Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Cobalt-Catalyzed Aminocarbonylation of Alkyl Tosylates: Stereospecific Synthesis of Amides

*Brendon T. Sargent and Erik J. Alexanian**

anie_201905173_sm_miscellaneous_information.pdf

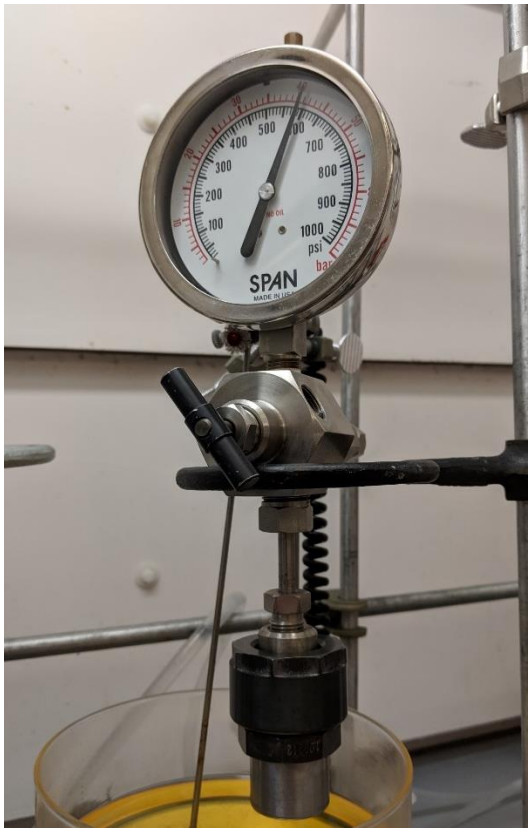
Supporting Information

Table of Contents

General Methods and Materials

Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker Avance III 600 CryoProbe (^{1}H NMR 600 MHz and ^{13}C at 151 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CHCl_3$ at 7.285 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{1}H NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectrometry samples were analyzed with a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer. Samples were introduced via a microelectrospray at a flow rate of 10 µL/min in methanol. Xcalibur (ThermoFisher, Breman, Germany) was used to analyze the data. HPLC analysis was performed on a Shimadzu SPD-M20A photodiode array (PDA) system equipped with Daicel Chiralpak IE, IF, IG, and OJ-H (4.6 mm x 250 mm x 5 µm) columns using a flow rate of 1 mL/min, unless otherwise indicated, with hexanes and isopropanol as eluent. Chiral supercritical fluid chromatography analysis was performed on a Waters Acquity UPC2 instrument at 35 °C equipped with Phenomenex Lux Cellulose-1, Cellulose-2, and Cellulose-3 (4.6 mm x 150 mm x 5 µm) columns using a flow rate of 2 mL/min with hexanes and isopropanol or methanol as eluent.

Analytical thin layer chromatography (TLC) was performed on SiliaPlate 250µm thick silica gel purchased from Silicycle. Visualization was accomplished with short-wave UV light (254 nm), iodine, Hanessian's stain, or ethanolic acidic p-anisaldehyde solution followed by heating when necessary. Purification of the reaction products was carried out by flash chromatography using Siliaflash P60 silica gel (40-63µm) purchased from Silicycle. Carbon monoxide, Research Purity 99.99% (part number CM R200) was purchased from Airgas. Tetrahydrofuran, diethyl ether, *N,N*-dimethylformamide, acetonitrile, and dichloromethane were dried by passage through a column of neutral alumina under nitrogen prior to use. *t*-Amyl alcohol was sparged with argon before storage over 3 Å molecular sieves in an argon filed glovebox. $Co_2(CO)_{10}$ was purchased from Strem Chemicals, stored in a glovebox at -30 °C, and used as received. $K[Co(CO)_4]$ was synthesized according to Ellis and co-workers.[1] All liquid amine nucleophiles and 2,2,6,6-tetramethylpiperidine were distilled prior to being stored in a glovebox. All other reagents were obtained from commercial sources and used without further purification, unless otherwise noted. In addition, all reactions were carried out under an atmosphere of dry argon in flame or oven-dried glassware with magnetic stirring. The pressure reactors used were purchased from Parr Instrument Company.



Parr reactor for aminocarbonylation

List of Abbreviations

DCM = dichloromethane
DIAD = diisopropyl azodicarboxylate
DMAP = 4-dimethylaminopyridine
DMF = *N,N*-dimethylformamide
EtOAc = ethyl acetate
MeCN = acetonitrile
Pin = pinacol
TBAF = tetrabutylammonium fluoride
TBS = *tert*-butyldimethylsilyl
TEA = triethylamine
THF = tetrahydrofuran
TMP = 2,2,6,6-tetramethylpiperidine
TsCl = 4-toluenesulfonyl chloride

Substrate Preparation

General Procedure A: Tosylation of Secondary Alcohols.

Tosylates were synthesized using a modified procedure from Tanabe, et. al.[2] To a 0 ºC ice bath cooled solution of TsCl (1.5 equiv) and trimethylamine hydrochloride (0.1 equiv) in DCM (1 M with respect to the alcohol) was added TEA (2.5 equiv) dropwise. To this solution was added a solution of the alcohol in DCM (1 M), the solution was then stirred for 1 hour at 0 ºC, monitoring by TLC. The reaction was quenched by addition of *N,N*-dimethyldiaminopropane (2.0 equiv) and stirred for 20 additional minutes while warming to room temperature. The reaction mixture was poured into water and separated. The organic layer was washed sequentially with 1 M HCl, a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

General Procedure B: Mitsunobu of Phenols

This procedure was adapted from Lepore and He.[3] The corresponding alcohol (1.05 equiv), substituted phenol (1 equiv), and triphenylphosphine (1.05 equiv) were dissolved in toluene (0.25 M) and sonicated for 5 minutes. DIAD (1.05 equiv) was added dropwise over the course of 3 minutes and the reaction was sonicated for 1 hour until complete consumption of the phenol, monitored by TLC. The solution was concentrated under reduced pressure and the crude product was purified by flash chromatography.

General Procedure C: Acylation of Primary Alcohols

To a mixture of primary alcohol (1 equiv), DMAP (0.2 equiv), and TEA (2 equiv) in DCM (0.4 M) was added the respective acid chloride (1.1 equiv, 1 M in DCM) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 minutes, then warmed to room temperature and stirred 2-16 hours. Upon completion of the reaction, the mixture was quenched with a saturated solution of $NaHCO_3$ and extracted 3 times with DCM. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography.

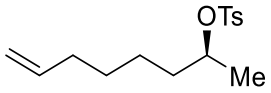
General Procedure D: TBS Deprotection

To a solution of TBS protected alcohol (1 equiv) in THF (0.5 M) was added 1 M TBAF in THF (2 equiv) and heated to 55 °C ON. After completion of reaction, the mixture was cooled to room temperature, diluted with water, and extracted twice with EtOAc. The combined organic layers were washed twice with water, once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography.

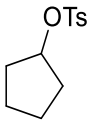
General Procedure E: TBS Deprotection

This procedure was adapted from Martinez-Solorio and Jennings.[4] To a solution of TBS protected alcohol (1 equiv) in MeOH (0.1 M) was added pyridinium perbromide (5 mol %) at 0 °C. The solution was allowed to stir overnight, warming to room temperature. After completion of reaction, the solution was quenched with a saturated aqueous solution of $NaHCO_3$, and extracted three times with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography.

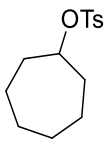
Tosylates:



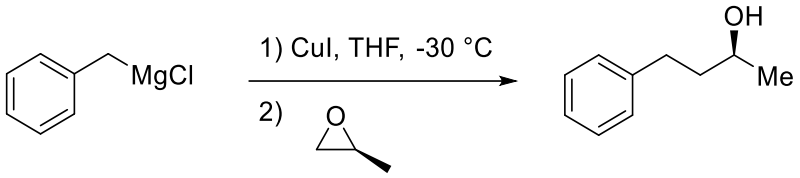
(*S*)-oct-7-en-2-yl 4-methylbenzenesulfonate (SI-1) was prepared in 97% *ee* according to a published procedure; physical and spectral data were in accordance with literature data.[5]



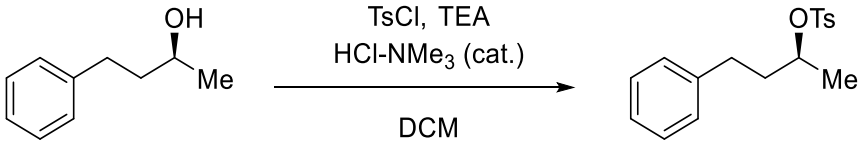
Cyclopentyl 4-methylbenzenesulfonate (SI-2) was prepared according to a published procedure; physical and spectral data were in accordance with literature data.[6]



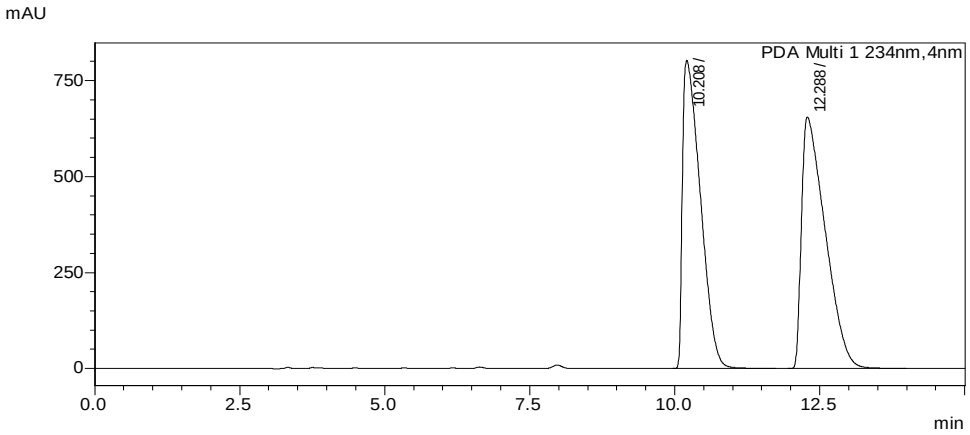
Cycloheptyl 4-methylbenzenesulfonate (SI-3) was prepared according to a published procedure; physical and spectral data were in accordance with literature data.[6]



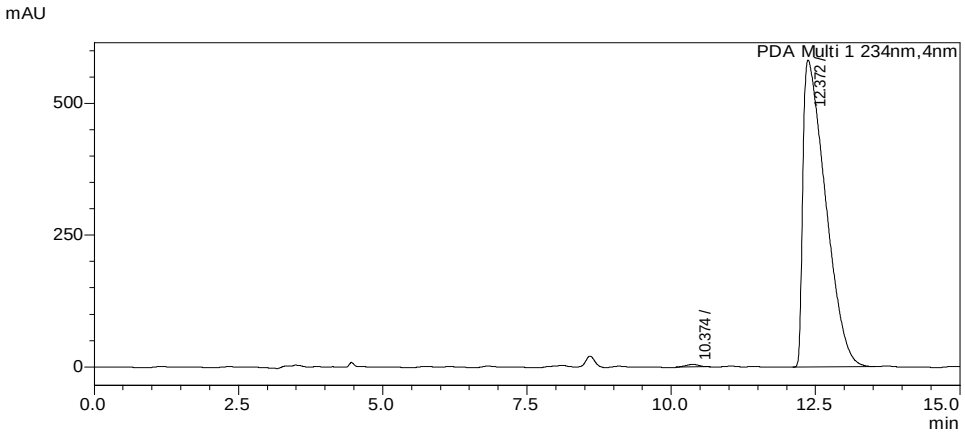
(*S*)-4-phenylbutan-2-yl 4-methylbenzenesulfonate (SI-4) was prepared using a modified literature procedure.[5] Benzylmagnesium chloride (13 mL, 26 mmol, 2.0 M THF) was added dropwise to a -30 °C suspension of CuI (4.9 g, 26 mmol) in THF (38 mL) and stirred for 5 minutes. (*S*)-Propylene oxide (1.2 mL, 17 mmol) was added and the reaction was warmed to 0 °C and stirred for an additional 2.5 hours. The reaction was then quenched with an aqueous saturated solution of NH_4Cl and warmed to room temperature. Ether was added and the mixture was filtered through Celite before the layers were separated. The organic layer was washed sequentially with a saturated aqueous solution of $NaHCO_3$, then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography in 20% EtOAc/hexanes to provide 2.5 g (98%) of **SI-4** as a pale yellow oil. Physical and spectral data were in accordance with literature data.[7]



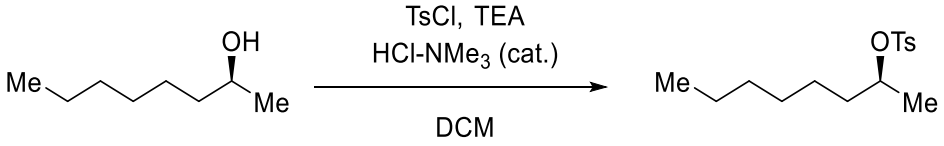
(*S*)-4-phenylbutan-2-yl 4-methylbenzenesulfonate (1) was synthesized by tosylating **SI-4** (2.0 g, 13 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 3.7 g (91%) of tosylate **1** as a colorless oil. Physical and spectral data were in accordance with literature data.[5] **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 99%.



Peak#	Ret. Time	Area	Area%
1	10.208	17241843	48.127
2	12.288	18584150	51.873
Total		35825993	100

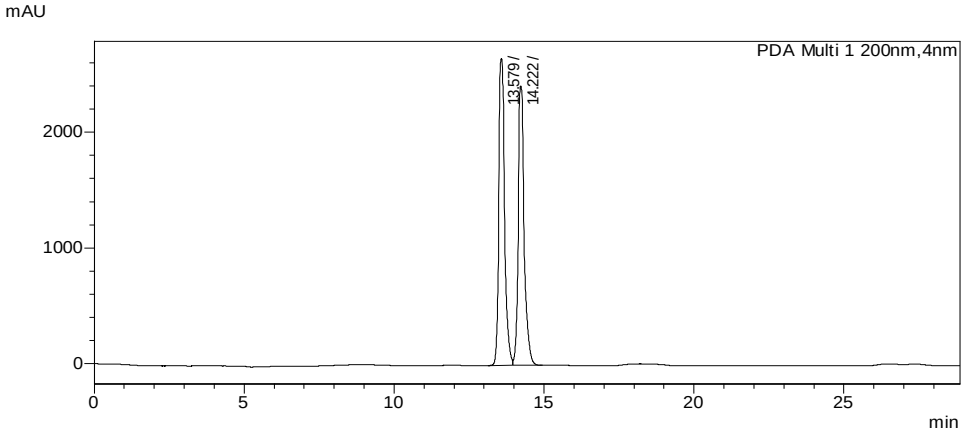


Peak#	Ret. Time	Area	Area%
1	10.374	83943	0.526
2	12.372	15862476	99.474
Total		15946419	100

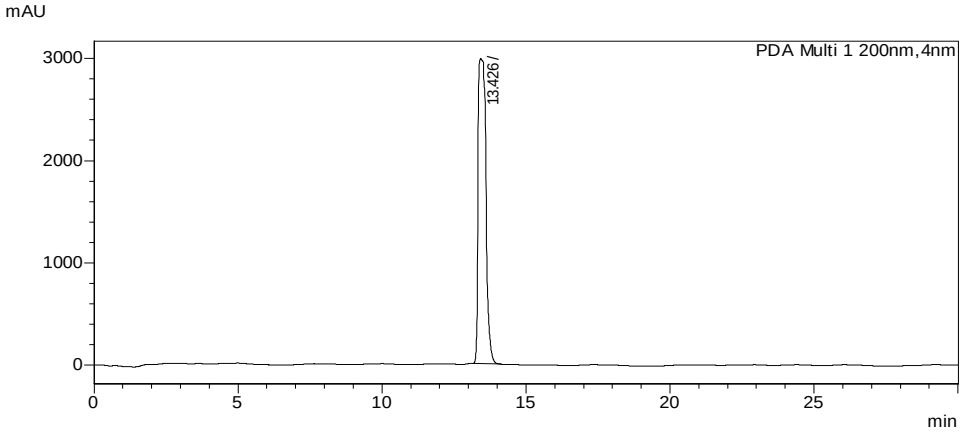


(*S*)-octan-2-yl 4-methylbenzenesulfonate (SI-5) was synthesized by tosylating (*S*)-2-octanol (1.6 g, 12 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 3.2 g (94%) of

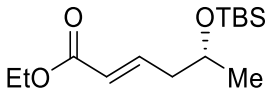
tosylate **SI-5** as a colorless oil. Physical and spectral data were in accordance with literature data.[6] **Chiral HPLC** (Chiralpak IE, 95:5 hexanes:isopropanol): *ee* = >99%.



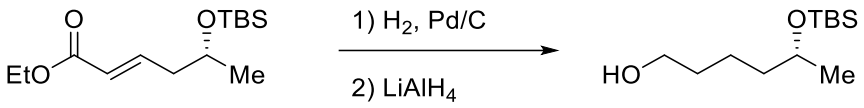
Peak#	Ret. Time	Area	Area%
1	13.579	35789238	51.792
2	14.222	33312280	48.208
Total		69101518	100



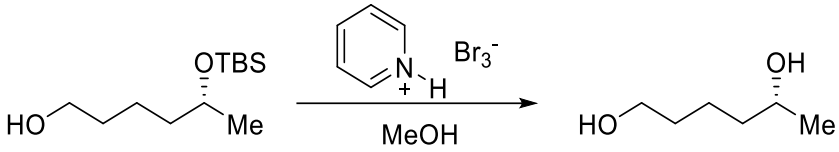
Peak#	Ret. Time	Area	Area%
1	13.426	56057566	100
Total		56057566	100



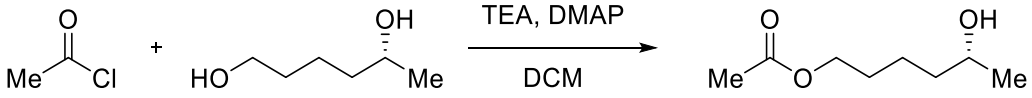
Ethyl (*R*,*E*)-5-((tert-butyldimethylsilyl)oxy)hex-2-enoate (SI-6) was prepared according to a published procedure; physical and spectral data were in accordance with literature data.[8]



(*R*)-5-((tert-butyldimethylsilyl)oxy)hexan-1-ol (SI-7) was synthesized by the 2 step sequence shown above. 10% w/w palladium on carbon (5.4 g) was suspended in EtOH and **SI-6** (27 g, 99 mmol) was added. The flask was evacuated and back-filled with hydrogen. The reaction was allowed to stir overnight at room temperature under a balloon of hydrogen. The reaction was filtered through Celite and concentrated under reduced pressure to provide 23.7 g of the crude product (87%). A solution of the crude product (23.7 g, 86.3 mmol) in Et_2O (50 mL) was added dropwise to a suspension of $LiAlH_4$ (3.28 g, 86.3 mmol) in Et_2O (125 mL) at 0 ºC. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was cooled to 0 ºC and quenched by sequential dropwise addition of water (3.3 mL), 3 M NaOH (3.3 mL), and water (9.9 mL). The slurry was warmed to room temperature, dried with $MgSO_4$, filtered through a pad of Celite, and concentrated under reduced pressure. Crude product **SI-7** (19.5 g, 97%) was used without further purification. Physical and spectral data were in accordance with literature data.[8]

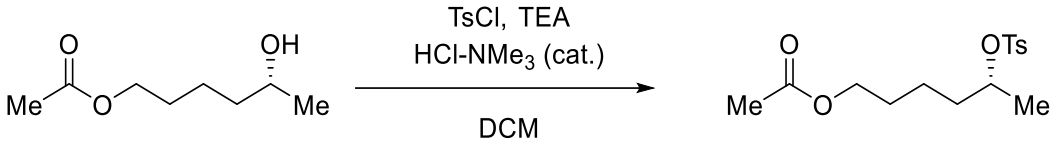


(*R*)-hexane-1,5-diol (SI-8) was synthesized by subjecting **SI-7** (2.0 g, 8.6 mmol) to General Procedure E. The crude product was purified via flash chromatography using a gradient of 75-100% EtOAc/hexanes to provide 0.76 g (75%) of **SI-8** as a colorless oil. Physical and spectral data were in accordance with literature data.[9]

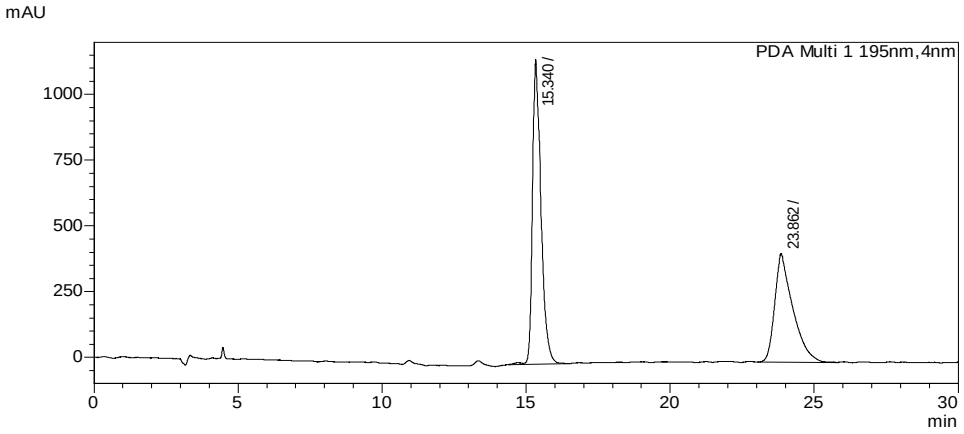


(*R*)-5-hydroxyhexyl acetate (SI-9) was synthesized by subjecting **SI-8** (0.70 g, 5.9 mmol) to General Procedure C. The crude product was purified via flash chromatography

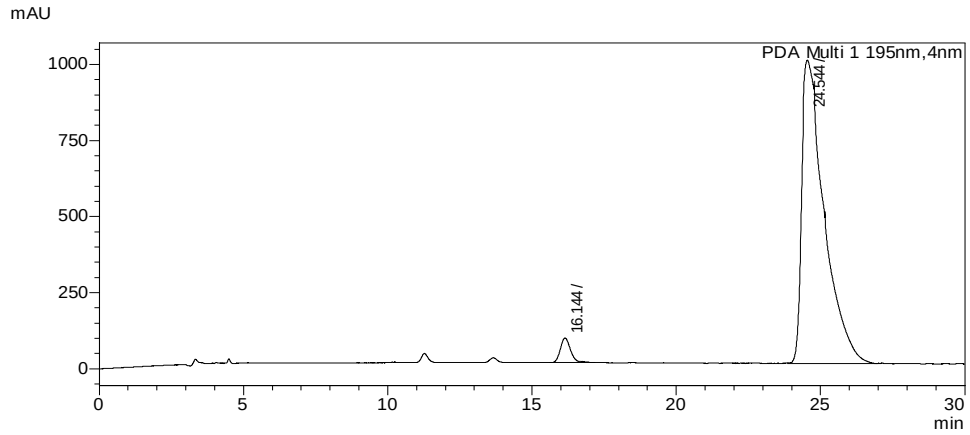
in 30% EtOAc/hexanes to provide 0.62 g (65%) of **SI-9** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.02 (tt, *J* = 6.7, 1.5 Hz, 2H), 3.74 (qq, *J* = 6.5, 4.4, 3.5 Hz, 1H), 2.23 – 2.14 (m, 1H), 2.01 – 1.96 (m, 3H), 1.65 – 1.53 (m, 2H), 1.48 – 1.28 (m, 4H), 1.14 (dt, *J* = 6.3, 1.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.3, 67.6, 64.4, 38.7, 28.6, 23.4, 22.1, 20.9. **HRMS** (ESI) calculated for $[C_8H_{16}O_3+H]^+$ 161.1178, found 161.1168.



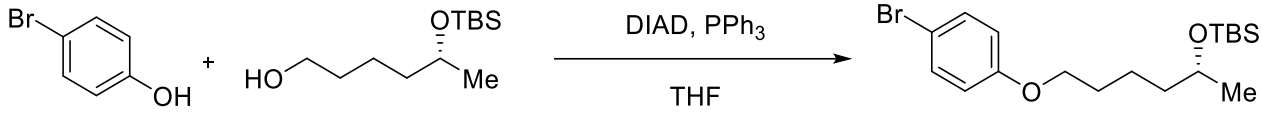
(*R*)-5-(tosyloxy)hexyl acetate (SI-10) was synthesized by tosylating **SI-9** (0.62 g, 3.9 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 1.0 g (85%) of tosylate **SI-10** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.84 – 7.79 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.69 – 4.60 (m, 1H), 3.99 (t, *J* = 6.6 Hz, 2H), 2.47 (s, 3H), 2.06 (s, 3H), 1.67 (dddd, *J* = 14.1, 10.4, 7.4, 5.2 Hz, 1H), 1.61 – 1.51 (m, 3H), 1.38 (ddtd, *J* = 13.0, 10.3, 7.4, 5.1 Hz, 1H), 1.33 – 1.22 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.1, 144.5, 134.6, 129.8, 127.7, 80.1, 64.1, 36.1, 28.1, 21.6, 21.4, 21.0, 20.8. **HRMS** (ESI) calculated for $[C_{15}H_{22}O_5S+H]^+$ 315.1266, found 315.1248. **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 93%.



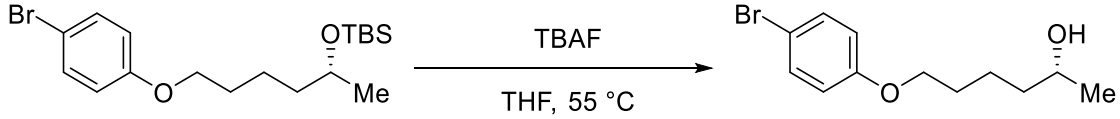
Peak#	Ret. Time	Area	Area%
1	15.34	23746237	57.019
2	23.862	17899936	42.981
Total		41646173	100



Peak#	Ret. Time	Area	Area%
1	16.144	2003435	3.593
2	24.544	53762974	96.407
Total		55766409	100

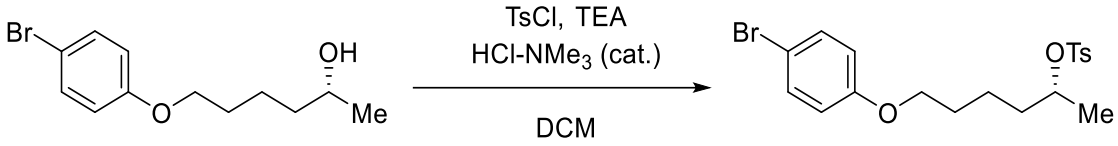


(*R*)-((6-(4-bromophenoxy)hexan-2-yl)oxy)(*tert*-butyl)dimethylsilane (SI-11) was synthesized by subjecting **SI-7** (0.50 g, 2.2 mmol) and 4-bromophenol (0.35 g, 2.0 mmol) to General Procedure B. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 0.64 g (81%) of **SI-11** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.41 – 7.32 (m, 2H), 6.82 – 6.75 (m, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 3.83 (td, *J* = 6.3, 4.9 Hz, 1H), 1.84 – 1.74 (m, 2H), 1.59 – 1.41 (m, 4H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.91 (s, 9H), 0.07 (d, *J* = 2.6 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2, 132.2, 116.3, 112.6, 68.4, 68.2, 39.4, 29.3, 25.9, 23.8, 22.2, 18.2, -4.3, -4.7. **HRMS** (ESI) calculated for $[C_{18}H_{31}BrO_2Si+Na]^+$ 409.1174, found 409.1157.

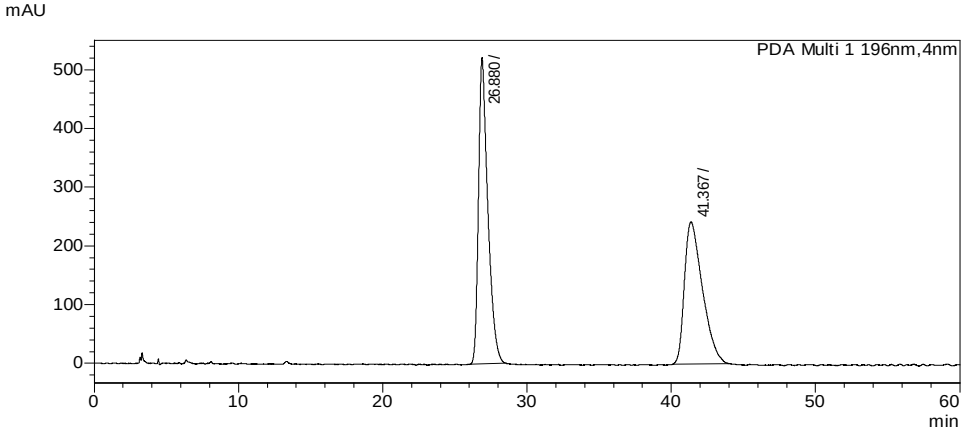


(*R*)-6-(4-bromophenoxy)hexan-2-ol (SI-12) was synthesized by deprotecting **SI-11** (0.75 g, 1.9 mmol) according to General Procedure D. The crude product was purified via flash chromatography in 30% EtOAc/hexanes to provide 0.31 g (59%) of alcohol **SI-12** as an off-white solid. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.40 – 7.35 (m, 2H), 6.81 – 6.76

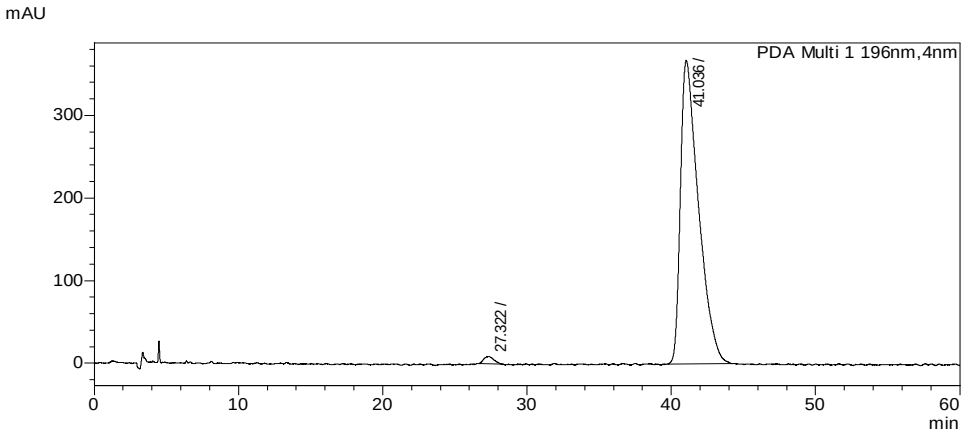
(m, 2H), 3.94 (t, *J* = 6.4 Hz, 2H), 3.88 – 3.82 (m, 1H), 1.88 – 1.75 (m, 2H), 1.65 – 1.47 (m, 5H), 1.23 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.2, 132.2, 116.3, 112.7, 68.06, 67.97, 38.9, 29.2, 23.6, 22.3. **HRMS** (ESI) calculated for $[C_{12}H_{17}BrO_2+Na]^+$ 295.0310, found 295.0295.



(*R*)-6-(4-bromophenoxy)hexan-2-yl 4-methylbenzenesulfonate (SI-13) was synthesized by tosylating **SI-12** (0.31 g, 1.1 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 0.47 g (97%) of tosylate **SI-13** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.83 – 7.79 (m, 2H), 7.41 – 7.36 (m, 2H), 7.35 – 7.31 (m, 2H), 6.79 – 6.73 (m, 2H), 4.71 – 4.62 (m, 1H), 3.85 (t, *J* = 6.3 Hz, 2H), 2.43 (s, 3H), 1.75 – 1.66 (m, 3H), i1.64 – 1.55 (m, 1H), 1.52 – 1.42 (m, 1H), 1.42 – 1.32 (m, 1H), 1.28 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.1, 144.5, 134.5, 132.2, 129.8, 127.7, 116.2, 112.7, 80.2, 67.7, 36.2, 28.7, 21.6, 21.5, 20.8. **HRMS** (ESI) calculated for $[C_{19}H_{23}BrO_4S+Na]^+$ 449.0398, found 449.0383. **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 97%.

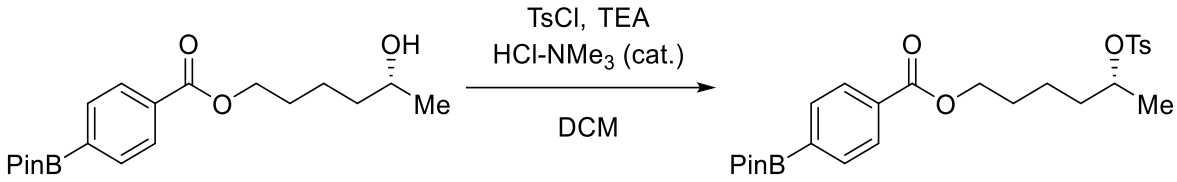


Peak#	Ret. Time	Area	Area%
1	26.88	23462248	52.779
2	41.367	20991569	47.221
Total		44453817	100

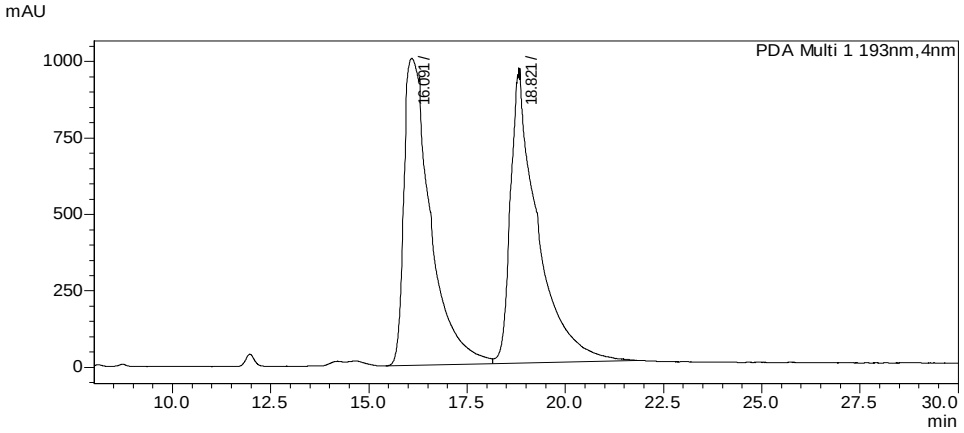


Peak#	Ret. Time	Area	Area%
1	27.322	430506	1.327
2	41.036	32020267	98.673
Total		32450774	100

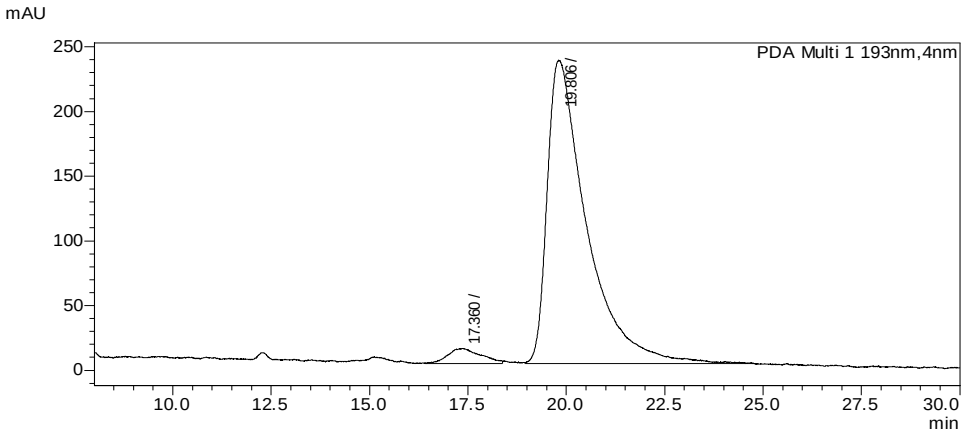
(*R*)-5-hydroxyhexyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (SI-14) was synthesized by first preparing the acid chloride by dissolving 4-carboxyphenylboronic acid pinacol ester (5.0 g, 20 mmol) and 2 drops of DMF in DCM (60 mL) at 0 °C. Oxalyl chloride (2.6 mL, 30 mmol) was added dropwise and the reaction was stirred for 15 minutes before warming to room temperature and stirring for 1 hour. The mixture was evaporated to dryness and the acid chloride was used crude as an orange solid in the subsequent step. The title compound was synthesized by subjecting **SI-7** (0.76 g, 6.4 mmol) to General Procedure C. The crude product was purified via flash chromatography using a gradient of 20-30% EtOAc/hexanes to provide 1.4 g (63%) of **SI-14** as an orange oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.05 – 8.01 (m, 2H), 7.90 – 7.86 (m, 2H), 4.35 (t, *J* = 6.6 Hz, 2H), 3.85 (q, *J* = 6.1 Hz, 1H), 1.83 (dtt, *J* = 12.5, 10.0, 6.5 Hz, 2H), 1.64 – 1.48 (m, 4H), 1.47 (br s, 1H), 1.37 (s, 12H), 1.22 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.7, 134.7, 132.6, 128.6, 84.2, 67.9, 65.0, 38.8, 28.7, 24.9, 23.62, 22.3. **HRMS** (ESI) calculated for $[C_{19}H_{29}BO_5+H]^+$ 349.2186, found 349.2196.



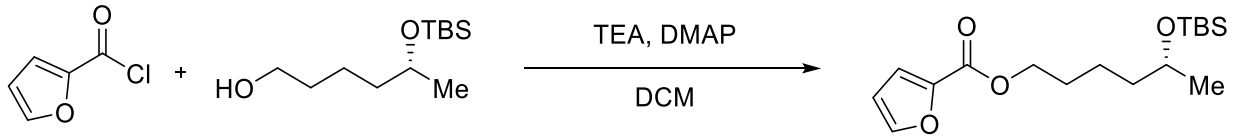
(*R*)-5-(tosyloxy)hexyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (SI-15) was synthesized by tosylating **SI-14** (1.4 g, 4.4 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 1.5 g (72%) of tosylate **SI-15** as a viscous, pale yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.04 – 7.99 (m, 2H), 7.92 – 7.88 (m, 2H), 7.83 – 7.78 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.70 – 4.61 (m, 1H), 4.23 (tt, *J* = 6.6, 3.4 Hz, 2H), 2.43 (s, 3H), 1.75 – 1.64 (m, 3H), 1.64 – 1.55 (m, 1H), 1.52 – 1.40 (m, 1H), 1.39 (s, 12H), 1.36 – 1.31 (m, 0H), 1.36 – 1.29 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.6, 144.6, 134.7, 134.4, 132.5, 129.8, 128.6, 127.7, 84.2, 80.1, 64.7, 36.1, 28.2, 24.9, 21.63, 21.56, 21.0. **HRMS** (ESI) calculated for $[C_{26}H_{35}BO_7S+H]^+$ 503.2275, found 503.2259. **Chiral HPLC** (Chiralpak IF, 95:5 (2 mL/min) hexanes:isopropanol): *ee* = 92%.



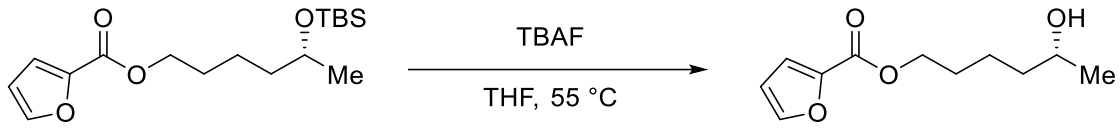
Peak#	Ret. Time	Area	Area%
1	16.091	62877023	50.688
2	18.822	61169201	49.312
Total		124046224	100



Peak#	Ret. Time	Area	Area%
1	17.36	682114	4.013
2	19.806	16313494	95.987
Total		16995609	100

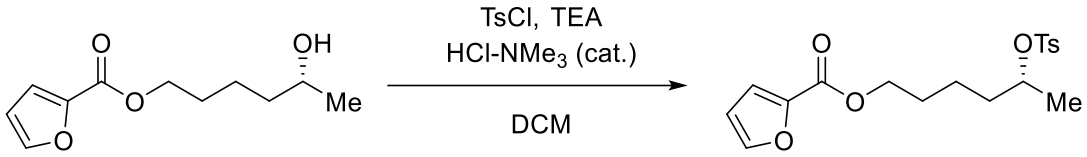


(*R*)-5-((*tert*-butyldimethylsilyl)oxy)hexyl furan-2-carboxylate (SI-16) was synthesized by subjecting **SI-7** (1.0 g, 4.3 mmol) and furan-2-carbonyl chloride (0.47 mL, 4.7 mmol) to General Procedure C. The crude product was purified via flash chromatography in 15% EtOAc/hexanes to provide 1.3 g (93%) of **SI-16** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.59 (dt, *J* = 1.8, 0.9 Hz, 1H), 7.18 (dt, *J* = 3.6, 0.9 Hz, 1H), 6.52 (dt, *J* = 2.9, 1.4 Hz, 1H), 4.32 (td, *J* = 6.7, 1.0 Hz, 2H), 3.86 – 3.78 (m, 1H), 1.82 – 1.71 (m, 2H), 1.63 – 1.38 (m, 4H), 1.15 (dd, *J* = 6.0, 1.0 Hz, 3H), 0.90 (d, *J* = 1.2 Hz, 9H), 0.08 – 0.04 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.9, 146.2, 144.9, 117.7, 111.8, 68.4, 65.0, 39.3, 28.8, 25.9, 23.8, 22.2, 18.1, -4.4, -4.8. **HRMS** (ESI) calculated for $[C_{17}H_{30}O_4Si+H]^+$ 327.1992, found 327.1976.

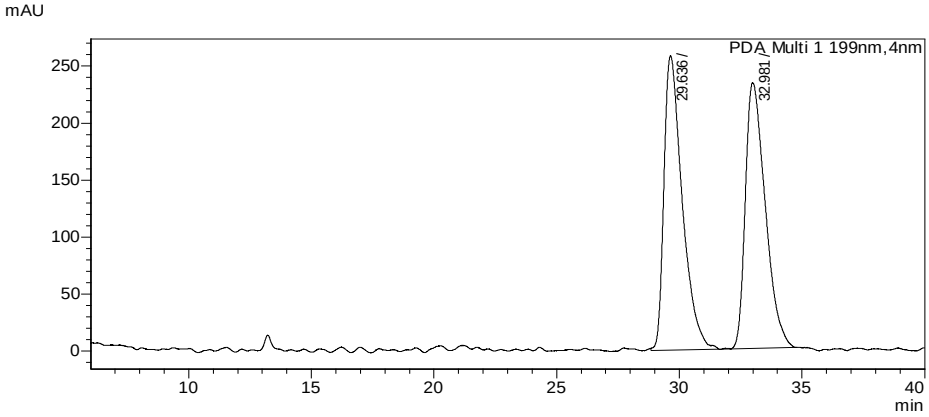


(*R*)-5-hydroxyhexyl furan-2-carboxylate (SI-17) was synthesized by subjecting **SI-16** (1.3 g, 4.0 mmol) to General Procedure D. The crude product was purified via flash

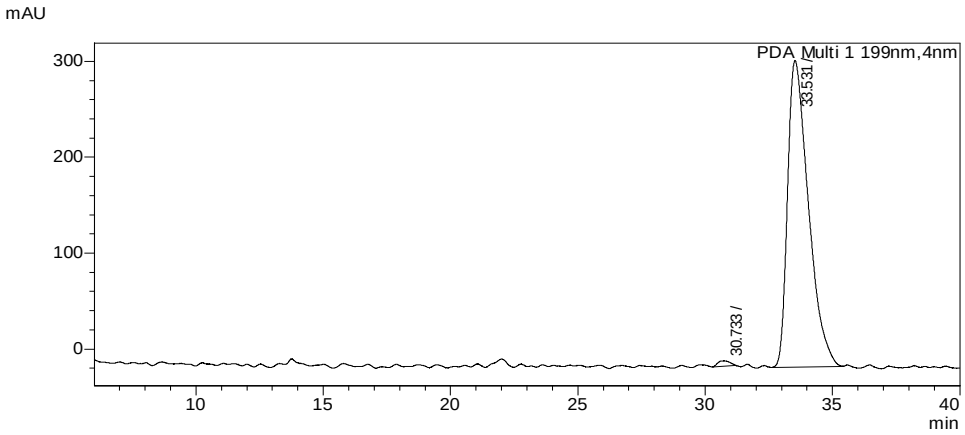
chromatography in 30% EtOAc/hexanes to provide 0.6 g (71%) of **SI-17** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.53 – 7.49 (m, 1H), 7.10 (dd, *J* = 3.6, 1.0 Hz, 1H), 6.43 (dd, *J* = 3.6, 1.8 Hz, 1H), 4.23 (t, *J* = 6.8 Hz, 2H), 3.77 – 3.69 (m, 1H), 2.33 (s, 1H), 1.77 – 1.63 (m, 2H), 1.54 – 1.32 (m, 4H), 1.11 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.8, 146.2, 144.7, 117.8, 111.8, 67.6, 64.9, 38.7, 28.6, 23.4, 22.1. **HRMS** (ESI) calculated for $[C_{11}H_{16}O_4+H]^+$ 213.1127, found 213.1114.



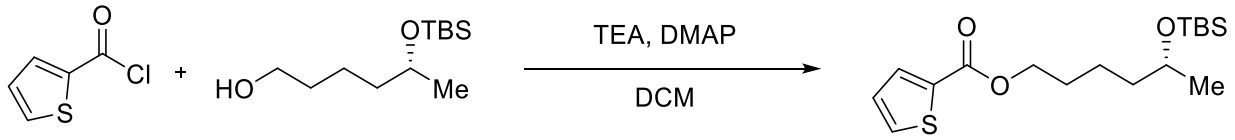
(*R*)-5-(tosyloxy)hexyl furan-2-carboxylate (SI-18) was synthesized by tosylating **SI-17** (0.57 g, 2.7 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 25% EtOAc/hexanes to provide 0.75 g (76%) of tosylate **SI-18** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.83 – 7.77 (m, 2H), 7.60 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.18 (dd, *J* = 3.5, 0.9 Hz, 1H), 6.53 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.68 – 4.60 (m, 1H), 4.21 (td, *J* = 6.6, 0.9 Hz, 2H), 2.44 (s, 3H), 1.73 – 1.61 (m, 3H), 1.61 – 1.53 (m, 1H), 1.47 – 1.36 (m, 1H), 1.35 – 1.25 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.7, 146.3, 144.7, 144.6, 134.5, 129.8, 127.7, 117.9, 111.9, 80.1, 64.5, 36.1, 28.2, 21.6, 21.4, 20.9 **HRMS** (ESI) calculated for $[C_{18}H_{22}O_6S+H]^+$ 367.1215, found 367.1196. **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 98%.



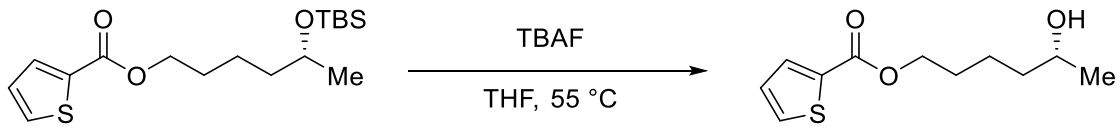
Peak#	Ret. Time	Area	Area%
1	29.636	13393753	50.459
2	32.981	13149822	49.541
Total		26543575	100



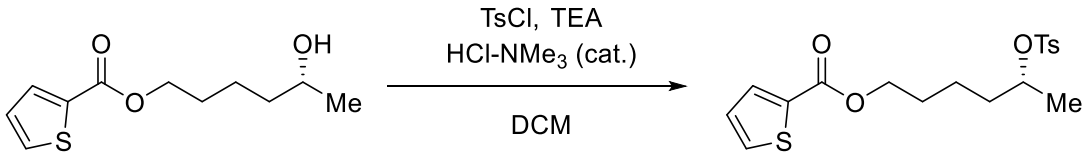
Peak#	Ret. Time	Area	Area%
1	30.733	187755	1.021
2	33.531	18204952	98.979
Total		18392707	100



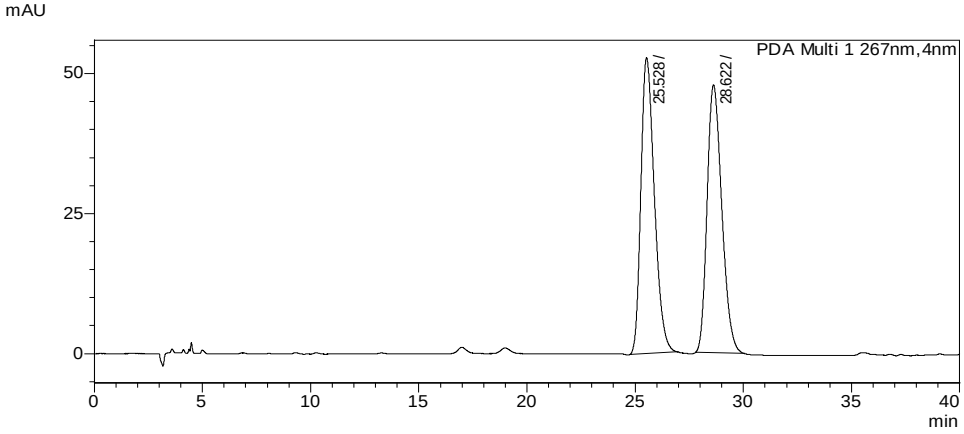
(*R*)-5-((*tert*-butyldimethylsilyl)oxy)hexyl thiophene-2-carboxylate (SI-19) was synthesized by subjecting **SI-7** (2.0 g, 8.6 mmol) and thiophene-2-carbonyl chloride (1.0 mL, 9.5 mmol) to General Procedure C. The crude product was purified via flash chromatography in 5% EtOAc/hexanes to provide 2.6 g (88%) of **SI-19** as a colorless liquid. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.56 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.12 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.31 (td, *J* = 6.7, 3.1 Hz, 2H), 3.82 (dq, *J* = 10.9, 6.1 Hz, 1H), 1.76 (dqd, *J* = 8.1, 6.5, 1.7 Hz, 2H), 1.60 – 1.37 (m, 3H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 8H), 0.10 – 0.04 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.3, 134.1, 133.2, 132.2, 127.9, 68.4, 65.2, 39.3, 28.8, 25.9, 23.9, 22.2, 18.1, -4.4, -4.7. **HRMS** (ESI) calculated for $[C_{17}H_{30}O_3SSi+H]^+$ 343.1763, found 343.1748.



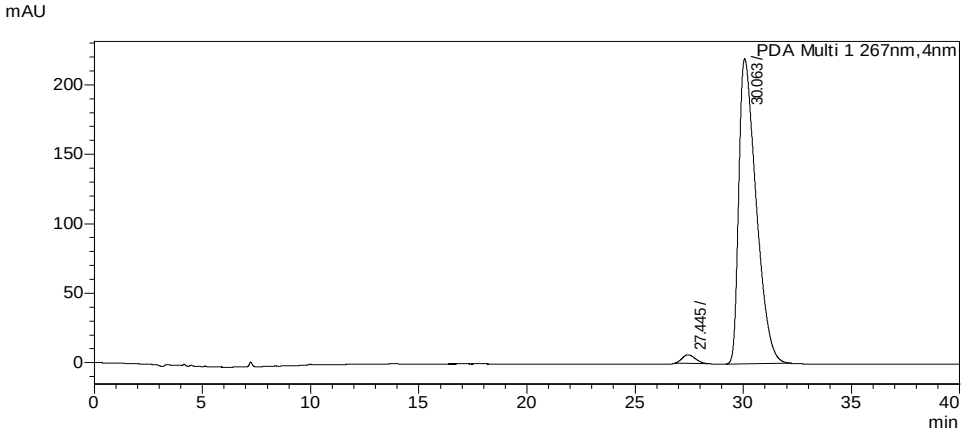
(*R*)-5-hydroxyhexyl thiophene-2-carboxylate (SI-20) was synthesized by subjecting **SI-19** (0.50 g, 1.5 mmol) to General Procedure D. The crude product was purified via flash chromatography in 30% EtOAc/hexanes to provide 0.31 g (93%) of **SI-20** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.80 (dt, *J* = 3.8, 1.2 Hz, 1H), 7.55 (dt, *J* = 5.1, 1.2 Hz, 1H), 7.10 (ddd, *J* = 5.0, 3.8, 1.3 Hz, 1H), 4.31 (td, *J* = 6.6, 1.5 Hz, 2H), 3.86 – 3.80 (m, 1H), 1.78 (tdt, *J* = 7.6, 5.5, 3.7 Hz, 2H), 1.69 – 1.42 (m, 5H), 1.21 (dd, *J* = 6.2, 1.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.4, 134.0, 133.3, 132.3, 127.7, 67.9, 65.1, 38.8, 28.7, 23.6, 22.2. **HRMS** (ESI) calculated for $[C_{11}H_{16}O_3S+H]^+$ 229.0898, found 229.0888.



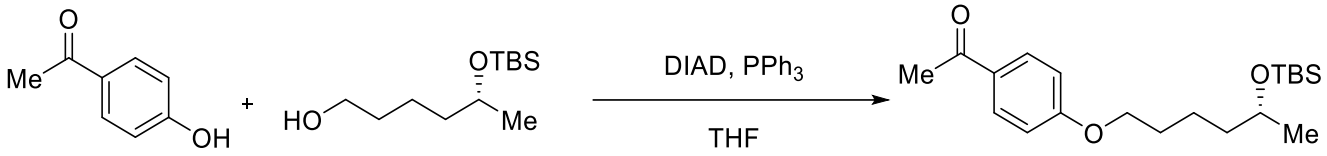
(*R*)-5-(tosyloxy)hexyl thiophene-2-carboxylate (SI-21) was synthesized by tosylating **SI-20** (0.31 g, 1.4 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 0.38 g (73%) of tosylate **SI-21** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.83 – 7.76 (m, 3H), 7.57 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.12 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.69 – 4.60 (m, 1H), 4.20 (td, *J* = 6.6, 1.5 Hz, 2H), 2.43 (s, 3H), 1.74 – 1.62 (m, 3H), 1.58 (ddt, *J* = 14.0, 10.5, 5.4 Hz, 1H), 1.47 – 1.37 (m, 1H), 1.36 – 1.25 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.2, 144.6, 134.5, 133.9, 133.4, 132.3, 129.8, 127.8, 127.7, 80.1, 64.7, 36.1, 28.2, 21.6, 21.5, 20.9. **HRMS** (ESI) calculated for $[C_{18}H_{22}O_5S_2+H]^+$ 383.0987, found 383.0971. **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 96%.



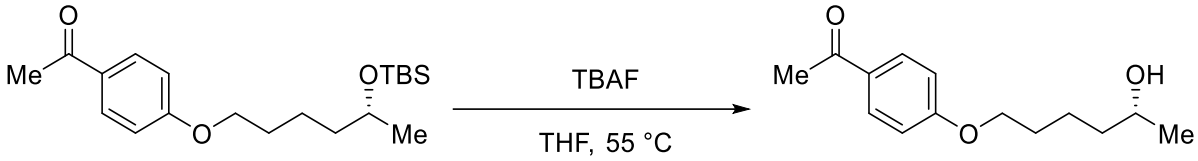
Peak#	Ret. Time	Area	Area%
1	25.528	2288037	50.278
2	28.622	2262710	49.722
Total		4550748	100



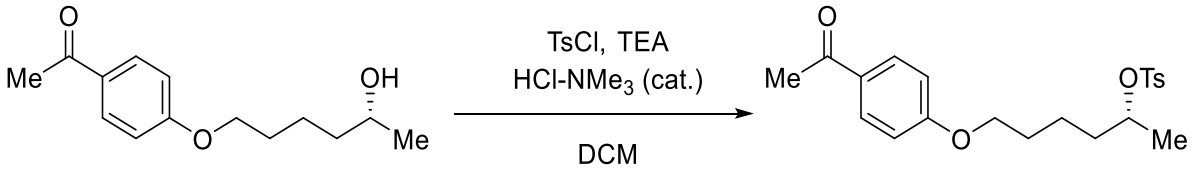
Peak#	Ret. Time	Area	Area%
1	27.445	265207	2.122
2	30.063	12234052	97.878
Total		12499259	100



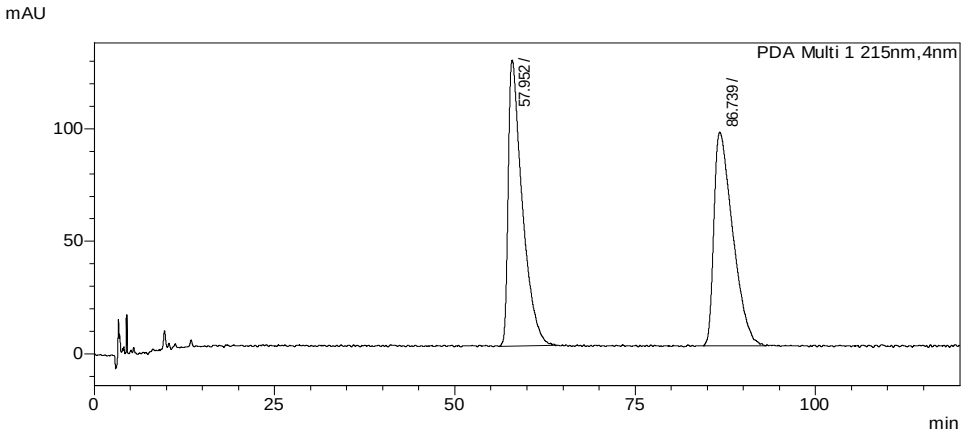
(*R*)-1-(4-((5-((*tert*-butyldimethylsilyl)oxy)hexyl)oxy)phenyl)ethan-1-one (SI-22) was synthesized by subjecting **SI-7** (1.5 g, 6.5 mmol) and 4-hydroxyacetophenone (0.84 g, 6.5 mmol) to General Procedure B. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.5 g (70%) of **SI-22** as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.97 – 7.88 (m, 2H), 6.96 – 6.87 (m, 2H), 4.04 (t, *J* = 6.5 Hz, 2H), 3.83 (dt, *J* = 11.1, 5.6 Hz, 1H), 2.58 (s, 3H), 1.86 – 1.77 (m, 2H), 1.61 – 1.40 (m, 4H), 1.16 (d, *J* = 6.0 Hz, 3H), 0.91 (s, 9H), 0.08 – 0.06 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.9, 163.1, 130.6, 130.1, 114.1, 68.4, 68.1, 39.3, 29.2, 26.4, 25.9, 23.9, 22.2, 18.2, -4.3, -4.7. **HRMS** (ESI) calculated for $[C_{20}H_{34}O_3Si+H]^+$ 351.2355, found 351.2361.



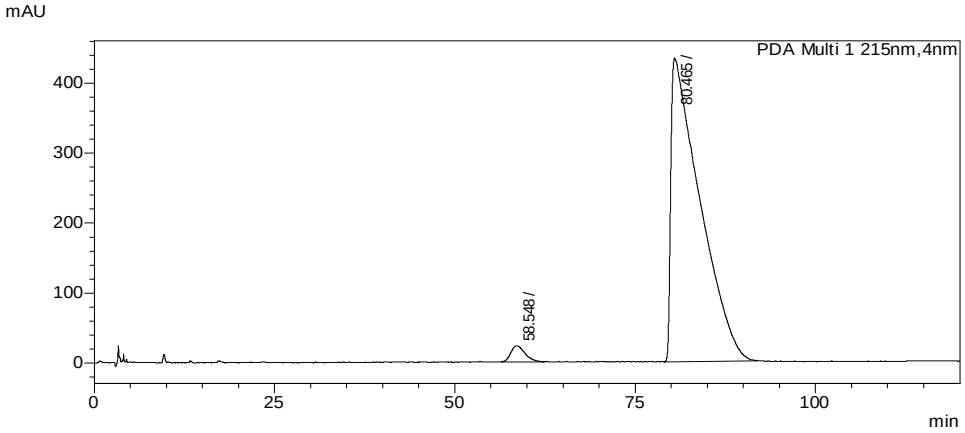
(*R*)-1-(4-((5-hydroxyhexyl)oxy)phenyl)ethan-1-one (SI-23) was synthesized by deprotecting **SI-22** (1.5 g, 4.3 mmol) according to General Procedure D. The crude product was purified via flash chromatography in 40% EtOAc/hexanes to provide 0.80 g (79%) of alcohol **SI-23** as an off-white solid. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.97 – 7.90 (m, 2H), 6.95 – 6.89 (m, 2H), 4.03 (q, *J* = 6.4, 5.0 Hz, 2H), 3.89 – 3.80 (m, 1H), 2.56 (s, 3H), 1.83 (dq, *J* = 15.5, 6.4 Hz, 2H), 1.75 (br s, 1H), 1.72 – 1.43 (m, 4H), 1.22 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 197.0, 163.0, 130.6, 130.1, 114.1, 68.1, 67.9, 38.9, 29.1, 26.4, 23.6, 22.3. **HRMS** (ESI) calculated for $[C_{14}H_{20}O_3+H]^+$ 237.1491, found 237.1493.



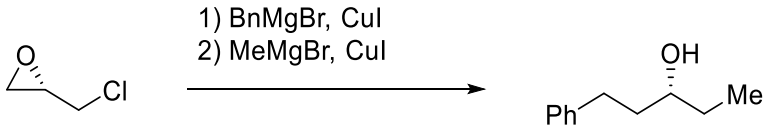
(*R*)-6-(4-acetylphenoxy)hexan-2-yl 4-methylbenzenesulfonate (SI-24) was synthesized by tosylating **SI-23** (0.80 g, 4.2 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 30% EtOAc/hexanes to provide 1.1 g (83%) of tosylate **SI-24** as an ivory white solid. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.97 – 7.92 (m, 2H), 7.83 – 7.78 (m, 2H), 7.35 – 7.30 (m, 2H), 6.93 – 6.87 (m, 2H), 4.70 – 4.62 (m, 1H), 3.94 (t, *J* = 6.3 Hz, 2H), 2.57 (s, 3H), 2.41 (s, 3H), 1.77 – 1.67 (m, 3H), 1.64 – 1.55 (m, 1H), 1.53 – 1.45 (m, 1H), 1.44 – 1.34 (m, 1H), 1.27 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.9, 162.9, 144.6, 134.4, 130.6, 130.2, 129.8, 127.7, 114.1, 80.2, 67.8, 36.2, 28.6, 26.4, 21.6, 21.5, 20.8. **HRMS** (ESI) calculated for $[C_{21}H_{26}O_5S+H]^+$ 391.1579, found 391.1583. **Chiral HPLC** (Daicel OJ-H, 70:30 hexanes:isopropanol): *ee* = 95%.



Peak#	Ret. Time	Area	Area%
1	57.952	17196346	49.976
2	86.739	17212767	50.024
Total		34409113	100

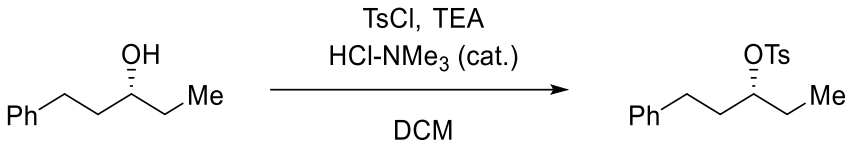


Peak#	Ret. Time	Area	Area%
1	58.547	3328932	2.538
2	80.466	127820507	97.462
Total		131149439	100

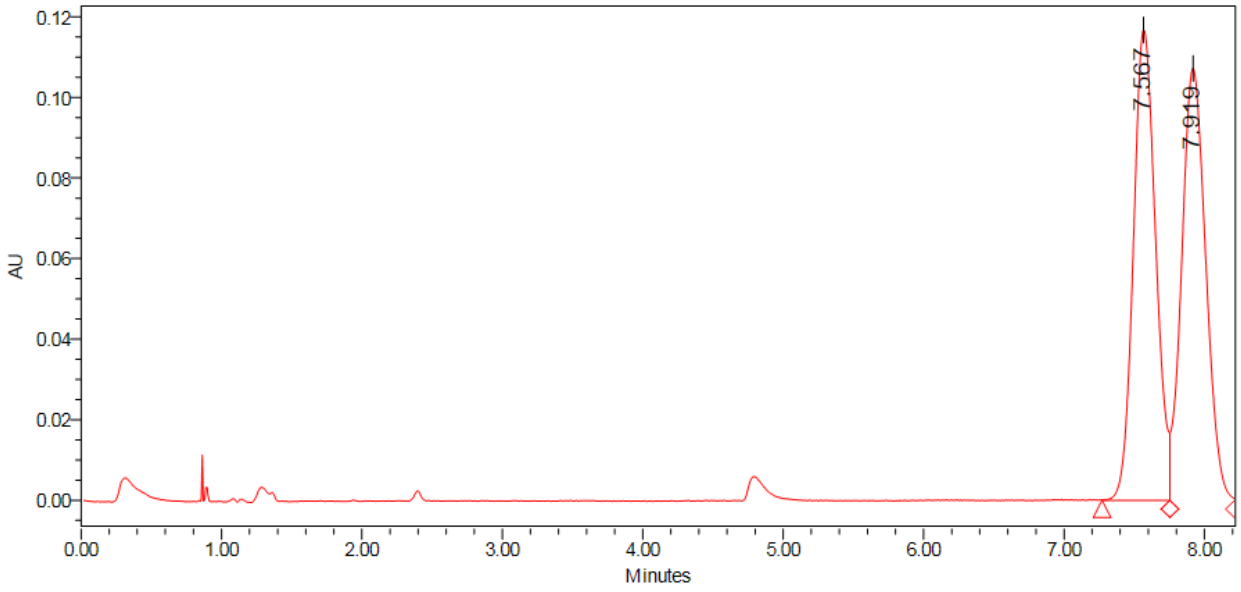


(*R*)-1-phenylpentan-3-ol (SI-25) was synthesized using the 2-step sequence shown above. To a -78 °C suspension of CuI (4.6 g, 24 mmol) in THF (15 mL) was added benzylmagnesium bromide (12 mL, 2.0 M in THF, 24 mmol) and stirred for 5 minutes. (*S*)-epichlorohydrin (1.3 mL g, 16 mmol) was added and the reaction was warmed to 0 °C

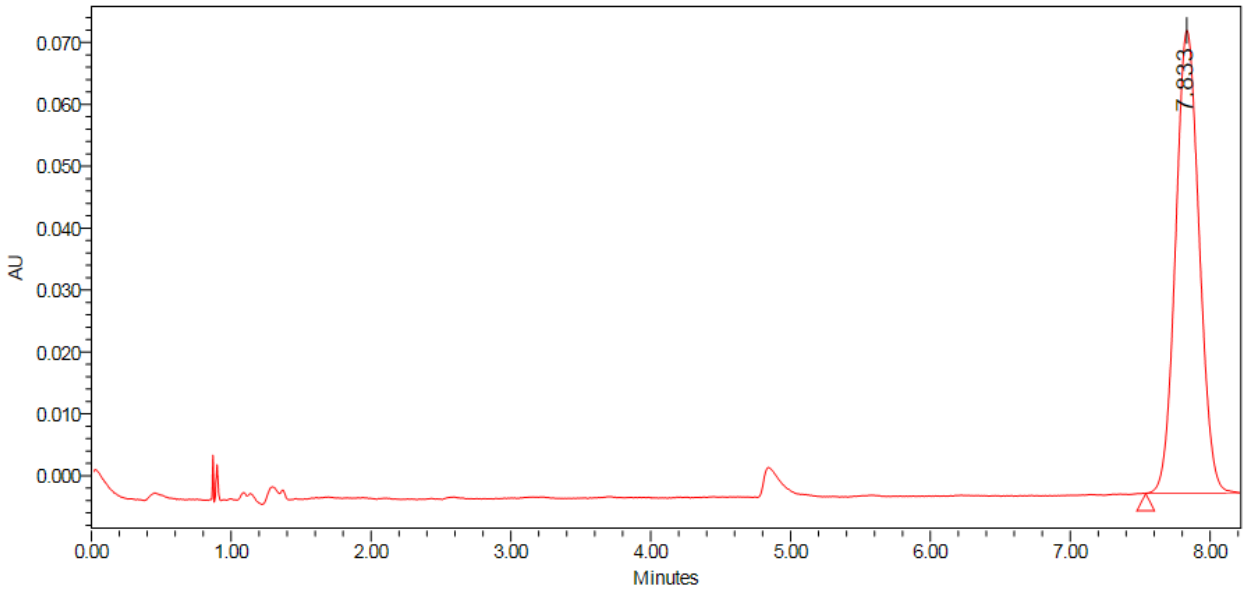
for 3 hours with stirring. The reaction was then stirred overnight at room temperature. The mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.3 g (54%) of the enantioenriched oxirane intermediate as a colorless oil. Physical and spectral data were in accordance with literature data.[10] To a -78 °C suspension of CuI (2.3 g, 12 mmol) in THF (8 mL) was added methylmagnesium bromide (3 mL, 3.0 M in Et_2O, 8 mmol) and stirred for 5 minutes. A solution of the oxirane intermediate (1.2 g, 8 mmol) in THF (5 mL) was then added and the reaction was warmed to 0 °C for 3 hours with stirring. The mixture was quenched with an aqueous saturated solution of NH_4Cl and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 0.92 g (69%) of alcohol **SI-25** as a colorless oil. Physical and spectral data were in accordance with literature data.[11]



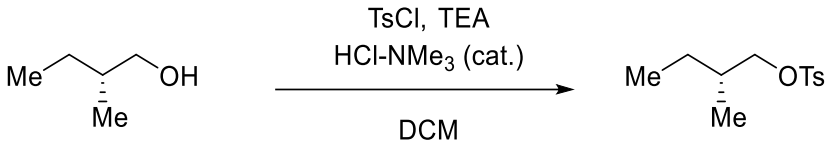
(*R*)-1-phenylpentan-3-yl 4-methylbenzenesulfonate (SI-26) was synthesized by tosylating **SI-25** (0.80 g, 4.9 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.1 g (71%) of tosylate **SI-26** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.86 – 7.81 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.19 (m, 1H), 7.13 – 7.08 (m, 2H), 4.63 – 4.56 (m, 1H), 2.63 (ddd, *J* = 13.8, 10.3, 6.1 Hz, 1H), 2.55 (ddd, *J* = 13.9, 10.2, 5.9 Hz, 1H), 2.48 (s, 3H), 1.99 – 1.85 (m, 2H), 1.77 – 1.64 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.6, 141.1, 134.6, 129.8, 128.5, 128.3, 127.8, 126.1, 84.8, 35.3, 31.1, 27.1, 21.7, 9.1. **HRMS** (ESI) calculated for $[C_{18}H_{22}O_3S+Na]^+$ 341.1187, found 341.1155. **Chiral SFC** (Cellulose-2, 99:1 hexanes:isopropanol): *ee* = >99%.



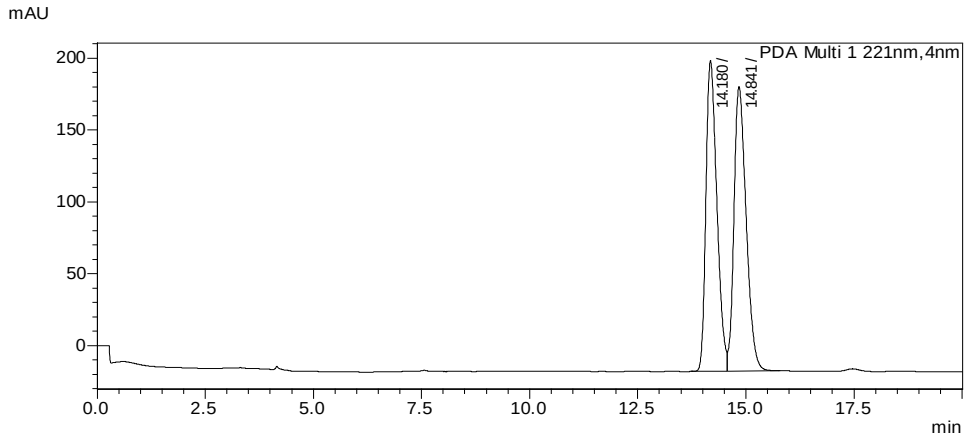
Peak#	Ret. Time	Area%
1	7.567	52.13
2	7.919	47.87
Total		100



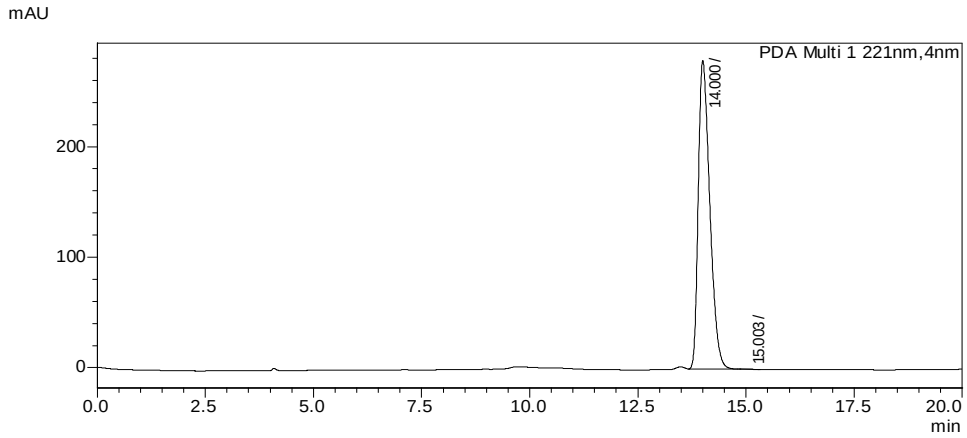
Peak#	Ret. Time	Area%
1	7.833	100
Total		100



(*S*)-2-methylbutyl 4-methylbenzenesulfonate (SI-27) was synthesized by tosylating (*S*)-2-methylbutan-1-ol (5.0 mL, 55 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 5% EtOAc/hexanes to provide 9.8 g (74%) of tosylate **SI-27** as a colorless liquid. Physical and spectral data were in accordance with literature data.[12] **Chiral HPLC** (Daicel OJ-H, 99.5:0.5 hexanes:isopropanol): *ee* = >99%.



Peak#	Ret. Time	Area	Area%
1	14.18	3808916	49.505
2	14.841	3885086	50.495
Total		7694002	100

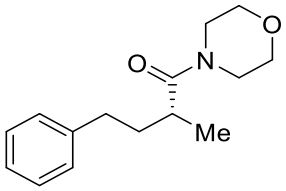


Peak#	Ret. Time	Area	Area%

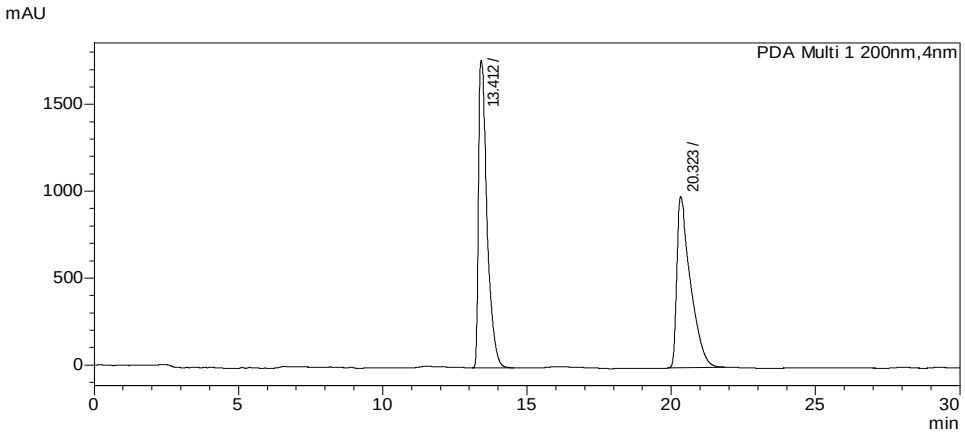
1	14	5164457	99.869
2	15.003	6767	0.131
Total		5171224	100

Cobalt-Catalyzed Reactions

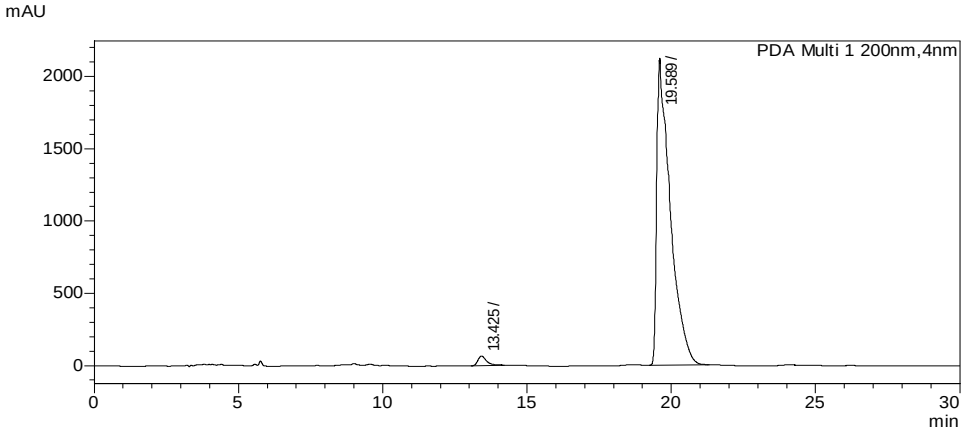
General Carbonylation Procedure A: In a glovebox under an argon atmosphere, alkyl tosylate (0.25 mmol) was combined with $Co_2(CO)_8$ (8.5 mg, 0.025 mmol), TMP (84 µL, 0.50 mmol), amine (.325 mmol), and *t*-amyl alcohol (1 mL) in a Parr reactor. The vessel was sealed with a regulator and removed from the glovebox. Subsequently, the reactor was pressurized with 40 atm CO and stirred for 48 hours (unless otherwise noted) at 70 ºC. The reaction mixture was cooled to room temperature, depressurized, and 3 mL HCl (1 M) was added. The mixture was extracted three times with EtOAc and the combined organic layers were allowed to sit open to air for two hours to decompose the cobalt complex. The combined organic layers were filtered through a plug of SiO_2, eluting with EtOAc, and concentrated under reduced pressure. The crude product was purified by flash chromatography.



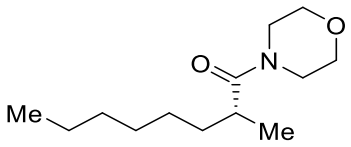
(*R*)-2-methyl-1-morpholino-4-phenylbutan-1-one (3) was obtained from General Carbonylation Procedure A and the crude product (85% NMR yield) was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **3** as a colorless oil (45 mg, 73%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.15 (m, 3H), 3.78 – 3.60 (m, 3H), 3.59 (t, *J* = 5.0 Hz, 2H), 3.36 – 3.28 (m, 2H), 2.76 – 2.53 (m, 3H), 2.07 (dtd, *J* = 13.8, 8.1, 6.6 Hz, 1H), 1.71 (ddt, *J* = 13.3, 8.5, 6.6 Hz, 1H), 1.15 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.8, 141.7, 128.5, 128.4, 126.0, 67.1, 66.8, 45.8, 42.1, 35.4, 34.0, 33.4, 17.5. **HRMS** (ESI) calculated for $[C_{15}H_{21}NO_2+H]^+$ 248.1651, found 248.1637. **Chiral HPLC** (Daicel OJ-H, 90:10 hexanes:isopropanol): *ee* = 96%, es = 97%.



Peak#	Ret. Time	Area	Area%
1	13.412	36422131	53.109
2	20.323	32158108	46.891
Total		68580239	100

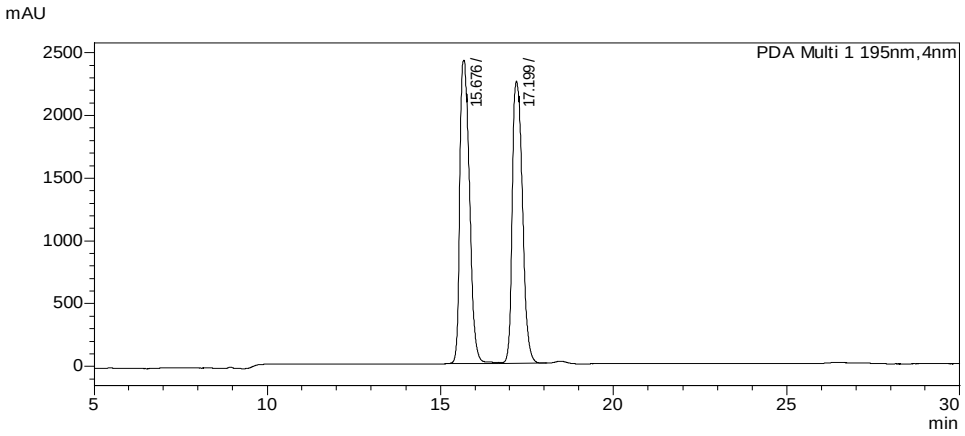


Peak#	Ret. Time	Area	Area%
1	13.425	1377020	1.955
2	19.589	69045255	98.045
Total		70422275	100

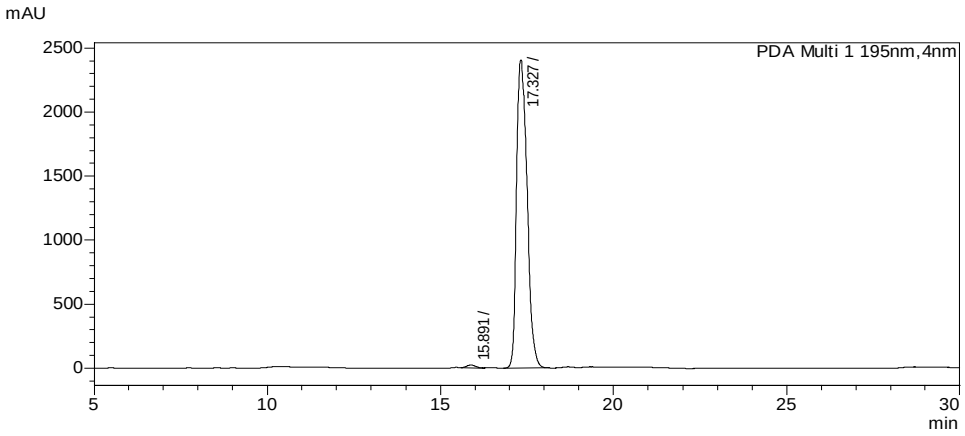


(*R*)-2-methyl-1-morpholinooctan-1-one (4) was obtained from General Carbonylation Procedure A (24 h) and the crude product was purified via flash chromatography using a gradient of 10-75% EtOAc/hexanes yielding **4** as a colorless oil (29 mg, 51%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 3.67 (t, *J* = 5.1 Hz, 4H), 3.67 – 3.62 (m, 2H), 3.52 (q, *J* = 3.9

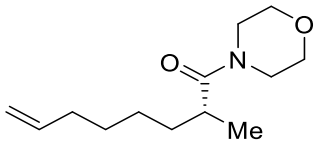
Hz, 2H), 2.65 (h, *J* = 6.8 Hz, 1H), 1.67 (dt, *J* = 13.5, 6.8 Hz, 1H), 1.39 (dt, *J* = 14.2, 7.0 Hz, 1H), 1.34 – 1.24 (m, 8H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.3, 67.1, 66.9, 46.1, 42.1, 35.1, 34.1, 31.8, 29.4, 27.4, 22.6, 17.5, 14.1. **HRMS** (ESI) calculated for $[C_{13}H_{25}NO_2+H]^+$ 228.1964, found 228.1951. **Chiral HPLC** (Chiralpak IG, 95:5 hexanes:isopropanol): *ee* = 99%, es = 99%.



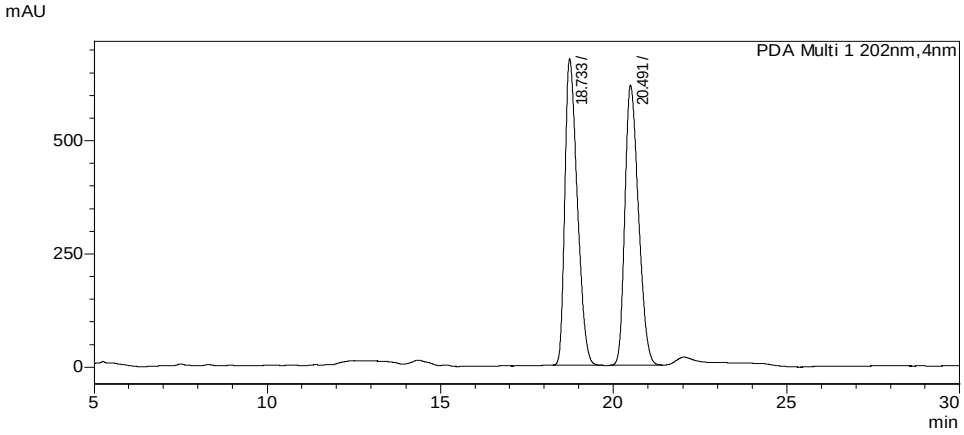
Peak#	Ret. Time	Area	Area%
1	15.676	47291170	50.641
2	17.199	46094846	49.359
Total		93386017	100



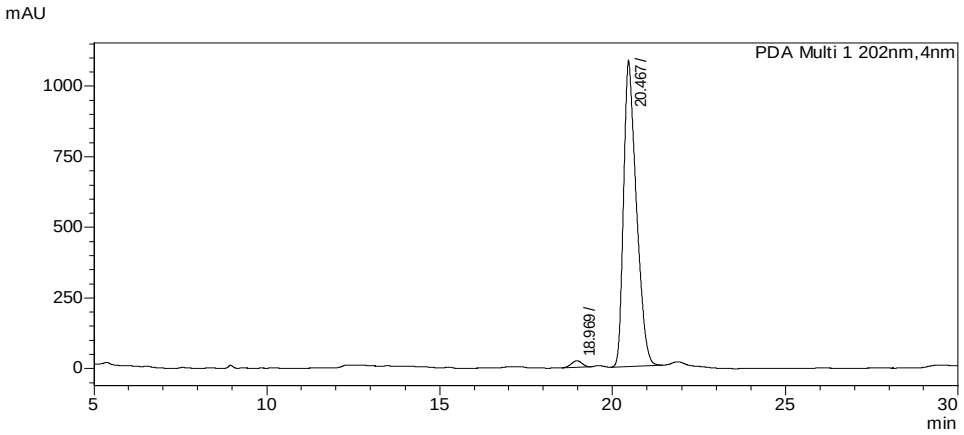
Peak#	Ret. Time	Area	Area%
1	15.891	368388	0.717
2	17.327	51041381	99.283
Total		51409769	100



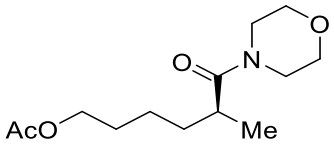
(*R*)-2-methyl-1-morpholinooct-7-en-1-one (5) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-75% EtOAc/hexanes yielding **5** as a colorless oil (30.2 mg, 54%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 5.80 (ddt, *J* = 13.4, 10.1, 6.7 Hz, 1H), 5.00 (dt, *J* = 17.1, 1.7 Hz, 1H), 4.94 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.70 – 3.63 (m, 6H), 3.52 (q, *J* = 3.9 Hz, 2H), 2.65 (h, *J* = 6.8 Hz, 1H), 2.05 (qt, *J* = 7.3, 1.5 Hz, 2H), 1.74 – 1.65 (m, 1H), 1.46 – 1.34 (m, 3H), 1.36 – 1.24 (m, 2H), 1.12 (dd, *J* = 6.9, 1.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.2, 138.8, 114.4, 67.1, 66.9, 46.1, 42.1, 35.1, 33.9, 33.6, 29.0, 26.9, 17.6. **HRMS** (ESI) calculated for $[C_{13}H_{23}NO_2+H]^+$ 226.1807, found 226.1794. **Chiral HPLC** (Chiralpak IG, 95:5 hexanes:isopropanol): *ee* = 97%, es = >99%.



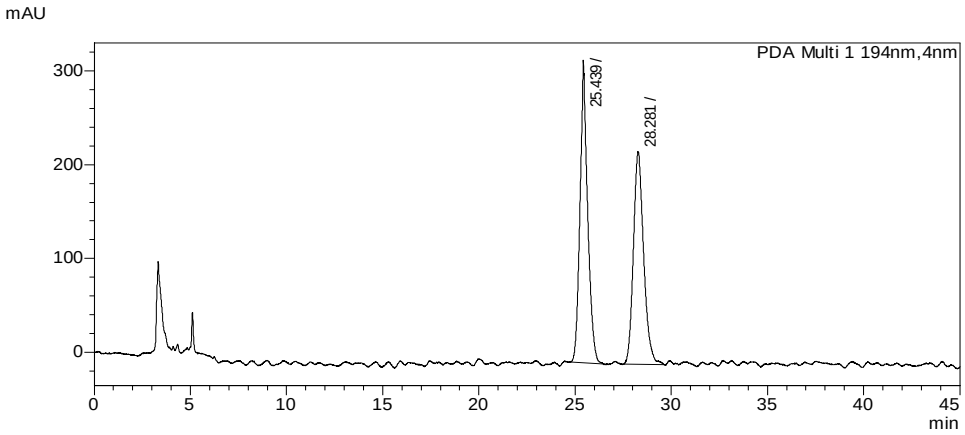
Peak#	Ret. Time	Area	Area%
1	18.733	16898844	50.047
2	20.491	16866822	49.953
Total		33765666	100



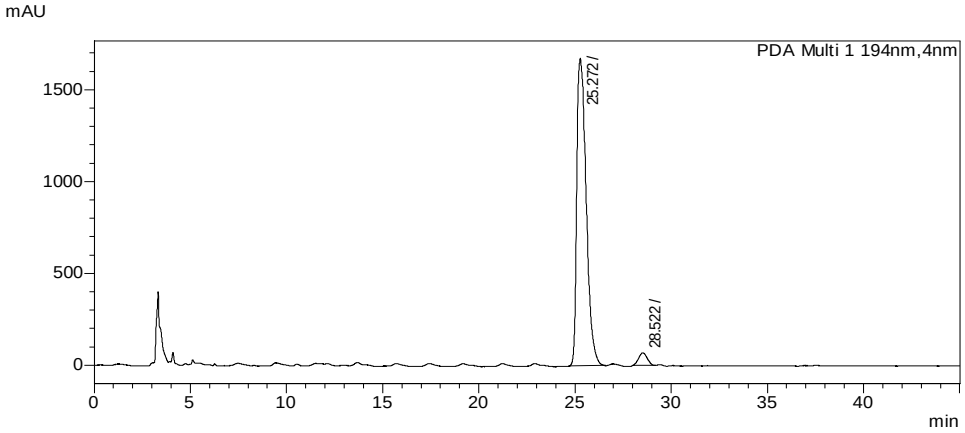
Peak#	Ret. Time	Area	Area%
1	18.969	495532	1.748
2	20.467	27848703	98.252
Total		28344235	100



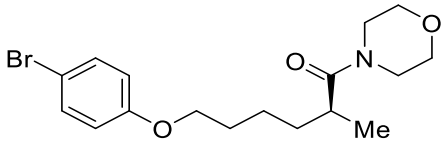
(*S*)-5-methyl-6-morpholino-6-oxohexyl acetate (6) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 20-75% EtOAc/hexanes yielding **6** as a colorless oil (45 mg, 70%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.05 (t, *J* = 6.7 Hz, 2H), 3.73 – 3.60 (m, 6H), 3.53 (dd, *J* = 6.1, 3.7 Hz, 2H), 2.66 (h, *J* = 6.8 Hz, 1H), 2.05 (d, *J* = 1.0 Hz, 3H), 1.78 – 1.66 (m, 1H), 1.63 (ddt, *J* = 15.2, 8.4, 6.2 Hz, 2H), 1.46 – 1.36 (m, 1H), 1.33 (p, *J* = 7.7 Hz, 2H), 1.12 (dd, *J* = 6.8, 1.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.9, 171.2, 67.1, 66.9, 64.3, 46.1, 42.1, 35.1, 33.6, 28.7, 23.9, 21.0, 17.6. **HRMS** (ESI) calculated for $[C_{13}H_{23}NO_4+H]^+$ 258.1705, found 258.1691. **Chiral HPLC** (Chiralpak IE, 80:20 hexanes:isopropanol): *ee* = 93%, es = >99%.



Peak#	Ret. Time	Area	Area%
1	25.439	8842230	51.196
2	28.281	8429232	48.804
Total		17271461	100

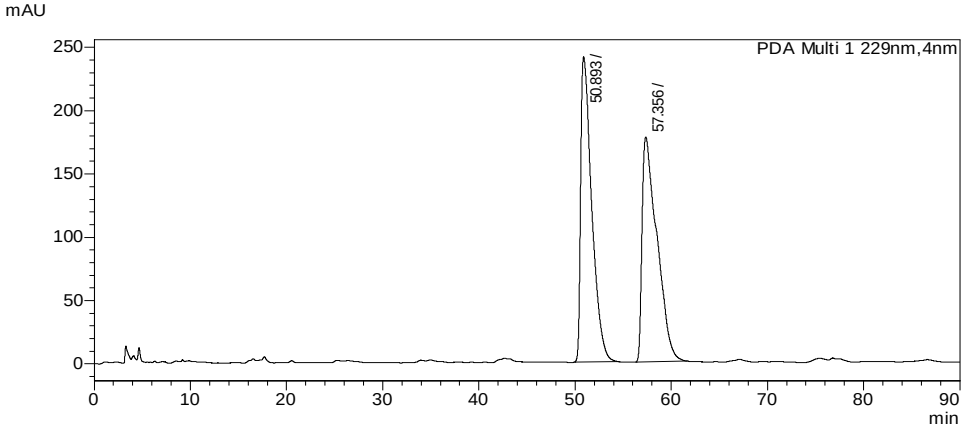


Peak#	Ret. Time	Area	Area%
1	25.272	56932706	96.442
2	28.522	2100495	3.558
Total		59033201	100

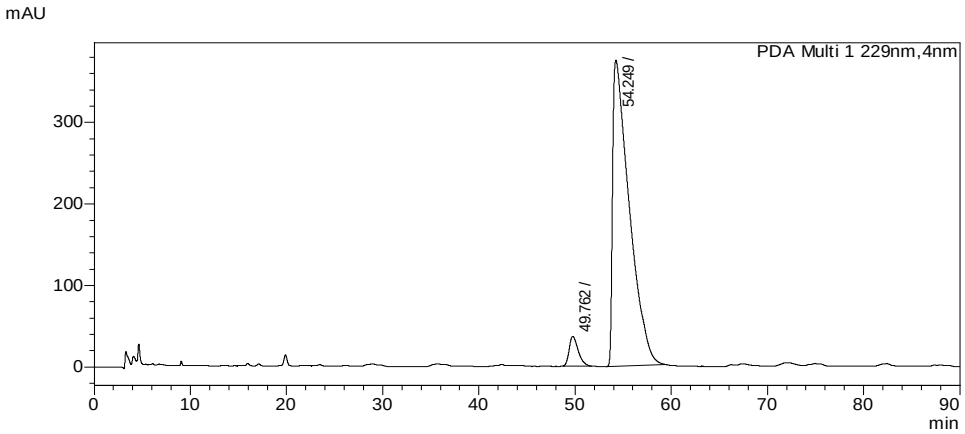


(*S*)-6-(4-bromophenoxy)-2-methyl-1-morpholinohexan-1-one (7) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 20-75% EtOAc/hexanes yielding **7** as a cream colored solid (52 mg, 56%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.40 – 7.34 (m, 2H), 6.80

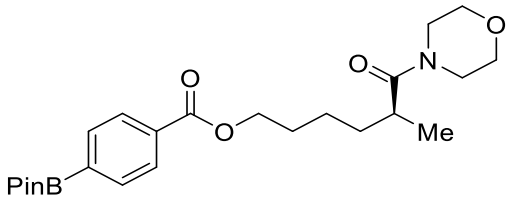
– 6.74 (m, 2H), 3.97 – 3.86 (m, 2H), 3.74 – 3.60 (m, 6H), 3.53 (t, *J* = 4.9 Hz, 2H), 2.73 – 2.64 (m, 1H), 1.84 – 1.72 (m, 3H), 1.51 – 1.40 (m, 3H), 1.14 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.0, 158.1, 132.2, 116.3, 112.7, 67.9, 67.1, 66.9, 46.1, 42.1, 35.2, 33.7, 29.3, 24.0, 17.7. **HRMS** (ESI) calculated for $[C_{17}H_{24}BrNO_3+H]^+$ 370.1018, found 370.1024. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 90%, es = 93%.



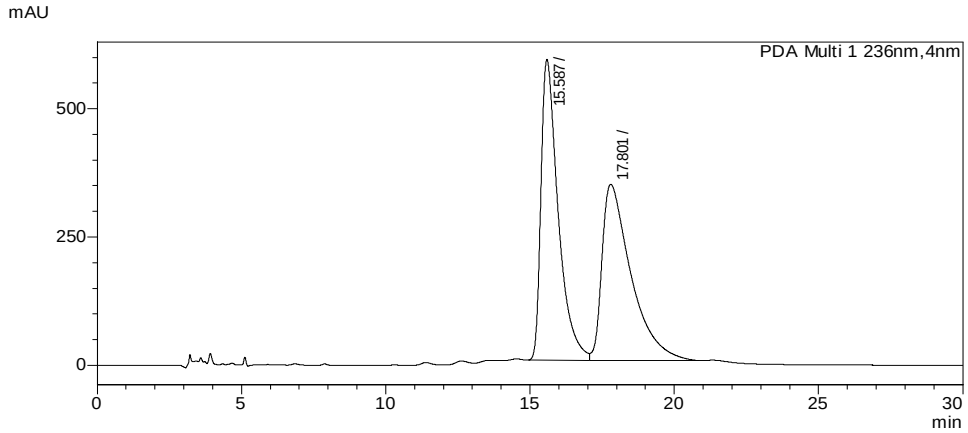
Peak#	Ret. Time	Area	Area%
1	50.893	19283341	50.175
2	57.356	19148686	49.825
Total		38432028	100



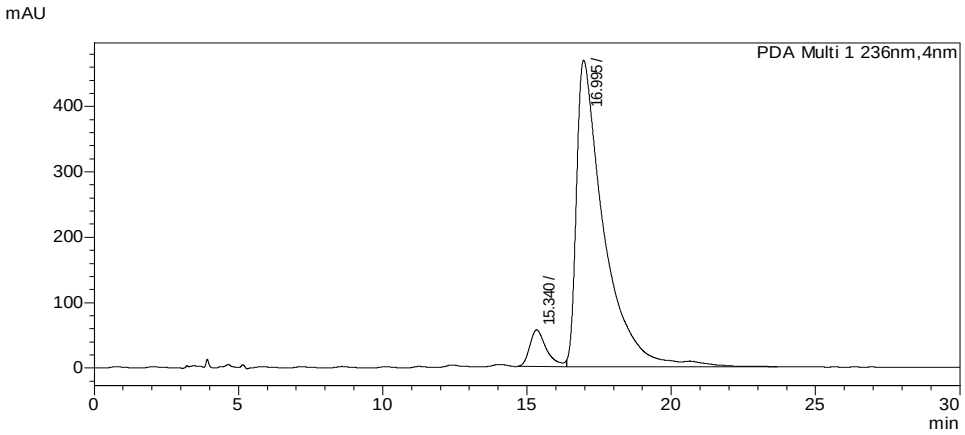
Peak#	Ret. Time	Area	Area%
1	49.762	2363057	4.971
2	54.249	45177434	95.029
Total		47540491	100



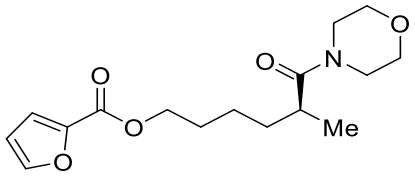
(*S*)-5-methyl-6-morpholino-6-oxohexyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (8) was obtained from General Carbonylation Procedure A and the crude product (71% NMR yield) was purified via flash chromatography using a gradient of 20-75% EtOAc/hexanes yielding **8** as a viscous, pale yellow oil (50 mg, 48%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.04 – 7.99 (m, 2H), 7.89 – 7.85 (m, 2H), 4.32 (td, *J* = 6.6, 1.1 Hz, 2H), 3.69 – 3.59 (m, 6H), 3.52 (td, *J* = 4.5, 2.4 Hz, 2H), 2.72 – 2.63 (m, 1H), 1.84 – 1.71 (m, 3H), 1.52 – 1.37 (m, 3H), 1.36 (s, 12H), 1.13 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.0, 166.7, 134.7, 132.5, 128.6, 84.2, 67.1, 66.9, 64.9, 46.0, 42.1, 35.1, 33.6, 28.8, 24.89, 24.85, 24.0, 17.7. **HRMS** (ESI) calculated for $[C_{24}H_{36}BNO_6+H]^+$ 446.2714, found 446.2721. **Chiral HPLC** (Chiralpak IF, 80:20 hexanes:isopropanol): *ee* = 86%, es = 93%.



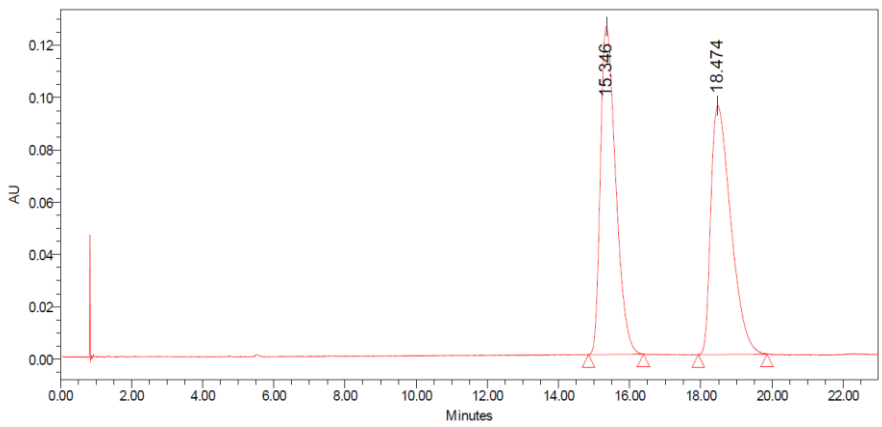
Peak#	Ret. Time	Area	Area%
1	15.587	24342286	50.362
2	17.801	23992087	49.638
Total		48334373	100



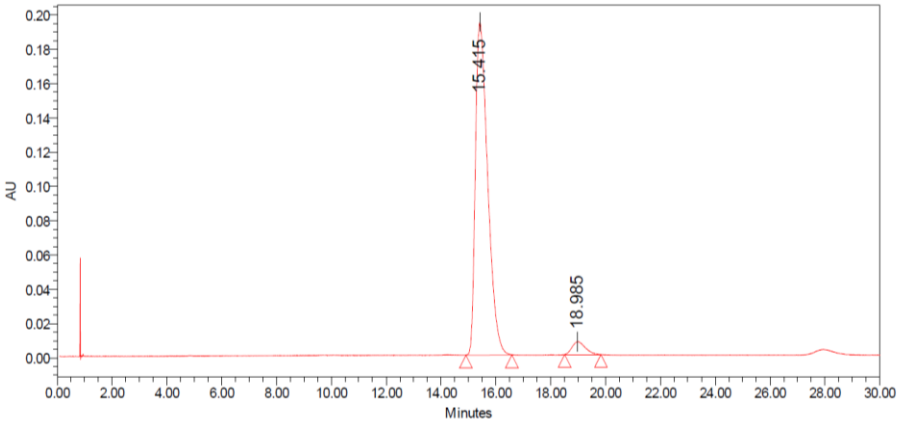
Peak#	Ret. Time	Area	Area%
1	15.34	2267568	6.825
2	16.995	30955789	93.175
Total		33223357	100



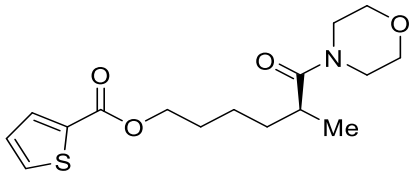
(*S*)-5-methyl-6-morpholino-6-oxohexyl furan-2-carboxylate (9) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 40-100% EtOAc/hexanes yielding **9** as a yellow oil (40 mg, 52%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.59 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.18 (dd, *J* = 3.5, 1.0 Hz, 1H), 6.52 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.31 (td, *J* = 6.7, 1.3 Hz, 2H), 3.74 – 3.58 (m, 6H), 3.53 (q, *J* = 4.1 Hz, 2H), 2.68 (h, *J* = 6.8 Hz, 1H), 1.82 – 1.69 (m, 3H), 1.52 – 1.35 (m, 3H), 1.13 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.9, 158.8, 146.2, 144.8, 117.8, 111.8, 67.1, 66.9, 64.8, 46.1, 42.1, 35.1, 33.5, 28.8, 23.9, 17.7. **HRMS** (ESI) calculated for $[C_{16}H_{23}NO_5+H]^+$ 310.1654, found 310.1640 **Chiral SFC** (Phenomenex Lux Cellulose-1, 95:5 CO_2:isopropanol): *ee* = 92%, es = 94%.



Peak#	Ret. Time	Area%
1	15.346	50.12
2	18.474	49.88
Total		100

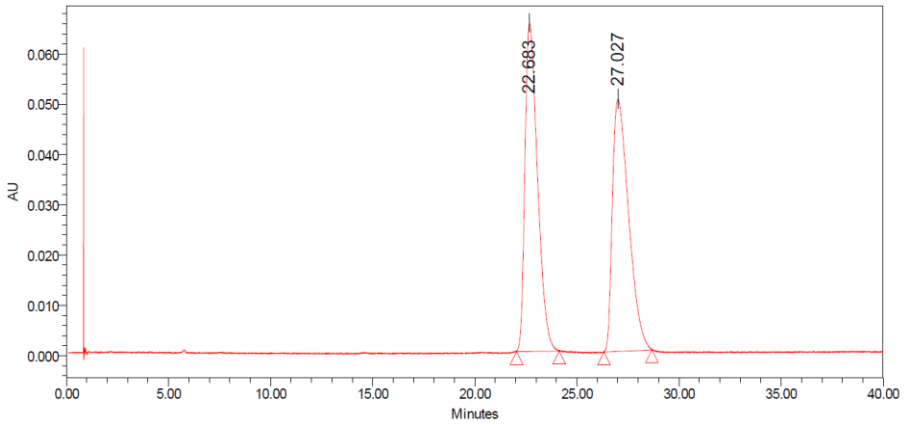


Peak#	Ret. Time	Area%
1	15.415	95.96
2	18.985	4.04
Total		100

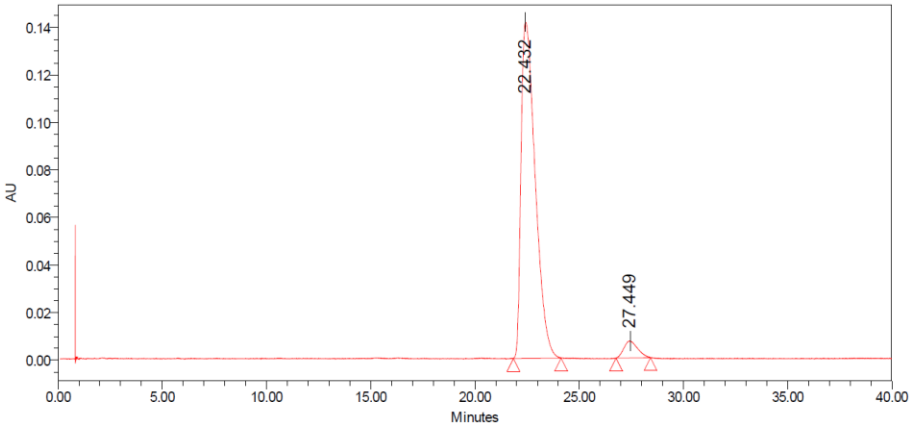


(*S*)-5-methyl-6-morpholino-6-oxohexyl thiophene-2-carboxylate (10) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 50-100% EtOAc/hexanes yielding **10** as a pale yellow oil (48.4 mg, 60%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 3.8, 1.3 Hz, 1H),

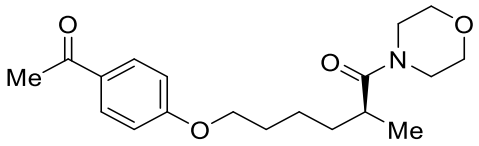
7.56 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.30 (td, *J* = 6.6, 2.5 Hz, 2H), 3.75 – 3.59 (m, 6H), 3.53 (q, *J* = 4.0 Hz, 2H), 2.68 (h, *J* = 6.8 Hz, 1H), 1.82 – 1.69 (m, 3H), 1.51 – 1.36 (m, 3H), 1.13 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.9, 162.3, 133.9, 133.3, 132.3, 127.8, 67.1, 66.9, 64.9, 46.1, 42.1, 35.1, 33.6, 28.8, 23.9, 17.6. **HRMS** (ESI) calculated for $[C_{16}H_{23}NO_4S+H]^+$ 326.1426, found 326.1412. **Chiral SFC** (Phenomenex Lux Cellulose-1, 95:5 CO_2:isopropanol): *ee* = 91%, es = 95%.



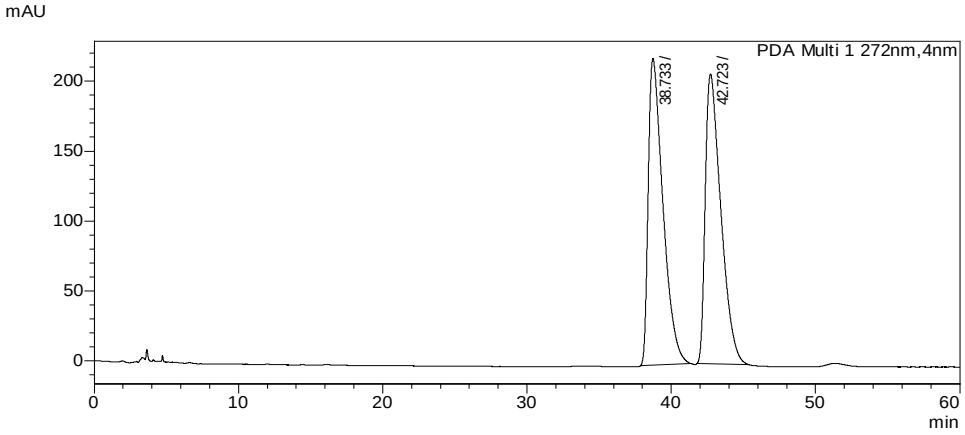
Peak#	Ret. Time	Area%
1	22.683	50.19
2	27.027	49.81
Total		100



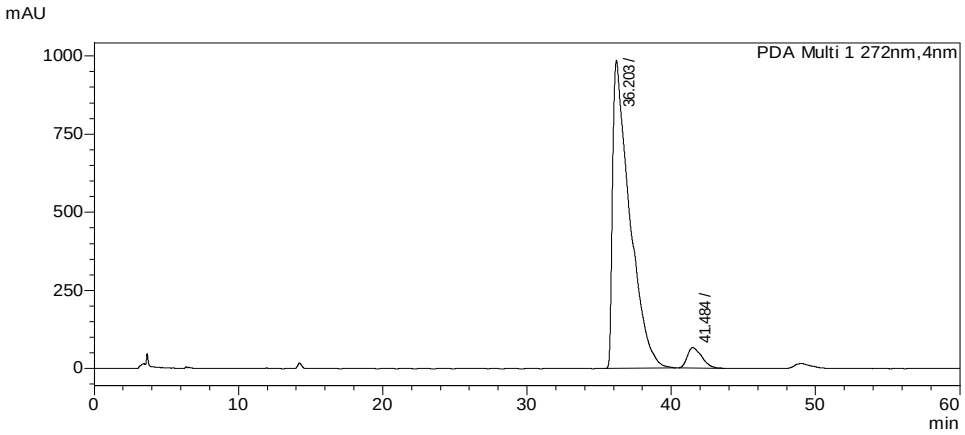
Peak#	Ret. Time	Area%
1	22.432	95.32
2	27.449	4.68
Total		100



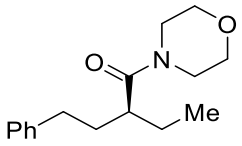
(*S*)-6-(4-acetylphenoxy)-2-methyl-1-morpholinohexan-1-one (11) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 40-75% EtOAc/hexanes yielding **11** as a colorless oil (52 mg, 62%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.95 – 7.90 (m, 2H), 6.94 – 6.88 (m, 2H), 4.06 – 3.97 (m, 2H), 3.70 – 3.65 (m, 5H), 3.65 – 3.58 (m, 1H), 3.53 (t, *J* = 4.8 Hz, 2H), 2.73 – 2.65 (m, 1H), 2.56 (s, 3H), 1.81 (dddd, *J* = 18.3, 13.5, 9.2, 7.6 Hz, 3H), 1.52 – 1.42 (m, 3H), 1.14 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.8, 175.0, 163.0, 130.6, 130.2, 114.1, 67.9, 67.1, 66.9, 46.1, 42.1, 35.2, 33.7, 29.2, 26.4, 24.0, 17.8. **HRMS** (ESI) calculated for $[C_{19}H_{27}NO_4+H]^+$ 334.2018, found 334.2003. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 90%, es = 95%.



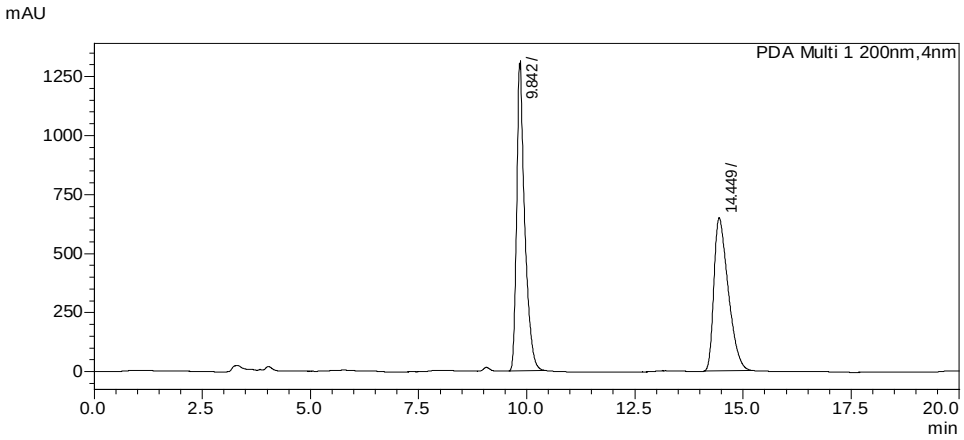
Peak#	Ret. Time	Area	Area%
1	38.733	15517933	49.97
2	42.723	15536754	50.03
Total		31054687	100



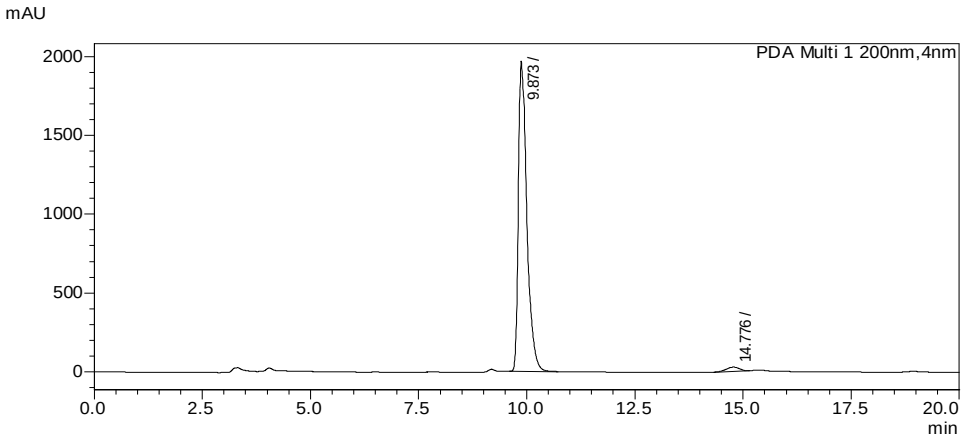
Peak#	Ret. Time	Area	Area%
1	36.203	83864254	94.774
2	41.485	4624130	5.226
Total		88488384	100



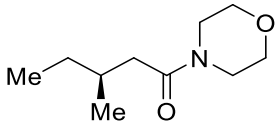
(*S*)-2-ethyl-1-morpholino-4-phenylbutan-1-one (12) was obtained from General Carbonylation Procedure A (43% NMR yield) and the crude product was purified via flash chromatography using a gradient of 20-75% EtOAc/hexanes yielding **12** as a colorless oil (19.5 mg, 30%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.30 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.20 – 7.16 (m, 2H), 3.69 (d, *J* = 2.6 Hz, 4H), 3.60 (t, *J* = 4.8 Hz, 2H), 3.37 (dtt, *J* = 18.3, 13.4, 4.3 Hz, 2H), 2.68 (ddd, *J* = 14.4, 8.8, 5.9 Hz, 1H), 2.58 – 2.48 (m, 2H), 2.06 (dtd, *J* = 14.4, 8.6, 5.9 Hz, 1H), 1.83 – 1.65 (m, 2H), 1.59 – 1.49 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.3, 141.8, 128.43, 128.41, 126.0, 67.2, 66.9, 46.0, 42.1, 41.1, 33.8, 33.5, 25.9, 12.0. **HRMS** (ESI) calculated for $[C_{16}H_{23}NO_2+H]^+$ 262.1807, found 262.1782. **Chiral HPLC** (Daicel OJ-H, 90:10 hexanes:isopropanol): *ee* = 96%, es = 97%.



Peak#	Ret. Time	Area	Area%
1	9.855	38711492	49.541
2	14.448	39428521	50.459
Total		78140013	100

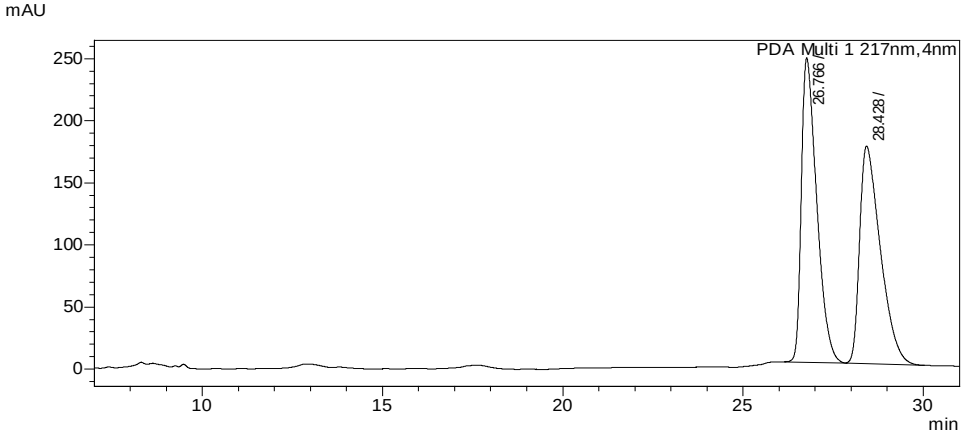


Peak#	Ret. Time	Area	Area%
1	9.873	26943391	97.887
2	14.776	581570	2.113
Total		27524961	100

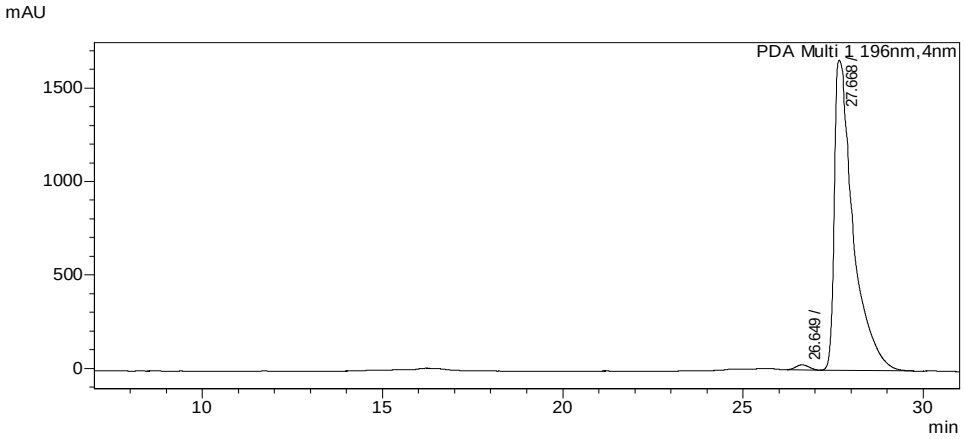


(*S*)-3-methyl-1-morpholinopentan-1-one (13) was obtained from General Carbonylation Procedure A (53% NMR yield) and the crude product was purified via flash chromatography using a gradient of 20-50% EtOAc/hexanes yielding **13** as a colorless oil (19 mg, 41%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 3.71 – 3.62 (m, 6H), 3.52 – 3.48 (m,

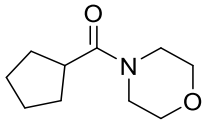
2H), 2.33 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.14 (dd, *J* = 14.6, 8.2 Hz, 1H), 1.97 – 1.86 (m, 1H), 1.46 – 1.37 (m, 1H), 1.30 – 1.18 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.4, 67.1, 66.8, 46.3, 41.9, 40.0, 32.0, 29.7, 19.5, 11.5. **HRMS** (ESI) calculated for $[C_{10}H_{19}NO_2+H]^+$ 186.1494, found 186.1475. **Chiral HPLC** (Chiralpak IF, 98:2 hexanes:isopropanol): *ee* = 98%.



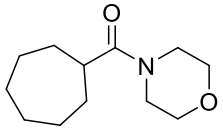
Peak#	Ret. Time	Area	Area%
1	26.767	30912633	56.41
2	28.428	23886895	43.59
Total		54799528	100



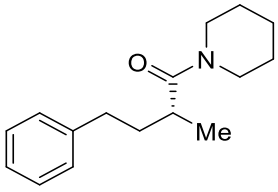
Peak#	Ret. Time	Area	Area%
1	26.649	695291	1.151
2	27.668	59721506	98.849
Total		60416796	100



Cyclopentyl(morpholino)methanone (14) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-50% EtOAc/hexanes yielding **14** as a colorless oil (27 mg, 59%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 3.70 – 3.66 (m, 4H), 3.64 (dd, *J* = 5.8, 3.9 Hz, 2H), 3.56 – 3.51 (m, 2H), 2.87 (p, *J* = 8.0 Hz, 1H), 1.91 – 1.78 (m, 4H), 1.81 – 1.74 (m, 1H), 1.76 – 1.69 (m, 1H), 1.64 – 1.53 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.8, 67.0, 66.8, 46.0, 42.2, 40.9, 30.1, 26.0. **HRMS** (ESI) calculated for $[C_{10}H_{17}NO_2+H]^+$ 184.1338, found 184.1327.

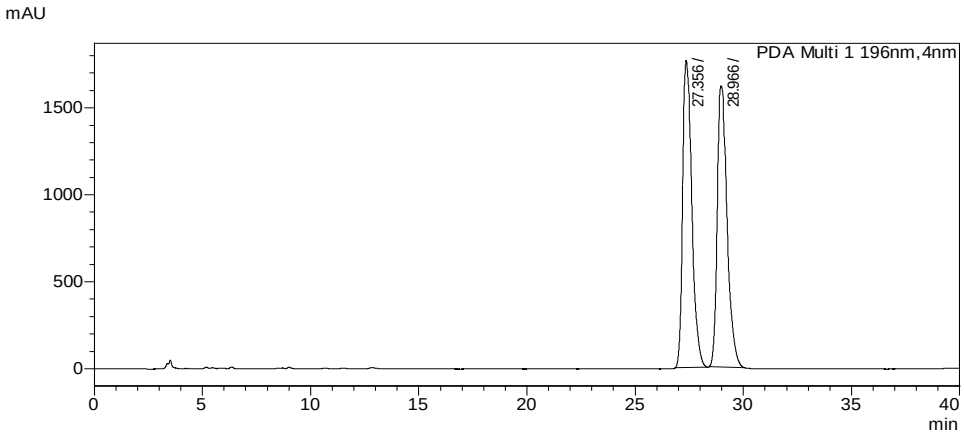


Cycloheptyl(morpholino)methanone (15) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-50% EtOAc/hexanes yielding **15** as a white solid (31 mg, 59%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 3.68 (t, *J* = 5.5 Hz, 4H), 3.62 (t, *J* = 4.7 Hz, 2H), 3.50 (t, *J* = 4.8 Hz, 2H), 2.61 (tt, *J* = 9.7, 3.7 Hz, 1H), 1.86 – 1.78 (m, 2H), 1.81 – 1.76 (m, 2H), 1.75 – 1.66 (m, 2H), 1.58 (dq, *J* = 8.7, 5.5, 4.0 Hz, 4H), 1.46 (tdd, *J* = 15.4, 8.8, 4.1 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.9, 67.1, 66.8, 46.1, 42.0, 41.4, 31.2, 28.2, 26.7. **HRMS** (ESI) calculated for $[C_{12}H_{21}NO_2+H]^+$ 212.1651, found 212.1641.

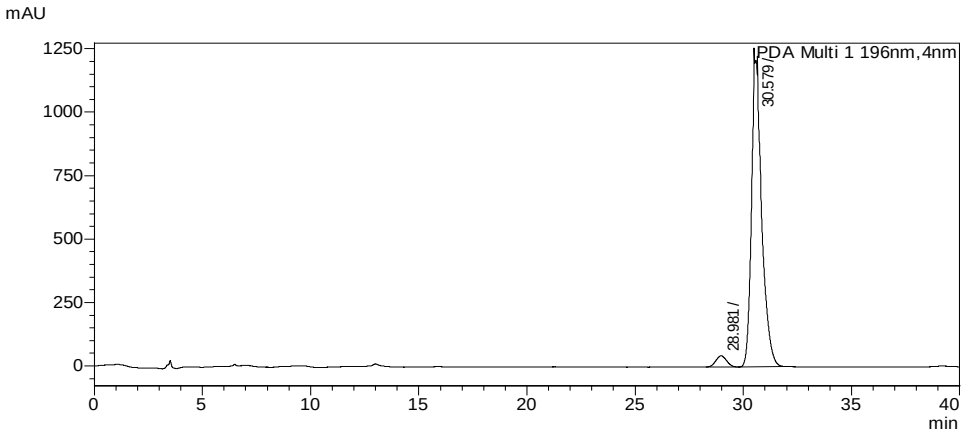


(*R*)-2-methyl-4-phenyl-1-(piperidin-1-yl)butan-1-one (16) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-40% EtOAc/hexanes yielding **16** as a pale yellow oil (37.5 mg, 61%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.33 – 7.26 (m, 2H), 7.23 – 7.17 (m, 3H), 3.65

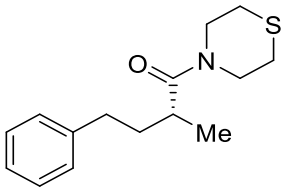
(ddd, *J* = 13.2, 6.7, 4.4 Hz, 1H), 3.54 (ddd, *J* = 13.0, 7.0, 4.3 Hz, 1H), 3.33 (qt, *J* = 13.4, 5.5 Hz, 2H), 2.73 – 2.63 (m, 2H), 2.60 (ddd, *J* = 13.7, 8.8, 6.7 Hz, 1H), 2.08 (dddd, *J* = 13.6, 9.0, 7.5, 6.2 Hz, 1H), 1.76 – 1.59 (m, 3H), 1.60 – 1.48 (m, 3H), 1.15 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.4, 142.1, 128.5, 128.3, 125.8, 46.4, 42.9, 35.6, 34.3, 33.6, 26.8, 25.8, 24.7, 17.7. **HRMS** (ESI) calculated for $[C_{16}H_{23}NO+H]^+$ 246.1858, found 246.1860. **Chiral HPLC** (Chiralpak IE, 95:5 hexanes:isopropanol): *ee* = 93%, es = 94%.



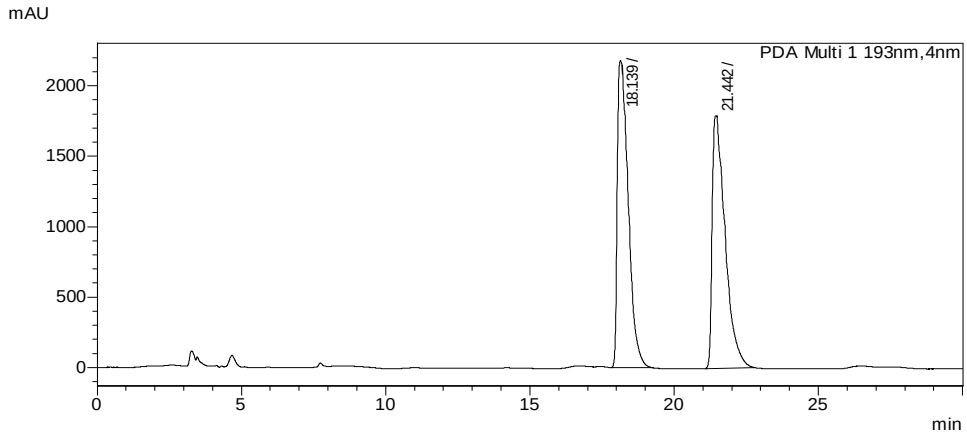
Peak#	Ret. Time	Area	Area%
1	27.356	52206489	50.462
2	28.966	51250763	49.538
Total		103457252	100



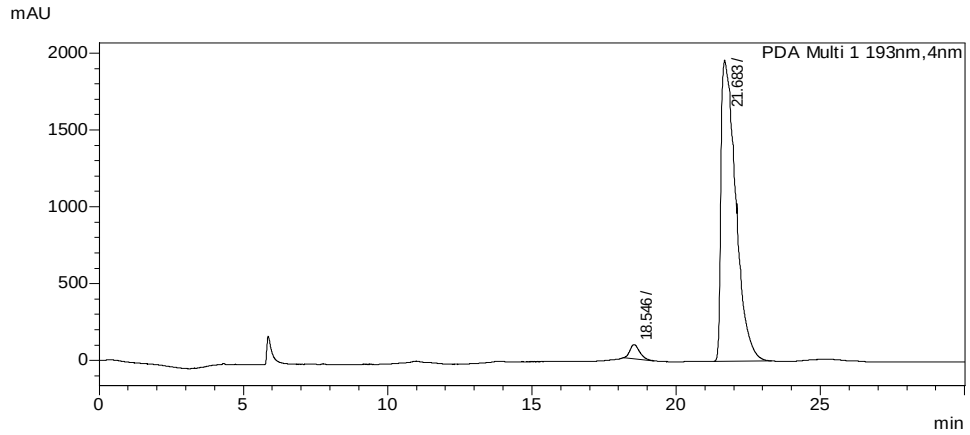
Peak#	Ret. Time	Area	Area%
1	28.981	1536174	3.69
2	30.579	40089340	96.31
Total		41625513	100



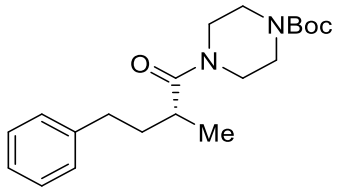
(*R*)-2-methyl-4-phenyl-1-thiomorpholinobutan-1-one (17) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **17** as a pale yellow oil (39.2 mg, 60%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.41 – 7.26 (m, 2H), 7.26 – 7.11 (m, 3H), 3.98 (dt, *J* = 14.2, 4.9 Hz, 1H), 3.86 (qd, *J* = 12.4, 10.3, 5.3 Hz, 1H), 3.62 (qt, *J* = 14.1, 5.1 Hz, 2H), 2.64 (tdd, *J* = 14.3, 12.2, 6.7 Hz, 6H), 2.52 (t, *J* = 5.1 Hz, 2H), 2.08 (tdd, *J* = 13.7, 8.8, 6.6 Hz, 1H), 1.83 – 1.66 (m, 2H), 1.16 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.7, 141.7, 128.5, 128.4, 126.0, 48.0, 44.4, 35.5, 34.3, 33.4, 28.1, 27.6, 17.7. **HRMS** (ESI) calculated for $[C_{15}H_{22}NOS+H]^+$ 264.1422, found 264.1407. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 94%, es = 95%.



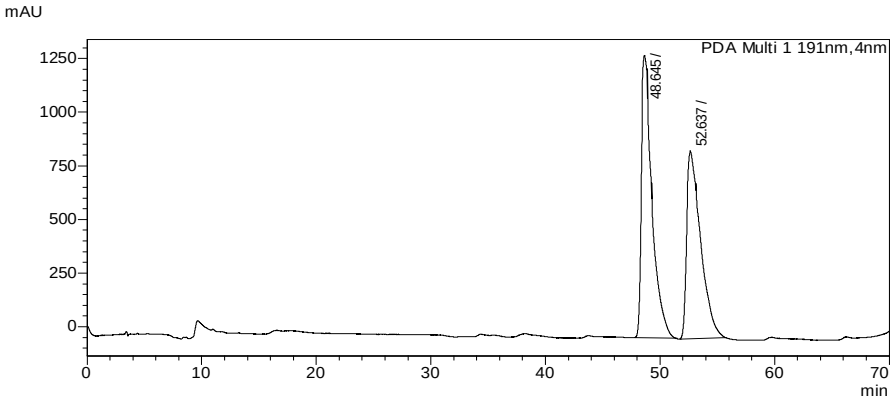
Peak#	Ret. Time	Area	Area%
1	18.139	57516633	50.782
2	21.442	55745812	49.218
Total		113262445	100



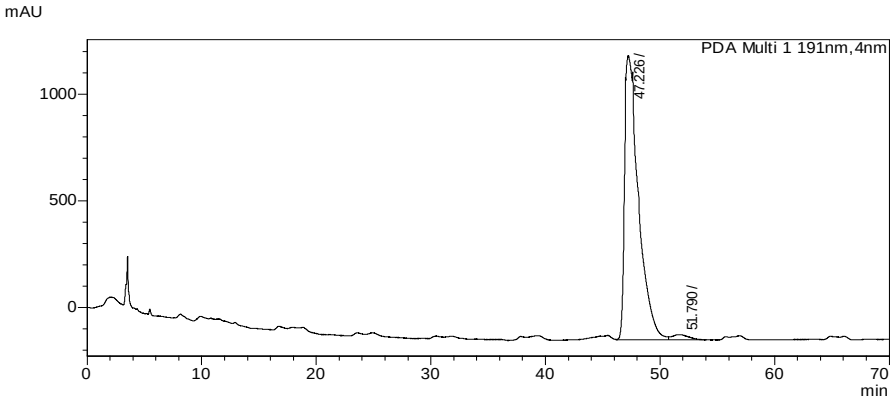
Peak#	Ret. Time	Area	Area%
1	18.546	2175038	3.03
2	21.683	69614730	96.97
Total		71789768	100



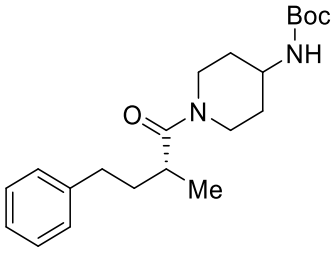
***tert*-Butyl (*R*)-4-(2-methyl-4-phenylbutanoyl)piperazine-1-carboxylate (18)** was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **18** as a colorless oil in a mixture of conformers (61 mg, 70%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 2H), 7.22 – 7.13 (m, 3H), 4.67 – 4.48 (m, 2H), 3.73 – 3.62 (m, 2H), 3.03 – 2.96 (m, 1H), 2.80 – 2.69 (m, 1H), 2.69 – 2.52 (m, 3H), 2.09 – 2.01 (m, 1H), 2.00 – 1.91 (m, 1H), 1.72 – 1.63 (m, 1H), 1.51 – 1.41 (m, 9H), 1.28 – 1.16 (m, 1H), 1.15 – 1.10 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 174.5, 155.1, 141.9, 141.8, 128.47, 128.45, 128.38, 128.35, 125.94, 125.90, 79.5, 48.0, 44.1, 40.8, 40.7, 35.53, 35.51, 34.3, 34.2, 33.5, 33.41, 33.39, 33.3, 32.3, 32.1, 28.4, 17.8, 17.5. **HRMS** (ESI) calculated for $[C_{20}H_{30}N_2O_3+H]^+$ 347.2335, found 347.2321. **Chiral HPLC** (Chiralpak IE, 95:5 hexanes:isopropanol): *ee* = 96%, es = 97%.



Peak#	Ret. Time	Area	Area%
1	48.645	84196139	53.353
2	52.637	73612782	46.647
Total		157808921	100

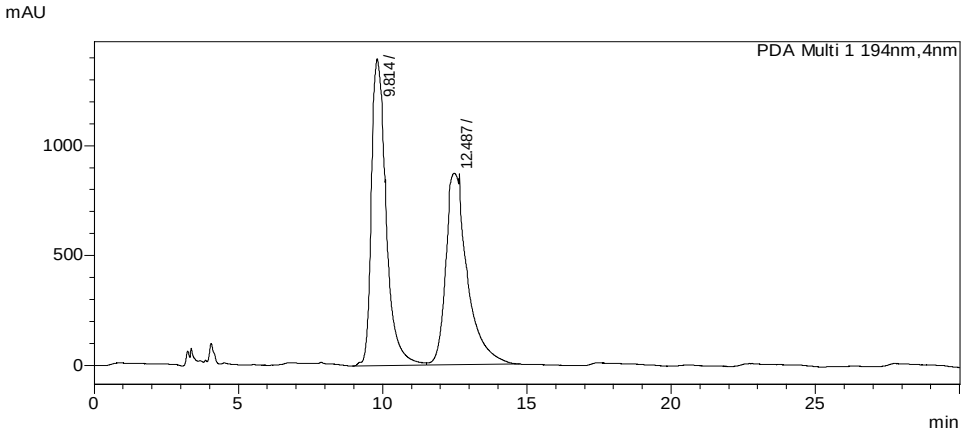


Peak#	Ret. Time	Area	Area%
1	47.226	111938873	97.818
2	51.79	2496843	2.182
Total		114435716	100

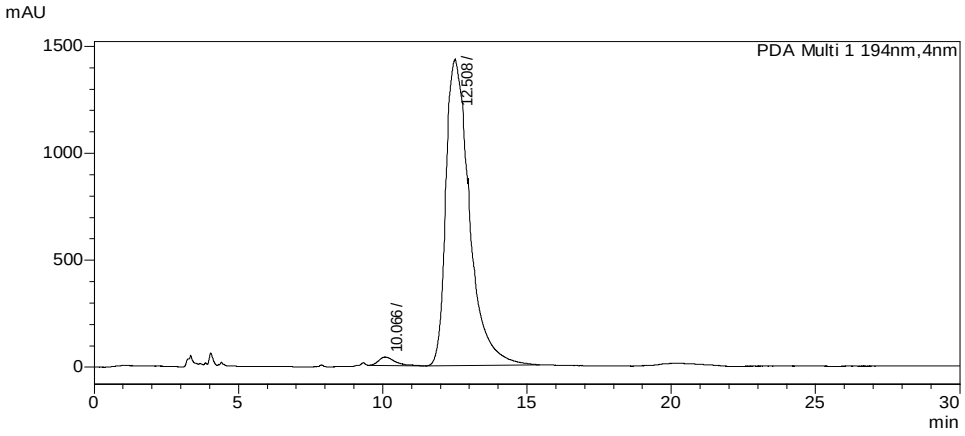


***tert*-Butyl (*R*)-(1-(2-methyl-4-phenylbutanoyl)piperidin-4-yl)carbamate (19)** was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **19** as a pale

yellow solid in a mixture of rotamers (55 mg, 61%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 2H), 7.18 (dt, *J* = 18.1, 7.8 Hz, 3H), 4.55 (t, *J* = 11.6 Hz, 2H), 3.72 – 3.62 (m, 2H), 3.01 (ddd, *J* = 14.2, 11.7, 2.8 Hz, 1H), 2.75 (dd, *J* = 22.7, 11.9 Hz, 1H), 2.62 (dtd, *J* = 45.5, 14.6, 14.1, 7.2 Hz, 3H), 2.09 – 2.00 (m, 1H), 1.99 – 1.91 (m, 2H), 1.69 (dt, *J* = 13.6, 6.9 Hz, 1H), 1.46 (d, *J* = 4.4 Hz, 9H), 1.33 – 1.18 (m, 2H), 1.13 (t, *J* = 5.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 174.5, 155.1, 141.9, 141.8, 128.5, 128.38, 128.36, 125.94, 125.90, 79.6, 48.0, 44.1, 40.8, 40.7, 35.5, 34.28, 34.25, 33.5, 33.41, 33.40, 33.3, 32.4, 32.2, 28.4, 17.7, 17.5. **HRMS** (ESI) calculated for $[C_{21}H_{32}N_2O_3+H]^+$ 361.2491, found 361.2473. **Chiral HPLC** (Daicel OJ-H, 90:10 hexanes:isopropanol): *ee* = 96%, es = 97%.

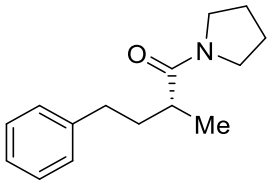


Peak#	Ret. Time	Area	Area%
1	9.814	49648452	52.317
2	12.487	45250134	47.683
Total		94898586	100

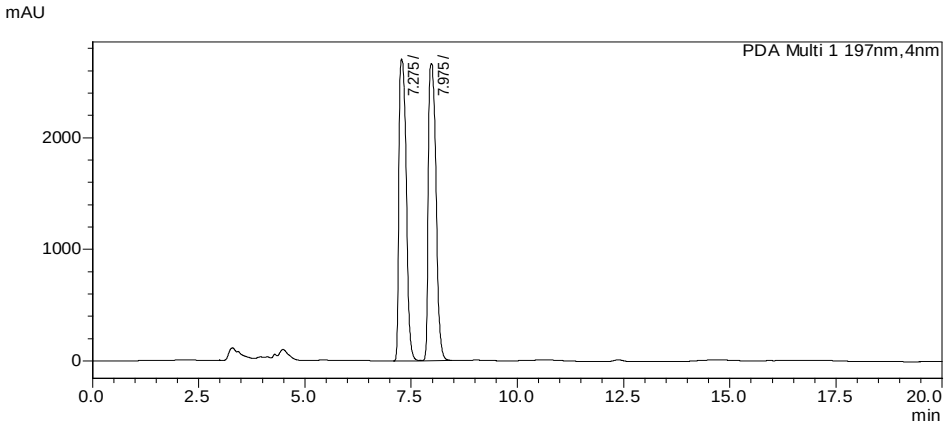


Peak#	Ret. Time	Area	Area%
1	10.066	1563424	1.887

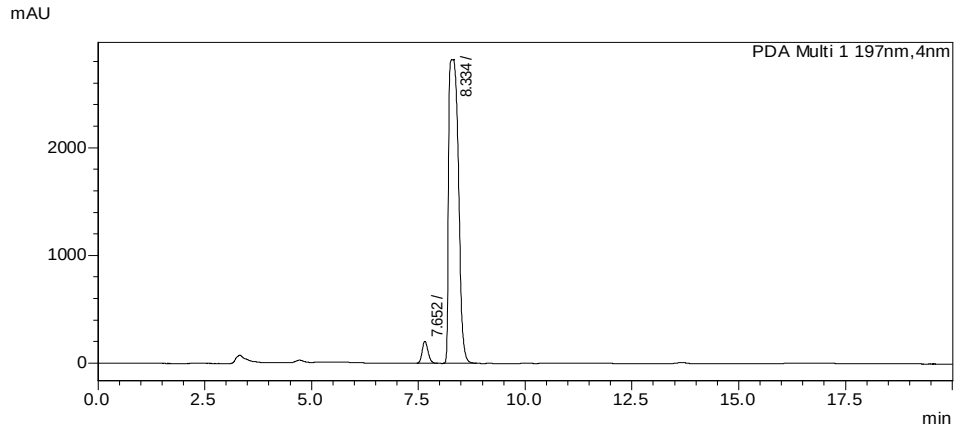
2	12.508	81307904	98.113
Total		82871328	100



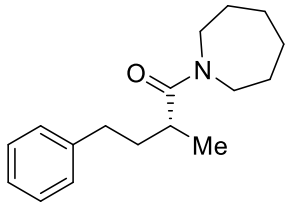
(*R*)-2-methyl-4-phenyl-1-(pyrrolidin-1-yl)butan-1-one (20) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 20-75% EtOAc/hexanes yielding **20** as a pale yellow oil (35 mg, 61%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.25 – 7.17 (m, 3H), 3.50 (t, *J* = 6.8 Hz, 2H), 3.33 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.25 (dt, *J* = 9.8, 6.7 Hz, 1H), 2.68 (ddd, *J* = 14.6, 8.9, 5.9 Hz, 1H), 2.61 (ddd, *J* = 13.6, 8.8, 7.0 Hz, 1H), 2.50 (ddd, *J* = 10.0, 8.2, 4.4 Hz, 1H), 2.14 – 2.04 (m, 1H), 1.97 – 1.82 (m, 4H), 1.71 (dddd, *J* = 13.1, 8.9, 7.0, 5.8 Hz, 1H), 1.16 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.8, 142.0, 128.5, 128.3, 125.8, 46.3, 45.7, 37.1, 35.3, 33.6, 26.1, 24.4, 17.4. **HRMS** (ESI) calculated for $[C_{15}H_{21}NO+H]^+$ 232.1701, found 232.1704. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 92%, es = 93%.



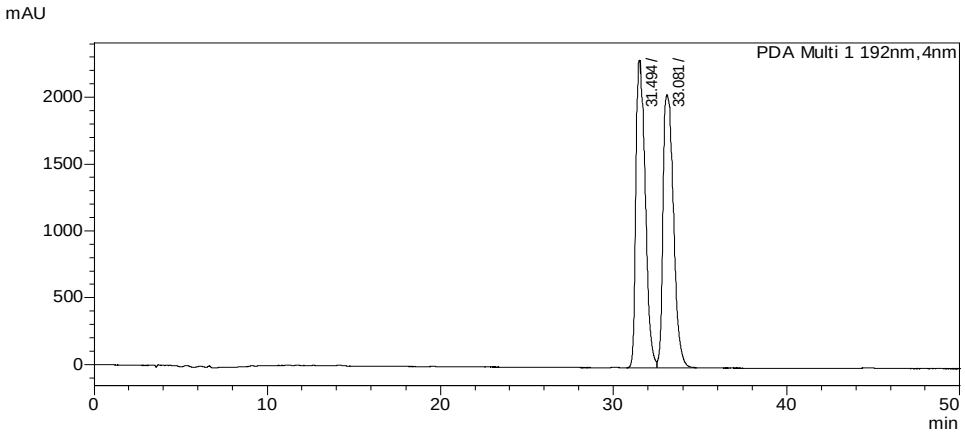
Peak#	Ret. Time	Area	Area%
1	7.275	32231433	49.195
2	7.975	33285894	50.805
Total		65517327	100



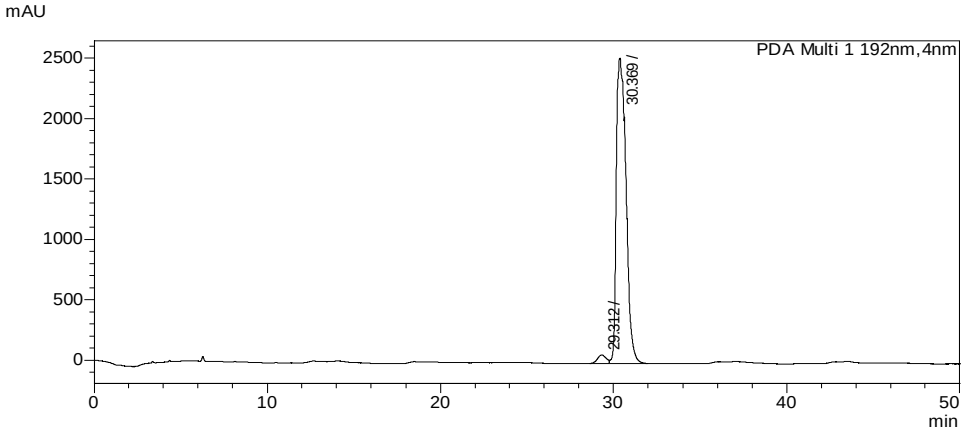
Peak#	Ret. Time	Area	Area%
1	7.652	1932688	4.16
2	8.334	44527812	95.84
Total		46460501	100



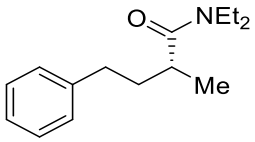
(*R*)-1-(azepan-1-yl)-2-methyl-4-phenylbutan-1-one (21) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-50% EtOAc/hexanes yielding **21** as a colorless oil (35 mg, 54%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.19 (dd, *J* = 8.5, 7.1 Hz, 2H), 3.59 (dt, *J* = 13.8, 6.2 Hz, 1H), 3.52 (dt, *J* = 13.7, 6.1 Hz, 1H), 3.40 – 3.28 (m, 2H), 2.66 (ddd, *J* = 15.6, 9.4, 6.5 Hz, 2H), 2.60 (ddd, *J* = 13.7, 9.1, 6.4 Hz, 1H), 2.13 – 2.04 (m, 1H), 1.77 – 1.68 (m, 3H), 1.68 – 1.51 (m, 6H), 1.17 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.9, 142.1, 128.4, 128.3, 125.8, 47.7, 46.2, 35.8, 34.9, 33.7, 29.4, 27.8, 26.8, 26.8, 18.1. **HRMS** (ESI) calculated for $[C_{17}H_{25}NO+H]^+$ 260.2014, found 260.2000. **Chiral HPLC** (Chiralpak IE, 95:5 hexanes:isopropanol): *ee* = 95%, es = 96%.



Peak#	Ret. Time	Area	Area%
1	31.494	86771051	50.174
2	33.081	86168470	49.826
Total		172939521	100

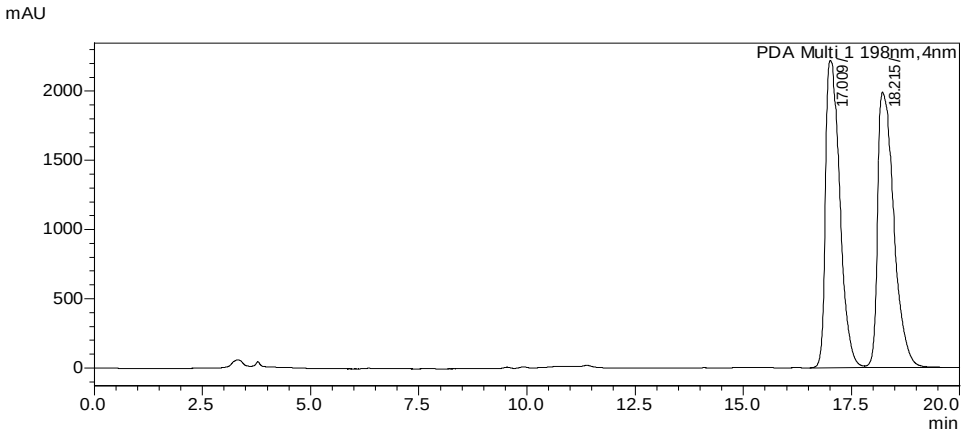


Peak#	Ret. Time	Area	Area%
1	29.312	2455913	2.431
2	30.369	98564417	97.569
Total		101020330	100

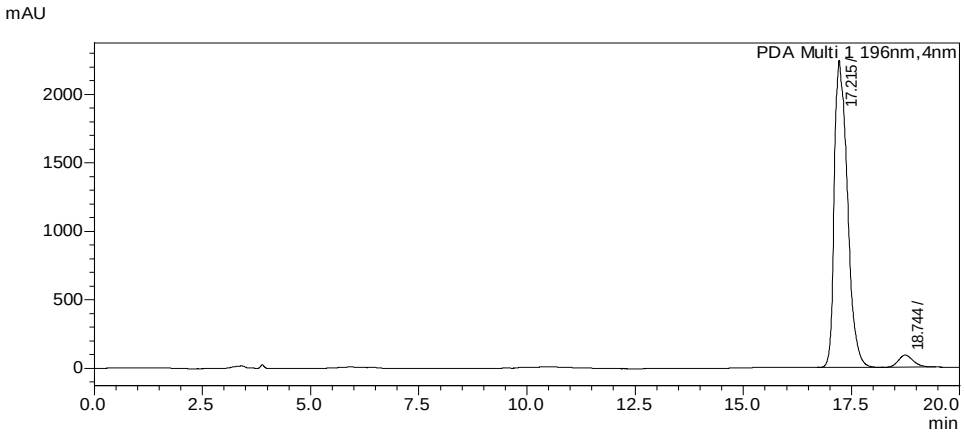


(*R*)-*N*,*N*-diethyl-2-methyl-4-phenylbutanamide (22) was obtained from General Carbonylation Procedure A (24 h) and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **22** as a pale yellow oil (32 mg, 55%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.22 – 7.17

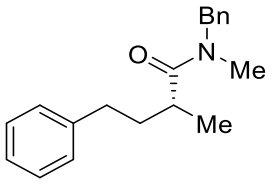
(m, 3H), 3.45 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.34 (dq, *J* = 14.0, 7.1 Hz, 1H), 3.25 – 3.16 (m, 2H), 2.69 – 2.56 (m, 3H), 2.06 (dddd, *J* = 13.9, 9.1, 7.8, 6.3 Hz, 1H), 1.77 – 1.67 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.6, 142.0, 128.5, 128.3, 125.8, 41.8, 40.3, 35.9, 34.7, 33.6, 18.1, 14.8, 13.2. **HRMS** (ESI) calculated for $[C_{15}H_{23}NO+H]^+$ 234.1858, found 234.1860. **Chiral HPLC** (Chiralpak IF, 98:2 hexanes:isopropanol): *ee* = 91%, es = 92%.



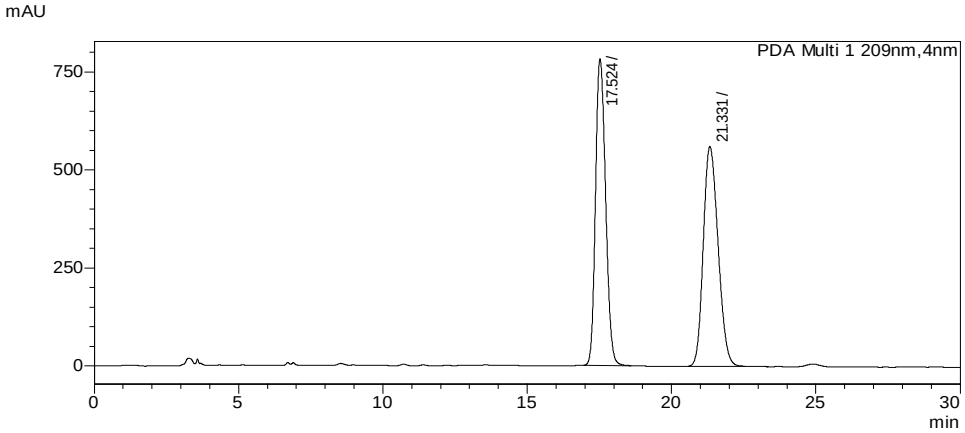
Peak#	Ret. Time	Area	Area%
1	17.009	51182177	49.666
2	18.215	51871090	50.334
Total		103053267	100



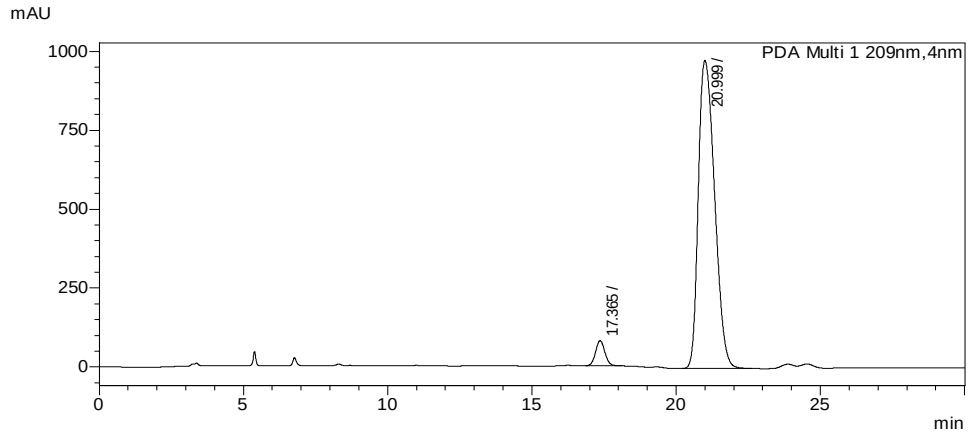
Peak#	Ret. Time	Area	Area%
1	17.215	47336897	95.612
2	18.739	2172677	4.388
Total		49509574	100



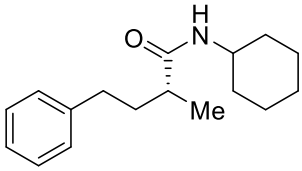
(*R*)-*N*-benzyl-*N*,2-dimethyl-4-phenylbutanamide (23) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **23** as a pale yellow oil in a mixture of rotamers (51 mg, 72%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.44 – 7.23 (m, 12H), 7.18 (ddd, *J* = 18.1, 10.8, 7.3 Hz, 6H), 7.11 (d, *J* = 7.6 Hz, 2H), 4.70 (d, *J* = 14.6 Hz, 1H), 4.59 (d, *J* = 14.6 Hz, 1H), 4.52 – 4.42 (m, 2H), 3.01 (s, 3H), 2.84 (s, 3H), 2.73 (ddt, *J* = 13.6, 9.4, 6.4 Hz, 3H), 2.64 (dq, *J* = 13.5, 6.0 Hz, 2H), 2.57 (ddd, *J* = 19.7, 9.9, 5.2 Hz, 1H), 2.20 – 2.05 (m, 2H), 1.75 (ddt, *J* = 13.6, 9.1, 6.4 Hz, 2H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.18 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.0, 176.3, 142.0, 141.9, 137.7, 137.0, 128.9, 128.6, 128.5, 128.40, 128.38, 128.0, 127.5, 127.3, 126.3, 125.9, 53.1, 50.9, 35.9, 35.6, 35.0, 34.8, 34.6, 34.4, 33.6, 18.0, 17.6. **HRMS** (ESI) calculated for $[C_{19}H_{23}NO+H]^+$ 282.1858, found 282.1844. **Chiral HPLC** (Chiralpak IF, 95:5 hexanes:isopropanol): *ee* = 91%, es = 92%.



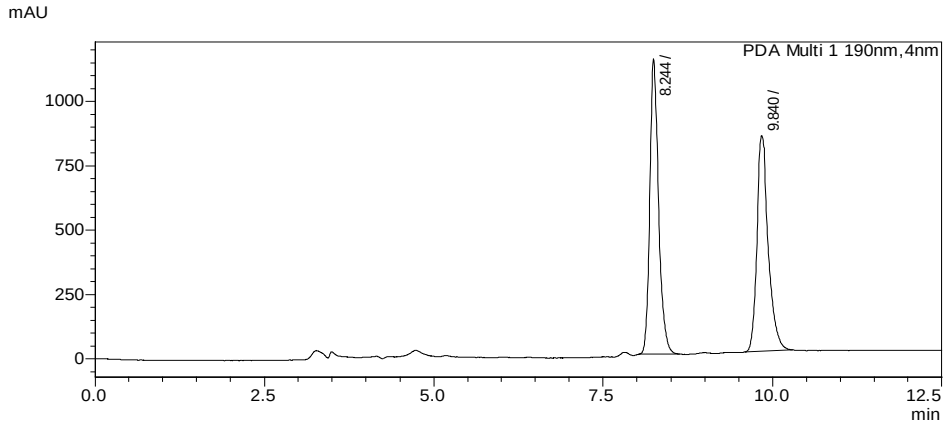
Peak#	Ret. Time	Area	Area%
1	17.524	18224315	48.844
2	21.331	19086603	51.156
Total		37310918	100



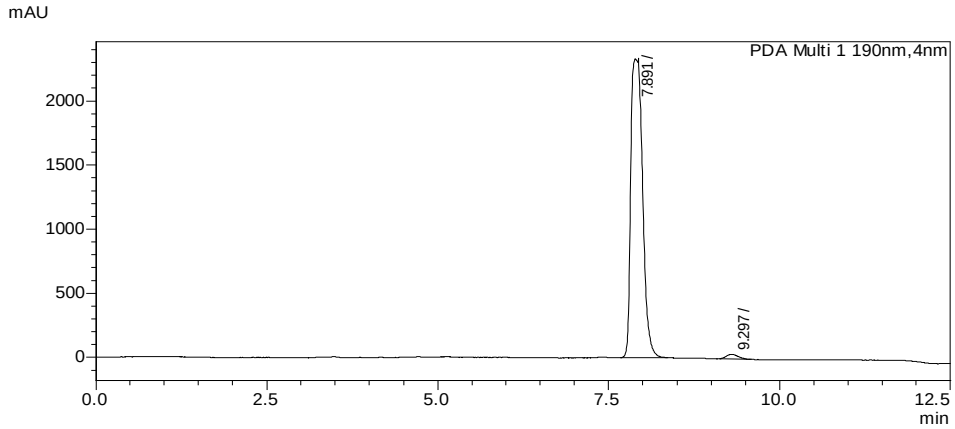
Peak#	Ret. Time	Area	Area%
1	17.365	1800513	4.492
2	20.999	38284961	95.508
Total		40085474	100



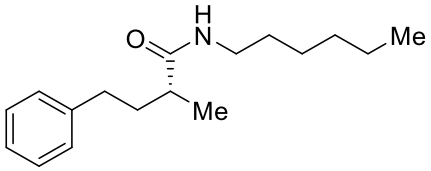
(*R*)-*N*-cyclohexyl-2-methyl-4-phenylbutanamide (24) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **24** as a colorless oil (43.3 mg, 67%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 7.7 Hz, 2H), 7.20 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 3H), 5.32 (s, 1H), 3.82 (dddd, *J* = 14.7, 10.8, 8.1, 3.9 Hz, 1H), 2.68 (ddd, *J* = 14.7, 9.5, 5.6 Hz, 1H), 2.59 (ddd, *J* = 13.8, 9.3, 6.9 Hz, 1H), 2.17 – 2.10 (m, 1H), 2.06 – 1.95 (m, 2H), 1.92 (dtd, *J* = 12.0, 3.8, 1.8 Hz, 1H), 1.78 – 1.68 (m, 3H), 1.67 – 1.61 (m, 1H), 1.39 (dddd, *J* = 13.6, 12.1, 10.4, 6.1 Hz, 2H), 1.25 – 1.08 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.1, 141.9, 128.43, 128.39, 125.9, 47.9, 40.9, 35.8, 33.6, 33.4, 33.2, 25.6, 24.9, 18.1. **HRMS** (ESI) calculated for $[C_{17}H_{25}NO+H]^+$ 260.2014, found 260.2000. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 97%, es = 98%.



Peak#	Ret. Time	Area	Area%
1	8.244	10305665	51.644
2	9.84	9649363	48.356
Total		19955028	100

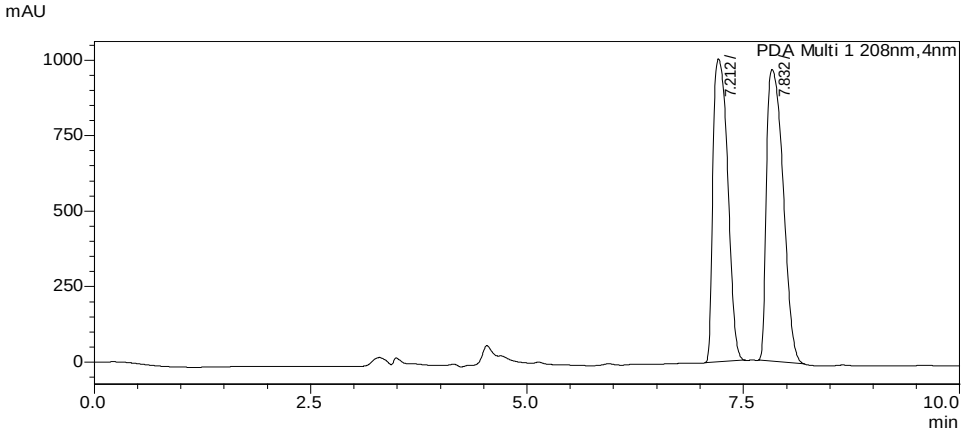


Peak#	Ret. Time	Area	Area%
1	7.891	27986470	98.426
2	9.297	447648	1.574
Total		28434118	100

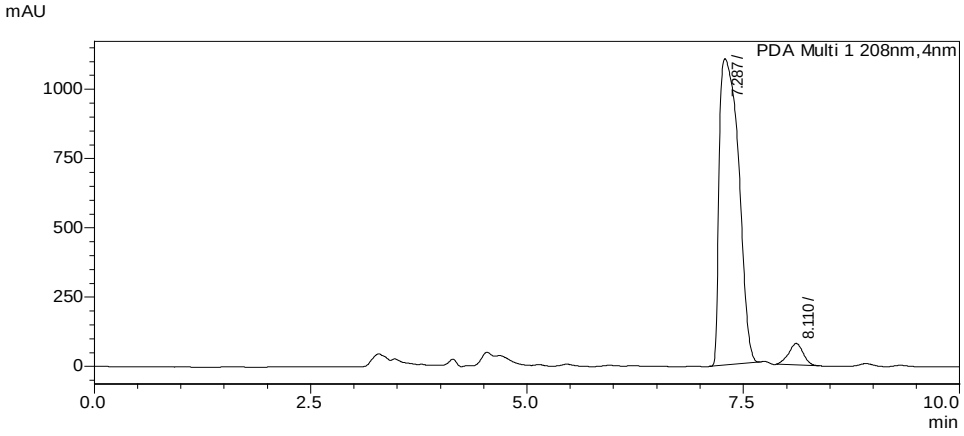


(*R*)-*N*-hexyl-2-methyl-4-phenylbutanamide (25) was obtained from General Carbonylation Procedure A (24 h) and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **25** as a colorless oil

(39 mg, 60%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 – 7.28 (m, 2H), 7.23 – 7.17 (m, 3H), 5.49 (t, *J* = 5.7 Hz, 1H), 3.27 (dtdd, *J* = 20.5, 13.3, 7.2, 5.7 Hz, 2H), 2.67 (ddd, *J* = 14.8, 9.5, 5.8 Hz, 1H), 2.59 (ddd, *J* = 13.9, 9.3, 6.8 Hz, 1H), 2.22 – 2.13 (m, 1H), 2.03 (dtd, *J* = 14.3, 8.9, 5.8 Hz, 1H), 1.71 (ddt, *J* = 12.9, 9.5, 6.3 Hz, 1H), 1.52 (dd, *J* = 10.6, 4.5 Hz, 2H), 1.39 – 1.26 (m, 6H), 1.18 (d, *J* = 6.9 Hz, 3H), 0.93 – 0.88 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.0, 141.8, 128.40, 128.39, 125.9, 40.9, 39.4, 35.7, 33.6, 31.5, 29.7, 26.6, 22.6, 18.1, 14.0. **HRMS** (ESI) calculated for $[C_{17}H_{27}NO+H]^+$ 262.2171, found 262.2156. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 91%, es = 92%.

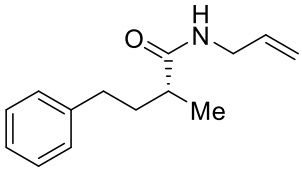


Peak#	Ret. Time	Area	Area%
1	7.212	11845806	47.882
2	7.832	12893954	52.118
Total		24739760	100

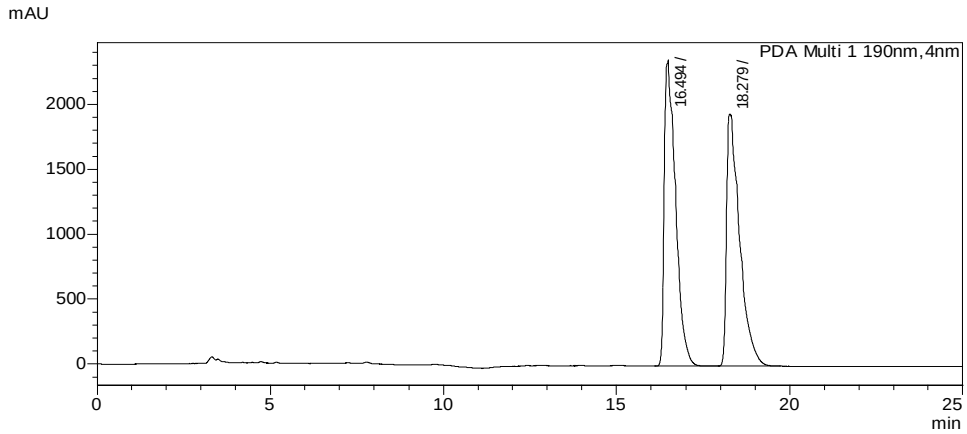


Peak#	Ret. Time	Area	Area%
1	7.288	16315738	95.579
2	8.11	754612	4.421

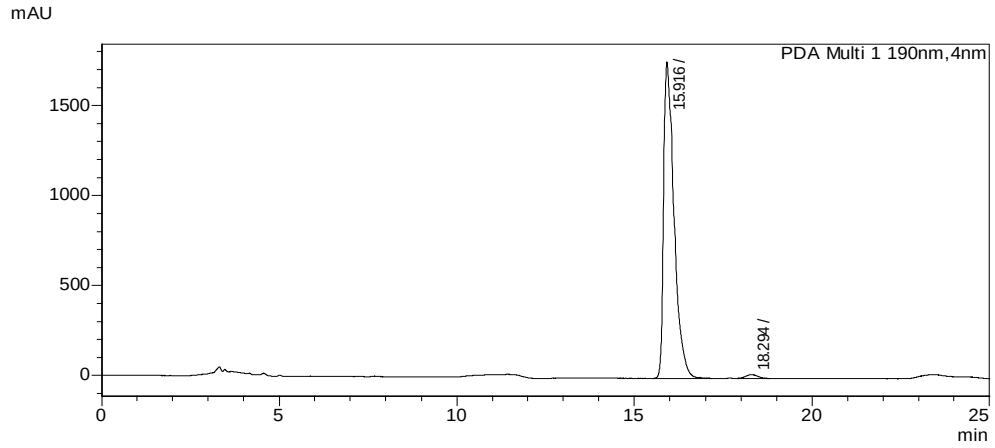
Total		17070350	100



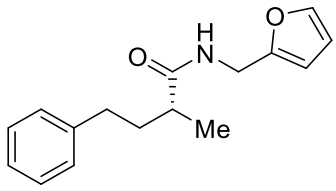
(*R*)-*N*-allyl-2-methyl-4-phenylbutanamide (26) was obtained from General Carbonylation Procedure A (24 h) and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **26** as a cream colored solid (35 mg, 64%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 5.87 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.64 (t, *J* = 5.9 Hz, 1H), 5.21 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.16 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.92 (qt, *J* = 5.7, 1.6 Hz, 2H), 2.68 (ddd, *J* = 13.7, 9.5, 5.9 Hz, 1H), 2.61 (ddd, *J* = 13.8, 9.3, 6.6 Hz, 1H), 2.28 – 2.19 (m, 1H), 2.04 (dddd, *J* = 14.0, 9.3, 8.3, 5.9 Hz, 1H), 1.73 (dddd, *J* = 13.5, 9.5, 6.6, 5.9 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.0, 141.8, 134.4, 128.4, 125.9, 116.4, 41.8, 40.8, 35.7, 33.6, 18.1. **HRMS** (ESI) calculated for $[C_{14}H_{19}NO+H]^+$ 218.1545, found 218.1534. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 97%, es = 98%.



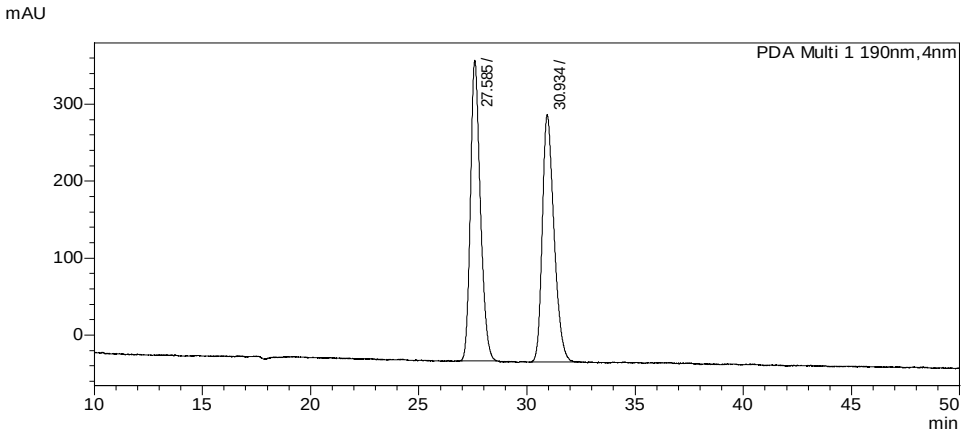
Peak#	Ret. Time	Area	Area%
1	16.494	53722713	51.194
2	18.279	51217627	48.806
Total		104940339	100



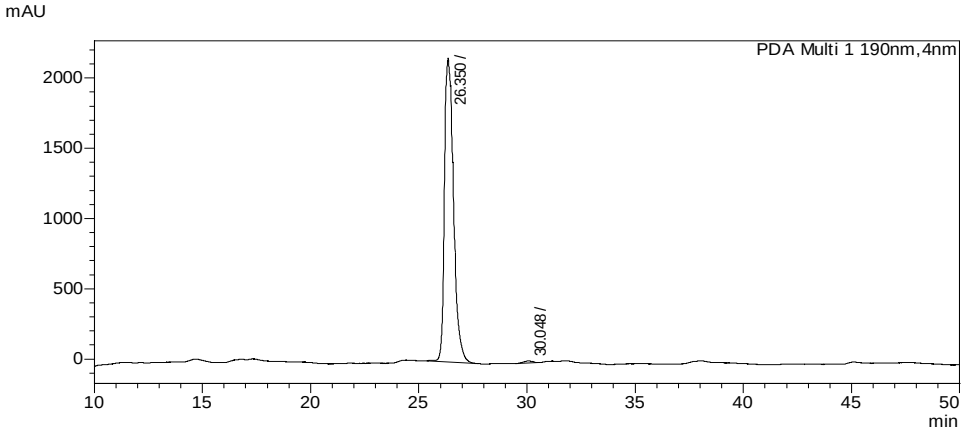
Peak#	Ret. Time	Area	Area%
1	15.916	35869165	98.65
2	18.294	490741	1.35
Total		36359905	100



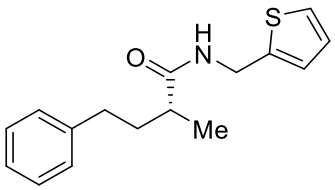
(*R*)-*N*-(furan-2-ylmethyl)-2-methyl-4-phenylbutanamide (27) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 20-40% EtOAc/hexanes yielding **27** as a white, fluffy solid (43 mg, 67%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 1.8 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.24 – 7.17 (m, 1H), 7.18 – 7.14 (m, 2H), 6.35 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.26 (d, *J* = 3.2 Hz, 1H), 5.87 (t, *J* = 5.6 Hz, 1H), 4.52 (dd, *J* = 15.5, 5.7 Hz, 1H), 4.42 (dd, *J* = 15.5, 5.3 Hz, 1H), 2.66 (ddd, *J* = 14.7, 9.4, 5.7 Hz, 1H), 2.58 (ddd, *J* = 13.8, 9.2, 6.9 Hz, 1H), 2.26 – 2.17 (m, 1H), 2.08 – 1.99 (m, 1H), 1.73 (dddd, *J* = 13.1, 9.4, 6.9, 5.7 Hz, 1H), 1.20 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.9, 151.5, 142.2, 141.7, 128.4, 125.9, 110.5, 107.4, 40.7, 36.4, 35.7, 33.5, 18.0. **HRMS** (ESI) calculated for $[C_{16}H_{19}NO_2+H]^+$ 258.1494, found 258.1481. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 99%, es = 99%.



Peak#	Ret. Time	Area	Area%
1	27.585	12432345	50.591
2	30.934	12142105	49.409
Total		24574450	100

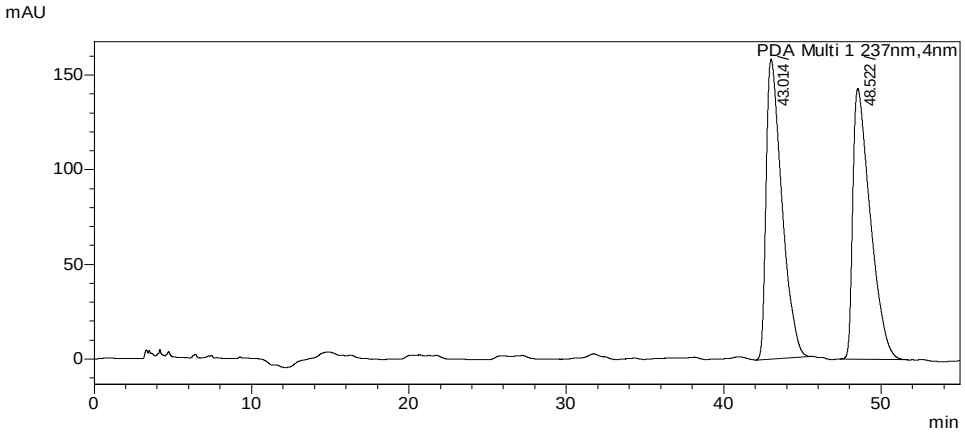


Peak#	Ret. Time	Area	Area%
1	26.35	62863396	99.305
2	30.048	439810	0.695
Total		63303206	100

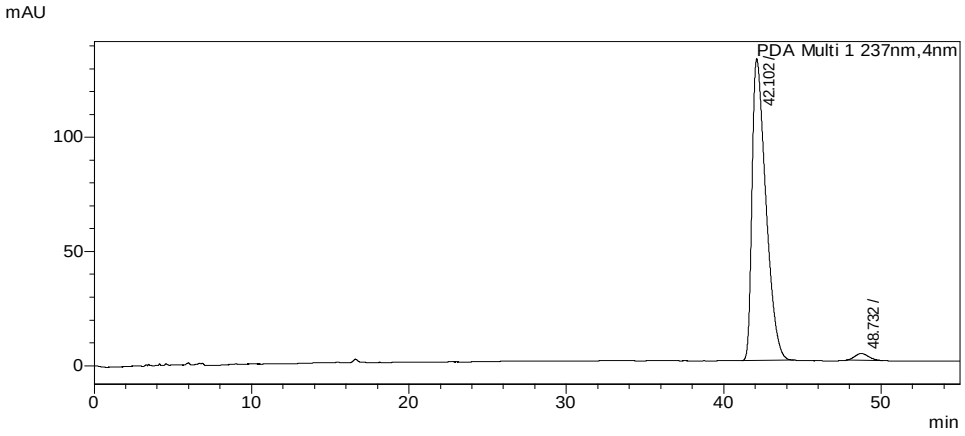


(*R*)-2-methyl-4-phenyl-*N*-(thiophen-2-ylmethyl)butanamide (28) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 20-40% EtOAc/hexanes yielding **28** as a cream

colored solid (48 mg, 70%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.25 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.20 – 7.14 (m, 2H), 7.01 – 6.95 (m, 2H), 5.90 (t, *J* = 5.7 Hz, 1H), 4.68 (ddd, *J* = 15.3, 5.8, 0.8 Hz, 1H), 4.60 (ddd, *J* = 15.2, 5.6, 0.8 Hz, 1H), 2.68 (ddd, *J* = 14.8, 9.5, 5.7 Hz, 1H), 2.59 (ddd, *J* = 13.8, 9.3, 6.8 Hz, 1H), 2.26 – 2.17 (m, 1H), 2.10 – 2.01 (m, 1H), 1.74 (dddd, *J* = 13.5, 9.5, 6.8, 5.7 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.6, 141.7, 141.3, 128.43, 128.42, 126.9, 125.95, 125.92, 125.2, 40.7, 38.2, 35.7, 33.5, 18.0. **HRMS** (ESI) calculated for $[C_{16}H_{19}NOS+H]^+$ 274.1266, found 274.1268. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 96%, es = 97%.

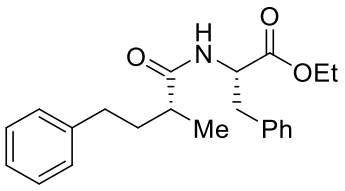


Peak#	Ret. Time	Area	Area%
1	43.014	11032049	49.96
2	48.522	11049670	50.04
Total		22081719	100

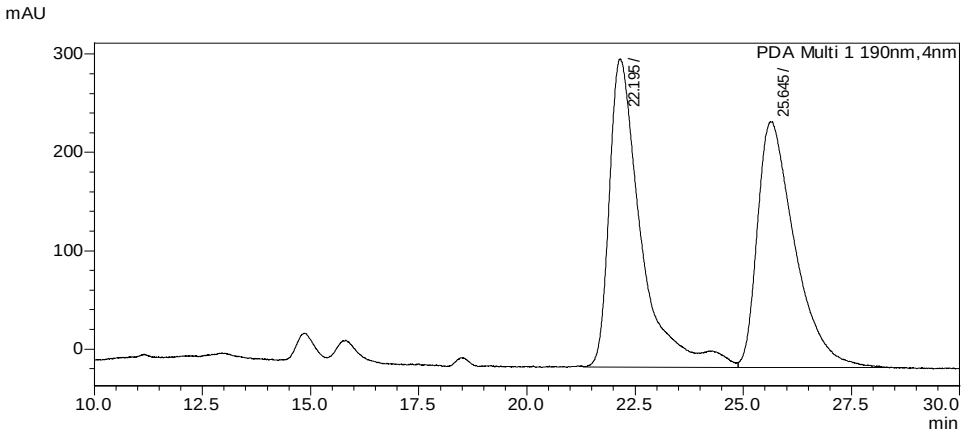


Peak#	Ret. Time	Area	Area%
1	42.102	8044176	97.812

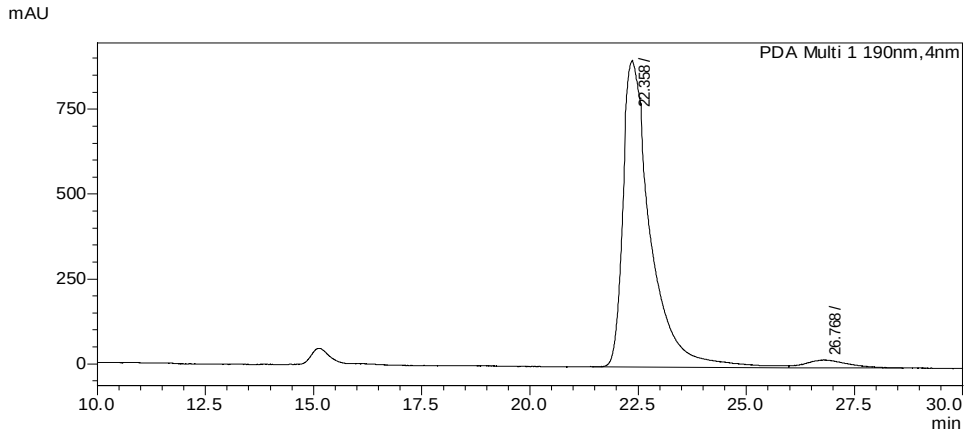
2	48.732	179955	2.188
Total		8224131	100



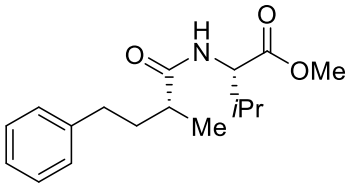
Ethyl ((*R*)-2-methyl-4-phenylbutanoyl)-L-phenylalaninate (29) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes yielding **29** as a white solid (55 mg, 62%). Major diastereomer: **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 7.24 – 7.07 (m, 6H), 6.01 – 5.90 (m, 1H), 4.95 (dt, *J* = 7.9, 6.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.20 (dd, *J* = 14.0, 5.9 Hz, 1H), 3.16 – 3.07 (m, 1H), 2.70 – 2.46 (m, 2H), 2.27 – 2.16 (m, 1H), 1.98 (dddd, *J* = 14.0, 9.3, 8.3, 5.8 Hz, 1H), 1.74 – 1.61 (m, 2H), 1.34 – 1.22 (m, 4H), 1.16 (d, *J* = 6.9 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.8, 171.9, 141.7, 136.0, 129.3, 128.6, 128.42, 128.40, 127.2, 125.9, 61.6, 52.8, 40.6, 38.1, 35.7, 33.4, 17.9, 14.2. **HRMS** (ESI) calculated for $[C_{22}H_{27}NO_3+H]^+$ 354.2069, found 354.2053. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 93%, es = 94%.



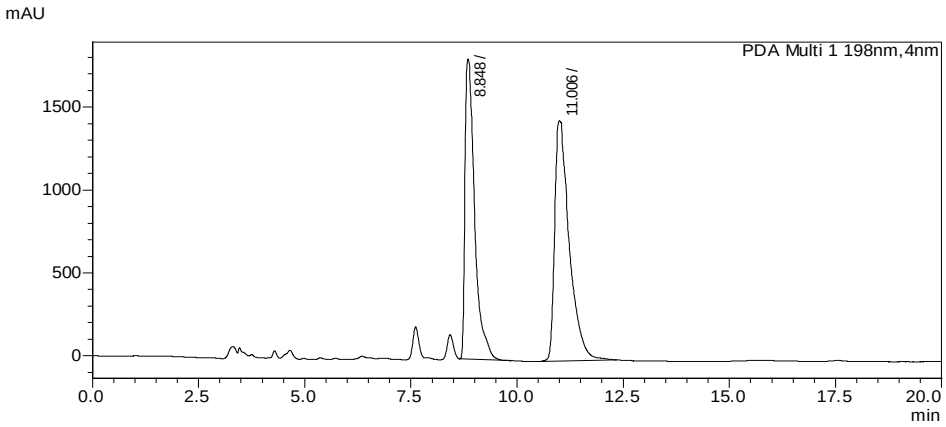
Peak#	Ret. Time	Area	Area%
1	22.195	15991103	51.559
2	25.645	15024192	48.441
Total		31015294	100



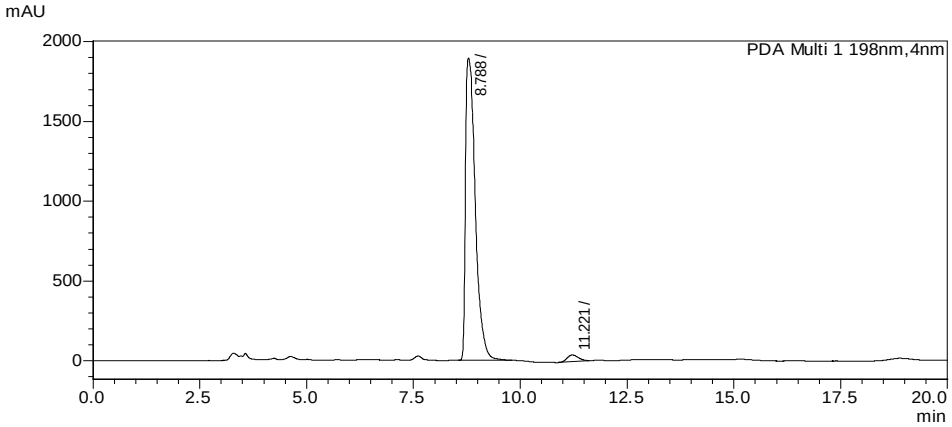
Peak#	Ret. Time	Area	Area%
1	22.358	39991153	96.345
2	26.768	1517183	3.655
Total		41508336	100



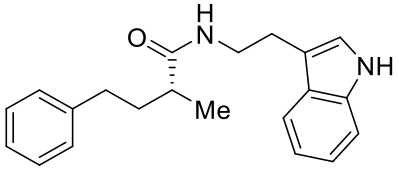
Methyl ((*R*)-2-methyl-4-phenylbutanoyl)-L-valinate (30) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-20% EtOAc/hexanes yielding **30** as a white solid (48 mg, 66%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.30 (dd, *J* = 8.6, 6.7 Hz, 2H), 7.21 (dd, *J* = 8.6, 7.0 Hz, 3H), 6.00 (d, *J* = 8.8 Hz, 1H), 4.64 (dd, *J* = 8.8, 4.8 Hz, 1H), 3.76 (s, 3H), 2.69 (ddd, *J* = 13.9, 9.9, 5.7 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.36 – 2.26 (m, 1H), 2.26 – 2.15 (m, 1H), 2.11 – 2.00 (m, 1H), 1.73 (dddt, *J* = 16.7, 8.8, 6.3, 4.4 Hz, 1H), 1.20 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.1, 172.8, 141.7, 128.42, 128.40, 126.0, 56.8, 52.2, 40.9, 35.9, 33.6, 31.3, 19.1, 17.93, 17.87. **HRMS** (ESI) calculated for $[C_{17}H_{25}NO_3+H]^+$ 292.1913, found 292.1916. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 95%, es = 96%.



Peak#	Ret. Time	Area	Area%
1	8.848	28583027	45.259
2	11.006	34570896	54.741
Total		63153922	100

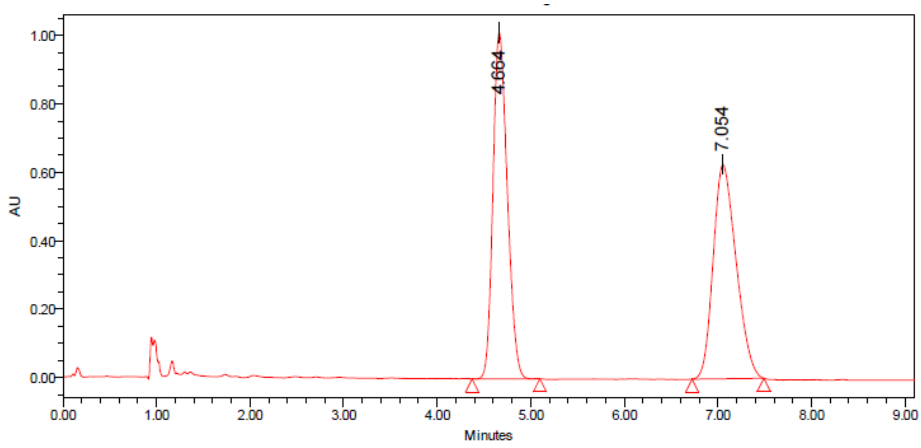


Peak#	Ret. Time	Area	Area%
1	8.788	30136282	97.553
2	11.221	756043	2.447
Total		30892325	100

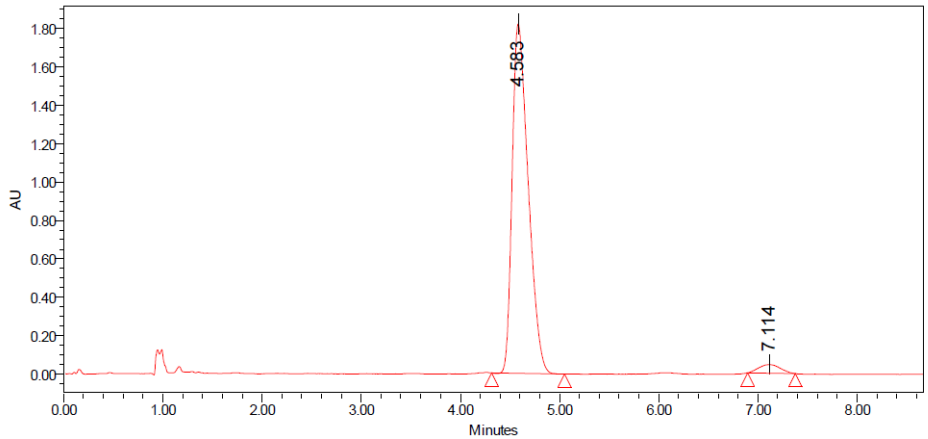


(*R*)-*N*-(2-(1H-indol-3-yl)ethyl)-2-methyl-4-phenylbutanamide (31) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **31** as a viscous

yellow oil (49 mg, 61%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.39 (br s, 1H), 7.66 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.41 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.30 – 7.10 (m, 7H), 7.03 (d, *J* = 2.3 Hz, 1H), 5.58 (t, *J* = 5.9 Hz, 1H), 3.67 (tq, *J* = 13.1, 6.6 Hz, 2H), 3.06 – 2.98 (m, 2H), 2.63 (ddd, *J* = 14.8, 9.5, 5.7 Hz, 1H), 2.54 (ddd, *J* = 13.8, 9.2, 6.7 Hz, 1H), 2.15 – 2.06 (m, 1H), 2.05 – 1.96 (m, 1H), 1.68 (dddd, *J* = 13.4, 9.6, 6.7, 5.7 Hz, 1H), 1.16 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.3, 141.8, 136.5, 128.4, 127.4, 125.9, 122.20, 122.17, 119.5, 118.7, 112.9, 111.4, 40.9, 39.6, 35.7, 33.5, 25.5, 18.1. **HRMS** (ESI) calculated for $[C_{21}H_{24}N_2O+H]^+$ 321.1967, found 321.1971. **Chiral SFC** (Phenomenex Lux Cellulose-3, 60:40 CO_2:methanol): *ee* = 94%, es = 95%.

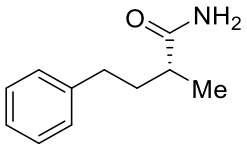


Peak#	Ret. Time	Area%
1	4.664	50.27
2	7.054	49.73
Total		100

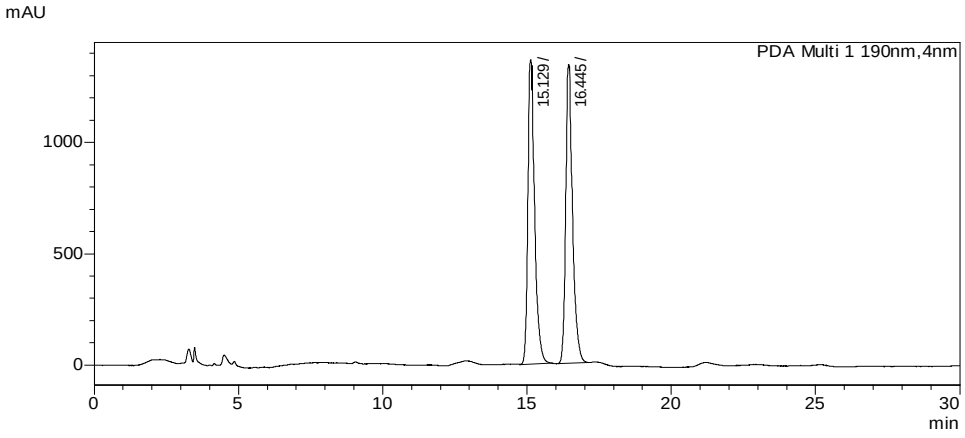


Peak#	Ret. Time	Area%
1	4.583	96.79

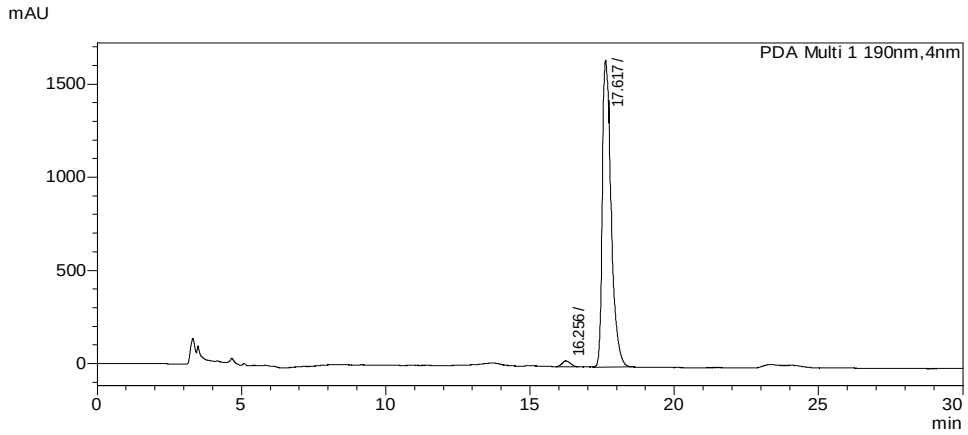
2	7.114	3.21
Total		100



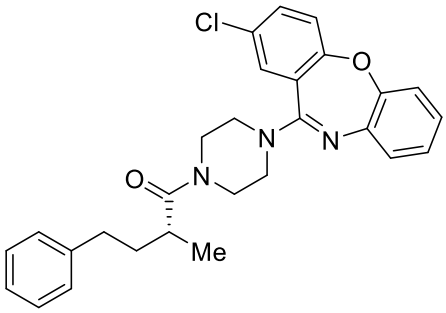
(*R*)-2-methyl-4-phenylbutanamide (32) was obtained from General Carbonylation Procedure A (using 1.3 equiv ammonium carbamate in place of the amine) and the crude product was purified via flash chromatography using a gradient of 30-75% EtOAc/hexanes yielding **32** as a white solid (36.4 mg, 82%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 5.87 (br s, 1H), 5.49 (br s, 1H), 2.71 (ddd, *J* = 15.0, 9.5, 5.9 Hz, 1H), 2.65 (ddd, *J* = 13.9, 9.3, 6.7 Hz, 1H), 2.29 (dt, *J* = 8.2, 6.5 Hz, 1H), 2.03 (dddd, *J* = 13.9, 9.3, 8.2, 5.9 Hz, 1H), 1.74 (ddt, *J* = 13.1, 9.5, 6.4 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.9, 141.7, 128.4, 126.0, 40.0, 35.7, 33.5, 18.0. **HRMS** (ESI) calculated for $[C_{11}H_{15}NO+H]^+$ 178.1232, found 178.1234. **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 97%, es = 98%.



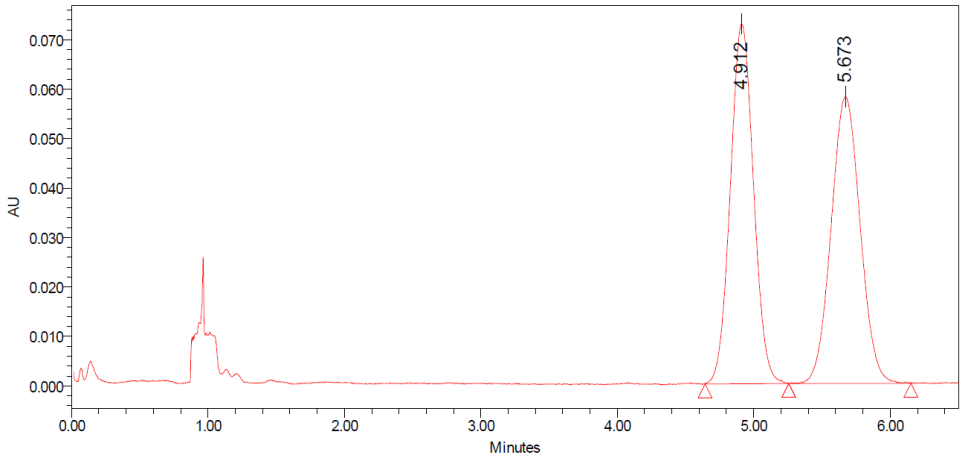
Peak#	Ret. Time	Area	Area%
1	15.129	22129938	50.277
2	16.445	21885968	49.723
Total		44015906	100



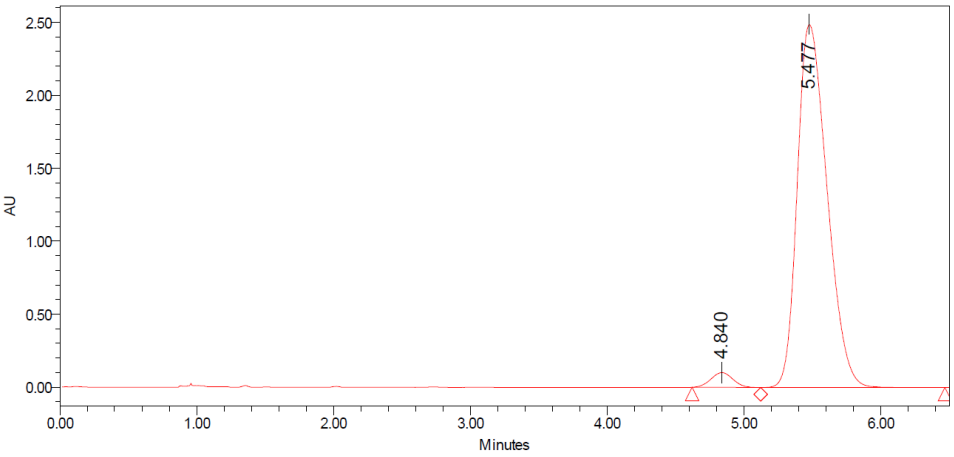
Peak#	Ret. Time	Area	Area%
1	16.256	597088	1.68
2	17.617	34942891	98.32
Total		35539979	100



(*R*)-1-(4-(2-chlorodibenzo[b,f][1,4]oxazepin-11-yl)piperazin-1-yl)-2-methyl-4-phenylbutan-1-one (37) was obtained from General Carbonylation Procedure A and the crude product was purified via flash chromatography using a gradient of 10-50% EtOAc/hexanes yielding **37** as a cream colored, waxy solid (51 mg, 43%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.36 – 7.27 (m, 3H), 7.25 – 7.16 (m, 5H), 7.16 – 7.10 (m, 2H), 7.05 (td, *J* = 7.6, 1.7 Hz, 1H), 3.79 (s, 2H), 3.52 (s, 6H), 2.70 (ddt, *J* = 12.1, 8.6, 4.6 Hz, 2H), 2.63 (dt, *J* = 14.1, 7.6 Hz, 1H), 2.16 – 2.06 (m, 1H), 1.74 (ddt, *J* = 13.2, 8.5, 6.6 Hz, 1H), 1.19 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.9, 159.4, 158.8, 151.8, 141.8, 139.8, 132.9, 130.5, 128.9, 128.5, 128.5, 127.1, 126.0, 125.9, 125.0, 124.8, 122.9, 120.2, 47.9 (br), 47.5 (br), 45.0, 41.5, 35.4, 34.3, 33.4, 17.7. **HRMS** (ESI) calculated for $[C_{28}H_{29}ClN_3O_2+H]^+$ 474.1948, found 474.1954. **Chiral SFC** (Phenomenex Lux Cellulose-3, 80:20 CO_2:methanol): *ee* = 94%, es = 95%.



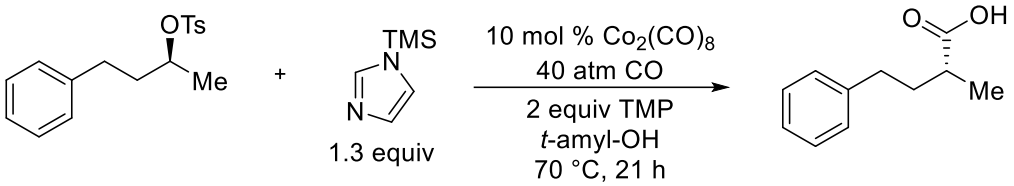
Peak#	Ret. Time	Area%
1	4.912	50.07
2	5.673	49.93
Total		100



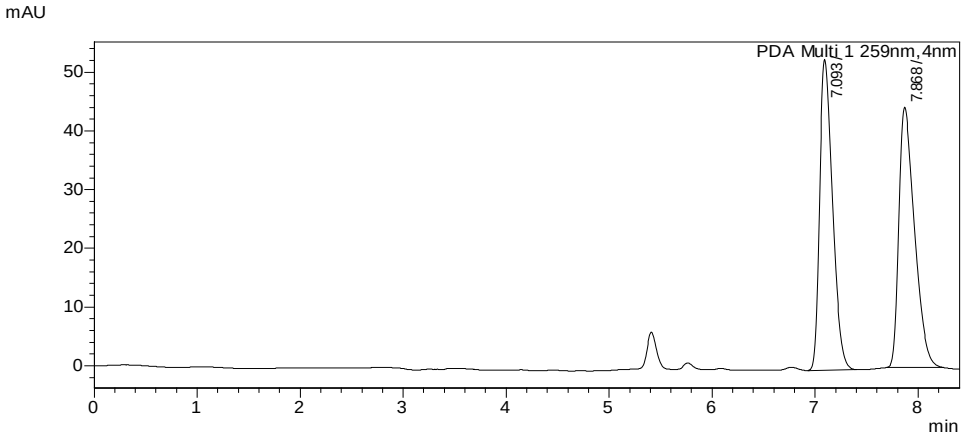
Peak#	Ret. Time	Area%
1	4.84	2.89
2	5.477	97.11
Total		100

Post-Reaction Transformations

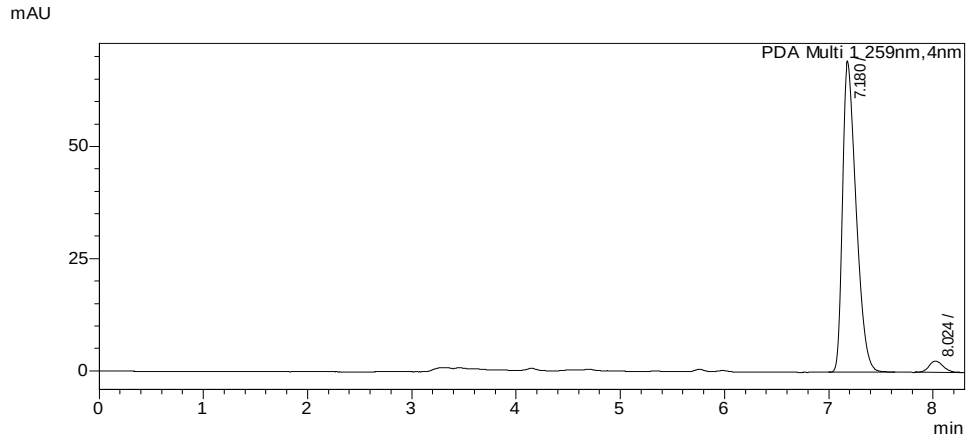
One-Pot Stereospecific Synthesis of Carboxylic Acids



(*R*)-2-methyl-4-phenylbutanoic acid (34) was obtained from General Carbonylation Procedure A (21 h) with 1-(trimethylsilyl)imidazole (1.3 equiv) as the coupling partner. Hydrolysis to the carboxylic acid was accomplished by stirring the crude reaction mixture open to air with 1 M HCl for 20 minutes at room temperature, then worked up as described in General Carbonylation Procedure A. The crude product was purified via flash chromatography using a gradient of 10-30% EtOAc/hexanes with 0.1% AcOH yielding **34** as a yellow oil (36 mg, 81%). Physical and spectral data were in accordance with literature data.[13] **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 93%, es = 94%.

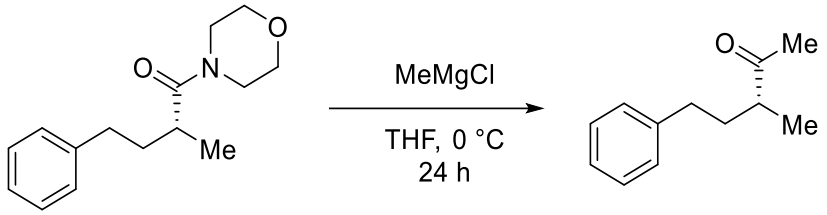


Peak#	Ret. Time	Area	Area%
1	7.093	460958	49.633
2	7.868	467767	50.367
Total		928725	100

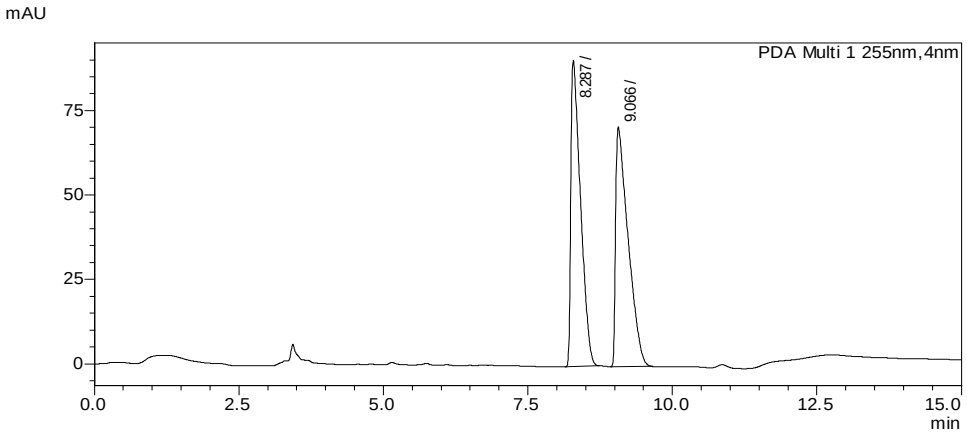


Peak#	Ret. Time	Area	Area%
1	7.18	634510	96.36
2	8.024	23971	3.64
Total		658481	100

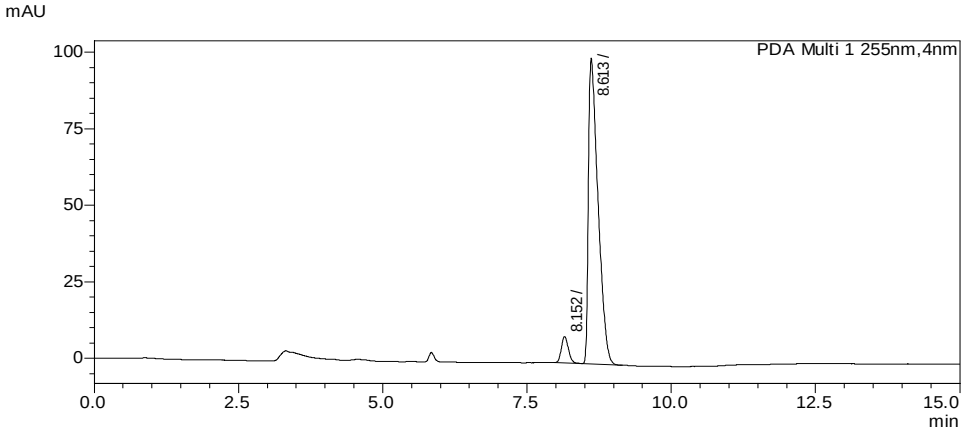
Organometallic Reagent Addition for Asymmetric Chiral Ketone Synthesis:



(*R*)-3-methyl-5-phenylpentan-2-one (35) was prepared using a modified procedure from Vilarrasa and co-workers.[14] To a 0 °C cryobath cooled solution of amide **3** (62 mg, 0.25 mmol, 90% *ee*, synthesized below) in THF (2.5 mL) was added methylmagnesium chloride (0.5 mL, 1.5 mmol, 3.0 M). The reaction mixture was stirred at 0 °C in a cryobath for 24 hours. Upon completion of the reaction, the mixture was quenched, still at 0 °C, with a saturated solution of NH_4Cl and extracted 3 times with DCM. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified via flash chromatography in 5% EtOAc/hexanes yielding **35** as a yellow oil (40 mg, 91%). Physical and spectral data were in accordance with literature data.[15] **Chiral HPLC** (Daicel OJ-H, 95:5 hexanes:isopropanol): *ee* = 88%, es = 98%.

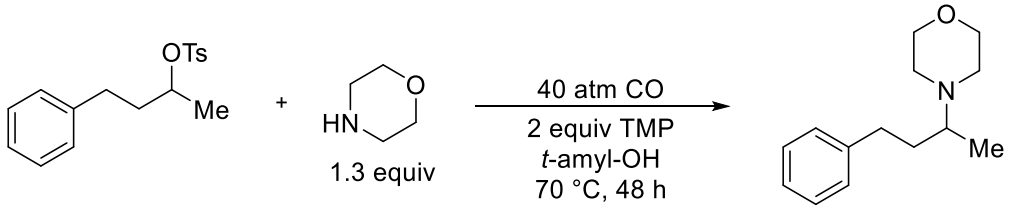


Peak#	Ret. Time	Area	Area%
1	8.287	1082319	49.812
2	9.066	1090471	50.188
Total		2172790	100



Peak#	Ret. Time	Area	Area%
1	8.152	72791	5.925
2	8.613	1155803	94.075
Total		1228595	100

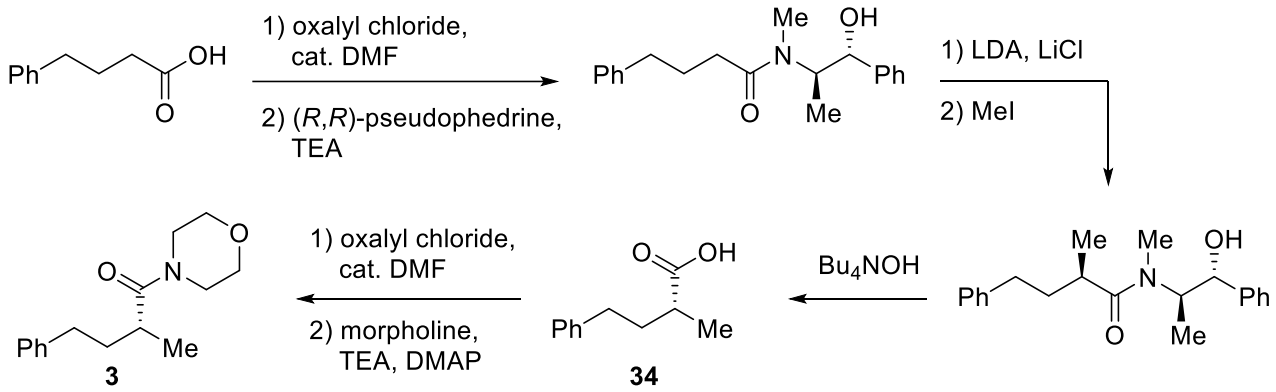
Competitive Alkylation of Morpholine:

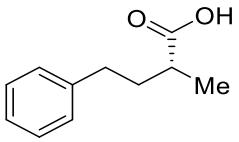


4-(4-phenylbutan-2-yl)morpholine (38) was obtained from General Carbonylation Procedure A (without any cobalt carbonyl added, 45% conversion), substituting the aqueous wash with 1 M NaOH, and the crude product was purified via flash chromatography using a gradient of 10-75% EtOAc/hexanes yielding **38** as a colorless oil (20 mg, 36%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.31 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.18 (m, 3H), 3.79 – 3.70 (m, 4H), 2.76 – 2.63 (m, 2H), 2.63 – 2.51 (m, 3H), 2.48 (ddd, *J* = 11.4, 6.0, 3.3 Hz, 2H), 1.88 (ddt, *J* = 13.4, 9.7, 6.1 Hz, 1H), 1.60 (ddt, *J* = 13.6, 9.6, 6.9 Hz, 1H), 1.04 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.7, 128.5, 128.3, 125.7, 67.5, 58.4, 48.7, 35.3, 32.8, 13.9. **HRMS** (ESI) calculated for $[C_{14}H_{21}NO+H]^+$ 220.1701, found 220.1693.

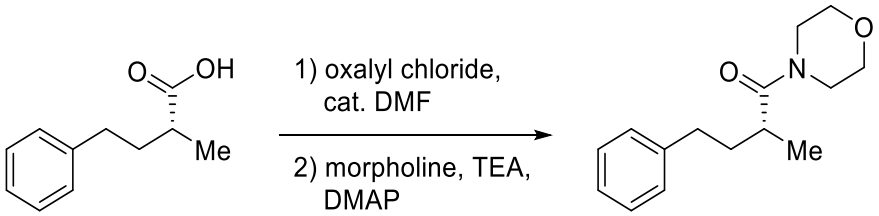
Mechanistic Experiments

Absolute Stereochemistry Determination: An independent HPLC standard of morpholine amide **3** was independently synthesized, using the chiral auxiliary route shown below, to prove that the carbonylation proceeds via inversion. This suggests an S_N2 oxidative addition is operative in the reaction mechanism.



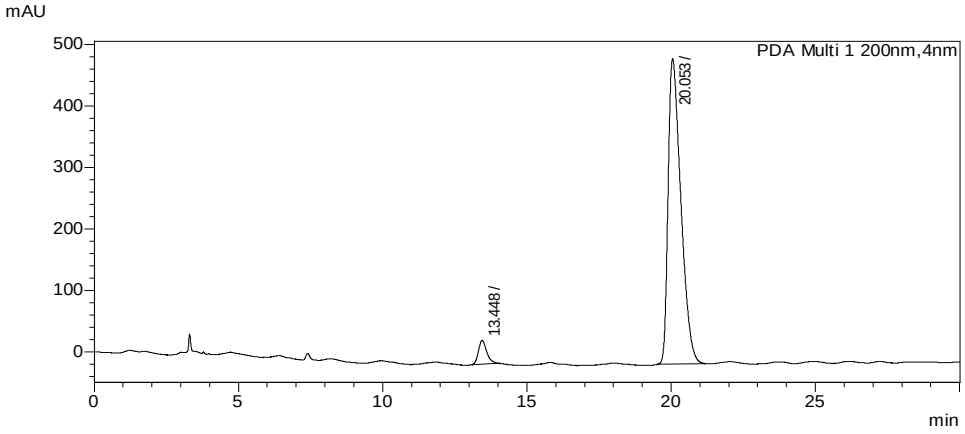


(*R*)-2-methyl-4-phenylbutanoic acid (34) was prepared according to a published procedure and used without further purification.[5]



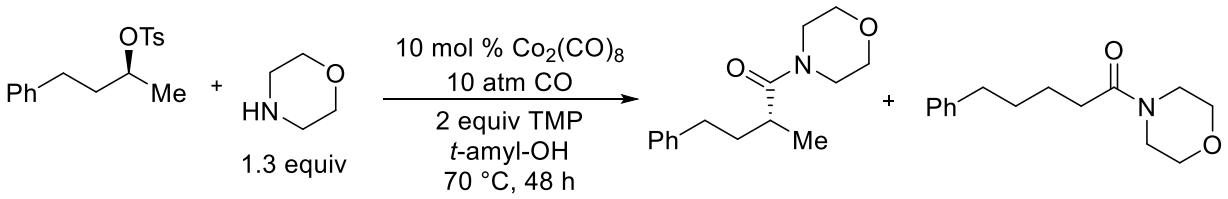
(*R*)-2-methyl-1-morpholino-4-phenylbutan-1-one (3) was synthesized by adding a few drops of DMF to a solution of **34** (0.40 g, 2.2 mmol) in DCM (8 mL) at 0 ºC. To this stirred solution was added oxalyl chloride (0.38 mL, 4.5 mmol) dropwise. The reaction was stirred at 0 ºC for 15 minutes and warmed to room temperature for 30 minutes. Solvent and excess oxalyl chloride were removed under reduced pressure and the mixture was brought up in DCM (2 mL). This solution was added dropwise to a stirred solution of

morpholine (0.17 mL, 2.0 mmol), DMAP (24 mg, 0.20 mmol), and TEA (0.36 mL, 2.6 mmol) in DCM (4 mL) at 0 ºC for 10 minutes. The reaction was then warmed to room temperature for 45 minutes and quenched with water. The organic layer was separated and washed twice with brine, once with a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified via flash chromatography in 40% EtOAc/hexanes to provide 0.47 g (95%) of **3** as a colorless oil. **Chiral HPLC** (Daicel OJ-H, 90:10 hexanes:isopropanol): *ee* = 90%.



Peak#	Ret. Time	Area	Area%
1	13.448	779154	4.866
2	20.053	15233092	95.134
Total		16012246	100

Low Pressure Aminocarbonylations:

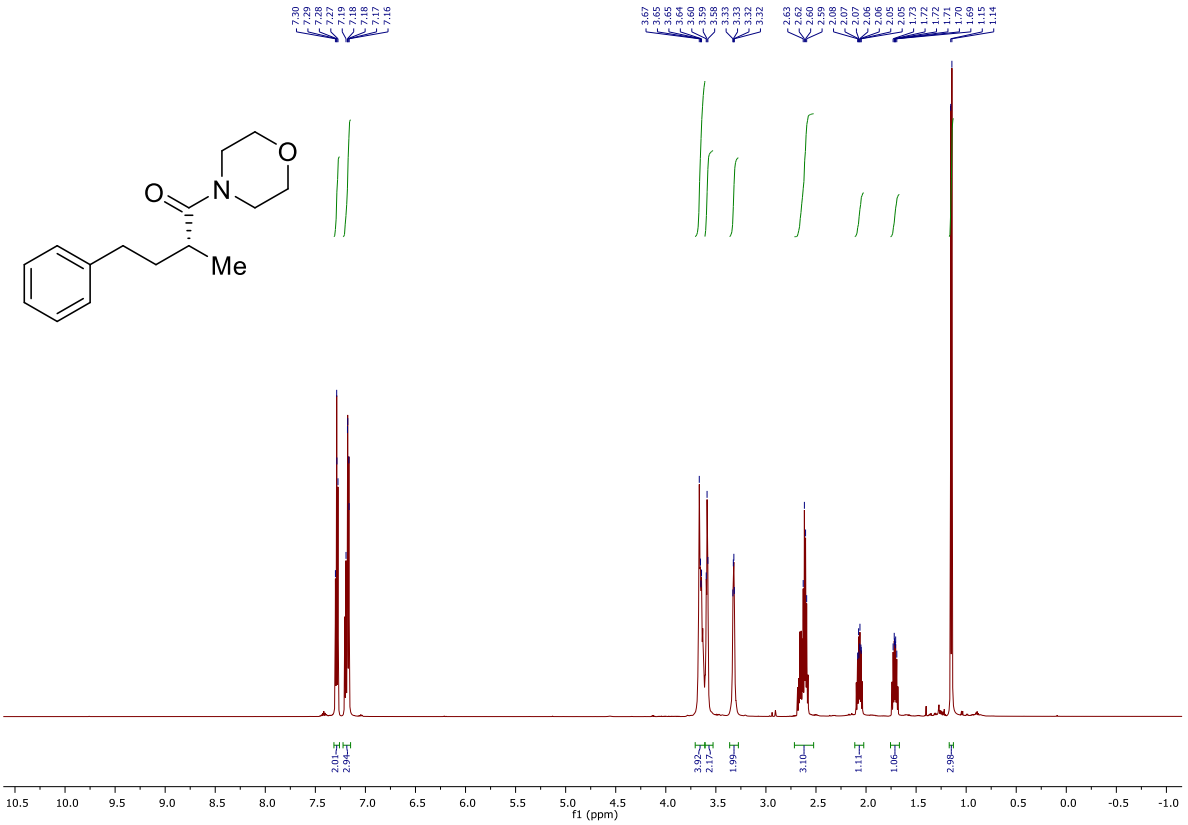


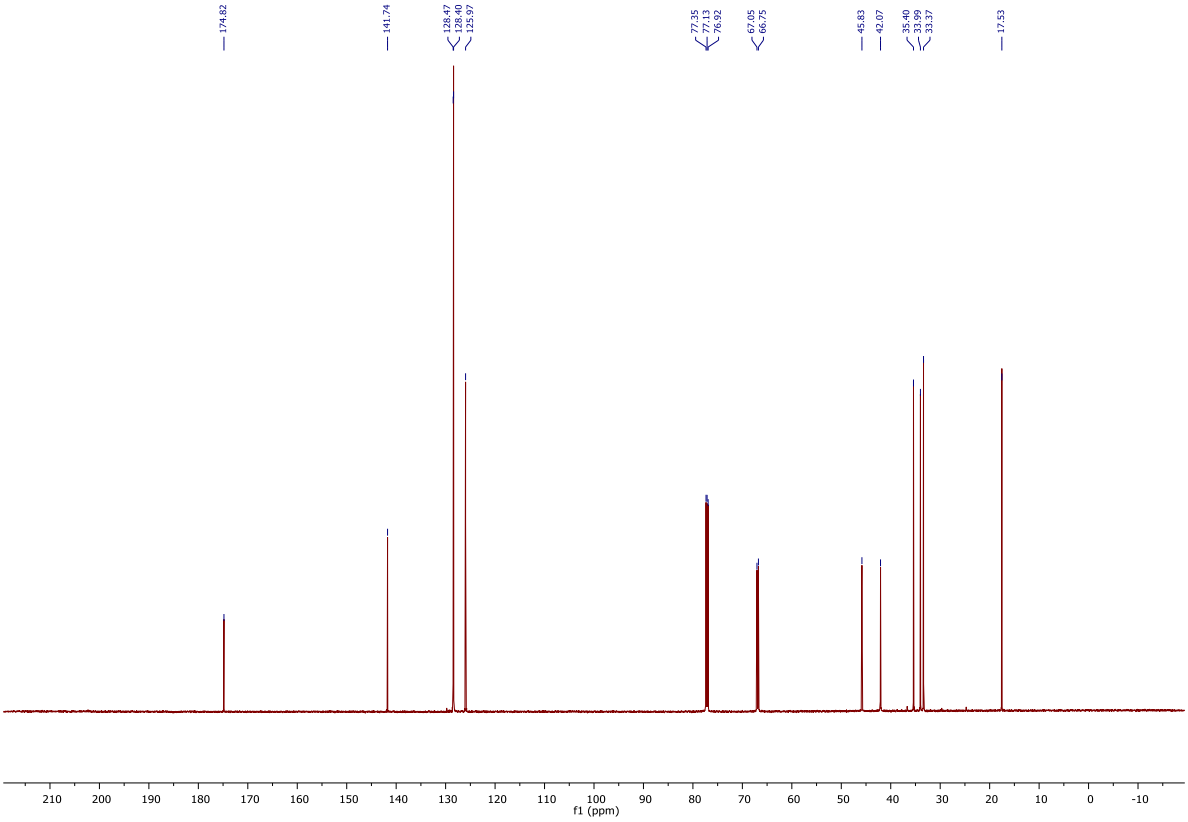
1-Morpholino-5-phenylpentan-1-one (SI-28) was observed in General Carbonylation Procedure A at lower pressures (using 10 atm, 45% NMR yield secondary amide, 11% primary amide). Physical and spectral data for **SI-28** were in accordance with literature data.[16]

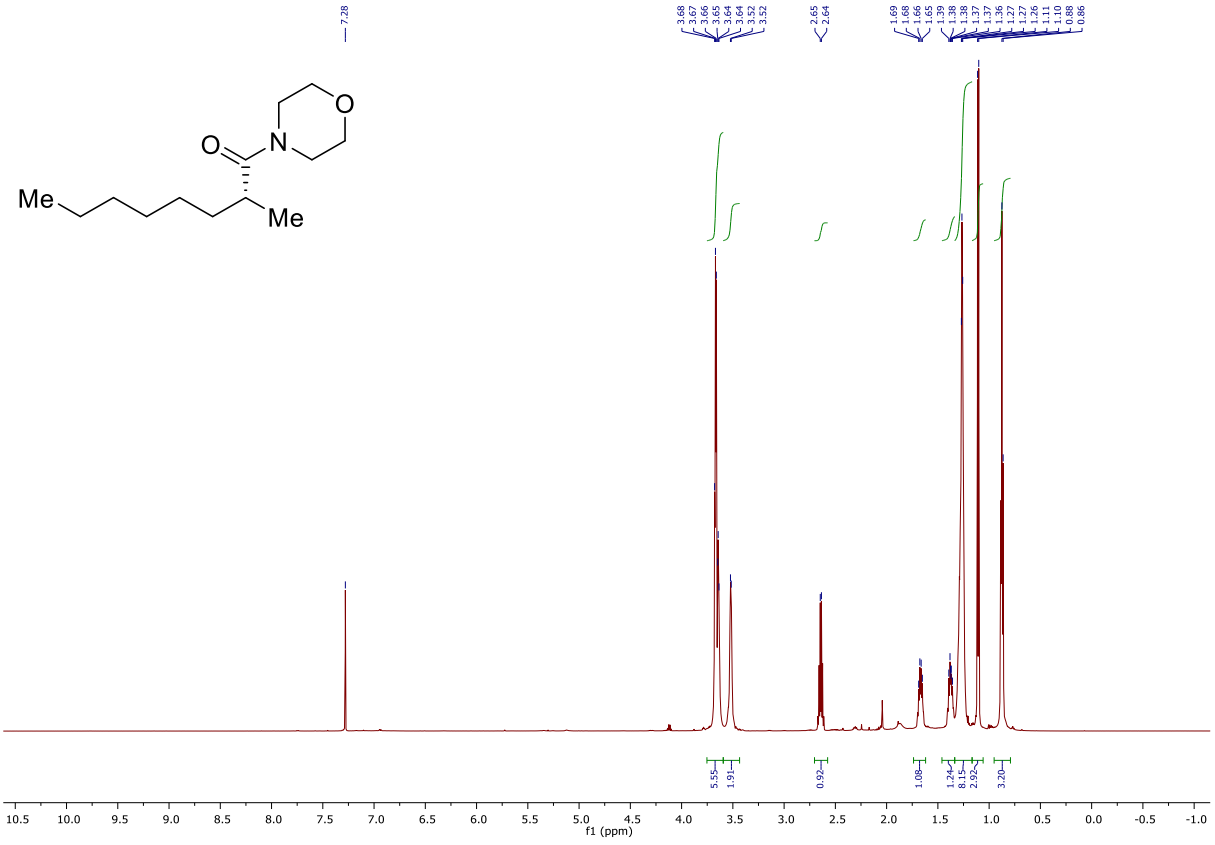
References:

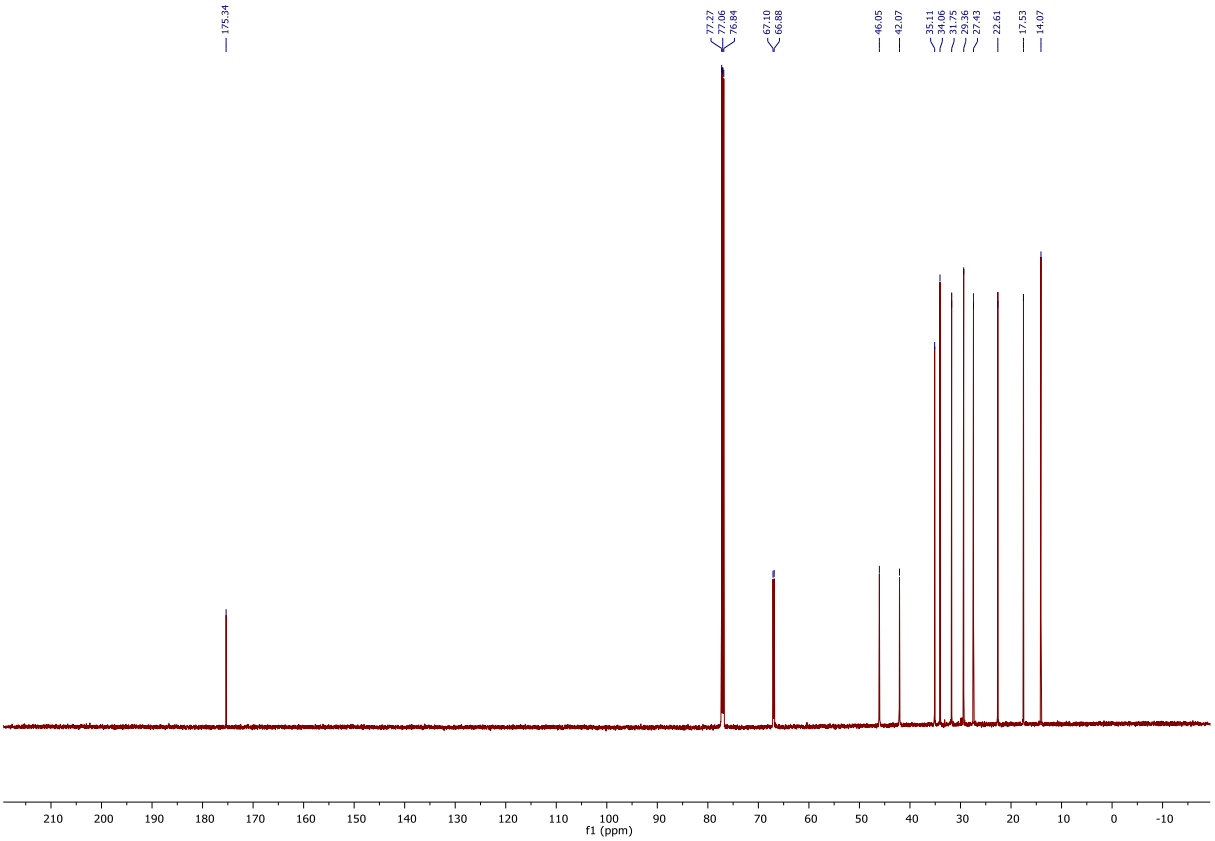
[1] J. E. Ellis, P. T. Barger, M. L. Winzenburg, G. F. Warnock, *J. Organomet. Chem.* **1990**, *383*, 521–530.
[2] Y. Yoshida, Y. Sakakura, N. Aso, S. Okada, Y. Tanabe, *Tetrahedron* **1999**, *55*, 2183–2192.
[3] S. D. Lepore, Y. He, *J. Org. Chem.* **2003**, *68*, 8261–8263.
[4] D. Martinez-Solorio, M. P. Jennings, *Tetrahedron Lett.* **2008**, *49*, 5175–5178.
[5] B. T. Sargent, E. J. Alexanian, *J. Am. Chem. Soc.* **2017**, *139*, 12438–12440.
[6] J. E. Roque Peña, E. J. Alexanian, *Org. Lett.* **2017**, *19*, 4413–4415.
[7] G. Bastug, S. Dierick, F. Lebreux, I. E. Markó, *Org. Lett.* **2012**, *14*, 1306–1309.
[8] V. Rawat, P. V. Chouthaiwale, G. Suryavanshi, A. Sudalai, *Tetrahedron Asymmetry* **2009**, *20*, 2173–2177.
[9] X.-H. Yang, K. Wang, S.-F. Zhu, J.-H. Xie, Q.-L. Zhou, *J. Am. Chem. Soc.* **2014**, *136*, 17426–17429.
[10] B. Srinivas, D. S. Reddy, N. A. Mallampudi, D. K. Mohapatra, *Org. Lett.* **2018**, *20*, 6910–6914.
[11] Z. Liu, B. Breit, *Angew. Chem. Int. Ed.* **2016**, *55*, 8440–8443.
[12] S. A. Cochrane, C. T. Lohans, M. J. van Belkum, M. A. Bels, J. C. Vederas, *Org. Biomol. Chem.* **2015**, *13*, 6073–6081.
[13] M. Gaydou, T. Moragas, F. Juliá-Hernández, R. Martin, *J. Am. Chem. Soc.* **2017**, *139*, 12161–12164.
[14] R. Martín, P. Romea, C. Tey, F. Urpí, J. Vilarrasa, *Synlett* **1997**, *12*, 1414–1416.
[15] S. D. Holmbo, N. A. Godfrey, J. J. Hirner, S. V. Pronin, *J. Am. Chem. Soc.* **2016**, *138*, 12316–12319.
[16] N. Deibl, R. Kempe, *J. Am. Chem. Soc.* **2016**, *138*, 10786–10789.

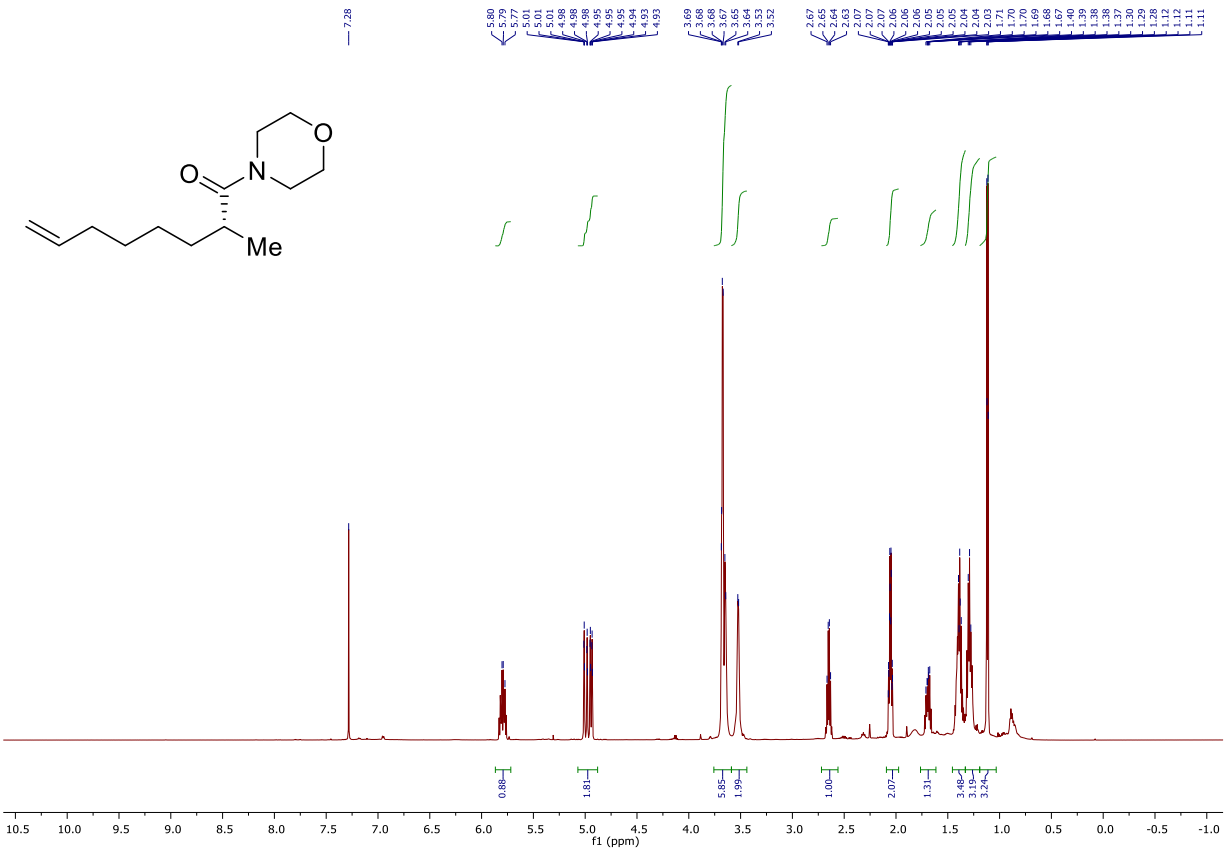
^{1}H and ^{13}C NMR Spectra

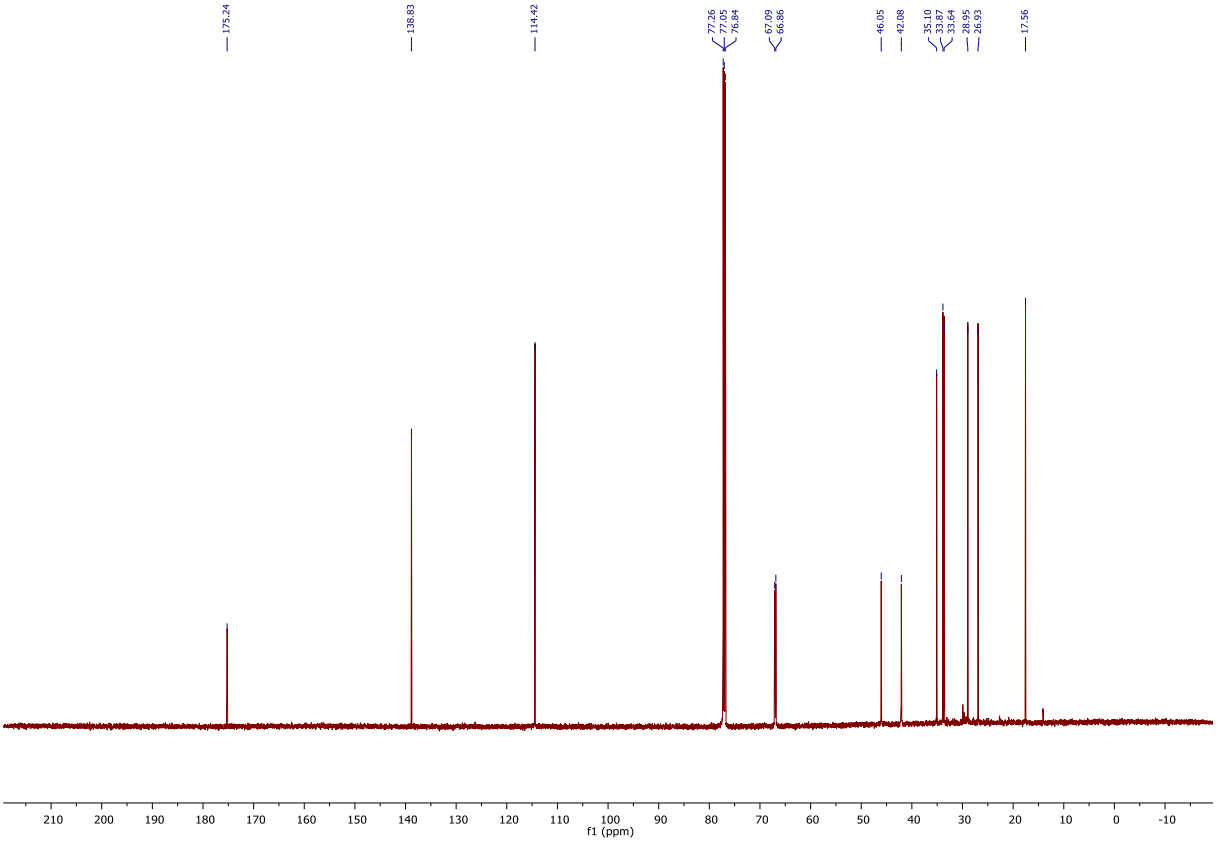


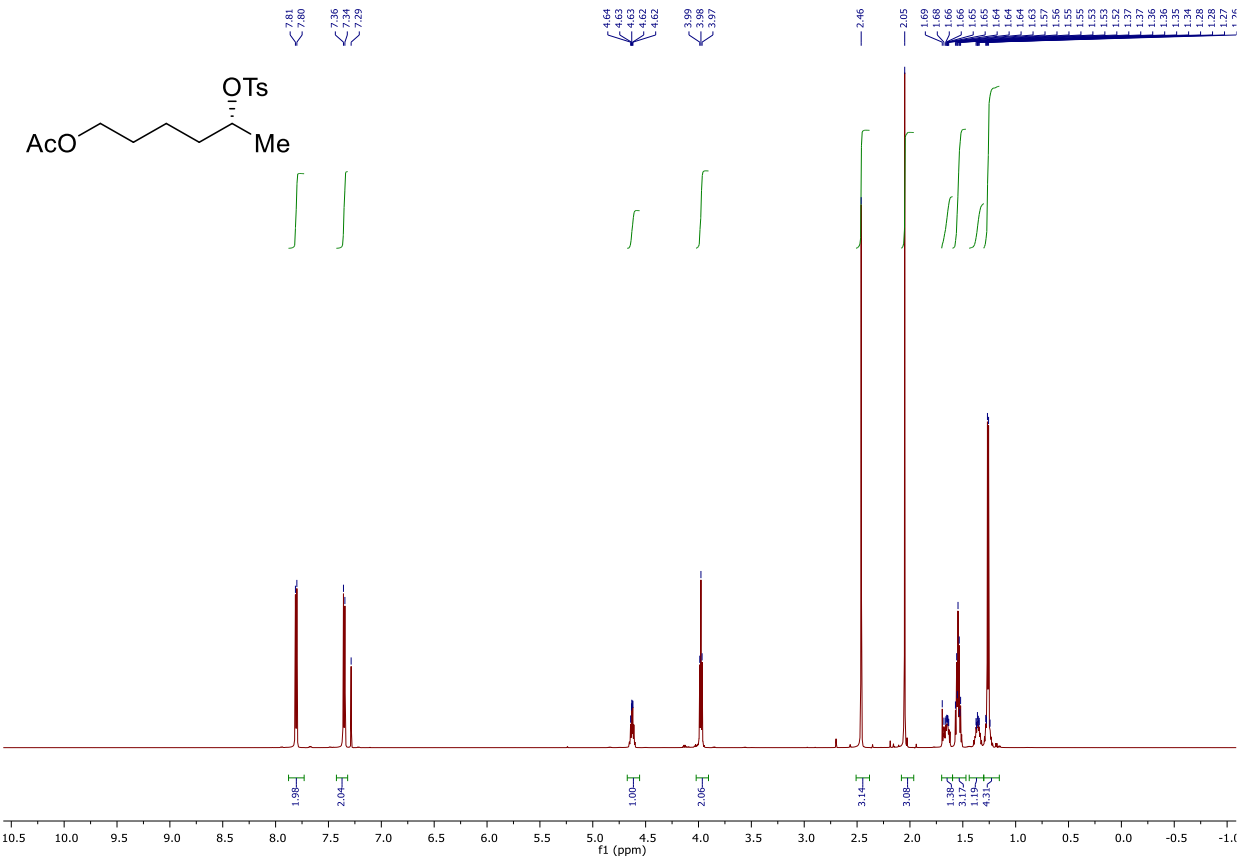


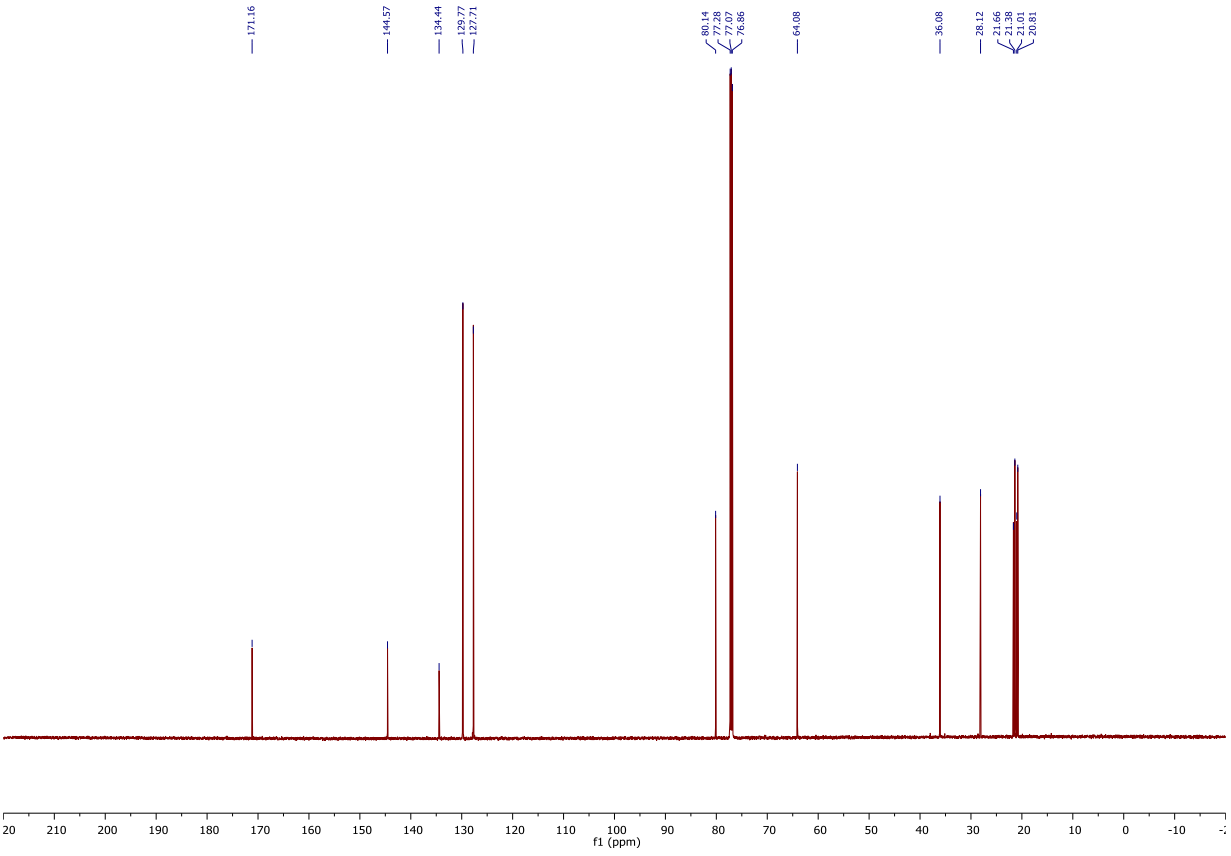

7.28
3.68
3.67
3.66
3.65
3.64
3.64
3.52
3.52
2.65
2.64
1.69
1.68
1.66
1.65
1.39
1.38
1.38
1.37
1.37
1.36
1.27
1.27
1.26
1.11
1.10
0.88
0.86
O
N
O
Me
Me
5.55
1.91
0.92
1.08
1.24
8.15
2.92
3.20
f1 (ppm)

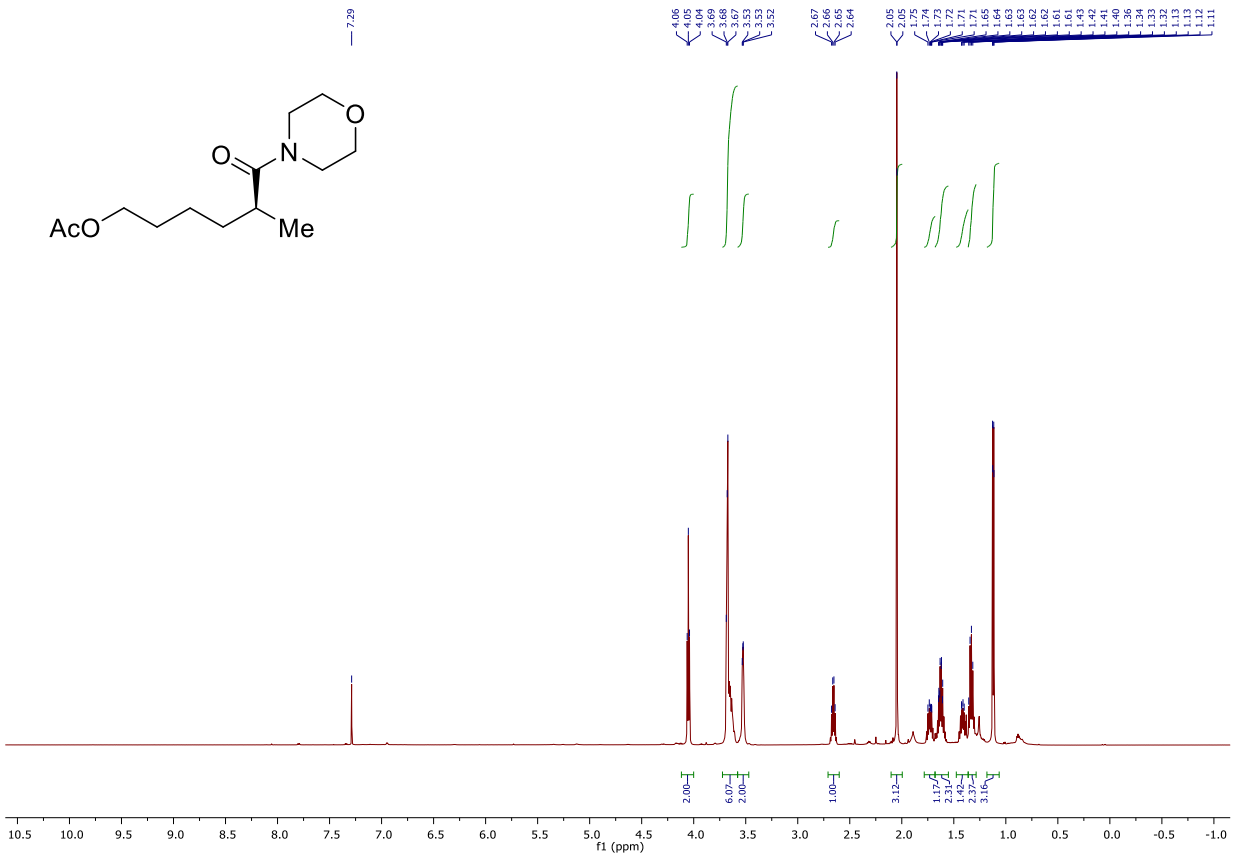

175.34
77.27
77.06
76.84
67.10
66.88
46.05
42.07
35.11
34.06
31.75
29.36
27.43
22.61
17.53
14.07
f1 (ppm)

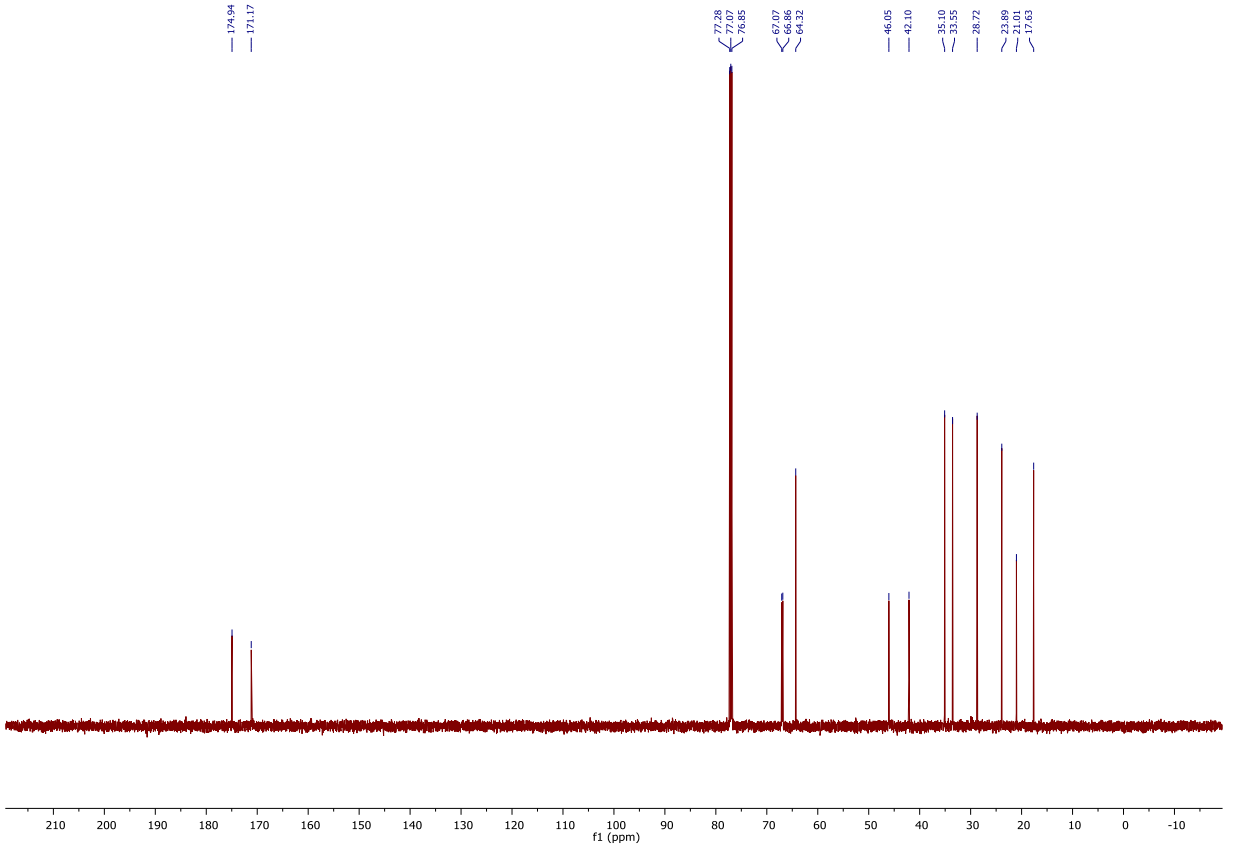

O
N
O
Me
f1 (ppm)

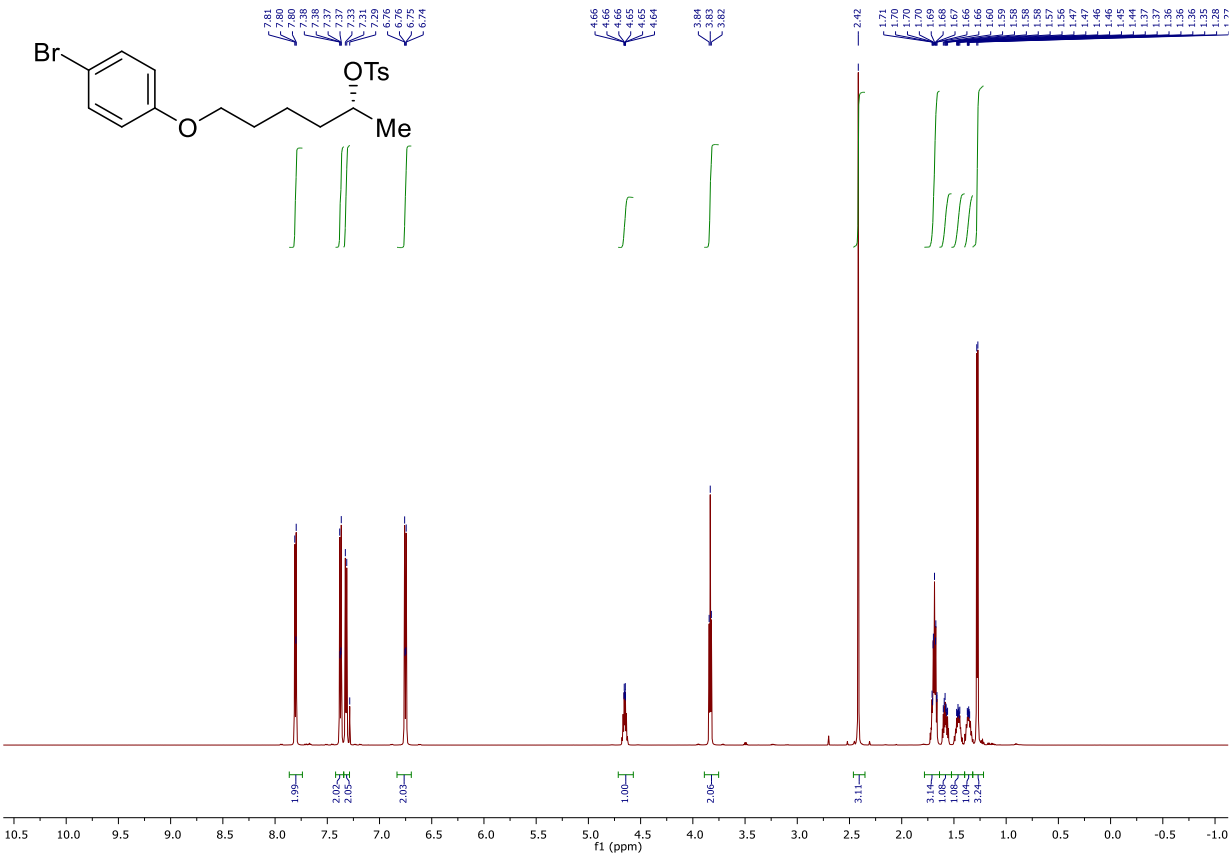

f1 (ppm)

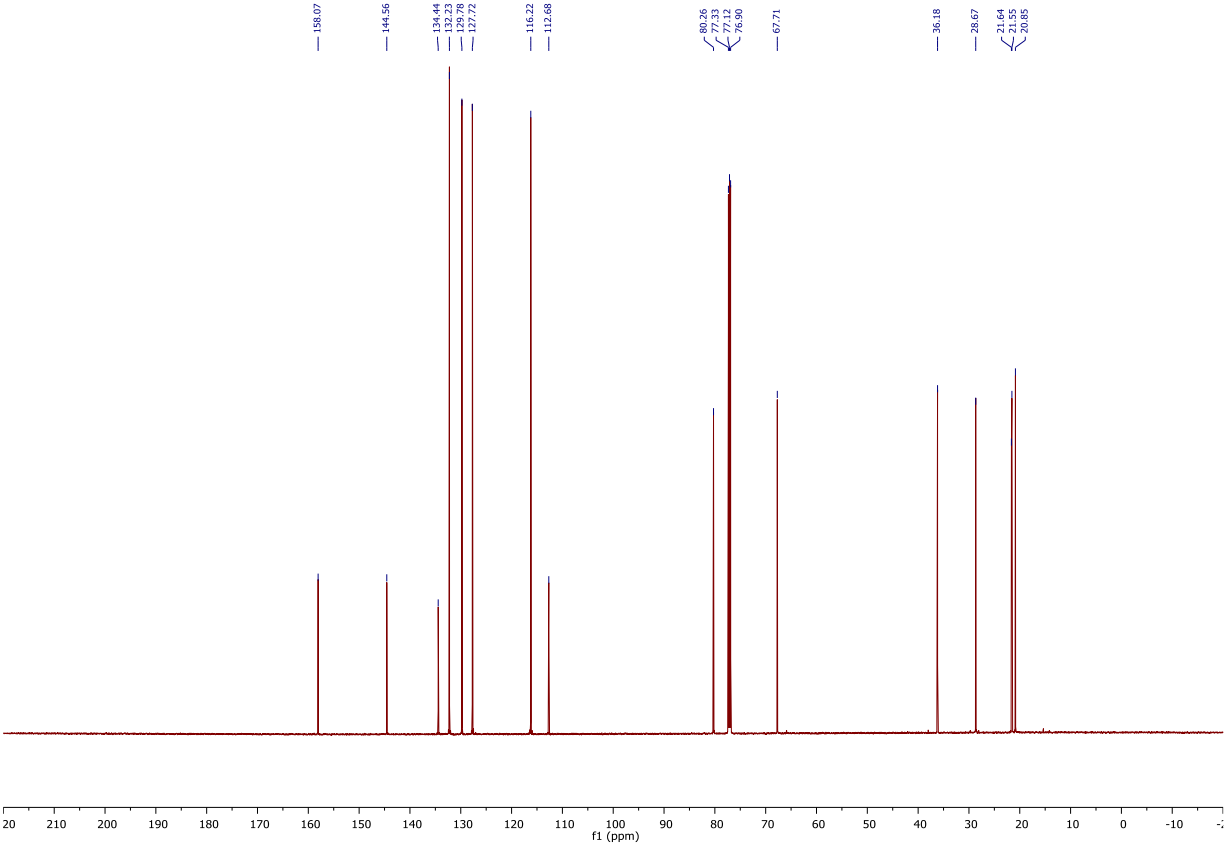

OTs
AcO
Me
f1 (ppm)

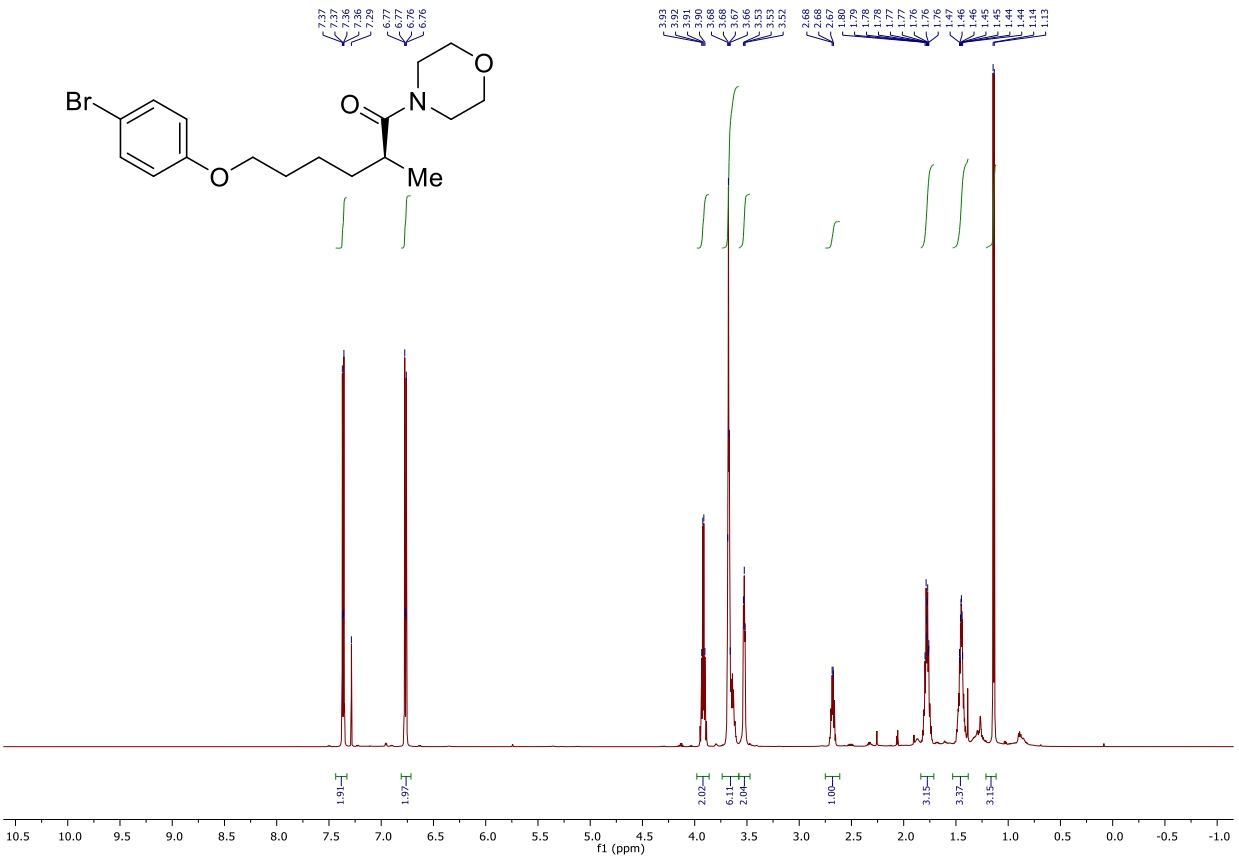

f1 (ppm)

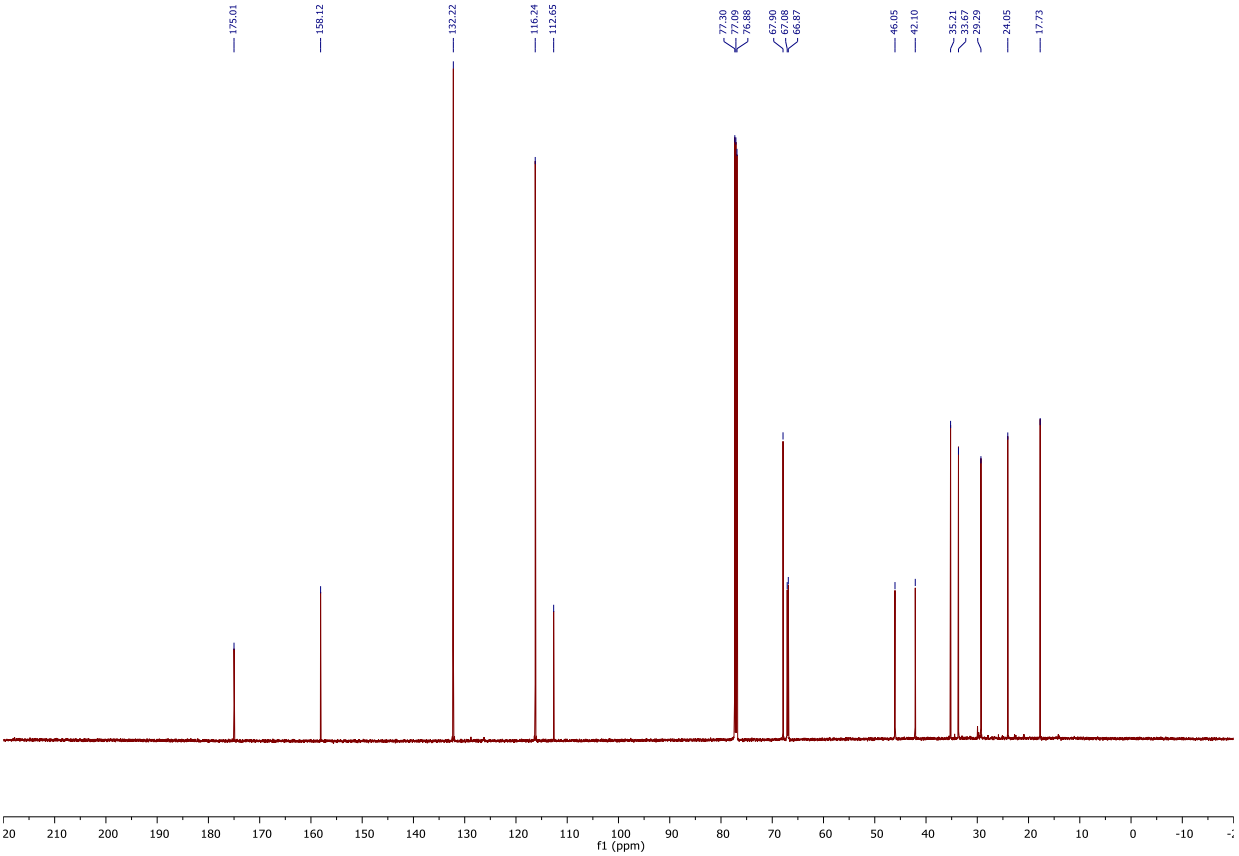

7.29
4.06
4.05
4.04
3.69
3.68
3.67
3.53
3.52
2.67
2.66
2.65
2.64
2.05
2.05
1.75
1.74
1.73
1.72
1.71
1.71
1.65
1.64
1.63
1.63
1.62
1.62
1.61
1.61
1.43
1.42
1.41
1.40
1.36
1.34
1.33
1.32
1.13
1.13
1.12
1.11
O
O
N
AcO
Me
2.00
6.07
2.00
1.00
3.12
1.17
2.31
1.43
2.37
3.16
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

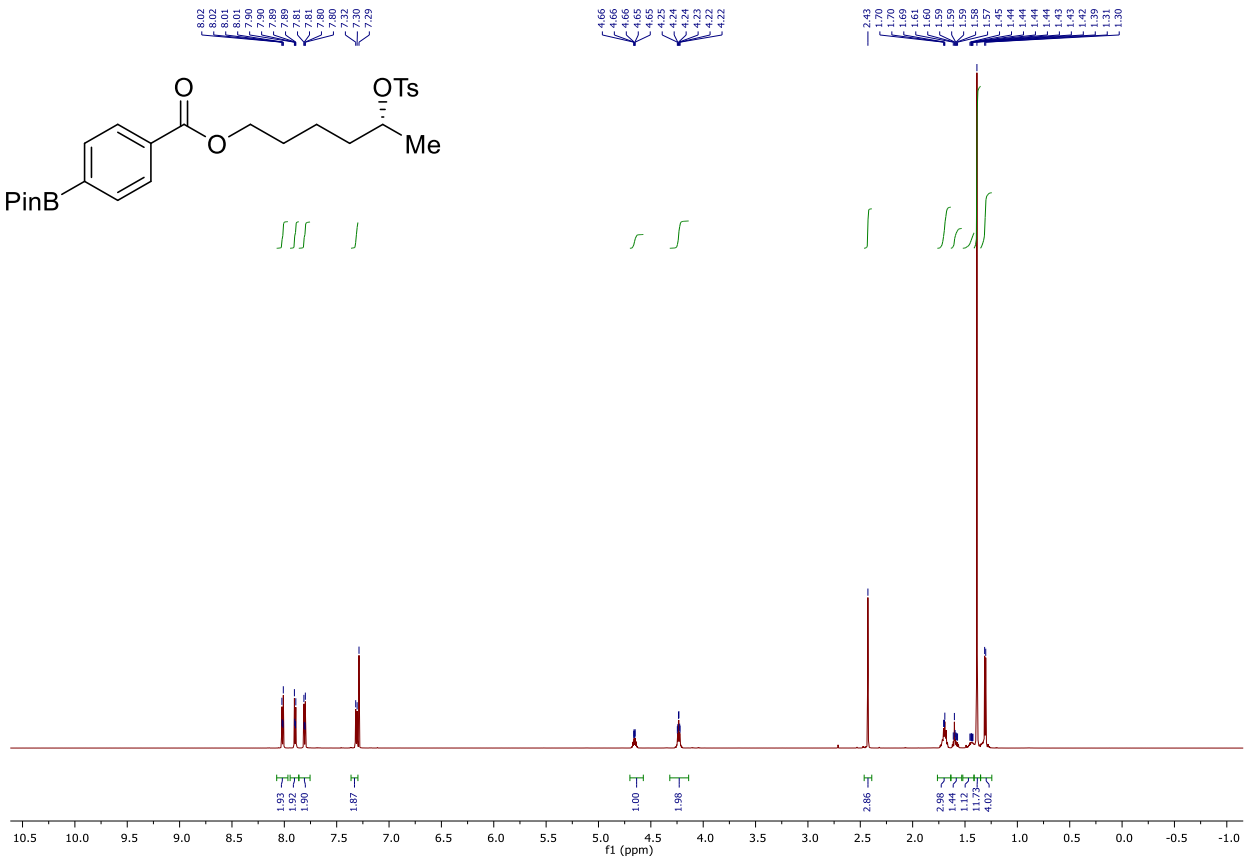

174.94
171.17
77.28
77.07
76.85
67.07
66.86
64.32
46.05
42.10
35.10
33.55
28.72
23.89
21.01
17.63
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

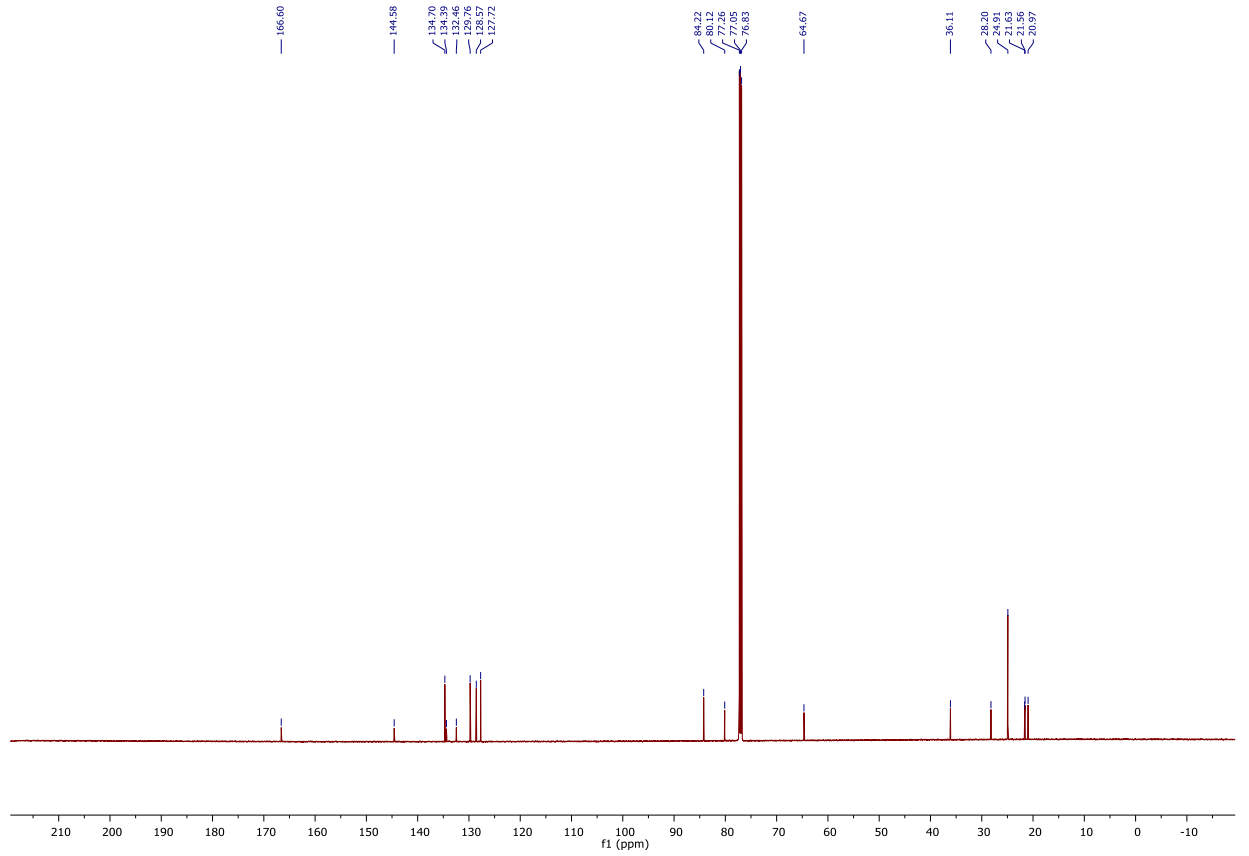

Br
OTs
O
Me
f1 (ppm)

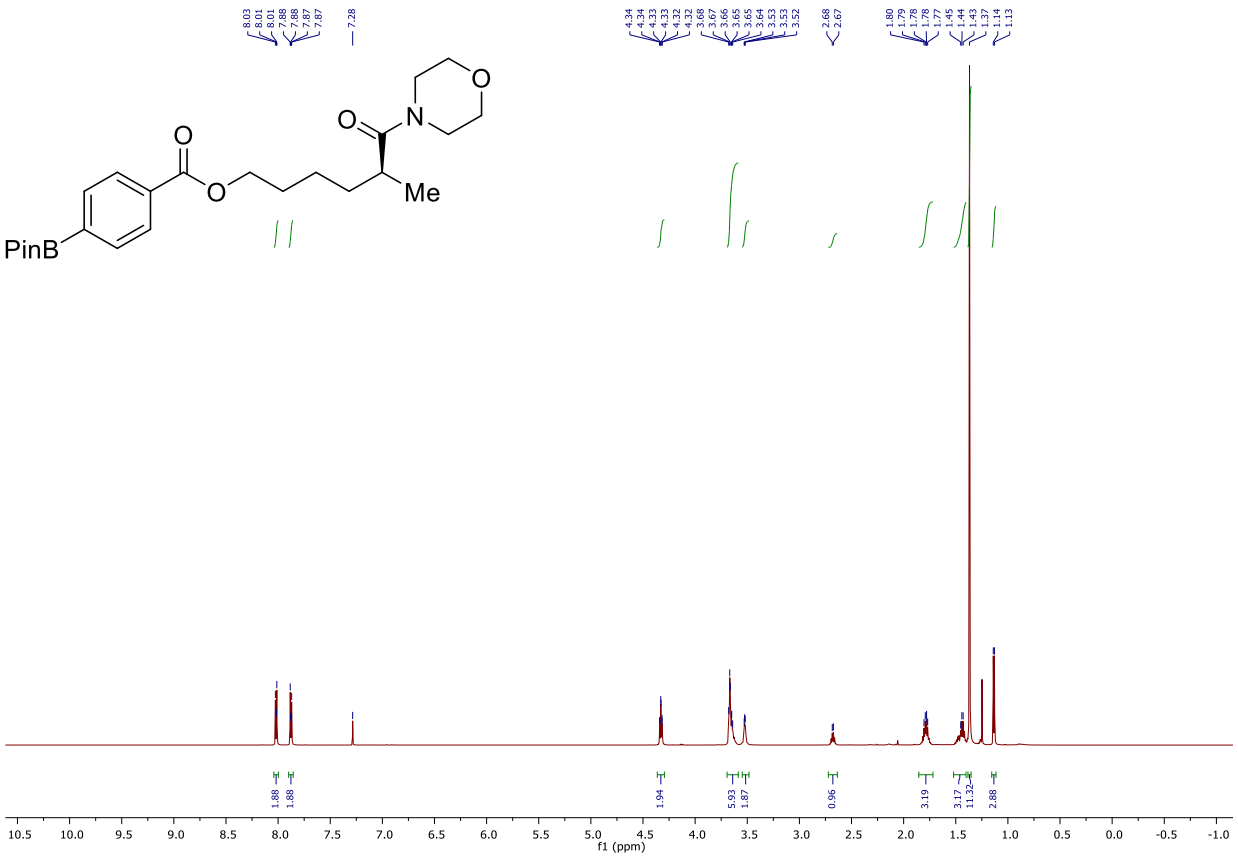

f1 (ppm)

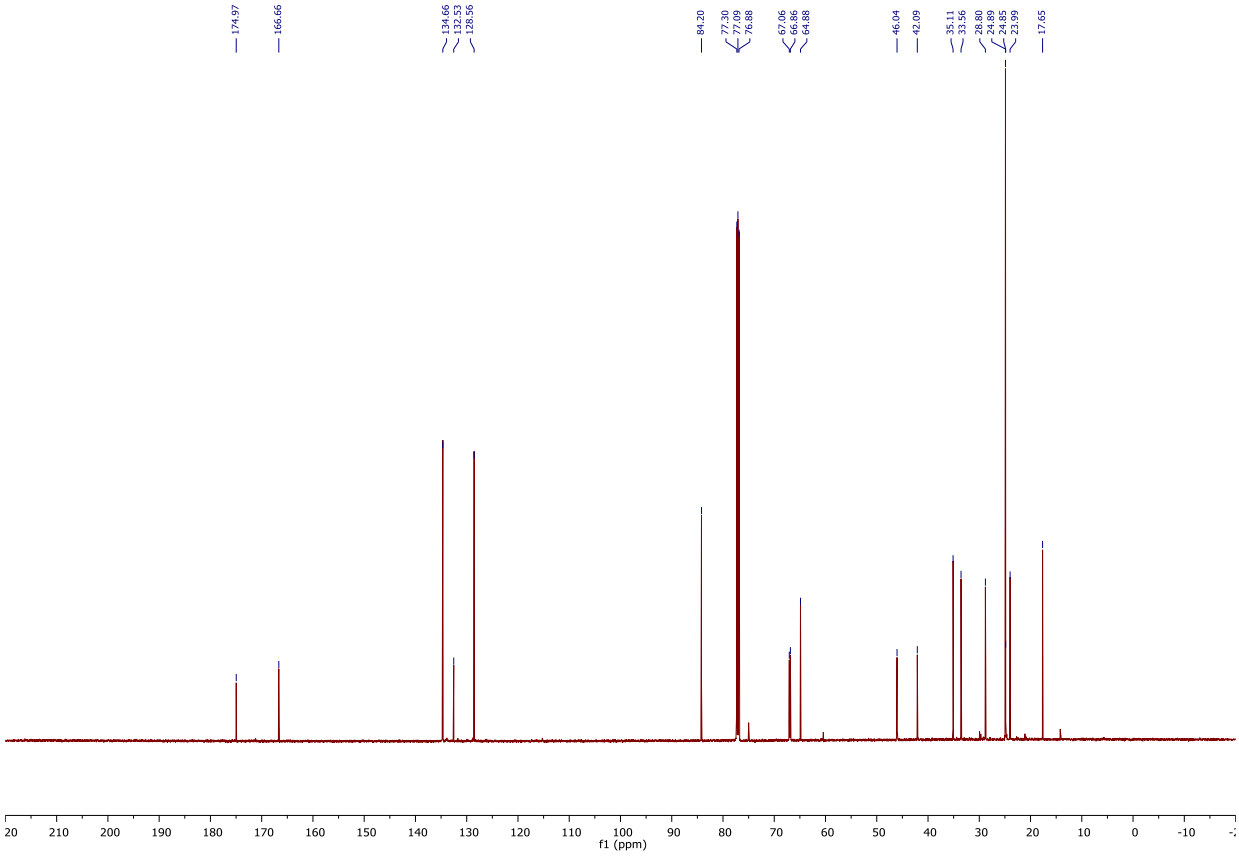

Br
O
N
O
O
Me
f1 (ppm)

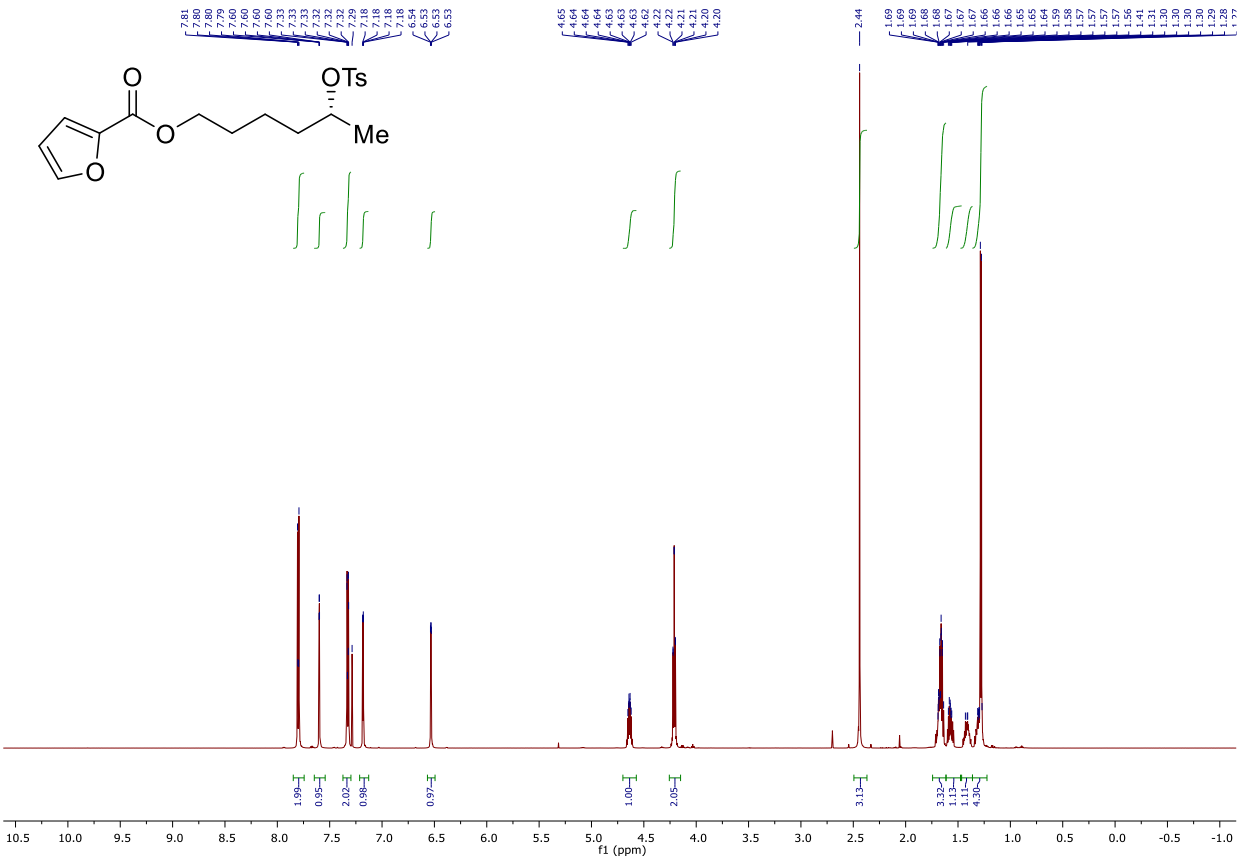

f1 (ppm)

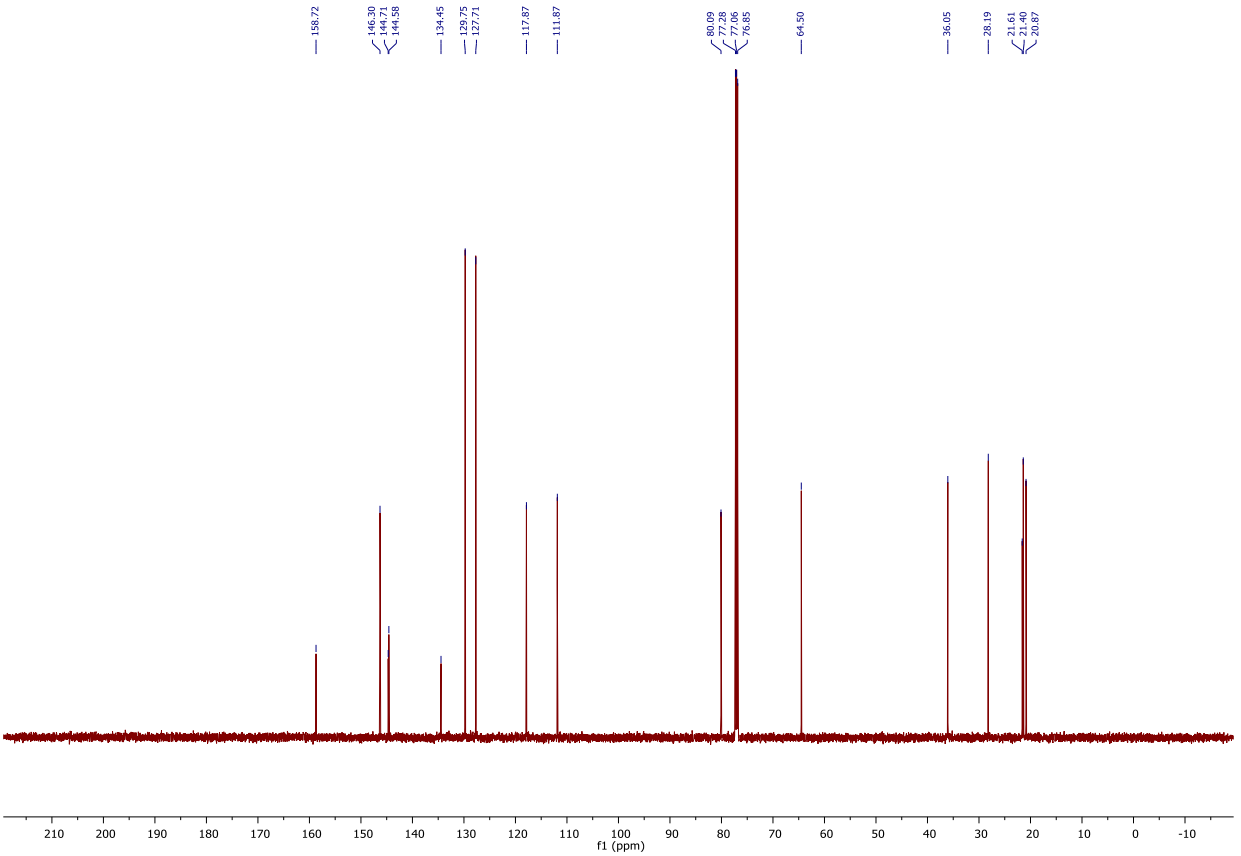

O
OTs
O
Me
PinB
f1 (ppm)

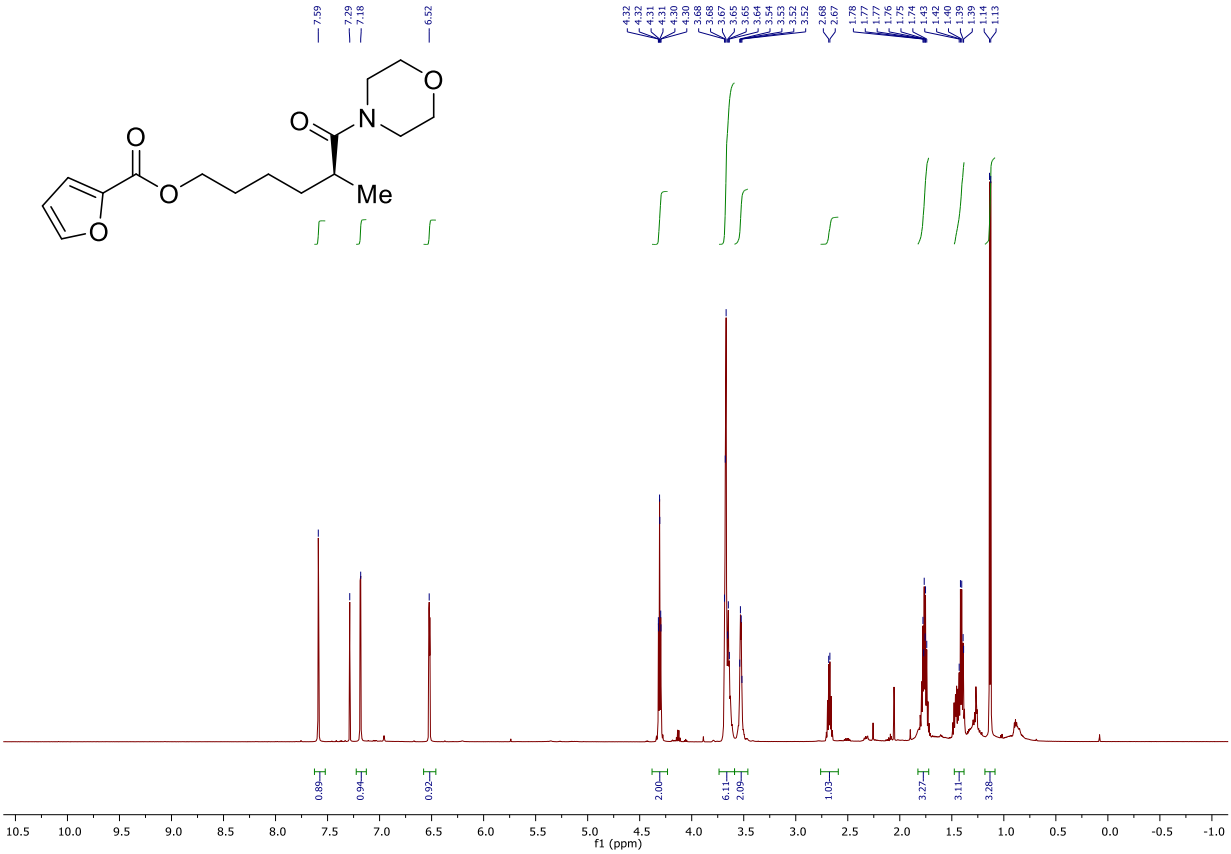

f1 (ppm)

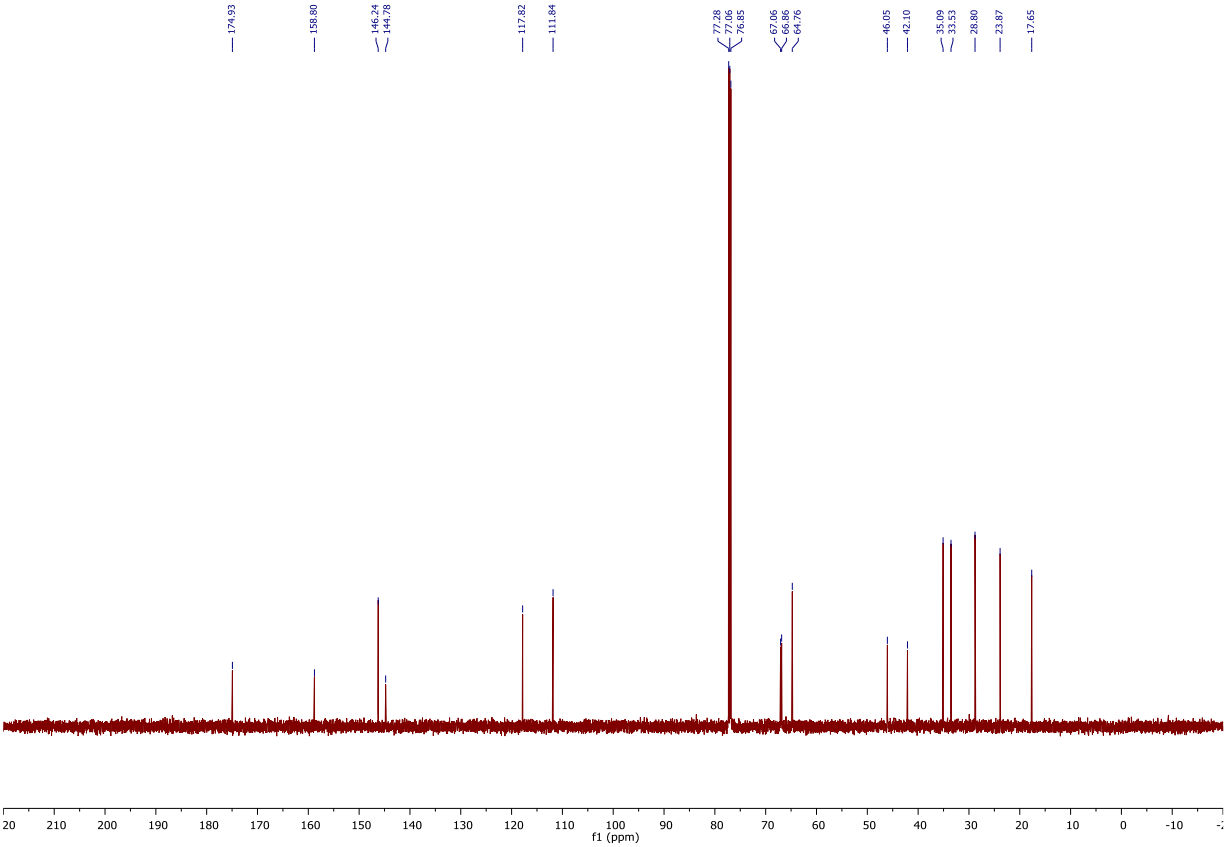

8.03
8.01
8.01
7.88
7.88
7.87
7.87
7.28
4.34
4.34
4.33
4.33
4.32
4.32
3.68
3.67
3.66
3.65
3.65
3.64
3.53
3.53
3.52
2.68
2.67
1.80
1.79
1.78
1.78
1.77
1.45
1.44
1.43
1.37
1.14
1.13
O
O
N
O
O
Me
PinB
1.88
1.88
1.94
5.93
1.87
0.96
3.19
3.17
11.32
2.88
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

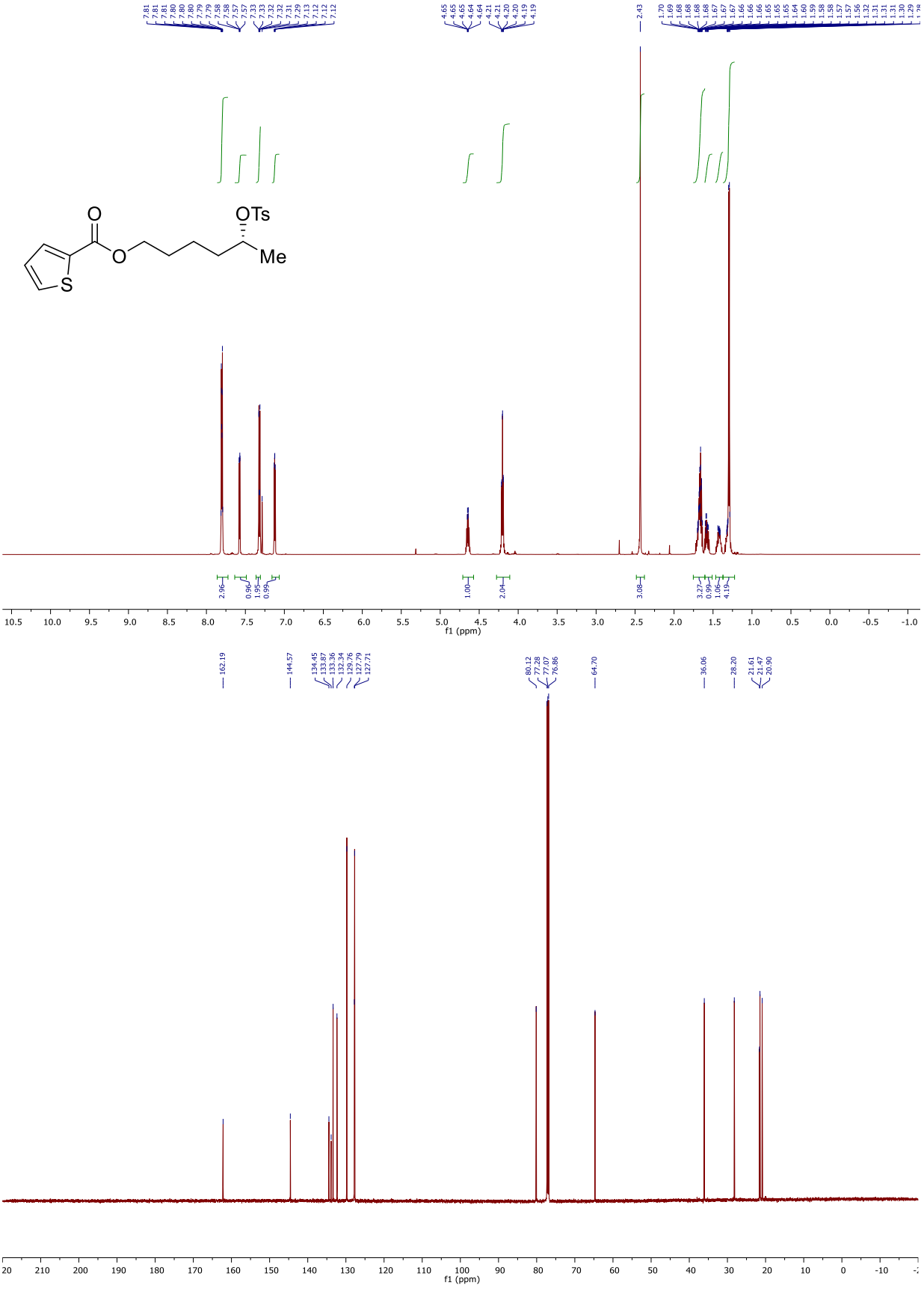

174.97
166.66
134.66
132.53
128.56
84.20
77.30
77.09
76.88
67.06
66.86
64.88
46.04
42.09
35.11
33.56
28.80
24.89
24.85
23.99
17.65
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

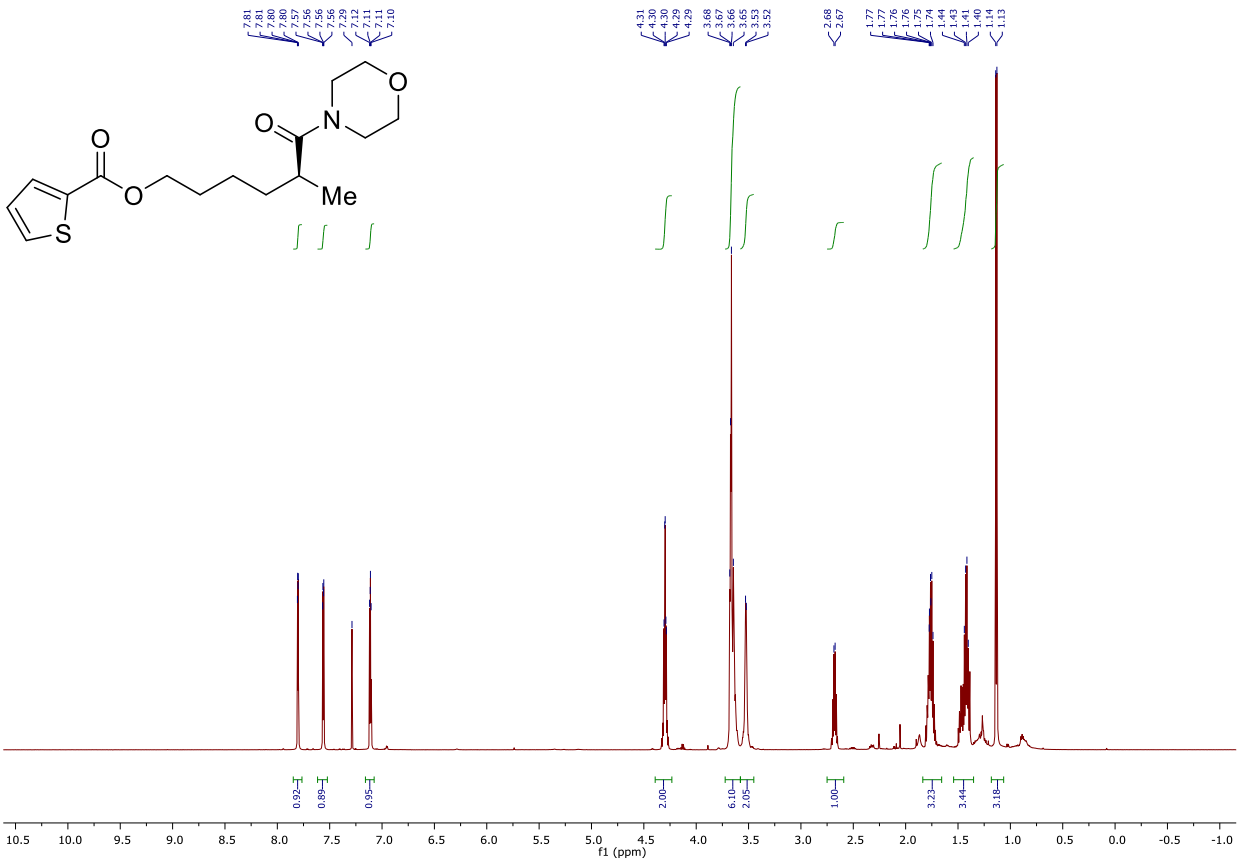

OTs
Me
f1 (ppm)

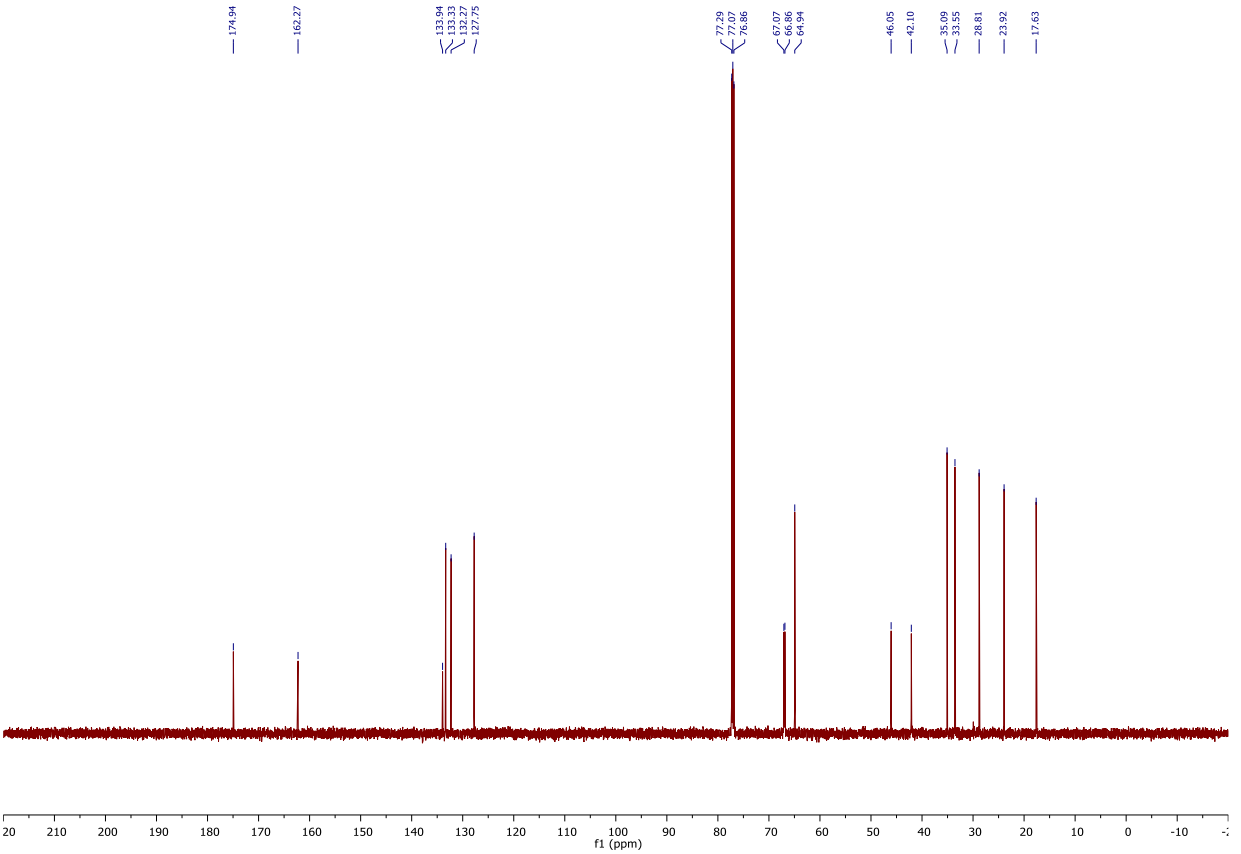

f1 (ppm)

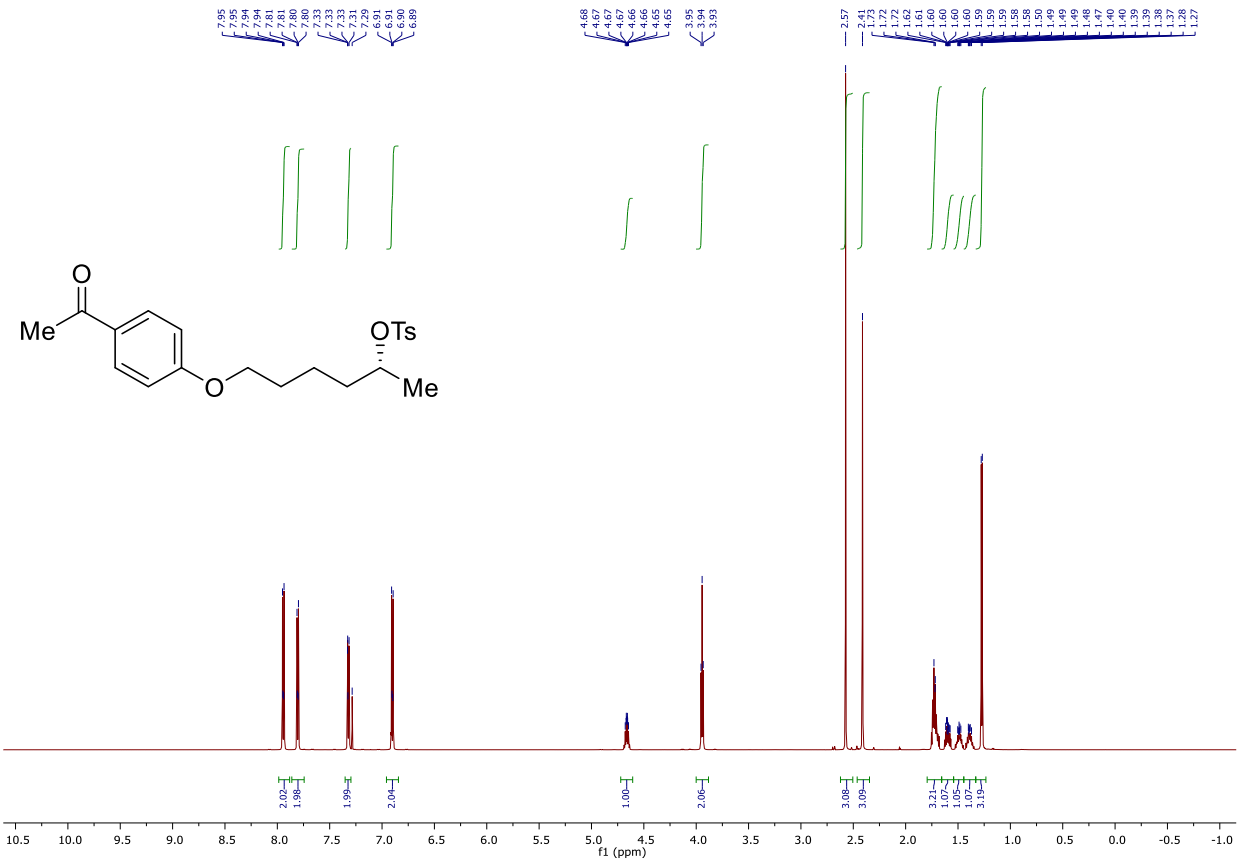

7.59
7.29
7.18
6.52
4.32
4.32
4.31
4.31
4.30
4.30
3.68
3.68
3.67
3.67
3.65
3.64
3.54
3.53
3.52
3.52
2.68
2.67
1.78
1.77
1.77
1.76
1.75
1.74
1.43
1.42
1.40
1.39
1.39
1.14
1.13
O
O
O
N
O
O
Me
0.89
0.94
0.92
2.00
6.11
2.09
1.03
3.27
3.11
3.28
f1 (ppm)

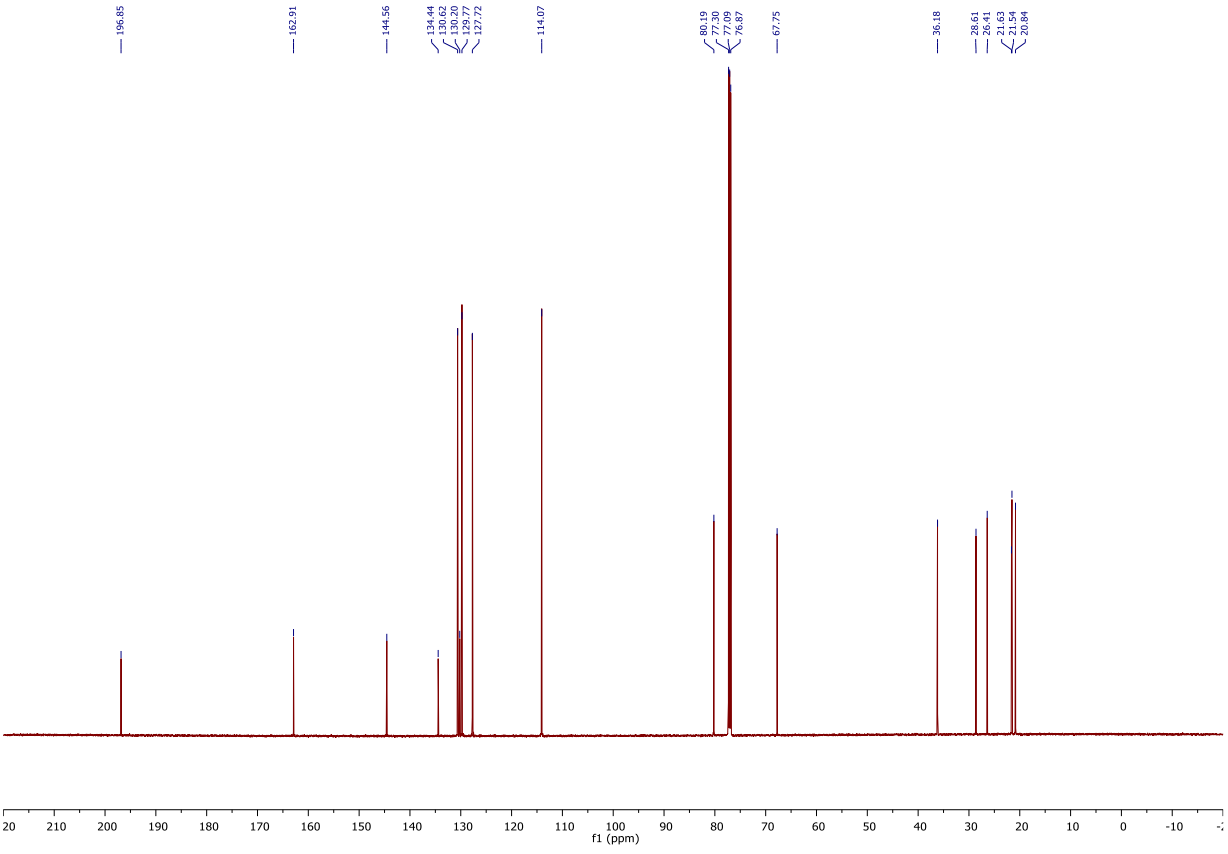

174.93
158.80
146.24
144.78
117.82
111.84
77.28
77.06
76.85
67.06
66.86
64.76
46.05
42.10
35.09
33.53
28.80
23.87
17.65
f1 (ppm)

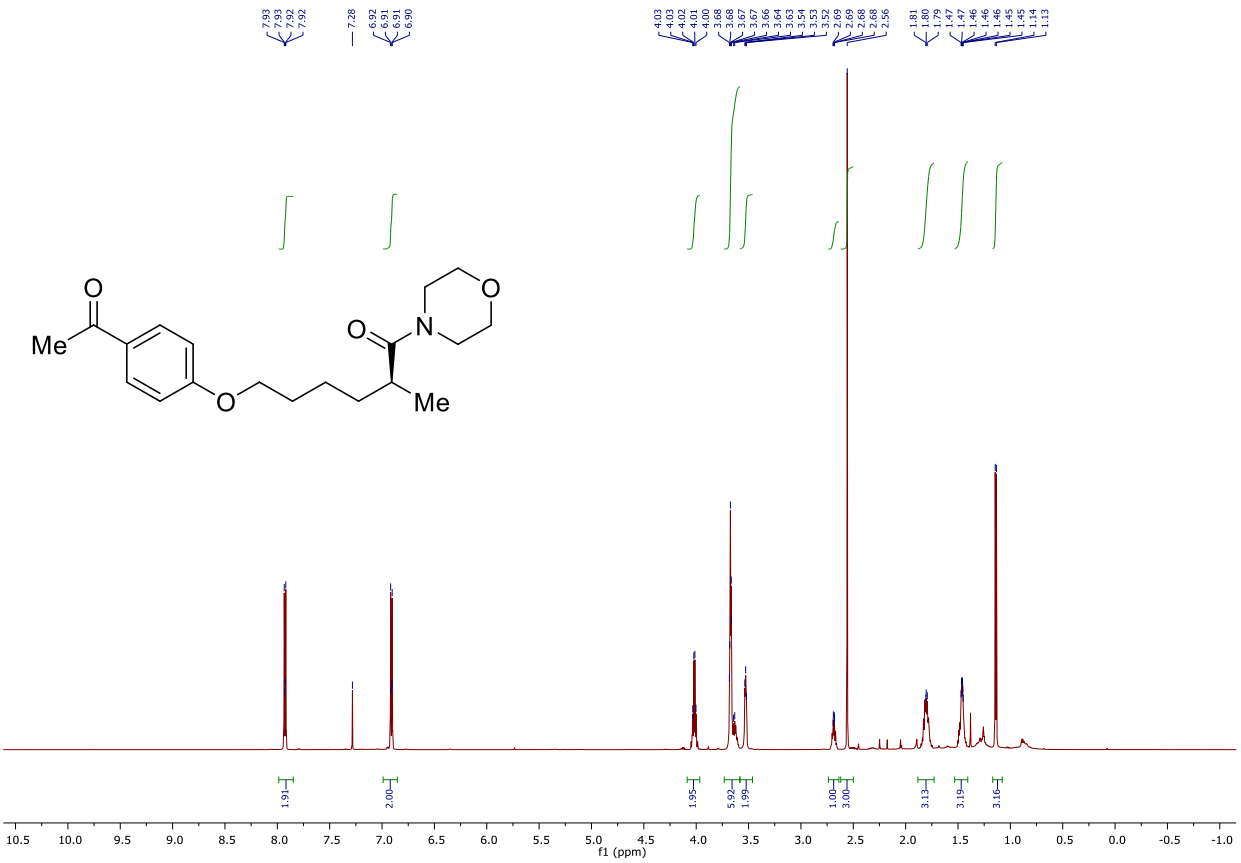

O
OTs
O
Me
S
f1 (ppm)
f1 (ppm)

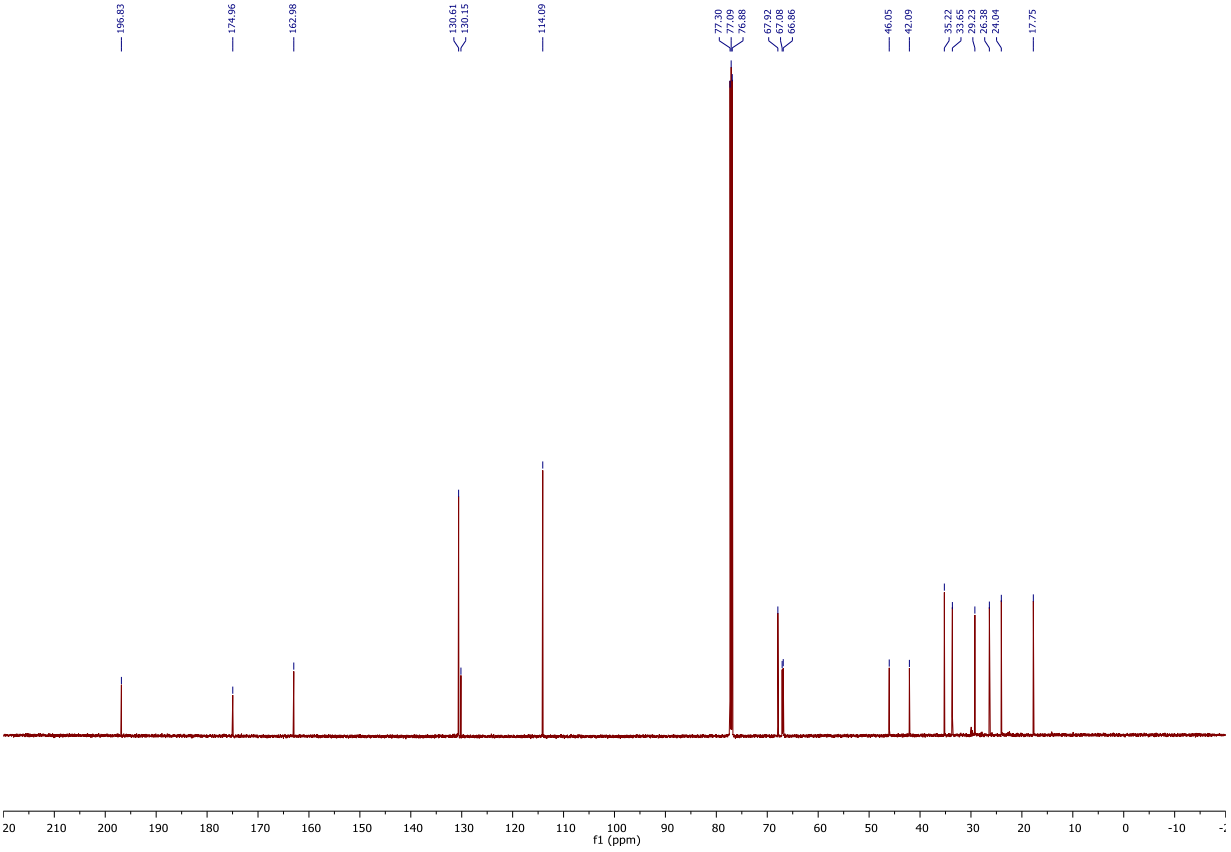

7.81
7.81
7.80
7.80
7.57
7.56
7.56
7.56
7.39
7.12
7.11
7.11
7.10
4.31
4.30
4.30
4.29
4.29
3.68
3.67
3.66
3.65
3.53
3.52
2.68
2.67
1.77
1.77
1.76
1.76
1.75
1.74
1.44
1.43
1.41
1.40
1.14
1.13
O
O
N
O
O
Me
S
0.92
0.89
0.95
2.00
6.10
2.05
1.00
3.23
3.44
3.18
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

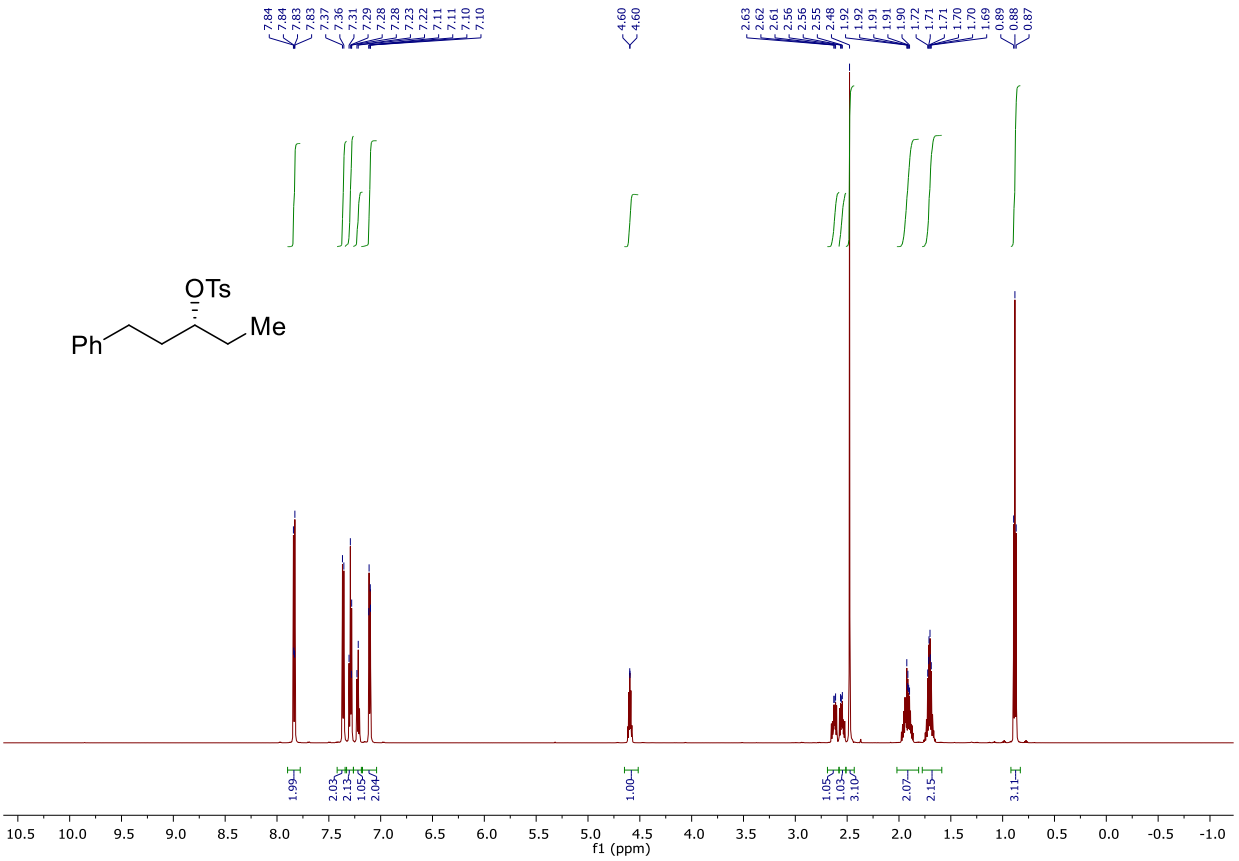

174.94
162.27
133.94
133.33
132.27
127.75
77.29
77.07
76.86
67.07
66.86
64.94
46.05
42.10
35.09
33.55
28.81
23.92
17.63
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

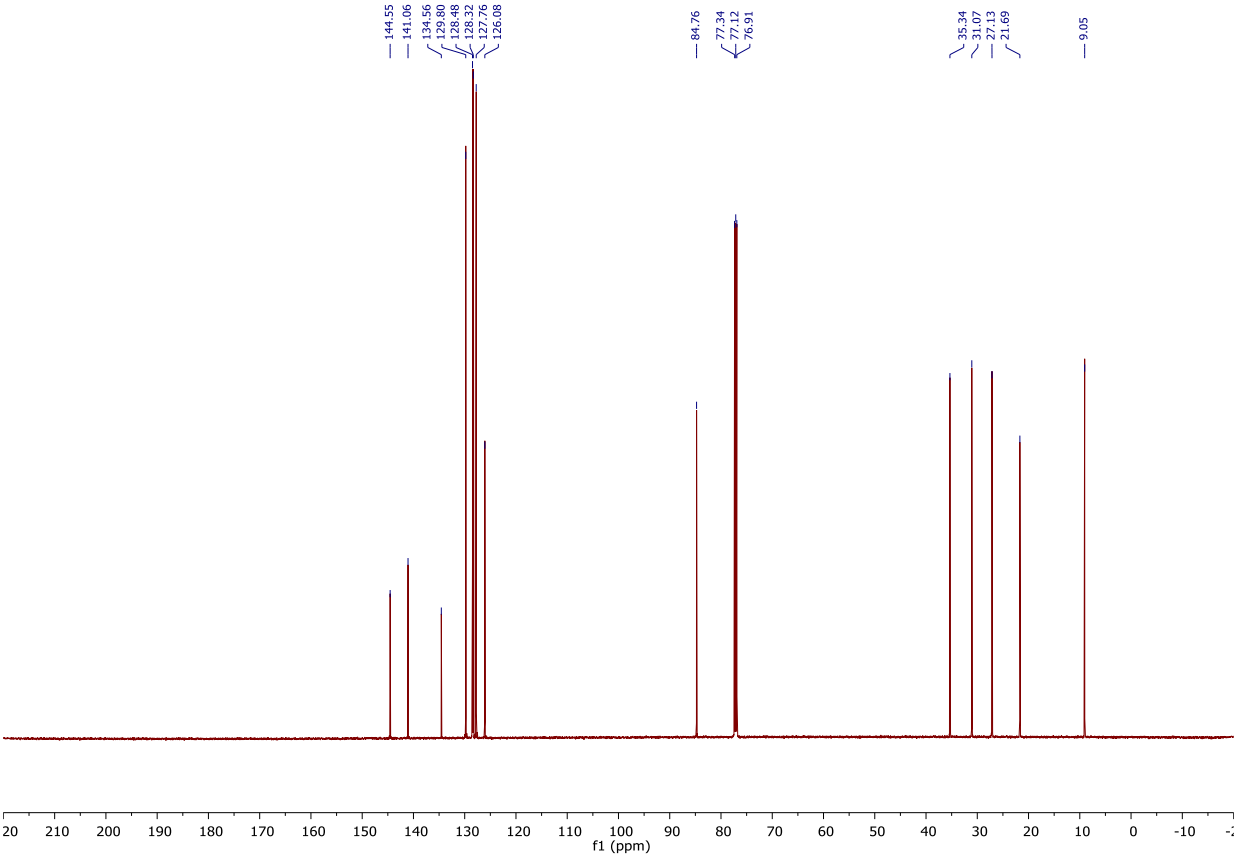

Me
O
O
OTs
Me
f1 (ppm)

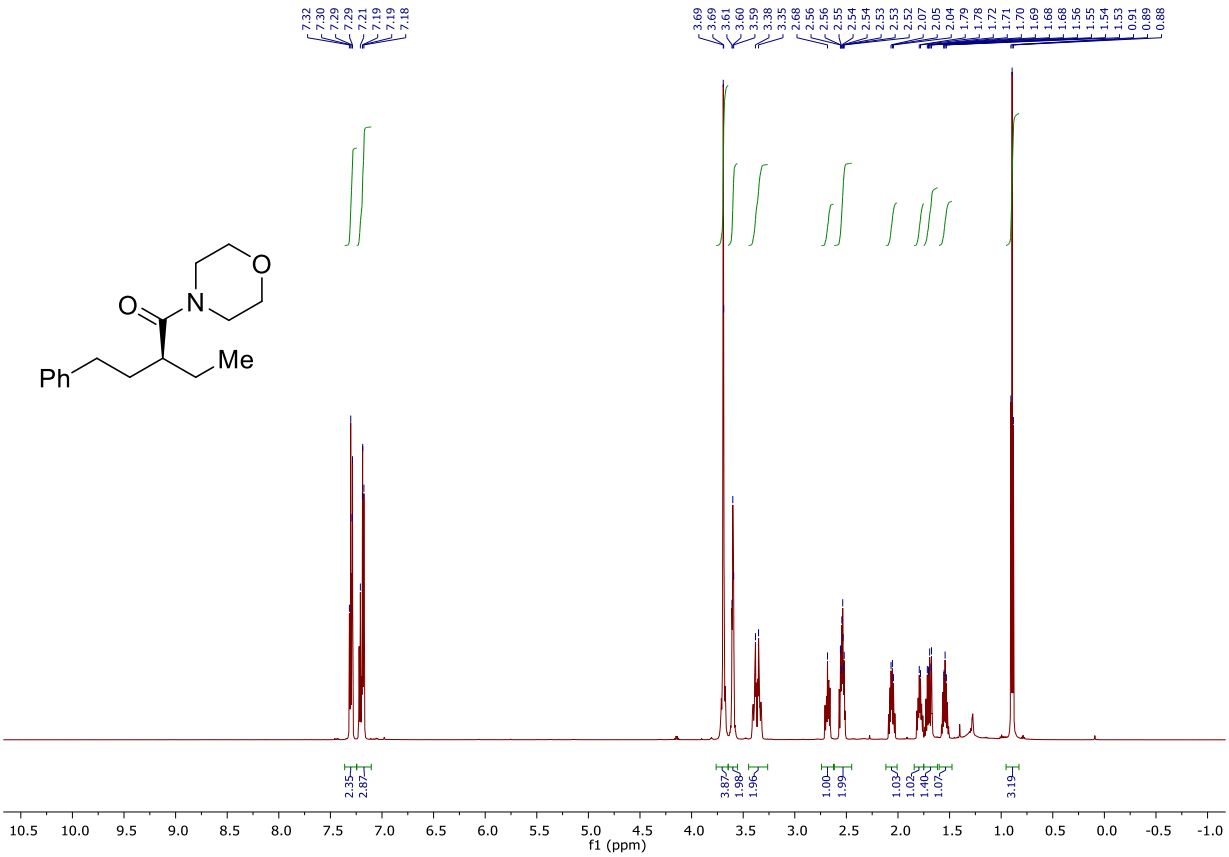

f1 (ppm)

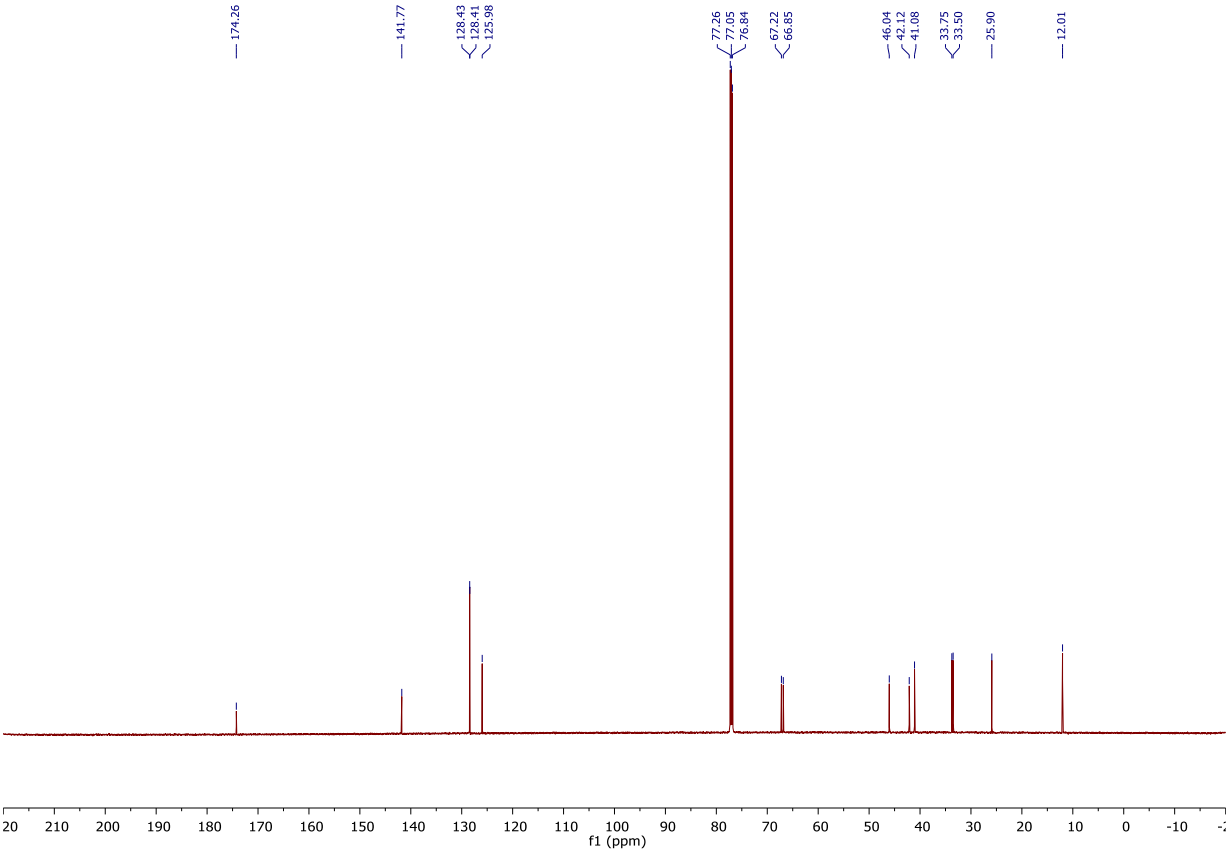

7.93
7.93
7.92
7.92
7.28
6.92
6.91
6.91
6.90
4.03
4.03
4.02
4.01
4.00
3.68
3.68
3.67
3.67
3.66
3.64
3.63
3.54
3.53
3.52
2.69
2.69
2.68
2.68
2.56
1.81
1.80
1.79
1.47
1.47
1.46
1.46
1.46
1.45
1.45
1.14
1.13
O
Me
O
N
O
O
Me
1.91
2.00
1.95
5.92
1.99
1.00
3.00
3.13
3.19
3.16
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

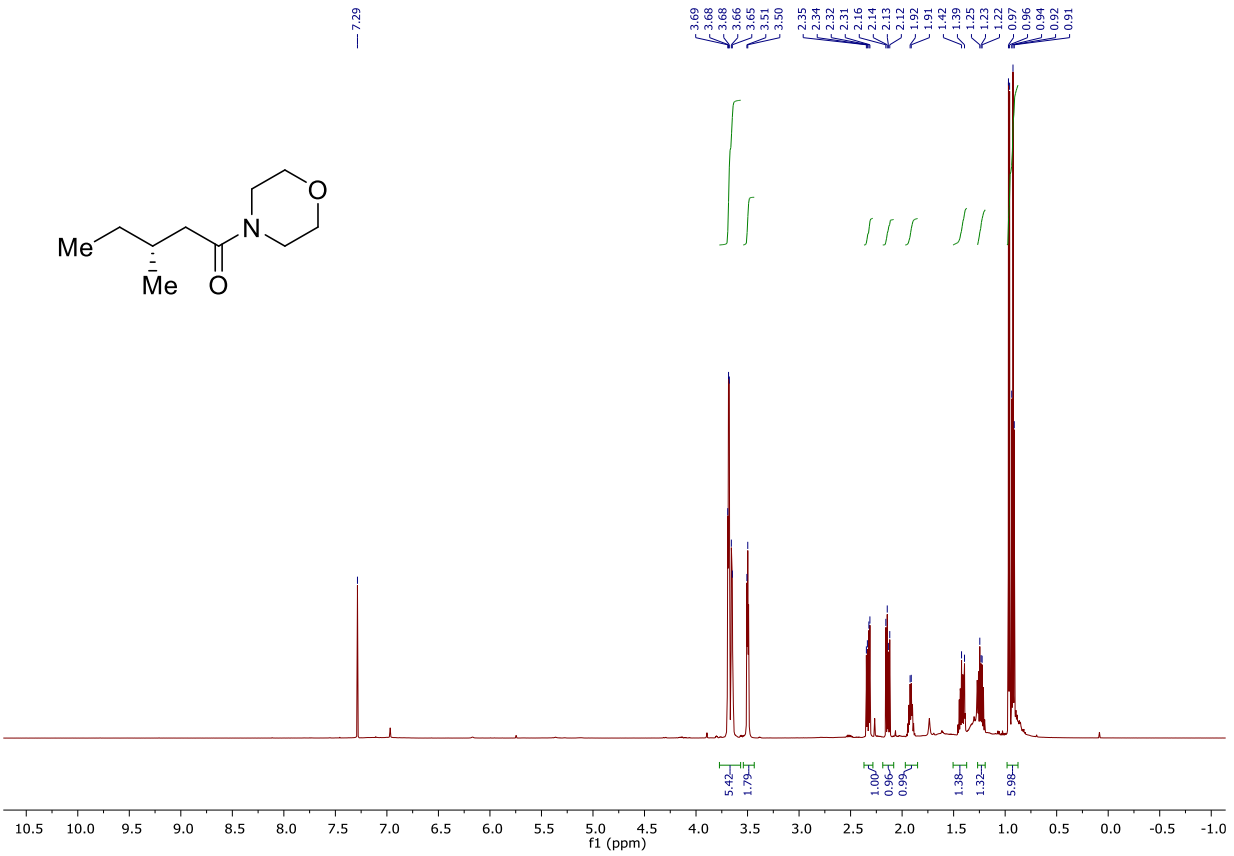

196.83
174.96
162.98
130.61
130.15
114.09
77.30
77.09
76.88
67.92
67.08
66.86
46.05
42.09
35.22
33.65
29.23
26.38
24.04
17.75
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

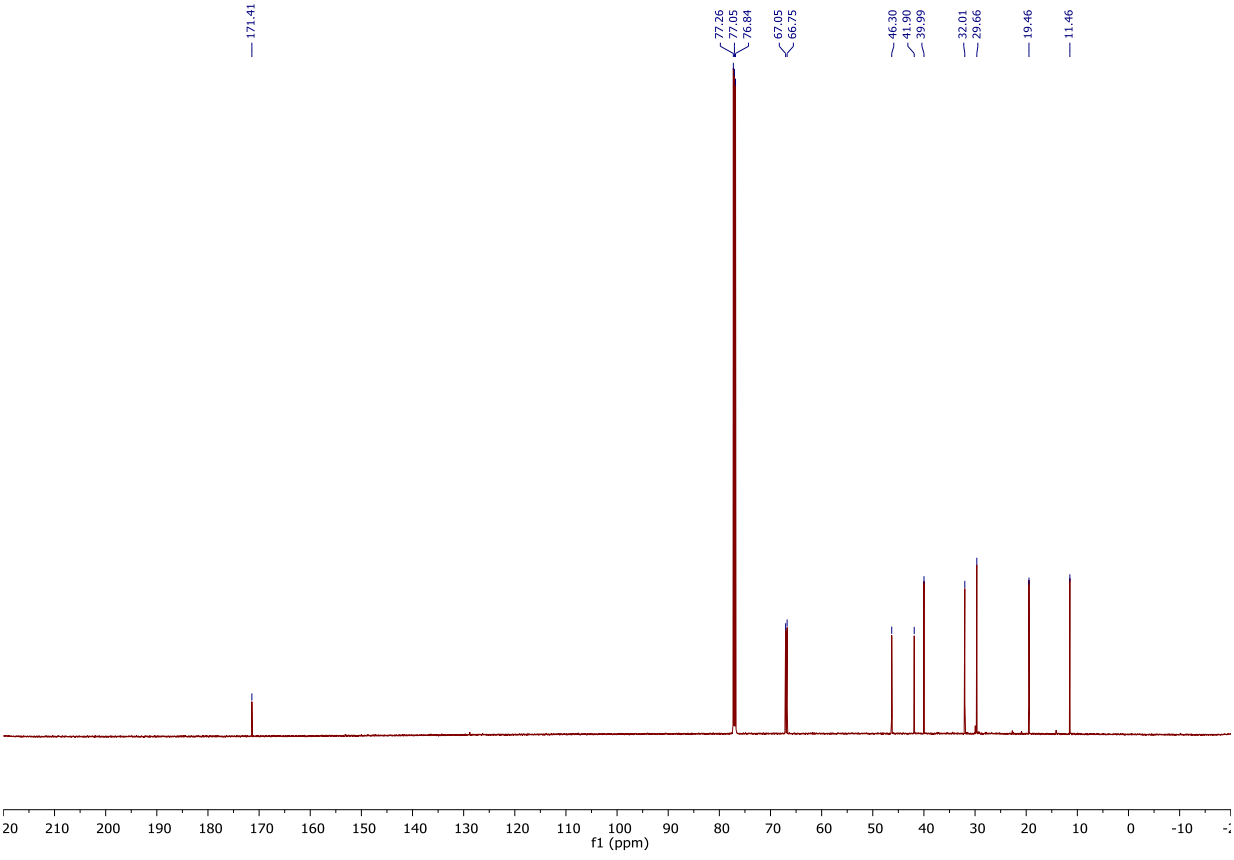

OTs
Me
Ph
f1 (ppm)

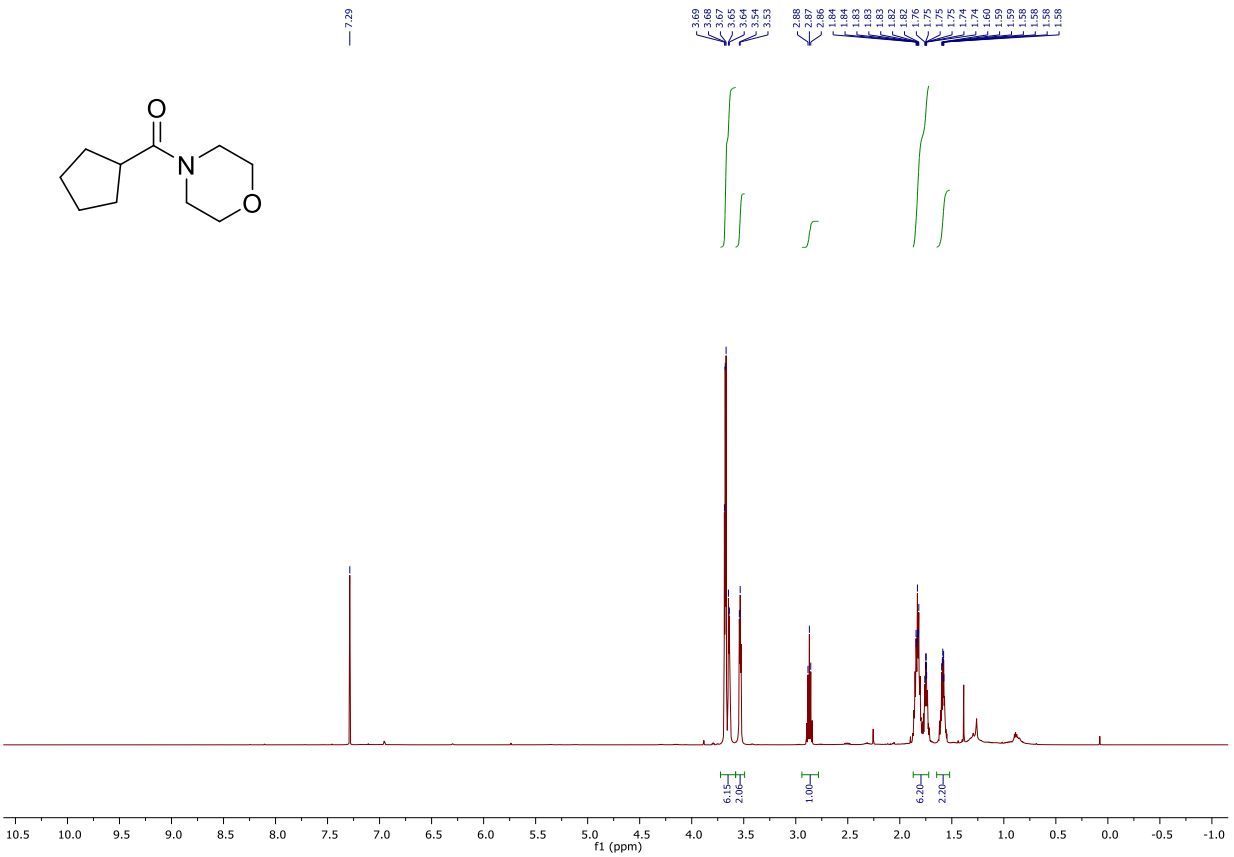

f1 (ppm)

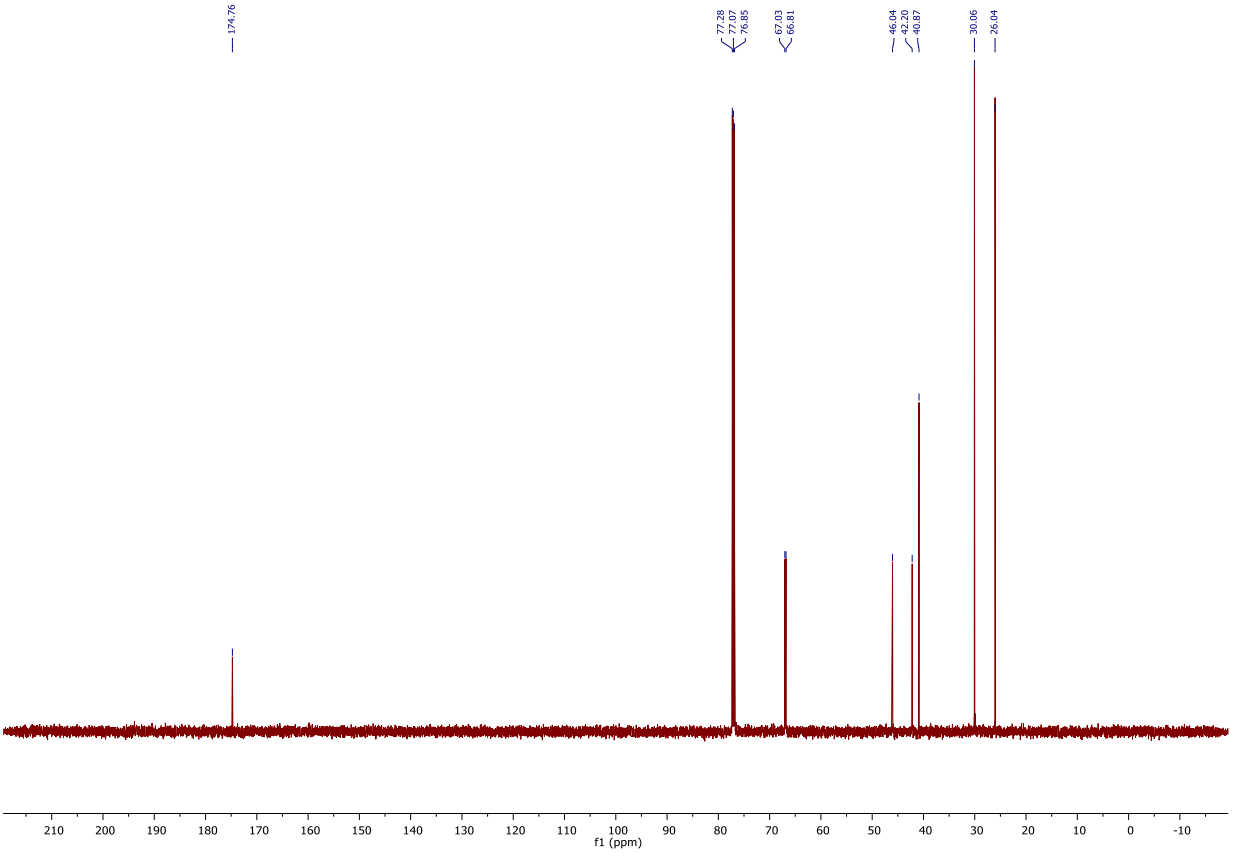

7.32
7.30
7.29
7.29
7.21
7.19
7.19
7.18
3.69
3.69
3.61
3.60
3.59
3.38
3.35
2.68
2.56
2.56
2.55
2.54
2.54
2.53
2.53
2.52
2.07
2.05
2.04
1.79
1.78
1.72
1.71
1.70
1.69
1.68
1.68
1.56
1.55
1.54
1.53
0.91
0.89
0.88
O
N
O
Me
Ph
2.35
2.87
3.87
1.98
1.96
1.00
1.99
1.03
1.02
1.40
1.07
3.19
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

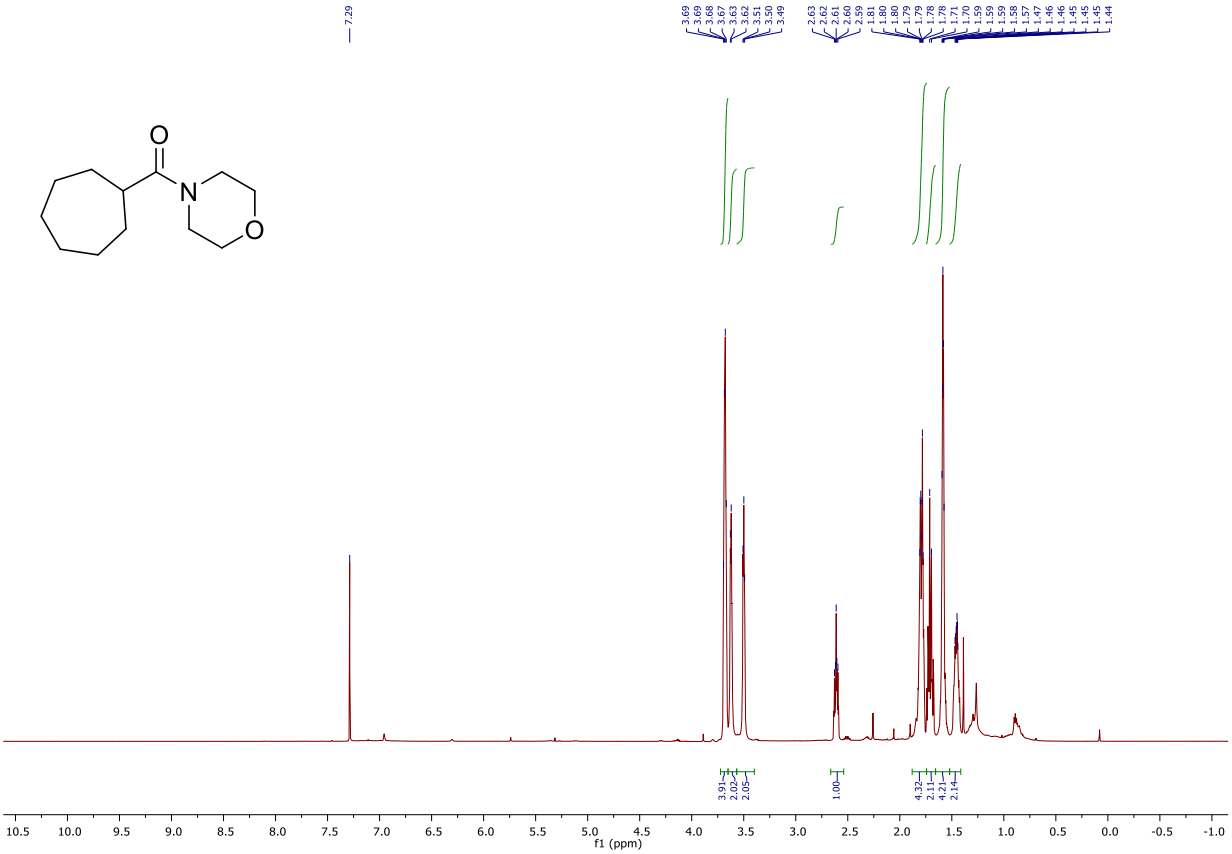

174.26
141.77
128.43
128.41
125.98
77.26
77.05
76.84
67.22
66.85
46.04
42.12
41.08
33.75
33.50
25.90
12.01
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

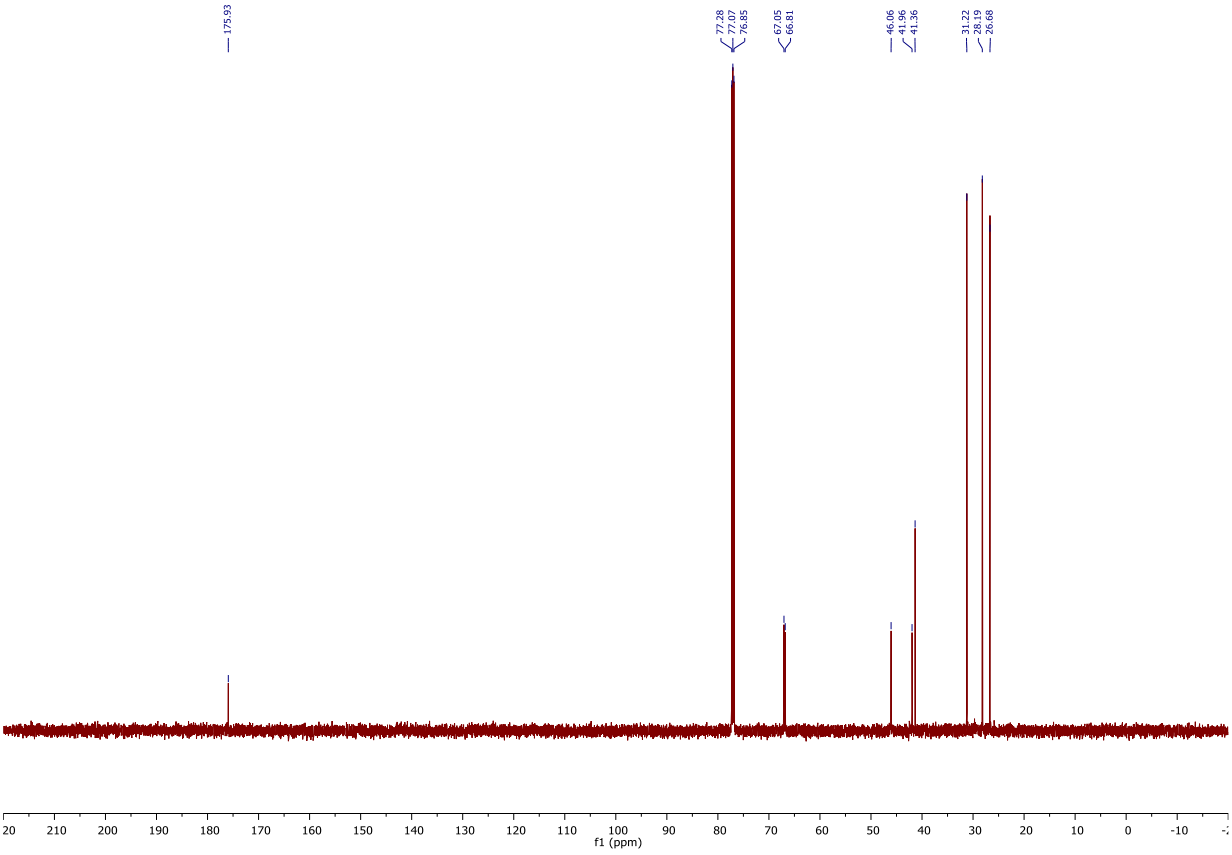

7.29
3.69
3.68
3.68
3.66
3.65
3.51
3.50
2.35
2.34
2.32
2.31
2.16
2.14
2.13
2.12
1.92
1.91
1.42
1.39
1.25
1.23
1.22
0.97
0.96
0.94
0.92
0.91
Me
Me
O
N
O
5.42
1.79
1.00
0.96
0.99
1.38
1.32
5.98
f1 (ppm)

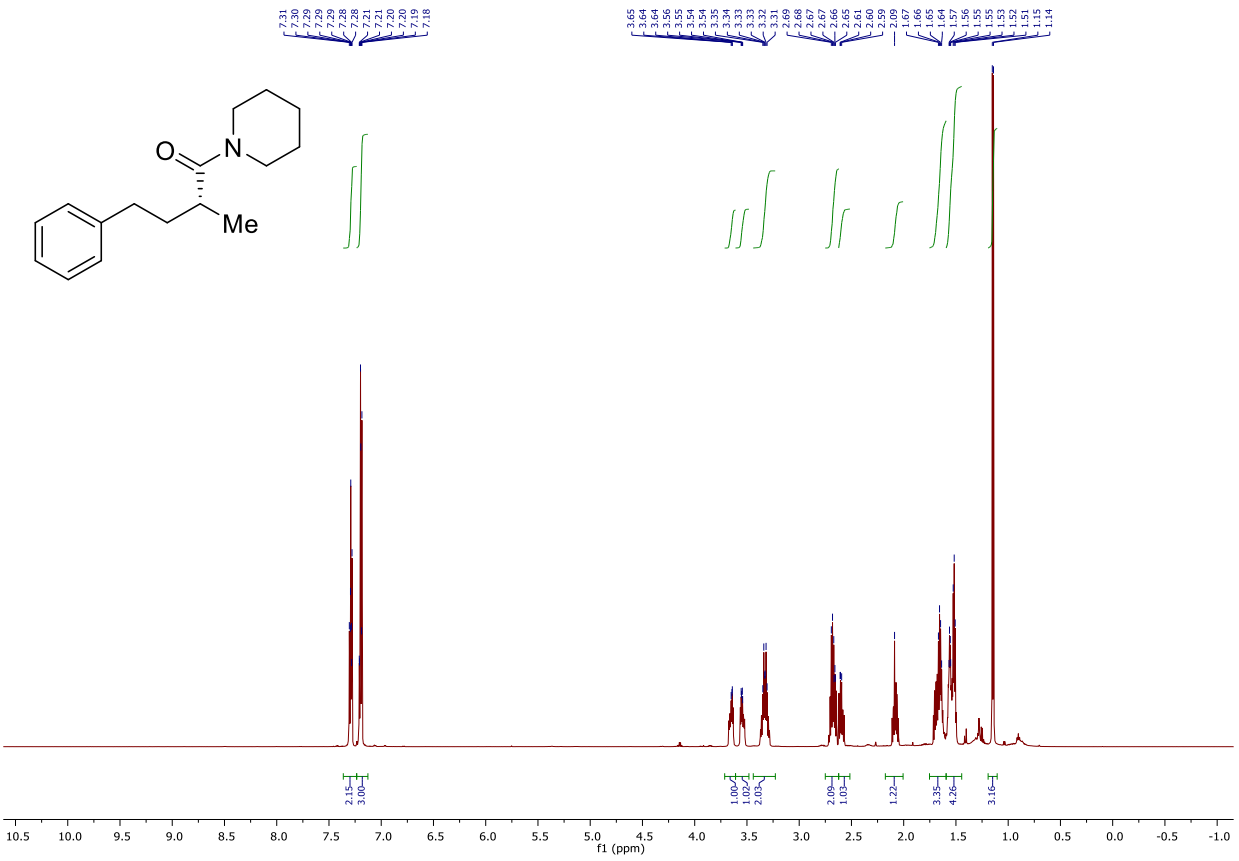

171.41
77.26
77.05
76.84
67.05
66.75
46.30
41.90
39.99
32.01
29.66
19.46
11.46
f1 (ppm)

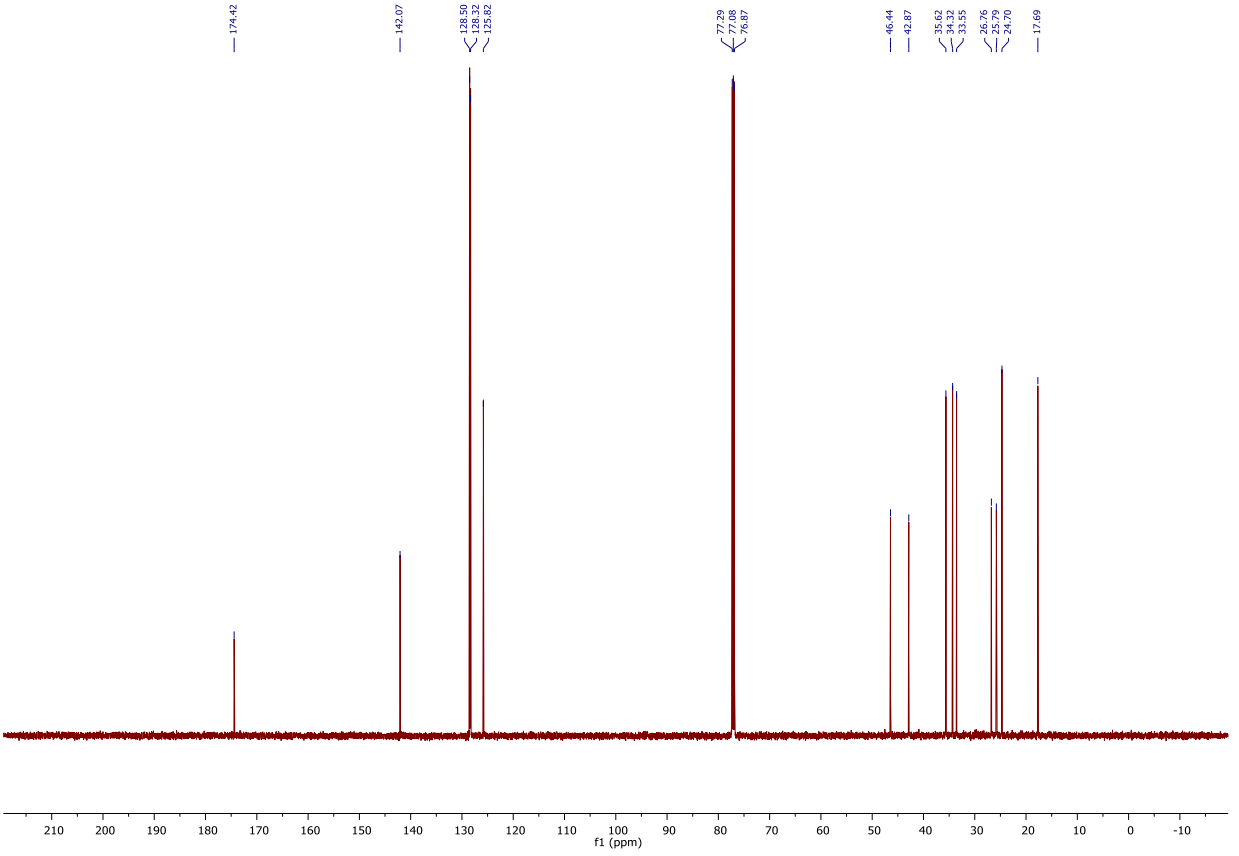

7.29
3.69
3.68
3.67
3.65
3.64
3.54
3.53
2.88
2.87
2.86
1.84
1.83
1.83
1.82
1.82
1.76
1.75
1.75
1.75
1.74
1.74
1.60
1.59
1.59
1.58
1.58
1.58
1.58
6.15
2.06
1.00
6.20
2.20
f1 (ppm)

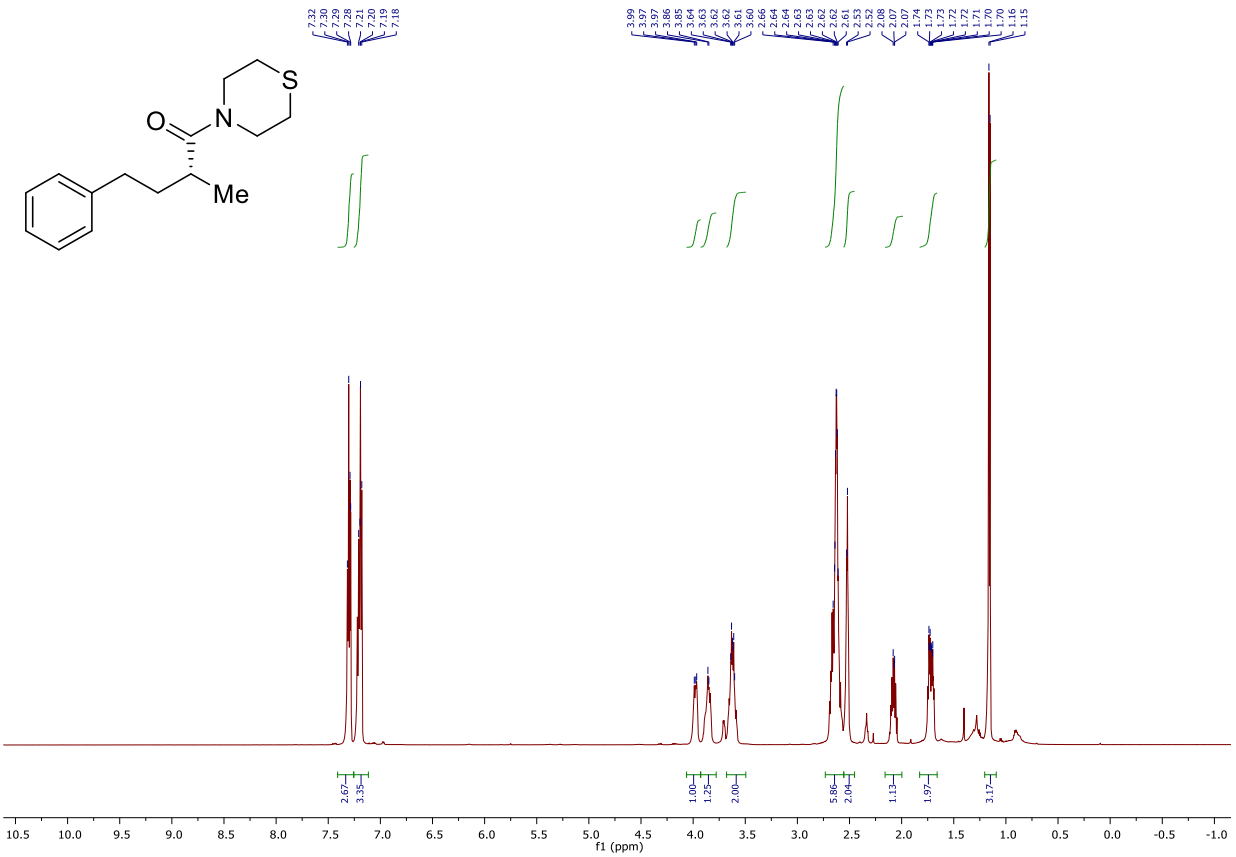

174.76
77.28
77.07
76.85
67.03
66.61
46.04
42.20
40.87
30.06
26.04
f1 (ppm)

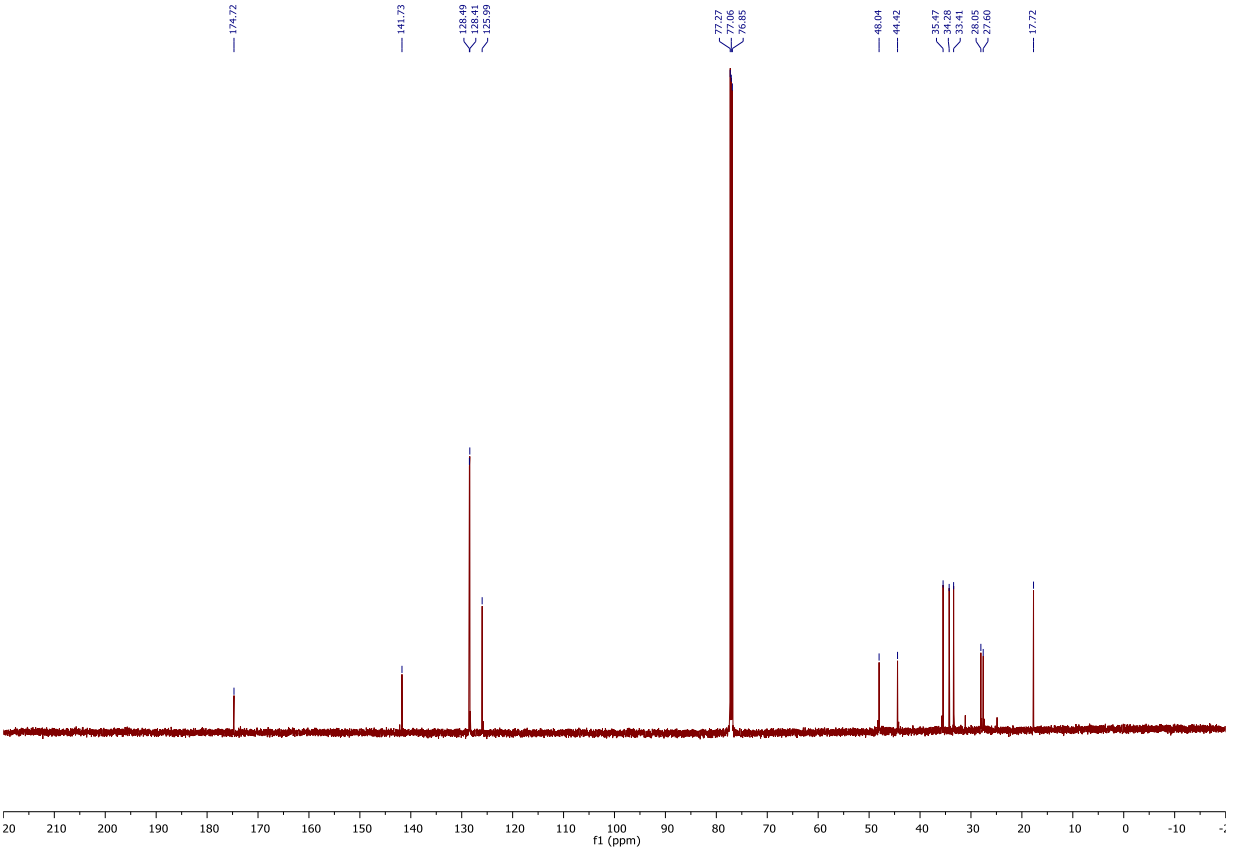

7.29
3.69
3.69
3.68
3.67
3.65
3.62
3.51
3.50
3.49
2.63
2.62
2.61
2.60
2.59
1.81
1.80
1.80
1.79
1.79
1.78
1.78
1.71
1.70
1.59
1.59
1.59
1.58
1.57
1.47
1.46
1.46
1.45
1.45
1.45
1.44
O
N
O
3.01
2.02
2.05
1.00
4.32
2.11
4.21
2.14
f1 (ppm)

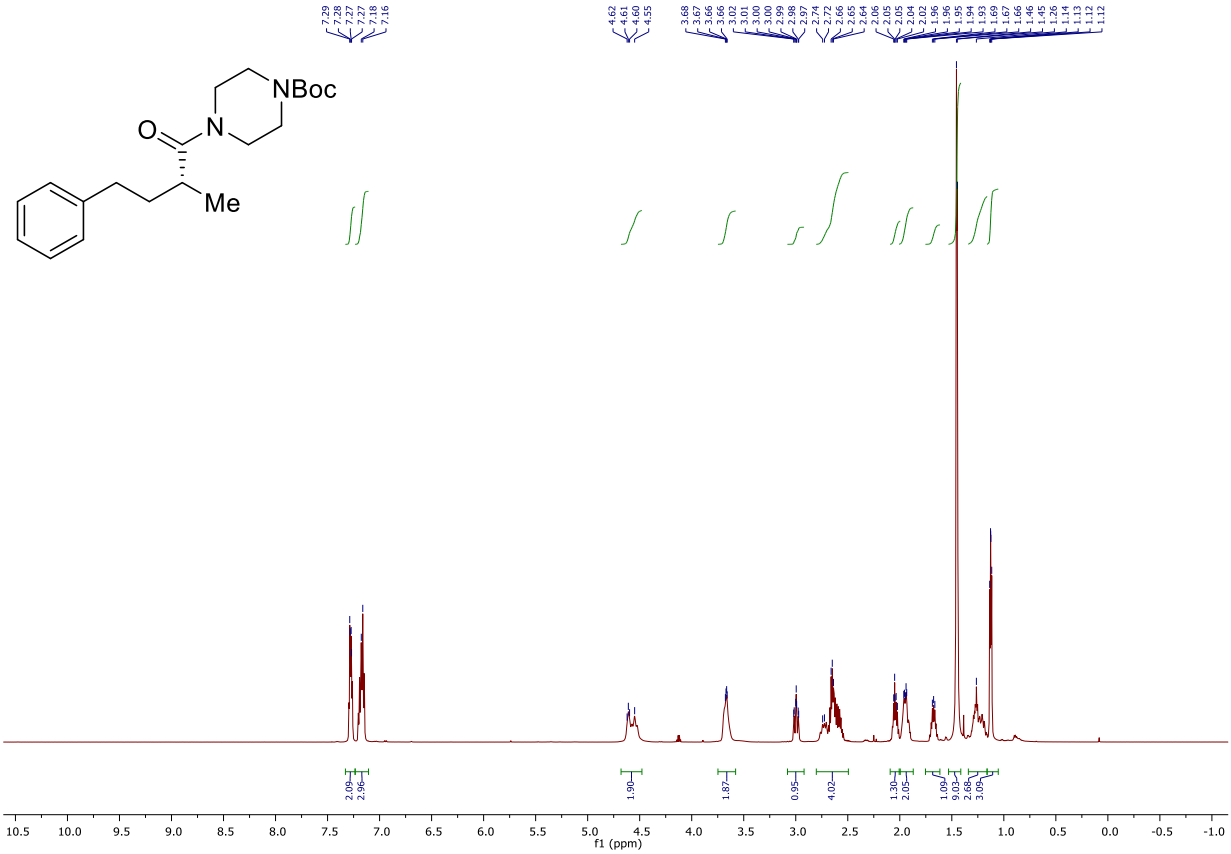

175.93
77.28
77.07
76.85
67.05
66.61
46.06
41.96
41.36
31.22
28.19
26.68
f1 (ppm)

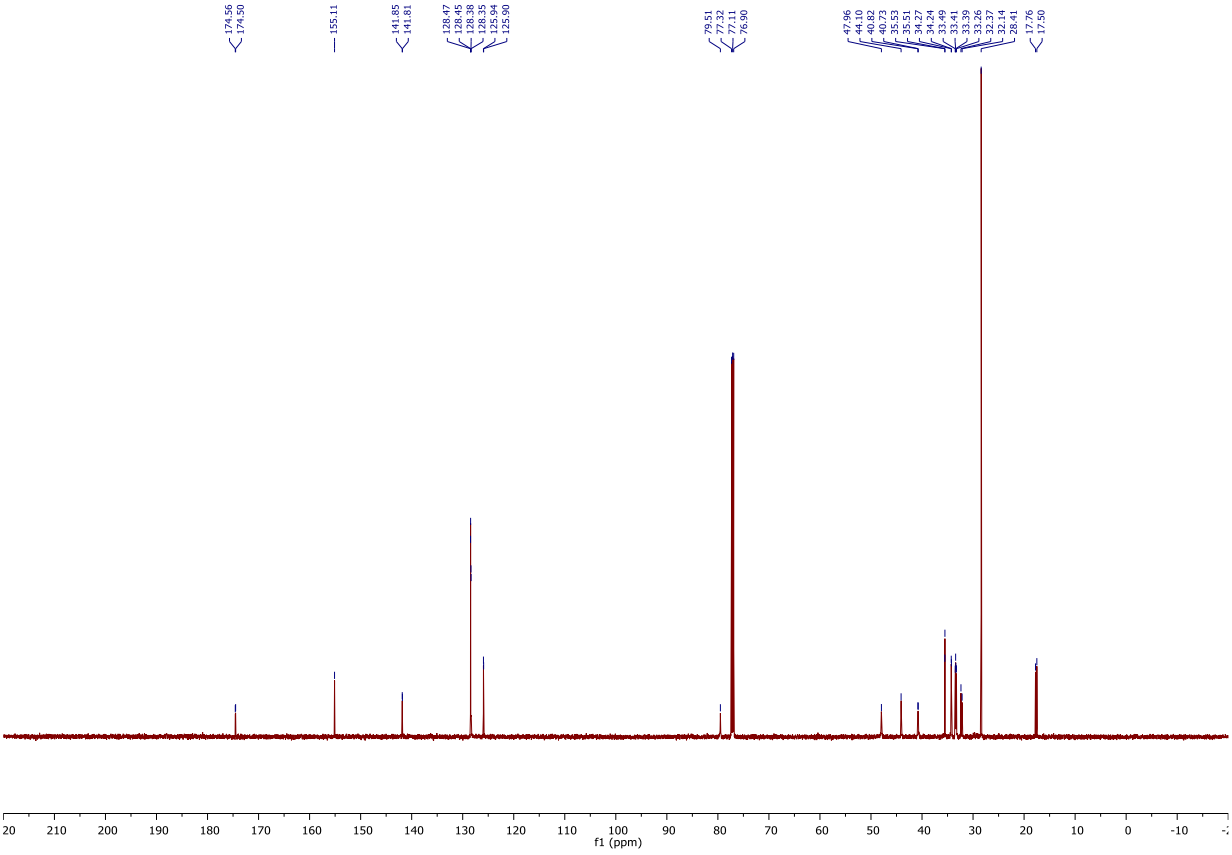

O
N
Me
f1 (ppm)

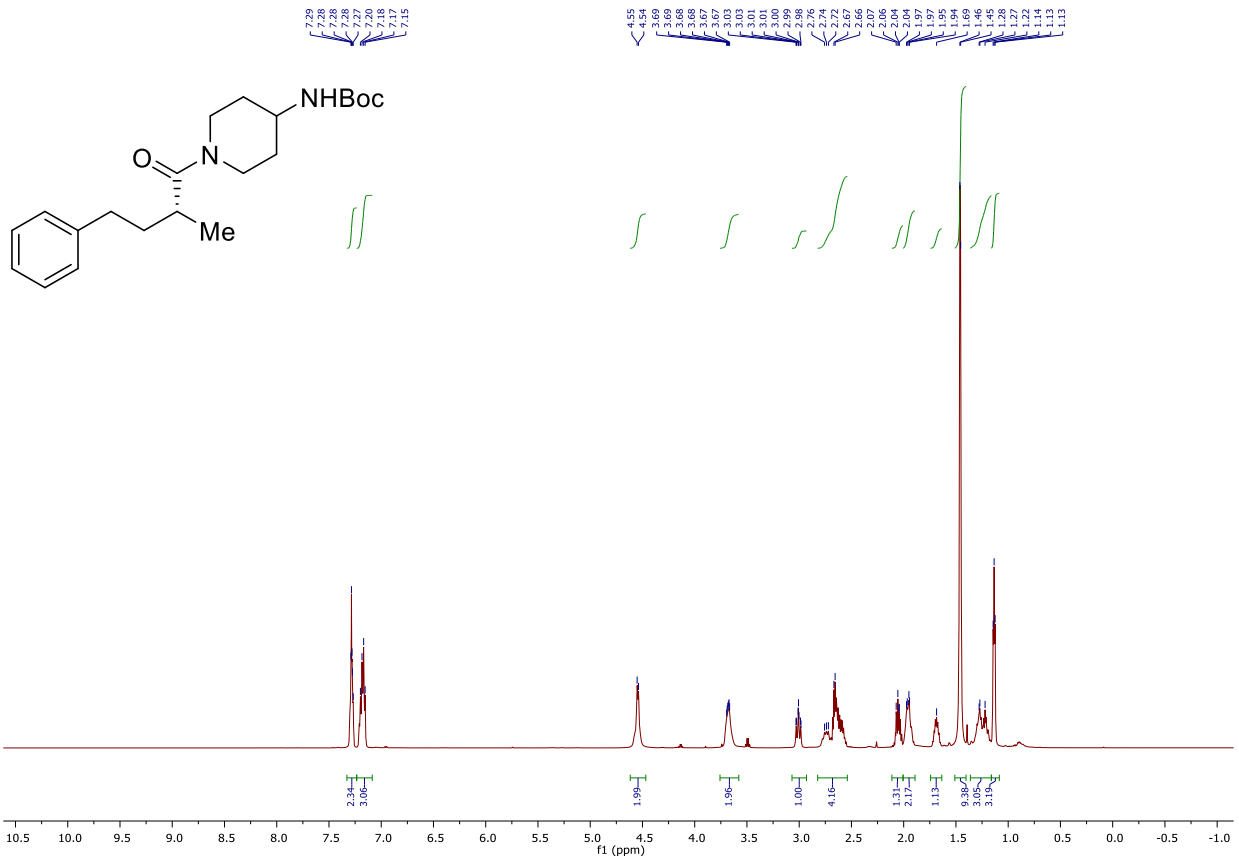

f1 (ppm)

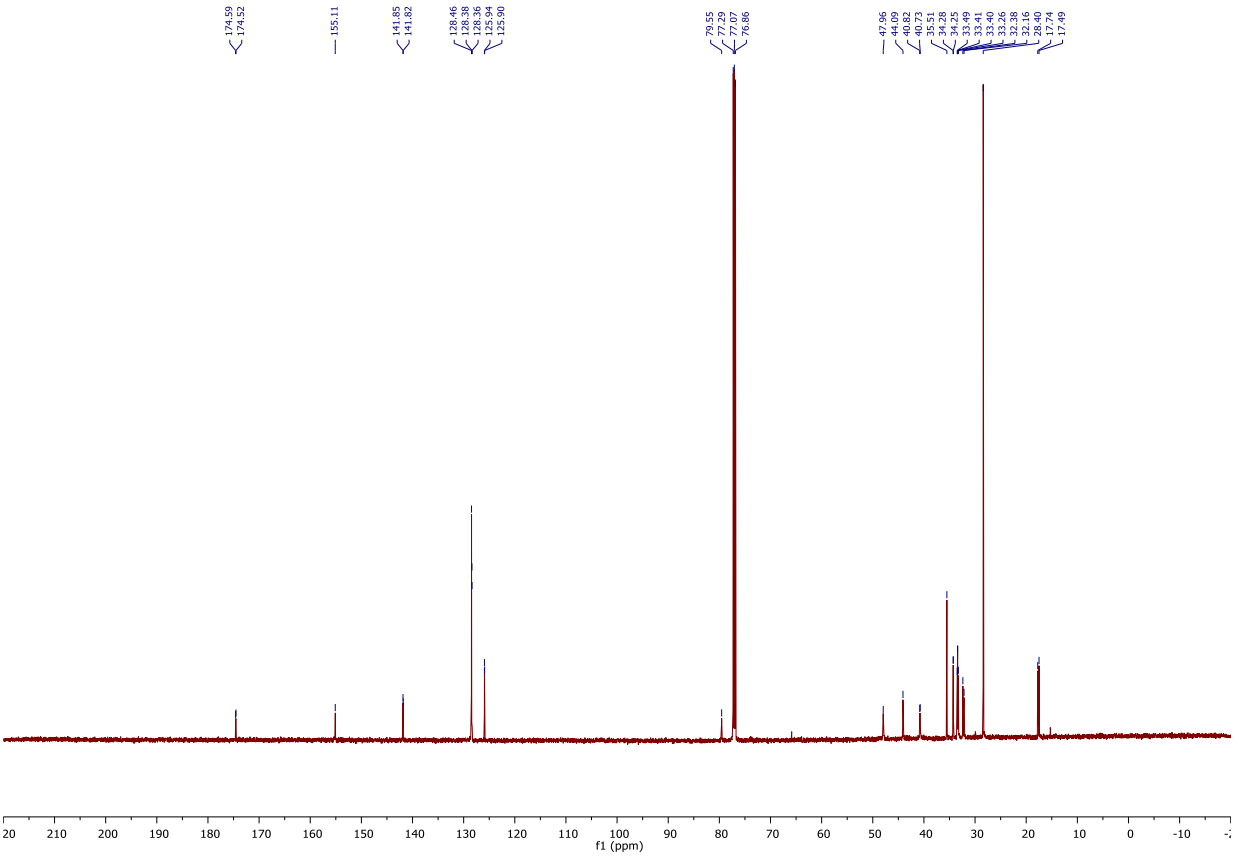

O
N
S
Me
f1 (ppm)

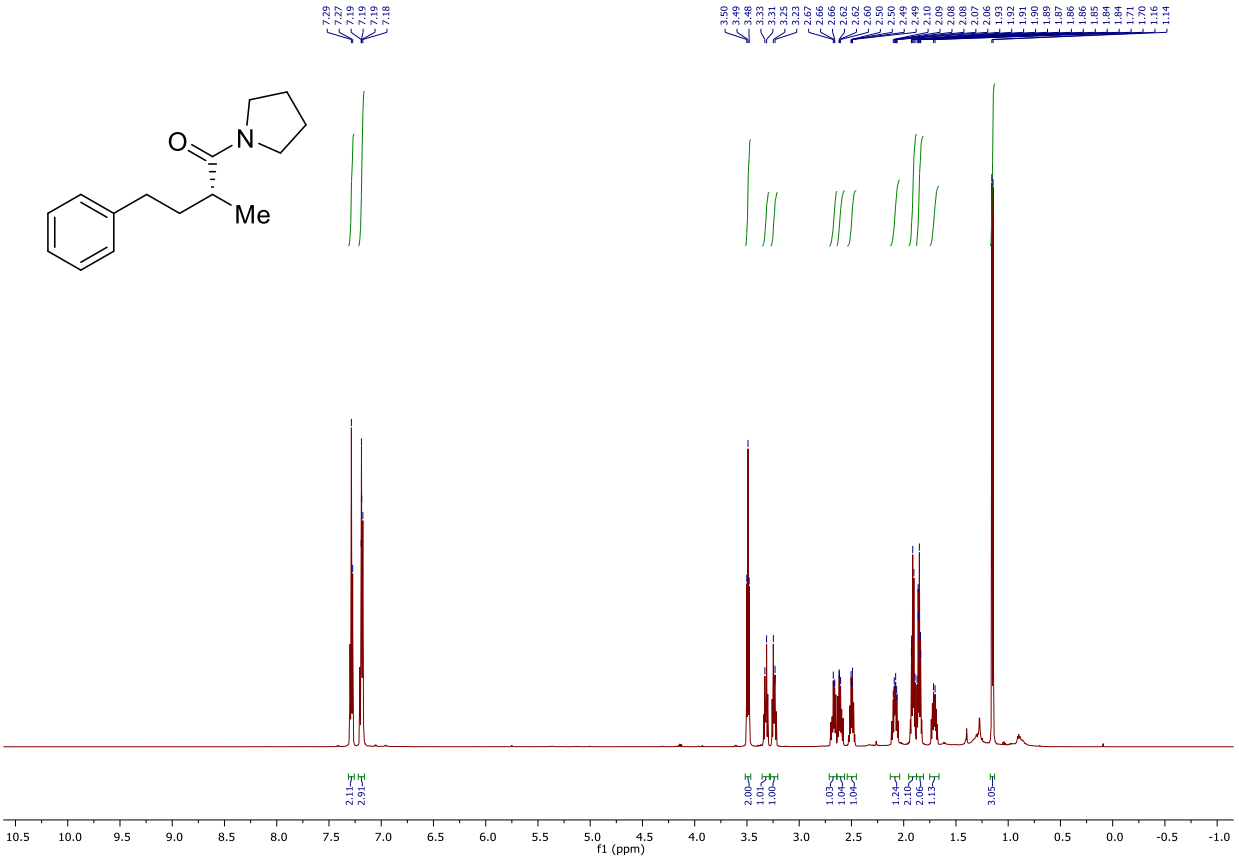

f1 (ppm)

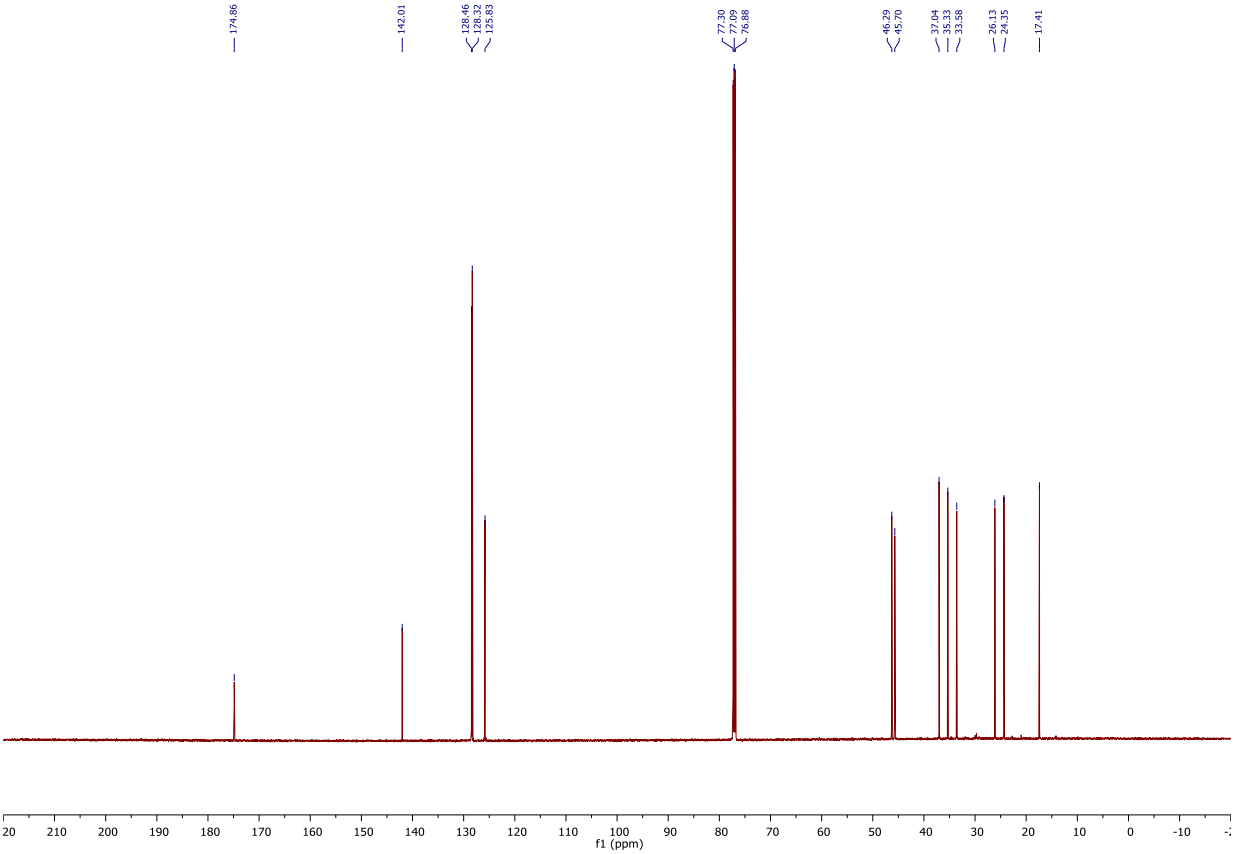

NBoc
O
N
Me
f1 (ppm)

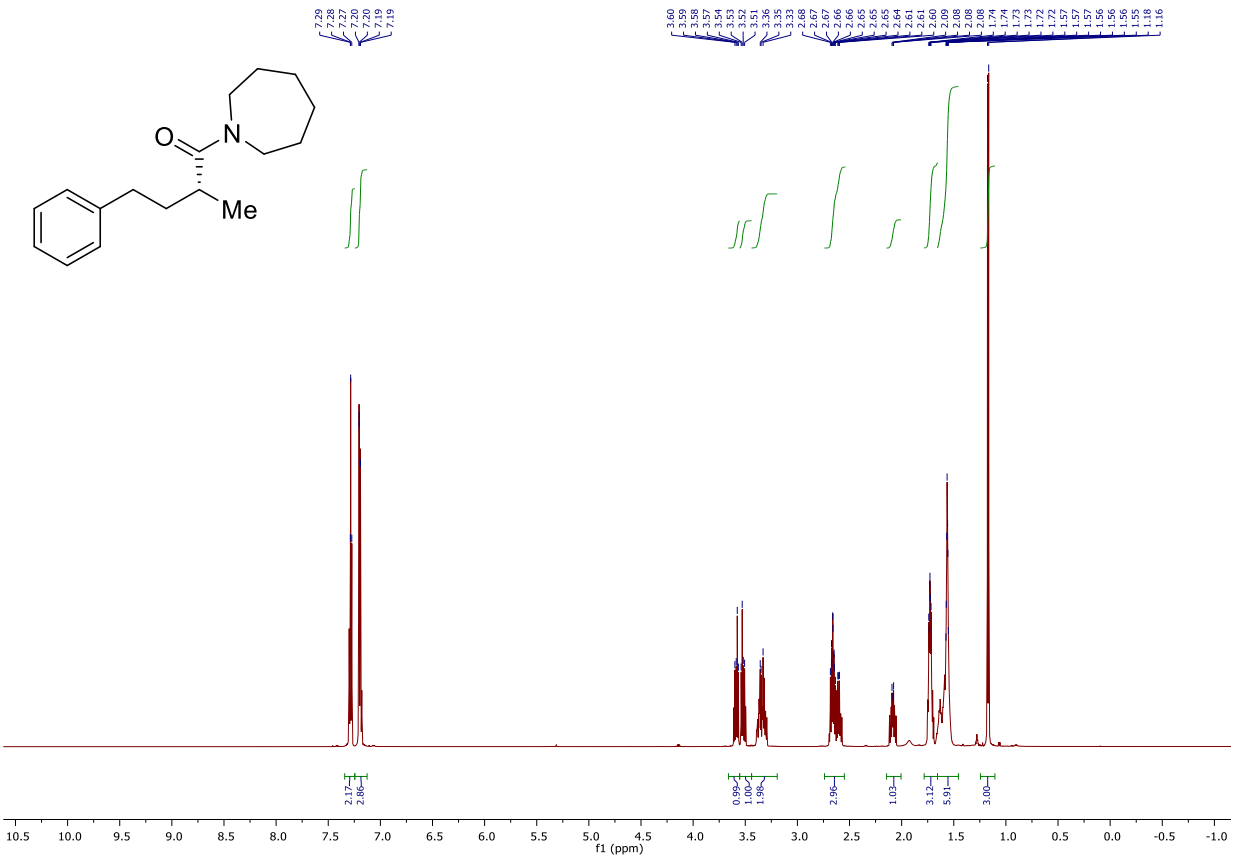

f1 (ppm)

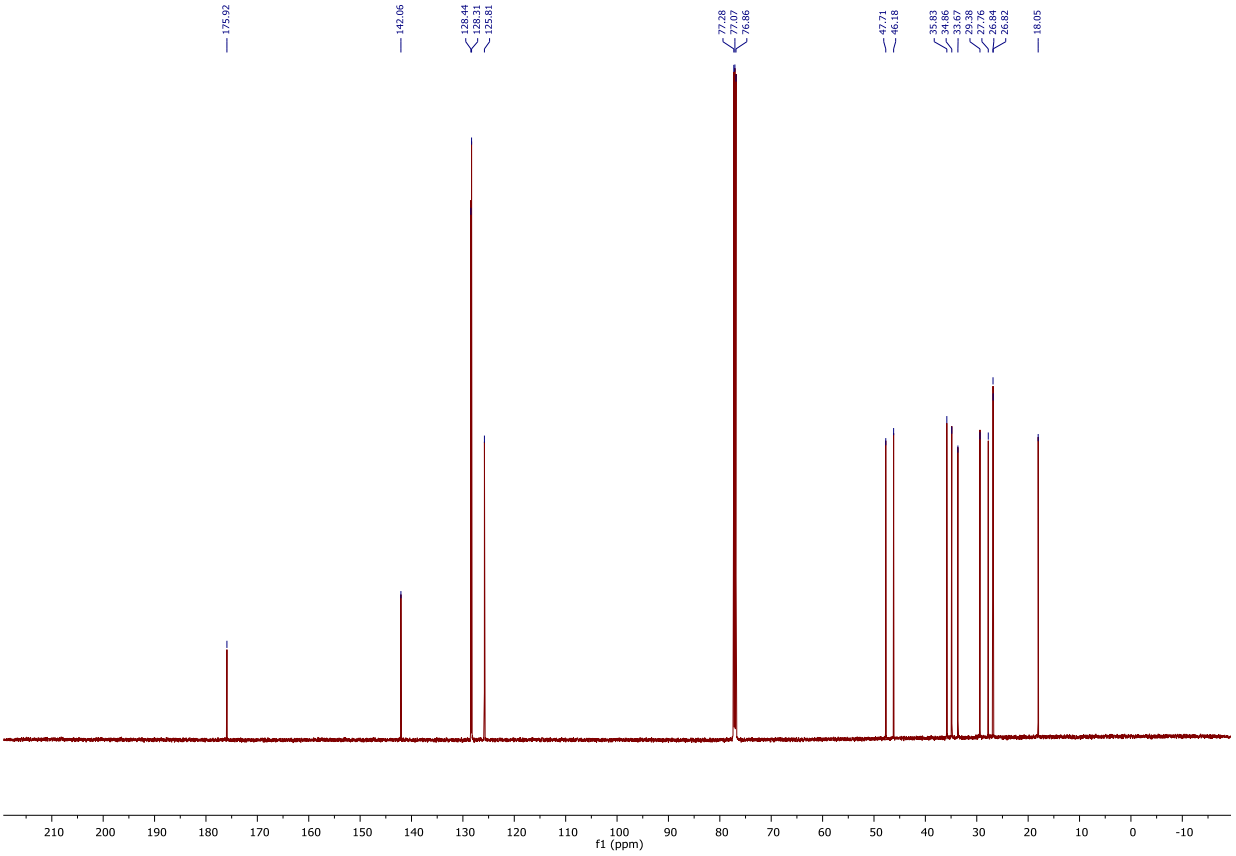

NHBoc
O
N
Me
f1 (ppm)

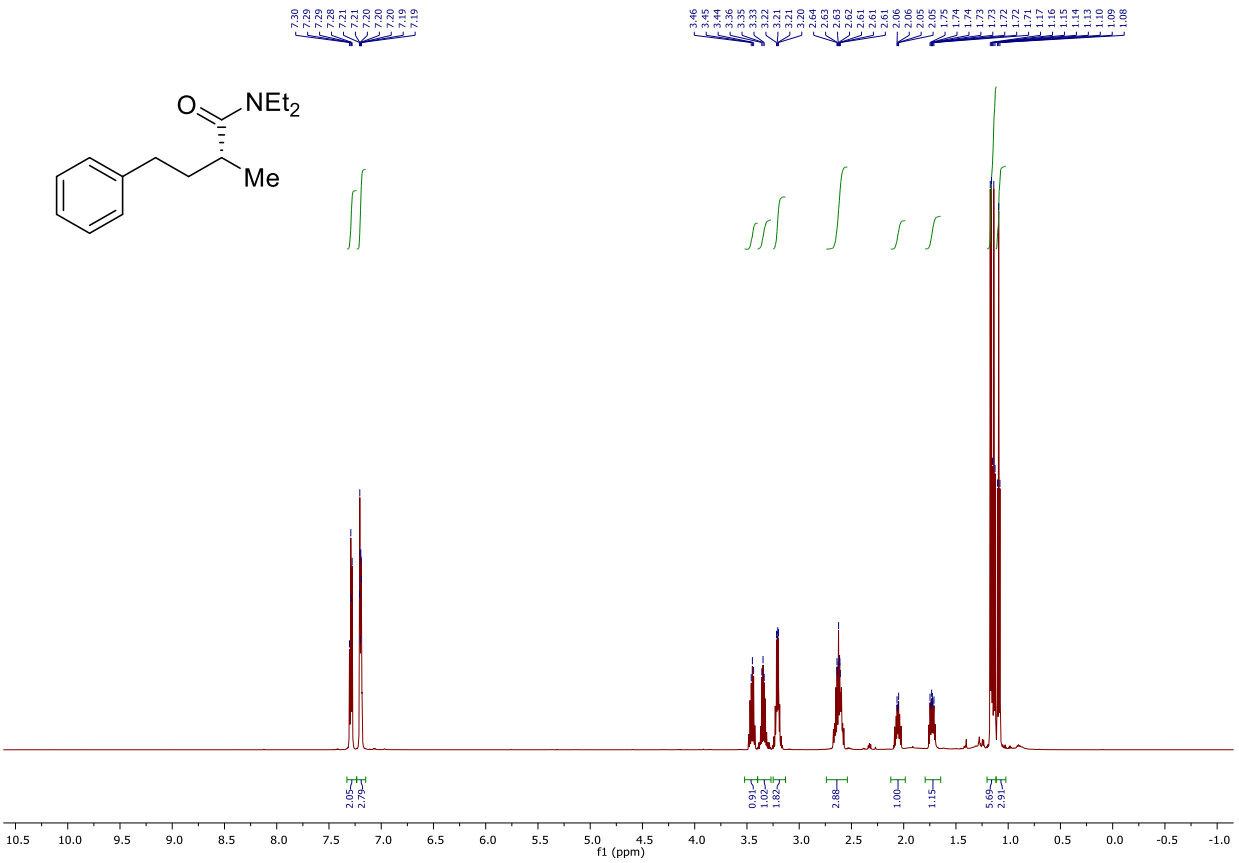

f1 (ppm)

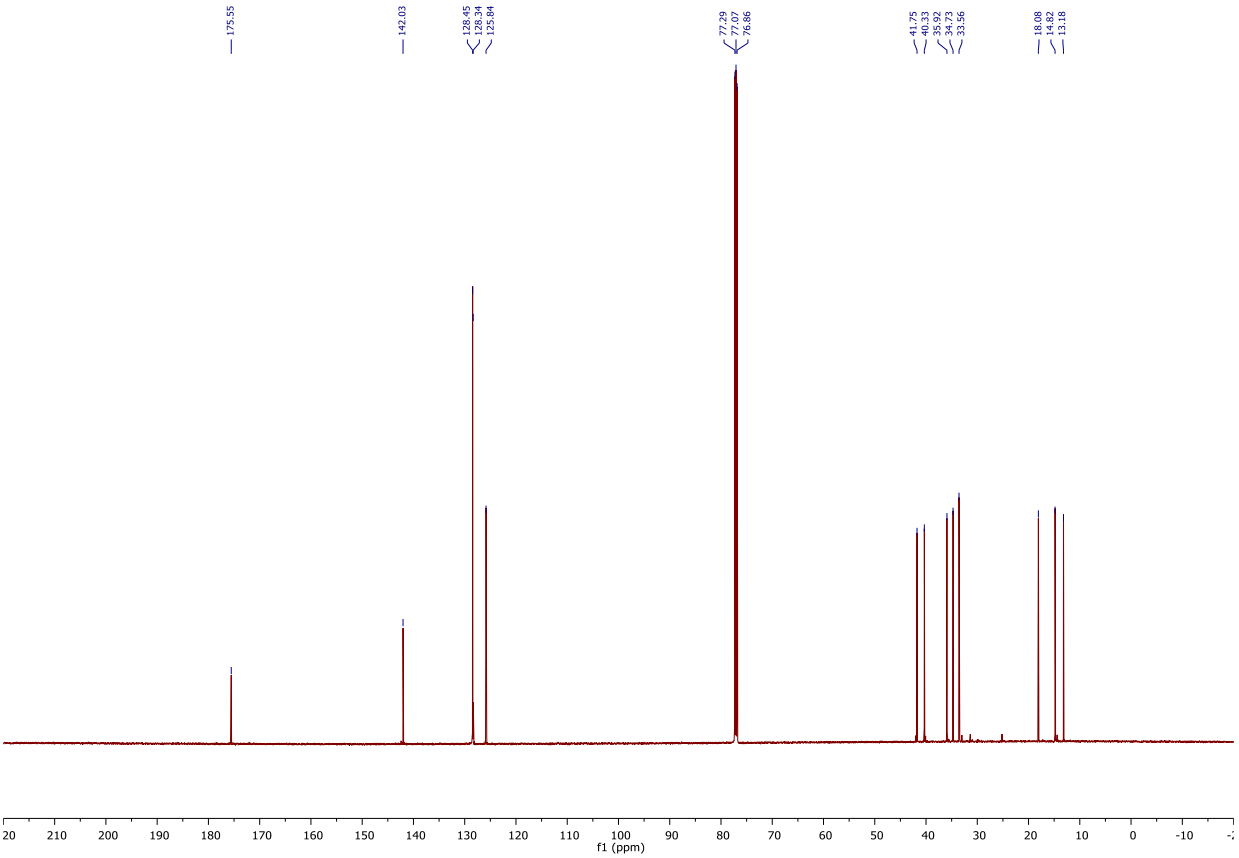

O
N
Me
f1 (ppm)

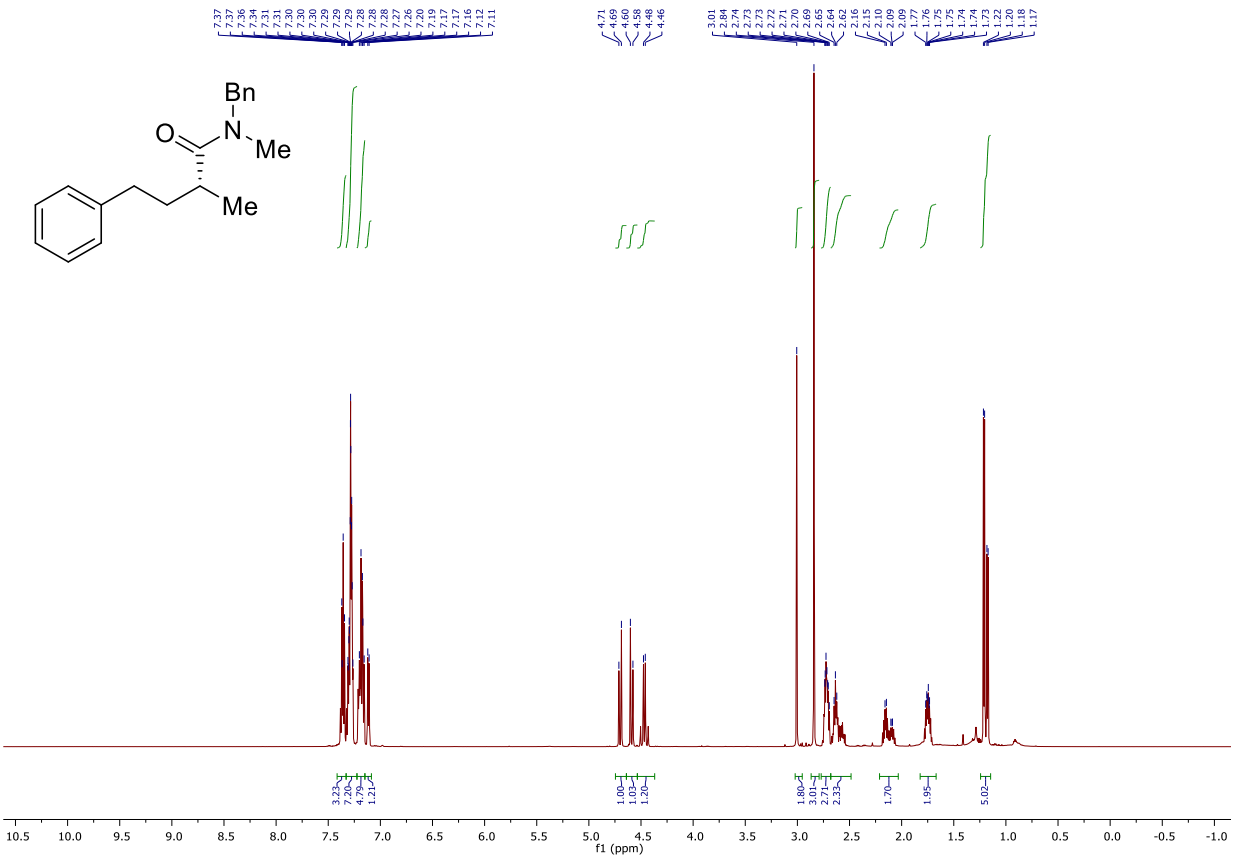

f1 (ppm)

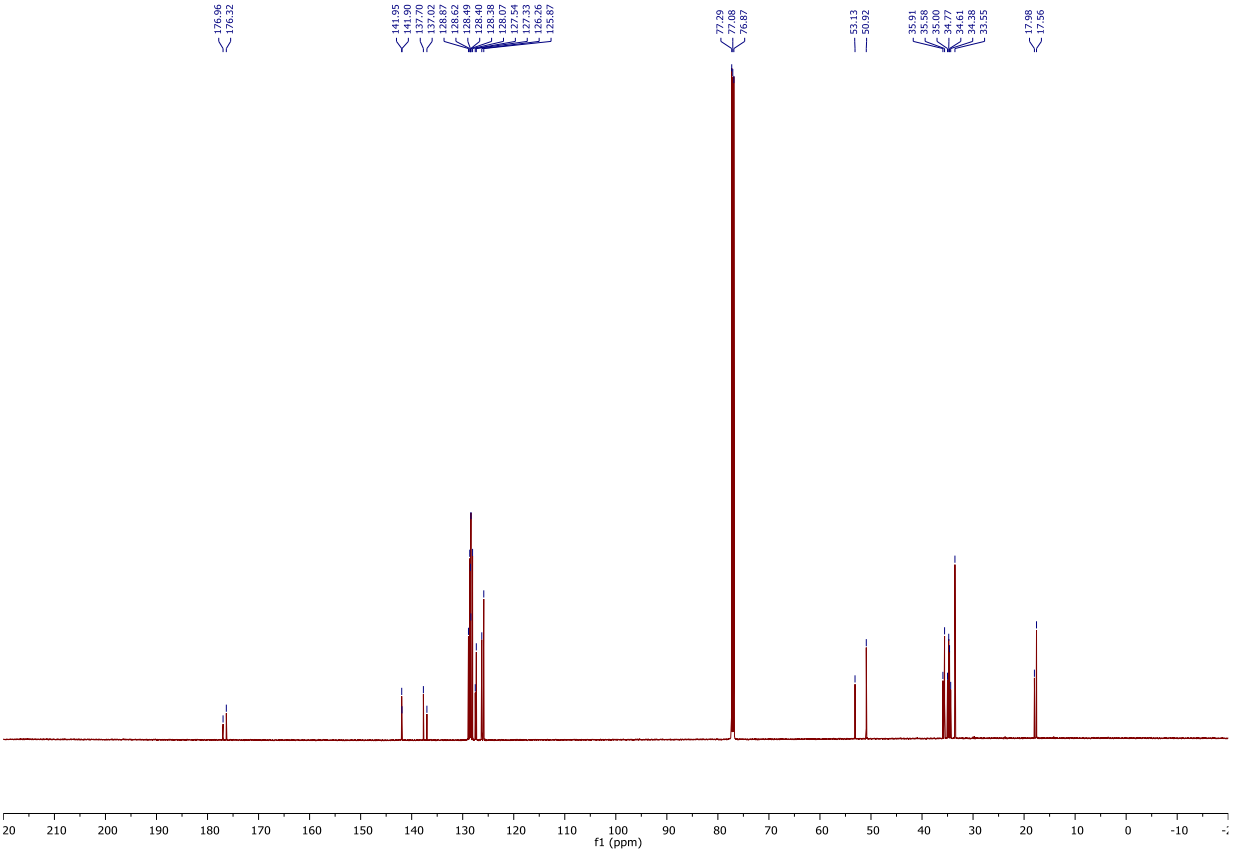

O
N
Me
7.29
7.28
7.27
7.20
7.20
7.19
7.19
3.60
3.59
3.58
3.57
3.54
3.53
3.52
3.51
3.36
3.35
3.33
2.68
2.67
2.67
2.66
2.66
2.65
2.65
2.64
2.61
2.61
2.60
2.09
2.08
2.08
2.08
1.74
1.74
1.73
1.73
1.72
1.72
1.57
1.57
1.57
1.56
1.56
1.56
1.55
1.18
1.16
2.17
2.86
0.98
1.00
1.98
2.96
1.03
3.12
5.91
3.00
f1 (ppm)

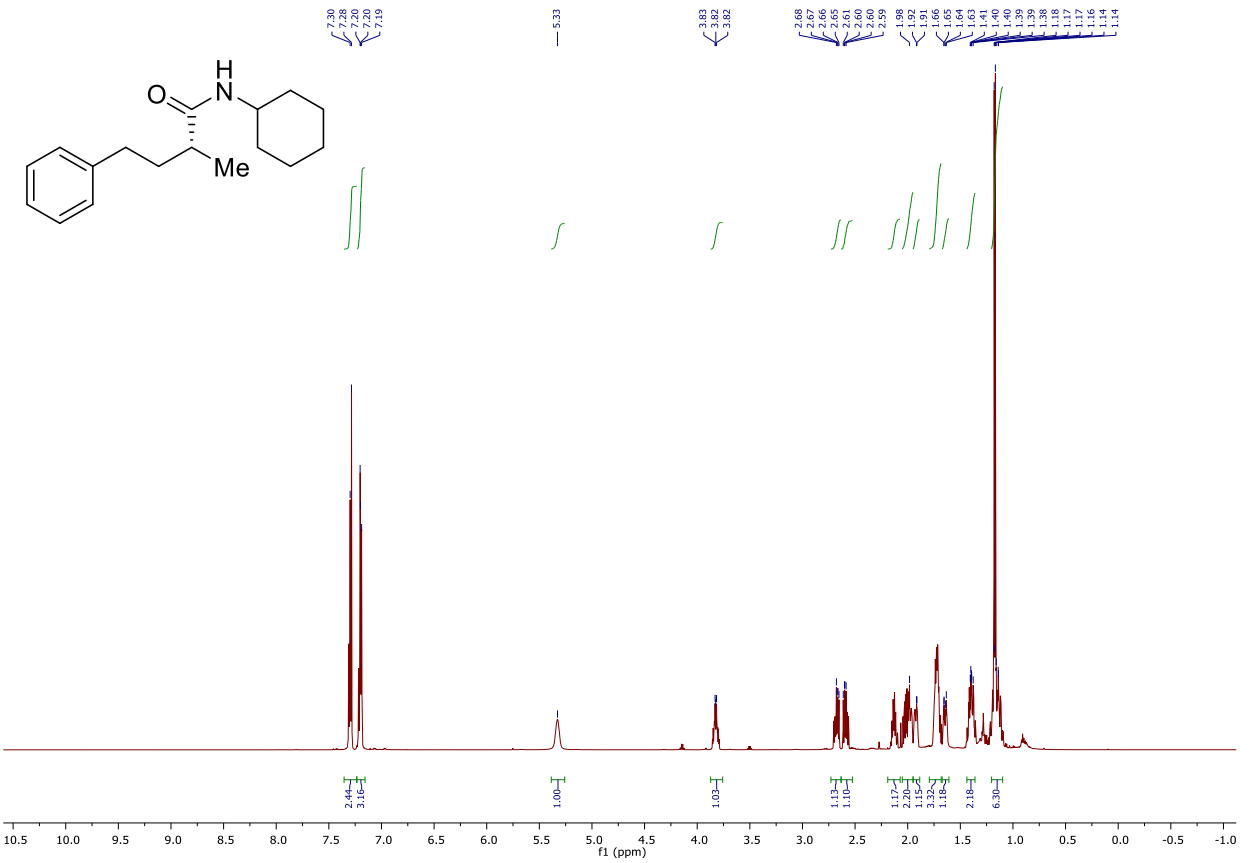

175.92
142.06
128.44
128.31
125.81
77.28
77.07
76.86
47.71
46.18
35.83
34.86
33.67
29.38
27.76
26.84
26.82
18.05
f1 (ppm)

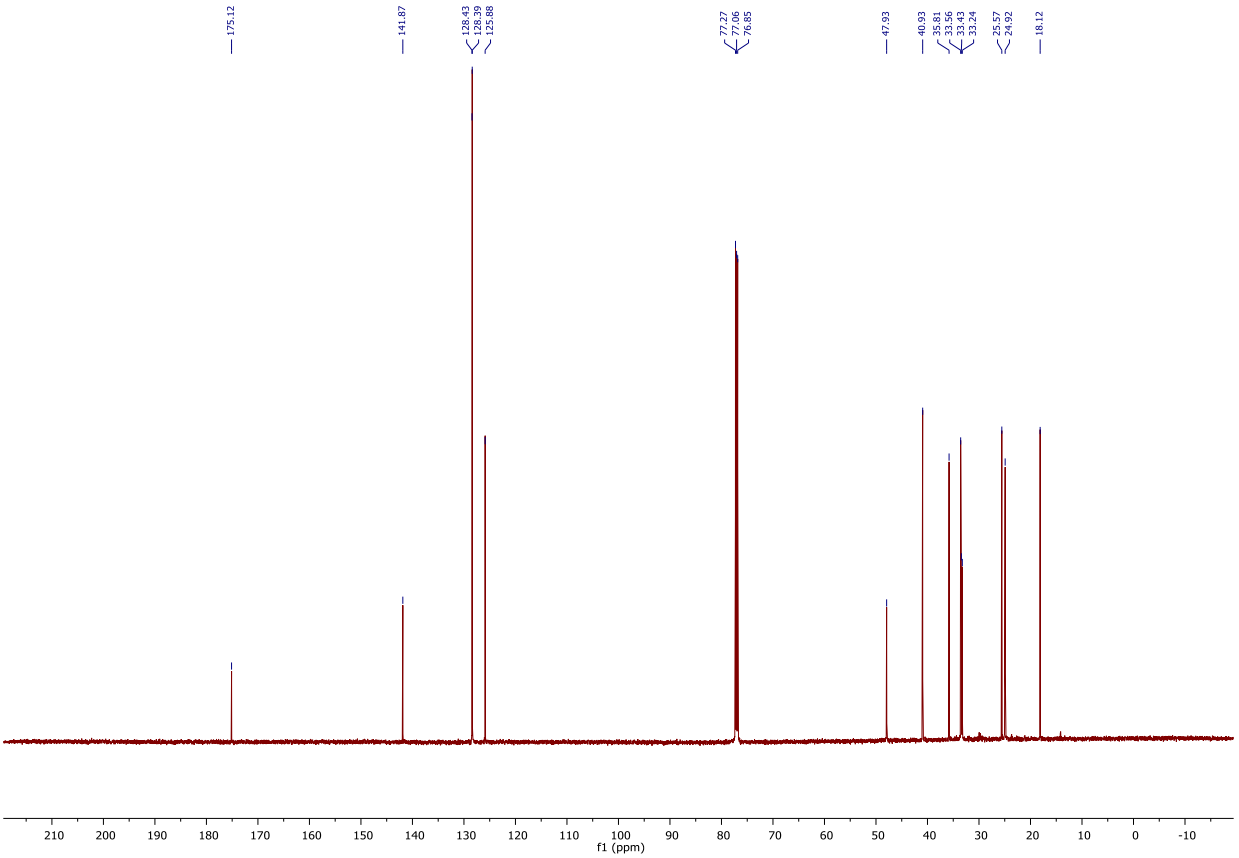

O
NEt2
Me
f1 (ppm)

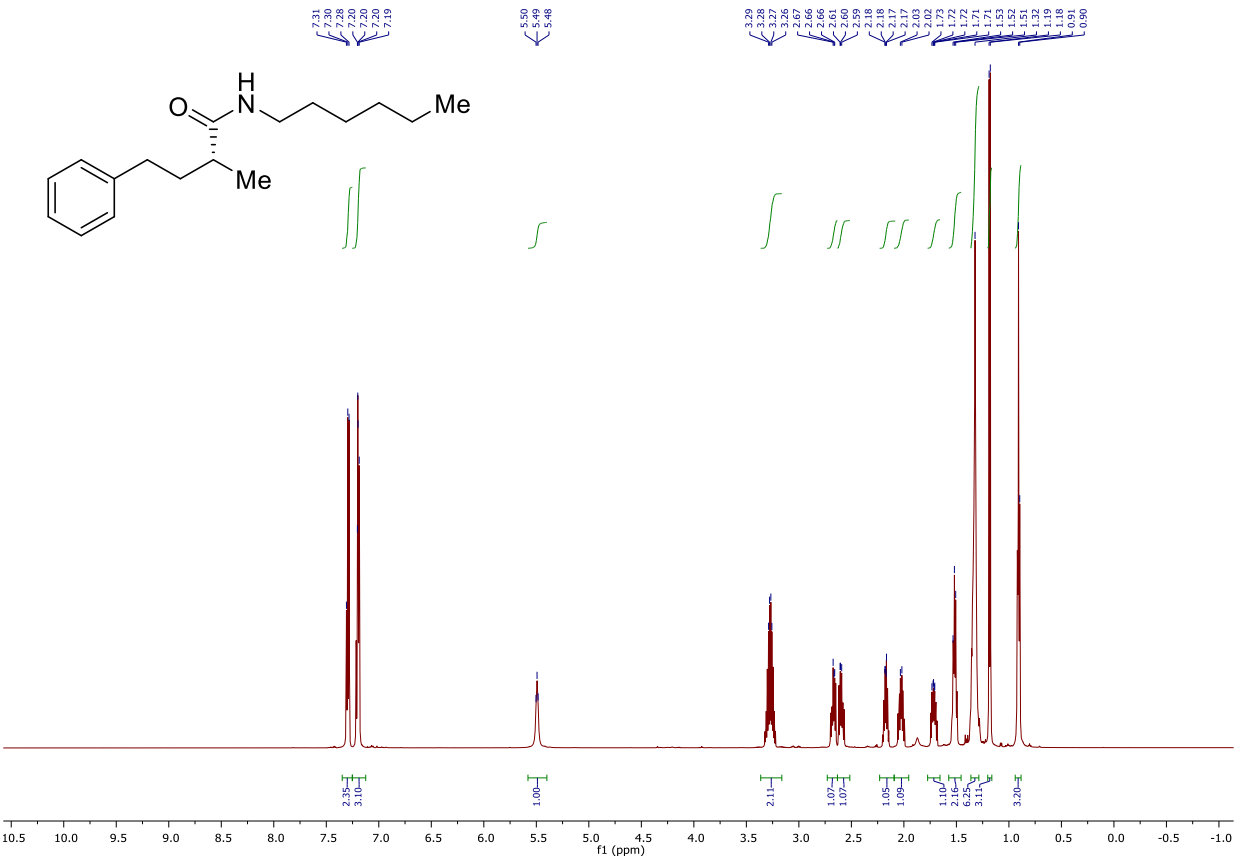

f1 (ppm)

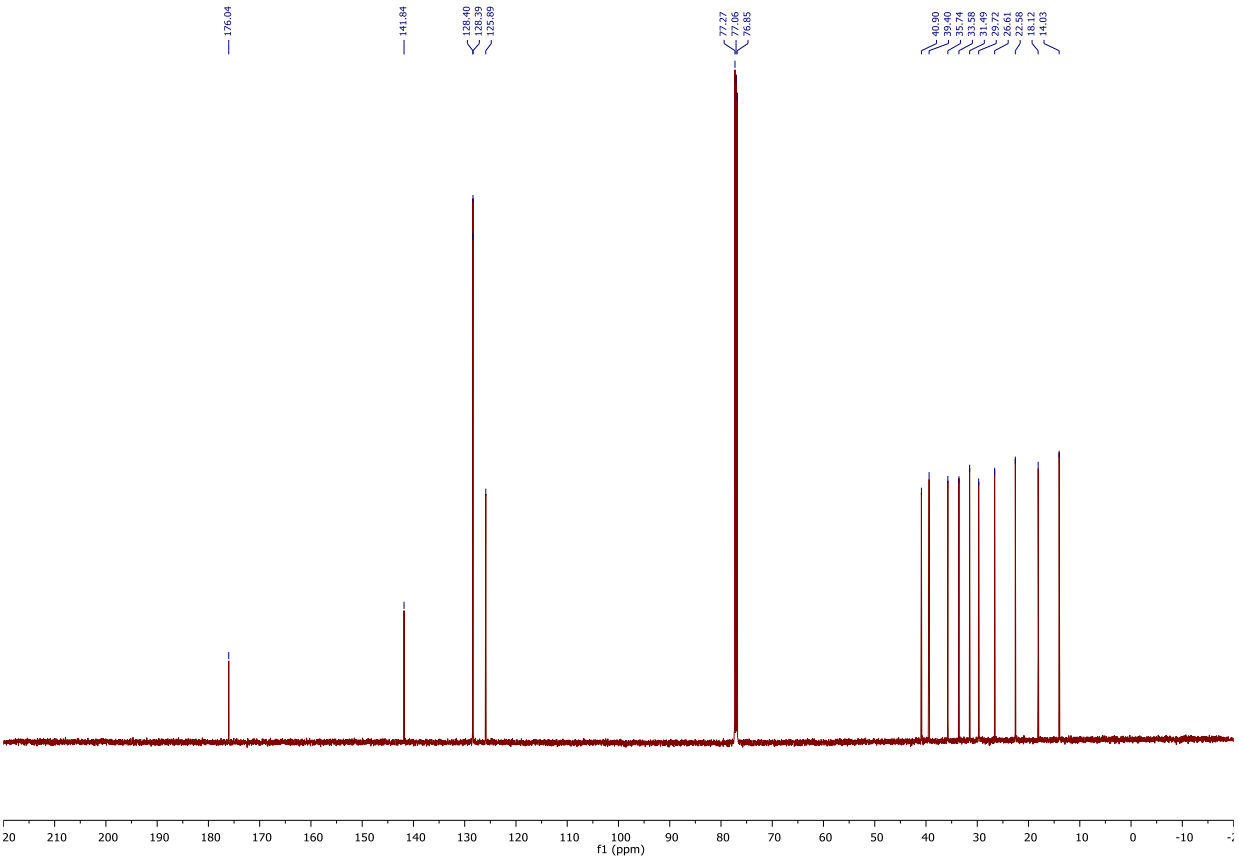

Bn
N
O
Me
Me
f1 (ppm)

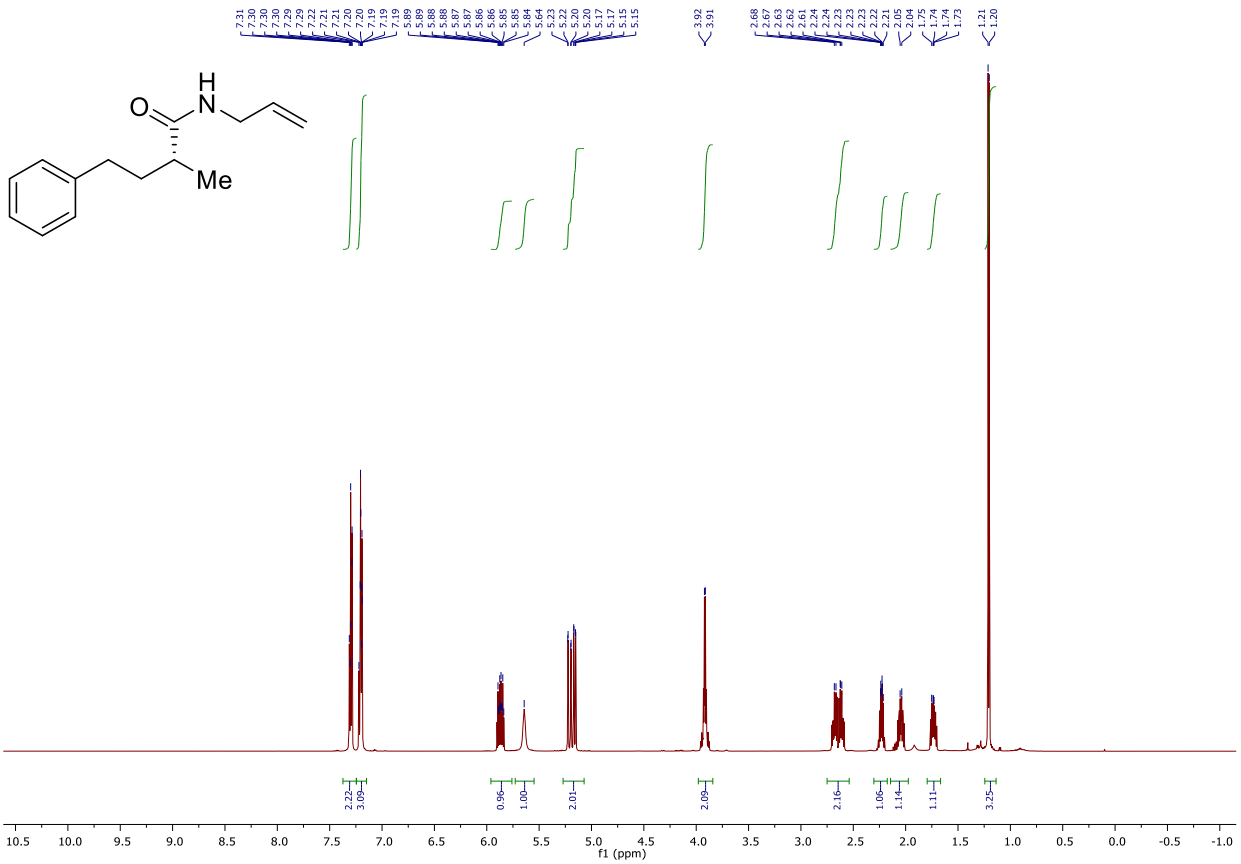

f1 (ppm)

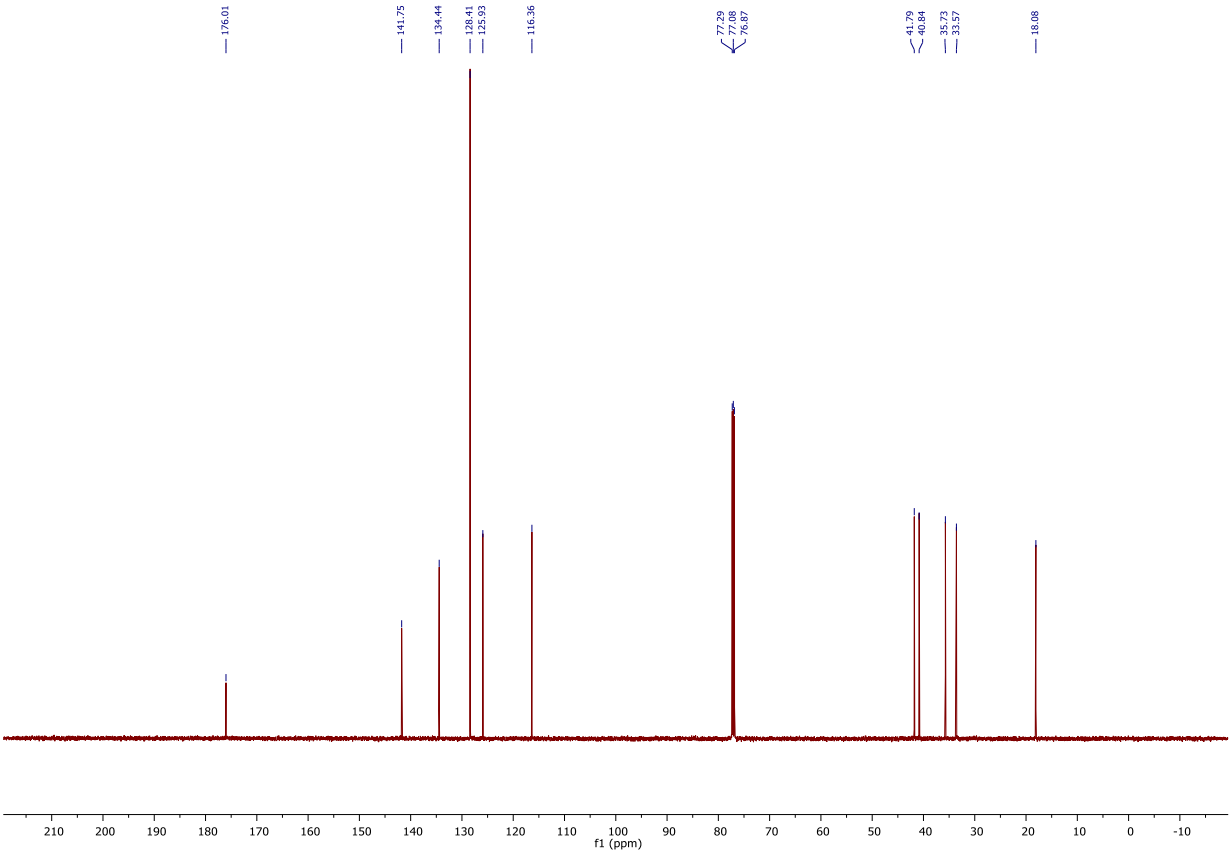

7.30
7.28
7.20
7.20
7.19
5.33
3.83
3.82
3.82
2.68
2.67
2.66
2.65
2.61
2.60
2.60
2.59
1.98
1.92
1.91
1.66
1.65
1.64
1.63
1.41
1.40
1.40
1.39
1.39
1.38
1.18
1.17
1.17
1.16
1.14
1.14
O
H
N
Me
2.44
3.16
1.00
1.03
1.13
1.10
1.17
2.26
1.15
3.32
1.18
2.18
6.30
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

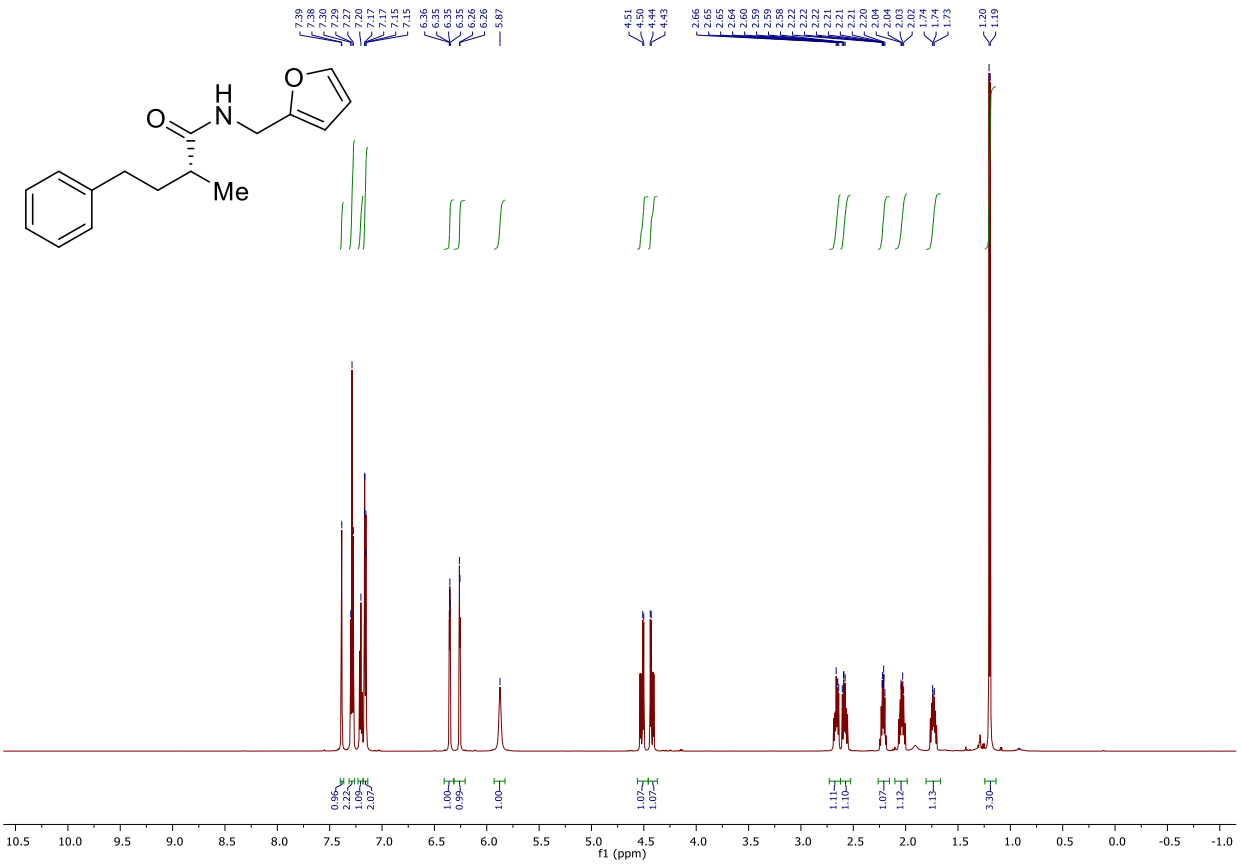

175.12
141.87
128.43
128.39
125.88
77.27
77.06
76.85
47.93
40.93
35.81
33.56
33.43
33.24
25.57
24.92
18.12
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

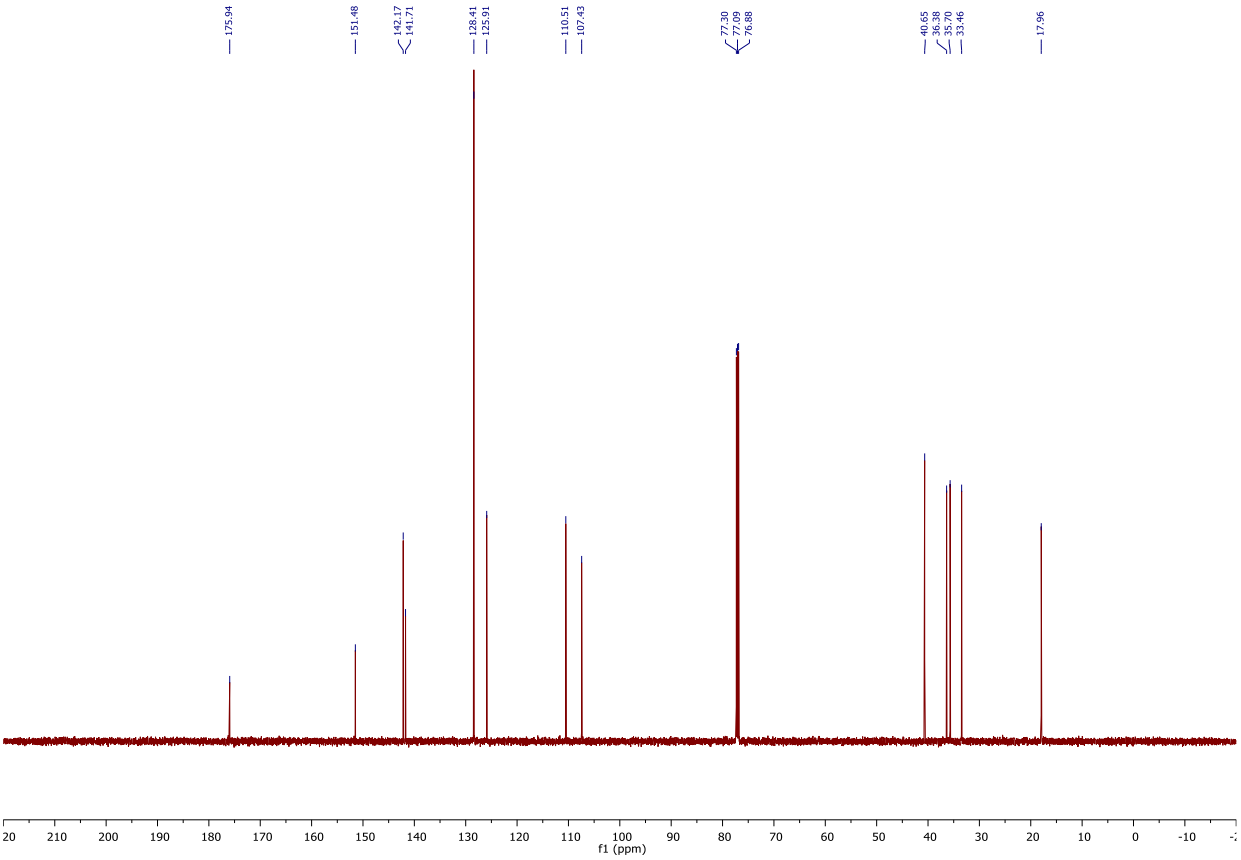

7.31
7.30
7.28
7.20
7.20
7.20
7.19
5.50
5.49
5.48
3.29
3.28
3.27
3.26
2.67
2.66
2.66
2.61
2.60
2.59
2.18
2.18
2.17
2.17
2.03
2.02
1.73
1.72
1.72
1.71
1.71
1.53
1.52
1.51
1.32
1.19
1.18
0.91
0.90
O
H
N
Me
Me
2.35
3.10
1.00
2.11
1.07
1.07
1.05
1.09
1.10
2.16
6.25
3.11
3.20
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

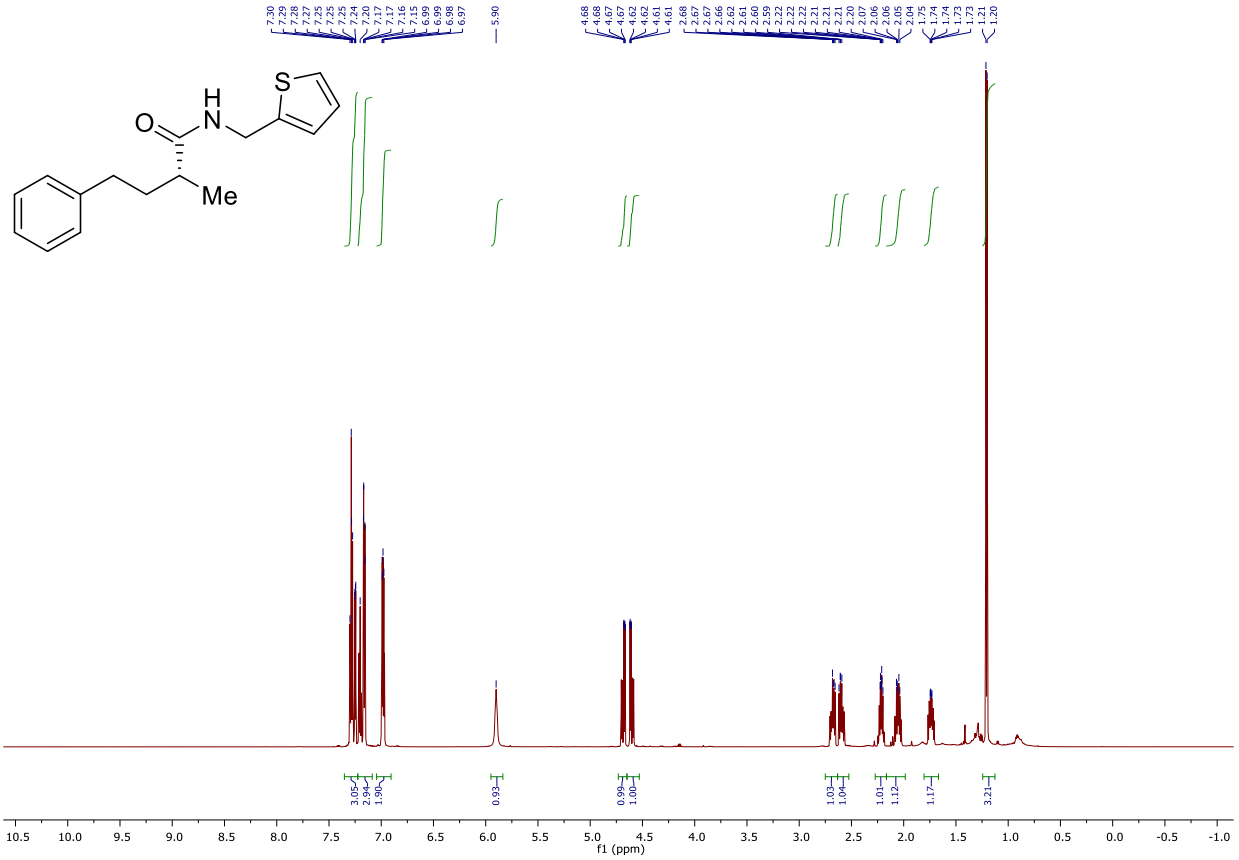

176.04
141.84
128.40
128.39
125.89
77.27
77.06
76.85
40.90
39.40
33.74
33.58
31.49
29.72
26.61
22.58
18.12
14.03
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

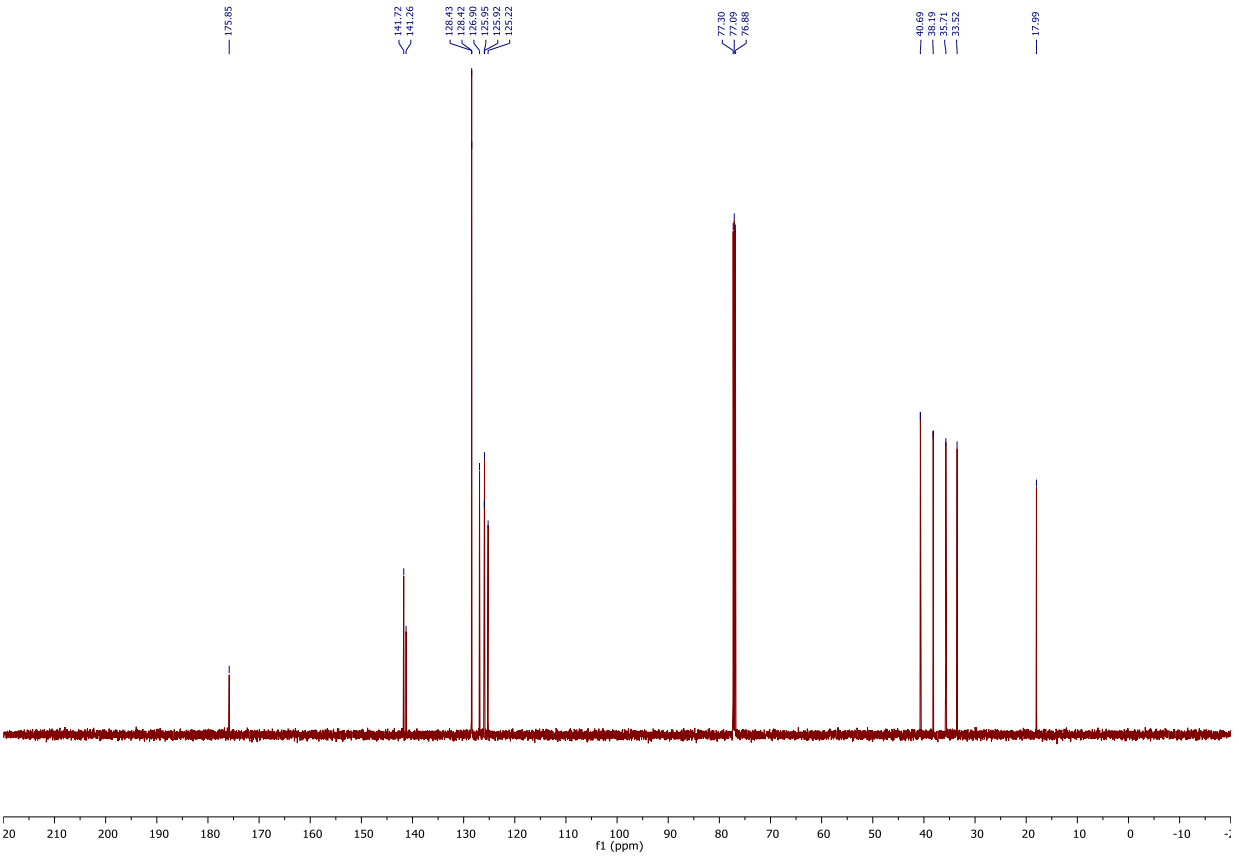

H
N
O
Me
f1 (ppm)

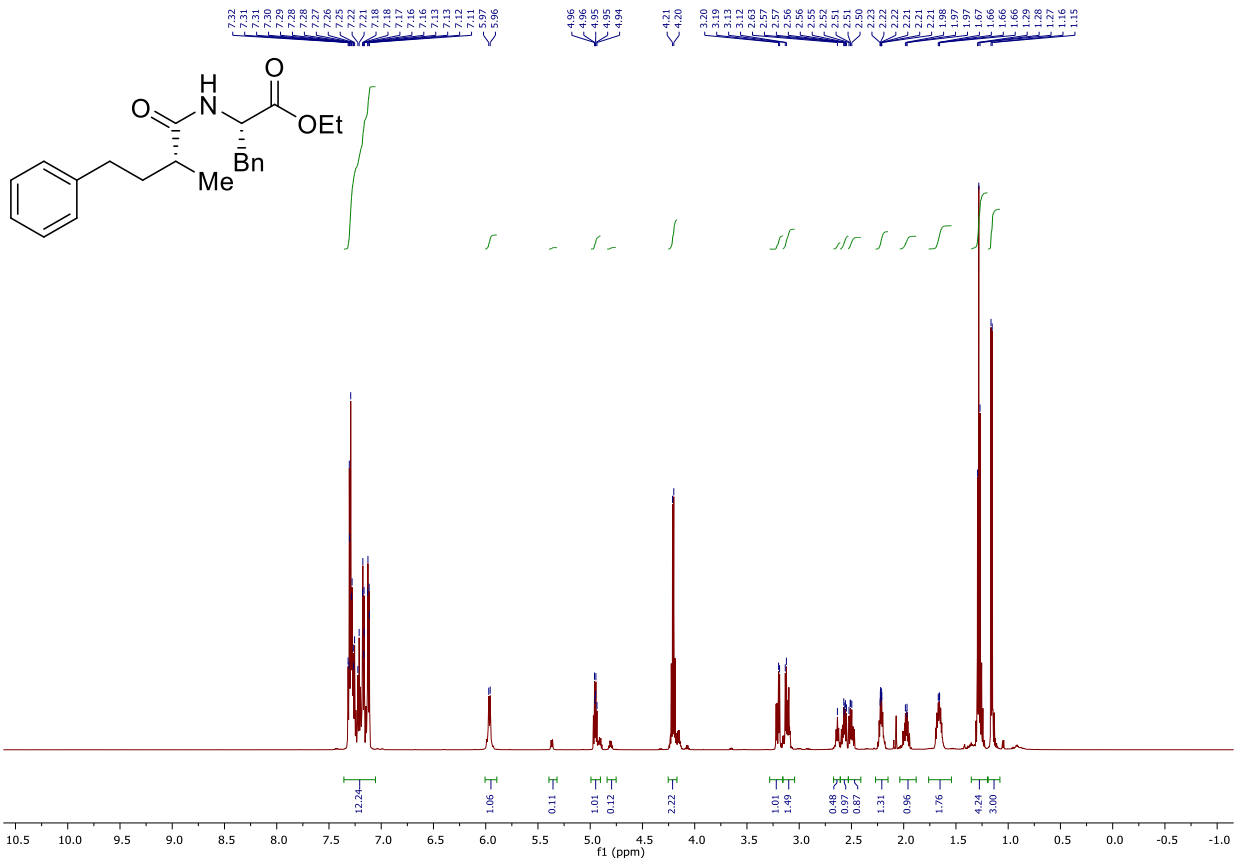

f1 (ppm)

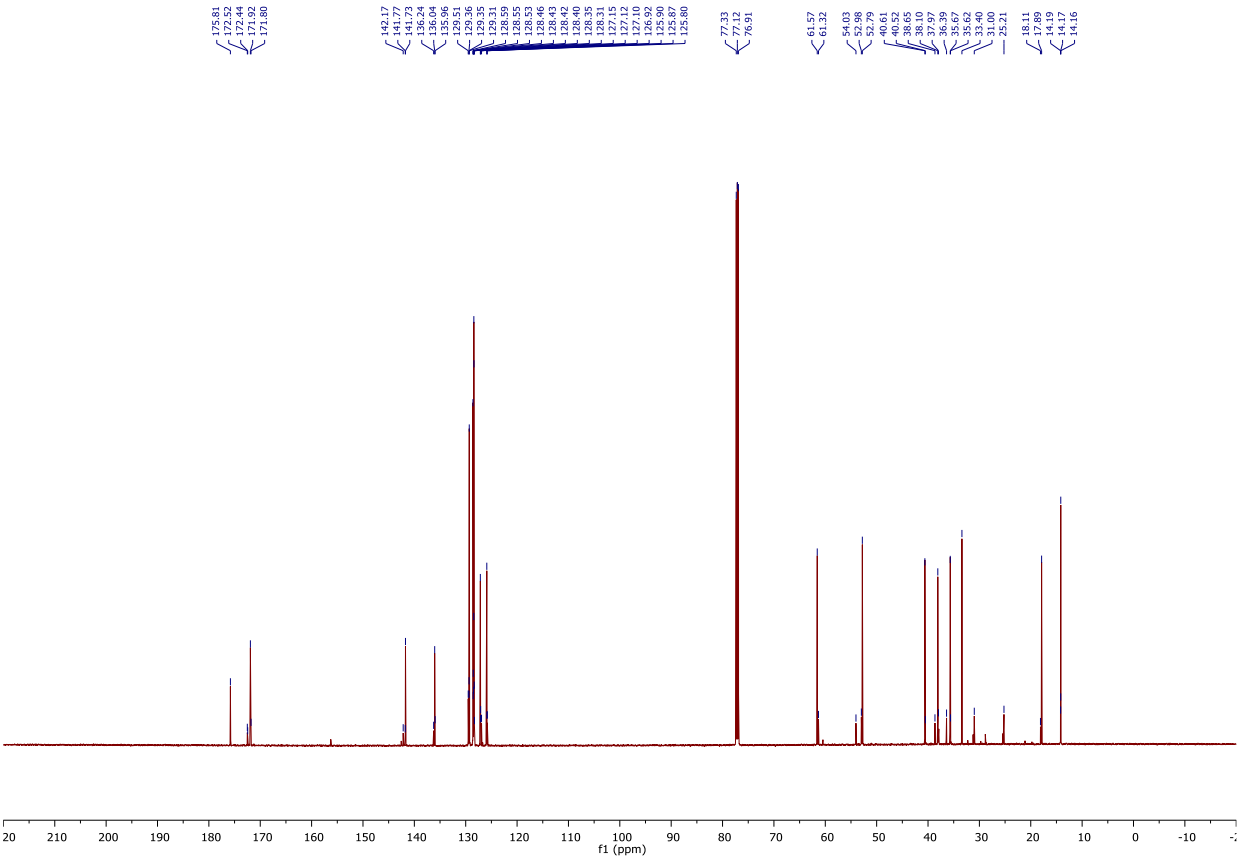

7.39
7.38
7.30
7.29
7.27
7.20
7.17
7.15
7.15
6.36
6.35
6.35
6.26
6.26
5.87
4.51
4.50
4.44
4.43
2.66
2.65
2.65
2.64
2.60
2.59
2.58
2.22
2.22
2.21
2.21
2.20
2.04
2.03
2.02
1.74
1.74
1.73
1.20
1.19
O
H
N
O
Me
0.96
2.22
1.09
2.07
1.00
0.99
1.00
1.07
1.07
1.11
1.10
1.07
1.12
1.13
3.30
f1 (ppm)

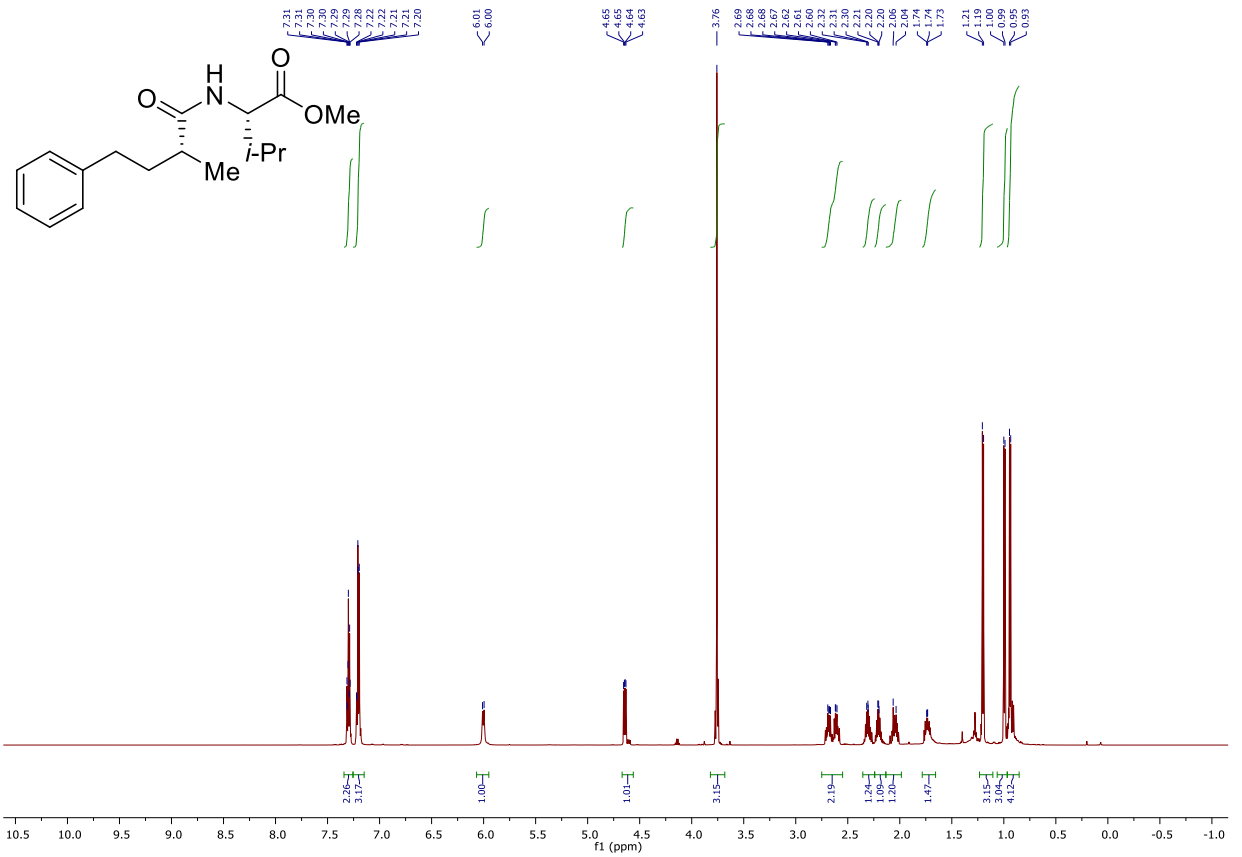

175.94
151.48
142.17
141.71
128.41
125.91
110.51
107.43
77.30
77.09
76.88
40.65
36.38
35.70
33.46
17.96
f1 (ppm)

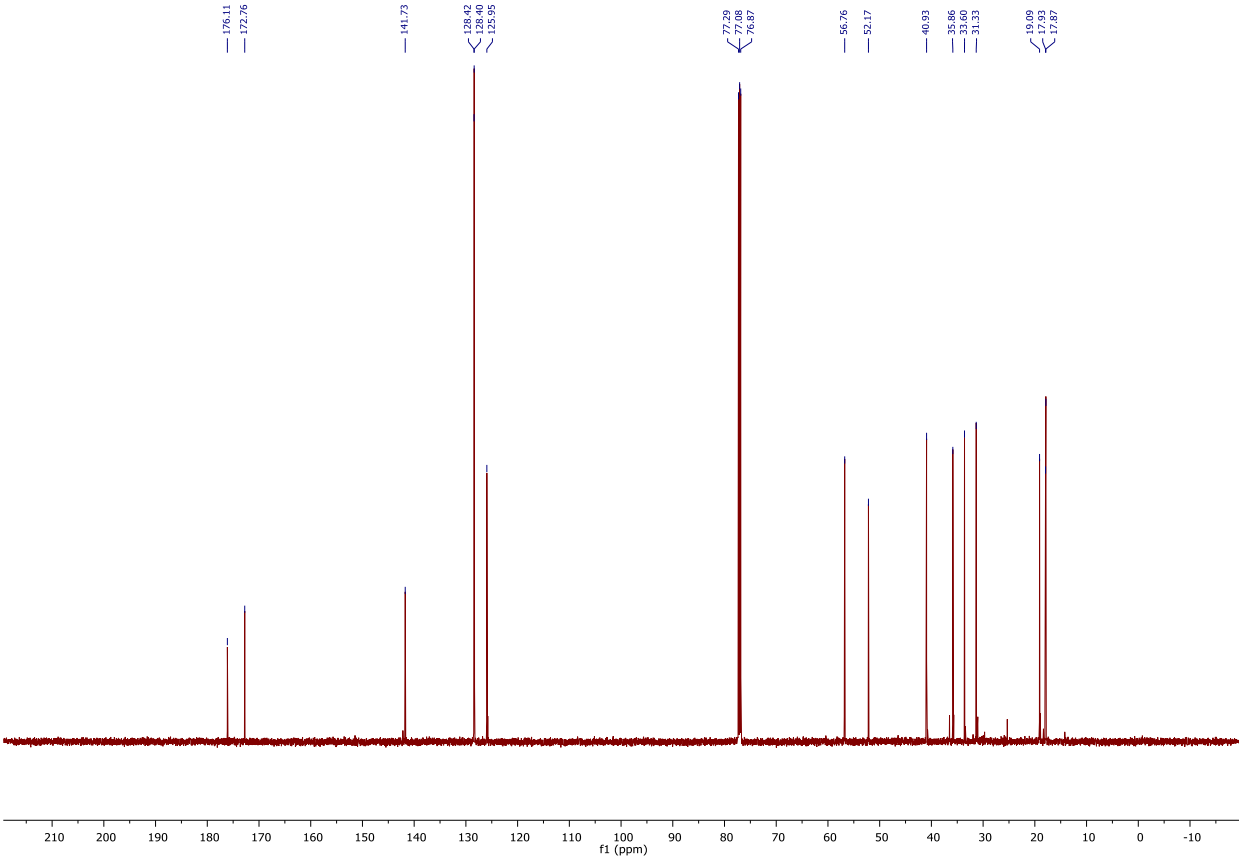

7.30
7.29
7.28
7.27
7.25
7.25
7.25
7.24
7.20
7.17
7.17
7.16
7.15
6.99
6.98
6.97
5.90
4.68
4.68
4.67
4.67
4.62
4.62
4.61
4.61
2.68
2.67
2.67
2.66
2.62
2.61
2.60
2.59
2.22
2.22
2.22
2.21
2.21
2.20
2.07
2.06
2.05
2.04
1.75
1.74
1.74
1.73
1.21
1.20
H
N
O
S
Me
3.05
2.94
1.90
0.93
0.99
1.00
1.03
1.04
1.01
1.12
1.17
3.21
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

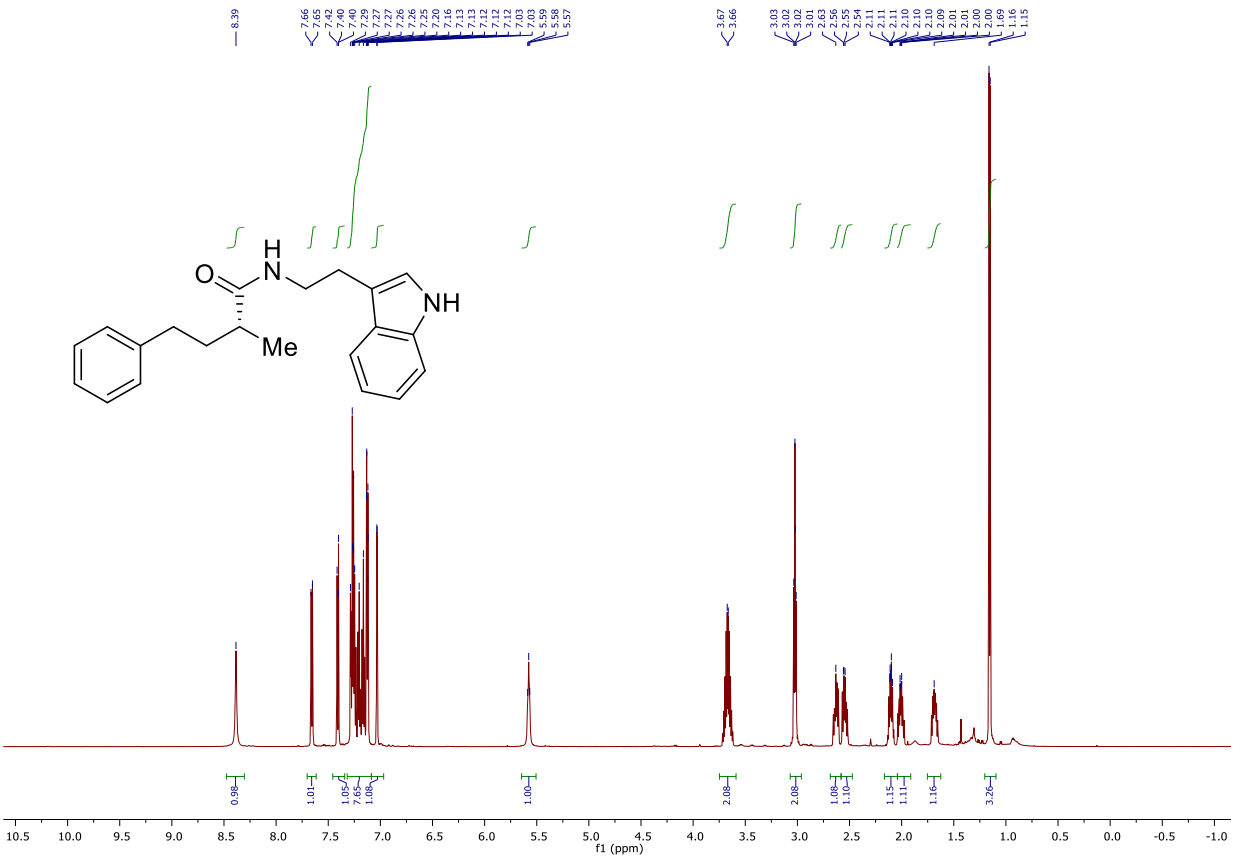

175.85
141.72
141.26
128.43
128.42
126.90
125.95
125.50
125.22
77.30
77.09
76.88
40.69
38.19
37.71
33.52
17.99
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

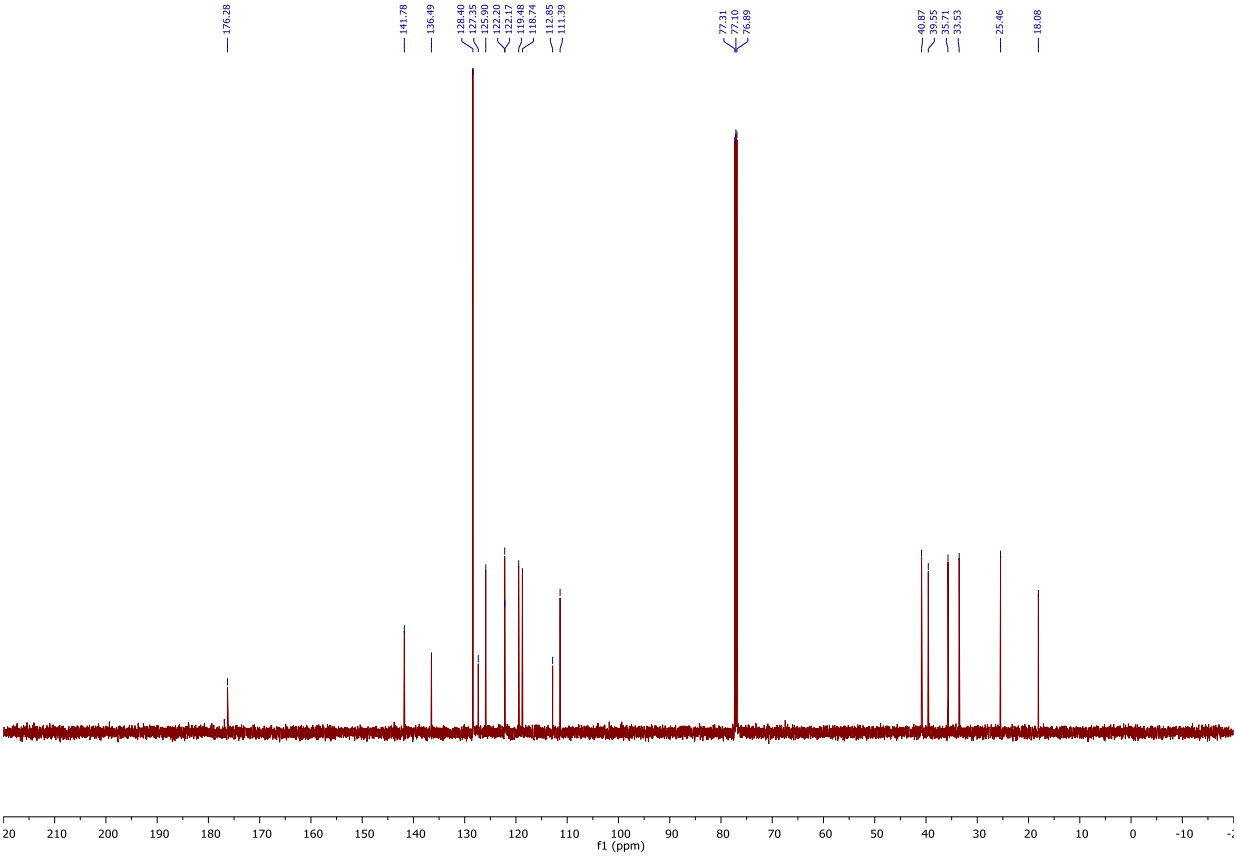

O
H
N
O
OEt
Bn
Me
f1 (ppm)

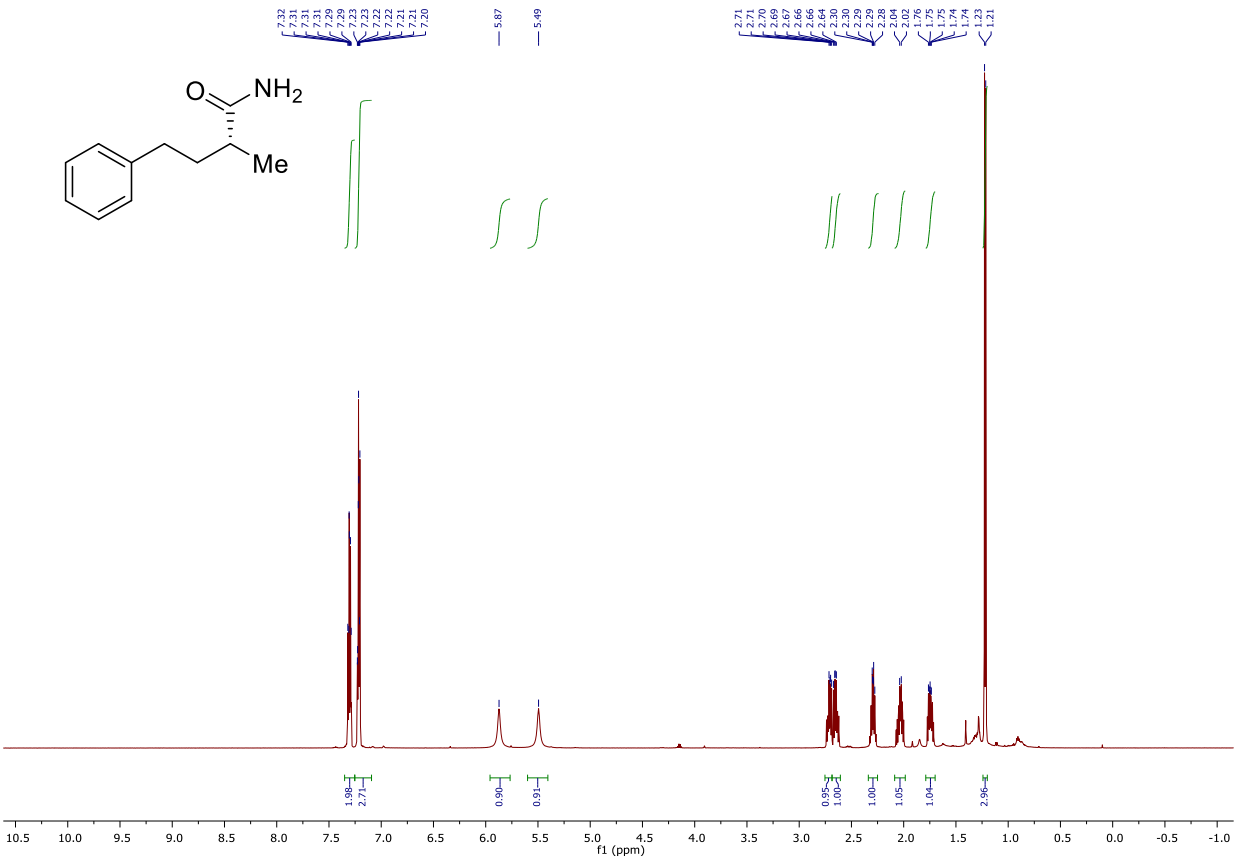

f1 (ppm)

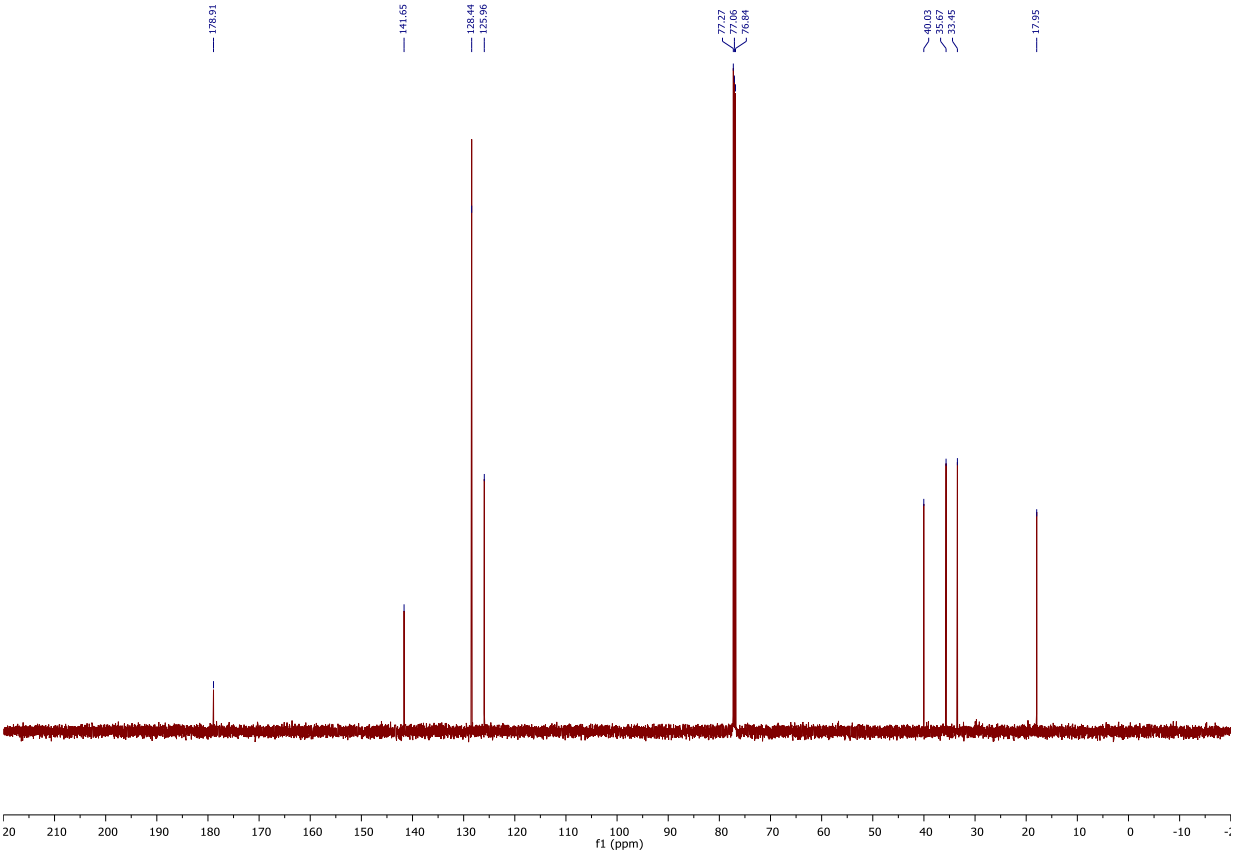

7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.22
7.22
7.21
7.21
7.20
6.01
6.00
4.65
4.65
4.64
4.63
3.76
2.69
2.68
2.68
2.67
2.62
2.61
2.60
2.32
2.31
2.30
2.21
2.20
2.20
2.06
2.04
1.74
1.74
1.73
1.21
1.19
1.00
0.99
0.95
0.93
O
H
N
O
OMe
i-Pr
Me
2.26
3.17
1.00
1.01
3.15
2.19
1.24
1.09
1.20
1.47
3.15
3.04
4.12
f1 (ppm)

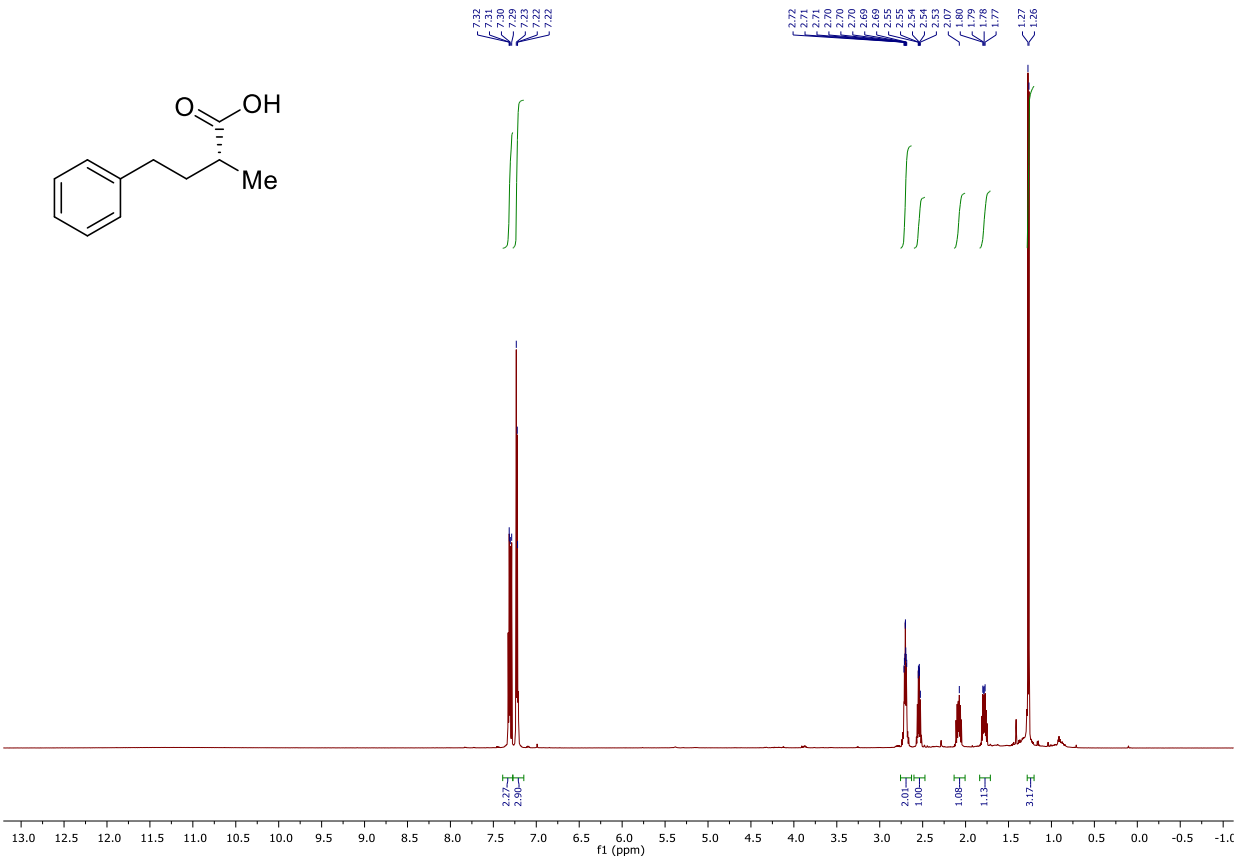

176.11
172.76
141.73
128.42
128.40
125.95
77.29
77.08
76.87
56.76
52.17
40.93
35.86
33.60
31.33
19.09
17.93
17.87
f1 (ppm)

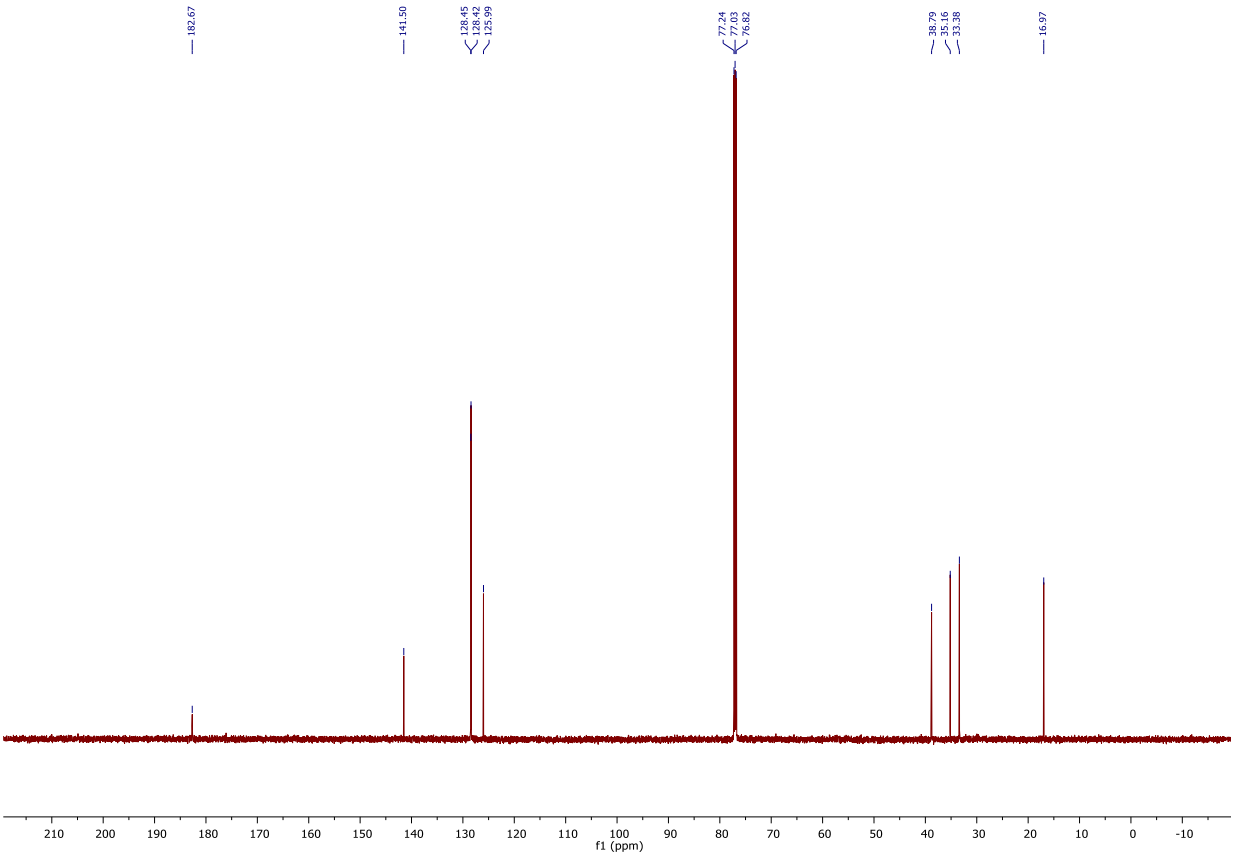

8.39
7.66
7.65
7.42
7.40
7.29
7.27
7.27
7.26
7.26
7.25
7.20
7.16
7.13
7.13
7.12
7.12
7.03
7.03
5.59
5.58
5.57
3.67
3.66
3.03
3.02
3.02
3.01
2.63
2.56
2.55
2.54
2.11
2.11
2.11
2.10
2.10
2.09
2.01
2.01
2.00
2.00
1.69
1.16
1.15
O
H
N
NH
Me
0.98
1.01
1.05
1.65
1.08
1.00
2.08
2.08
1.08
1.10
1.15
1.11
1.16
3.26
f1 (ppm)

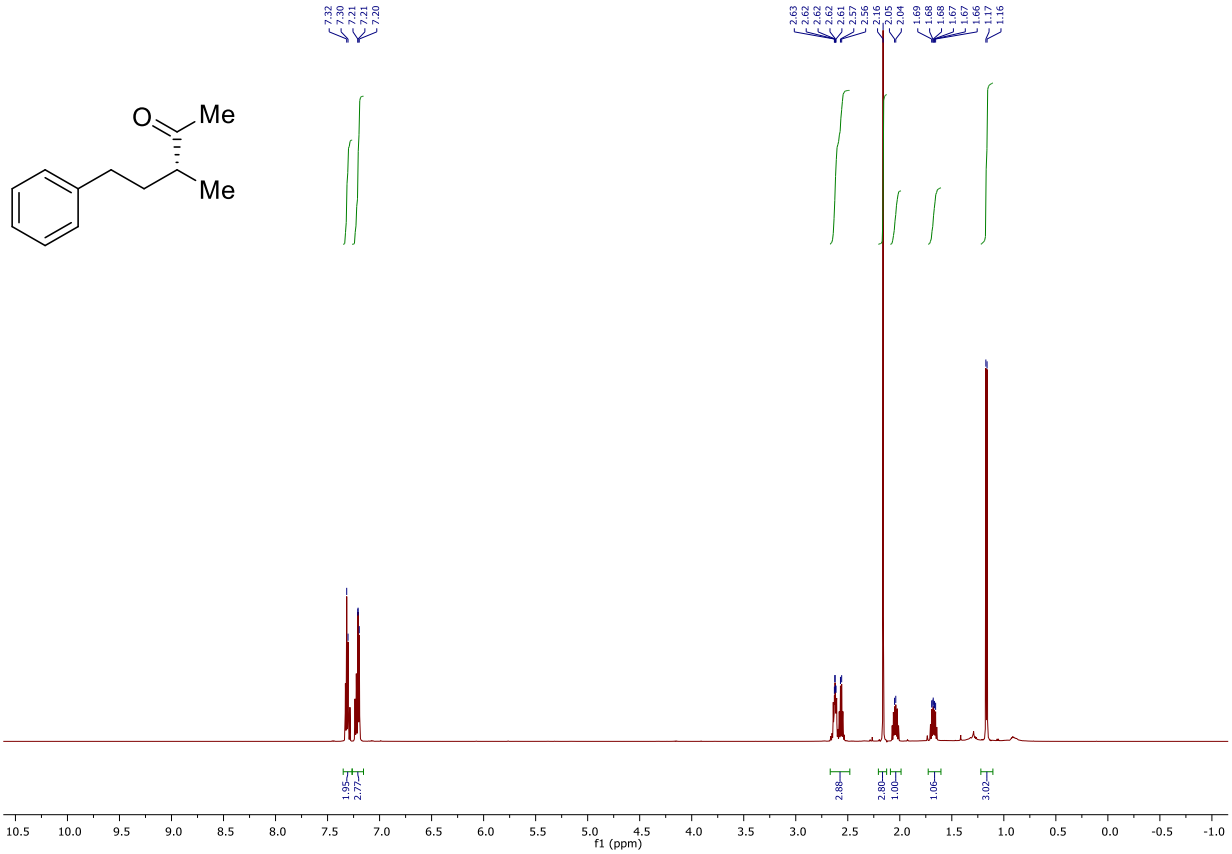

176.28
141.78
136.49
128.40
127.35
125.90
122.20
122.17
119.48
118.74
112.85
111.39
77.31
77.10
76.89
40.87
39.55
35.71
33.53
25.46
18.08
f1 (ppm)

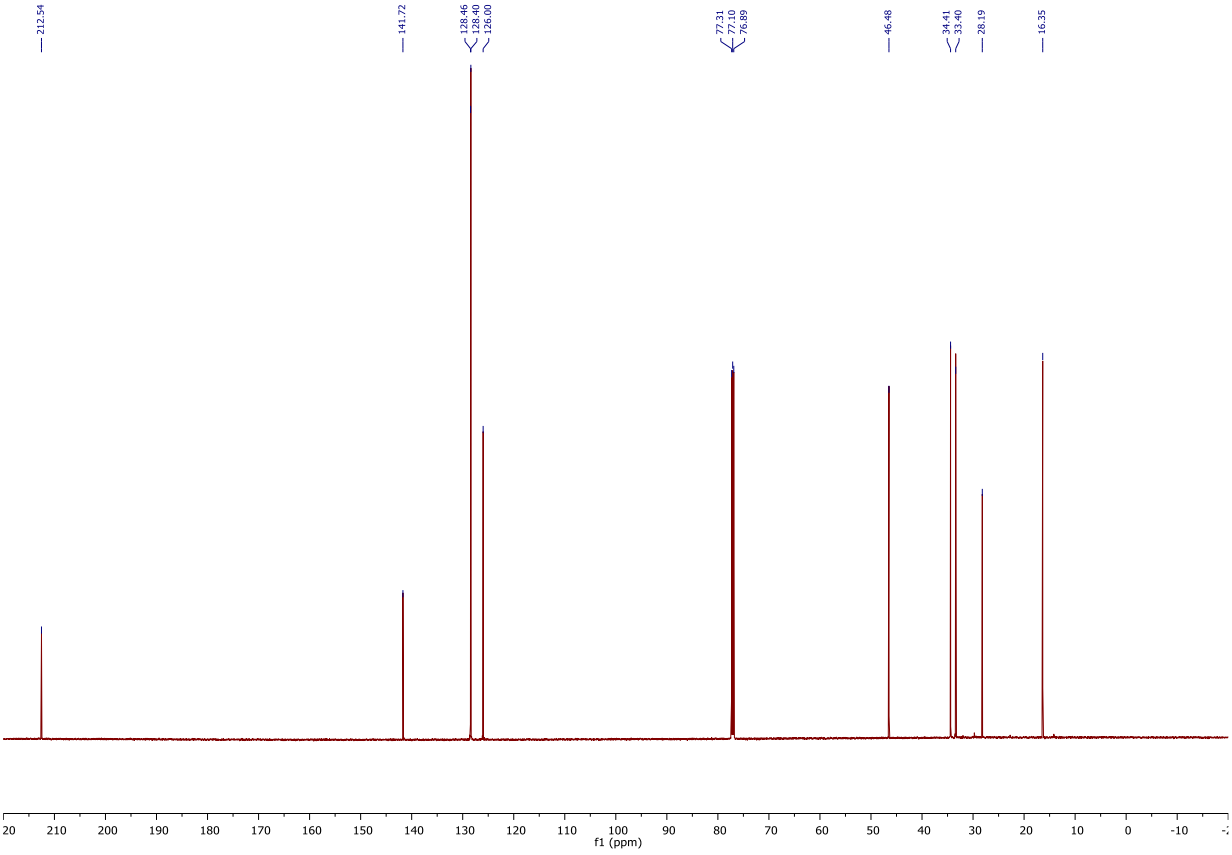

O
NH2
Me
7.32
7.31
7.31
7.31
7.29
7.29
7.23
7.23
7.22
7.21
7.21
7.20
5.87
5.49
2.71
2.71
2.70
2.69
2.67
2.66
2.66
2.64
2.30
2.30
2.29
2.29
2.28
2.04
2.02
1.76
1.75
1.74
1.74
1.23
1.21
1.98
2.71
0.90
0.91
0.95
1.00
1.00
1.05
1.04
2.96
f1 (ppm)

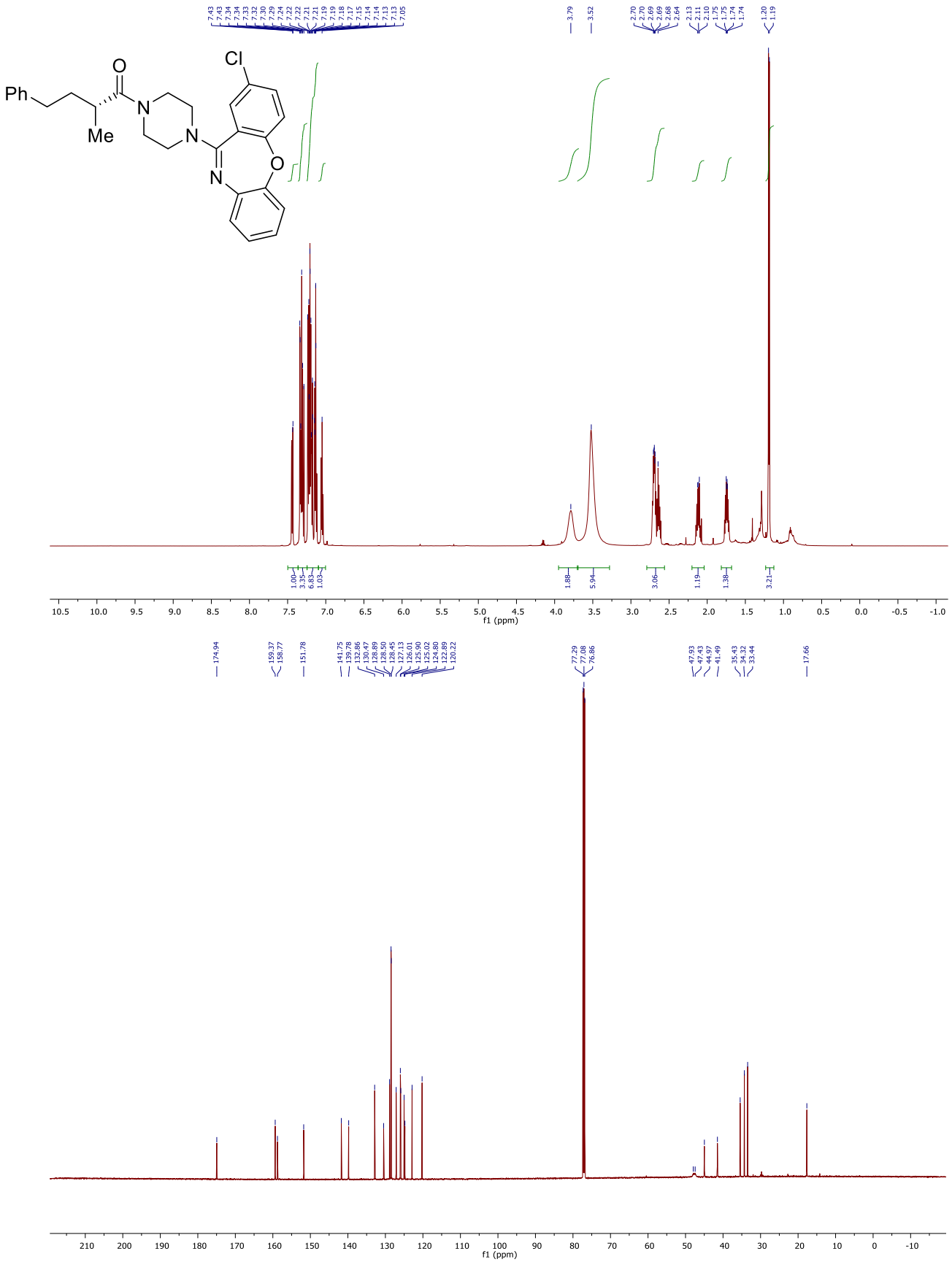

178.91
141.65
128.44
125.96
77.27
77.06
76.84
40.03
35.67
33.45
17.95
f1 (ppm)

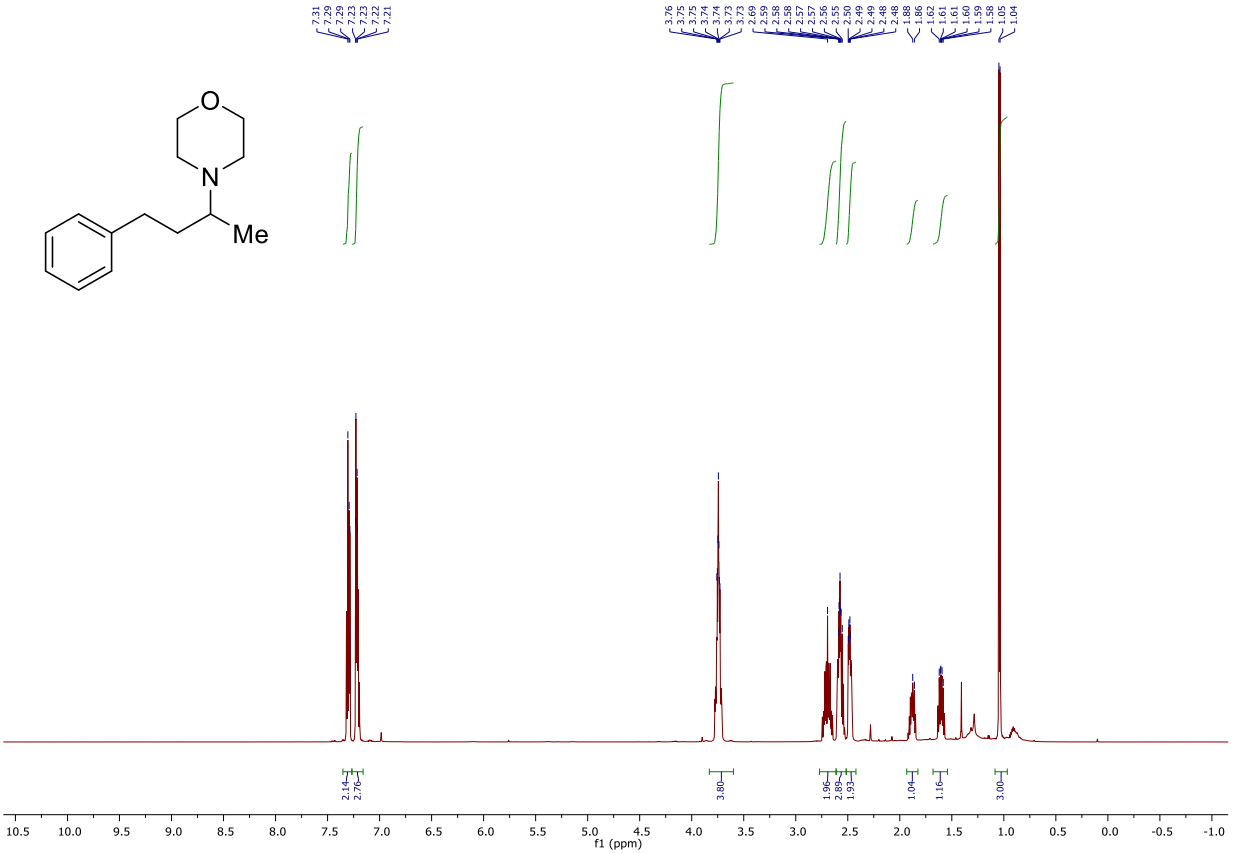

O
OH
Me
7.32
7.31
7.30
7.29
7.23
7.22
7.22
2.72
2.71
2.71
2.70
2.70
2.70
2.69
2.69
2.55
2.55
2.54
2.54
2.53
2.07
1.80
1.79
1.78
1.77
1.27
1.26
2.27
2.90
2.01
1.00
1.08
1.13
3.17
f1 (ppm)

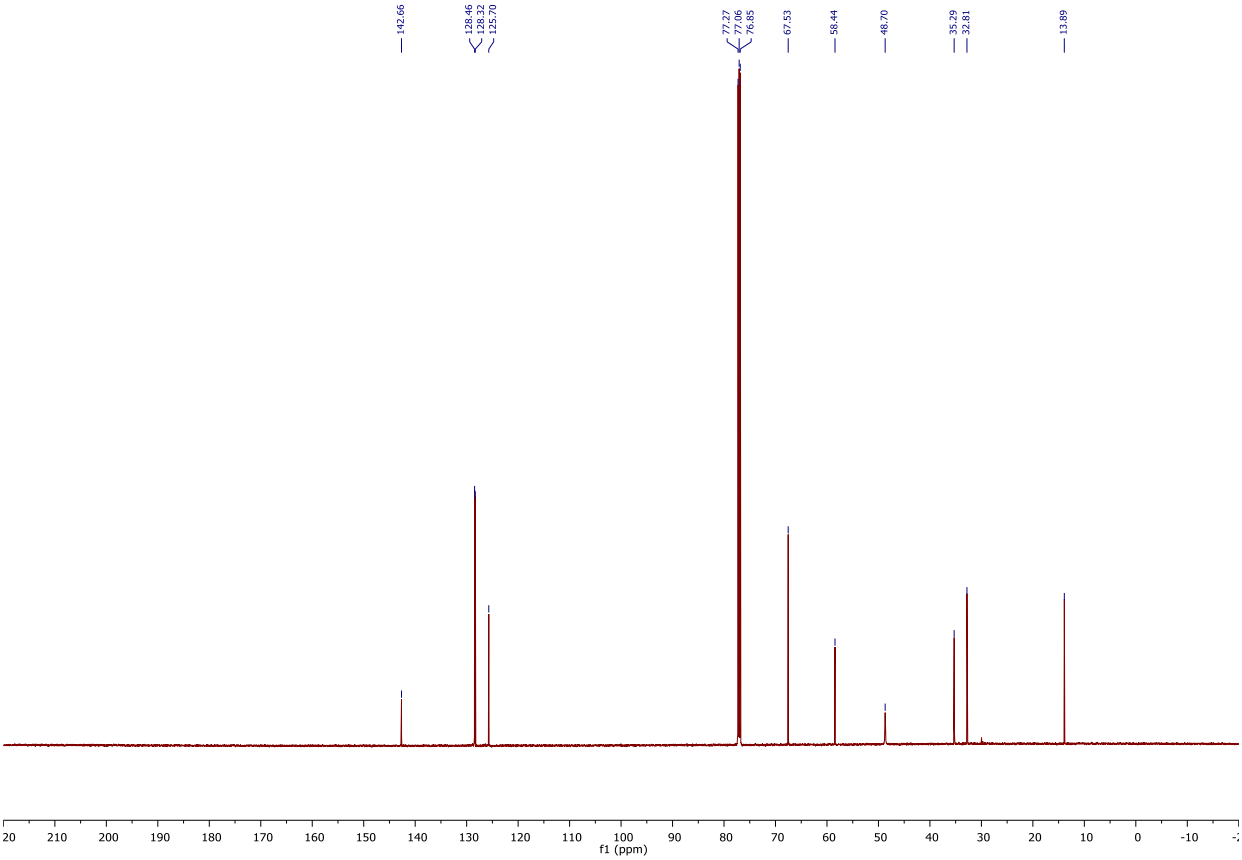

182.67
141.50
128.45
128.42
125.99
77.24
77.03
76.82
38.79
33.16
33.38
16.97
f1 (ppm)


O
Me
Me
7.32
7.30
7.21
7.21
7.20
2.63
2.62
2.62
2.62
2.61
2.57
2.56
2.16
2.05
2.04
1.69
1.68
1.68
1.67
1.67
1.66
1.17
1.16
1.95
2.77
2.88
2.80
1.00
1.06
3.02
f1 (ppm)


212.54
141.72
128.46
128.40
126.00
77.31
77.10
76.89
46.48
34.41
33.40
28.19
16.35
f1 (ppm)


Ph
Me
O
N
N
N
O
Cl
f1 (ppm)
f1 (ppm)


O
N
Me
f1 (ppm)


142.66
128.46
128.32
125.70
77.27
77.06
76.85
67.53
58.44
48.70
35.29
32.81
13.89
f1 (ppm)