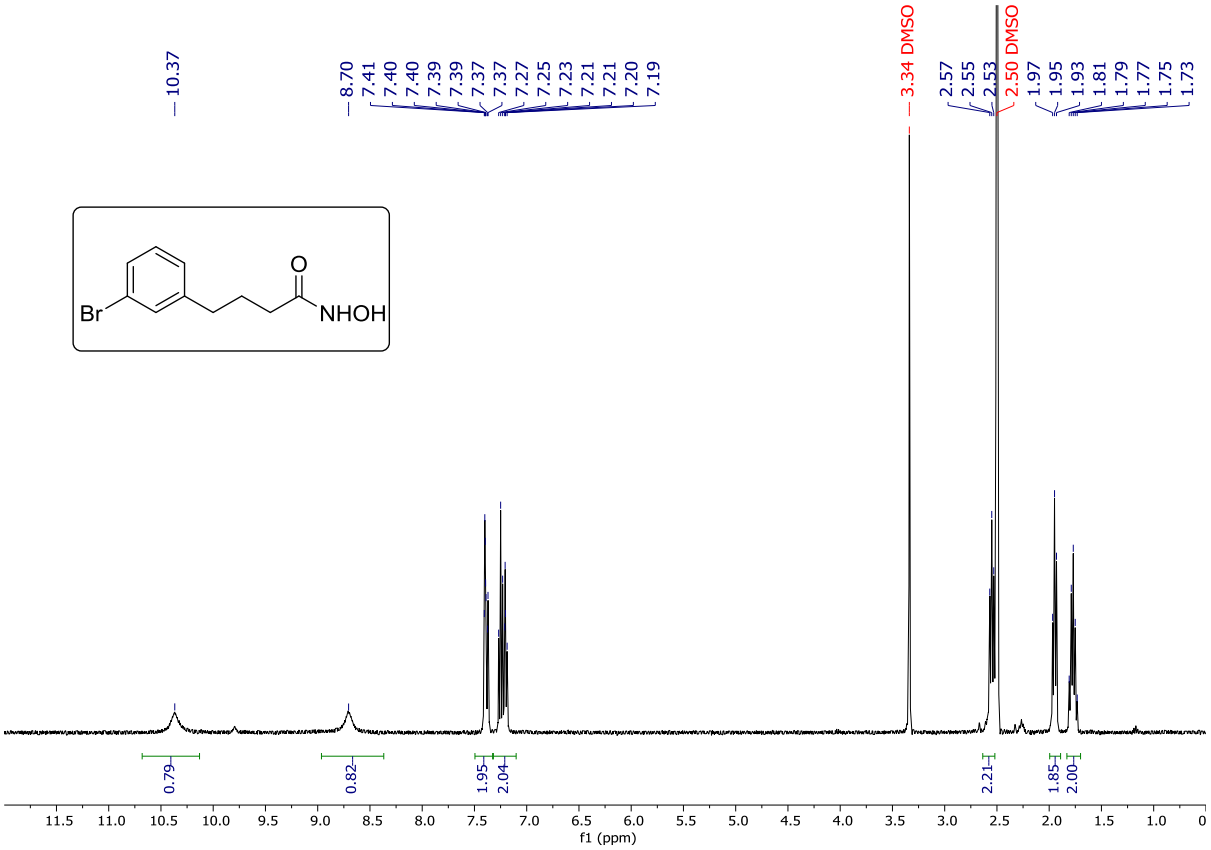
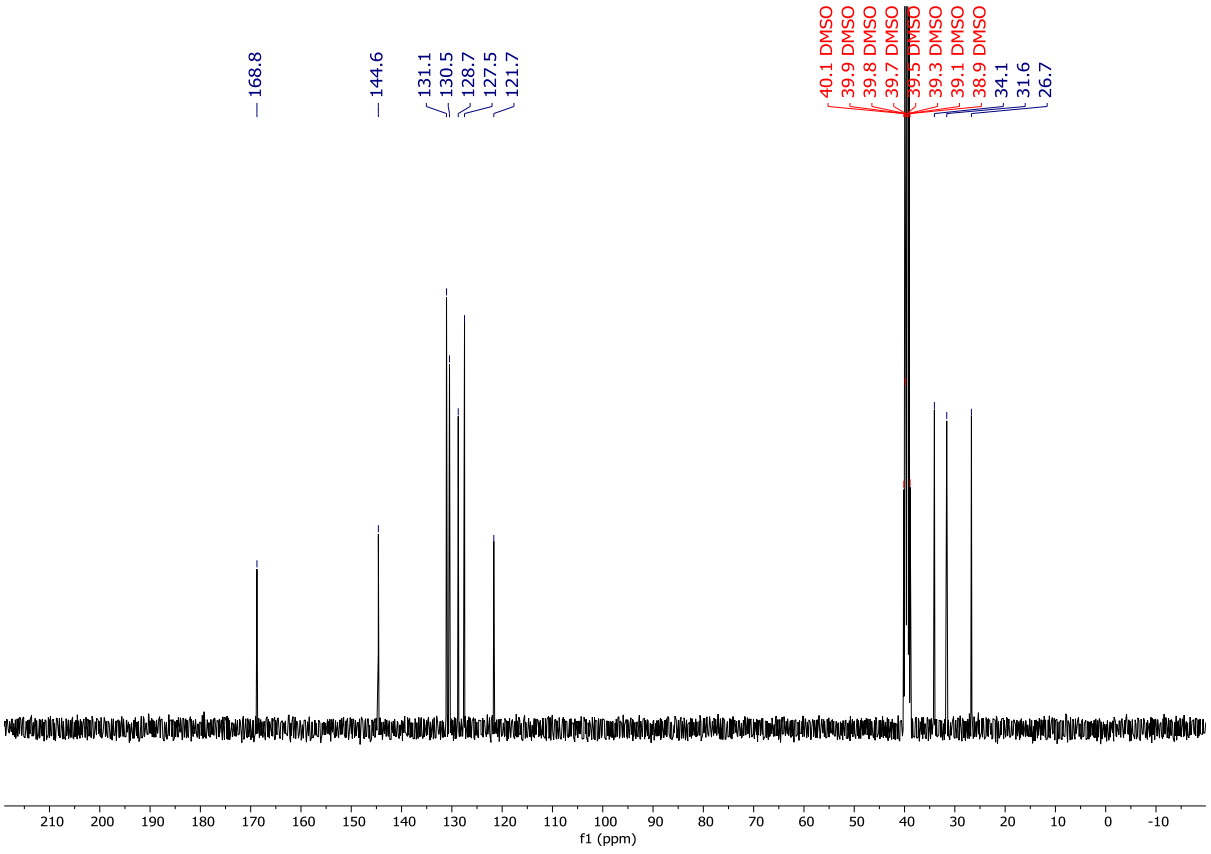
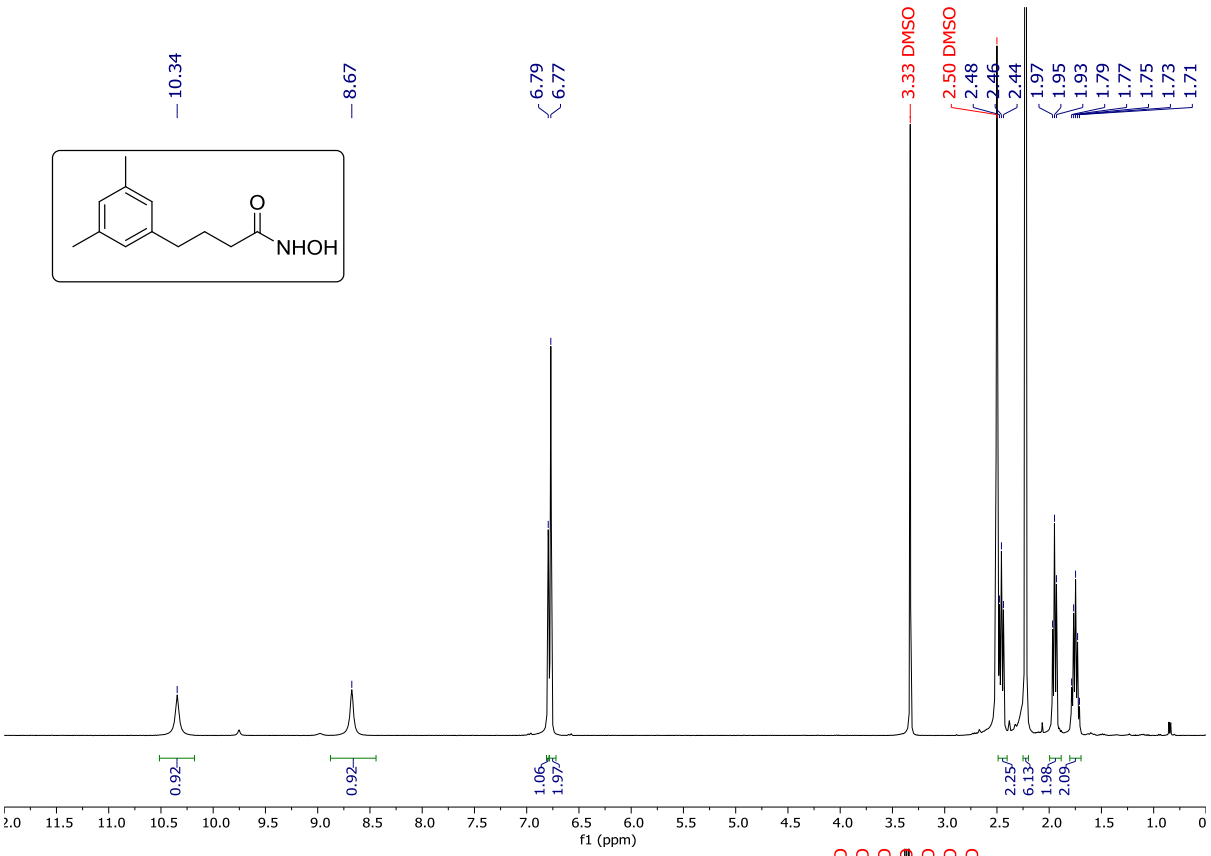
-150
-160
-170
-180
-190
-20
f1 (ppm)

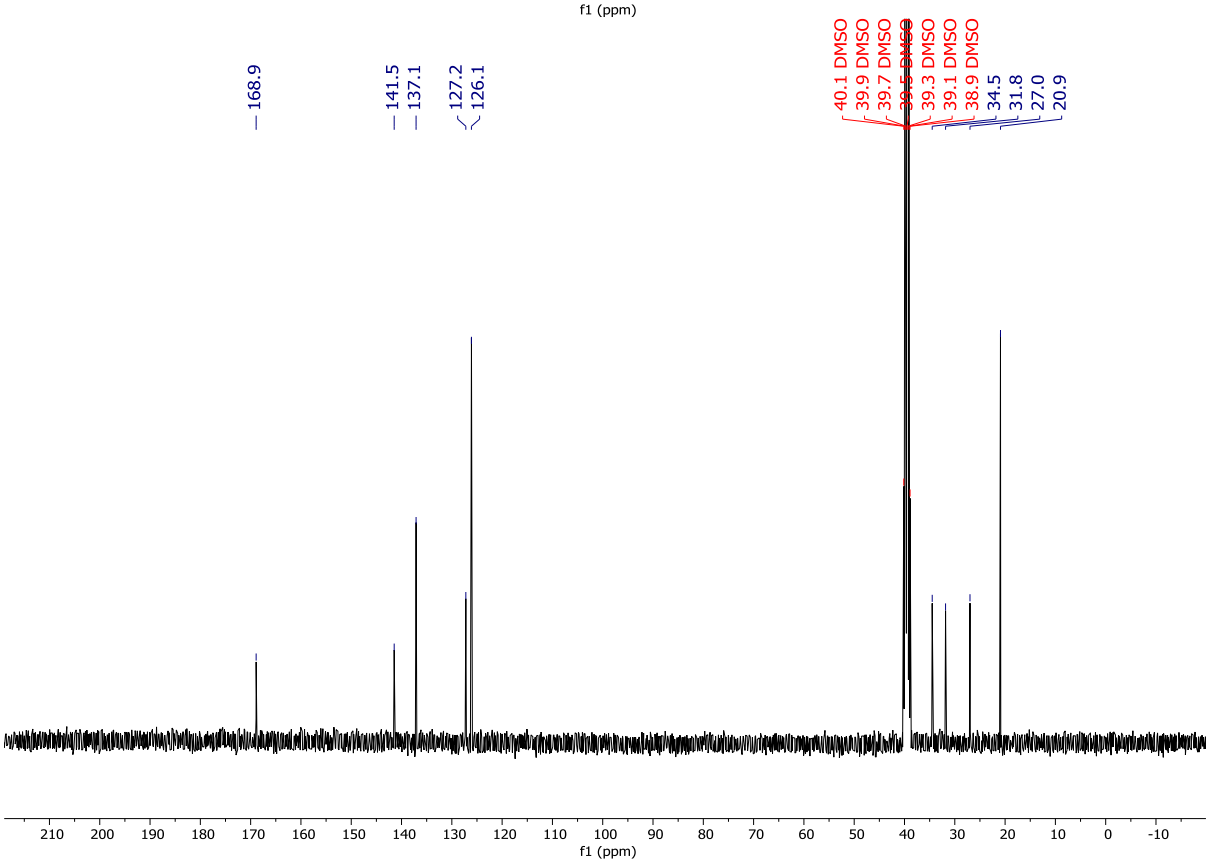
4-(3-Bromophenyl)-*N*-hydroxybutanamide



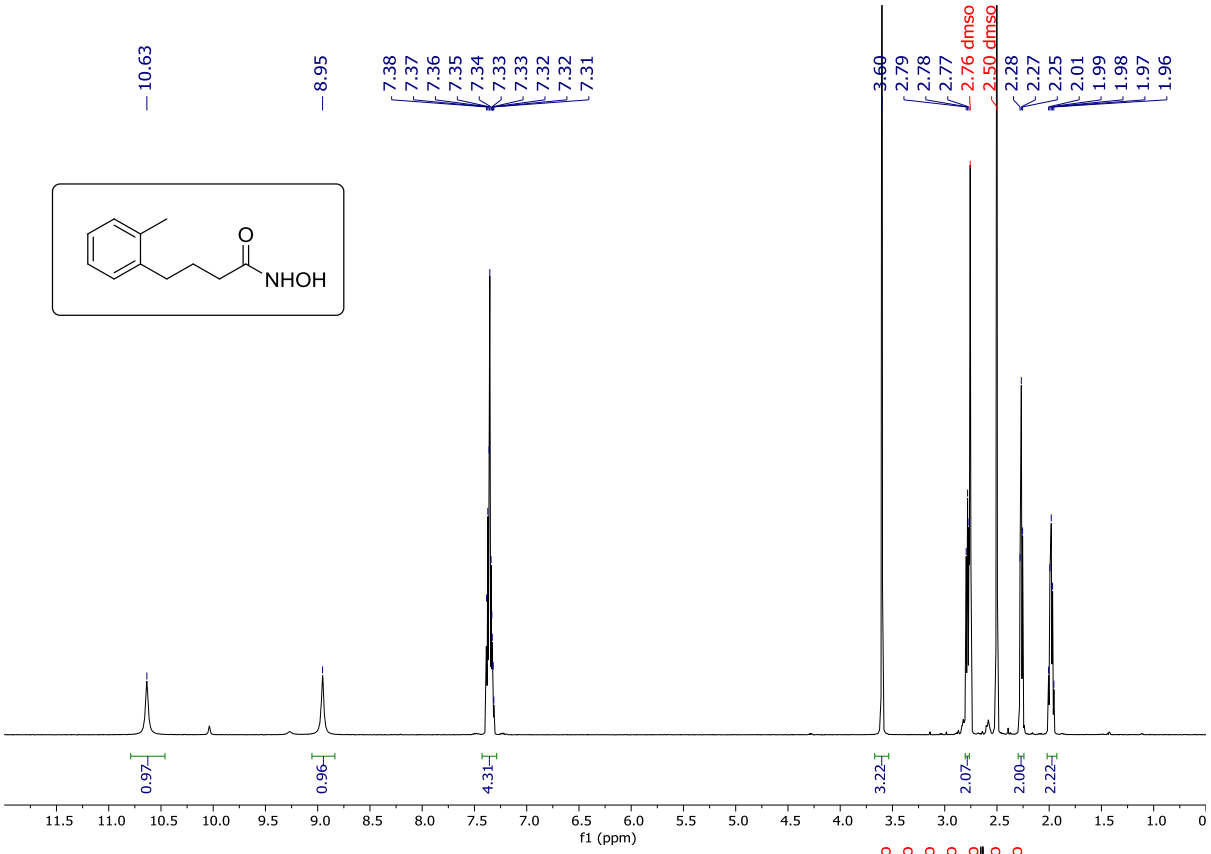


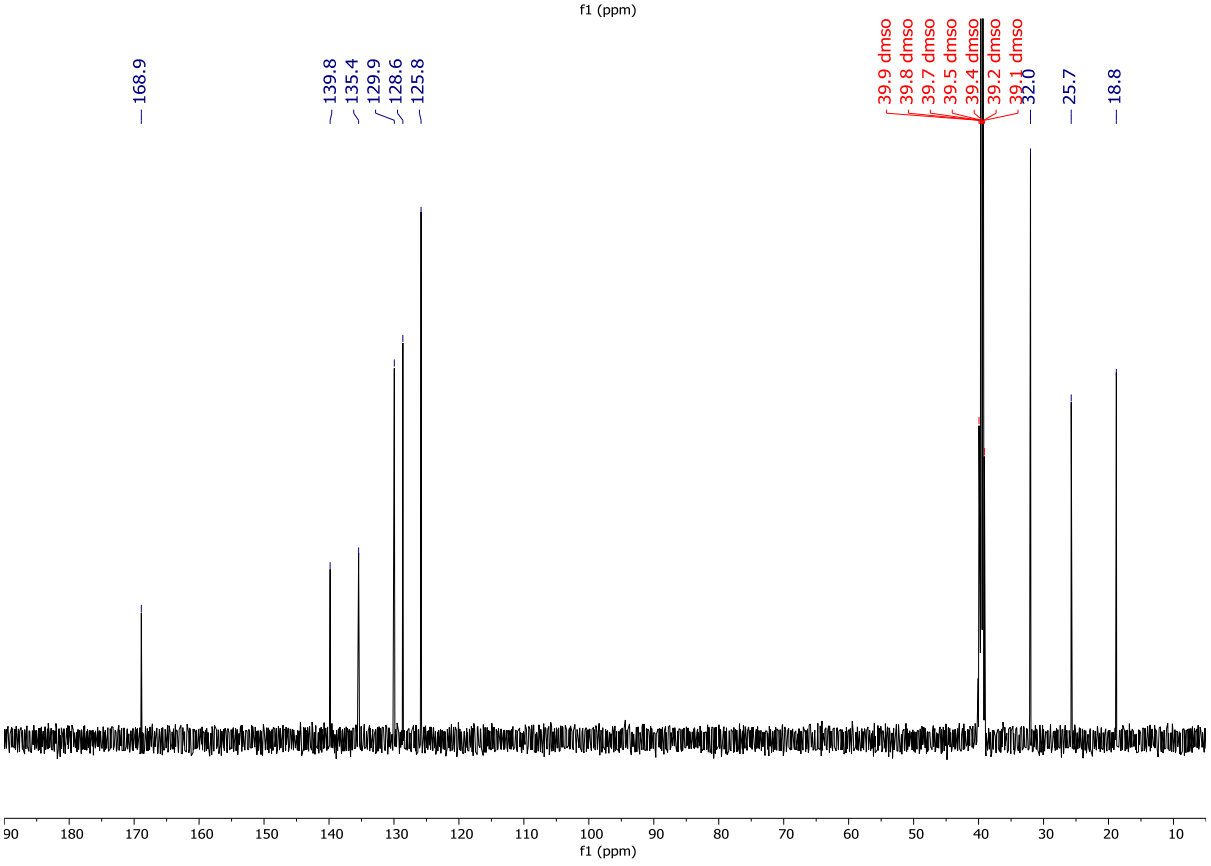
4-(3,5-Dimethylphenyl)-*N*-hydroxybutanamide



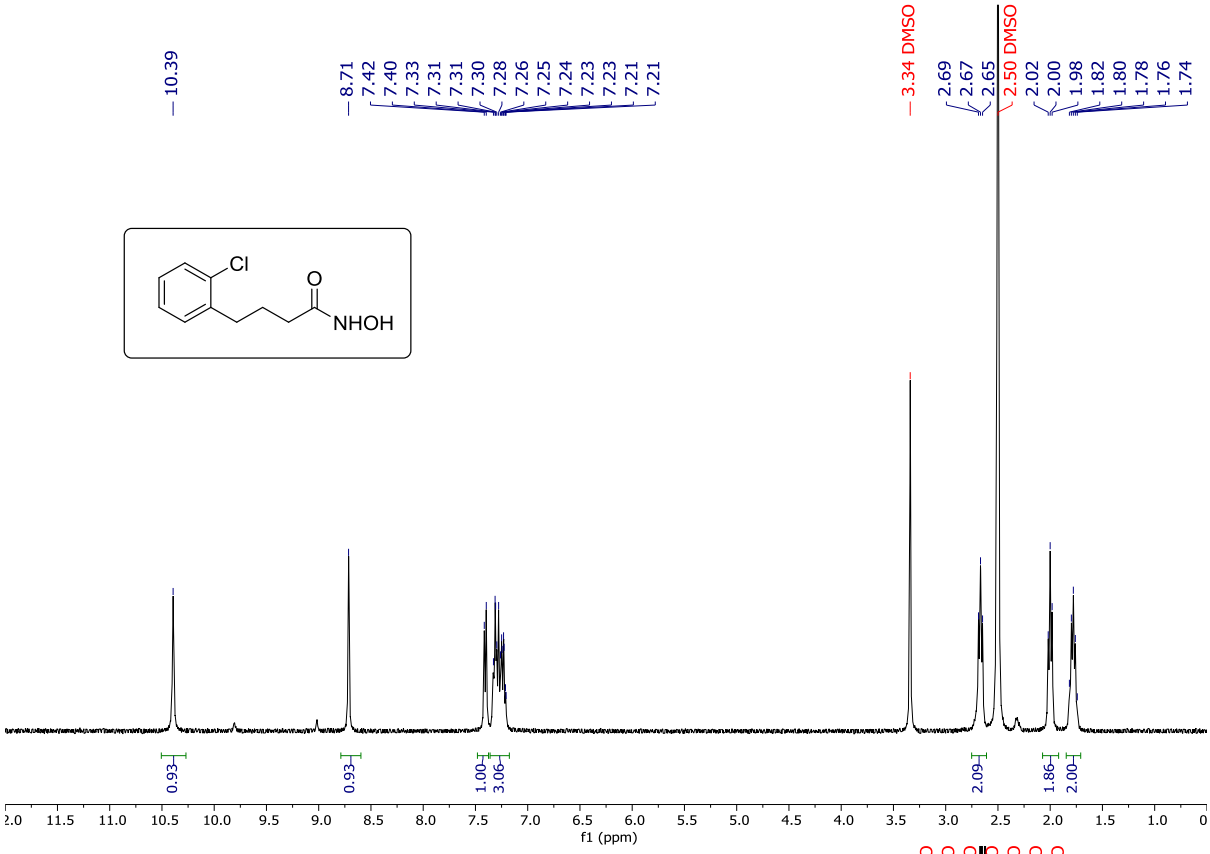


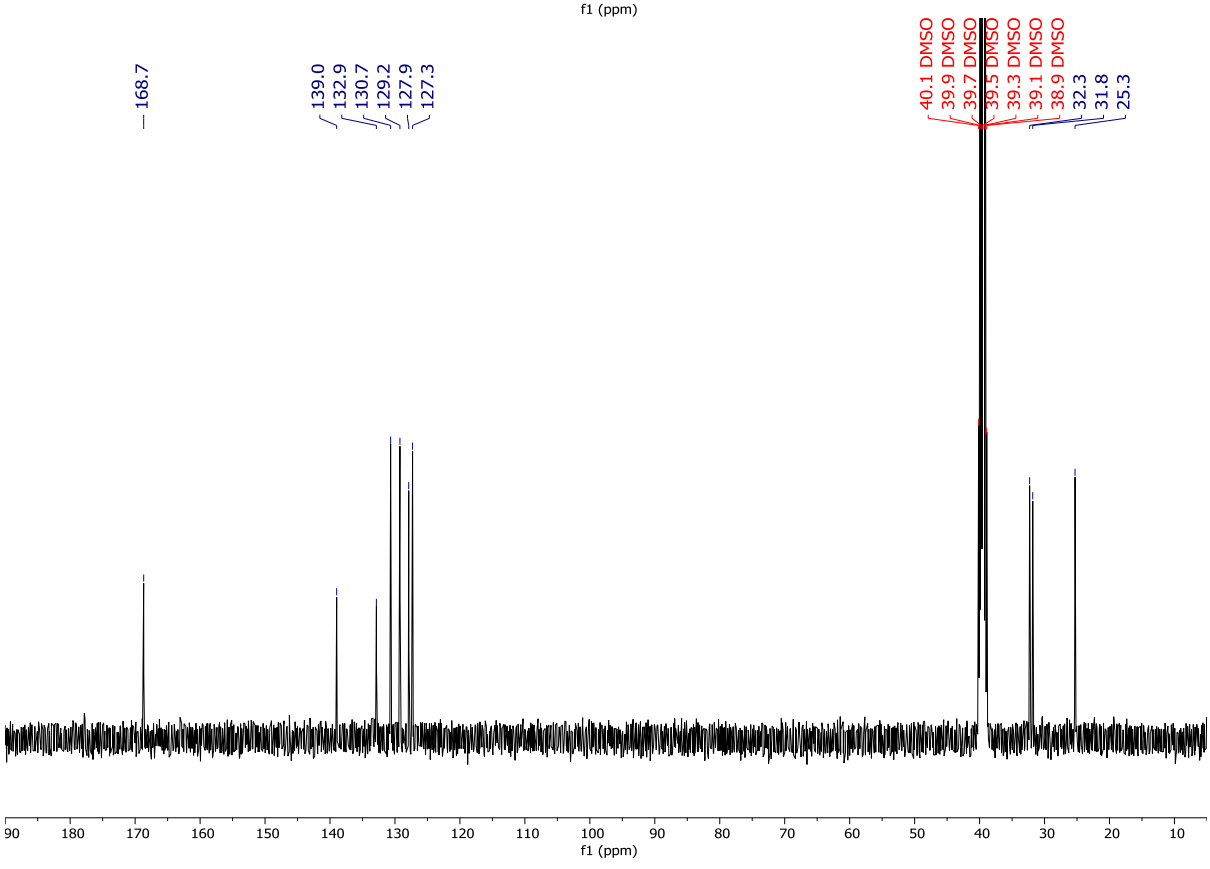
N-Hydroxy-4-(*o*-tolyl)butanamide



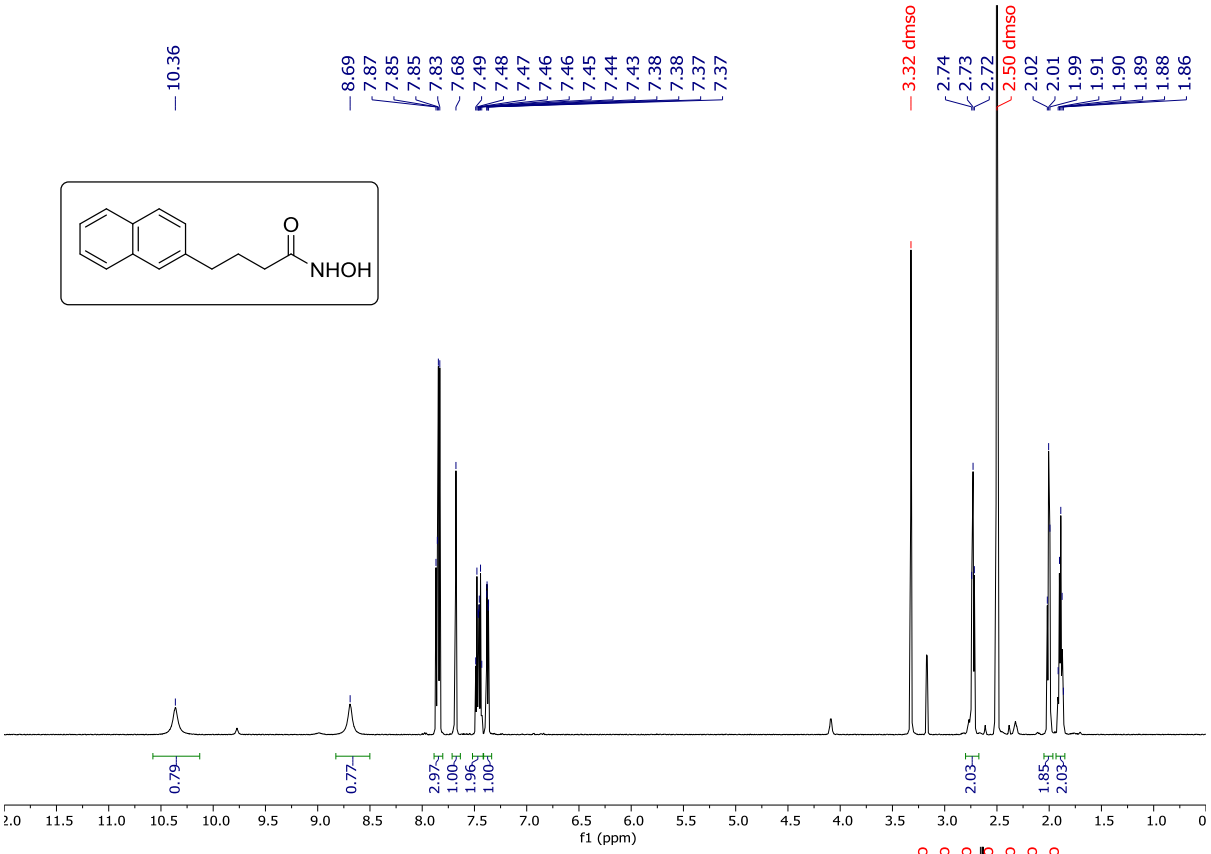


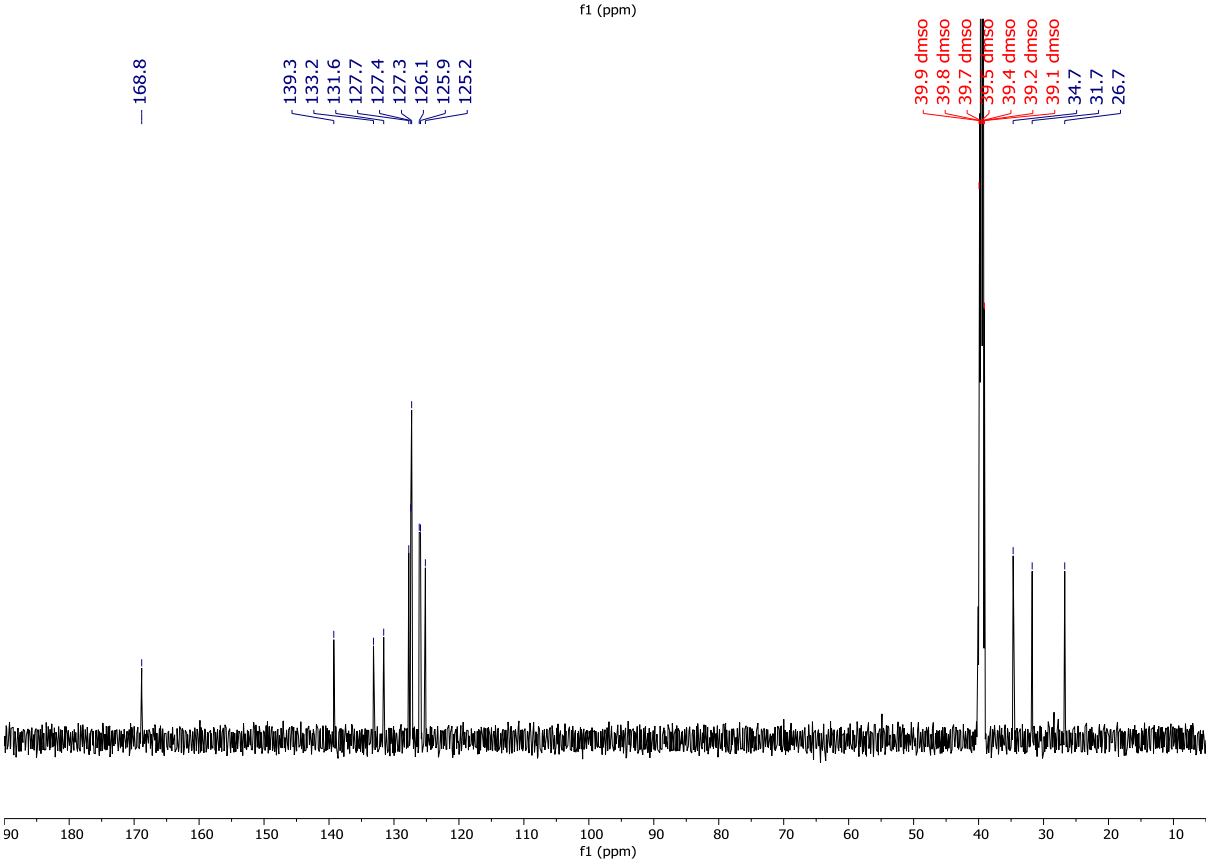
4-(2-Chlorophenyl)-*N*-hydroxybutanamide



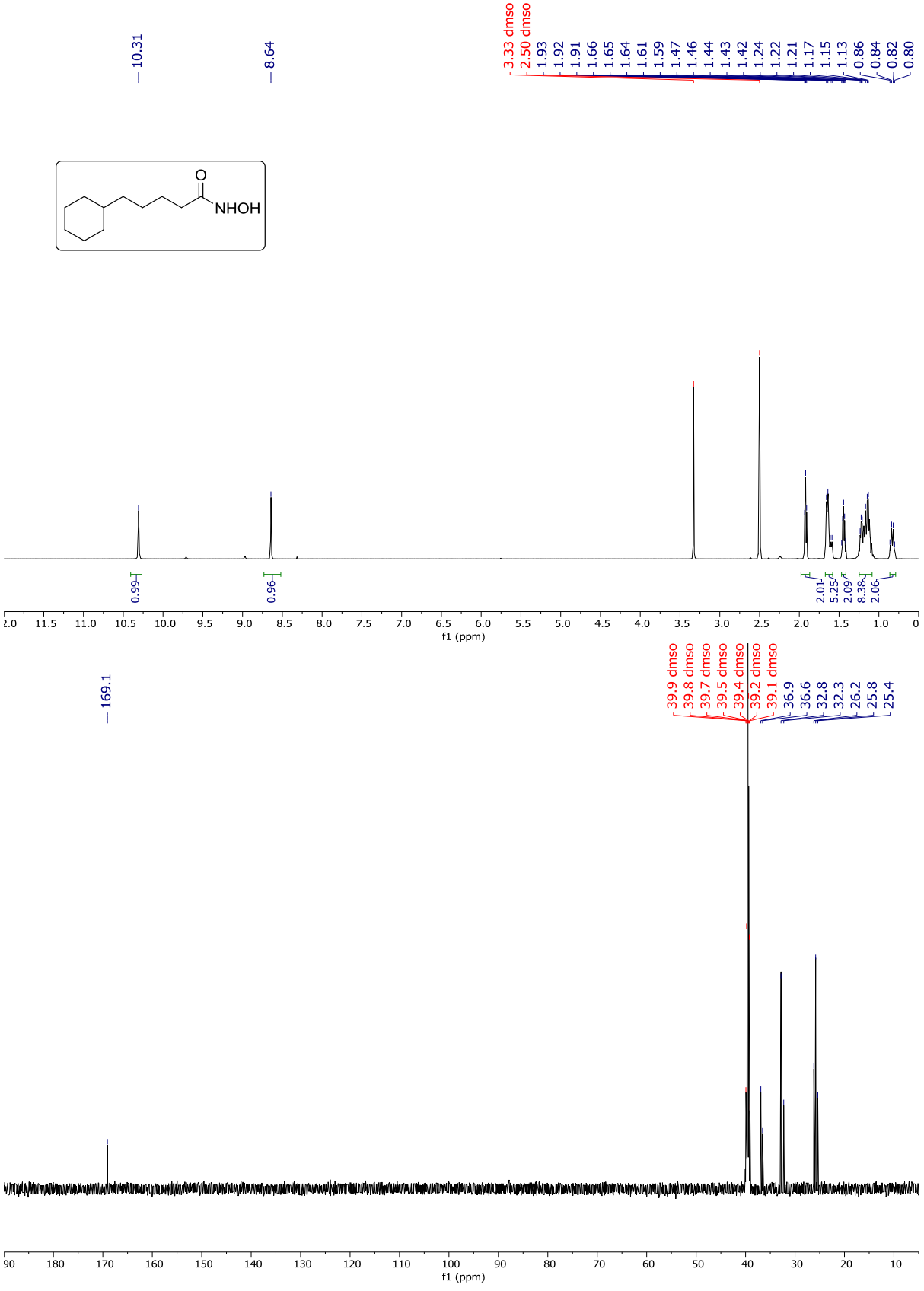


N-Hydroxy-4-(naphthalen-2-yl)butanamide

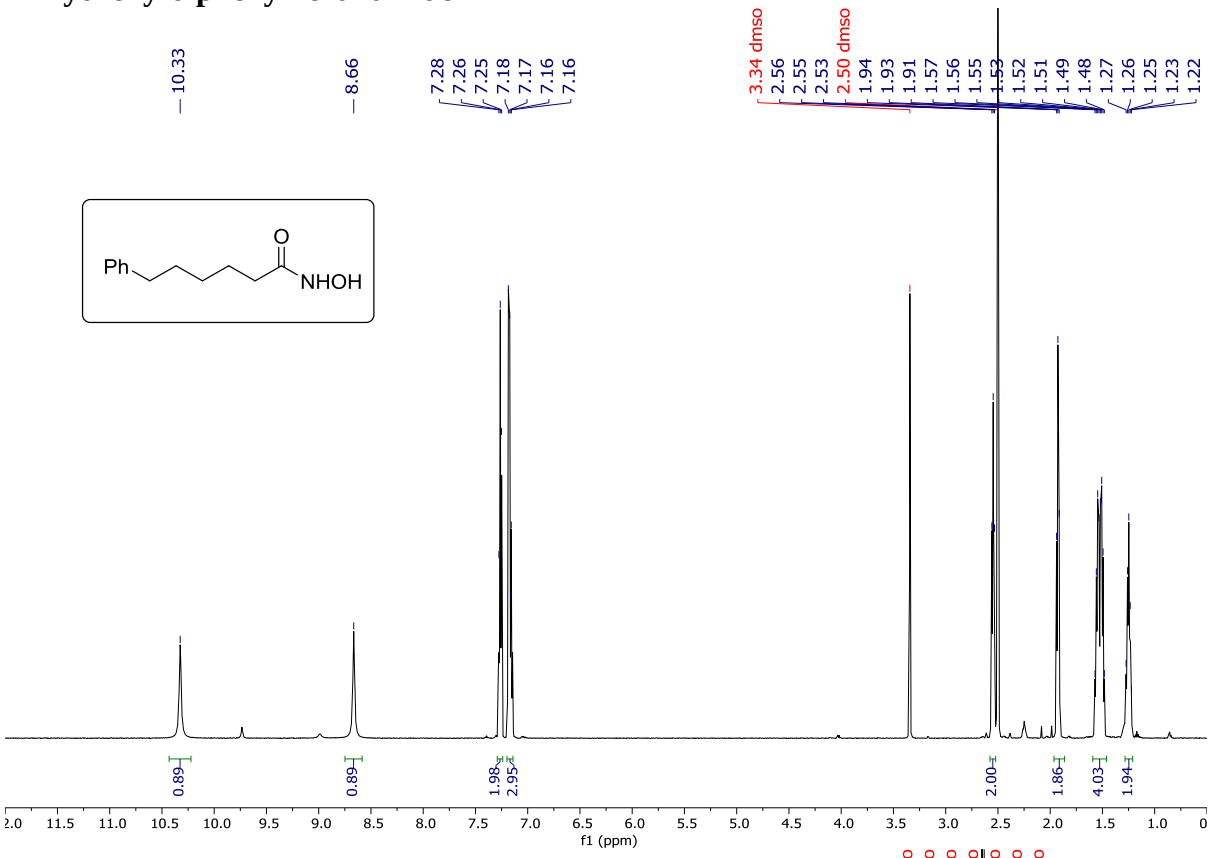


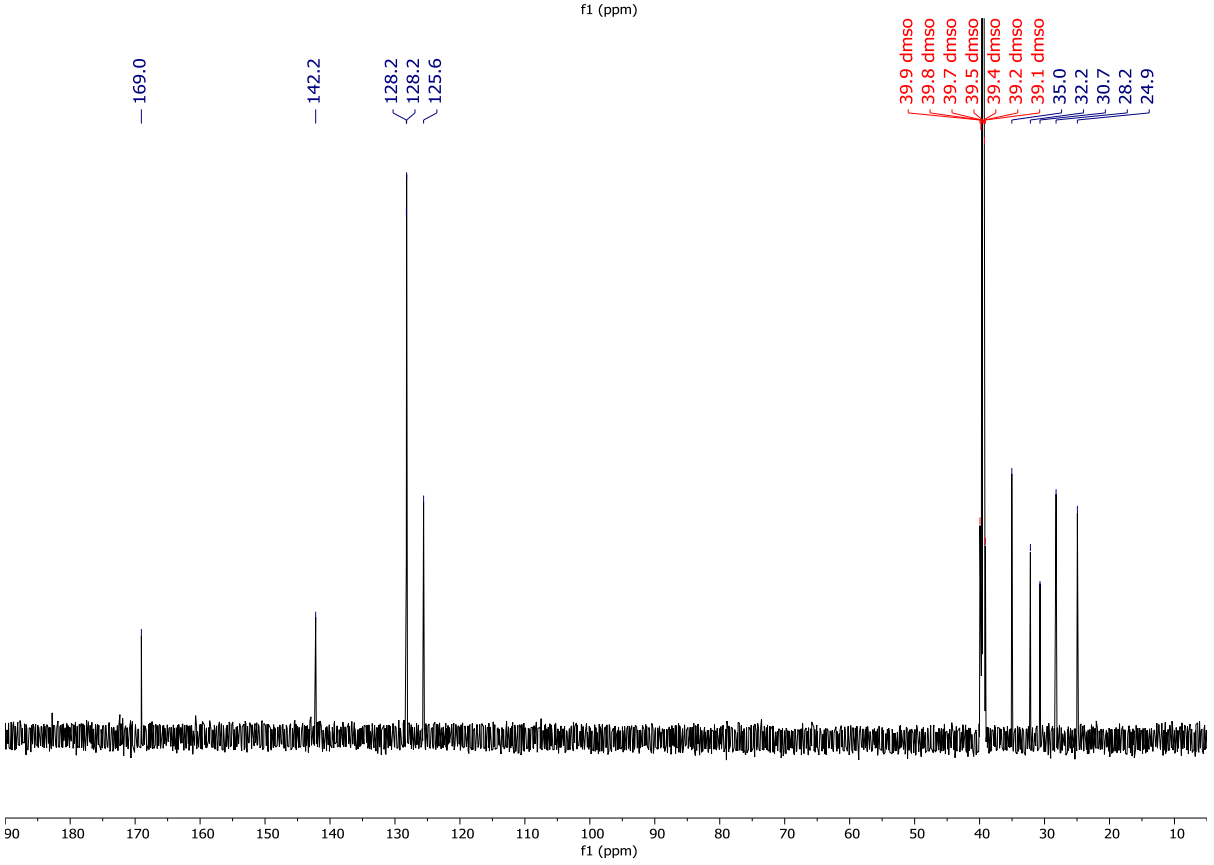


5-Cyclohexyl-*N*-hydroxypentanamide

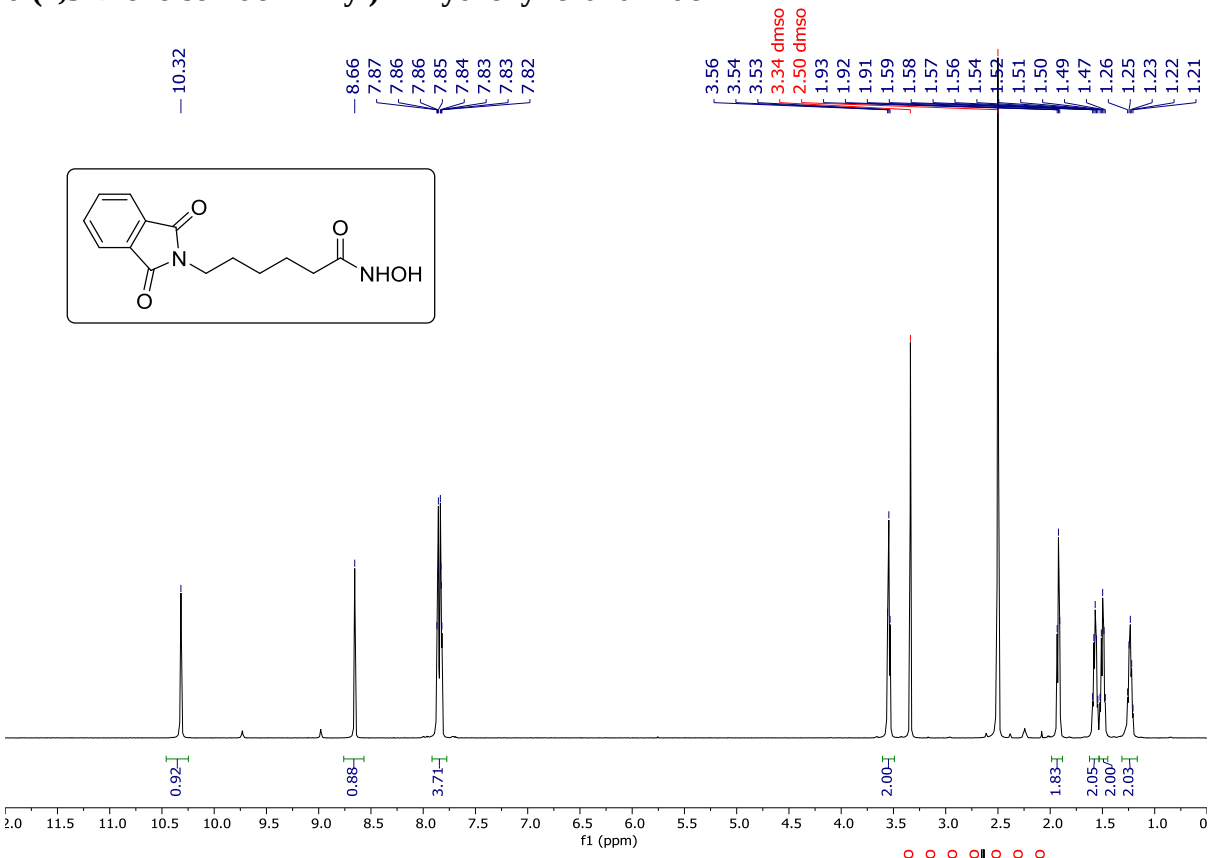


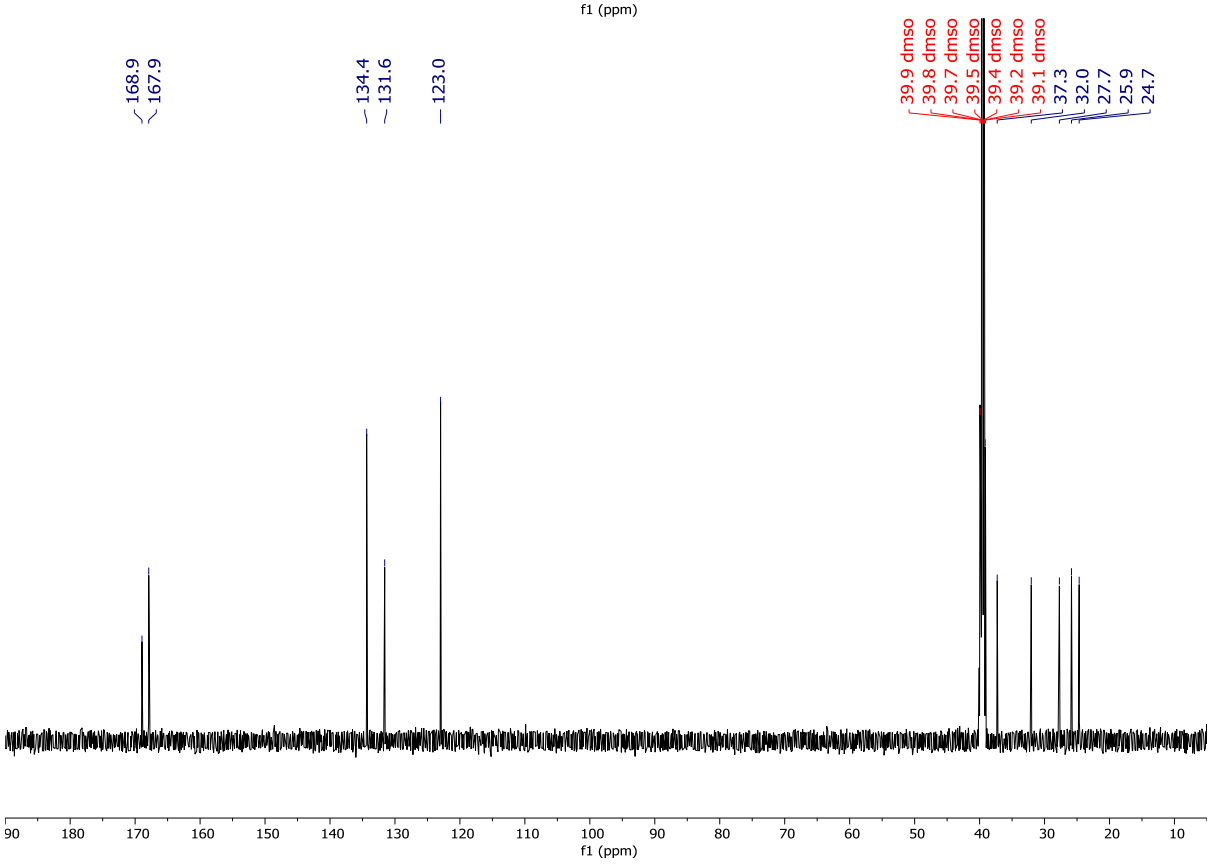
N-Hydroxy-6-phenylhexanamide



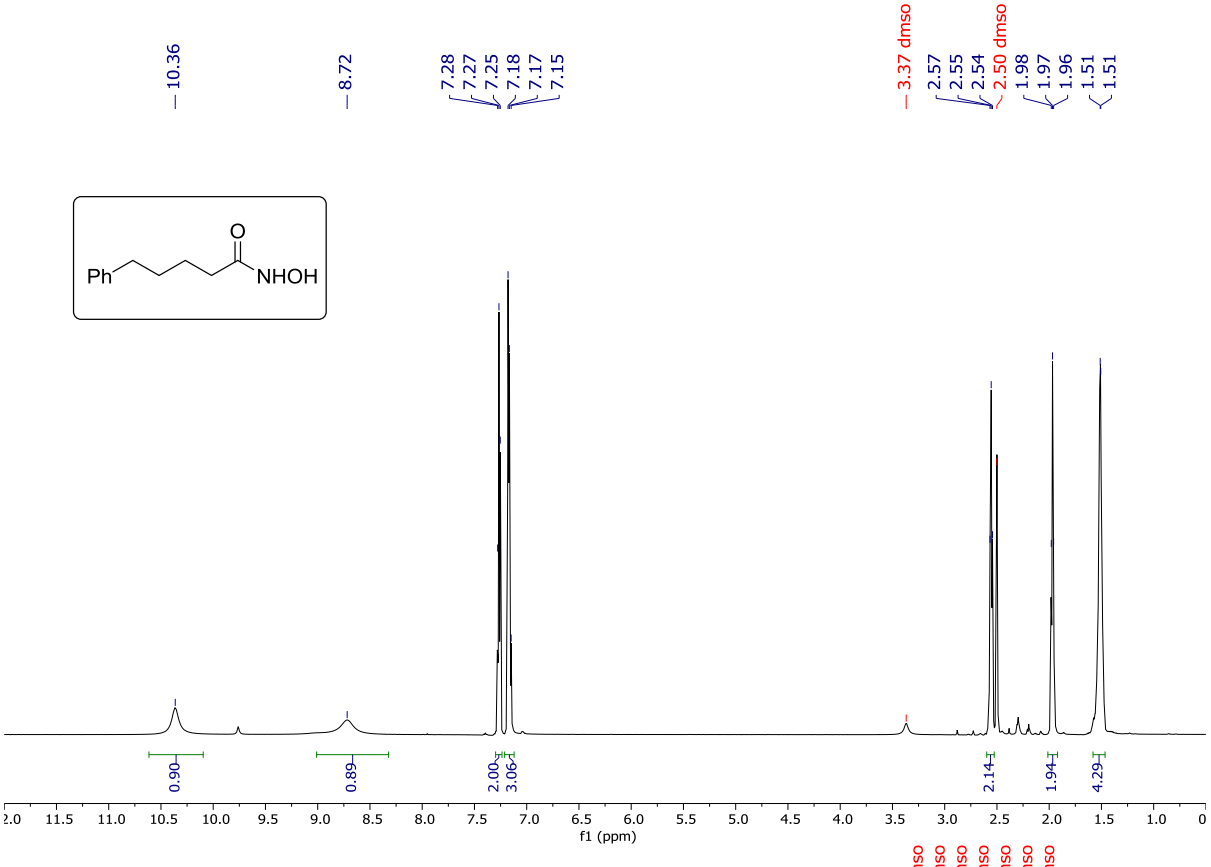


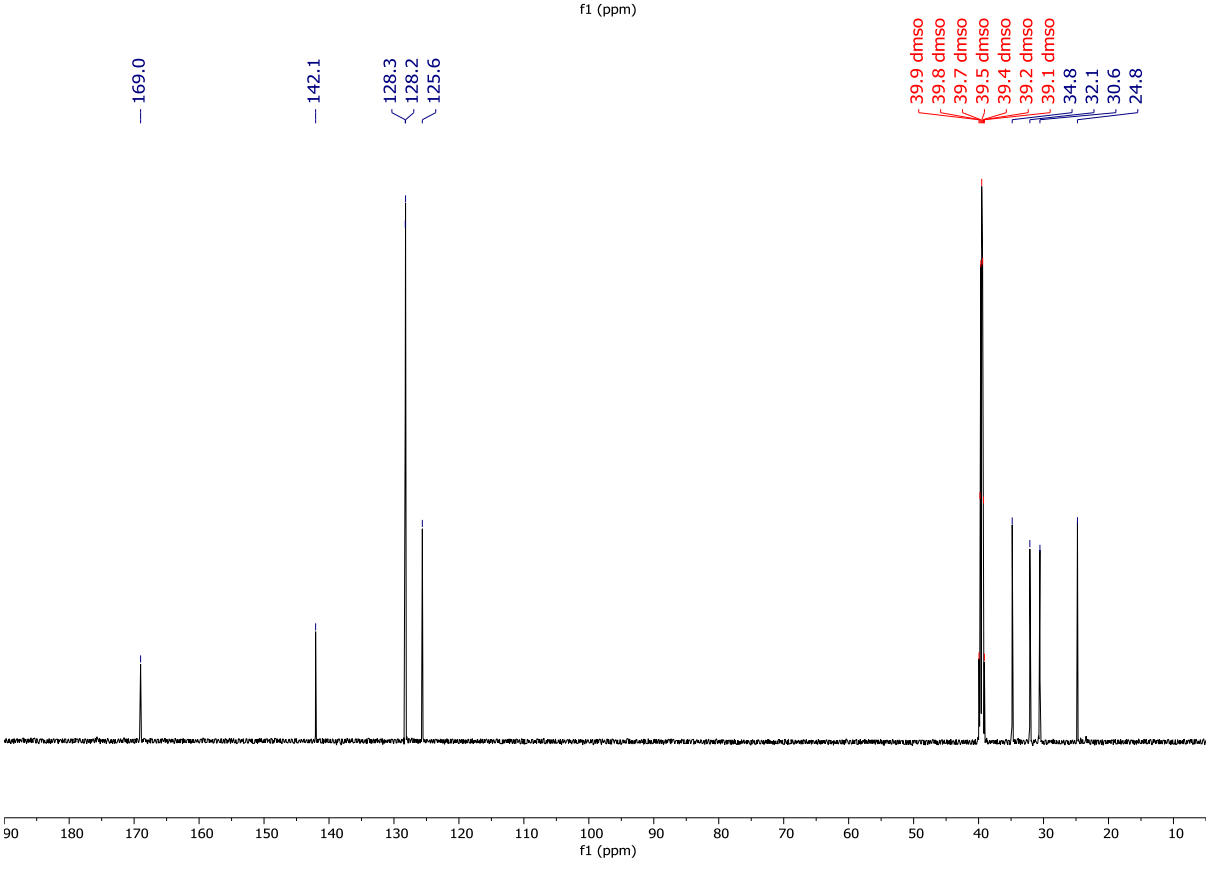
6-(1,3-Dioxoisoindolin-2-yl)-*N*-hydroxyhexanamide



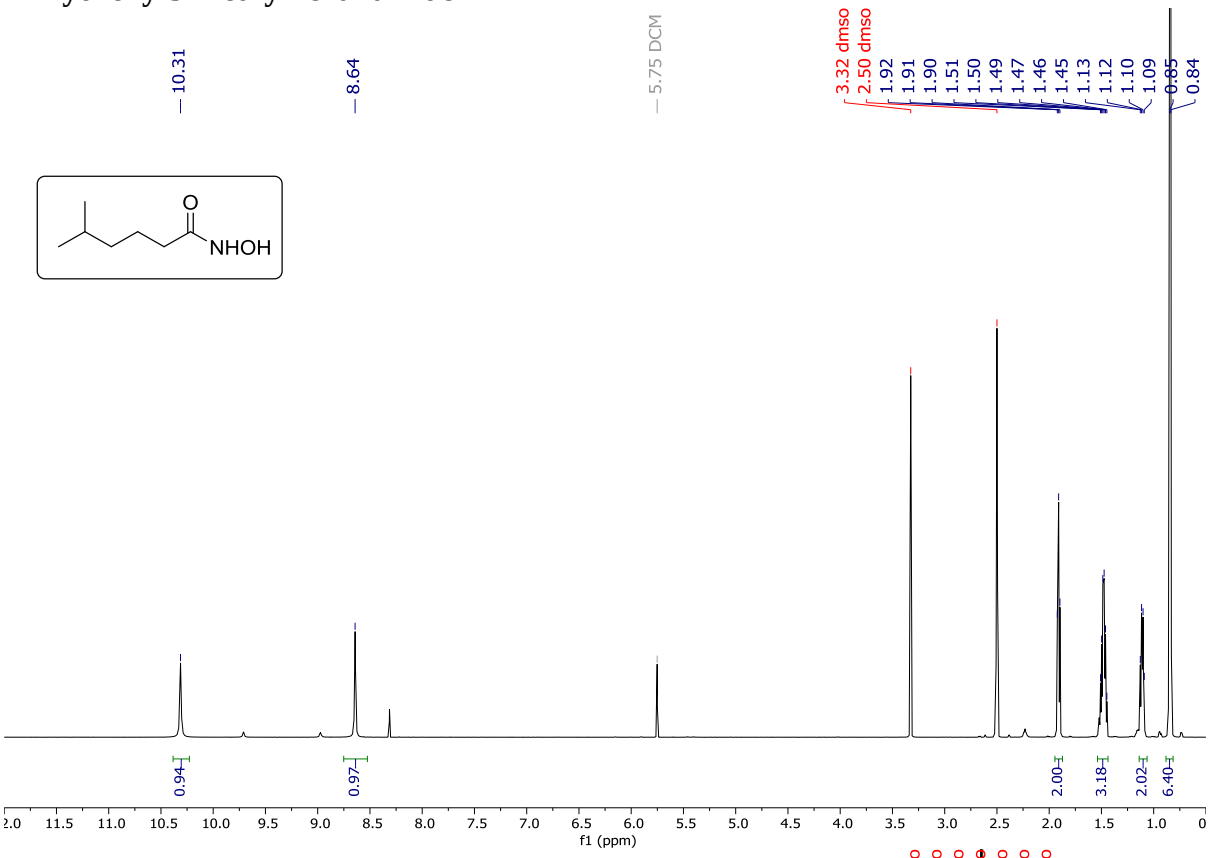


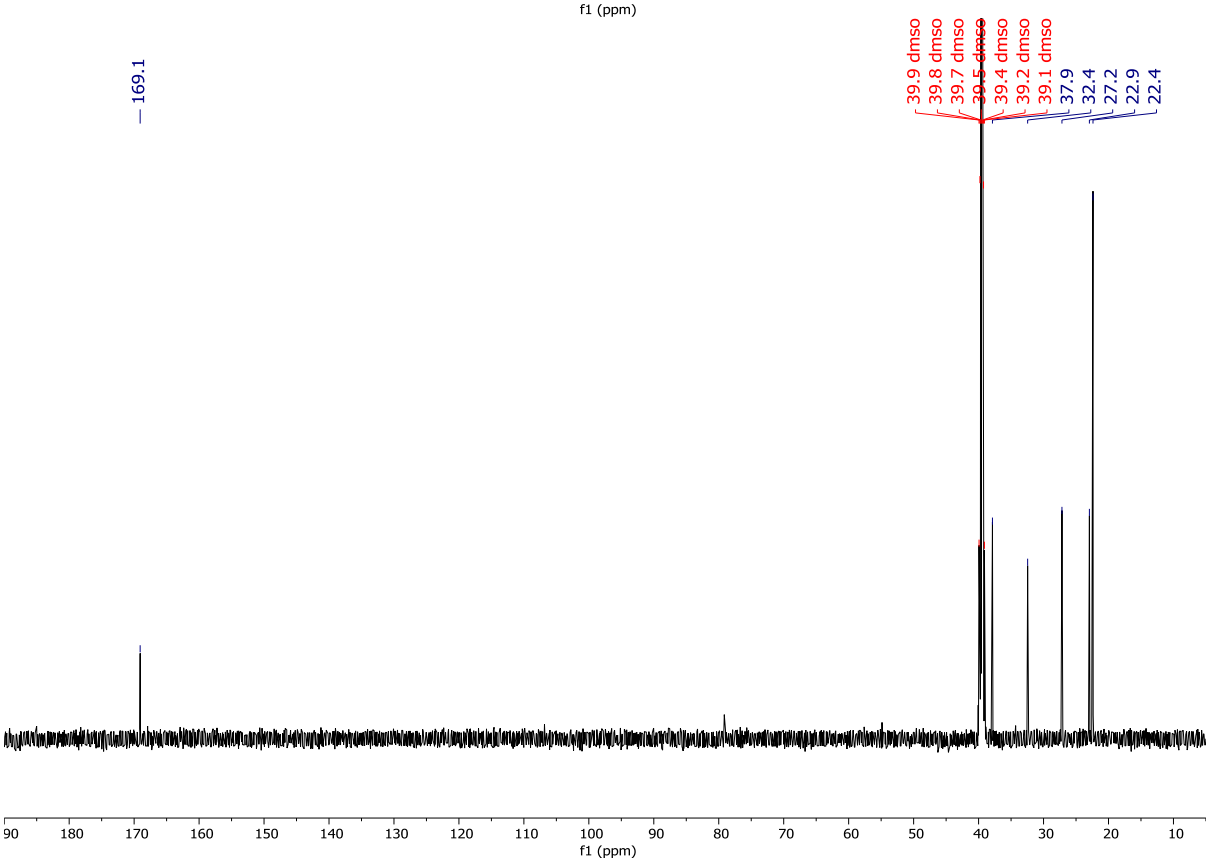
N-Hydroxy-5-phenylpentanamide



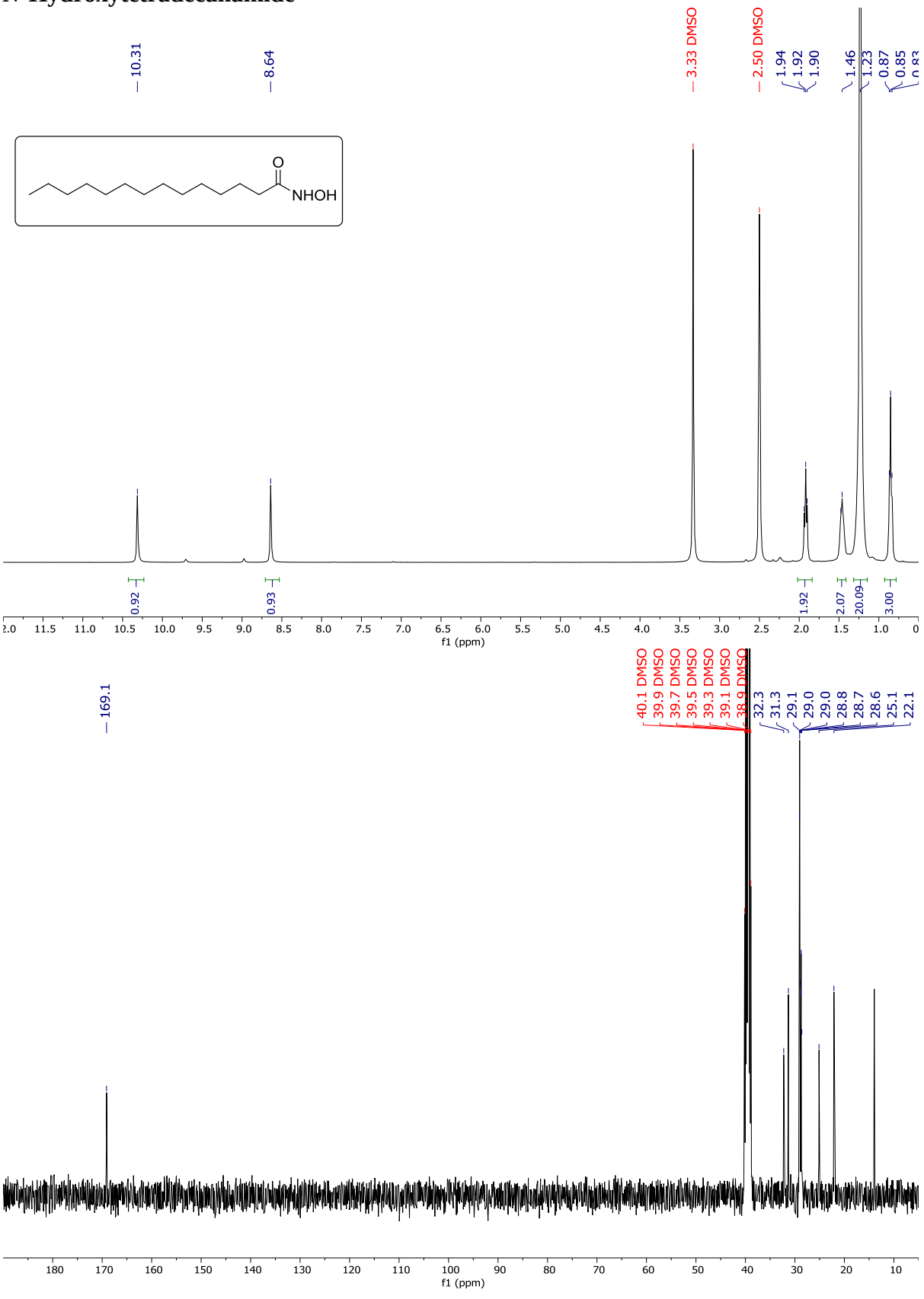


N-Hydroxy-5-methylhexanamide

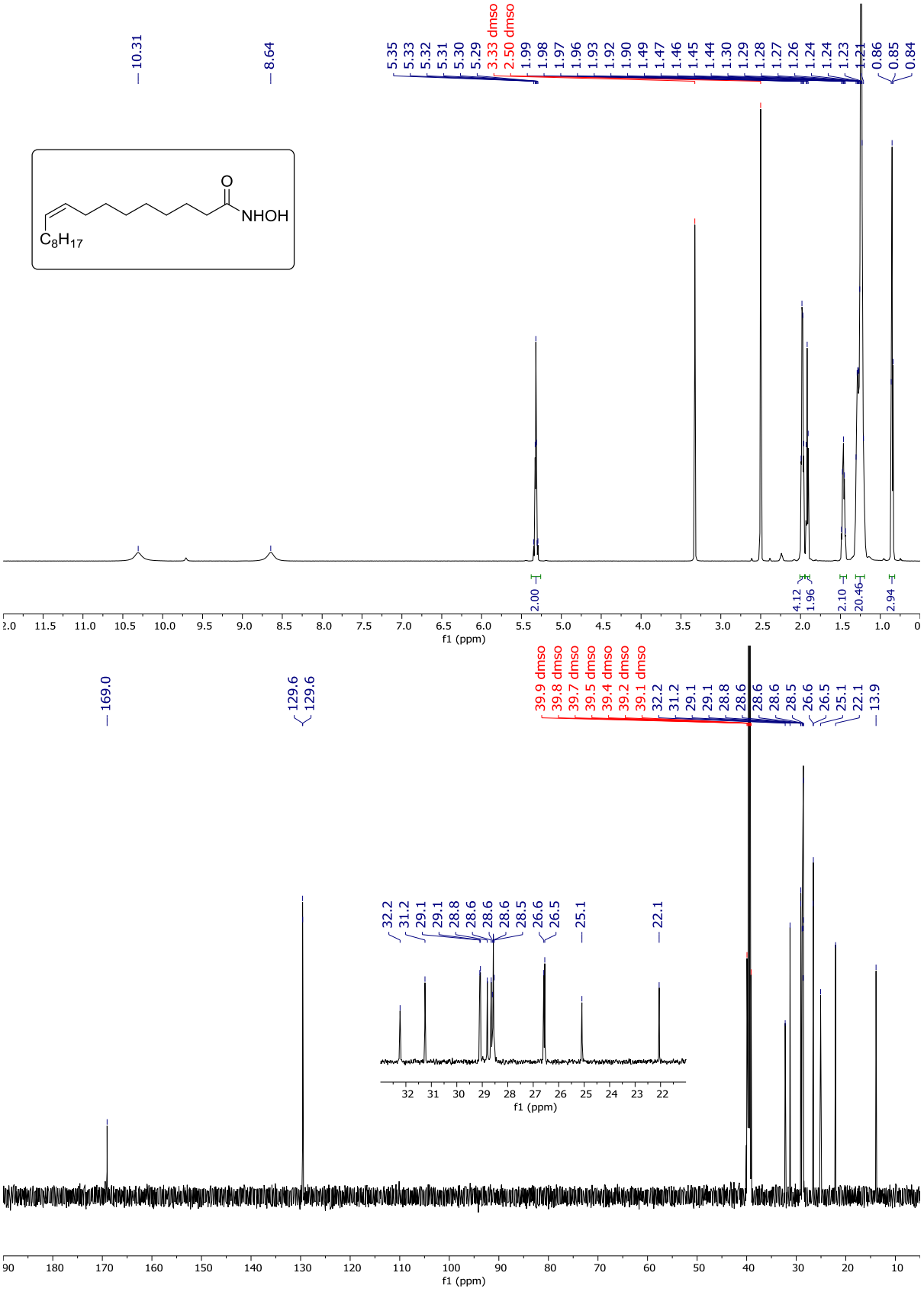




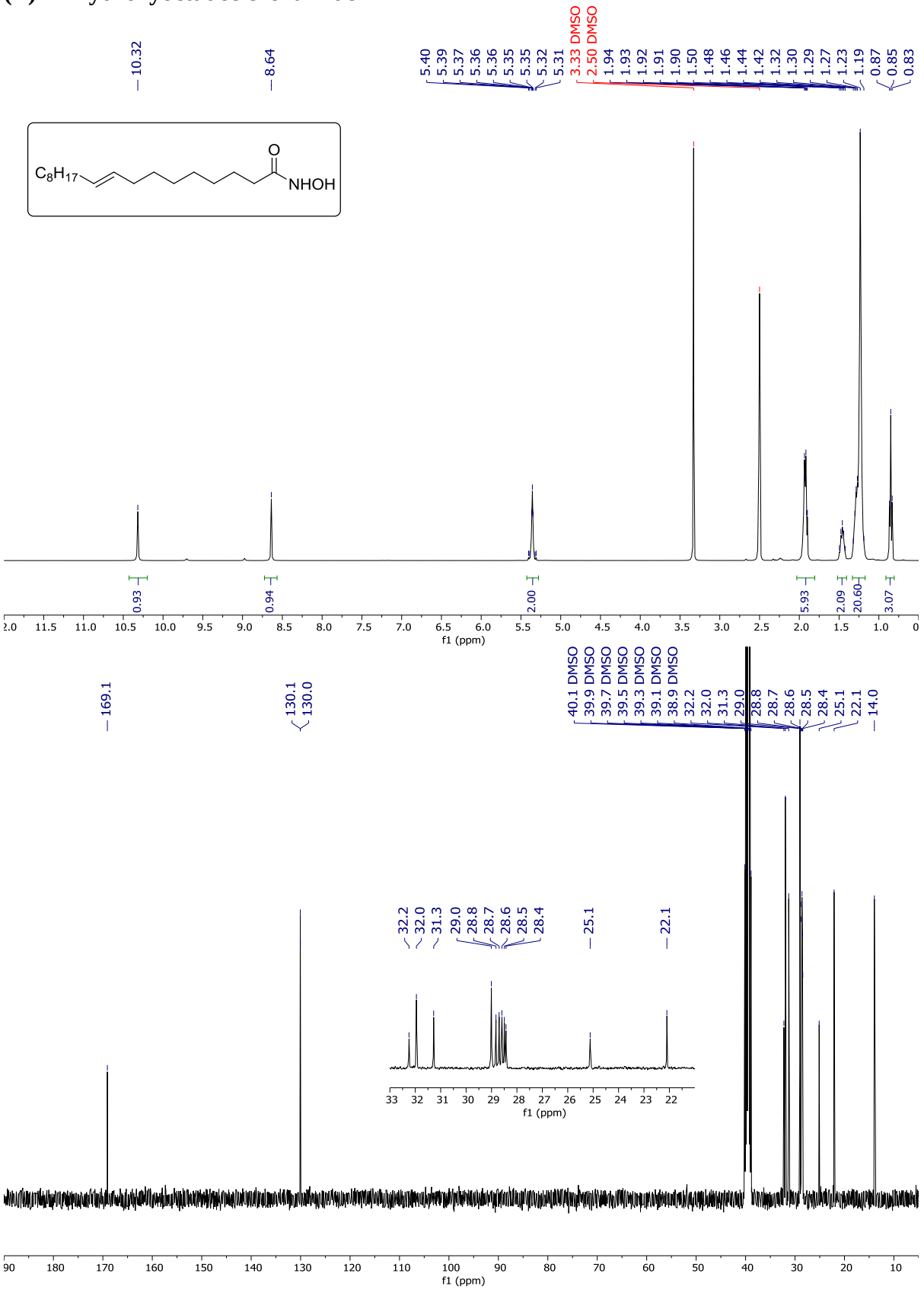
N-Hydroxytetradecanamide



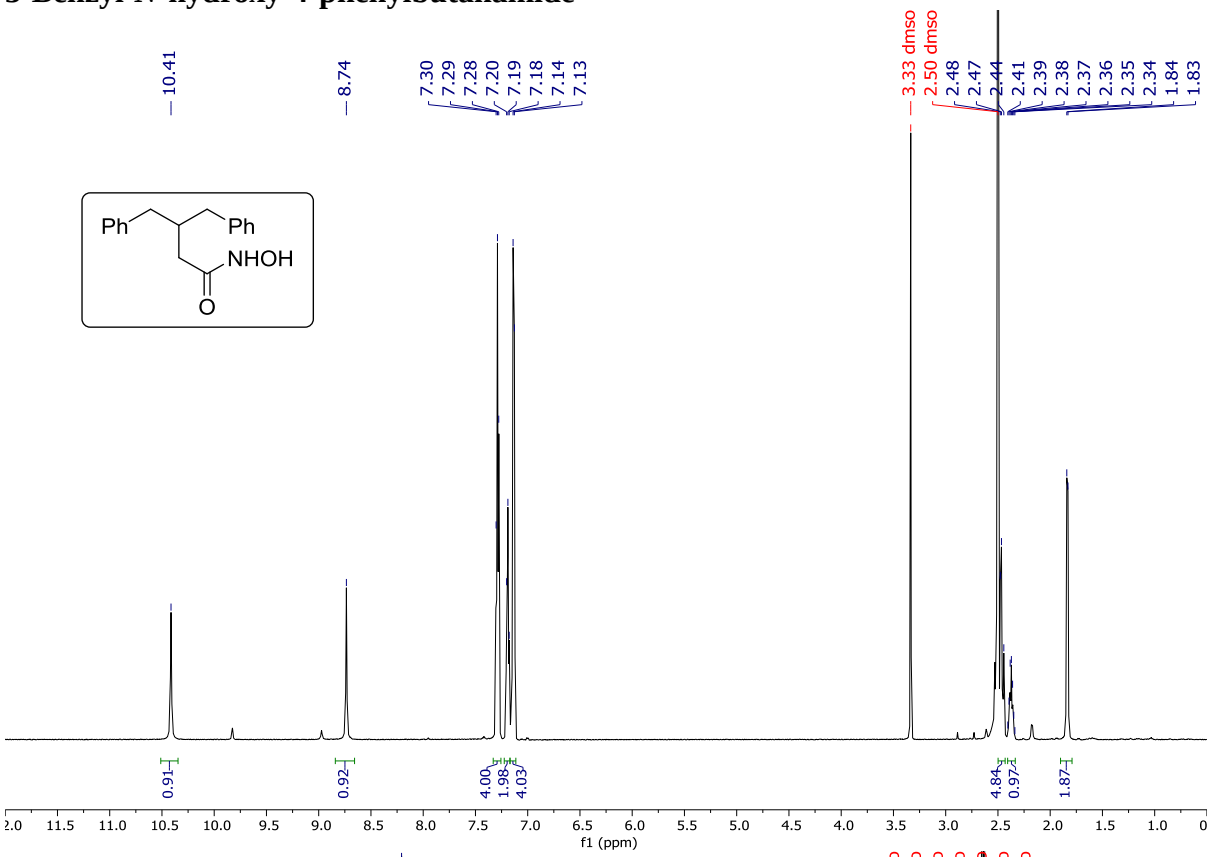
N-Hydroxyoleamide

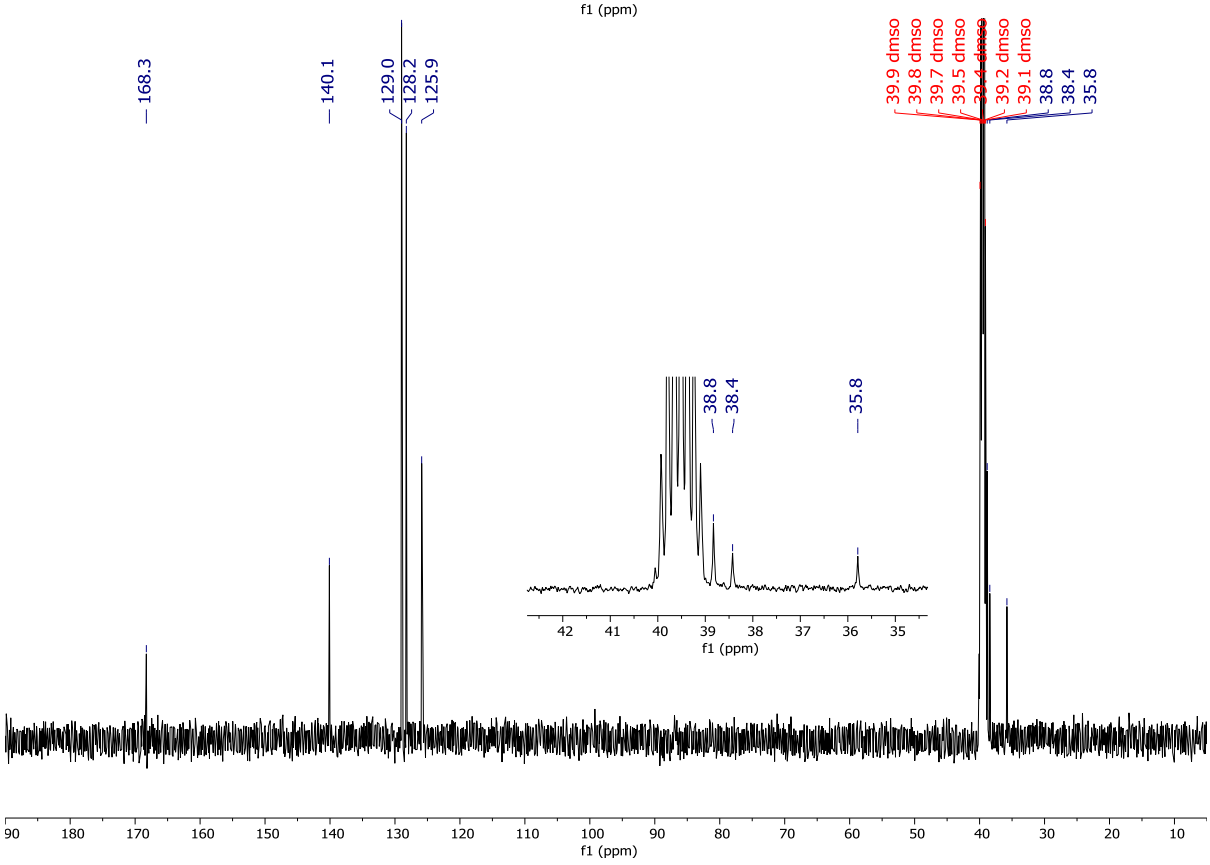


(*E*)-*N*-Hydroxyoctadec-9-enamide

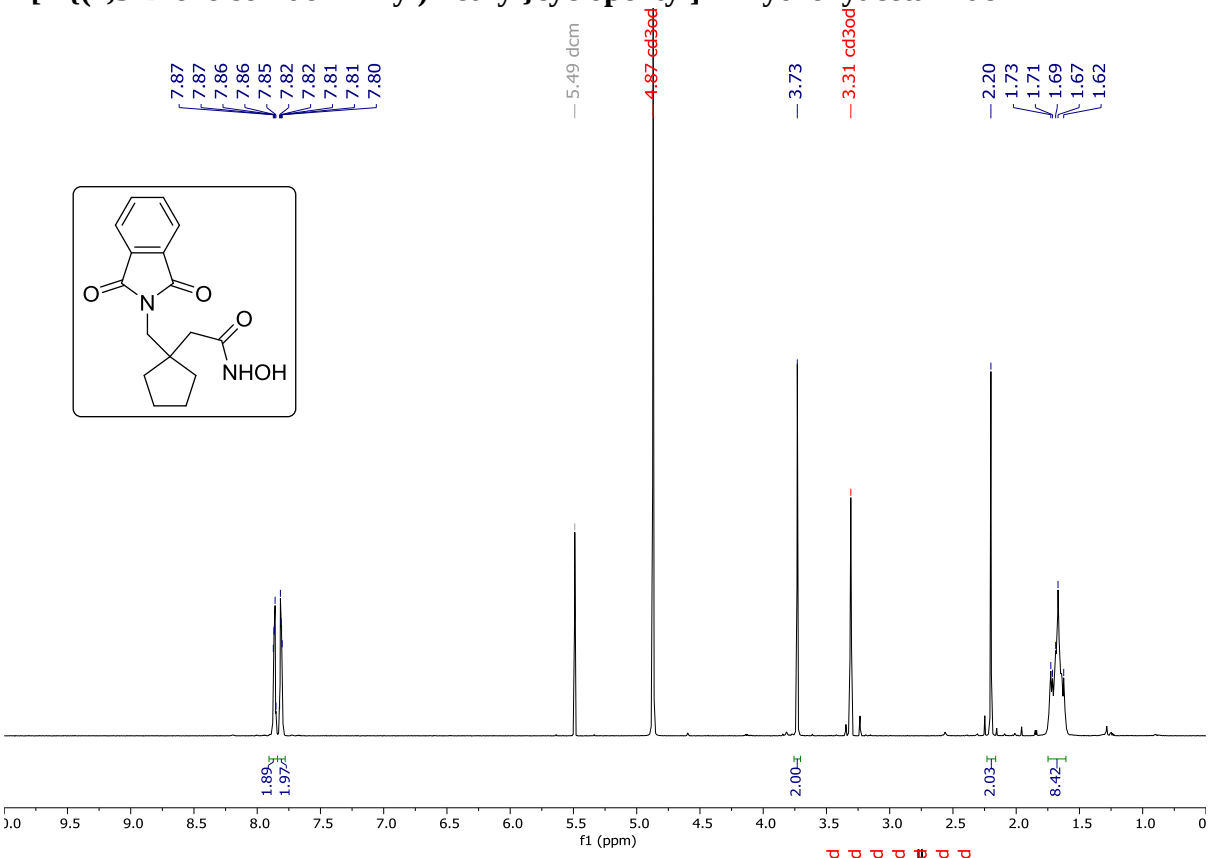


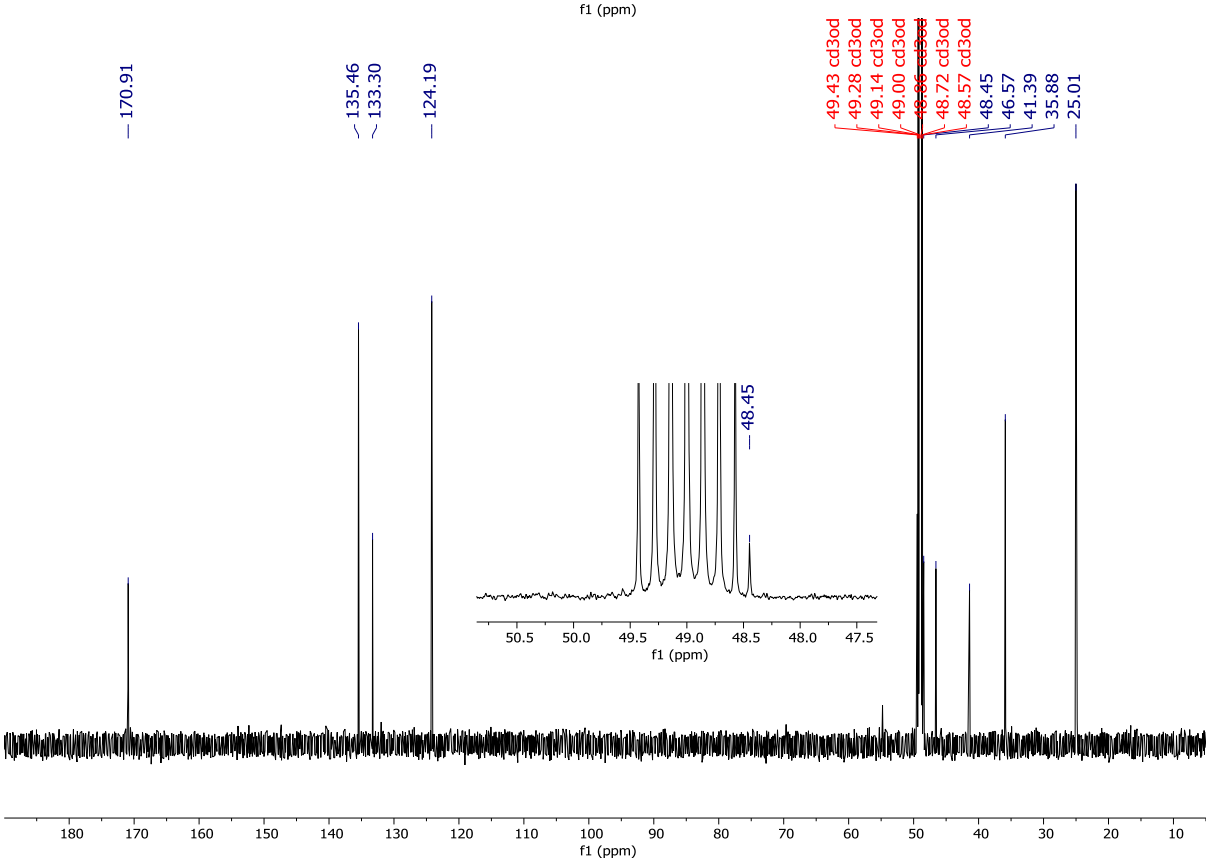
3-Benzyl-*N*-hydroxy-4-phenylbutanamide



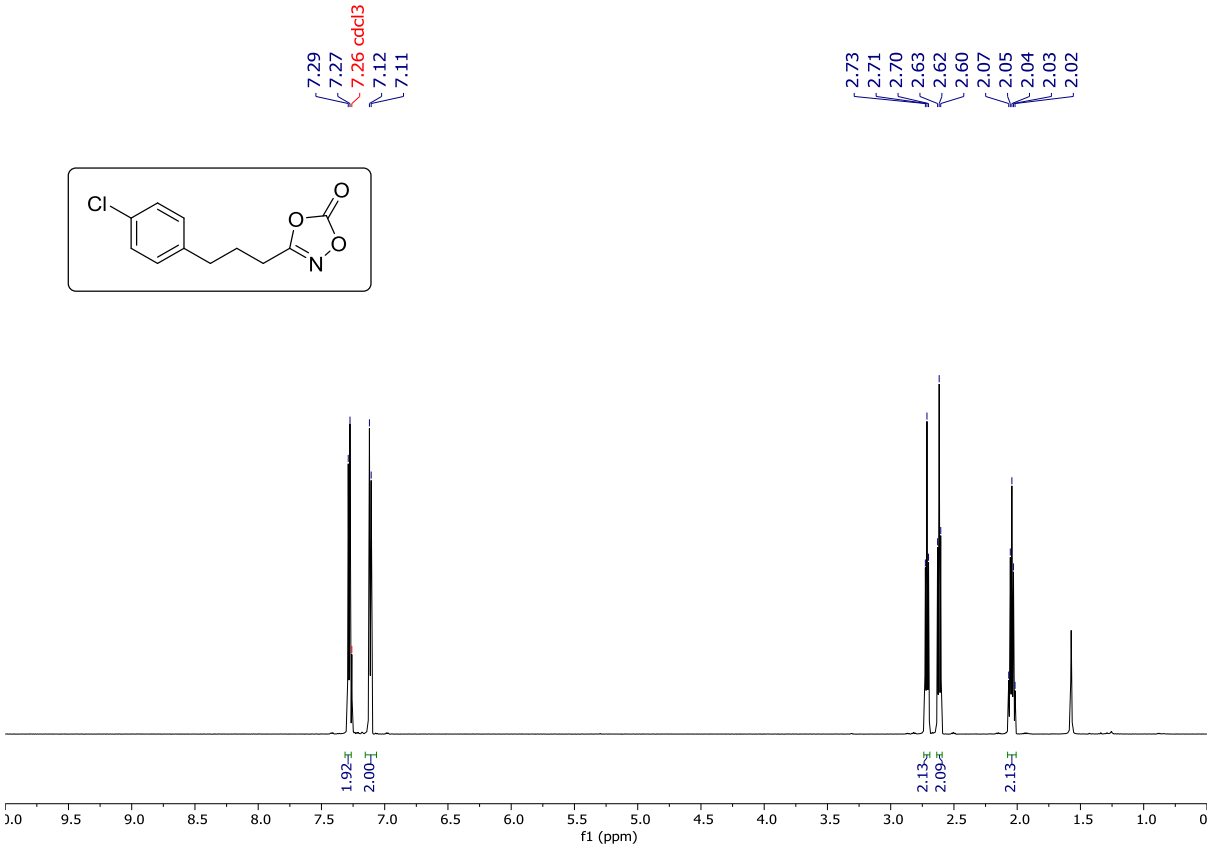


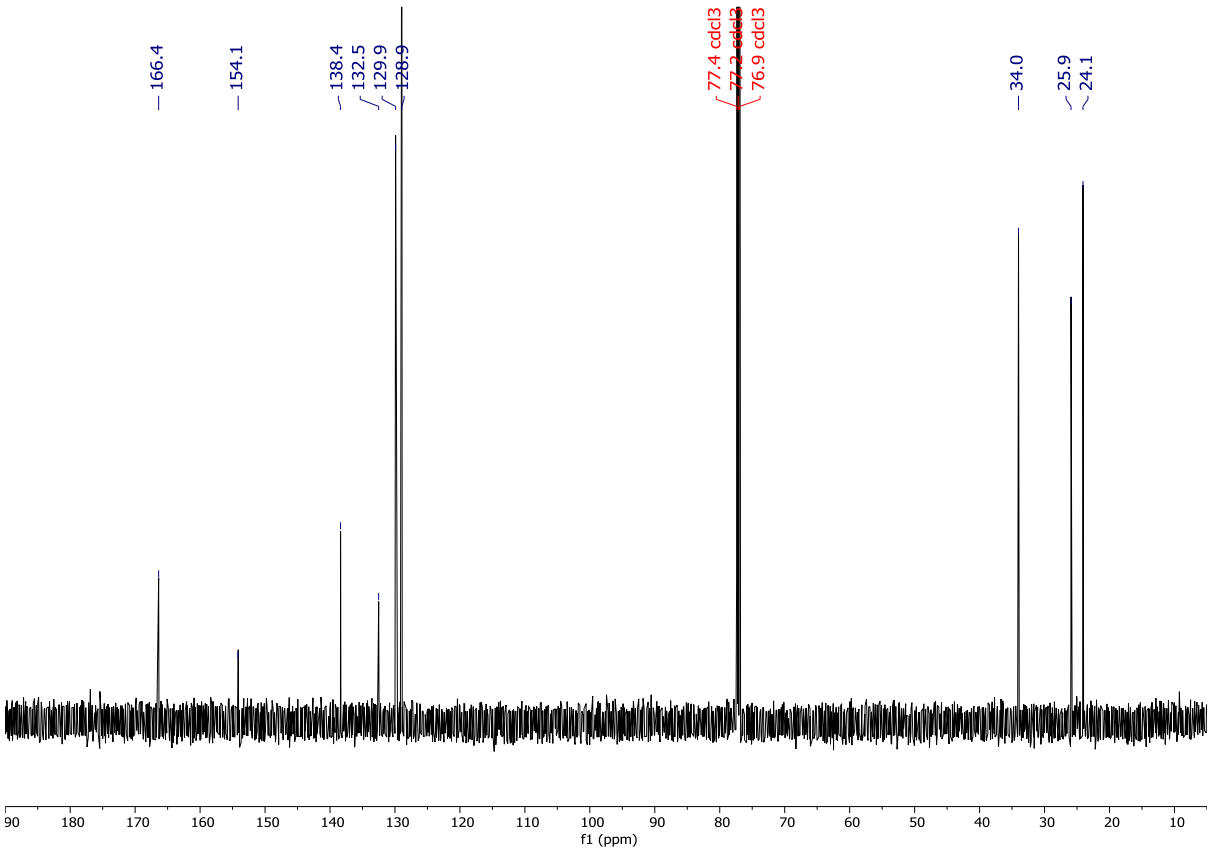
2-[1-{(1,3-Dioxoisoindolin-2-yl)methyl}cyclopentyl]-*N*-hydroxyacetamide



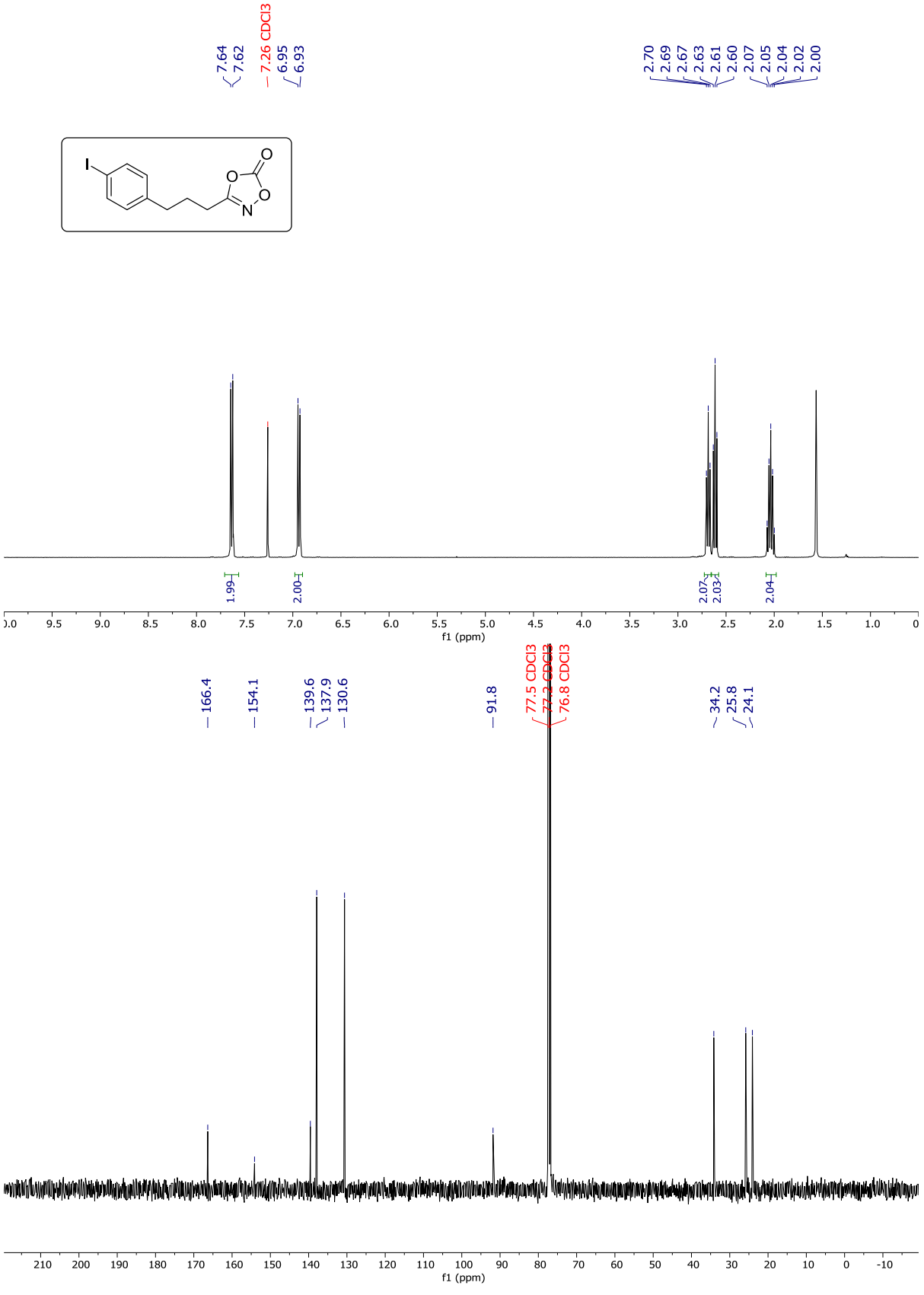


3-(3-(4-chlorophenyl)propyl)-1,4,2-dioxazol-5-one

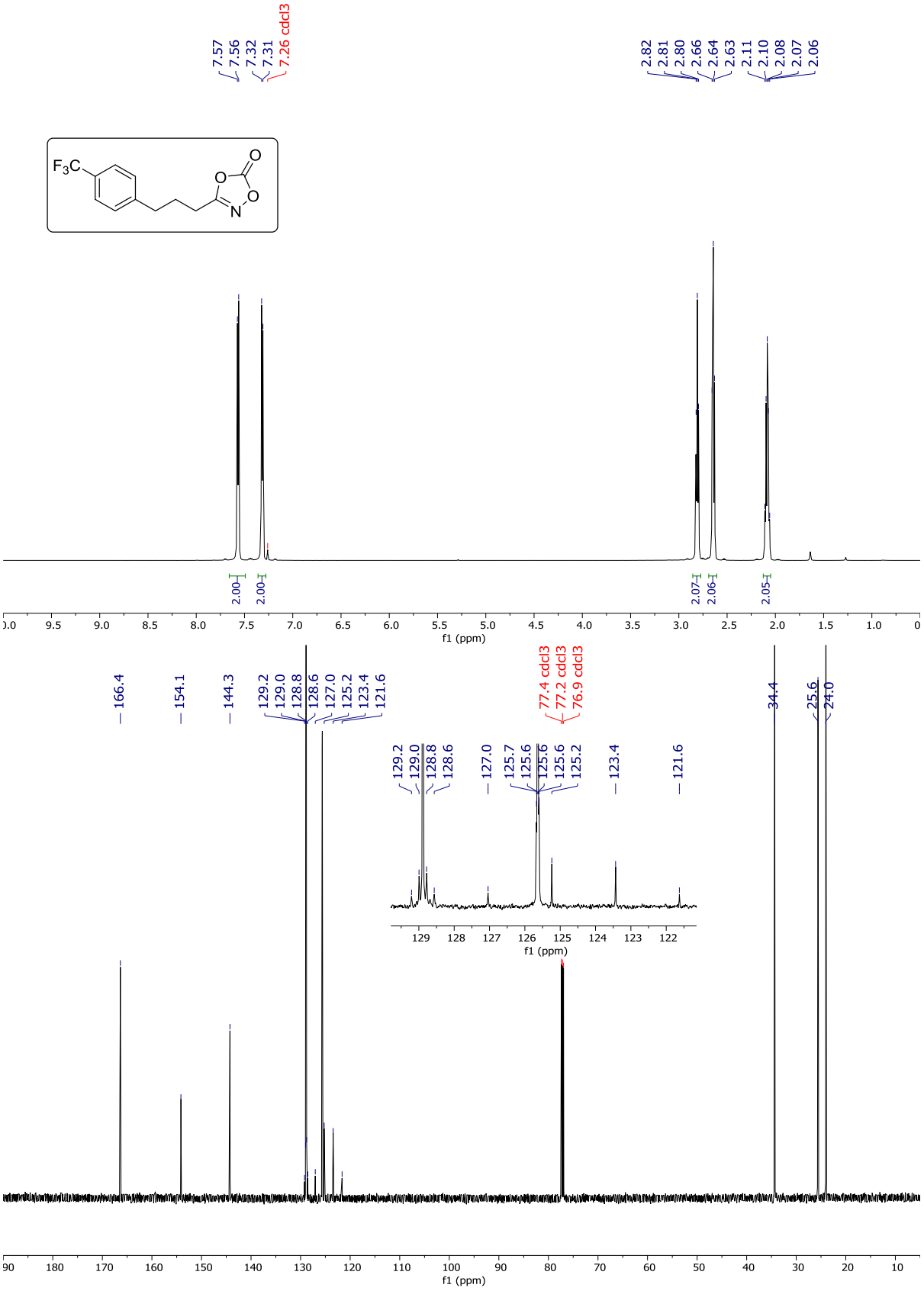


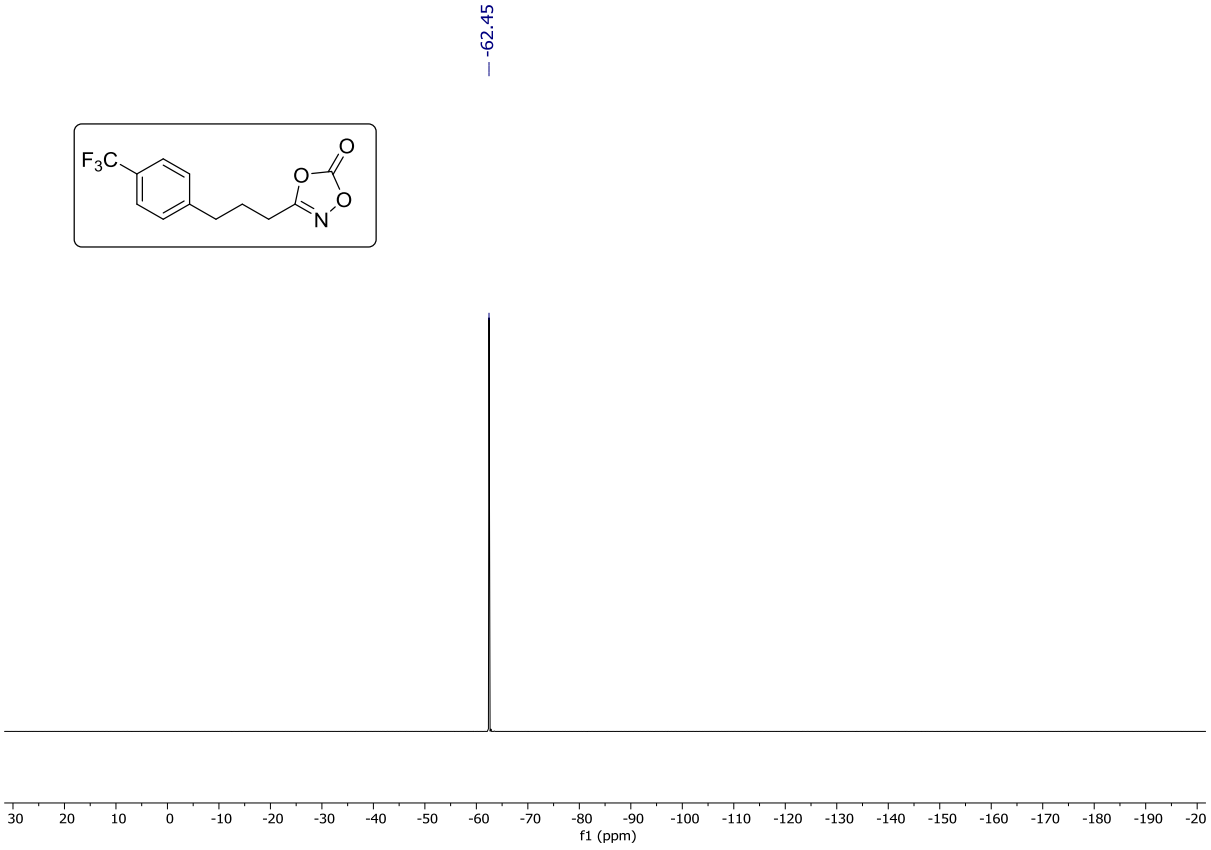


3-{3-(4-iodophenyl)propyl}-1,4,2-dioxazol-5-one

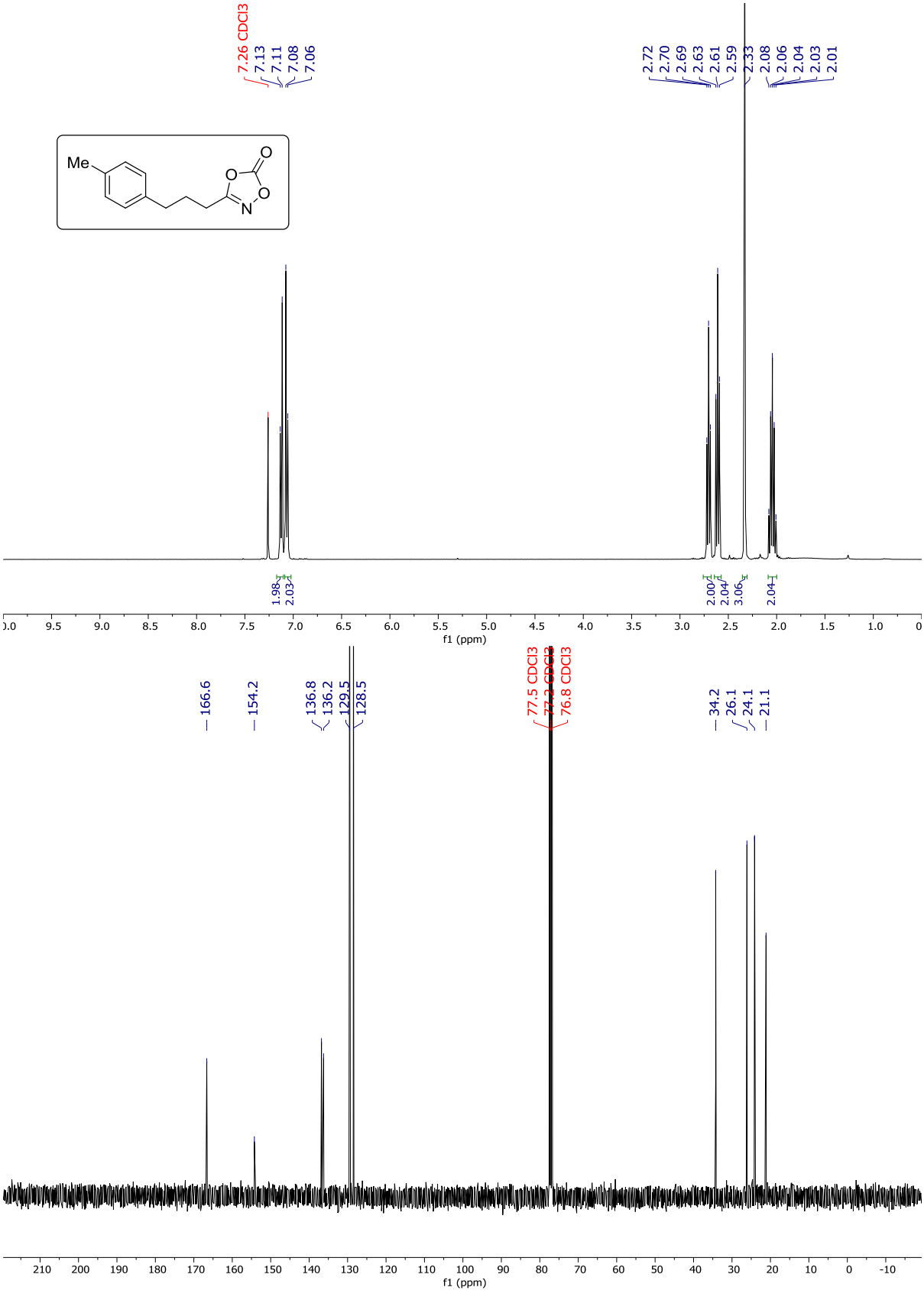


3-[3-{4-(Trifluoromethyl)phenyl}propyl]-1,4,2-dioxazol-5-one

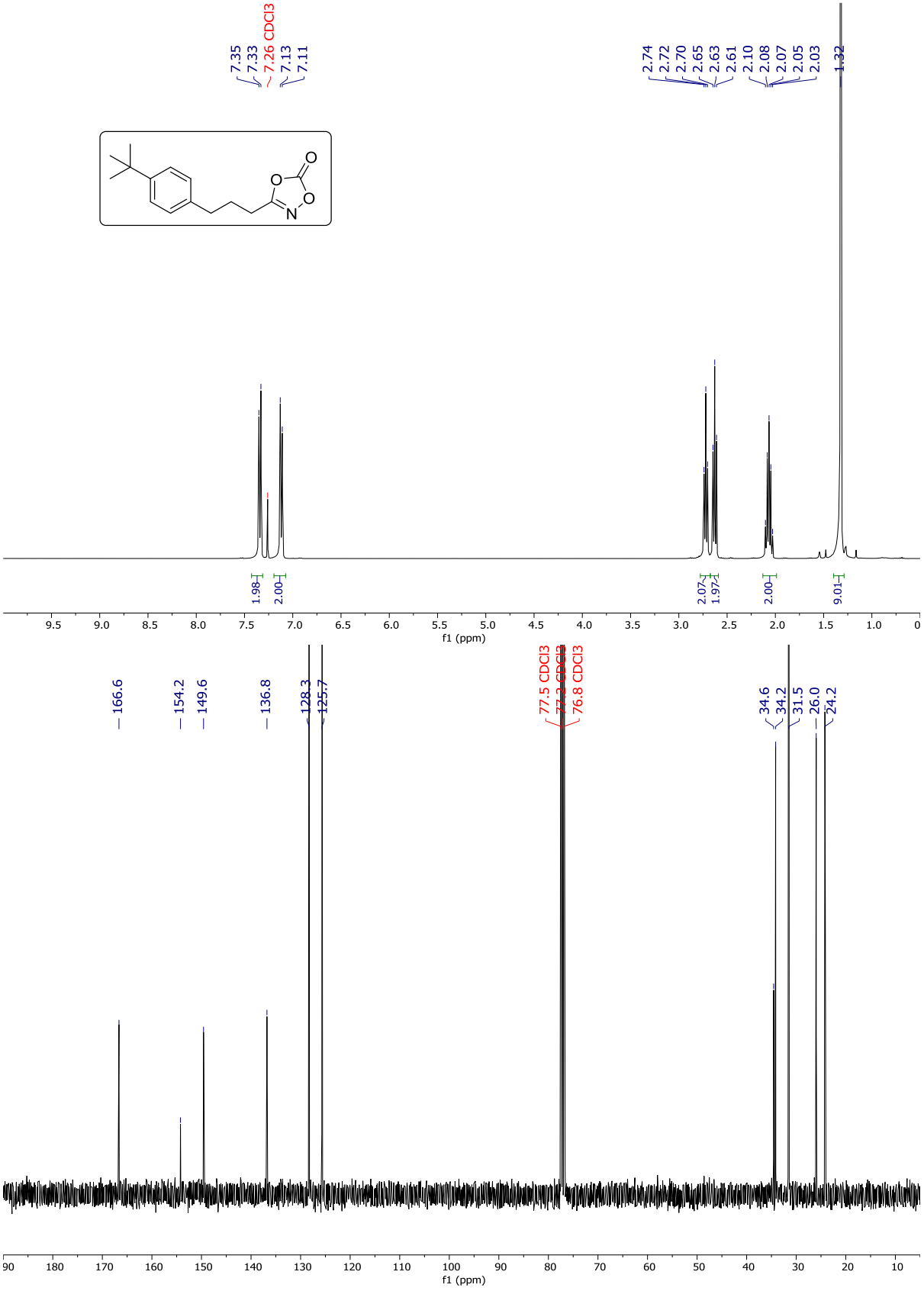



-62.45
F3C
O
O
O
N
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)

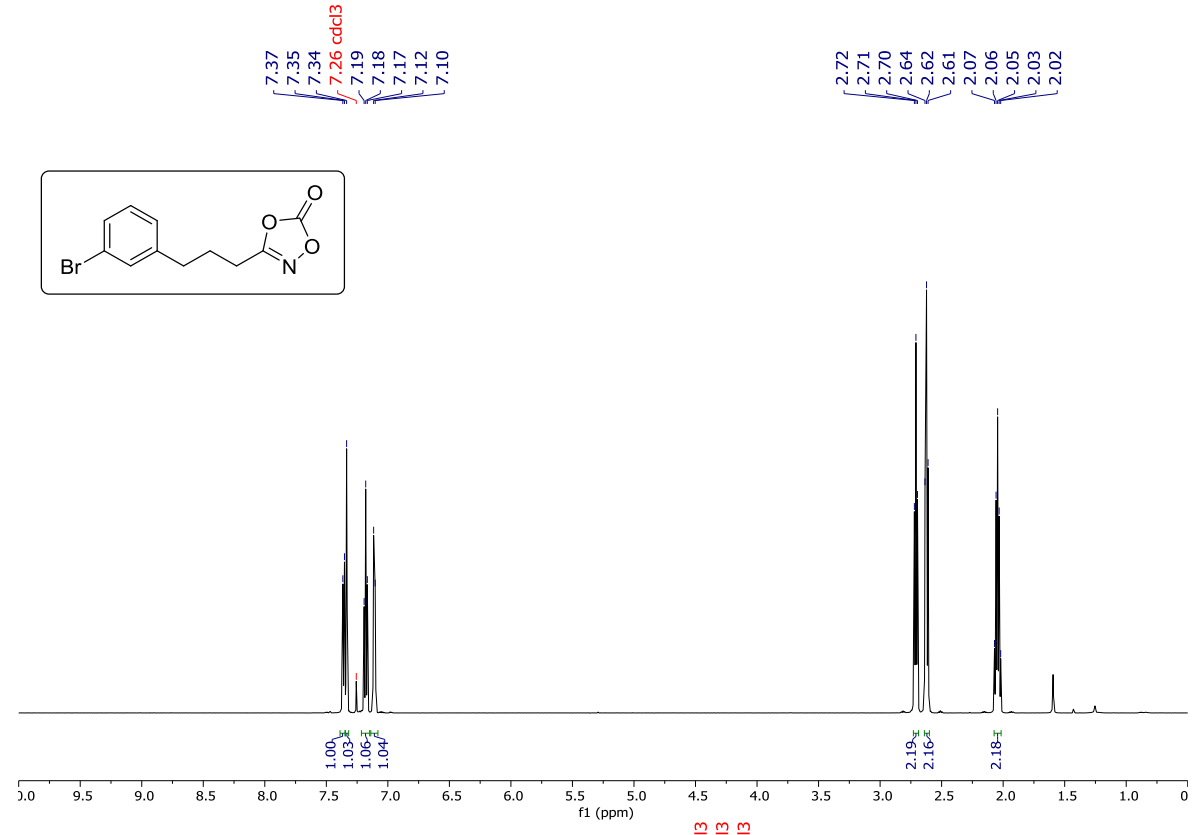
3-{3-(*p*-Tolyl)propyl}-1,4,2-dioxazol-5-one

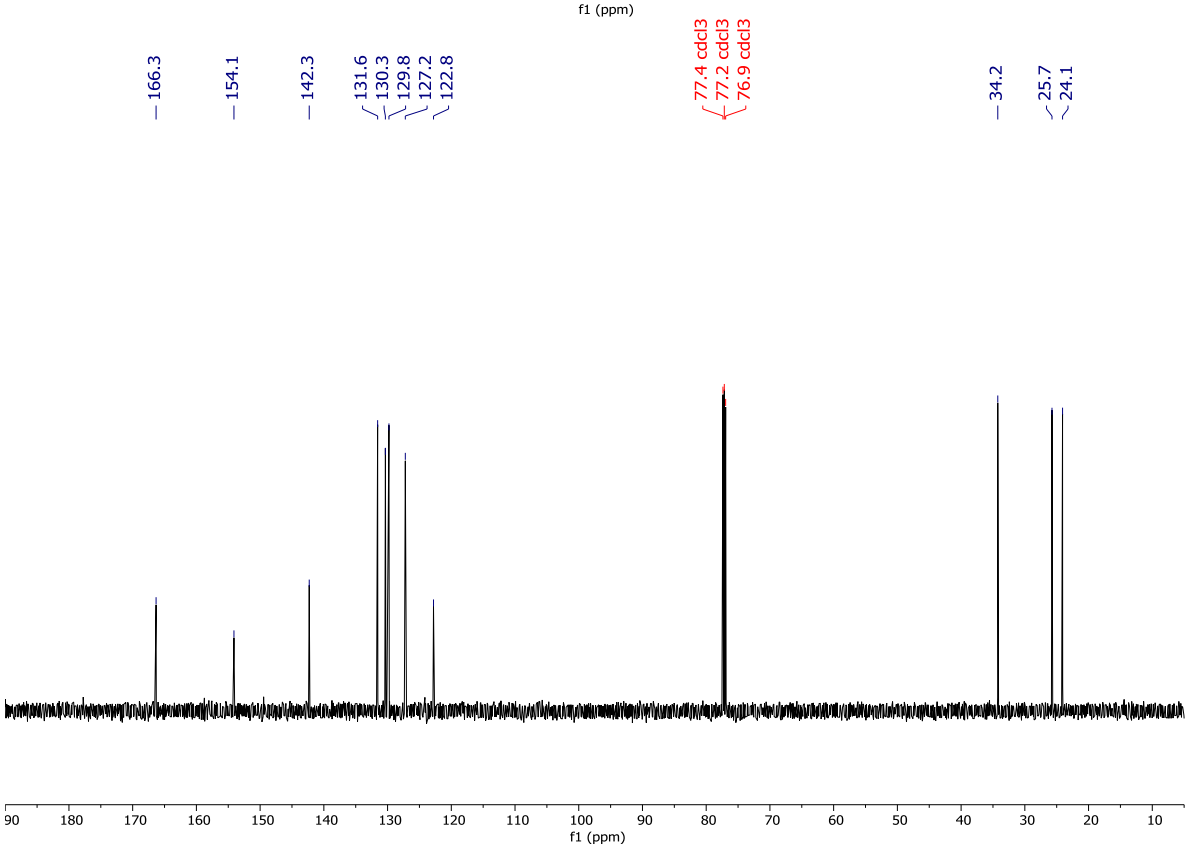


3-[3-{4-(*tert*-butyl)phenyl}propyl]-1,4,2-dioxazol-5-one

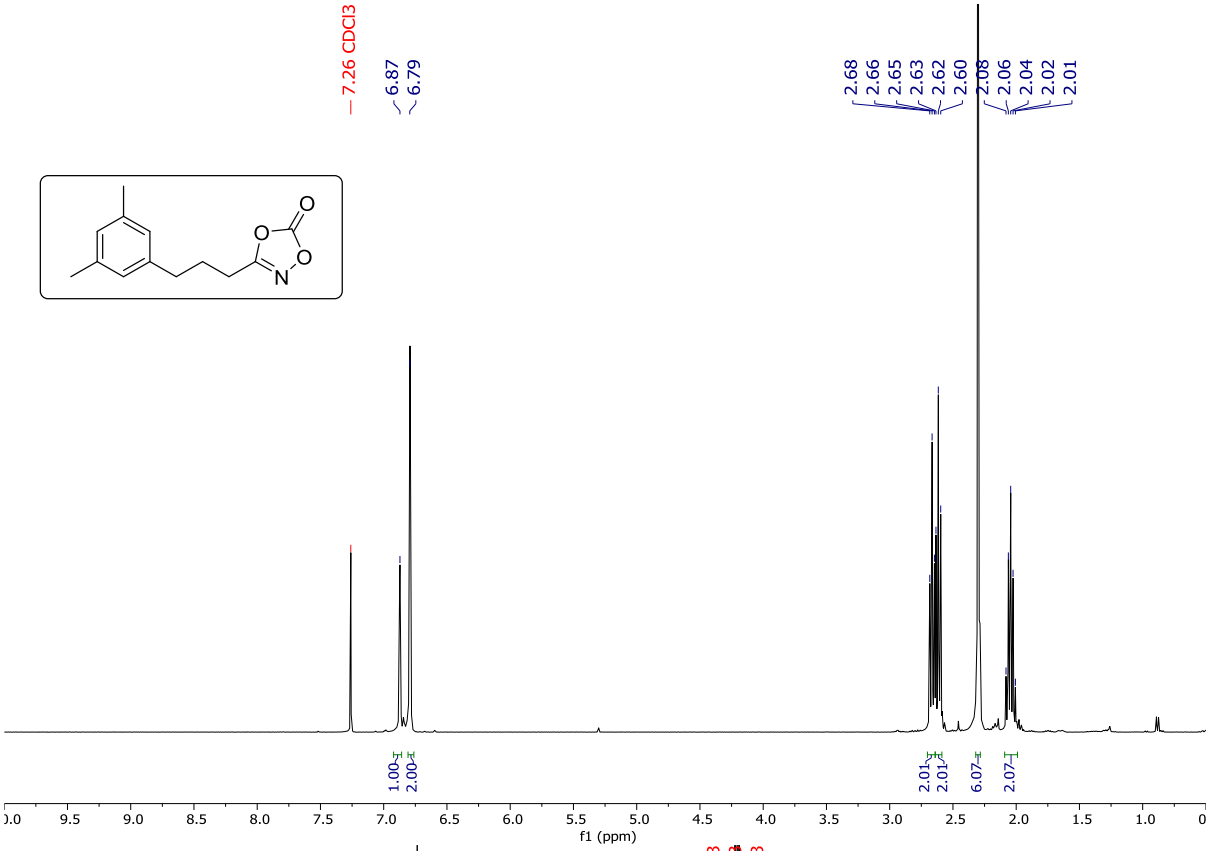


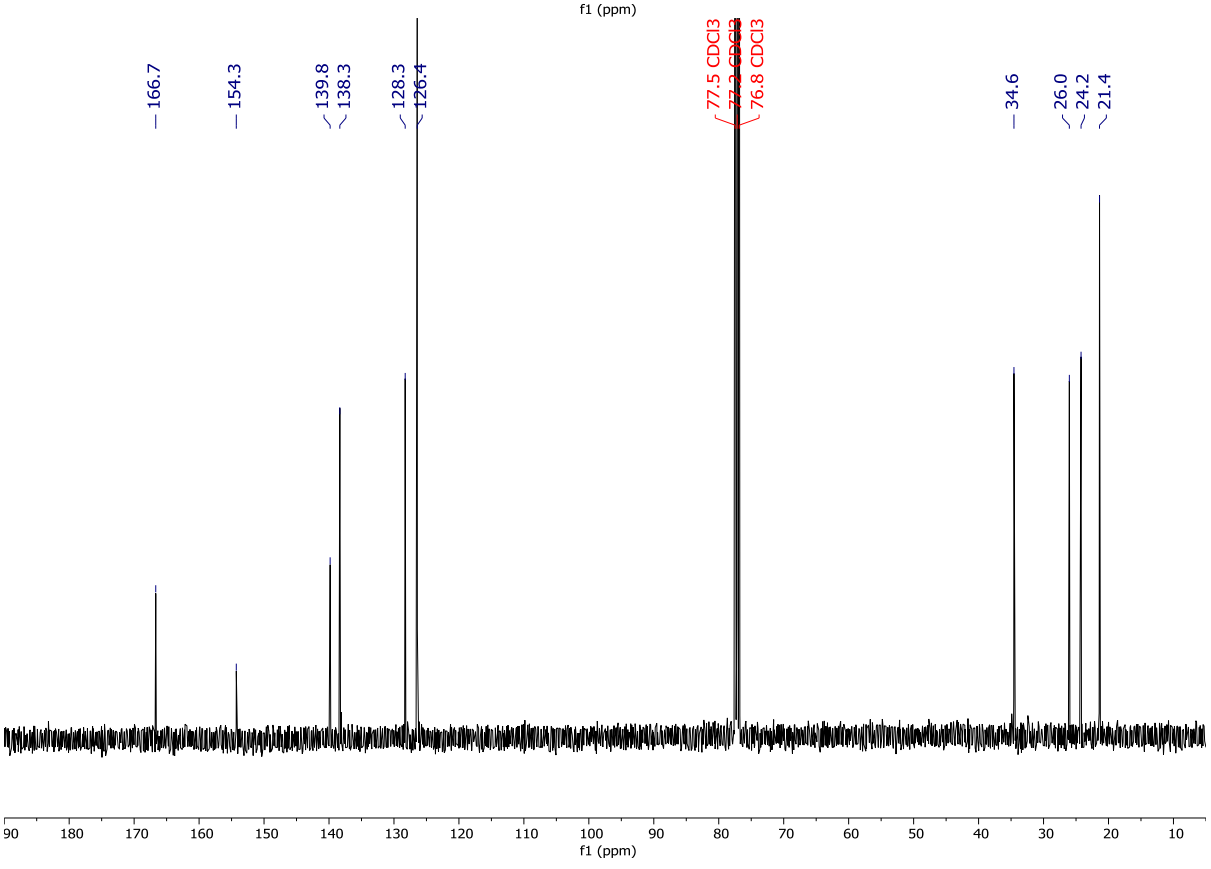
3-{3-(3-Bromophenyl)propyl}-1,4,2-dioxazol-5-one



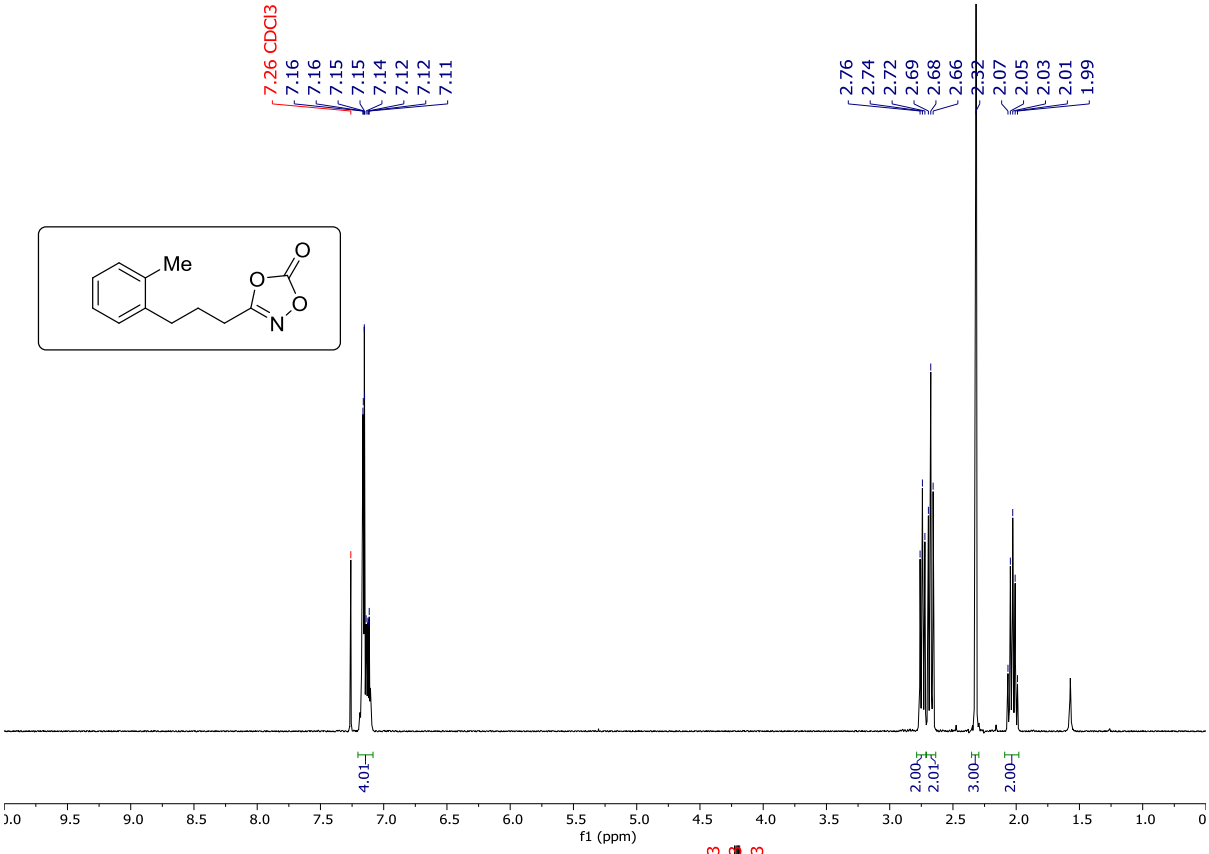


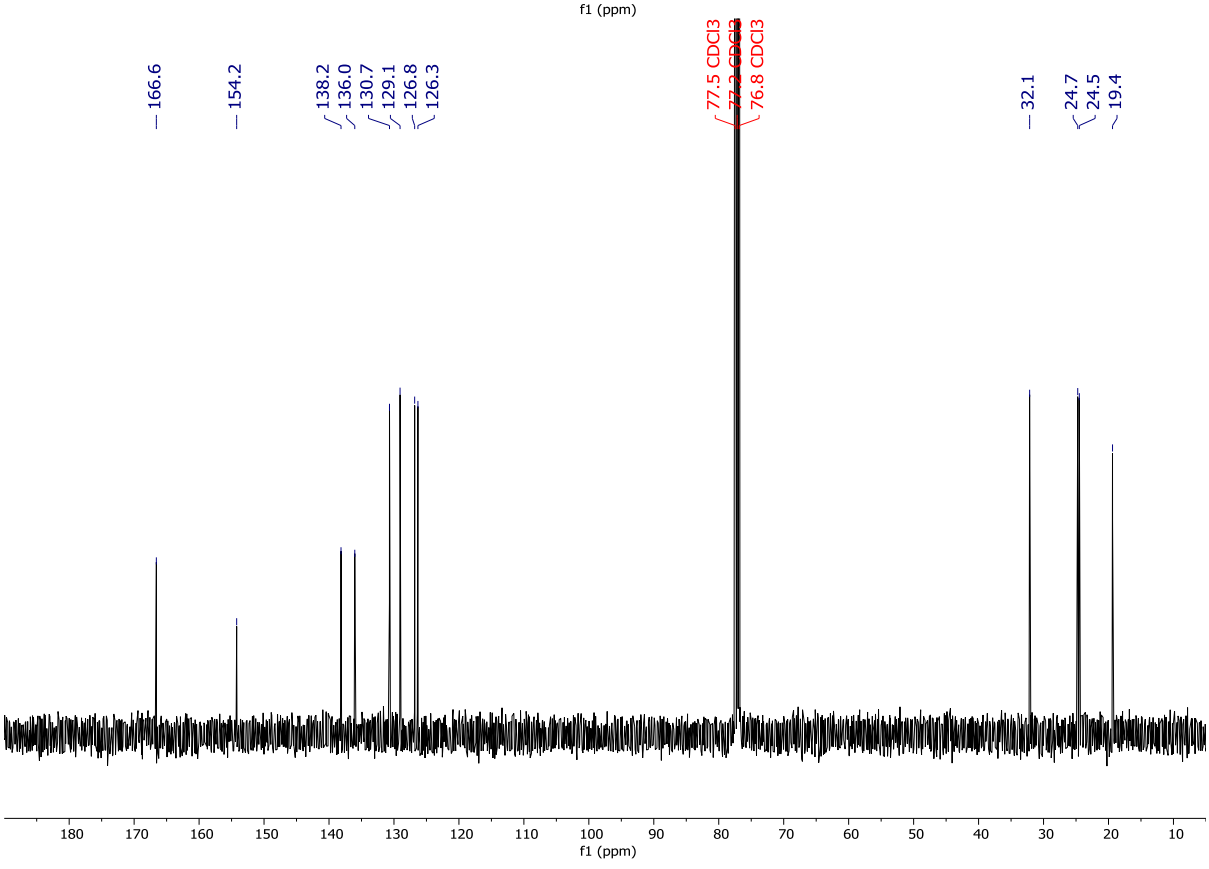
3-{3-(3,5-dimethylphenyl)propyl}-1,4,2-dioxazol-5-one



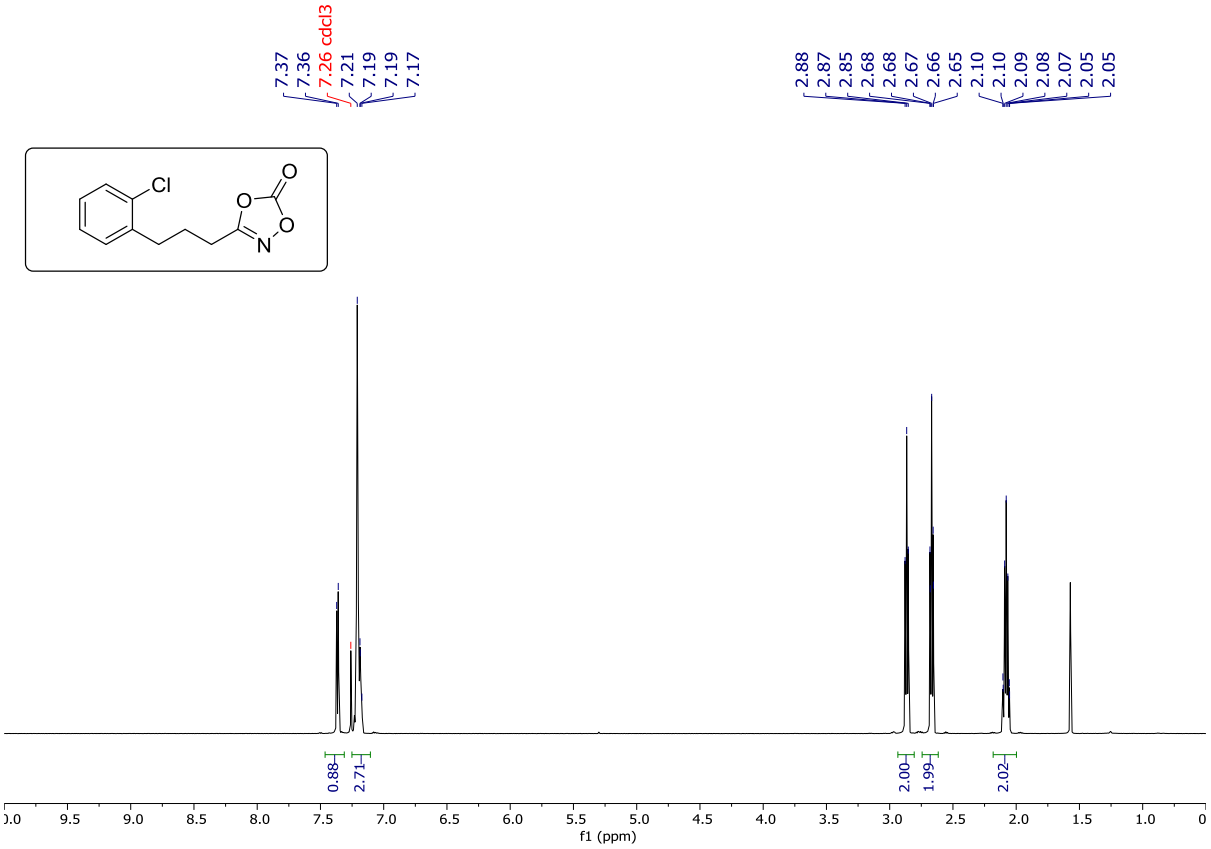


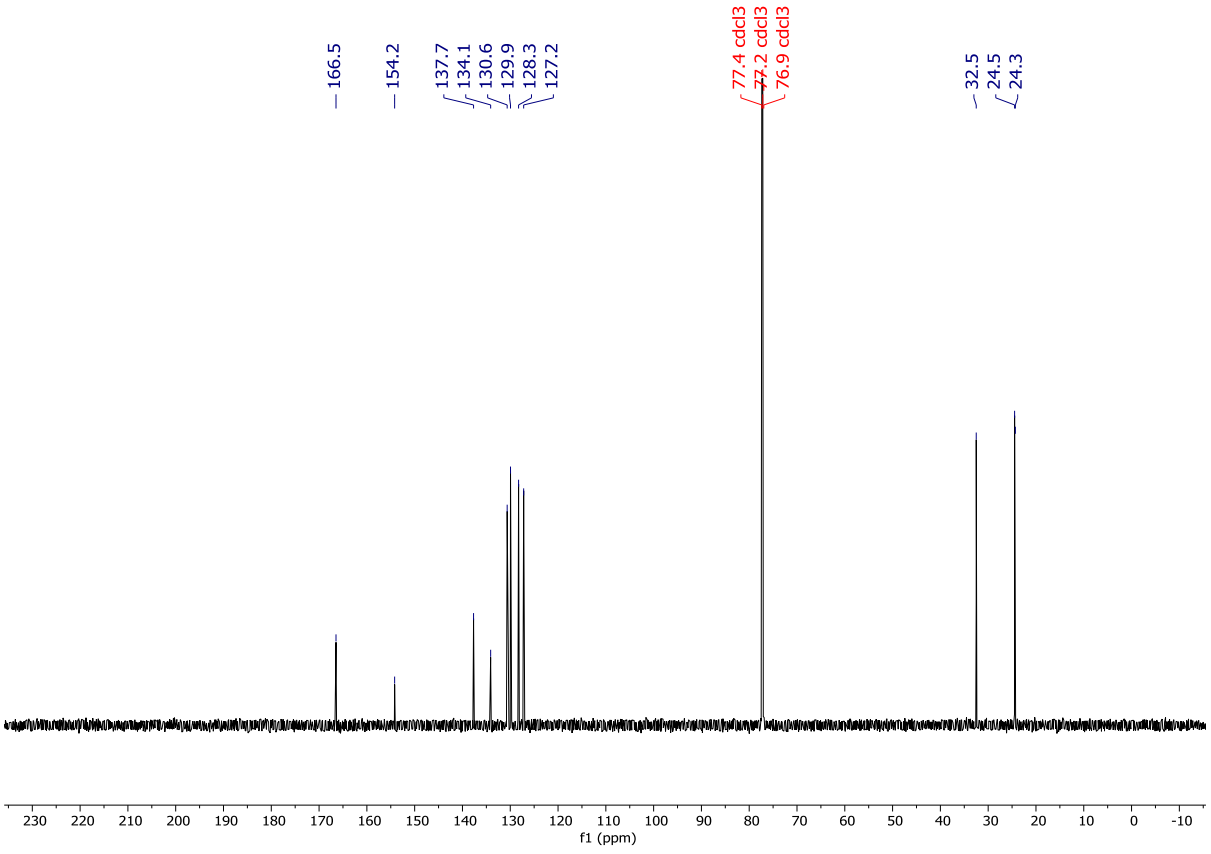
3-{3-(*o*-Tolyl)propyl}-1,4,2-dioxazol-5-one



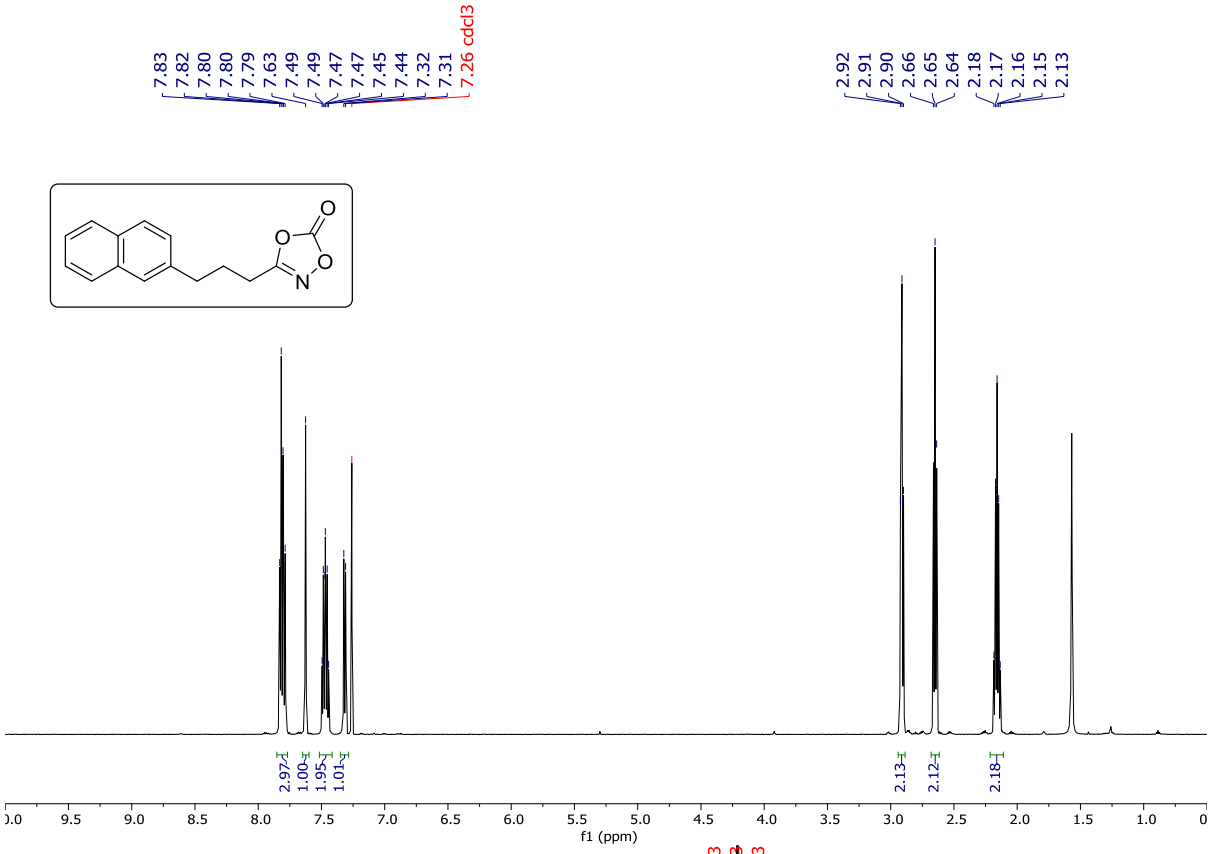


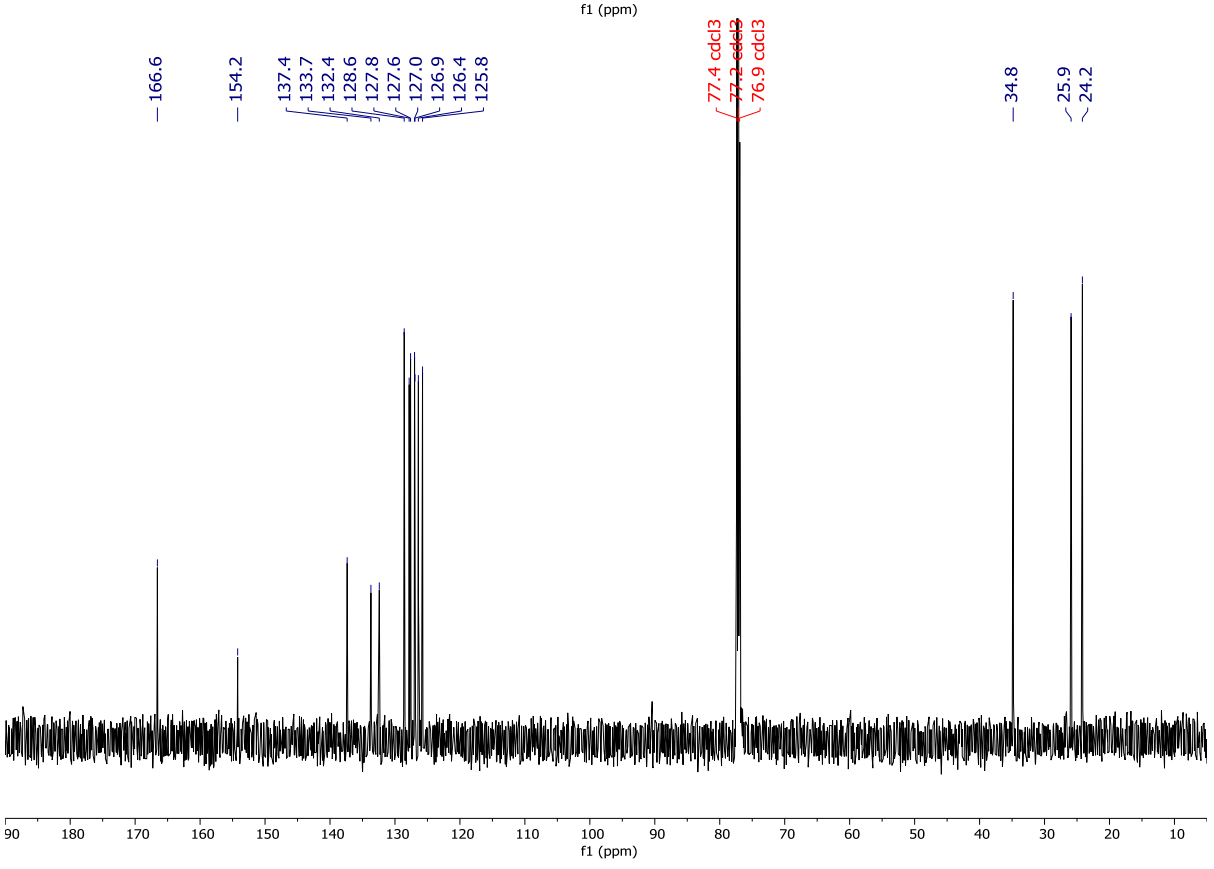
3-{3-(2-Chlorophenyl)propyl}-1,4,2-dioxazol-5-one



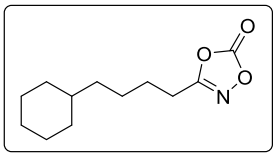


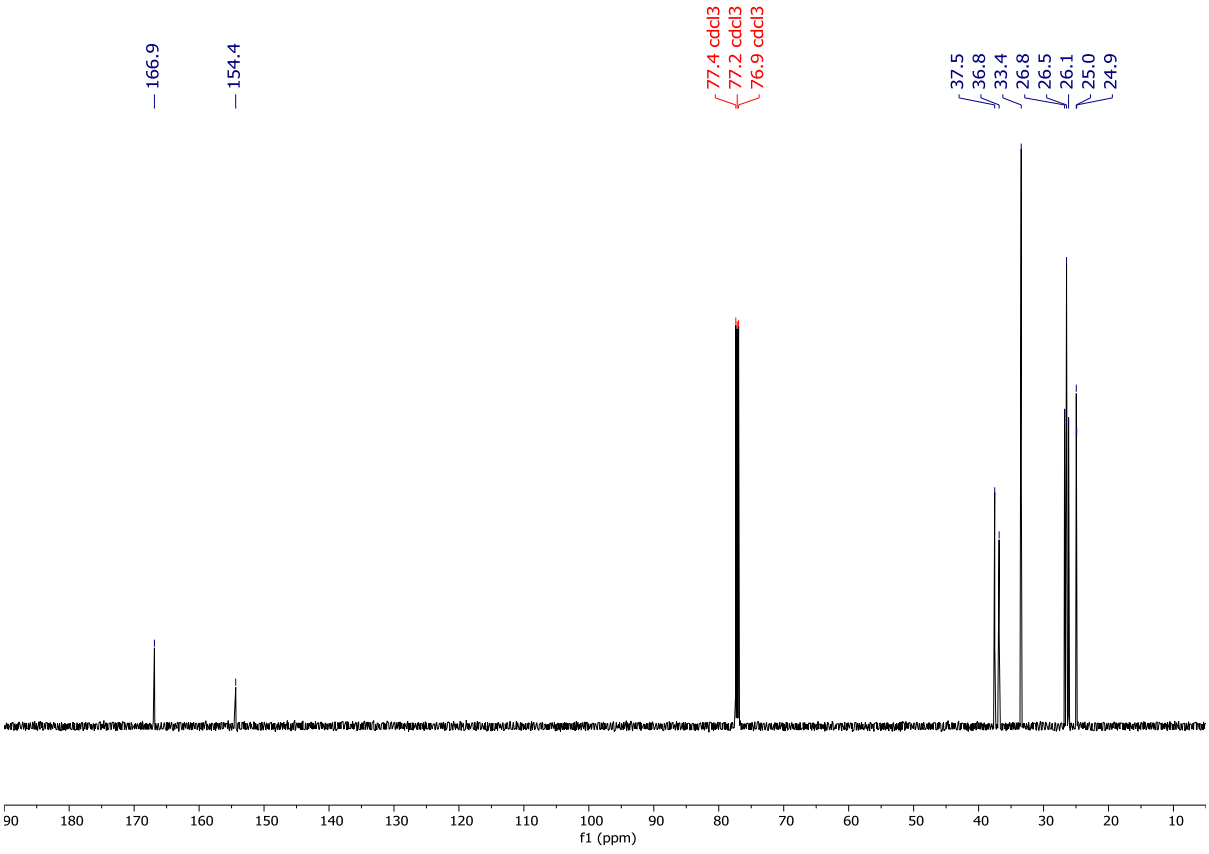
3-{3-(Naphthalen-2-yl)propyl}-1,4,2-dioxazol-5-one



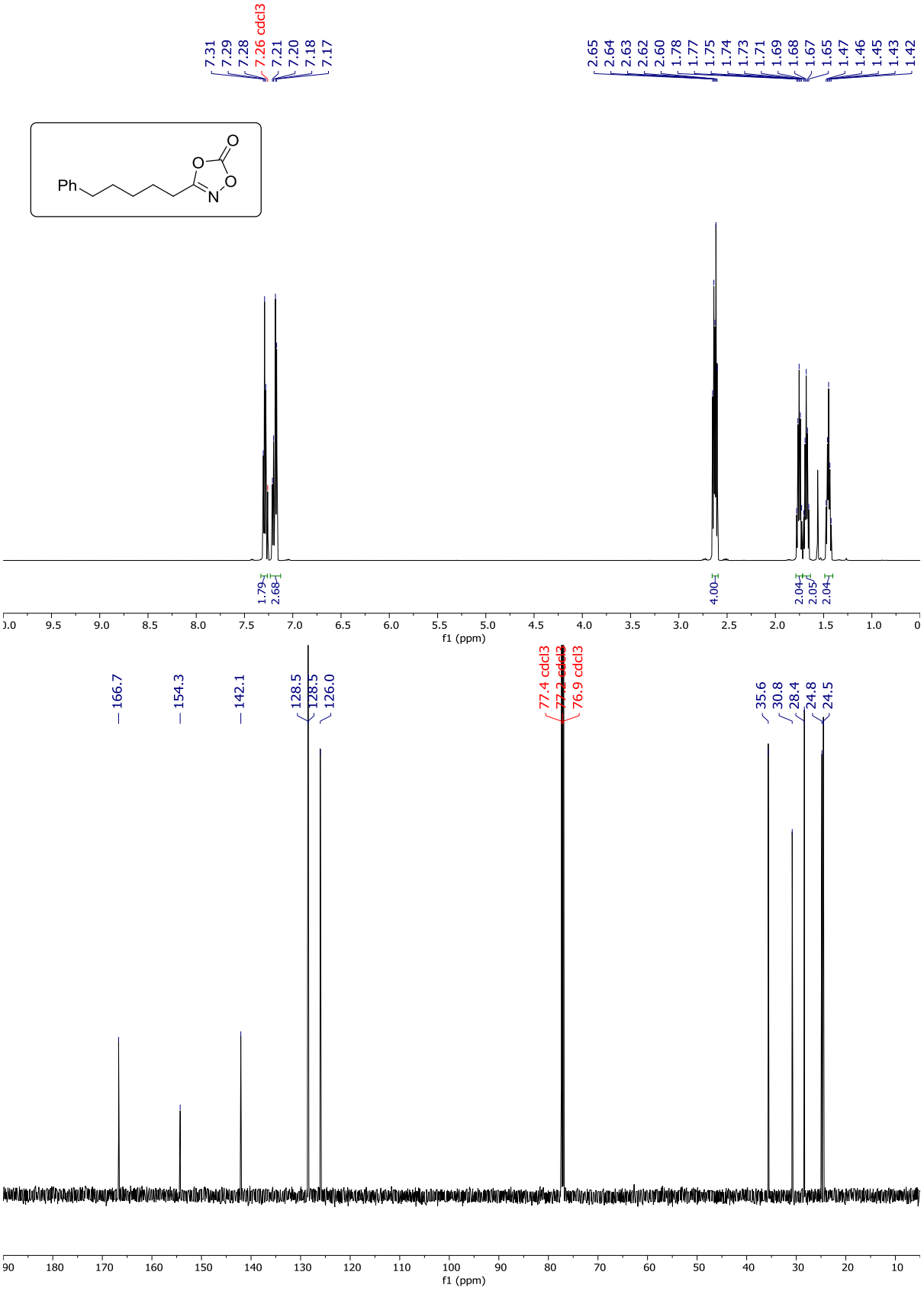


3-(4-Cyclohexylbutyl)-1,4,2-dioxazol-5-one

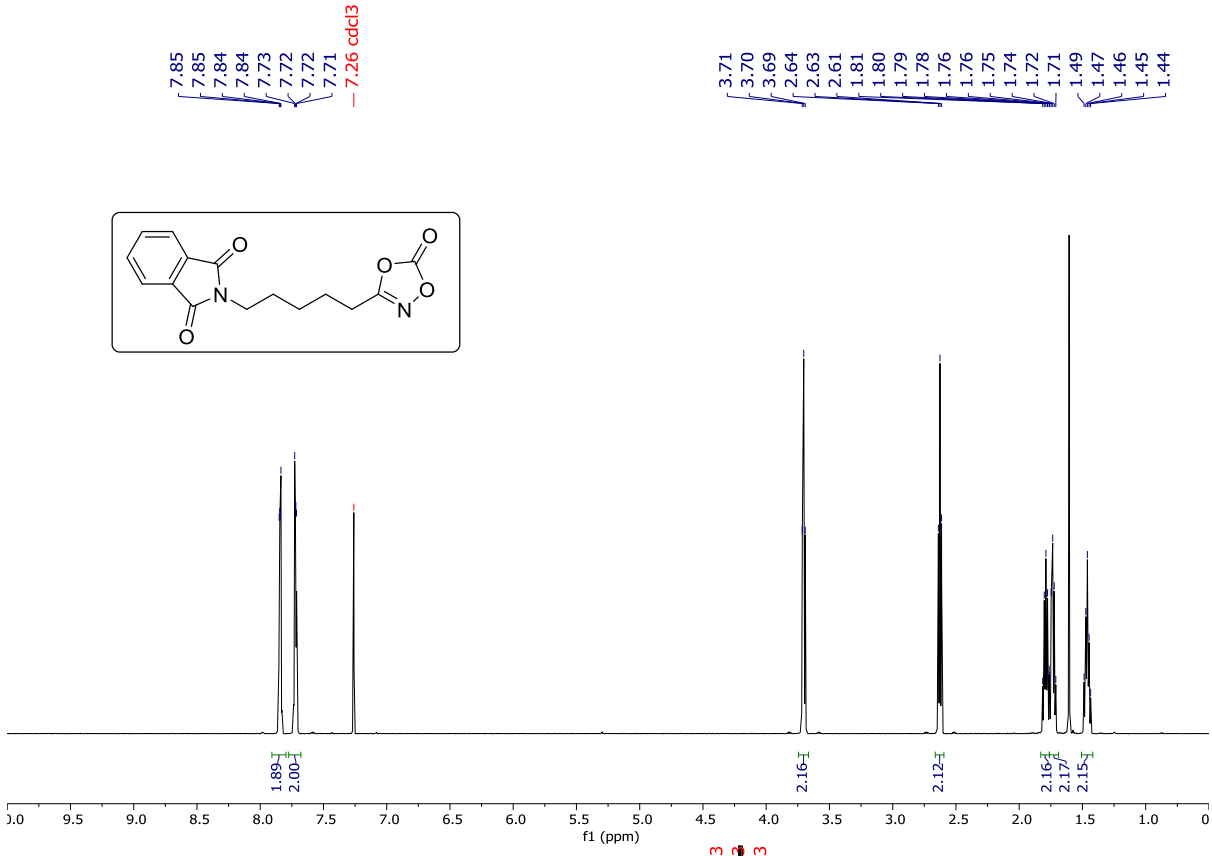


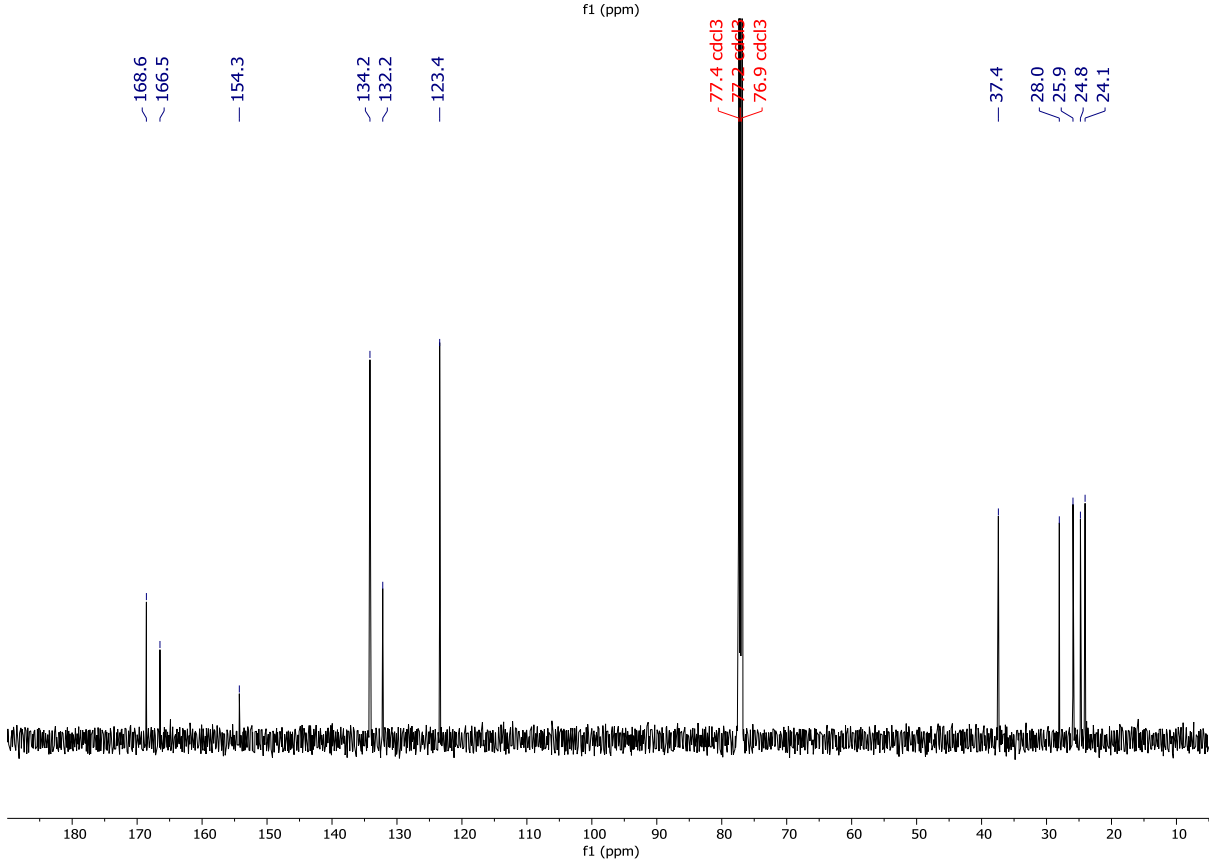


3-(5-Phenylpentyl)-1,4,2-dioxazol-5-one

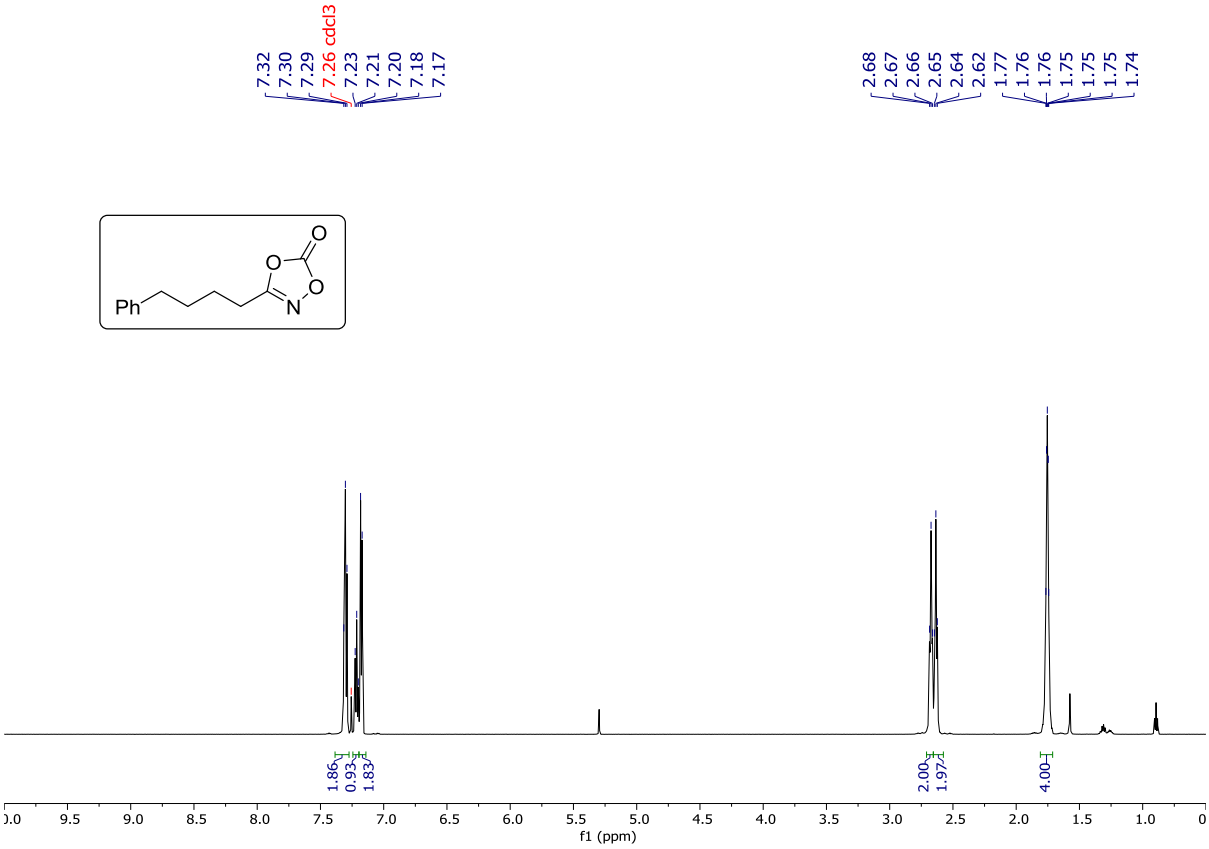


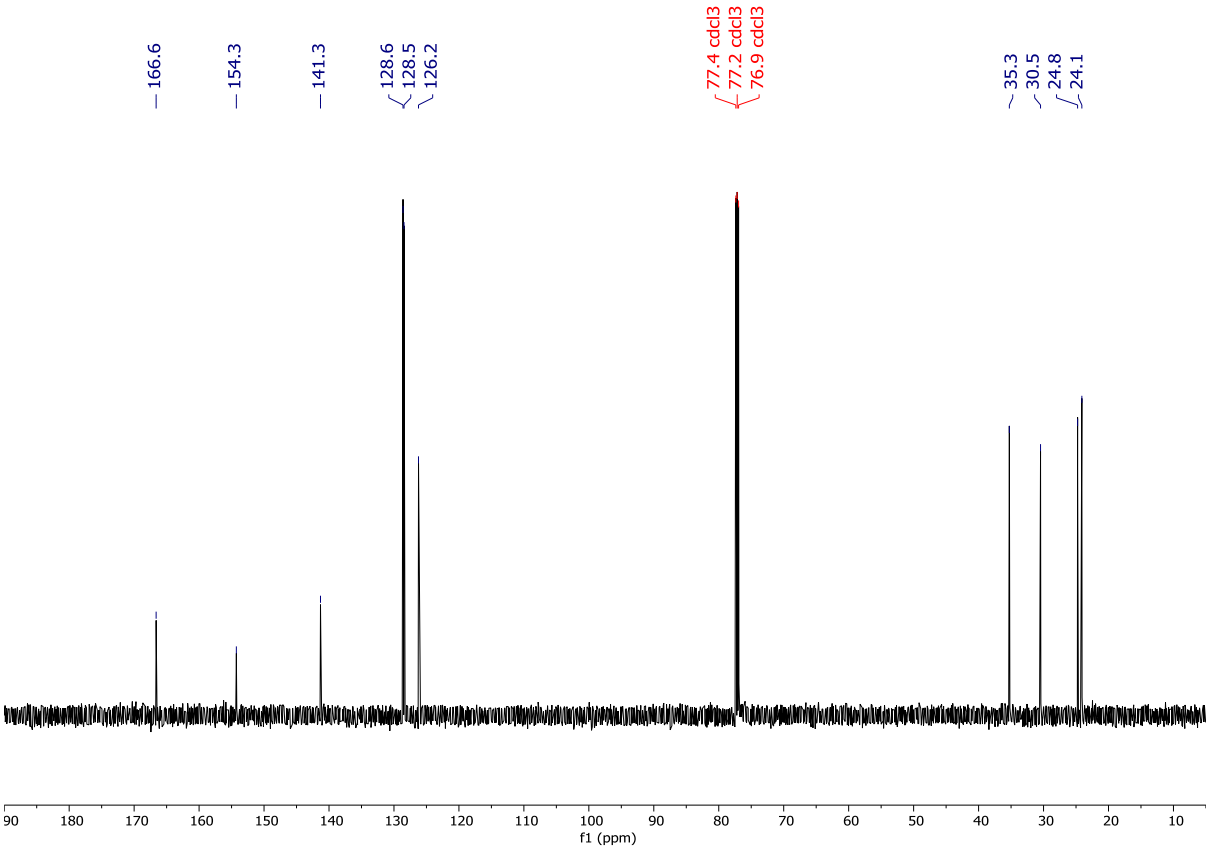
2-{5-(5-Oxo-1,4,2-dioxazol-3-yl)pentyl}isoindoline-1,3-dione



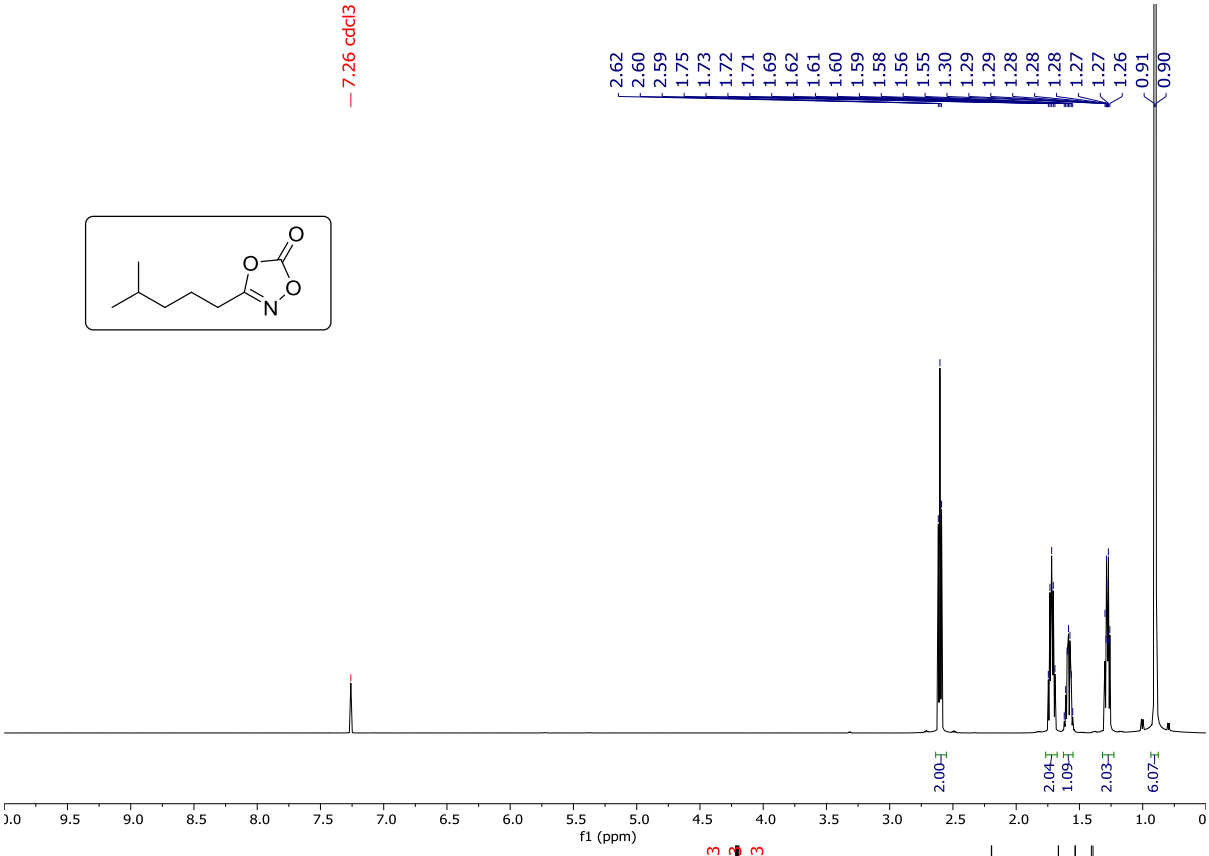


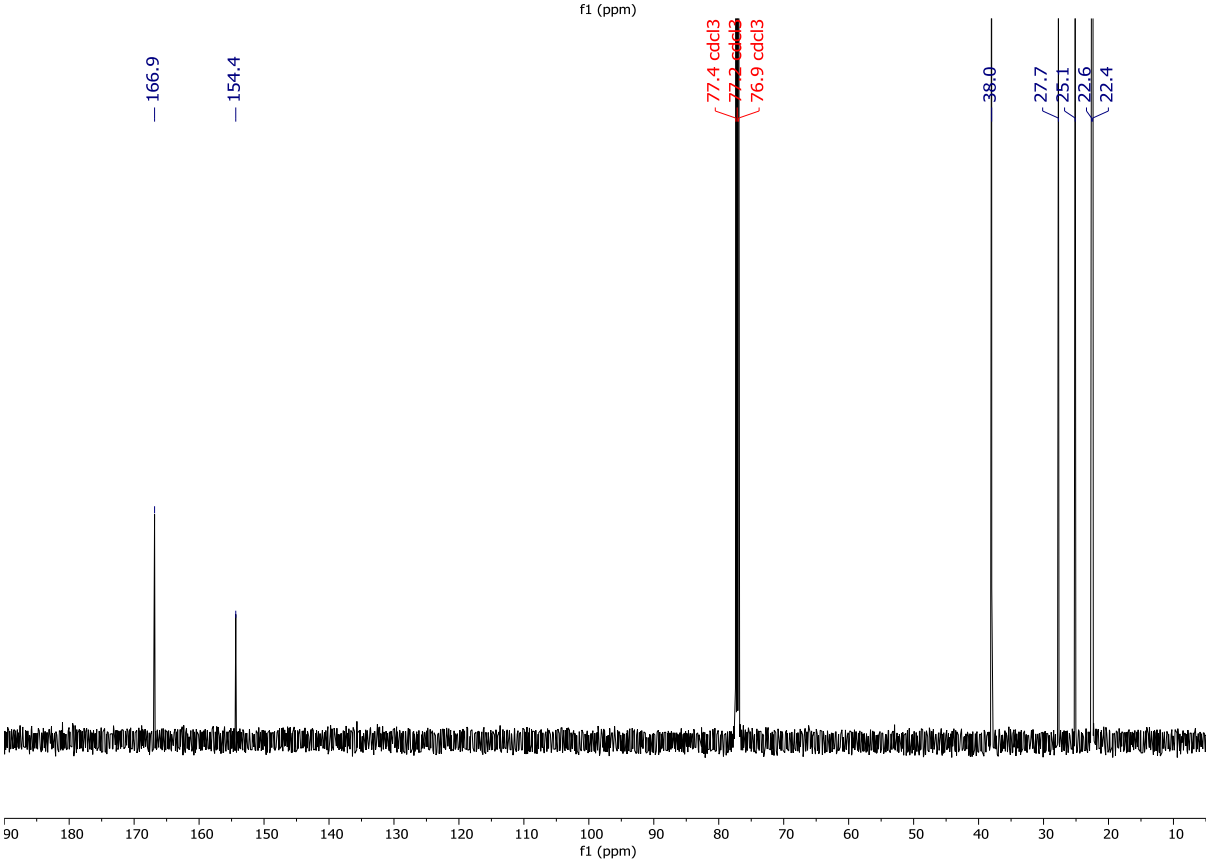
3-(4-Phenylbutyl)-1,4,2-dioxazol-5-one



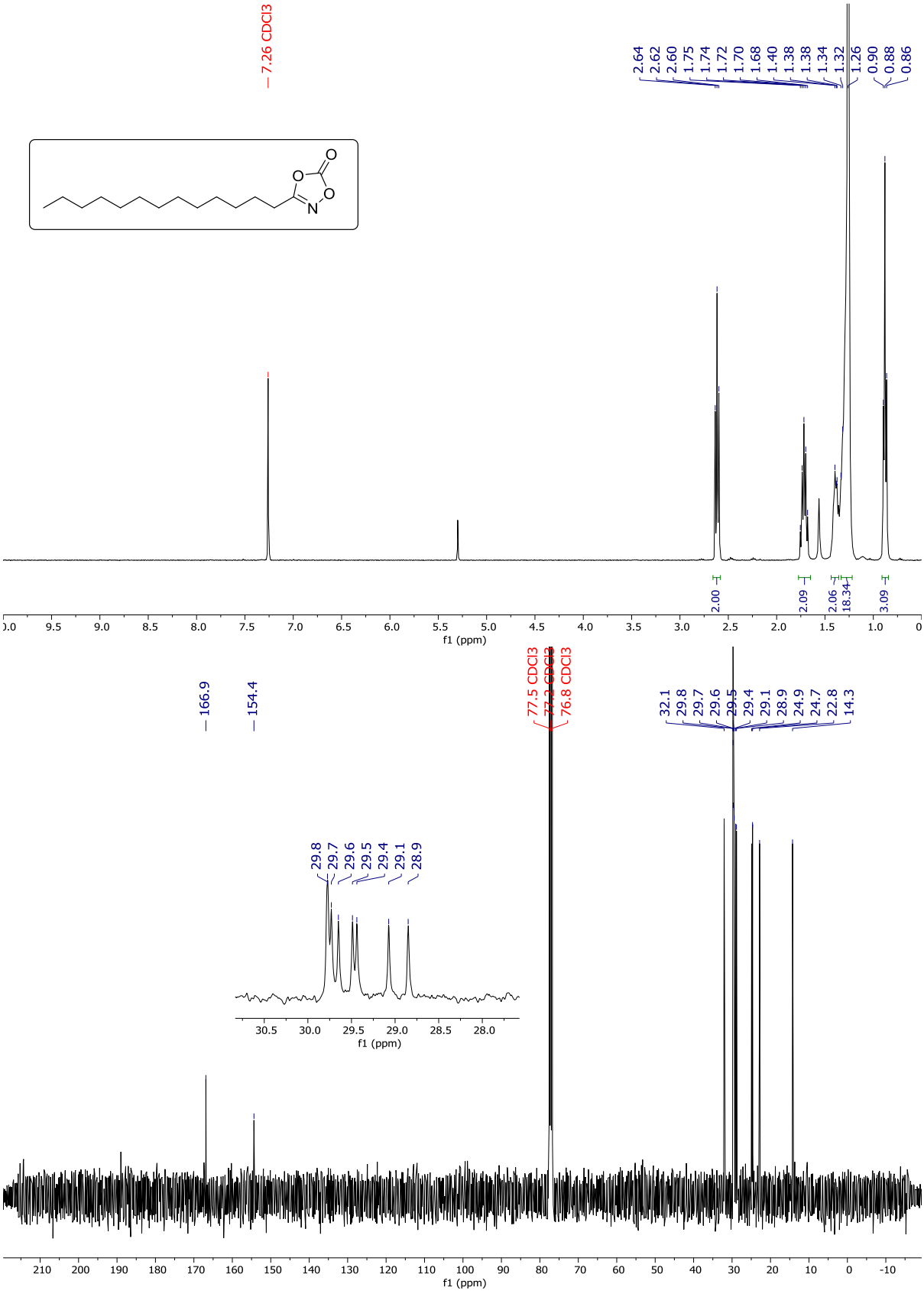


3-(4-Methylpentyl)-1,4,2-dioxazol-5-one

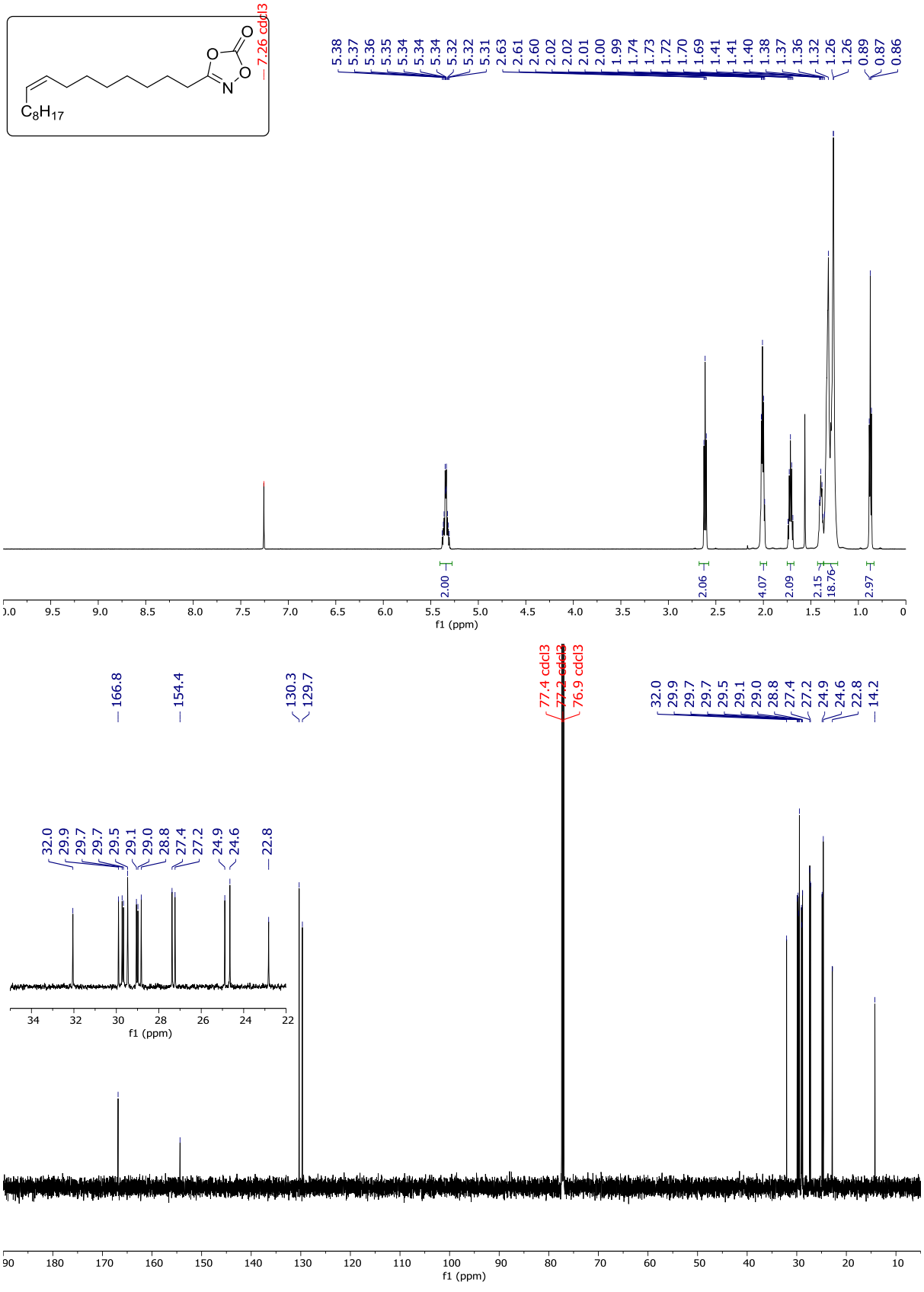




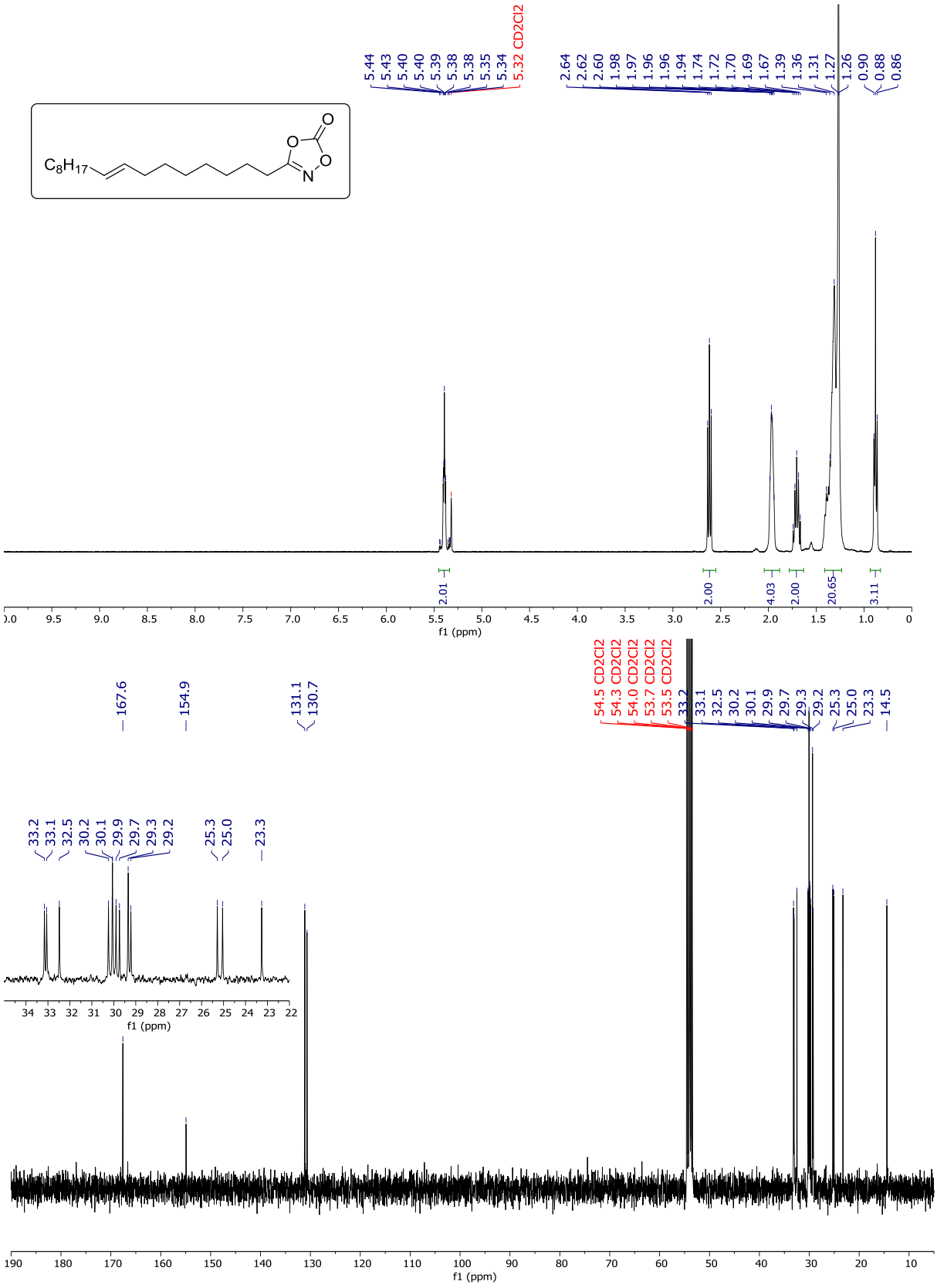
3-Tridecyl-1,4,2-dioxazol-5-one



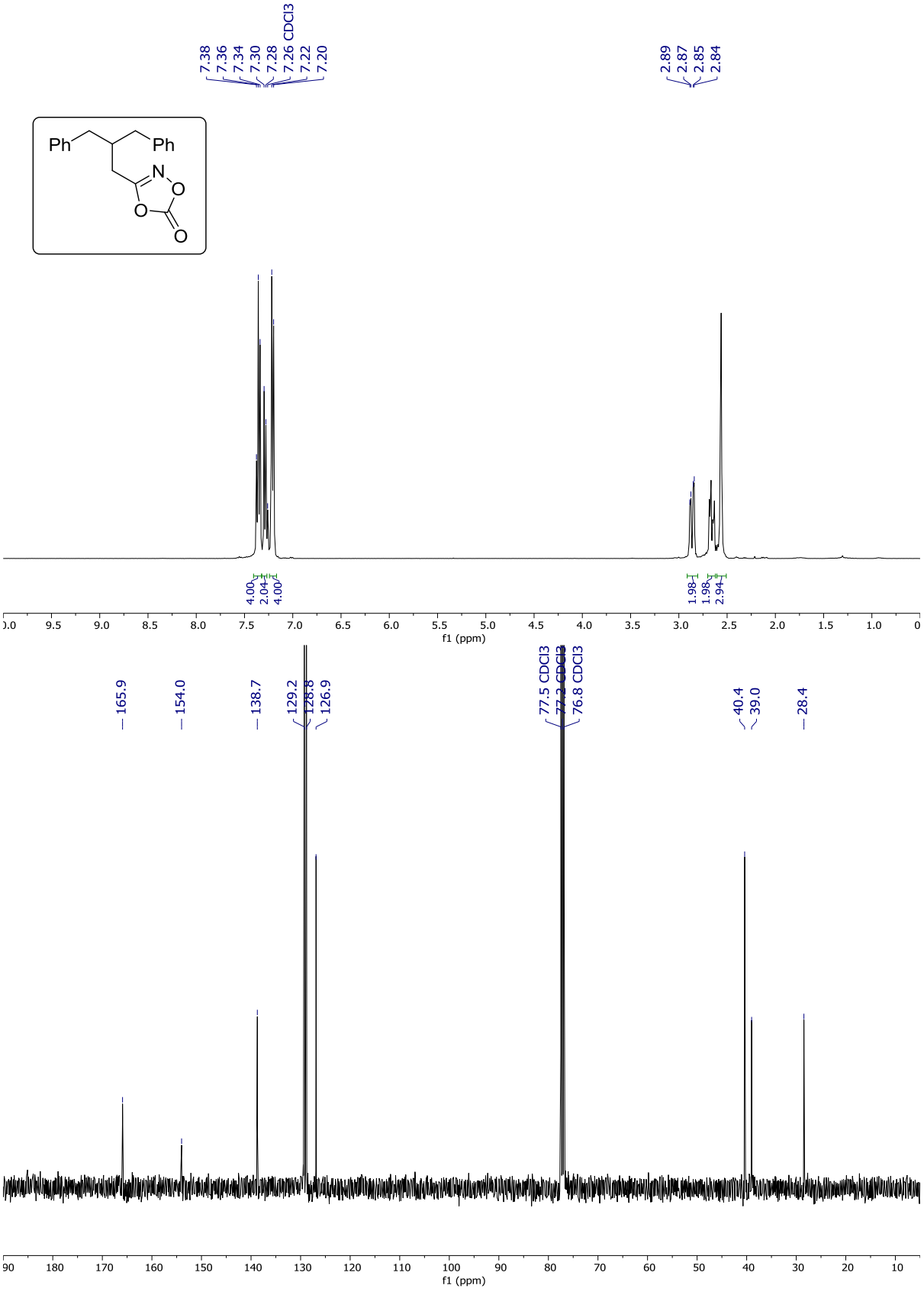
(*Z*)-3-(Heptadec-8-en-1-yl)-1,4,2-dioxazol-5-one



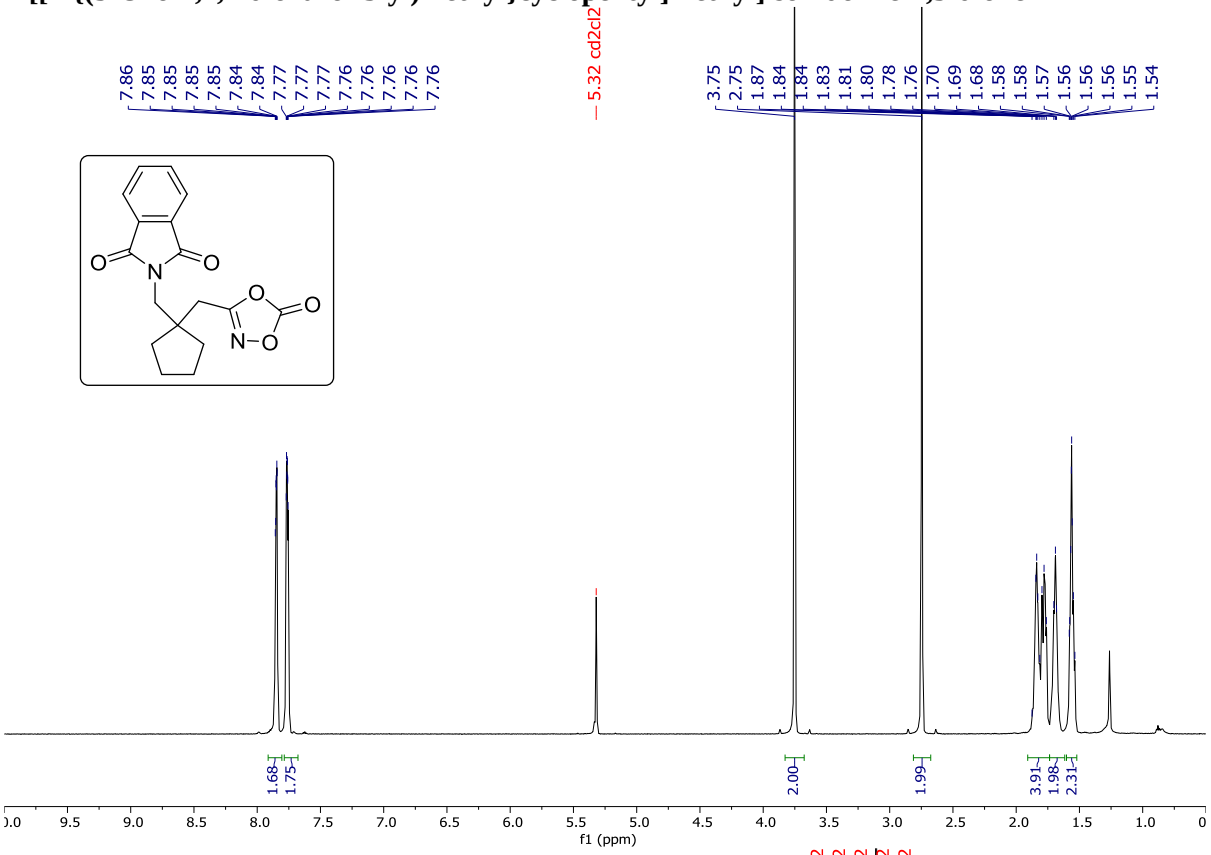
(*E*)-3-(Heptadec-8-en-1-yl)-1,4,2-dioxazol-5-one

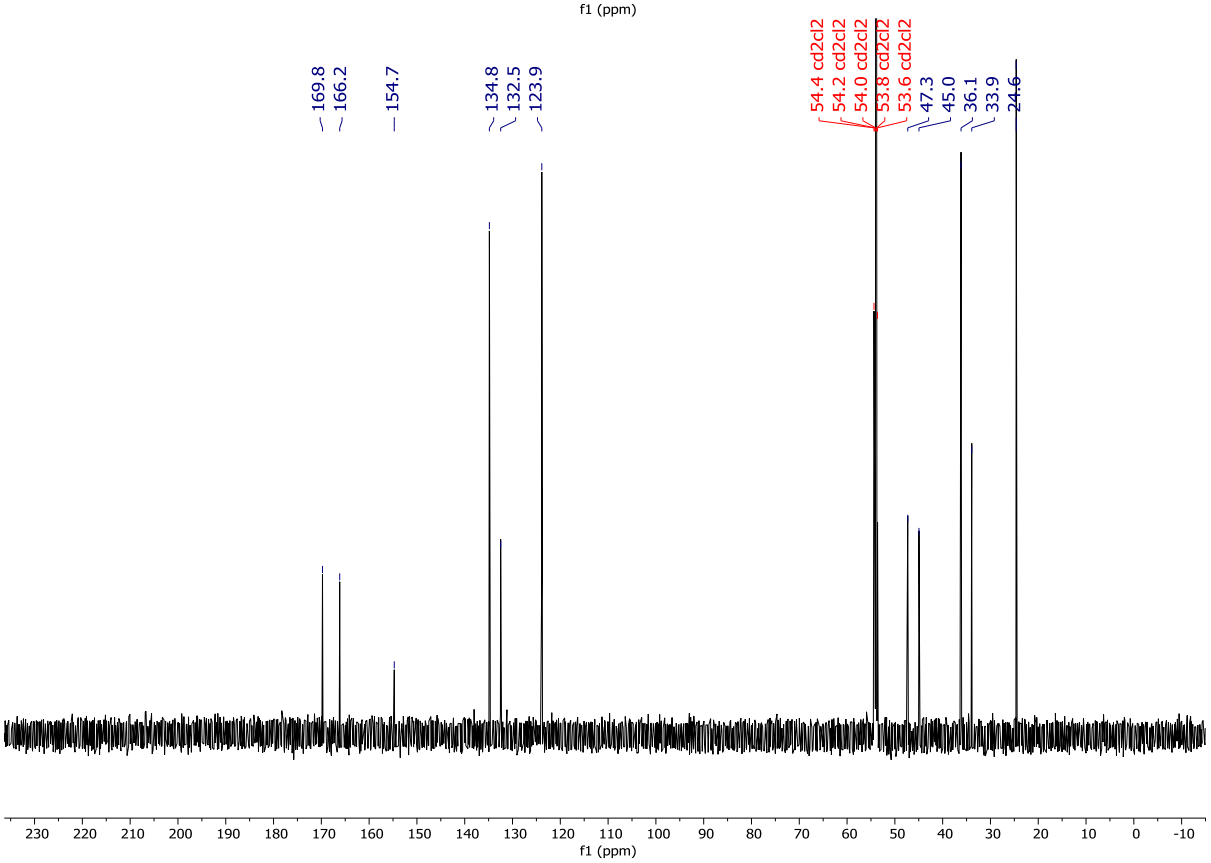


3-(2-Benzyl-3-phenylpropyl)-1,4,2-dioxazol-5-one

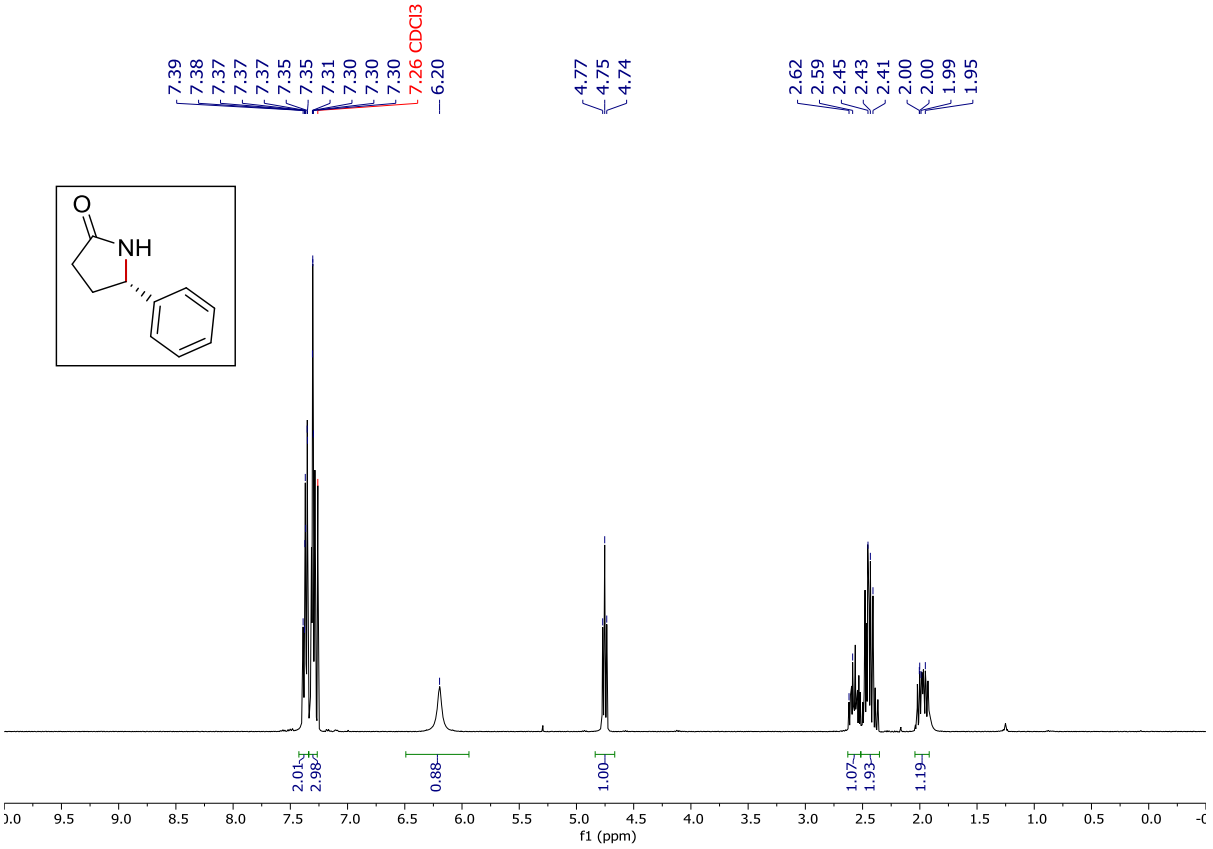


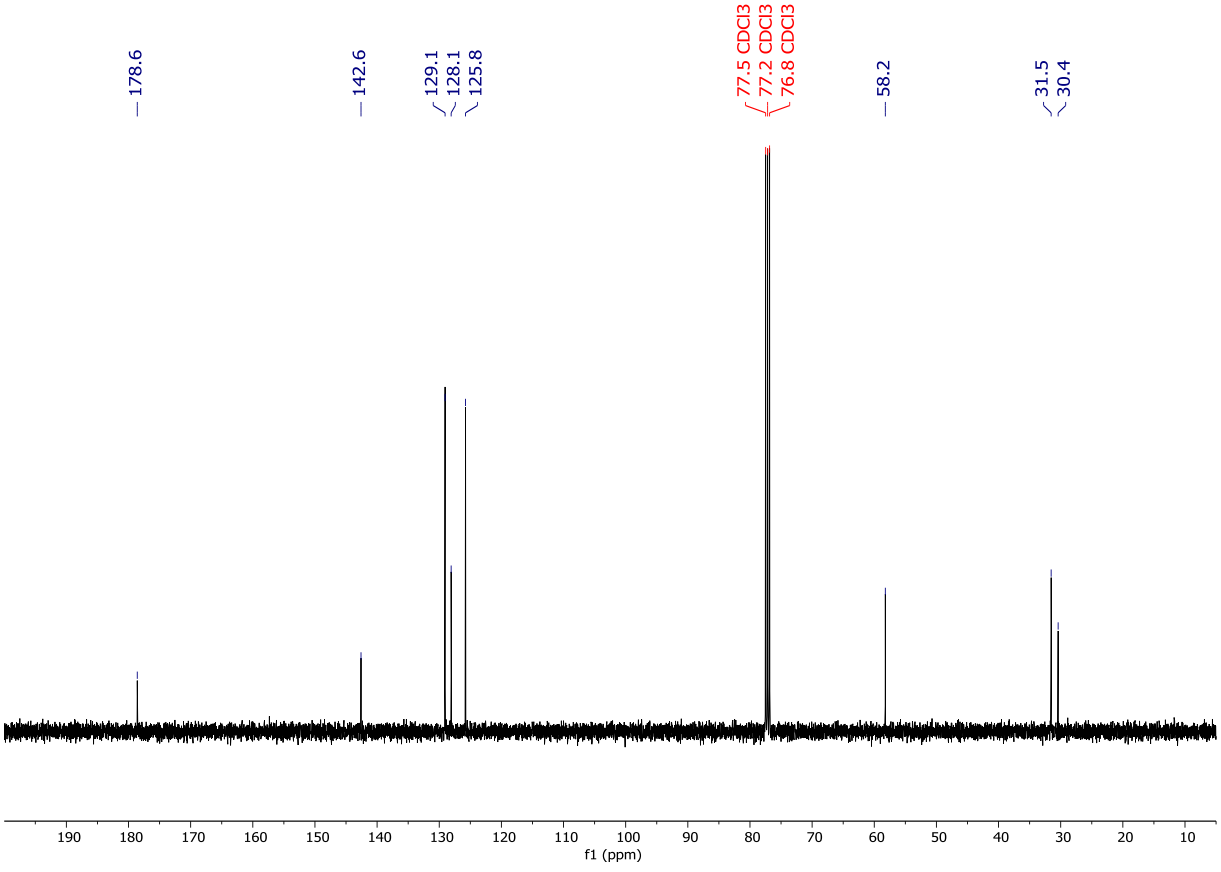
2-[[1-{(5-Oxo-1,4,2-dioxazol-3-yl)methyl}cyclopentyl]methyl]isoindoline-1,3-dione



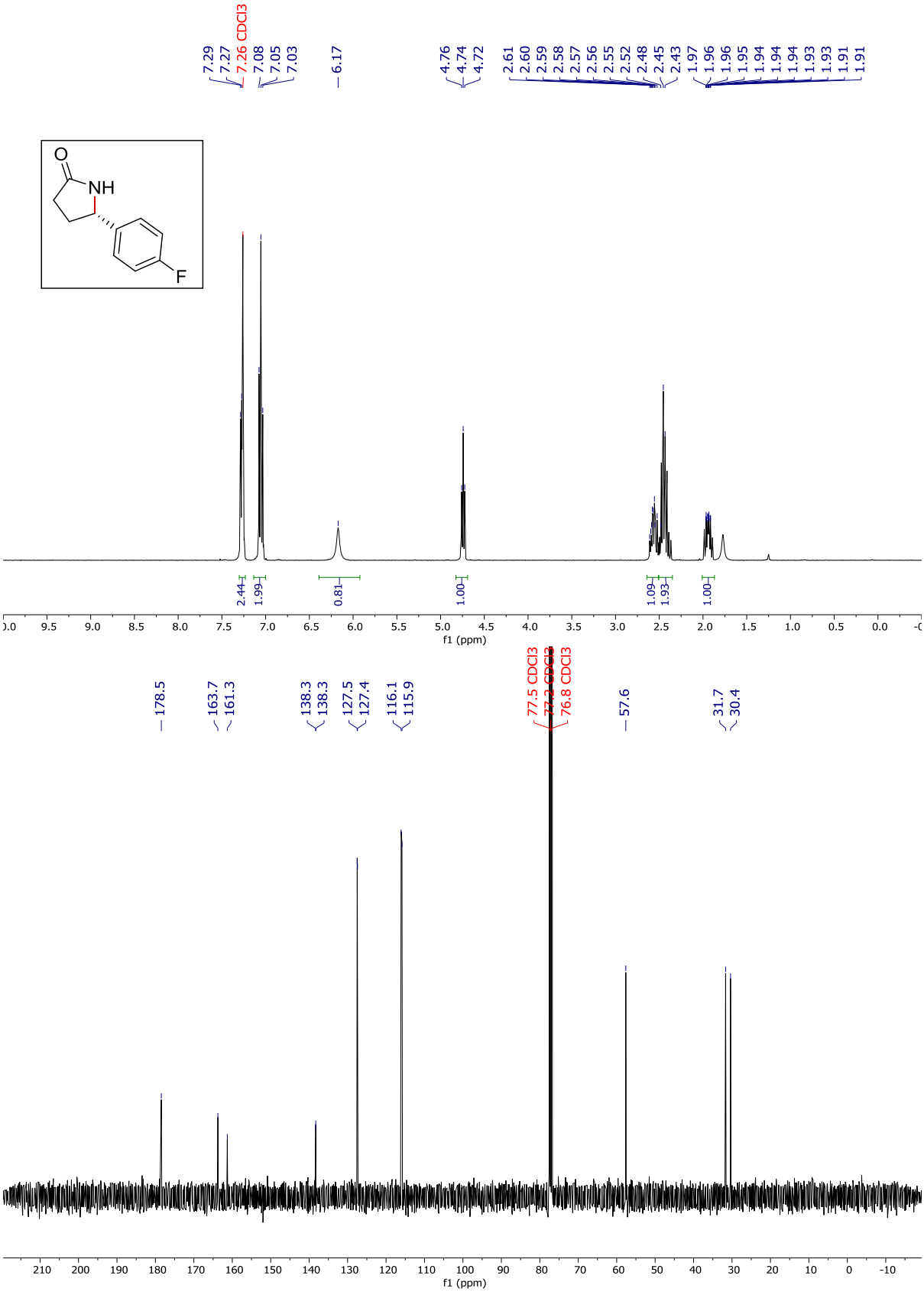


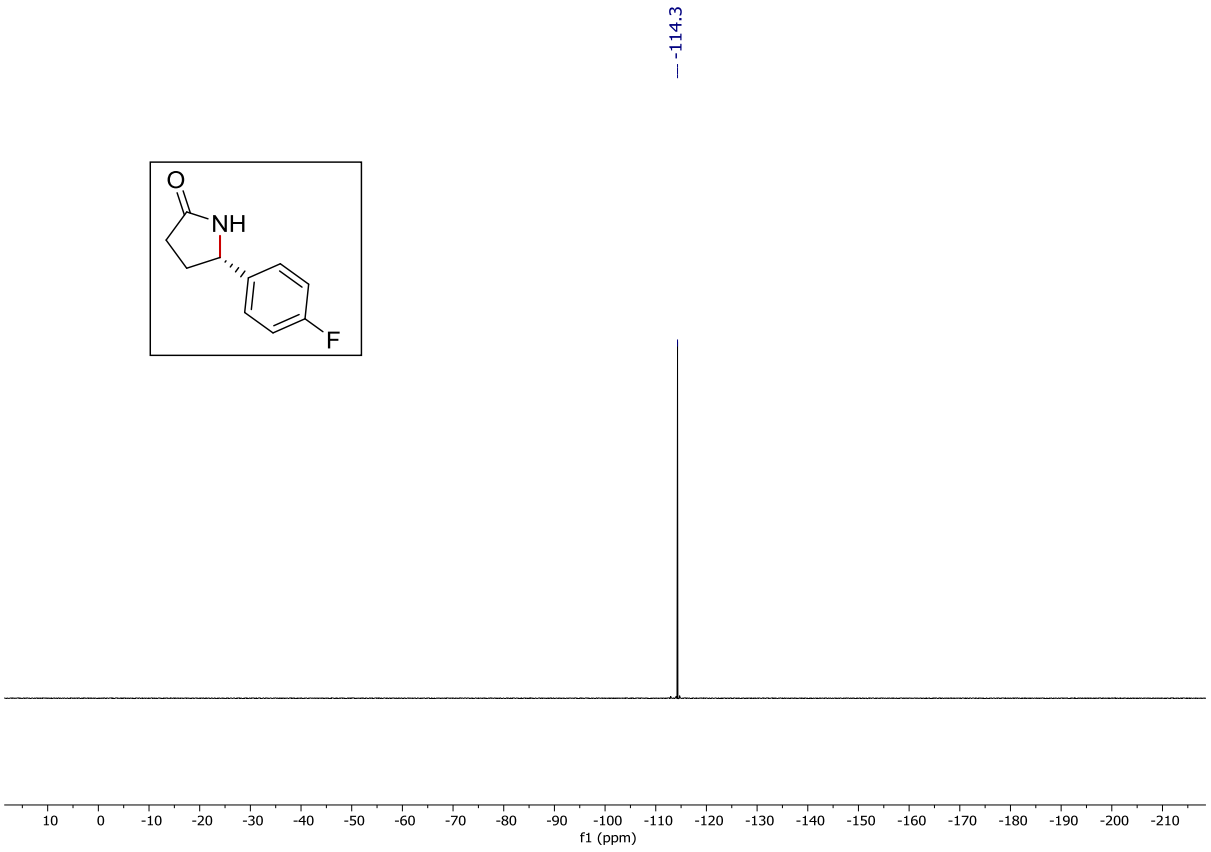
5-Phenylpyrrolidin-2-one (2)



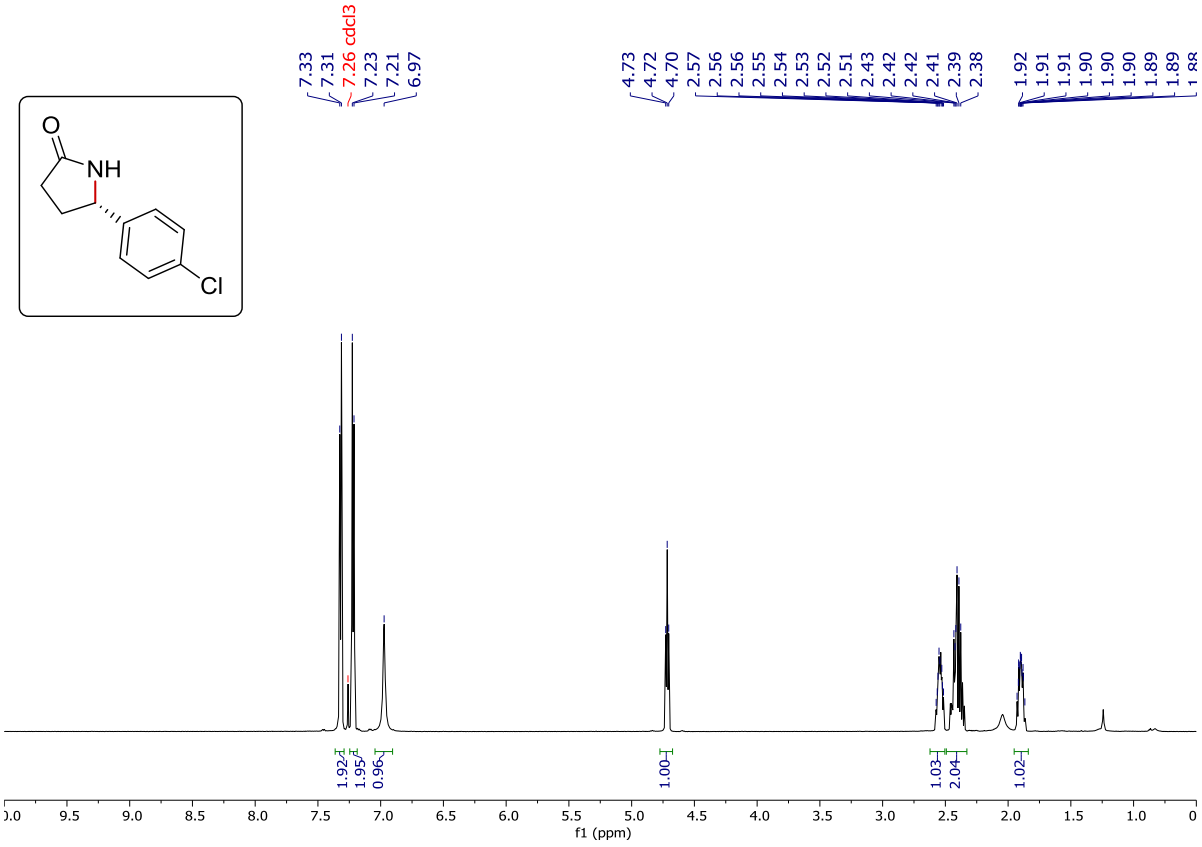


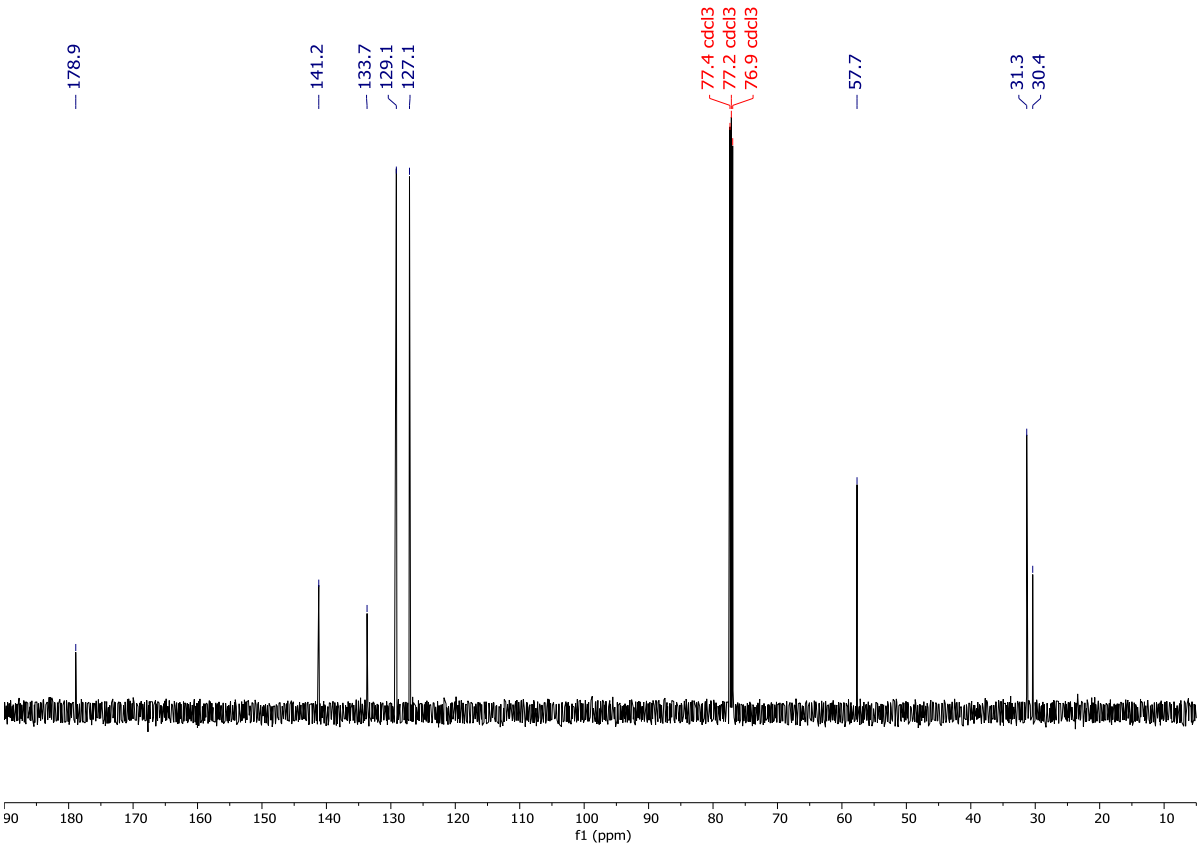
5-(4-Fluorophenyl)pyrrolidin-2-one (4)



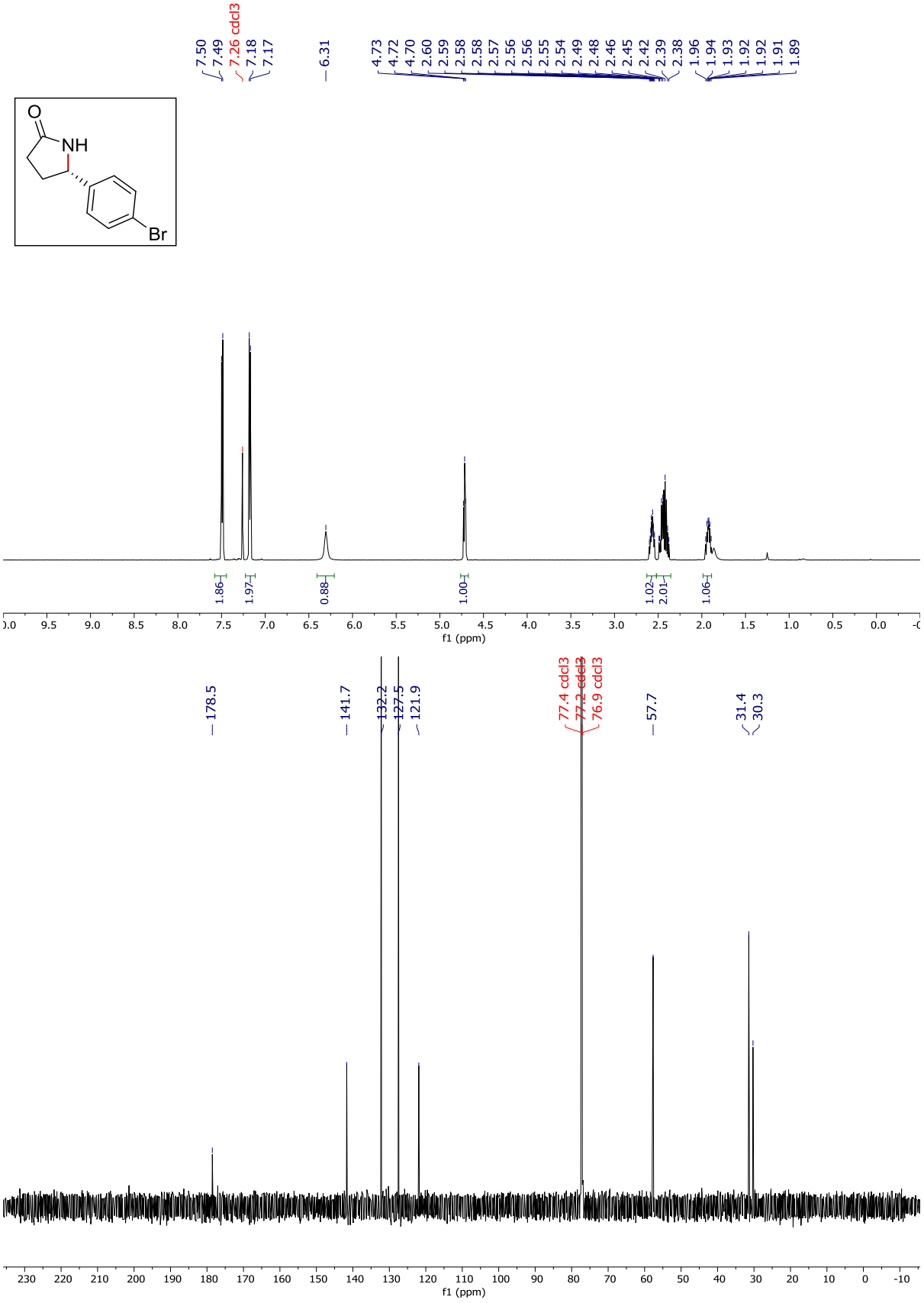

-114.3
O
NH
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

5-(4-Chlorophenyl)pyrrolidin-2-one (5)

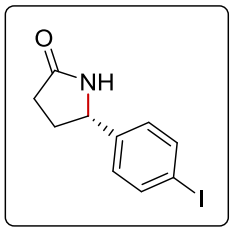


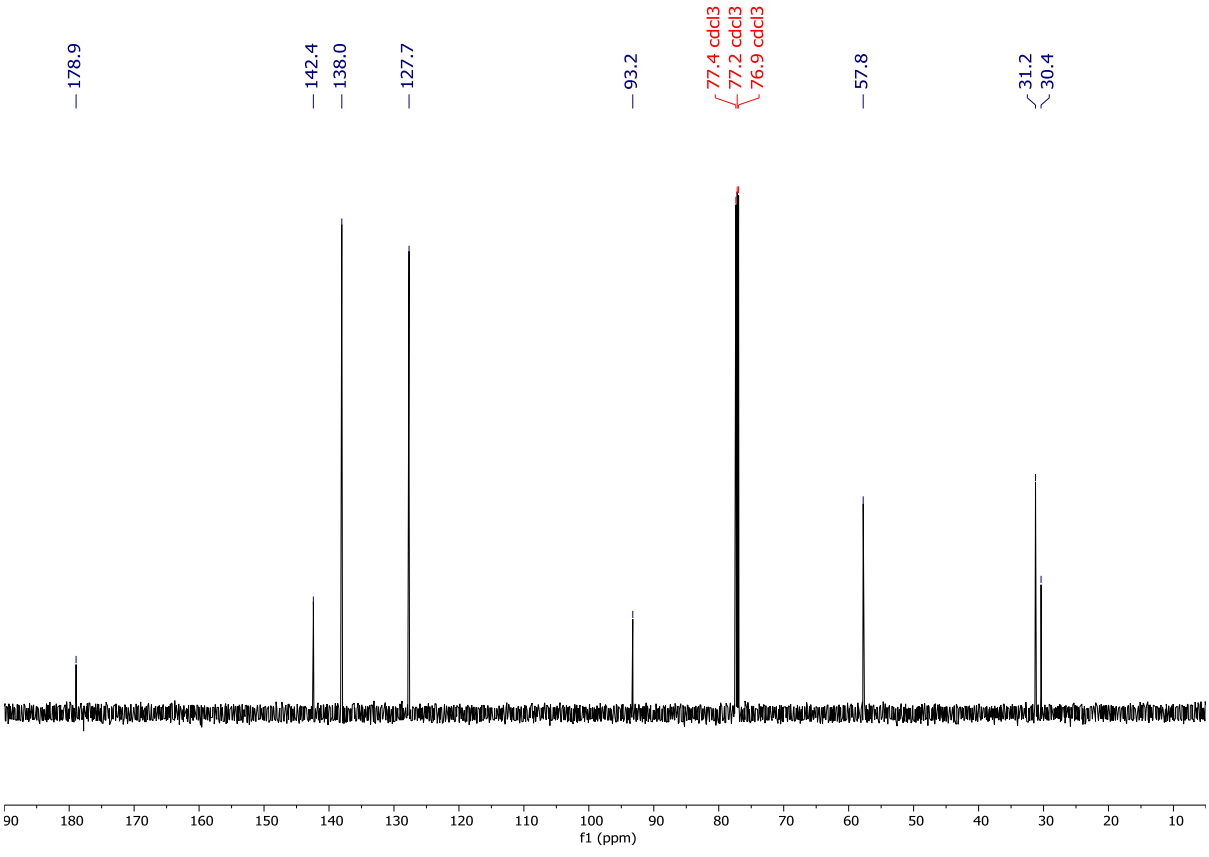


5-(4-Bromophenyl)pyrrolidin-2-one (6)

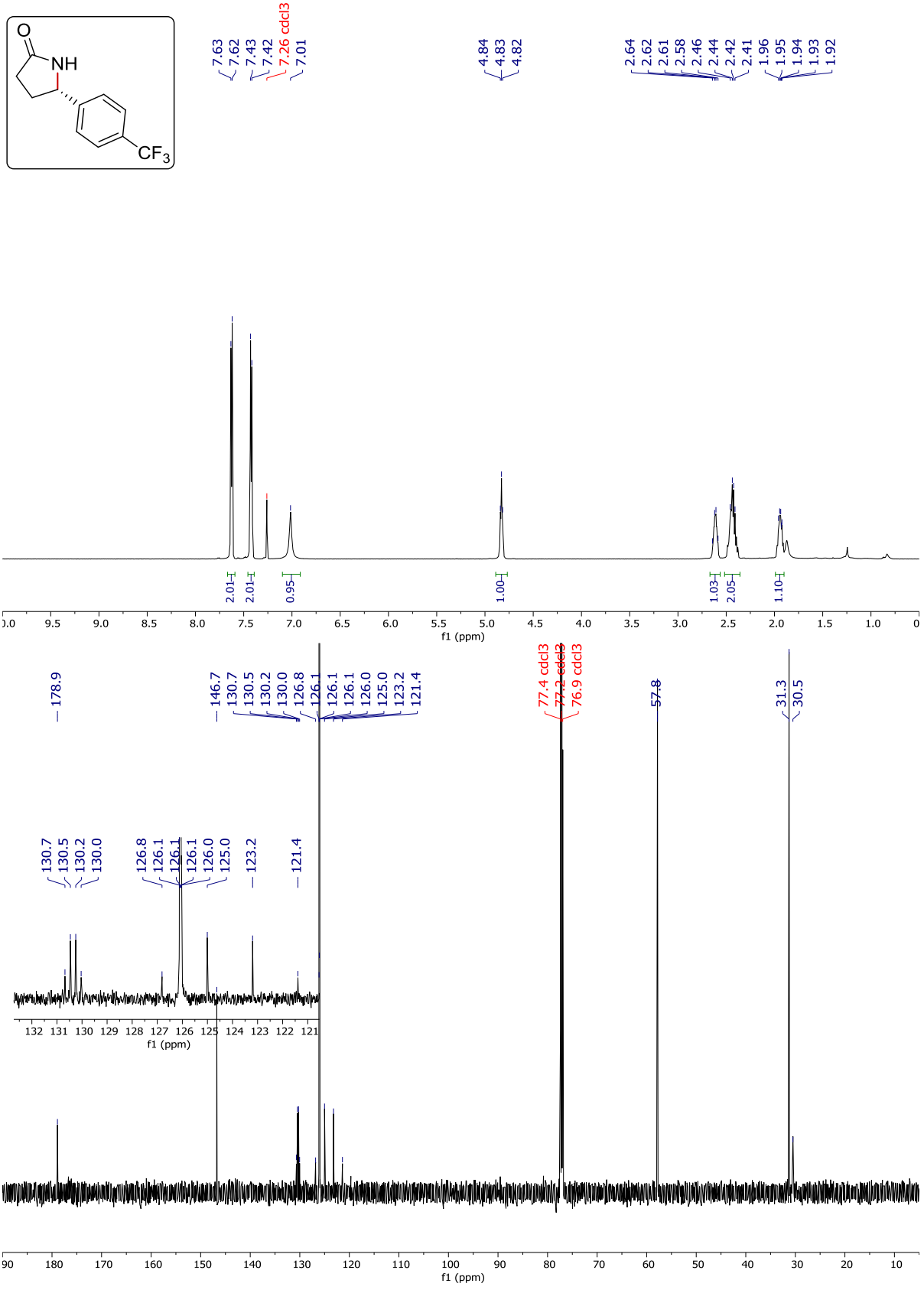


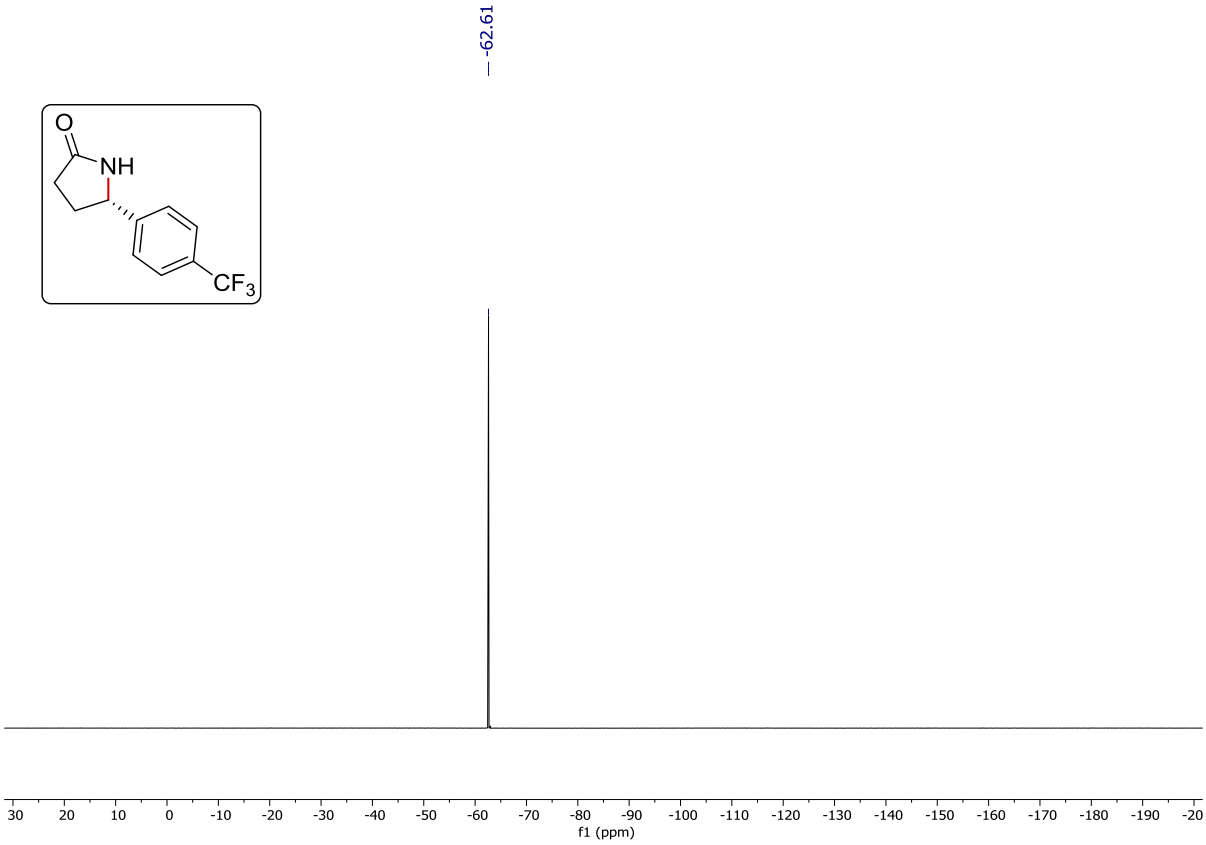
5-(4-Iodophenyl)pyrrolidin-2-one (7)



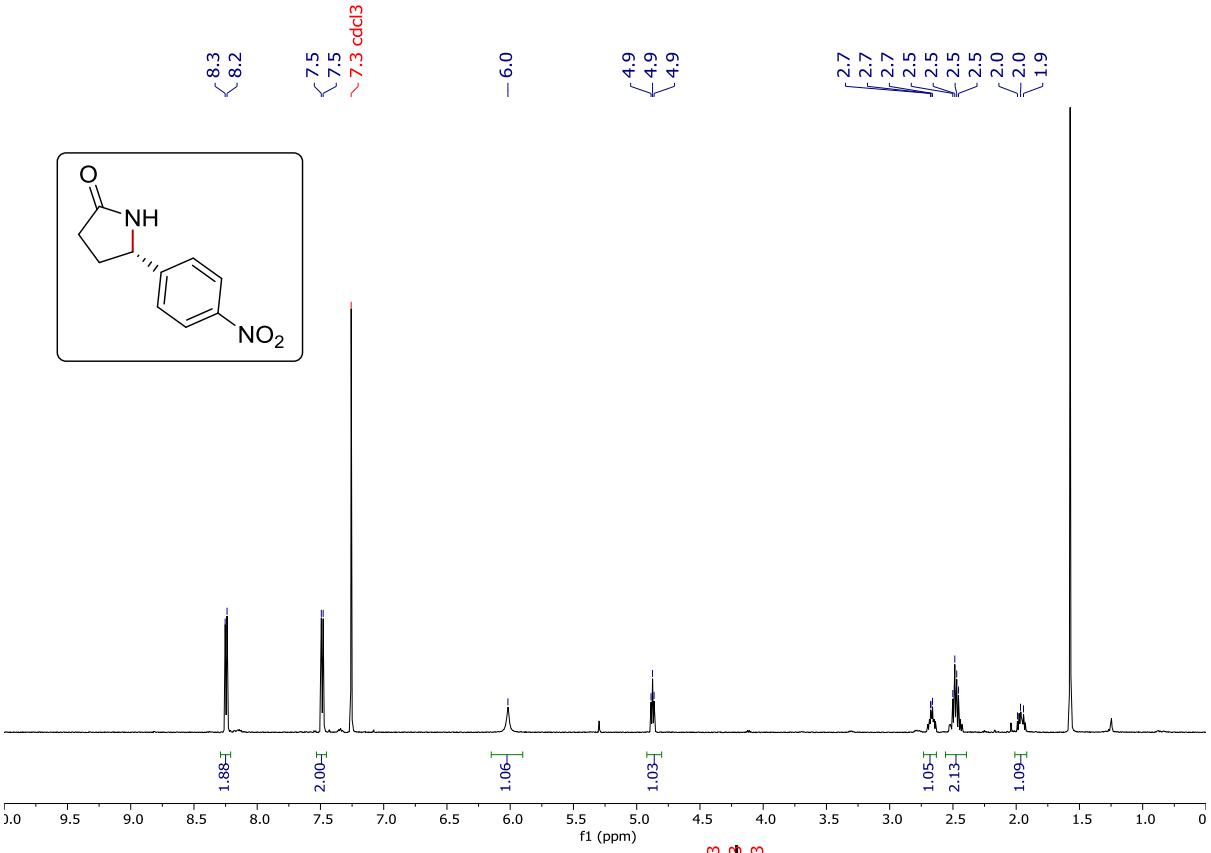


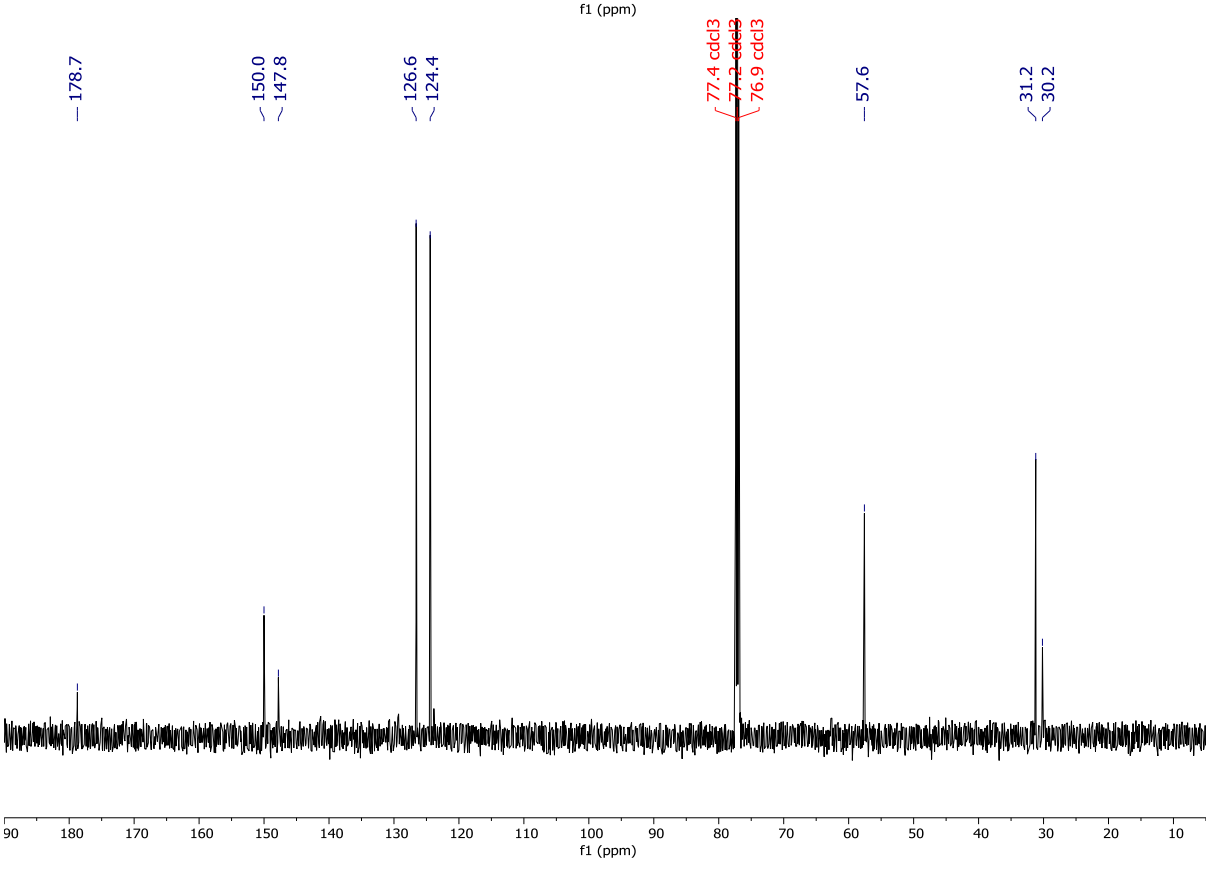
5-{4-(Trifluoromethyl)phenyl}pyrrolidin-2-one (8)



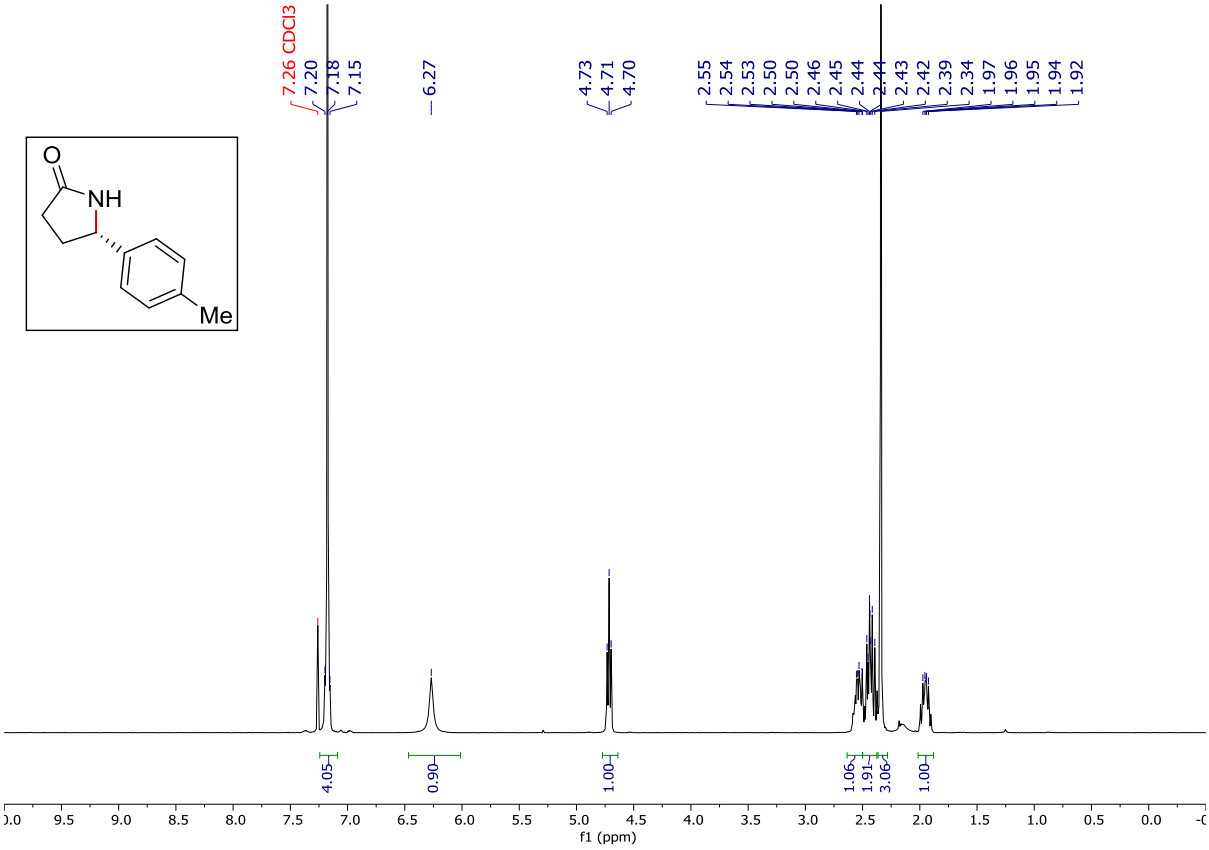

-62.61
O
NH
CF3
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)

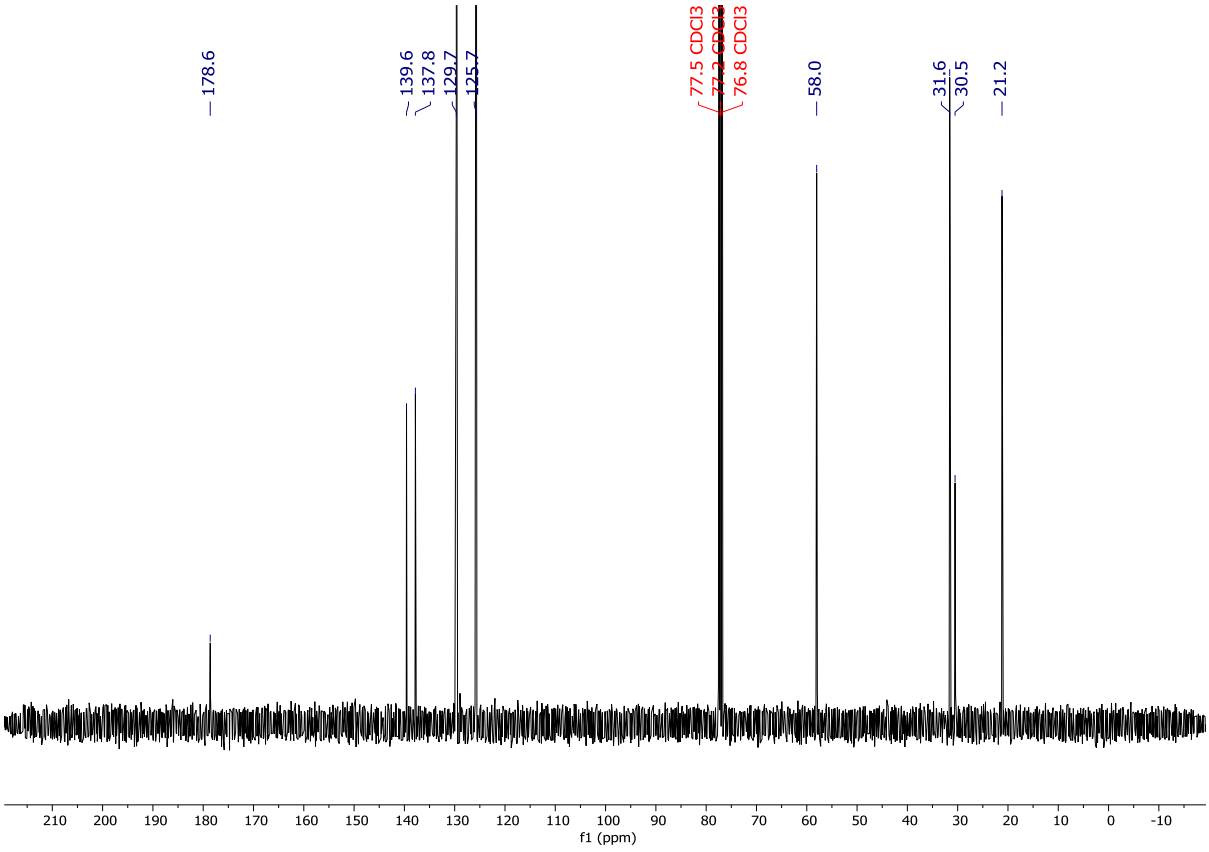
5-(4-Nitrophenyl)pyrrolidin-2-one (9)



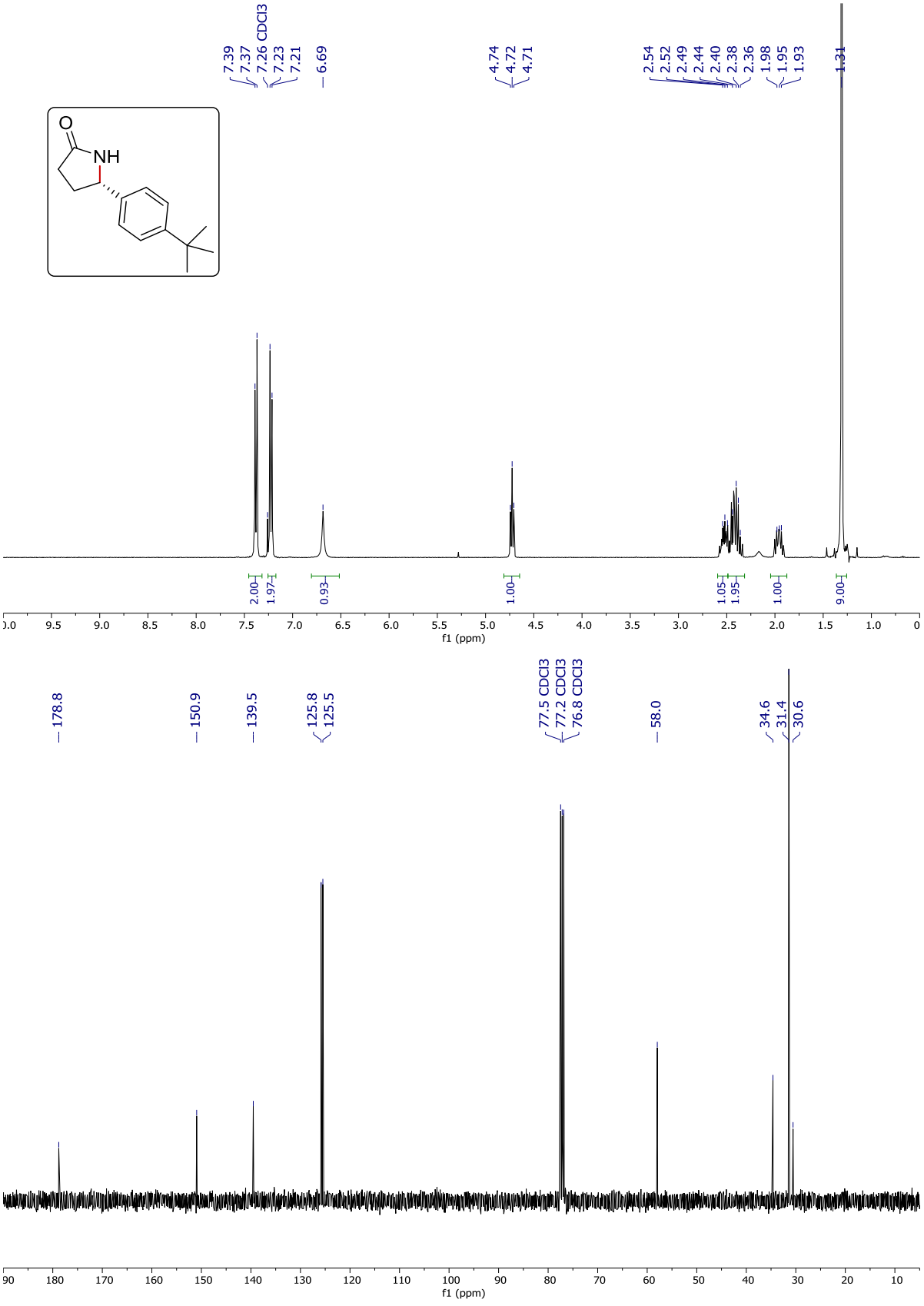


5-(*p*-Tolyl)pyrrolidin-2-one (10)

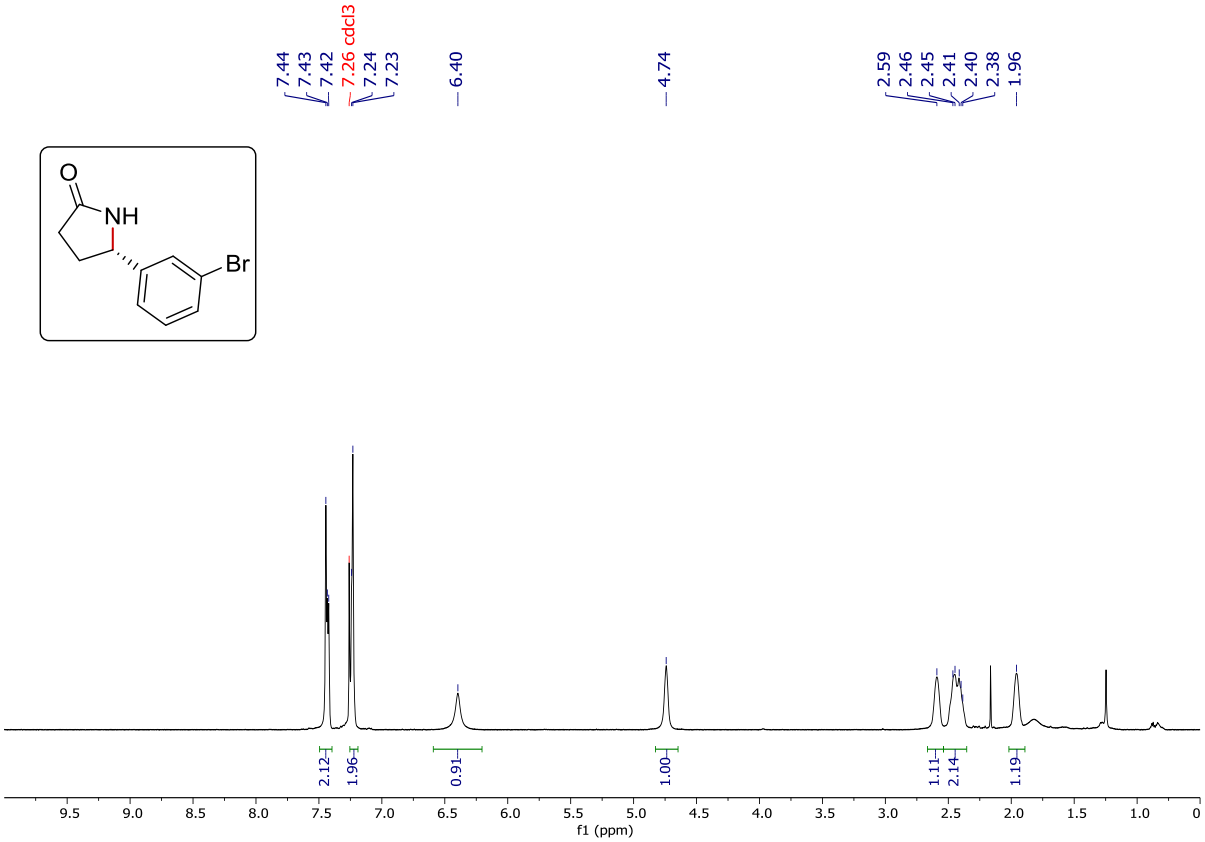


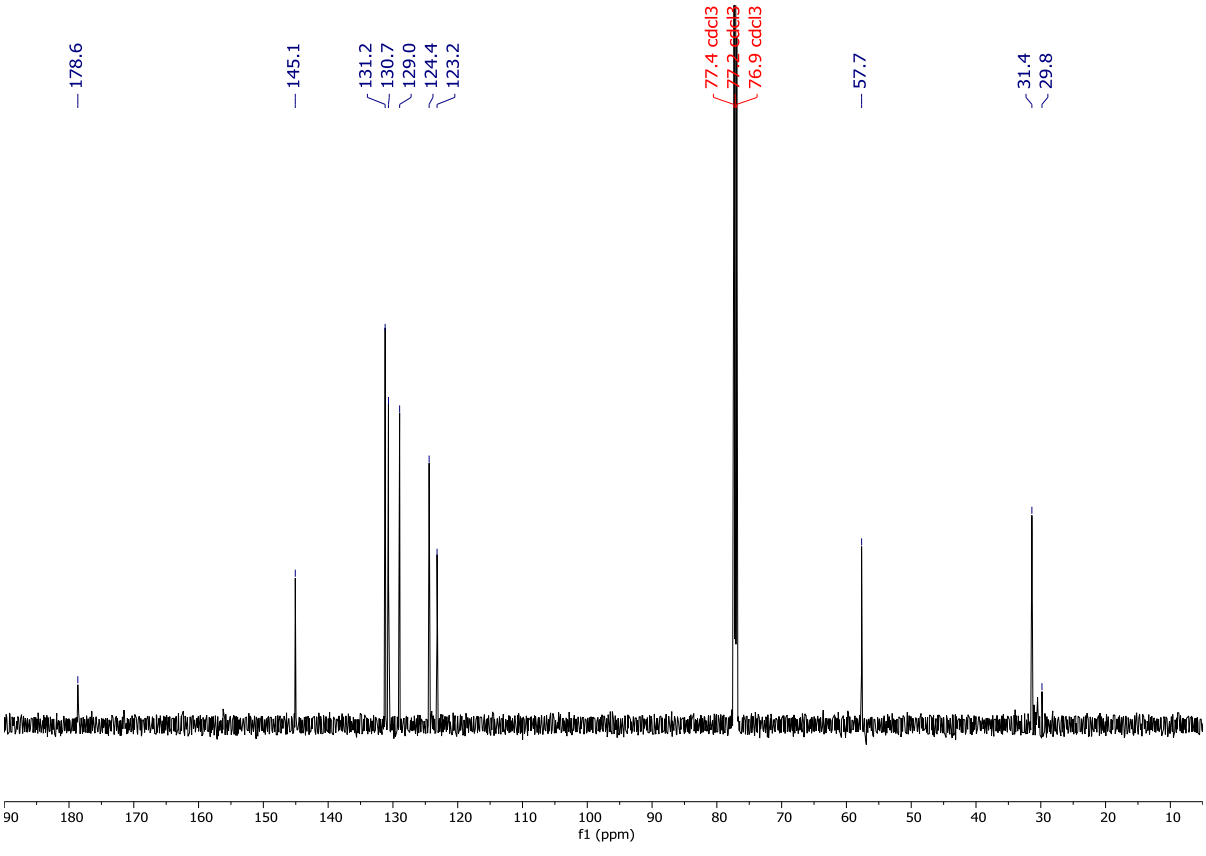


5-{4-(*tert*-Butyl)phenyl}pyrrolidin-2-one (11)

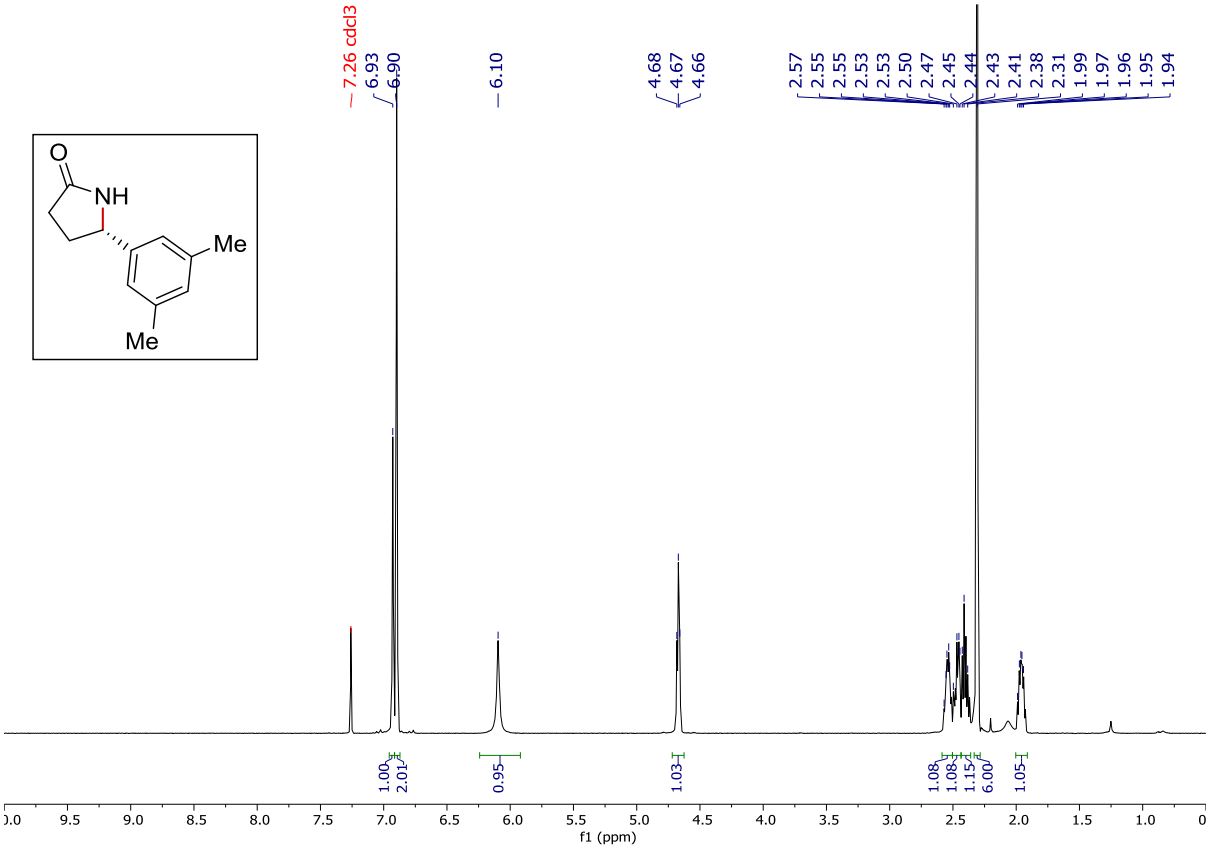


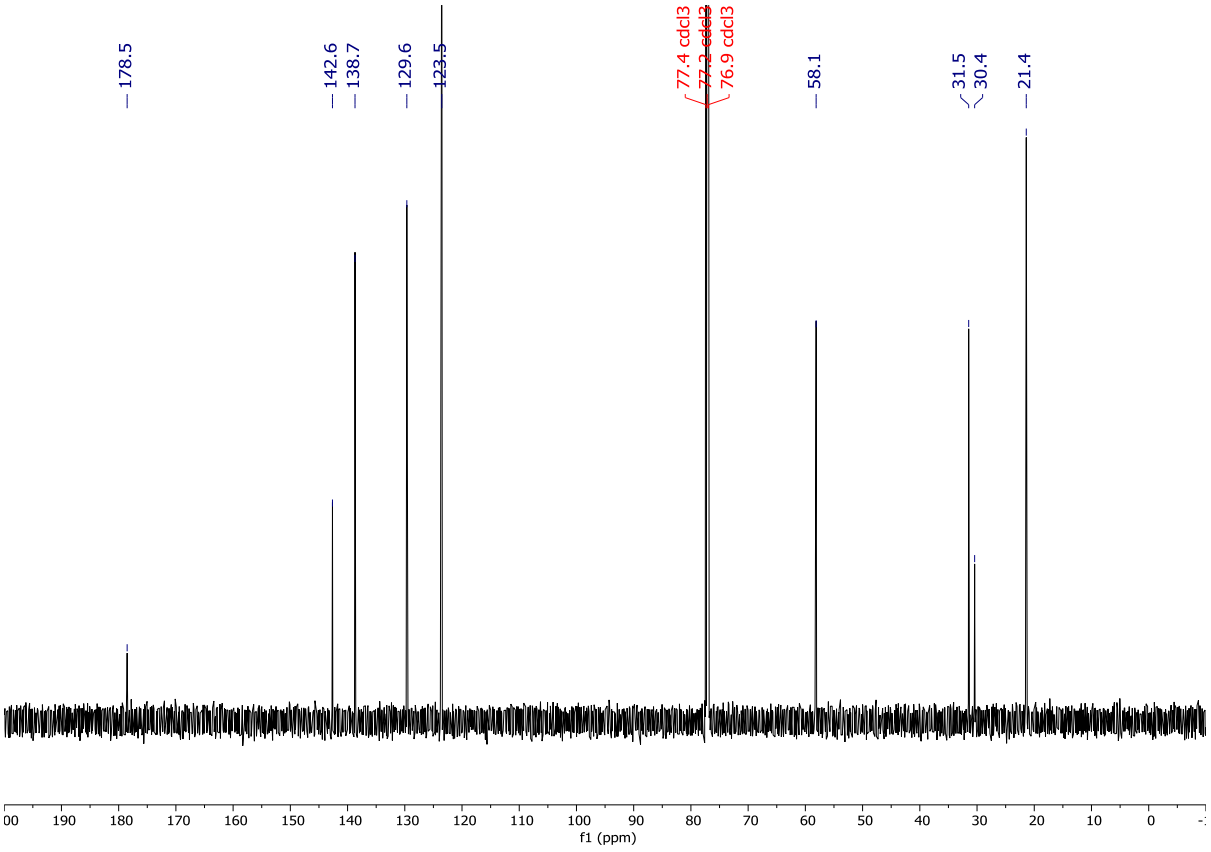
5-(3-Bromophenyl)pyrrolidin-2-one (12)



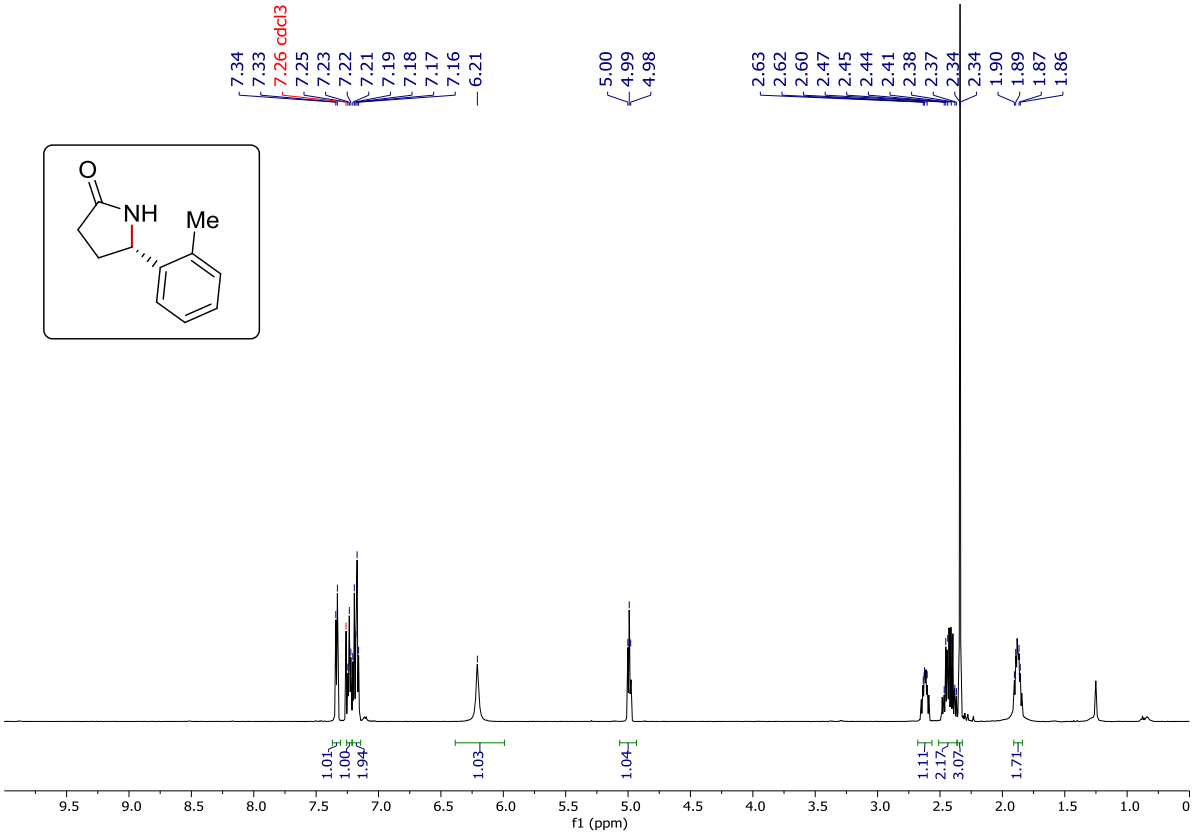


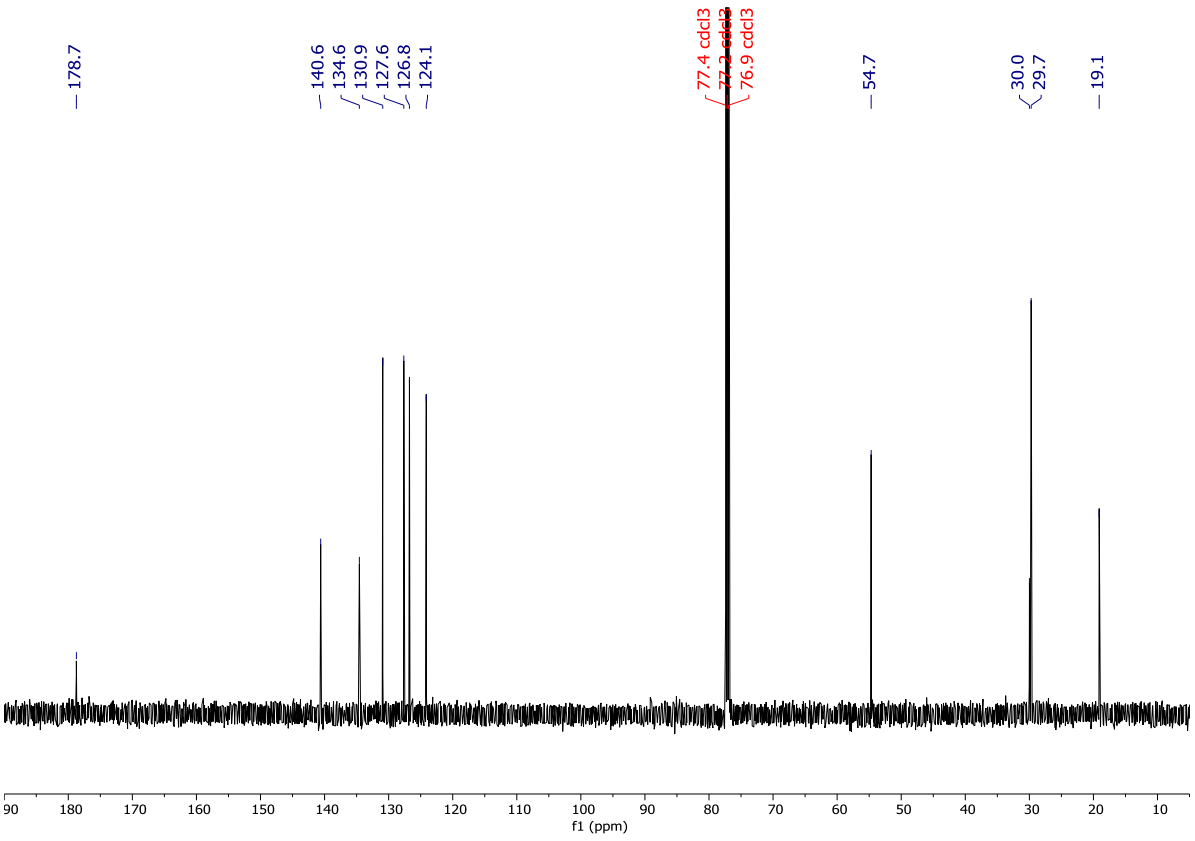
5-(3,5-Dimethylphenyl)pyrrolidin-2-one (13)



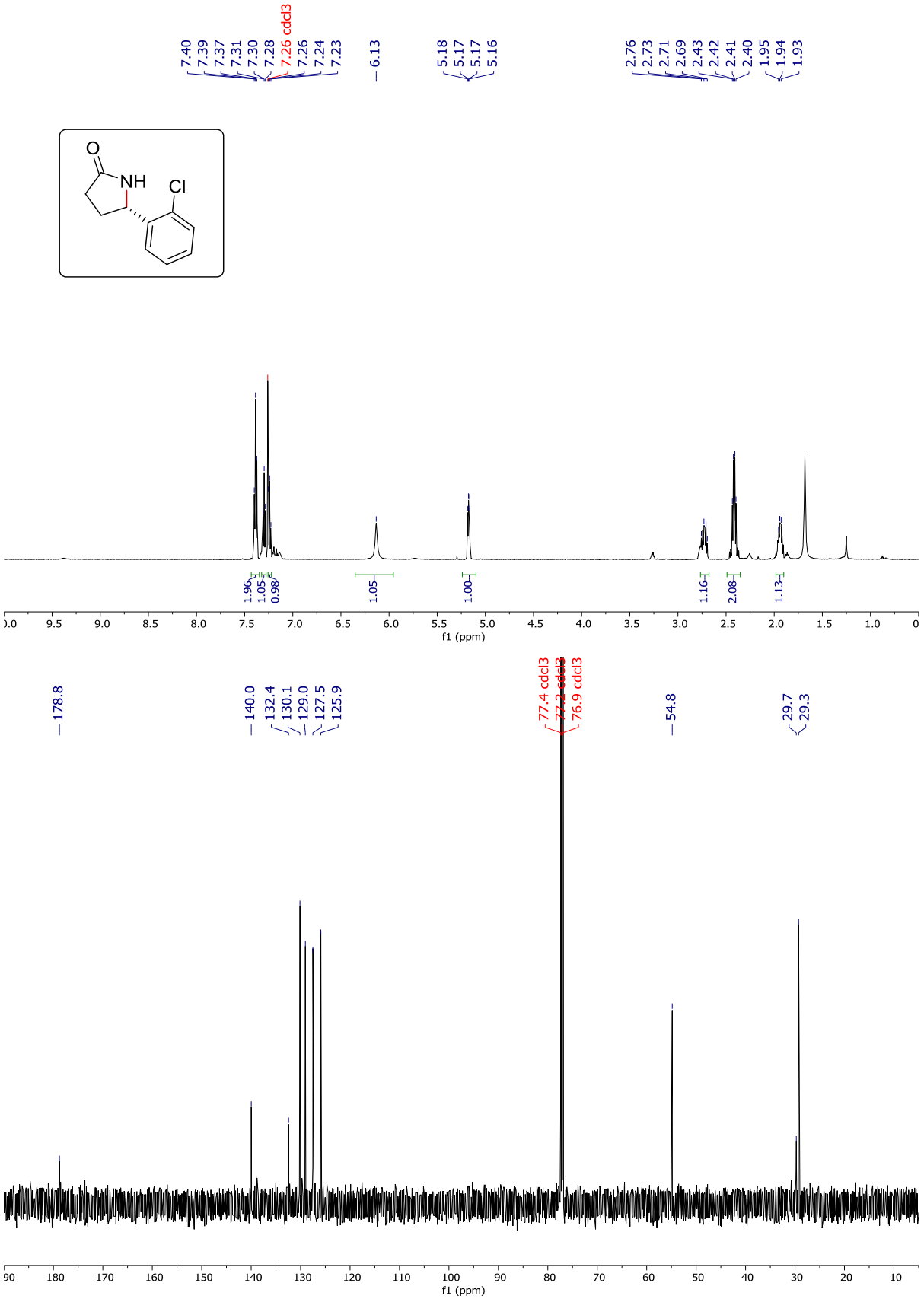


5-(*o*-Tolyl)pyrrolidin-2-one (14)

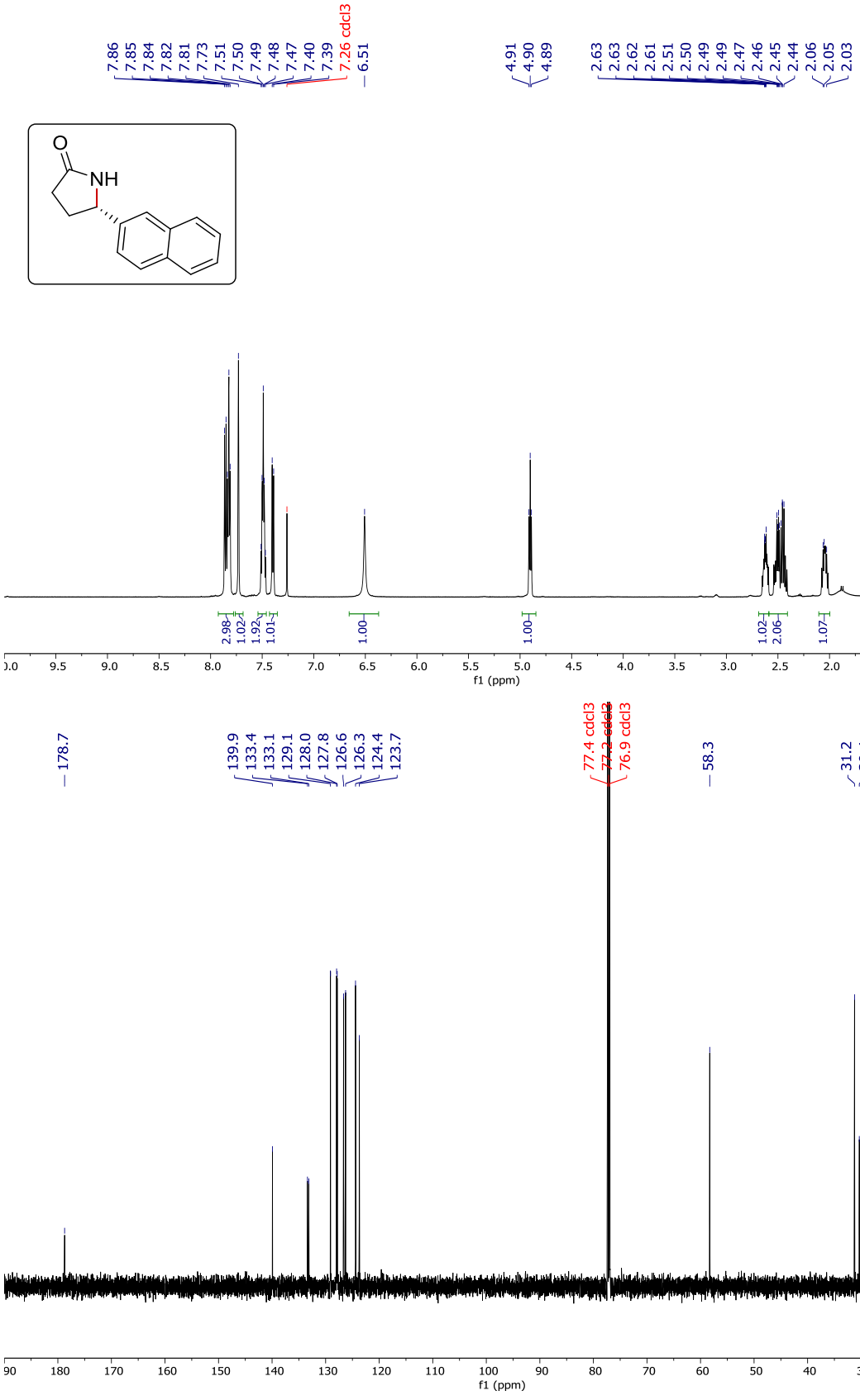




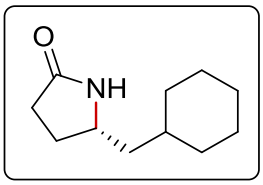
5-(2-Chlorophenyl)pyrrolidin-2-one (15)

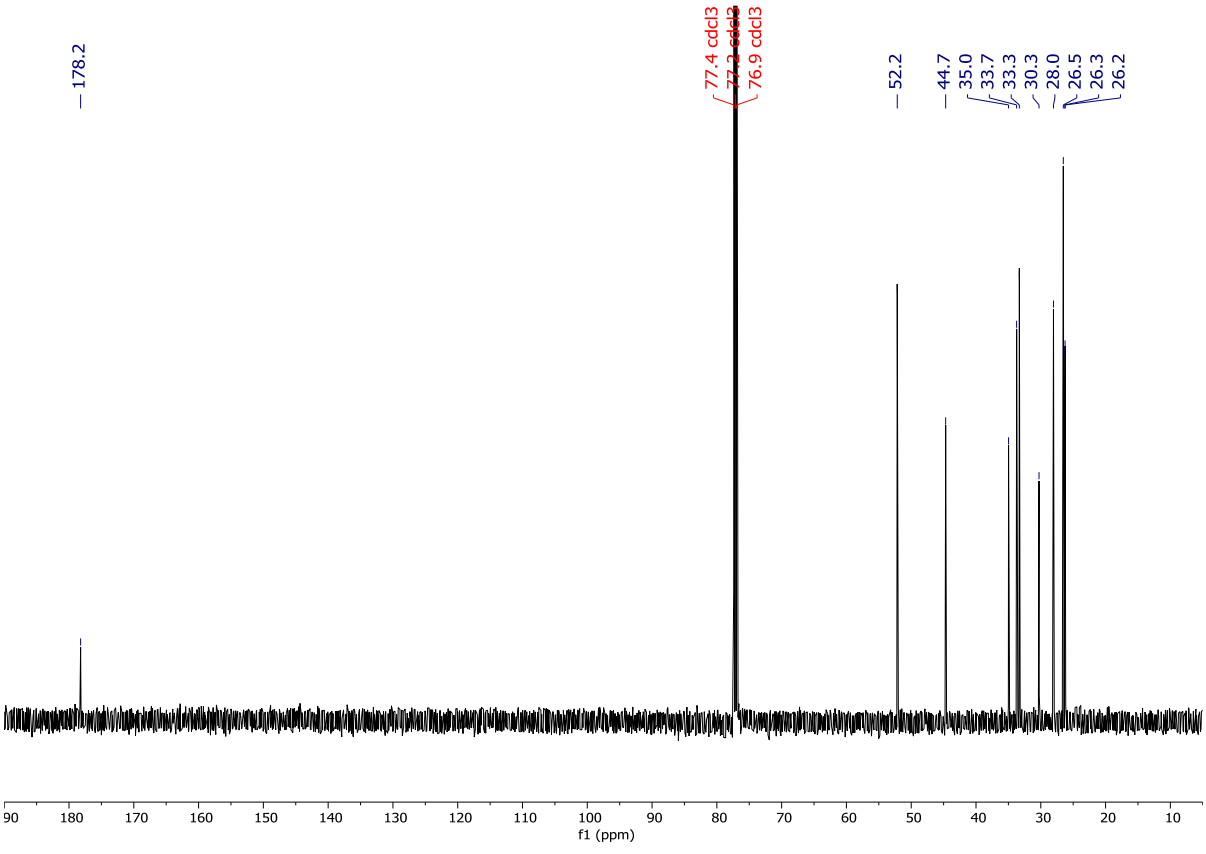


5-(Naphthalen-2-yl)pyrrolidin-2-one (16)

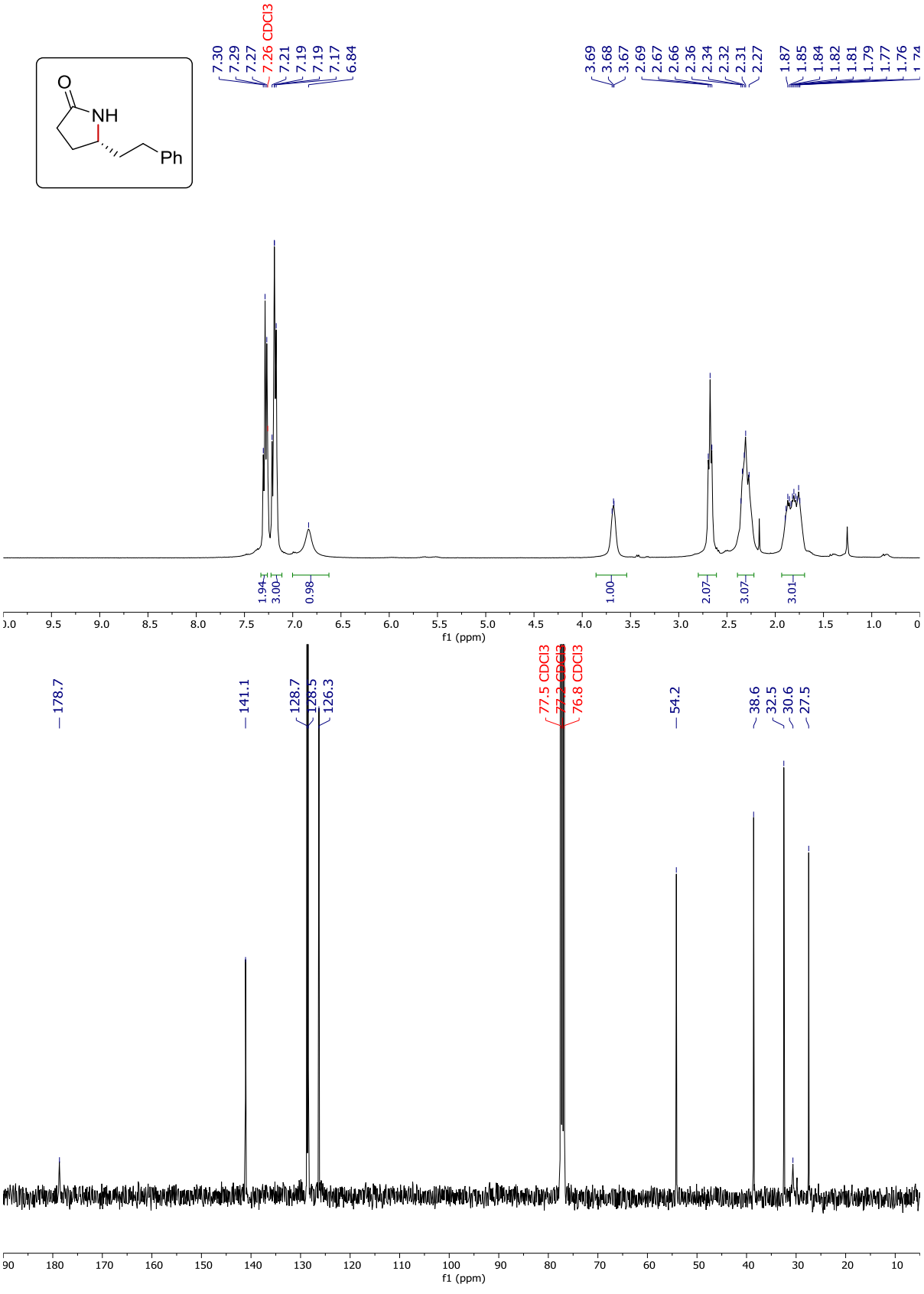


5-(Cyclohexylmethyl)pyrrolidin-2-one (17)

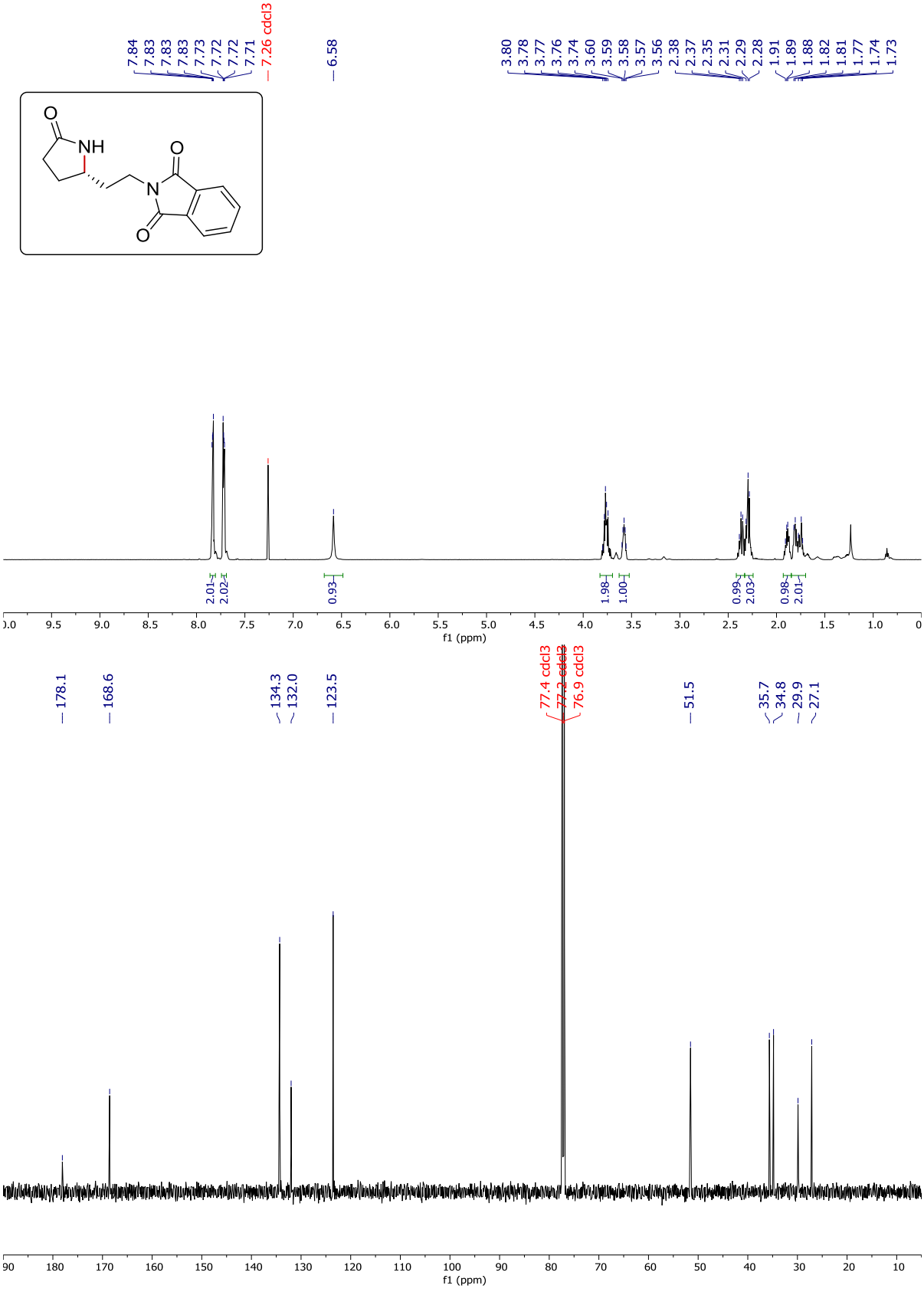




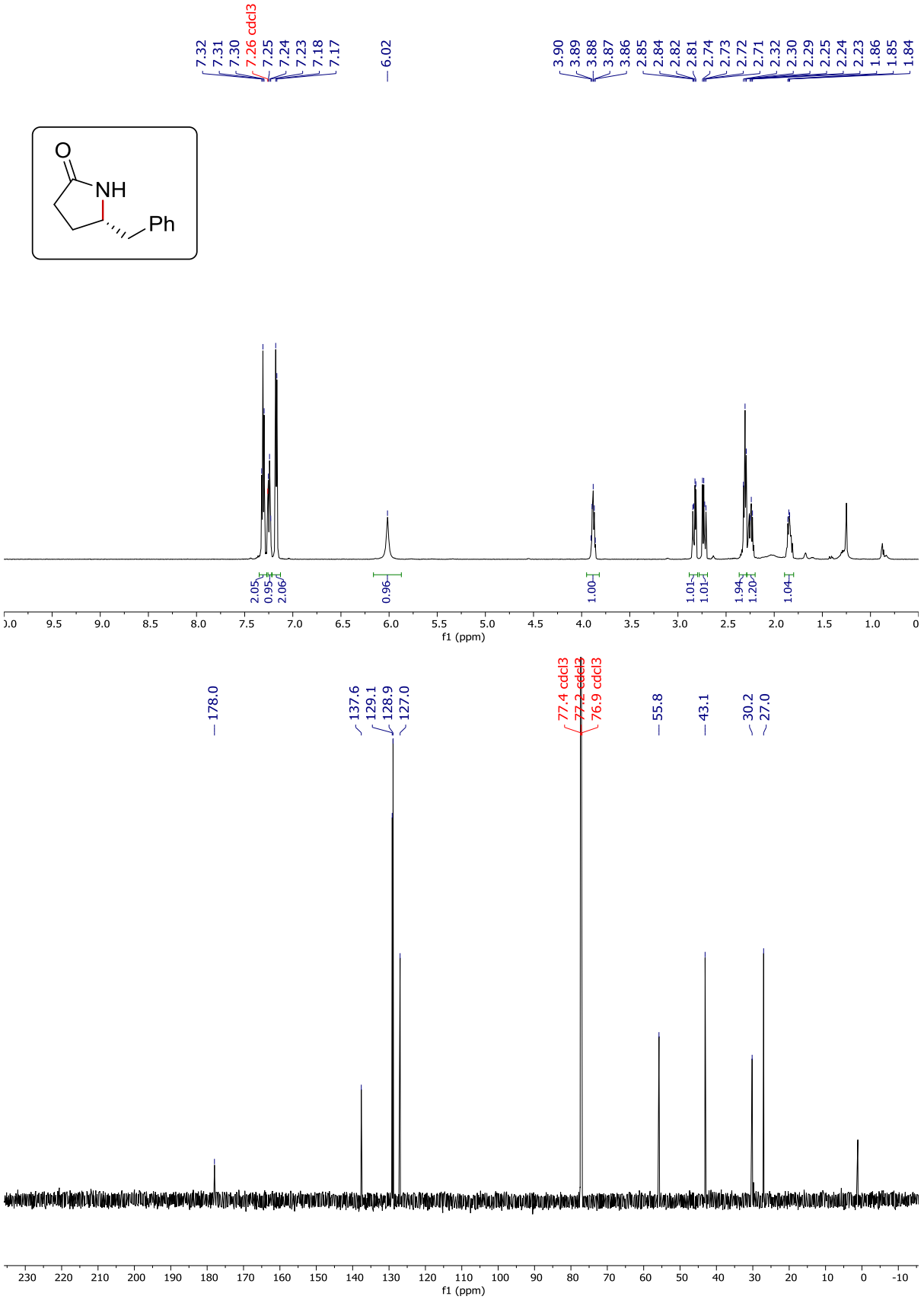
5-Phenethylpyrrolidin-2-one (18)



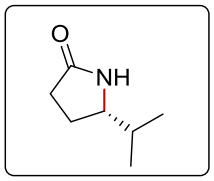
2-{2-(5-Oxopyrrolidin-2-yl)ethyl}isoindoline-1,3-dione (19)

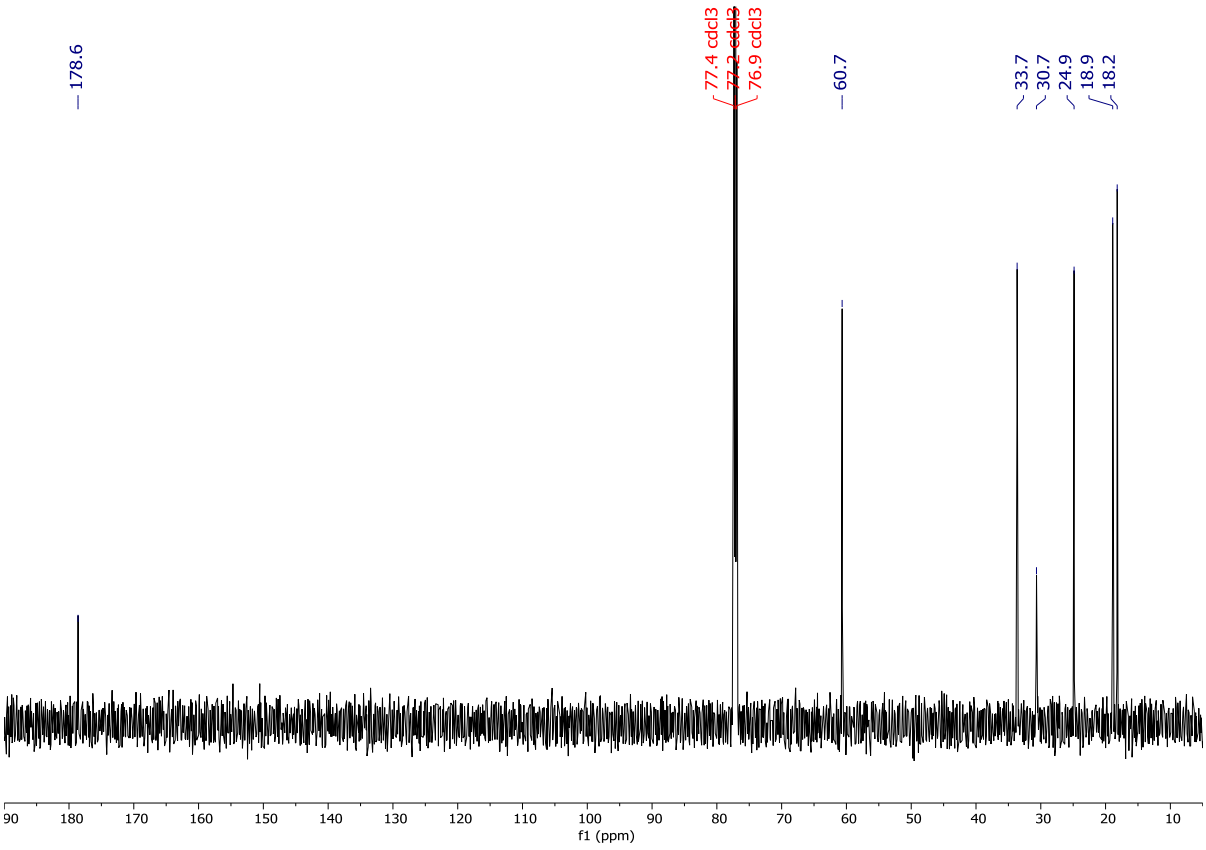


5-Benzylpyrrolidin-2-one (20)

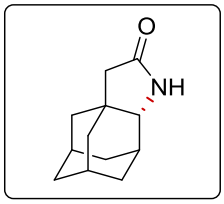


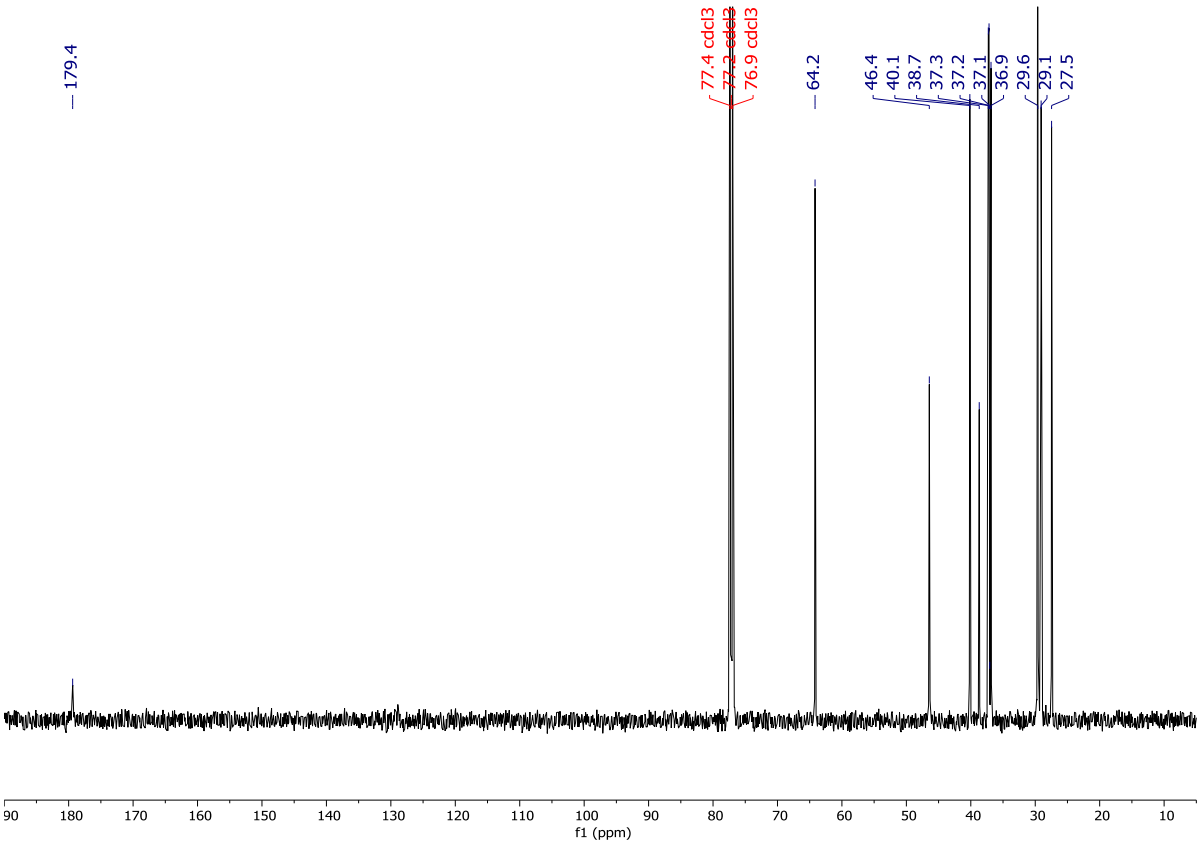
5-Isopropylpyrrolidin-2-one (21)



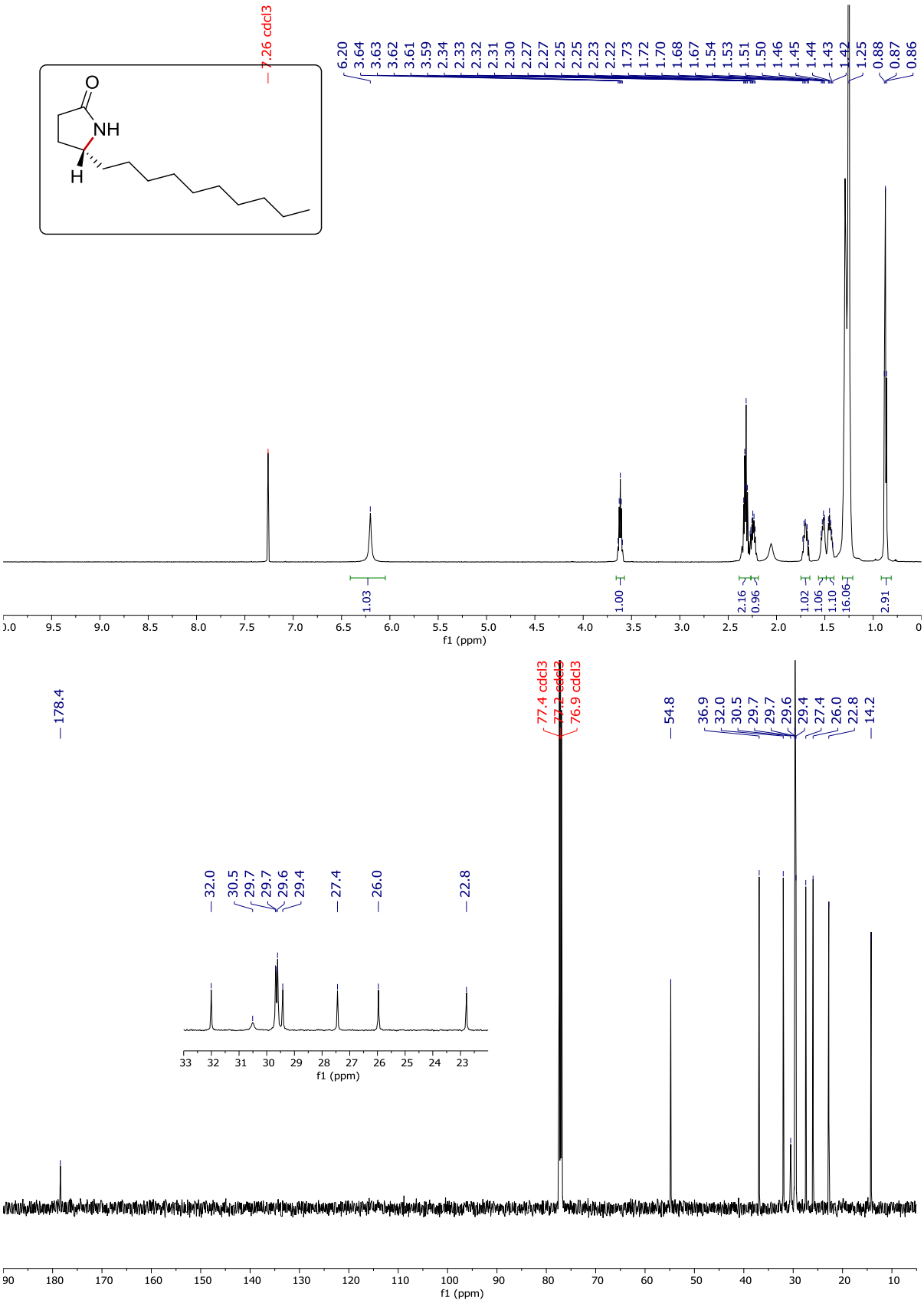


Octahydro-3a,7:5,9-dimethanocycloocta[b]pyrrol-2(*3H*)-one (22)

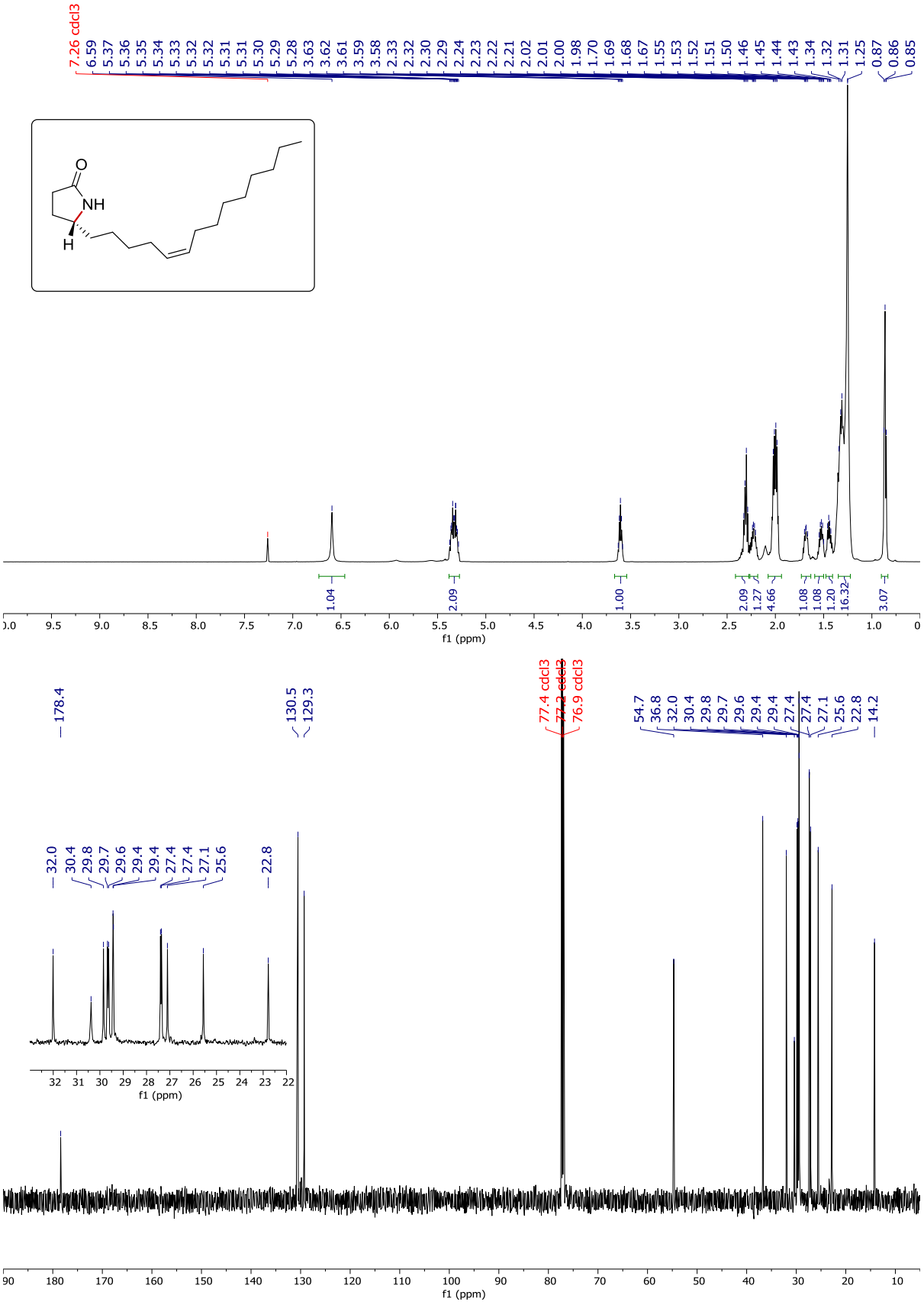




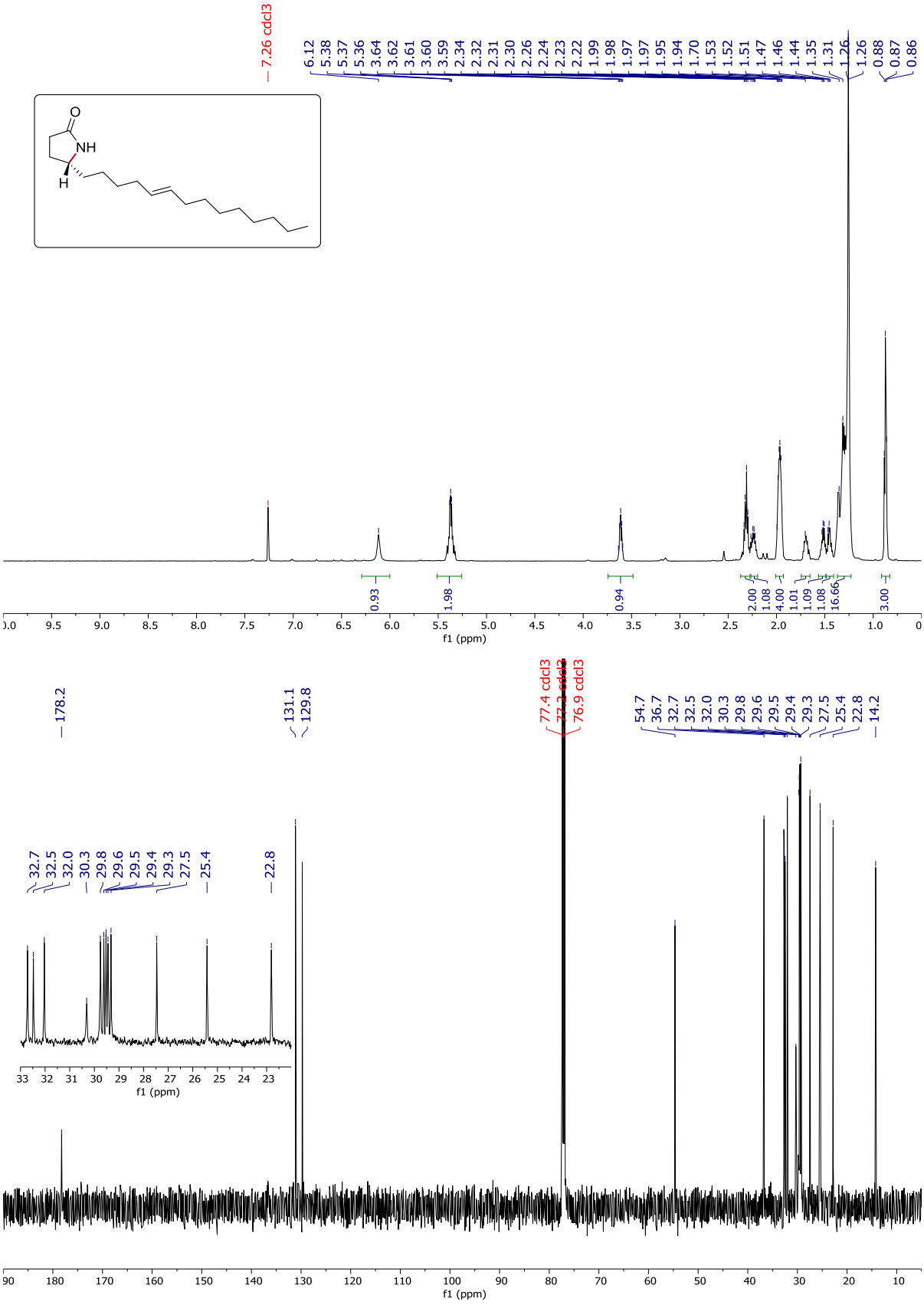
5-Decylpyrrolidin-2-one (23)



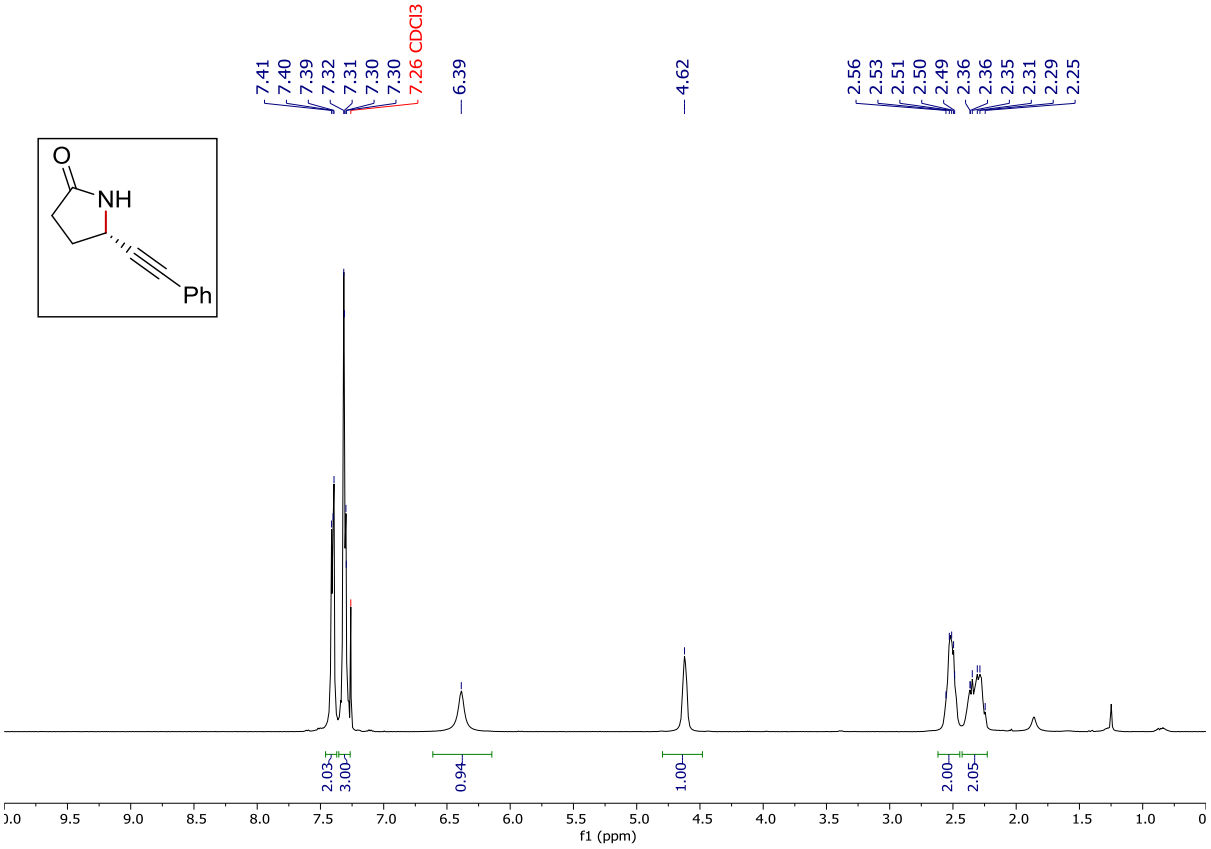
(*Z*)-5-(Tetradec-5-en-1-yl)pyrrolidin-2-one (24)

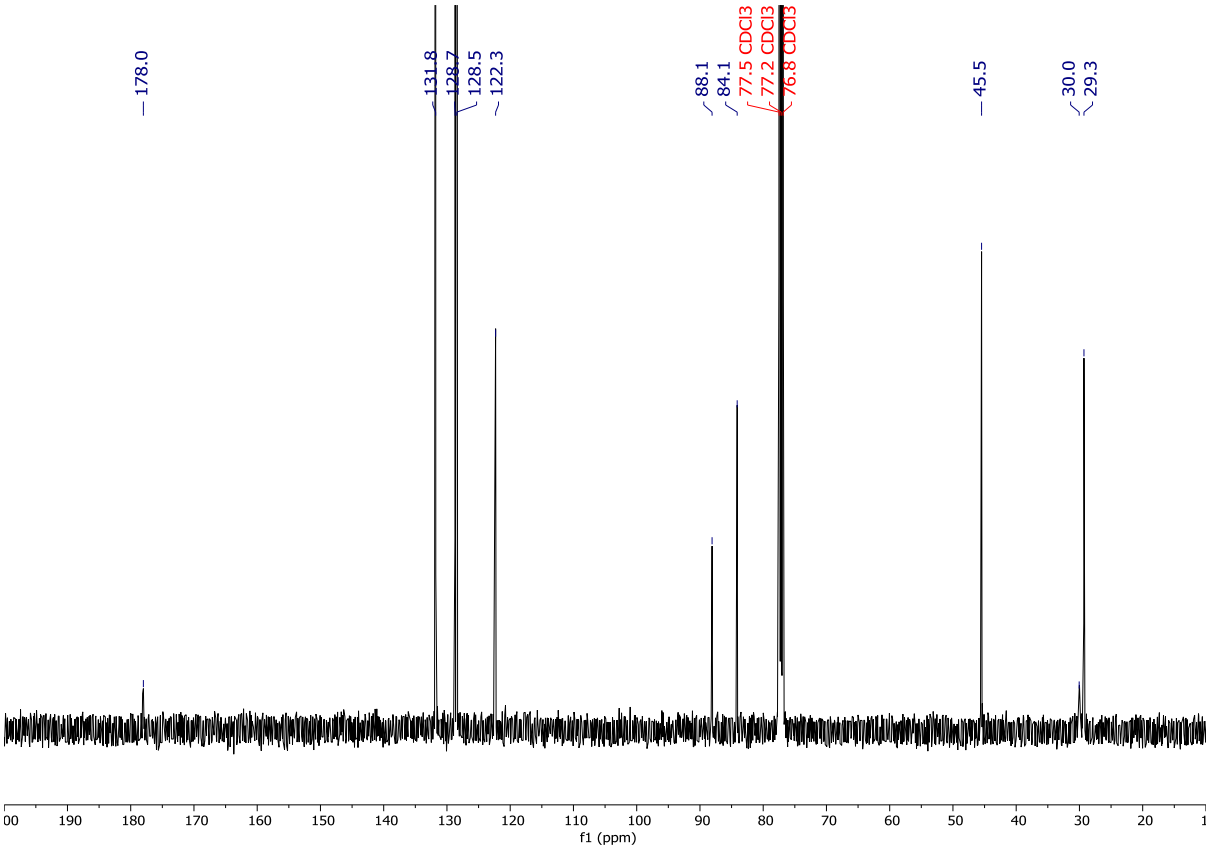


(*E*)-5-(tetradec-5-en-1-yl)pyrrolidin-2-one (25)

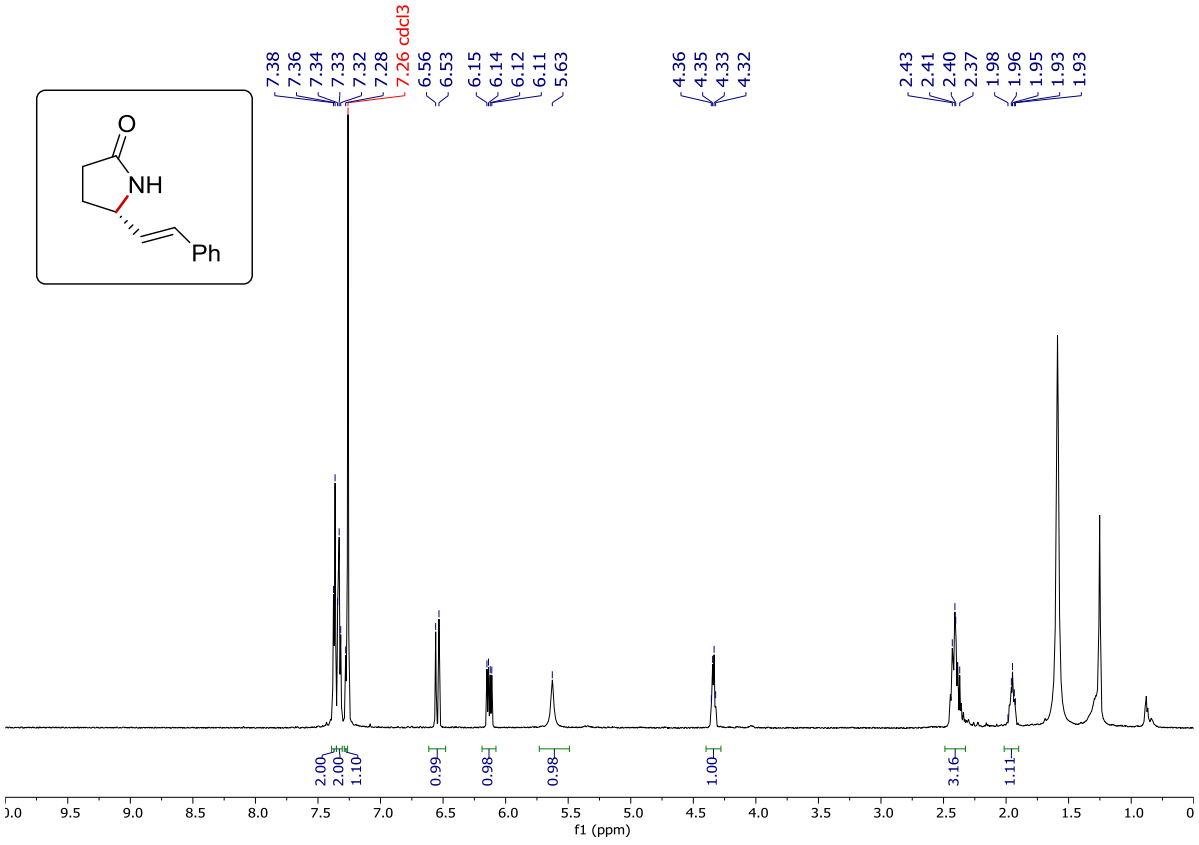


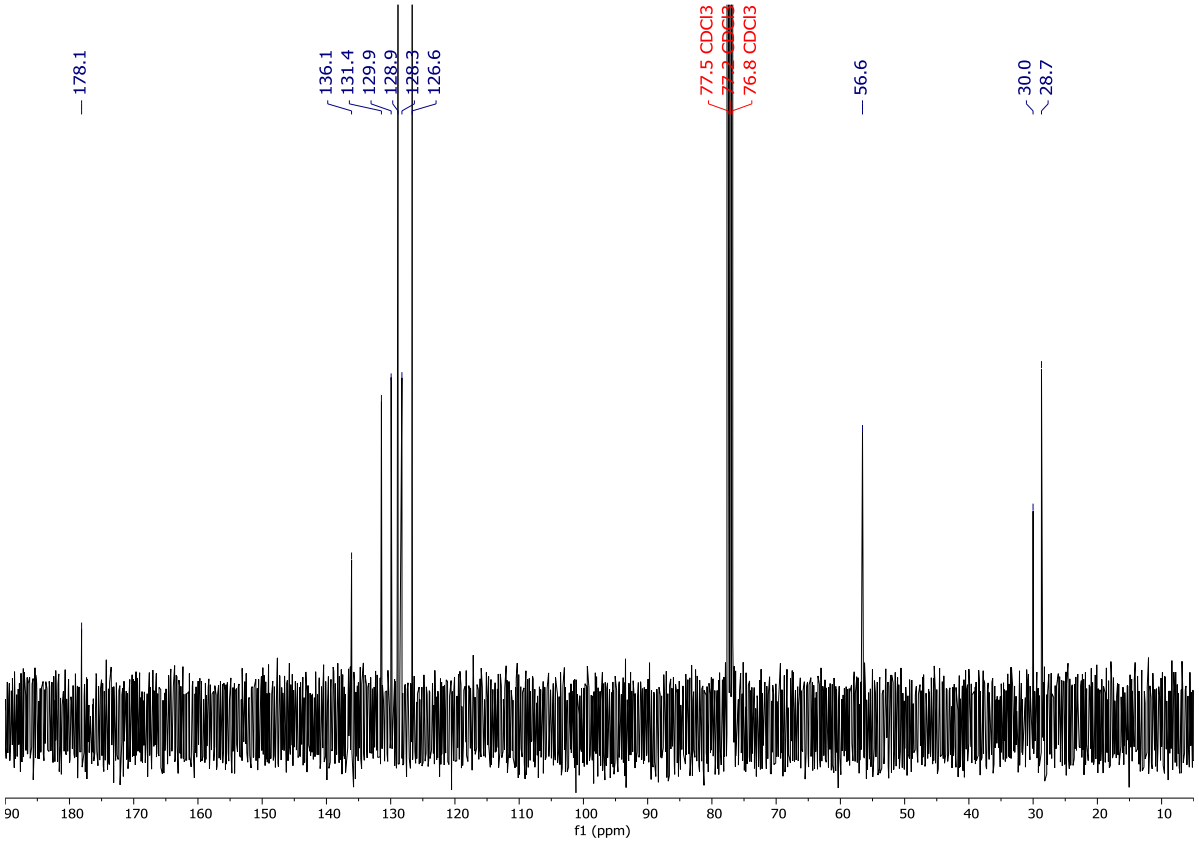
5-(Phenylethynyl)pyrrolidin-2-one (26)



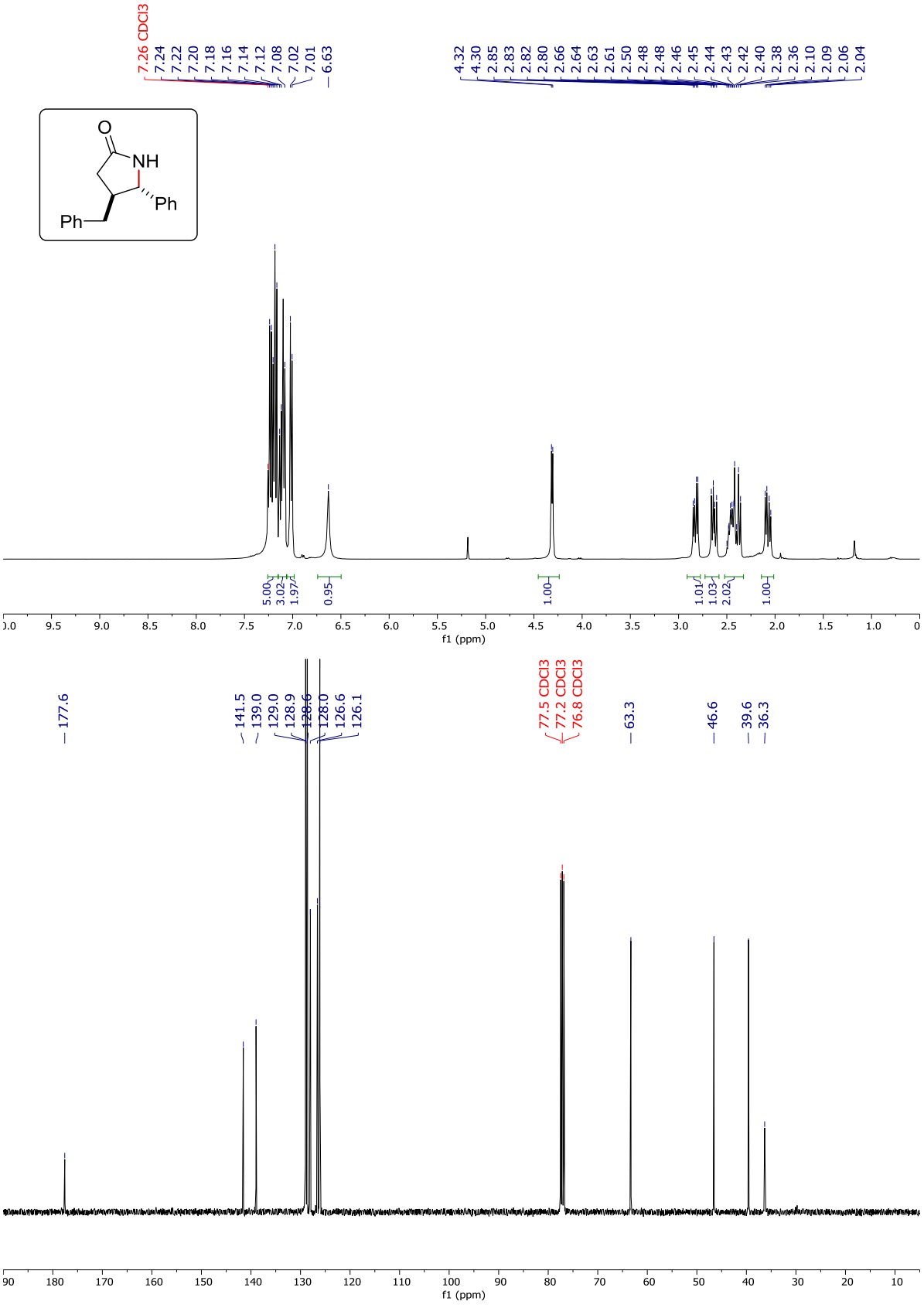


(*E*)-5-Styrylpyrrolidin-2-one (27)

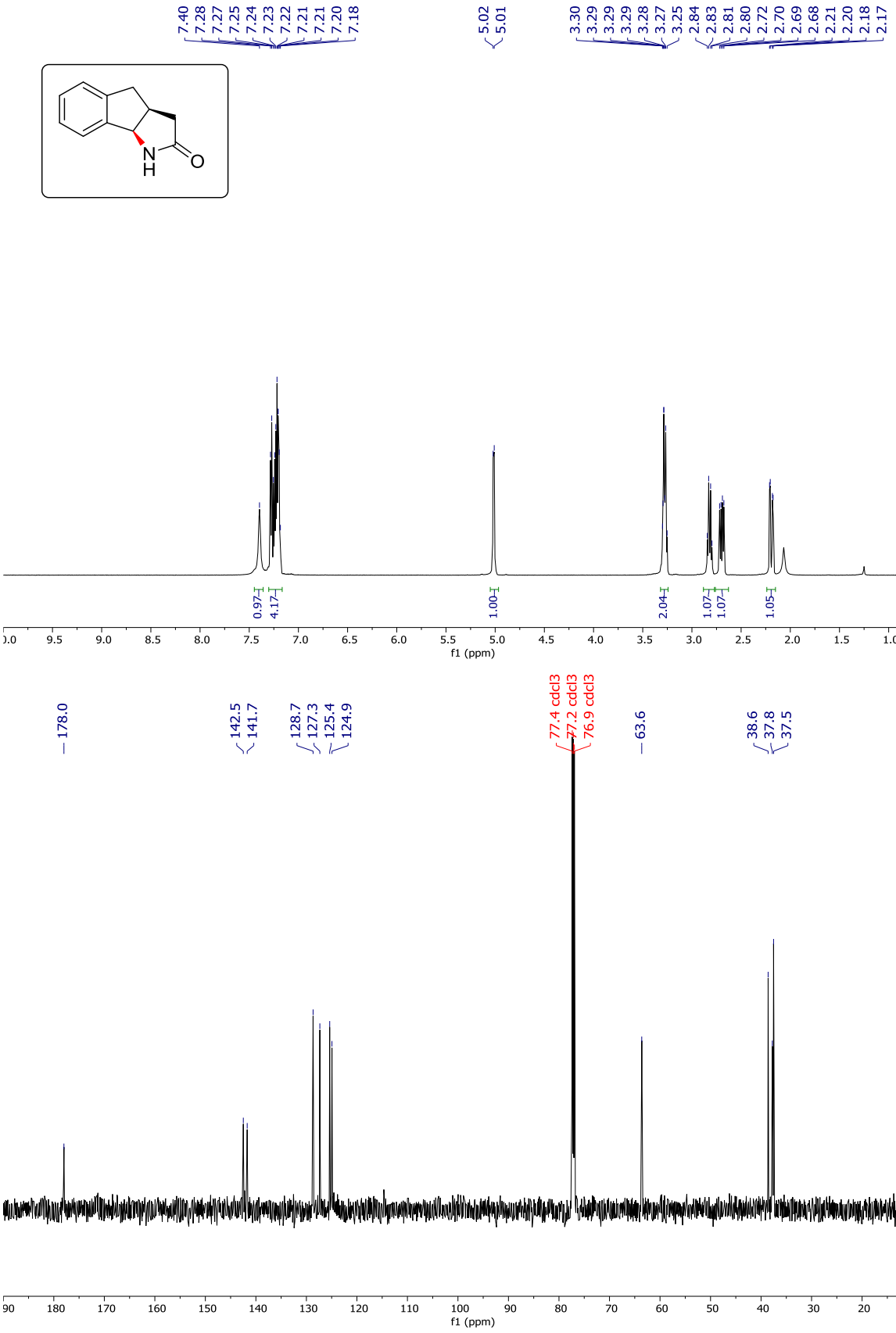




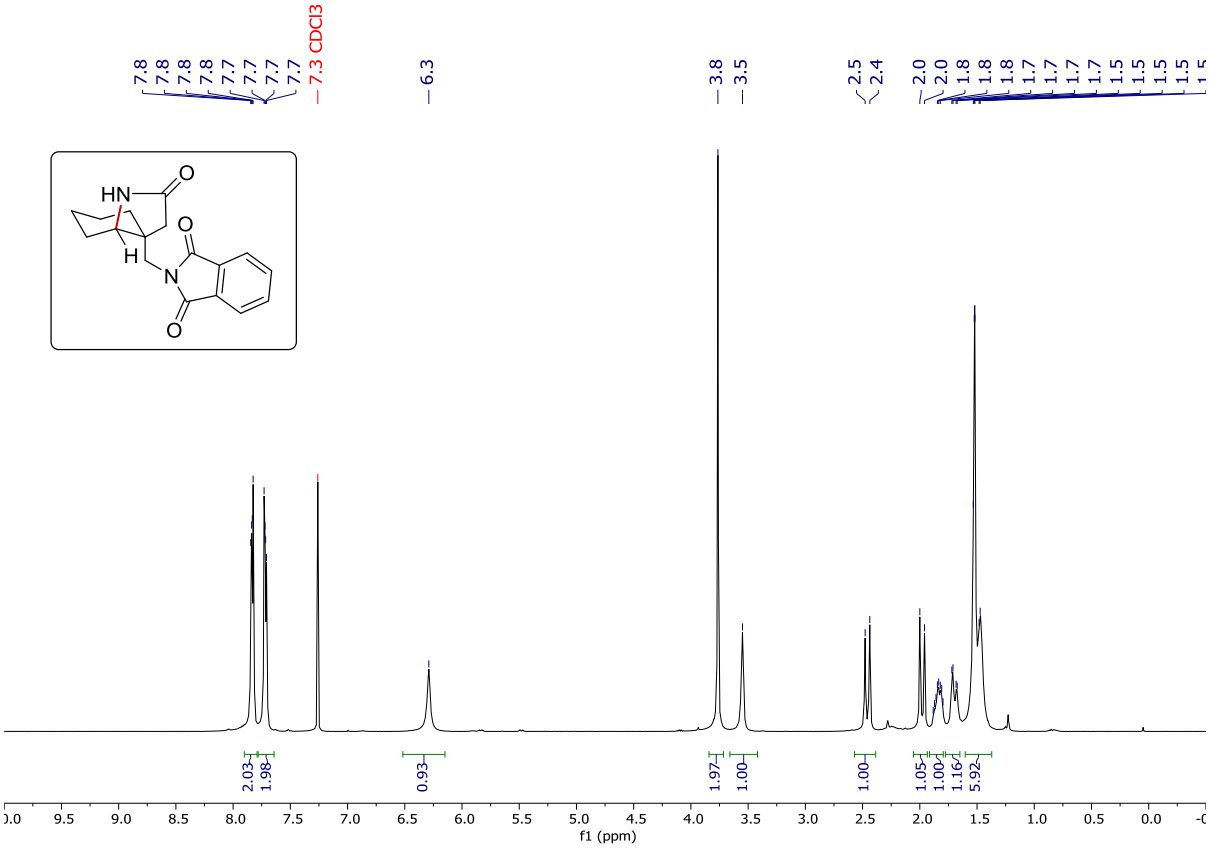
anti-4-Benzyl-5-phenylpyrrolidin-2-one (28)

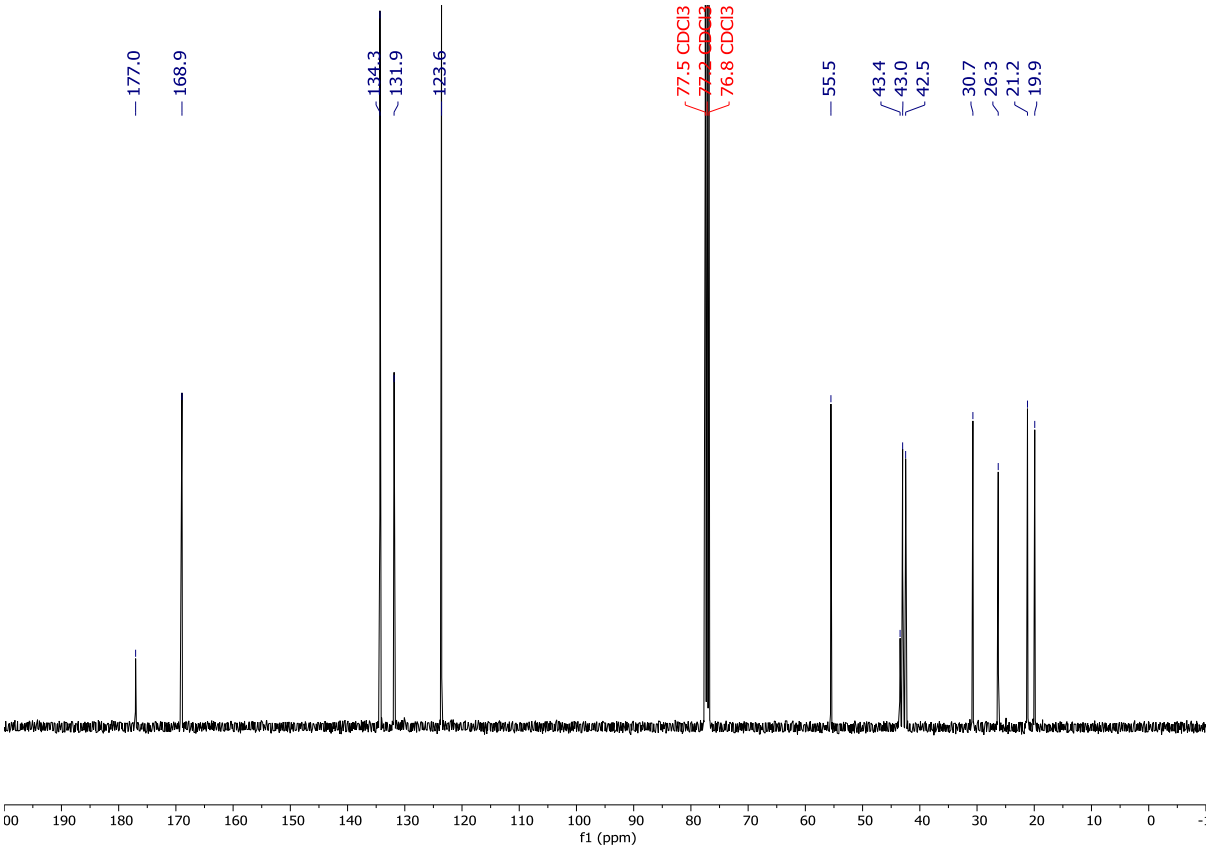


syn-3,3a,4,8b-Tetrahydroindeno[1,2-b]pyrrol-2(*1H*)-one (29)

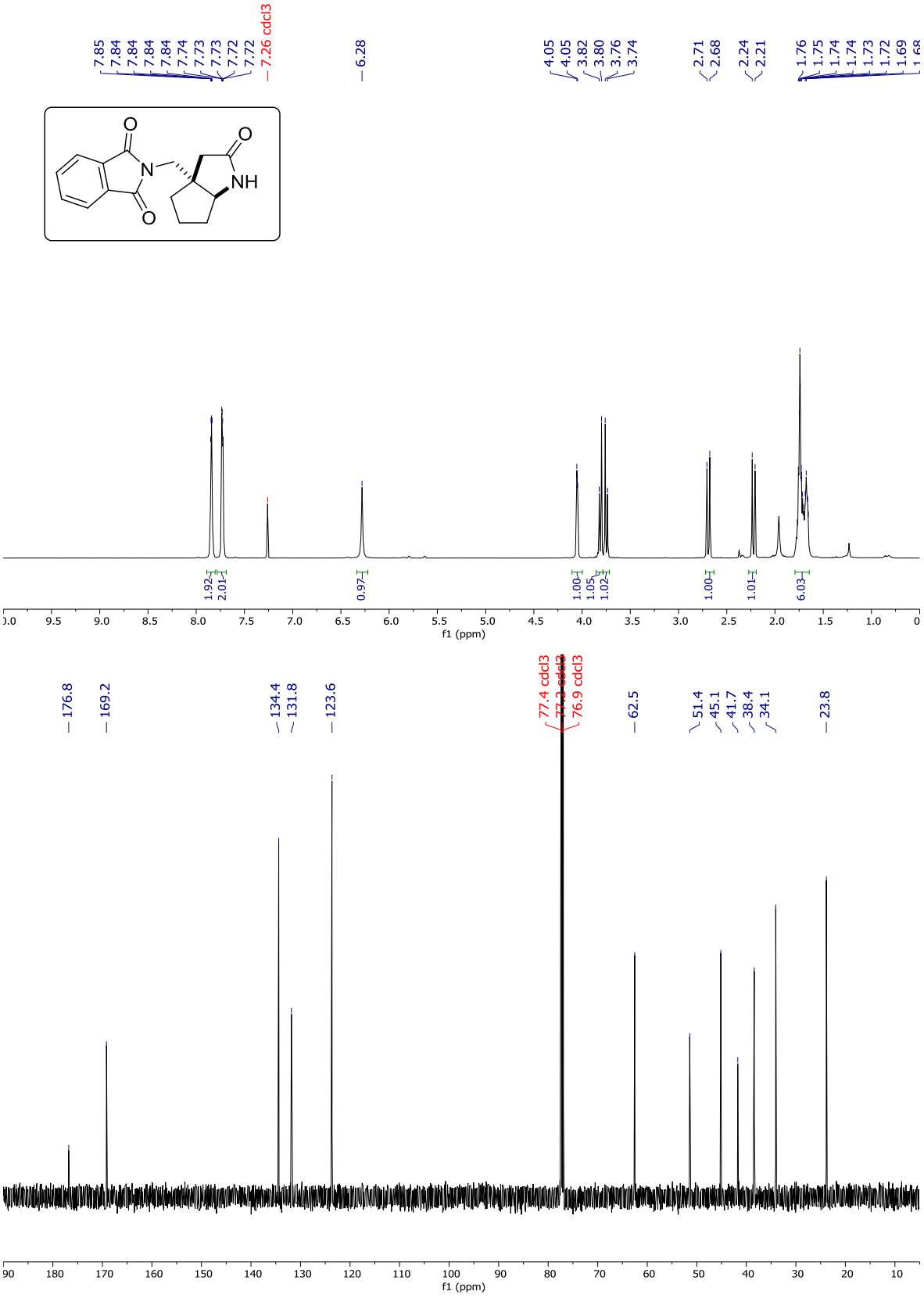


2-{(2-Oxooctahydro-3aH-indol-3a-yl)methyl}isoindoline-1,3-dione (30)

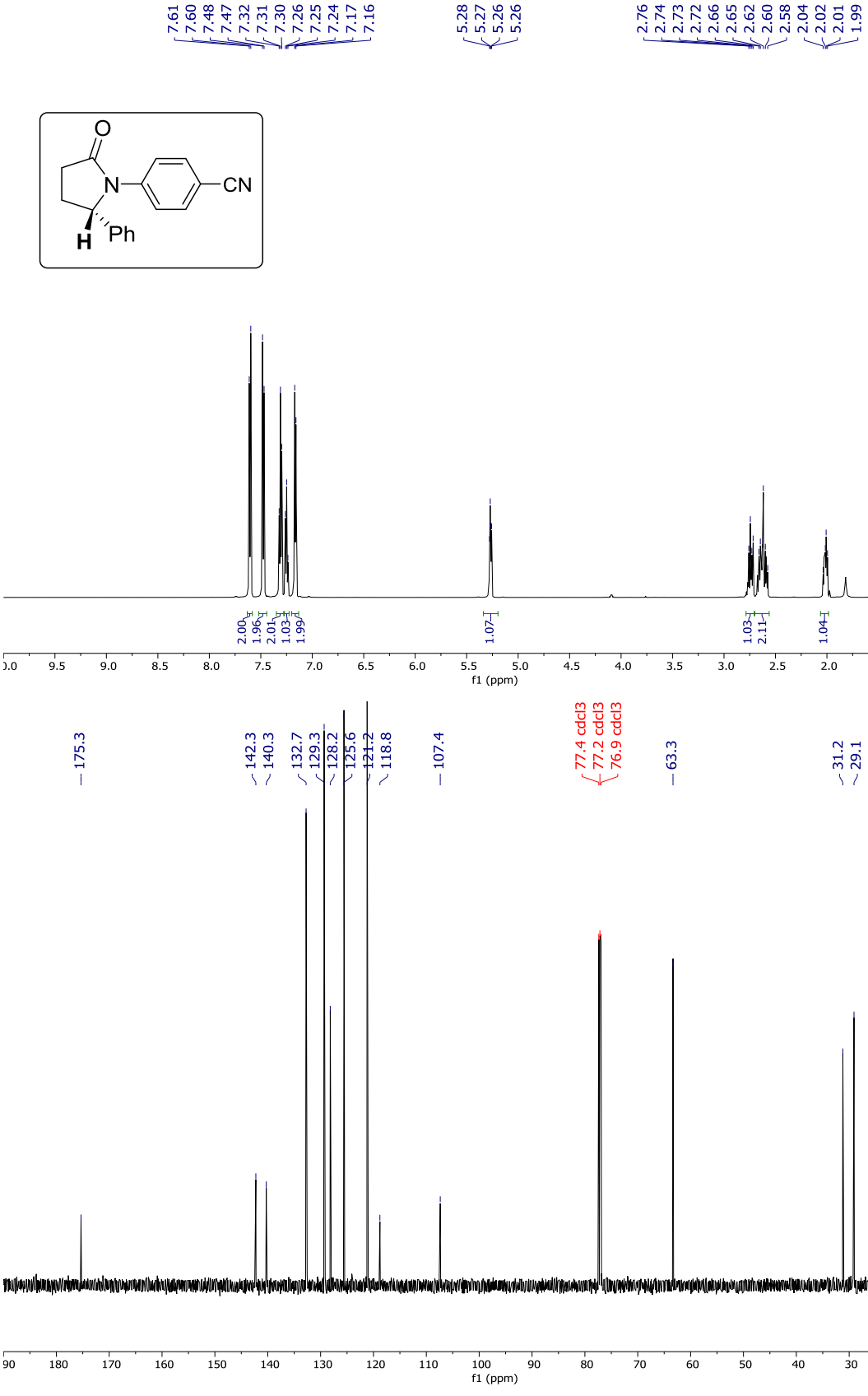




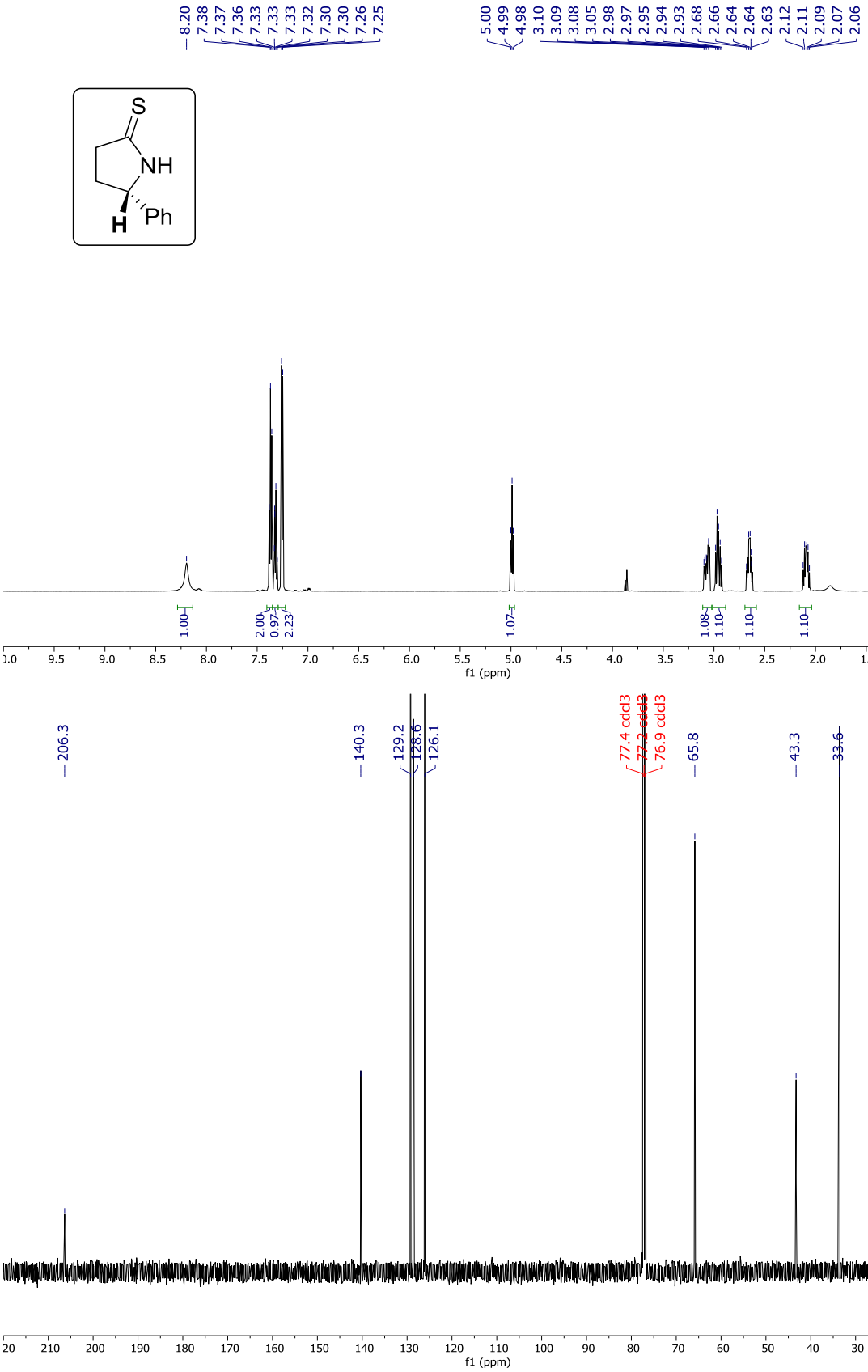
2-[{*syn*-2-Oxohexahydrocyclopenta[b]pyrrol-3a(*1H*)-yl}methyl]isoindoline-1,3-dione (31)



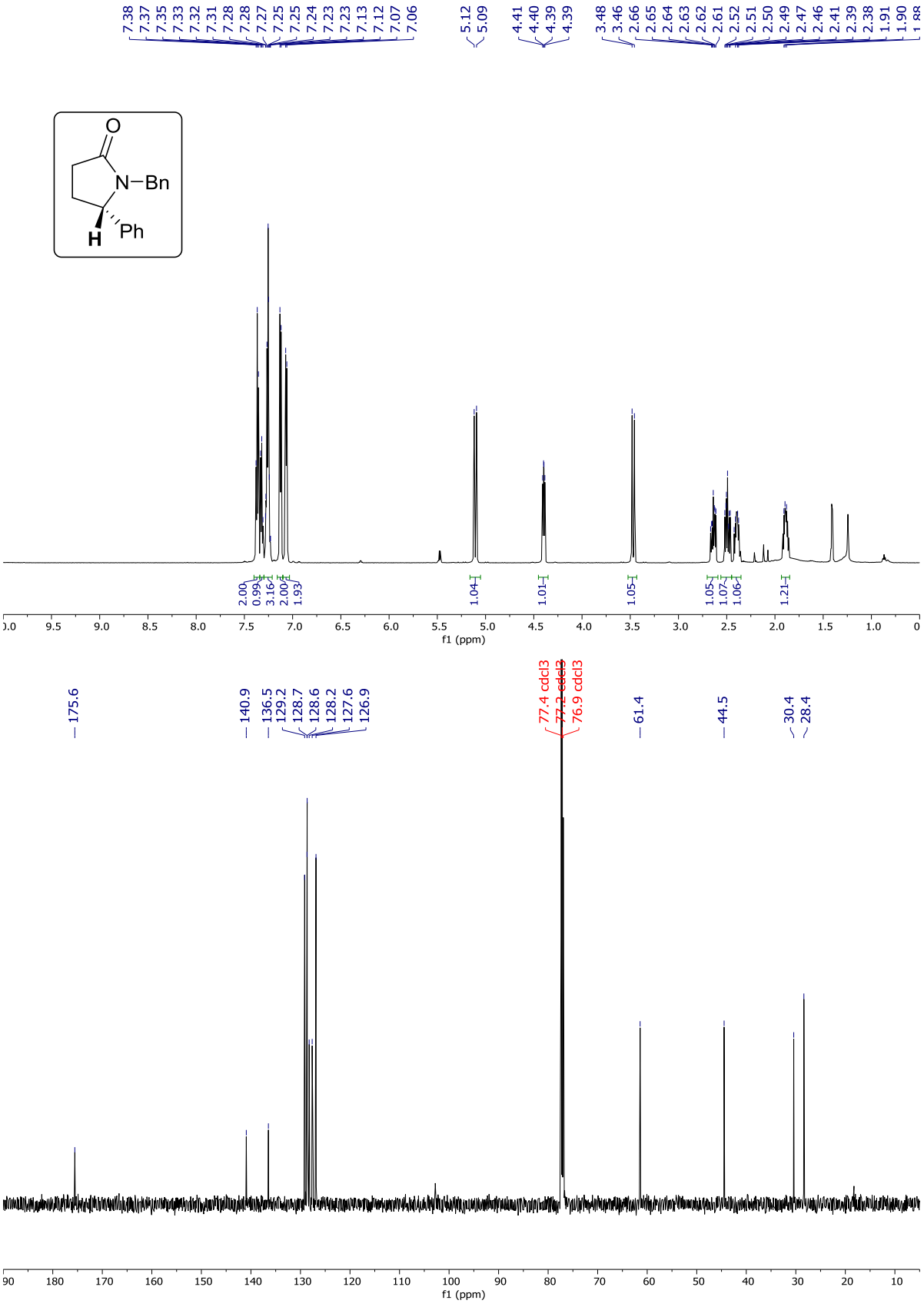
4-(2-Oxo-5-phenylpyrrolidin-1-yl)benzonitrile (32)



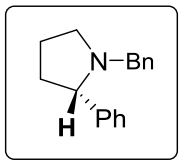
5-Phenylpyrrolidine-2-thione (33)

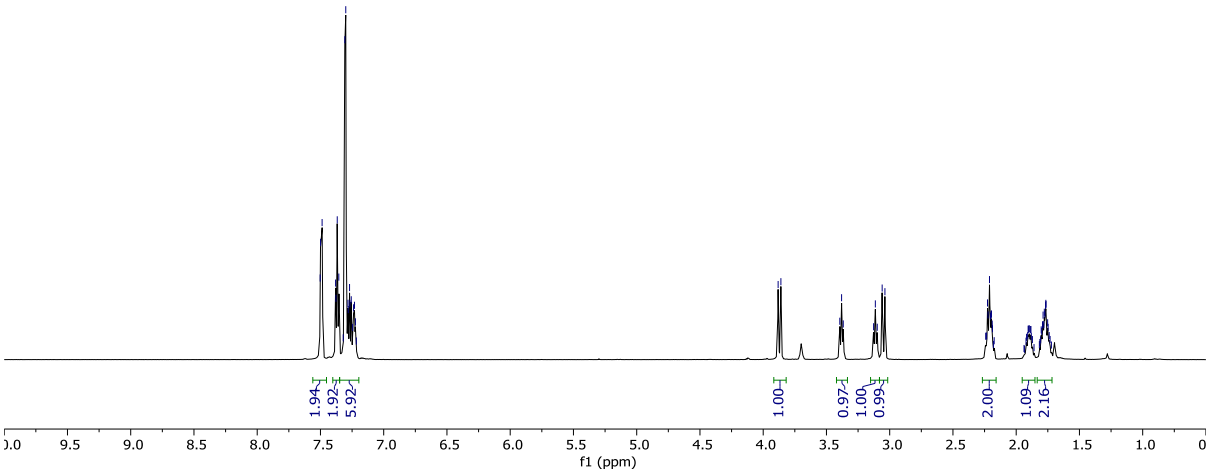


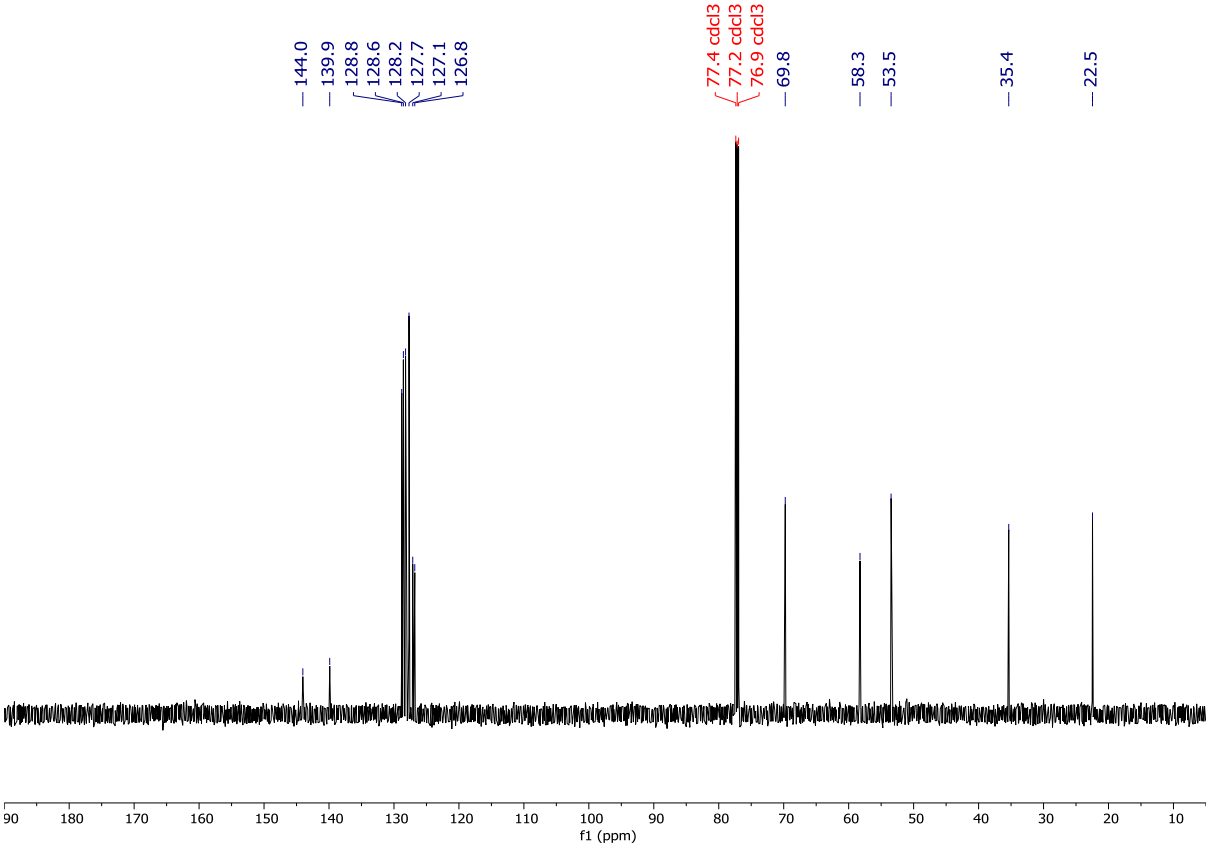
N-Benzyl-5-phenylpyrrolidin-2-one



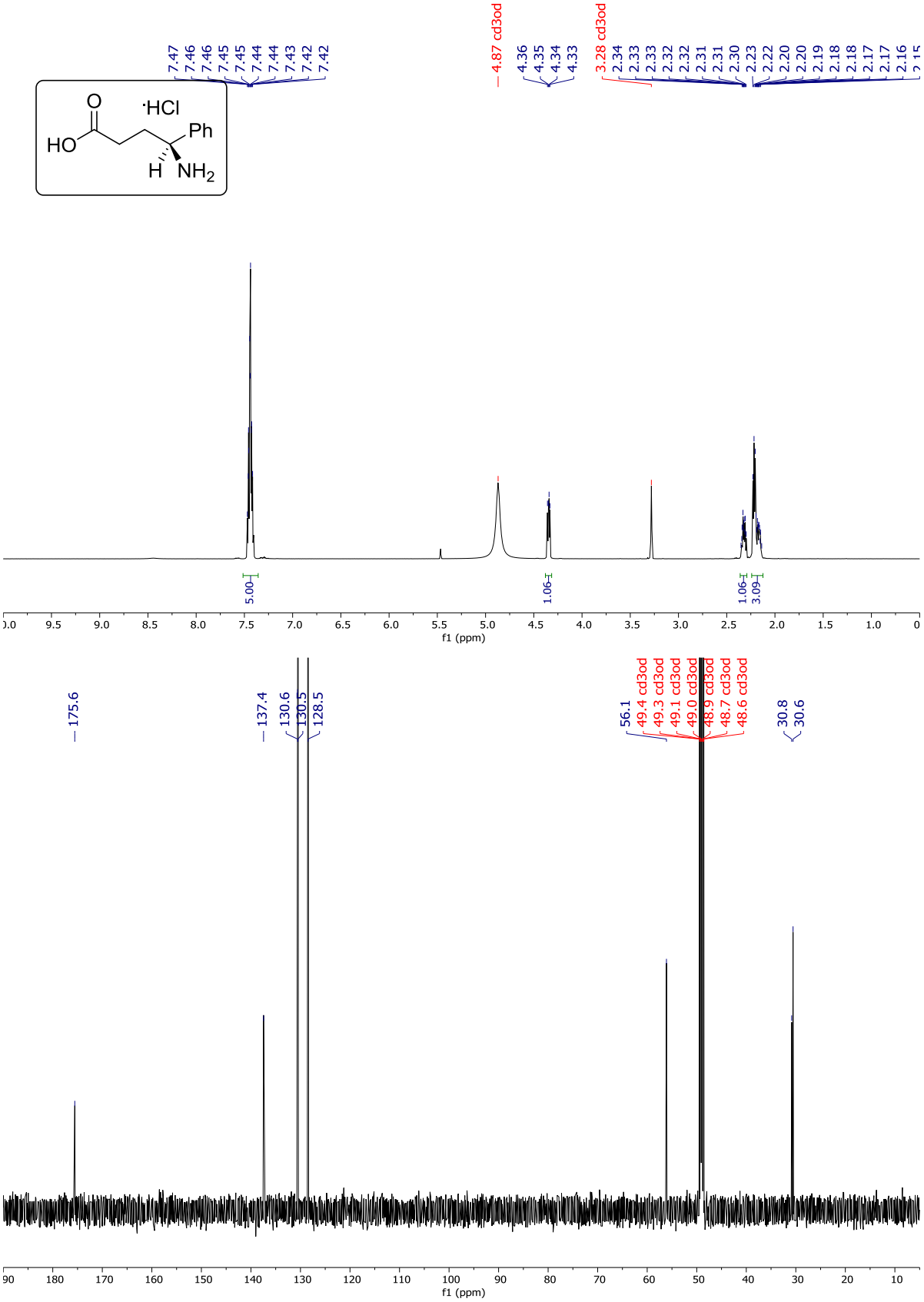
N-Benzyl-2-phenylpyrrolidine (34)



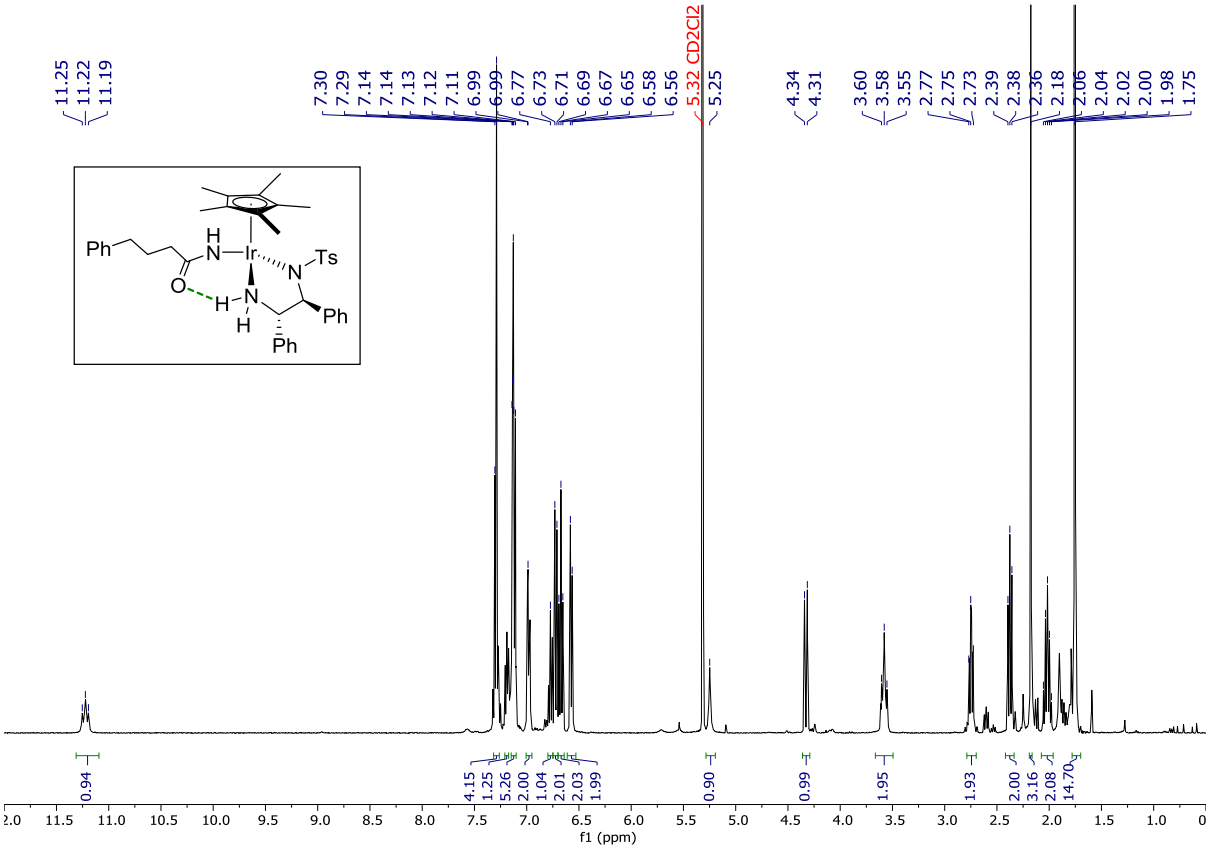




4-Amino-4-phenylbutanoic acid hydrochloride (35)



Ir12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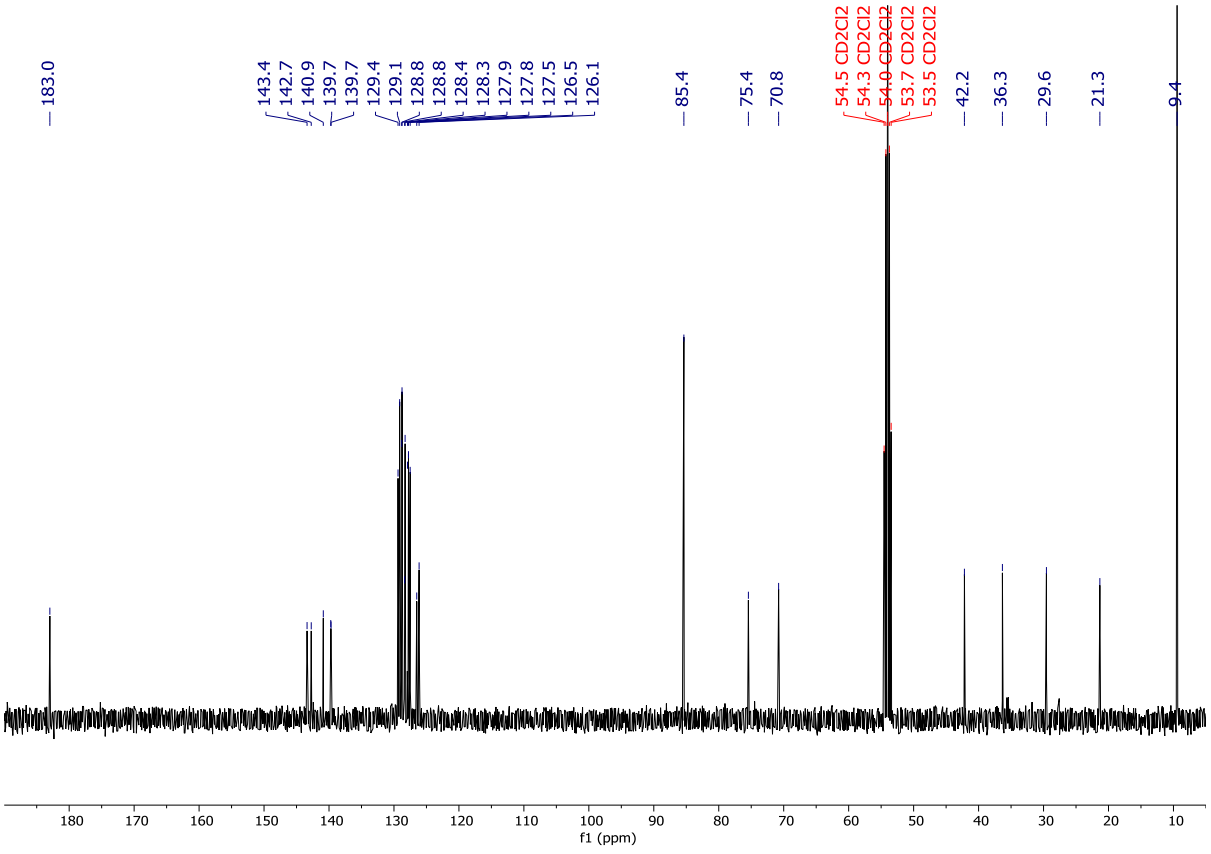
11.22
11.19
7.30
7.29
7.14
7.14
7.13
7.12
7.11
6.99
6.99
6.77
6.73
6.71
6.69
6.67
6.65
6.58
6.56
5.32 CD2Cl2
5.25
4.34
4.31
3.60
3.58
3.55
2.77
2.75
2.73
2.39
2.38
2.36
2.18
2.06
2.04
2.02
2.00
1.98
1.75
Ph
H
N
Ir
N
Ts
O
H
N
H
Ph
Ph
0.94
4.15
1.25
5.26
2.00
1.04
2.01
2.03
1.99
0.90
0.99
1.95
1.93
2.00
3.16
2.08
14.70
f1 (ppm)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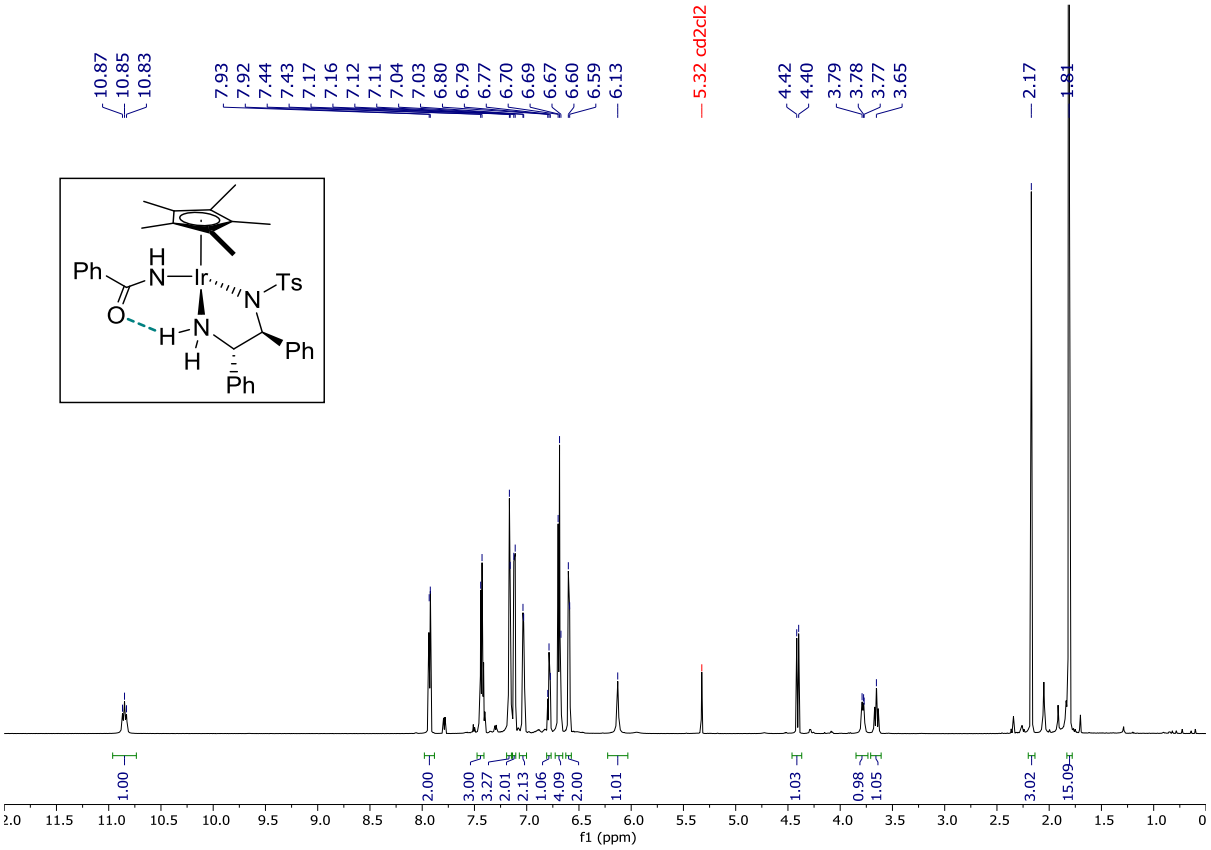
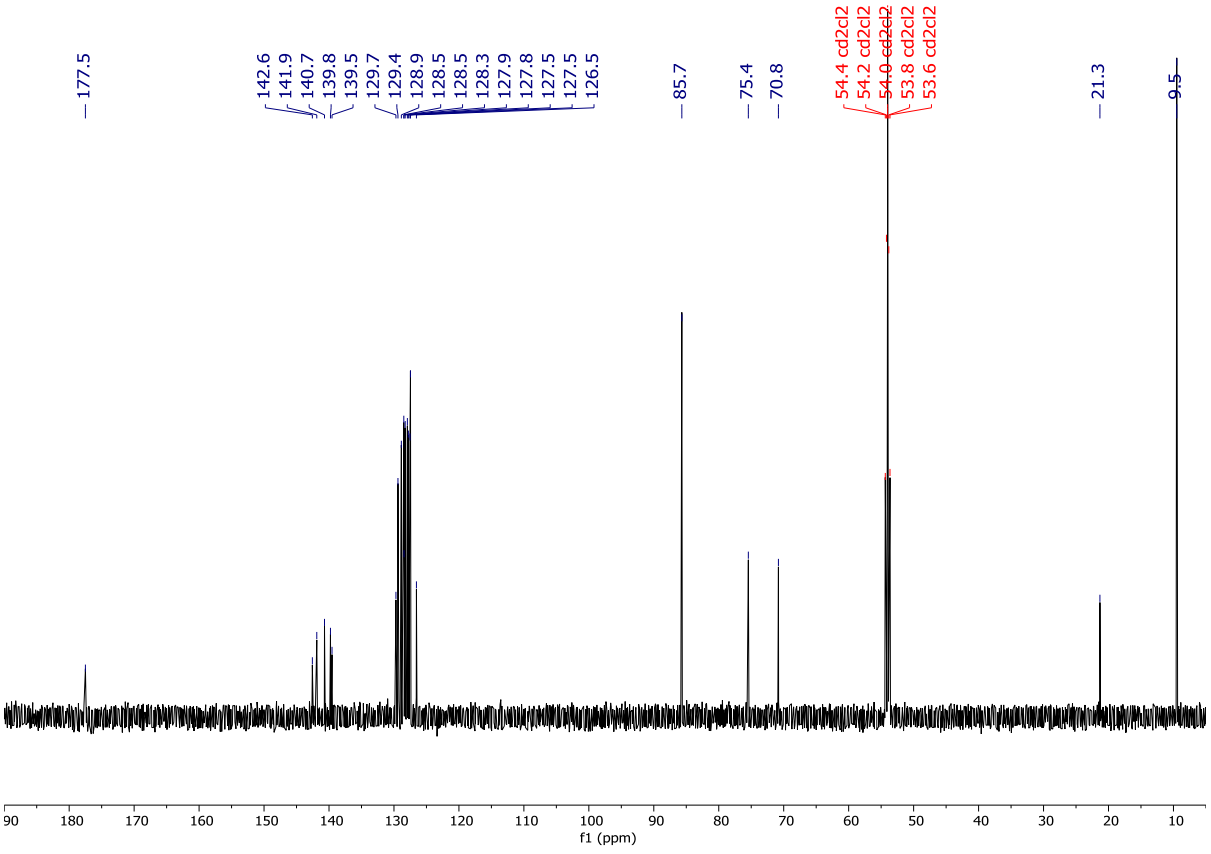
142.7
140.9
139.7
139.7
129.4
129.1
128.8
128.8
128.4
128.3
127.9
127.8
127.5
126.5
126.1
85.4
75.4
70.8
54.5 CD2Cl2
54.3 CD2Cl2
54.0 CD2Cl2
53.7 CD2Cl2
53.5 CD2Cl2
42.2
36.3
29.6
21.3
9.4
f1 (ppm)

Ir13


10.87
10.85
10.83
7.93
7.92
7.44
7.43
7.17
7.16
7.12
7.11
7.04
7.03
6.80
6.79
6.77
6.70
6.69
6.67
6.60
6.59
6.13
5.32 cd2cl2
4.42
4.40
3.79
3.78
3.77
3.65
2.17
1.81
Ph
H
N
Ir
Ts
N
O
H
N
H
Ph
Ph
1.00
2.00
3.00
3.27
2.01
2.13
1.06
4.09
2.00
1.01
1.03
0.98
1.05
3.02
15.09
f1 (ppm)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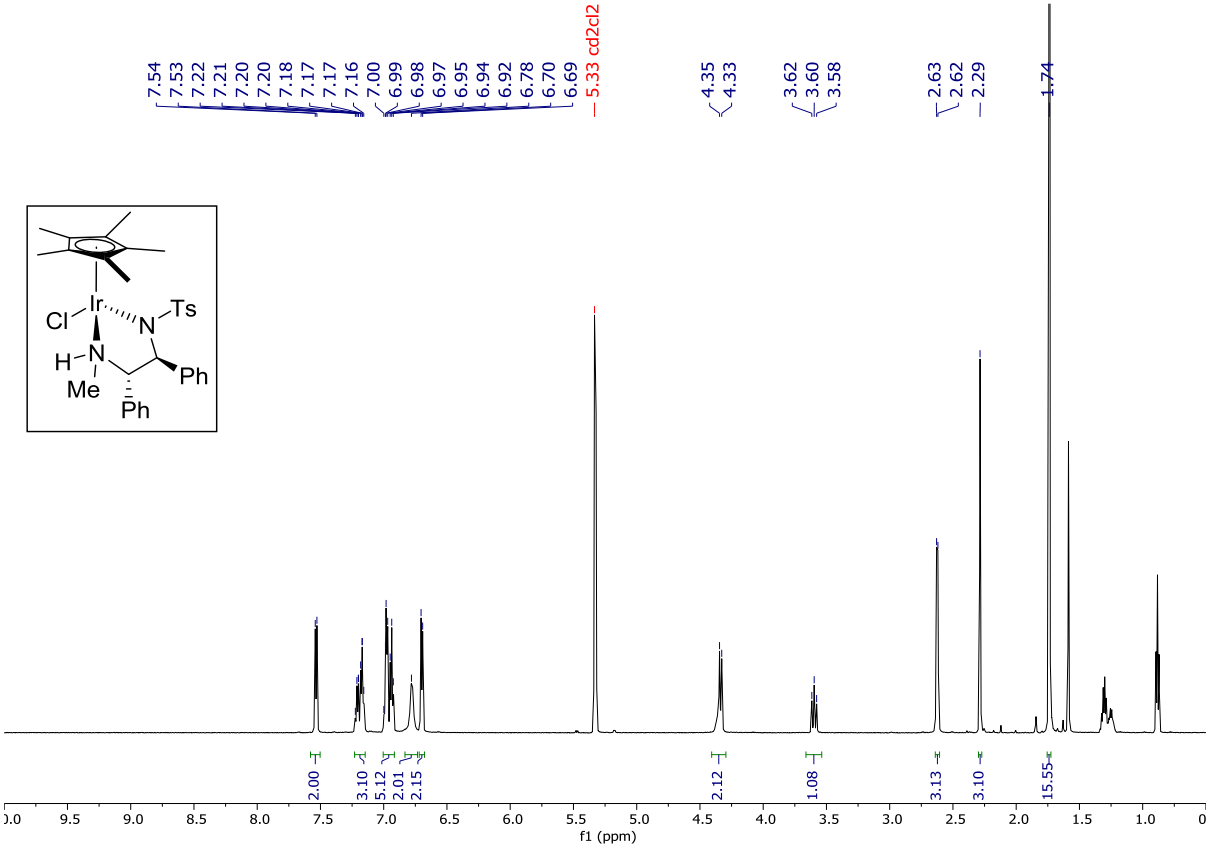
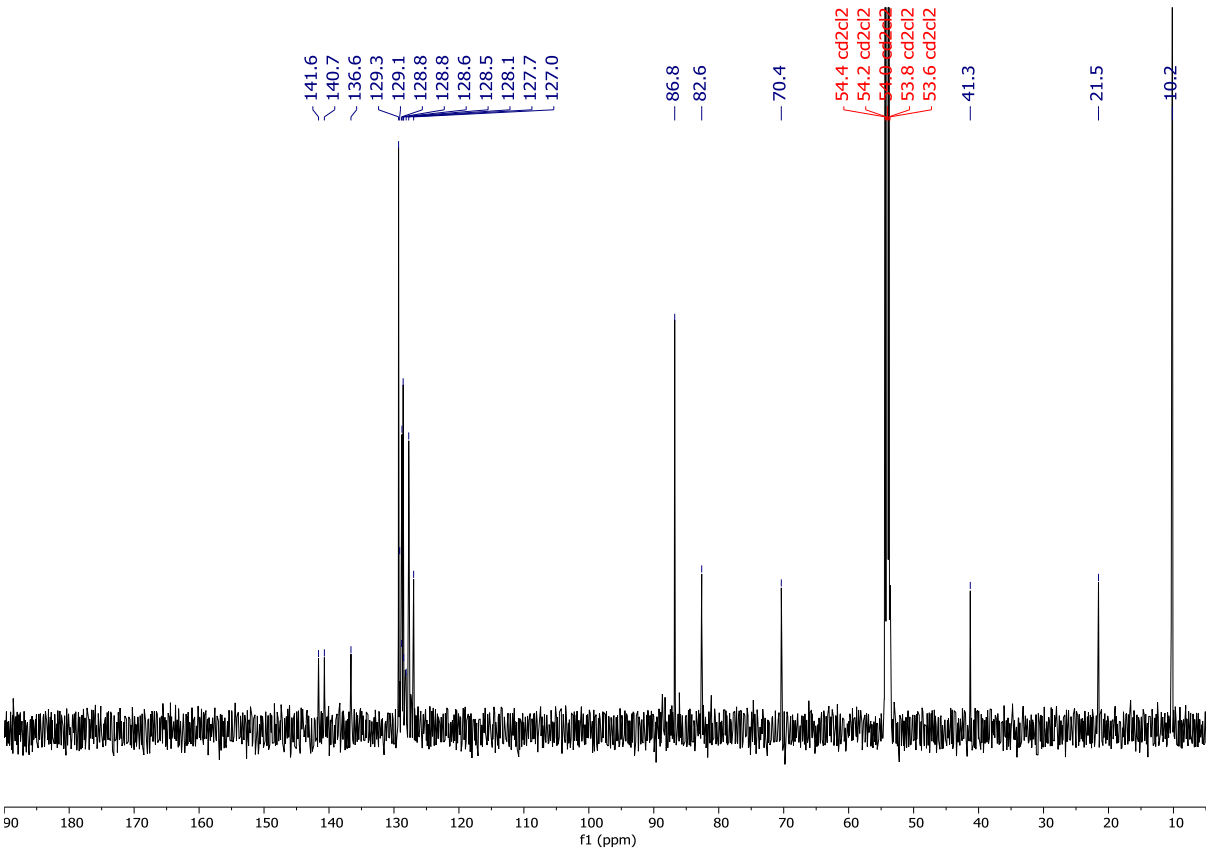
141.9
140.7
139.8
139.5
129.7
129.4
128.9
128.5
128.5
128.3
127.9
127.8
127.5
127.5
126.5
85.7
75.4
70.8
54.4 cd2cl2
54.2 cd2cl2
54.0 cd2cl2
53.8 cd2cl2
53.6 cd2cl2
21.3
9.5
f1 (ppm)

Ir14


7.54
7.53
7.22
7.21
7.20
7.20
7.18
7.17
7.17
7.16
7.00
6.99
6.98
6.97
6.95
6.94
6.92
6.78
6.70
6.69
5.33 cd2cl2
4.35
4.33
3.62
3.60
3.58
2.63
2.62
2.29
1.74
Cl
Ir
N
Ts
H
N
Me
Ph
Ph
2.00
3.10
5.12
2.01
2.15
2.12
1.08
3.13
3.10
15.55
f1 (ppm)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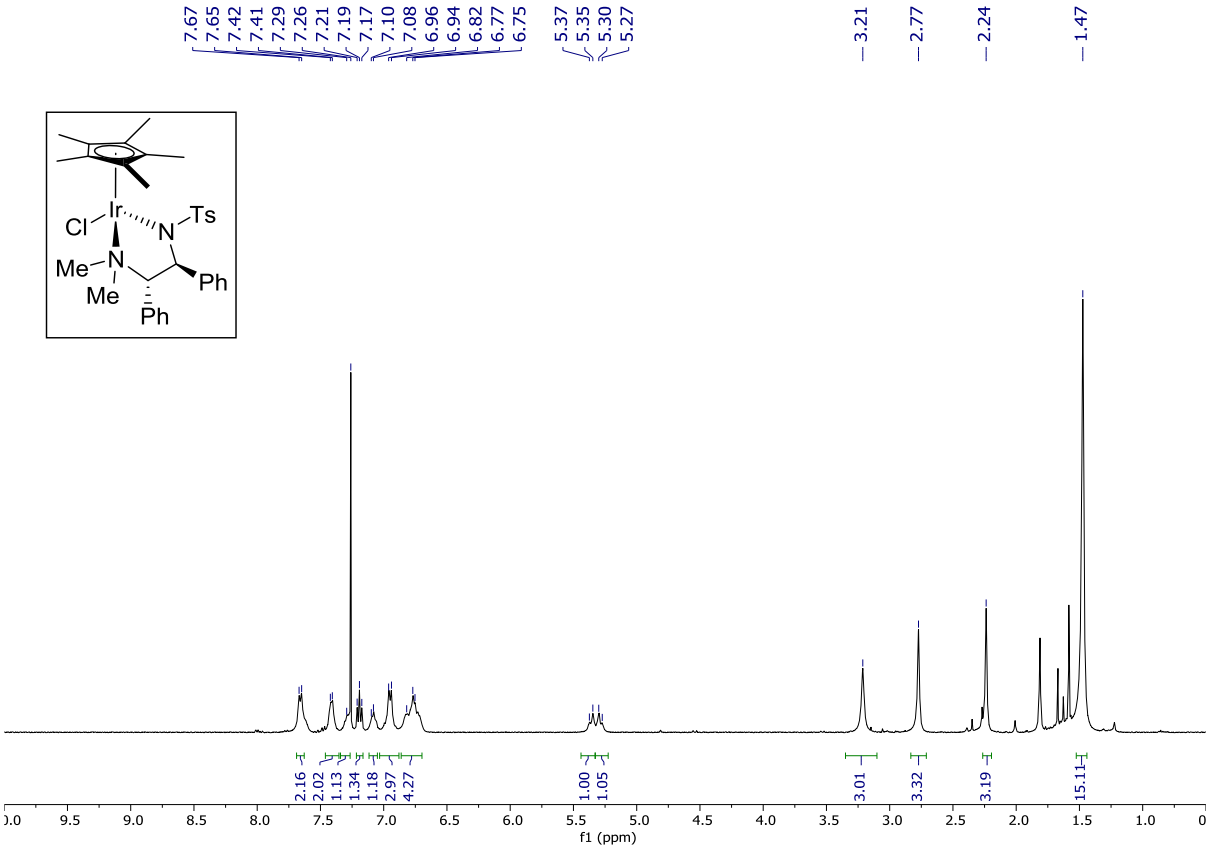
140.7
136.6
129.3
129.1
128.8
128.8
128.6
128.5
128.1
127.7
127.0
86.8
82.6
70.4
54.4 cd2cl2
54.2 cd2cl2
54.0 cd2cl2
53.8 cd2cl2
53.6 cd2cl2
41.3
21.5
19.2
f1 (ppm)

Ir15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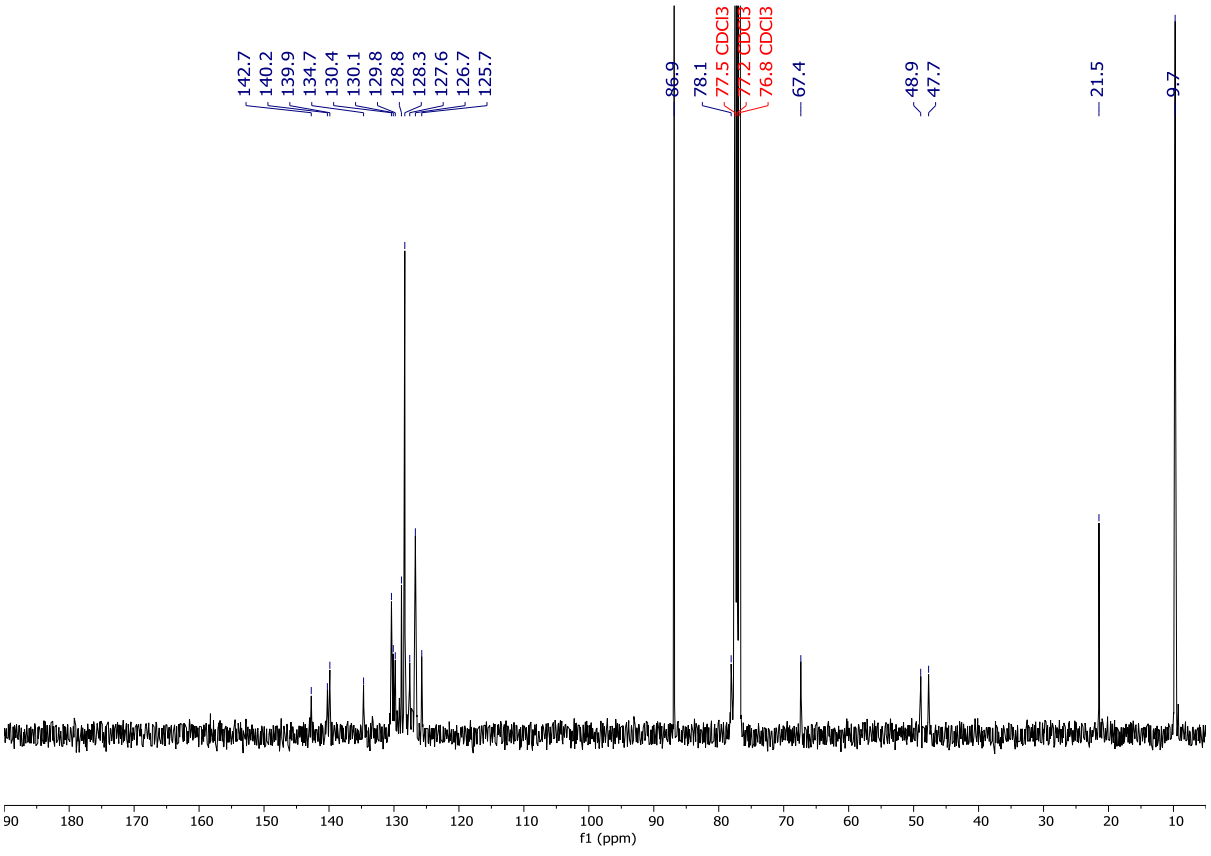
7.65
7.42
7.41
7.29
7.26
7.21
7.19
7.17
7.10
7.08
6.96
6.94
6.82
6.77
6.75
5.37
5.35
5.30
5.27
3.21
2.77
2.24
1.47
Cl
Ir
N
Ts
Me
N
Me
Ph
Ph
2.16
2.02
1.13
1.34
1.18
2.97
4.27
1.00
1.05
3.01
3.32
3.19
15.11
f1 (ppm)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140.2
139.9
134.7
130.4
130.1
129.8
128.8
128.3
127.6
126.7
125.7
86.9
78.1
77.5 CDCl3
77.2 CDCl3
76.8 CDCl3
67.4
48.9
47.7
21.5
9.7
f1 (ppm)