Supporting Information

Direct Electrochemical Synthesis of Pentafluorophenyl Esters via Oxyl-Radical-Promoted Nucleophilic Aromatic Substitution

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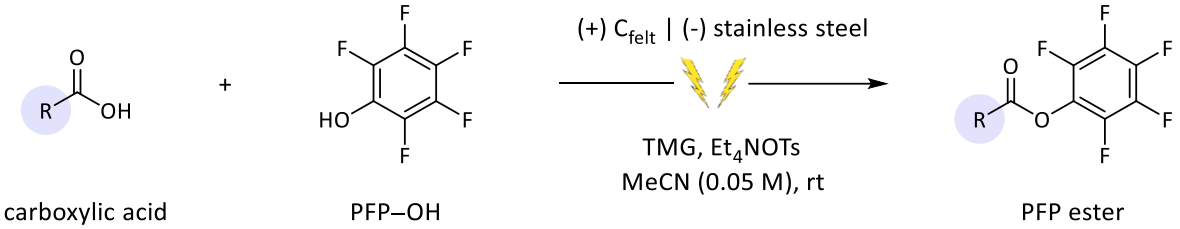
I. General Information

All procedures were performed under air unless stated otherwise. Acetonitrile, dimethylformamide, dimethyl sulfoxide, methanol, tetrahydrofuran, and toluene were dried using a solvent purification system. All starting materials and reagents were used as received. Reactions were monitored by thin-layer chromatography (TLC), gas chromatography-mass spectrometry (GC-MS), or liquid chromatography-mass spectrometry (LC-MS). TLC was performed on Silicycle 250-micron silica-gel F-254 plates and visualized by UV fluorescence (254 nm), $KMnO_4$ stain or ninhydrin stain for Boc-protected amino acid derived products. GC-MS (electron impact) spectra were recorded on Agilent 8890 GC and 5977B Series MSD systems. Low-resolution mass spectra (LRMS) and the yield for **9** were obtained by ^{19}F NMR on a Bruker NEO 400 MHz spectrometer against a α,α,α-trifluorotoluene standard. Organic solutions were concentrated under reduced pressure on a Heidolph rotary evaporator. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel. NMR spectra were recorded on a Bruker NEO 400 MHz spectrometer. Chemical shifts were internally referenced to residual protic solvent signals of $CDCl_3$ (7.26 ppm for ^1H, 77.16 ppm for ^{13}C), DMSO-d_6 (2.50 ppm for ^1H, 39.53 ppm for ^{13}C) or CD_3CN (1.97 ppm for ^1H, 118.26 and 1.32 ppm for ^{13}C). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift and, if applicable, multiplicity and coupling constant (Hz). Cyclic voltammetry (CV) experiments were performed using a CH Instruments 600E electrochemical analyzer, a 3-mm glassy carbon disk working electrode (polished with 0.05-μm MicroPolish powder on a Microcloth polishing pad), a platinum-wire counter electrode, and a $Ag/AgNO_3$ reference electrode with NEt_4OTs as the electrolyte. Potentials were corrected to SCE by adding 0.05 V (we measured $E_{1/2}[Fc^+/Fc] = +0.35$ V vs. $Ag/AgNO_3$, which is at +0.40 V vs. SCE). [1] High-resolution mass spectra (ESI-HRMS) were obtained on a ThermoFisher Scientific UHPLC/QExactive HF-X mass spectrometer equipped with a C_{18} column.

II. General Procedures for Pentafluorophenyl Esterification



General Procedure A

Carboxylic acid (0.50 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (301.44 mg, 1.0 mmol, 2.0 equiv.), pentafluorophenol (276 mg, 1.50 mmol, 3.0 equiv.), tetramethylguanidine (~62 µL, 0.50 mmol, 1 equiv.), and acetonitrile (10 mL, 0.05 M in carboxylic acid) were added to a 20-mL vial equipped with a magnetic stir bar and sealed with a septum cap. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup") at 3.0 V for 3–4 hours. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure A (Scale-up)

Carboxylic acid (2.00 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (1.21 g, 4.00 mmol, 2.0 equiv.), pentafluorophenol (1.10 g, 6.00 mmol, 3.0 equiv.), tetramethylguanidine (~0.25 mL, 2 mmol, 1 equiv.), and acetonitrile (40 mL, 0.05 M in carboxylic acid) were added to a 55-mL test tube equipped with a magnetic stir bar and sealed with a 24/40 septum. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup") at 3.0 V for 6–8 hours. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure B

Carboxylic acid (0.50 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (301.44 mg, 1.0 mmol, 2.0 equiv.), pentafluorophenol (276 mg, 1.50 mmol, 3.0 equiv.), tetramethylguanidine (~62 μL, 0.50 mmol, 1 equiv.), and acetonitrile (10 mL, 0.05 M in carboxylic acid) were added to a 20-mL vial equipped with a magnetic stir bar and sealed with a septum cap. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup") at 3.0 V for 3 hours. Additional pentafluorophenol (184 mg, 1.00 mmol. 2.0 equiv.) and tetramethylguanidine (~31 μL, 0.25 mmol, 0.5 equiv.) was added to the reaction mixture. The solution was sparged and sealed and was electrolyzed for 1–1.5 hours until the reaction yield plateaued. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure B (Scale-up)

Carboxylic acid (2.00 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (1.21 g, 4.00 mmol, 2.0 equiv.), pentafluorophenol (1.10 g, 6.00 mmol, 3.0 equiv.), tetramethylguanidine (~0.25 mL, 2 mmol, 1 equiv.), and acetonitrile (40 mL, 0.05 M in carboxylic acid) were added to a 55-mL test tube equipped with a magnetic stir bar and sealed with a 24/40 septum. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup") at 3.0 V for 6–8 hours. Additional pentafluorophenol (552 mg, 3.00 mmol. 2.0 equiv.) and tetramethylguanidine (~0.13 mL, 0.1 mmol, 0.5 equiv.) were added to the reaction mixture. The solution was sparged and sealed and was electrolyzed for 2–3 hours until the reaction yield plateaued. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure C

Carboxylic acid (0.50 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (301.44 mg, 1.0 mmol, 2.0 equiv.), pentafluorophenol (460 mg, 1.50 mmol, 3.0 equiv.), tetramethylguanidine (~94 μL, 0.75 mmol, 1 equiv.), and acetonitrile (10 mL, 0.05 M in carboxylic acid) were added to a 20-mL vial equipped with a magnetic stir bar and sealed with a septum cap. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup"") at 3.0 V for 3–4 hours. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure C (Scale-up)

Carboxylic acid (2.00 mmol, 1.0 equiv.), tetraethylammonium toluenesulfonate (1.21 g, 4.00 mmol, 2.0 equiv.), pentafluorophenol (1.84 g, 10.00 mmol, 5.0 equiv.,), tetramethylguanidine (~0.37 mL, 3 mmol, 1.5 equiv.), and acetonitrile (40 mL, 0.05 M in carboxylic acid) were added to a 55-mL test tube equipped with a magnetic stir bar and sealed with a 24/40 septum. The resulting mixture was thoroughly shaken and sparged with nitrogen for 10 minutes. The degassed mixture was electrolyzed (see "Section III. Electrochemistry Setup") at 3.0 V for 6–8 hours. The electrodes were removed and washed with acetone into the reaction mixture and the solution was concentrated. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the product. Some products required initial elution with hexanes to remove a yellow oil by-product.

General Procedure (A, B or C) – Product Characterization as *N*-Benzylamide

For PFP esters that proved inseparable from any byproduct(s) by silica-gel chromatography

Electrosyntheses were performed the same manner as above. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the partially purified product. This residue was then dissolved in acetonitrile (5 mL), and benzylamine (~1.50 equiv.) and triethylamine (~1 equiv.) were added to the solution. The reaction was stirred for 6 hours and concentrated. The

residue was dissolved in ethyl acetate (10 mL) and washed with 1 M HCl (2 × 10 mL), saturated Na_2CO_3 solution (10 mL), and distilled water (10 mL). The organic layer was then dried over sodium sulfate and concentrated to a green-white residue. The residue was purified by silica-gel chromatography with hexanes/ethyl acetate to afford the *N*-benzylamide derivative.

III. Electrochemistry Setup

Electrochemical Setup for Small-Scale Reactions

Figure S1. Photograph of the in-house electrolytic cell used for the reactions (0.5 mmol scale).

An electrochemical reaction was conducted using a SKY TOPPOWER (PS3010H) DC power source supply. 6-cm piece of OOK 14-gauge galvanized steel wire were bent at one end to form a hook. For the carbon felt electrodes, a 0.5 cm wide, 1.2 cm long, and 3.3 cm high piece of carbon felt was attached to the end of the wire. The hook was crimped with pliers to secure the carbon felt. For the stainless-steel electrodes, a 20 cm piece of 100 lb. braided OOK hanging wire was unbraided. The single strand of wire was wrapped around the galvanized steel wire to create a spring-like structure, and the hook of the galvanized wire was crimped to secure the electrode. This flat stainless-steel wire was then coiled using another piece of galvanized steel wire. Both electrodes were then pierced through a septum cap that would fit onto a 20 mL vial. The vial was charged with a stir bar and the septum cap bearing the electrodes was screwed on. The DC power supply was set to the appropriate potential and then connected to the vial using alligator clips.

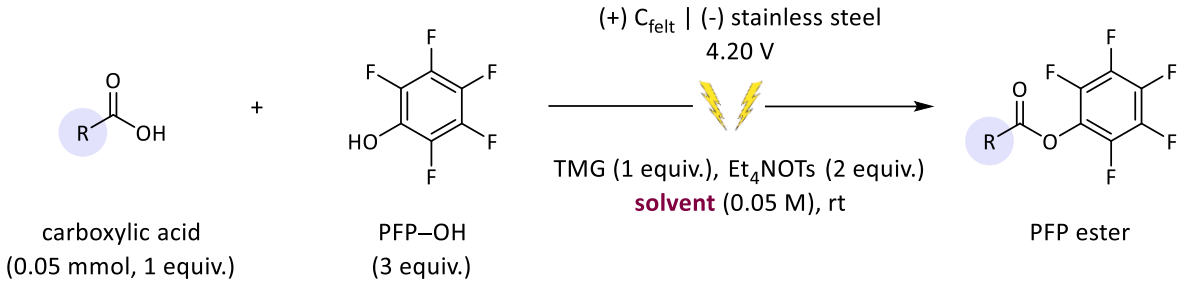
Electrochemical Setup for Large-Scale Reactions

Figure S2. Photograph of the in-house electrolytic cell used for the large-scale reactions (2 mmol scale).

An electrochemical reaction was conducted using a SKY TOPPOWER (PS3010H) DC power source supply. A 7.5-cm piece of OOK 14-gauge galvanized steel wire were bent at one end to form a hook. For the carbon felt electrodes, a 0.5 cm wide, 0.5 cm long, and 11 cm high piece of carbon felt was attached to the end of the wire. The hook was crimped with pliers to secure the carbon felt. For the stainless-steel electrodes, a 31 cm piece of 100 lb. braided OOK hanging wire was unbraided. An individual piece of the wire was wrapped around the galvanized steel wire to create a spring-like structure, and the hook of the galvanized wire was crimped to secure the electrode. This flat stainless-steel wire was then coiled using another piece of galvanized steel wire. Both electrodes were then inserted into a septum stopper for a 24/40 outer joint, which can be fitted into a 15 cm diameter by 25 cm height test tube. The tube was charged with a stir bar and the septum stopper bearing the electrodes was screwed on. Electrical tape was wrapped around the cap to prevent it from popping out during the reaction. The DC power supply was set to the appropriate potential and then connected to the tube using alligator clips.

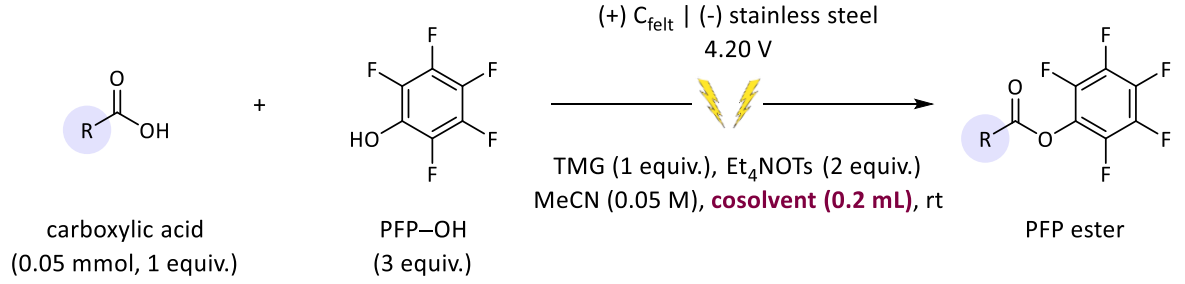
IV. Optimization

Table S1. Impact of solvents on model esterification. Yields determined by ^{19}F NMR.



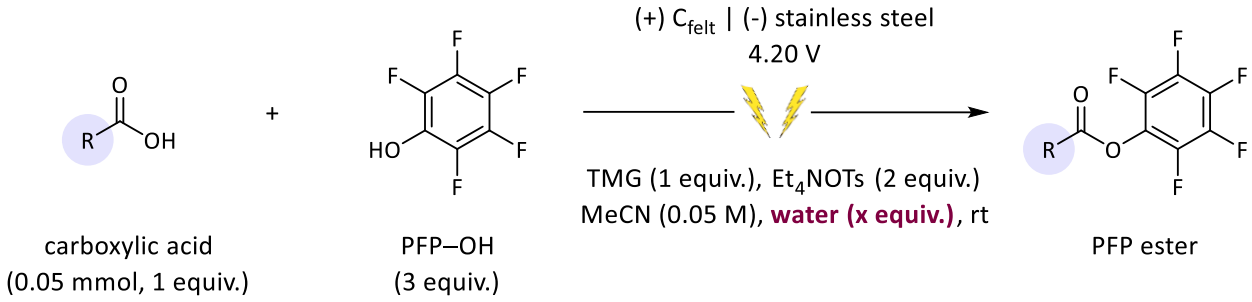
entry	solvent	Time (h)	yield (%)
1	MeCN	1	80
2	MeOH	1	Trace
3	DMF	3	67
4	DMSO	3	38

Table S2. Impact of cosolvents on model esterification. Yields determined by ^{19}F NMR.



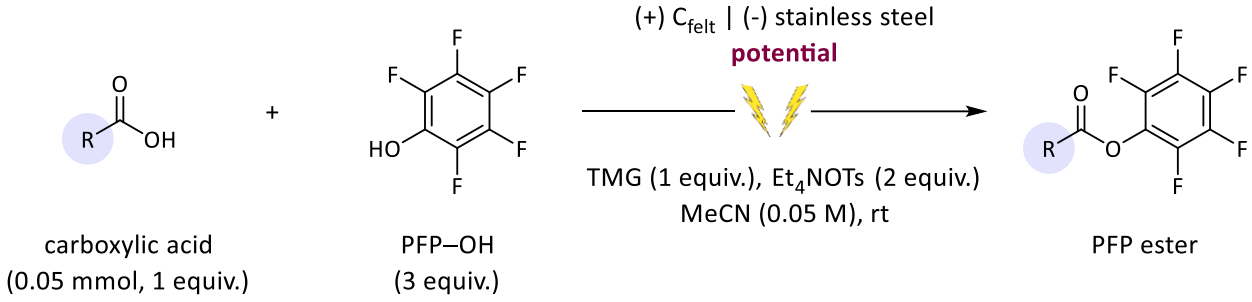
entry	solvent	Time (h)	yield (%)
1	HFIP	1	46
2	TFE	1	60
3	MeOH	1	54
4	*i*-PrOH	1	66
5	none	1	82

Table S3. Impact of water on model esterification. Yields determined by ^{19}F NMR.



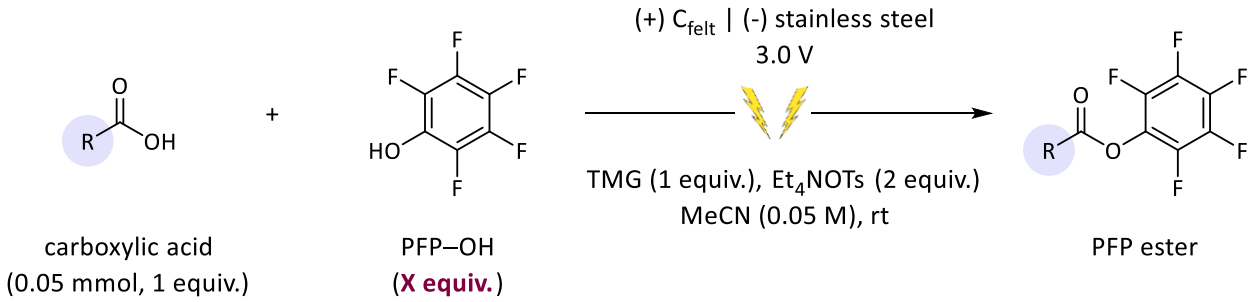
entry	Equivalents of H_2O	Time (h)	yield (%)
1	none	1	82
2	2 equiv.	1	82
3	8 equiv.	1	76
4	10 equiv.	1	63
5	cosolvent (2.5 mL)	1	39

Table S4. Impact of reaction potential on model esterification. Yields determined by ^{19}F NMR.



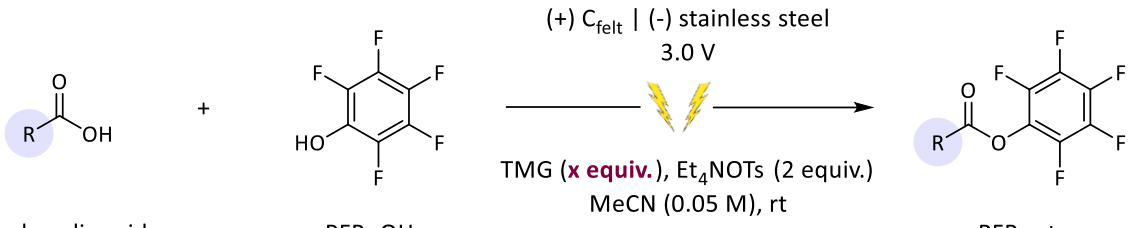
entry	Potential	Time (h)	yield (%)
1	4.0 V	1.0	82
2	3.5 V	1.5	83
3	3.0 V	2.0	85
4	2.5 V	6.5	68

Table S5. Impact of PFPOH stoichiometry on model esterification. Yields determined by ^{19}F NMR.



entry	Equiv. of PFPOH	Time (h)	yield (%)
1	1	0.5	13
2	2	1.5	42
3	3	2.5	83
4	4	3.0	82
5	5	3.0	79
6	6	3.0	48
7	7	3.0	35

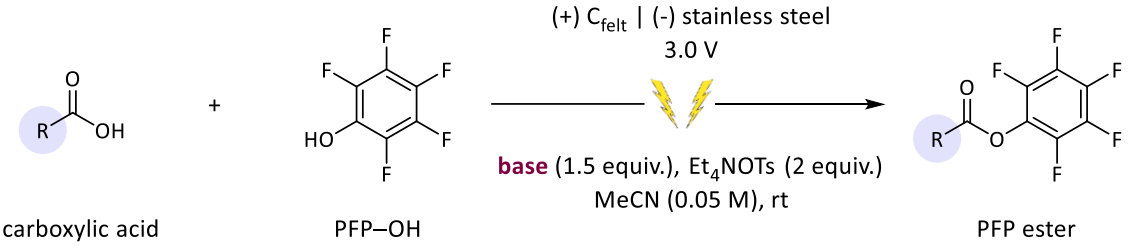
Table S6. Impact of base stoichiometry on model esterification. Yields determined by ^{19}F NMR.



carboxylic acid (0.05 mmol, 1 equiv.) | PFP–OH (5 equiv.) | PFP ester

entry	Equiv. of base	Time (h)	yield (%)
1	0	2.5	None
2	0.5	4.5	44
3	1.0	3.0	79
4	1.5	2.5	82
5	2.0	2.5	90

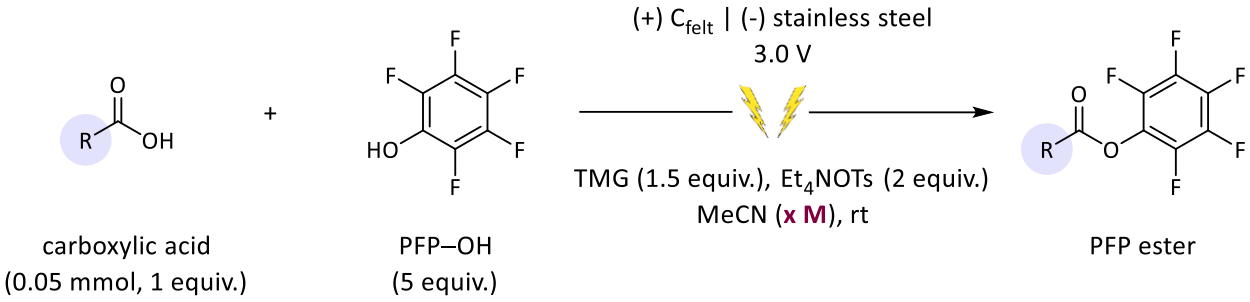
Table S7. Impact of base identity on model esterification. Yields determined by ^{19}F NMR.



carboxylic acid (0.05 mmol, 1 equiv.) | PFP–OH (5 equiv.) | PFP ester

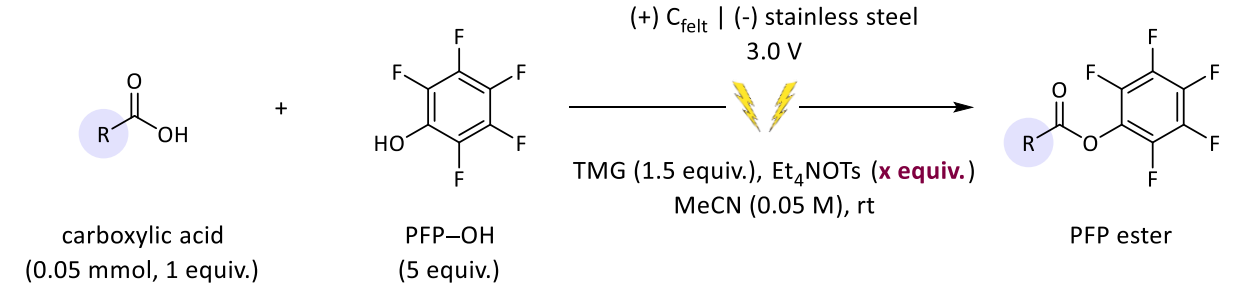
entry	Base (pK_a in MeCN)	Time (h)	yield (%)
1	NEt_3 (18.8)[2]	2.5	None
2	DBU (24.3)[2]	4.5	44
3	DABCO (18.3)[2]	3.0	79
4	Pyridine (12.5)[2]	2.5	82
5	TMG (23.35)[2]	2.5	90

Table S8. Impact of concentration on model esterification. Yields determined by ^{19}F NMR.



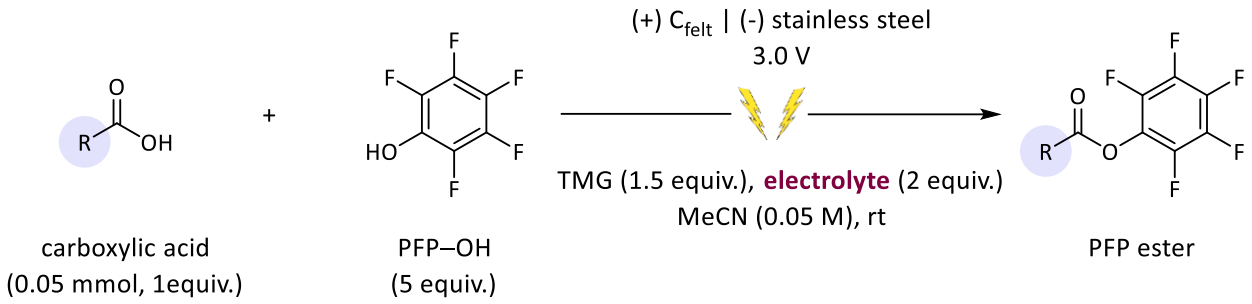
entry	concentration	Time (h)	yield (%)
1	0.025 M	2.5	88
2	0.05 M	2.5	88
3	0.075 M	4.0	78
4	0.10 M	4.0	73
5	0.25 M	8.0	55

Table S9. Impact of electrolyte stoichiometry on model esterification. Yields determined by ^{19}F NMR.



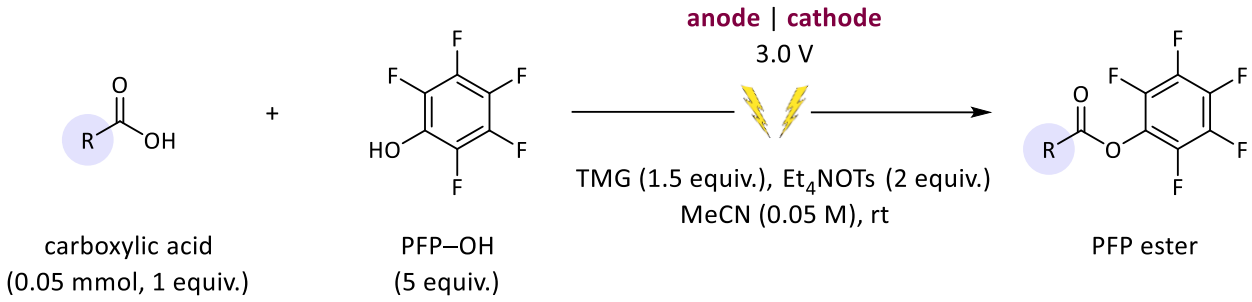
entry	Equivalents of Et4NOTs	Time (h)	yield (%)
1	0	6.0	0
2	1	3.0	14
3	2	2.5	89
4	3	2.5	85

Table S10. Impact of electrolyte identity on model esterification. Yields determined by ^{19}F NMR.



entry	electrolyte	Time (h)	yield (%)
1	Bu_4NBr	2.5	75
2	Bu_4NCl	2.0	75
3	Et_4NCl	2.0	80
4	Et_4NOTs	2.5	87
5	Et_4NBF_4	2.0	68
6	Et_4NPF_6	2.0	68
7	$LiPF_6$	2.5	1
8	$NMe_4OH \bullet 5H_2O$	1.5	35
9	$NMe_4OH \bullet 5H_2O$ (no TMG)	2.5	80

Table S11. Impact of electrode materials on model esterification. Yields determined by ^{19}F NMR.



entry	cathode	anode	Time (h)	yield (%)
1	C	SS	2.5	89
2	RVC	SS	3.0	81
3	C	SS	4.0	78
4	C	C	2.0	53
5	C	Pt	2.5	88
6	C	Cu	2.0	76
7	C	Sn	2.5	73
8	C	Ti	3.0	77
9	C	Zn	3.0	76

V. Electrochemical Studies

Cyclic Voltammetry

General Procedure

A solution of analytes(s) (0.003 M) and tetrabutylammonium hexafluorophosphate (0.1 M) in acetonitrile (10 mL) was prepared in a 10-mL three-neck flask (undivided cell) at room temperature. All measurements were scanned oxidatively, from 0 V vs. $Ag/AgNO_3$ to 2.5 V vs. $Ag/AgNO_3$, and then reductively, to 0 V vs. $Ag/AgNO_3$, at 500 mV/s. Cyclic voltammograms are shown in Figures S3-S8.

Analysis

Figure S3 shows the cyclic voltammogram (oxidative side) of pentafluorophenol (PFPOH) with the electrolyte. Under neutral conditions, pentafluorophenol is oxidized at +1.58 V vs SCE. Upon the addition on 1 equivalent of the base, tetramethylguanidine (TMG), the oxidation of pentafluorophenol becomes more facile, +0.27 V vs. SCE (Figure S4). The use of a different base, tetrabutylammonium hydroxide, resulted in a similar potential, +0.29 V vs. SCE (Figure S5).

3-phenylpropanoic acid has a high oxidation potential under neutral conditions. We did not observe a peak before the limit of oxidation that acetonitrile has (Figure S6).[3] Unsurprisingly, the addition of TMG makes the oxidation of the carboxylic acid possible at +0.96 V (Figure S7). Like with PFPOH, treatment of 3-phenylpropanoic acid with TBAOH, resulted in a near identical potential for oxidation, +0.95 V vs. SCE (Figure S8).

We then took a cyclic voltammogram of a solution that has the equivalencies of acid (1 equiv., 0.003 M), base (1.5 equiv.) and PFPOH (5 equiv.) that is the similar to that of the optimized reaction conditions (Figure S9). We observed a peak at +0.46 V which more closely resembles the oxidation of PFPOH than the oxidation of the acid. We also note that there is no peak close to +0.96 V showing that the acid is most likely. This observation supports our proposed mechanism that the reaction is initiated by the formation of an oxyl radical while the acid is unaffected by the electrolysis. This is also consistent with pka measurements made that shows that PFPOH is more acidic than aliphatic carboxylic acids.[4]

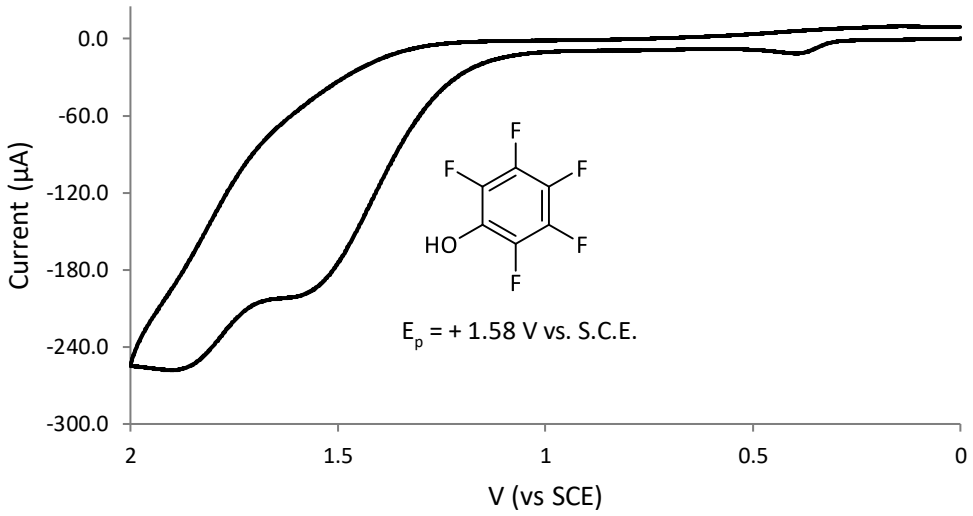


Figure S3. Cyclic voltammogram of PFPOH, at 100 mV/s.

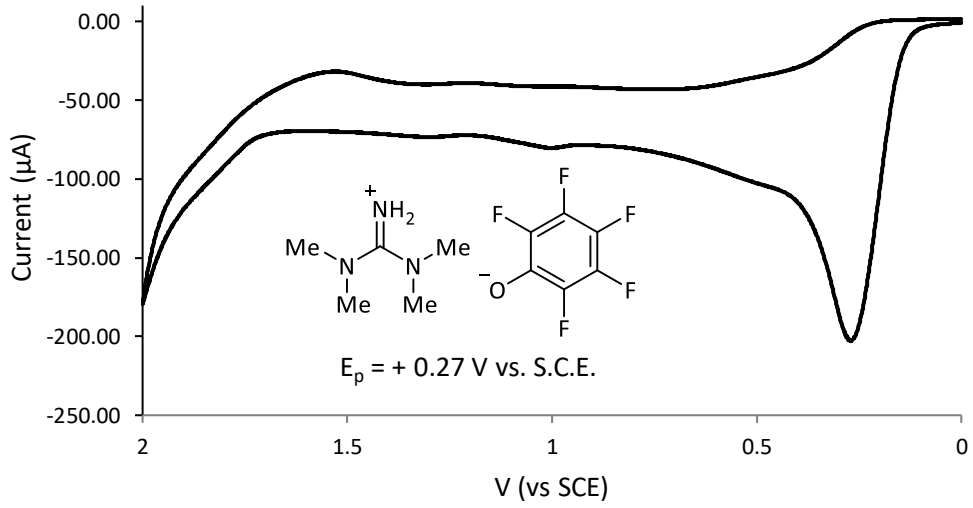


Figure S4. Cyclic voltammogram of PFPOH with one equivalent of TMG, at 100 mV/s.

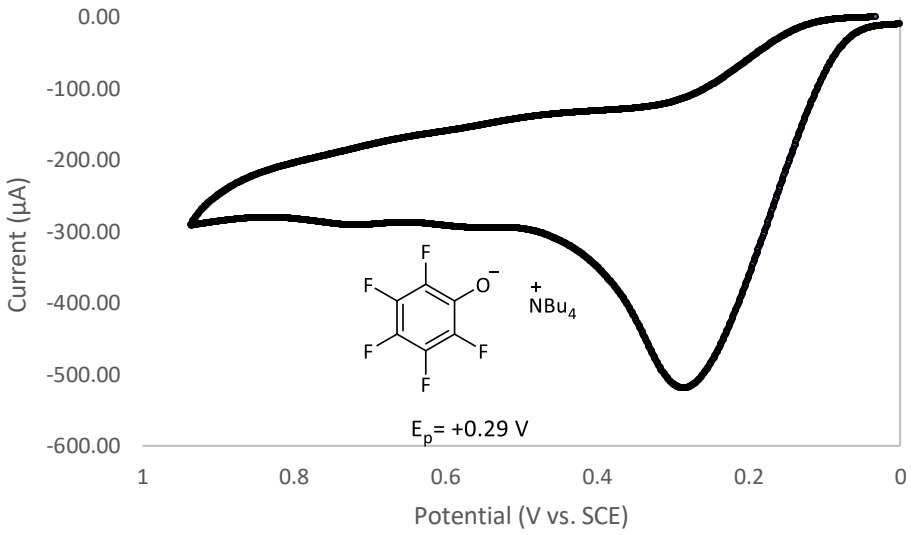


Figure S5. Cyclic voltammogram of PFPOH with one equivalent of tetrabutylammonium hydroxide (as an alternative base for deprotonation), at 100 mV/s.

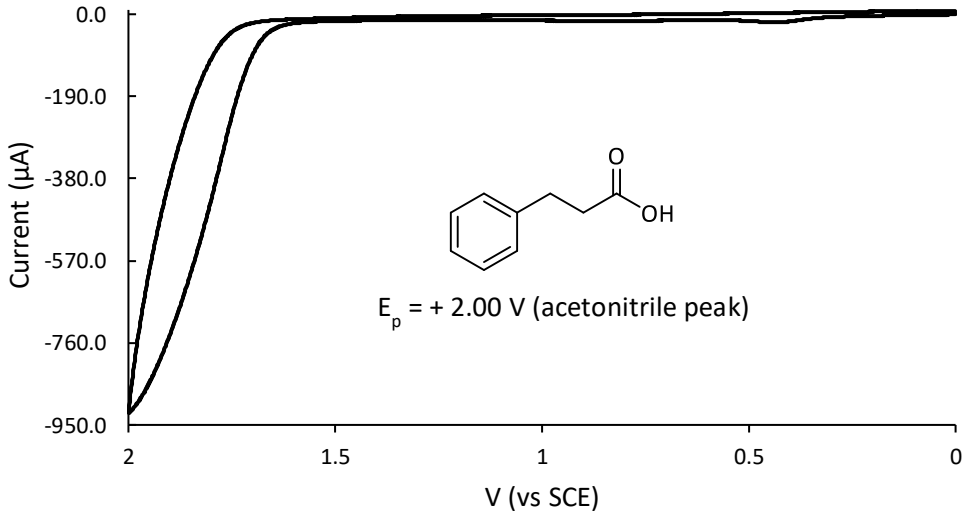


Figure S6. Cyclic voltammogram of 3-phenylpropionic acid, at 100 mV/s.

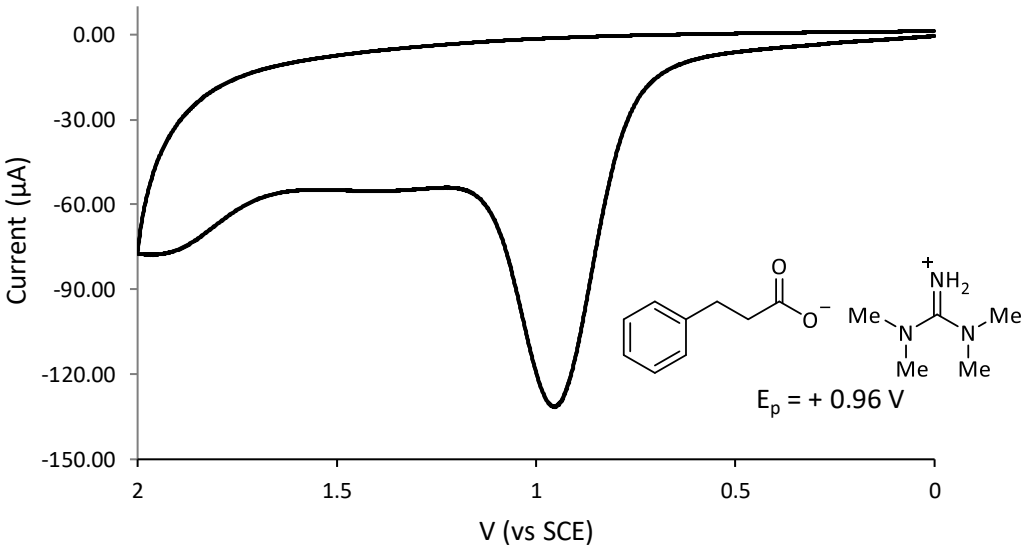


Figure S7. Cyclic voltammogram of 3-phenylpropionic acid with one equivalent of TMG, at 100 mV/s.

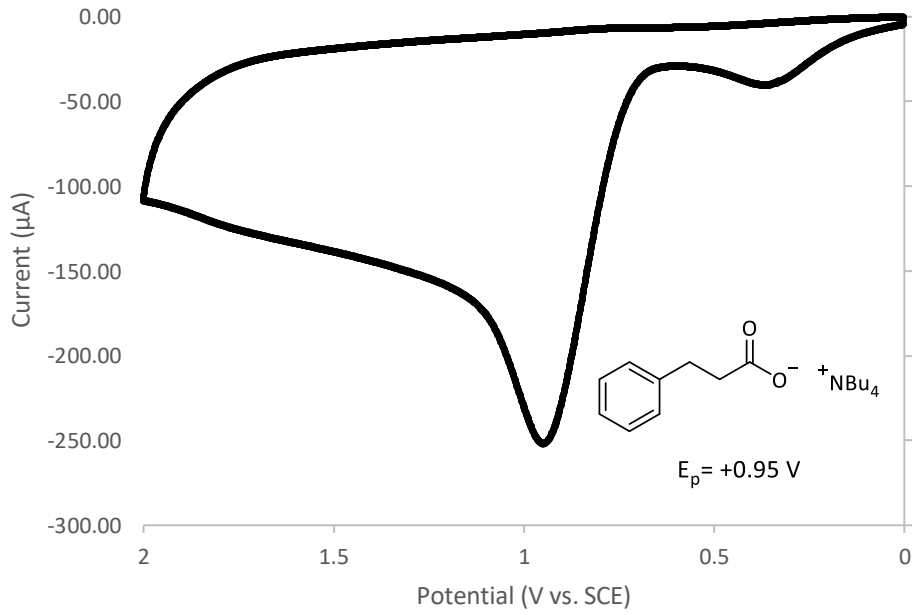


Figure S8. Cyclic voltammogram of 3-phenylpropionic acid with one equivalent of TMG, at 100 mV/s.

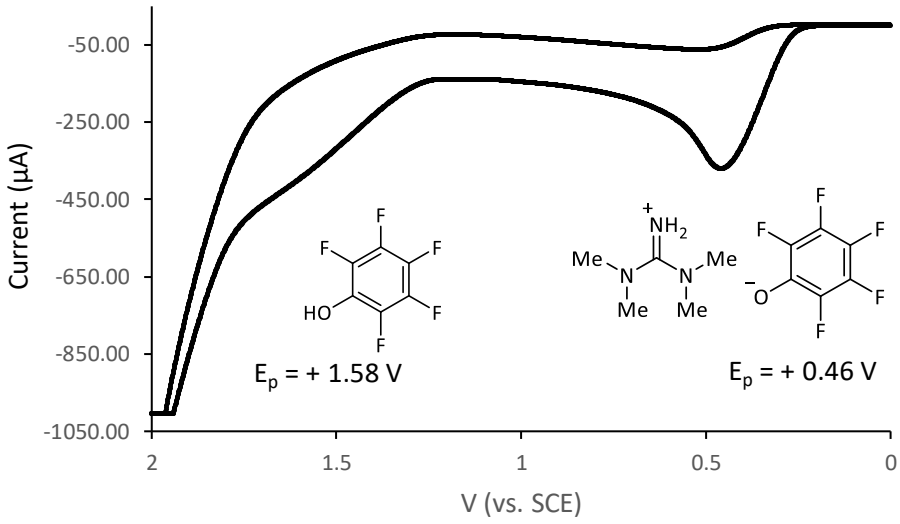


Figure S9. Cyclic voltammogram of the model reaction, at 100 mV/s.

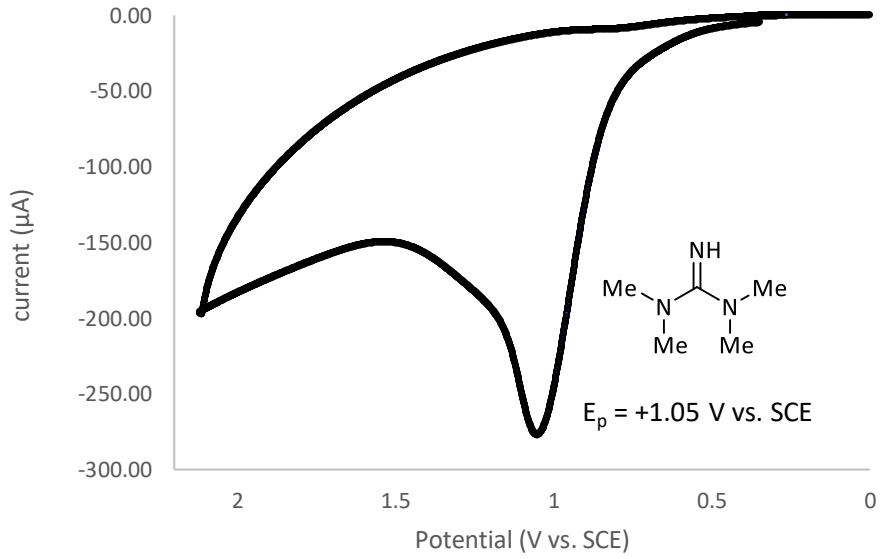


Figure S10. Cyclic voltammogram of 1,1,3,3-tetramethylguanidine, at 100 mV/s. We expect TMG to not have an influence on the electrochemistry in the reaction due to the acidity and excess amount of pentafluorophenol which causes TMG to be fully protonated (see S9 for fully protonated CV of TMG).

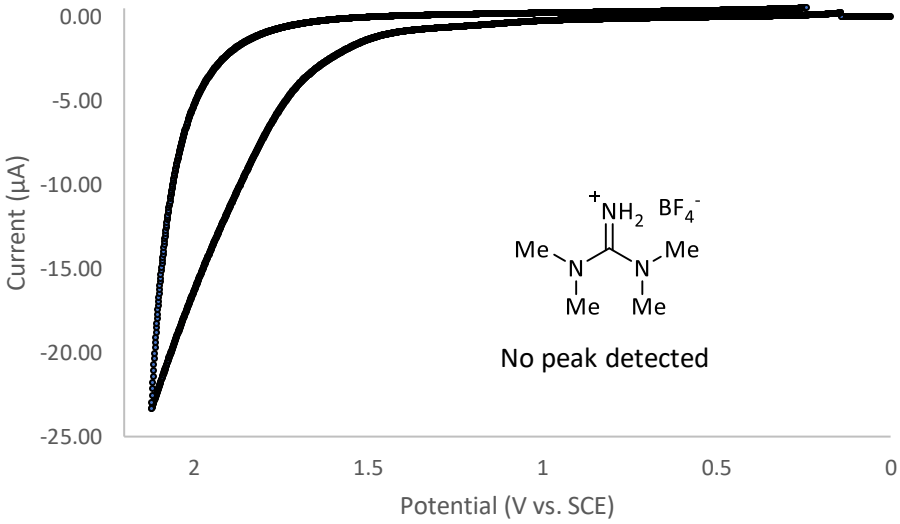


Figure S11. Cyclic voltammogram of 1,1,3,3-tetramethylguanidine with one equivalent of HBF_4 (as a representative of a non-oxidizable strong acid), at 100 mV/s.

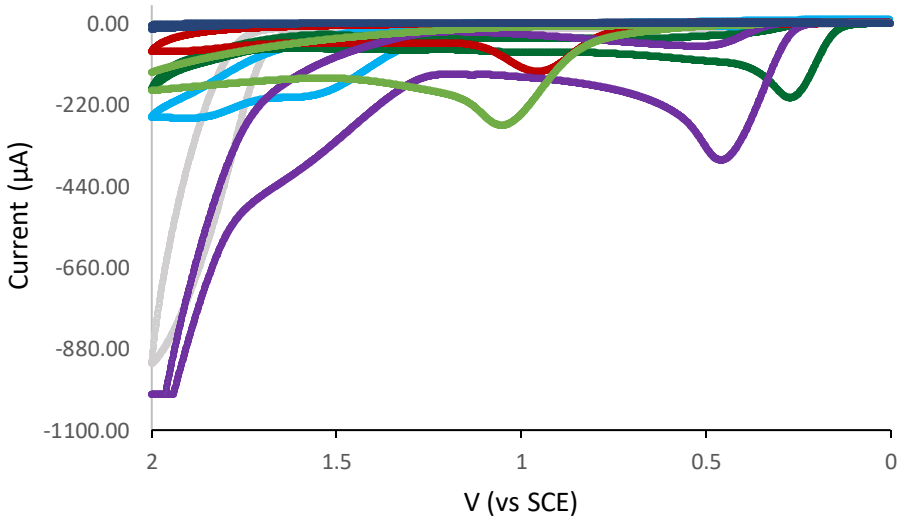


Figure S12. An overlay of the five cyclic voltammograms (Figure S3 in blue, Figure S4 in green, Figure S6 in grey, Figure S7 in red, Figure S9 in purple, Figure S10 in lime green and Figure S11 in dark blue [nearly flat line] in). The reaction CV (purple) most resembles the PFPOH with 1 equiv. of TMG (green).

Measurement of Cathode and Anode Potentials

An electrochemical cell was prepared in the same way as described in Section III. "Electrochemical Setup for Small-Scale Reactions". In addition, a $Ag/AgNO_3$ reference electrode (filled with a solution of $AgNO_3$ (10 mM) and Et_4NOTs (100 mM) in acetonitrile) was added in between the anode and cathode. A solution composed of 3-phenylpropionic acid (75 mg, 0.5 mmol, 1 equiv.), tetramethylguanidine (94 µL, 0.75 mmol, 1.5 equiv.), tetraethylammonium toluenesulfonate (301 mg, 1.00 mmol, 2.0 equiv.), pentafluorophenol (460 mg, 2.5 mmol, 5.0 equiv.) and acetonitrile (20 mL, 0.05 M in 3-phenylpropionic acid) was added to the constructed cell. The power source was connected to the respective electrodes (anode: carbon felt, cathode: stainless steel) and an OWON B35T+ digital multimeter was connected to the reference electrode and the electrode of interest. The multimeter was set to record the potential every 1 minute for 3 hours and the power source was then turned on and set to 3.0 V and the solution was electrolyzed for 3 hours. The recorded potentials are shown in Figures S9-S11.

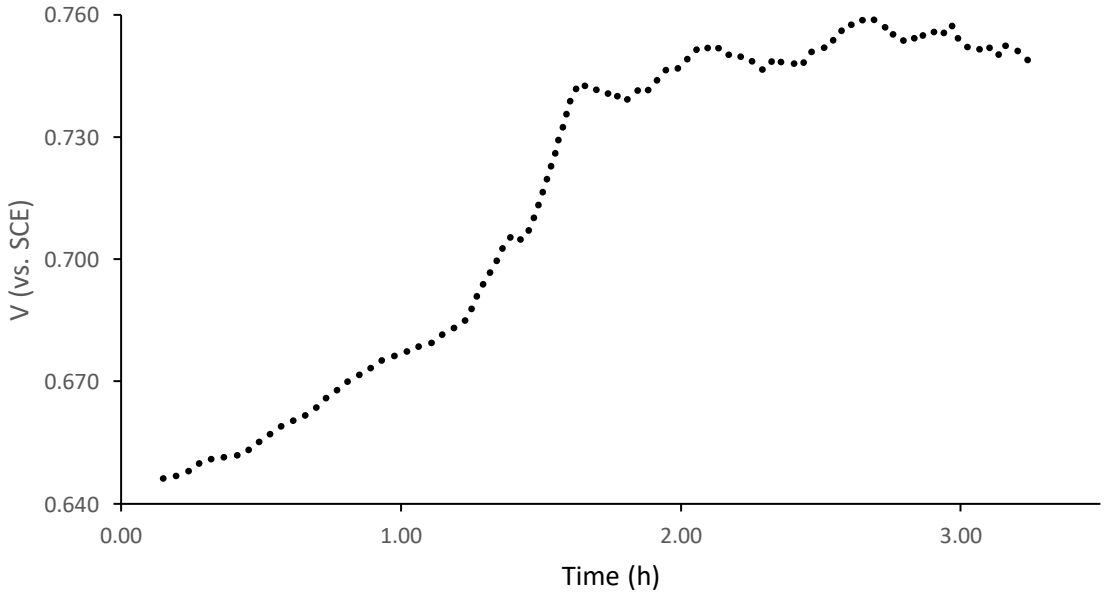


Figure S13. Recorded potential of the carbon felt anode vs. SCE. Moving average (period =10).

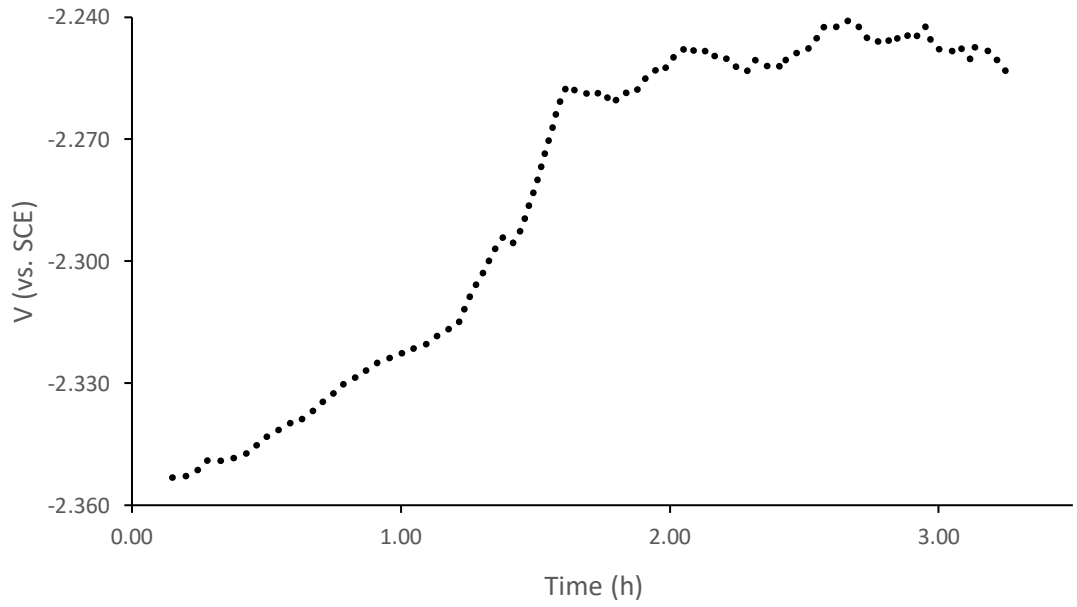


Figure S14. Recorded potential of the stainless-steel cathode vs. SCE. Moving average (period =10).

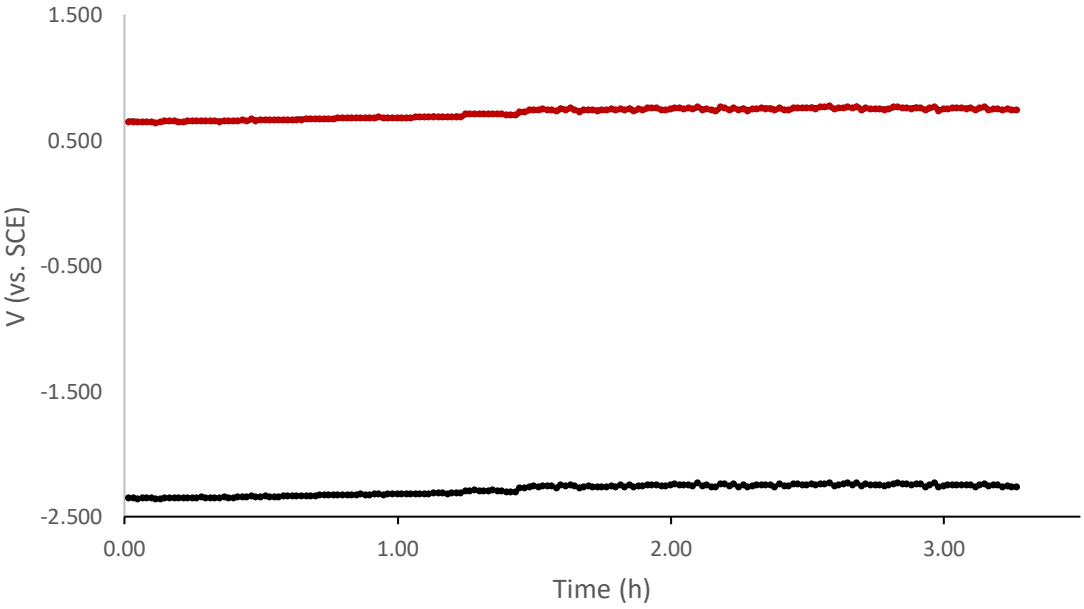


Figure S15. Combined potentials of cathode (black) and anode (red).

VI. Other Mechanistic Studies

Setup for Measurement of Hydrogen Gas Evolution

An electrochemical cell was prepared in the same way as described in Section III, "Electrochemical Setup for Small-Scale Reactions". The reaction mixture was composed of 3-phenylpropionic acid (75 mg, 0.50 mmol, 1 equiv.), tetramethylguanidine (94 μL, 0.50 mmol, 1.5 equiv.), tetraethylammonium toluenesulfonate (301 mg, 0.50 mmol, 2.0 equiv.), pentafluorophenol (460 mg, 2.50 mmol, 5.0 equiv.) and acetonitrile (10 mL, 0.05 M in 3-phenylpropionic acid). The reaction was electrolyzed incompletely (~30 minutes to 1 hr). After electrolysis, a SKY3000 GAS DETECTOR from SAFEGAS equipped with a needle at the end of the propylene tube was used to detect the amount of H_2 gas in the test tube by sticking the needle in the septa, a smaller gauge needle was also added to function as a vent needle to prevent the pump in the detector from malfunctioning. The calculation and analysis can be found below.

Calculations and Analysis of Hydrogen Gas Evolution

We initially determined the total volume of the reaction vessel with the septa on in order to approximate the total headspace available. This was done by completely filling the test tube with water and placing the septa equipped with a needle to allow excess water to exit the vessel. We then accounted for the volume of the stir bar which was done by preparing the 10-mL solution indicated above in a graduated cylinder and placing the stir bar to determine the total volume occupied by the solution. We determined the headspace to be 45 mL.

The output of the detector was reported as the lower explosive limit (LEL) which can be converted to parts per million through a factor specific to the gas.[5] For hydrogen 1% LEL = 4% H_2 or 4000 ppm H_2.

$$[\mathrm{H_2}] = (95\ \mathrm{LEL})\left(\frac{400\ \mathrm{ppm\ H_2}}{1\ \mathrm{LEL}}\right) = 38000\ \mathrm{ppm\ H_2}$$

We then estimated the volume of hydrogen occupying the headspace using the calculated

concentration of H_2.

$$\text{volume } H_2 = \left(\frac{38000}{1000000}\right) 45 \text{ mL} = 1.71 \text{ mL}$$

This value was then converted into mmol by assuming the molar volume of H_2 approximates to the molar volume of an ideal gas at SATP, 24.5 mL/mmol

$$\text{n } H_2 = \left(\frac{1.71 \text{ mL}}{24.5 \text{ mL}}\right) \text{mmol} = 0.070 \text{ mmol}$$

We then determined the yield of the reaction at this point by using ^{19}F NMR, which was 14%.

$$\text{n product} = 0.14(0.5 \text{ mmol}) = 0.070 \text{ mmol}$$

Isolation and Structural Determination of Byproduct 62

An electrochemical cell was prepared in the same way as described in Section III, "Electrochemical Setup for Large-Scale Reactions". The reaction mixture was composed of 3-phenylpropionic acid (300 mg, 2.00 mmol, 1 equiv.), tetramethylguanidine (0.38 mL, 3.00 mmol, 1.5 equiv.), tetraethylammonium toluenesulfonate (1.20 g, 4.00 mmol, 2.0 equiv.), pentafluorophenol (1.84 g, 10.0 mmol, 5.0 equiv.) and acetonitrile (40 mL, 0.05 M in 3-phenylpropionic acid). The reaction was then concentrated, and the byproduct was isolated from a standard reaction mixture using column chromatography with basified silica using triethylamine (TEA) and hexanes/ethyl acetate as the eluent.

Analysis and Structure Determination

We initially noticed the presence of a byproduct that was being formed at a similar amount (roughly a 1:1 ratio) to the product during the optimization. Initial efforts to isolate this byproduct led to the complete loss of the signals in the ^{19}F NMR due to an apparent instability in acidic conditions. We then isolated the byproduct in basic conditions in what we postulated would be in its triethylammonium salt form.

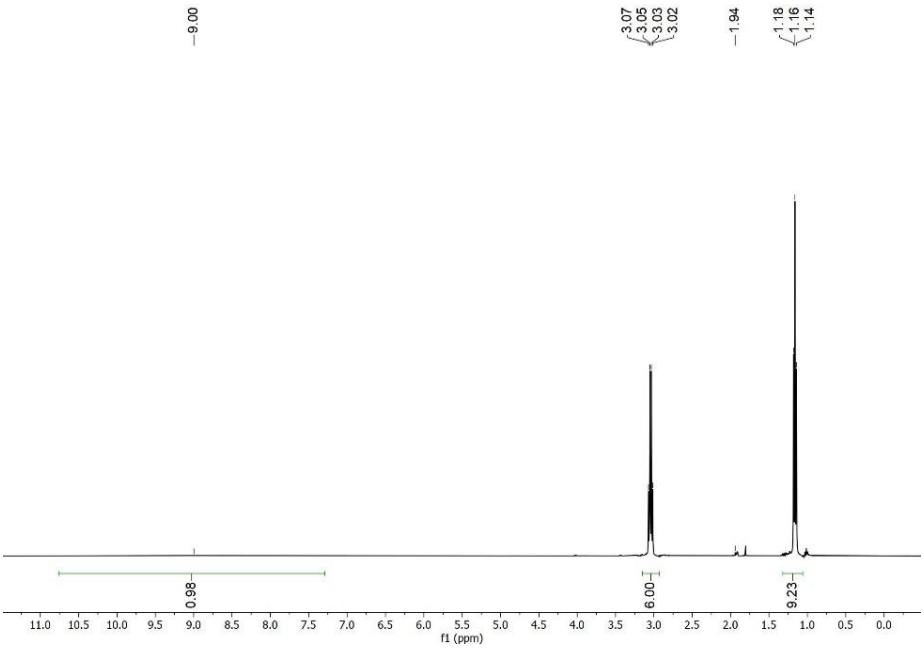


Figure S16. ^{1}H NMR of the isolated by product.

Using negative-mode direct injection HRMS, we were able to confirm that our isolated compound had an anion that had the formula $C_{12}F_9O_3$ by obtaining a m/z of 362.9707 (computed: 362.9709).

The ^{1}H NMR (Figure S12) of the isolated by product did not show any protons corresponding to the structure of anion, the byproduct of interest. Instead, what we saw a spectrum corresponding to triethylammonium, the cation of the isolated salt. This is consistent with chemical formula found in the HRMS analysis, $C_{12}F_9O_3$.

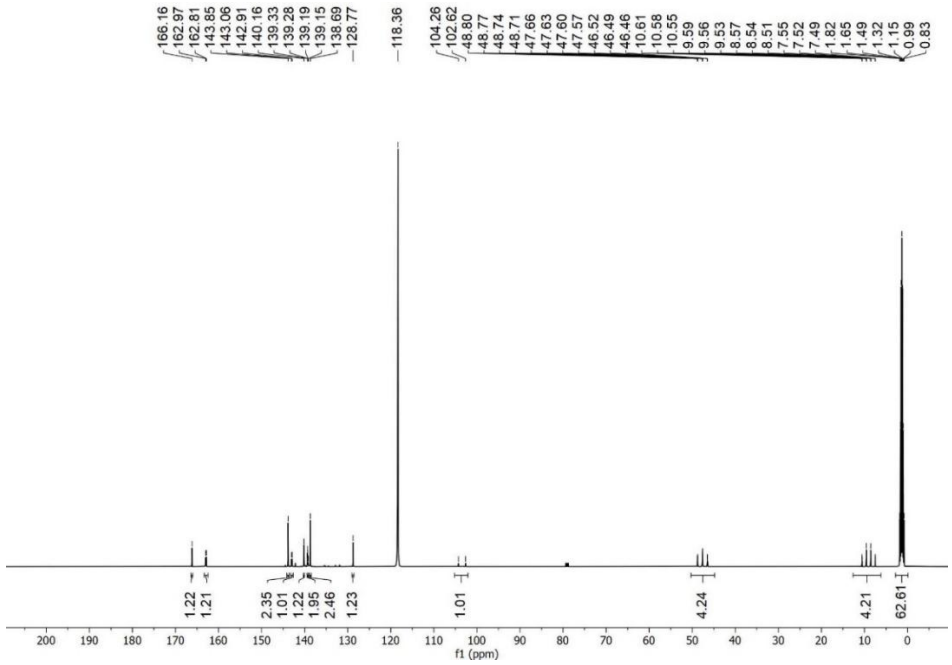


Figure S17. ^{19}F decoupled ^{13}C NMR of the isolated by product.

The ^{13}C NMR (Figure S13) of the isolated by product can be divided into two regions: upfield of the acetonitrile solvent peak (at 118.26 ppm) and downfield of the acetonitrile solvent peak (at 118.26 ppm). In order to avoid high multiplicities, we performed ^{19}F-decoupled ^{13}C NMR. Upfield of the solvent peak, the two peaks corresponding to the cation, triethylammonium can be seen. Downfield of the acetonitrile peak, 12 peaks corresponding to each of the carbons of the anion (Figure S14). ^{1}H-decoupled spectra (not shown) multiplicities were too high for each peak that the spectra was not interpretable.

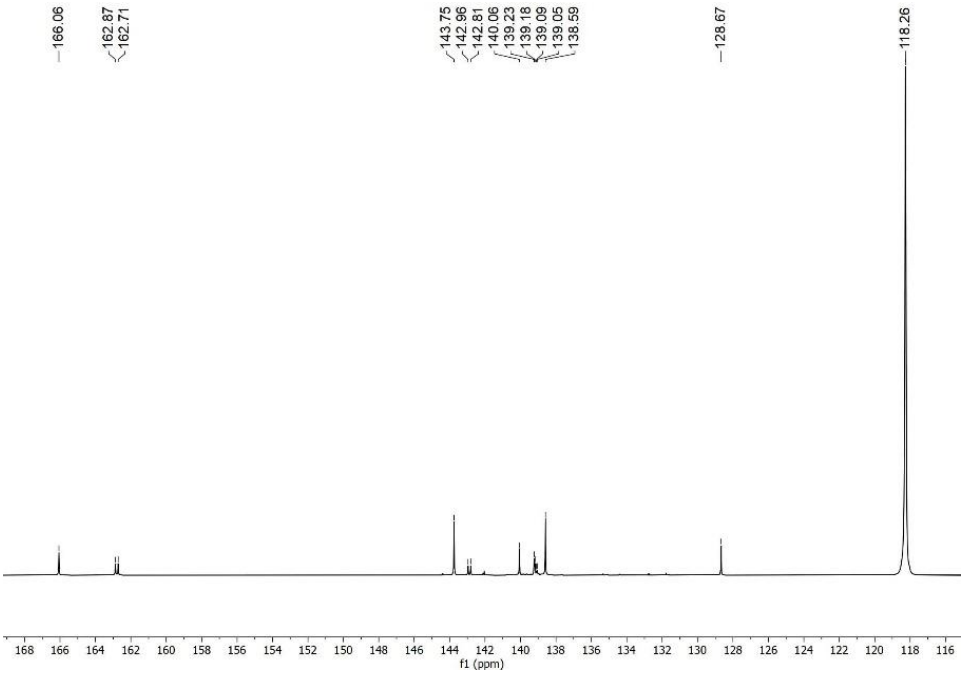


Figure S18. ^{19}F decoupled ^{13}C NMR of the isolated by product (downfield of solvent peak).

^{19}F NMR (Figure S15) and ^{19}F COSY (Figure S16) allowed us to propose a structure for the byproduct. Peak B, E, and F were a familiar pattern to us, as it the common peak pattern for a pentafluorophenyl ring. We hypothesized that the fluorine that corresponds to peak A is most likely attached to the carbon connected to the pentafluorophenol group. Two correlations between A → C, A → D or A → G convinced us that fluorine A was adjacent to two fluorines. A correlation found between C → G and D → G also gave us an indication that fluorine G must be adjacent to one of these fluorine. After building up this rudimentary skeleton, we then completed the structure to fit our chemical formula, due to the lack of hydrogens, we propose quinone-like structures (Figure S17).

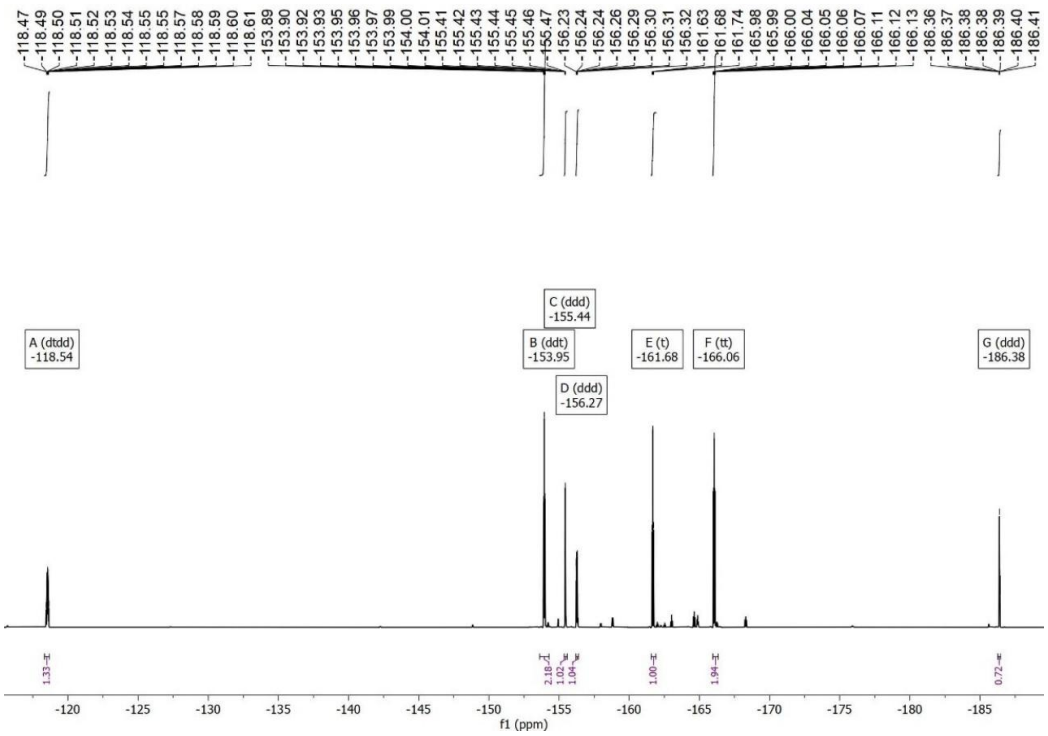


Figure S19. ^{19}F NMR of the isolated product.

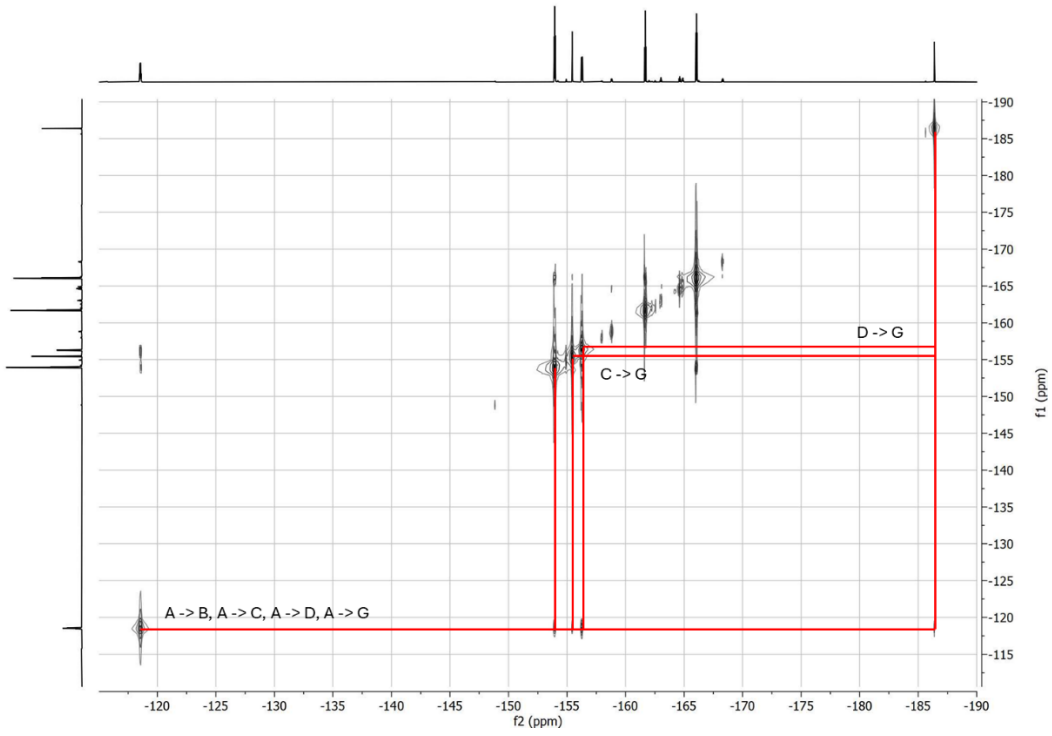
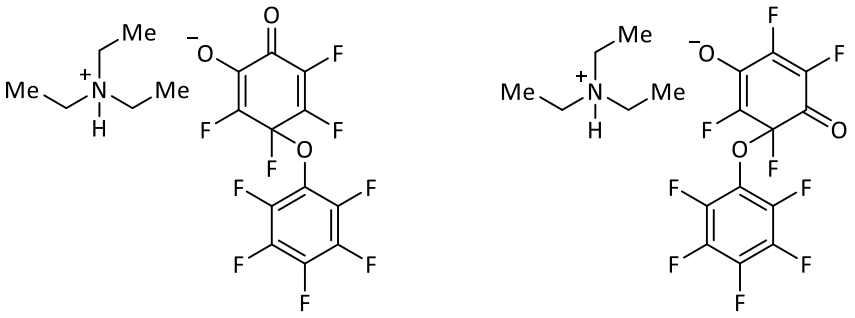


Figure S20. ^{19}F COSY NMR of the isolated product.

Based on the stronger correlation between A → C and A → D (two ^{3}J), we believe that **structure I** is the more likely structure. Structure II should have fluorine A have a strong correlation to one fluorine and two weaker ones (^{4}J and ^{5}J).



I II

Figure S21. Two possible structures of the byproduct. Structure I is favored (see discussion).

Trapping of the Pentafluorophenoxyl Radical.

An electrochemical cell was prepared in the same way as described in Section III, "Electrochemical Setup for Small-Scale Reactions" using an 8-mL vial. The reaction mixture was composed of 3-phenylpropionic acid (38 mg, 0.25 mmol, 1 equiv.), tetramethylguanidine (47 µL, 0.25 mmol, 1.5 equiv.), tetraethylammonium toluenesulfonate (150 mg, 0.38 mmol, 2.0 equiv.), pentafluorophenol (230 mg, 1.25 mmol, 5.0 equiv.) and acetonitrile (10 mL, 0.05 M in 3-phenylpropionic acid). 5-diisopropoxy-phosphoryl-5-methyl-1-pyrroline-N-oxide (66 mg, 0.25 mmol, 1 equiv.) was added to the solution and was electrolyzed for 3 hours at 3.00 V. The crude solution was analyzed via ^{31}P NMR and LC-HRMS.

Analysis

In order to support our hypothesis, we attempted to trap the pentafluorophenyl radical. We chose to use 5-diisopropoxy-phosphoryl-5-methyl-1-pyrroline-N-oxide (DIPPMPO) as the radical trap because of its ability to trap oxygen-centered radicals.[6] The ^{31}P NMR shows a signal at 24.28 ppm which is consistent with DIPPMPO trapping a phenoxy radical. The original DIPPMPO signal (22.2 ppm) is shifted downfield to around 24-25 ppm.[6] In order to confirm, the presence of the correct species, we analyzed the sample using negative-mode HRMS and found the mass 446.1144 m/z ($[M–H]^-$) which is within acceptable error (< 5 ppm, actual error = 1.3 ppm) to the calculated mass of 446.1150 m/z.

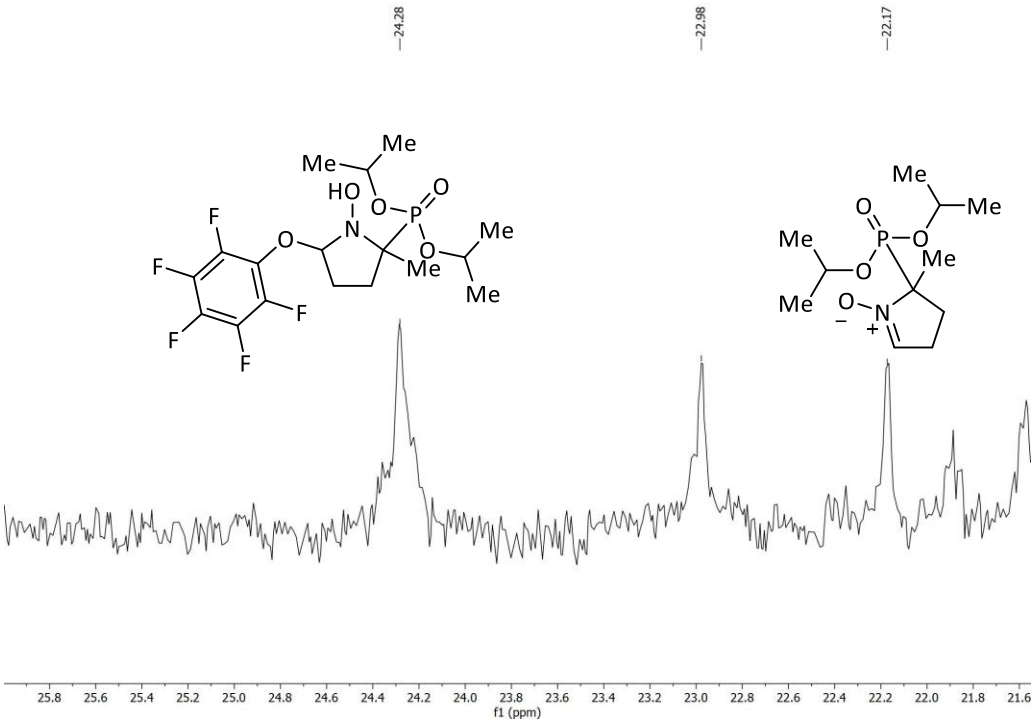
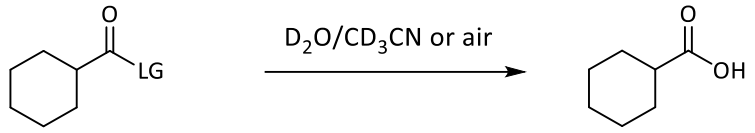


Figure S22. ^{31}P NMR of partially purified sample of model reaction electrolyzed in the presence of the radical trap, DIPPMPO.

VII. Stability Studies



activated acid

Air Stability Determination

A 2-dram vial was charged with an activated form of cyclohexane carboxylic acid (100 mg for solids, 1 mL for liquids). A small aliquot of the substance was taken by dipping the pipette into the sample and passing $CDCl_3$ through the pipette into an NMR tube. The sample was monitored periodically and the ratio of the alpha hydrogen of the activated acid to the alpha hydrogen of cyclohexane carboxylic acid was used to monitor the progress of hydrolysis. The results can be seen in Tables S12-S15.

Water Stability Determination

An activated form of cyclohexane carboxylic acid (0.025 mmol) was dissolved in 0.5 mL of a solution composed of D_2O and acetonitrile (1:4 ratio). The solution was monitored periodically and the ratio of the alpha hydrogen of the activated acid to the alpha hydrogen of cyclohexane carboxylic acid was used to monitor the progress of hydrolysis. The results can be seen in Tables S16-S19.

Table S12. Decomposition of cyclohexanecarbonyl chloride in air.

Time (h)	% remaining
0.00	100.00
1.00	97.00
3.00	84.00
5.00	79.00
22.00	56.00
32.00	30.00
48.00	23.00
60.00	10.00
72.00	0.00

Table S13. Decomposition of cyclohexanecarboxylic anhydride in air.

Time (h)	% remaining
0.00	100.00
48.00	75.00
96.00	59.00
168.00	29.00
240.00	10.00
284.00	0.00

Table S14. Decomposition of pentafluorophenyl cyclohexanecarboxylate in air.

Time (h)	% remaining
0.00	100.00
160.00	100.00
336.00	100.00
504.00	100.00
1008.00	100.00
3600.00	100.00

Table S15. Decomposition of 2,5-dioxopyrrolidin-1-yl cyclohexanecarboxylate (NHS ester) in air.

Time (h)	% remaining
0.00	100.00
72.00	100.00
168.00	100.00

Table S16. Decomposition of cyclohexanecarbonyl chloride in 1:4 D_2O/CD_3CN.

Time (h)	% remaining
0.00	100.00
0.13	2.00
0.27	0.00

Table S17. Decomposition of cyclohexanecarboxylic anhydride in 1:4 D_2O/CD_3CN.

Time (h)	% remaining
0.00	100.00
0.25	70.00
5.00	68.00
24.00	65.00
47.00	61.00
72.00	57.00
142.00	50.00
190.00	46.00
214.00	43.00
310.00	33.00
358.00	27.00
381.00	21.00

Table S18. Decomposition of pentafluorophenyl cyclohexanecarboxylate in 1:4 D_2O/CD_3CN.

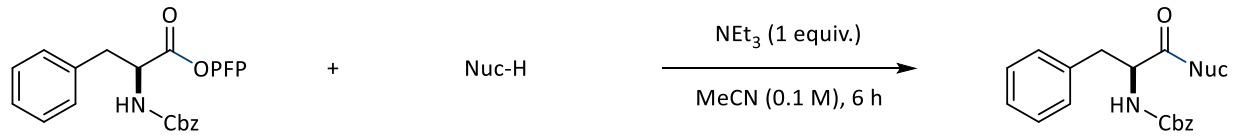
Time (h)	% remaining
0.00	100.00
0.52	100.00
5.00	100.00
24.00	100.00
47.00	100.00
72.00	99.00
142.00	99.00

190.00	99.00
214.00	99.00
310.00	99.00
358.00	98.00
381.00	98.00

Table S19. Decomposition of 2,5-dioxopyrrolidin-1-yl cyclohexanecarboxylate (NHS ester) in 1:4 D_2O/CD_3CN.

Time (h)	% remaining
0.00	100.00
0.38	100.00
5.00	99.00
24.00	99.00
48.00	98.00
72.00	96.00
142.00	94.00
190.00	93.00
214.00	93.00
310.00	91.00
358.00	90.00
381.00	90.00

VIII. Derivatization Procedures



Cbz-Phe-OPFP (0.5 mmol) nucleophile (1.1 equiv.)

General Nucleophilic Substitution Procedure

Cbz-Phe-OPFP (233 mg, 0.50 mmol, 1.0 equiv.) was dissolved in acetonitrile (5 mL). Triethylamine (70 µL, 0.50 mmol, 1.0 equiv.) and the nucleophile (0.55 mol, 1.1 equiv.) was added to the solution and was stirred for 6 hours. The reaction mixture was concentrated and redissolved in ethyl acetate (10 mL). The solution was then washed with 1 M HCl (10 mL), saturated Na_2CO_3 (10 mL) and distilled water (10 mL). The organic layer was then dried and concentrated. A resulting solid residue was recrystallized with hexanes/ethyl acetate while an oil was purified via column chromatography using hexanes/ethyl acetate.

General Peptide Coupling Procedure

Cbz-Phe-OPFP (233 mg, 0.50 mmol, 1.0 equiv.) and the amino acid hydrochloride salt (0.55 mmol, 1.1 equiv.) was suspended in acetonitrile (5 mL). Triethylamine (70 µL, 0.50 mmol, 2.1 equiv.) was added to the solution and was stirred for 6 hours. The reaction mixture was concentrated and redissolved in ethyl acetate (10 mL). The solution was then washed with 1 M HCl (10 mL), saturated Na_2CO_3 (10 mL), and water (10 mL). The organic layer was then dried and concentrated. The resulting solid residue was recrystallized with hexanes/ethyl acetate, more polar dipeptides such as tryptophan containing dipeptides, required the use of isopropyl alcohol/water.

Note: Amino acid-PFP esters that are Fmoc-protected required DMF as a solvent. Acetonitrile did not solubilize the reaction mixture and led to the loss of the Fmoc group and a mixture of products.

Mosher Acid Test (e.e. determination for amides and ester derivatives of Cbz-Phe)

Cbz-Phe-OPFP derivative (0.08 mmol, 1.0 equiv.) and Pd/C (5 mg, 0.05 mmol, 0.6 equiv.) was placed in an evacuated flask equipped with a pierceable septa. The solids were suspended in methanol (2 mL) and a balloon filled with hydrogen gas was used to fill the flask with hydrogen. The solution was stirred for 3 hours. The solution was filtered and concentrated to a yellow oil and was used without further purification.

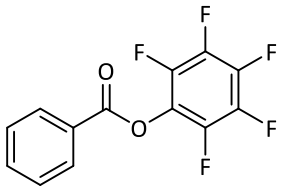
The oil was dissolved in DCM and (*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoyl chloride or (*rac*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl (40 mg, 0.16 mmols, 2 equiv.) prepared using a previously adapted method was added.[7] Triethylamine (~11µL, 0.08 mmol, 1 equiv.) was added to the solution was stirred overnight. The resulting reaction mixture was concentrated and was analyzed using ^{19}F NMR.

Direct amine substitution (e.e. determination for chiral amino acid-derived PFP esters and Thioesters of Cbz-Phe-OPFP)

The amino acid-derived PFP ester (0.08 mmol, 1.0 equiv.), (*R*)-1-phenylethan-1-amine or (*rac*)-1-phenylethan-1-amine (10 mg, 0.08 mmol, 1.0 equiv.) and diisopropylethylamine (10 mg, ~0.08 mmol. 1.0 equiv.) was dissolved in THF (2 mL). The solution was cooled to 0 °C and was stirred overnight. The reaction mixture was then concentrated and redissolved in ethyl acetate (5 mL). The ethyl acetate solution was then washed with 1 M HCl (5 mL), saturated sodium carbonate (5 mL) and water (5 mL) and dried over anhydrous sodium sulfate. The dried organic layer was then concentrated to dryness and was analyzed by ^{1}H NMR.

IX. Characterization Data for Substrate Scope Entries

Pentafluorophenyl benzoate (10a)[8]



Prepared according to "Section II. General Procedure B".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Physical Characteristics: white solid

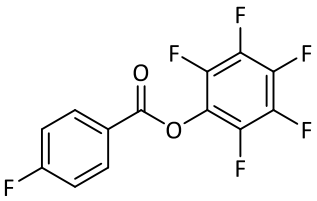
Yield: 118 mg (82% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 7.7 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.75, 141.56 (ddq, *J* = 251.52 Hz, 12.43 Hz, 4.18 Hz), 139.70 (dtt, *J* = 253.11 Hz, 13.53 Hz, 3.88 Hz), 138.12 (dm, *J* = 254.51 Hz) 134.83, 130.14, 129.01, 127.10 (tdt, *J* = 14.62 Hz, 4.87 Hz, 1.99 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -151.86 – -153.35 (m, 2F), -158.20 (t, *J* = 21.5 Hz), -162.09 – -162.94 (m).

Pentafluorophenyl 4-fluorobenzoate (10b)[9]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Physical characteristics: white solid

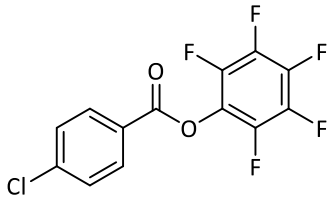
Yield: 108 mg (71% yield))

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 – 8.15 (m, 2H), 7.36 – 7.14 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.25, 165.97 (d, *J* = 257.54 Hz), 161.77, 141.53 (ddq, *J* = 251.57 Hz, 12.68 Hz, 3.81 Hz), 139.77 (dtt, *J* = 253.70 Hz, 13.72 Hz, 4.00 Hz), 138.12 (dm, *J* = 254.58 Hz), 133.65 (d, *J* = 9.77 Hz), 125.59 – 125.20 (m), 123.36 (d, *J* = 2.63 Hz), 116.42 (d, *J* = 22.35 Hz)

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.88 (s, 1F), -152.47 (d, *J* = 17.2 Hz, 2F), -157.68 (t, *J* = 21.6 Hz, 1F), -161.66 – -162.74 (m, 2F).

Pentafluorophenyl 4-chlorobenzoate (10c)[9]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Physical characteristics: white solid

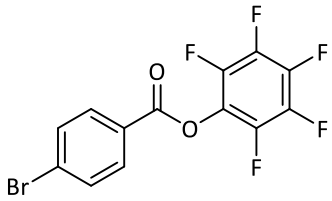
Yield: 119 mg (74% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.95, 141.67, 141.47 (ddq, *J* = 251.55 Hz, 12.55 Hz, 4.41 Hz), 139.80 (dtt, *J* = 254.23 Hz, 13.70 Hz, 4.21 Hz), 138.12 (dm, *J* = 255.00 Hz), 132.20, 129.50, 129.51, 125.50-129.12 (m).

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.28 – -152.64 (m), -157.57 (t, *J* = 21.6 Hz), -162.10 (dd, *J* = 21.7, 17.1 Hz).

Pentafluorophenyl 4-bromobenzoate (10d)[10]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Physical characteristics: white solid

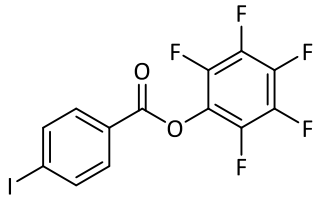
Yield: 153 mg (83% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 8.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.12, 141.45 (ddq, *J* = 251.41 Hz, 12.47 Hz, 4.16 Hz), 139.80 (dtt, *J* = 253.93 Hz, 13.63 Hz, 3.96 Hz), 138.10 (dm, *J* = 152.28), 132.50, 132.24, 130.43, 125.96, 125.26 (tdt, *J* = 14.43 Hz, 4.81 Hz, 2.36 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.23 – -152.61 (m), -157.53 (t, *J* = 21.7 Hz), -161.81 – -162.24 (m).

Pentafluorophenyl 4-iodobenzoate (10e)[11]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Physical characteristics: white solid

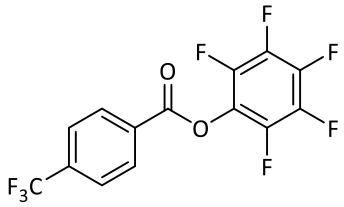
Yield: 145 mg (70% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.6 Hz, 2H), 7.89 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.40, 141.44 (ddq, *J* = 251.73 Hz, 12.52 Hz, 4.14 Hz), 141.23 – 138.40 (m), 138.51, 138.10 (dm, *J* = 252.29), 132.02, 126.51, 125.45 – 125.11 (m), 103.30.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.14 – -152.65 (m), -157.51 (t, *J* = 21.8 Hz), -161.71 – -162.44 (m).

Pentafluorophenyl 4-(trifluoromethyl)benzoate (10f)[11]



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 0-3% ethyl acetate/hexanes

Physical characteristics: white solid

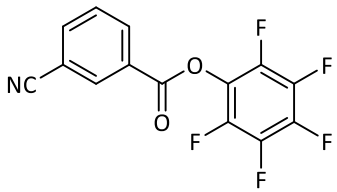
Yield: 141 mg (72% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.70, 141.52 (ddq, *J* = 251.93 Hz, 12.56 Hz, 4.09 Hz), 140.02 (dtt, *J* = 254.02 Hz, 13.56 Hz, 3.99 Hz), 138.24 (dtdd, *J* = 252.93 Hz, 13.79 Hz, 6.00 Hz, 3.00 Hz), 136.32 (q, *J* = 32.90 Hz), 131.27, 130.45, 126.10 (q, *J* = 3.71 Hz), 125.26 (tdt, *J* = 14.48 Hz, 4.92 Hz, 1.88 Hz), 123.56 (q, *J* = 272.33 Hz)

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.76, -152.71 – -153.01 (m), -157.70 (t, *J* = 21.5 Hz), -162.39 (td, *J* = 22.0, 5.0 Hz).

Pentafluorophenyl 3-cyanobenzoate (10g)



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 5-10% ethyl acetate/hexanes

Physical characteristics: white solid

Yield: 105 mg (67% yield)

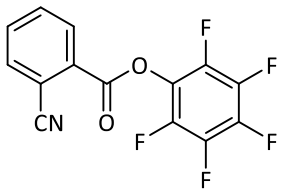
HRMS: m/z calculated for $C_{14}H_4F_5NO_5$ $[M+H]^+$ 336.0054, found 336.0054

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.46 – 8.35 (m, 1H), 7.99 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 160.95, 140.98 (ddq, *J* = 252.36 Hz, 12.68 Hz, 3.99 Hz), 140.01 (dtt, *J* = 254.20 Hz, 13.74 Hz, 3.79 Hz), 138.13 (dm, *J* = 253.06 Hz), 137.73, 136.73, 134.69, 134.32, 130.20, 128.50, 125.12-124.76 (m), 117.42, 113.89.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.15 – -152.36 (m, 2F), -156.75 (t, *J* = 21.6 Hz, 1F), -161.45 – -161.72 (m, 2F).

Pentafluorophenyl 2-cyanobenzoate (10h)



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 5-10% ethyl acetate/hexanes

Physical characteristics: white solid

Yield: 78 mg (50% yield)

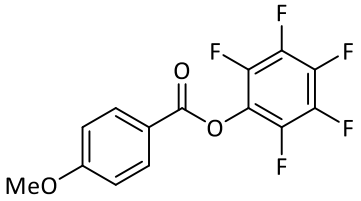
HRMS: m/z calculated for $C_{14}H_4F_5NO_5$ $[M+H]^+$ 336.0054, found 336.0052

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 – 8.29 (m, 1H), 8.01 – 7.89 (m, 1H), 7.89 – 7.75 (m, 2H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 160.23, 141.33 (ddq, *J* = 252.34 Hz, 12.46 Hz, 4.08 Hz), 1, 140.03 (dtt, *J* = 252.51 Hz, 13.67 Hz, 4.13 Hz), 138.09 (dm, *J* = 252.64 Hz), 135.54, 134.62, 133.05, 132.35, 128.99, 124.95 - 124.60 (m), 116.67, 114.11.

^{19}F NMR (376 MHz, $CDCl_3$) δ -151.79 – -152.03 (m, 2F), -156.69 (t, *J* = 21.7 Hz, 1F), -161.51 – -161.81 (m, 2F).

Pentafluorophenyl 4-methoxybenzoate (10i)[12]



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 0-2% ethyl acetate/hexanes

Physical characteristics: white solid

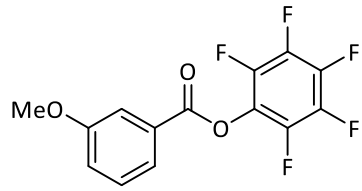
Yield: 108 mg (61% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.9 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.95, 162.40, 141.61 (ddq, *J* = 251.30 Hz, 12.34 Hz, 4.18 Hz), 139.56 (dtt, *J* = 252.77 Hz, 13.80 Hz, 3.97 Hz), 138.07 (dm, *J* = 251.93 Hz), 133.14, 125.85-125.47 (m), 119.20, 114.35, 55.77.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.53 – -152.75 (m), -158.45 (t, *J* = 21.6 Hz), -162.64 (td, *J* = 22.1, 5.2 Hz).

Pentafluorophenyl 3-methoxybenzoate (10j)[12]



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 0-3% ethyl acetate/hexanes

Physical characteristics: white solid

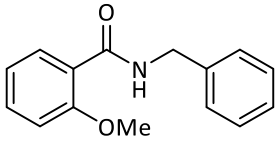
Yield: 115 mg (72% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.70 – 7.56 (m, 1H), 7.09 – 7.05 (m, 2H), 3.96 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.21, 160.84, 141.78 (ddq, *J* = 251.43 Hz, 12.39 Hz, 4.30 Hz), 139.48 (dtt, *J* = 252.77 Hz, 13.62 Hz, 4.10 Hz), 138.03 (dm, *J* = 251.74 Hz), 125.57 (tdt, *J* = 14.42 Hz, 4.77 Hz, 1.97 Hz), 135.88, 132.96, 120.42, 116.06, 112.42, 56.14.

^{19}F NMR (376 MHz, $CDCl_3$) δ -149.31 – -154.42 (m), -158.45 (t, *J* = 21.7 Hz), -160.31 – -164.85 (m).

N-benzyl-2-methoxybenzamide (10k – amide)[13]



Prepared according to "Section II. General Procedure B - Amidation".

Chromatography solvent 1: 0-3% ethyl acetate/hexanes

Chromatography solvent 2: 15-30% ethyl acetate/hexanes

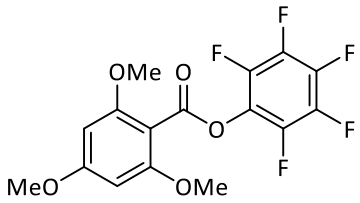
Physical characteristics: white solid

Yield: 72 mg (60% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 7.8, 1.9 Hz, 1H), 8.18 (s, 1H), 7.44 (ddd, *J* = 8.5, 7.3, 1.9 Hz, 1H), 7.40 – 7.25 (m, 5H), 7.13 – 7.04 (m, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 4.68 (d, *J* = 5.6 Hz, 2H), 3.91 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.32, 157.50, 138.80, 132.82, 132.32, 128.61, 127.47, 127.20, 121.38, 121.26, 111.34, 55.90, 43.70.

Pentafluorophenyl 2,4,6-trimethoxybenzoate (10l)



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 0-10% ethyl acetate/hexanes

Physical characteristics:

Yield: 97 mg (51% yield)

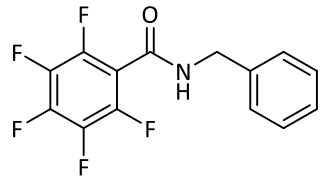
HRMS: m/z calculated for $C_{16}H_{11}F_5O_5$ $[M+H]^+$ 379.0599, found 379.0599.

^{1}H NMR (400 MHz, CD_3CN): δ 6.25 (s, 2H), 3.85-3.84 (m, 9H)

^{13}C NMR (100 MHz, CD_3CN): δ 165.42, 162.87, 160.73, 142.41 (ddq, *J* = 249.51 Hz, 12.17 Hz, 4.33 Hz), 140.50 (dtt, *J* = 250.02 Hz, 13.62 Hz, 4.13 Hz), 139.12 (dm, *J* = 249.72 Hz), 126.29 (tdt, *J* = 1.84 Hz, 4.73 Hz, 14.92 Hz) 102.66, 91.92, 56.98, 56.49.

^{19}F NMR (376 MHz, CD_3CN): δ -151.42 – -151.82 (m, 2F), -158.90 (t, *J* = 21.6 Hz, F), -162.67 – -163.28 (m, 2F).

N-benzylpentafluorobenzamide (10m – amide)[14]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Chromatography solvent 2: 10 - 25% ethyl acetate/hexanes

Physical characteristics: white solid

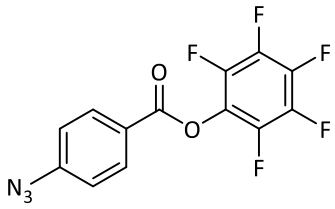
Yield: 69 mg (46 yield%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.30 (m, 5H), 6.22 (s, 1H), 4.65 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.46, 144.31 (dm, *J* = 256.95 Hz), 142.47 (dm, *J* = 258.38 Hz), 137.75 (dm, *J* = 251.57 Hz), 136.84, 129.06, 128.13, 127.87, 111.74 – 111.28 (m), 44.50.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.15 – -152.36 (m, 2F), -156.75 (t, *J* = 21.6 Hz, 1F), -161.45 – -161.72 (m, 2F).

Pentafluorophenyl 4-azidobenzoate (10n)[15]



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 0-3% ethyl acetate/hexanes

Physical characteristics: white solid

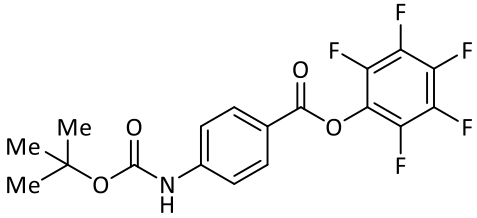
Yield: 100 mg (61 yield%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.87, 146.78, 141.51 (ddq, *J* = 251.42 Hz, 12.54 Hz, 4.27 Hz), 139.69 (dtt, *J* = 253.47 Hz, 13.65 Hz, 4.09 Hz), 138.08 (dm, *J* = 251.98 Hz) 132.69, 125.41 (tdt, *J* = 14.40 Hz, 4.64 Hz, 2.04 Hz), 123.30, 119.38.

^{19}F NMR (376 MHz, $CDCl_3$) δ -151.44 – -153.21 (m), -157.78 (t, *J* = 21.7 Hz), -161.23 – -163.65 (m).

Pentafluorophenyl 4-((tert-butoxycarbonyl)amino)benzoate (10o)[16]



Prepared according to "Section II. General Procedure A".

Chromatography solvent: 2-7% ethyl acetate/hexanes

Physical characteristics: white solid

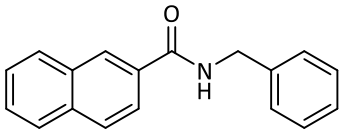
Yield: 181 mg (90% yield); 0.645 g (80% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 6.77 (s, 1H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.37, 152.26, 144.73, 141.54 (ddq, *J* = 251.44 Hz, 12.49 Hz, 4.08 Hz), 139.53 (dtt, *J* = 253.14 Hz, 13.51 Hz, 3.82 Hz), 138.02 (dm, *J* = 252.38 Hz), 132.29, 125.76 – 125.39 (m), 120.67, 117.70, 81.72, 28.26.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.37 – -152.72 (m, 2F), -158.29 (t, *J* = 21.7 Hz, 1F), -162.37 – -162.74 (m, 2F).

N-benzyl-2-naphthamide (10p – amide)[12]



Prepared according to "Section II. General Procedure B".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Chromatography solvent 1: 5-20% ethyl acetate/hexanes

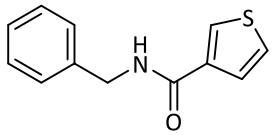
Physical characteristics: white solid

Yield: 106 mg (81% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, *J* = 1.6 Hz, 1H), 7.84 (dq, *J* = 6.9, 2.7 Hz, 4H), 7.52 (dddd, *J* = 19.5, 8.2, 6.8, 1.3 Hz, 2H), 7.42 – 7.25 (m, 5H), 6.91 (t, *J* = 5.7 Hz, 1H), 4.67 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.62, 138.37, 134.81, 132.67, 131.65, 129.00, 128.84, 128.51, 128.00, 127.80, 127.72, 127.64, 127.60, 126.79, 123.74, 77.16, 44.27.

N-benzylthiophene-3-carboxamide (11)[17]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-1% ethyl acetate/hexanes

Chromatography solvent 2: 10 - 25% ethyl acetate/hexanes

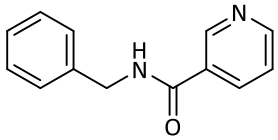
Physical characteristics: white solid

Yield: 85 mg (78% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.39 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.33 – 7.18 (m, 6H), 7.01 (d, *J* = 6.0 Hz, 1H), 4.50 (d, *J* = 5.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.17, 138.31, 137.36, 128.82, 128.53, 127.95, 127.65, 126.57, 126.21, 77.16, 43.88.

N-benzylnicotinamide (12 – amide)[18]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 5-15% ethyl acetate/hexanes

Chromatography solvent 1: 25-50% ethyl acetate/hexanes

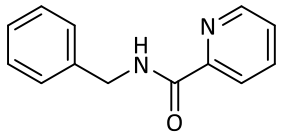
Physical characteristics: white solid

Yield: 76 mg (72% yield)

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.47 (t, *J* = 6.0 Hz, 1H), 9.08 (d, *J* = 2.3 Hz, 1H), 8.70 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.27 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.50 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.39 – 7.11 (m, 5H), 4.50 (d, *J* = 5.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.85, 151.90, 148.57, 139.40, 135.06, 128.32, 127.31, 126.83, 123.46, 42.69, 39.53.

N-benzylpicolinamide (13 – amide)[19]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 5-20% ethyl acetate/hexanes

Chromatography solvent 1: 25-50% ethyl acetate/hexanes

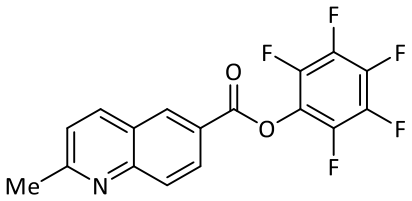
Physical characteristics: white solid

Yield: 77 mg (73% yield)

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.35 (t, *J* = 6.5 Hz, 1H), 8.64 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.06 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.99 (td, *J* = 7.7, 1.7 Hz, 1H), 7.59 (ddd, *J* = 7.5, 4.8, 1.3 Hz, 1H), 7.39 – 7.16 (m, 5H), 4.51 (d, *J* = 6.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.05, 150.07, 148.51, 139.63, 137.84, 128.31, 127.43, 126.81, 126.59, 122.06, 42.47.

Pentafluorophenyl 2-methylquinoline-6-carboxylate (14)



Prepared according to "Section II. General Procedure A".

Chromatography solvent: 5-20% ethyl acetate/hexanes

Physical characteristics: yellowish brown solid

Yield: 140 mg (79% yield)

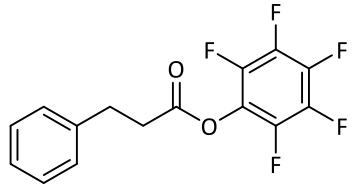
HRMS: m/z calculated for $C_{17}H_8F_5NO_2$ $[M+H]^+$ 354.0548, found 354.0546.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 1.9 Hz, 1H), 8.36 (dd, *J* = 8.8, 2.0 Hz, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.9 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 2.80 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.05, 162.50, 150.63, 141.58 (ddq, *J* = 251.36 Hz, 12.03 Hz, 4.16 Hz), 139.81 (dtt, *J* = 253.63 Hz, 13.43 Hz, 3.68 Hz), 138.17 (dm, *J* = 252.66 Hz), 137.61, 132.80, 129.88, 129.39, 125.86, 125.72 – 125.34 (m), 124.11, 123.55, 25.92.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.04 – -152.77 (m, 2F), -157.73 (t, *J* = 21.6 Hz, 1F), -161.90 – -162.64 (m, 2F).

Pentafluorophenyl 3-phenylpropanoate (15a)[20]



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 0%-5% ethyl acetate/hexanes

Physical Characteristics: White solid, low melting.

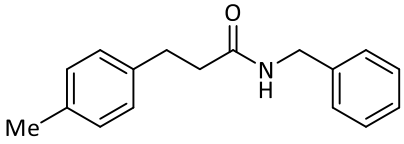
Yield: 136 mg (82% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.29 (m, 2H), 7.28 – 7.22 (m, 4H), 3.14 – 3.06 (m, 2H), 2.99 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3) δ 168.89, 141.26 (ddq, *J* = 251.50 Hz, 12.77 Hz, 3.78 Hz), 139.60 (dtt, *J* = 253.30, 13.53, 3.97), 139.43, 139.38 – 136.65 (dm, *J* = 254.81), 128.83, 128.37, 126.83, 125.17 (m), 35.06, 30.79

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.46 – -152.63 (m, 2F), -157.99 (t, *J* = 21.7 Hz, 1F), -162.31 (dt, *J* = 21.7, 4.8 Hz, 2F).

N-benzyl-3-(p-tolyl)propanamide (15b – amide)[21]



Prepared according to "Section II. General Procedure C - Amidation".

Chromatography solvent 1: 0%-5% ethyl acetate/hexanes

Chromatography solvent 2: 15%-35% ethyl acetate/hexanes

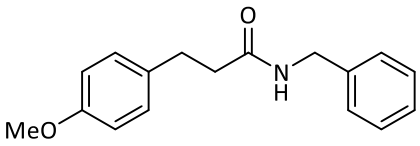
Physical Characteristics: White solid

Yield: 105 mg (83% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.23 (m, 3H), 7.18 – 7.11 (m, 2H), 7.09 (s, 4H), 5.62 (s, 1H), 4.40 (d, *J* = 5.6 Hz, 2H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.50 (t, *J* = 7.6 Hz, 2H), 2.32 (s, 3H).

^{13}C NMR (100 MHz, CDCl3): δ 172.10, 138.29, 137.78, 135.89, 129.37, 128.76, 128.41, 127.90, 127.58, 43.71, 38.81, 31.45, 21.16.

N-benzyl-3-(4-methoxyphenyl)propanamide (15c – amide)[22]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 5%-10% ethyl acetate/hexanes

Chromatography solvent 2: 25-40% ethyl acetate/hexanes

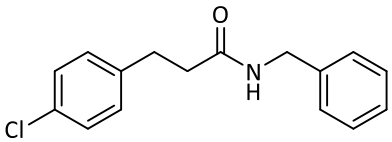
Physical Characteristics: White solid

Yield: 104 mg (78% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.20 (m, 3H), 7.19 – 7.04 (m, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 5.75 (s, 1H), 4.37 (d, *J* = 5.7 Hz, 2H), 2.92 (t, *J* = 7.5 Hz, 2H), 2.46 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 171.55, 140.52, 138.14, 137.67, 130.66, 128.81, 127.81, 127.63, 91.51, 43.67, 38.26, 31.24.

N-benzyl-3-(4-chlorophenyl)propanamide (15d – amide)[23]



Prepared according to "Section II. General Procedure C - Amidation".

Chromatography solvent: 2%-5% ethyl acetate/hexanes

Recrystallization solvent: Isopropyl alcohol/water

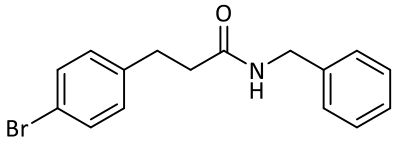
Physical Characteristics: White solid

Yield: 116 mg (85% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.25 (m, 3H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.18 – 6.97 (m, 4H), 6.11 (t, *J* = 5.8 Hz, 1H), 4.35 (d, *J* = 5.8 Hz, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.47 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ δ 171.59, 139.34, 138.15, 132.16, 129.95, 128.82, 128.76, 127.84, 127.67, 43.71, 38.43, 31.10.

N-benzyl-3-(4-bromophenyl)propanamide (15e – amide)[24]



Prepared according to "Section II. General Procedure C - Amidation".

Chromatography solvent 1: 2%-5% ethyl acetate/hexanes

Chromatography solvent 2: 20%-35% ethyl acetate/hexanes

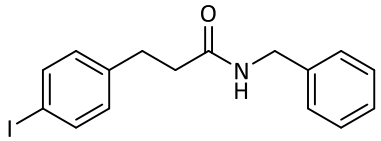
Physical Characteristics: White solid

Yield: 146 mg (92% yield)

^{1}H NMR (400 MHz, $CDCl_3$): 7.43 – 7.35 (m, 2H), 7.35 – 7.24 (m, 3H), 7.17 – 7.09 (m, 2H), 7.09 – 6.99 (m, 2H), 6.01 (s, 1H), 4.37 (d, *J* = 5.8 Hz, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.48 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 171.52, 139.87, 138.15, 131.75, 130.38, 128.86, 127.88, 127.71, 120.23, 43.76, 38.42, 31.18.

N-benzyl-3-(4-iodophenyl)propanamide (15f – amide)



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 2%-5% ethyl acetate/hexanes

Chromatography solvent 2: 20%-35% ethyl acetate/hexanes

Physical Characteristics: White solid

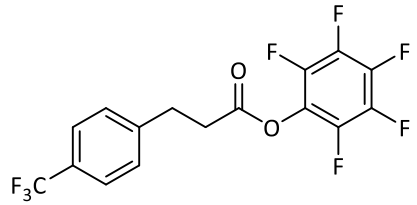
Yield: 100 mg (55% yield)

ESI-HRMS: m/z calculated for $C_{16}H_{16}INO$ $[M+H]^+$ 366.0349, found 366.0348

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.20 (m, 3H), 7.16 – 7.04 (m, 2H), 6.92 (d, *J* = 8.3 Hz, 2H), 5.74 (s, 1H), 4.35 (d, *J* = 5.7 Hz, 2H), 2.90 (t, *J* = 7.5 Hz, 2H), 2.45 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 171.55, 140.53, 138.15, 137.67, 130.67, 128.82, 127.81, 127.63, 91.51, 43.67, 38.26, 31.24.

Pentafluorophenyl 3-(4-(trifluoromethyl)phenyl)propanoate (15g)[25]



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 0%-5% ethyl acetate/hexanes

Physical Characteristics: White solid

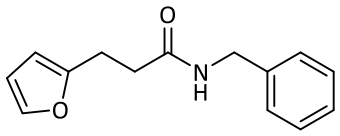
Yield: 150 mg (78% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 3.15 (t, *J* = 7.5 Hz, 2H), 3.02 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3) : δ 168.56, 143.49, 141.23 (ddq, *J* = 251.15 Hz, 12.65 Hz, 4.25 Hz), 139.71 (dtt, *J* = 253.49 Hz, 13.50 Hz, 4.04 Hz), 138.04 (dm, *J* = 252.60 Hz), 129.31 (q, *J* = 32.47 Hz), 125.80 (q, *J* = 3.77 Hz), 125.27 - 124.88 (m), 124.36 (q, *J* = 272.07 Hz), 34.58, 30.51.

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.52 (m, 3F), -152.00 – -153.42 (m, 2F), -157.72 (t, *J* = 21.7 Hz, 1F), -161.59 – -162.72 (m, 2F).

N-benzyl-3-(furan-2-yl)propanamide (16 – amide)[26]



Prepared according to "Section II. General Procedure C - Amidation".

Chromatography solvent 1: 2.5-7.5% ethyl acetate/hexanes

Chromatography solvent 2: 25-40% ethyl acetate/hexanes

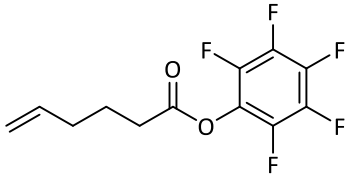
Physical Characteristics: White solid

Yield: 91 mg (79% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.20 (m, 6H), 6.29 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.05 (dd, *J* = 3.2, 1.0 Hz, 1H), 5.78 (s, 1H), 4.44 (d, *J* = 5.8 Hz, 2H), 3.09 – 2.99 (m, 2H), 2.57 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 171.64, 154.39, 141.34, 138.25, 128.81, 127.90, 127.64, 110.39, 105.77, 43.76, 35.19, 24.22.

Pentafluorophenyl hex-5-enoate (17)[27]



Prepared according to "Section II. General Procedure B".

Chromatography solvent: 0-0.4% ethyl acetate/hexanes

Physical Characteristics: colorless oil, slight foul odor

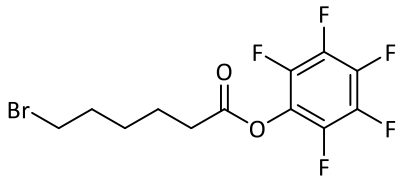
Yield: 82 mg (58% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.14 – 5.00 (m, 2H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.32 – 2.15 (m, 2H), 1.88 (p, *J* = 7.4 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 169.55, 141.31 (ddq, *J* = 250.98 Hz, 12.32 Hz, 4.32 Hz), 138.08 (dtt, *J* = 253.09 Hz, 13.39 Hz, 3.93 Hz), 138.03 (dtdd, *J* = 252.91 Hz, 13.76 Hz, 5.02 Hz, 2.24 Hz), 137.10, 125.46 – 125.09 (m), 116.19, 32.85, 32.59, 23.92.

^{19}F NMR (376 MHz, $CDCl_3$): δ -149.87 – -155.77 (m, 2F), -158.15 (t, *J* = 21.6 Hz, 1F), -161.35 – -164.92 (m, 2F).

Pentafluorophenyl 6-bromohexanoate (18)[28]



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 0-3% ethyl acetate/hexanes

Physical Characteristics: clear oil

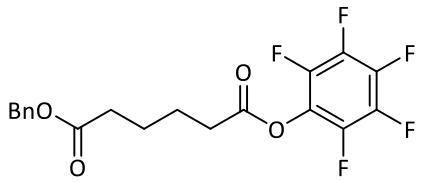
Yield: 134 mg (74% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 (t, *J* = 6.7 Hz, 2H), 2.69 (t, *J* = 7.4 Hz, 2H), 1.98 – 1.87 (m, 2H), 1.81 (dt, *J* = 15.2, 7.4 Hz, 2H), 1.63 – 1.53 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.36, 141.26 (ddq, *J* = 251.19 Hz, 12.46 Hz, 4.43 Hz), 139.58 (dtt, *J* = 253.25 Hz, 13.70 Hz, 4.02 Hz), 138.00 (dm, *J* = 254.79 Hz), 125.37 – 125.00 (m), 33.30, 33.22, 32.36, 27.50, 24.03z.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.60 – -152.76 (m, 2F), -157.59 (t, *J* = 21.8 Hz, 1F), -162.13 – -162.36 (m, 2F).

Benzyl pentafluorphenyl hexanedioate (19)[29]



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 2-10% ethyl acetate/hexanes

Physical Characteristics: clear oil

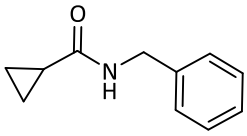
Yield: 131 mg (65% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.28 (m, 5H), 5.15 (s, 2H), 2.76 – 2.63 (m, 2H), 2.45 (t, *J* = 6.8 Hz, 2H), 1.81 (dtq, *J* = 6.9, 4.9, 2.3 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.91, 169.16, 141.21 (ddq, *J* = 251.19 Hz, 12.04 Hz, 4.20 Hz), 139.51 (dtt, *J* = 253.06 Hz, 13.54 Hz, 4.11 Hz), 137.95 (dm, *J* = 254.37 Hz), 136.04, 128.60, 128.28, 128.26, 125.22 – 124.85 (m), 66.34, 33.74, 32.97, 24.18, 24.14.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.72 – -153.17 (m, 2F), -158.18 (t, *J* = 21.6 Hz, 1F), -162.33 – -162.63 (m, 2F).

N-benzylcyclopropanecarboxamide (20 – amide)[30]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-2.5% ethyl acetate/hexanes

Chromatography solvent 2: 15-30% ethyl acetate/hexanes

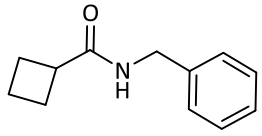
Physical Characteristics: White solid

Yield: 58 mg (64% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.30 (m, 2H), 7.30 – 7.21 (m, 3H), 6.25 (s, 1H), 4.42 (d, *J* = 5.8 Hz, 2H), 1.38 (ddd, *J* = 7.9, 4.5, 3.3 Hz, 1H), 1.03 – 0.90 (m, 2H), 0.73 (dt, *J* = 8.0, 3.4 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 173.65, 138.62, 128.72, 127.86, 127.47, 43.83, 14.75, 7.26.

N-benzylcyclobutanecarboxamide (21 – amide)[30]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-2.5% ethyl acetate/hexanes

Chromatography solvent 2: 15-30% ethyl acetate/hexanes

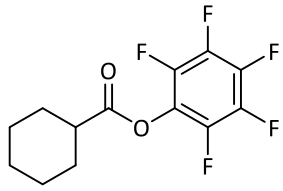
Physical Characteristics: White solid

Yield: 63 mg (64% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 7.0 Hz, 2H), 7.29 – 7.21 (m, 3H), 5.89 (s, 1H), 4.41 (d, *J* = 5.7 Hz, 2H), 3.03 (p, *J* = 8.5 Hz, 1H), 2.30 (pd, *J* = 9.1, 2.3 Hz, 2H), 2.20 – 2.08 (m, 2H), 2.02 – 1.80 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.93, 138.61, 128.73, 127.82, 127.48, 43.50, 39.95, 25.44, 18.25.

Pentafluorophenyl cyclohexanecarboxylate (22)[31]



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 0-2.5% ethyl acetate/hexanes

Physical Characteristics: Transparent oily solid, low melting

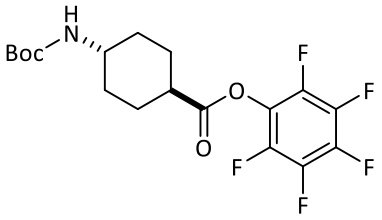
Yield: 109 mg (64% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (tt, *J* = 11.0, 3.8 Hz, 1H), 2.07 (dt, *J* = 13.2, 4.1 Hz, 2H), 1.83 (dt, *J* = 12.8, 3.8 Hz, 2H), 1.64 (tp, *J* = 16.2, 4.8 Hz, 3H), 1.47 – 1.23 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.01, 141.36 (ddq, *J* = 251.32 Hz, 12.52 Hz, 4.17 Hz), 139.49 (dtt, *J* = 252.88 Hz, 13.67 Hz, 3.90 Hz), 138.04 (dm, *J* = 254.26 Hz), 125.36 42.51, 28.97, 25.69, 25.26.

^{19}F NMR (376 MHz, $CDCl_3$) δ -155.07 – -155.81 (m, 2F), -160.76 (t, *J* = 20.9 Hz, 1F), -164.49 – -165.07 (m, 2F).

Pentafluorophenyl trans-4-((tert-butoxycarbonyl)amino)cyclohexane-1-carboxylate (23)



Prepared according to "Section II. General Procedure A".

Chromatography solvent: 0%-12% ethyl acetate/hexanes

Physical Characteristics: White solid,

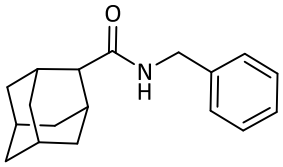
Yield: 170 mg (83% yield)

ESI-HRMS: m/z calculated for $C_{18}H_{20}F_5NO_4$ $[M+Na]^+$ 432.1205, found 432.1202

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.42 (d, *J* = 8.1 Hz, 1H), 3.48 (s, 1H), 2.61 (tt, *J* = 12.2, 3.5 Hz, 1H), 2.25 – 2.11 (m, 4H), 1.69 (qd, *J* = 13.9, 3.8 Hz, 2H), 1.45 (s, 9H), 1.21 (qd, *J* = 13.5, 3.8 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3) δ δ 171.38, 141.21 (ddq, *J* = 251.35 Hz, 12.54 Hz, 4.34 Hz), 139.51 (dtt, *J* = 252.97, 13.62, 3.92), 137.96 (dm, *J* = 253.95), 155.26, 125.27, 79.47, 48.85, 41.98, 32.29, 28.48, 27.77.

N-benzyladamantane-2-carboxamide (24 – amide)



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-3% ethyl acetate/hexanes

Chromatography solvent 2: 15-30% ethyl acetate/hexanes

Physical Characteristics: White solid

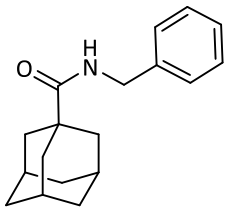
Yield: 104 mg (77% yield)

ESI-HRMS: m/z calculated for $C_{18}H_{23}NO$ $[M+H]^+$ 270.1852, found 270.1853

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.29 (m, 2H), 7.27 (d, *J* = 7.3 Hz, 3H), 6.07 (s, 1H), 4.47 (d, *J* = 5.7 Hz, 2H), 2.50 (s, 1H), 2.28 (s, 2H), 1.99 (d, *J* = 12.7 Hz, 2H), 1.94 – 1.80 (m, 4H), 1.75 (d, *J* = 10.9 Hz, 4H), 1.62 (d, *J* = 12.7 Hz, 2H).

^{13}C NMR (100 MHz, CDCl3): δ 174.13, 138.90, 128.70, 127.78, 127.38, 77.16, 50.06, 43.44, 38.41, 37.42, 33.40, 30.06, 27.55, 27.45.

N-benzyladamantane-1-carboxamide (25 – amide)[25]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-3% ethyl acetate/hexanes

Chromatography solvent 2: 15-30% ethyl acetate/hexanes

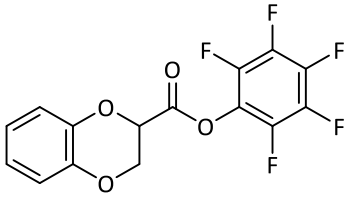
Physical Characteristics: White solid

Yield: 96 mg (71% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (dd, *J* = 7.9, 6.3 Hz, 2H), 7.28 – 7.21 (m, 3H), 5.87 (s, 1H), 4.41 (d, *J* = 5.5 Hz, 2H), 2.02 (p, *J* = 3.1 Hz, 3H), 1.86 (d, *J* = 3.0 Hz, 6H), 1.76 – 1.63 (m, 6H).

^{13}C NMR (100 MHz, CDCl3): δ 177.94, 138.80, 128.81, 127.76, 127.51, 43.45, 40.78, 39.43, 36.63, 28.25.

Pentafluorophenyl 2,3-dihydrobenzo[b][1,4]dioxine-2-carboxylate (26)



Prepared according to "Section II. General Procedure C".

Chromatography solvent 1: 2-10% ethyl acetate/hexanes

Physical Characteristics: Transparent oily solid, low melting

Yield: 123 mg (71% yield)

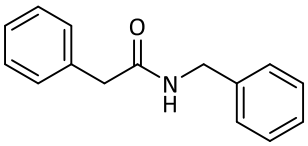
ESI HRMS: m/z calculated for $C_{15}H_7F_5O_4Na$ $[M+Na]^+$ 369.0157, found 369.0151

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 – 6.99 (m, 1H), 6.97 – 6.88 (m, 3H), 5.24 (dd, *J* = 4.0, 2.8 Hz, 1H), 4.62 (dd, *J* = 11.6, 4.0 Hz, 1H), 4.49 (dd, *J* = 11.5, 2.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): 164.69, 142.96, 141.83, 139.05 (ddq, *J* = 252.63 Hz, 12.69 Hz, 4.29 Hz), 138.78 (dtt, *J* = 254.55 Hz, 13.60 Hz, 4.11 Hz), 138.04 (dm, 255.49 Hz), 124.70 – 124.28 (m) 122.67, 122.52, 117.70, 117.53, 71.86, 64.75.

^{19}F NMR (376 MHz, $CDCl_3$) δ -152.09 – -152.39 (m, 2F), -156.64 (t, *J* = 21.8 Hz, 1F), -161.42 – -161.71 (m, 2F).

N-benzyl-2-phenylacetamide (27 – amide)[32]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent 1: 0-5% ethyl acetate/hexanes

Chromatography solvent 2: 20-35% ethyl acetate/hexanes

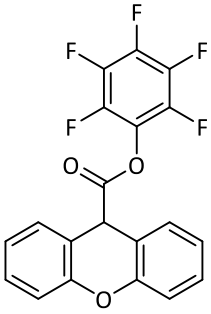
Physical Characteristics: White solid

Yield: 93 mg (82% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.21 (m, 8H), 7.21 – 7.13 (m, 2H), 5.84 (s, 1H), 4.40 (d, *J* = 5.8 Hz, 2H), 3.62 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.04, 138.22, 134.88, 129.55, 129.15, 128.75, 127.59, 127.53, 127.50, 43.88, 43.68.

Pentafluorophenyl 9H-xanthene-9-carboxylate (28)



Prepared according to "Section II. General Procedure A".

Chromatography solvent 1: 2-15% ethyl acetate/hexanes

Physical Characteristics: white solid

Yield: 140 mg (71% yield)

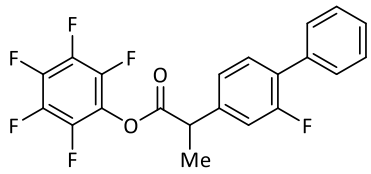
ESI HRMS: m/z calculated for $C_{20}H_{11}F_5O_3Na$ $[M+Na]^+$ 417.0521, found 417.0518

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.33 (m, 4H), 7.24 – 7.11 (m, 4H), 5.38 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.90, 151.27, 141.11 (ddq, *J* = 252.35 Hz, 12.68 Hz, 4.23 Hz), 139.69 (dtt, *J* = 253.53 Hz, 13.66 Hz, 4.13 Hz), 137.91 (dm, *J* = 252.55 Hz), 130.02, 129.00, 125.16 (m), 123.80, 117.48, 116.44, 44.88.

^{19}F NMR (376 MHz, CDCl3): δ -152.60 – -152.76 (m, 2F), -157.59 (t, J = 21.8 Hz, 1F), -162.13 – -162.36 (m, 2F).

Pentafluorophenyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (29)



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 0-2% ethyl acetate/hexanes

Physical characteristics: white solid

Yield: 143 mg (70% yield)

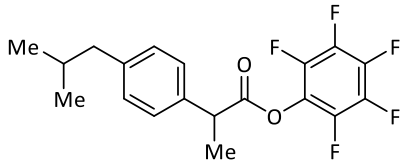
ESI HRMS: m/z calculated for $C_{21}H_{12}F_6O_2Na$ $[M+Na]^+$ 433.0634, found 433.0627

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (dt, *J* = 8.2, 1.5 Hz, 2H), 7.46 (td, *J* = 7.8, 3.5 Hz, 3H), 7.42 – 7.35 (m, 1H), 7.25 – 7.17 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 1H), 1.70 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.23, 159.95 (d, *J* = 249.1 Hz), 141.24 (ddq, *J* = 250.03 Hz, 12,26 Hz, 4.13 Hz), 139.98 (d, *J* = 7.8 Hz), 139.67 (dtt, *J* = 253.24 Hz, 13.84 Hz, 4.37 Hz), 138.00 (dm, *J* = 252.63), 135.36 (d, *J* = 1.3 Hz), 131.32 (d, *J* = 4.0 Hz), 129.10 (d, *J* = 3.0 Hz), 128.78, 128.63, 127.99, 125.42-125.07 (m), 123.66 (d, *J* = 3.5 Hz), 115.50 (d, *J* = 24.1 Hz), 44.66, 18.57.

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.94 (s, 1F), -149.87 – -155.43 (m, 2F), -157.73 (t, *J* = 21.7 Hz, 1F), -161.11 – -163.67 (m, 2F).

Pentafluorophenyl 2-(4-isobutylphenyl)propanoate (30)[33]



Prepared according to "Section II. General Procedure C".

Chromatography solvent: 0-2% ethyl acetate/hexanes

Physical characteristics: white solid

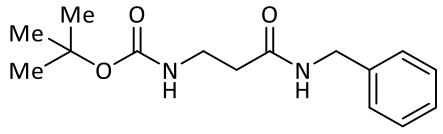
Yield: 132 mg (71% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 1H), 2.53 (d, *J* = 7.2 Hz, 2H), 1.91 (n, *J* = 6.8 Hz, 1H), 1.69 (d, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.93, 141.48, 141.27 (ddq, *J* = 248.90 Hz, 12.40 Hz, 4.44 Hz), 139.53 (dtt, *J* = 253.35 Hz, 13.57 Hz, 3.98 Hz), 137.95 (dm, *J* = 252.18 Hz), 136.09, 129.78, 127.31, 125.59 – 125.22 (m), 45.19, 44.84, 30.34, 22.49, 22.47, 18.66.

^{19}F NMR (376 MHz, $CDCl_3$): δ -147.52 – -155.21 (m, 2F), -158.25 (t, *J* = 21.7 Hz, 1F), -161.26 – -164.99 (m, 2F).

tert-butyl (3-(benzylamino)-3-oxopropyl)carbamate (31 – amide)[34]



Prepared according to "Section II. General Procedure B - Amidation".

Physical characteristics: White powder

Chromatography solvent: 3-7% ethyl acetate/hexanes

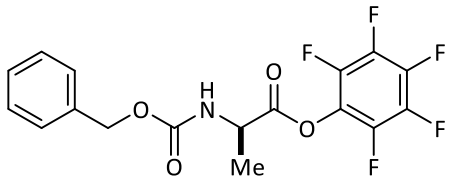
Chromatography solvent 2: 30-45% ethyl acetate/hexanes

Yield: 104 mg (75% yield)

^{1}H NMR (400 MHz, CD_3CN): δ 7.34 – 7.28 (m, 2H), 7.28 – 7.22 (m, 3H), 6.63 (s, 1H), 5.06 (s, 1H), 4.43 (d, *J* = 5.8 Hz, 2H), 4.19 (s, 1H), 1.40 (s, 9H), 1.37 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, CD_3CN): δ 172.69, 155.72, 138.20, 128.80, 127.70, 127.58, 80.32, 50.30, 43.52, 28.40, 18.40.

Pentafluorophenyl ((benzyloxy)carbonyl)-D-alaninate (32)



Prepared according to "Section II. General Procedure B".

Physical characteristics: white solid

Chromatography solvent: 2-5% ethyl acetate/hexanes

Yield: 146 mg (75% yield)

ESI-HRMS: m/z calculated for $C_{17}H_{12}F_5NO_4Na$ $[M+Na]^+$ 412.0579, found 412.0576

$[\alpha]_D^{30}$ = +24.5 ± 0.9 (c=0.5) EtOAc

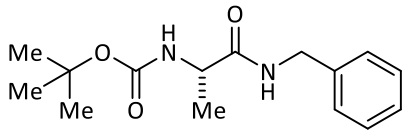
Enantiomeric excess (determined by amidation) = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.32 (m, 5H), 5.26 (d, *J* = 7.9 Hz, 1H), 5.15 (d, *J* = 3.9 Hz, 2H), 4.76 (p, *J* = 7.2 Hz, 1H), 1.62 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.59, 155.83, 141.05 (ddq, *J* = 251.67 Hz, 12.74 Hz, 3.93 Hz), 139.67 (dtt, *J* = 253.73 Hz, 13.67 Hz, 3.91 Hz), 137.89 (dtdd, *J* = 252.71 Hz, 13.44 Hz, 5.56 Hz, 2.91 Hz) 136.09, 128.50, 128.22, 128.12, 125.03 – 124.66 (m), 67.24, 49.59, 17.81.

^{19}F NMR (376 MHz, CDCl3): δ -151.29 – -154.49 (m, 2F), -157.72 (t, J = 21.4 Hz, 1F), -160.88 – -164.57 (m, 2F).

tert-butyl (S)-(1-(benzylamino)-1-oxopropan-2-yl)carbamate (33 – amide)[35]



Prepared according to "Section II. General Procedure A - Amidation".

Chromatography solvent: 3-7% ethyl acetate/hexanes

Chromatography solvent 2: 30-45% ethyl acetate/hexanes

Physical characteristics: white solid

Yield: 113 mg (81% yield)

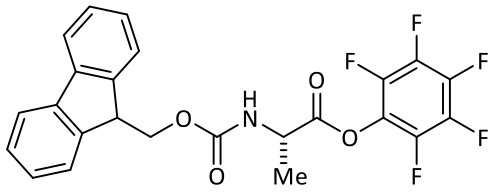
$[\alpha]_D^{30}$ = - 20.4 ± 0.4 (c=0.5) CH_2Cl_2

Enantiomeric excess (determined by diastereomeric amidation) = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.28 – 7.22 (m, 3H), 6.63 (s, 1H), 5.06 (s, 1H), 4.43 (d, *J* = 5.8 Hz, 2H), 4.19 (s, 1H), 1.40 (s, 9H), 1.37 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.69, 155.71, 138.19, 128.80, 127.70, 127.58, 80.32, 77.16, 50.29, 43.52, 28.40, 18.40.

Pentafluorophenyl (((9H-fluoren-9-yl)methoxy)carbonyl)-L-alaninate (34)[36]



Prepared according to "Section II. General Procedure C".

Physical characteristics: white solid

Chromatography solvent: 5-15% ethyl acetate/hexanes

Yield: 193 mg (81% yield)

$[\alpha]_D^{30}$ = - 33.6 ± 2.2 (c=0.5) CH_2Cl_2

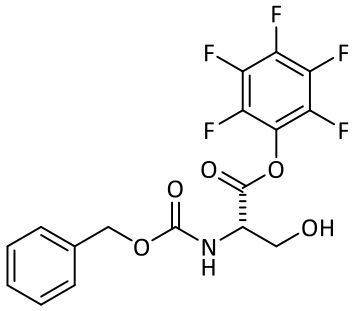
Enantiomeric excess (determined by diastereomeric amidation) = >99%

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.18 (d, 7.1 Hz, 1H), 7,78 (d, *J* = 7.1 Hz, 2H) 7.72 (dd, *J* = 7.5, 3.4 Hz, 2H), 7.48 – 7.24 (m, 4H), 4.53 (t, *J* = 7.1 Hz, 1H), 4.45 – 4.16 (m, 3H), 1.49 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 169.80, 155.94, 143.74, 143.71, 140.77, 140.52 (dm, *J* = 250.69 Hz), 139.28 (dm, *J* = 252.39 Hz), 137.49 (dm, *J* = 251.08 Hz), 127.65, 127.07, 125.15, 125.13, 124.56 – 124.20 (m), 120.14, 65.83, 49.34, 46.59, 39.53, 16.57.

^{19}F NMR (376 MHz, DMSO-d_6): δ -153.56 (d, *J* = 23.1 Hz), -157.83 (t, *J* = 23.1 Hz), -162.52 (t, *J* = 23.1,)

Pentafluorophenyl ((benzyloxy)carbonyl)-L-serinate (35)



Prepared according to "Section II. General Procedure A".

Physical characteristics: White needle-like crystals

Chromatography solvent: 10-25% ethyl acetate/hexanes

Yield: 105 mg (52% yield)

ESI-HRMS: m/z calculated for $C_{17}H_{12}F_5NO_5Na$ $[M+Na]^+$ 428.0528, found 428.0525

$[\alpha]_D^{30}$ = - 18.3 ± 1.1 (c=0.5) EtOAc

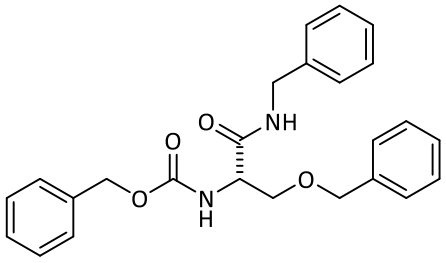
Enantiomeric excess (determined by diastereomeric amidation) = >99%

^{1}H NMR (400 MHz, CD_3CN): δ 7.50 – 7.20 (m, 5H), 6.32 (d, J = 7.9 Hz, 1H), 5.13 (s, 2H), 4.69 (dt, J = 8.3, 4.2 Hz, 1H), 4.06 (dd, J = 11.4, 4.5 Hz, 1H), 3.94 (dd, J = 11.3, 4.0 Hz, 1H), 3.50 (s, 1H).

^{13}C NMR (100 MHz, CD_3CN): δ 168.46, 157.18, 141.99 (ddq, *J* = 249.49 Hz, 12.17 Hz, 4.14 Hz), 140.65 (dtt, *J* = 250. 51 Hz, 13.66 Hz, 4.30 Hz), 138.98 (dm, *J* = 249.35 Hz), 137.79, 129.40, 128.94, 128.68, 125.91–125.55, 67.48, 62.38, 57.23.

^{19}F NMR (376 MHz, CD_3CN): δ -153.88 – -154.76 (m, 2F), -159.94 (t, *J* = 21.0 Hz, 1F), -163.76 – -164.78 (m, 2F).

Benzyl (S)-(1-(benzylamino)-3-(benzyloxy)-1-oxopropan-2-yl)carbamate (36 – amide)



Prepared according to "Section II. General Procedure B - Amidation".

Physical characteristics: White powder

Chromatography solvent: 5-12% ethyl acetate/hexanes

Chromatography solvent 2: 40-65% ethyl acetate/hexanes

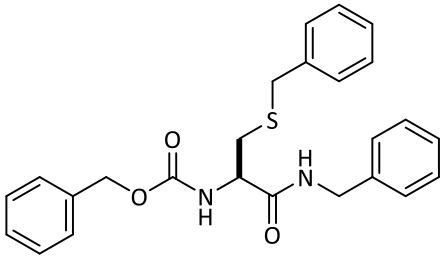
Yield: 151 mg (72% yield)

ESI-HRMS: m/z calculated for $C_{25}H_{27}N_2O_4$ $[M+H]^+$ 419.1965, found 419.1963

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.13 (m, 15H), 6.79 (t, *J* = 5.8 Hz, 1H), 5.95 – 5.63 (m, 1H), 5.11 (s, 2H), 4.47 (tq, *J* = 15.3, 8.9 Hz, 5H), 3.96 (dd, *J* = 9.4, 3.8 Hz, 1H), 3.60 (dd, *J* = 9.2, 6.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.90, 156.17, 137.89, 137.34, 136.11, 128.77, 128.66, 128.60, 128.37, 128.24, 128.05, 127.88, 127.65, 127.56, 73.62, 69.99, 67.30, 54.51, 43.64.

Benzyl (R)-(1-(benzylamino)-3-(benzylthio)-1-oxopropan-2-yl)carbamate (37 – amide)



Prepared according to "Section II. General Procedure A - Amidation".

Physical characteristics: White powder

Chromatography solvent: 5-12% ethyl acetate/hexanes

Chromatography solvent 2: 40-65% ethyl acetate/hexanes

Yield: 151 mg (72% yield)

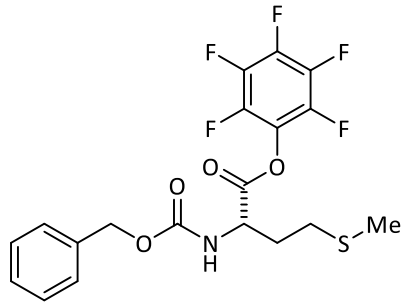
$[\alpha]_D^{30}$ = +8.4 ± 0.2 (c=0.5) CH_2Cl_2 **Enantiomeric excess (determined by amidation) =** >99%

ESI-HRMS: m/z calculated for $C_{25}H_{27}N_2O_3S$ $[M+H]^+$ 435.1737, found 435.1736

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 6.59 (m, 16H), 5.90 (d, *J* = 8.1 Hz, 1H), 4.95 (q, *J* = 12.2 Hz, 2H), 4.29 (ddd, *J* = 39.0, 15.1, 6.0 Hz, 3H), 3.62 (s, 2H), 2.75 (qd, *J* = 13.9, 6.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.34, 156.10, 137.92, 137.62, 136.01, 128.97, 128.64, 128.57, 128.51, 128.20, 128.02, 127.66, 127.49, 127.18, 67.09, 54.31, 43.55, 36.52, 33.98.

Pentafluorophenyl ((benzyloxy)carbonyl)-L-methioninate (38)



Prepared according to "Section II. General Procedure A (3.50 V)".

Physical characteristics: Clear blocky crystals

Chromatography solvent: 5-10% ethyl acetate/hexanes

Yield: 198 mg (88% yield)

ESI-HRMS: m/z calculated for $C_{19}H_{17}F_5NO_4S$ $[M+H]^+$ 450.0793, found 450.0796

$[\alpha]_D^{30}$ = - 15.7 ± 1.4 (c=0.5) CH_2Cl_2

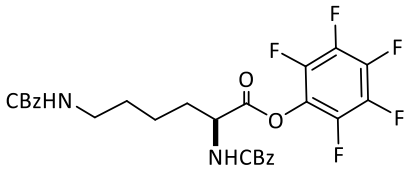
Enantiomeric excess (determined by diastereomeric amidation) = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.26 (m, 5H), 5.75 (d, *J* = 8.5 Hz, 1H), 5.15 (s, 2H), 4.90 (td, *J* = 8.2, 4.6 Hz, 1H), 2.62 (tq, *J* = 11.1, 5.0 Hz, 2H), 2.31 (tt, *J* = 7.9, 4.0 Hz, 1H), 2.20-2.12 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.66, 155.96, 141.02 (ddq, *J* = 251.82 Hz, 12.79 Hz, 4.02 Hz), 139.77 (dtt, *J* = 254.19 Hz, 13.24 Hz, 4.02 Hz), 137.92 (dtdd, *J* = 252.73 Hz, 13.70 Hz, 5.75 Hz, 2.83 Hz), 135.96, 128.57, 128.34, 128.19, 124.70 (tdt, *J* = 14.66 Hz, 4.57 Hz, 1.94 Hz) 67.45, 53.12, 31.41, 29.80, 15.38.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.15 – -152.86 (m, 2F), -157.20 (t, *J* = 21.7 Hz, 1F), -161.60 – -162.26 (m, 2F).

Pentafluorophenyl N^2,N^6-bis((benzyloxy)carbonyl)-L-lysinate (39)



Prepared according to "Section II. General Procedure B".

Physical characteristics: White powder

Chromatography solvent: 10-20% ethyl acetate/hexanes

Yield: 215 mg (74% yield)

ESI-HRMS: m/z calculated for $C_{27}H_{24}F_5NO_5Na$ $[M+Na]^+$ 560.1467, found 560.1469

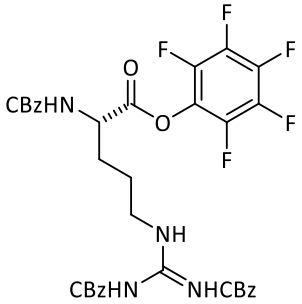
$[\alpha]_D^{31}$ = -10.0 ± 0.2 (c=0.5) EtOAc **Enantiomeric excess (determined by amidation) =** 99%

^{1}H NMR (400 MHz, CD_3CN): δ 7.64 – 7.05 (m, 10H), 6.43 (d, *J* = 7.2 Hz, 1H), 5.73 (t, *J* = 6.0 Hz, 1H), 5.22 – 4.98 (m, 4H), 4.66 – 4.39 (m, 1H), 3.14 (q, *J* = 6.4 Hz, 2H), 2.07 – 1.81 (m, 2H), 1.51 (tt, *J* = 7.4, 3.7 Hz, 4H).

^{13}C NMR (100 MHz, CD_3CN) δ 169.95, 164.59, 161.67, 157.19, 156.70, 141.94 (ddq, *J* = 249.80 Hz, 12.70 Hz, 4.13 Hz), 140.52 (dtt, *J* = 251.12 Hz, 13.31 Hz, 3.64 Hz), 138.89 (dm, *J* = 249.59 Hz), 138.31, 137.80, 136.25, 129.55, 129.39, 129.26, 129.00, 128.93, 128.71, 128.60, 125.76 (tdt, *J* = 14.77 Hz, 4.40 Hz, 2.13 Hz), 69.59, 67.48, 67.44, 54.97, 44.81, 28.87, 25.78,.

^{19}F NMR (376 MHz, CD_3CN): δ -154.43 (d, *J* = 17.0 Hz, 2F), -159.98 (t, *J* = 21.0 Hz, 1F), -164.27 (dd, *J* = 21.0, 17.0 Hz, 2F).

Pentafluorophenyl (E)-N^2,N^ω,$N^{\omega'}$-tris((benzyloxy)carbonyl)-L-argininate (40)



Prepared according to "Section II. General Procedure B".

Physical characteristics: White powder

Chromatography solvent: 13-25% ethyl acetate/hexanes

Yield: 319 mg (86% yield); 1.203 g (81% yield)

ESI-HRMS: m/z calculated for $C_{36}H_{32}F_5N_4O_8$ $[M+H]^+$ 743.2135, found 743.2137

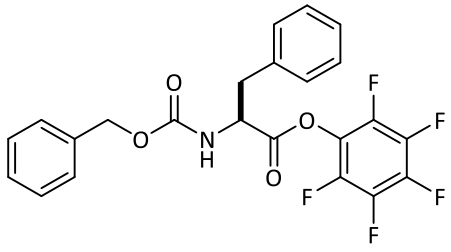
$[\alpha]_D^{30}$ = +2.52 ± 0.1 (c=0.5) CH_2Cl_2 **Enantiomeric excess (determined by amidation) =** >99%

^{1}H NMR (400 MHz, CD_3CN): δ 9.43 (s, 1H), 9.25 (s, 1H), 7.46 – 7.27 (m, 15H), 6.49 (d, *J* = 7.8 Hz, 1H), 5.27 (s, 2H), 5.16 – 5.08 (m, 4H), 4.63 (td, *J* = 8.2, 5.1 Hz, 1H), 4.05 (h, *J* = 7.3 Hz, 2H), 2.01 – 1.74 (m, 4H).

^{13}C NMR (100 MHz, CD_3CN): δ 170.16, 157.59, 157.26, 142.02 (ddq, *J* = 249.92 Hz, 12.55 Hz, 4.15 Hz), 140.60 (dtt, *J* = 250.64 Hz, 13.76 Hz, 3.96 Hz), 138.97 (dm, *J* = 249.18 Hz), 138.38, 137.83, 129.41, 129.35, 128.95, 128.74, 128.70, 128.58, 125.98 – 125.57 (m), 67.41, 66.74, 55.10, 40.87, 31.23, 29.98

^{19}F NMR (376 MHz, CD_3CN): δ -154.22 – -154.51 (m, 2F), -159.80 (t, *J* = 21.0 Hz, 1F), -163.88 – -164.40 (m, 2F).

Pentafluorophenyl ((benzyloxy)carbonyl)-L-phenylalaninate (41)[37]



Prepared according to "Section II. General Procedure C".

Physical characteristics: slightly off-white solid

Chromatography solvent: 2-7% ethyl acetate/hexanes

Yield: 165 mg (71% yield); 633 mg (68% yield); 1.06 g (65% yield)

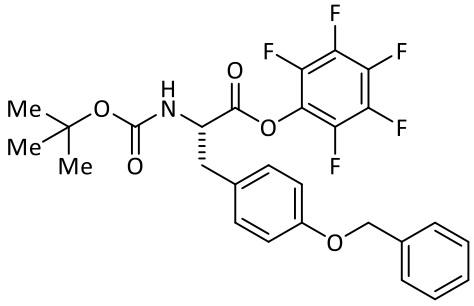
$[\alpha]_D^{20}$ = -27.0 ± 0.1 (c=0.5) $CHCl_3$ **Enantiomeric excess (determined by amidation) =** >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.04 (m, 10H), 5.23 (d, *J* = 8.3 Hz, 1H), 5.13 (d, *J* = 2.2 Hz, 2H), 5.02 (dt, *J* = 8.2, 6.1 Hz, 1H), 3.34 (dd, *J* = 14.2, 5.9 Hz, 1H), 3.24 (dd, *J* = 14.2, 6.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.22, 155.72, 141.11 (ddq, *J* = 252.35 Hz, 11.98 Hz, 4.08 Hz), 139.85 (dtt, *J* = 254.45 Hz, 13.62 Hz, 3.97 Hz), 138.00 (dtdd, *J* = 2.91 Hz, 5.74 Hz, 13.76 Hz, 253.17 Hz), 136.02, 134.70, 129.36, 129.02, 128.65, 128.41, 128.27, 127.70, 125.01 – 124.55, 67.45, 54.77, 37.85.

^{19}F NMR (376 MHz, $CDCl_3$): δ -151.49 – -152.29 (m), -157.07 (t, *J* = 21.8 Hz), -161.56 – -161.94 (m).

Pentafluorophenyl (S)-3-(4-(benzyloxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanoate (42)



Prepared according to "Section II. General Procedure B".

Physical characteristics: white solid

Chromatography solvent: 2-7% ethyl acetate/hexanes

Yield: 175 mg (65% yield)

HRMS: m/z calculated for $C_{27}H_{24}F_5NO_5Na$ $[M+Na]^+$ 560.1467, found 560.1469

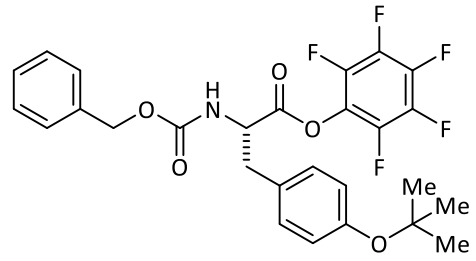
$[\alpha]_D^{32}$ = -16.5 ± 0.8 (c=0.5) **Enantiomeric excess (determined by amidation) =** 98%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.43 (m, 2H), 7.43 – 7.37 (m, 2H), 7.37 – 7.30 (m, 1H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 5.07 (s, 2H), 5.01 (d, *J* = 8.4 Hz, 1H), 4.89 (q, *J* = 6.9 Hz, 1H), 3.26 (dd, *J* = 14.2, 5.9 Hz, 1H), 3.17 (dd, *J* = 14.2, 6.6 Hz, 1H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.23, 155.72, 154.96, 141.07 (ddq, *J* = 252.14 Hz, 12.40 Hz, 4.26 Hz), 139.77 (dtt, *J* = 253.99 Hz, 13.42 Hz, 3.87 Hz), 137.95 (dtdd, *J* = 253.14 Hz, 13.86 Hz, 5.85 Hz, 3.05 Hz), 136.03, 129.81, 129.40, 128.60, 128.36, 128.23, 124.94 – 124.50 (m), 124.50, 78.64, 67.39, 54.86, 37.16, 28.85.

^{19}F NMR (376 MHz, $CDCl_3$): δ -150.46 – -153.08 (m), -157.40 (t, *J* = 21.7 Hz), -160.57 – -163.37 (m).

Pentafluorophenyl (S)-2-(((benzyloxy)carbonyl)amino)-3-(4-(tert-butoxy)phenyl)propanoate (43)



Prepared according to "Section II. General Procedure B".

Physical characteristics: white solid

Chromatography solvent: 2-7% ethyl acetate/hexanes

Yield: 183 mg (68% yield)

HRMS: m/z calculated for $C_{27}H_{24}F_5NO_5Na$ $[M+Na]^+$ 560.1467, found 560.1464

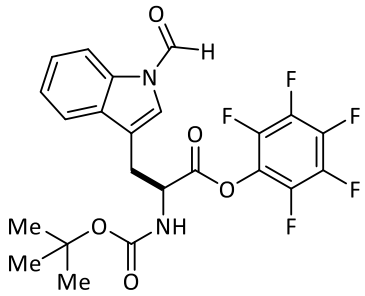
$[\alpha]_D^{32}$ = -17.4 ± 0.9 (c=0.5) CH_2Cl_2 **Enantiomeric excess (determined by amidation) =** 96%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.21 (m, 5H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 5.41 (d, *J* = 8.4 Hz, 1H), 5.13 (s, 2H), 5.00 (q, *J* = 6.9 Hz, 1H), 3.28 (dd, *J* = 14.2, 6.0 Hz, 1H), 3.19 (dd, *J* = 14.2, 6.7 Hz, 1H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.59, 158.34, 155.08, 141.16 (ddq, *J* = 252.07 Hz, 12.65 Hz, 4.28 Hz), 139.77 (dtt, *J* = 253.67 Hz, 13.63 Hz, 4.10 Hz), 138.00 (dm, *J* = 252.42 Hz), 137.00, 130.48, 128.69, 128.10, 127.55, 127.20, 125.09 – 124.72 (m), 115.29, 80.68, 70.12, 54.61, 37.10, 28.32.

^{19}F NMR (376 MHz, $CDCl_3$): δ -149.96 – -153.98 (m), -157.28 (t, *J* = 21.5 Hz), -159.97 – -162.79 (m).

pentafluorophenyl N$^{\alpha}$-(tert-butoxycarbonyl)-1-formyl-L-tryptophanate (44)



Prepared according to "Section II. General Procedure A".
Physical characteristics: pale slightly brown powder

Chromatography solvent: 5-12% ethyl acetate/hexanes

Yield: 157 mg (63% yield)

HRMS: m/z calculated for $C_{23}H_{20}F_5N_2O_5$ $[M+H]^+$ 499.1287, found 499.1277

$[\alpha]_D^{32}$ = -14.4 ± 1.1 (c=0.5) CH_2Cl_2

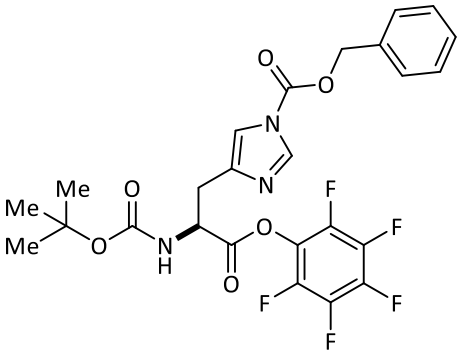
Enantiomeric excess (determined by amidation) = >99%

^{1}H NMR (400 MHz, CD_3CN): δ 9.09 (s, 1H, another singlet can be found most likely due to different conformations), 8.45 – 7.31 (m, 5H), 6.06 (d, *J* = 8.5 Hz, 1H), 4.87 (td, *J* = 8.5, 5.4 Hz, 1H), 3.44 (dd, *J* = 15.1, 5.4 Hz, 1H), 3.32 (dd, *J* = 15.1, 8.5 Hz, 1H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, CD_3CN): δ 169.50, 161.29, 156.35, 135.16, 142.04 (ddq, *J* = 250.16 Hz, 12.77 Hz, 4.08 Hz), 140.62 (dtt, *J* = 250.70 Hz, 13.48 Hz, 4.08 Hz), 138.98 (dtdd, *J* = 249.81 Hz, 14.10 Hz, 5.14 Hz, 3.02 Hz), 131.93, 126.11, 125.98-125.63 (m), 125.78, 125.29, 124.71, 120.09, 116.54, 80.67, 54.57, 27.40.

^{19}F NMR (376 MHz, CD_3CN): δ -154.07 (d, *J* = 20 Hz, 2F), -159.83 (t, *J* = 20 Hz, 1F), -164.20 (t, *J* = 20 Hz, 2F).

benzyl (S)-4-(2-((tert-butoxycarbonyl)amino)-3-oxo-3-(perfluorophenoxy)propyl)-1H-imidazole-1-carboxylate (45)



Prepared according to "Section II. General Procedure A".
Chromatography solvent: 10-25% ethyl acetate/hexanes

NMR Yield: 55% yield

Low Resolution LCMS: m/z calculated for $C_{25}H_{22}F_5N_3O_6$ $[M+H]^+$ 556.1, found 556.1

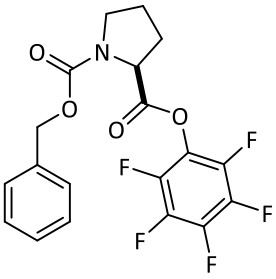
(Spectral data are from partially purified sample)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.68 – 7.12 (m, 6H), 5.88 (d, *J* = 8.3 Hz, 1H), 5.45 (s, 2H), 4.93 (q, *J* = 6.6 Hz, 1H), 3.31 – 3.21 (m, 2H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.19, 155.61, 148.24, 141.17 (ddq, *J* = 254.96 Hz, 12.47 Hz, 4.10 Hz), 139.89 (dtt, *J* = 253.97 Hz, 13.83 Hz, 3.53 Hz), 138.132 (dm, *J* = 253.86 Hz) 137.85, 137.52, 133.84, 129.55, 129.12, 129.03, 125.07 – 124.77, 115.53, 81.02, 77.26, 70.60, 53.62, 29.83, 28.31.

^{19}F NMR (376 MHz, $CDCl_3$): δ -151.37 – -152.75 (m), -156.74 – -157.79 (m), -161.49 – -162.29 (m).

1-benzyl 2-(perfluorophenyl) (S)-pyrrolidine-1,2-dicarboxylate (46)[38]



Prepared according to "Section II. General Procedure B".

Physical characteristics: pale yellow liquid

Chromatography solvent: 5-12% ethyl acetate/hexanes

Yield: 137 mg (68% yield)

$[\alpha]_D^{32}$ = -59.6 ± 2.3 (c=0.5) CH_2Cl_2

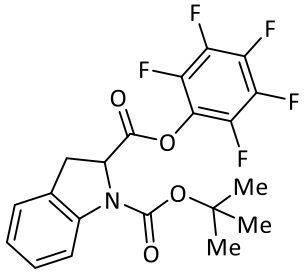
Enantiomeric excess (determined by amidation) = 96%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.24 (m, 3H), 5.29 – 5.17 (m, 1H), 5.13 (dd, *J* = 29.2, 12.4 Hz, 1H), 4.71 (ddd, *J* = 20.3, 8.8, 3.8 Hz, 1H), 3.76 – 3.50 (m, 2H), 2.43 (ttd, *J* = 14.3, 9.0, 7.4 Hz, 1H), 2.32 – 2.18 (m, 1H), 2.16 – 1.95 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.05, 168.86, 154.94, 154.19, 141.13 (dm, *J* = 253.80 Hz), 139.66 (dm, *J* = 253.61 Hz), 137.93 (dm, *J* = 252.02 Hz) 136.48, 136.20, 128.54, 128.49, 128.15, 128.05, 128.00, 125.22 – 124.74 (m), 67.59, 67.44, 58.96, 58.50, 47.04, 46.55, 31.28, 30.19, 24.47, 23.56.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.28 – -153.21 (m, 2F), -157.59 (dt, *J* = 130.9, 21.6 Hz, 1F), -162.11 (dtd, *J* = 88.1, 22.0, 4.8 Hz, 2F).

1-(tert-butyl) 2-(pentafluorophenyl) indoline-1,2-dicarboxylate (47)



Prepared according to "Section II. General Procedure B".

Physical characteristics: pale yellow powder

Chromatography solvent: 3-7% ethyl acetate/hexanes

Yield: 133 mg (61% yield)

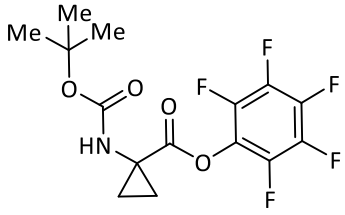
HRMS: m/z calculated for $C_{20}H_{16}F_5NO_4Na$ $[M+Na]^+$ 452.0892, found 452.0889

^{1}H NMR (400 MHz, CD_3CN): δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 2H), 7.00 (t, *J* = 7.5 Hz, 1H), 5.28 (d, *J* = 12.0 Hz, 1H), 3.75 (dd, *J* = 17.0, 12.0 Hz, 1H), 3.30 (dd, *J* = 17.0, 4.0 Hz, 1H), 1.59 – 1.51 (two singlets at 1.59 and 1.51 with a 1:4 ratio due to rotamers, 9H).

^{13}C NMR (100 MHz, CD_3CN): δ 169.46, 152.19, 142.14 (ddq, *J* = 249.31 Hz, 12.85 Hz, 4.01 Hz), 140.77 (dtt, *J* = 250.86 Hz, 13.40 Hz, 4.10 Hz), 139.04 (dtdd, *J* = 249.77 Hz, 13.76 Hz, 5.83 Hz, 3.30 Hz), 128.93, 126.14 – 125.61 (m, overlaps with peak at 125.86), 125.86, 123.85, 115.04, 82.77, 60.81, 33.51, 28.24.

^{19}F NMR (376 MHz, CD_3CN) δ -154.66 – 154.78 (mainly a doublet with *J* = 20.9 Hz), -159.24 – -160.19 (m, two triplets due to rotamers with a 3:1 ratio *J* = 20.9 Hz), -164.02 – -164.28 (m, mainly a triplet with a side peak, *J* = 20.9 Hz).

Pentafluorophenyl 1-((tert-butoxycarbonyl)amino)cyclopropane-1-carboxylate (48)



Prepared according to "Section II. General Procedure A".

Physical characteristics: slightly off-white solid

Chromatography solvent: 2-7% ethyl acetate/hexanes

Yield: 105 mg (57% yield)

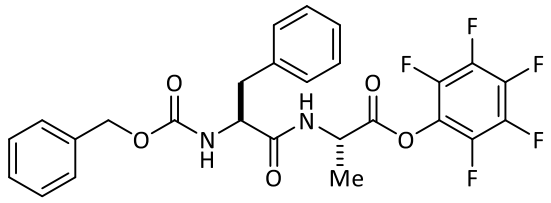
HRMS: m/z calculated for $C_{15}H_{14}F_5NO_4Na$ $[M+Na]^+$ 390.0735, found 390.0732

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.37 (s, 1H), 1.77 (d, *J* = 9.3 Hz, 2H), 1.46 – 1.40 (m, 11H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.78, 155.74, 141.26 (ddq, *J* = 251.92 Hz, 12.28 Hz, 4.20 Hz), 139.64 (dtt, *J* = 253.39 Hz, 13.23 Hz), 137.98 (dm, *J* = 251.50 Hz), 125.49-125.11 (m), 80.68, 34.24, 28.26, 20.36, 19.38.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.77 (dd, *J* = 263.7, 21.4 Hz), -157.96 (dt, *J* = 100.5, 21.9 Hz), -162.39 (dt, *J* = 70.1, 21.5 Hz).

Pentafluorophenyl ((benzyloxy)carbonyl)-L-phenylalanyl-L-alaninate (49)



Prepared according to "Section II. General Procedure B".

Physical characteristics: white powder

Chromatography solvent: 20-40% ethyl acetate/hexanes

Yield: 172 mg (64% yield)

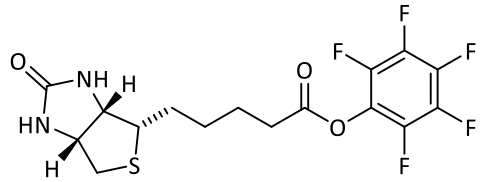
HRMS: m/z calculated for $C_{26}H_{22}F_5N_2O_5$ $[M+H]^+$ 537.1443, found 537.1435

^{1}H NMR (400 MHz, CD_3CN): δ 7.35–7.25 (m, 11H), 5.93 (d, *J* = 8.8 Hz, 1H), 4.99 (q, *J* = 12.8 Hz, 2H), 4.68 (dt, *J* = 15.5, 7.7 Hz, 1H), 4.40 (s, 1H), 3.16 (d, *J* = 14.6 Hz, 1H), 2.92 – 2.72 (m, 1H), 1.54 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, CD_3CN): δ 172.58, 170.09, 156.90, 142.07 (dm, *J* = 251.21 Hz), 140.59 (dm, *J* = 250.89 Hz), 138.96 (dm, *J* = 249.60 Hz), 125.96 –125.63 (m), 138.30, 138.02, 130.24, 129.36, 129.27, 128.79, 128.47, 127.58, 67.01, 56.85, 49.12, 38.58, 17.07.

^{19}F NMR (376 MHz, CD_3CN): δ -154.69 (d, *J* = 20.0 Hz), -160.09 (t, *J* = 20.0 Hz), -164.40 (t, *J* = 20.0 Hz).

Pentafluorophenyl 5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanoate (50)[39]



Prepared according to "Section II. General Procedure B".

Physical characteristics: white powder

Chromatography solvent: 20-40% ethyl acetate/hexanes

Yield: 134 mg (65% yield)

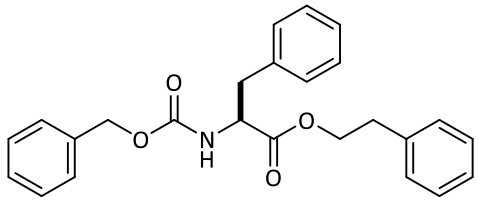
^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 6.48 (s, 1H), 6.39 (s, 1H), 4.32 (dd, *J* = 7.8, 4.5 Hz, 1H), 4.16 (ddd, *J* = 7.8, 4.5, 1.8 Hz, 1H), 3.13 (ddd, *J* = 7.8, 6.2, 4.5 Hz, 1H), 2.91 – 2.56 (m, 4H), 1.79 – 1.33 (m, 6H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 169.53, 162.78, 140.60 (ddq, *J* = 248.54 Hz, 12.49 Hz, 4.37 Hz), 138.94 (dtt, *J* = 250.14 Hz, 14.01 Hz, 3.75 Hz), 137.50 (dm, *J* = 247.29 Hz), 124.70 – 124.33 (m), 61.07, 59.24, 55.30, 39.52, 32.33, 27.95, 27.72, 24.34.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -153.62 (d, *J* = 19.1 Hz), -158.26 (t, *J* = 22.9 Hz), -162.74 (dd, *J* = 22.9, 19.1 Hz).

X. Characterization Data for Z-Phe Derivatives

Phenethyl ((benzyloxy)carbonyl)-L-phenylalaninate (51)



Chromatography solvent: 10-25% ethyl acetate/hexanes

Physical Characteristics: clear viscous liquid

Yield: 174 mg (86% yield)

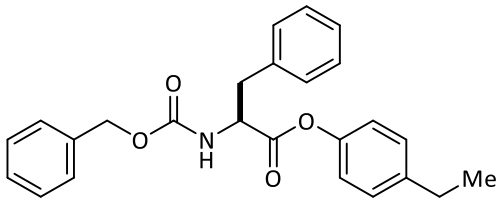
HRMS: m/z calculated for $C_{25}H_{25}NO_4Na$ $[M+Na]^+$ 426.1676, found 426.1674

$[\alpha]_D^{20}$ **=** + 13.2 (c=1) $CHCl_3$**Enantiomeric excess (determined by Mosher amide) =** 97%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.34 (m, 7H), 7.34 – 7.19 (m, 6H), 7.07 (dd, *J* = 7.1, 2.8 Hz, 2H), 5.51 – 5.26 (m, 1H), 5.21 – 5.10 (m, 2H), 4.73 (q, *J* = 7.0 Hz), 4.38 (t, *J* = 7.0 Hz, 2H), 3.16 (dd, *J* = 13.8, 6.1 Hz, 1H), 3.08 (dd, *J* = 13.8, 6.1 Hz, 1H), 2.96 (t, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.42, 155.65, 137.41, 136.27, 135.72, 129.25, 128.87, 128.54, 128.49, 128.46, 128.11, 128.02, 127.00, 126.69, 66.86, 65.88, 54.85, 38.05, 34.82.

4-ethylphenyl ((benzyloxy)carbonyl)-L-phenylalaninate (52)



Recrystallization solvent: hexanes

Physical Characteristics: white solid with a slight phenolic smell

Yield: 191 mg (95% yield)

HRMS: m/z calculated for $C_{25}H_{25}NO_4Na$ $[M+Na]^+$ 426.1676, found 426.1675

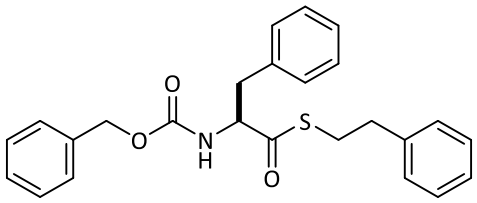
$[\alpha]_D^{20}$ = + 6.6 (c=1) $CHCl_3$

Enantiomeric excess (determined by Mosher amide) = 99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.28 (m, 8H), 7.28 – 7.23 (m, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 5.43 (d, *J* = 8.3 Hz, 1H), 5.16 (d, *J* = 2.6 Hz, 2H), 4.94 (dt, *J* = 8.3, 6.0 Hz, 1H), 3.29 (d, *J* = 6.0 Hz, 2H), 2.67 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.45, 155.77, 148.24, 142.20, 136.26, 135.58, 129.55, 128.86, 128.80, 128.62, 128.29, 128.20, 127.39, 121.02, 67.15, 55.05, 38.34, 28.34, 15.62.

S-phenethyl (S)-2-(((benzyloxy)carbonyl)amino)-3-phenylpropanethioate (53)



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white solid with a pungent rubbery smell

Yield: 176 mg (84% yield)

HRMS: m/z calculated for $C_{25}H_{25}NO_3SNa$ $[M+Na]^+$ 442.1447, found 442.1448

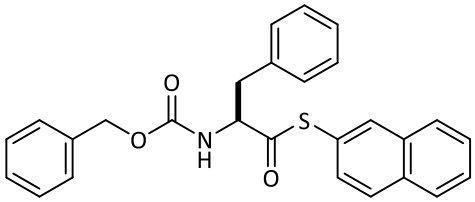
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ = + 19.9 (c=0.2) $CHCl_3$

Enantiomeric excess (determined by direct substitution with chiral amine) = 98%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.23 (m, 11H), 7.21 (d, *J* = 7.6 Hz, 2H), 7.13 (dd, *J* = 7.7, 1.8 Hz, 2H), 5.17 – 5.03 (m, 3H), 4.73 (ddd, *J* = 8.8, 7.1, 5.5 Hz, 1H), 3.20 – 2.91 (m, 4H), 2.85 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.37, 155.74, 139.89, 136.21, 135.51, 129.49, 128.84, 128.73, 128.67, 128.65, 128.36, 128.22, 127.34, 126.72, 67.32, 61.59, 38.53, 35.71, 30.48.

S-(naphthalen-2-yl) (S)-2-(((benzyloxy)carbonyl)amino)-3-phenylpropanethioate (54)



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white solid with a pungent rubbery smell

Yield: 201 mg (91% yield)

HRMS: m/z calculated for $C_{27}H_{23}NO_3SNa$ $[M+Na]^+$ 464.1291, found 464.1293

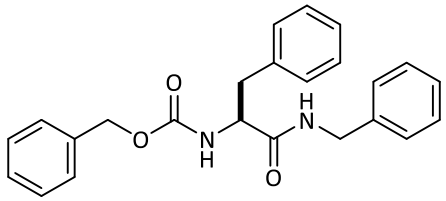
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ = – 92.6 (c=0.5) $CHCl_3$

Enantiomeric excess (determined by direct substitution with chiral amine) = 96%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.77 (m, 4H), 7.59 – 7.49 (m, 2H), 7.42 – 7.27 (m, 9H), 7.21 (d, *J* = 6.25), 5.27 (d, *J* = 8.9 Hz, 3H), 5.16 (d, *J* = 2.3 Hz), 4.88 (dt, *J* = 6.8 Hz, 8.9 Hz) 3.25 – 3.15 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 199.14, 155.80, 136.17, 135.41, 134.75, 133.69, 133.56, 130.99, 129.58, 129.04, 128.94, 128.71, 128.42, 128.26, 128.10, 127.96, 127.48, 127.39, 126.75, 124.39, 67.48, 61.55, 38.54.

benzyl (S)-(1-(benzylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (55)[40]



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white solid

Yield: 191 mg (98% yield)

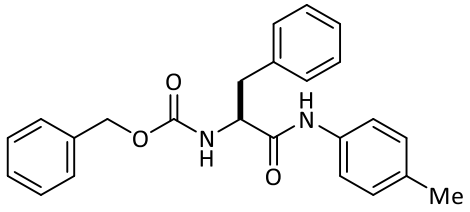
$[\alpha]_D^{20}$ = +7.6 (c=0.877) $CHCl_3$

Enantiomeric excess (determined by Mosher amide) = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 6.94 (m, 15H), 6.31 (s, 1H), 5.56 (d, *J* = 8.4 Hz, 1H), 5.01 (d, *J* = 2.8 Hz, 2H), 4.61 – 4.15 (m, 3H), 3.14 (dd, *J* = 13.7, 6.4 Hz, 1H), 3.07 (dd, *J* = 13.7, 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 199.14, 155.80, 136.17, 135.41, 134.75, 133.69, 133.56, 130.99, 129.58, 129.04, 128.94, 128.71, 128.42, 128.26, 128.10, 127.96, 127.48, 127.39, 126.75, 124.39, 67.48, 61.55, 38.54.

benzyl (S)-(1-(benzylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (56)



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white solid

Yield: 179 mg (92% yield)

$[\alpha]_D^{20}$ = – 5.8 (c=1) $CHCl_3$

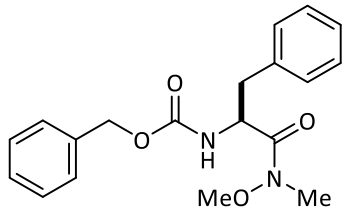
Enantiomeric excess (determined by Mosher amide) = >99%

HRMS: m/z calculated for $C_{24}H_{24}N_2O_4Na$ $[M+Na]^+$ 411.1679, found 411.1678

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 30.1 Hz, 1H), 7.43 – 7.11 (m, 12H), 7.07 (dd, *J* = 8.2, 5.6 Hz, 2H), 6.02 (d, *J* = 8.2 Hz, 2 doublets with a 1:2 ratio, 1H), 5.10 (dd, *J* = 12.4, 6.0 Hz, 1H), 5.04 (dd, *J* = 12.4, 4.8 Hz, 1H), 4.72 (q, *J* = 7.8 Hz, 1H), 3.19 – 3.05 (m, 2H), 2.32 (s, two singlets with 1:2 ratio at 2.33 and 2.32 most likely due to amide conformations, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.53, 169.44, 156.42, 136.58, 136.55, 136.15, 134.83, 134.18, 129.45, 129.42, 128.73, 128.67, 128.61, 128.26, 127.94, 127.86, 127.07, 127.02, 120.36, 120.34, 67.17, 57.13, 39.16 (has a peak at 39.48 that most likely corresponds to the methyl group in a different amide conformation), 20.96.

benzyl (S)-(1-(methoxy(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (57)



Chromatography Solvent: 20 – 40% hexanes/ethyl acetate

Physical Characteristics: clear viscous liquid

Yield: 164 mg (96% yield)

$[\alpha]_D^{20}$ = + 17.1 (c=1) $CHCl_3$

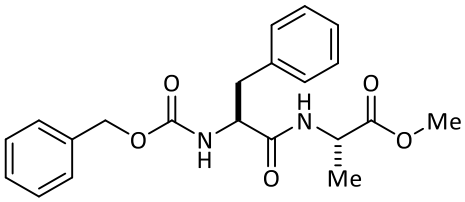
Enantiomeric excess (determined by Mosher amide) = 99%

HRMS: m/z calculated for $C_{19}H_{22}N_2O_4$ $[M+H]^+$ 343.1652, found 343.1652

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.12 (m, 7H), 7.12 – 7.04 (m, 2H), 5.40 (d, *J* = 8.9 Hz, 1H), 4.99 (q, *J* = 12.3 Hz, 3H), 3.61 (s, 3H), 3.11 (s, 3H), 3.01 (dd, *J* = 13.7, 6.0 Hz, 1H), 2.84 (dd, *J* = 13.7, 7.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.00, 155.91, 136.46, 136.38, 129.54, 128.60, 128.53, 128.19, 128.08, 127.01, 66.90, 61.68, 52.21, 38.77, 32.19.

methyl ((benzyloxy)carbonyl)-L-phenylalanyl-L-alaninate (58)[41]



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white powder

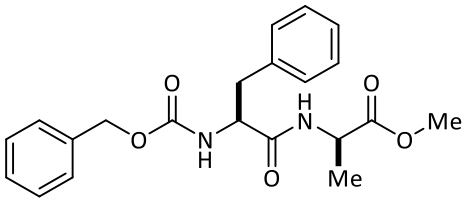
Yield: 177 mg (92% yield)

Diasteriomeric ratio = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.23 (m, 8H), 7.20 (d, *J* = 7.3 Hz, 2H), 6.28 (d, *J* = 7.3 Hz, 1H), 5.29 (s, 1H), 5.10 (s, 2H), 4.51 (p, *J* = 7.2 Hz, 1H), 4.43 (d, *J* = 9.0 Hz, 1H), 3.72 (s, 3H), 3.13 (dd, *J* = 14.0, 6.3 Hz, 1H), 3.05 (dd, *J* = 13.8, 6.9 Hz, 1H), 1.34 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ δ 172.92, 170.47, 156.02, 136.33, 136.25, 129.48, 128.81, 128.66, 128.33, 128.16, 127.19, 67.20, 56.15, 52.60, 48.27, 38.64, 18.41.

methyl ((benzyloxy)carbonyl)-L-phenylalanyl-D-alaninate (59)[42]



Recrystallization solvent: hexanes/ethyl acetate

Physical Characteristics: white powder

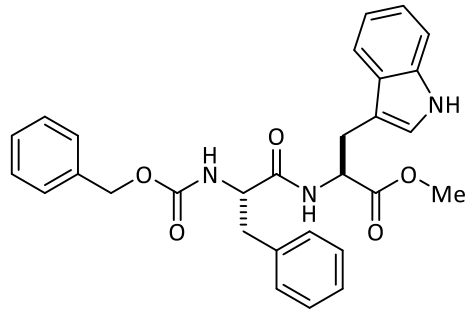
Yield: 177 mg (92% yield)

Diasteriomeric ratio = >99%

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.13 (m, 10H), 6.59 (d, *J* = 7.5 Hz, 1H), 5.73 (d, *J* = 8.3 Hz, 1H), 5.22 – 4.95 (m, 2H), 4.70 – 4.33 (m, 2H), 3.71 (s, 3H), 3.28 – 2.93 (m, 2H), 1.25 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.07, 170.50, 156.01, 136.53, 136.25, 129.39, 128.66, 128.54, 128.17, 128.01, 127.01, 67.00, 56.19, 52.48, 47.94, 38.93, 18.02.

methyl ((benzyloxy)carbonyl)-L-phenylalanyl-L-tryptophanate (60)



Recrystallization solvent: water/isopropanol

Physical Characteristics: beige powder

Yield: 175 mg (70% yield)

Diasteriomeric ratio = 98%

HRMS: m/z calculated for $C_{29}H_{30}N_3O_5$ $[M+H]^+$ 500.2180, found 500.2177

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.16 (s, 1H), 7.50 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.39 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.37 – 6.91 (m, 14H), 5.85 (d, *J* = 8.6 Hz, 1H), 4.97 (q, *J* = 12.5 Hz, 2H), 4.70 (ddd, *J* = 7.6, 6.7, 5.7 Hz, 1H), 4.33 (td, *J* = 9.0, 5.0 Hz, 1H), 3.62 (s, 3H), 3.29 – 3.14 (m, 2H), 3.09 (dd, *J* = 14.1, 5.0 Hz, 1H), 2.77 (dd, *J* = 14.1, 9.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.97, 156.85, 130.22, 129.38, 129.25, 128.78, 128.44, 127.53, 124.77, 122.51, 120.00, 119.20, 112.34, 110.33, 66.98, 57.04, 54.06, 52.72, 38.46, 28.10.

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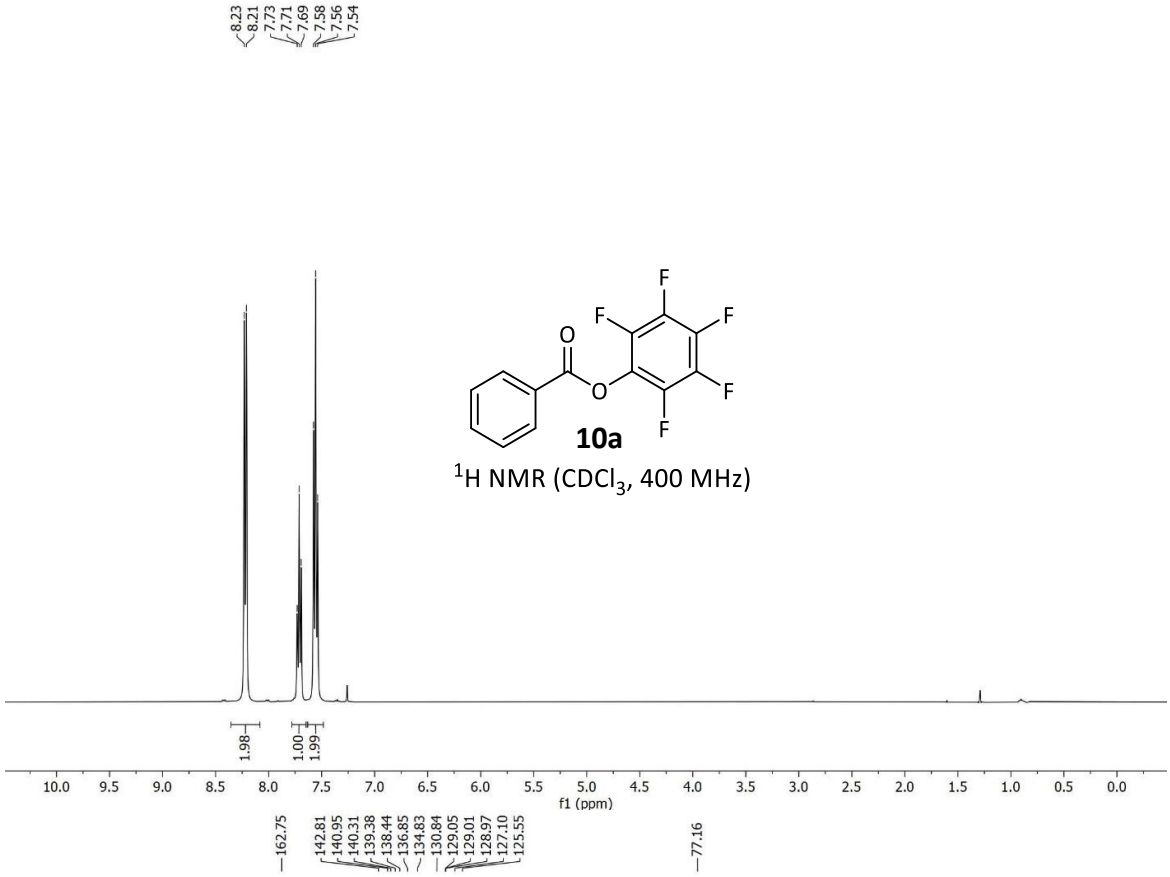
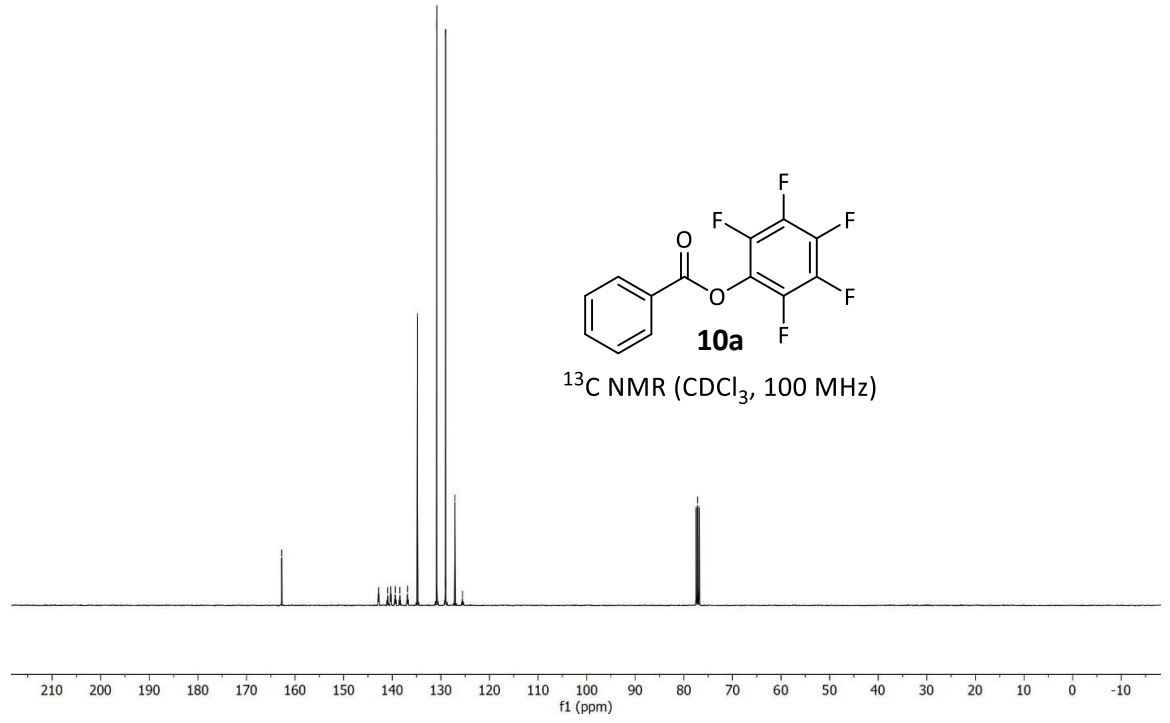
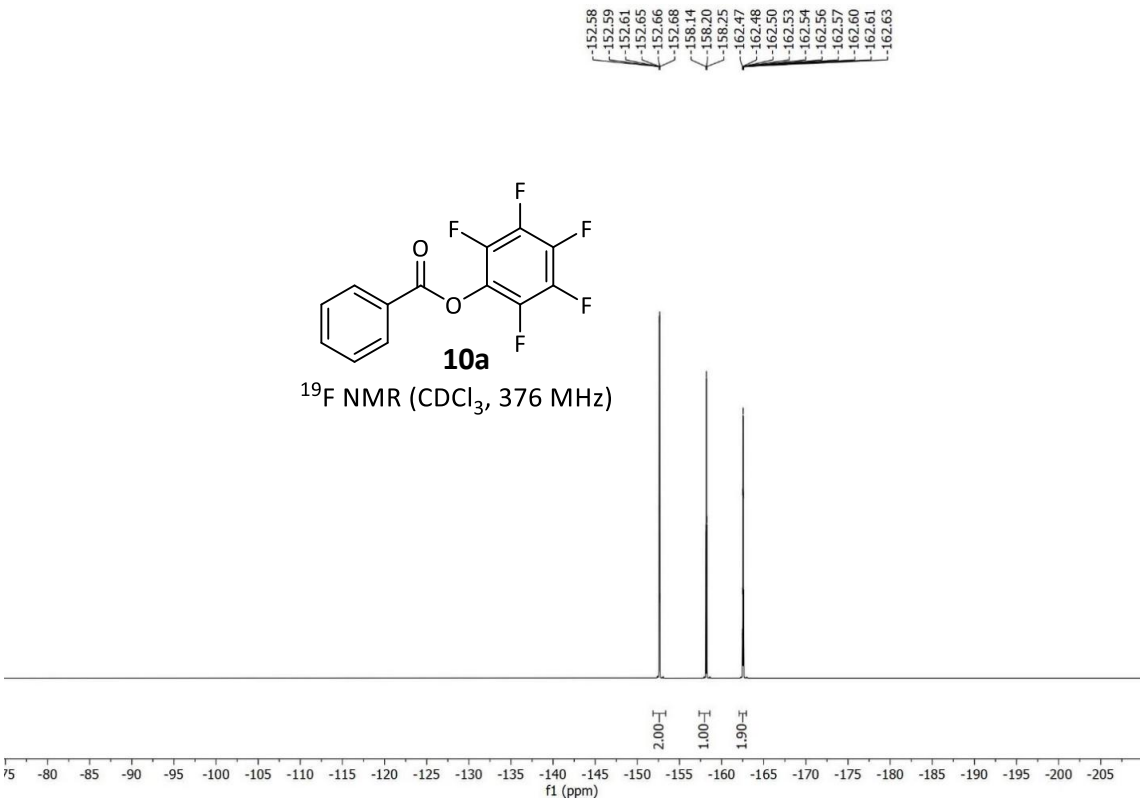
XII. NMR Spectra for Substrate Scope Entries

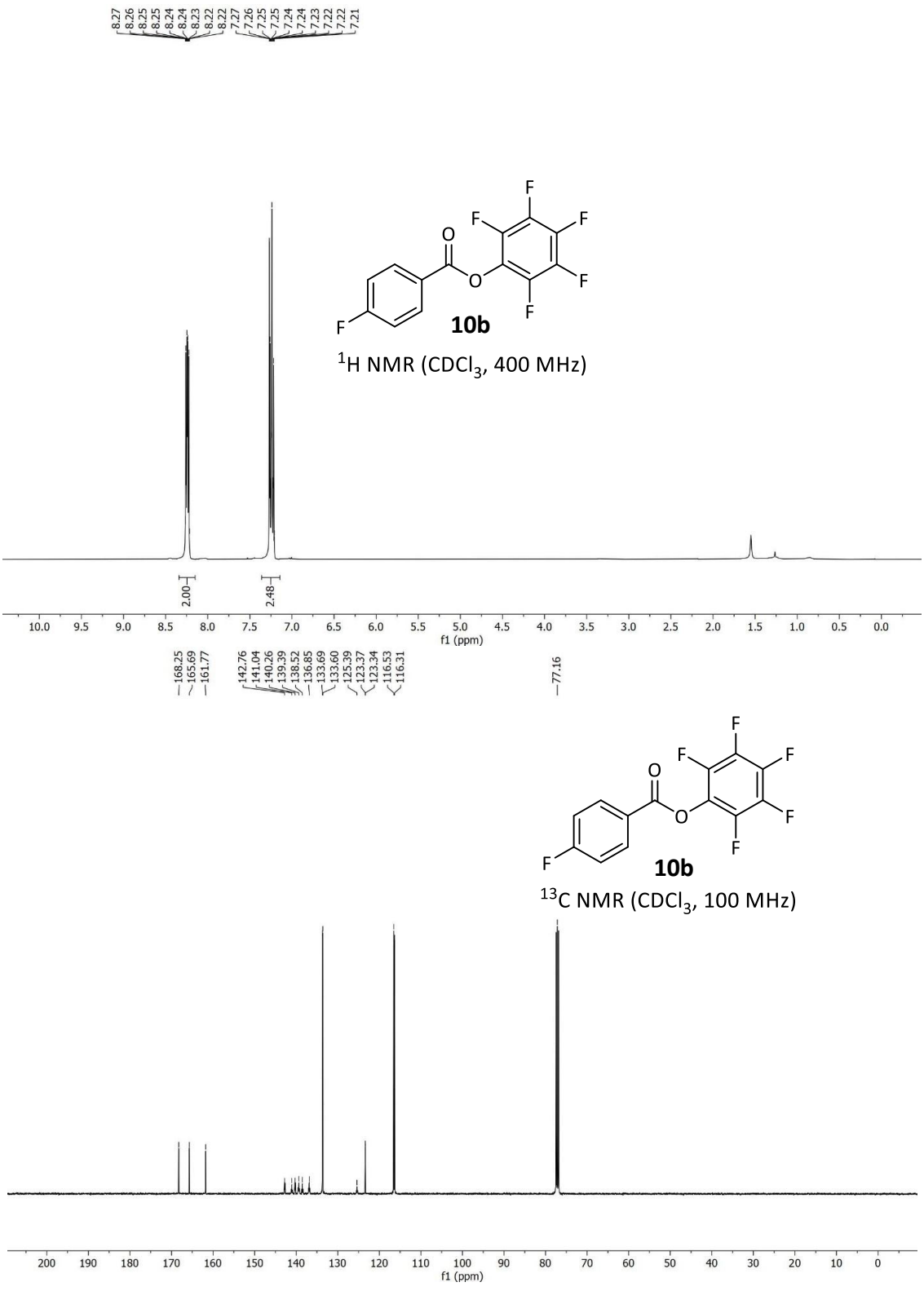






10a

^{19}F NMR ($CDCl_3$, 376 MHz)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F
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O
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F
F
F
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4.0
3.5
3.0
2.5
2.0
1.5
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0.0
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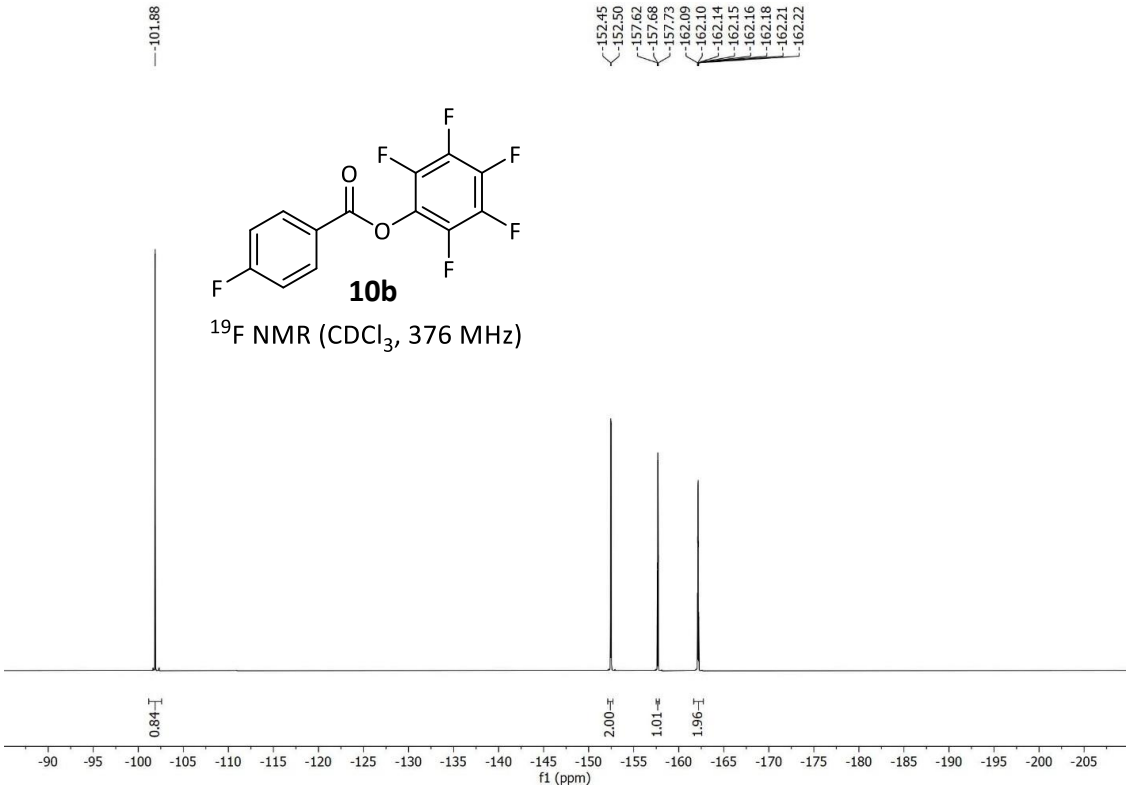
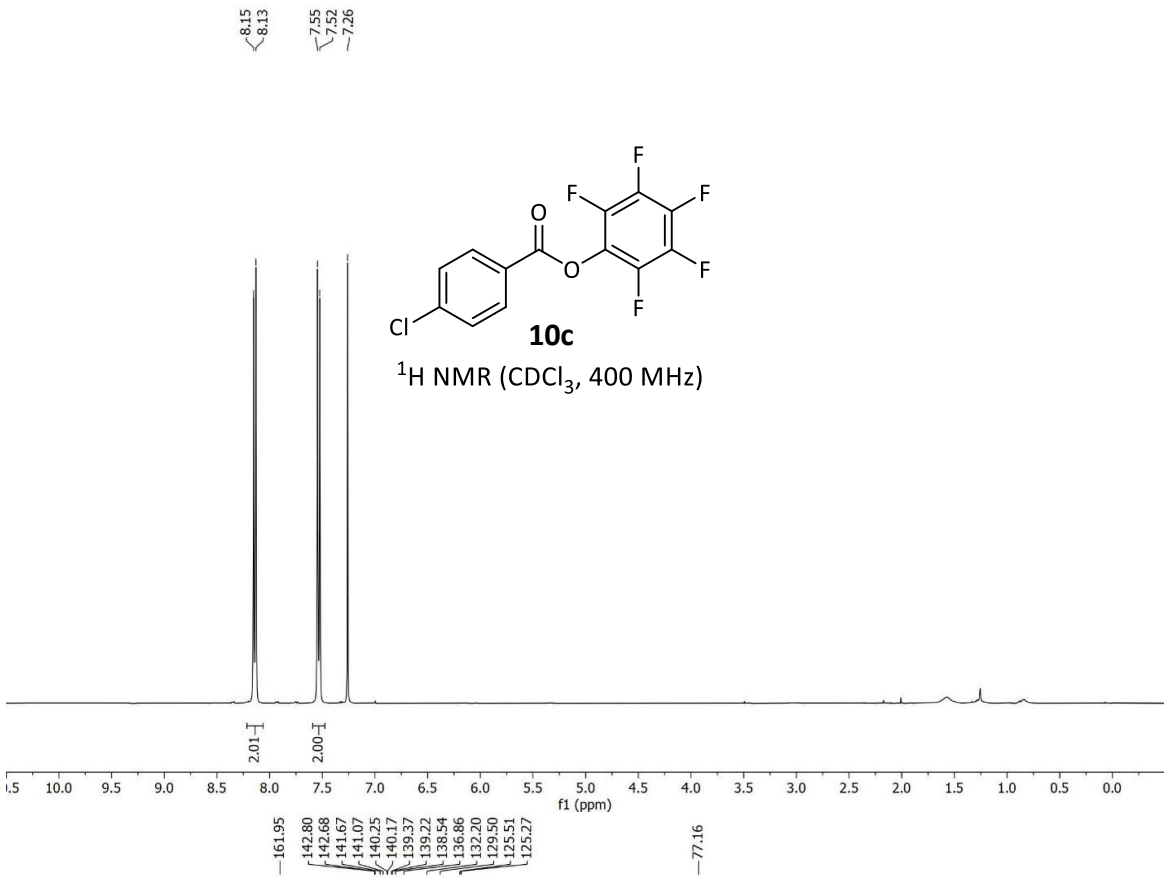
168.25
165.69
161.77
142.76
141.04
140.26
139.39
138.52
136.85
133.69
133.60
125.39
123.37
123.34
116.53
116.31
77.16
F
F
F
O
O
F
F
F
10b
13C NMR (CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



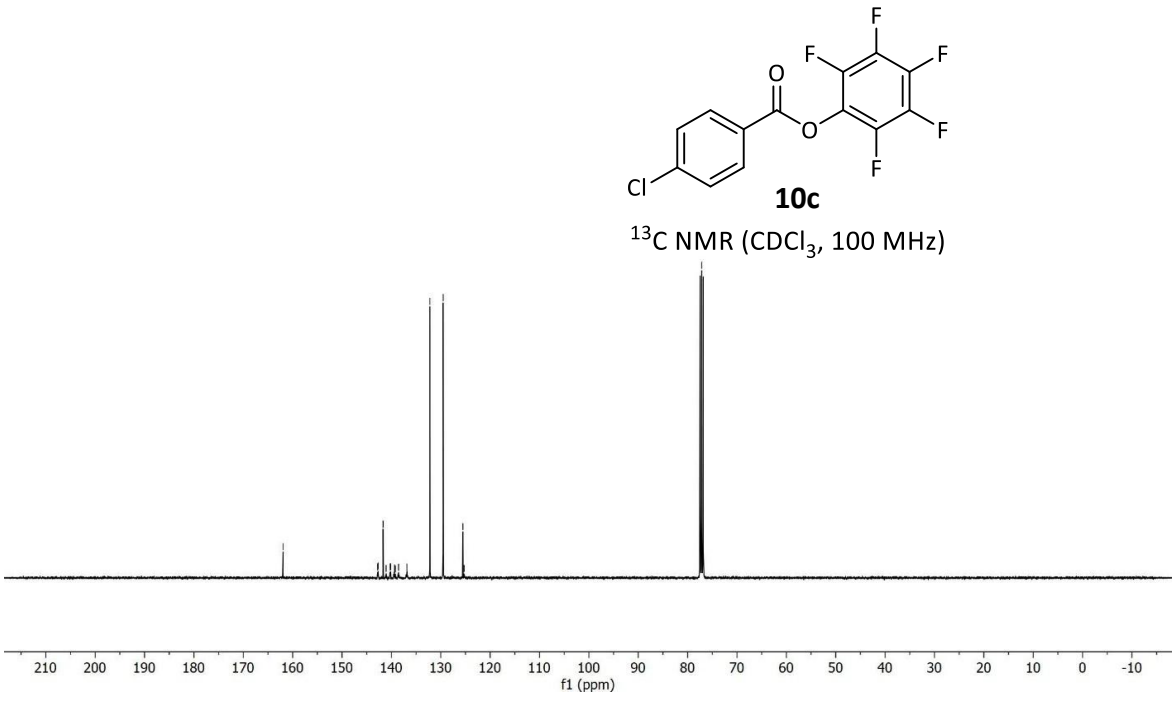
10b

^{19}F NMR ($CDCl_3$, 376 MHz)



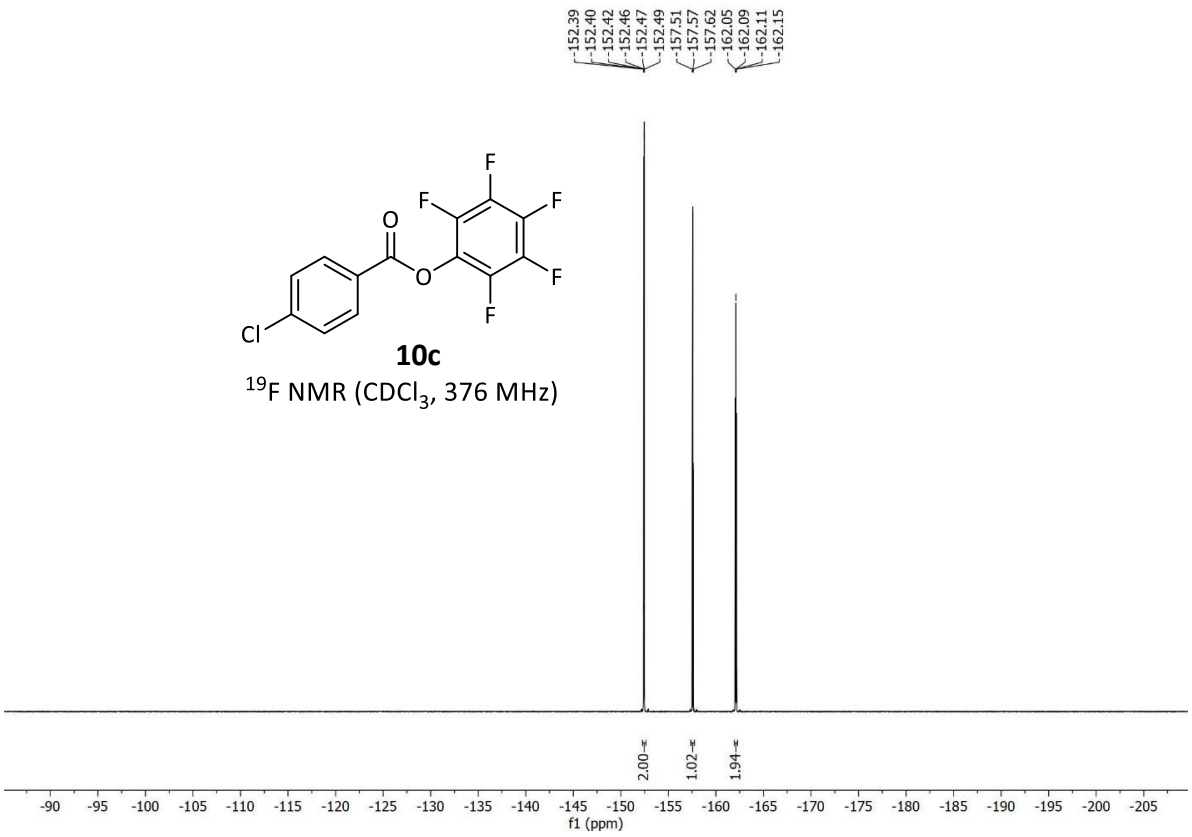
10c

^{1}H NMR ($CDCl_3$, 400 MHz)



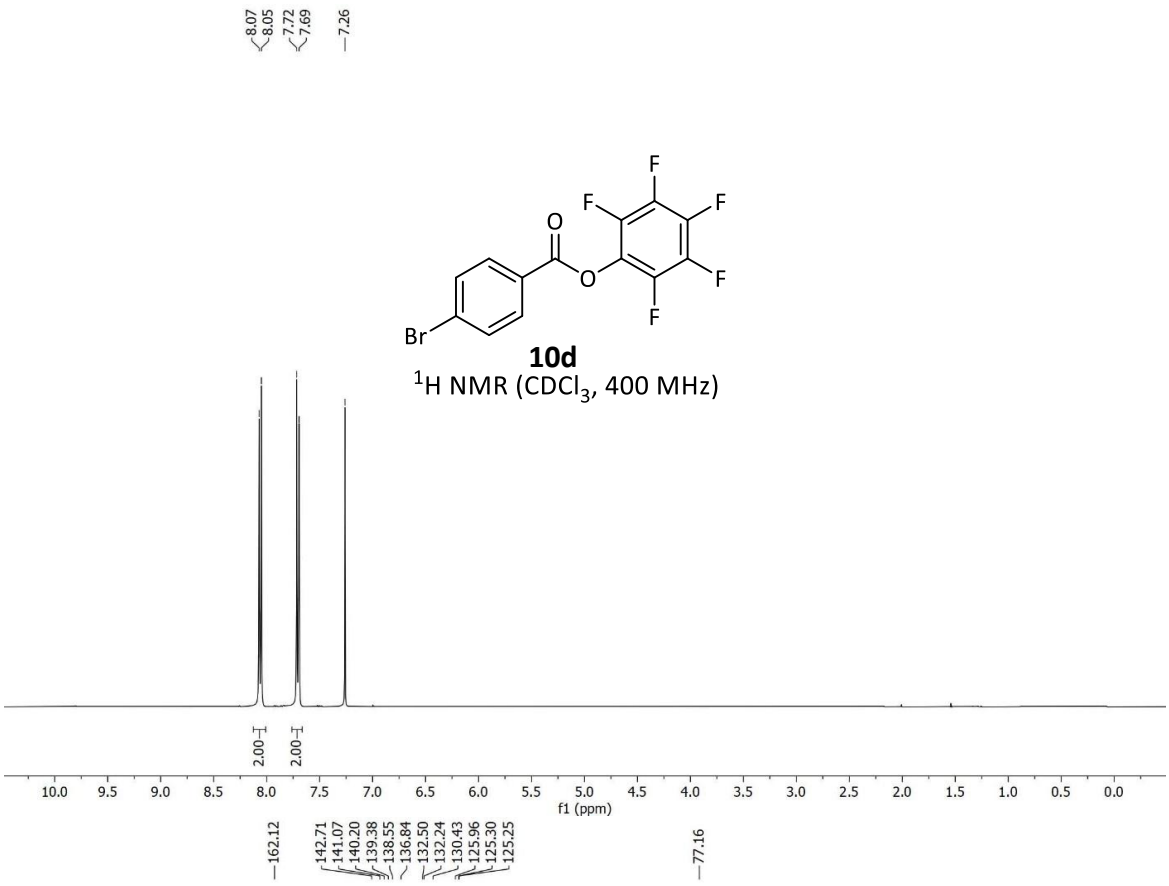
10c

^{13}C NMR ($CDCl_3$, 100 MHz)



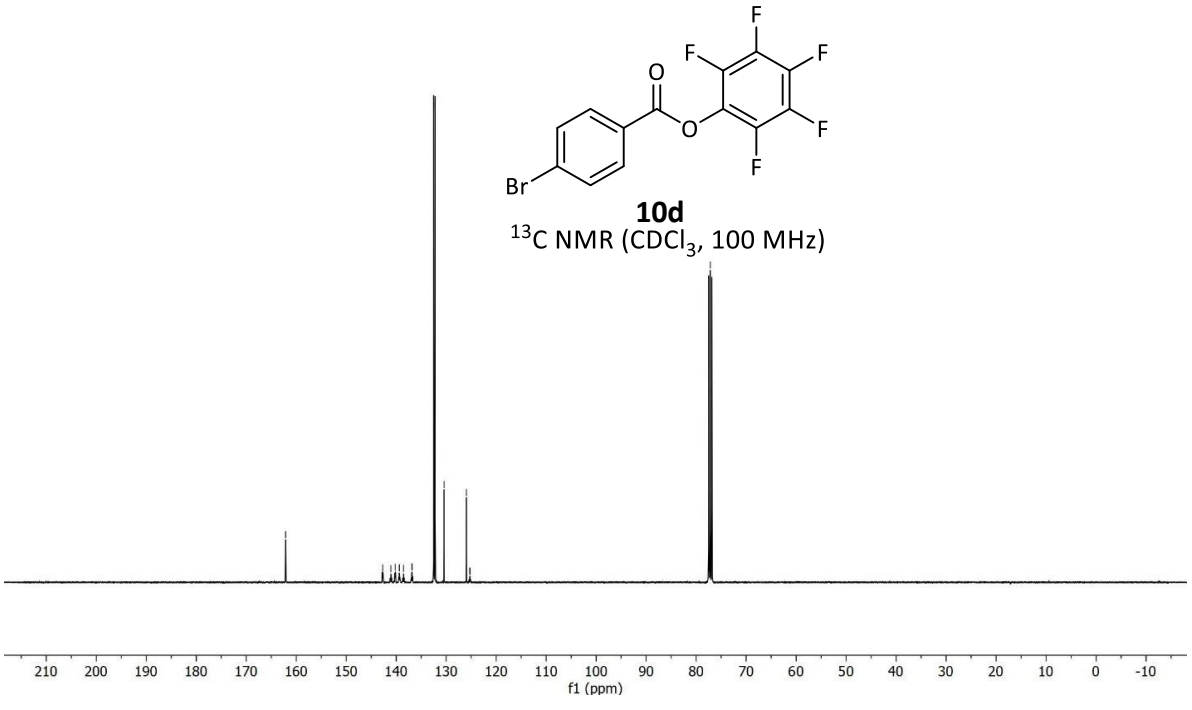
10c

^{19}F NMR ($CDCl_3$, 376 MHz)



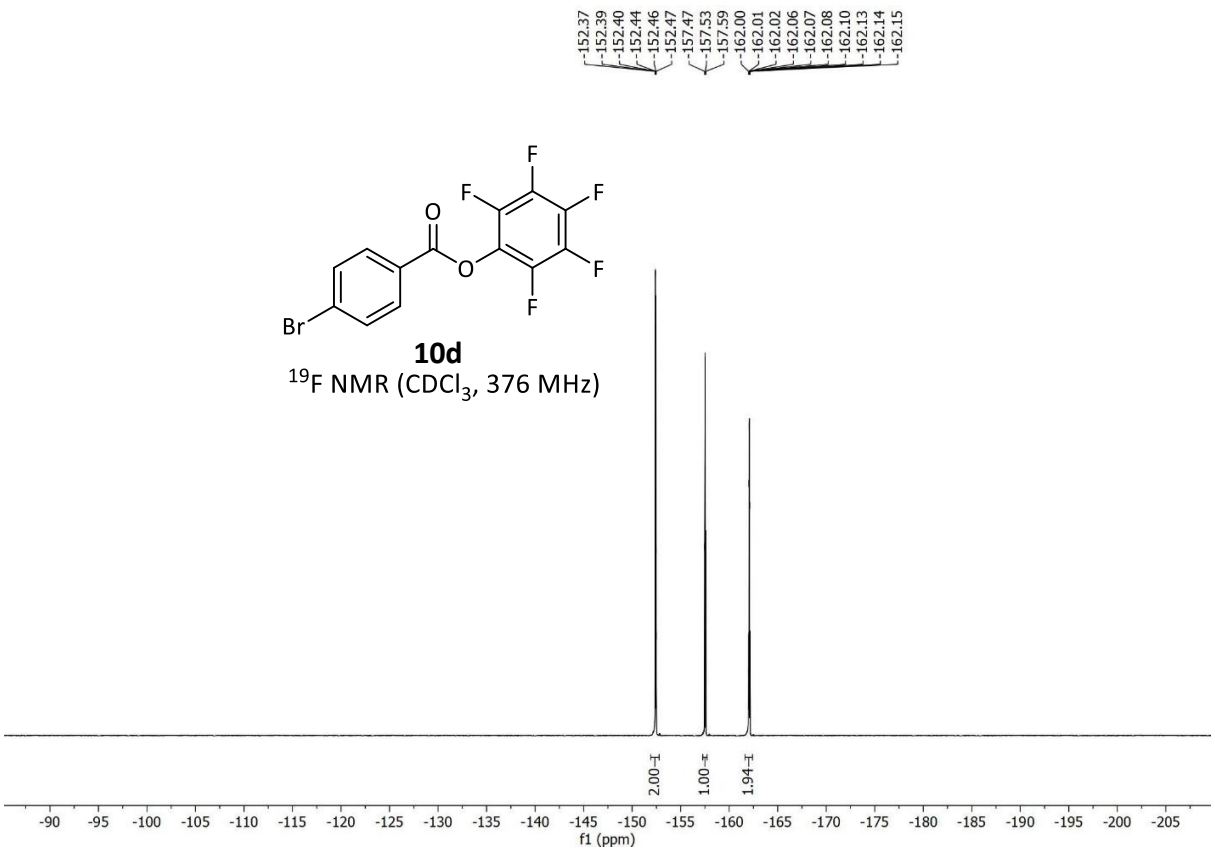
10d

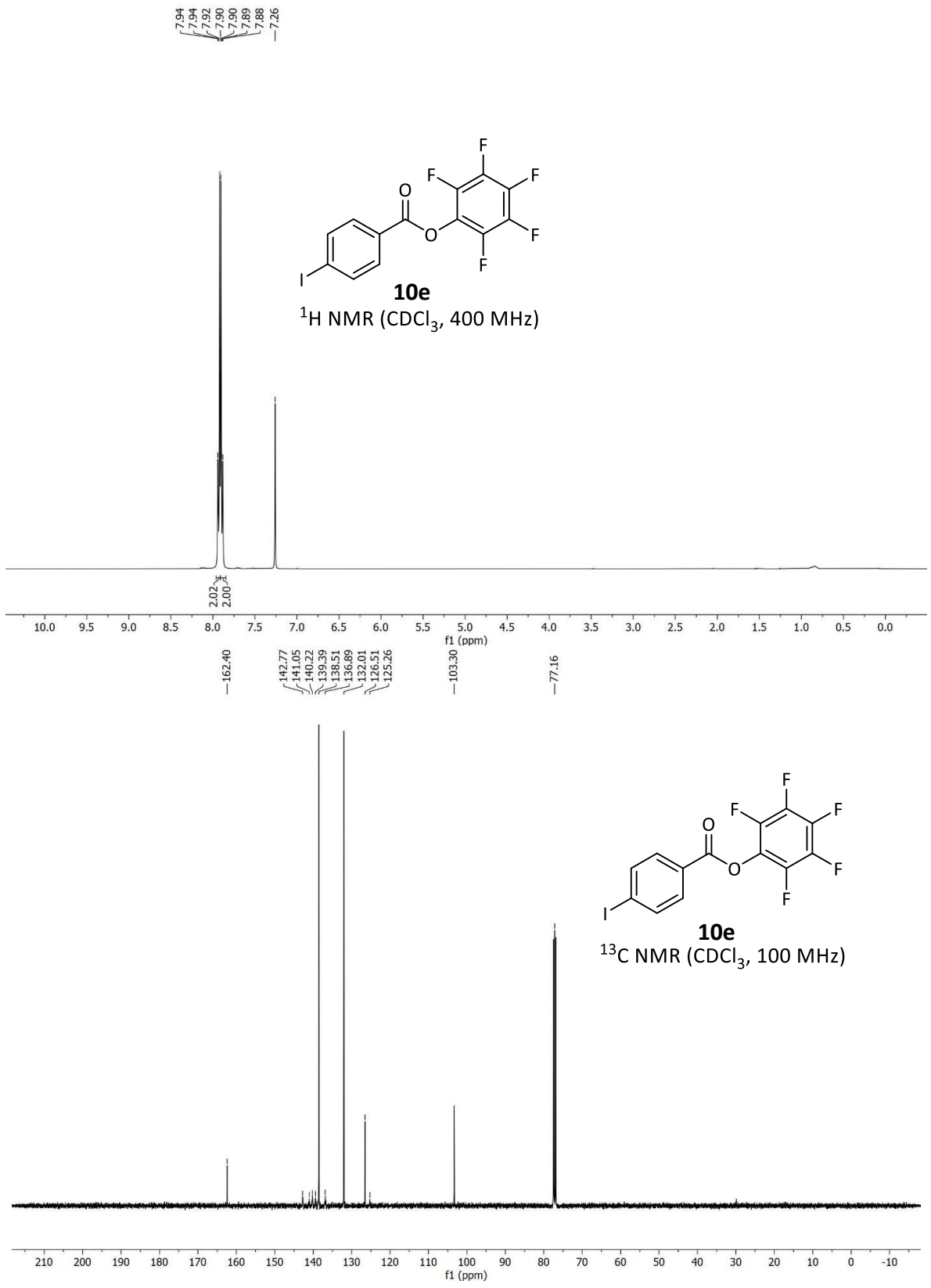
^{1}H NMR ($CDCl_3$, 400 MHz)

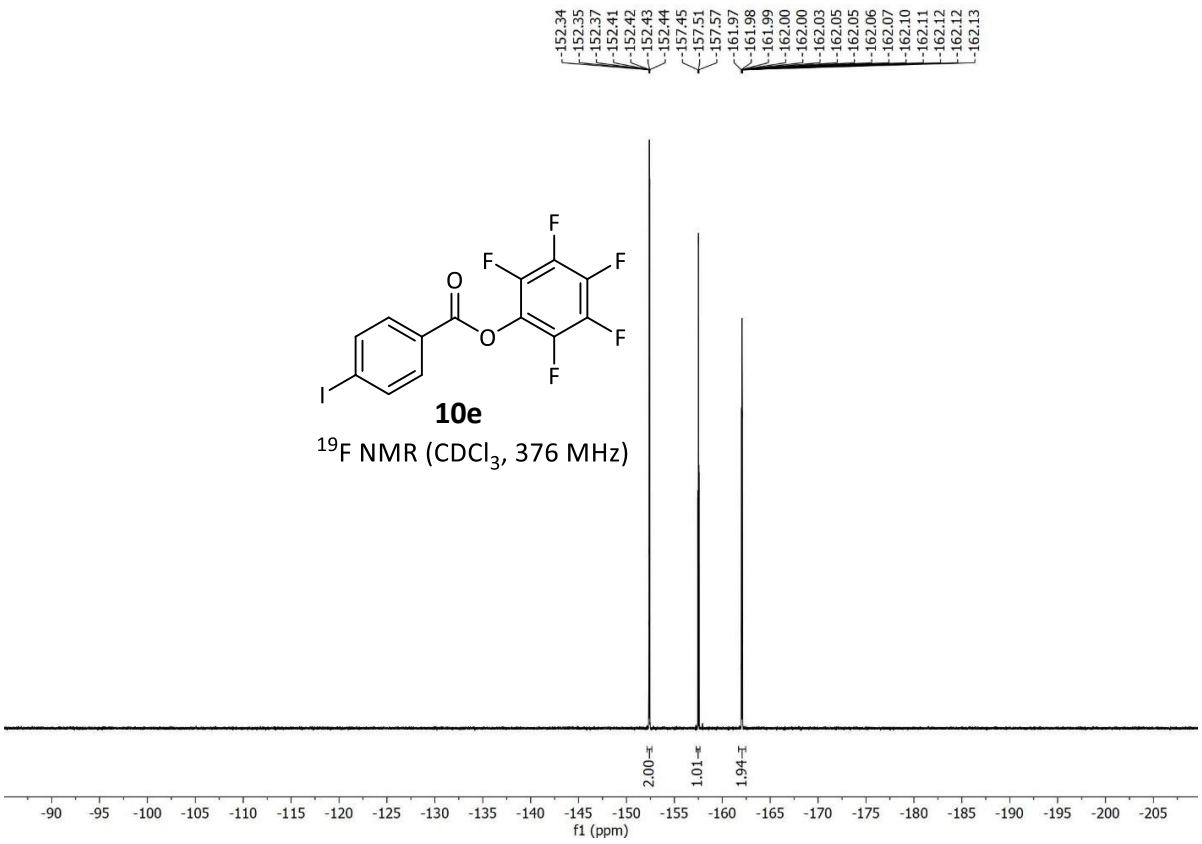


10d

^{13}C NMR ($CDCl_3$, 100 MHz)

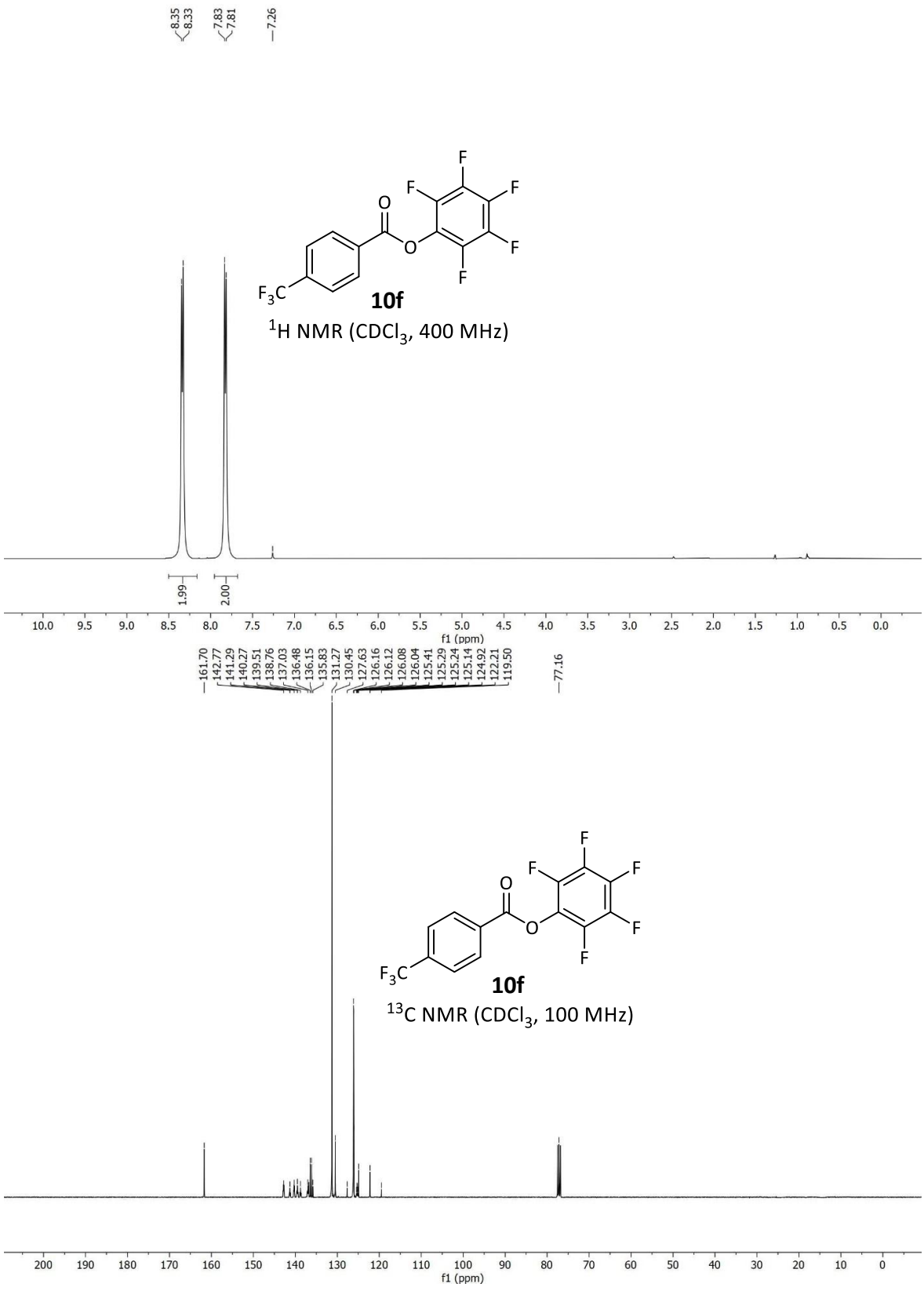

-152.37
-152.39
-152.40
-152.44
-152.46
-152.47
-157.47
-157.53
-157.59
-162.00
-162.01
-162.02
-162.06
-162.07
-162.08
-162.10
-162.13
-162.14
-162.15
F
F
F
O
O
F
F
Br
10d
19F NMR (CDCl3, 376 MHz)
2.00
1.00
1.94
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)


7.94
7.94
7.92
7.90
7.90
7.89
7.88
7.26
F
F
F
F
F
O
O
I
10e
1H NMR (CDCl3, 400 MHz)
2.02
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
162.40
142.77
141.05
140.22
139.39
138.51
136.89
132.01
126.51
125.26
103.30
77.16
F
F
F
F
F
O
O
I
10e
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



10e

^{19}F NMR ($CDCl_3$, 376 MHz)

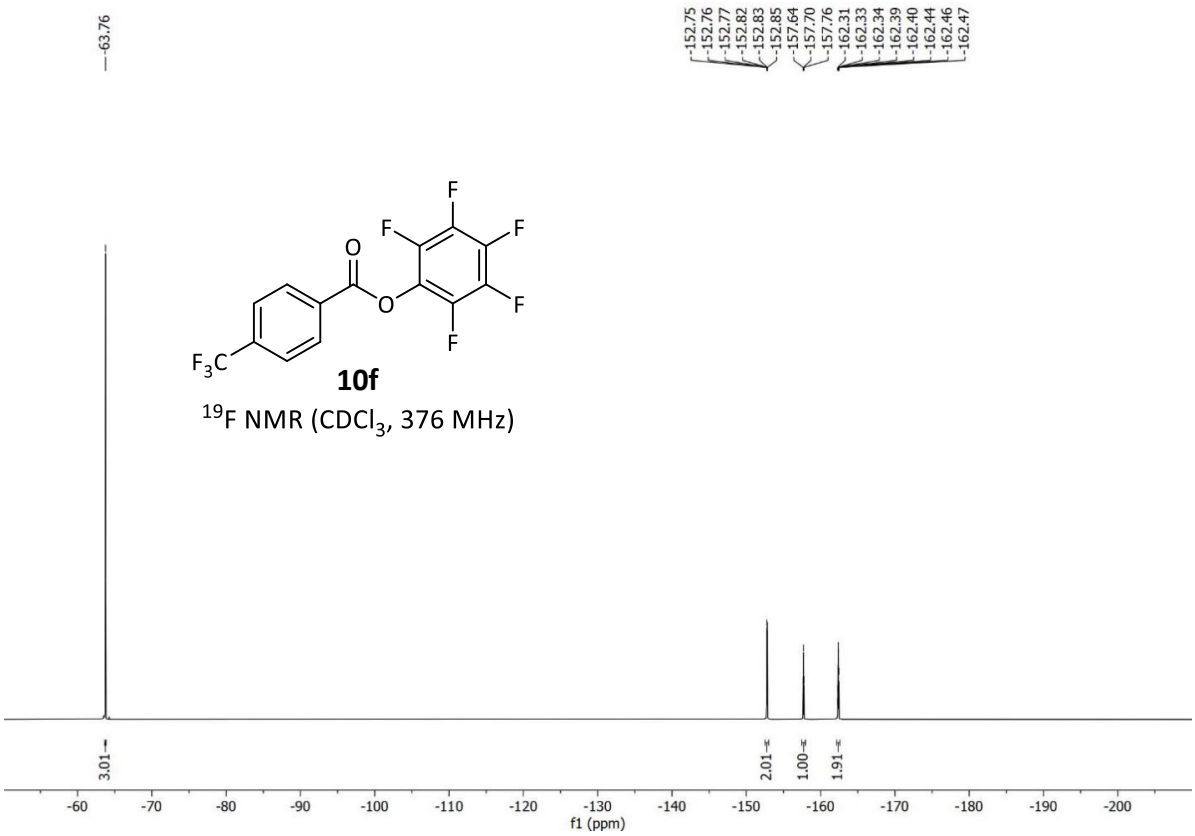


10f

^{1}H NMR ($CDCl_3$, 400 MHz)

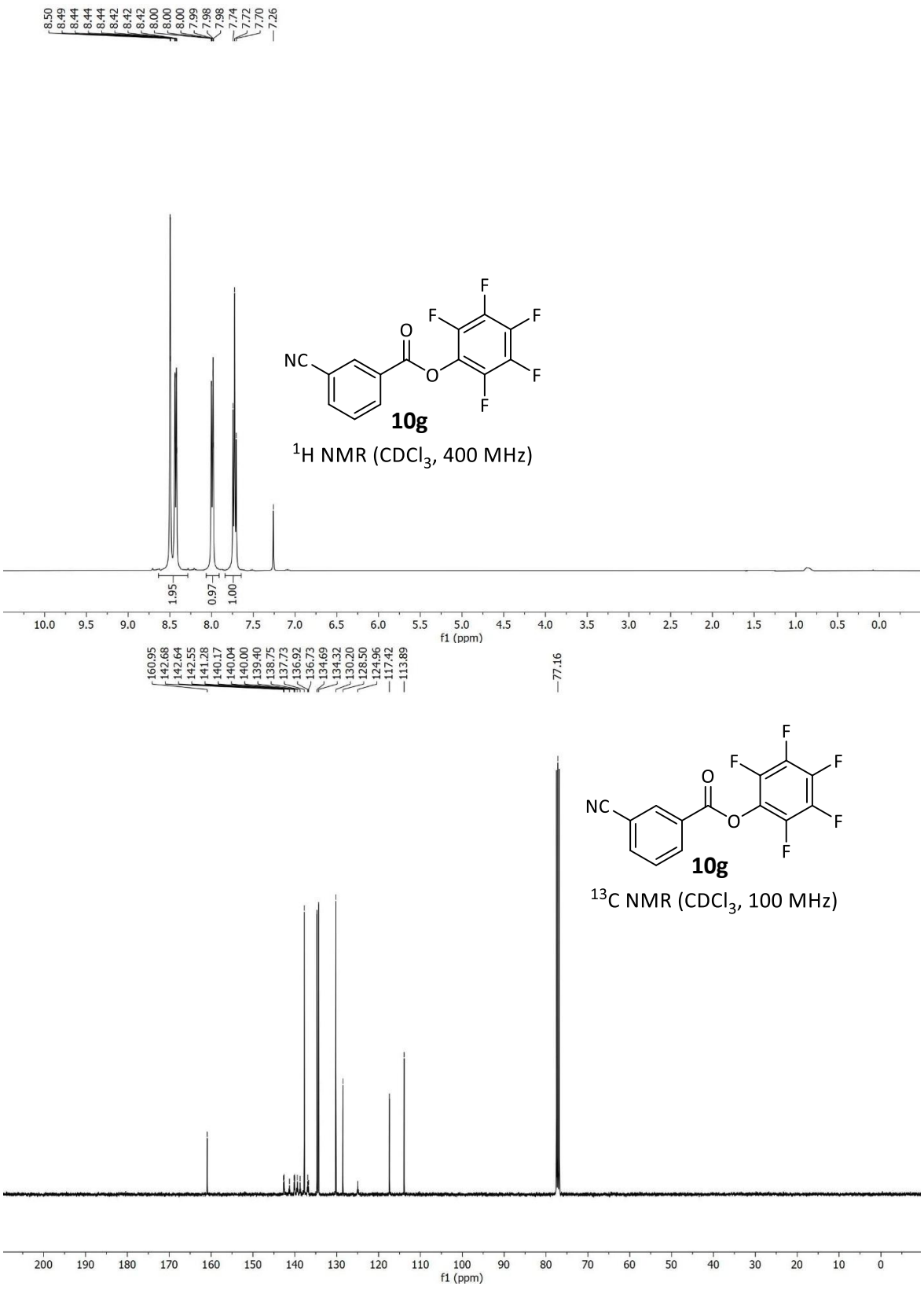
10f

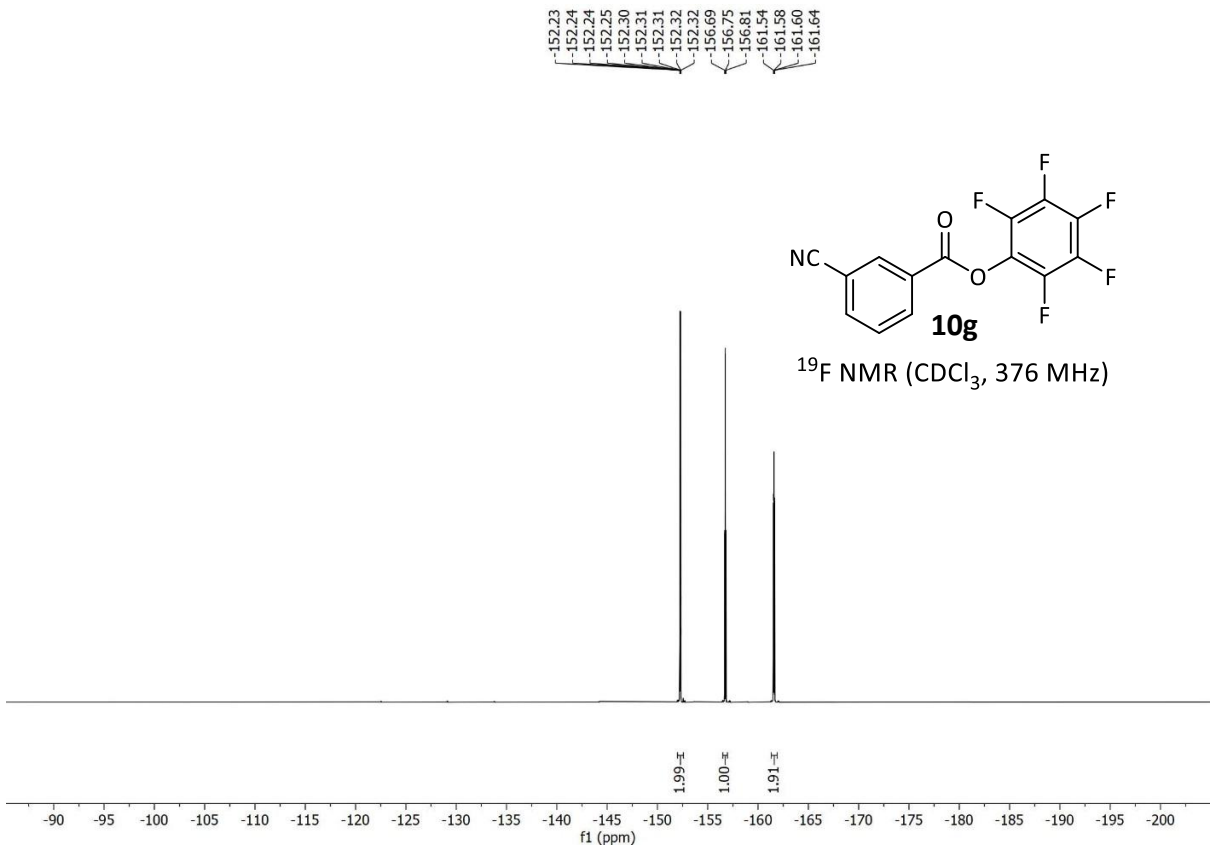
^{13}C NMR ($CDCl_3$, 100 MHz)

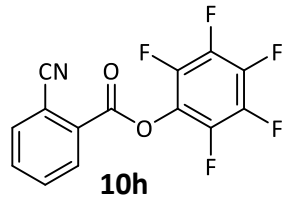


10f

^{19}F NMR ($CDCl_3$, 376 MHz)

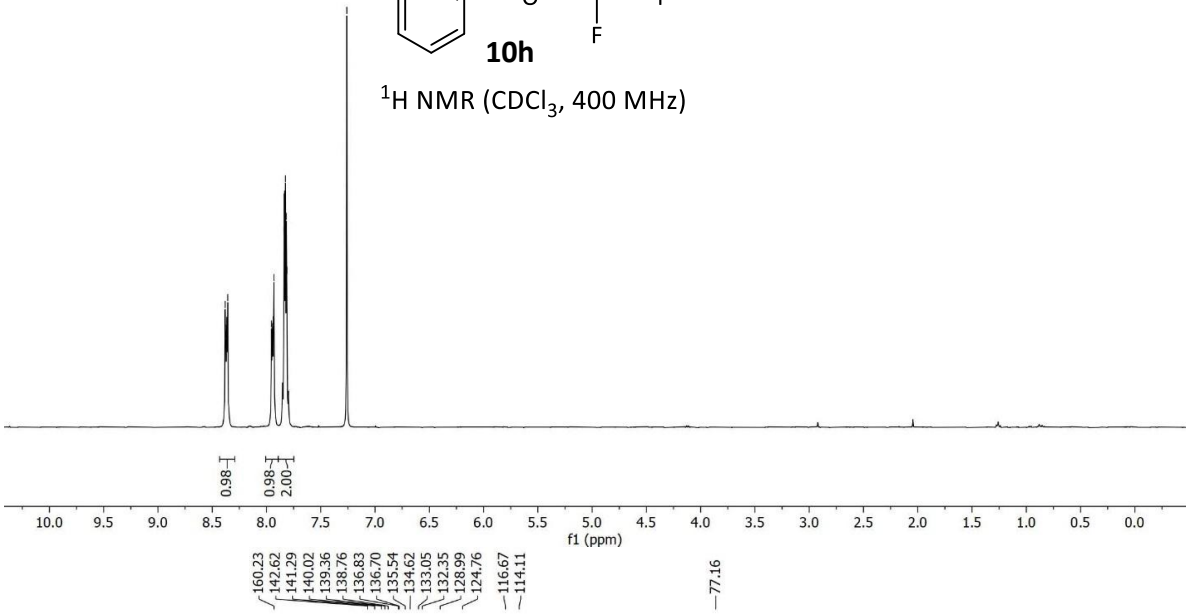

8.50
8.49
8.44
8.44
8.44
8.42
8.42
8.42
8.00
8.00
8.00
7.99
7.98
7.98
7.74
7.72
7.70
7.26
NC
O
O
F
F
F
F
F
10g
1H NMR (CDCl3, 400 MHz)
1.95
0.97
1.00
f1 (ppm)
160.95
142.68
142.64
142.55
141.28
140.17
140.04
140.00
139.40
138.75
137.73
136.92
136.73
134.69
134.32
130.20
128.50
124.96
117.42
113.89
77.16
10g
13C NMR (CDCl3, 100 MHz)
f1 (ppm)

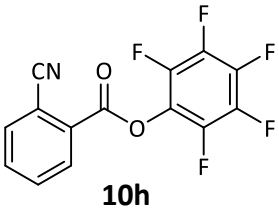

-152.23
-152.24
-152.24
-152.25
-152.30
-152.31
-152.31
-152.32
-152.32
-156.69
-156.75
-156.81
-161.54
-161.58
-161.60
-161.64
F
F
F
O
NC
O
F
F
10g
19F NMR (CDCl3, 376 MHz)
1.99
1.00
1.91
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200
f1 (ppm)



10h

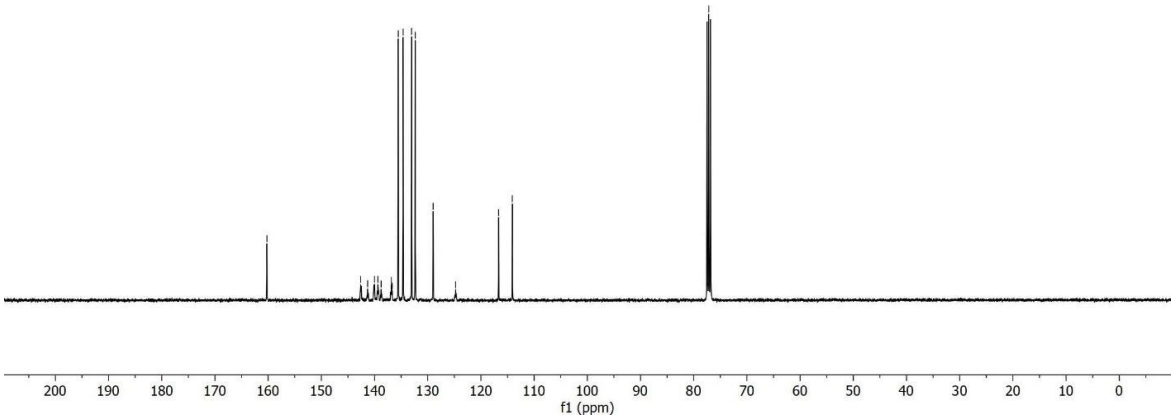
^{1}H NMR ($CDCl_3$, 400 MHz)

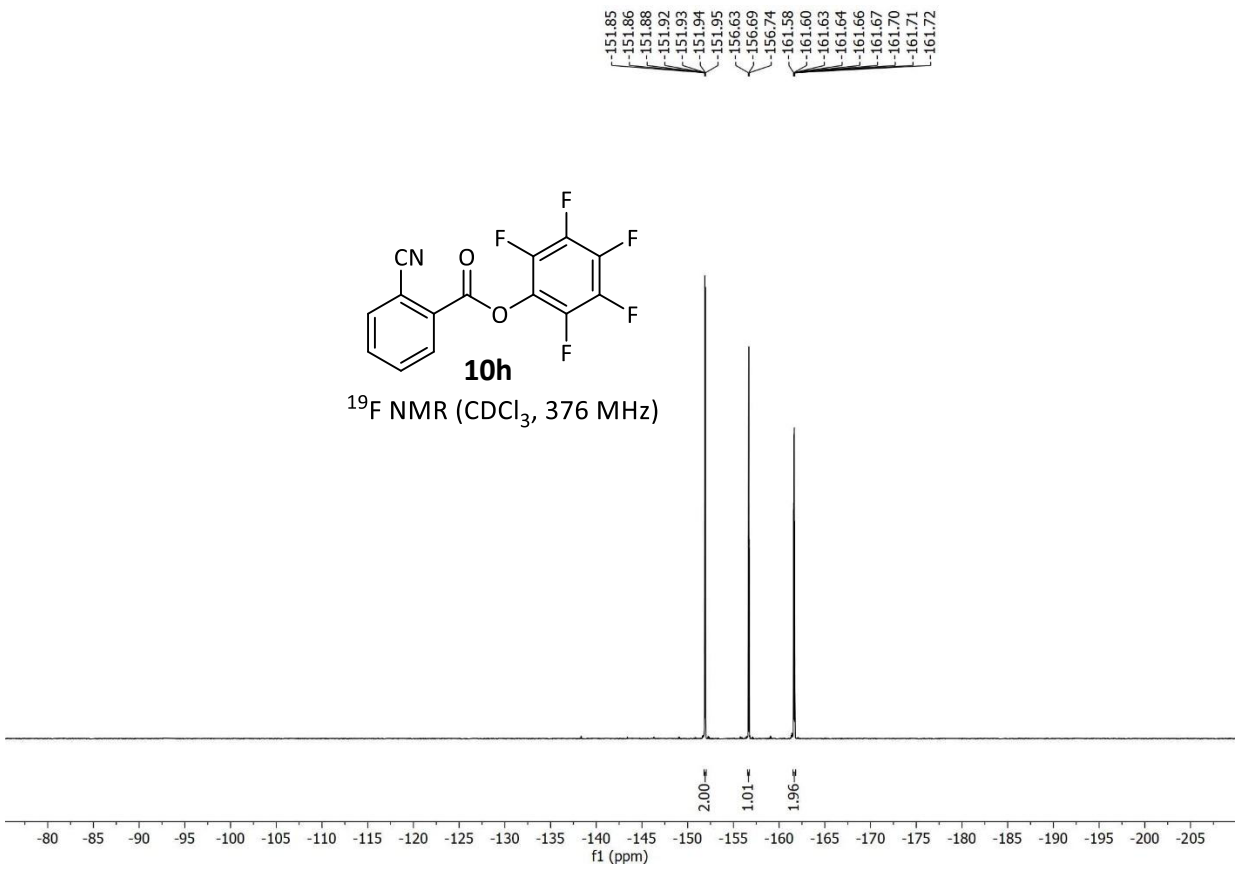




10h

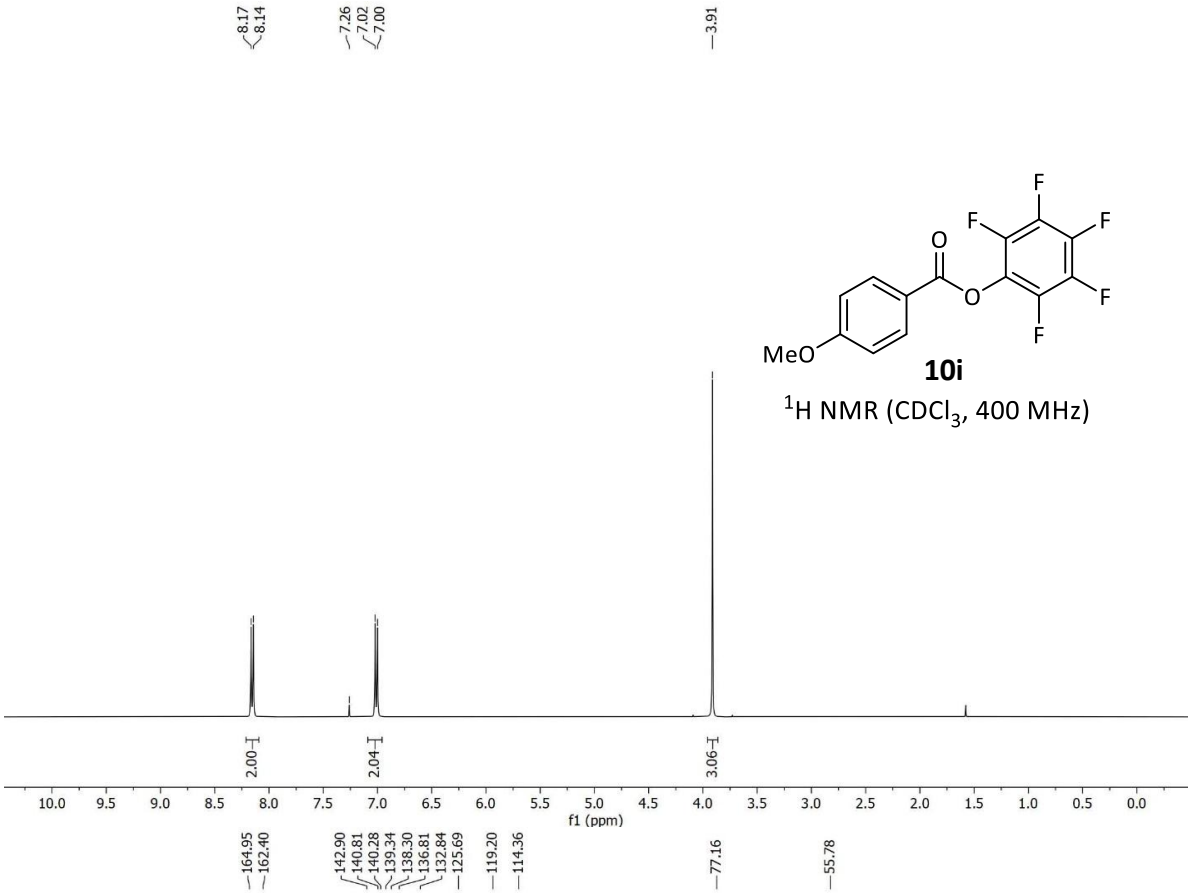
^{13}C NMR ($CDCl_3$, 100 MHz)





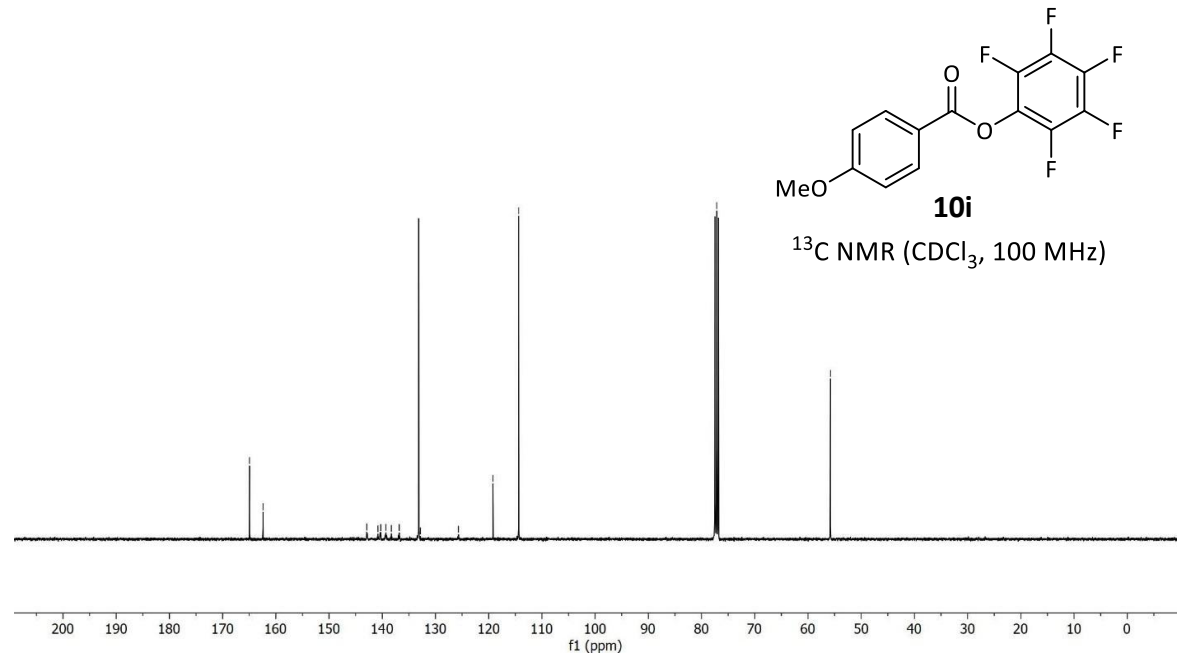
10h

^{19}F NMR ($CDCl_3$, 376 MHz)



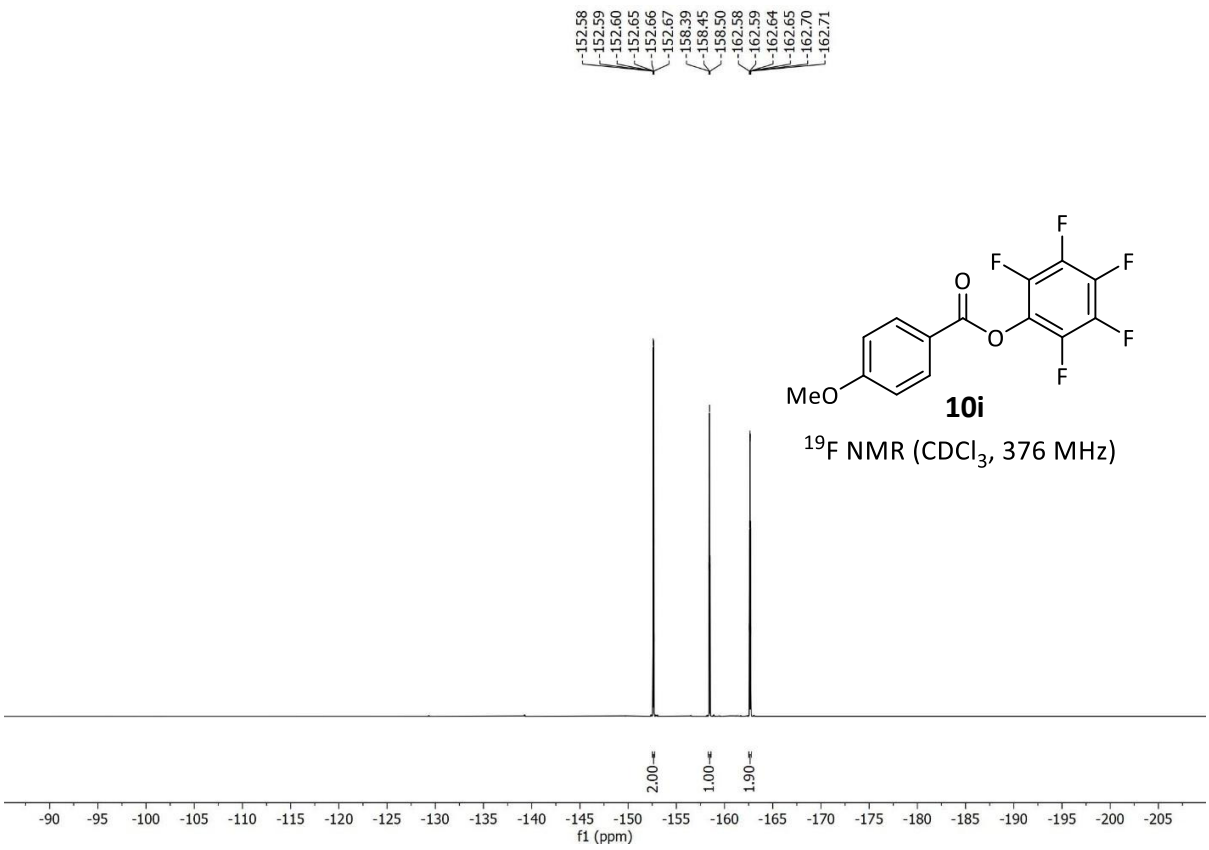
10i

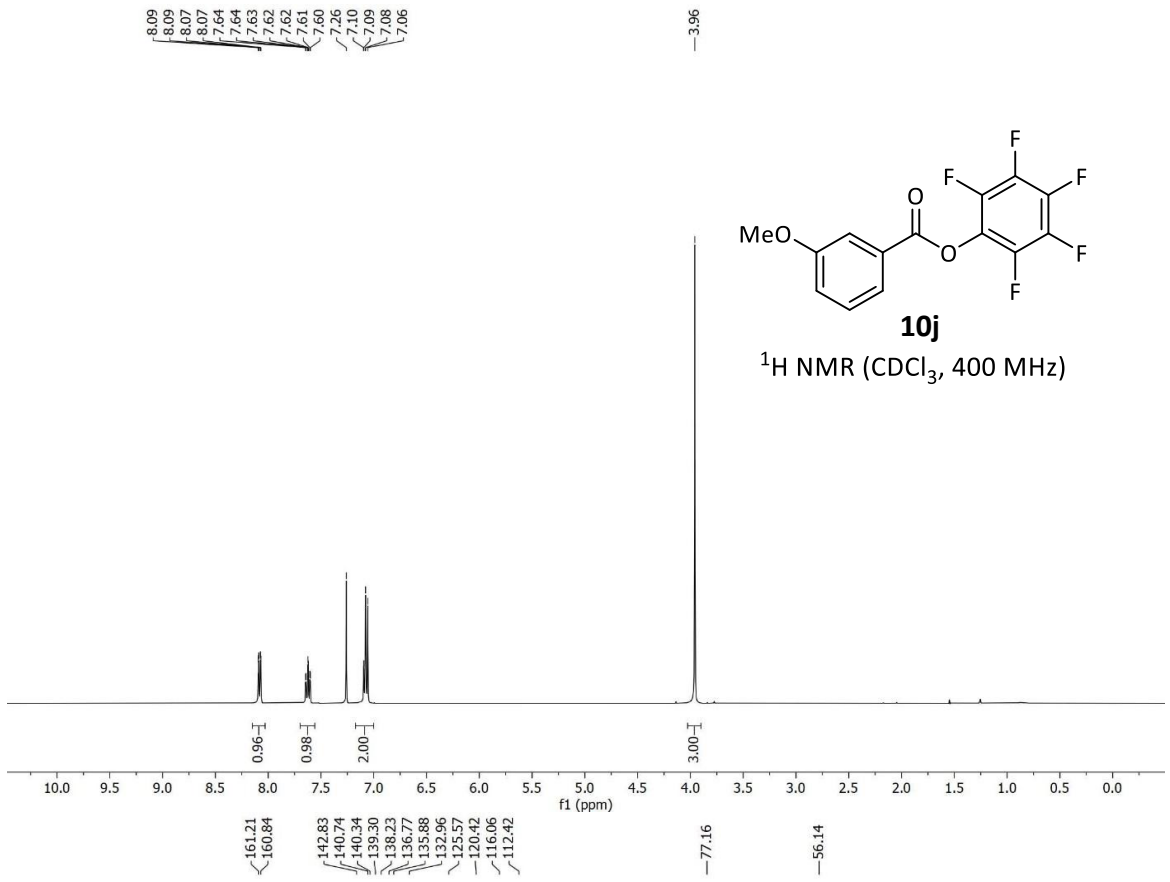
^{1}H NMR ($CDCl_3$, 400 MHz)



10i

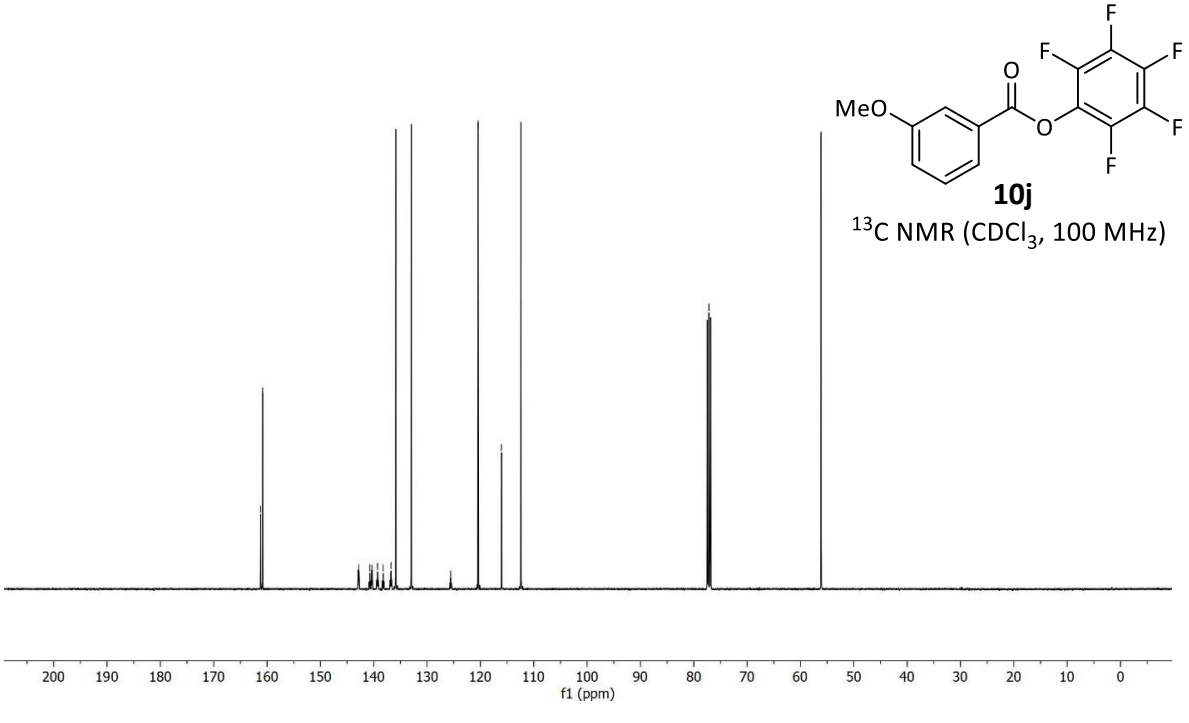
^{13}C NMR ($CDCl_3$, 100 MHz)


-152.58
-152.59
-152.60
-152.65
-152.66
-152.67
-158.39
-158.45
-158.50
-162.58
-162.59
-162.64
-162.65
-162.70
-162.71
F
F
F
O
O
F
F
MeO
10i
19F NMR (CDCl3, 376 MHz)
2.00
1.00
1.90
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)



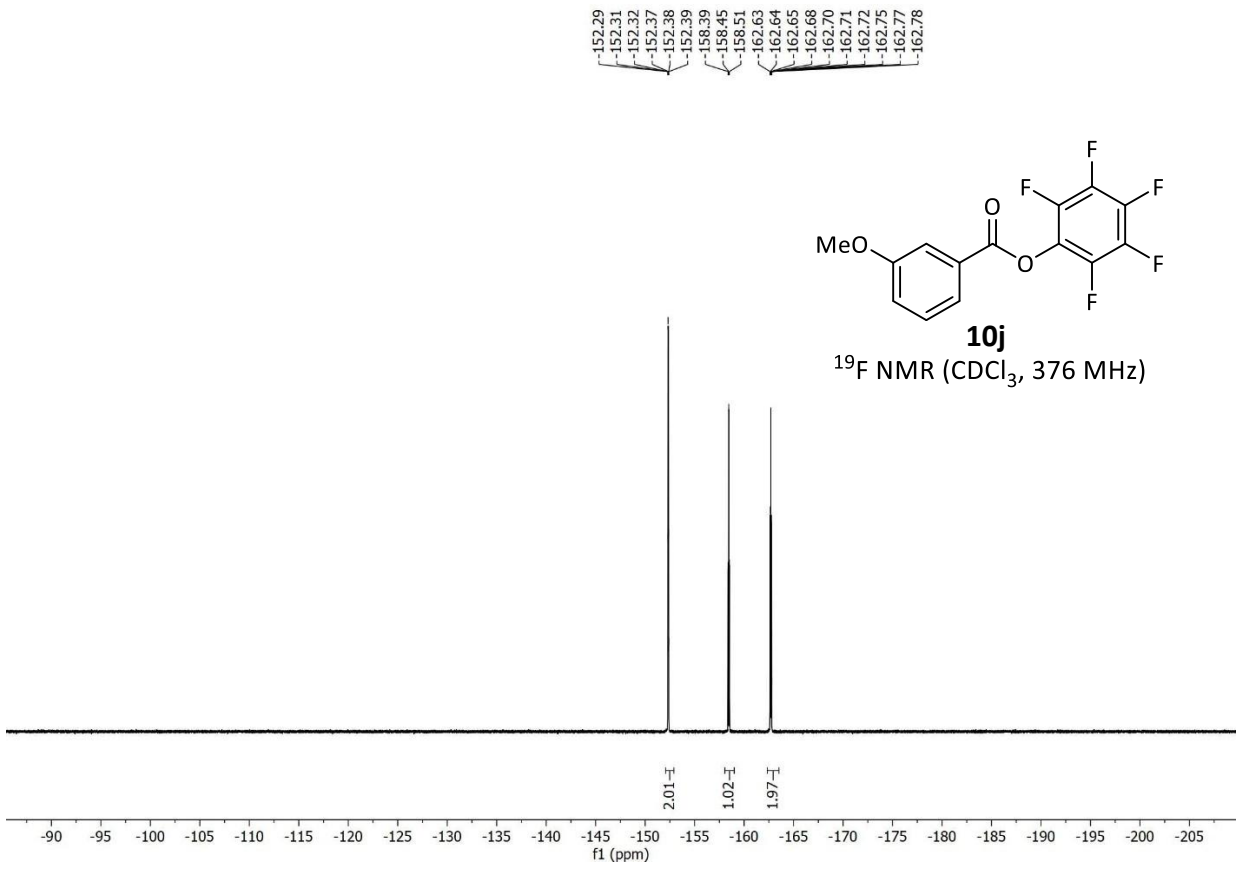
10j

^{1}H NMR ($CDCl_3$, 400 MHz)



10j

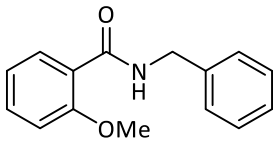
^{13}C NMR ($CDCl_3$, 100 MHz)



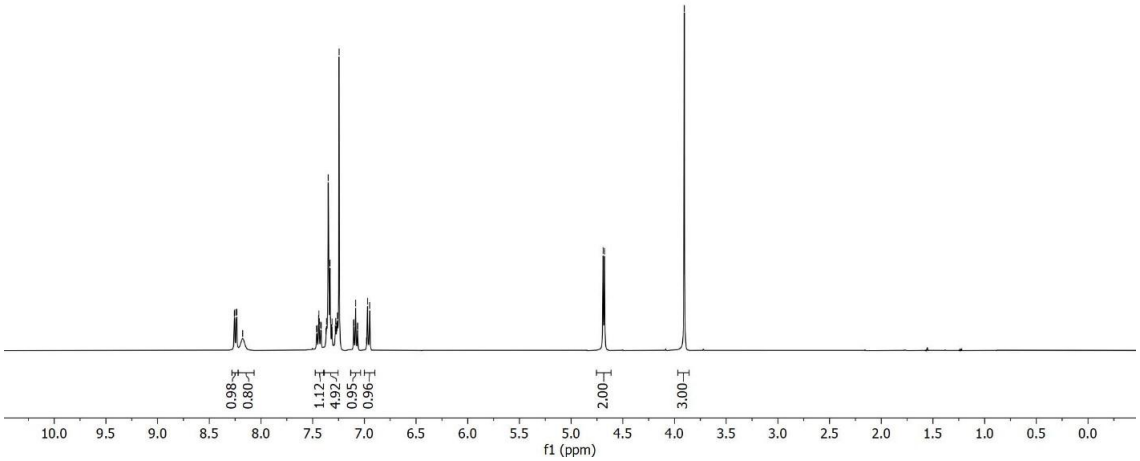
10j

^{19}F NMR ($CDCl_3$, 376 MHz)

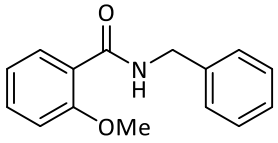
10k – amide



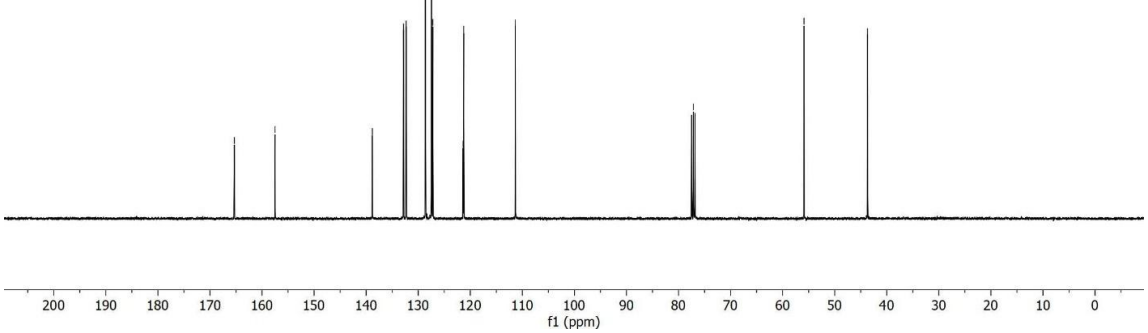
^{1}H NMR ($CDCl_3$, 400 MHz)

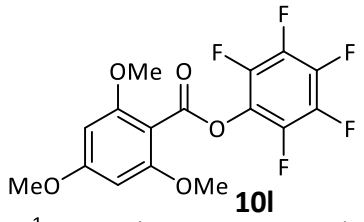


10k – amide



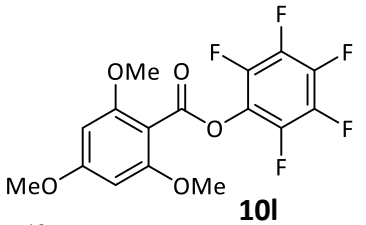
^{13}C NMR ($CDCl_3$, 100 MHz)





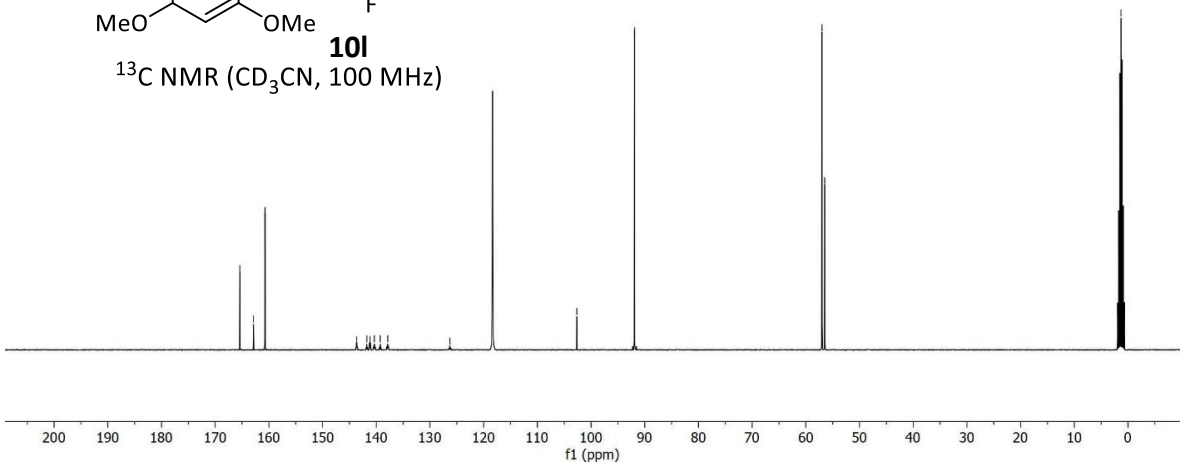
10l

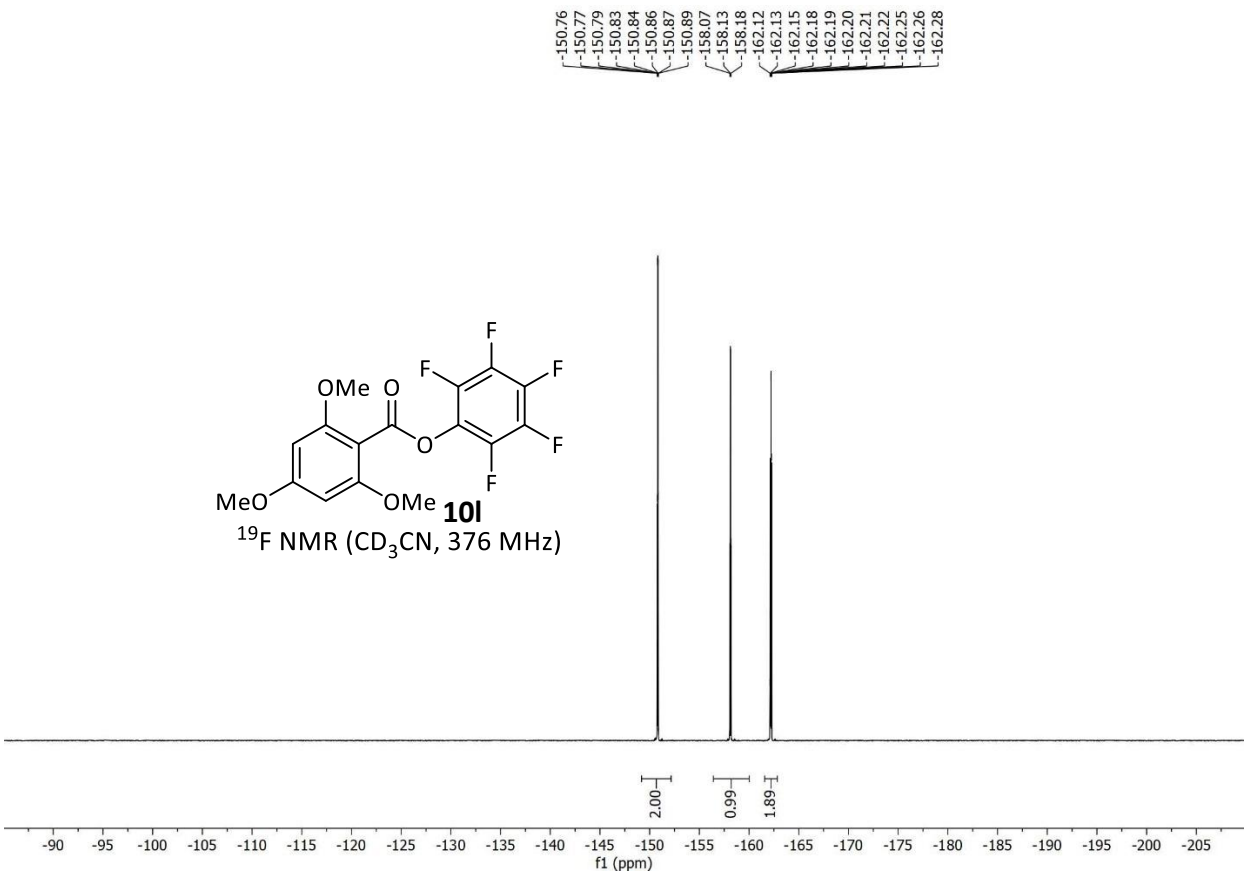
^{1}H NMR (CD_3CN, 400 MHz)



10l

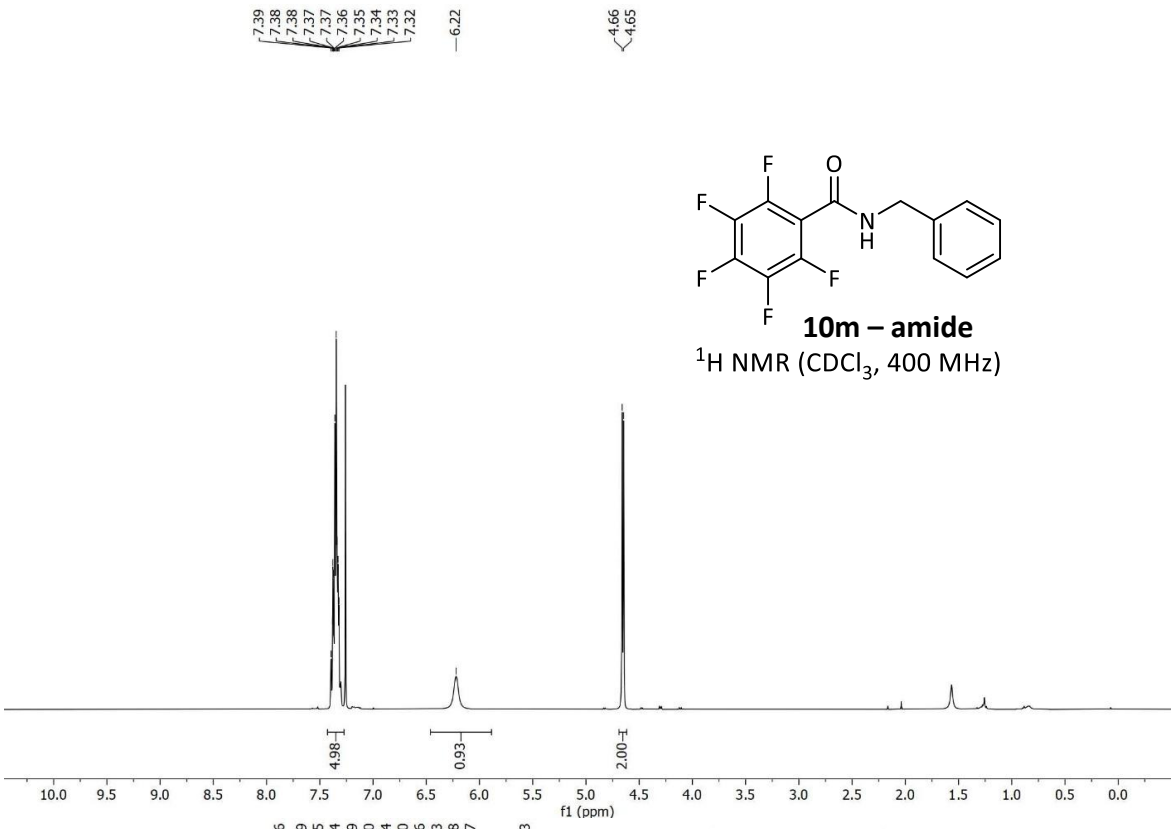
^{13}C NMR (CD_3CN, 100 MHz)





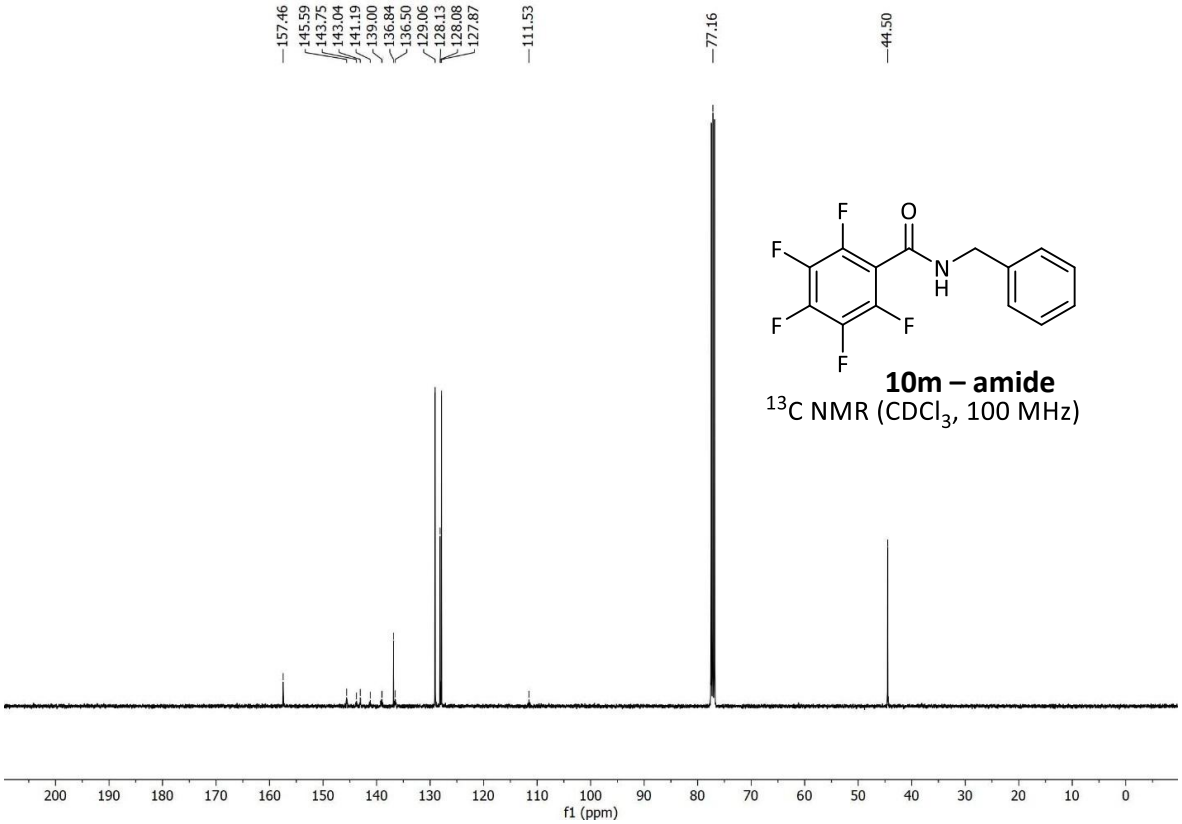
10l

^{19}F NMR (CD_3CN, 376 MHz)



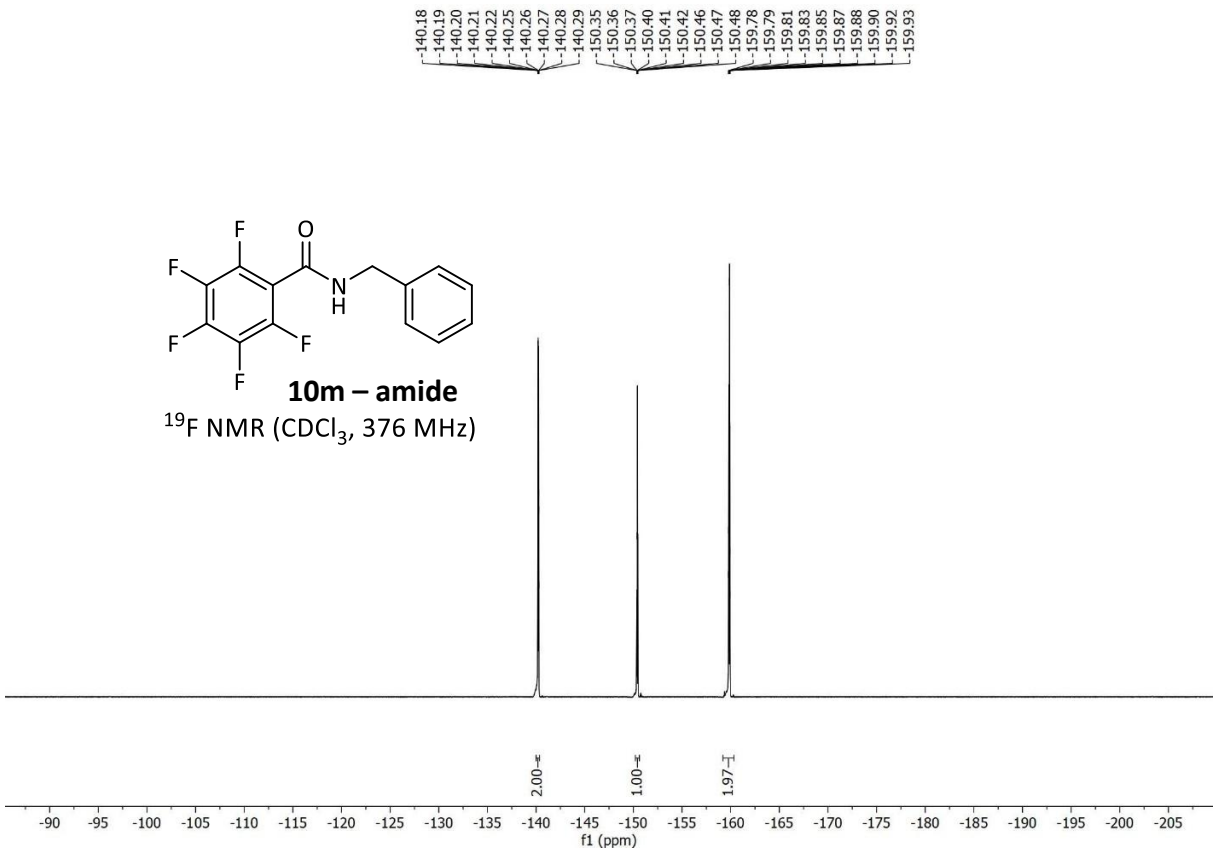
10m – amide

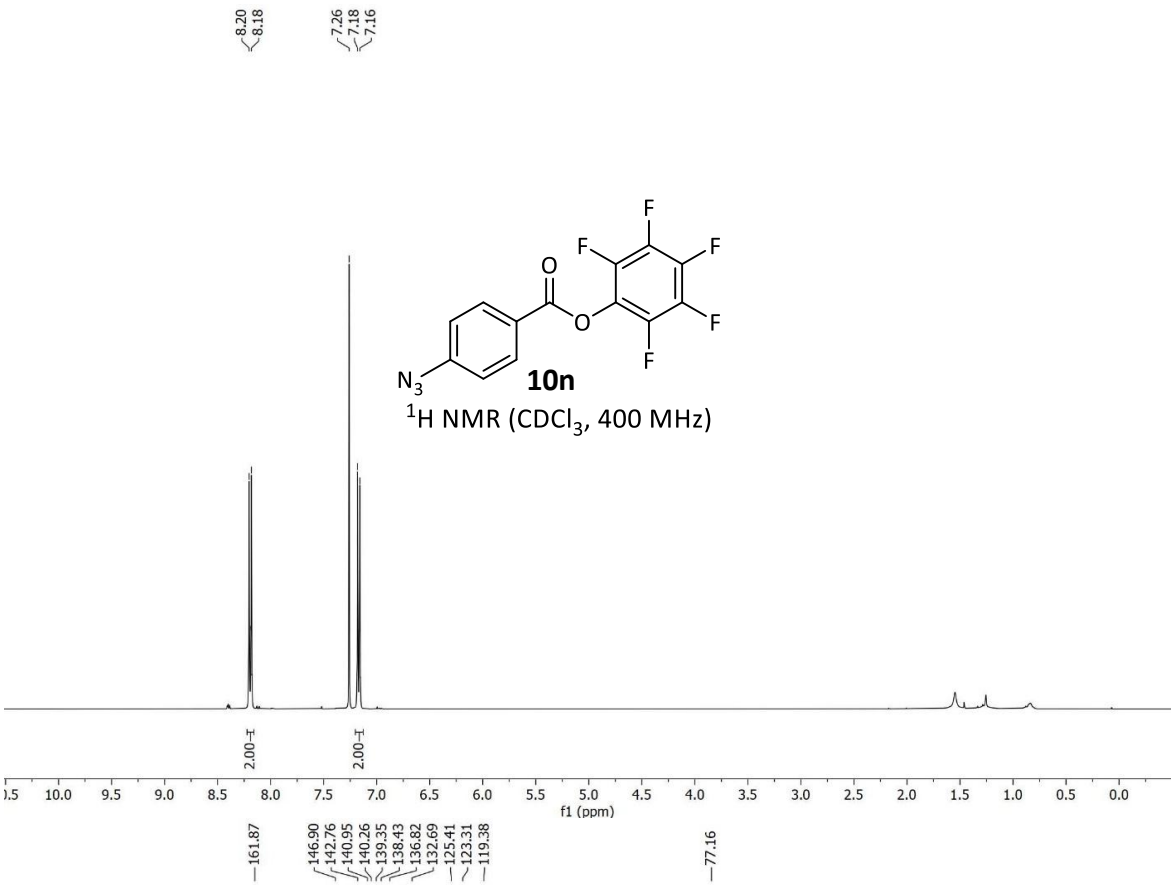
^{1}H NMR ($CDCl_3$, 400 MHz)

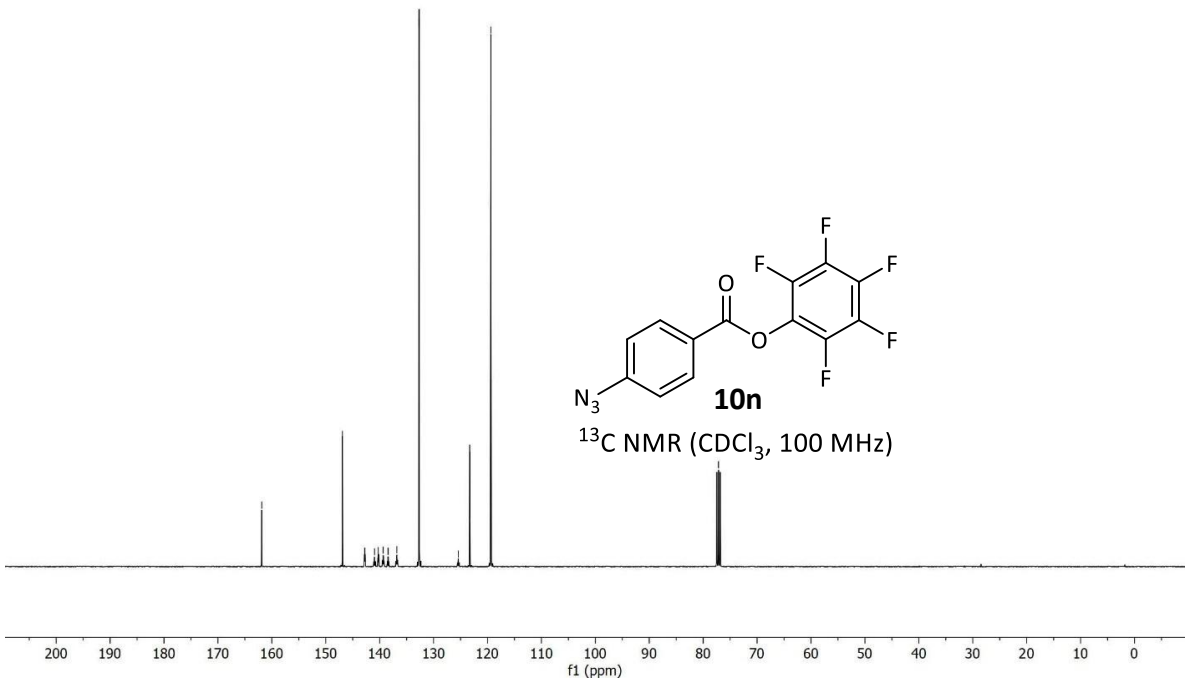


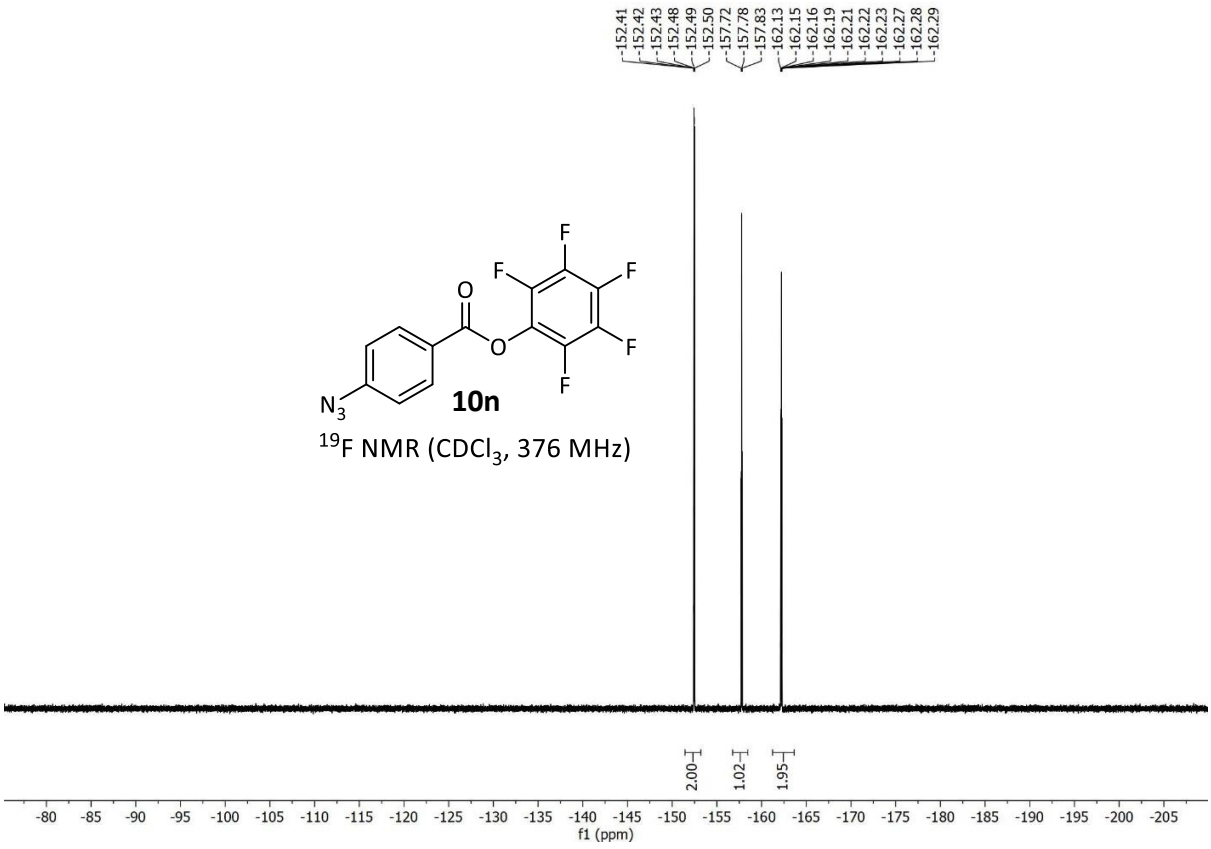
10m – amide

^{13}C NMR ($CDCl_3$, 100 MHz)


-140.18
-140.19
-140.20
-140.21
-140.22
-140.25
-140.26
-140.27
-140.28
-140.29
-150.35
-150.36
-150.37
-150.40
-150.41
-150.42
-150.46
-150.47
-150.48
-159.78
-159.79
-159.81
-159.83
-159.85
-159.87
-159.88
-159.90
-159.92
-159.93
F
O
F
N
H
F
F
F
10m – amide
^{19}F NMR ($CDCl_3$, 376 MHz)
2.00
1.00
1.97
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)

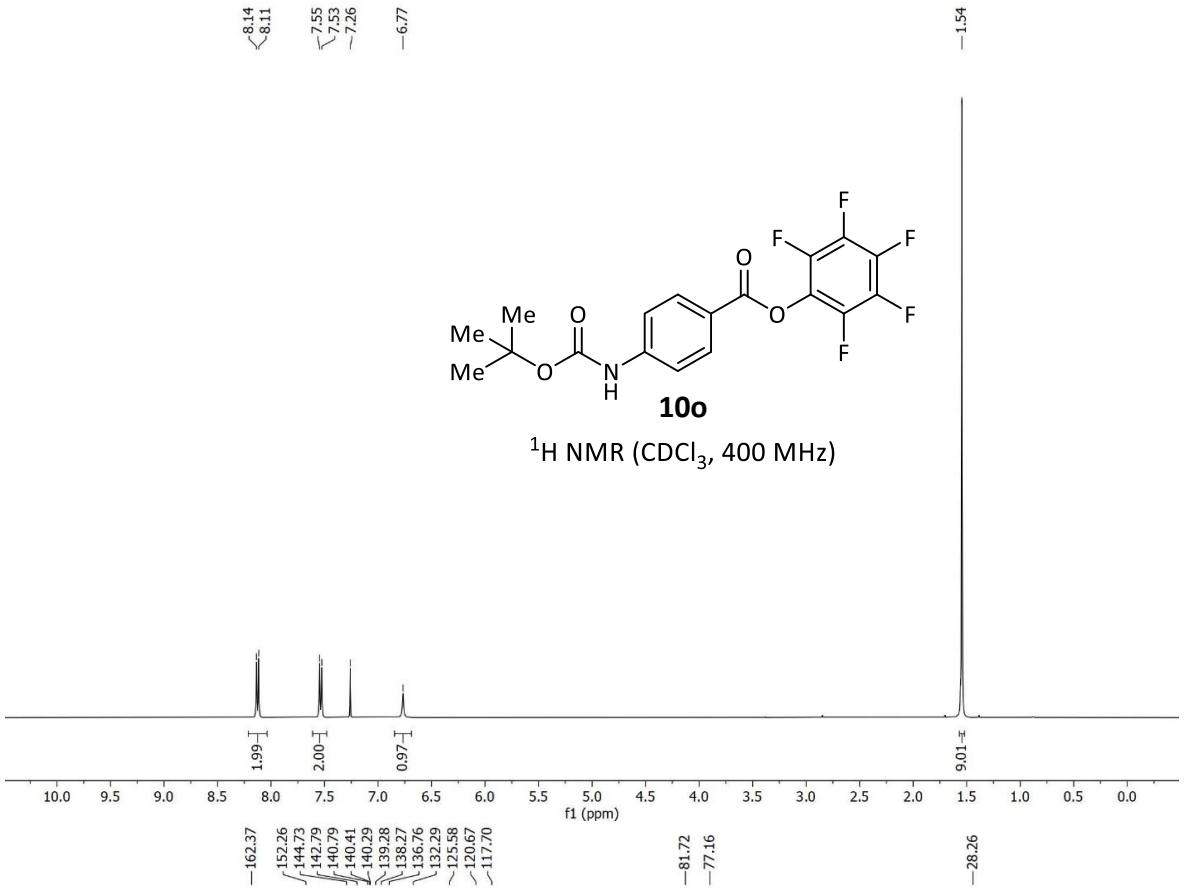

8.20
8.18
7.26
7.18
7.16
F
F
F
F
F
O
O
N3
10n
1H NMR (CDCl3, 400 MHz)
2.00
2.00
f1 (ppm)
161.87
146.90
142.76
140.95
140.26
139.35
138.43
136.82
132.69
125.41
123.31
119.38
77.16


F
F
F
F
F
O
O
N3
10n
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



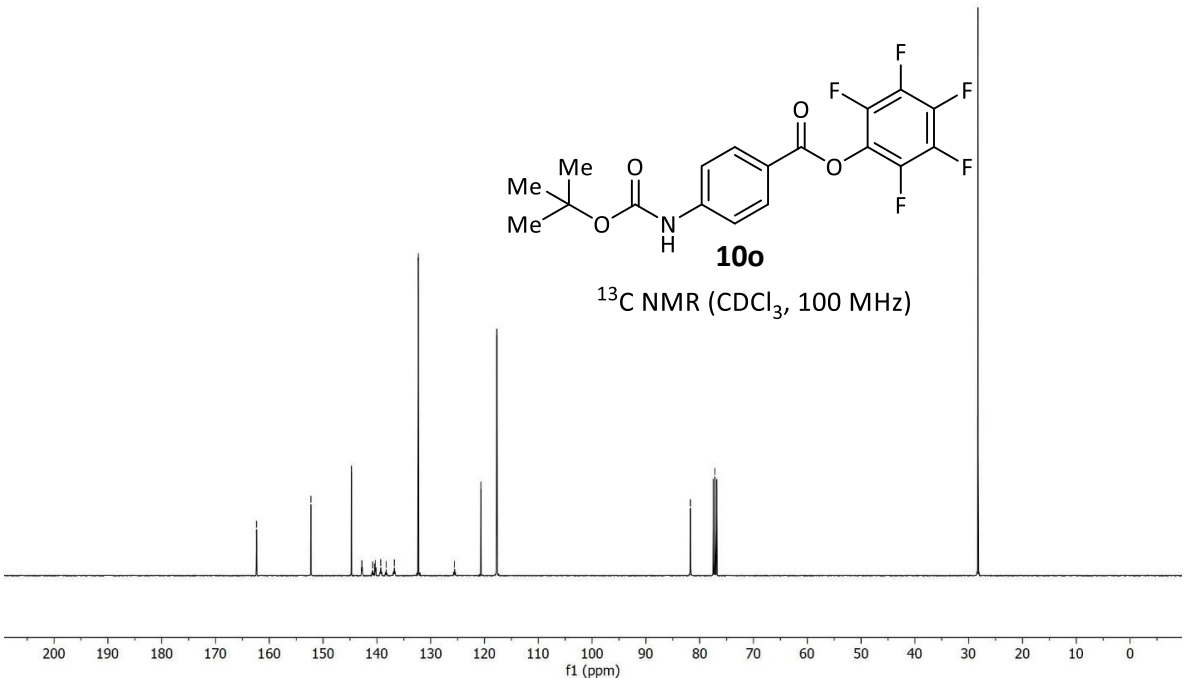
10n

^{19}F NMR ($CDCl_3$, 376 MHz)



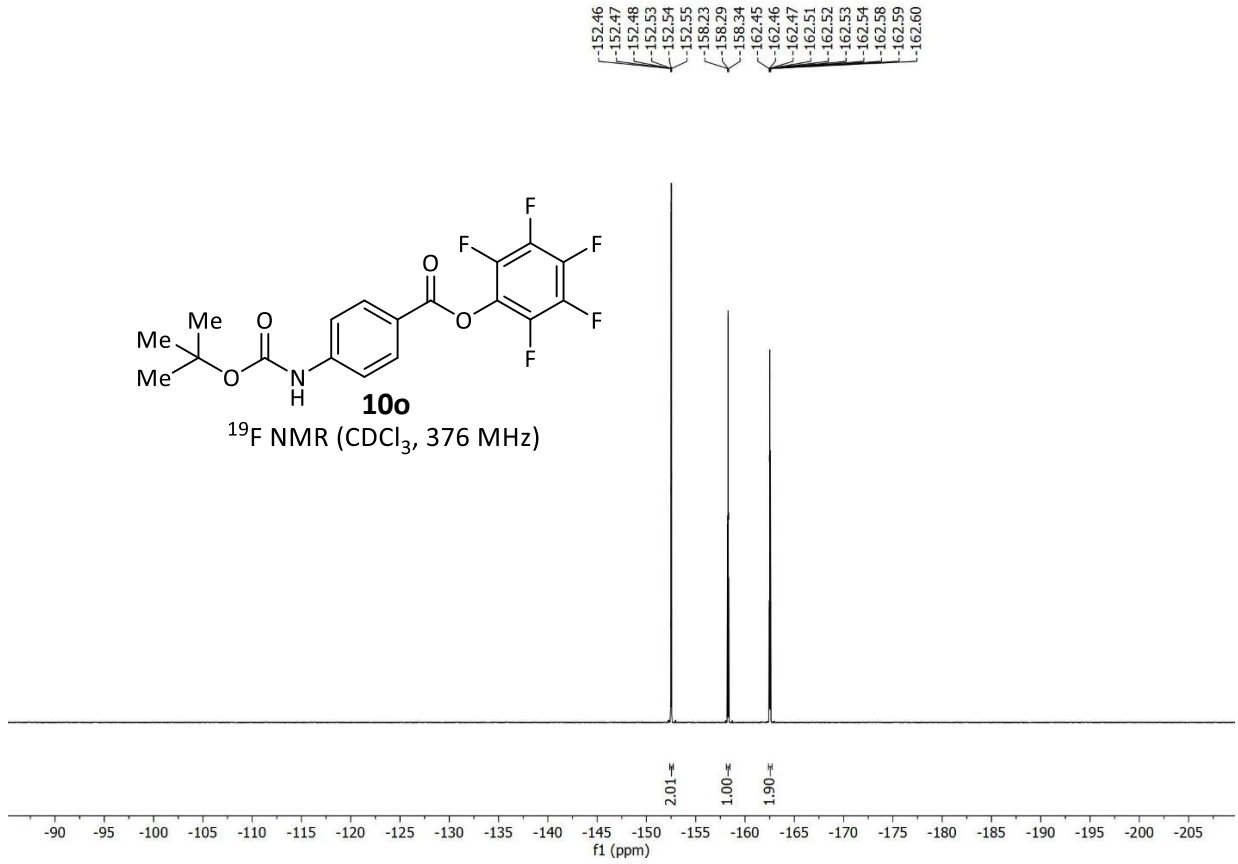
10o

^{1}H NMR ($CDCl_3$, 400 MHz)



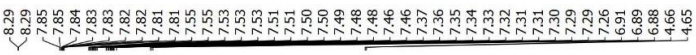
10o

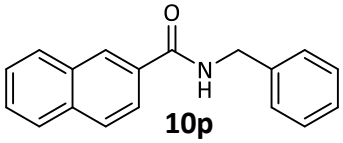
^{13}C NMR ($CDCl_3$, 100 MHz)



10o

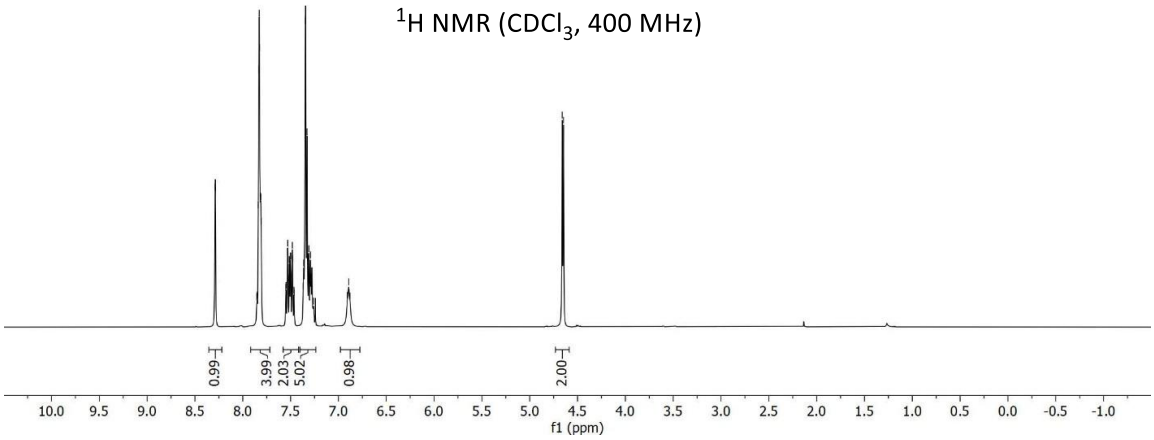
^{19}F NMR ($CDCl_3$, 376 MHz)

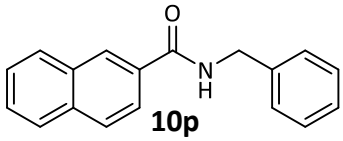




10p

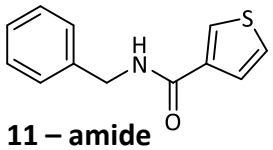
^{1}H NMR ($CDCl_3$, 400 MHz)





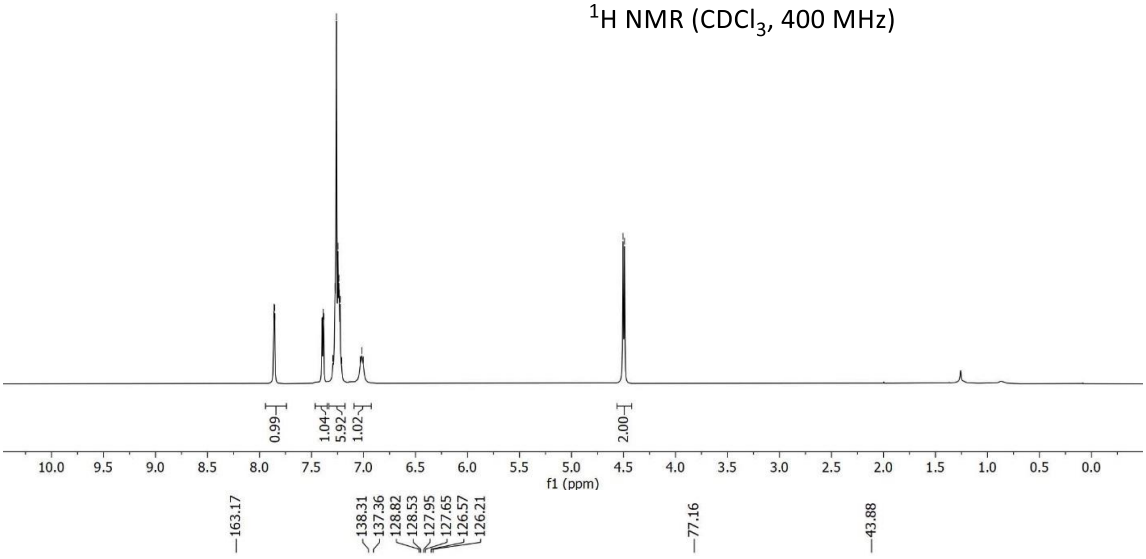
10p

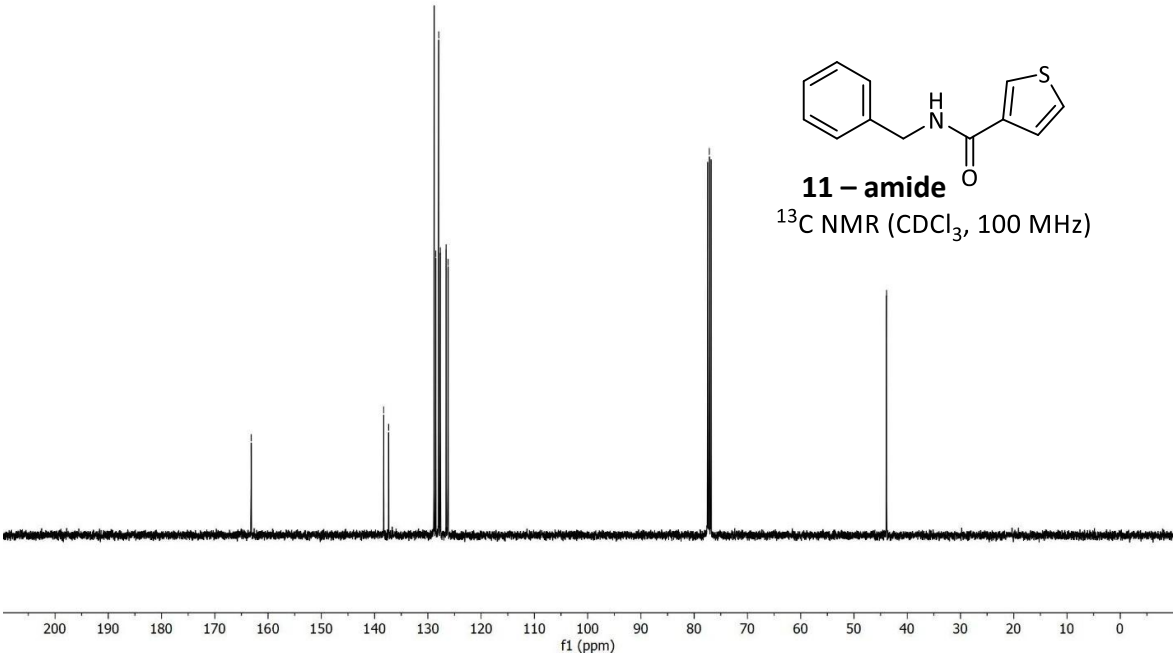
^{13}C NMR ($CDCl_3$, 100 MHz)



11 – amide

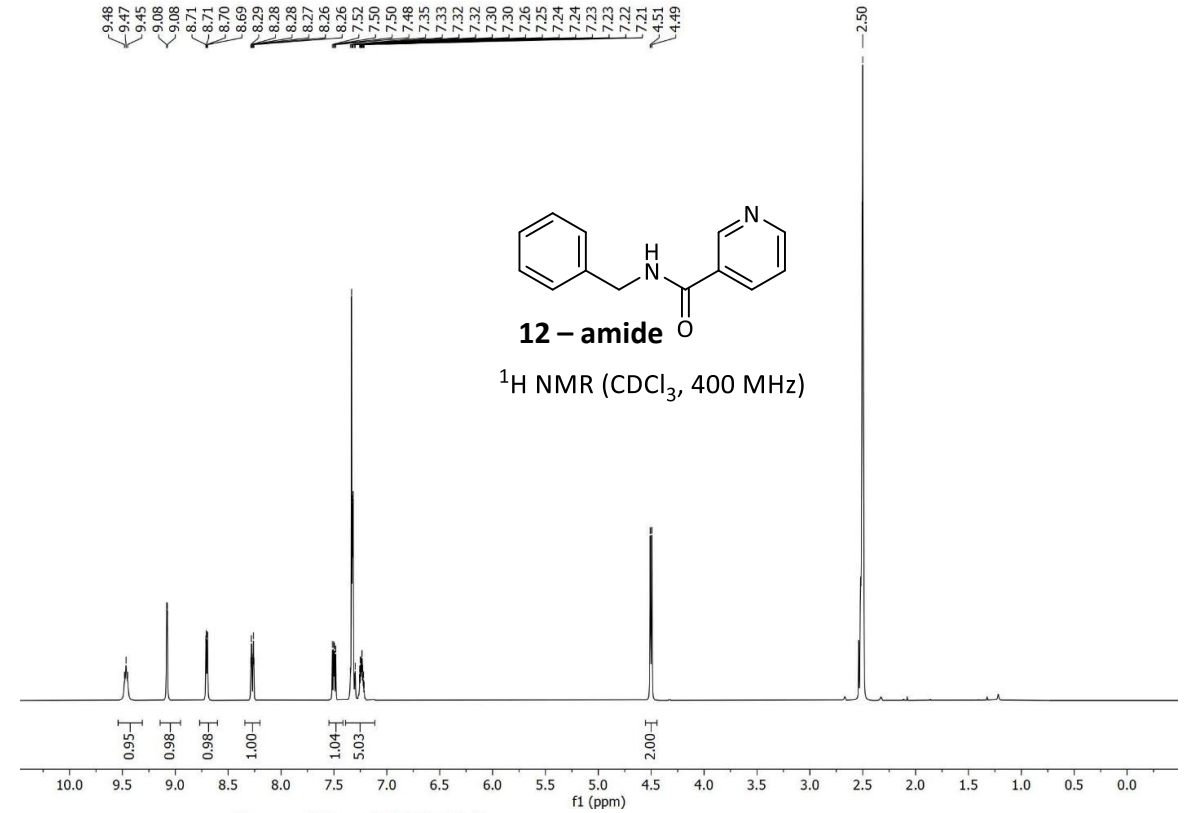
^{1}H NMR ($CDCl_3$, 400 MHz)



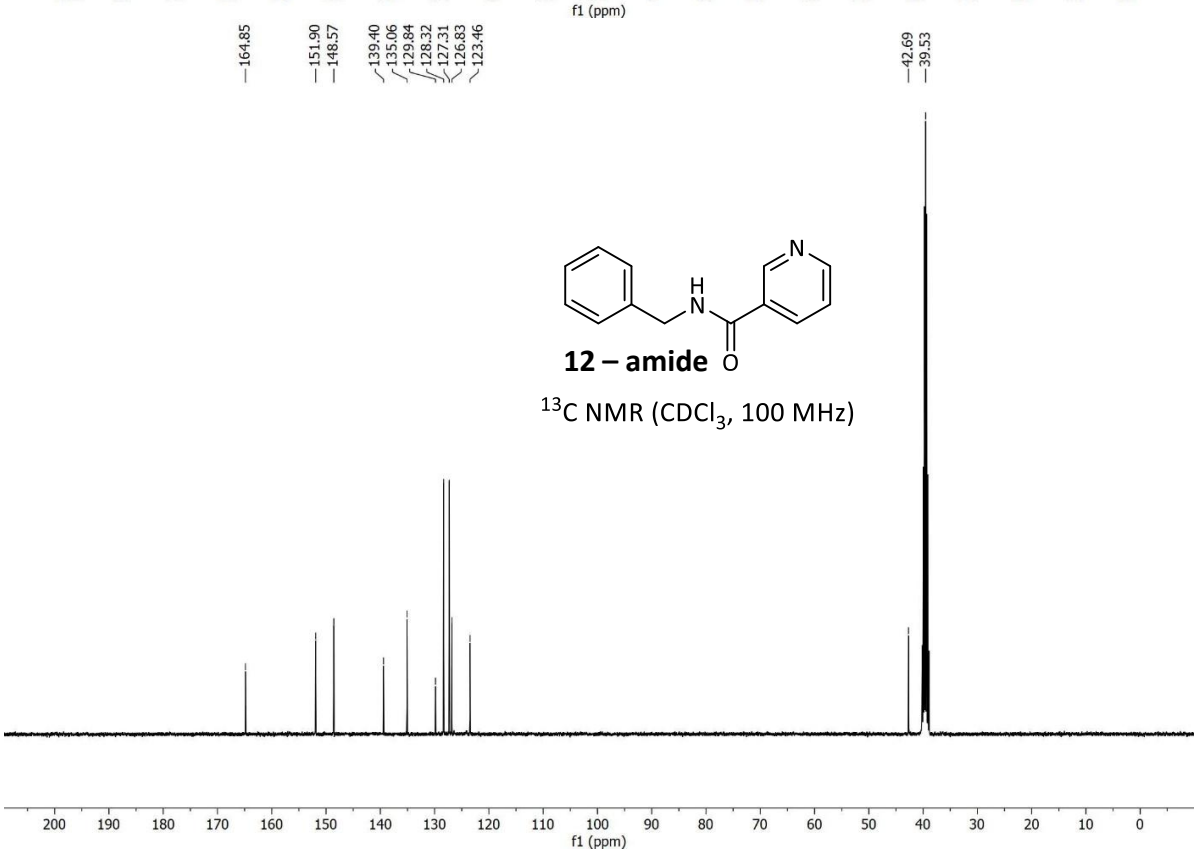


11 – amide

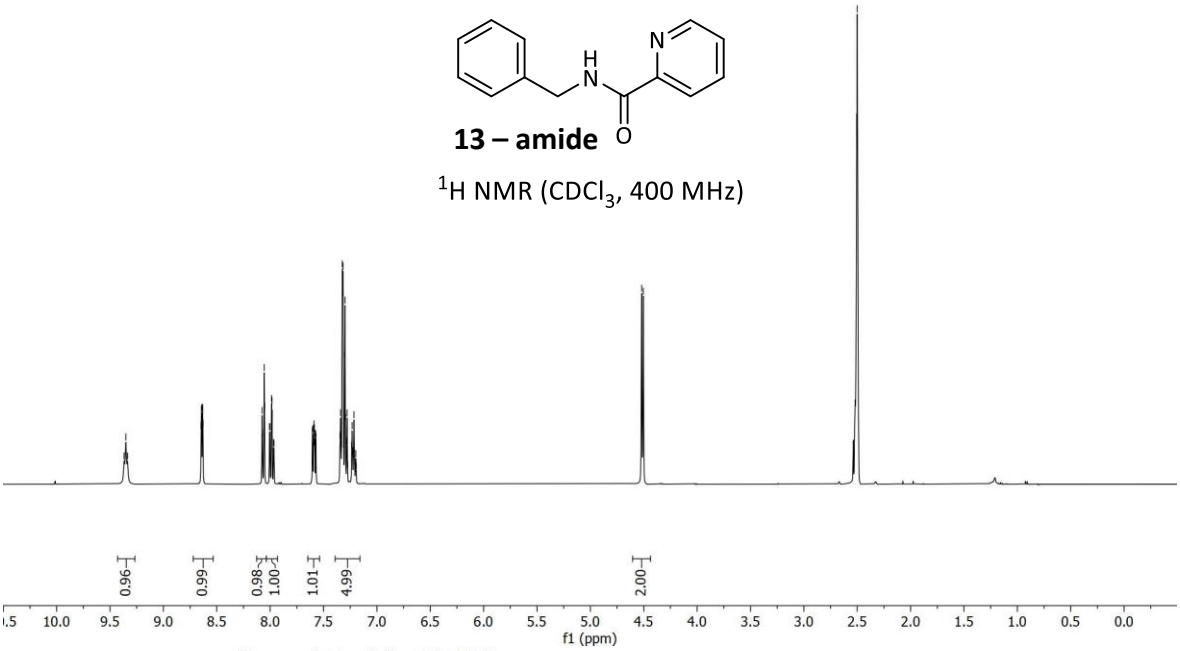
^{13}C NMR ($CDCl_3$, 100 MHz)

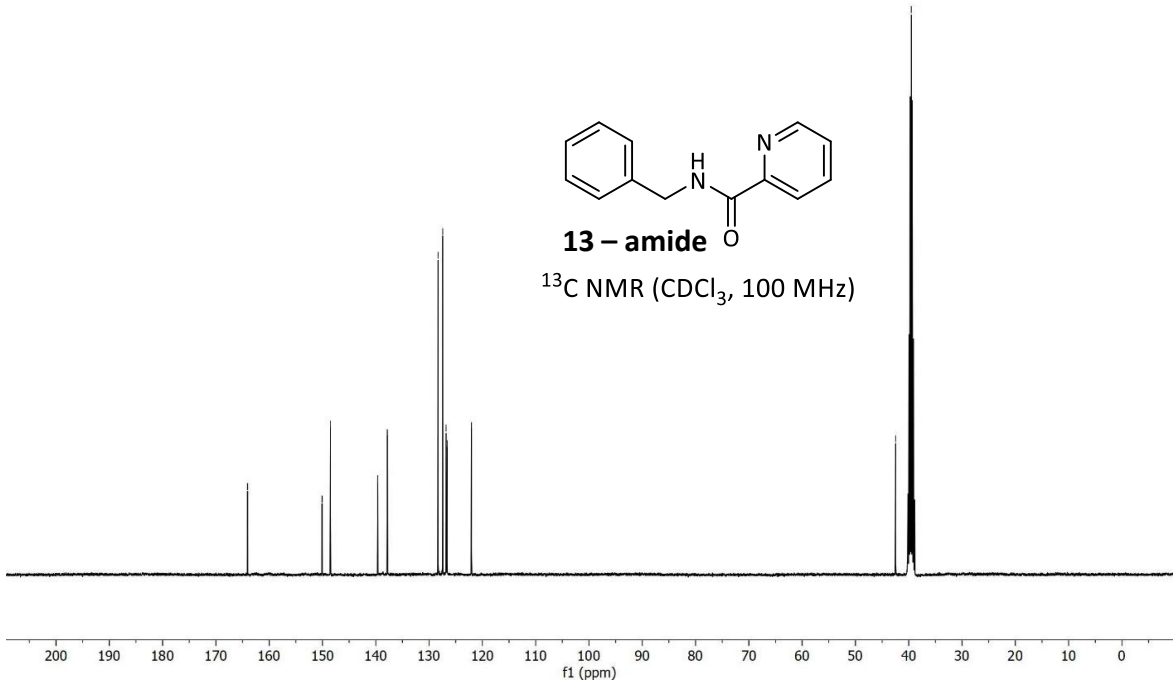


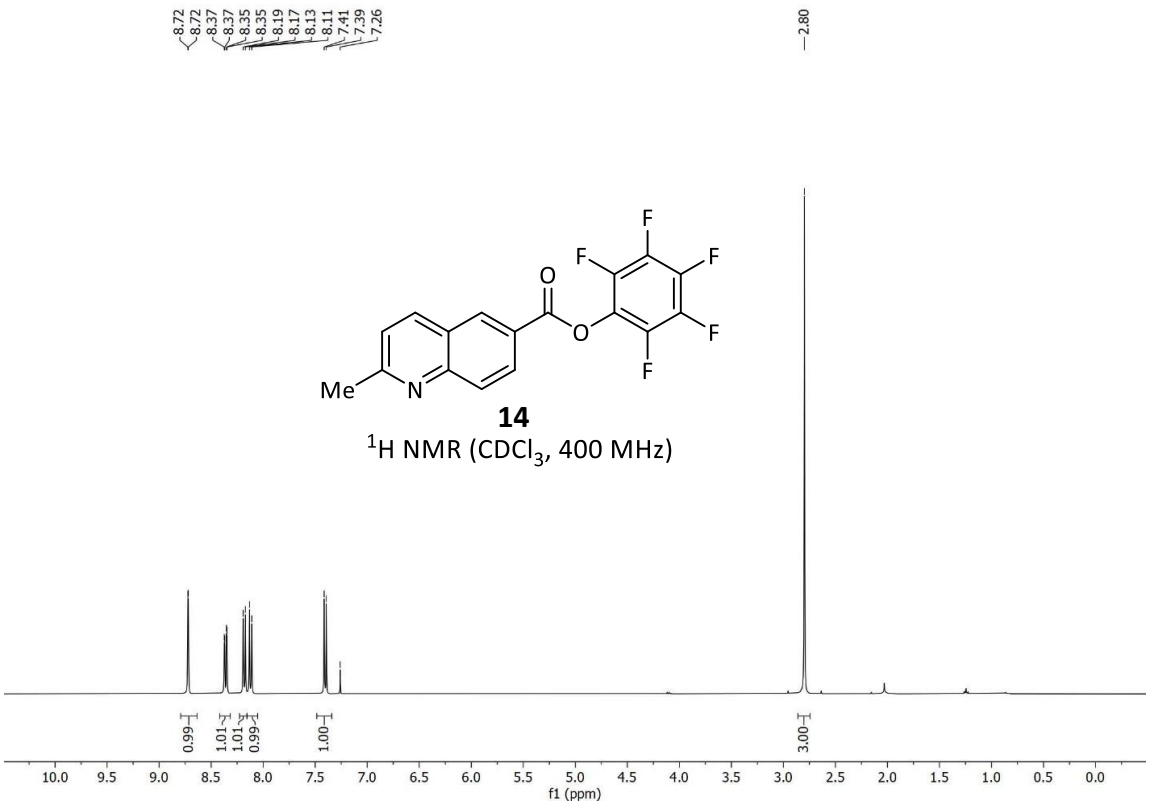
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)

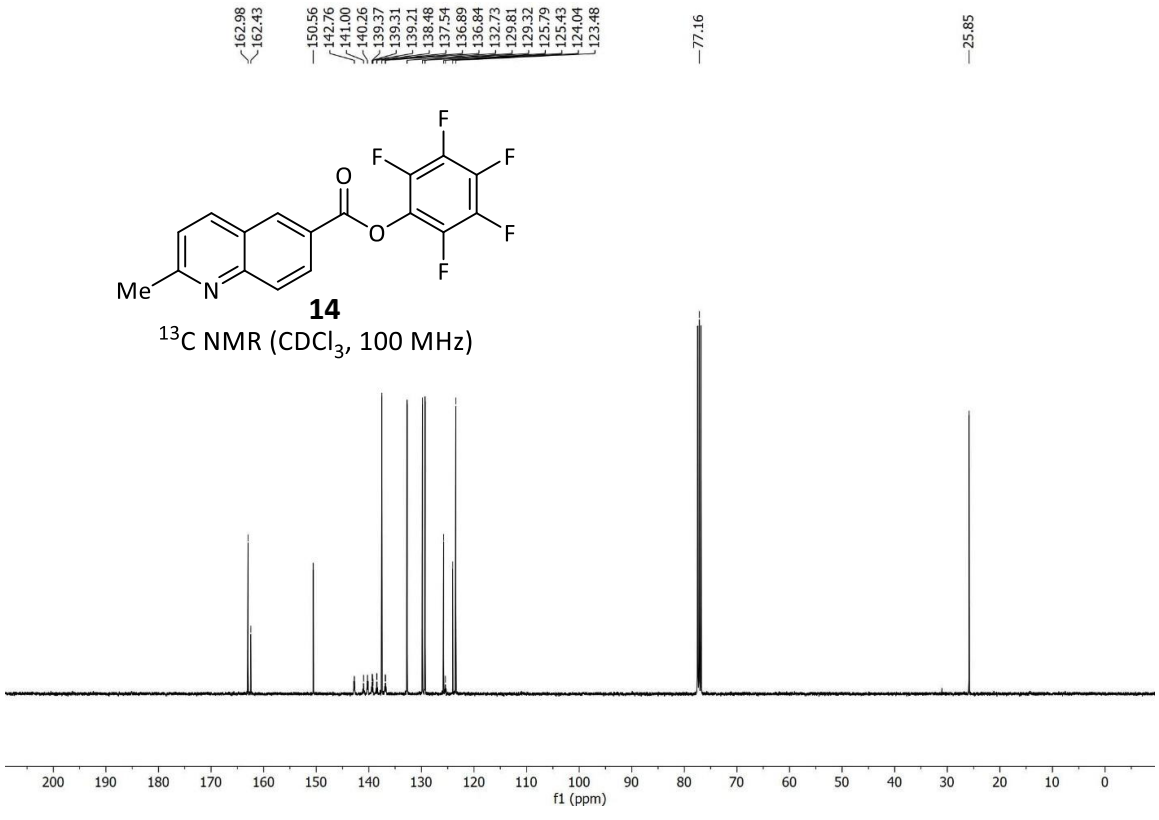

13 – amide
1H NMR (CDCl3, 400 MHz)
0.96
0.99
0.98
1.00
1.01
4.99
2.00
f1 (ppm)


164.05
150.07
148.51
139.63
137.84
128.31
127.43
126.81
126.59
122.06
42.47
39.53
13 – amide
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



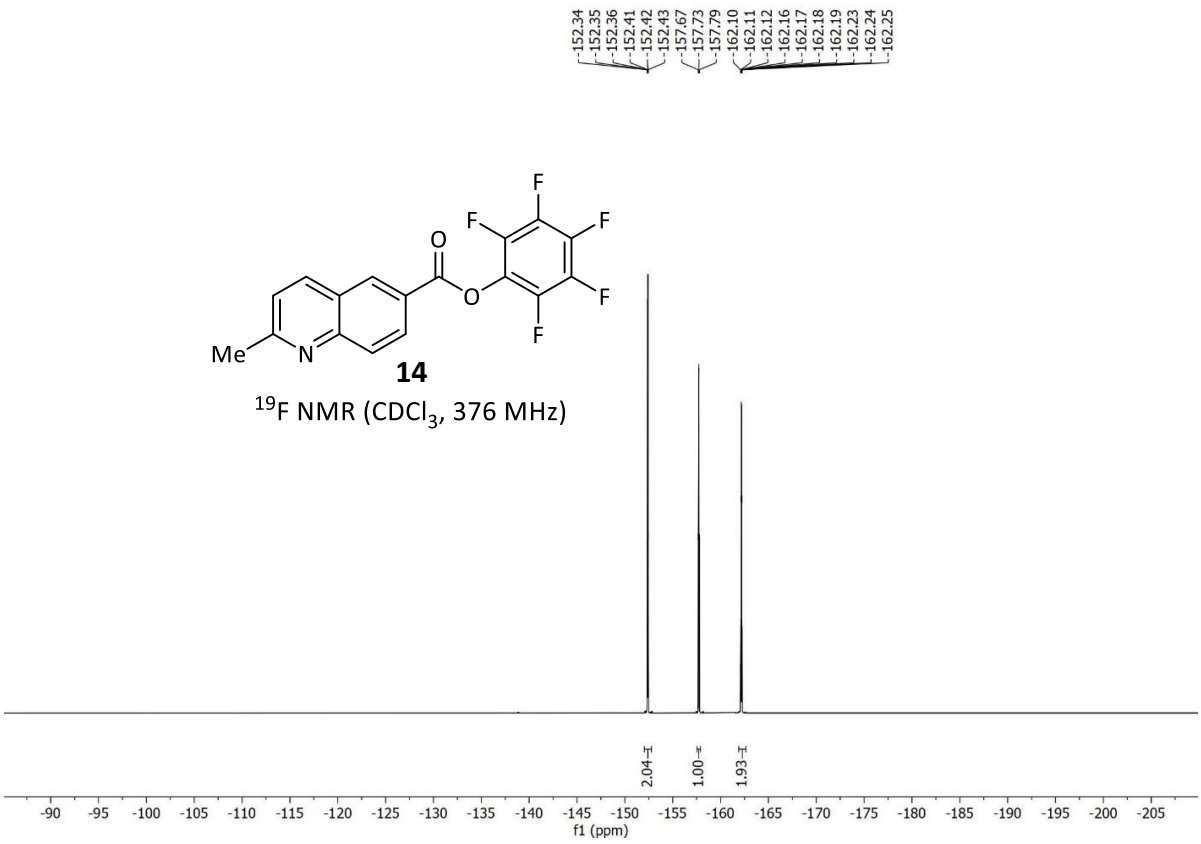
14

^{1}H NMR ($CDCl_3$, 400 MHz)



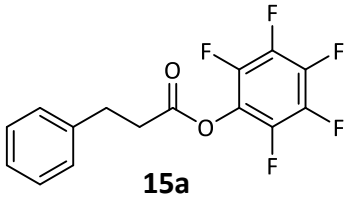
14

^{13}C NMR ($CDCl_3$, 100 MHz)



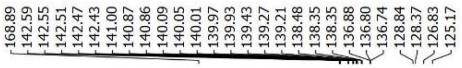
14

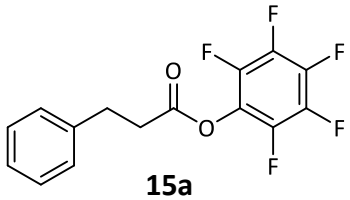
^{19}F NMR ($CDCl_3$, 376 MHz)



15a

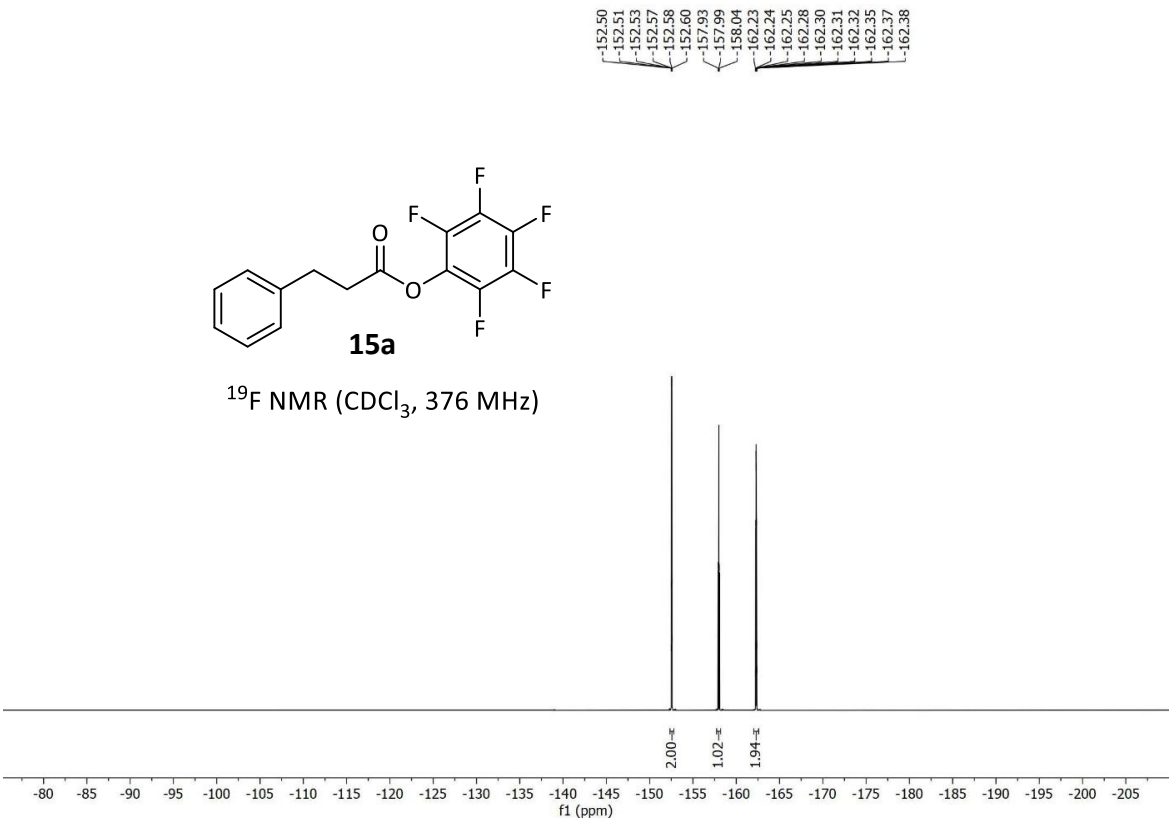
^{1}H NMR ($CDCl_3$, 400 MHz)





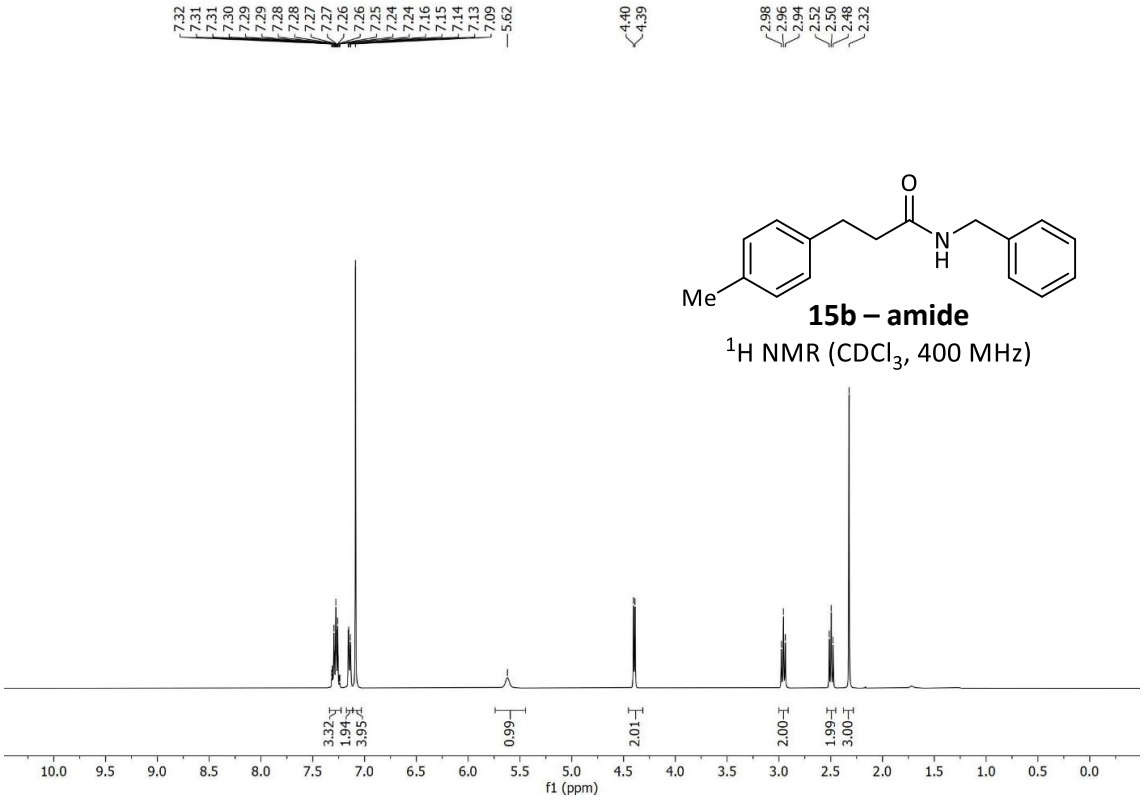
15a

^{13}C NMR ($CDCl_3$, 100 MHz)



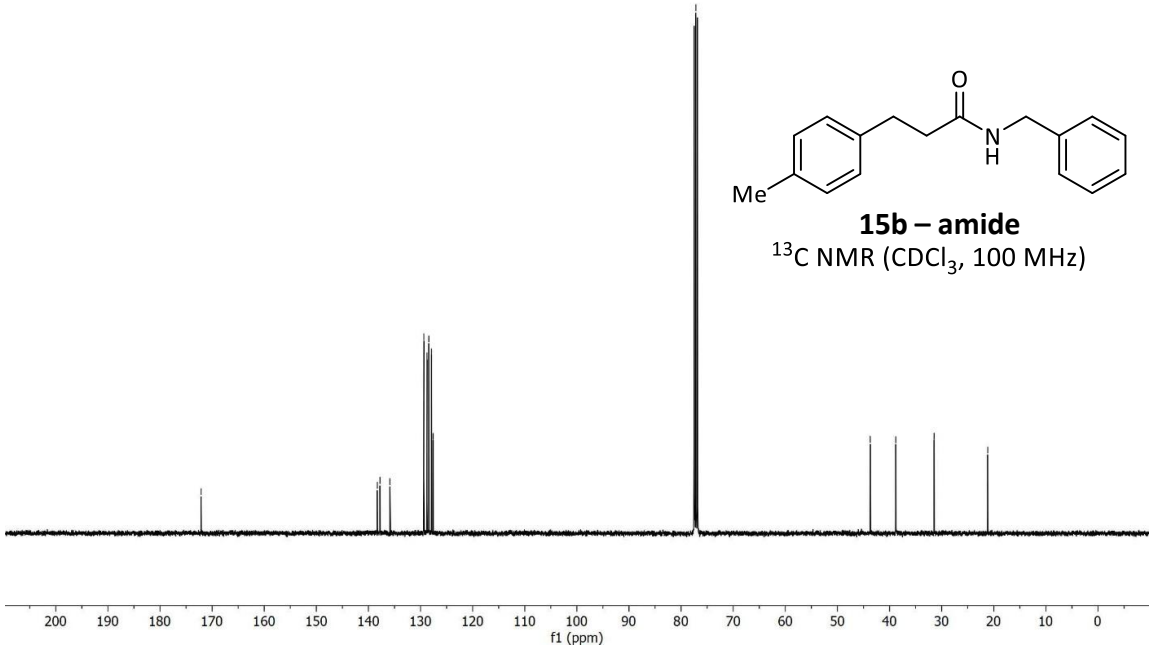
15a

^{19}F NMR ($CDCl_3$, 376 MHz)



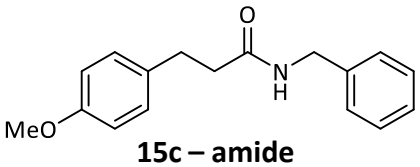
15b – amide

^{1}H NMR ($CDCl_3$, 400 MHz)



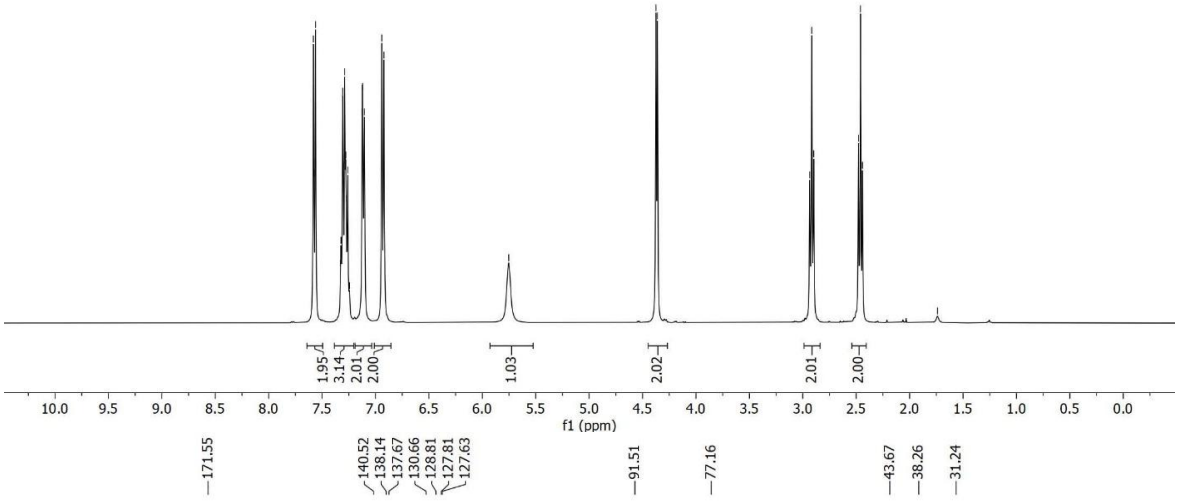
15b – amide

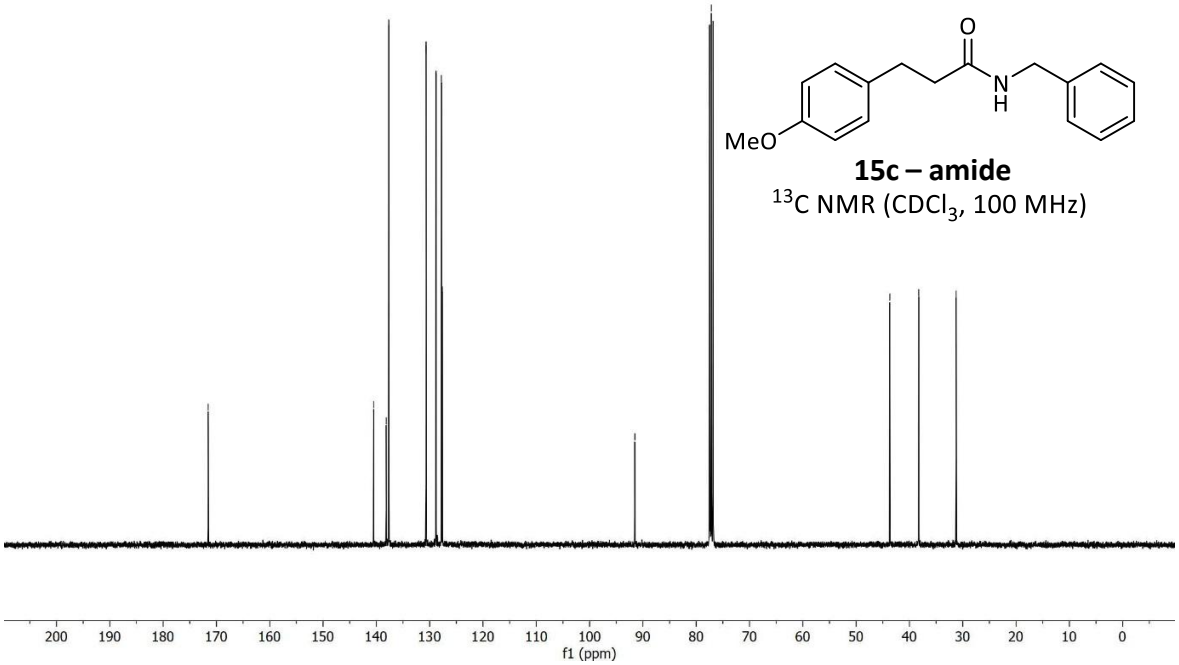
^{13}C NMR ($CDCl_3$, 100 MHz)



15c – amide

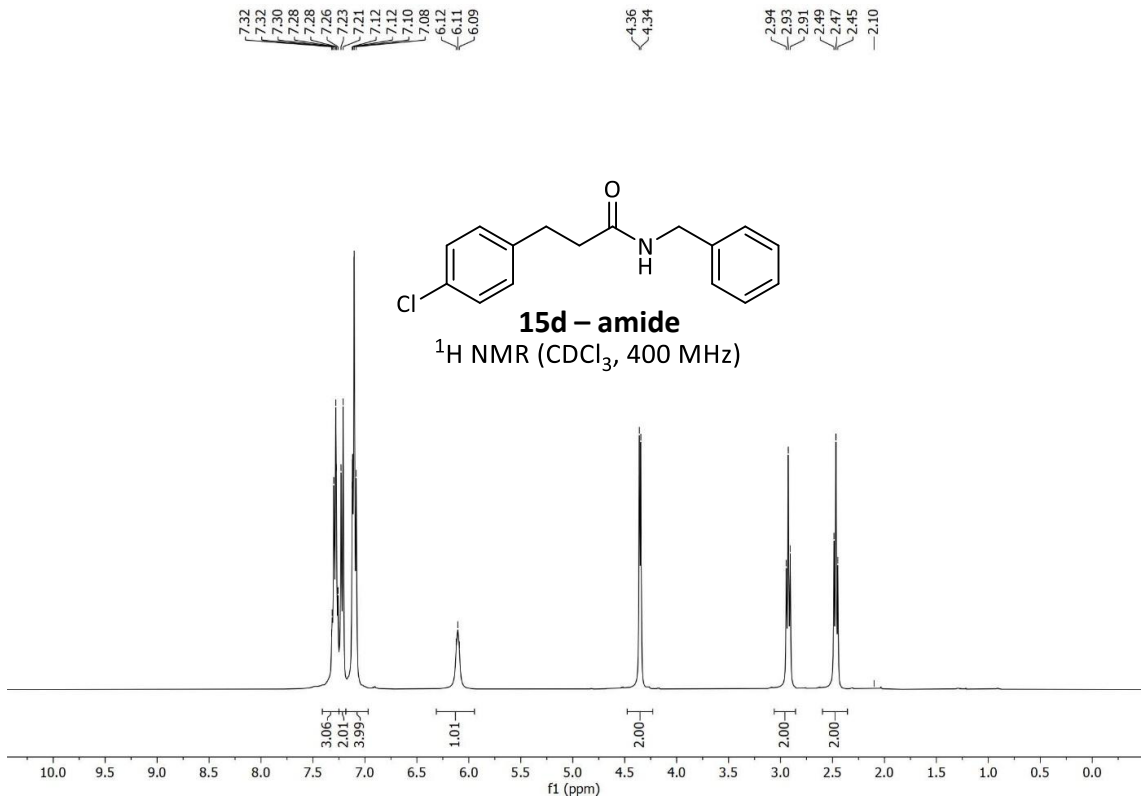
^{1}H NMR ($CDCl_3$, 400 MHz)

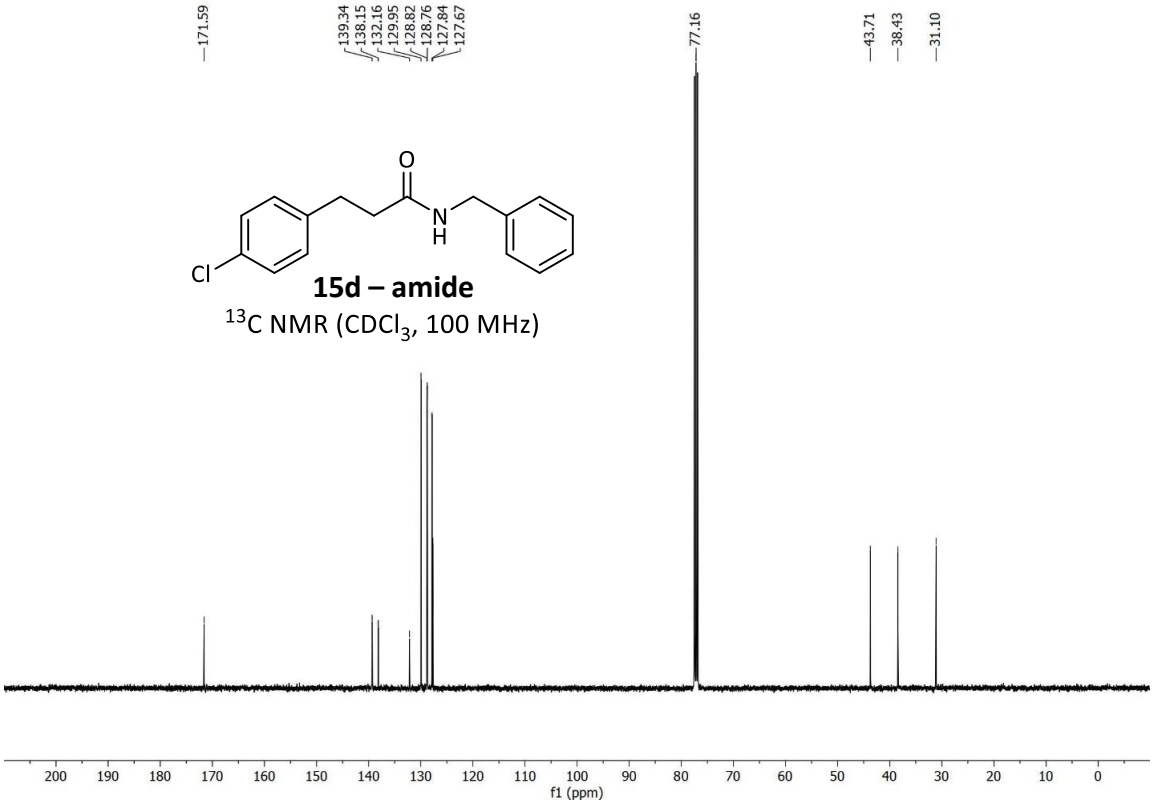


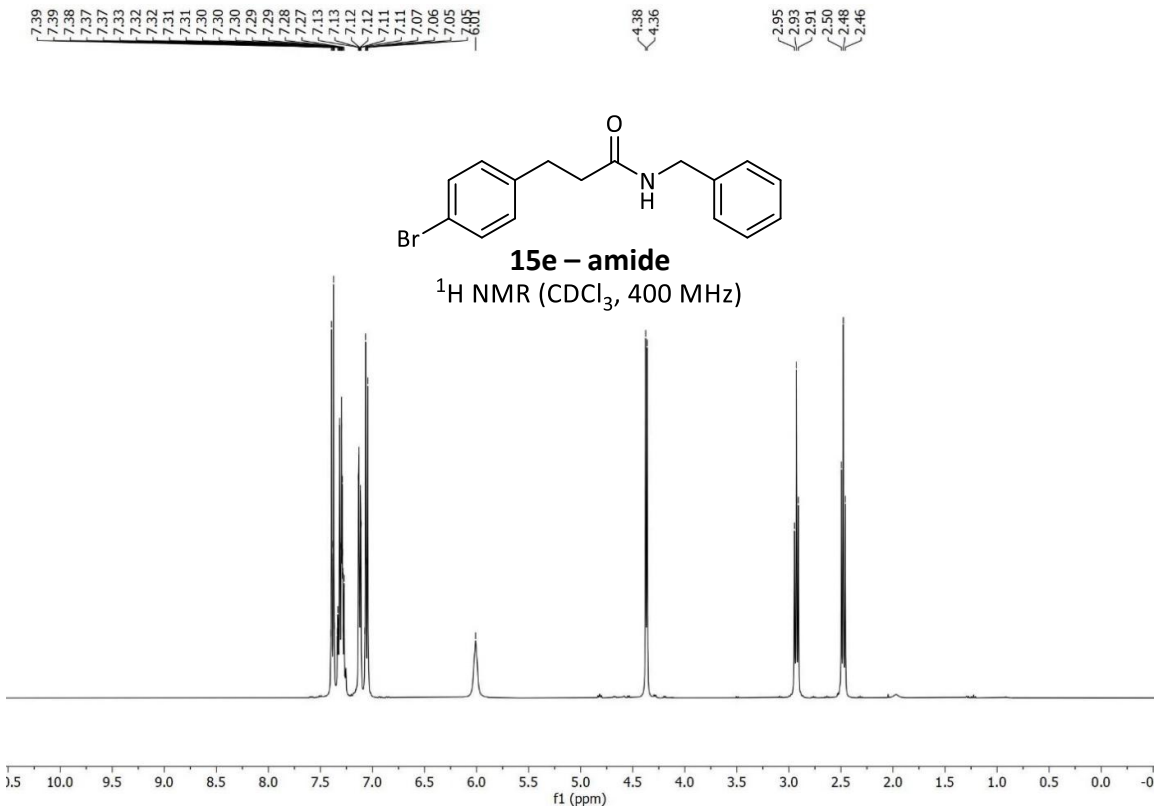


15c – amide

^{13}C NMR ($CDCl_3$, 100 MHz)

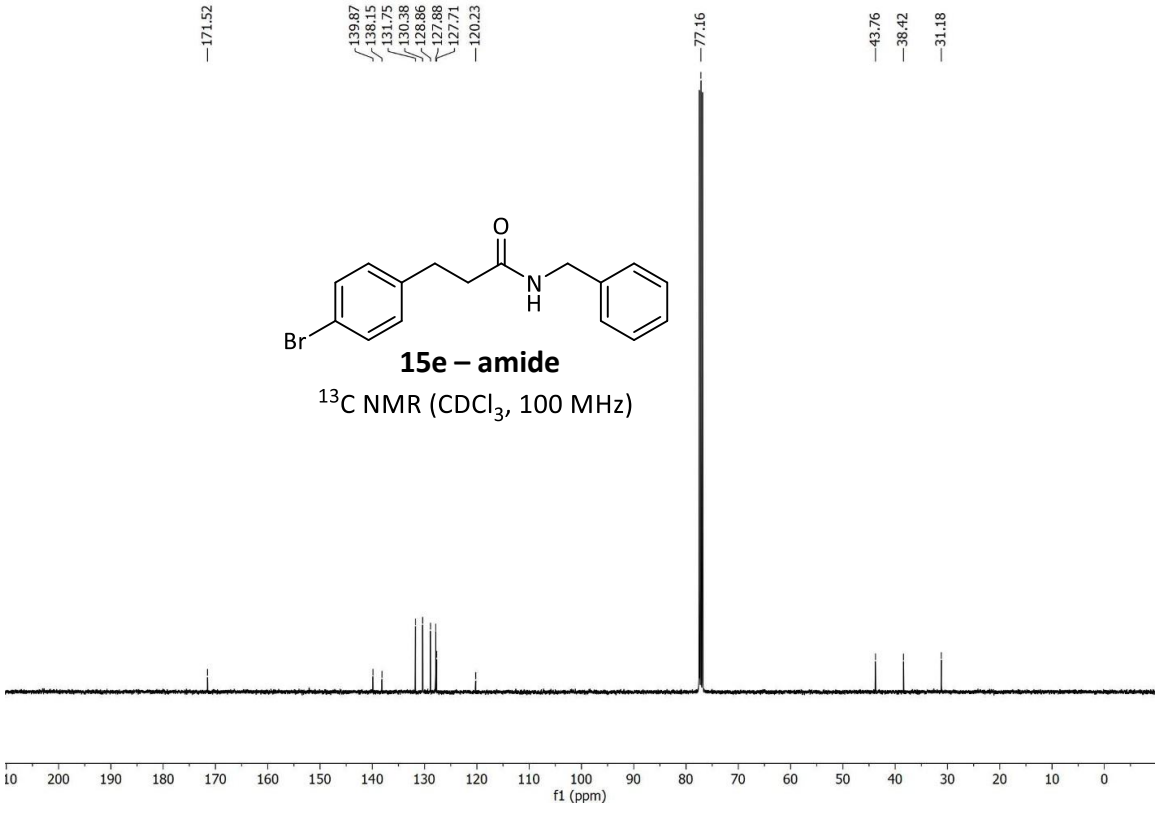

7.32
7.32
7.30
7.28
7.28
7.26
7.23
7.21
7.12
7.12
7.10
7.08
6.12
6.11
6.09
4.36
4.34
2.94
2.93
2.91
2.49
2.47
2.45
2.10
O
N
H
Cl
15d – amide
1H NMR (CDCl3, 400 MHz)
3.06
2.01
3.99
1.01
2.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.59
139.34
138.15
132.16
129.95
128.82
128.76
127.84
127.67
77.16
43.71
38.43
31.10
O
N
H
Cl
15d – amide
13C NMR (CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



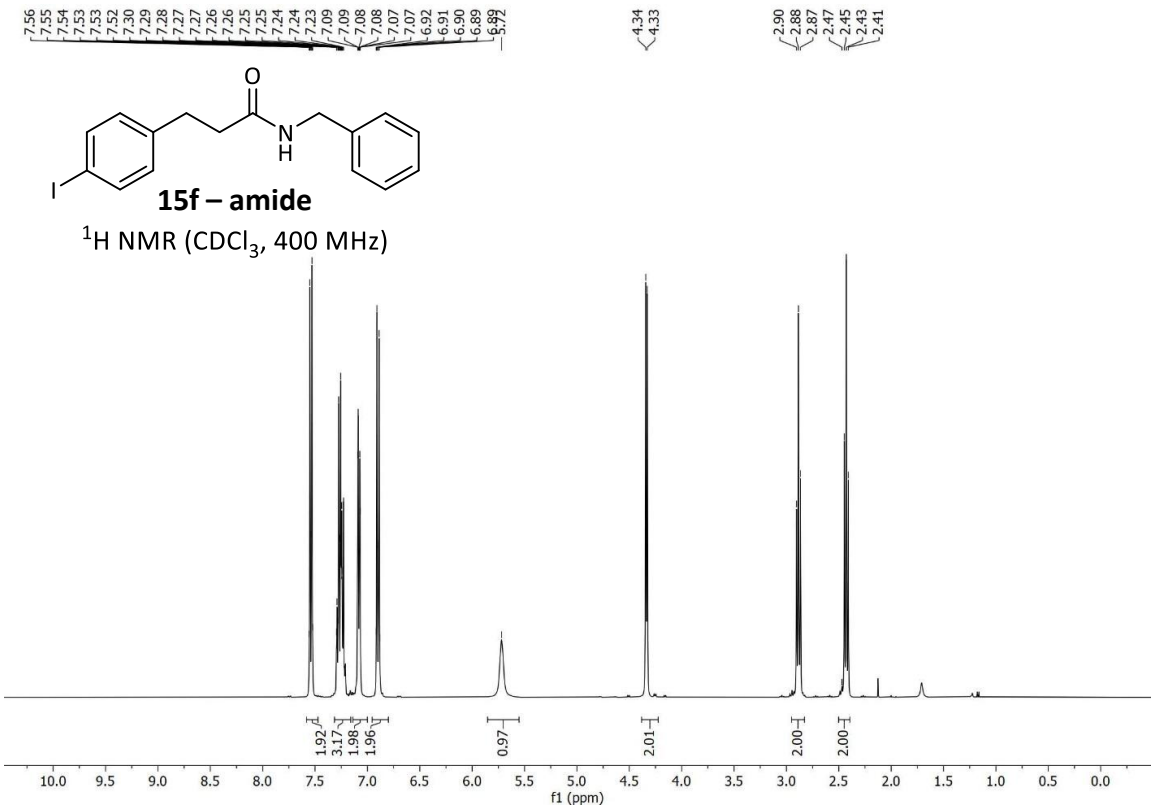
15e – amide

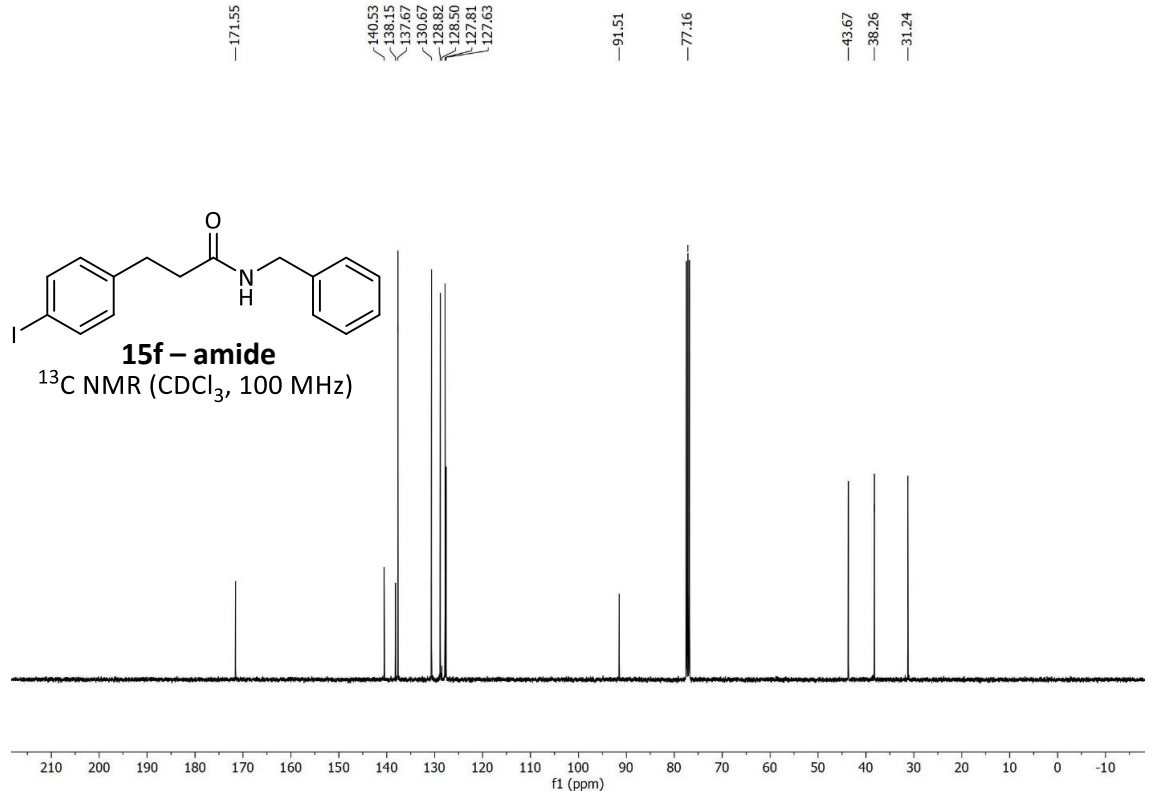
^{1}H NMR ($CDCl_3$, 400 MHz)

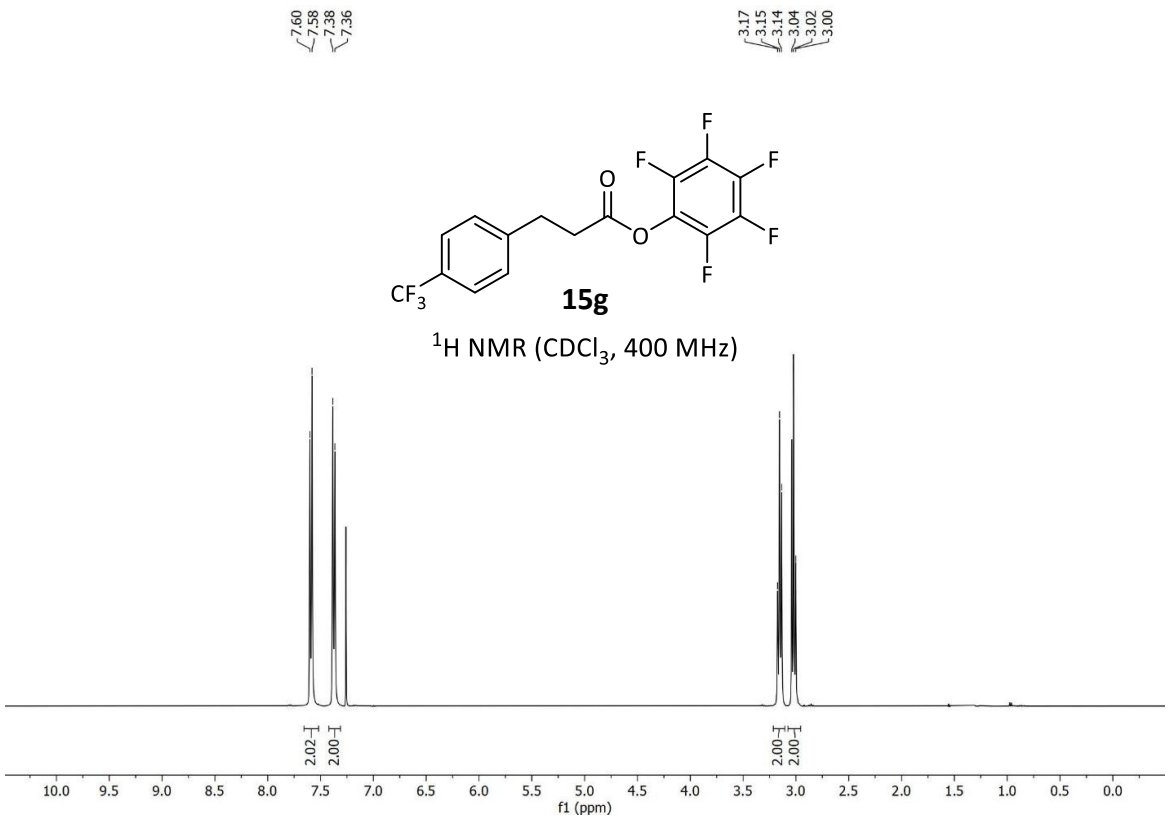


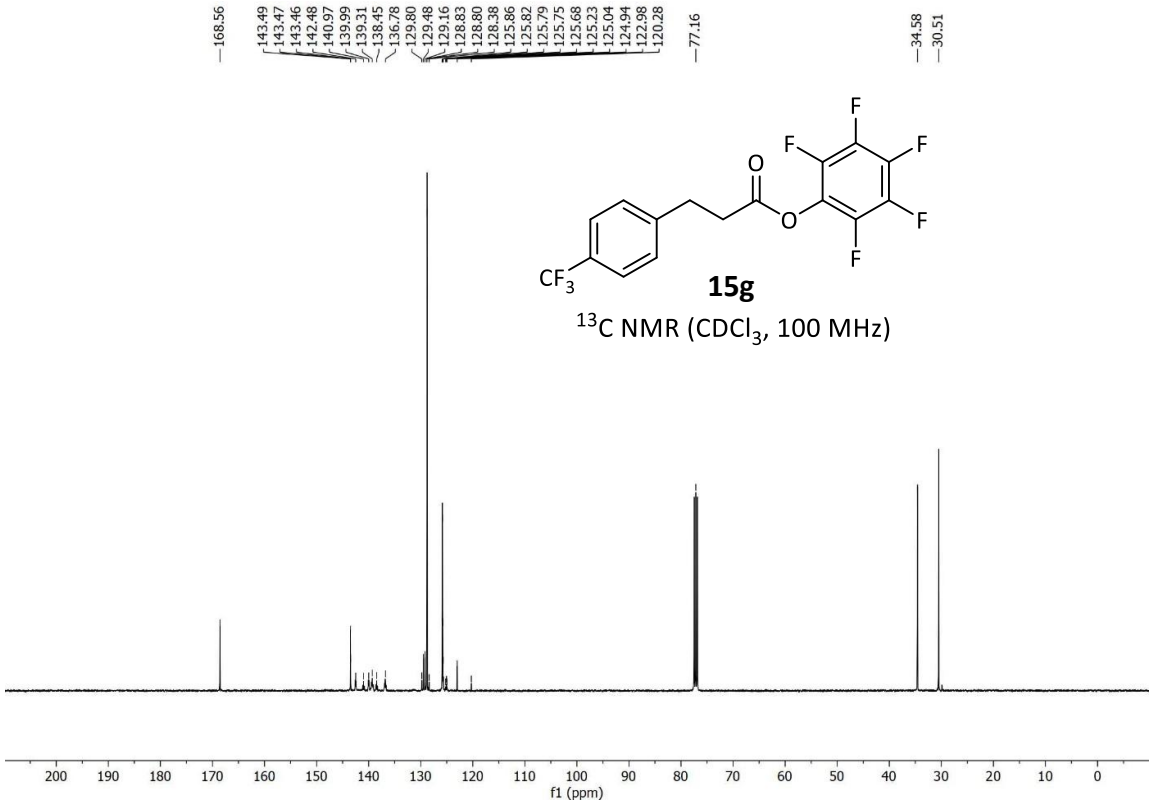
15e – amide

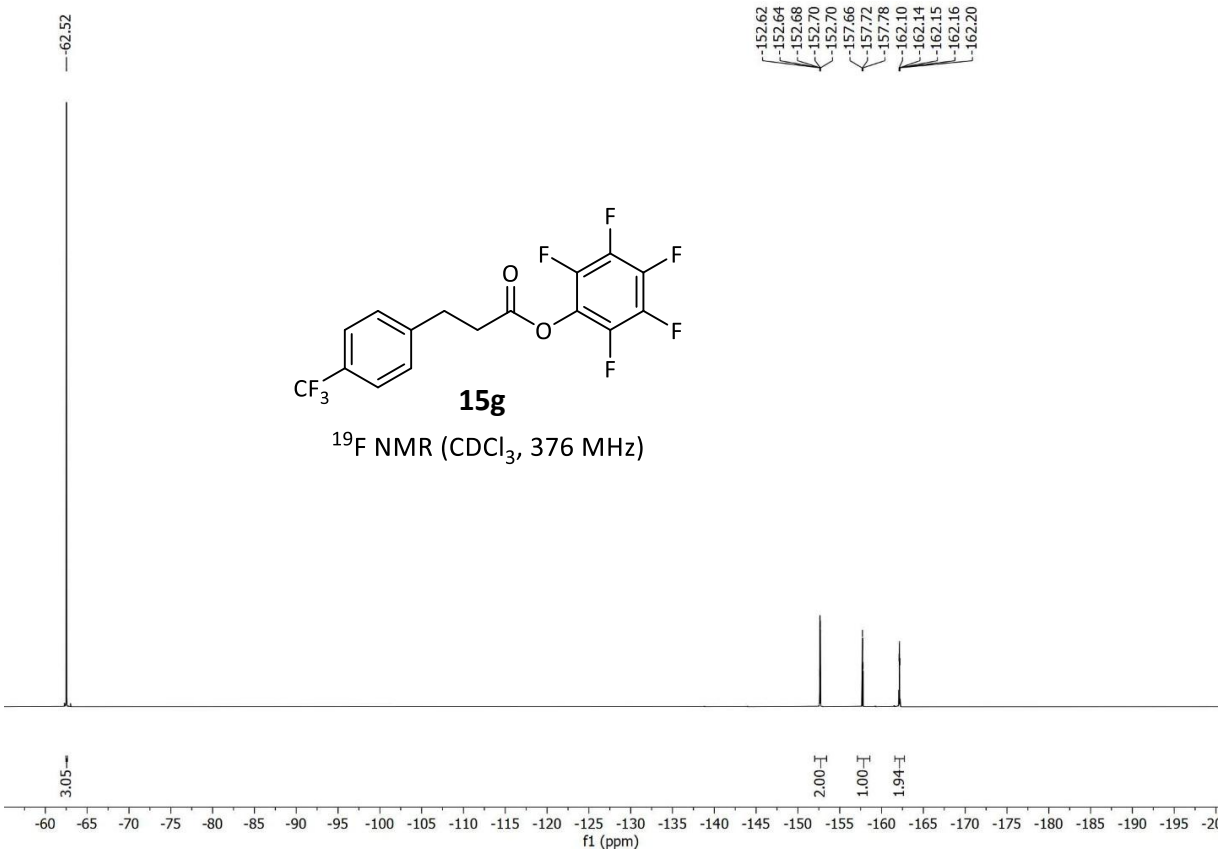
^{13}C NMR ($CDCl_3$, 100 MHz)


7.56 7.55 7.54 7.53 7.53 7.52 7.30 7.29 7.28 7.27 7.27 7.26 7.26 7.25 7.25 7.24 7.24 7.23 7.09 7.09 7.08 7.08 7.07 7.07 6.92 6.91 6.90 6.89 6.89 6.88
4.34 4.33
2.90 2.88 2.87 2.47 2.45 2.43 2.41
O
N
H
I
15f – amide
1H NMR (CDCl3, 400 MHz)
1.92 3.17 1.98 1.96 0.97 2.01 2.00 2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


171.55
140.53 138.15 137.67 130.67 128.82 128.50 127.81 127.63
91.51
77.16
43.67 38.26 31.24
O
N
H
I
15f – amide
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

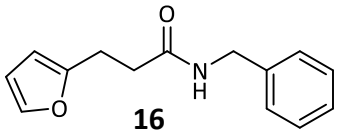

7.60
7.58
7.38
7.36
3.17
3.15
3.14
3.04
3.02
3.00
F
F
F
F
F
O
O
CF3
15g
1H NMR (CDCl3, 400 MHz)
2.02
2.00
2.00
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


168.56
143.49
143.47
143.46
142.48
140.97
139.99
139.31
138.45
136.78
129.80
129.48
129.16
128.83
128.80
128.38
125.86
125.82
125.79
125.75
125.68
125.23
125.04
124.94
122.98
120.28
77.16
34.58
30.51
F
F
F
F
F
O
O
CF3
15g
13C NMR (CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



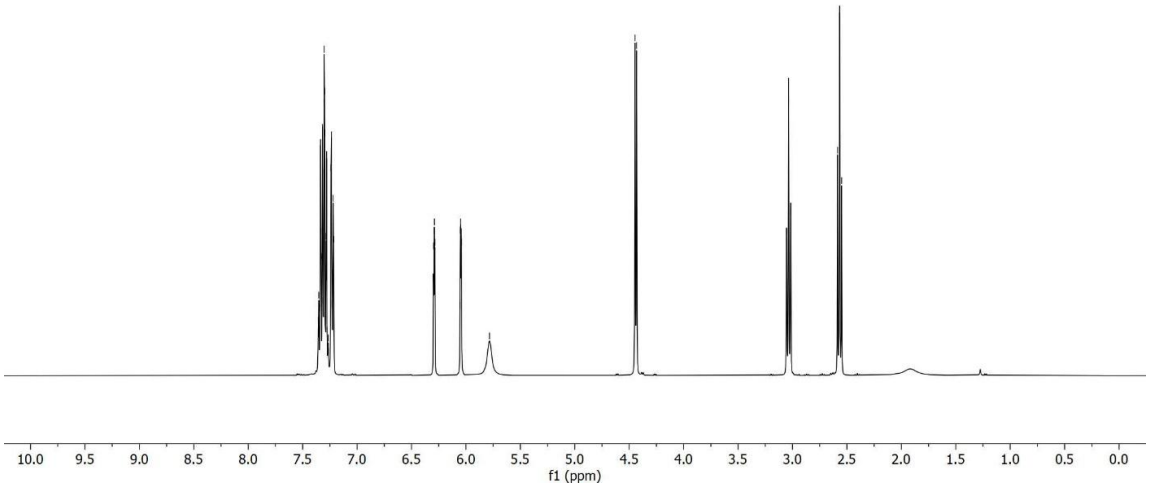
15g

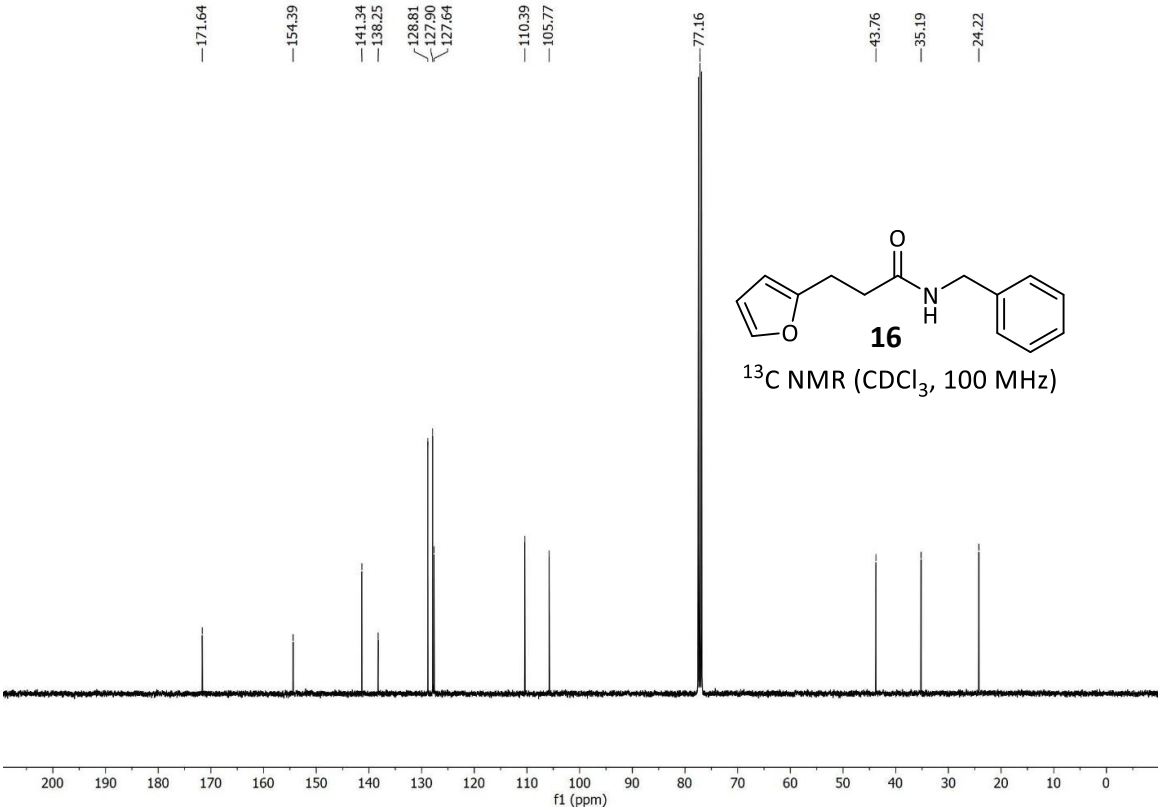
^{19}F NMR ($CDCl_3$, 376 MHz)



16

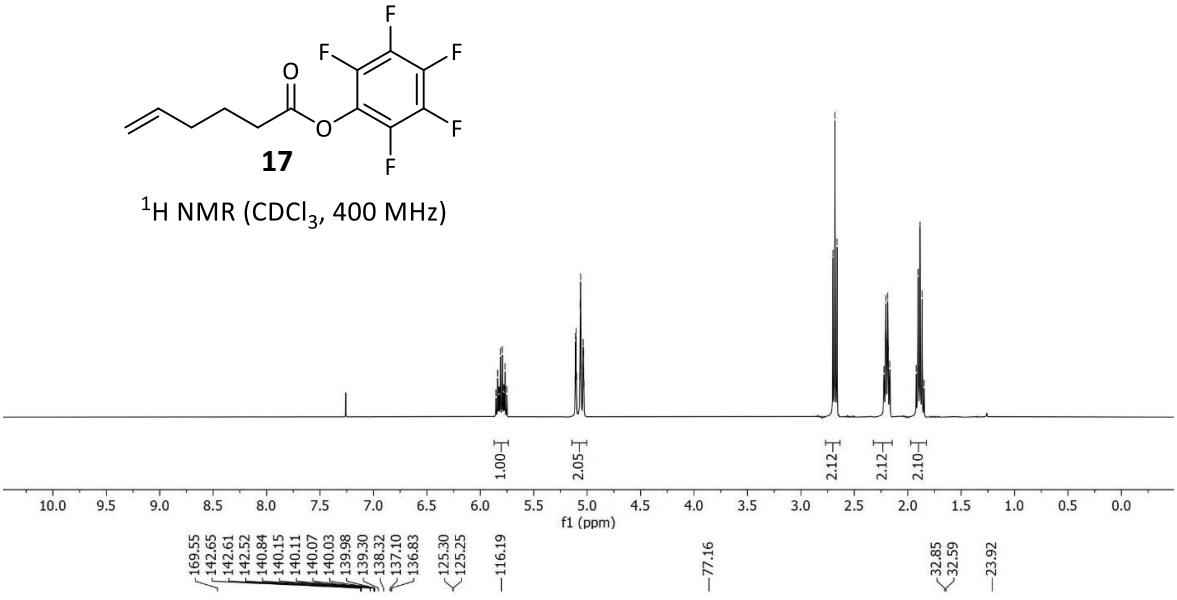
^{1}H NMR ($CDCl_3$, 400 MHz)



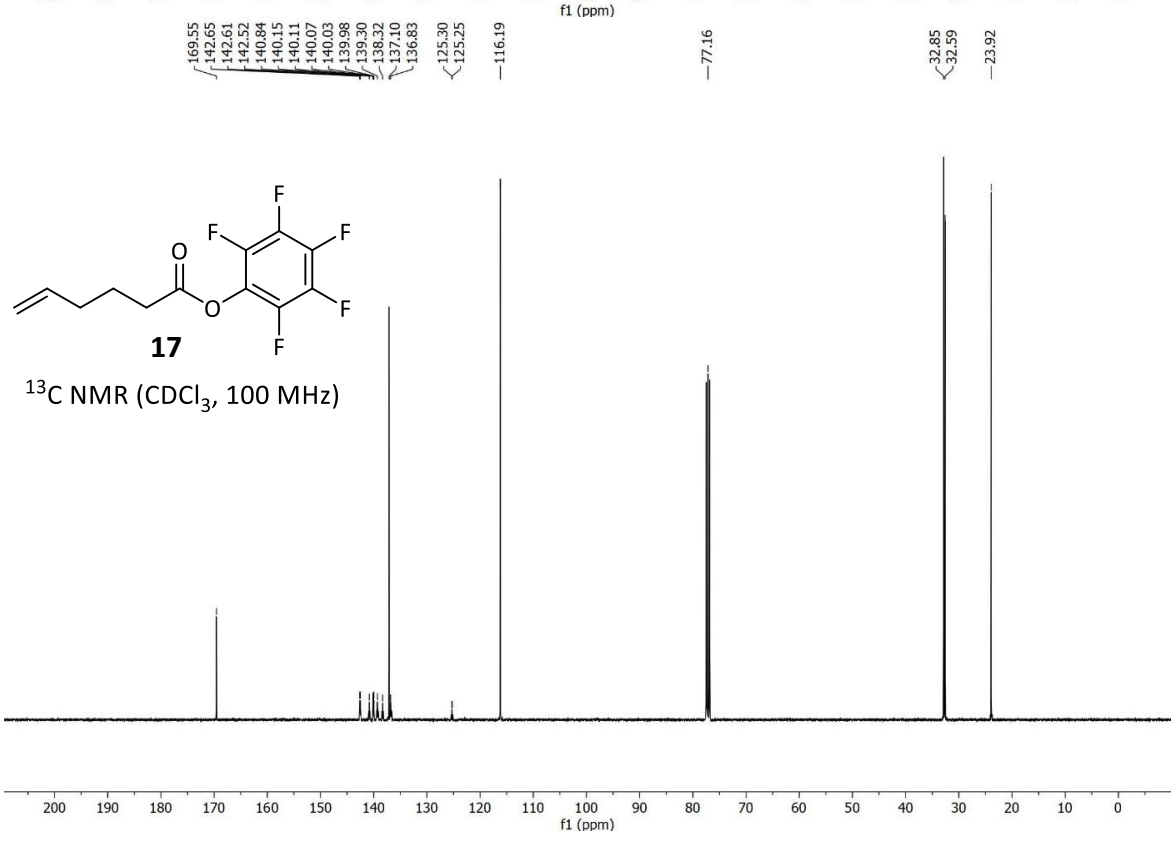


16

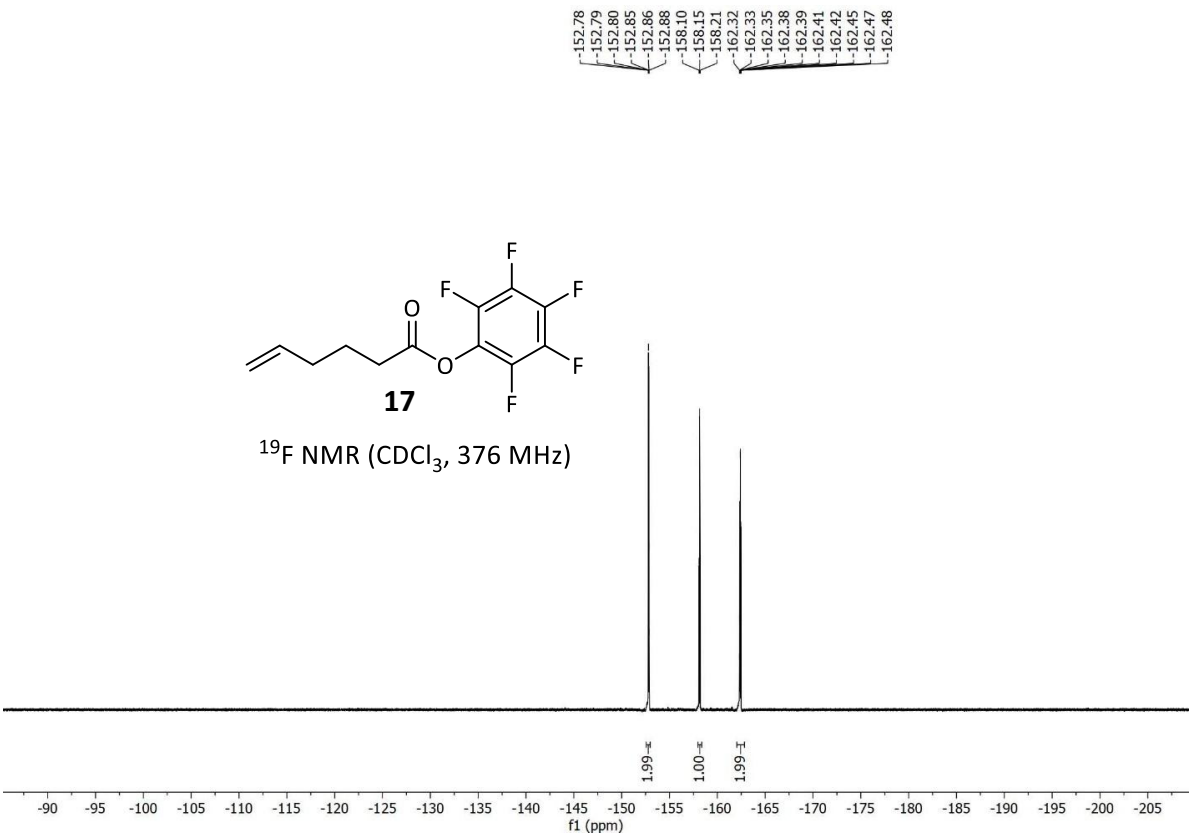
^{13}C NMR ($CDCl_3$, 100 MHz)

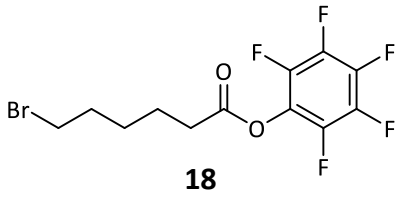


^{1}H NMR ($CDCl_3$, 400 MHz)



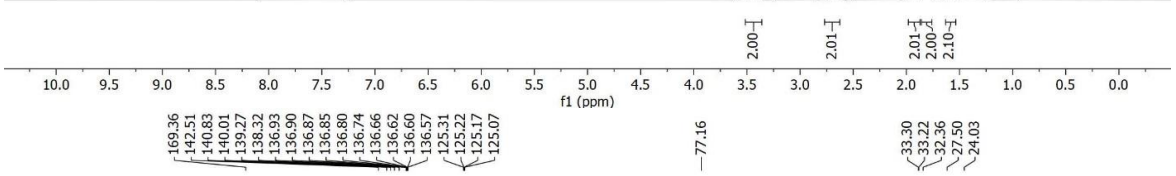
^{13}C NMR ($CDCl_3$, 100 MHz)

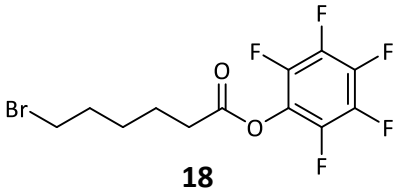

-152.78
-152.79
-152.80
-152.85
-152.86
-152.88
-158.10
-158.15
-158.21
-162.32
-162.33
-162.35
-162.38
-162.39
-162.41
-162.42
-162.45
-162.47
-162.48
F
F
F
O
O
F
F
17
19F NMR (CDCl3, 376 MHz)
1.99
1.00
1.99
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)



18

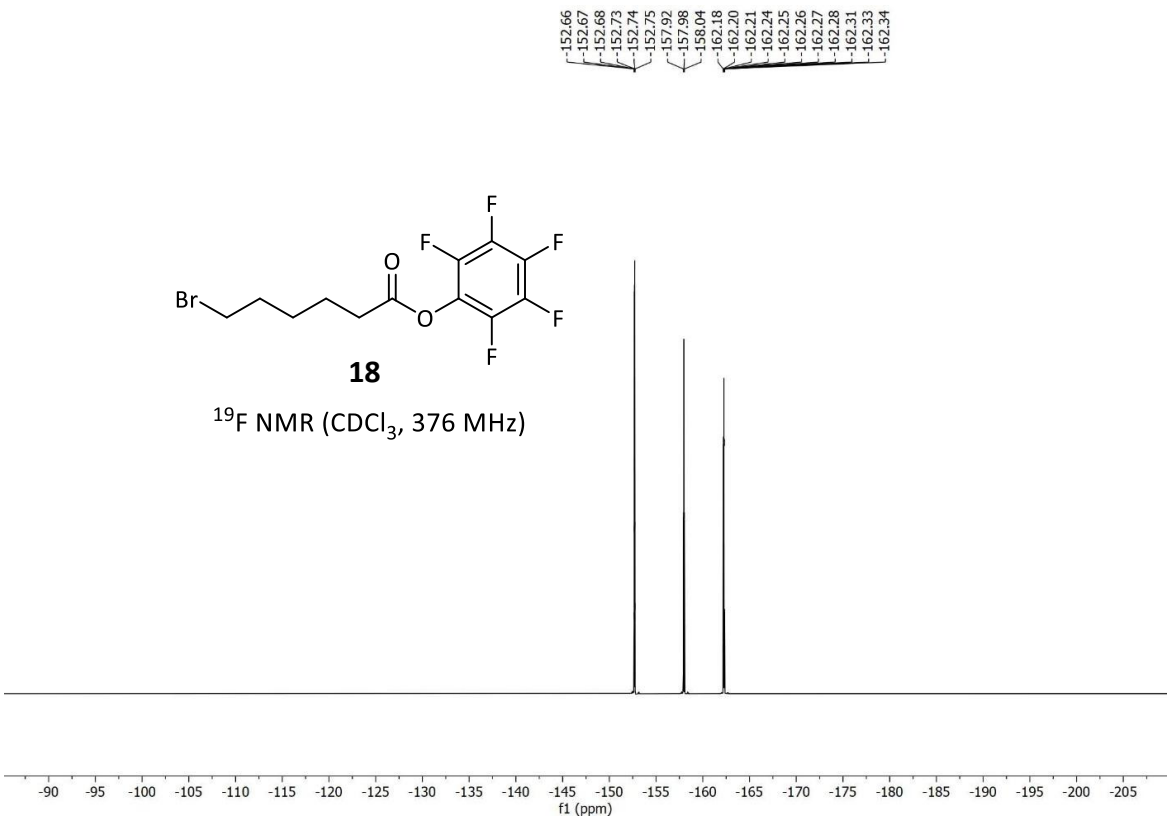
^{1}H NMR ($CDCl_3$, 400 MHz)





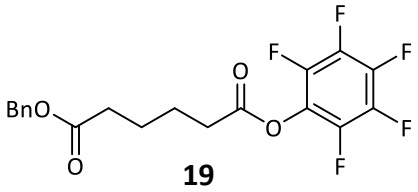
18

^{13}C NMR ($CDCl_3$, 100 MHz)



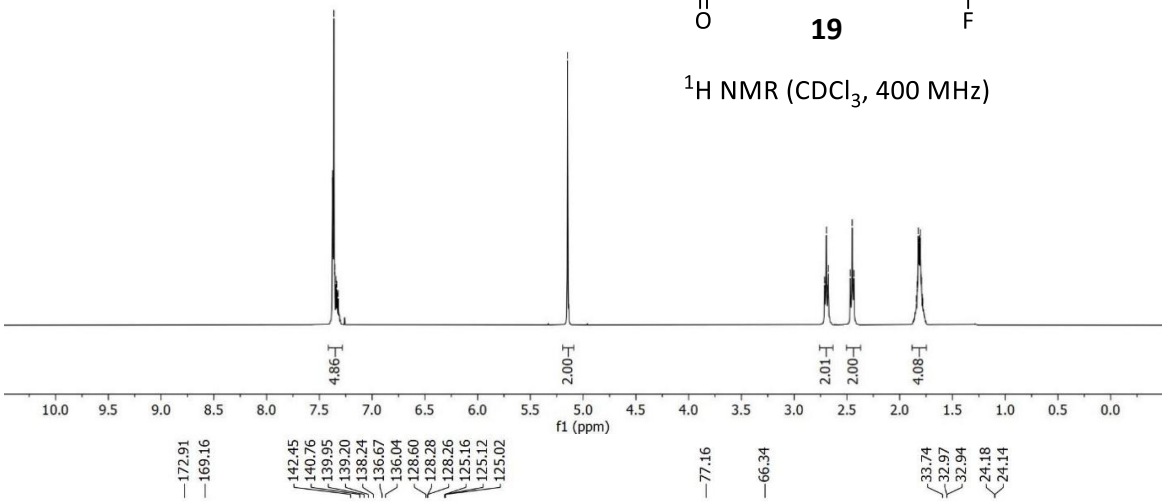
18

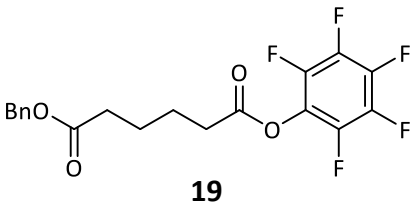
^{19}F NMR ($CDCl_3$, 376 MHz)



19

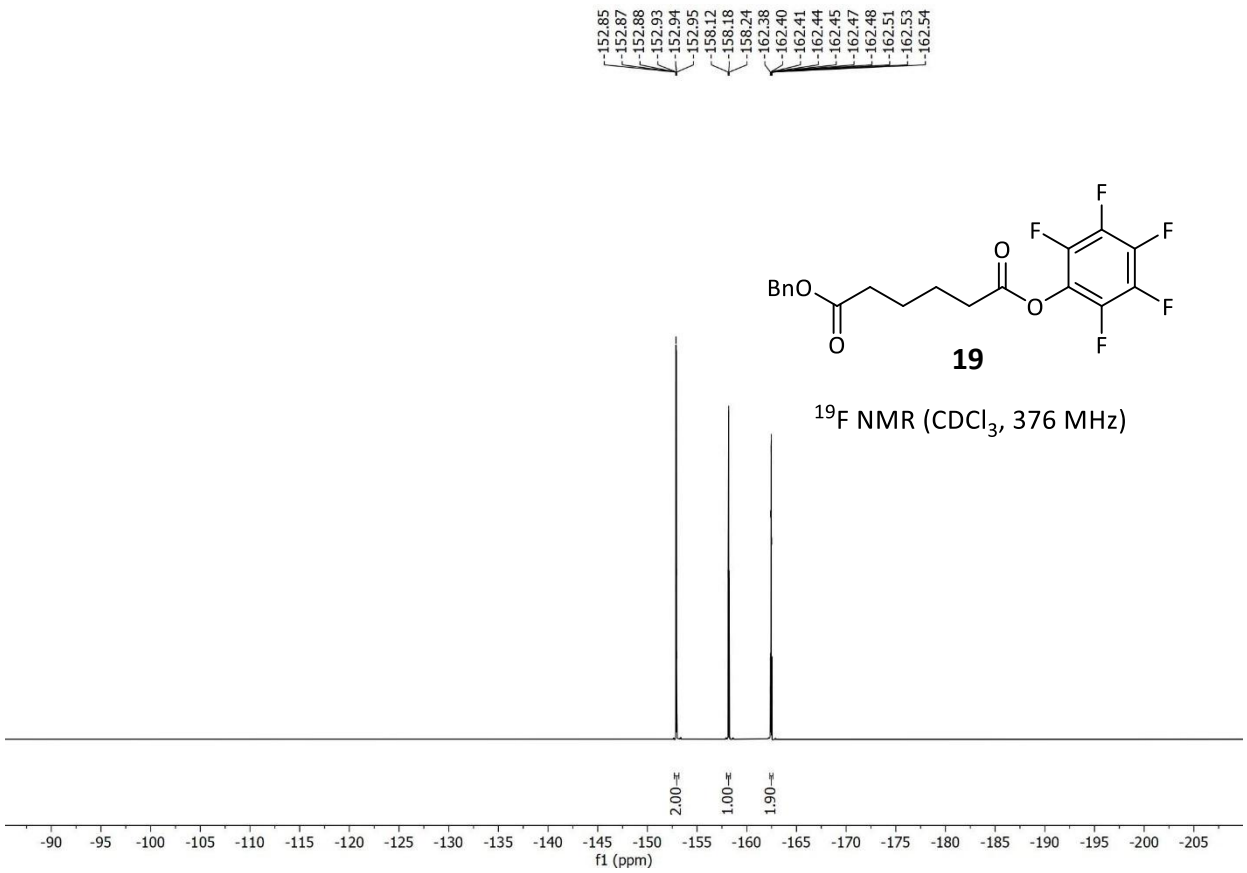
^{1}H NMR ($CDCl_3$, 400 MHz)

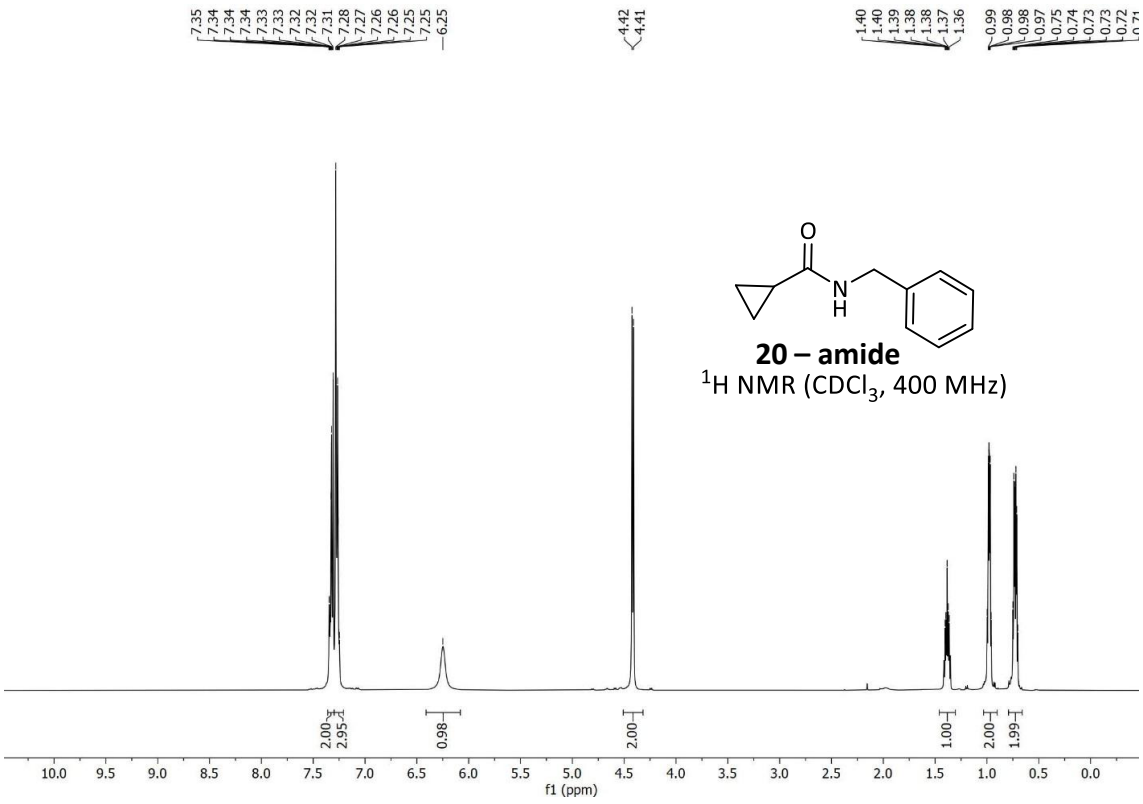


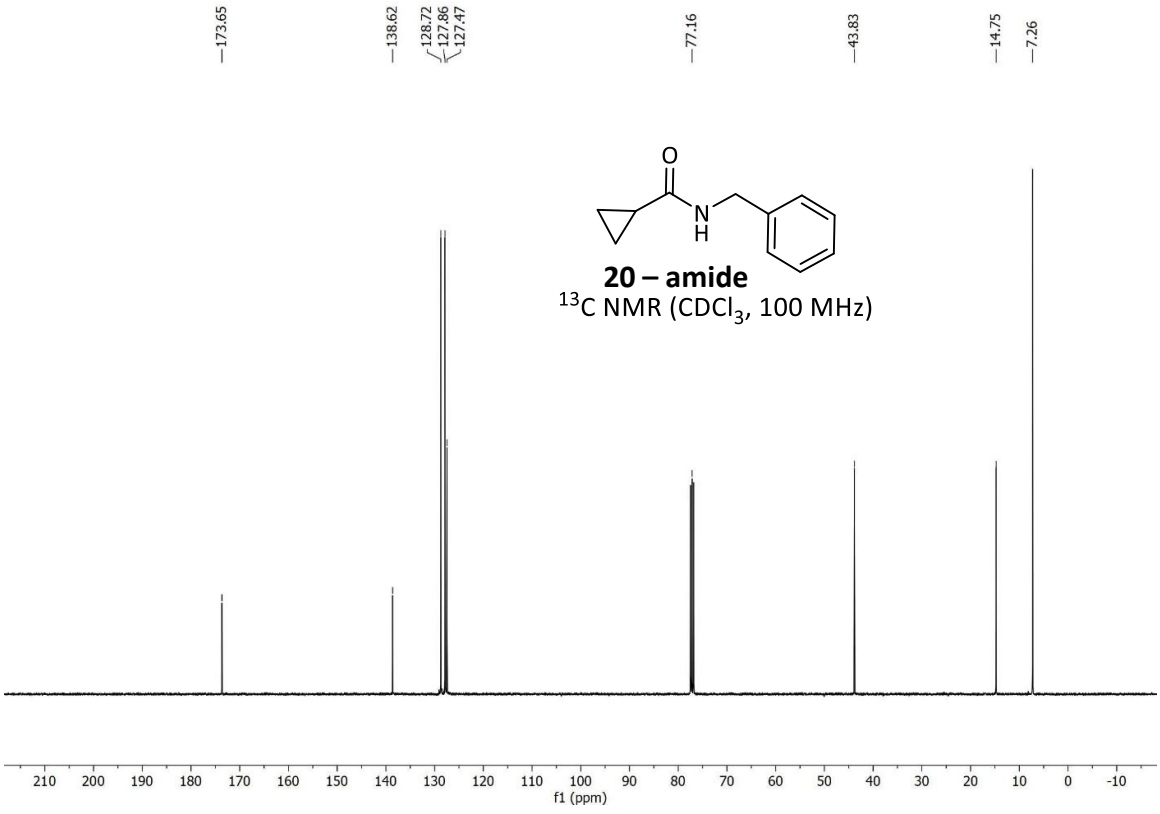


19

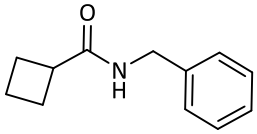
^{13}C NMR ($CDCl_3$, 100 MHz)


-152.85
-152.87
-152.88
-152.93
-152.94
-152.95
-158.12
-158.18
-158.24
-162.38
-162.40
-162.41
-162.44
-162.45
-162.47
-162.48
-162.51
-162.53
-162.54
F
F
F
O
BnO
O
F
O
F
19
^{19}F NMR ($CDCl_3$, 376 MHz)
2.00
1.00
1.90
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)


7.35
7.34
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.28
7.27
7.26
7.26
7.25
7.25
6.25
4.42
4.41
1.40
1.40
1.39
1.38
1.38
1.37
1.36
0.99
0.98
0.98
0.97
0.75
0.74
0.73
0.73
0.72
O
N
H
20 – amide
1H NMR (CDCl3, 400 MHz)
2.00
2.95
0.98
2.00
1.00
2.00
1.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

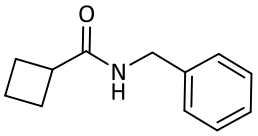

173.65
138.62
128.72
127.86
127.47
77.16
43.83
14.75
7.26
O
N
H
20 – amide
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

21 – amide

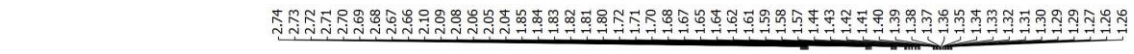


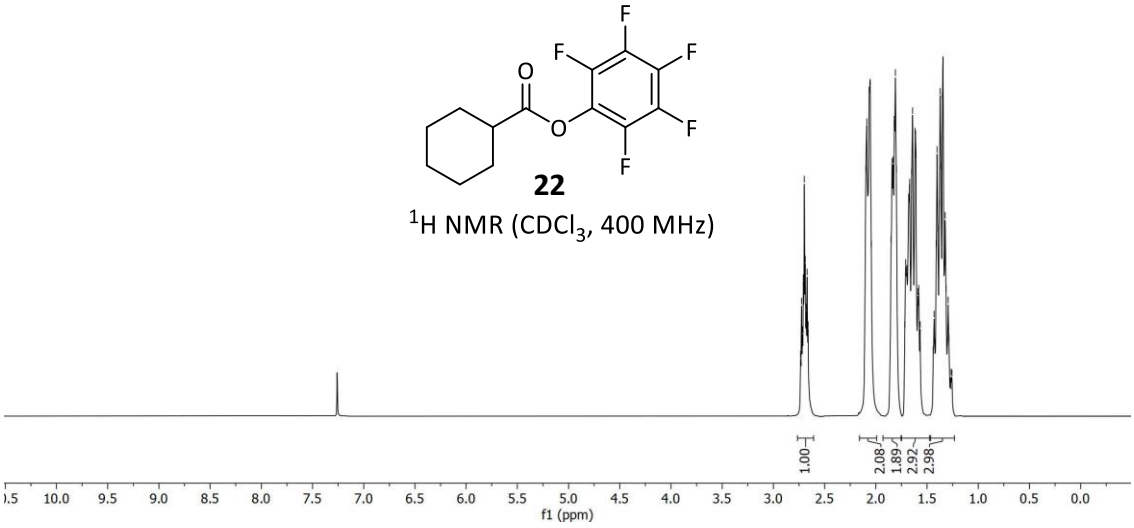
^{1}H NMR ($CDCl_3$, 400 MHz)

21 – amide

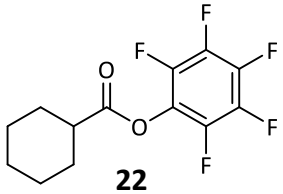


^{13}C NMR ($CDCl_3$, 100 MHz)

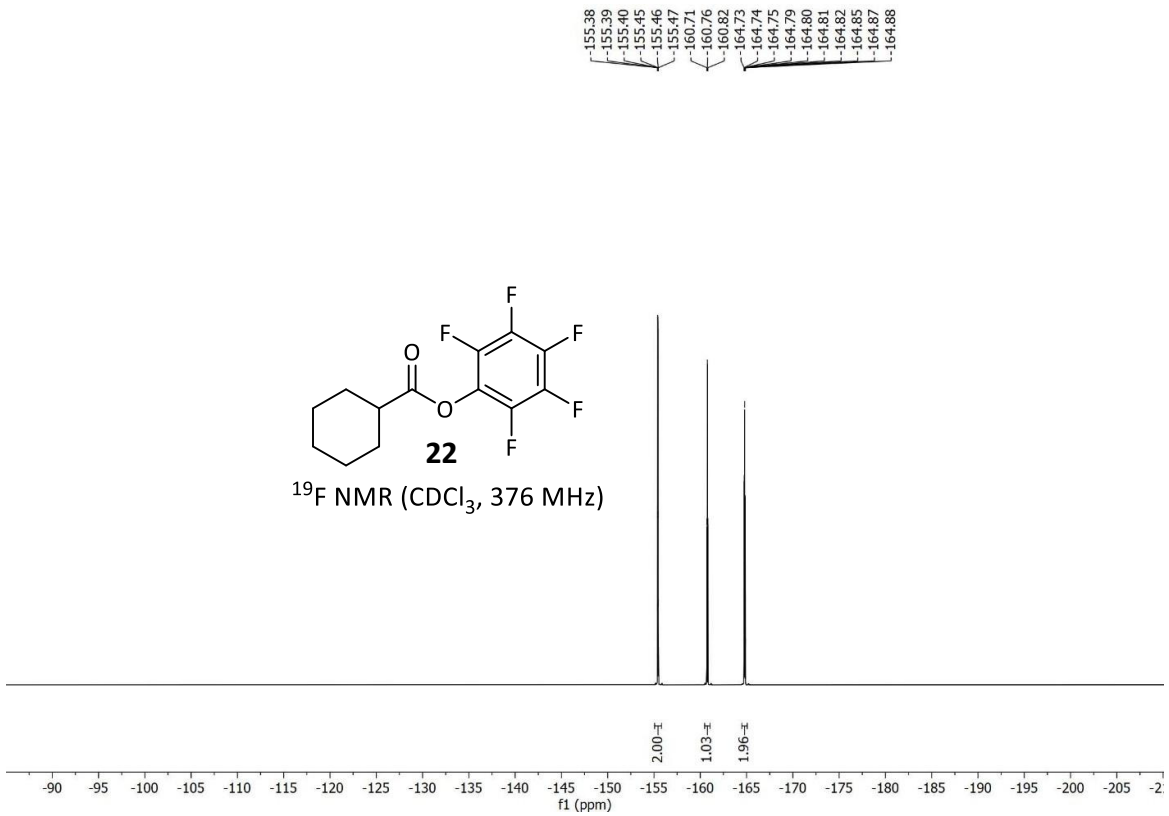


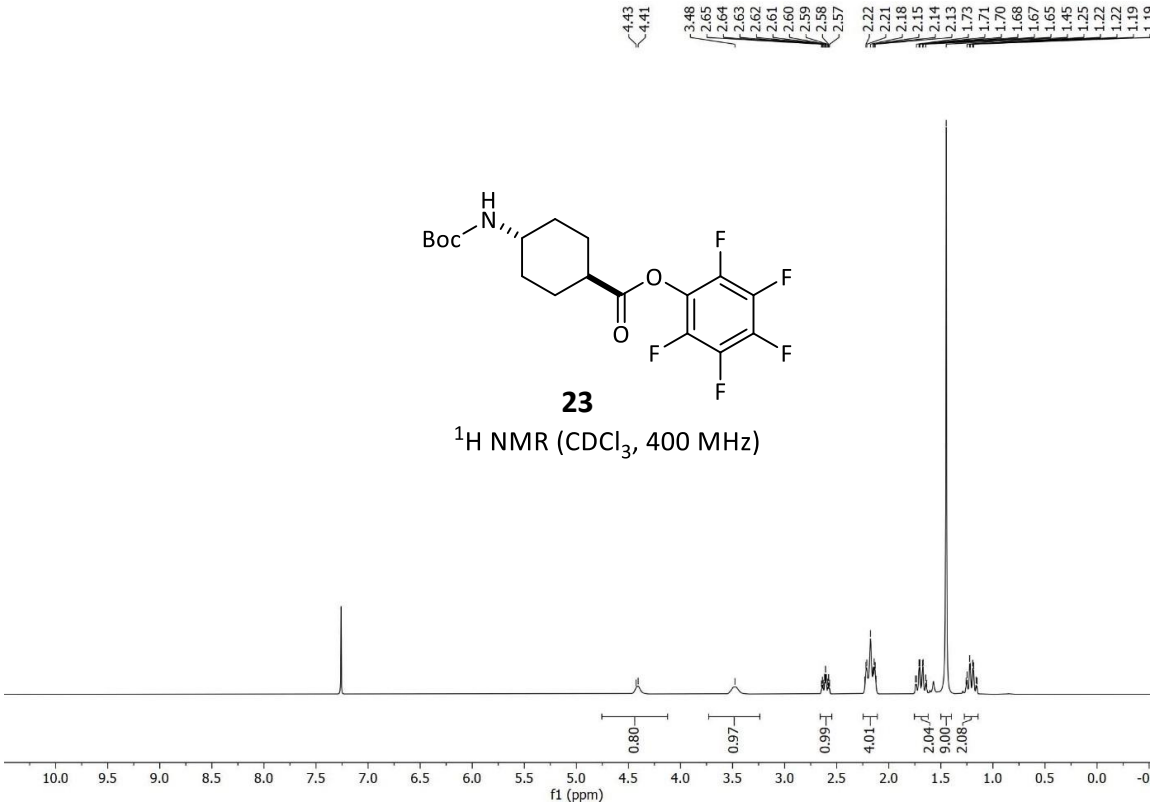


^{1}H NMR ($CDCl_3$, 400 MHz)



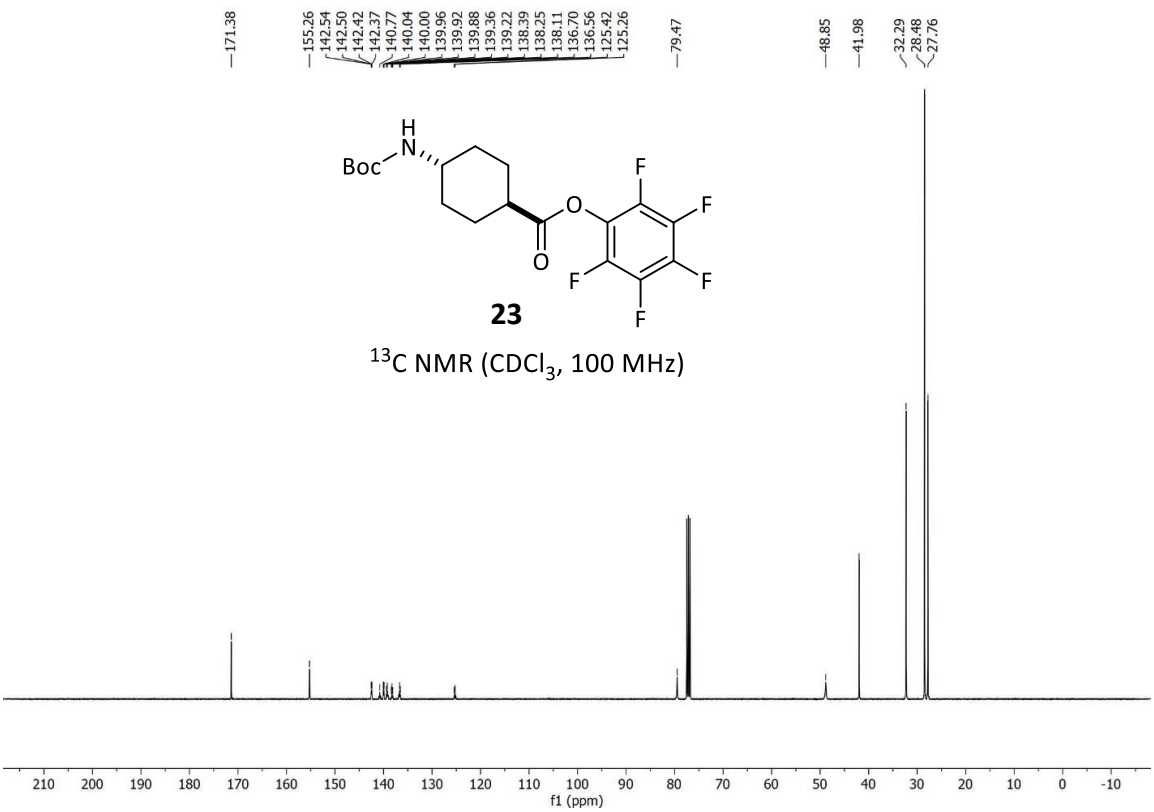
^{13}C NMR ($CDCl_3$, 100 MHz)


-155.38
-155.39
-155.40
-155.45
-155.46
-155.47
-160.71
-160.76
-160.82
-164.73
-164.74
-164.75
-164.79
-164.80
-164.81
-164.82
-164.85
-164.87
-164.88
F
F
F
O
O
F
F
22
^{19}F NMR ($CDCl_3$, 376 MHz)
2.00
1.03
1.96
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)



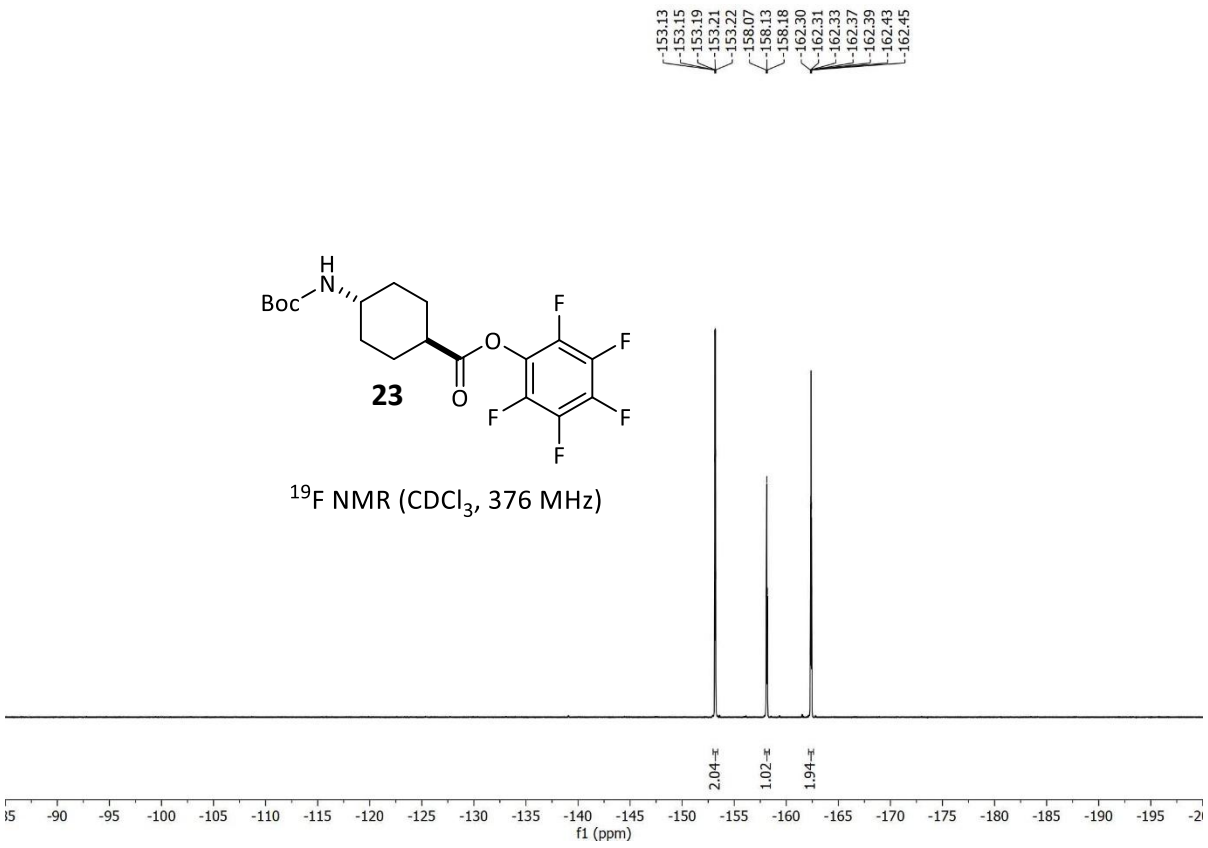
23

^{1}H NMR ($CDCl_3$, 400 MHz)

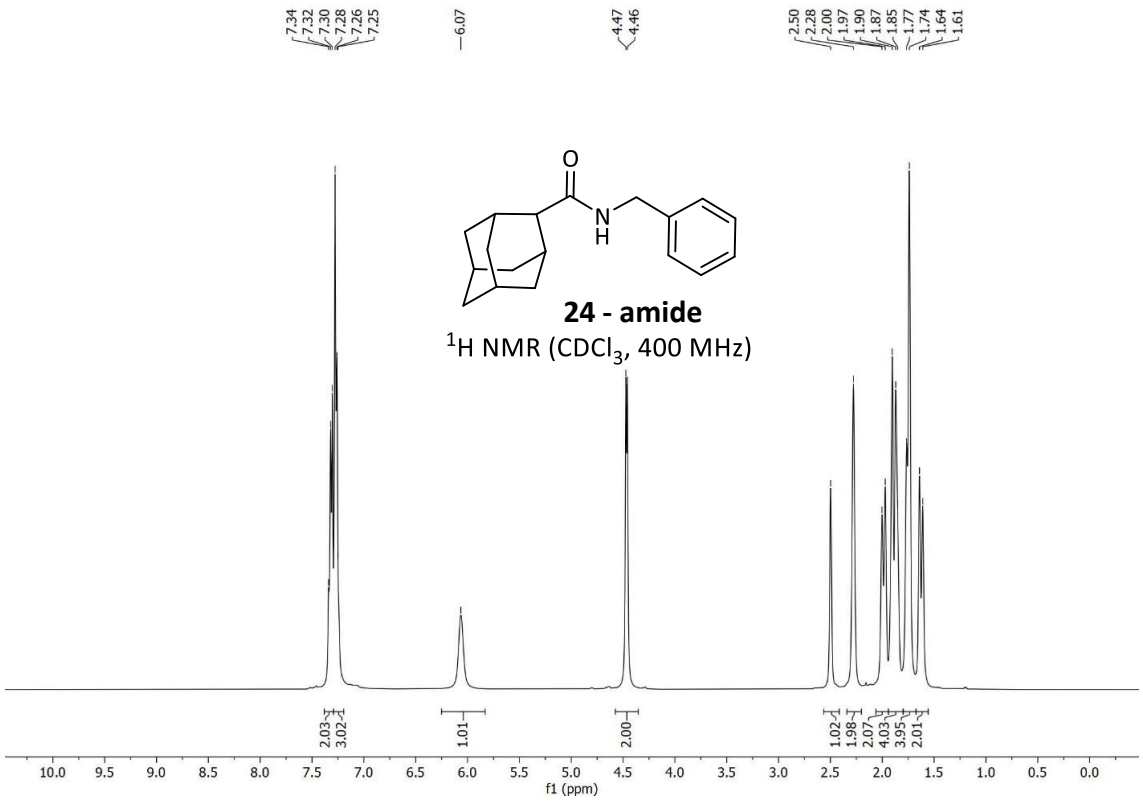


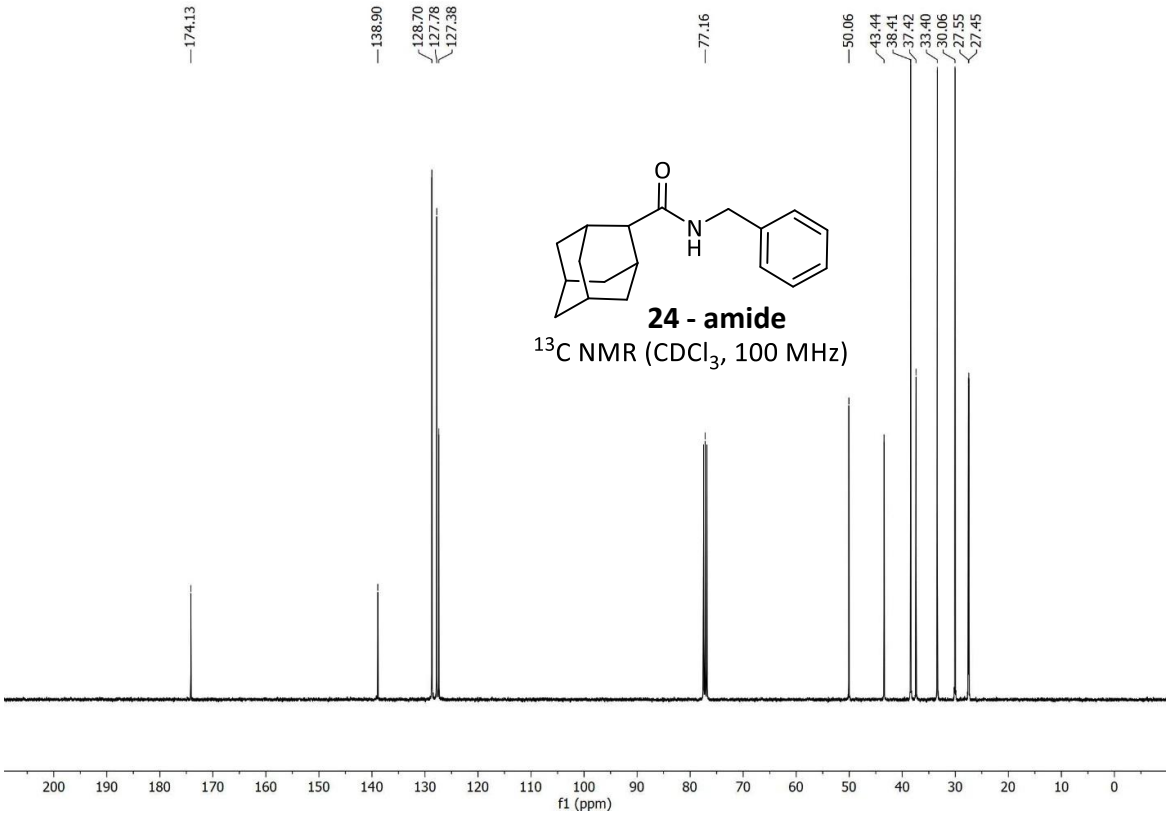
23

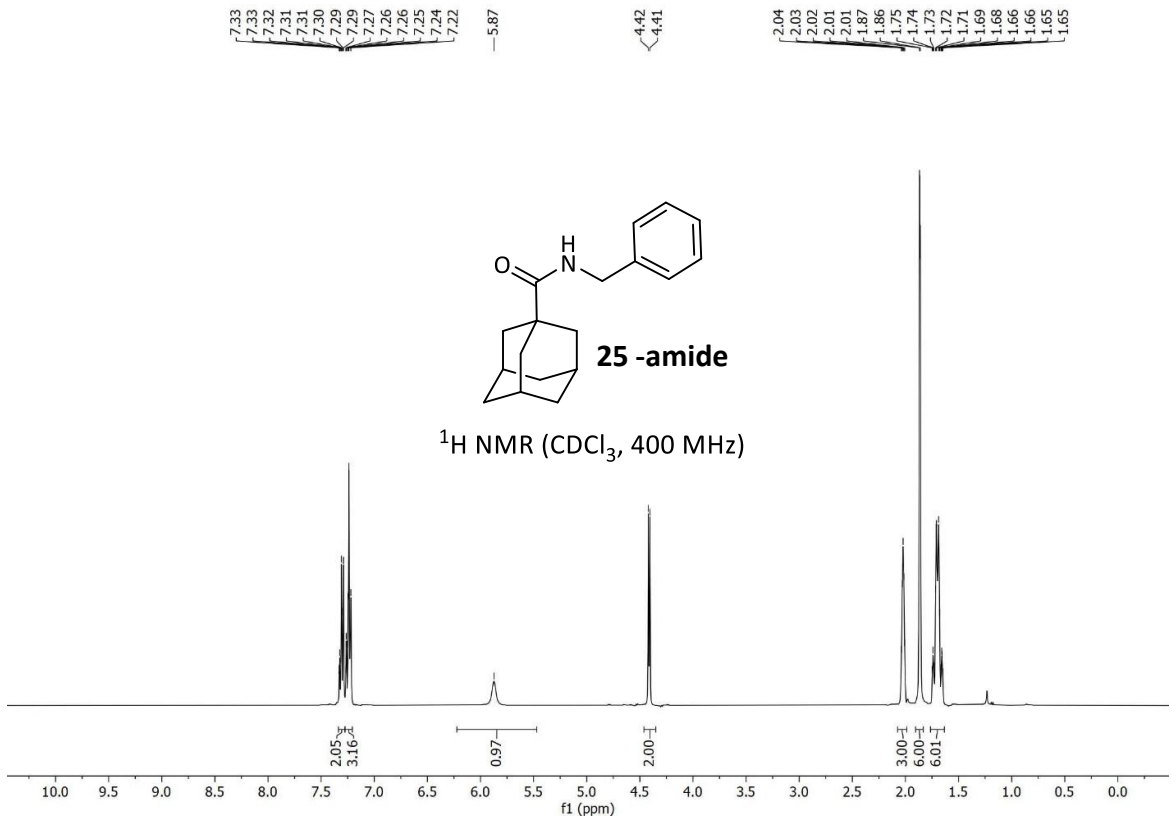
^{13}C NMR ($CDCl_3$, 100 MHz)

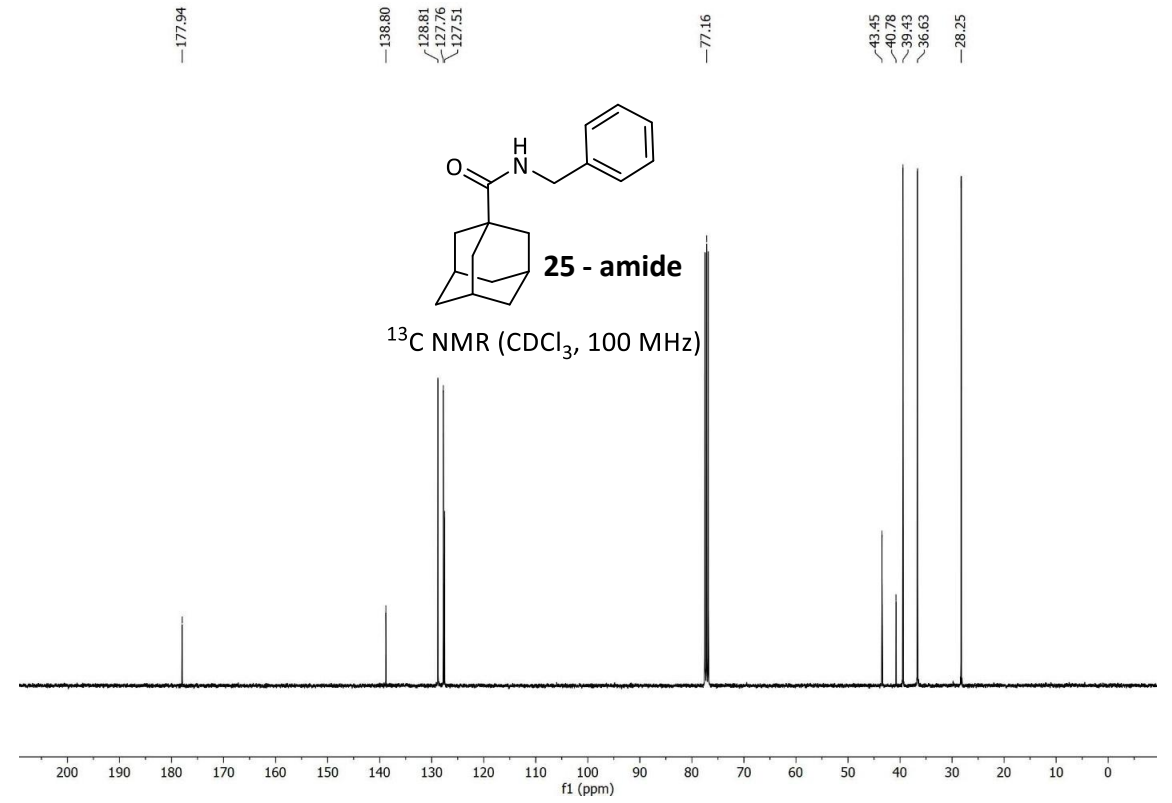


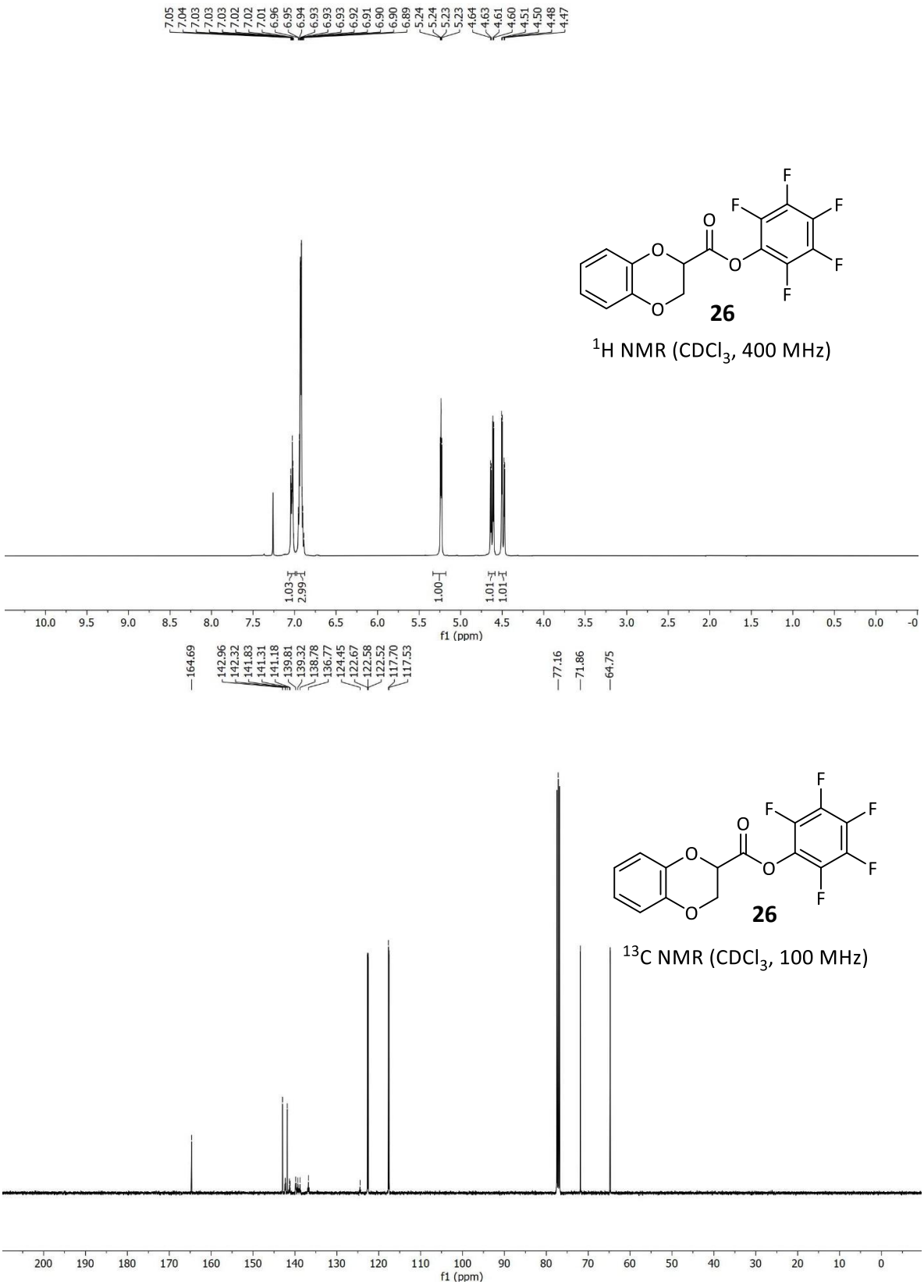
^{19}F NMR ($CDCl_3$, 376 MHz)

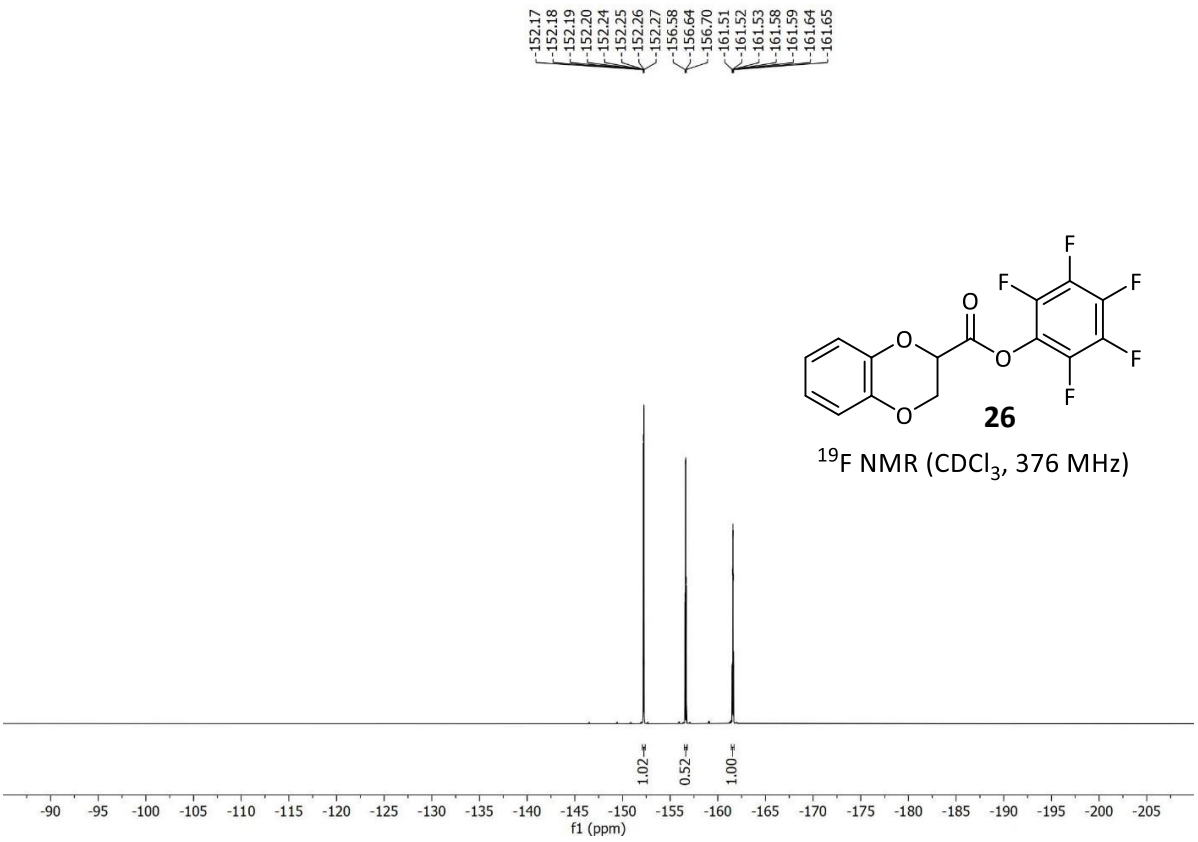

7.34
7.32
7.30
7.28
7.26
7.25
6.07
4.47
4.46
2.50
2.28
2.00
1.97
1.90
1.87
1.85
1.77
1.74
1.64
1.61
O
N
H
24 - amide
1H NMR (CDCl3, 400 MHz)
2.03
3.02
1.01
2.00
1.02
1.98
2.07
4.03
3.95
2.01
f1 (ppm)


174.13
138.90
128.70
127.78
127.38
77.16
50.06
43.44
38.41
37.42
33.40
30.06
27.55
27.45
O
N
H
24 - amide
13C NMR (CDCl3, 100 MHz)
f1 (ppm)


7.33
7.33
7.32
7.31
7.31
7.30
7.29
7.29
7.27
7.26
7.26
7.25
7.24
7.22
5.87
4.42
4.41
2.04
2.03
2.02
2.01
2.01
1.87
1.86
1.75
1.74
1.73
1.72
1.71
1.69
1.68
1.66
1.66
1.65
1.65
H
N
O
25 -amide
1H NMR (CDCl3, 400 MHz)
2.05
3.16
0.97
2.00
3.00
6.00
6.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

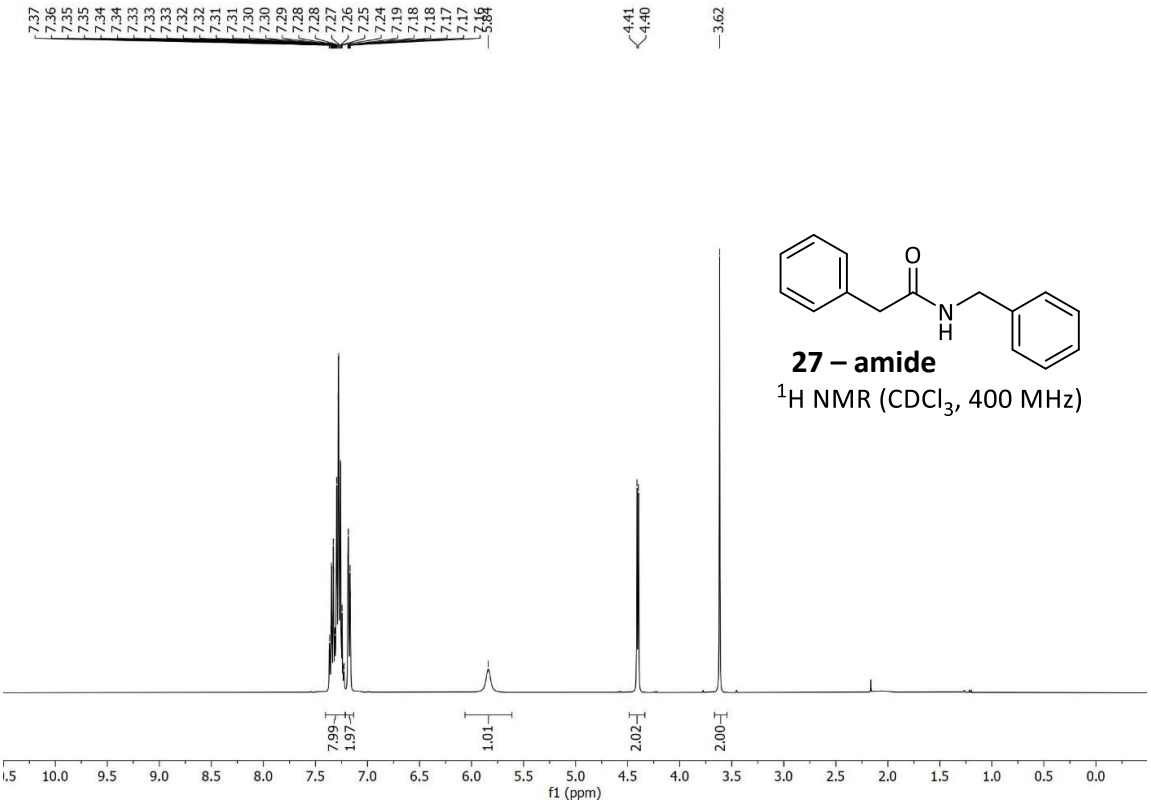

177.94
138.80
128.81
127.76
127.51
77.16
43.45
40.78
39.43
36.63
28.25
H
N
O
25 - amide
13C NMR (CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

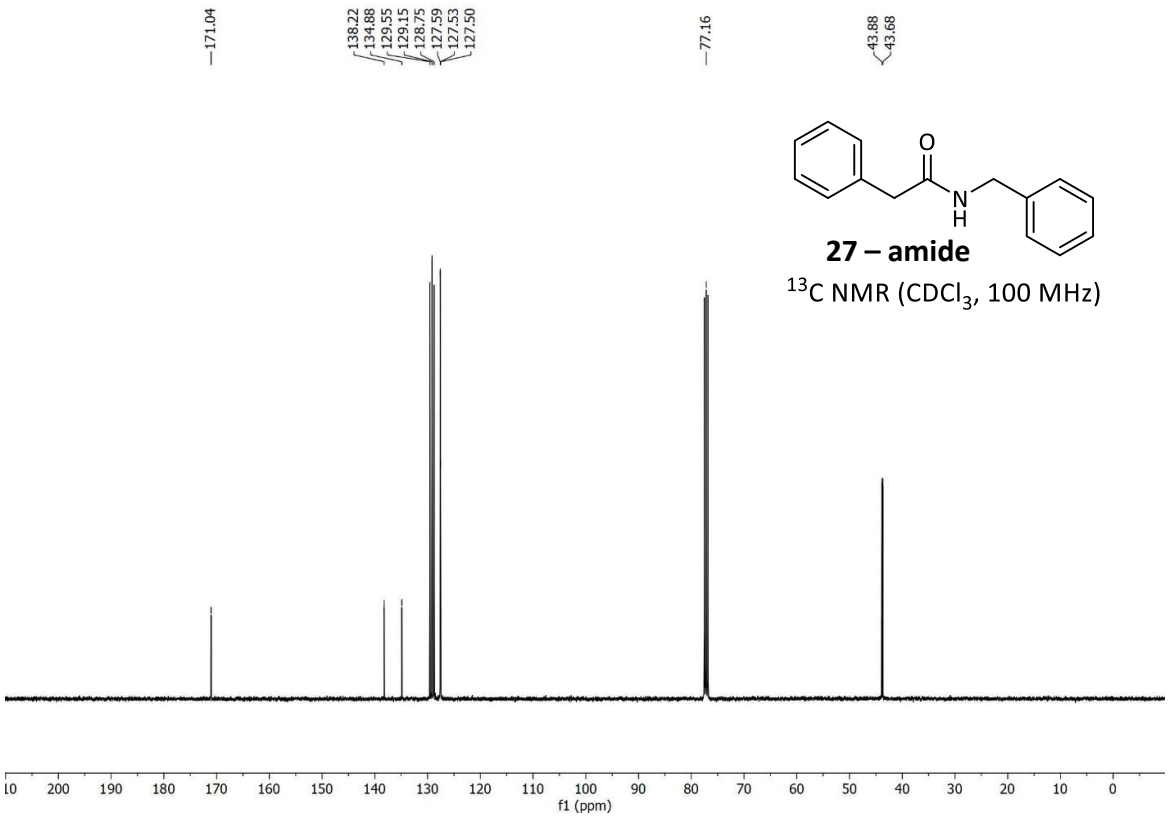

7.05
7.04
7.03
7.03
7.03
7.02
7.02
7.01
6.96
6.95
6.94
6.93
6.93
6.93
6.92
6.91
6.90
6.90
6.89
5.24
5.24
5.23
5.23
4.64
4.63
4.61
4.60
4.51
4.50
4.48
4.47
F
F
F
O
O
O
F
F
26
1H NMR (CDCl3, 400 MHz)
1.03
2.99
1.00
1.01
1.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)
164.69
142.96
142.32
141.83
141.31
141.18
139.81
139.32
138.78
136.77
124.45
122.67
122.58
122.52
117.70
117.53
77.16
71.86
64.75
F
F
F
O
O
O
F
F
26
13C NMR (CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

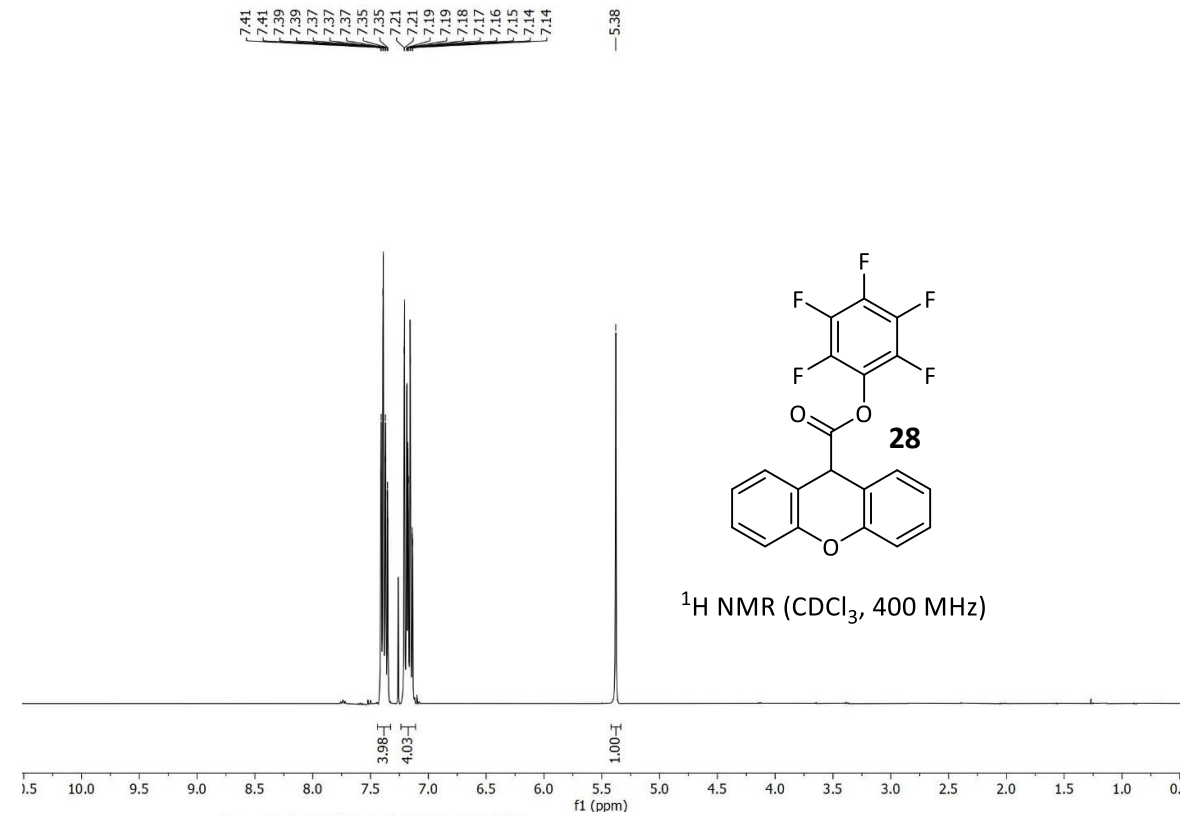


26

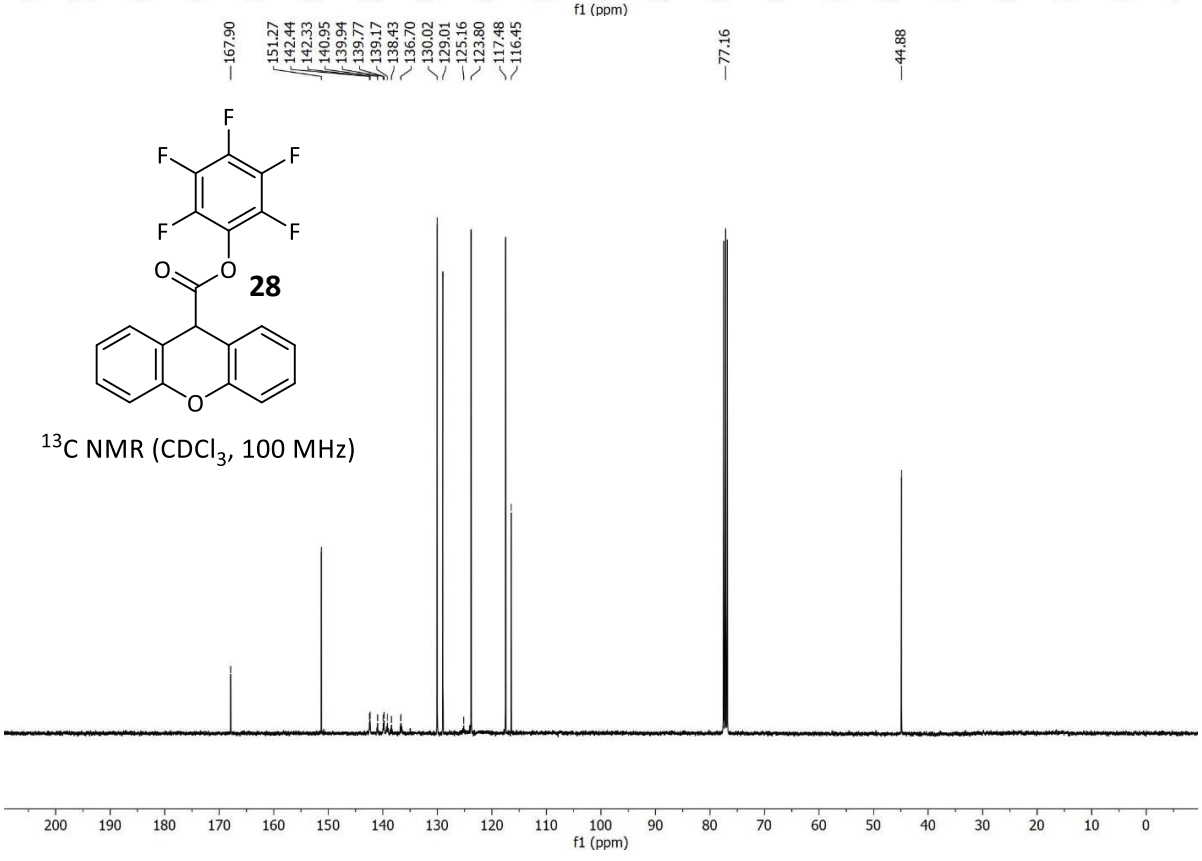
^{19}F NMR ($CDCl_3$, 376 MHz)


7.37
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.26
7.25
7.24
7.19
7.18
7.18
7.17
7.17
5.84
4.41
4.40
3.62
O
N
H
27 – amide
1H NMR (CDCl3, 400 MHz)
7.99
1.97
1.01
2.02
2.00
f1 (ppm)

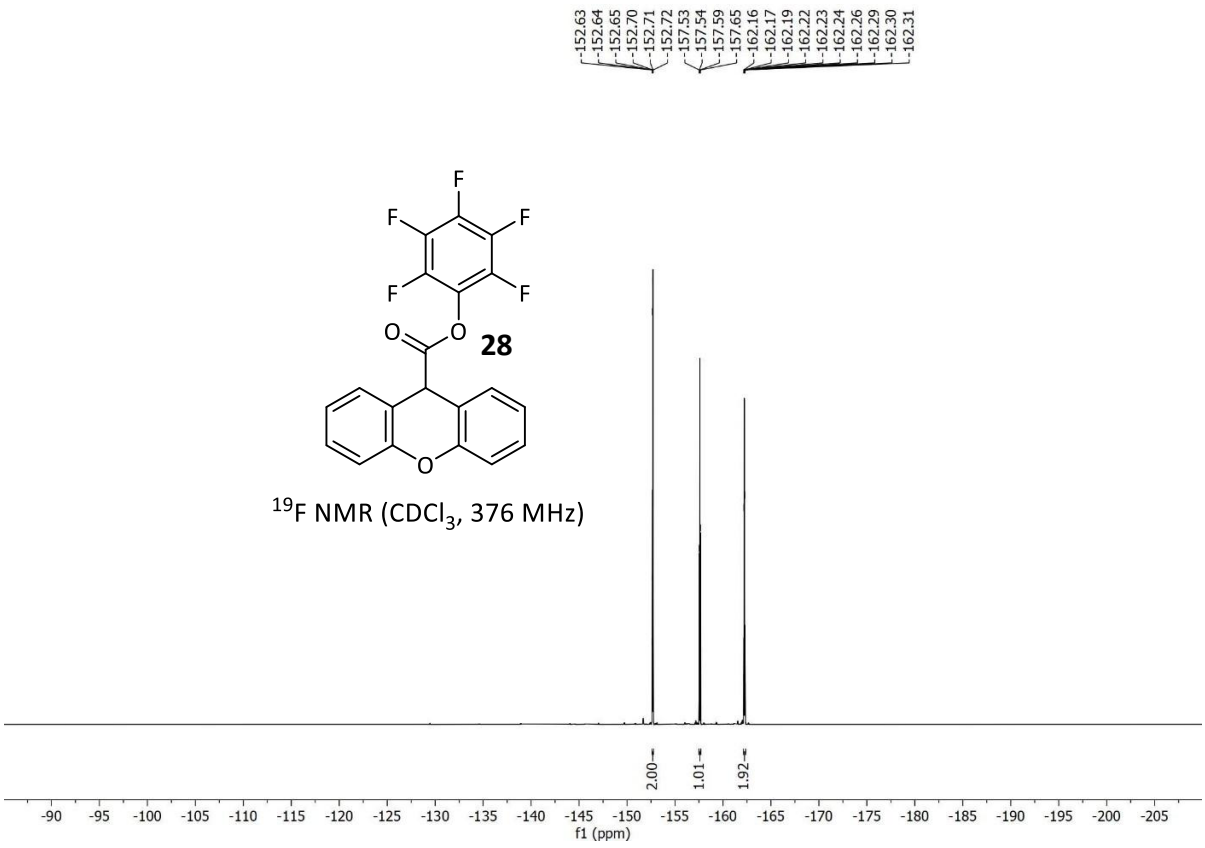

171.04
138.22
134.88
129.55
129.15
128.75
127.59
127.53
127.50
77.16
43.88
43.68
O
N
H
27 – amide
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



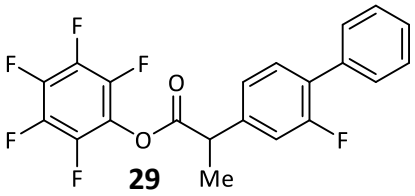
^{1}H NMR ($CDCl_3$, 400 MHz)



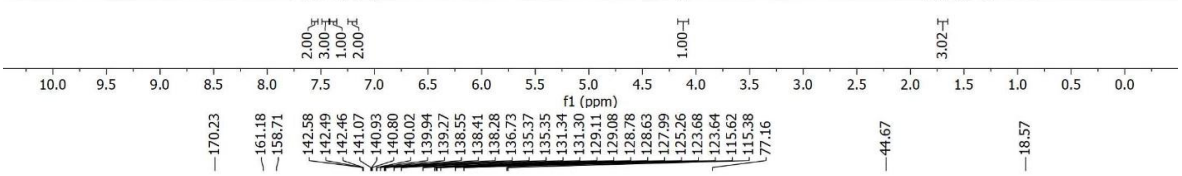
^{13}C NMR ($CDCl_3$, 100 MHz)

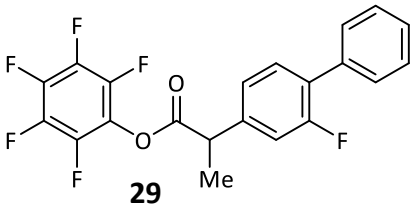


^{19}F NMR ($CDCl_3$, 376 MHz)

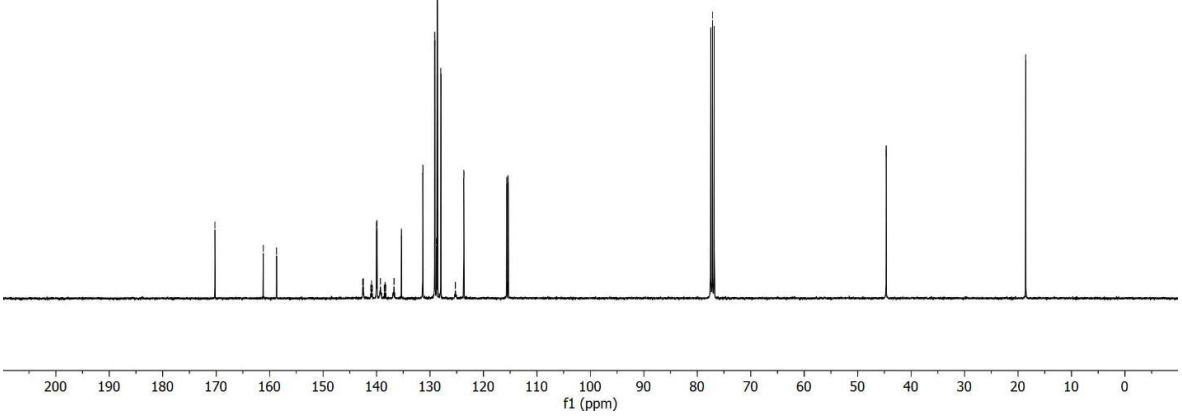


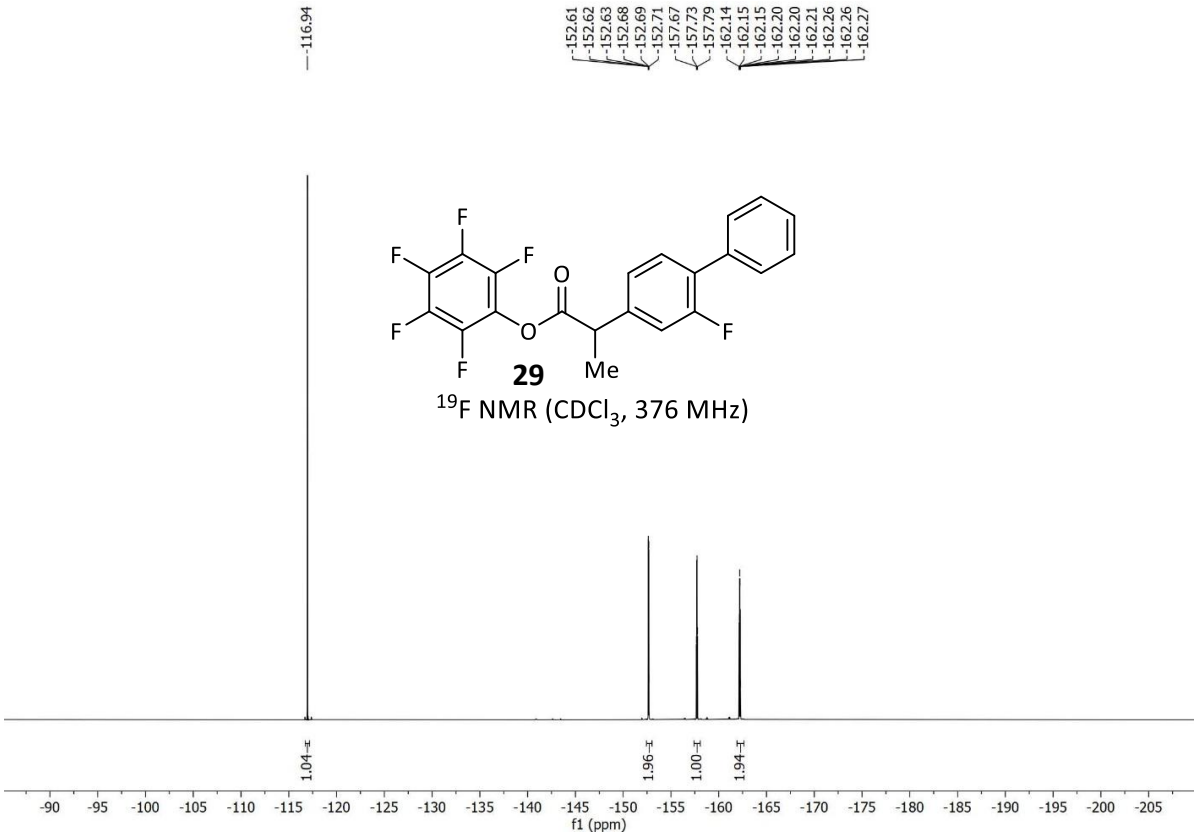
^{1}H NMR ($CDCl_3$, 400 MHz)





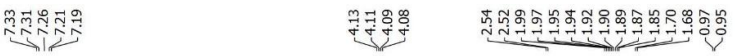
^{13}C NMR ($CDCl_3$, 100 MHz)

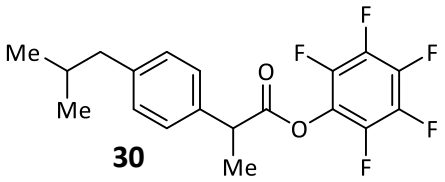




29

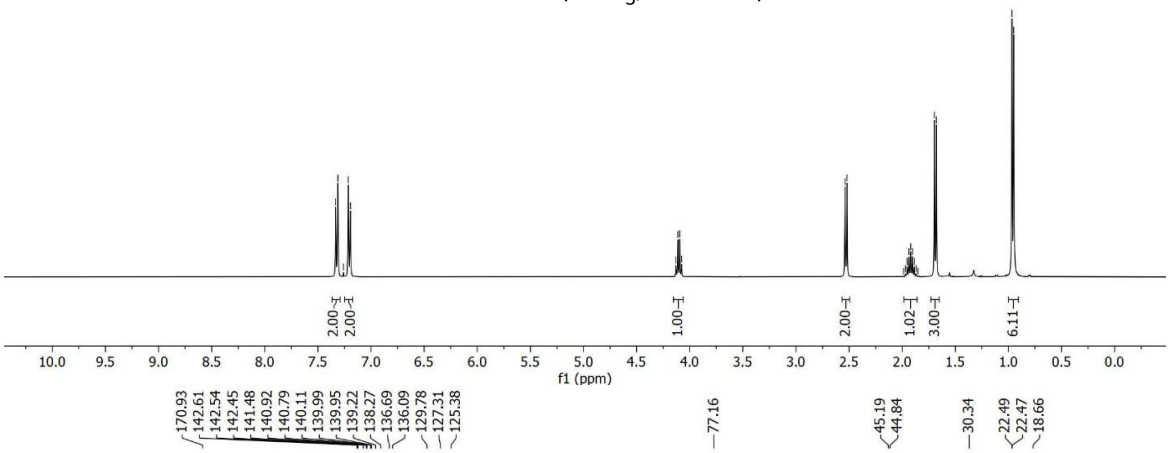
^{19}F NMR ($CDCl_3$, 376 MHz)

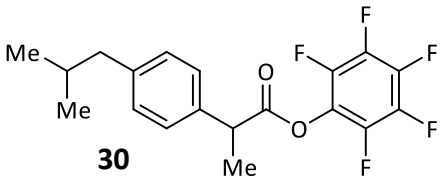




30

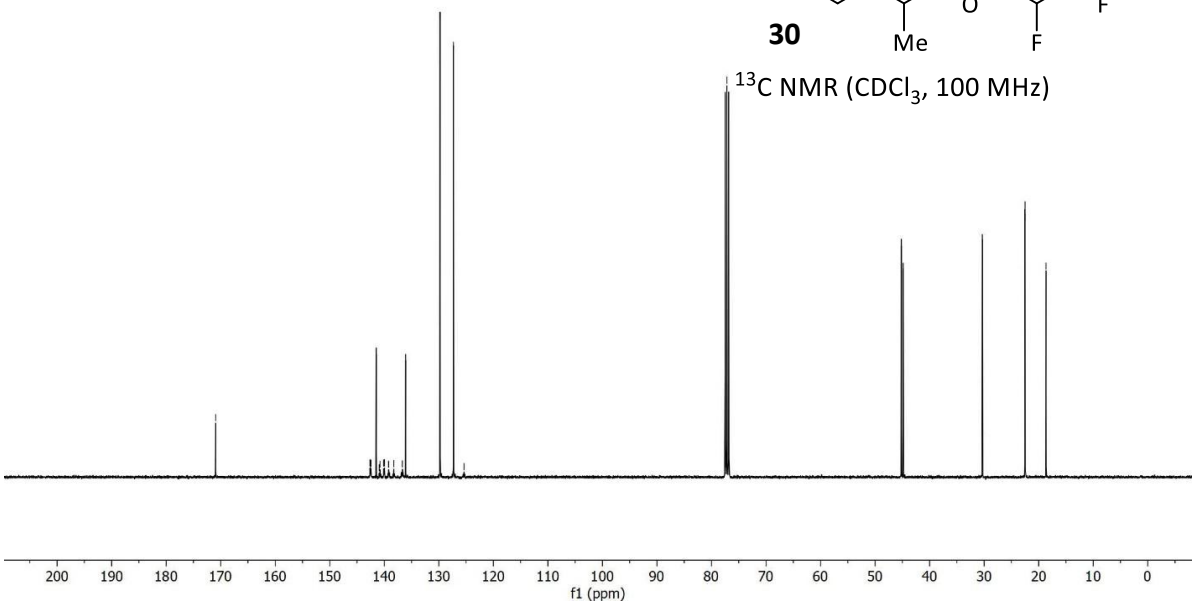
^{1}H NMR ($CDCl_3$, 400 MHz)

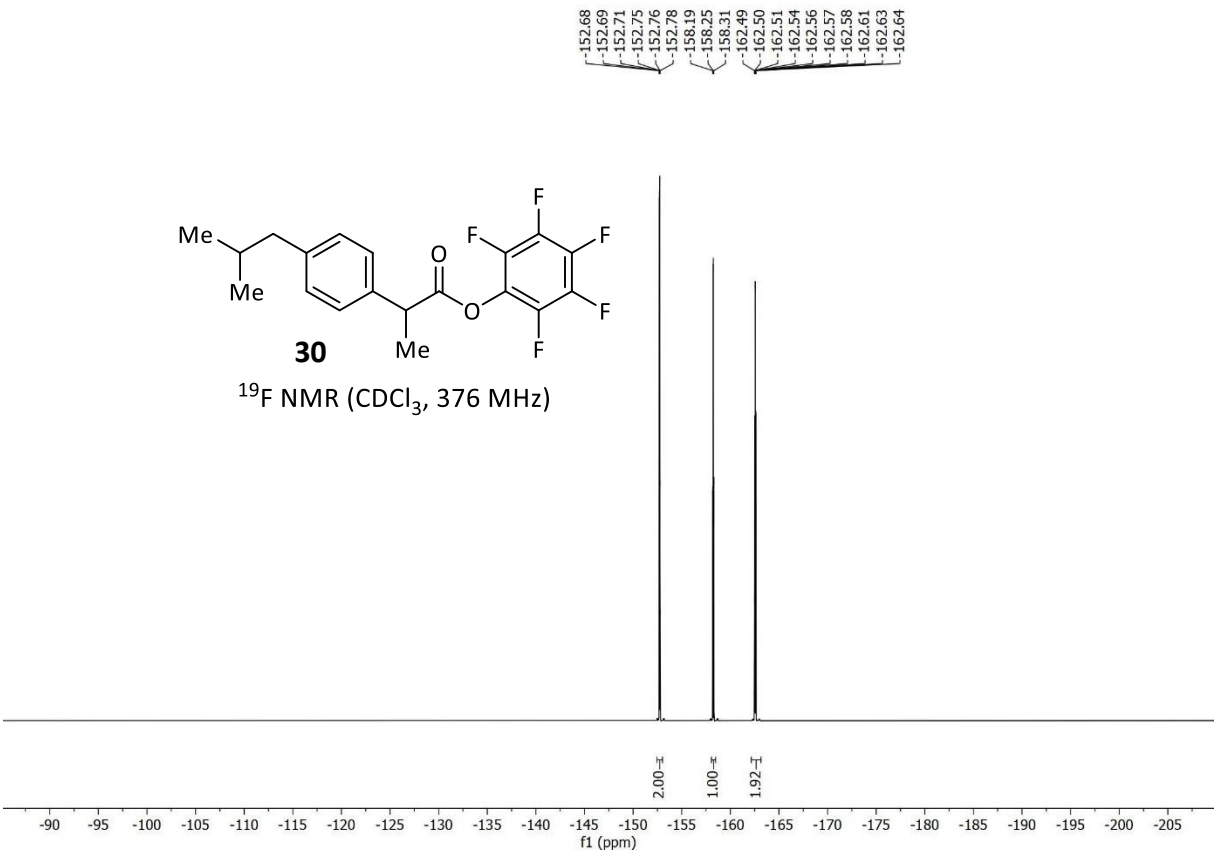


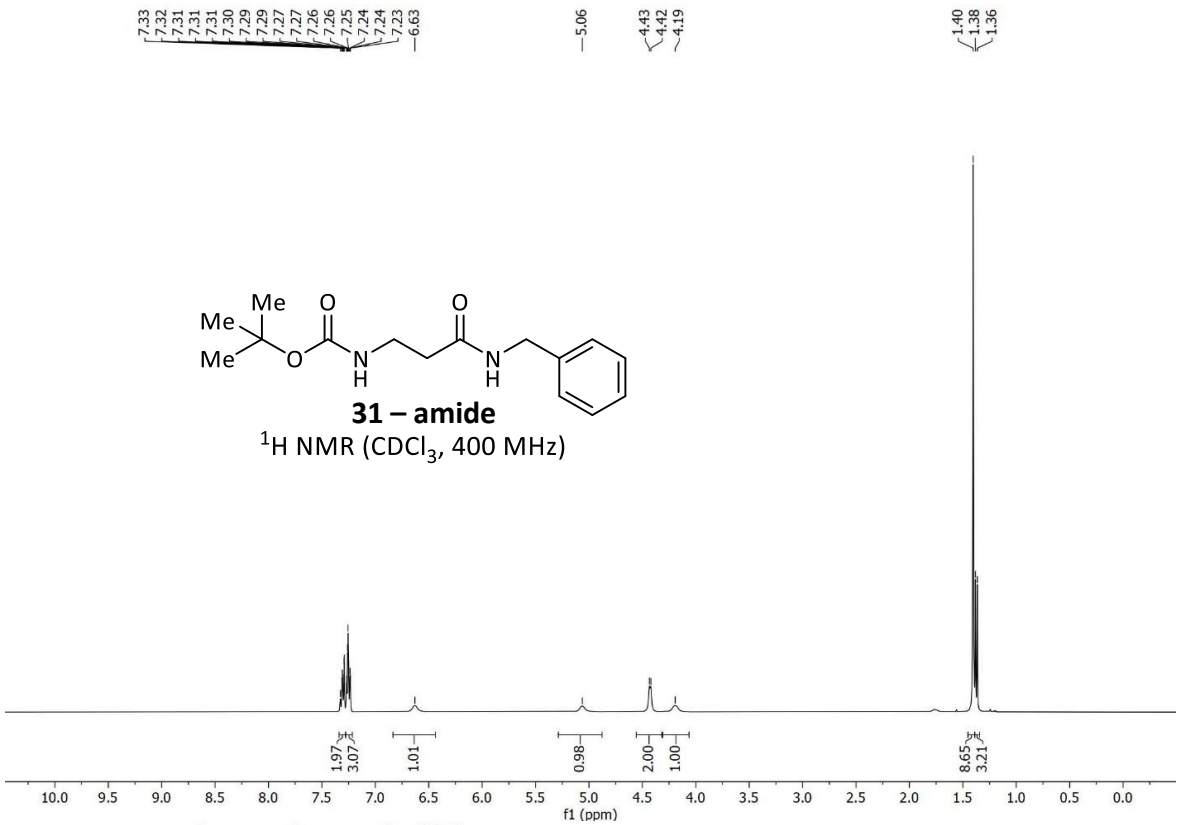


30

^{13}C NMR ($CDCl_3$, 100 MHz)

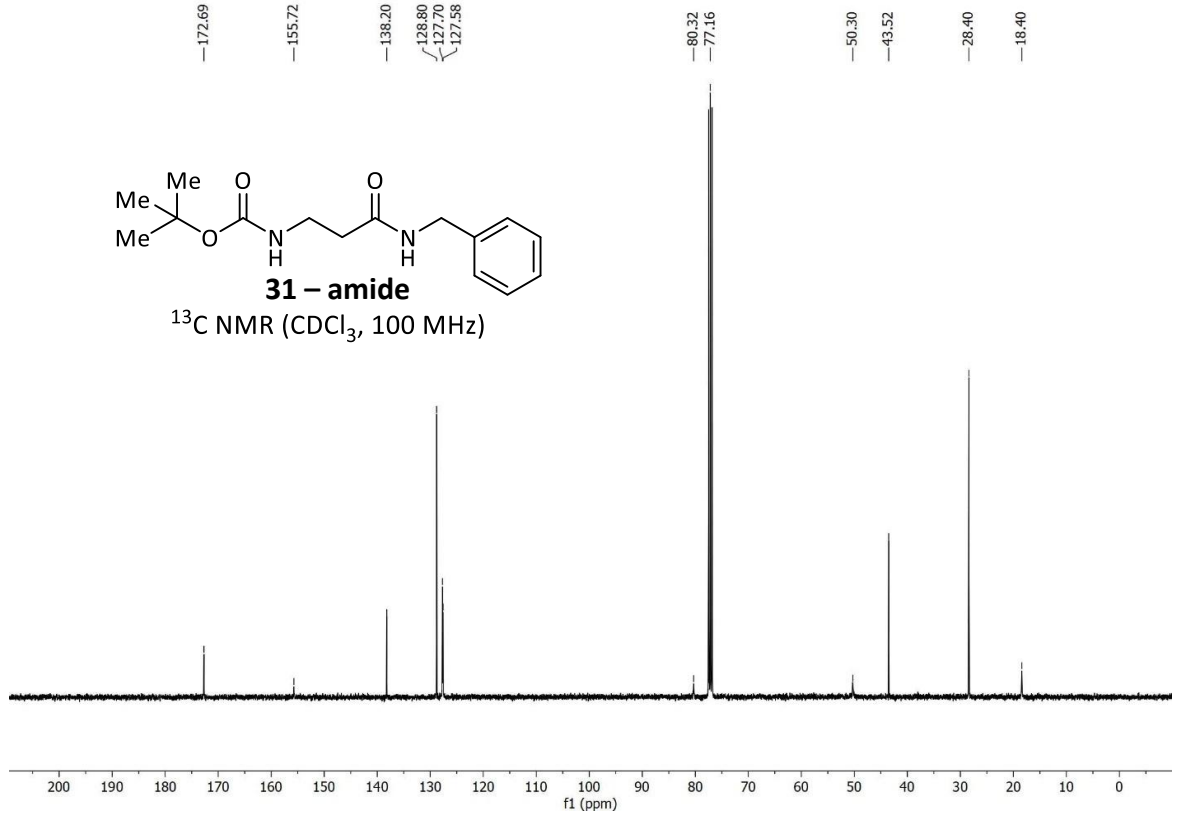



-152.68
-152.69
-152.71
-152.75
-152.76
-152.78
-158.19
-158.25
-158.31
-162.49
-162.50
-162.51
-162.54
-162.56
-162.57
-162.58
-162.61
-162.63
-162.64
Me
Me
O
O
F
F
F
F
F
Me
30
^{19}F NMR ($CDCl_3$, 376 MHz)
2.00
1.00
1.92
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)



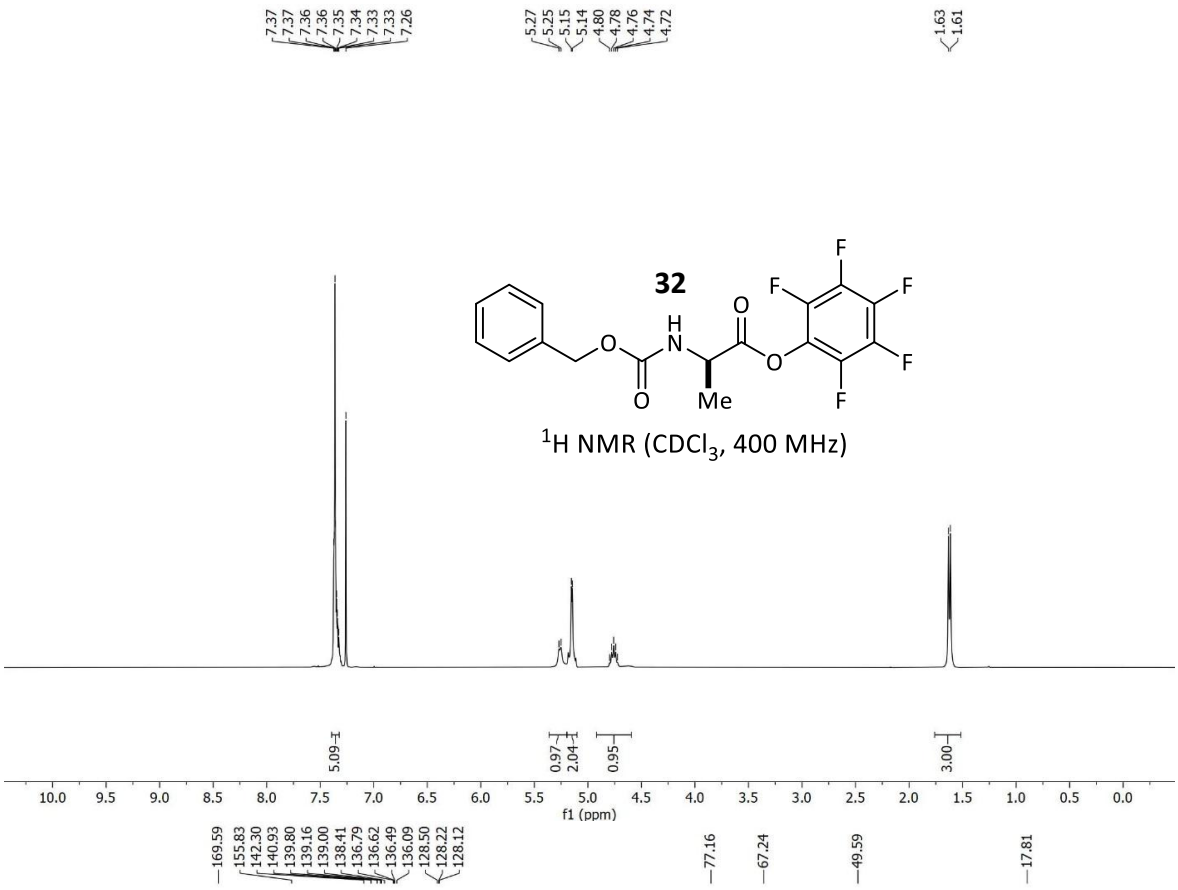
31 – amide

^{1}H NMR ($CDCl_3$, 400 MHz)

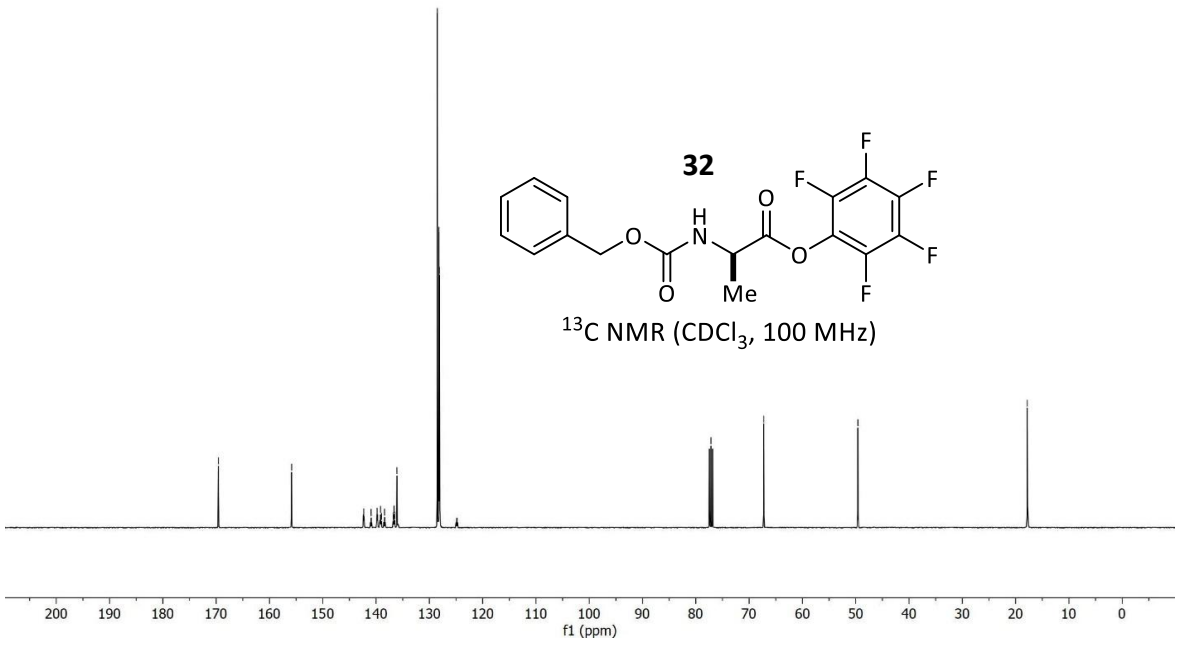


31 – amide

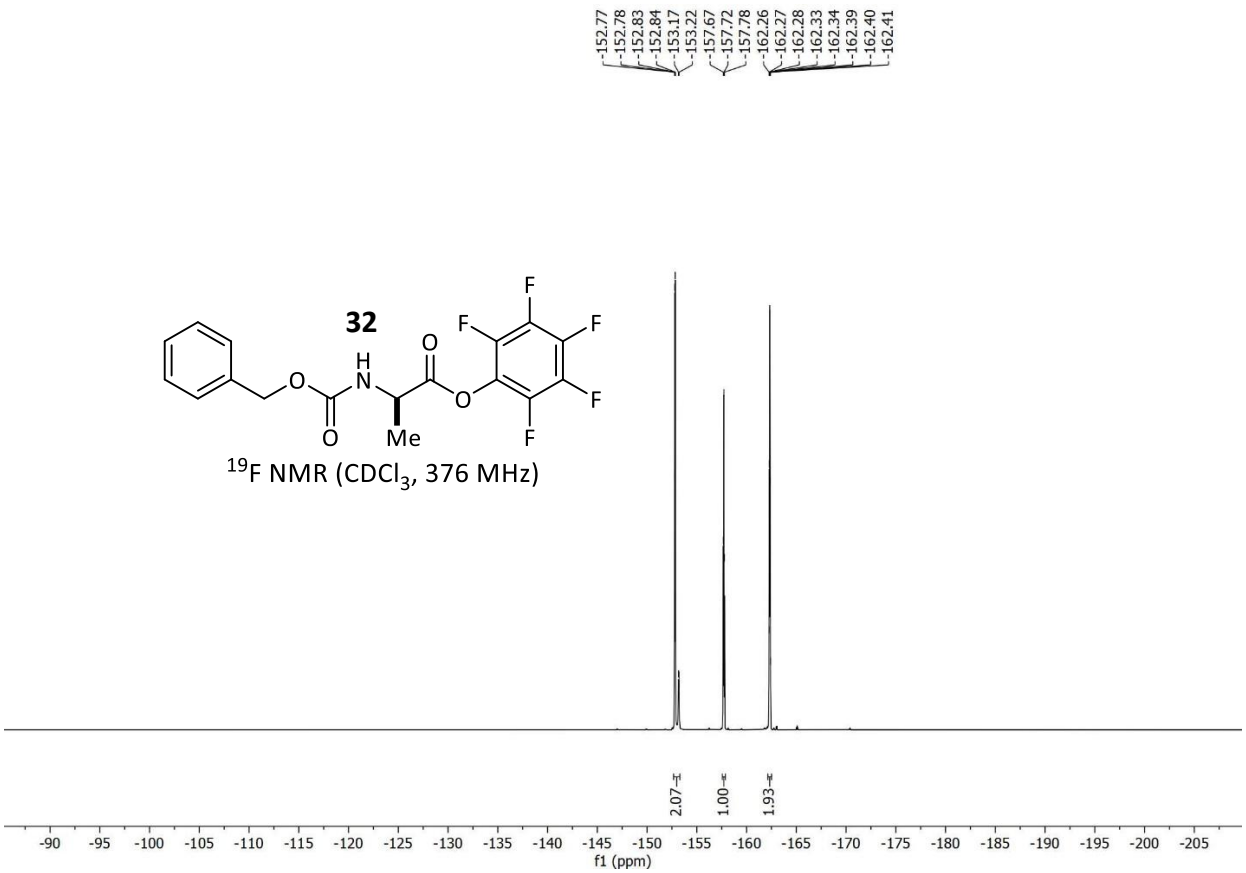
^{13}C NMR ($CDCl_3$, 100 MHz)

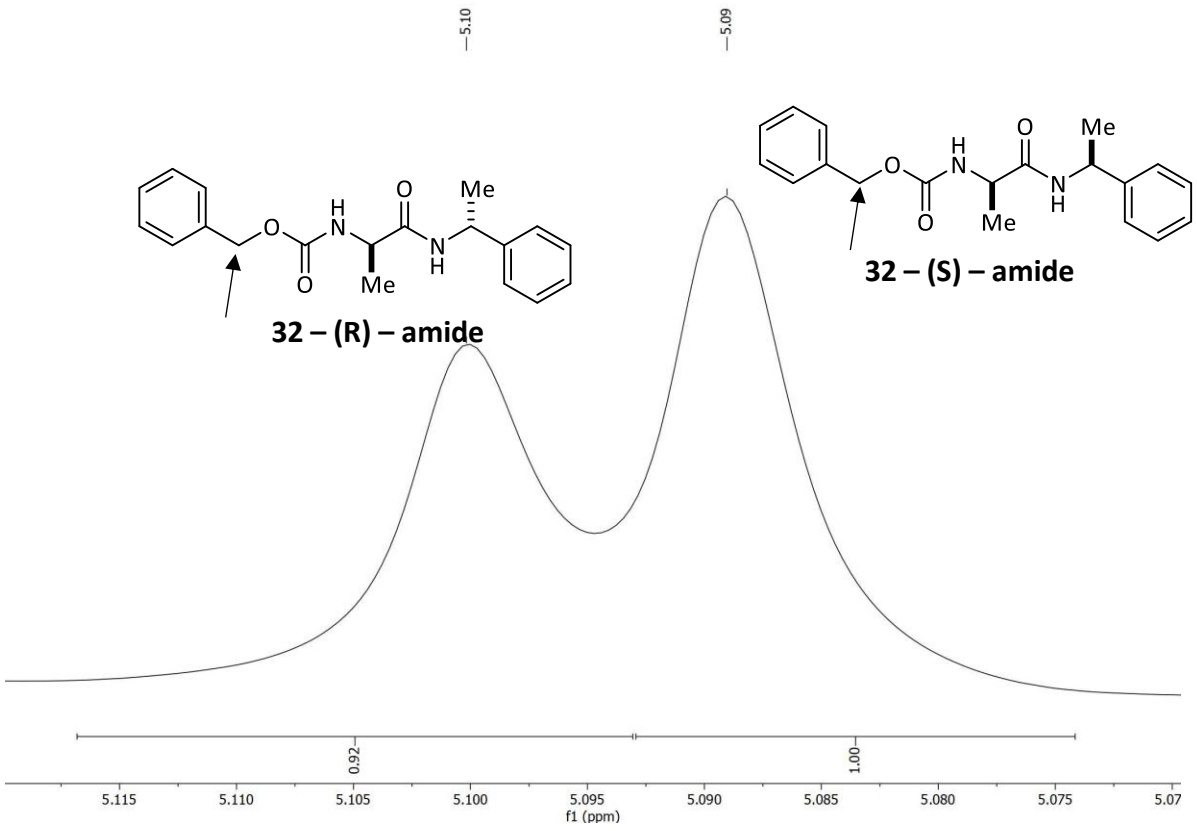


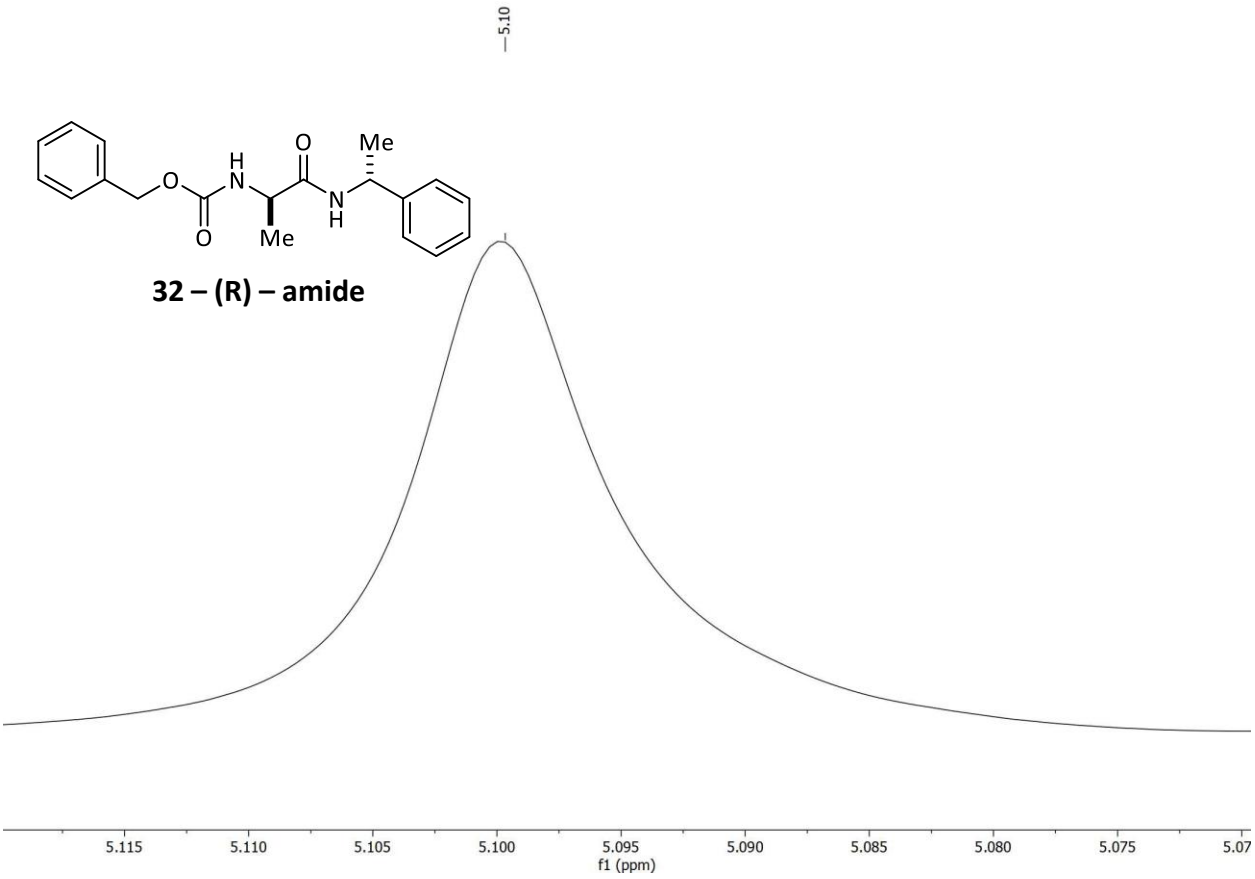
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)

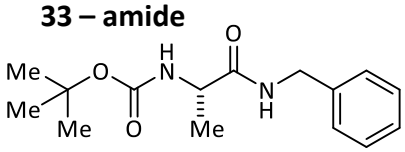

-152.77
-152.78
-152.83
-152.84
-153.17
-153.22
-157.67
-157.72
-157.78
-162.26
-162.27
-162.28
-162.33
-162.34
-162.39
-162.40
-162.41
32
F
F
F
F
F
O
H
N
O
O
O
Me
19F NMR (CDCl3, 376 MHz)
2.07
1.00
1.93
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)


5.10
5.09
32 – (R) – amide
32 – (S) – amide
0.92
1.00
5.115 5.110 5.105 5.100 5.095 5.090 5.085 5.080 5.075 5.07
f1 (ppm)


5.10
O
Me
H
N
O
N
H
O
Me
5.115
5.110
5.105
5.100
5.095
5.090
5.085
5.080
5.075
5.07
f1 (ppm)

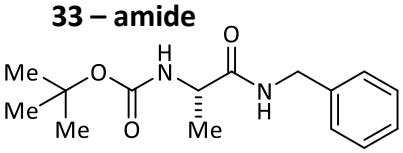
32 – (R) – amide

33 – amide

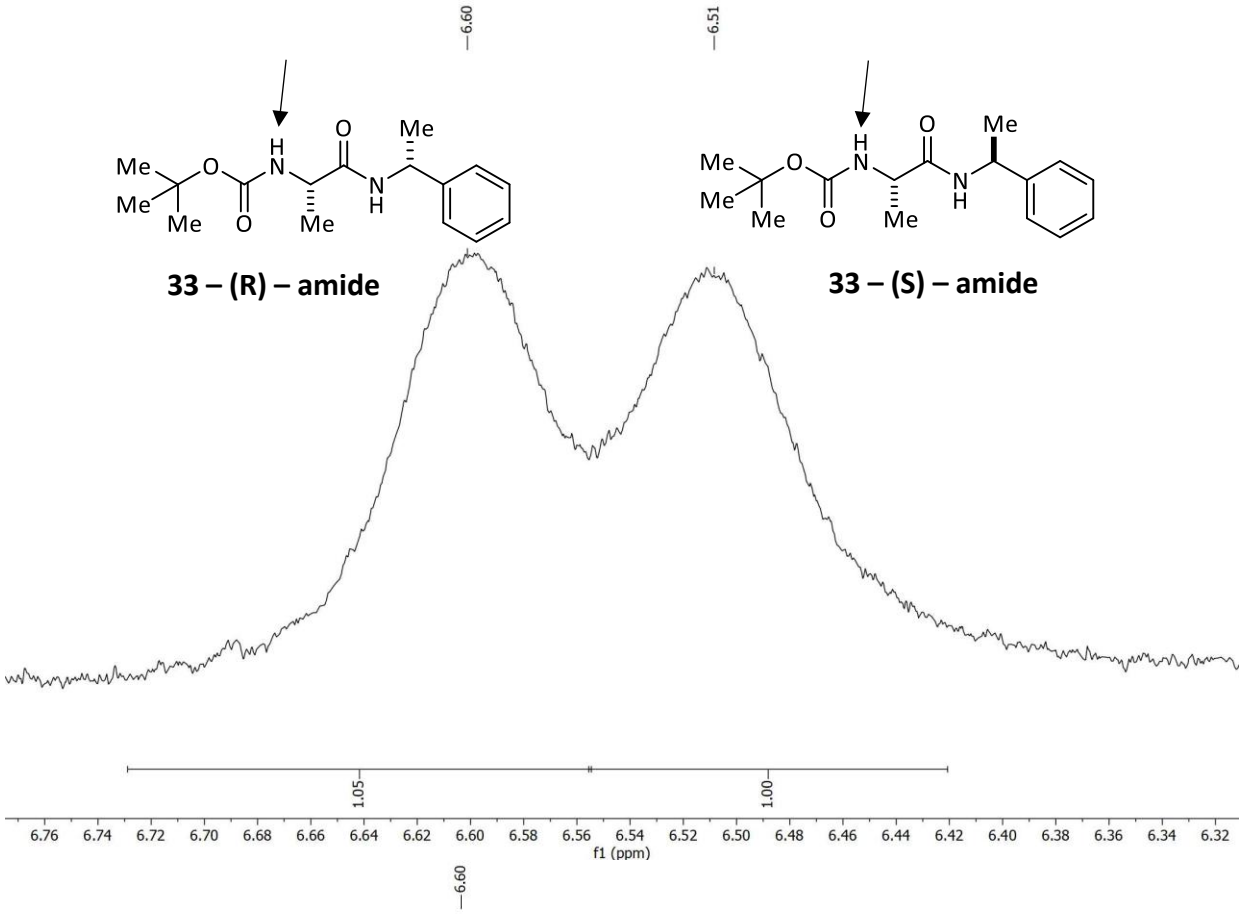


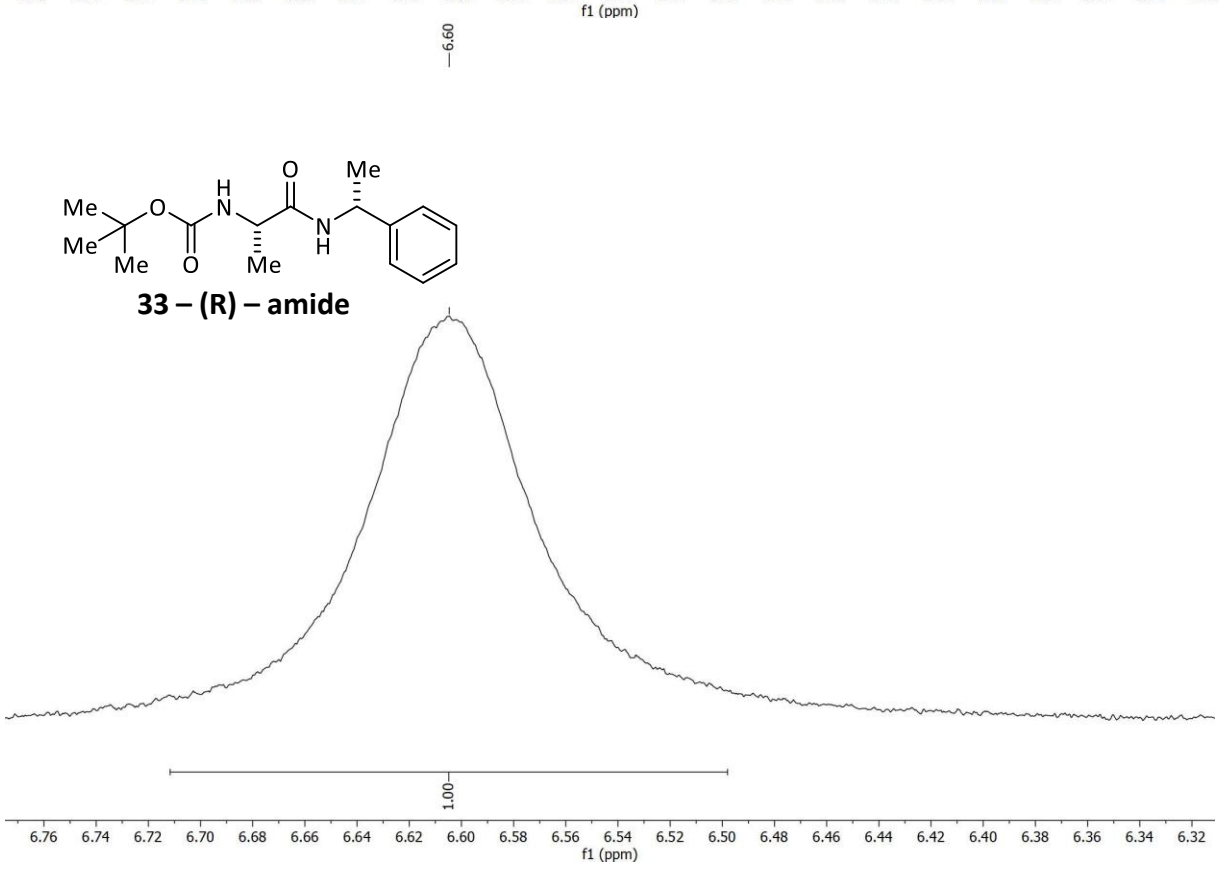
^{1}H NMR ($CDCl_3$, 400 MHz)

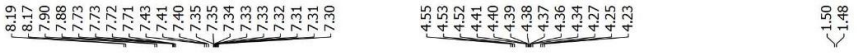
33 – amide

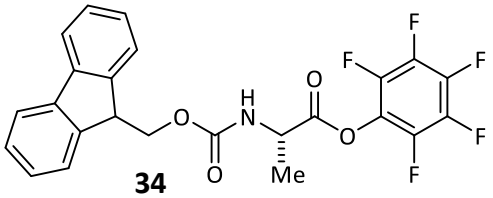


^{13}C NMR ($CDCl_3$, 100 MHz)


6.60
6.51
33 – (R) – amide
33 – (S) – amide
1.05
1.00
6.76 6.74 6.72 6.70 6.68 6.66 6.64 6.62 6.60 6.58 6.56 6.54 6.52 6.50 6.48 6.46 6.44 6.42 6.40 6.38 6.36 6.34 6.32
f1 (ppm)

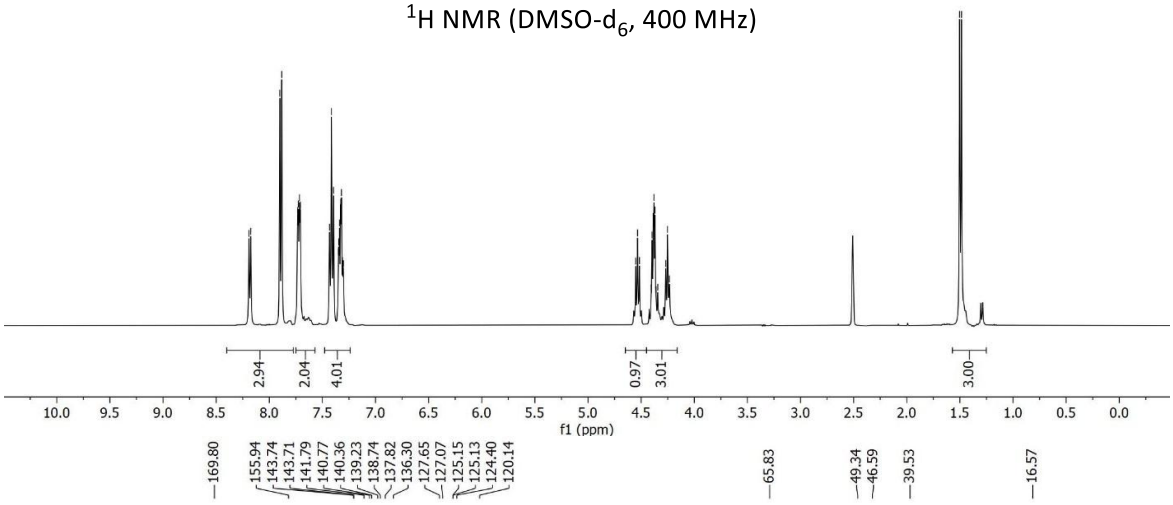

6.60
33 – (R) – amide
1.00
6.76 6.74 6.72 6.70 6.68 6.66 6.64 6.62 6.60 6.58 6.56 6.54 6.52 6.50 6.48 6.46 6.44 6.42 6.40 6.38 6.36 6.34 6.32
f1 (ppm)

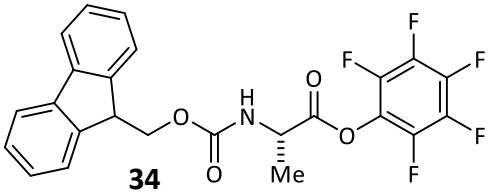




34

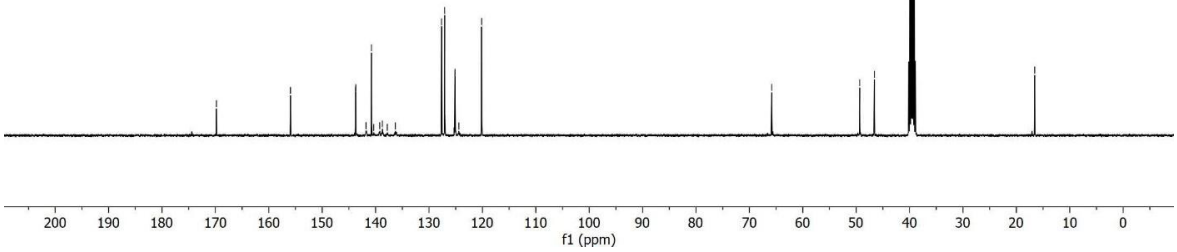
^{1}H NMR (DMSO-d_6, 400 MHz)

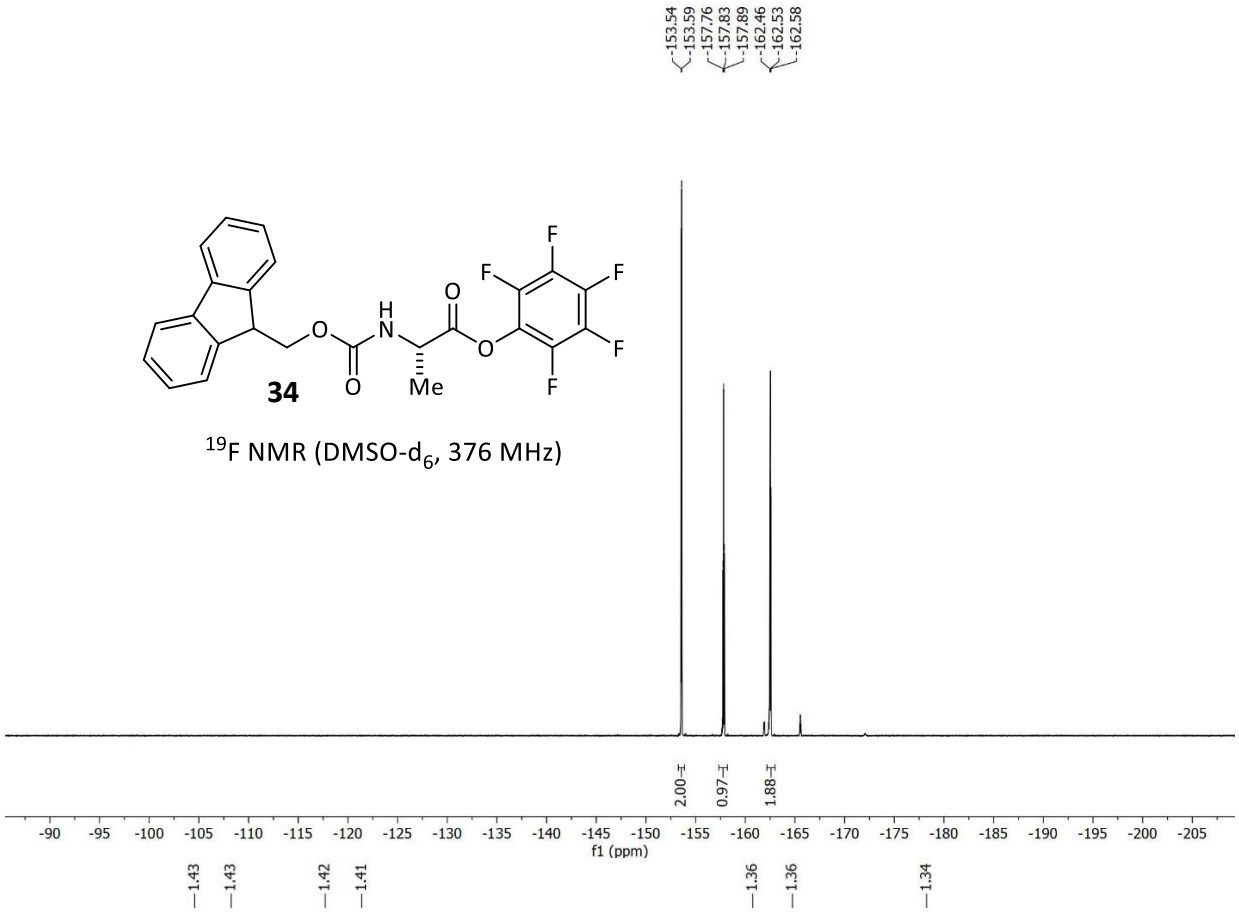




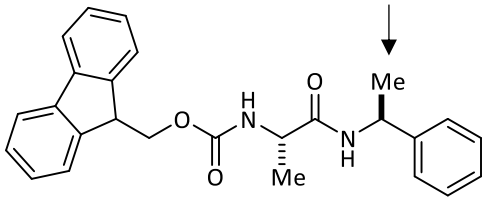
34

^{13}C NMR (DMSO-d_6, 100 MHz)

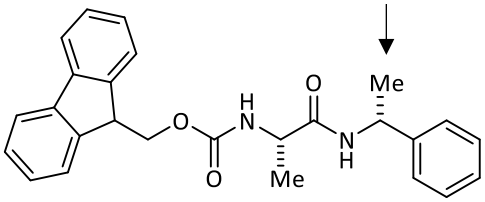




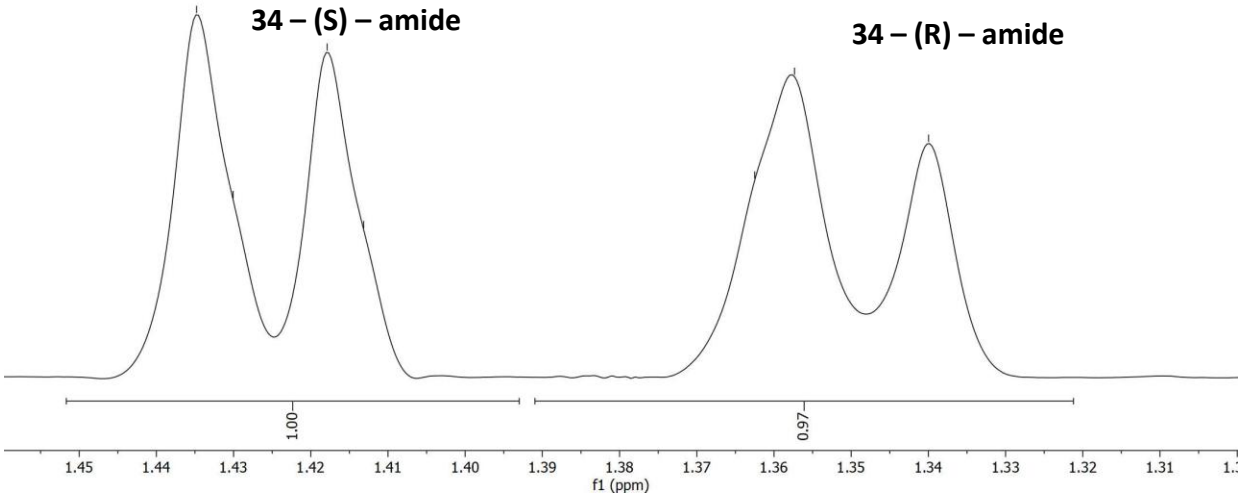
^{19}F NMR (DMSO-d_6, 376 MHz)

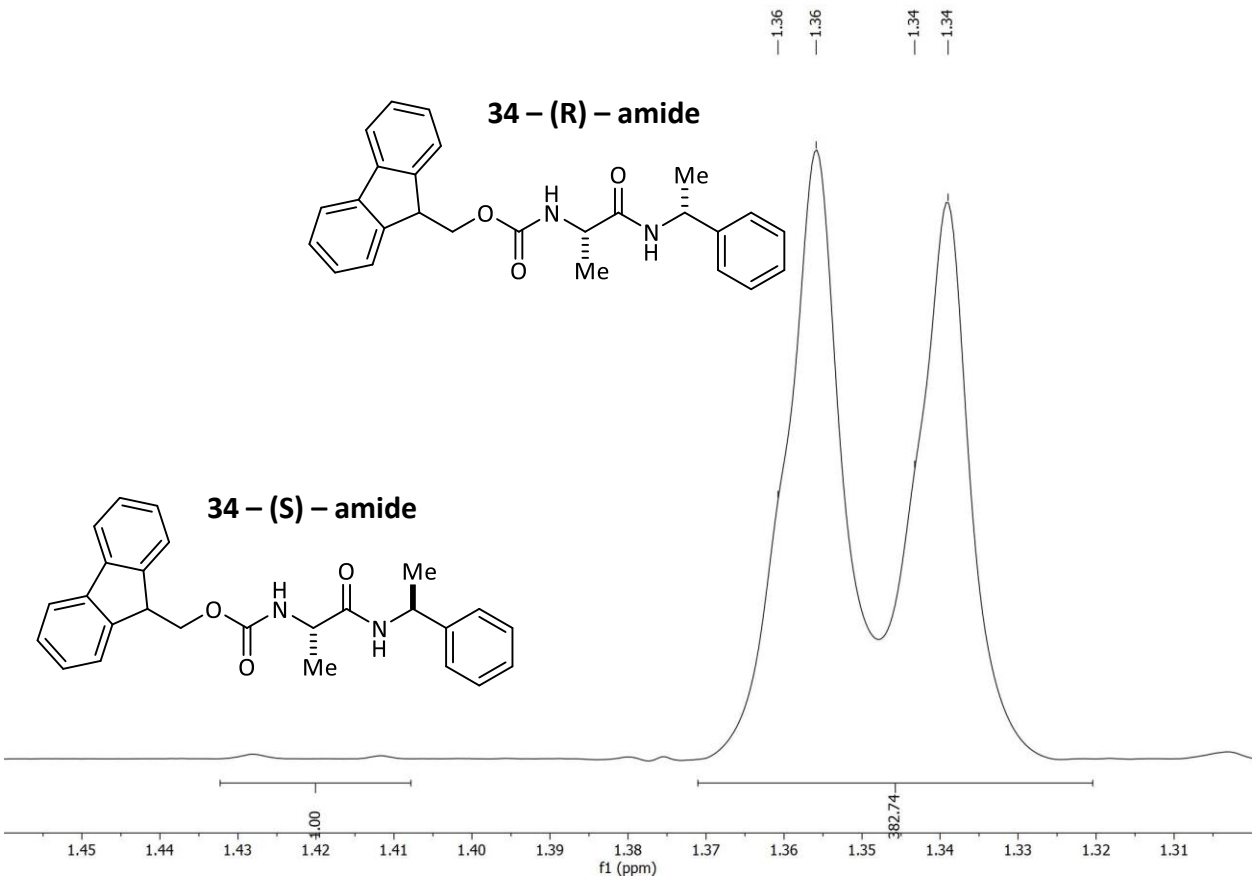


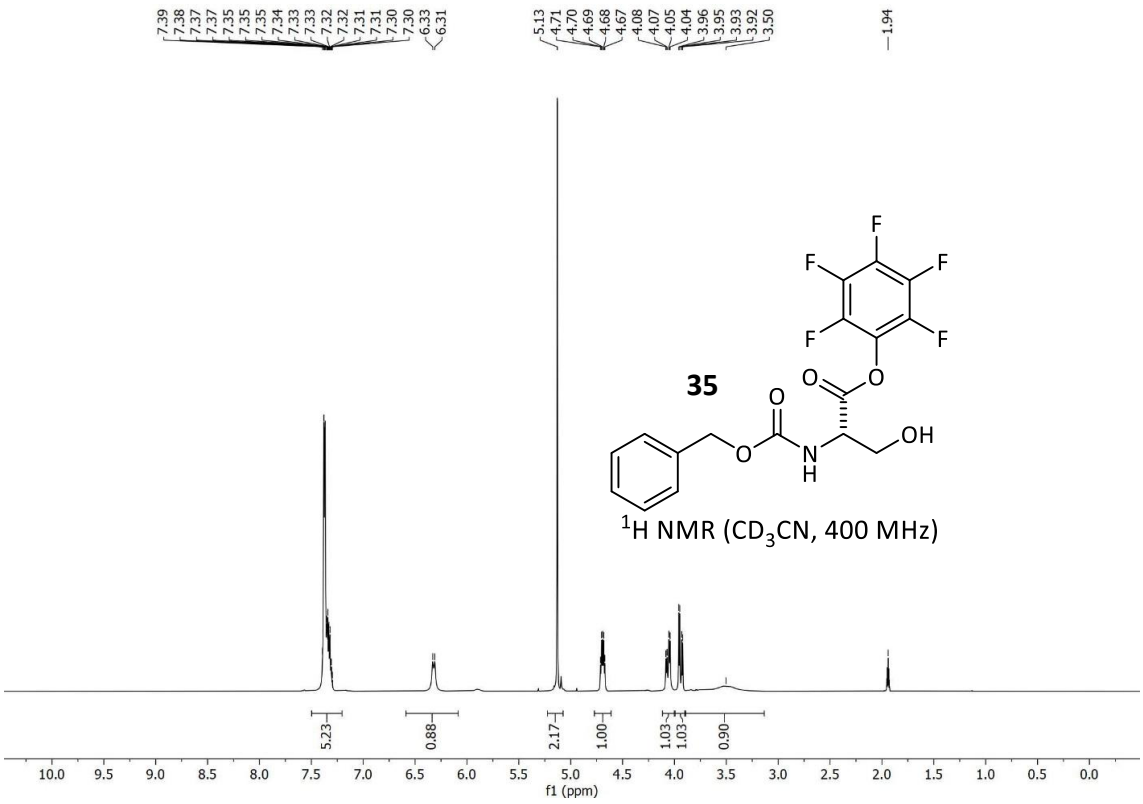
34 – (S) – amide

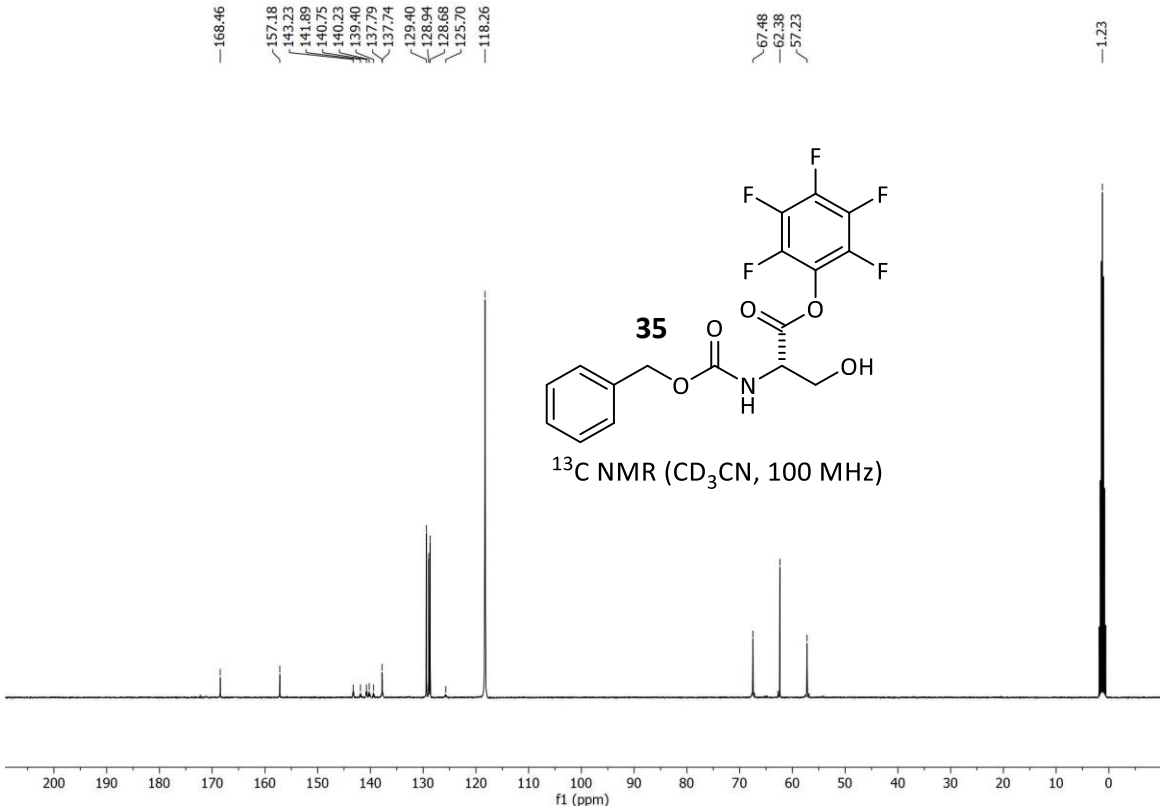


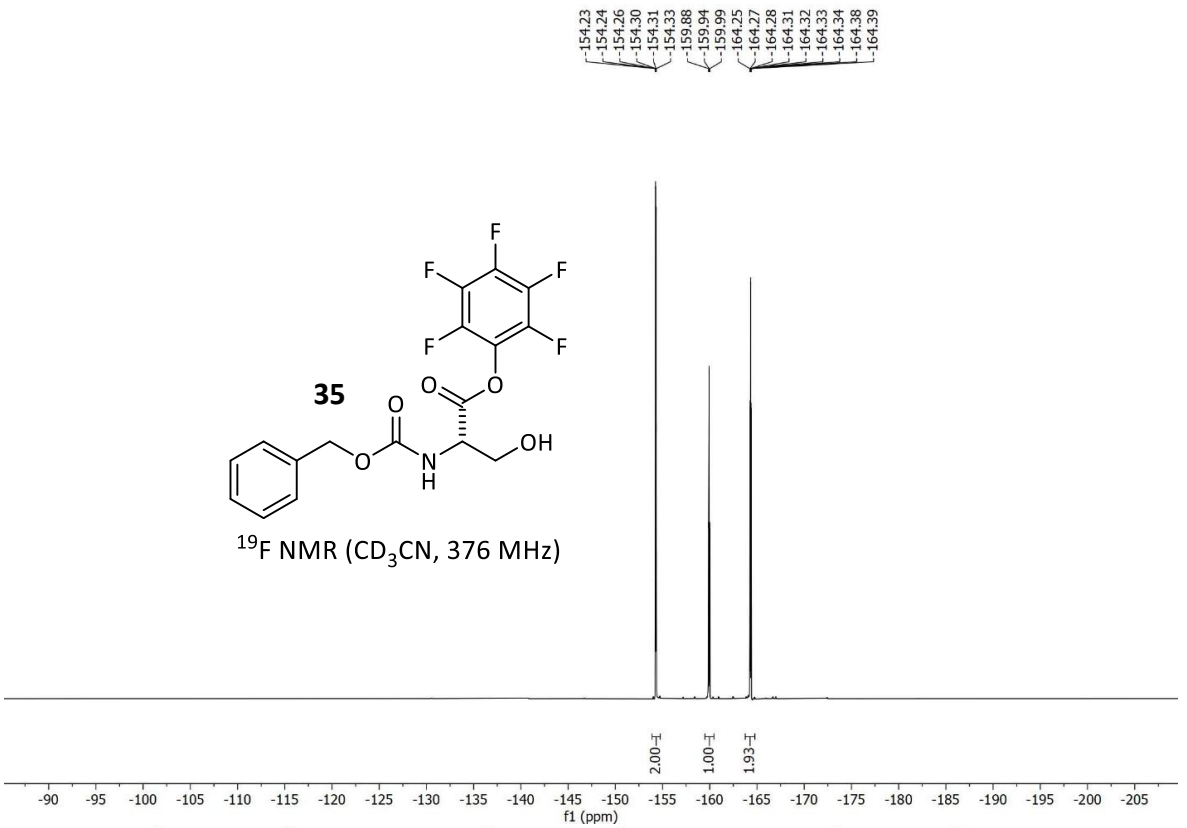
34 – (R) – amide

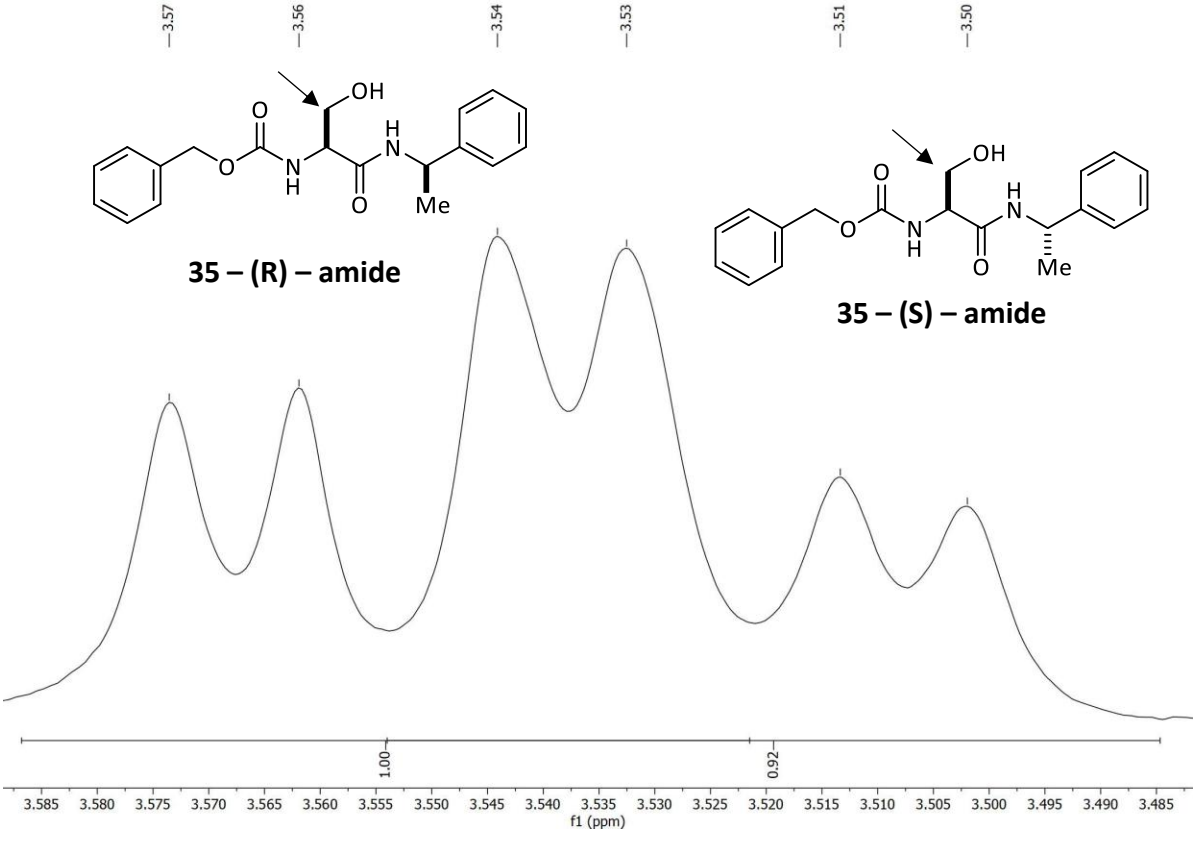


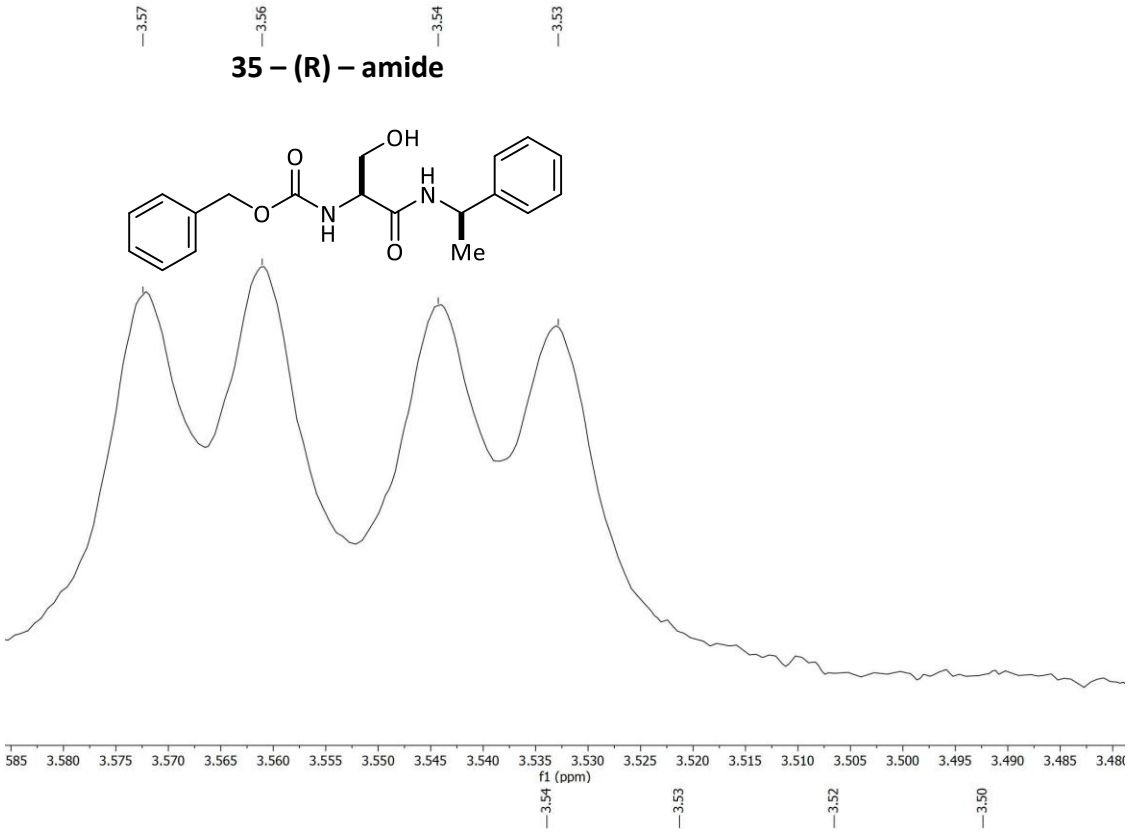

34 – (R) – amide
34 – (S) – amide
1.36
1.36
1.34
1.34
1.00
382.74
1.45
1.44
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.32
1.31
f1 (ppm)


35
^{1}H NMR (CD_3CN, 400 MHz)
f1 (ppm)

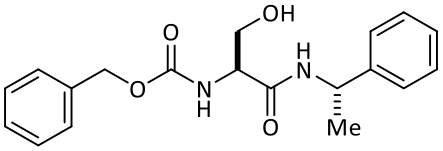

35
^{13}C NMR (CD_3CN, 100 MHz)
f1 (ppm)


154.23
154.24
154.26
154.30
154.31
154.33
159.88
159.94
159.99
164.25
164.27
164.28
164.31
164.32
164.33
164.34
164.38
164.39
35
19F NMR (CD3CN, 376 MHz)
2.00
1.00
1.93
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)

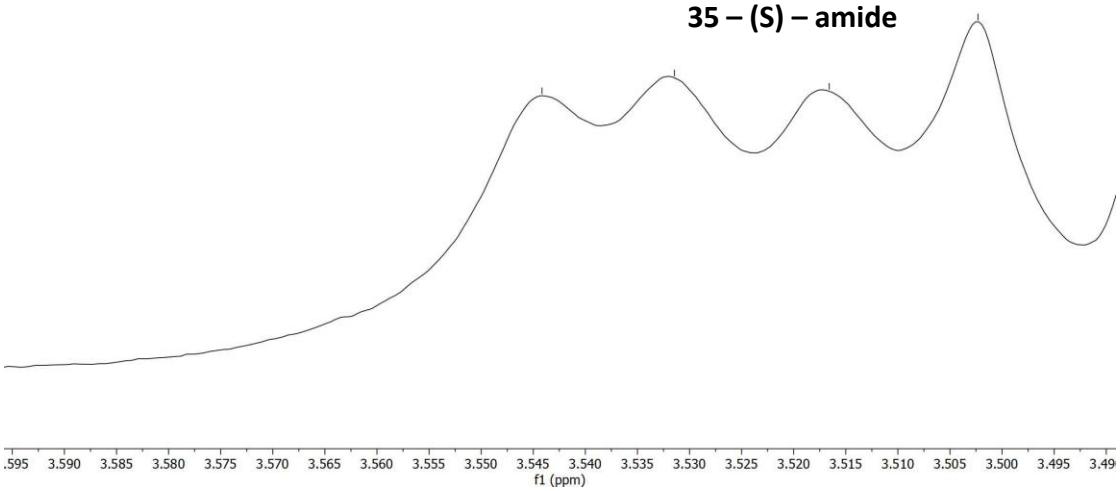

3.57
3.56
3.54
3.53
3.51
3.50
35 – (R) – amide
35 – (S) – amide
1.00
0.92
3.585 3.580 3.575 3.570 3.565 3.560 3.555 3.550 3.545 3.540 3.535 3.530 3.525 3.520 3.515 3.510 3.505 3.500 3.495 3.490 3.485
f1 (ppm)

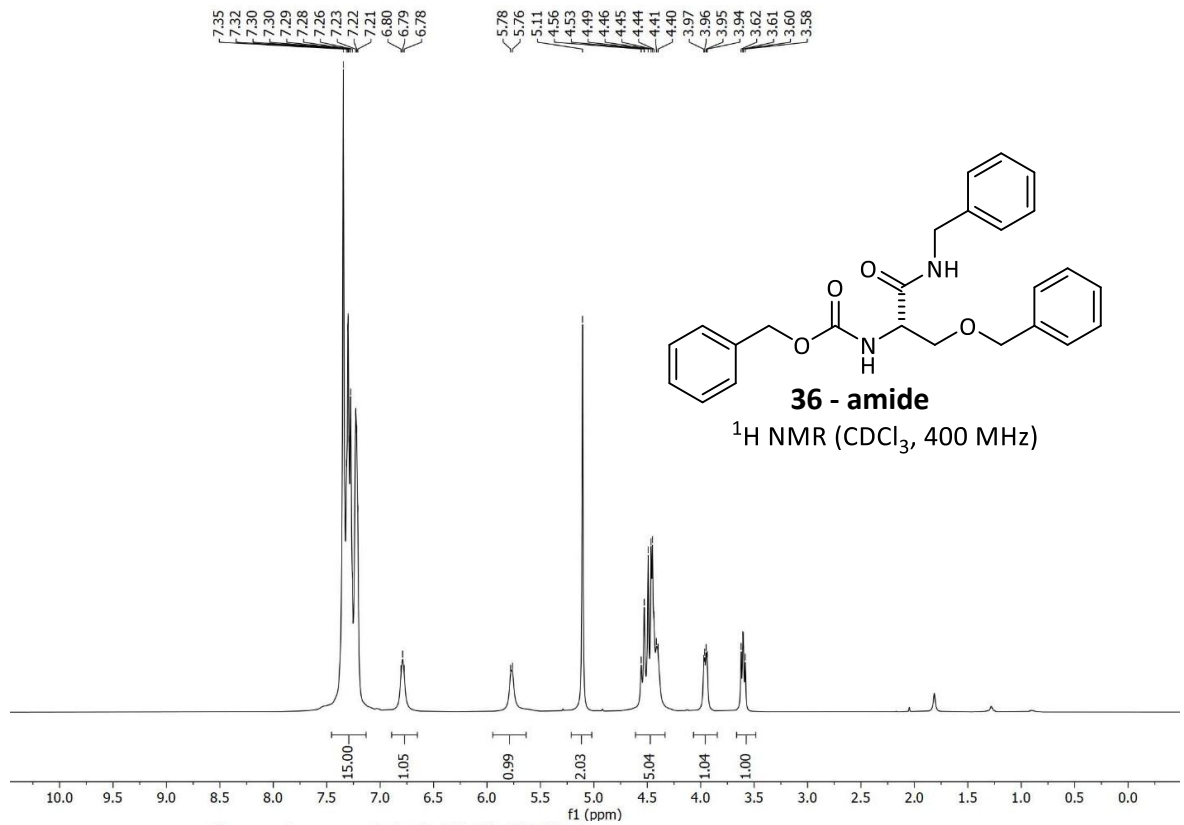


35 – (R) – amide



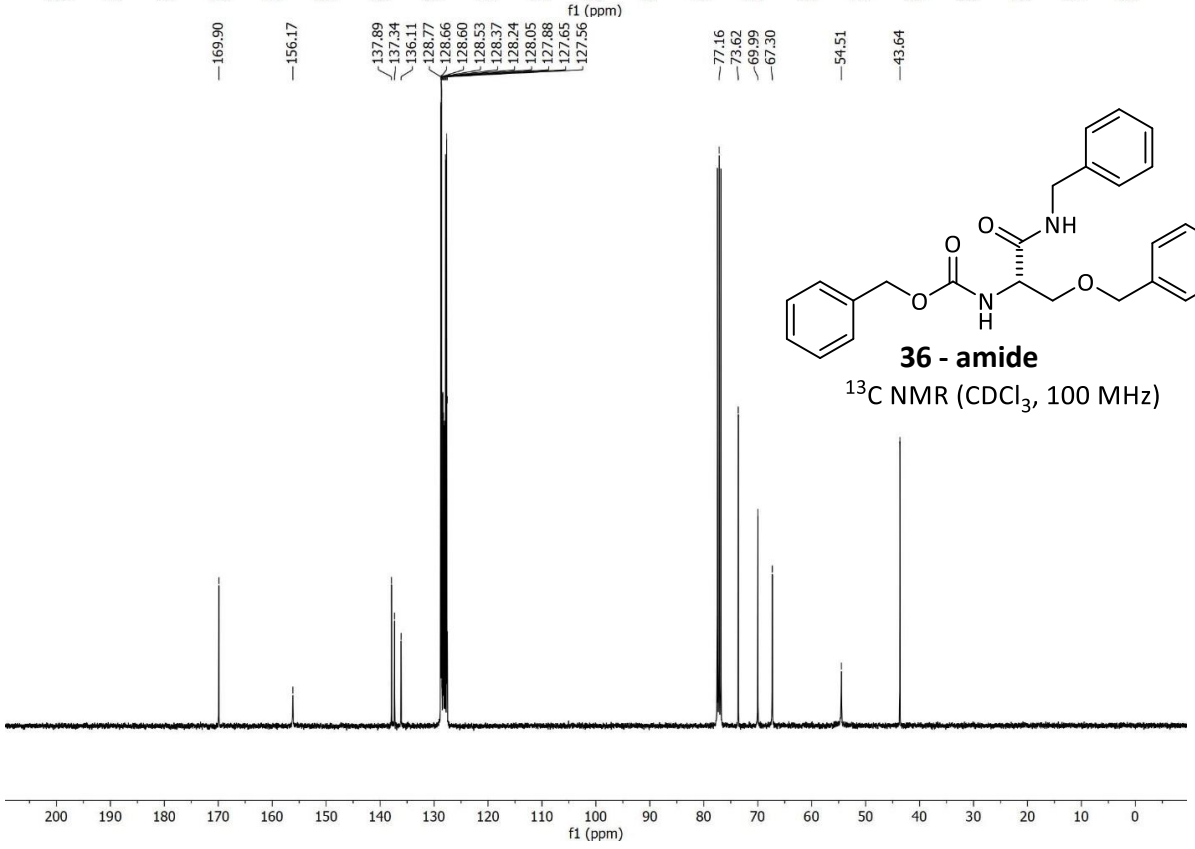
35 – (S) – amide





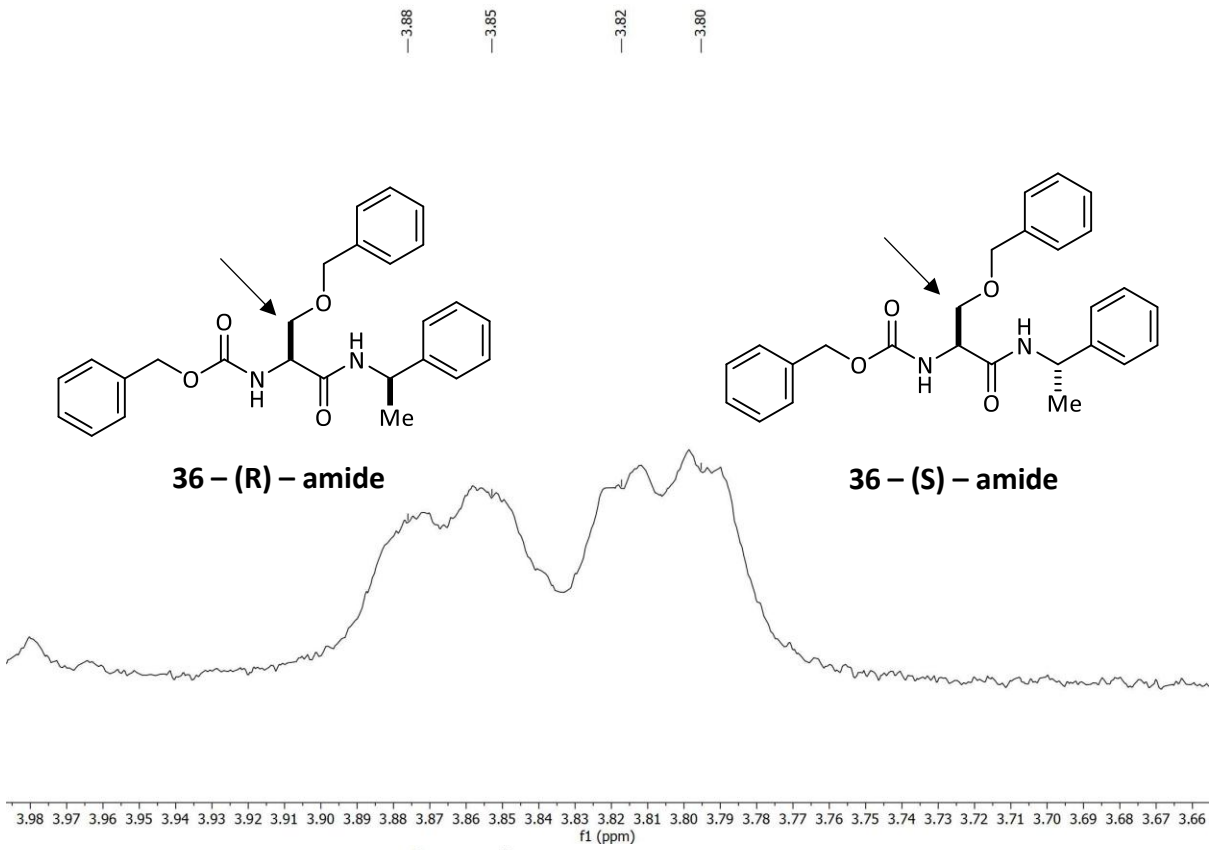
36 - amide

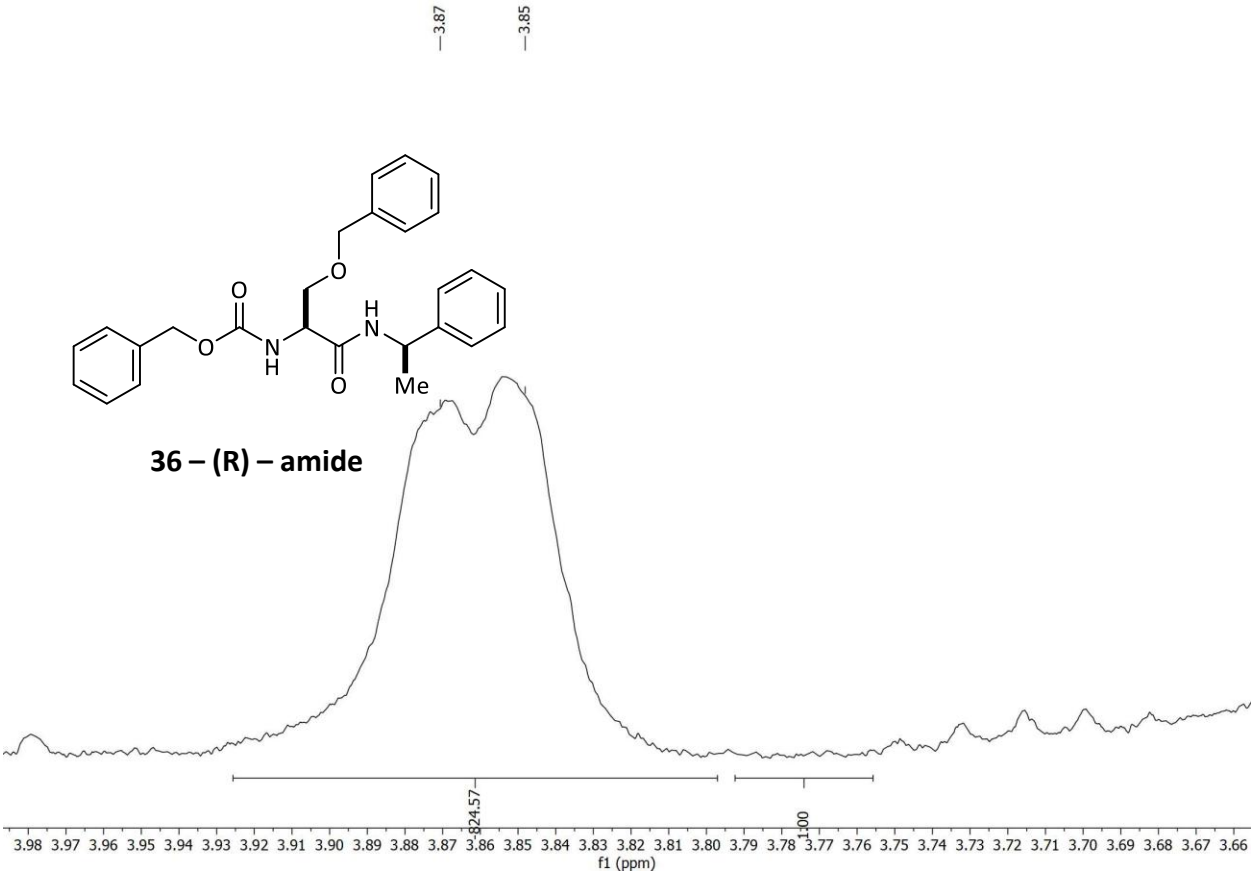
^{1}H NMR ($CDCl_3$, 400 MHz)

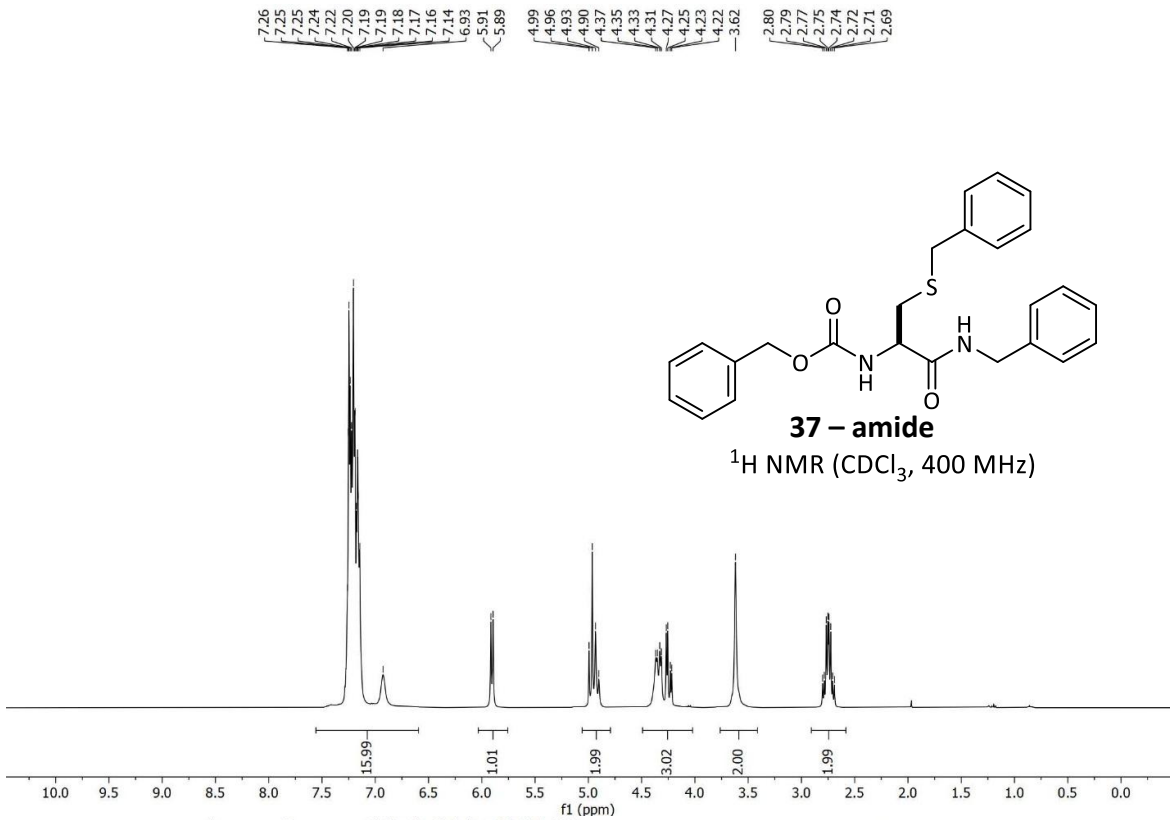


36 - amide

^{13}C NMR ($CDCl_3$, 100 MHz)

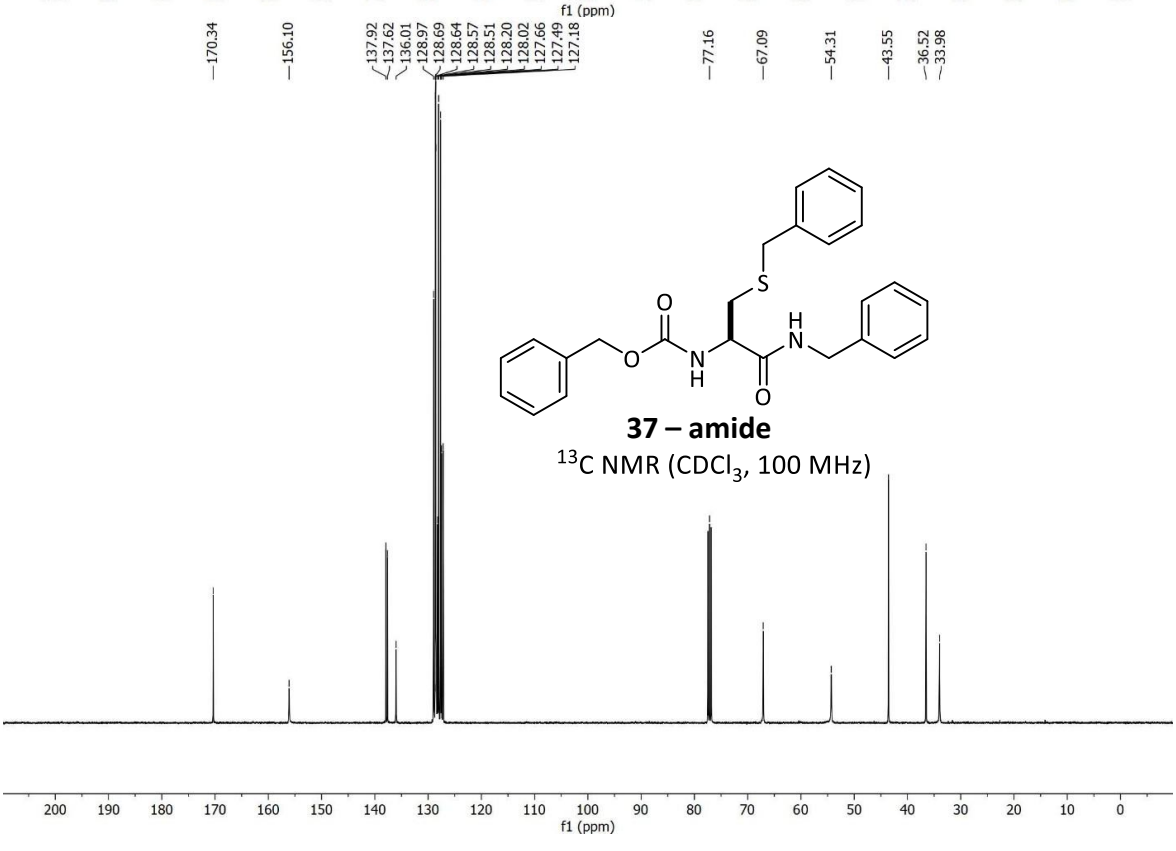

3.88
3.85
3.82
3.80
O
O
N
H
O
H
N
O
Me
36 – (R) – amide
36 – (S) – amide
3.98 3.97 3.96 3.95 3.94 3.93 3.92 3.91 3.90 3.89 3.88 3.87 3.86 3.85 3.84 3.83 3.82 3.81 3.80 3.79 3.78 3.77 3.76 3.75 3.74 3.73 3.72 3.71 3.70 3.69 3.68 3.67 3.66
f1 (ppm)


3.87
3.85
O
O
N
H
O
H
N
O
Me
36 – (R) – amide
824.57
100
3.98 3.97 3.96 3.95 3.94 3.93 3.92 3.91 3.90 3.89 3.88 3.87 3.86 3.85 3.84 3.83 3.82 3.81 3.80 3.79 3.78 3.77 3.76 3.75 3.74 3.73 3.72 3.71 3.70 3.69 3.68 3.67 3.66
f1 (ppm)



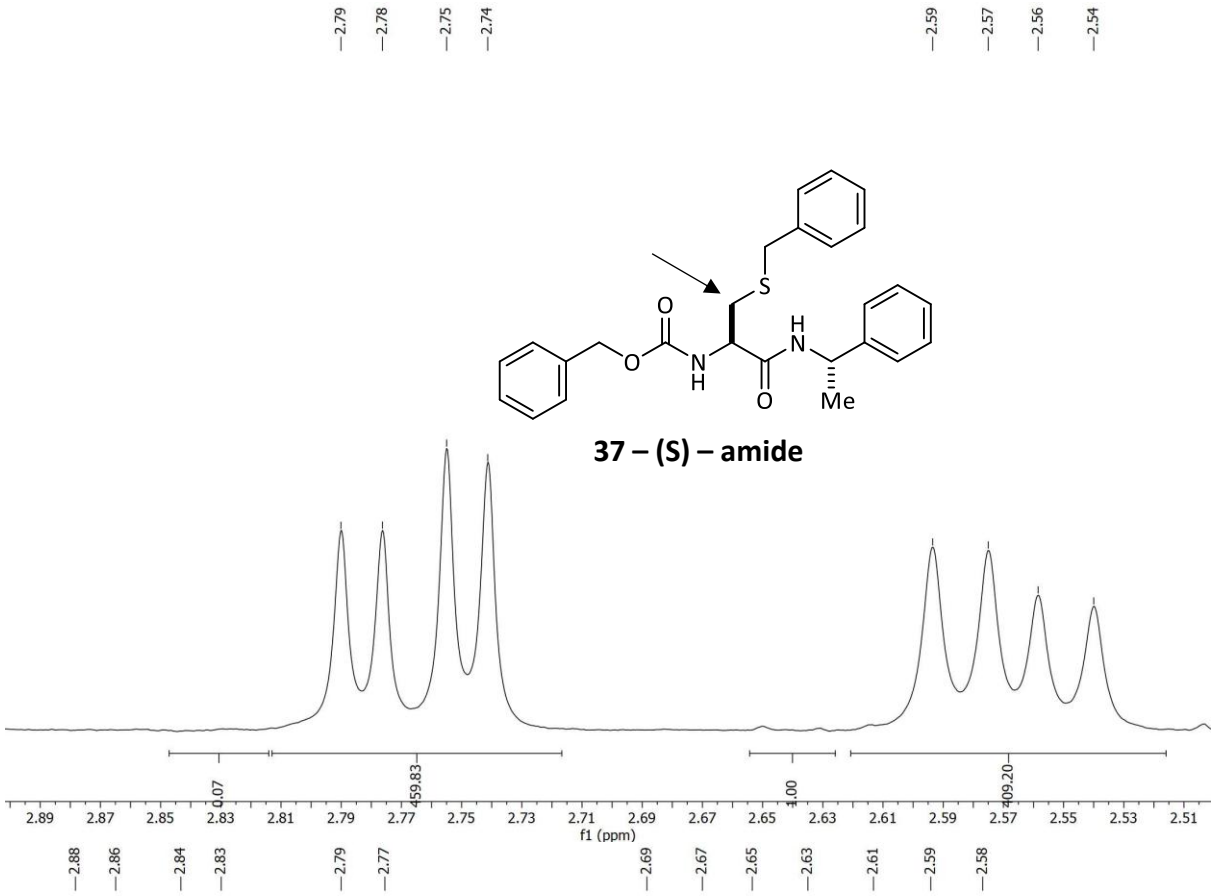
37 – amide

^{1}H NMR ($CDCl_3$, 400 MHz)

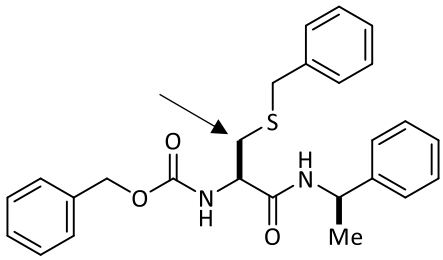


37 – amide

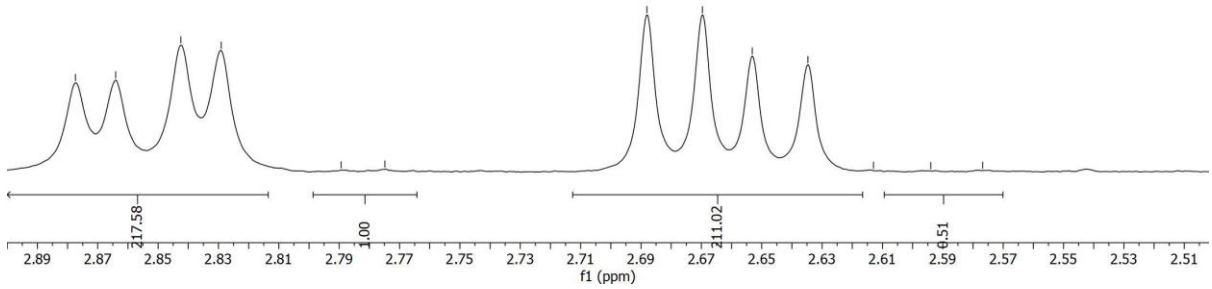
^{13}C NMR ($CDCl_3$, 100 MHz)

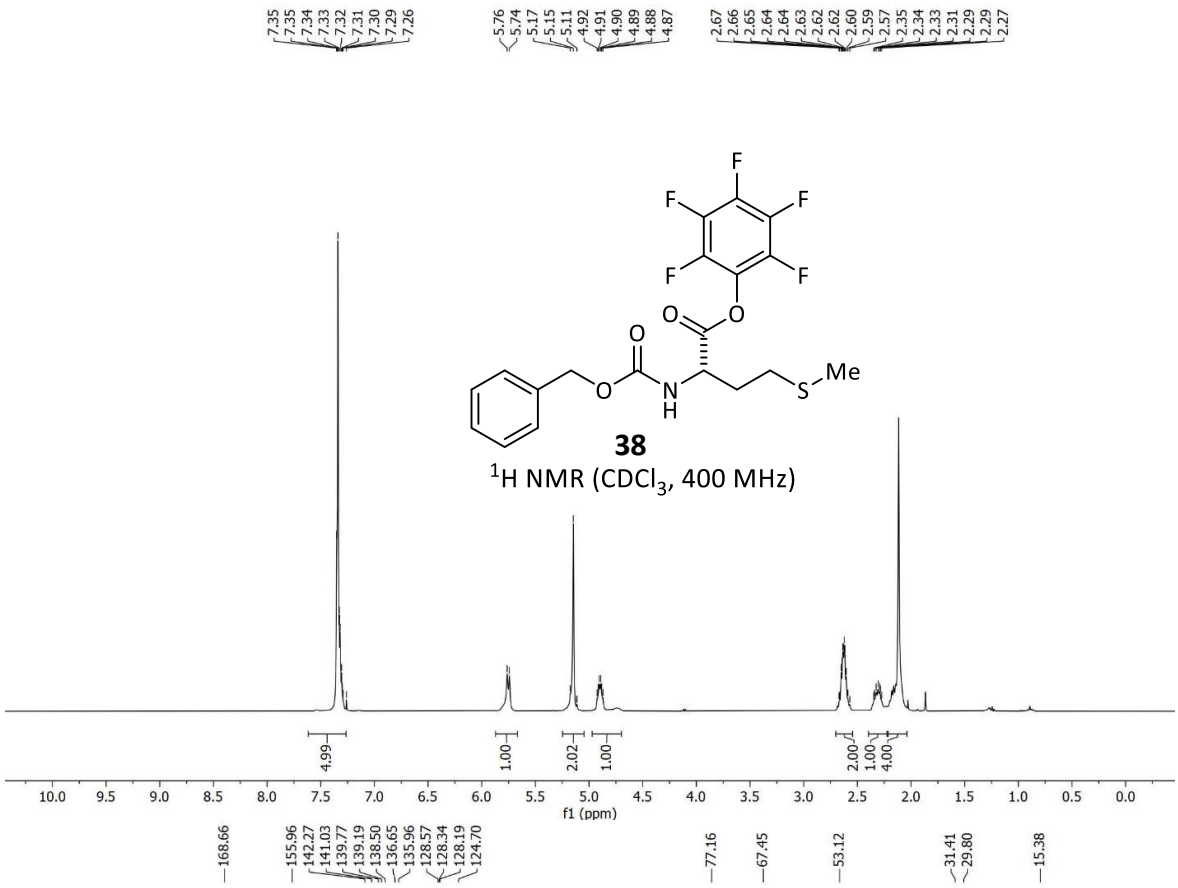


37 – (S) – amide



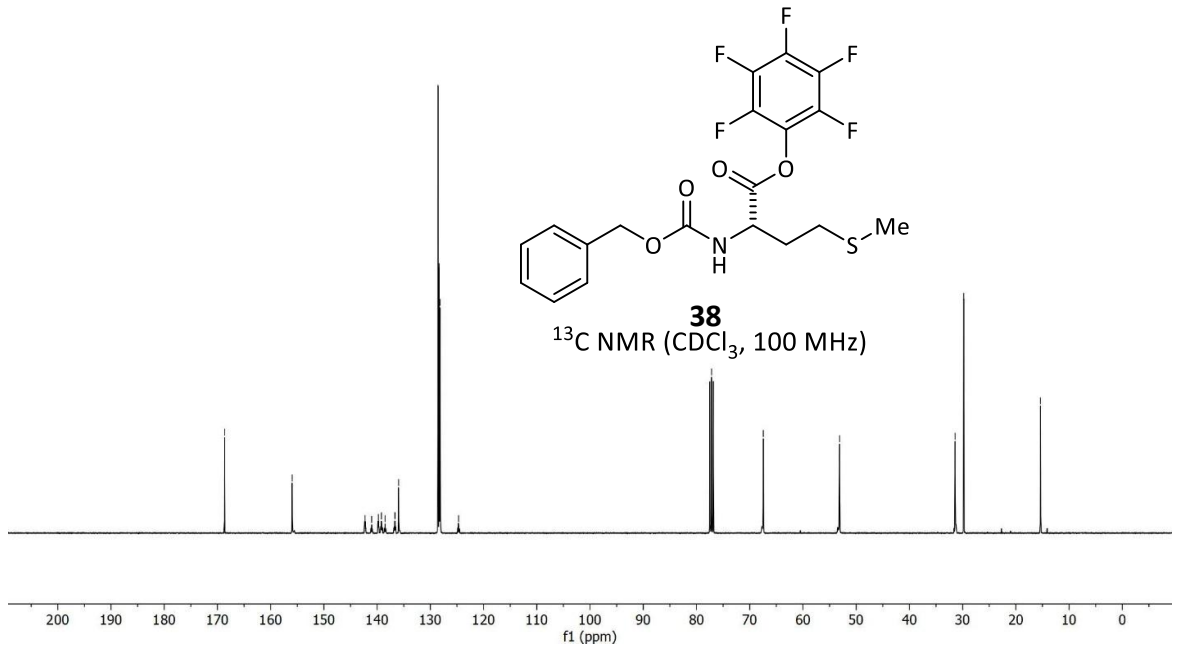
37 – (R) – amide





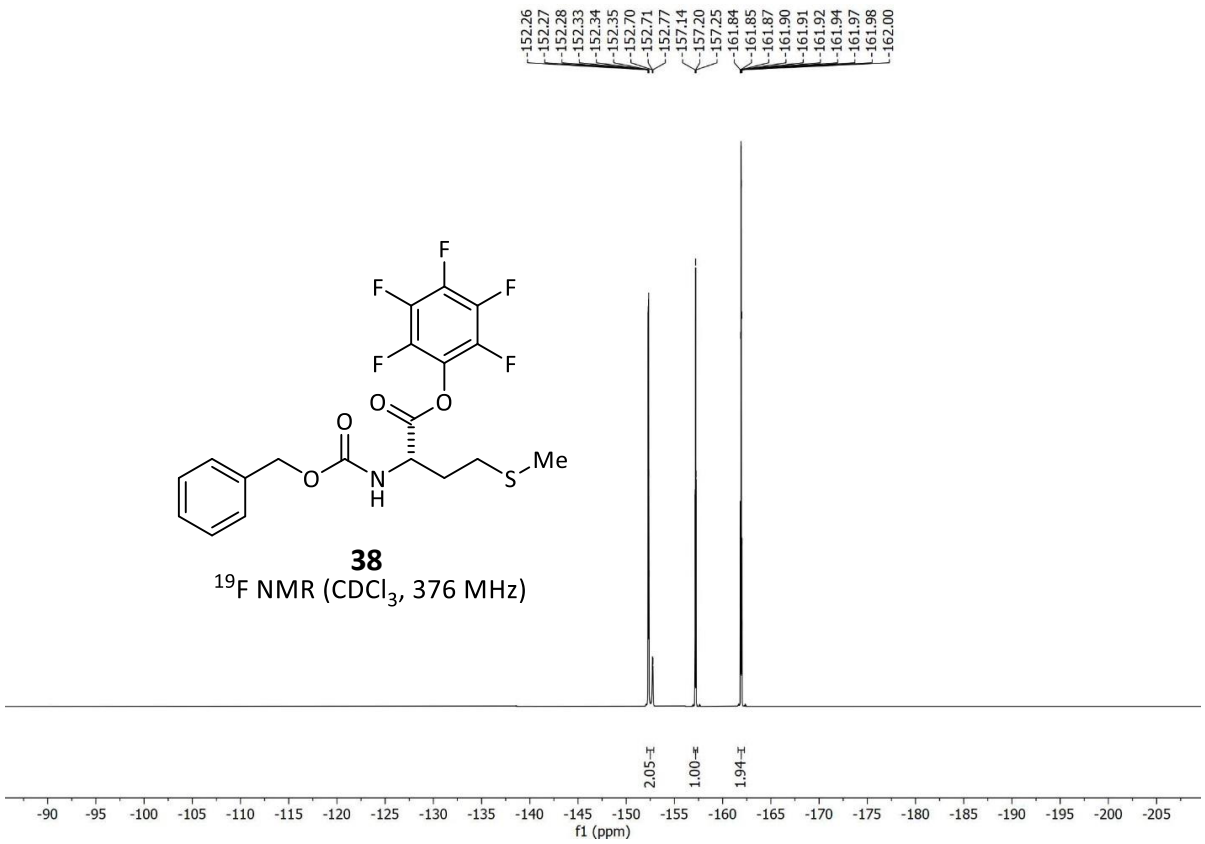
38

^{1}H NMR ($CDCl_3$, 400 MHz)



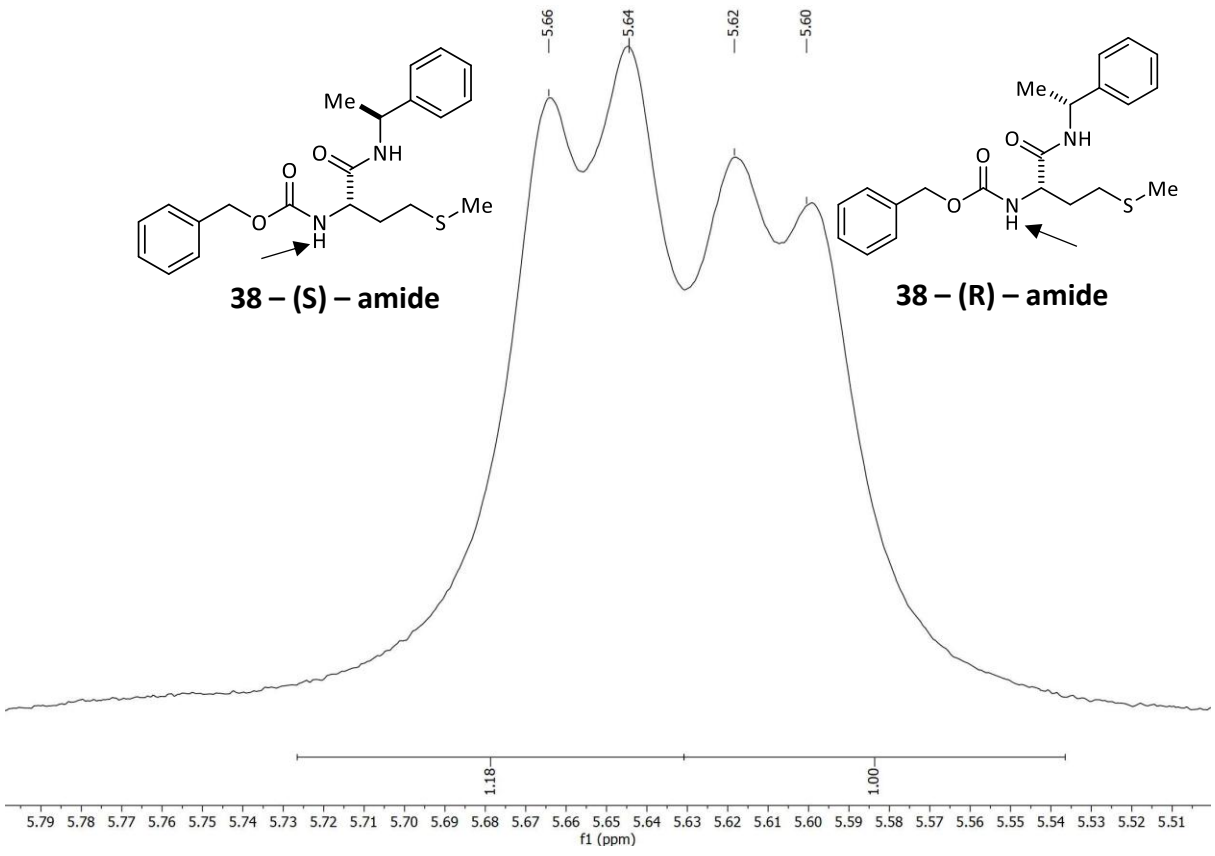
38

^{13}C NMR ($CDCl_3$, 100 MHz)



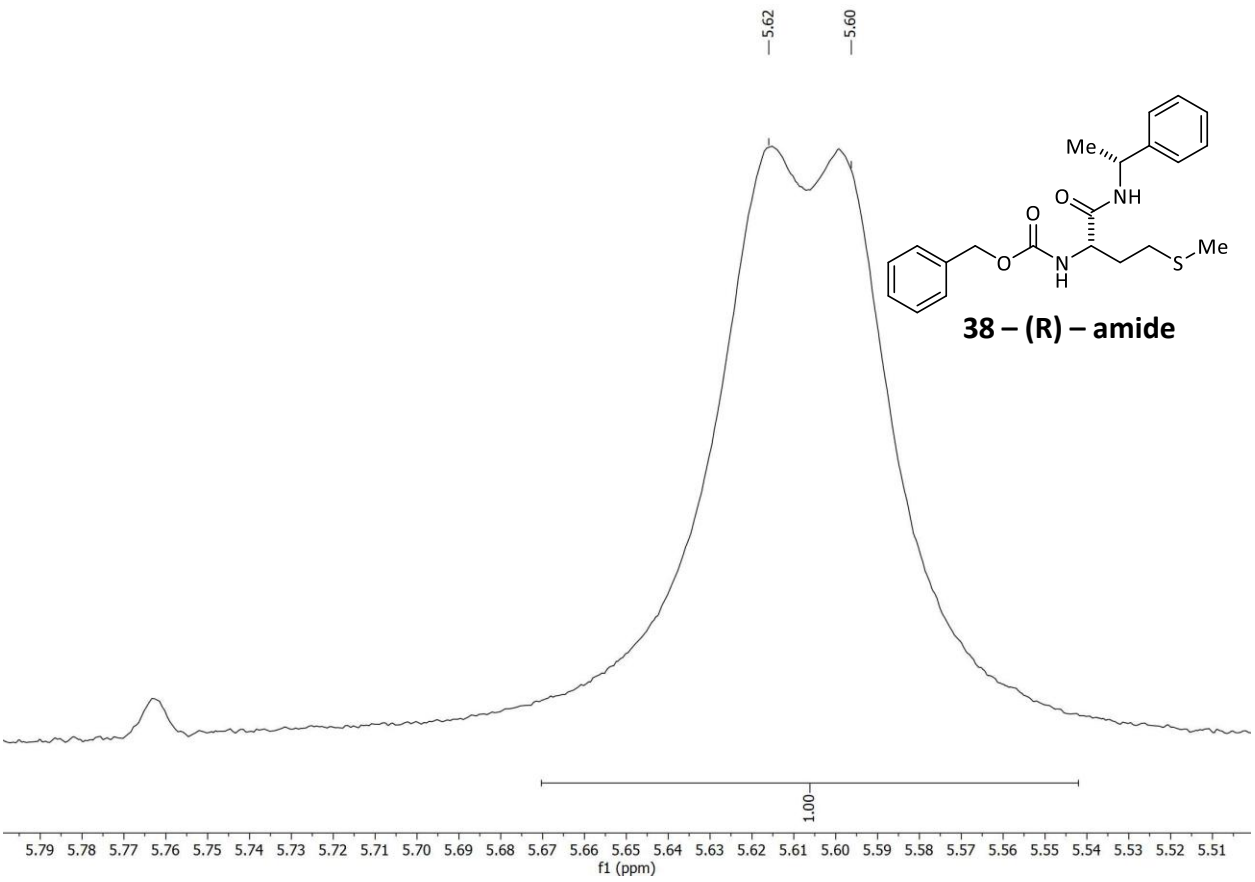
38

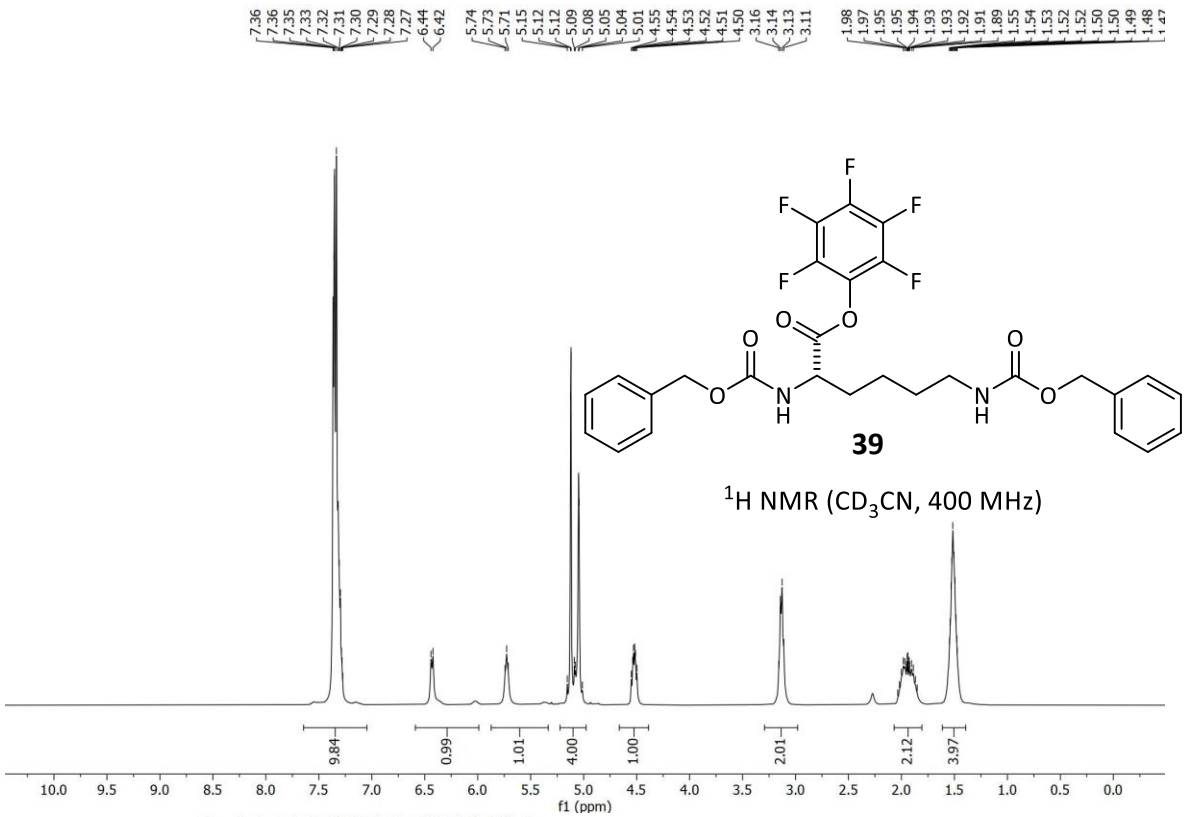
^{19}F NMR ($CDCl_3$, 376 MHz)

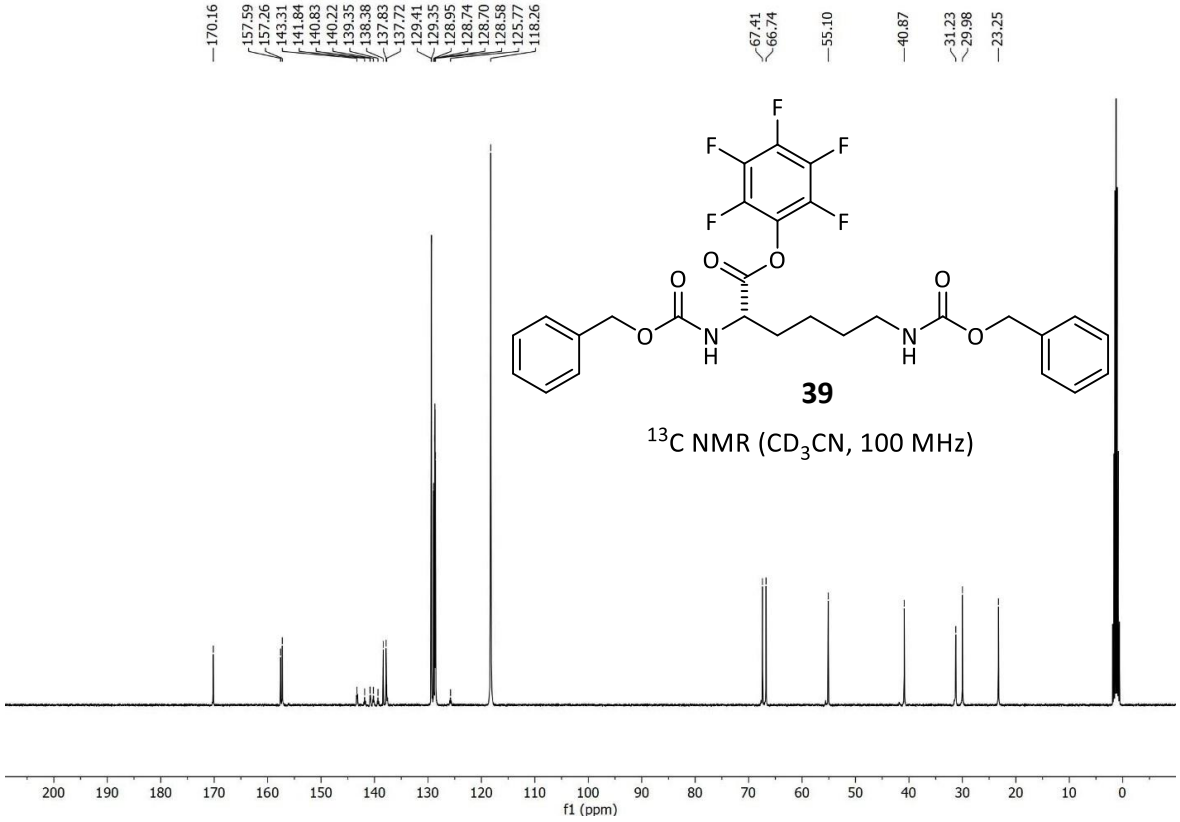


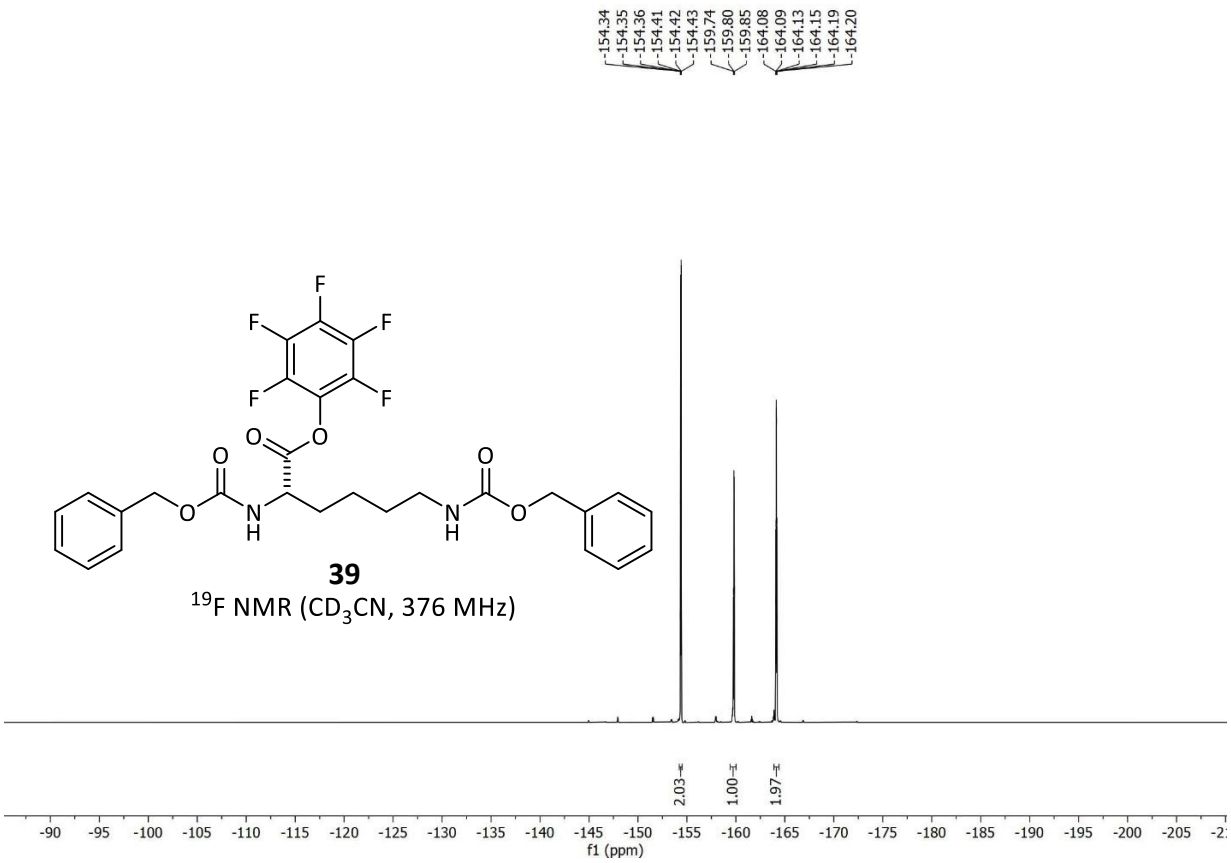
38 – (S) – amide

38 – (R) – amide


5.62
5.60
Me
O
NH
O
O
N
H
S
Me
38 – (R) – amide
1.00
5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.72 5.71 5.70 5.69 5.68 5.67 5.66 5.65 5.64 5.63 5.62 5.61 5.60 5.59 5.58 5.57 5.56 5.55 5.54 5.53 5.52 5.51
f1 (ppm)

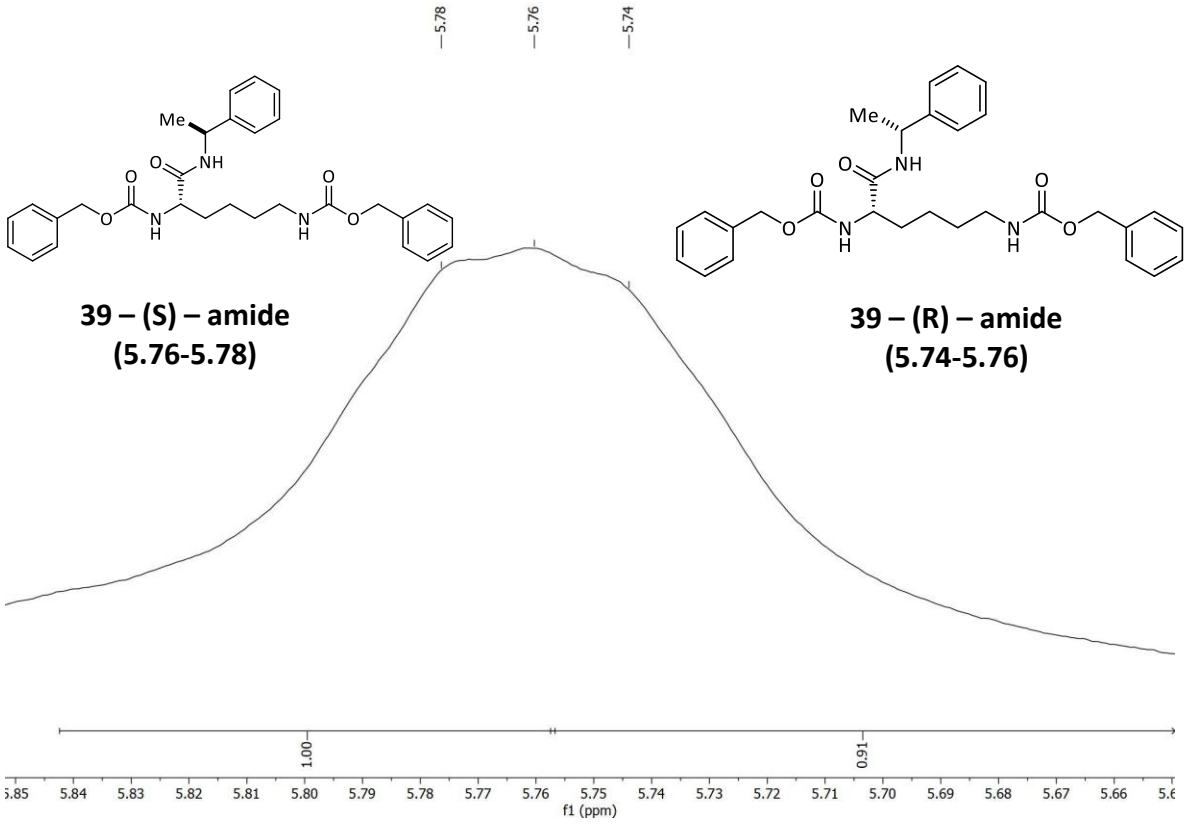

39
^{1}H NMR (CD_3CN, 400 MHz)
f1 (ppm)


39
^{13}C NMR (CD_3CN, 100 MHz)
f1 (ppm)



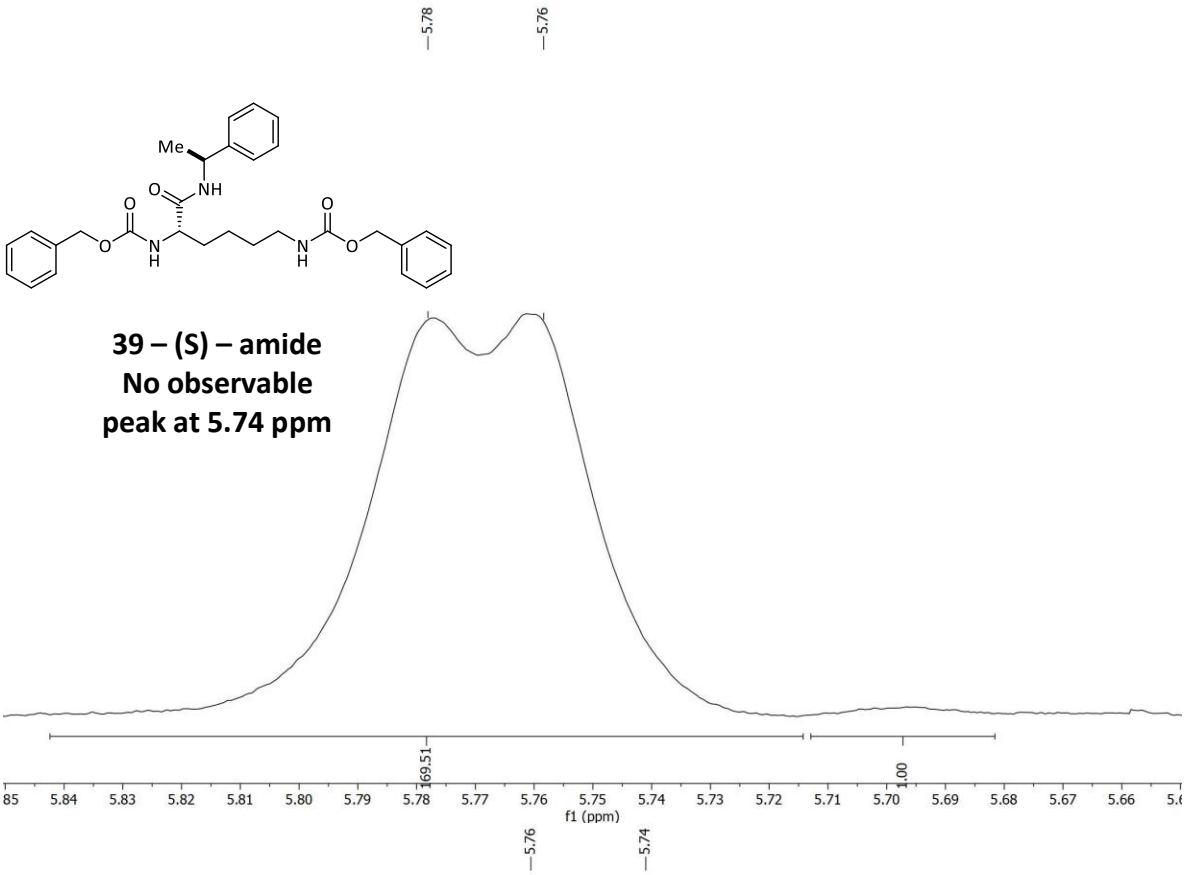
39

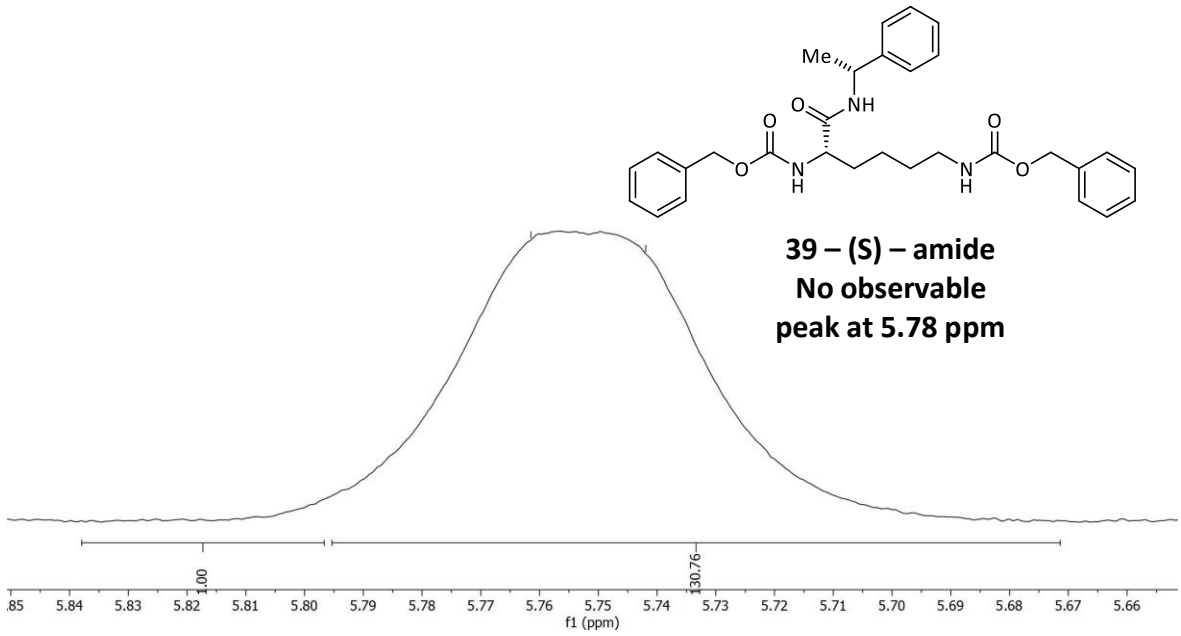
^{19}F NMR (CD_3CN, 376 MHz)

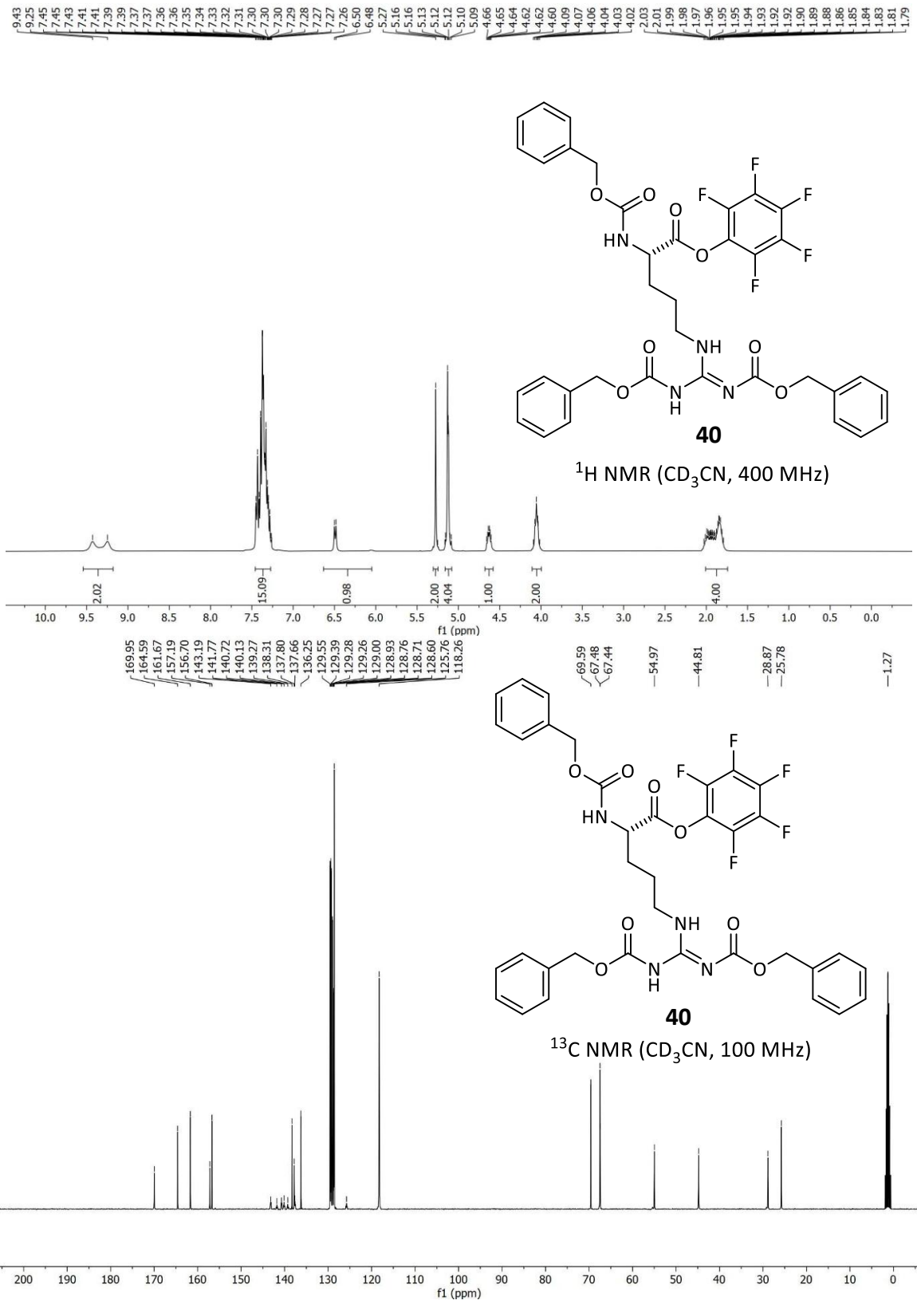


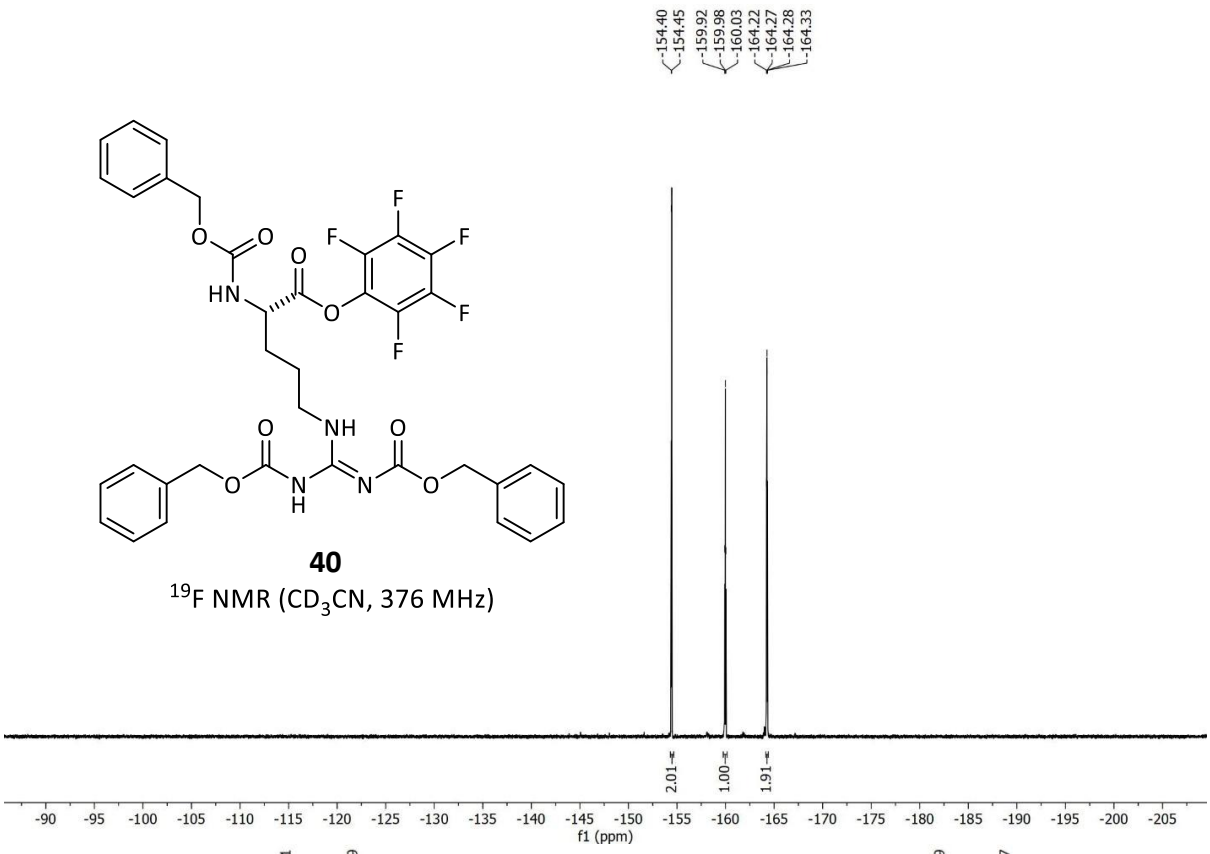
39 – (S) – amide
(5.76-5.78)

39 – (R) – amide
(5.74-5.76)


5.78
5.76
Me
NH
O
O
O
N
H
N
H
O
O
39 – (S) – amide
No observable
peak at 5.74 ppm
169.51
1.00
85 5.84 5.83 5.82 5.81 5.80 5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.72 5.71 5.70 5.69 5.68 5.67 5.66
f1 (ppm)
5.76
5.74

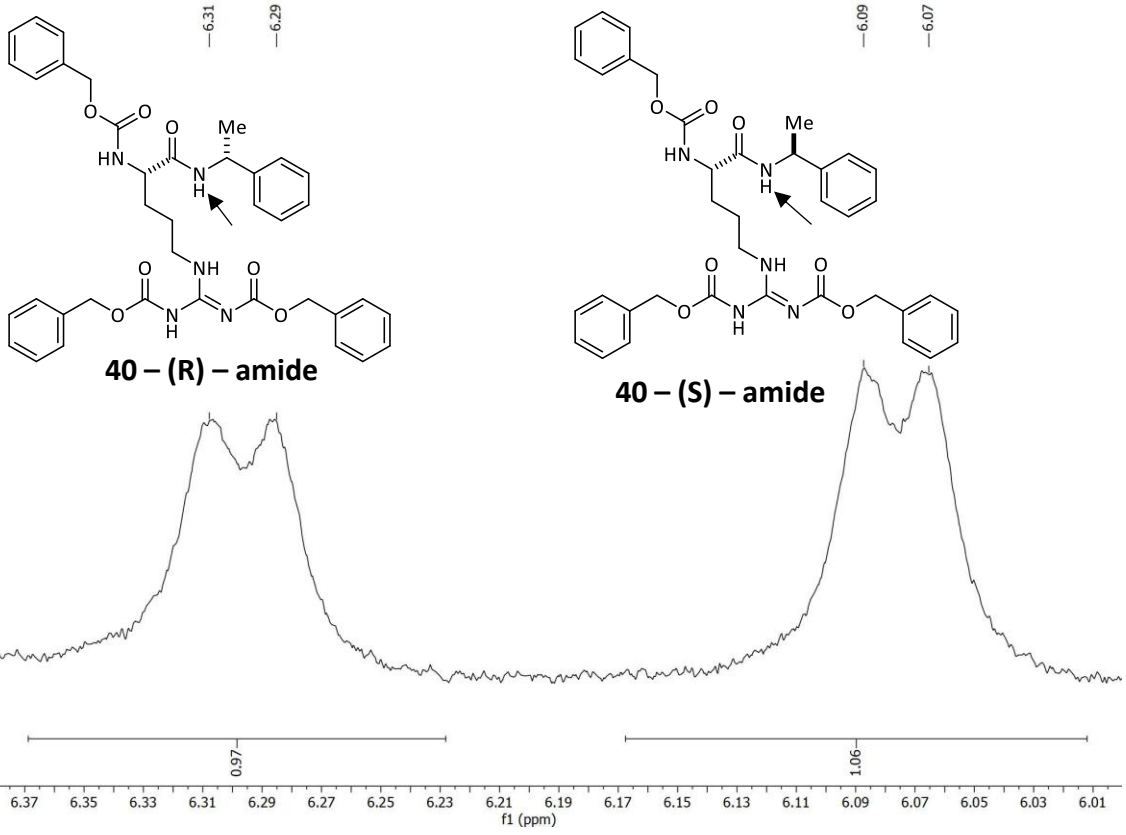

Me
NH
O
O
O
N
H
N
H
O
O
39 – (S) – amide
No observable
peak at 5.78 ppm
1.00
130.76
85 5.84 5.83 5.82 5.81 5.80 5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.72 5.71 5.70 5.69 5.68 5.67 5.66
f1 (ppm)


40
^{1}H NMR (CD_3CN, 400 MHz)
40
^{13}C NMR (CD_3CN, 100 MHz)



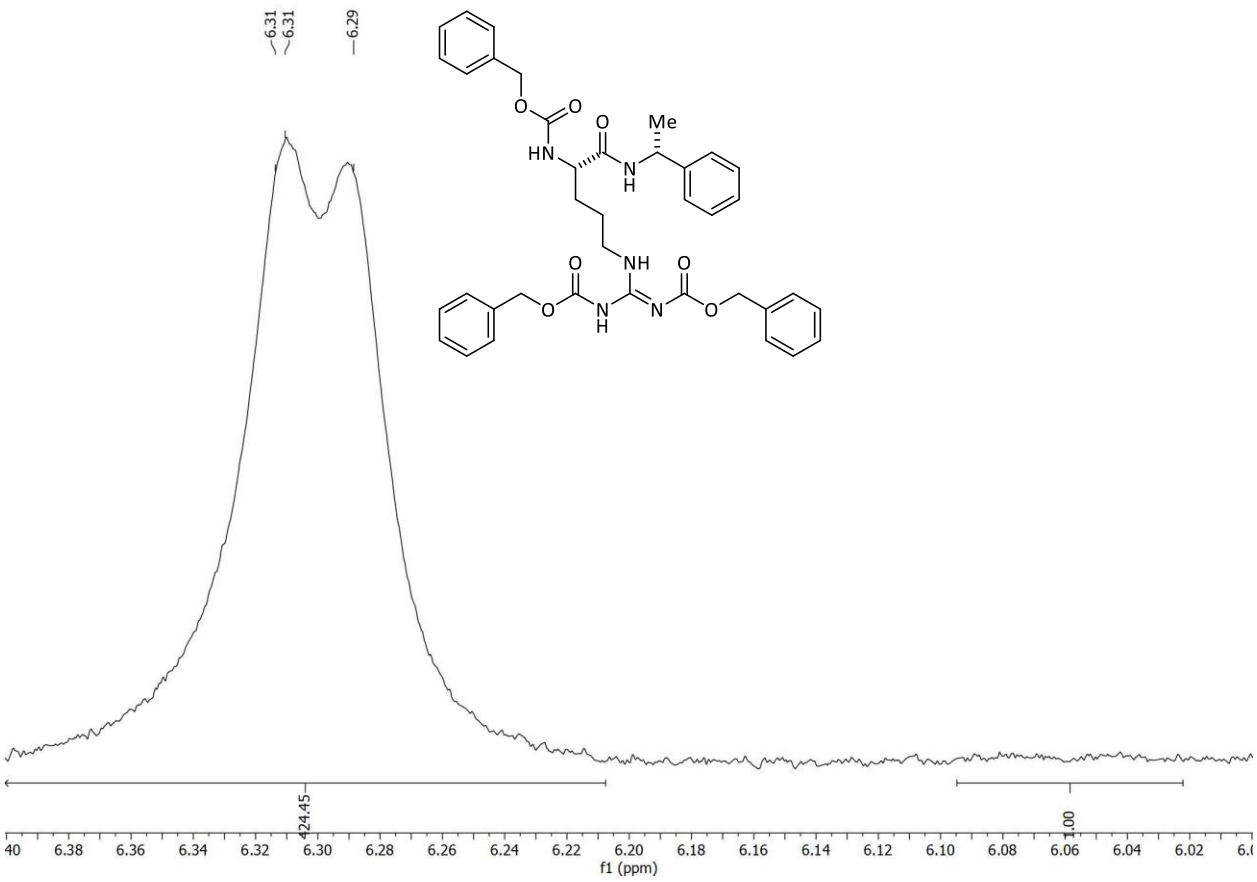
40

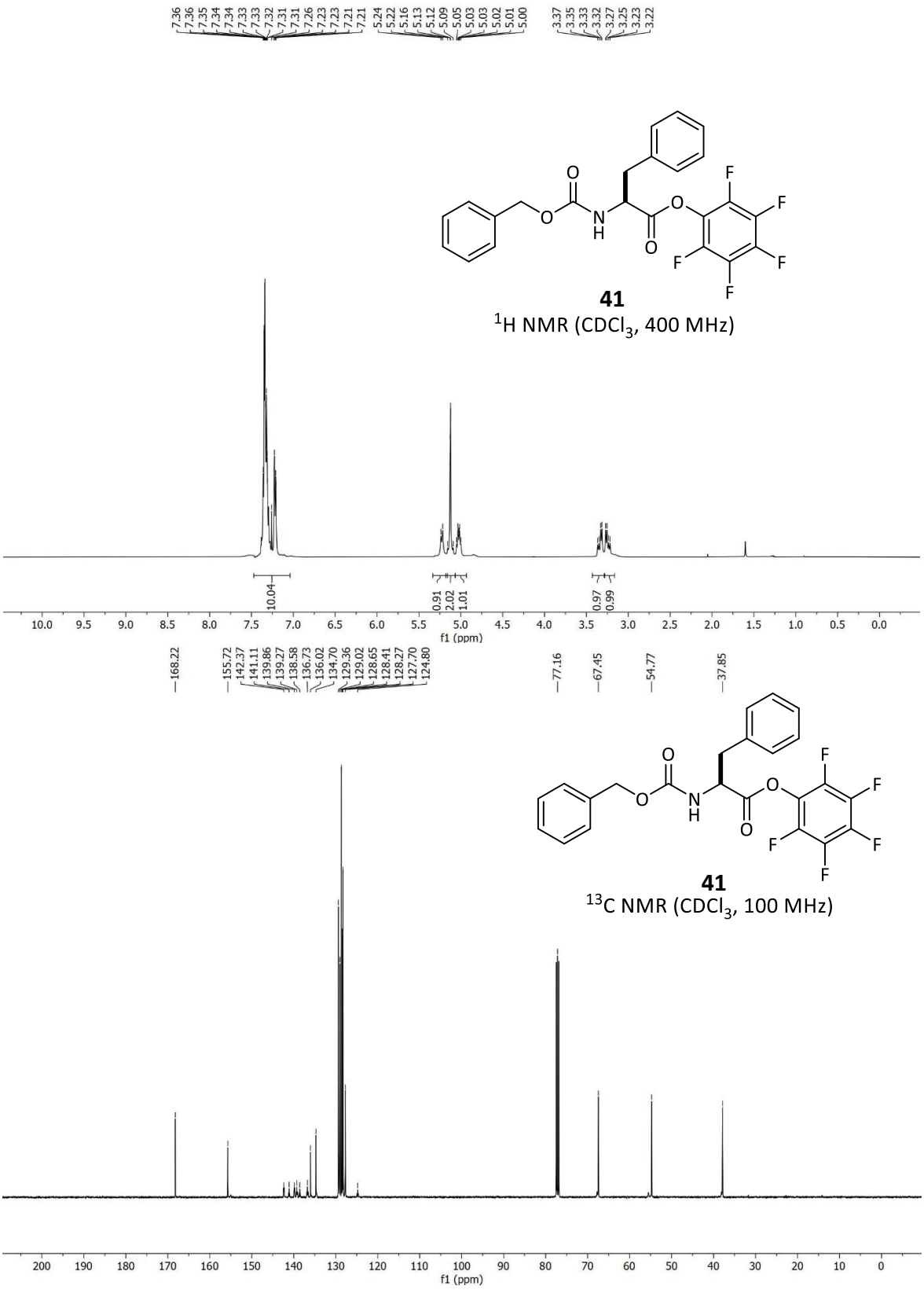
^{19}F NMR (CD_3CN, 376 MHz)

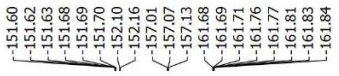


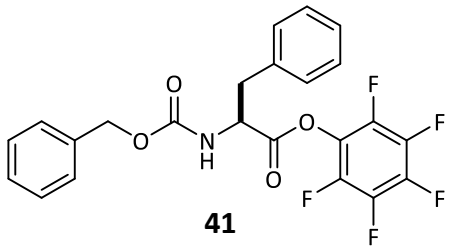
40 – (R) – amide

40 – (S) – amide


6.31
6.31
6.29
O
O
HN
O
N
H
Me
NH
O
O
N
H
N
O
O
424.45
1.00
40
6.38
6.36
6.34
6.32
6.30
6.28
6.26
6.24
6.22
6.20
6.18
6.16
6.14
6.12
6.10
6.08
6.06
6.04
6.02
f1 (ppm)

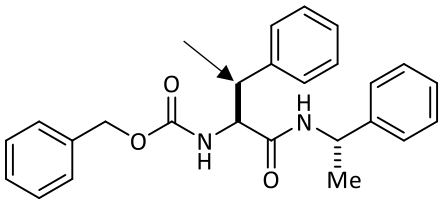

7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.32
7.31
7.31
7.26
7.23
7.23
7.21
7.21
5.24
5.22
5.16
5.13
5.12
5.09
5.05
5.03
5.03
5.02
5.01
5.00
3.37
3.35
3.33
3.32
3.27
3.25
3.23
3.22
O
O
N
H
O
O
F
F
F
F
F
41
1H NMR (CDCl3, 400 MHz)
10.04
0.91
2.02
1.01
0.97
0.99
f1 (ppm)
168.22
155.72
142.37
141.11
139.86
139.27
138.58
136.73
136.02
134.70
129.36
129.02
128.65
128.41
128.27
127.70
124.80
77.16
67.45
54.77
37.85
41
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



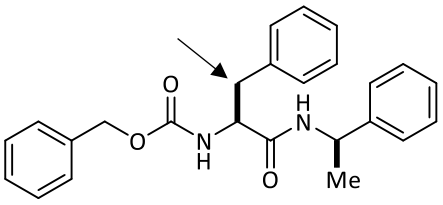


41

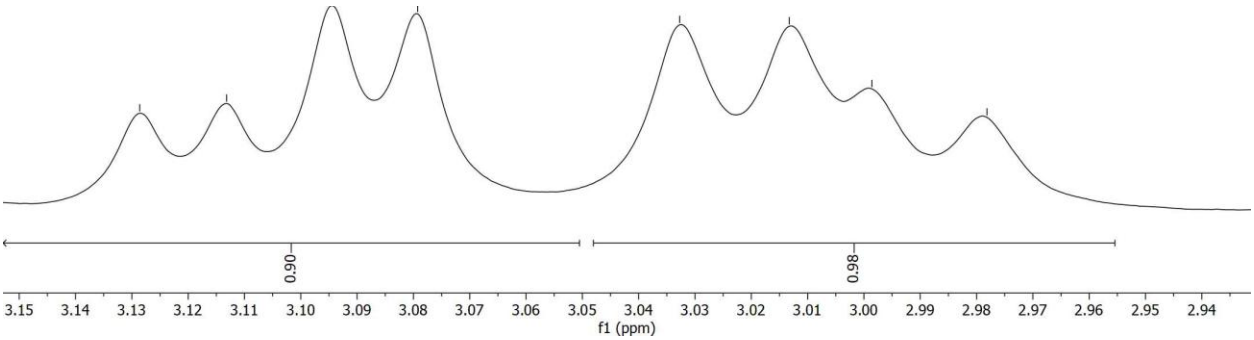
^{19}F NMR ($CDCl_3$, 376 MHz)

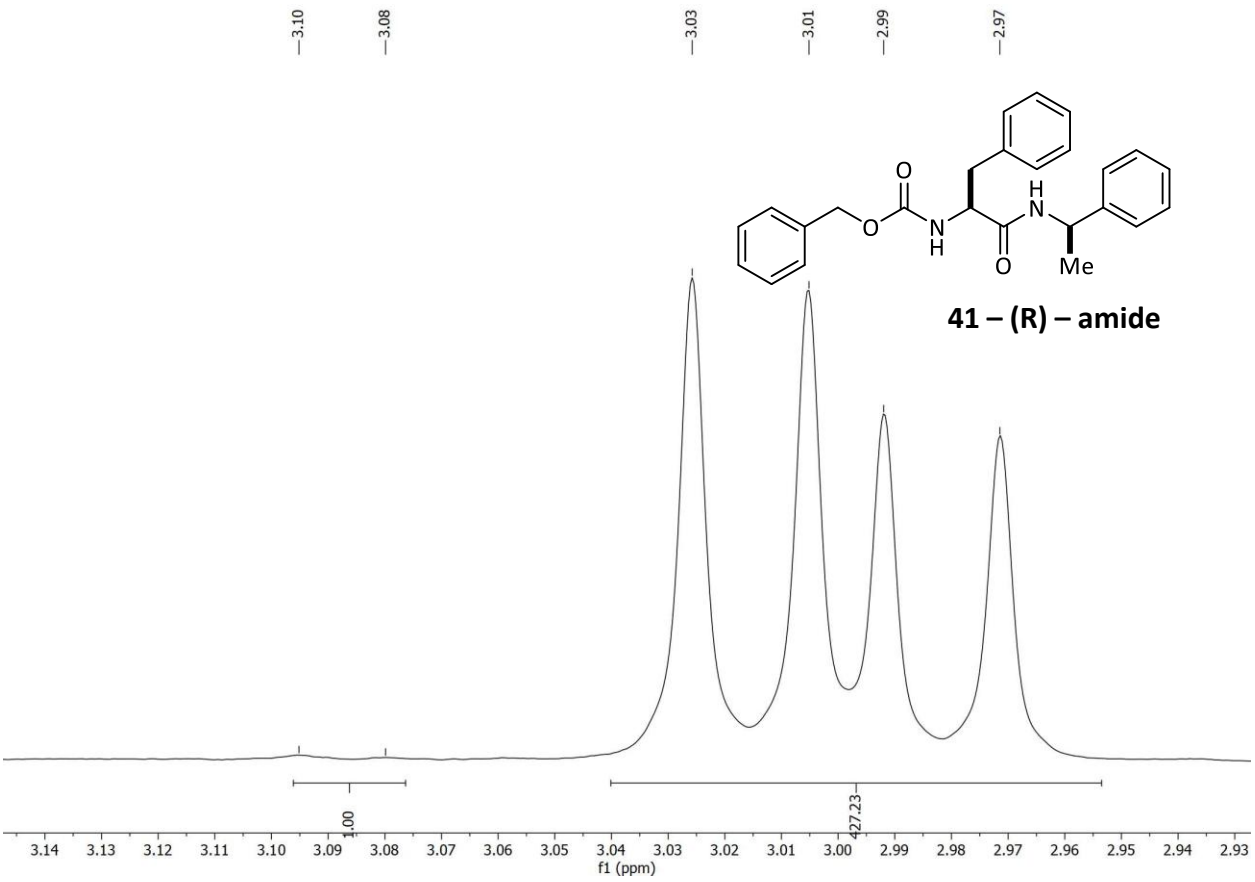


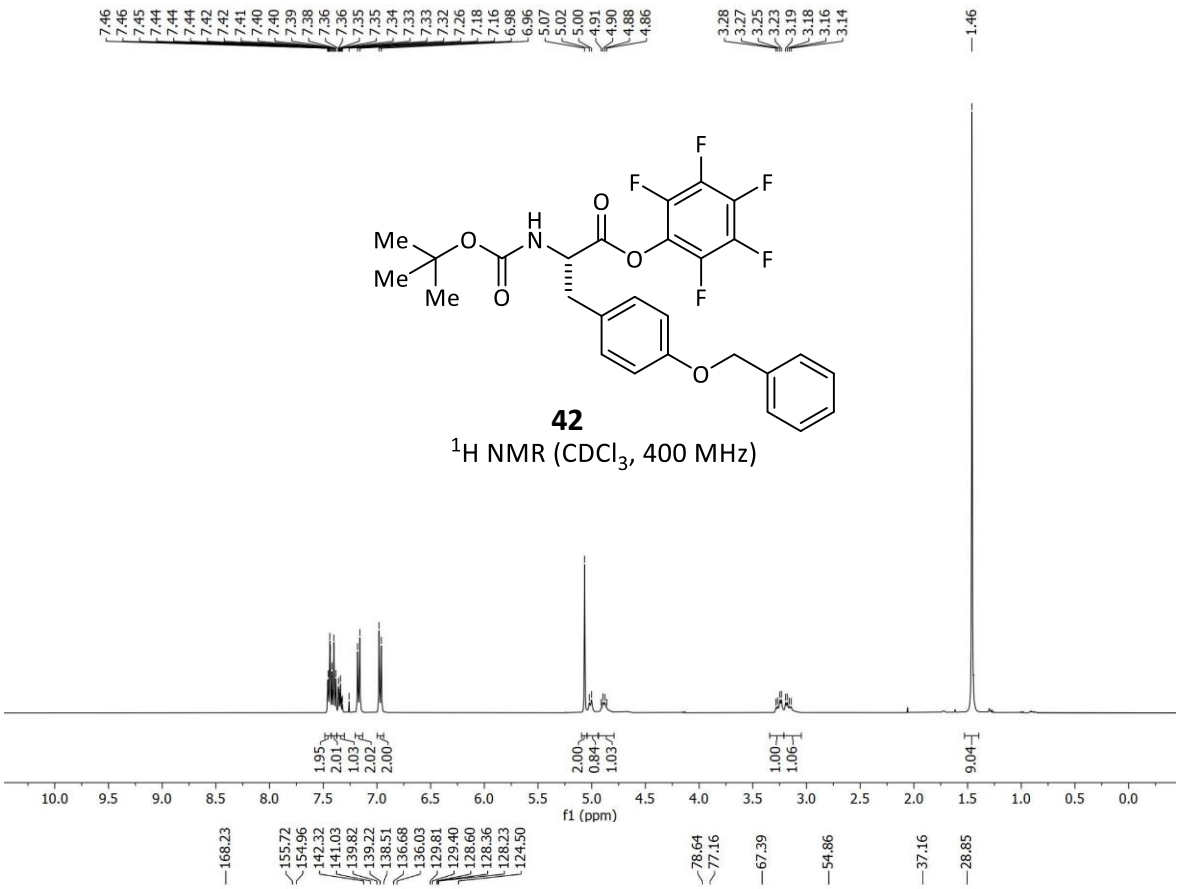
42 – (S) – amide



42 – (R) – amide

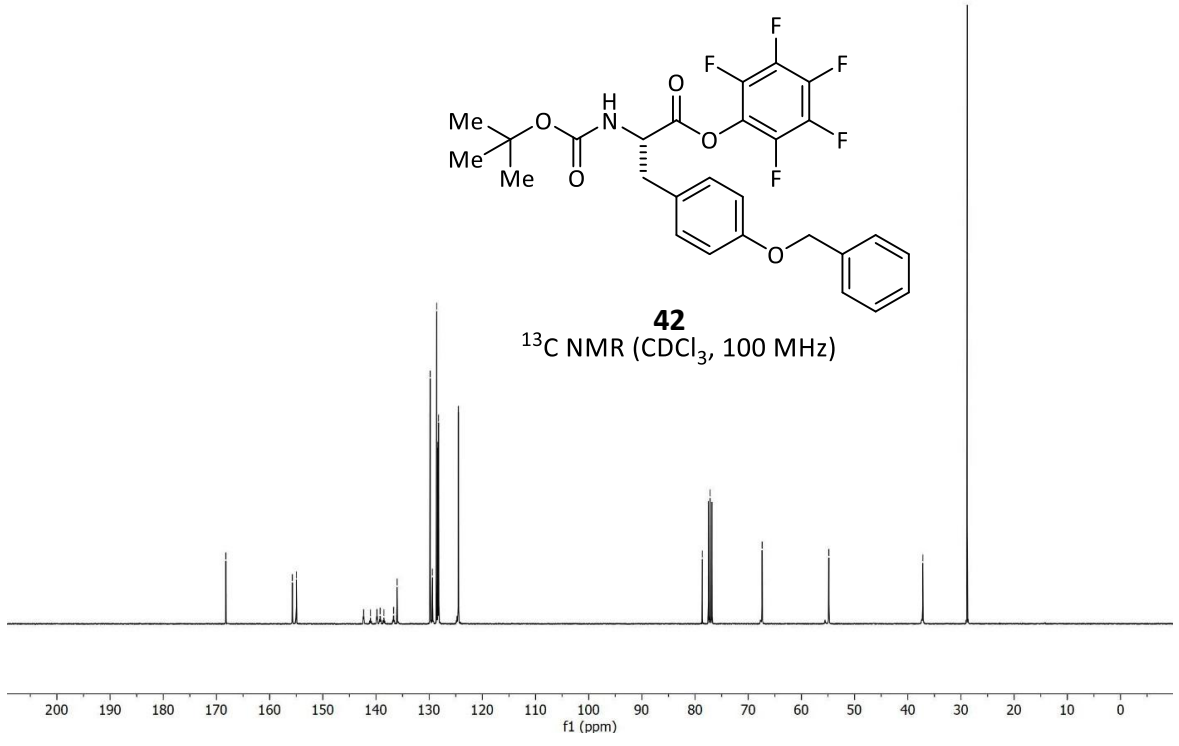



3.10
3.08
3.03
3.01
2.99
2.97
O
O
N
H
H
N
O
Me
41 – (R) – amide
1.00
427.23
3.14 3.13 3.12 3.11 3.10 3.09 3.08 3.07 3.06 3.05 3.04 3.03 3.02 3.01 3.00 2.99 2.98 2.97 2.96 2.95 2.94 2.93
f1 (ppm)



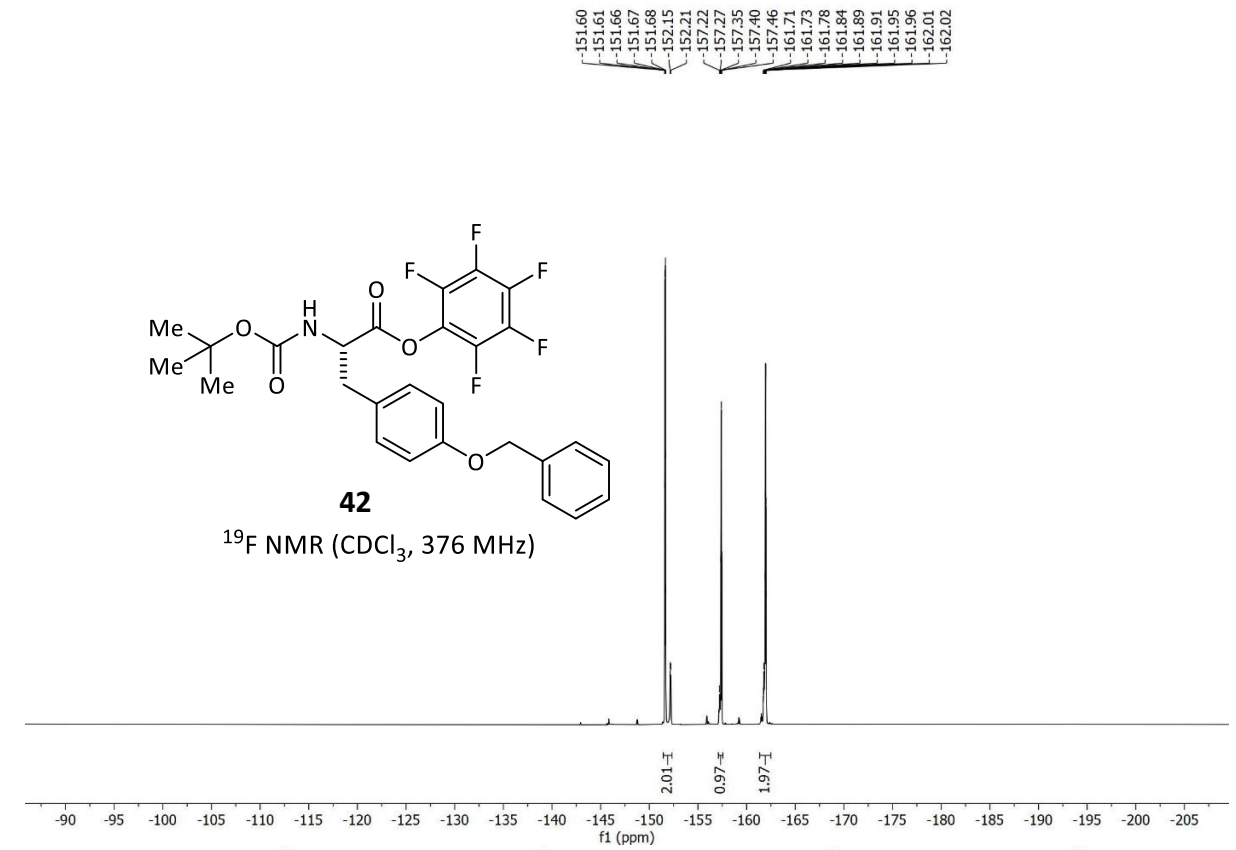
42

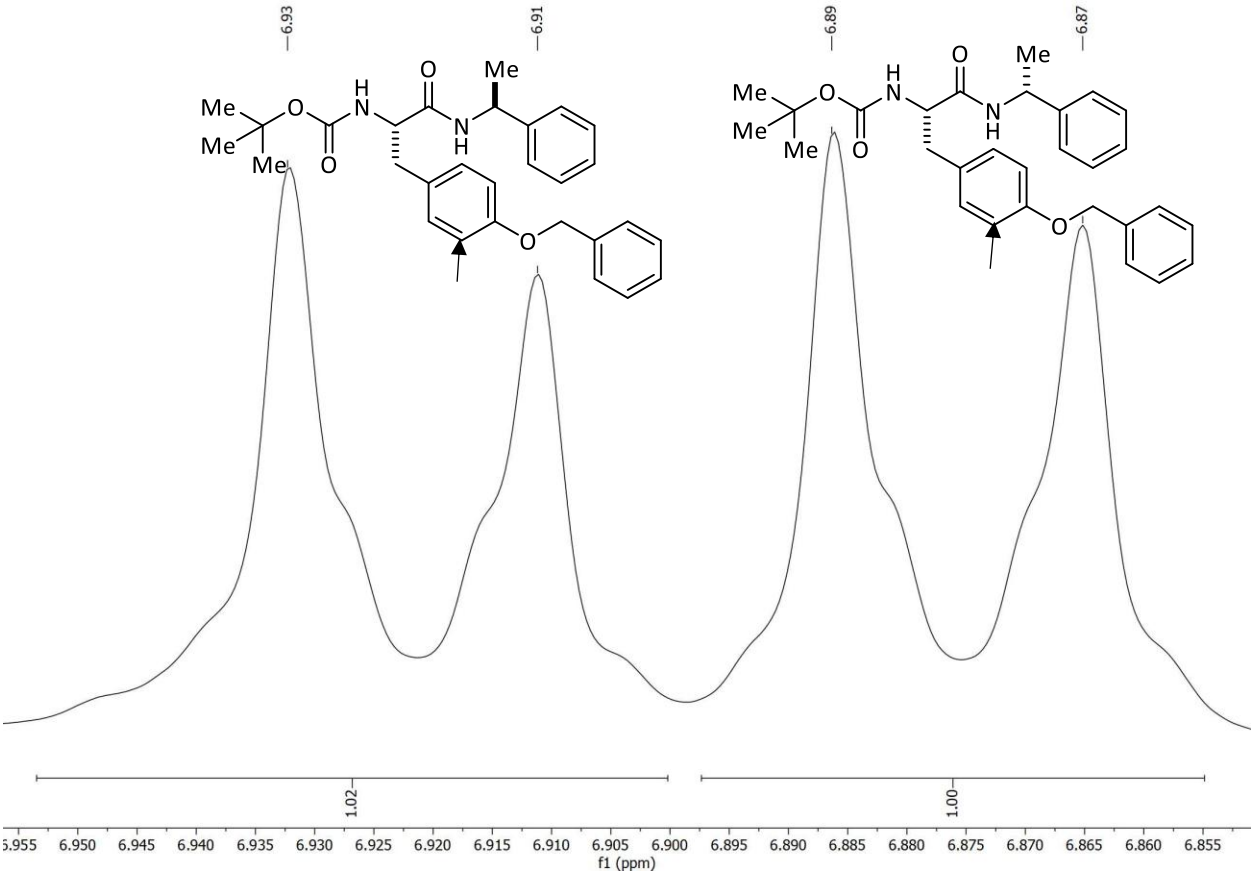
^{1}H NMR ($CDCl_3$, 400 MHz)

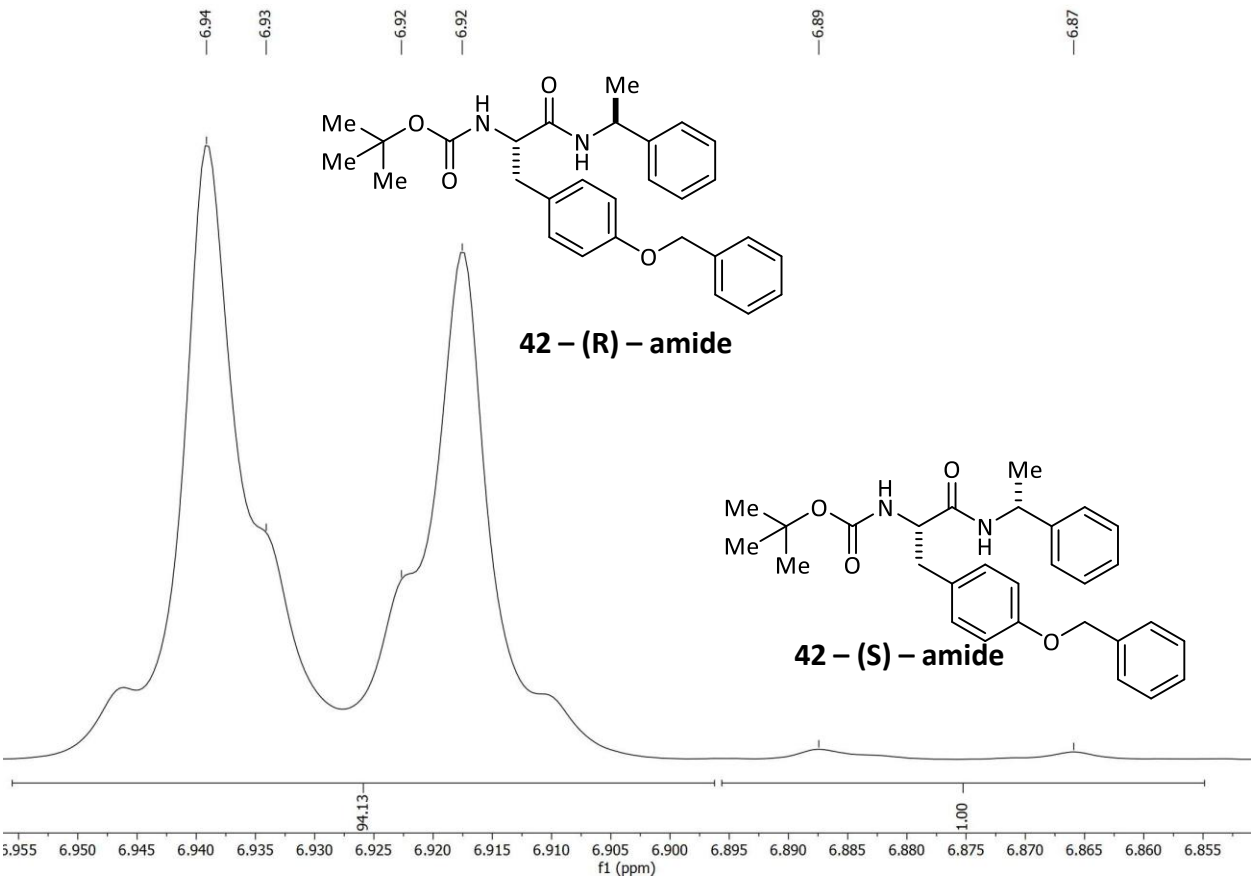


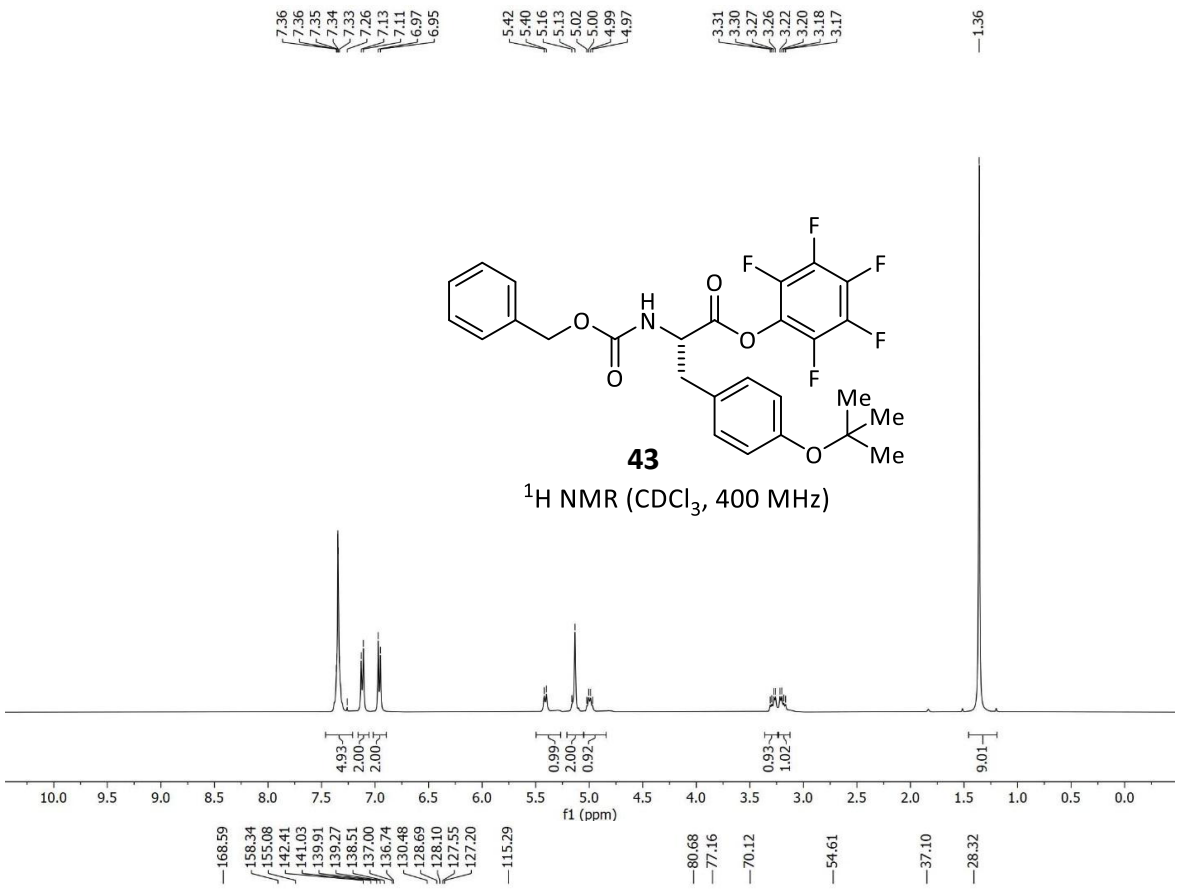
42

^{13}C NMR ($CDCl_3$, 100 MHz)


151.60
151.61
151.66
151.67
151.68
152.15
152.21
157.22
157.27
157.35
157.40
157.46
161.71
161.73
161.78
161.84
161.89
161.91
161.95
161.96
162.01
162.02
F
F
F
F
F
Me
Me
Me
O
O
H
N
O
O
O
O
42
^{19}F NMR ($CDCl_3$, 376 MHz)
2.01
0.97
1.97
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)

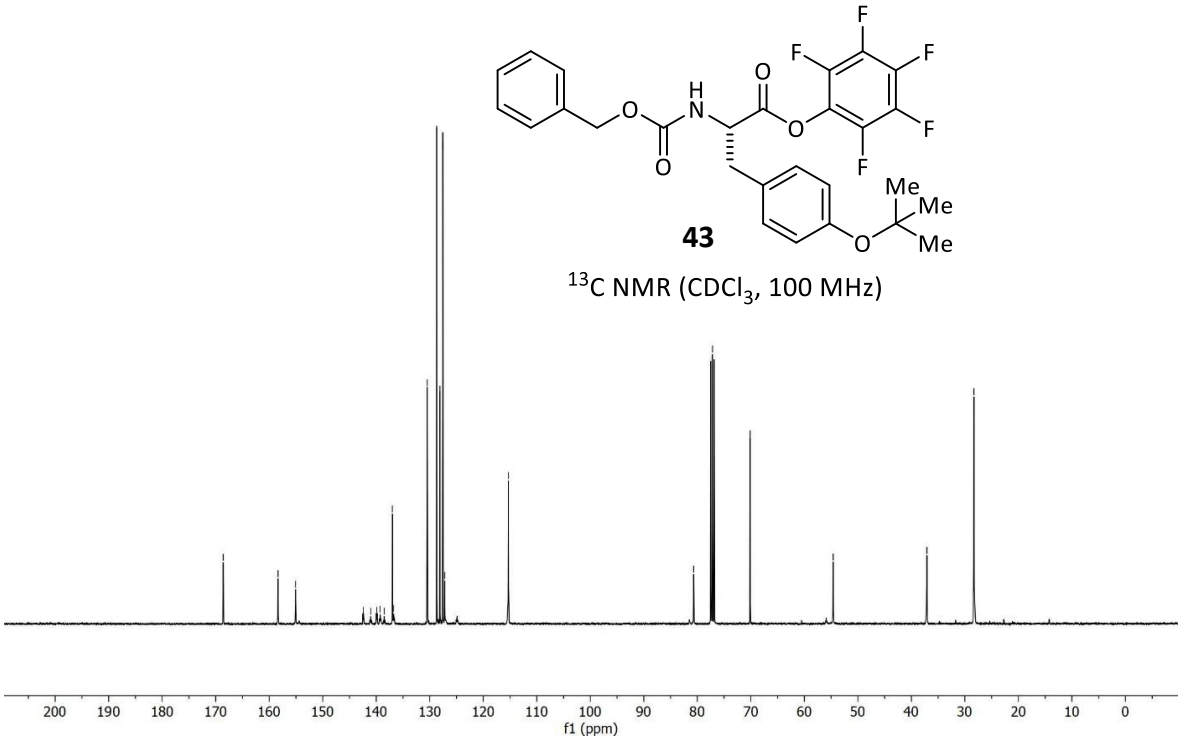

6.93
6.91
6.89
6.87
Me
Me
Me
O
O
H
N
O
Me
N
H
O
1.02
1.00
6.955 6.950 6.945 6.940 6.935 6.930 6.925 6.920 6.915 6.910 6.905 6.900 6.895 6.890 6.885 6.880 6.875 6.870 6.865 6.860 6.855
f1 (ppm)


6.94
6.93
6.92
6.92
6.89
6.87
42 – (R) – amide
42 – (S) – amide
94.13
1.00
6.955 6.950 6.945 6.940 6.935 6.930 6.925 6.920 6.915 6.910 6.905 6.900 6.895 6.890 6.885 6.880 6.875 6.870 6.865 6.860 6.855
f1 (ppm)



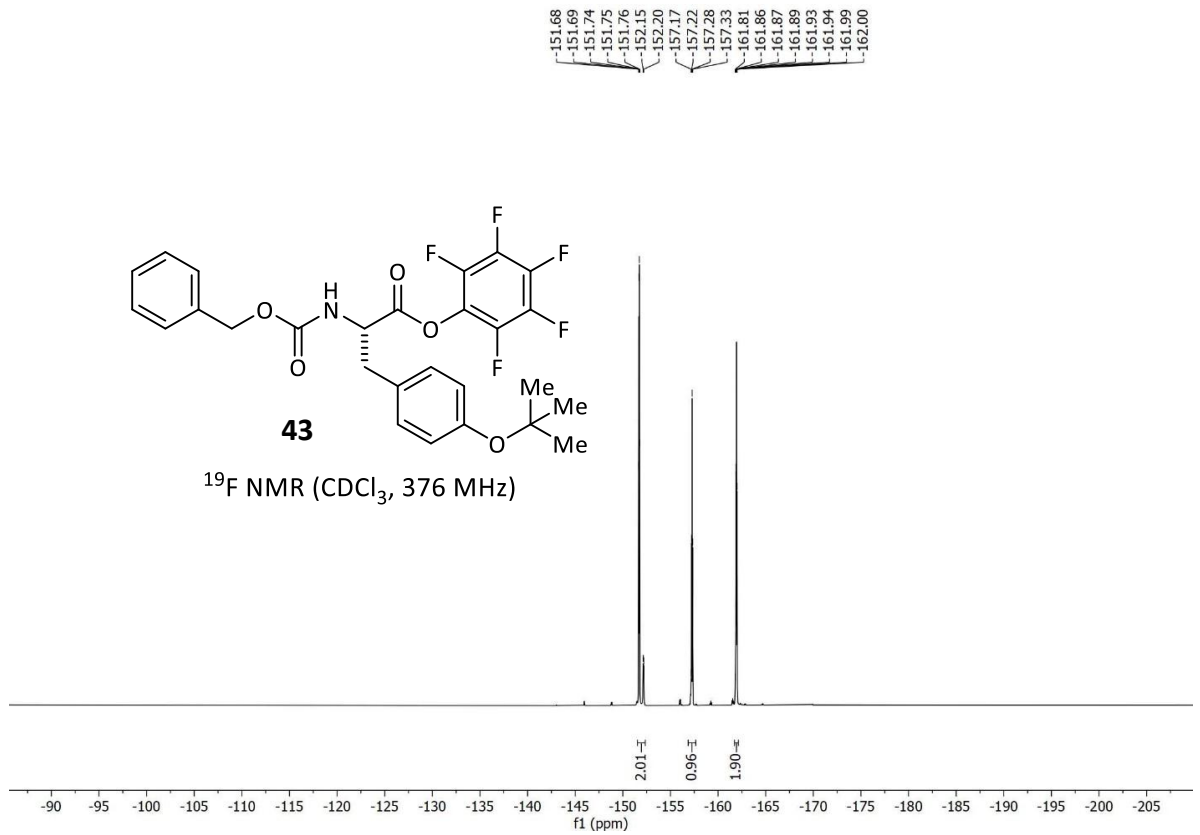
43

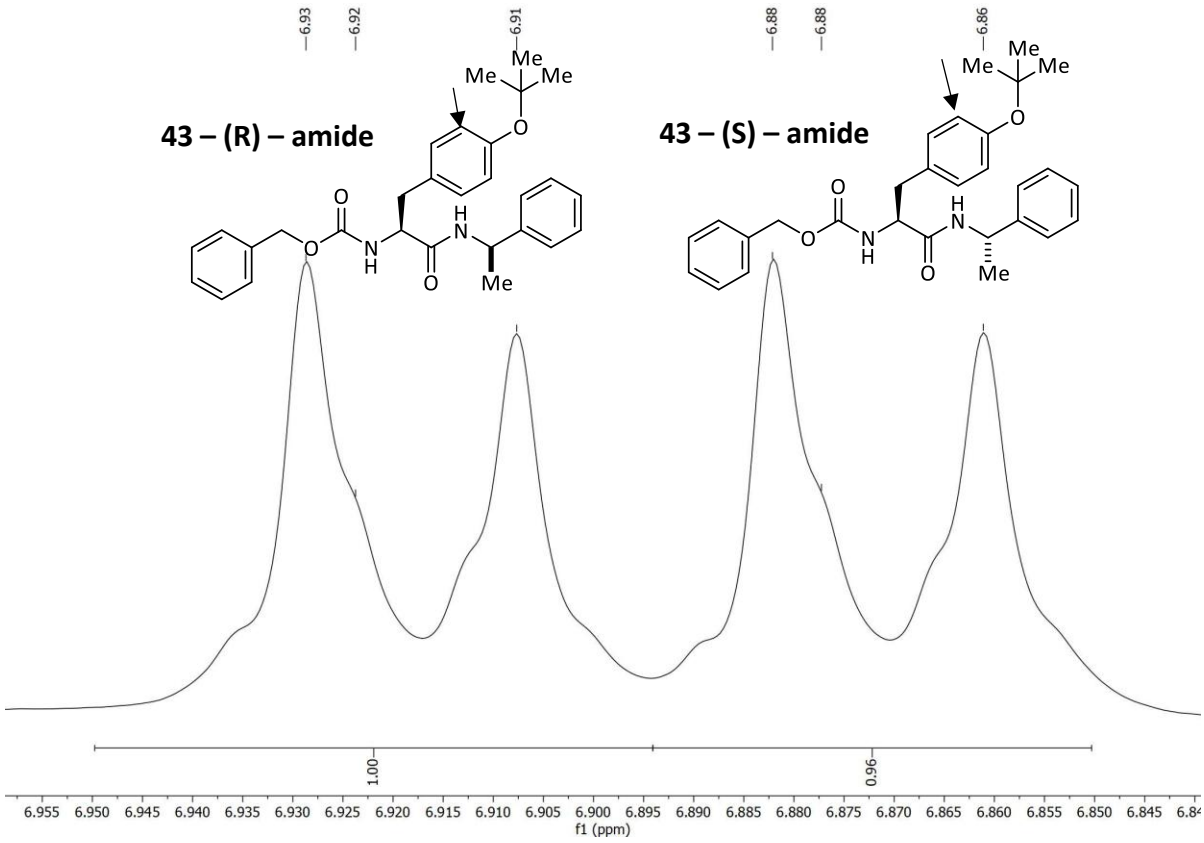
^{1}H NMR ($CDCl_3$, 400 MHz)

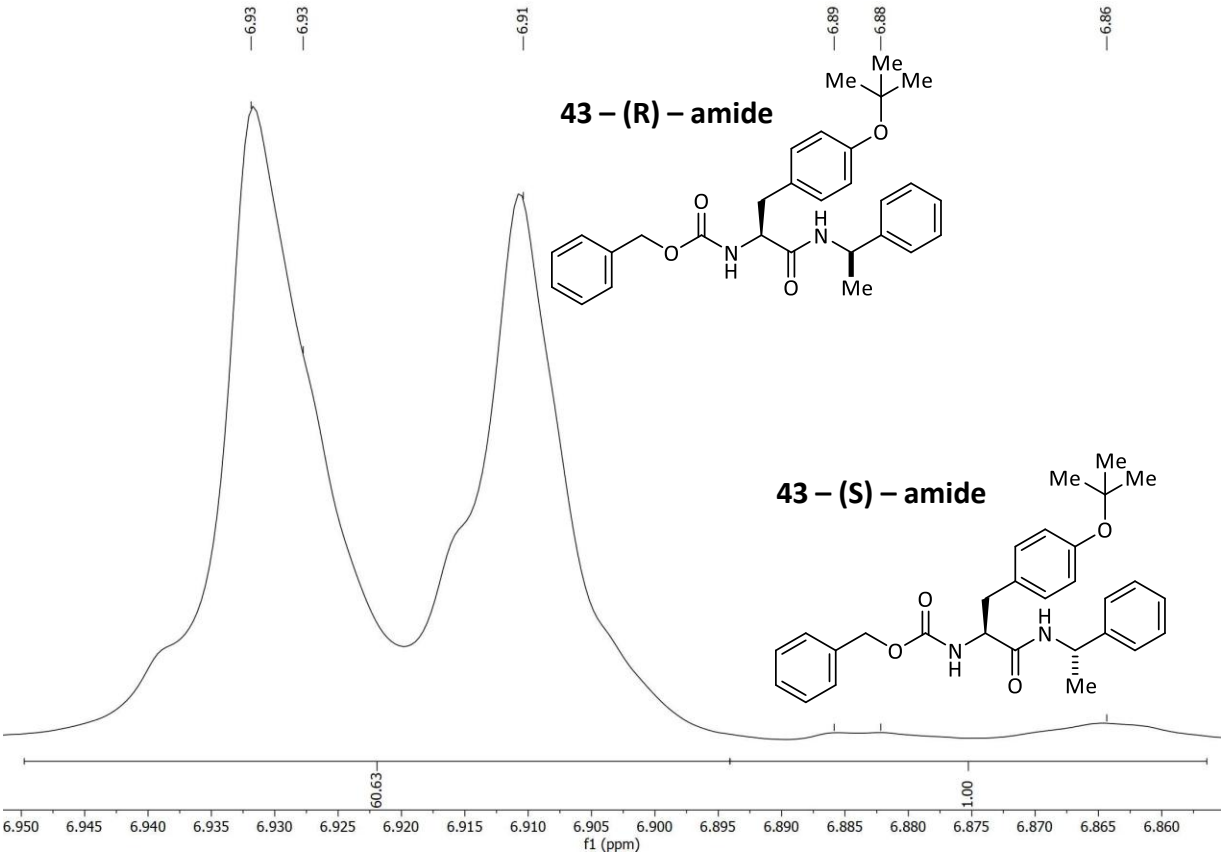


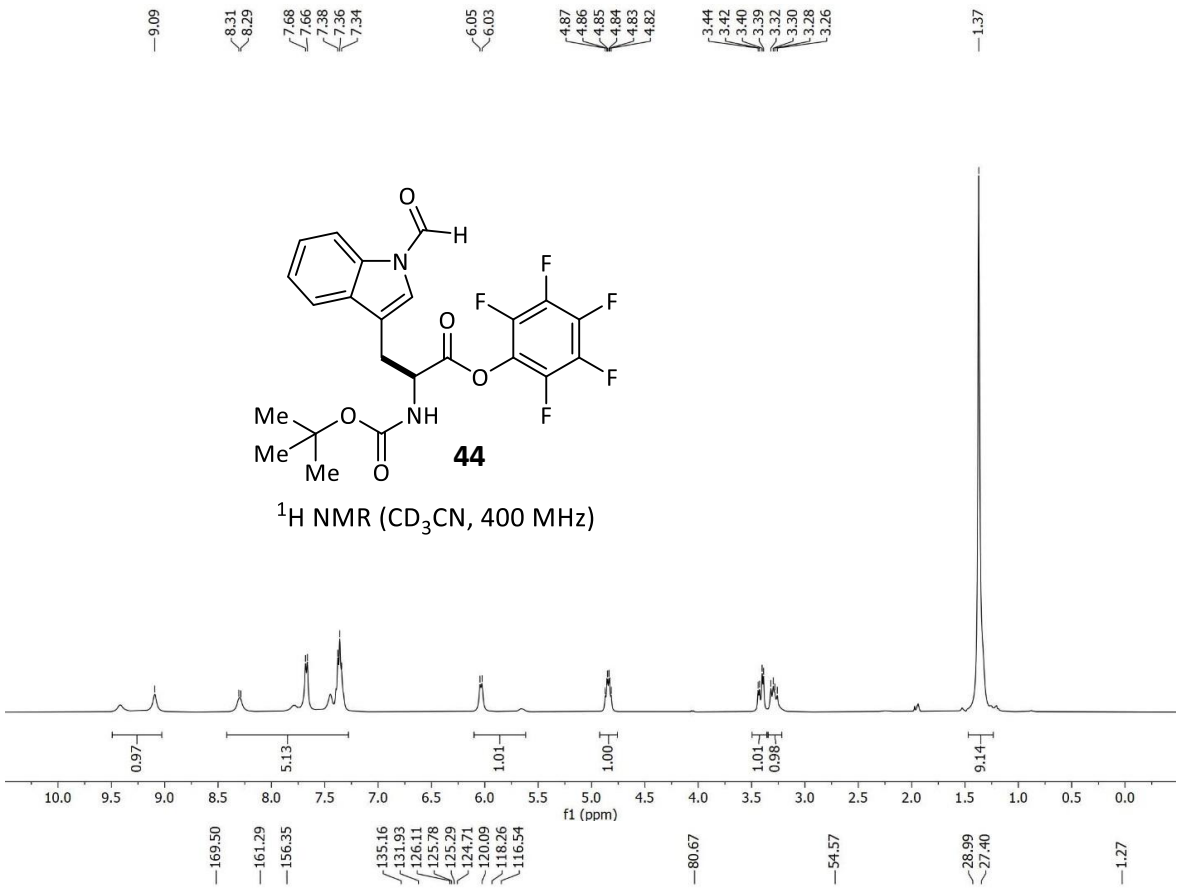
43

^{13}C NMR ($CDCl_3$, 100 MHz)

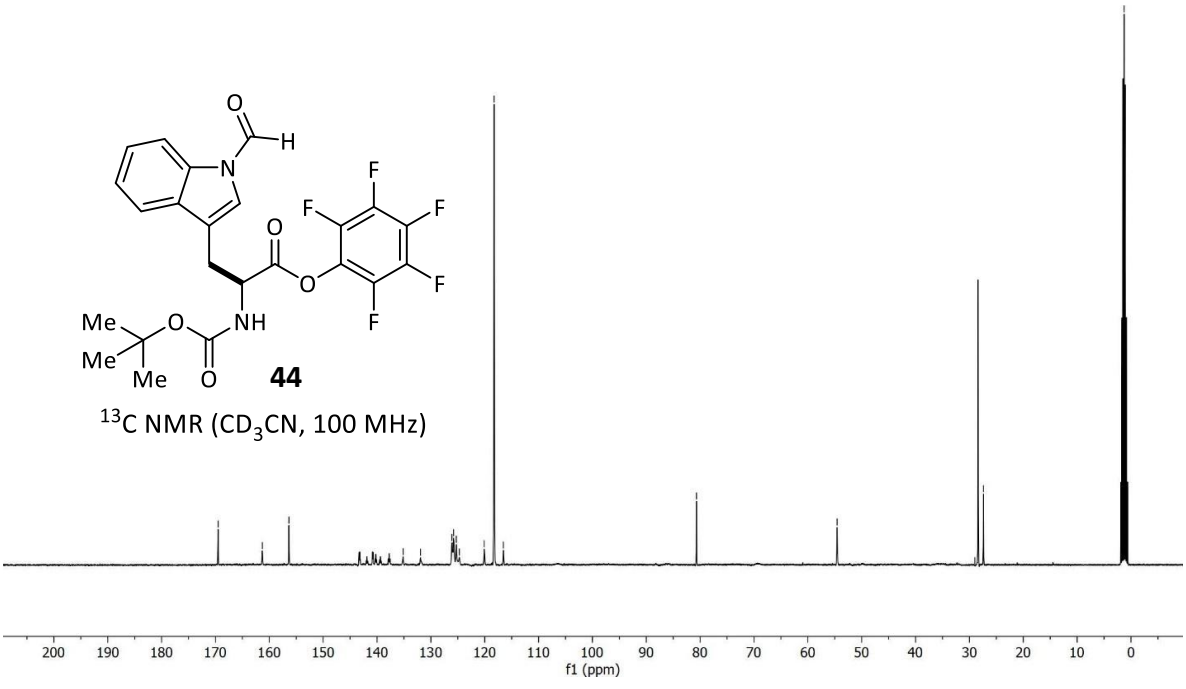

151.68
151.69
151.74
151.75
151.76
152.15
152.20
157.17
157.22
157.28
157.33
161.81
161.86
161.87
161.89
161.93
161.94
161.99
162.00
43
19F NMR (CDCl3, 376 MHz)
2.01
0.96
1.90
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)


6.93
6.92
6.91
43 – (R) – amide
6.88
6.88
6.86
43 – (S) – amide
1.00
0.96
6.955 6.950 6.945 6.940 6.935 6.930 6.925 6.920 6.915 6.910 6.905 6.900 6.895 6.890 6.885 6.880 6.875 6.870 6.865 6.860 6.855 6.850 6.845
f1 (ppm)

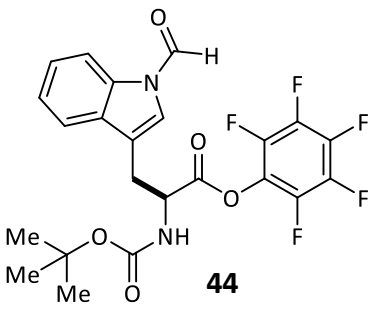

6.93
6.93
6.91
6.89
6.88
6.86
43 – (R) – amide
43 – (S) – amide
Me
Me
Me
O
O
O
N
H
H
N
O
Me
60.63
1.00
6.950 6.945 6.940 6.935 6.930 6.925 6.920 6.915 6.910 6.905 6.900 6.895 6.890 6.885 6.880 6.875 6.870 6.865 6.860
f1 (ppm)



^{1}H NMR (CD_3CN, 400 MHz)

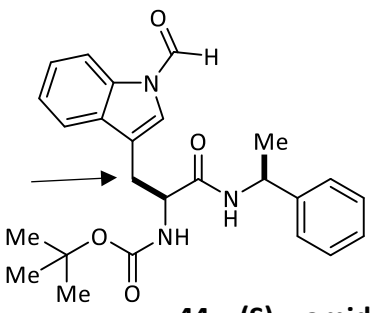


^{13}C NMR (CD_3CN, 100 MHz)

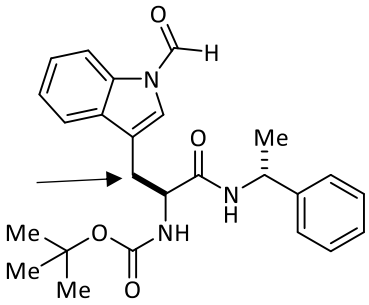


44

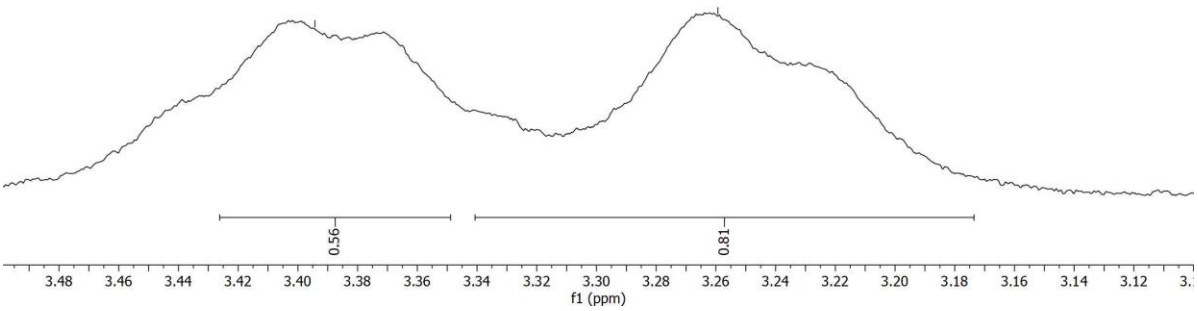
^{19}F NMR (CD_3CN, 100 MHz)

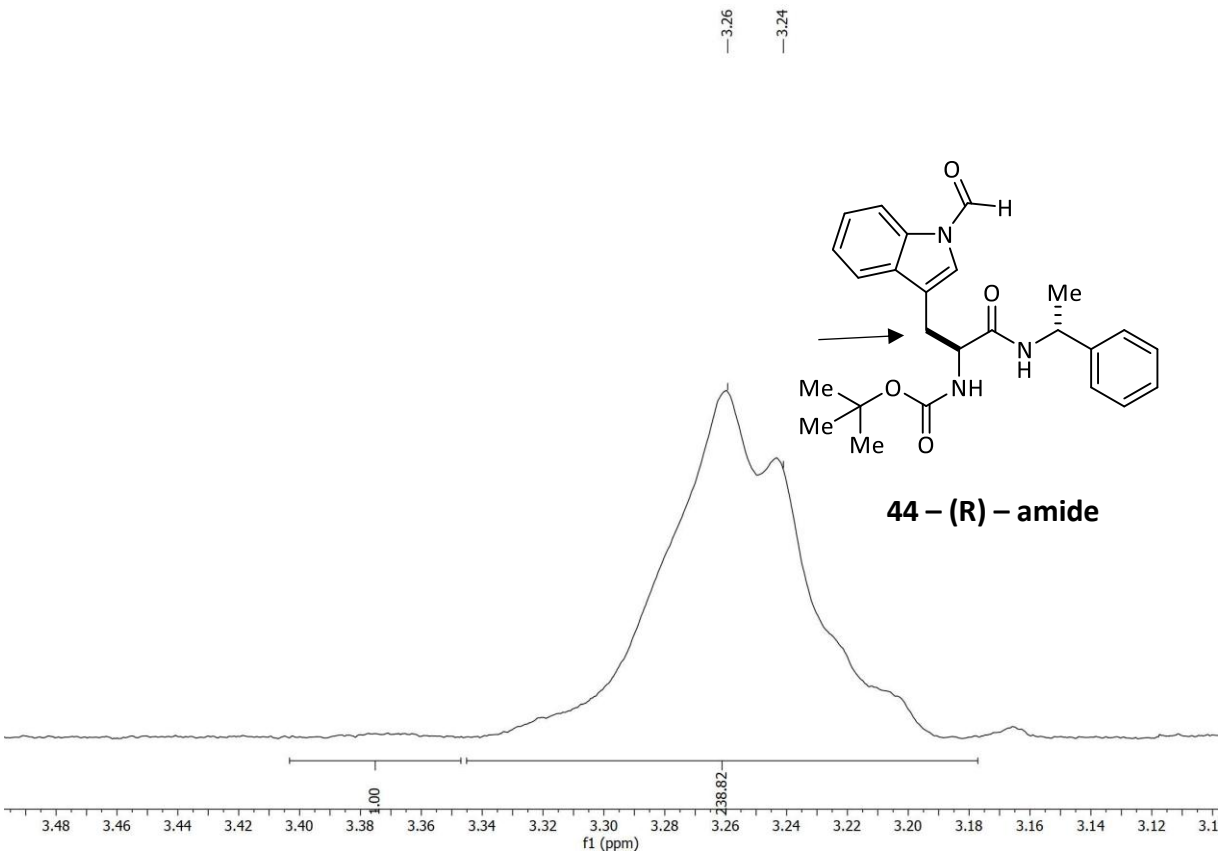


44 – (S) – amide

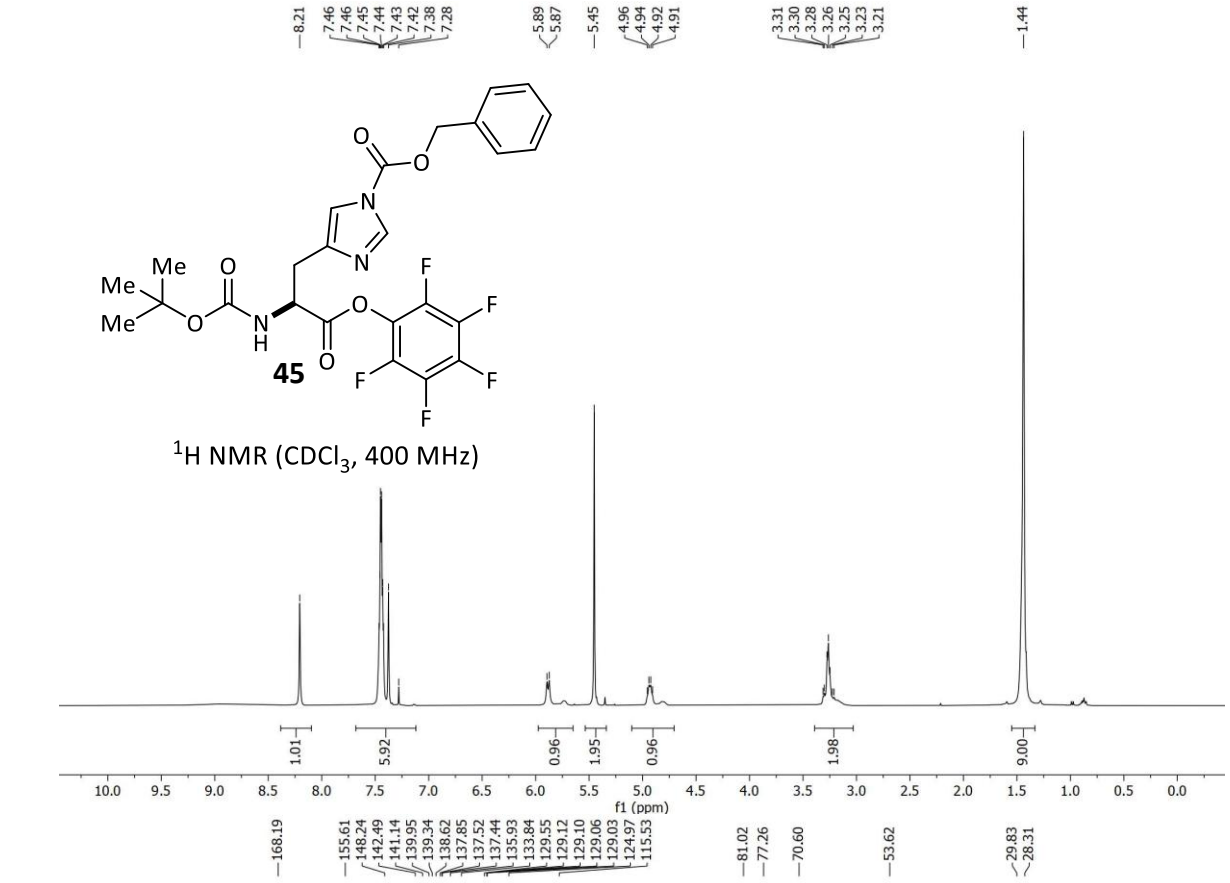


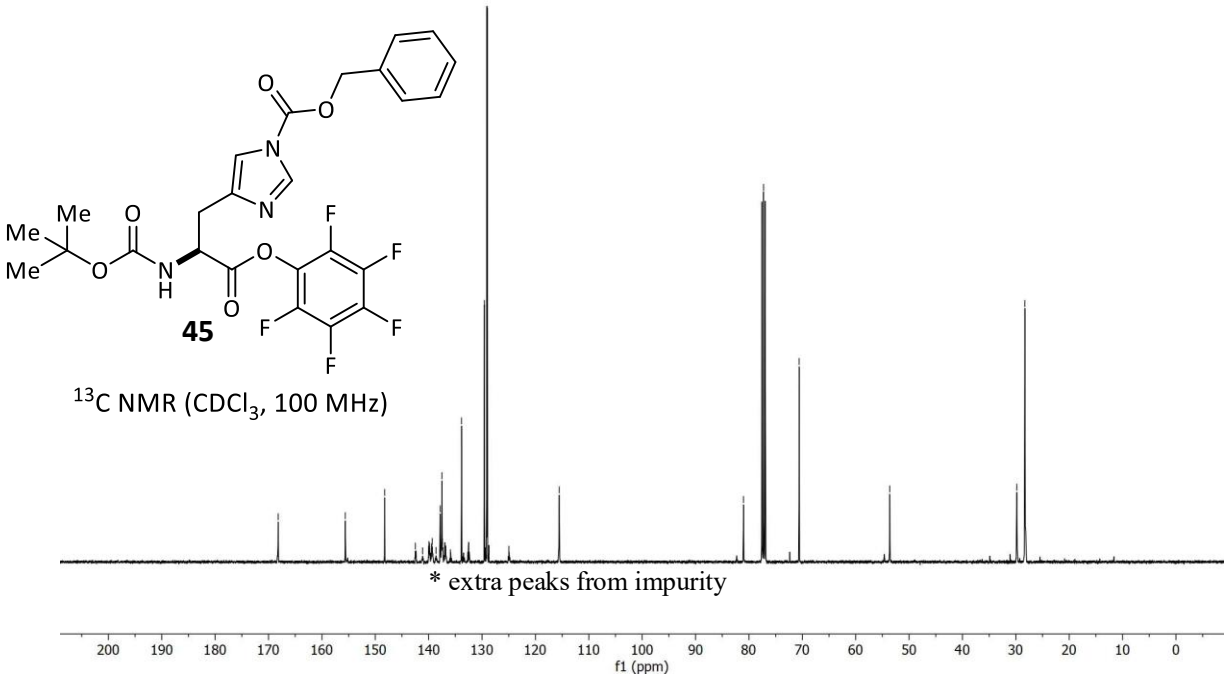
44 – (R) – amide

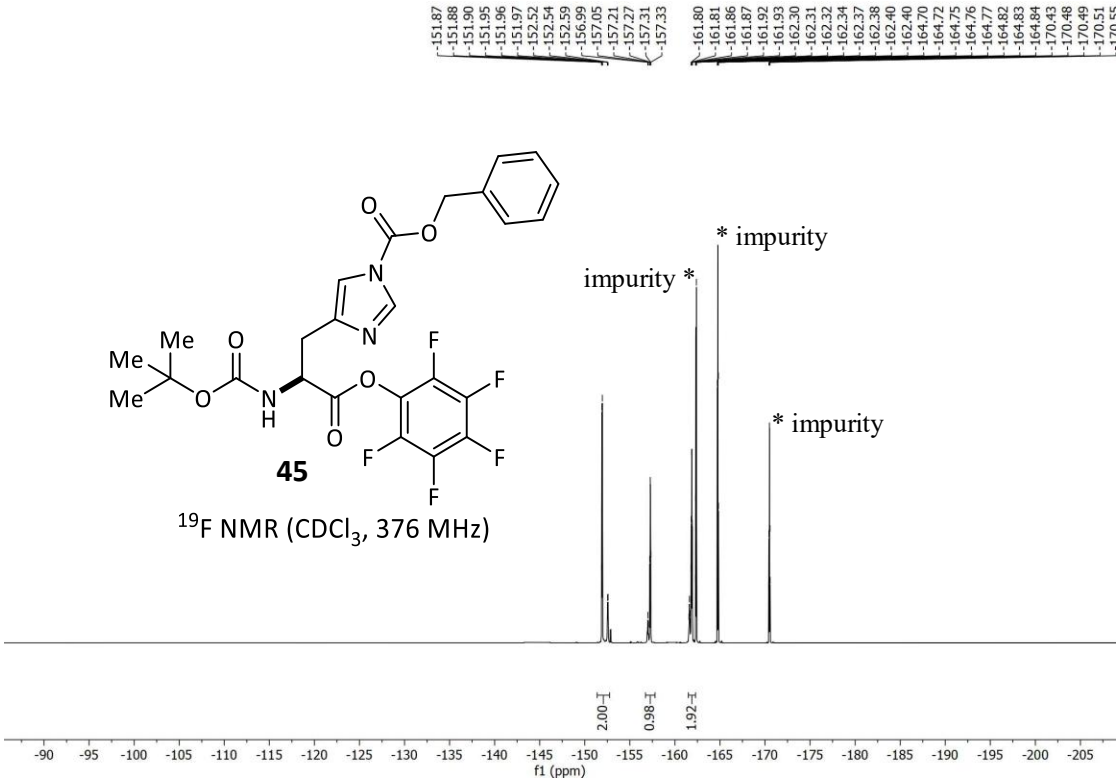


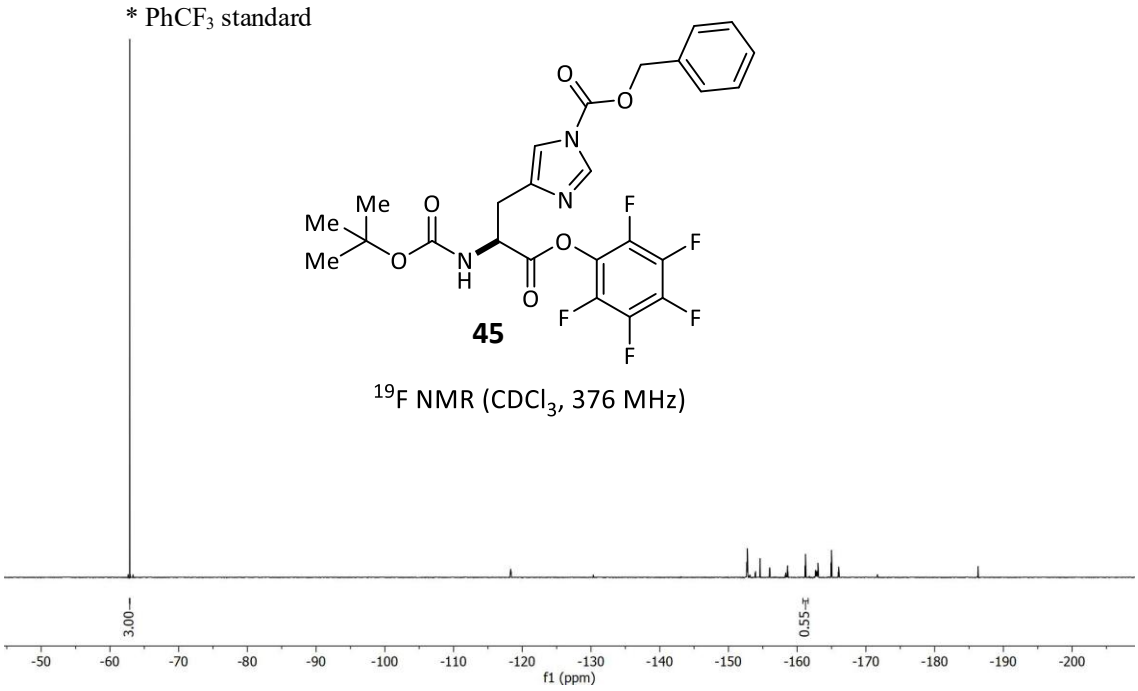

3.26
3.24
O
H
N
O
Me
N
H
Me
O
NH
Me
Me
O
Me
1.00
38.82
3.48
3.46
3.44
3.42
3.40
3.38
3.36
3.34
3.32
3.30
3.28
3.26
3.24
3.22
3.20
3.18
3.16
3.14
3.12
3.1
f1 (ppm)

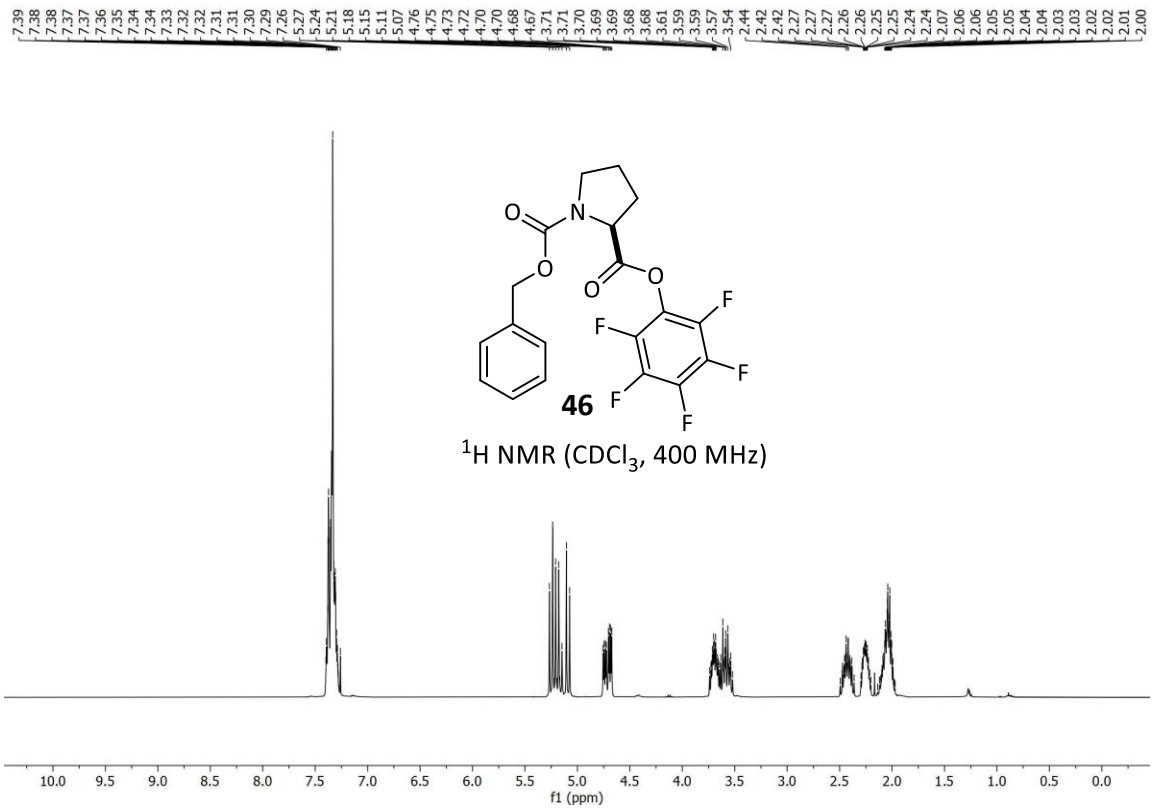
44 – (R) – amide

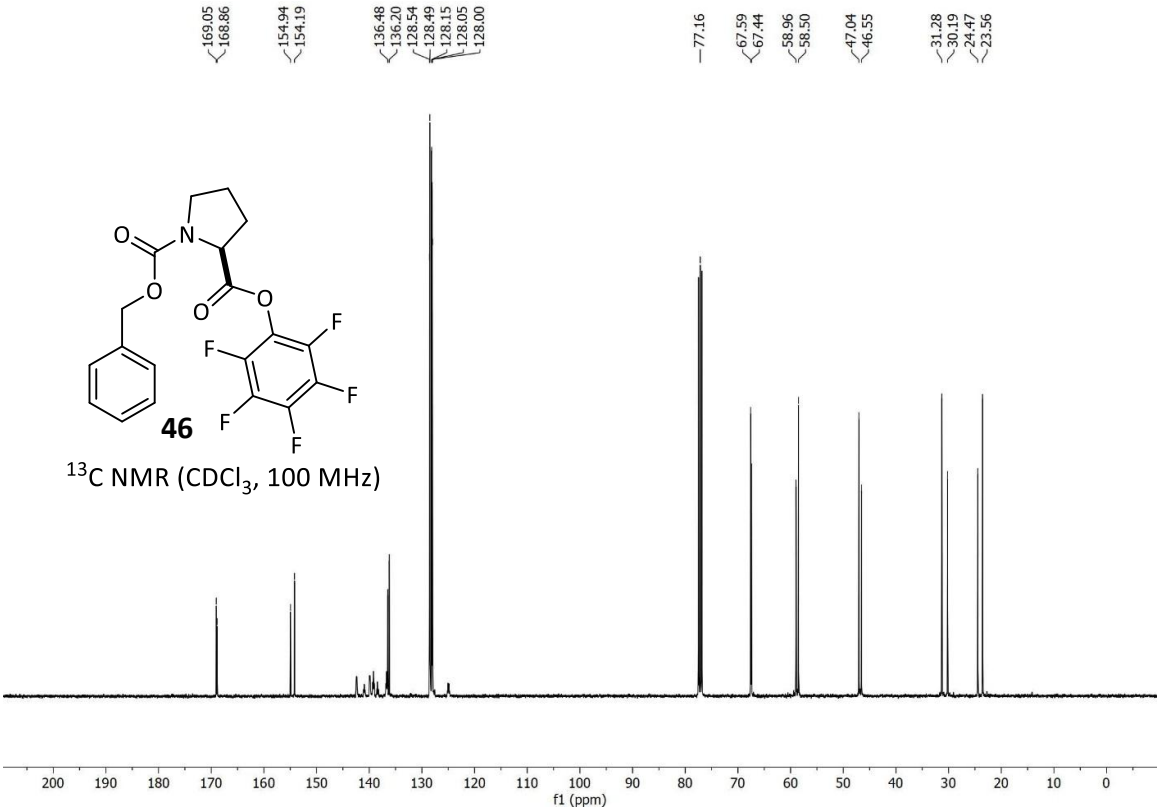

45
1H NMR (CDCl3, 400 MHz)
f1 (ppm)

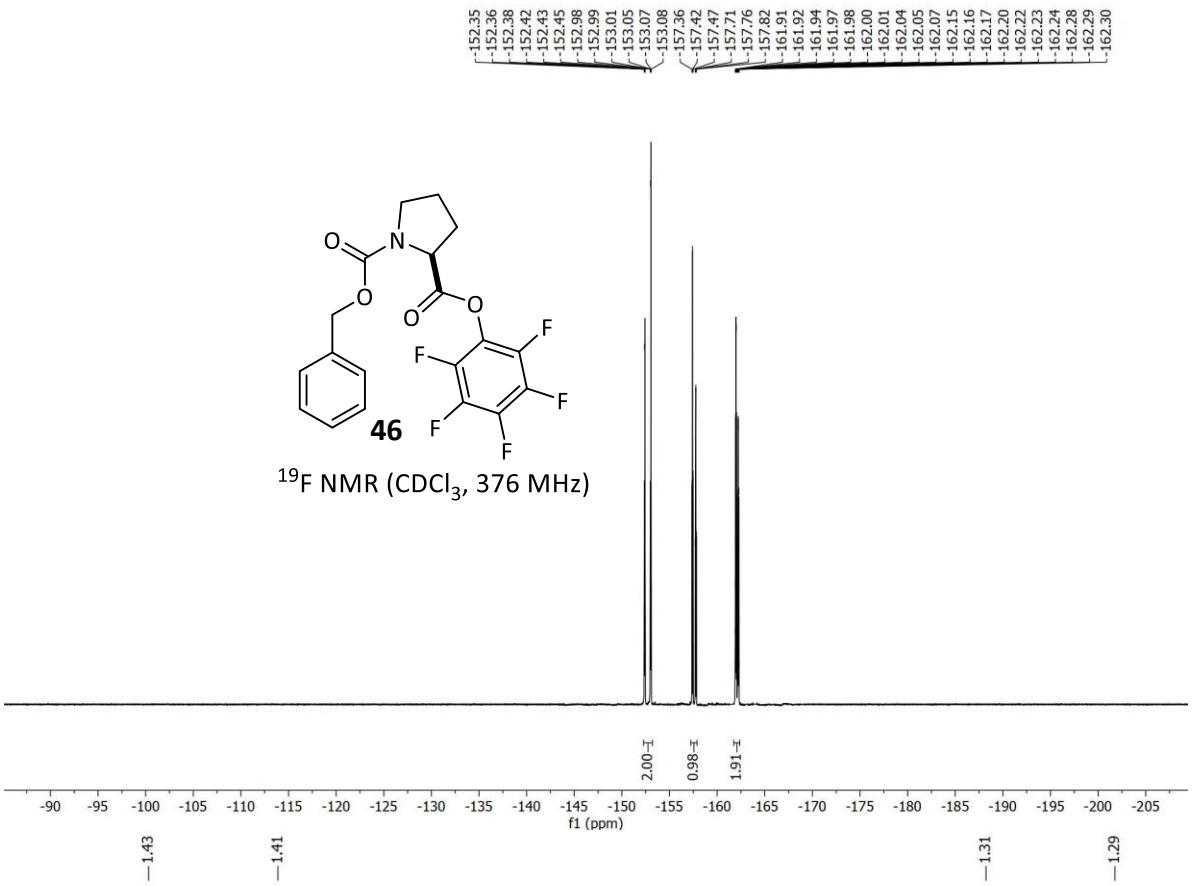

45
13C NMR (CDCl3, 100 MHz)
* extra peaks from impurity
f1 (ppm)

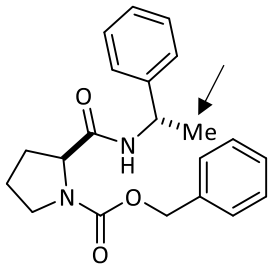

45
^{19}F NMR (CDCl$_3$, 376 MHz)
* impurity
impurity *
* impurity
2.00
0.98
1.92
f1 (ppm)


* PhCF$_3$ standard
45
^{19}F NMR (CDCl$_3$, 376 MHz)
3.00
0.55
f1 (ppm)

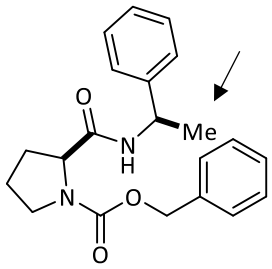

46
1H NMR (CDCl3, 400 MHz)
f1 (ppm)


46
13C NMR (CDCl3, 100 MHz)
f1 (ppm)

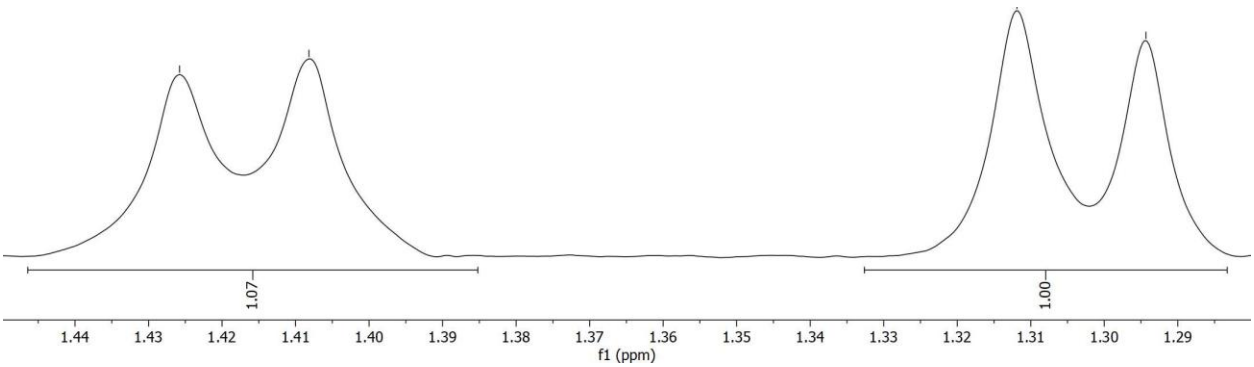


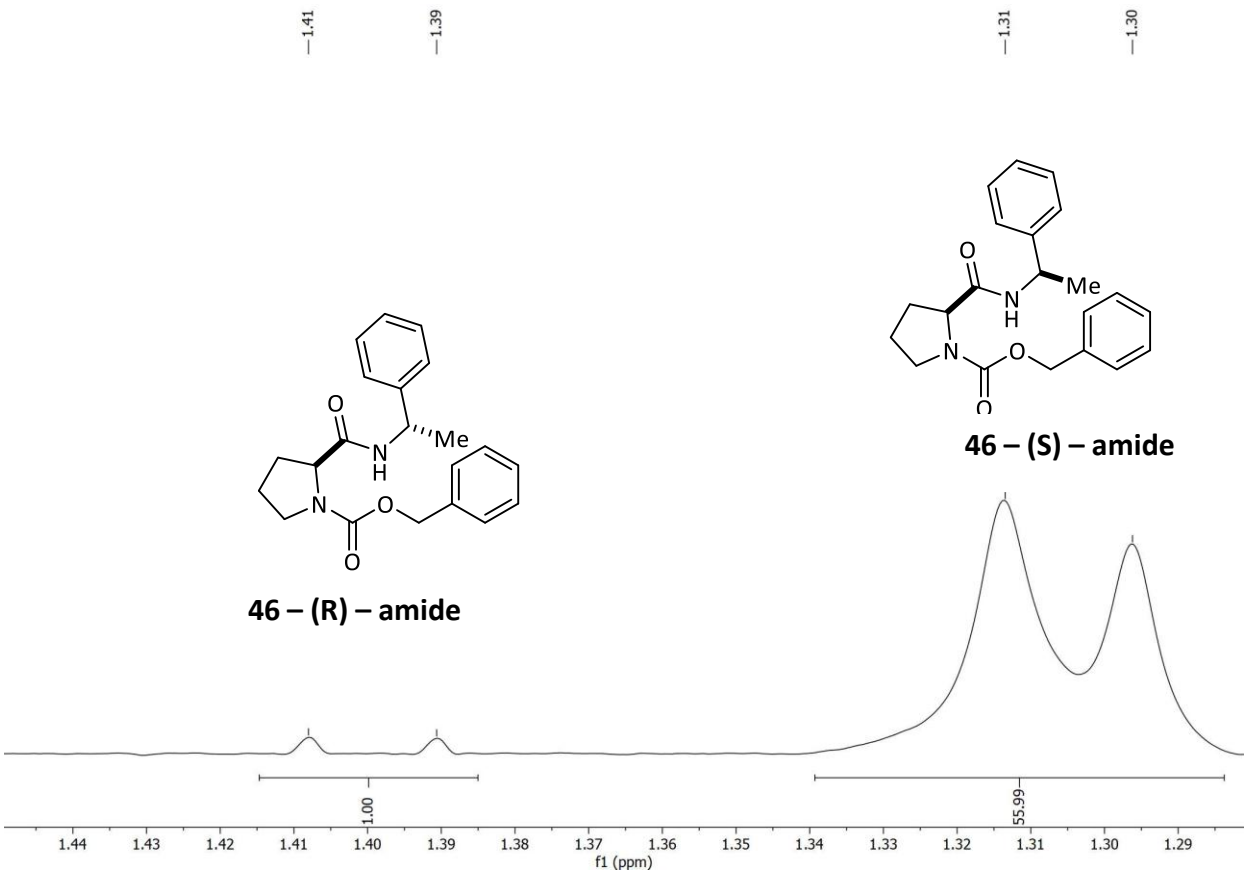


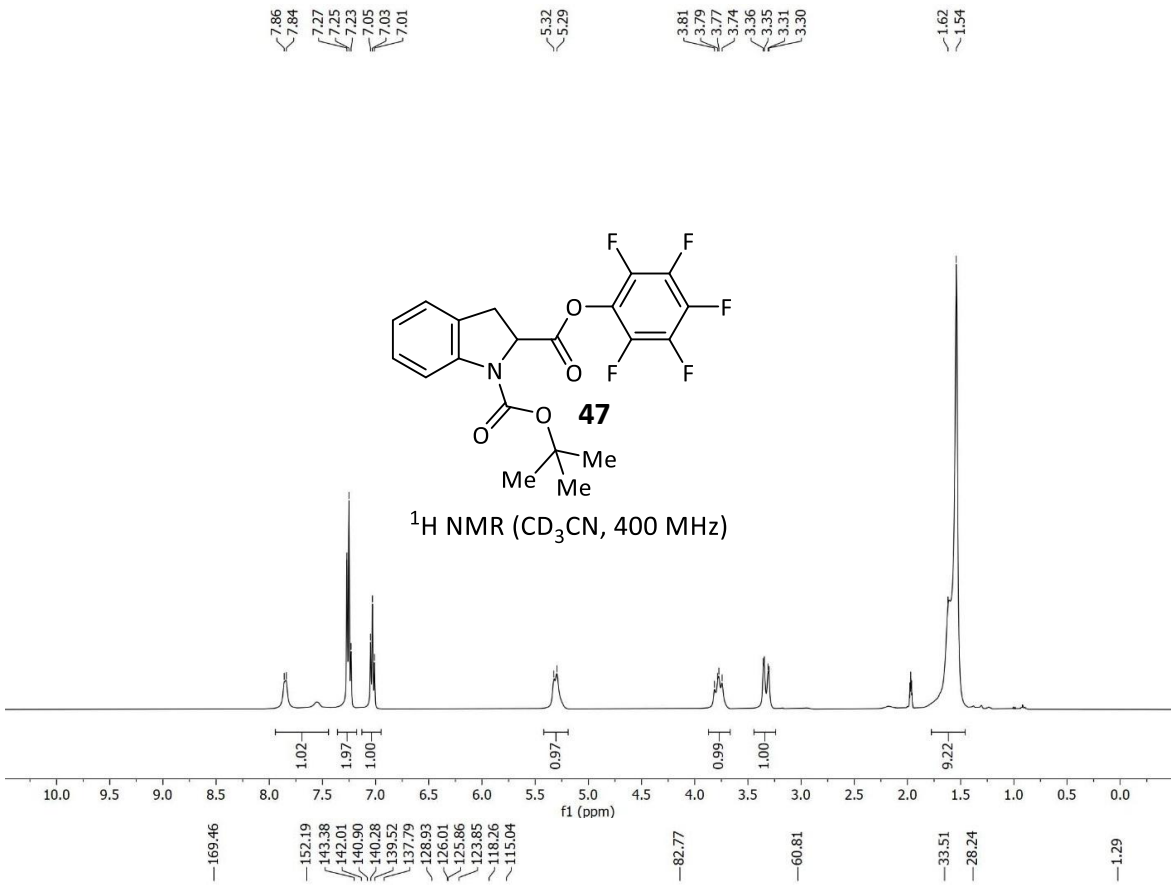
46 – (R) – amide

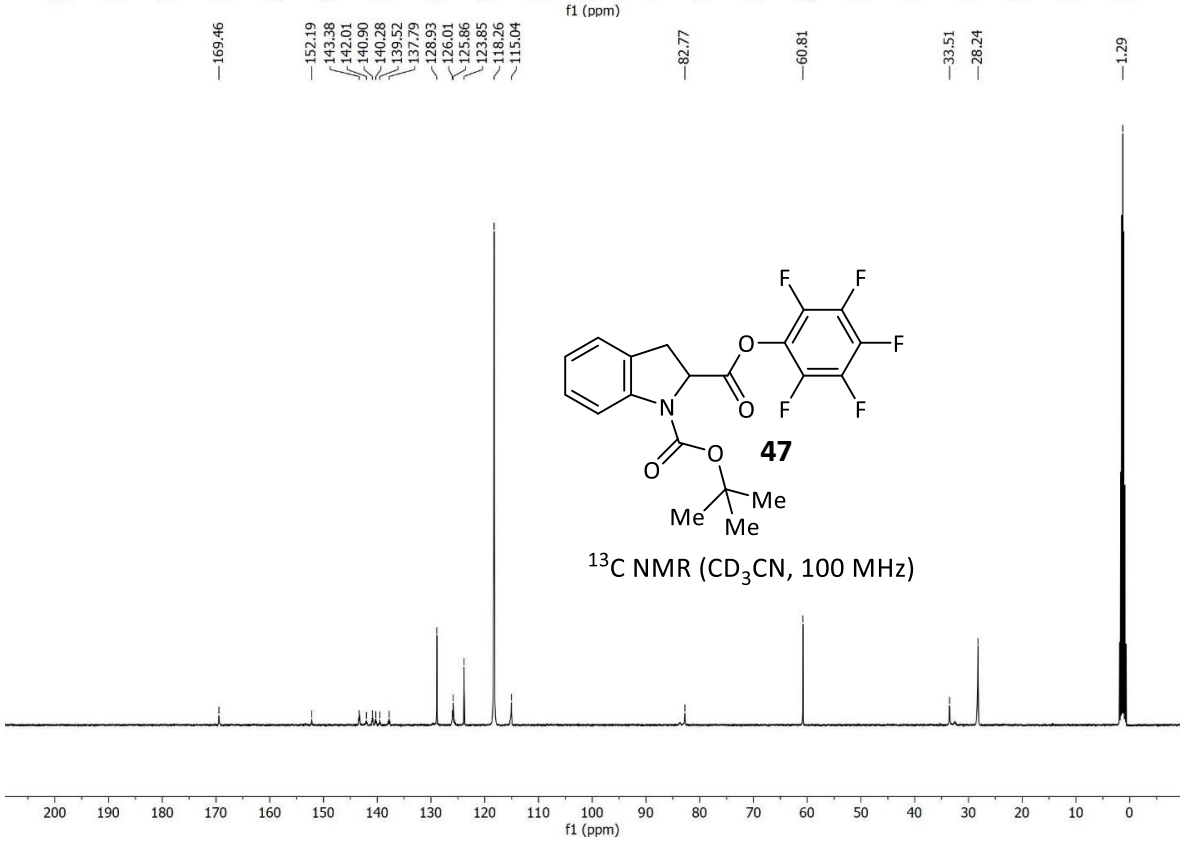


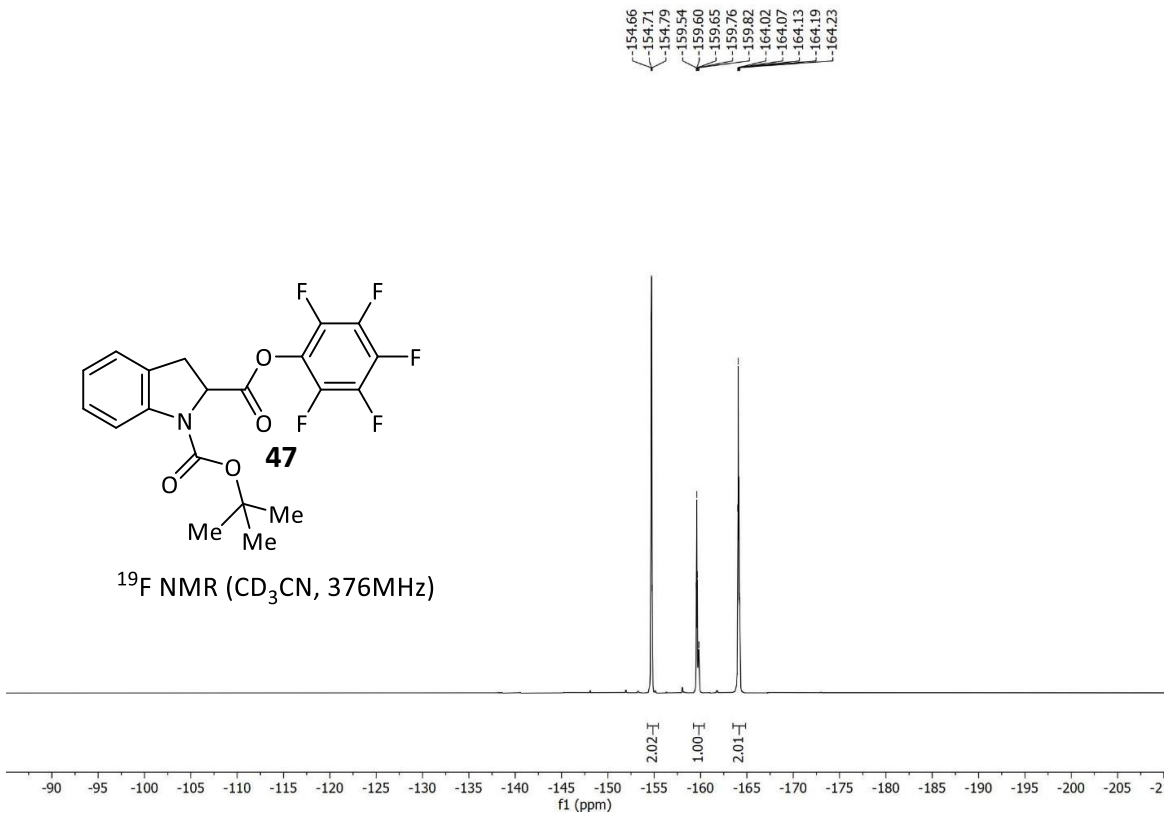
46 – (S) – amide

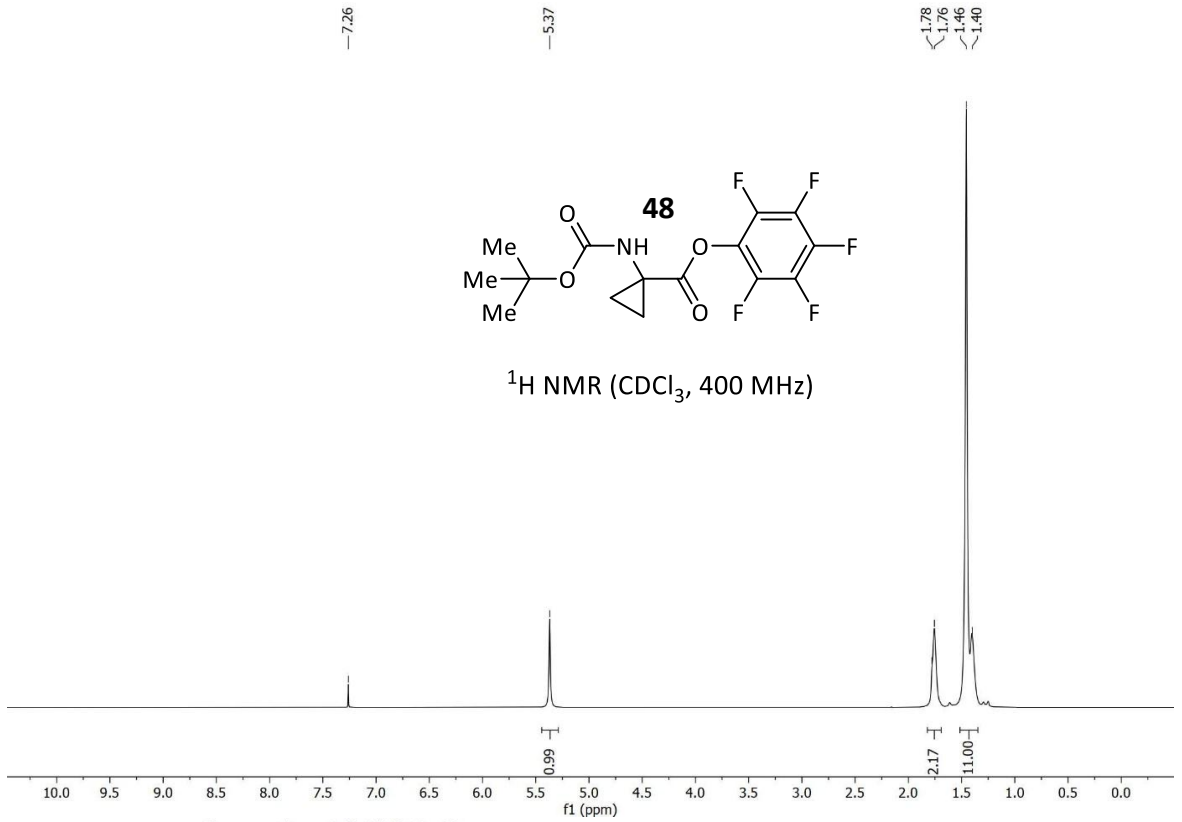



1.41
1.39
1.31
1.30
46 – (S) – amide
46 – (R) – amide
1.00
55.99
1.44
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.32
1.31
1.30
1.29
f1 (ppm)

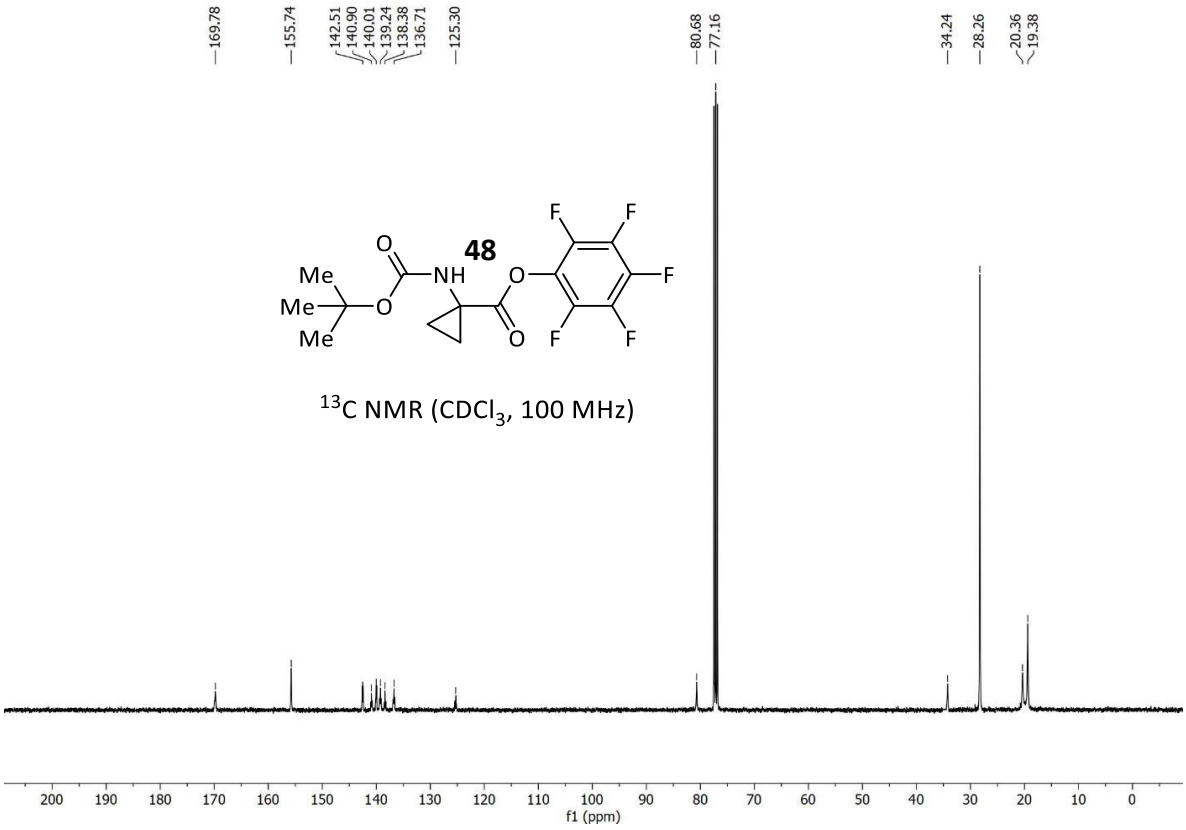

7.86
7.84
7.27
7.25
7.23
7.05
7.03
7.01
5.32
5.29
3.81
3.79
3.77
3.74
3.36
3.35
3.31
3.30
1.62
1.54
F
F
F
F
F
O
O
N
O
O
Me
Me
Me
47
1H NMR (CD3CN, 400 MHz)
1.02
1.97
1.00
0.97
0.99
1.00
9.22
f1 (ppm)


169.46
152.19
143.38
142.01
140.90
140.28
139.52
137.79
128.93
126.01
125.86
123.85
118.26
115.04
82.77
60.81
33.51
28.24
1.29
F
F
F
F
F
O
O
N
O
O
Me
Me
Me
47
13C NMR (CD3CN, 100 MHz)
f1 (ppm)

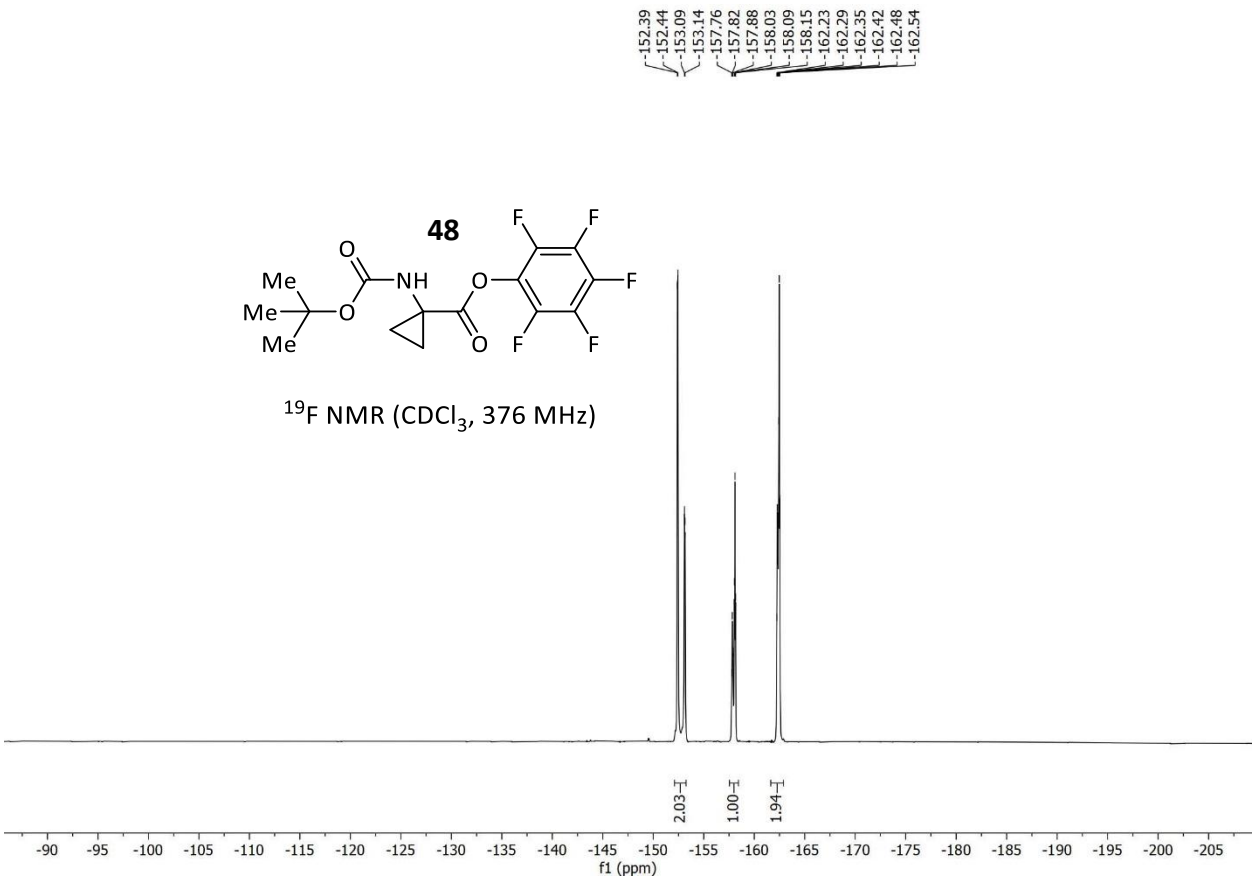

154.66
154.71
154.79
159.54
159.60
159.65
159.76
159.82
164.02
164.07
164.13
164.19
164.23
F
F
F
F
F
O
O
O
N
O
O
Me
Me
Me
47
19F NMR (CD3CN, 376MHz)
2.02
1.00
2.01
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
-200
-205
f1 (ppm)

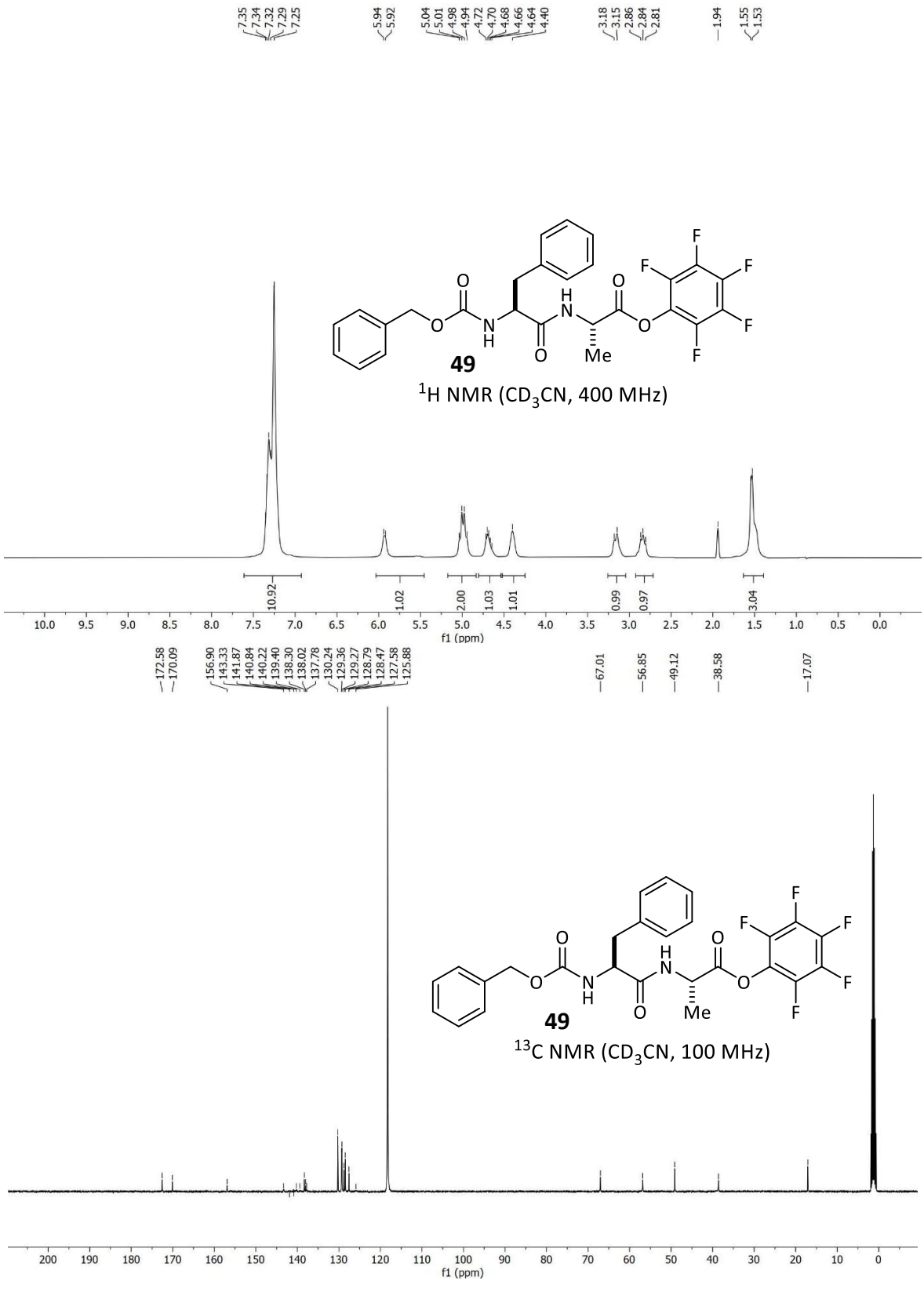


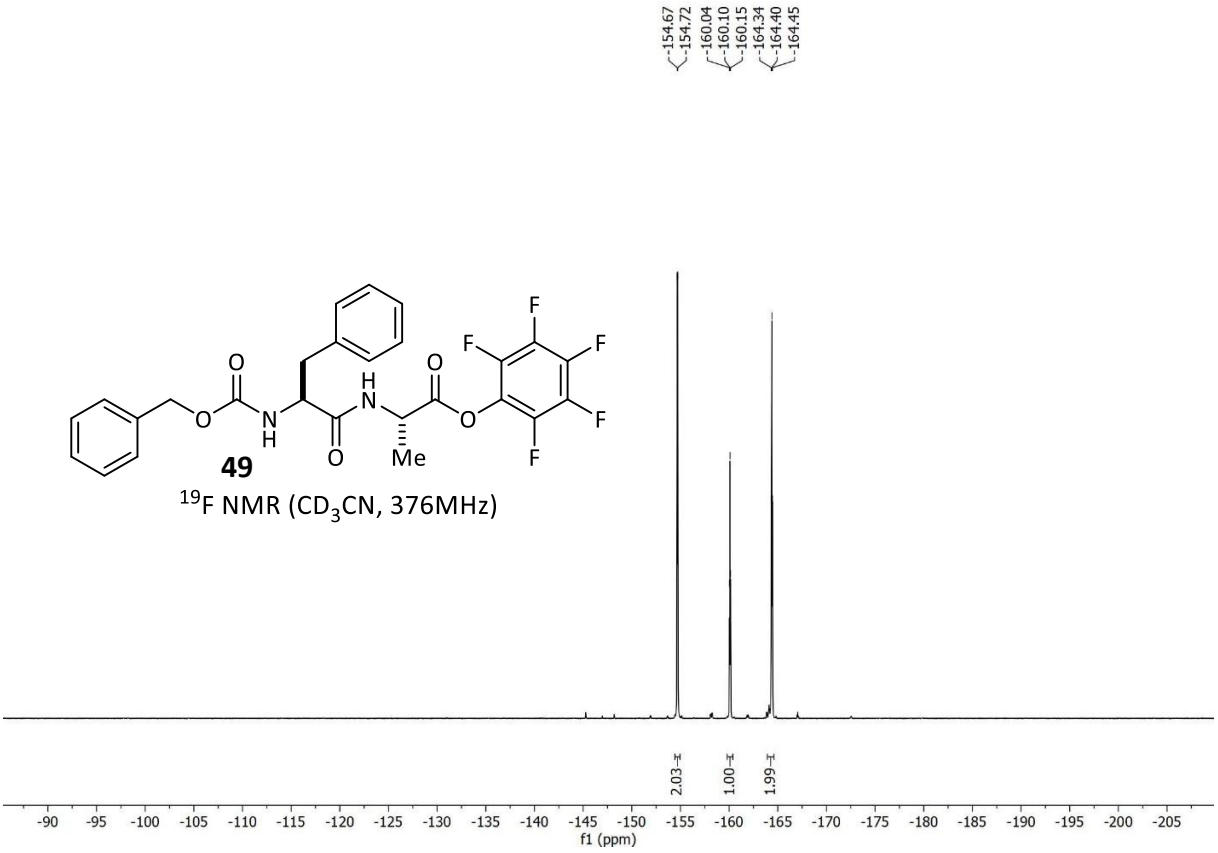
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)

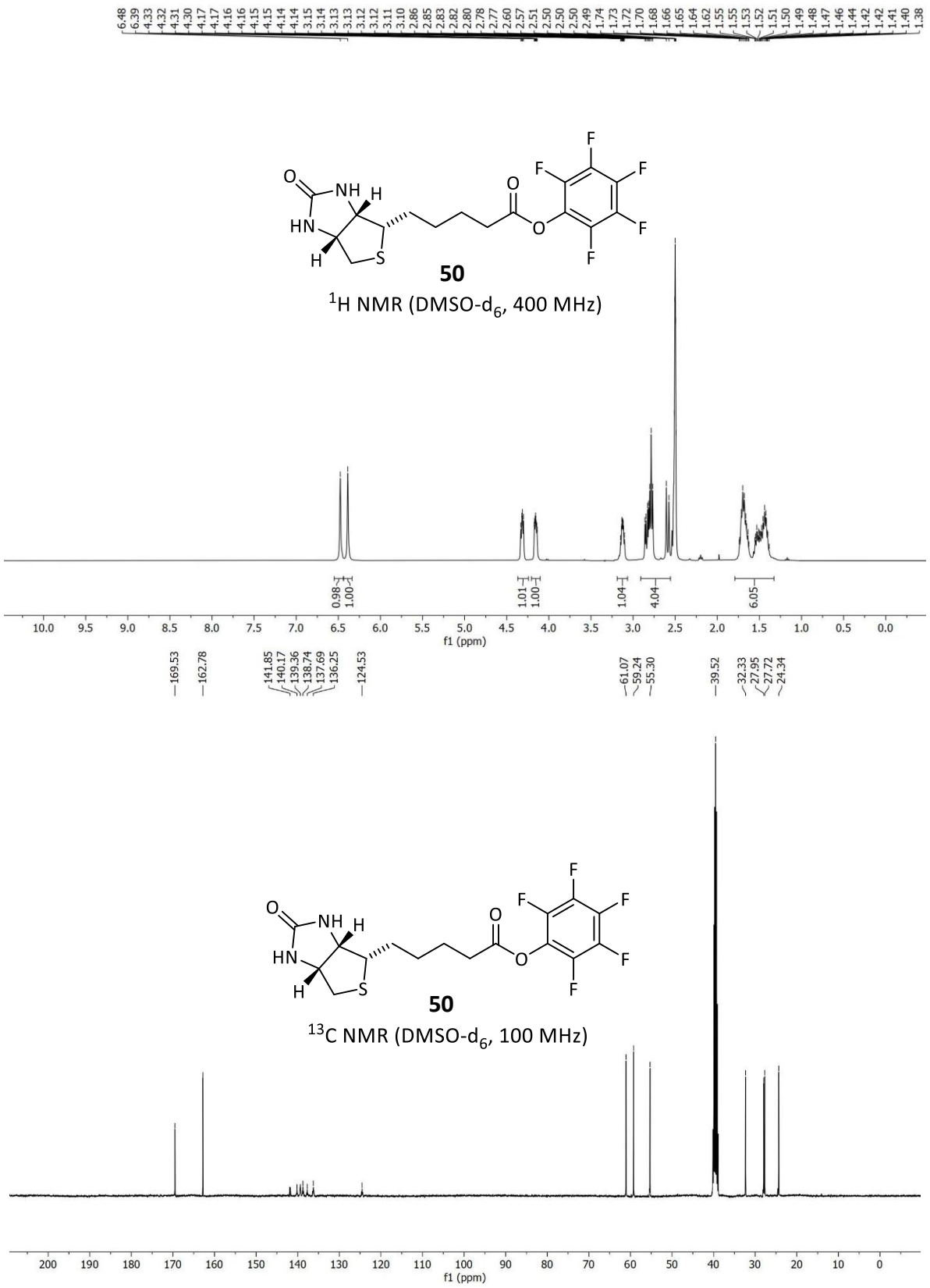

-152.39
-152.44
-153.09
-153.14
-157.76
-157.82
-157.88
-158.03
-158.09
-158.15
-162.23
-162.29
-162.35
-162.42
-162.48
-162.54
48
Me
Me
Me
O
O
NH
O
O
F
F
F
F
F
^{19}F NMR ($CDCl_3$, 376 MHz)
2.03
1.00
1.94
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205
f1 (ppm)

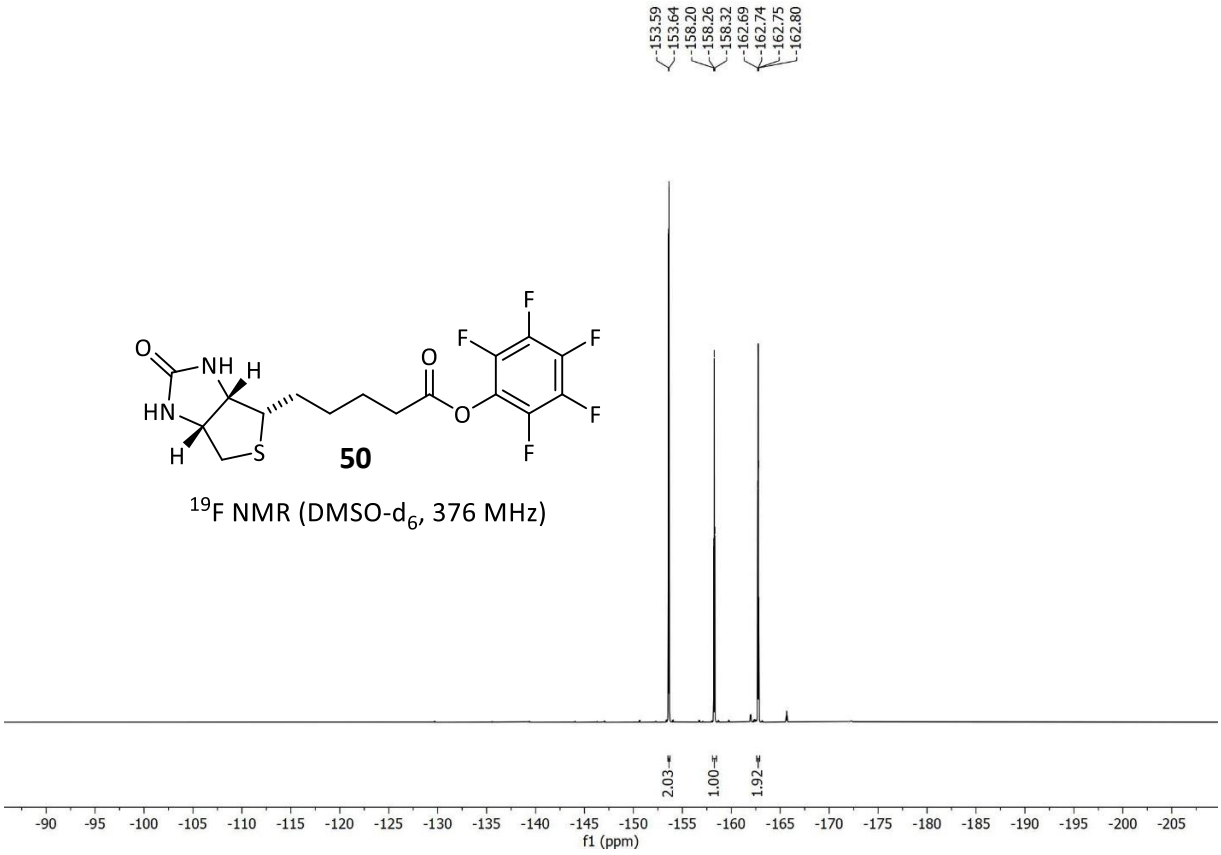

7.35
7.34
7.32
7.29
7.25
5.94
5.92
5.04
5.01
4.98
4.94
4.72
4.70
4.68
4.66
4.64
4.40
3.18
3.15
2.86
2.84
2.81
1.94
1.55
1.53
49
1H NMR (CD3CN, 400 MHz)
10.92
1.02
2.00
1.03
1.01
0.99
0.97
3.04
f1 (ppm)
172.58
170.09
156.90
143.33
141.87
140.84
140.22
139.40
138.30
138.02
137.78
130.24
129.36
129.27
128.79
128.47
127.58
125.88
67.01
56.85
49.12
38.58
17.07
49
13C NMR (CD3CN, 100 MHz)
f1 (ppm)



49

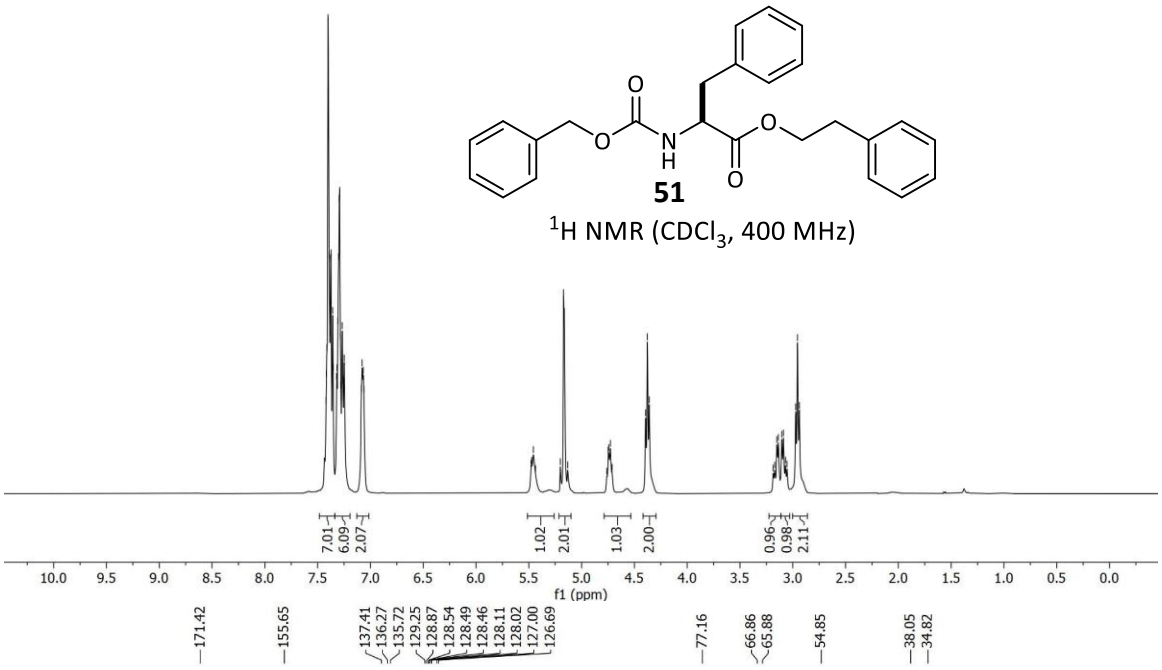
^{19}F NMR (CD_3CN, 376MHz)


6.48 6.39 4.33 4.32 4.31 4.30 4.17 4.17 4.16 4.16 4.15 4.15 4.14 4.14 3.15 3.14 3.13 3.13 3.12 3.12 3.11 3.10 2.86 2.85 2.83 2.82 2.80 2.78 2.77 2.60 2.57 2.51 2.50 2.50 2.50 2.49 1.74 1.73 1.72 1.70 1.68 1.66 1.65 1.64 1.62 1.55 1.55 1.53 1.52 1.51 1.50 1.49 1.48 1.47 1.46 1.44 1.42 1.41 1.40 1.38
50
1H NMR (DMSO-d6, 400 MHz)
0.98 1.00 1.01 1.00 1.04 4.04 6.05
f1 (ppm)
169.53 162.78 141.85 140.17 139.36 138.74 137.69 136.25 124.53 61.07 59.24 55.30 39.52 32.33 27.95 27.72 24.34
50
13C NMR (DMSO-d6, 100 MHz)
f1 (ppm)



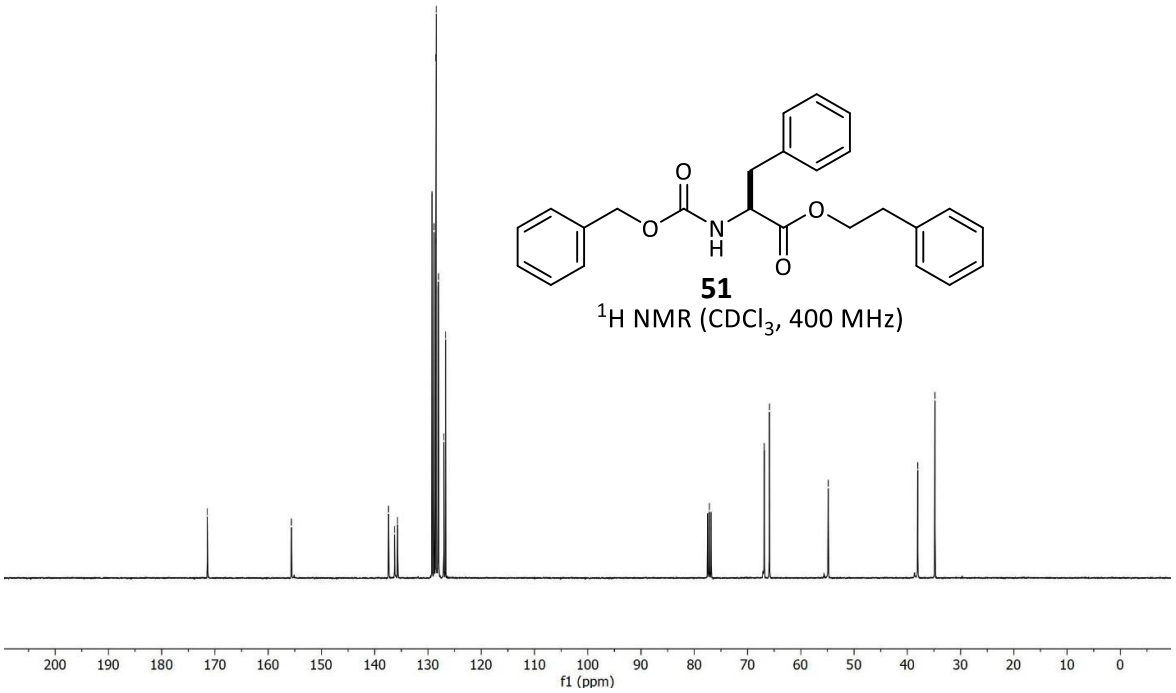
^{19}F NMR (DMSO-d_6, 376 MHz)

XIII. NMR Spectra for Z-Phe Derivatives



51

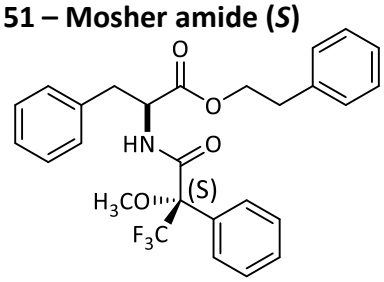
^{1}H NMR ($CDCl_3$, 400 MHz)



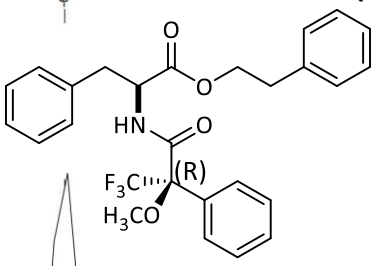
51

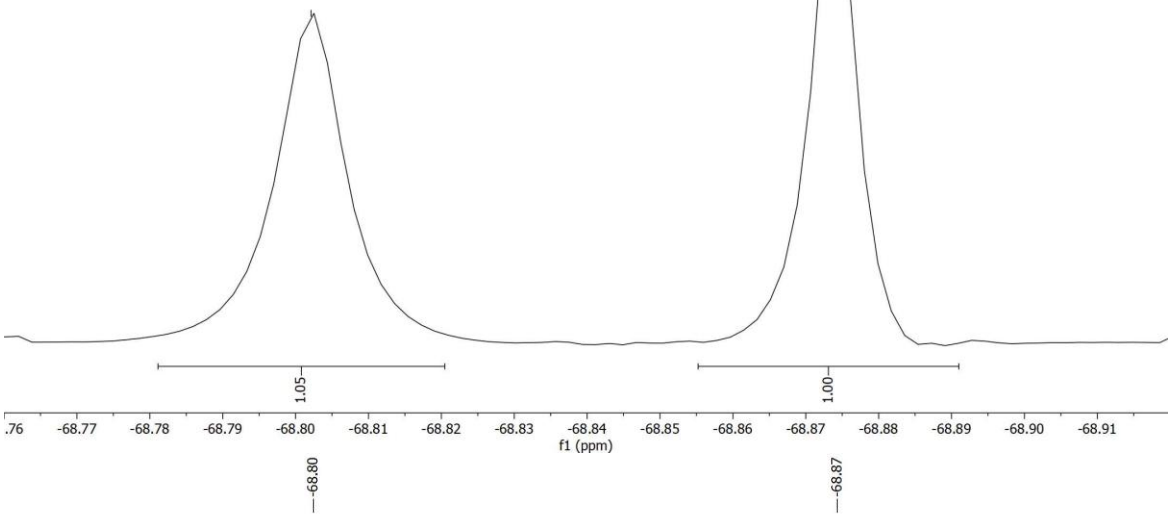
^{1}H NMR ($CDCl_3$, 400 MHz)

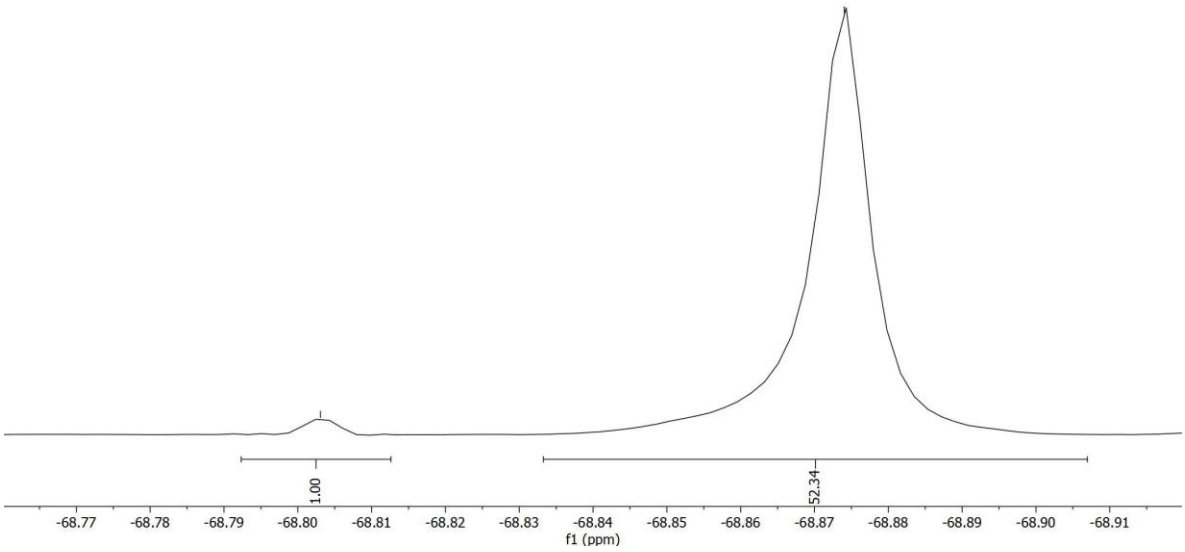
51 – Mosher amide (*S*)

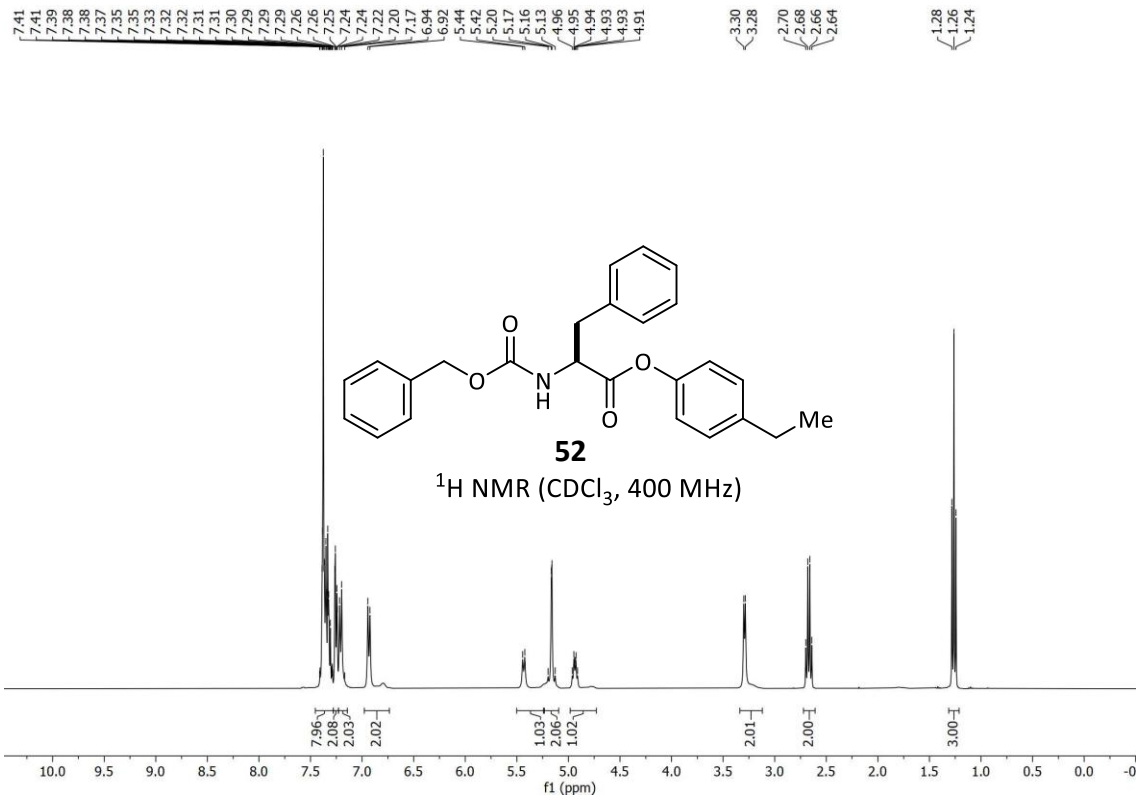


51 – Mosher amide (*R*)



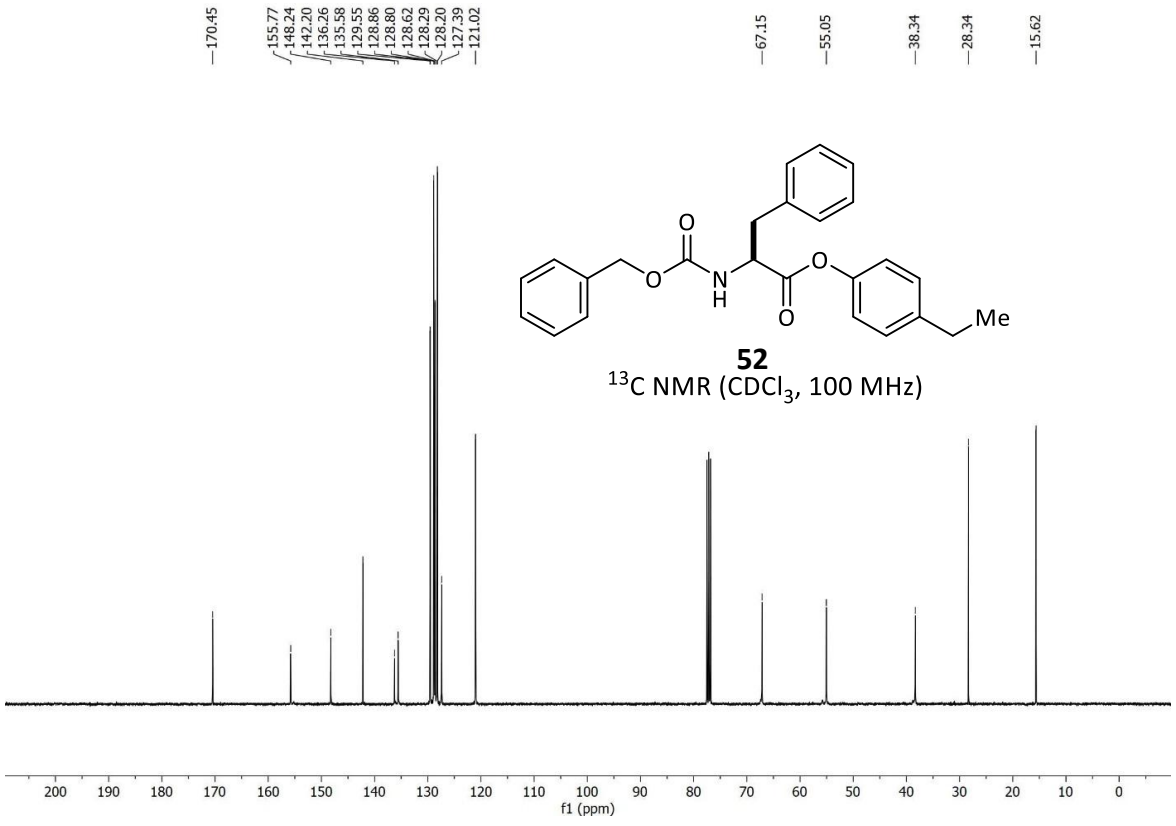






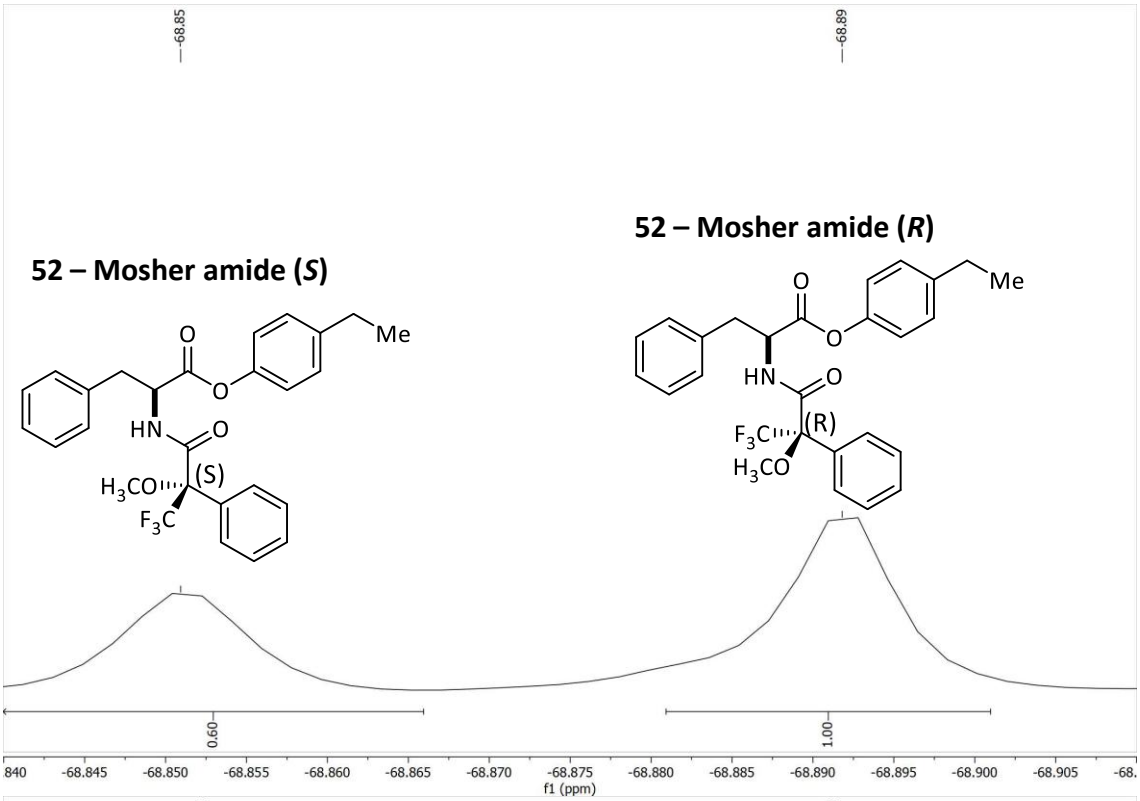
52

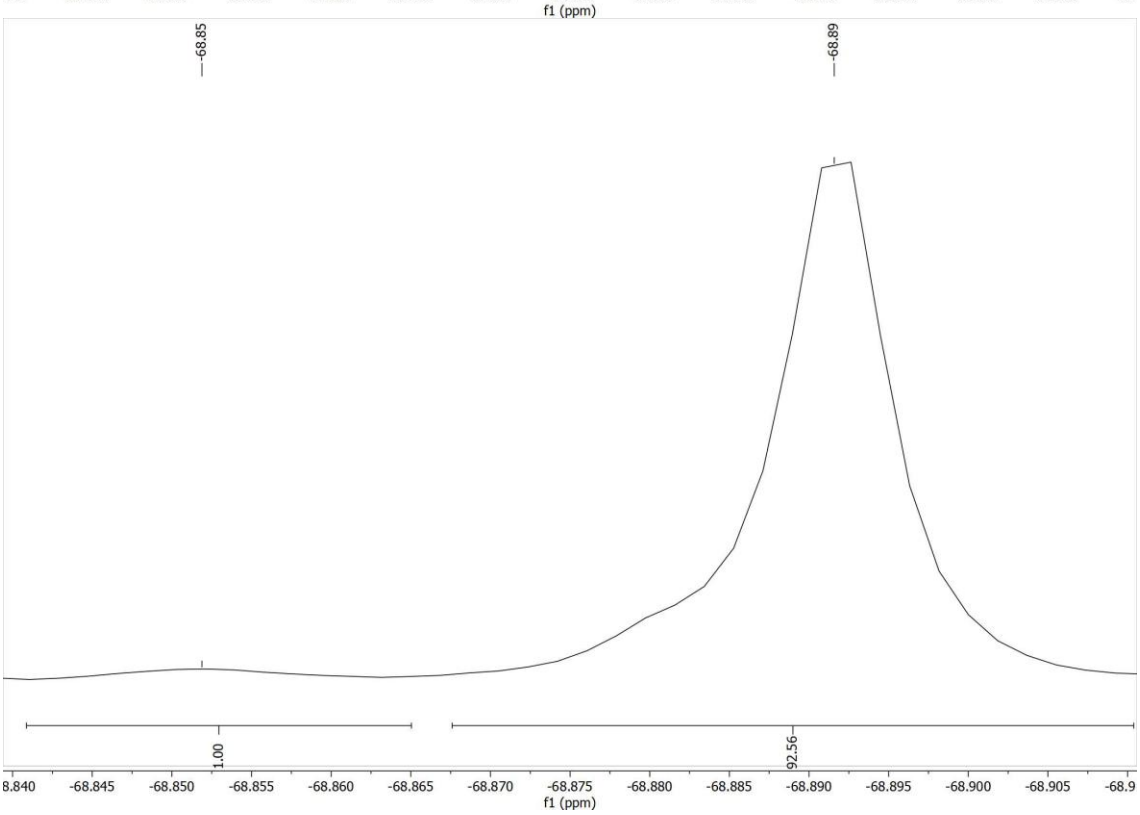
^{1}H NMR ($CDCl_3$, 400 MHz)

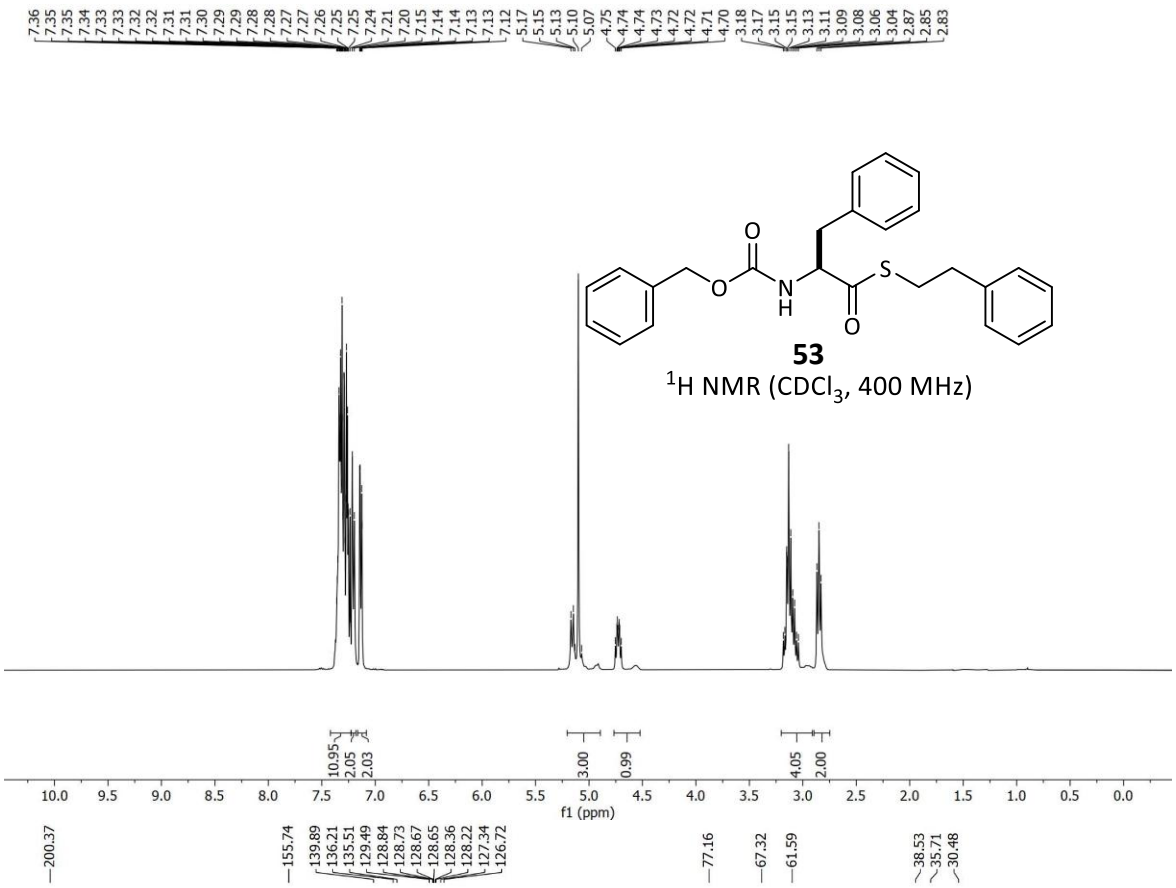


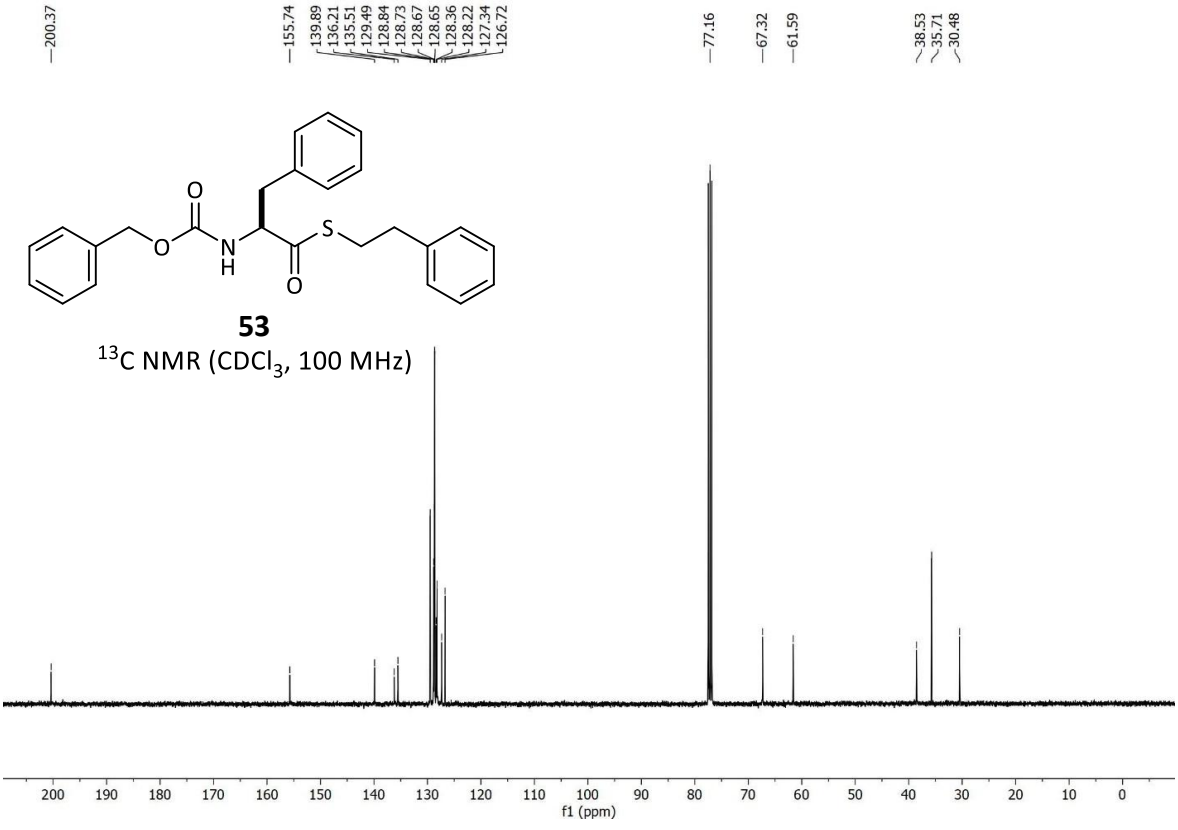
52

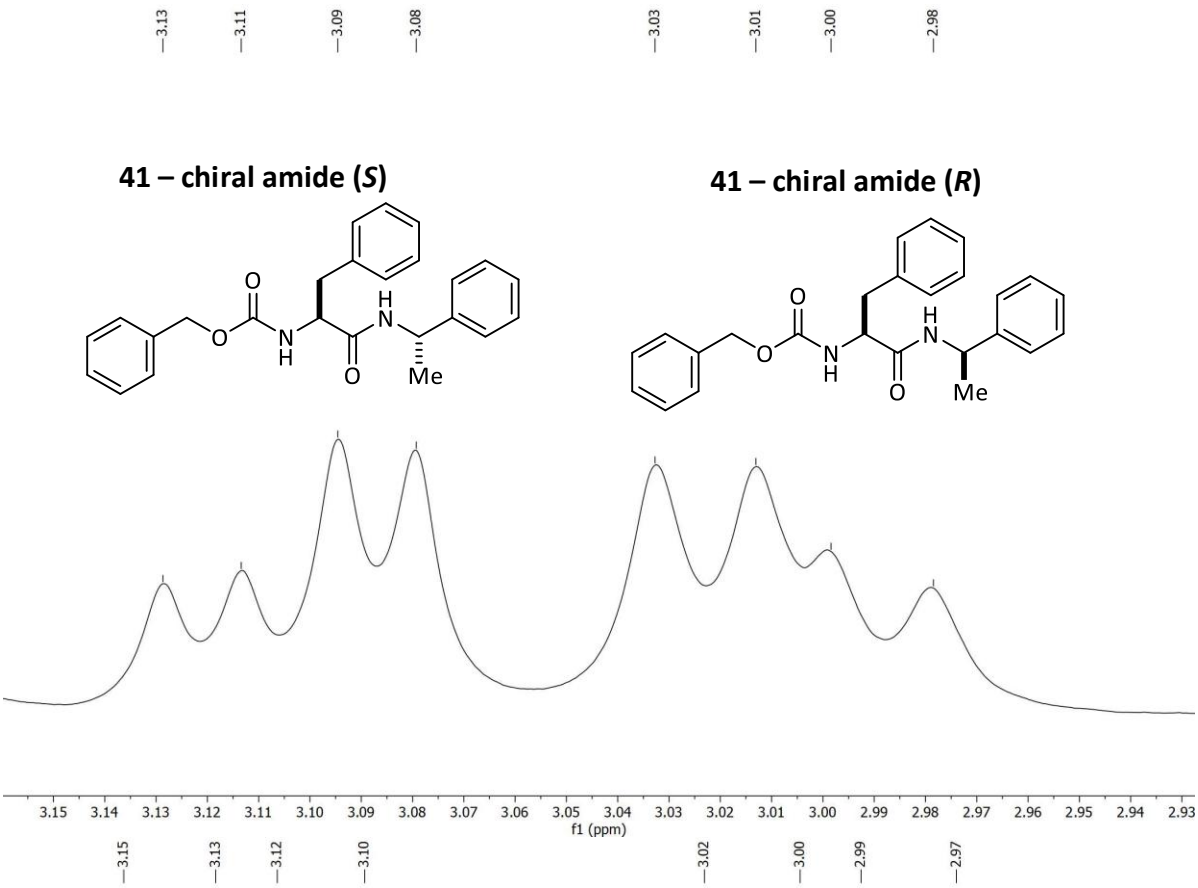
^{13}C NMR ($CDCl_3$, 100 MHz)

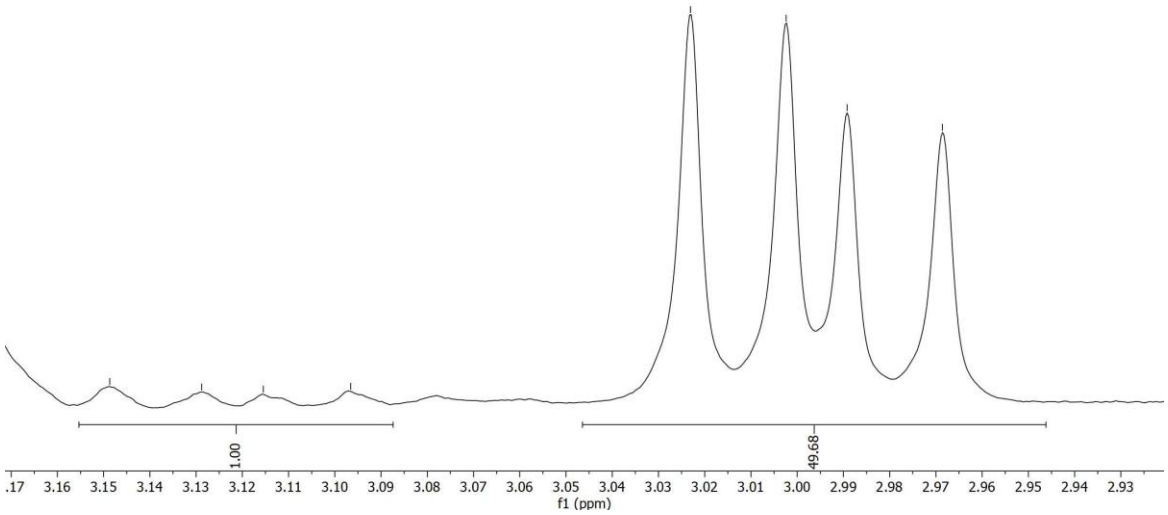

-68.85
-68.89
52 – Mosher amide (S)
52 – Mosher amide (R)
Me
O
HN
(S)
(R)
H_3CO
F_3C
0.60
1.00
-68.840
-68.845
-68.850
-68.855
-68.860
-68.865
-68.870
-68.875
-68.880
-68.885
-68.890
-68.895
-68.900
-68.905
f1 (ppm)

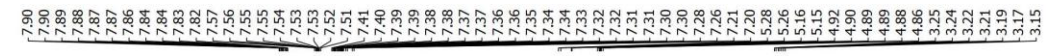

-68.85
-68.89
1.00
92.56
-68.840
-68.845
-68.850
-68.855
-68.860
-68.865
-68.870
-68.875
-68.880
-68.885
-68.890
-68.895
-68.900
-68.905
f1 (ppm)

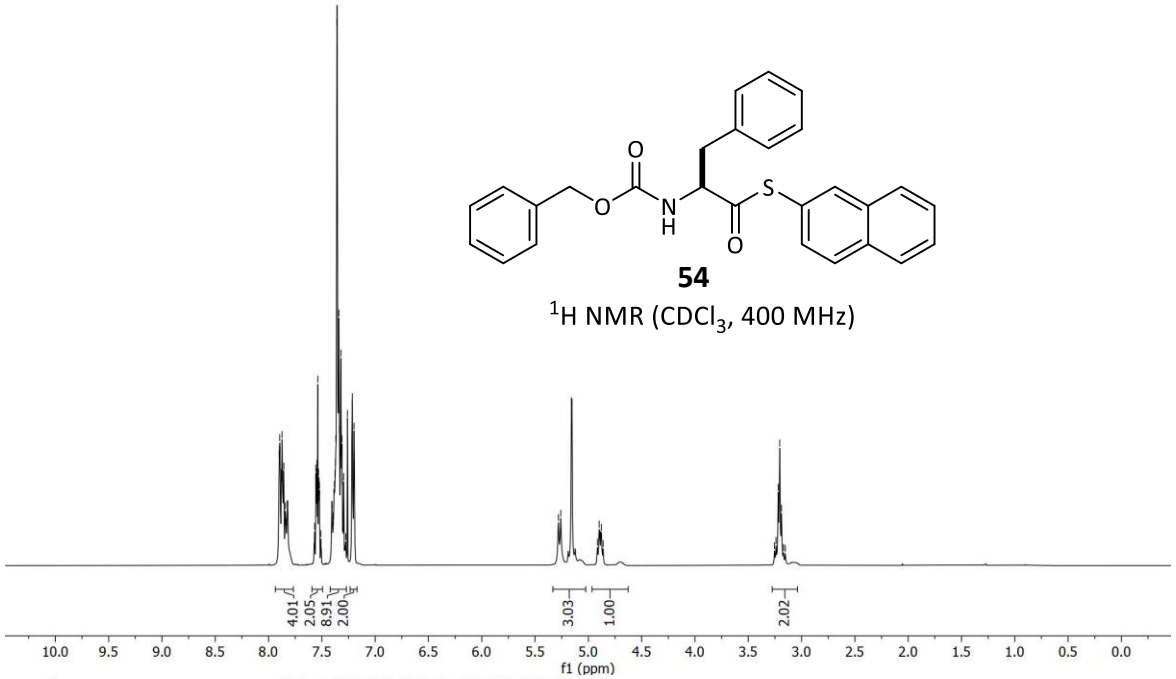

7.36 7.35 7.35 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.26 7.25 7.25 7.24 7.21 7.20 7.15 7.14 7.14 7.13 7.13 7.12 5.17 5.15 5.13 5.10 5.07 4.75 4.74 4.74 4.73 4.72 4.72 4.71 4.70 3.18 3.17 3.15 3.15 3.13 3.11 3.09 3.08 3.06 3.04 2.87 2.85 2.83
O
O
N
H
S
O
53
1H NMR (CDCl3, 400 MHz)
10.95
2.05
2.03
3.00
0.99
4.05
2.00
f1 (ppm)


200.37
155.74
139.89
136.21
135.51
129.49
128.84
128.73
128.67
128.65
128.36
128.22
127.34
126.72
77.16
67.32
61.59
38.53
35.71
30.48
O
O
N
H
S
O
53
13C NMR (CDCl3, 100 MHz)
f1 (ppm)


3.13
3.11
3.09
3.08
3.03
3.01
3.00
2.98
41 – chiral amide (S)
41 – chiral amide (R)
O
O
N
H
H
N
O
Me
3.15 3.14 3.13 3.12 3.11 3.10 3.09 3.08 3.07 3.06 3.05 3.04 3.03 3.02 3.01 3.00 2.99 2.98 2.97 2.96 2.95 2.94 2.93
f1 (ppm)
3.15
3.13
3.12
3.10
3.02
3.00
2.99
2.97

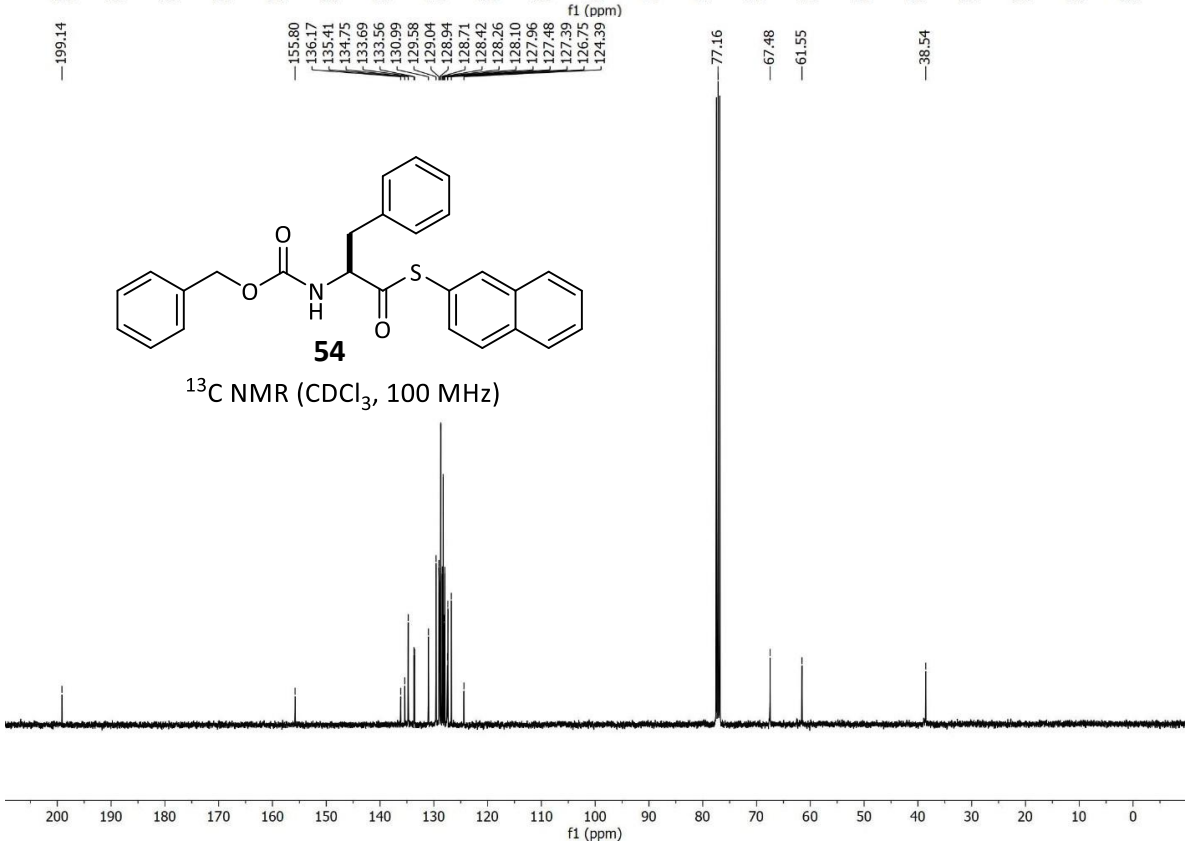

1.00
49.68
.17 3.16 3.15 3.14 3.13 3.12 3.11 3.10 3.09 3.08 3.07 3.06 3.05 3.04 3.03 3.02 3.01 3.00 2.99 2.98 2.97 2.96 2.95 2.94 2.93
f1 (ppm)





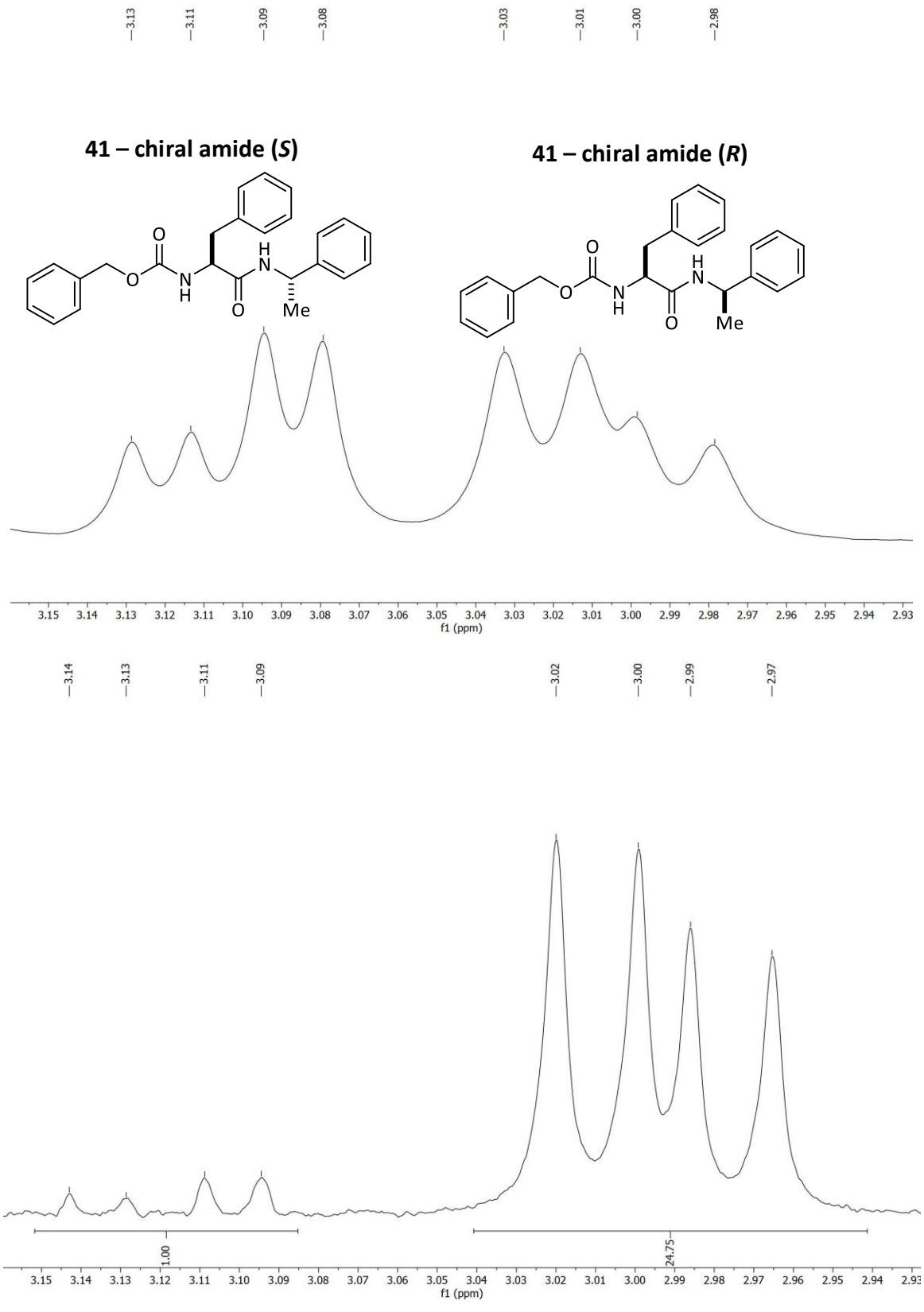
54

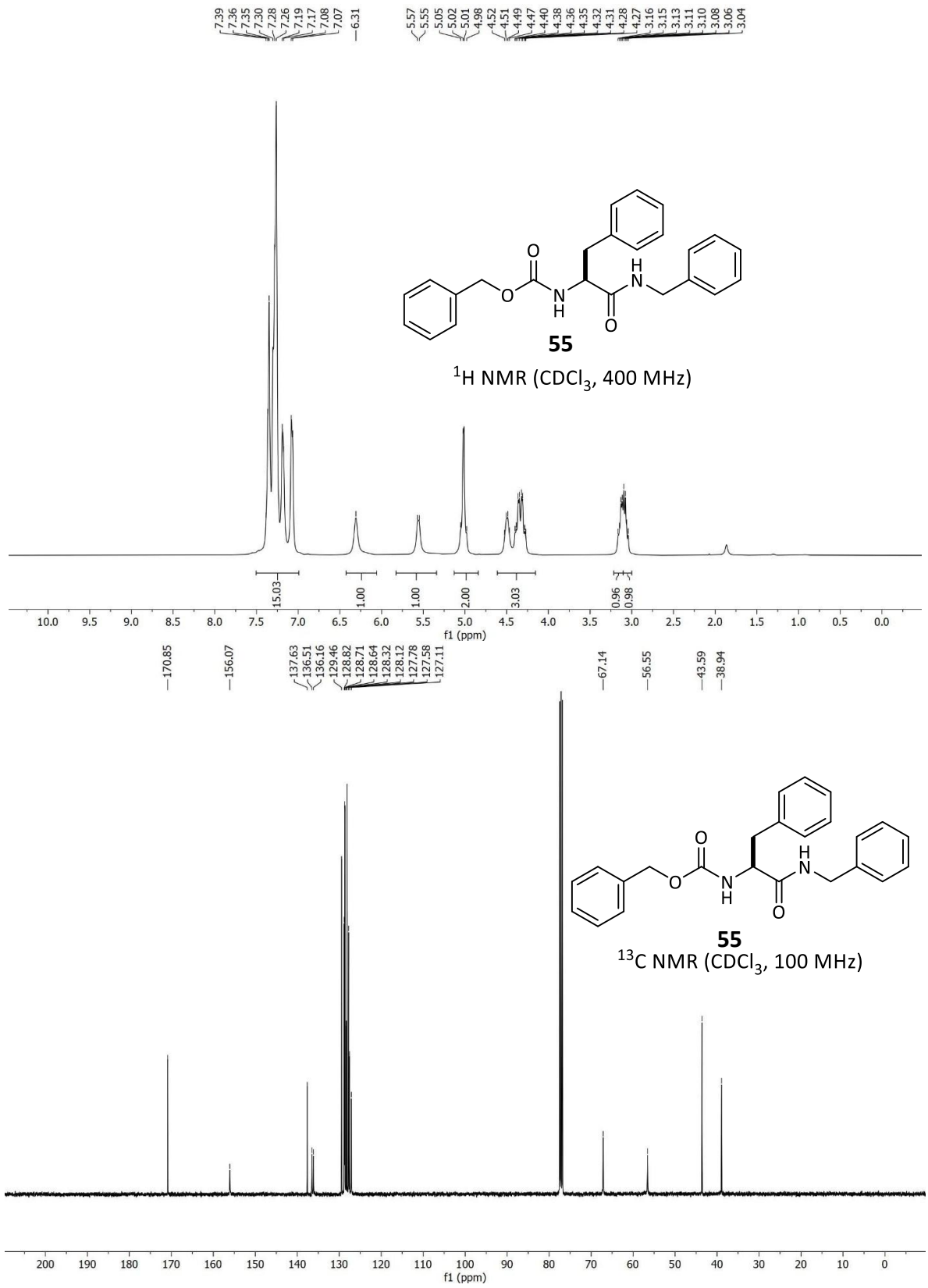
^{1}H NMR ($CDCl_3$, 400 MHz)



54

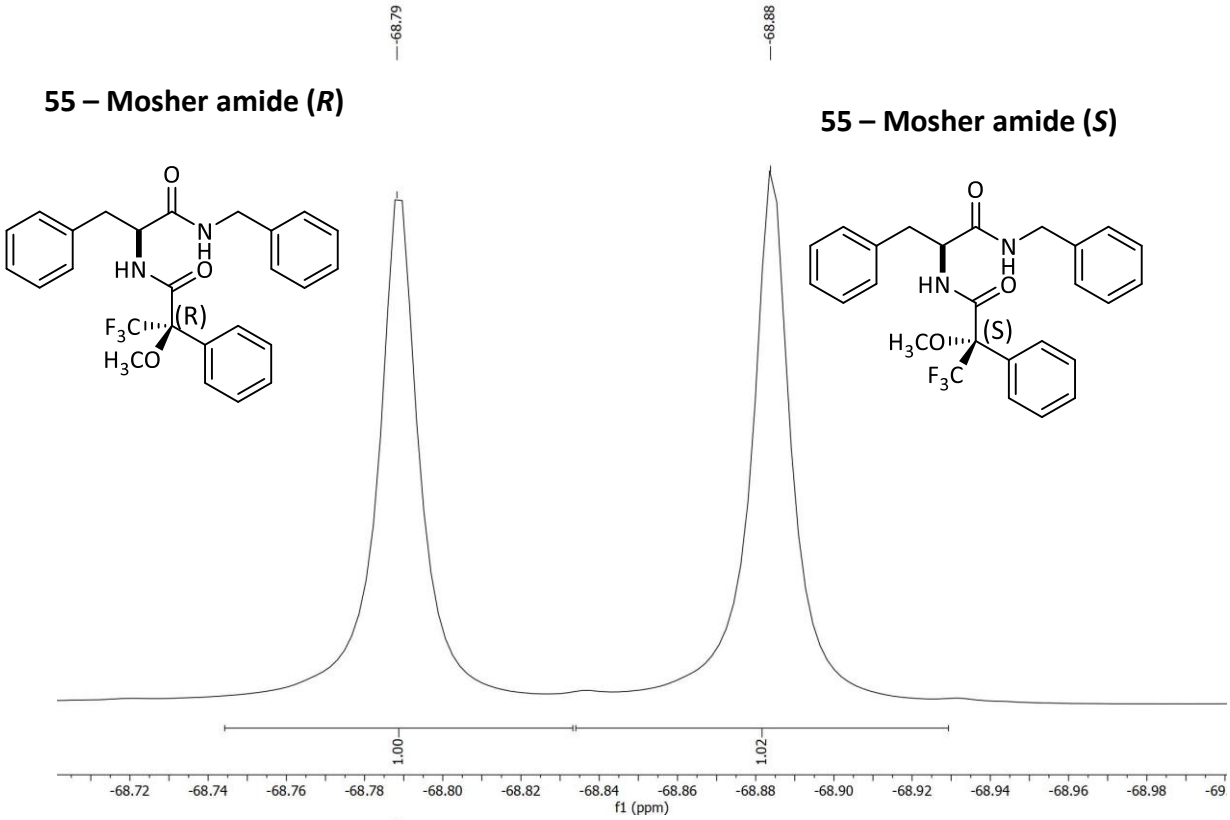
^{13}C NMR ($CDCl_3$, 100 MHz)

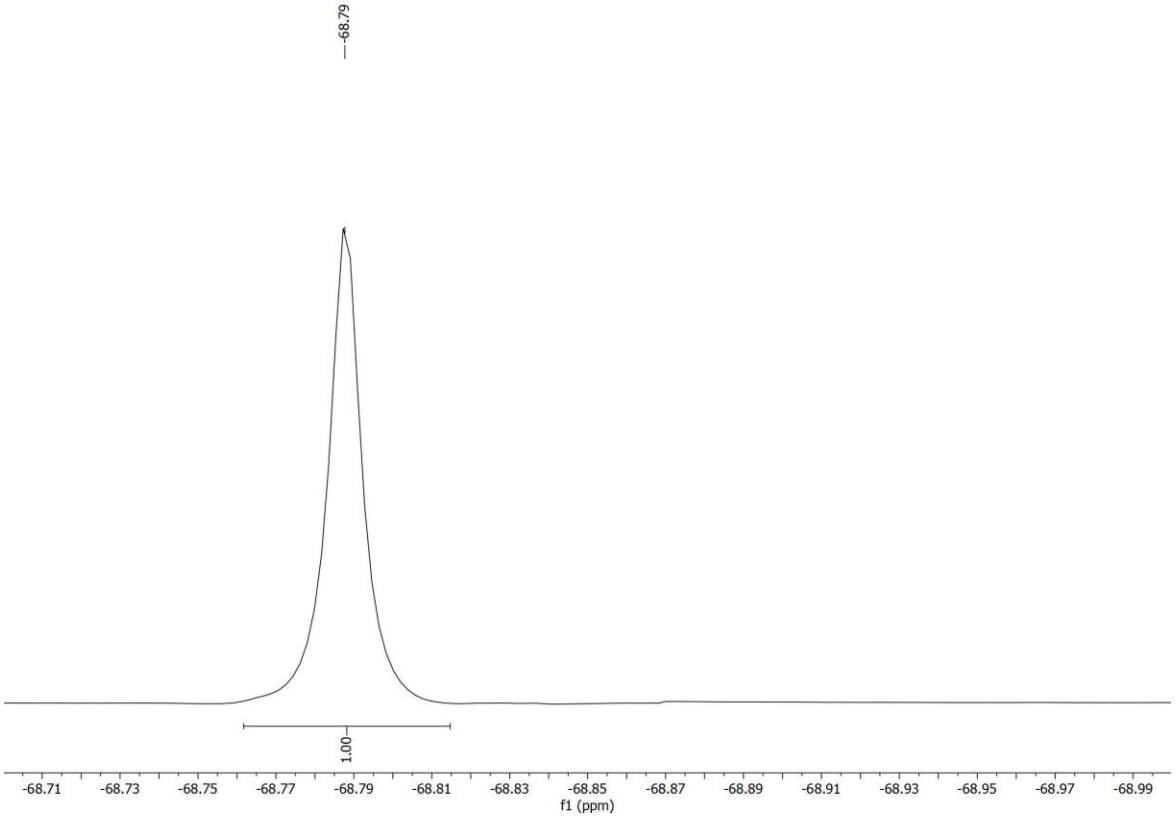

3.13
3.11
3.09
3.08
3.03
3.01
3.00
2.98
41 – chiral amide (S)
41 – chiral amide (R)
O
N
H
O
H
N
O
Me
3.15 3.14 3.13 3.12 3.11 3.10 3.09 3.08 3.07 3.06 3.05 3.04 3.03 3.02 3.01 3.00 2.99 2.98 2.97 2.96 2.95 2.94 2.93
f1 (ppm)
3.14
3.13
3.11
3.09
3.02
3.00
2.99
2.97
1.00
24.75
3.15 3.14 3.13 3.12 3.11 3.10 3.09 3.08 3.07 3.06 3.05 3.04 3.03 3.02 3.01 3.00 2.99 2.98 2.97 2.96 2.95 2.94 2.93
f1 (ppm)

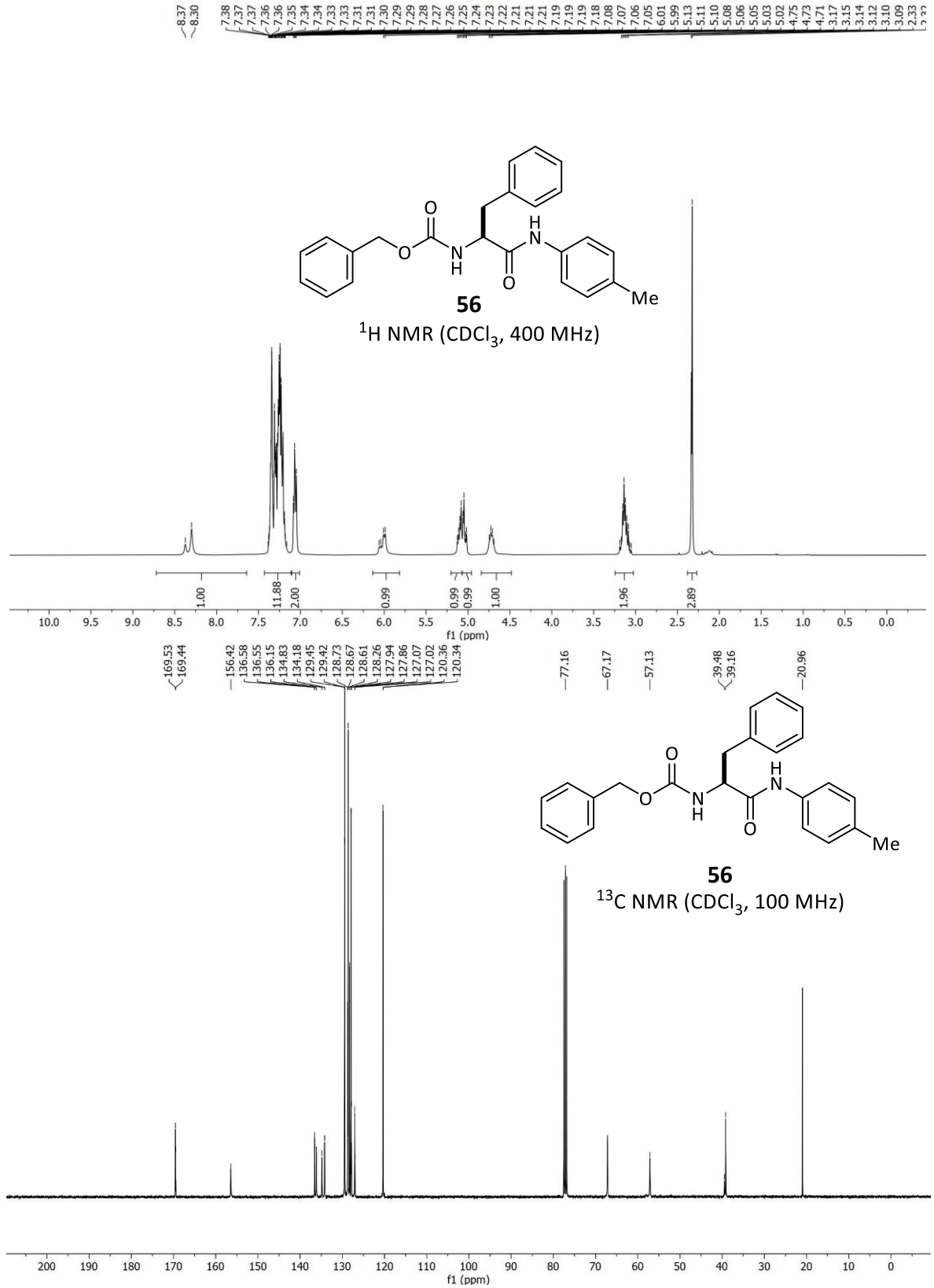

7.39
7.36
7.35
7.30
7.28
7.26
7.19
7.17
7.08
7.07
6.31
5.57
5.55
5.05
5.02
5.01
4.98
4.52
4.51
4.49
4.47
4.40
4.38
4.36
4.35
4.32
4.31
4.28
4.27
3.16
3.15
3.13
3.11
3.10
3.08
3.06
3.04
O
O
N
H
O
H
N
O
55
1H NMR (CDCl3, 400 MHz)
15.03
1.00
1.00
2.00
3.03
0.96
0.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
170.85
156.07
137.63
136.51
136.16
129.46
128.82
128.71
128.64
128.32
128.12
127.78
127.58
127.11
67.14
56.55
43.59
38.94
O
O
N
H
H
N
O
55
13C NMR (CDCl3, 100 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

55 – Mosher amide (*R*)

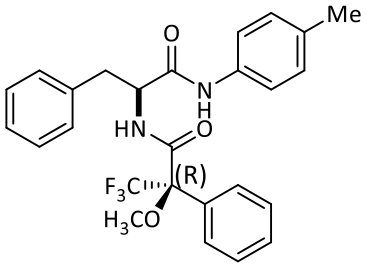
55 – Mosher amide (*S*)



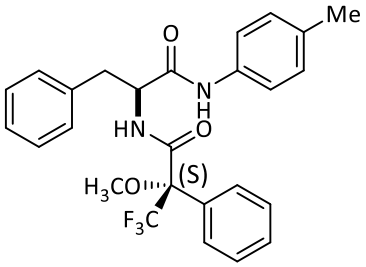


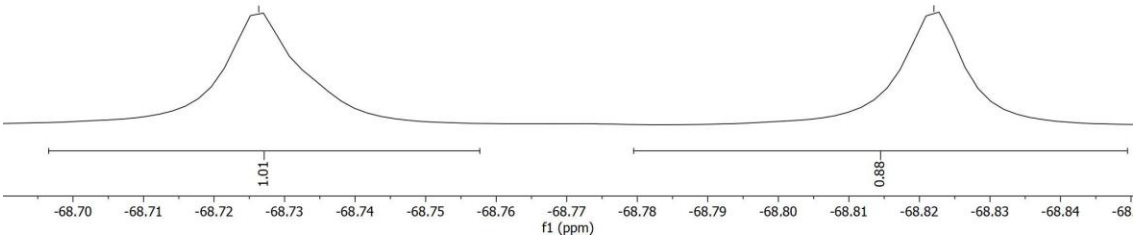

56
1H NMR (CDCl3, 400 MHz)
56
13C NMR (CDCl3, 100 MHz)

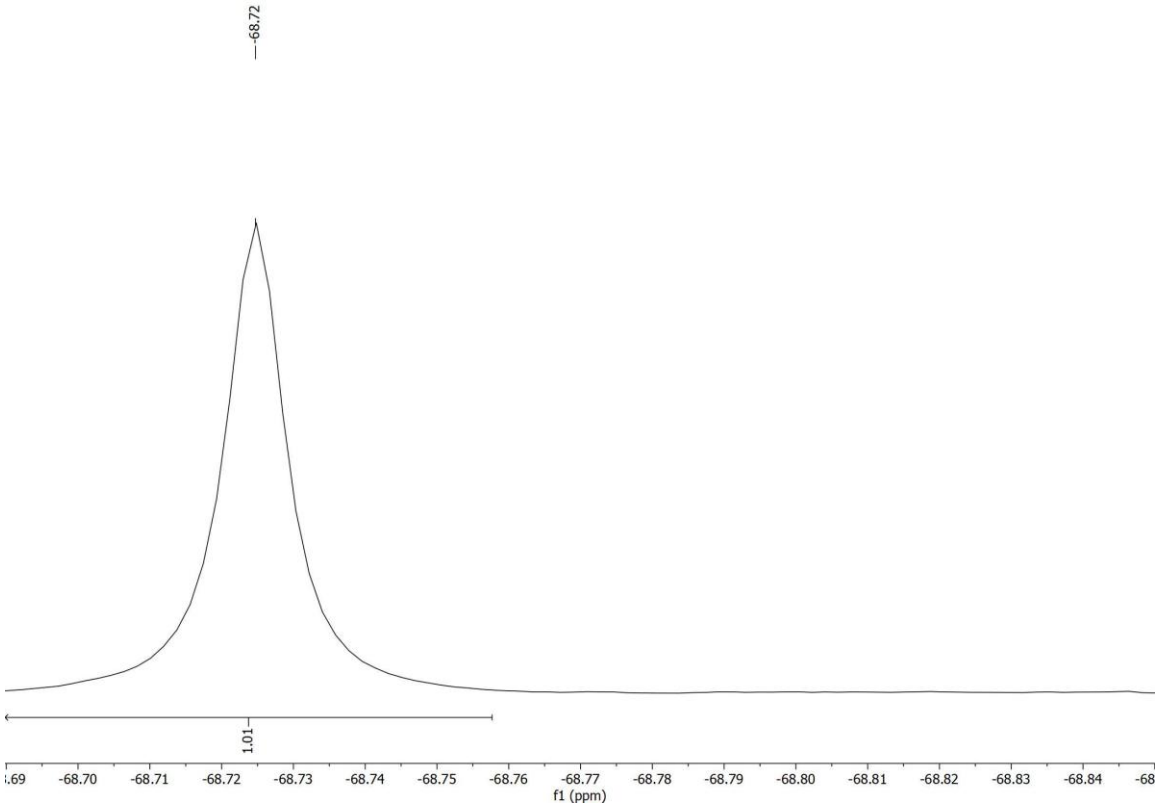
56 – Mosher amide (*R*)

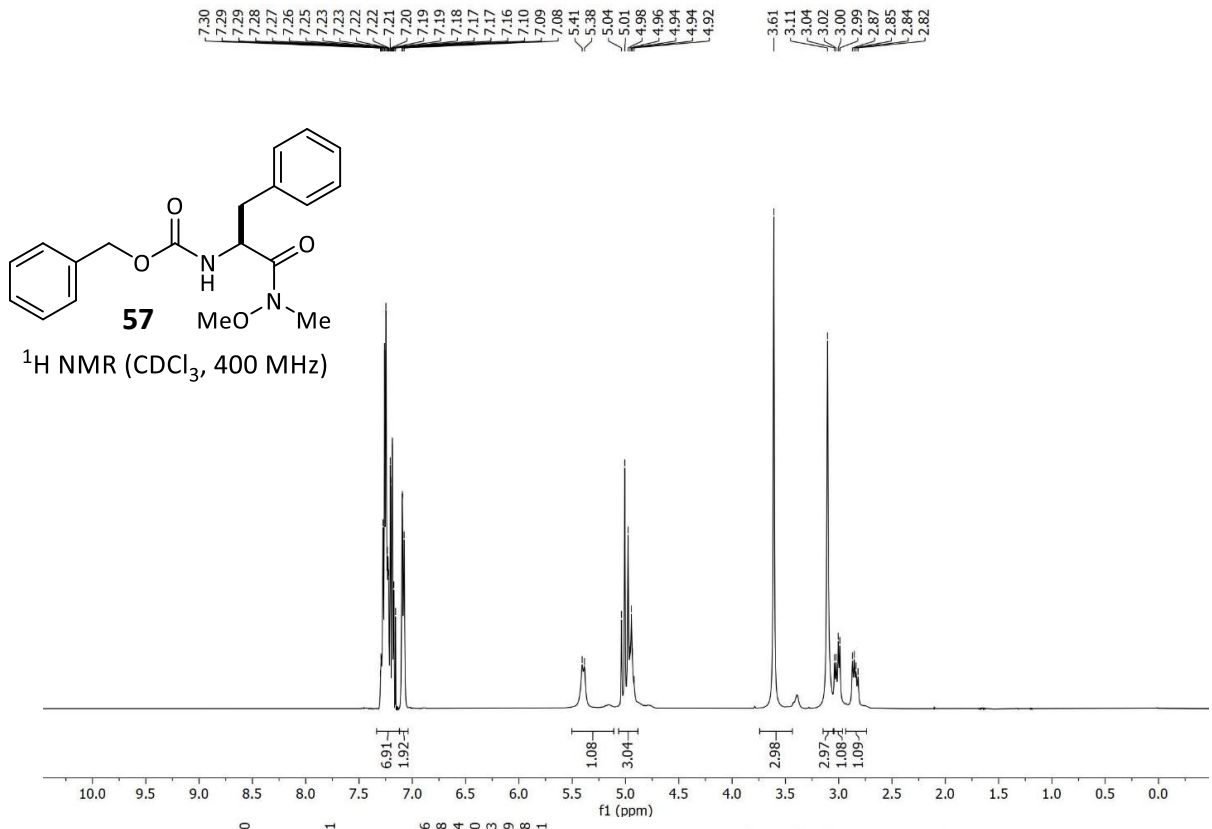


56 – Mosher amide (*S*)

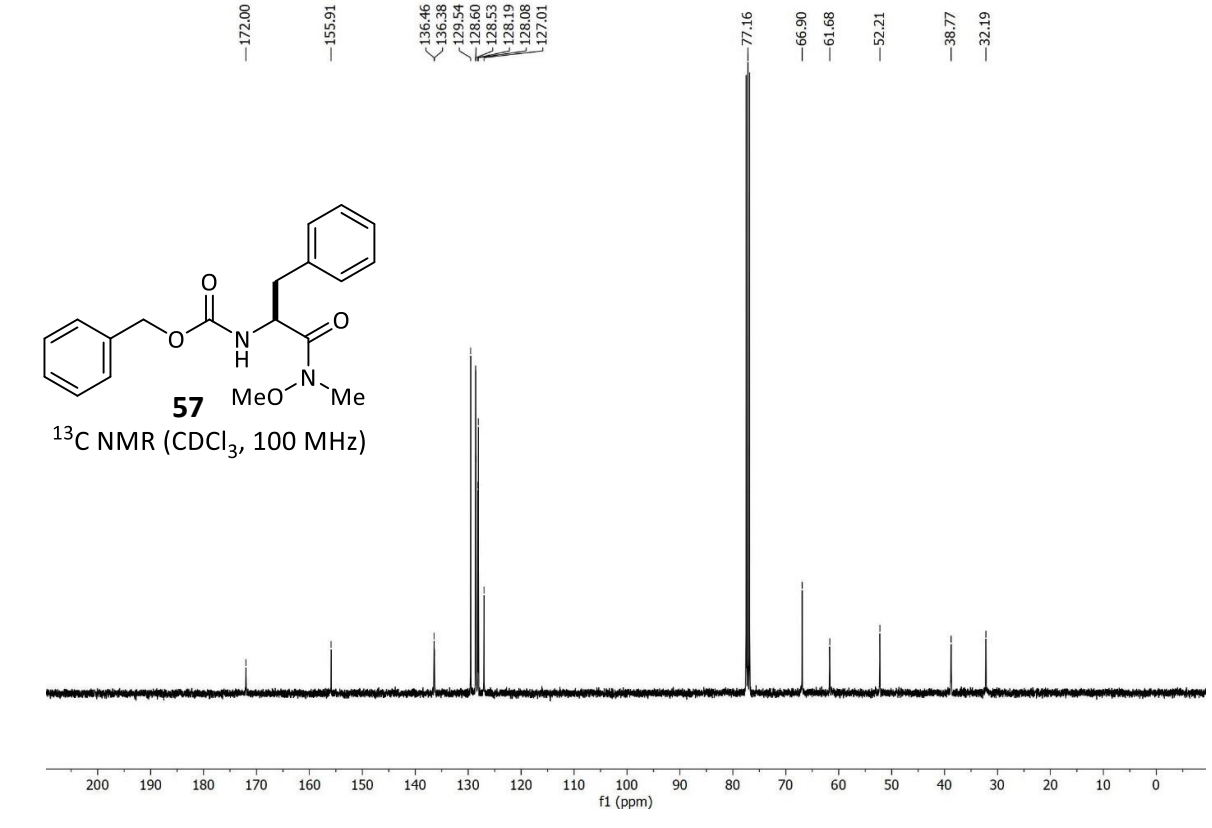




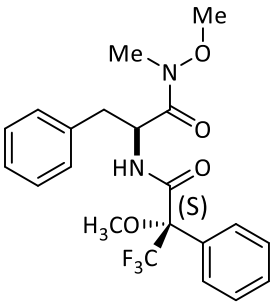




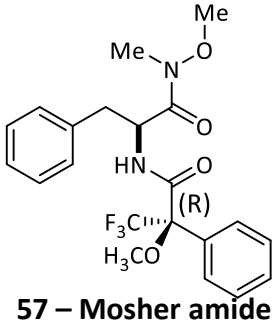
^{1}H NMR ($CDCl_3$, 400 MHz)



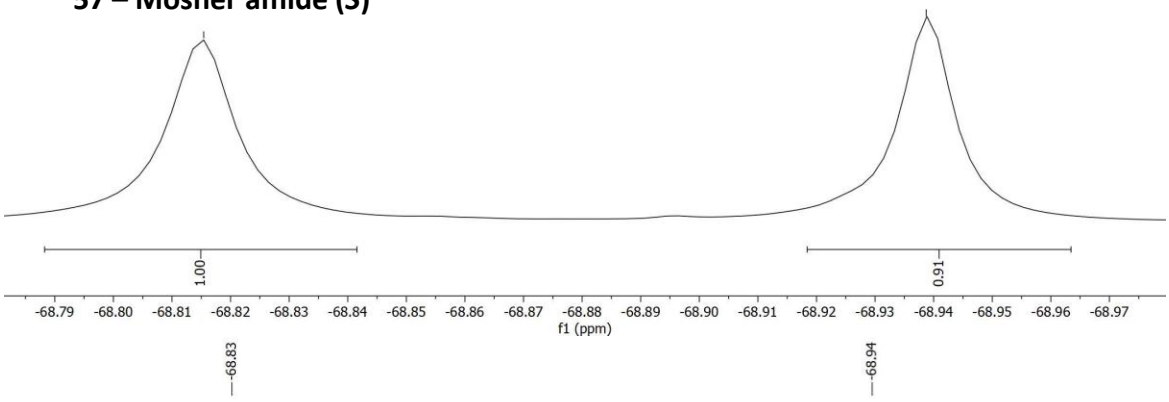
^{13}C NMR ($CDCl_3$, 100 MHz)

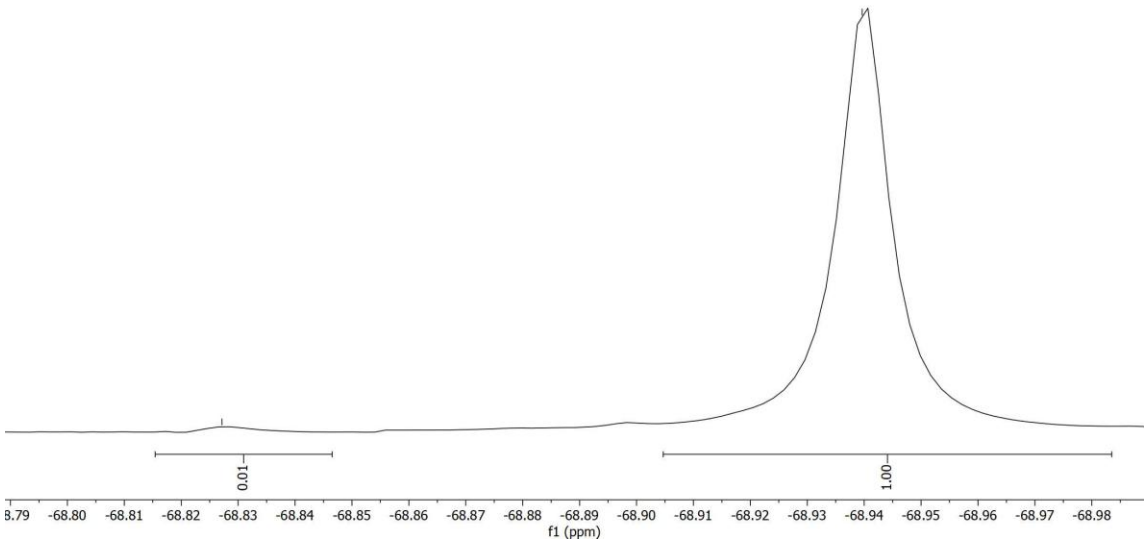


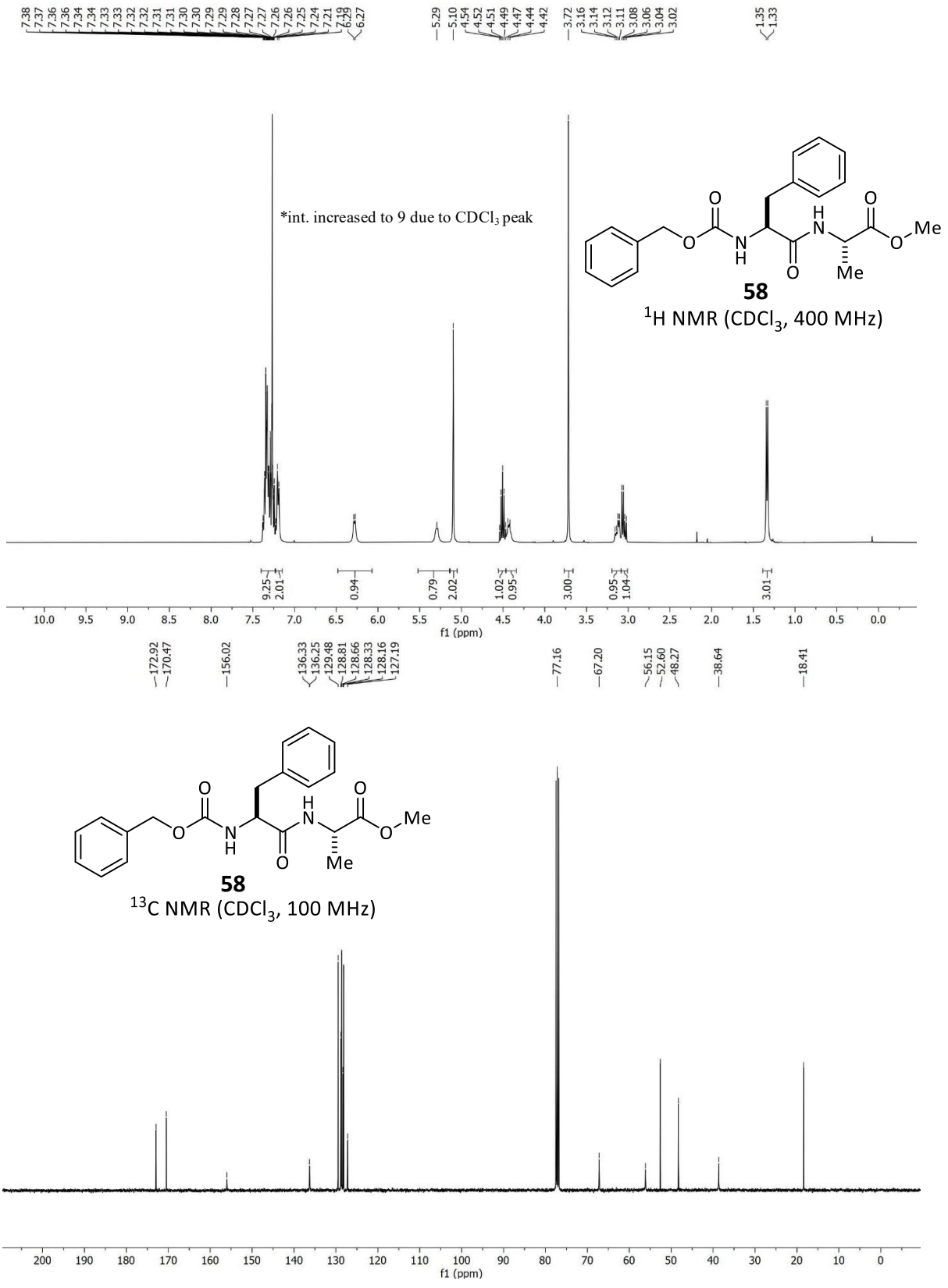
57 – Mosher amide (*S*)

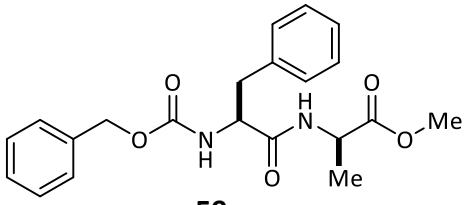


57 – Mosher amide (*R*)



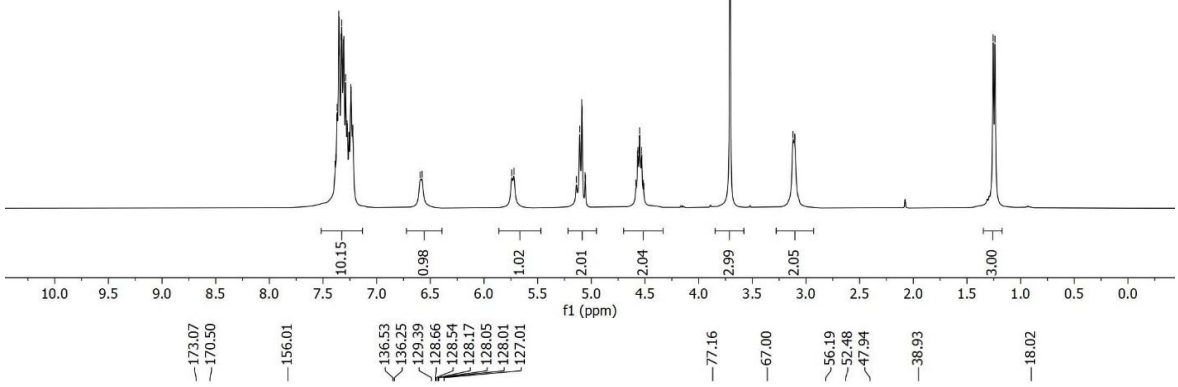


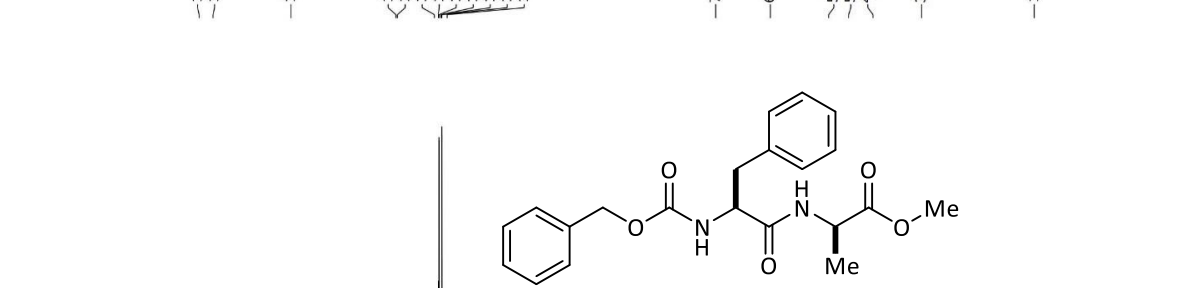

*int. increased to 9 due to CDCl3 peak
58
1H NMR (CDCl3, 400 MHz)
f1 (ppm)
58
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



59

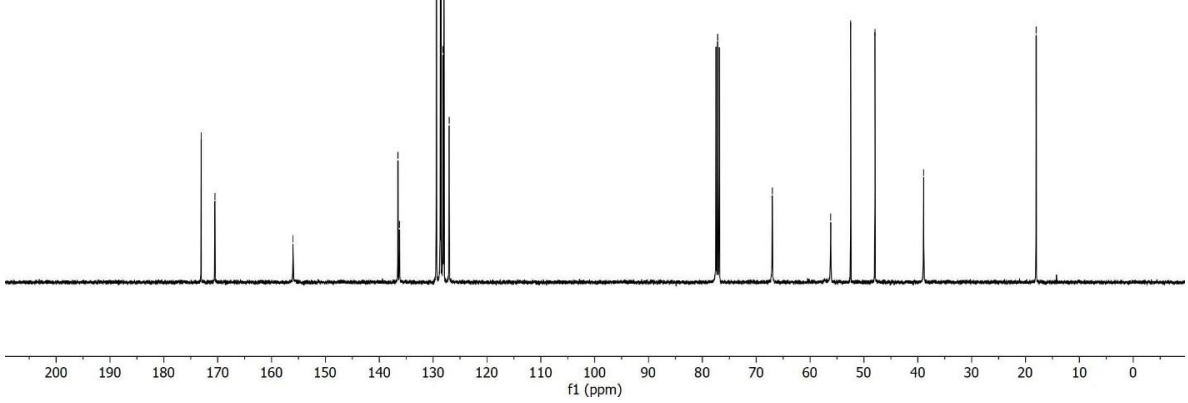
^{1}H NMR ($CDCl_3$, 400MHz)

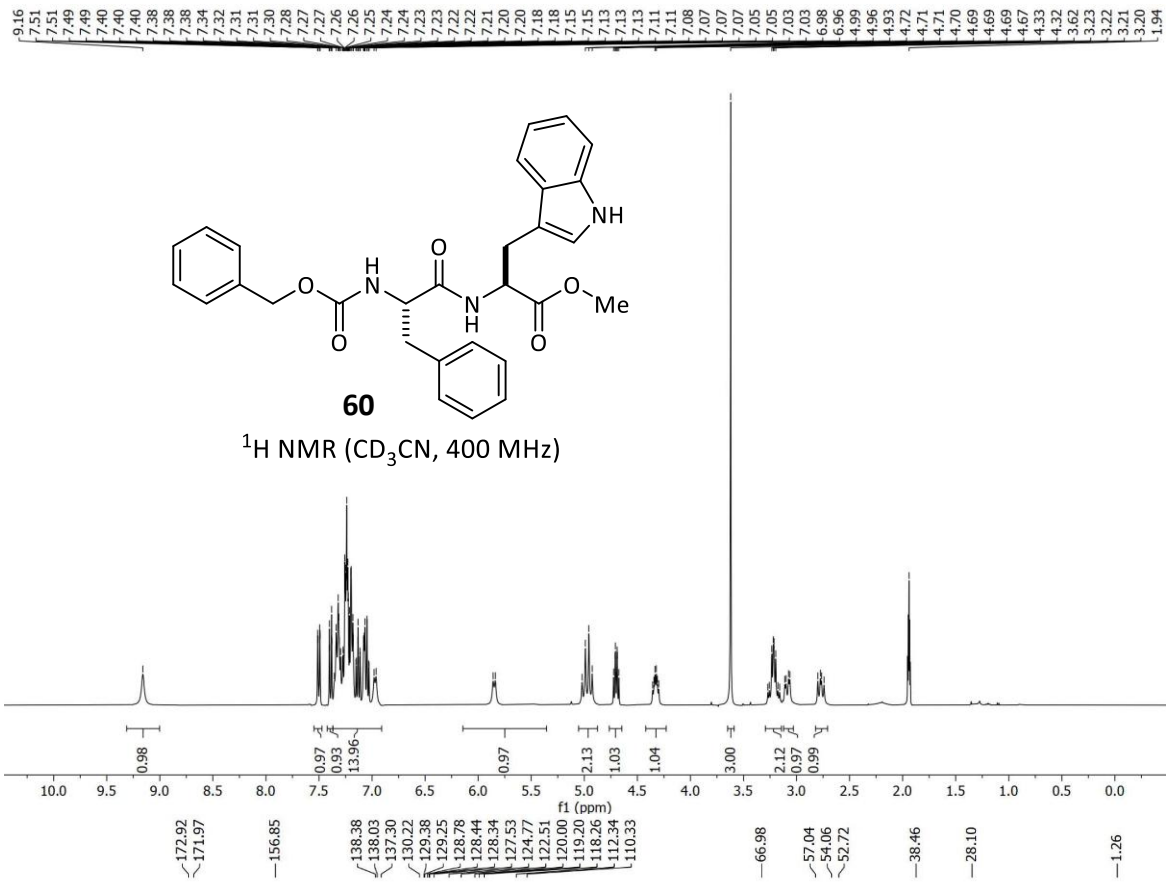




59

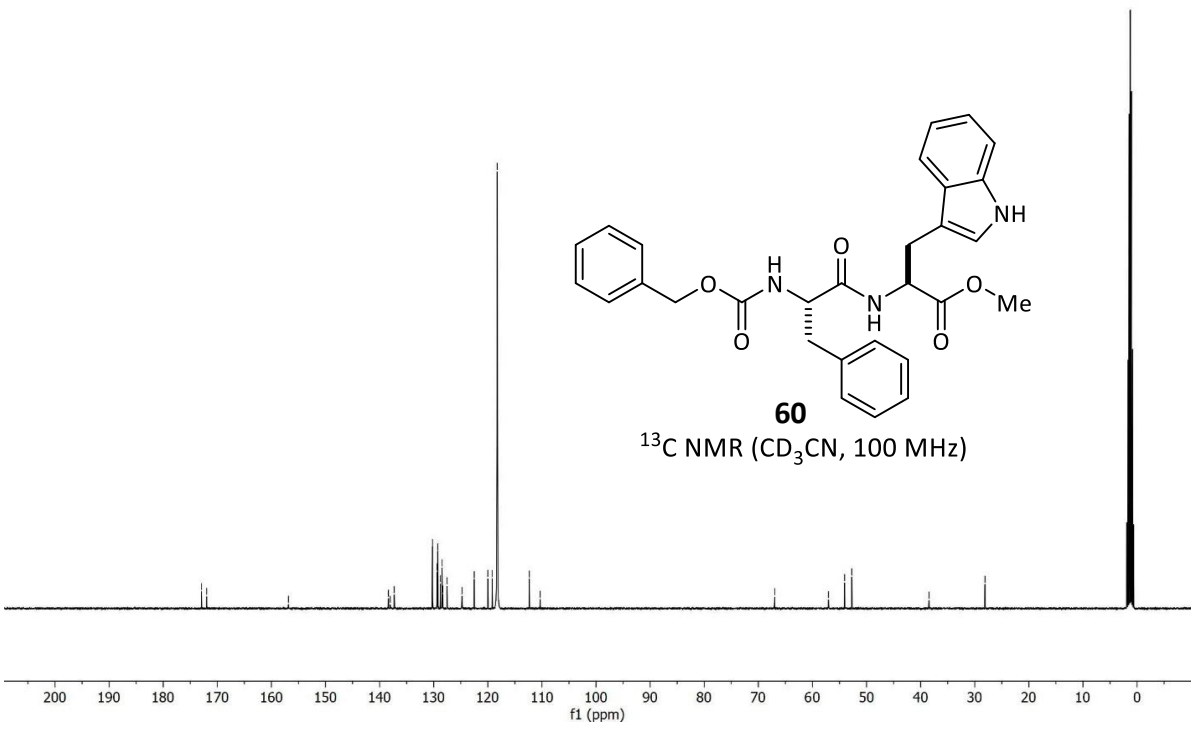
^{13}C NMR ($CDCl_3$, 100MHz)





60

^{1}H NMR (CD_3CN, 400 MHz)



60

^{13}C NMR (CD_3CN, 100 MHz)