Electronic Supplementary Material (ESI) for RSC Advances.

Development of Fluorous Boronic Acid Catalysts Integrated with Sulfur for Enhanced Amidation Efficiency

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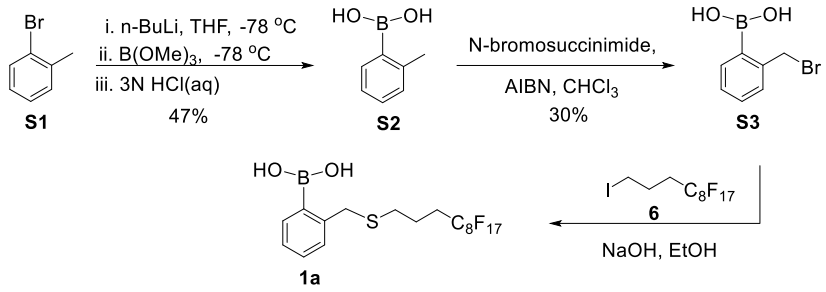
Synthesis of Fluorous Boronic Acid Catalyst 1a



Unless otherwise stated, all starting materials and chemical reagents were purchased from Acros, Fluorochem, Sigma-Aldrich, Strem or TCI and used without further purification. Moisture-sensitive reactions were carried out under nitrogen atmosphere with commercially obtained anhydrous solvents. Analytical thin-layer chromatography (TLC) was carried out on precoated plates (Merck silica gel 60, F254) and visualized with UV light (254 nm) and/or stained with the appropriate staining reagents (described in the reaction procedure below). Purification by column chromatography was performed with either Kieselgel 60 silica gel (Merck, 70-230 mesh or 230 – 400 mesh). NMR spectra (^{1}H and ^{13}C), while purification by fluorous solid-phase extraction (F-SPE) was performed using FluoroFlash® F-SPE cartridges (10g, 60 mL tube) that was commercially available and pre-packed in a proprietary silica gel bonded with perfluoroalkyl chains. ^{1}H NMR (400 MHz). ^{13}C NMR (100 MHz), ^{19}F NMR (376 MHz) and ^{11}B NMR (128 MHz) were recorded at 298 K on a Bruker AVIII (400 MHz) or Bruker DPX (400 MHz) Fourier Transform spectrometer. Chemical shifts are expressed in terms of δ (ppm) relative to δ_H 7.26/ δ_X 77.0 for $CDCl_3$, δ_H 3.31/ δ_X 49.00 for CD_3OD and δ_H 2.50/ δ_X 39.52 for DMSO-*d*$_6$. Coupling constants (*J*) are given in hertz (Hz) and the splitting patterns are reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Infrared spectroscopy (IR) spectra were obtained using Varian 640 FT-IR instrument by applying 1% of sample with KBr. IR absorption data are reported in cm^{-1}. Electrospray ionization high resolution mass spectrometry (ESI-HRMS) data were obtained on Waters LCT Premier XE mass spectrometer. Melting points were recorded uncorrected on Fisher-Johns melting point apparatus from Fischer Scientific.

o-tolylboronic acid (S2): To a stirred solution of 2-bromotoluene **S1** (5.0 g, 29.2 mmol) in 60 ml anhydrous THF was added n-BuLi (2.5 M in hexanes, 17.5 mL, 43.8 mmol) dropwise at -78 °C. The pale yellow reaction mixture was then stirred for 60 min under argon atmosphere, while the temperature was raised slowly to -60 °C. The temperature was decreased to -78 °C again and trimethyl borate (9.8 mL, 87.7 mmol) was added dropwise. The resulting solution was allowed to warm slowly to room temperature and stirred for another 60 min. The cloudy white mixture was acidified with 1 M HCl (aq) (8 mL) and stirred for 30 min at room temperature. The mixture was then extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. A minimum amount of CH_2Cl_2 (5 mL) was added to dissolve the mixture

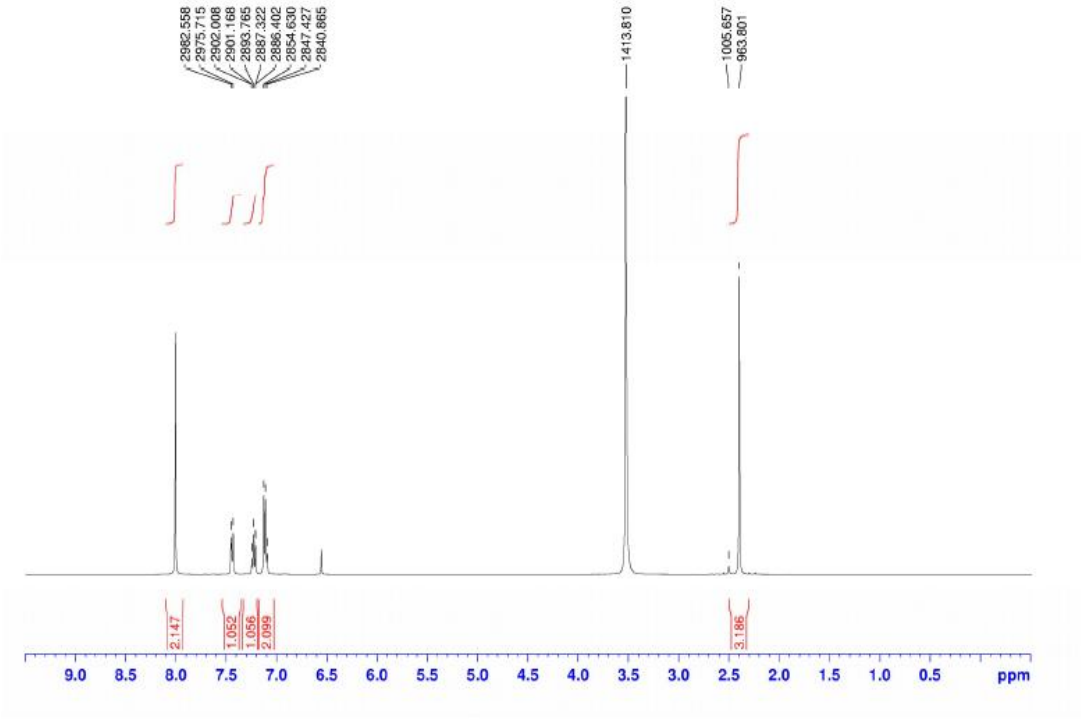
and precipitation from excess hexanes yielded the desired pure product as a white solid (1.9 g, 47%). R_f = 0.20 (hexane:EtOAc = 8:2, UV, PMA). Mp = 162-164 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.87 (d, *J* = 7.4 Hz, 1H), 7.27-7.23 (m, 1H), 7.17-7.13 (m, 2H), 2.65 (s, 3H) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 141.5 (C), 133.5 (CH), 129.6 (CH), 129.2 (CH), 124.8 (CH), 22.6 (CH_3) ppm. Boron-bound carbon was not detected due to quadrupolar relaxation. ^{11}B NMR (128 MHz, DMSO-d_6): δ 30.4 (s, 1B) ppm. IR (KBr): 3073, 3285, 1600, 1446, 1360, 1138, 1101, 1020, 828, 731, 645, 604 cm^{-1}. EI-TOF-MS for $C_7H_9O_2B$ (M^+) cald. 103.0696, found 136.06092.

(2-(bromomethyl)phenyl)boronic acid (S3). A mixture of *o*-tolylboronic acid **S2** (501 mg, 3.7 mmol) azobisisobutyronitrile (12.1 mg, 0.071 mmol) and N-bromosuccinimide (787.1 mg, 4.4 mmol, recrystallizaed from hot water) in $CHCl_3$ (53 mL) was refluxed for 2 h under argon atmosphere. The resulting yellow rection mixture was cooled to room temperature and evaporated to dryness under reduced pressure. The crude product was dissolved in a minimum amount of $CHCl_3$ (2 mL) and precipitation from excess hexanes yielded (2-(bromomethyl)phenyl)boronic acid **S3** as a pale yellow solid (238 mg, 30%). R_f = 0.18 (hexane:EtOAc = 8:2, UV, PMA). Mp = 153-155 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.74 (d, *J* = 7.3 Hz, 1H), 7.49-7.45 (m, 1H), 7.41-7.39 (m, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 4.96 (s, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.3 (C), 131.0 (CH), 130.9 (CH), 127.2 (CH), 121.8 (CH), 70.4 (CH_2) ppm. Boron-bound carbon was not detected due to quadrupolar relaxation. ^{11}B NMR (128 MHz, DMSO-d_6): δ 29.0 (s, 1B) ppm. IR (KBr): 3354, 3297, 1749, 1724, 1606, 1445, 1344, 1213, 1083, 1017, 809, 760, 690, 600 cm^{-1}. EI-TOF-MS for $C_7H_8O_2{}^{79}BrB$ (M^+) cald. 213.9801, found 213.9797 and $C_7H_8O_2{}^{81}BrB$ (M^+) cald 215.9780, found 215.9774.

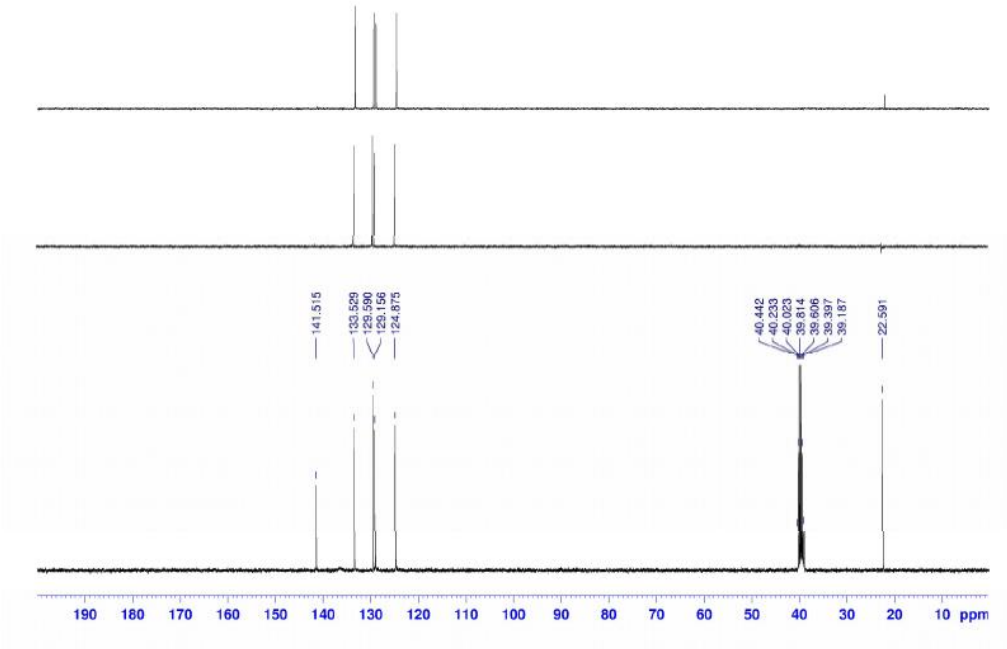
(2-(((4,4,5,5,6,6,7,7,8,8,9,9,10.10,11,11,11-heptadecafluoroundecyl)thio)methyl)phenyl)boronic acid (1a). To a stirred solution of sodium hydrosulfide (96 mg, 1.7 mmol) in EtOH (3 mL) was added to compound **6** (503 mg, 0.86 mmol) dissolved in EtOH (5 mL) dropwise and stirred at room temperature for 30 min under argon atmosphere. NaOH (342 mg, 8.6 mmol) dissolved in EtOH (5 mL) was added dropwise into the white cloudy reaction mixture and stirred at room temperature for another 15 min. Compound **S3** (205.9 mg, 0.94 mmol) dissolved in EtOH (5 mL) was added dropwise into the reaction mixture and stirred at room temperature for 17 h. After the completion of reaction, iced-cold deionized water (15 mL) was added into the mixture and the mixture was then extracted with CH_2Cl_2 (3 x 50 mL), brine (1 x 50 mL), dried over Na_2SO_4 and concentrated under reduced pressure, Crude product was purified by fluorous solid-phase extraction (F-SPE) using FluoroFlash® F-SPE cartridges (10g, 60 mL tube). The cartridge was first washed with 20% H_2O in MeOH to obtain fractions containing the organic compounds (excess (2-(bromomethyl)phenyl)boronic acid and unwanted by-products) and then washed with 100% MeOH to obtain the fractions containing fluorous compounds. Final product was obtained as a white solid (215 mg, 40%) after evaporation to dryness under vacuum. R_f = 0.25 (hexane:EtOAc = 8:2, UV, PMA). Mp = 77-78 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.02 (2, 2H, OH), 7.50-7.48 (d, *J* = 7.1 Hz, 1H), 7.27-7.18 (m, 3H), 3.94 (s, 2H), 2.48-

2.46 (m, 2H), 2.34-2.20 (m, 2H), 1.77-1.70 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 143.2 (C), 134.6 (CH), 129.2 (CH), 128.8 (CH), 126.1 (CH), 35.2 (CH_2), 29.9 (CH_2), 29.2 (t, J = 22.2 Hz, CH_2), 20.0 (CH_2) ppm. ^{19}F NMR (376 MHz, DMSO-d_6): δ -80.7 (t, J = 9.9 Hz, 3F), -113.9 - -114.1 (m, 2F), -121.7 - -121.9 (m, 6F), -122.7 (s, 2F), -123.4 (s. 2F). -126.1 (s, 2F) ppm. ^{11}B NMR (128 MHz, DMSO-d_6): δ 29.7 (s, 1B) ppm. IR (KBr): 3469, 3339, 1593, 1141, 1094, 1009, 978, 953, 802, 771, 636, 559, 530 cm^{-1}. EI-TOF-MS for $C_{18}H_{14}BO_2F_{17}S$ (M - H) cald. 627.0458, found 627.0438.

NMR Spectra of Compounds



^{1}H NMR spectrum of compound **S2**



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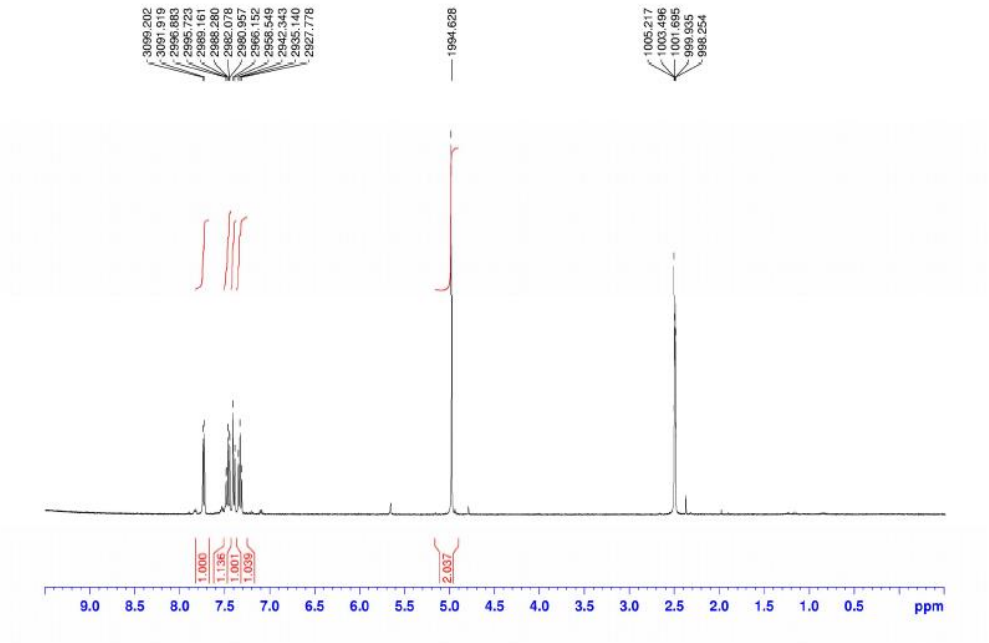
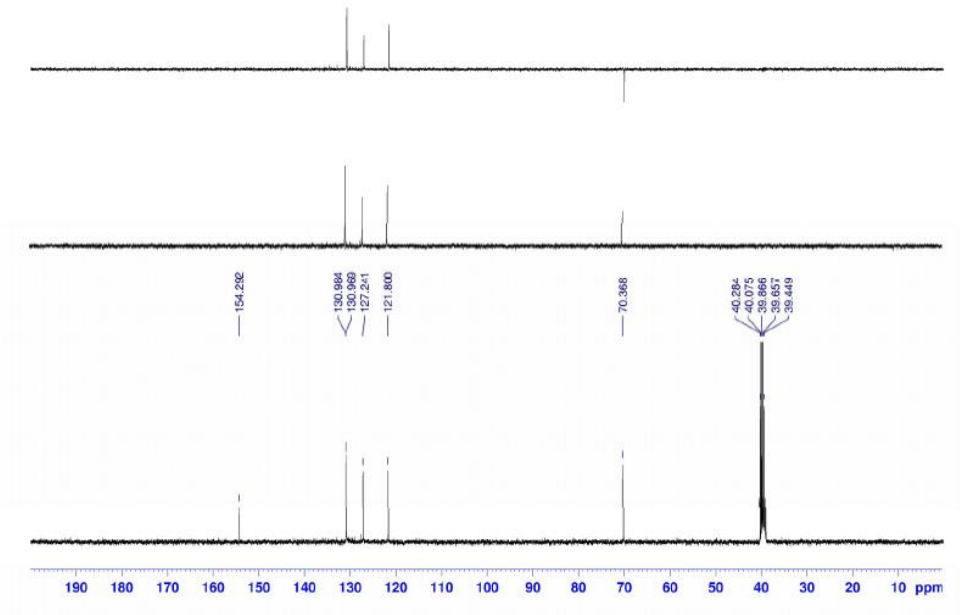
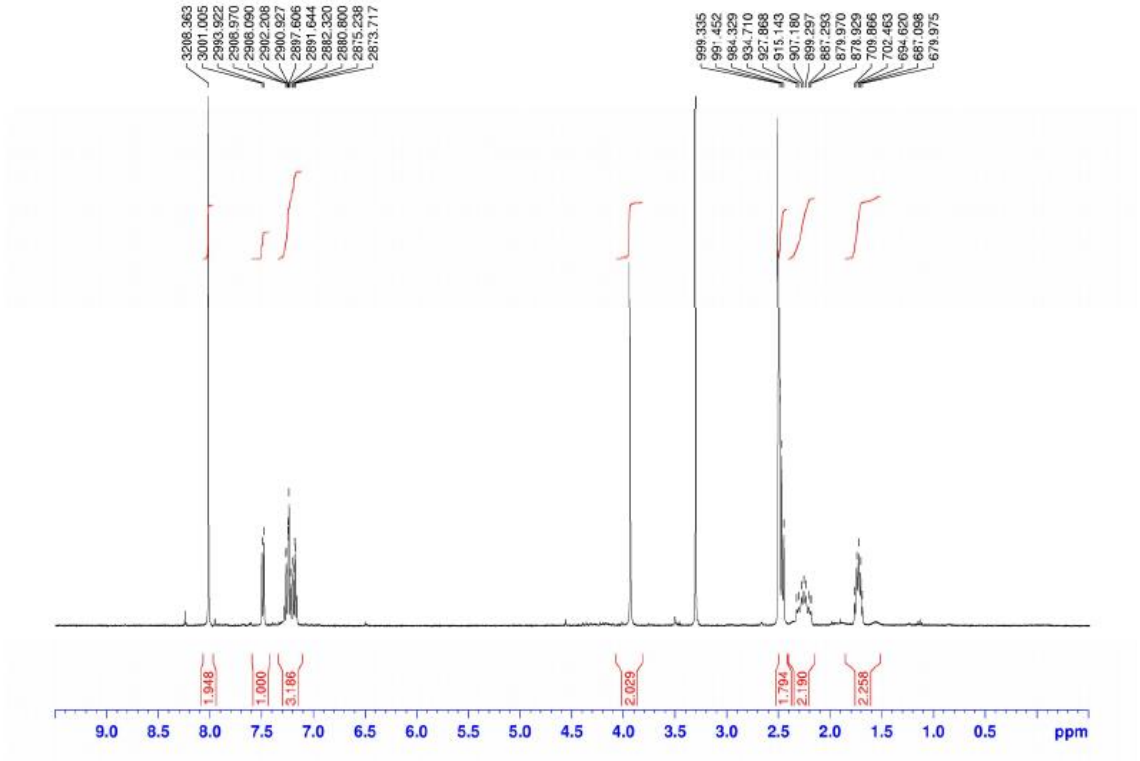


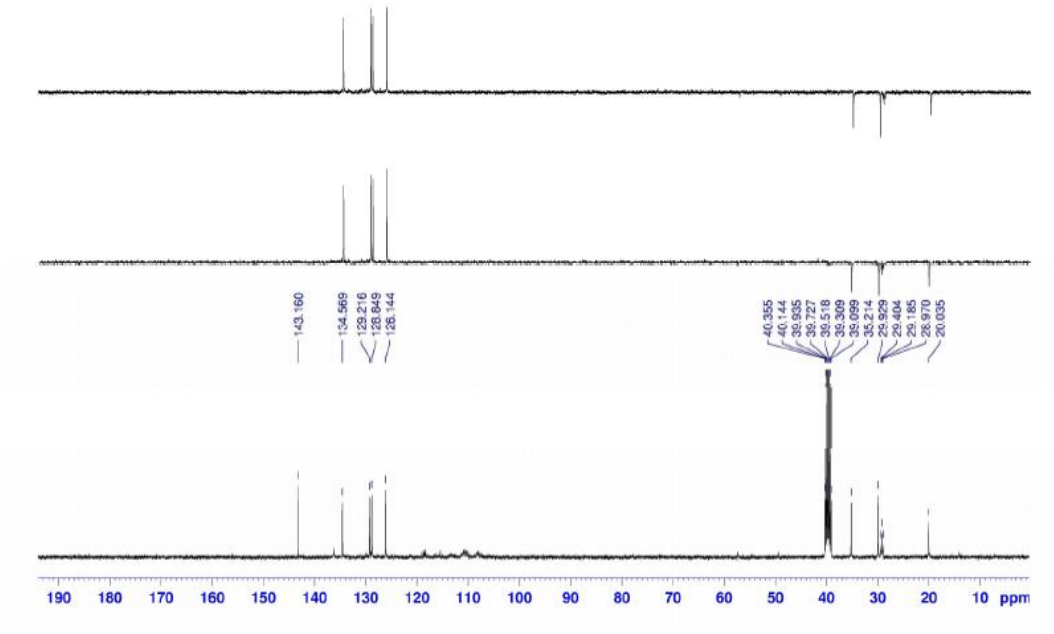
^{1}H NMR spectrum of compound **S3**



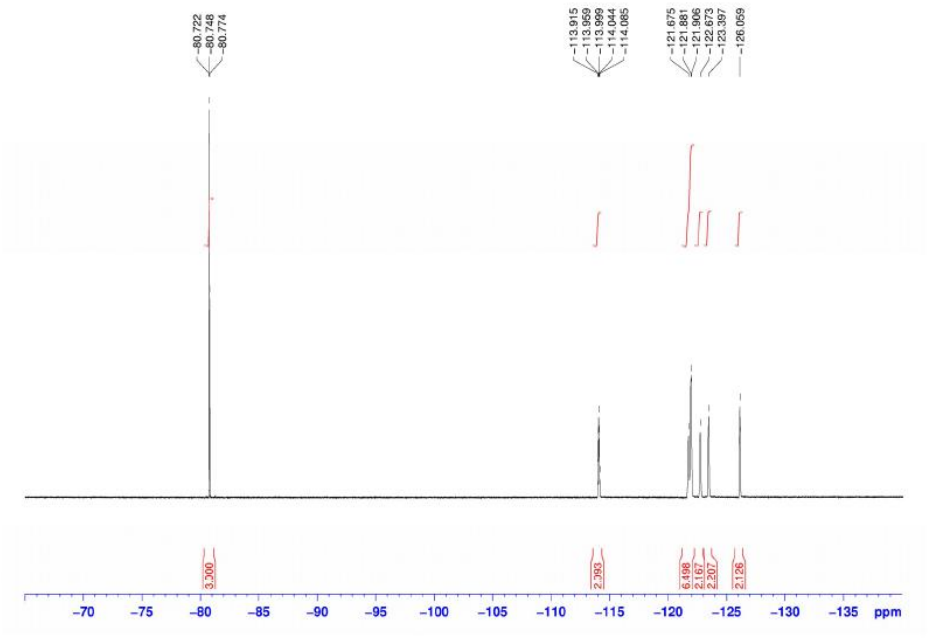
^{13}C, DEPT 90 and 135 NMR spectra of compound **S3**



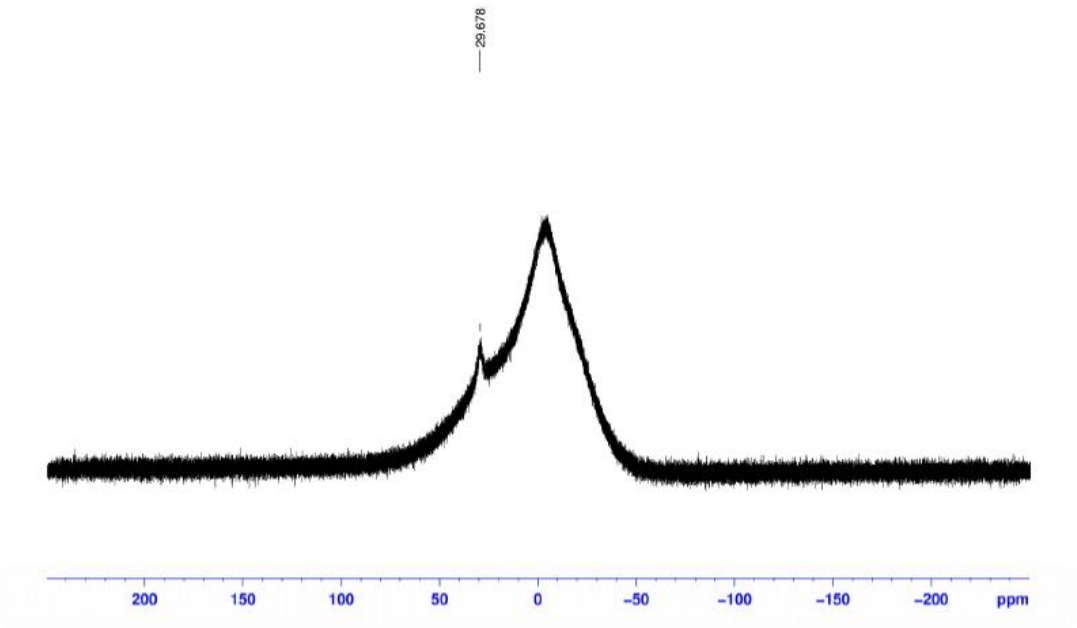
^{1}H NMR spectrum of catalyst **1a**



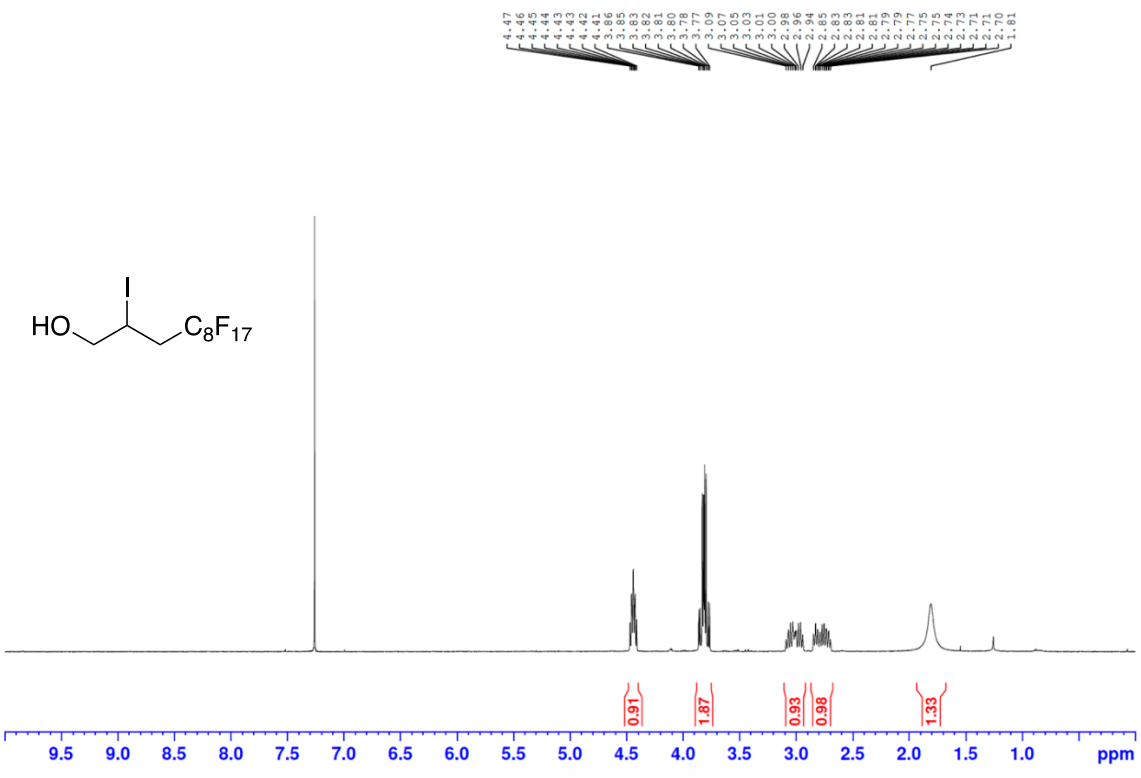
^{13}C, DEPT 90 and 135 NMR spectra of catalyst **1a**



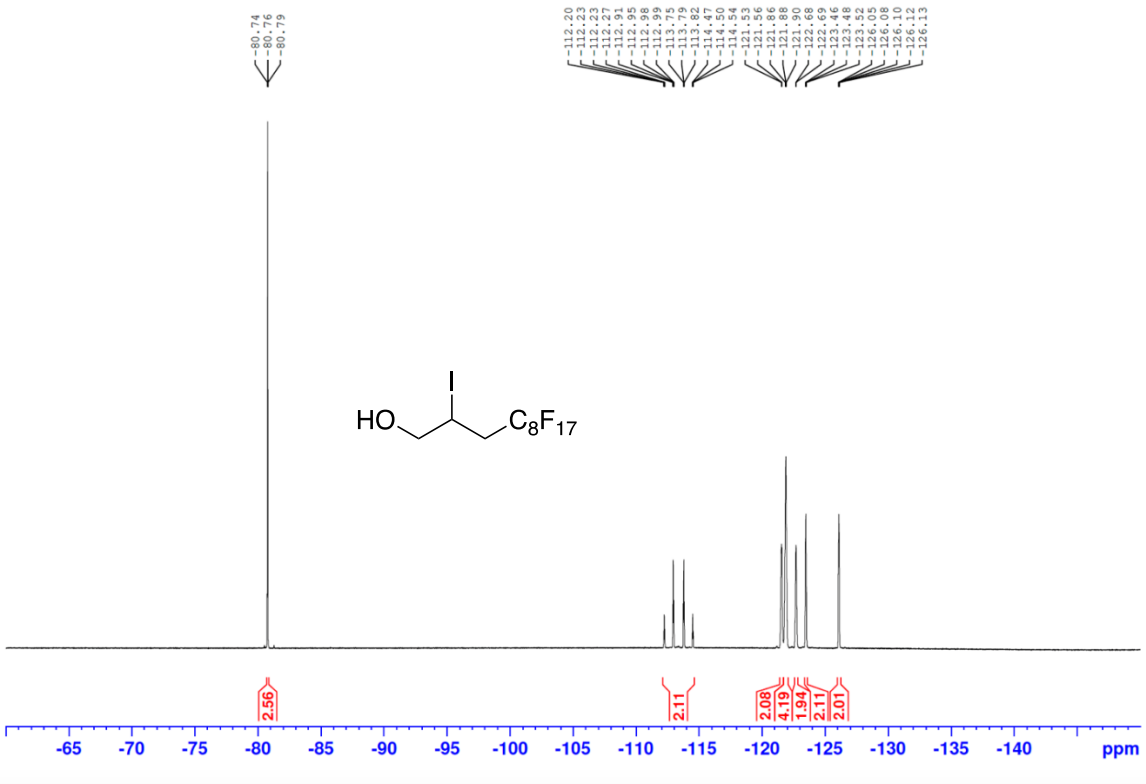
^{19}F NMR spectrum of catalyst **1a**



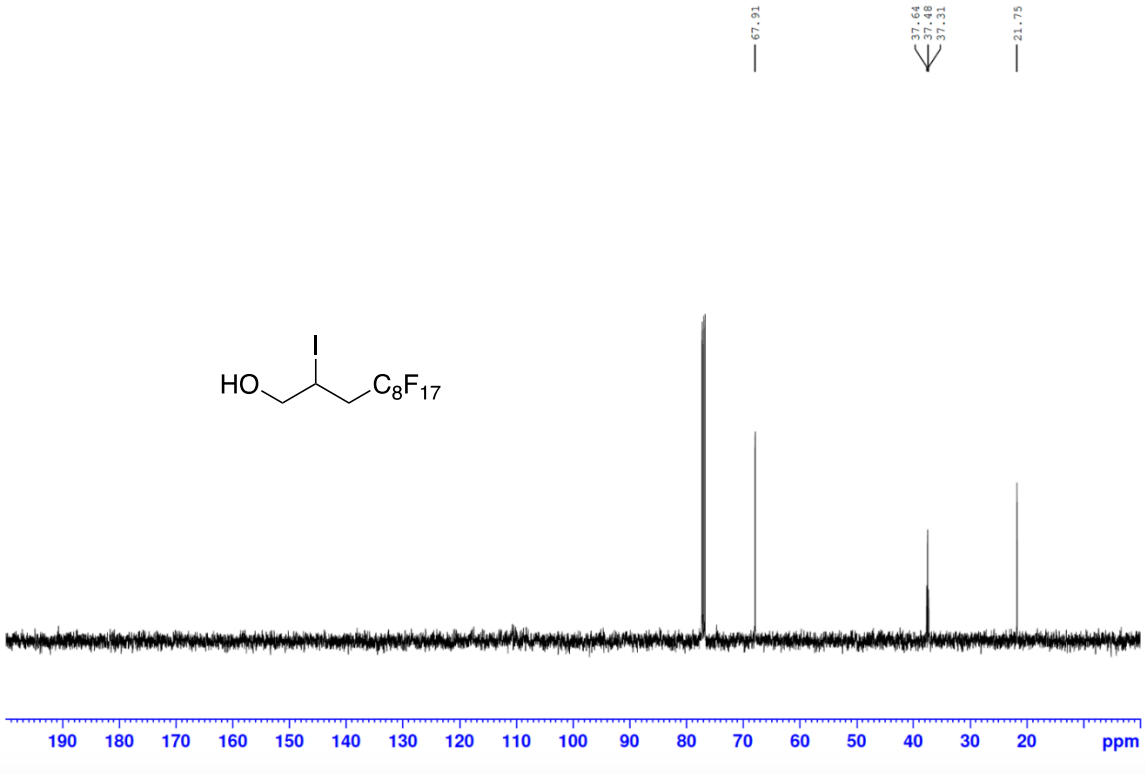
^{11}B NMR spectrum of catalyst **1a**



^{1}H NMR spectrum of compound **4**



^{13}C NMR spectrum of compound **4**



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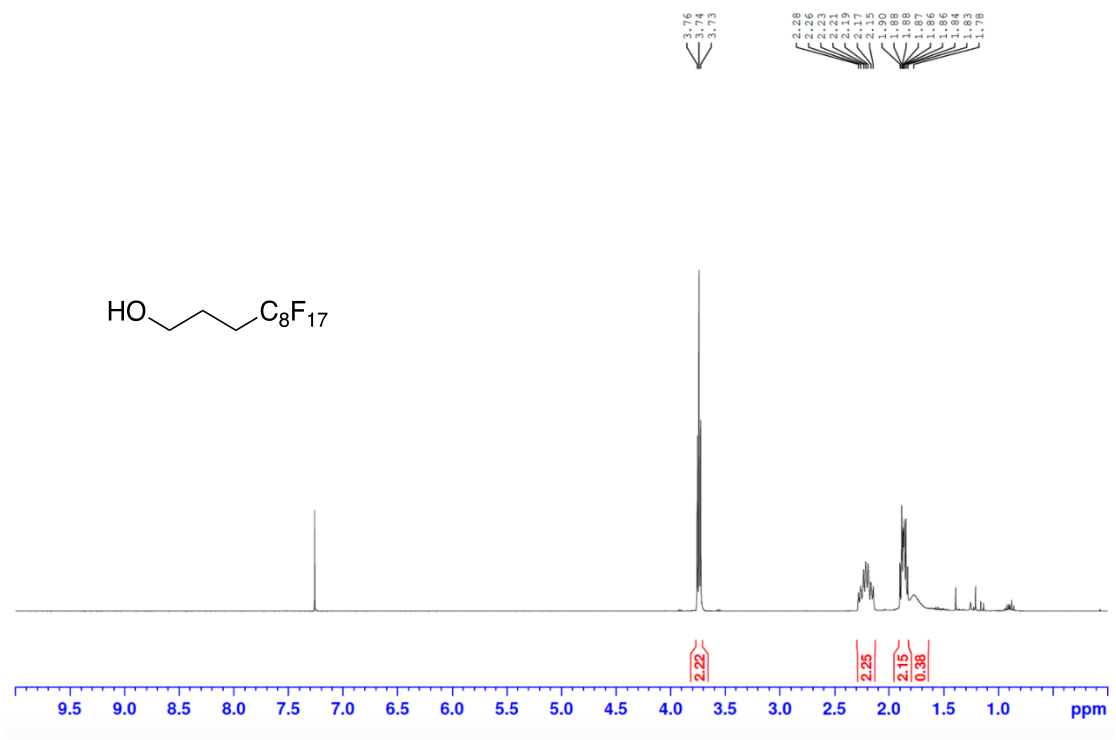
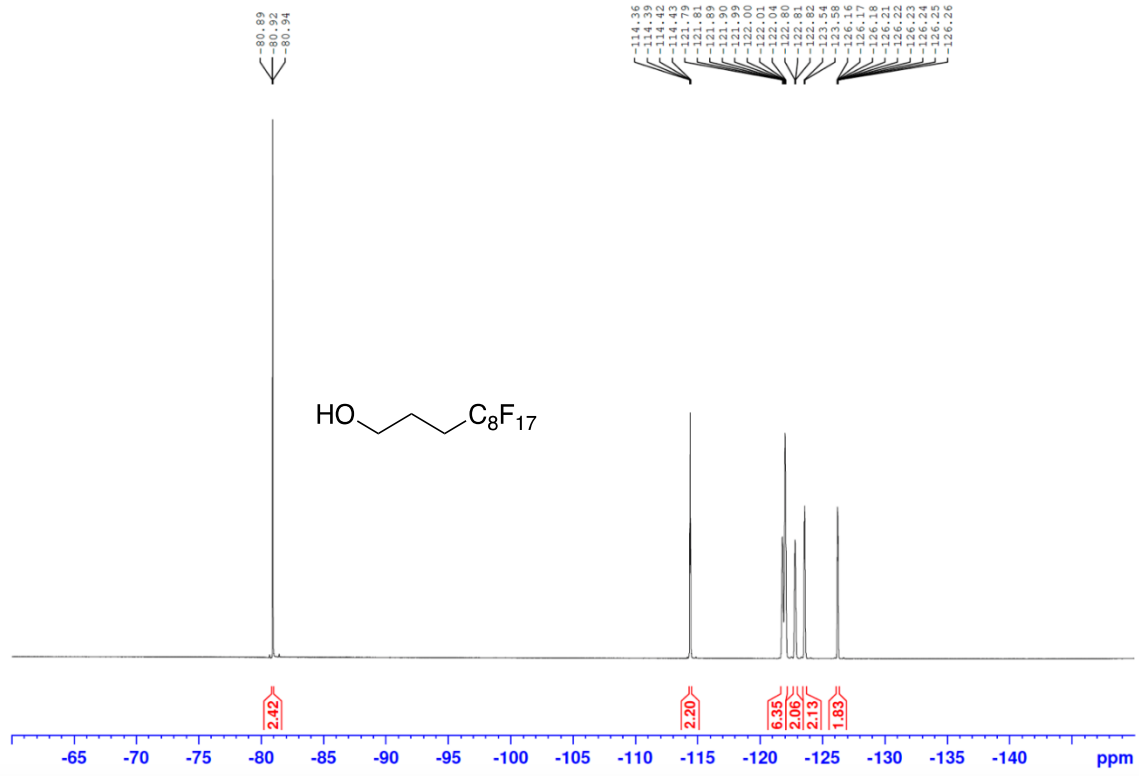
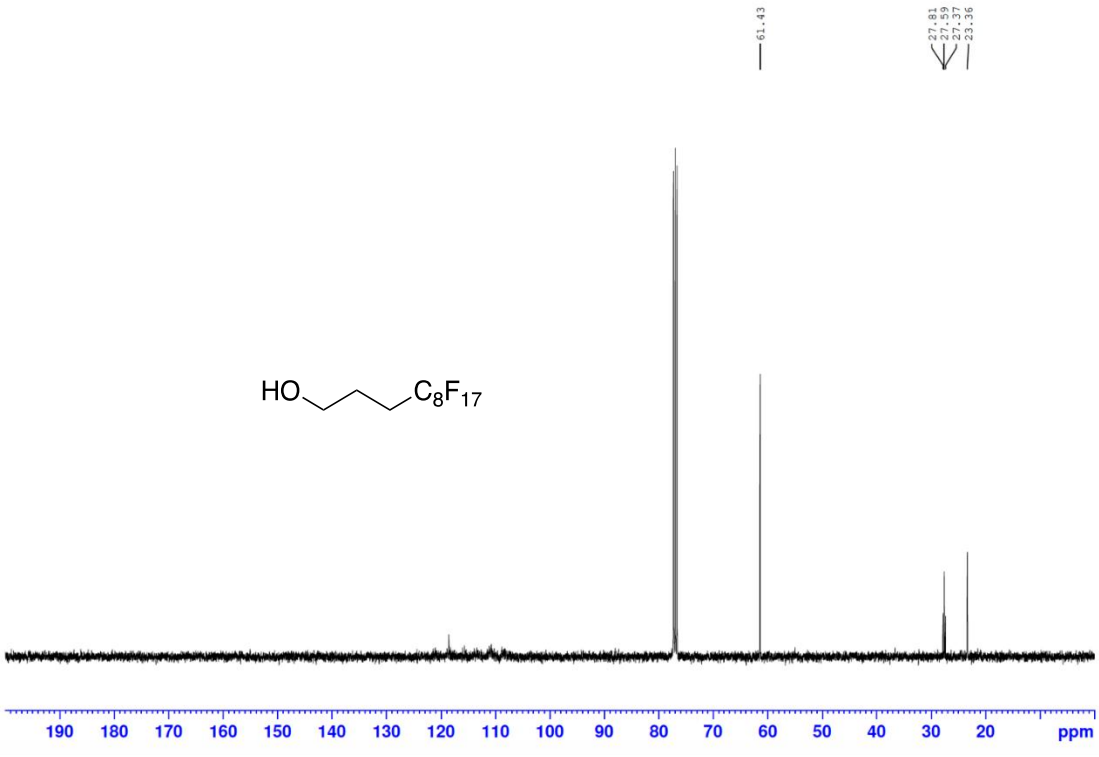


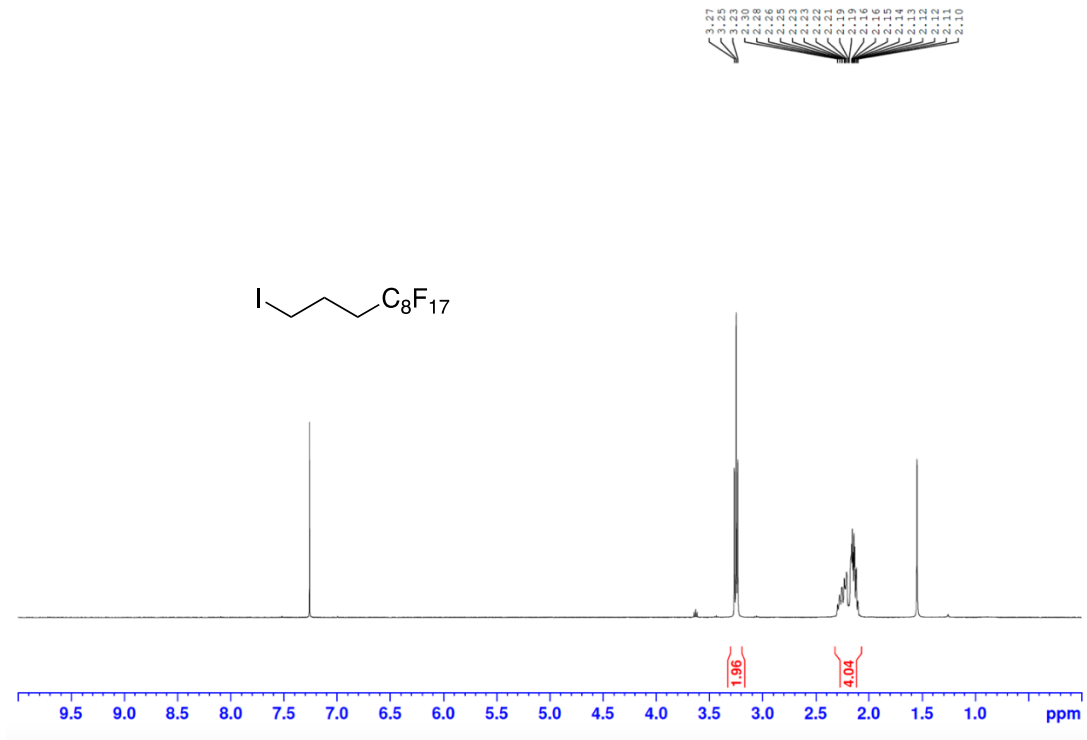
^{1}H NMR spectrum of compound **5**



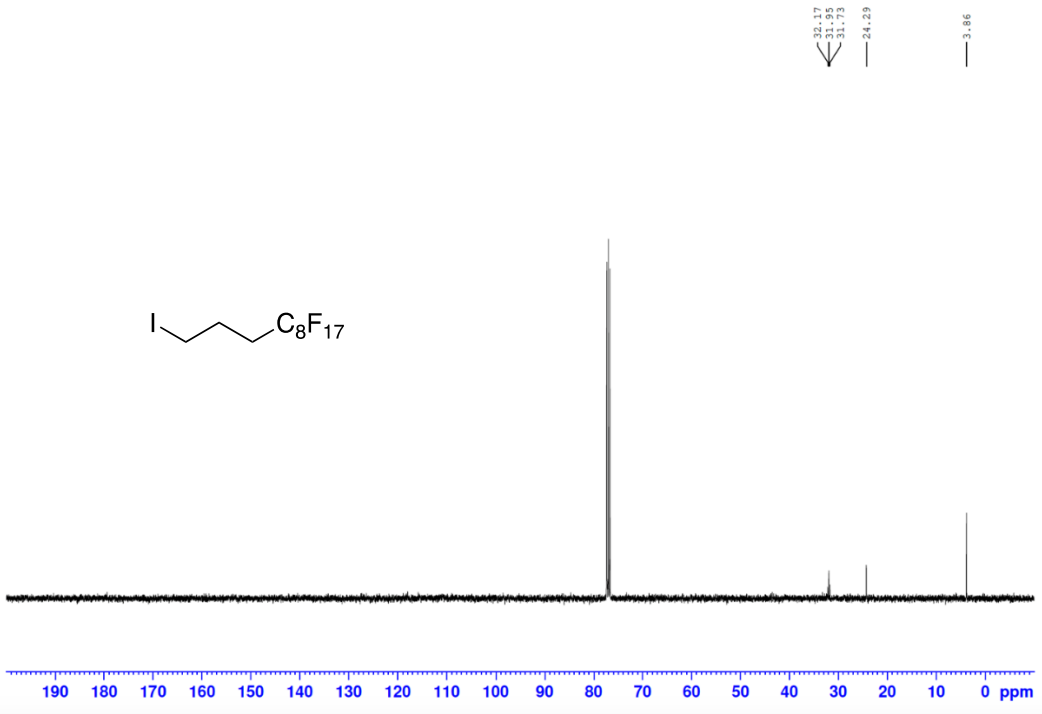
^{13}C NMR spectrum of compound **5**



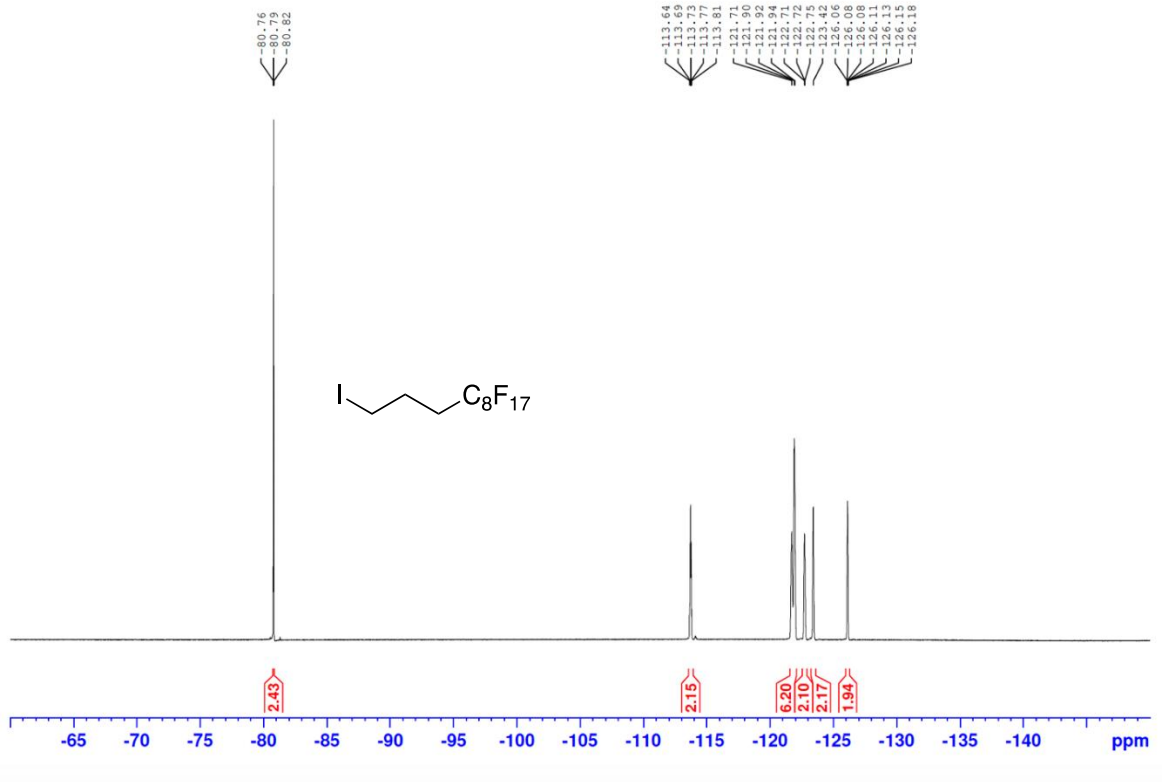
^{19}F NMR spectrum of compound **5**



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



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



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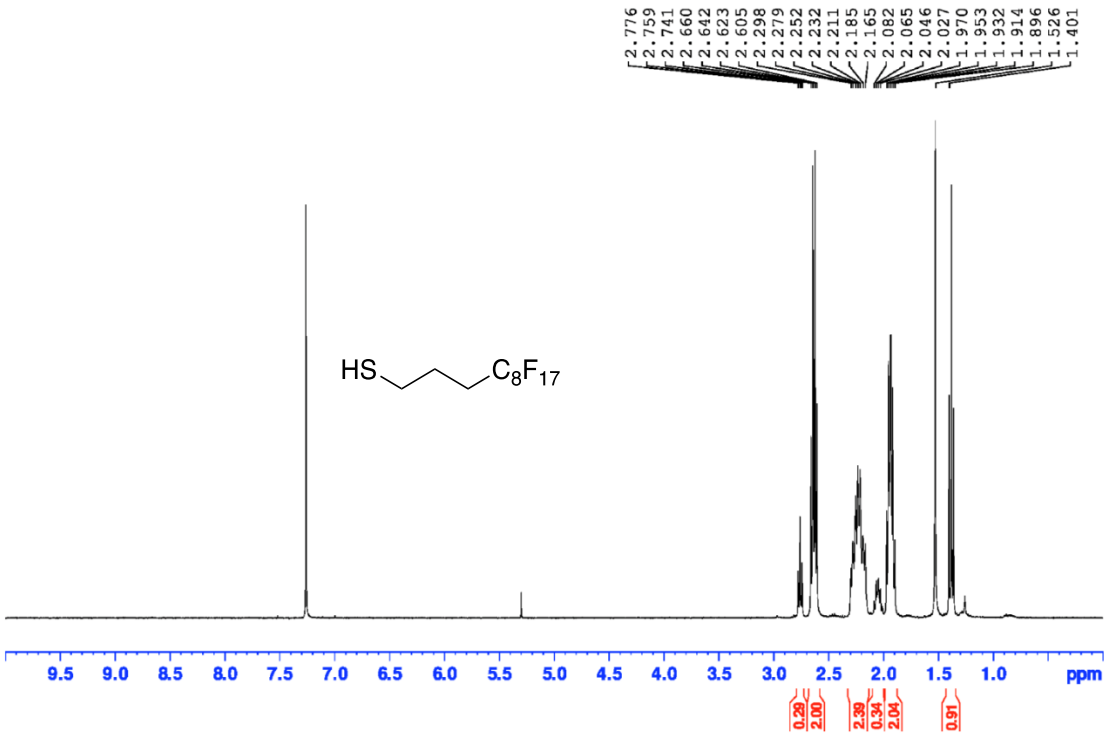

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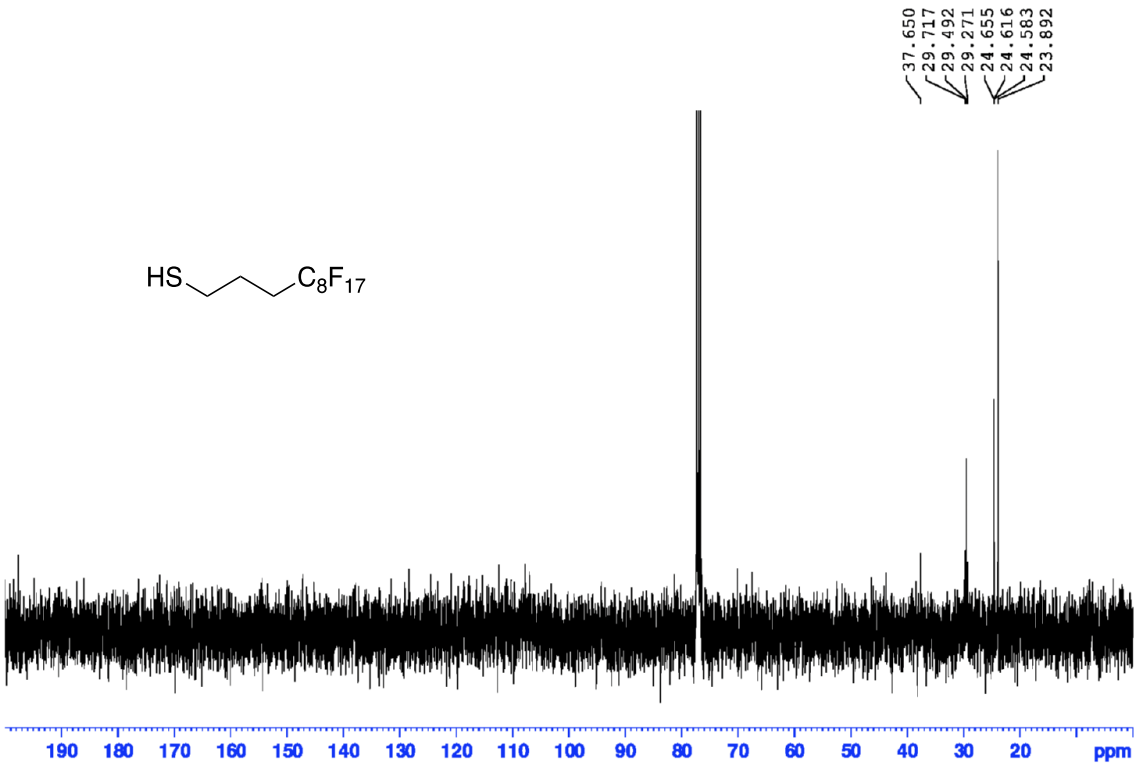
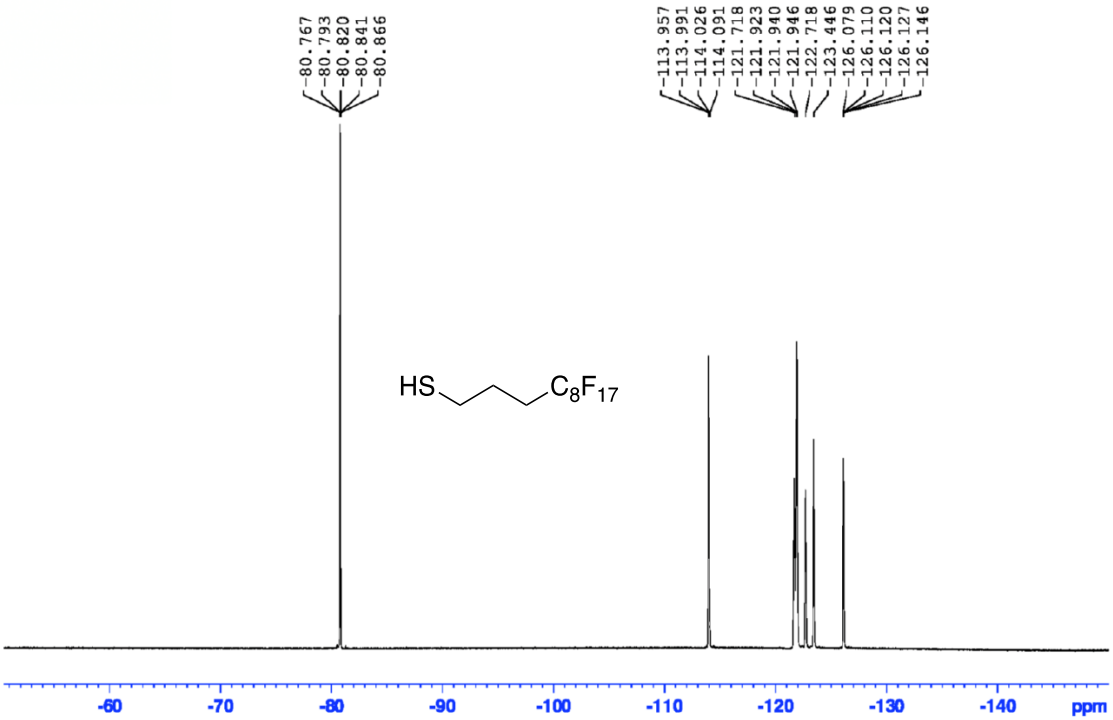
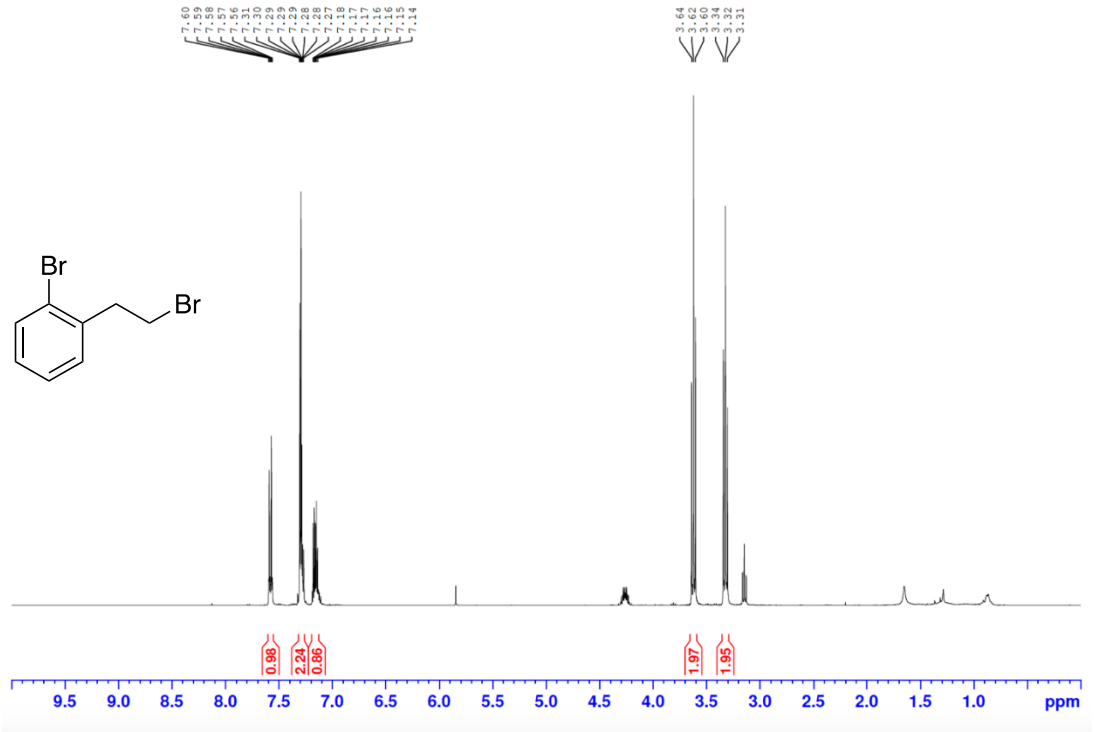


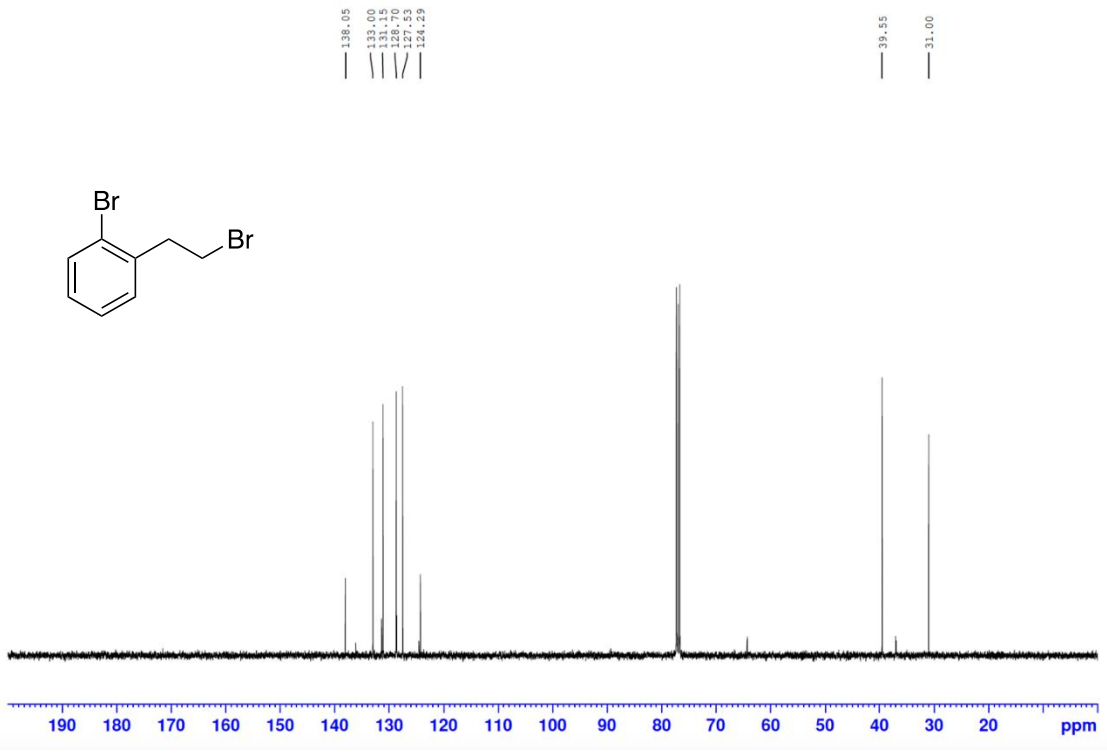
^{13}C NMR spectrum of compound **7**



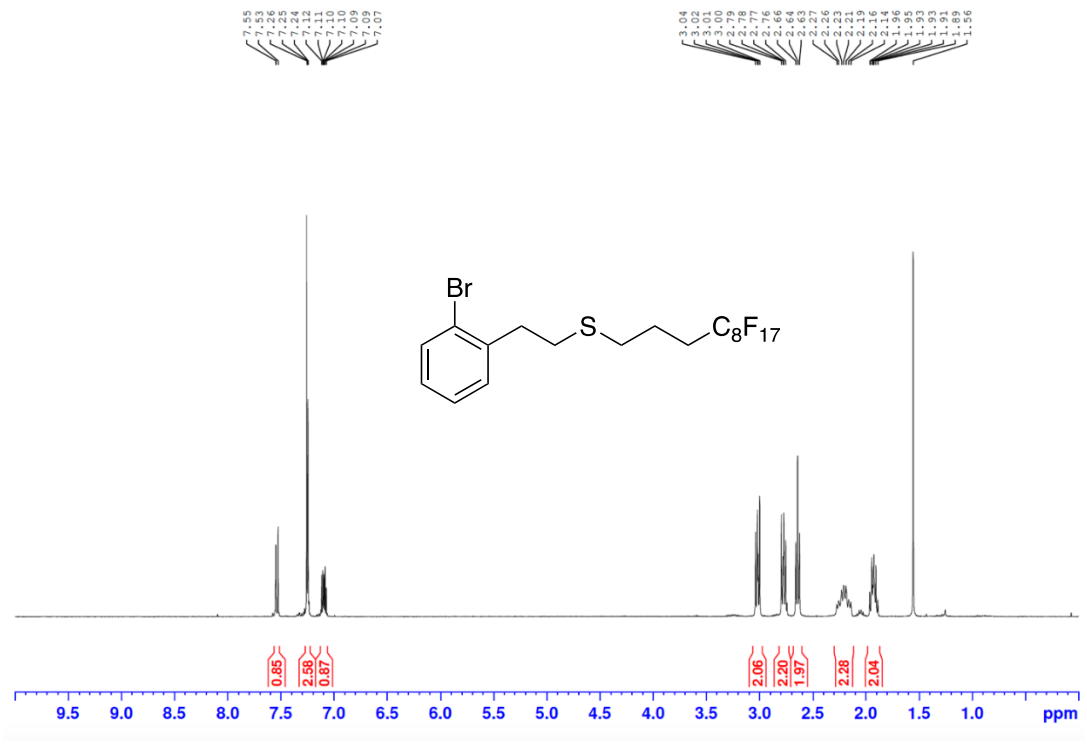
^{19}F NMR spectrum of compound **7**



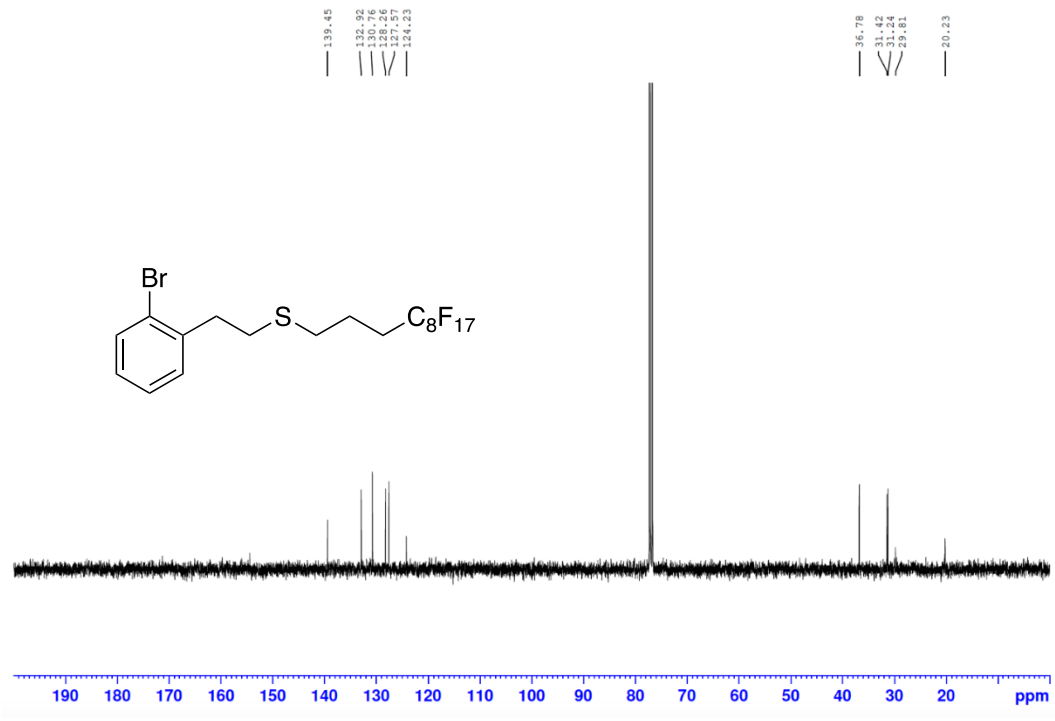
^{1}H NMR spectrum of compound **9**



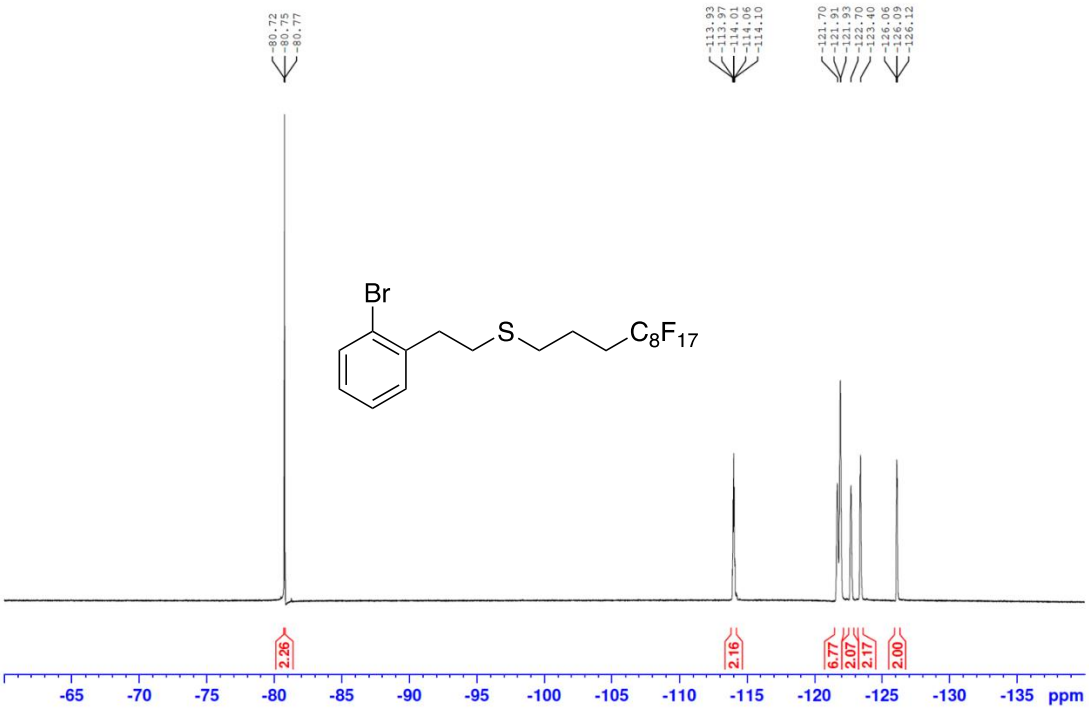
^{13}C NMR spectrum of compound **9**



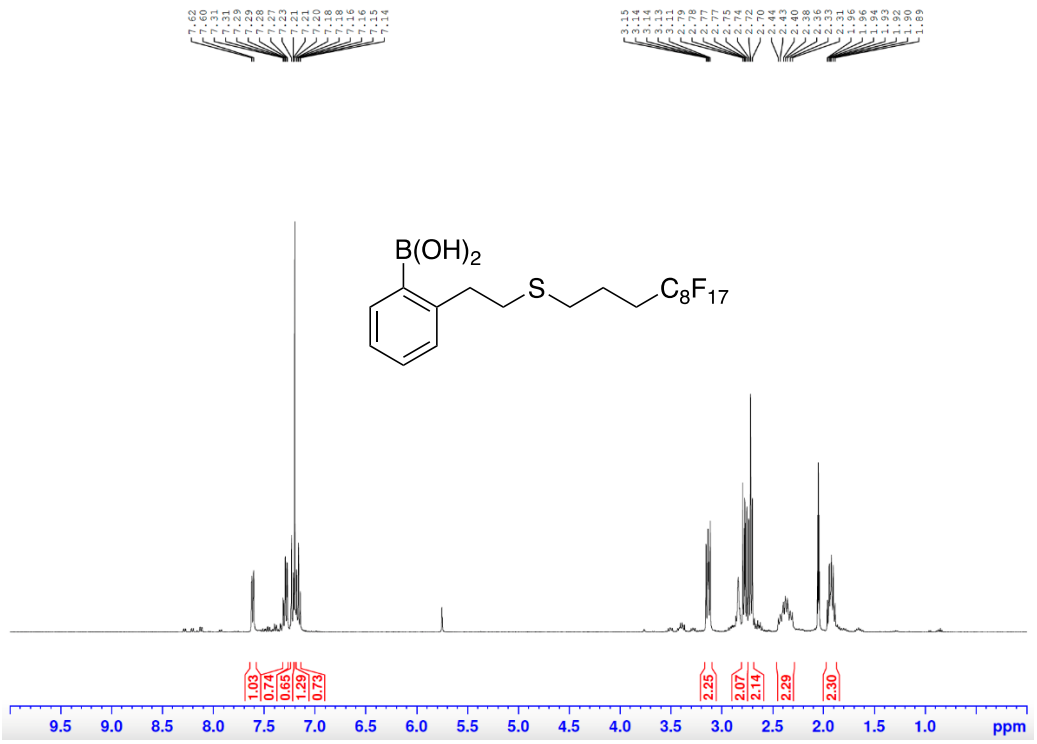
^{1}H NMR spectrum of compound **10**



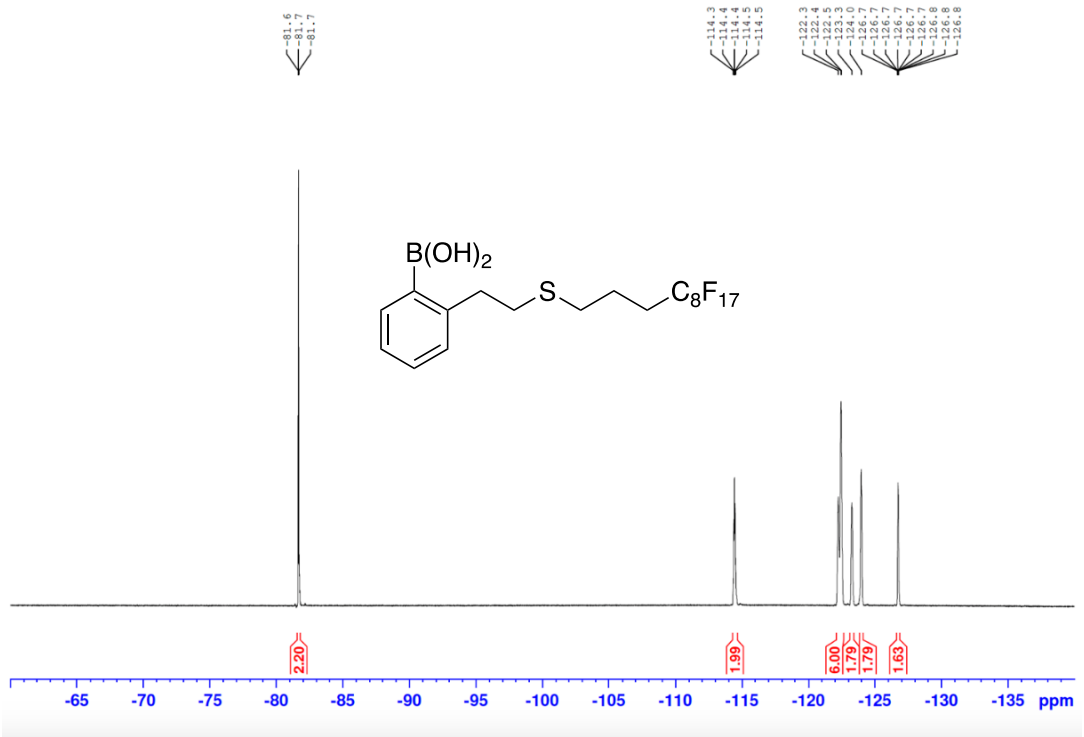
^{13}C NMR spectrum of compound **10**



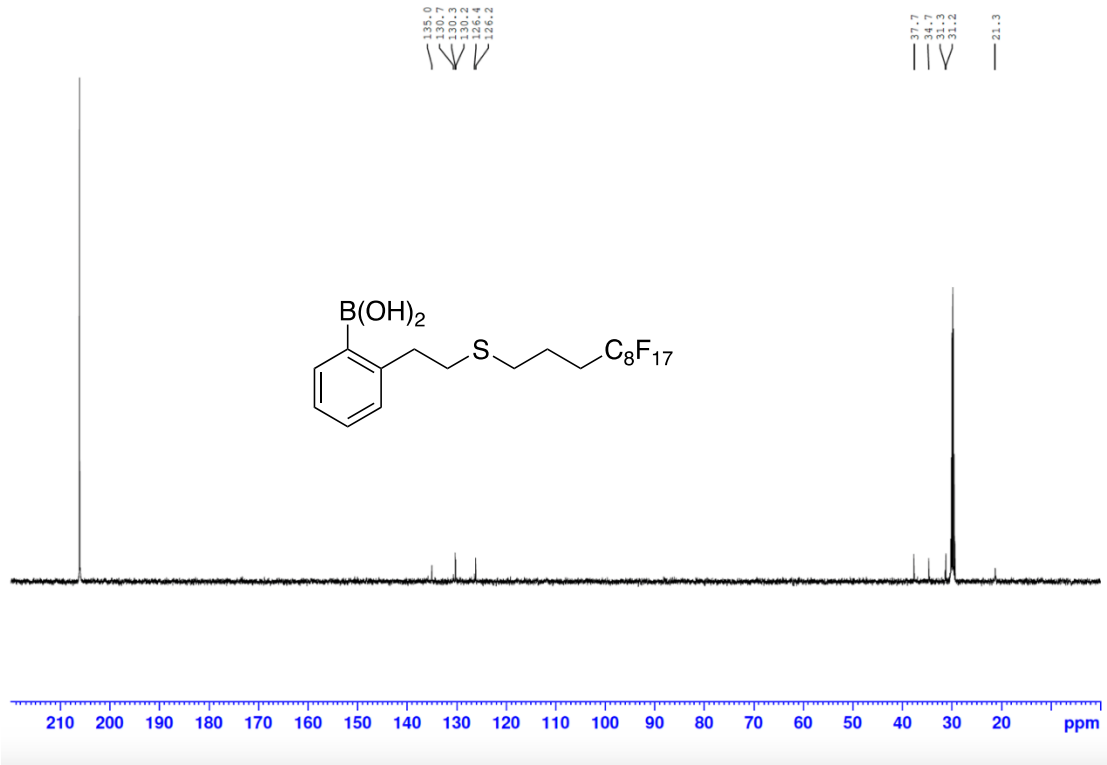
^{19}F NMR spectrum of compound **10**



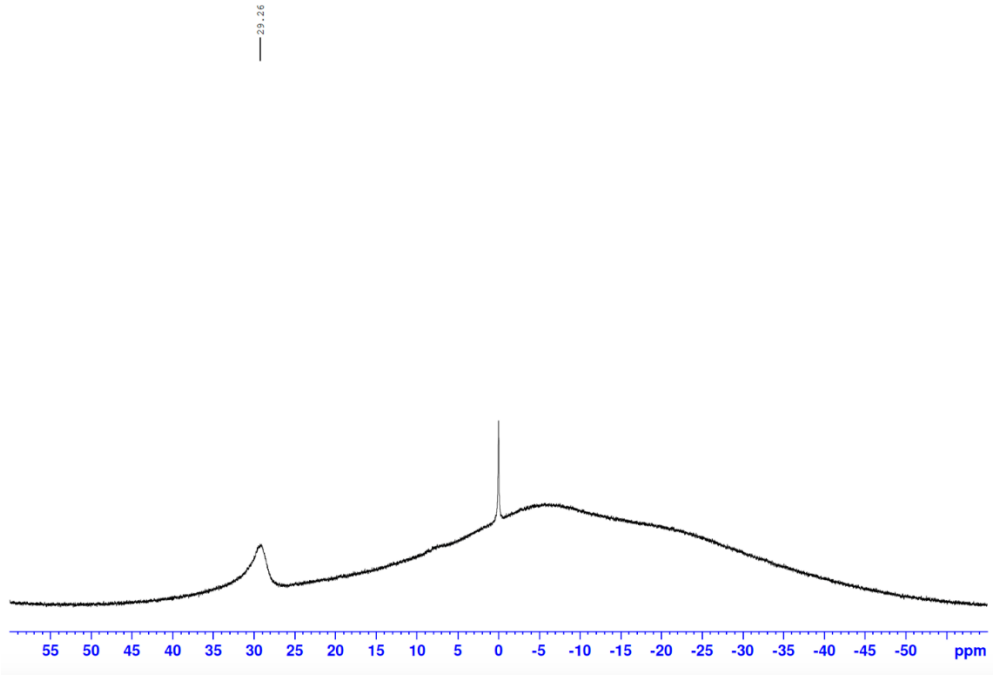
^{1}H NMR spectrum of catalyst **1b**



^{13}C NMR spectrum of catalyst **1b**



^{19}F NMR spectrum of catalyst **1b**



^{11}B NMR spectrum of catalyst **1b**

Meas. m/z	#	Formula	Calc. Mass	Err [ppm]
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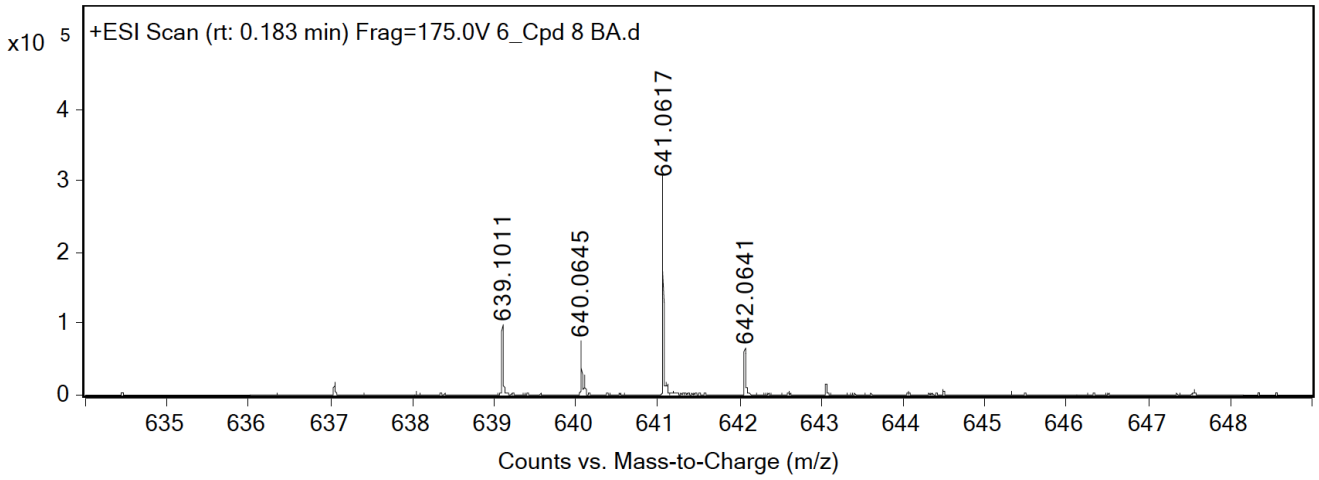
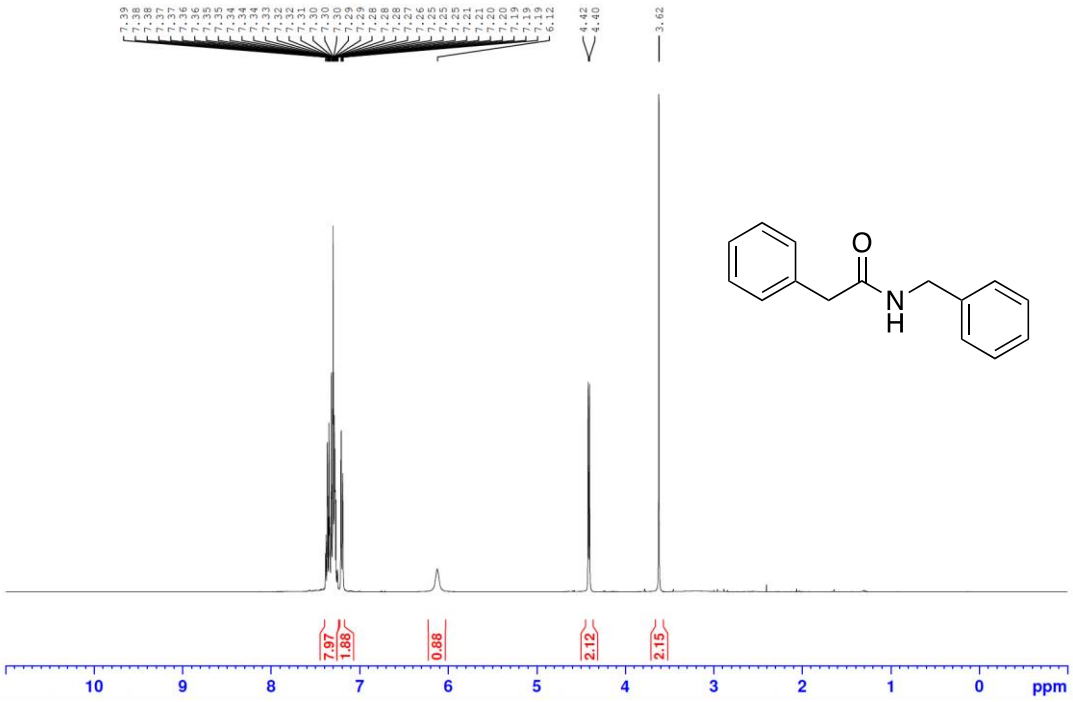
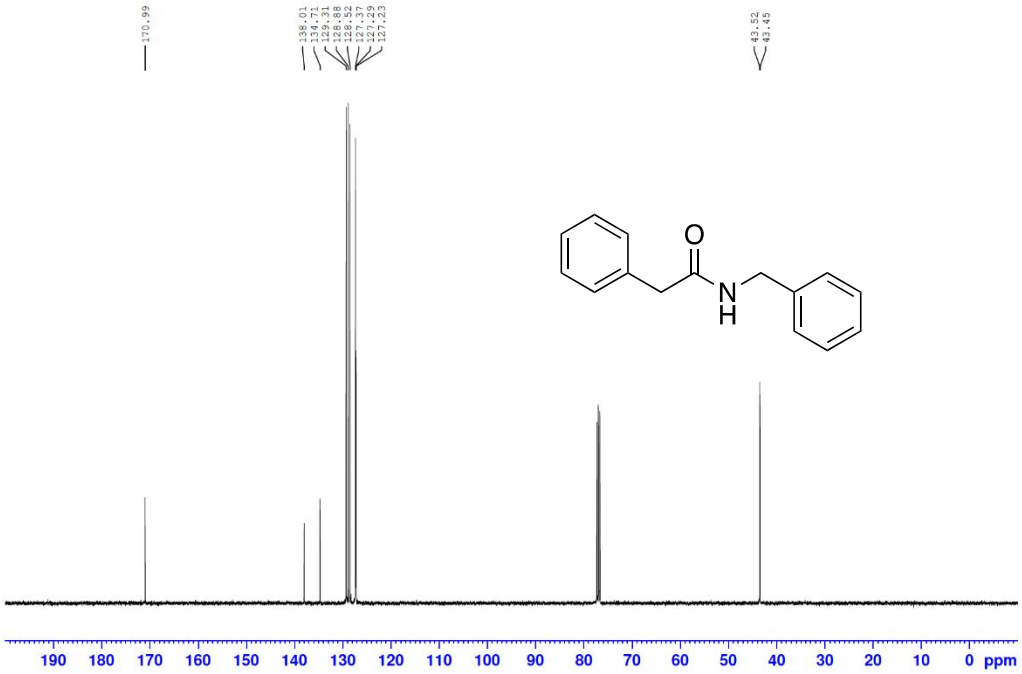


High-resolution mass spectrum for catalyst **1b**

***N*-Benzyl-2-phenylacetamide (2a)** White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.25 (m, 8H), 7.21-7.19 (m, 2H), 6.12 (s, 1H), 4.42 (d, *J* = 8 Hz, 2H), 3.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 138.0, 134.7, 129.3, 128.9, 128.5, 127.4, 127.3, 127.2, 43.5, 43.4. HRMS (+ESI) calcd. for $C_{15}H_{16}NO$: 226.1226; found: 226.1225.

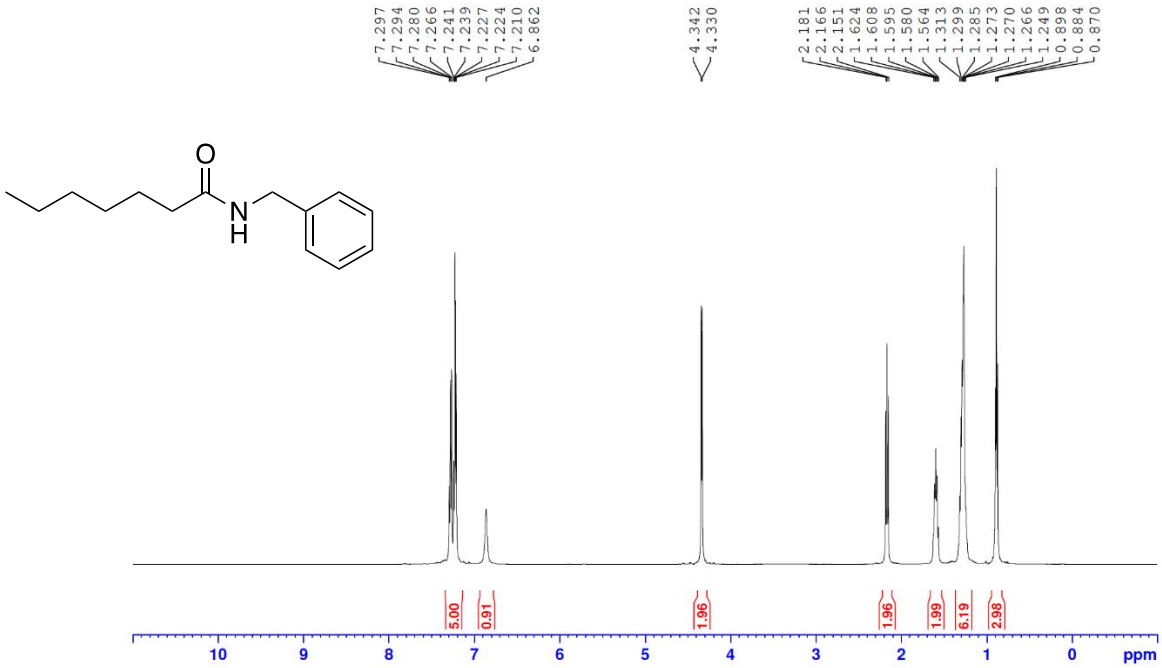


^{1}H NMR spectrum of compound **2a**

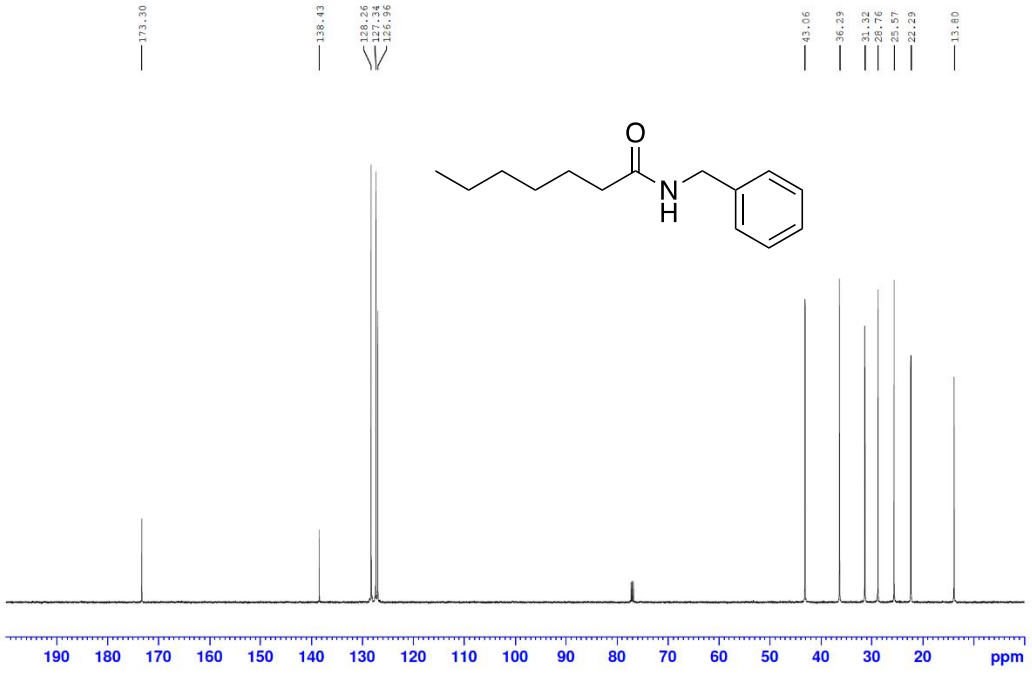


^{13}C NMR spectrum of compound **2a**

***N*-Benzylheptanamide (2b)** Off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.21 (m, 5H), 6.86 (s, 1H), 4.34 (d, *J* = 6 Hz, 2H), 2.17 (t, J = 6 Hz, 2H), 1.62-1.56 (quint, J = 8 Hz, 2H), 1.31-1.25 (m, 6H), 0.88 (t, J = 5.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 138.4, 128.3, 127.3, 126.9, 43.1, 36.3, 31.3, 28.8, 25.6, 22.3, 13.8. HRMS (+ESI) calcd. for $C_{14}H_{22}NO$: 220.1696; found: 220.1695.

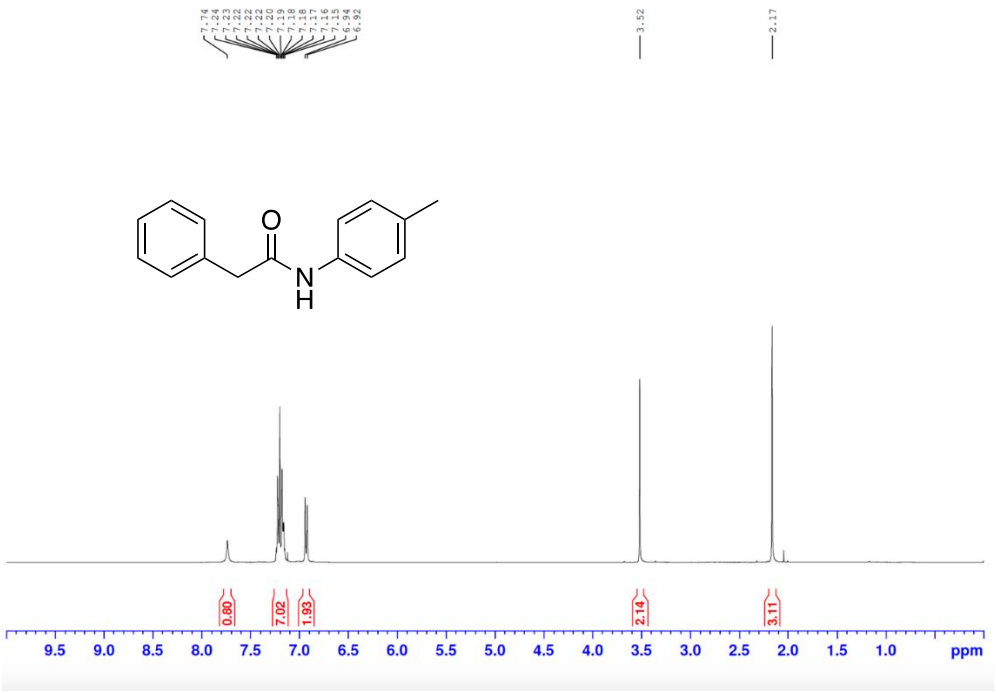


^{1}H NMR spectrum of compound **2b**

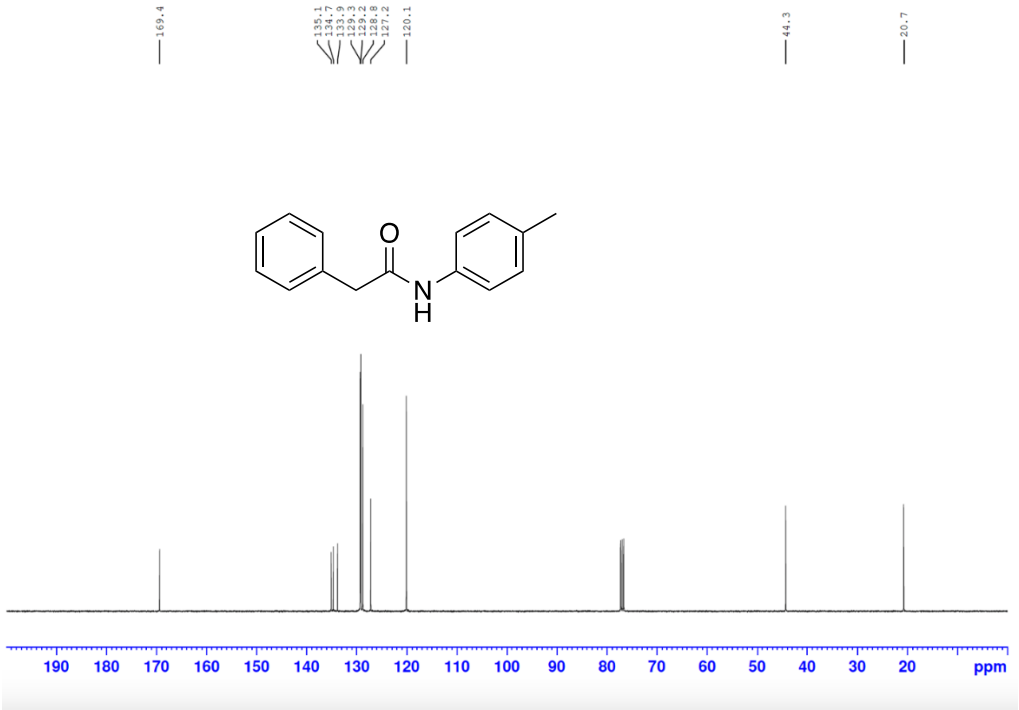


^{13}C NMR spectrum of compound **2b**

2-Phenyl-*N*-(*p*-tolyl)acetamide (2c) Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.24-7.15 (m, 7H), 6.94 (d, J = 8.2 Hz, 2H), 3.52 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 135.1, 134.7, 133.9, 129.3, 129.2, 128.8, 127.2, 120.1, 44.3, 20.7. HRMS (+ESI) calcd. for $C_{15}H_{16}NO$: 226.1226; found: 226.1228.

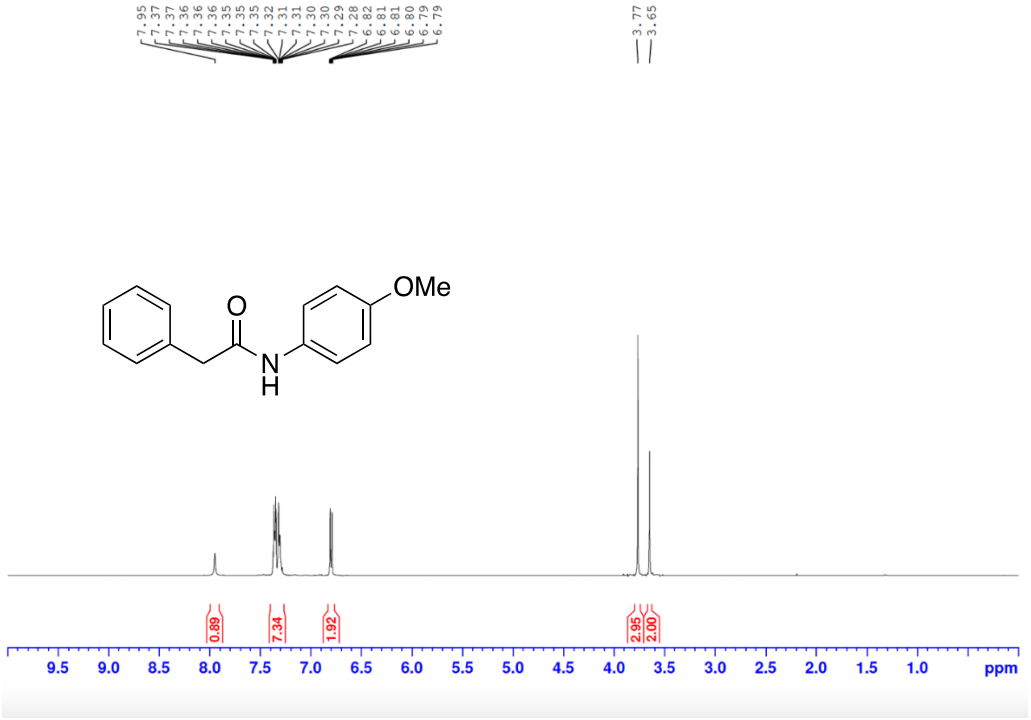


^{1}H NMR spectrum of compound **2c**

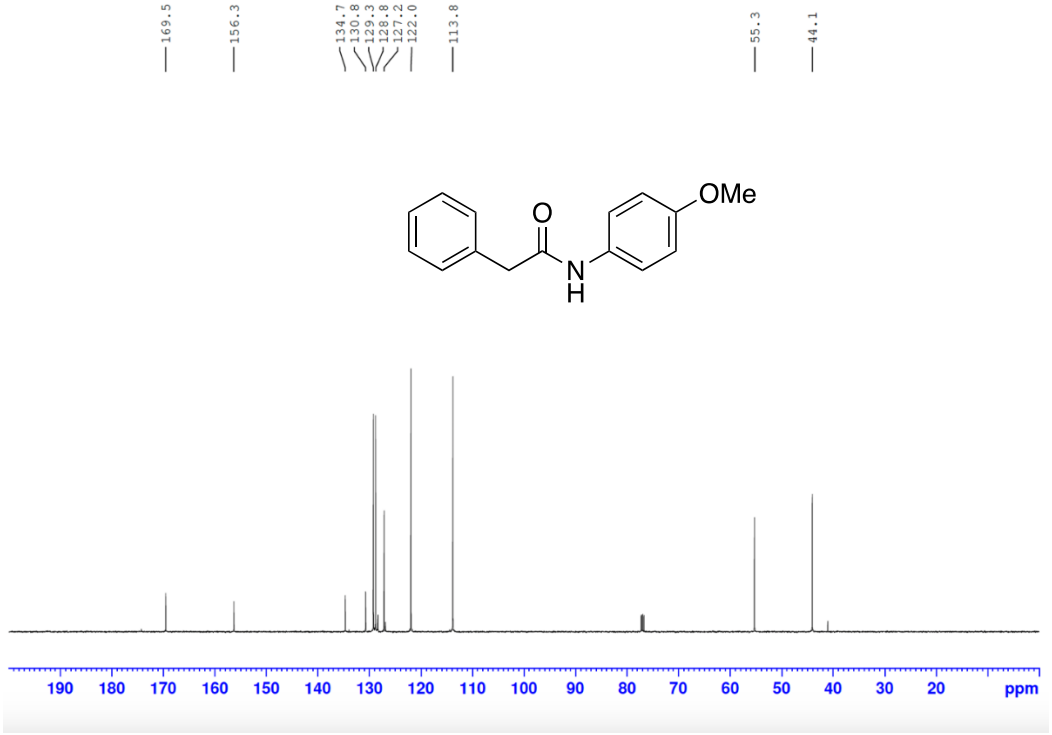


^{13}C NMR spectrum of compound **2c**

***N*-(4-Methoxyphenyl)-2-phenylacetamide (2d)** Light brown solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.37-7.28 (m, 7H), 6.82-6.79 (m, 2H), 3.77 (s, 3H), 3.65 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 156.3, 134.7, 130.8, 129.3, 128.8, 127.2, 122.0, 113.8, 55.3, 44.1. HRMS (+ESI) calcd. for $C_{15}H_{16}NO_2$: 242.1176; found: 242.1179.

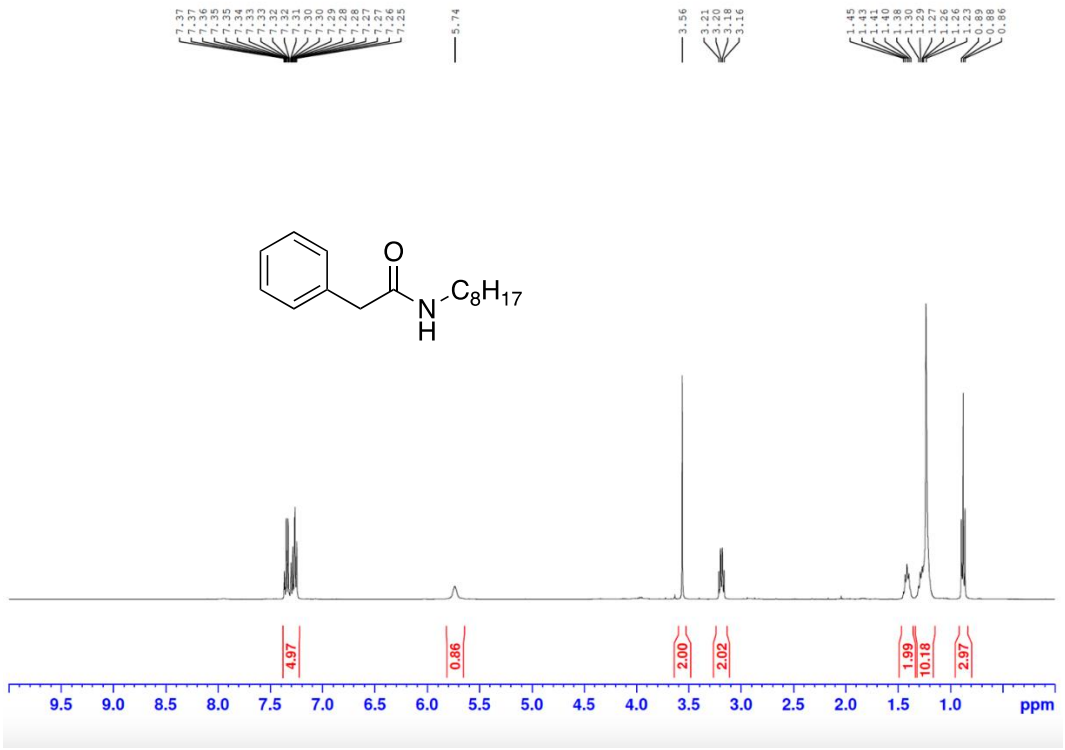


^{1}H NMR spectrum of compound **2d**

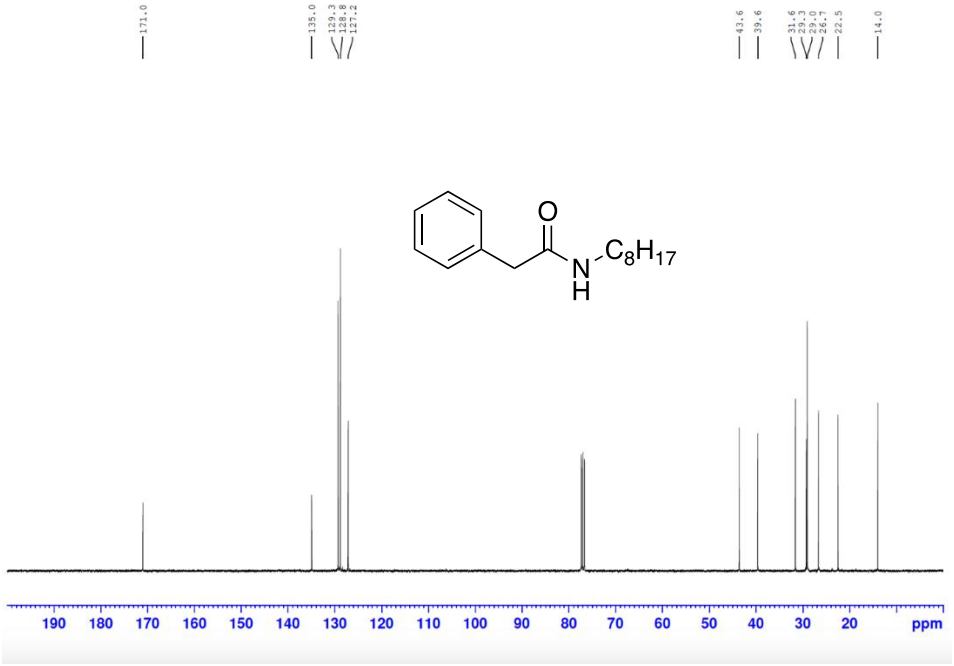


^{13}C NMR spectrum of compound **2d**

***N*-Octyl-2-phenylacetamide (2e)** Off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.25 (m, 5H), 5.74 (s, 1H), 3.36 (s, 2H), 3.21-3.16 (q, J = 7 Hz, 2H), 1.41 (quint, J = 7.4 Hz, 2H), 1.30-1.23 (m, 10H), 0.88 (t, J = 6.84 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 135.0, 129.3, 128.8, 127.2, 43.6, 39.6, 31.6, 29.3, 29.0, 26.7, 22.5, 14.0. HRMS (+ESI) calcd. for $C_{16}H_{26}NO$: 248.2009; found: 248.2010.

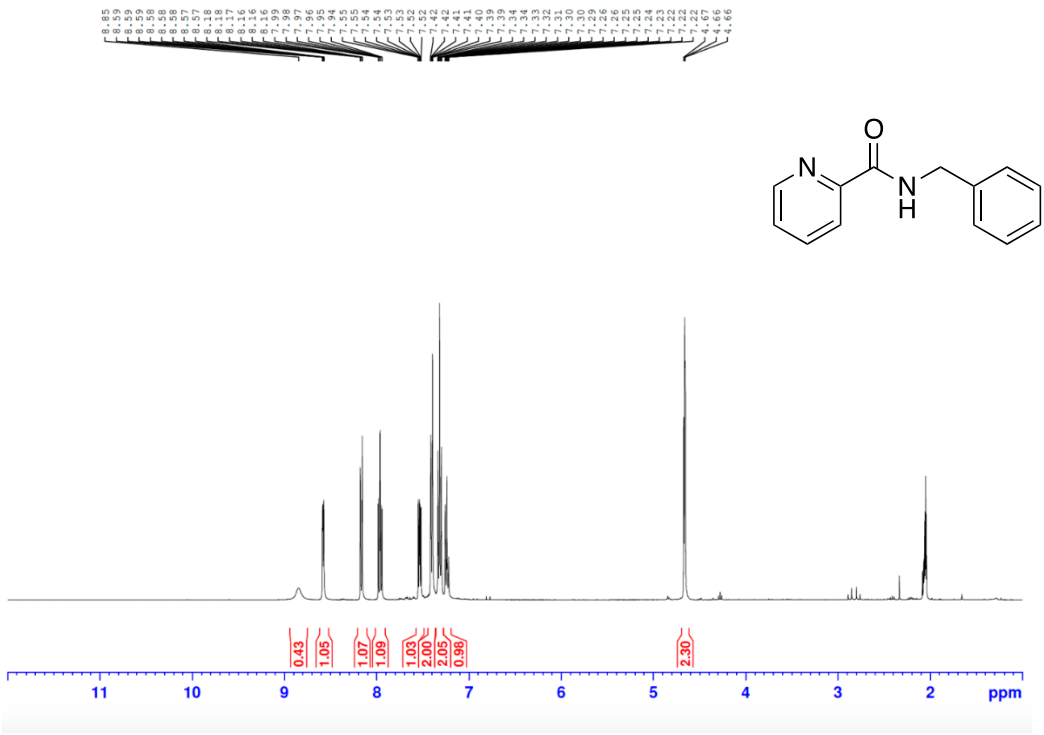


^{1}H NMR spectrum of compound **2e**

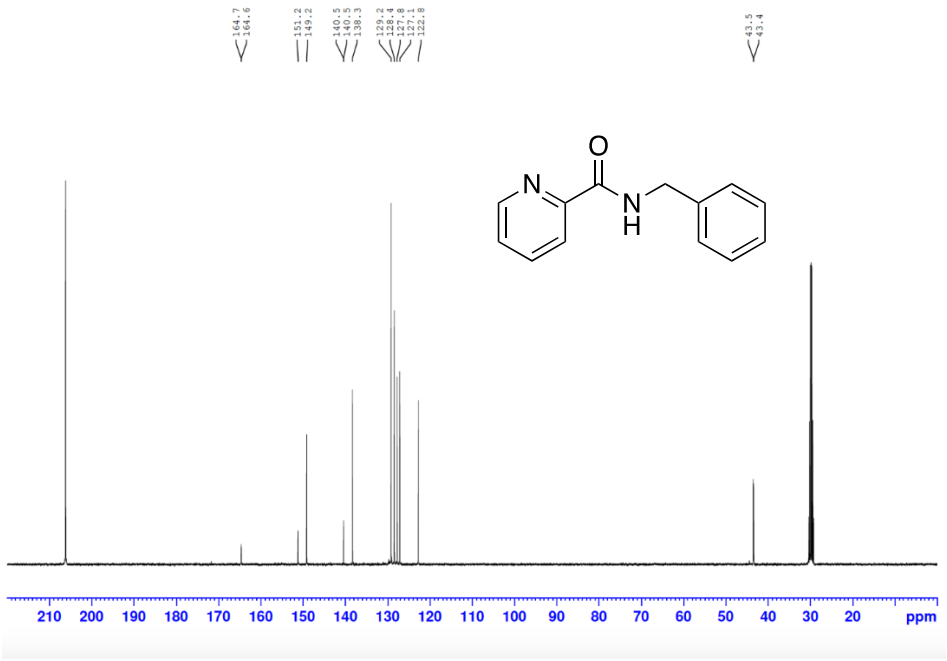


^{13}C NMR spectrum of compound **2e**

***N*-Benzylpicolinamide (2f)** Brownish liquid. ^{1}H NMR (400 MHz, Acetone-d_6): δ 8.85 (br s, 1H), 8.59-8.57 (dq, J = 4.76, 0.92 Hz, 1H), 8.18-8.16 (dt, J = 7.8, 1.08 Hz, 1H), 7.99-7.94 (td, J = 7.72, 1.72 Hz, 1H), 7.55-7.52 (ddd, J = 7.6, 4.76, 1.24 Hz, 1H), 7.42-7.39 (m, 2H), 7.34-7.29 (m, 2H), 7.26-7.22 (m, 1H), 4.67-4.66 (m, 2H). ^{13}C NMR (100 MHz, Acetone-d_6): δ 164.7, 164.6, 151.2, 149.2, 140.5, 140.5, 138.3, 129.2, 128.4, 127.8, 127.1, 122.8, 43.5, 43.4. HRMS (+ESI) calcd. for $C_{13}H_{13}N_2O$: 213.1022; found: 213.1019.

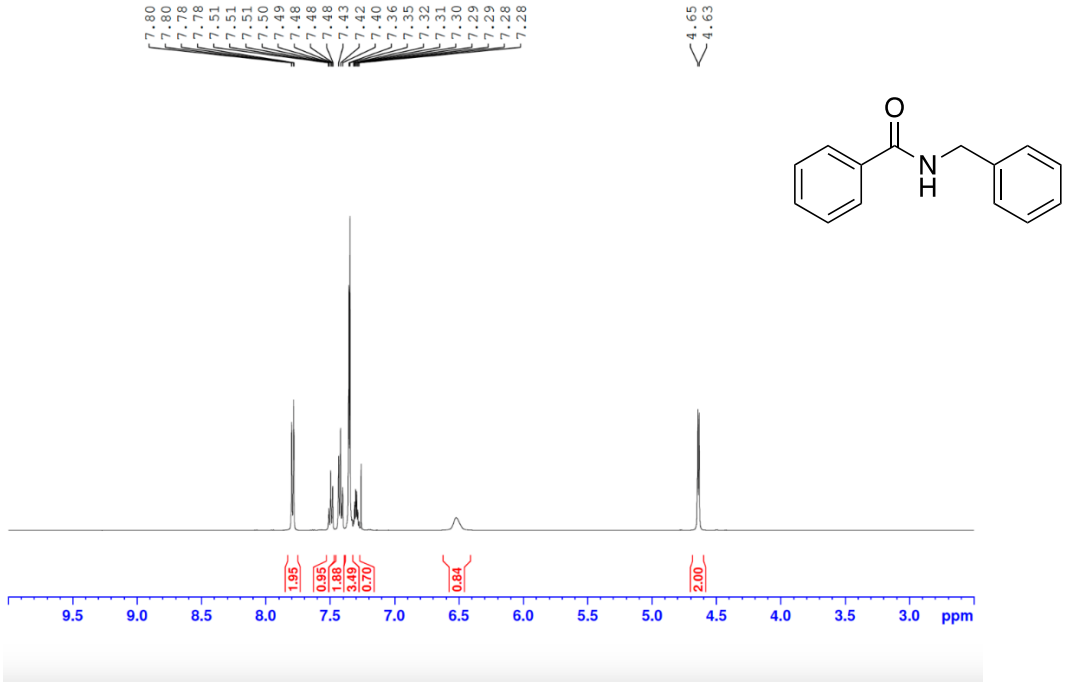


^{1}H NMR spectrum of compound **2f**

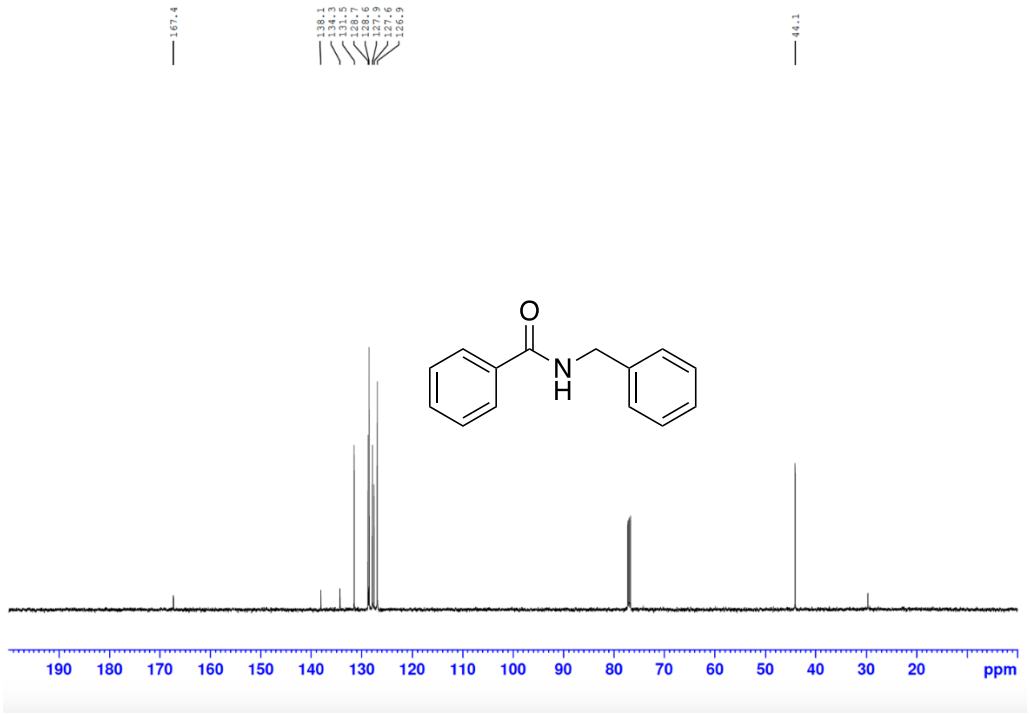


^{13}C NMR spectrum of compound **2f**

***N*-Benzylbenzamide (2g)** Light brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.78 (m, 2H), 7.51-7.48 (m, 1H), 7.43-7.40 (m, 2H), 7.36-7.35 (m, 4H), 7.32-7.28 (m, 1H), 6.52 (s, 1H), 4.65 (d, *J* = 5.65 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 138.1, 134.3, 131.5, 128.7, 128.6, 127.9, 127.6, 126.9, 44.1. HRMS (+ESI) calcd. for $C_{14}H_{14}NO$: 212.1070; found: 212.1066.

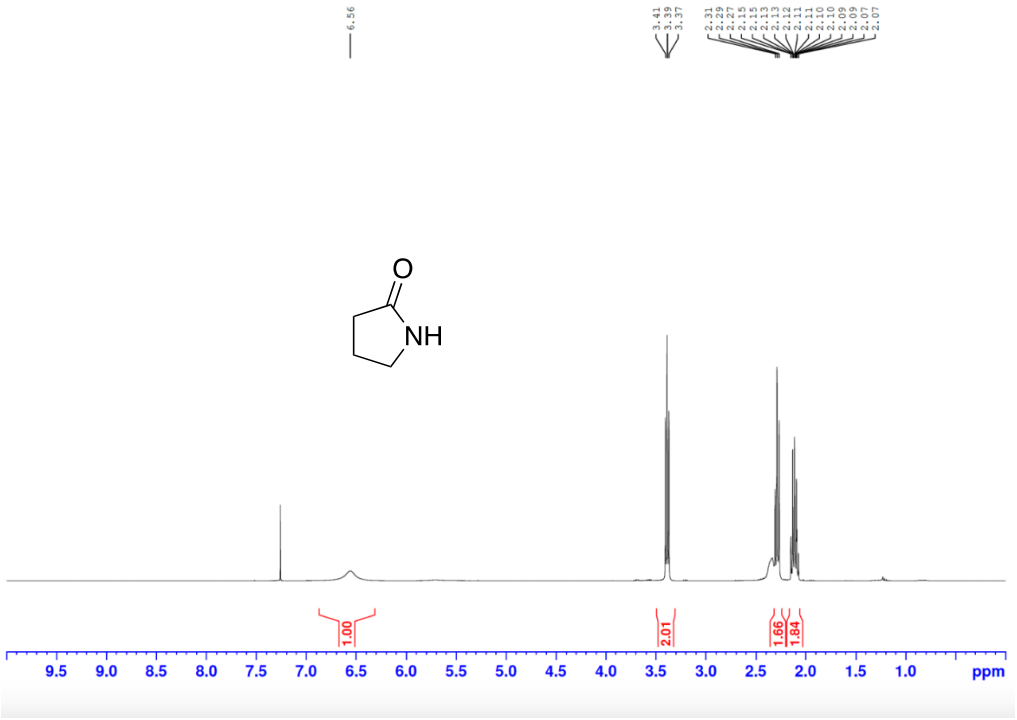


^{1}H NMR spectrum of compound **2g**

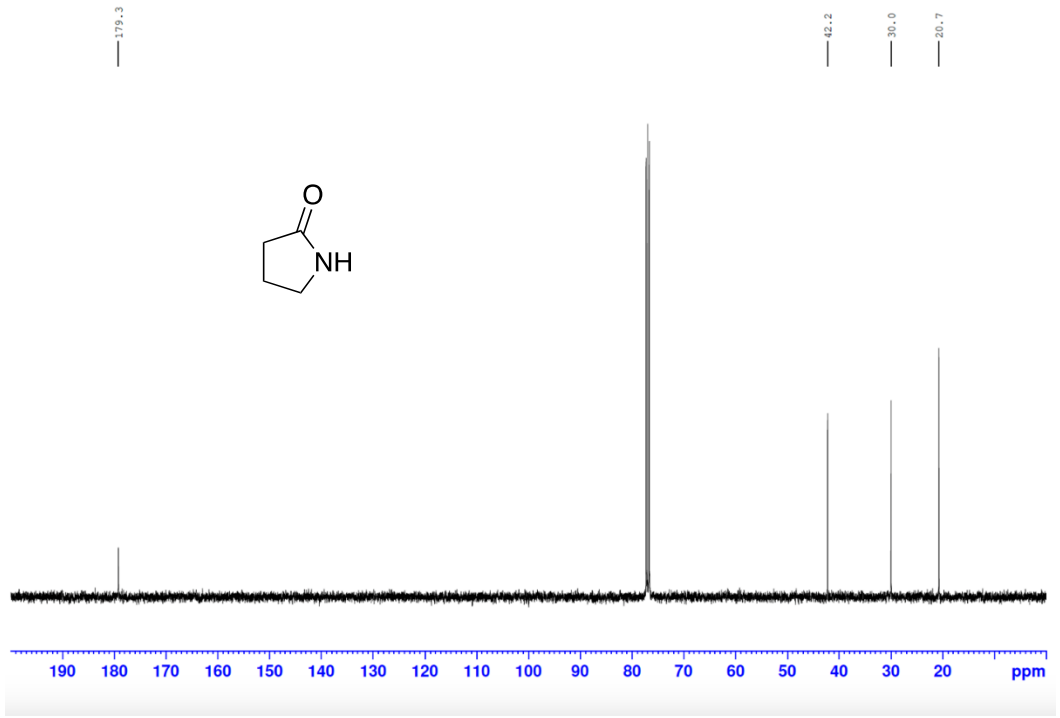


^{13}C NMR spectrum of compound **2g**

Pyrrolidin-2-one (2h) Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.56 (br s, 1H), 3.39 (t, J = 7 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 2.15-2.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 42.2, 30.0, 20.7. HRMS (+ESI) calcd. for C_4H_8NO: 86.0600; found: 86.0601.

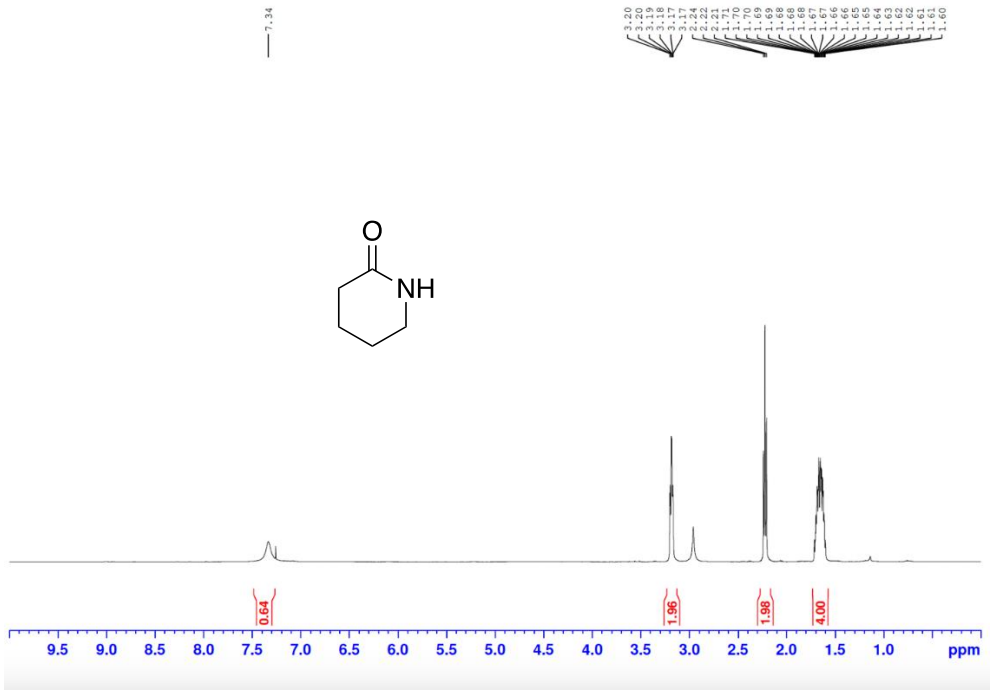


^{1}H NMR spectrum of compound **2h**

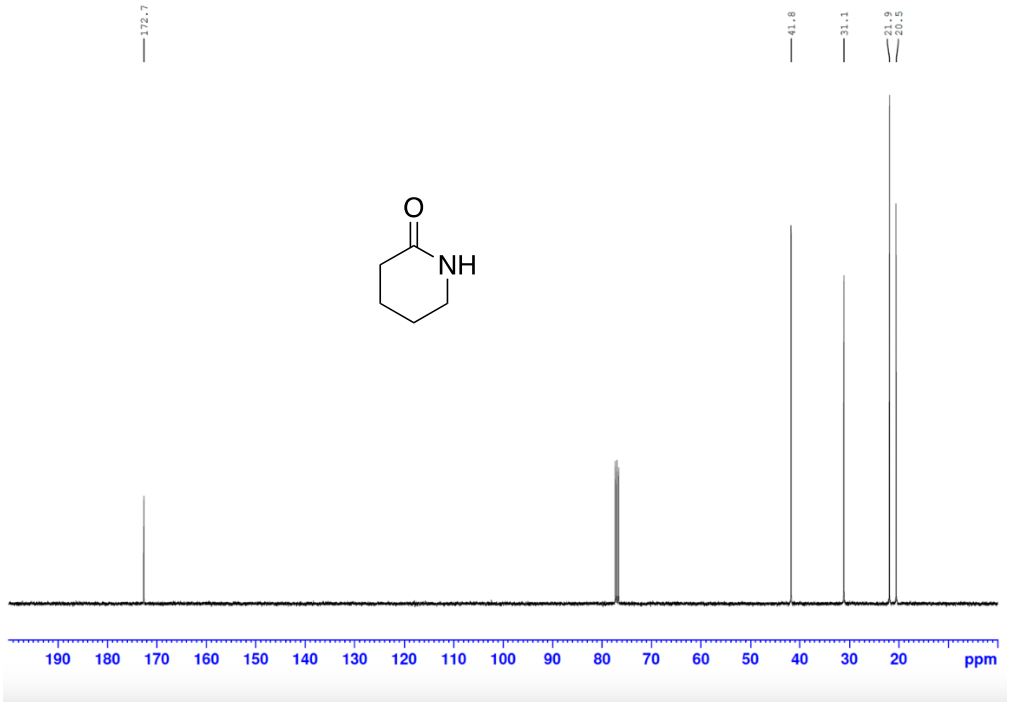


^{13}C NMR spectrum of compound **2h**

Piperidin-2-one (2i) Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (br s, 1H), 3.20-3.17 (m, 2H), 2.22 (t, J = 6.36 Hz, 2H), 1.71-1.60 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 41.8, 31.1, 21.9, 20.5. HRMS (+ESI) calcd. for C_5H_9NaNO: 122.0576; found: 122.0577.

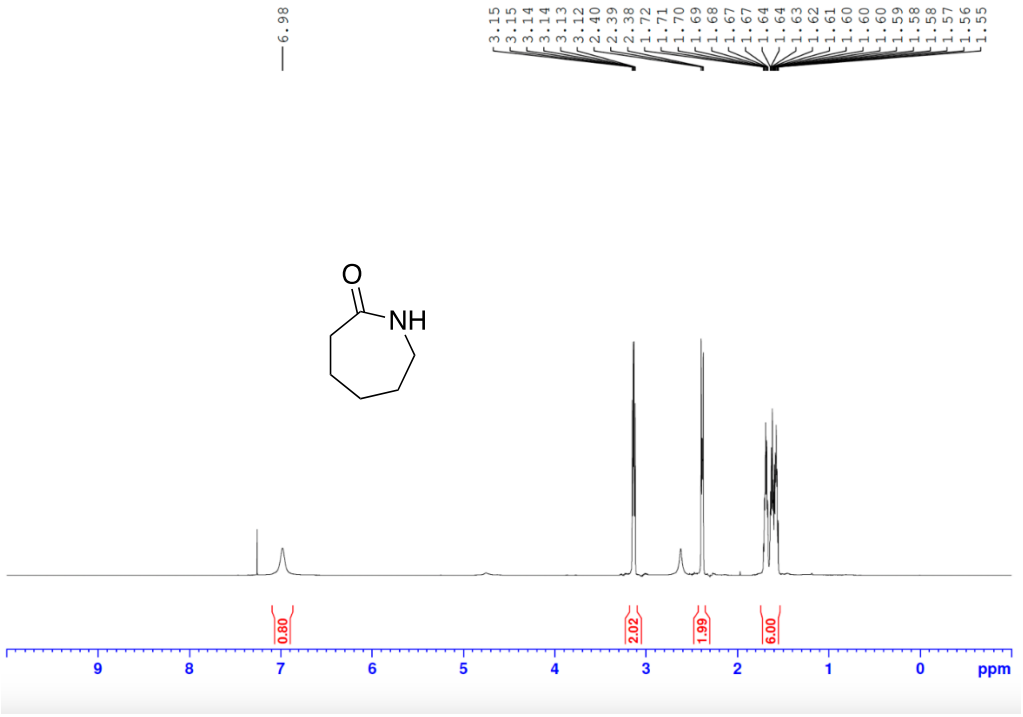


^{1}H NMR spectrum of compound **2i**

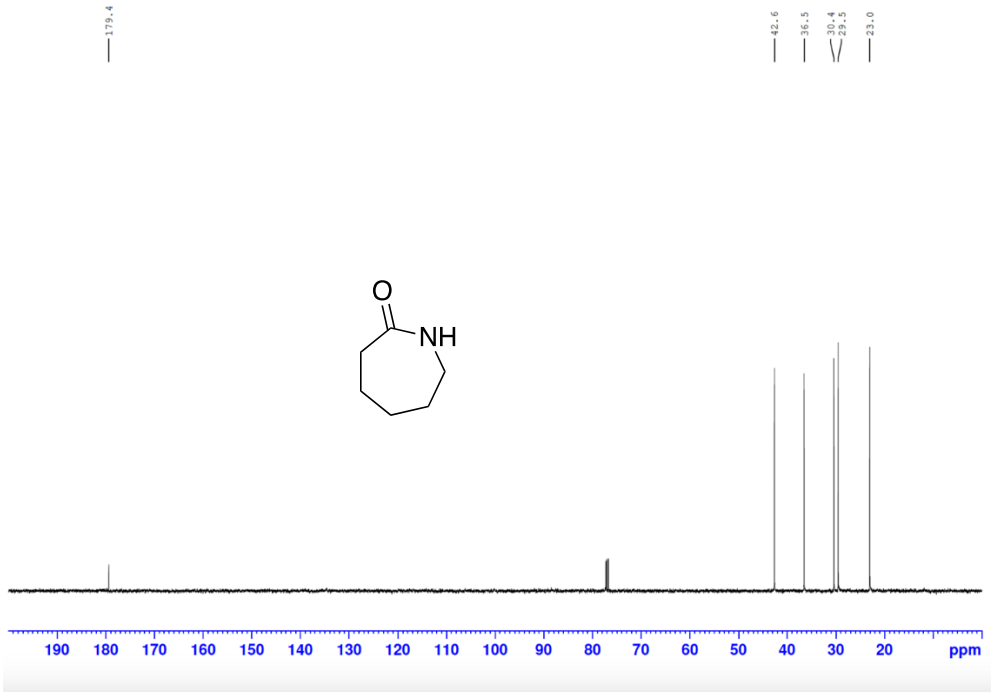


^{13}C NMR spectrum of compound **2i**

Azepan-2-one (2j) Colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (br s, 1H), 3.15-3.12 (m, 2H), 2.40-2.38 (m, 2H), 1.72-1.55 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.4, 42.6, 36.5, 30.4, 29.5, 23.0. HRMS (+ESI) calcd. for $C_6H_{12}NO$: 114.0913; found: 114.0913.

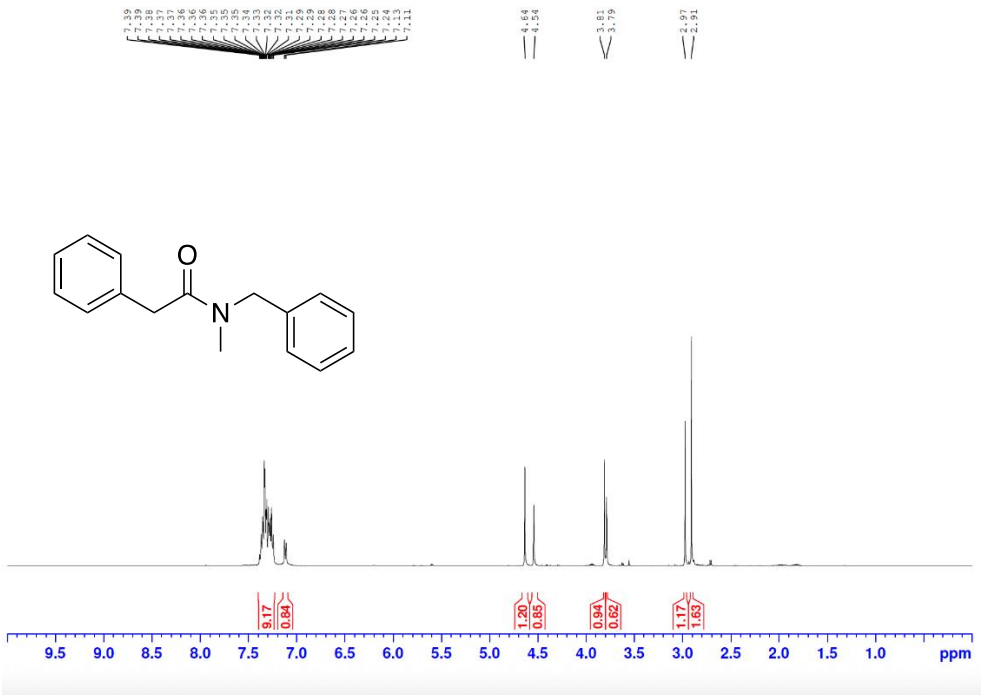


^{1}H NMR spectrum of compound **2j**

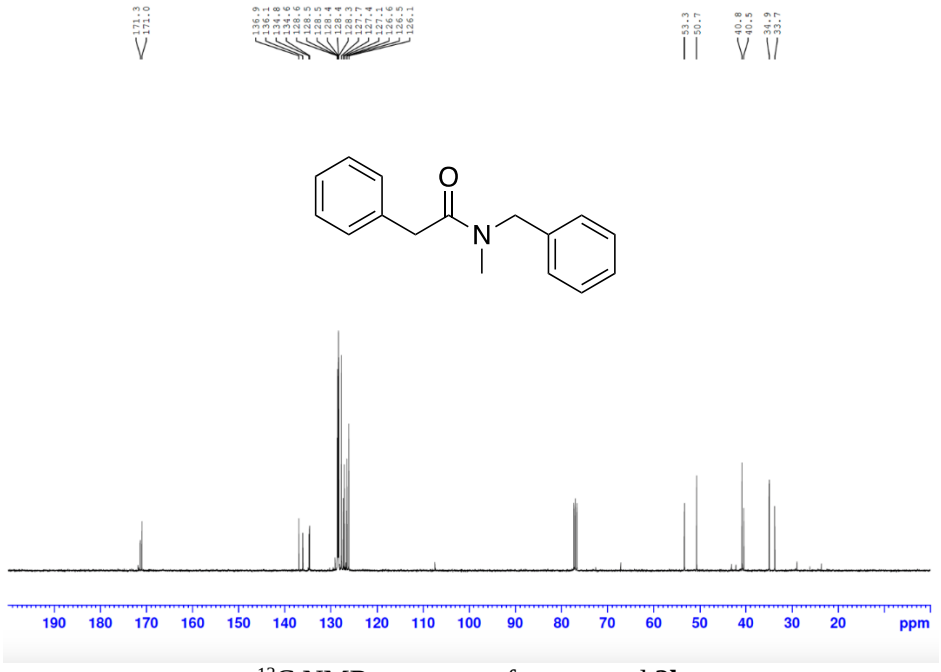


^{13}C NMR spectrum of compound **2j**

***N*-Benzyl-*N*-methyl-2-phenylacetamide (2k)** Brownish liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.24 (m, 9H), 7.13-7.11 (d, 1H), 4.64 (s, 1.2H), 4.54 (s, 0.8H), 3.81 (s, 1H), 3.79 (s, 1H), 2.97 (s, 1H), 2.91 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 171.0, 136.9, 136.1, 134.8, 134.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 127.7, 127.4, 127.1, 126.6, 126.5, 126.1, 53.3, 50.7, 40.8, 40.5, 34.9, 33.7. HRMS (+ESI) calcd. for $C_{14}H_{14}NO$: 240.1383; found: 240.1379.

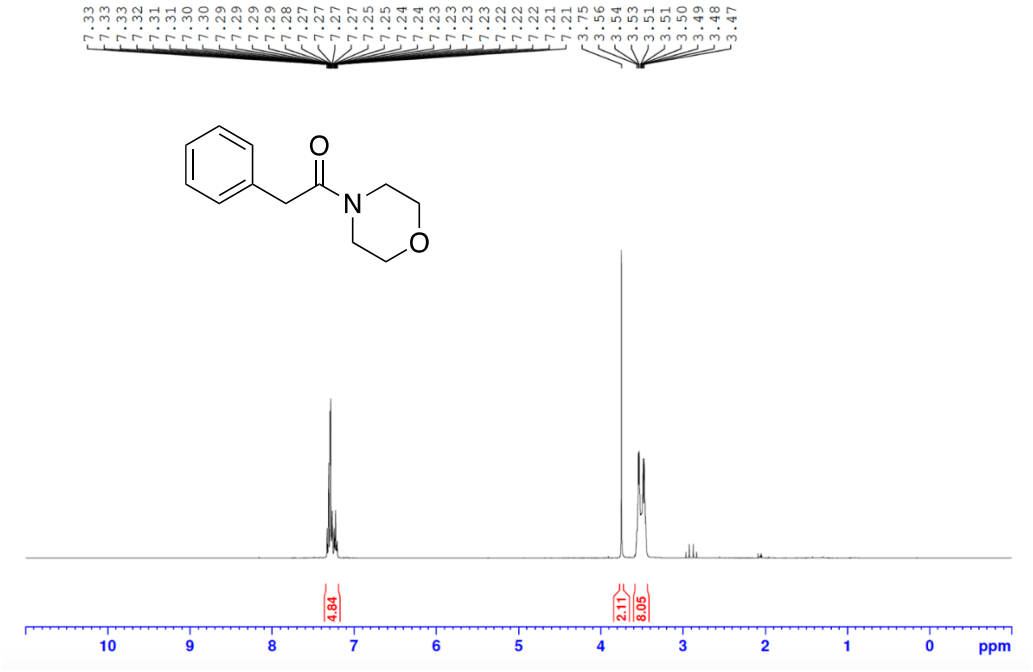


^{1}H NMR spectrum of compound **2k**

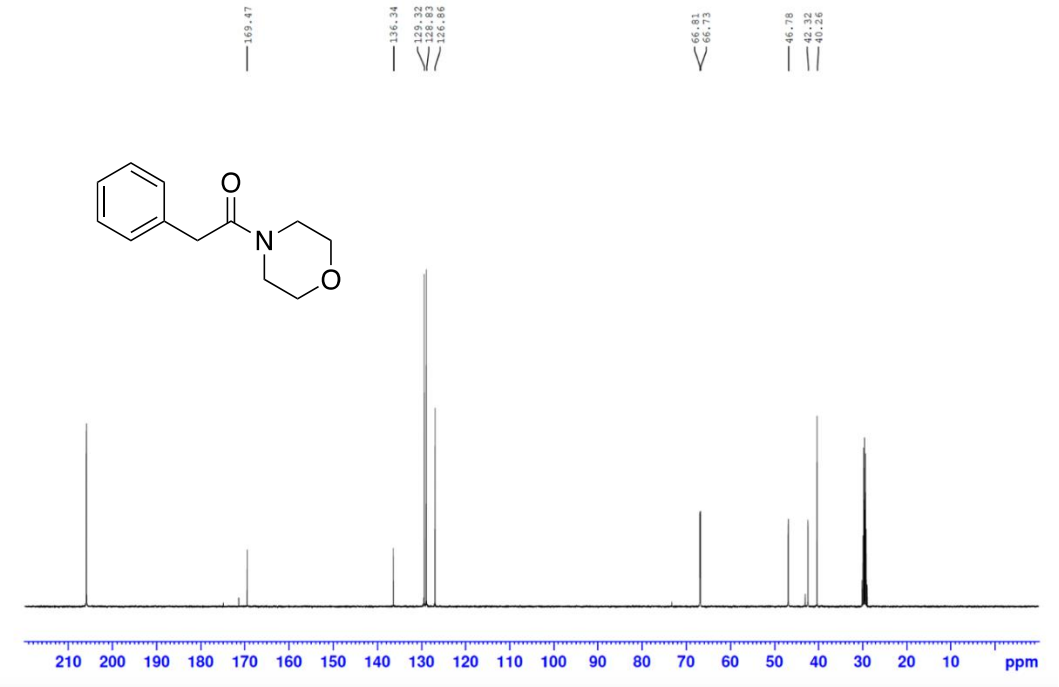


^{13}C NMR spectrum of compound **2k**

1-Morpholino-2-phenylethan-1-one (2l) Brownish solid. ^{1}H NMR (400 MHz, Acetone-d_6): δ 7.33-7.21 (m, 5H), 3.75 (s, 2H), 3.56-3.47 (m, 8H). ^{13}C NMR (100 MHz, Acetone-d_6): δ 169.5, 136.3, 129.3, 128.8, 126.9, 66.8, 66.7, 46.8, 42.3, 40.3. HRMS (+ESI) calcd. for $C_{12}H_{16}NO_2$: 206.1176; found: 206.1172.

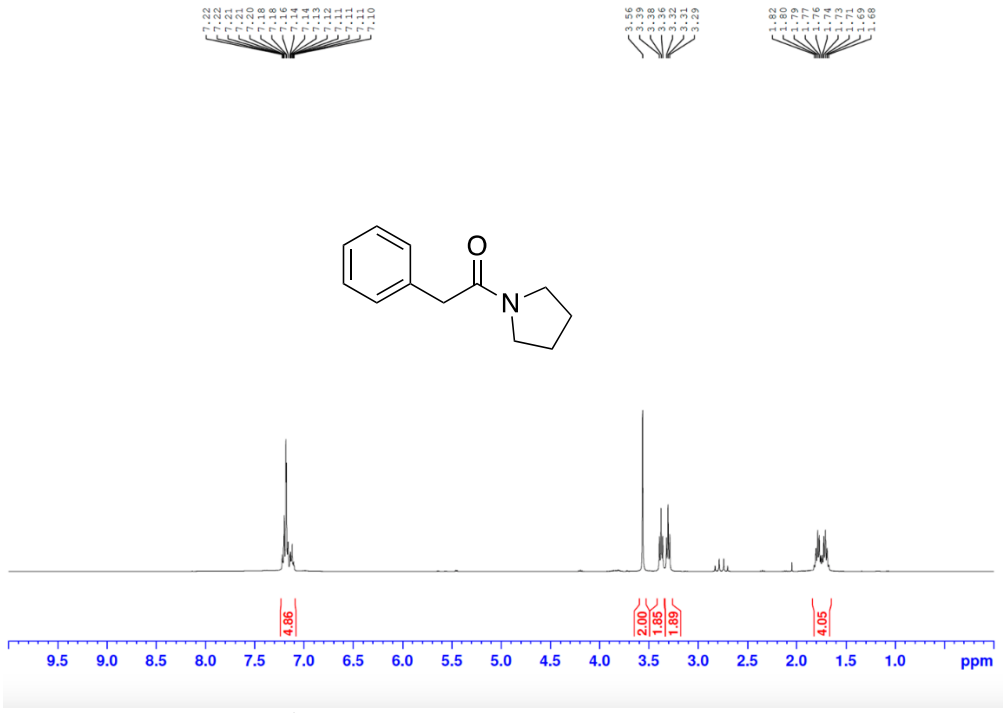


^{1}H NMR spectrum of compound **2l**

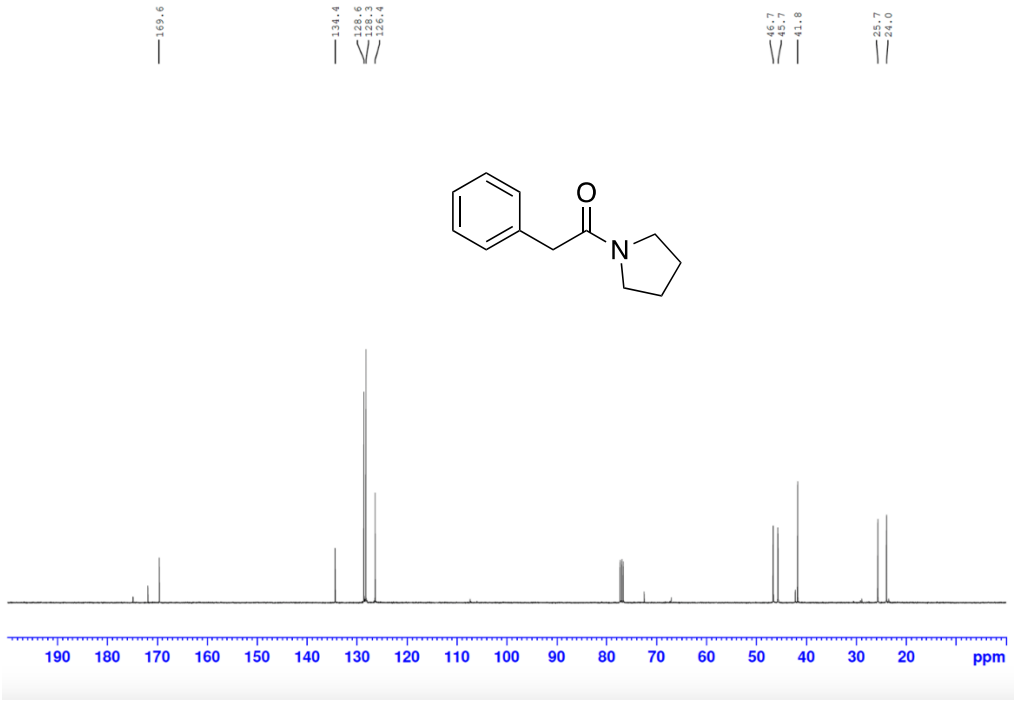


^{13}C NMR spectrum of compound **2l**

2-Phenyl-1-(pyrrolidin-1-yl)ethan-1-one (2m) Dark brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.10 (m, 5H), 3.56 (s, 2H), 3.38 (t, J = 6.88 Hz, 2H), 3.31 (t, J = 6.64 Hz, 2H), 1.82-1.68 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 134.4, 128.6, 128.3, 126.4, 46.7, 45.7, 41.8, 25.7, 24.0. HRMS (+ESI) calcd. for $C_{12}H_{16}NO$: 190.1226; found: 190.1229.

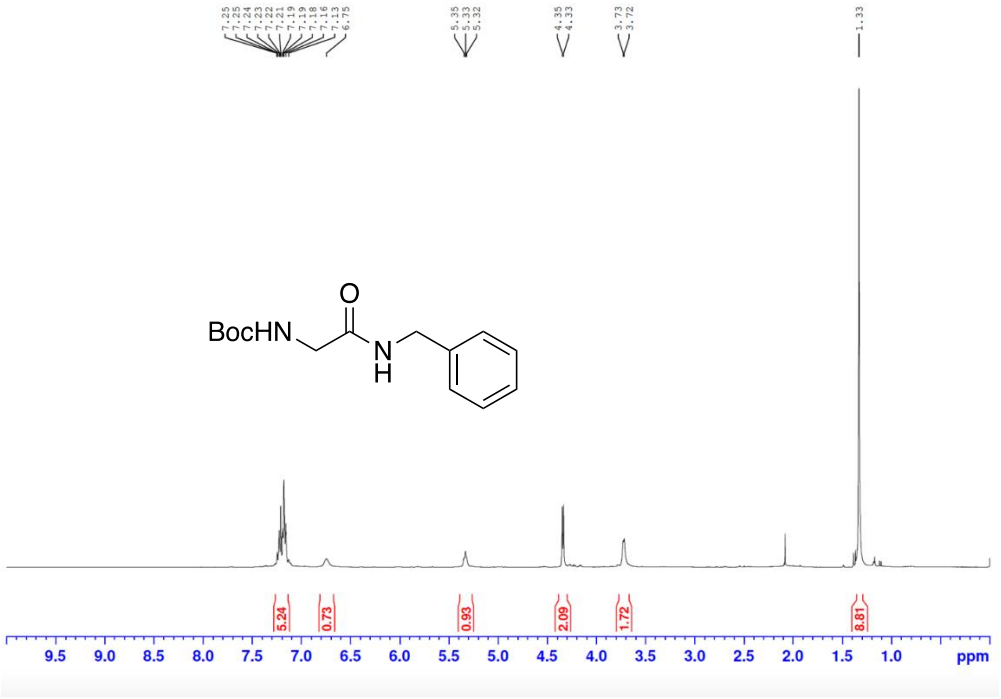


^{1}H NMR spectrum of compound **2m**

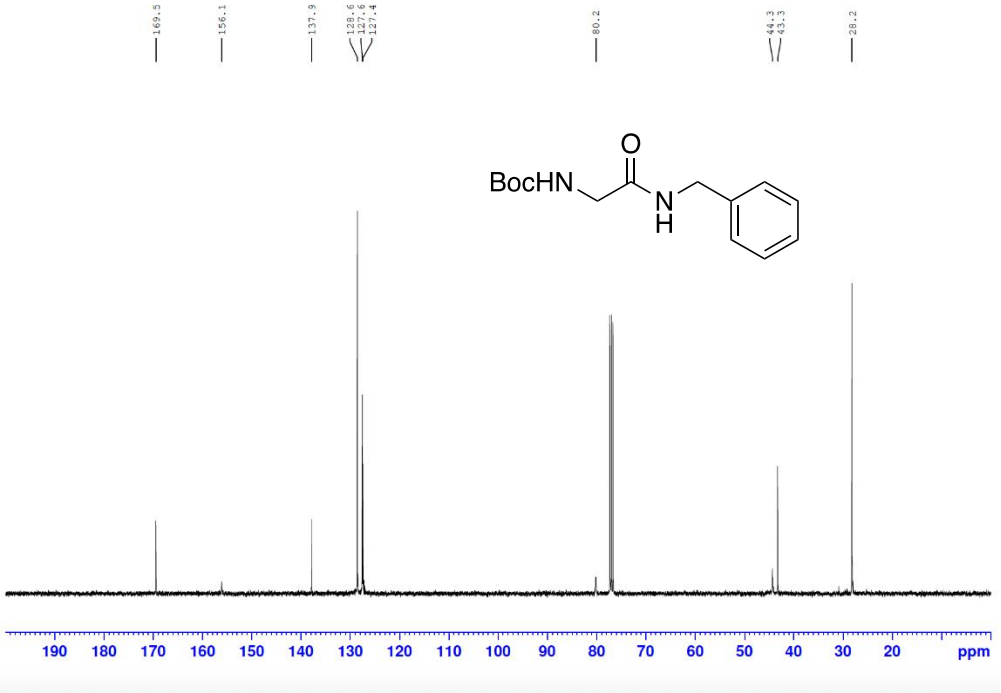


^{13}C NMR spectrum of compound **2m**

***tert*-Butyl (2-(benzylamino)-2-oxoethyl)carbamate (2n)** Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.13 (m, 5H), 6.75 (br s, 1H), 5.35-5.32 (m, 2H), 4.35 (d, J = 5.76 Hz, 2H), 3.73 (d, J = 4.72 Hz, 2H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 156.1, 137.9, 128.6, 127.6, 127.4, 80.2, 44.3, 43.3, 28.2. HRMS (+ESI) calcd. for $C_{14}H_{20}NaN_2O_3$: 287.1366; found: 287.1368.

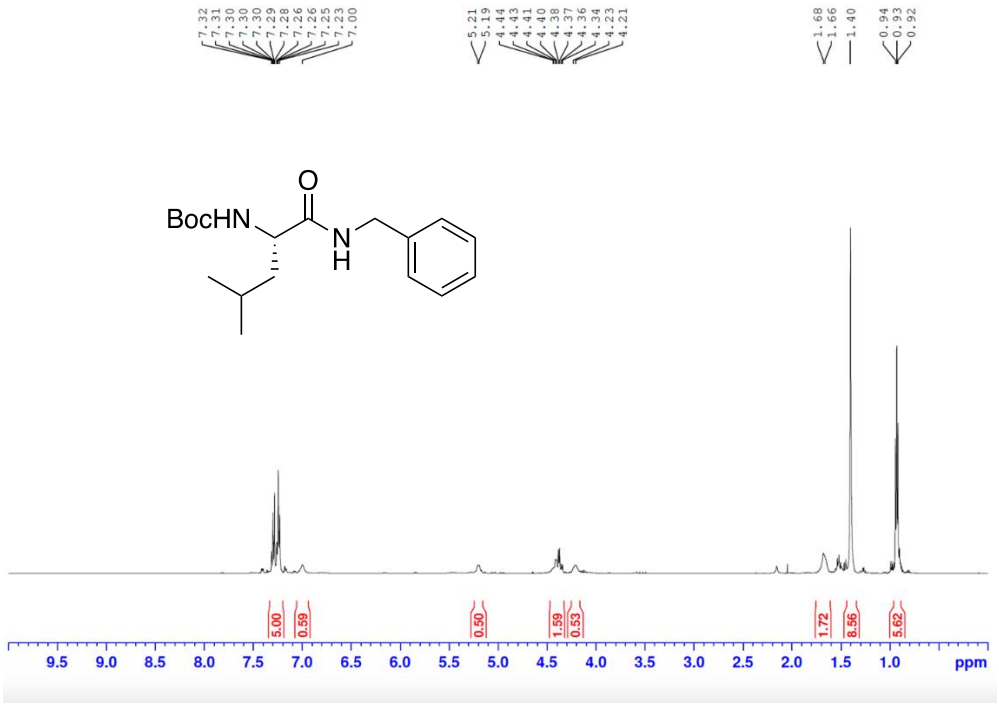


^{1}H NMR spectrum of compound **2n**

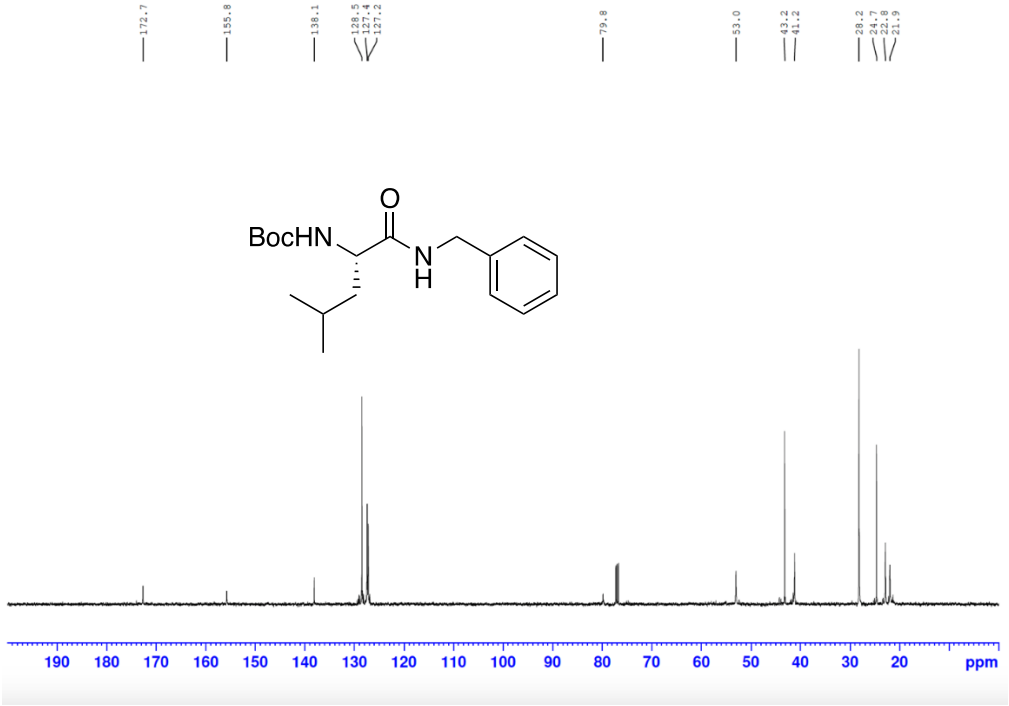


^{13}C NMR spectrum of compound **2n**

***tert*-Butyl (*S*)-(1-(benzylamino)-4-methyl-1-oxopentan-2-yl)carbamate (2o)** Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.23 (m, 5H), 6.99 (br s, 1H), 5.21-5.19 (m, 1H), 4.44-4.34 (m, 2H), 4.23-4.21 (m, 1H), 1.68 (m, 2H), 1.40 (s, 9H), 0.94 (d, J = 6.65 Hz, 3H), 0.93 (d, J = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 155.8, 138.1, 128.5, 127.4, 127.2, 79.8, 53.0, 43.2, 41.2, 28.2, 24.7, 22.8, 21.9. HRMS (+ESI) calcd. for $C_{18}H_{29}N_2O_3$: 321.2173; found: 321.2175.

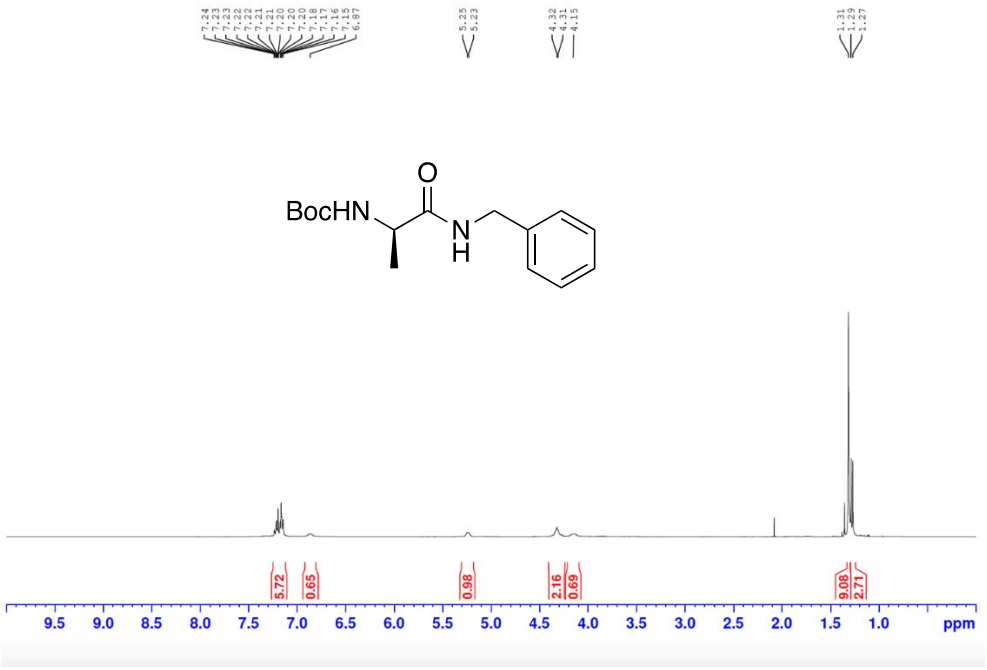


^{1}H NMR spectrum of compound **2o**

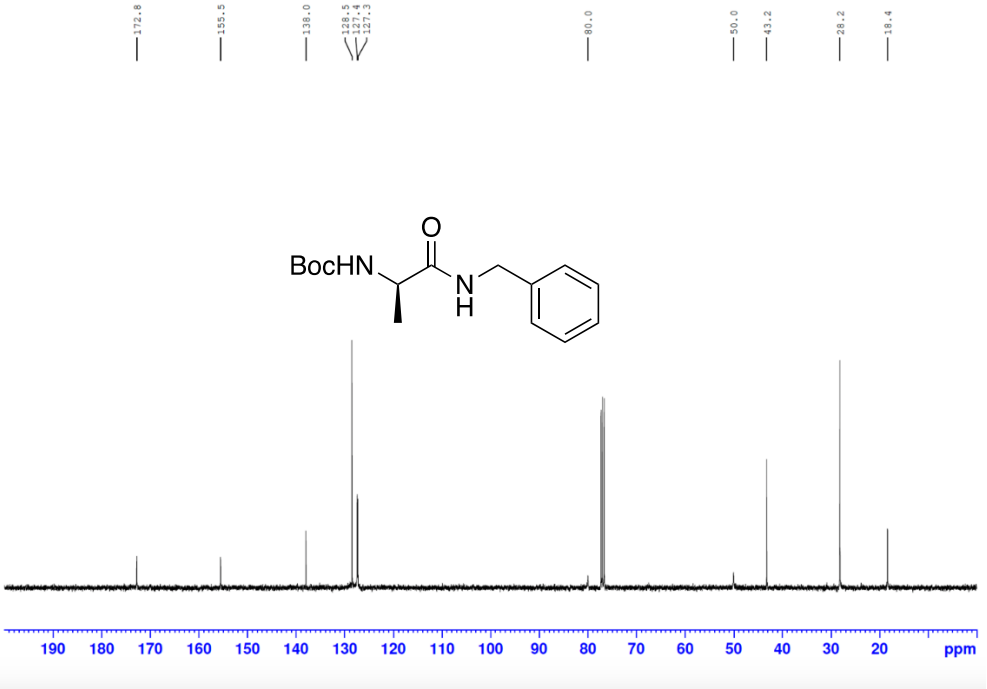


^{13}C NMR spectrum of compound **2o**

***tert*-Butyl (*R*)-(1-(benzylamino)-1-oxopropan-2-yl)carbamate (2p)** Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24-7.15 (m, 5H), 6.87 (br s, 1H), 5.25-5.23 (m, 1H), 4.32-4.31 (m, 2H), 4.15 (br s, 1H), 1.31 (s, 9H), 1.29 (d, J = 7.04 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 155.5, 138.0, 128.5, 127.4, 127.3, 80.0, 50.0, 43.2, 28.2, 18.4. HRMS (+ESI) calcd. for $C_{15}H_{22}NaN_2O_3$: 301.1523; found: 301.1525.

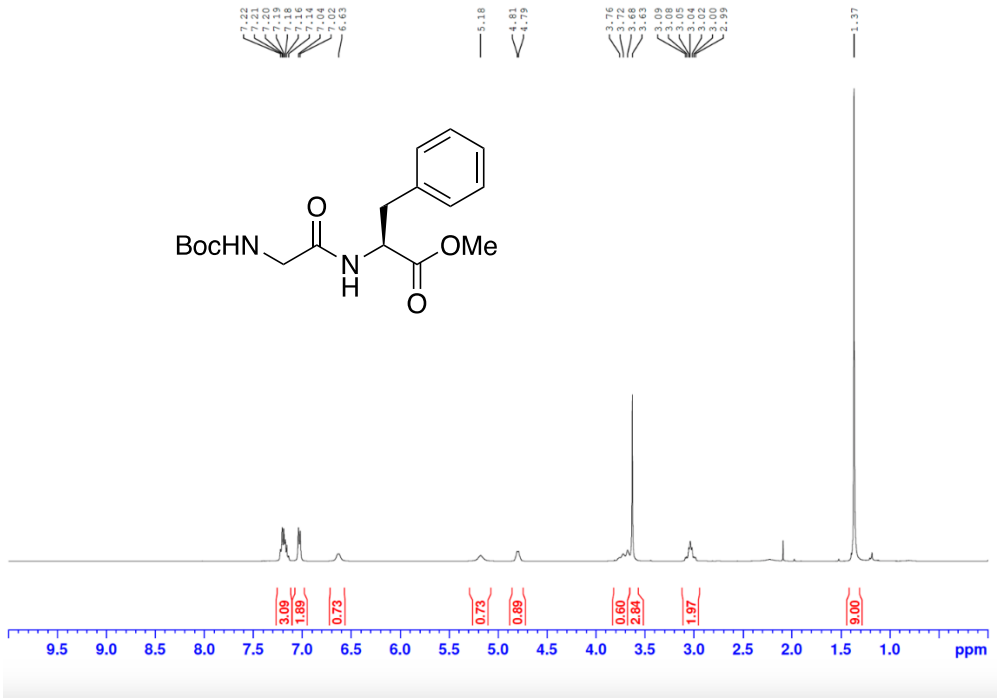


^{1}H NMR spectrum of compound **2p**

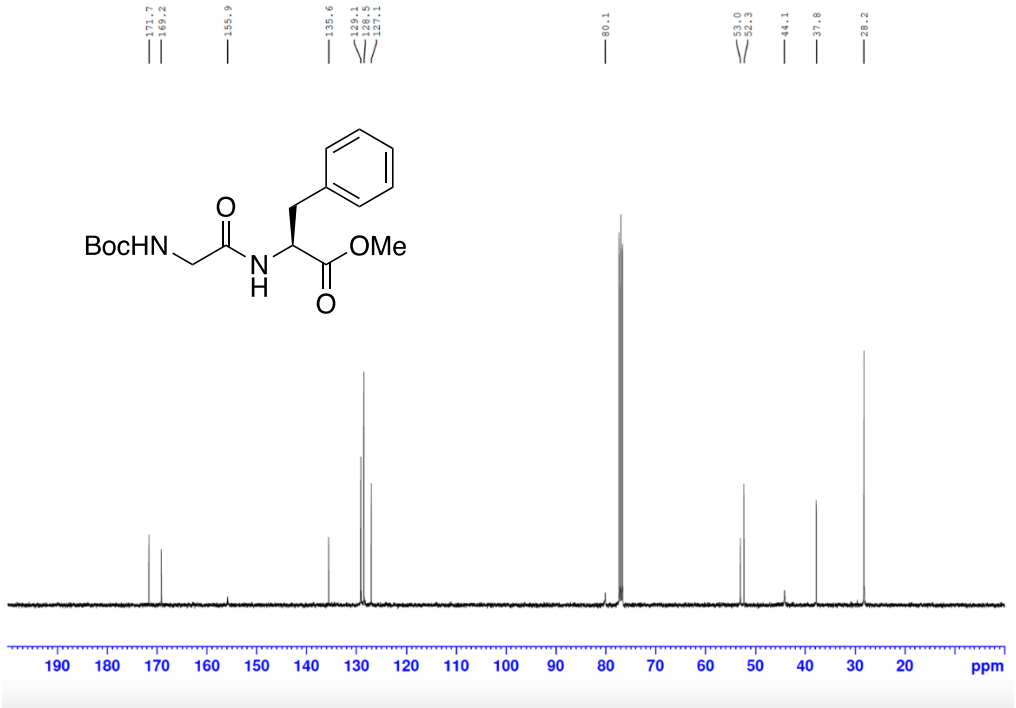


^{13}C NMR spectrum of compound **2p**

Methyl (*tert*-butoxycarbonyl)glycyl-*L*-phenylalaninate (2q) Colorless paste. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.14 (m, 3H), 7.04-7.02 (d, J = 8 Hz, 2H), 6.63 (br s, 1H), 5.18 (s, 1H), 4.81-4.80 (m, 1H), 3.76-3.68 (m, 1H), 3.63 (s, 3H), 3.09-2.99 (m, 2H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 169.2, 155.9, 135.6, 129.1, 128.7, 127.1, 80.1, 53.0, 52.3, 44.1, 37.8, 28.2. HRMS (+ESI) calcd. for $C_{17}H_{24}NaN_2O_5$: 359.1577; found: 359.1580.

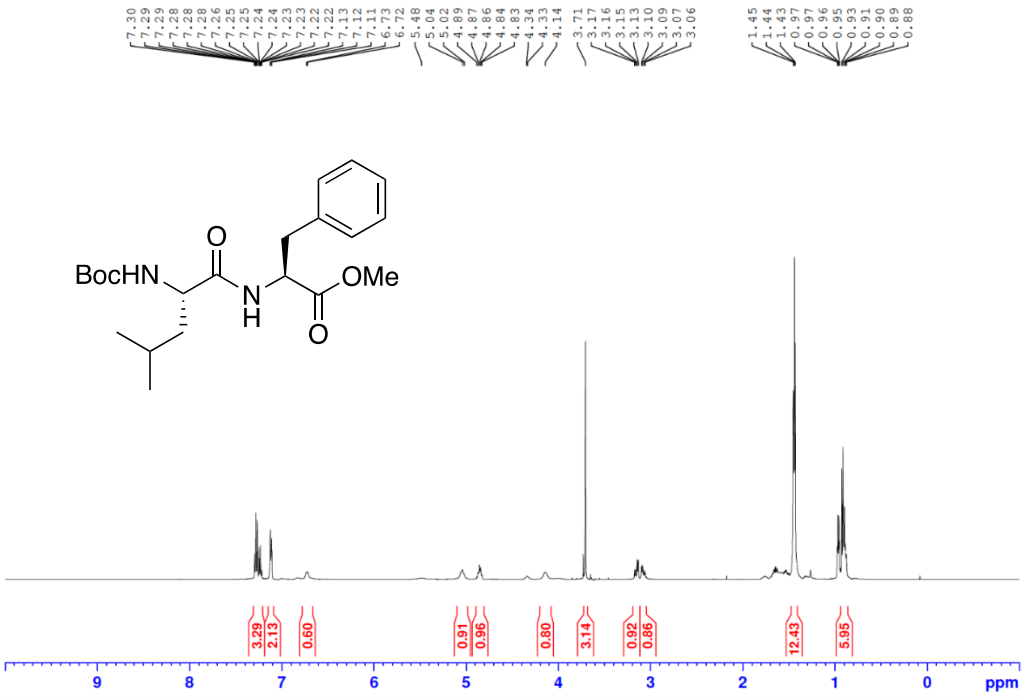


^{1}H NMR spectrum of compound **2q**

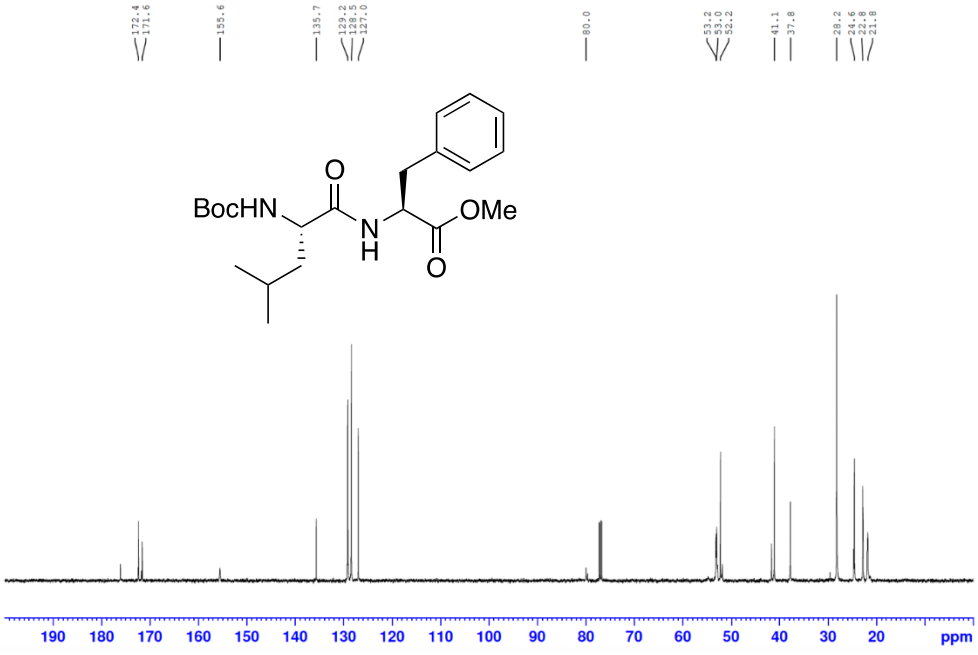


^{13}C NMR spectrum of compound **2q**

Methyl (*tert*-butoxycarbonyl)-*L*-leucyl-*L*-phenylalaninate (2r) Yellowish paste. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.22 (m, 3H), 7.13-7.11 (m, 2H), 6.73-6.72 (m, 1H) 5.04-5.02 (m, 1H), 4.89-4.83 (m, 1H), 4.14 (s, 1H), 3.71 (s, 3H), 3.17-3.13 (dd, J = 13.9, 5.9 Hz, 1H), 3.10-3.06 (dd, J = 13.75, 6.15 Hz, 1H), 1.45-1.43 (m, 12H), 0.97-0.88 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 171.6, 155.6, 135.7, 129.2, 128.5, 127.0, 80.0, 53.2, 53.0, 52.2, 41.1, 37.8, 28.2, 24.6, 22.8, 21.8. HRMS (+ESI) calcd. for $C_{21}H_{33}N_2O_5$: 393.2384; found: 393.2386.

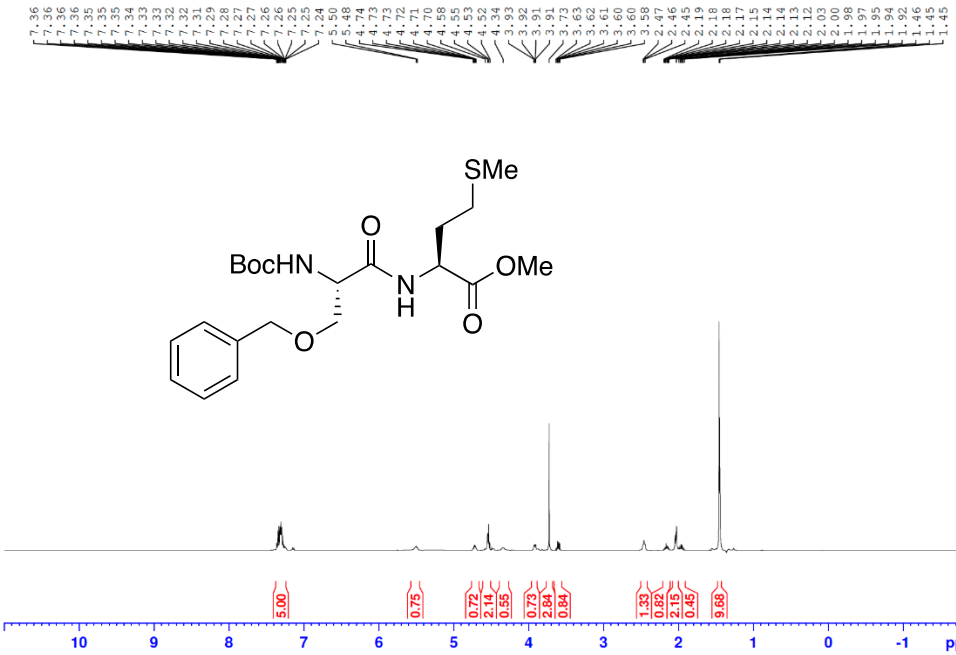


^{1}H NMR spectrum of compound **2r**

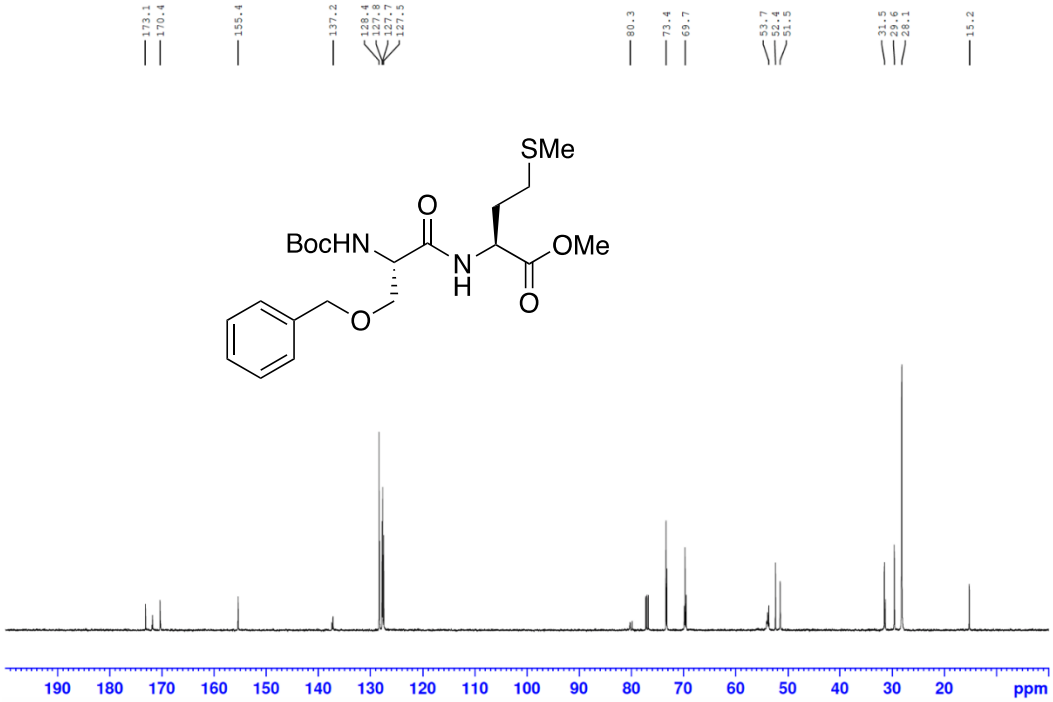


^{13}C NMR spectrum of compound **2r**

Methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-seryl-*L*-methioninate (2s) Yellowish paste. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36-7.25 (m, 5H), 5.50-5.48 (m, 1H), 4.73-4.70 (m, 1H), 4.55-4.52 (m, 2H), 4.34 (s, 1H), 3.93-3.91 (m, 1H), 3.73 (s, 3H), 3.63-3.58 (m, 1H), 2.47-2.45 (m, 2H), 2.19-2.12 (m, 1H), 2.03 (s, 3H), 2.00-1.92 (m, 1H), 1.45 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 170.4, 155.4, 137.2, 128.4, 127.8, 127.7, 127.5, 80.3, 73.4, 69.7, 53.7, 52.4, 51.5, 31.5, 29.6, 28.1, 15.2. HRMS (+ESI) calcd. for $C_{21}H_{32}NaN_2O_6S$: 463.1873; found: 463.1875.

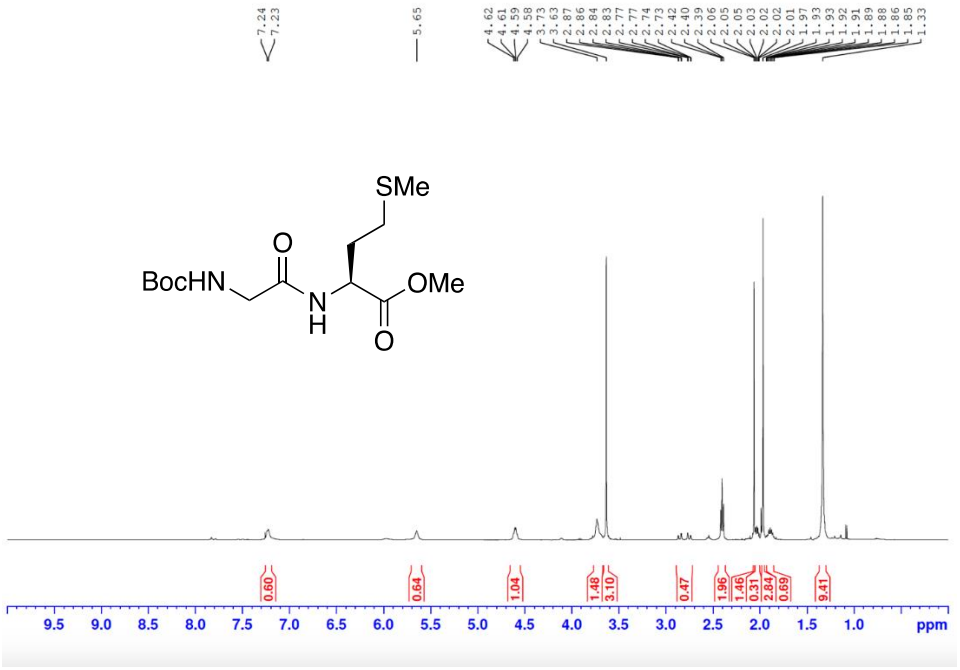


^{1}H NMR spectrum of compound **2s**

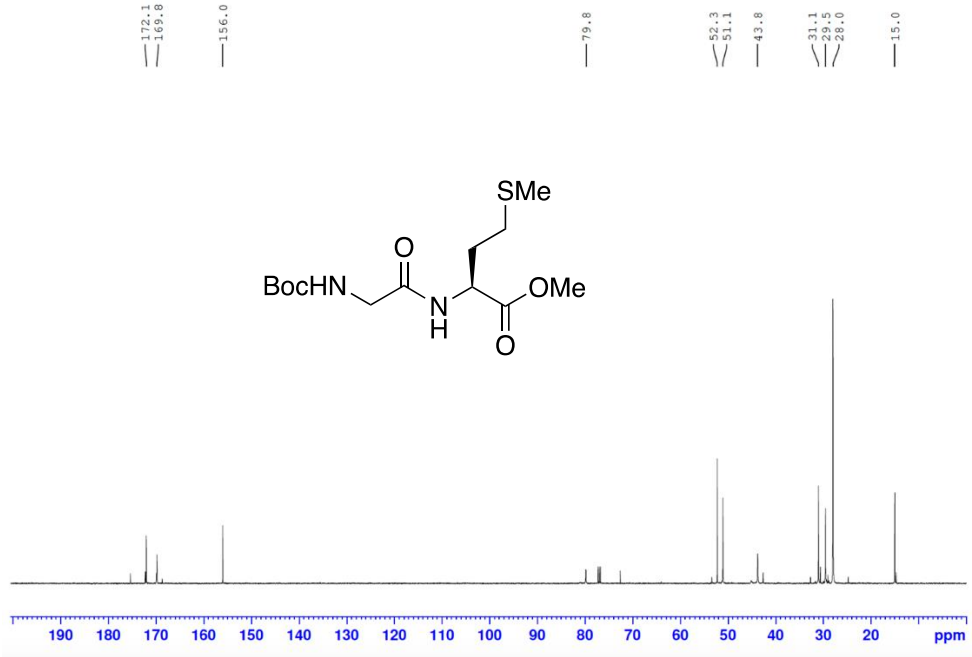


^{13}C NMR spectrum of compound **2s**

Methyl (*tert*-butoxycarbonyl)glycyl-*L*-methioninate (2t) Yellowish paste. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.23 (m, 1H), 5.65 (s, 1H), 4.62-4.58 (m, 1H), 3.73 (br s, 2H), 3.63 (s, 3H), 2.87-2.73 (m, 1H), 2.40 (t, J = 7.7 Hz, 2H), 2.06 (s, 2H), 1.97 (s, 3H), 1.93-1.85 (m, 1H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 171.6, 155.6, 135.7, 129.2, 128.5, 127.0, 80.0, 53.2, 53.0, 52.2, 41.1, 37.8, 28.2, 24.6, 22.8, 21.8. HRMS (+ESI) calcd. for $C_{13}H_{24}NaN_2O_5S$: 343.1298; found: 343.1300.



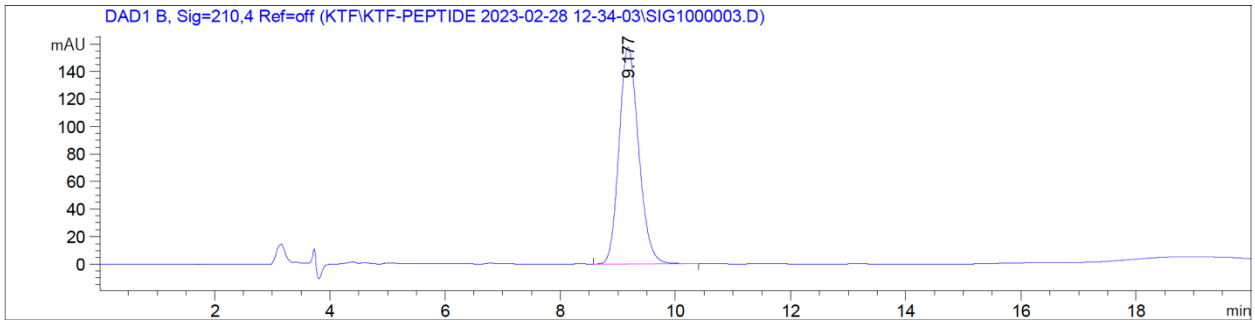
^{1}H NMR spectrum of compound **2t**



^{13}C NMR spectrum of compound **2t**

HPLC chromatograms of dipeptides

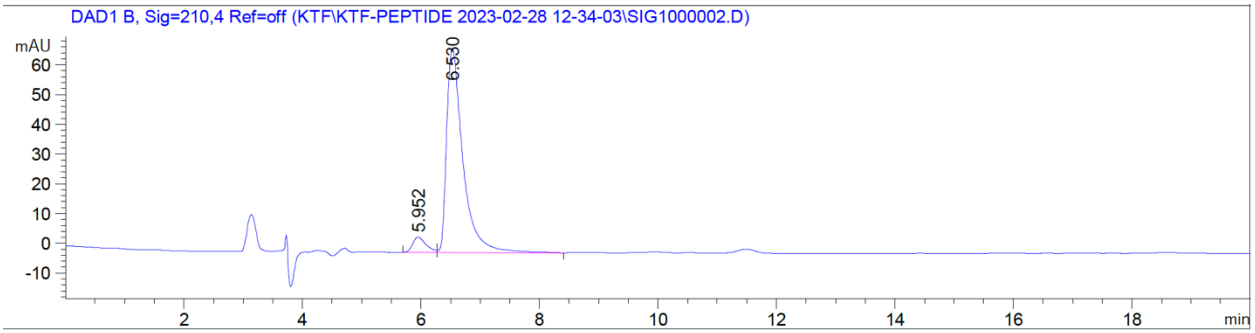
Methyl (*tert*-butoxycarbonyl)-*L*-leucyl-*L*-phenylalaninate (2r)



Signal 2: DAD1 B, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.177	BB	0.3653	3723.48755	157.80589	100.0000
Totals :				3723.48755	157.80589	

Methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-seryl-*L*-methioninate (2s)



Signal 2: DAD1 B, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.952	BV	0.2345	80.17085	5.12392	5.7432
2	6.530	VB	0.2894	1315.74500	68.72381	94.2568
Totals :				1395.91585	73.84772	