

SUPPORTING INFORMATION

Base-Catalyzed Synthesis of Aryl Amides from Aryl Azides and Aldehydes

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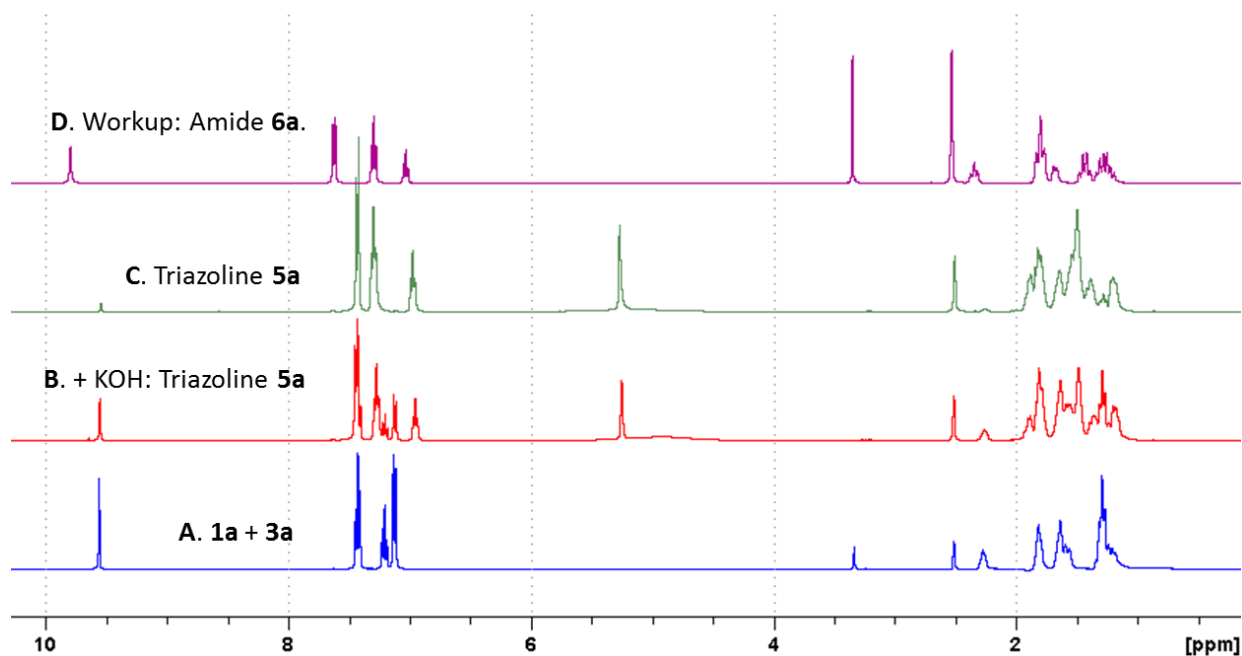
Table of Contents

General procedures	S1
Figure S1. ¹ H NMR spectra of model reaction.....	S2
Figure S2. Azide decomposition temperatures.....	S2
Table S1. Optimization of conditions for reaction of α -unsubstituted aldehyde with phenyl azide.	S3
Synthesis of azides.....	S3
Synthesis of products.....	S7
References	S16
Characterization Spectra.....	S18

General procedures

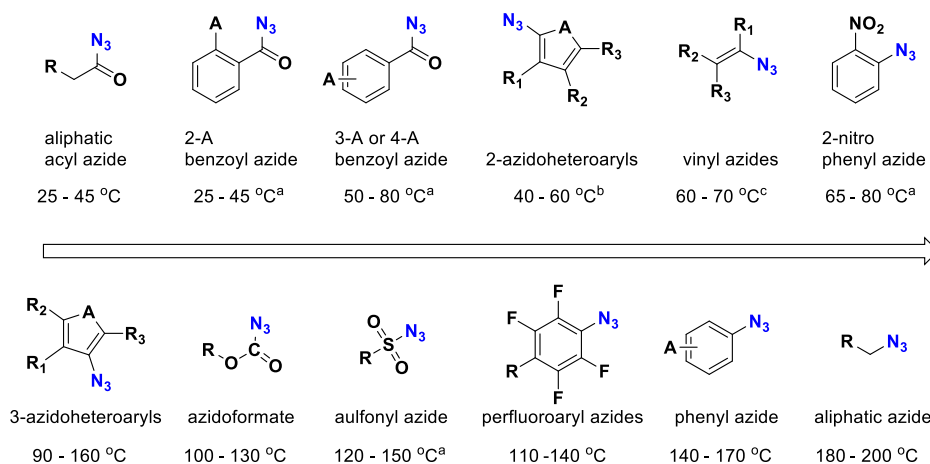
All reagents and solvents were used as received from Sigma Aldrich, Alfa Aesar, Fluka, and Merck. Thin-layer chromatography was conducted using TLC silica gel 60 F₂₅₄ (Merck Co.), visualized with ultraviolet light. ¹H-, ¹³C- and ¹⁹F-NMR data were recorded on a Bruker AscendTM 400 instrument or a Bruker DMX 500 instrument. Chemical shifts are reported as δ values (ppm) with CDCl₃ (¹H: δ = 7.26, ¹³C: δ = 77.16), DMSO-d₆ (¹H: δ = 2.50, ¹³C: δ = 39.52) or acetone-d₆ (¹H: δ = 2.05, ¹³C: δ = 29.84) as the internal standard. ¹⁹F NMR signals were referenced to hexafluorobenzene (δ = -161.75 in CDCl₃ or -162.65 in DMSO-d₆) unless noted otherwise. High resolution electrospray ionization (HRMS-ESI) mass spectrometry data were obtained from the Mass Spectrometry Lab at the University of Illinois at Urbana-Champaign. IR spectra were recorded on ReactIRTM IC10 (Mettler Toledo Co.) for liquid samples, or SPECTRUM 2000 (Perkin Elmer) for solid samples in the ATR mode.

Figure S1. ¹H NMR spectra of model reaction

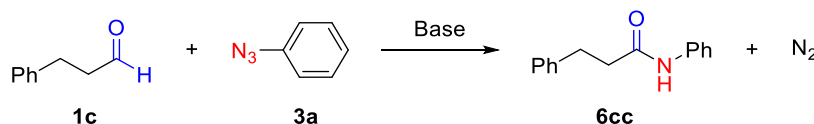


A). Azide and aldehyde in DMSO-d₆; B). Triazoline **5a** formed after addition of KOH; C). Triazoline **5a** formed exclusively (6 h); D). Aqueous acidic workup yielding amide **6a**.

Figure S2. Azide decomposition temperatures*



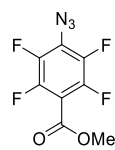
*The temperature range was determined where the rate constant for the decomposition of azide was 10^{-5} to 10^{-4} s⁻¹ ($t_{0.5} = 2 - 24$ h), following the suggestion in ref. 1. ^aRef. 1 and references therein; ^bref. 2; ^cref. 3; ^dref. 4.

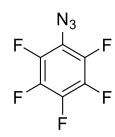
Table S1. Optimization of conditions for reaction of α -unsubstituted aldehyde with phenyl azide.^a

Entry	Base (eq.)	Solvent (v:v)	1c (eq.)	Temp. /Time.	Conv. ^b of 3a (%)	Yield ^c of 6cc (%)
1	t-BuOK (0.5)	THF/ <i>t</i> -BuOH (3:1)	3.0	20 °C/10 min	10	8
2	t-BuOK (1.1)	THF/ <i>t</i> -BuOH (3:1)	3.0	20 °C/6 min	70	48 (66 ^d)
3	t-BuOK (1.5)	THF/ <i>t</i> -BuOH (3:1)	4.0	20 °C/5 min	71	57 (86 ^d)
4	t-BuOK (2.0)	THF/ <i>t</i> -BuOH (3:1)	4.0	20 °C/5 min	> 95	68

^aProtocol: to a solution of **3a** (1 mmol) and base in THF/*t*-BuOH (1 mL/0.5 mL) under vigorous stirring, aldehyde **1c** in THF (0.5 mL) was added dropwise during 0.5 min. After the reaction was completed, the solution was quenched by aq. AcOH (1.5 M, 2 mL). ^bDetermined by ¹H NMR. ^cIsolated yield. ^dYield based on recycled azide.

Synthesis of azides

 **Methyl 4-azido-2,3,5,6-tetrafluorobenzoate.**⁵**General procedure A:** Methyl pentafluorobenzoate (9.5 g, 40 mmol) was dissolved in a 2:1 (v/v) mixture of acetone and water (90 mL). Sodium azide (3.40 g, 52 mmol, 1.3 equiv.) was added to the flask and the mixture was refluxed at 85 °C for 6 h. The mixture was subsequently cooled to r.t., diluted with water (150 mL), and extracted with diethyl ether (3 x 150 mL). The extract was dried over MgSO₄ and the solvent evaporated under reduced pressure, yielding the product as colorless crystals (9.5 g, 95%). Further purification was performed by flash column chromatography using EtOAc:hexanes (1:40) as the eluent. The compounds were stored in the dark to prevent extensive light exposure. ¹H NMR (400 MHz, CDCl₃): δ 3.97 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 160.0, 145.5 (dm, $J_{\text{C-F}} = 260.1$ Hz), 140.6 (dm, $J_{\text{C-F}} = 250.1$ Hz), 123.5, 107.8, 53.4; ¹⁹F NMR (376 MHz, CDCl₃): δ -138.62 (m, 2F), -150.91 (m, 2F).

 **1-Azido-2,3,4,5,6-pentafluorobenzene.**⁶**General procedure B:** Aniline (20 mmol) was dissolved in TFA (25 mL) and cooled to -2 °C using an immersion cooler. After ~15 min, NaNO₂ (12 mmol) was added in portions while stirring. After stirred at 0 °C for 1h, sodium azide (30 mmol) was added and the mixture was stirred at -2-0 °C for 1h. The mixture was diluted with

Et₂O (50 mL) and washed with water and then saturated NaHCO₃ and dried over MgSO₄. After removal of solvent, the residue was purified by flash column using pentane as eluent to give a pale brown liquid in 82% yield. ¹³C NMR (125 MHz, CDCl₃): δ 115.89 (dt, J = 4.63, 12.5 Hz), 138.14 (dm, J = 261.30 Hz), 141.02 (dm, J = 250.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃): -151.48 (m, 2F), -159.62 (m, 1F), -161.11 (m, 2F).



4-Azido-2,3,5,6-tetrafluorobenzonitrile. Synthesized according to general procedure A. The product was purified by column chromatography using hexanes:EtOAc mixture as eluent to give a light yellow liquid in 65% yield. ¹³C NMR (125 MHz, CDCl₃): δ 89.1 (t, 1C, CN, J = 17.5 Hz), 107.2 (t, 1C, J = 3.6 Hz), 126.7 (m, 1C), 140.3 (dm, 2C, J_{C-F} = 252.4 Hz), 147.5 (dm, 2C, J_{C-F} = 261.5 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -132.05 (m, 2F), -148.68 (m, 2F).



1-Azido-2,3,5,6-tetrafluoro-4-nitrobenzene. Synthesized according to general procedure A. The product was purified by column chromatography using hexanes:EtOAc (70:1) mixture as eluent to give a pale yellow liquid in 67% yield. ¹³C NMR (100 MHz, CDCl₃): δ 125.4 (t, 1C, J = 3.6 Hz), 126.6 (m, 1C), 140.7 (dm, 2C, J_{C-F} = 252.0 Hz), 141.4 (dm, 2C, J_{C-F} = 264.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -145.65 (m, 2F), -148.76 (m, 2F).

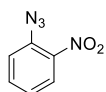


4-Azido-2,3,5,6-tetrafluoropyridine.⁷ The product was purified by distillation using a Büchi Kügelrohr apparatus to give a colorless liquid in 68% yield. ¹³C NMR (125 MHz, CDCl₃): δ 132.2 (m, C₍₄₎-N₃), 135.4 (dm, 2C, J_{C-F} = 261.8 Hz), 143.6 (dm, 2C, J_{C-F} = 244.1 Hz). ¹⁹F NMR (376 MHz, CDCl₃): δ -89.59 (m, 2F), -152.91 (m, 2F).

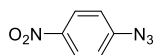
Phenyl Azide (6).⁸ **General procedure C:** To a 250 mL round-bottom flask, charged with aniline (0.02 mol) and water (40 mL), was added concentrated HCl (20.0 mL, 0.21 mol) under vigorous stirring while cooling using an immersion cooler. After stirring at -2 °C for 20-30 min, a freshly prepared, ice-cold solution of sodium nitrite (1.9 g, 0.03 mol) in water (10 mL) was added dropwise and the mixture was stirred for an additional 10-20 min. A freshly prepared solution of sodium azide (2.5 g, 0.03 mol) in water (20 mL) was then added dropwise to the reaction mixture while maintaining the temperature below 5 °C, after which the reaction mixture was stirred for an additional 20–30 min at 0 °C, followed by stirring at rt for 1 h. Afterwards, the solution was extracted with EtOAc (50 mL x 3), washed with saturated NaHCO₃ solution and brine (75 mL), and dried over Na₂SO₄. After removal of solvent, the crude mixture was purified by column chromatography using hexanes as eluent to give an orange oil in 63% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.04 (d, 2H, J=8.2 Hz), 7.15 (t, 1H, J=8.2 Hz), 7.36 (t, 2H, J=8.2 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 119.1 (2C), 124.9, 129.8 (2C), 140.0.

Benzyl azide.⁹ The product was purified by column chromatography using pentane to give a colorless oil in 90% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.35 (m, 5H, Ar), 4.35 (s, 2H, CH₂); ¹³C NMR (125 MHz, CDCl₃): δ 146.3, 135.6, 130.4, 127.6, 21.8.

Tosyl Azide.¹⁰ Colorless oil in 98% yield. ¹H NMR (500 MHz, CDCl₃): δ 2.48 (s, 3H, CH₃), 7.41 (d, 2H, J=8.4 Hz), 7.84 (d, 2H, J=8.4 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 21.8, 127.6 (2C), 130.3 (2C), 135.6, 146.4.



1-Azido-2-nitrobenzene.¹¹ A mixture of *o*-nitroaniline (2.8 g, 0.02 mol), water (80 ml) and concentrated hydrochloric acid (45 mL, 0.54 mmol) was placed in a 500 mL flask. The flask was cooled to 0°C and sodium nitrite (1.45 g, 0.021 mol) in water (10 mL) was added dropwise. After 30 min stirring at 0°C, sodium azide (13.0 g, 0.20 mol) in water (10 mL) was added dropwise, during which the product precipitated out as an off-white solid. After the nitrogen evolution had ceased, the product was collected on a Büchner funnel and washed twice with ice-cold water and then dried in air overnight to give the product as pale yellow needles (2.1 g, 88 %). ¹³C NMR (125 MHz, CDCl₃): δ 140.9, 134.8, 134.1, 126.1, 125.1, 120.8; ¹H NMR (400 MHz, CDCl₃): δ 7.92 (dd, 1H, J = 8.1, 1.5 Hz), 7.60 (dt, 1H, J = 7.9, 1.4 Hz), 7.31 (dd, 1H, J = 8.4, 1.0 Hz), 7.23 (dt, 1H, J = 7.7, 1.1 Hz).



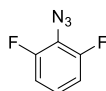
1-Azido-4-nitrobenzene.¹² (0.02 mol scale) Synthesized according to general procedure C. The product was purified by column chromatography using hexanes: DCM 1:1 mixture as eluent to give a yellow white solid in 48% yield (1.5 g). ¹³C NMR (125 MHz, CDCl₃): δ 146.9, 144.6, 125.6, 119.4; ¹H NMR (400 MHz, CDCl₃): δ 8.24 (dm, 2H, J = 8.9 Hz), 7.14 (dm, 2H, J = 9.0 Hz).



1-Azido-2-bromobenzene.¹² (0.02 mol scale) Synthesized according to general procedure B. The product was purified by column chromatography using hexanes as eluent to give a light yellow liquid in 90 % yield. ¹³C NMR (125 MHz, CDCl₃): δ 138.7, 134.0, 128.7, 126.1, 119.5, 114.0; ¹H NMR (400 MHz, CDCl₃): δ 7.55 (dd, 1H, J = 8.0, 1.1 Hz), 7.34 (app t, 1H, J = 7.6 Hz), 7.17 (dd, 1H, J = 8.0, 1.1 Hz), 7.01 (app t, 1H, J = 7.6 Hz).



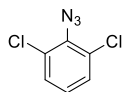
1-Azido-2-fluorobenzene.¹³ (0.02 mol scale) Synthesized according to general procedure B. The product was purified by column chromatography using hexanes as eluent to give a light yellow liquid in 68% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.10 (m, 4H, J = 8.0); ¹³C NMR (100 MHz, CDCl₃): δ 154.9 (d, J = 249 Hz), 127.9 (d, J = 11 Hz), 125.8 (d, J = 7 Hz), 124.9 (d, J = 4 Hz), 121.0, 116.7 (d, J = 19 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -126.25 (s).



1-azido-2,6-difluorobenzene.¹³ (0.02 mol scale) Synthesized according to general procedure B. The product was purified by column chromatography using hexanes as eluent to give white crystals in 33% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.02 (m, 1 H), 6.89 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ 155.8 (dd, J = 4, 250 Hz), 124.8 (t, J = 9 Hz), 117.5 (t, J = 14 Hz), 112.1 (dd, J = 5, 18 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -122.80 (s, 2F).



1-Azido-2-chlorobenzene.¹⁴ (0.02 mol scale) Synthesized according to general procedure C. The product was purified by column chromatography using pentane as eluent to give a light yellow liquid in 88% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.31 (d, 2H, J = 8.7 Hz), 6.96 (d, 2H, J = 8.7 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 138.7, 130.2, 129.8, 120.3.



1-Azido-2,6-dichlorobenzene.¹⁵ (0.02 mol scale) Synthesized according to general procedure B. The product was purified by column chromatography using pentane as eluent to give a light yellow oil in 67% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.30 (d, 2H, J = 8.2 Hz), 7.05 (t, 1H, J = 8.2 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 134.2, 129.6, 129.0, 126.4.



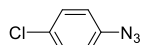
1-Azido-2-methylbenzene.¹⁶(0.02 mol scale) Synthesized according to general procedure C.

The product was purified by column chromatography using pentane as eluent to give a light yellow liquid in 81% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.26 (t, 1H, J = 7.4 Hz), 7.19 (d, 1H, J = 7.3 Hz), 7.15 (d, 1H, J = 7.3 Hz), 7.07 (t, 1H, J = 7.4 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 138.4, 131.1, 129.6, 127.1, 124.6, 117.9, 17.2.



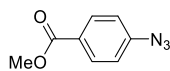
1-Azido-2,6-dimethylbenzene.¹⁵(0.02 mol scale) Synthesized according to general procedure

C. The product was purified by column chromatography using hexanes as eluent to give a light yellow liquid in 86% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.02 (m, 3H), 2.38 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 137.0, 132.2, 128.9, 125.7, 18.2.



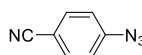
1-Azido-4-chlorobenzene.¹⁵(0.02 mol scale) Synthesized according to general procedure

C. The product was purified by column chromatography using pentane as eluent to give a light yellow liquid in 88% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.31 (app d, 2H, J = 8.6 Hz), 6.98 (app d, 2H, J = 8.6 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 138.7, 130.2, 129.9, 120.3.



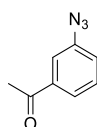
Methyl 4-azidobenzoate.¹⁷(0.02 mol scale) Synthesized according to general procedure

C. The product was purified by column chromatography using hexanes:EtOAc as eluent to give a pale solid in 62 % yield. ¹H NMR (400 MHz, CDCl₃): δ 8.03 (app d, 2H, J = 8.6 Hz), 7.05 (app d, 2H, J = 8.6 Hz), 3.90 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 166.3, 144.7, 131.4, 126.7, 118.9, 52.2.



4-Azidobenzonitrile.¹⁸(0.02 mol scale) Synthesized according to general procedure C. The

product was purified by column chromatography using hexanes:EtOAc (9:1) as eluent to give a pale yellow solid in 80% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.02 (m, 3H), 2.38 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 137.0, 132.2, 128.9, 125.7, 18.2.



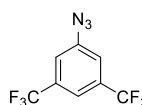
3-Azidoacetophenone.¹⁹(0.02 mol scale) Synthesized according to general procedure C. The

product was purified by column chromatography using hexanes:EtOAc 9:1 as eluent to give an orange liquid in 70 % yield. ¹H NMR (400 MHz, CDCl₃): δ 7.70 (app d, 1H, J = 7.7 Hz), 7.60 (app t, 1H, J = 1.9 Hz), 7.44 (t, 1H, J = 7.7 Hz), 7.23 (app dd, 1H, J = 7.7, 1.9 Hz), 2.62 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 197.1, 140.9, 138.7, 130.0, 124.9, 123.5, 118.5, 26.7.



3-Azidoacetophenone.¹⁴(0.02 mol scale) Synthesized according to general procedure C.

Extracted with diethyl ether instead of EtOAc. The product was purified by column chromatography using pentane as eluent to give a light yellow oil in 80% yield. ¹H NMR (400 MHz, CDCl₃): δ 7.26 (t, 1H, J = 8.2 Hz), 6.72 (dd, 1H, J = 8.2, 2.0 Hz), 6.65 (dd, 1H, J = 8.2, 2.0 Hz), 6.56 (t, 1H, J = 2.0 Hz), 3.81 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 160.8, 141.3, 130.4, 111.3, 110.7, 104.9, 55.4.



1-Azido-3,5-bis(trifluoromethyl)benzene.²⁰(0.02 mol scale) Synthesized according to general procedure C. The product was purified by column chromatography using pentane

as eluent to give a pale yellow liquid in 65% yield. ^1H NMR (400 MHz, CDCl_3): δ 7.65 (s, 1H), 7.45 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 142.4 (1C), 133.1 (2C, q, $J = 34$ Hz), 122.8 (2 CF_3 , q, $J = 271$ Hz), 119.1 (2C, m), 118.3 (C, m); ^{19}F NMR (376 MHz, CDCl_3): δ -63.17 (m, 6F).



3-Azidopyridine.²¹ (0.02 mol scale) Synthesized according to **general procedure C**. The product was purified by column chromatography using hexanes:EtOAc 1:4 as eluent to give an amber liquid in 69% yield. ^1H NMR (400 MHz, CDCl_3): δ 8.35(app d, 1H, $J = 4.5$ Hz), 8.31(d, 1H, $J = 2.1$ Hz), 7.26(dm, 1H, $J = 8.1$ Hz), 7.22 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 146.0, 141.3, 137.1, 125.9, 124.1.



3-Azidothiophene.²² Synthesized using a modified version of a reported procedure.²³ To a solution of 3-bromothiophene (0.03 mmol) in anhydrous ether (80 mL) at -70°C under nitrogen, was added *n*-butyl lithium (24 mL, 1.6 M solution in hexane) while stirring. The mixture was stirred for 30 min at -70°C , to which was added *p*-toluenesulfonyl azide (0.07 mol) dropwise. The reaction mixture was stirred for 3 h at -70°C , after which the temperature was allowed to increase to -40°C over 1 h. A solution of ethylenediaminetetraacetic acid disodium salt (11.4 g, 0.05 mol) in water (100 mL), was added, while maintaining the temperature below 0°C . After stirring for 15 min at 0°C , the reaction mixture was allowed to reach rt, and stirred for another 12 h. The mixture was extracted with ether and washed with water, dried over MgSO_4 , filtered, and evaporated. The red-brown residue was purified by column chromatography using pentane as eluent to give an amber liquid in 22% yield. ^1H NMR (400 MHz, CDCl_3): δ 7.30 (dd, 1H, $J = 3.2, 5.2$ Hz), 6.82 (dd, 1H, $J = 5.2, 1.5$ Hz), 6.80 (dd, 1H, $J = 3.2, 1.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 137.7, 126.7, 120.6, 109.8.

Synthesis of products

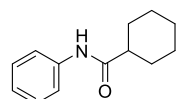
General procedure A (Table 1, Figure 1). In a microwave vial (2 mL) charged with azide (1.0 mmol) and aldehyde (1.1 mmol) in DMSO (2.0 mL), was added base (0.1 mmol) and the reaction mixture was stirred at elevated temperature under microwave irradiation for 0.5-2 h. The crude reaction mixture was added to aqueous NH_4Cl solution (20 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic layers were washed with water and then dried over Na_2SO_4 , filtered and concentrated. The products were obtained by column chromatography (silica gel, hexanes/EtOAc).

General procedure B (Figure 1). In a flask (10 mL) charged with azide (1.0 mmol) and aldehyde (1.2 – 1.5 mmol) in DMSO (2.0 mL), was added base (0.1 mmol) and the reaction mixture was stirred at rt. When NMR analysis ($\text{DMSO}-d_6$) indicated complete conversion, an aq. AcOH solution (2 mL, 1.5 M) was added dropwise and the reaction mixture was stirred for 1 h. The resulting solution was extracted with EtOAc (3 x 30 mL), and the combined organic layers were washed with 0.5 M aq. HCl (10 mL), dried over Na_2SO_4 , filtered and concentrated. The products were obtained by column chromatography (silica gel, hexanes/EtOAc).

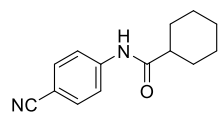
General procedure C (Table 2 and S1). In a vial (10 mL) charged with azide (1.0 mmol) in THF (1 mL) and *t*-BuOH (0.5 mL), *t*-BuOK (1.2 – 2.0 mmol) was added and the reaction mixture was stirred vigorously at room temperature. Afterwards, aldehyde (4 mmol) in THF (0.5 mL) was added dropwise within 0.5 - 1 minute. After the reaction time (1-5 minutes), the mixture was quickly quenched by 2 mL

aq. AcOH (1.5 M) and stirred for another 1 hours. The mixture was then extracted with ethyl acetate (3 x 30 mL). The combined organic layers were then dried over Na₂SO₄, filtered and concentrated. Amides were obtained by column chromatography (silica gel, hexanes/EtOAc).

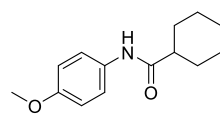
General procedure D (Figure 2). In a flask (5 mL) charged with azide (1.0 mmol) and aldehyde (1.1 mmol) in DMSO (2.0 mL), was added base (0.1 mmol) and the reaction mixture was stirred at room temperature while the flask remained open. After complete conversion, as indicated by ¹⁹F-NMR spectroscopy, the reaction mixture was added to an aq. NH₄Cl solution (20 mL), and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with water and concentrated. The products were obtained by column chromatography (silica gel, hexanes/EtOAc).



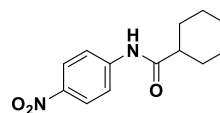
N-Phenylcyclohexanecarboxamide (**6a**).²⁴ White solid. *R*_f = 0.28 (hexanes/EtOAc = 5:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.24 – 1.35 (m, 3H), 1.54 (quartet, 2H, CH, *J* = 12.3 Hz), 1.70 (m, 1H, CH), 1.83 (m, 2H), 1.96 (d, 2H, CH, *J* = 13.2 Hz), 2.23 (tt, 1H, CH, *J* = 11.6, 3.6 Hz), 7.09 (t, 1H, *J* = 7.5 Hz), 7.10 (br. s, 1H, NH), 7.31 (t, 2H, *J* = 7.5 Hz), 7.52 (d, 2H, *J* = 7.5 Hz); ¹³C NMR (100 MHz, CDCl₃): δ_C 25.8 (3C), 29.7 (2C), 46.7, 119.8, 119.9, 124.2, 129.1, 138.2, 174.4.



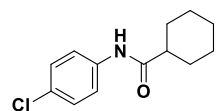
N-(4-Cyanophenyl)cyclohexanecarboxamide (**6b**). White powder. *R*_f = 0.20 (hexanes/EtOAc = 4:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.21 – 1.39 (m, 3H), 1.52 (quartet, 2H, CH, *J* = 12.8 Hz), 1.72 (m, 1H, CH), 1.84 (m, 2H, CH₂), 1.96 (d, 2H, CH, *J* = 13.0 Hz), 2.26 (tt, 1H, CH, *J* = 3.5, 11.8 Hz), 7.34 (br. s, 1H, NH), 7.60 (d, 1H, *J* = 8.6 Hz), 7.67 (d, 1H, *J* = 8.6 Hz); ¹³C NMR (100 MHz, CDCl₃): δ_C 25.7 (3C), 29.7 (2C), 46.8, 107.1, 119.0, 119.6, 133.4, 142.3, 174.8. ESI-HRMS: Calcd. for C₁₄H₁₇N₂O [M+H]⁺: 229.1335, found 229.1340. IR (ATR), see attached spectrum.



N-(4-Methoxyphenyl)cyclohexanecarboxamide (**6c**).³⁵ White solid. *R*_f = 0.21 (hexanes/EtOAc = 4:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.23 – 1.33 (m, 3H), 1.53 (quartet, 2H, CH, *J* = 12.8 Hz), 1.72 (m, 1H, CH), 1.84 (m, 2H), 1.95 (d, 2H, CH, *J* = 13.2 Hz), 2.20 (tt, 1H, CH, *J* = 3.4, 12.0 Hz), 3.78 (s, 3H, OCH₃), 6.85 (d, 2H, *J* = 8.2 Hz), 7.06 (br. s, 1H, NH), 7.42 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ_C 25.9 (3C), 29.9 (2C), 46.6, 55.6, 114.3, 121.8, 131.3, 156.4, 174.2.

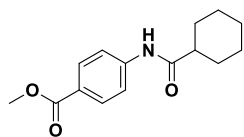


N-(4-Nitrophenyl)cyclohexanecarboxamide (**6d**).³⁰ Yellow powder. *R*_f = 0.36 (hexanes/EtOAc = 3:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.31 (m, 3H), 1.54 (quartet, 2H, CH, *J* = 12.8 Hz), 1.71 (m, 1H, CH), 1.85 (m, 2H, CH₂), 1.98 (d, 2H, CH, *J* = 13.2 Hz), 2.29 (tt, 1H, CH, *J* = 3.4, 12.0 Hz), 7.54 (br. s, 1H, NH), 7.72 (d, 1H, *J* = 9.0 Hz), 8.20 (d, 1H, *J* = 9.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ_C 25.7 (3C), 29.7 (2C), 46.8, 119.1, 125.2, 143.5, 144.1, 174.9.

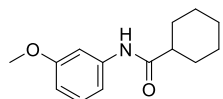


N-(4-Chlorophenyl)cyclohexanecarboxamide (**6e**).³¹ White powder. *R*_f = 0.43 (hexanes/EtOAc = 9:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.22 – 1.35 (m, 3H), 1.52

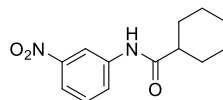
(quartet, 2H, CH, J = 12.8 Hz), 1.70 (m, 1H, CH), 1.83 (m, 2H, CH₂), 1.94 (d, 2H, CH, J = 13.0 Hz), 2.22 (tt, 1H, CH, J = 3.5, 11.6 Hz), 7.26 (br. s, 1H, NH), 7.26 (d, 1H, J = 9.0 Hz), 7.47 (d, 1H, J = 9.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 25.8 (3C), 29.8 (2C), 46.6, 121.2, 129.1, 129.2, 136.8, 174.5.



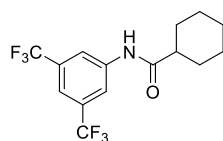
Methyl 4-(cyclohexanecarboxamido)benzoate(**6f**).³² White powder. R_f = 0.20 (hexanes/EtOAc= 4:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.22 – 1.33 (m, 3H), 1.54 (quartet, 2H, CH, J = 12.8 Hz), 1.71 (m, 1H, CH), 1.83 (m, 2H, CH₂), 1.96 (d, 2H, CH, J = 13.0 Hz), 2.25 (tt, 1H, CH, J = 3.5, 11.6 Hz), 3.89 (s, 3H, OCH₃), 7.38 (br. s, 1H, NH), 7.61 (d, 1H, J = 8.7 Hz), 7.99 (d, 1H, J = 8.7 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 25.8 (3C), 29.7 (2C), 46.8, 52.1, 118.9, 125.6, 131.0, 142.4, 166.8, 174.7.



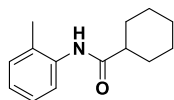
N-(3-Methoxyphenyl)cyclohexanecarboxamide(**6g**). White solid. R_f = 0.47 (hexanes/EtOAc= 3:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.22 – 1.40 (m, 3H), 1.54 (app quartet, 2H, CH, J = 12.8 Hz), 1.71 (m, 1H, CH), 1.84 (m, 2H), 1.96 (app d, 2H, CH, J = 13.2 Hz), 2.22 (tt, 1H, CH, J = 3.4, 11.8 Hz), 3.80 (s, 3H, OCH₃), 6.65 (app d, 1H, J = 8.3 Hz), 6.94 (app d, 1H, J = 7.8 Hz), 7.14 (br. s, 1H, NH), 7.19 (t, 1H, J = 8.1 Hz), 7.37 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 25.8 (3C), 29.8 (2C), 46.7, 55.4, 105.4, 110.2, 111.9, 129.7, 139.6, 160.2, 174.7; ESI-HRMS: Calcd. for C₁₄H₂₀NO₂ [M+H]⁺: 234.1494, found 234.1502. IR(ATR), see attached spectrum.



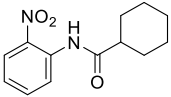
N-(3-Nitrophenyl)cyclohexanecarboxamide(**6h**).³³ Yellow powder. R_f = 0.50 (hexanes/EtOAc= 4:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.21 – 1.40 (m, 3H), 1.55 (quartet, 2H, CH, J = 12.8 Hz), 1.72 (m, 1H, CH), 1.85 (dm, 2H, CH, J = 12.8 Hz), 1.97 (d, 2H, CH, J = 13.2 Hz), 2.29 (tt, 1H, CH, J = 3.4, 11.8 Hz), 7.47 (t, 1H, J = 8.1 Hz), 7.54 (br. s, 1H, NH), 7.93 (dd, 1H, J = 8.2, 1.5 Hz), 7.96 (dd, 1H, J = 8.2, 1.5 Hz), 8.38 (t, 1H, J = 2.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 25.7 (3C), 29.7 (2C), 46.6, 114.6, 118.8, 125.6, 130.0, 139.4, 148.7, 174.9.

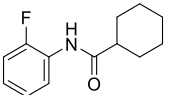


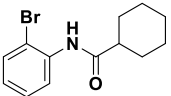
N-(3,5-Bis(trifluoromethyl)phenyl)cyclohexanecarboxamide(**6i**).³⁴ White solid. R_f = 0.57 (hexanes/EtOAc= 4:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.21 – 1.40 (m, 3H), 1.55 (quartet, 2H, CH, J = 12.8 Hz), 1.72 (m, 1H, CH), 1.86 (m, 2H), 1.96 (d, 2H, CH, J = 13.2 Hz), 2.27 (tt, 1H, CH, J = 3.4, 11.8 Hz), 7.49 (br. s, 1H, NH), 7.58 (s, 1H), 8.05 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 25.7 (3C), 29.7 (2C), 46.6, 117.5 (m), 119.5 (m), 123.2 (quartet, 1C, J_{CF} = 272 Hz, CF₃), 132.5 (quartet, 1C, J_{CF} = 33 Hz), 139.6, 174.9; ¹⁹F NMR (376 MHz, CDCl₃): δ -63.07 (m, 6F); ESI-HRMS: Calcd. for C₁₅H₁₆F₆NO [M+H]⁺: 340.1136, found 340.1134. IR(ATR), see attached spectrum.

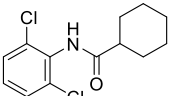


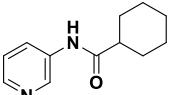
N-(o-Tolyl)cyclohexanecarboxamide(**6j**).²⁷ White powder. R_f = 0.50 (hexanes/EtOAc= 3:1). ¹H NMR (400 MHz, CDCl₃): δ_H 1.22 – 1.34 (m, 3H), 1.55 (quartet, 2H, CH, J = 12.8 Hz), 1.70 (m, 1H, CH), 1.82 (m, 2H), 1.99 (d, 2H, CH, J = 13.2 Hz), 2.22 – 2.30 (m, 4H, CH & CH₃), 6.95 (br. s, 1H, NH), 7.04 (t, 1H, J = 7.5 Hz), 7.14 – 7.20 (m, 2H), 7.82 (d, 1H, J = 7.9 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 17.9, 25.9, 30.0, 46.6, 123.2, 125.1, 126.9, 128.9, 130.5, 135.9, 174.3.

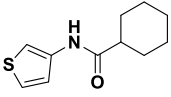
 *N*-(2-Nitrophenyl)cyclohexanecarboxamide (**6k**).²⁵ Yellow powder. $R_f = 0.42$ (hexanes/EtOAc= 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.25 – 1.42 (m, 3H), 1.55 (quartet, 2H, CH, $J = 12.8$ Hz), 1.72 (m, 1H), 1.85 (dm, 2H, CH, $J = 12.8$ Hz), 2.03 (d, 2H, CH, $J = 13.2$ Hz), 2.36 (tt, 1H, CH, $J = 3.4, 11.6$ Hz), 7.16 (t, 1H, $J = 7.7$ Hz), 7.63 (t, 1H, $J = 7.7$ Hz), 8.21 (dd, 1H, $J = 8.4, 1.3$ Hz), 8.82 (d, 1H, $J = 8.4$ Hz), 10.44 (br. s, 1H, NH); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.7, 25.8, 29.7, 47.3, 122.4, 123.1, 125.9, 135.4, 136.1, 136.4, 175.4$.

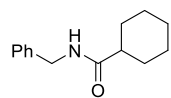
 *N*-(2-Fluorophenyl)cyclohexanecarboxamide (**6l**).²⁸ White powder. $R_f = 0.28$ (hexanes/EtOAc= 9:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.24 – 1.36 (m, 3H), 1.55 (quartet, 2H, CH, $J = 12.8$ Hz), 1.72 (m, 1H, CH), 1.84 (dm, 2H, CH, $J = 12.8$ Hz), 1.97 (d, 2H, CH, $J = 13.2$ Hz), 2.28 (tt, 1H, CH, $J = 3.5, 12.0$ Hz), 7.05 (m, 3H), 7.38 (br. s, 1H, NH), 8.35 (t, 1H, $J = 9.5$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.76, 25.79, 29.8, 46.7, 114.8}$ (d, $J_{\text{CF}} = 19$ Hz), 121.8, 124.1 (d, $J_{\text{CF}} = 8$ Hz), 124.7 (d, $J_{\text{CF}} = 4$ Hz), 126.7 (d, $J_{\text{CF}} = 10$ Hz), 152.4 (d, $J_{\text{CF}} = 242$ Hz), 174.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -131.96 (m).

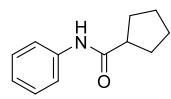
 *N*-(2-Bromophenyl)cyclohexanecarboxamide (**6m**).²⁶ White powder. $R_f = 0.35$ (hexanes/EtOAc= 12:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.22 – 1.36 (m, 3H), 1.55 (app quartet, 2H, CH, $J = 12.8$ Hz), 1.72 (m, 1H, CH), 1.86 (app dm, 2H, CH, $J = 12.8$ Hz), 2.03 (d, 2H, CH, $J = 13.2$ Hz), 2.32 (tt, 1H, CH, $J = 3.4, 12.0$ Hz), 6.96 (td, 1H, $J = 1.5, 7.8$ Hz), 7.31 (t, 1H, $J = 7.8$ Hz), 7.52 (dd, 1H, $J = 8.1, 1.2$ Hz), 7.70 (br. s, 1H, NH), 8.38 (d, 1H, $J = 8.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.8, 25.9, 29.8, 46.8, 122.0, 125.1, 128.6, 132.3, 136.0, 174.4$.

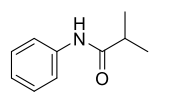
 *N*-(2,6-Dichlorophenyl)cyclohexanecarboxamide (**6n**).²⁹ White powder. $R_f = 0.16$ (hexanes/EtOAc= 9:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.22 – 1.36 (m, 3H), 1.55 (m, 2H), 1.72 (m, 1H, CH), 1.86 (dm, 2H, CH, $J = 12.8$ Hz), 2.04 (d, 2H, CH, $J = 13.2$ Hz), 2.34 (t, 1H, CH, $J = 12.0$ Hz), 6.93 (br. s, 1H, NH), 7.16 (t, 1H, $J = 8.0$ Hz), 7.36 (d, 2H, $J = 8.0$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.8, 25.9, 29.8, 45.7, 128.4, 128.5, 132.3, 133.8, 174.1$.

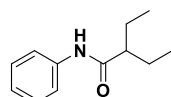
 *N*-(Pyridin-3-yl)cyclohexanecarboxamide (**6p**).³⁶ White solid. Yield > 95%. $R_f = 0.17$ (hexanes/EtOAc= 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.21 – 1.39 (m, 3H), 1.55 (quartet, 2H, CH, $J = 12.8$ Hz), 1.71 (m, 1H, CH), 1.83 (m, 2H), 1.95 (d, 2H, CH, $J = 13.2$ Hz), 2.29 (tt, 1H, CH, $J = 11.6, 3.3$ Hz), 7.27 (dd, 1H, $J = 8.0, 1.4$ Hz), 7.74 (br. s, 1H, NH), 8.24 (dd, 1H, Ar-H, $J = 8.0, 1.4$ Hz), 8.32 (s, 1H), 8.57 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.7}$ (3C), 29.7 (2C), 46.5, 123.9, 127.5, 135.4, 140.9, 144.8, 175.2.

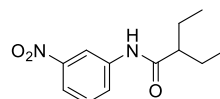
 *N*-(Thiophen-3-yl)cyclohexanecarboxamide (**6q**). White solid. $R_f = 0.33$ (hexanes/EtOAc= 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.22 – 1.39 (m, 3H), 1.52 (quartet, 2H, CH, $J = 12.8$ Hz), 1.71 (m, 1H, CH), 1.83 (m, 2H), 1.94 (d, 2H, CH, $J = 13.2$ Hz), 2.22 (tt, 1H, CH, $J = 3.4, 11.8$ Hz), 7.49 (br. s, 1H, NH), 6.99 (dd, 1H, Ar-H, $J = 5.2, 1.2$ Hz), 7.21 (dd, 1H, Ar-H, $J = 5.2, 3.2$ Hz), 7.58 (br. s, 1H, NH), 7.59 (m, 1H, NH); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta_{25.8}$ (3C), 29.8 (2C), 46.1, 110.1, 121.1, 124.6, 135.8, 173.7; ESI-HRMS: Calcd. for $\text{C}_{11}\text{H}_{16}\text{NOS}$ $[\text{M}+\text{H}]^+$: 210.0953, found 210.0955. IR(ATR), see attached spectrum.

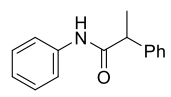
 *N*-Benzylcyclohexanecarboxamide (**6s**).³⁷ White powder. $R_f = 0.2$ (hexanes/EtOAc= 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.18 – 1.30 (m, 3H), 1.47 (m, 2H), 1.67 (m, 1H, *CH*), 1.78 (dm, 2H, *CH*, $J = 12.8$ Hz), 1.87 (d, 2H, *CH*, $J = 13.2$ Hz), 2.11 (tt, 1H, *CH*, $J = 3.6$, 12.0 Hz), 5.85 (br. s, 1H, *NH*), 7.30 (m, 5H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 25.9, 29.8, 43.5, 45.7, 127.5, 127.8, 128.8, 138.7, 176.1.

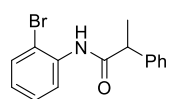
 *N*-Phenylcyclopentanecarboxamide (**6t**).⁴⁰ White powder. $R_f = 0.17$ (hexanes/EtOAc= 9:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.61 (m, 2H), 1.79 (m, 2H), 1.92 (m, 4H), 2.68 (quintet, 1H, *CH*, $J = 8.3$ Hz), 7.09 (t, 1H, $J = 7.5$ Hz), 7.16 (br. s, 1H, *NH*), 7.31 (t, 2H, $J = 7.5$ Hz), 7.52 (d, 2H, $J = 7.5$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 26.2, 30.7, 47.1, 119.8, 124.2, 129.1, 138.3, 174.7.

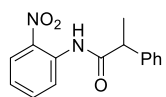
 *N*-Phenylisobutyramide (**6v**).³⁸ White powder. $R_f = 0.33$ (hexanes/EtOAc= 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.25 (d, 6H, CH_3 , $J = 7.4$ Hz), 2.51 (m, 1H, *CH*), 7.09 (t, 1H, $J = 7.9$ Hz), 7.23 (br. s, 1H, *NH*), 7.31 (t, 2H, $J = 7.9$ Hz), 7.53 (d, 2H, $J = 7.9$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 19.8, 36.9, 119.9, 124.3, 129.1, 138.2, 175.4.

 2-Ethyl-*N*-phenylbutanamide (**6w**).³⁹ White powder. $R_f = 0.26$ (hexanes/EtOAc= 20:3). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 0.96 (t, 6H, CH_3 , $J = 7.4$ Hz), 1.57 (m, 2H, CH_2), 1.72 (m, 2H, CH_2), 2.03 (septet, 1H, *CH*, $J = 4.9$ Hz), 7.10 (t, 1H, $J = 7.8$ Hz), 7.15 (br. s, 1H, *NH*), 7.32 (t, 2H, $J = 7.8$ Hz), 7.55 (d, 2H, $J = 8.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 12.3, 26.0, 52.7, 120.0, 124.4, 129.1, 138.1, 174.3.

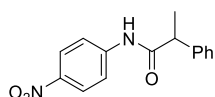
 2-Ethyl-*N*-(3-nitrophenyl)butanamide (**6x**).^{25a} White powder. $R_f = 0.42$ (hexanes/EtOAc= 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 0.97 (t, 6H, $J = 7.4$ Hz), 1.60 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 2.09 (septet, 1H, *CH*, $J = 4.9$ Hz), 7.41 (br. s, 1H, *NH*), 7.49 (t, 1H, $J = 8.0$ Hz), 7.96 (dd, 1H, $J = 8.2$, 1.6 Hz), 7.99 (d, 1H, $J = 8.0$ Hz), 8.40 (t, 1H, $J = 1.6$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 12.2, 25.9, 52.6, 114.7, 119.0, 125.7, 130.0, 139.1, 148.7, 174.8; ESI-HRMS: Calcd. for $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 237.1239, found 237.1247. IR(ATR), see attached spectrum.

 *N*,2-Diphenylpropanamide (**6y**).⁴¹ White solid. $R_f = 0.55$ (hexanes/EtOAc= 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.60 (d, 3H, CH_3 , $J = 7.1$ Hz), 3.23 (quartet, 1H, *CH*), 7.07 (t, 1H, $J = 7.5$ Hz), 7.12 (br. s, 1H, *NH*), 7.25 – 7.28 (m, 2H), 7.30 – 7.33 (m, 1H), 7.36 – 7.42 (m, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.7, 48.3, 119.8, 124.4, 127.7, 128.4, 129.0, 129.3, 138.0, 141.1, 172.4.

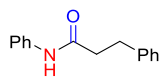
 *N*-(2-Bromophenyl)-2-phenylpropanamide (**6z**).⁴² pale yellow solid. $R_f = 0.25$ (hexanes/EtOAc= 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.65 (d, 3H, CH_3 , $J = 7.2$ Hz), 3.80 (quartet, 1H, *Ar-CH*, $J = 7.2$ Hz), 6.92 (app t, 1H, *Ar-H*, $J = 7.8$ Hz), 7.28 (t, 1H, $J = 7.8$ Hz), 7.33 (m, 1H), 7.38-7.44 (m, 5H, *Ar-H*), 7.61 (br, 1H, *N-H*), 8.36 (d, 1H, $J = 8.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.1, 48.6, 113.3, 121.5, 125.1, 128.0, 128.1, 128.4, 129.4, 132.3, 135.9, 140.4, 172.6.



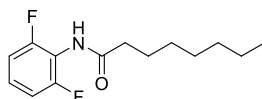
N-(2-Nitrophenyl)-2-phenylpropanamide(**6aa**). Yellowish solid. $R_f = 0.30$ (hexanes/EtOAc = 6:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.65 (d, 3H, CH_3 , $J = 7.1$ Hz), 3.82 (quartet, 1H, Ar- CH , $J = 7.1$ Hz), 7.13 (t, 1H, Ar- H , $J = 7.8$ Hz), 7.30-7.46 (m, 5H, Ar- H), 7.61 (t, 1H, Ar- H , $J = 7.8$ Hz), 8.15 (dd, 1H, $J = 8.6, 1.4$ Hz), 8.80 (d, 1H, $J = 8.6$ Hz), 10.31 (s, 1H, N- H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.1, 49.3, 122.1, 123.2, 125.8, 127.9, 128.1, 129.4, 135.2, 136.0, 136.3, 140.0, 173.6. ESI-HRMS: Calcd. for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 271.1077, found 271.1076. IR(ATR), see attached spectrum.



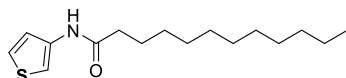
N-(4-Nitrophenyl)-2-phenylpropanamide(**6bb**).³⁰Yellowish solid. $R_f = 0.31$ (hexanes/EtOAc = 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.60 (d, 3H, CH_3 , $J = 7.1$ Hz), 3.76 (quartet, 1H, Ar- CH , $J = 7.1$ Hz), 7.33-7.40 (m, 5H, Ar- H), 7.49 (s, 1H, N- H), 7.61 (d, 1H, Ar- H , $J = 9.1$ Hz), 8.14 (d, 1H, $J = 9.1$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.6, 48.4, 119.1, 125.1, 127.8, 128.1, 129.5, 140.3, 143.6, 143.8, 172.9.



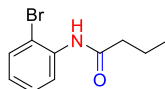
N,3-Diphenylpropanamide(**6cc**).⁴³ Colorless solid. $R_f = 0.23$ (hexanes/EtOAc = 6:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 2.66 (t, 2H, $J = 7.7$ Hz), 3.06 (t, 2H, $J = 7.7$ Hz), 7.08 (br. s, 1H, NH), 7.10 (t, 1H, $J = 7.2$ Hz), 7.24 (m, 3H), 7.30 (m, 4H), 7.43 (d, 2H, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 31.7, 39.7, 120.0, 124.5, 126.6, 128.6, 128.8, 129.1, 137.9, 140.8, 170.5.



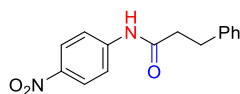
N-(2,6-Difluorophenyl)octanamide(**6dd**). Colorless solid. $R_f = 0.32$ (hexanes/EtOAc = 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 0.88 (t, 3H, $J = 6.3$ Hz), 1.31 (m, 8H), 1.73 (m, 2H), 2.4 (m, 2H), 6.80 (br. s, 1H, NH), 6.94 (t, 2H, $J = 8.1$ Hz), 7.19 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 14.2, 22.7, 25.7, 29.1, 29.2, 31.7, 31.8, 36.6, 111.7, 111.9, 127.7, 158.1(d, 1C, $J_{\text{CF}} = 250$ Hz), 171.7; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -118.00 (m); ESI-HRMS: Calcd. for $\text{C}_{14}\text{H}_{20}\text{NOF}_2$ $[\text{M}+\text{H}]^+$: 256.1507, found 256.1509. IR(ATR), see attached spectrum.



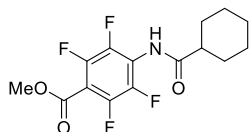
N-(Thiophen-3-yl)dodecanamide(**6ee**). White solid. $R_f = 0.47$ (hexanes/EtOAc = 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 0.88 (t, 3H, $J = 6.3$ Hz), 1.25 (m, 16H), 1.70 (quintet, 2H, $J = 7.2$ Hz), 2.33 (t, 2H, $J = 7.2$ Hz), 6.98 (dd, 1H, Ar- H , $J = 5.1, 1.1$ Hz), 7.22 (dd, 1H, Ar- H , $J = 5.2, 3.2$ Hz), 7.42 (br. s, 1H, NH), 7.57 (d, 1H, $J = 2.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 14.3, 22.8, 25.8, 29.4, 29.5(2C), 29.6, 29.8(2C), 30.1, 37.4, 110.2, 131.0, 124.6, 135.7, 170.7; ESI-HRMS: Calcd. for $\text{C}_{16}\text{H}_{28}\text{NOS}$ $[\text{M}+\text{H}]^+$: 282.1866, found 282.1866. IR(ATR), see attached spectrum.



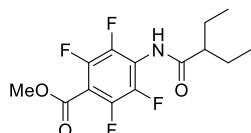
N-(2-Bromophenyl)butyramide(**6ff**).⁴⁴Colorless solid. $R_f = 0.51$ (hexanes/EtOAc = 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.04 (t, 2H, $J = 7.3$ Hz), 1.79 (sextet, 2H, $J = 7.3$ Hz), 2.41 (t, 2H, $J = 7.3$ Hz), 6.97 (t, 1H, $J = 7.5$ Hz), 7.31 (t, 1H, $J = 7.5$ Hz), 7.53 (d, 1H, $J = 7.5$ Hz), 7.62 (br. s, 1H, NH), 8.36 (d, 1H, $J = 7.5$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 13.9, 19.2, 40.1, 113.3, 122.0, 125.2, 128.6, 132.3, 135.9, 171.3.



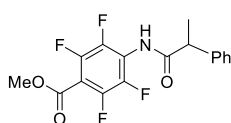
N-(4-Nitrophenyl)-3-phenylpropanamide(**6gg**).⁴⁵ Yellowish solid. $R_f = 0.19$ (hexanes/EtOAc= 6:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 2.73 (t, 2H, $J = 7.7$ Hz), 3.06 (t, 2H, $J = 7.7$ Hz), 7.23 (tm, 3H, $J = 7.7$ Hz), 7.30 (t, 1H, $J = 7.7$ Hz), 7.61 (br. s, 1H, *NH*), 7.62 (d, 2H, $J = 9.3$ Hz), 8.16 (d, 2H, $J = 9.3$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 31.4, 39.6, 119.2, 125.2, 126.7, 128.4, 128.8, 140.2, 143.5, 143.8, 171.1.



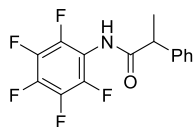
Methyl 4-(cyclohexanecarboxamido)-2,3,5,6-tetrafluorobenzoate(**6hh**). White solid. $R_f = 0.47$ (hexanes/EtOAc= 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.21 – 1.39 (m, 3H), 1.56 (quartet, 2H, *CH*, $J = 12.8$ Hz), 1.72 (m, 1H, *CH*), 1.89 (d, 2H, *CH*, $J = 12.8$ Hz), 1.99 (d, 2H, *CH*, $J = 12.8$ Hz), 2.40 (tt, 1H, *CH*, $J = 3.5, 11.5$ Hz), 3.97 (s, 3H, OCH_3), 7.09 (br, 1H, *NH*); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 25.6, 25.7, 29.7, 45.4, 53.4, 109.9 (m), 119.7 (m), 142.1 (dm, 2C, $J_{\text{CF}} = 250$ Hz), 145.1 (dm, 2C, $J_{\text{CF}} = 258$ Hz), 160.2, 174.0; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -139.60 (m, 2F), -144.32 (m, 2F). ESI-HRMS: Calcd. for $\text{C}_{15}\text{H}_{16}\text{F}_4\text{NO}_3$ $[\text{M}+\text{H}]^+$: 334.1066, found 334.1068. IR(ATR), see attached spectrum.



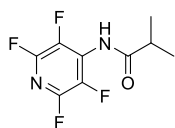
Methyl 4-(2-ethylbutanamido)-2,3,5,6-tetrafluorobenzoate(**6ii**). White powder. $R_f = 0.2$ (hexanes/EtOAc= 6:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 0.96 (t, 6H, $J = 7.4$ Hz), 1.60 (m, 2H, CH_2), 1.72 (m, 2H, CH_2), 2.23 (septet, 1H, *CH*, $J = 5.0$ Hz), 3.97 (s, 3H, OMe), 7.17 (br. s, 1H, *NH*); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 11.9, 25.9, 51.4, 53.4, 110.0 (m), 119.5 (m), 142.0 (dm, 2C, $J_{\text{CF}} = 250$ Hz), 145.0 (dm, 2C, $J_{\text{CF}} = 250$ Hz), 160.4, 174.2; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -139.63 (m, 2F), -144.00 (m, 2F); ESI-HRMS: Calcd. for $\text{C}_{14}\text{H}_{16}\text{F}_4\text{NO}_3$ $[\text{M}+\text{H}]^+$: 322.1066, found 322.1071. IR (ATR), see attached spectrum.



Methyl 2,3,5,6-tetrafluoro-4-(2-phenylpropanamido)benzoate(**6jj**). White solid. $R_f = 0.33$ (3:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.59 (d, 3H, CH_3 , $J = 7.2$ Hz), 3.84 (quartet, 1H, *Ar-CH*, $J = 7.2$ Hz), 3.95 (s, 3H, OCH_3), 7.03 (br, 1H, *NH*), 7.31 – 7.41 (m, 5H, *Ar-H*); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.6, 47.3, 53.4, 109.9 (m), 119.5 (m), 127.8, 128.0, 129.5, 140.2, 142.0 (dm, 2C, $J_{\text{CF}} = 243$ Hz), 144.7 (dm, 2C, $J_{\text{CF}} = 256$ Hz), 159.8, 169.4; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -139.54 (m, 2F), -144.20 (m, 2F); ESI-HRMS: Calcd. for $\text{C}_{17}\text{H}_{14}\text{F}_4\text{NO}_3$ $[\text{M}+\text{H}]^+$: 356.0901, found 356.0910. IR(ATR), see attached spectrum.

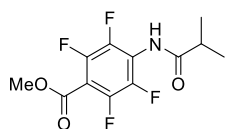


N-(Perfluorophenyl)-2-phenylpropanamide(**6kk**).⁴⁶ White solid. $R_f = 0.30$ (10:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.60 (d, 3H, CH_3 , $J = 7.1$ Hz), 3.82 (quartet, 1H, *Ar-CH*, $J = 7.1$ Hz), 6.77 (br, 1H, *NH*), 7.27–7.42 (m, 5H, *Ar-H*); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 18.6, 47.2, 112.0 (m), 127.8, 128.0, 129.4, 140.2, 137.8 (dm, 2C, $J_{\text{CF}} = 247$ Hz), 140.3 (dm, 1C, $J_{\text{CF}} = 232$ Hz), 140.4, 143.1 (dm, 2C, $J_{\text{CF}} = 252$ Hz), 173.0; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -145.00 (m, 2F), -156.54 (m, 1F), -156.54 (m, 2F). IR(ATR), see attached spectrum.

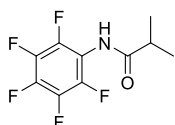


N-(Perfluoropyridin-4-yl)isobutyramide (**6ll**). White solid. $R_f = 0.25$ (hexanes/EtOAc= 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 1.30 (d, 6H, CH_3 , $J = 6.9$ Hz), 2.70 (septet, 1H, *CH*, $J = 6.9$ Hz), 7.19 (s, 1H, *NH*); $^{13}\text{C NMR}$ (100 MHz, DMSO): δ 19.2, 34.0, 130.0 (m), 136.7 (dm, 2C, $J_{\text{CF}} = 258$ Hz), 142.9 (dm, 2C, $J_{\text{CF}} = 240$ Hz), 174.7; $^{19}\text{F NMR}$ (376 MHz, DMSO):

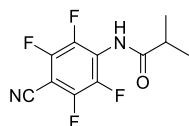
δ -92.67 (m, 2F), -145.58 (m, 2F).ESI-HRMS: Calcd. for $C_9H_9F_4N_2O$ $[M+H]^+$: 237.0651, found 237.0648. IR(ATR), see attached spectrum.



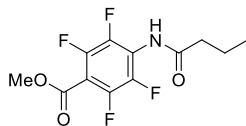
Methyl 2,3,5,6-tetrafluoro-4-isobutyramidobenzoate (**6mm**). White solid. R_f = 0.24 (hexanes/EtOAc= 3:1). 1H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (d, 6H, CH_3 , J = 6.9 Hz), 2.67 (septet, 1H, CH , J = 6.9 Hz), 3.95 (s, 3H, OCH_3), 7.03 (br, 1H, NH), 7.31 - 7.41 (m, 5H, Ar- H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5, 35.9, 53.4, 110.0 (m), 119.7 (m), 142.1 (dm, 2C, J_{CF} = 252 Hz), 145.1 (dm, 2C, J_{CF} = 256 Hz), 159.8, 169.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -139.60 (m, 2F), -144.42 (m, 2F);ESI-HRMS: Calcd. for $C_{12}H_{12}F_4NO_3$ $[M+H]^+$: 294.0753, found 294.0744. IR(ATR), see attached spectrum.



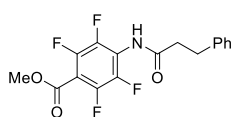
N-(Perfluorophenyl)isobutyramide (**6nn**). White solid. R_f = 0.44 (hexanes/EtOAc= 3:1). 1H NMR (400 MHz, $CDCl_3$): δ_H 1.29 (d, 6H, CH_3 , J = 6.9 Hz), 2.65 (septet, 1H, CH , J = 6.9 Hz), 6.77 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.6, 35.7, 112.1 (m), 137.8 (dm, 2C, J_{CF} = 248 Hz), 140.3 (dm, 1C, J_{CF} = 241 Hz), 143.2 (dm, 2C, J_{CF} = 250 Hz), 175.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -145.21 (m, 2F), -156.63 (m, 1F), -162.46 (m, 2F). ESI-HRMS: Calcd. for $C_{15}H_{16}NO$ $[M+H]^+$: 226.1232, found 226.1236. IR(ATR), see attached spectrum.



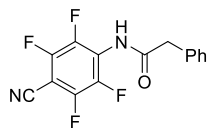
N-(4-Cyano-2,3,5,6-tetrafluorophenyl)isobutyramide (**6oo**). White solid. R_f = 0.26 (hexanes/EtOAc= 3:1). 1H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (d, 6H, CH_3 , J = 6.9 Hz), 2.69 (septet, 1H, CH , J = 6.9 Hz), 7.43 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 35.9, 91.2 (m, CN), 107.5 (m), 123.1 (m), 141.8 (dm, 2C, J_{CF} = 254 Hz), 147.5 (dm, 2C, J_{CF} = 261 Hz), 175.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ -132.78 (m, 2F), -141.80 (m, 2F);ESI-HRMS: Calcd. for $C_{11}H_9F_4N_2O$ $[M+H]^+$: 261.0651, found 261.0652. IR (ATR), see attached spectrum.



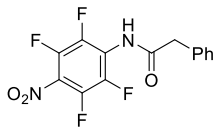
Methyl 4-butyramido-2,3,5,6-tetrafluorobenzoate (**6pp**). White solid. R_f = 0.23 (hexanes/EtOAc= 9:1). 1H NMR (400 MHz, $CDCl_3$): δ_H 1.02 (t, 3H, CH_3 , J = 7.4 Hz), 1.77 (sextet, 2H, CH_2CH_3 , J = 7.4 Hz), 2.44 (t, 3H, CH_3 , J = 7.4 Hz), 3.97 (s, 3H, OCH_3), 7.22 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 19.0, 38.3, 53.4, 110.1 (m), 119.5 (m), 142.1 (dm, 2C, J_{CF} = 250 Hz), 145.1 (dm, 2C, J_{CF} = 256 Hz), 160.2, 171.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -139.52 (m, 2F), -144.15 (m, 2F).ESI-HRMS: Calcd. for $C_{12}H_{12}F_4NO_3$ $[M+H]^+$: 294.0753, found 294.0745. IR (ATR), see attached spectrum.



Methyl 2,3,5,6-tetrafluoro-4-(3-phenylpropanamido)benzoate (**6qq**). White solid. R_f = 0.29 (hexanes/EtOAc = 3:1). 1H NMR (400 MHz, $CDCl_3$): δ_H 2.76 (t, 2H, CH_2 , J = 7.5 Hz), 3.03 (t, 2H, Ar- CH_2 , J = 7.5 Hz), 3.96 (s, 3H, OCH_3), 7.49 (br, 1H, NH), 7.19-7.26 (m, 3H, Ar- H), 7.27- 7.31 (m, 2H, Ar- H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.3, 38.0, 53.5, 109.9 (m), 119.3 (m), 126.7, 128.4, 128.8, 140.0, 142.0 (dm, 2C, J_{CF} = 251 Hz), 145.0 (dm, 2C, J_{CF} = 257 Hz), 160.2, 170.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -139.46 (m, 2F), -143.80 (m, 2F);ESI-HRMS: Calcd. for $C_{17}H_{14}F_4NO_3$ $[M+H]^+$: 356.0910, found 356.0913. IR (ATR), see attached spectrum.



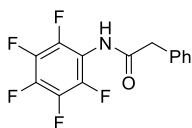
N-(4-Cyano-2,3,5,6-tetrafluorophenyl)-2-phenylacetamide(**6rr**). White solid. $R_f = 0.23$ (3:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 3.80 (s, 2H, Ar- CH_2), 7.26-7.35 (m, 5H, Ar- H), 10.81 (s, 1H, NH); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 41.8, 90.2 (CN), 108.2 (m), 123.5 (m), 126.8, 128.4, 129.1, 134.9, 141.4 (dm, 2C, $J_{\text{CF}} = 250$ Hz), 145.0 (dm, 2C, $J_{\text{CF}} = 258$ Hz), 169.0; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -130.25 (m, 2F), -137.63 (m, 2F); ESI-HRMS: Calcd. for $\text{C}_{15}\text{H}_9\text{F}_4\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 309.0651, found 309.0652. IR (ATR), see attached spectrum.



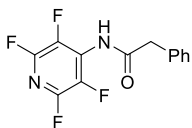
2-Phenyl-*N*-(2,3,5,6-tetrafluoro-4-nitrophenyl)acetamide(**6ss**). White powder. $R_f = 0.36$ (3:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, DMSO): δ_{H} 3.80 (s, 1H, Ar- CH_2), 10.8 (br, 1H, NH), 7.27-7.35 (m, 5H, Ar- H); $^{13}\text{C NMR}$ (100 MHz, DMSO): δ 41.7, 111.3 (m), 122.0 (m), 126.8, 128.4, 129.1, 134.9, 141.1 (dm, 2C, $J_{\text{CF}} = 257$ Hz), 141.7 (dm, 2C, $J_{\text{CF}} = 253$ Hz), 169.0; $^{19}\text{F NMR}$ (376 MHz, DMSO): δ -142.67 (m, 2F), -147.08 (m, 2F). ESI-HRMS: Calcd. for $\text{C}_{14}\text{H}_9\text{F}_4\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 329.0549, found 329.0549. IR (ATR), see attached spectrum.



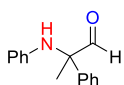
Methyl 2,3,5,6-tetrafluoro-4-(2-phenylacetamido)benzoate(**6tt**). White solid. $R_f = 0.30$ (7:2 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ_{H} 3.82 (s, 2H, Ar- CH_2), 3.96 (s, 3H, OCH_3), 7.10 (br, 1H, NH), 7.34 (m, 3H, Ar- H), 7.40 (m, 2H, Ar- H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 & DMSO- d_6): δ 42.6, 53.0, 109.0 (m), 120.2 (m), 126.8, 128.1, 128.4, 128.9, 134.4, 142.1 (dm, 2C, $J_{\text{CF}} = 240$ Hz), 145.1 (dm, 2C, $J_{\text{CF}} = 255$ Hz), 160.1, 172.3; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -139.37 (m, 2F), -143.99 (m, 2F); ESI-HRMS: Calcd. for $\text{C}_{16}\text{H}_{12}\text{F}_4\text{NO}_3$ $[\text{M}+\text{H}]^+$: 342.0748, found 342.0743. IR (ATR), see attached spectrum.



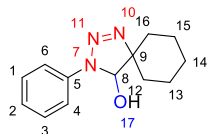
N-(Perfluorophenyl)-2-phenylacetamide(**6uu**).⁴⁷ White solid. $R_f = 0.42$ (3:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, DMSO): δ_{H} 3.82 (s, 1H, Ar- CH_2), 10.3 (br, 1H, NH), 7.26-7.34 (m, 5H, Ar- H); $^{13}\text{C NMR}$ (100 MHz, DMSO): δ 41.7, 112.9 (m), 126.0 (m), 126.7, 128.4, 129.0, 135.2, 137.3 (dm, 2C, $J_{\text{CF}} = 248$ Hz), 139.0 (dm, 1C, $J_{\text{CF}} = 243$ Hz), 142.6 (dm, 2C, $J_{\text{CF}} = 246$ Hz), 173.0; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -145.40 (m, 2F), -158.19 (m, 1F), -163.55 (m, 2F). IR (ATR), see attached spectrum.



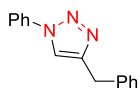
N-(Perfluoropyridin-4-yl)-2-phenylacetamide(**6vv**). White solid. $R_f = 0.24$ (5:1 hexanes/EtOAc). $^1\text{H NMR}$ (400 MHz, DMSO): δ_{H} 3.82 (s, 2H, Ar- CH), 7.26-7.35 (m, 5H, Ar- H), 10.99 (s, 1H, NH); $^{13}\text{C NMR}$ (100 MHz, DMSO): δ 41.8, 126.8, 128.4, 129.1, 129.6 (m), 134.8, 136.6 (dm, 2C, $J_{\text{CF}} = 257$ Hz), 142.9 (dm, 2C, $J_{\text{CF}} = 240$ Hz), 168.7; $^{19}\text{F NMR}$ (376 MHz, DMSO): δ -95.25 (m, 2F), -145.17 (m, 2F); ESI-HRMS: Calcd. for $\text{C}_{13}\text{H}_9\text{F}_4\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 285.0651, found 285.0646. IR (ATR), see attached spectrum.



2-Phenyl-2-(phenylamino)propanal(**7**). Gray solid. $R_f = 0.68$ (hexanes/EtOAc = 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 1.85 (s, 3H), 5.22 (br. s, 1H, NH), 6.44 (d, 2H, J), 6.44 (d, 2H, J = 8.0 Hz), 6.67 (t, 1H, J = 7.3 Hz), 7.06 (t, 2H, J = 8.0 Hz), 7.36 (t, 1H, J = 7.3 Hz), 7.42 (t, 2H, J = 8.0 Hz), 7.50 (d, 2H, J = 7.3 Hz), 9.30 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 19.7, 66.4, 115.3, 117.8, 127.4, 128.3, 129.1, 129.4, 137.8, 144.4, 196.8; ESI-HRMS: Calcd. for $\text{C}_{15}\text{H}_{16}\text{NO}$ $[\text{M}+\text{H}]^+$: 226.1226, found 226.1230. IR (ATR), see attached spectrum.



3-Phenyl-1,2,3-triazaspiro[4.5]dec-1-en-4-ol (**5a**). Triazoline **6a** decomposed during SiO₂-gel column chromatography separation and was characterized from the crude product. ¹H NMR (400 MHz, DMSO): δ_H 1.19 – 1.88 (m, 10H), 5.26 (s, 1H, C₍₈₎H), 4.10 – 6.50 (br. s, 1H, OH), 6.97 (t, 1H, C₍₂₎H, J = 7.5 Hz), 7.29 (t, 2H, C_(1,3)H, J = 7.5 Hz), 7.43 (d, 2H, C_(4,6)H, J = 8 Hz); ¹³C NMR (100 MHz, DMSO): δ_C 22.7, 23.4, 25.5, 27.8, 32.4, 82.7 (C₍₉₎), 83.1(C₍₈₎), 115.5, 122.2, 129.5, 140.8.



4-Benzyl-1-phenyl-1*H*-1,2,3-triazole(**8**).⁴⁸ White solid. R_f = 0.25 (6:1 hexanes/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ 7.68 (m, 2H), 7.60 (s, 1H), 7.50 (m, 2H), 7.42 (m, 1H), 7.33 (m, 4H), 7.26 (m, 1H), 4.18 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 32.5, 119.8, 120.6, 126.8, 128.7, 128.9, 129.0, 129.8, 137.3, 139.0, 148.7.

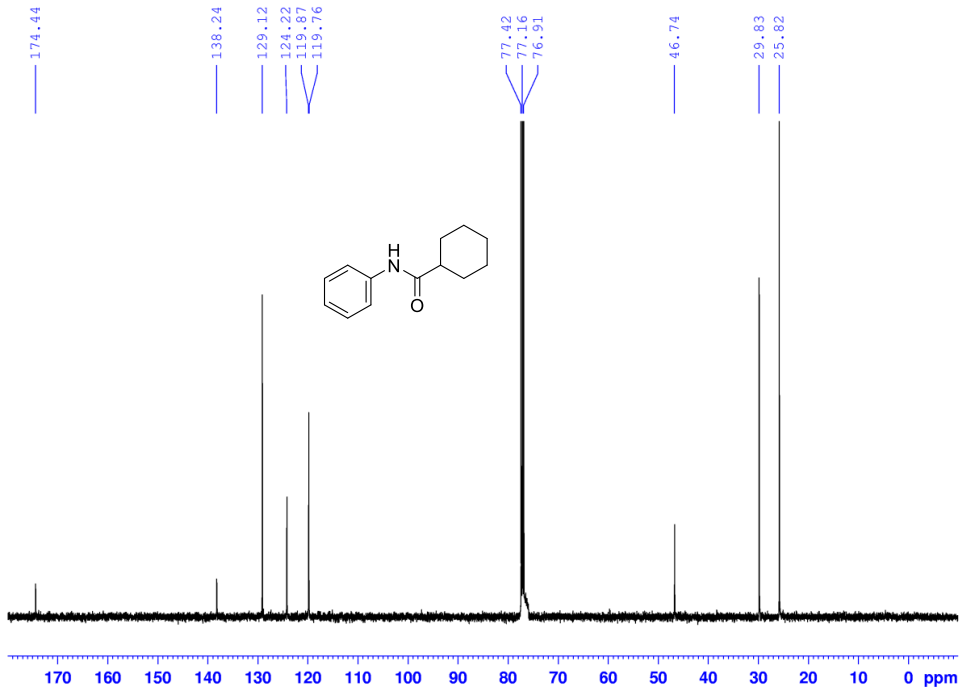
References

- (1) L'Abbe, G., *Chem. Rev.* **1969**, *69*, 345.
- (2) Zanirato, P., *Arkivoc* **2009**, 97.
- (3) L'Abbe, G.; Mathys, G., *J. Org. Chem.* **1974**, *39*, 1778.
- (4) Xie, S.; Lopez, S. A.; Ramstrom, O.; Yan, M.; Houk, K. N., *J. Am. Chem. Soc.* **2015**, *137*, 2958.
- (5) Keana, J. F. W.; Cai, S. X., *J. Org. Chem.* **1990**, *55*, 3640.
- (6) Jin, L. M.; Xu, X.; Lu, H.; Cui, X.; Wojtas, L.; Zhang, X. P., *Angew. Chem. Int. Ed.* **2013**, *52*, 5309.
- (7) Chapyshev, S. V., *Chem. Heterocycl. Compd.* **2001**, *37*.
- (8) Berger, O.; Kaniti, A.; van Ba, C.; Vial, H.; Ward, S.; Biagini, G.; Bray, P.; O'Neill, P., *ChemMedChem* **2011**, *6*, 2094.
- (9) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M., *Eur. J. Org. Chem.* **2010**, *2010*, 1875.
- (10) Serwinski, P.; Esat, B.; Lahti, P.; Liao, Y.; Walton, R.; Lan, J., *J. Org. Chem.* **2004**, *69*, 5247.
- (11) Ueno, M.; Hori, C.; Suzawa, K.; Ebisawa, M.; Kondo, Y., *Eur. J. Org. Chem.* **2005**, *2005*, 1965.
- (12) Kwok, S. W.; Fotsing, J. R.; Fraser, R. J.; Rodionov, V. O.; Fokin, V. V., *Org. Lett.* **2010**, *12*, 4217.
- (13) Jin, L. M.; Xu, X.; Lu, H.; Cui, X.; Wojtas, L.; Zhang, X. P., *Angew. Chem. Int. Ed.* **2013**, *52*, 5309.
- (14) Hu, M.; Li, J.; Yao, S. Q., *Org. Lett.* **2008**, *10*, 5529.
- (15) Kitamura, M.; Kato, S.; Yano, M.; Tashiro, N.; Shiratake, Y.; Sando, M.; Okauchi, T., *Org. Biomol. Chem.* **2014**, *12*, 4397.
- (16) Morawietz, J.; Sander, W.; Traubel, M., *J. Org. Chem.* **1995**, *60*, 6368.
- (17) Chitre, K. P.; Guillén, E.; Yoon, A. S.; Galoppini, E., *Eur. J. Inorg. Chem.* **2012**, *2012*, 5461.
- (18) Nicolaidis, A.; Enyo, T.; Miura, D.; Tomioka, H., *J. Am. Chem. Soc.* **2001**, *123*, 2628.
- (19) Smith, C. D.; Greaney, M. F., *Org. Lett.* **2013**, *15*, 4826.
- (20) Laitar, D. S.; Mathison, C. J.; Davis, W. M.; Sadighi, J. P., *Inorg. Chem.* **2003**, *42*, 7354.
- (21) Tran, A. T.; Cergol, K. M.; Britton, W. J.; Imran Bokhari, S. A.; Ibrahim, M.; Lapthorn, A. J.; Payne, R. J., *MedChemComm* **2010**, *1*, 271.
- (22) Potratz, S.; Mishra, A.; Bauerle, P., *Beilstein. J. Org. Chem.* **2012**, *8*, 683.
- (23) Yarovenko, V. N.; Smirnova, N. G.; Bulgakova, V. N.; Zavarzin, I. V.; Krayushkin, M. M., *RUSS. J. ORG. CHEM.* **2003**, *39*, 1161.
- (24) Liu, H.; Yan, N.; Dyson, P. J., *Chem. Commun.* **2014**, *50*, 7848.

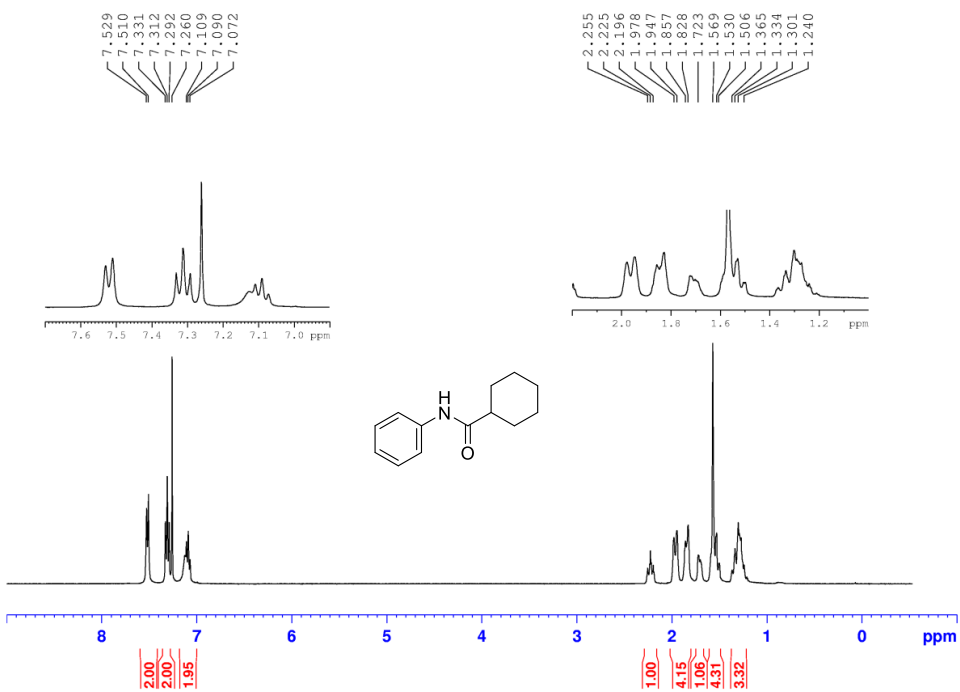
- (25) (a) Herbst, R. M.; Roberts, C. W.; Givens, H. T. F.; Harvill, E. K., *J. Org. Chem.* **1952**,*17*, 262. (b) Suzuki, Y. U., Jpn. Kokai Tokkyo Koho (**2011**), JP 2011128469 A 20110630.
- (26) Park, Y.-T.; Kim, M.-S.; Kwak, Y.-W.; Lee, J.-K.; Yoh, S.-D.; Kim, W.-S., *J. Photosci.* **2000**,*7*, 135.
- (27) La Regina, G.; Bai, R.; Rensen, W. M.; Di Cesare, E.; Coluccia, A.; Piscitelli, F.; Famiglini, V.; Reggio, A.; Nalli, M.; Pelliccia, S.; Da Pozzo, E.; Costa, B.; Granata, I.; Porta, A.; Maresca, B.; Soriani, A.; Iannitto, M. L.; Santoni, A.; Li, J.; Miranda Cona, M.; Chen, F.; Ni, Y.; Brancale, A.; Dondio, G.; Vultaggio, S.; Varasi, M.; Mercurio, C.; Martini, C.; Hamel, E.; Lavia, P.; Novellino, E.; Silvestri, R., *J. med. chem.***2013**,*56*, 123.
- (28) Beyer, A.; Buendia, J.; Bolm, C., *Org. Lett.* **2012**,*14*, 3948.
- (29) Nakatsuji, H.; Morimoto, M.; Misaki, T.; Tanabe, Y., *Tetrahedron* **2007**,*63*, 12071.
- (30) Carbone, G.; Burnley, J.; Moses, J. E., *Chem. Commun.* **2013**,*49*, 2759.
- (31) (a) Hara, T.; Wada, N.; Iwamura, H., *J. Agric. Food Chem.* **1992**,*40*, 1692. (b) Li, W.; Wu, X. F., *J. Org. Chem.* **2014**,*79*, 10410.
- (32) Coppo, F. T.; Maskell, E. S. L.; Redshaw, S., WO 2009071519 A1,**2009**.
- (33) (a) Mohmeyer, N.; Schmidt, H. W., *Chemistry* **2007**,*13*, 4499. (b) Flaherty, D. P.; Simpson, D. S.; Miller, M.; Maki, B. E.; Zou, B. Y.; Shi, J.; Wu, M.; McManus, O. B.; Aube, J.; Li, M.; Golden, J. E., *Bioorg. Med. Chem. Lett.***2014**,*24*, 3968.
- (34) (a) Takahashi, N. A., Osamu, Eur. Pat. Appl. (**1998**), EP 878741 A2 19981118. (b) Ono, H. T., Noriaki; Ando, Osamu; Takeuchi, Masako, Jpn. Kokai Tokkyo Koho (1997), JP 09160301 A 19970620.
- (35) Fors, B. P.; Krattiger, P.; Strieter, E.; Buchwald, S. L., *Org. Lett.* **2008**,*10*, 3505.
- (36) Fors, B. P.; Dooleweerd, K.; Zeng, Q.; Buchwald, S. L., *Tetrahedron* **2009**,*65*, 6576.
- (37) Morimoto, H.; Fujiwara, R.; Shimizu, Y.; Morisaki, K.; Ohshima, T., *Org. Lett.* **2014**,*16*, 2018.
- (38) Xiang, S. K.; Zhang, D. X.; Hu, H.; Shi, J. L.; Liao, L. G.; Feng, C.; Wang, B. Q.; Zhao, K. Q.; Hu, P.; Yang, H.; Yu, W. H., *Adv. Synth. Catal.***2013**,*355*, 1495.
- (39) (a) Baigrie, L. M.; Lenoir, D.; Seikaly, H. R.; Tidwell, T. T., *J. Org. Chem.* **1985**,*50*, 2105. (B) Cooke, M. P.; Pollock, C. M., *J. Org. Chem.* **1993**,*58*, 7474.
- (40) Ye, W.; Mo, J.; Zhao, T.; Xu, B., *Chem. Commun.* **2009**, 3246.
- (41) Dunetz, J. R.; Xiang, Y.; Baldwin, A.; Ringling, J., *Org. Lett.* **2011**,*13*, 5048.
- (42) Jia, Y. X.; Katayev, D.; Bernardinelli, G.; Seidel, T. M.; Kundig, E. P., *Chem. Eur. J.* **2010**,*16*, 6300.
- (43) Bures, J.; Martin, M.; Urpi, F.; Vilarrasa, J., *J. Org. Chem.* **2009**,*74*, 2203.
- (44) Muñoz, J. d. M.; Alcázar, J.; de la Hoz, A.; Díaz-Ortiz, Á.; Alonso de Diego, S.-A., *Green Chem.* **2012**,*14*, 1335.
- (45) Upadhayaya, R. S.; Kulkarni, G. M.; Vasireddy, N. R.; Vandavasi, J. K.; Dixit, S. S.; Sharma, V.; Chattopadhyaya, J., *Bioorg. Med. Chem.* **2009**,*17*, 4681.
- (46) Li, J.; Subramaniam, K.; Smith, D.; Qiao, J. X.; Li, J. J.; Qian-Cutrone, J.; Kadow, J. F.; Vite, G. D.; Chen, B. C., *Org. Lett.* **2012**,*14*, 214.
- (47) Chiang, Y.; Grant, A. S.; Guo, H. X.; Kresge, A. J.; Paine, S. W., *J. Org. Chem.* **1997**,*62*, 5363.
- (48) Macdonald, J. E.; Kelly, J. A.; Veinot, J. G., *Langmuir* **2007**,*23*, 9543.

Characterization Spectra

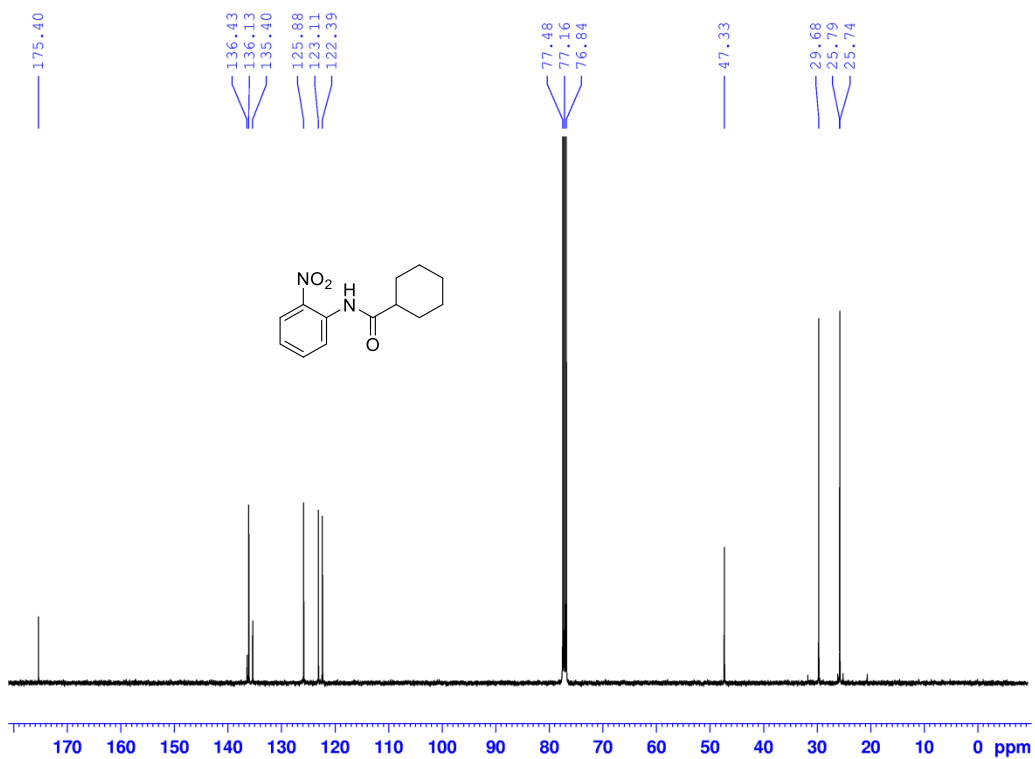
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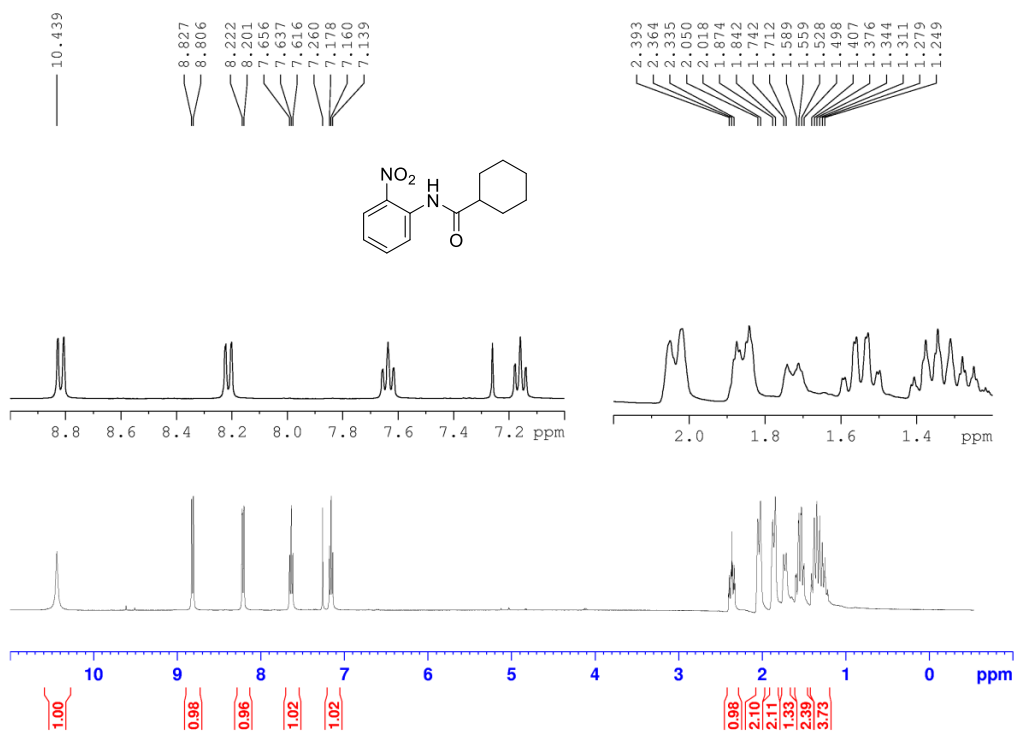
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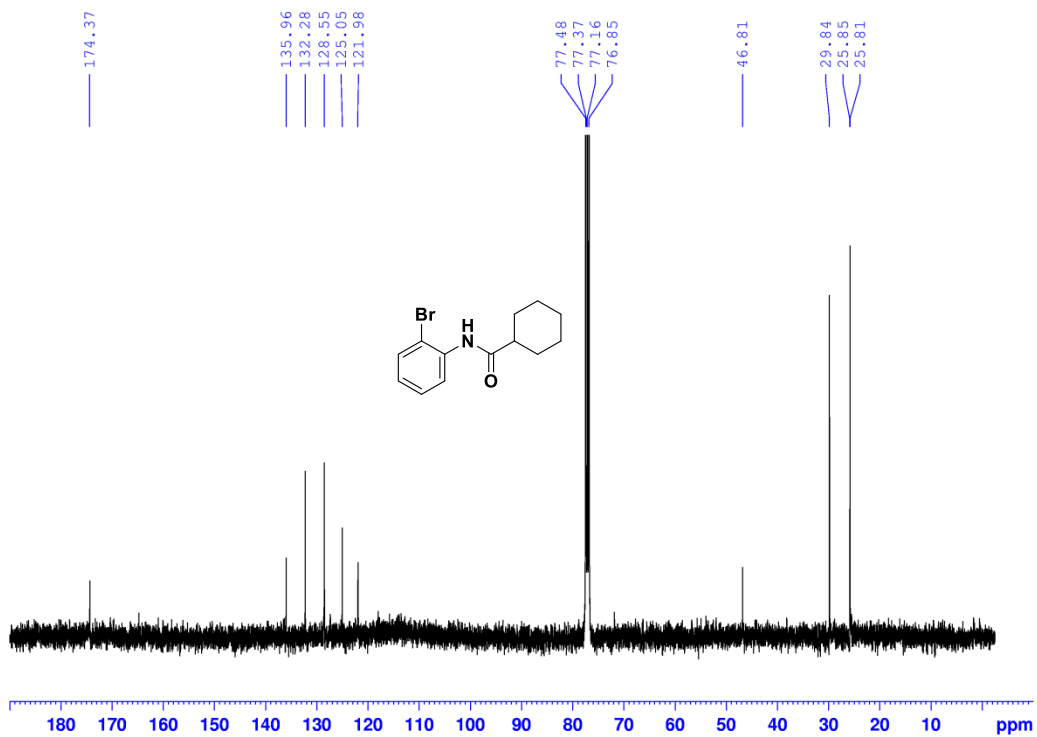
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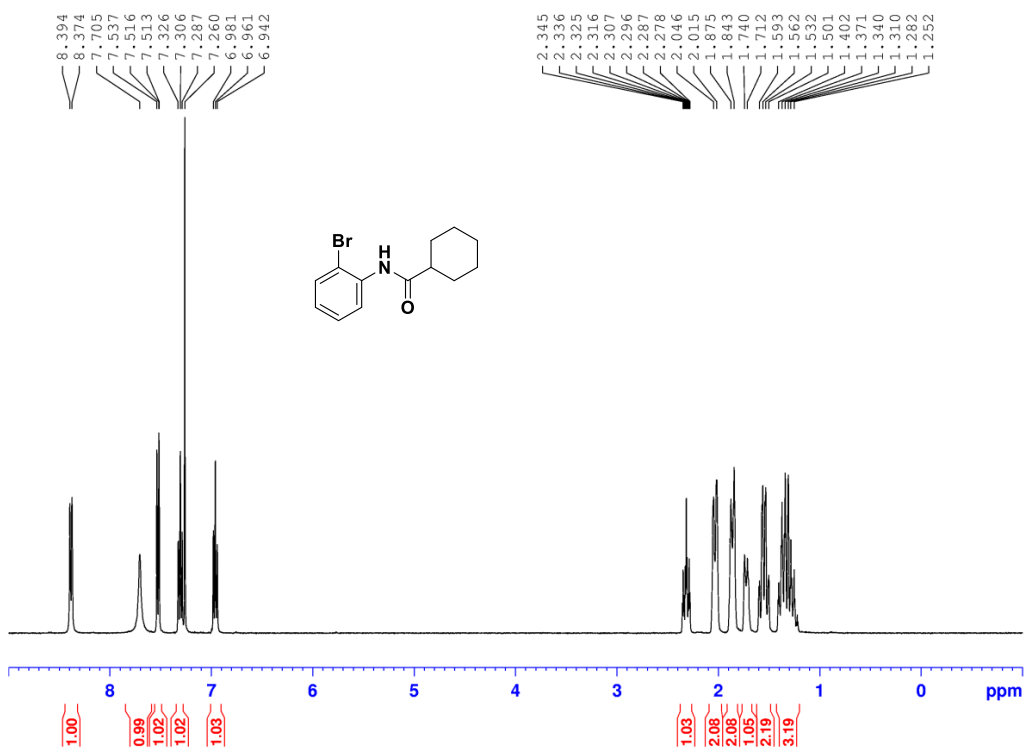
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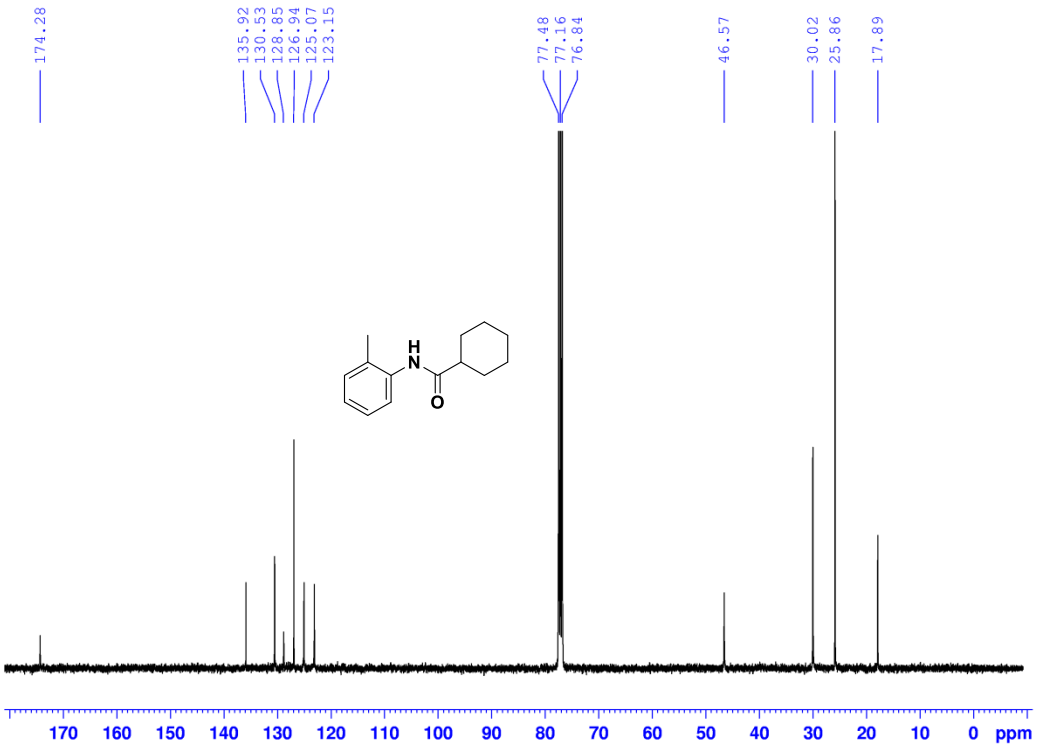
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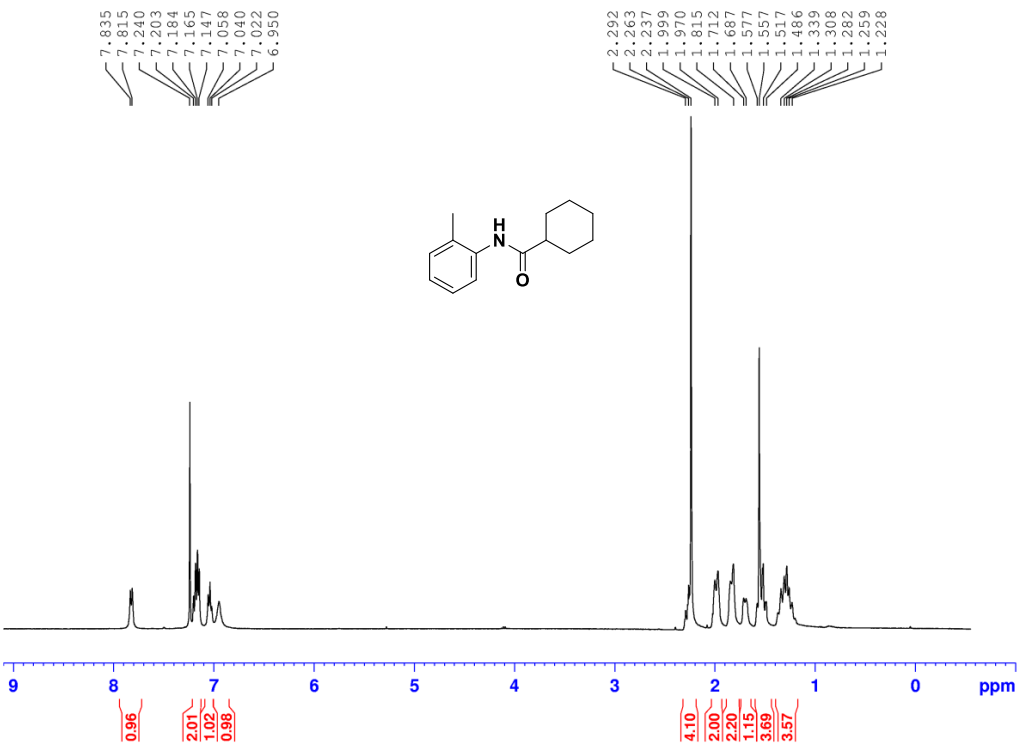
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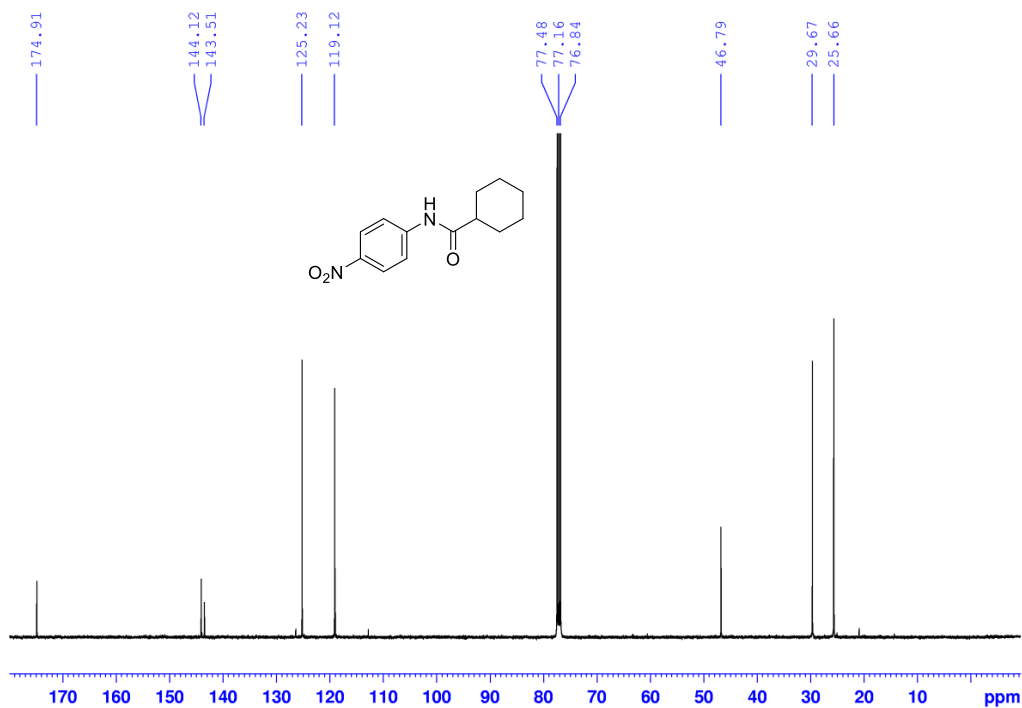
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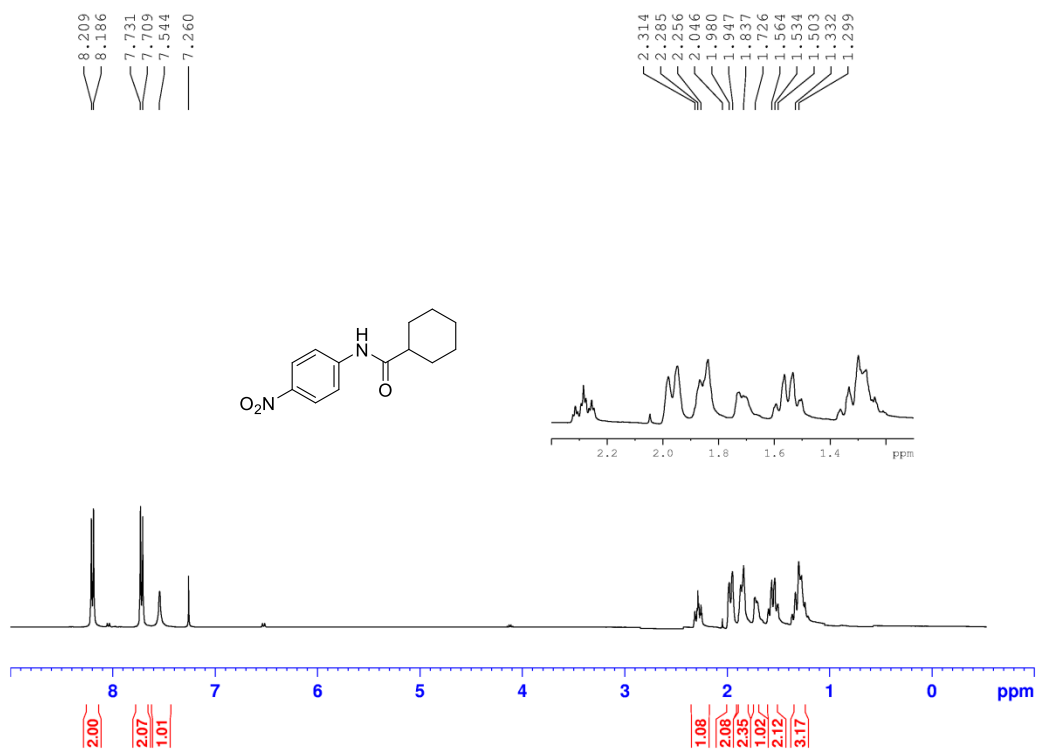
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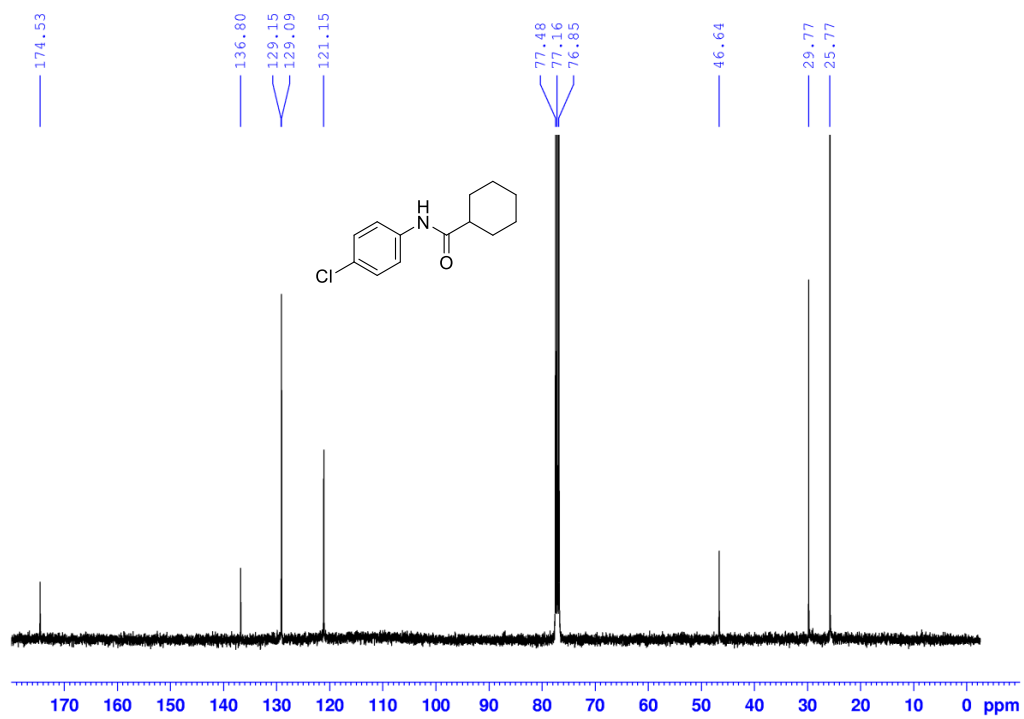
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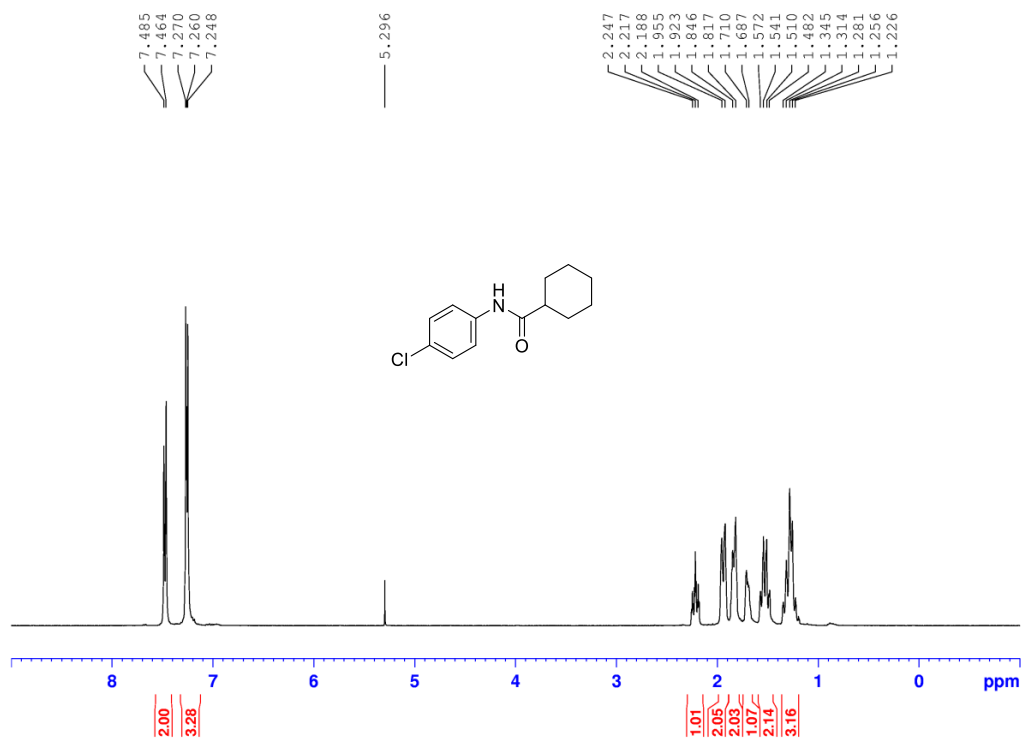
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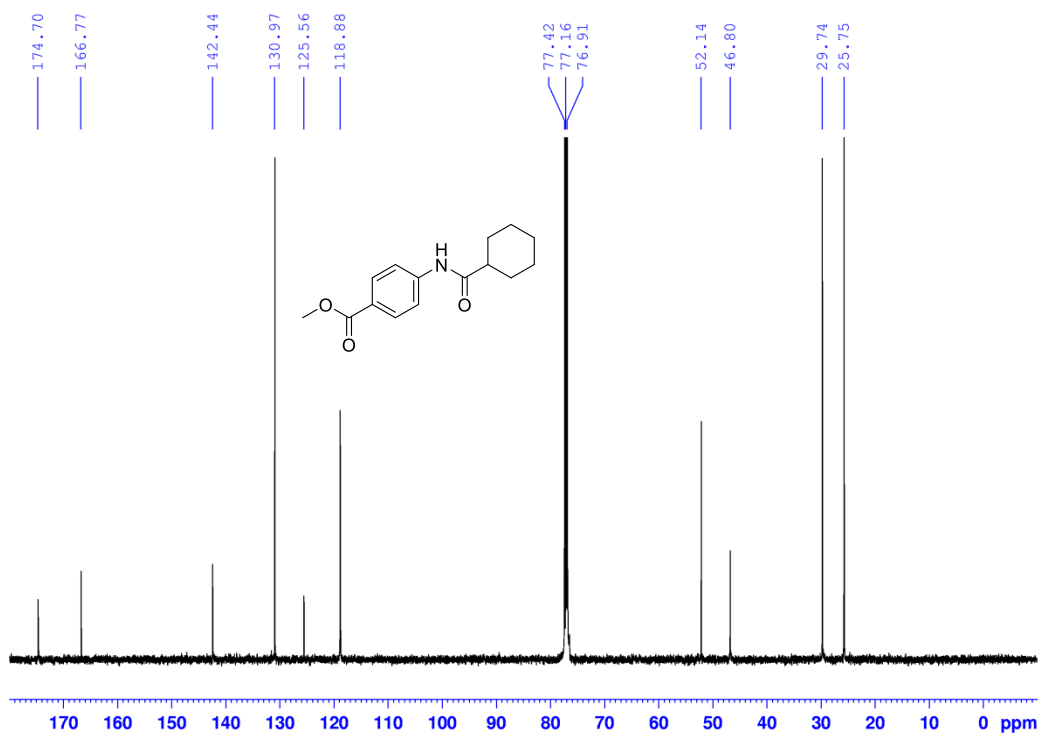
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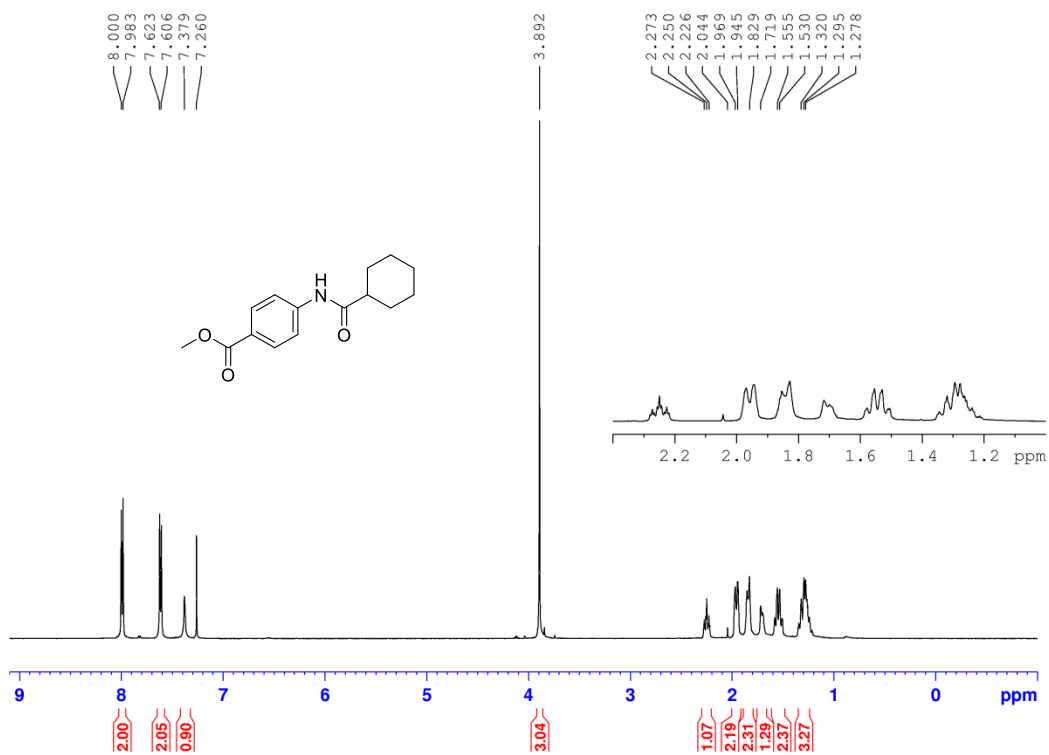
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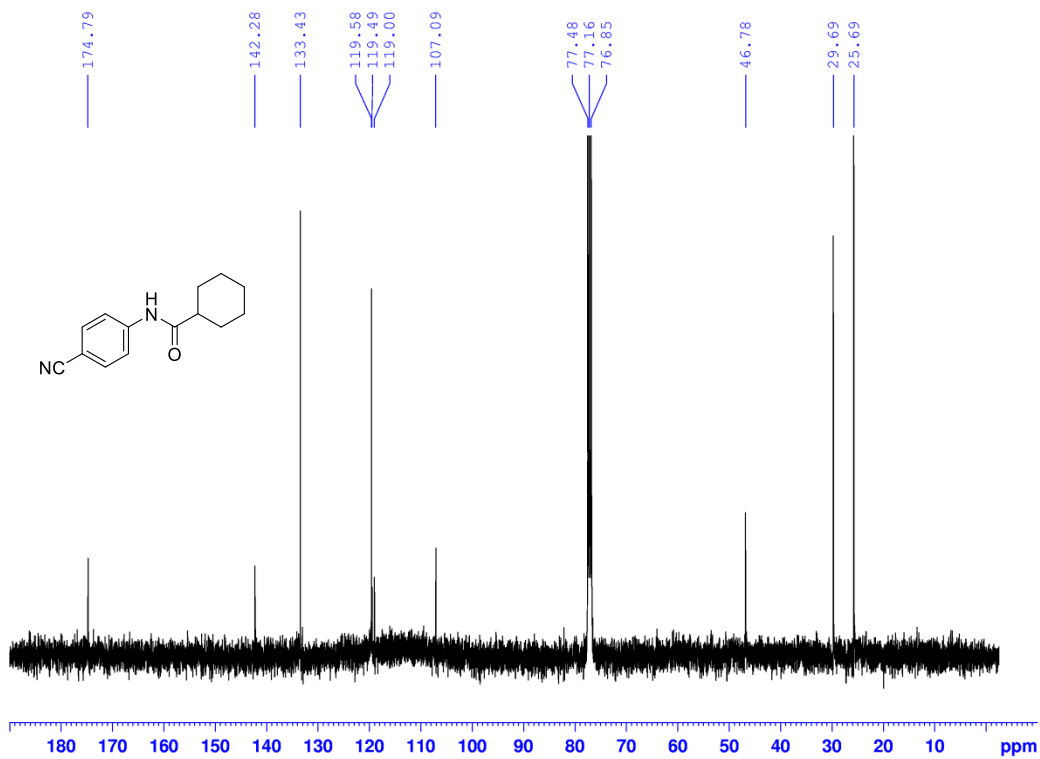
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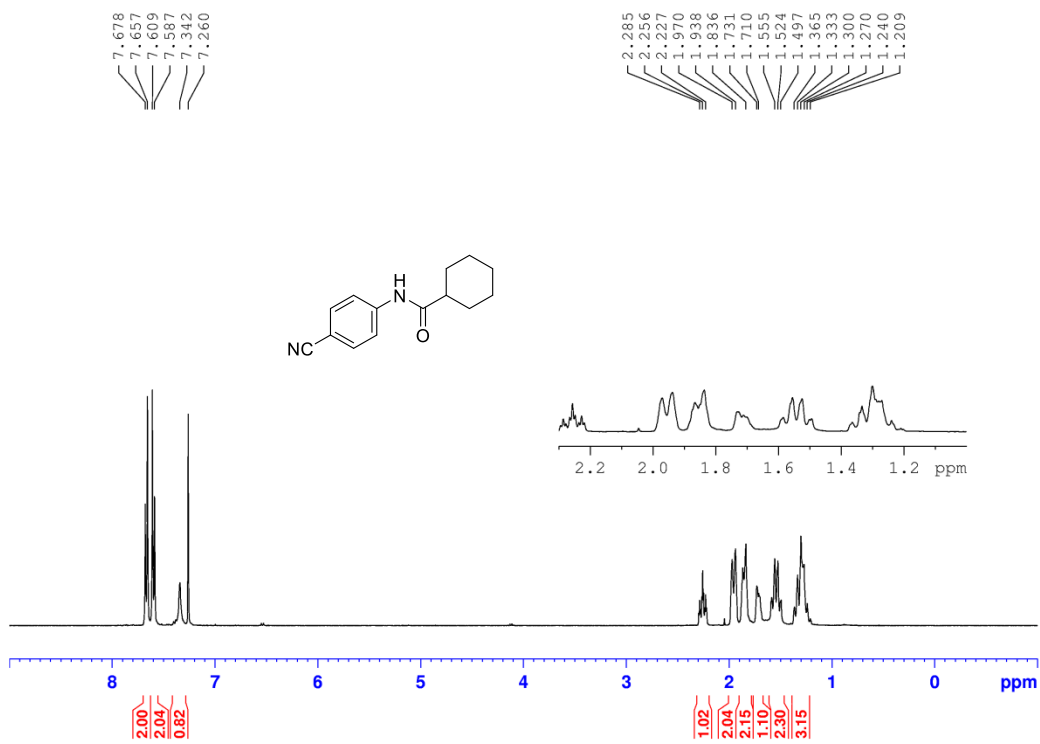
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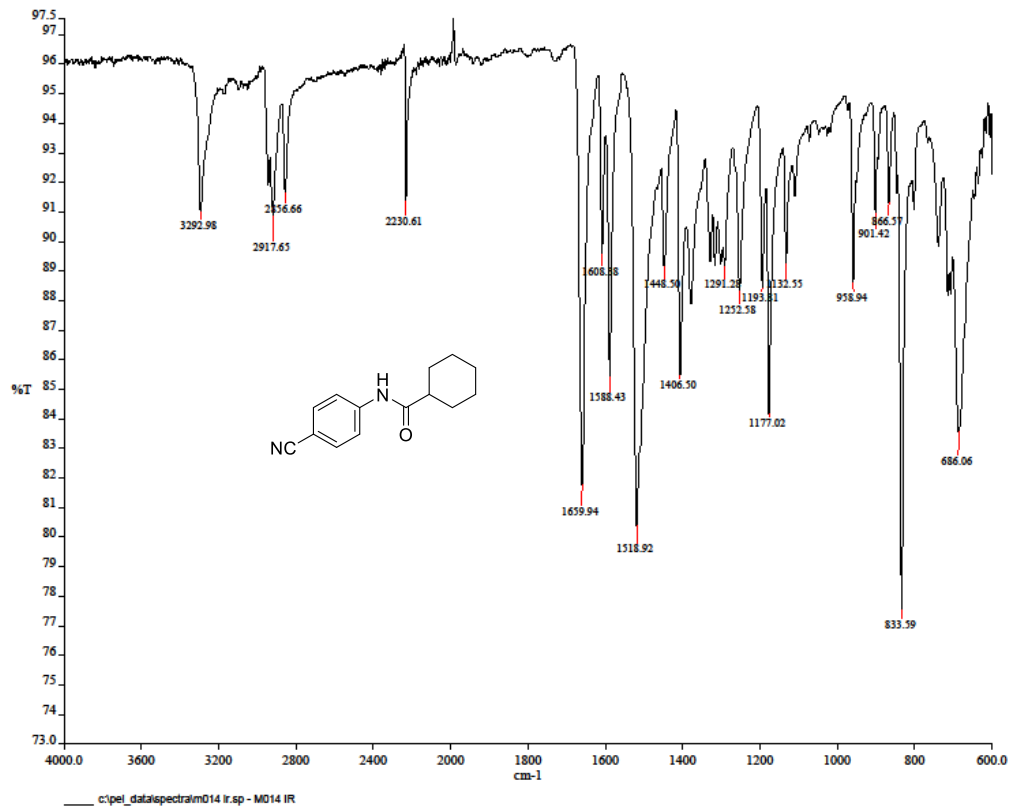


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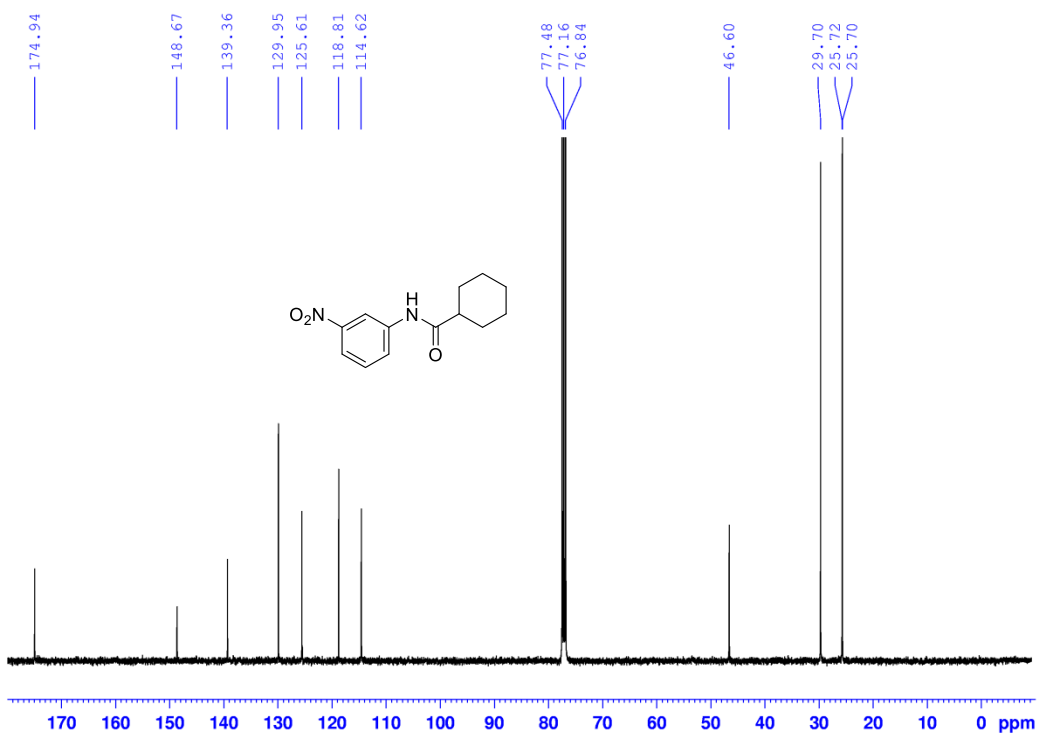


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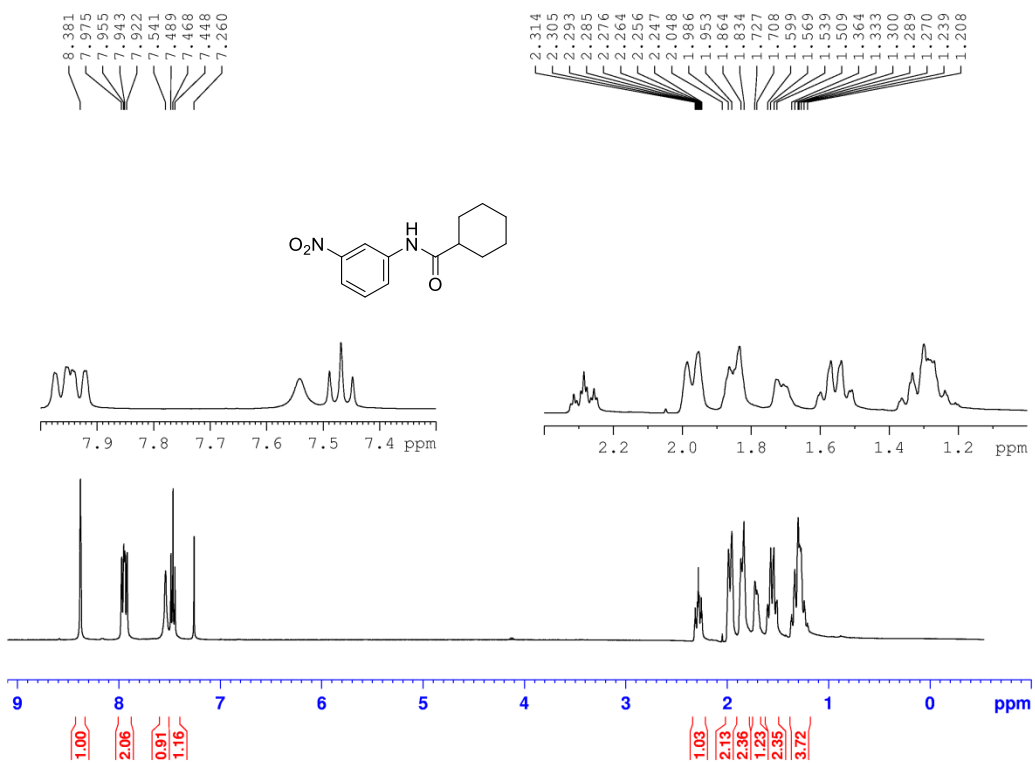




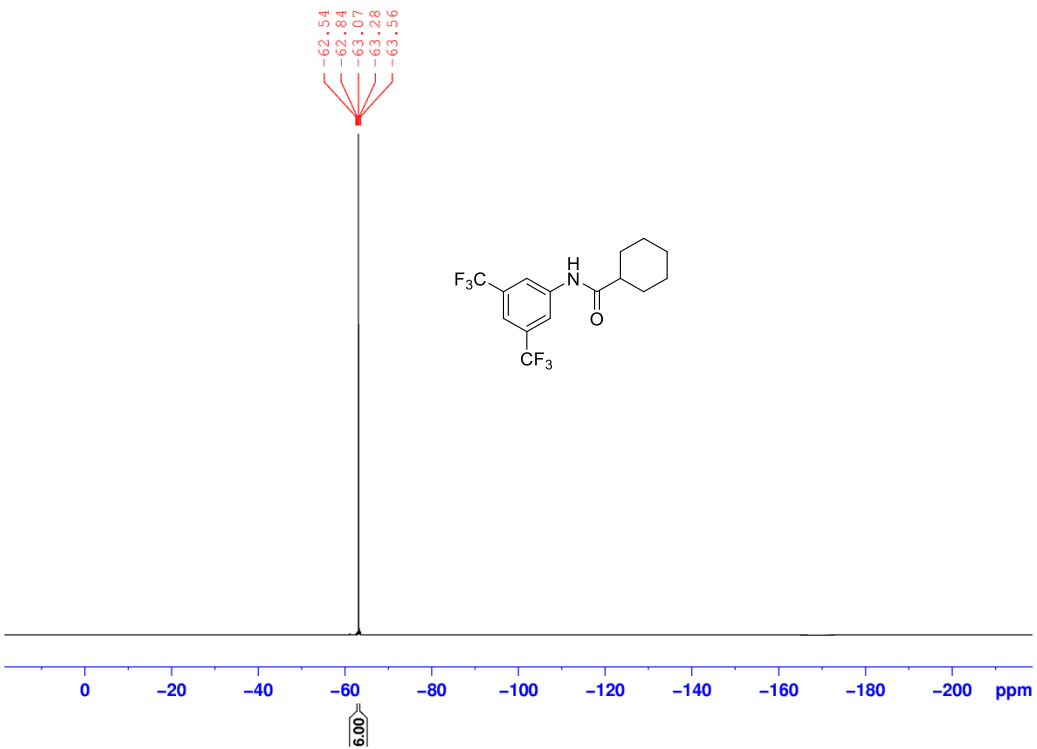
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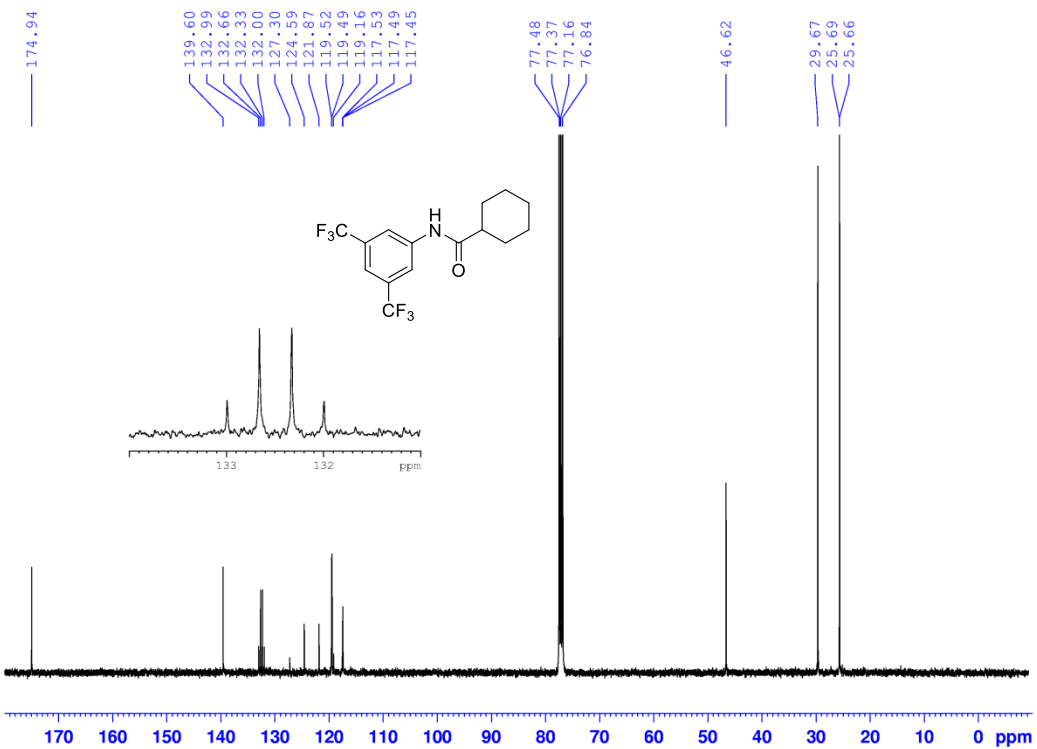
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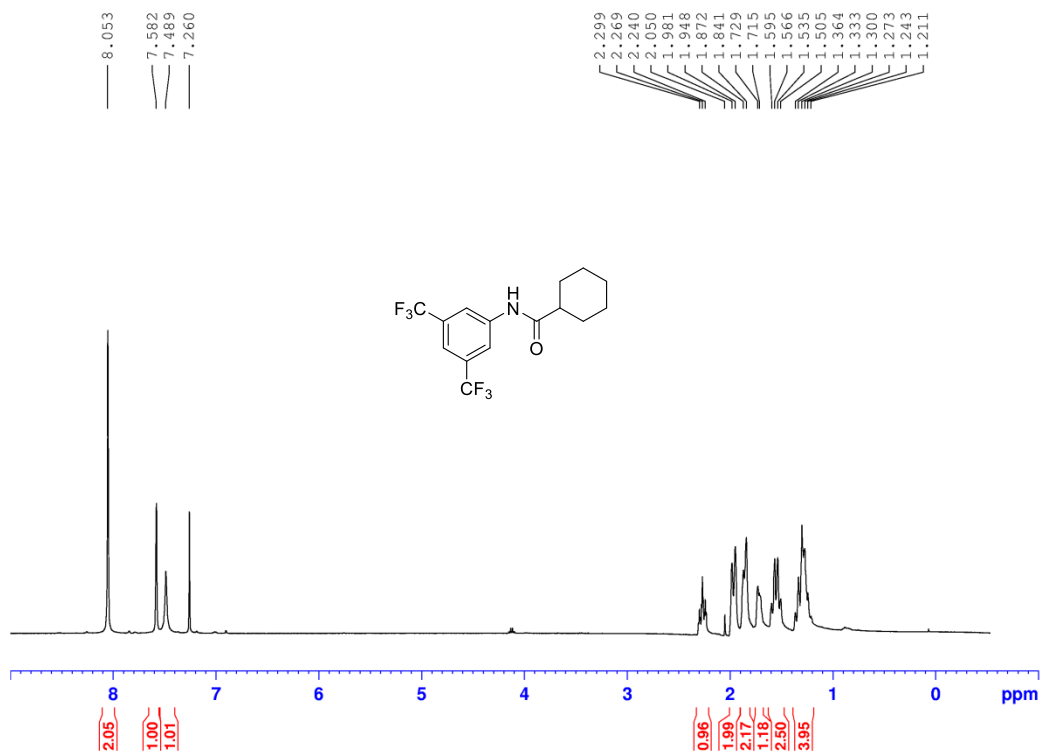
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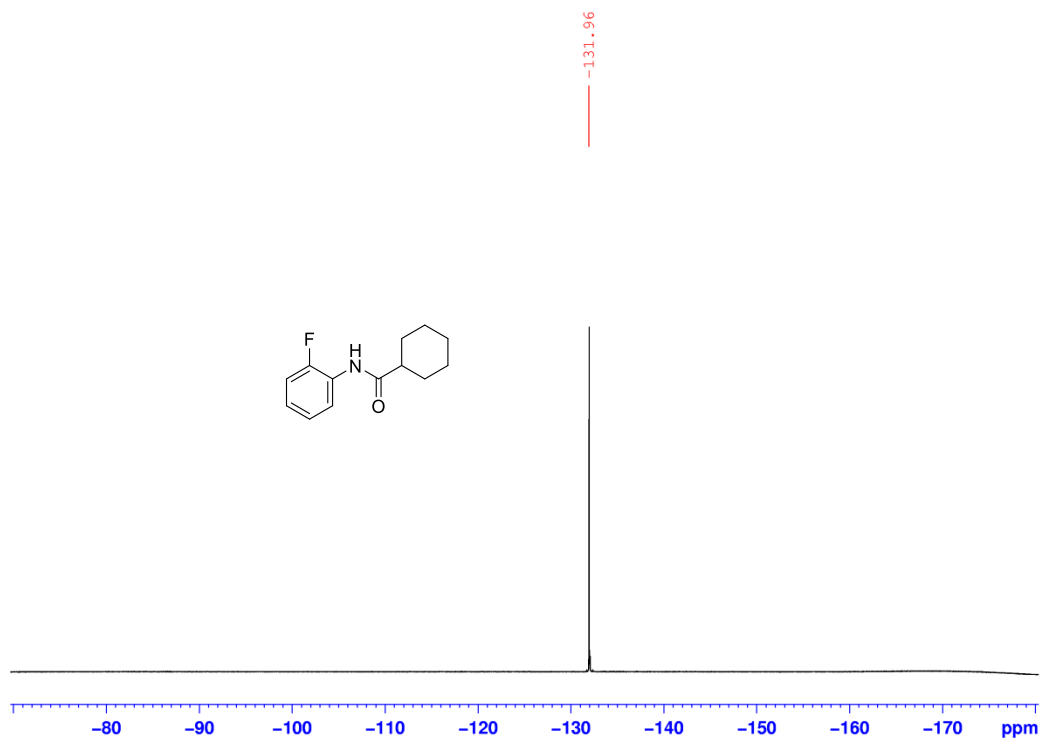
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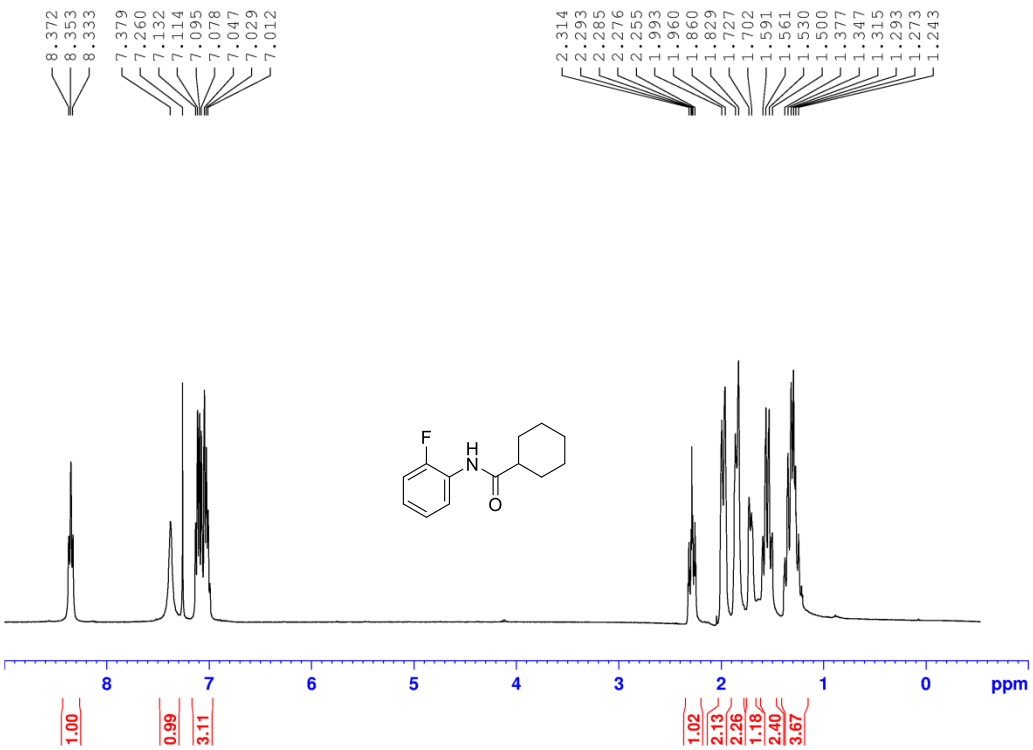
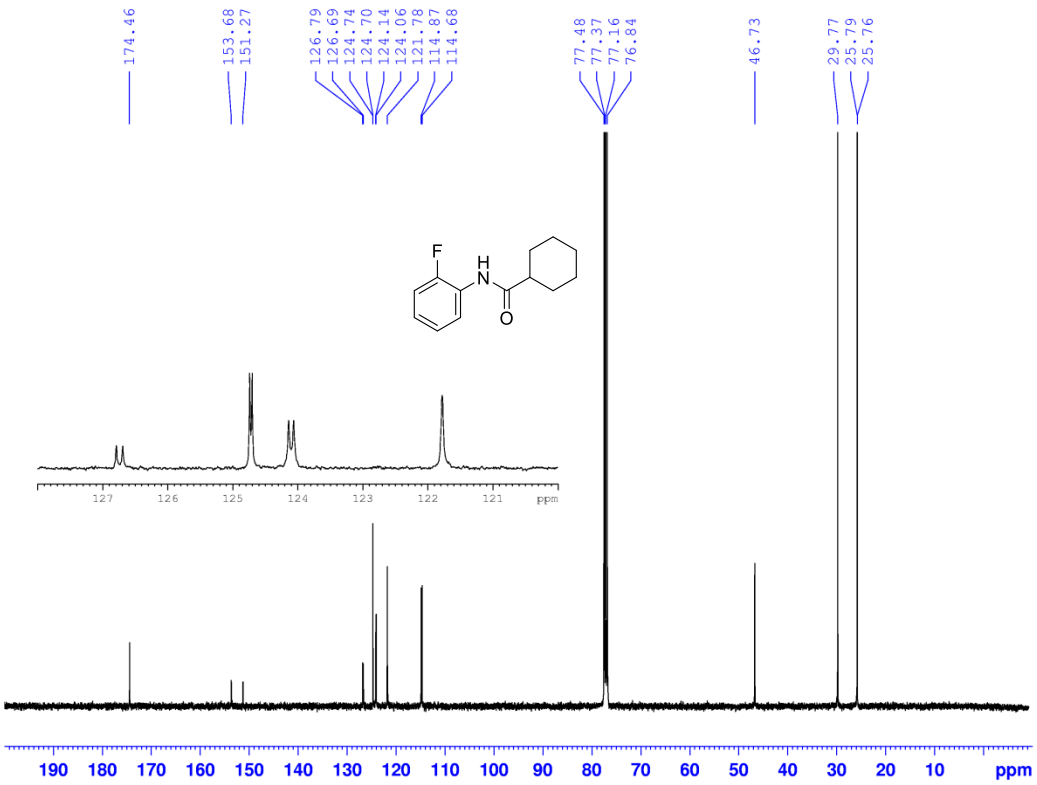


HNMR M013

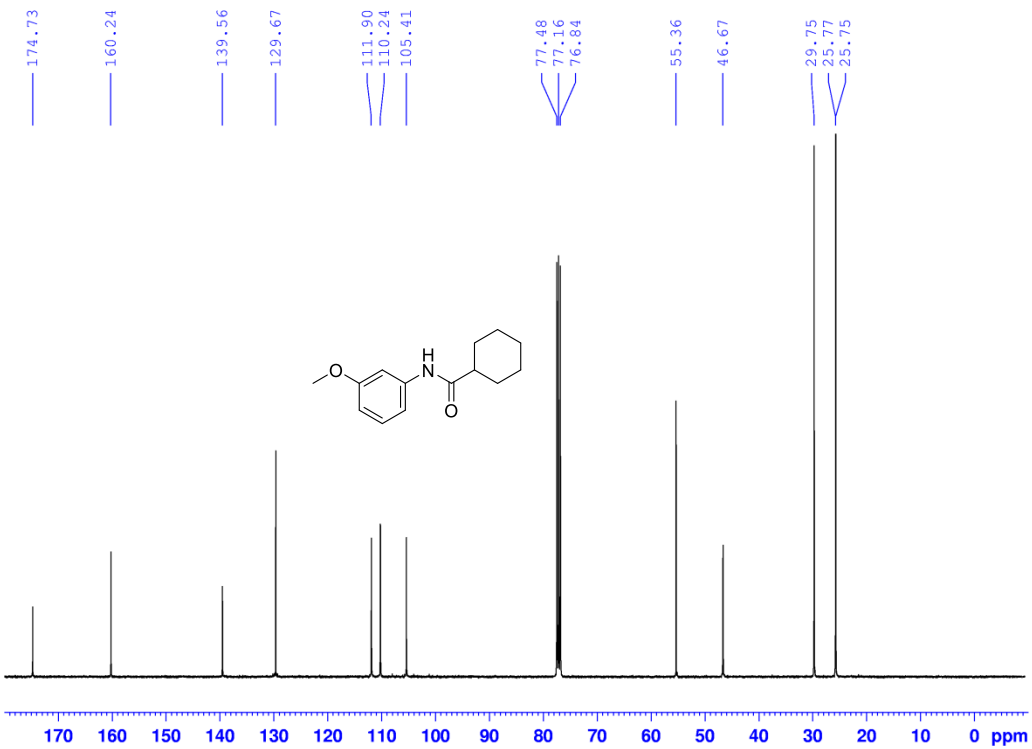


F19, CDCl3

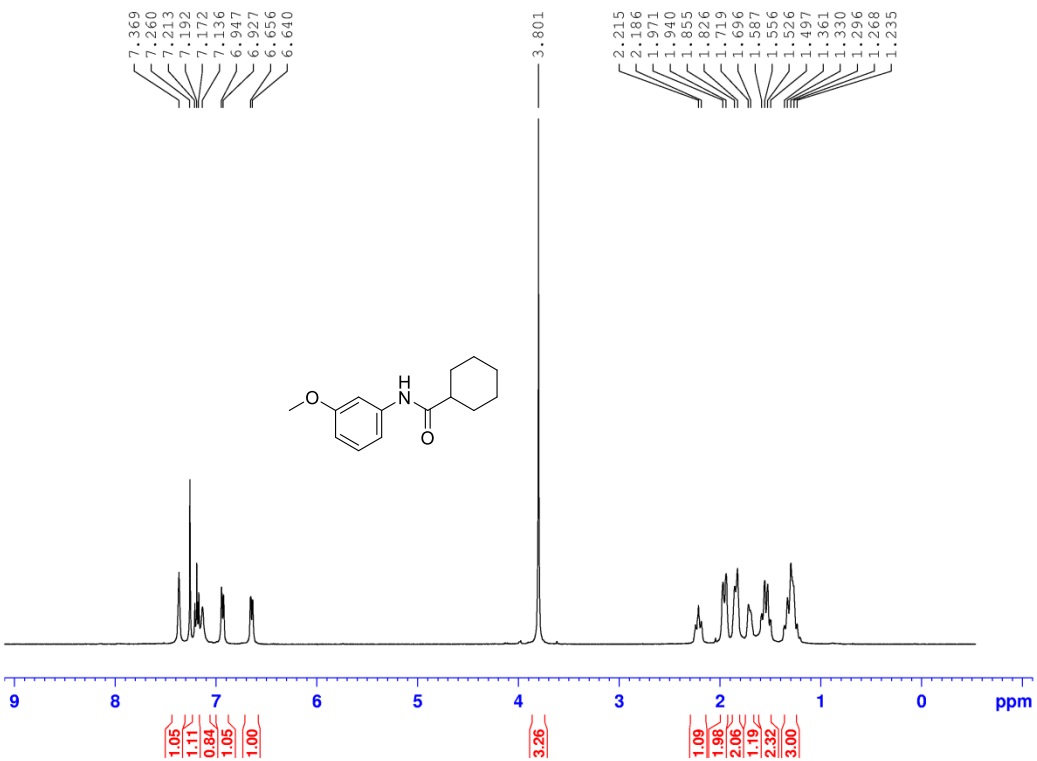


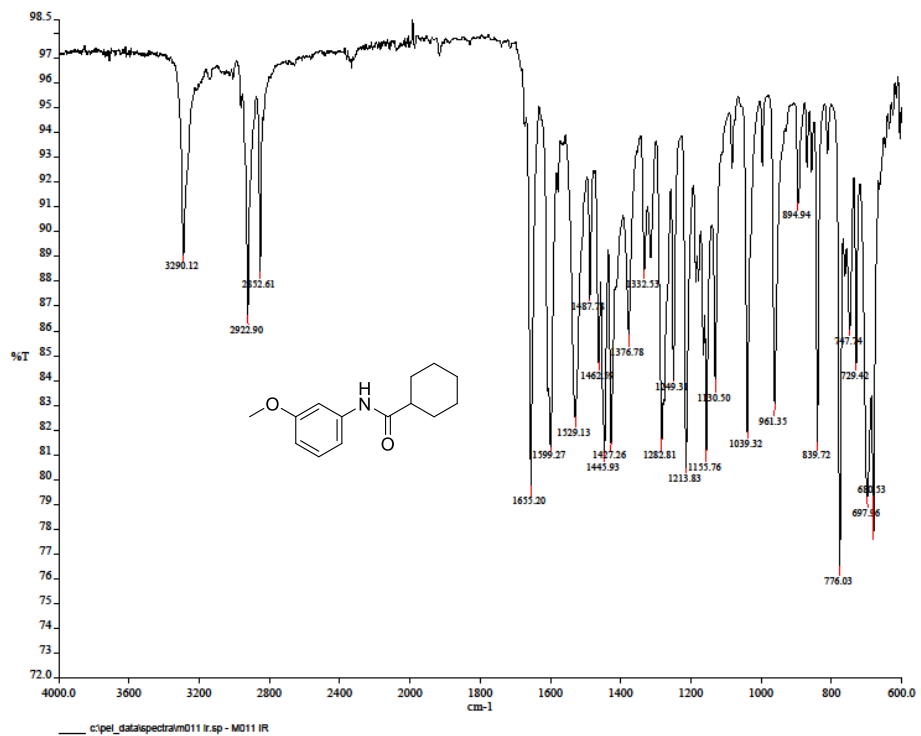


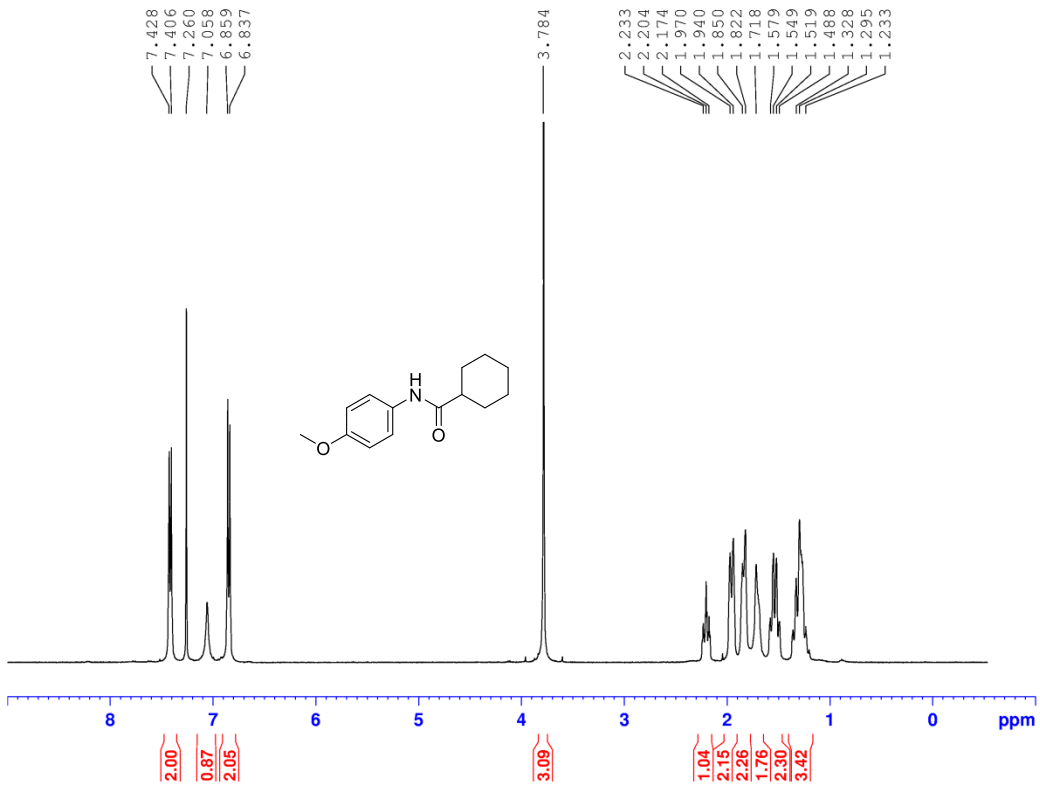
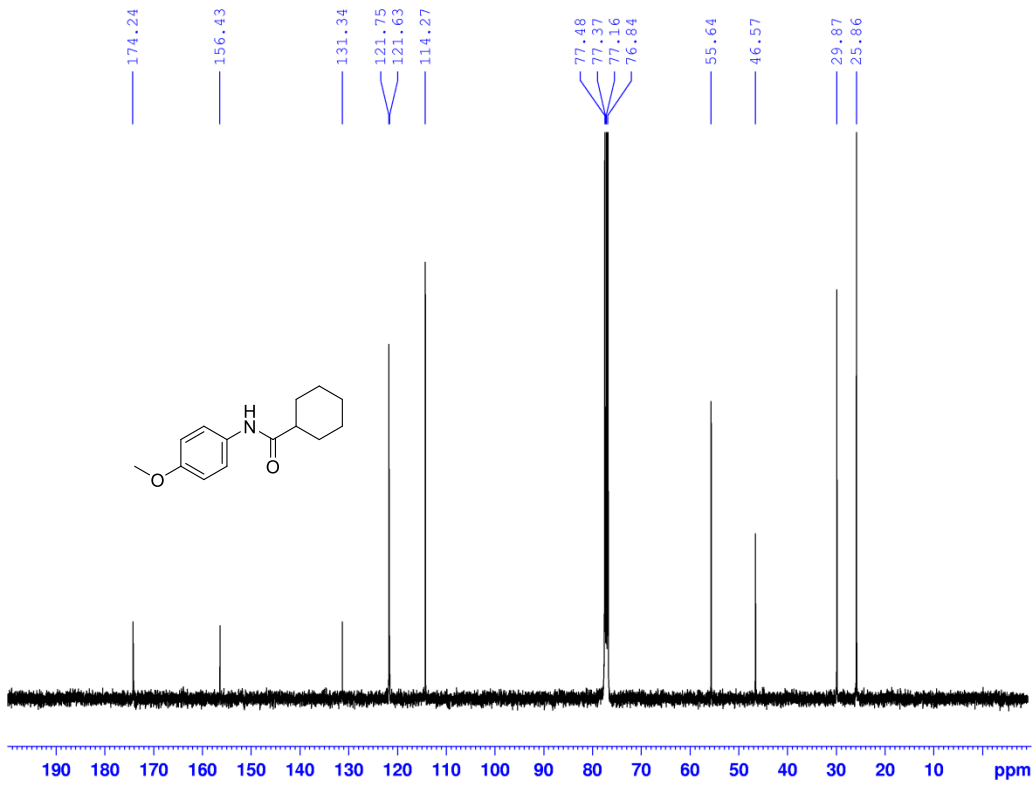
C13NMR M011



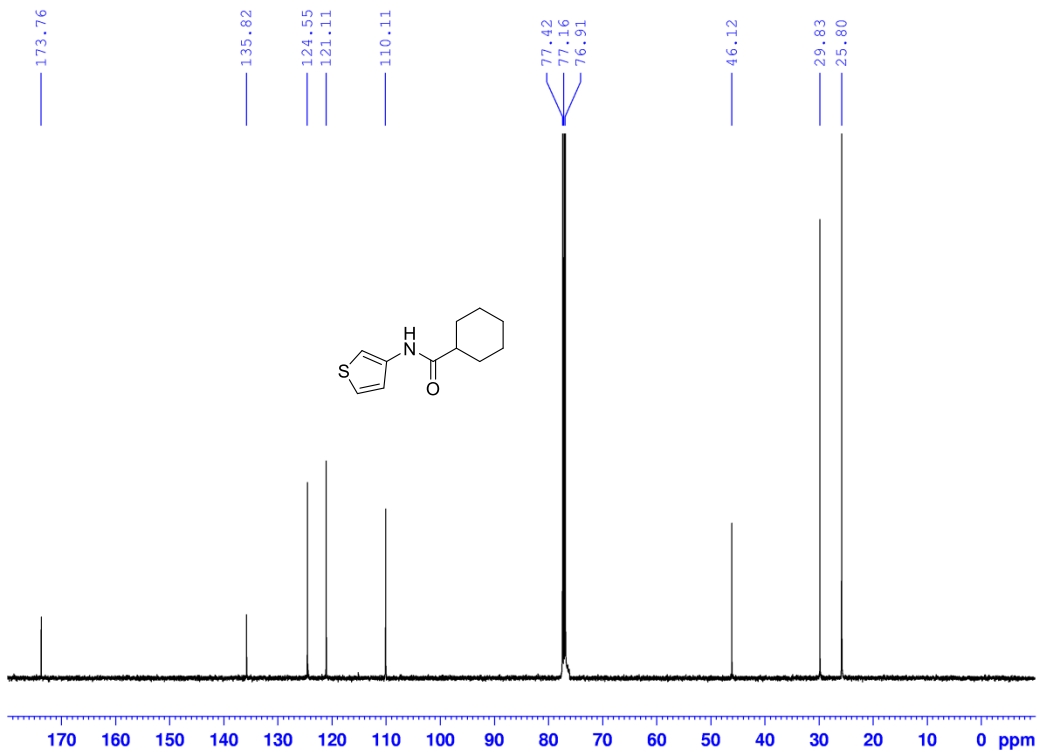
HNMR M011



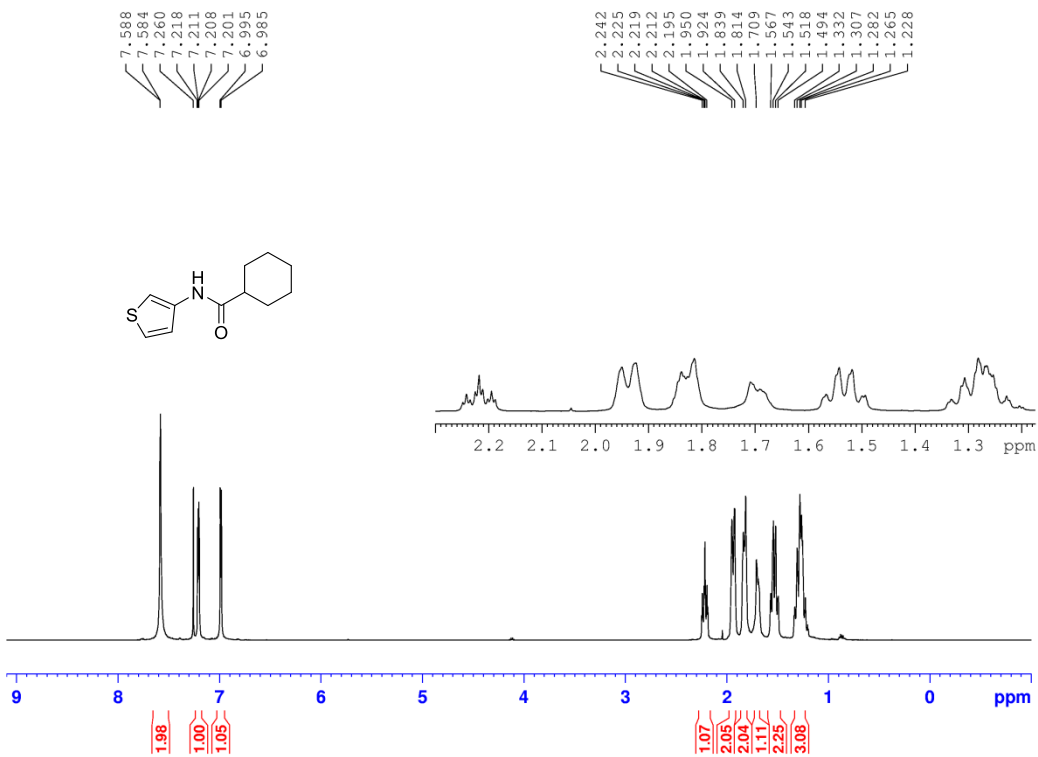


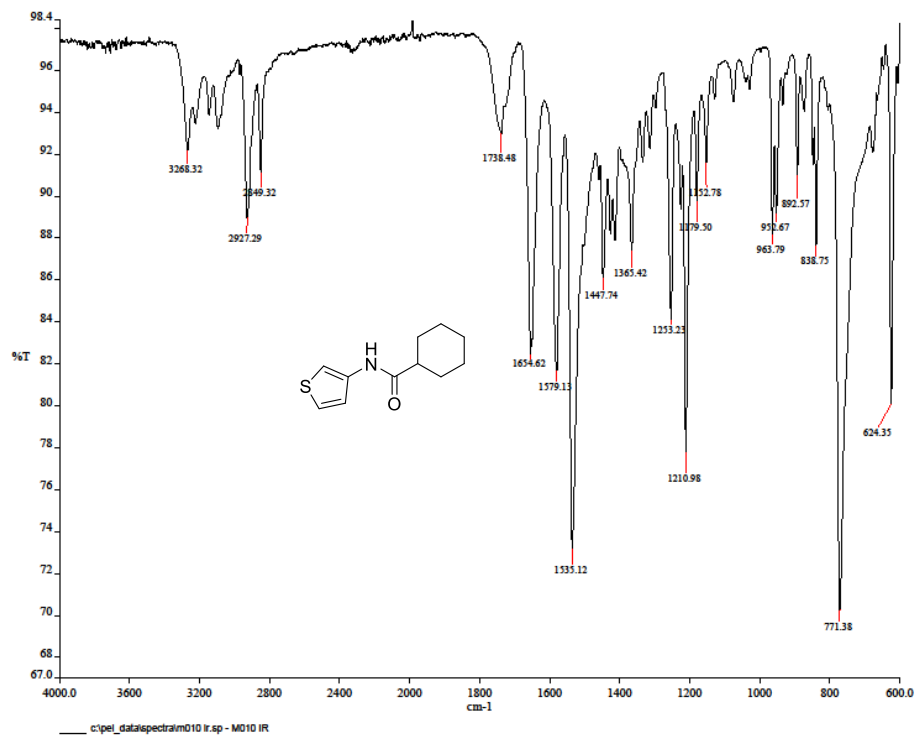


C13NMR M010

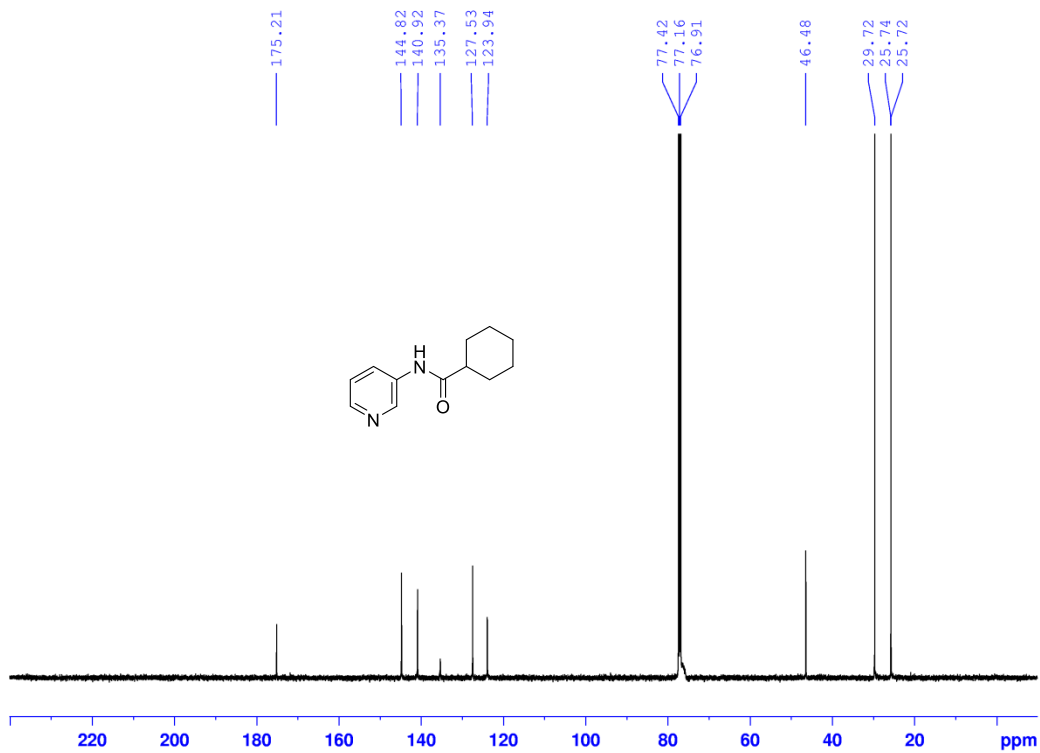


HNMR M010

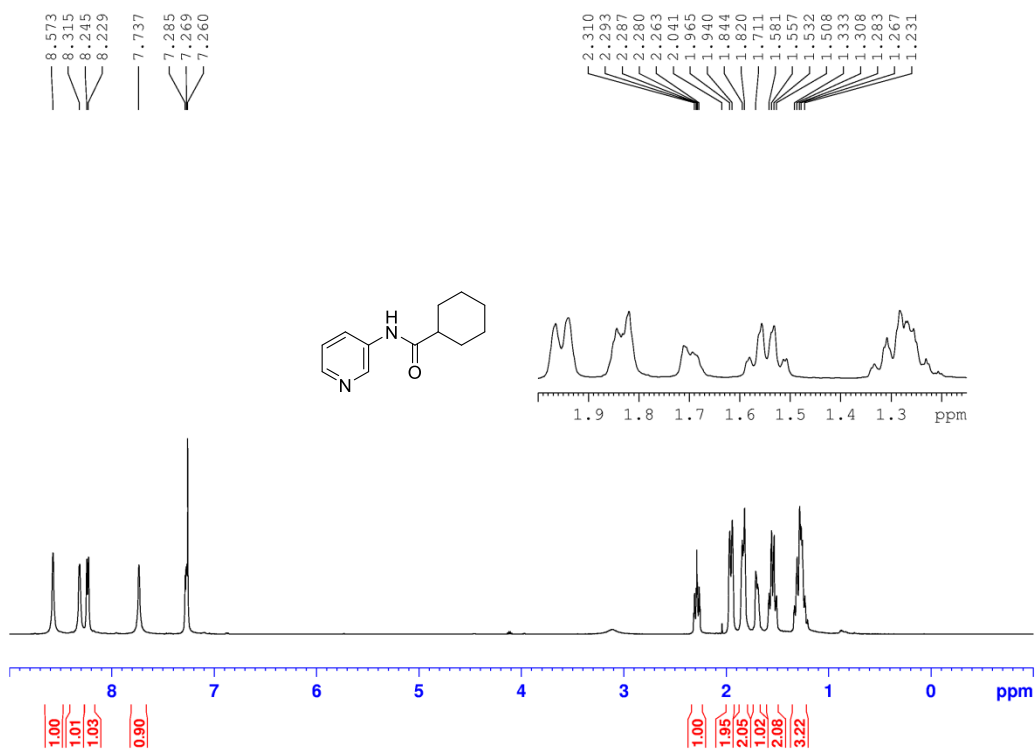


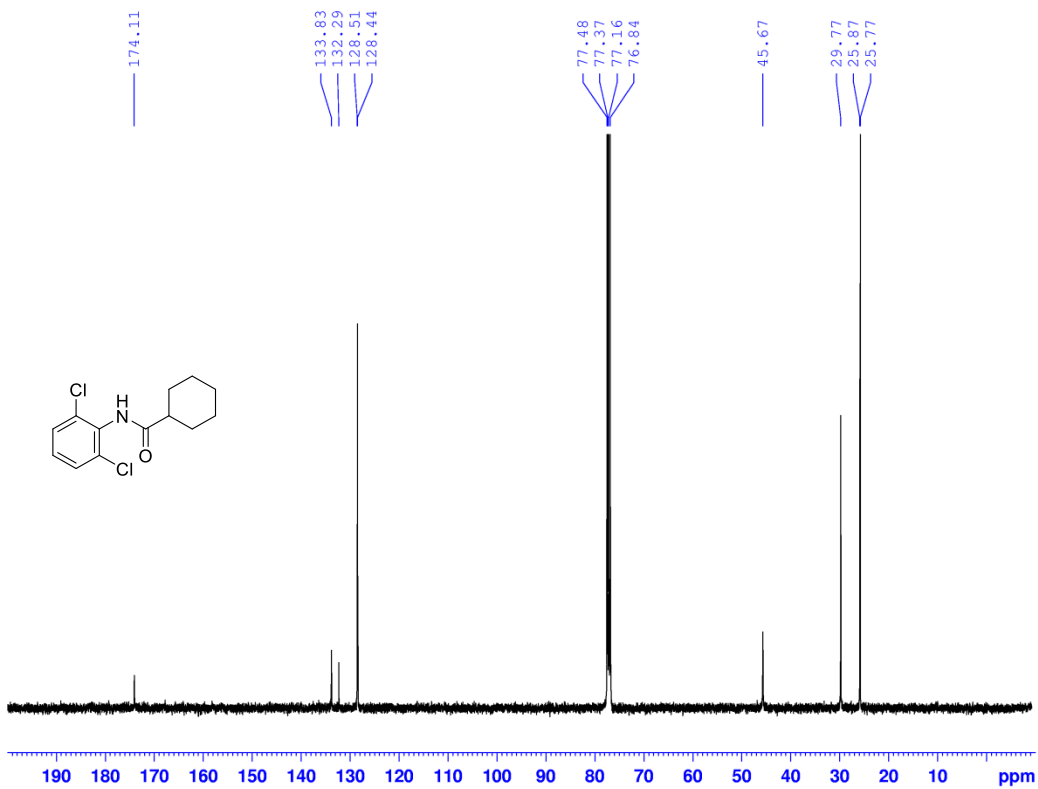


C13NMR M009

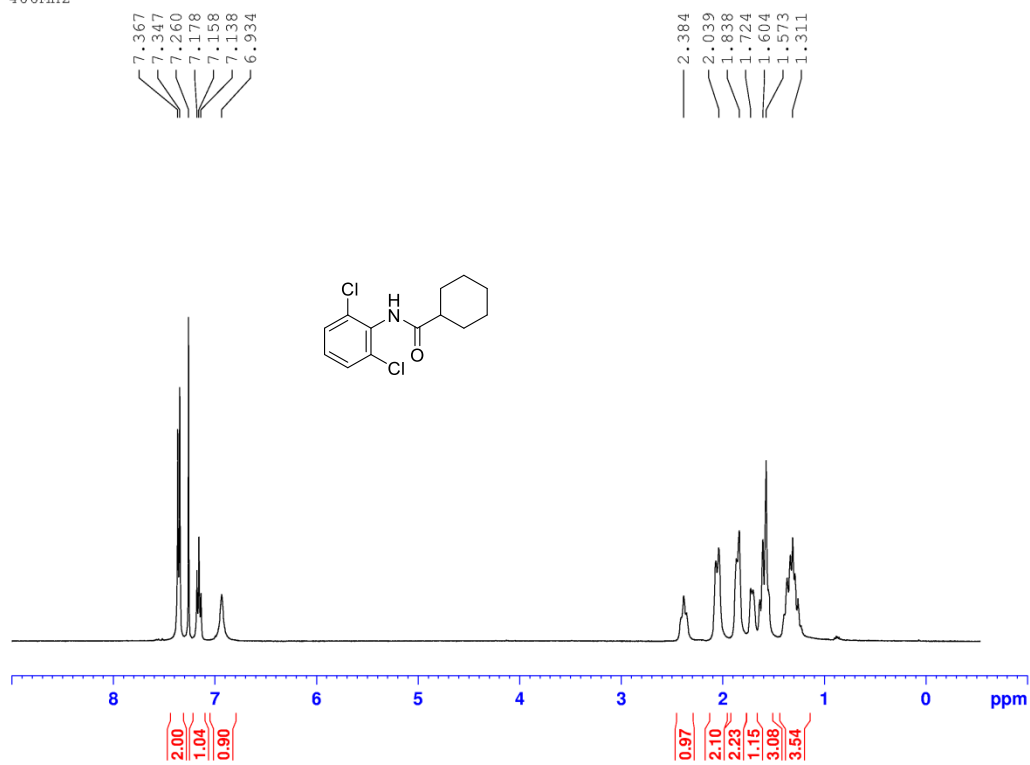


HNMR M009

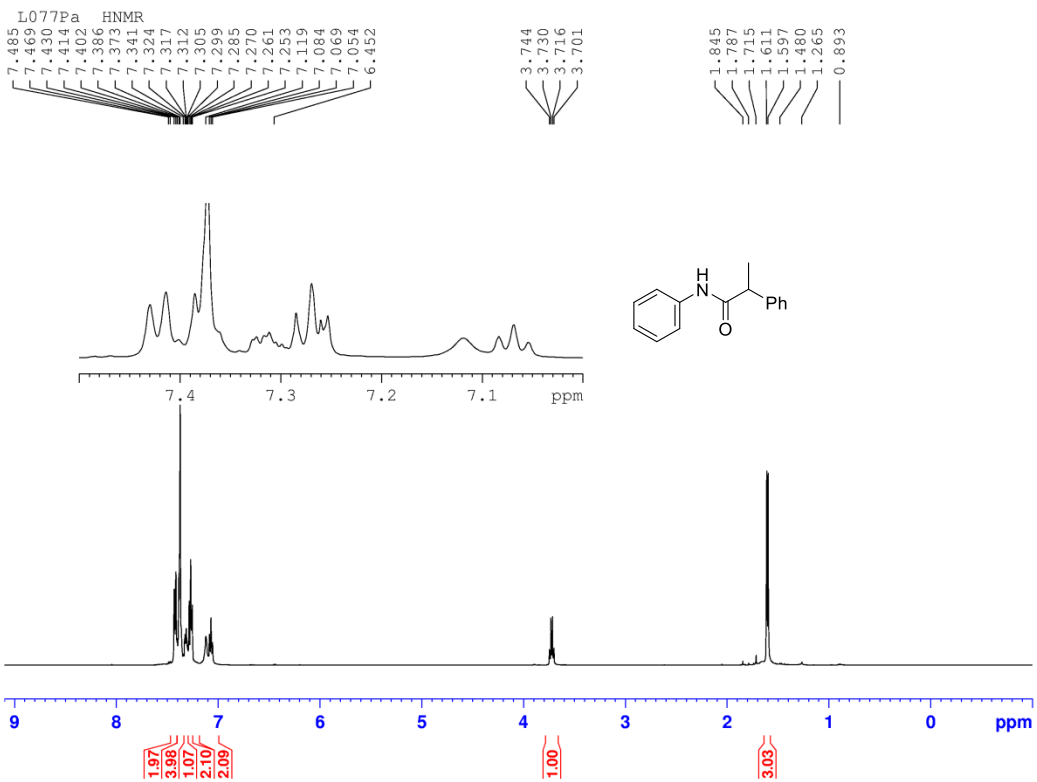
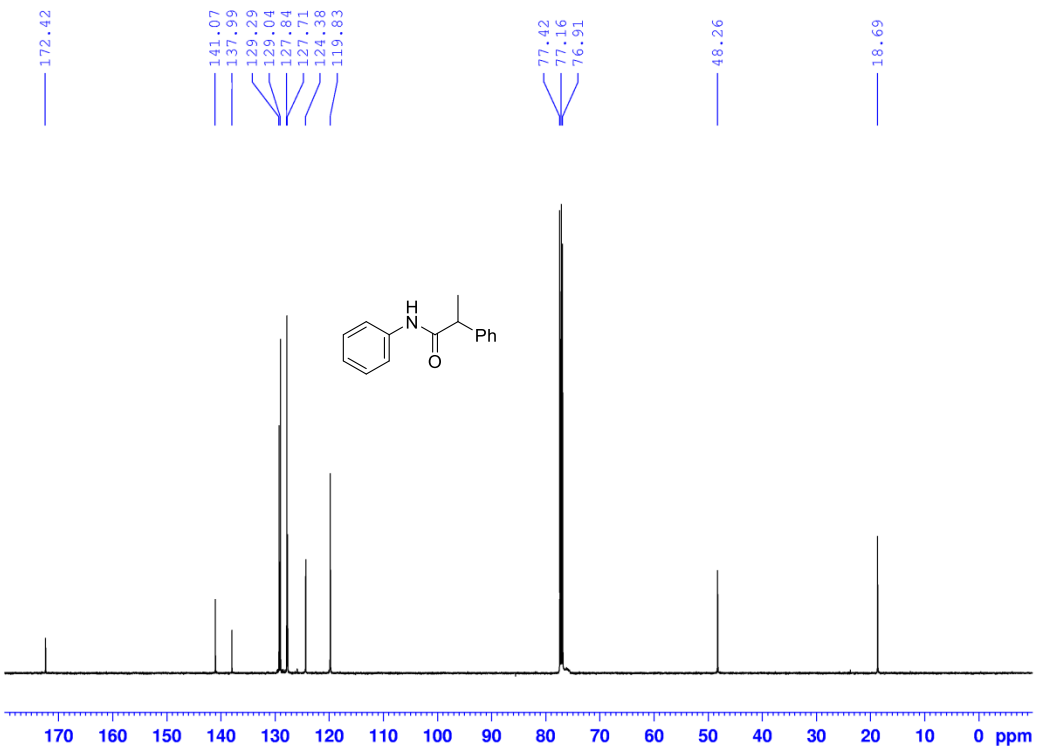




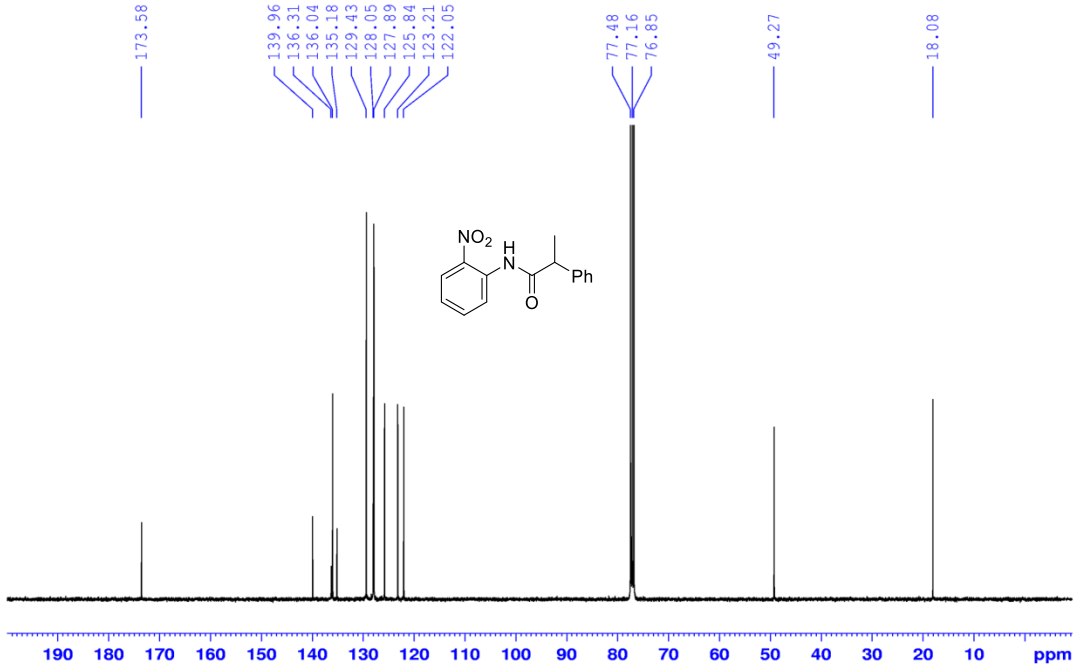
400MHz



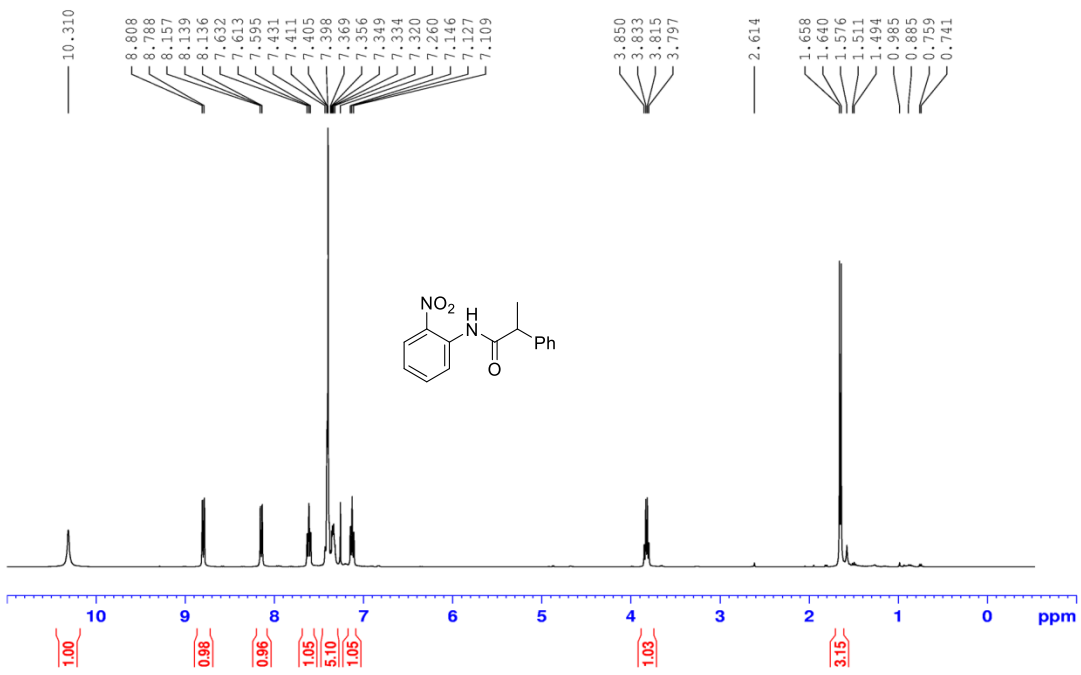
C13NMR L077Pa



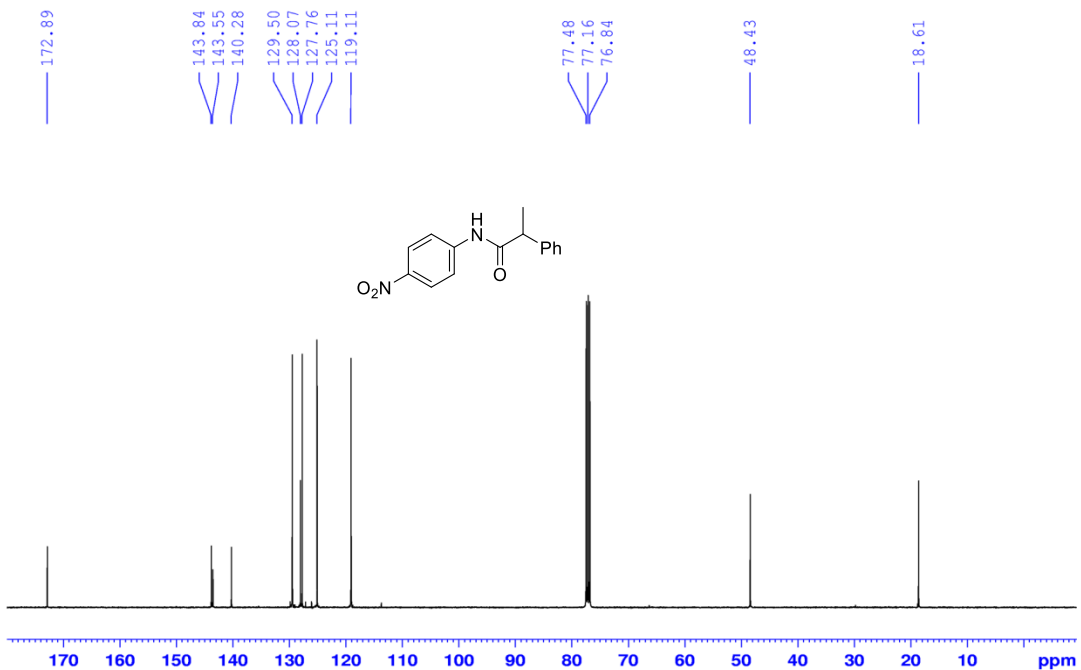
C-NMR L076



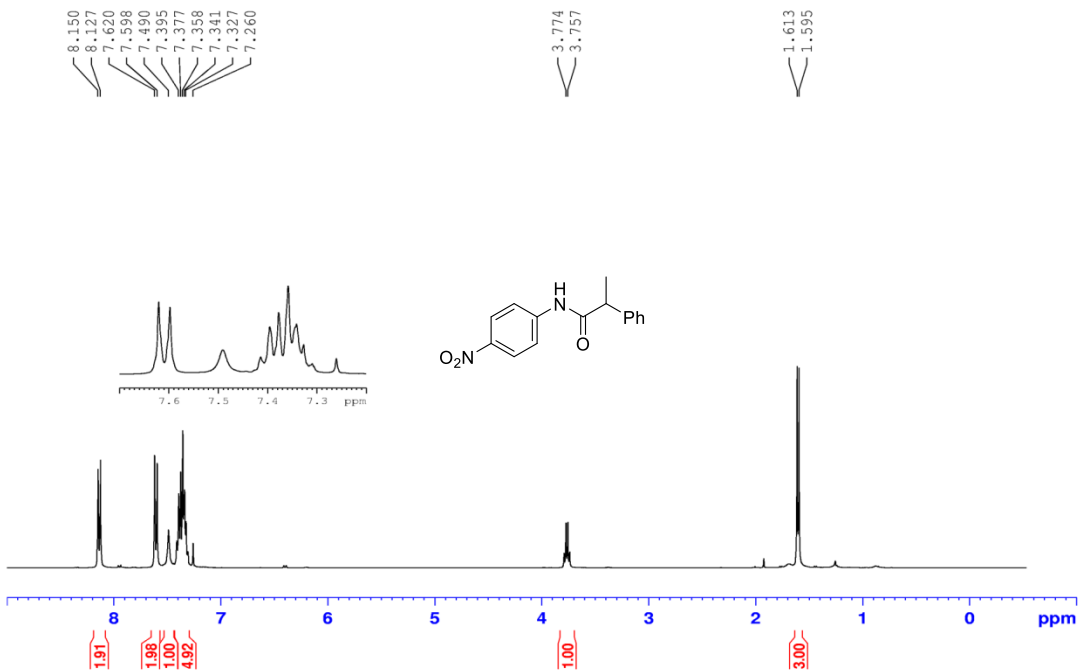
H-NMR L076



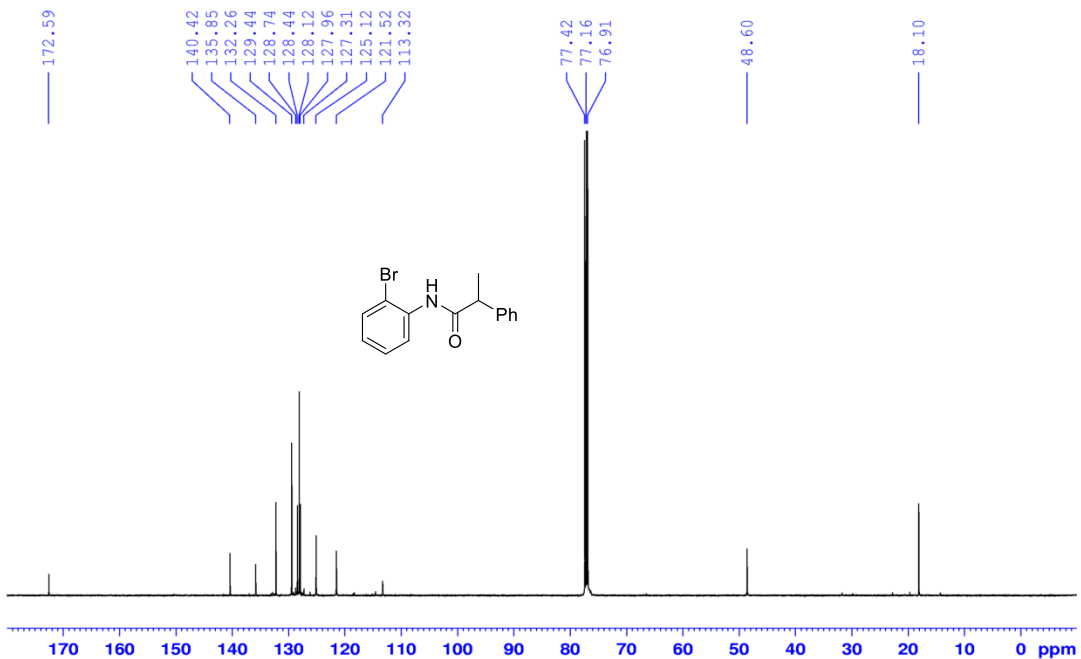
C-NMR L078



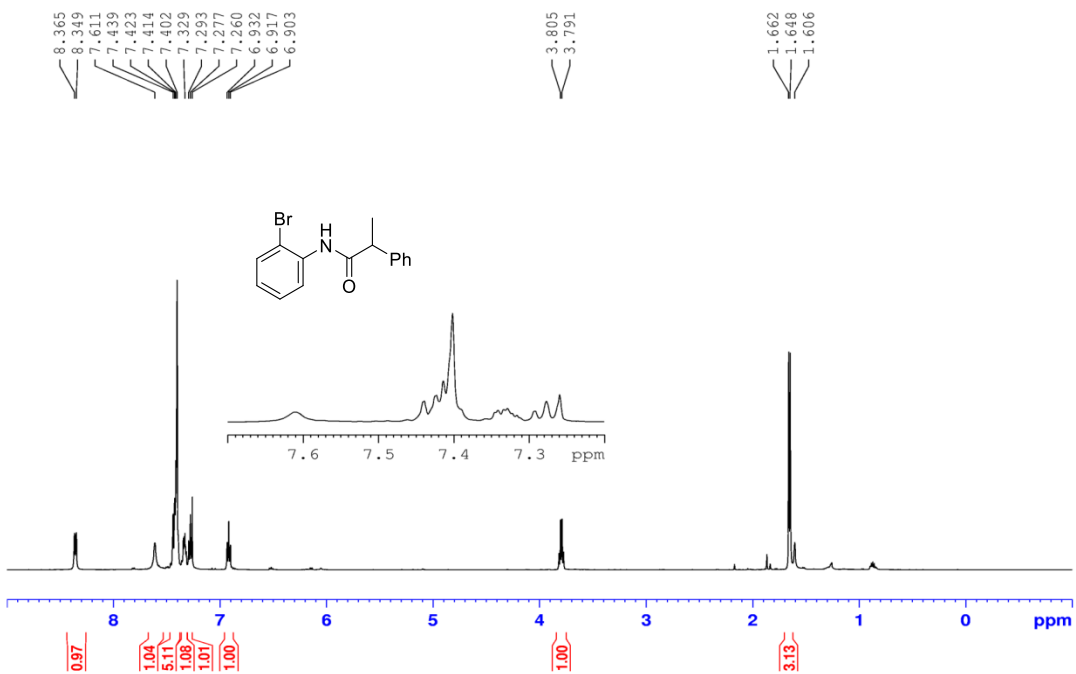
HNMR L078



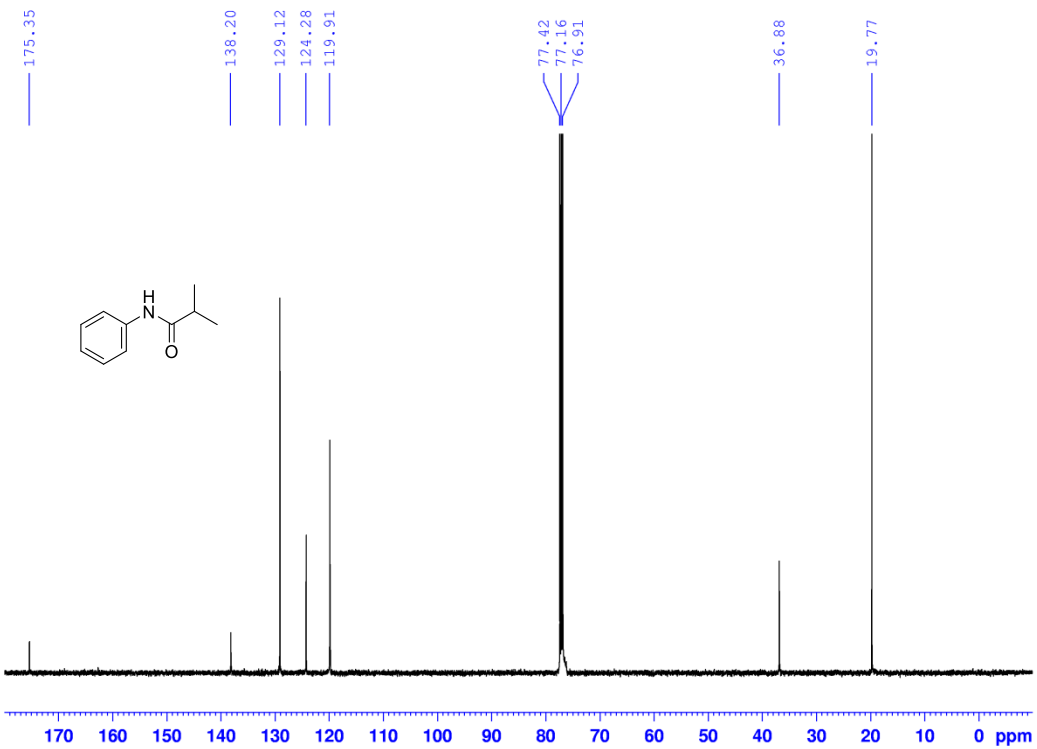
CNMR L082



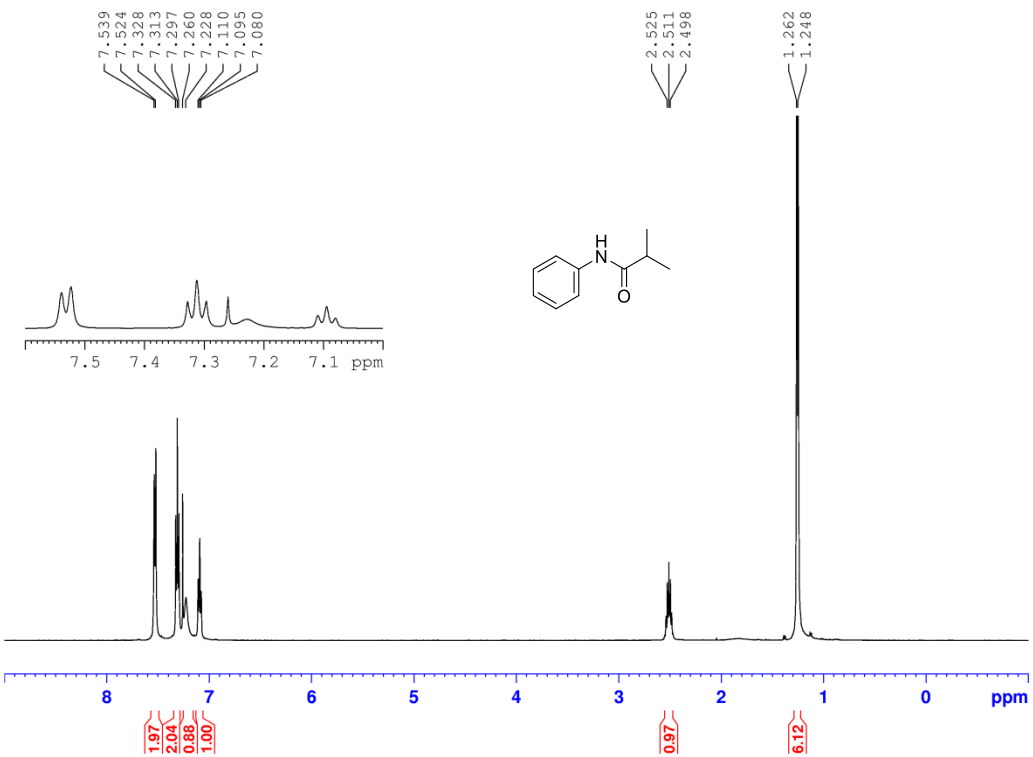
HNMR L082



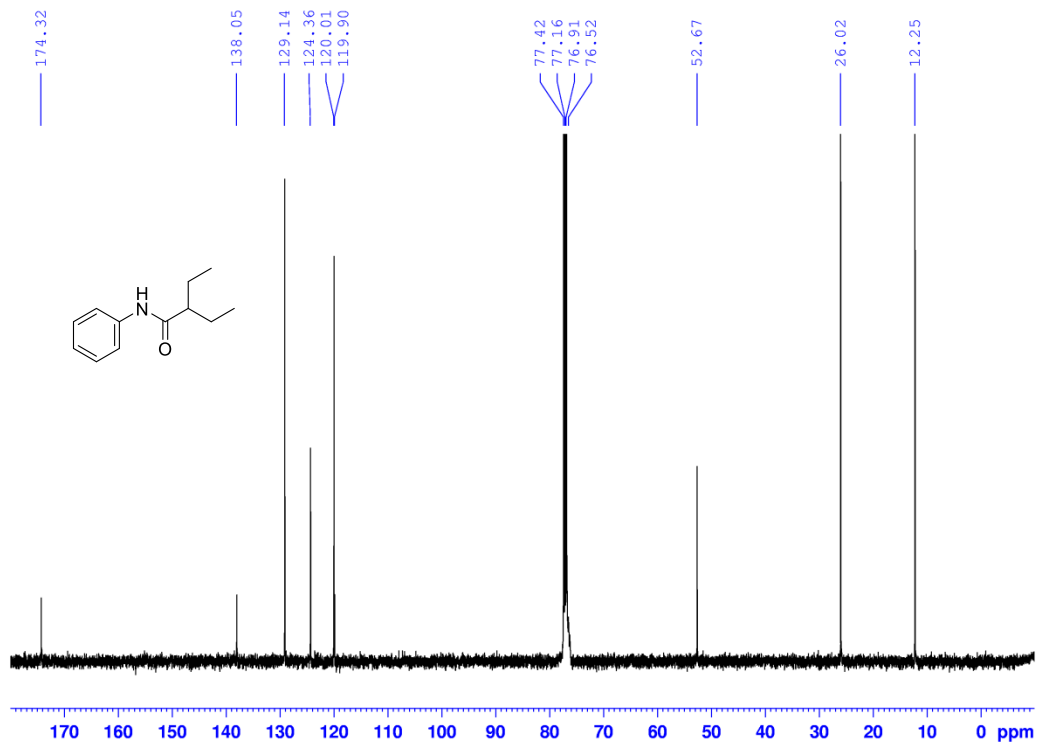
CNMR L102



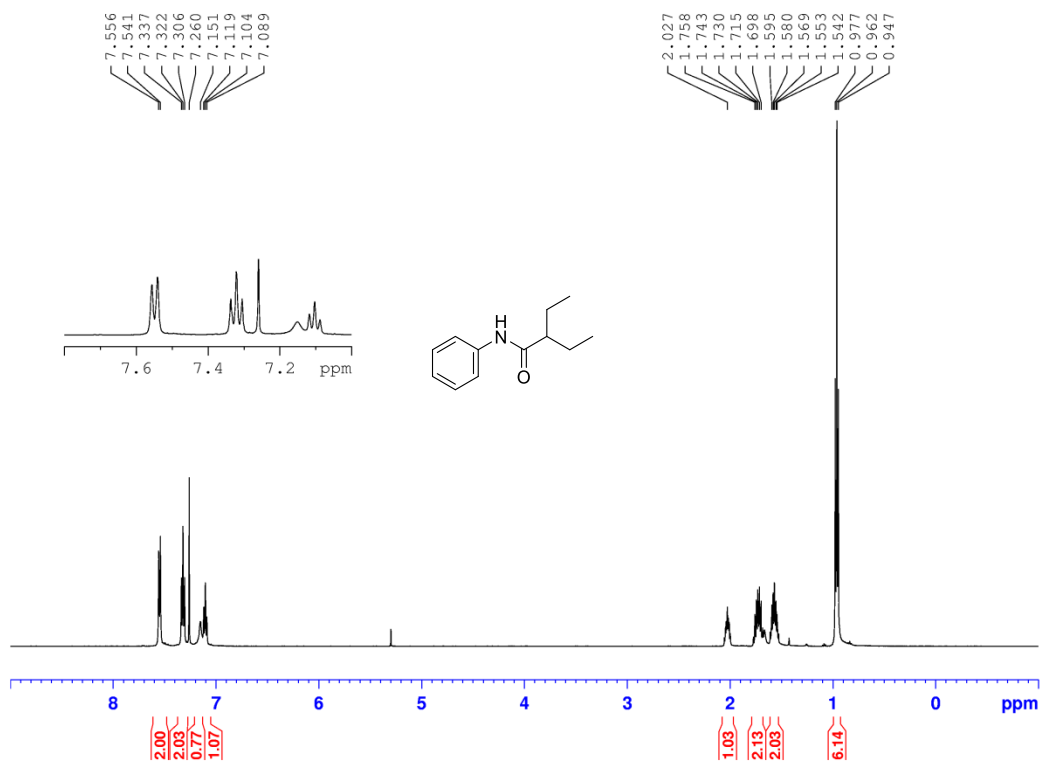
HNMR L102

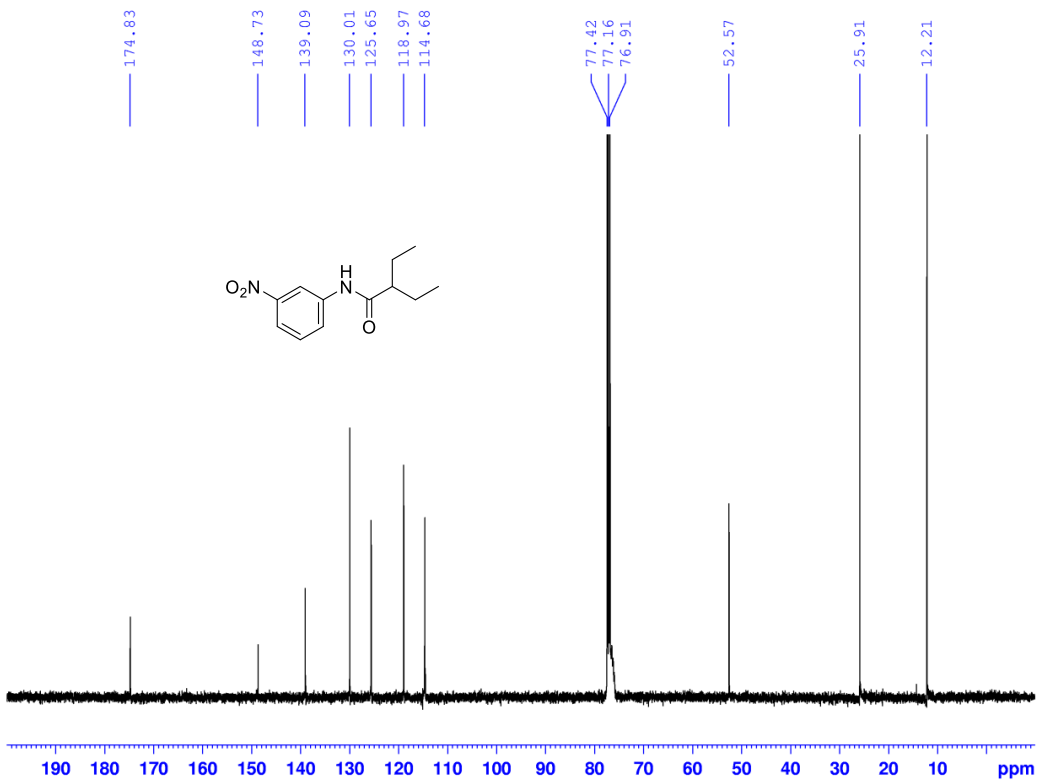
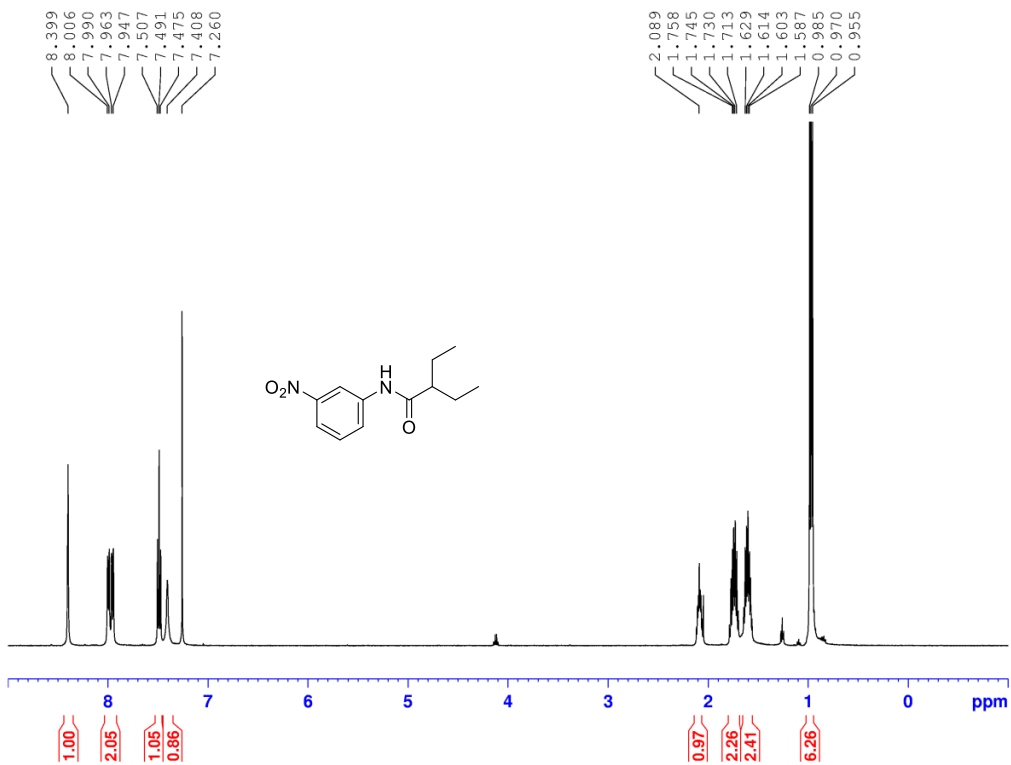


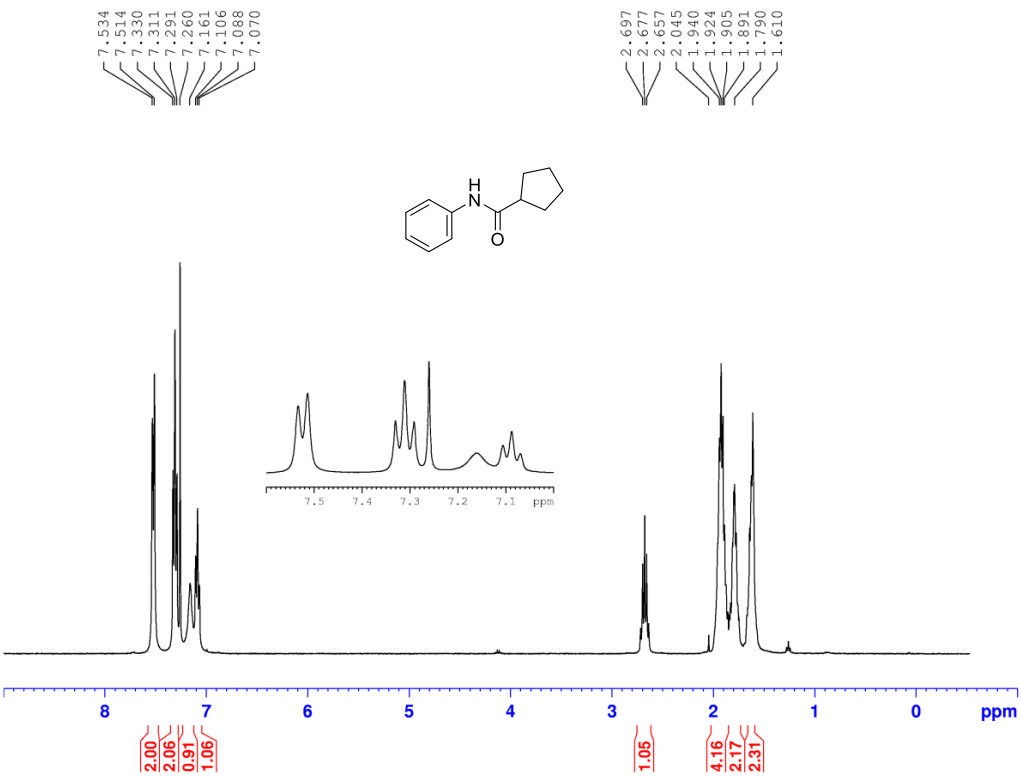
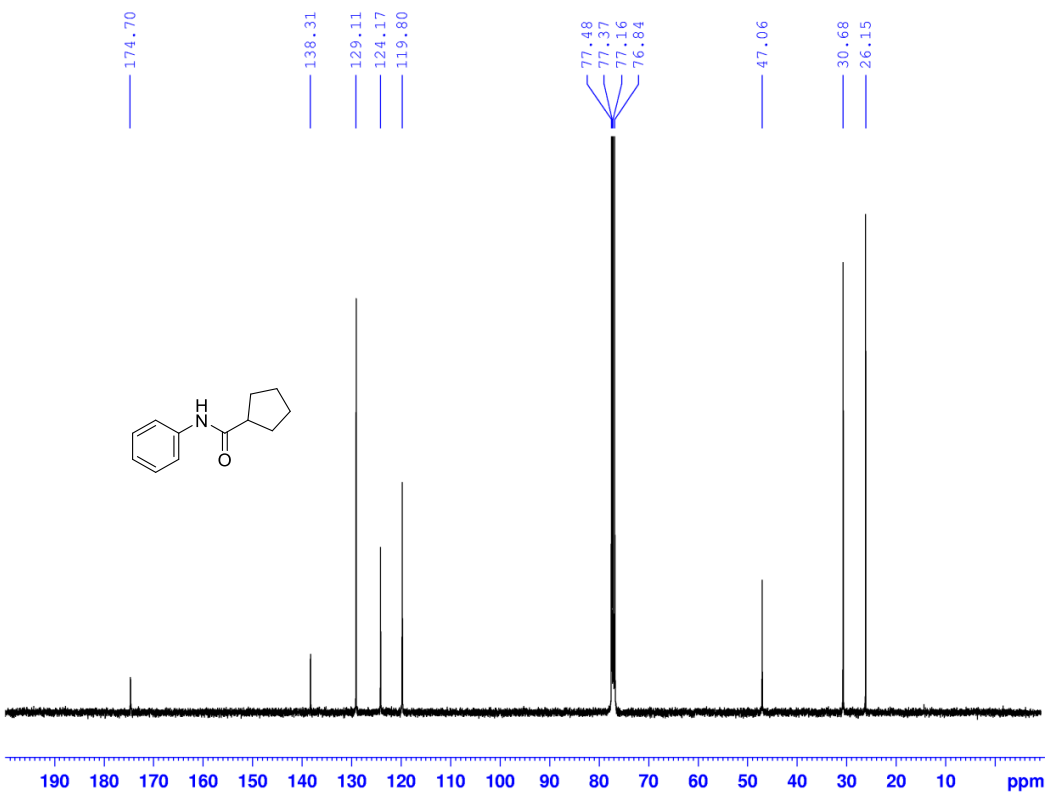
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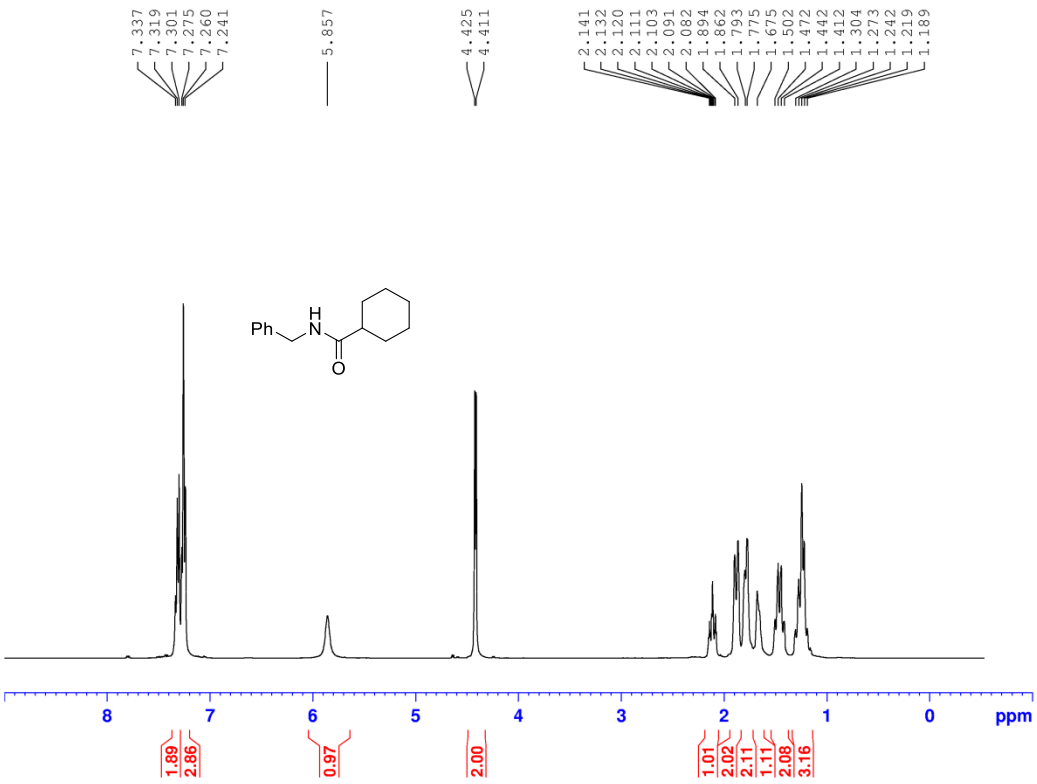
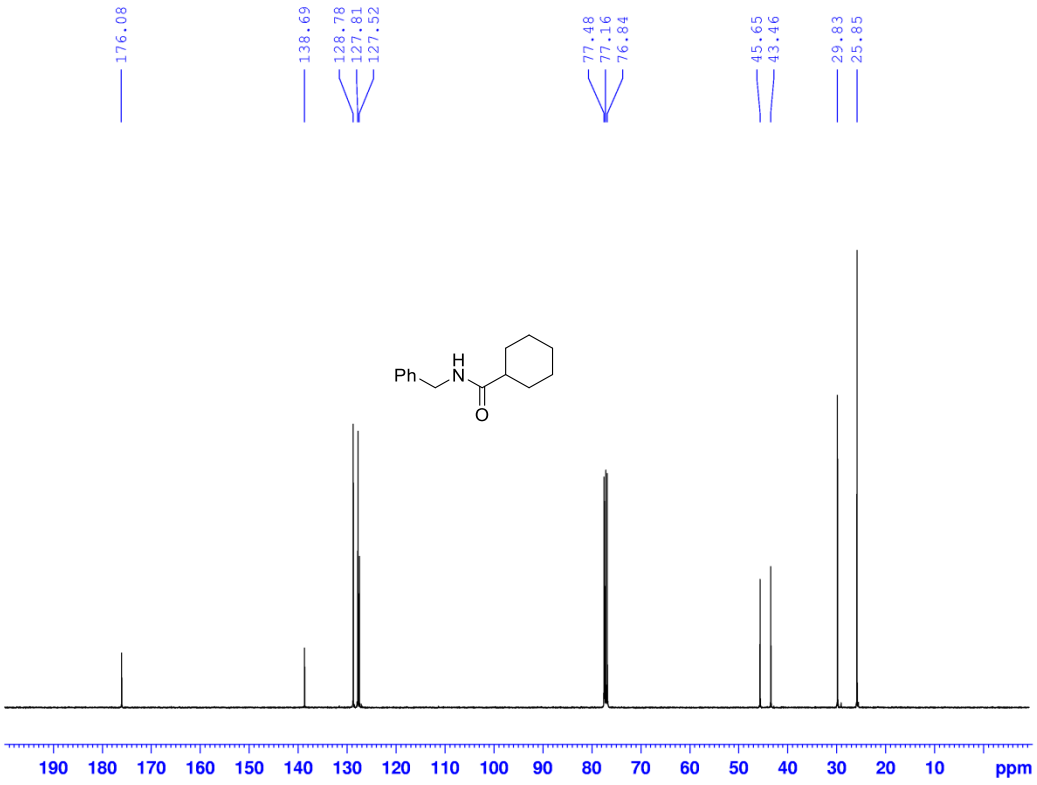


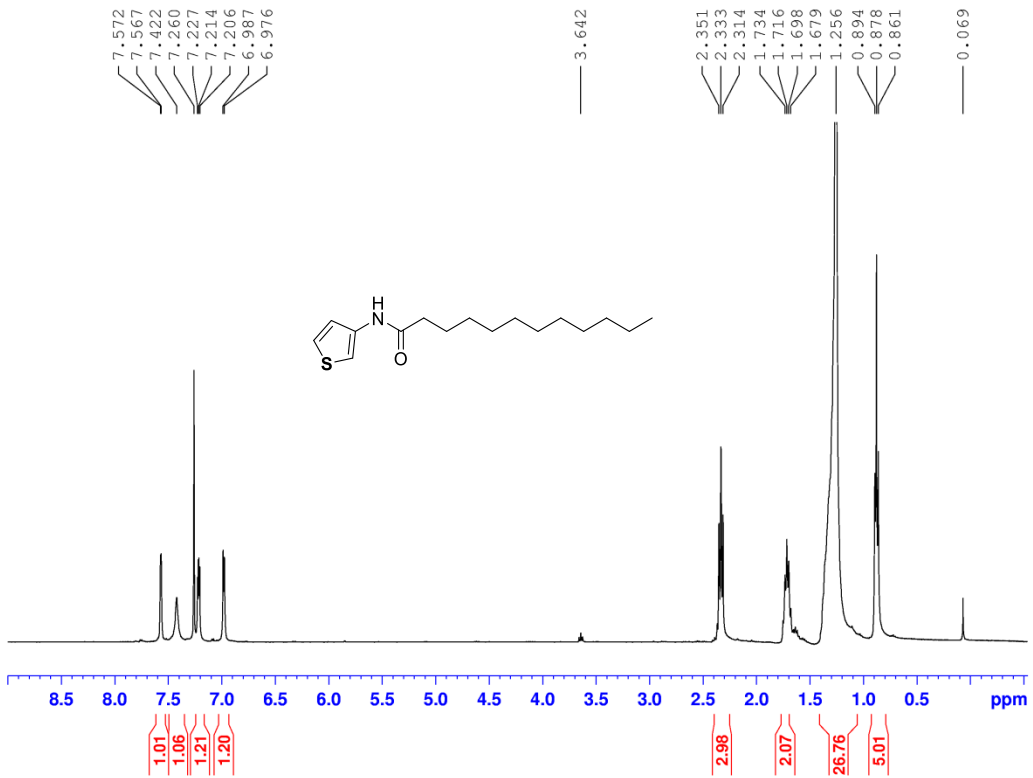
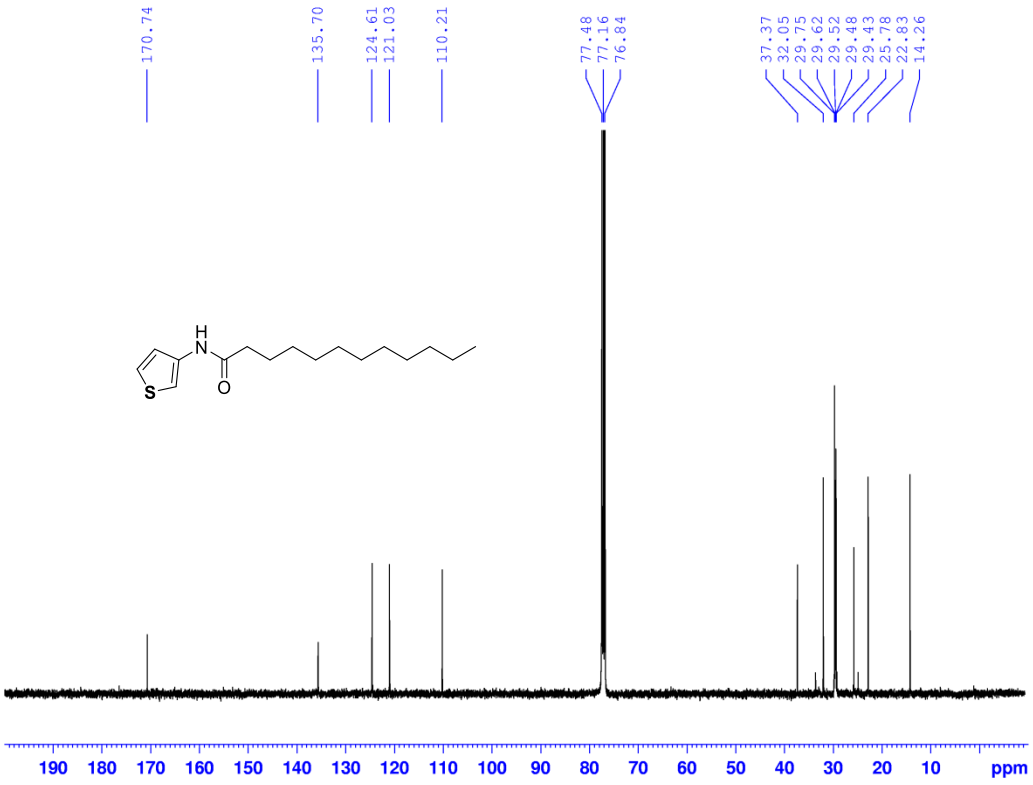
HNMR L100

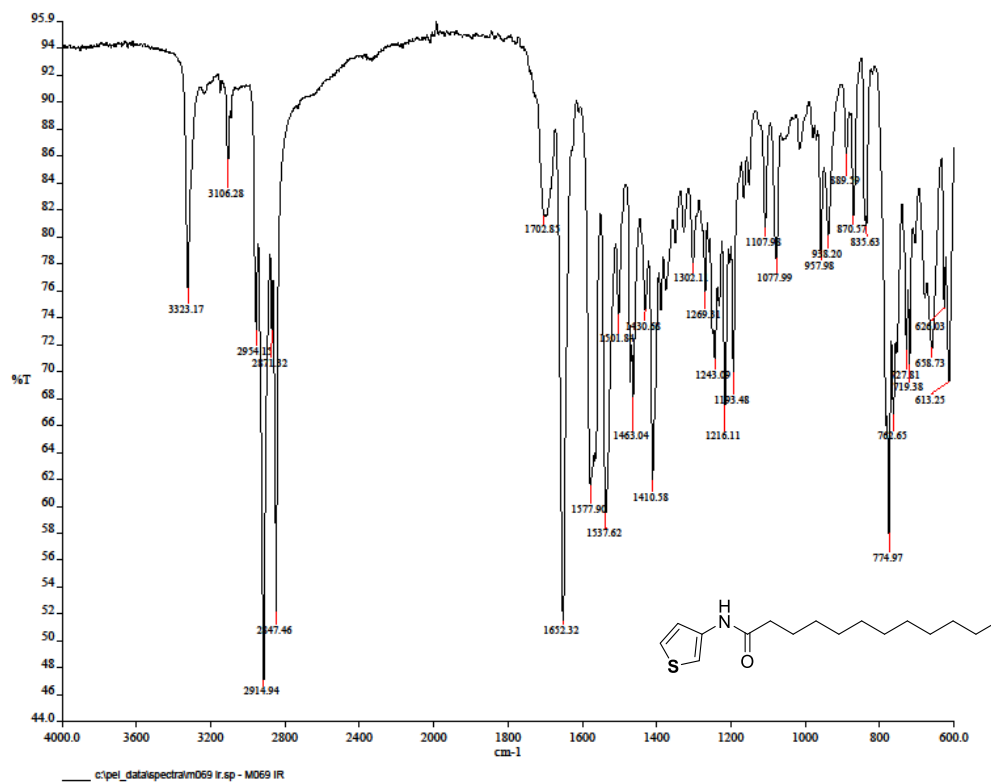


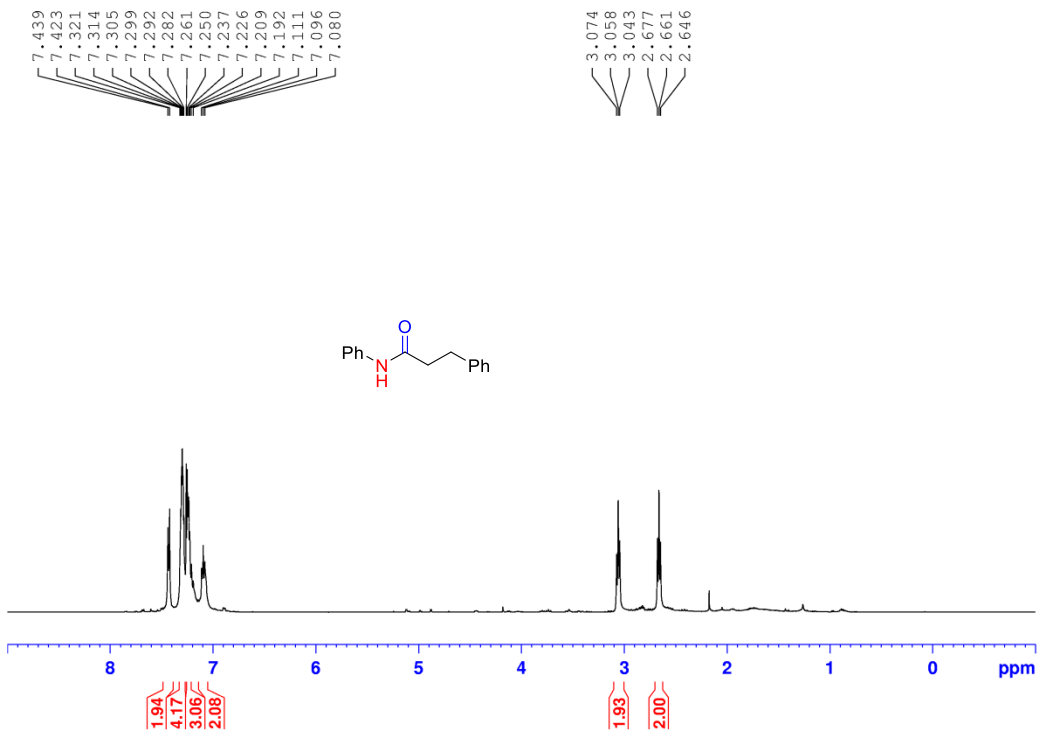
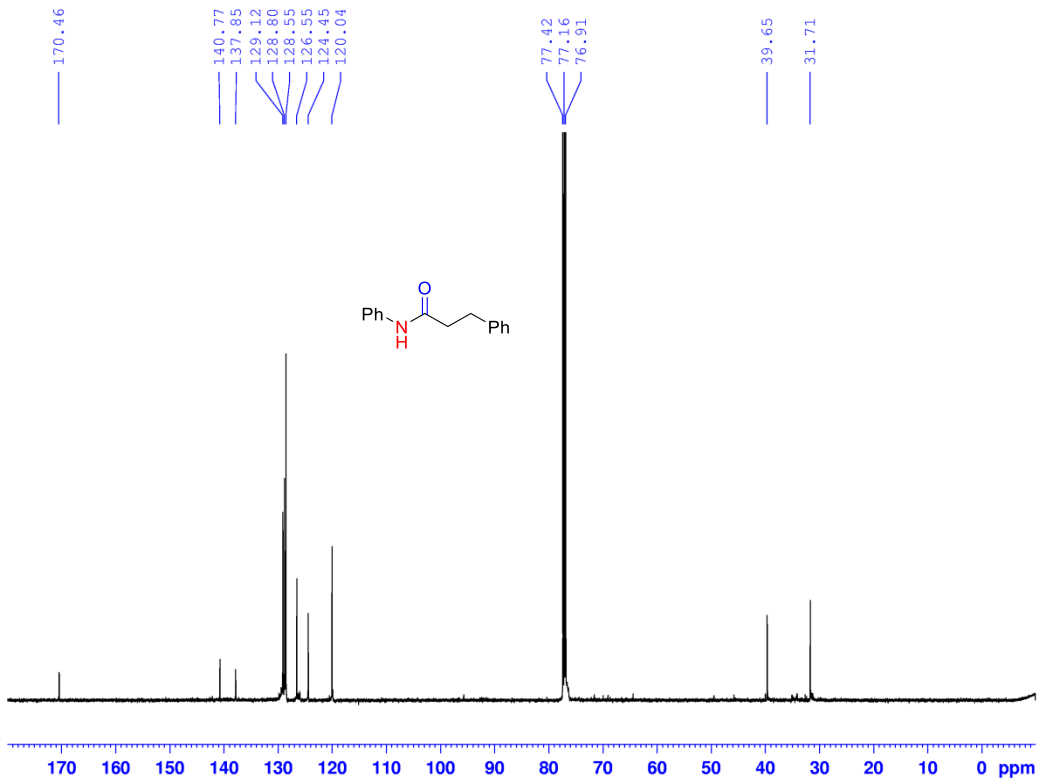


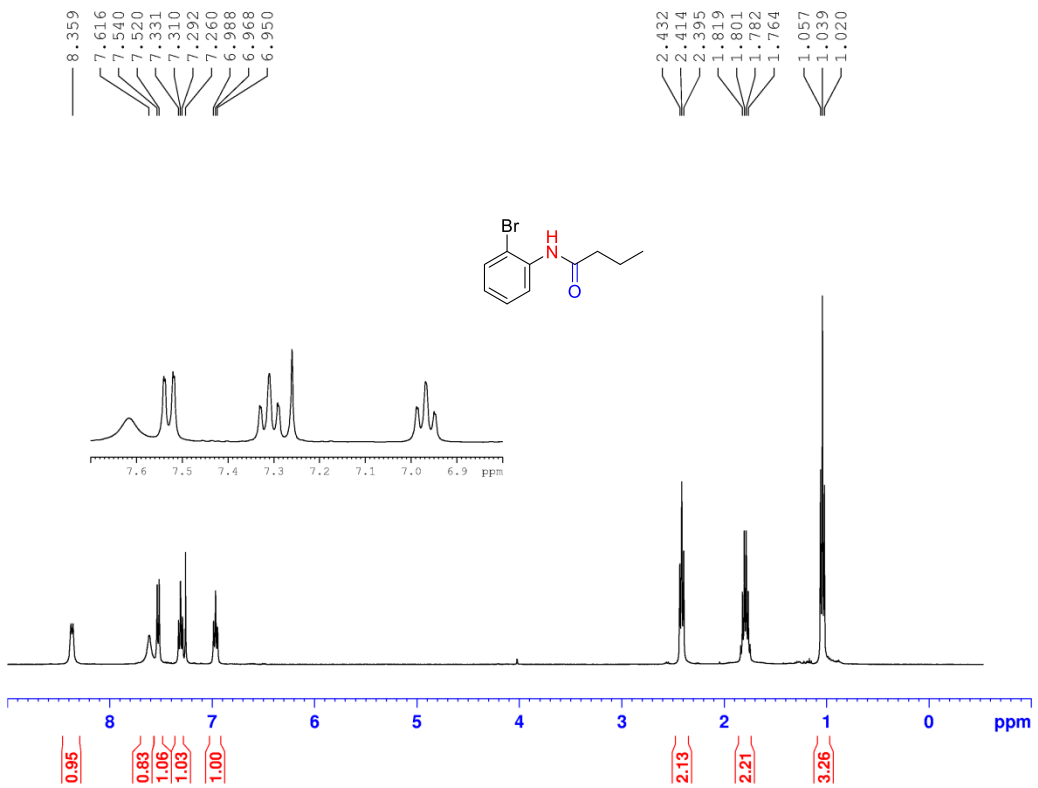
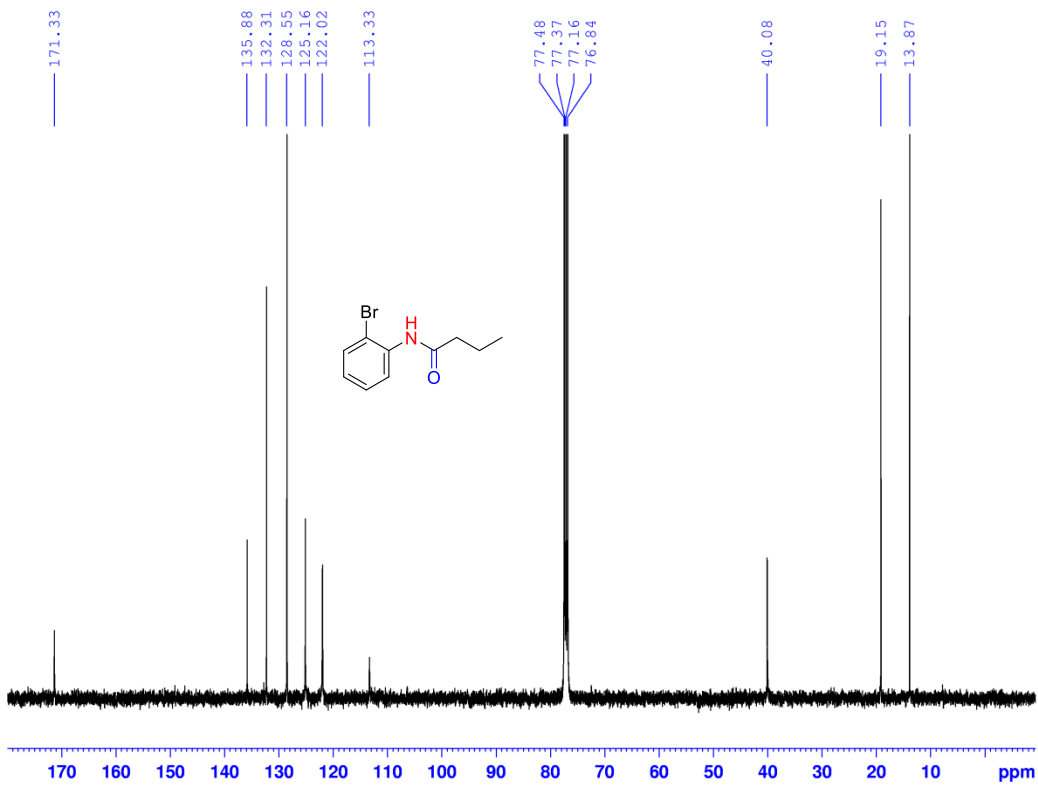


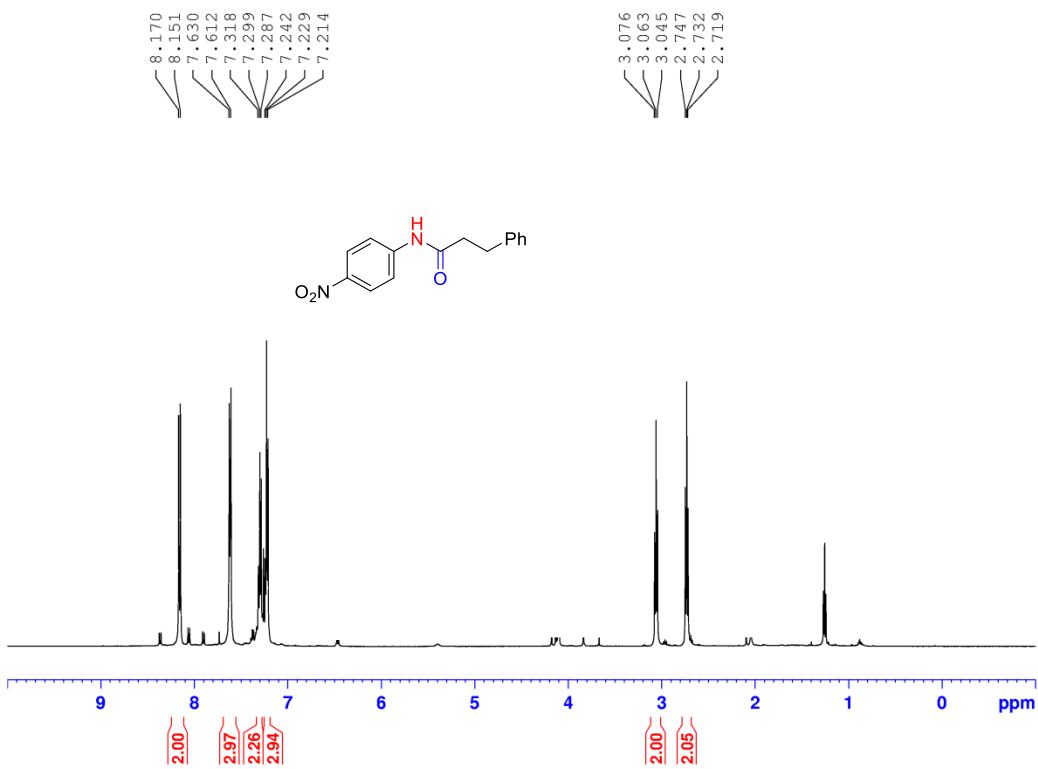
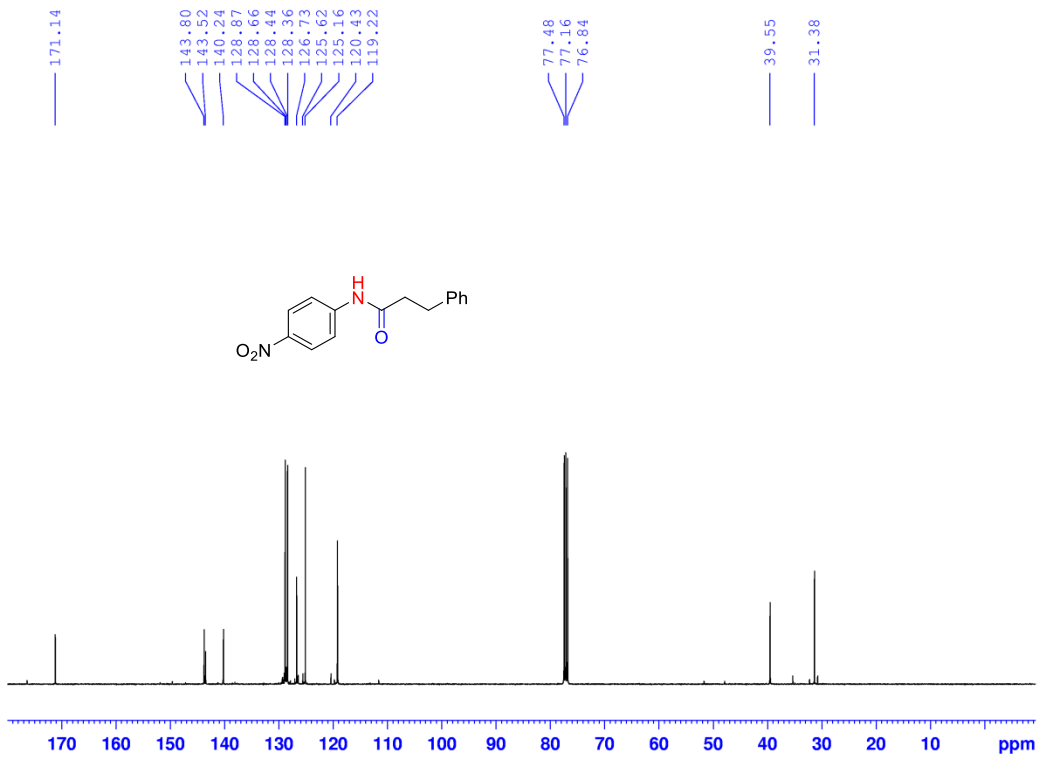




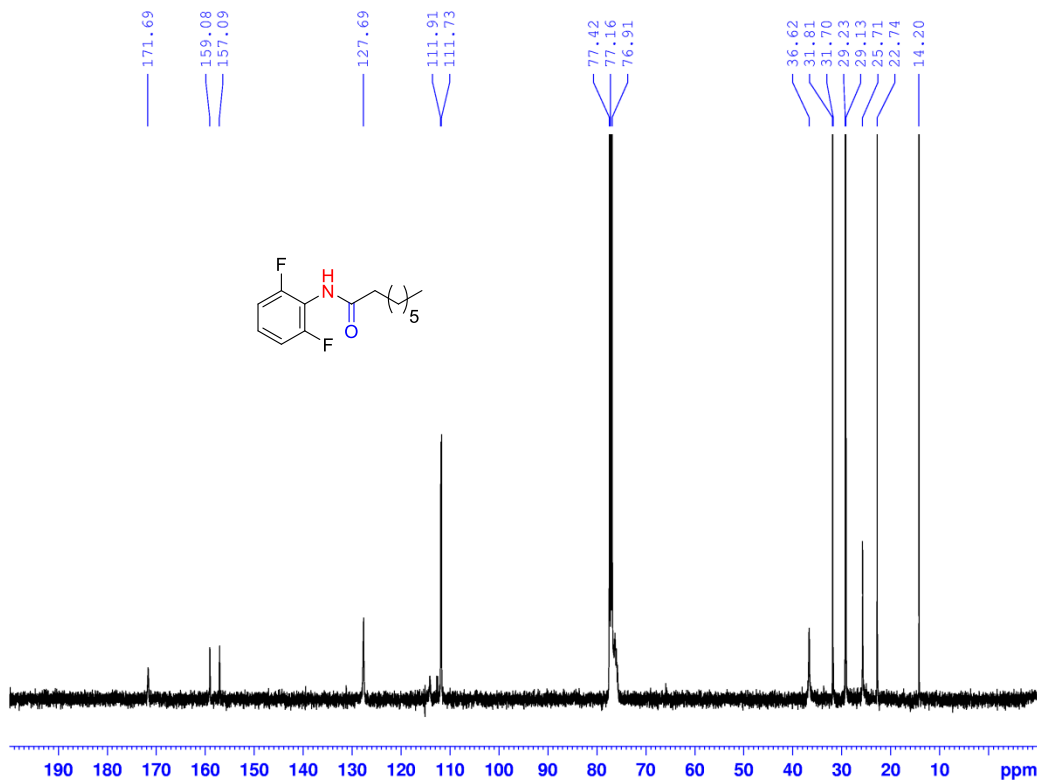
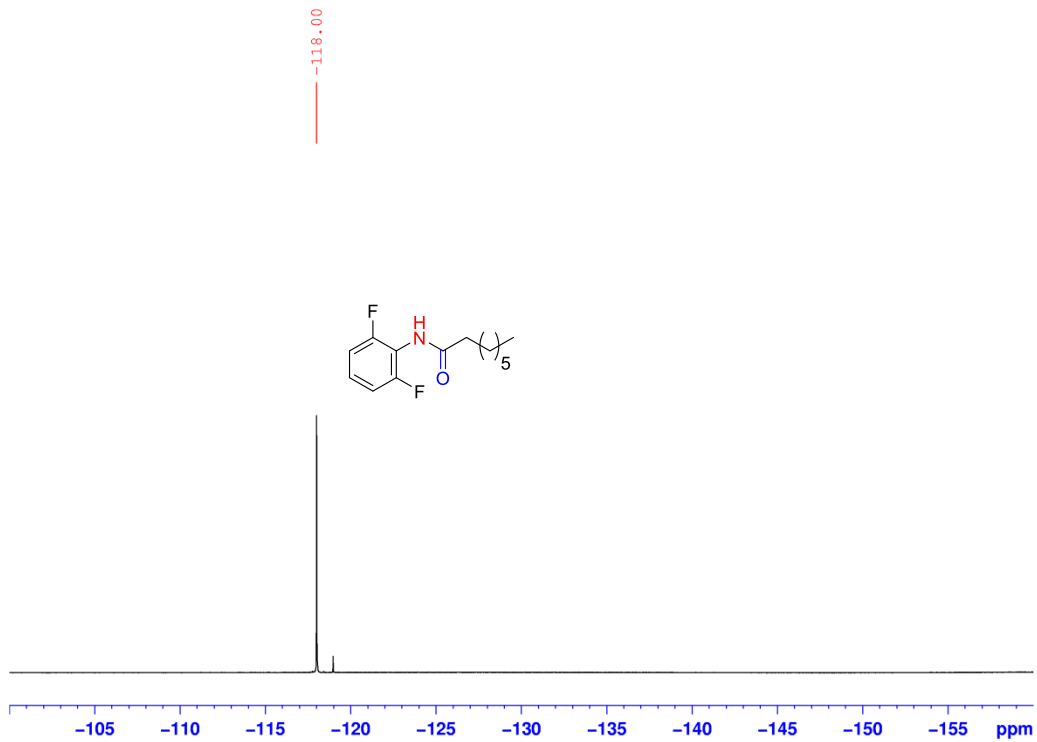


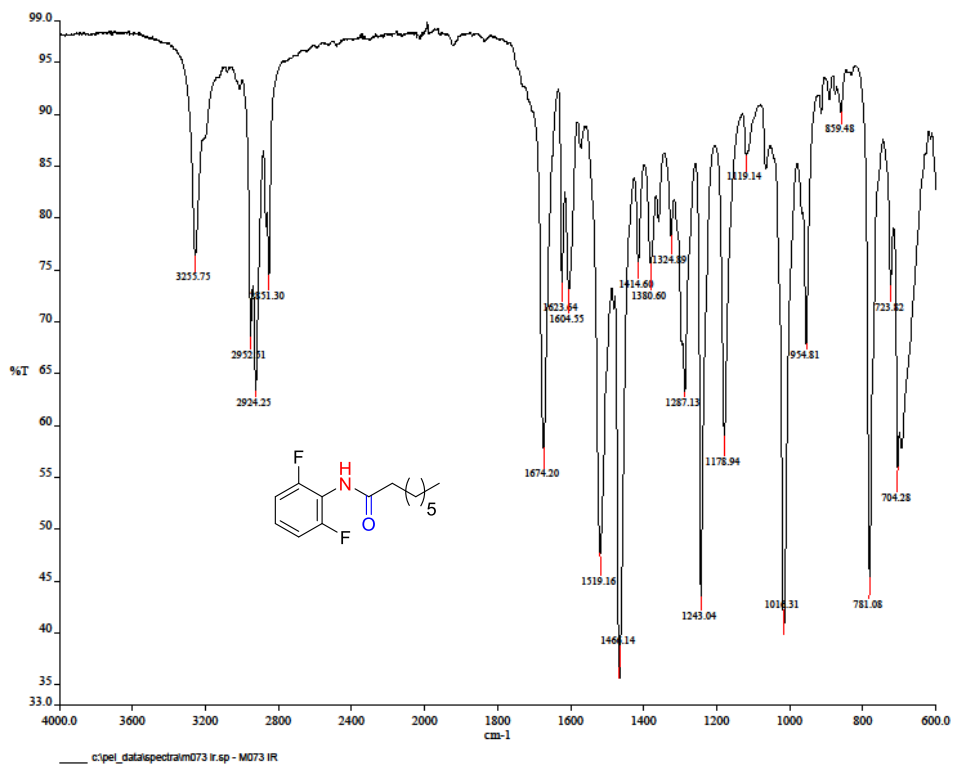
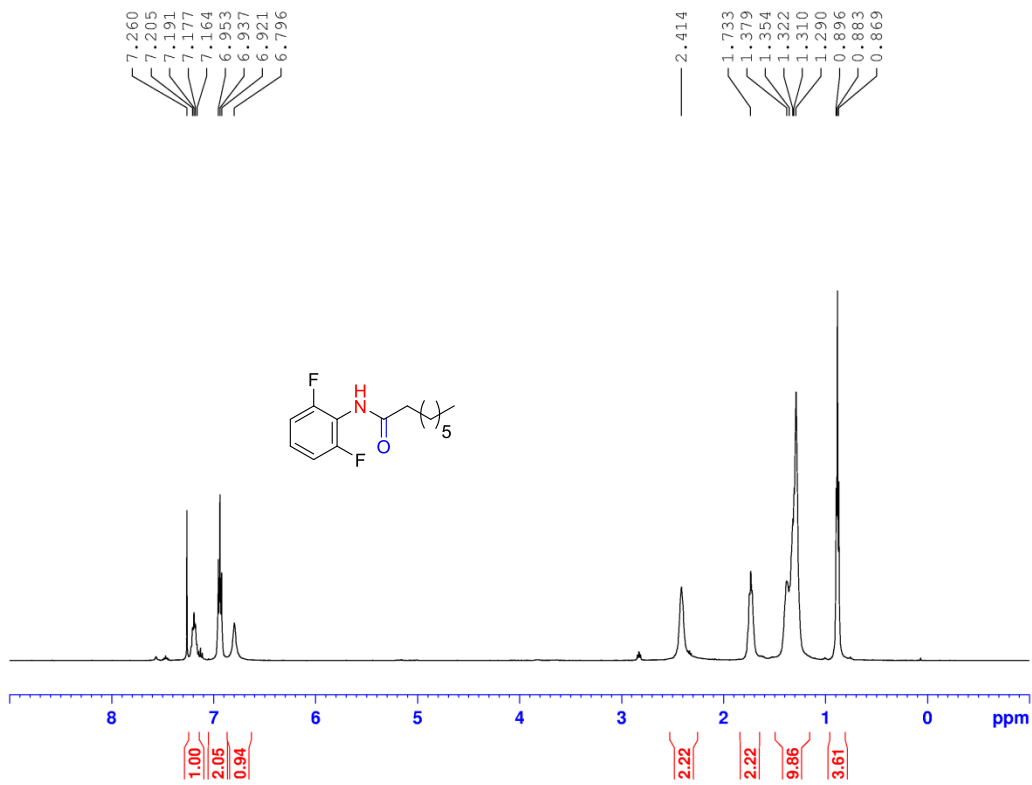




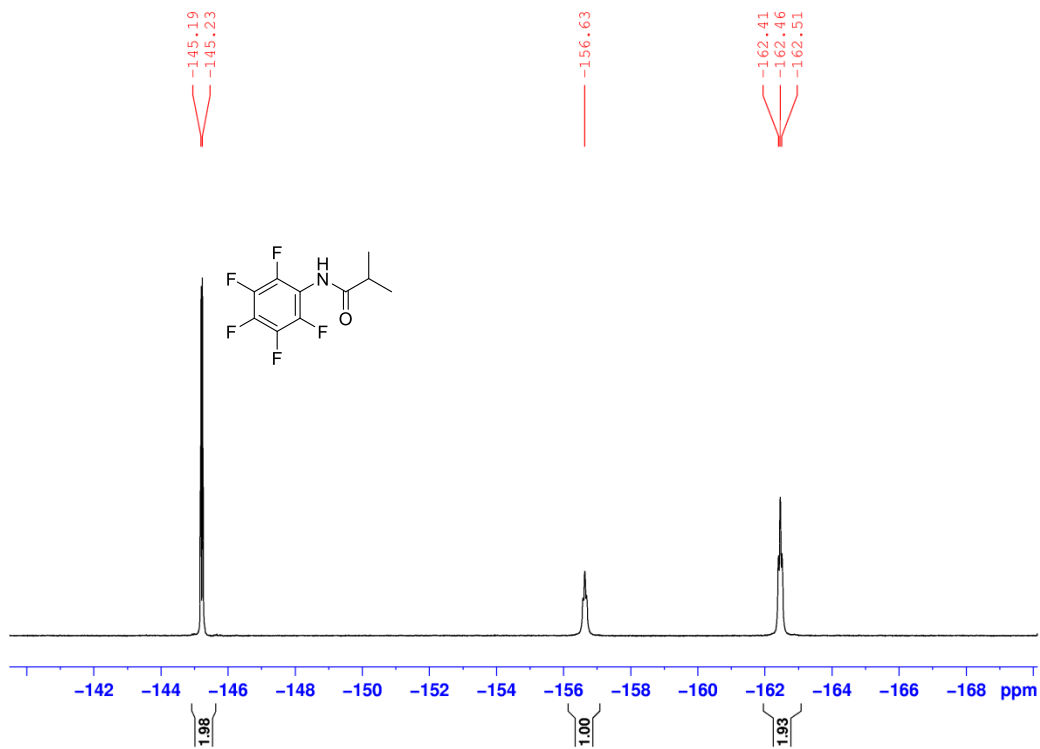


F19 CDCl3

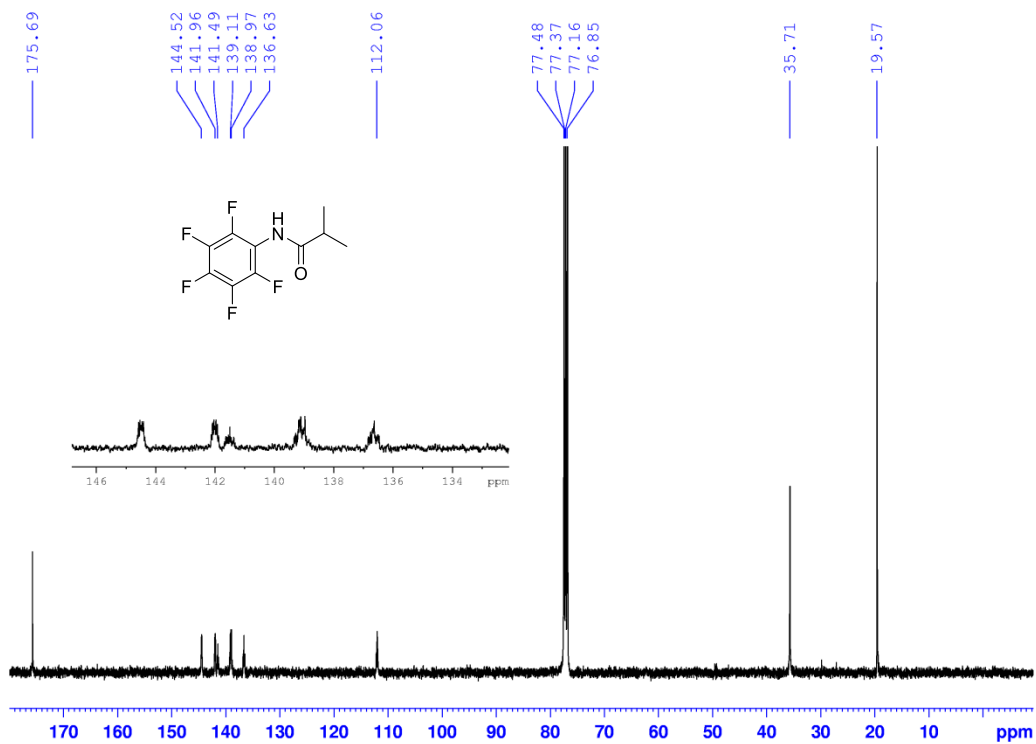




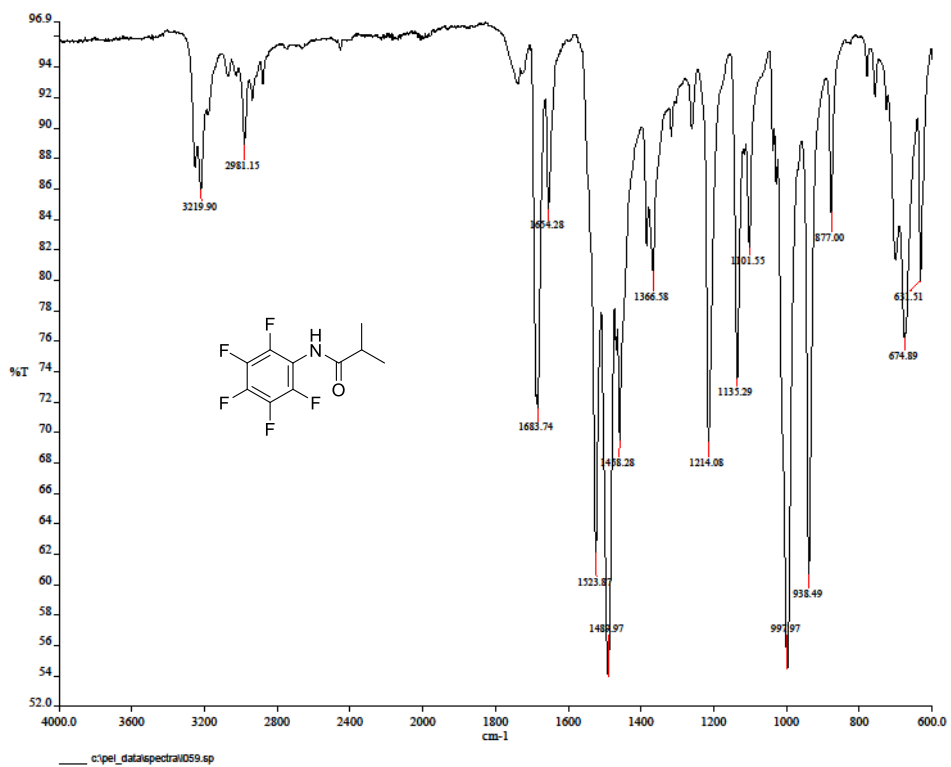
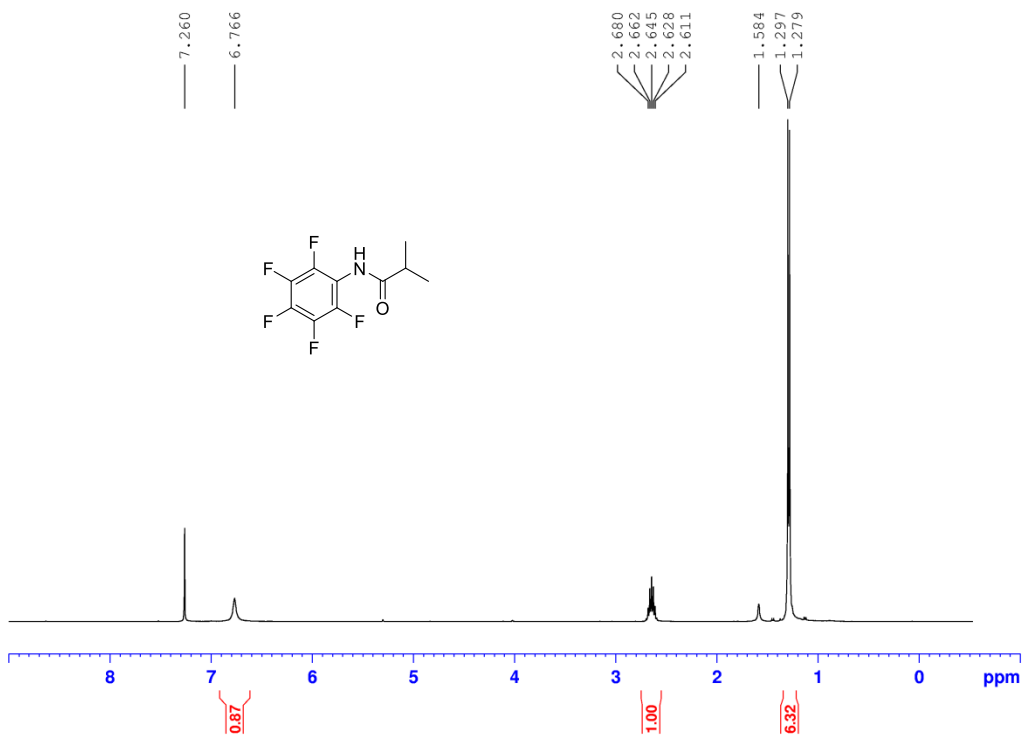
F-NMR L059



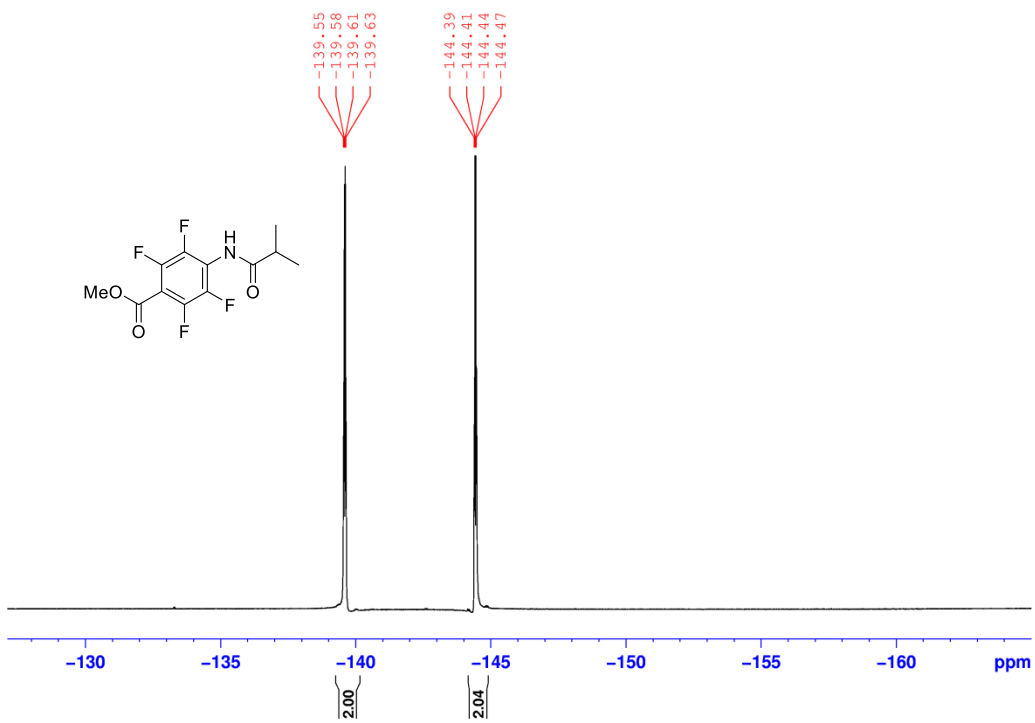
C-NMR L059



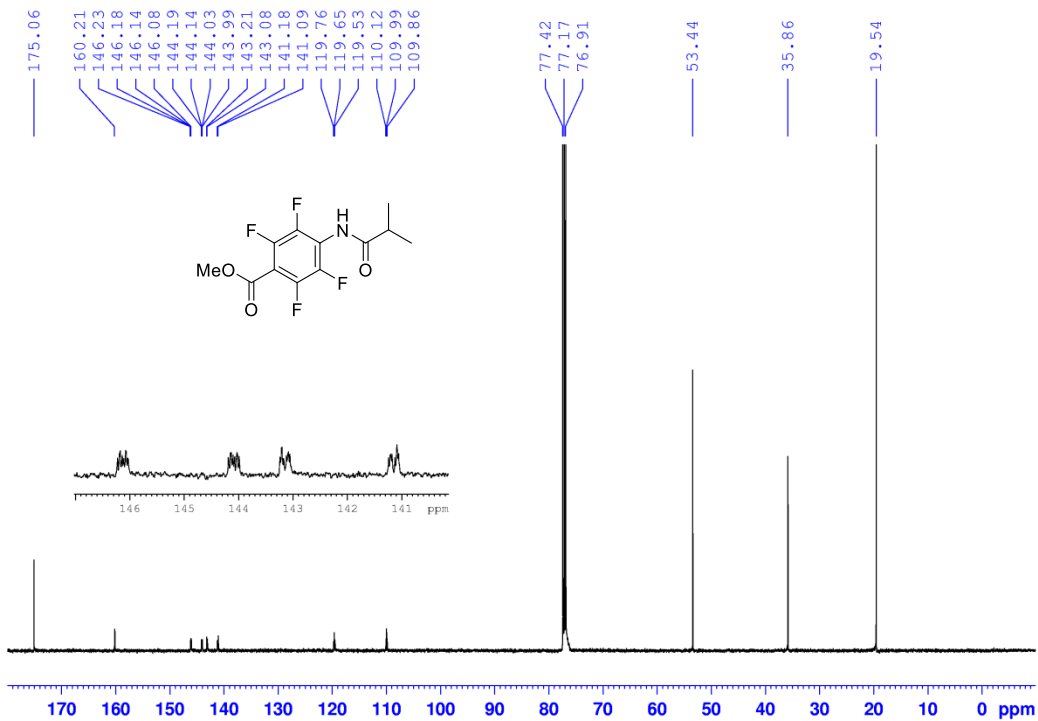
H-NMR L059



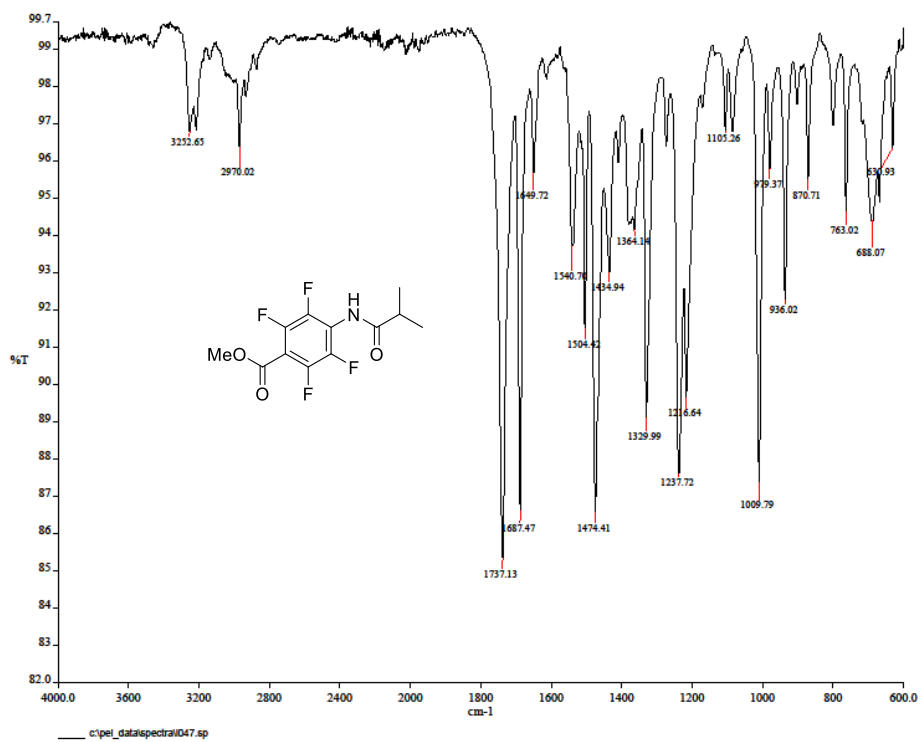
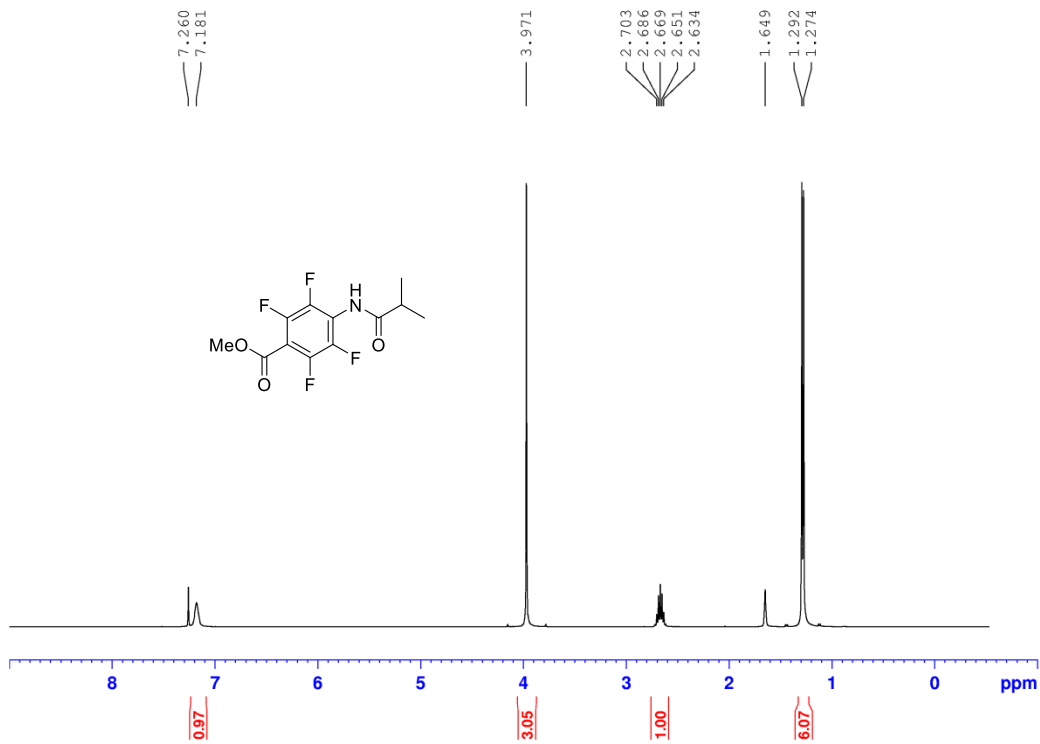
FNMR L047 CDC13 376MHz



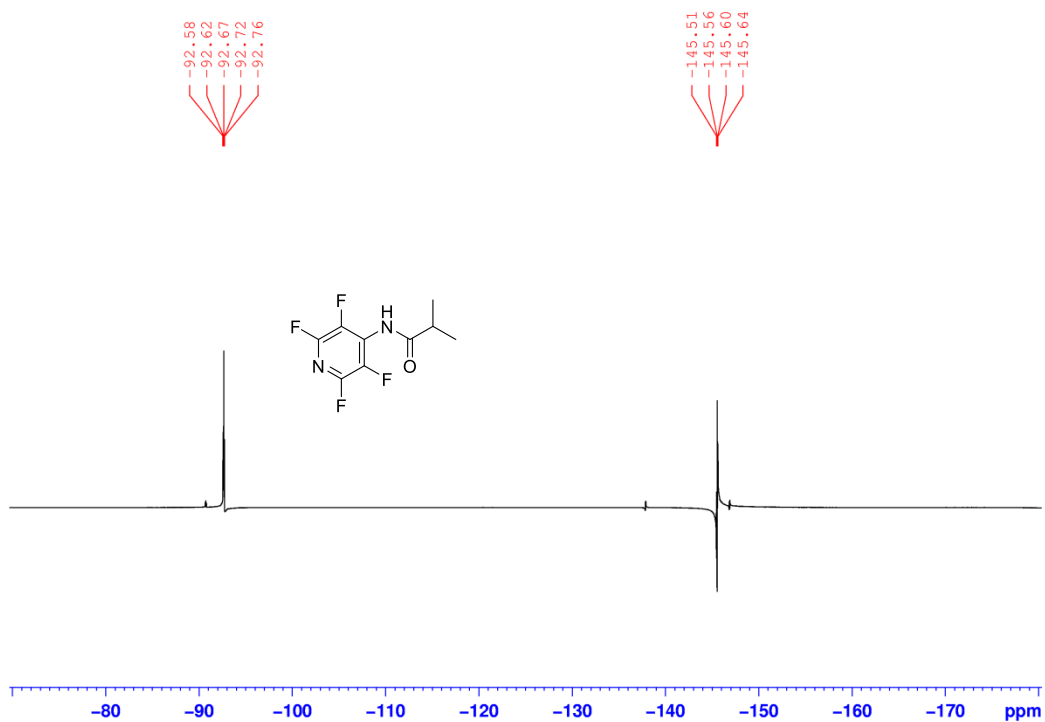
C13 L047 CDC13 100MHz



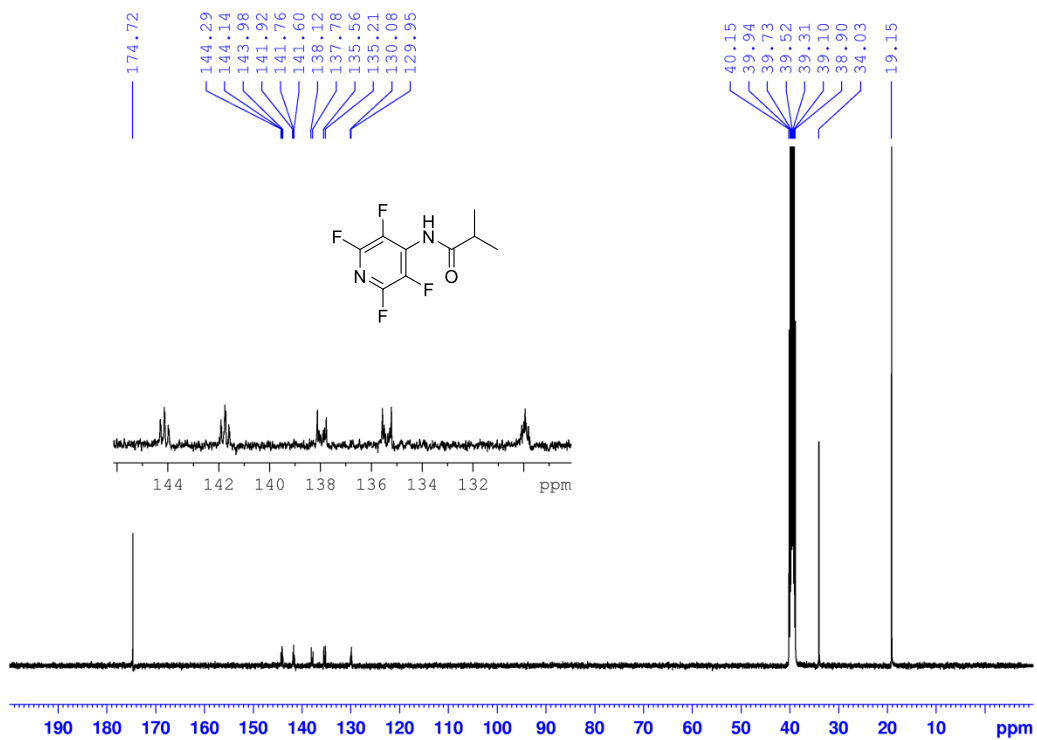
HNMR L047 CDC13



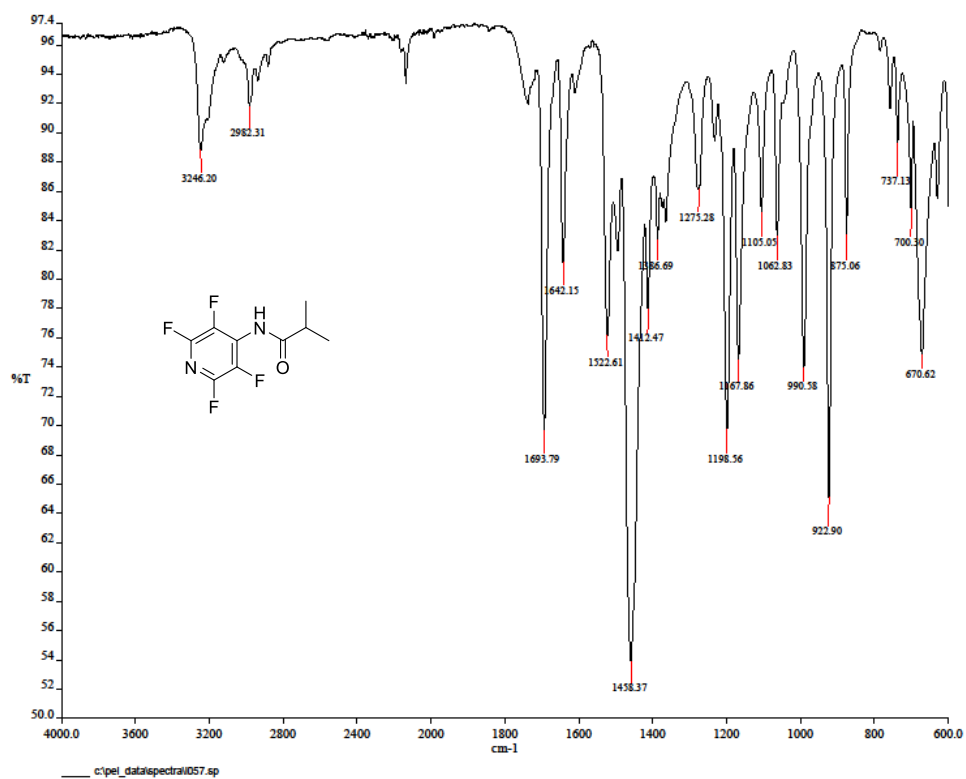
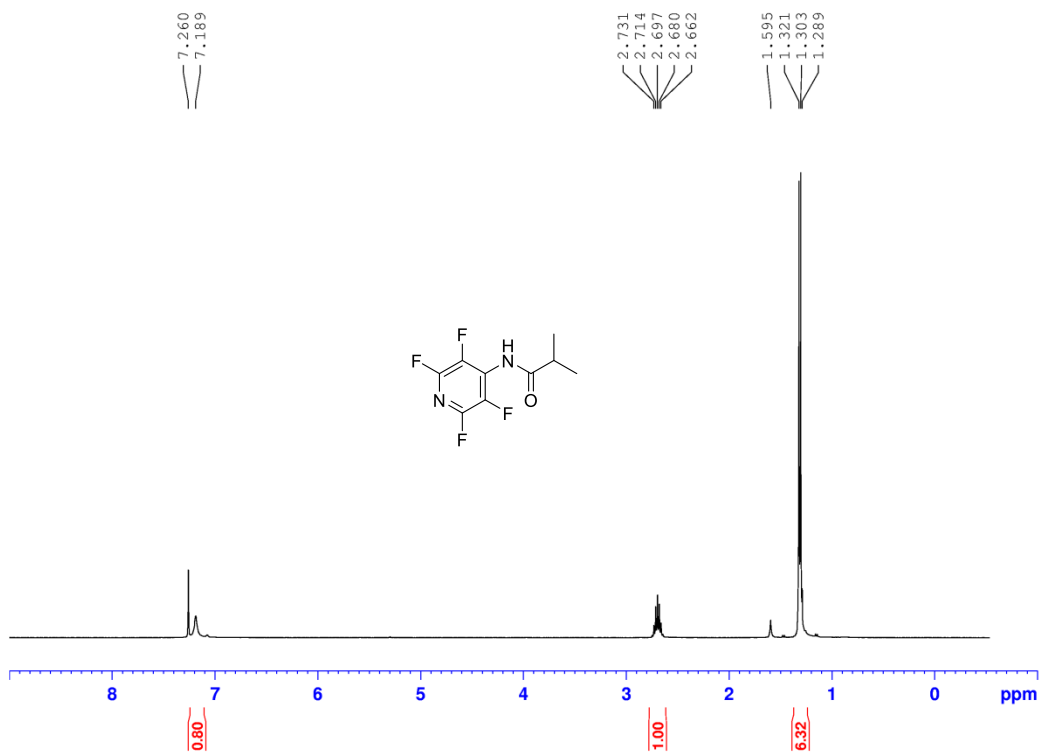
F-NMR L057, without phase procession



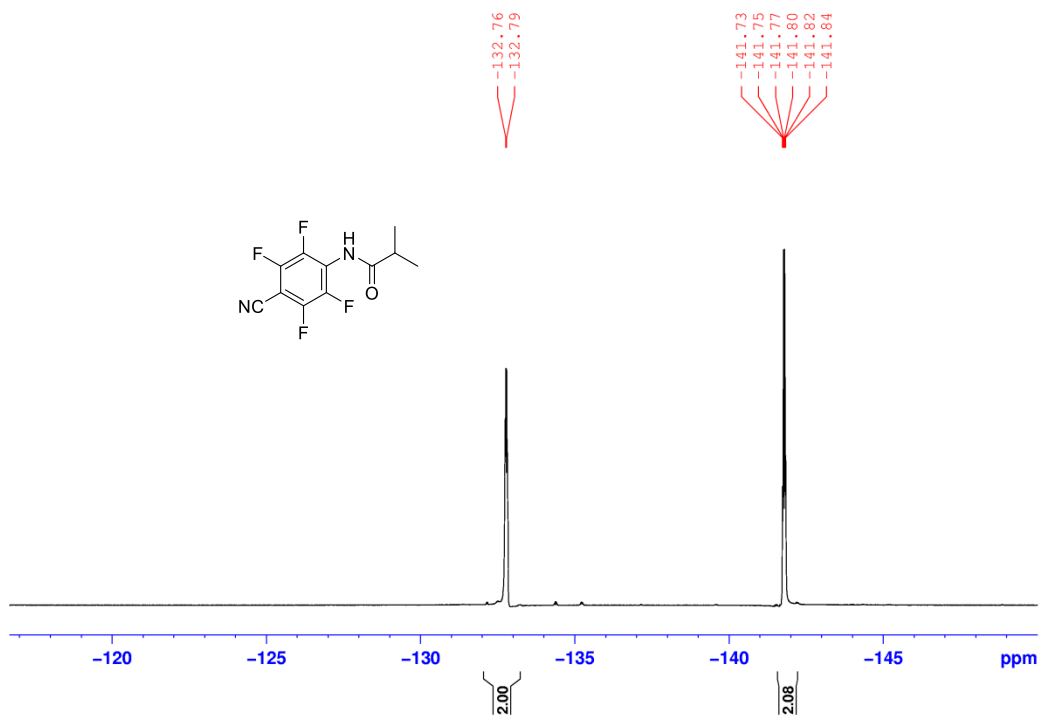
C-NMR L057



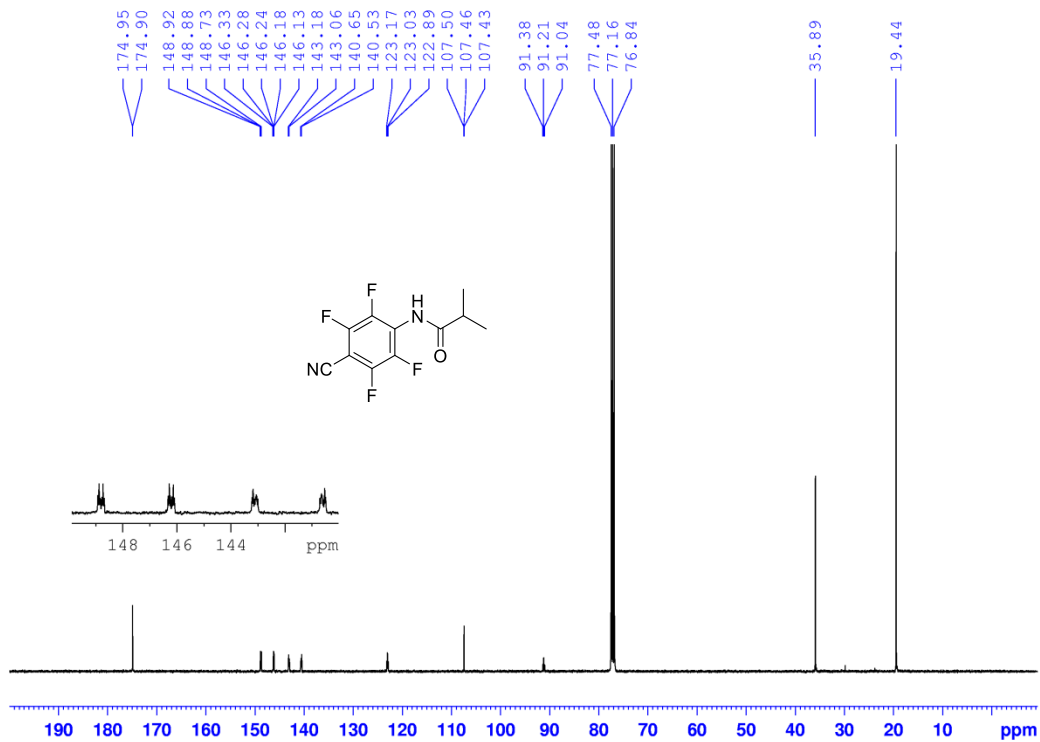
H-NMR L057



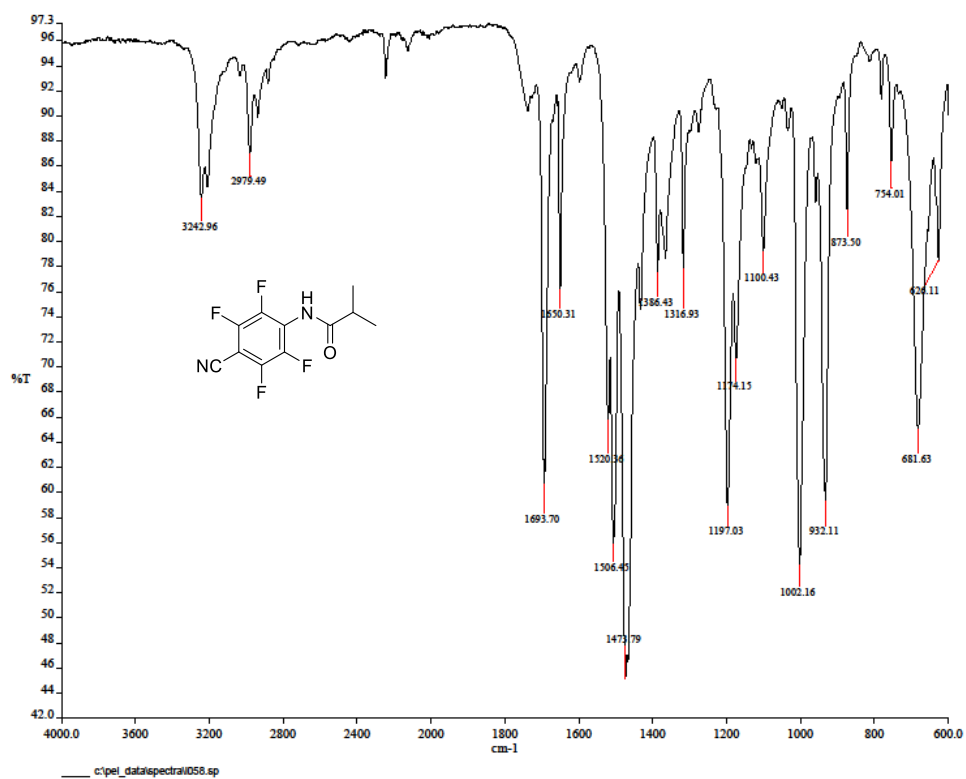
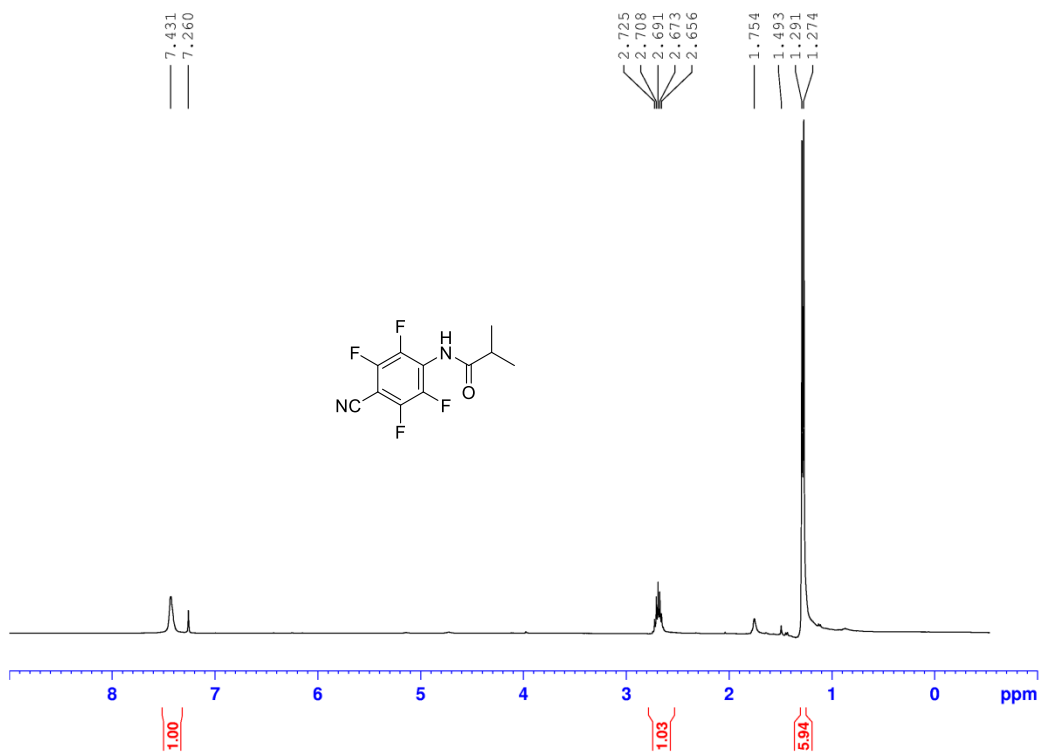
F-NMR L058



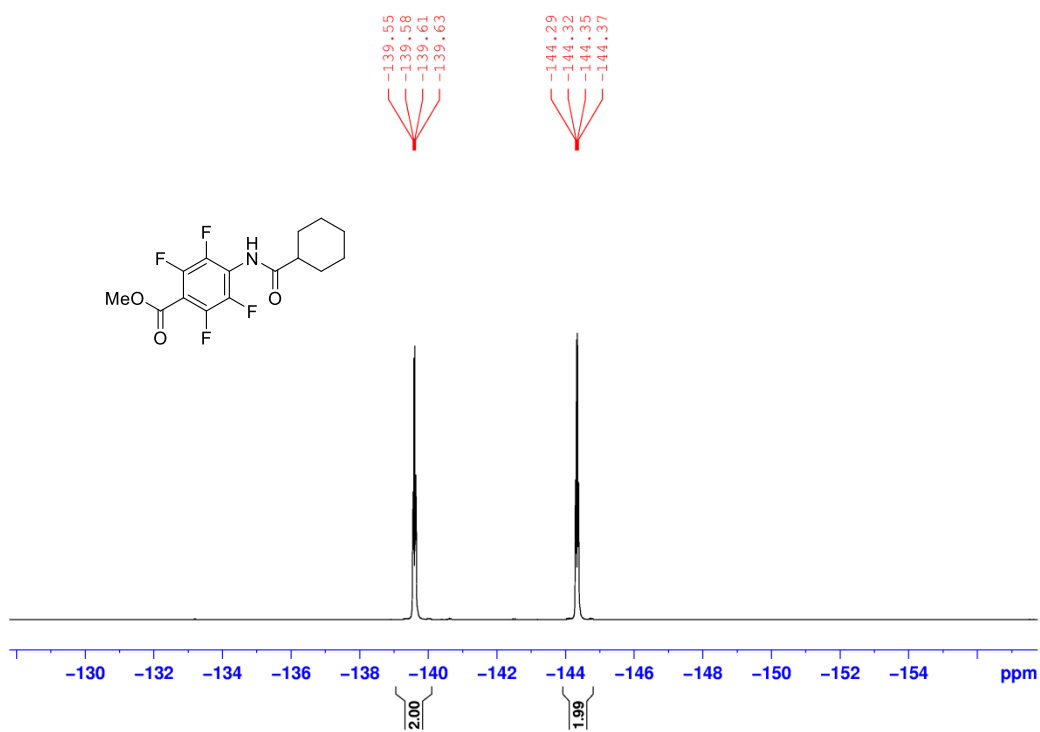
C-NMR L058



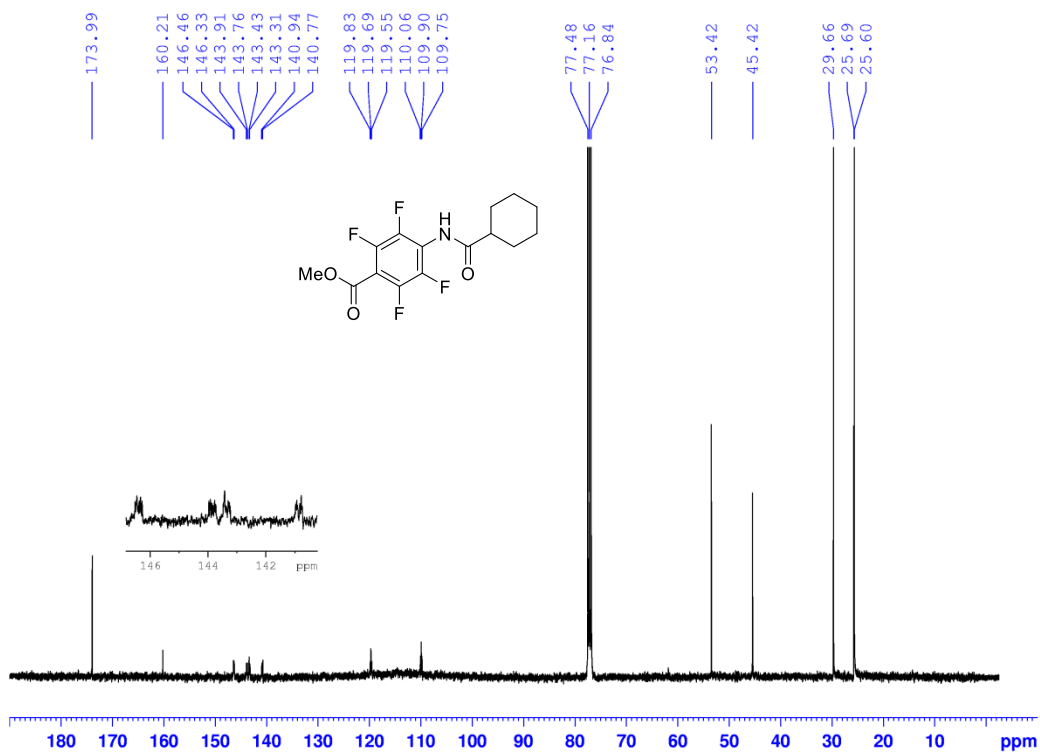
H-NMR L058

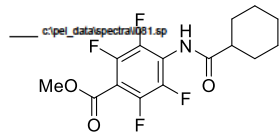
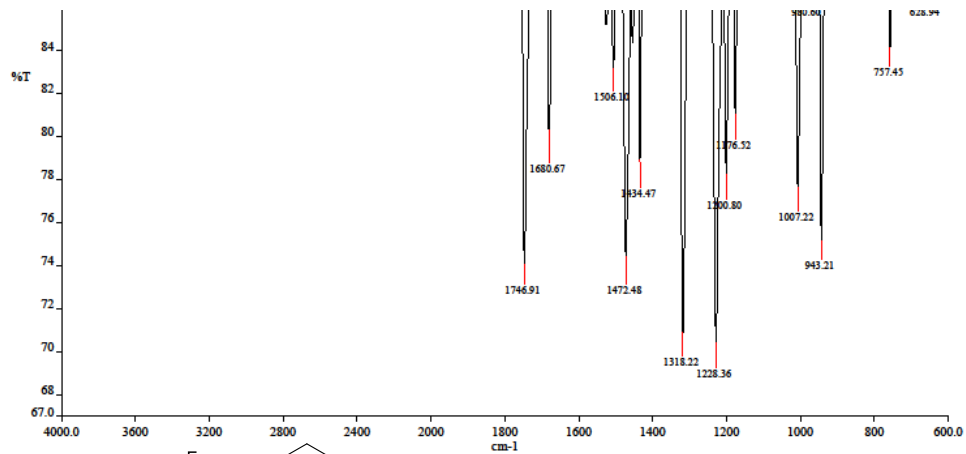


FNMR L082

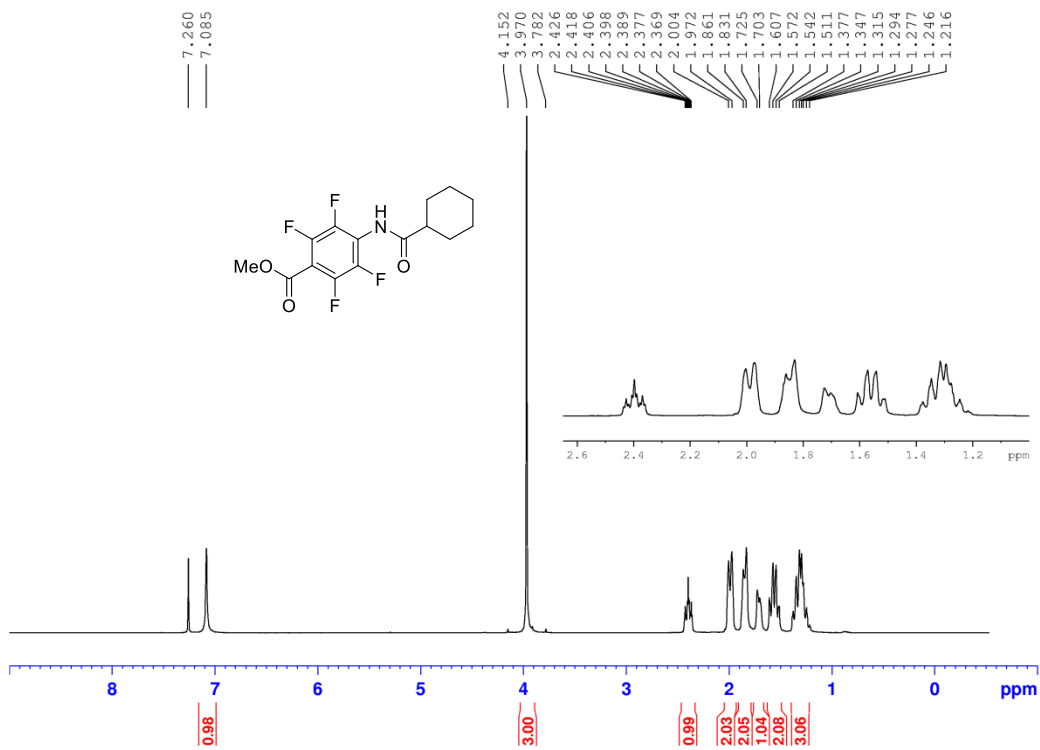


CNMR L081

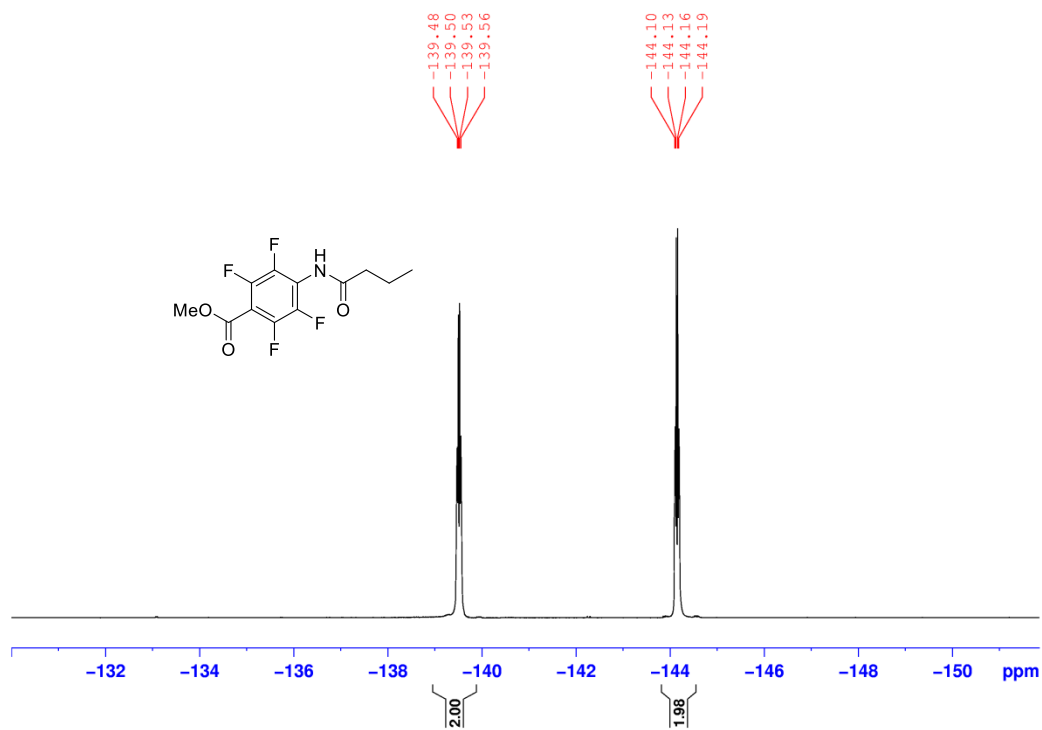




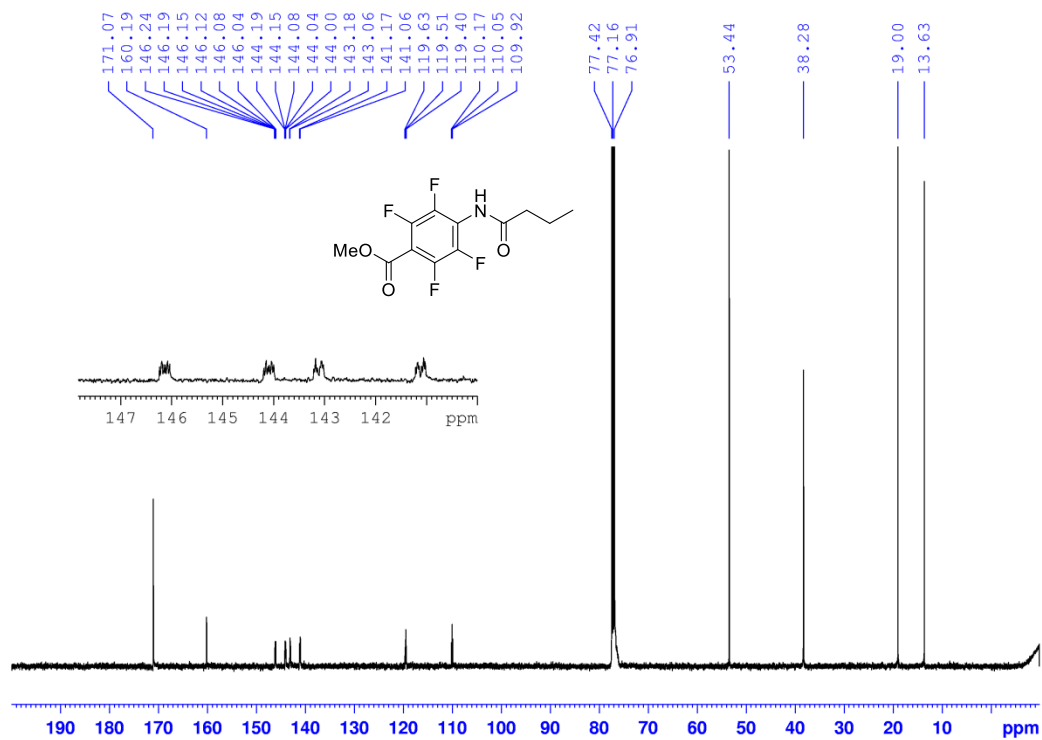
HNMR L081



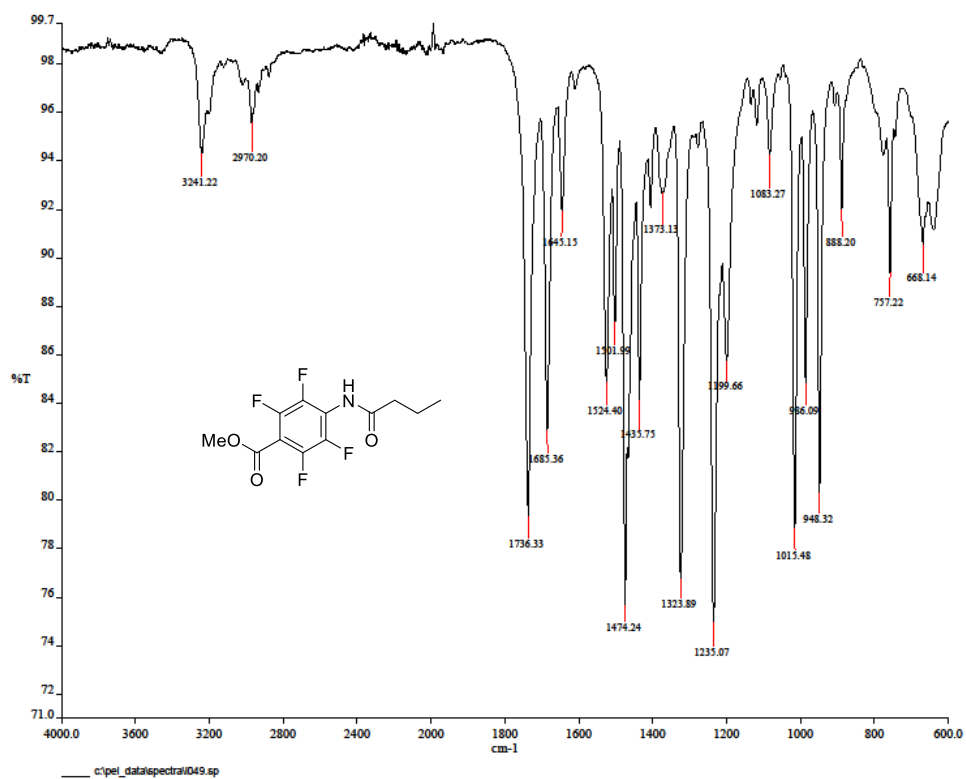
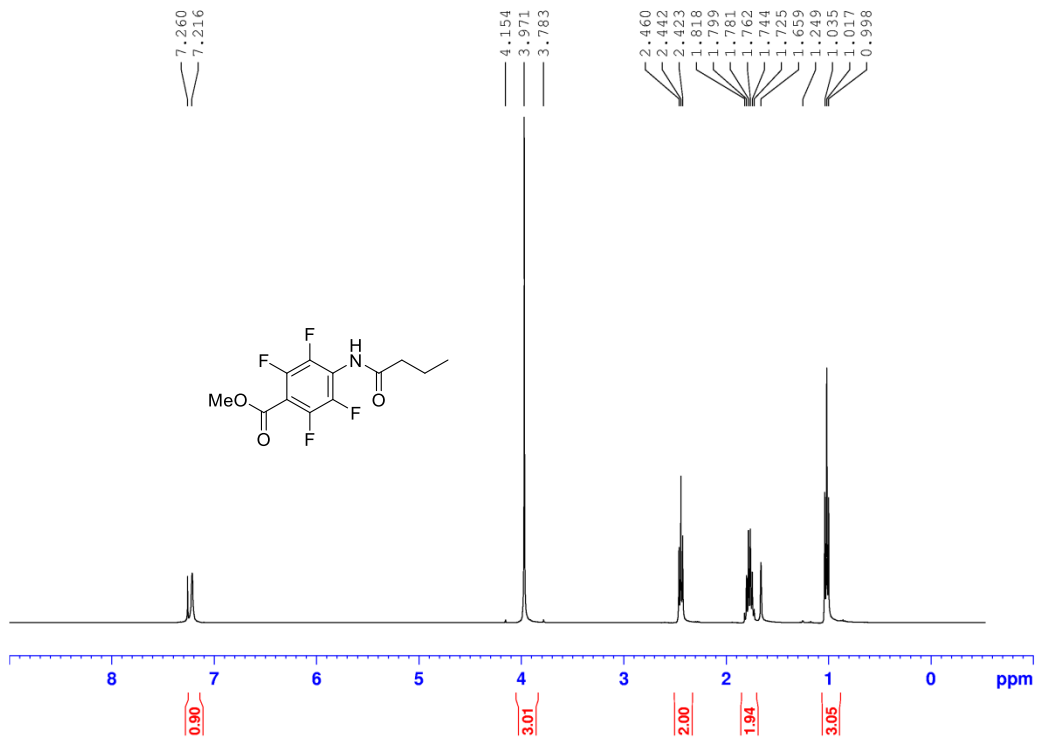
F-NMR L049 CDC13

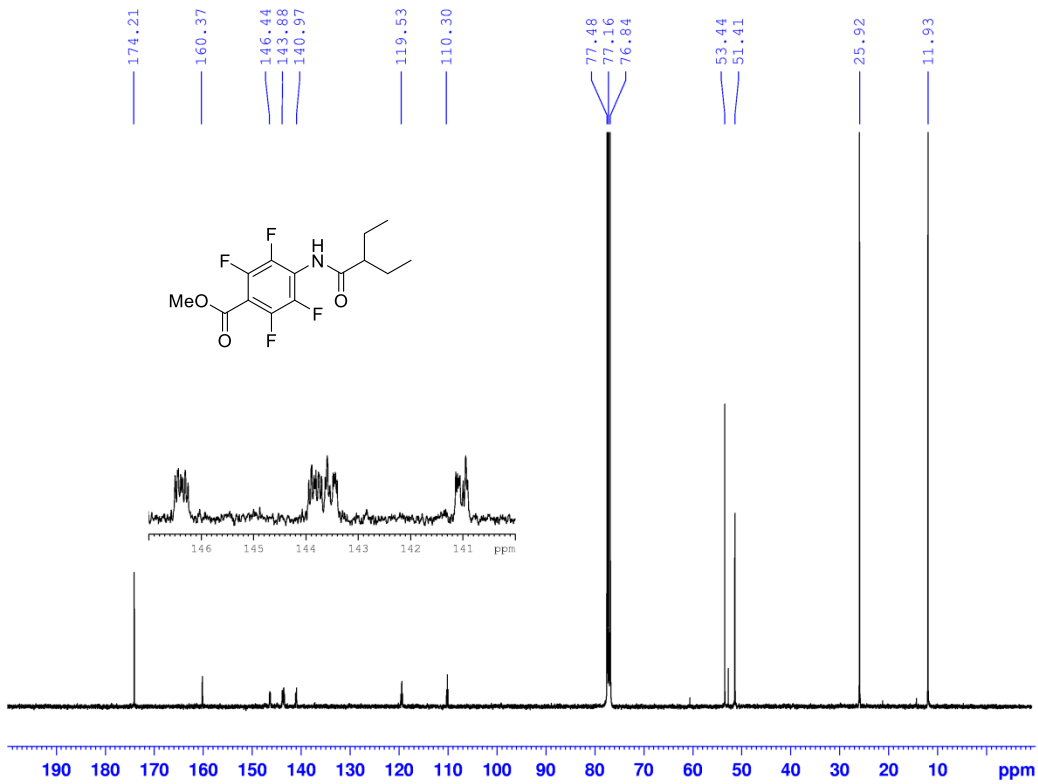
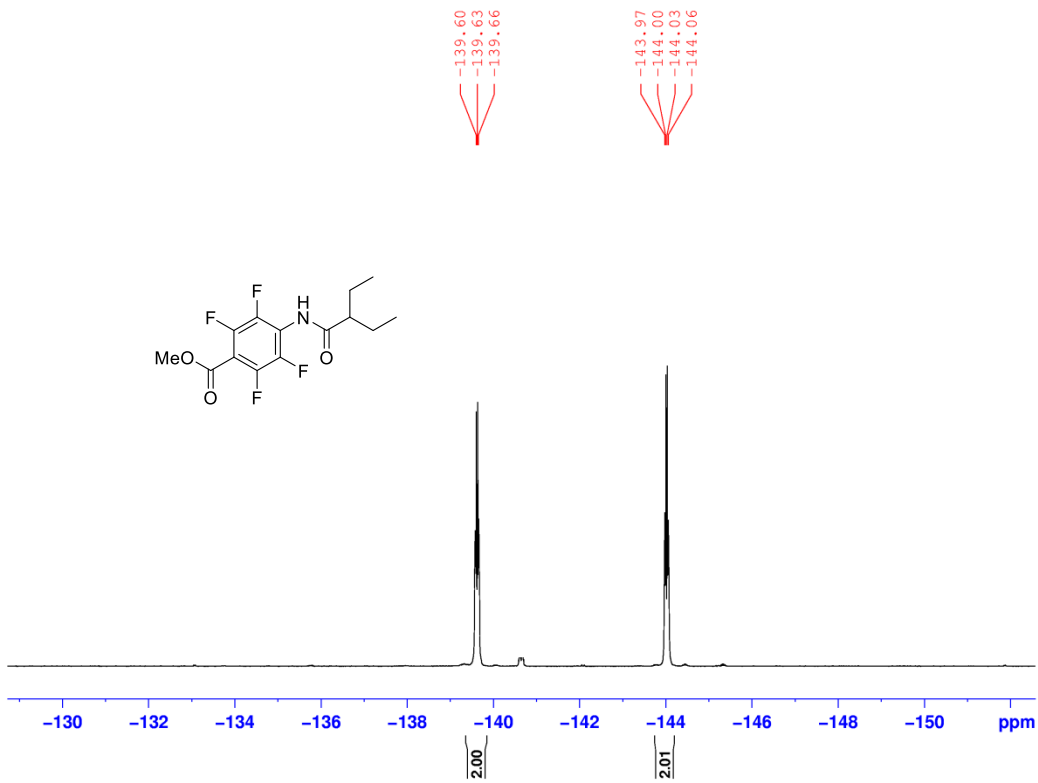


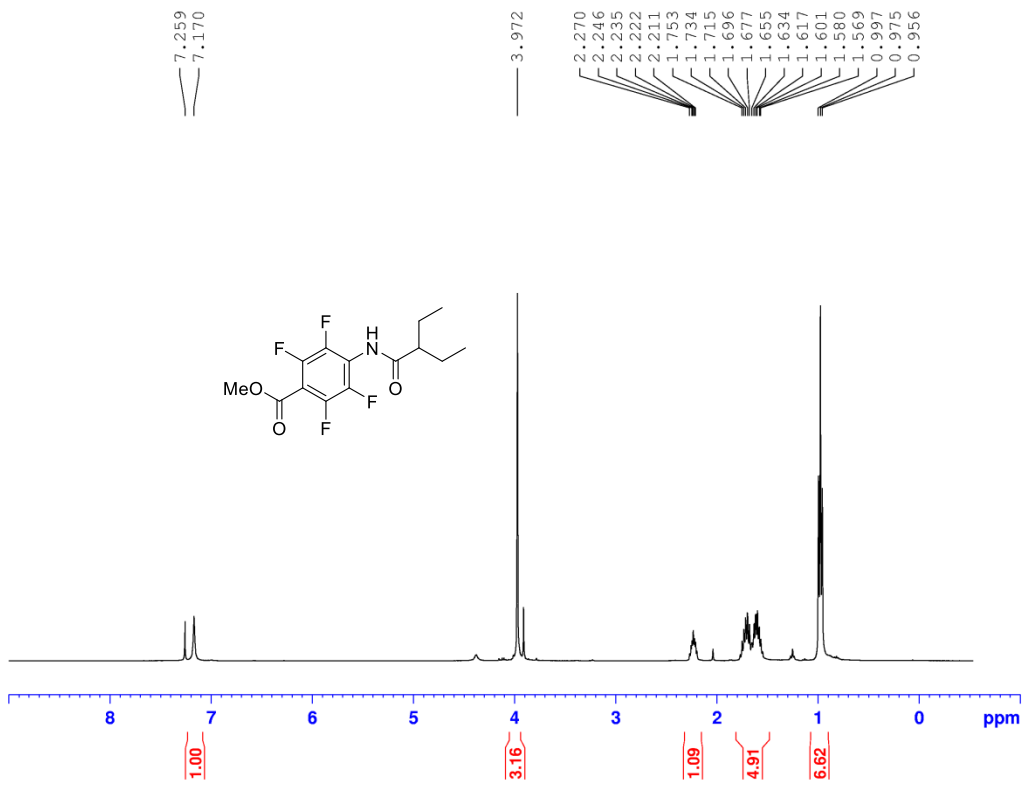
C13-NMR L049 CDC13 100MHz

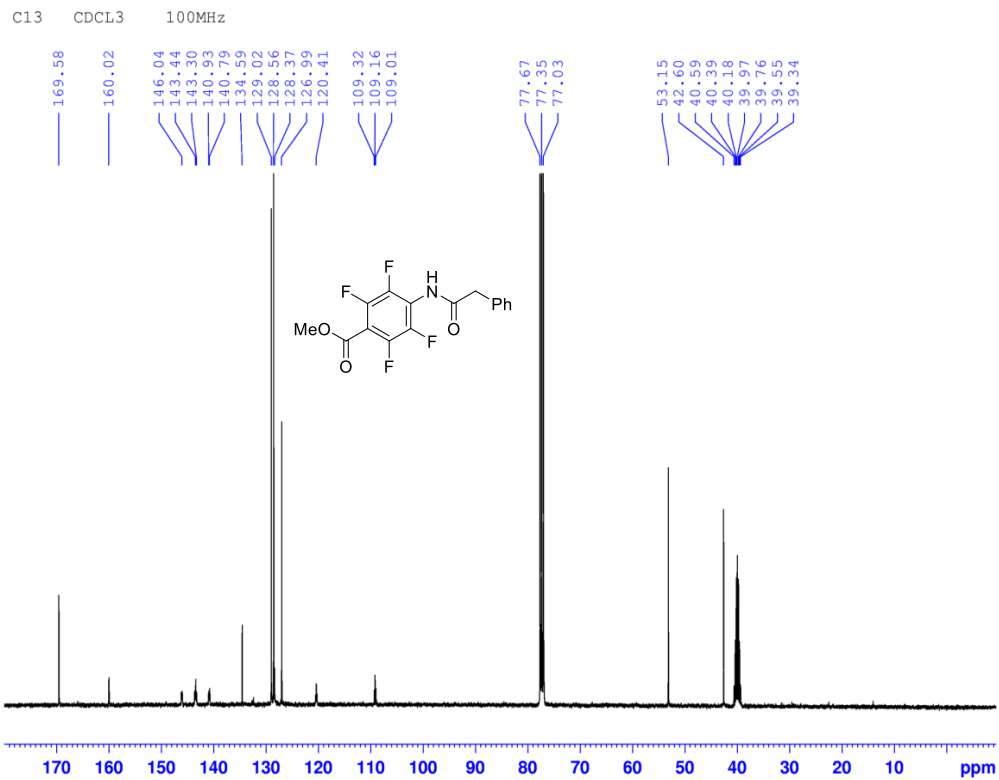
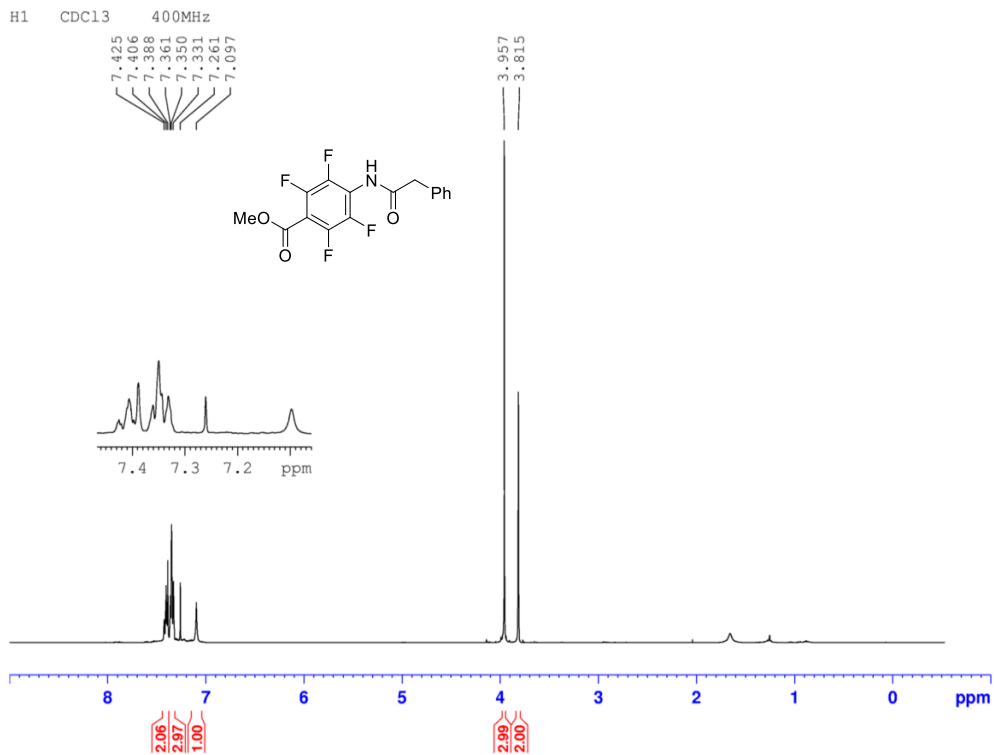


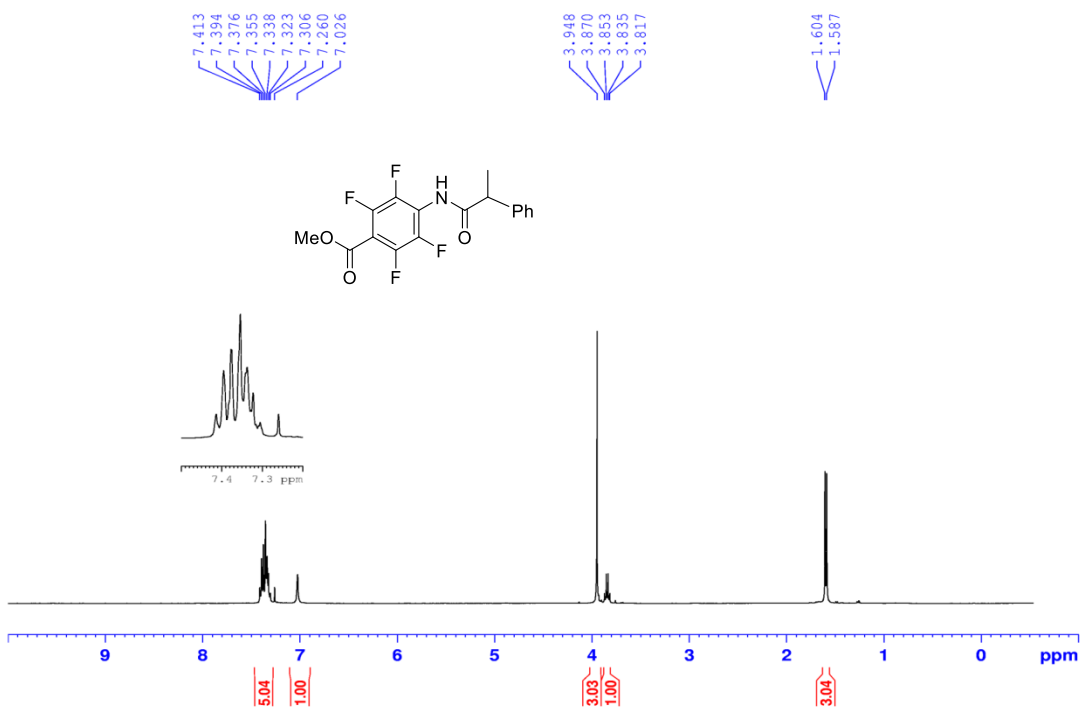
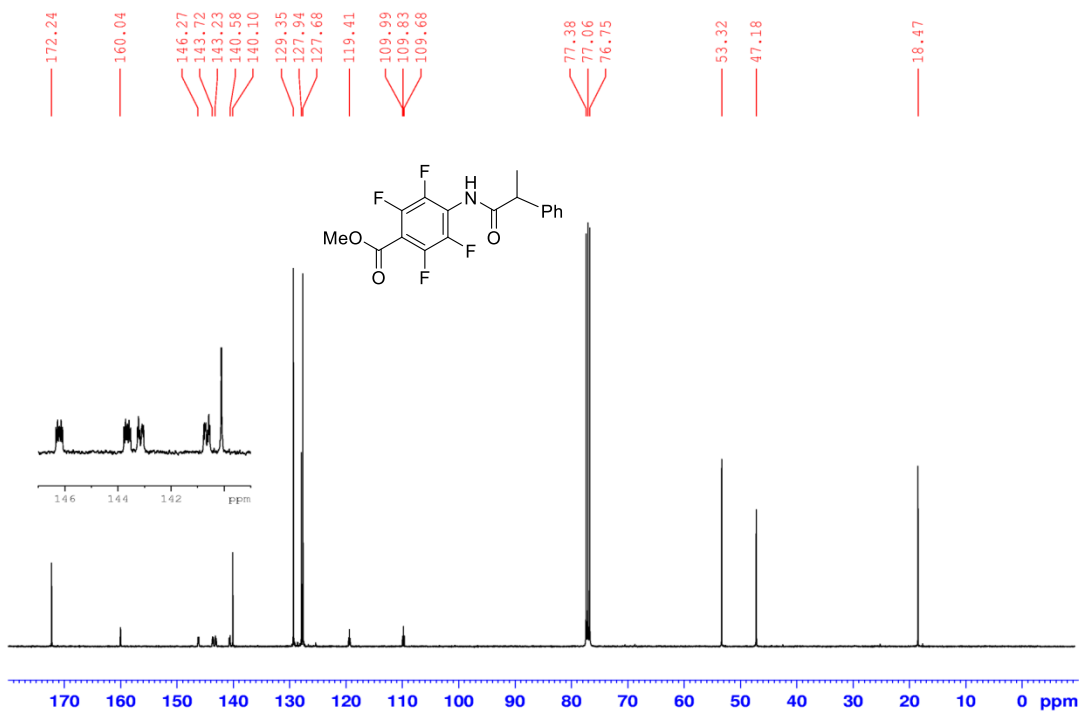
H-NMR L049 CDC13 400MHz



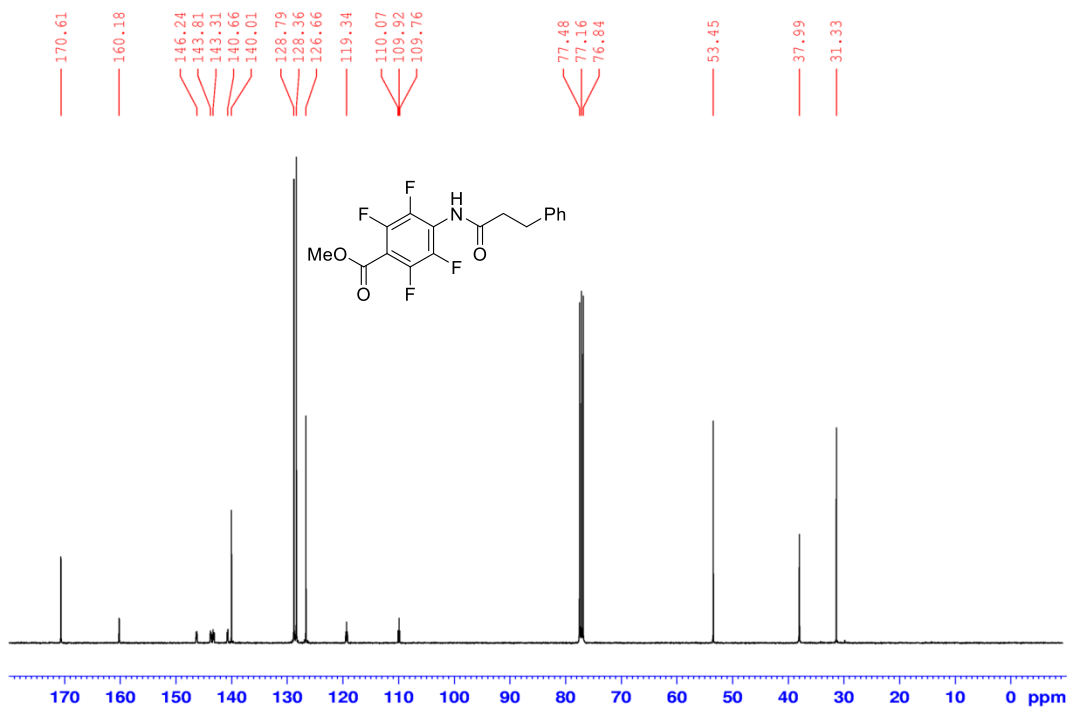
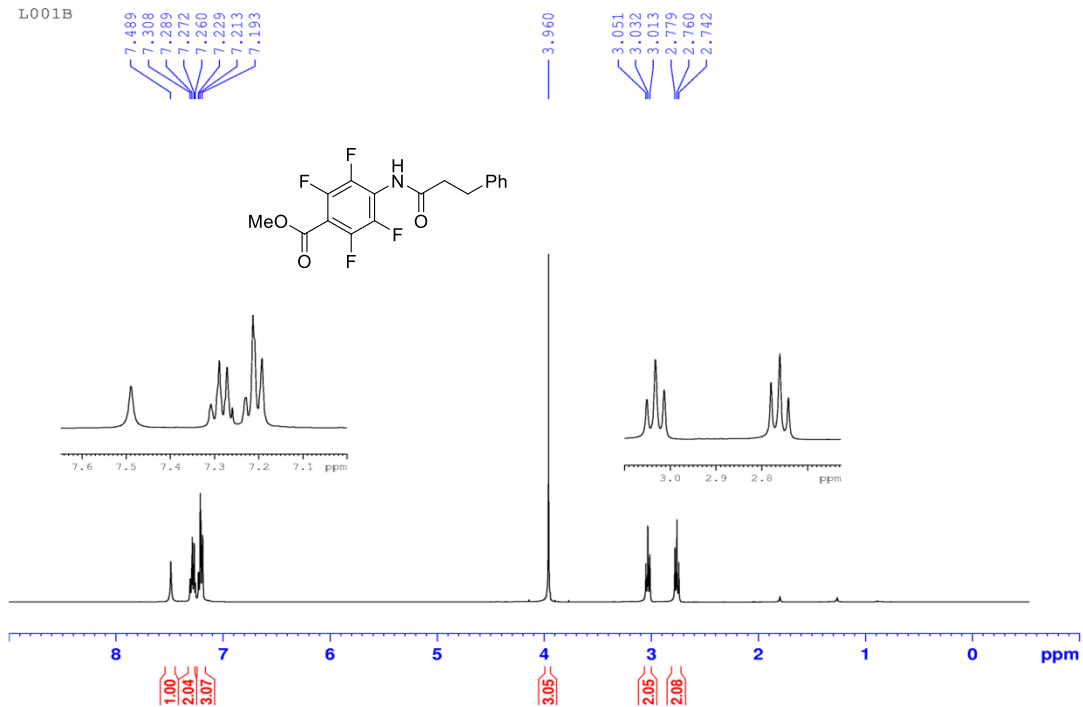




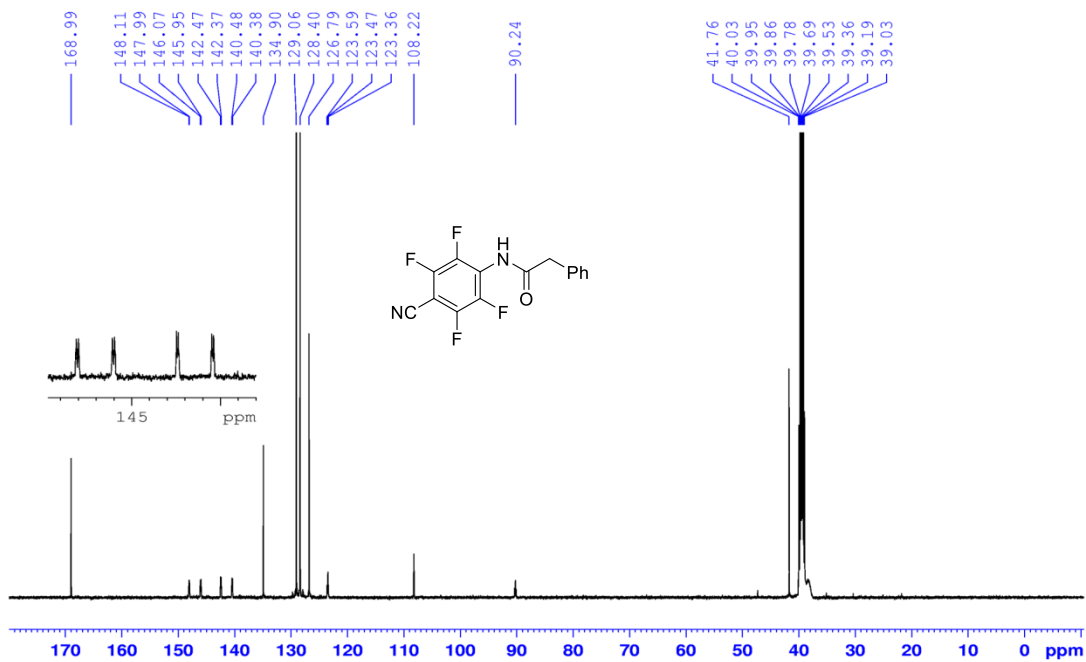




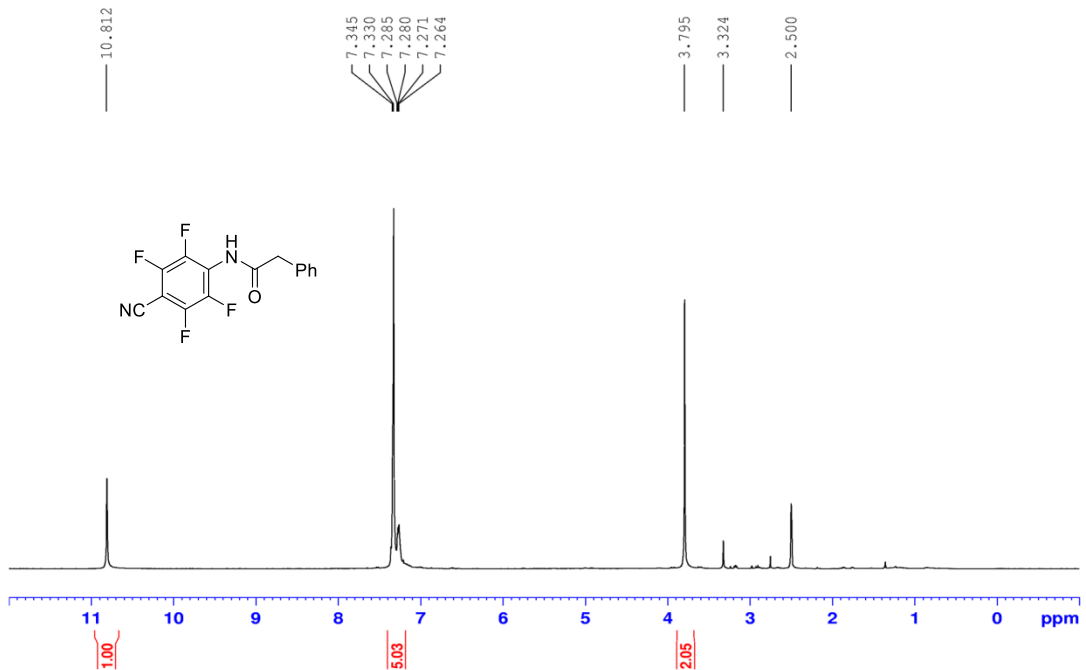
L001B

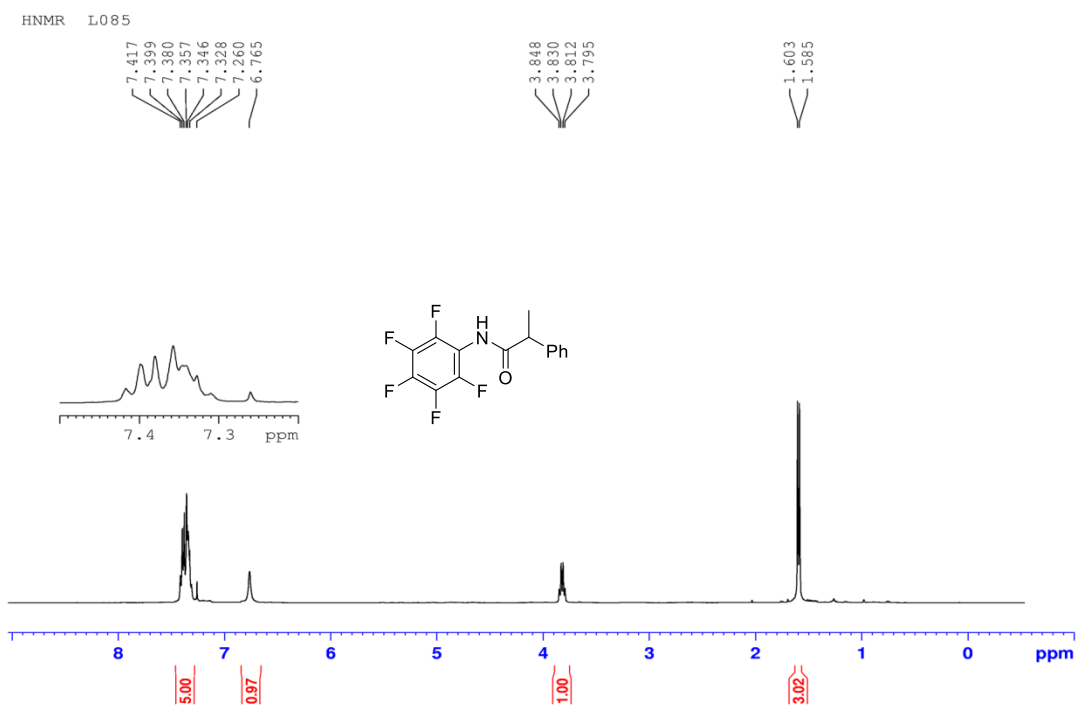
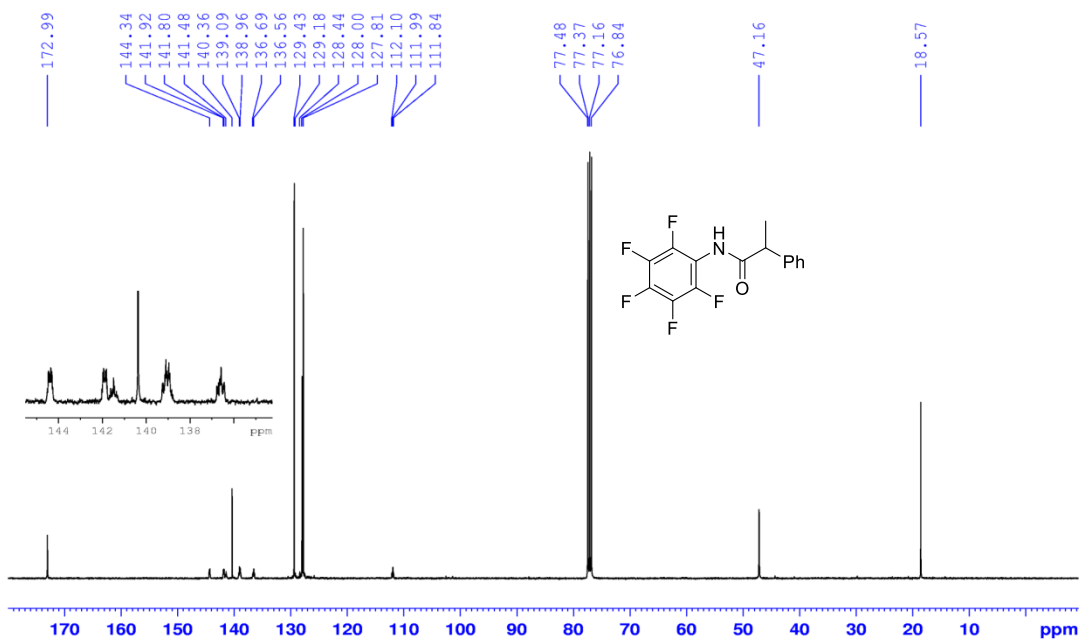


C13-NMR L055 CDC13 100MHz

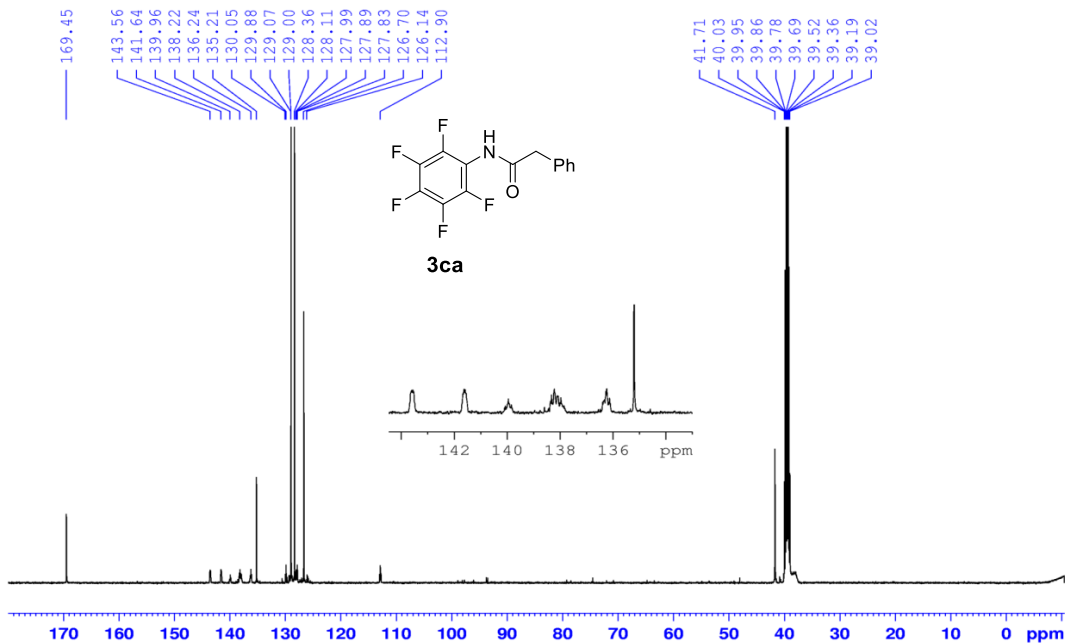


H-NMR L055

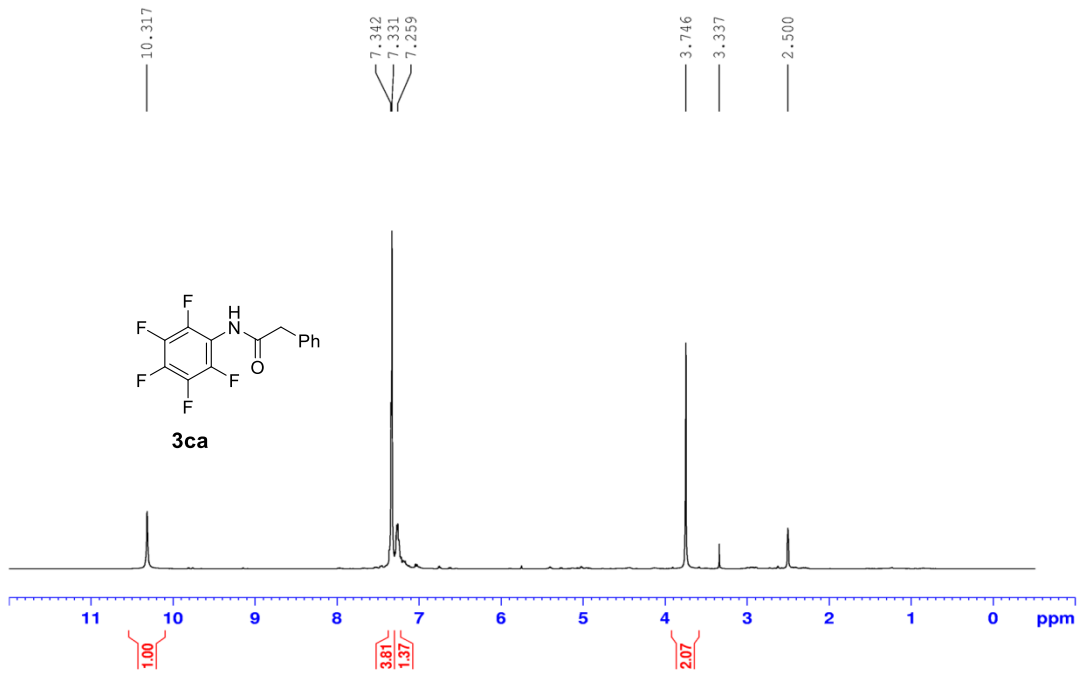




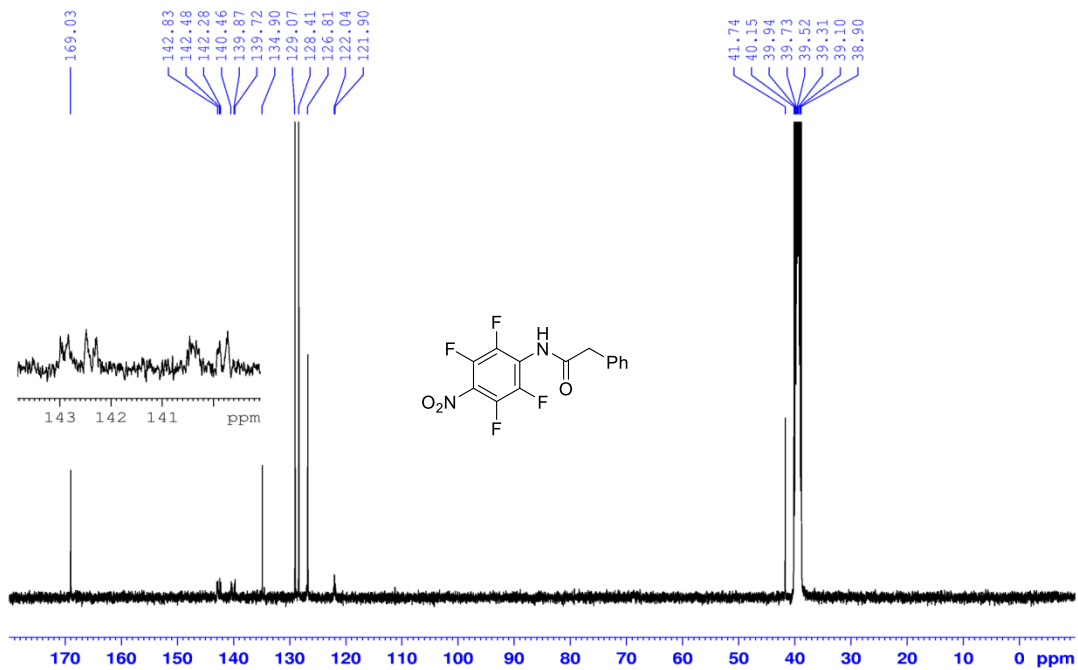
C13-NMR L054B CDC13 100MHz



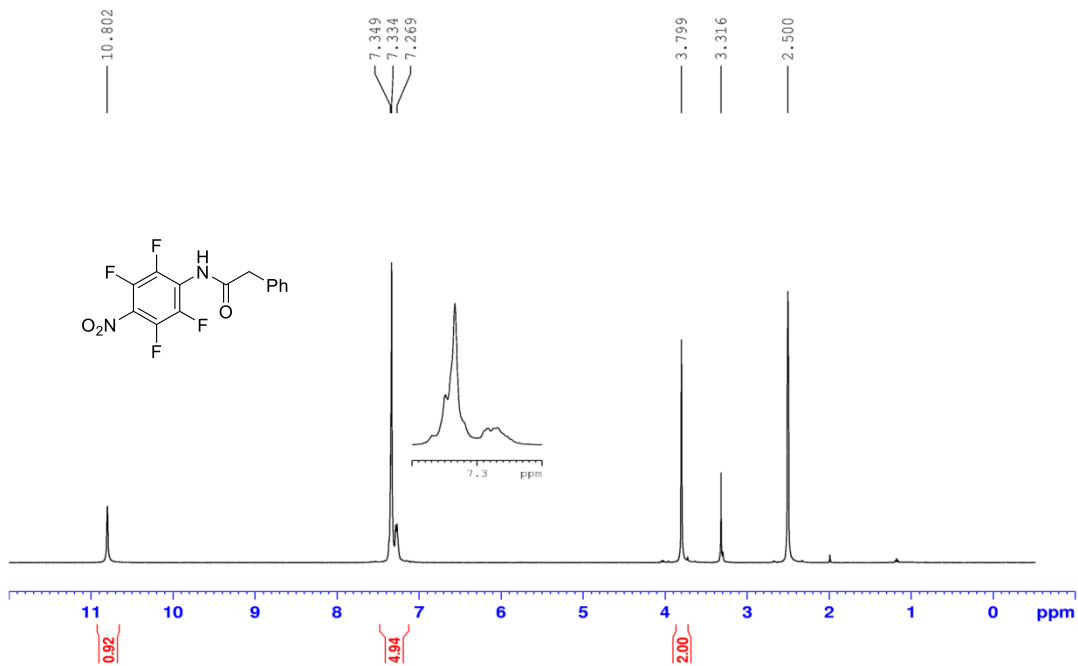
H-NMR L054B DMSO 400MHz



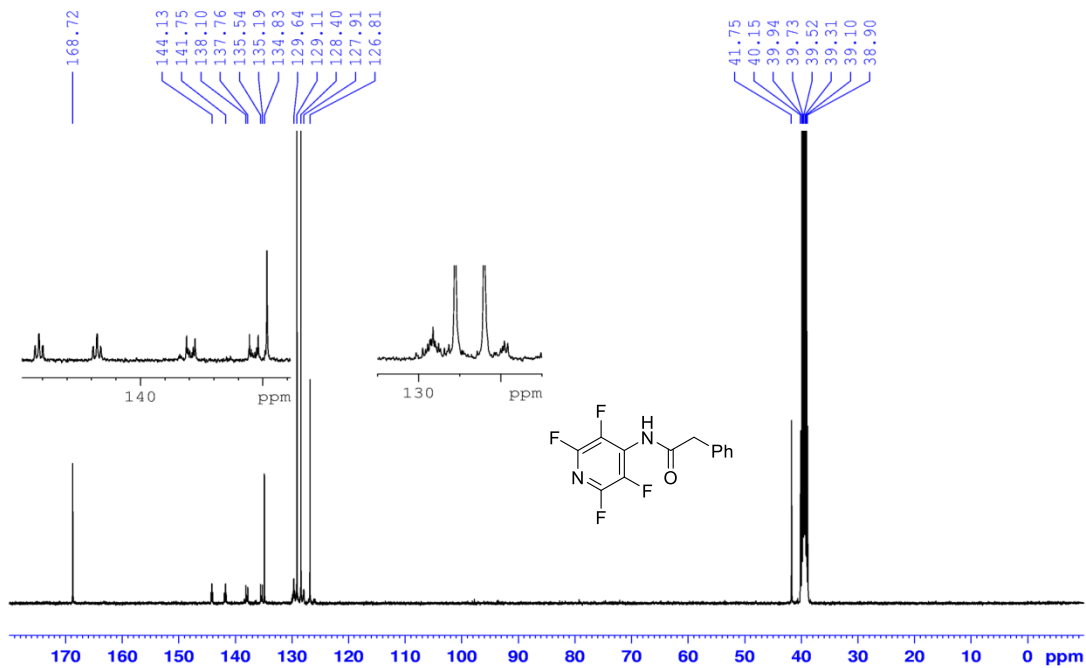
CNMR L089



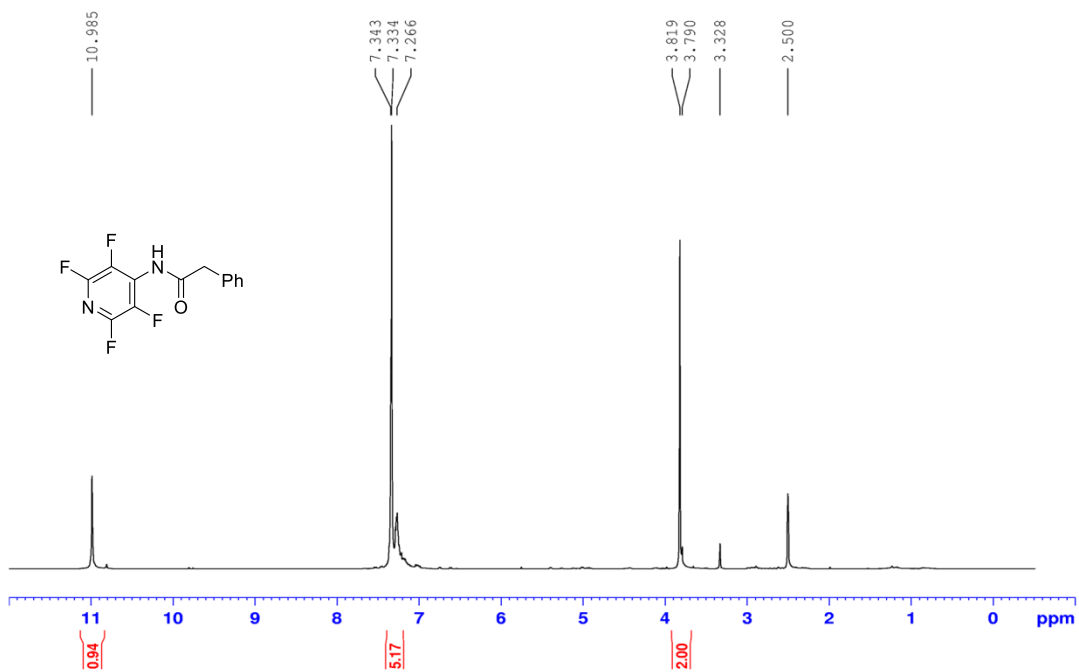
HNMR L089



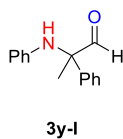
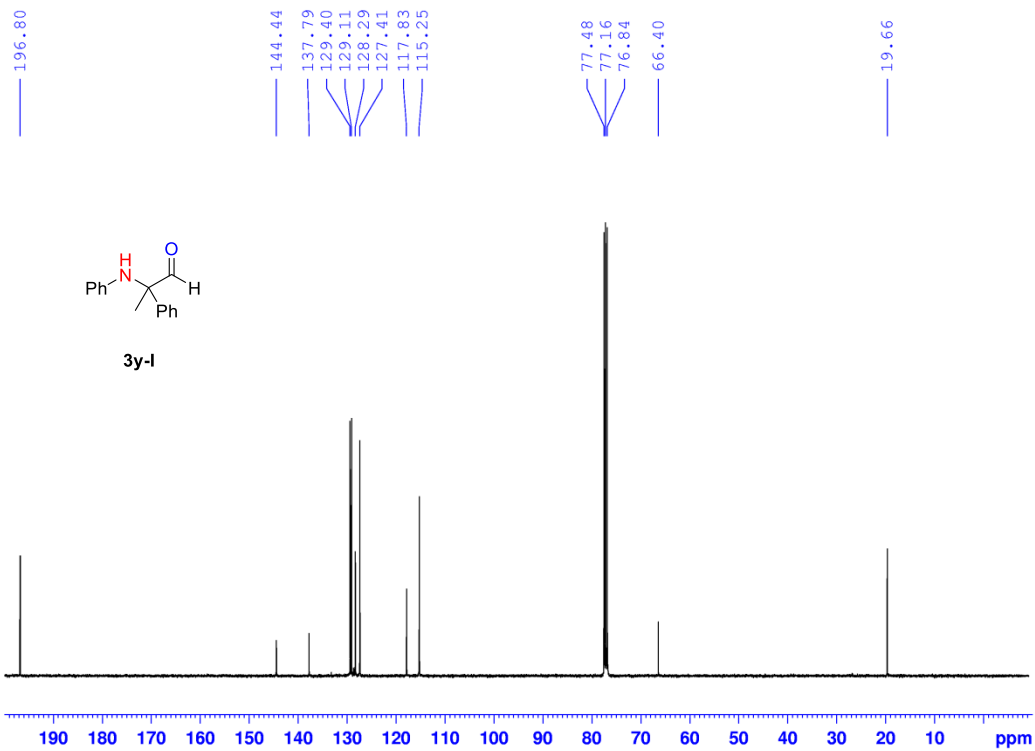
C-NMR L056



H-NMR L056



CNMR L083A



HNMR L083A

