Electronic Supplementary Material (ESI) for Chemical Science.

Supplementary Information

Catalytic Intramolecular Aminoarylation of Unactivated Alkenes with Aryl Sulfonamides

Efrey A. Noten, Rory C. McAtee, and Corey R. J. Stephenson*

Department of Chemistry, University of Michigan, 930 N. University Ave, Ann Arbor, MI 48109

*Corresponding author. crjsteph@umich.edu

1. Experimental details

1a. General considerations

All chemicals were used as received and stored as recommended by the supplier. All solvents were dried by passage through activated alumina columns or by overnight storage over flame-dried 3Å molecular sieves, unless otherwise noted.

Reactions were monitored by thin layer chromatography (TLC) using glass-backed plates pre-coated with 230–400 mesh silica gel (250 mm thickness) with fluorescent indicator F254, available from EMD Millipore (cat. #: 1.05715.0001). Plates were visualized with a dual short wave/long wave UV lamp. Column flash chromatography was performed using 230-400 mesh silica (SiliCycle cat. #: R12030B) gel or via automated column chromatography.

NMR spectra were recorded on Varian MR400, Bruker Ascend 500, Varian Inova 500, Varian VNMRS 500, Varian VNMRS 600, or Varian VNMRS 700 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26 ppm and for DMSO 2.50 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77.16 ppm and for DMSO at 39.52 ppm for the center of the septet. ^{19}F NMR chemical shifts were reported as δ, parts per million, relative to $CFCl_3$ at 0.0 ppm. The abbreviations app. s, br. s, d, dd, br. d, ddd, t, q, p, sext, sept, and m stand for the following resonance multiplicities, respectively: apparent singlet, broad singlet, doublet, doublet of doublets, broad doublet, doublet of doublet of doublets, triplet, quartet, pentet, sextet, septet, and multiplet. All ^{13}C NMR spectra are proton-decoupled and fluorine-coupled. All ^{19}F NMR spectra are proton-coupled.

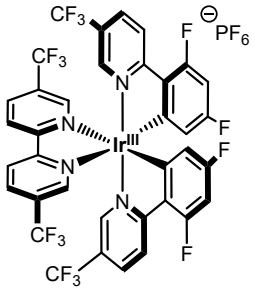
IR spectra were recorded on a Perkin-Elmer Spectrum BX FT-IR spectrometer fitted with an ATR accessory.

Mass spectra were recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan on an Agilent Q-TOF HPCL-MS with a high resolution mass spectrometer using electrospray ionization (ESI). We thank Dr. James Windak and Dr. Russel Bornschein for conducting a portion of these experiments.

X-ray diffraction data collection and processing was conducted by Dr. Jeff. W. Kampf.

1b. Reaction optimization

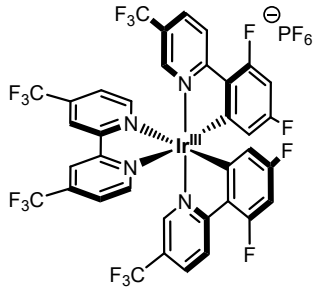
Photoredox catalysts evaluated in optimization process



$[Ir(dF(CF_3)ppy)_2(5,5'd(CF_3)bpy)]PF_6$

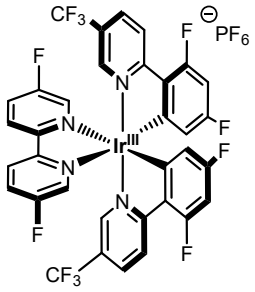
PC1: $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}d(CF_3)bpy)]PF_6$ was prepared according to a procedure previously reported in the literature. Spectral data matched values reported therein.[1]

PC2: $[Ir(dF(CF_3)ppy)_2(4,4'\text{-}d(CF_3)bpy)]PF_6$ was prepared according to a procedure previously reported in the literature. Spectral data matched values reported therein.[1]



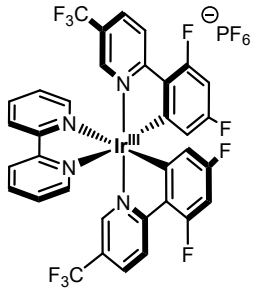
$[Ir(dF(CF_3)ppy)_2(4,4'\text{-}d(CF_3)bpy)]PF_6$

PC3: $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dFbpy)]PF_6$ was prepared as previously reported in the literature. Spectral data matched values reported therein.[1]



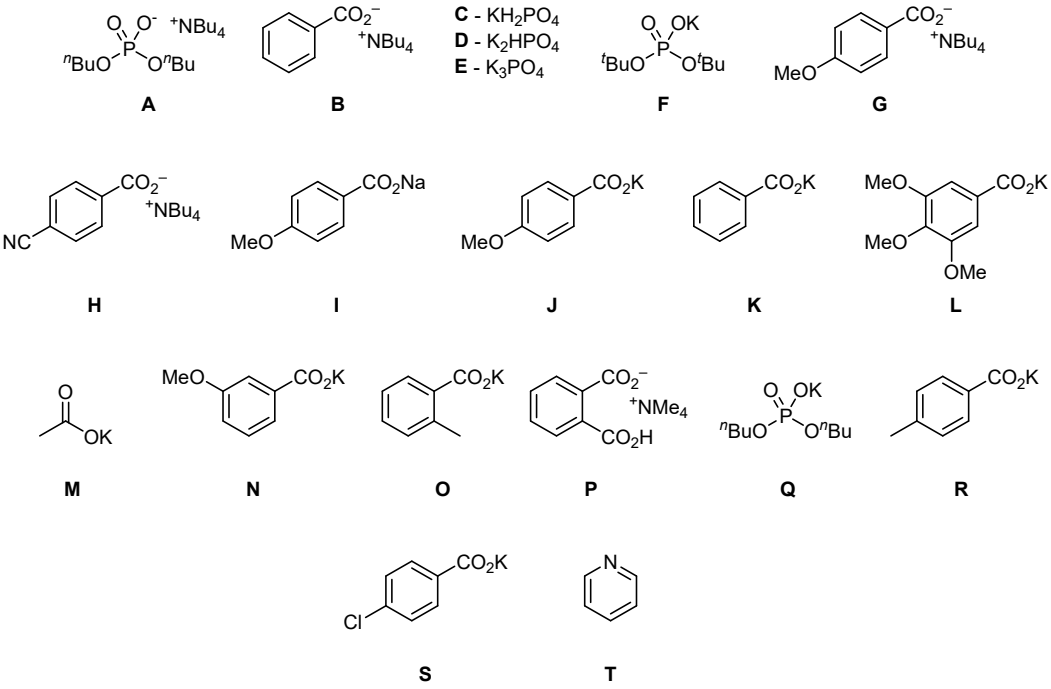
$[Ir(dF(CF_3)ppy)_2(5,5'dFbpy)]PF_6$

PC4: $[Ir(dF(CF_3)ppy)_2bpy]PF_6$ was prepared according to a procedure reported in the literature. Spectral data matched values reported therein.[2]



$[Ir(dF(CF_3)ppy)_2bpy]PF_6$

Bases evaluated in optimization process



General procedure for optimization experiments

To an oven-dried 1 dram vial with a stir bar was added N-((2,6-difluorophenyl)sulfonyl)-5-methylhex-4-enamide (30.3 mg, 0.10 mmol, 1.0 equiv.) (**1d**), base (if solid), and photocatalyst. Solvent was added under ambient atmosphere, then base (if liquid). The vial was sealed with a PTFE septum cap. The reaction mixture was sparged with argon for 5–10 minutes, then sealed with electrical tape. The reaction was irradiated by two blue Kessil H150 lamps for 16–18 hours, then concentrated under reduced pressure. The residue was diluted with $CDCl_3$ before 4-fluorobromobenzene (17.5 mg, 11.0 µL, 1.0 equiv.) was added via microsyringe. Assay yields were obtained by ^{19}F NMR spectroscopy.

Trial	Solvent	Base, equiv.	Photocat., mol %	Temp.	NMR yield
1	1:1 0.05 M bottle $PhCF_3$/*t*-BuOH	**A**, 0.65	PC1, 1	ambient	45% (isolated)
2	1:1 0.05 M dry DCE/tBuOH	**A**, 0.65	PC1, 2	ambient	42%
3	0.05 M dry $PhCF_3$	**A**, 0.65	PC1, 2	ambient	52%
4	0.05 M dry $PhCF_3$	**A**, 0.65	PC1, 1	ambient	68%
5	0.05 M bottle $PhCF_3$ + 5 uL H_2O	**A**, 0.65	PC1, 1	ambient	61%
6	0.05 M bottle $PhCF_3$	**A**, 0.33	PC1, 1	ambient	64%
7	0.05 M bottle $PhCF_3$	**A**, 1.0	PC1, 1	ambient	55%
8	0.05 M bottle $PhCF_3$	**B**, 0.65	PC1, 1	ambient	65%
9[a]	0.05 M bottle $PhCF_3$	**A**, 0.65	PC1, 1	ambient	39%
10	0.05 M dry $PhCF_3$	**A**, 0.65	PC1, 0.5	ambient	55%
11	0.1 M dry $PhCF_3$	**A**, 0.65	PC1, 1	ambient	39%
12	0.1 M dry $PhCF_3$	**A**, 0.65	PC1, 0.5	ambient	37%
13	0.05 M dry $PhCF_3$	**A**, 0.33	PC1, 0.5	ambient	50%
14	0.1 M dry $PhCF_3$	**A**, 0.33	PC1, 1	ambient	44%
15	0.1 M dry $PhCF_3$	**A**, 0.33	PC1, 0.5	ambient	43%
16	0.05 M bottle DCE	**A**, 0.65	PC1, 1	ambient	60%
17	0.05 M bottle acetone	**A**, 0.65	PC1, 1	ambient	64%
18	0.05 M dry CH_3CN	**A**, 0.65	PC1, 1	ambient	70%
19	0.05 M dry $PhCF_3$	**A**, 0.65	PC1, 1	ambient	60%
20	0.05 M bottle $PhCF_3$	**A**, 0.65	PC1, 1	ambient	65%
21	0.05 M dry CH_3CN	**A**, 0.65	PC1, 1	60 °C	63%
22	0.05 M dry CH_3CN	**A**, 0.65	PC1, 0.5	60 °C	62%
23	0.05 M dry CH_3CN	**B,** 0.65	PC1, 0.5	ambient	15%
24	0.05 M dry CH_3CN	**B,** 0.65	PC1, 1	ambient	44%
25	0.05 M dry CH_3CN	**A,** 0.65	PC1, 0.5	ambient	69%
26	0.05 M dry CH_3CN +50 uL H_2O)	**C**, 0.65	PC1, 1	ambient	0%
27	0.05 M dry CH_3CN +50 uL H_2O	**D**, 0.65	PC1, 1	ambient	33%
28	0.05 M dry CH_3CN +50 uL H_2O	**E**, 0.65	PC1, 1	ambient	22%
29	0.05 M dry CH_3CN	**A**, 0.65	PC2, 1	ambient	67%
30	0.05 M dry CH_3CN	**A**, 0.65	PC3, 1	ambient	44%
31	0.05 M dry CH_3CN	**A**, 0.65	PC4, 1	ambient	43%
32	0.05 M dry CH_3CN	**F**, 0.65	PC1, 1	ambient	38%
33	0.05 M dry DMF	**A,** 0.65	PC1, 1	ambient	53%
34	0.05 M dry toluene	**A,** 0.65	PC1, 1	ambient	64%
35[b]	0.05 M dry DCM	**A,** 0.65	PC1, 1	ambient	58%
36	0.05 M bottle $PhCF_3$	**A**, 0.65	PC1, 1	60 °C	74%
37	0.05 M bottle $PhCF_3$	**B,** 0.65	PC1, 1	60 °C	67%
38	0.05 M bottle $PhCF_3$	**G**, 0.65	PC1, 1	60 °C	60%
39	0.05 M bottle $PhCF_3$	**H**, 0.65	PC1, 1	60 °C	61%

Trial	Solvent	Base, equiv	Photocat. mol %	Temp	NMR yield
40	0.05 M bottle $PhCF_3$	**G**, 0.33	PC1, 1	60 °C	66%
41	0.05 M bottle $PhCF_3$	**I**, 0.65	PC1, 1	60 °C	45%
42	0.05 M bottle $PhCF_3$	**J**, 0.65	PC1, 1	60 °C	77%
43	0.05 M bottle $PhCF_3$	**K**, 0.65	PC1, 1	60 °C	71%
44	0.05 M bottle $PhCF_3$	**L**, 0.65	PC1, 1	60 °C	47%
45	0.05 M bottle $PhCF_3$	**M**, 0.65	PC1, 1	60 °C	70%
46	0.05 M bottle $PhCF_3$	**N,** 0.65	PC1, 1	60 °C	53%
47	0.05 M bottle $PhCF_3$	**O**, 0.65	PC1, 1	60 °C	54%
48	0.05 M bottle $PhCF_3$	**P**, 0.65	PC1, 1	60 °C	68%
49	0.05 M bottle $PhCF_3$	**Q**, 0.65	PC1, 1	60 °C	70%
50	0.05 M bottle $PhCF_3$	**R**, 0.65	PC1, 1	60 °C	74%
51	0.05 M bottle $PhCF_3$	**S**, 0.65	PC1, 1	60 °C	78%
52	0.05 M bottle $PhCF_3$	**S**, 0.8	PC1, 1	60 °C	78%
53	0.05 M bottle $PhCF_3$	**S**, 0.5	PC1, 1	60 °C	70%
54	0.05 M bottle $PhCF_3$	**S**, 0.65	–	60 °C	0%
55	0.05 M bottle $PhCF_3$	–	PC1, 1	60 °C	< 5%
56[c]	0.05 M bottle $PhCF_3$	**S**, 0.65	PC1, 1	60 °C	0%
57[d]	0.05 M bottle $PhCF_3$	**S**, 0.65	PC1, 1	60 °C	70%
58	0.05 M bottle $PhCF_3$	**T,** 0.65	PC1, 1	60 °C	12%

Notes: Solvents indicated as “dry” were stored under nitrogen atmosphere overnight over flame-dried 3Å molecular sieves. Solvents with “bottle” quality had been stored under ambient atmosphere for > 1 year before use without further drying.

[a] Reaction conducted without degassing.

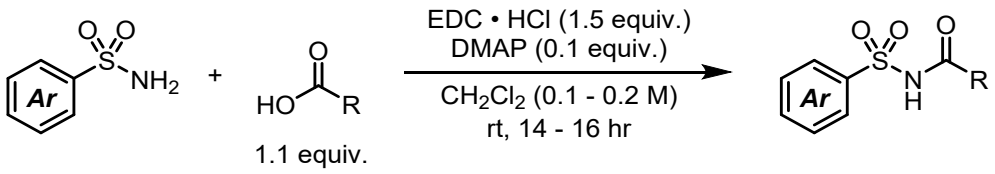
[b] Reaction solvent degassed by three freeze-pump-thaw cycles.

[c] Reaction conducted in an aluminum foil-covered vial to exclude light.

[d] Reaction conducted in a 2 dram vial.

1c. Synthetic Procedures

General Procedure 1 (GP1): Sulfonamide coupling with carboxylic acids



In a flame-dried round bottom flask with a stir bar under ambient atmosphere, carboxylic acid (1.1 equiv.) was dissolved in dry CH_2Cl_2 (0.1M – 0.2M with respect to sulfonamide). Aryl sulfonamide (1.0 equiv.) and 4-dimethylaminopyridine (0.1 equiv) were added together in one portion, and the resulting suspension was stirred for 1-2 minutes. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (1.5 equiv) was added in one portion with stirring. A rubber septum was used to seal the flask, and the headspace was purged with nitrogen for 2-3 minutes. The reaction was stirred at room temperature overnight under nitrogen atmosphere, typically between 14-16 hours. Upon completion, the reaction was concentrated under reduced pressure and the resulting viscous oil was purified using flash chromatography on silica gel (0 to 10% acetone in CH_2Cl_2 gradient) to obtain the desired *N*-acylated sulfonamide.

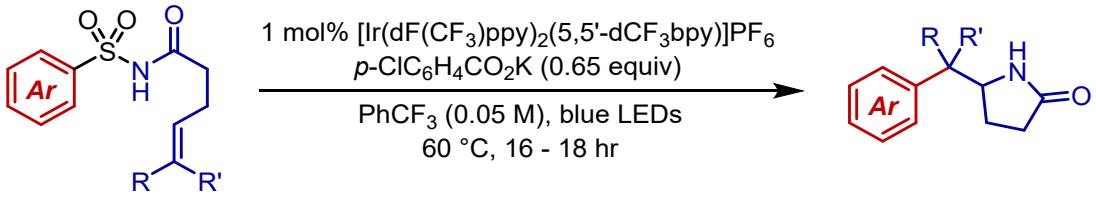
Comments:

- If the aryl sulfonamide was not commercially available, it was synthesized from the corresponding sulfonyl chloride according to published procedures.[3]

- Although coupling reactions were conducted overnight, full conversion could be observed sooner (3-4 hours).

- If complete consumption of the primary sulfonamide did not occur, its separation from the N*-acylated product by chromatography was not always trivial. Basic extraction (1M NaOH) from either EtOAc or CH_2Cl_2 was usually sufficient to partition the unreacted sulfonamide and the desired product between the organic and aqueous phases, respectively. Acidification of the aqueous phase with concentrated HCl to pH = 1, followed by extraction with CH_2Cl_2 gave the* N*-acyl sulfonamide in sufficient purity.*

General Procedure 2 (GP2): Alkene aminoarylation



1 **2**

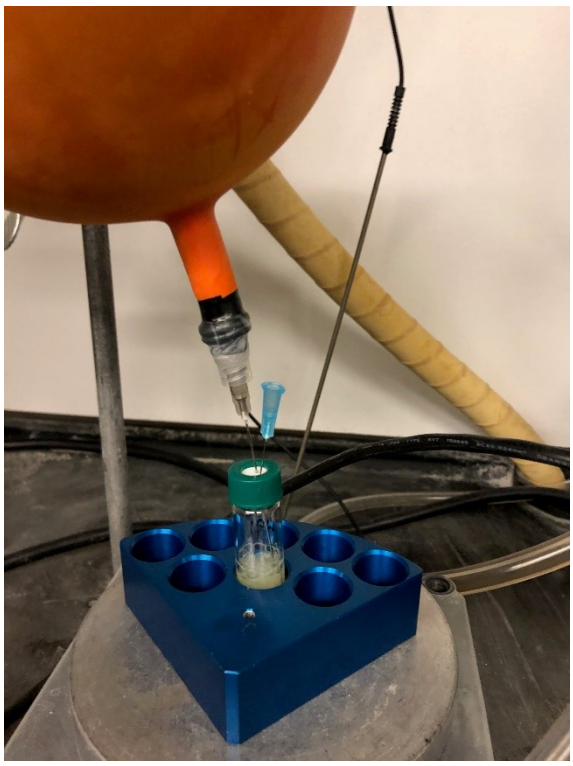
To an oven-dried 2-dram vial with a stir bar under ambient atmosphere was added acyl sulfonamide **1** (0.2 mmol, 1.0 equiv), potassium *para*-chlorobenzoate (25.3 mg, 0.13 mmol, 0.65 equiv.), and iridium photocatalyst (2.3 mg, 2.0 µmol, 0.01 equiv.). The solids were suspended in 4 mL $PhCF_3$ (0.05 M with respect to acyl sulfonamide **1**) and the vial was sealed with a PTFE-lined septum screw cap. The reaction mixture was degassed by sparging with either nitrogen or argon for 10 minutes while stirring. After sequentially removing the venting needle (25 gauge) and gas inlet needle (22 gauge), the pierced septum and vial/cap junction were both quickly sealed with electrical tape. The reaction was secured in a pre-heated oil bath set at 60 °C and irradiated by Kessil H150 blue LEDs for 16-18 hours while stirring at 700 rpm. Upon cooling to room temperature, the contents of the vial were transferred to a separatory funnel using 15 mL EtOAc. The organic phase was washed once with 30 mL saturated aqueous $NaHCO_3$ solution, and the aqueous phase was washed with additional EtOAc (2 x 5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified with flash chromatography on silica gel (0 to 10% acetone in CH_2Cl_2, then isocratic hold at 10% acetone in CH_2Cl_2) to give the aminoarylation product.

Comments:

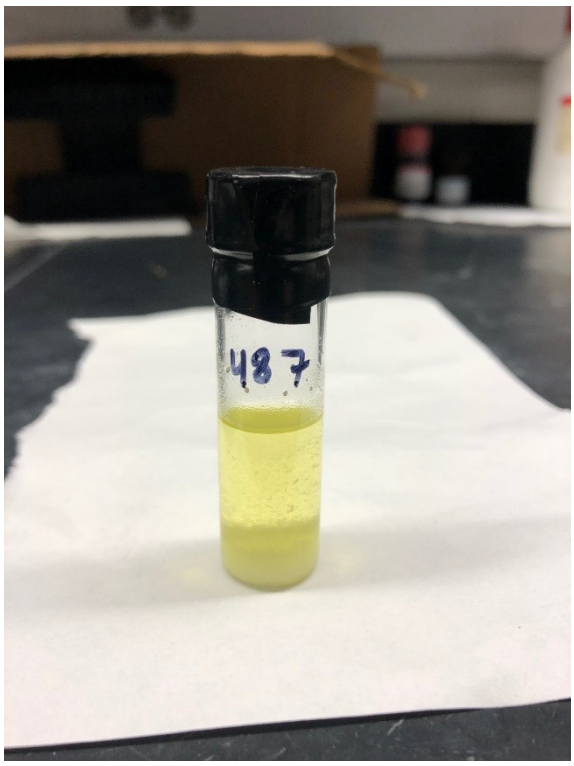
- 2 dram vials were purchased from Fisher Scientific (product number 03-339-22D) and had a 17 mm external diameter.

- $PhCF_3$ was not dried prior to use and was stored under ambient atmosphere. Control experiments in which the solvent was dried over activated 3Å molecular sieves overnight or in which a small amount (5-10 µL) of water were added did not show substantial changes in yield, indicating that this reaction is not appreciably moisture sensitive.

- Oil in the heating bath should be totally clear and colorless to ensure efficient light penetration into the reaction vessel.

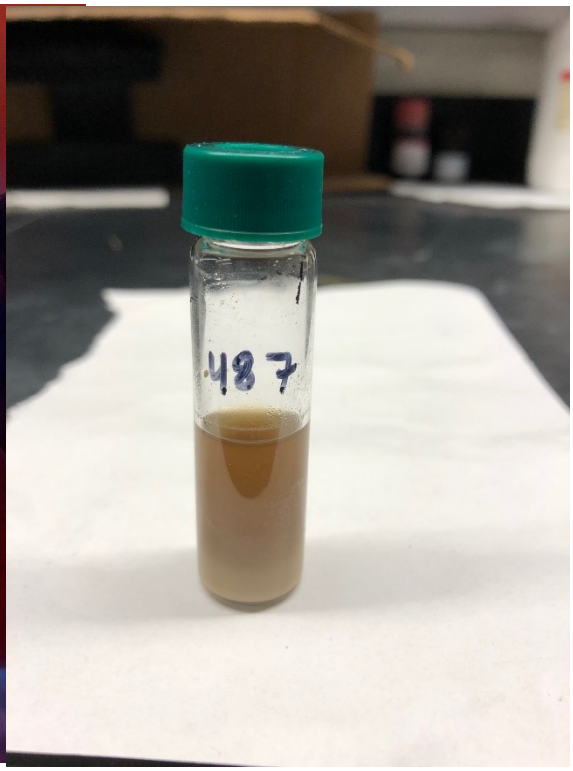


Degassing the reaction mixture with an argon balloon and vent needle



Typical appearance of the sealed reaction mixture prior to irradiation.

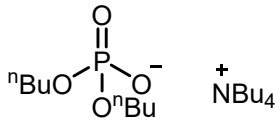
Typical reaction setup with heating in a silicone oil bath.



Typical appearance of the reaction mixture after irradiation for 16 hours.

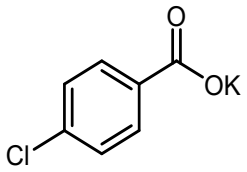
1d. Synthesis and characterization of reagents and precursors

Bases



Tetrabutylammonium dibutylphosphate (Note: all bases used as tetrabutylammonium salts in the optimization process which were unavailable commercially were synthesized analogously to the titled compound)

In a flame-dried flask under inert atmosphere, dibutyl phosphate (2.10 g, 10.0 mmol, 1.00 equiv.) was dissolved in 10.0 mL anhydrous MeOH. Tetrabutylammonium dibutyl phosphate (1.0 M solution in MeOH, 10 mL, 10 mmol, 1.0 equiv.) was added via syringe and the reaction was stirred at room temperature for three hours. The solvent was removed under reduced pressure, first by a rotary evaporator at 50 °C, and then under high vacuum at 70 °C for 72 hours to obtain the product (4.06 g, 9.0 mmol, 90% yield) as a colorless solid. Spectral data matches literature values.[4] This compound was stored in the glovebox, but small quantities (100 – 200 mg) were removed in vials and handled under ambient atmosphere.



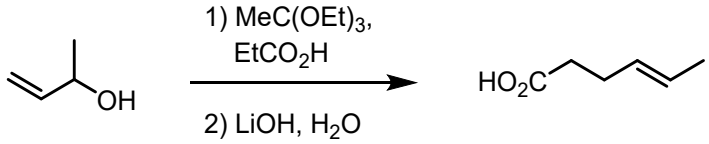
Potassium *p*-chlorobenzoate (Note: all bases used as potassium salts in the optimization process which were unavailable commercially were synthesized analogously and on the same scale as the titled compound)

To a 0 °C solution of *p*-chlorobenzoic acid (1.58 g, 10.1 mmol, 1.01 equiv) in 15 mL anhydrous THF under inert atmosphere was added a solution of potassium *tert*-butoxide (1.12 g, 10.0 mmol, 1.0 equiv) in 15 mL anhydrous THF via syringe over one minute. The product quickly precipitated as a colorless solid. The reaction was allowed to warm to room temperature and stirred for an additional 20 minutes. The precipitate was loosened to a fine slurry by addition of 30 mL diethyl ether. The solid was collected by filtration and washed with additional diethyl ether, then with pentane. The solid was transferred into a vial and ground to a fine powder with a glass rod. Yield: 1.7 g, 8.8 mmol, 88%. This compound was stored under ambient atmosphere.

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 167.4, 140.2, 132.9, 130.7, 126.9.

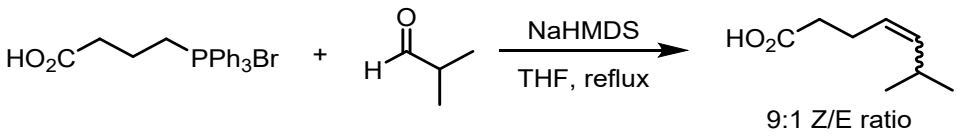
Unsaturated carboxylic acids



(*E*)-hex-4-enoic acid. To a 20 mL microwave reaction vial with a stir bar was added but-3-en-2-ol (1.5 g, 21 mmol, 1 equiv.), triethyl orthoacetate (11 mL, 60. mmol, 3.0 equiv) and propanoic acid (0.16 mL, 2.1 mmol, 0.10 equiv.) under ambient atmosphere. The vial was sealed with a crimp cap and the reaction was heated by microwave irradiation to 150 °C for 90 minutes. Upon cooling to room temperature, the reaction contents were diluted in 100 mL diethyl ether and transferred to a separatory funnel. The organic phase was washed with 100 mL 1M HCl, 100 mL sat. aq. $NaHCO_3$, 100 mL sat. aq. NaCl, dried over $MgSO_4$, and filtered. Careful concentration of the filtrate under reduced pressure gave the intermediate ester ethyl (*E*)-hex-4-enoate as a colorless, fragrant oil which was used directly in the next step without additional purification.

Under ambient atmosphere, the crude ester was dissolved in 105 mL of a 1:1:1 THF:MeOH:water mixture. LiOH (1.5 g, 62 mmol, 3.0 equiv) was added in one portion with stirring and the mixture was heated to 60 °C for 12 hours. Over this time, the reaction changed appearance from a clear, colorless solution to a cloudy yellow mixture. Upon cooling to room temperature, 50 mL water was added and the reaction mixture was concentrated under reduced pressure to remove most THF and MeOH. The concentrated mixture was transferred to a separatory funnel and washed with 2 x 50 mL diethyl ether. These first organic washes were discarded. The aqueous phase was acidified with concentrated HCl to pH 1, and the desired product was extracted with 3x50 mL diethyl ether. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated to obtain the desired acid as a yellow oil without further purification (1.8 g, 21 mmol, 76% yield over 2 steps). Spectral data match literature values.[5]

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.85 (br s, 1H), 5.56 – 5.37 (m, 2H), 2.44 – 2.39 (m, 2H), 2.34 – 2.28 (m, 2H), 1.65 (dd, *J* = 6.0, 1.6 Hz, 3H).

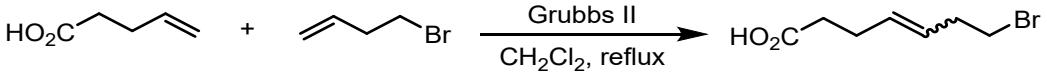


6-methylhept-4-enoic acid. To a suspension of (3-carboxypropyl)triphenylphosphonium bromide (1.5 equiv., 2.58 g, 6.0 mmol) in 20 mL anhydrous THF was added sodium bis(trimethylsilyl)amide (6 mL, 12 mmol, 3 equiv., 2 M in THF). The bright orange mixture was stirred at room temperature for 20 minutes. Isobutyraldehyde (4.0 mmol, 0.37 mL) was added dropwise and the reaction was refluxed (75 °C) for 2 hours. Upon cooling, the reaction contents were quenched with 10 mL sat. aq. NH4Cl and concentrated under reduced pressure. The concentrated mixture was partitioned between EtOAc (50 mL) and 60 mL sat. aq. NaHCO3. The aqueous phase was washed once more with 30 mL EtOAc and acidified with conc. HCl until the solution was cloudy and white. The aqueous phase was washed with hexane (3x40 mL) and the organic phase was dried over MgSO4, filtered, and concentrated to give the product as a clear colorless oil and as a 9:1 mixture of Z/E isomers (393 mg, 2.8 mmol, 69% yield). Spectral data match literature values.[6]

Z isomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.29 – 5.18 (m, 2H), 2.62 (dsept, *J* = 9.1, 6.6 Hz, 1H), 2.43 – 2.35 (m, 4H), 0.95 (d, *J* = 6.6 Hz, 6H).

Z isomer **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.4, 139.3, 124.5, 34.3, 26.5, 23.1, 22.6.

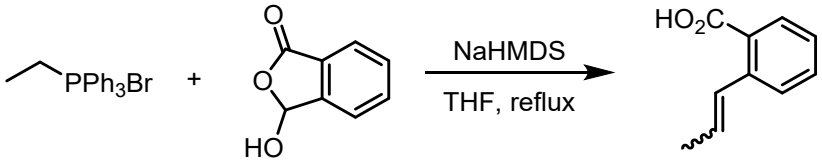
E isomer partial **^{1}H NMR** (600 MHz, $CDCl_3$) 5.45 (ddt, *J* = 15.4, 6.6, 1.0 Hz, 1H), 5.36 (dtd, *J* = 15.4, 6.6, 1.0 Hz, 1H).



7-bromohept-4-enoic acid. In a 25 mL round bottom flask with a stir bar under ambient atmosphere, 4-pentenoic acid (0.20 mL, 200 mg, 2.0 mmol, 1.0 equiv.) and 4-bromo-1-butene (1.0 mL, 1.35 g, 10.0 mmol, 5.0 equiv) were added to 10 mL CH_2Cl_2. 2nd-generation Grubbs catalyst (85 mg, 0.1 mmol, 0.05 equiv) was added, then a water-cooled condenser was affixed to the flask with a nitrogen inlet and outlet needle. The reaction was heated to 45 °C and stirred overnight under nitrogen atmosphere. The reaction was diluted with 20 mL DCM and transferred to a separatory funnel. The organic phase was washed with sat. aq. $NaHCO_3$ (2 x 20 mL). The combined aqueous phase was washed once with 10 mL CH_2Cl_2, then acidified to pH 1 with dropwise addition of concentrated aqueous HCl. The aqueous phase was washed with diethyl ether (3x15 mL) and the combined diethyl ether washes were dried over Na_2SO_4, filtered, and concentrated to obtain the product as a brown oil in an undetermined E/Z ratio (306 mg, 1.48 mmol, 74% yield).

E isomer **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.60 – 5.52 (m, 1H), 5.52 – 5.43 (m, 1H), 3.36 (t, *J* = 7.1 Hz, 2H), 2.56 (q, *J* = 7.0 Hz, 2H), 2.48 – 2.43 (m, 2H), 2.38 – 2.32 (m, 2H).

E isomer **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.15, 131.26, 128.38, 35.95, 33.84, 32.68, 27.60.



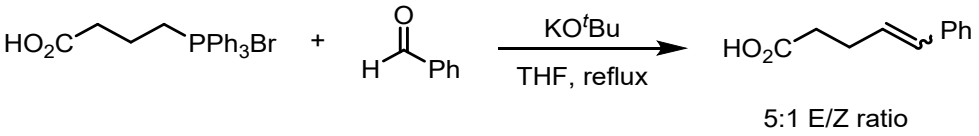
2-(prop-1-en-1-yl)benzoic acid. To a suspension of ethyltriphenylphosphonium bromide (2.0 equiv., 2.97 g, 8.0 mmol) in 20 mL anhydrous THF was added KO^{t}Bu (1.347 g, 12.0 mmol, 3.0 equiv) as a 1M solution in 12 mL THF. The bright orange mixture was stirred at room temperature for 20 minutes. 2-carboxybenzaldehyde (4.0 mmol, 601 mg) was added in one portion and the reaction was refluxed (75 °C) for 20 hours under argon atmosphere. Upon cooling, the reaction contents were quenched with 10 mL sat. aq. NH_4Cl and concentrated under reduced pressure. The concentrated mixture was partitioned between CH_2Cl_2 (50 mL) and 50 mL 1M NaOH. The organic layer was set aside and later discarded. The aqueous phase was acidified with conc. HCl to pH = 1, then washed with diethyl ether (3x40 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated to give the product as a pale yellow oil that crystallized to a

colorless solid upon standing (559 mg, 3.5 mmol, 86% yield, 2:1 E/Z ratio). Spectral data match literature values.[7]

E isomer **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.49 (td, *J* = 7.9, 1.4 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.30 – 7.27 (m, 1H), 6.19 (dq, *J* = 15.6, 6.6 Hz, 1H), 1.95 (dd, *J* = 6.6, 1.8 Hz, 3H).

Z isomer partial **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 8.2, 1.4 Hz, 1H), 6.98 – 6.93 (m, 1H), 5.88 (dq, *J* = 11.6, 7.1 Hz, 1H), 1.76 (dd, *J* = 7.1, 1.8 Hz, 3H).

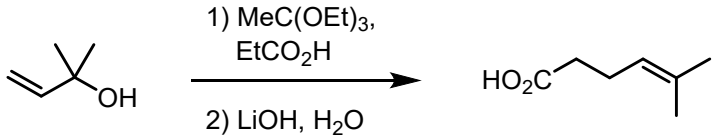
E/Z isomer mixture **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.31, 172.33, 140.8, 139.8, 133.0, 132.6, 131.6, 131.4, 131.3, 129.9, 129.8, 129.3, 128.0, 127.6, 126.9, 126.8, 126.72, 126.68, 19.0, 14.5.



5-phenylpent-4-enoic acid. A solution of potassium *tert*-butoxide (561 mg, 2.0 equiv., 5.00 mmol) in 5 mL THF was added to a suspension of (3-carboxypropyl)triphenylphosphonium bromide (1.0 equiv., 2.15 g, 5.0 mmol) in 10 mL THF at 0 °C. The reaction was stirred for 15 minutes, at which point benzaldehyde (531 mg, 0.51 mL, 1.0 equiv, 5.0 mmol) was added dropwise over 30 seconds and the reaction was allowed to warm to room temperature and stir for 2 hr. The reaction contents were partitioned between 40 mL CH_2Cl_2 and 40 mL 1M NaOH. The organic layer was isolated and the aqueous layer was washed with 50 mL additional CH_2Cl_2. The aqueous layer was isolated and the combined organics were washed with 20 mL 1M NaOH. The combined aqueous layers were acidified with dropwise addition of concentrated aqueous HCl until the solution became cloudy. The aqueous layer was extracted with diethyl ether (3x20 mL). The combined diethyl ether washes were dried over MgSO4, filtered, and concentrated to give the product as a colorless waxy solid (580 mg, 3.3 mmol, 66% yield, 5:1 E/Z ratio). Partial characterization is provided below.

E isomer **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.15 (m, 5H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.28 – 6.14 (m, 1H), 2.58 – 2.53 (m, 4H).

Z isomer partial **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.15 (m, 5H), 5.64 (dt, *J* = 11.6, 7.1 Hz, 1H), 2.71 – 2.63 (app q, 2H).

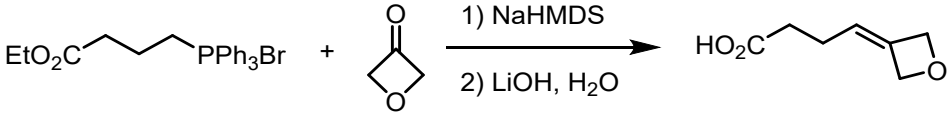


5-methylhex-4-enoic acid. Step 1: To a 20 mL microwave reaction vial with a stir bar was added 2-methylbut-3-en-2-ol (2.6 mL, 25 mmol, 1 equiv.), triethyl orthoacetate (14

mL, 76 mmol, 3.0 equiv), and propanoic acid (0.19 mL, 2.5 mmol, 0.10 equiv) under ambient atmosphere. The vial was sealed with a crimp cap and the reaction was heated by microwave irradiation to 150 °C for 90 minutes. A second, identical reaction was conducted in parallel and the contents of the two vials were combined, diluted with 100 mL diethyl ether, and transferred to a separatory funnel. The organic phase was washed with 100 mL 1M HCl, 100 mL sat. aq. $NaHCO_3$, 100 mL sat. aq. NaCl, dried over $MgSO_4$, and filtered. Careful concentration of the filtrate under reduced pressure gave the intermediate ester ethyl 5-methylhex-4-enoate as a colorless oil which was used directly in the next step without additional purification.

Step 2: Under ambient atmosphere, the crude ester was dissolved in 100 mL of a 1:1:1 THF:MeOH:water mixture. $LiOH•H_2O$ (8.4 g, 200 mmol, 4 equiv) was added in one portion with stirring and the mixture was heated to 60 °C for 90 minutes. Upon cooling to room temperature, 50 mL water was added and the reaction mixture was concentrated under reduced pressure to remove most THF and MeOH. The concentrated mixture was transferred to a separatory funnel and washed with 2 x 50 mL diethyl ether. These first organic washes were discarded. The aqueous phase was acidified with concentrated HCl to pH 1, and the desired product was extracted with 3x50 mL diethyl ether. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated to obtain the crude acid as a pale yellow oil. Purification was achieved by distillation under vacuum at 90 °C to obtain the product as a clear, colorless oil (3.33 g, 26 mmol, 52% yield over 2 steps). Spectral data match literature values.[8]

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.46 (br s, 1H), 5.13 – 5.07 (m, 1H), 2.40 – 2.35 (m, 2H), 2.35 – 2.28 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H).



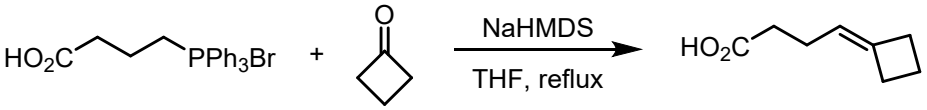
4-(oxetan-3-ylidene)butanoic acid. Step 1: To a stirred suspension of (3-ethoxycarbonylpropyl)triphenylphosphonium bromide (3.43 g, 7.5 mmol, 1.5 equiv) in 20 mL anhydrous THF was added sodium bis(trimethylsilyl)amide (3.8 mL, 7.5 mmol, 3.0 equiv., 2.0 M in THF). The bright orange mixture was stirred at room temperature for 20 minutes. 3-oxetanone (5.0 mmol, 360 mg) was added dropwise as a solution in 5 mL THF, and the reaction was heated to reflux (75 °C) under inert atmosphere for 3 hours, then was allowed to cool and stir overnight. The reaction was quenched by pouring into 50 mL sat. aq. NH_4Cl in a separatory funnel. The aqueous phase was extracted with diethyl ether (3x50 mL), then washed with sat. aq. NaCl. The combined organic phases were dried over MgSO4, filtered, and concentrated to give a yellow oil. Purification by silica gel chromatography (0 to 20% EtOAc in hexanes) gave the intermediate ester product ethyl 4-(oxetan-3-ylidene)butanoate as a clear, colorless oil.

Intermediate ester **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.25 – 5.20 (m, 2H), 5.18–5.14 (m, 2H), 5.14 – 5.10 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.34 (t, *J* = 7.3 Hz, 2H), 2.20 – 2.14 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

Step 2: Under ambient atmosphere, the ester was dissolved in 45 mL of a 1:1:1 THF/MeOH/water solution. LiOH (479 mg, 20.0 mmol, 4.0 equiv) was added and the reaction was stirred for 1 hour at 60 °C. Upon cooling, the contents of the reaction were transferred to a separatory funnel using 50 mL water. The aqueous phase was washed with 30 mL ether. This ether layer was later discarded. The aqueous phase was acidified to pH = 1 by dropwise addition of conc. HCl, then extracted with diethyl ether (3 x 30 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated to give the product as a pale yellow oil (245 mg, 1.7 mmol, 35% yield over 2 steps).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.27 – 5.23 (m, 2H), 5.20 – 5.17 (m, 2H), 5.15 (tp, *J* = 7.2, 2.4 Hz, 1H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.22 – 2.16 (m, 2H).

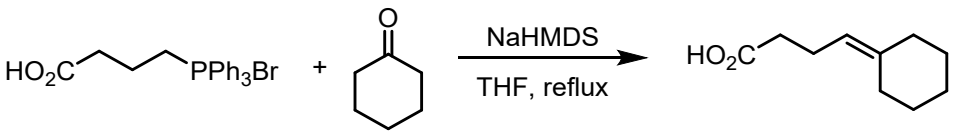
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.3, 135.7, 117.6, 79.5, 78.9, 33.5, 23.5.



4-cyclobutylidenebutanoic acid. To a suspension of (3-carboxypropyl)triphenylphosphonium bromide (1.5 equiv., 1.93 g) in 20 mL anhydrous THF was added sodium bis(trimethylsilyl)amide (4.5 mL, 9.0 mmol, 3.0 equiv., 2.0 M in THF). The bright orange mixture was stirred at room temperature for 20 minutes. Cyclobutanone (3.0 mmol, 0.22 mL) was added dropwise, and the reaction was heated to reflux (75 °C) under inert atmosphere for 12 hours. Upon cooling, the reaction contents were diluted with CH_2Cl_2 (100 mL) and 75 mL 1M NaOH. The aqueous phase was washed once more with 50 mL CH_2Cl_2 and acidified with conc. HCl until the solution was cloudy. The aqueous phase was washed with ether (3x40 mL) and the organic phase was dried over $MgSO_4$, filtered, and concentrated. Pentane (30 mL) was added to the residue to precipitate any remaining $OPPh_3$, and the resulting suspension was filtered through a Celite plug. The clear, colorless filtrate was concentrated to give the product as a clear pale yellow oil (183 mg, 1.3 mmol, 44% yield). Spectral data match literature values.[9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.43 (br s, 1H), 5.04 (app tp, J = 7.2, 2.6 Hz, 1H), 2.69 – 2.58 (m, 4H), 2.37 (t, J = 7.4 Hz, 2H), 2.20 (q, J = 7.2 Hz, 2H), 1.93 (p, J = 7.9 Hz, 2H).

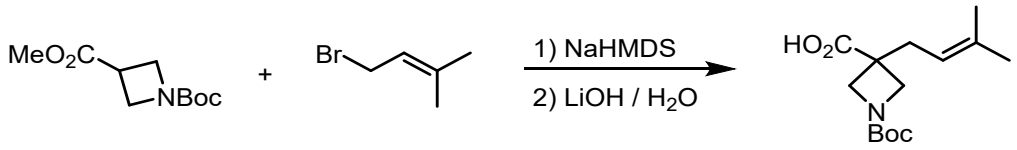
^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8, 142.2, 117.9, 34.3, 31.0, 29.3, 23.4, 17.1.



4-cyclohexylidenebutanoic acid. To a suspension of (3-carboxypropyl)triphenylphosphonium bromide (1.3 equiv., 1.93 g) in 20 mL anhydrous

THF was added sodium bis(trimethylsilyl)amide (9.0 mL, 9.0 mmol, 2.6 equiv., 1.0 M in THF). The bright orange mixture was stirred at room temperature for 20 minutes. Cyclohexanone (3.5 mmol, 0.36 mL) was added dropwise, and the reaction was heated to reflux (75 °C) under inert atmosphere for 6 hours. Upon cooling, the reaction contents were diluted with CH_2Cl_2 (100 mL) and 75 mL 1M NaOH. The aqueous phase was washed once more with 50 mL CH_2Cl_2 and acidified with conc. HCl until the solution turned cloudy. The aqueous phase was washed with ether (3x40 mL) and the organic phase was dried over $MgSO_4$, filtered, and concentrated. Pentane (30 mL) was added to the residue to precipitate any remaining $O=PPh_3$, and the resulting suspension was filtered through a Celite plug. The clear, colorless filtrate was concentrated to give the product as a clear colorless oil (535 mg, 3.2 mmol, 91% yield). Spectral data match literature values.[10]

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.06 (t, *J* = 7.0 Hz, 1H), 2.40 – 2.35 (m, 2H), 2.35 – 2.30 (m, 2H), 2.15 – 2.10 (m, 2H), 2.09 – 2.03 (m, 2H), 1.56 – 1.46 (m, 6H).



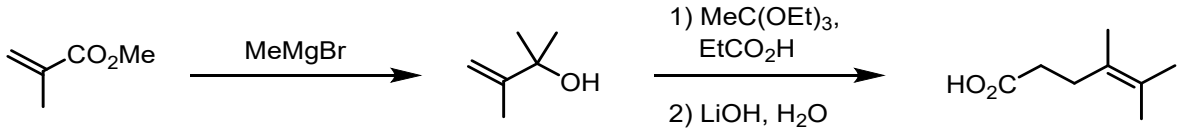
1-(tert-butoxycarbonyl)-3-(3-methylbut-2-en-1-yl)azetidine-3-carboxylic acid. Step 1: To a 0 °C solution of 1-(tert-butyl) 3-methyl azetidine-1,3-dicarboxylate (1.07 g, 5.0 mmol, 1.0 equiv) in 20 mL anhydrous THF was added NaHMDS (3.0 mL, 6.0 mmol, 1.2 equiv, 2.0 M THF solution) dropwise over 3 minutes. The reaction was stirred at this temperature for 30 min, then 1-bromo-3-methylbut-2-ene (0.7 mL, 6.0 mmol, 1.2 equiv.) was added dropwise over 2 minutes. Let warm to room temperature and stirred for 48 hours. Quenched by addition of sat. aq. NH_4Cl (2-3 mL), then transferred to separatory funnel with 50 mL CH_2Cl_2 and 50 mL water. The layers were separated, and the aqueous phase was washed with additional CH_2Cl_2 (2x50mL). Combined organics were dried over $MgSO_4$, filtered, and concentrated. Residue was purified by flash chromatography on silica gel (0 to 30% EtOAc in hexane over 12 column volumes) to give the intermediate ester 1-(tert-butyl) 3-methyl 3-(3-methylbut-2-en-1-yl)azetidine-1,3-dicarboxylate as a pale yellow oil (1.08 g, 3.8 mmol, 76% yield).

Intermediate ester **^{1}H NMR** (401 MHz, $CDCl_3$) δ 5.06 – 4.98 (m, 1H), 4.14 (d, *J* = 8.8 Hz, 2H), 3.73 (s, 3H), 3.72 (d, *J* = 8.8 Hz, 2H), 2.57 (d, *J* = 7.3 Hz, 2H), 1.70 (s, 3H), 1.64 (s, 3H), 1.43 (s, 9H).

Step 2: Under ambient atmosphere, the ester (1.08 g, 3.8 mmol, 1.0 equiv) was dissolved in 30 mL of a 1:1:1 THF/MeOH/water solution. LiOH (365 mg, 15.2 mmol, 4.0 equiv) was added in one portion and the reaction was stirred for 1 hour at 60 °C. Upon cooling, the reaction was concentrated to remove volatile components, then diluted with 50 mL water. The aqueous mixture was washed with 30 mL ether. This ether layer was later discarded. The aqueous phase was acidified to pH = 1 by dropwise addition of conc. HCl, then extracted with diethyl ether (3 x 30 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated to give the product as a colorless solid (860 mg, 3.2 mmol, 84% yield).

^{1}H NMR (401 MHz, $CDCl_3$) δ 5.10 – 5.03 (m, 1H), 4.18 (d, *J* = 8.8 Hz, 2H), 3.75 (d, *J* = 8.7 Hz, 2H), 2.61 (d, *J* = 7.3 Hz, 2H), 1.72 (s, 3H), 1.66 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.6, 156.5, 136. 6, 117.4, 80.1, 56.2, 42.8, 34.4, 28.5, 26.1, 18.2.



4,5-dimethylhex-4-enoic acid. Step 1: A solution of methylmagnesium bromide (21 mL, 63 mmol, 2.1 equiv., 3.0 M in diethyl ether) was diluted with 21 mL additional anhydrous diethyl ether in a flame-dried round bottom flask and cooled to 0 °C under nitrogen atmosphere. Methyl methacrylate (3.2 mL, 3.0 g, 30 mmol, 1.0 equiv) in 20 mL diethyl ether was added via syringe over 5 minutes. A white precipitate formed during the addition. The reaction was allowed to warm to room temperature and stir for 15 hours overnight. Quenched by careful addition of water (100 mL) and saturated aqueous NH_4Cl (25 mL). Transferred to separatory funnel and isolated organic phase. The aqueous phase was washed with diethyl ether (2 x 20 mL) and the combined organics were dried over Na_2SO_4, filtered, and partially concentrated to get the intermediate tertiary alcohol product (2,3-dimethylbut-3-en-2-ol) as a pale yellow oil (2.35 g, 23.5 mmol, 78% yield).

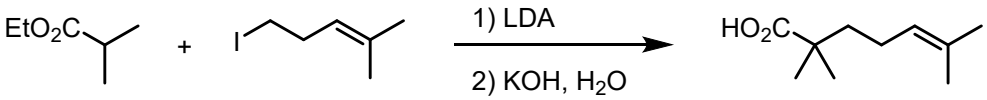
Intermediate alcohol **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.03 – 4.96 (m, 1H), 4.80 – 4.70 (m, 1H), 1.82 – 1.78 (m, 3H), 1.34 (s, 6H).

Step 2: 2,3-dimethylbut-3-en-2-ol (1.65 g, 14.8 mmol, 1.0 equiv.), triethyl orthoacetate (9.5 mL, 52 mmol, 3.5 equiv.), and propionic acid (0.11 mL, 1.5 mmol, 0.10 equiv.) were added to a 20 mL microwave vial with a stir bar under ambient atmosphere. The vial was sealed with a crimp cap and heated with microwave irradiation at 150 °C for 3 hours and 30 minutes. The contents of the vial were diluted in 100 mL diethyl ether and transferred to a separatory funnel. The organic phase was washed with 75 mL 1M HCl, 75 mL sat. aq. $NaHCO_3$, 75 mL water, dried over $MgSO_4$, and filtered. Careful concentration of the filtrate under reduced pressure gave the intermediate ester (ethyl 4,5-dimethylhex-4-enoate) as a colorless oil (contaminated with unreacted allylic alcohol starting material) which was used directly in the next step without additional purification.

Step 3: Under ambient atmosphere, the crude ester was dissolved in 75 mL of a 1:1:1 THF/MeOH/water mixture. LiOH (1.4 g, 59 mmol, 4.0 equiv) was added in one portion with stirring and the mixture was heated to 60 °C for 90 minutes. Over this time, the reaction changed appearance from a clear, colorless solution to a cloudy yellow mixture. Upon cooling to room temperature, 50 mL water was added and the reaction mixture was concentrated under reduced pressure to remove most THF and MeOH. The concentrated mixture was transferred to a separatory funnel and washed with 3 x 30 mL diethyl ether. These first organic washes were discarded. The aqueous phase was acidified with concentrated HCl to pH 1, and the desired product was extracted with 3 x 30 mL diethyl

ether. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated to obtain the desired acid as a yellow oil without further purification (553 mg, 14.8 mmol, 26% yield over 2 steps). Spectral data match literature values.[10]

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 – 2.34 (m, 4H), 1.67 (s, 3H), 1.64 (app s, 6H).



2,2,6-trimethylhept-5-enoic acid. Step 1: To a solution of diisopropylamine (2.83 mL, 20.2 mmol, 1.2 equiv) in THF (20 mL) was added n-BuLi (2.6 M solution in hexane; 7.77 mL, 20.2 mmol, 1.2 equiv.) slowly at 0 °C, and stirred at that temperature for 30 min. To this solution was added ethyl isobutyrate (2.26 mL, 1.95 g, 16.8 mmol, 1 equiv.). The reaction mixture was allowed to warm to rt and stirred for an additional 30 min, then cooled back down to 0 °C. 5-iodo-2-methylpent-2-ene[11] (4.23 g, 20.2 mmol, 1.2 equiv) was added dropwise and the resulting solution was stirred at room temperature for 7 hours. The reaction was quenched by addition of 1 mL aqueous 1 M HCl, then poured into a separatory funnel containing 50 mL aqueous 1 M HCl. The aqueous phase was washed with Et_2O (3 x 50 mL) and the combined organics were washed with saturated aqueous NaCl solution, dried over Na_2SO_4, and partially concentrated to get the intermediate ester (ethyl 2,2,6-trimethylhept-5-enoate) as a pale yellow oil. All material was taken forward to the saponification without additional purification.

Intermediate ester **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.13 – 5.02 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.94 – 1.87 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.56 – 1.50 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 6H).

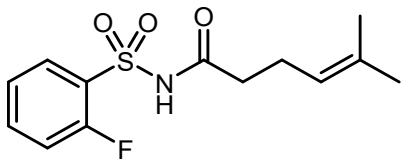
Step 2: 2,2,6-trimethylhept-5-enoate was dissolved in 75 mL 200 proof ethanol under an inert atmosphere. In a separate beaker, potassium hydroxide (9.42 g, 168 mmol, 10 equiv.) was dissolved in 250 mL DI water; this solution was then slowly poured into the ethanolic solution while stirring. The mixture was refluxed under argon atmosphere at 100 °C for 16 hrs. Upon cooling to room temp, 200 mL diethyl ether was added, and the phases were separated (discarding the ether layer). The aqueous layer was acidified to pH ~ 1 with addition of 2 M HCl and was then extracted with three 200 mL portions of ether. The combined organics were washed with 200 mL saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum to obtain the product as a clear pale yellow oil (2.69 g, 15.8 mmol, 94% yield over 2 steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.11 – 5.06 (m, 1H), 2.00 – 1.93 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.61 – 1.54 (m, 2H), 1.21 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 184.9, 132.1, 124.0, 42.2, 40.6, 25.8, 25.1, 23.8, 17.7.

2. Characterization data

2a. **<u>Characterization data and NMR spectra for aminoarylation substrates (1a – 1ae)</u>**



1a: N-((2-fluorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.7 mmol 2-fluorobenzenesulfonamide and 5-methylhex-4-enoic acid. 99 mg, 0.35 mmol, 50% yield. Colorless solid.

^{1}H NMR (401 MHz, $CDCl_3$) δ 8.57 (br s, 1H), 8.10 (td, *J* = 7.6, 1.8 Hz, 1H), 7.69 – 7.61 (m, 1H), 7.35 (td, *J* = 7.7, 1.1 Hz, 1H), 7.22 (ddd, *J* = 9.7, 8.4, 1.1 Hz, 1H), 5.04 – 4.97 (m, 1H), 2.36 – 2.30 (m, 2H), 2.30 – 2.22 (m, 2H), 1.67 (s, 3H), 1.57 (s, 3H).

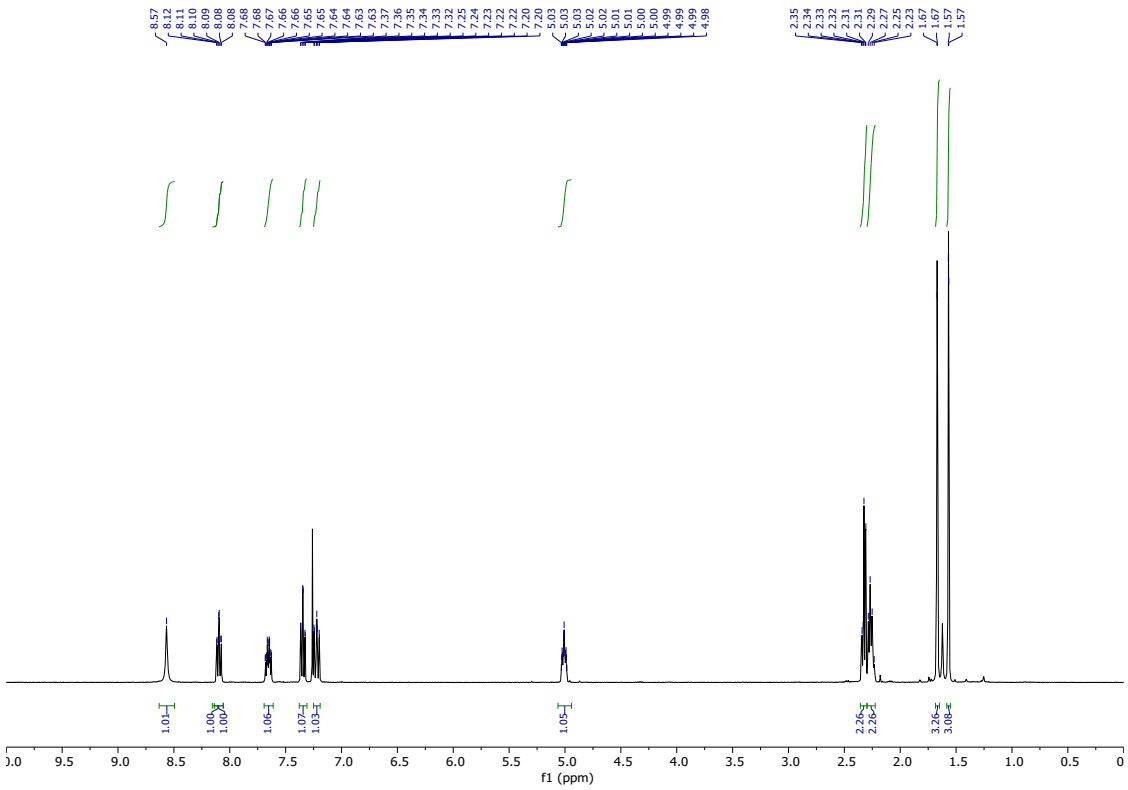
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.67, 159.1 (d, *J* = 257 Hz), 136.5 (d, *J* = 8.7 Hz), 134.8, 132.2, 126.71 (d, *J* = 12.5 Hz), 124.8 (d, *J* = 3.8 Hz), 121.5, 117.15 (d, *J* = 20.8 Hz), 36.6, 25.8, 23.1, 17.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -109.69 – -109.82 (m).

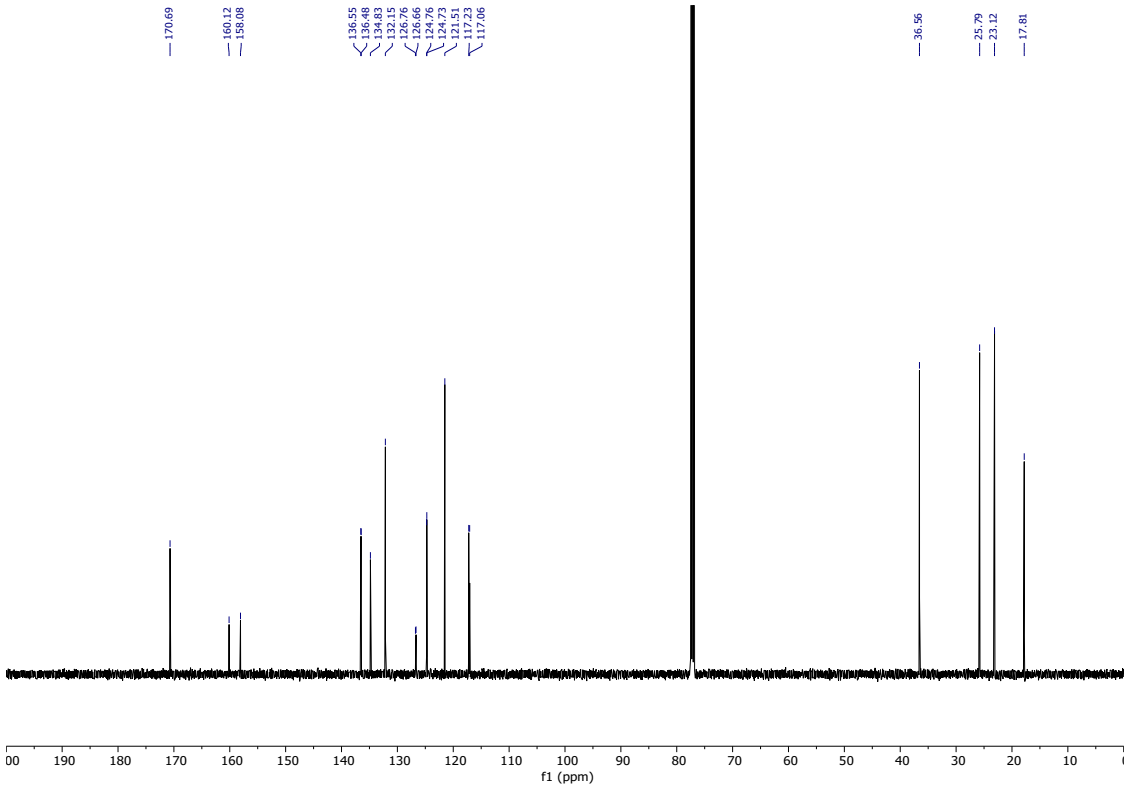
IR (neat) 3239, 2963, 2923, 2861, 1734, 1599, 1584, 1477, 1441, 1412 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{16}FNO_3SNa^+$ $[M+Na]^+$: 308.0728, found 308.0723.

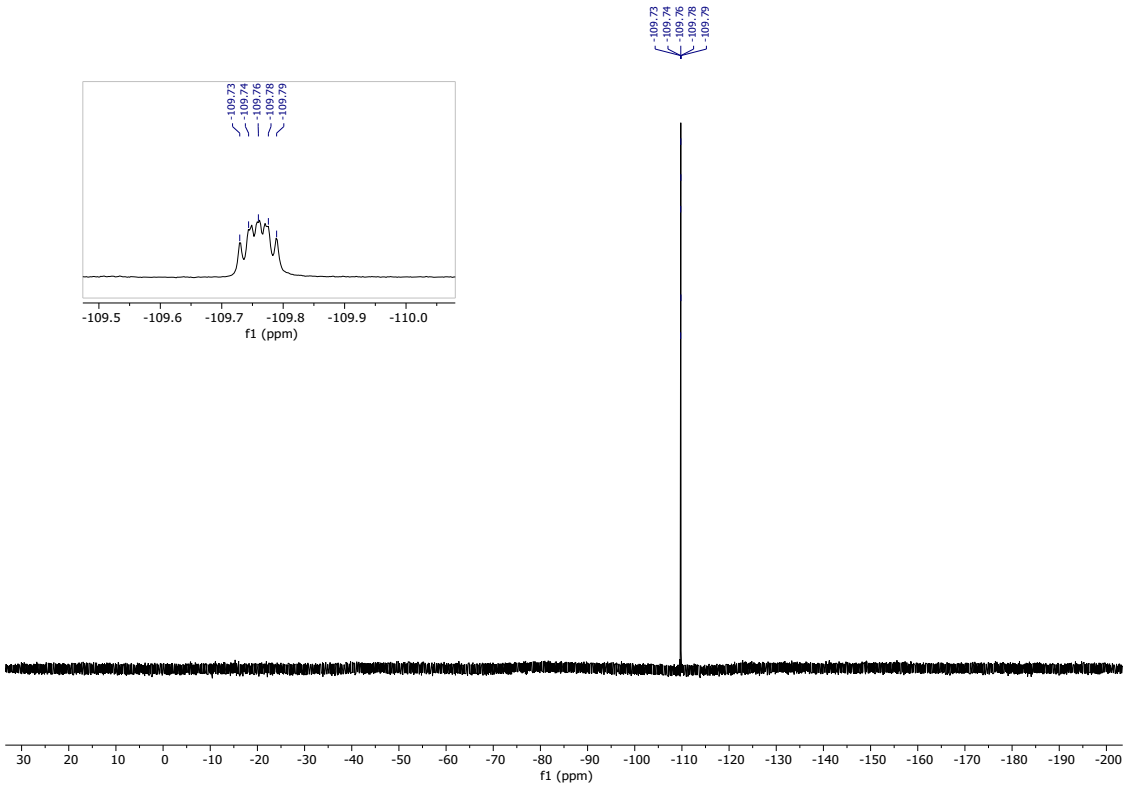
^{1}H NMR – 1a

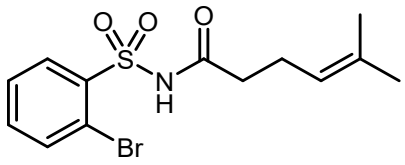


^{13}C NMR – 1a



^{19}F NMR – 1a


-109.73
-109.74
-109.76
-109.78
-109.79
-109.5
-109.6
-109.7
-109.8
-109.9
-110.0
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



1b: N-((2-bromophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 2.8 mmol 2-bromobenzenesulfonamide and 5-methylhex-4-enoic acid. 695 mg, 2.0 mmol, 72% yield. Colorless solid.

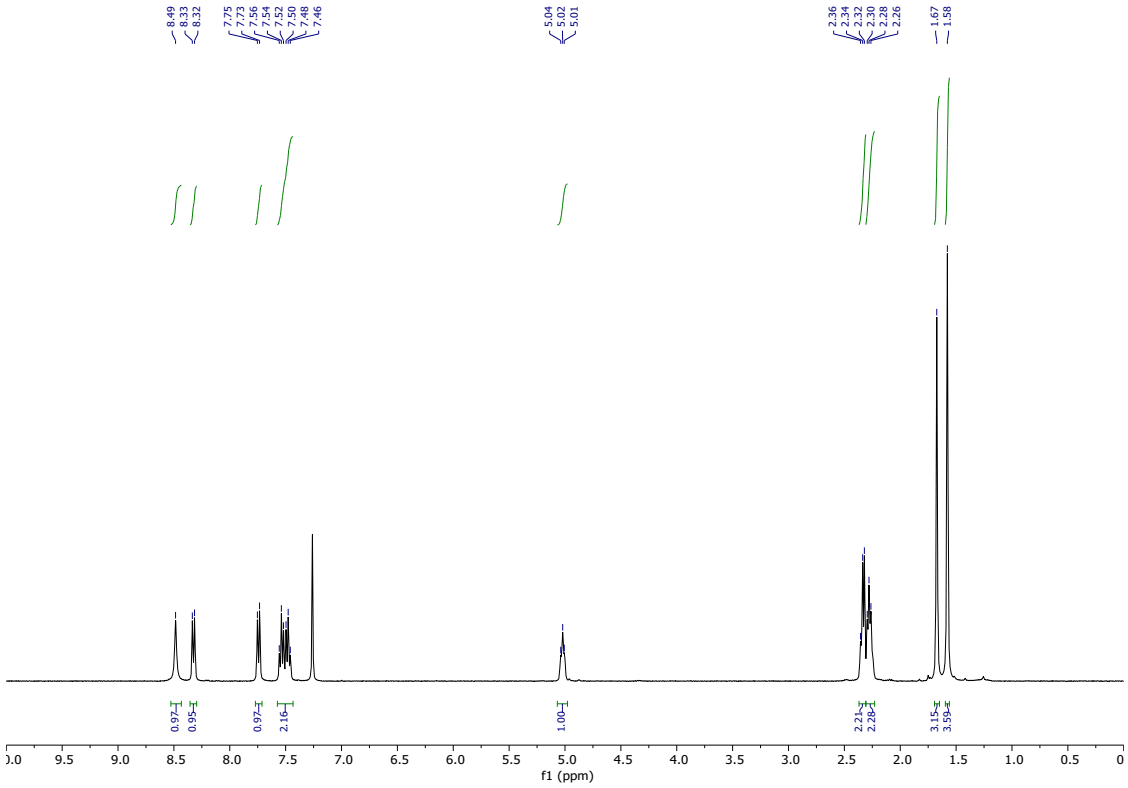
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (br s, 1H), 8.33 (m, 1H), 7.74 (m, 1H), 7.57 – 7.43 (m, 2H), 5.07 – 4.98 (m, 1H), 2.37 – 2.31 (m, 2H), 2.31 – 2.23 (m, 2H), 1.67 (s, 3H), 1.58 (s, 4H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 170.4, 137.8, 135.3, 135.0, 134.8, 133.5, 128.1, 121.6, 120.1, 36.6, 25.8, 23.1, 17.9.

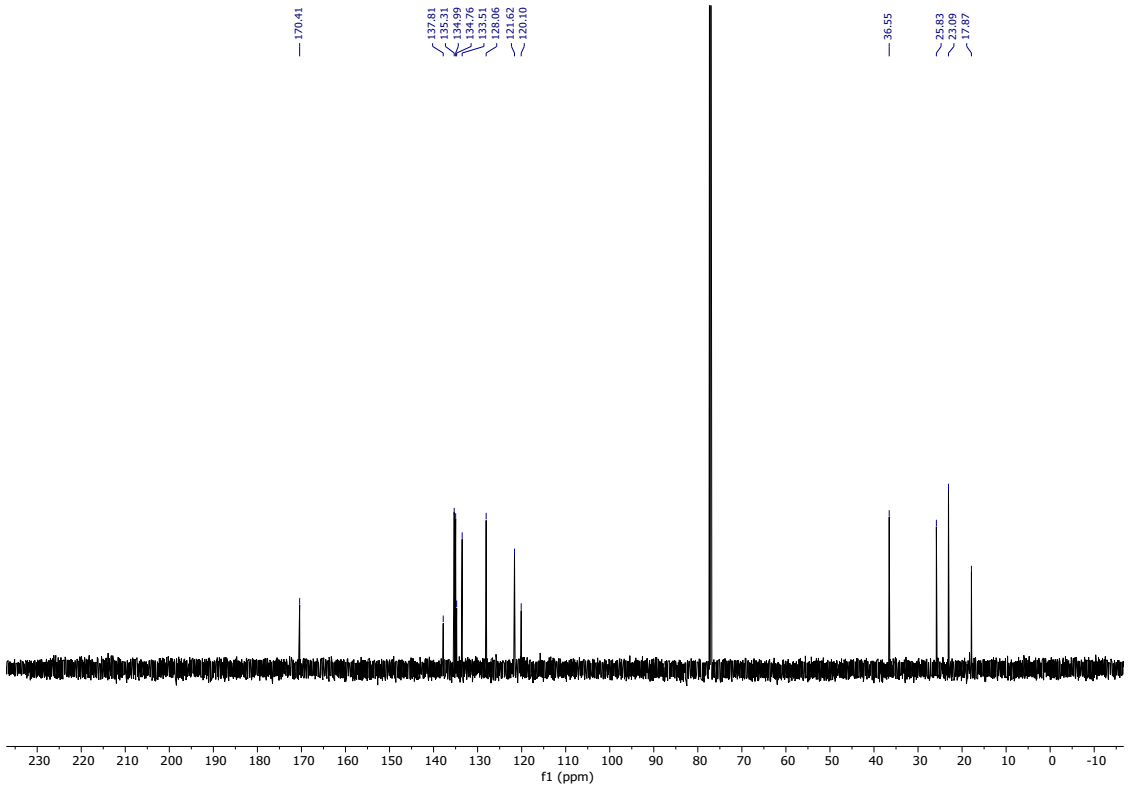
IR (neat) 3231, 2972, 2932, 1726, 1576, 1430, 1375, 1340, 1259, 1167 cm^{-1}

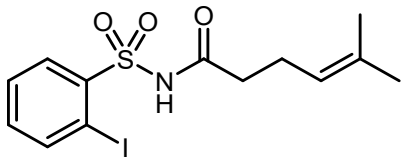
HRMS (ESI+) m/z calculated for $C_{13}H_{16}BrNO_3SNa^+$ $[M+Na]^+$: 367.9926, found 367.9912.

^{1}H NMR – 1b



^{13}C NMR – 1b





1c: N-((2-iodophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.7 mmol 2-iodobenzenesulfonamide and 5-methylhex-4-enoic acid. 169 mg, 0.43 mmol, 61% yield. Colorless solid.

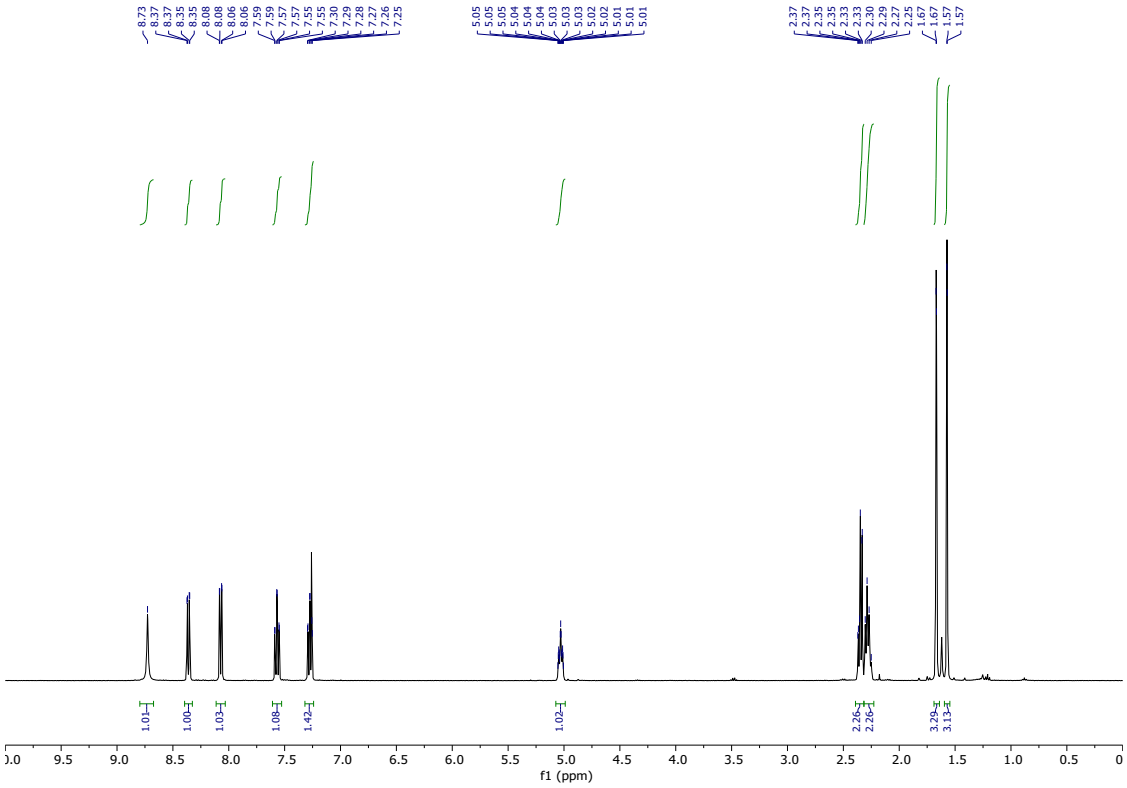
^{1}H NMR (401 MHz, $CDCl_3$) δ 8.73 (br s, 1H), 8.36 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.07 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.57 (td, *J* = 7.7, 1.2 Hz, 1H), 7.27 (td, *J* = 7.7, 1.6 Hz, 1H), 5.07 – 4.99 (m, 1H), 2.39 – 2.32 (m, 2H), 2.32 – 2.23 (m, 2H), 1.67 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 142.5, 140.9, 134.7, 134.7, 133.3, 128.8, 121.7, 92.2, 36.5, 25.9, 23.1, 17.9.

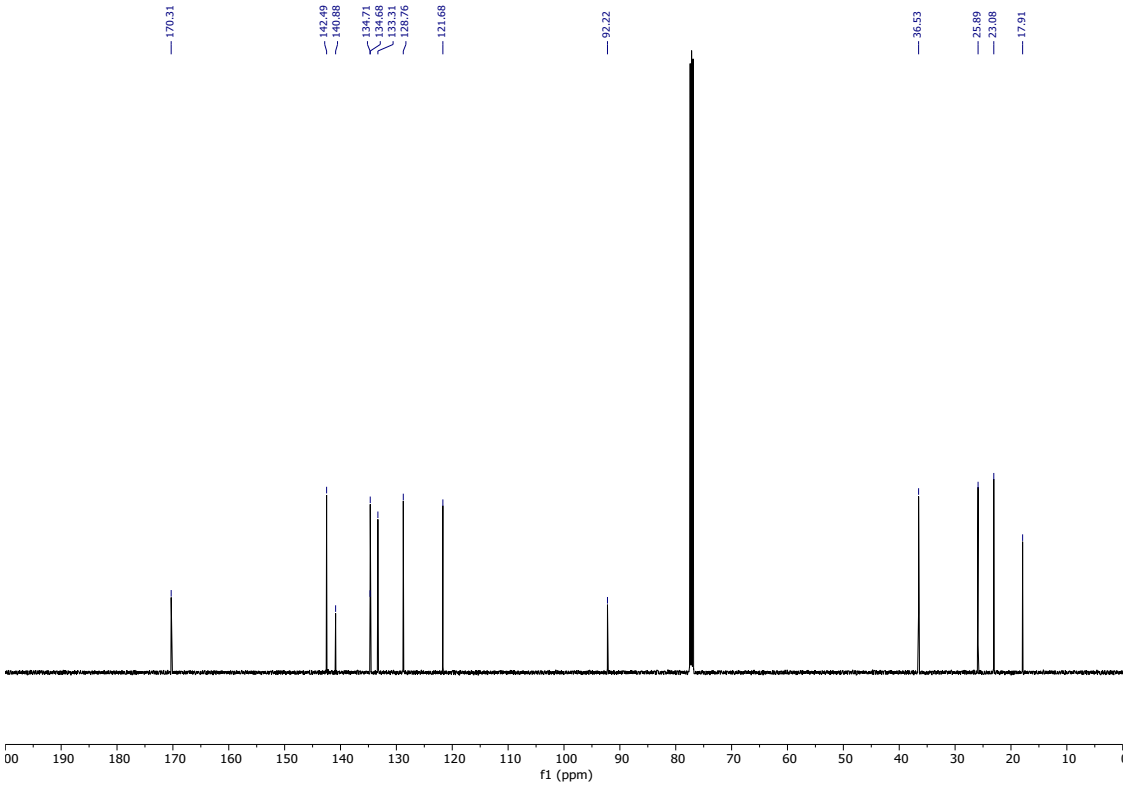
IR (neat) 3229, 2974, 2914, 2861, 1711, 1571, 1445, 1426, 1380, 1334 cm^{-1}

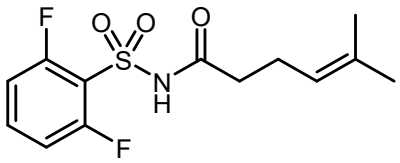
HRMS (ESI+) m/z calculated for $C_{13}H_{16}INO_3SNa^+$ $[M+Na]^+$: 415.9788, found 415.9782 .

^{1}H NMR – 1c



^{13}C NMR – 1c





1d. N-((2,6-difluorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 2.0 mmol 2,6-difluorobenzenesulfonamide and 5-methylhex-4-enoic acid. 403 mg, 1.3 mmol, 66% yield. Colorless solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.59 (tt, *J* = 8.4, 5.9 Hz, 1H), 7.06 (t, *J* = 8.7 Hz, 2H), 5.03 (t, *J* = 7.1 Hz, 1H), 2.37 (t, *J* = 7.1 Hz, 2H), 2.29 (q, *J* = 7.1 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H).

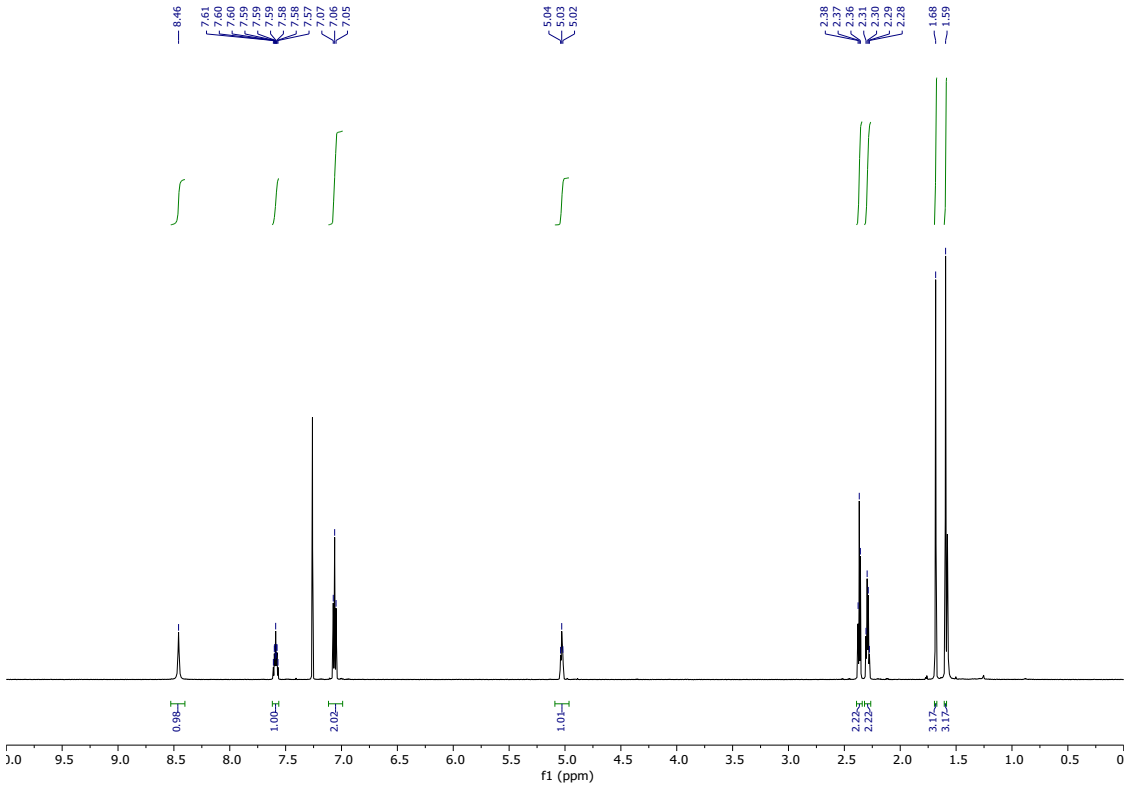
^{13}C NMR (176 MHz, $CDCl_3$) δ 171.2, 160.2 (dd, *J* = 262, 2.8 Hz), 136.0 (t, *J* = 11.2 Hz), 134.8, 121.5, 116.9 (t, *J* = 14.5 Hz), 113.4 (dd, *J* = 22.7, 3.7 Hz), 36.5, 25.8, 23.1, 17.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -106.28 (dd, *J* = 8.7, 5.9 Hz).

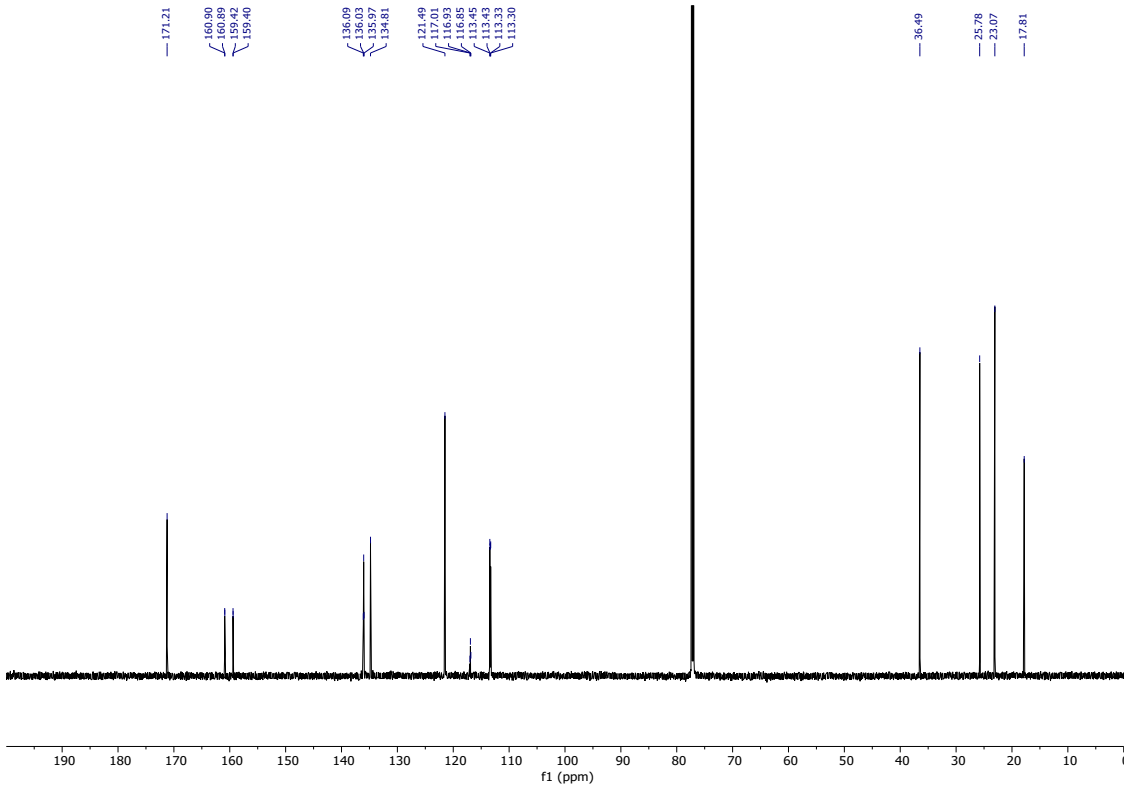
IR (neat) 3228, 3097, 2922, 2881, 1729, 1683, 1613, 1591, 1475, 1436 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{15}F_2NO_3SNa^+$ $[M+Na]^+$: 326.0633, found 326.0627.

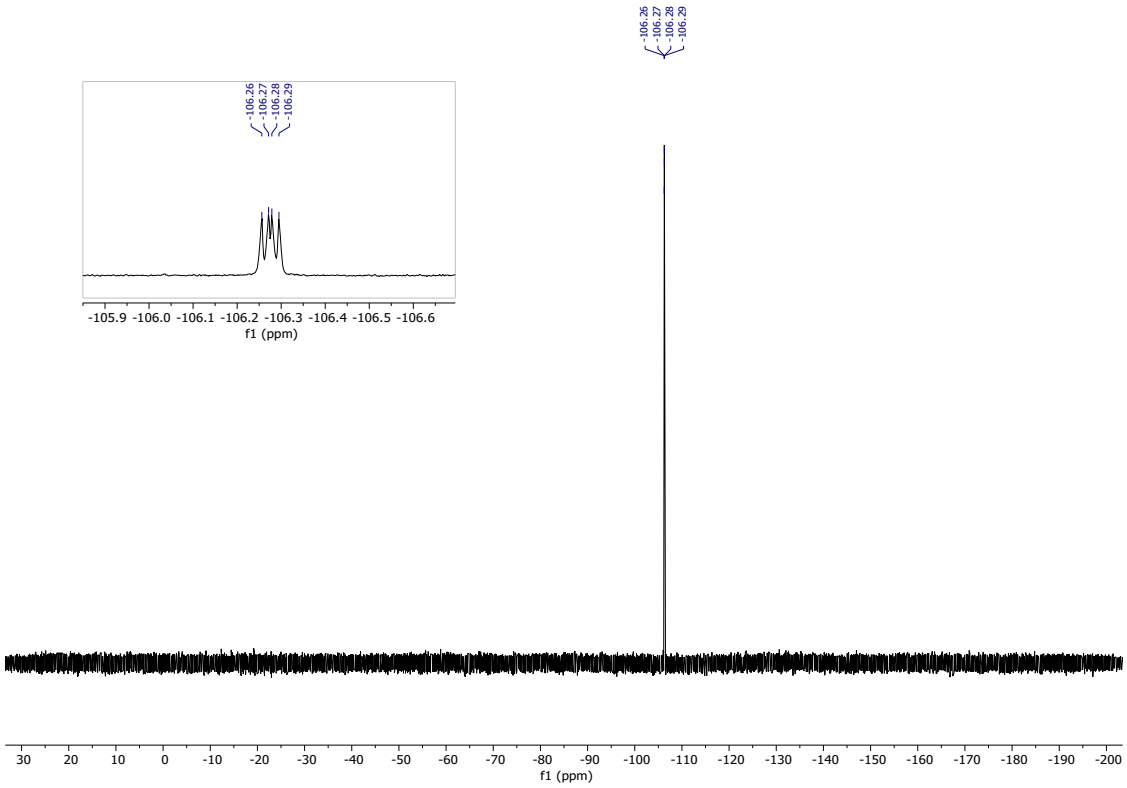
^{1}H NMR – 1d

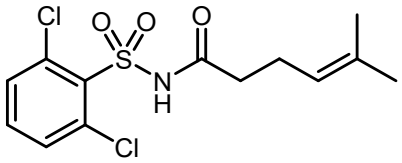


^{13}C NMR – 1d



^{19}F NMR – 1d


-106.26
-106.27
-106.28
-106.29
-105.9 -106.0 -106.1 -106.2 -106.3 -106.4 -106.5 -106.6
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1e. N-((2,6-dichlorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 1.0 mmol 2,6-dichlorobenzenesulfonamide and 5-methylhex-4-enoic acid. 242 mg, 0.72 mmol, 72% yield. Colorless solid.

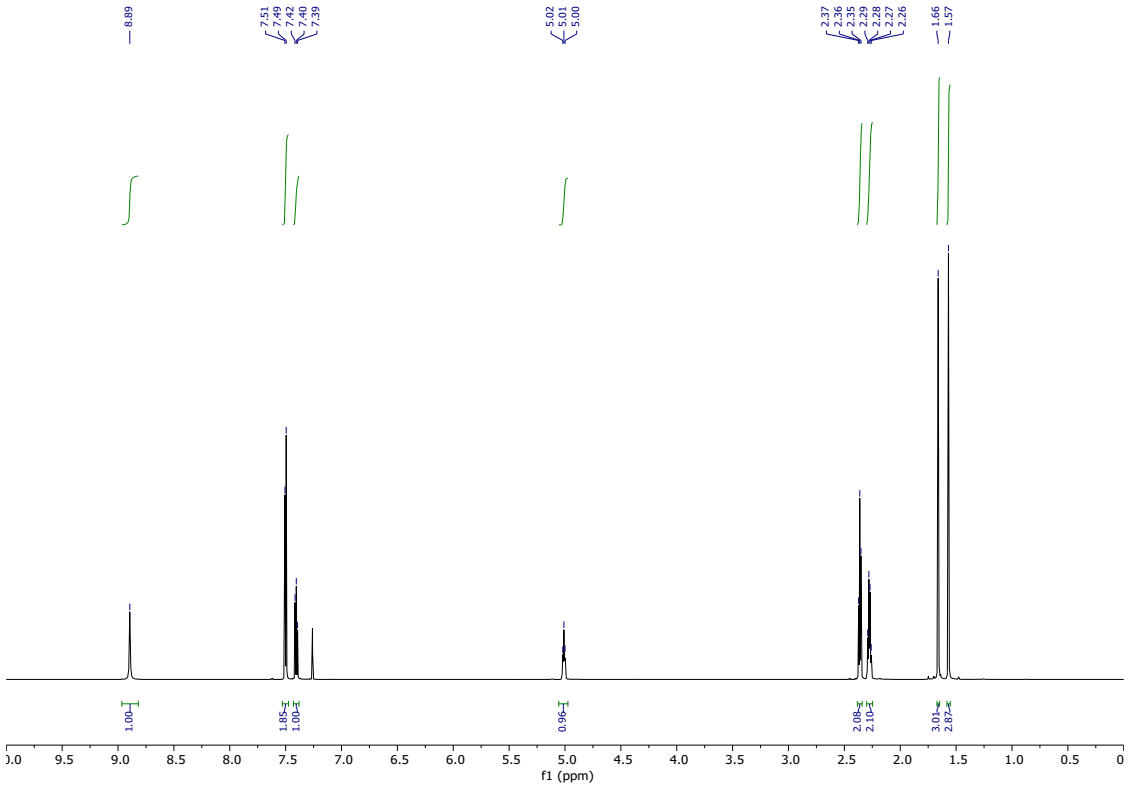
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.89 (br s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 8.1 Hz, 1H), 5.01 (t, *J* = 7.1 Hz, 1H), 2.36 (t, *J* = 7.3 Hz, 2H), 2.28 (q, *J* = 7.2 Hz, 2H), 1.66 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 171.2, 136.2, 134.7, 133.9, 133.7, 131.8, 121.6, 36.4, 25.8, 23.0, 17.9.

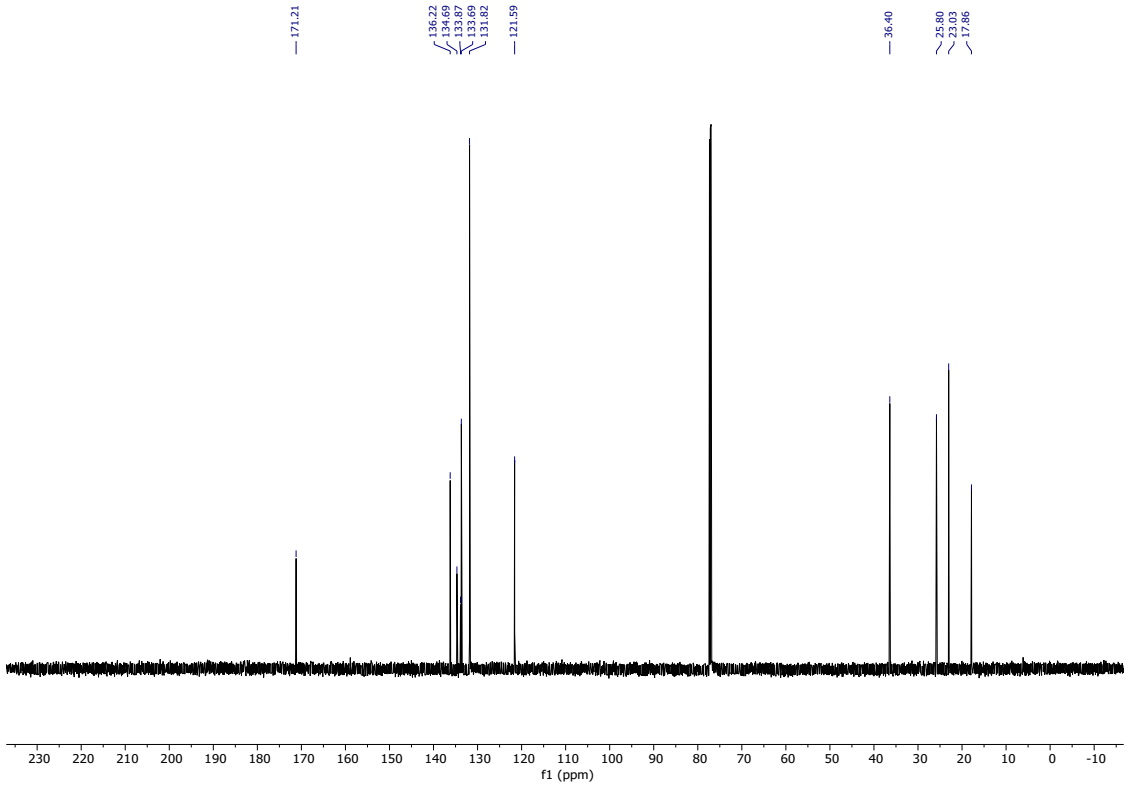
IR (neat) 3234, 2970, 2921, 1734, 1559, 1428, 1411, 1356, 1240, 1186 cm^{-1}

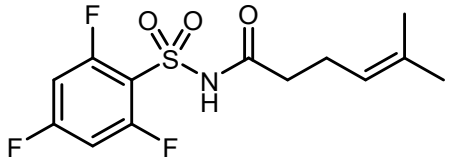
HRMS (ESI+) m/z calculated for $C_{13}H_{15}Cl_2NO_3SNa^+$ $[M+Na]^+$: 358.0042, found 358.0039.

^{1}H NMR – 1e



^{13}C NMR – 1e





1f. N-((2,4,6-trifluorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 1.0 mmol 2,4,6-trifluoromethylbenzenesulfonamide and 5-methylhex-4-enoic acid. 190 mg, 0.59 mmol, 59% yield. Colorless solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 6.82 (t, *J* = 8.5 Hz, 2H), 5.03 (t, *J* = 7.1 Hz, 1H), 2.36 (t, *J* = 7.0 Hz, 2H), 2.30 (q, *J* = 7.1 Hz, 2H), 1.69 (s, 3H), 1.61 (s, 3H).

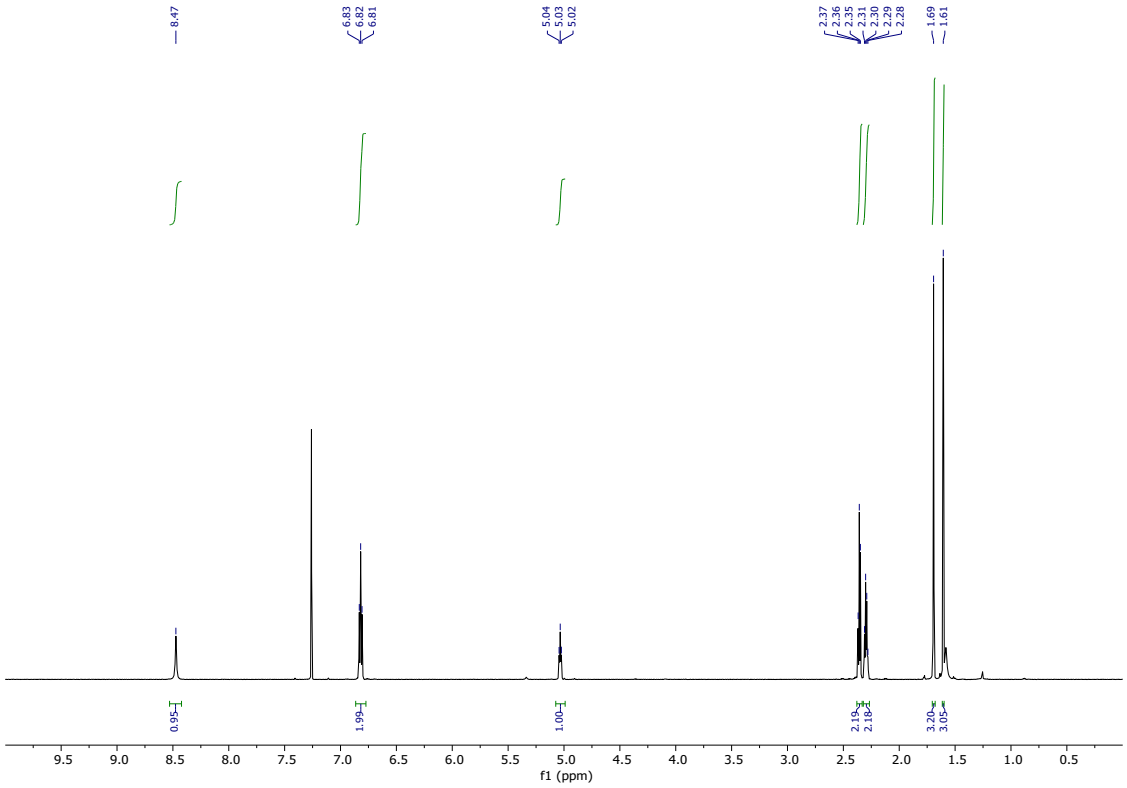
^{13}C NMR (176 MHz, $CDCl_3$) δ 171.2, 166.2 (dt, *J* = 260, 15.6 Hz), 161.3 (ddd, *J* = 263, 15.5, 5.4 Hz), 135.0, 121.4, 113.8 (td, *J* = 15.6, 5.4 Hz), 102.4 (td, *J* = 26.2, 4.1 Hz), 36.5, 25.8, 23.1, 17.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -95.97 (tt, *J* = 12.3, 8.3 Hz), -102.05 (dd, *J* = 12.2, 8.4 Hz).

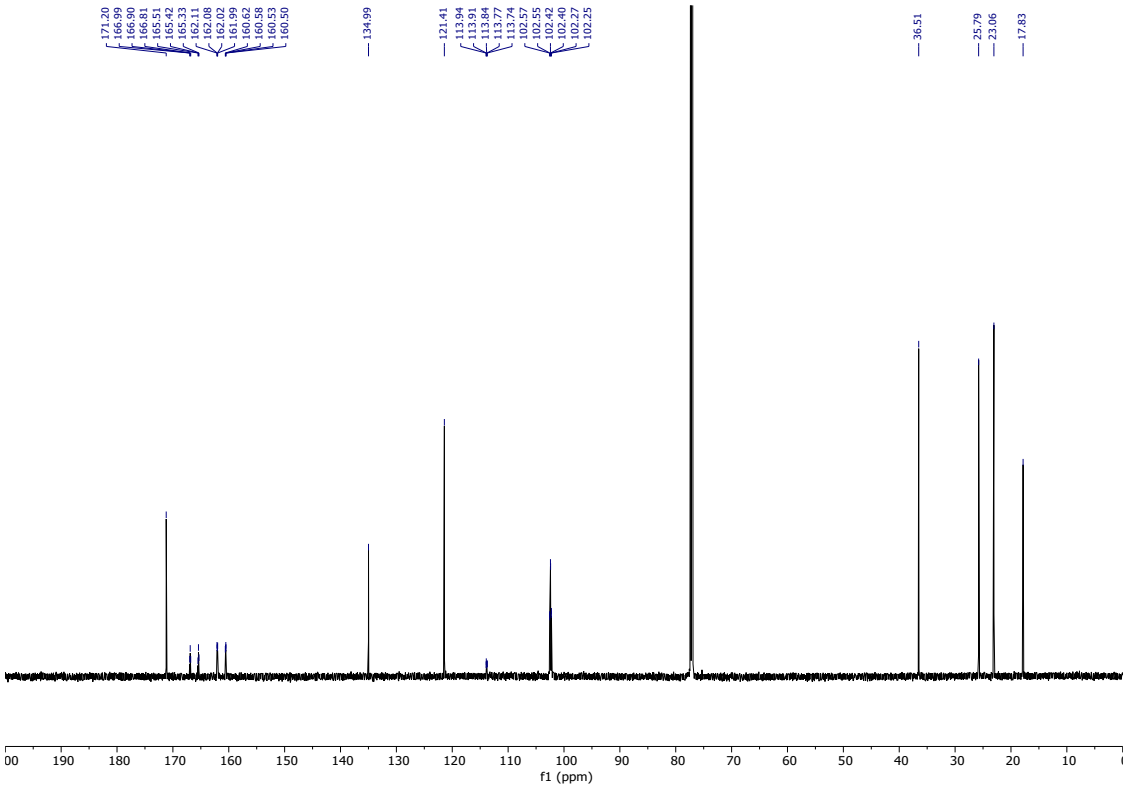
IR (neat) 3096, 2887, 1684, 1646, 1610, 1597, 1461, 1434, 1369, 1252 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{14}F_3NO_3SNa^+$ $[M+Na]^+$: 344.0539, found 344.0532.

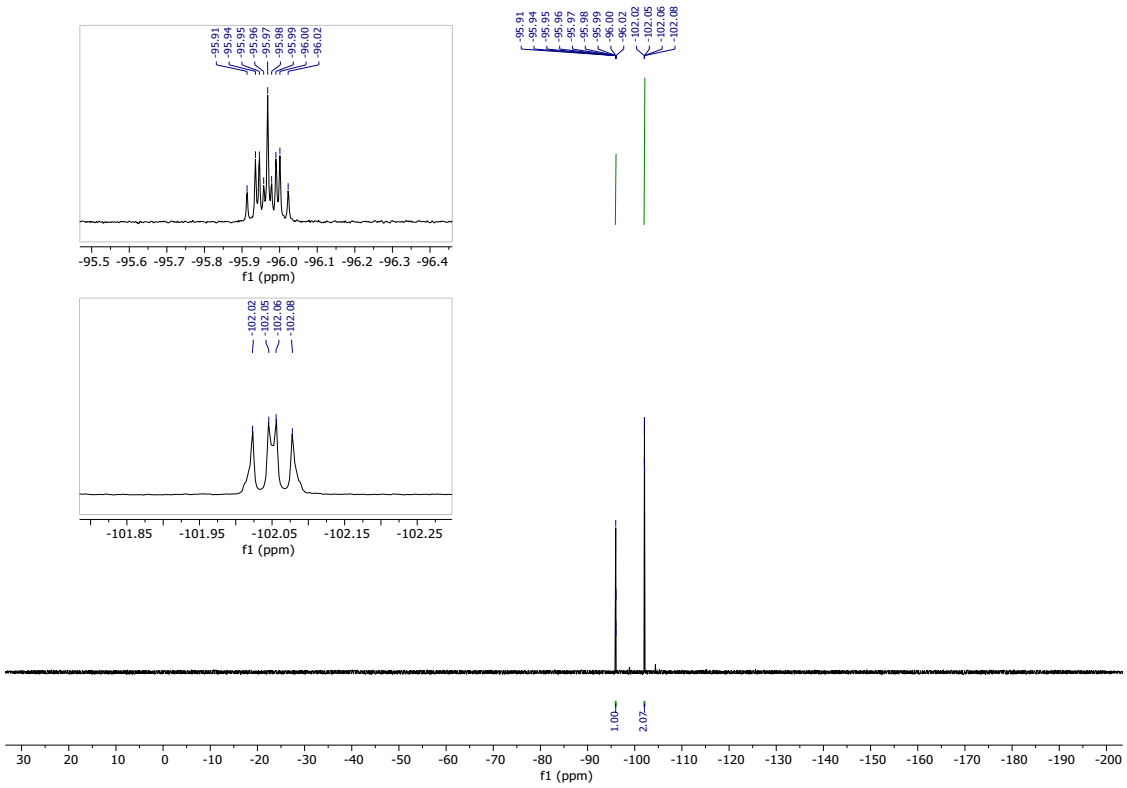
^{1}H NMR – 1f

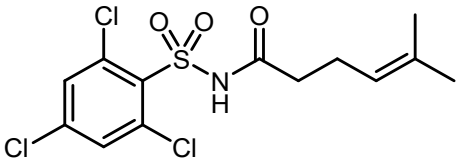


^{13}C NMR – 1f



^{19}F NMR – 1f


-95.91
-95.94
-95.95
-95.96
-95.97
-95.98
-95.99
-96.00
-96.02
-95.5 -95.6 -95.7 -95.8 -95.9 -96.0 -96.1 -96.2 -96.3 -96.4
f1 (ppm)
-102.02
-102.05
-102.06
-102.08
-101.85 -101.95 -102.05 -102.15 -102.25
f1 (ppm)
1.00
2.07
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1g. N-((2,4,6-trichlorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2,4,6-trichlorobenzenesulfonamide and 5-methylhex-4-enoic acid. 116 mg, 0.31 mmol, 52% yield. Colorless solid.

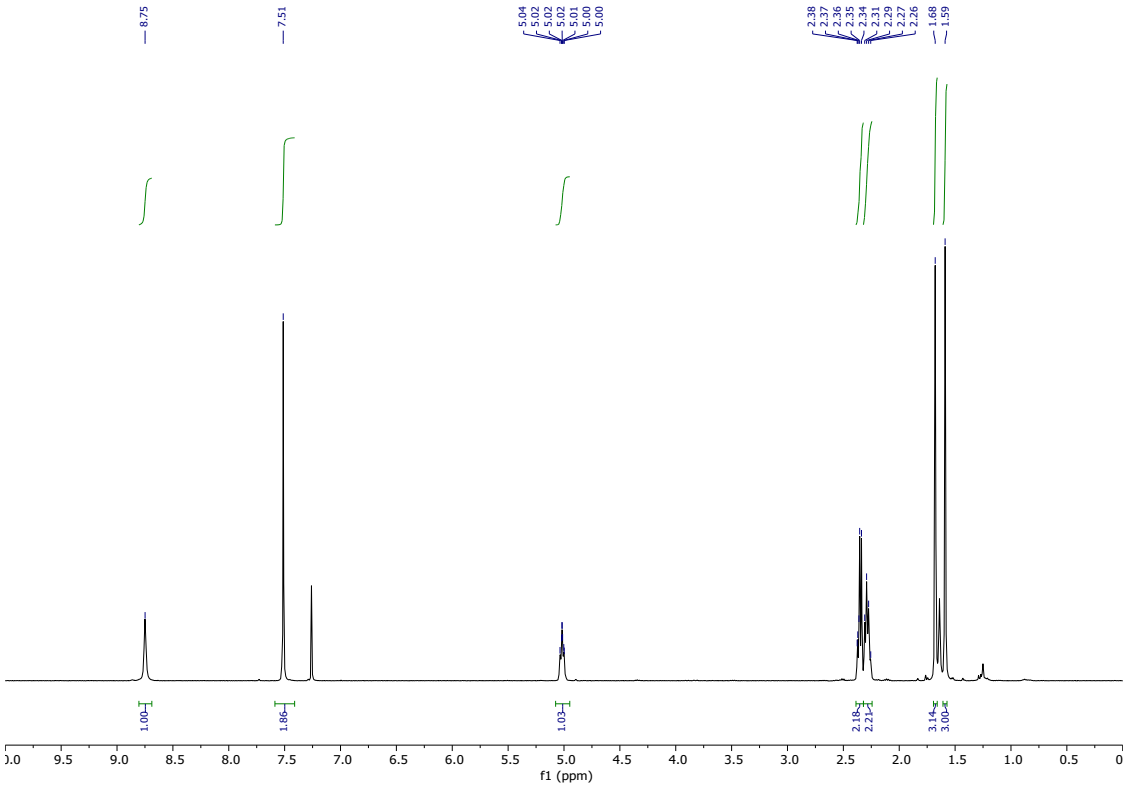
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 7.51 (s, 2H), 5.07 – 4.95 (m, 1H), 2.39 – 2.32 (m, 2H), 2.32 – 2.24 (m, 2H), 1.68 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 139.7, 137.0, 135.0, 132.5, 131.6, 121.5, 36.4, 25.8, 23.0, 17.9.

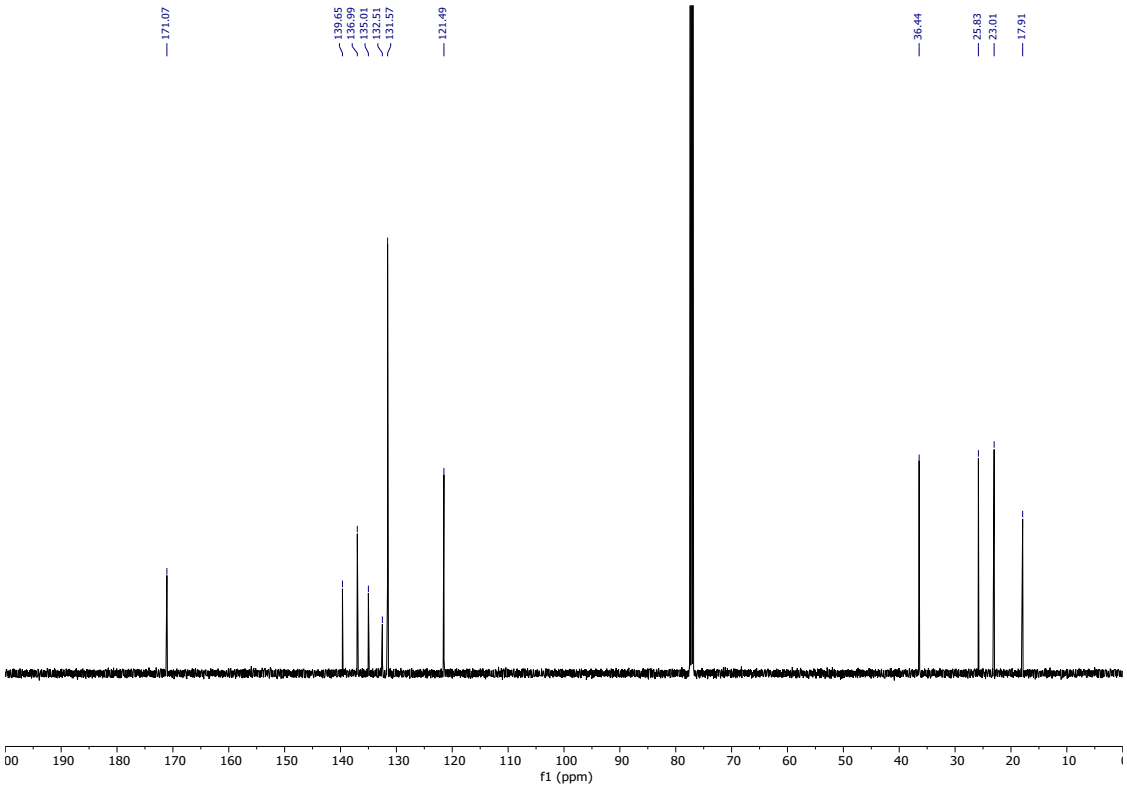
IR (neat) 3060, 2975, 2888, 1674, 1561, 1540, 1447, 1376, 1255, 1181 cm^{-1}

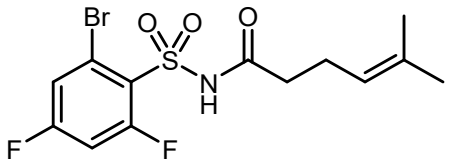
HRMS (ESI+) m/z calculated for $C_{13}H_{14}Cl_3NO_3SNa^+$ $[M+Na]^+$: 391.9653, found 391.9652.

^{1}H NMR – 1g



^{13}C NMR – 1g





1h. N-((2-bromo-4,6-difluorophenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2-bromo-4,6-difluorobenzenesulfonamide and 5-methylhex-4-enoic acid. 134 mg, 0.35 mmol, 58% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.36 (dt, *J* = 7.7, 2.2 Hz, 1H), 6.99 (ddd, *J* = 10.7, 8.0, 2.6 Hz, 1H), 5.06 – 5.00 (m, 1H), 2.38 – 2.33 (m, 2H), 2.32 – 2.25 (m, 2H), 1.68 (s, 3H), 1.59 (s, 3H).

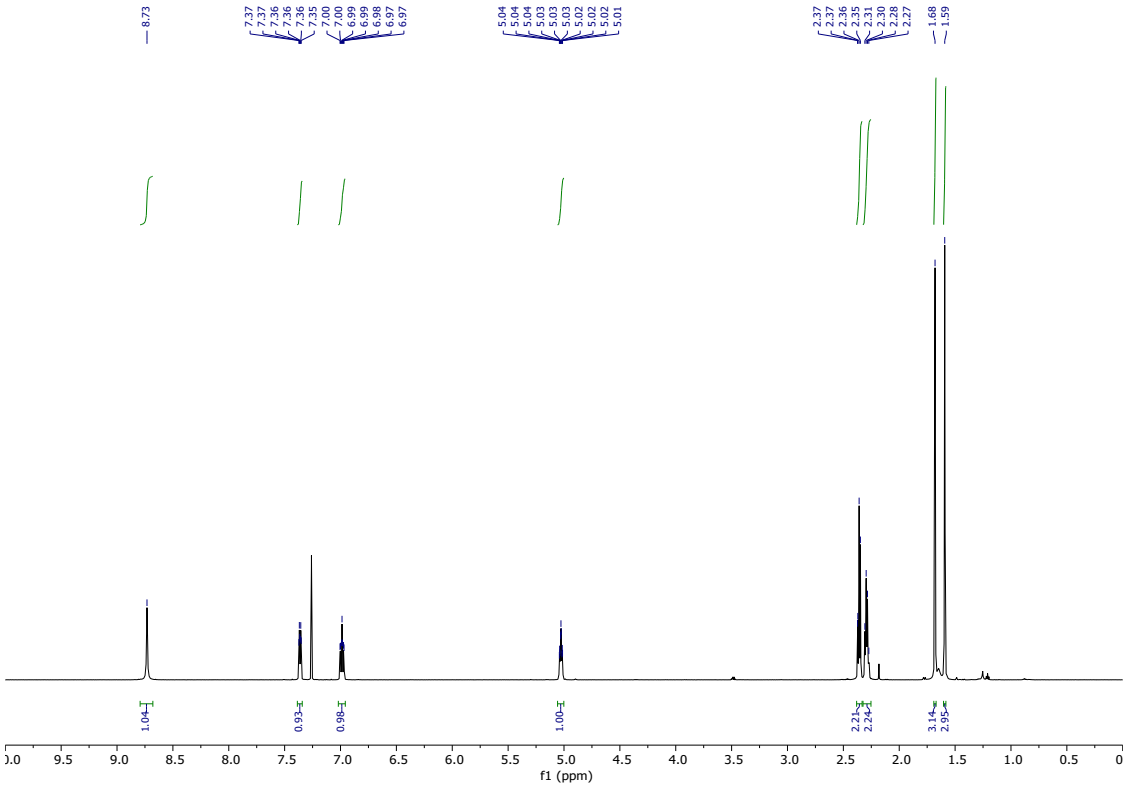
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 164.9 (dd, *J* = 262, 14.3 Hz), 162.5 (dd, *J* = 267, 13.8 Hz), 134.7, 124.0 (d, *J* = 12.1 Hz), 123.4 (dd, *J* = 11.4, 4.7 Hz), 121.49, 119.8 (dd, *J* = 24.7, 3.8 Hz), 106.0 (dd, *J* = 28.2, 25.1 Hz), 36.4, 25.8, 23.0, 17.8.

^{19}F NMR (564 MHz, $CDCl_3$) δ -96.32 (ddd, *J* = 13.2, 10.7, 1.8 Hz), -99.24 (dt, *J* = 13.9, 7.8 Hz).

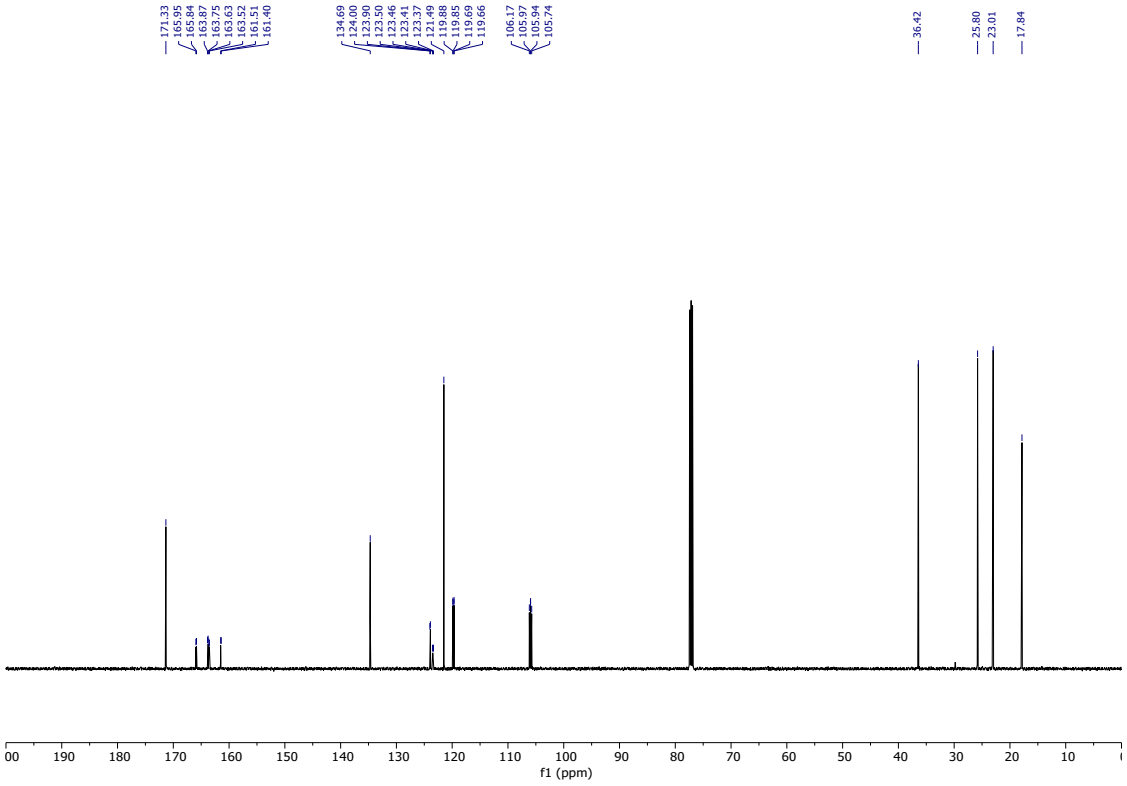
IR (neat) 3074, 2969, 2891, 1674, 1600, 1584, 1445, 1410, 1370, 1177 cm^{-1}

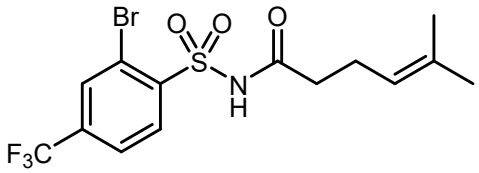
HRMS (ESI+) m/z calculated for $C_{13}H_{14}BrF_2NO_3SNa^+$ $[M+Na]^+$: 403.9739, found 403.9733

^{1}H NMR – 1h



^{13}C NMR – 1h





1i. N-((2-bromo-4-(trifluoromethyl)phenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2-bromo-4-(trifluoromethyl)benzenesulfonamide and 5-methylhex-4-enoic acid. 175 mg, 0.42 mmol, 70% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.45 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 5.03 (t, *J* = 7.0 Hz, 1H), 2.35 (t, *J* = 6.9 Hz, 2H), 2.28 (q, *J* = 7.0 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H).

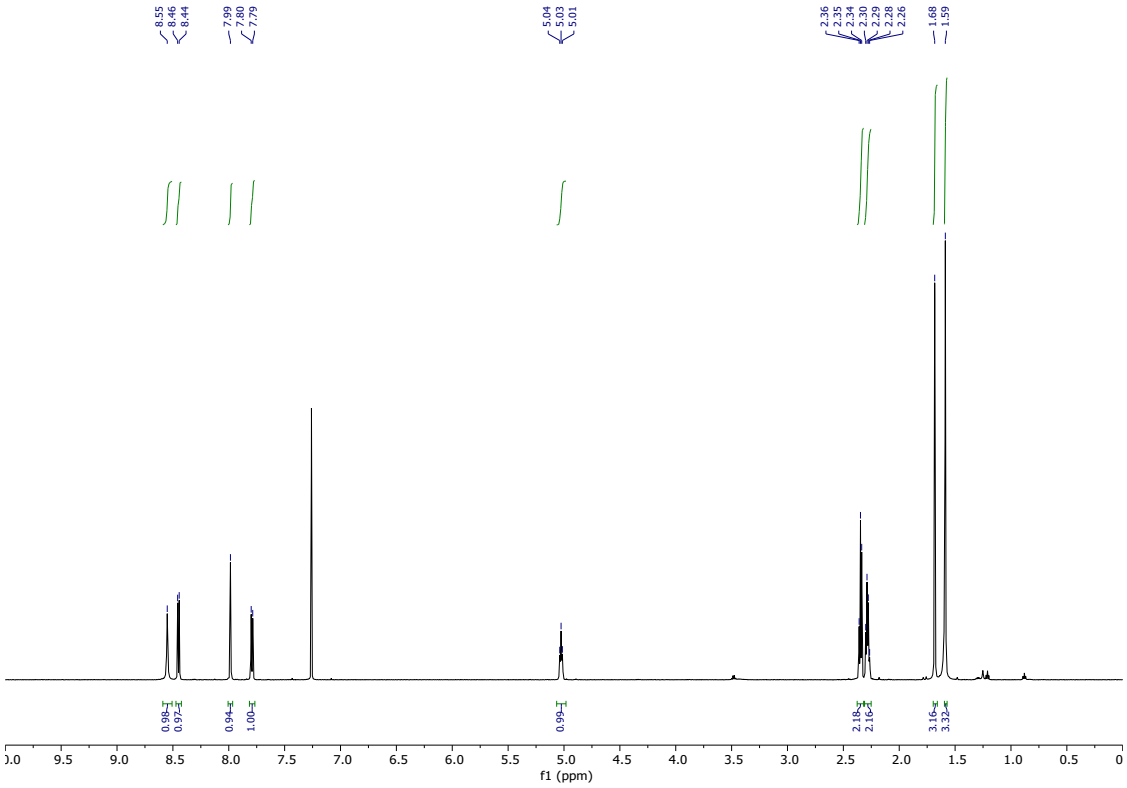
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 141.0, 136.5 (q, *J* = 33.9 Hz), 134.7, 134.2, 132.4 (q, *J* = 3.7 Hz), 125.1 (q, *J* = 3.6 Hz), 122.2 (q, *J* = 274 Hz), 121.4, 120.8, 36.5, 25.8, 23.0, 17.8.

^{19}F NMR (564 MHz, $CDCl_3$) δ -63.37.

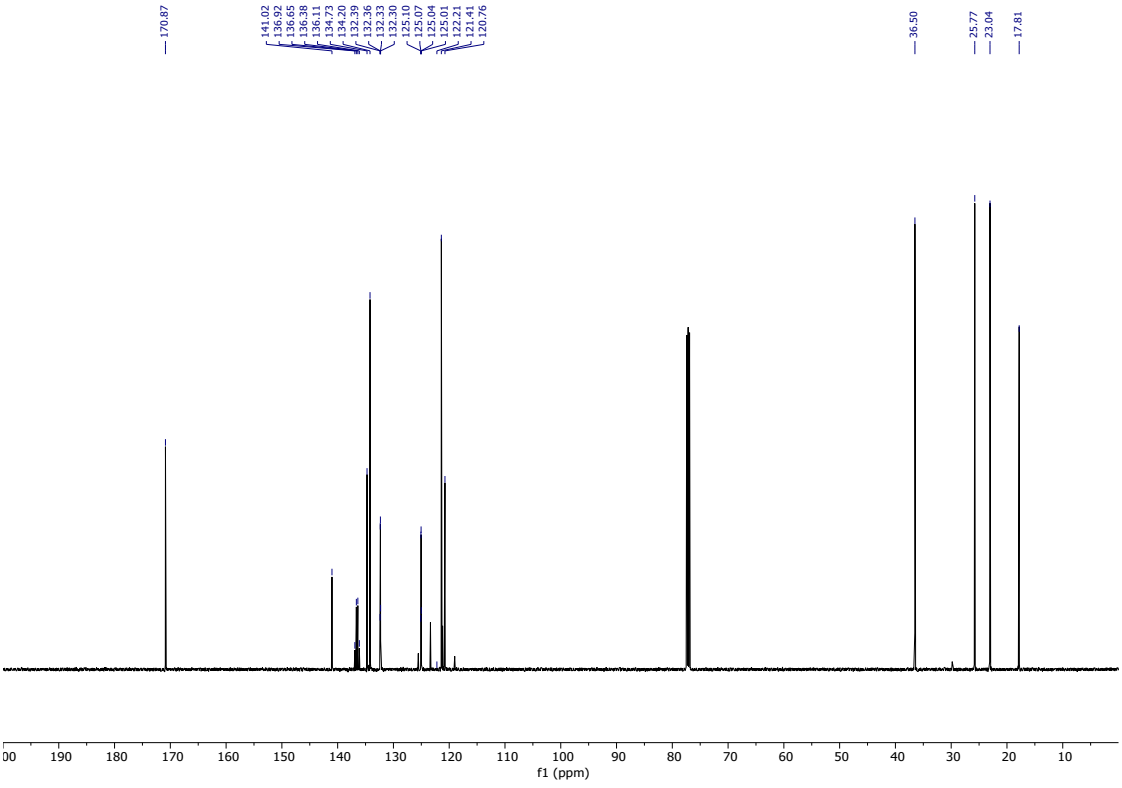
IR (neat) 3241, 3110, 2963, 1741, 1567, 1424, 1409, 1391, 1348, 1322 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{15}BrF_3NO_3SNa^+$ $[M+Na]^+$: 435.9801, found 435.9794.

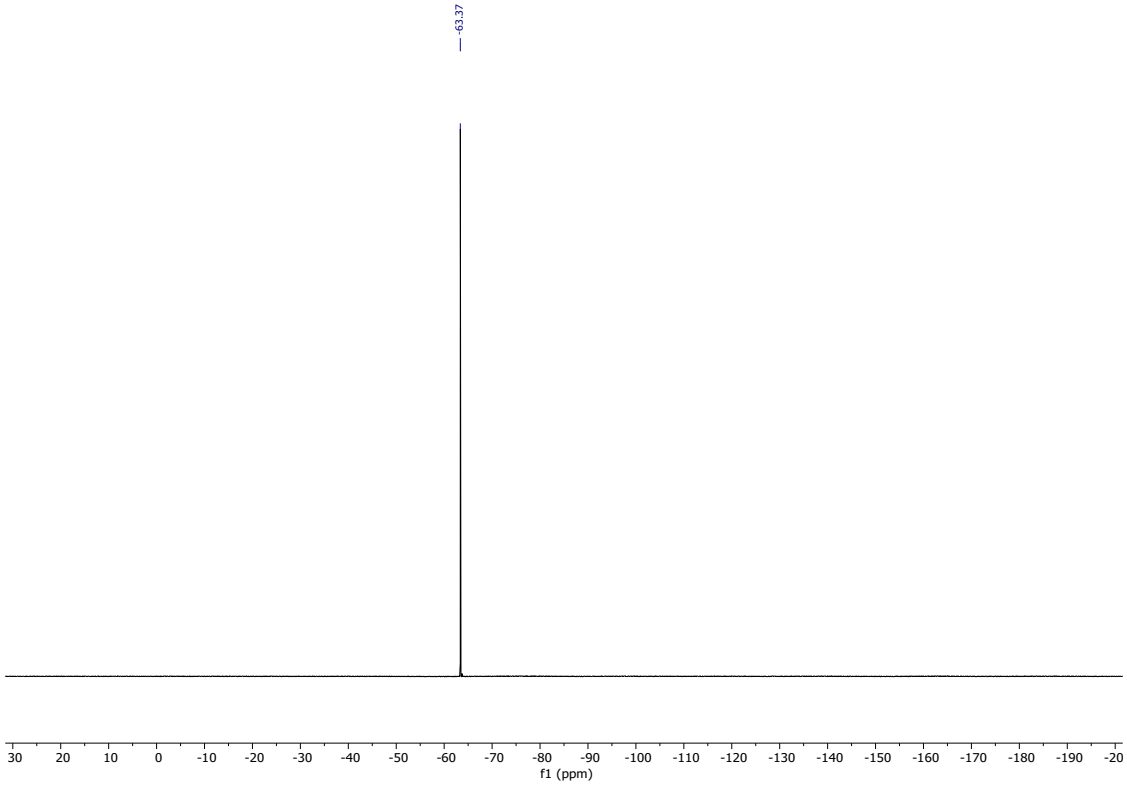
^{1}H NMR – 1i

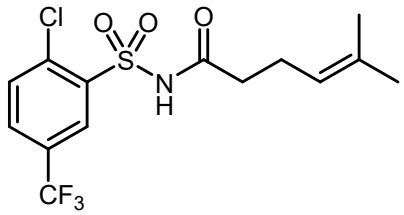


^{13}C NMR – 1i



^{19}F NMR – 1i


-63.37
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



1j. N-((2-chloro-5-(trifluoromethyl)phenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2-chloro-5-(trifluoromethyl)benzenesulfonamide and 5-methylhex-4-enoic acid. 158 mg, 0.43 mmol, 71% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.53 (d, *J* = 2.2 Hz, 1H), 7.82 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 5.03 – 4.98 (m, 1H), 2.37 – 2.31 (m, 2H), 2.27 (q, *J* = 7.2 Hz, 2H), 1.66 (s, 3H), 1.56 (s, 3H).

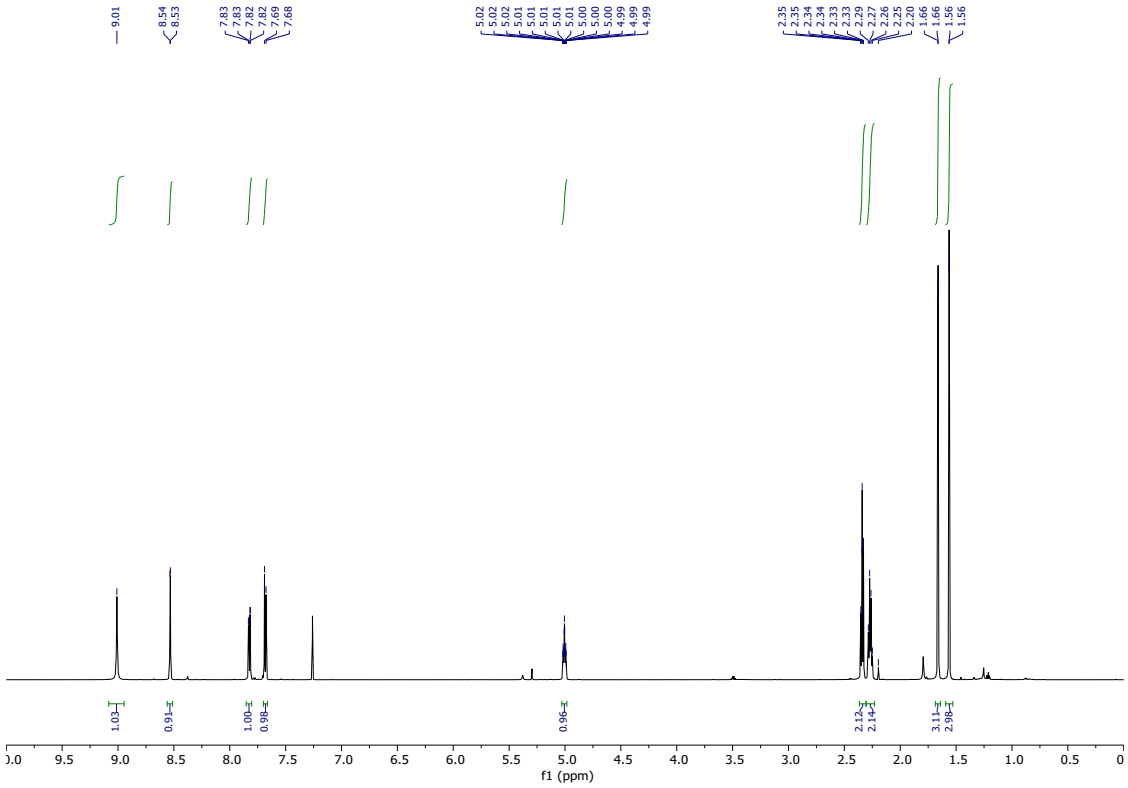
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8, 137.2, 135.9, 134.9, 132.6, 131.6 (q, *J* = 3.0 Hz), 130.4 (q, *J* = 3.9 Hz), 130.3 (q, *J* = 34.3 Hz), 122.9 (q, *J* = 273 Hz), 121.4, 36.6, 25.8, 23.1, 17.8.

^{19}F NMR (564 MHz, $CDCl_3$) δ -62.73.

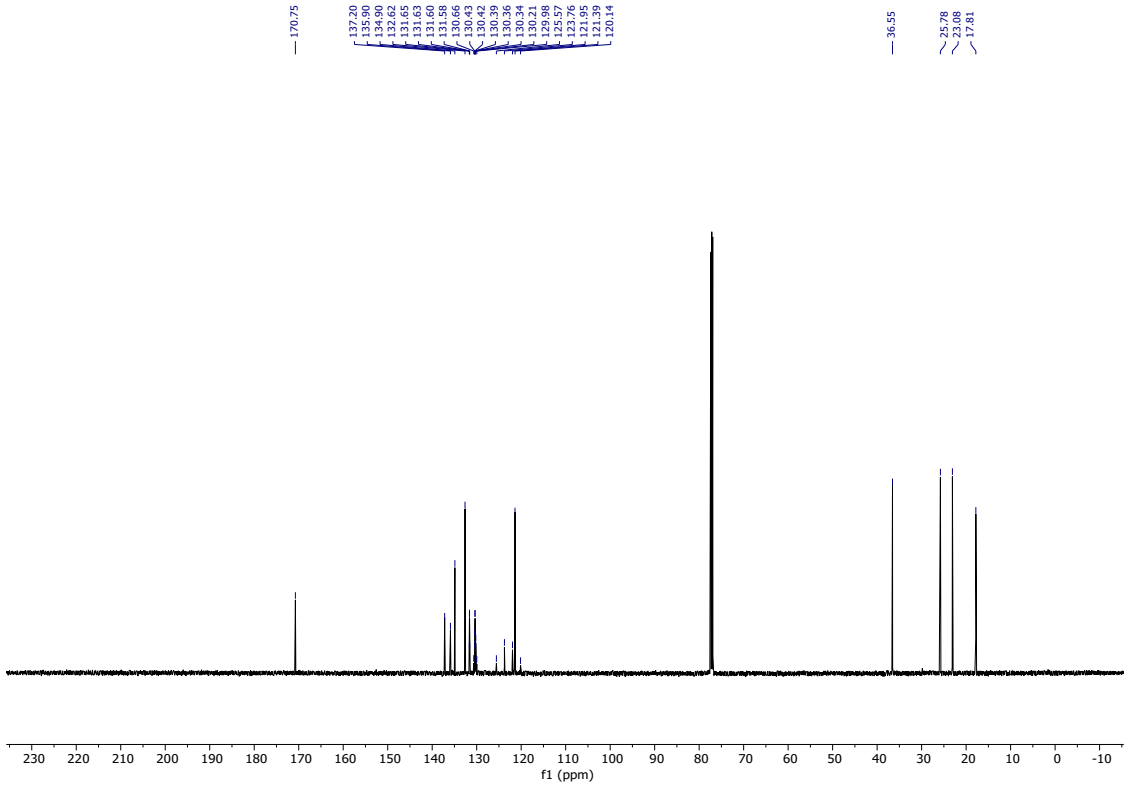
IR (neat) 3218, 2919, 1730, 1607, 1435, 1322, 1254, 1175, 1128 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{15}ClF_3NO_3S^+$ $[M+H]^+$: 392.0306, found 392.0306.

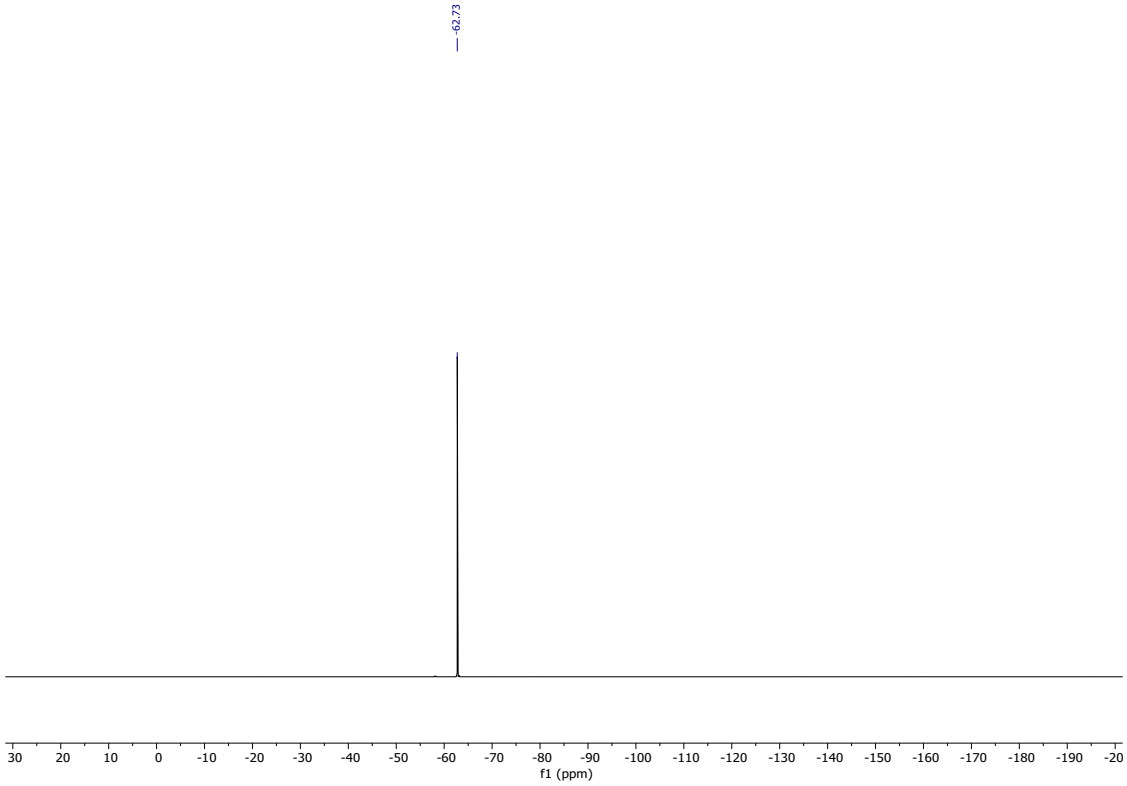
^{1}H NMR – 1j

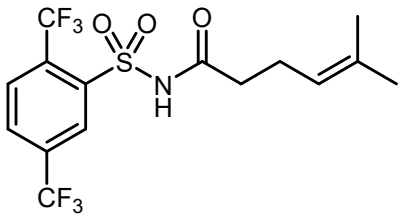


^{13}C NMR – 1j



^{19}F NMR – 1j


-62.73
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



1k. N-((2,5-bis(trifluoromethyl)phenyl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2,5-bis(trifluoromethyl)benzenesulfonamide and 5-methylhex-4-enoic acid. 170 mg, 0.42 mmol, 70%. Colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.22 (s, 1H), 8.06 – 8.00 (m, 2H), 5.07 – 4.96 (m, 1H), 2.37 – 2.22 (m, 4H), 1.68 (s, 3H), 1.59 (s, 3H).

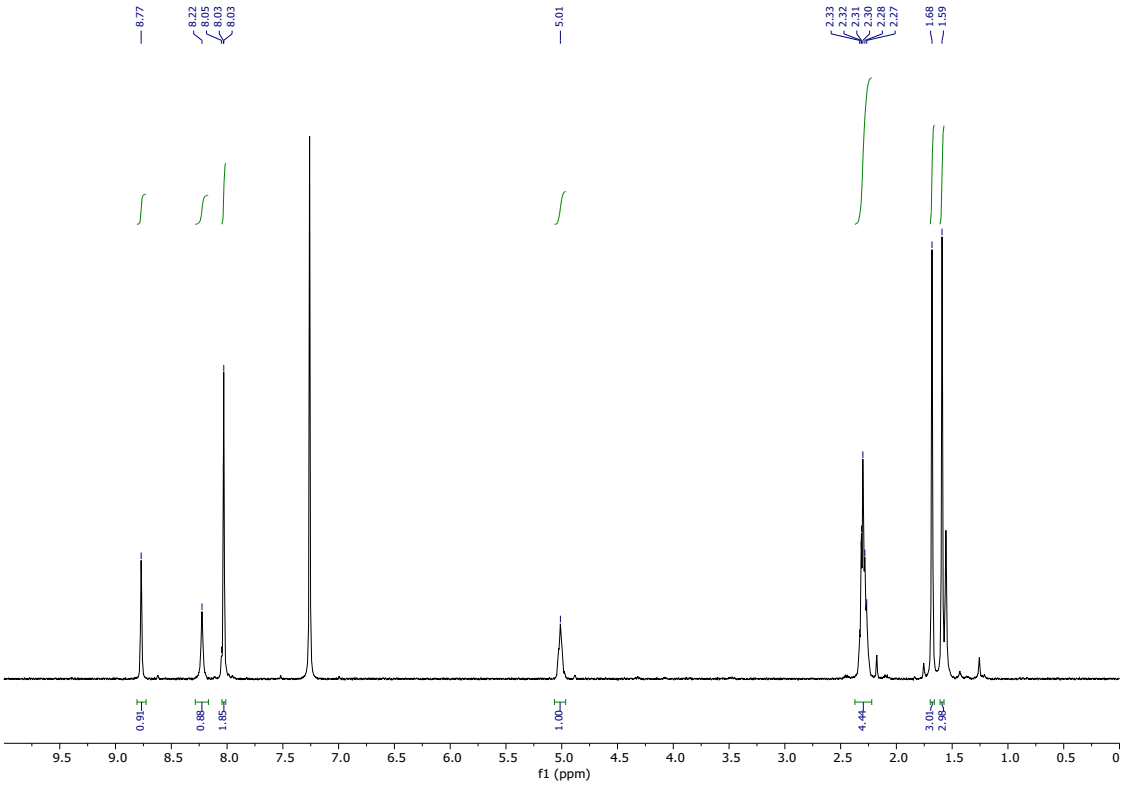
^{13}C NMR ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 138.6, 135.1, 134.8 (q, *J* = 34.5 Hz), 131.7 (q, *J* = 3.7 Hz), 131.2 (q, *J* = 34.2 Hz), 131.0 (q, *J* = 3.5 Hz), 129.3 (q, *J* = 6.2 Hz), 122.5 (q, *J* = 274 Hz), 122.2 (q, *J* = 274 Hz), 121.3, 36.5, 25.7, 23.0, 17.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -58.13, -63.35.

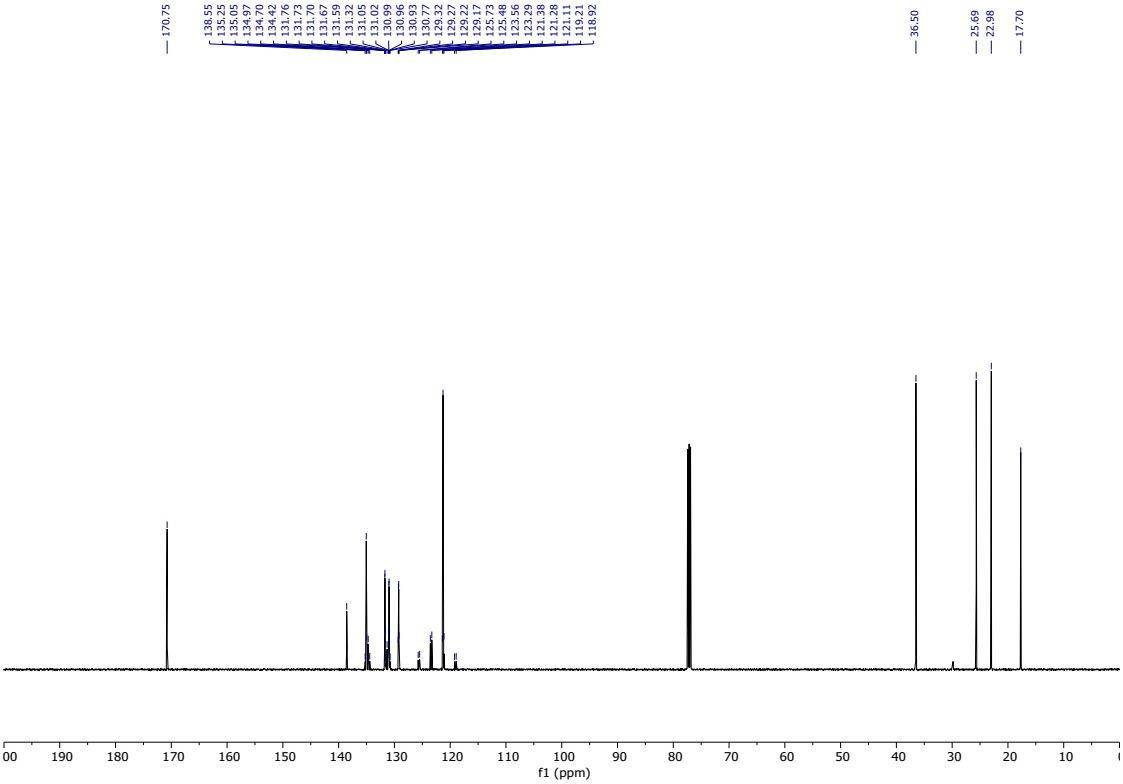
IR (neat) 3102, 2920, 1690, 1451, 1400, 1370, 1331, 1309, 1267, 1161 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{15}H_{15}F_6NO_3SNa^+$ $[M+Na]^+$: 426.0570, found 426.0569.

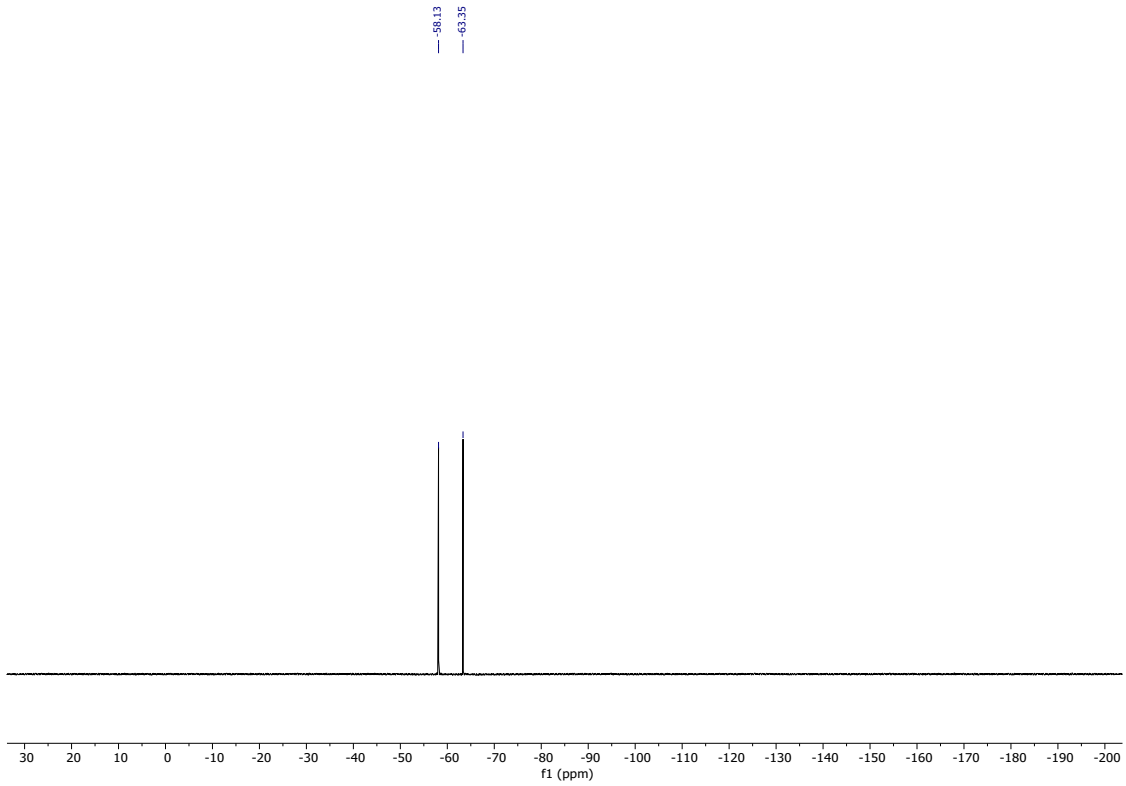
^{1}H NMR – 1k

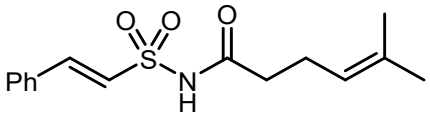


^{13}C NMR – 1k



^{19}F NMR – 1k


-58.13
-63.35
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1*l*. (E)-5-methyl-N-(styrylsulfonyl)hex-4-enamide. Prepared according to **GP1** with 1.5 mmol (E)-2-phenylethenesulfonamide and 5-methylhex-4-enoic acid. 332 mg, 1.1 mmol, 75% yield. Colorless solid.

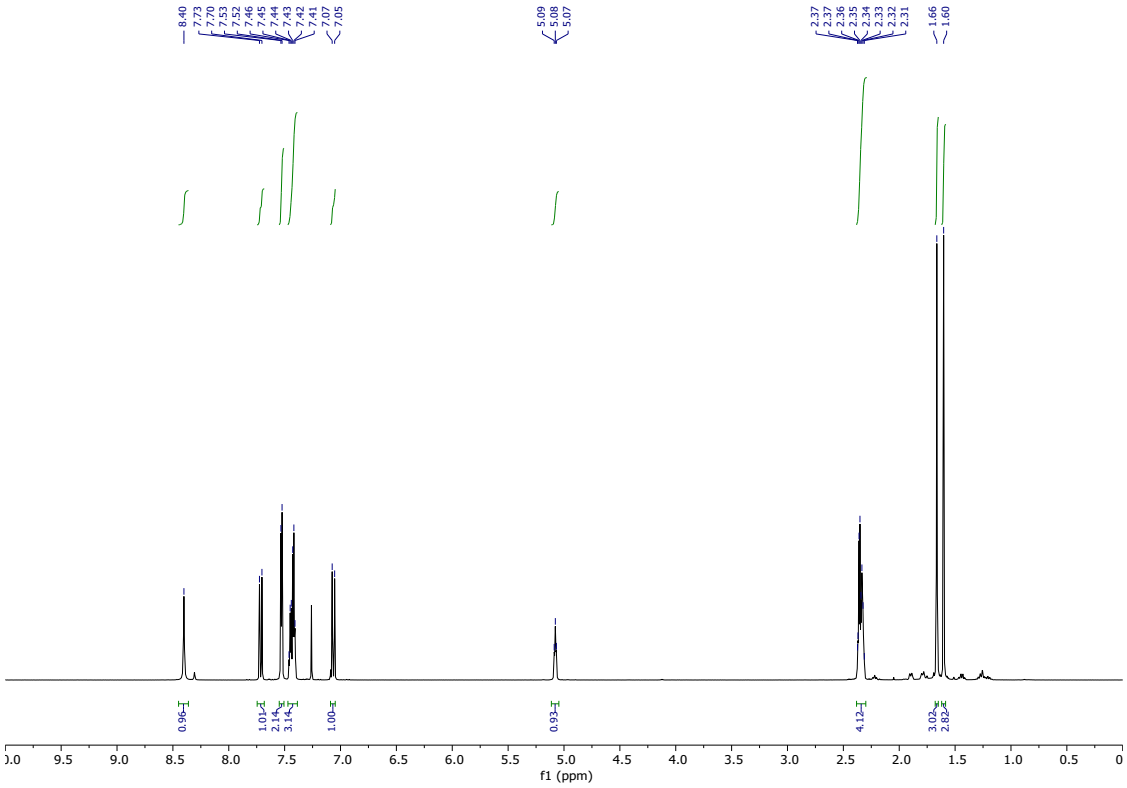
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.71 (d, *J* = 15.5 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.47 – 7.39 (m, 3H), 7.06 (d, *J* = 15.4 Hz, 1H), 5.08 (t, *J* = 6.9 Hz, 1H), 2.38 – 2.30 (m, 4H), 1.66 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 171.1, 145.0, 134.6, 131.9, 131.6, 129.1, 128.8, 123.9, 121.6, 36.5, 25.7, 23.1, 17.7.

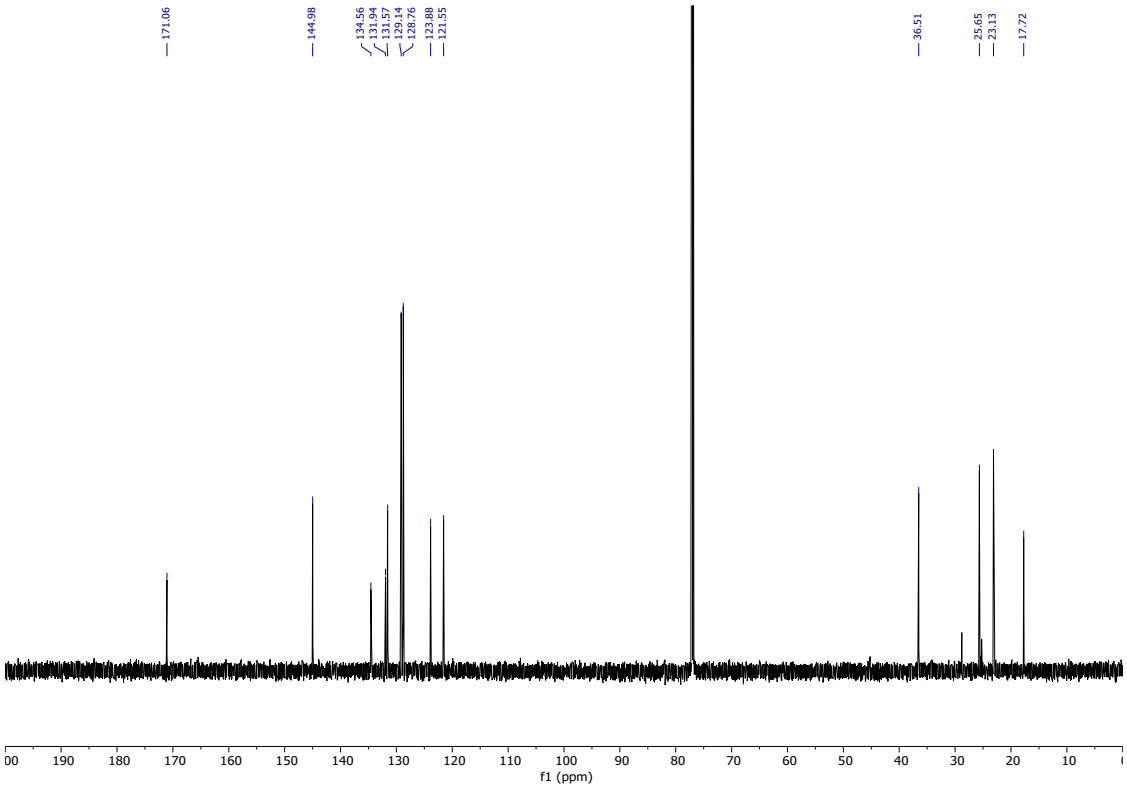
IR (neat) 3237, 3049, 2930, 1726, 1624, 1578, 1440, 1381, 1322, 1201 cm^{-1}

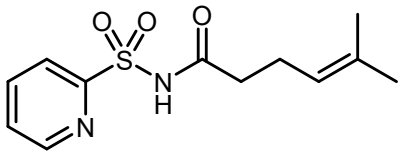
HRMS (ESI+) m/z calculated for $C_{15}H_{19}NO_3SNa^+$ $[M+Na]^+$: 316.0978, found 316.0977.

^{1}H NMR – 1*l*



^{13}C NMR – 1*l*





1m. 5-methyl-N-(pyridin-2-ylsulfonyl)hex-4-enamide. Prepared according to **GP1** with 1.5 mmol pyridine-2-sulfonamide and 5-methylhex-4-enoic acid. 155 mg, 0.58 mmol, 39% yield. Colorless solid.

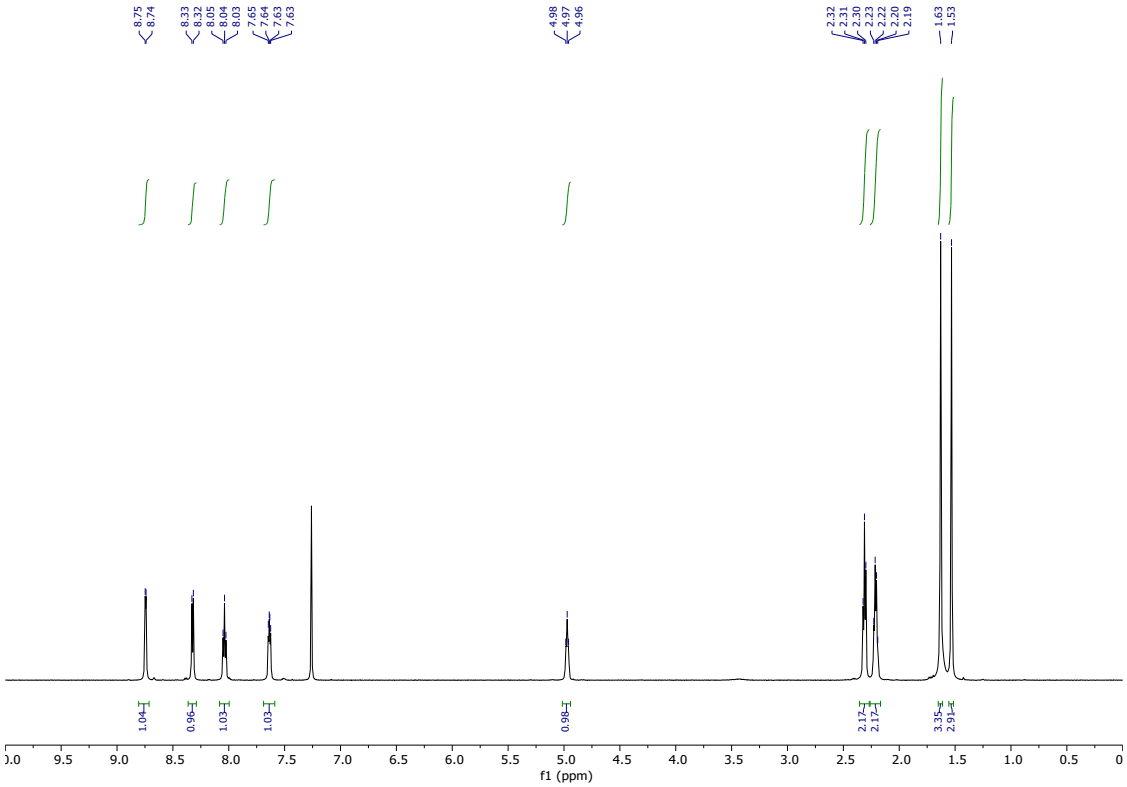
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.74 (d, *J* = 4.7 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 8.04 (t, *J* = 7.8 Hz, 1H), 7.64 (dd, *J* = 7.7, 4.7 Hz, 1H), 4.97 (t, *J* = 7.3 Hz, 1H), 2.31 (t, *J* = 7.4 Hz, 2H), 2.21 (q, *J* = 7.1 Hz, 2H), 1.63 (s, 3H), 1.53 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6, 155.6, 149.3, 138.6, 133.9, 127.9, 125.2, 121.7, 36.1, 25.6, 22.7, 17.6.

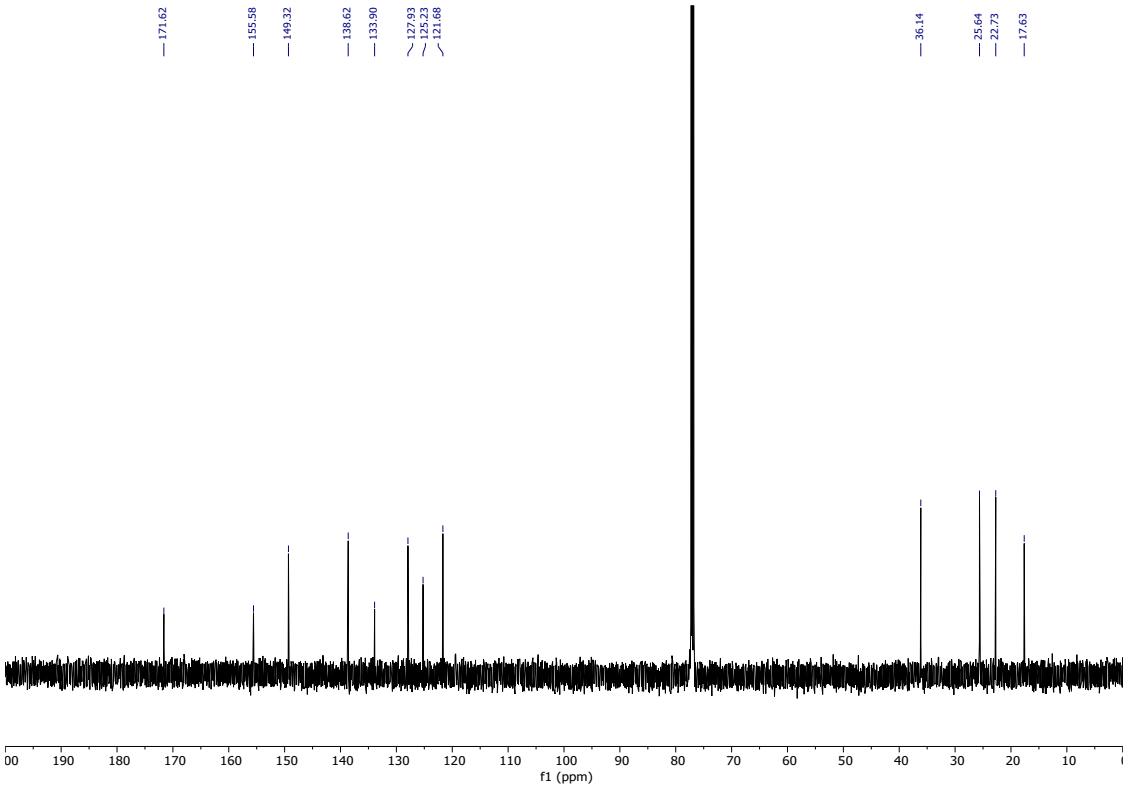
IR (neat) 3007, 2911, 2857, 2770, 1715, 1586, 1463, 1427, 1413, 1341 cm^{-1}

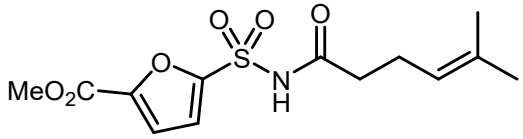
HRMS (ESI+) m/z calculated for $C_{12}H_{16}N_2O_3SNa^+$ $[M+Na]^+$: 291.0774, found 291.0772.

^{1}H NMR – 1m



^{13}C NMR – 1m





1n. Methyl 5-(N-(5-methylhex-4-enoyl)sulfamoyl)furan-2-carboxylate. Prepared according to **GP1** with 1.0 mmol methyl 5-sulfamoylfuran-2-carboxylate and 5-methylhex-4-enoic acid. 106 mg, 0.34 mmol, 34% yield. Colorless solid.

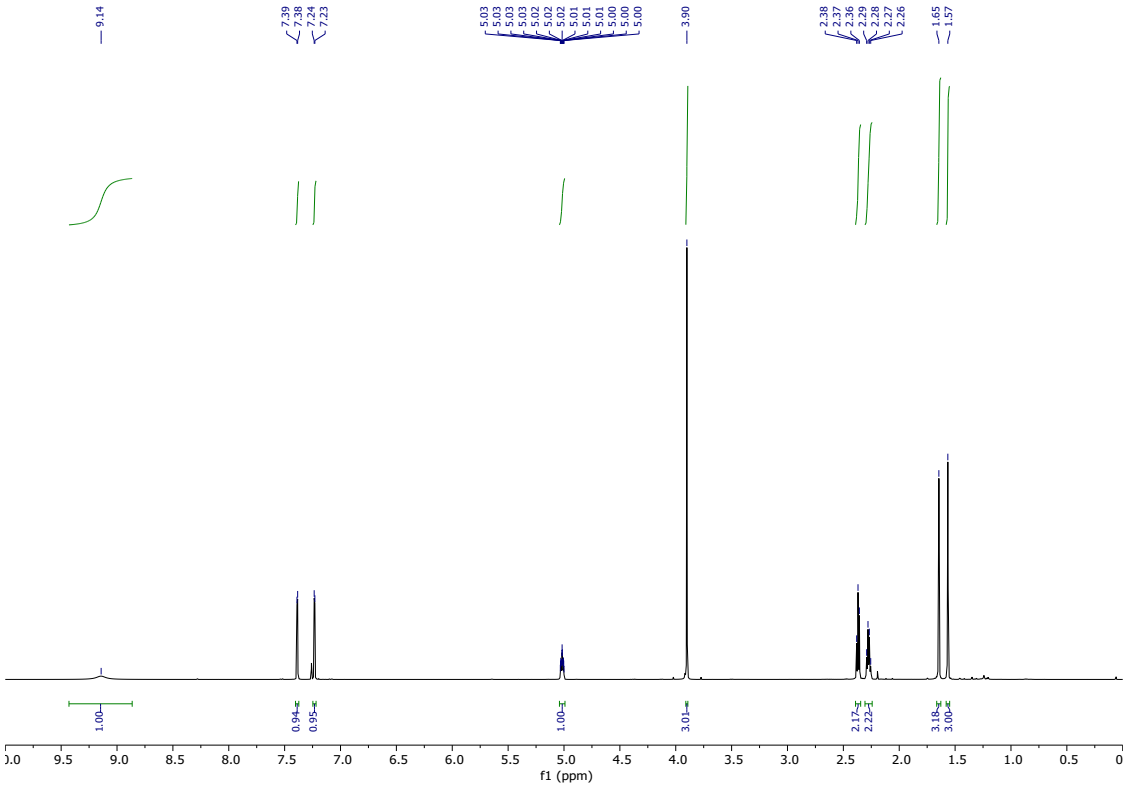
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.39 (d, *J* = 3.7 Hz, 1H), 7.23 (d, *J* = 3.7 Hz, 1H), 5.04 – 4.99 (m, 1H), 3.90 (s, 3H), 2.37 (t, *J* = 7.4 Hz, 2H), 2.27 (q, *J* = 7.3 Hz, 2H), 1.65 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0, 158.2, 149.2, 147.3, 134.5, 121.5, 120.5, 118.2, 52.9, 36.6, 25.7, 23.0, 17.7.

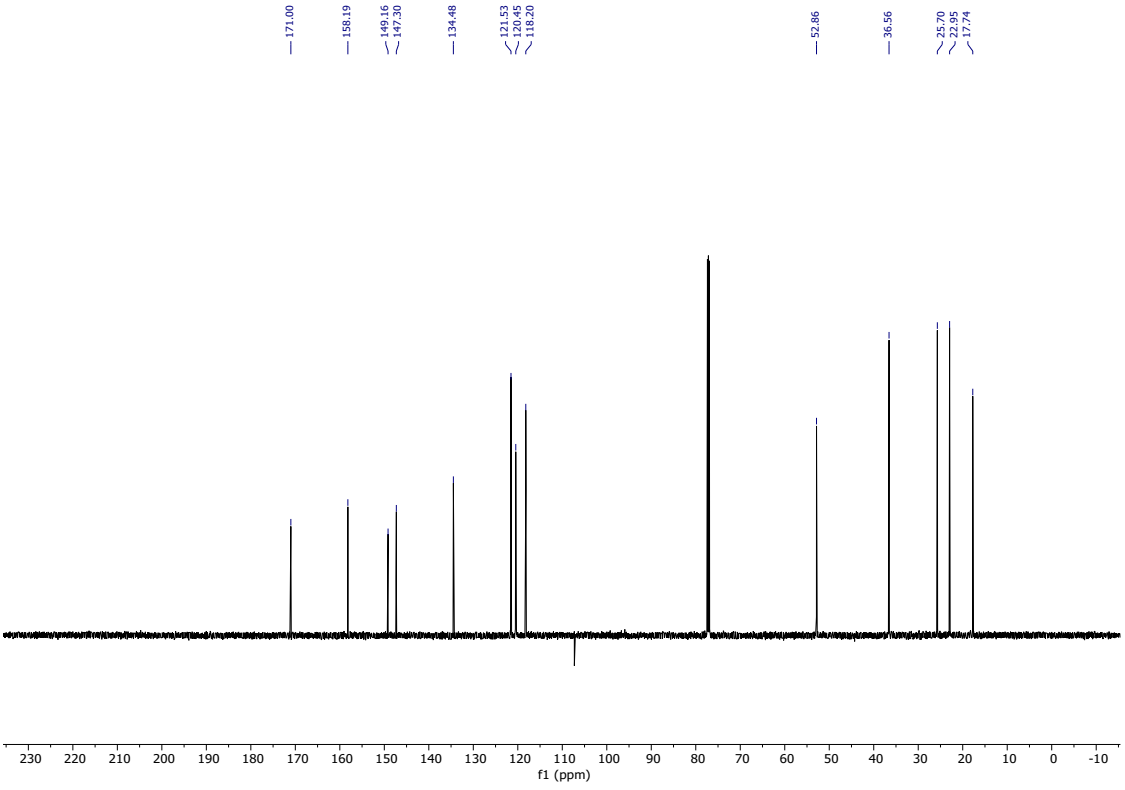
IR (neat) 3272, 3155, 2955, 2923, 2861, 1731, 1573, 1488, 1432, 1412 cm^{-1}

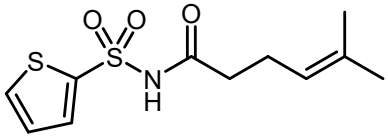
HRMS (ESI+) m/z calculated for $C_{13}H_{17}NO_6SNa^+$ $[M+Na]^+$: 338.0669, found 338.0668.

^{1}H NMR – 1n



^{13}C NMR – 1n





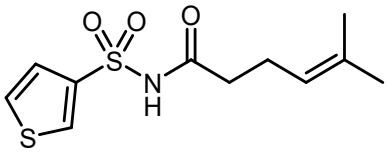
1o. 5-methyl-N-(thiophen-2-ylsulfonyl)hex-4-enamide. Prepared according to **GP1** with 1.0 mmol thiophene-2-sulfonamide and 5-methylhex-4-enoic acid. 230 mg, 0.84 mmol, 84% yield. Colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.89 (d, *J* = 3.5 Hz, 1H), 7.69 (d, *J* = 4.9 Hz, 1H), 7.12 (t, *J* = 4.4 Hz, 1H), 5.01 (t, *J* = 6.9 Hz, 1H), 2.40 – 2.18 (m, 4H), 1.64 (s, 3H), 1.55 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 138.8, 135.3, 134.5, 134.1, 127.6, 121.6, 36.6, 25.8, 23.2, 17.8.

IR (neat) 3243, 3103, 2974, 2921, 2876, 1718, 1681, 1505, 1447, 1401 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{11}H_{15}NO_3S_2Na^+$ $[M+Na]^+$: 296.0386, found 296.0376.

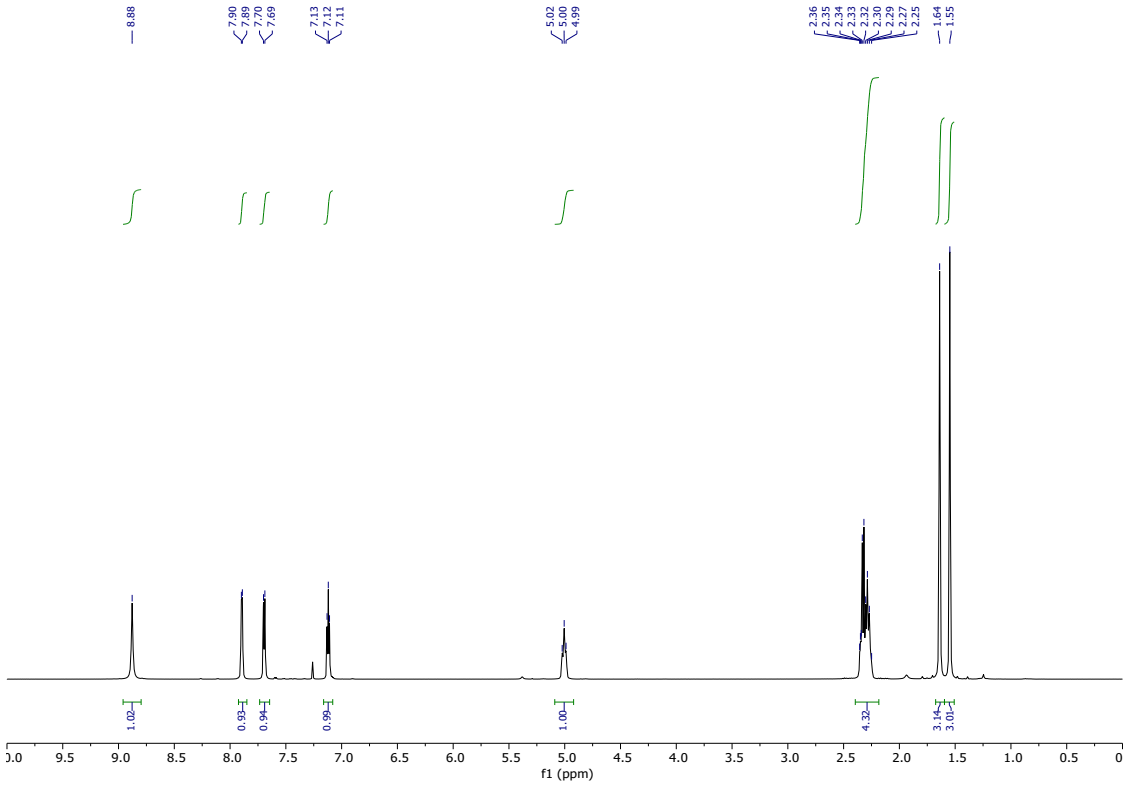


1o': 5-methyl-N-(thiophen-3-ylsulfonyl)hex-4-enamide. Prepared according to **GP1** with 0.8 mmol thiophene-3-sulfonamide and 5-methylhex-4-enoic acid. 190 mg, 0.70 mmol, 87% yield. Colorless solid. Partial characterization provided below:

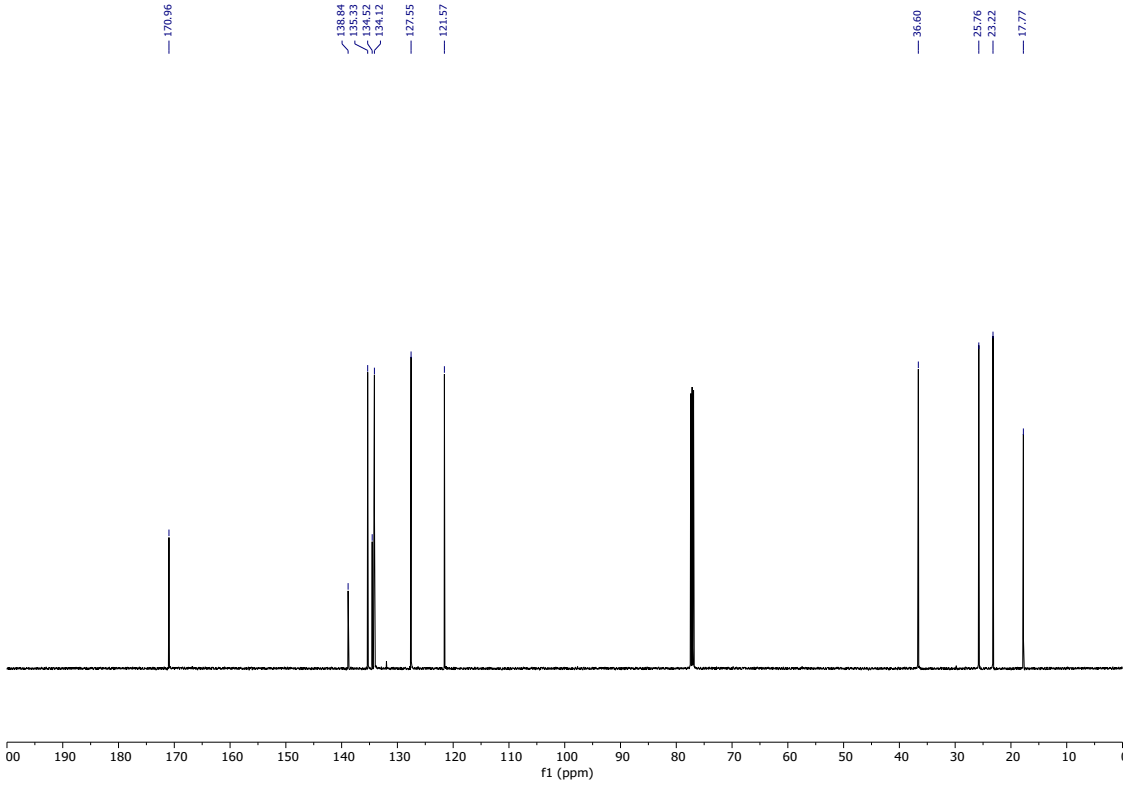
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (br s, 1H), 8.26 (dd, *J* = 3.1, 1.3 Hz, 1H), 7.52 (dd, *J* = 5.2, 1.3 Hz, 1H), 7.42 (dd, *J* = 5.2, 3.1 Hz, 1H), 5.03 – 4.95 (m, 1H), 2.35 – 2.23 (m, 4H), 1.64 (s, 3H), 1.54 (s, 3H).

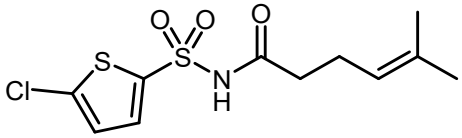
^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0, 138.4, 134.4, 133.7, 127.7, 126.3, 121.6, 36.6, 25.8, 23.2, 17.8.

^{1}H NMR – 1o



^{13}C NMR – 1o





1p. N-((5-chlorothiophen-2-yl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 1.0 mmol 5-chlorothiophene-2-sulfonamide and 5-methylhex-4-enoic acid. 201 mg, 0.65 mmol, 65% yield. Colorless solid.

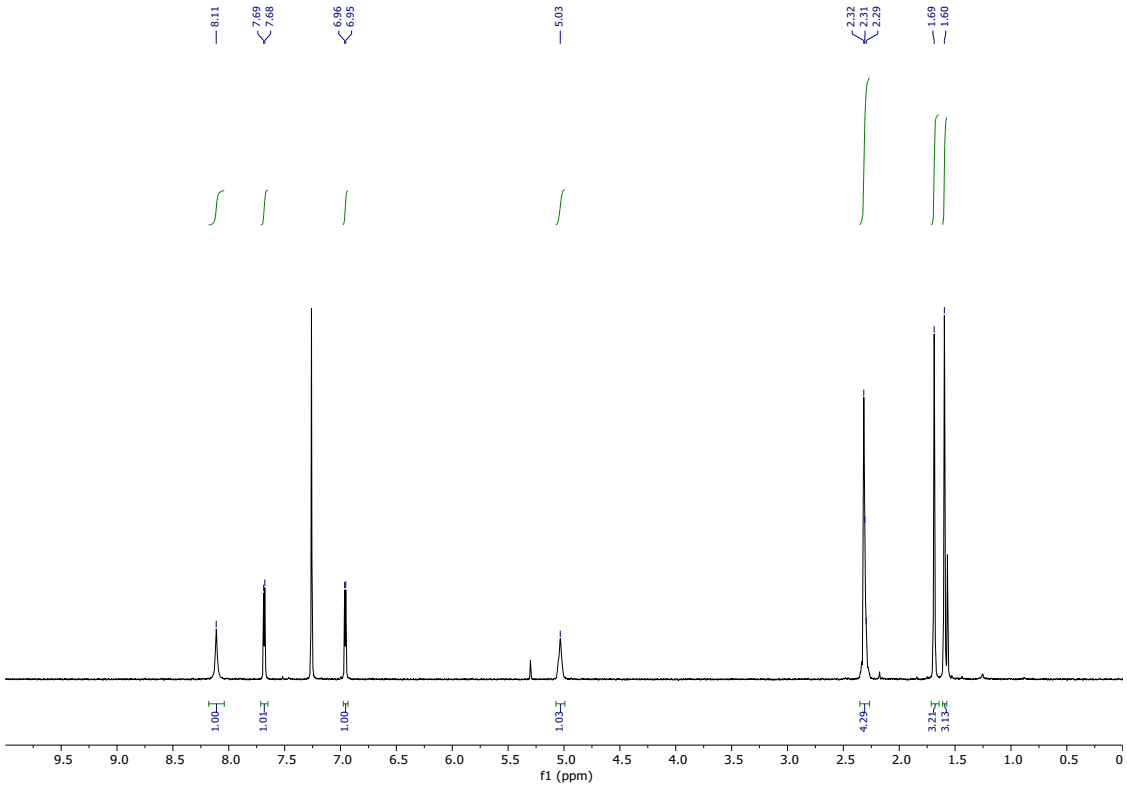
^{1}H NMR (401 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.68 (d, *J* = 4.1 Hz, 1H), 6.96 (d, *J* = 4.1 Hz, 1H), 5.03 (s, 1H), 2.35 – 2.27 (m, 4H), 1.69 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 139.9, 136.4, 135.0, 134.9, 126.9, 121.5, 36.7, 25.8, 23.2, 17.8.

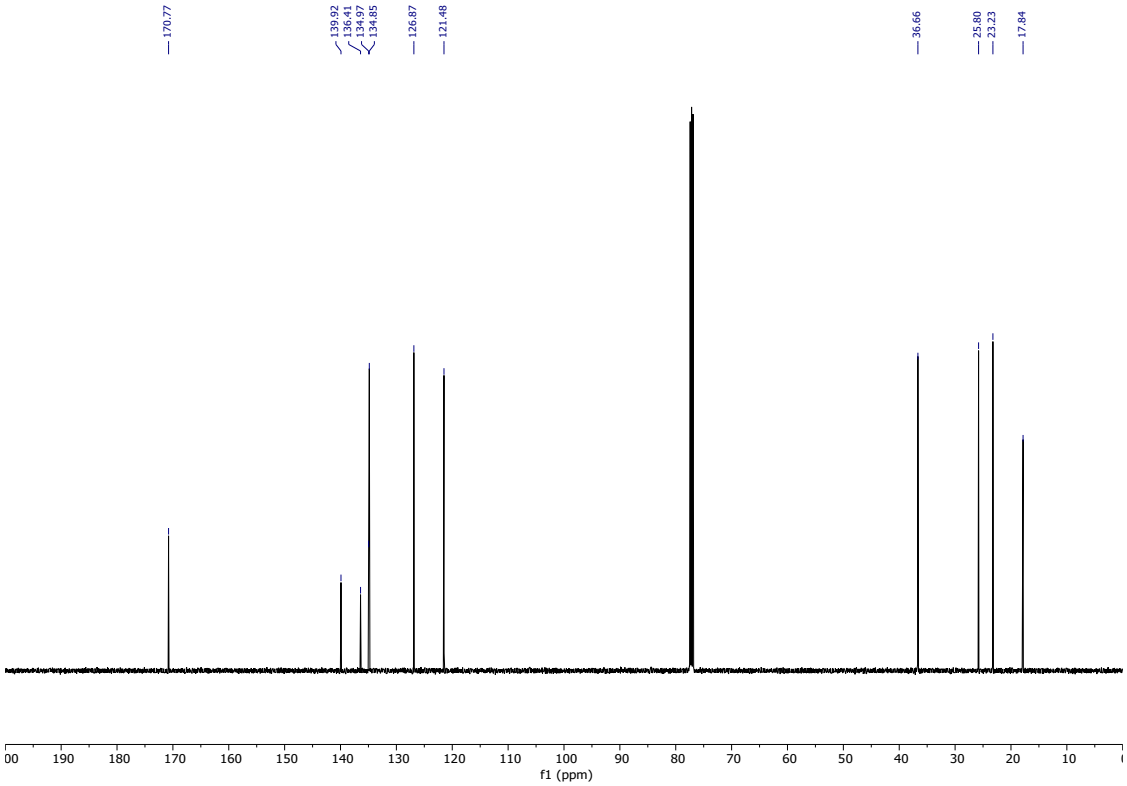
IR (neat) 3193, 3148, 2911, 1703, 1522, 1445, 1406, 1382, 1355, 1317 cm^{-1}

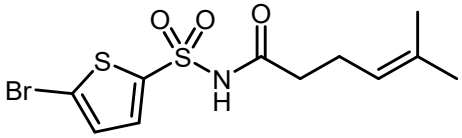
HRMS (ESI+) m/z calculated for $C_{11}H_{14}NO_3S_2ClNa^+$ $[M+Na]^+$: 329.9996, found 329.9997.

^{1}H NMR – 1p



^{13}C NMR – 1p





1q. N-((5-bromothiophen-2-yl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 1.0 mmol 5-bromothiophene-2-sulfonamide and 5-methylhex-4-enoic acid. 217 mg, 0.62 mmol, 62% yield. Colorless solid.

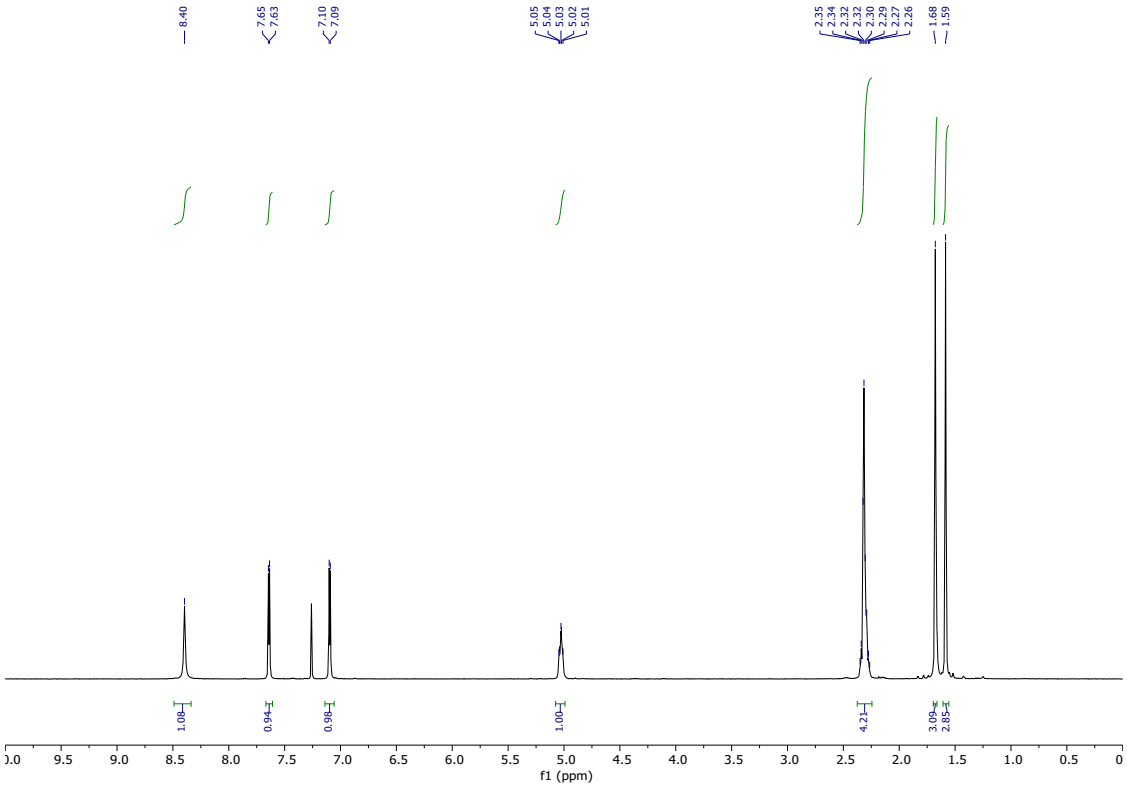
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.64 (d, *J* = 4.1 Hz, 1H), 7.10 (d, *J* = 4.1 Hz, 1H), 5.08 – 4.99 (m, 1H), 2.38 – 2.24 (m, 4H), 1.68 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 139.3, 135.5, 135.1, 130.5, 122.7, 121.5, 36.7, 25.8, 23.3, 17.9.

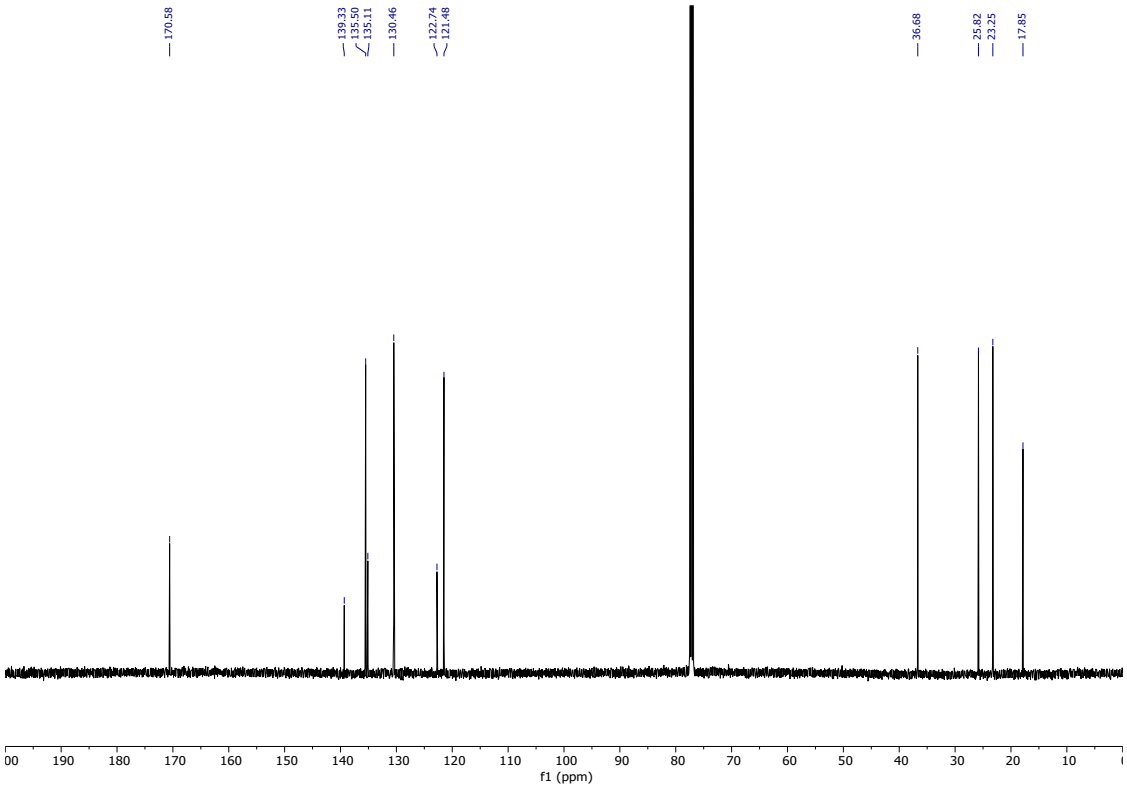
IR (neat) 3190, 3148, 2921, 1704, 1444, 1400, 1383, 1360, 1209, 1175 cm^{-1}

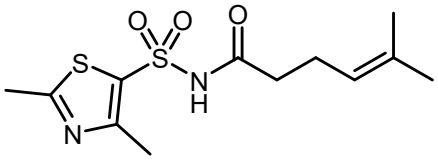
HRMS (ESI+) m/z calculated for $C_{11}H_{14}BrNO_3S_2Na^+$ $[M+Na]^+$: 373.9491, found 373.9488

^{1}H NMR – 1q



^{13}C NMR – 1q





1r. N-((2,4-dimethylthiazol-5-yl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 2,4-dimethylthiazole-5-sulfonamide and 5-methylhex-4-enoic acid. 146 mg, 0.48 mmol, 81% yield. Colorless solid.

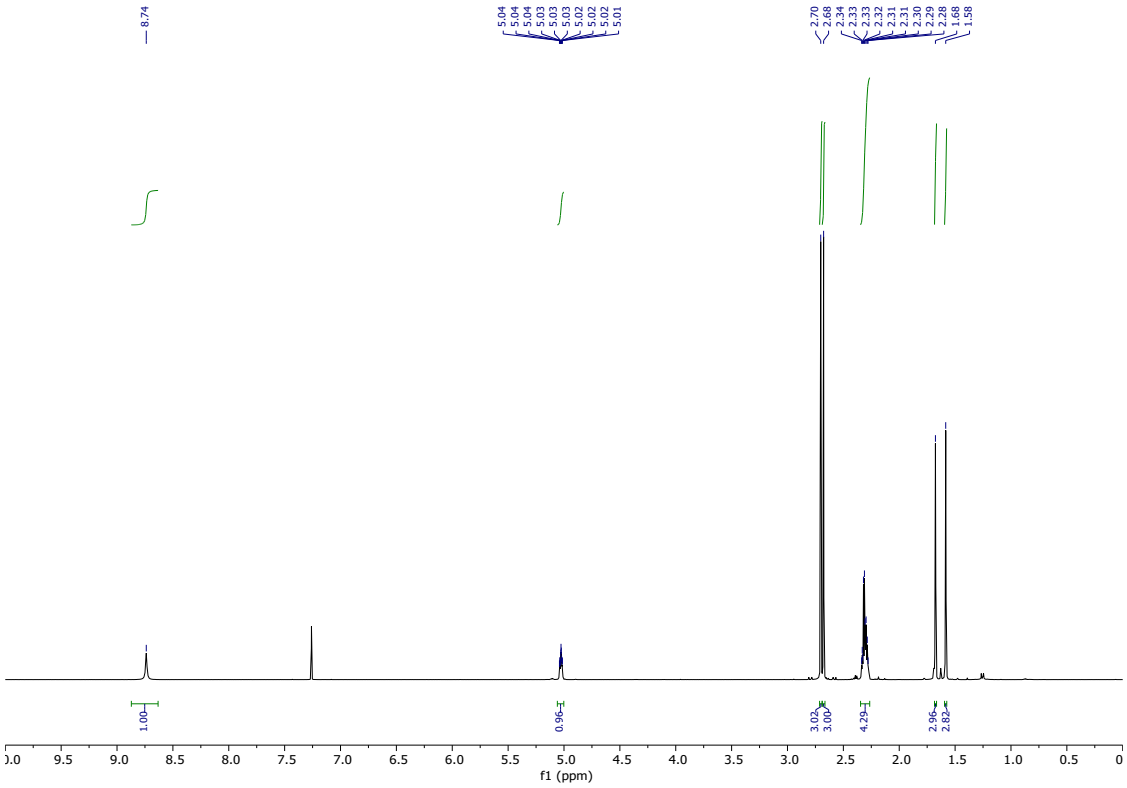
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 5.05 – 5.00 (m, 1H), 2.70 (s, 3H), 2.68 (s, 3H), 2.35 – 2.26 (m, 4H), 1.68 (s, 3H), 1.58 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1, 170.8, 159.3, 135.0, 127.7, 121.5, 36.6, 25.8, 23.2, 19.7, 17.9, 16.9.

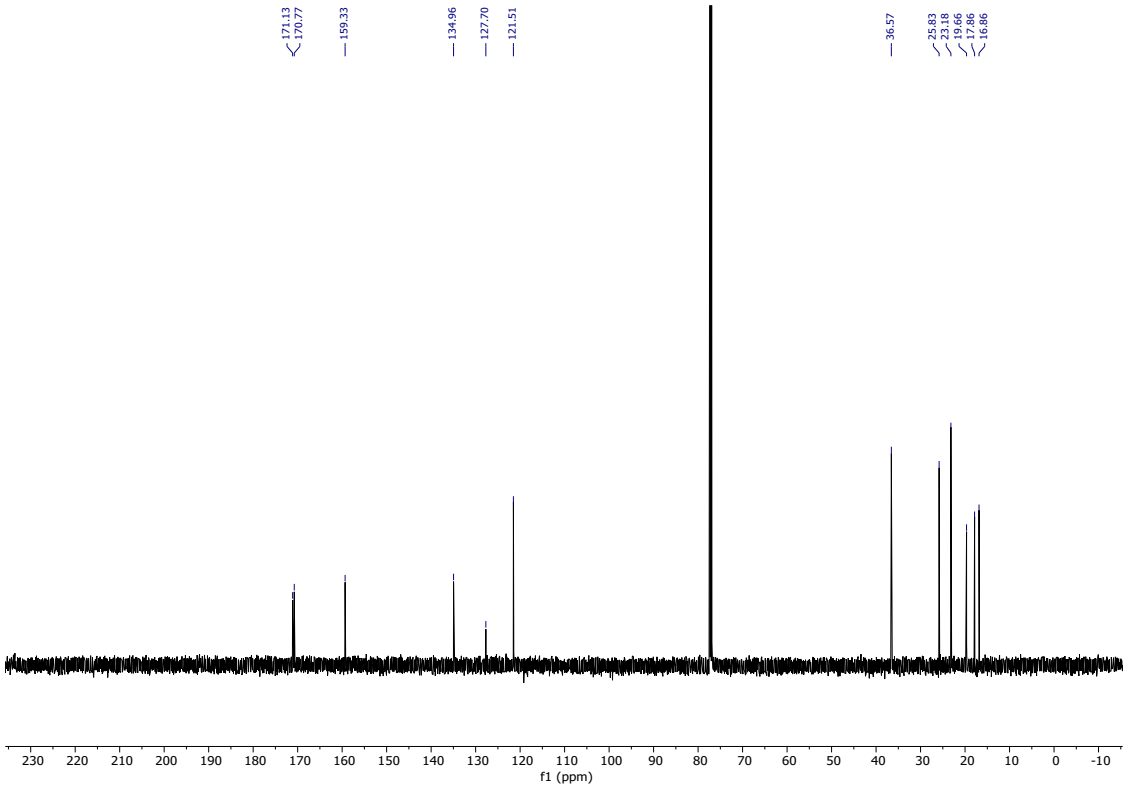
IR (neat) 2969, 2927, 2854, 2752, 1719, 1524, 1434, 1348, 1296, 1247 cm^{-1}

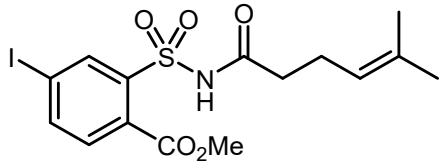
HRMS (ESI+) m/z calculated for $C_{12}H_{18}N_2O_3S_2Na^+$ $[M+Na]^+$: 325.0652, found 325.0650.

^{1}H NMR – 1r



^{13}C NMR – 1r





1s. Methyl 4-iodo-2-(N-(5-methylhex-4-enoyl)sulfamoyl)benzoate. Prepared according to **GP1** with 0.6 mmol methyl 4-iodo-2-sulfamoylbenzoate and 5-methylhex-4-enoic acid. 185 mg, 0.41 mmol, 68% yield. Colorless solid.

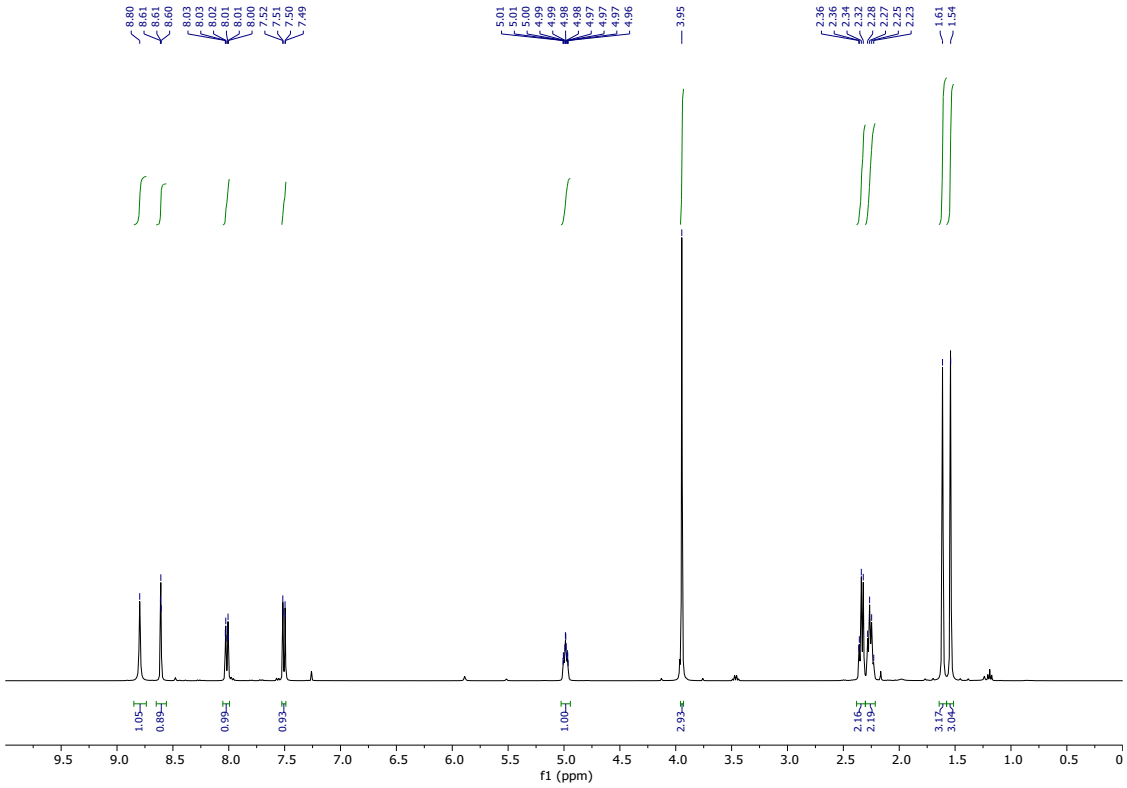
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.61 (t, *J* = 1.4 Hz, 1H), 8.02 (dt, *J* = 8.1, 1.4 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 5.03 – 4.94 (m, 1H), 3.95 (s, 3H), 2.38 – 2.30 (m, 2H), 2.30 – 2.21 (m, 2H), 1.61 (s, 3H), 1.54 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 166.8, 142.7, 140.1, 138.9, 134.2, 131.7, 130.2, 121.5, 97.9, 53.6, 37.0, 25.7, 23.0, 17.8.

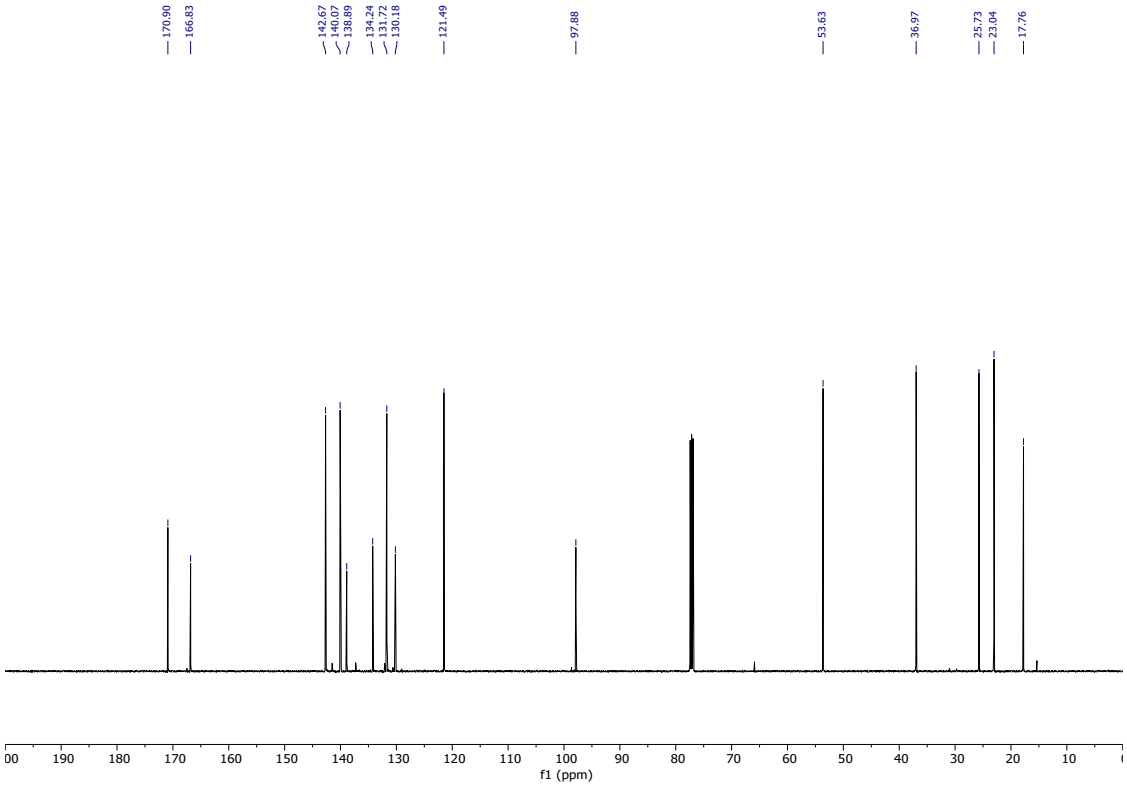
IR (neat) 3286, 2935, 2864, 1737, 1716, 1579, 1423, 1373, 1350, 1283 cm^{-1}

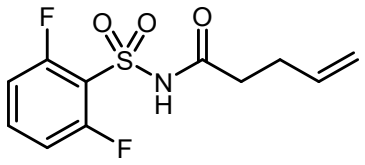
HRMS (ESI+) m/z calculated for $C_{15}H_{18}INO_5SNa^+$ $[M+Na]^+$: 473.9843, found 473.9839.

^{1}H NMR – 1s



^{13}C NMR – 1s





1t. N-((2,6-difluorophenyl)sulfonyl)pent-4-enamide. Prepared according to **GP1** with 1.0 mmol 2,6-difluorobenzenesulfonamide and commercially available 4-pentenoic acid. 211 mg, 0.77 mmol, 77% yield. Colorless solid.

^{1}H NMR (401 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.60 (tt, *J* = 8.5, 5.9 Hz, 1H), 7.07 (t, *J* = 8.7 Hz, 2H), 5.75 (ddt, *J* = 16.7, 10.2, 6.4 Hz, 1H), 5.07 – 4.96 (m, 2H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.35 (q, *J* = 6.8 Hz, 2H).

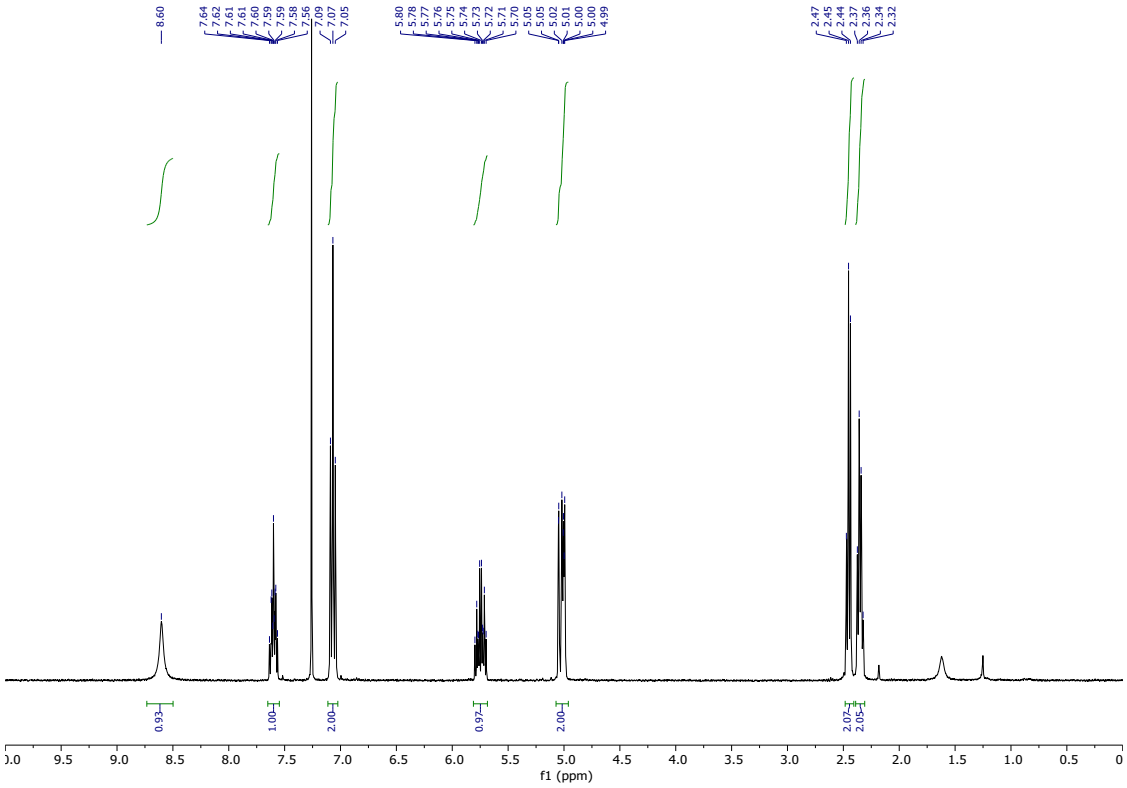
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 160.1 (dd, *J* = 262, 3.0 Hz), 136.2 (t, *J* = 11.2 Hz), 135.7, 116.8 (t, *J* = 14.3 Hz), 116.5, 113.4 (dd, *J* = 22.6, 3.9 Hz), 35.5, 28.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -106.22 (dd, *J* = 8.8, 5.9 Hz).

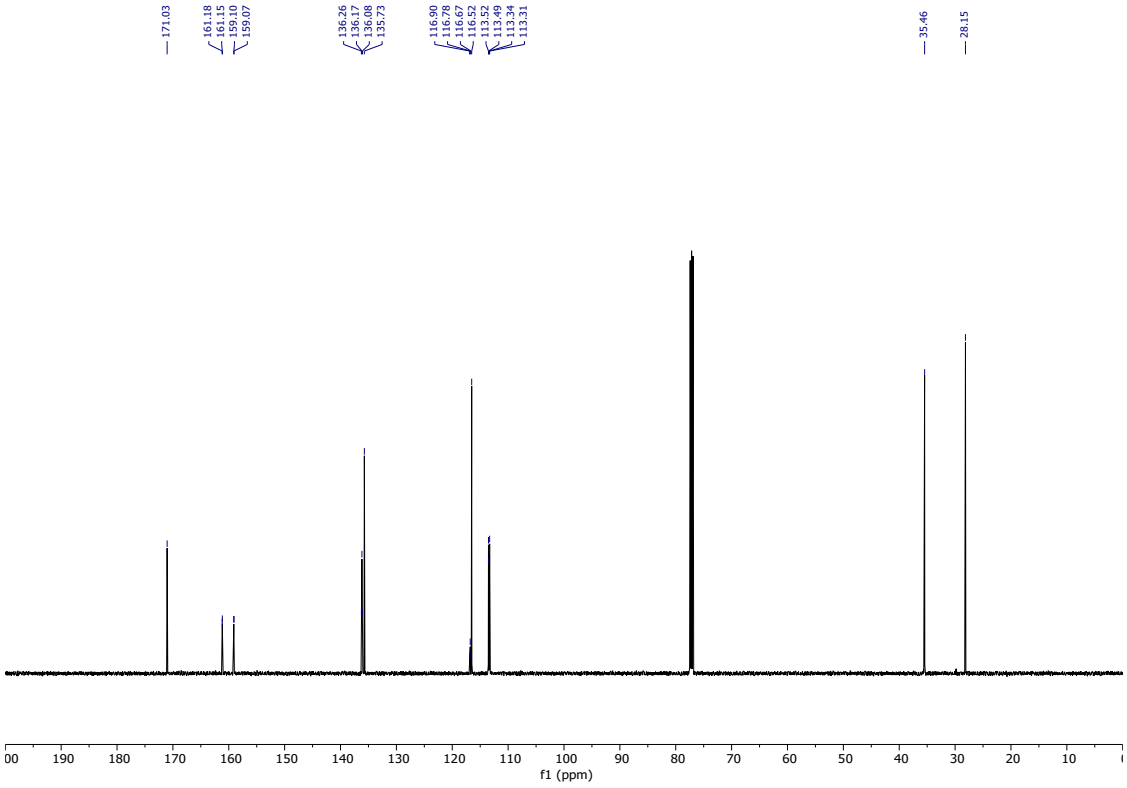
IR (neat) 3075, 2872, 1681, 1615, 1591, 1566, 1471, 1444, 1365, 1241 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{11}H_{11}F_2NO_3SNa^+$ $[M+Na]^+$: 298.0320, found 298.0318.

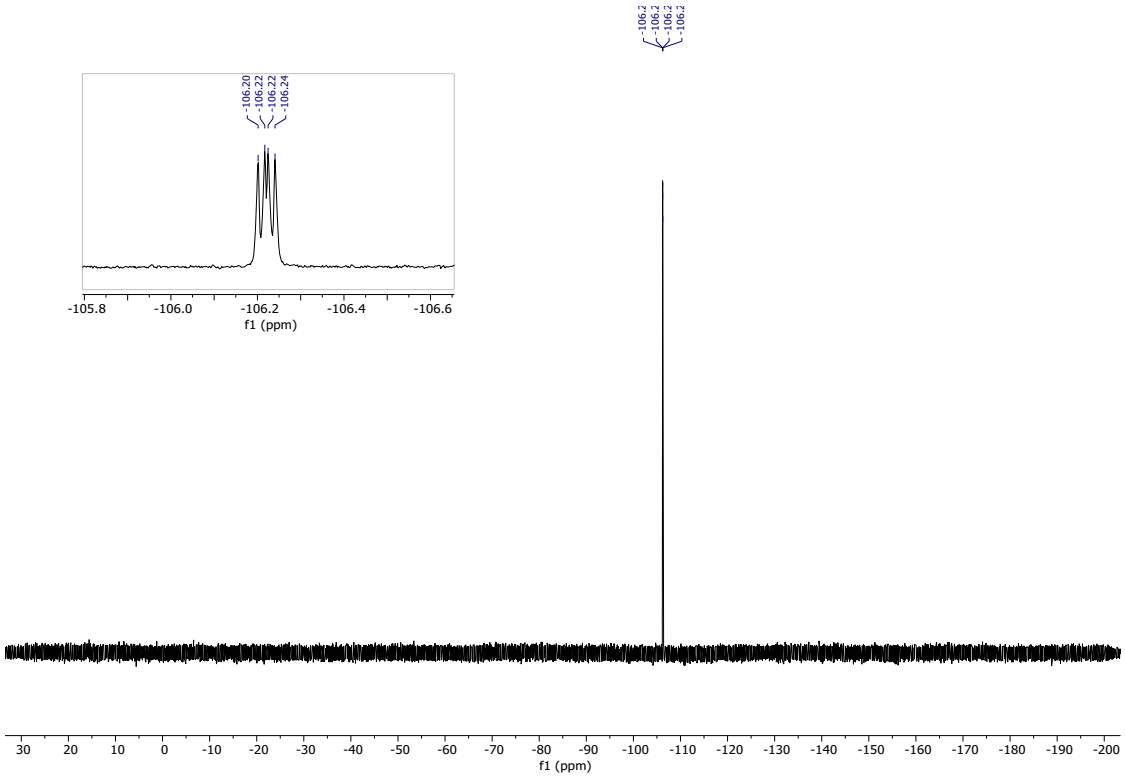
^{1}H NMR – 1t

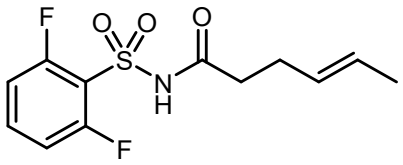


^{13}C NMR – 1t



^{19}F NMR – 1t


-106.20
-106.22
-106.22
-106.24
-105.8
-106.0
-106.2
-106.4
-106.6
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



1u. (E)-N-((2,6-difluorophenyl)sulfonyl)hex-4-enamide. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and (E)-hex-4-enoic acid. 100 mg, 0.35 mmol, 43% yield. Colorless solid.

^{1}H NMR (401 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.60 (tt, *J* = 8.5, 5.9 Hz, 1H), 7.07 (t, *J* = 8.6 Hz, 2H), 5.54 – 5.42 (m, 1H), 5.40 – 5.27 (m, 1H), 2.44 – 2.37 (m, 2H), 2.32 – 2.22 (m, 2H), 1.62 (dd, *J* = 6.3, 1.4 Hz, 3H).

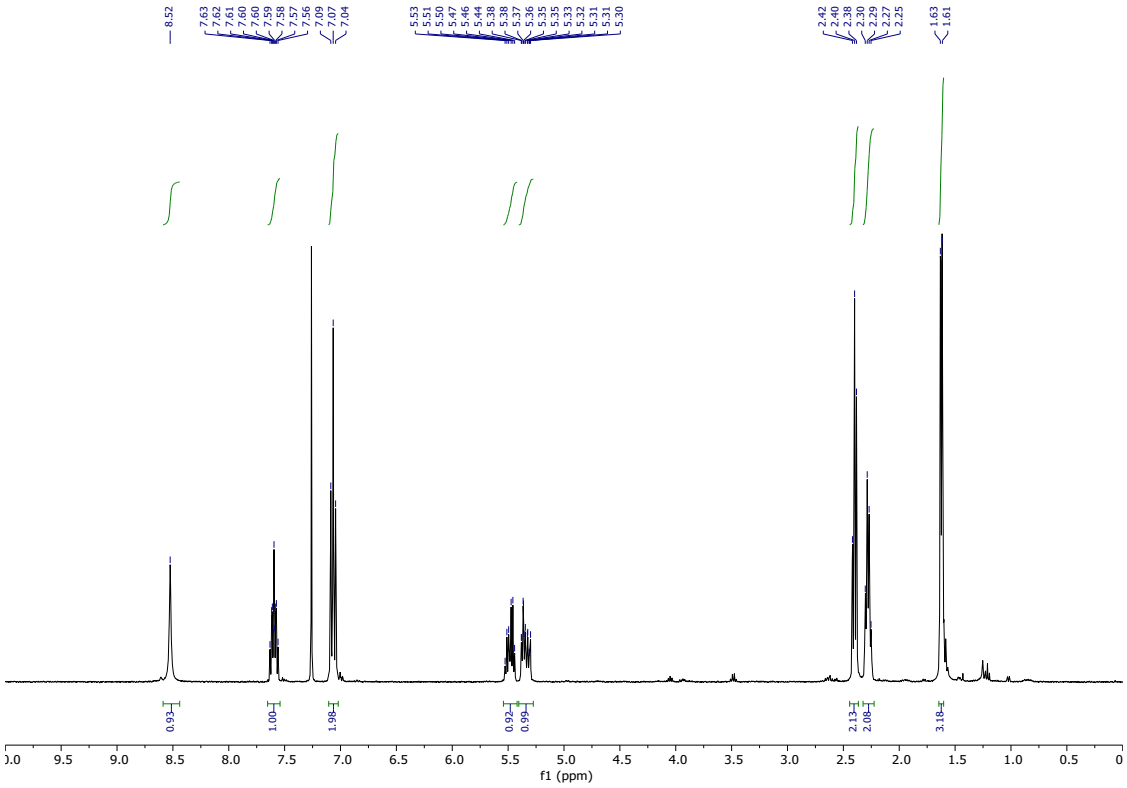
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 160.1 (dd, *J* = 262, 3.0 Hz), 136.1 (t, *J* = 11.2 Hz), 128.3, 127.6, 116.9 (t, *J* = 14.4 Hz), 113.4 (dd, *J* = 22.5, 4.0 Hz), 36.2, 27.2, 18.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -106.28 (dd, *J* = 9.1, 6.0 Hz).

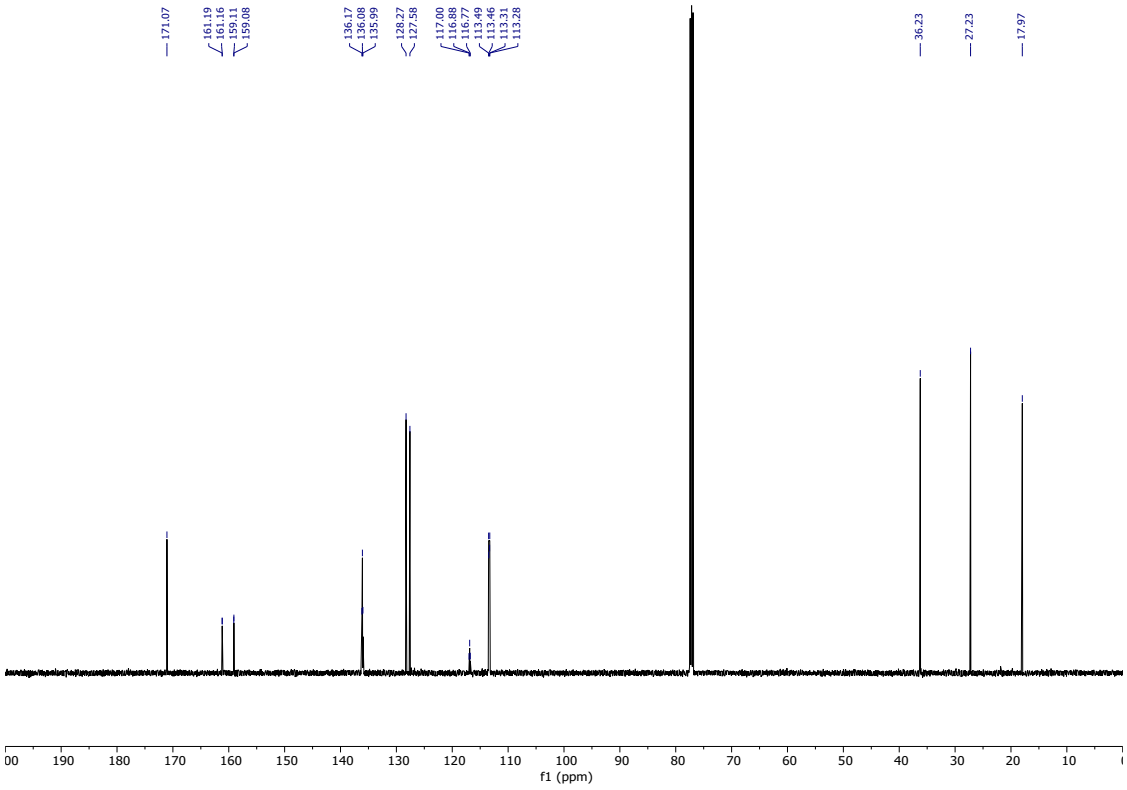
IR (neat) 3101, 2921, 2880, 1684, 1613, 1590, 1565, 1474, 1446, 1371 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{12}H_{13}F_2NO_3SNa^+$ $[M+Na]^+$: 312.0477, found 312.0480.

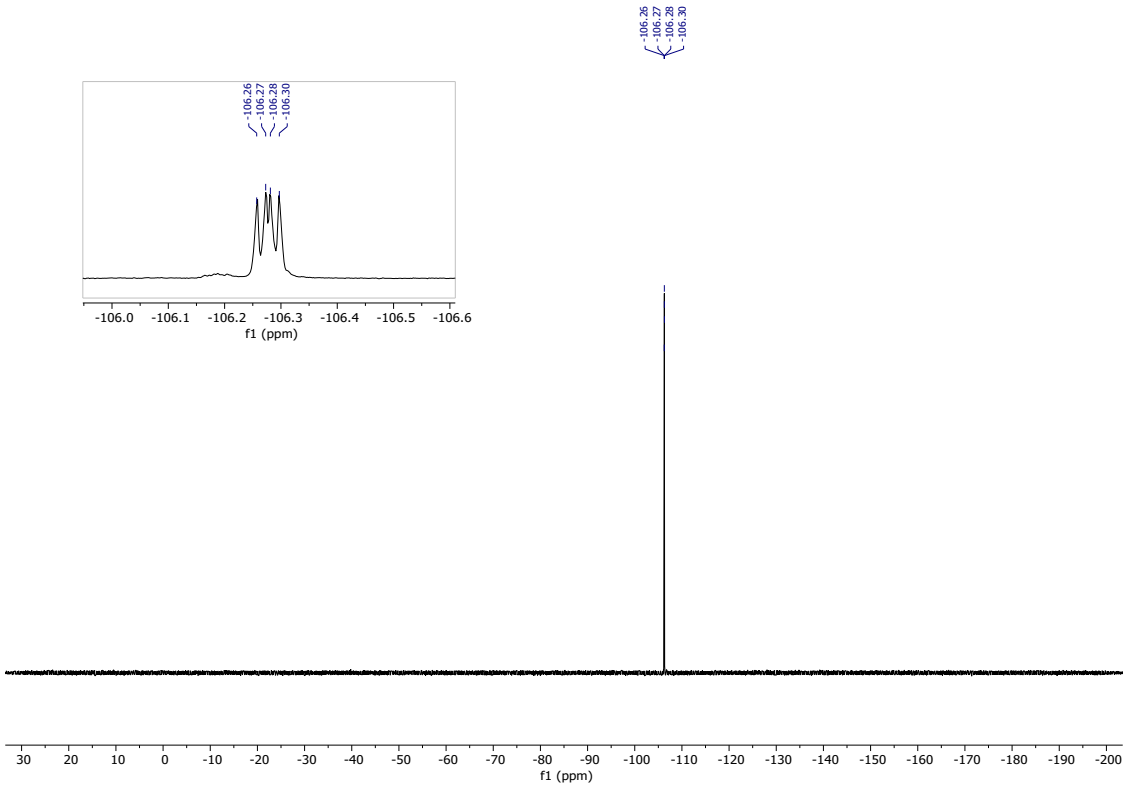
^{1}H NMR – 1u

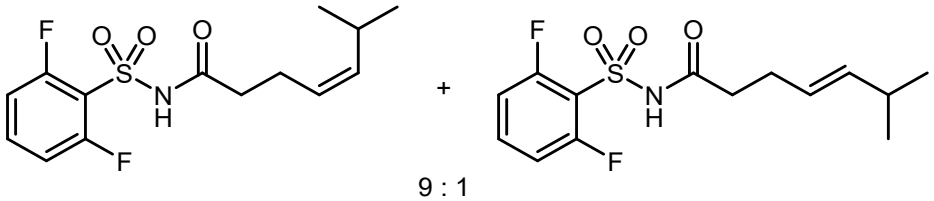


^{13}C NMR – 1u



^{19}F NMR – 1u


-106.26
-106.27
-106.28
-106.30
-106.0
-106.1
-106.2
-106.3
-106.4
-106.5
-106.6
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



9 : 1

1v. N-((2,6-difluorophenyl)sulfonyl)-6-methylhept-4-enamide. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and 6-methylhept-4-enoic acid. 141 mg, 0.44 mmol, 56% yield. Colorless solid, ~ 9:1 Z/E ratio

Z isomer **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.59 (tt, *J* = 8.4, 4.2 Hz, 1H), 7.06 (t, *J* = 9.0 Hz, 2H), 5.25 – 5.17 (m, 1H), 5.15 – 5.06 (m, 1H), 2.58 – 2.47 (m, 1H), 2.44 – 2.29 (m, 4H), 0.86 (d, *J* = 6.7 Hz, 6H).

Z isomer **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.5, 160.1 (dd, *J* = 262, 2.8 Hz), 139.9, 136.2 (t, *J* = 11.2 Hz), 124.0, 116.8 (t, *J* = 14.4 Hz), 113.4 (dd, *J* = 22.6, 3.8 Hz), 36.4, 26.6, 23.1, 22.2.

Z isomer **^{19}F NMR** (564 MHz, $CDCl_3$) δ -106.24 (dd, *J* = 9.1, 5.9 Hz).

E isomer partial **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.42 (dd, *J* = 15.4, 6.7 Hz, 1H), 2.26 (q, *J* = 7.1 Hz, 2H), 2.23 – 2.14 (m, 1H), 0.91 (d, *J* = 6.8 Hz).

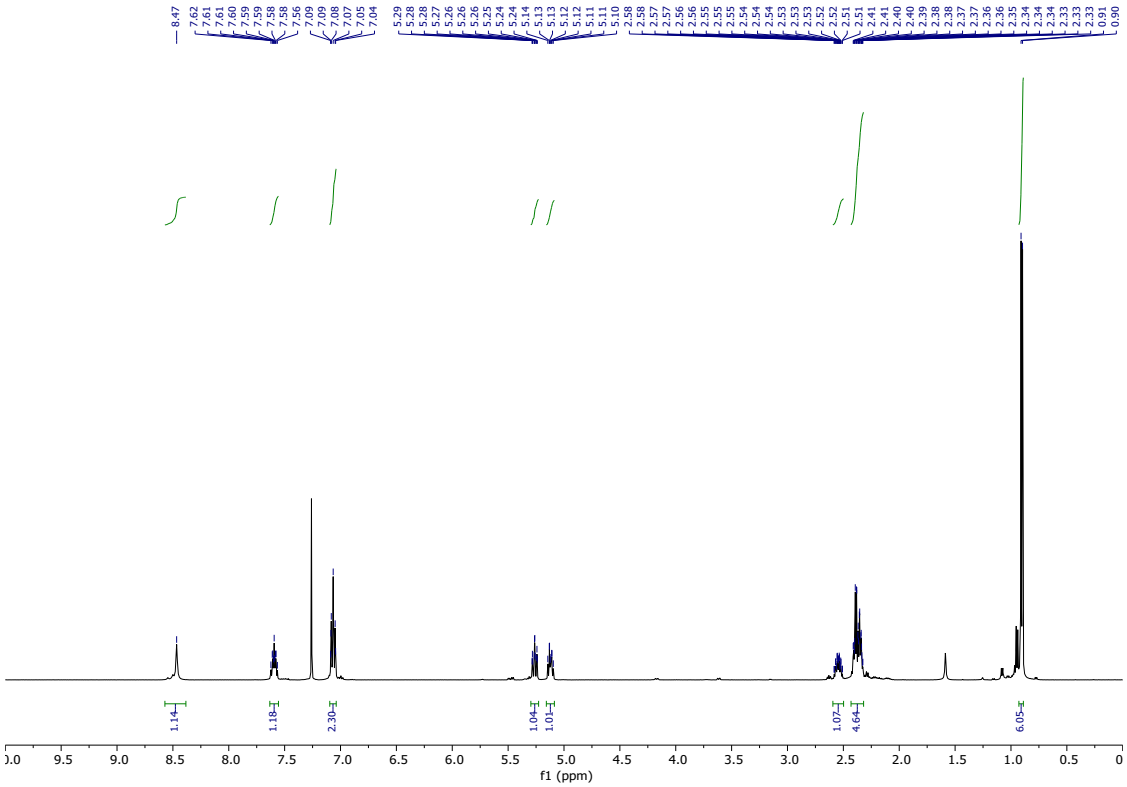
E isomer partial **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.0, 136.1 (t, *J* = 11.2 Hz), 124.1, 36.3, 31.0, 27.1, 22.4.

E isomer **^{19}F NMR** (564 MHz, $CDCl_3$) δ -106.30 (dd, *J* = 9.1, 5.9 Hz).

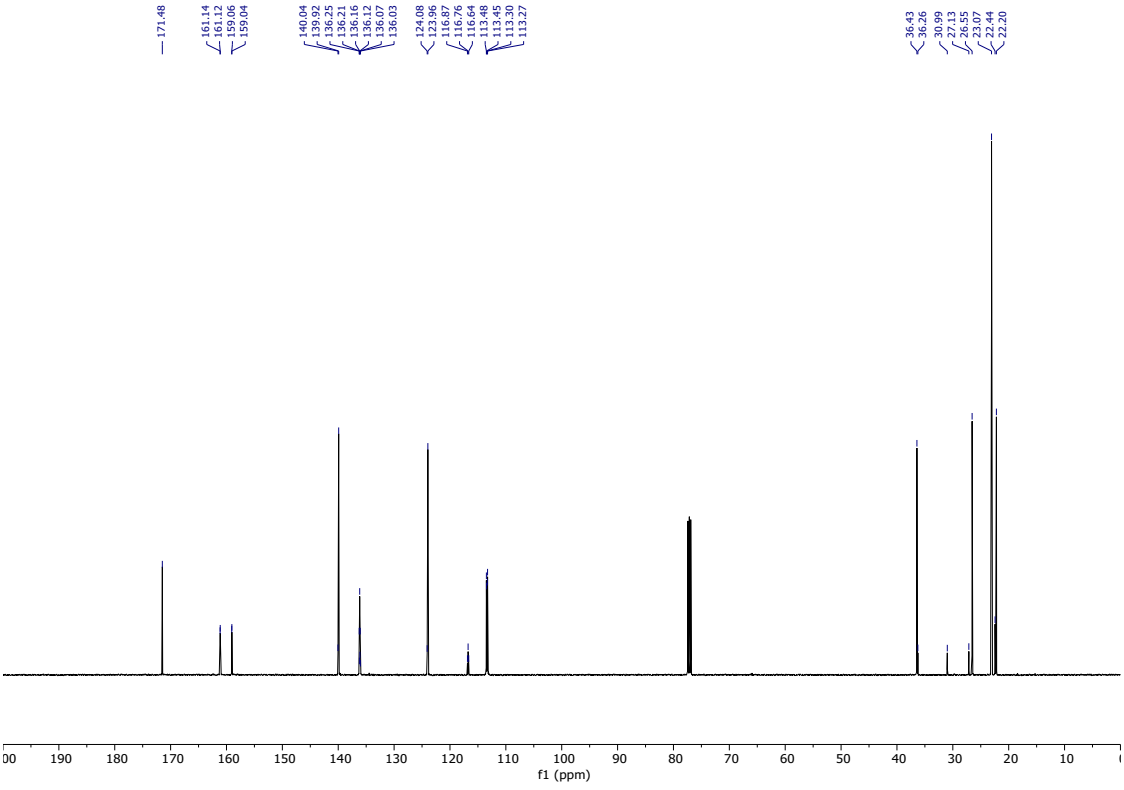
IR (neat) 3255, 2959, 2871, 1731, 1613, 1590, 1471, 1433, 1354, 1178 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{17}F_2NO_3SNa^+$ $[M+Na]^+$: 340.0790, found 340.0789.

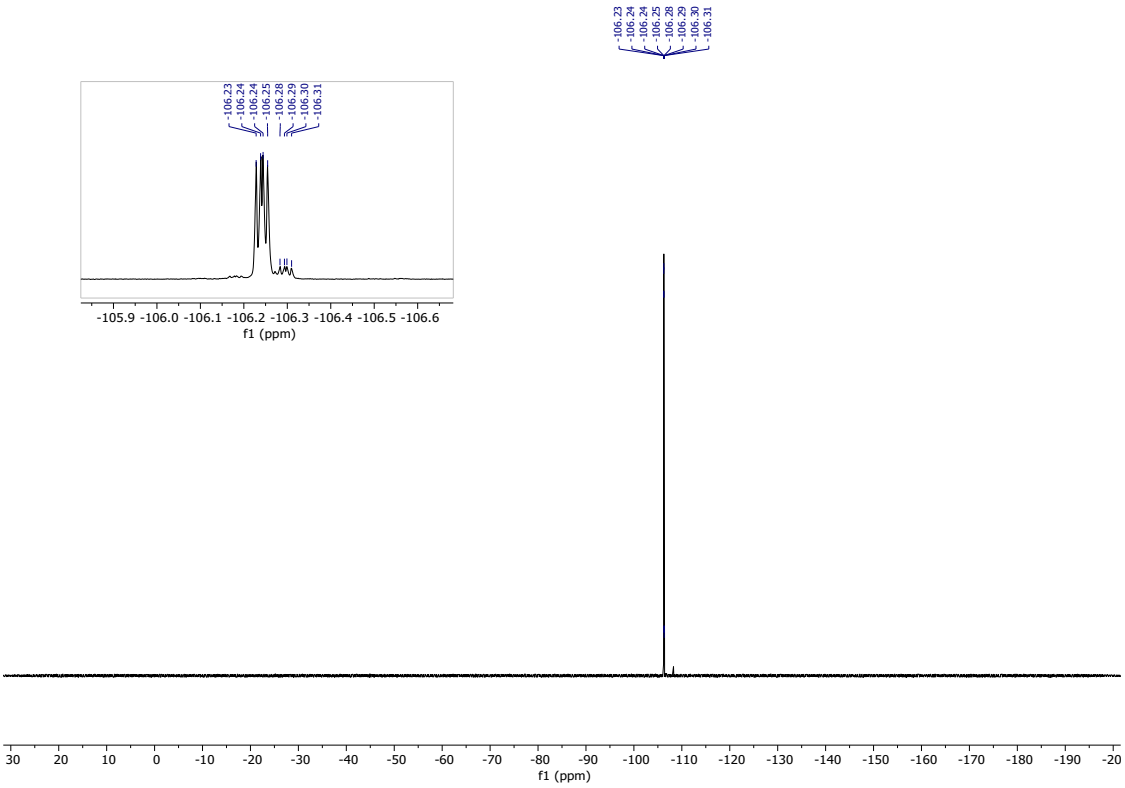
^{1}H NMR - 1v

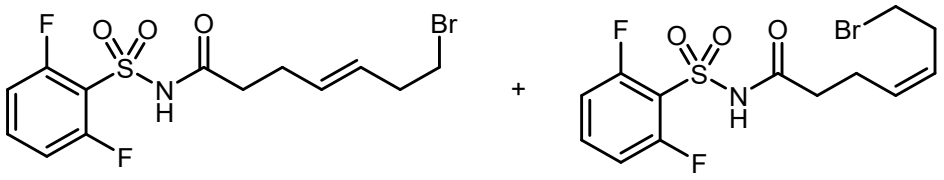


^{13}C NMR – 1v



^{19}F NMR – 1v


-106.23
-106.24
-106.24
-106.25
-106.28
-106.29
-106.30
-106.31
-105.9 -106.0 -106.1 -106.2 -106.3 -106.4 -106.5 -106.6
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



9 : 1

1w. 7-bromo-N-((2,6-difluorophenyl)sulfonyl)hept-4-enamide. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and 7-bromohept-4-enoic acid. 201 mg, 0.53 mmol, 66% yield. Colorless solid, ~9:1 E/Z ratio.

E/Z mixture **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.65 – 7.57 (m, 1H), 7.11 – 7.04 (m, 2H), 5.79 – 5.41 (m, 2H), 3.50 – 3.30 (m, 2H), 2.67 – 2.49 (m, 2H), 2.46 – 2.40 (m, 2H), 2.39 – 2.29 (m, 2H).

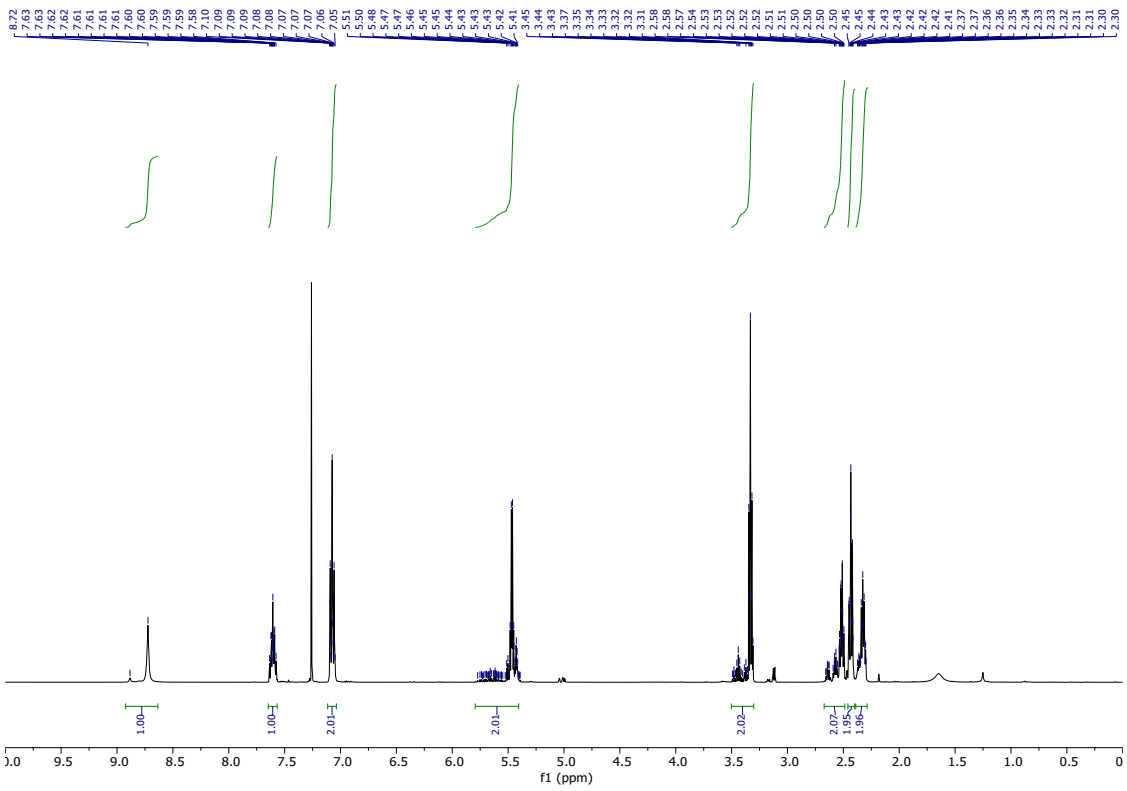
E isomer **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.6, 160.1 (dd, *J* = 262, 2.9 Hz), 136.14 (t, *J* = 11.2 Hz), 130.6, 129.1, 116.9 (t, *J* = 14.3 Hz) 113.44 (dd, *J* = 22.3, 3.7 Hz), 35.97, 35.83, 32.51, 27.06.

E/Z mixture **^{19}F NMR** (471 MHz, $CDCl_3$) δ -106.13 – -106.27 (m).

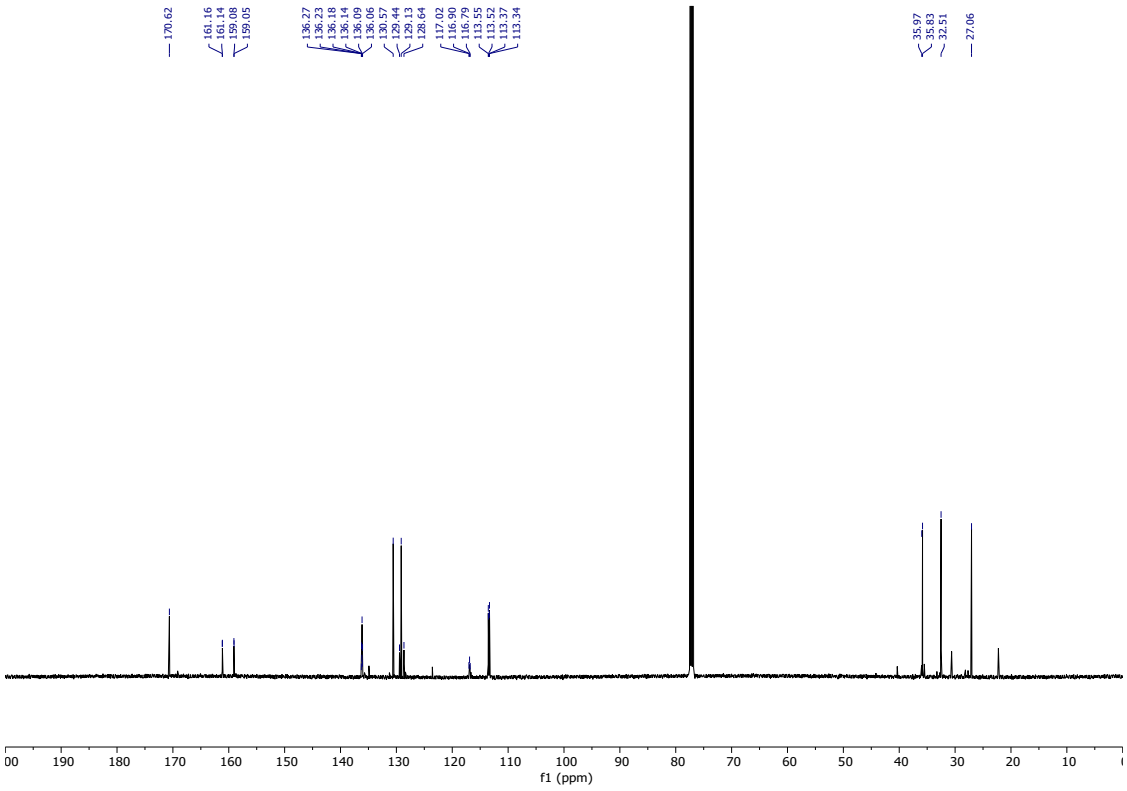
IR (neat) 3292, 3092, 2935, 1722, 1614, 1589, 1469, 1425, 1349, 1296 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{14}BrF_2NO_3SNa^+$ $[M+Na]^+$: 403.9738, found 403.9734.

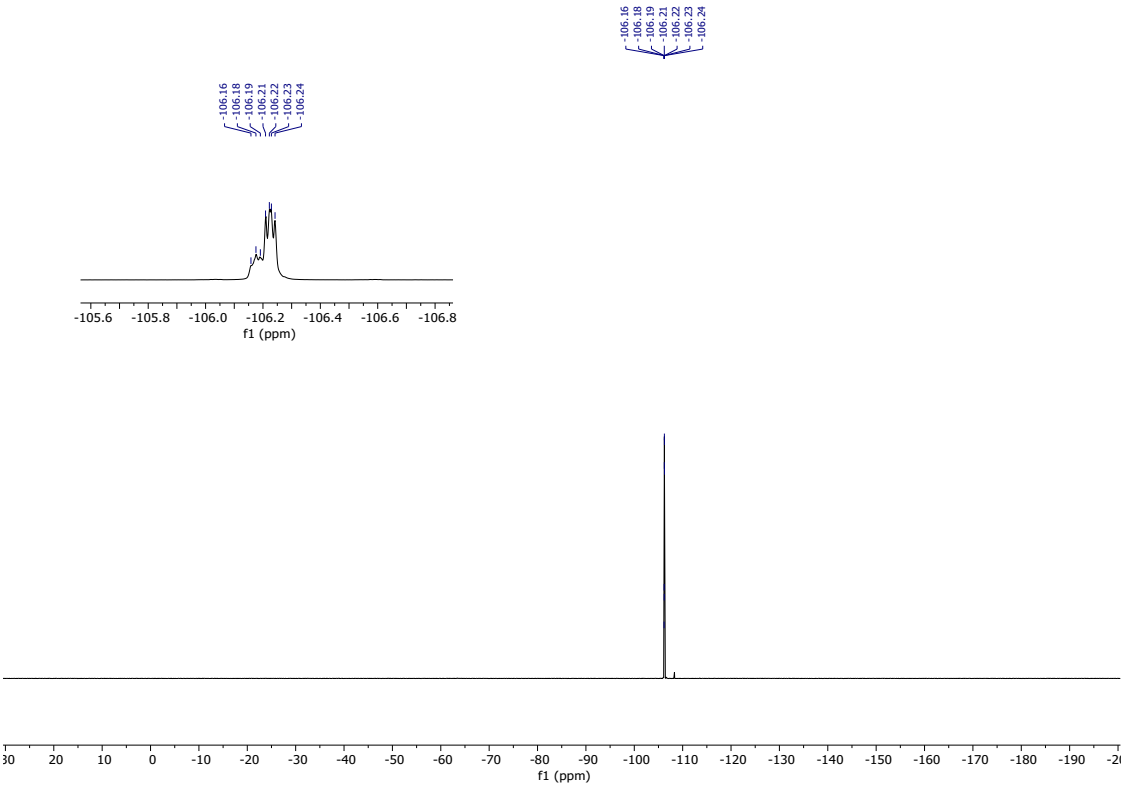
^{1}H NMR – 1w

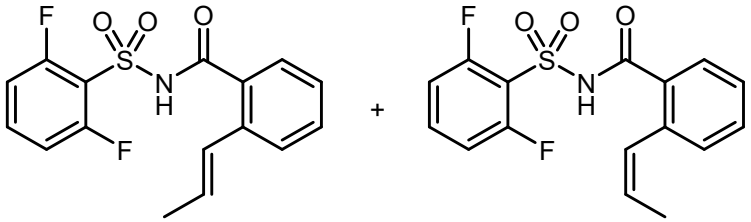


^{13}C NMR – 1w



^{19}F NMR – 1w


-106.16
-106.18
-106.19
-106.21
-106.22
-106.23
-106.24
-105.6
-105.8
-106.0
-106.2
-106.4
-106.6
-106.8
f1 (ppm)
f1 (ppm)



1 : 1

1x. N-((2,6-difluorophenyl)sulfonyl)-2-(prop-1-en-1-yl)benzamide. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and 2-(prop-1-en-1-yl)benzoic acid. 133 mg, 0.39 mmol, 49% yield. Colorless solid, 1:1 E/Z ratio.

E/Z mixture **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (br s, 1H), 8.71 (br s, 1H), 7.86 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.66 – 7.55 (m, 2H), 7.56 – 7.50 (m, 2H), 7.48 – 7.45 (m, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.33 – 7.24 (m, 2H), 7.10 (t, J = 8.7 Hz, 2H), 7.07 (t, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 11.4 Hz, 1H), 6.65 (dq, *J* = 15.7, 1.9 Hz, 1H), 6.26 – 6.13 (m, 2H), 1.91 (dd, *J* = 6.6, 1.8 Hz, 3H), 1.75 (dd, *J* = 7.0, 1.9 Hz, 3H).

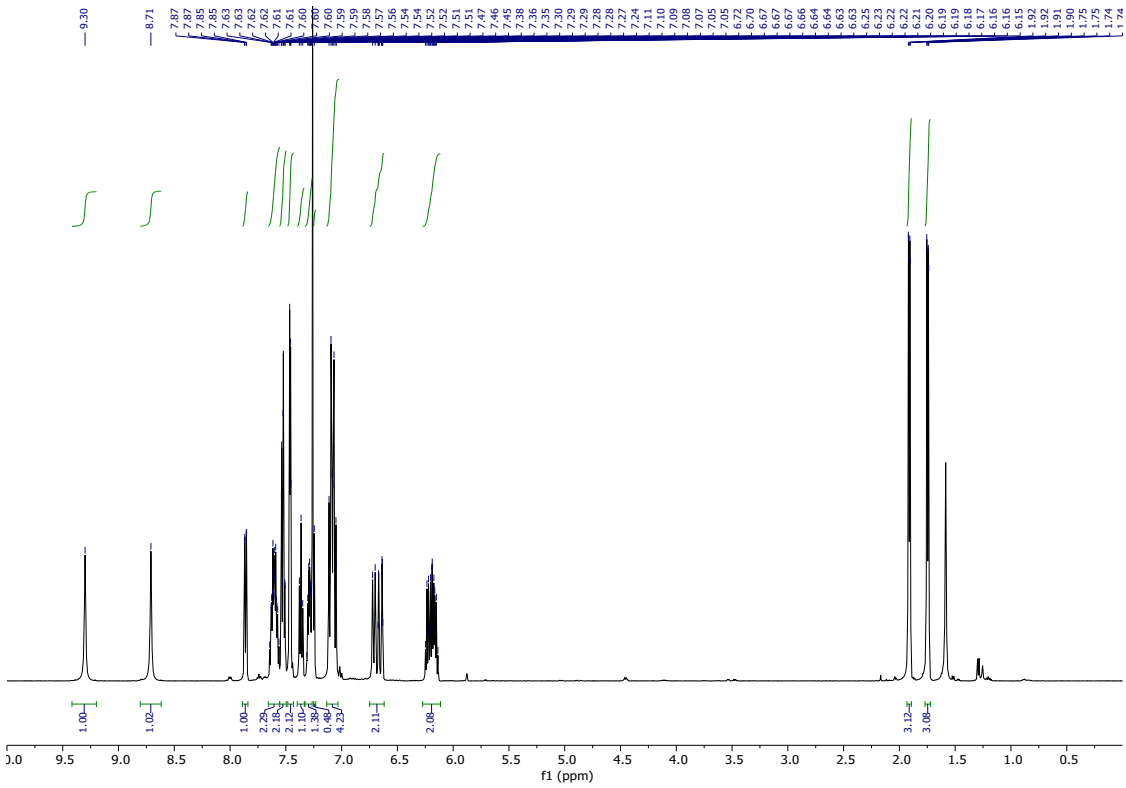
E/Z mixture **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.5, 165.6, 160.3 (dd, *J* = 262, 2.6 Hz), 160.2 (dd, *J* = 262, 2.6 Hz) 137.6, 136.2, 136.13 (t, *J* = 11.0 Hz), 136.06 (t, *J* = 11.2 Hz), 132.7, 132.4, 132.3, 131.7, 130.8, 130.3, 130.0, 129.9, 128.3, 127.9, 127.7, 127.6, 127.2, 116.9 (t, *J* = 14.2 Hz), 116.8 (t, *J* = 14.4 Hz), 113.39 (dd, *J* = 22.5, 4.1 Hz), 113.35 (dd, *J* = 22.5, 4.2 Hz), 18.8, 14.5.

E/Z mixture **^{19}F NMR** (377 MHz, $CDCl_3$) δ -106.04, (dd, *J* = 8.7, 6.0 Hz), -106.10 (dd, *J* = 8.6, 5.9 Hz).

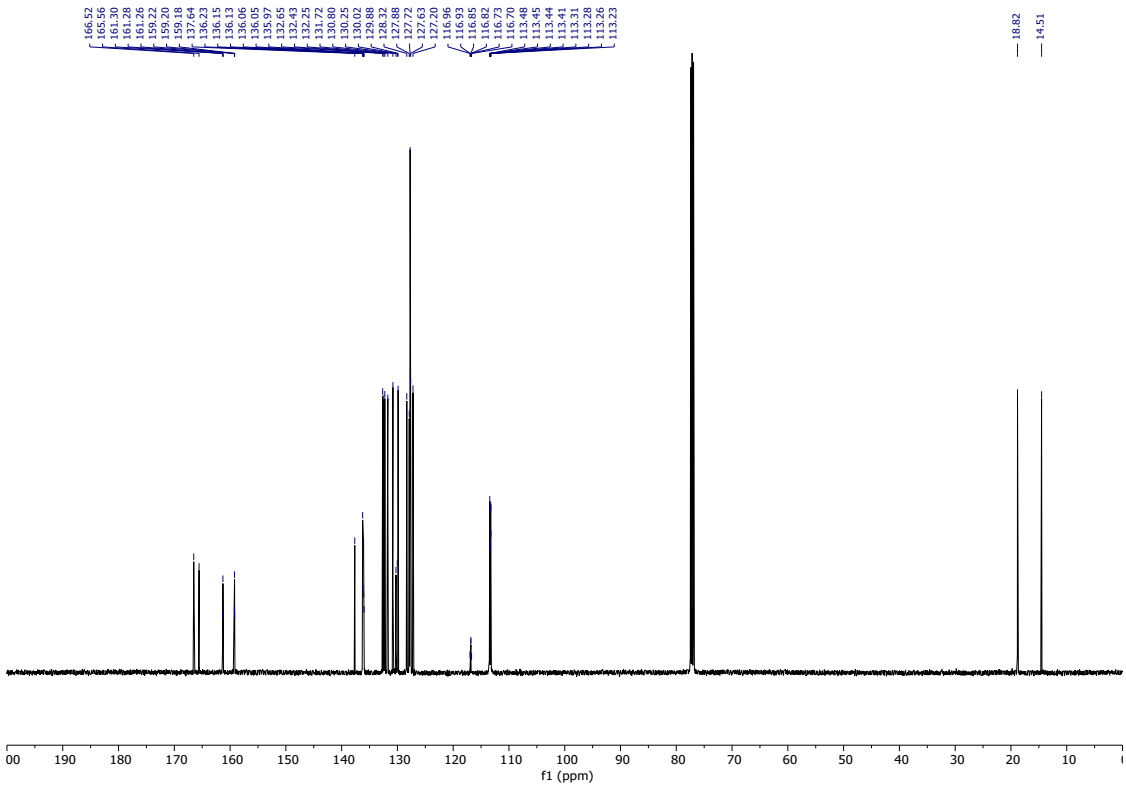
IR (neat) 3228, 3107, 1699, 1612, 1590, 1568, 1470, 1411, 1363, 1289 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{16}H_{13}F_2NO_3SNa^+$ $[M+Na]^+$: 360.0477, found 360.0476.

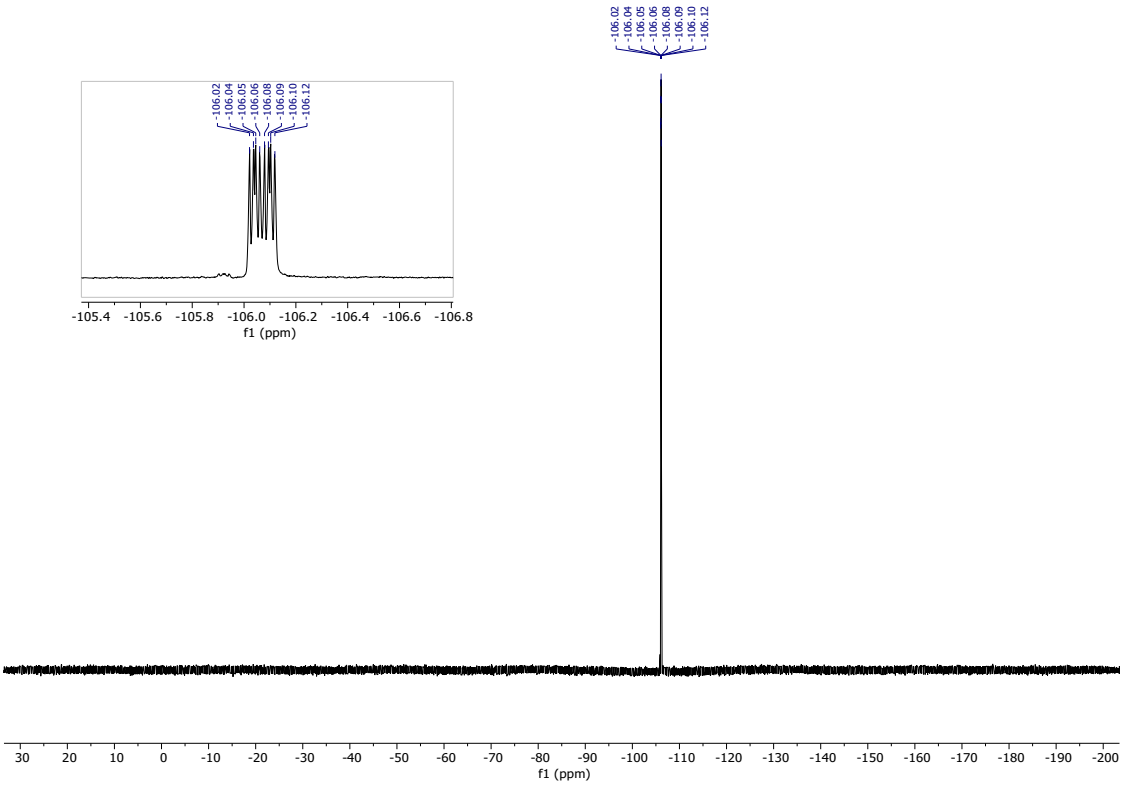
^{1}H NMR – 1x

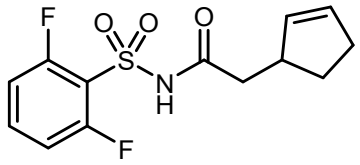


^{13}C NMR – 1x



^{19}F NMR – 1x


-106.02
-106.04
-106.05
-106.06
-106.08
-106.09
-106.10
-106.12
-105.4 -105.6 -105.8 -106.0 -106.2 -106.4 -106.6 -106.8
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1y. 2-(cyclopent-2-en-1-yl)-N-((2,6-difluorophenyl)sulfonyl)acetamide. Prepared according to **GP1** with 1.0 mmol 2,6-difluorobenzenesulfonamide and commercially available 2-cyclopentene-1-acetic acid. 151 mg, 0.50 mmol, 50% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.60 (tt, *J* = 8.5, 5.9 Hz, 1H), 7.09 – 7.05 (m, 2H), 5.80 – 5.76 (m, 1H), 5.61 – 5.55 (m, 1H), 3.10 – 3.02 (m, 1H), 2.41 (dd, *J* = 15.5, 6.8 Hz, 1H), 2.37 – 2.24 (m, 3H), 2.12 – 2.05 (m, 1H), 1.40 (ddt, *J* = 13.2, 9.0, 6.1 Hz, 1H).

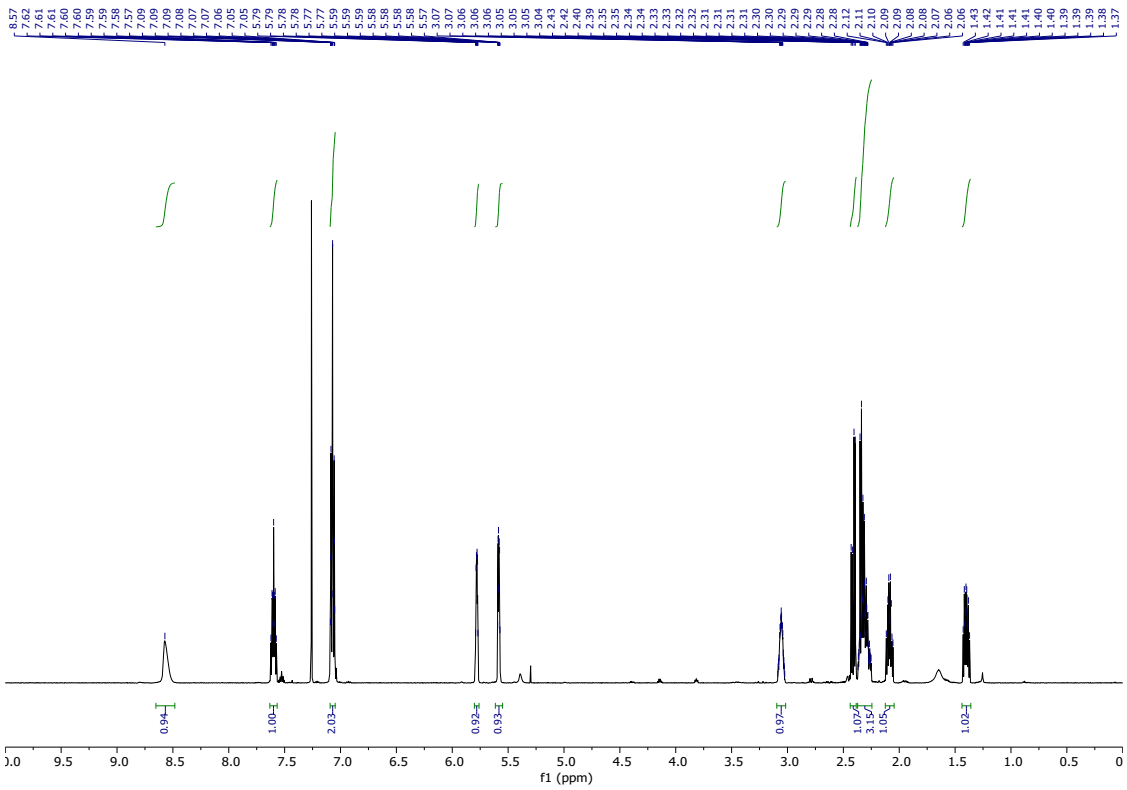
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 160.1 (dd, *J* = 262, 3.0 Hz), 136.1 (t, *J* = 11.2 Hz), 132.8, 132.7, 116.9 (t, J = 14.5 Hz), 113.4 (dd, *J* = 22.6, 4.0 Hz), 42.4, 41.6, 31.9, 29.4.

^{19}F NMR (564 MHz, $CDCl_3$) δ -106.23 (dd, *J* = 9.3, 5.9 Hz).

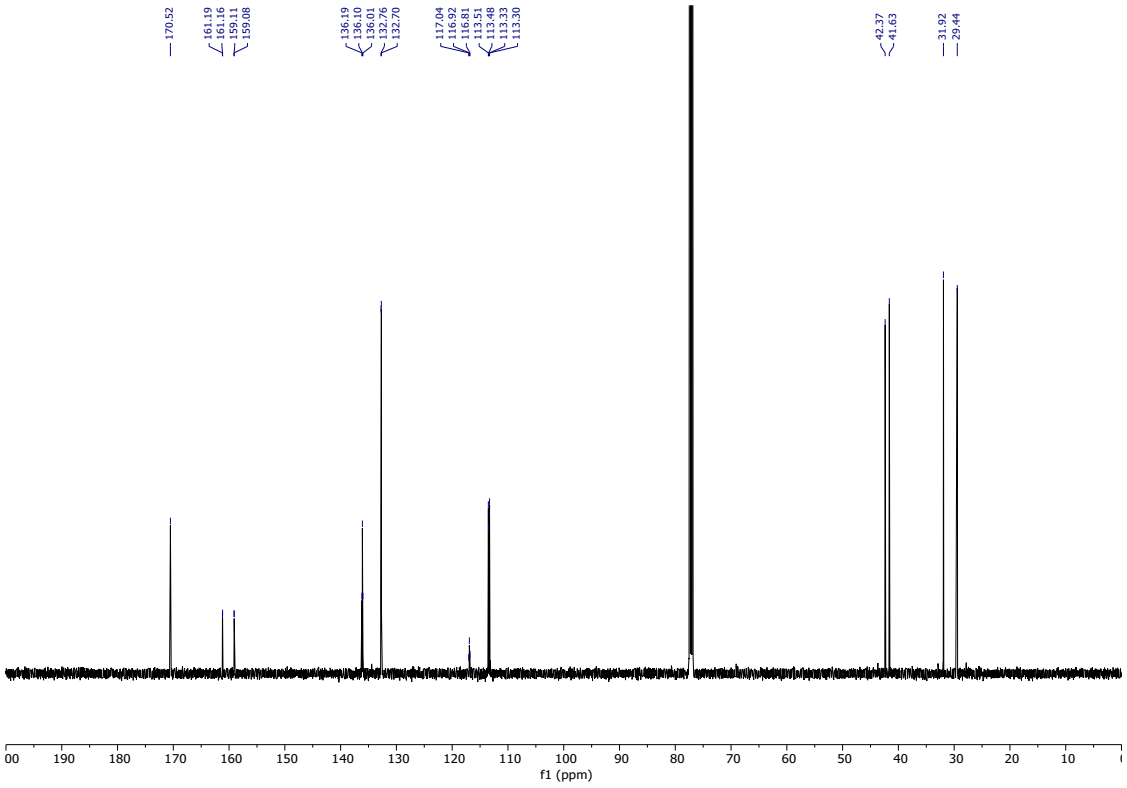
IR (neat) 3094, 2840, 2869, 2847, 1682, 1614, 1589, 1473, 1442, 1368 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{13}F_2NO_3SNa^+$ $[M+Na]^+$: 324.0477, found 324.0473.

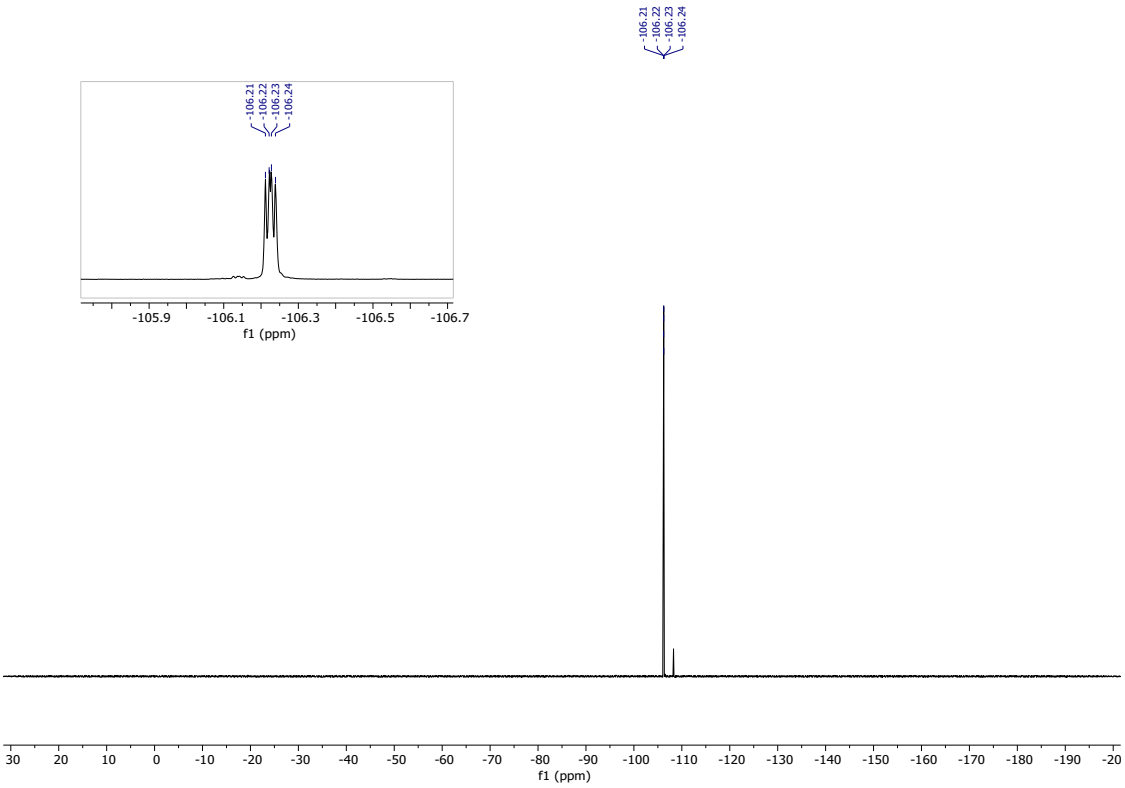
^{1}H NMR – 1y

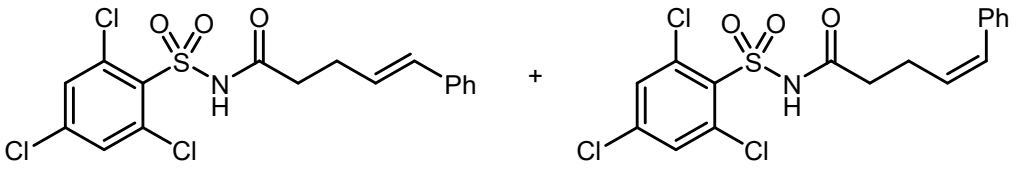


^{13}C NMR – 1y



^{19}F NMR – 1y


-106.21
-106.22
-106.23
-106.24
-105.9
-106.1
-106.3
-106.5
-106.7
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)



5 : 1

1z. N-((2,4,6-trichlorophenyl)sulfonyl)-5-phenylpent-4-enamide. Prepared according to **GP1** with 0.88 mmol 2,4,6-trichlorobenzenesulfonamide and 5-phenylpent-4-enoic acid. 195 mg, 0.46 mmol, 53% yield. Colorless solid, ~ 5:1 E/Z ratio

E isomer **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.37 (s, 2H), 7.34 – 7.18 (m, 5H), 6.34 (d, *J* = 15.7 Hz, 1H), 6.12 – 6.04 (m, 1H), 2.53 – 2.49 (m, 4H).

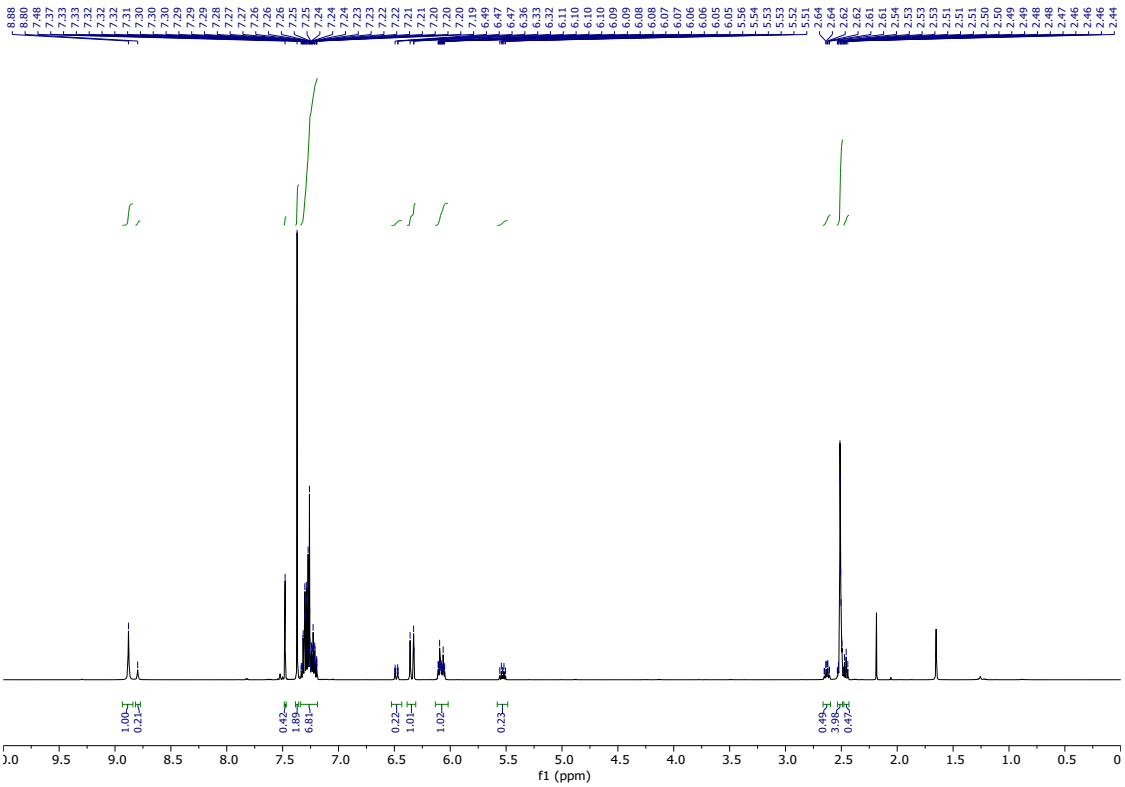
Z isomer partial **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.48 (s, 2H), 6.48 (dt, *J* = 11.6, 1.9 Hz, 1H), 5.53 (dt, *J* = 11.5, 7.1 Hz, 1H), 2.63 (app qd, *J* = 7.3, 1.8 Hz, 2H), 2.46 (t, *J* = 7.5 Hz, 3H).

E + Z isomer mixture **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.6, 139.8, 139.7, 137.0, 136.94, 136.87, 136.8, 132.4, 132.3, 132.1, 131.61, 131.59, 131.4, 129.0, 128.8, 128.7, 128.5, 127.6, 127.2, 127.0, 126.3, 36.3, 36.0, 27.6, 23.3.

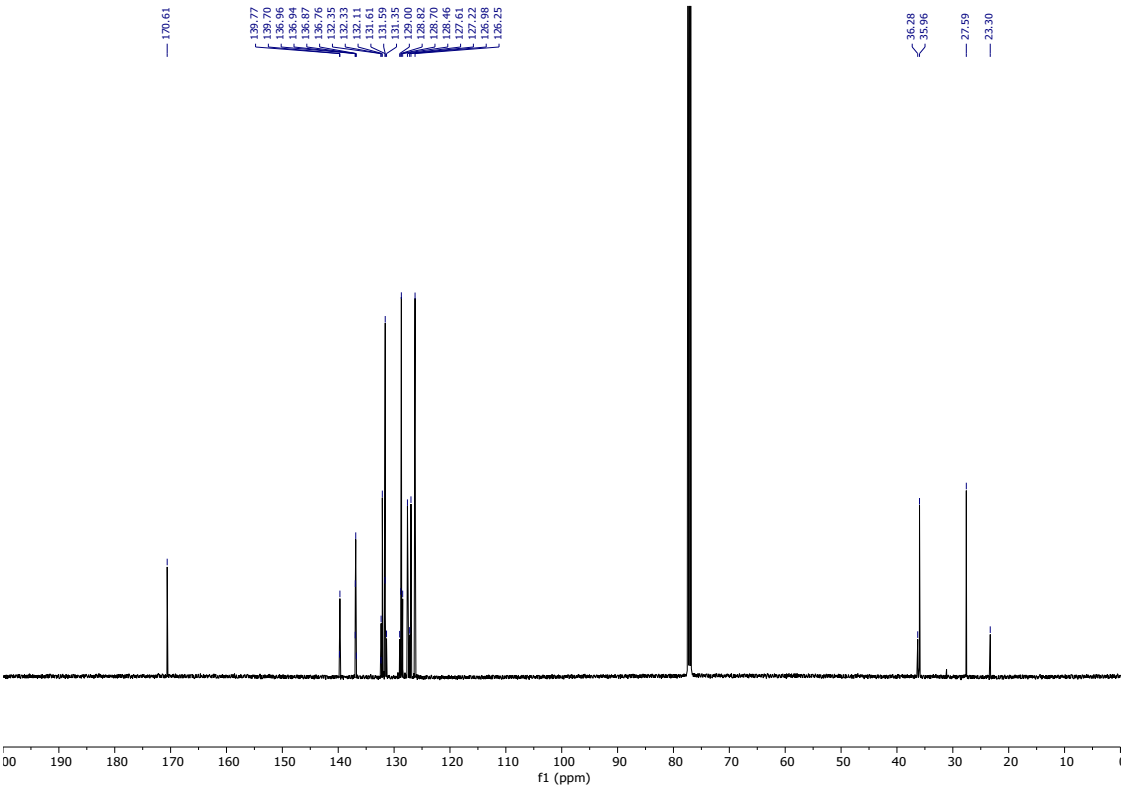
IR (neat) 3178, 3113, 2882, 1679, 1563, 1539, 1440, 1372, 1179, 1119 cm^{-1}

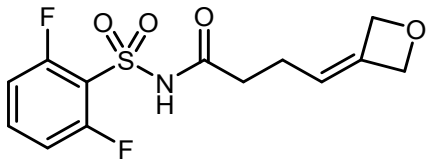
HRMS (ESI+) m/z calculated for $C_{17}H_{14}Cl_3NO_3SNa^+$ $[M+Na]^+$: 439.9652, found 439.9648.

^{1}H NMR – 1z



^{13}C NMR – 1z





1aa. N-((2,6-difluorophenyl)sulfonyl)-4-(oxetan-3-ylidene)butanamide. Prepared according to **GP1** with 0.7 mmol 2,6-difluorobenzenesulfonamide and 4-(oxetan-3-ylidene)butanoic acid. 83 mg, 0.26 mmol, 37% yield. Colorless solid.

^{1}H NMR (401 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.61 (tt, *J* = 8.5, 5.8 Hz, 1H), 7.13 – 6.99 (m, 2H), 5.19 – 5.13 (m, 4H), 5.07 (tp, *J* = 7.1, 2.3 Hz, 1H), 2.38 (t, *J* = 7.2 Hz, 2H), 2.19 – 2.10 (m, 2H).

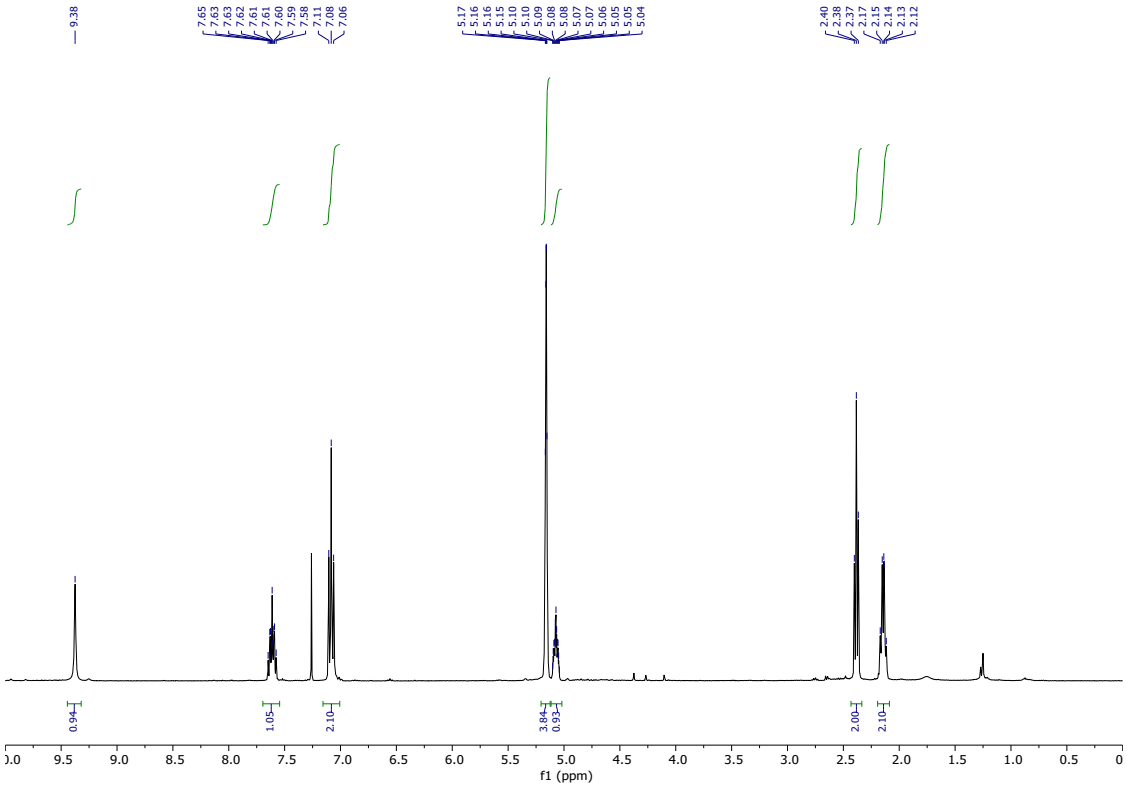
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 160.1 (dd, *J* = 262, 2.9 Hz), 136.3, 136.2 (t, *J* = 11.2 Hz), 117.0, 116.9 (t, *J* = 14.5 Hz), 113.4 (dd, *J* = 22.4, 3.8 Hz), 79.5, 78.8, 35.5, 23.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -106.31 (dd, *J* = 9.0, 5.8 Hz).

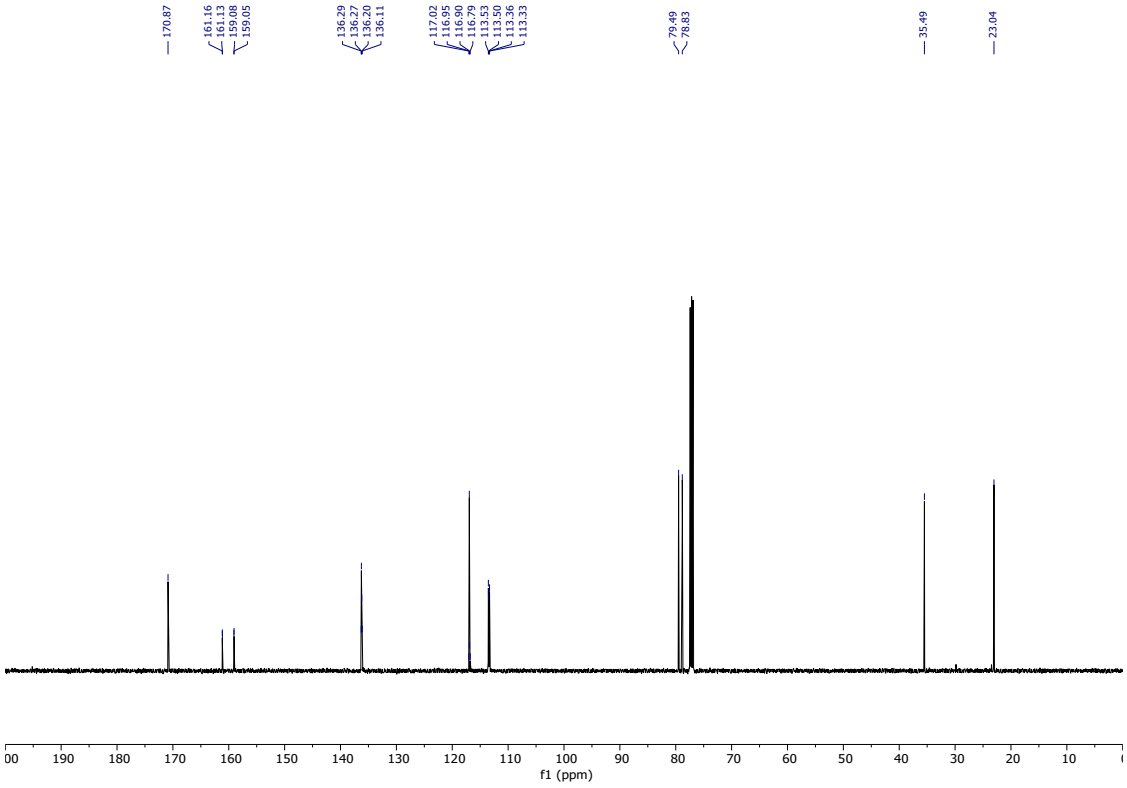
IR (neat) 3094, 2936, 2868, 1720, 1612, 1589, 1470, 1447, 1362, 1239 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{14}F_2NO_4S^+$ $[M+H]^+$: 318.0607, found 318.0604.

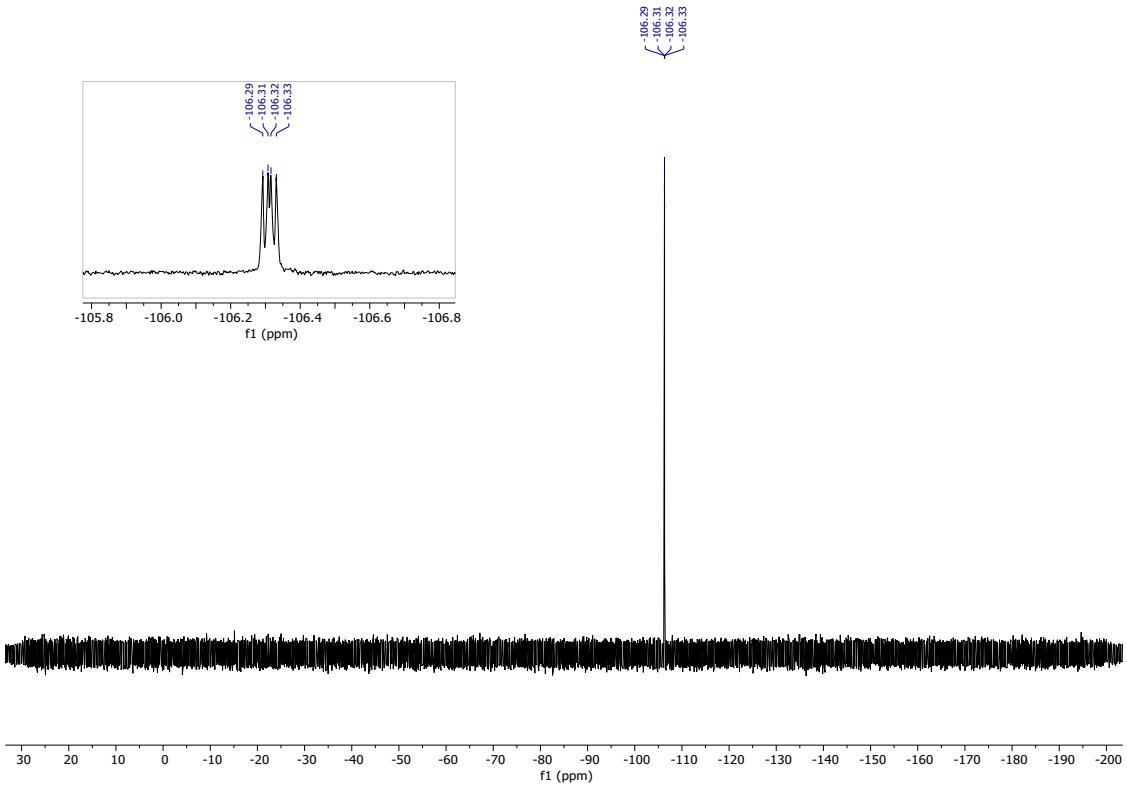
^{1}H NMR – 1aa

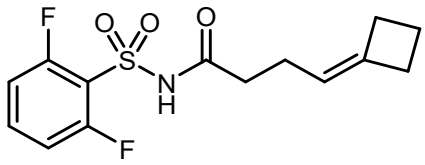


^{13}C NMR – 1aa



^{19}F NMR – 1aa


-106.29
-106.31
-106.32
-106.33
-105.8
-106.0
-106.2
-106.4
-106.6
-106.8
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



1ab. 4-cyclobutylidene-N-((2,6-difluorophenyl)sulfonyl)butanamide. Prepared according to **GP1** with 0.7 mmol 2,6-difluorobenzenesulfonamide and 4-cyclobutylidenebutanoic acid. 90 mg, 0.29 mmol, 41% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (br s, 1H), 7.59 (tt, *J* = 8.5, 5.9 Hz, 1H), 7.09 – 7.04 (m, 2H), 4.97 (tp, *J* = 7.2, 2.4 Hz, 1H), 2.64 – 2.56 (m, 4H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.20 – 2.14 (m, 2H), 1.91 (p, *J* = 7.9 Hz, 2H).

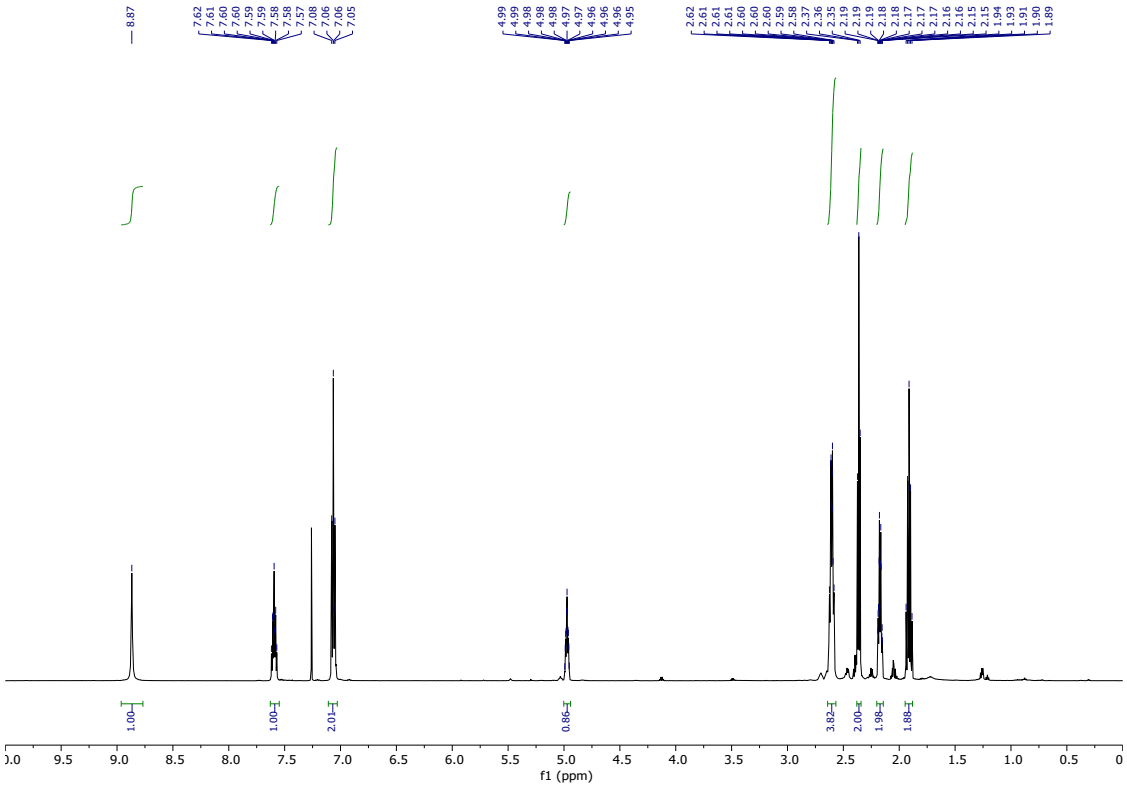
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 160.2 (dd, *J* = 262, 2.9 Hz), 143.6, 136.0 (t, *J* = 11.2 Hz), 117.3, 116.9 (*J* = 14.4 Hz), 113.4 (dd, *J* = 22.5, 3.9 Hz), 36.4, 31.0, 29.3, 23.0, 17.0.

^{19}F NMR (564 MHz, $CDCl_3$) δ -106.27 (dd, *J* = 8.8, 5.9 Hz).

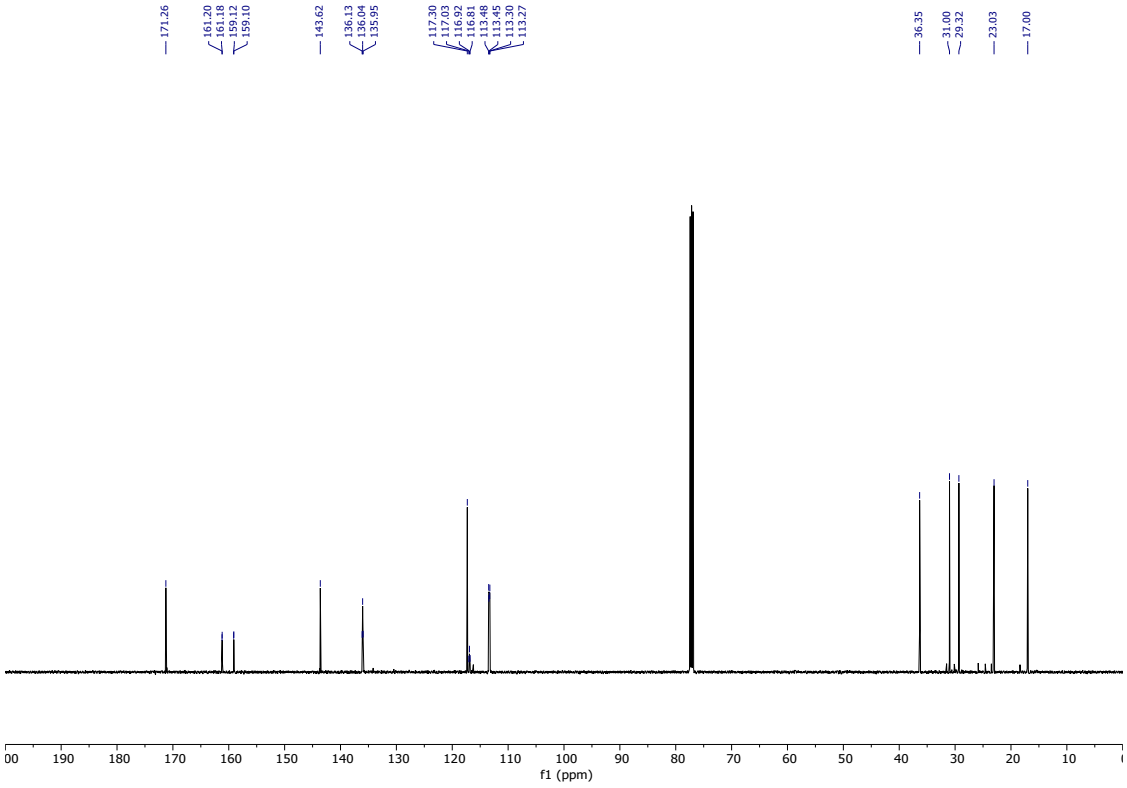
IR (neat) 3197, 2923, 1694, 1612, 1590, 1565, 1471, 1438, 1367, 1240 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{15}F_2NO_3SNa^+$ $[M+Na]^+$: 338.0633, found 338.0627.

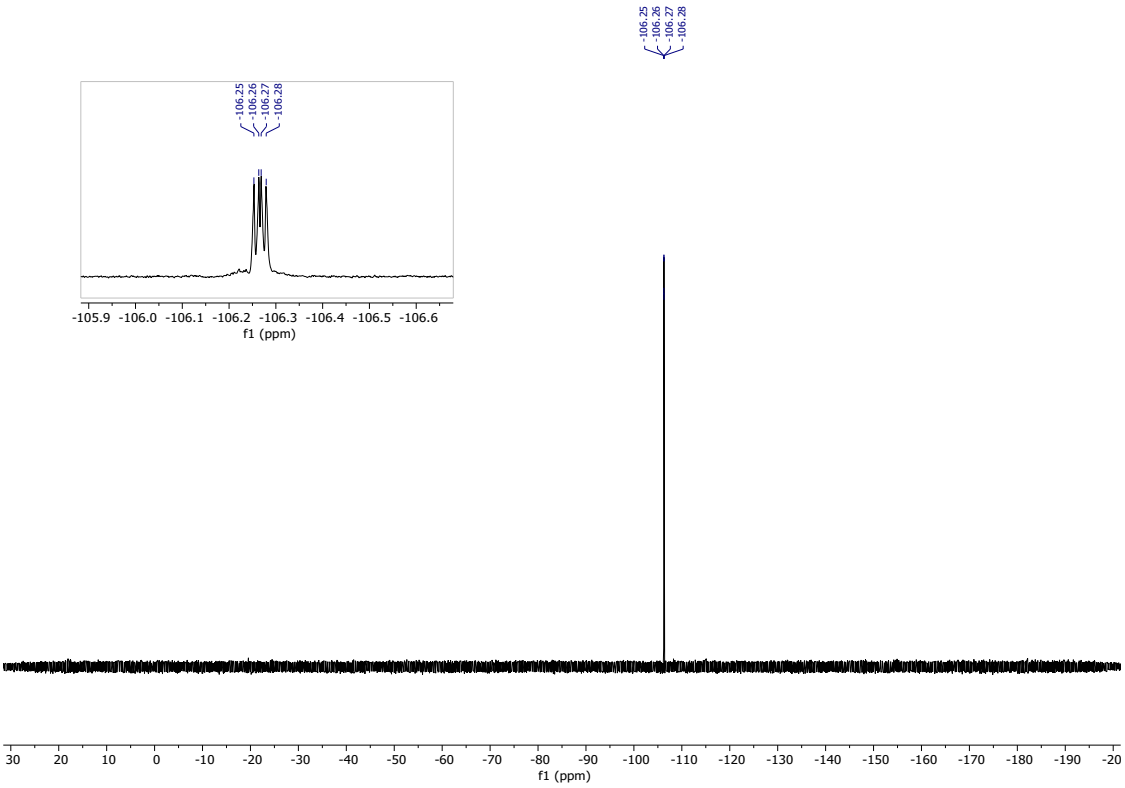
^{1}H NMR – 1ab

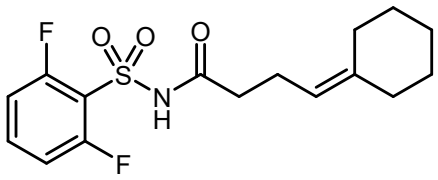


^{13}C NMR – 1ab



^{19}F NMR – 1ab


-106.25
-106.26
-106.27
-106.28
-105.9 -106.0 -106.1 -106.2 -106.3 -106.4 -106.5 -106.6
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



1ac. 4-cyclohexylidene-N-((2,6-difluorophenyl)sulfonyl)butanamide. Prepared according to **GP1** with 1.0 mmol 2,6-difluorobenzenesulfonamide and 4-cyclohexylidenebutanoic acid. 216 mg, 0.63 mmol, 63% yield. Colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.59 (tt, *J* = 8.6, 5.9 Hz, 1H), 7.06 (t, *J* = 8.9 Hz, 2H), 4.96 (t, *J* = 7.1 Hz, 1H), 2.41 – 2.32 (m, 2H), 2.32 – 2.24 (m, 2H), 2.11 – 2.04 (m, 2H), 2.05 – 1.99 (m, 2H), 1.56 – 1.39 (m, 6H).

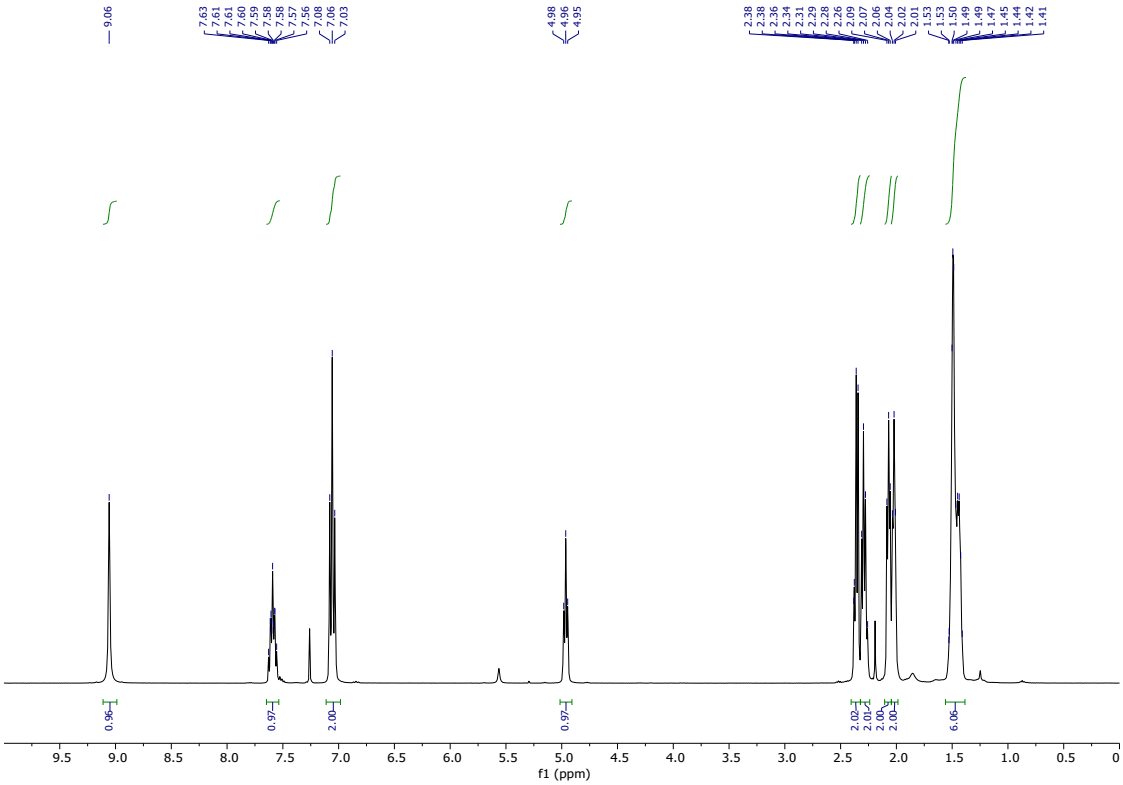
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 160.1 (dd, *J* = 262, 3.0 Hz), 142.8, 136.0 (t, *J* = 11.2 Hz), 118.1, 116.9 (t, *J* = 14.4 Hz) 113.4 (dd, *J* = 22.6, 3.9 Hz), 37.1, 36.8, 28.7, 28.6, 27.7, 26.8, 22.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -106.22 (dd, *J* = 9.5, 6.0 Hz).

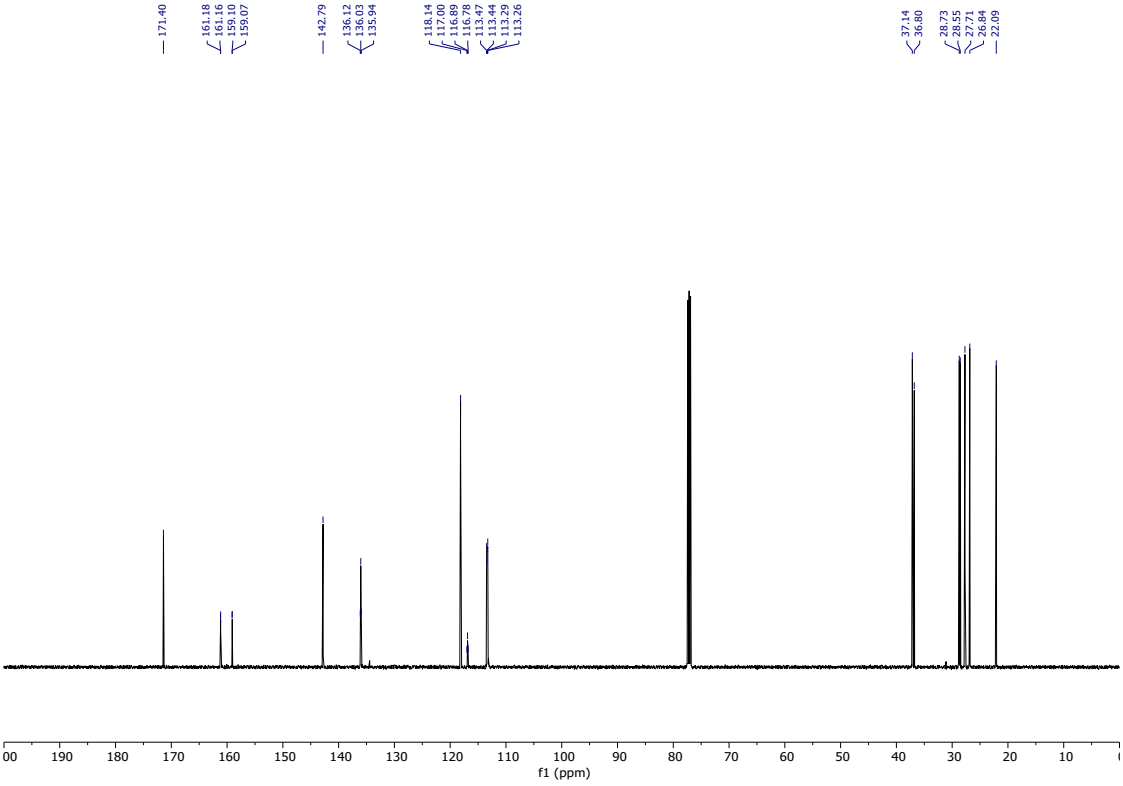
IR (neat) 3247, 2931, 2855, 1729, 1613, 1590, 1563, 1471, 1431, 1353 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{16}H_{19}F_2NO_3SNa^+$ $[M+Na]^+$: 366.0946, found 366.0942.

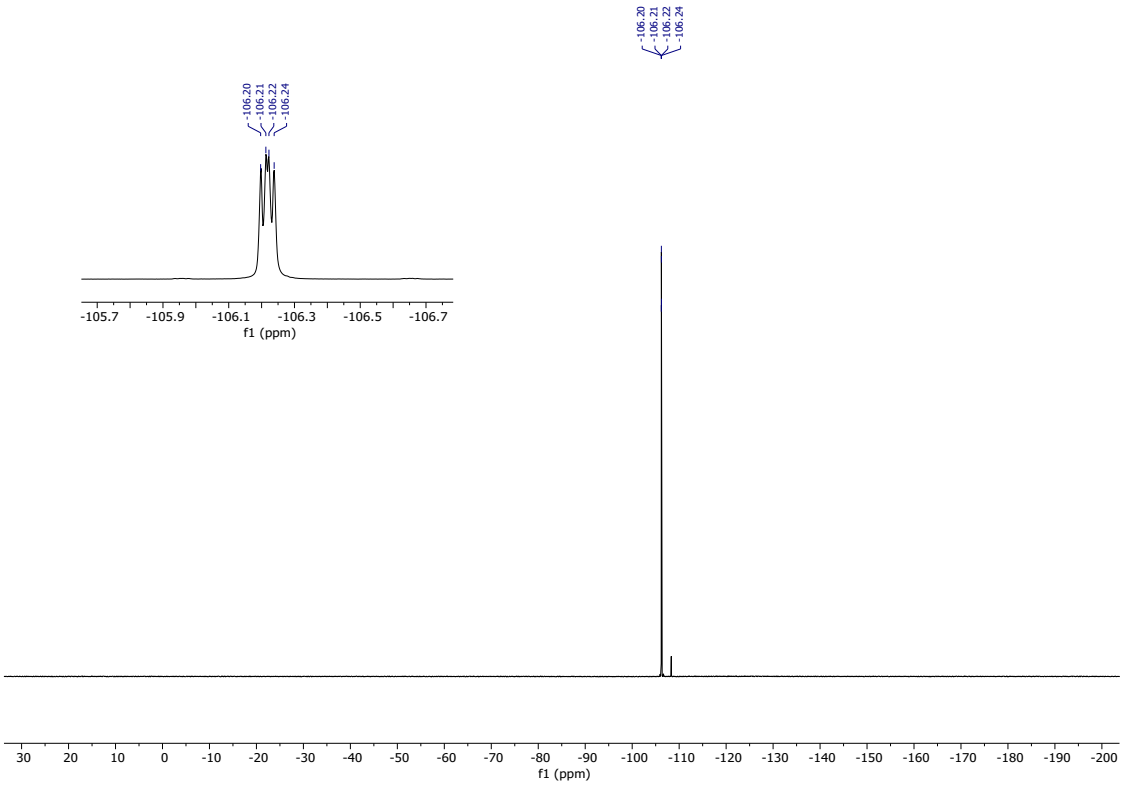
^{1}H NMR – 1ac

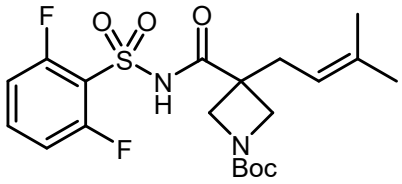


^{13}C NMR – 1ac



^{19}F NMR – 1ac


-106.20
-106.21
-106.22
-106.24
-105.7
-105.9
-106.1
-106.3
-106.5
-106.7
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



1ad. tert-butyl 3-(((2,6-difluorophenyl)sulfonyl)carbamoyl)-3-(3-methylbut-2-en-1-yl)azetidine-1-carboxylate. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and 1-(tert-butoxycarbonyl)-3-(3-methylbut-2-en-1-yl)azetidine-3-carboxylic acid. 219 mg, 0.49 mmol, 62% yield. Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.61 (tt, *J* = 8.2, 5.7 Hz, 1H), 7.07 (t, *J* = 9.0 Hz, 2H), 5.04 – 4.95 (m, 1H), 4.09 (d, *J* = 8.7 Hz, 2H), 3.71 (d, *J* = 8.7 Hz, 2H), 2.58 (d, *J* = 7.2 Hz, 2H), 1.72 (s, 3H), 1.68 (s, 3H), 1.42 (s, 9H).

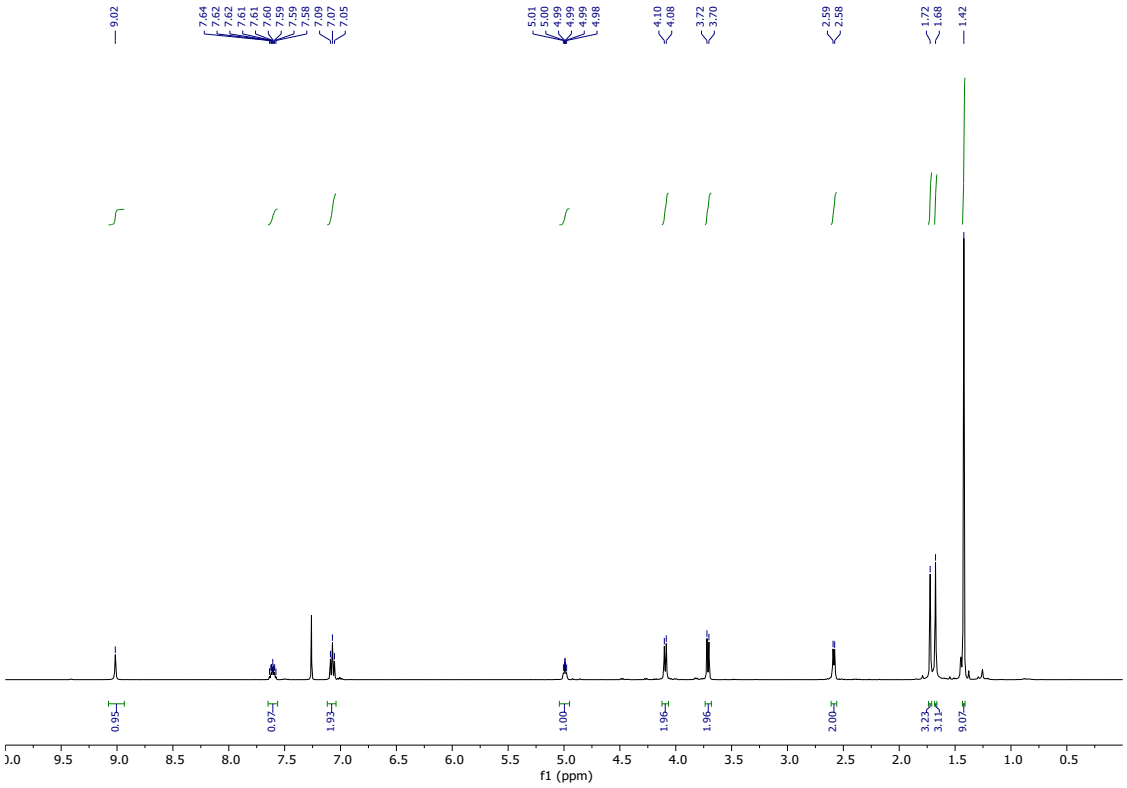
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 160.2 (dd, J = 262, 2.8 Hz), 156.4, 138.6, 136.2 (t, *J* = 11.1 Hz), 116.62, 116.59 (t, *J* = 14.4 Hz), 113.4 (dd, *J* = 22.4, 3.8 Hz), 80.5, 55.8, 43.9, 34.1, 28.4, 26.1, 18.4.

^{19}F NMR (471 MHz, $CDCl_3$) δ -106.16 (dd, *J* = 9.3, 5.9 Hz).

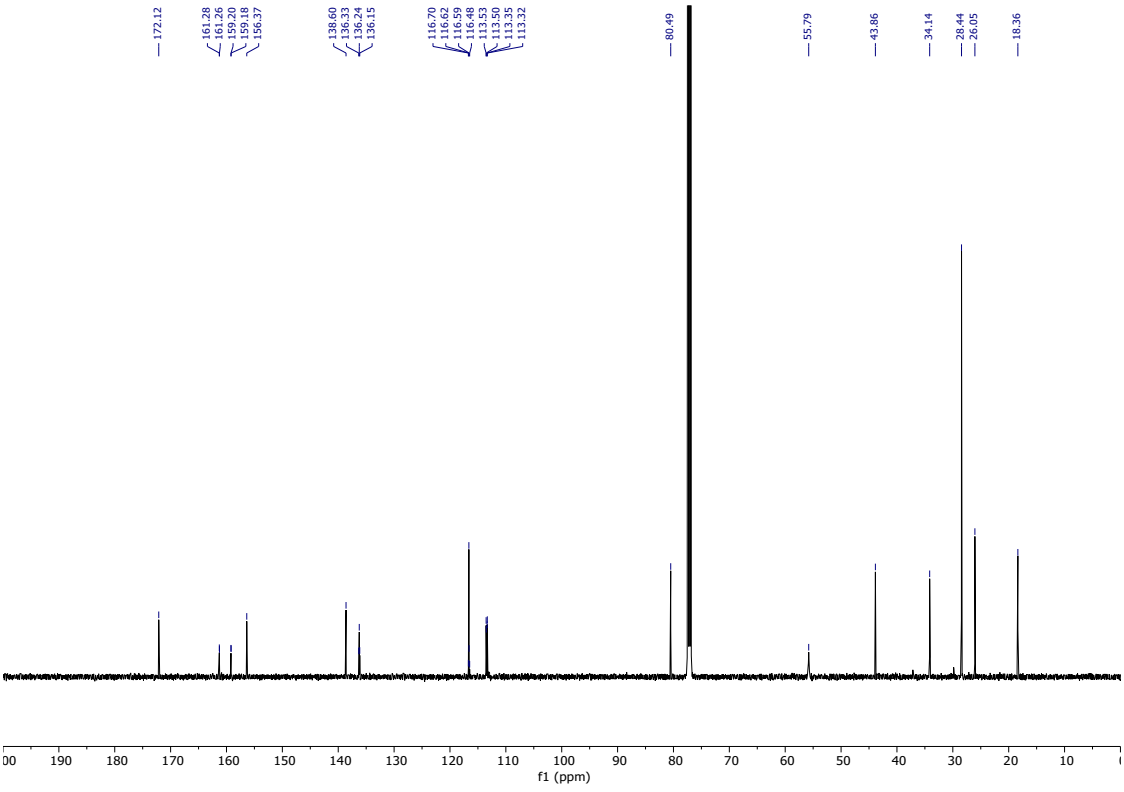
IR (neat) 2978, 1721, 1663, 1613, 1590, 1552, 1472, 1416, 1366, 1239 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{20}H_{26}F_2N_2O_5SNa^+$ $[M+Na]^+$: 467.1423, found 467.1415.

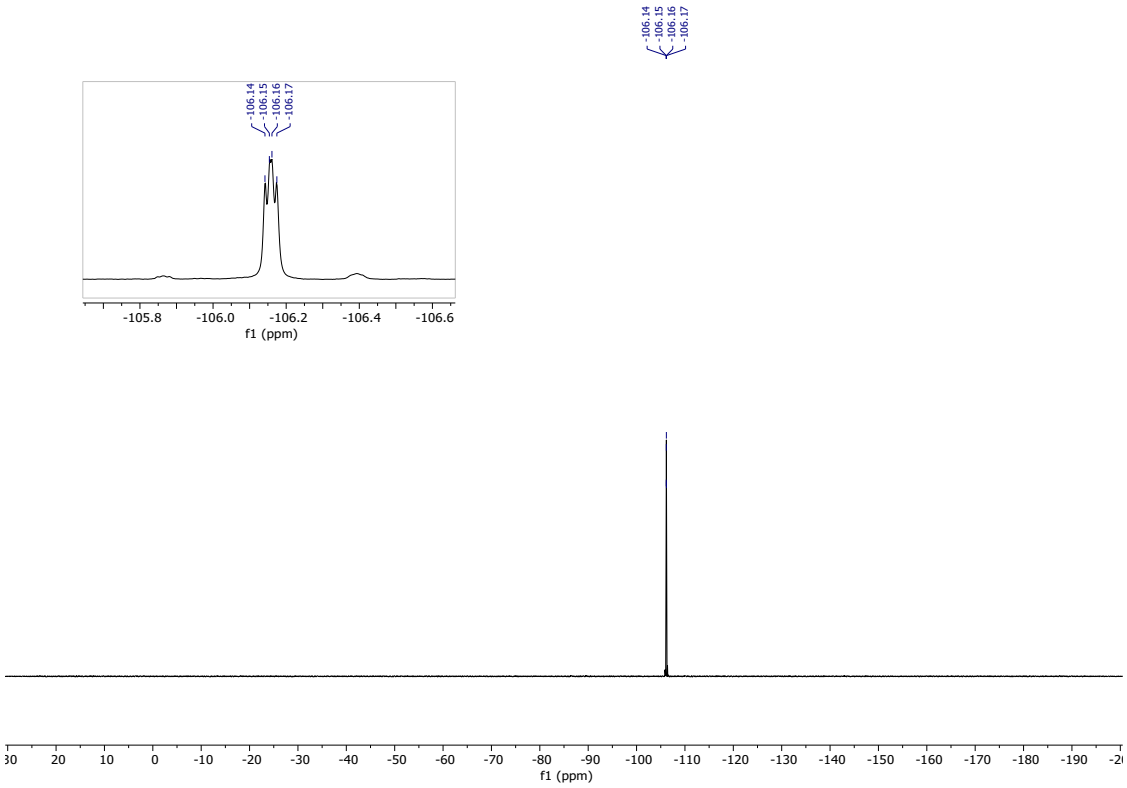
^{1}H NMR – 1ad

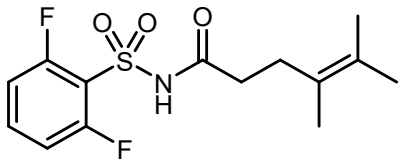


^{13}C NMR – 1ad



^{19}F NMR – 1ad


-106.14
-106.15
-106.16
-106.17
-105.8
-106.0
-106.2
-106.4
-106.6
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)



1ae. N-((2,6-difluorophenyl)sulfonyl)-4,5-dimethylhex-4-enamide. Prepared according to **GP1** with 0.8 mmol 2,6-difluorobenzenesulfonamide and 4,5-dimethylhex-4-enoic acid. 167 mg, 0.53 mmol, 66% yield. Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (br s, 1H), 7.59 (tt, *J* = 8.5, 5.8 Hz, 1H), 7.06 (t, *J* = 8.8 Hz, 2H), 2.41 – 2.36 (m, 2H), 2.36 – 2.30 (m, 2H), 1.63 (s, 3H), 1.62 (s, 3H), 1.59 (s, 3H).

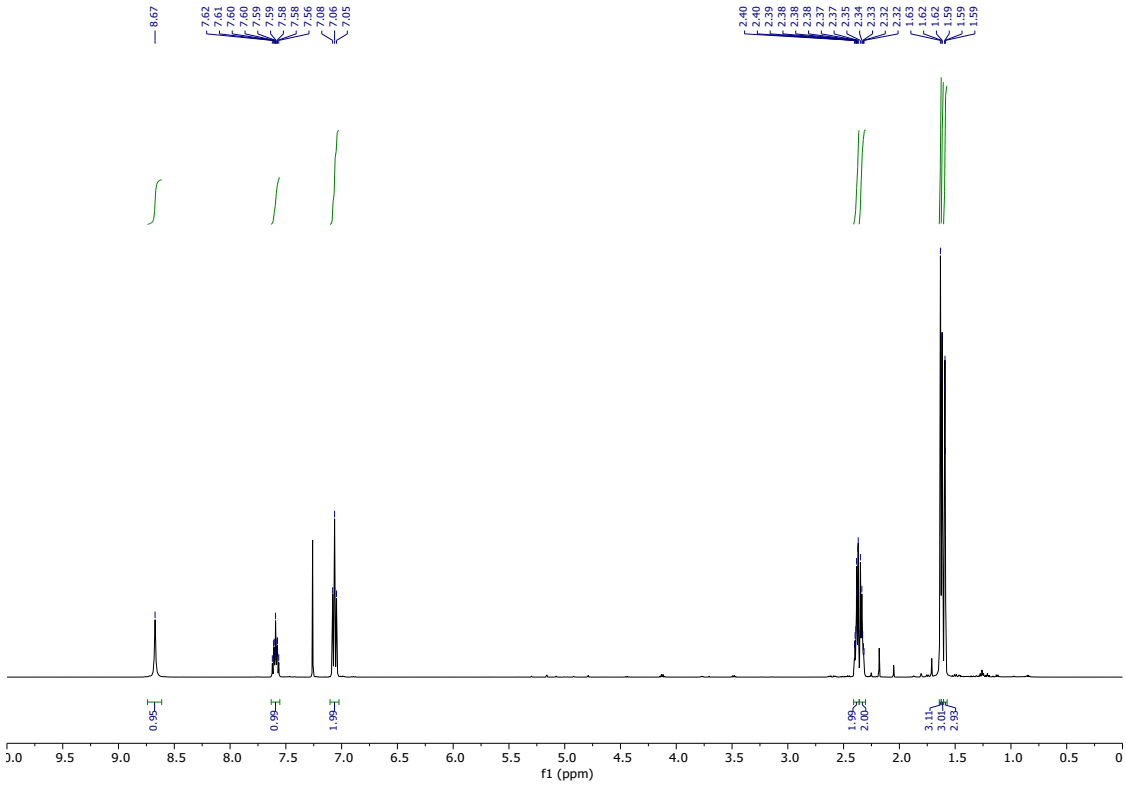
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 160.2 (dd, J = 262, 3.0 Hz), 136.0 (t, *J* = 11.3 Hz), 127.5, 124.9, 116.9 (t, *J* = 14.4 Hz), 113.4 (dd, J = 22.5, 3.9 Hz), 34.9, 29.1, 20.8, 20.3, 17.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -106.3 (dd, J = 8.9, 5.9 Hz).

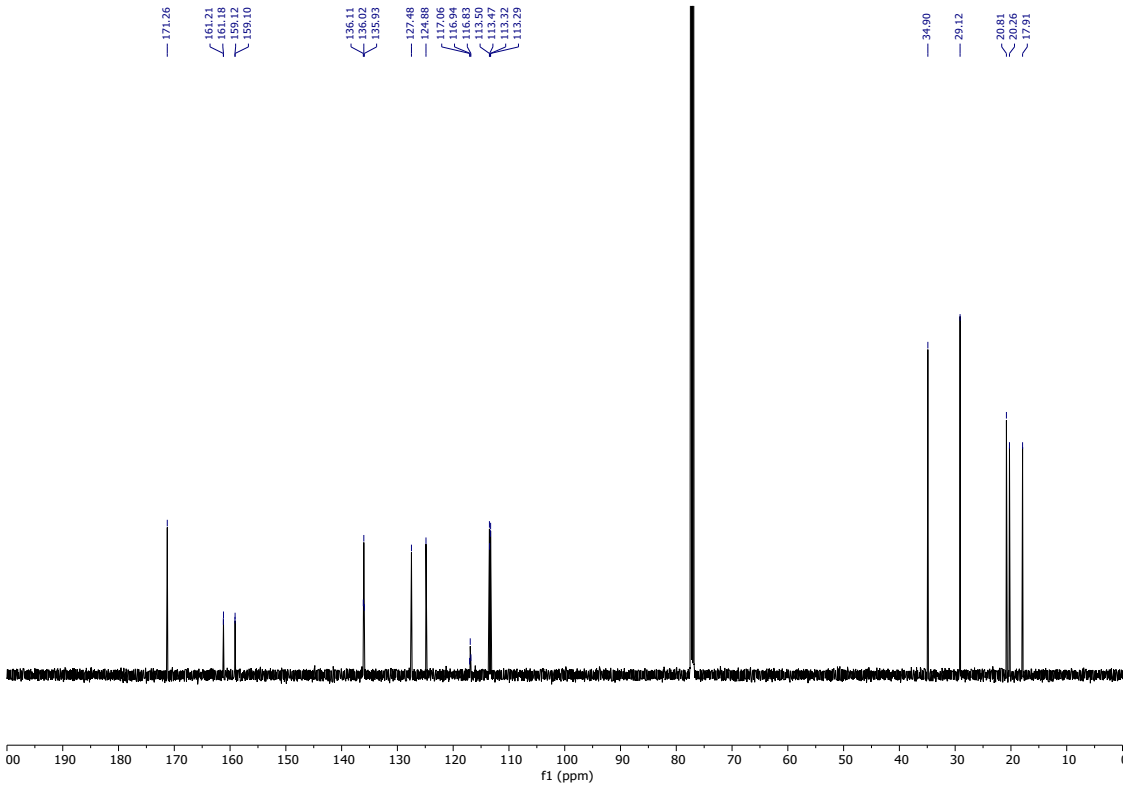
IR (neat) 3242, 3099, 2921, 2864, 1729, 1612, 1589, 1563, 1471, 1427 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{17}F_2NO_3SNa^+$ $[M+Na]^+$: 340.0790, found 340.0785.

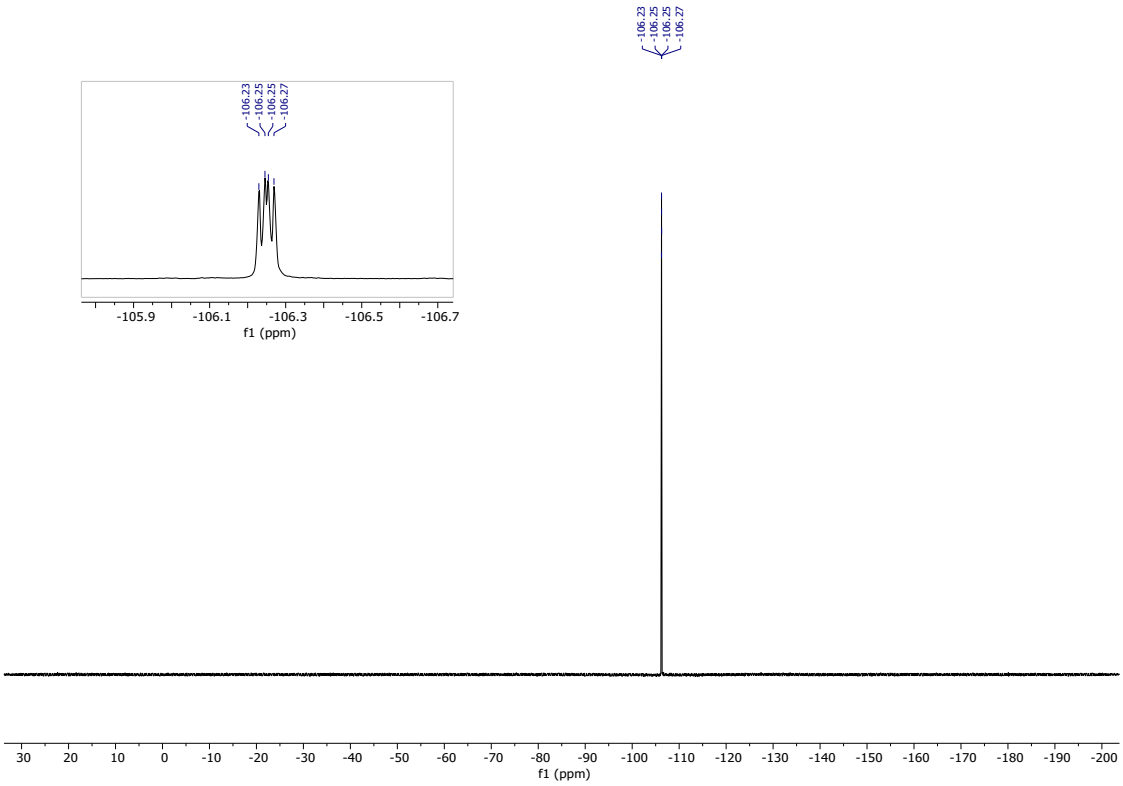
^{1}H NMR – 1ae

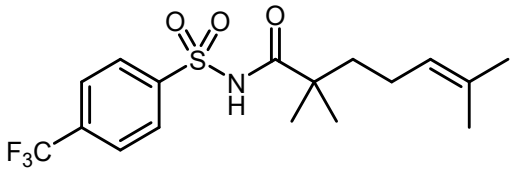


^{13}C NMR – 1ae



^{19}F NMR - 1ae


-106.23
-106.25
-106.25
-106.27
-105.9
-106.1
-106.3
-106.5
-106.7
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1af. 2,2,6-trimethyl-N-((4-(trifluoromethyl)phenyl)sulfonyl)hept-5-enamide. Prepared according to **GP1** with 1.0 mmol 4-trifluoromethylbenzenesulfonamide and 2,2,6-trimethylhept-5-enoic acid. 224 mg, 0.59 mmol, 59% yield. Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.2 Hz, 2H), 8.18 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 2H), 4.95 (t, *J* = 7.2 Hz, 1H), 1.78 – 1.69 (m, 2H), 1.63 (s, 3H), 1.49 – 1.43 (m, 2H), 1.45 (s, 3H), 1.15 (s, 6H).

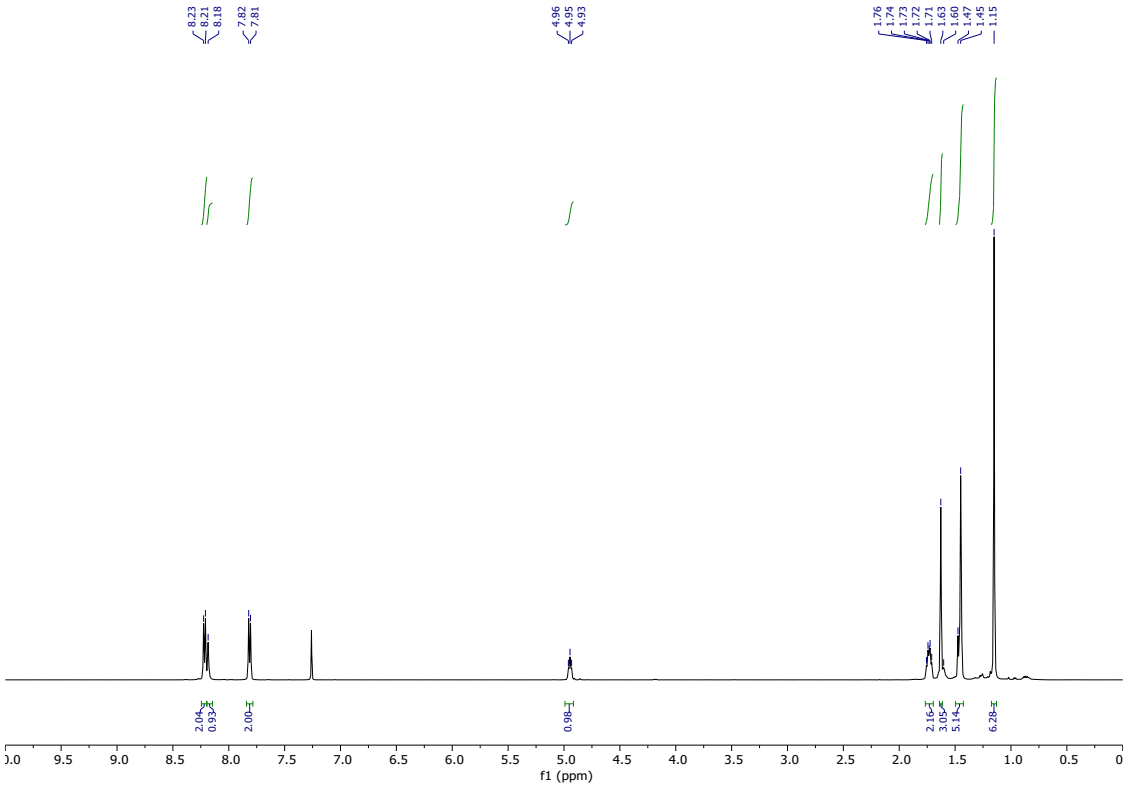
^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 142.0, 135.7 (q, *J* = 33.3 Hz), 132.8, 129.3, 126.3 (q, *J* = 3.5 Hz), 123.2 (q, *J* = 273 Hz), 122.9, 43.7, 41.0, 25.7, 24.7, 23.3, 17.6.

^{19}F NMR (471 MHz, $CDCl_3$) δ -63.32.

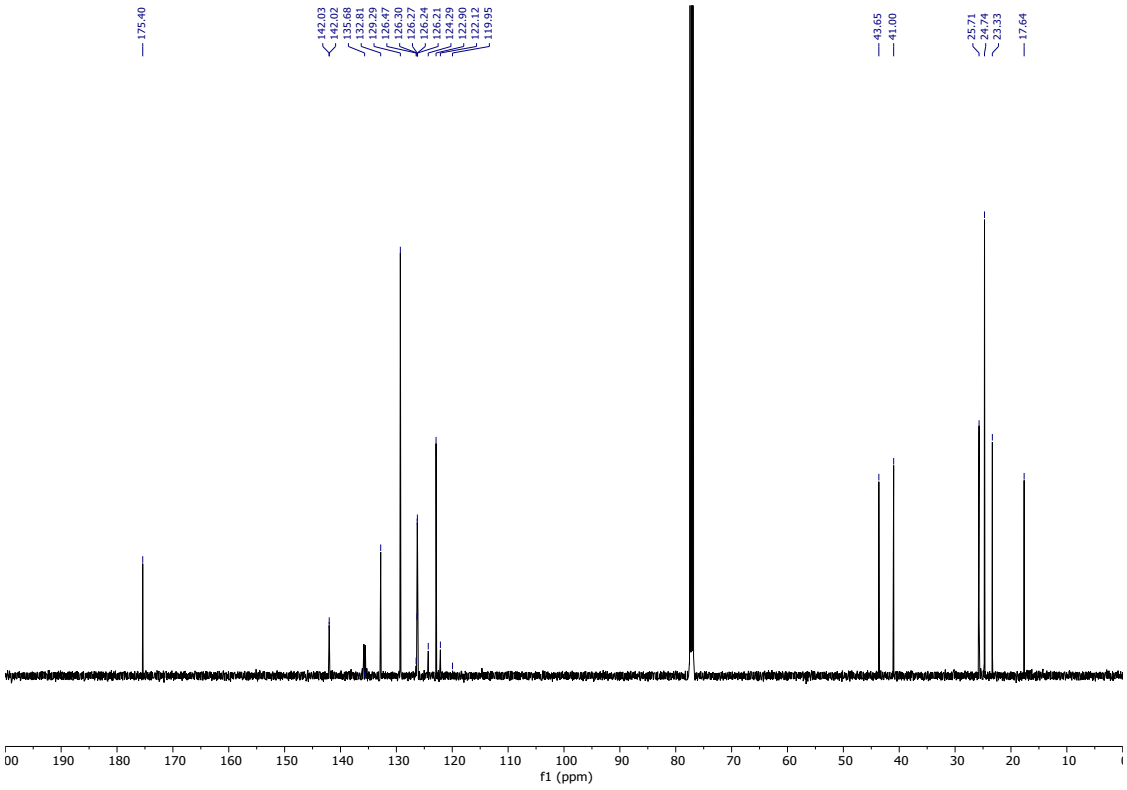
IR (neat) 3280, 2923, 2855, 1713, 1467, 1404, 1344, 1321, 1165, 1128 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{17}H_{22}F_3NO_3SNa^+$ $[M+Na]^+$: 400.1165, found 400.1160.

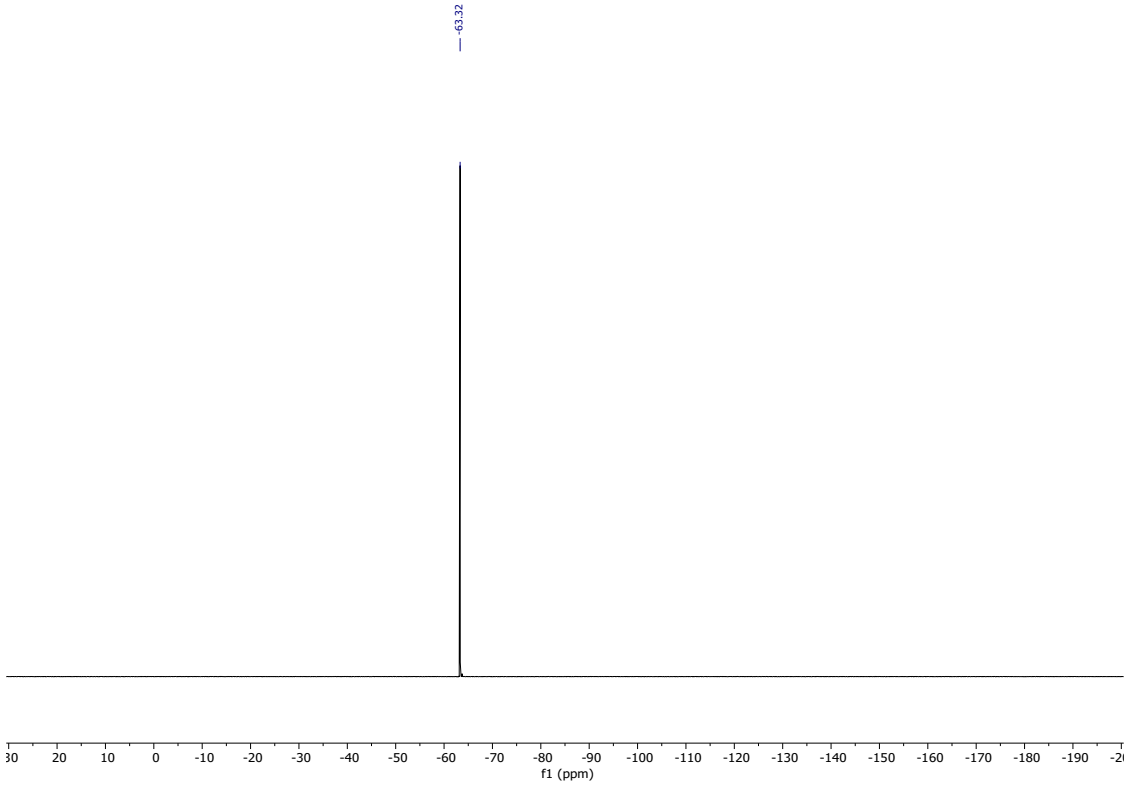
^{1}H NMR – 1af

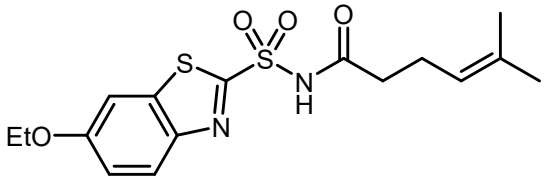


^{13}C NMR – 1af



^{19}F NMR – 1af


-63.32
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)



1ag. N-((6-ethoxybenzo[d]thiazol-2-yl)sulfonyl)-5-methylhex-4-enamide. Prepared according to **GP1** with 0.6 mmol 6-ethoxybenzo[d]thiazole-2-sulfonamide and 5-methylhex-4-enoic acid (87 mg, 0.24 mmol, 39% yield). Colorless solid.

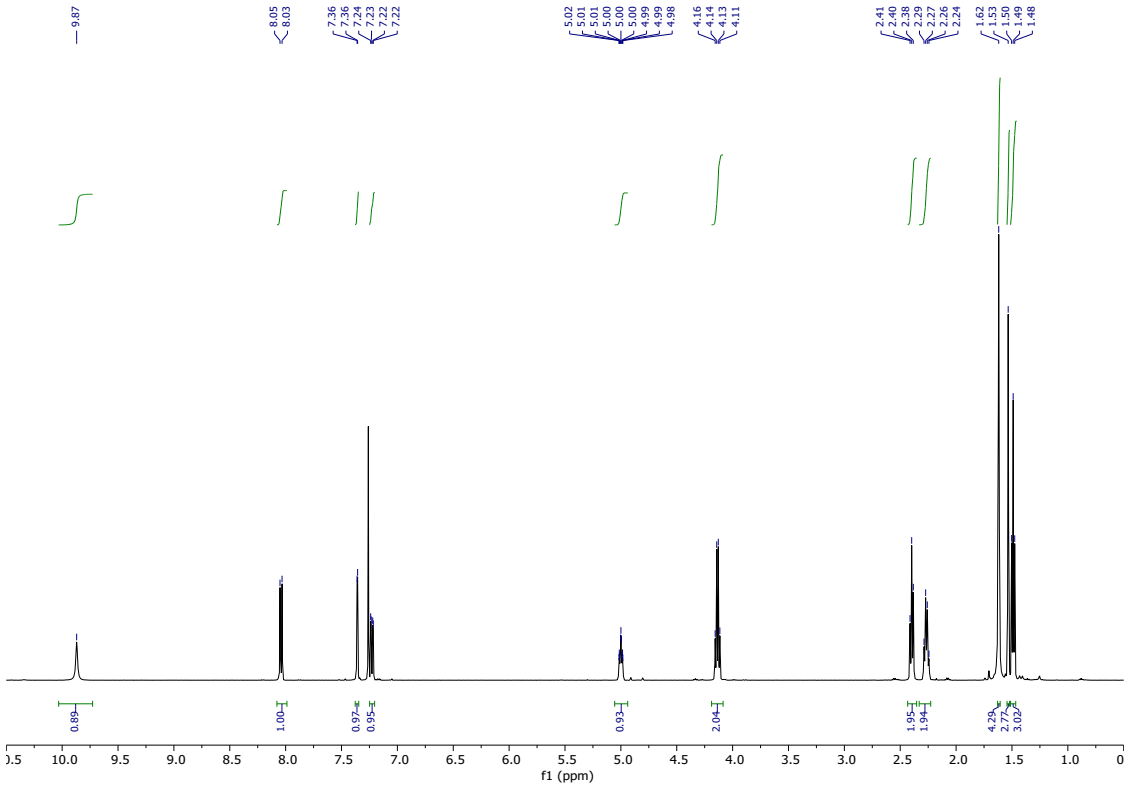
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.36 (d, *J* = 2.4 Hz, 1H), 7.23 (dd, *J* = 9.1, 2.4 Hz, 1H), 5.03 – 4.97 (m, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 2.40 (t, *J* = 7.3 Hz, 2H), 2.27 (q, *J* = 7.4 Hz, 2H), 1.62 (s, 3H), 1.53 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 161.2, 159.6, 146.1, 139.4, 134.6, 125.7, 121.6, 119.2, 104.0, 64.6, 36.5, 25.8, 22.9, 17.8, 14.8.

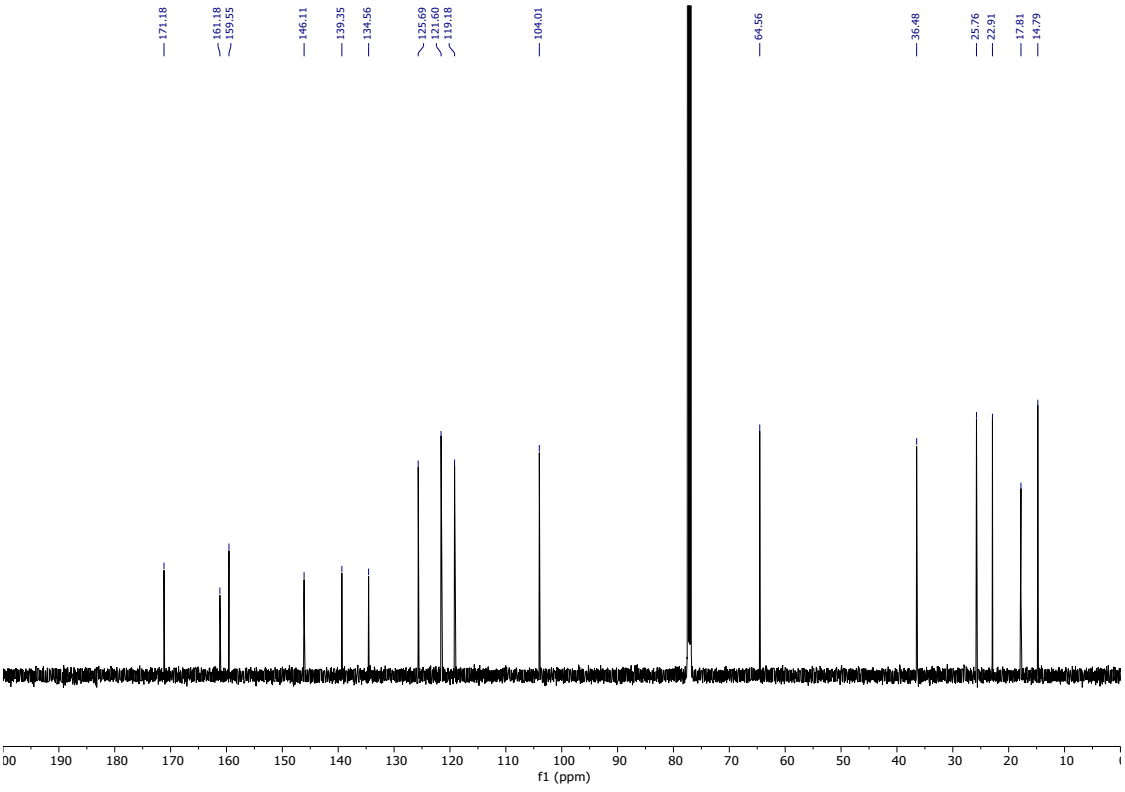
IR (neat) 2988, 2853, 2779, 1725, 1601, 1551, 1482, 1455, 1356, 1262 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{16}H_{20}N_2O_4S_2Na^+$ $[M+Na]^+$: 391.0757, found 391.0752.

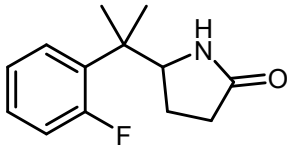
^{1}H NMR – 1ag



^{13}C NMR – 1ag



2b. <u>Characterization data and NMR spectra for Smiles-Truce rearrangement products</u>



2a. 5-(2-(2-fluorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1a**. 20.6 mg, 0.093 mmol, 47% yield. Light brown solid.

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 1H), 7.26 – 7.22 (m, 1H), 7.11 (td, *J* = 7.6, 1.4 Hz, 1H), 7.03 (ddd, *J* = 13.1, 8.0, 1.4 Hz, 1H), 5.41 (br s, 1H), 4.25 (dd, *J* = 8.3, 5.3 Hz, 1H), 2.29 (t, *J* = 8.3 Hz, 2H), 2.06 (dq, *J* = 13.5, 8.2 Hz, 1H), 1.82 (dtd, *J* = 13.6, 8.3, 5.4 Hz, 1H), 1.38 (d, *J* = 1.0 Hz, 3H), 1.36 (s, 3H).

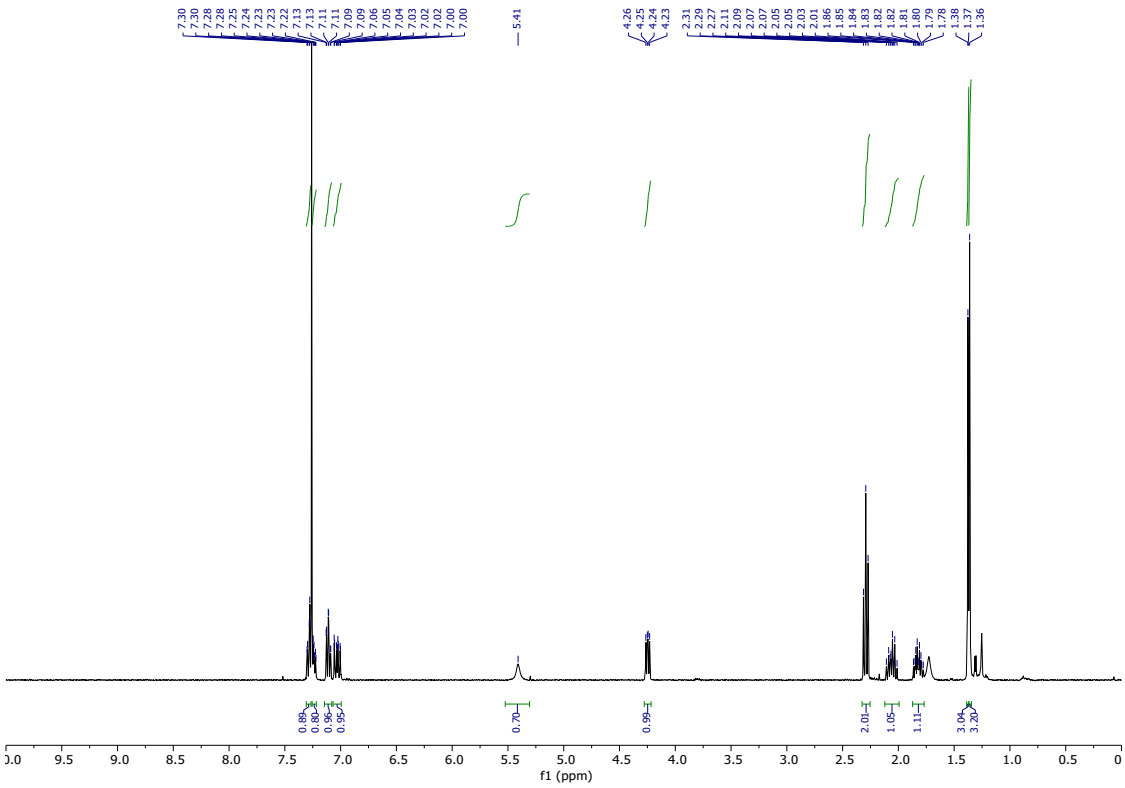
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.3, 161.7 (d, *J* = 248 Hz), 132.5 (d, *J* = 10.9 Hz), 129.0 (d, *J* = 9.1 Hz), 128.6 (d, *J* = 5.7 Hz), 124.4 (d, *J* = 3.2 Hz), 116.9 (d, *J* = 24.8 Hz), 60.6 (d, *J* = 5.0 Hz), 41.6 (d, *J* = 4.6 Hz), 30.4, 23.0 (d, *J* = 2.8 Hz), 22.8 (d, *J* = 4.2 Hz), 22.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ -107.91 – -108.06 (m).

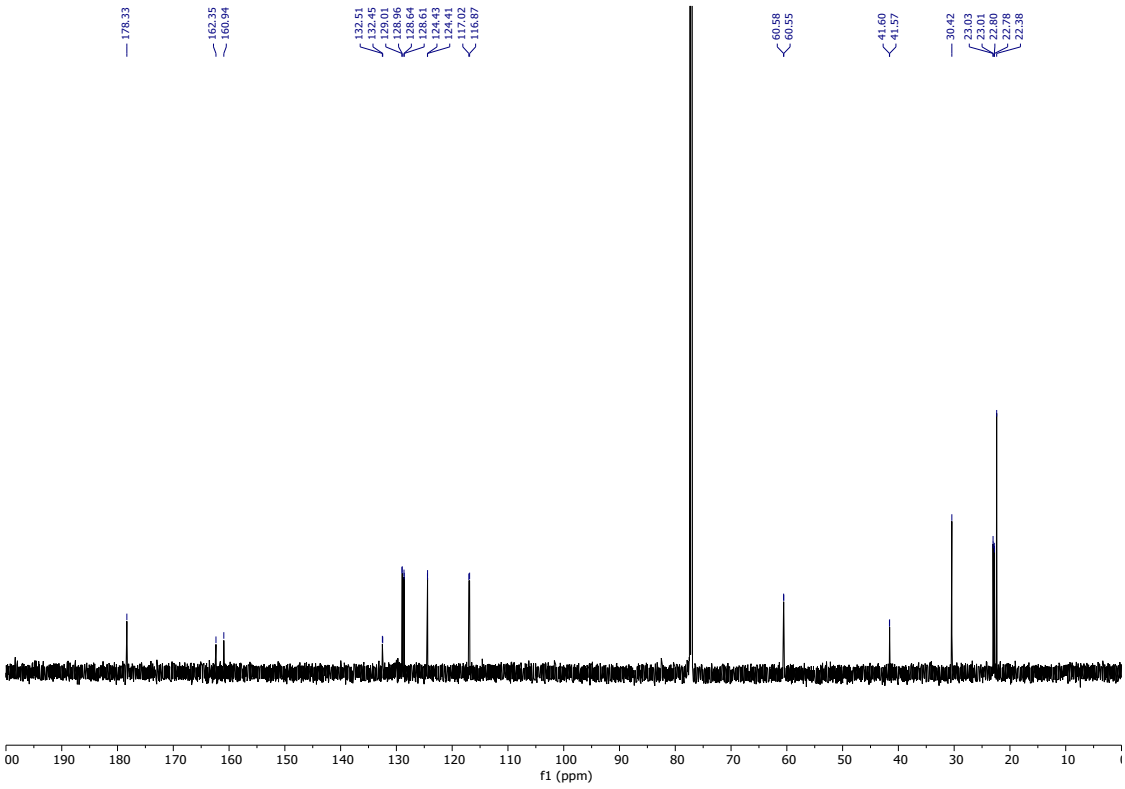
IR (neat) 3174, 3079, 2966, 1694, 1682, 1490, 1446, 1386, 1344, 1313 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{17}FNO^+$ $[M+H]^+$: 222.1289, found 222.1289.

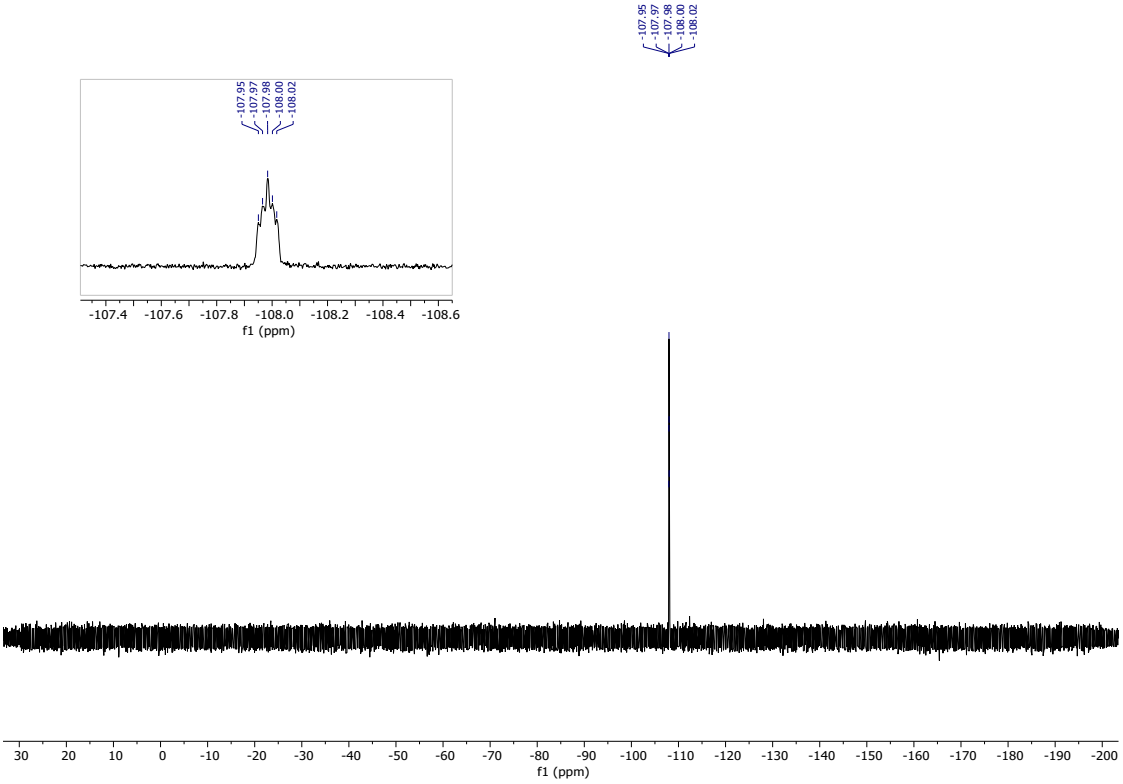
^{1}H NMR – 2a

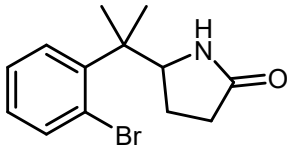


^{13}C NMR – 2a



^{19}F NMR – 2a


-107.95
-107.97
-107.98
-108.00
-108.02
-107.4
-107.6
-107.8
-108.0
-108.2
-108.4
-108.6
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2b. 5-(2-(2-bromophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1b**. 29.1 mg, 0.103 mmol, 52% yield. Light brown solid.

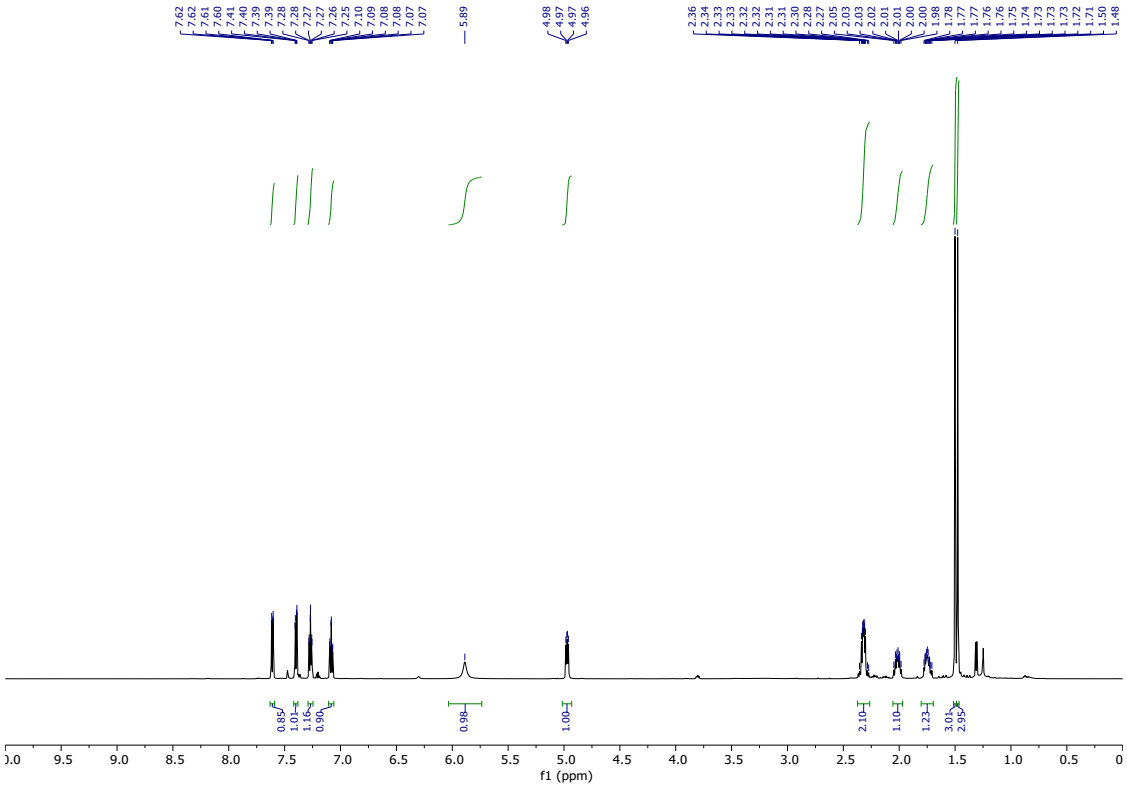
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.40 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.11 – 7.06 (m, 1H), 5.89 (br s, 1H), 4.97 (dd, *J* = 8.4, 5.3 Hz, 1H), 2.37 – 2.26 (m, 2H), 2.06 – 1.97 (m, 1H), 1.80 – 1.70 (m, 1H), 1.50 (s, 3H), 1.48 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.5, 143.8, 136.5, 129.8, 128.6, 127.7, 122.0, 58.2, 43.5, 30.6, 23.5, 22.8, 22.2.

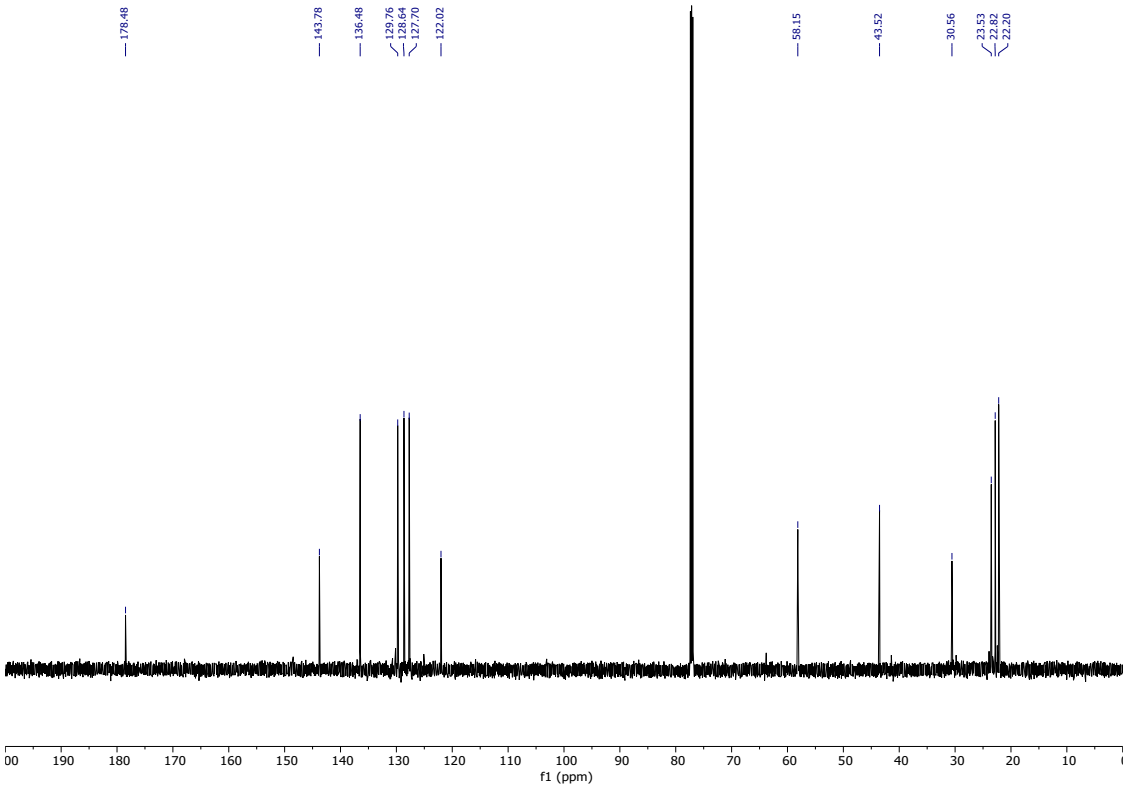
IR (neat) 3186, 2970, 2924, 2853, 1687, 1592, 1465, 1421, 1381, 1346 cm^{-1}

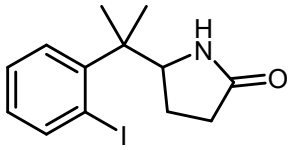
HRMS (ESI+) m/z calculated for $C_{13}H_{17}BrNO^+$ $[M+H]^+$: 282.0488, found 282.0489.

^{1}H NMR – 2b



^{13}C NMR – 2b





2c. 5-(2-(2-iodophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1c**. 28.0 mg, 0.085 mmol, 43% yield. Light brown solid.

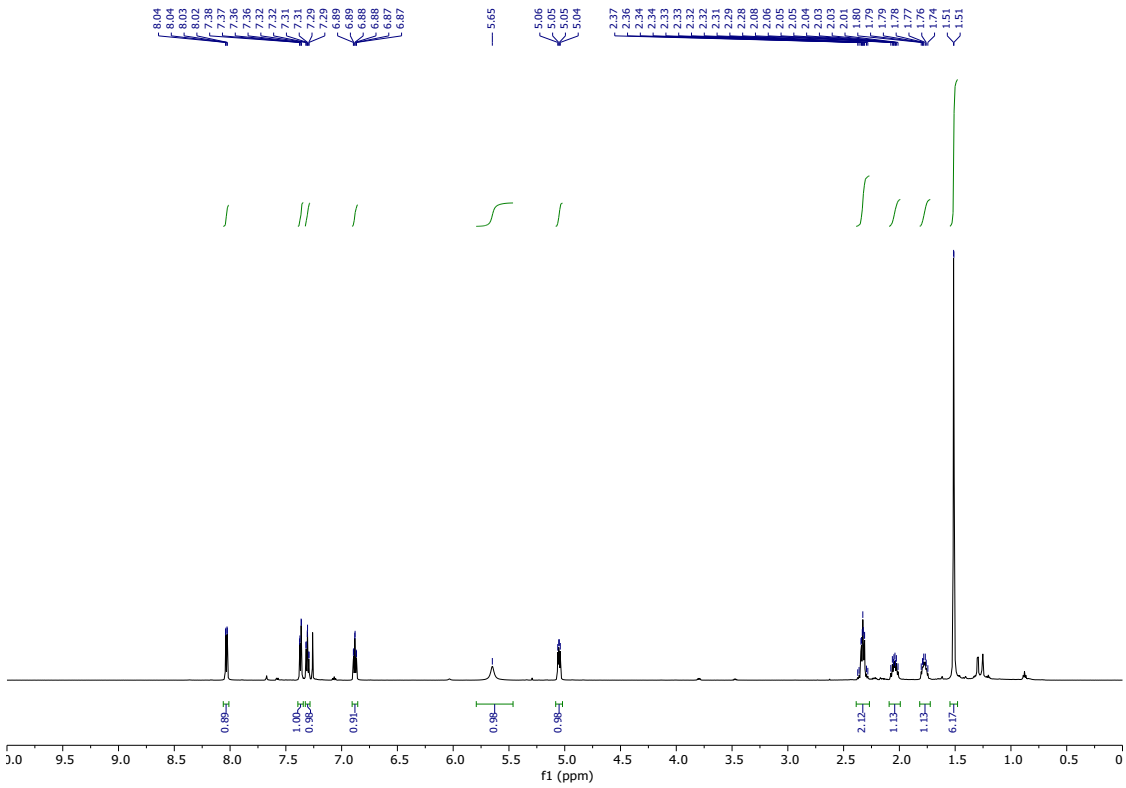
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.37 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.31 (td, *J* = 7.6, 1.5 Hz, 1H), 6.88 (td, *J* = 7.5, 1.7 Hz, 1H), 5.65 (br s, 1H), 5.05 (dd, *J* = 8.4, 5.3 Hz, 1H), 2.39 – 2.27 (m, 2H), 2.09 – 1.99 (m, 1H), 1.82 – 1.72 (m, 1H), 1.51 (app d, *J* = 2.3 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.3, 146.3, 144.5, 129.6, 128.8, 128.4, 94.0, 58.1, 43.0, 30.6, 23.6, 23.1, 22.1.

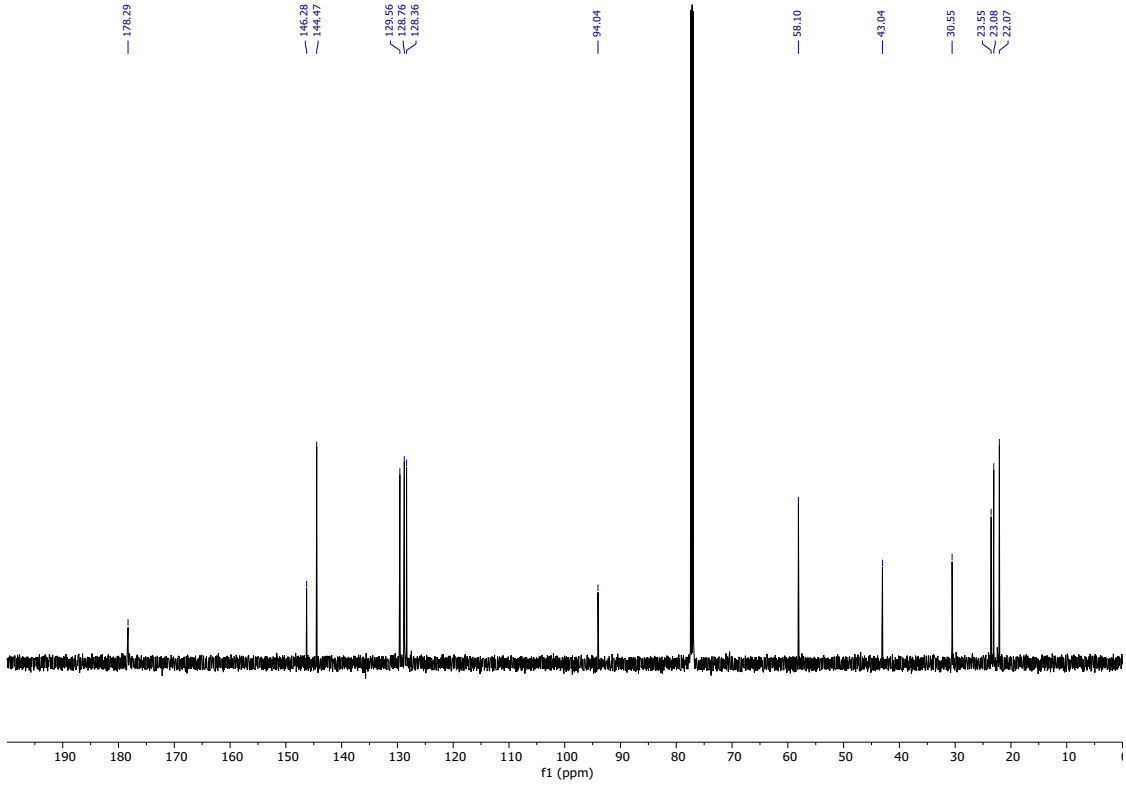
IR (neat) 3176, 3074, 2976, 2924, 1686, 1462, 1419, 1382, 1346, 1316 cm^{-1}

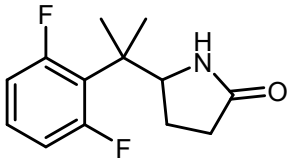
HRMS (ESI+) m/z calculated for $C_{13}H_{17}INO^+$ $[M+H]^+$: 330.0349, found 330.0345.

^{1}H NMR – 2c



^{13}C NMR – 2c





2d. 5-(2-(2,6-difluorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1d**. 30.4 mg, 0.127 mmol, 64% yield. Light brown solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.17 (tt, *J* = 8.2, 5.9 Hz, 1H), 6.83 (dd, *J* = 11.3, 8.3 Hz, 2H), 6.52 (br s, 1H), 4.20 (dd, *J* = 8.3, 5.0 Hz, 1H), 2.33 – 2.23 (m, 2H), 2.07 – 2.00 (m, 1H), 1.87 – 1.80 (m, 1H), 1.49 (t, *J* = 2.5 Hz, 3H), 1.47 (t, *J* = 3.2 Hz, 3H).

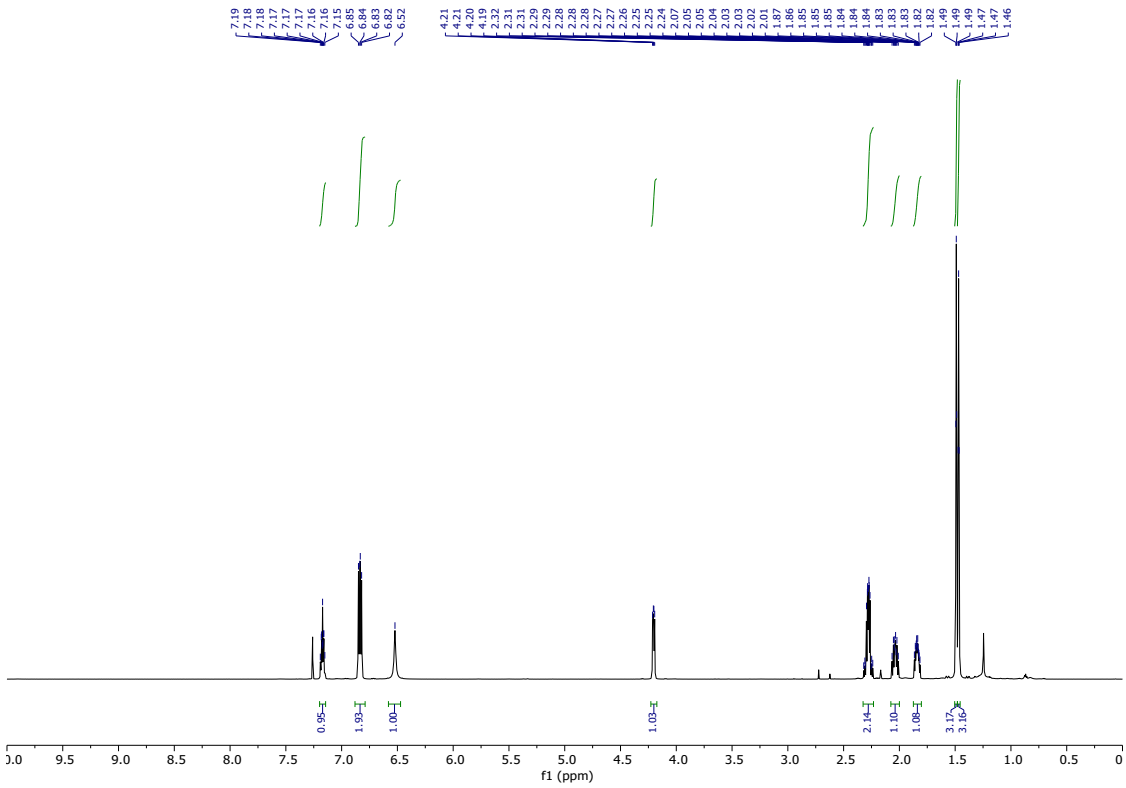
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.7, 162.0 (dd, *J* = 249, 9.9 Hz), 128.5 (t, *J* = 12.0 Hz), 120.5 (t, *J* = 14.3 Hz), 112.9 (dd, *J* = 26.1, 4.4 Hz), 61.1 (t, *J* = 3.6 Hz), 43.1 (t, *J* = 4.3 Hz), 30.3, 25.4 (t, *J* = 6.2 Hz), 23.4 (t, *J* = 7.2 Hz), 22.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -104.37 – -104.49 (m).

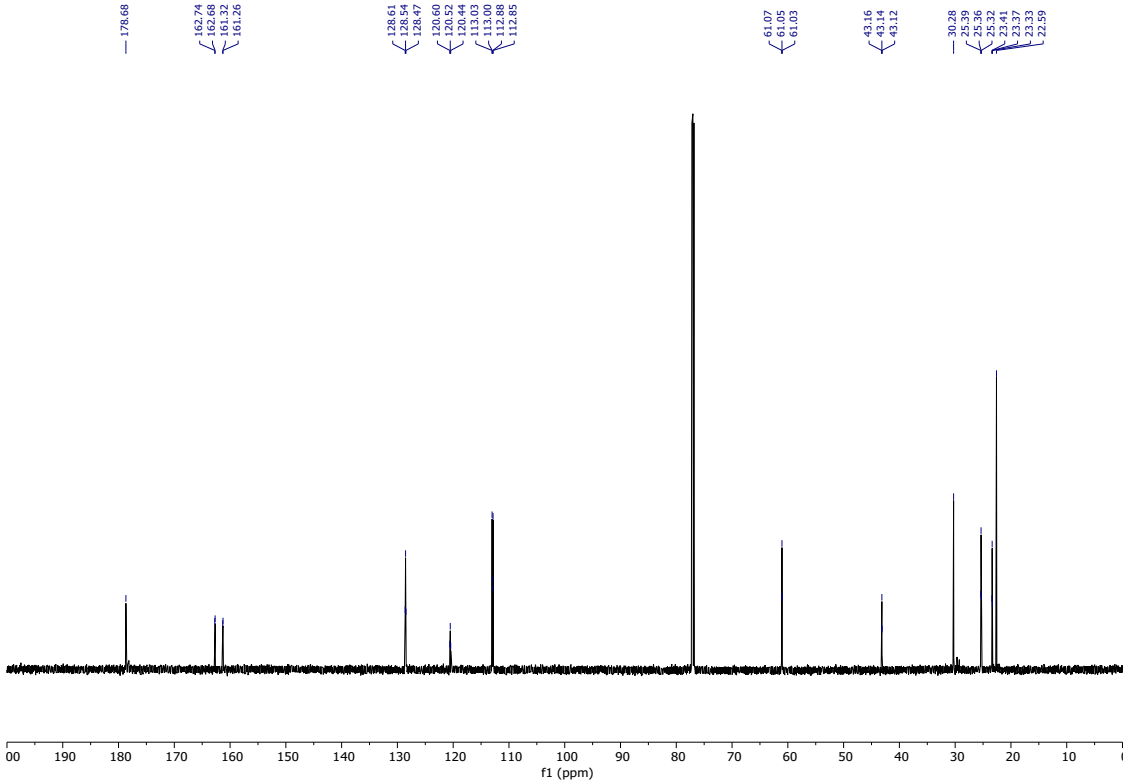
IR (neat) 3187, 3094, 2987, 1684, 1684, 1619, 1573, 1461, 1446, 1423, 1350 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{16}F_2NO^+$ $[M+H]^+$: 240.1194, found 240.1203.

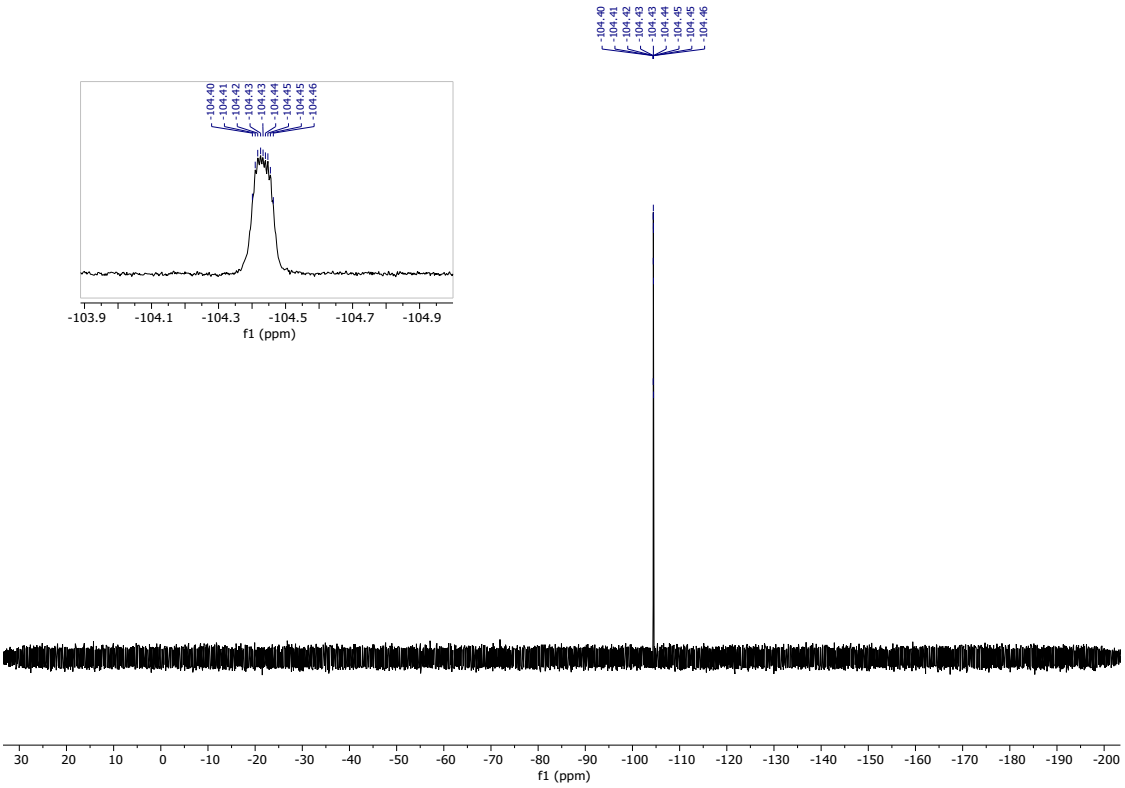
^{1}H NMR – 2d

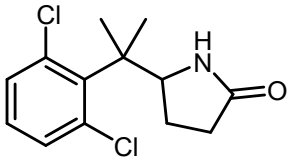


^{13}C NMR – 2d



^{19}F NMR – 2d


-104.40
-104.41
-104.42
-104.43
-104.43
-104.44
-104.45
-104.45
-104.46
-103.9
-104.1
-104.3
-104.5
-104.7
-104.9
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2e. 5-(2-(2,6-dichlorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1e**. (30.4 mg, 0.112 mmol, 56% yield. Light brown solid.

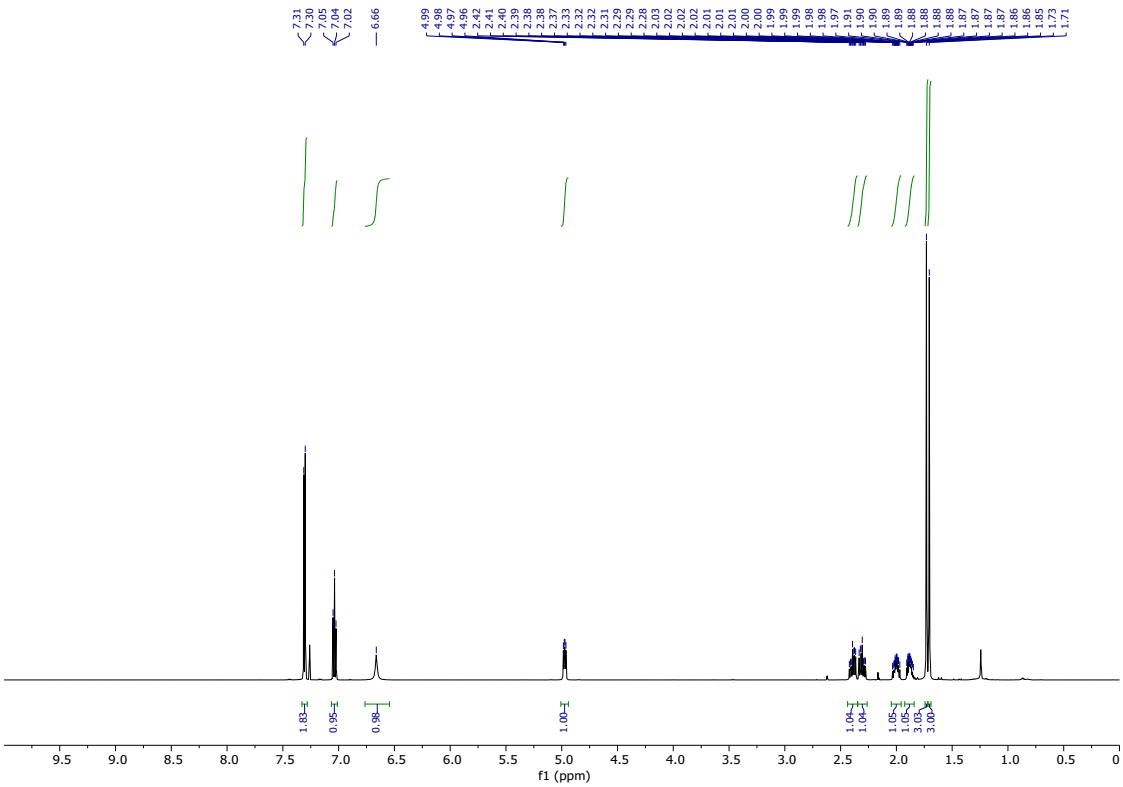
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.9 Hz, 2H), 7.04 (t, *J* = 7.9 Hz, 1H), 6.66 (s, 1H), 4.97 (dd, *J* = 8.5, 5.1 Hz, 1H), 2.39 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H), 2.31 (ddd, *J* = 17.2, 10.4, 6.4 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.93 – 1.84 (m, 1H), 1.73 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 179.0, 140.1, 136.1, 132.5, 128.1, 58.9, 47.1, 30.7, 27.1, 26.3, 22.6.

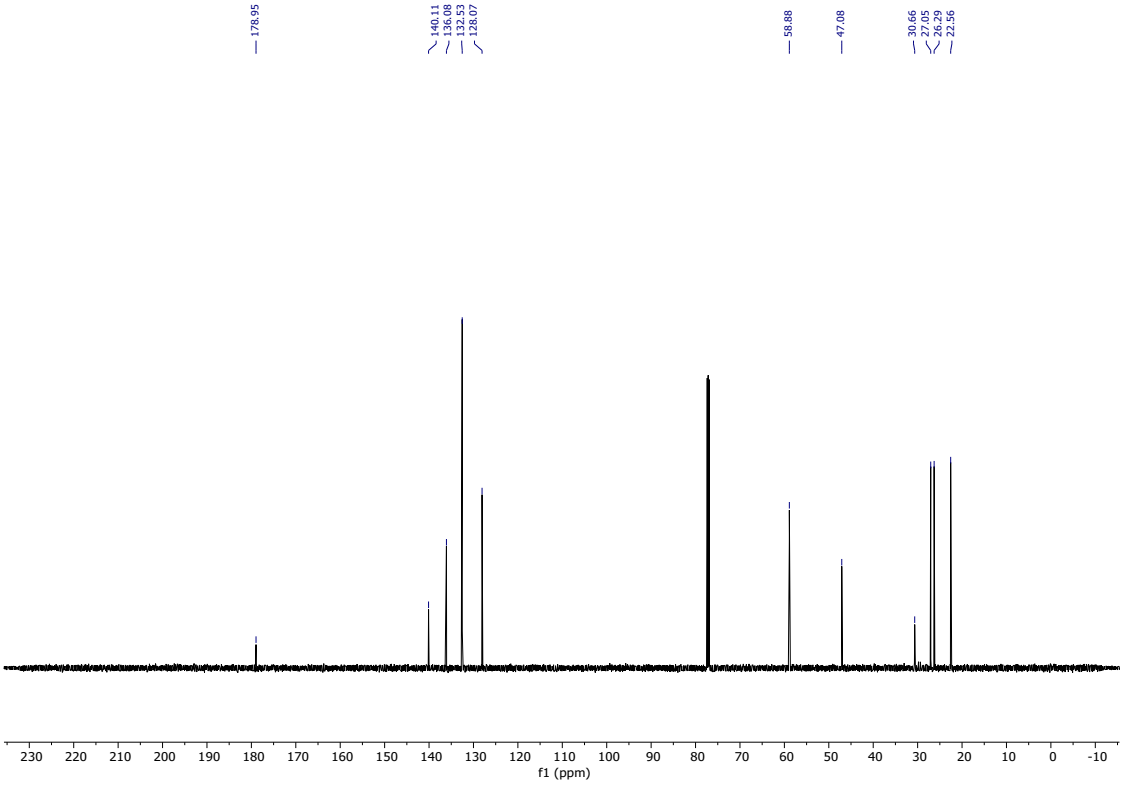
IR (neat) 3182, 3088, 2923, 1689, 1576, 1553, 1470, 1418, 1385, 1346 cm^{-1}

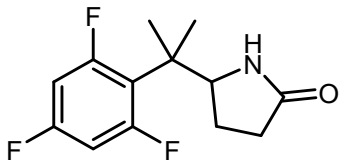
HRMS (ESI+) m/z calculated for $C_{13}H_{16}Cl_2NO^+$ $[M+H]^+$: 272.0604, found 272.0608.

^{1}H NMR – 2e



^{13}C NMR – 2e





2f. 5-(2-(2,4,6-trifluorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1f**. 21.7 mg, 0.084 mmol, 42% yield. Light yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.74 – 6.49 (m, 3H), 4.15 (dd, *J* = 8.4, 5.0 Hz, 1H), 2.35 – 2.25 (m, 2H), 2.05 (dq, *J* = 13.5, 8.4 Hz, 1H), 1.86 – 1.78 (m, 1H), 1.47 (t, *J* = 2.6 Hz, 3H), 1.45 (t, *J* = 3.3 Hz, 3H).

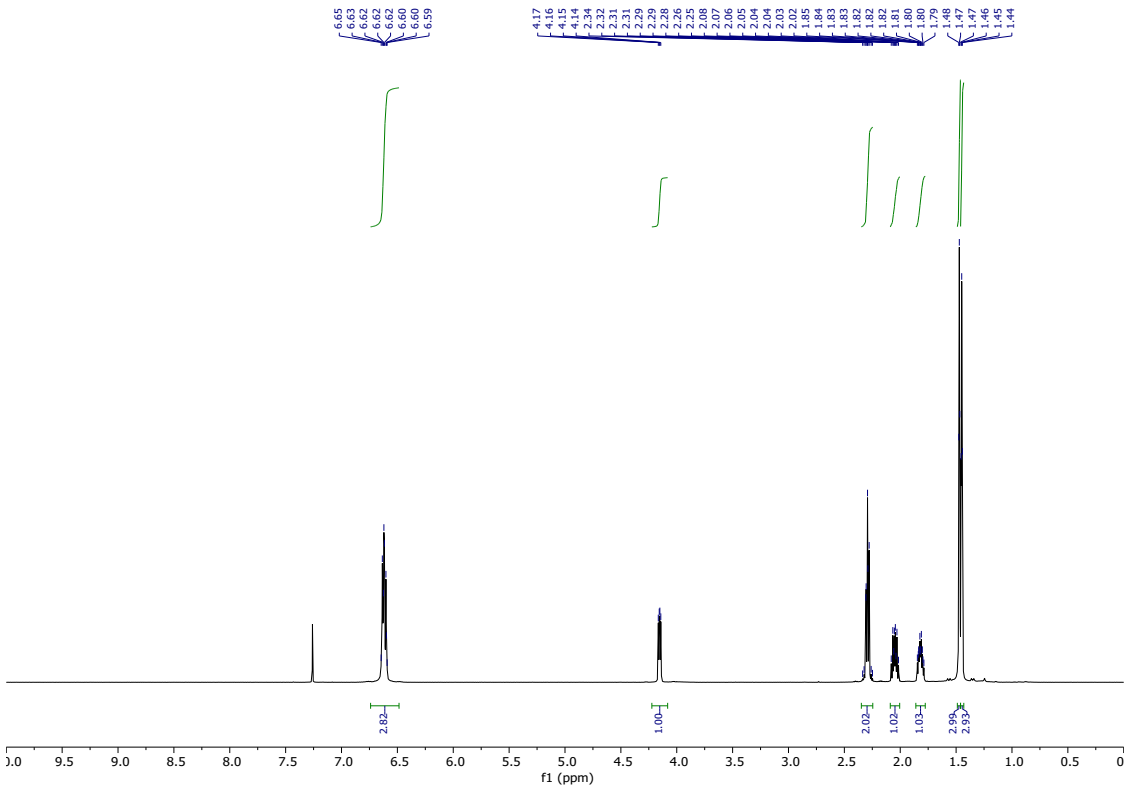
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.9, 162.4 (ddd, *J* = 251, 14.0, 13.1 Hz), 161.4 (dt, *J* = 250, 17.5 Hz), 117.0 (td, *J* = 14.8, 5.3 Hz), 101.6 (ddd, *J* = 32.6, 24.5, 2.9 Hz), 61.3 (t, *J* = 3.0 Hz), 43.2, (t, *J* = 4.4 Hz), 30.4, 25.6 (t, *J* = 6.1 Hz), 23.4 (t, *J* = 7.2 Hz), 22.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -101.11 (m, 2F), -110.68 (p, *J* = 7.9 Hz, 1F).

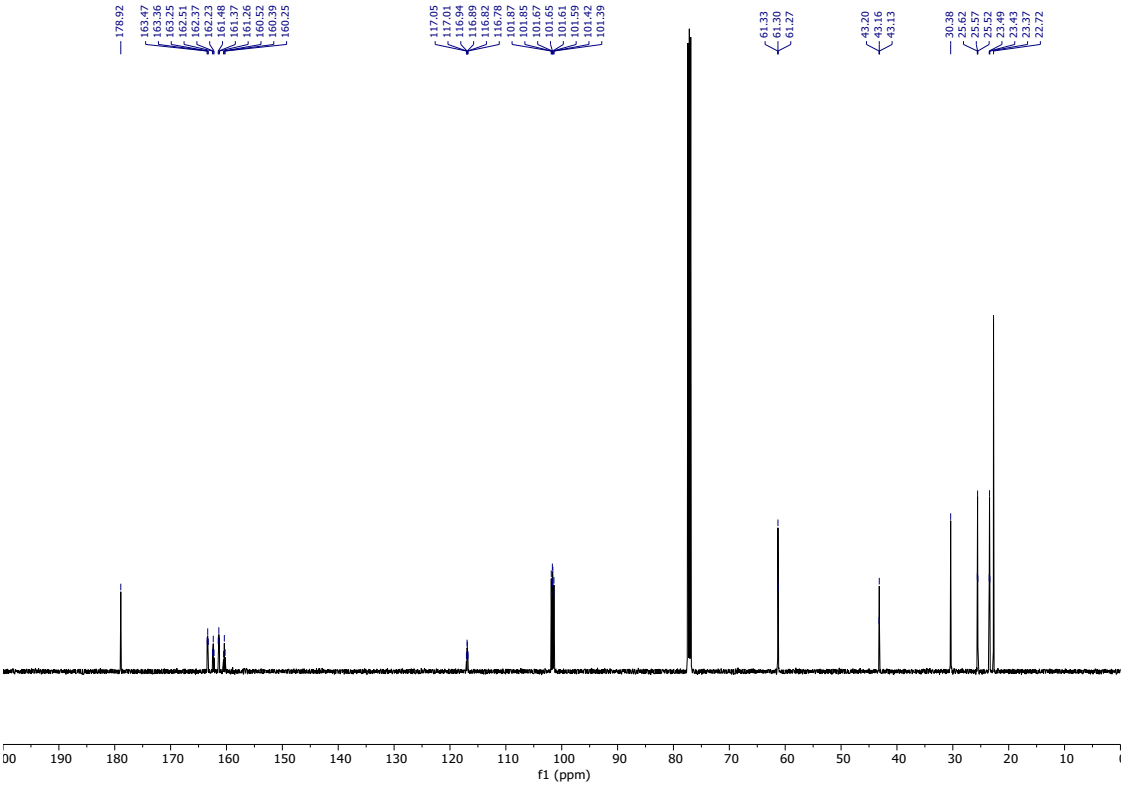
IR (neat) 3173, 3083, 2924, 2855, 1701, 1686, 1623, 1594, 1481, 1424 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{15}F_3NO^+$ $[M+H]^+$: 258.1101, found 258.1097.

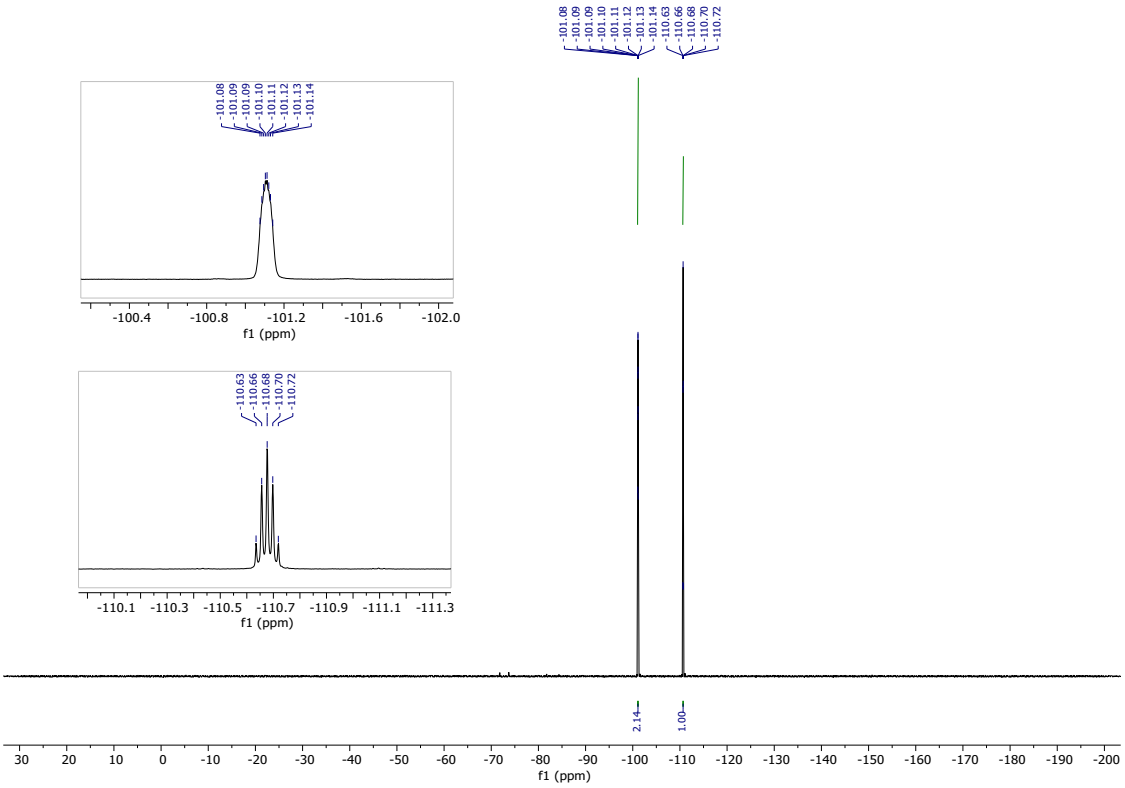
^{1}H NMR – 2f

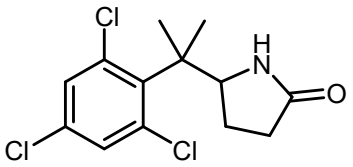


^{13}C NMR – 2f



^{19}F NMR – 2f


-101.08
-101.09
-101.09
-101.10
-101.11
-101.12
-101.13
-101.14
-110.63
-110.66
-110.68
-110.70
-110.72
-100.4
-100.8
-101.2
-101.6
-102.0
f1 (ppm)
-110.1
-110.3
-110.5
-110.7
-110.9
-111.1
-111.3
f1 (ppm)
2.14
1.00
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2g. 5-(2-(2,4,6-trichlorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1g**. 35.4 mg, 0.115 mmol, 58% yield. Colorless solid.

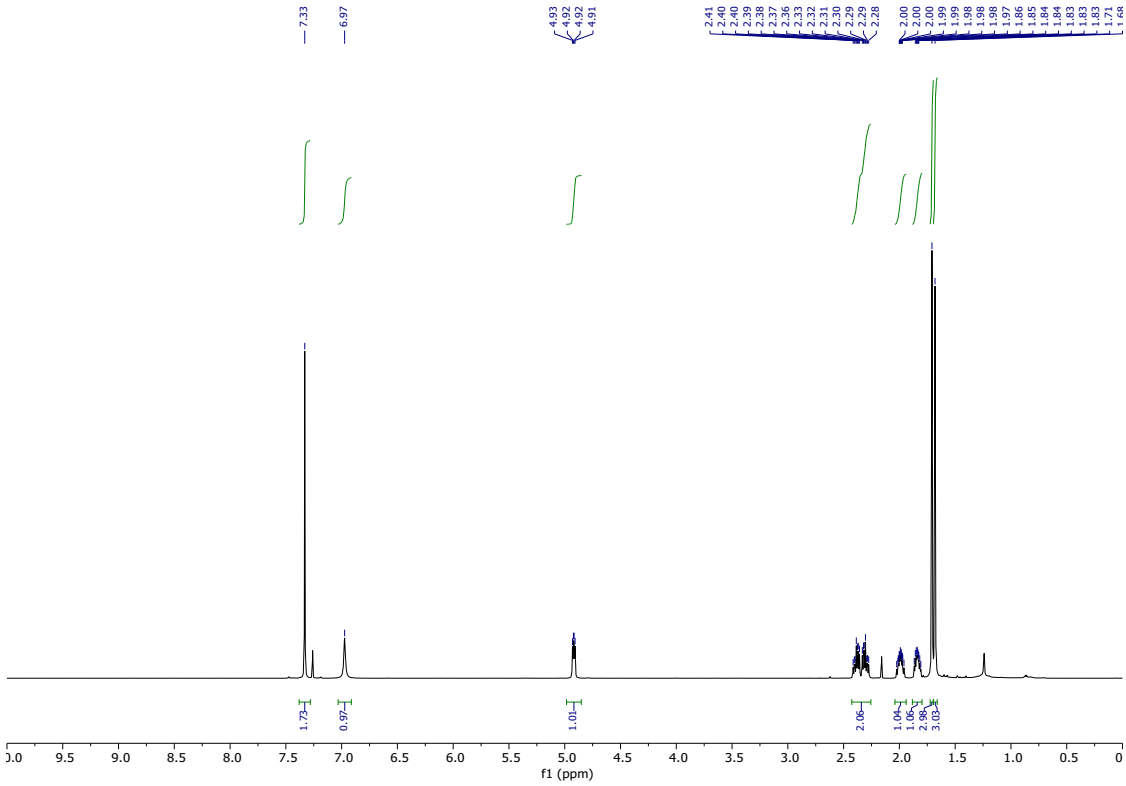
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (s, 2H), 6.97 (br s, 1H), 4.92 (dd, *J* = 8.6, 5.1 Hz, 1H), 2.43 – 2.26 (m, 2H), 2.04 – 1.94 (m, 1H), 1.88 – 1.80 (m, 1H), 1.71 (s, 3H), 1.68 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 179.1, 138.9, 136.6, 132.8, 132.0, 58.8, 47.1, 27.1, 26.1, 22.6.

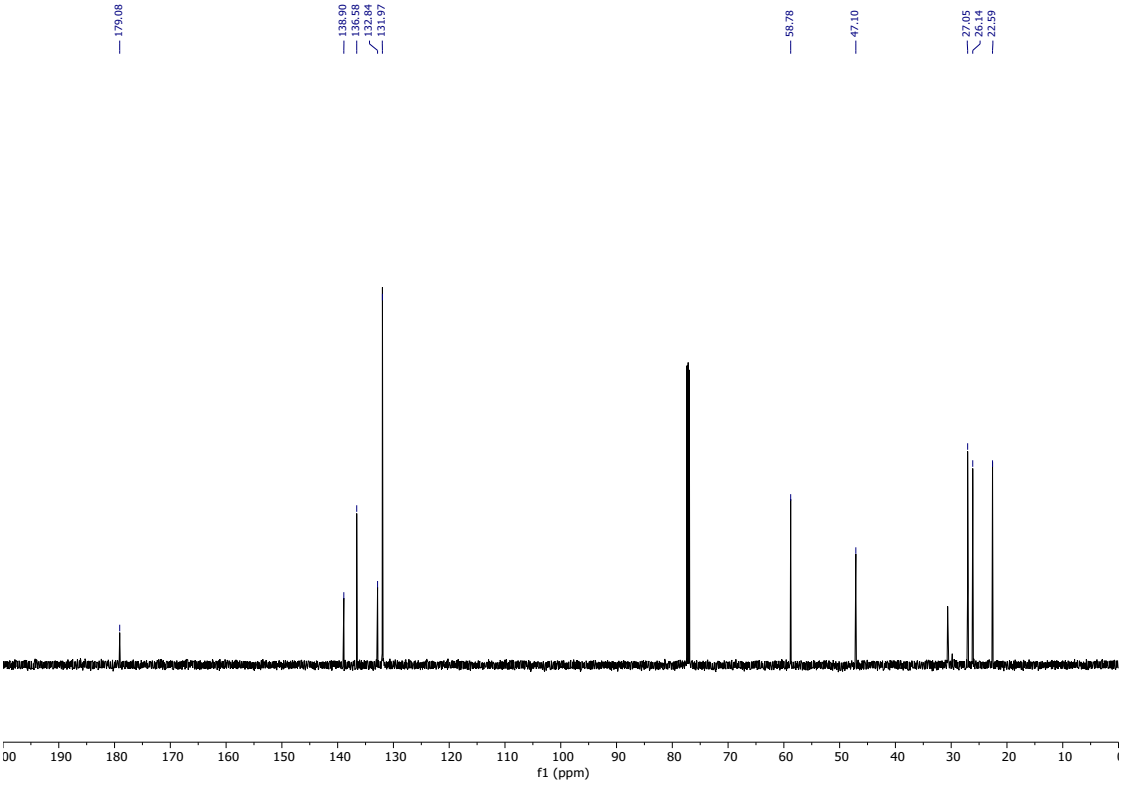
IR (neat) 3158, 3075, 2924, 1692, 1573, 1538, 1471, 1387, 1361, 1315 cm^{-1}

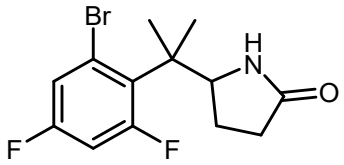
HRMS (ESI+) m/z calculated for $C_{13}H_{15}Cl_3NO^+$ $[M+H]^+$: 306.0214, found 306.0215.

^{1}H NMR – 2g



^{13}C NMR – 2g





2h. 5-(2-(2-bromo-4,6-difluorophenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1h**. 14.6 mg, 0.046 mmol, 23% yield. Brown solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (ddd, *J* = 7.7, 2.9, 1.9 Hz, 1H), 6.78 (ddd, *J* = 14.1, 7.9, 2.9 Hz, 1H), 6.36 (br s, 1H), 4.70 (dd, *J* = 8.5, 5.0 Hz, 1H), 2.41 – 2.28 (m, 2H), 2.03 (dddd, *J* = 13.5, 10.4, 8.5, 6.6 Hz, 1H), 1.87 – 1.79 (m, 1H), 1.62 (d, *J* = 3.6 Hz, 3H), 1.57 (d, *J* = 5.5 Hz, 3H).

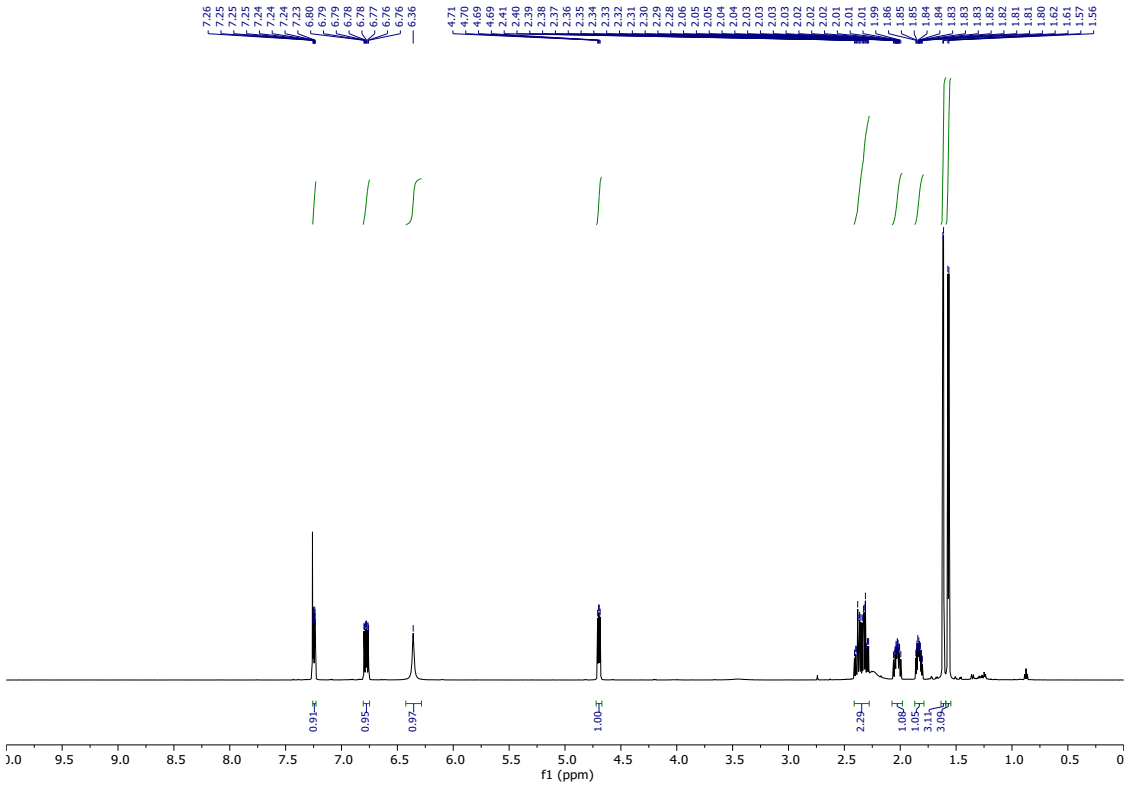
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.9, 162.8 (dd, *J* = 254, 11.9 Hz), 160.6 (dd, *J* = 252, 16.1 Hz), 127.9 (dd, *J* = 12.5, 5.1 Hz), 123.2 (dd, *J* = 10.9, 8.6 Hz), 120.4 (dd, *J* = 23.4, 3.4 Hz), 105.4 (dd, *J* = 33.5, 23.7 Hz), 59.5, 45.0 (d, *J* = 4.8 Hz), 30.5, 26.0 (d, *J* = 7.8 Hz), 24.5 (d, *J* = 10.6 Hz), 22.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.22 (m, 1F), -112.81 (q, *J* = 8.2 Hz, 1F).

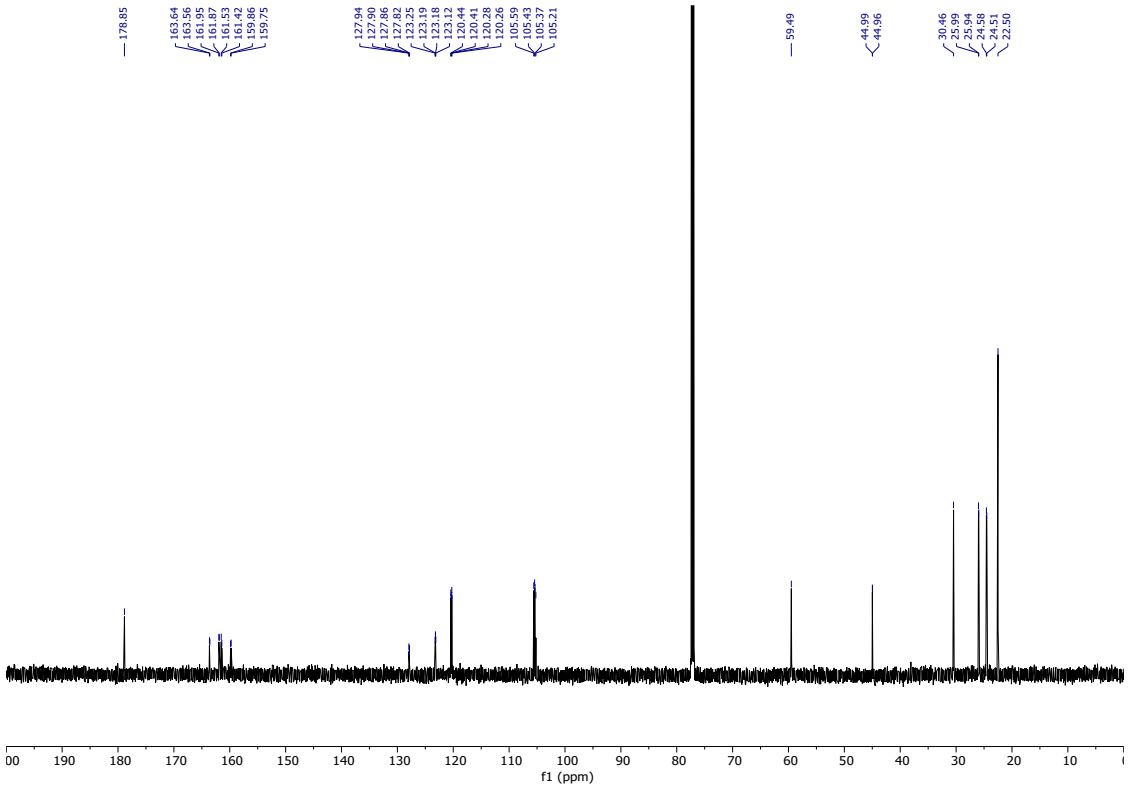
IR (neat) 3182, 3069, 1686, 1606, 1581, 1442, 1403, 1348, 1272, 1166 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{15}BrF_2NO^+$ $[M+H]^+$: 318.0300, found 318.0300.

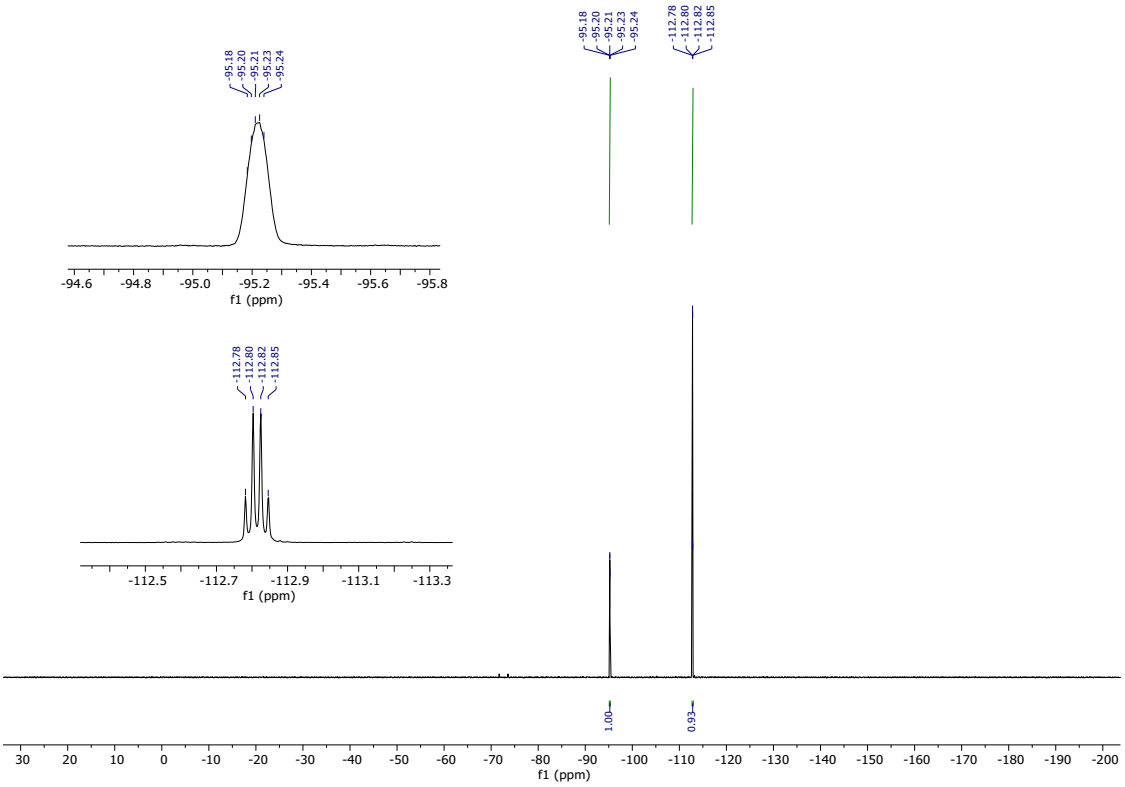
^{1}H NMR – 2h

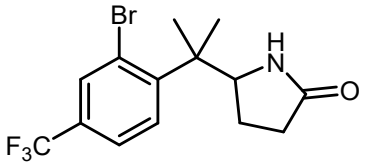


^{13}C NMR – 2h



^{19}F NMR – 2h


-95.18
-95.20
-95.21
-95.23
-95.24
-112.78
-112.80
-112.82
-112.85
-94.6
-94.8
-95.0
-95.2
-95.4
-95.6
-95.8
f1 (ppm)
-112.5
-112.7
-112.9
-113.1
-113.3
f1 (ppm)
1.00
0.93
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2i. 5-(2-(2-bromo-4-(trifluoromethyl)phenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1i**. 35.2 mg, 0.101 mmol, 50% yield. Colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.53 (app s, 2H), 6.67 (br s, 1H), 4.98 (dd, *J* = 8.5, 5.2 Hz, 1H), 2.36 – 2.26 (m, 2H), 2.02 – 1.93 (m, 1H), 1.69 – 1.61 (m, 1H), 1.56 (s, 3H), 1.47 (s, 3H).

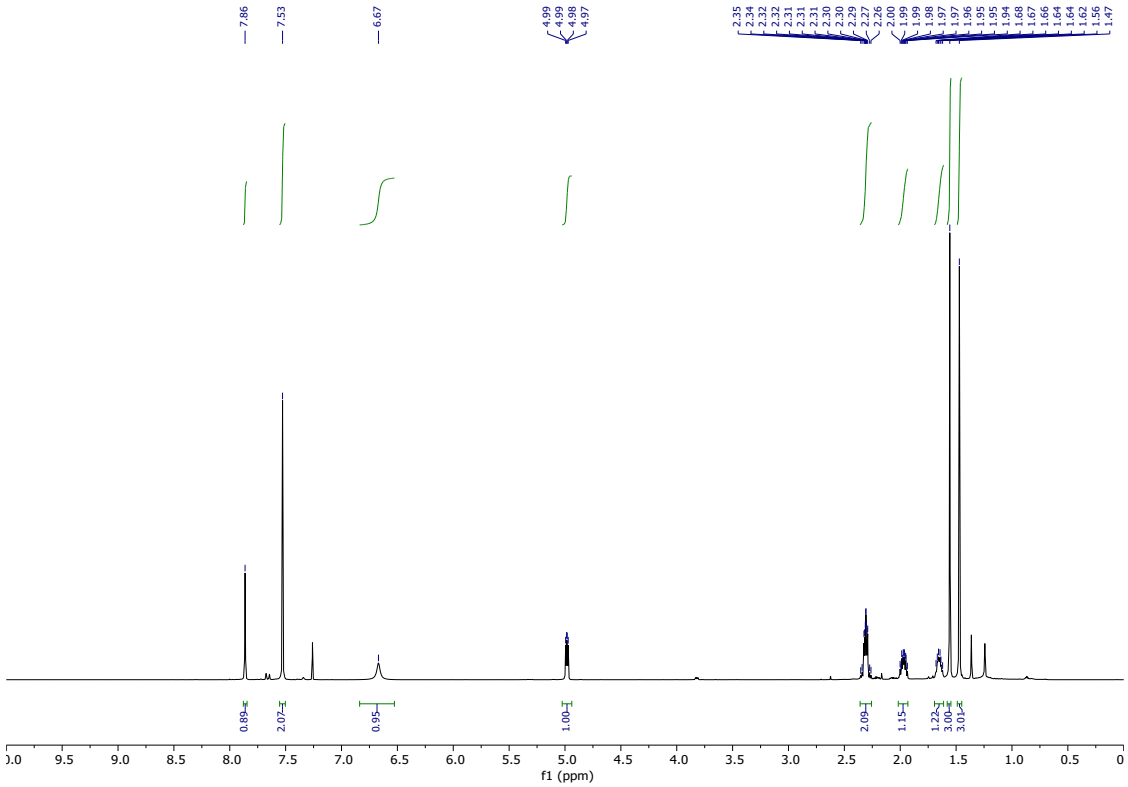
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.8, 148.1, 133.2 (q, *J* = 3.8 Hz), 130.7 (q, *J* = 33.5 Hz), 130.2, 124.4 (q, *J* = 3.7 Hz), 123.1 (q, *J* = 272 Hz), 122.1, 57.9, 44.1, 30.5, 23.7, 22.5, 22.3.

^{19}F NMR (564 MHz, $CDCl_3$) δ -62.85.

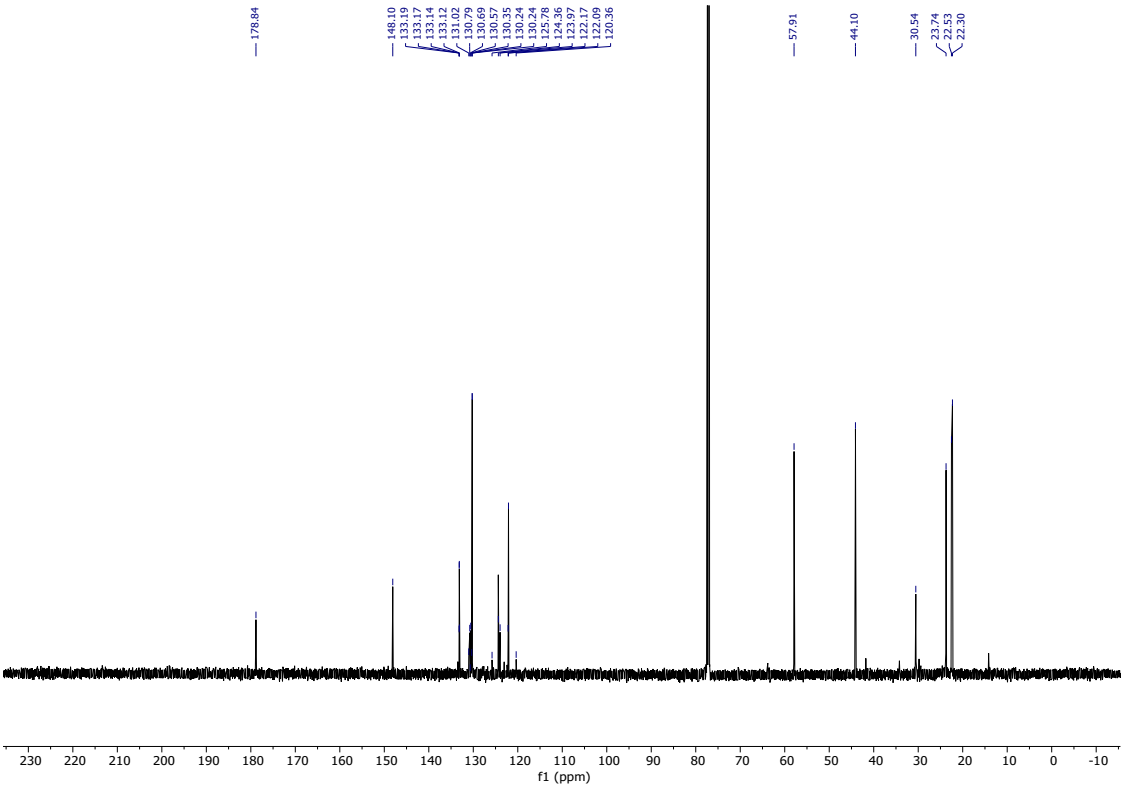
IR (neat) 3165, 3079, 2981, 1690, 1612, 1475, 1385, 1323, 1273, 1175 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{16}BrF_3NO^+$ $[M+H]^+$: 350.0362, found 350.0363.

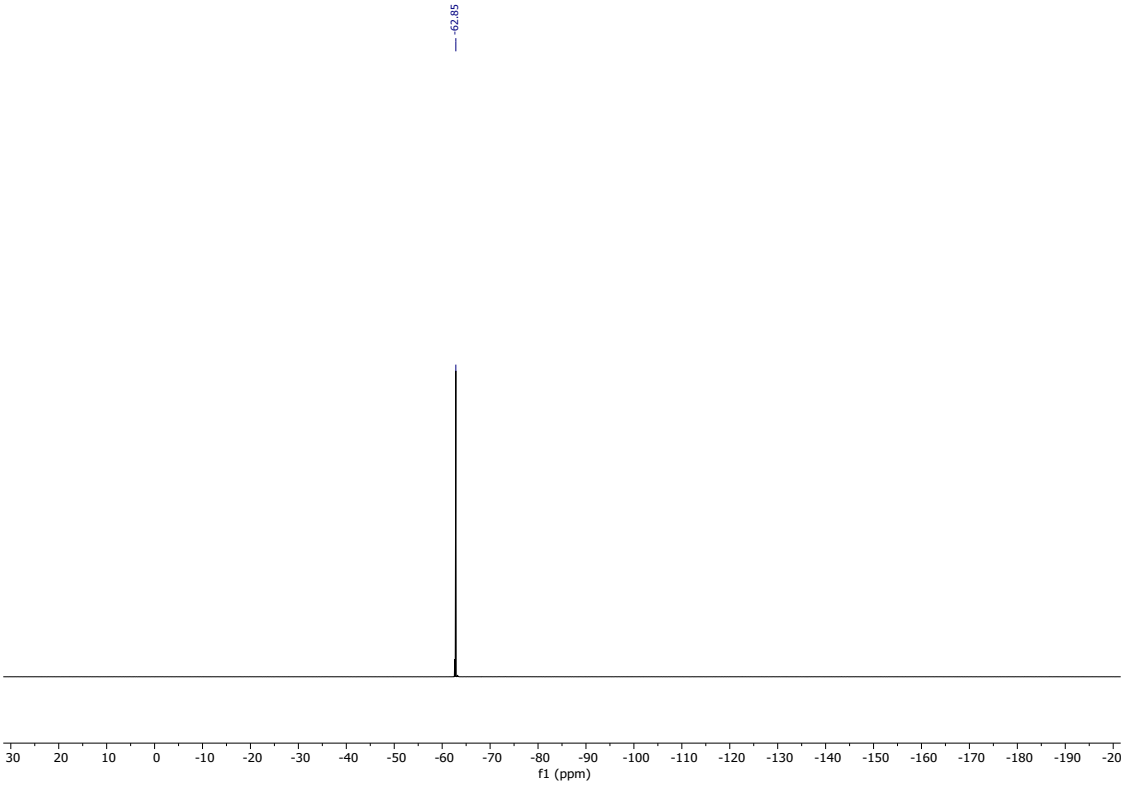
^{1}H NMR – 2i

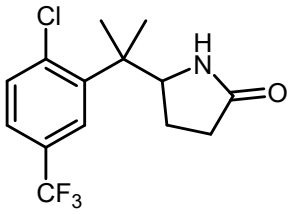


^{13}C NMR – 2i



^{19}F NMR – 2i


-62.85
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



2j. 5-(2-(2-chloro-5-(trifluoromethyl)phenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1j**. 39.3 mg, 0.129 mmol, 64% yield. Pale yellow solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.48 – 7.45 (m, 1H), 5.38 (br s, 1H), 4.84 (dd, *J* = 8.5, 5.2 Hz, 1H), 2.39 – 2.29 (m, 2H), 2.09 – 2.02 (m, 1H), 1.80 – 1.72 (m, 1H), 1.50 (s, 3H), 1.49 (s, 3H).

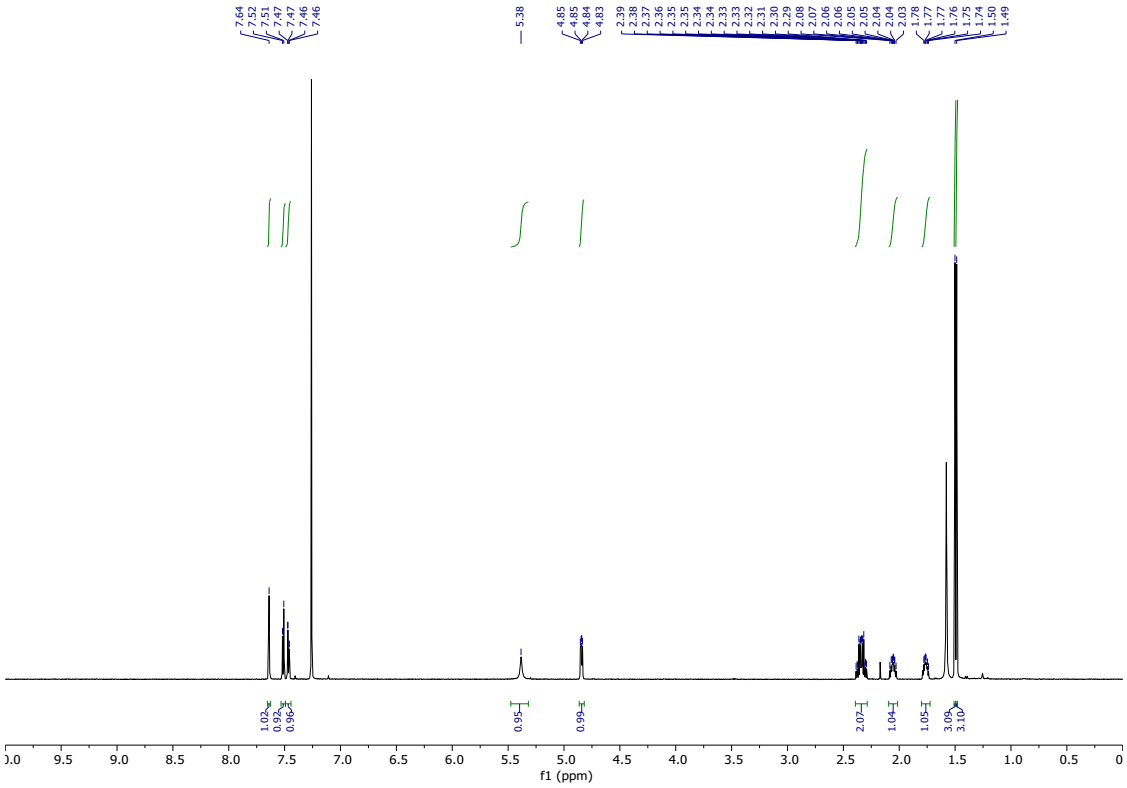
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.9, 143.8, 137.1, 133.1, 129.5 (q, *J* = 32.7 Hz), 126.3 (q, *J* = 3.7 Hz), 125.1 (q, *J* = 3.5 Hz), 123.9 (q, *J* = 273 Hz), 58.2, 43.7, 30.5, 23.7, 22.38, 22.35.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.56.

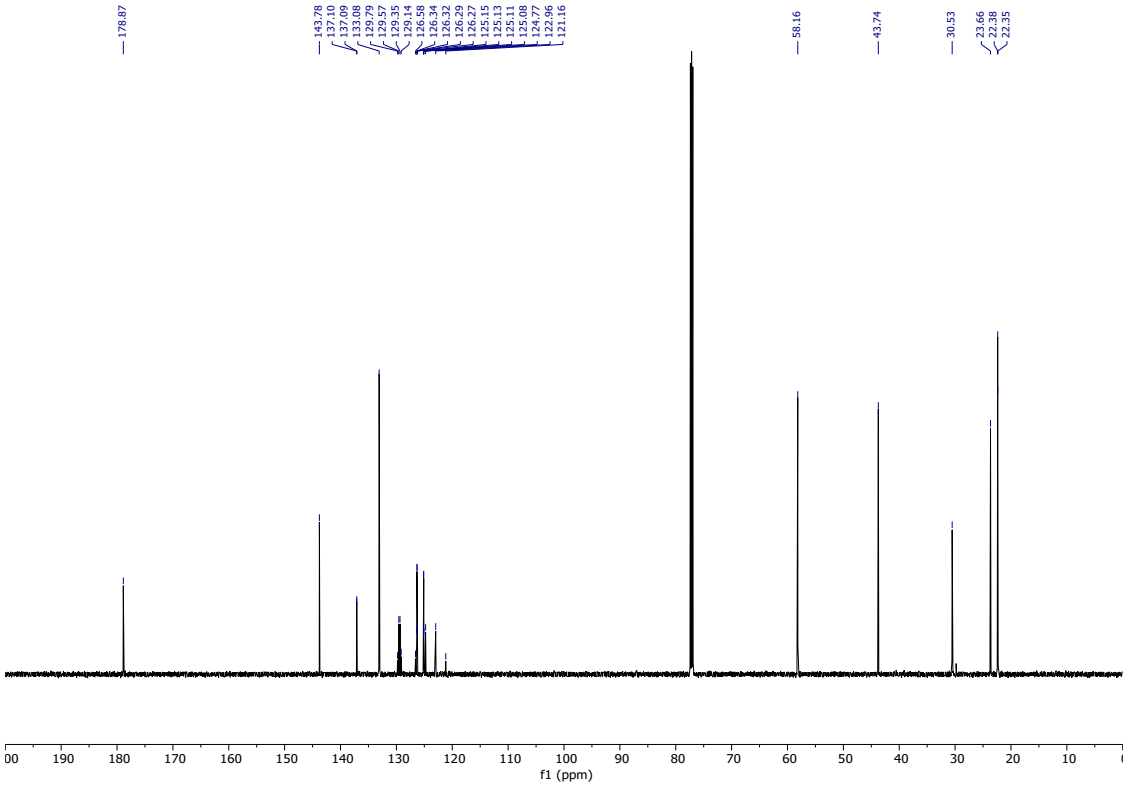
IR (neat) 3179, 3096, 2985, 1707, 1676, 1610, 1471, 1454, 1390, 1327 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{16}ClF_3NO^+$ $[M+H]^+$: 306.0867, found 306.0863.

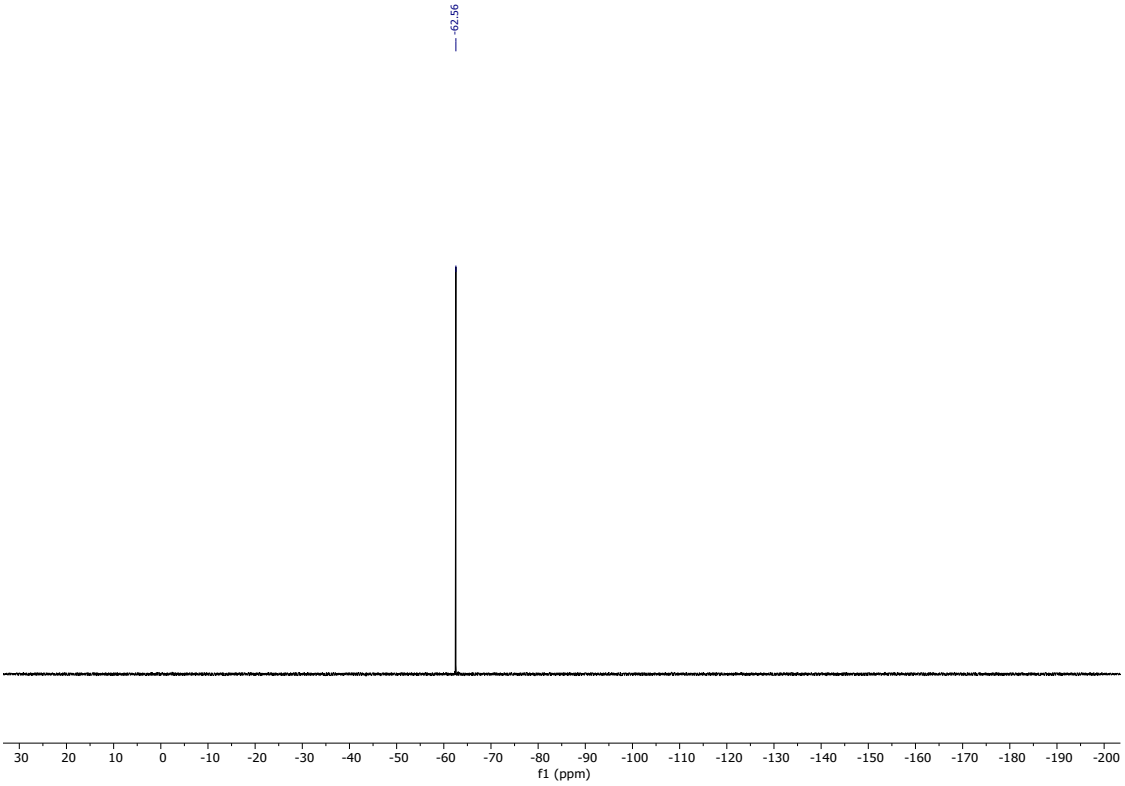
^{1}H NMR – 2j

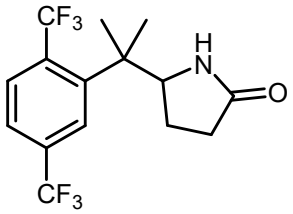


^{13}C NMR – 2j



^{19}F NMR – 2j


-62.56
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2k. 5-(2-(2,5-bis(trifluoromethyl)phenyl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1k**. 42.0 mg, 0.120 mmol, 62% yield. Light brown solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, 1H), 7.85 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 6.95 (br s, 1H), 4.28 (dd, *J* = 8.3, 5.4 Hz, 1H), 2.35 – 2.23 (m, 2H), 1.99 – 1.89 (m, 1H), 1.77 – 1.68 (m, 1H), 1.51 (s, 3H), 1.48 (s, 3H).

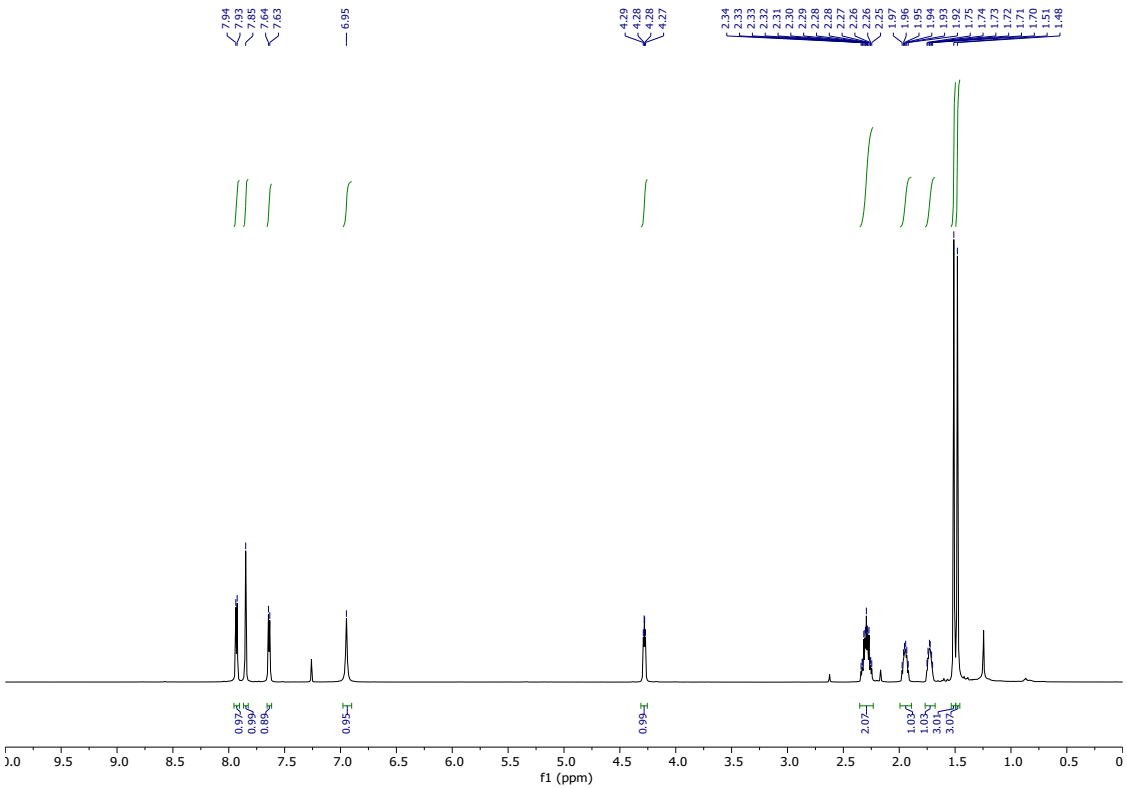
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.9, 146.6, 133.8 (q, *J* = 32.8 Hz), 132.0 (q, *J* = 31.0 Hz), 129.9 (q, *J* = 7.7 Hz), 127.2 (q, *J* = 3.5 Hz), 124.3 (q, *J* = 275 Hz), 124.0 (q, *J* = 3.4 Hz), 123.5 (q, *J* = 273 Hz), 61.0 (q, *J* = 3.9 Hz), 44.2, 30.5, 25.7 (q, *J* = 3.0 Hz), 24.1 (q, *J* = 3.2 Hz), 22.55.

^{19}F NMR (376 MHz, $CDCl_3$) δ -52.83, -63.31.

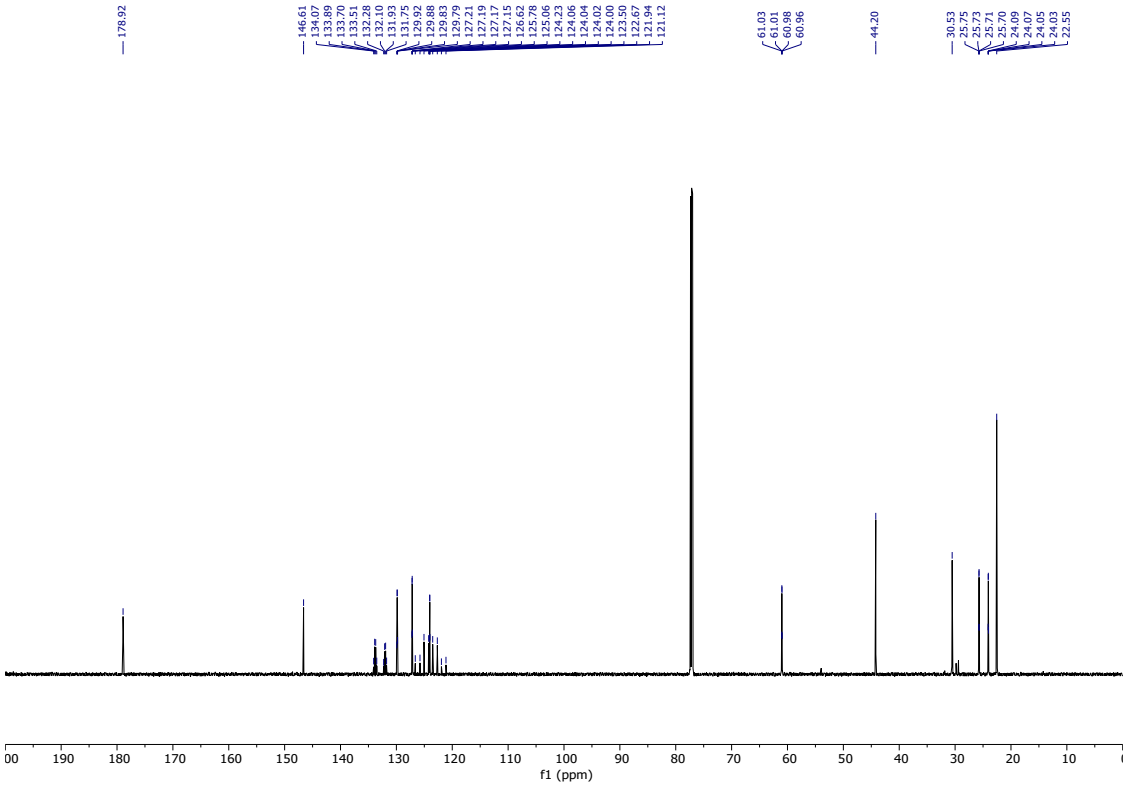
IR (neat) 318,,t3096, 2924, 1702, 1687, 1408, 1334, 1290, 1258, 1182 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{15}H_{16}F_6NO^+$ $[M+H]^+$: 340.1131, found 340.1132.

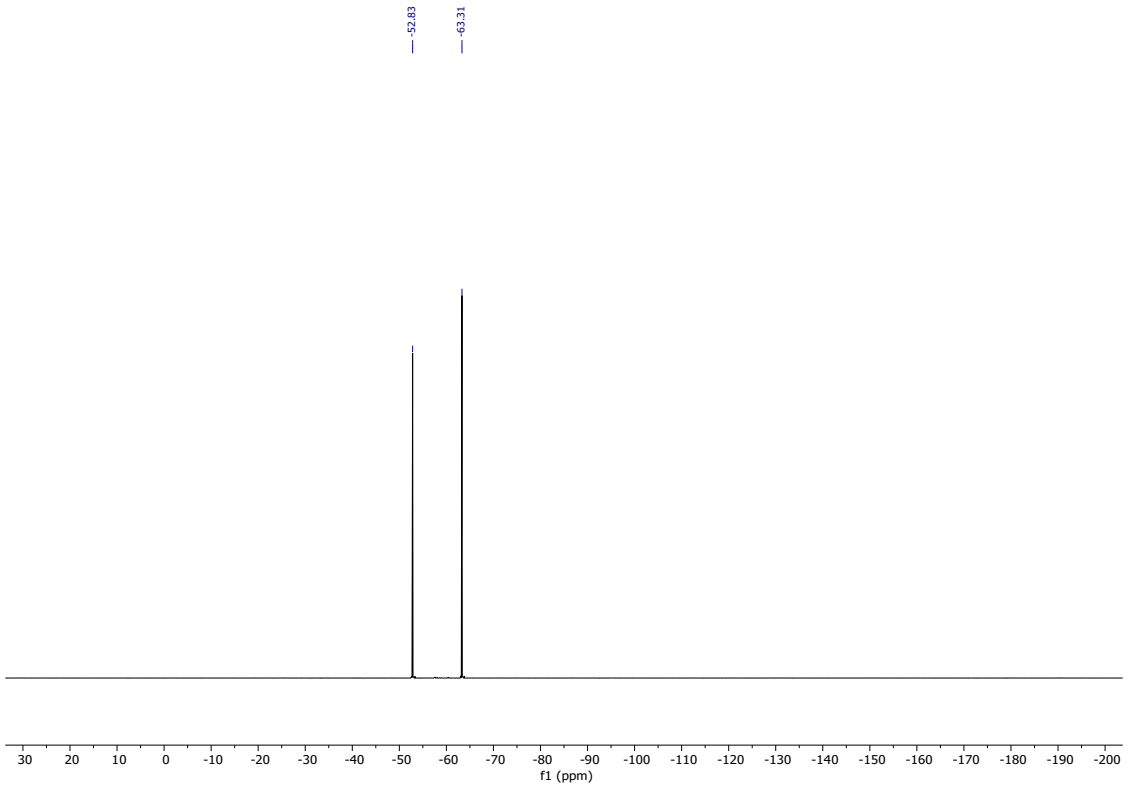
1H NMR – 2k

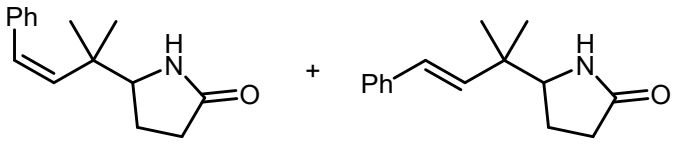


^{13}C NMR – 2k



^{19}F NMR – 2k


-52.83
-63.31
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



4.2 : 1

2*l*. 5-(2-methyl-4-phenylbut-3-en-2-yl)pyrrolidin-2-one. Isolated as a 4.2:1 mixture of *Z*/E alkene isomers. Prepared according to **GP2** with 0.2 mmol **1*l***. 15.0 mg, 0.065 mmol, 33% yield. Light brown solid.

Z isomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 – 7.13 (m, 5H), 6.63 (d, *J* = 12.8 Hz, 1H), 6.45 (br s, 1H), 5.52 (d, *J* = 12.8 Hz, 1H), 3.50 (dd, *J* = 8.1, 5.7 Hz, 1H), 2.36 – 2.24 (m, 2H), 2.09 – 2.01 (m, 1H), 1.92 – 1.83 (m, 1H), 0.94 (s, 3H), 0.87 (s, 3H).

Z isomer **^{13}C NMR** (176 MHz, $CDCl_3$) δ 178.8, 138.9, 137.0, 130.9, 128.6, 128.0, 126.8, 63.5, 41.0, 30.5, 25.1, 24.5, 22.34.

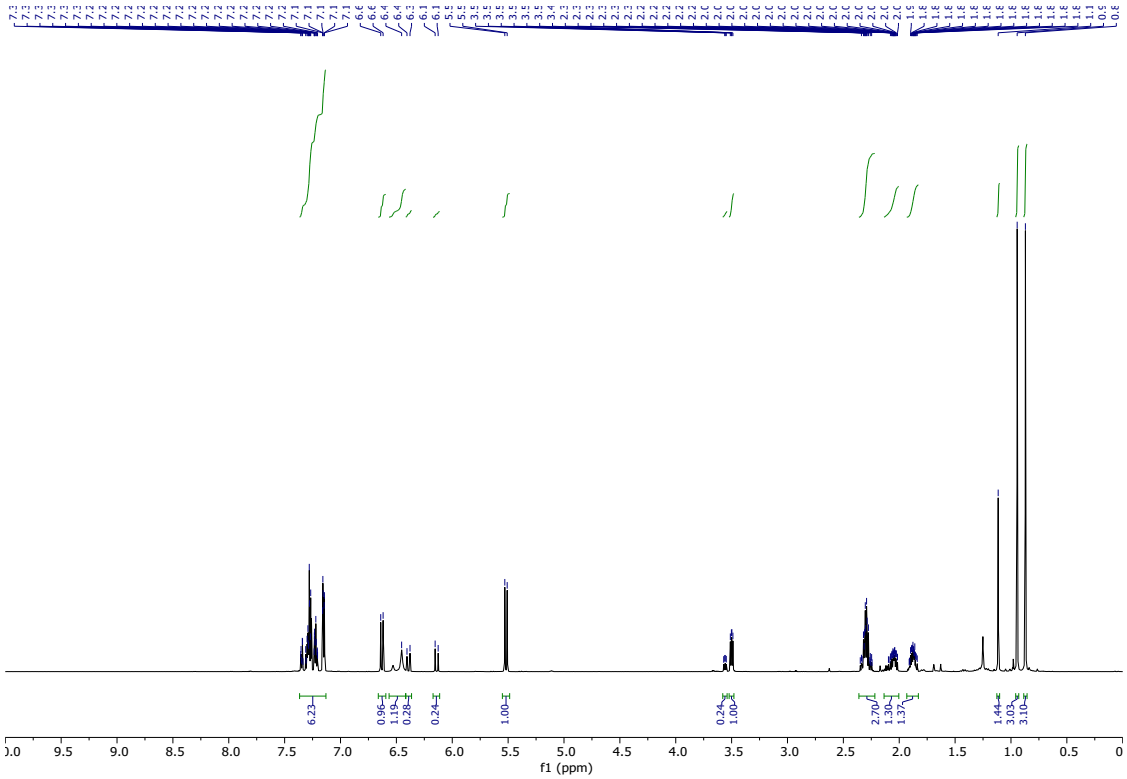
E isomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 – 7.13 (m, 5H), 6.53 (br s, 1H), 6.39 (d, *J* = 16.2 Hz, 1H), 6.14 (d, *J* = 16.2 Hz, 1H), 3.56 (dd, *J* = 8.1, 5.7 Hz, 1H), 2.36 – 2.24 (m, 2H), 2.13 – 2.00 (m, 1H), 1.92 – 1.83 (m, 1H), 1.11 (s, 6H).

E isomer **^{13}C NMR** (176 MHz, $CDCl_3$) δ 178.7, 137.2, 135.5, 129.0, 128.7, 127.6, 126.4, 63.0, 40.0, 29.8, 25.8, 24.1, 22.26.

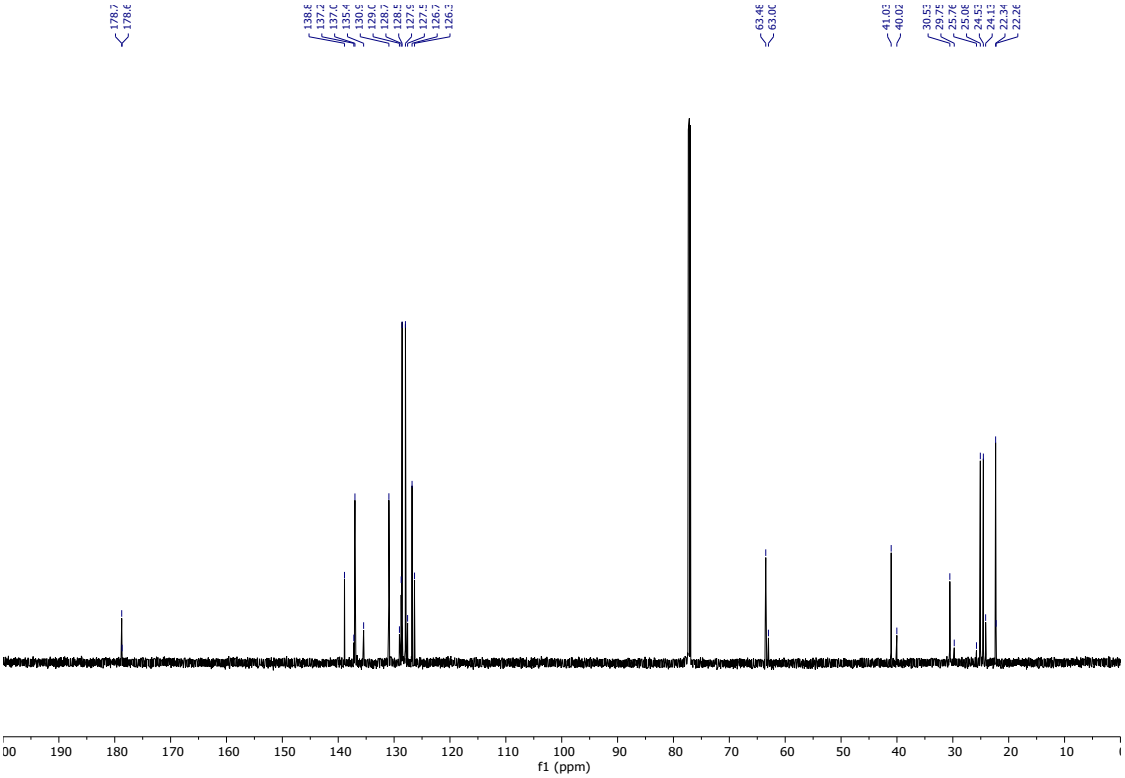
IR (neat) 3198, 2970, 2870, 1678, 1494, 1444, 1423, 1386, 1347, 1282 cm^{-1}

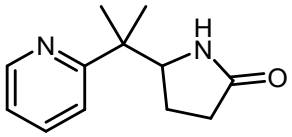
HRMS (ESI+) m/z calculated for $C_{15}H_{20}NO^+$ $[M+H]^+$: 230.1540, found 230.1541.

^{1}H NMR – 2*l*



^{13}C NMR – 2*l*





2m. 5-(2-(pyridin-2-yl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1m**. 13.8 mg, 0.068 mmol, 34% yield. Colorless solid.

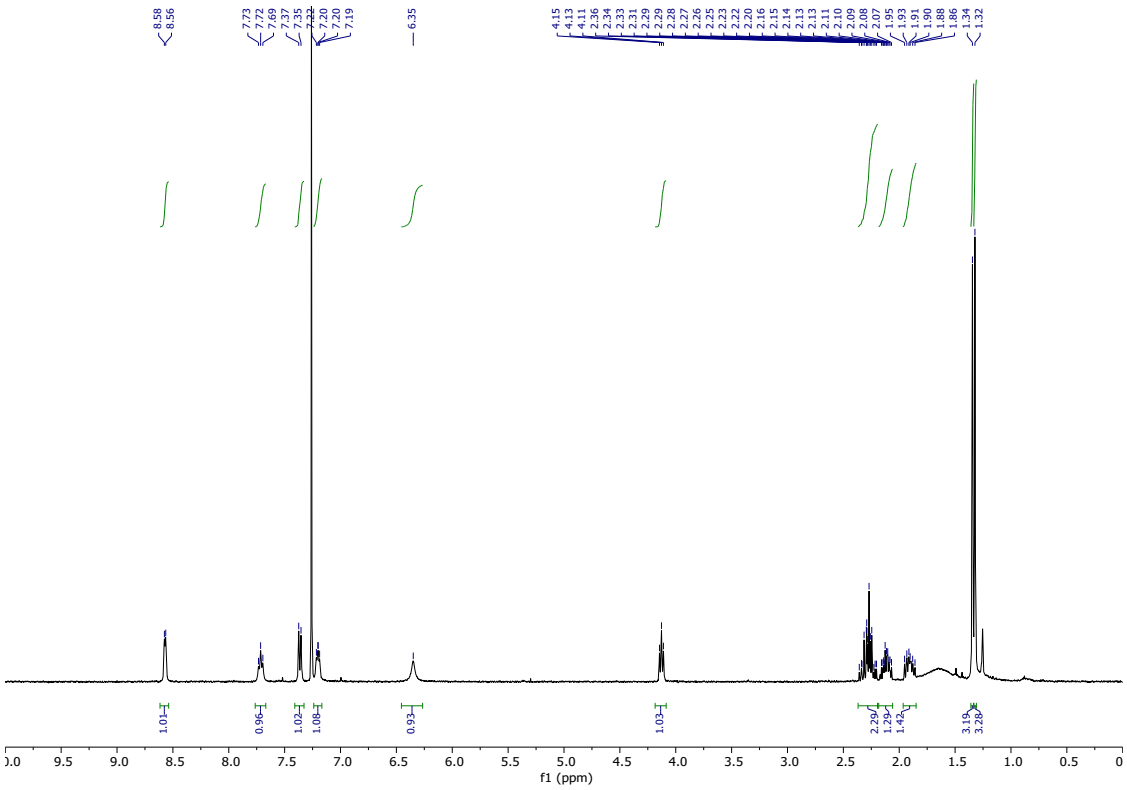
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.9 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.24 – 7.17 (m, 1H), 6.35 (br s, 1H), 4.13 (t, *J* = 7.1 Hz, 1H), 2.37 – 2.19 (m, 2H), 2.18 – 2.06 (m, 1H), 1.96 – 1.85 (m, 1H), 1.34 (s, 3H), 1.32 (s, 3H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 178.1, 166.4, 148.8, 136.9, 121.6, 120.4, 61.8, 43.5, 30.6, 23.8, 22.6, 22.1.

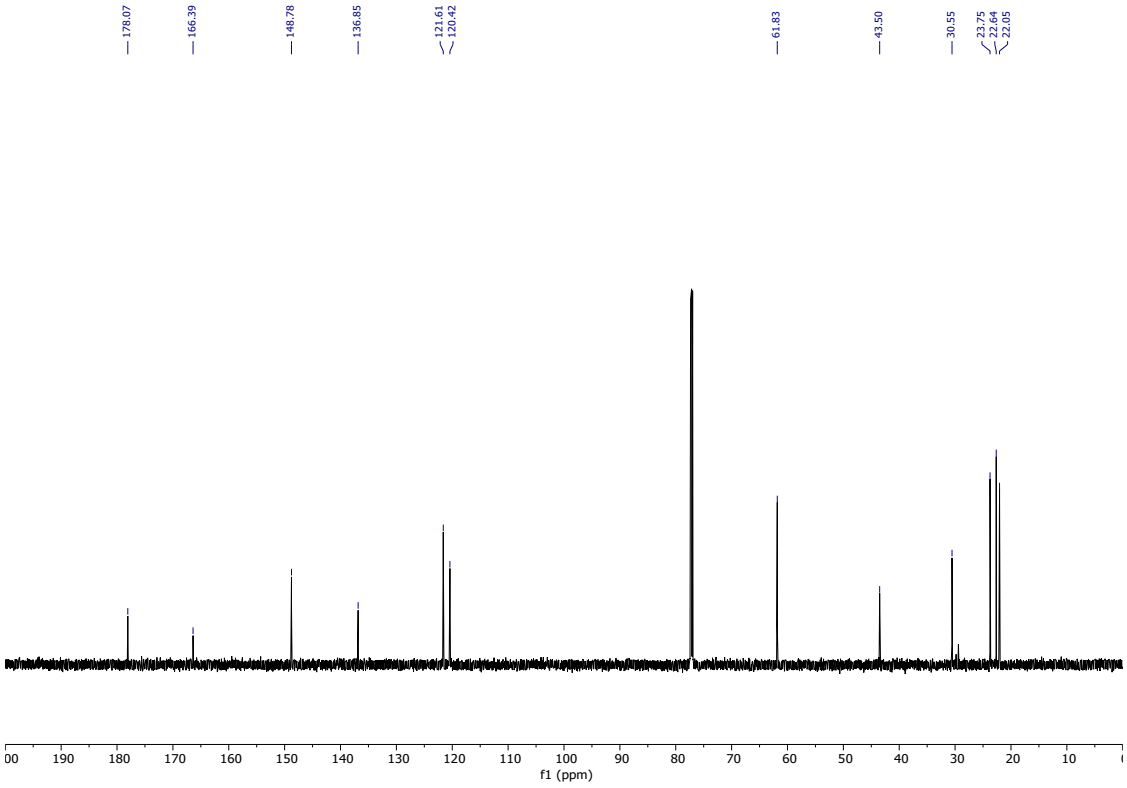
IR (neat) 3185, 3086, 2973, 2924, 1674, 1588, 1567, 1476, 1429, 1393 cm^{-1}

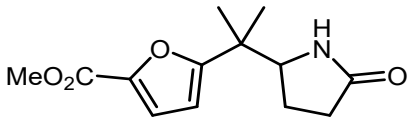
HRMS (ESI+) m/z calculated for $C_{12}H_{16}N_2ONa^+$ $[M+Na]^+$: 227.1155, found 227.1156.

^{1}H NMR – 2m



^{13}C NMR – 2m





2n. Methyl 5-(2-(5-oxopyrrolidin-2-yl)propan-2-yl)furan-2-carboxylate. Prepared according to **GP2** with 0.2 mmol **1n**. 29.8 mg, 0.119 mmol, 59%. Brown solid.

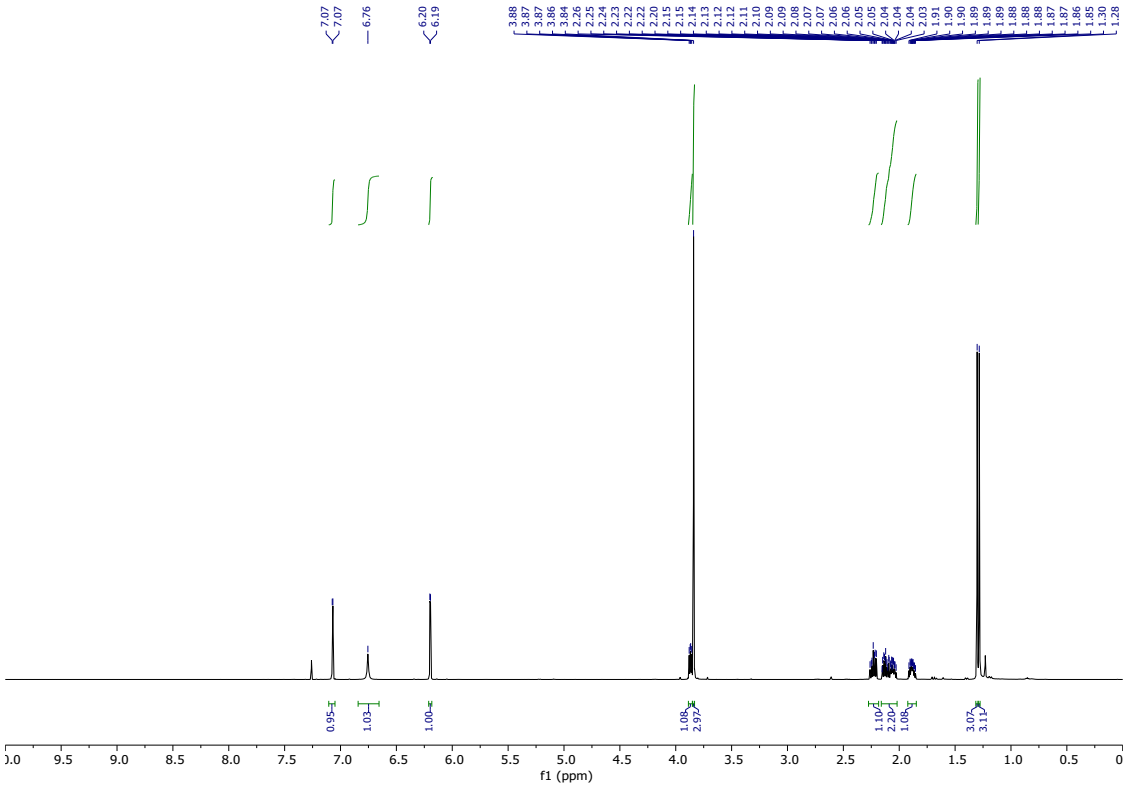
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.07 (d, *J* = 3.5 Hz, 1H), 6.76 (br s, 1H), 6.20 (d, *J* = 3.5 Hz, 1H), 3.87 (dd, *J* = 8.0, 5.4 Hz, 1H), 3.84 (s, 3H), 2.23 (ddd, *J* = 16.8, 10.2, 6.6 Hz, 1H), 2.16 – 2.02 (m, 2H), 1.92 – 1.85 (m, 1H), 1.30 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.7, 164.3, 159.1, 143.7, 118.9, 107.9, 61.9, 51.9, 40.1, 30.1, 22.39, 22.37, 22.3.

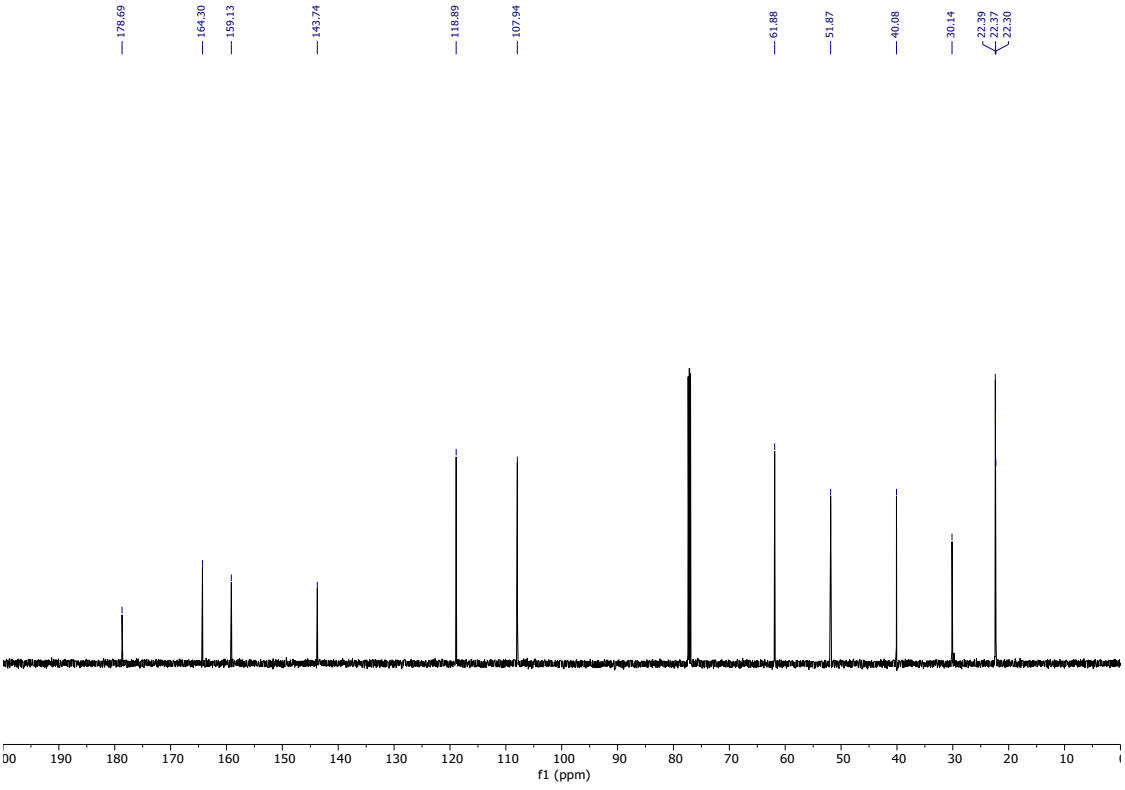
IR (neat) 3176, 3084, 2975, 1695, 1591, 1529, 1442, 1386, 1302, 1276 cm^{-1}

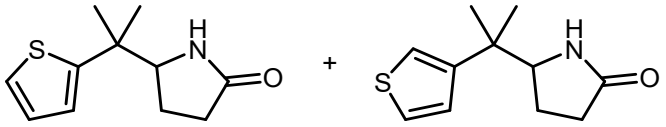
HRMS (ESI+) m/z calculated for $C_{13}H_{17}NO_4Na^+$ $[M+Na]^+$: 274.1050, found 274.1046.

^{1}H NMR – 2n



^{13}C NMR – 2n





2o 7 : 1 **2o'**

2o [5-(2-(thiophen-2-yl)propan-2-yl)pyrrolidin-2-one], **2o'** [5-(2-(thiophen-3-yl)propan-2-yl)pyrrolidin-2-one]. Prepared according to **GP2** with 0.2 mmol **1o**. 26.2 mg, 0.125 mmol, 63% yield. Colorless solid.

2o ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.95 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.87 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.78 (br s, 1H), 3.76 (dd, *J* = 8.1, 5.0 Hz, 1H), 2.25 – 2.15 (m, 1H), 2.10 – 1.97 (m, 3H), 1.89 – 1.76 (m, 1H), 1.37 (d, *J* = 5.7 Hz, 6H).

2o ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.0, 150.8, 126.8, 124.1, 123.8, 64.5, 41.1, 30.4, 26.2, 25.2, 22.5.

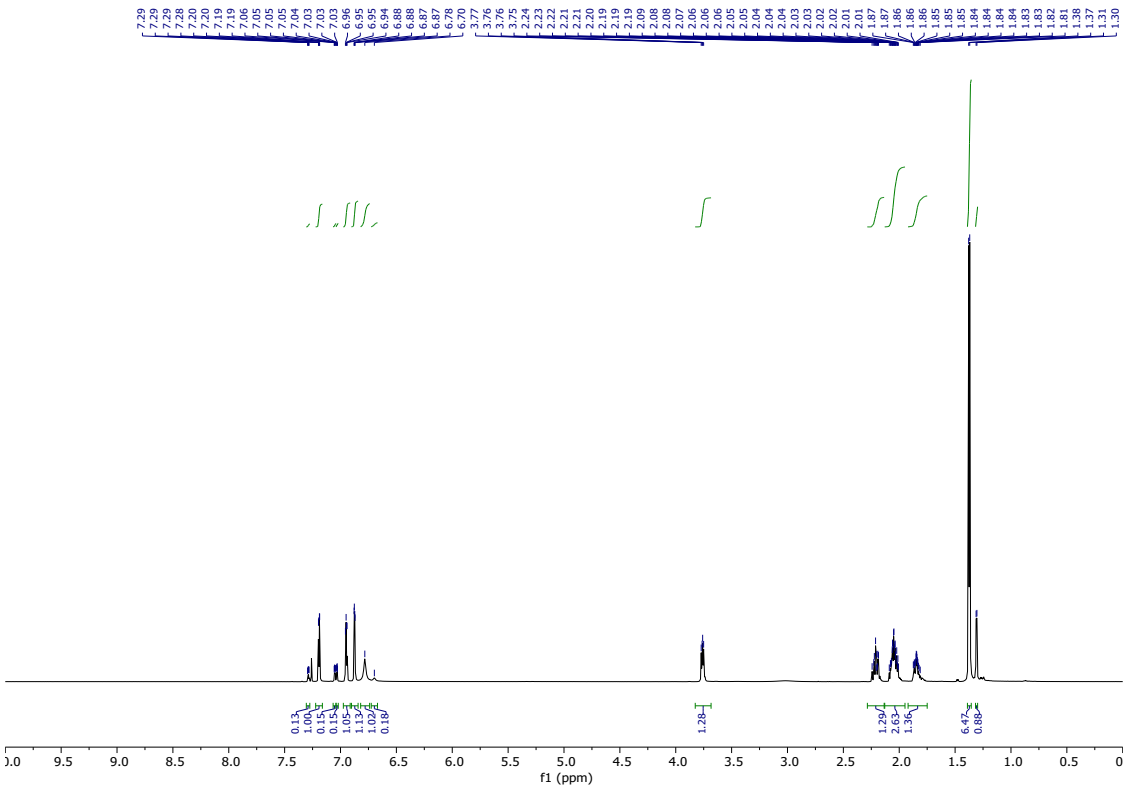
2o' partial **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.05 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.03 (dd, *J* = 3.0, 1.4 Hz, 1H), 6.70 (br s, 1H), 1.31 (d, *J* = 4.4 Hz, 6H).

2o' partial **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.4, 126.4, 125.9, 120.5, 63.7, 40.0, 25.0, 24.1, 22.4.

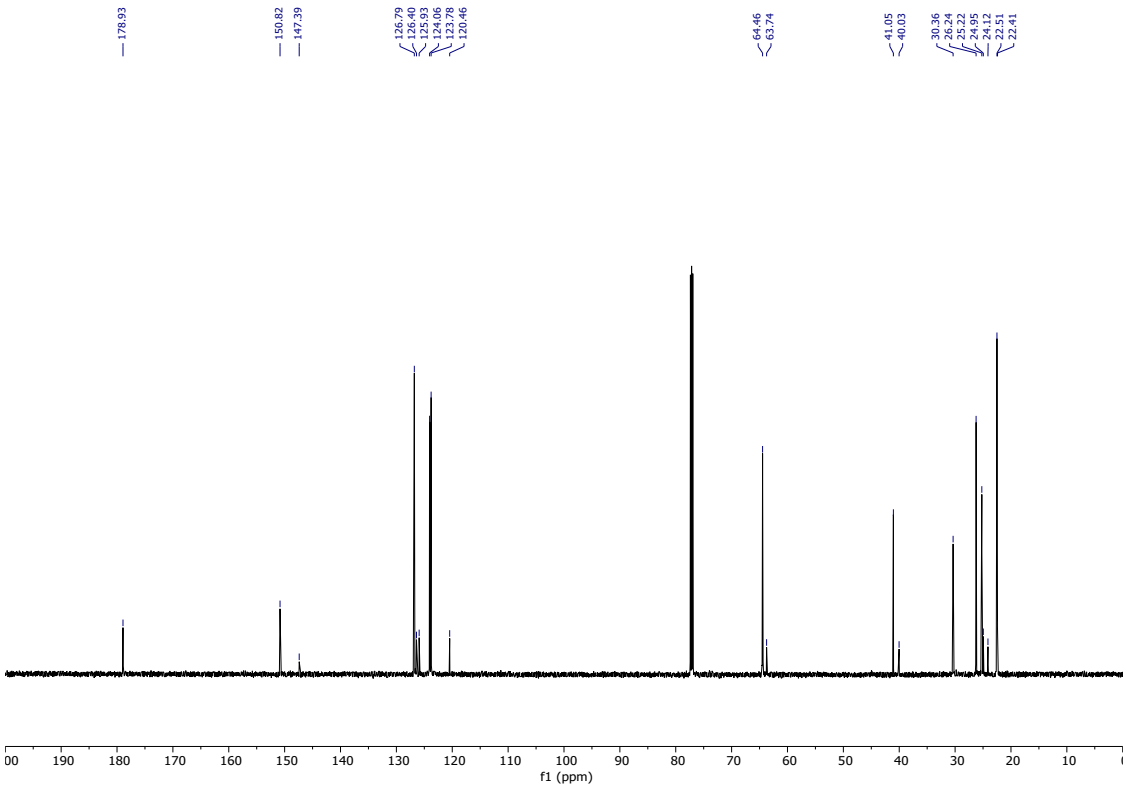
IR (neat) 3172, 3080, 2967, 2922, 2879, 1677, 1471, 1443, 1392, 1312 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{11}H_{16}NOS^+$ $[M+H]^+$: 210.0947, found 210.0954.

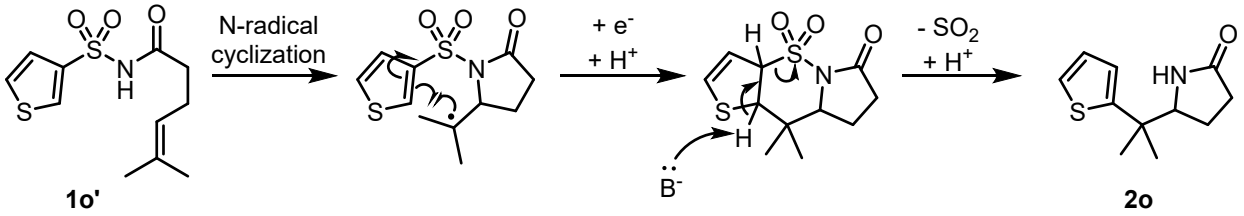
^{1}H NMR – 2o + 2o’



^{13}C NMR – 2o + 2o’

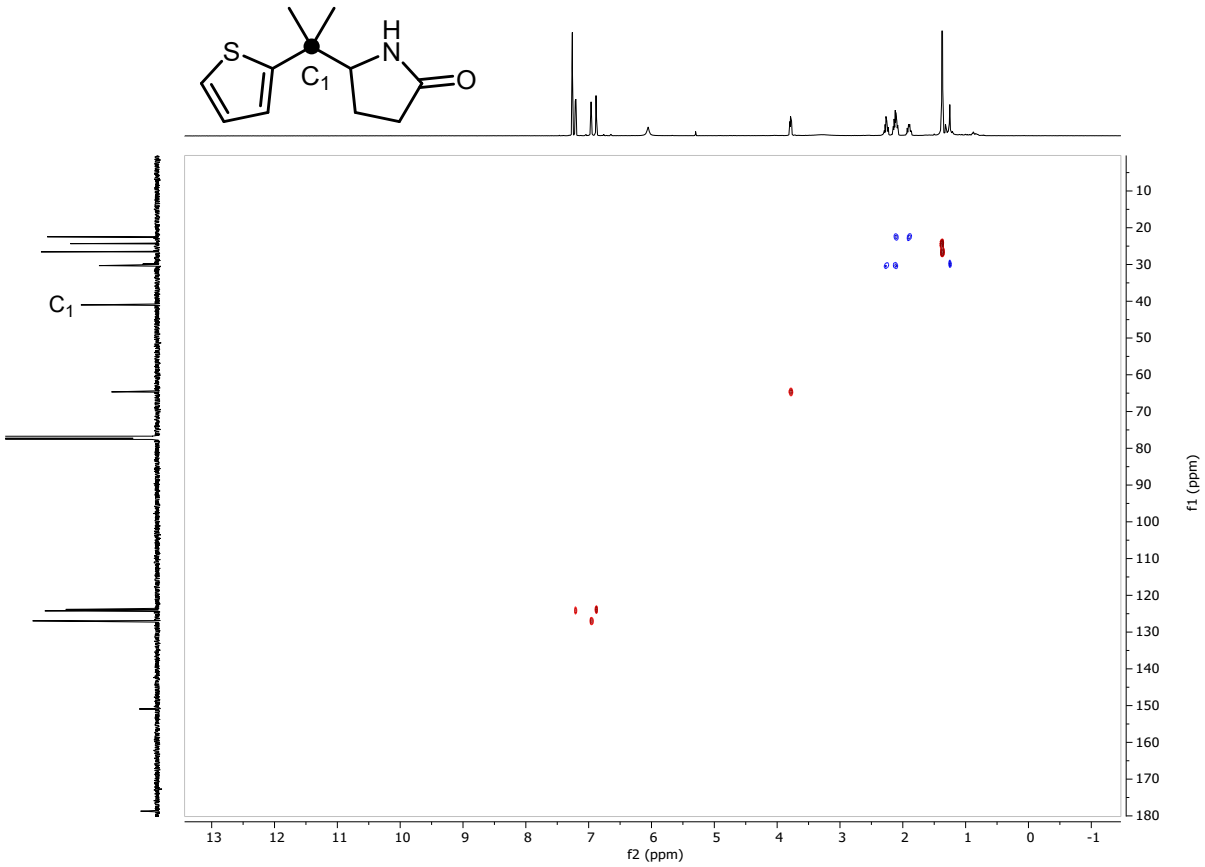


To provide additional evidence for the structure of **2o'**, **1o'** was subjected to **GP2**. The only aminoarylation product isolated from the reaction was identified as **2o** (6.9 mg, 16%) *via* analyses of HSQC and HMBC spectra (see following page). A mechanism for this transformation is proposed below:

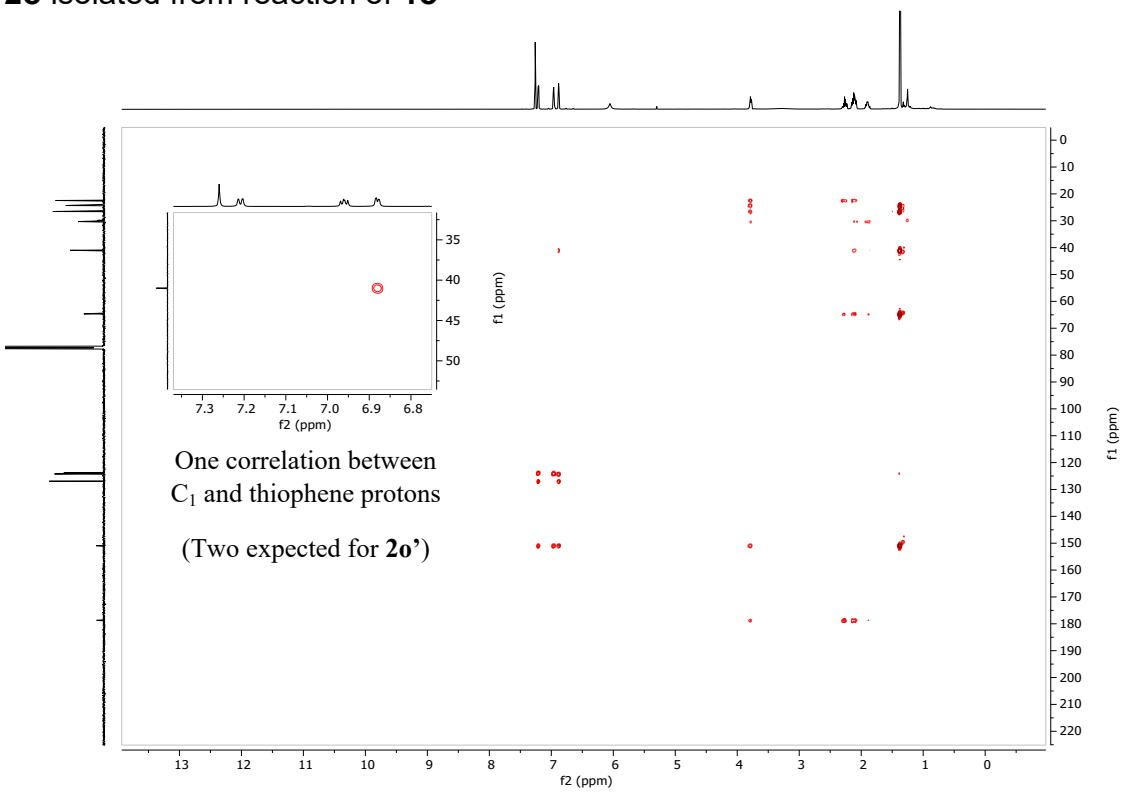


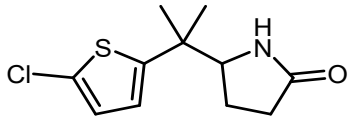
This experiment confirms that *cine* substitution on the thiophene ring can occur; therefore, the analogous reaction on **1o** is a plausible pathway by which **2o'** forms.

HSQC – 2o isolated from reaction of **1o'**:



HMBC – 2o isolated from reaction of **1o'**





2p. 5-(2-(5-chlorothiophen-2-yl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1p**. 24.9 mg, 0.102 mmol, 51% yield. Brown solid.

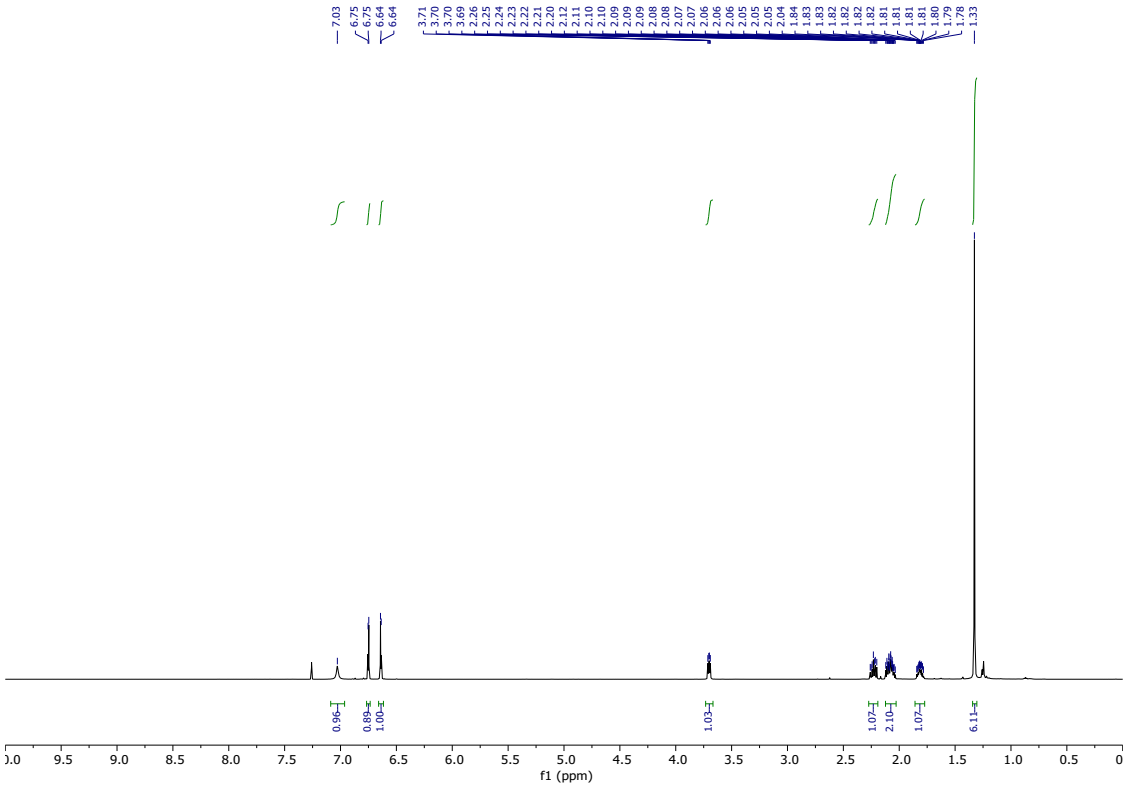
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.03 (br s, 1H), 6.75 (d, *J* = 3.8 Hz, 1H), 6.64 (d, *J* = 3.8 Hz, 1H), 3.70 (dd, *J* = 8.0, 5.1 Hz, 1H), 2.27 – 2.19 (m, 1H), 2.12 – 2.03 (m, 2H), 1.86 – 1.77 (m, 1H), 1.33 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 179.0, 149.3, 128.4, 125.8, 123.3, 64.2, 41.6, 30.4, 26.0, 25.2, 22.5.

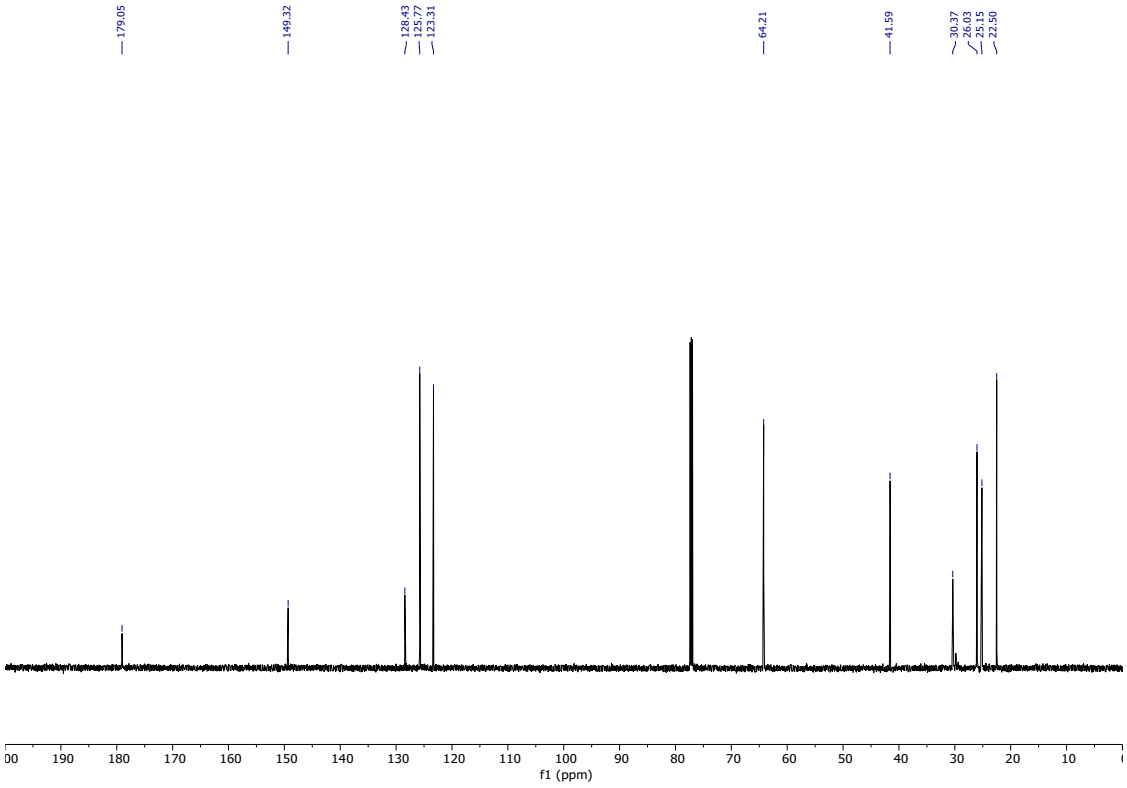
IR (neat) 3190, 3085, 2968, 2923, 1677, 1532, 1463, 1444, 1390, 1340 cm^{-1}

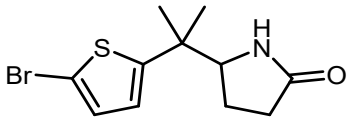
HRMS (ESI+) m/z calculated for $C_{11}H_{15}ClNOS^+$ $[M+H]^+$: 244.0558, found 244.0560.

^{1}H NMR – 2p



^{13}C NMR – 2p





2q. 5-(2-(5-bromothiophen-2-yl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1q**. 26.0 mg, 0.090 mmol, 45% yield. Light brown solid.

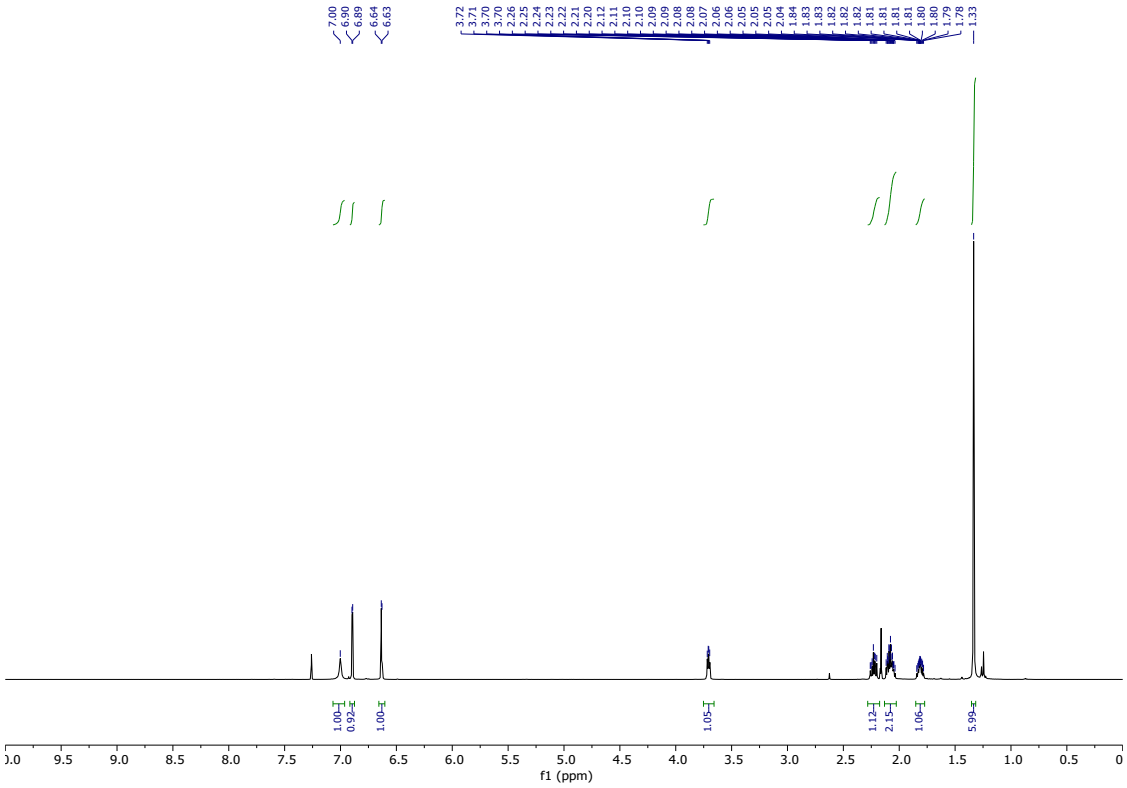
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.00 (br s, 1H), 6.89 (d, *J* = 3.8 Hz, 1H), 6.63 (d, *J* = 3.8 Hz, 1H), 3.71 (dd, *J* = 8.0, 5.1 Hz, 1H), 2.28 – 2.18 (m, 1H), 2.13 – 2.03 (m, 2H), 1.85 – 1.77 (m, 1H), 1.33 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 179.0, 152.3, 129.6, 124.4, 110.6, 64.2, 41.7, 30.4, 26.1, 25.2, 22.5.

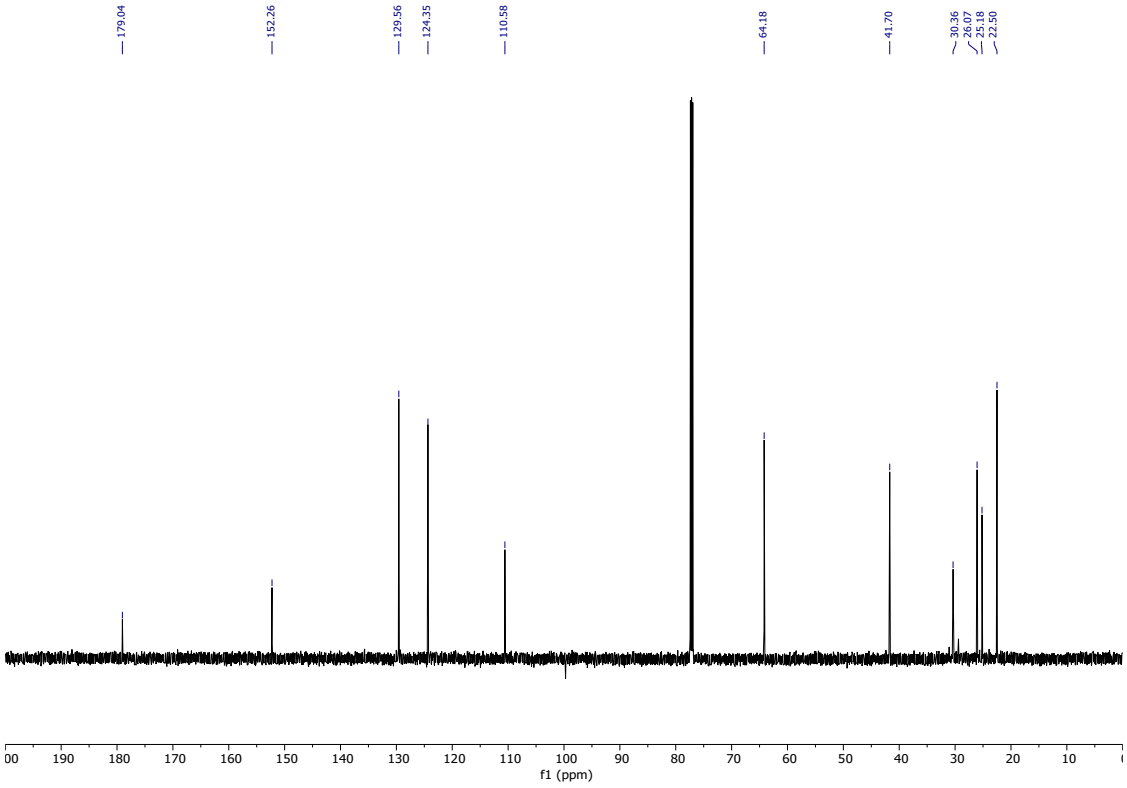
IR (neat) 3187, 3067, 2969, 2924, 2876, 1674, 1440, 1391, 1340, 1279 cm^{-1}

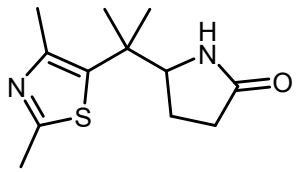
HRMS (ESI+) m/z calculated for $C_{11}H_{15}BrNOS^+$ $[M+H]^+$: 288.0053, found 288.0051.

^{1}H NMR – 2q



^{13}C NMR – 2q





2r. 5-(2-(2,4-dimethylthiazol-5-yl)propan-2-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1r**. 21.3 mg, 0.894 mmol, 45% yield. Tan solid.

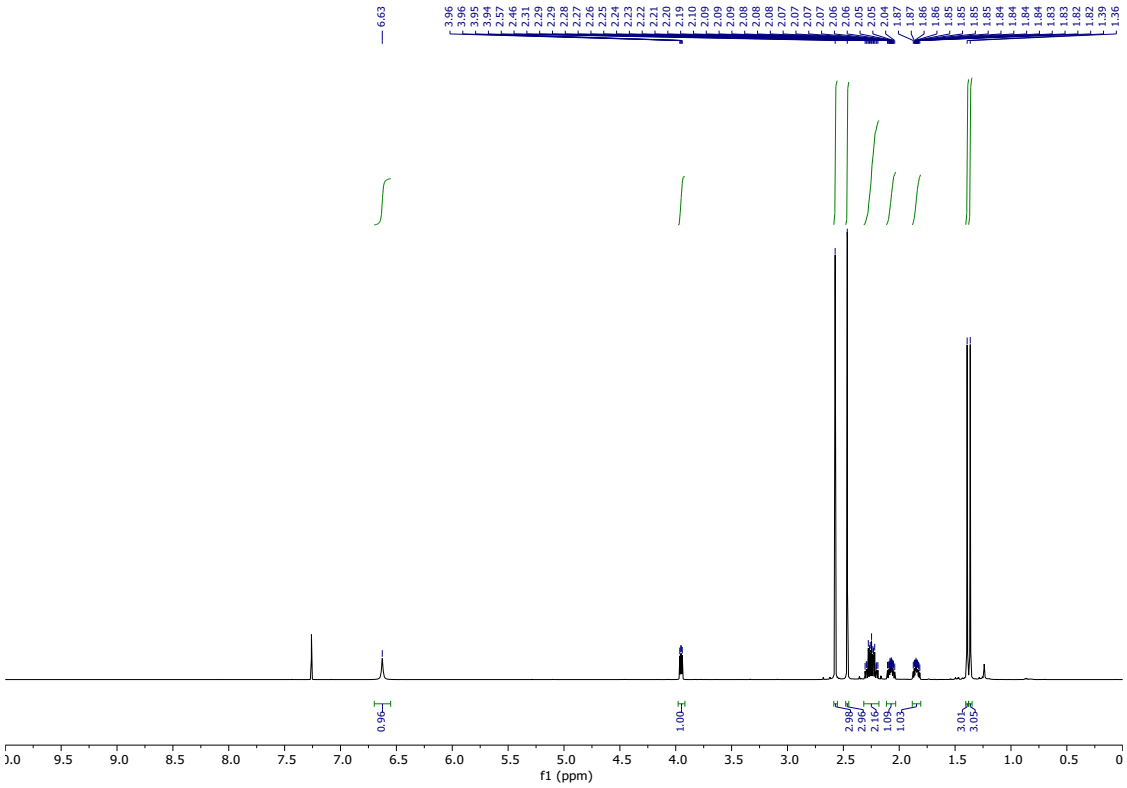
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.63 (br s, 1H), 3.95 (dd, *J* = 8.2, 5.2 Hz, 1H), 2.57 (s, 3H), 2.46 (s, 3H), 2.31 – 2.18 (m, 2H), 2.11 – 2.03 (m, 1H), 1.88 – 1.81 (m, 1H), 1.39 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.7, 161.6, 146.6, 136.8, 62.7, 40.2, 30.4, 25.8, 25.2, 22.5, 18.9, 18.1.

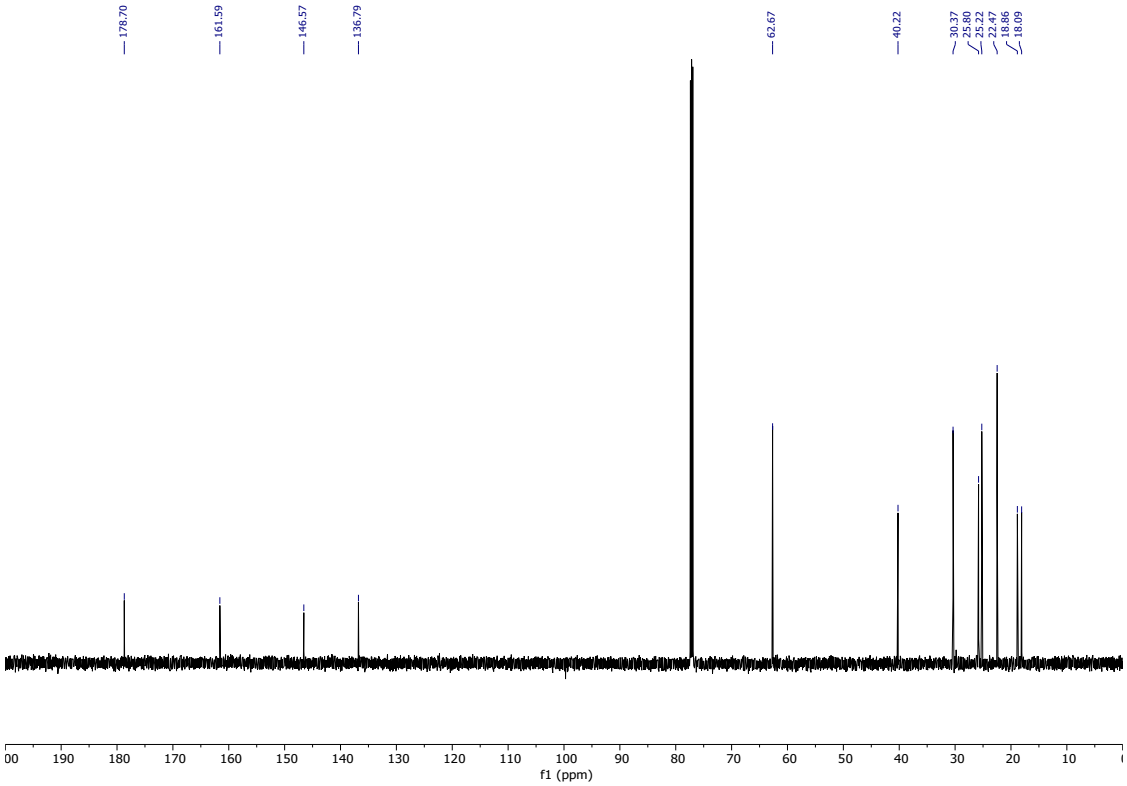
IR (neat) 3181, 3089, 2971, 2936, 1694, 1530, 1464, 1376, 1343, 1286 cm^{-1}

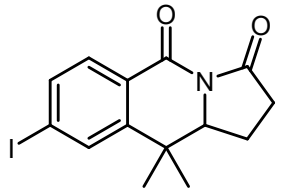
HRMS (ESI+) m/z calculated for $C_{12}H_{19}N_2OS^+$ $[M+H]^+$: 239.1213, found 239.1214.

^{1}H NMR – 2r



^{13}C NMR – 2r





2s. 8-iodo-10,10-dimethyl-1,2,10,10a-tetrahydropyrrolo[1,2-b]isoquinoline-3,5-dione. Prepared according to **GP2** with 0.2 mmol **1s**. 36.7 mg, 0.103 mmol, 52% yield. Colorless solid.

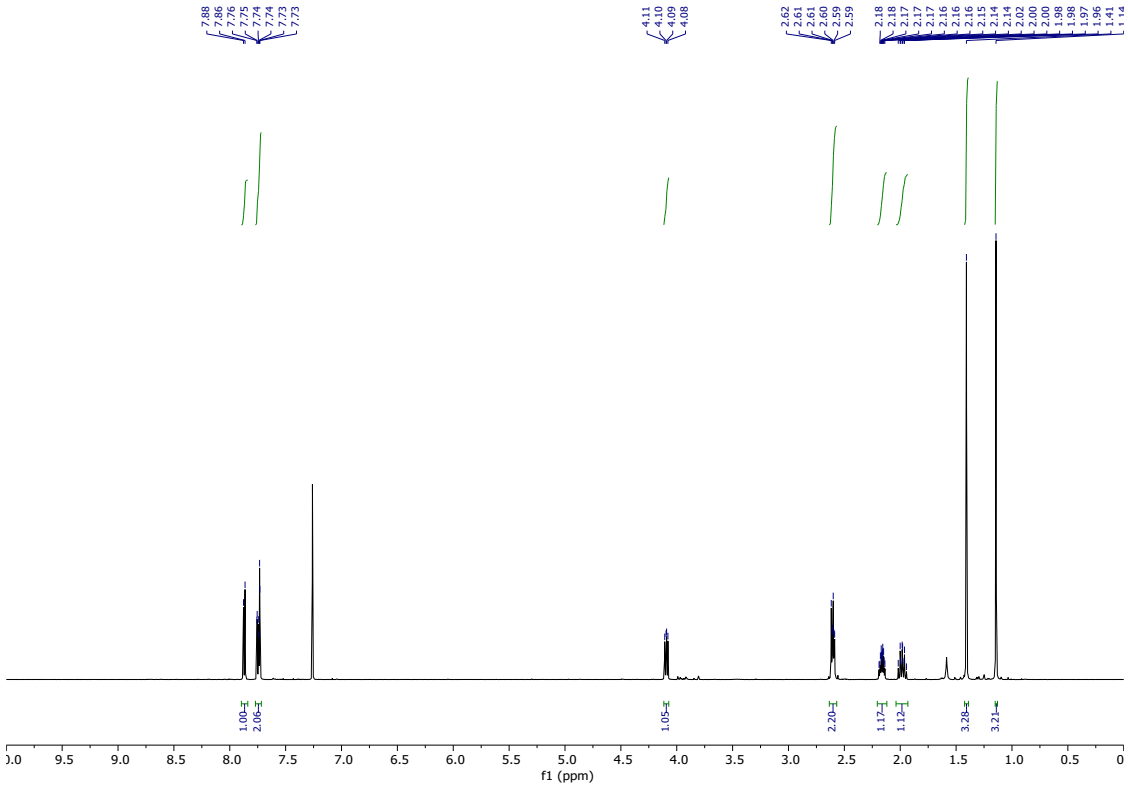
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 1H), 7.77 – 7.72 (m, 2H), 4.09 (dd, *J* = 10.0, 6.9 Hz, 1H), 2.63 – 2.57 (m, 2H), 2.16 (dtd, *J* = 12.6, 7.0, 4.4 Hz, 1H), 1.98 (dq, *J* = 12.8, 10.3 Hz, 1H), 1.41 (s, 3H), 1.14 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.8, 162.2, 149.9, 136.9, 133.2, 131.5, 127.6, 102.3, 63.8, 37.6, 31.7, 23.0, 22.2, 19.5.

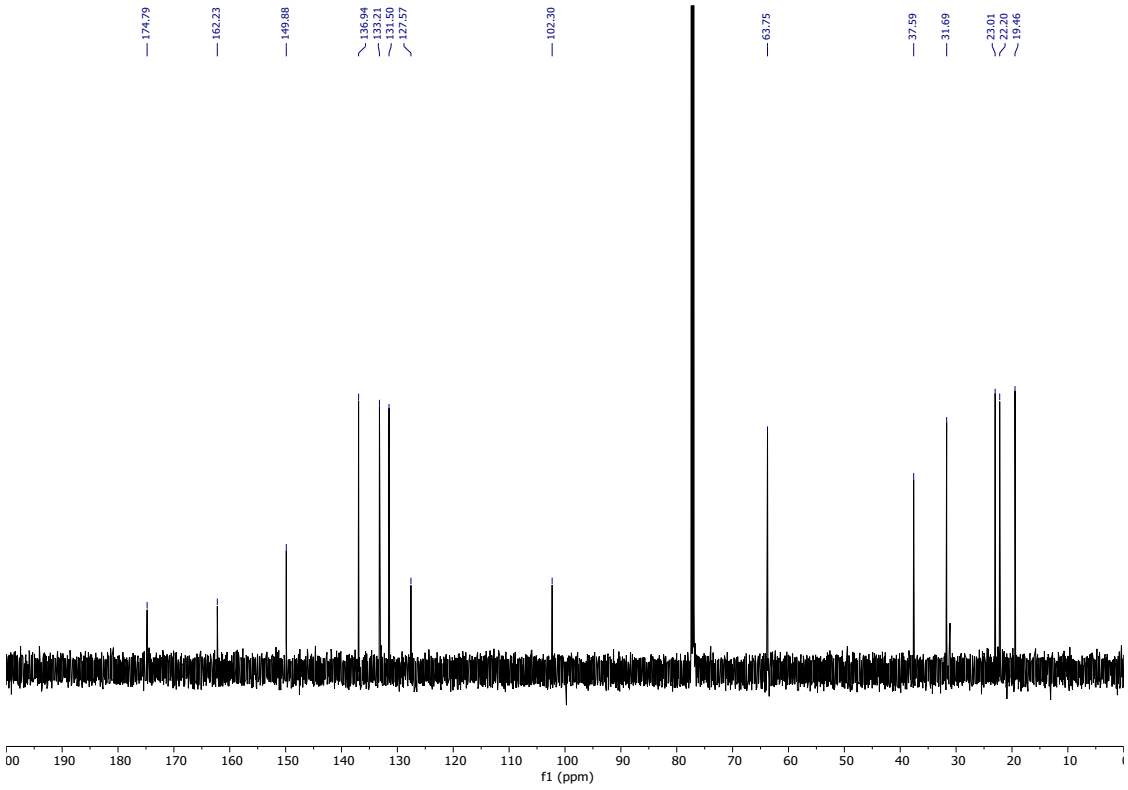
IR (neat) 2963, 2937, 1756, 1668, 1583, 1555, 1470, 1393, 1362, 1346 cm^{-1}

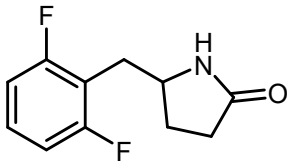
HRMS (ESI+) m/z calculated for $C_{14}H_{15}INO_2^+$ $[M+H]^+$: 356.0142, found 356.0140.

^{1}H NMR – 2s



^{13}C NMR – 2s





2t. 5-(2,6-difluorobenzyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1t**. 19.2 mg, 0.0904 mmol, 45% yield. Yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (tt, *J* = 8.4, 6.5 Hz, 1H), 6.93 – 6.85 (m, 2H), 5.96 (br s, 1H), 3.95 (p, *J* = 6.5 Hz, 1H), 2.90 (dt, *J* = 6.5, 1.4 Hz, 2H), 2.39 – 2.18 (m, 3H), 1.90 – 1.82 (m, 1H).

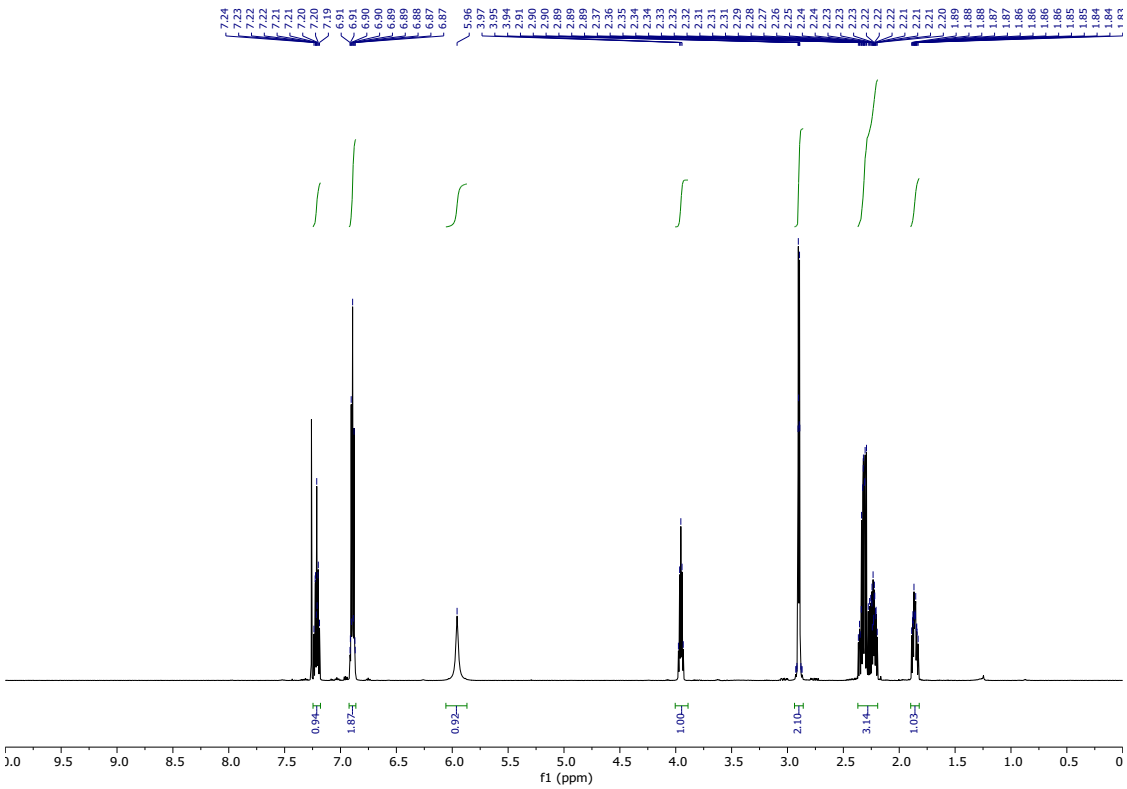
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.0, 161.7 (dd, *J* = 247, 8.5 Hz), 128.9 (t, *J* = 10.2 Hz), 113.1 (t, *J* = 20.2 Hz), 111.5 (dd, *J* = 21.2, 4.9 Hz), 54.0, 30.0, 28.9, 26.7.

^{19}F NMR (564 MHz, $CDCl_3$) ^{19}F NMR (564 MHz, Chloroform-*d*) δ -114.37 (t, *J* = 6.8 Hz).

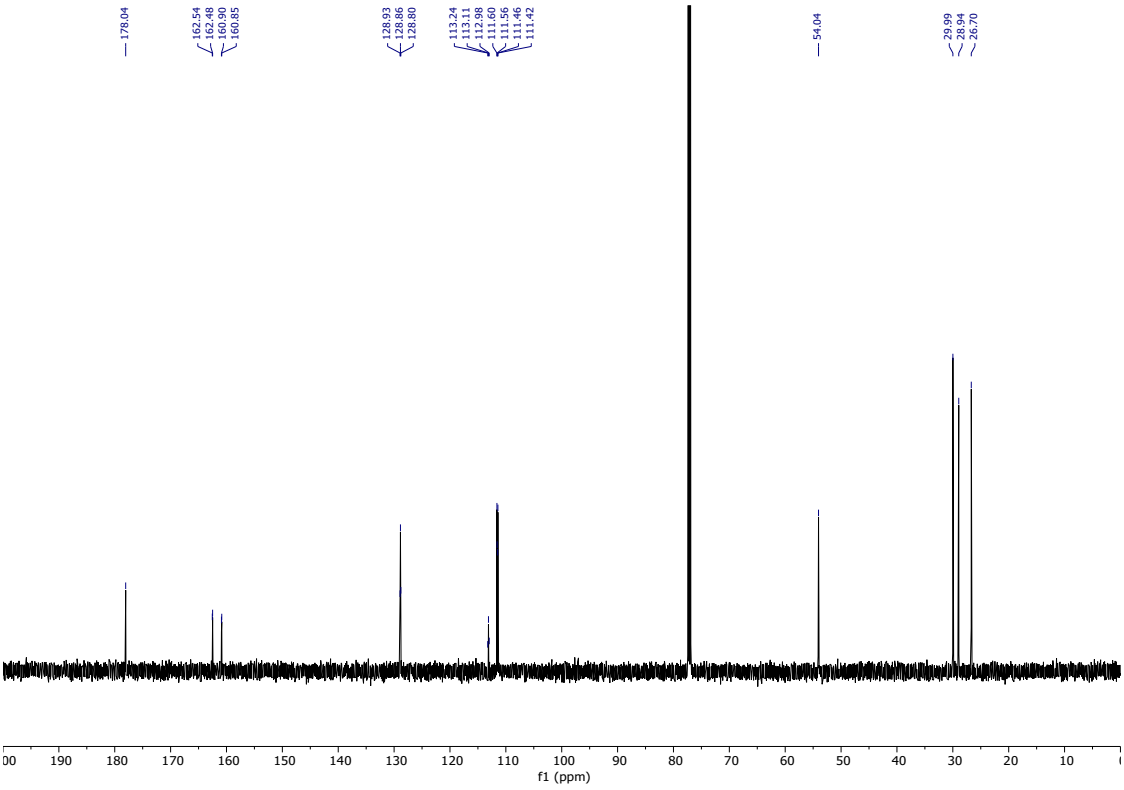
IR (neat) 3185, 3092, 2938, 1688, 1626, 1591, 1468, 1358, 1327, 1262 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{11}H_{12}F_2NO^+$ $[M+H]^+$: 212.0882, found 212.0885.

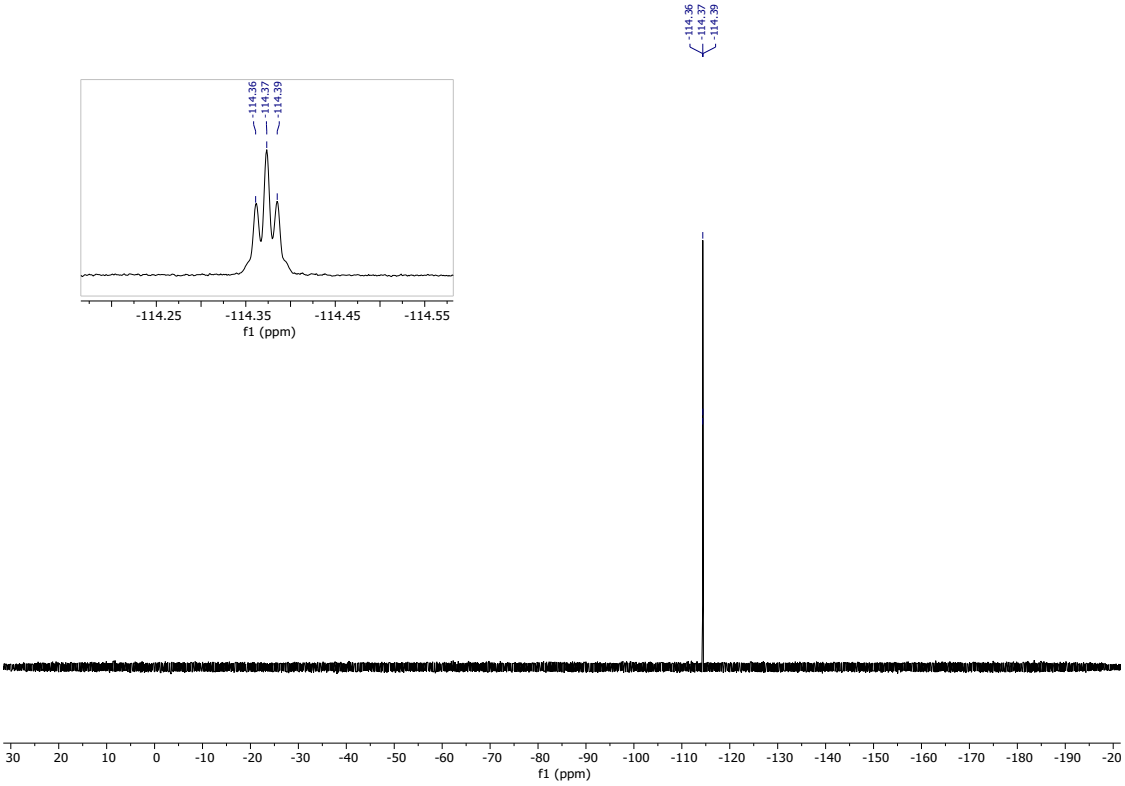
^{1}H NMR – 2t

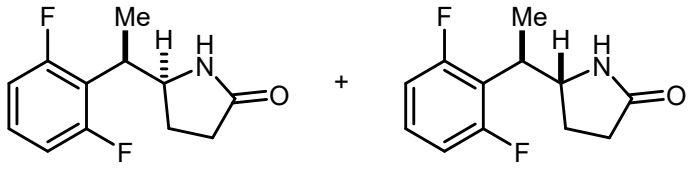


^{13}C NMR – 2t



^{19}F NMR – 2t


-114.36
-114.37
-114.39
-114.25
-114.35
-114.45
-114.55
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



9 : 1

2u. 5-(1-(2,6-difluorophenyl)ethyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1u**. 33.3 mg, 0.148 mmol, 74% yield. Beige solid.

Major diastereomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.18 (tt, *J* = 8.3, 6.3 Hz, 1H), 6.85 (t, *J* = 8.7 Hz, 2H), 5.62 (br s, 1H), 4.04 – 3.95 (m, 1H), 3.16 (dq, *J* = 9.3, 7.2 Hz, 1H), 2.41 – 2.18 (m, 3H), 1.91 – 1.79 (m, 1H), 1.32 (d, *J* = 7.1 Hz, 3H).

Major diastereomer **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.7, 161.5 (dd, *J* = 248, 8.9 Hz), 128.8 (t, *J* = 10.6 Hz), 118.3 (t, *J* = 17.8 Hz), 112.0, 57.7 (t, *J* = 1.7 Hz), 36.5, 30.2, 26.7, 15.8 (t, *J* = 2.1 Hz).

Major diastereomer **^{19}F NMR** (377 MHz, $CDCl_3$) δ -112.8.

Minor diastereomer partial **^{1}H NMR** (600 MHz, $CDCl_3$) δ 2.02 – 2.94 (m, 1H), 1.64 – 1.57 (m, 1H), 1.38 (d, J = 7.0 Hz, 3H).

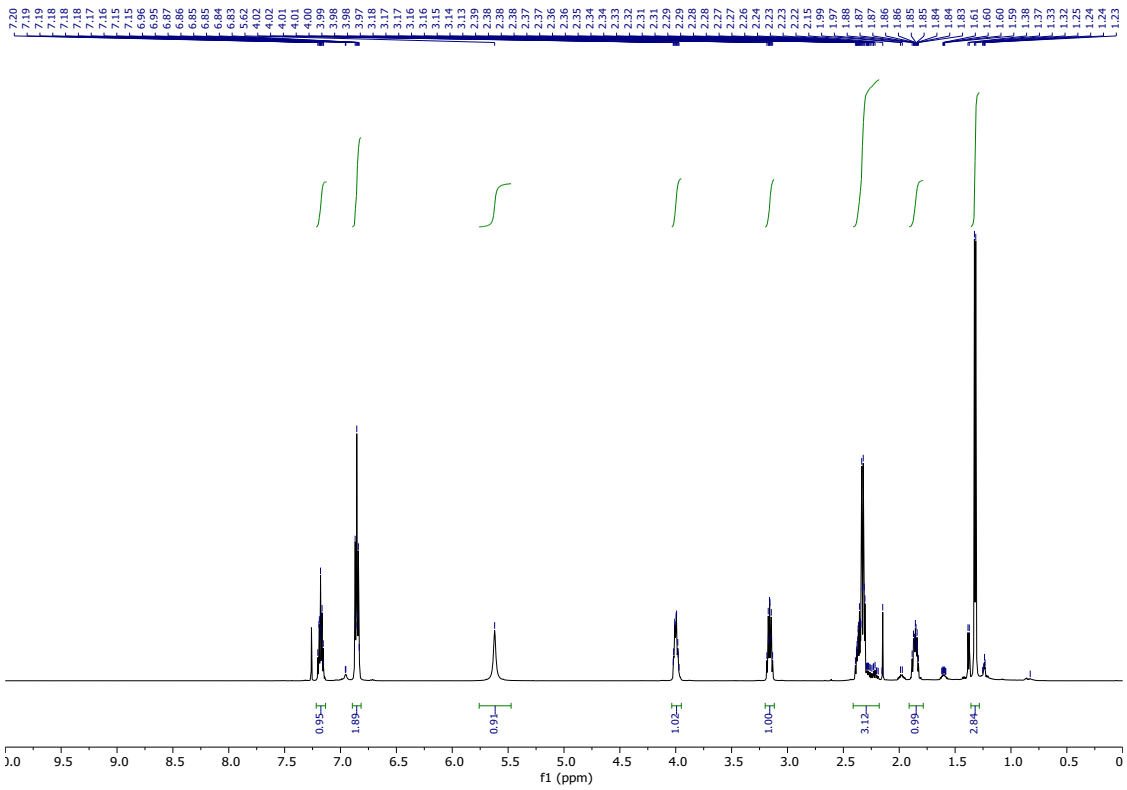
Minor diastereomer partial **^{13}C NMR** (151 MHz, $CDCl_3$) δ 128.5 (t, *J* = 10.6 Hz), 111.8, 57.8 (t, *J* = 2.2 Hz), 36.2, 30.0, 26.0, 16.8 (t, *J* = 1.9 Hz).

Minor diastereomer **^{19}F NMR** (377 MHz, $CDCl_3$) δ -112.5.

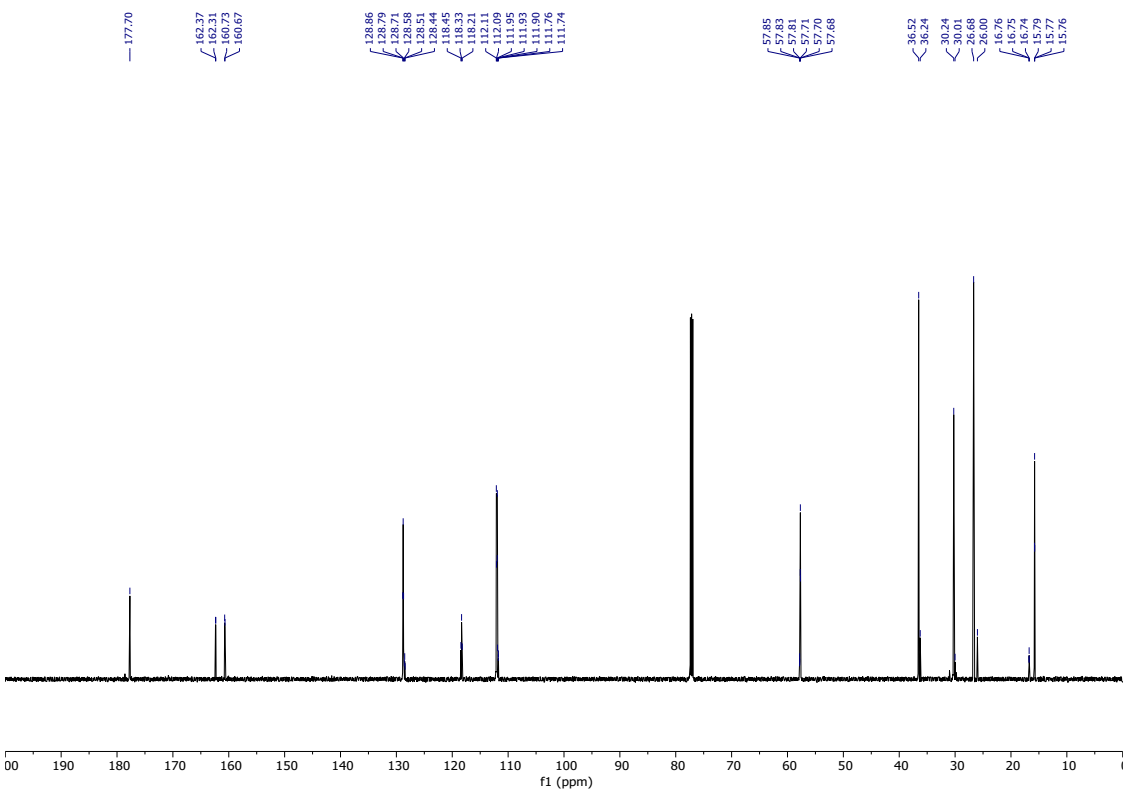
IR (neat) 3172, 3099, 2979, 1695, 1623, 1590, 1467, 1452, 1387, 1335 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{12}H_{14}F_2NO^+$ $[M+H]^+$: 226.1038, found 226.1046.

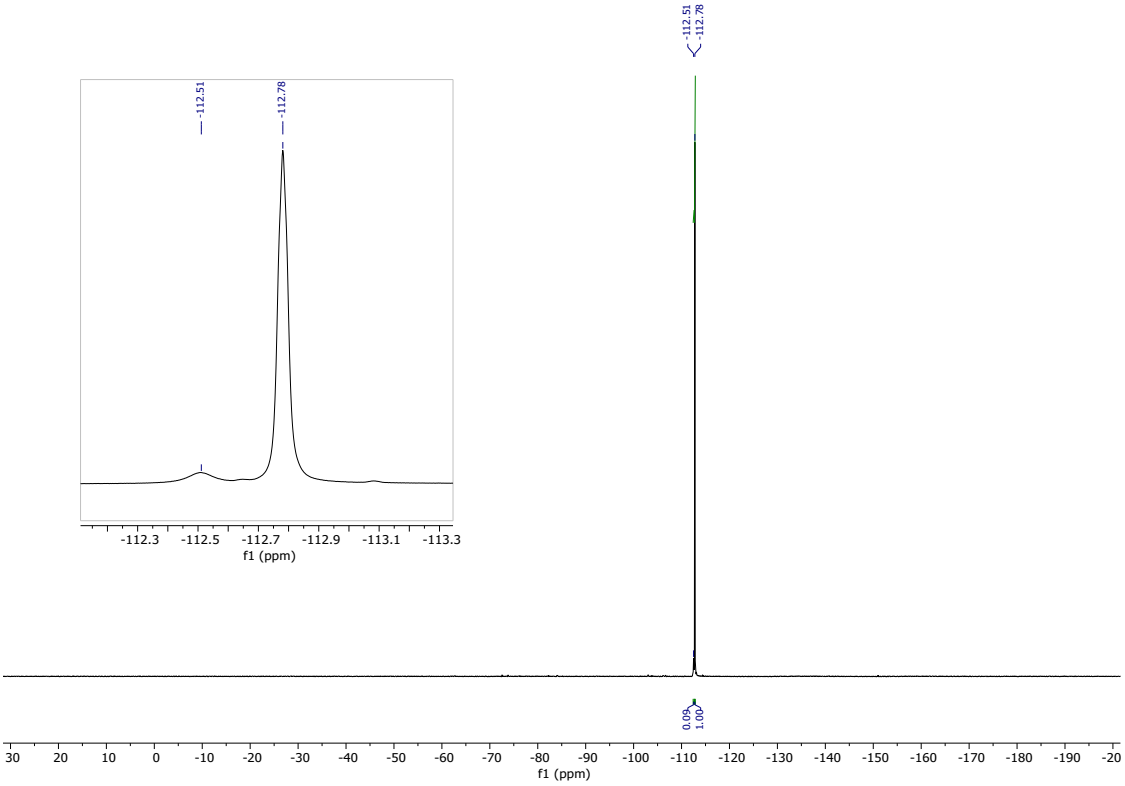
^{1}H NMR – 2u

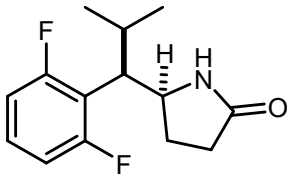


^{13}C NMR – 2u



^{19}F NMR – 2u


-112.51
-112.78
-112.3
-112.5
-112.7
-112.9
-113.1
-113.3
f1 (ppm)
0.09
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



2v. 5-(1-(2,6-difluorophenyl)-2-methylpropyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1v**. 40.3 mg, 0.159 mmol, 80% yield. Tan solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (tt, *J* = 8.4, 6.3 Hz, 1H), 6.91 – 6.81 (m, 2H), 5.77 (br s, 1H), 4.30 – 4.24 (m, 1H), 2.92 (t, *J* = 7.4 Hz, 1H), 2.34 (dddd, *J* = 12.6, 9.7, 7.3, 5.2 Hz, 1H), 2.28 – 2.15 (m, 2H), 2.08 (ddd, *J* = 17.0, 9.7, 5.2 Hz, 1H), 1.78 (ddt, *J* = 13.1, 9.5, 6.9 Hz, 1H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.7 Hz, 3H).

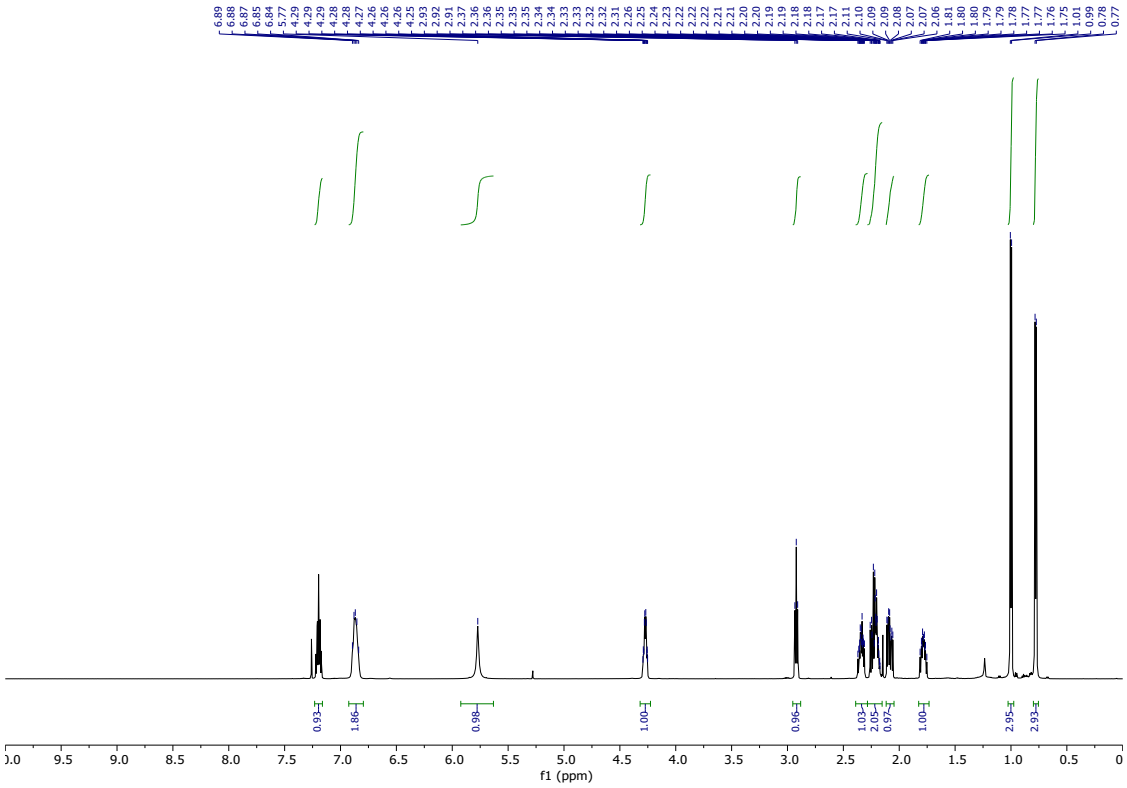
^{13}C NMR (151 MHz, $CDCl_3$) δ 177.8, 162.1 (d, *J* = 246 Hz), 161.7 (d, *J* = 246 Hz), 129.0 (t, *J* = 10.7 Hz), 115.2 (t, *J* = 18.5 Hz), 112.3 (d, *J* = 24.5 Hz), 111.6 (d, *J* = 25.0 Hz), 54.7 (t, *J* = 2.0 Hz), 48.9 (d, *J* = 1.8 Hz), 30.0, 28.9 (t, *J* = 1.5 Hz), 27.3, 21.9, 20.3. *Note*: at 25 °C, the hindered arene rotation leads to inequivalent aromatic sp^2 ^{13}C NMR signals.

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.36, -111.86. *Note*: at 25 °C, the hindered arene rotation leads to two well-resolved ^{19}F NMR signals.

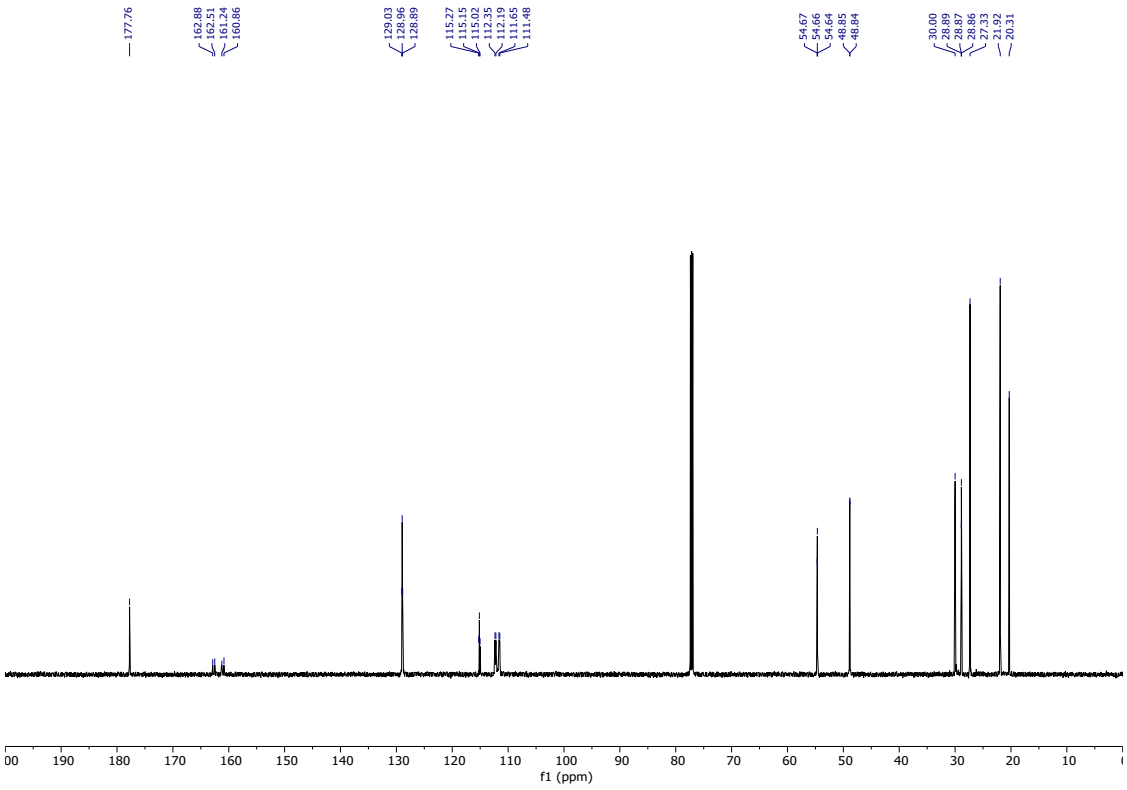
IR (neat) 3183, 3100, 2969, 1687, 1660, 1620, 1589, 1460, 1387, 1290 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{18}F_2NO^+$ $[M+H]^+$: 254.1351, found 254.1357.

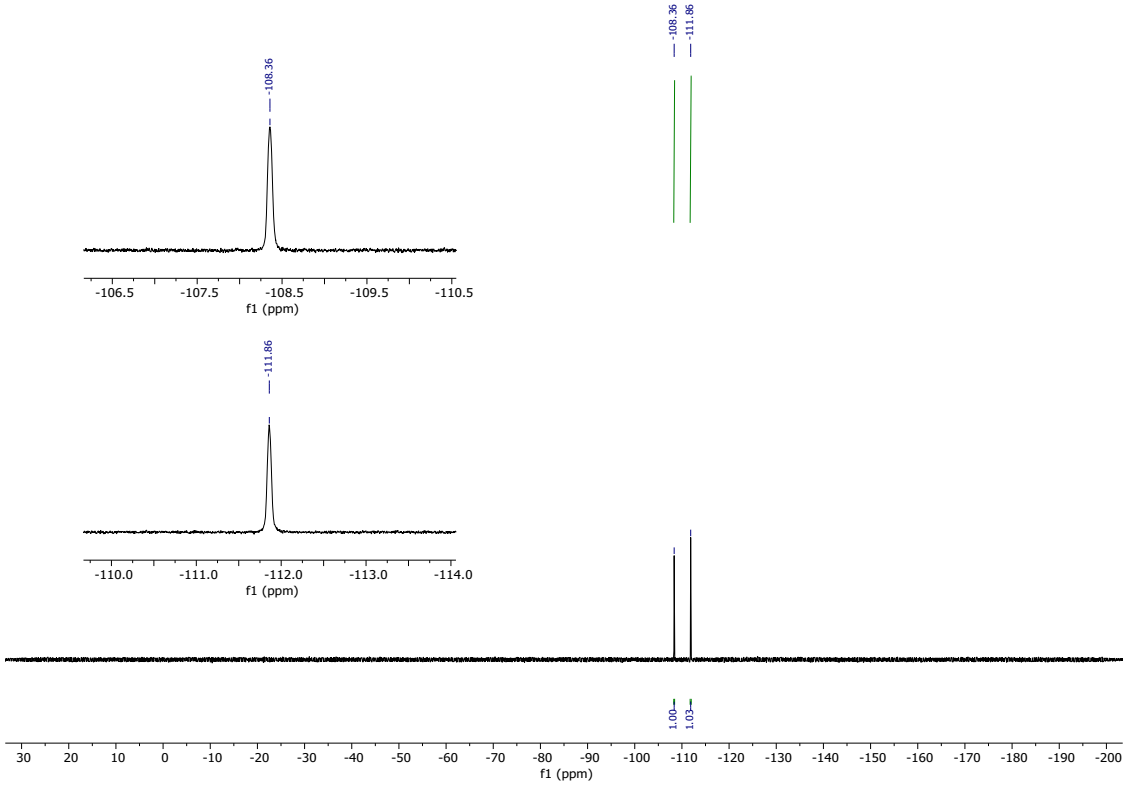
^{1}H NMR – 2v

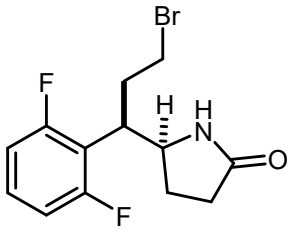


^{13}C NMR – 2v



^{19}F NMR – 2v


-108.36
-111.86
-106.5
-107.5
-108.5
-109.5
-110.5
f1 (ppm)
-110.0
-111.0
-112.0
-113.0
-114.0
1.00
1.03
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200



2w. 5-(3-bromo-1-(2,6-difluorophenyl)propyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1w**. 28.2 mg, 0.089 mmol, 44% yield. Light brown solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (tt, *J* = 6.4, 8.4 Hz, 1H), 6.97 – 6.88 (m, 2H), 5.30 (br s, 1H), 4.13 – 4.02 (m, 1H), 3.41 – 3.32 (m, 2H), 3.10 (td, *J* = 9.8, 6.3 Hz, 1H), 2.48 – 2.31 (m, 4H), 2.19 (dddd, *J* = 14.0, 9.4, 7.0, 3.9 Hz, 1H), 1.98 – 1.88 (m, 1H).

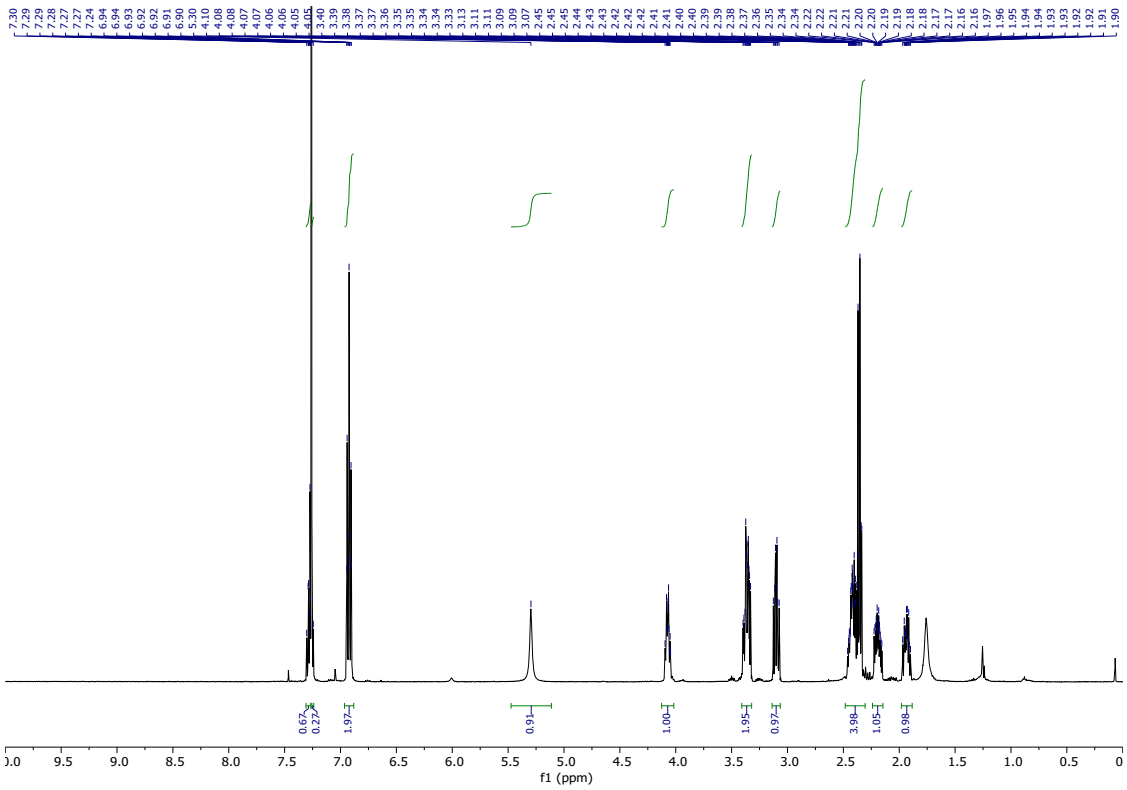
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 161.9 (dd, *J* = 248, 8.4 Hz), 129.8 (t, *J* = 10.6 Hz), 114.7 (t, *J* = 17.9 Hz), 112.4 (dd, J = 23.3, 3.4 Hz), 56.5 (t, *J* = 2.0 Hz), 41.1, 33.0 (*t*, J = 2.3 Hz), 30.7, 30.1, 26.8.

^{19}F NMR (564 MHz, $CDCl_3$) δ -111.64.

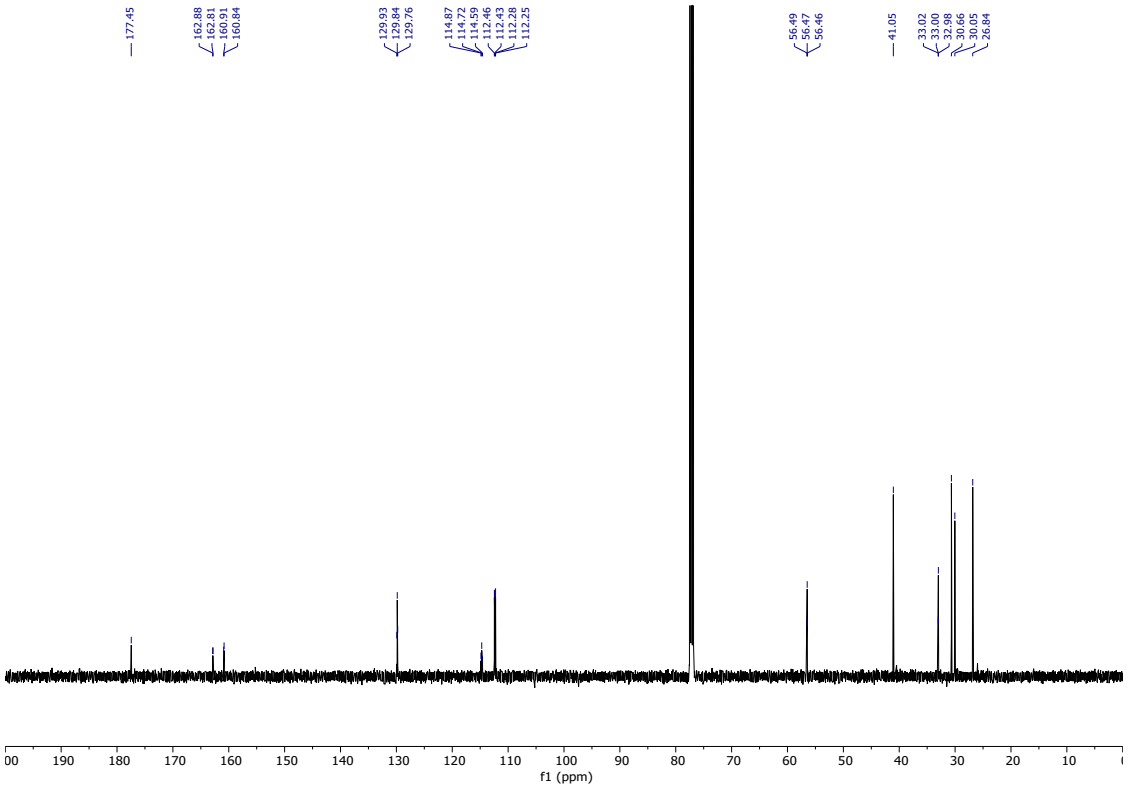
IR (neat) 3199, 2931, 2229, 1675, 1621, 1587, 1465, 1263, 1234, 1192 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{15}F_2BrNO^+$ $[M+H]^+$: 318.0300, found 318.0299.

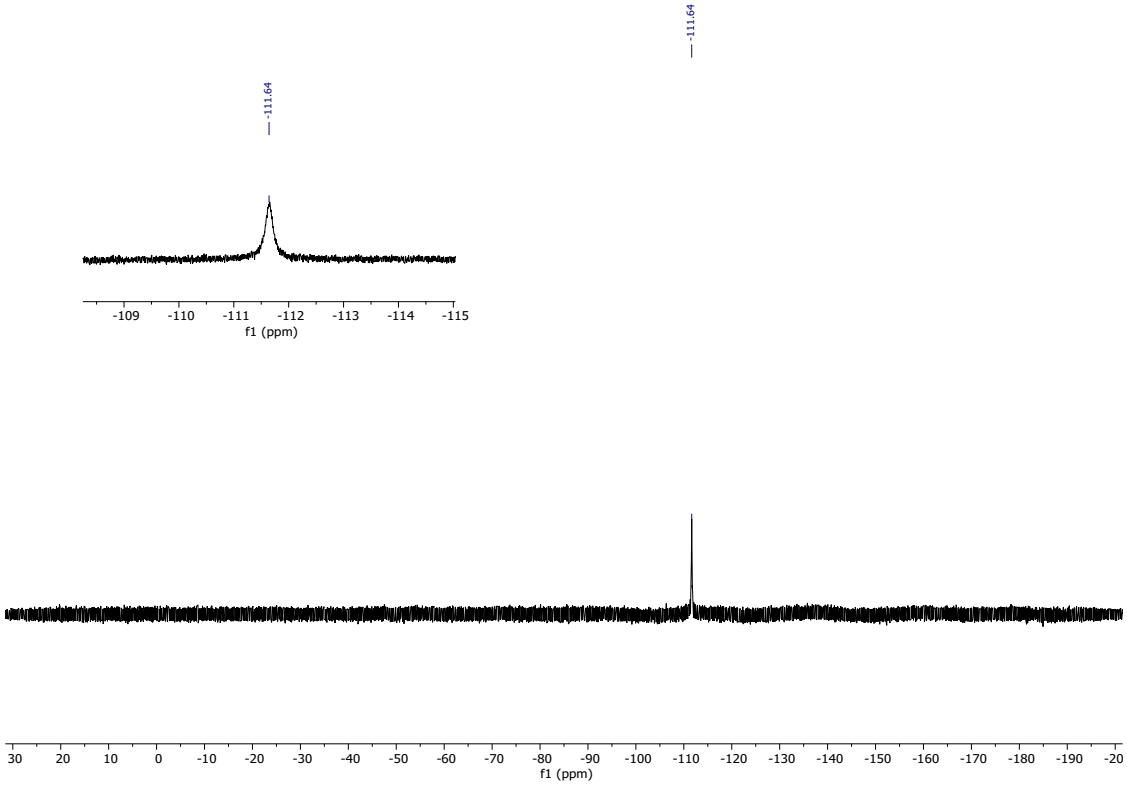
^{1}H NMR – 2w

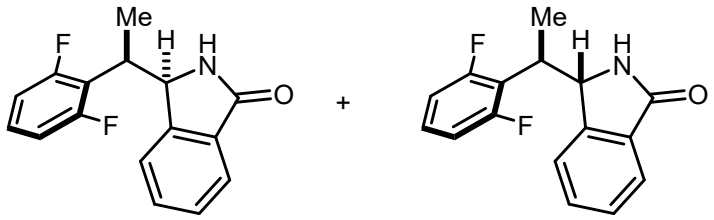


^{13}C NMR – 2w



^{19}F NMR – 2w


-111.64
-111.64
-109
-110
-111
-112
-113
-114
-115
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)



3.2 : 1

2x. 3-(1-(2,6-difluorophenyl)ethyl)isoindolin-1-one. Prepared according to **GP2** with 0.2 mmol **1x**. 25.5 mg, 0.093 mmol, 47%. Dark red solid.

Major diastereomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.56 (td, *J* = 7.4, 1.2 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.16 (tt, *J* = 8.4, 6.3 Hz, 1H), 6.83 (t, *J* = 8.6 Hz, 2H), 6.41 (br s, 1H), 4.93 (d, *J* = 8.0 Hz, 1H), 3.49 (p, *J* = 7.4 Hz, 1H), 1.67 (d, *J* = 7.2 Hz, 3H).

Major diastereomer **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.4, 161.4 (dd, *J* = 248, 8.7 Hz), 146.0, 132.0, 131.7, 129.0 (t, *J* = 10.6 Hz), 128.6, 124.0, 123.8, 117.7 (t, *J* = 17.9 Hz), 112.1 (m), 60.5, 35.3, 17.1 (t, *J* = 2.5 Hz).

Major diastereomer **^{19}F NMR** (471 MHz, $CDCl_3$) δ -111.66 – -111.81 (m).

Minor diastereomer **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.40 (td, *J* = 7.5, 1.3 Hz, 1H), 7.29 (tt, *J* = 8.3, 6.4 Hz, 1H), 7.09 (br s, 1H), 6.94 (t, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 4.91 (d, *J* = 7.6 Hz, 1H), 3.42 (p, *J* = 7.2 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 3H).

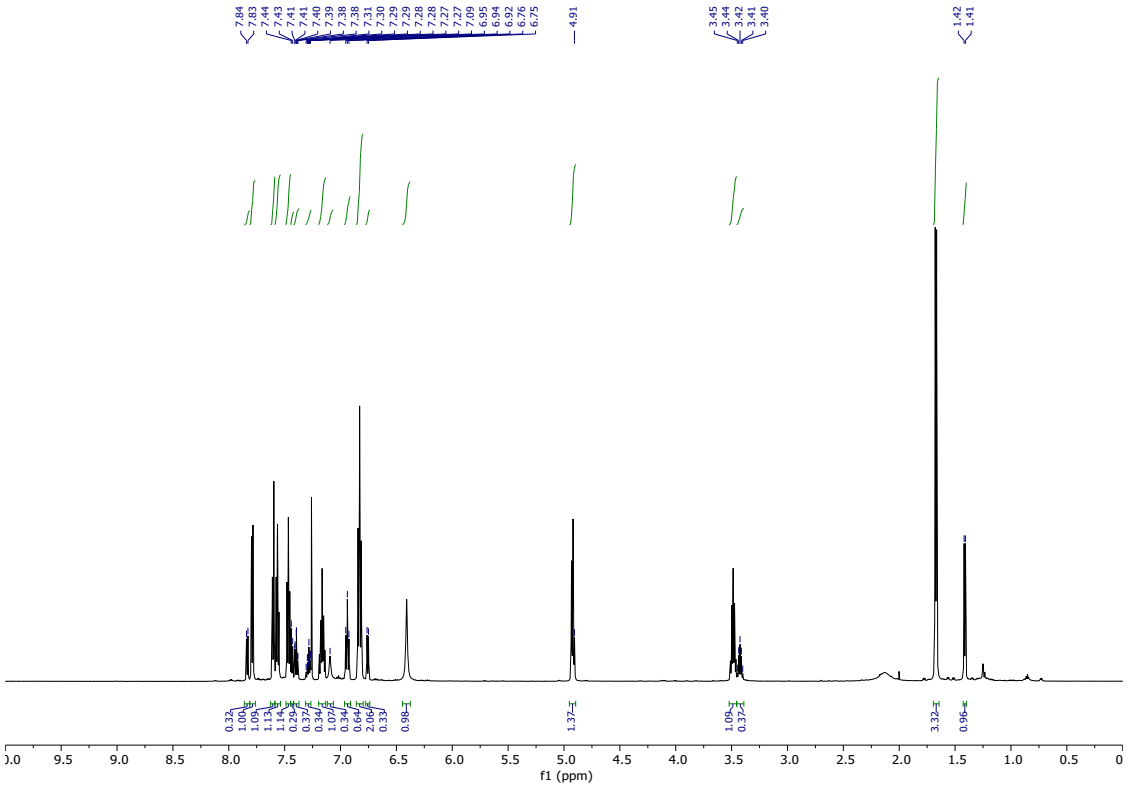
Minor diastereomer partial **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.1, 161.6 (dd, *J* = 247, 8.8 Hz), 146.2, 131.9, 129.0 (t, *J* = 10.6 Hz), 128.5, 124.0, 122.8, 118.8 (t, *J* = 18.1 Hz), 112.09 (m), 59.9, 35.1, 16.08 (t, *J* = 2.2 Hz).

Minor diastereromer **^{19}F NMR** (471 MHz, $CDCl_3$) -112.35 – -112.47 (m).

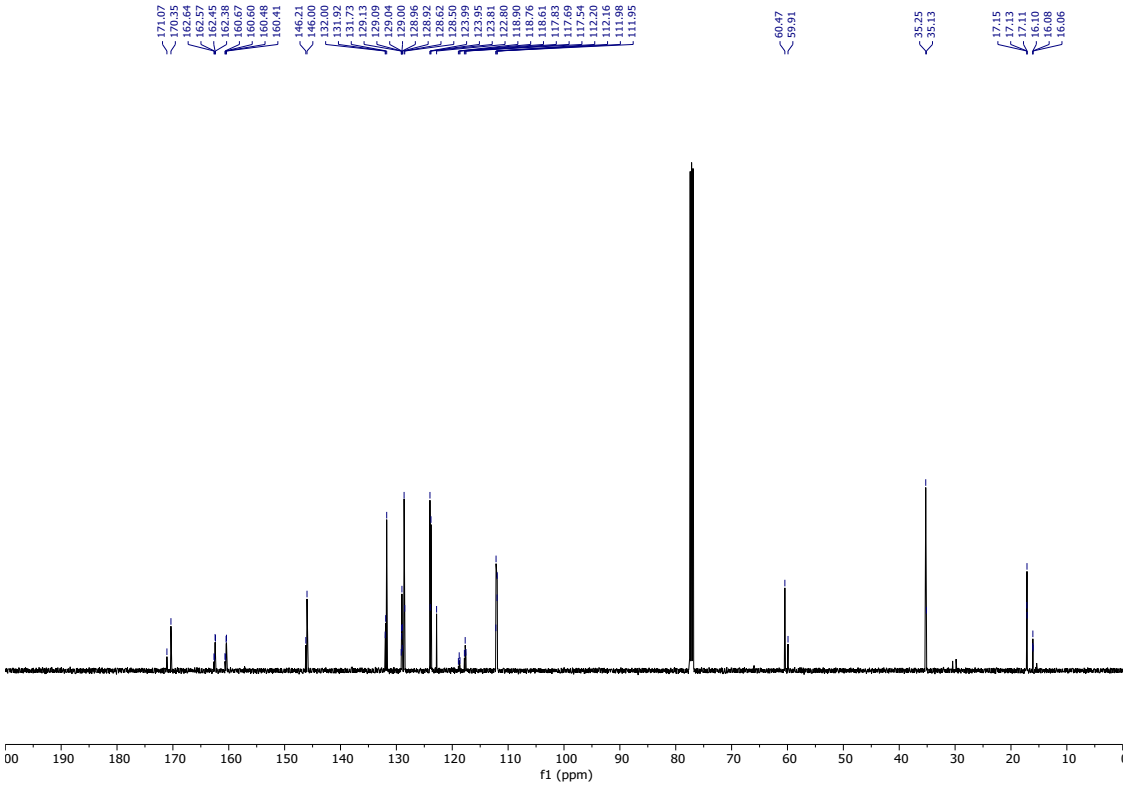
IR (neat) 3172, 3084, 2941, 2887, 1689, 1623, 1590, 1469, 1456, 1360 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{16}H_{14}F_2NO^+$ $[M+H]^+$: 274.1038, found 274.1036.

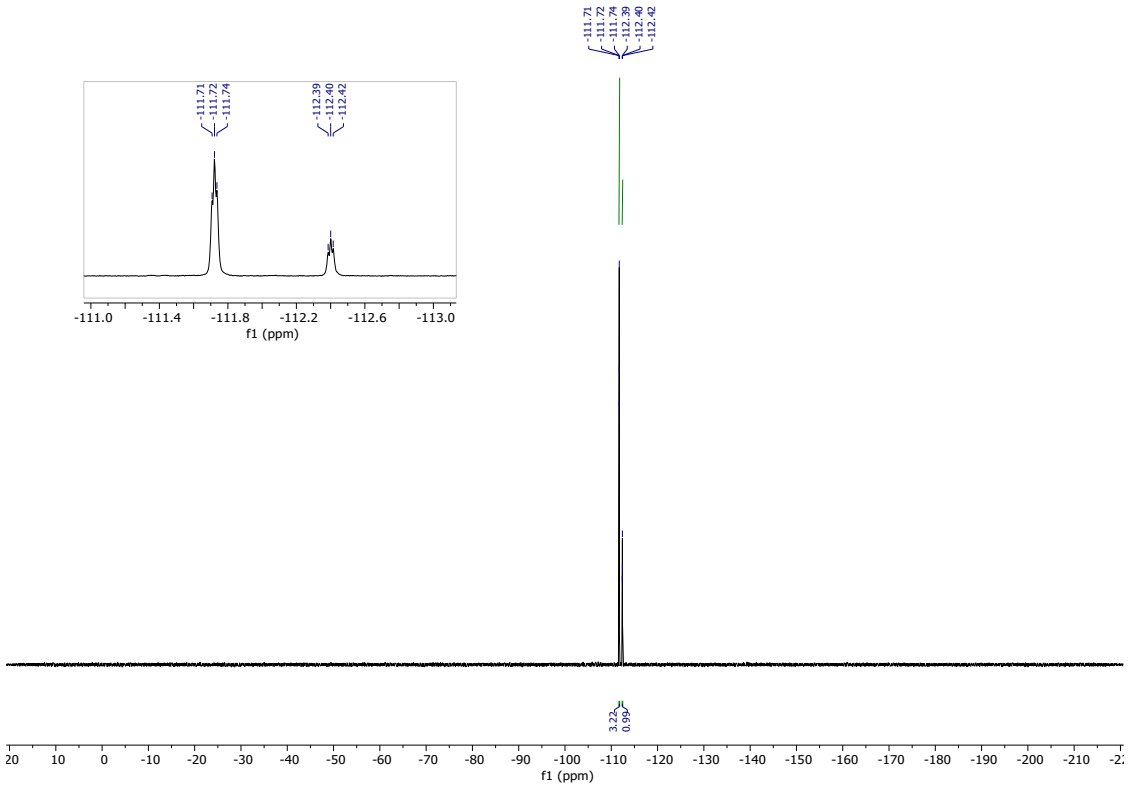
^{1}H NMR – 2x

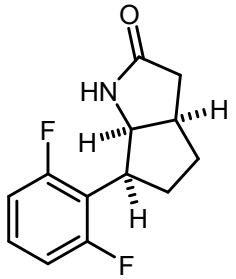


^{13}C NMR – 2x



^{19}F NMR – 2x


-111.71
-111.72
-111.74
-112.39
-112.40
-112.42
-111.0
-111.4
-111.8
-112.2
-112.6
-113.0
f1 (ppm)
3.22
0.99
f1 (ppm)



2y. 6-(2,6-difluorophenyl)hexahydrocyclopenta[b]pyrrol-2(1H)-one. Prepared according to **GP2** with 0.2 mmol **1y**. 20.7 mg, 0.087 mmol, 44% yield. Colorless solid.

Major diastereomer **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.23 – 7.17 (m, 1H), 6.91 – 6.85 (m, 2H), 5.09 (br s, 1H), 4.28 (t, *J* = 6.7 Hz, 1H), 3.27 (dt, *J* = 12.5, 6.0 Hz, 1H), 3.08 – 3.02 (m, 1H), 2.71 (dd, *J* = 17.8, 10.6 Hz, 1H), 2.47 (qd, *J* = 12.8, 6.2 Hz, 1H), 2.15 (dd, *J* = 17.8, 4.3 Hz, 1H), 1.98 (dt, *J* = 12.4, 6.1 Hz, 1H), 1.91 – 1.83 (m, 1H), 1.74 (dd, *J* = 13.1, 6.4 Hz, 1H).

Major diastereomer **^{13}C NMR** (176 MHz, $CDCl_3$) δ 178.2, 162.2 (dd, *J* = 248, 8.9 Hz), 128.7 (*t*, *J* = 10.7 Hz), 114.7 (t, *J* = 17.5 Hz), 112.0 (dd, *J* = 23.0, 4.4 Hz), 61.5, 42.4, 36.5, 33.6, 26.2 (t, *J* = 5.0 Hz).

Major diastereomer **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.95 – -111.16 (app t, J = 6.9 Hz).

Minor diastereomer partial **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.66 (br s, 1H), 4.25 – 4.20 (m, 1H), 3.34 – 3.30 (m, 1H), 2.63 (dd, *J* = 17.4, 9.7 Hz, 1H), 2.28 – 2.22 (m, 1H), 2.20 (dd, *J* = 17.5, 3.3 Hz, 1H).

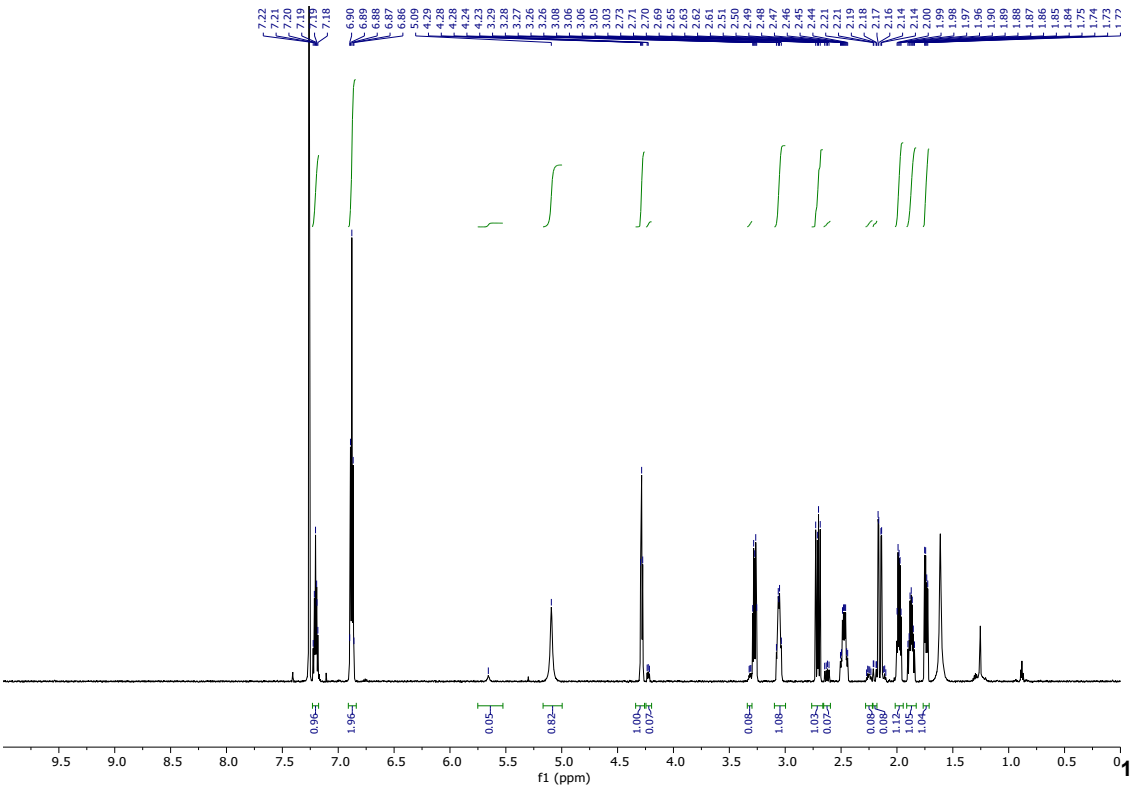
Minor diastereomer partial **^{13}C NMR** (176 MHz, $CDCl_3$) δ 43.6, 39.0, 34.1.

Minor diastereomer **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.75 – -113.87 (app t, J = 6.9 Hz).

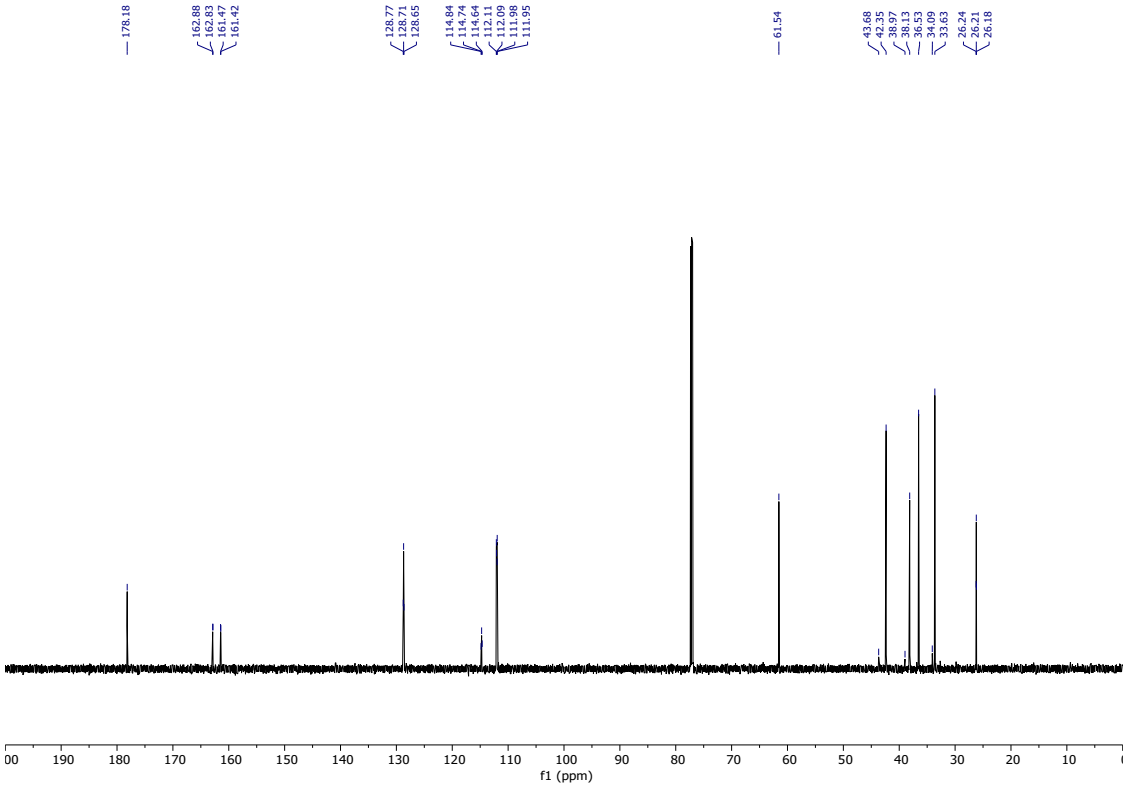
IR (neat) 3265, 2978, 1949, 2872, 1698, 1666, 1625, 1593, 1468, 1425 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{14}F_2NO^+$ $[M+H]^+$: 238.1038, found 238.1036.

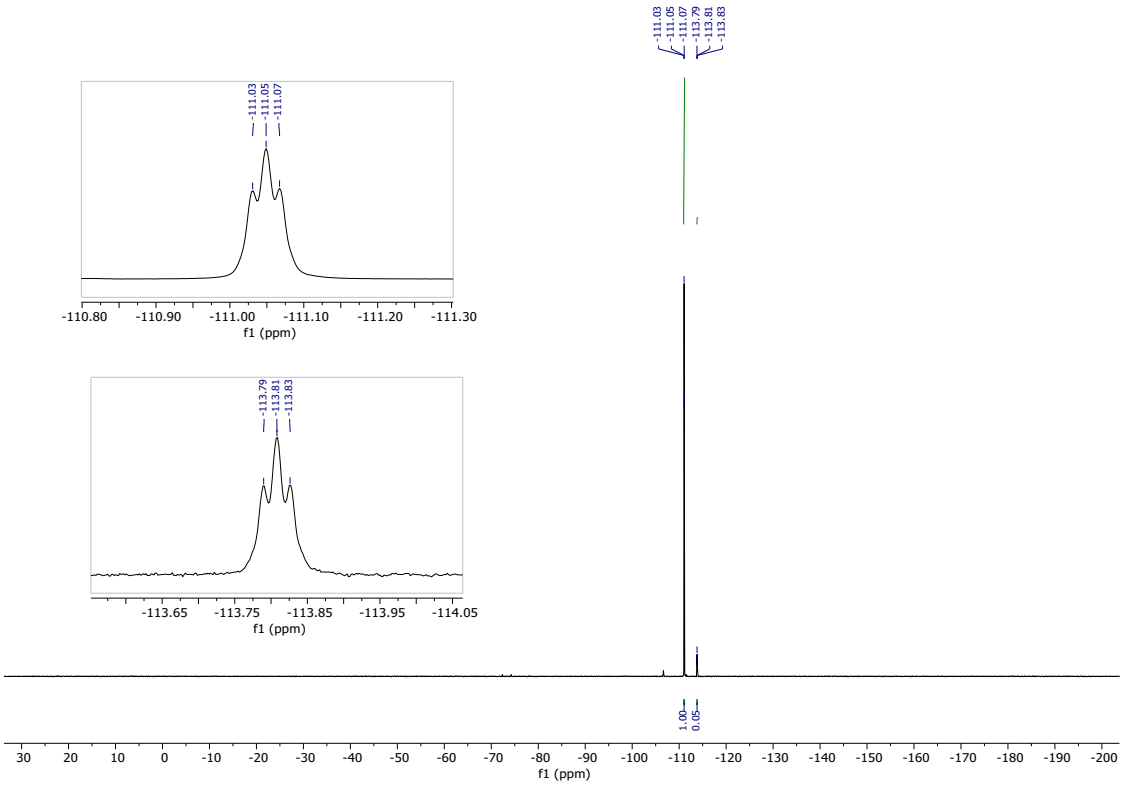
^{1}H NMR – 2y

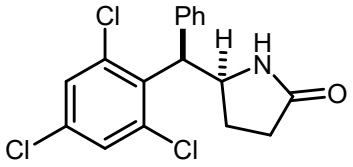


^{13}C NMR – 2y



^{19}F NMR – 2y


-111.03
-111.05
-111.07
-113.79
-113.81
-113.83
-110.80
-110.90
-111.00
-111.10
-111.20
-111.30
f1 (ppm)
-113.65
-113.75
-113.85
-113.95
-114.05
f1 (ppm)
1.00
0.05
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2z. 5-(phenyl(2,4,6-trichlorophenyl)methyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1z**. 46.6 mg, 0.13 mmol, 66% yield. Brown solid.

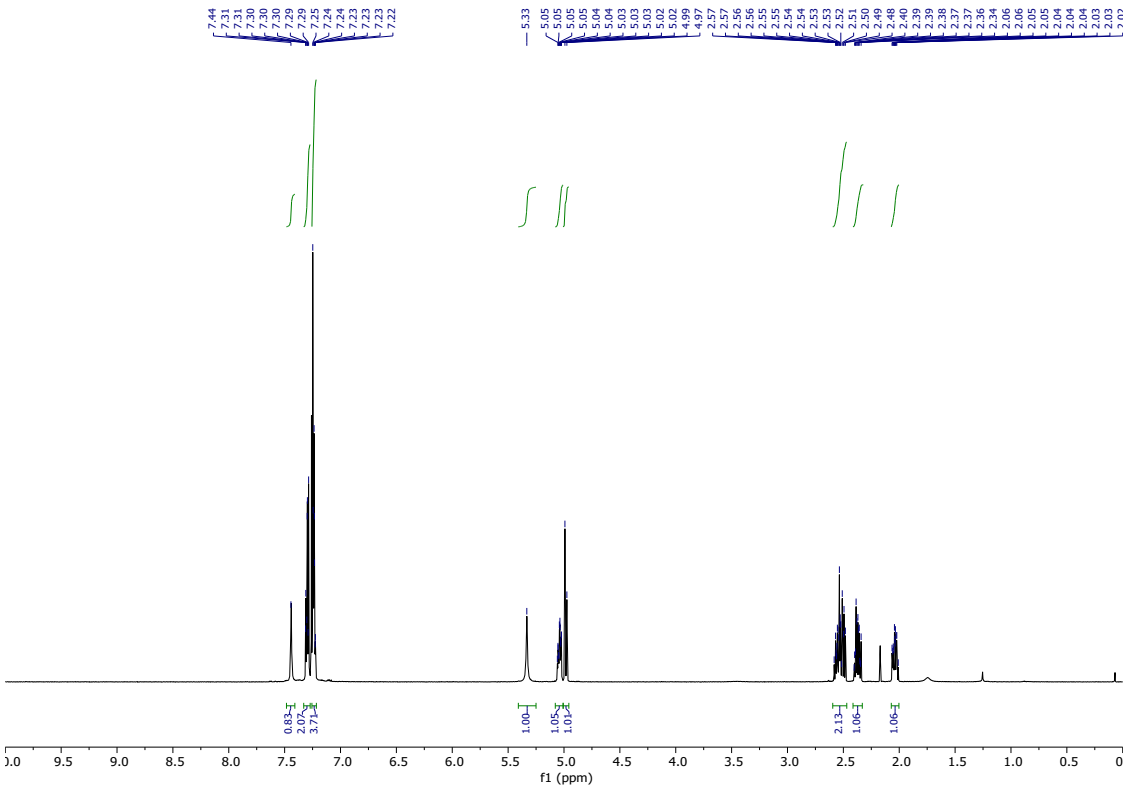
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.33 – 7.27 (m, 2H), 7.26 – 7.22 (m, 4H), 5.33 (br s, 1H), 5.08 – 5.01 (m, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 2.59 – 2.47 (m, 2H), 2.41 – 2.33 (m, 1H), 2.07 – 2.00 (m, 1H). *Note*: at 25 °C, the hindered arene rotation leads to inequivalent ^{1}H NMR signals from the trichlorobenzene ring.

^{13}C NMR (151 MHz, $CDCl_3$) δ 177.6, 138.2, 138.0, 135.9, 135.4, 134.1, 130.5, 129.0, 128.5, 128.5, 127.2, 53.3, 52.2, 29.4, 27.5. *Note*: at 25 °C, the hindered arene rotation leads to inequivalent ^{13}C NMR signals from the trichlorobenzene ring.

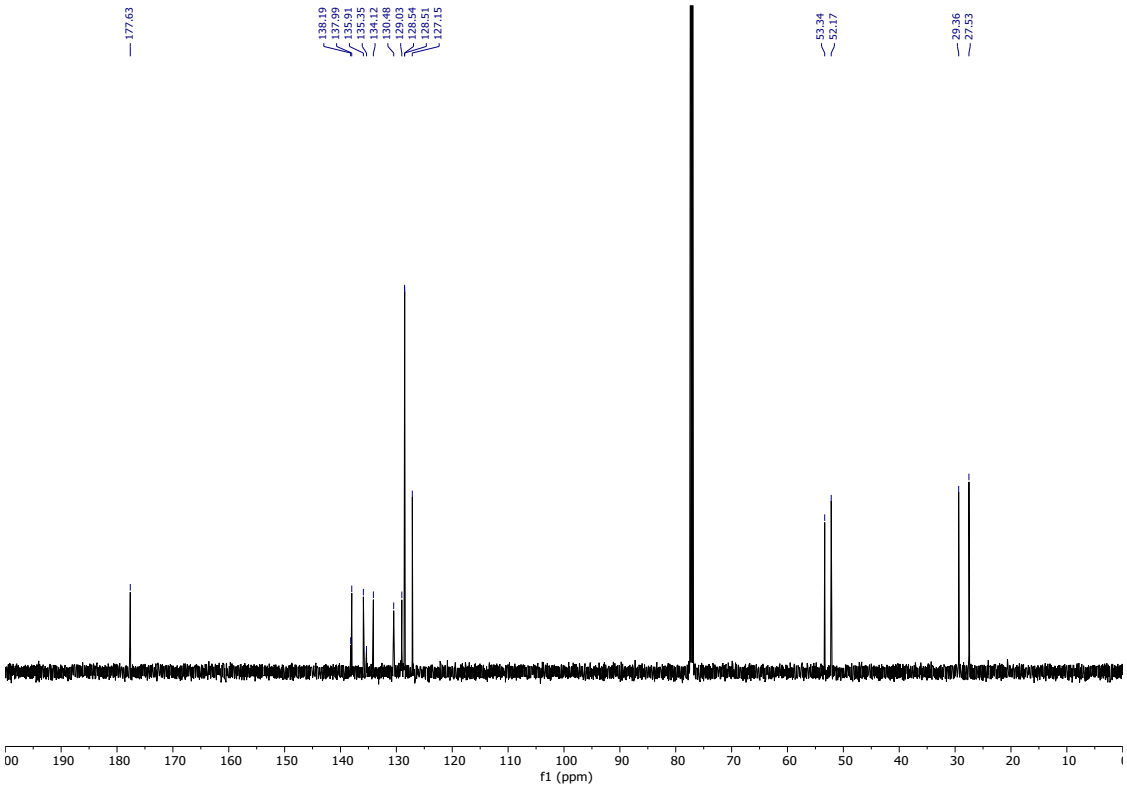
IR (neat) 3188, 3089, 3069, 2975, 1692, 1577, 1548, 1498, 1445, 1377 cm^{-1}

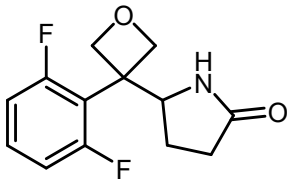
HRMS (ESI+) m/z calculated for $C_{17}H_{15}Cl_3NO^+$ $[M+H]^+$: 354.0214, found 354.0212.

^{1}H NMR – 2z



^{13}C NMR – 2z





2aa. 5-(3-(2,6-difluorophenyl)oxetan-3-yl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1aa**. 18.3 mg, 0.072 mmol, 36% yield. Light brown solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.28 (tt, *J* = 8.2, 6.7 Hz, 1H), 6.91 (t, *J* = 8.9 Hz, 2H), 6.67 (br s, 1H), 5.08 (d, *J* = 6.9 Hz, 1H), 5.03 (d, *J* = 6.6 Hz, 1H), 4.69 (d, *J* = 6.7 Hz, 1H), 4.63 (d, *J* = 7.0 Hz, 1H), 4.50 – 4.43 (m, 1H), 2.31 – 2.18 (m, 2H), 2.08 – 1.98 (m, 2H).

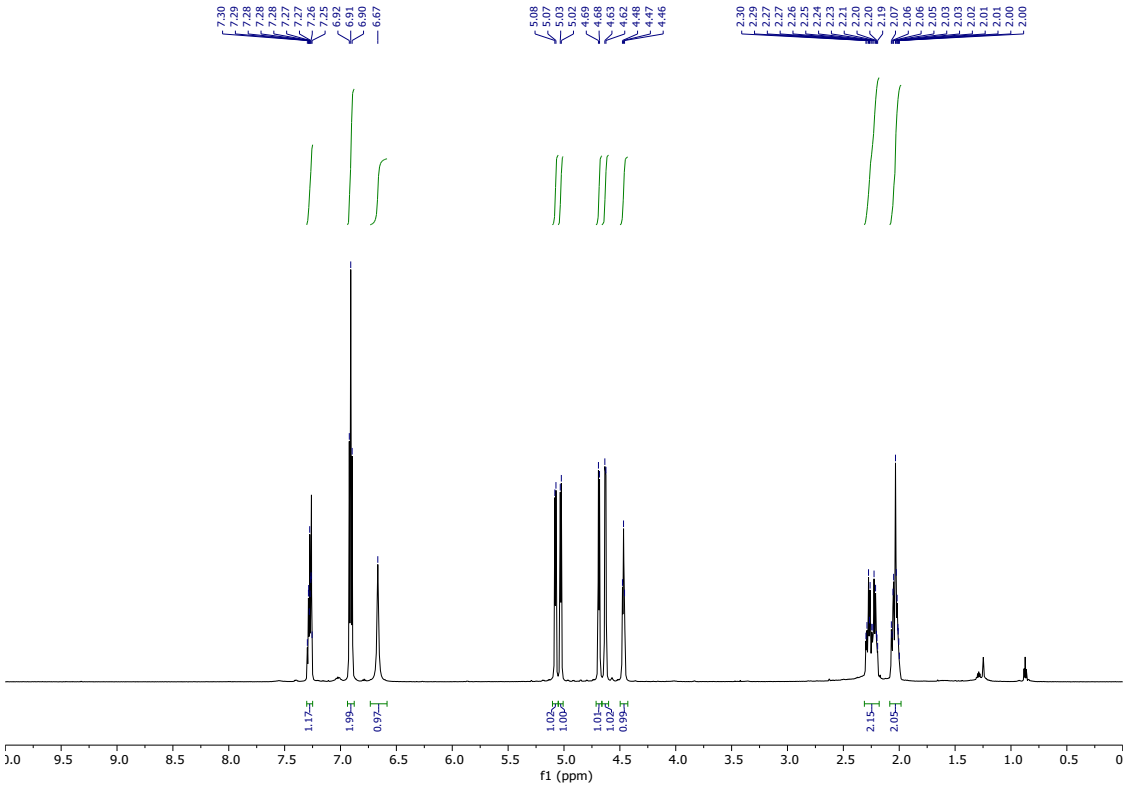
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.5, 160.8 (m), 129.9 (t, *J* = 10.6 Hz), 115.8 (t, *J* = 18.5 Hz), 112.2 (d, *J* = 22.6 Hz), 78.0 (t, *J* = 5.0 Hz), 77.9 (t, *J* = 5.0 Hz), 60.1, 46.8 (t, *J* = 1.9 Hz), 30.1, 22.6.

^{19}F NMR (564 MHz, $CDCl_3$, 50 °C) δ -113.41. *Note*: at room temperature, the ^{19}F resonance appears as a broad doublet. Warming the sample to 50 °C causes the signal to coalesce to a broad singlet (see attached spectrum).

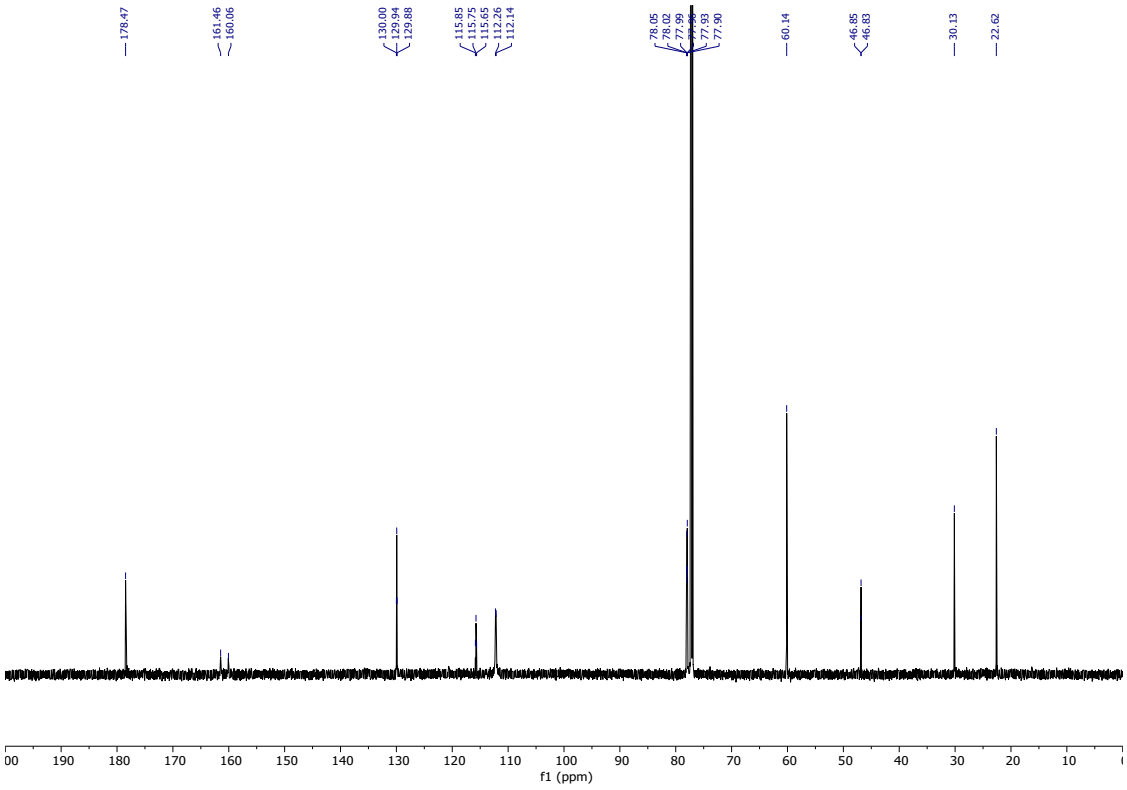
IR (neat) 3198, 3101, 2966, 2885, 1695, 1626, 1583, 1460, 1425, 1395 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{14}F_2NO_2Na^+$ $[M+H]^+$: 254.0988, found 254.0987.

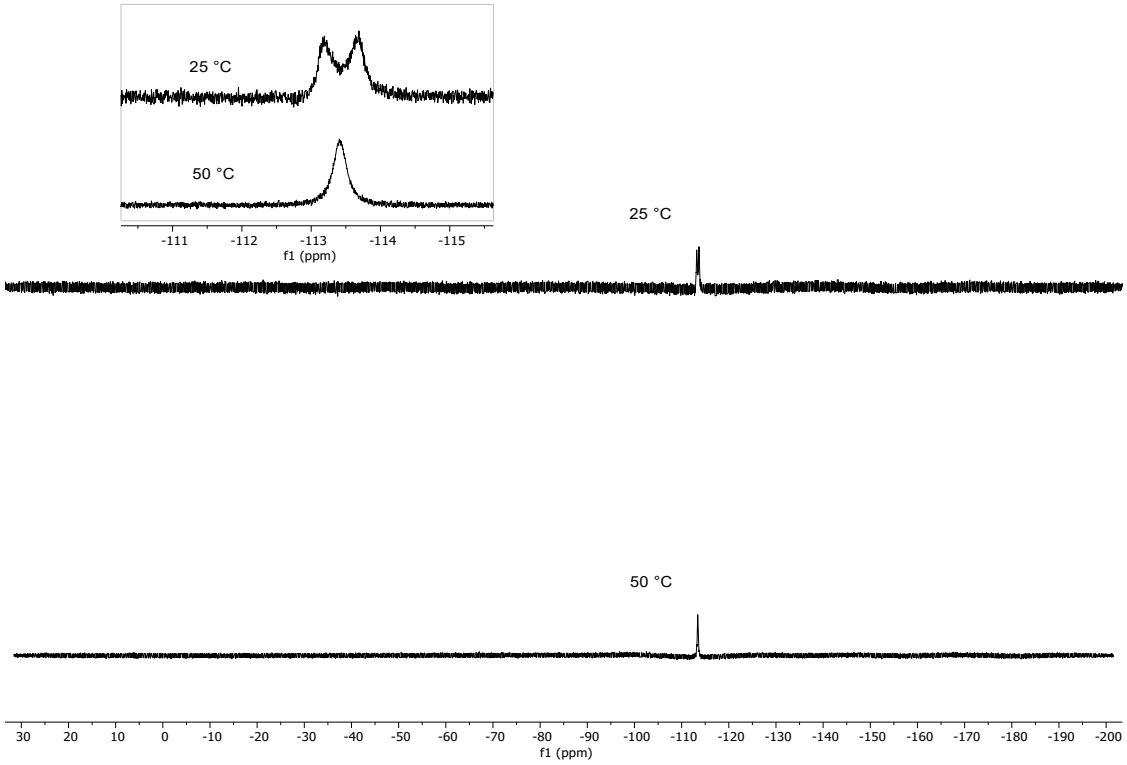
^{1}H NMR – 2aa

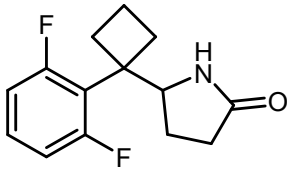


^{13}C NMR – 2aa



^{19}F NMR – 2aa


25 °C
50 °C
-111
-112
-113
-114
-115
f1 (ppm)
25 °C
50 °C
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2ab. 5-(1-(2,6-difluorophenyl)cyclobutyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1ab**. 22.7 mg, 0.090 mmol, 45% yield. Yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (tt, *J* = 8.3, 6.2 Hz, 1H), 6.83 (t, *J* = 9.2 Hz, 2H), 6.63 (br s, 1H), 4.31 – 4.25 (m, 1H), 2.67 – 2.53 (m, 2H), 2.40 – 2.32 (m, 1H), 2.32 – 2.25 (m, 1H), 2.21 – 2.12 (m, 2H), 2.12 – 2.04 (m, 1H), 1.96 – 1.80 (m, 3H).

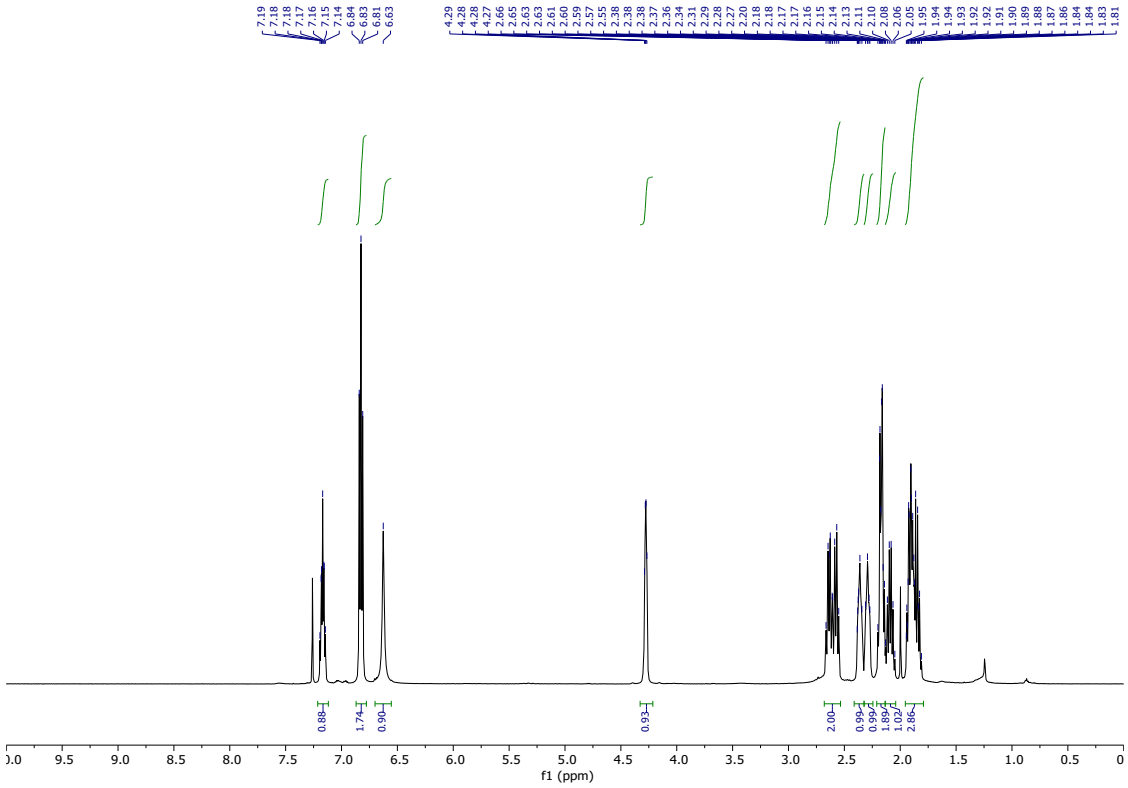
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.6, 161.4 (dd, *J* = 247, 9.0 Hz) 128.7 (t, *J* = 10.8 Hz), 120.1 (t, *J* = 17.2 Hz), 112.0 (d, *J* = 23.9 Hz), 60.9, 46.4, 32.2 (t, *J* = 2.7 Hz), 31.3 (t, *J* = 2.8 Hz) 30.2, 22.7 (t, *J* = 2.0 Hz), 17.5 (t, *J* = 2.2 Hz).

^{19}F NMR (564 MHz, $CDCl_3$, 50 °C) δ -110.90. *Note*: at 25 °C, the ^{19}F resonance appears as a broad singlet. Warming the sample to 50 °C causes the signal to sharpen (see spectrum).

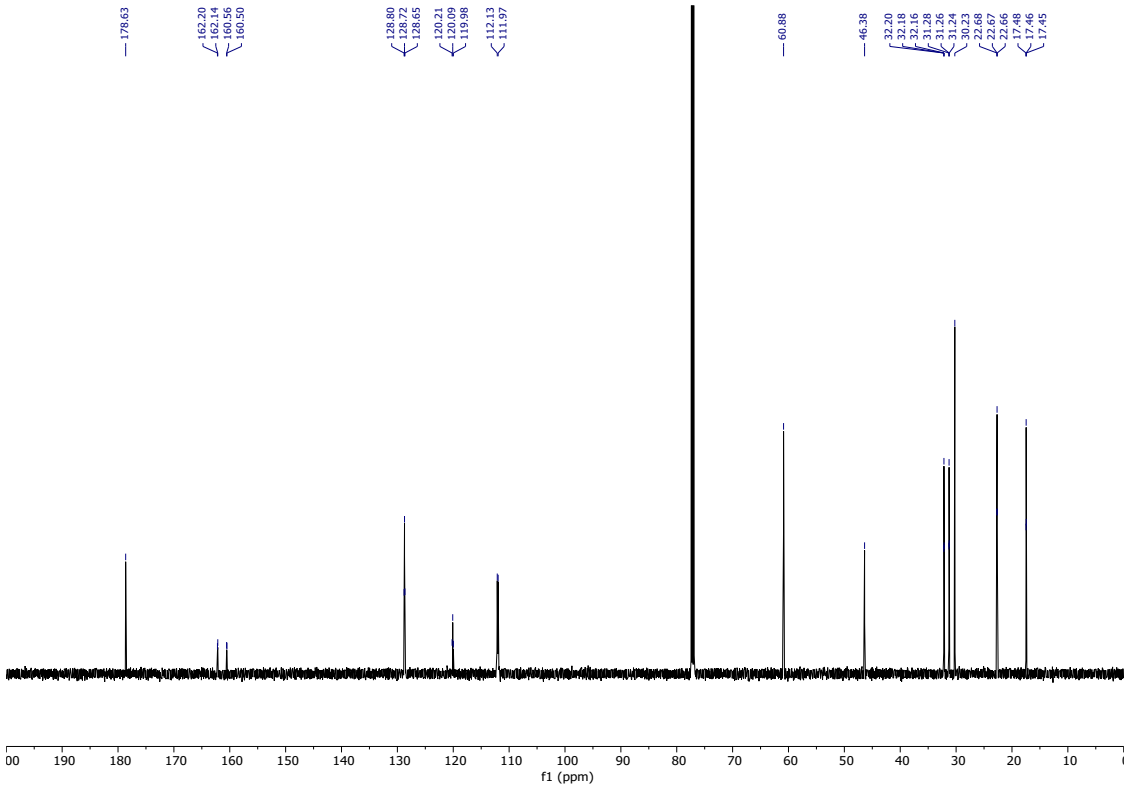
IR (neat) 3177, 3101, 2949, 1688, 1666, 1621, 1577, 1459, 1396, 1358 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{16}F_2NO^+$ $[M+H]^+$: 252.1195, found 252.1184

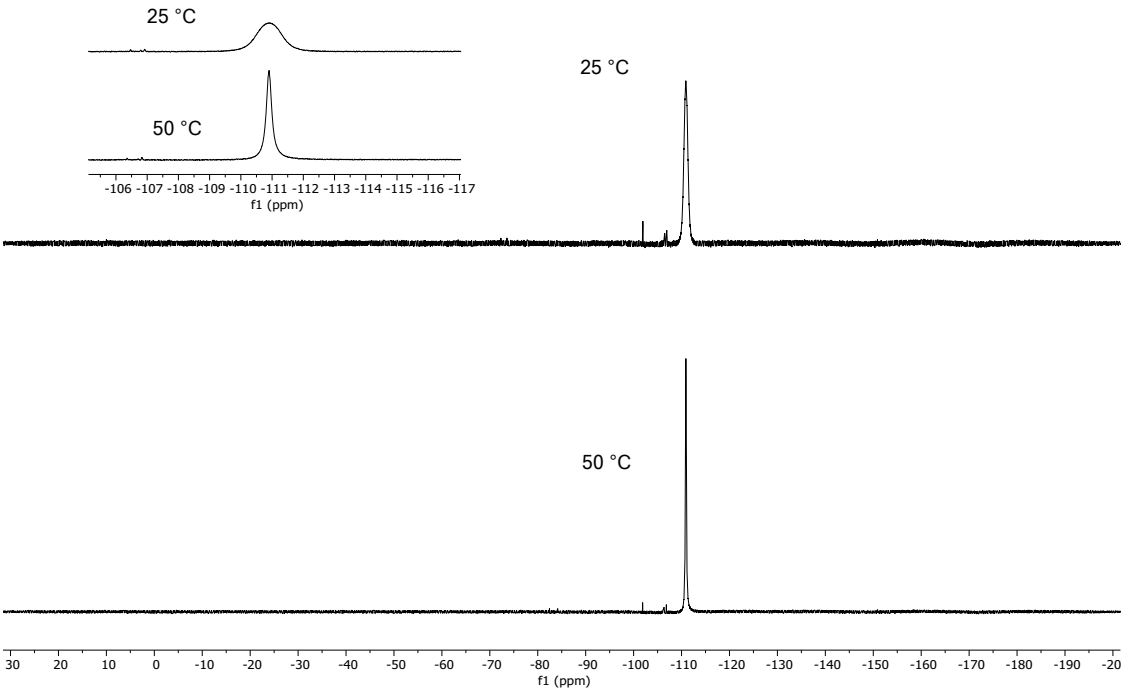
^{1}H NMR – 2ab

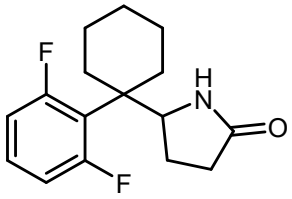


^{13}C NMR – 2ab



^{19}F NMR – 2ab


25 °C
50 °C
-106 -107 -108 -109 -110 -111 -112 -113 -114 -115 -116 -117
f1 (ppm)
25 °C
50 °C
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



2ac. 5-(1-(2,6-difluorophenyl)cyclohexyl)pyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1ac**. 23.9 mg, 0.086 mmol, 43% yield. Light brown solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (tt, *J* = 8.3, 5.9 Hz, 4H), 6.92 – 6.84 (m, 2H), 5.76 (br s, 1H), 3.75 (app t, *J* = 6.6 Hz, 1H), 2.79 – 2.69 (m, 2H), 2.21 – 2.13 (m, 1H), 2.11 – 1.90 (m, 3H), 1.75 – 1.69 (m, 2H), 1.64 – 1.60 (m, 1H), 1.34 – 1.17 (m, 5H).

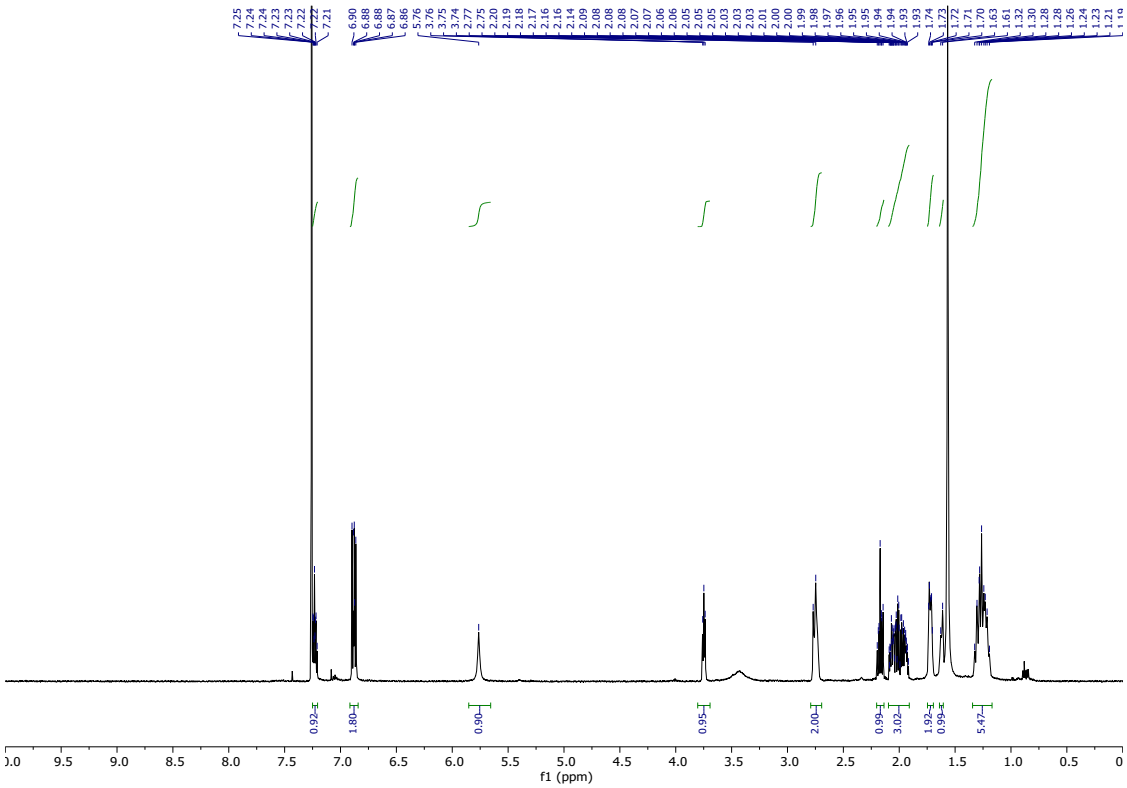
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.6, 163.0 (dd, *J* = 249, 10.1 Hz), 129.1 (t, *J* = 12.6 Hz), 116.4 (t, *J* = 14.3 Hz), 113.3 (dd, *J* = 28.4, 2.5 Hz), 63.6, 49.6 (t, *J* = 4.5 Hz), 34.5 (t, *J* = 7.4 Hz), 34.1 (t, *J* = 7.5 Hz), 30.1, 26.5, 23.2, 23.2, 22.3.

^{19}F NMR (564 MHz, $CDCl_3$, 50 °C) δ -103.68. *Note*: at 25 °C, the ^{19}F resonance appears as a broad singlet. Warming the sample to 50 °C causes the signal to sharpen (see spectrum).

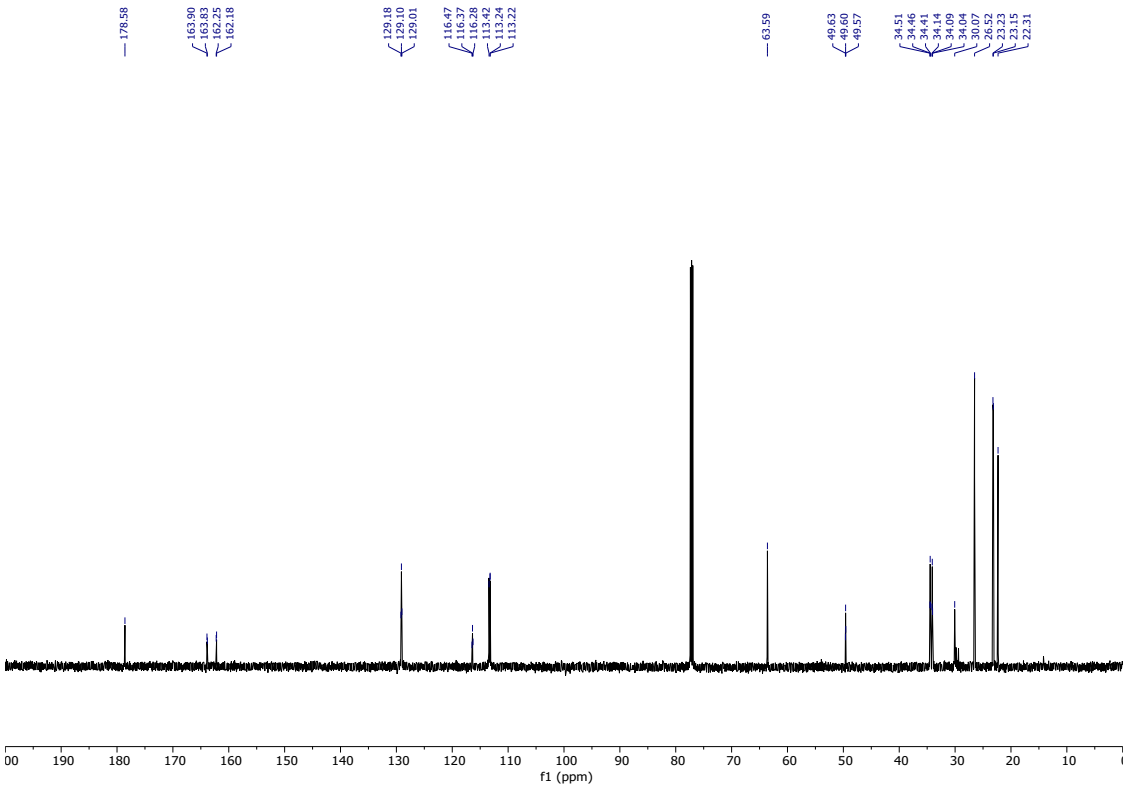
IR (neat) 3208, 3093, 2928, 1688, 1617, 1572, 1450, 1365, 1268, 1229 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{17}H_{19}F_2NO^+$ $[M+H]^+$: 280.1507, found 280.1505.

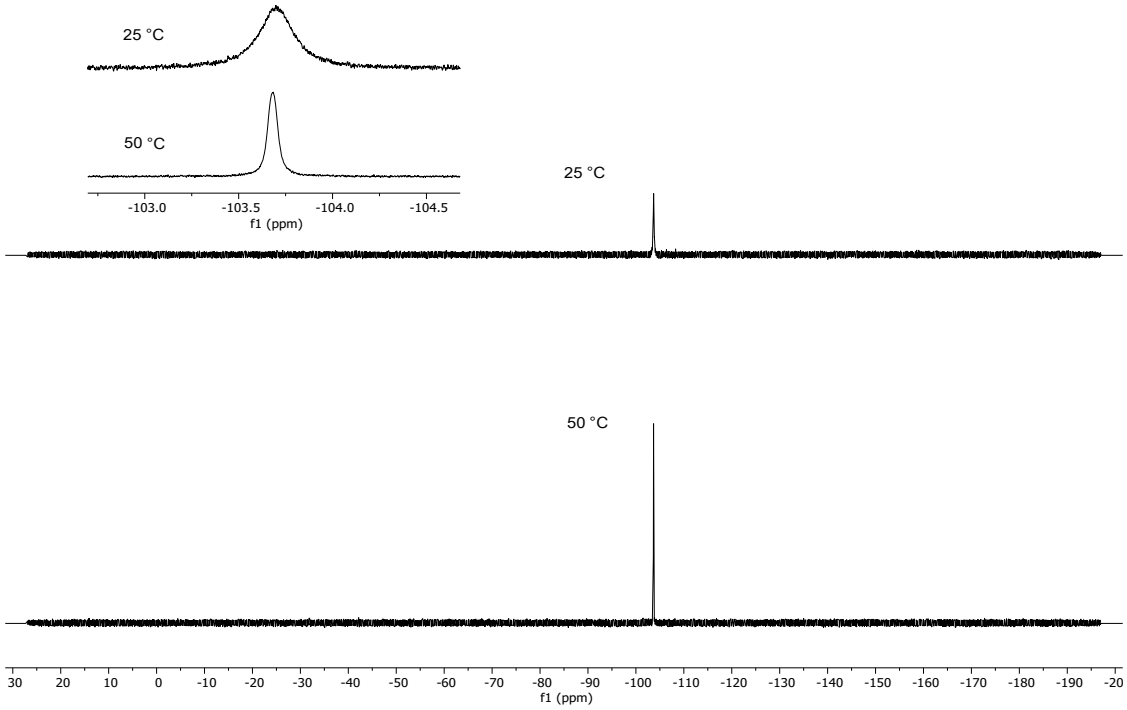
^{1}H NMR – 2ac

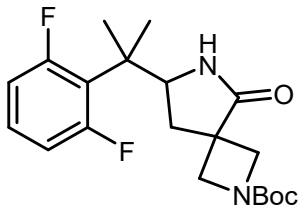


^{13}C NMR - 2ac



^{19}F NMR - 2ac


25 °C
50 °C
-103.0
-103.5
-104.0
-104.5
f1 (ppm)
25 °C
50 °C
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)



2ad. Tert-butyl 7-(2-(2,6-difluorophenyl)propan-2-yl)-5-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate. Prepared according to **GP2** with 0.2 mmol **1ad**. 31.0 mg, 0.082 mmol, 41% yield. Beige solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (tt, *J* = 8.3, 5.9 Hz, 1H), 6.90 – 6.82 (m, 2H), 5.73 (br s, 1H), 4.18 (d, *J* = 8.2 Hz, 1H), 4.14 (d, *J* = 8.4 Hz, 1H), 4.10 (dd, *J* = 8.1, 5.1 Hz, 1H), 3.72 (d, *J* = 8.2 Hz, 1H), 3.66 (d, *J* = 8.4 Hz, 1H), 2.36 (dd, *J* = 14.2, 8.2 Hz, 1H), 2.15 (dd, *J* = 14.2, 5.1 Hz, 1H), 1.45 (t, *J* = 2.8 Hz, 3H), 1.44 – 1.41 (m, 12H).

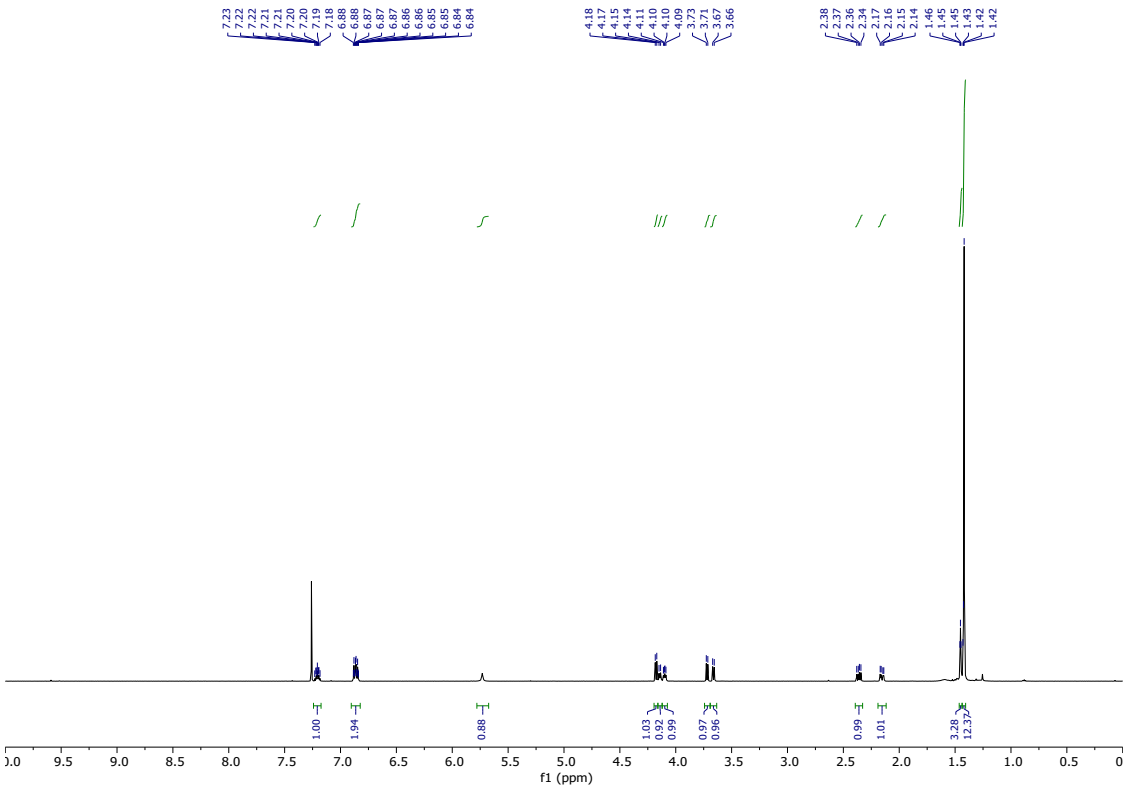
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.6, 162.1 (dd, *J* = 249, 9.8 Hz), 156.0, 129.0 (t, *J* = 12.1 Hz), 120.1 (t, *J* = 14.4 Hz), 113.2, 79.8, 58.8, 54.0, 42.5 (t, *J* = 4.2 Hz), 39.8, 35.6, 29.4, 28.5, 25.5 (t, *J* = 6.3 Hz), 23.7 (t, *J* = 6.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -104.32.

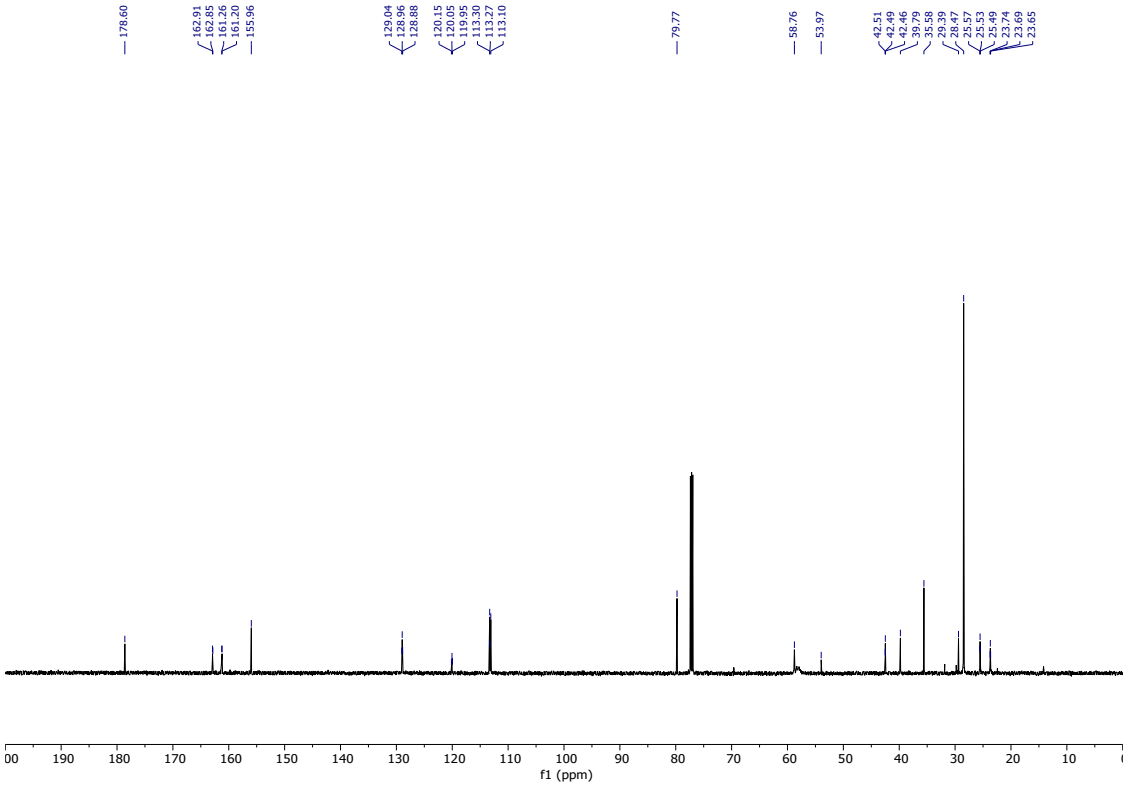
IR (neat) 3205, 2979, 2877, 2259, 1689, 1619, 1572, 1463, 1408, 1386 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{20}H_{26}F_2N_2O_3Na^+$ $[M+Na]^+$: 403.1804, found 403.1802.

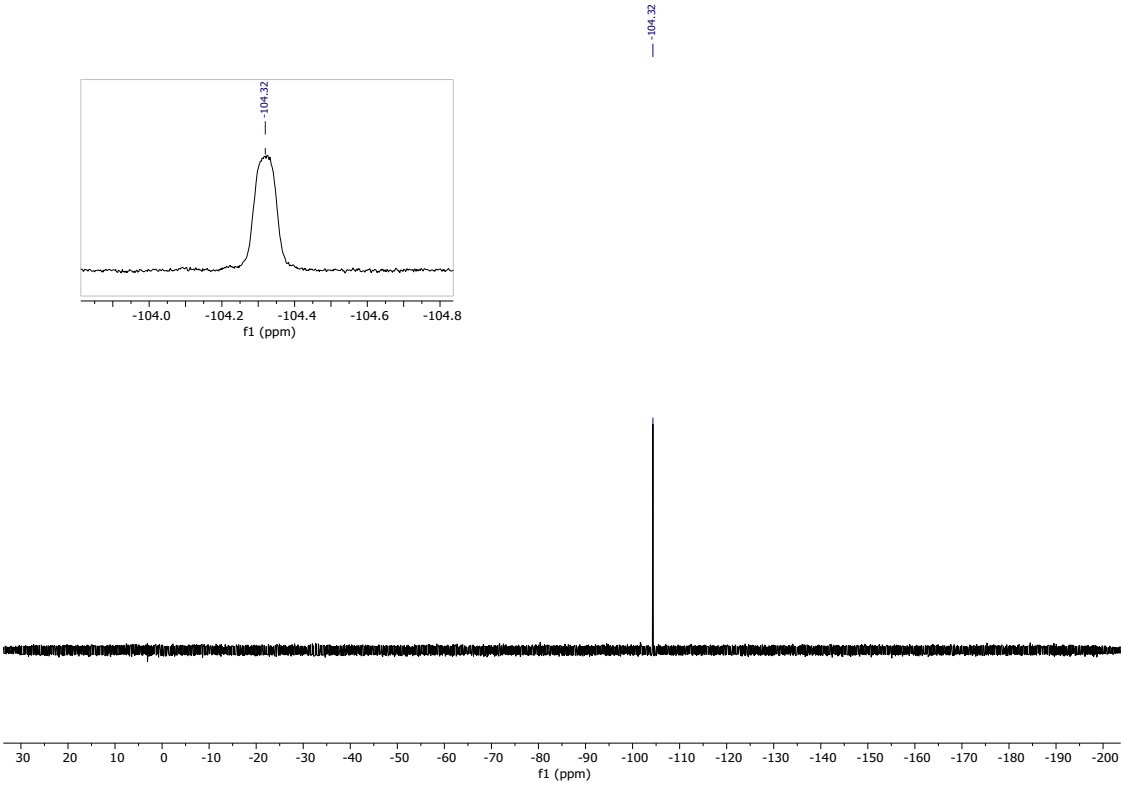
^{1}H NMR – 2ad

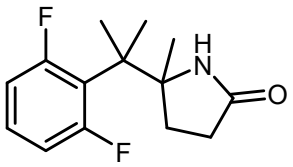


^{13}C NMR – 2ad



^{19}F NMR – 2ad


-104.32
-104.32
-104.0
-104.2
-104.4
-104.6
-104.8
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2ae. 5-(2-(2,6-difluorophenyl)propan-2-yl)-5-methylpyrrolidin-2-one. Prepared according to **GP2** with 0.2 mmol **1ae**. 15.5 mg, 0.061 mmol, 31% yield. Colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (tt, *J* = 8.2, 5.9 Hz, 1H), 6.85 (dd, *J* = 12.1, 8.3 Hz, 2H), 6.26 (br s, 1H), 2.36 – 2.24 (m, 2H), 2.00 – 1.88 (m, 1H), 1.83 – 1.73 (m, 1H), 1.60 – 1.55 (m, 6H), 1.31 (s, 3H).

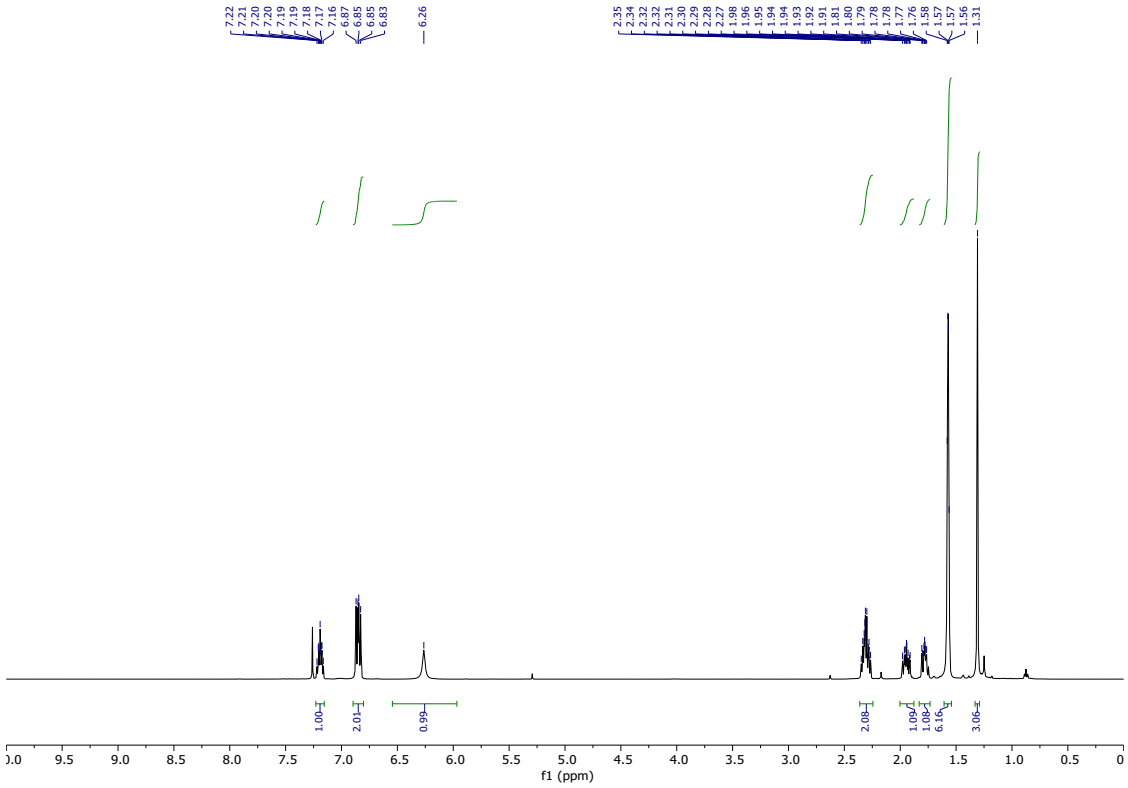
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 162.3 (dd, *J* = 249, 9.9 Hz), 129.1 (t, *J* = 12.4 Hz), 120.8 (t, *J* = 14.3 Hz), 113.17 (dd, *J* = 28.6, 2.9 Hz), 66.3, 46.5 (t, *J* = 4.0 Hz), 30.33, 30.1 (t, *J* = 1.3 Hz), 26.61 (t, *J* = 7.7 Hz), 26.49 (t, *J* = 7.8 Hz), 24.27.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.04.

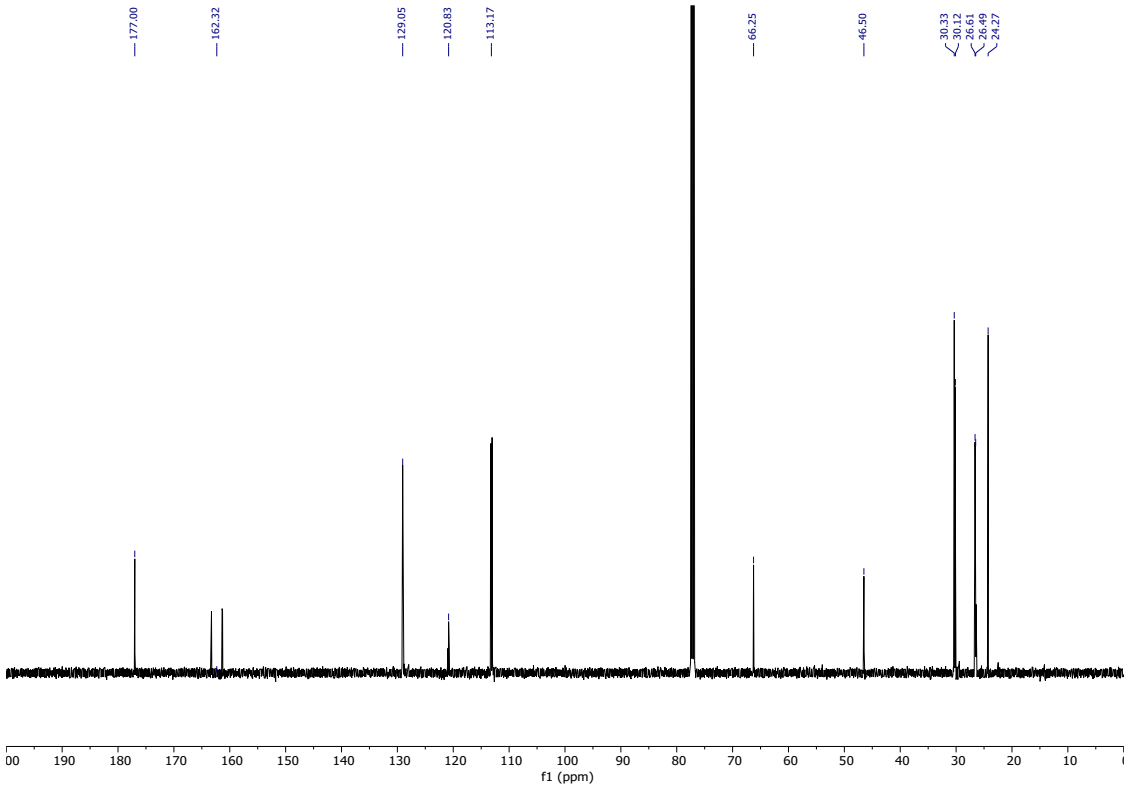
IR (neat) 3170, 3070, 2971, 1695, 1616, 1569, 1457, 1400, 1372, 1262 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{14}H_{18}F_2NO^+$ $[M+H]^+$: 254.1351, found 254.1360.

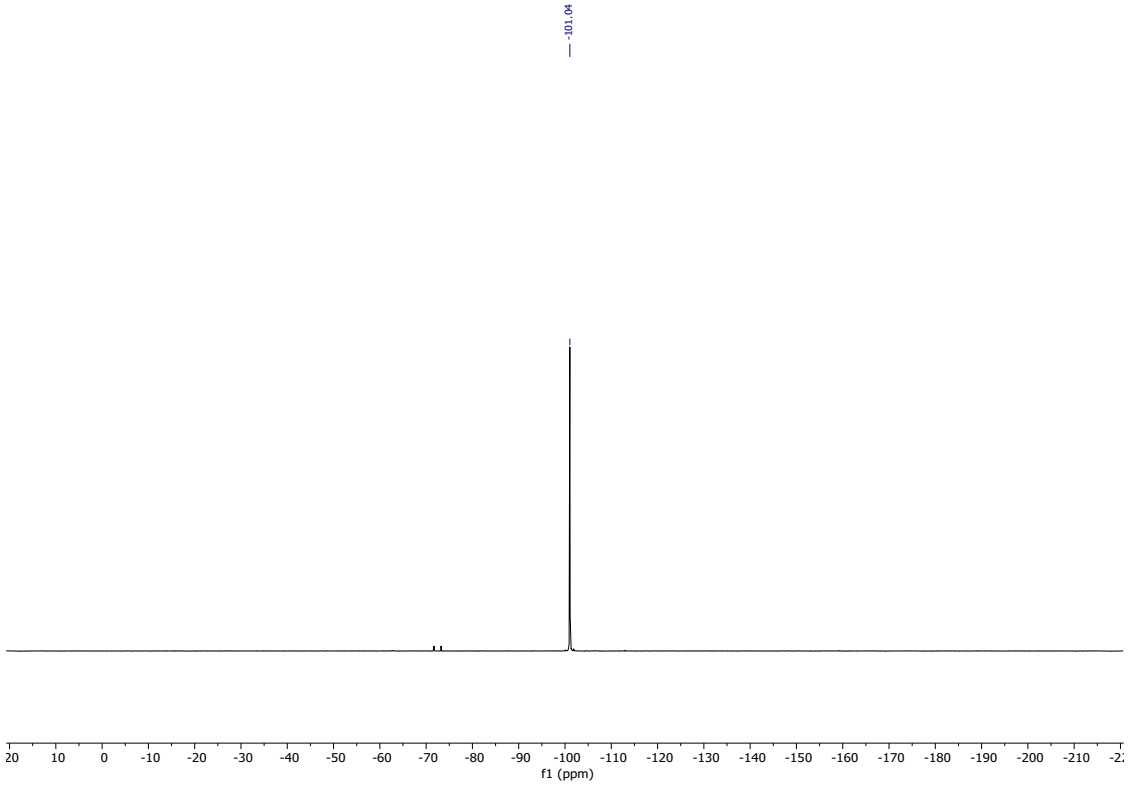
^{1}H NMR – 2ae

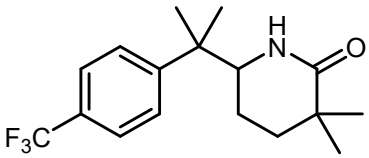


^{13}C NMR – 2ae



^{19}F NMR – 2ae


-101.04
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



2af. 3,3-dimethyl-6-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)piperidin-2-one. Prepared according to **GP2** with 0.2 mmol **1af**. 10.5 mg, 0.034 mmol, 17% yield. Yellow solid. Isolated with a minor inseparable impurity (<10%).

^{1}H NMR (401 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 5.65 (br s, 1H), 3.65 – 3.53 (m, 1H), 1.72 – 1.57 (m, 4H), 1.39 (s, 3H), 1.35 (s, 3H), 1.17 (s, 3H), 1.14 (s, 3H).

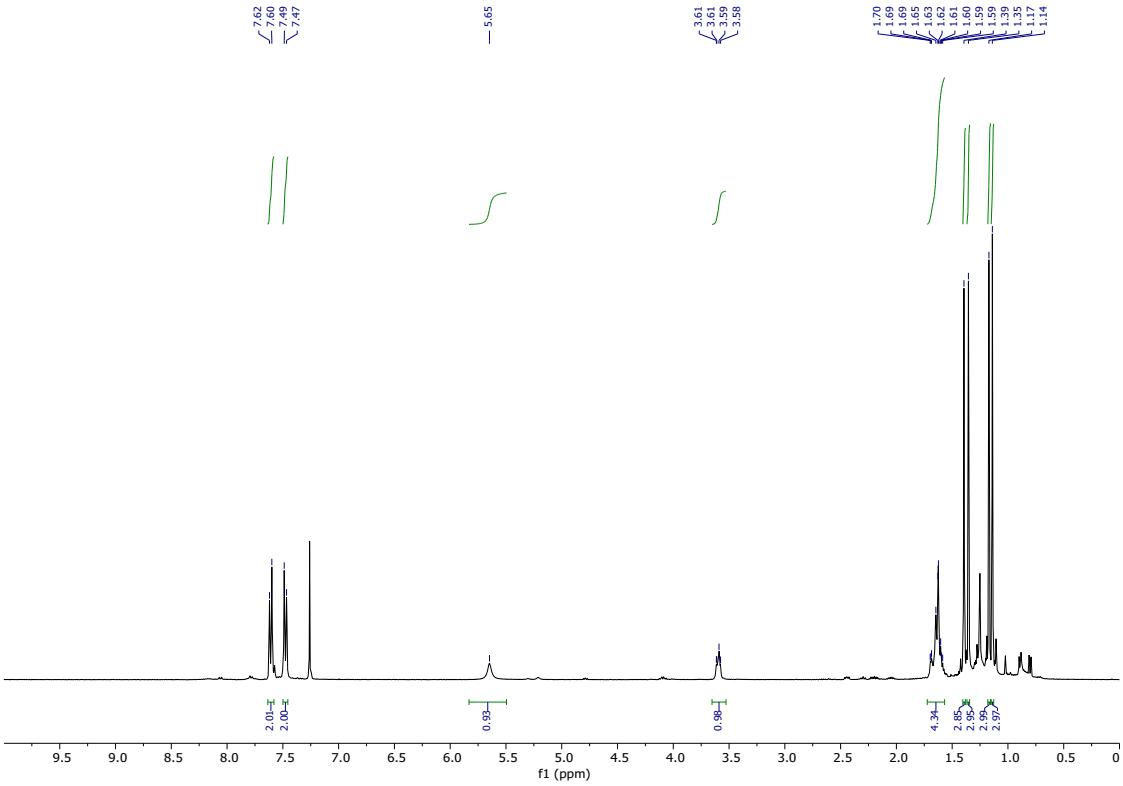
^{13}C NMR (126 MHz, $CDCl_3$) δ 179.3, 149.9, 129.2 (q, *J* = 32.5 Hz), 126.8, 125.6 (q, *J* = 3.6 Hz), 124.0 (q, *J* = 272 Hz), 62.8, 41.4, 37.2, 35.0, 27.0, 26.6, 24.9, 22.1, 20.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.63.

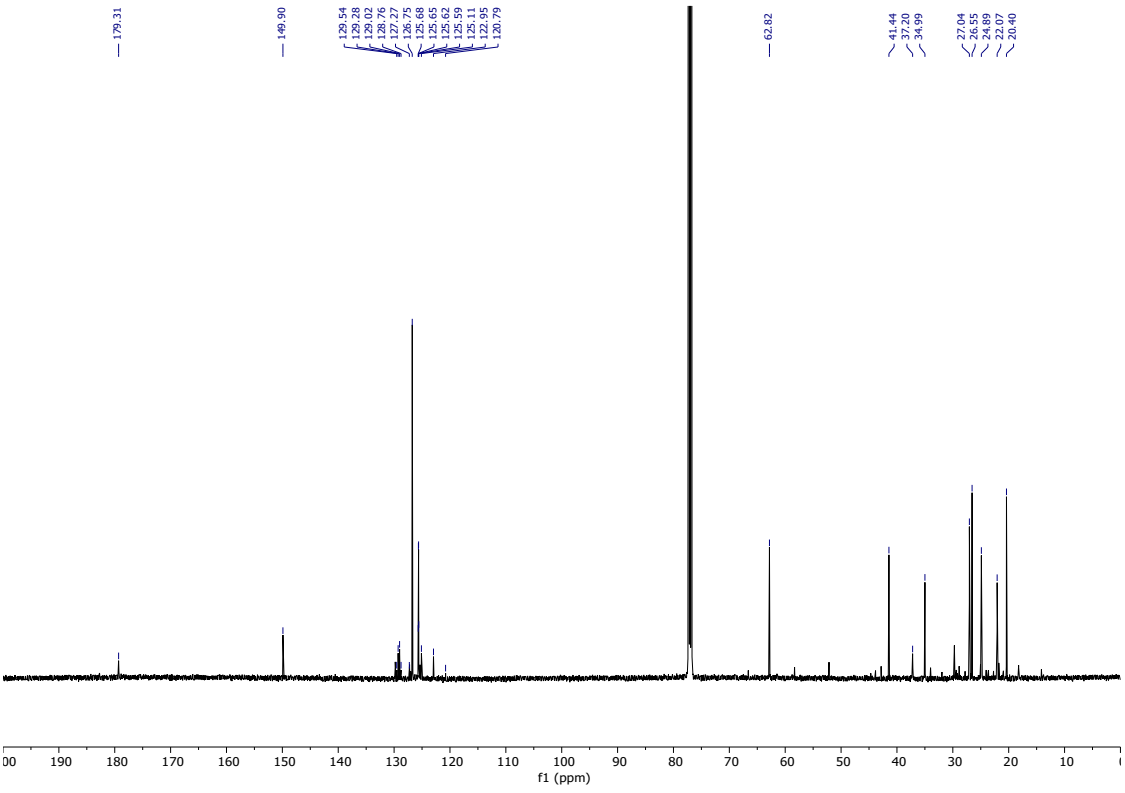
IR (neat) 3197, 3057, 2964, 2934, 1634, 1618, 1474, 1411, 1326, 1161 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{17}H_{23}F_3NO^+$ $[M+H]^+$: 314.1727, found 314.1724.

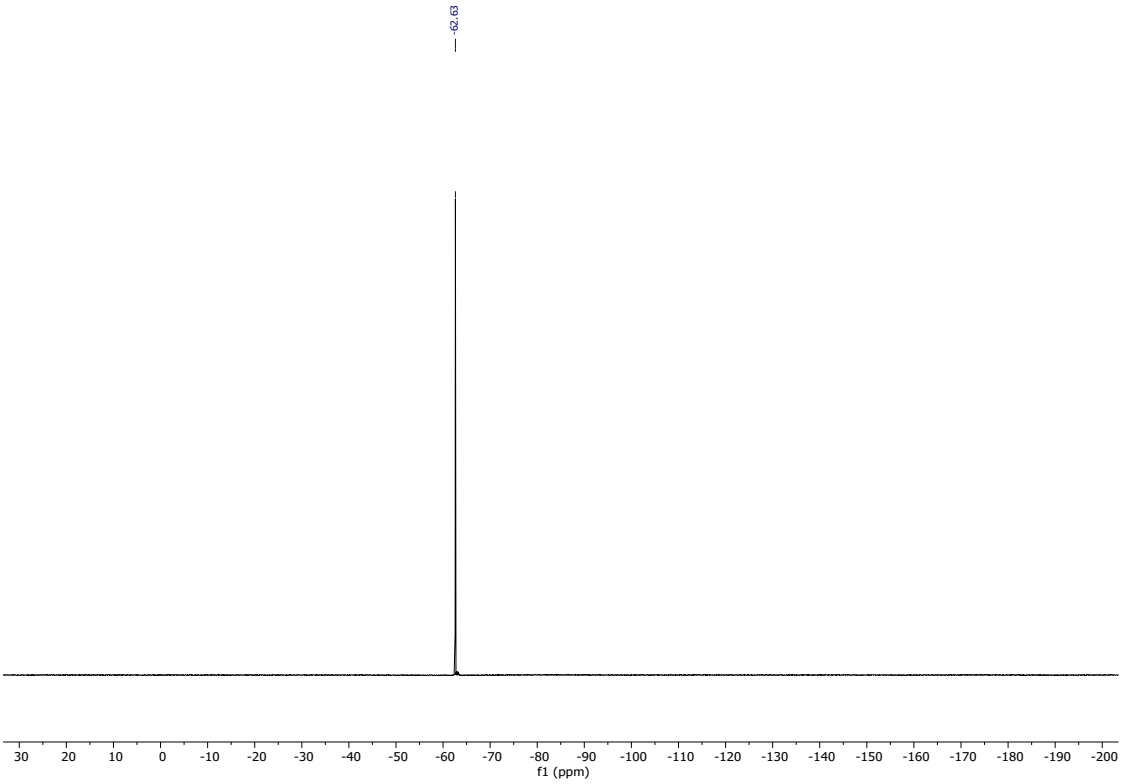
^{1}H NMR – 2af

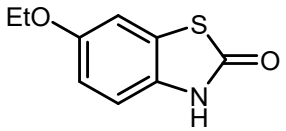


^{13}C NMR – 2af



^{19}F NMR – 2af


-62.63
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



1ag'. 6-ethoxybenzo[d]thiazol-2(3H)-one. Prepared according to **GP2** with 0.2 mmol **1ag**. 19.4 mg, 0.099 mmol, 50% yield. Tan solid.

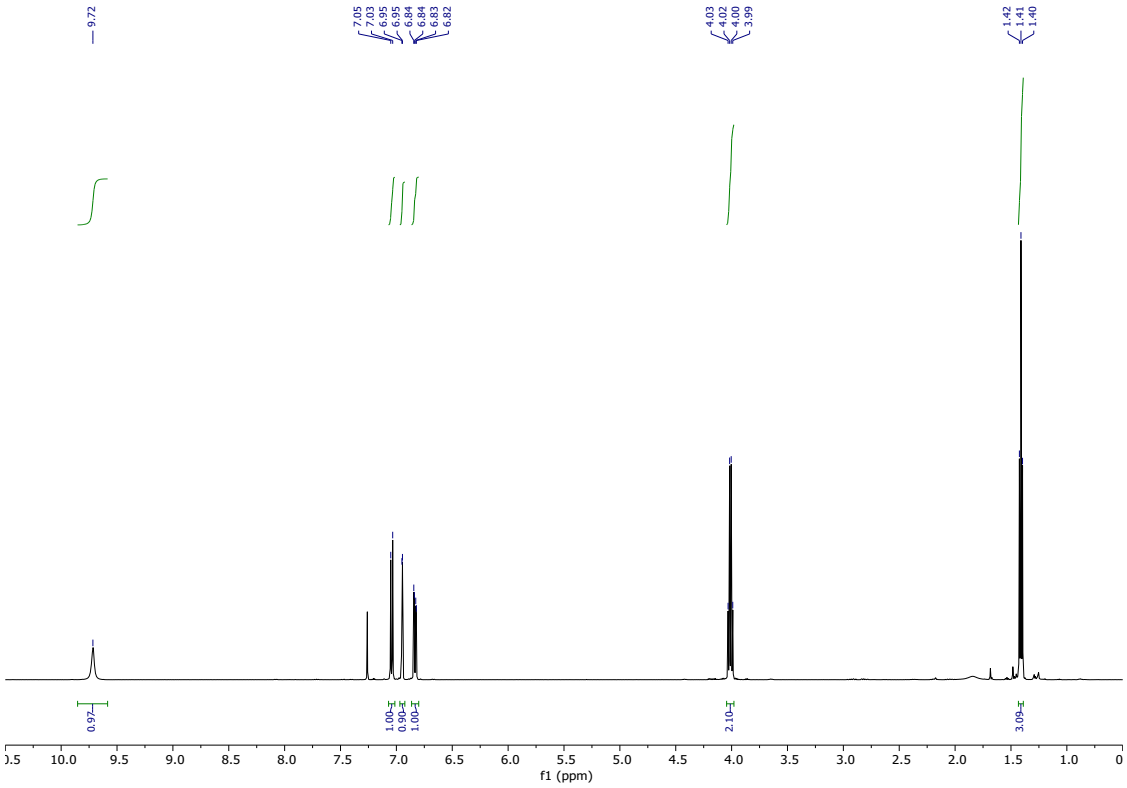
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.72 (br s, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.5 Hz, 1H), 4.01 (q, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 155.6, 129.1, 125.1, 114.1, 112.4, 108.4, 64.4, 15.0.

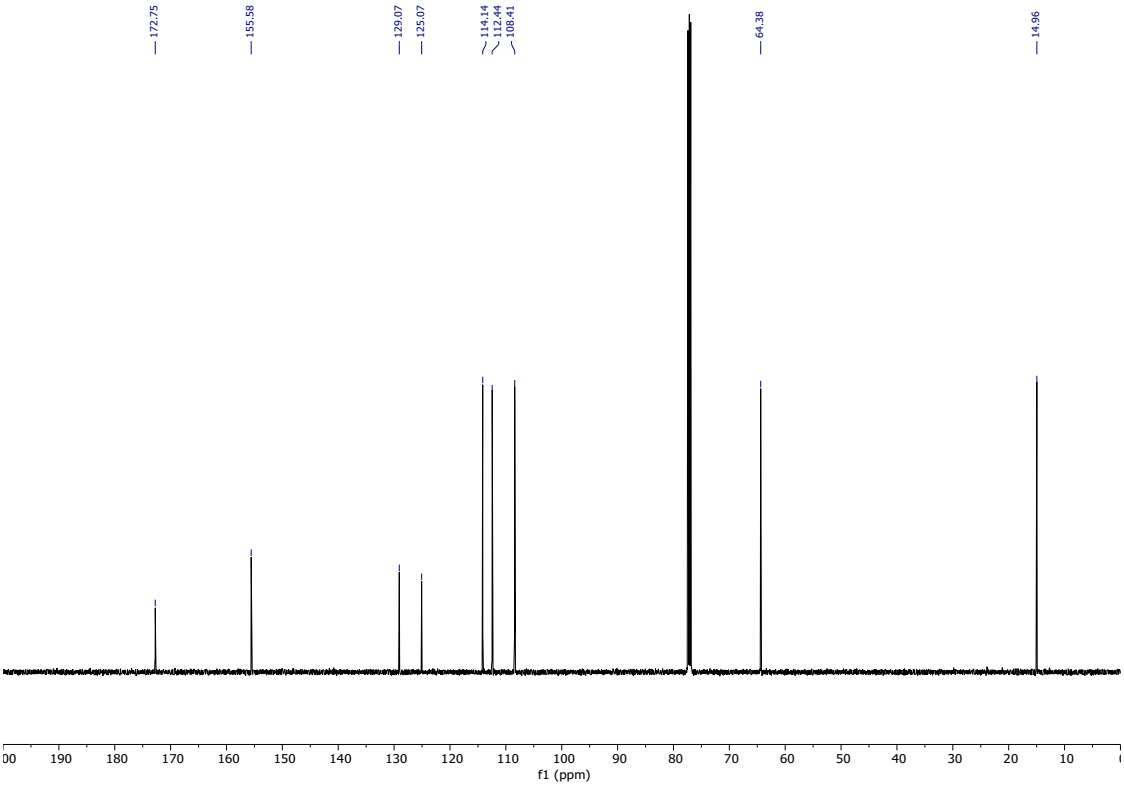
IR (neat) 3130, 3070, 2984, 2846, 1674, 1615, 1588, 1484, 1471, 1455 cm^{-1}

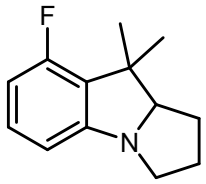
HRMS (ESI+) m/z calculated for $C_9H_{10}NO_2S^+$ $[M+H]^+$: 196.0427, found 196.0428.

^{1}H NMR – 1ag’



^{13}C NMR – 1ag’





3d. 8-fluoro-9,9-dimethyl-2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]indole. In a flame-dried 10 mL round-bottom flask, $LiAlH_4$ (9.5 mg, 0.25 mmol, 2.0 equiv.) was suspended in 1 mL anhydrous THF under nitrogen atmosphere and cooled to 0 °C. A room temperature solution of **2d** (30 mg, 0.13 mmol, 1.0 equiv) in 1 mL THF was added dropwise at room temperature over one minute. The reaction was removed from the ice bath and a water-cooled reflux condenser with a nitrogen inlet was attached. The reaction was stirred at 67 °C under a dynamic nitrogen atmosphere for 15 hours. Upon cooling to room temperature, the reflux condenser was removed and the reaction was quenched by piecewise addition of Na_2SO_4•$10H_2O$ (Glauber's salt). The quenched mixture was diluted with CH_2Cl_2 and filtered through a pad of Celite. Concentration of the filtrate affords the title product **3d** as a pale yellow oil without further purification. 21.3 mg, 0.104 mmol, 83% yield. This compound slowly turns red/pink on extended storage at –20 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.03 (td, *J* = 8.0, 5.6 Hz, 1H), 6.41 (ddd, *J* = 9.8, 8.2, 0.8 Hz, 1H), 6.32 (app d, *J* = 7.7 Hz, 1H), 3.48 (dd, *J* = 11.0, 5.3 Hz, 1H), 3.44 (ddd, *J* = 10.6, 9.0, 2.8 Hz, 1H), 3.14 (dt, *J* = 10.6, 8.4 Hz, 1H), 1.95 (dtdd, *J* = 12.3, 7.7, 2.7, 1.7 Hz, 1H), 1.84 (dddd, *J* = 18.0, 12.4, 8.9, 6.4 Hz, 1H), 1.69 (dddd, *J* = 11.8, 6.7, 5.2, 1.6 Hz, 1H), 1.46 (s, 3H), 1.40 (s, 3H), 1.39 – 1.33 (m, 1H).

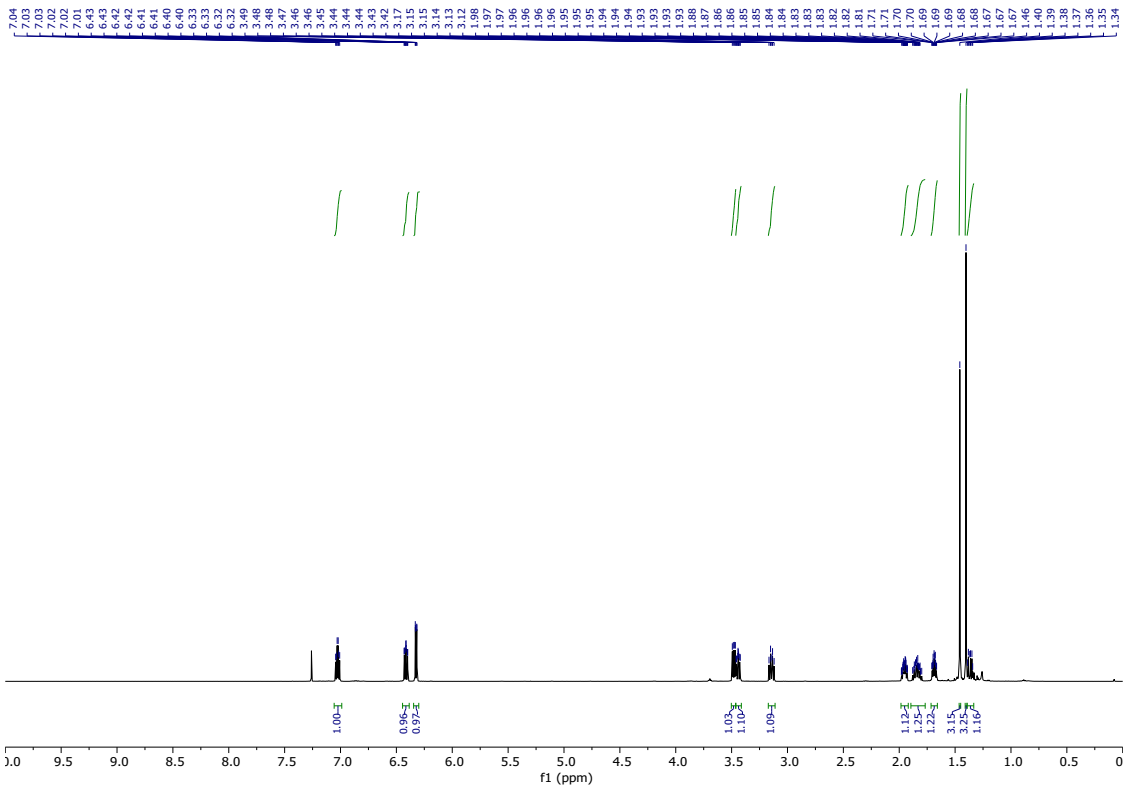
^{13}C NMR (126 MHz, $CDCl_3$, 50 °C) δ 160.4 (d, J = 245 Hz), 156.4 (d, *J* = 9.2 Hz), 129.3 (d, *J* = 9.0 Hz), 123.5 (d, *J* = 17.9 Hz), 106.7 (d, *J* = 21.7 Hz), 106.5 (d, *J* = 2.6 Hz), 79.0, 51.8, 42.2 (d, J = 2.0 Hz), 30.0, 26.8, 26.2, 22.6 (d, J = 3.0 Hz).

^{19}F NMR (564 MHz, $CDCl_3$, 50 °C) δ -124.09 (dd, *J* = 10.0, 5.7 Hz).

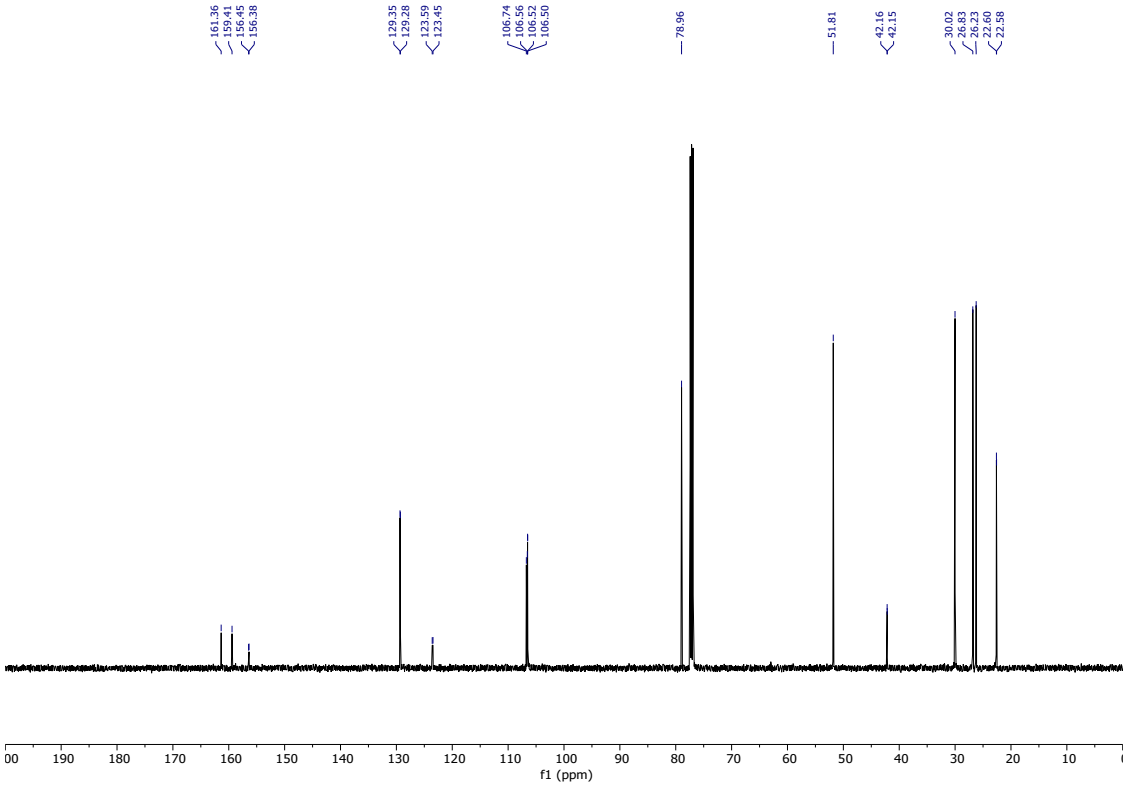
IR (neat) 2966, 2934, 2880, 1617, 1590, 1477, 1456, 1364, 1312, 1281 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{13}H_{17}FN^+$ $[M+H]^+$: 206.1340, found 206.1338.

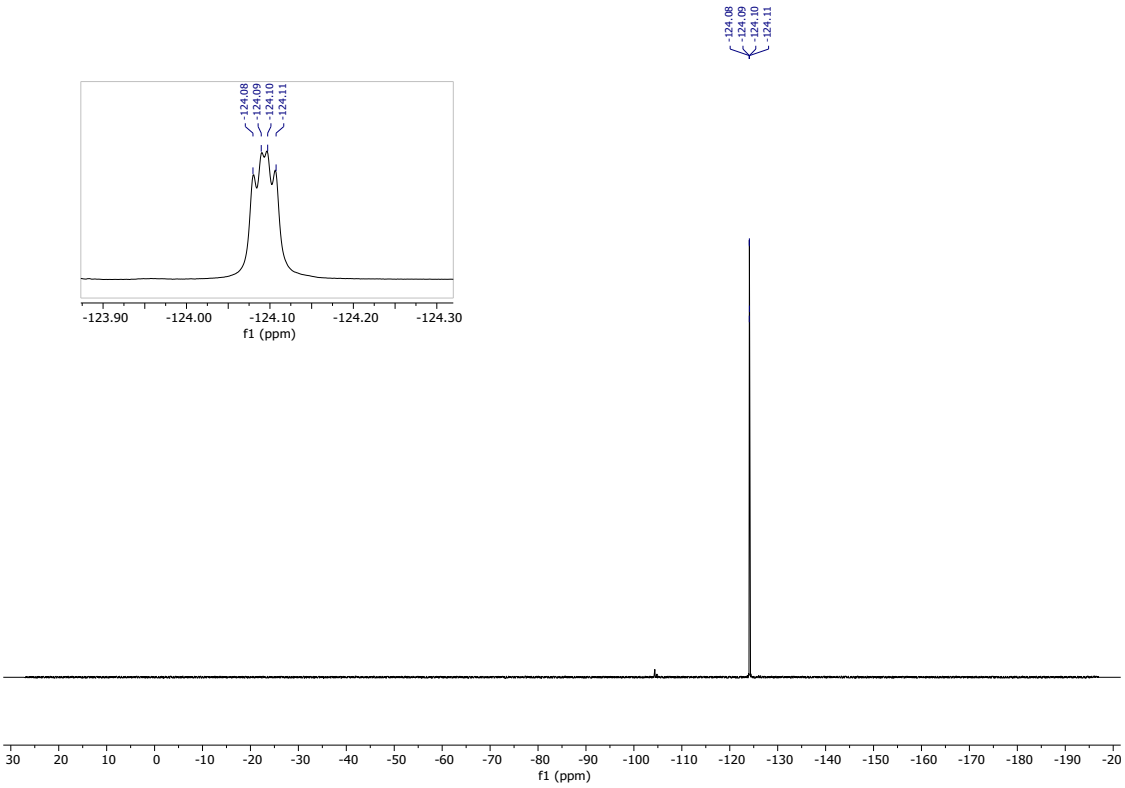
^{1}H NMR – 3d

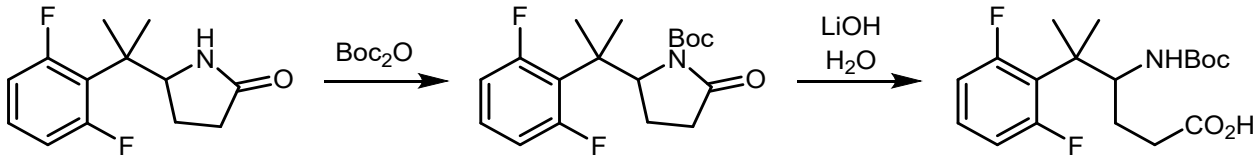


^{13}C NMR – 3d



^{19}F NMR – 3d


-124.08
-124.09
-124.10
-124.11
-123.90
-124.00
-124.10
-124.20
-124.30
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)



2d **4d**

4d. 4-((tert-butoxycarbonyl)amino)-5-(2,6-difluorophenyl)-5-methylhexanoic acid.

Step 1: In a 1 dram vial, **2d** (29.4 mg, 0.12 mmol, 1.0 equiv.) and DMAP (15.0 mg, 0.12 mmol, 1.0 equiv) were dissolved in 0.2 mL CH_2Cl_2. Triethylamine (17 µL, 0.12 mmol, 1.0 equiv.) was added via syringe, followed by di-*tert*-butyl decarbonate (50 uL, 0.22 mmol, 1.8 equiv.) in one portion. The reaction was allowed to stir at room temperature for 20 hours. Once complete, direct column chromatography purification of the reaction mixture was conducted (0 to 10% acetone in CH_2Cl_2) to obtain the Boc-protected lactam as a clear, colorless oil. Partial characterization data are provided below:

N-Boc lactam **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.19 (tt, *J* = 8.4, 5.7 Hz, 1H), 6.85 (dd, *J* = 11.3, 8.3 Hz, 2H), 4.95 (d, *J* = 9.5 Hz, 1H), 2.51 (ddd, *J* = 18.6, 11.1, 9.4 Hz, 1H), 2.40 (ddd, *J* = 18.4, 10.8, 1.7 Hz, 1H), 2.05 (dq, *J* = 14.0, 10.7 Hz, 1H), 1.76 (dd, *J* = 13.4, 9.7 Hz, 1H), 1.51 (s, 9H), 1.50 – 1.46 (m, 6H).

Step 2: In a 2 dram vial, the intermediate *N*-Boc lactam was dissolved in 0.35 mL THF. 0.22 mL of a 1 M aqueous LiOH solution was added and the reaction was stirred at room temperature for 2 hours under ambient atmosphere. Upon completion, 10 mL diethyl ether was used to transfer the vial contents to a separatory funnel containing 5 mL 1 M aqueous LiOH solution. After this first extraction, the organic layer was set aside to be discarded. The aqueous layer was acidified to pH ~1 with dropwise addition of concentrated aqueous HCl until the solution became cloudy. The acidic aqueous phase was washed with CH_2Cl_2 (3x5 mL) and EtOAc (5 mL). The combined organics were washed sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under vacuum to give the amino acid product **4d** as a colorless foam. 22 mg, 62 µmol, 49% yield over 2 steps.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (tt, *J* = 8.2, 5.8 Hz, 1H), 6.85 – 6.77 (m, 2H), [5.80 (d, J = 10.3 Hz), 4.50 (d, *J* = 10.7 Hz), 1H] 4.24 – 4.16 (m, 1H), 2.45 – 2.22 (m, 2H), 1.84 – 1.73 (m, 1H), 1.69 – 1.51 (m, 1H), 1.51 – 1.44 (m, 6H), 1.37 – 1.34 (m, 9H).

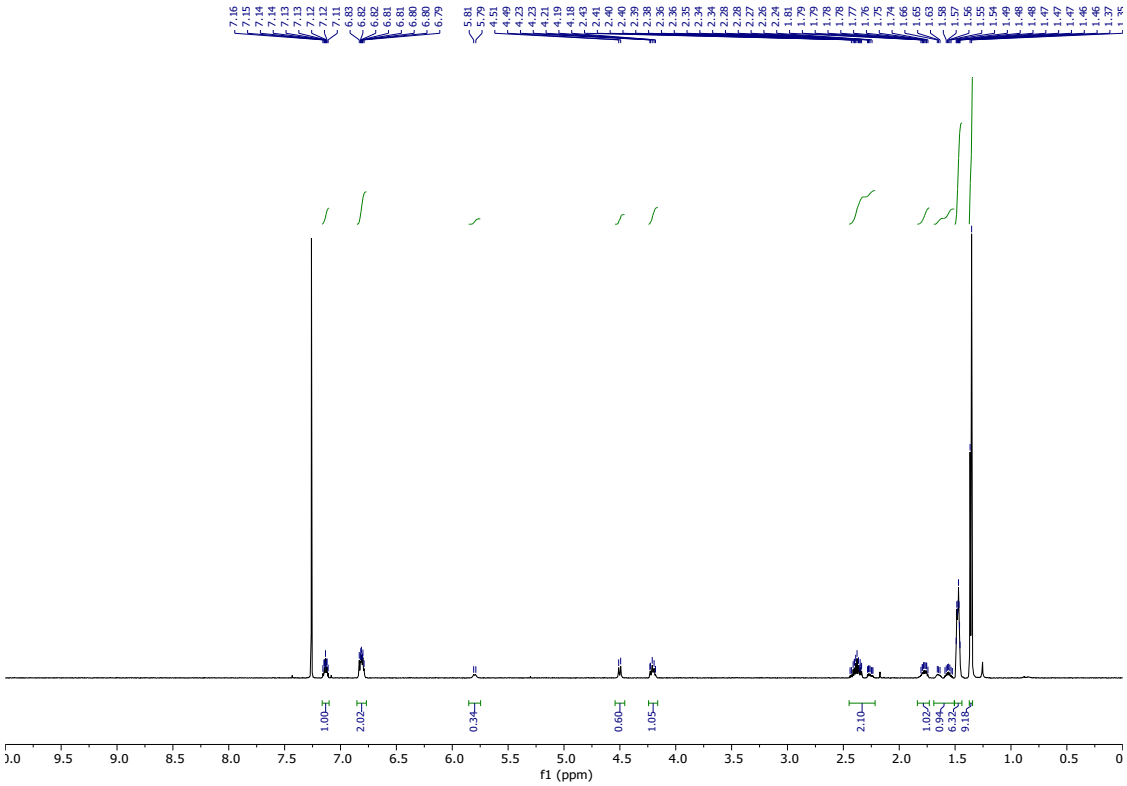
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 178.3, 162.32 (dd, *J* = 250, 5.0 Hz), 162.25 (dd, *J* = 250, 5.0 Hz), 157.8, 156.10, 128.2 (t, *J* = 11.9 Hz), 128.0 (t, *J* = 11.9 Hz), 122.4 (t, *J* = 14.1 Hz), 121.7 (t, *J* = 14.1 Hz), 112.8 (m), 80.7, 79.5, 58.3 (t, *J* = 3.0 Hz), 56.6 (t, *J* = 3.0 Hz), 43.8 (t, *J* = 3.6 Hz), 43.7 (t, *J* = 3.6 Hz), 32.1, 31.7, 28.4, 28.2, 26.2, 26.1, 25.9 (t, *J* = 5.9 Hz), 25.31 (t, *J* = 5.9 Hz), 24.5 (t, *J* = 7.3 Hz), 24.3 (t, *J* = 7.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -104.75, -105.04.

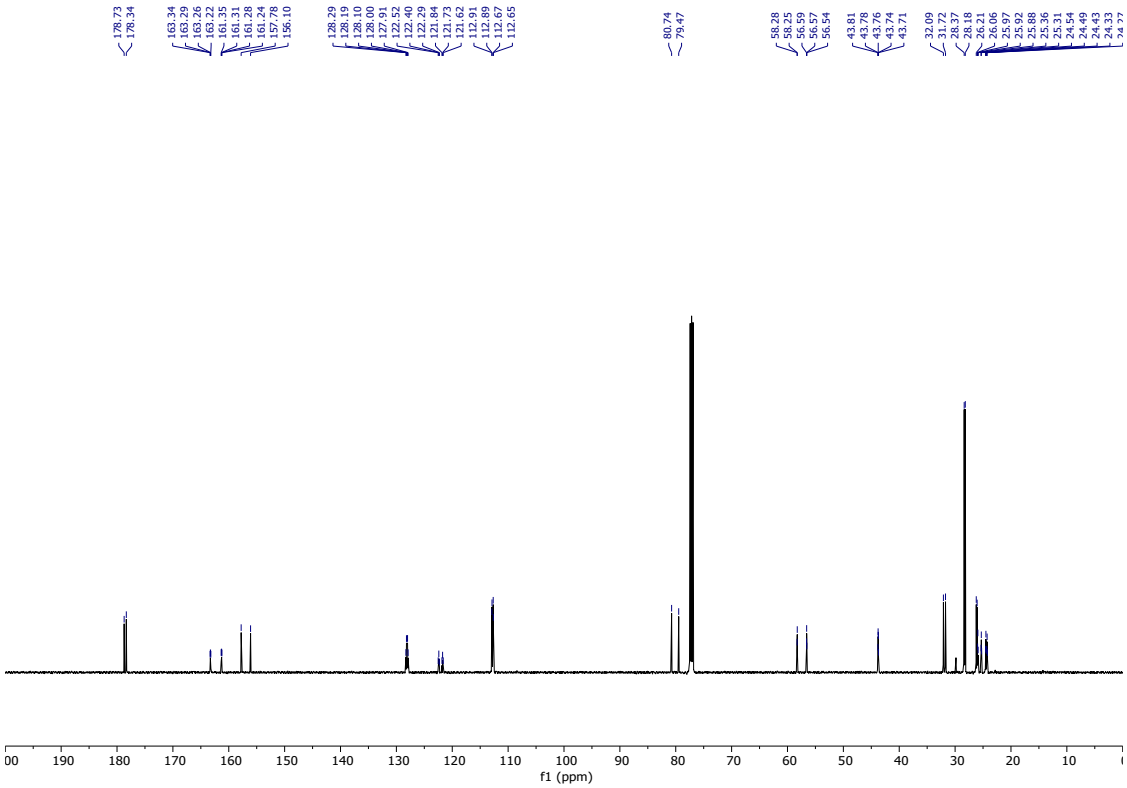
IR (neat) 3310, 3252, 2986, 2924, 1709, 1646, 1620, 1573, 1452, 1412 cm^{-1}

HRMS (ESI+) m/z calculated for $C_{18}H_{25}F_2NO_4Na^+$ $[M+Na]^+$: 380.1644, found 380.1644.

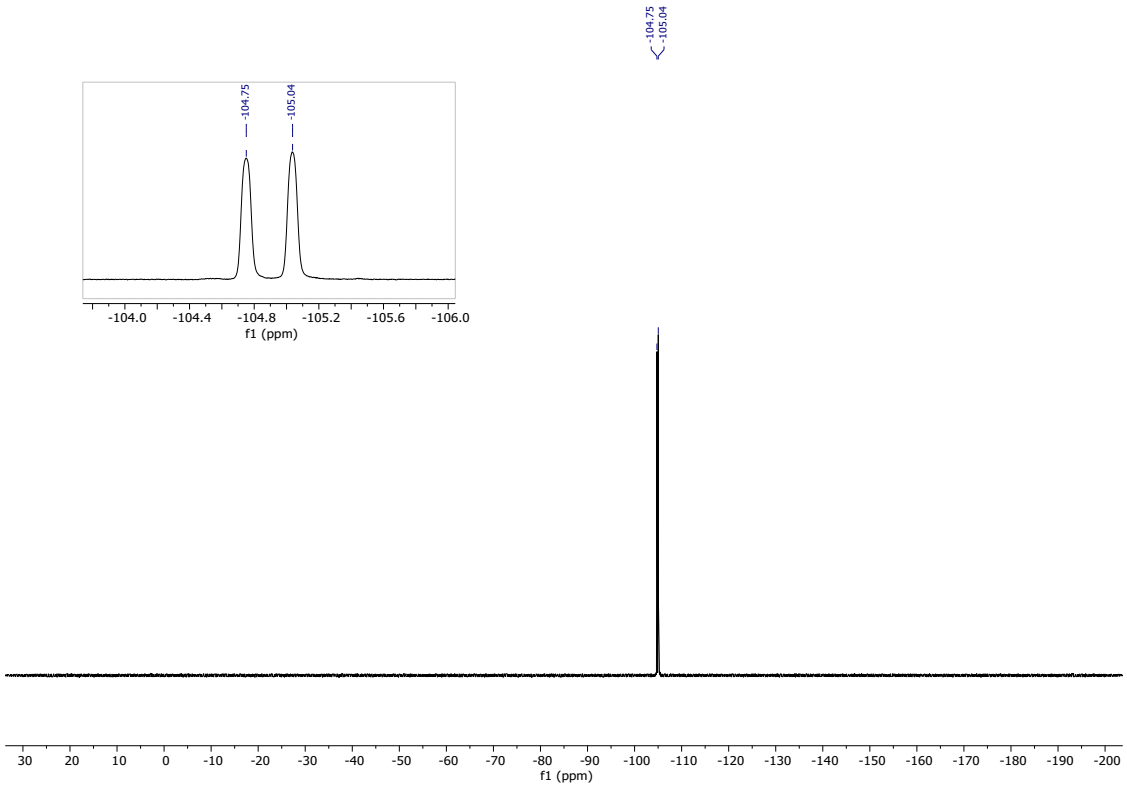
^{1}H NMR – 4d

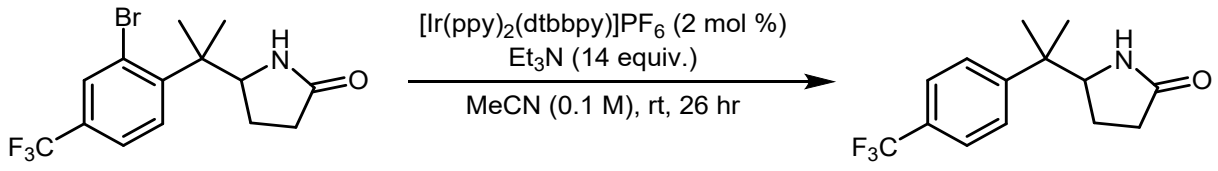


^{13}C NMR – 4d


178.73
178.34
163.34
163.29
163.26
161.72
161.35
161.31
161.28
161.24
157.78
156.10
128.29
128.19
128.10
128.00
127.91
122.52
122.40
122.29
121.84
121.73
121.62
112.91
112.89
112.67
112.65
80.74
79.47
58.28
58.25
56.59
56.57
56.54
43.81
43.78
43.76
43.74
43.71
32.09
31.72
28.37
28.18
26.21
26.06
25.97
25.92
25.88
25.36
25.31
24.54
24.49
24.43
24.33
14.17
f1 (ppm)

^{19}F NMR – 4d


-104.75
-105.04
-104.75
-105.04
-104.0
-104.4
-104.8
-105.2
-105.6
-106.0
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



2i **3i**

3i. 5-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)pyrrolidin-2-one. Adapted from a literature report.[12] In a 1.5 mL GC vial with a stir bar, aryl bromide **2i** (8.6 mg, 25 µmol, 1.0 equiv.) was dissolved in anhydrous MeCN (0.30 mL). Triethylamine (50 µL, 36 mg, 14 equiv.) was added and a snap-on GC vial cap with a pierceable septum was attached to seal the vial. The vial was partially submerged in an ice bath to prevent excessive evaporation of triethylamine in the degassing step. An argon balloon and outlet needle were inserted through the septum and the solution was sparged for 5 minutes at 0 °C. Only the outlet needle was removed and the reaction was irradiated at ambient temperature for 26 hours. The contents of the reaction vial were transferred to a 3-dram vial using 3 mL diethyl ether, and the organic phase was washed with 1 M aq. HCl. The aqueous phase was washed with 2 x 2 mL diethyl ether and the combined organics were concentrated under reduced pressure. 0.25 mL of a 0.1 mM solution of 1,3,5-trimethoxybenzene in $CDCl_3$ was added to the residue. Additional $CDCl_3$ was used to dilute the sample. Yield was calculated vs. the 1.0 equiv. of trimethoxybenzene present. (4.7 mg, 17 µmol, 69% yield). A pipette-scale flash chromatography column (9:1 CH_2Cl_2:acetone) on silica gel was conducted to obtain material of higher purity for characterization purposes.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 5.47 (br s, 1H), 3.84 (dd, *J* = 8.2, 5.4 Hz, 1H), 2.25 (ddd, *J* = 16.8, 10.4, 6.4 Hz, 1H), 2.19 – 2.02 (m, 2H), 1.87 – 1.77 (m, 1H), 1.36 (s, 3H), 1.34 (s, 3H).

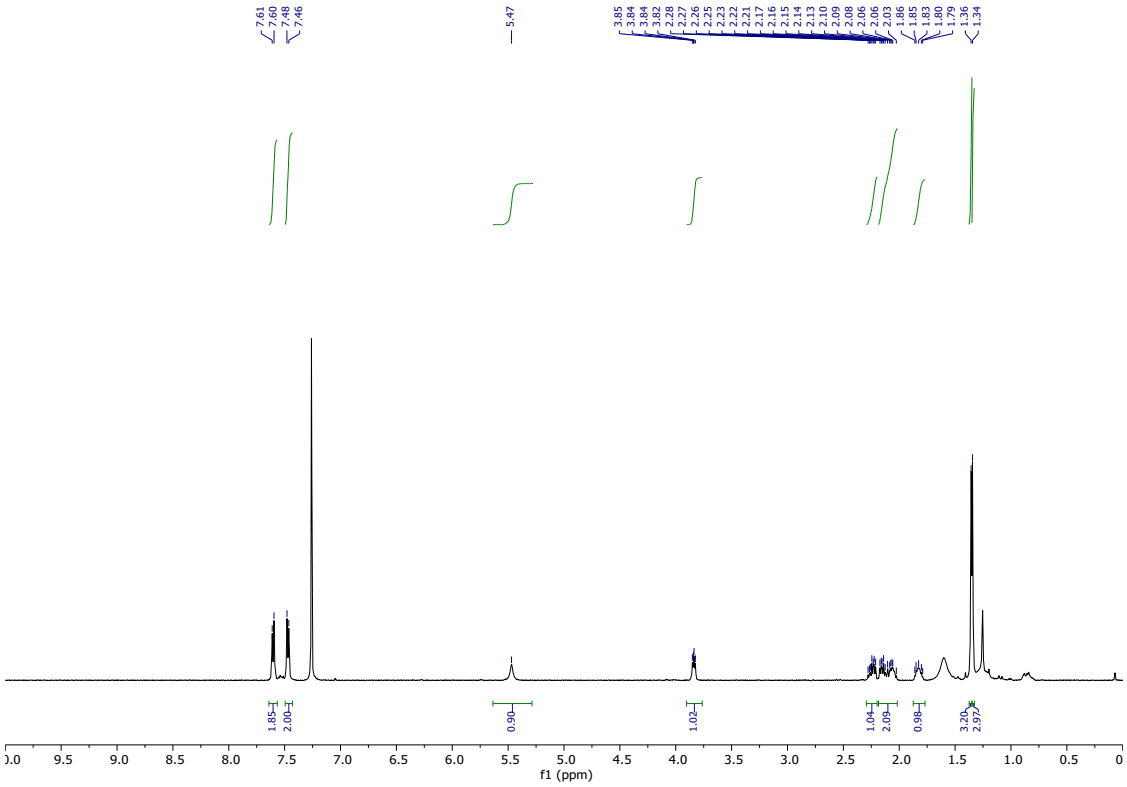
^{13}C NMR (176 MHz, $CDCl_3$) δ 178.3, 150.0, 129.14 (q, *J* = 32.8 Hz), 126.8, 125.6 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 272 Hz), 63.6, 41.6, 30.2, 24.1, 23.3, 22.4.

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.59.

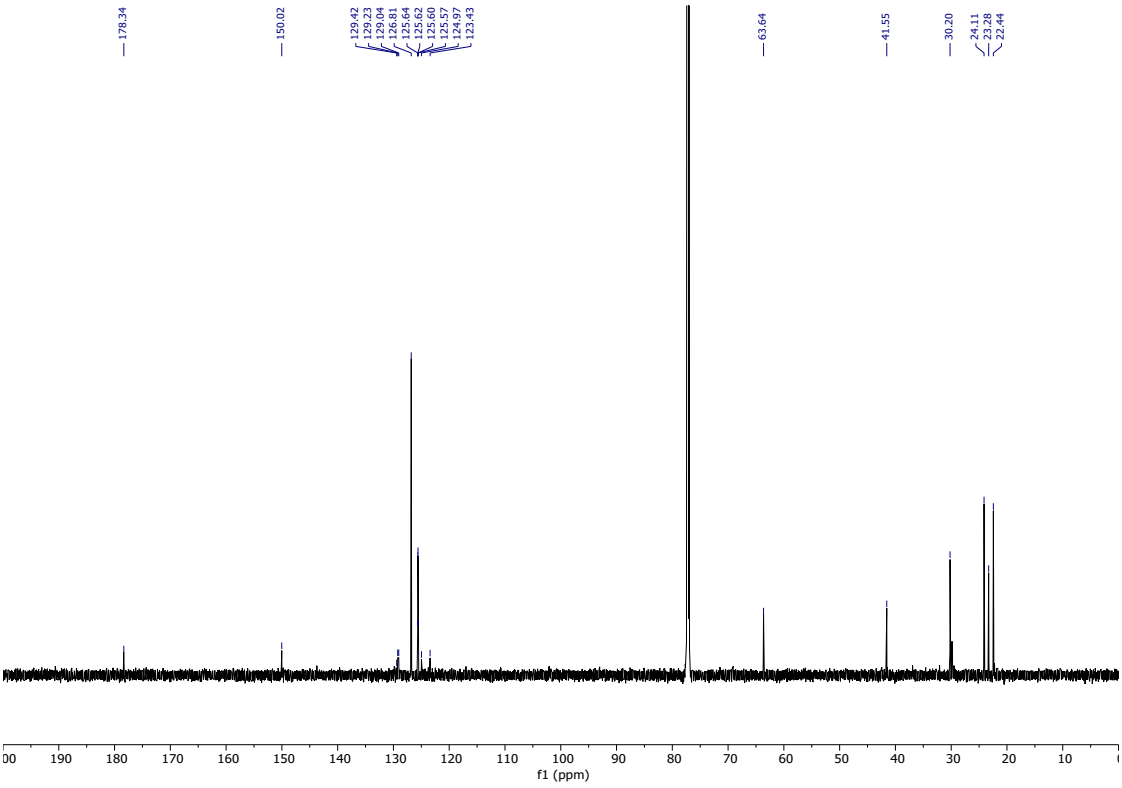
IR (neat) 3204, 2973, 2927, 1689, 1618, 1467, 1410, 1326, 1304, 1164 cm^{-1}

HRMS (ESI+) calculated for $C_{14}H_{17}F_3NO^+$ $[M+H]^+$: 272.1257, found 272.1254.

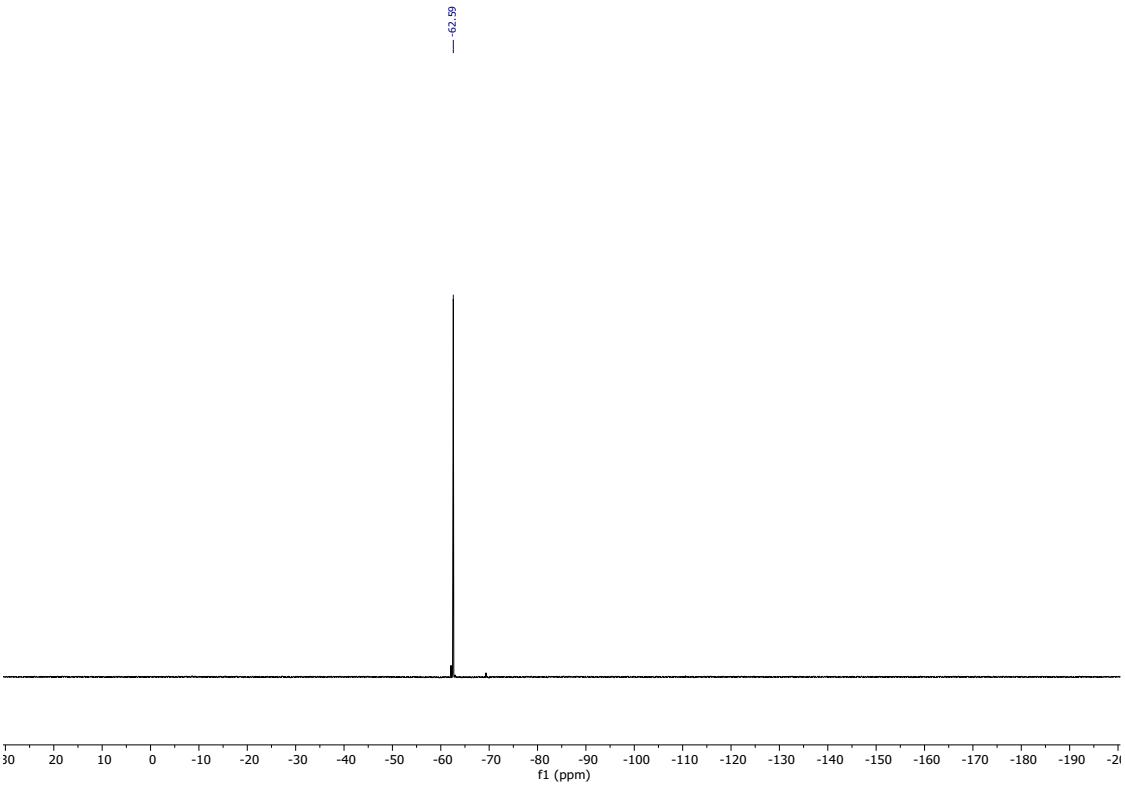
^{1}H NMR – 3i



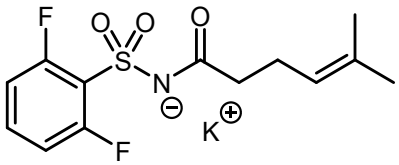
^{13}C NMR – 3i



^{19}F NMR – 3i


-62.59
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

3. Mechanistic experiments



K$^+$[1d]$^-$. Potassium ((2,6-difluorophenyl)sulfonyl)(5-methylhex-4-enoyl)amide. To a room temperature solution of KO^{t}Bu (31.0 mg, 0.276 mmol, 1.0 equiv.) in 1.25 mL THF under a nitrogen atmosphere was added **1d** (88.0 mg, 0.29 mmol, 1.05 equiv.) as a solution in 1.25 mL THF. The reaction was allowed to stir for 15 minutes at room temperature before the solvent was removed under reduced pressure. The resulting solid was washed by decanting with diethyl ether (3 x 5 mL) and dried under vacuum to give the title product (46.7 mg, 0.14 mmol, 50%) as a colorless solid.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.38 (tt, J = 8.3, 5.9 Hz, 1H), 7.00 – 6.93 (m, 2H), 5.08 – 4.99 (m, 1H), 2.04 (q, J = 7.6 Hz, 2H), 1.94 – 1.87 (m, 2H), 1.61 (s, 3H), 1.52 (s, 3H).

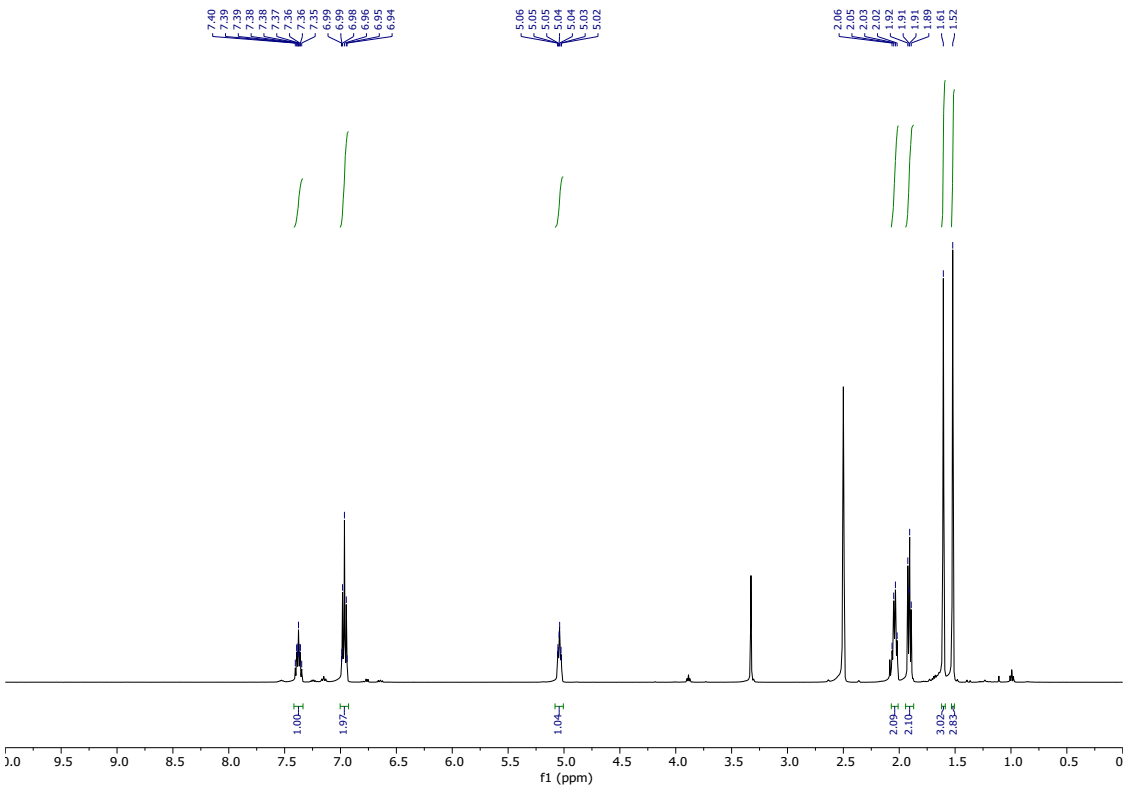
^{13}C NMR (126 MHz, DMSO-d_6) δ 177.8, 159.2 (dd, J = 253, 6.1 Hz), 131.1 (t, J = 10.8 Hz), 130.0, 124.7, 124.0 (t, J = 17.9 Hz), 112.08 (dd, J = 22.3, 5.0 Hz), 39.3, 25.5, 24.5, 17.5.

^{19}F NMR (471 MHz, DMSO-d_6) δ -108.11 – -108.20 (dd, J = 8.4, 6.1 Hz).

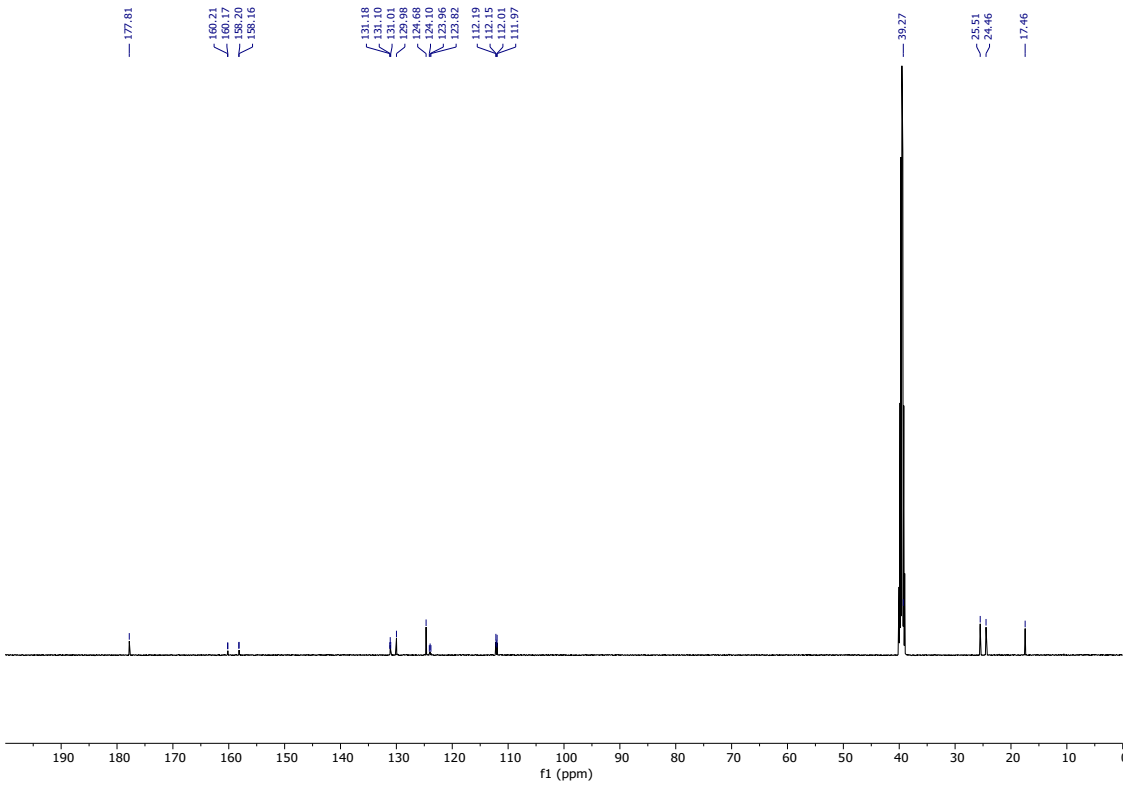
IR (neat) 2970, 2922, 1612, 1590, 1463, 1366, 1346, 1255, 1225, 1135 cm^{-1}

HRMS (ESI-) m/z calculated for $C_{13}H_{14}F_2NO3S^-$ [M$^-$]: 302.0667, found 302.0653

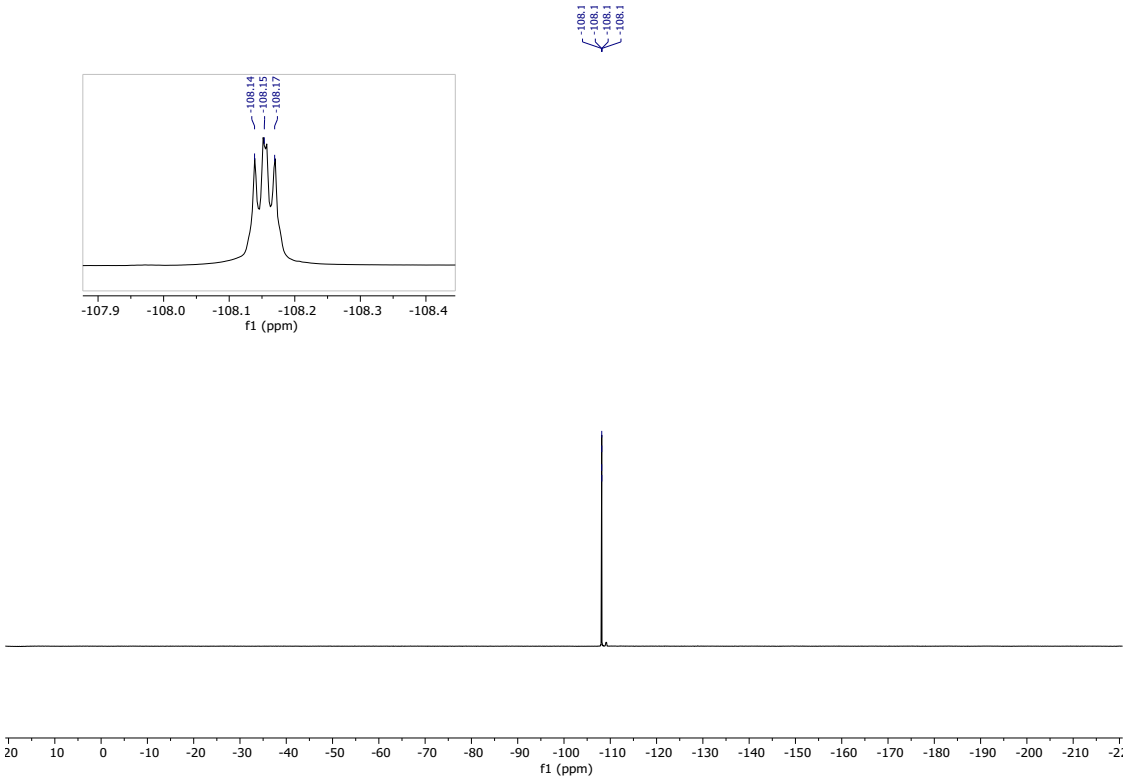
^{1}H NMR – K^{+}[1d]$^{-}$



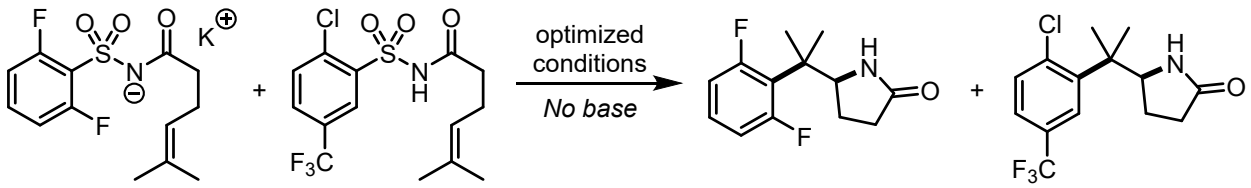
^{13}C NMR – K^{+}[1d]$^{-}$



^{19}F NMR – $K^+[1d]^-$


-108.14
-108.15
-108.17
-107.9
-108.0
-108.1
-108.2
-108.3
-108.4
f1 (ppm)
-108.1
-108.1
-108.1
-108.1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

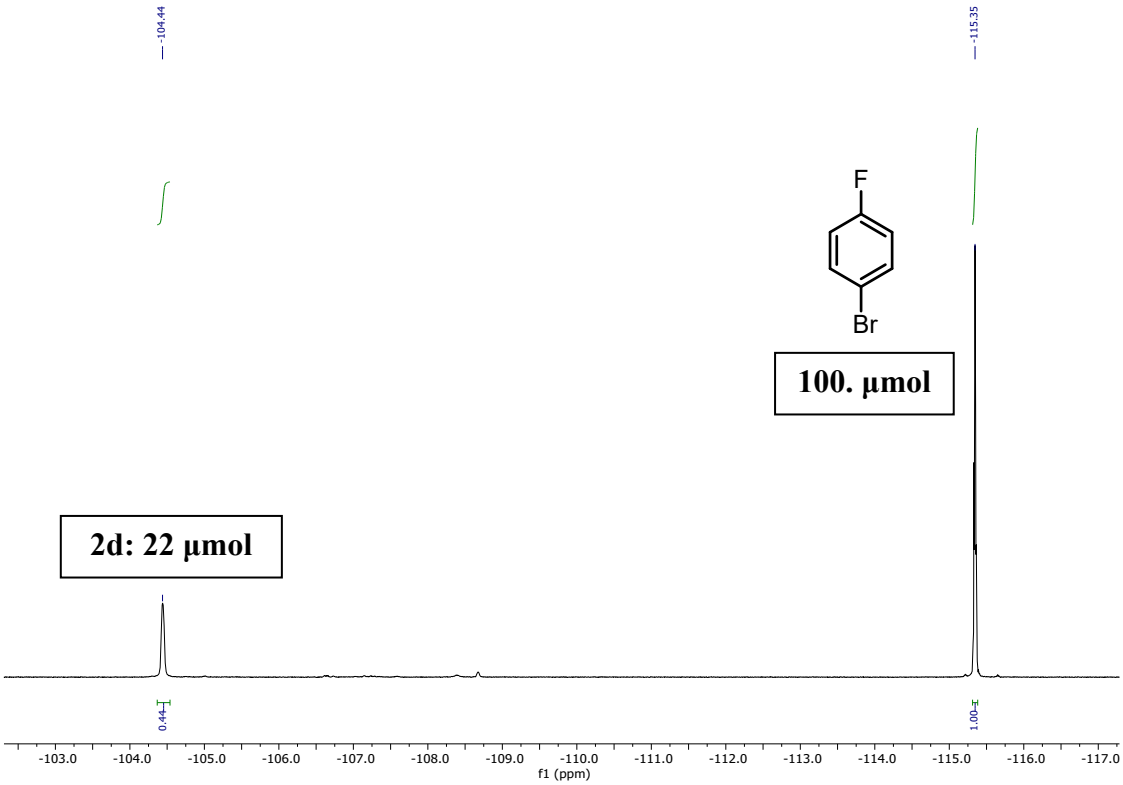
Substrate reactivity experiment



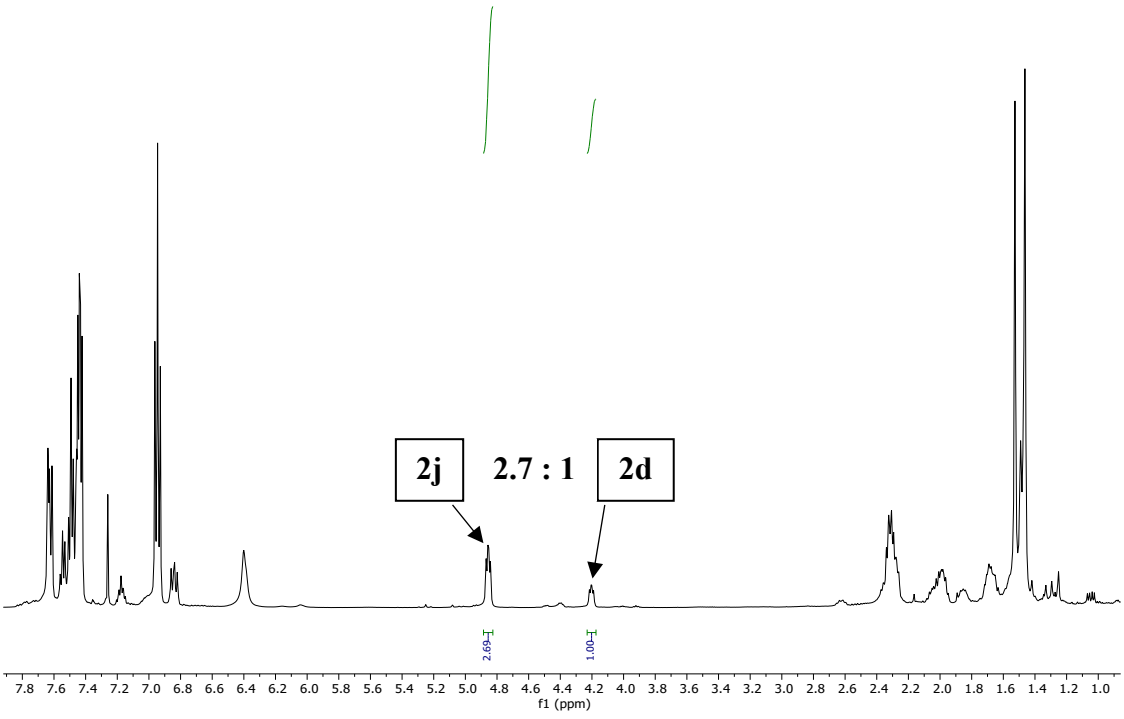
K^+[1d]$^-$: 1 equiv. **1j:** 2.3 equiv. **2d:** 73% **2j:** 84%

The reaction setup was conducted in a 1 dram vial according to **GP2** (excluding *p*-$ClC_6H_4CO_2K$) with a mixture of **K^+[1d]$^-$** (10.2 mg, 30.0 μmol) and **1j** (21.4 mg, 70.0 μmol) in 2.0 mL $PhCF_3$. After 16 hours, the reaction mixture was concentrated under reduced pressure and redissolved in 0.5 mL $CDCl_3$. 4-Fluorobromobenzene (17.5 mg, 11.0 μL, 1.0 equiv.) was added so that assay yields of **2d** and **2j** could be obtained by ^{19}F NMR spectroscopy of the crude mixture. Only the assay yield of **2d** was obtained by ^{19}F NMR due to signal overlap between **2j** and residual $PhCF_3$. As a result, yield of **2j** was obtained indirectly by finding the relative ratio of **2j** to **2d** through integration of their representative ^1H NMR signals.

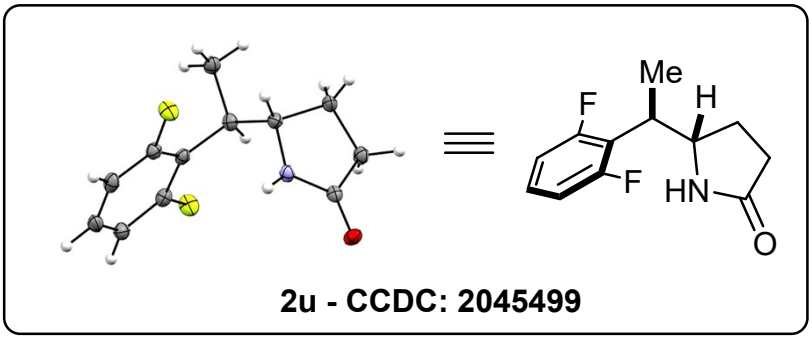
^{19}F NMR – Crude reaction mixture of K$^+$[1d]$^-$ and 1j



^{1}H NMR – Crude reaction mixture of K$^+$[1d]$^-$ and 1j



4. X-ray crystallography data



2u - CCDC: 2045499

2u - Structure Determination

Colorless plates of **2u** were grown from a dichloromethane/diethyl ether solution of the compound at 22 °C. A crystal of dimensions 0.16 x 0.16 x 0.10 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (l = 1.54187 Å) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in w. The exposure times were 1 sec. for the low angle images, 4 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 16093 reflections to a maximum 2q value of 138.74° of which 1976 were independent and 1969 were greater than 2s(I). The final cell constants (Table 1) were based on the xyz centroids of 13269 reflections above 10s(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group P2(1)2(1)2(1) with Z = 4 for the formula $C_{12}H_{13}NOF_2$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in a combination of refined and idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0269 and wR2 = 0.0698 [based on I > 2σ(I)], R1 = 0.0271 and wR2 = 0.0699 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

Crystal data and structure refinement for **2u**.

Identification code	ean223
Empirical formula	C12 H13 F2 N O
Formula weight	225.23
Temperature	85(2) K
Wavelength	1.54184 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.32492(6) A alpha = 90 deg. b = 7.77679(5) A beta = 90 deg. c = 18.64270(13) A gamma = 90 deg.
Volume	1061.969(14) $Å^3$
Z, Calculated density	4, 1.409 Mg/m^3
Absorption coefficient	0.964 mm^{-1}
F(000)	472
Crystal size	0.160 x 0.160 x 0.100 mm
Theta range for data collection	4.744 to 69.368 deg.
Limiting indices	-8<=h<=8, -9<=k<=9, -22<=l<=22
Reflections collected / unique	16093 / 1976 [R(int) = 0.0574]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.93266
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1976 / 0 / 151
Goodness-of-fit on F^2	1.074
Final R indices [I>2σ(I)]	R1 = 0.0269, wR2 = 0.0698
R indices (all data)	R1 = 0.0271, wR2 = 0.0699
Absolute structure parameter	0.23(5)
Extinction coefficient	0.0066(10)
Largest diff. peak and hole	0.169 and -0.189 $eÅ^{-3}$

5. References

1. G. J. Choi, Q. Zhu, D. C. Miller, C. J. Gu and R. R. Knowles, *Nature*, 2016, **539**, 268-271.
2. M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Pascal, G. G. Malliaras and S. Bernhard, *Chemistry of Materials*, 2005, **17**, 5712-5719.
3. T. M. Monos, R. C. McAtee and C. R. J. Stephenson, *Science*, 2018, **361**, 1369-1373.
4. C. M. Morton, Q. Zhu, H. Ripberger, L. Troian-Gautier, Z. S. D. Toa, R. R. Knowles and E. J. Alexanian, *J. Am. Chem. Soc.*, 2019, **141**, 13253-13260.
5. A. J. Cresswell, S. T. C. Eey and S. E. Denmark, *Nat. Chem.*, 2015, **7**, 146-152.
6. D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick and S. F. Martin, *J. Am. Chem. Soc.*, 2012, **134**, 11128-11131.
7. S. A. Shahzad, C. Vivant and T. Wirth, *Org. Lett.*, 2010, **12**, 1364-1367.
8. D. Staveness, T. M. Sodano, K. Li, E. A. Burnham, K. D. Jackson and C. R. J. Stephenson, *Chem*, 2019, **5**, 215-226.
9. R. C. McAtee, E. A. Noten and C. R. J. Stephenson, *Nat. Commun.*, 2020, **11**, 2528.
10. T. R. Huffman, Y. Wu, A. Emmerich and R. A. Shenvi, *Angew. Chem. Int. Ed.*, 2019, **58**, 2371-2376.
11. A. T. Placzek and R. A. Gibbs, *Org. Lett.*, 2011, **13**, 3576-3579.
12. T. U. Connell, C. L. Fraser, M. L. Czyz, Z. M. Smith, D. J. Hayne, E. H. Doeven, J. Agugiaro, D. J. D. Wilson, J. L. Adcock, A. D. Scully, D. E. Gómez, N. W. Barnett, A. Polyzos and P. S. Francis, *J. Am. Chem. Soc.*, 2019, **141**, 17646-17658.