Supporting Information

Stereospecific Cross-Coupling of Secondary Alkyl β-Trifluoroboratoamides

Deidre L. Sandrock,[†] Ludivine Jean-Gérard,[†] Cheng-yi Chen,[‡] Spencer D. Dreher,[‡] and Gary A. Molander[†]*

[†]Roy and Diana Vagelos Laboratories, Penn/Merck Laboratory for High-Throughput Experimentation, Department of Chemistry, University of Pennsylvania, 231 South 34th Street, Philadelphia, PA 19104-6323, and [‡]Department of Process Research and the Catalytic Reactions Discovery and Development Laboratory, Merck and Co. Inc., 126 East Lincoln Avenue, Rahway, NJ, USA 07065

Contents:

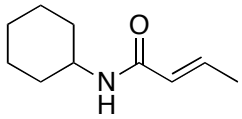
General. $Pd(OAc)_2$, XPhos (2-dicyclohexylphosphino-2',4',6'-diisopropyl-1,1'-biphenyl), SPhos (2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl), K_2CO_3, and Cs_2CO_3 were used as received. Toluene, THF, and CPME were distilled from sodium/benzophenone prior to use. H_2O was degassed prior to use. Standard benchtop techniques were employed for handling air–sensitive reagents. Melting points (°C) are uncorrected. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded at 500.39, 125.75, and 470.55 MHz, respectively. ^{19}F NMR chemical shifts were referenced to external $CFCl_3$ (0.0 ppm). ^{11}B NMR spectra at 128.4 MHz were obtained on a spectrometer equipped with the appropriate decoupling accessories. All ^{11}B NMR chemical shifts were referenced to external $BF_3 \cdot OEt_2$ (0.0 ppm) with a negative sign indicating an upfield shift. Analytical thin–layer chromatography (TLC) was performed on TLC silica gel plates (0.25 mm) precoated with a fluorescent indicator. Standard flash chromatography procedures[11] were followed using 32–63 μm silica gel.

Preparation of α,β-unsaturated amide starting materials:

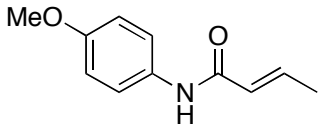
α,β-Unsaturated amides were prepared according to the following procedure.[2] Those derived from the reaction of dimethylamine,[3] piperidine,[4] pyrrolidine,[5] and dibenzylamine[6] with crotonoyl chloride; and pyrrolidine[7] with cinnamoyl chloride were prepared following this procedure and were in accordance with the spectral data reported in the literature. (*E*)-*N*-Ethyl-*N*-(*o*-tolyl)but-2-enamide was available commercially.

Procedure: Crotonoyl chloride (1.12 g, 10.7 mmol, 1.2 equiv) was dissolved in CH_2Cl_2 (100 mL) in a dry 250 mL flask that was purged with N_2 (three times) and the reaction

mixture was cooled to 0 °C. To this soln were added dropwise the amine (8.9 mmol, 1 equiv) and Et_3N (1.49 mL, 10.7 mmol, 1.2 equiv). Following addition, the reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was then concentrated and redissolved in EtOAc (50 mL) and washed with H_2O (2 x 20 mL), sat. $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated to provide the crude amide that could be purified by column chromatography or by distillation.



***(E)-N*-Cyclohexylbut-2-enamide.** According to the general procedure using cyclohexylamine (0.88 g, 8.9 mmol, 1 equiv) and crotonoyl chloride (1.12 g, 10.7 mmol, 1.2 equiv), the product was obtained in 79% yield (1.18 g, 7.06 mmol) as a white solid after silica gel column chromatography (elution with hexane/EtOAc 7:3). mp = 113-115 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.78-6.85 (dq, *J* = 13.8, 6.9 Hz, 1H), 5.73-5.76 (d, *J* = 15.0 Hz, 1H), 5.23 (br s, 1H), 3.83-3.85 (m, 1H), 1.93-1.96 (m, 2H), 1.83-1.84 (d, *J* = 6.9 Hz, 3H), 1.61-1.73 (m, 3H), 1.34-1.43 (m, 2H), 1.09-1.20 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 165.1, 139.3, 125.7, 48.1, 33.3, 25.6, 25.0, 17.7; IR (neat) 3286, 3082, 2931, 2854, 1627, 1552 cm^{-1}; HRMS (CI) calcd. for $C_{10}H_{18}NO$ $[M+H]^+$ 168.1388, found 168.1389.



(*E*)-*N*-(4-Methoxyphenyl)but-2-enamide. According to the general procedure using *p*-anisidine (1.10 g, 8.9 mmol, 1 equiv) and crotonoyl chloride (1.12 g, 10.7 mmol, 1.2 equiv), the product was obtained in 82% yield (1.39 g, 7.29 mmol) as an off-white solid after silica gel column chromatography (gradient elution with hexane/EtOAc 4:1 to 1:1). mp = 119-120 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45-7.47 (d, *J* = 8.5, 2H), 7.26 (br s, 1H), 6.92-6.99 (dq, *J* = 13.9, 6.8 Hz, 1H), 6.84-6.86 (d, *J* = 8.5, 2H), 5.91-5.95 (dd, *J* = 15.1, 1.6 Hz, 1H), 3.79 (s, 3H), 0.88-1.89 (d, *J* = 7.0, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 164.2, 156.5, 141.0, 131.4, 125.6, 122.0, 114.2, 55.6, 17.9; IR (neat) 3290, 2967, 1669, 1628, 1532, 1510, 1244 cm^{-1}; HRMS (CI) calcd. for $C_{11}H_{14}NO_2$ $[M+H]^+$ 192.1025, found 192.1027.

General Procedure for the Preparation of Racemic Secondary Potassium β-Trifluoroboratoamides:[8]

A flask was charged with CuCl (14.6 mg, 0.15 mmol, 0.03 equiv), NaO*t*-Bu (42.6 mg, 0.44 mmol, 0.09 equiv), and DPEPhos (79.2 mg, 0.15 mmol, 0.03 equiv) and purged with N_2 (three times). THF (5 mL) was added and the reaction mixture was stirred at rt for 30 min. After 30 min, a soln of bis(pinacolato)diboron (1.56 g, 6.15 mmol, 1.25 equiv) in THF (5 mL, prepared in a separate flask under a N_2 atmosphere) was added and the flask containing the bis(pinacolato)diboron was rinsed with additional THF (5 mL) and also added to the reaction mixture. After stirring for 10 min, the α,β-unsaturated amide (4.92 mmol, 1.00 equiv) and MeOH (398 μL, 9.84 mmol, 2 equiv) were added, and the reaction

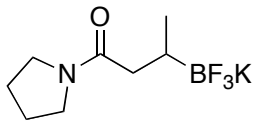
was stirred at rt until no starting material amide was observed by TLC or ^{1}H NMR spectroscopy. The reaction mixture was filtered through a pad of Celite and rinsed with EtOAc and concentrated to give the crude borylated compound. The crude borylated compound was dissolved in MeCN (10 mL) and sat. aq. KHF_2 (4.5 M, 4.37 mL, 19.7 mmol, 4 equiv) was added. The reaction mixture was stirred for 2 h, concentrated, azeotroped with wet MeOH[9] or EtOH, and placed on the high vacuum overnight. The crude product was extracted with hot acetone or CH_3CN (3 x 10 mL), filtered, and then concentrated. To the resulting crude material, Et_2O was added (10 mL), and the mixture was sonicated for 30 min and filtered to yield the desired β-trifluoroboratoamides. (N.B. In some cases, the purification of the RBPin material was made easier by purification by column chromatography before quench with KHF_2).

General Procedure for the Preparation of Enantioenriched Secondary Potassium β-Trifluoroboratoamides:[8]

A flask was charged with CuCl (17.8 mg, 0.18 mmol, 0.03 equiv), NaO*t*-Bu (51.7 mg, 0.54 mmol, 0.09 equiv), and (*R*)-(*S*)-JosiPhos (115 mg, 0.18 mmol, 0.03 equiv) and purged with N_2 (three times). THF (5 mL) was added and the reaction mixture was stirred at rt for 30 min. After 30 min, a soln of bis(pinacolato)diboron (1.90 g, 7.47 mmol, 1.25 equiv) in THF (5 mL, prepared in a separate flask under a N_2 atmosphere) was added, and the flask containing the bis(pinacolato)diboron was rinsed with additional THF (5 mL) and then added to the reaction mixture. After stirring for 10 min, the α,β-unsaturated amide (5.98 mmol, 1.00 equiv) and MeOH (485 μL, 12.0 mmol, 2 equiv) were added, and the reaction was stirred at rt until no starting material amide was

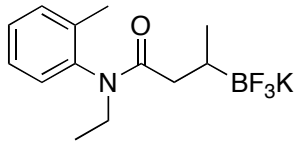
observed by TLC or ^{1}H NMR spectroscopy. The reaction mixture was filtered through a pad of Celite and rinsed with EtOAc and concentrated to give the crude borylated compound. The crude borylated compound was dissolved in MeCN (10 mL) and sat. aq KHF_2 (4.5 M, 4.37 mL, 19.7 mmol, 4 equiv) was added. The reaction mixture was stirred for 2 h, concentrated, azeotroped with wet MeOH or EtOH, and placed on the high vacuum overnight. The crude product was extracted with hot acetone or CH_3CN (3 x 10 mL), filtered, and then concentrated. To the resulting crude material, Et_2O was added (10 mL), and the mixture was sonicated for 30 min and filtered to yield the desired β-boratoamidohomoenolate.

Compound characterization of β-Trifluoroboratoamides:[10]

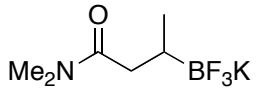


Potassium 1-(Pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one. According to the general procedure for the racemic preparation using (*E*)-1-(pyrrolidin-1-yl)but-2-en-1-one (1.37 g, 9.84 mmol), the boronate ester was obtained in 89% yield (2.33 g, 8.76 mmol) after purification by column chromatography (elution in hexanes/EtOAc 4:1). A portion of this product (1.82 g, 6.81 mmol) was subjected to the general procedure for trifluoroborate preparation, and after extraction with acetone (3 x 20 mL) and sonication with Et_2O (10 mL) for 30 min, the title compound was obtained as a white solid in 84% yield (1.43 g, 5.78 mmol) for an overall yield of 75% from the corresponding alkene. mp = 119-121 °C. ^{1}H NMR (500 MHz, acetone-d_6): δ 3.37-3.51 (m, 2H), 3.29-3.32 (m, 2H), 2.19-2.23 (dd, J = 13.4, 6.6 Hz, 1H), 1.70-1.98 (m, 5H), 0.79 (m, 4H). ^{13}C NMR (125.8

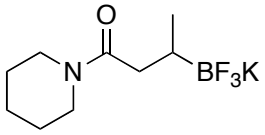
MHz, acetone-d_6): δ 173.7, 46.1, 45.0, 38.6, 25.8, 24.0, 16.1. ^{19}F NMR (470.8 MHz, acetone-d_6): δ -148.0. ^{11}B NMR (128.4 MHz, acetone-d_6): δ 5.21. IR (KBr) 2966, 2877, 1620, 1458, 1343, 1314 cm^{-1}. HRMS (ESI) calcd. for $C_9H_{17}BNO_2$ [M(-F_3K)(+OMe)]$^+$ 182.1352, found 182.1344.



Potassium *N*-Ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide. According to the general procedure for the racemic preparation using (*E*)-*N*-ethyl-*N*-(*o*-tolyl)but-2-enamide (10.0 g, 49.2 mmol) and azeotroping with EtOH, the product was obtained as a white crystalline solid in 93% yield (14.2 g, 45.8 mmol). The title compound was purified by continuous Soxhlet extraction with acetone (100 mL), and the resulting solution was concentrated until minimally soluble in hot acetone, and then Et_2O (~50 mL) was added to precipitate. mp = 229-231 °C. ^{1}H NMR (500 MHz, asterisk denotes minor rotamer peaks, DMSO-d_6): δ 7.17-7.32 (m, 3H), 7.05 (m, 1H), 3.88-3.99 (m, 1H), 3.12-3.16* (m, 1H), 2.97-3.01 (m, 1H), 2.07-2.14 (m, 3H), 1.74-1.82 (m, 1H), 1.43-1.49* (m, 1H), 1.27-1.32 (m, 1H), 0.95-1.02 (m, 3H), 0.53-0.74 (m, 4H). ^{13}C NMR (125.8 MHz, asterisk denotes rotamer peaks, DMSO-d_6): δ 174.7, 174.2*, 142.2, 141.9*, 136.2, 135.6*, 131.4, 131.4*, 130.0, 129.8*, 128.0, 127.9*, 127.2, 127.1*, 42.6, 42.2*, 38.5, 37.2*, 17.6, 16.5, 16.3*, 13.4, 13.2*. ^{19}F NMR (470.8 MHz, DMSO-d_6): δ -145.7. ^{11}B NMR (128.4 MHz, DMSO-d_6): δ 4.80. IR (KBr) 2938, 2870, 1648, 1492, 1458, 1409, 1294 cm^{-1}. HRMS (ESI) calcd. for $C_{14}H_{21}BNO_2$ [M(-F_3K)(+OMe)]$^+$ 246.1665, found 246.1677.

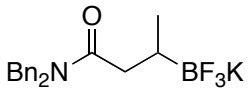


Potassium *N*,*N*-Dimethyl-3-(trifluoroborato)butanamide. According to the general procedure for the racemic preparation using (*E*)-*N*,*N*-dimethylbut-2-enamide (2.23 g, 19.7 mmol), the product was obtained as a white amorphous solid in 83% yield (3.62 g, 16.4 mmol). The title compound was extracted with hot acetone (3 x 15 mL) and concentrated. The crude substrate was dissolved in CH_3CN (5 mL) and washed with hexanes (5 mL) to provide the title compound. ^{1}H NMR (500 MHz, acetone-d_6): δ 3.00 (s, 3H), 2.82 (s, 3H), 2.24-2.29 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.03-2.07 (m, 1H), 0.80-0.81 (m, 4H). ^{13}C NMR (125.8 MHz, acetone-d_6): δ 176.6, 38.8, 37.8, 35.2, 17.1. ^{19}F NMR (470.8 MHz, acetone-d_6): δ -147.4. ^{11}B NMR (128.4 MHz, acetone-d_6): δ 5.68. IR (neat) 2943, 2858, 1614 cm^{-1}. HRMS (ESI) calcd. for $C_7H_{15}BNO_2$ $[M(-F_3K)(+OMe)]^+$ 156.1196, found 156.1182.

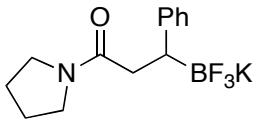


Potassium 1-(Piperidin-1-yl)-3-(trifluoroborato)butan-1-one. According to the general procedure for the racemic preparation using (*E*)-1-(piperidin-1-yl)but-2-en-1-one (754 mg, 4.92 mmol), the product was obtained as a light yellow amorphous solid in 81% yield (1.04 mg, 3.98 mmol) after hot filtration with acetone (3 x 10 mL), concentration, and sonication with Et_2O (10 mL). ^{1}H NMR (500 MHz, acetone-d_6): δ 3.42-3.43 (m, 4H), 2.22-2.23 (dd, *J* = 13.3, 8.1 Hz, 1H), 2.05-2.06 (m, 1H), 1.43-1.60 (m, 6H), 0.80-

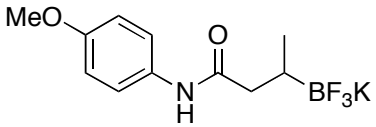
0.81 (d, J = 7.0 Hz, 3H), 0.71 (br s, 1H). ^{13}C NMR (125.8 MHz, acetone-d_6): δ 173.4, 46.2, 41.5, 37.4, 26.3, 25.6, 24.3, 15.8. ^{19}F NMR (470.8 MHz, acetone-d_6): δ -148.0. ^{11}B NMR (128.4 MHz, acetone-d_6): δ 5.60. IR (neat) 2937, 2861, 1606, 1471, 1446, 1274 cm^{-1}. HRMS (ESI) calcd. for $C_{10}H_{19}BNO_2$ [M(-F_3K)(+OMe)]$^+$ 196.1509, found 196.1511.



Potassium *N,N*-Dibenzyl-3-(trifluoroborato)butanamide. According to the general procedure for the racemic preparation using (*E*)-*N,N*-dibenzylbut-2-enamide (1.31 g, 4.92 mmol), the product was obtained as a white crystalline solid in 70% yield (1.28 g, 3.42 mmol) after hot filtration with acetone (5 x 20 mL) and sonication with Et_2O (10 mL). mp = 238-240 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.13-7.40 (m, 10H), 4.66-4.69 (d, J = 15.1 Hz, 1H), 4.57-4.61 (d, J = 17.1 Hz, 1H), 4.30-4.33 (d, J = 17.1 Hz, 1H), 4.17-4.20 (d, J = 15.1 Hz, 1H), 2.39-2.43 (dd, J = 13.9, 2.9 Hz, 1H), 1.80-1.85 (dd, J = 13.9, 11.4 Hz, 1H), 0.73-0.75 (d, J = 7.0 Hz, 3H), 0.62 (br s, 1H). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 175.7, 138.4, 137.8, 128.7, 128.4, 127.4, 127.1, 126.8, 126.4, 49.7, 47.1, 37.2, 16.1. ^{19}F NMR (470.8 MHz, DMSO-d_6): δ -145.7. ^{11}B NMR (128.4 MHz, DMSO-d_6): δ 4.67. IR (KBr) 3064, 3028, 2939, 2864, 1628, 1447, 1429, 1313 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{23}BNO_2$ [M(-F_3K)(+OMe)]$^+$ 308.1826, found 308.1836.

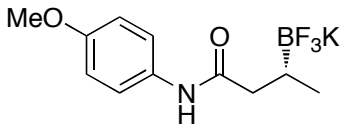


Potassium 3-Phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one. According to the general procedure for the racemic preparation using (*E*)-3-phenyl-1-(pyrrolidin-1-yl)prop-2-en-1-one (250 mg, 1.24 mmol), the product was obtained as a white amorphous solid in 86% yield (331 mg, 1.07 mmol). The title compound was extracted via hot filtration with CH_3CN (3 x 10 mL) and purified by concentration until minimally soluble, followed by addition of Et_2O (~5 mL), and sonication. The supernatant was decanted off, providing the title compound. ^{1}H NMR (500 MHz, acetone-d_6): δ 7.19-7.21 (d, J = 7.5, 2H), 7.05-7.08 (t, J = 7.5, 2H), 6.90-6.93 (t, J = 7.5, 1H), 3.31-3.43 (m, 1H), 3.21-3.30 (m, 3H), 2.61-2.65 (dd, J = 14.0, 7.4 Hz, 1H), 2.42-2.46 (dd, J = 14.0, 7.5 Hz, 1H), 2.20 (m, 1H), 1.69-1.85 (m, 4H). ^{13}C NMR (125.8 MHz, acetone-d_6): δ 174.3, 150.7, 129.3, 127.9, 123.9, 47.1, 46.0, 39.3, 26.8, 25.0. ^{19}F NMR (470.8 MHz, acetone-d_6): δ -144.4. ^{11}B NMR (128.4 MHz, acetone-d_6): δ 5.16. IR (KBr) 3079, 3023, 2971, 2886, 1617, 1470, 1452 cm^{-1}. HRMS (ESI) calcd. for $C_{14}H_{19}BNO_2$ $[M(-F_3K)(+OMe)]^+$ 244.1509, found 244.1507.

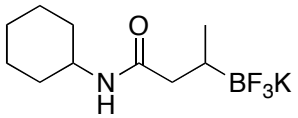


Potassium *N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide. According to the general procedure for the racemic preparation using (*E*)-*N*-(4-methoxyphenyl)but-2-enamide (956 mg, 5.00 mmol), the product was obtained as a white crystalline solid in 84% yield (1.26 g, 4.23 mmol). The title compound was obtained after hot filtration with

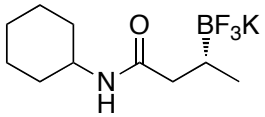
CH_3CN (3 x 20 mL), concentration until minimally soluble in CH_3CN and precipitation with Et_2O (~20 mL). mp = 169-171 °C. ^{1}H NMR (500 MHz, acetone-d_6): δ 8.84 (br s, 1H), 7.57-7.59 (d, J = 8.5 Hz, 2H), 6.80-6.82 (d, J = 8.5 Hz, 2H), 3.74 (s, 3H), 2.33-2.37 (m, 1H), 2.00-2.05 (m, 1H), 0.83 (m, 4H). ^{13}C NMR (125.8 MHz, acetone-d_6): δ 175.1, 156.2, 134.3, 121.6, 114.4, 55.6, 43.0, 16.6. ^{19}F NMR (470.8 MHz, acetone-d_6): δ -147.2. ^{11}B NMR (128.4 MHz, acetone-d_6): δ 5.28. IR (KBr) 3300, 3068, 2954, 2871, 1637, 1609, 1516, 1459, 1412, 1302, 1251 cm^{-1}. HRMS (ESI) calcd. for $C_{12}H_{17}BNO_3$ [M(-F_3K)(+OMe)]$^+$ 234.1301, found 234.1309.



Potassium (*R*)-*N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide. According to the general procedure for the enantioenriched preparation using (*E*)-*N*-(4-methoxyphenyl)but-2-enamide (373 mg, 1.95 mmol), the product was obtained as an off-white solid in 78% yield (458 mg, 1.53 mmol) with an enantiomeric ratio of 7:93 after filtration with CH_3CN (5 x 10 mL) and sonication with Et_2O (10 mL) with spectra in accordance with that described above. $[\alpha]_D^{20}$ = +10.8 (c = 0.2, MeOH). The absolute configuration (*R*) of the major enantiomer was determined on the basis of the experiments performed with 3-hydroxy-*N*-(4-methoxyphenyl)butanamide described below and the results obtained by Yun and coworkers.[8a]



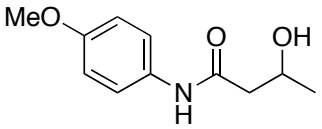
Potassium *N*-Cyclohexyl-3-(trifluoroborato)butanamide. According to the general procedure for the racemic preparation using (*E*)-*N*-cyclohexylbut-2-enamide (0.50 g, 2.99 mmol), the product was obtained as a white crystalline solid in 79% yield (649 mg, 2.36 mmol) after hot filtration with CH_3CN (5 x 10 mL) and sonication with Et_2O (10 mL). mp = 214-215 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.16-7.17 (d, J = 7.8 Hz, 1H), 3.48-3.49 (m, 1H), 1.96-2.00 (dd, J = 13.6, 3.8 Hz, 1H), 1.55-1.66 (m, 6H), 1.07-1.21 (m, 5H), 0.59-0.60 (d, J = 7.0 Hz, 3H), 0.49 (br s, 1H). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 174.2, 47.0, 40.4, 32.8, 32.6, 25.4, 24.7, 15.6. ^{19}F NMR (470.8 MHz, DMSO-d_6): δ -144.7. ^{11}B NMR (128.4 MHz, DMSO-d_6): δ 4.64. IR (KBr) 3350, 2928, 2856, 1620, 1537, 1452 cm^{-1}. HRMS (ESI) calcd. for $C_{10}H_{18}BF_3NO$ $[M\text{-}K]^-$ 236.1434, found 236.1433.



Potassium (*R*)-*N*-Cyclohexyl-3-(trifluoroborato)butanamide. According to the general procedure for the enantioenriched preparation using (*E*)-*N*-cyclohexylbut-2-enamide (1.00 g, 5.98 mmol), the product was obtained as a white crystalline solid in 74% yield (1.22 g, 4.42 mmol) with an enantiomeric ratio of 6:94 after filtration with CH_3CN (5 x 10 mL) and sonication with Et_2O (10 mL) with spectra in accordance with that described above. $[\alpha]_D^{20}$ = +9.8 (c = 0.2, MeOH). The absolute configuration (*R*) of the major enantiomer was deduced on the basis of the experiments performed with 3-

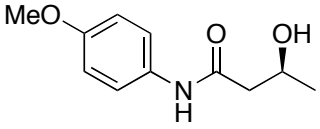
hydroxy-*N*-(4-methoxyphenyl)butanamide described below and the results obtained by Yun and coworkers.[8a]

Determination of Absolute Configuration and Enantiomeric Ratio of Enantioenriched Potassium Trifluoroboratohomoenolates:

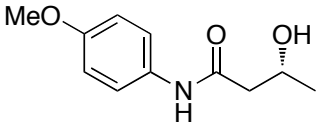


3-Hydroxy-*N*-(4-methoxyphenyl)butanamide. Before quench of the borylation reaction of (*E*)-*N*-(4-methoxyphenyl)but-2-enamide (186 mg, 0.58 mmol, 1.0 equiv) with KHF_2, an aliquot was removed and concentrated. The crude borylated material was dissolved in THF (2.5 mL) and H_2O (2.5 mL) and sodium perborate (449 mg, 2.92 mmol, 5.0 equiv) was added to the mixture and was stirred vigorously at rt for 2 h. The crude reaction mixture was purified by silica gel column chromatography (elution with hexane/EtOAc 1:1) and the title compound was obtained in 80% yield (98.1 mg, 0.47 mmol) as a white crystalline solid. mp = 135-137 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (br s, 1H), 7.38-7.39 (d, *J* = 9.0 Hz, 2H), 6.84-6.85 (d, *J* = 9.0 Hz, 2H), 4.26-4.29 (m, 1H), 3.78 (s, 3H), 3.44 (d, *J* = 2.9 Hz, 1H), 2.41-2.51 (m, 2H), 1.27-1.28 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.6, 156.8, 130.8, 122.3, 114.4, 65.2, 55.7, 45.1, 23.2; IR (neat) 3242, 3131, 3076, 2962, 1654, 1604, 1549, 1513, 1237 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{16}NO_3$ $[M+H]^+$ 210.1130, found 210.1127. A method was developed to separate the enantiomers using SFC analysis (Column OD-H, 8% *i*-PrOH, 4 mL, 12MPa); (*S*)-isomer t_r = 4.9 min and (*R*)-isomer t_r = 5.5 min. The determination of absolute configuration of the enantiomers was determined via derivation of (*S*)-

hydroxybutyric acid described below.

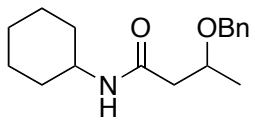


(*S*)-3-Hydroxy-*N*-(4-methoxyphenyl)butanamide. A dry flask was purged with N_2 and charged with (*S*)-3-hydroxybutyric acid (26.0 mg, 0.25 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL), and the reaction vessel was cooled to 0 °C. To the reaction mixture was added *i*-Pr_2NEt (153 μL, 0.88 mmol, 3.5 equiv), HATU (114 mg, 0.30 mmol, 1.2 equiv), and *p*-anisidine (33.9 mg, 0.28 mmol, 1.1 equiv). Following the addition of reagents, the reaction mixture was allowed to warm to rt and stir overnight. The title compound was isolated in 75% yield (39.1 mg, 0.19 mmol) after purification by column chromatography (elution with hexane/EtOAc 1:1) with spectra in accordance with that described above for the racemate. $[\alpha]_D^{20}$ = +14.5 (c = 0.2, MeOH). Using SFC analysis, co-injection of the (*S*)-enantiomer with the racemate was used to identify the corresponding retention time of each compound.



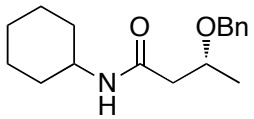
(*R*)-3-Hydroxy-*N*-(4-methoxyphenyl)butanamide. Following the procedure described above for oxidation using the enantioselective borylated intermediate, the title compound was obtained in 56% yield (48.8 mg, 0.23 mmol) as a white crystalline solid with spectra in accordance with that described above for the racemate. Using SFC analysis (Column OD-H, 8% *i*-PrOH, 4 mL, 12MPa); the enantiomeric ratio was measured to be 7:93 with

the major enantiomer having an absolute configuration of *R*. (*S*)-isomer t_r = 4.9 min and (*R*)-isomer t_r = 5.5 min.



3-(Benzyloxy)-*N*-cyclohexylbutanamide. Before quench of the borylation reaction of (*E*)-*N*-cyclohexylbut-2-enamide with KHF_2, an aliquot was removed and concentrated. The crude borylated material (302 mg, 1.02 mmol) was dissolved in THF (5 mL) and H_2O (5 mL), and sodium perborate (788 mg, 5.10 mmol, 5 equiv) was added and stirred vigorously at rt for 2 h. The reaction was diluted with H_2O and extracted with EtOAc (2 x 5 mL). The combined organic layers were washed with brine (5 mL), dried (Mg_2SO_4), and concentrated. The crude reaction mixture was purified by silica gel column chromatography (elution with hexane/EtOAc 1:1). The resulting solid was dissolved in THF (15 mL) under a dry, N_2 atmosphere and cooled to 0 °C. To the soln was added NaH (60%, 40.8 mg, 1.02 mmol, 1 equiv), and the reaction mixture was stirred for 30 min, and then BnBr (175 mg, 1.02 mmol, 1.00 equiv) was added. The reaction mixture was allowed to warm to rt and stirred until no starting material was detected by TLC. The reaction mixture was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried (Mg_2SO_4), filtered, and concentrated and purified by column chromatography (elution with hexanes/EtOAc 4:1) to give the title compound as a white solid in 59% yield (166 mg, 0.60 mmol). mp = 74-76 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.36 (m, 5H), 6.11 (br s, 1H), 4.62-4.64 (d, *J* = 11.5 Hz, 1H), 4.45-4.48 (d, *J* = 11.5 Hz, 1H), 3.95-4.00 (m, 1H), 3.74-3.80 (m, 1H), 2.38-2.40 (m, 2H),

1.85-1.87 (m, 2H), 1.59-1.66 (m, 4H), 1.06-1.36 (m, 7H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.2, 138.4, 128.7, 128.0, 128.0, 73.0, 71.1, 48.0, 44.4, 33.2, 25.8, 24.9, 19.8; IR (neat) 3291, 3066, 2931, 2855, 1638, 1549 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{25}NO_2Na$ $[M+Na]^+$ 298.1783, found 298.1793. Using the title compound, a chiral HPLC method was developed (Column AS-H, 5% *i*-PrOH, 0.7 mL). (*S*)-isomer t_r = 47.2 min and (*R*)-isomer t_r = 42.3 min.[11]



(*R*)-3-(Benzyloxy)-*N*-cyclohexylbutanamide. Following the procedure described above for oxidation and benzylation using the enantioselective borylated intermediate, the title compound was obtained in 57% yield in accordance the spectral data for the racemate. Using the HPLC method described above (Column AS-H, 5% *i*-PrOH, 0.7 mL), the product has an enantiomeric ratio of 6:94 *S*:*R*. with an absolute configuration assumed to be *R*. $[\alpha]_D^{20}$ = -13.1 (*c* = 0.2, MeOH).

Procedure for the Suzuki-Miyaura Cross-Coupling with Aryl Electrophiles:

To a 10 mL Biotage Microwave vial were added $Pd(OAc)_2$ (5.6 mg, 0.03 mmol, 0.1 equiv), ligand (0.05 mmol, 0.20 equiv), base (0.75 mmol, 3 equiv), aryl electrophile (0.25 mmol, 1 equiv), and potassium β-trifluoroboratoamide (0.25 mmol, 1 equiv). This mixture was sealed in the microwave vial and purged with N_2 (three times). To the vial was added CPME (1.0 mL) and H_2O (0.15 mL), and then the reaction was heated to 95 ºC for 20-24 h. The reaction mixture was allowed to cool to rt and quenched with H_2O (1

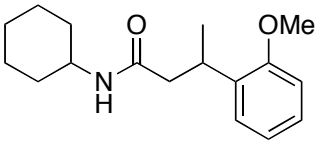
mL). The organic layer was separated and the aqueous layer was washed with EtOAc (3 x 1 mL). The resulting soln was concentrated and purified by silica gel column chromatography.

Condition A: 10 mol % of $Pd(OAc)_2$, 20 mol % of XPhos, 3 equiv K_2CO_3, and 6.7:1 CPME/H_2O (0.25 M)

Condition B: 10 mol % of $Pd(OAc)_2$, 20 mol % of XPhos, 3 equiv Cs_2CO_3, and 6.7:1 CPME/H_2O (0.25 M)

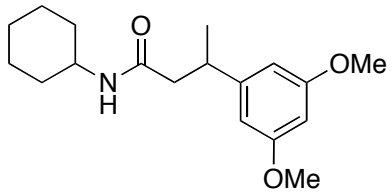
Condition C: 10 mol % of $Pd(OAc)_2$, 20 mol % of SPhos, 3 equiv Cs_2CO_3, and 6.7:1 CPME/H_2O (0.25 M)

Compound Characterization of Cross-Coupled Products:



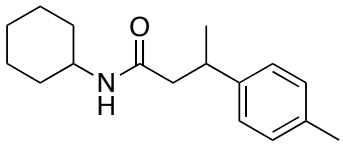
***N*-Cyclohexyl-3-(2-methoxyphenyl)butanamide.** According to the general procedure using 2-chloroanisole on a 0.25 mmol scale, the product was obtained in 90% yield (61.6 mg, 0.22 mmol) as a white solid after silica gel column chromatography (elution with 2% MeOH in CH_2Cl_2). mp: 105-107 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16-7.20 (m, 2H), 6.90-6.93 (m, 1H), 6.85-6.86 (d, J = 8.1 Hz, 1H), 5.25-5.29 (m, 1H), 3.84 (s, 3H), 3.65-3.70 (m, 1H), 3.55-3.62 (m, 1H), 2.52-2.57 (dd, J = 14.1, 7.5 Hz, 1H), 2.33-2.37 (dd, J = 14.1, 7.5 Hz, 1H), 1.71-1.77 (m, 2H), 1.54-1.61 (m, 3H), 1.27-1.35 (m, 5H), 0.88-1.13 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 171.2, 156.9, 134.0, 127.5, 127.4, 121.0, 110.8, 55.49, 47.9, 44.5, 33.2, 33.1, 30.9, 25.7, 24.9, 20.6; IR (neat) 3287, 3065, 2930, 2848, 1636, 1545, 1242 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{26}NO_2$ $[M+H]^+$ 276.1964, found 276.1968.

The title compound was also prepared according to the general procedure using 2-bromoanisole (46.8 mg, 0.25 mmol) and was isolated as a white solid in 63% yield (43.1 mg, 0.16 mmol) with spectral data in accordance with data listed above.

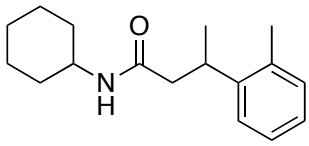


***N*-Cyclohexyl-3-(3,5-dimethoxyphenyl)butanamide.** According to the general procedure using 1-chloro-3,5-dimethoxybenzene on a 0.25 mmol scale, the product was obtained in 72% yield (55.1 mg, 0.18 mmol) as a white solid after silica gel column chromatography (elution with hexane/EtOAc 7:3). mp: 102-103 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.37-6.38 (m, 2H), 6.30-6.31 (m, 1H), 5.13-5.14 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 6H), 3.66-3.72 (m, 1H), 3.16-3.23 (m, 1H), 2.29-2.39 (qd, *J* = 13.7, 7.5 Hz, 2H), 1.80-1.82 (m, 1H), 1.69-1.71 (m, 1H), 1.54-1.63 (m, 3H), 1.26-1.35 (m, 5H), 0.87-1.11 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.7, 161.0, 148.7, 105.1, 98.3, 55.4, 48.0, 46.2, 37.6, 33.2, 33.1, 25.6, 24.8, 24.8, 21.6; IR (neat) 3289, 3077, 2931, 2854, 1638, 1597, 1550, 1460, 1205, 1154 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{27}NO_3Na$ $[M+Na]^+$ 328.1889, found 328.1879.

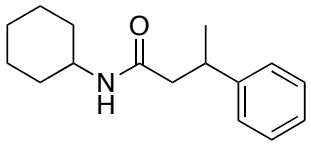
The title compound was also prepared according to the general procedure using 1-bromo-3,5-dimethoxybenzene (54.3 mg, 0.25 mmol) and was isolated as a white solid in 74% yield (56.4 mg, 0.18 mmol) with spectral data in accordance with data listed above.



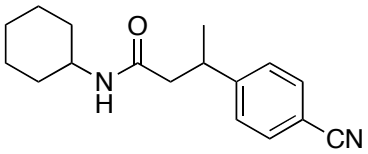
***N*-Cyclohexyl-3-(p-tolyl)butanamide.** According to the general procedure using 4-chlorotoluene on a 0.25 mmol scale, the product was obtained in 91% yield (55.8 mg, 0.23 mmol) as an off-white solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (s, 4H), 5.01 (br s, 1H), 3.67-3.69 (m, 1H), 3.20-3.25 (dd, J = 14.4, 7.2 Hz, 1H), 2.23-2.39 (m, 2H), 2.31 (s, 3H), 1.80-1.82 (m, 1H), 1.55-1.69 (m, 4H), 1.25-1.35 (m, 5H) 0.87-1.11 (m, 3H). ^{3}C-NMR (125.8 MHz, $CDCl_3$): δ 170.8, 143.1, 136.1, 129.4, 126.8, 48.0, 46.4, 36.9, 33.2, 33.1, 25.7, 24.9, 24.8, 21.9, 21.1; IR (neat) 3287, 3065, 2930, 2854, 1638, 1550, 1450 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{26}NO$ $[M+H]^+$ 260.2014, found 260.2019.



***N*-Cyclohexyl-3-(*o*-tolyl)butanamide.** According to the general procedure using 2-chlorotoluene on a 0.25 mmol scale, the product was obtained in 88% yield (56.7 mg, 0.22 mmol) as a white solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 105-106 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07-7.19 (m, 4H), 5.04-5.05 (m, 1H), 3.63-3.70 (m, 1H), 3.51-3.58 (m, 1H), 2.31-2.43 (m, 5H), 1.80-1.82 (m, 1H), 1.54-1.66 (m, 4H), 1.20-1.32 (m, 5H), 0.81-1.05 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.9, 144.3, 135.8, 130.7, 126.4, 126.2, 125.1, 48.0, 45.6, 33.2, 32.9, 32.2, 25.6, 24.8, 24.8, 21.6, 19.7; IR (neat) 3292, 3075, 2930, 2848, 1637, 1546, 1450 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{26}NO$ $[M+H]^+$ 260.2014, found 260.2013.



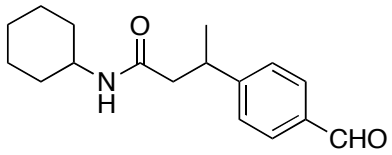
***N*-Cyclohexyl-3-phenylbutanamide.** According to the general procedure using chlorobenzene on a 0.25 mmol scale, the product was obtained in 81% yield (49.4 mg, 0.20 mmol) as a white solid after silica gel column chromatography (elution with 2% MeOH in CH_2Cl_2). mp: 92-94 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.31 (m, 2H), 7.18-7.23 (m, 3H), 5.07 (s, 1H), 3.63-3.71 (dtt, *J* = 12.2, 8.1, 3.9 Hz, 1H), 3.23-3.30 (m, 1H), 2.37-2.38 (d, 2H), 1.80-1.82 (m, 1H), 1.54-1.59 (m, 4H), 1.24-1.34 (m, 5H), 0.95-1.12 (m, 2H), 0.81-0.89 (m, 1H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): δ 170.5, 145.8, 128.5, 126.8, 126.3, 47.7, 46.2, 37.1, 33.0, 32.8, 25.4, 24.6, 24.6, 21.6; IR (neat) 3299, 3059, 2932, 2854, 1636, 1544, 1450 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{23}NONa$ $[M+Na]^+$ 268.1677, found 268.1684.



3-(4-Cyanophenyl)-*N*-cyclohexylbutanamide. According to the general procedure using 4-chlorobenzonitrile on a 0.25 mmol scale, the product was obtained in 76% yield (51.3 mg, 0.19 mmol) as an off-white solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 108-110 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.58 (d, *J* = 8.3 Hz, 2H), 7.32-7.33 (d, *J* = 8.3 Hz, 2H), 5.18-5.20 (d, *J* = 7.4 Hz, 1H), 3.63 (dtt, *J* = 12.1, 8.1, 3.9 Hz, 1H), 3.34-3.41 (m, 1H), 2.31 (qd, *J* = 14.0, 7.5 Hz, 2H), 1.82-1.84 (m, 1H), 1.55-1.67 (m, 4H), 1.24-1.35 (m, 5H), 0.85-1.14 (m, 3H). ^{13}C-NMR (125.8

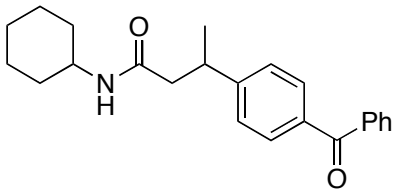
MHz, $CDCl_3$): 169.8, 151.7, 132.5, 127.9, 119.1, 110.3, 48.2, 45.5, 37.2, 33.2, 33.2, 25.6, 24.9, 24.8, 21.4; IR (neat) 3293, 3070, 2932, 2855, 2228, 1641, 1548, 1451 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{23}N_2O$ $[M+H]^+$ 271.1810, found 271.1822.

The title compound was also prepared according to the general procedure using 4-bromobenzonitrile (45.5 mg, 0.25 mmol) and was isolated as an off-white solid in 72% yield (48.9 mg, 0.18 mmol) with spectral data in accordance with data listed above.

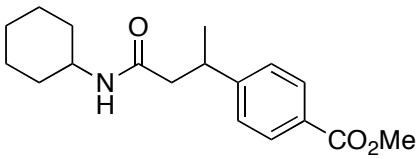


***N*-Cyclohexyl-3-(4-formylphenyl)butanamide.** According to the general procedure using 4-chlorobenzaldehyde on a 0.25 mmol scale, the product was obtained in 66% yield (45.1 mg, 0.16 mmol) as a white crystalline solid after silica gel column chromatography (elution with hexane/EtOAc 3:2). mp: 110-111 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.81-7.83 (d, *J* = 8.1 Hz, 2H), 7.39-7.40 (d, *J* = 8.1 Hz, 2H), 5.08 (s, 1H), 3.64-3.72 (m, 1H), 3.37-3.43 (m, 1H), 2.35-2.43 (m, 2H), 1.82-1.84 (m, 1H), 1.57-1.67 (m, 4H), 1.24-1.36 (m, 5H), 0.98-1.13 (m, 2H), 0.83-0.91 (m, 1H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): δ 192.1, 170.0, 153.4, 135.1, 130.2, 127.8, 48.2, 45.7, 37.4, 33.3, 33.1, 25.6, 24.9, 24.8, 21.4; IR (neat) 3293, 3068, 2930, 2854, 1702, 1639, 1607, 1546, 1214, 1170 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{24}NO_2$ $[M+H]^+$ 274.1807, found 274.1806.

The title compound was also prepared according to the general procedure using 4-bromobenzaldehyde (68.8 mg, 0.25 mmol) and was isolated as a white crystalline solid in 46% yield (31.1 mg, 0.11 mmol) with spectral data in accordance with data listed above.

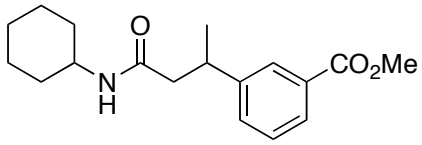


3-(4-Benzoylphenyl)-*N*-cyclohexylbutanamide. According to the general procedure using 4-chlorobenzophenone on a 0.25 mmol scale, the product was obtained in 72% yield (63.3 mg, 0.18 mmol) as an off-white solid after silica gel column chromatography (gradient elution with hexane/EtOAc 4:1 to 3:2). mp: 119-121 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75-7.79 (m, 4H), 7.57-7.60 (m, 1H), 7.46-7.49 (t, *J* = 7.7 Hz, 2H), 7.33-7.35 (d, *J* = 8.2 Hz, 2H), 5.09-5.11 (d, *J* = 7.9 Hz, 1H), 3.67-3.73 (m, 1H), 3.38-3.42 (m, 1H), 2.37-2.44 (m, 2H), 1.84-1.85 (m, 1H), 1.56-1.70 (m, 4H), 1.34-1.36 (d, *J* = 7.0 Hz, 3H), 1.25-1.31 (m, 2H), 1.00-1.11 (m, 2H), 0.87-0.93 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 196.5, 170.2, 151.1, 137.9, 135.9, 132.4, 130.6, 130.1, 128.4, 127.0, 48.1, 48.5, 37.3, 33.2, 33.2, 25.6, 24.9, 24.9, 21.5; IR (neat) 3295, 3064, 2930, 2854, 1642, 1606, 1546, 1280 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{28}NO_2$ $[M+H]^+$ 350.2120, found 350.2119.

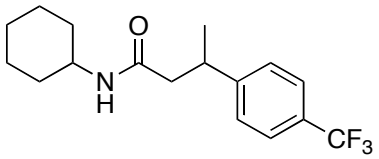


Methyl 4-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate. According to the general procedure using methyl 4-bromobenzoate on a 0.25 mmol scale, the product was obtained in 92% yield (69.8 mg, 0.23 mmol) as a white solid after silica gel column chromatography (elution with hexane/EtOAc 3:2)**.** mp: 138-139 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95-7.97 (d, *J* = 8.3 Hz, 2H), 7.28-7.30 (d, *J* = 8.3 Hz, 2H), 5.10-5.11 (d, *J* = 7.6 Hz, 1H), 3.90 (s, 3H), 3.65-3.70 (m, 1H), 3.32-3.39 (m, 1H), 2.36-2.39 (dd, *J* = 11.2, 4.0 Hz, 2H), 1.81-1.83 (m, 1H), 1.56-1.67 (m, 4H), 1.24-1.35 (m, 5H), 0.83-1.12 (m, 3H).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.2, 167.2, 151.5, 130.0, 128.5, 127.1, 52.2, 48.1, 45.8, 37.2, 33.2, 33.1, 25.6, 24.9, 24.8, 21.5; IR (neat) 3276, 3085, 2922, 2856, 1719, 1634, 1555, 1282 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{26}NO_3$ $[M+H]^+$ 304.1913, found 304.1922.

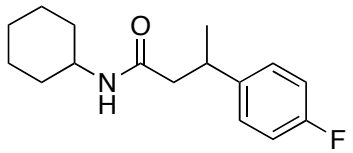


Methyl 3-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate. According to the general procedure using methyl 3-chlorobenzoate on a 0.25 mmol scale, the product was obtained in 83% yield (63.1 mg, 0.21 mmol) as a white solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86-7.89 (m, 2H), 7.41-7.42 (d, *J* = 7.7 Hz, 1H), 7.33-7.36 (t, *J* = 7.6 Hz, 1H), 5.13-5.15 (d, *J* = 7.6 Hz, 1H), 3.90 (s, 3H), 3.63-3.70 (dtt, *J* = 12.1, 8.1, 3.9 Hz, 1H), 3.31-3.38 (m, 1H), 2.34-2.41 (m, 2H), 1.80-1.82 (m, 1H), 1.54-1.66 (m, 4H), 1.31-1.32 (d, *J* = 7.0 Hz, 3H), 1.23-1.34 (m, 2H), 0.81-1.11 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.3, 167.3, 146.4, 132.1, 130.5, 128.7, 127.8, 127.7, 52.2, 48.1, 46.0, 37.1, 33.2, 33.1, 25.6, 24.9, 24.8, 21.6; IR (neat) 3291, 3065, 2931, 2855, 1725, 1640, 1548, 1288 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{26}NO_3$ $[M+H]^+$ 304.1913, found 304.1907.

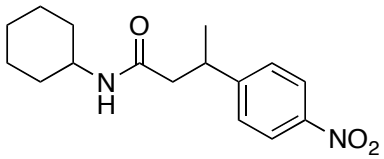


***N*-Cyclohexyl-3-(4-(trifluoromethyl)phenyl)butanamide.** According to the general procedure using 1-chloro-4-trifluoromethylbenzene on a 0.25 mmol scale, the product was obtained in 80% yield (62.9 mg, 0.20 mmol) as a white solid after silica gel column

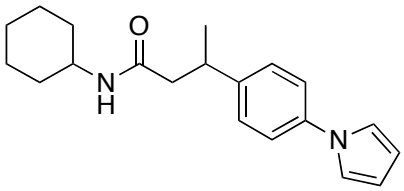
chromatography (elution with hexane/EtOAc 4:1). mp: 129-130 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52-7.54 (d, *J* = 8.1 Hz, 2H), 7.32-7.33 (d, *J* = 8.1 Hz, 2H), 5.19-5.20 (d, *J* = 7.2 Hz, 1H), 3.62-3.72 (m, 1H), 3.32-3.41 (m, 1H), 2.31-2.41 (m, 2H), 1.81-1.83 (m, 1H), 1.54-1.63 (m, 4H), 1.30-1.32 (d, *J* = 7.0, 3H), 1.22-1.35 (m, 2H), 0.97-11.14 (m, 2H), 0.82-0.92 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 169.9, 149.9, 128.2-129.0 (q, *J* = 33.0 Hz), 127.1, 125.3-125.4 (q, *J* = 4.0 Hz), 120.9-127.4 (q, *J* = 120.9 Hz), 47.9, 45.6, 36.8, 33.0, 32.8, 25.3, 24.6, 24.6, 21.2; IR (neat) 3293, 3070, 2921, 2855, 1635, 1551, 1333, 1118 cm^{-1}; HRMS (CI) calcd. for $C_{17}H_{22}NOF_2$ $[M-F]^+$ 294.1669, found 294.1660.



***N*-Cyclohexyl-3-(4-fluorophenyl)butanamide.** According to the general procedure using methyl 4-chlorofluorobenzene on a 0.25 mmol scale, the product was obtained in 92% yield (60.5 mg, 0.23 mmol) as a white crystalline solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15-7.18 (dd, *J* = 8.5, 5.5 Hz, 2H), 6.94-6.97 (apparent t, *J* = 8.6 Hz, 2H), 5.15-5.17 (d, *J* = 6.7 Hz, 1H), 3.63-3.69 (m, 1H), 3.24-3.29 (m, 1H), 2.28-2.34 (qd, *J* = 13.7, 7.5 Hz, 2H), 1.80-1.82 (m, 1H), 1.53-1.67 (m, 4H), 1.26-1.28 (d, *J* = 7.0 Hz, 3H), 1.25-1.33 (m, 2H), 0.97-1.12 (m, 2H), 0.84-0.91 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.5, 160.6-162.5 (d, *J* = 244 Hz), 141.7 (d, *J* = 3.77 Hz), 128.3-128.4 (d, *J* = 8.81 Hz), 115.2-115.4 (d, *J* = 21.4 Hz), 48.0, 46.4, 36.5, 33.2, 33.1, 25.6, 24.9, 24.8, 21.8; IR (neat) 3289, 3072, 2931, 2855, 1638, 1551, 1511, 1224 cm^{-1}; HRMS (CI) calcd. for $C_{16}H_{23}NOF$ $[M+H]^+$ 264.1764, found 264.1758.



***N*-Cyclohexyl-3-(4-nitrophenyl)butanamide.** According to the general procedure using methyl 4-chloronitrobenzene, SPhos, and Cs_2CO_3 on a 0.25 mmol scale, the product was obtained in 71% yield (51.7 mg, 0.18 mmol) as a white crystalline solid after silica gel column chromatography (gradient elution with hexane/EtOAc 4:1 to 3:2). mp: 119-120 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15-8.16 (d, *J* = 8.8 Hz, 2H), 7.38-7.40 (d, *J* = 8.8 Hz, 2H), 5.11-5.13 (d, *J* = 7.1 Hz, 1H), 3.65-3.71 (dtt, *J* = 12.0, 8.1, 3.9 Hz, 1H), 3.44-3.48 (m, 1H), 2.34-2.44 (qd, *J* = 14.1, 7.5 Hz, 2H), 1.84-1.86 (m, 1H), 1.58-1.70 (m, 4H), 1.33-1.34 (d, *J* = 7.0 Hz, 3H), 1.25-1.36 (m, 2H), 0.88-1.11 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 169.7, 153.9, 146.7, 127.9, 123.9, 48.3, 45.5, 37.0, 33.3, 33.2, 25.6, 24.9, 24.8, 21.3; IR (neat) 3399, 3291, 3078, 2932, 2855, 1640, 1520, 1347 cm^{-1}; HRMS (CI) calcd. for $C_{16}H_{23}N_2O_3$ $[M+H]^+$ 291.1709, found 291.1714.

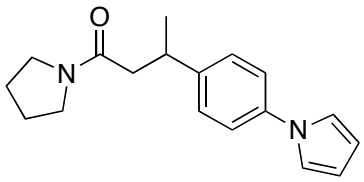


3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-cyclohexylbutanamide. According to the general procedure using potassium *N*-cyclohexyl-3-(trifluoroborato)butanamide and condition A on a 0.25 mmol scale, the product was obtained in 84% yield (65.1 mg, 0.21 mmol) as an off-white solid after silica gel column chromatography (elution with hexane/EtOAc 1:1). mp: 155-156 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.33 (d, *J* = 8.5 Hz, 2H), 7.27-7.28 (d, *J* = 8.5 Hz, 2H), 7.05 (m, 2H), 6.33-6.34 (m, 2H), 5.04-5.05 (d, *J* = 7.4 Hz, 1H), 3.65-3.74 (m, 1H), 3.30-3.35 (m, 1H), 2.34-2.42 (m, 2H), 1.81-1.82 (m, 1H), 1.56-1.66 (m,

4H), 1.31-1.32 (d, J = 7.0 Hz, 3H), 1.26-1.34 (m, 2H), 0.87-1.14 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.2, 143.3, 139.1, 127.8, 120.6, 119.3, 110.1, 47.8, 46.1, 36.5, 33.0, 32.9, 25.4, 24.6, 24.6, 21.5; IR (neat) 3289, 2930, 2848, 1636, 1548, 1526 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{27}N_2O$ $[M+H]^+$ 311.2123, found 311.2116.

The title compound was also prepared according to the general procedure using condition B and was isolated as a pale yellow solid in 89% yield (69.4 mg, 0.22 mmol) with spectral data in accordance with data listed above.

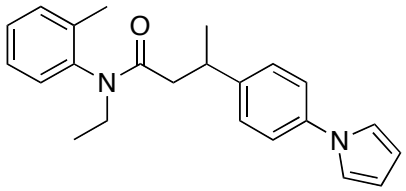
The title compound was also prepared according to the general procedure using condition C and was isolated as a pale yellow solid in 78% yield (60.9 mg, 0.20 mmol) with spectral data in accordance with data listed above.



3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(pyrrolidin-1-yl)butan-1-one. According to the general procedure using potassium 1-(pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one and condition A on a 0.25 mmol scale, the product was obtained in 92% yield (65.1 mg, 0.23 mmol) as a light yellow oil after silica gel column chromatography (elution with hexane/EtOAc 7:3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (s, 4H), 7.05-7.06 (m, 2H), 6.32-6.33 (m, 2H), 3.33-3.43 (m, 4H), 3.16-3.21 (m, 1H), 2.47-2.57 (qd, J = 14.9, 7.2 Hz, 2H), 1.75-1.90 (m, 4H), 1.35-1.36 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.3, 144.1, 139.2, 128.1, 120.7, 119.5, 110.3, 46.9, 45.8, 43.6, 36.0, 26.2, 24.5, 21.7; IR (neat) 3132, 3101, 2967, 2873, 1634, 1523, 1434, 1328 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{23}N_2O$ $[M+H]^+$ 283.1810, found 283.1817.

The title compound was also prepared according to the general procedure using condition B and was isolated as a light yellow oil in 84% yield (59.5 mg, 0.21 mmol) with spectral data in accordance with data listed above.

The title compound was also prepared according to the general procedure using condition C and was isolated as a light yellow oil in 93% yield (65.8 mg, 0.23 mmol) with spectral data in accordance with data listed above.

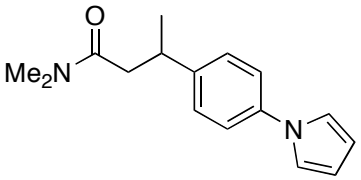


3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-ethyl-*N*-(*o*-tolyl)butanamide. According to the general procedure using potassium *N*-ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide and condition A on a 0.25 mmol scale, the product was obtained in 87% yield (75.8 mg, 0.22 mmol) as a pale yellow solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 89-91 °C. ^{1}H NMR (500 MHz, asterisk denotes minor rotamer peaks, $CDCl_3$): δ 7.02-7.29 (m, 10H), 6.51-6.52* (m, 1H), 6.33-6.34 (m, 2H), 6.31-6.32* (m, 2H), 4.08-4.15* (m, 1H), 4.01-4.07 (m, 1H), 3.39-3.46 (m, 1H), 3.07-3.20 (m, 1H), 2.07-2.24 (m, 2H), 2.21 (s, 3H), 1.94* (s, 3H), 1.21-1.23 (m, 3H), 1.09-1.12* (t, J = 7.1 Hz, 3H), 1.01-1.04* (t, J = 7.1 Hz, 3H). ^{13}C NMR (125.8 MHz, asterisk denotes rotamer peaks, $CDCl_3$): δ 171.3, 171.2*, 144.3, 143.9*, 141.0, 141.0*, 139.2, 139.2*, 136.2, 135.9*, 131.7, 131.5*, 129.7, 129.5*, 128.5, 128.4*, 128.4, 128.2*, 127.2, 127.1*, 120.8, 120.6*, 119.6, 110.4, 110.3*, 43.3, 43.2*, 43.0, 42.9*, 36.2, 35.9*, 21.7, 21.6*, 17.8, 17.5*, 13.1, 13.0*; IR (neat) 3039, 2966, 2920, 2863, 1652, 1523, 1404, 1329 cm^{-1};

HRMS (ESI) calcd. for $C_{23}H_{26}N_2ONa$ $[M+Na]^+$ 369.1943, found 369.1931.

The title compound was also prepared according to the general procedure using condition B and was isolated as a pale yellow solid in 99% yield (85.5 mg, 0.25 mmol) with spectral data in accordance with data listed above.

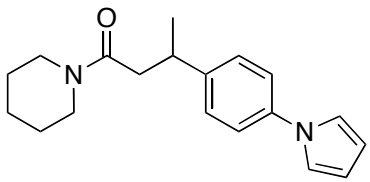
The title compound was also prepared according to the general procedure using condition C and was isolated as a pale yellow solid in 98% yield (85.1 mg, 0.25 mmol) with spectral data in accordance with data listed above.



3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dimethylbutanamide. According to the general procedure using potassium *N*,*N*-dimethyl-3-(trifluoroborato)butanamide and condition A on a 0.25 mmol scale, the product was obtained in 72% yield (46.3 mg, 0.18 mmol) as a tan solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 47-49 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.33 (m, 4H), 7.06-7.07 (m, 2H), 6.33-6.34 (m, 2H), 3.38-3.45 (m, 1H), 2.92 (s, 3H), 2.91 (s, 3H), 2.61-2.65 (dd, *J* = 15.1, 6.6 Hz, 1H), 2.51-2.56 (dd, *J* = 15.2, 7.6 Hz, 1H), 1.34-1.35 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 171.7, 144.3, 139.3, 128.2, 120.8, 119.5, 110.4, 42.0, 37.5, 36.1, 35.7, 22.0; IR (neat) 3101, 3039, 2957, 2930, 2863, 1644, 1523, 1398, 1329 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{21}N_2O$ $[M+H]^+$ 257.1654, found 257.1644.

The title compound was also prepared according to the general procedure using condition B and was isolated as a tan solid in 78% yield (50.1 mg, 0.20 mmol) with spectral data in accordance with data listed above.

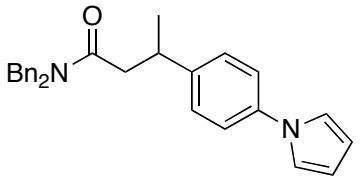
The title compound was also prepared according to the general procedure using condition C and was isolated as a tan solid in 64% yield (41.1 mg, 0.16 mmol) with spectral data in accordance with data listed above.



3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(piperidin-1-yl)butan-1-one. According to the general procedure using potassium 1-(piperidin-1-yl)-3-(trifluoroborato)butan-1-one and condition A on a 0.25 mmol scale, the product was obtained in 89% yield (65.9 mg, 0.22 mmol) as a light yellow oil after silica gel column chromatography (elution with hexane/EtOAc 7:3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.33 (m, 4H), 7.05-7.06 (m, 2H), 6.33-6.34 (m, 2H), 3.54-3.59 (m, 1H), 3.45-3.50 (m, 1H), 3.27-3.41 (m, 3H), 2.62 (dd, *J* = 14.8, 6.7 Hz, 1H), 2.50-2.55 (dd, *J* = 14.8, 7.7 Hz, 1H), 1.43-1.60 (m, 6H), 1.34-1.36 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.0, 144.4, 139.3, 128.2, 120.9, 119.6, 110.4, 47.0, 43.0, 41.8, 36.4, 26.7, 25.8, 24.7, 22.0; IR (neat) 3127, 3096, 2934, 2855, 1637, 1523, 1442, 1329 cm^{-1}; HRMS (CI) calcd. for $C_{19}H_{25}N_2O$ $[M+H]^+$ 297.1967, found 297.1955.

The title compound was also prepared according to the general procedure using condition B and was isolated as a light yellow oil in 96% yield (70.9 mg, 0.24 mmol) with spectral data in accordance with data listed above.

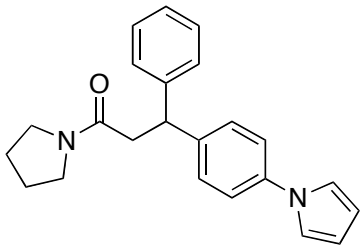
The title compound was also prepared according to the general procedure using condition C and was isolated as a light yellow oil in 89% yield (66.1 mg, 0.22 mmol) with spectral data in accordance with data listed above.



3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dibenzylbutanamide. According to the general procedure using potassium *N*,*N*-dibenzyl-3-(trifluoroborato)butanamide and condition A on a 0.25 mmol scale, the product was obtained in 79% yield (80.8 mg, 0.20 mmol) as a pale yellow amorphous solid after silica gel column chromatography (elution with hexane/EtOAc 9:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.34 (m, 10H), 7.04-7.10 (m, 6H), 6.33-6.34 (m, 2H), 4.63-4.66 (d, *J* = 14.8 Hz, 1H), 4.44-4.47 (d, *J* = 14.8 Hz, 1H), 4.29-4.38 (m, 2H), 3.51-3.58 (m, 1H), 2.72 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.60-2.64 (dd, *J* = 15.2, 6.8 Hz, 1H), 1.33-1.35 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 172.2, 143.8, 139.3, 137.4, 136.6, 129.1, 128.7, 128.4, 128.3, 127.8, 127.5, 126.4, 120.7, 119.5, 110.4, 50.0, 48.4, 41.7, 36.4, 22.0; IR (neat) 3059, 3030, 2962, 1644, 1522, 1451, 1329 cm^{-1}; HRMS (ESI) calcd. for $C_{28}H_{28}N_2ONa$ $[M+Na]^+$ 431.2099, found 431.2092.

The title compound was also prepared according to the general procedure using condition B and was isolated as a pale yellow amorphous solid in 91% yield (93.2 mg, 0.23 mmol) with spectral data in accordance with data listed above.

The title compound was also prepared according to the general procedure using condition C and was isolated as a pale yellow amorphous solid in 86% yield (87.9 mg, 0.22 mmol) with spectral data in accordance with data listed above.

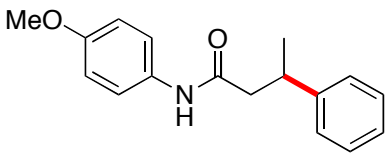


3-(4-(1*H*-Pyrrol-1-yl)phenyl)-3-phenyl-1-(pyrrolidin-1-yl)propan-1-one. According to the general procedure using potassium 3-phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one and condition A on a 0.25 mmol scale, the product was obtained in 94% yield (80.9 mg, 0.23 mmol) as a white solid after silica gel column chromatography (elution with 1% MeOH in CH_2Cl_2). mp: 97-99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.30 (m, 8H), 7.18-7.21 (t, *J* = 7.0 Hz, 1H), 7.03 (m, 2H), 6.31 (m, 2H), 4.72-4.75 (t, *J* = 7.5 Hz, 1H), 3.37-3.40 (t, *J* = 6.8 Hz, 2H), 3.21-3.29 (m, 2H), 2.95-3.04 (m, 2H), 1.73-1.84 (m, 4H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 169.7, 144.3, 142.0, 139.3, 129.2, 128.7, 128.1, 126.7, 120.7, 119.5, 110.4, 46.8, 46.5, 45.8, 41.2, 26.2, 24.5; IR (neat) 3054, 3023, 2971, 2873, 1638, 1521, 1434, 1329 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{25}N_2O$ $[M+H]^+$ 345.1967, found 345.1971.

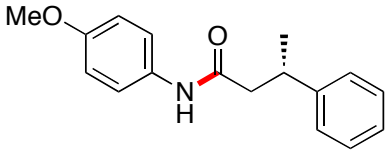
The title compound was also prepared according to the general procedure using condition B and was isolated as a white solid in 79% yield (67.8 mg, 0.20 mmol) with spectral data in accordance with data listed above.

The title compound was also prepared according to the general procedure using condition C and was isolated as an off-white solid in 89% yield (76.7 mg, 0.22 mmol) with spectral data in accordance with data listed above.

Determination of Absolute Configuration and Enantiomeric Ratio of Enantioenriched Cross-Coupled Products:

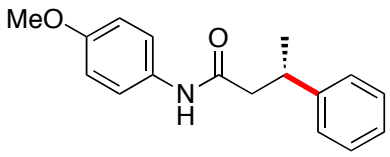


***N*-(4-Methoxyphenyl)-3-phenylbutanamide.** Using the general procedure described for the Suzuki-Miyaura cross-coupling of β-trifluoroboratoamides using potassium *N*-(4-methoxyphenyl)-3-(trifluoroborato)butanamide and chlorobenzene under condition A on 0.25 mmol scale, the title compound was obtained in 84% yield as an off-white solid after silica gel column chromatography (elution with hexane/EtOAc 4:1). mp: 125-127 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.31 (t, *J* = 7.5 Hz, 2H), 7.20-7.26 (m, 5H), 6.96 (br s, 1H), 6.77-6.80 (d, *J* = 9.0 Hz, 2H), 3.75 (s, 3H), 3.34-3.38 (m, 1H), 2.52-2.61 (qd, *J* = 14.0, 7.4 Hz, 2H), 1.35-1.37 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 170.1, 156.6, 145.9, 131.0, 128.9, 127.0, 126.8, 122.2, 114.3, 55.7, 46.8, 37.3, 21.9; IR (neat) 3289, 3062, 2961, 2931, 1652, 1604, 1538, 1513, 1246 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{19}NO_2Na$ $[M+Na]^+$ 292.1313, found 292.1309. Using the racemate of this material, a method for enantiomer separation was attained using SFC analysis (Column OJ-H, 10% *i*-PrOH, 4 mL, 12 MPa).

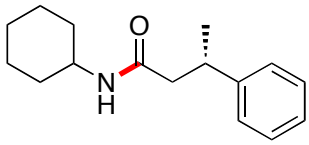


(*S*)-*N*-(4-Methoxyphenyl)-3-phenylbutanamide. A dry flask was purged with N_2 and charged with (*S*)-3-phenylbutyric acid (41.1 mg, 0.25 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL), and the reaction vessel was cooled to 0 °C. To the reaction mixture was added *i*-

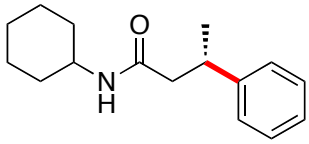
Pr_2NEt (153 μL, 0.88 mmol, 3.5 equiv), HATU (114 mg, 0.30 mmol, 1.2 equiv), and *p*-anisidine (33.9 mg, 0.28 mmol, 1.1 equiv). Following the addition of reagents, the reaction mixture was allowed to warm to rt and to stir overnight. The title compound was obtained in 84% yield (56.8 mg, 0.21 mmol) as a white crystalline solid after silica gel column chromatography (elution with hexanes/EtOAc 4:1) with spectral data in accordance with that obtained via the cross-coupling reaction described above. $[\alpha]_D^{20}$ = +64.7 (c = 0.2, MeOH). Using SFC analysis, co-injection of the racemate described above with the title compound provided absolute configuration identity to the enantiomer peaks. [(*S*)-isomer t_r = 5.3 min and (*R*)-isomer t_r = 6.1 min].



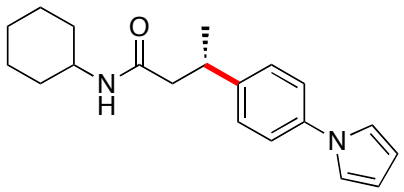
(*S*)-*N*-(4-Methoxyphenyl)-3-phenylbutanamide. Using the general procedure described for the Suzuki-Miyaura cross-coupling of β-trifluoroboratoamides using potassium (*R*)-*N*-(4-methoxyphenyl)-3-(trifluoroborato)butanamide and chlorobenzene under condition A on a 0.25 mmol scale, the title compound was obtained as an off-white solid in 82% yield (55.1 mg, 0.21 mmol) with spectral data in accordance with that described for the racemate. The title compound was found to have an enantiomeric ratio of 93:7 with an absolute configuration of *S* for the major enantiomer using SFC analysis. $[\alpha]_D^{20}$ = +46.8 (*c* = 0.2, MeOH).



(*S*)-*N*-Cyclohexyl-3-phenylbutanamide. Using cyclohexylamine and (*S*)-3-phenylbutyric acid and the procedure described above for the preparation of (*S*)-*N*-(4-methoxyphenyl)-3-phenylbutanamide on a 0.25 mmol scale, the title compound was prepared in 79% yield (48.5 mg, 0.20 mmol) with spectral data in accordance with that obtained via the cross-coupling reaction described above. $[\alpha]_D^{20}$ = +35.0 (*c* = 0.2, MeOH). Using the racemate of this material, a method for enantiomer separation was attained using HPLC analysis (Column AS-H, 6% *i*-PrOH, 0.5 mL). Co-injection of the racemate with the title compound provided absolute configuration identity to the enantiomer peaks. [(*S*)-isomer t_r = 81.2 min and (*R*)-isomer t_r = 74.5 min].



(*S*)-*N*-Cyclohexyl-3-phenylbutanamide. Using the general procedure described for the Suzuki-Miyaura cross-coupling of β-trifluoroboratoamides using potassium (*R*)-*N*-cyclohexyl-3-(trifluoroborato)butanamide and chlorobenzene under condition B on 0.25 mmol scale, the title compound was obtained as a white solid in 96% yield (58.9 mg, 0.24 mmol) with spectral data in accordance with that described for the racemate. The title compound was found to have an enantiomeric ratio of 92:8 with an absolute configuration of *S* for the major enantiomer using HPLC analysis. $[\alpha]_D^{20}$ = +29.7 (*c* = 0.2, MeOH).

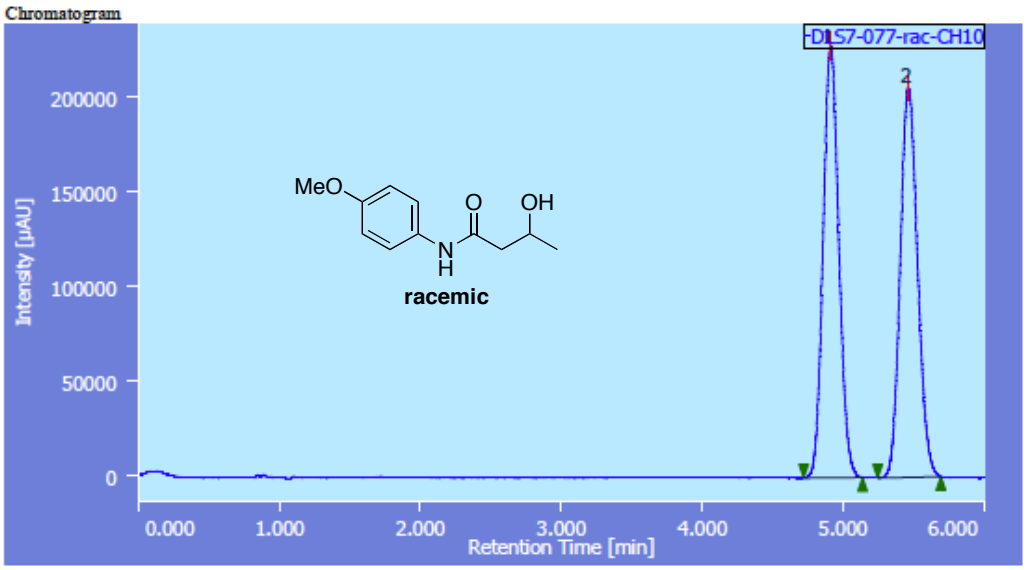


(*S*)-3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-cyclohexylbutanamide. Using the general procedure described for the Suzuki-Miyaura cross-coupling of β-trifluoroboratoamides using potassium (*R*)-*N*-cyclohexyl-3-(trifluoroborato)butanamide and chlorobenzene under condition B on a 0.25 mmol scale, the title compound was obtained as a white solid in 91% yield (70.8, 0.23 mmol) with spectral data in accordance with that described for the racemate. The title compound was found to have an enantiomeric ratio of 92:8 assumed to have an absolute configuration of *S* for the major enantiomer using HPLC analysis [Column AS-H, 10% *i*-PrOH, 1.0 mL; (*S*)-isomer t_r = 37.3 min and (*R*)-isomer t_r = 27.4 min]. $[\alpha]_D^{20}$ = +33.1 (*c* = 0.2, MeOH). This assumption was made on the basis that we and Yun and coworkers[8a] both observed that (*R*)-(*S*)-Josiphos provides this enantiomer in the borylation of a,β-unsaturated amides.

Chromatograms:

Analysis of 3-Hydroxy-*N*-(4-Methoxyphenyl)butanamide using SFC. Analysis was performed using Column OD-H, 8% *i*-PrOH, 4 mL, 12MPa. (*S*)-isomer t_r = 4.9 min and (*R*)-isomer t_r = 5.5 min.

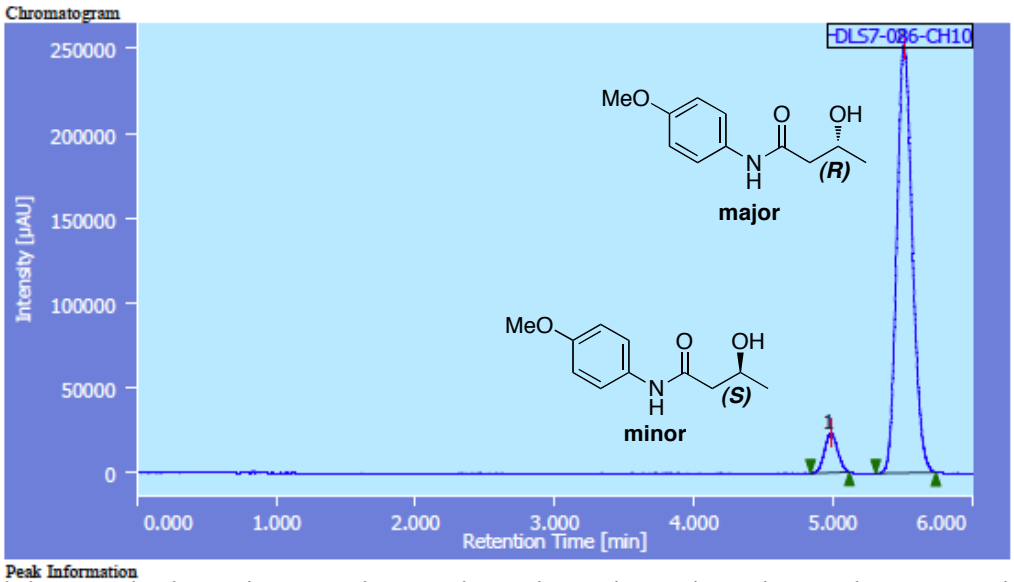
Chromatogram of oxidized racemic borylation product:



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	10	4.910	1756448	227514	50.091	52.586	N/A	9278	2.574	1.100	
2	Unknown	10	5.462	1750051	205141	49.909	47.414	N/A	9355	N/A	1.123	

Chromatogram of oxidized enantioenriched borylation product:

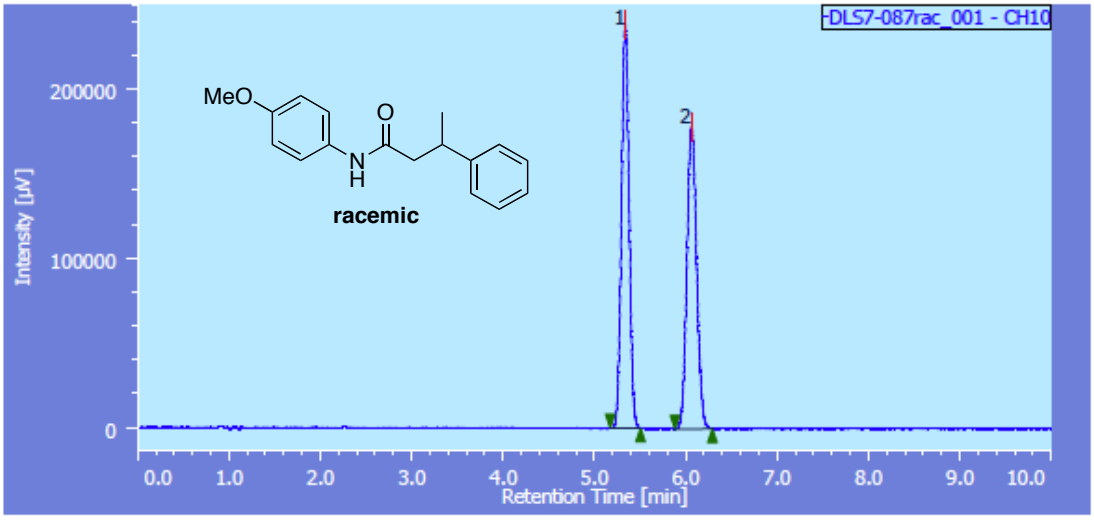


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	10	4.983	153309	23316	7.286	8.468	N/A	12860	2.775	1.053	
2	Unknown	10	5.508	1950936	252031	92.714	91.532	N/A	11703	N/A	1.157	

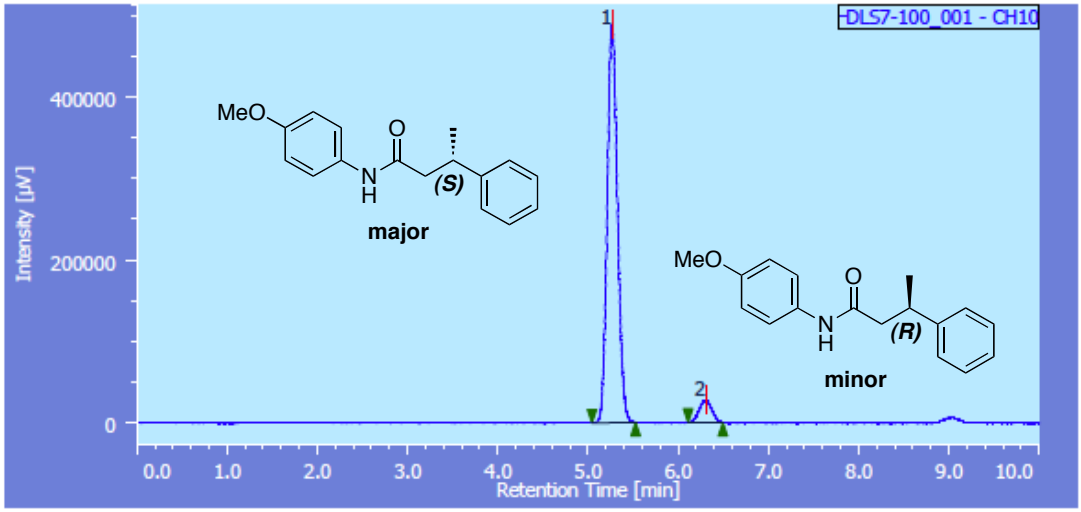
Analysis of *N*-(4-methoxyphenyl)-3-phenylbutanamide using SFC. Analysis was performed using Column OJ-H, 10% *i*-PrOH, 4 mL, 12 MPa.. (*S*)-isomer t_r= 5.3 min and (*R*)-isomer t_r = 6.1 min.

Chromatogram of racemic cross-coupled product:



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	10	5.337	1387751	238202	51.208	57.171	N/A	19167	4.158	1.036	
2	Unknown	10	6.063	1322277	178450	48.792	42.829	N/A	15268	N/A	1.074	

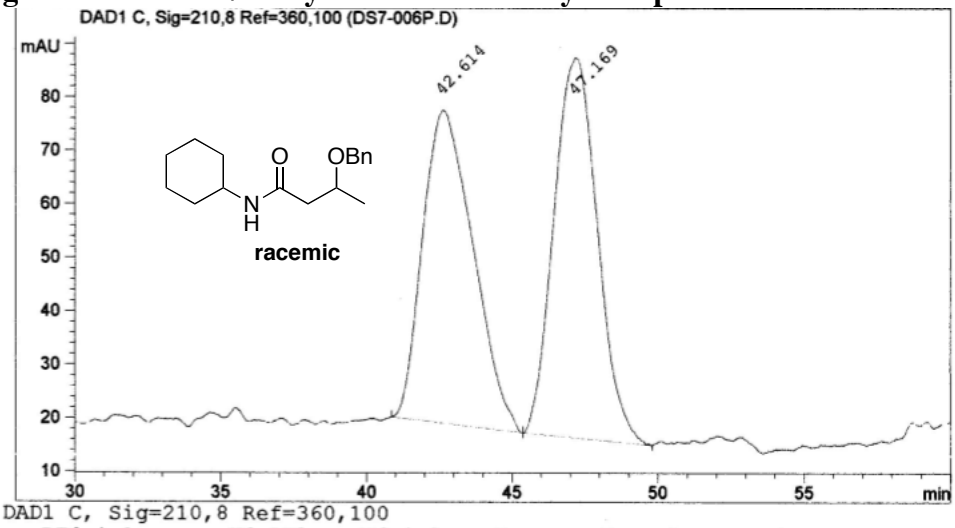
Chromatogram of cross-coupled product from enantioenriched trifluoroborate:



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	10	5.265	3862590	488998	93.433	94.656	N/A	10214	4.411	1.120	
2	Unknown	10	6.305	271492	27606	6.567	5.344	N/A	9099	N/A	0.980	

Analysis of 3-(benzyloxy)-N-cyclohexylbutanamide using chiral HPLC. Analysis was performed using Column AS-H, 5% *i*-PrOH, 0.7 mL. (*S*)-isomer t_r = 47.2 min and (*R*)-isomer t_r = 42.3 min.

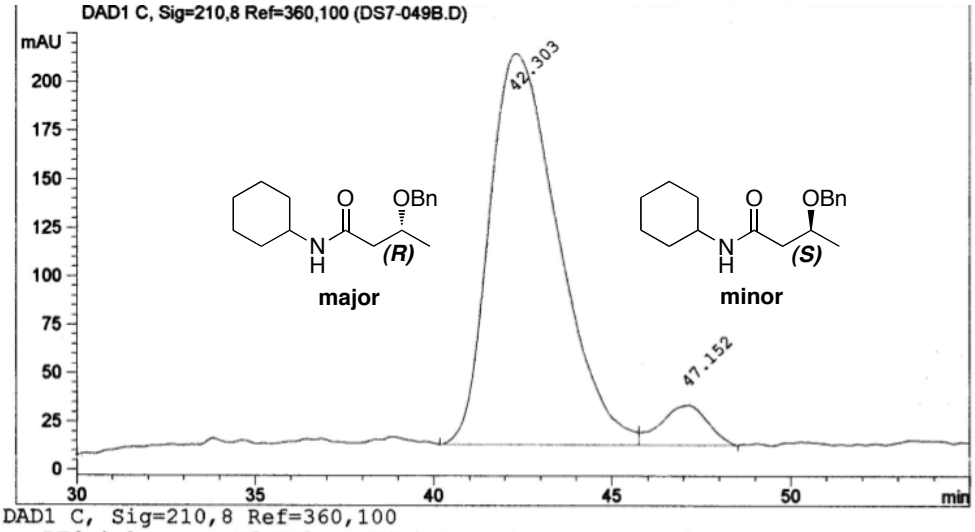
Chromatogram of oxidized/benzylated racemic borylated product:



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	BP	42.61	58.6	1.42	7057.4	48.80	
2	VP	47.17	71.1	1.23	7403.5	51.20	

Chromatogram of oxidized/benzylated enantioenriched borylated product:

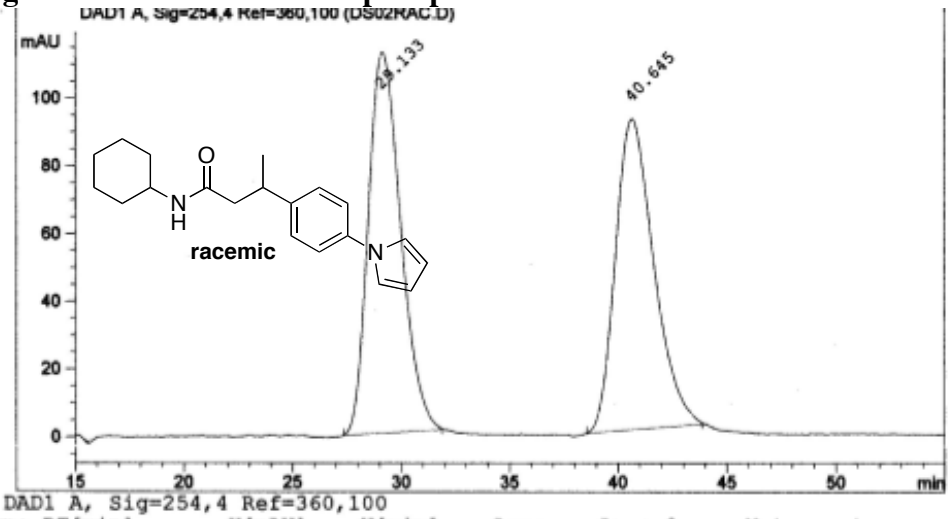


ignal 1: DAD1 C, Sig=210,8 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	PV	42.30	201.5	1.59	27162.6	93.54	
2	VP	47.15	20.6	1.07	1875.2	6.46	

Analysis of 3-(4-(1*H*-pyrrol-1-yl)phenyl)-*N*-cyclohexylbutanamide using chiral HPLC. Analysis was performed using Column AS-H, 10% *i*-PrOH, 1.0 mL. (*S*)-isomer t_r = 37.3 min and (*R*)-isomer t_r = 27.4 min.

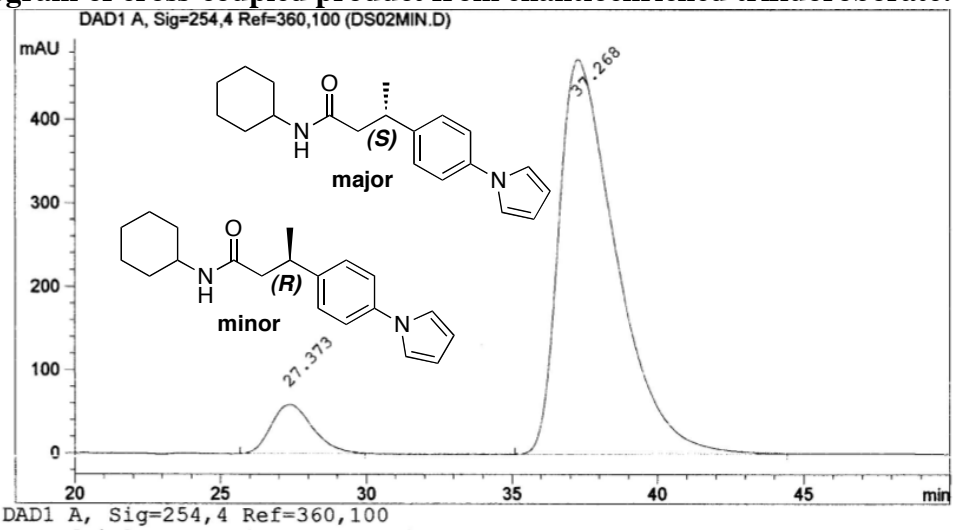
Chromatogram of racemic cross-coupled product:



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	BB	29.13	112.5	1.39	11698.7	50.94	
2	BB	40.64	91.8	1.49	11265.2	49.06	

Chromatogram of cross-coupled product from enantioenriched trifluoroborate:

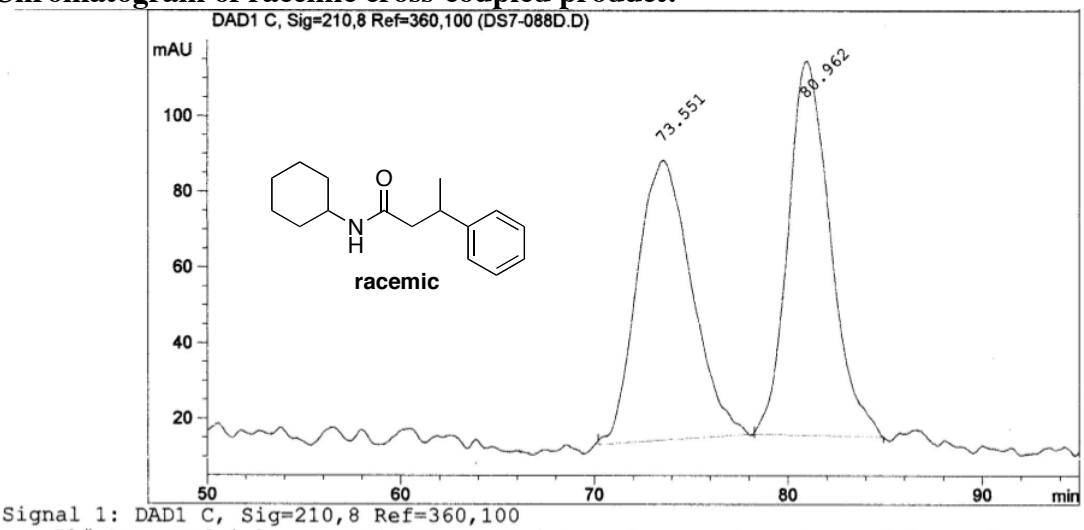


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	BB	27.37	59.0	1.22	5813.7	8.21	
2	MM	37.27	473.5	2.29	65017.4	91.79	

Analysis of *N*-cyclohexyl-3-(*p*-tolyl)butanamide using chiral HPLC. Analysis was performed using Column AS-H, 6% *i*-PrOH, 0.5 mL. (*S*)-isomer t_r = 81.2 min and (*R*)-isomer t_r = 74.5 min.

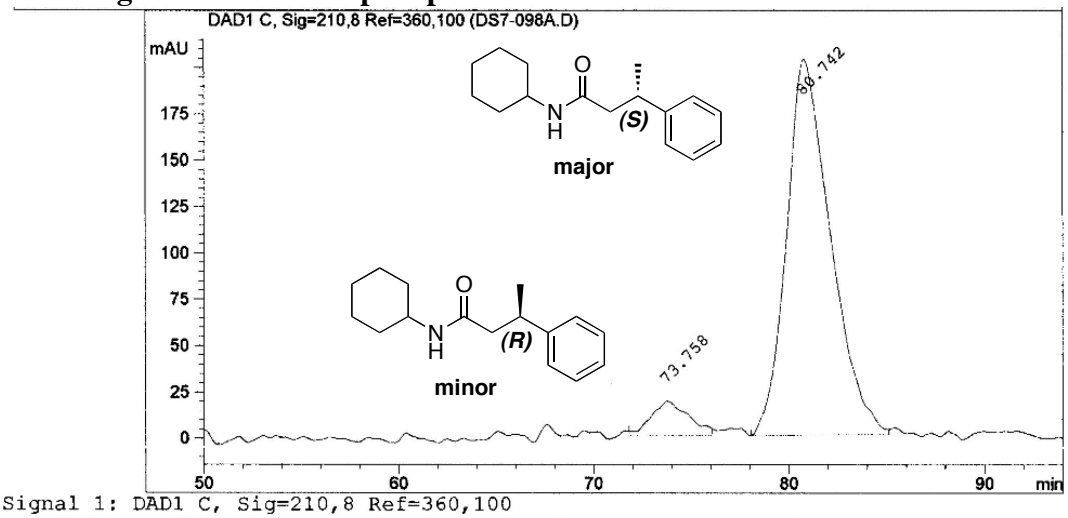
Chromatogram of racemic cross-coupled product:



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	MM	73.55	74.0	3.26	14490.7	49.11	
2	MM	80.96	99.0	2.53	15015.1	50.89	

Chromatogram of cross-coupled product from enantioenriched trifluoroborate:



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Pk#	Type	RT[min]	H[mAU]	W[min]	Area	Area %	Notes, etc.
1	MM	73.76	18.6	2.22	2483.8	7.24	
2	VV	80.74	202.9	1.85	31831.7	92.76	

References and Notes

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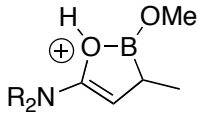
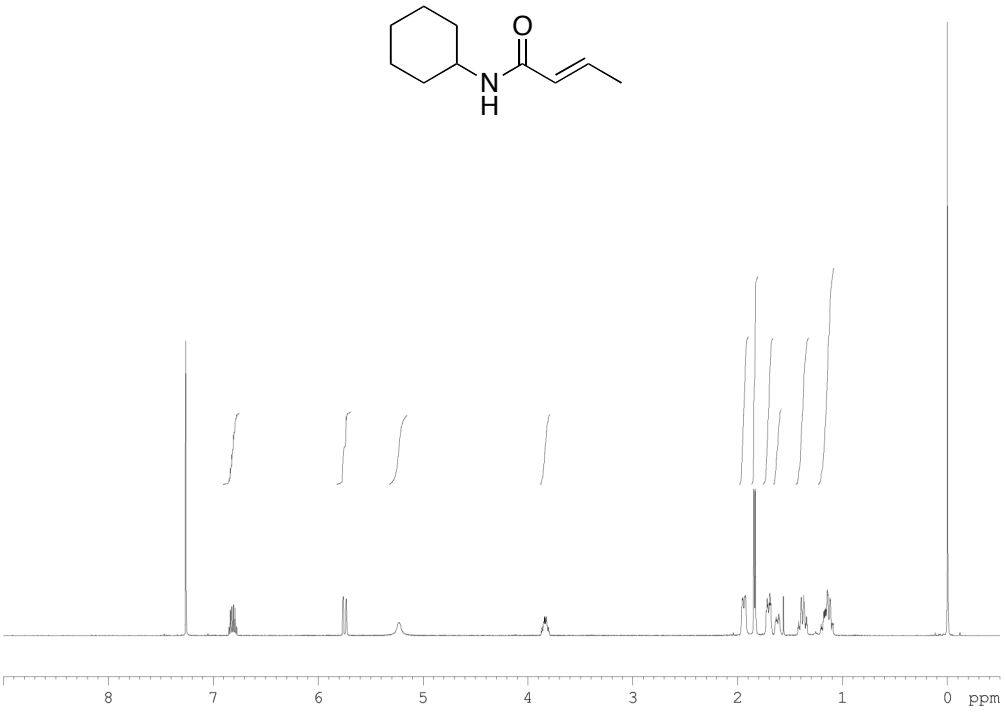
8) (a) Chea, H.; Sim, H.-S.; Yun, J. *Adv. Synth. Catal.* **2009**, *351*, 855. (b) Molander, G. A.; Petrillo, D. E. *Org. Lett.* **2008**, *10*, 1795.

9) Bagutski, V.; Ros, A.; Aggarwal, V. K. *Tetrahedron* **2009**, *65*, 9956.

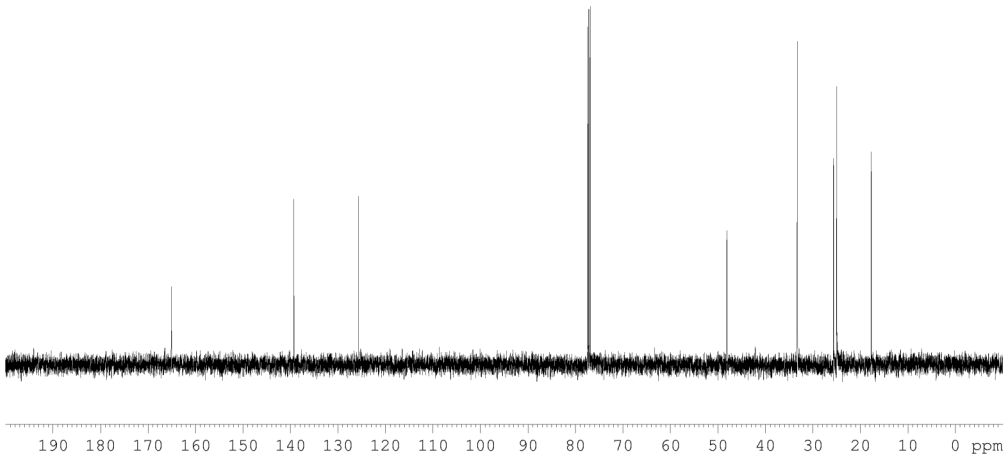
10) Owing to the rapid hydrolysis that occurs with this family of β-boratoamidohomoenolates, many of the high resolution mass spectrometry values found correspond to hydrolyzed structure in the following form:

$[M(-F_3K)(+OCH_3)]^+$: 

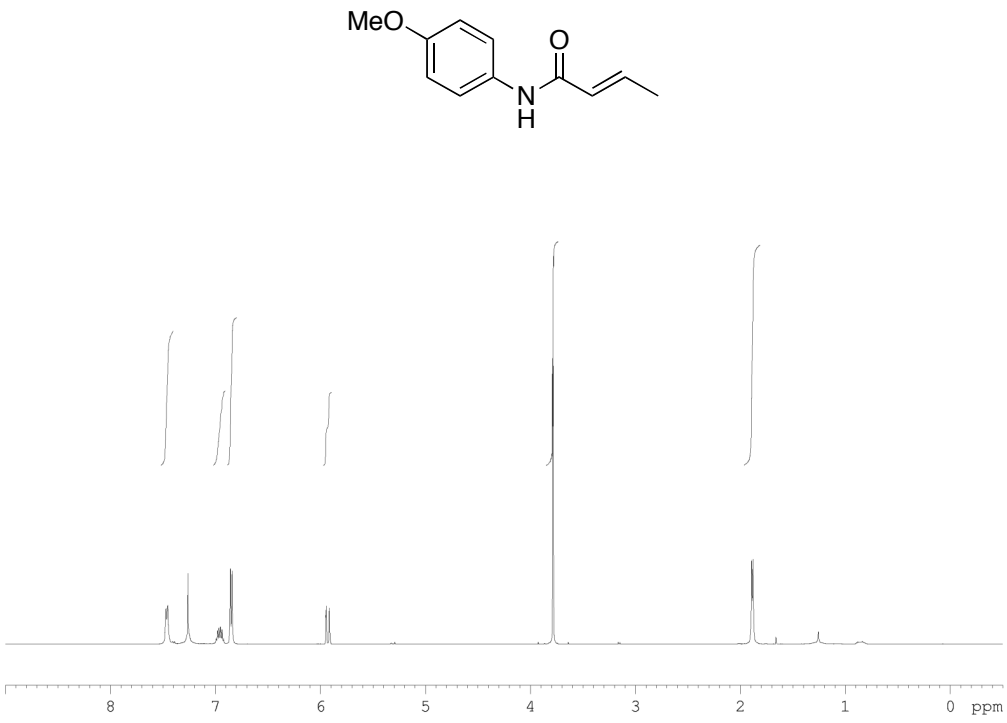
11) The absolute configurations of *R* and *S* were assigned on the basis of the absolute determination of *p*-anisidine derivative.



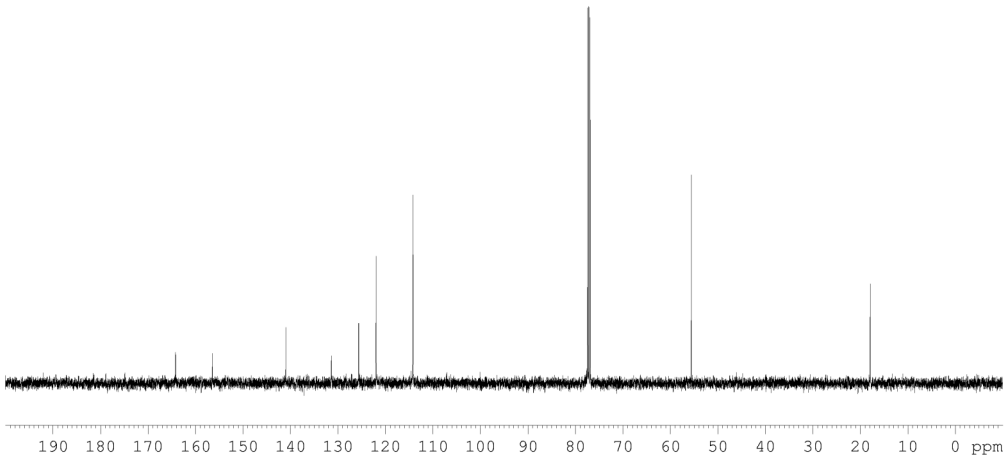
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *(E)-N*-Cyclohexylbut-2-enamide



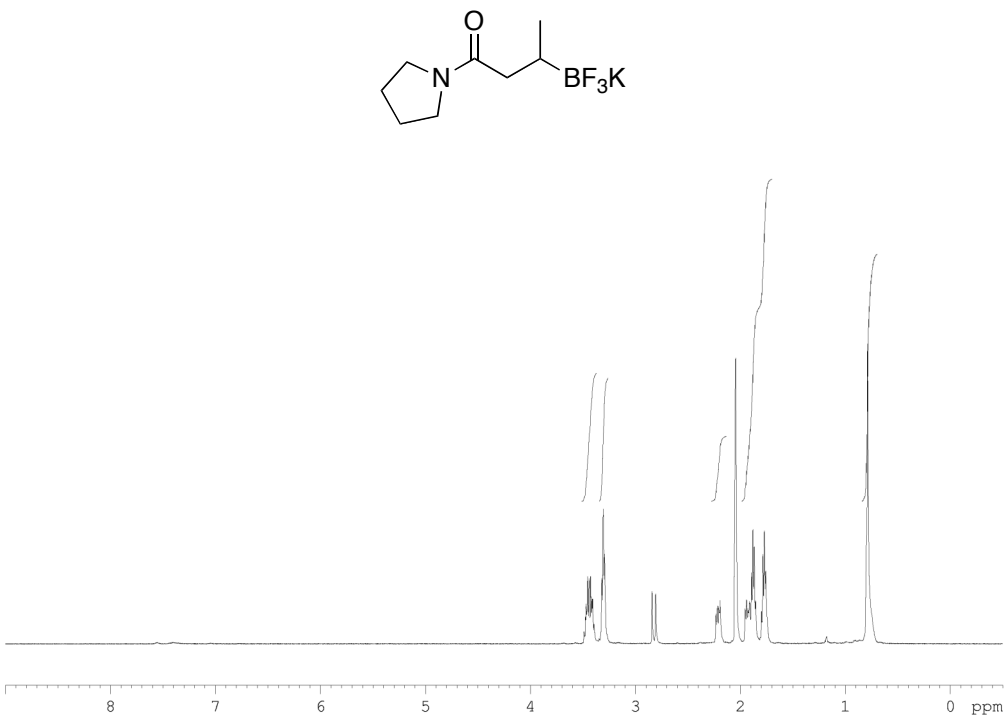
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *(E)-N*-Cyclohexylbut-2-enamide



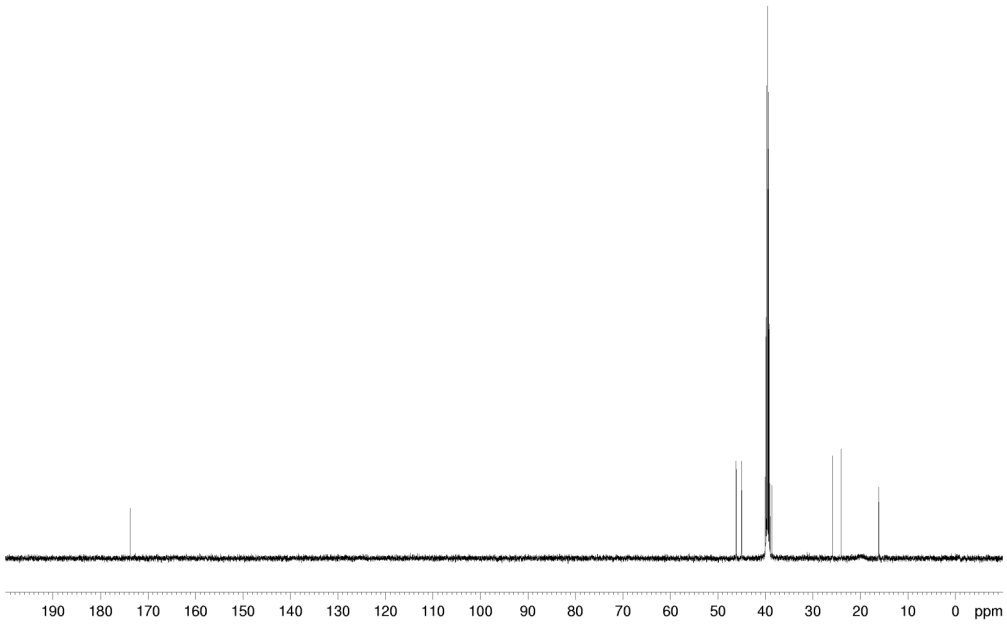
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of (*E*)-*N*-(4-Methoxyphenyl)but-2-enamide



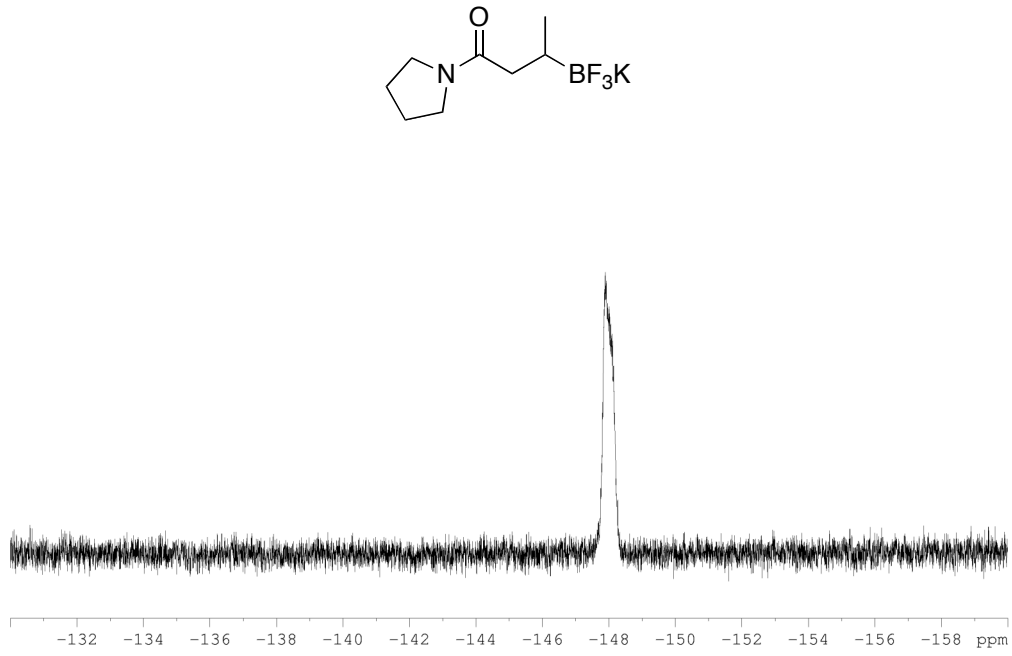
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of (*E*)-*N*-(4-Methoxyphenyl)but-2-enamide



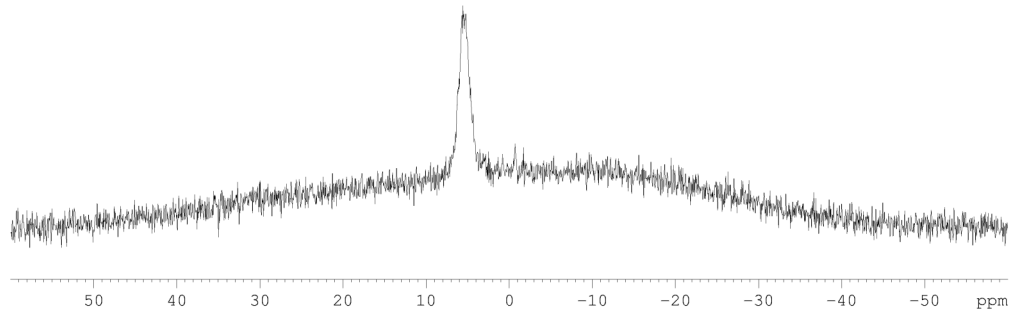
^{1}H NMR (500 MHz, acetone-d_6) Spectrum of Potassium 1-(Pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one



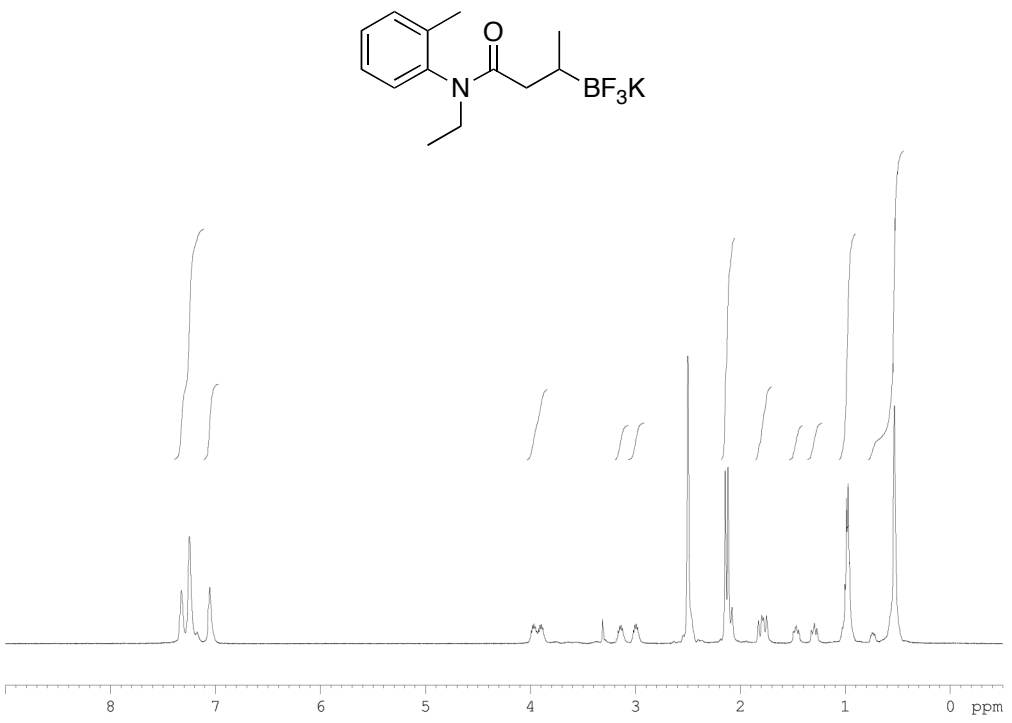
^{13}C NMR (125.8 MHz, acetone-d_6) Spectrum of Potassium 1-(Pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one



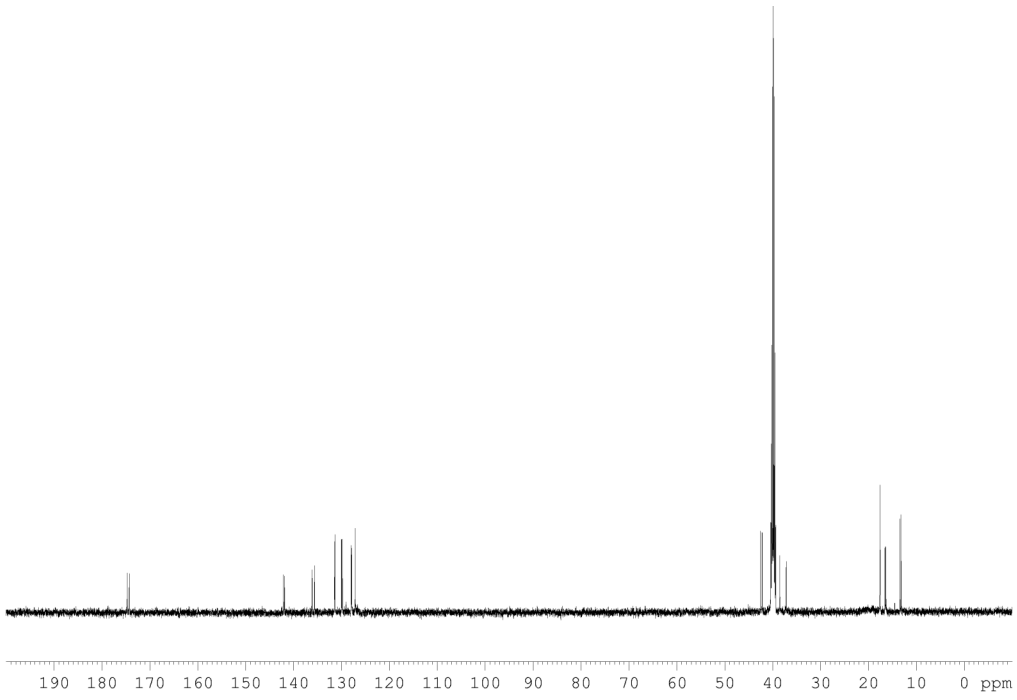
^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum of Potassium 1-(Pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one



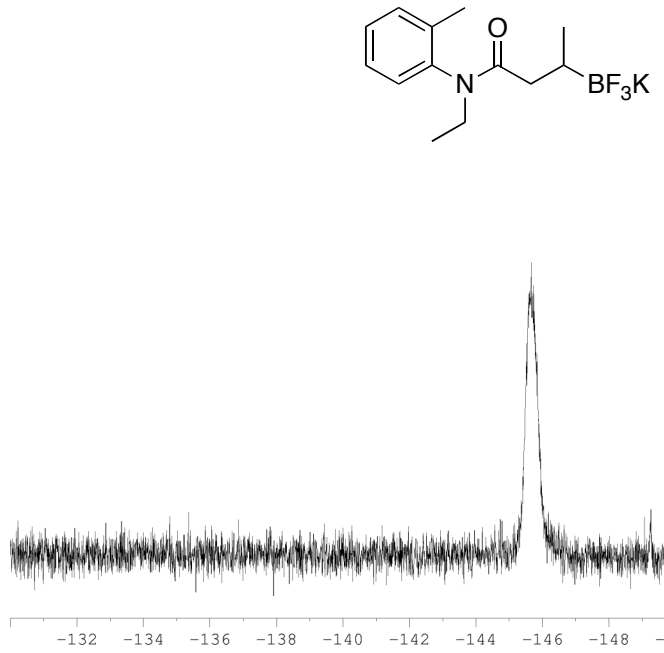
^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum of Potassium 1-(Pyrrolidin-1-yl)-3-(trifluoroborato)butan-1-one



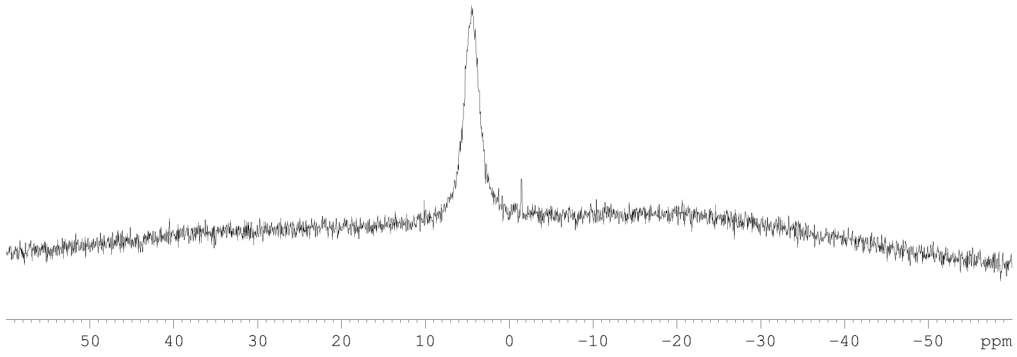
^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of Potassium *N*-Ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide



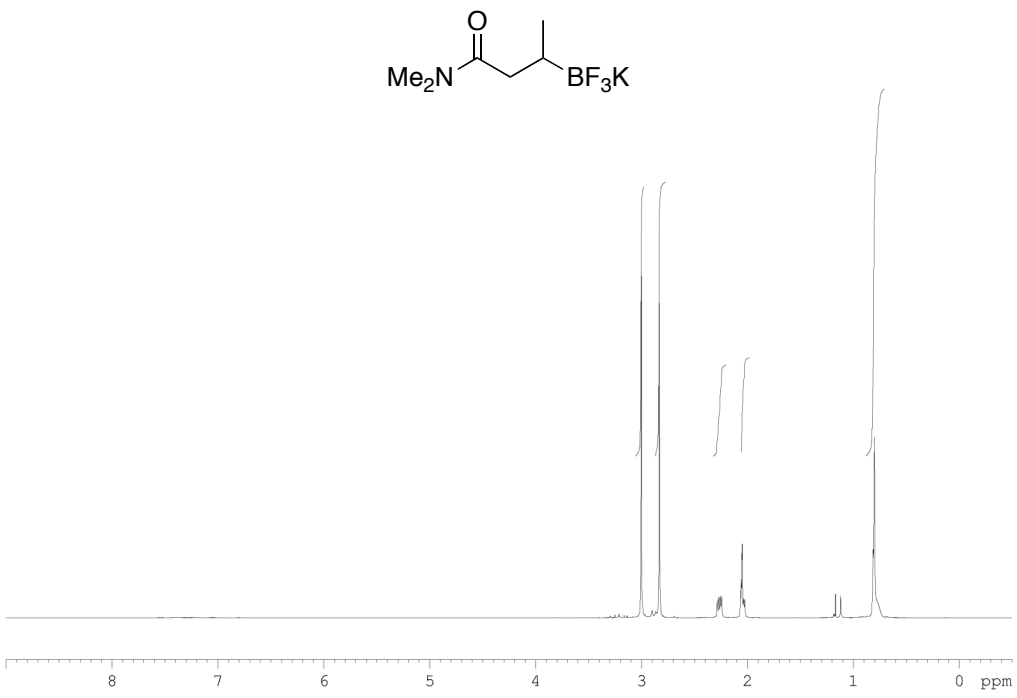
^{13}C NMR (125.8 MHz, DMSO-d_6) Spectrum of Potassium *N*-Ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide



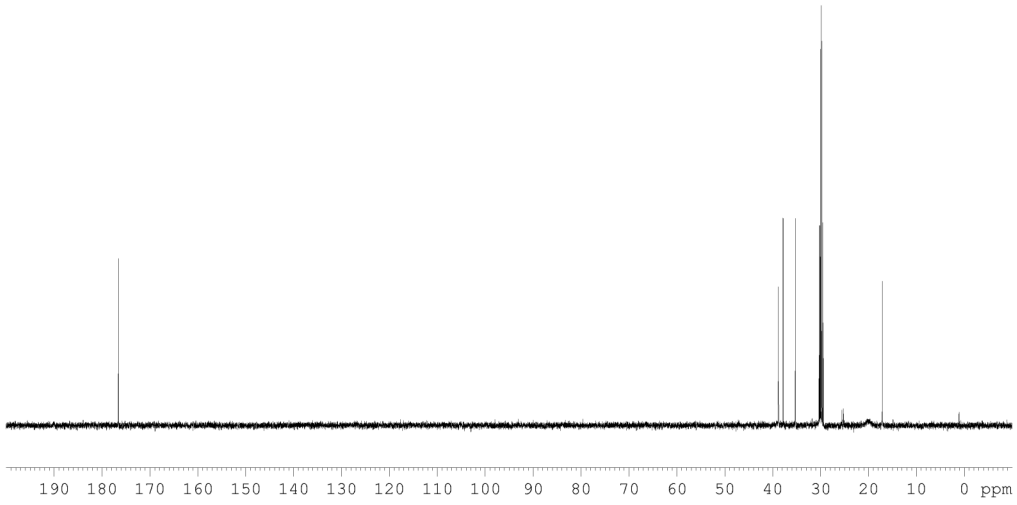
^{19}F NMR (470.8 MHz, DMSO-d_6) Spectrum of Potassium *N*-Ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide



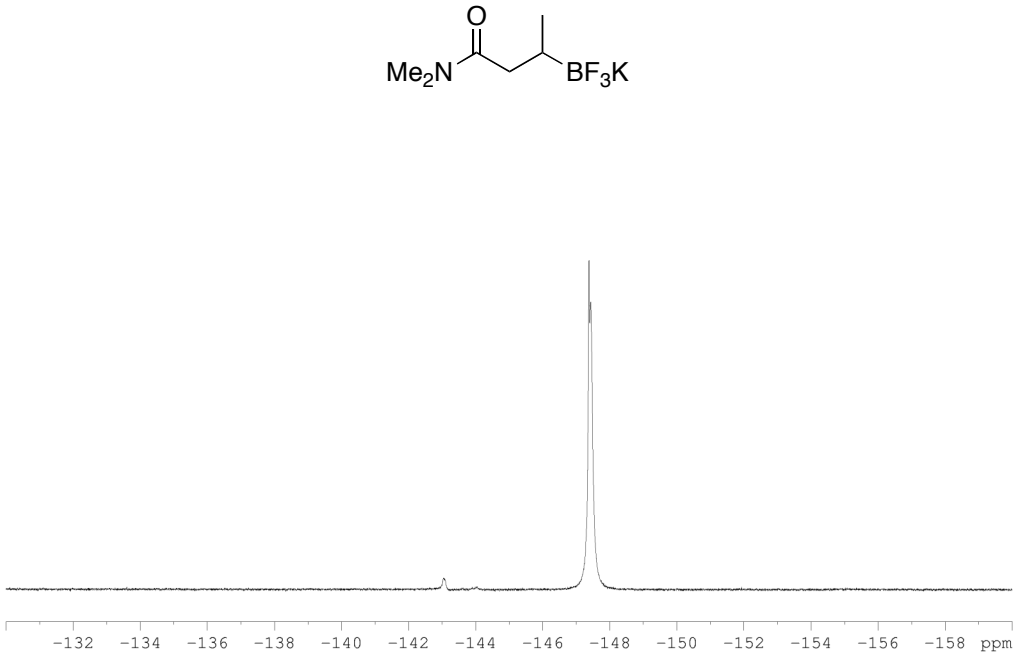
^{11}B NMR (128.4 MHz, DMSO-d_6) Spectrum of Potassium *N*-Ethyl-*N*-(*o*-tolyl)-3-(trifluoroborato)butanamide



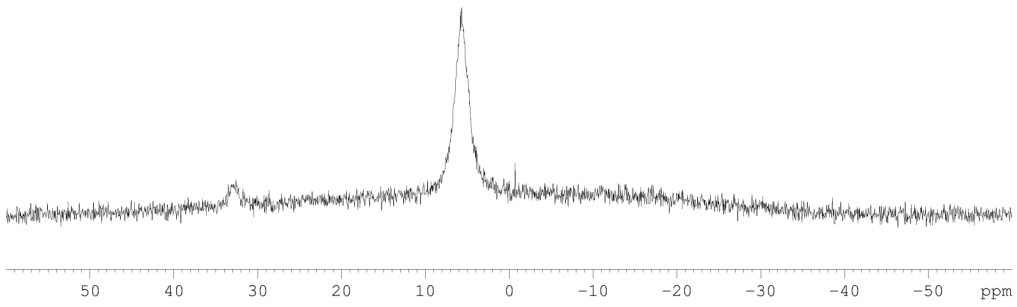
^{1}H NMR (500 MHz, acetone-d_6) Spectrum of Potassium *N*,*N*-Dimethyl-3-(trifluoroborato)butanamide



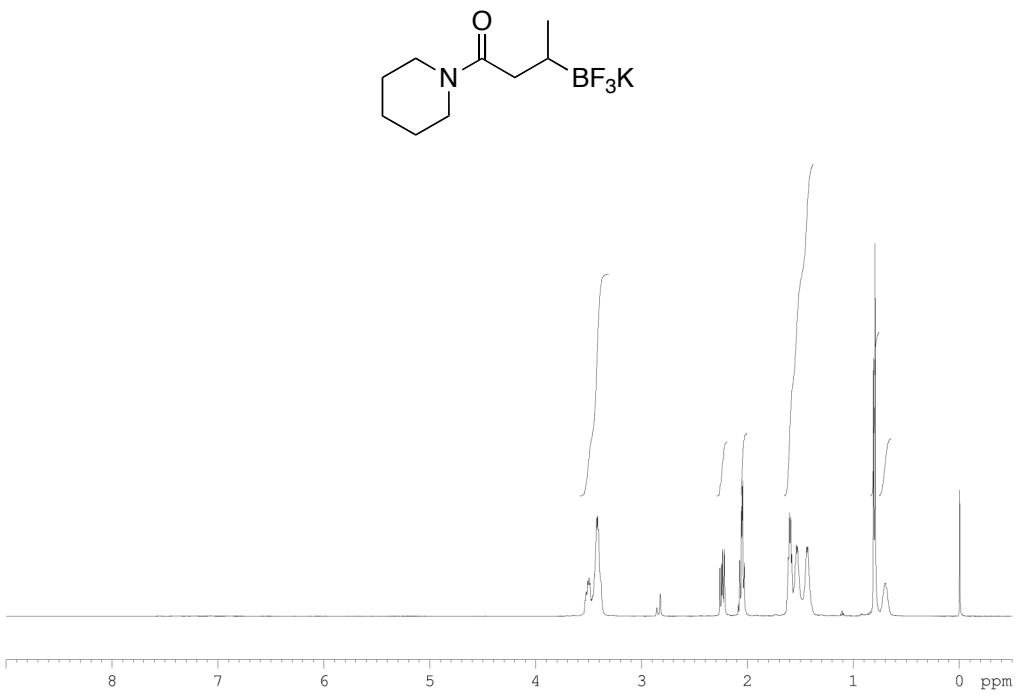
^{13}C NMR (125.8 MHz, acetone-d_6) Spectrum of Potassium *N*,*N*-Dimethyl-3-(trifluoroborato)butanamide



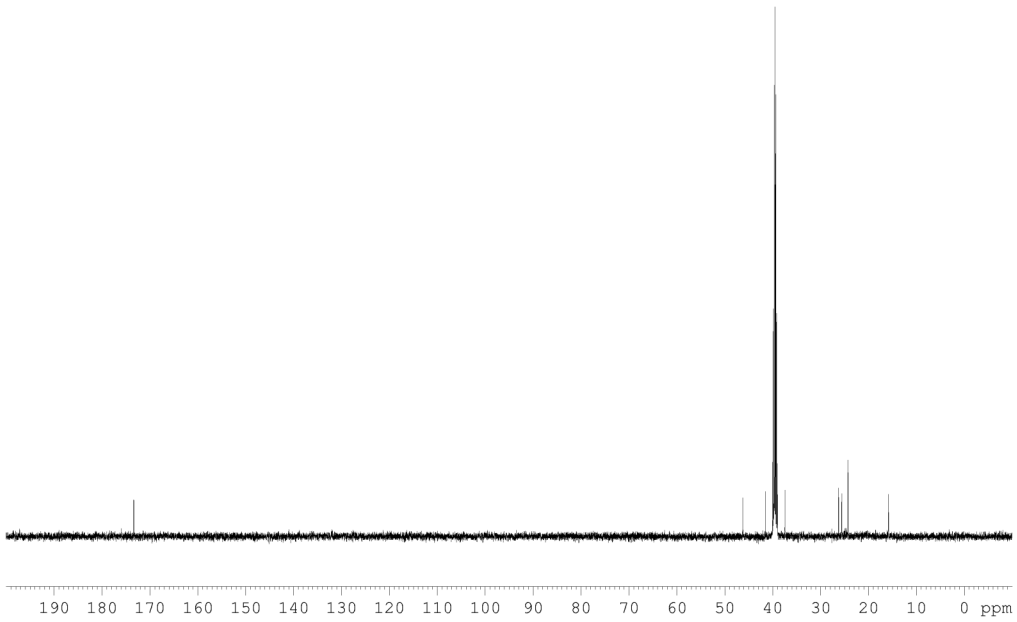
^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum of Potassium *N*,*N*-Dimethyl-3-(trifluoroborato)butanamide



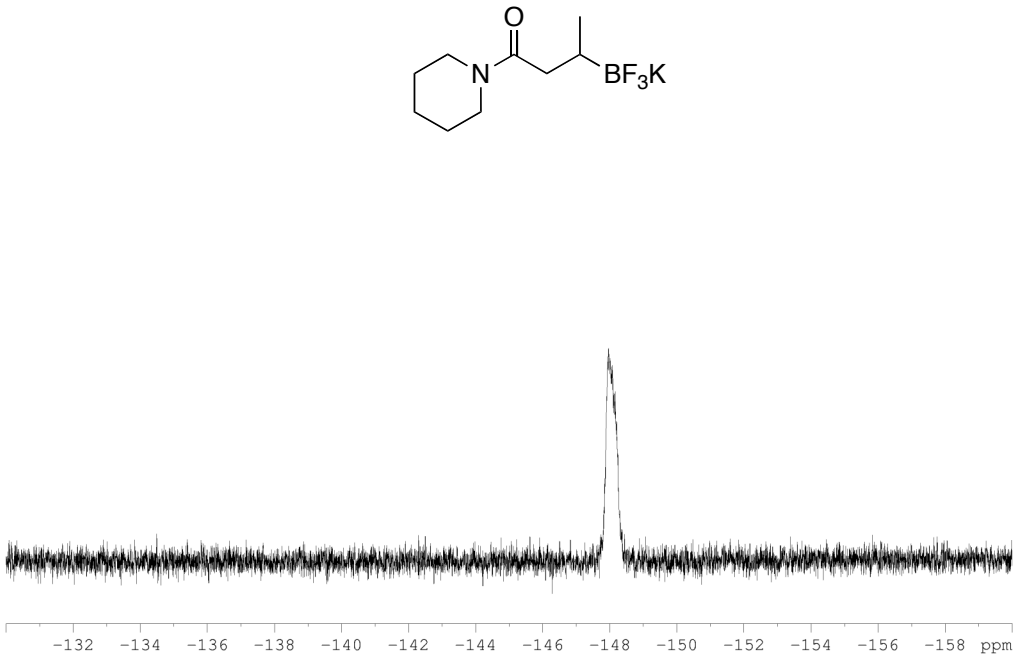
^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum of Potassium *N*,*N*-Dimethyl-3-(trifluoroborato)butanamide



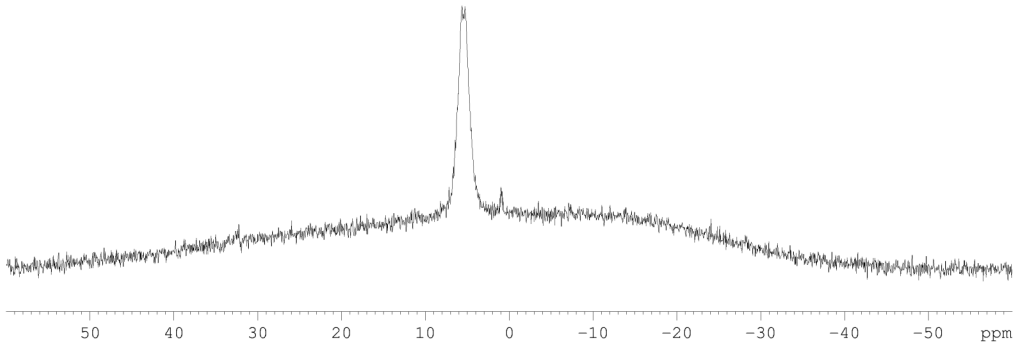
^{1}H NMR (500 MHz, acetone-d_6) Spectrum of Potassium 1-(Piperidin-1-yl)-3-(trifluoroborato)butan-1-one



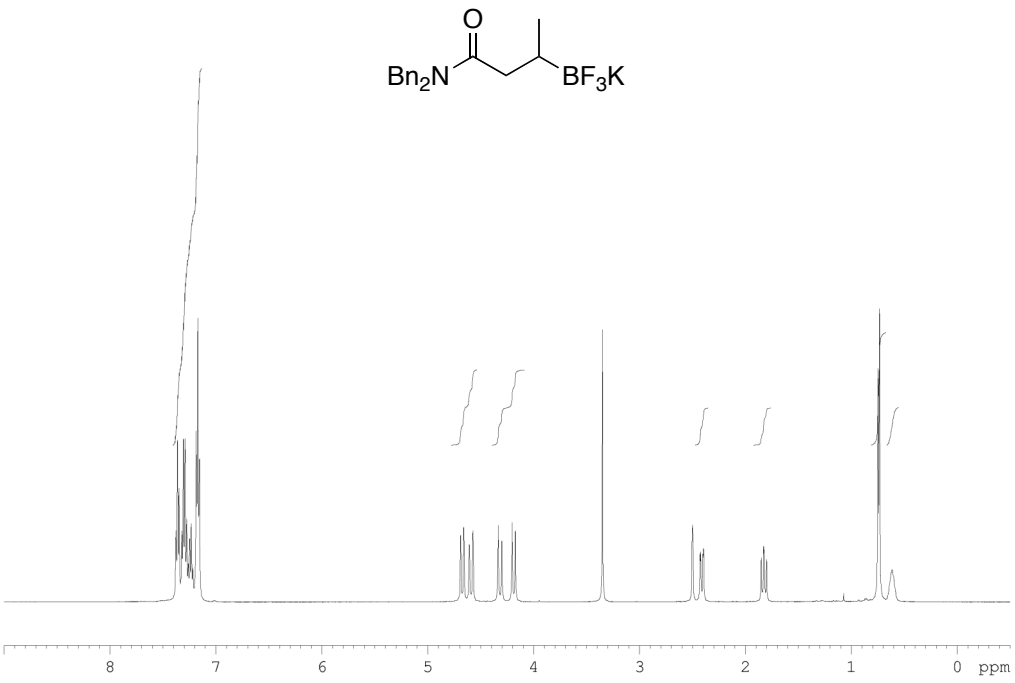
^{13}C NMR (125.8 MHz, acetone-d_6) Spectrum of Potassium 1-(Piperidin-1-yl)-3-(trifluoroborato)butan-1-one



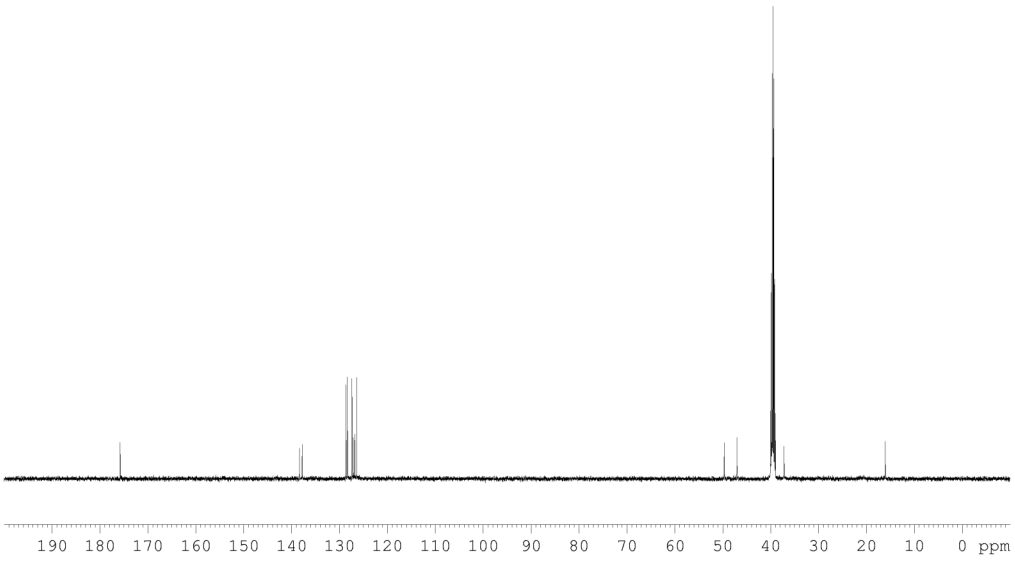
^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum of Potassium 1-(Piperidin-1-yl)-3-(trifluoroborato)butan-1-one



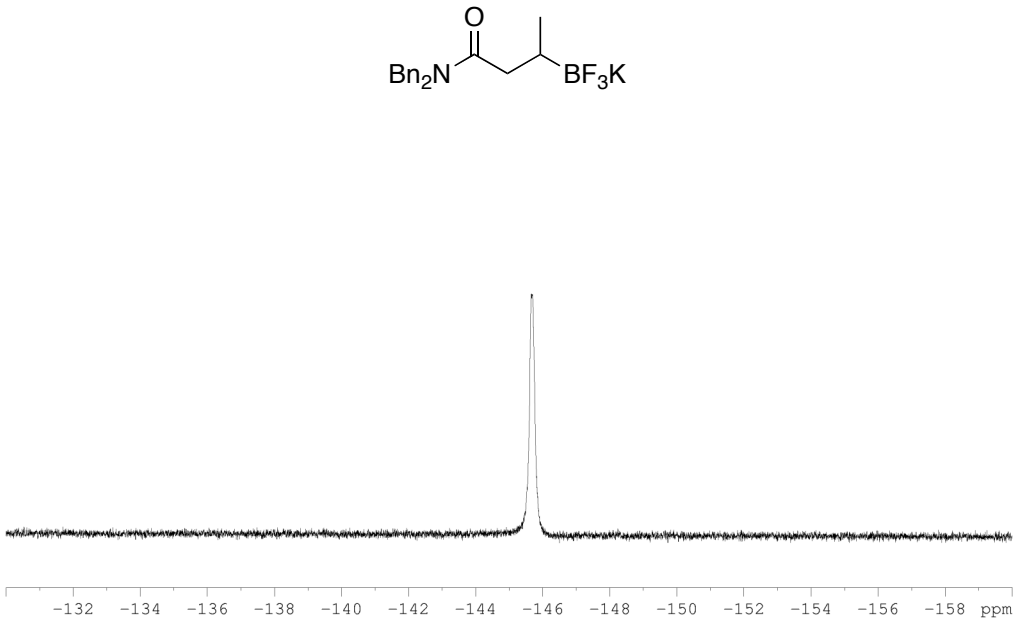
^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum of Potassium 1-(Piperidin-1-yl)-3-(trifluoroborato)butan-1-one



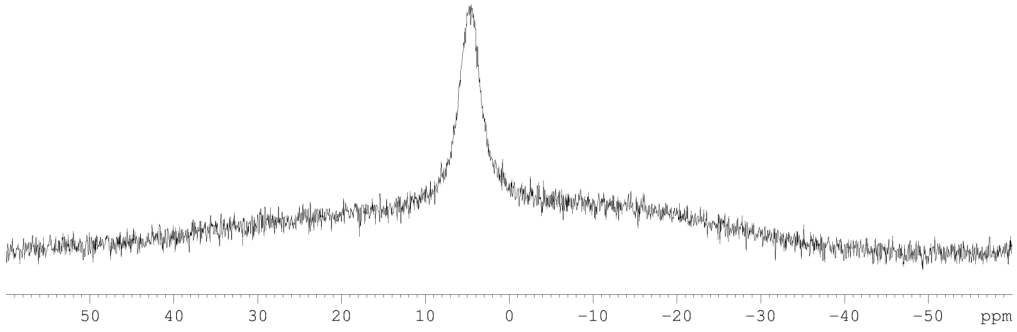
^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of Potassium *N*,*N*-Dibenzyl-3-(trifluoroborato)butanamide



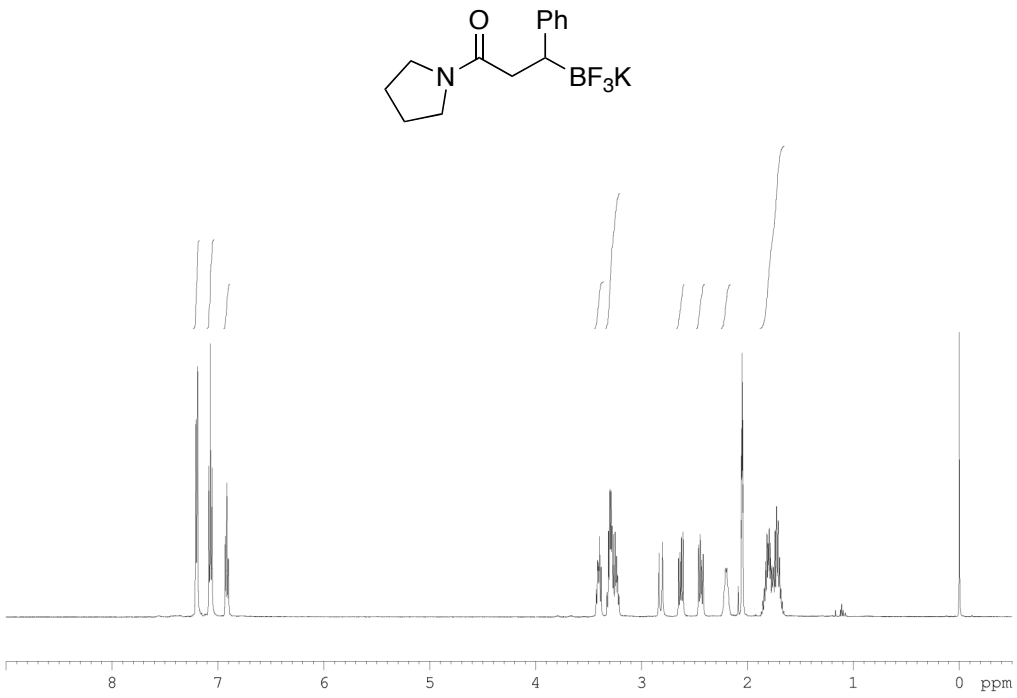
^{13}C NMR (125.8 MHz, DMSO-d_6) Spectrum of Potassium *N*,*N*-Dibenzyl-3-(trifluoroborato)butanamide



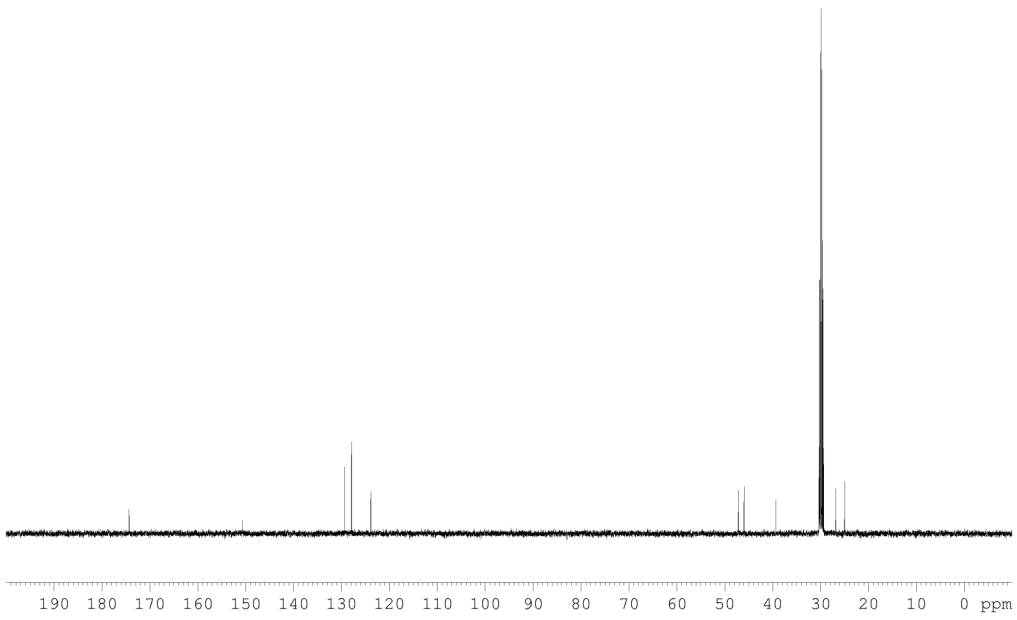
^{19}F NMR (470.8 MHz, DMSO-d_6) Spectrum of Potassium *N*,*N*-Dibenzyl-3-(trifluoroborato)butanamide



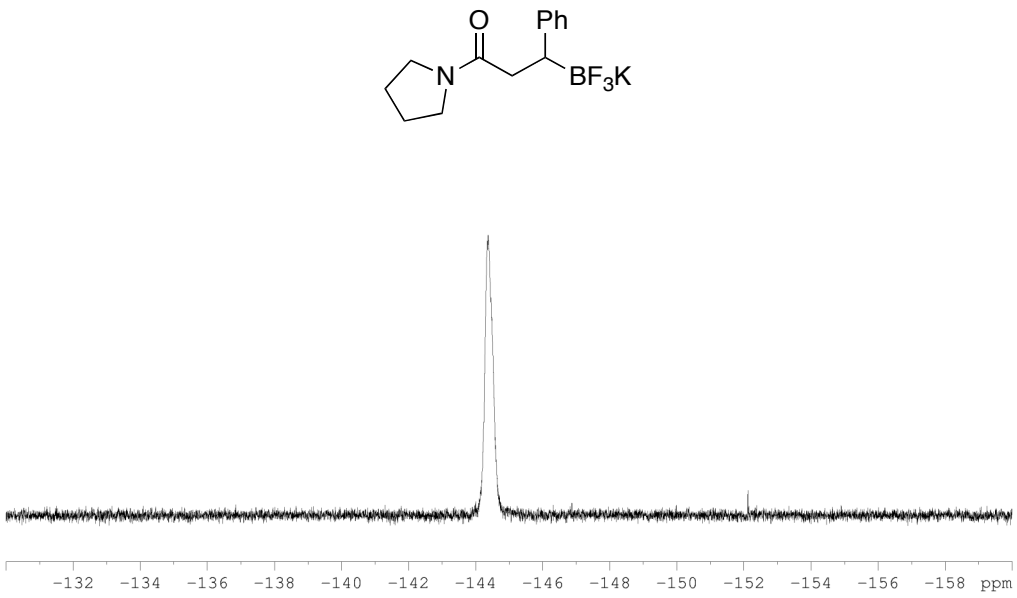
^{11}B NMR (128.4 MHz, DMSO-d_6) Spectrum of Potassium *N*,*N*-Dibenzyl-3-(trifluoroborato)butanamide



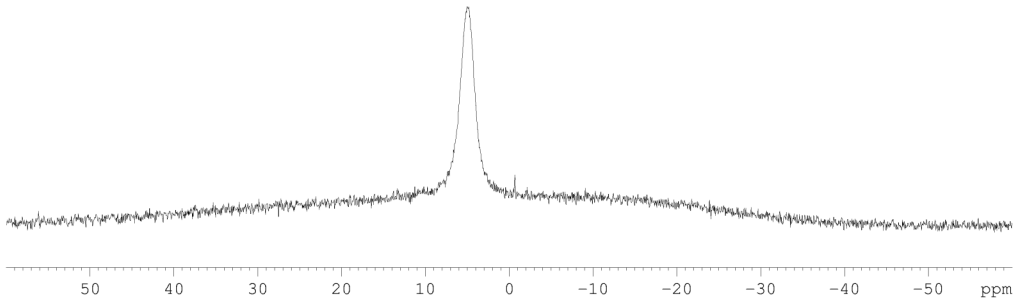
^{1}H NMR (500 MHz, acetone-d_6) Spectrum of Potassium 3-Phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one



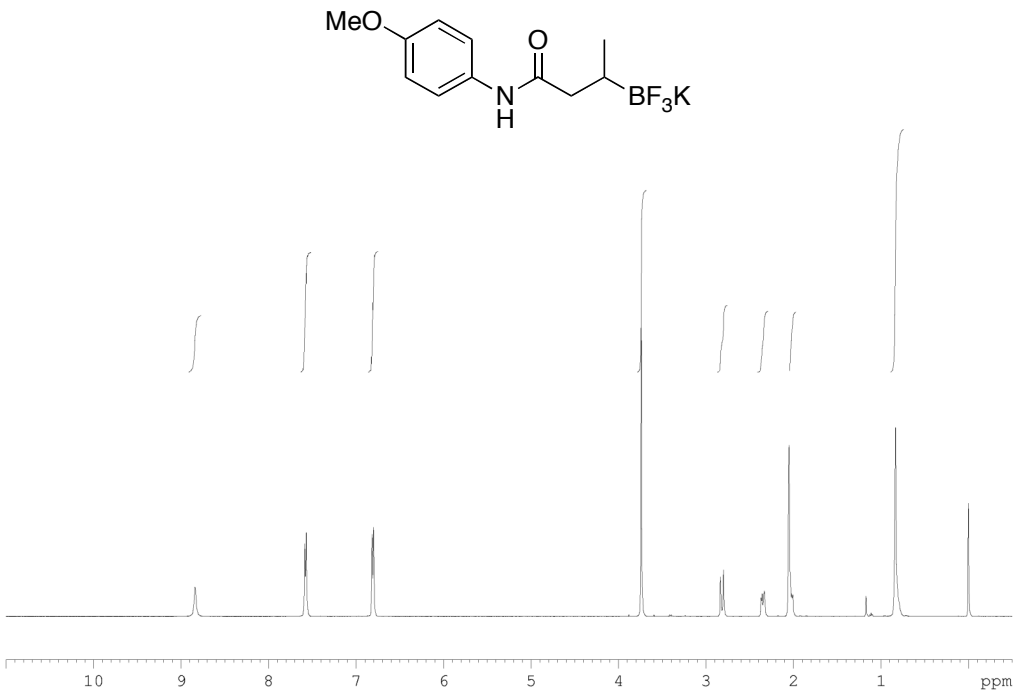
^{13}C NMR (125.8 MHz, acetone-d_6) Spectrum of Potassium 3-Phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one



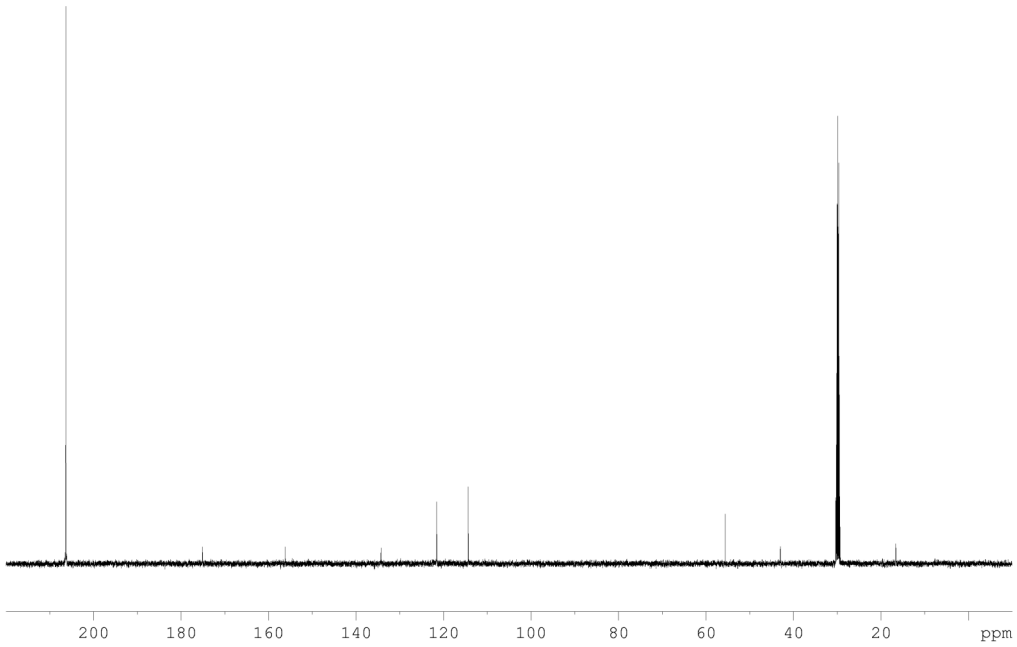
^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum of Potassium 3-Phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one



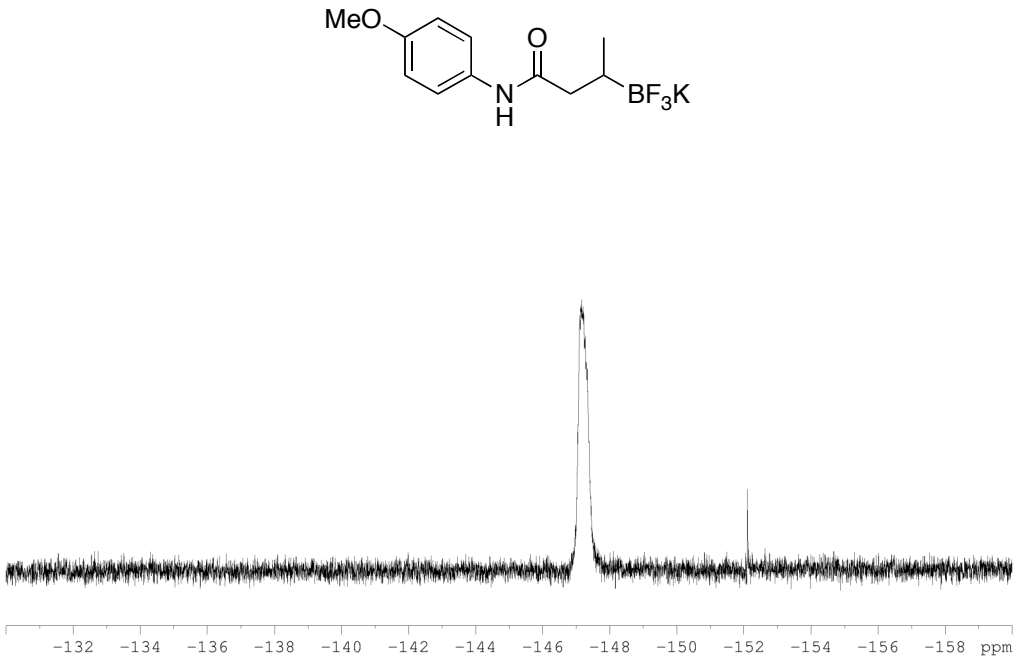
^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum of Potassium 3-Phenyl-1-(pyrrolidin-1-yl)-3-(trifluoroborato)propan-1-one



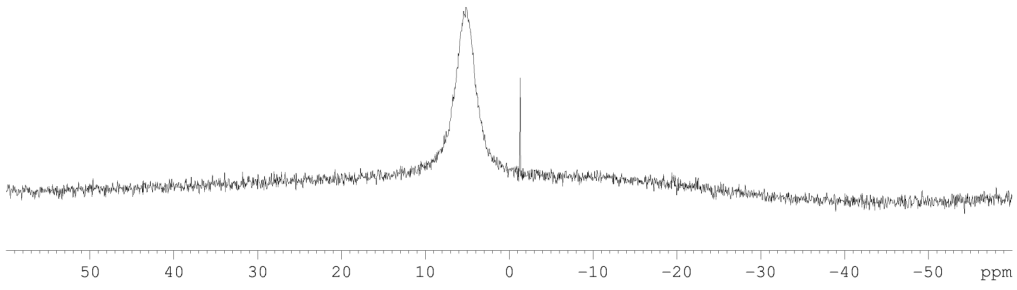
^{1}H NMR (500 MHz, acetone-d_6) Spectrum of Potassium *N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide



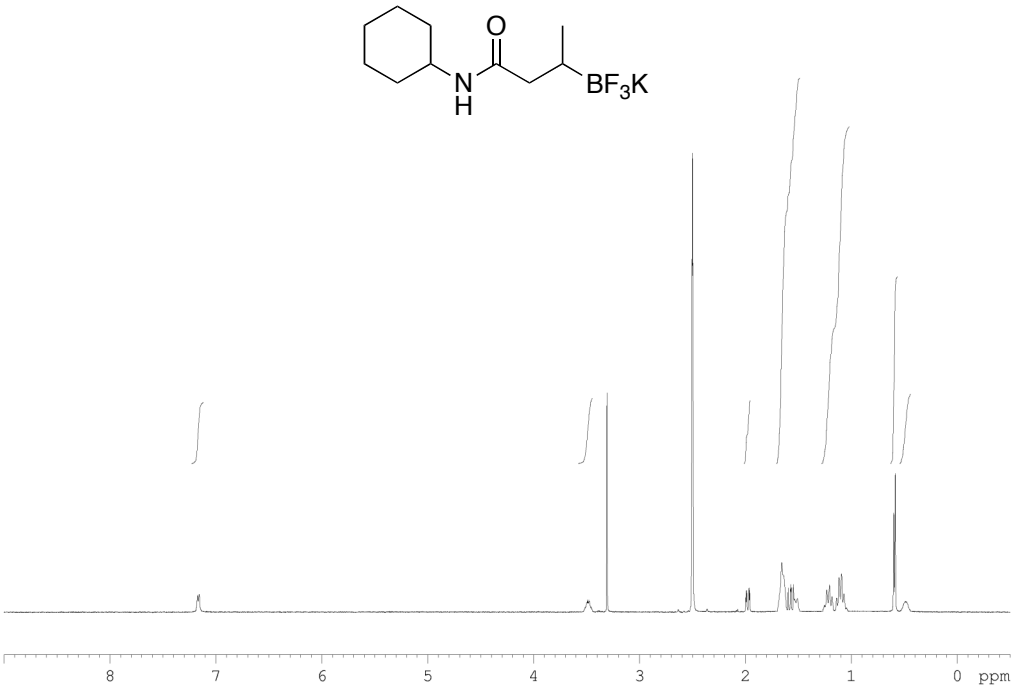
^{13}C NMR (125.8 MHz, acetone-d_6) Spectrum of Potassium *N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide



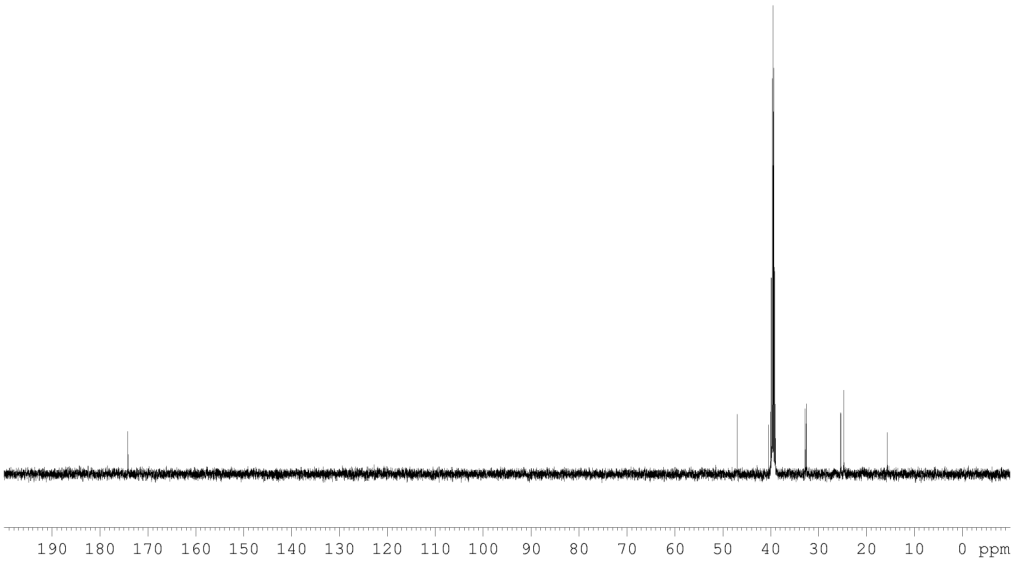
^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum of Potassium *N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide



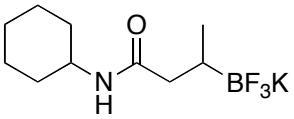
^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum of Potassium *N*-(4-Methoxyphenyl)-3-(trifluoroborato)butanamide

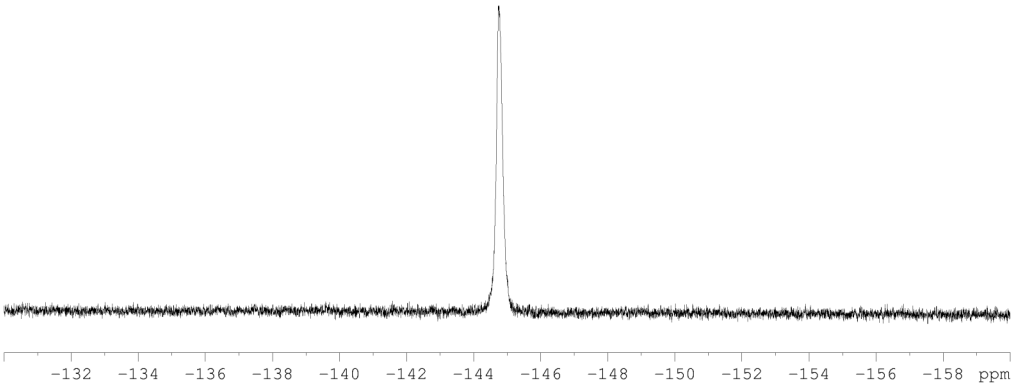


^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of Potassium *N*-Cyclohexyl-3-(trifluoroborato)butanamide

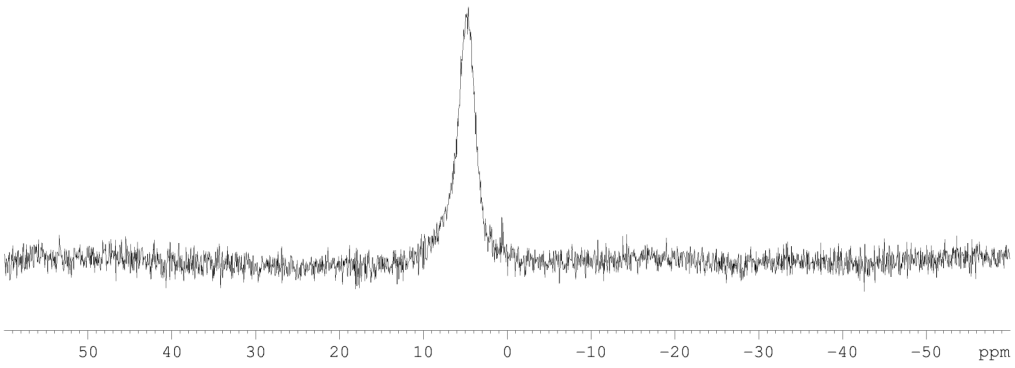


^{13}C NMR (125.8 MHz, DMSO-d_6) Spectrum of Potassium *N*-Cyclohexyl-3-(trifluoroborato)butanamide

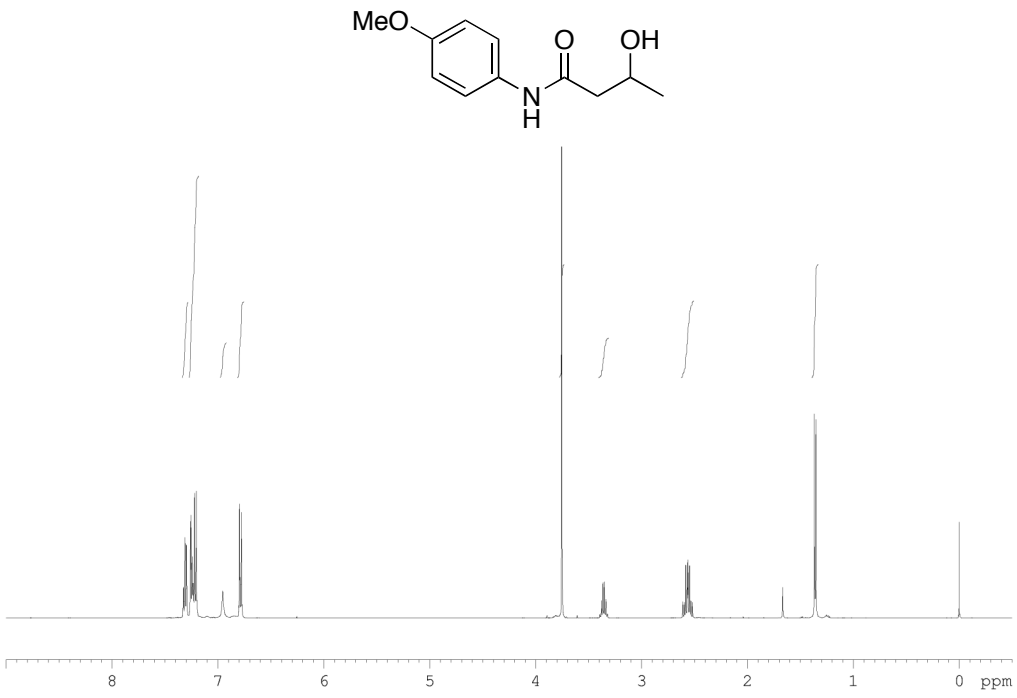




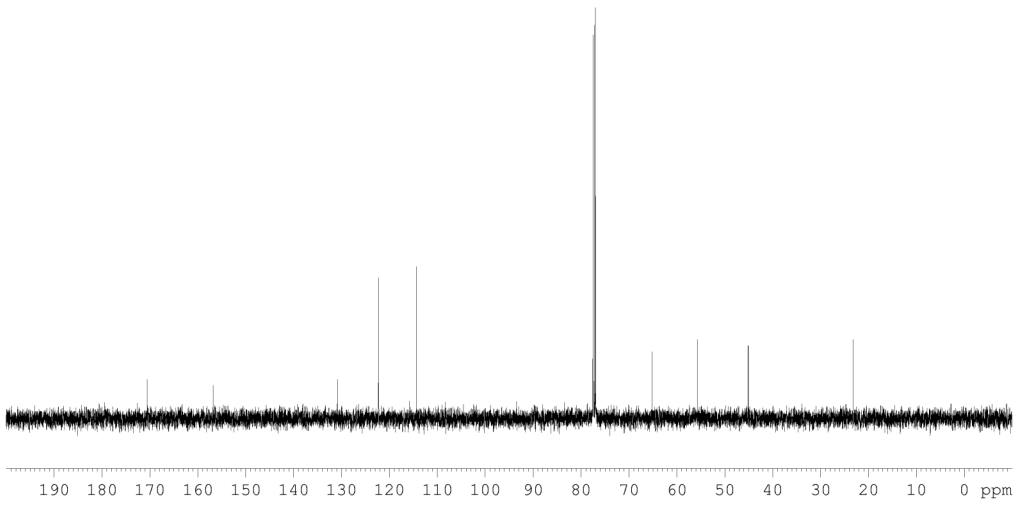
^{19}F NMR (470.8 MHz, DMSO-d_6) Spectrum of Potassium *N*-Cyclohexyl-3-(trifluoroborato)butanamide



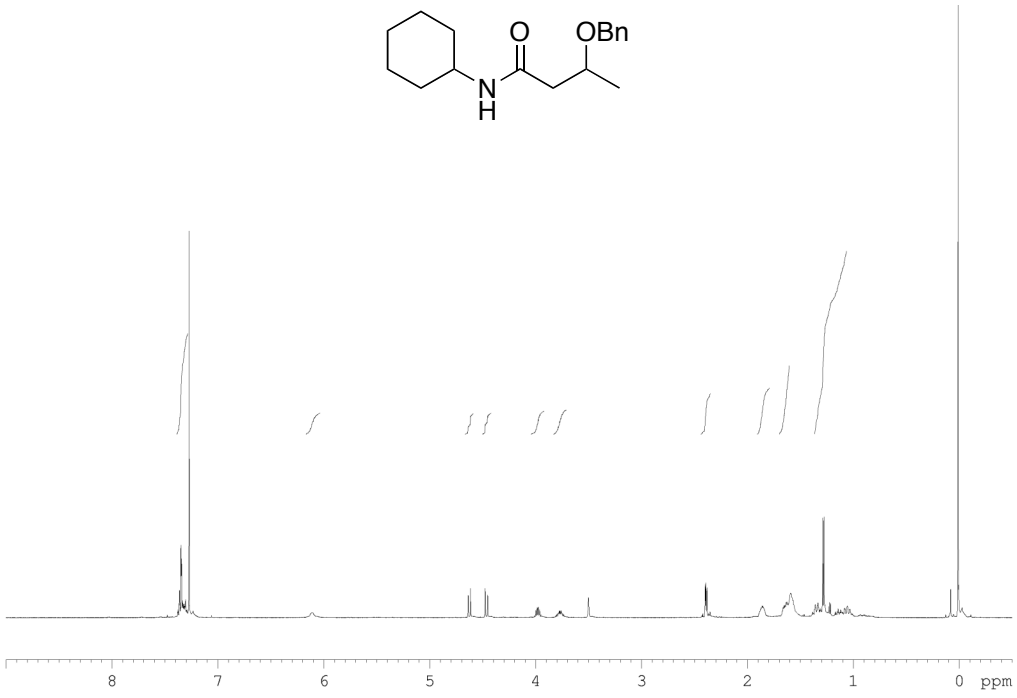
^{11}B NMR (128.4 MHz, DMSO-d_6) Spectrum of Potassium *N*-Cyclohexyl-3-(trifluoroborato)butanamide



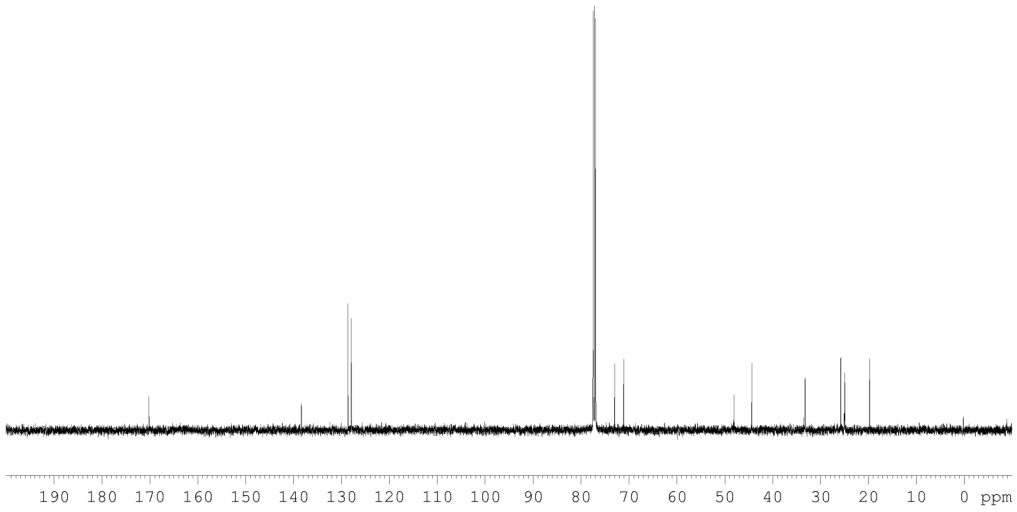
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-Hydroxy-*N*-(4-methoxyphenyl)butanamide



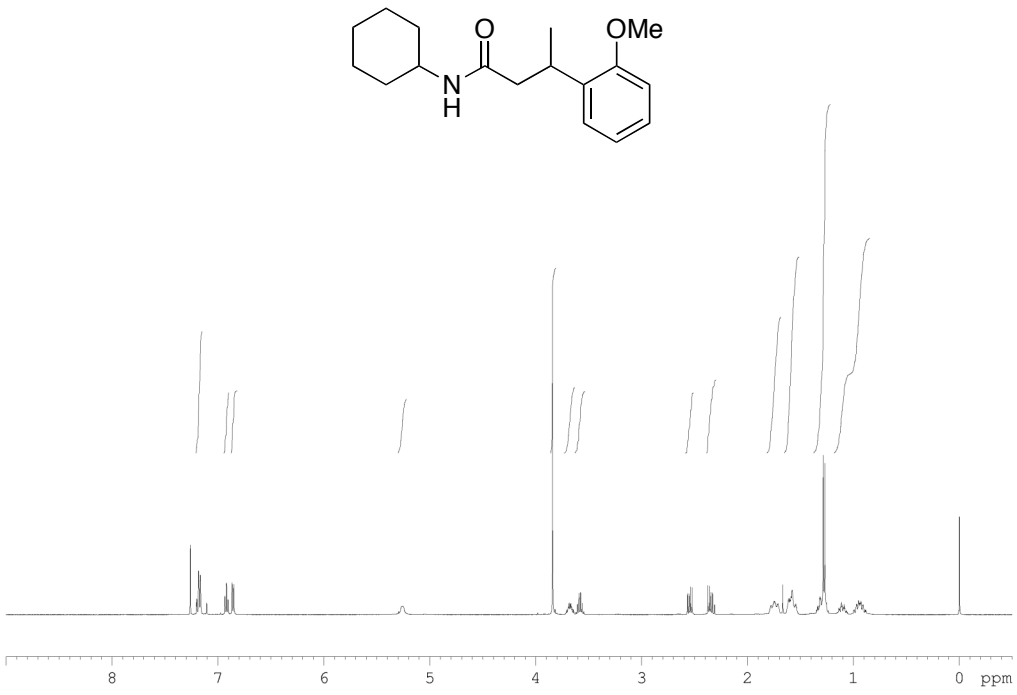
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-Hydroxy-*N*-(4-methoxyphenyl)butanamide



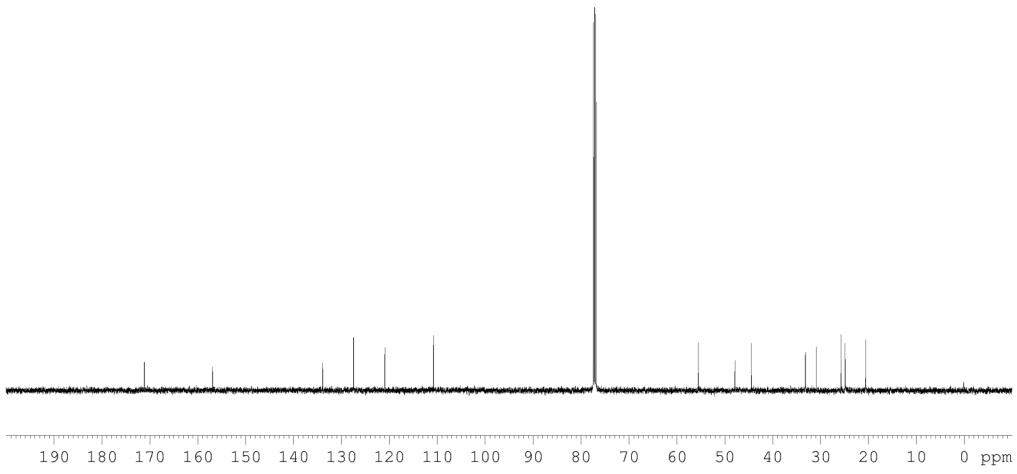
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(Benzyloxy)-*N*-cyclohexylbutanamide



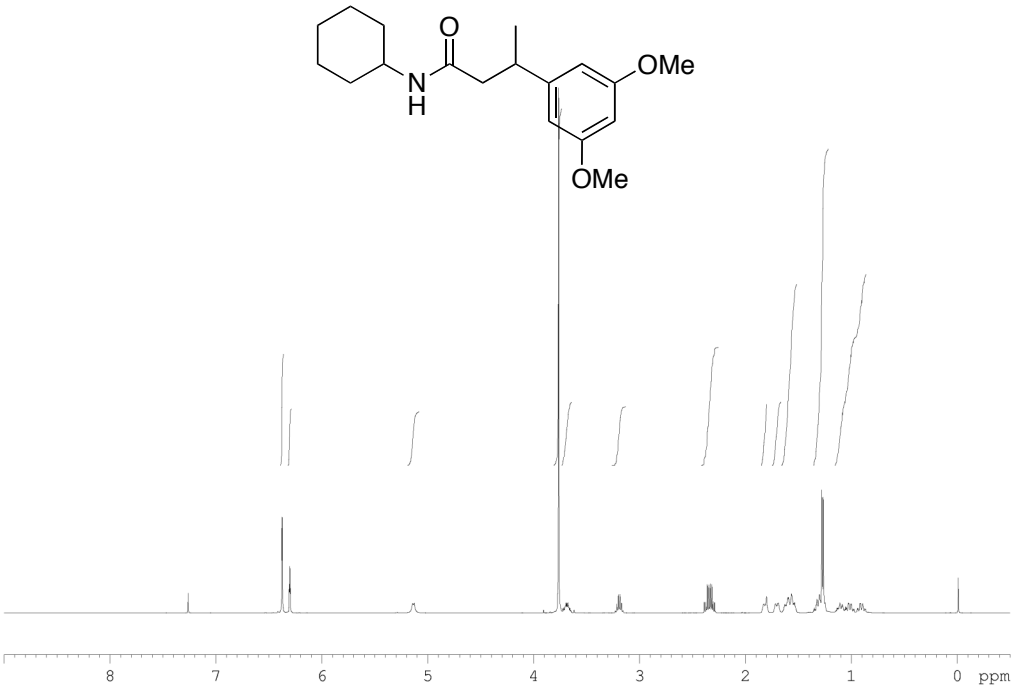
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(Benzyloxy)-*N*-cyclohexylbutanamide



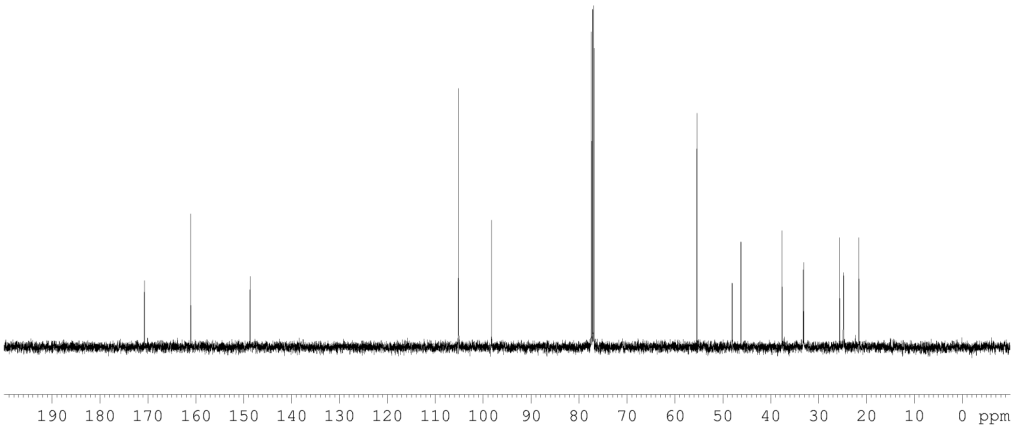
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(2-methoxyphenyl)butanamide



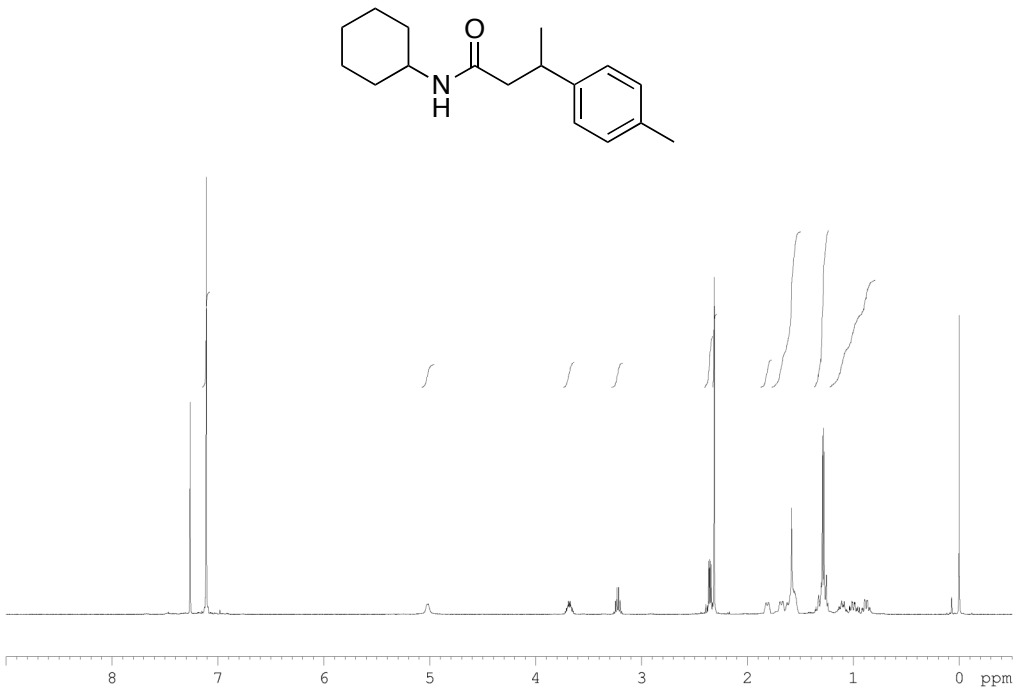
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(2-methoxyphenyl)butanamide



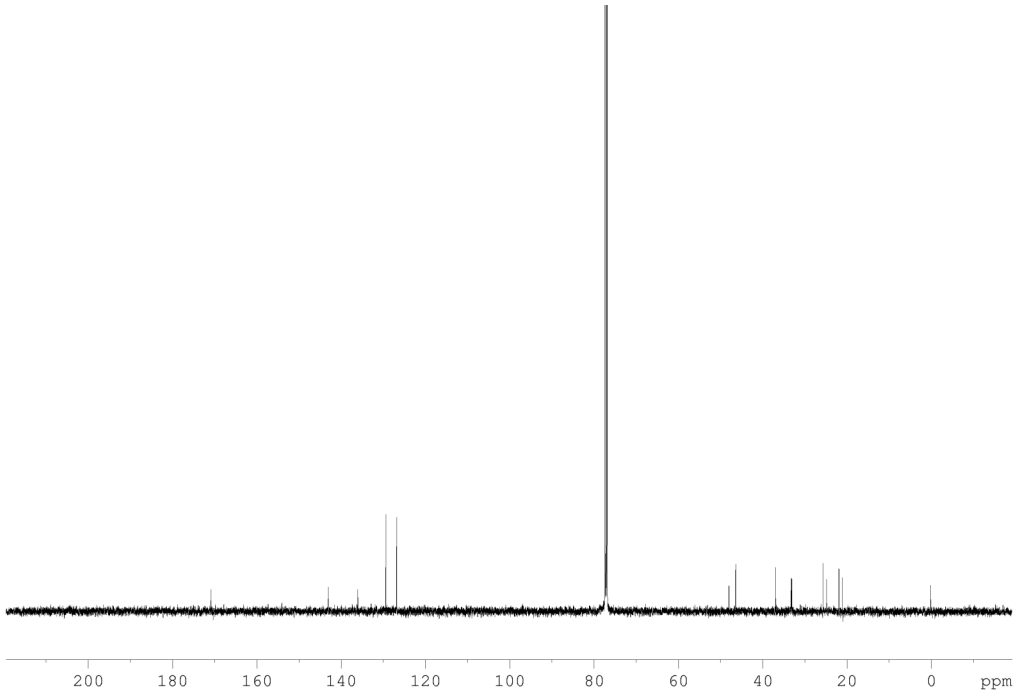
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(3,5-dimethoxyphenyl)butanamide



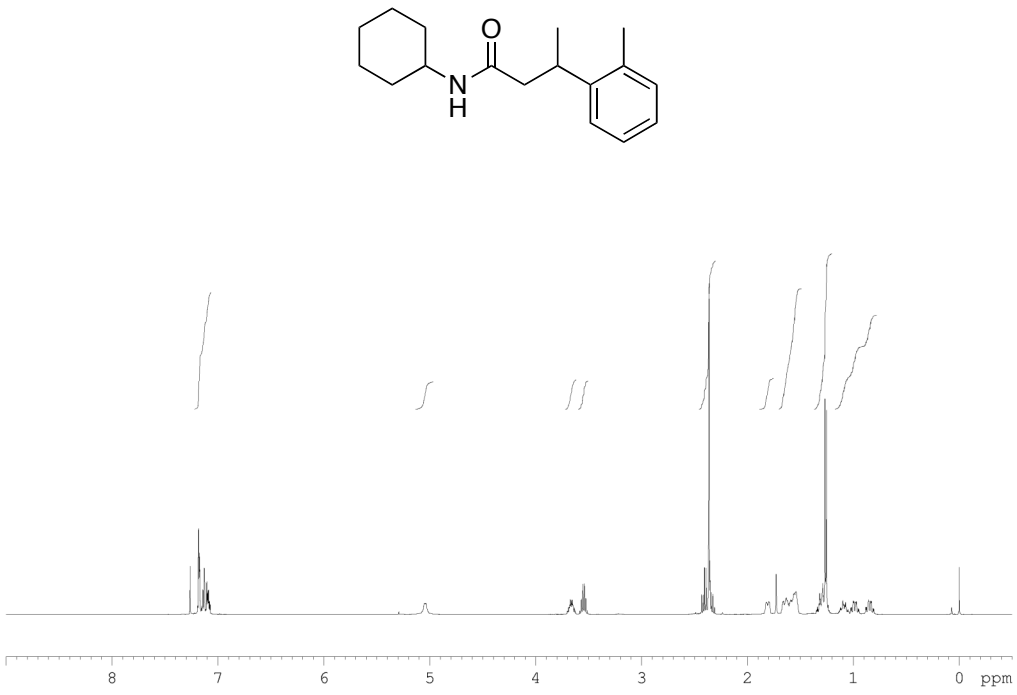
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(3,5-dimethoxyphenyl)butanamide



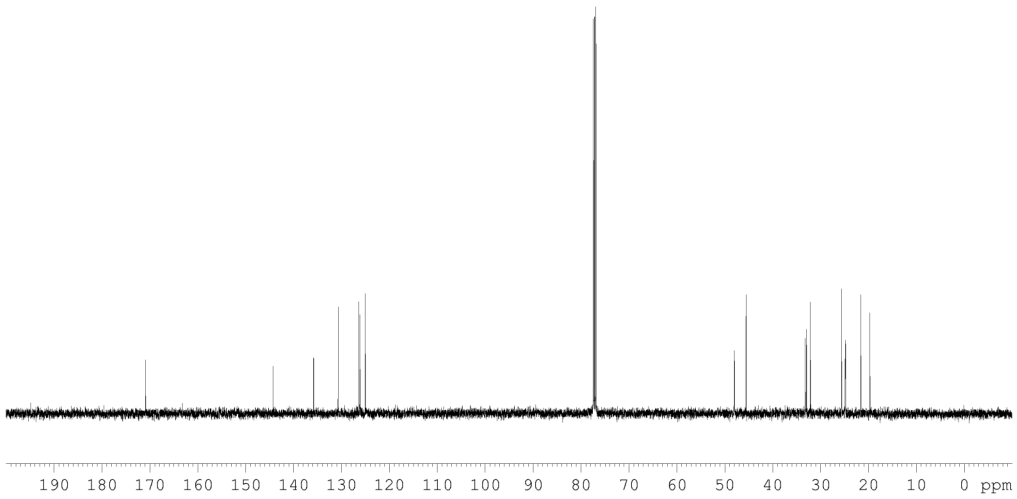
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(*p*-tolyl)butanamide



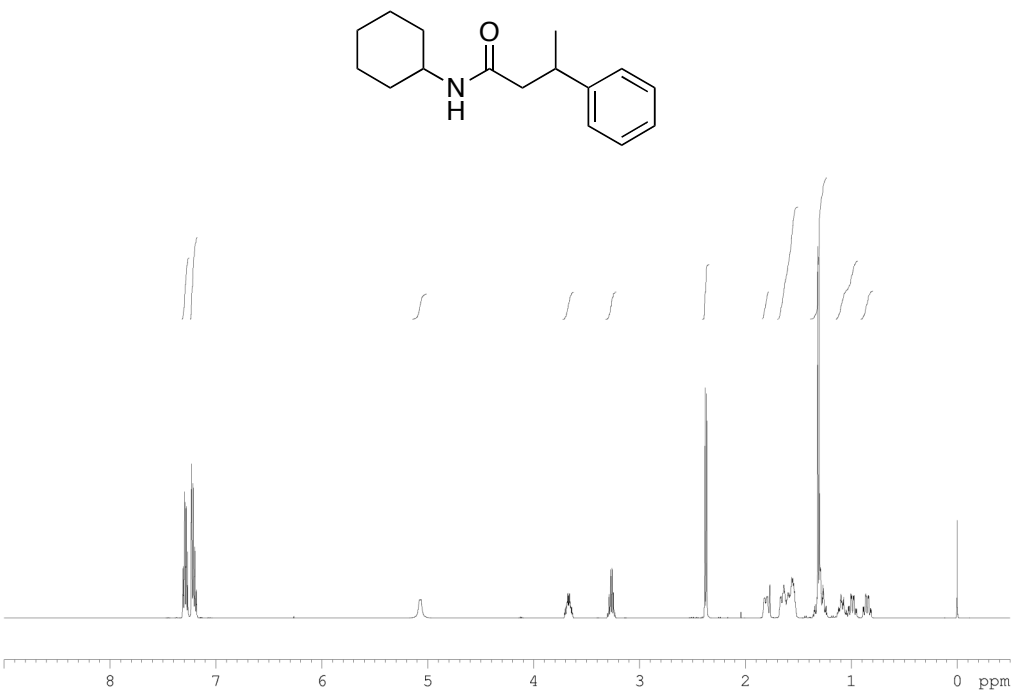
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(*p*-tolyl)butanamide



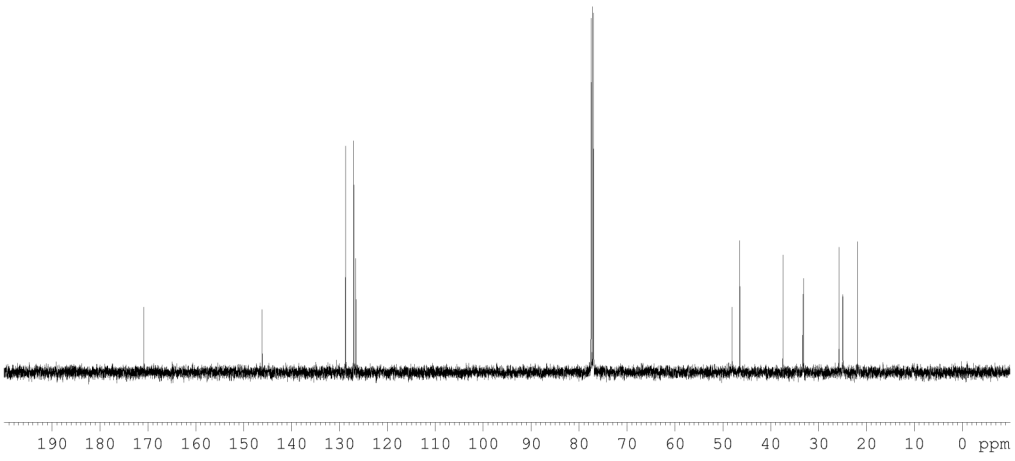
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(*o*-tolyl)butanamide



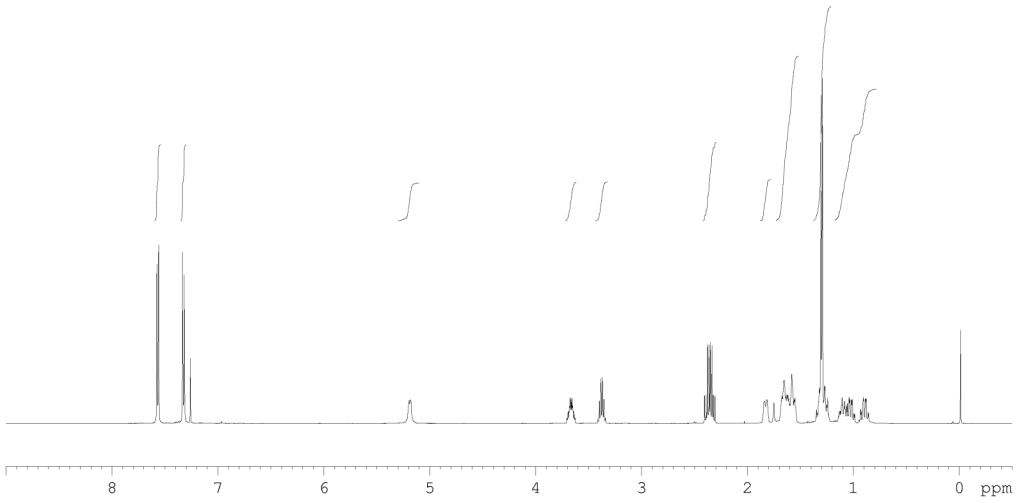
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(*o*-tolyl)butanamide



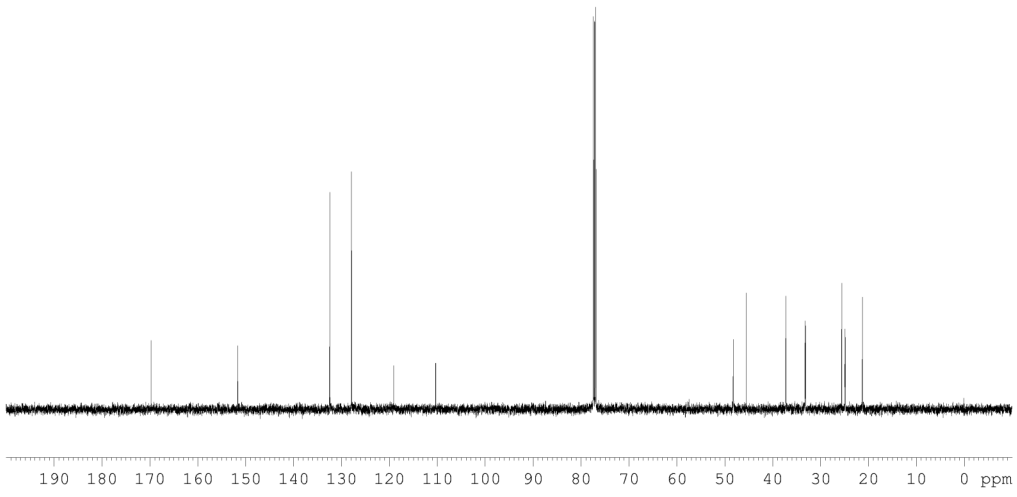
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-phenylbutanamide



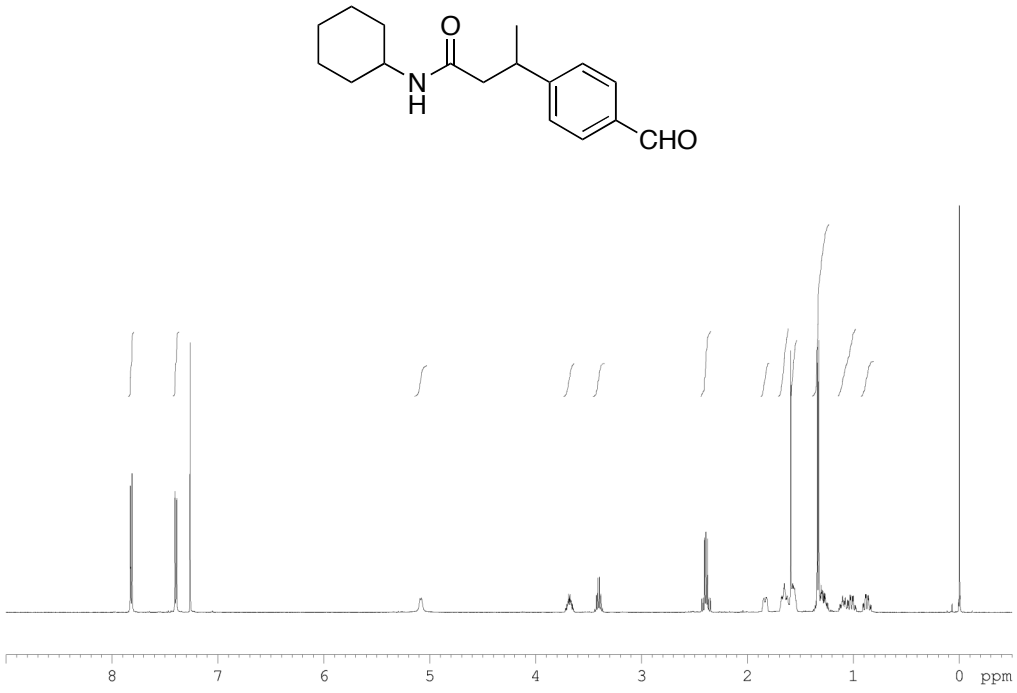
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-phenylbutanamide



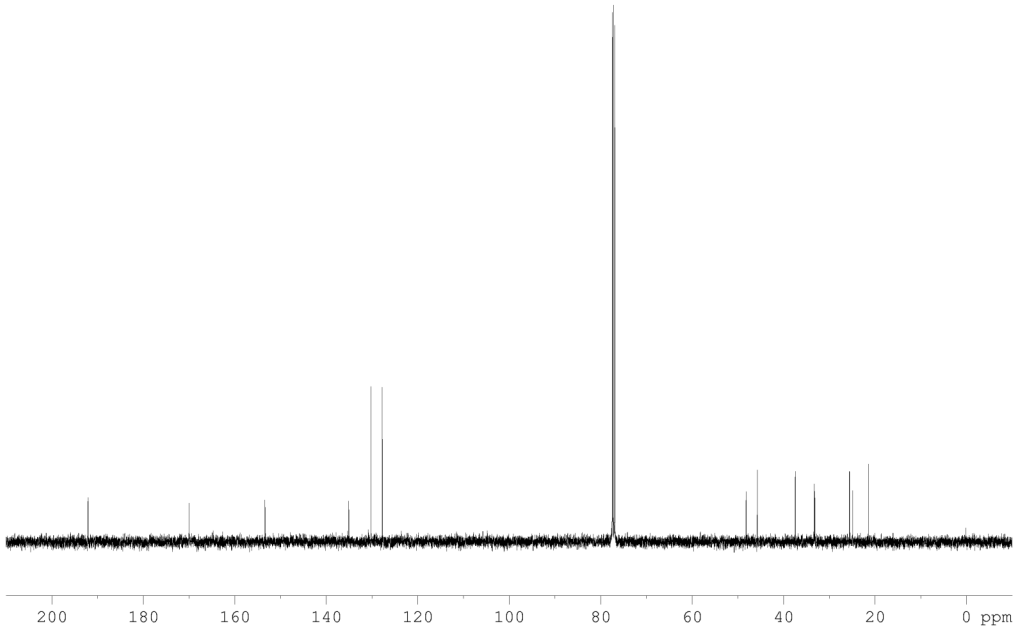
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-Cyanophenyl)-*N*-cyclohexylbutanamide



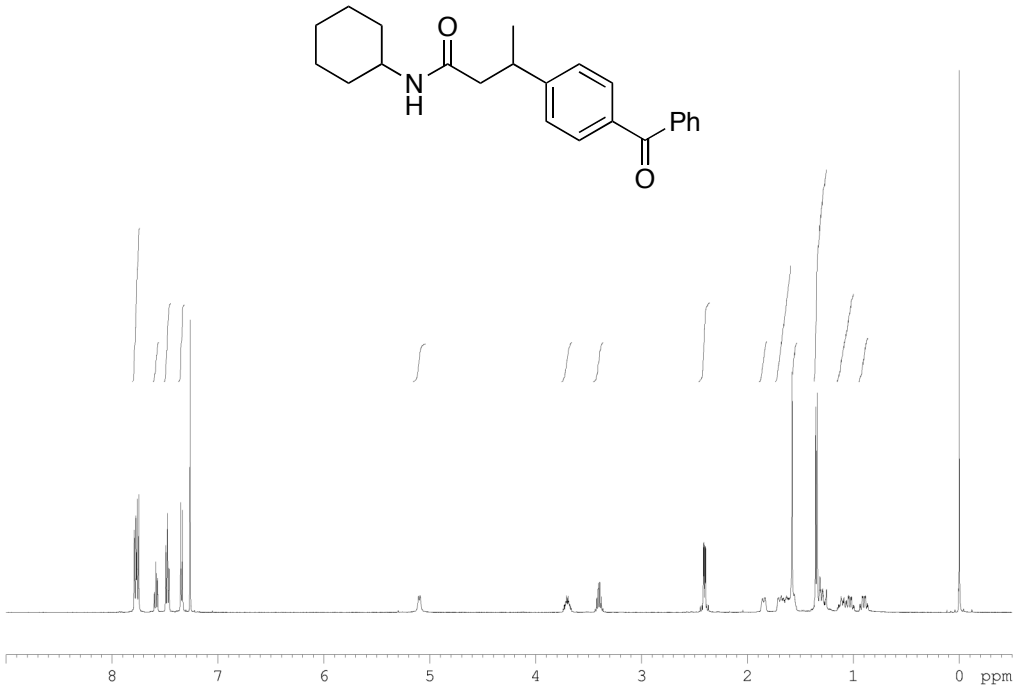
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-Cyanophenyl)-*N*-cyclohexylbutanamide



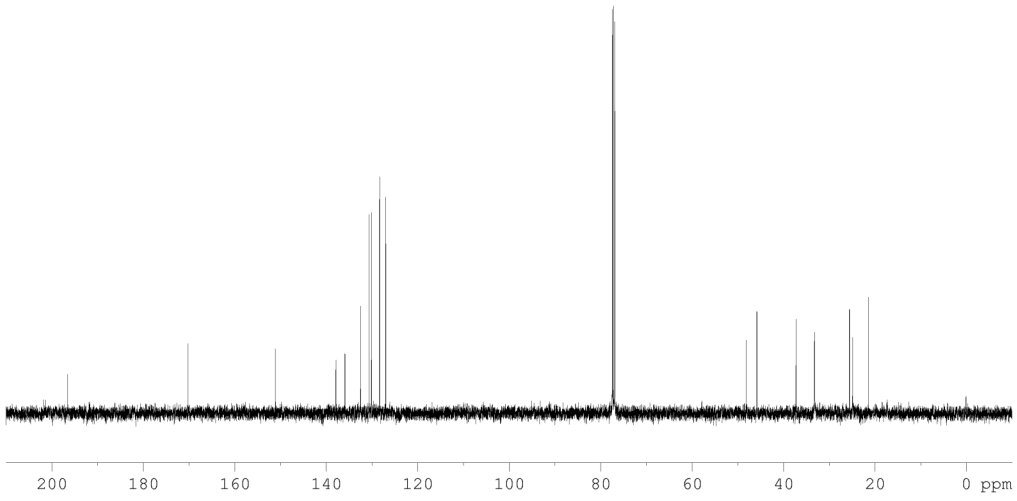
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-formylphenyl)butanamide



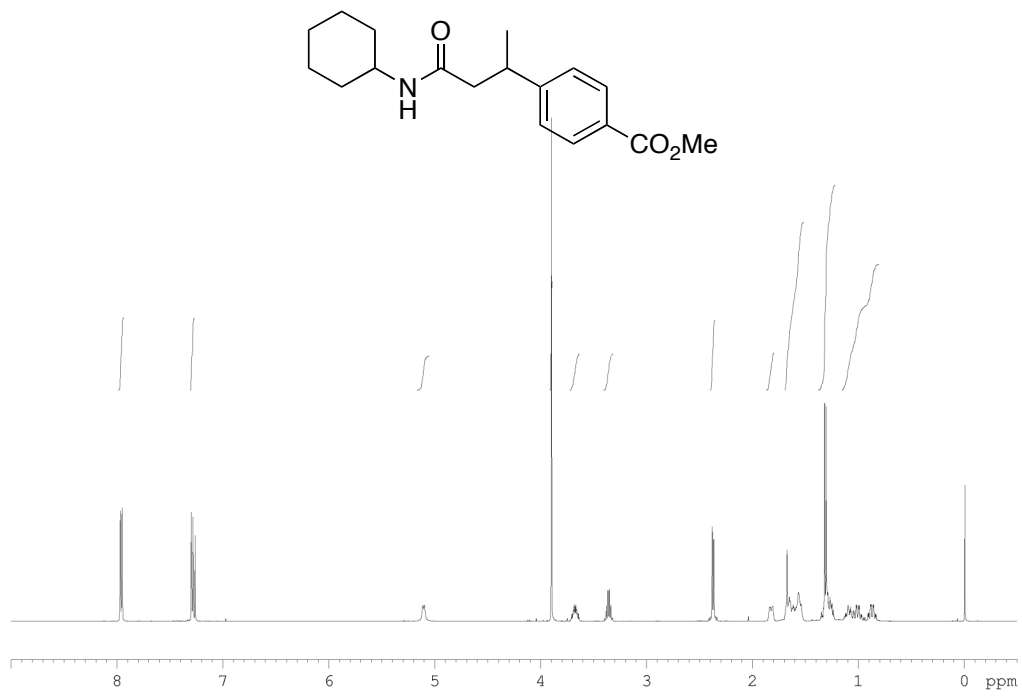
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-formylphenyl)butanamide



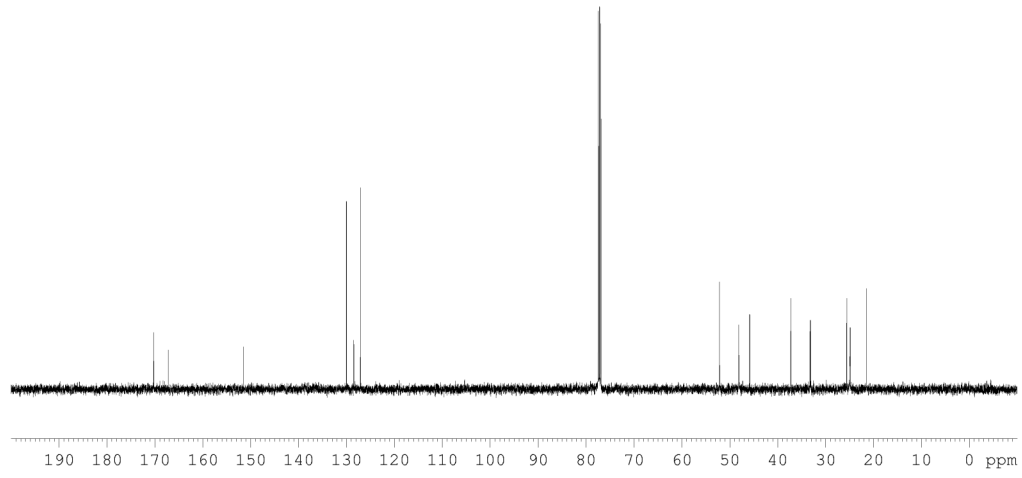
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-Benzoylphenyl)-*N*-cyclohexylbutanamide



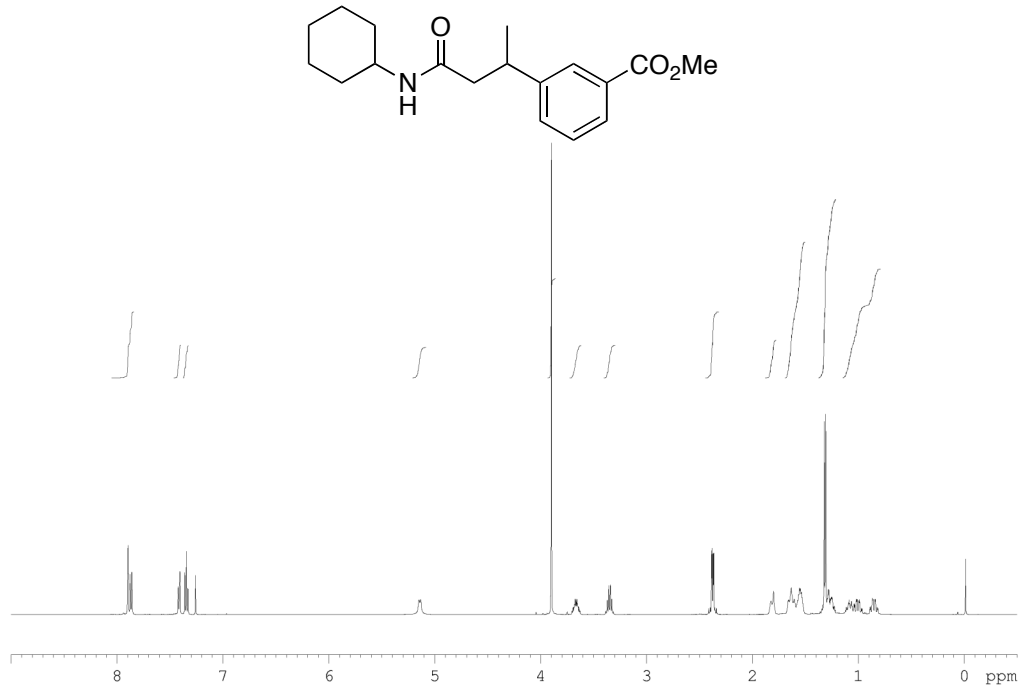
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-Benzoylphenyl)-*N*-cyclohexylbutanamide



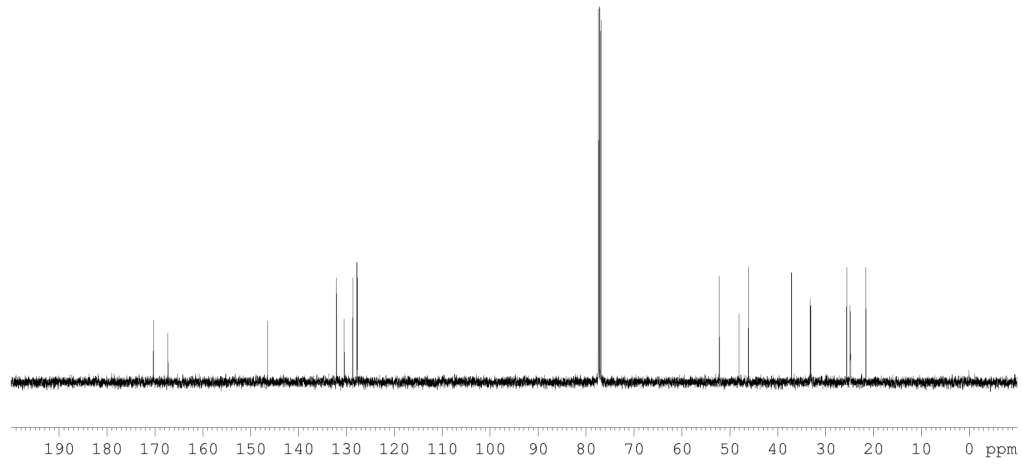
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Methyl 4-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate



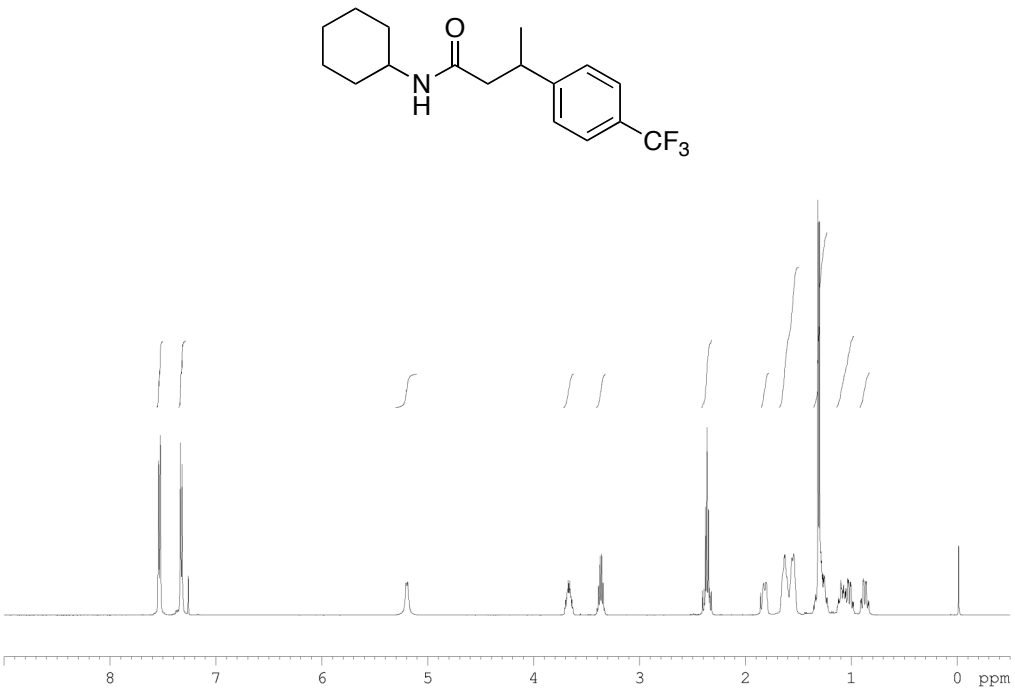
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of Methyl 4-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate



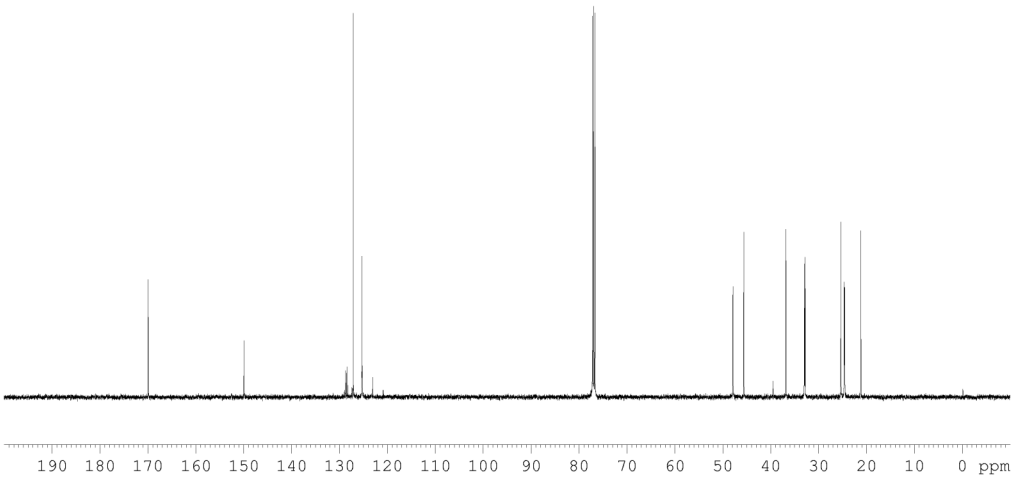
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Methyl 3-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate



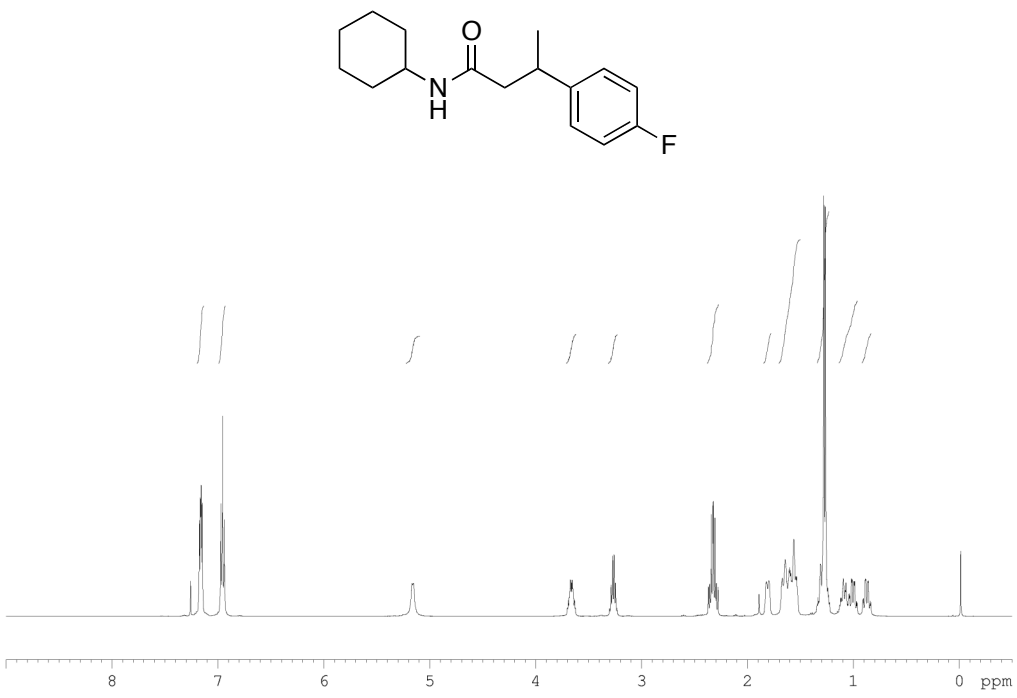
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of Methyl 3-(4-(Cyclohexylamino)-4-oxobutan-2-yl)benzoate



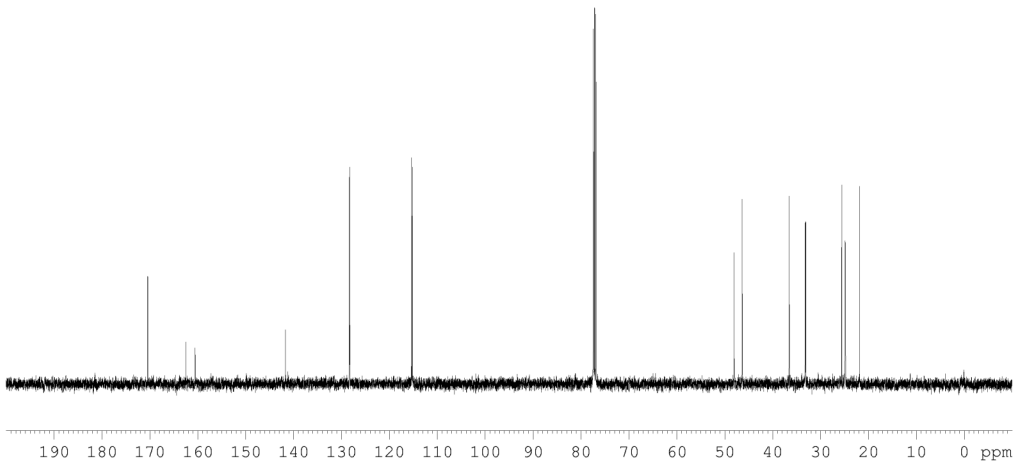
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-(trifluoromethyl)phenyl)butanamide



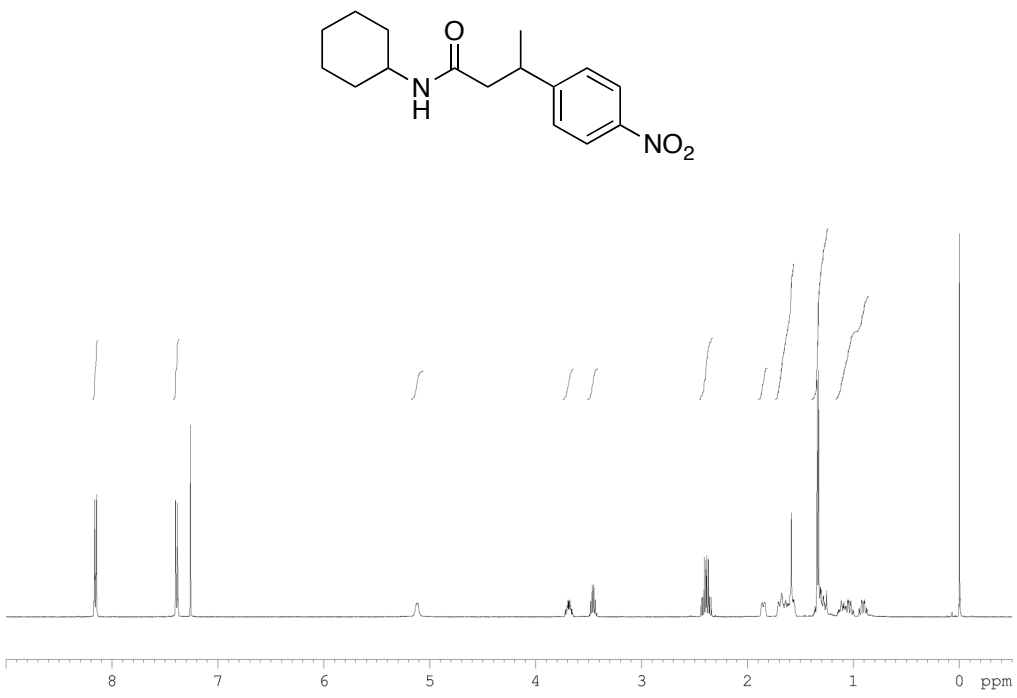
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-(trifluoromethyl)phenyl)butanamide



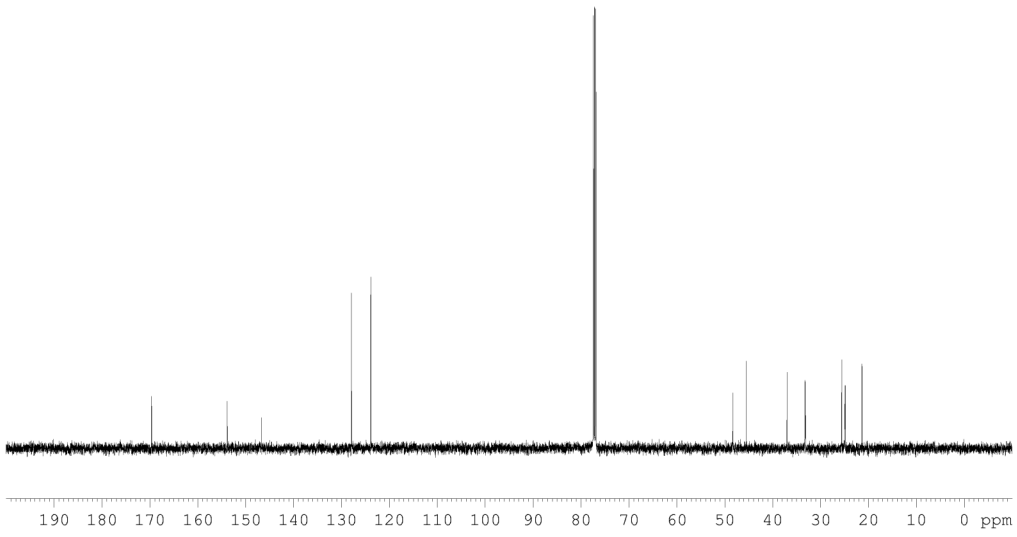
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-fluorophenyl)butanamide



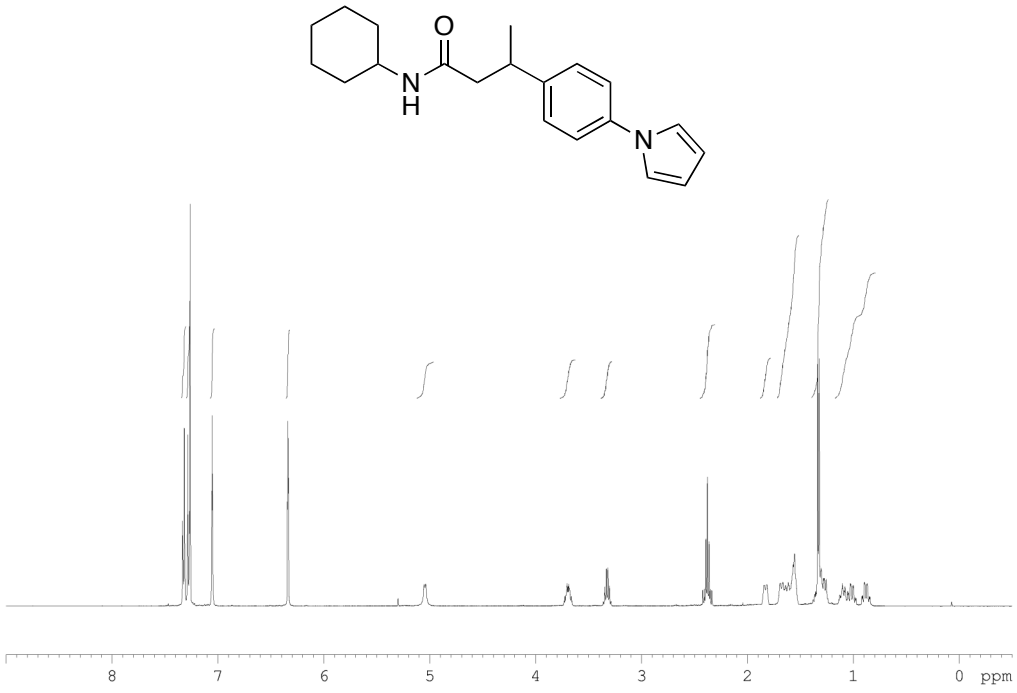
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-fluorophenyl)butanamide



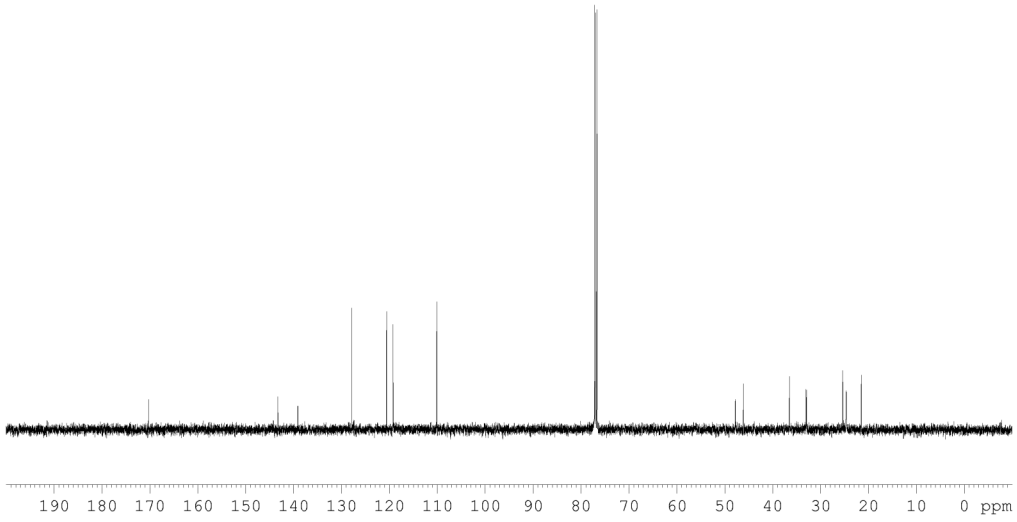
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-nitrophenyl)butanamide



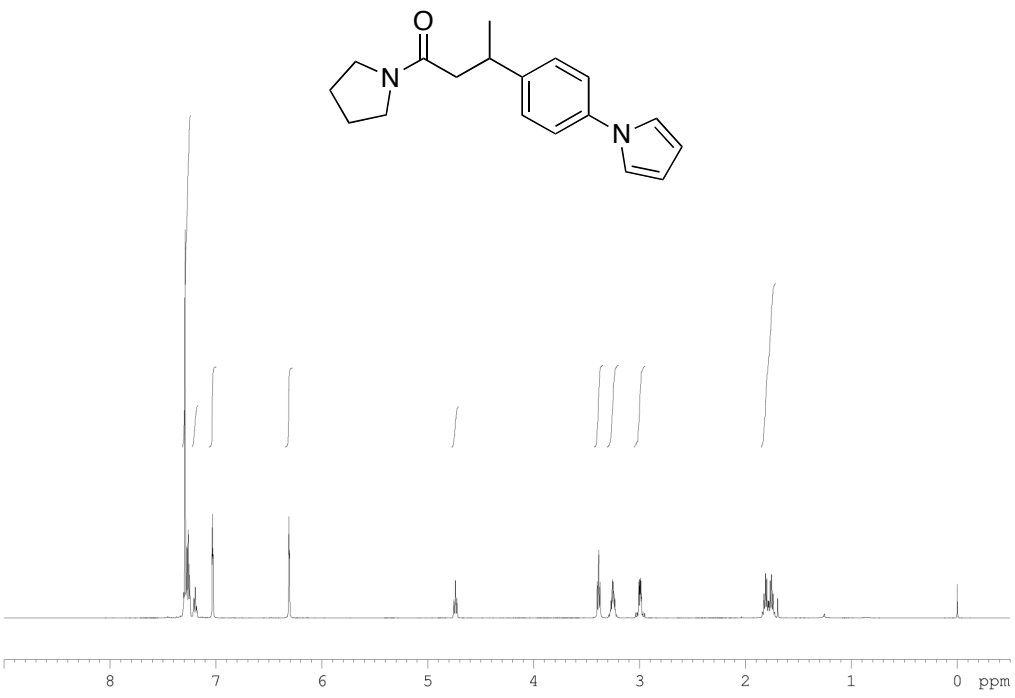
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-Cyclohexyl-3-(4-nitrophenyl)butanamide



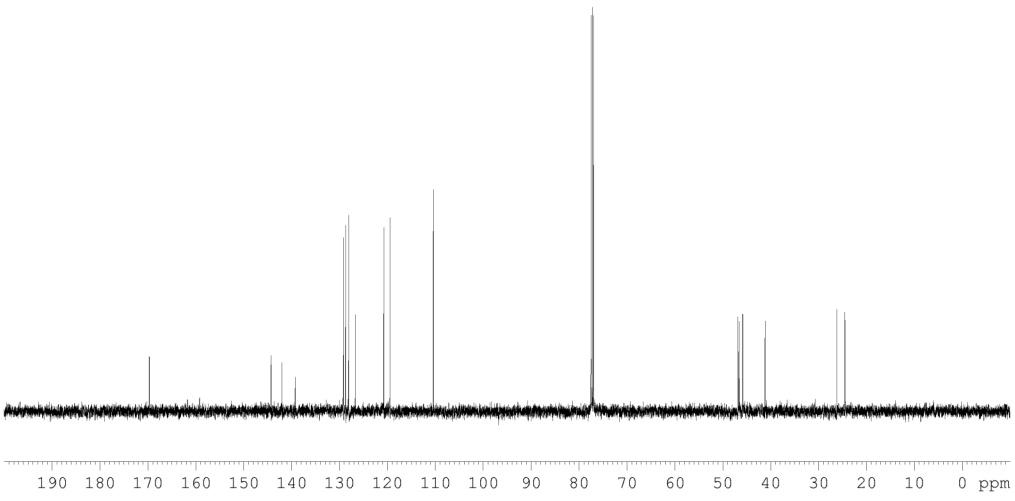
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-cyclohexylbutanamide



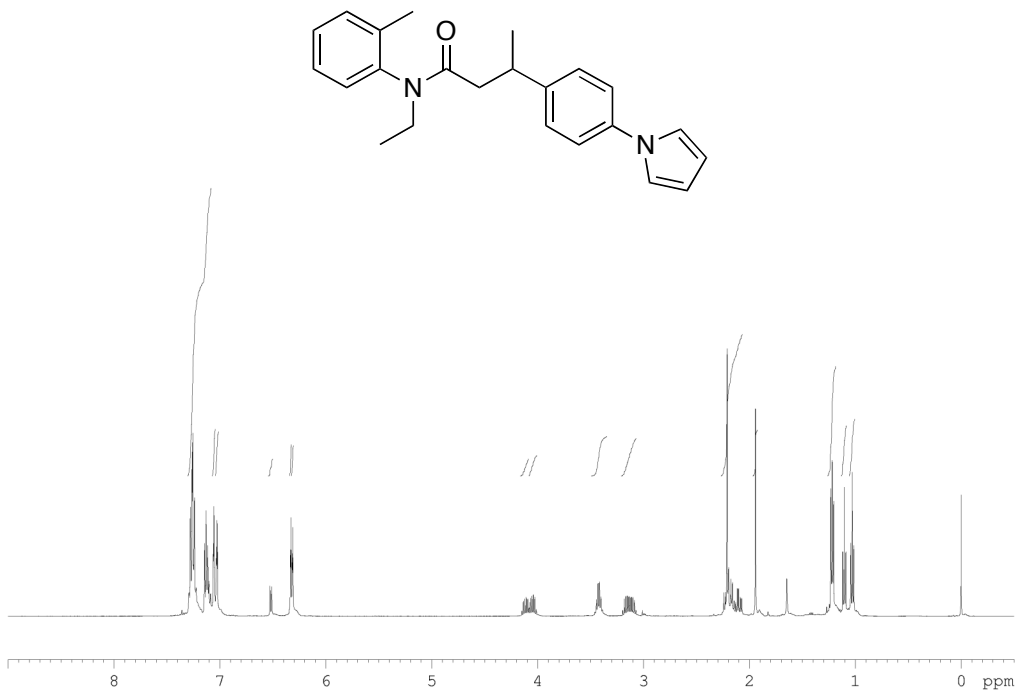
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-cyclohexylbutanamide



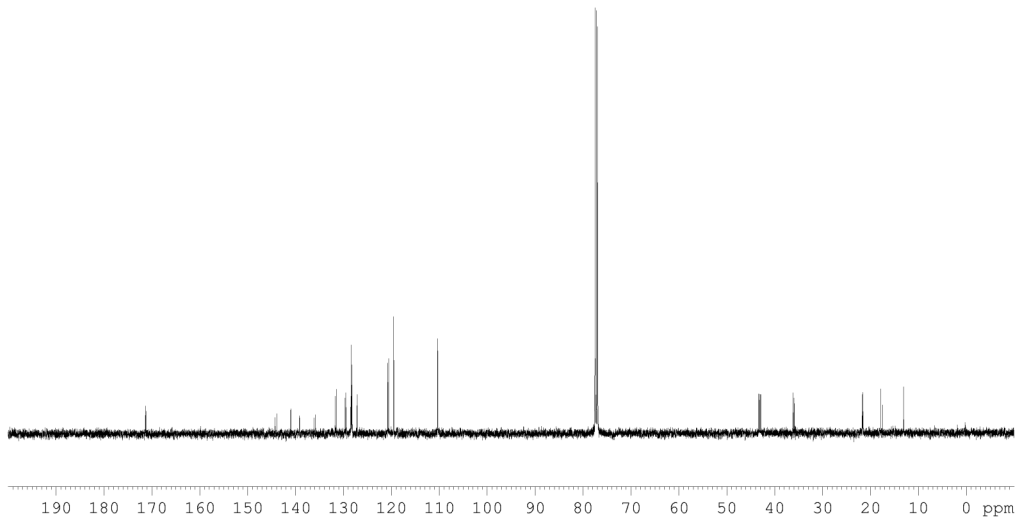
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(pyrrolidin-1-yl)butan-1-one



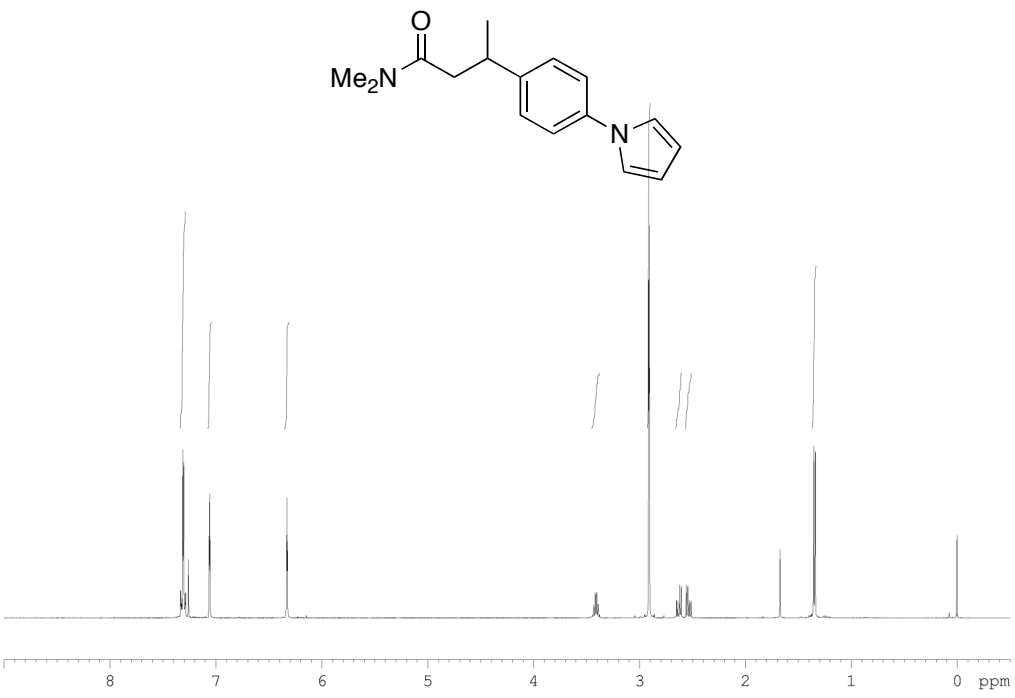
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(pyrrolidin-1-yl)butan-1-one



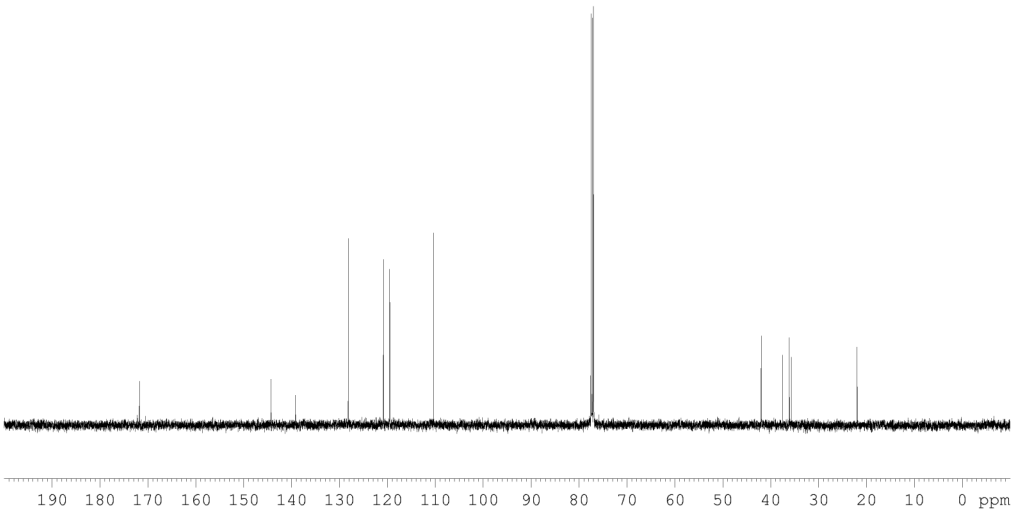
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-ethyl-*N*-(*o*-tolyl)butanamide



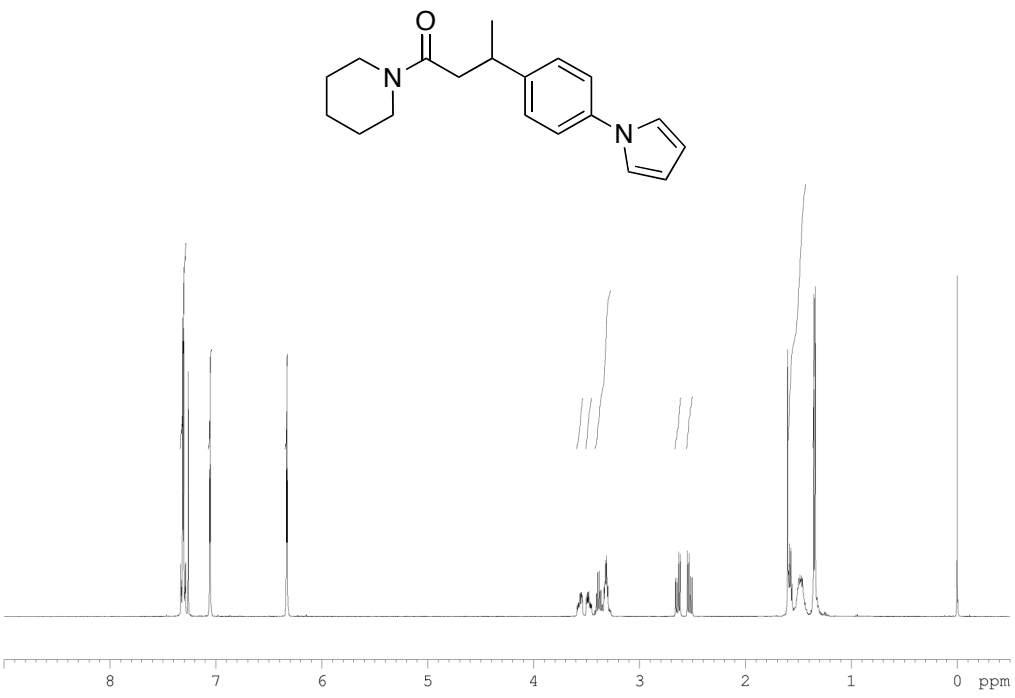
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-ethyl-*N*-(*o*-tolyl)butanamide



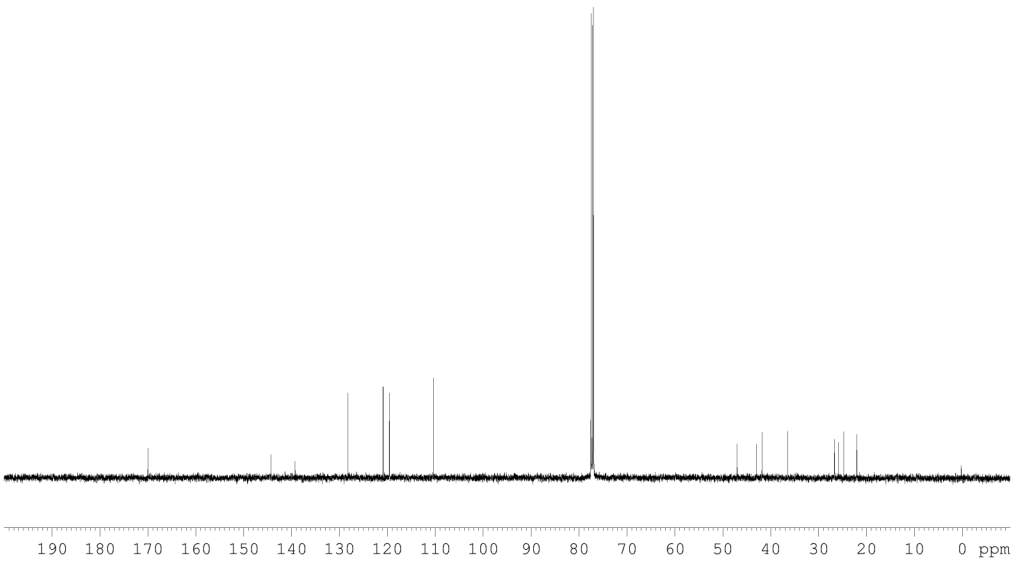
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dimethylbutanamide



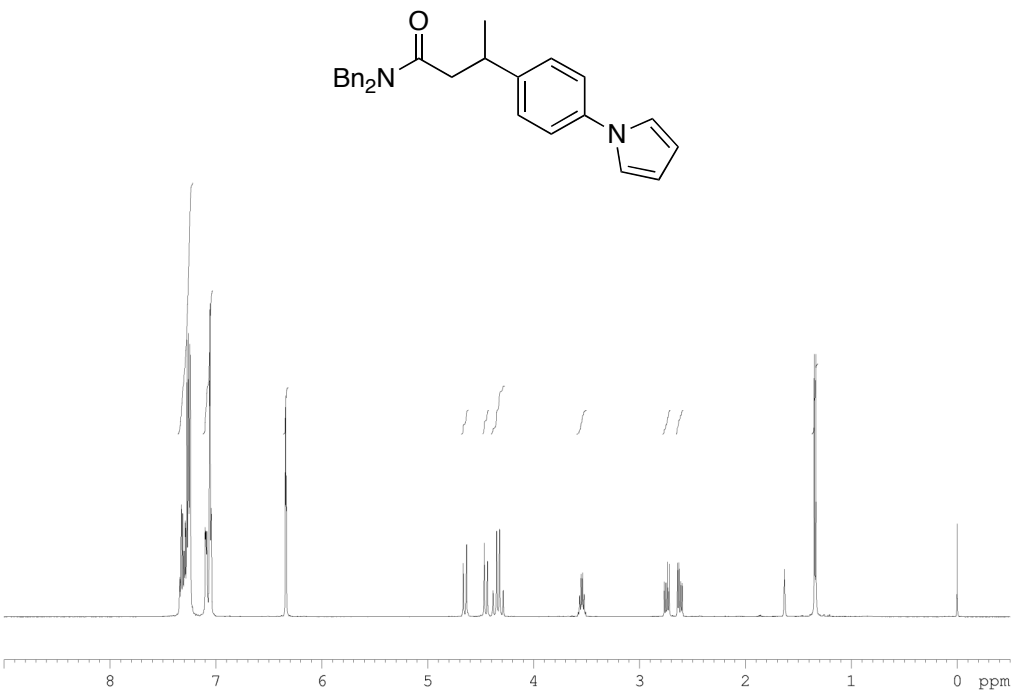
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dimethylbutanamide



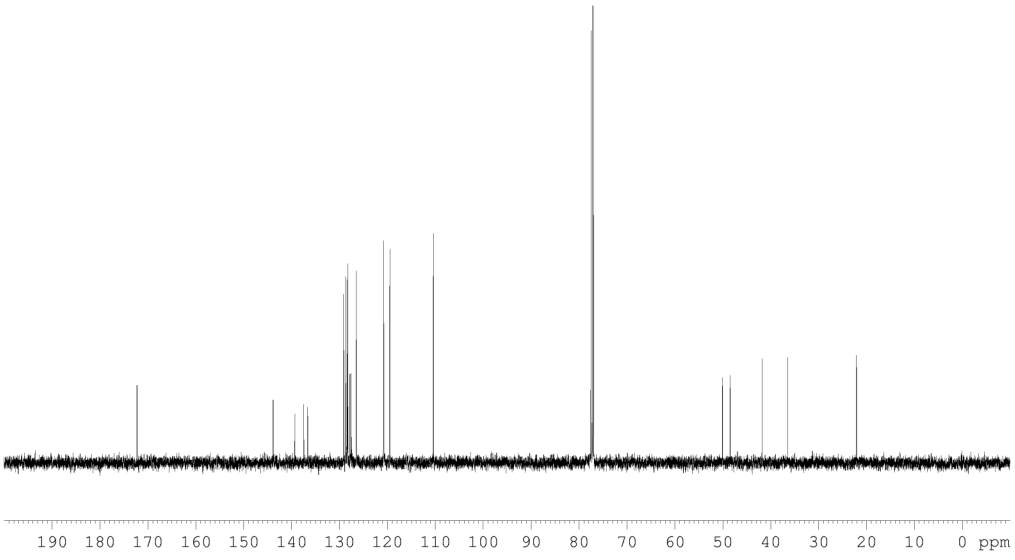
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(piperidin-1-yl)butan-1-one



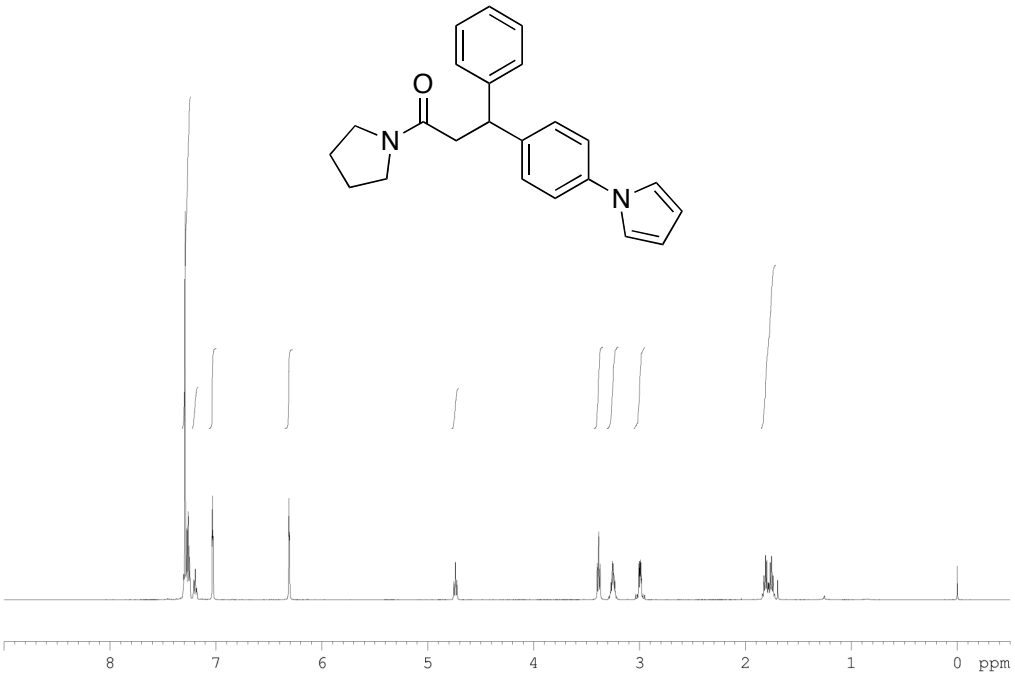
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-1-(piperidin-1-yl)butan-1-one



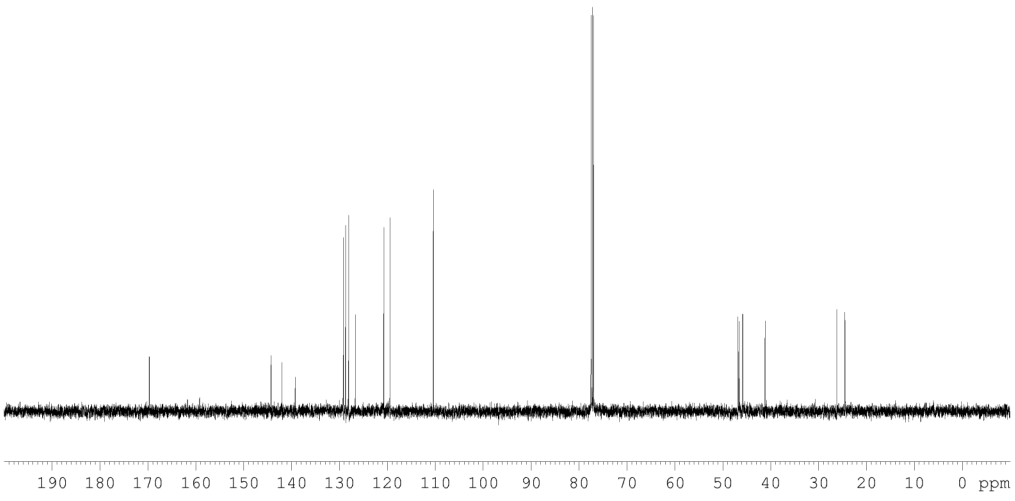
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dibenzylbutanamide



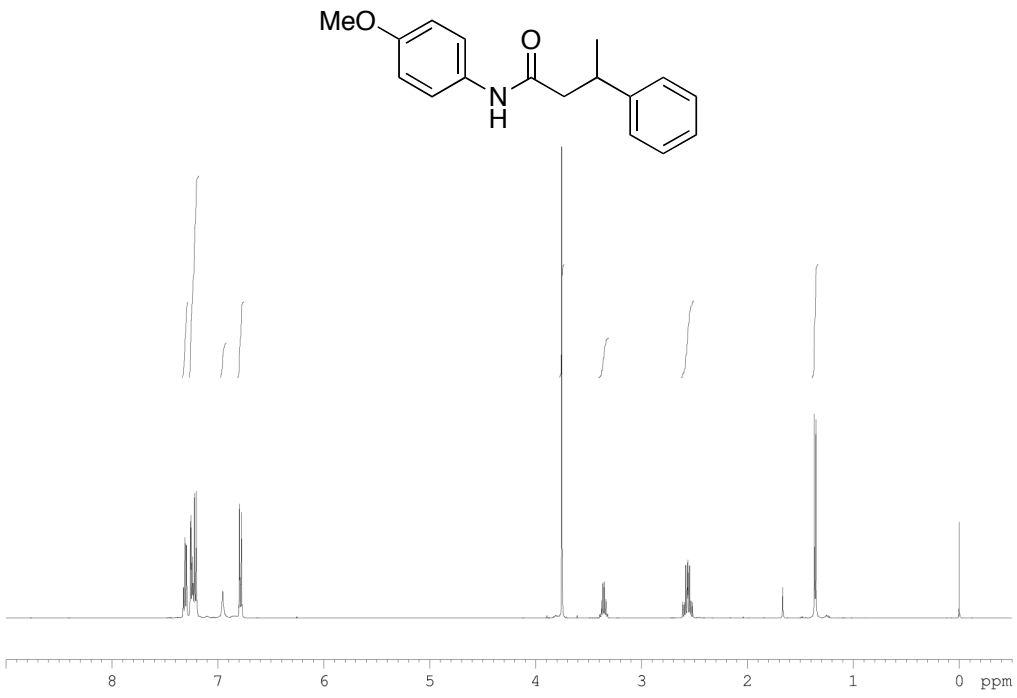
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*,*N*-dibenzylbutanamide



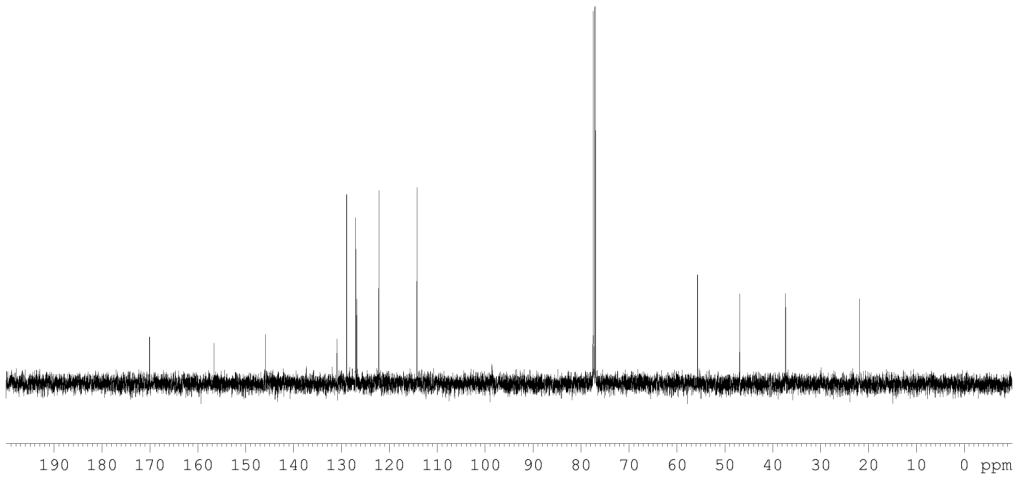
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-3-phenyl-1-(pyrrolidin-1-yl)propan-1-one



^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of 3-(4-(1*H*-Pyrrol-1-yl)phenyl)-3-phenyl-1-(pyrrolidin-1-yl)propan-1-one



^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of *N*-(4-Methoxyphenyl)-3-phenylbutanamide



^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of *N*-(4-Methoxyphenyl)-3-phenylbutanamide