Electronic Supplementary Material (ESI) for ChemComm.

Robust and General Procedure for Carbon Isotope Labeling of Linear Urea Derivatives with Carbon Dioxide

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Supporting Information

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1. General information

Reactants and solvents

Unless otherwise noted, all reactions were out in oven-dried glassware. Commercially available chemicals were purchased from ABCR, Acros Organics, Sigma-Aldrich, Alfa Aesar, Combi-Blocks, Carbolution, Fluorochem, and TCI Europe and used received unless otherwise stated. The following solvents were dried by distillation over the drying agents indicated in parentheses: THF (Sodium), Dichloromethane (CaH_2). Additional anhydrous solvents were purchased from Acros Organics, Sigma-Aldrich, Alfa Aesar and stored over molecular sieves under argon atmosphere.

Purifications

Flash chromatography were perfomred on silica gel (Merck Kieselgel 60, grading 40-63 µm) or using automate Puriflash XS 520 Plus with pre-packed column RediSep® Rf (grading 35-70 µm).
Chiral HPLC chromatograms were recorded using a JASCO SFC apparatus with CHIRALCEL IA chiral column (250 mm x 4.6 mm x 5 µm), mobile phase: CO_2/*i*PrOH: 10/90, flow rate 1.0 mL.min^{-1} at 25 °C, UV detection (300 nm).

Analysis

Reactions were monitored by TLC carried out on silica 0.25 mm (60 F254, Merck), using UV light as visualizing agent. For staining, the TLC plates were dipped into a solution of basic aqueous permanganate (1 g $KMnO_4$, 6 g K_2CO_3 and 0.1 g KOH in 100 mL of H_2O) and developed with a heat gun. *Nuclear Magnetic Resonance (NMR) Spectroscopy:* ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (376 MHz) were measured on a Bruker Avance 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from residual solvents peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (br, s), doublet (d), triplet (t), quartet (q), quintet (quint.), multiplet (m). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m). *Electrospray mass spectra* were obtained using an ESI-Quadripole autopurify, Waters (pump: 2545, mass: ZQ2000) mass Spectrometer. LC-MS spectra were recorded on a Waters Acquity UPLC® equipped PDA eλ Detector and SQ Detector 2, mobile phase A: H_2O + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid.*High-Resolution Mass Spectra* (HRMS) were performed on a Bruker maXis mass spectrometer by the "Fédération de Recherche" ICOA/CBM (FR2708) platform (University of Orléans).*Infrared spectra* (IR) were obtained on a Perkin Elmer UATR TWI FTIR spectrophotometer and are reported as wavelength number (cm^{-1}). *Melting points* (Mp) were obtained on a BÜCHI Melting Point B-545 and are reported in °C.

Carbon-14 radiolabeling

Carbon-14 reagents and compounds were handled by experimentalist uniquely trained in working with radioactive materials and operating in specialized laboratories.

Carbon-14 radioactivity was measured either with a PerkinElmer Ultra Gold liquid scintillation cocktail or with a PerkinElmer 3110TR liquid scintillation analyzer.

RadioHPLC and HPLC-UV analyses were conducted with a Waters Alliance 2695 connected to a MS detector Waters ZQ 2000 and a Scintillation Analyzer Berthold 514 (column Xbridge BEH C18 100 x 4.6 mm, 3.5 µm). Alternatively, they were also conducted on a Waters Acquity UPLC® equipped PDA eλ Detector and SQ Detector 2, mobile phase A: H_2O + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid and a Scintillation Analyzer Berthold 509 (Xbridge BEH C18 50 x 2.1, 1.7).

When using $^{14}CO_2$: $^{14}CO_2$ (2.172 GBq.mmol^{-1}) was generated using a $^{14}CO_2$ manifold system (RC Tritec AG). Mass spectra (ESI) for the calculation of molar activities (A_m) were obtained using a Waters Micromass ZQ spectrometer. Radiochemical purities were determined by Thin Layer Chromatography on TLC silica gel 60F254 glass plates (Merck) using a RITA scanner (Raytest) for the radioactive detection.

2. Materials and Methods

2.1. Procedures for azide preparation

General procedure GP1

In a solution of NaN_3 (**1.1 equiv.**) in DMSO (**2 mL.mmol^{-1}**) was added the aryl bromide (**1 equiv.**). The solution was stirred overnight and water was added (**8 mL.mmol^{-1}**). The aqueous layer was extracted three times with Et_2O (**1 mL.mmol^{-1}**) and the organic layer was dried over $MgSO_4$ filtrated and concentrated under vacuum.

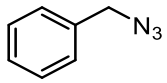
General procedure GP2

A solution of the aromatic amine (**1 equiv.**) in HCl 1.2 M (**4 mL.mmol^{-1}**) was cooled to 0°C in an ice bath. To this stirred mixture was added a solution of $NaNO_2$ (**1.2 equiv.**) in water. The solution was stirred 30 min at 0 °C and a solution of NaN_3 (**1.5 equiv.**) in water was added dropwise. The resulting solution was stirred at room temperature for 1 hour and was extracted twice with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtrated and concentrated under vacuum.

General procedure GP3

A solution of the aromatic amine (**1 equiv.**) in HCl 1.2 M (**4 mL.mmol^{-1}**) was cooled to 0°C in an ice bath. To this stirred mixture was added a solution of $NaNO_2$ (**1.2 equiv.**) in water. The solution was stirred 30 min at 0 °C and a solution of NaN_3 (**1.5 equiv.**) in water was added dropwise. The resulting solution was stirred at room temperature for 1 hour and pH was adjusted to pH = 8 with a saturated solution of $NaHCO_3$. The aqueous layer was extracted twice with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtrated and concentrated under vacuum.

*Benzyl azide **(S1)***

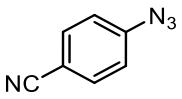


$C_7H_7N_3$
MW: 133.06 g.mol^{-1}
Yield: 85%
Yellow oil

Starting from benzyl bromide (700 µL, 5.85 mmol) and using *the general procedure **GP1***. The crude mixture affording the expected compound as a yellow oil without further purification (660 mg, 5.00 mmol, **85%**). Data are consistent with literature values. [1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42-7.30 (m, 5H), 4.35 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5, 129.0 (2C), 128.4, 128.4 (2C), 54.9.

*4-azidobenzonitrile **(S2)***

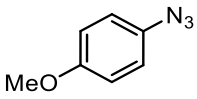


$C_7H_4N_4$
MW: 144.04 g.mol^{-1}
Yield: 90%
Yellow solid

Starting from p-aminobenzonitrile (590 mg, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow solid without further purification (650 mg, 4.50 mmol, **90%**). Data are consistent with literature values. [2]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59-7.54 (m, 2H), 7.06-7.01 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.6, 133.6 (2C), 119.5 (2C), 118.2, 108.0.

*1-azido-4-methoxybenzene **(S3)***

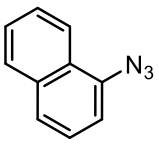


$C_7H_7N_3O$
MW: 149.06 g.mol^{-1}
Yield: 54%
Dark yellow oil

Starting from 4-methoxyaniline (615 mg, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a dark yellow oil without further purification (400 mg, 2.70 mmol, **54%**). Data are consistent with literature values. [3]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98-6.93 (m, 2H), 6.91-6.86 (m, 2H), 3.80 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 132.5, 120.1 (2C), 115.3 (2C), 55.7.

*1-azidonaphtalene **(S4)***

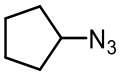


$C_{10}H_7N_3$
MW: 169.06 g.mol^{-1}
Yield: 95%
Dark yellow oil

Starting from naphthalen-1-amine (572 mg, 4.00 mmol) and using the *general procedure **GP2***. The crude mixture was purified by silica gel chromatography using *n*-heptane as eluent affording the expected compound as a dark yellow oil (642 mg, 3.80 mmol, **95%**). Data are consistent with literature values. [3]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14-8.08 (m, 1H), 7.86-7.80 (m, 1H), 7.66-7.62 (m, 1H), 7.55-7.45 (m, 3H), 7.27 (d, J = 7.3 Hz, J = 1.0 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.6, 134.5, 127.9, 127.0, 126.5, 126.3, 125.8, 124.8, 122.7, 114.0.

*Cyclopentylazide **(S5)***

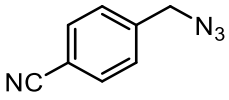


$C_5H_9N_3$
MW: 111.08 g.mol^{-1}
Yield: 72%
colorless oil

Starting from Bromocyclopentane (1.07 mL, 10.0 mmol) and using *the general procedure **GP1***. The crude mixture affording the expected compound as yellow oil without further purification (800 mg, 7.20 mmol, **72%**). Data are consistent with literature values. [4]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.97-3.89 (m, 1H), 1.88-1.58 (m, 8H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.1, 32.2 (2C), 23.6 (2C).

*1-(azidomethyl)-4-cyanobenzene **(S6)***

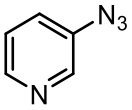


$C_8H_6N_4$
MW: 158.06 g.mol^{-1}
Yield: 93%
Colorless oil

Starting from 4-cyanobenzyl bromide (490 mg, 2.50 mmol) and using *the general procedure **GP1***. The crude mixture affording the expected compound as a colorless oil without further purification (370 mg, 2.32 mmol, **93%**). Data are consistent with literature values. [5]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70-7.66 (m, 2H), 7.46-7.41 (m, 2H), 4.45 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.9, 132.8 (2C), 128.6 (2C), 118.6, 112.3, 54.2.

*3-azidopyridine **(S7)***

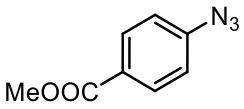


$C_5H_4N_4$
MW: 120.04 g.mol^{-1}
Yield: 60%
Dark yellow oil

Starting from 3-aminopyridine (675 mg, 7.17 mmol) and using *the general procedure **GP3***. The crude mixture was purified by silica gel chromatography using *n*-heptane/AcOEt (60/40) as eluent affording the expected compound as a dark yellow oil (504 mg, 4.30 mmol, **60%**). Data are consistent with literature values. [2]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 4.7 Hz, *J* = 1.4 Hz, 1H), 8.37 (d, *J* = 2.6 Hz, 1H), 7.35 (ddd, *J* = 8.2 Hz, *J* = 2.6 Hz, *J* = 1.4 Hz, 1H), 7.26 (dd, *J* = 8.2 Hz, *J* = 4.7 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.2, 141.5, 137.2, 126.0, 124.3.

*Methyl-4-aminobenzoate **(S8)***

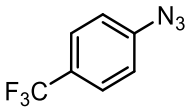


$C_8H_7N_3O_2$
MW: 177.05 g.mol^{-1}
Yield: 97%
Yellow oil

Starting from methyl-4-aminobenzoate (377 mg, 2.50 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow oil without further purification (430 mg, 2.43 mmol, **97%**). Data are consistent with literature values. [2]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06-8.00 (m, 2H), 7.09-7.03 (m, 2H), 3.91 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 144.9, 131.6 (2C), 126.9, 119.0 (2C), 52.3.

*1-azido-4-(trifluoromethyl)benzene **(S9)***

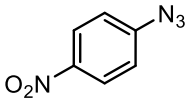


$C_7H_4F_3N_3$
MW: 187.04 g.mol^{-1}
Yield: 64%
Yellow oil

Starting from p-(trifluoromethyl)aniline (315 µL, 2.50 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow oil without further purification (300 mg, 1.60 mmol, **64%**). Data are consistent with literature values. [1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64-7.58 (m, 2H), 7.15-7.09 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9-143.8 (m), 127.6 (q, *J* = 257 Hz), 127.2 (q, *J* = 4 Hz, 2C), 122.7, 119.4 (2C).

*1-azido-4-nitrobenzene **(S10)***

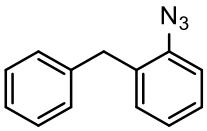


$C_6H_4N_4O_2$
MW: 164.03 g.mol^{-1}
Yield: 97%
Yellow solid

Starting from p-nitroaniline (400 mg, 2.89 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow solid without further purification (460 mg, 2.80 mmol, **97%**). Data are consistent with literature values. [2]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26-8.19 (m, 2H), 7.16-7.09 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.0, 144.7, 125.7 (2C), 119.5 (2C).

*1-azido-2-benzylbenzene **(S11)***

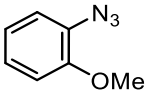


$C_{13}H_{11}N_3$
MW: 209.10 g.mol^{-1}
Yield: 75%
Orange oil

Starting from 2-benzylaniline (915 mg, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as an orange oil without further purification (780 mg, 3.75 mmol, **75%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.25 (m, 3H), 7.23-7.13 (m, 5H), 7.10-7.05 (m, 1H), 3.94 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.4, 138.3, 132.5, 131.2, 129.0 (2C), 128.6 (2C), 127.9, 126.2, 124.9, 118.3, 37.0.
IR (cm^{-1}): 3026, 2115, 1493, 1449, 1282, 695.

*1-azido-2-methoxybenzene **(S12)***

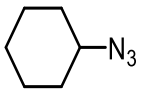


$C_7H_7N_3O$
MW: 149.06 g.mol^{-1}
Yield: 94%
Orange oil

Starting from 2-methoxyaniline (452 mg, 4.00 mmol) and using the *general procedure **GP2***. The crude mixture was purified by silica gel chromatography using *n*-heptane/AcOEt (95/5) as eluant affording the expected compound as an orange yellow oil (560 mg, 3.76 mmol, **94%**). Data are consistent with literature values. [3]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (ddd, *J* = 8.1 Hz, *J* = 7.4 Hz, *J* = 1.7 Hz, 1H), 7.02 (ddd, *J* = 7.8 Hz, *J* = 1.7 Hz, 1H), 6.97-6.87 (m, 2H), 3.88 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.2, 128.4, 125.8, 121.4, 120.4, 112.2, 56.0.

*Cyclohexylazide **(S13)***

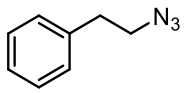


$C_6H_{11}N_3$
MW: 125.10 g.mol^{-1}
Yield: 97%
Colorless oil

Starting from Bromocyclohexane (1.23 mL, 10.0 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as yellow oil without further purification (800 mg, 9,70 mmol, **64%**). Data are consistent with literature values. [4]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38-3.27 (m, 1H), 1.95-1.84 (m, 2H), 1.79-1.70 (m, 2H), 1.62-1.50 (m, 2H), 1.44-1.50 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.0, 31.7 (2C), 25.4 (2C), 24.4.

2-(Azidoethyl)benzene ***(S14)***

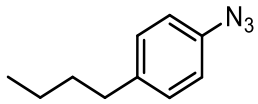


$C_8H_9N_3$
MW: 147.08 g.mol^{-1}
Yield: 82%
Colorless oil

Starting from 2-(bromoethyl)benzene (925 mg, 5.00 mmol) and using *the general procedure* ***GP1***. The crude mixture affording the expected compound as colorless oil without further purification (600 mg, 4,10 mmol, **82%**). Data are consistent with literature values. [1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.31 (m, 2H), 7.29-7.22 (m, 3H), 3.52 (t, *J* = 7.3 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 128.9 (2C), 128.8 (2C), 126.9, 52.6, 35.5.

1-azido-4-butylbenzene ***(S15)***

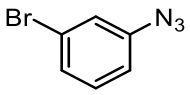


$C_{10}H_{13}N_3$
MW: 175.11 g.mol^{-1}
Yield: 72%
Dark yellow oil

Starting from 4-butylaniline (745 mg, 5.00 mmol) and using *the general procedure* ***GP2***. The crude mixture affording the expected compound as a dark yellow oil without further purification (630 mg, 3.60 mmol, **72%**). Data are consistent with literature values. [6]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19-7.12 (m, 2H), 6.98-6.90 (2H), 2.63-2.54 (m, 2H), 1.63-1.51 (m, 2H), 1.41-1.27 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 137.4, 129.9 (2C), 119.0 (2C), 35.1, 33.8, 22.4, 14.1.

1-azido-3-bromobenzene ***(S16)***

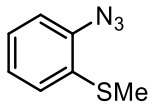


$C_9H_6BrN_3$
MW: 196.96 g.mol^{-1}
Yield: 97%
Dark yellow oil

Starting from 3-bromoaniline (370 µL, 3.40 mmol) and using *the general procedure* ***GP2***. The crude mixture affording the expected compound as a dark yellow oil without further purification (640 mg, 3.30 mmol, **97%**). Data are consistent with literature values. [7]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (ddd, *J* = 8.0 Hz, *J* = 1.7 Hz, *J* = 1.1 Hz, 1H), 7.23-7.21 (m, 1H), 7.19-7.18 (m, 1H), 6.96 (ddd, *J* = 7.9 Hz, *J* = 2.2 Hz, *J* = 1.1 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.7, 131.1, 128.1, 123.4, 122.3, 117.9.

*1-azido-2-(methyl)thiobenzene **(S17)***

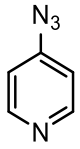


$C_7H_7N_3S$
MW: 165.04 g.mol^{-1}
Yield: 91%
Yellow oil

Starting from 2-(methylthio)aniline (625 µL, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow oil without further purification (750 mg, 4.55 mmol, **91%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23-7.18 (m, 2H), 7.15-7.10 (m, 2H), 2.45 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 129.9, 127.0, 126.3, 125.5, 118.3, 15.4.
IR (cm^{-1}): 2921, 2124, 2088, 1469, 1283, 741.

*4-azidopyridine **(S18)***

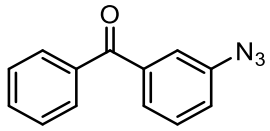


$C_5H_4N_4$
MW: 120.04 g.mol^{-1}
Yield: 69%
Orange oil

In a round bottom flask 4-bromopyridine hydrochloride (1.00 g, 5.14 mmol) was dissolved in water (5 mL) and the pH was adjusted to 6-7 using a solution of NaOH 1 M. Ethanol (5 mL) and NaN_3 (500 mg, 7.71 mmol) were added and the solution was refluxed for 16 h. The mixture was cooled down to room temperature and a saturated solution of $NaHCO_3$ was added. The organic layer was extracted twice with ethyl acetate, dried over $MgSO_4$ and evaporated affording the expected compound as an orange oil (425 mg, 3.55 mmol, **69%**). Data are consistent with literature values. [1]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56-8.50 (m, 2H), 6.96-6.92 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.3 (2C), 148.8, 114.2 (2C).

*3-azidobenzophenone **(S19)***

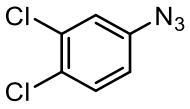


$C_{13}H_9N_3O$
MW: 223.07 g.mol^{-1}
Yield: 99%
Dark yellow oil

Starting from 3-aminobenzophenone (986 mg, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a dark yellow oil without further purification (1.11 g, 4.95 mmol, **99%**). Data are consistent with literature values. [8]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82-7.77 (m, 2H), 7.64-7.58 (m, 1H), 7.55-7.43 (m, 5H), 7.26-7.22 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.8, 140.8, 139.4, 137.2, 133.0, 130.2 (2C), 129.8, 128.6 (2C), 126.7, 122.9, 120.3.

*4-azido-1,2-dichlorobenzene **(S20)***

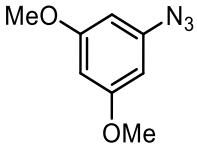


$C_6H_3Cl_2N_3$
MW: 186.97 g.mol^{-1}
Yield: 89%
Dark orange oil

Starting from 3,4-dichloroaniline (810 mg, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a yellow oil without further purification (840 mg, 4.45 mmol, **89%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.6 Hz, 1H), 7.12 (d, *J* = 2.6 Hz, 1H), 6.88 (dd, *J* = 8.6, *J* = 2.6 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 133.8, 131.4, 128.7, 121.1, 118.6.
IR (cm^{-1}): 2104, 1587, 1468, 1297, 805.

*1-azido-3,5-dimethoxybenzene **(S21)***

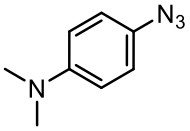


$C_8H_9N_3O_2$
MW: 179.07 g.mol^{-1}
Yield: 78%
Dark red oil

Starting from 3,5-dimethoxyaniline (765 mg, 5.00 mmol) and using *the general procedure **GP1***. The crude mixture affording the expected compound as a dark red oil without further purification (700 mg, 3.90 mmol, **78%**). Data are consistent with literature values. [9]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.26-6.23 (m, 1H), 6.20-6.17 (m, 2H), 3.78 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (2C), 142.1, 97.7 (2C), 97.4, 55.6 (2C).

*4-azido-N,N-dimethylaniline **(S22)***

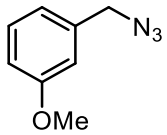


$C_8H_{10}N_4$
MW: 162.09 g.mol^{-1}
Yield: 68%
Dark solid

Starting from N^1,N^1-dimethylbenzene-1,4-diamine (681 mg, 5.00 mmol) and using *the general procedure **GP3***. The crude mixture affording the expected compound as a dark solid without further purification (530 mg, 3.40 mmol, **68%**). Data are consistent with literature values. [10]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95-6.90 (m, 2H), 6.75-6.69 (m, 2H), 2.93 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 128.4, 119.9 (2C), 114.0 (2C), 14.0 (2C).

*1-(azidomethyl)-3-methoxybenzene **(S23)***

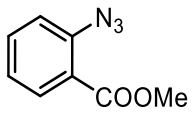


$C_8H_9N_3O$
MW: 163.07 g.mol^{-1}
Yield: 98%
Colorless oil

Starting from 3-methoxybenzyl bromide (770 µL, 5.00 mmol) and using *the general procedure **GP1***. The crude mixture affording the expected compound as a colorless oil without further purification (800 mg, 4.90 mmol, **98%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.27 (m, 1H), 6.93-6.84 (m, 3H), 4.32 (s, 2H), 3.83 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 137.0, 130.0, 120.5, 114.0, 113.8, 55.4, 54.9.
IR (cm^{-1}): 2952, 2838, 2094, 1586, 1264, 1040, 743.

*Methyl 2-azidobenzoate **(S24)***

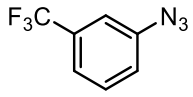


$C_8H_7N_3O_2$
MW: 177.05 g.mol^{-1}
Yield: 97%
Orange oil

Starting from methyl 2-aminobenzoate (647 µL, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as an orange oil without further purification (850 mg, 4.85 mmol, **97%**). Data are consistent with literature values. [8]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.83 (m, 1H), 7.56-7.49 (m, 1H), 7.26-7.22 (m, 1H), 7.21-7.14 (m, 1H), 3.91 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 140.2, 133.3, 132.0, 124.6, 122.8, 120.0, 52.5.

*1-azido-3-(trifluoromethyl)benzene **(S25)***



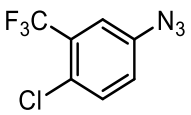
$C_7H_4F_3N_3$
MW: 187.04 g.mol^{-1}
Yield: 76%
Dark yellow oil

Starting from 3-(trifluoromethyl)aniline (617 µL, 5.00 mmol) and using *the general procedure **GP2***. The crude mixture affording the expected compound as a dark yellow oil without further purification (710 mg, 3.80 mmol, **76%**). Data are consistent with literature values. [11]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51-7.45 (m, 1H), 7.42-7.38 (m, 1H), 7.27-7.25 (m, 1H), 7.23-7.19 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.2, 132.5 (q, *J* = 33 Hz), 130.5, 126.4 (q, *J* = 273 Hz), 122.3, 121.7 (q, *J* = 4 Hz), 116.2 (q, *J* = 4 Hz).

4-azido-1-chloro-2-(trifluoromethyl)benzene ***(S26)***



$C_7H_3ClF_3N_3$
MW: 221.00 g.mol^{-1}
Yield: 63%
Orange yellow oil

Starting from 4-chloro-3-(trifluoromethyl)aniline (782 mg, 4.00 mmol) and using the *general procedure* ***GP2***. The crude mixture was purified by silica gel chromatography using *n*-heptane as eluant affording the expected compound as an orange yellow oil (560 mg, 2.52 mmol, **63%**). Data are consistent with literature values. [12]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.6 Hz), 7.32 (d, *J* = 2.7 Hz, 1H), 7.14 (dd, *J* = 8.6 Hz, *J* = 2.7 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.5, 133.0, 130.0 (q, *J* = 32 Hz), 128.1 (q, *J* = 2 Hz), 123.2, 122.4 (q, *J* = 272 Hz), 118.5 (q, *J* = 6 Hz).

2.2. Procedure for [^{13}C] urea labeling

General procedure GP4

Into a 1.0 mL vial, dimethylphenylphosphine was added to a solution containing the amine derivative, the azide and if noted an additive, in the suitable solvent (0.60 mL). The solution was transferred into a Wilmad® low pressure/*vacuum* NMR tube which was further frozen into N_2 bath, then gaseous $^{13}CO_2$ was precisely delivered using Tritec® (Figure S1). The NMR tube was then warmed up to room temperature, progressively brought to the indicated temperature and maintained at this temperature for a given time. After completion, the unreacted $^{13}CO_2$ was removed by opening the NMR tube and the solvent was evaporated. The crude mixture was purified by flash Chromatography affording the expected [^{13}C]labeled urea.

Materials

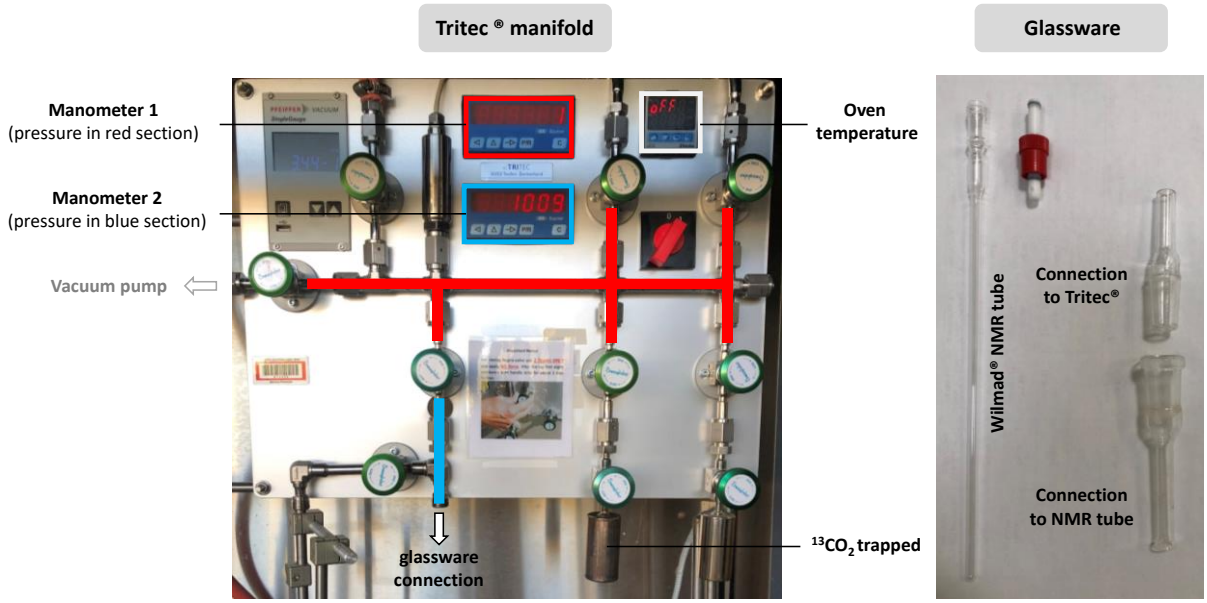


Figure S1: Tritec® manifold and specific glassware

Tritec® procedure

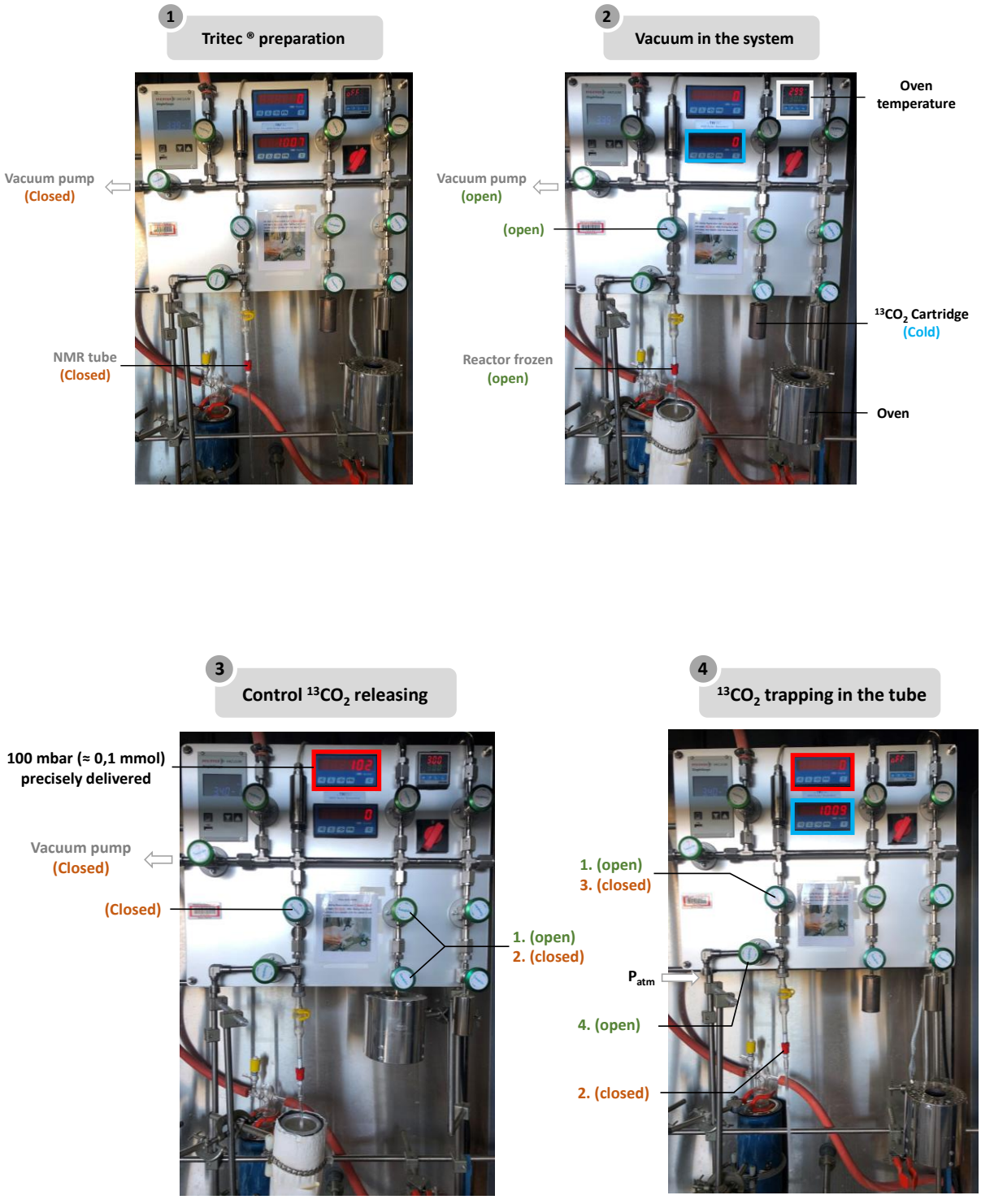
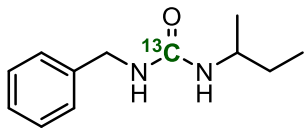


Figure S2: Sequence for $^{13}CO_2$ delivery in the reactor

2.3. Synthesis of ^{13}C-ureas from aliphatic azide and aliphatic amine

[^{13}C] 1-benzyl-3-(sec-butyl)urea **([^{13}C]1)**

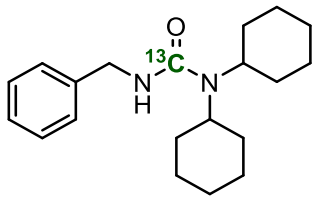


$C_{11}{}^{13}CH_{18}N_2O$
MW: 207.15 g.mol^{-1}
Yield: 85%
White solid

The [^{13}C] 1-benzyl-3-(sec-butyl)urea **[^{13}C]1** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), benzyl azide **S1** (13.3 mg, 0.10 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (30/70) as eluent affording the expected compound as a white solid (17.6 mg, 0.085 mmol, **85%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35-7.20 (m, 5H), 4.33 (d, *J* = 3.3 Hz, 2H), 3.70-3.60 (m, 1H), 1.41 (p, *J* = 7.4 Hz, 2H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9 (^{13}C), 139.4, 128.8 (2C), 127.6 (2C), 127.4, 47.7, 44.7, 30.3, 21.2, 10.4.
HRMS (ESI): calcd for $C_{11}{}^{13}CH_{18}N_2O$ $[M+H]^+$ 208.1525; found 208.1526.
Mp (°C): 88-89 °C

[^{13}C] 3-benzyl-1,1-dicyclohexylurea **([^{13}C]2)**

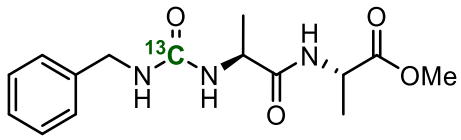


$C_{19}{}^{13}CH_{30}N_2O$
MW: 315.24 g.mol^{-1}
Yield: 73%
White solid

The [^{13}C] 3-benzyl-1,1-dicyclohexylurea **[^{13}C]2** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), benzyl azide **S1** (13.3 mg, 0.1 mmol) dicyclohexylamine (20 µL, 0.11 mmol), and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (20/80) as eluent affording the expected compound as a white solid (23 mg, 0.073 mmol, **73%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.22 (m, 5H), 4.55 (br s, 1H), 4.47-4.42 (m, 2H), 3.44-3.31 (m, 2H), 1.85-1.56 (m, 14H), 1.39-1.21 (m, 4H), 1.17-1.00 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6 (^{13}C), 140.2, 128.7 (2C), 127.6 (2C), 127.2, 55.4, 44.9 (2C), 32.0 (4C), 26.6 (4C), 25.7 (2C).
HRMS (ESI): calcd for $C_{19}{}^{13}CH_{31}N_2O_4$ $[M+H]^+$ 316.2464; found 316.2468.
Mp (°C): 138-140 °C

Methyl (benzylcarbamoyl-[^{13}C])-L-alanyl-L-alaninate **([^{13}C]3)**

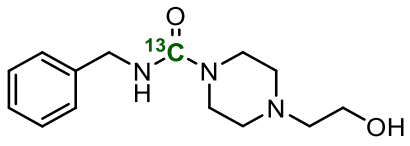


$C_{14}{}^{13}CH_{21}N_3O_4$
MW: 308.16 g.mol^{-1}
Yield: 51%
White solid

The Methyl (benzylcarbamoyl-[^{13}C])-*L*-alanyl-*L*-alaninate **[^{13}C]3** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), benzyl azide **S1** (13.3 mg, 0.1 mmol) H-Ala-Ala-OMe hydrochloride (21.3 mg, 0.10 mmol), DIPEA (32 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (80/20) as eluent affording the expected product as a white solid (15.7 mg, 0.051 mmol, **51%**).

^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 8.34 (d, *J* = 7.0 Hz, 1H), 7.34-7.27 (m, 2H), 7.26-7.19 (m, 3H), 6.53 (br, s), 6.15 (d, *J* = 7.0 Hz, 1H), 4.32-4.16 (m, 4H), 3.62 (s, 3H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, DMSO-d$_6$): δ = 173.2, 173.0, 157.3 (^{13}C), 140.7, 128.2 (2C), 127.0 (2C), 126.6, 51.9, 48.2, 47.4, 42.8, 19.6, 16.9.
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{22}N_3O_4$ $[M+H]^+$ 309.1638; found 309.1641.
Mp (°C): 213-214 °C

[^{13}C] *N*-benzyl-4-(2-hydroxyethyl)piperazine-1-carboxamide **([^{13}C]4)**

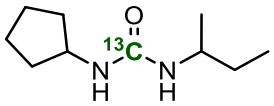


$C_{13}{}^{13}CH_{21}N_3O_2$
MW: 264.17 g.mol^{-1}
Yield: 51%
Colorless oil

The [^{13}C] *N*-benzyl-4-(2-hydroxyethyl)piperazine-1-carboxamide **[^{13}C]4** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), benzyl azide **S1** (13.3 mg, 0.1 mmol) *N*-2-hydroxyethyl)piperazine (13.1 mg, 0.11 mmol), and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using CH_2Cl_2/MeOH (92/8) as eluent affording the expected compound as a colorless oil (13.6 mg, 0.01 mmol, **51%**).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.35-7.18 (m, 5H), 4.35 (d, *J* = 4.0 Hz, 2H), 3.69 (t, *J* = 5.9 Hz, 2H), 3.47-3.42 (m, 4H), 2.57-2.48 (m, 6H).
^{13}C NMR (100 MHz, CDCl$_3$): δ = 160.1 (^{13}C), 141.5, 129.4 (2C), 128.2 (2C), 127.9, 61.3, 59.8, 54.3, 45.2, 44.6.
HRMS (ESI): calcd for $C_{13}{}^{13}CH_{22}N_3O_2$ $[M+H]^+$ 265.1740; found 265.1746.
Mp (°C): 102-104 °C

[^{13}C] *N*-benzyl-4-(2-hydroxyethyl)piperazine-1-carboxamide **([^{13}C]5)**

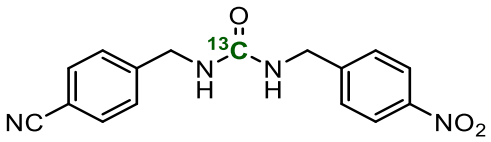


$C_9{}^{13}CH_{20}N_2O$
MW: 185.16 g.mol^{-1}
Yield: 55%
White solid

The [^{13}C] *N*-benzyl-4-(2-hydroxyethyl)piperazine-1-carboxamide **[^{13}C]5** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), cyclopentyl azide **S5** (11.0 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol), and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using CH_2Cl_2 as eluent affording the expected product as a white solid (9.7 mg, 0.055 mmol, **55%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.00-3.89 (m, 1H), 3.72.3.61 (m, 1H), 2.01-1.88 (m, 2H), 1.71-1.53 (m, 3H), 1.50-1.32 (m, 4H), 1.11 (d, *J* = 6.5 Hz, 3H), 0.90 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8 (^{13}C), 52.3, 47.6, 33.8, 30.4, 23.8, 21.2, 10.5.
HRMS (ESI): calcd for $C_9{}^{13}CH_{21}N_2O$ $[M+H]^+$ 186.1682; found 186.1685.
Mp (°C): 154-156 °C

[^{13}C] 1-(4-cyanobenzyl)-3-(4-nitrobenzyl)urea **([^{13}C]6)**



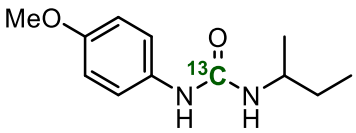
$C_{15}{}^{13}CH_{14}N_4O_3$
MW: 311.11 g.mol^{-1}
Yield: 84%
White solid

The [^{13}C] 1-(4-cyanobenzyl)-3-(4-nitrobenzyl)urea **[^{13}C]6** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 4-(azidomethyl)benzonitrile **S6** (15.8 mg, 0.10 mmol), 4-nitrobenzylamine hydrochloride (18.8 mg, 0.10 mmol), DIPEA (38 µL, 0.25 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (90/10) as eluent affording the expected compound as a white solid (26 mg, 0.084 mmol, **84%**).

^{1}H NMR (400 MHz, DMF-d_7): δ = 8.29-8.24 (m, 2H), 7.87-7.82 (m, 2H), 7.68.7.62 (m, 2H), 7.60-7.56 (m, 2H), 7.05-6.90 (m, 2H), 4.57-4.52 (m, 2H), 4.52-4.47 (m, 2H).
^{13}C NMR (100 MHz, DMF-d_7): δ = 159.5 (^{13}C), 150.8, 148.5, 147.8, 133.3 (2C), 129.1 (2C), 129.0 (2C), 124.5 (2C), 120.0, 110.9, 44.2, 44.1.
HRMS (ESI): calcd for $C_{15}{}^{13}CH_{14}N_4O_3$ $[M+H]^+$ 312.1172; found 312.1167.
Mp (°C): 227-229 °C

2.4. Synthesis of ^{13}C-ureas from aromatic azide and aliphatic amine

[^{13}C] 1-(sec-butyl)-3-(4-methoxyphenyl)urea **([^{13}C]7)**

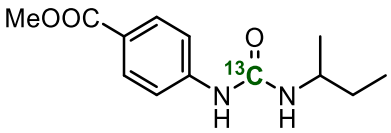


$C_{11}{}^{13}CH_{18}N_2O_2$
MW: 223.14 g.mol^{-1}
Yield: 77%
White solid

The [^{13}C] 1-(sec-butyl)-3-(4-methoxyphenyl)urea **[^{13}C]7** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-4-methoxybenzene **S3** (14.9 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (50/50) as eluent affording the expected product as a white solid (17 mg, 0.077 mmol, **77%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20-7.13 (m, 2H), 6.87-6.80 (m, 2H), 3.82-3.75 (m, 1H), 3.78 (s, 3H), 1.47-1.37 (m, 1H), 1.09 (d, *J* = 6.6 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 156.5 (^{13}C), 131.2, 124.7 (2C), 114.7 (2C), 55.6, 47.6, 30.1 (d, *J* = 2 Hz), 21.0 (d, *J* = 2 Hz), 10.5.
HRMS (ESI): calcd for $C_{12}{}^{13}CH_{19}N_2O_3$ $[M+H]^+$ 224.1475; found 224.1476.
Mp (°C): 119-121 °C

Methyl 4-(3-(sec-butyl)ureido-[^{13}C])benzoate **([^{13}C]8)**

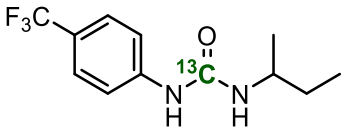


$C_{12}{}^{13}CH_{18}N_2O_3$
MW: 251.14 g.mol^{-1}
Yield: 44%
White solid

The Methyl 4-(3-(sec-butyl)ureido-[^{13}C])benzoate **[^{13}C]8** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), methyl 4-azidobenzoate **S8** (17.7 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (40/60) as eluent affording the expected product as a white solid (11 mg, 0.044 mmol, **44%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98-7.91 (m, 2H), 7.42-7.36 (m, 2H), 3.88 (s, 3H), 3.84-3.78 (m, 1H), 1.53-1.44 (m, 2H), 1.16 (d, *J* = 6.6 Hz, 1H), 0,93 (t, *J* = 7.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 154.6 (^{13}C), 143.5, 131.2 (2C), 124.4, 118.4 (d, *J* = 2 Hz, 2C), 52.1, 47.9, 30.1 (d, *J* = 2 Hz), 21.0 (d, *J* = 2 Hz), 10.5.
HRMS (ESI): calcd for $C_{12}{}^{13}CH_{19}N_2O_3$ $[M+H]^+$ 252.1424; found 252.1428.
Mp (°C): 114-116 °C

[^{13}C] 1-(sec-butyl)-3-(4-(trifluoromethyl)phenyl)urea **([^{13}C]9)**

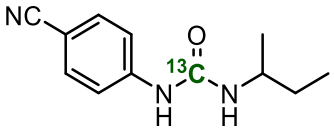


$C_{11}{}^{13}CH_{15}F_3N_2O$
MW: 261.12 g.mol^{-1}
Yield: 46%
White solid

The [^{13}C] 1-(sec-butyl)-3-(4-(trifluoromethyl)phenyl)urea **[^{13}C]9** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-4-(trifluoromethylbenzene) **S9** (18.7 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (20/80) as eluent affording the expected product as a white solid (12 mg, 0.046 mmol, **46%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49-7.44 (m, 2H), 7.41-7.36 (m, 2H), 3.82-3.71 (m, 1H), 1.49-1.39 (m, 2H), 1.12 (d, *J* = 6.6 Hz, 1H), 0.90 (t, *J* = 7.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1 (^{13}C), 142.3, 126.3 (q, *J* = 4 Hz, 2C), 124.6 (q, *J* = 33 Hz), 124.2 (q, *J* = 272 Hz), 118.7 (d, *J* = 2 Hz, 2C), 47.6, 30.0 (d, *J* = 2 Hz), 20.8 (d, *J* = 1 Hz), 10.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ = - 61.9.
HRMS (ESI): calcd for $C_{11}{}^{13}CH_{16}F_3N_2O$ $[M+H]^+$ 262.1246; found 262.1243.
Mp (°C): 129-131 °C

[^{13}C] 1-(sec-butyl)-3-(4-cyanophenyl)urea **([^{13}C]10)**

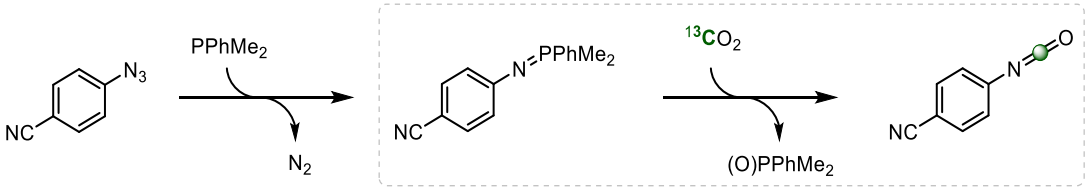


$C_{11}{}^{13}CH_{15}N_3O$
MW: 218.12 g.mol^{-1}
Yield: 73%
White solid

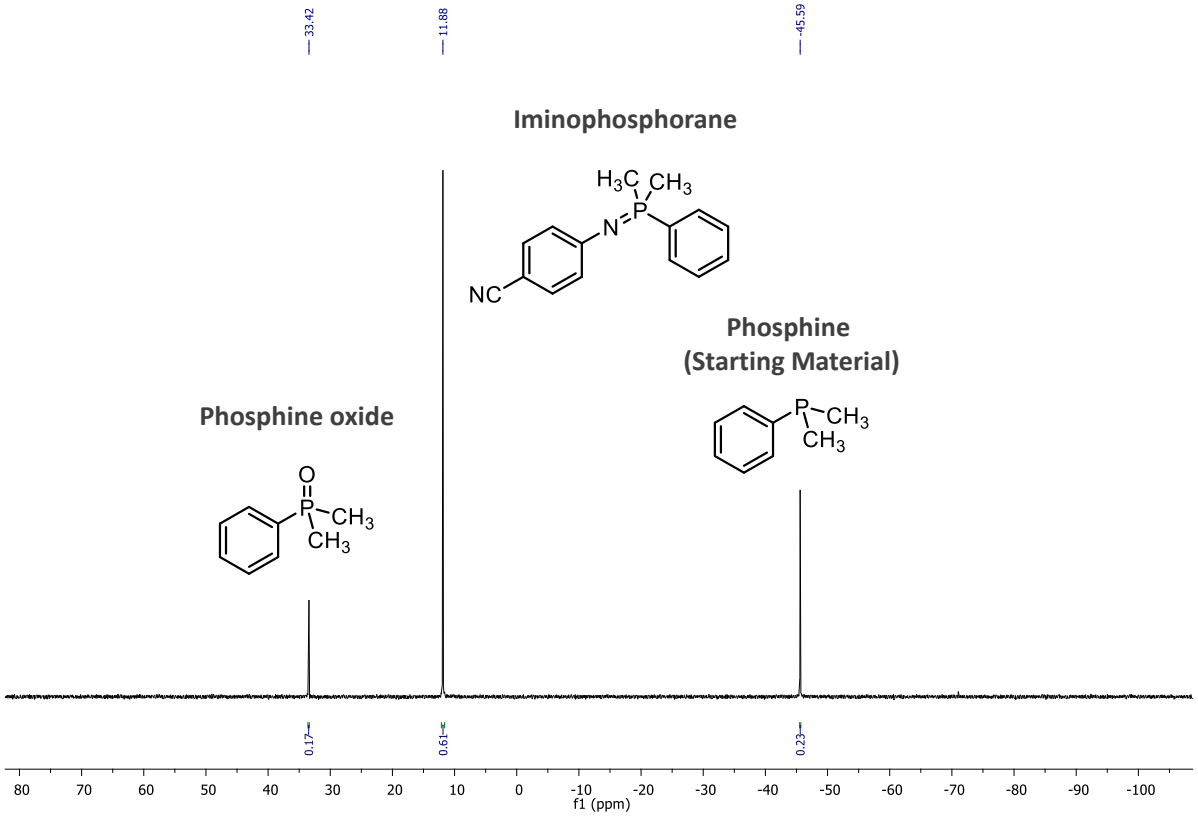
In a glovebox, the [^{13}C] 1-(sec-butyl)-3-(4-cyanophenyl)urea **[^{13}C]10** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-4-(cyanobenzene) **S2** (14.4 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) in CH_3CN. The NMR tube is then taken out of the glovebox and $^{13}CO_2$ (110 mbar, 0.11 mmol) was added. The reaction is kept for 10 minutes at 70°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (20/80) as eluent affording the expected product as a white solid (16 mg, **73%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.58 – 7.37 (m, 4H), 5.36 (d, *J* = 7.9 Hz, 1H), 3.77 (m, 1H), 1.53 – 1.37 (m, 2H), 1.13 (d, *J* = 6.6 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1 (^{13}C), 144.4, 133.7, 119.9, 118.8, 118.8, 104.88, 77.16, 47.96, 30.34, 30.33, 21.26, 10.77.
HRMS (ESI): calcd for $C_{11}{}^{13}CH_{16}N_3O$ $[M+H]^+$ 219.1326; found 219.1321.
Mp (°C): 147-148 °C

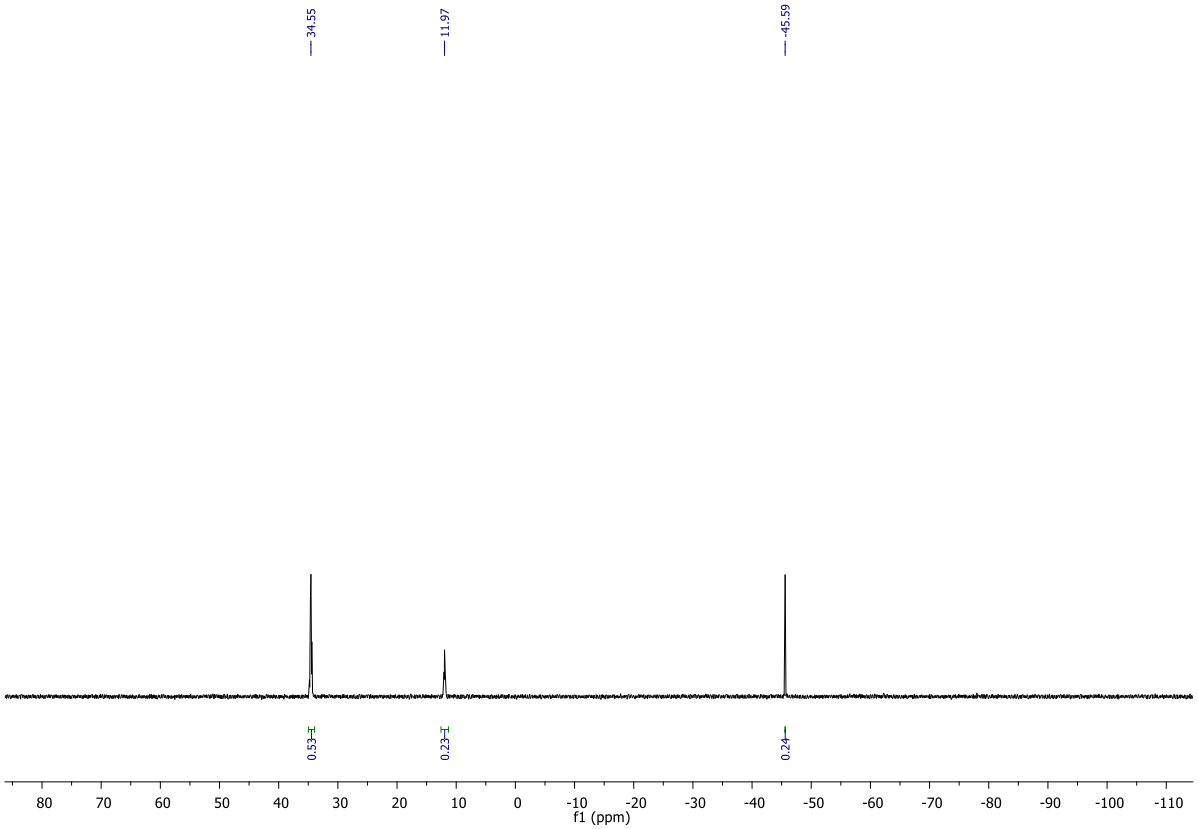
<u>Note</u>: The reaction was initially performed at room temperature, however, ^{31}P NMR follow-up of the reaction indicated the presence of iminophosphorane even after 60 min as shown on the following spectra. This suggest that the isocyanate formation is the rate determining step in that case.



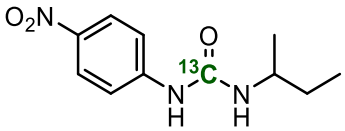
^{31}P NMR (CD_3CN, 162 MHz) at t = 10 min, 25 °C



^{31}P NMR (CD_3CN, 162 MHz) at t = 60 min, 25 °C



[^{13}C] 1-(sec-butyl)-3-(4-nitrophenyl)urea **([^{13}C]11)**

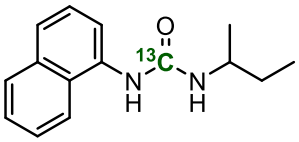


$C_{10}{}^{13}CH_{15}N_3O_3$
MW: 238.11 g.mol^{-1}
Yield: 68%
Yellow pale solid

In a glovebox, the [^{13}C] 1-(sec-butyl)-3-(4-nitrophenyl)urea **[^{13}C]11** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-4-(nitrobenzene) **S10** (16.4 mg, 0.1 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) in CH_3CN. The NMR tube is then taken out of the glovebox and $^{13}CO_2$ (110 mbar, 0.11 mmol) was added. The reaction is kept for 10 minutes at 70°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (20/80) as eluent affording the expected product as a white solid (16 mg, **68%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 9.2 Hz, 2H), 7.77 (s, 1H), 7.56 – 7.48 (m, 2H), 6.65 (d, *J* = 9.0 Hz, 1H), 3.80 (m, 1H), 1.49 (p, *J* = 7.2 Hz, 2H), 1.16 (d, *J* = 6.6 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.43 (^{13}C), 145.95, 141.87, 126.60, 125.32, 117.67, 113.56, 47.72, 29.90, 20.75, 10.32.
HRMS (ESI): calcd for $C_{10}{}^{13}CH_{16}N_3O_3$ $[M+H]^+$ 239.1224; found 239.1220.
Mp (°C): 133-134 °C

[^{13}C] 1-(sec-butyl)-3-(naphthalen-1-yl)urea **([^{13}C]12)**

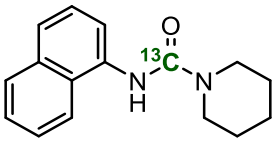


$C_{14}{}^{13}CH_{18}N_2O$
MW: 243.15 g.mol^{-1}
Yield: 69%
White solid

The [^{13}C] 1-isobutyl-3-(naphthalen-1-yl)urea **[^{13}C]12** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (40/60) as eluent affording the expected compound as a white solid (16.6 mg, 0.069 mmol, **69%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10-8.04 (m, 1H), 7.92-7.87 (m, 1H), 7.81-7.77 (m, 1H), 7.59-7.45 (m, 4H), 3.91-3.79 (m, 1H), 1.41-1.31 (m, 2H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 7.4 Hz, 3H)
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6-156.4 (m, ^{13}C), 134.7, 133.4, 128.6, 127.3, 127.0, 126.8, 126.0, 123.9, 122.4, 122.4, 47.8, 30.1, 21.0, 10.5.
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{18}N_2O$ $[M+H]^+$ 244.1525; found 244.1522.
Mp (°C): 134-136 °C

[^{13}C] *N*-(naphthalen-1-yl)piperidine-1-carboxamide **([^{13}C]13)**

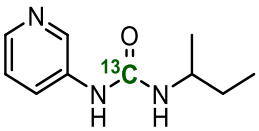


$C_{15}{}^{13}CH_{18}N_2O$
MW: 255.15 g.mol^{-1}
Yield: 53%
White solid

The [^{13}C] N-(naphthalen-1-yl)piperidine-1-carboxamide **[^{13}C]13** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), piperidine (9.8 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (40/60) as eluent affording the expected compound as a white solid (13.4 mg, 0.053 mmol, **53%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.82 (m, 2H), 7.70-7.62 (m, 2H), 7.53-7.41 (m, 3H), 6.69 (br s, 1H), 3.54-3.48 (m, 4H), 1.69-1.61 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0 (^{13}C), 134.3, 134.3, 128.8, 128.0 (d, *J* = 2 Hz), 126.1, 126.0, 125.9, 125.9, 124.9, 121.2, 120.6, 45.7 (2C), 25.9 (2C), 24.5.
HRMS (ESI): calcd for $C_{15}{}^{13}CH_{18}N_2O$ $[M+H]^+$ 256.1525; found 256.1526.
Mp (°C): 152-154 °C

[^{13}C] 1-(sec-butyl)-3-(pyridin-3-yl)urea **([^{13}C]14)**

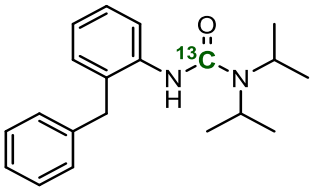


$C_9{}^{13}CH_{15}N_3O$
MW: 194.12 g.mol^{-1}
Yield: 85%
Amorphous solid

The [^{13}C] 1-(sec-butyl)-3-(pyridin-3-yl)urea **[^{13}C]14** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 3-azidopyridine **S7** (12.0 mg, 0.10 mmol), *sec*-butylamine (10.2 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc as eluent affording the expected compound as an amorphous solid (16.4 mg, 0.085 mmol, **85%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 2.4 Hz, 1H), 8.17 (dd, *J* = 4.7 Hz, *J* = 0.9 Hz, 1H), 8.04 (dd, *J* = 8.4 Hz, *J* = 1.4 Hz, 1H), 7.96 (br s, 1H), 7.20 (dd, *J* = 8.4 Hz, *J* = 4.7 Hz, 1H), 5.39 (br s, 1H), 3.85-3.72 (m, 1H), 1.45 (p, *J* = 7.3 Hz, 2H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6 (^{13}C), 143.0, 140.1 (d, *J* = 2.6 Hz), 137.0, 126.8, 124.2, 47.6, 30.1, 20.1 (d, *J* = 1.2 Hz), 10.5.
HRMS (ESI): calcd for $C_9{}^{13}CH_{15}N_3O$ $[M+H]^+$ 195.1321; found 195.1323.

[^{13}C] 3-(2-benzylphenyl)-1,1-diisopropylurea **([^{13}C]15)**

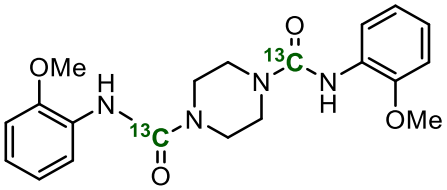


$C_{19}{}^{13}CH_{16}N_2O$
MW: 311.21 g.mol^{-1}
Yield: 62%
White solid

The [^{13}C] 3-(2-benzylphenyl)-1,1-diisopropylurea **[^{13}C]15** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-2-benzylbenzene **S11** (20.9 mg, 0.10 mmol), diisopropylamine (14 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (20/80) as eluent affording the expected compound as a white solid (19.1 mg, 0.062 mmol, **62%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 8.1 Hz, *J* = 0.9 Hz, 1H), 7.32-7.16 (m, 5H), 7.14-7.10 (m, 2H), 7.04 (td, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H), 5.84 (br s, 1H), 4.03 (s, 2H), 3.62-3.49 (m, 2H), 1.12 (d, *J* = 6.8 Hz, 12H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6 (^{13}C), 139.2, 137.9, 131.2, 129.6 (d, *J* = 3 Hz), 129.0 (2C), 128.4 (2C), 127.7, 126.8, 123.4, 123.3, 45.9 (2C), 38.8, 21.3 (4C).
HRMS (ESI): calcd for $C_{19}{}^{13}CH_{16}N_2O$ $[M+H]^+$ 312.2151; found 312.2149.
Mp (°C): 99-101 °C

N^1,*N*^{4}-bis(2-methoxyphenyl)piperazine-1,4-dicarboxamide-1,4-[^{13}C]$_2$ **([^{13}C]16)**



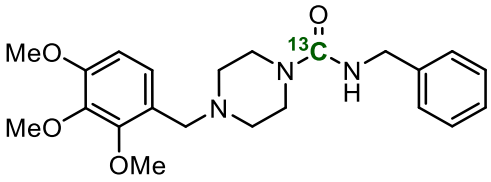
$C_{18}{}^{13}C_2H_{24}N_4O_4$
MW: 386.19 g.mol^{-1}
Yield: 34%
White solid

The *N*^{1},*N*^{4}-bis(2-methoxyphenyl)piperazine-1,4-dicarboxamide-1,4-[^{13}C]$_2$ **([^{13}C]16)** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-2-methoxybenzene **S12** (14.9 mg, 0.1 mmol), piperazine (8.6 mg, 0.05 mmol), and $^{13}CO_2$ (120 mbar, 0.12 mmol) in CH_3CN for 5 minutes at 25°C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (50/50) as eluent affording the expected product as a white solid (13 mg, 0.017 mmol, **34%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-8.12 (m, 2H), 7.11 (br s, 2H), 7.01-6.93 (m, 4H), 6.89-6.84 (m, 2H), 3.89 (s, 6H), 3.68-3.65 (m, 8H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7 (2^{13}C), 147.8 (2C), 128.6 (2C), 122.5 (2C), 121.4 (2C), 119.2 (2C), 109.9 (2C), 55.9 (4C), 43.3 (2C).
HRMS (ESI): calcd for $C_{18}{}^{13}CH_{25}N_4O_4$ $[M+H]^+$ 387.1937; found 387.1938.
Mp (°C): 205-207 °C

2.5. Late-stage diversification of drugs

[^{13}C] *N*-benzyl-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **([^{13}C]17)**

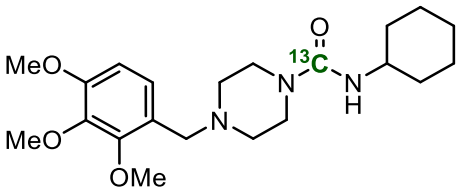


$C_{21}{}^{13}CH_{29}N_3O_4$
MW: 400.22 g.mol^{-1}
Yield: 60%
White solid

The [^{13}C] *N*-benzyl-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **[^{13}C]17** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), benzyl azide **S1** (13.3 mg, 0.1 mmol), trimetazidine dihydrochloride (38 mg, 0.11 mmol), DIPEA (38 µL, 0.25 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/CH_2Cl_2 (90/10) as eluent affording the expected compound as a white solid (24 mg, 0.060 mmol, **60%**). Data are consistent with literature values. [13]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35-7.22 (m, 5H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 1H), 4.74 (br s, 1H), 6.63 (dd, *J* = 5.4 Hz, *J* = 3.0 Hz, 2H), 3.87 (s 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.49 (s, 2H), 3.40-3.35 (m, 4H), 3.49-3.42 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7 (^{13}C), 153.2, 152.8, 142.4, 139.6 (*J* = 2 Hz), 128.7 (2C), 127.9 (2C), 127.4, 125.4, 123.4, 107.1, 61.3, 60.9, 56.6, 56.1, 52.6, 45.1 (2C), 43.9 (2C).
HRMS (ESI): calcd for $C_{21}{}^{13}CH_{30}N_3O_4$ $[M+H]^+$ 401.2264; found 401.2257.

[^{13}C] *N*-cyclohexyl-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **([^{13}C]18)**

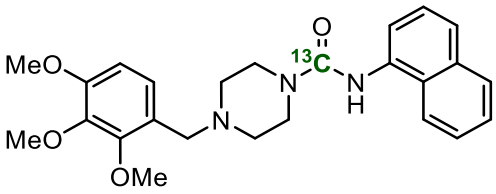


$C_{20}{}^{13}CH_{33}N_3O_4$
MW: 392.25 g.mol^{-1}
Yield: 44%
White solid

The [^{13}C] *N*-cyclohexyl-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **[^{13}C]18** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), azidocyclohexane **S13** (12.5 mg, 0.1 mmol), trimetazidine dihydrochloride (38 mg, 0.11 mmol), DIPEA (38 µL, 0.25 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/CH_2Cl_2 (80/20) as eluent affording the expected compound as a white solid (17.2 mg, 0.044 mmol, **44%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87-7.81 (m, 2H), 7.68-7.63 (m, 2H), 7.53-7.41 (m, 3H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 6.62 (br s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.60-3.51 (m, 6H), 2.59-2.50 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1 (^{13}C), 153.3, 152.8, 142.4, 125.4, 107.1, 61.4, 60.9, 56.5, 56.1, 52.5 (2C), 49.5, 43.8 (2C), 34.1 (2C), 25.8, 25.2 (2C).
HRMS (ESI): calcd for $C_{20}{}^{13}CH_{34}N_3O_4$ $[M+H]^+$ 393.2577; found 393.2257.
Mp (°C): 111-113 °C

[^{13}C] *N*-(naphthalen-1-yl)-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **([^{13}C]19)**

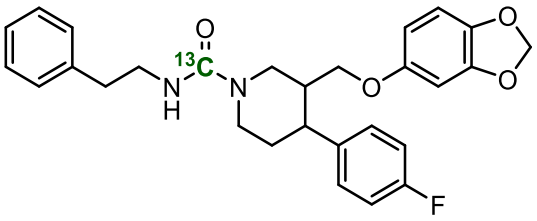


$C_{24}{}^{13}CH_{29}N_3O_4$
MW: 436.22 g.mol^{-1}
Yield: 77%
White solid

The [^{13}C] *N*-(naphthalen-1-yl)-4-(2,3,4-trimethoxybenzyl)piperazine-1-carboxamide **[^{13}C]19** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), trimetazidine dihydrochloride (38 mg, 0.11 mmol), DIPEA (38 µL, 0.25 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/CH_2Cl_2 (60/40) as eluent affording the expected compound as a white solid (32 mg, 0.077 mmol, **77%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87-7.81 (m, 2H), 7.68-7.63 (m, 2H), 7.53-7.41 (m, 3H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 6.62 (br s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.60-3.51 (m, 6H), 2.59-2.50 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1 (^{13}C), 153.2, 152.8, 142.4, 134.3, 134.1, 128.7, 128.2 (d, *J* = 2 Hz), 126.1, 126.0, 125.9, 125.3, 125.2, 123.5, 121.3, 121.0, 61.4, 60.9, 56.6, 56.1, 52.6 (2C), 44.4 (2C).
HRMS (ESI): calcd for $C_{24}{}^{13}CH_{30}N_3O_4$ $[M+H]^+$ 437.2264; found 437.2272.
Mp (°C): 137-139 °C

[^{13}C] 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-*N*-phenethylpiperidine-1-carboxamide **([^{13}C]20)**

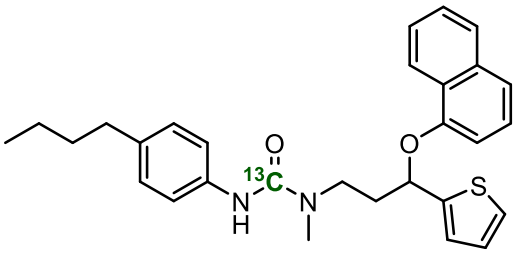


$C_{27}{}^{13}CH_{29}FN_2O_4$
MW: 477.21 g.mol^{-1}
Yield: 70%
Amorphous solid

The [^{13}C] 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-*N*-phenethylpiperidine-1-carboxamide **[^{13}C]20** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 2-phenylethyl azide **S14** (13.3 mg, 0.1 mmol) paroxetine hydrochloride (21.3 mg, 0.10 mmol), DIPEA (32 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (60/40) as eluent affording the expected product as an amorphous solid (15.7 mg, 0.072 mmol, **72%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35-7.29 (m, 2H), 7.26-7.20 (m, 3H), 7.15-7.09 (m, 2H), 7.02-6.95 (m, 2H), 6.63 (d, *J* = 8.5 Hz, 1H), 6.33 (d, *J* = 2.5 Hz, 1H), 6.12 (dd, *J* = 8.5 Hz, *J* = 2.5 Hz, 1H), 5.89 (s, 2H), 4.63 (br s, 1H), 4.17-4.08 (m, 1H), 4.08-4.00 (m, 1H), 3.61-3.50 (m, 3H), 3.44 (dd, *J* = 9.4 Hz, *J* = 7.0 Hz, 1H). 2.90-2.80 (m, 4H), 2.65 (td, *J* = 11.7 Hz, *J* = 4.0 Hz, 1H), 2.09-1.97 (m, 1H), 1.84-1.77 (m, 1H), 1.77-1.64 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (d, *J* = 245 Hz), 157.4 (^{13}C), 154.3, 148.4, 141.9, 139.5, 138.9 (d, *J* = 3 Hz), 129.0 (2C), 128.8 (d, *J* = 8 Hz, 2C), 128.8 (2C), 126.6, 115.7 (d, *J* = 21 Hz, 2C), 108.0, 105.7, 101.3, 98.1, 68.9, 48.0, 44.9, 44.2, 42.3, 14.8, 36.5, 33.8.
^{19}F NMR (376 MHz, $CDCl_3$): δ = - 115.9.
HRMS (ESI): calcd for $C_{27}{}^{13}CH_{30}FN_2O_4$ $[M+H]^+$ 478.2218; found 478.2218.

[^{13}C] 3-(4-butylphenyl)-1-methyl-1-(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)urea **([^{13}C]21)**



$C_{28}{}^{13}CH_{32}N_2O_2S$
MW: 473.22 g.mol^{-1}
Yield: 83%
Colorless oil

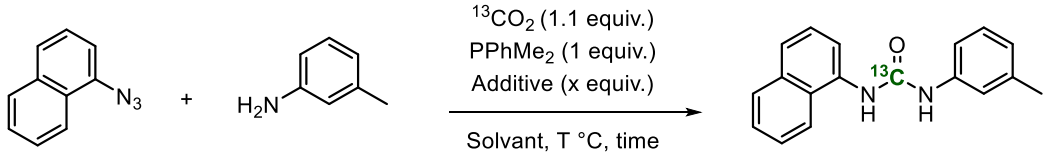
The [^{13}C] 3-(4-butylphenyl)-1-methyl-1-(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)urea **[^{13}C]21** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-4-butylbenzene **S15** (17.5 mg, 0.1 mmol), duloxetine hydrochloride (33.3 mg, 0.10 mmol), DIPEA (32 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-Heptane (40/60) as eluent affording the expected product as a colorless oil (37 mg, 0.083 mmol, **83%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39-8.33 (m, 2H), 7.82-7.76 (m, 2H), 7.53-7.47 (m, 2H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.25 (t, *J* = 8.1 Hz, 1H), 7.21 (dd, *J* = 5.0 Hz, *J* = 1.2 Hz, 1H), 7.11-7.07 (m, 1H), 7.01-6.95 (m, 4H), 6.93 (dd, *J* = 5.0 Hz, *J* = 3.5 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.27 (br s, 1H), 5.77 93 (dd, *J* = 8.3 Hz, *J* = 4.4 Hz, 1H), 3.73-3.58 (m, 2H), 3.00 (d, *J* = 2.9 Hz, 3H), 2.59-2.48 (m, 3H), 2.48-2.37 (m, 1H), 1.59-1.48 (m, 2H), 1.38-1.25 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7 (^{13}C), 152.8, 144.5, 137.6, 136.6, 134.8, 128.7 (2C), 127.8, 126.8, 126.6, 126.2, 125.9, 125.6, 125.2, 125.1, 121.9, 121.2, 120.0 (d, *J* = 2 Hz, 2C), 107.5, 73.8, 46.2, 37.5, 35.0, 35.0 (d, *J* = 2 Hz), 33.8, 22.4, 14.1.
HRMS (ESI): calcd for $C_{28}{}^{13}CH_{33}N_2O_2S$ $[M+H]^+$ 474.2291; found 474.2290.

2.6. Synthesis of ^{13}C-ureas from aromatic azide and aromatic amine

Optimizations

Into a 1.0 mL vial, $PPhMe_2$ **(1.00 equiv.)** was added to a solution of *o*-toluidine **(2.00 equiv.)**, 1-naphtylazide **(1.00 equiv.)** and additive **(2.00 equiv.)** in the appropriate solvent (0.60 mL). The solution was transferred into a Wilmad® low pressure/*vacuum* NMR tube which was further frozen into N_2 bath, then gaseous $^{13}CO_2$ **(1.10 equiv.)** was precisely delivered using Tritec®. The NMR tube was then warmed up to room temperature, progressively brought to the indicated temperature and maintained at this temperature for a given time. After completion, the unreacted $^{13}CO_2$ was removed by opening the NMR tube and MTBE **(1.00 equiv.)** was added as internal standard.



Entry	Solvent	Temperature	Time	Additive (n equiv.)	NMR yield (isolated)
1	CD_3CN	25 °C	10 min	-	15 %
2	DMF-d_7	25 °C	10 min	-	26 %
3	DMF-d_7	100 °C	10 min	-	20 %
4	DMF-d_7	25 °C	10 min	**A_1** (2)	30 %
5	DMF-d_7	25 °C	10 min	**A_2** (2)	46 %
6	DMF-d_7	25 °C	10 min	**A_3** (2)	57 %
7	DMF-d_7	25 °C	10 min	**A_4** (2)	51 %
8	DMF-d_7	25 °C	10 min	**A_5** (2)	59 %
9	DMF-d_7	80 °C	10 min	**A_5** (2)	67 % (62 %)

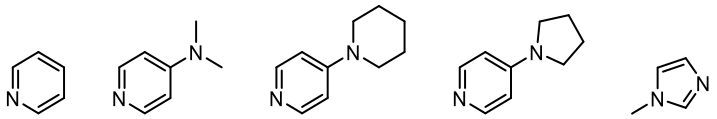
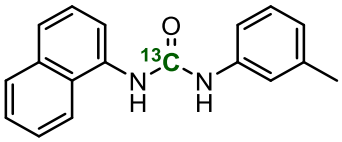


Table S1: Screening of solvent, temperature and additives

Note: Additive A_5 *N*-methylimidazole have already been described and used as an *N*-acyl transfer catalyst. [14]

[^{13}C] 1-(naphthalen-1-yl)-3-(m-tolyl)urea **([^{13}C]22)**

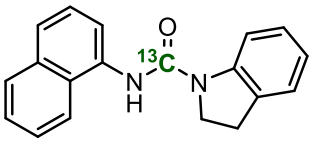


$C_{17}{}^{13}CH_{16}N_2O$
MW: 277.13 g.mol^{-1}
Yield: 62%
Beige solid

The [^{13}C] 1-(naphthalen-1-yl)-3-(m-tolyl)urea **[^{13}C]22** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.1 mmol), *o*-toluidine (21.8 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 10 minutes at 80 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using Dichloromethane/Methanol (from 100/0 to 99/1) as eluent affording the expected compound as a beige solid (24 mg, 0.062 mmol, **62%**).

^{1}H NMR (400 MHz, DMF-d_7): δ = 9.13 (br s), 8.83 (br s), 8.24-8.16 (m, 2H), 8.00-7.94 (m, 2H), 7.70-7.66 (m, 2H), 7.62-7.40 (m, 5H), 7.25-7.17 (m, 1H), 6.88-6.81 (m, 1H), 2.32 (s, 3H).
^{13}C NMR (100 MHz, DMF-d_7): δ = 154.5-154.0 (m, ^{13}C), 141.4, 139.4, 135.9, 135.4, 129.7, 129.7, 127.4 (d, *J* = 3.0 Hz), 127.0, 126.9, 126.9, 124.1, 123.8, 122.2, 120.0 (d, *J* = 2.2 Hz) , 118.6, 116.6 (d, *J* = 2.1 Hz), 21.9.
HRMS (ESI): calcd for $C_{17}{}^{13}CH_{16}N_2O$ $[M+H]^+$ 278.1369; found 278.1371.
Mp (°C): 239-241 °C

[^{13}C] *N*-(naphthalen-1-yl)indoline-1-carboxamide **([^{13}C]23)**

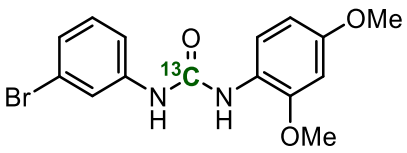


$C_{18}{}^{13}CH_{16}N_2O$
MW: 289.13 g.mol^{-1}
Yield: 59%
Grey solid

The [^{13}C] N-(naphthalen-1-yl)indoline-1-carboxamide **[^{13}C]23** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), indoline (22.4 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 10 minutes at 80 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (15/85) as eluent affording the expected compound as a grey solid (17.1 mg, 0.059 mmol, **59%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97-7.93 (m, 1H), 7.91-7.86 (m, 2H), 7.86-7.83 (m, 1H), 7.72-7.68 (m, 1H), 7.54-7.56 (m, 3H), 7.23-7.17 (m, 2H), 7.00-6.95 (m, 1H), 6.84 (br s, 1H), 4.20 (t, *J* = 8.5 Hz, 2H), 3.28 (t, *J* = 8.5 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.2 (^{13}C), 143.5 (d, *J* = 2.4 Hz), 134.4, 133.1, 130.7 (d, *J* = 4.0 Hz), 128.9, 128.0 (d, *J* = 2.1 Hz), 127.9, 126.4, 126.1, 126.0, 125.6, 124.9, 122.5, 121.2, 121.0, 115.2, 47.8, 28.1 (d, *J* = 1.9 Hz).
IR (cm^{-1}): 3287, 2952, 1621, 1520, 1479, 1345, 791, 751.
HRMS (ESI): calcd for $C_{18}{}^{13}CH_{16}N_2O$ $[M+H]^+$ 290.1369; found 290.1367.
Mp (°C): 174-176 °C

[^{13}C] 1-(3-bromophenyl)-3-(2,4-dimethoxyphenyl)urea **([^{13}C]24)**

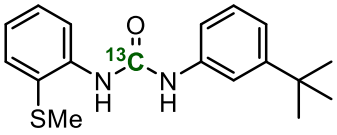


$C_{14}{}^{13}CH_{15}BrN_2O_3$
MW: 351.03 g.mol^{-1}
Yield: 57%
Purple solid

The [^{13}C] 1-(3-bromophenyl)-3-(2,4-dimethoxyphenyl)urea **[^{13}C]24** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-3-bromobenzene **S16** (19.8 mg, 0.10 mmol), 2,4-dimethoxyaniline (30 mg, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80 °C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 20/80) as eluent affording the expected compound as a purple solid (20.1 mg, 0.057 mmol, **57%**).

^{1}H NMR (400 MHz, CD_3OD): δ = 7.81 (d, *J* = 8.8 Hz, 1H), 7.77 (t, *J* = 1.9 Hz, 1H), 7.29 (ddd, *J* = 7.9 Hz, *J* = 1.9 Hz, *J* = 1.3 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 7.14-7.10 (m, 1H), 6.58 (d, *J* = 2.6 Hz, 1H), 6.49 (dd, *J* = 8.8 Hz, *J* = 2.7 Hz, 1H), 3.88 (s, 3H), 3.78 (s, 3H).
^{13}C NMR (100 MHz, CD_3OD): δ = 157.9, 155.3 (^{13}C), 155.3, 142.6, 131.3, 126.1, 123.4, 122.4 (d, *J* = 1.9 Hz), 122.4 (d, *J* = 0.8 Hz), 122.3, 118.3 (d, *J* = 2.5 Hz), 105.2, 99.7, 56.3, 56.0.
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{15}BrN_2O_3$ $[M+H]^+$ 352.0372; found 352.0369.
Mp (°C): 172-174 °C

[^{13}C] 1-(3-(tert-butyl)phenyl)-3-(2-(methylthio)phenyl)urea **([^{13}C]25)**

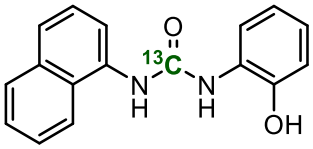


$C_{17}{}^{13}CH_{22}N_2OS$
MW: 315.15 g.mol^{-1}
Yield: 49%
Beige solid

The [^{13}C] 1-(3-(*tert*-butyl)phenyl)-3-(2-(methylthio)phenyl)urea **[^{13}C]25** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 2-(azidophenyl)methylsulfane **S17** (16.2 mg, 0.10 mmol), 3-(*tert*-butyl)aniline (30 mg, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 10 minutes at 80 °C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 20/80) as eluent affording the expected compound as a beige solid (15.4 mg, 0.049 mmol, **49%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1H), 7.71 (br s, 1H), 7.42-7.36 (m, 2H), 7.33-7.16 (m, 4H), 7.03-6.97 (m, 1H), 6.96 (br s, 1H), 2.92 (s, 3H), 1.31 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 153.0, 150.9, 138.6, 137.2; 132.6, 129.2, 128.9, 126.1 (d, *J* = 2 Hz), 123.9, 122.6, 121.0, 120.3, 34.9, 31.4 (3C), 18.5.
HRMS (ESI): calcd for $C_{17}{}^{13}CH_{22}N_2OS$ $[M+H]^+$ 316.1559; found 316.1556.
Mp (°C): 138-140 °C

[^{13}C] 1-(2-hydroxyphenyl)-3-(naphthalen-1-yl)urea **([^{13}C]26)**

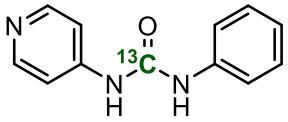


$C_{16}{}^{13}CH_{14}N_2O_2$
MW: 279.11 g.mol^{-1}
Yield: 54%
Beige solid

The [^{13}C] 1-(2-hydroxyphenyl)-3-(naphthalen-1-yl)urea **[^{13}C]26** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), 2-aminophenol (22 mg, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 10 minutes at 80 °C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 20/80) as eluent affording the expected compound as a beige solid (14.9 mg, 0.054 mmol, **54%**). Data are consistent with literature values. [15]

^{1}H NMR (400 MHz, CD_3OD): δ = 8.10 (dd, *J* = 8.1 Hz, *J* = 1.0 Hz, 1H), 7.93-7.86 (m, 2H), 7.79 (dd, *J* = 7.5 Hz, *J* = 0.8 Hz, 1H), 7.71-7.66 (m, 1H), 7.57-7.44 (m, 3H), 6.90-6.77 (m, 3H).
^{13}C NMR (100 MHz, CD_3OD): δ = 157.3-156.7 (m, ^{13}C), 148.0 (d, *J* = 2.9 Hz), 135.8, 135.0, 129.5, 129.4, 128.6, 127.1, 127.0, 126.7, 125.9, 124.1, 122.8, 121.8, 121.3, 120.7, 115.8.
HRMS (ESI): calcd for $C_{16}{}^{13}CH_{14}N_2O_2$ $[M+H]^+$ 280.1162; found 280.1162.

[^{13}C] 1-phenyl-3-(pyridin-4-yl)urea **([^{13}C]27)**

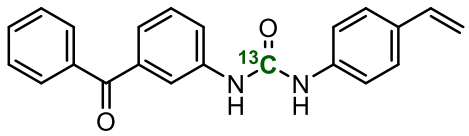


$C_{11}{}^{13}CH_{11}N_3O$
MW: 214.09 g.mol^{-1}
Yield: 65%
White solid

The [^{13}C] 1-phenyl-3-(pyridin-4-yl)urea **[^{13}C]27** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 4-azidopyridine **S18** (12.0 mg, 0.10 mmol), aniline (19 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80°C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 50/50) as eluent affording the expected compound as a white solid (13.9 mg, 0.065 mmol, **65%**). Data are consistent with literature values. [16]

^{1}H NMR (400 MHz, CD_3OD): δ = 8.48 (d, *J* = 6.8 Hz, 2H), 8.04 (d, *J* = 6.8 Hz, 2H), 7.55-7.49 (m, 2H), 7.36-7.30 (m, 2H), 7.13-7.07 (m, 1H).
^{13}C NMR (100 MHz, CD_3OD): δ = 152.8 (^{13}C), 152.6 (2C), 142.4, 139.3, 130.0 (2C), 125.1, 120.9 (d, *J* = 2.1 Hz, 2C), 114.6 (d, *J* = 2.5 Hz, 2C).
^{19}F NMR (376 MHz, CD_3OD): δ = -77.2.
HRMS (ESI): calcd for $C_{11}{}^{13}CH_{12}N_3O$ $[M+H]^+$ 215.1011; found 215.1008.

[^{13}C] 1-(3-benzoylphenyl)-3-(4-vinylphenyl)urea **([^{13}C]28)**

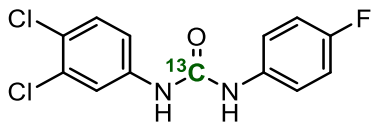


$C_{21}{}^{13}CH_{18}N_2O_2$
MW: 343.14 g.mol^{-1}
Yield: 38%
White solid

The [^{13}C] 1-(3-benzoylphenyl)-3-(4-vinylphenyl)urea **[^{13}C]28** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), (3-azidophenyl)(phenyl)methanone **S19** (22.3 mg, 0.10 mmol), 4-vinylaniline (24 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80°C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 20/80) as eluent affording the expected compound as a beige solid (13.0 mg, 0.038 mmol, **38%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91-7.88 (m, 1H), 7.83-7.78 (m, 2H), 7.76-7.71 (m, 1H), 7.68-7.62 (m, 1H), 7.67-7.52 (m, 2H), 7.49-7.43 (m, 1H), 7.43-7.34 (m, 5H), 6.68 (dd, *J* = 17.6 Hz, 10.9 Hz, 1H), 5.68 (dd, *J* = 17.6 Hz, 1.0 Hz, 1H), 5.13 (dd, *J* = 10.9 Hz, 1.0 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 155.1 (^{13}C), 141.0, 140.0, 139.5, 139.5, 138.8, 137.6, 133.9 (d, *J* = 2 Hz), 131.1 (2C), 130.0, 129.5 (2C), 127.8 (2C), 125.3, 124.2 (d, *J* = 2 Hz), 121.4 (d, *J* = 2 Hz), 120.3 (d, *J* = 2 Hz, 2C), 112.5.
HRMS (ESI): calcd for $C_{21}{}^{13}CH_{18}N_2O_2$ $[M+H]^+$ 344.1475; found 344.1467.

[^{13}C] 1-(3,4-dichlorophenyl)-3-(4-fluorophenyl)urea **([^{13}C]29)**



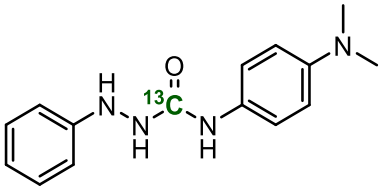
$C_{12}{}^{13}CH_9ClFN_2O$
MW: 299.01 g.mol^{-1}
Yield: 70%
White solid

The [^{13}C] 1-(3,4-dichlorophenyl)-3-(4-fluorophenyl)urea **[^{13}C]29** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azido-3,4-dichlorobenzene **S20** (18.8 mg, 0.10 mmol), 4-fluoroaniline (19 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80°C. The crude mixture was purified by flash chromatography on reverse phase using water/acetonitrile (from 95/5 to 20/80) as eluent affording the expected compound as a white solid (21 mg, 0.070 mmol, **70%**). Data are consistent with literature values. [17]

^{1}H NMR (400 MHz, CD_3OD): δ = 7.78 (d, *J* = 2.5 Hz, 1H), 7.45-7.36 (m, 3H), 7.28 (dd, *J* = 8.8 Hz, *J* = 2.5 Hz, 1H), 7.06-6.99 (m, 2H).
^{13}C NMR (100 MHz, CD_3OD): δ = 160.2 (d, *J* = 240 Hz), 155.0 (^{13}C), 140.8, 136.3 (d, *J* = 3 Hz), 133.3, 131.5 (2C), 126.2, 122.6 (dd, *J* = 8 Hz, *J* = 2 Hz), 121.5 (d, *J* = 2 Hz), 119.7 (d, *J* = 3 Hz), 116.3 (d, *J* = 23 Hz, 2C).
^{19}F NMR (376 MHz, CD_3OD): δ = -77.2.
HRMS (ESI): calcd for $C_{12}{}^{13}CH_{10}Cl_2N_2O$ $[M+H]^+$ 300.0185; found 300.0184.

2.7. Synthesis of [^{13}C] labeled urea derivatives

[^{13}C] *N*-(4-(dimethylamino)phenyl)-2-phenylhydrazine-1-carboxamide **([^{13}C]31)**

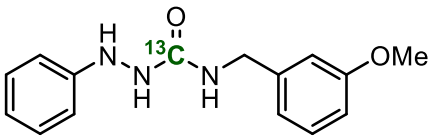


$C_{14}{}^{13}CH_{18}N_4O$
MW: 271.15 g.mol^{-1}
Yield: 56%
White solid

The [^{13}C] *N*-(4-(dimethylamino)phenyl)-2-phenylhydrazine-1-carboxamide **[^{13}C]31** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 4-azido-*N*,*N*-dimethylaniline **S22** (16.2 mg, 0.10 mmol), phenylhydrazine (9.90 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (50/50) as eluent affording the expected compound as a white solid (15.2 mg, 0.056 mmol, **56%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (br s, 1H), 7.33-7.26 (m, 4H), 7.01-6.96 (m, 1H), 6.94-6.90 (m, 2H), 6.73-6.67 (m, 2H), 6.12 (d, *J* = 6.1 Hz, 1H), 5.80 (d, *J* = 2.3 Hz, 1H), 2.90 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 157.0, 155.4 (2C), 147.3, 129.7 (2C), 122.2, 122.1, 113.7 (2C), 113.6 (2C), 41.3 (2C).
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{18}N_4O$ $[M+H]^+$ 272.1587; found 272.158
Mp (°C): 169-171 °C`

[^{13}C] *N*-(3-methoxybenzyl)-2-phenylhydrazine-1-carboxamide **([^{13}C]32)**

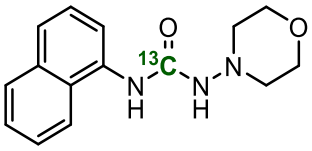


$C_{14}{}^{13}CH_{17}N_3O_2$
MW: 272.14 g.mol^{-1}
Yield: 67%
Yellow solid

The [^{13}C] *N*-(3-methoxybenzyl)-2-phenylhydrazine-1-carboxamide **[^{13}C]32** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-(azidomethyl)-3-methoxybenzene **S23** (16.3 mg, 0.10 mmol), phenylhydrazine (9.90 µL, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (70/30) as eluent affording the expected compound as a yellow solid (18.1 mg, 0.067 mmol, **67%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = .7.29-7.17 (m, 3H), 6.97-6.91 (m, 1H), 6.87-6.75 (m, 5H), 6.42-6.37 (d, *J* = 5.9 Hz, 1H), 6.25-6.19 (m, 1H), 5.75 (d, *J* = 2.0 Hz, 1H), 4.41 (dd, *J* = 6.0 Hz, *J* = 3.3 Hz, 2H), 3.74 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 159.4, 147.4, 140.7, 129.7, 129.6 (2C), 121.8, 119.8, 113.2 (2C), 113.0, 112.9, 55.3, 43.7.
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{17}N_3O_2$ $[M+H]^+$ 273.1427; found 273.1426.
Mp (°C): 108-110 °C

[^{13}C] 1-morpholino-3-(naphthalen-1-yl)urea **([^{13}C]33)**

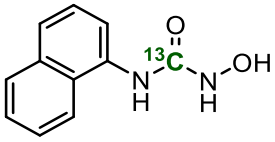


$C_{14}{}^{13}CH_{17}N_3O_2$
MW: 272.14 g.mol^{-1}
Yield: 57%
Beige solid

The [^{13}C] 1-morpholino-3-(naphthalen-1-yl)urea **[^{13}C]33** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), 4-amino-morpholine (9.64 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (40/60) as eluent affording the expected compound as a beige solid (15.2 mg, 0.056 mmol, **56%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (br s, 1H), 8.07-8.04 (m, 1H), 8.89-8.84 (m, 1H), 8.82-8.78 (m, 1H), 7.66-7.62 (m, 1H), 7.57-7.45 (m, 3H), 3.98 (br s, 2H), 3.81 (br s, 2H), 3.15 (br s, 2H), 2.78 (br s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.4 (^{13}C), 134.3, 132.8 (d, *J* = 1.1 Hz), 129.1, 126.6 (d, *J* = 2.7 Hz), 126.3, 126.2, 126.0, 124.4, 120.1, 128.6, 67.1 (2C), 57.0 (2C).
HRMS (ESI): calcd for $C_{14}{}^{13}CH_{17}N_3O_2$ $[M+H]^+$ 273.1427; found 273.1427.
Mp (°C): 206-208 °C

[^{13}C] 1-hydroxy-3-(naphthalen-1-yl)urea **([^{13}C]34)**

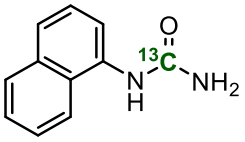


$C_{10}{}^{13}CH_{10}N_2O_2$
MW: 203.08 g.mol^{-1}
Yield: 45%
White solid

The [^{13}C] 1-hydroxy-3-(naphthalen-1-yl)urea **[^{13}C]34** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene **S4** (16.9 mg, 0.10 mmol), hydroxylamine hydrochloride (13.9 mg, 0.20 mmol), DIPEA (60 µL, 0.4 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 10 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (70/30) as eluent affording the expected compound as a white solid (8 mg, 0.045 mmol, **45%**). Data are consistent with literature values. [18]

^{1}H NMR (400 MHz, CD_3OD): δ = 8.02-7.97 (m, 1H), 7.91-7.86 (m, 1H), 7.76-7.71 (m, 1H), 7.68-7.64 (m, 1H), 7.56-7.44 (m, 3H).
^{13}C NMR (100 MHz, CD_3OD): δ = 162.6 (^{13}C), 135.8, 134.1, 130.2 (d, *J* = 1.8 Hz), 129.4, 127.2, 127.1, 126.8, 126.7, 123.1, 122.9.
LCMS (ESI) m/z $C_{10}{}^{13}CH_{11}N_2O_2$ $[M+H]^+$ 204.3.

[^{13}C] 1-(naphthalen-1-yl)urea **([^{13}C]35)**



$C_{10}{}^{13}CH_{10}N_2O$
MW: 187.08 g.mol^{-1}
Yield: 43%
White solid

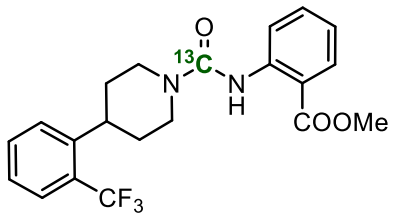
The [^{13}C] 1-(naphthalen-1-yl)urea **[^{13}C]35** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 1-azidonaphthalene (16.9 mg, 0.10 mmol), ammonia solution 7N in methanol (30.0 µL, 0.20 mmol), *N*-methylimidazole (16 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using EtOAc/*n*-Heptane (15/85) as eluent affording the expected compound as a grey solid (8.0 mg, 0.043 mmol, **43%**). Data are consistent with literature values. [19]

^{1}H NMR (400 MHz, CD_3OD): δ = 8.05-8.00 (m, 1H), 7.89-7.85 (m, 2H), 7.71-7.64 (m, 2H), 7.55-7.47 (m, 2H), 7.47-7.42 (m, 1H).
^{13}C NMR (100 MHz, CD_3OD): δ = 160.5 (^{13}C), 135.8, 135.1, 129.8, 129.4, 127.1, 127.0, 126.7, 126.2, 122.8, 122.3.
HRMS (ESI): calcd for $C_{10}{}^{13}CH_{12}N_2O$ $[M+H]^+$ 188.0899; found 188.0901.

2.8. Synthesis of ^{13}C-labeled biological relevant molecules

- *A-1120 methyl ester: RBP4 antagonist [^{13}C]36*

[^{13}C] Methyl 2-(4-(2-(trifluoromethyl)phenyl)piperidine-1-carboxamido)benzoate **([^{13}C]36)**

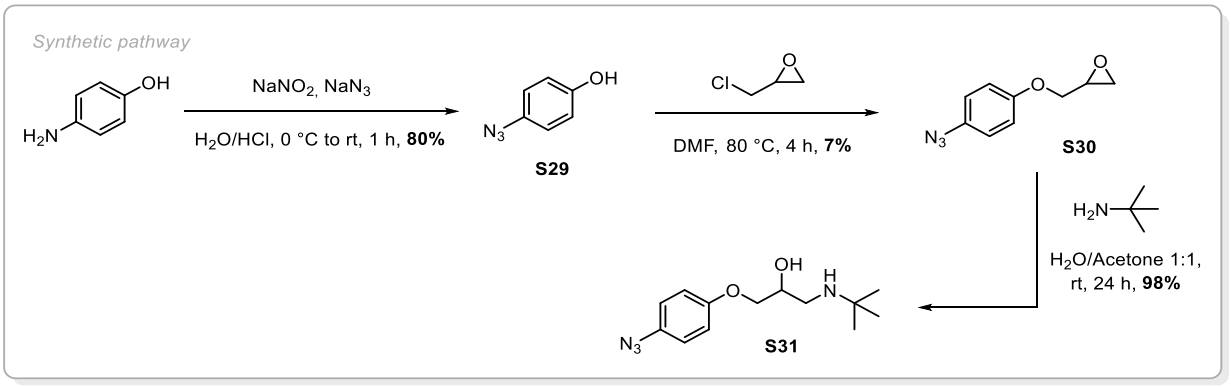


$C_{20}{}^{13}CH_{21}F_3N_2O_3$
MW: 407.15 g.mol^{-1}
Yield: 66%
White Solid

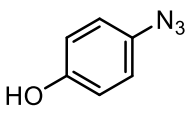
The [^{13}C] Methyl 2-(4-(2-(trifluoromethyl)phenyl)piperidine-1-carboxamido)benzoate **[^{13}C]36** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (0.10 mmol, 14.4 µL), methyl 2-azidobenzoate **S24** (0.10 mmol, 7.46 mg), 4-(2-(trifluoromethyl)phenyl)piperidine (25.2 mg, 0.11 mmol), and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using AcOEt/*n*-heptane (20/80) as eluent affording the expected compound as a white solid (27.0 mg, 0.066 mmol, **66%**). Data are consistent with literature values. [20]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.8 (s, 1H), 8.58 (dd, *J* = 8.6 Hz, *J* = 0.7 Hz, 1H), 8.01 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.55-7.48 (m, 2H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.01-6.95 (m, 1H), 4.46-4.37 (m, 2H), 3.91 (s, 3H), 3.24-3.14 (m, 1H), 3.09-2.99 (m, 2H), 1.96-1.87 (m, 2H), 1.84-1.72 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.6, 154.6 (^{13}C), 144.5 (q, *J* = 1.2 Hz), 143.8 (d, *J* = 0.5 Hz), 134.8, 132.2 (d, *J* = 0.5 Hz), 130.8, 128.1 (q, *J* = 30 Hz), 128.1, 126.4, 126.0 (q, *J* = 6 Hz), 124.8 (q, *J* = 274 Hz), 120.8, 119.8, 114.0 (d, *J* = 3.1 Hz), 52.4, 45.0, 38.7 (d, *J* = 1.6 Hz, 2C), 33.5 (2C).
^{19}F NMR (376 MHz, $CDCl_3$): δ = - 58.7.
IR (cm^{-1}): 3308, 2955, 1688, 1633, 1526, 1448, 1312, 1212, 1115, 1036, 753.
HRMS (ESI): calcd for $C_{20}{}^{13}CH_{21}F_3N_2O_3$ $[M+H]^+$ 408.1611; found 408.1612.

- *Talinolol: beta blocker [^{13}C]37*



4-azidophenol **(S29)**

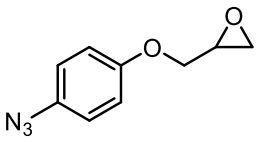


$C_6H_5N_3O$
MW: 135.04 g.mol^{-1}
Yield: 80%
Dark yellow oil

A solution of 4-aminophenol (545 mg, 5.00 mmol) in HCl 1.2 M (20 mL) was cooled to 0°C in an ice bath. To this stirred mixture was added a solution of $NaNO_2$ (360 mg, 5.50 mmol) in water. The solution was stirred 30min at 0 °C and a solution of NaN_3 (390 mg, 6 mmol) in water was added dropwise. The resulting solution was stirred at room temperature for 1 hour and was extracted twice with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtrated and concentrated under vacuum affording the expected compound as a dark yellow oil without further purification. (540 mg, 4.00 mmol, **80%**) Data are convenient with literature values. [21]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94-6.88 (m, 2H), 6.85-6.80 (m, 2H), 4.97 (br s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0, 132.7, 120.3 (2C), 116.8 (2C).

2-((4-azidophenoxy)methyl)oxirane (**S30)**

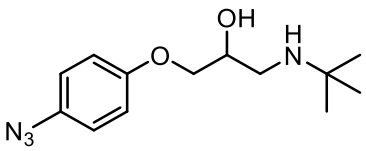


$C_9H_9N_3O_2$
MW: 191.07 g.mol^{-1}
Yield: 7%
Dark orange oil

In a round bottom flask 4-azidophenol **S29** (600 mg, 4.45 mmol), K_2CO_3 (920 mg, 6.68 mmol) and epichloridrine (520 µL, 6.68 mmol) were dissolved in DMF (15 mL). The reaction mixture was heated up to 80 °C for 4 hours. The mixture was cooled down to room temperature and water (15 mL) was added. The organic layer was extracted twice with DCM (15 mL) dried over $MgSO_4$ filtrated and evaporated. The crude mixture was purified by flash chromatography on SiO_2 gel using *n*-heptane/AcOEt (90/10) as eluent affording the expected compound as a dark orange oil (55 mg, 0.31 mmol, **7%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20-8.14 (m, 2H), 7.00-6.94 (m, 2H), 4.38 (dd, *J* = 11.1 Hz, *J* = 2.7 Hz, 1H), 3.98 (dd, *J* = 11.1 Hz, *J* = 6.0 Hz, 1H), 3.40-3.34 (m, 1H), 2.93 (dd, *J* = 4.7 Hz, *J* = 4.3 Hz, 1H), 2.77 (dd, *J* = 4.7 Hz, *J* = 2.7 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 141.9, 125.6 (2C), 114.7 (2C), 69.5, 49.8, 44.5.

1-(4-azidophenoxy)-3-(tert-butylamino)propan-2-ol **(S31)**

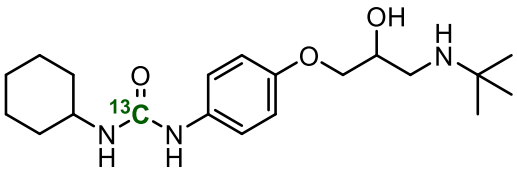


$C_{13}H_{20}N_4O_2$
MW: 264.16 g.mol^{-1}
Yield: 98%
Beige solid

In a round bottom flask 2-((4-azidophenoxy)methyl)oxirane **S30** (50 mg, 0.26 mmol) was dissolved in a mixture H_2O/Acetone (1/1) (1 mL). *Tert*-butyl amine (41 µL, 0.39 mmol) were added and the solution was stirred 24 hours at room temperature. Ethyl acetate (2 mL) was added and the solution was extracted twice (2 x 1 mL). The combined organic layers were dried over $MgSO_4$ filtrated and evaporated affording the expected compound as a beige solid without further purification (65 mg, 0.25 mmol, **98%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96-6.89 (m, 4H), 3.99-3.89 (m, 3H), 2.85 (dd, *J* = 12.0 Hz, *J* = 3.7 Hz, 1H), 2.66 (dd, *J* = 12.0 Hz, *J* = 7.4 Hz, 1H), 1.12 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 132.8, 120.1 (2C), 116.0 (2C), 71.1, 68.7, 50.5, 44.7, 29.3 (3C).
LCMS (ESI) m/z $C_{13}H_{21}N_4O_2$ $[M+H]^+$ 265.4.

[^{13}C] 1-(4-(3-(tert-butylamino)-2-hydroxypropoxy)phenyl)-3-cyclohexylurea **([^{13}C]37)**



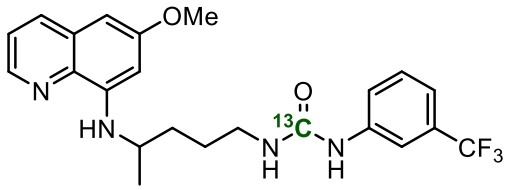
$C_{19}{}^{13}CH_{33}N_3O_3$
MW: 364.26 g.mol^{-1}
Yield: 91%
White Solid

The [^{13}C] 1-(4-(3-(tert-butylamino)-2-hydroxypropoxy)phenyl)-3-cyclohexylurea **[^{13}C]37** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (0.05 mmol, 7.20 µL), 1-(4-azidophenoxy)-3-(tert-butylamino)propan-2-ol **S31** (0.05 mmol, 13.2 mg), cyclohexylamine (28.0 µL, 0.25 mmol), and $^{13}CO_2$ (55 mbar, 0.055 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using Dichloromethane/methanol (90/10) + 1% NH_3 7N in MeOH as eluent affording the expected compound as a white solid (17.0 mg, 0.046 mmol, **91%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (br s, 1H), 7.08 (d, *J* = 8.9 Hz, 2H), 6.69 (d, *J* = 8.9 Hz, 2H), 5.37 (br s, 1H), 4.07-3.98 (m, 1H), 3.97-3.86 (m, 2H), 3.86-3.75 (m, 2H), 2.88 (dd, *J* = 11.9 Hz, *J* = 3.3 Hz, 1H), 2.72 (dd, *J* = 11.9 Hz, *J* = 8.4 Hz, 1H), 1.95-1.84 (m, 2H), 1.71-1.61 (m, 2H), 1.60-1.51 (m, 1H), 1.38-1.23 (m, 2H), 1.19 (s, 9H), 1.19-1.02 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (d, *J* = 1.5 Hz), 156.3 (^{13}C), 132.3, 123.3 (2C), 115.6 (2C), 70.7, 68.0, 52.6, 48.9, 45.0, 33.8 (2C), 28.3 (3C), 25.7, 25.1 (2C).
IR (cm^{-1}): 3301, 3045, 2928, 2853, 1542, 1508, 1210, 828.
HRMS (ESI): calcd for $C_{19}{}^{13}CH_{33}N_3O_3$ $[M+H]^+$ 365.2628; found 365.2629.

- *Primaquine derivative: antiproliferative agent [^{13}C]38*

[^{13}C] 1-(4-((6-methoxyquinolin-8-yl)amino)pentyl)-3-(3-(trifluoromethyl)phenyl)urea **([^{13}C]38)**

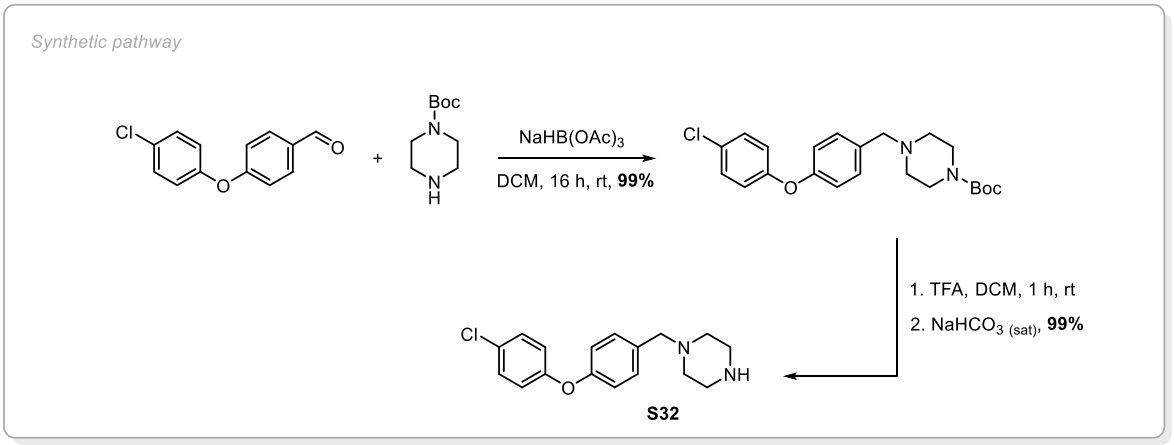


$C_{22}{}^{13}CH_{25}F_3N_4O_2$
MW: 447.20 g.mol^{-1}
Yield: 32%
Light yellow oil

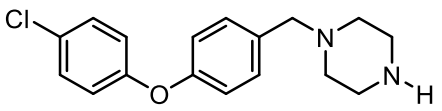
The [^{13}C] 1-(4-((6-methoxyquinolin-8-yl)amino)pentyl)-3-(3-(trifluoromethyl)phenyl)urea **[^{13}C]38** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), N^4-(6-methoxyquinolin-8-yl)pentane-1,4-diamine (0.10 mmol, 25.9 mg), 1-azido-3-(trifluoromethyl)benzene **S25** (18.7 mg, 0.10 mmol), and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using *n*-heptane/AcOEt 70/30 affording the expected compound as a light yellow oil (14.0 mg, 0.032 mmol, **32%**). Data are consistent with literature values. [22]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 4.2 Hz, *J* = 1.6 Hz, 1H), 7.94 (dd, *J* = 8.3 Hz, *J* = 1.6 Hz, 1H), 7.51-7.47 (m, 2H), 7.33-7.27 (m, 2H), 7.22-7.13 (m, 2H), 6.36 (d, *J* = 2.4 Hz, 1H), 6.30 (d, *J* = 2.4 Hz, 1H), 5.89 (d, *J* = 7.9 Hz, 1H), 5.23 (br s, 1H), 3.87 (s, 3H), 3.63-3.50 (m, 1H), 3.29-3.11 (m, 2H), 1.67-1.54 (m, 4H), 1.23 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 155.6 (m), 144.9, 144.5, 139.8, 135.4, 135.3, 131.4 (q, *J* = 32 Hz), 130.2, 129.6, 124.1 (q, *J* = 272 Hz), 122.4, 122.2, 119.3 (q, *J* = 5.4 Hz), 115.9 (q, *J* = 2.2 Hz), 97.4, 92.2, 55.4, 48.1, 40.3, 34.2, 26.6, 20.7.
^{19}F NMR (376 MHz, $CDCl_3$): δ = - 62.7.
IR (cm^{-1}): 3358, 2937, 1615, 1553, 1518, 1335, 1164, 1123, 791, 699.
HRMS (ESI): calcd for $C_{22}{}^{13}CH_{25}F_3N_4O_2$ $[M+H]^+$ 448.2036; found 448.2037.

- *JNJ-40355003 analogue: a potential FAAH inhibitor [^{13}C]39*



1-(4-(4-chlorophenoxy)benzyl)piperazine **(S32)**

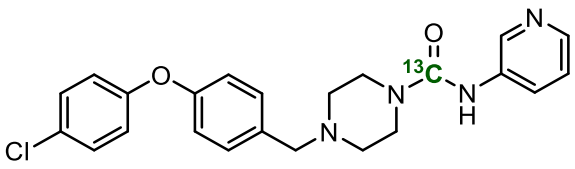


$C_{17}H_{19}ClNO_2$
MW: 302.12 g.mol^{-1}
Yield: 99%
Colorless oil

In a flask under argon was added 4-(4-chlorophenoxy)benzaldehyde (232 mg, 1.00 mmol) and *tert*-butyl piperazine-1-carboxylate (186 mg, 1.00 mmol) in dichloromethane (6 mL). Some drops of acetic acid was added and the solution was stirred at room temperature for 1 hour. Sodium triacetoxyborohydride (422 mg, 2.50 mmol) was added and the solution was stirred at room temperature for 16 hours. A saturated solution $NaHCO_3$ was added and the organic layer was extracted twice with dichloromethane. Combined organics layers were dried over $MgSO_4$, filtrated and evaporated affording *tert*-Butyl 4-(4-(4-chlorophenoxy)benzyl)piperazine-1-carboxylate as a colorless oil (400 mg, 0.99 mmol, **99%**).
tert-Butyl 4-(4-(4-chlorophenoxy)benzyl)piperazine-1-carboxylate (400 mg, 0.99 mmol) was dissolved in dichloromethane (10 mL). Trifluoroacetic acid was added (2 mL) and the solution was stirred one hour at room temperature. The solution was evaporated, dissolved in dichloromethane and evaporated another time. A saturated solution of $NaHCO_3$ (15 mL) was added and the solution was stirred 5 minutes at room temperature. The solution was extracted twice with dichloromethane and the combined organics layers were dried over $MgSO_4$, filtrated and evaporated affording the expected compound as a colorless oil (300 mg, 0.98 mmol, **99%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, , *J* = 2.5 Hz, 1H), 8.24 (dd, *J* = 4.7 Hz, *J* = 1.4 Hz, 1H), 7.96 (ddd, *J* = 8.4 Hz, *J* = 2.5 Hz, *J* = 1.4 Hz, 1H), 7.31-7.26 (m, 4H), 7.21 (dd, *J* = 8.4 Hz, *J* = 4.7 Hz, 1H), 6.97-6.91 (m, 4H), 6.91 (br s, 1H), 3.56-3.51 (m, 4H), 3.50 (s, 2H), 2.51-2.43 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 156.0, 154.9, 144.1, 141.3 (d, *J* = 3 Hz), 136.2, 132.9, 130.7 (2C), 129.9 (2C), 128.4, 127.6, 123.7, 120.2 (2C), 118.8 (2C), 63.3, 52.7 (d, *J* = 1 Hz, 2C), 44.3 (2C).
IR (cm^{-1}): 3296, 2811, 1612, 1504, 1483, 1419, 1235, 1001, 729.
LCMS (ESI) m/z $C_{17}H_{20}ClNO_2$ $[M+H]^+$ 303.3.

[^{13}C] 4-(4-(4-chlorophenoxy)benzyl)-*N*-(pyridin-3-yl)piperazine-1-carboxamide **([^{13}C]39)**

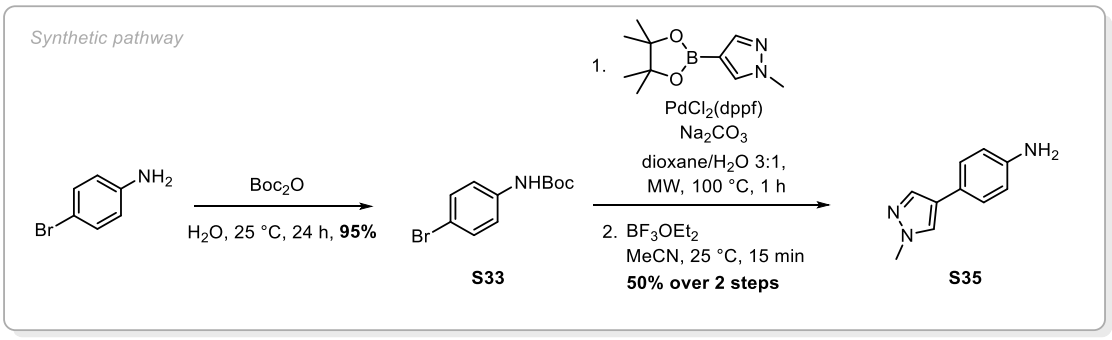


$C_{22}{}^{13}CH_{24}ClN_4O_2$
MW: 423.15 g.mol^{-1}
Yield: 71%
White Solid

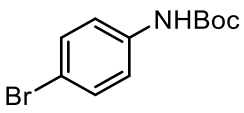
The [^{13}C] 4-(4-(4-chlorophenoxy)benzyl)-*N*-(pyridin-3-yl)piperazine-1-carboxamide **[^{13}C]39** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (0.10 mmol, 14.4 µL), 3-azidopyridine **S7** (0.1 mmol, 12.0 mg), 1-(4-(4-chlorophenoxy)benzyl)piperazine **S32** (33.3 mg, 0.11 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using CH_2Cl_2/MeOH (100/0 to 95/5) as eluent affording the expected compound as a white solid (30 mg, 0.071 mmol, **71%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, , *J* = 2.5 Hz, 1H), 8.24 (dd, *J* = 4.7 Hz, *J* = 1.4 Hz, 1H), 7.96 (ddd, *J* = 8.4 Hz, *J* = 2.5 Hz, *J* = 1.4 Hz, 1H), 7.31-7.26 (m, 4H), 7.21 (dd, *J* = 8.4 Hz, *J* = 4.7 Hz, 1H), 6.97-6.91 (m, 4H), 6.91 (br s, 1H), 3.56-3.51 (m, 4H), 3.50 (s, 2H), 2.51-2.43 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 156.0, 154.9, 144.1, 141.3 (d, *J* = 3 Hz), 136.2, 132.9, 130.7 (2C), 129.9 (2C), 128.4, 127.6, 123.7, 120.2 (2C), 118.8 (2C), 63.3, 52.7 (d, *J* = 1 Hz, 2C), 44.3 (2C).
IR (cm^{-1}): 3296, 2811, 1612, 1504, 1483, 1419, 1235, 1001, 729.
HRMS (ESI): calcd for $C_{22}{}^{13}CH_{24}ClN_4O_2$ $[M+H]^+$ 424.1616; found 424.1618.

- *Tau aggregate inhibitor: **[^{13}C]40***



tert-butyl (4-bromophenyl)carbamate **(S33)**

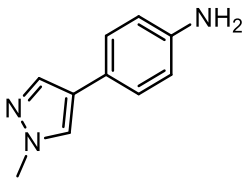


$C_{11}H_{14}BrNO_2$
MW: 272.02 g.mol^{-1}
Yield: 95%
White Solid

In a flask was added 4-bromoaniline (2.00 g, 11.6 mmol) and $(Boc)_2O$ (2.78 g, 12.7 mmol) in water (12 mL). The solution was stirred 24 hours and the white precipitate was filtrated and washed three times with heptane affording the expected compound without further purification (3.00 g, 11.0 mmol, **95%**). Data are consistent with literature values. [23]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41-7.36 (m, 2H), 7.28-7.22 (m, 2H), 6.47 (br s, 1H), 1.51 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 137.6, 132.0 (2C), 120.2, 115.6, 81.0, 28.4 (3C).

4-(1-methyl-1H-pyrazol-4-yl)aniline **(S35)**

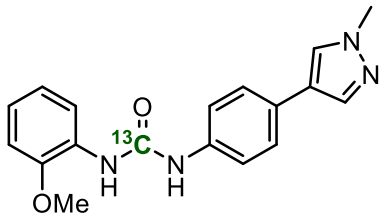


$C_{10}H_{11}N_3$
MW: 173.10 g.mol^{-1}
Yield: 72%
Grey Solid

In a microwave reactor was added tert-butyl-(4-bromophenyl)carbamate **S33** (300 mg, 1.08 mmol), 1-Methyl-1H-pyrazole-4-boronic acid pinacol ester (276 mg, 1.32 mmol), $PdCl_2$(dppf) (78 mg, 0.13 mmol), sodium carbonate (282 mg, 2.7 mmol) in a degazed solution of dioxane/water 4/1 (6 mL). The reaction mixture was heated to 100 °C for 1 hours under microwave and cooled down to room temperature. The solution was filtrated through a pad of celite®, extracted twice with AcOEt (2 x 10 mL) and the organic layer was washed once with water (10 mL) and once with brine (10 mL), dried over $MgSO_4$ and evaporated.
The crude mixture was dissolved in MeCN (10 mL) and the solution was cooled down to 0°C. Boron trifluoride etherate (450 µL, 3.66 mmol) was added dropwise. The solution was stirred 15 min at room temperature and was quenched with a saturated solution of $NaHCO_3$ (10 mL). The organic layer was extracted twice with DCM (10 mL), dried over $MgSO_4$ filtrated and evaporated. The crude mixture was purified by flash chromatography on SiO_2 gel using *n*-heptane/AcOEt (60/40 to 30/70) as eluent affording the expected compound as a grey solid (90 mg, 0.54 mmol, **50%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 0.6 Hz, 1H), 7.48 (d, *J* = 0.6 Hz, 1H), 7.29-7.24 (m, 4H), 6.72-6.66 (m, 2H), 3.91 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1, 136.4, 126.7 (2C), 126.2, 123.5, 123.3, 115.6 (2C), 39.1**.**
LCMS (ESI) m/z $C_{10}H_{12}N_3$ $[M+H]^+$ 174.3..

[^{13}C] 1-(2-methoxyphenyl)-3-(4-(1-methyl-1*H*-pyrazol-4-yl)phenyl)urea **([^{13}C]40)**



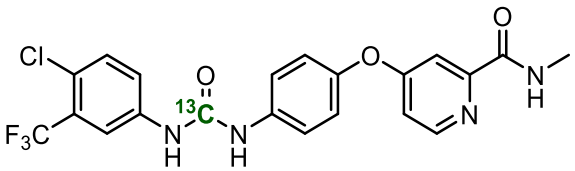
$C_{17}{}^{13}CH_{18}N_4O_2$
MW: 323.15 g.mol^{-1}
Yield: 36%
White Solid

The [^{13}C] 1-(2-methoxyphenyl)-3-(4-(1-methyl-1*H*-pyrazol-4-yl)phenyl)urea **[^{13}C]40** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (0.05 mmol, 7.20 µL), 1-azido-2-methoxybenzene **S12** (0.05 mmol, 7.46 mg), 4-(1-methyl-1*H*-pyrazol-4-yl)aniline **S35** (0.10 mmol, 17.3 mg), 1-methyl-imidazole (0.10 mmol, 8.00 µL) and $^{13}CO_2$ (55 mbar, 0.11 mmol) in DMF for 120 minutes at 80 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using CH_2Cl_2/MeOH (100/0 to 98/2) as eluent affording the expected compound as a white solid (5.8 mg, 0.018 mmol, **36%**). Data are consistent with literature values. [24]

^{1}H NMR (400 MHz, DMF-d_7): δ = 8.32 (dd, *J* = 7.3 Hz, *J* = 2.4 Hz, 1H), 8.09 (s, 1H), 7.85 (s, 1H), 7.64-7.52 (m, 4H), 7.06 (dd, *J* = 7.6 Hz, *J* = 1.9 Hz, 1H), 7.01-6.91 (m, 2H), 3.94 (s, 3H), 3.91 (s, 3H).
^{13}C NMR (100 MHz, DMF-d_7): δ = 153.9-153.7 (m, ^{13}C), 149.1-148.9 (m), 139.5, 136.8, 130.5-130.3 (m), 128.1, 128.0, 126.6 (2C), 123.6, 122.7, 121.7, 119.7-119.6 (m, 2C), 119.6-119.5 (m), 119.3, 119.2, 111.6, 56.6, 39.7.
IR (cm^{-1}): 3283, 2927, 1594, 1542, 1459, 1253, 746.
HRMS (ESI): calcd for $C_{17}{}^{13}CH_{18}N_4O_2$ $[M+H]^+$ 324.1536; found 324.1515.

- *Sorafenib: anti-cancer [^{13}C]41*

[^{13}C] *N*-[4-Chloro-3-(trifluoromethyl)phenyl]- ({4-[2-(*N*-methyl-carbamoyl)(4-pyridyloxy)] phenyl}amino)-carboxamide **([^{13}C]41)**

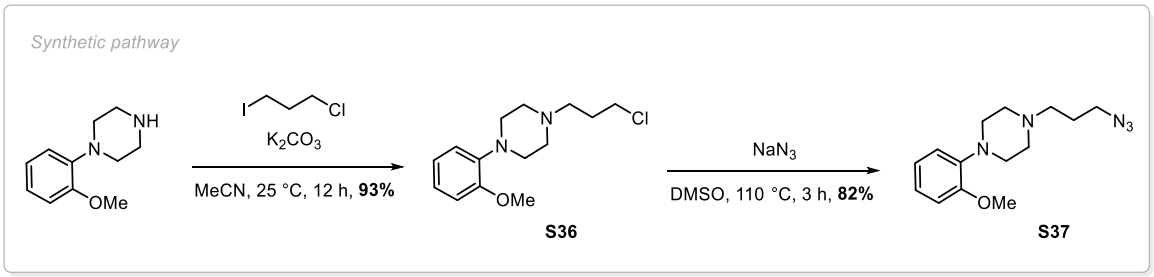


$C_{20}{}^{13}CH_{16}ClF_3N_4O_3$
MW: 465.09 g.mol^{-1}
Yield: 47%
White solid

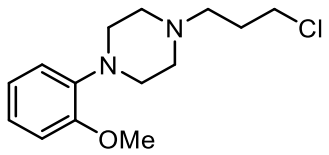
The [^{13}C] *N*-[4-Chloro-3-(trifluoromethyl)phenyl]- ({4-[2-(N-methyl-carbamoyl)(4-pyridyloxy)] phenyl}amino)-carboxamide **[^{13}C]41** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 4-(4-aminophenoxy)-*N*-methylpicolinamide (48.6 mg, 0.20 mmol), 4-azido-1-chloro-2-(trifluoromethyl)benzene **S26** (22.1 mg, 0.10 mmol), *N*-methylimidazole (16.0 µL, 0.20 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 120 minutes at 80 °C. The crude mixture was purified by reversed phase chromatography gel using water/acetonitrile (100/0 to 30/70) as eluent affording the expected compound as a white solid (22.1 mg, 0.047 mmol, **47%**). Data are consistent with literature values. [25]

^{1}H NMR (400 MHz, CD_3OD): δ = 8.52 (dd, *J* = 4.2 Hz, *J* = 1.6 Hz, 1H), 7.94 (dd, *J* = 8.3 Hz, *J* = 1.6 Hz, 1H), 7.51-7.47 (m, 2H), 7.33-7.27 (m, 2H), 7.22-7.13 (m, 2H), 6.36 (d, *J* = 2.4 Hz, 1H), 6.30 (d, *J* = 2.4 Hz, 1H), 5.89 (d, *J* = 7.9 Hz, 1H), 5.23 (br s, 1H), 3.87 (s, 3H), 3.63-3.50 (m, 1H), 3.29-3.11 (m, 2H), 1.67-1.54 (m, 4H), 1.23 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (100 MHz, CD_3OD): δ = 168.2, 167.0, 154.9-154.7 (m), 154.8 (^{13}C), 151.7, 150.3, 140.3, 128.2, 133.0, 129.5-129.2 (m), 125.7, 124.3, 124.3 (q, *J* = 272 Hz), 122.5 (2C), 122.4 (d, *J* = 2 Hz, 2C), 118.8-118.6 (m), 115.1, 110.7, 26.5.
^{19}F NMR (376 MHz, CD_3OD): δ = - 64.1.
IR (cm^{-1}): 3318, 1657, 1505, 1199, 1170, 1140, 843, 725.
HRMS (ESI): calcd for $C_{20}{}^{13}CH_{16}ClF_3N_4O_3$ $[M+H]^+$ 466.0969; found 466.0971.

- *APH199: Dopamine D4 receptor agonist [^{13}C]42*



1-(3-chloropropyl)-4-(2-methoxyphenyl)piperazine **(S36)**

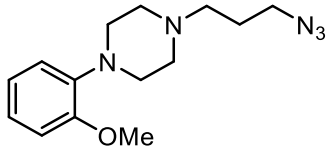


$C_{14}H_{21}ClN_2O$
MW: 268.13 g.mol^{-1}
Yield: 93%
Colorless oil

In a round bottom flask 1-(2-methoxyphenyl)piperazine (385 mg, 2.00 mmol), K_2CO_3 (276 mg, 4.00 mmol) and 3-chloro-1-iodopropane (290 µL, 2.20 mmol) were dissolved in MeCN (10 mL). The reaction mixture was stirred at room temperature for 12 hours and water (10 mL) was added. The organic layer was extracted twice with AcOEt (2 x 15 mL), dried over $MgSO_4$, filtrated and evaporated. The crude mixture was purified by flash chromatography on SiO_2 gel using *n*-heptane/AcOEt (40/60) as eluent affording the expected compound as a colorless oil (500 mg, 1.86 mmol, **93%**). Data are consistent with literature values. [26]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03-6.97 (m, 1H), 6.97-6.89 (m, 2H), 6.88-6.84 (m, 1H), 3.86 (s, 3H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.19-3.01 (m, 4H), 2.72-2.60 (m, 4H), 2.56 (t, *J* = 6.6 Hz, 2H), 2.00 (p, *J* = 6.6 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 141.4, 123.1, 121.1, 118.3, 111.3, 55.7, 55.5, 55.6 (2C), 50.8 (2C), 43.4, 30.1.

1-(3-azidopropyl)-4-(2-methoxyphenyl)piperazine **(S37)**

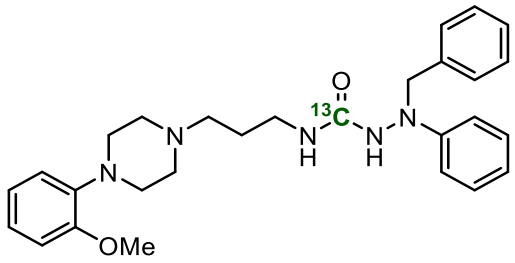


$C_{14}H_{21}N_5O$
MW: 275.17 g.mol^{-1}
Yield: 82%
Colorless oil

In a round bottom flask 1-(3-chloropropyl)-4-(2-methoxyphenyl)piperazine **S36** (480 mg, 1.80 mmol), and sodium azide (350 mg, 5.40 mmol) were dissolved in DMSO (10 mL). The reaction mixture was stirred at 110 °C for 3 hours and the solution was cooled down to room temperature. Water (40 mL) was added and the organic layer was extracted with Et_2O (3 x 10 mL), dried over $MgSO_4$, filtrated and evaporated affording the expected compound as a colorless oil without further purification (405 mg, 1.48 mmol, **82%**).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03-6.97 (m, 1H), 6.97-6.89 (m, 2H), 6.88-6.84 (m, 1H), 3.86 (s, 3H), 3.37 (t, *J* = 6.8 Hz, 2H), 3.18-3.01 (m, 4H), 2.70-2.59 (m, 4H), 2.50 (t, *J* = 6.8 Hz, 2H), 1.82 (p, *J* = 6.8 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 141.4, 123.1, 121.1, 118.3, 111.3, 55.5, 55.5, 53.5 (2C), 50.8 (2C), 49.8, 26.4.
^{19}F NMR (376 MHz, CD_3OD): δ = - 64.1.
LCMS (ESI) m/z $C_{14}H_{22}N_5O$ $[M+H]^+$ 277.0.

[^{13}C] 2-benzyl-*N*-(3-(4-(2-methoxyphenyl)piperazin-1-yl)propyl)-2-phenylhydrazine-1-carboxamide **[^{13}C]42**



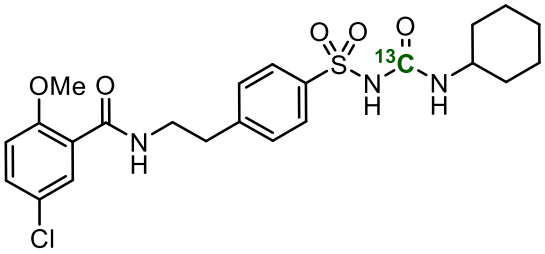
$C_{27}{}^{13}CH_{35}N_5O_2$
MW: 474.28 g.mol^{-1}
Yield: 66%
Pale yellow oil

The [^{13}C] 2-benzyl-*N*-(3-(4-(2-methoxyphenyl)piperazin-1-yl)propyl)-2-phenylhydrazine-1-carboxamide **[^{13}C]53** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), *N*-benzyl-*N*-phenylhydrazine (40.0 mg, 0.20 mmol), 1-(3-azidopropyl)-4-(2-methoxyphenyl)piperazine **S37** (27.5 mg, 0.10 mmol) and $^{13}CO_2$ (110 mbar, 0.11 mmol) in DMF for 5 minutes at 25 °C. The crude mixture was purified by reversed phase chromatography gel using water/acetonitrile (100/0 to 50/50) as eluent affording the expected compound as a pale yellow oil (31 mg, 0.066 mmol, **66%**). Data are consistent with literature values. [27]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36-7.26 (m, 7H), 7.13-7.05 (m, 3H), 7.00-6.86 (m, 5H), 6.27 (br s, 1H), 4.56 (s, 2H), 3.87 (s, 3H), 3.65-3.31 (m, 4H), 3.26-3.16 (m, 2H), 3.16-3.06 (m, 1H), 3.06-2.94 (m, 2H), 2.94-2.85 (m, 2H), 1.92-1.76 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6 (^{13}C), 152.2, 149.1, 138.5, 135.4, 129.6 (2C), 129.3 (2C), 128.9 (2C), 128.2, 125.0 (2C), 122.1, 121.4, 119.2, 115.7, 111.6, 59.4, 55.6, 54.8, 52.5 (2C), 47.6, 36.7, 24.6 (2C).
IR (cm^{-1}): 3262, 3030, 2838, 1674, 1500, 1198, 1172, 751.
HRMS (ESI): calcd for $C_{27}{}^{13}CH_{35}N_5O_2$ $[M+H]^+$ 475.2897; found 475.2902.

- *Glibenclamide [^{13}C]43*

5-chloro-N-(4-(*N*-(cyclohexylcarbamoyl-[^{13}C])sulfamoyl)phenethyl)-2-methoxybenzamide **([^{13}C]43)**



$C_{22}{}^{13}CH_{28}ClN_3O_5S$
MW: 494.15 g.mol^{-1}
Yield: 40%
White solid

In a vial 5-chloro-2-methoxy-N-(4-sulfamoylphenethyl)benzamide (36.8 mg, 0.10 mmol) was dissolved in 0.4 mL of dry DMF. NaH 95% (5 mg, 0.20 mmol) was added and the solution was stirred 15 minutes at room temperature. In a reactor (Figure S3) cyclohexylazide **S13** (12.5 mg, 0.1 mmol) and $PPhMe_2$ were dissolved in 0.4 mL of DMF and the solution containing the sulfonylamide was finally added. The reactor was freezed in to N_2 bath, then gaseous $^{13}CO_2$ (110 mbar, 0.11 mmol) was trapped using Tritec®. The mixture was maintained at room temperature for 5 minutes and heated to 80 °C for 5 min then the unreacted $^{13}CO_2$ was removed by opening the reactor and the solvent was evaporated. A white precipitate was obtained by centrifugation of the crude mixture in CH_2Cl_2, and was washed several times with CH_2Cl_2 affording the expected compound (19 mg, 0.04 mmol, **40%**).
Data are consistent with literature values. [28]

^{1}H NMR (400 MHz, DMF-d$_7$): δ = 8.385 (t, *J* = 5.5 Hz, 1H), 7.94 (d, *J* = 2.8 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.58 (dd, *J* = 8.9 Hz, *J* = 2.9 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.9 Hz, 1H), 5.75 (br s, 1H), 4.23 (br s, 1H), 3.93 (s, 3H), 3.72-3.65 (m, 2H), 3.44-3.33 (m, 1H), 3.00-2.95 (m, 2H), 1.86-1.71 (m, 2H), 1.71-1.60 (m, 2H), 1.59-1.49 (m, 1H), 1.32-1.19 (m, 2H), 1.18-1.02 (m, 2H).
^{13}C NMR (100 MHz, DMF-d$_7$): δ = 164.6, 162.6 (^{13}C), 157.5, 147.2, 142.2, 133.0, 131.4, 129.1, 127.6, 126.0, 125.3, 115.2, 57.2, 49.9, 49.3, 42.0, 34.6, 26.8, 26.1.
IR (cm^{-1}): 3367, 2929, 1647, 1545, 1482, 1238, 1125, 810.
HRMS (ESI): calcd for $C_{22}{}^{13}CH_{29}N_3O_5S$ $[M+H]^+$ 495.1546; found 495.1545.

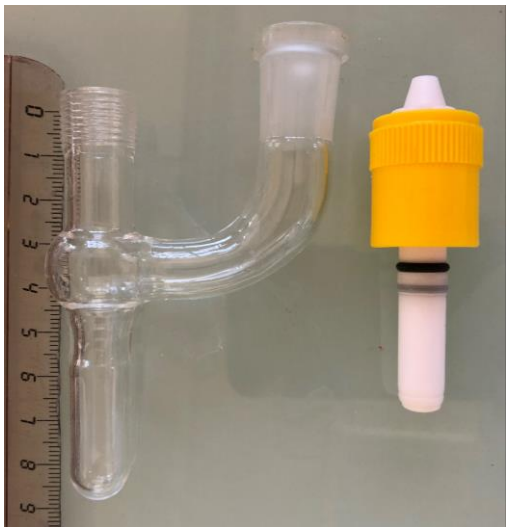


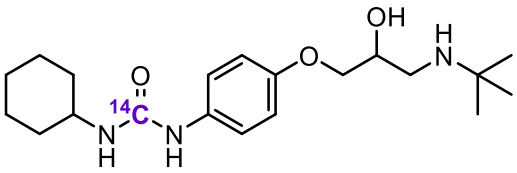
Figure S3: Specific reactor

3. Carbon labeling experiments

3.1. Synthesis of ^{14}C-labeled drug derivatives

3.1.1. [^{14}C]Talinolol

[^{14}C] 1-(4-(3-(tert-butylamino)-2-hydroxypropoxy)phenyl)-3-cyclohexylurea **([^{14}C]37)**

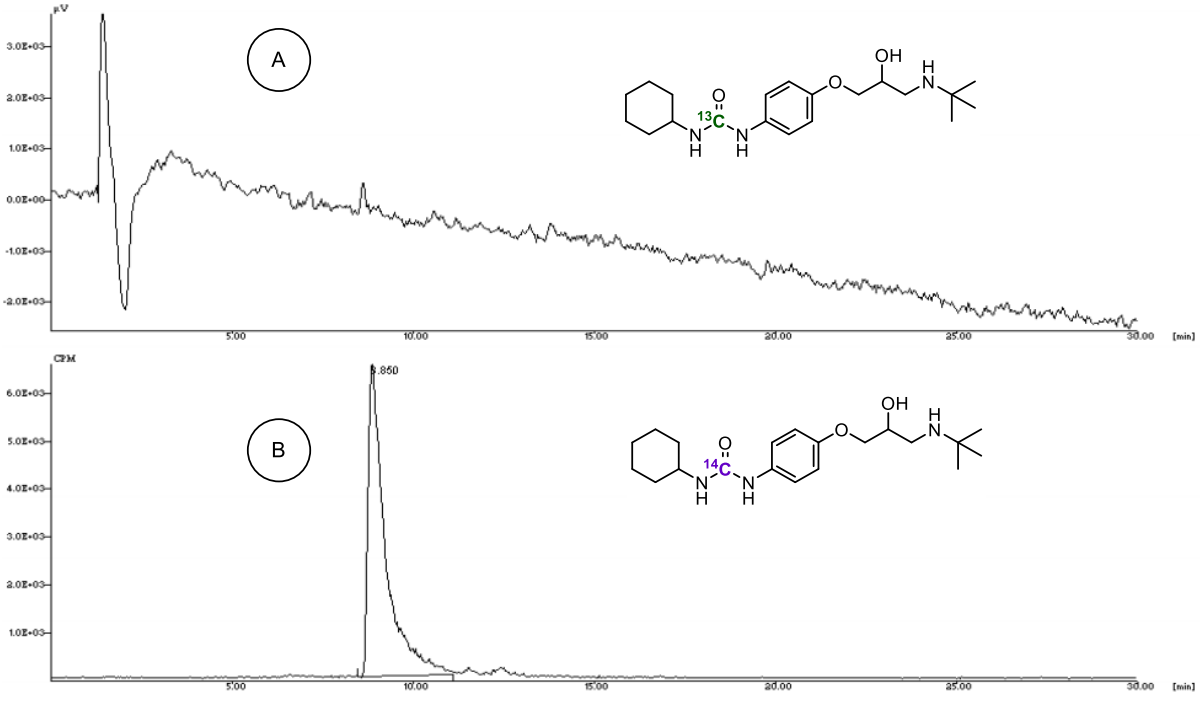


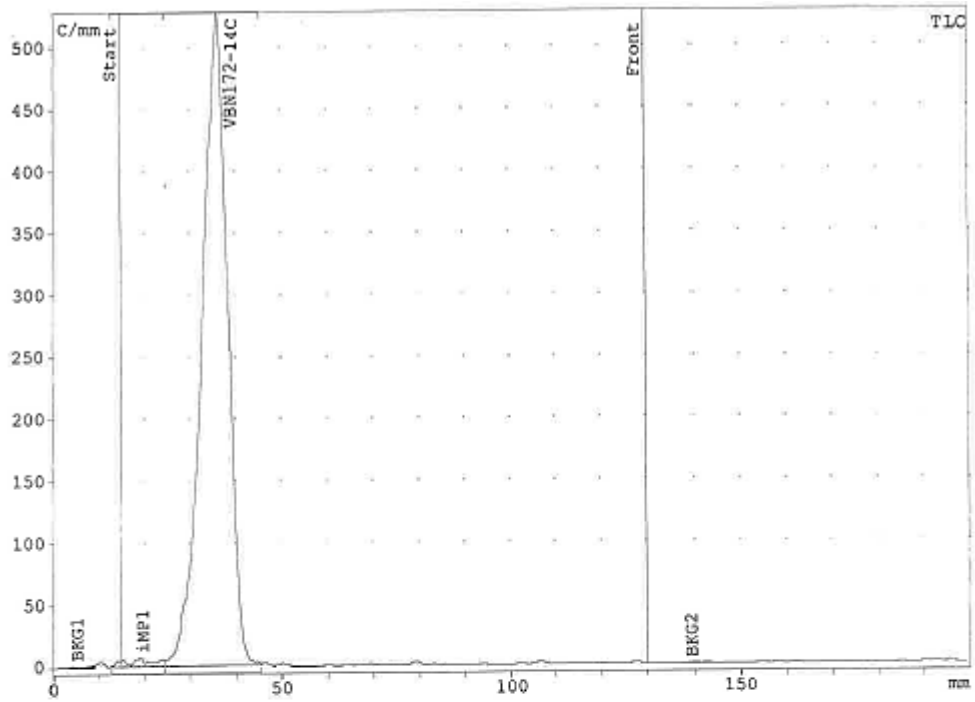
$C_{19}{}^{14}CH_{33}N_3O_3$
MW: 365.26 g.mol^{-1}
RCY: 82%

The [^{14}C] 1-(4-(3-(tert-butylamino)-2-hydroxypropoxy)phenyl)-3-cyclohexylurea **[^{14}C]37** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (0.05 mmol, 7.20 µL), 1-(4-azidophenoxy)-3-(tert-butylamino)propan-2-ol **S31** (0.05 mmol, 13.2 mg), cyclohexylamine (28.0 µL, 0.25 mmol), and $^{14}CO_2$ (0.058 mmol, 125.97 MBq (3.40 mCi)) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using Dichloromethane/methanol (90/10) + 1% NH_3 7N in MeOH as eluent affording the expected compound (84.73 MBq, 0.041 mmol, 82%)

$^{14}CO_2$ molar activity: 2.172 GBq.mmol^{-1}
Molar activity (MS (ESI)): 2.055 GBq.mmol^{-1}
TLC (silicagel 60F254, CH_2Cl_2/MeOH/ NH3 7N in MeOH (90/10/1)): Rf = 0.19
Radiochemical purity (TLC): 99%

A: UV chromatogram / B: Radiochromatogram





Description de l'échantillon

Etude:	OLIVIER		
Mesure:	VBN172-14C-Purified_02.rta, commencé: 02/10/2019 13:02		
Méthode:	C14		
Origine:	15 mm	Front 130 mm	
Meas. time:	0,3 min	Résolution: 0,4 mm	
Tray number:	1,0	Position de scan:	215,0 mm
Haute tension:	1620,0 V		

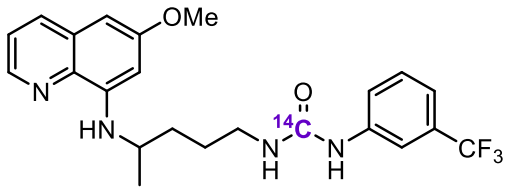
VBN172-14C Purified
Silicagel 60F254
CH2Cl2/MeOH/NH3 7N in MeOH (90/10/1)
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

Substance	R/F	Type	Aire	%Aire
			Counts	%
iMP1	0,035	DD	35,302	1,02
VBN172-14C	0,185	DD	3422,720	98,98
Sum in ROI			3458,022	
Aire totale			3506,864	
Aire RF			3488,273	
BKG1			1,1157	
BKG2			0,2479	
Remainder RF			30,25	0,87

3.1.2. [^{14}C]Primaquine derivative

[^{14}C] 1-(4-((6-methoxyquinolin-8-yl)amino)pentyl)-3-(3-(trifluoromethyl)phenyl)urea **([^{14}C]38)**

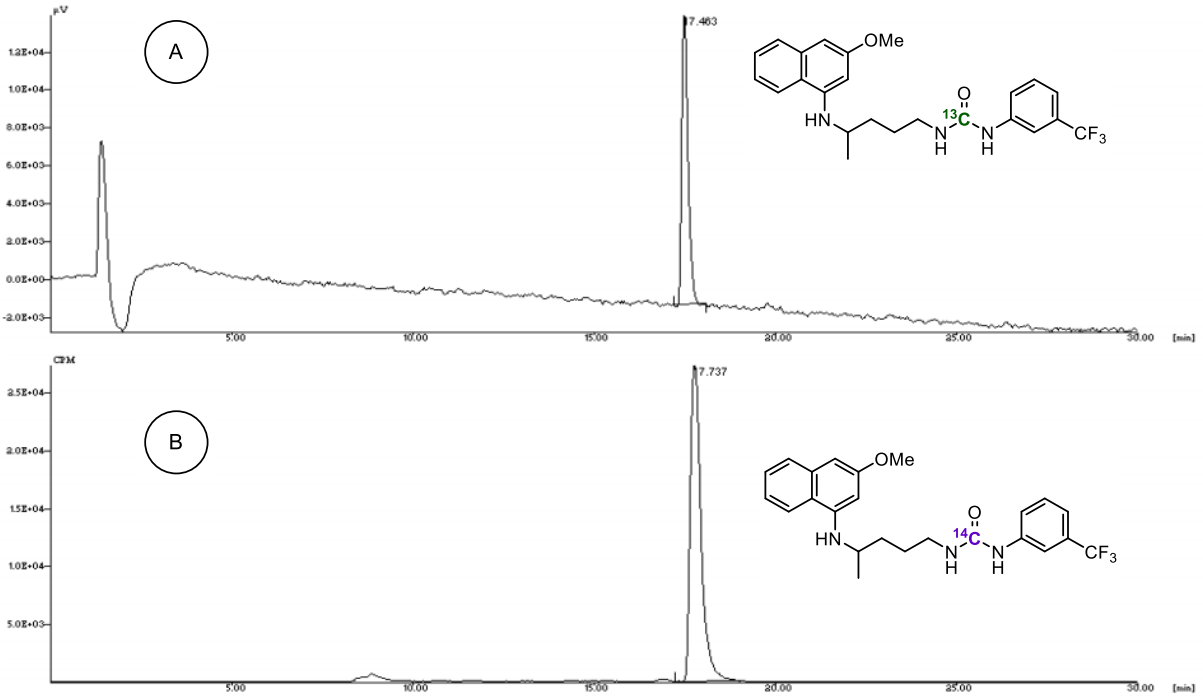


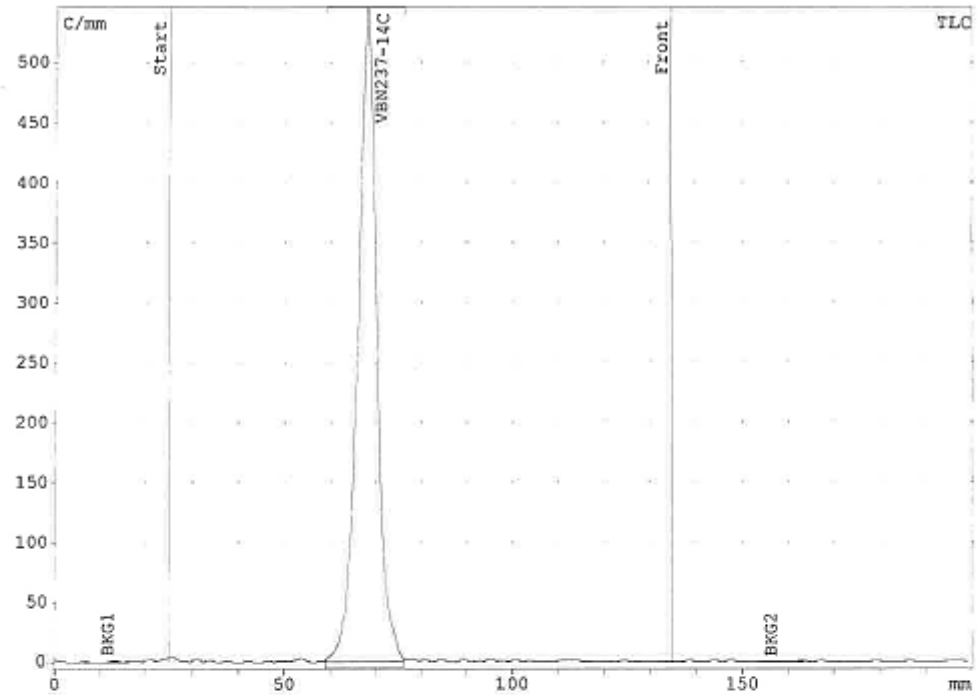
$C_{22}{}^{14}CH_{25}F_3N_4O_2$
MW: 448.20 g.mol^{-1}
RCY: 60%

The [^{14}C] 1-(4-((6-methoxyquinolin-8-yl)amino)pentyl)-3-(3-(trifluoromethyl)phenyl)urea **[^{14}C]38** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), N^4-(6-methoxyquinolin-8-yl)pentane-1,4-diamine (0.10 mmol, 25.9 mg), 1-azido-3-(trifluoromethyl)benzene **S25** (18.7 mg, 0.10 mmol), and $^{14}CO_2$ (0.104 mmol, 226.44 MBq (6.12 mCi)) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using *n*-heptane/AcOEt 70/30 affording the expected compound (108.04 MBq, 0.060 mmol, 60%)

$^{14}CO_2$ molar activity: 2.172 GBq.mmol^{-1}
Molar activity (MS (ESI)): 1.799 GBq.mmol^{-1}
TLC (silicagel 60F254, n-Heptane/AcOEt (50/50)): Rf = 0.39
Radiochemical purity (TLC): >99%

A: UV chromatogram / B: Radiochromatogram





Description de l'échantillon

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Méthode:	C14 de:	01/01/2000	
Origine:	25 mm	Front 135 mm	
Meas. time:	0,2 min	Résolution: 0,4 mm	

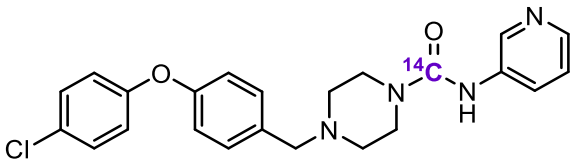
VBN237-14C-Pur
Silicagel Merck 60F254 - Heptane 50 AcOEt 50
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

Substance	R/F	Type	Aire	%Aire
			Counts	%
VBN237-14C	0,393	DD	2658,465	100,00
Sum in ROI			2658,465	
Aire totale			2719,861	
Aire RF			2704,075	
BKG1			0,2922	
BKG2			0,0682	
Remainder RF			45,61	1,69
Remainder (Tot)			61,40	2,26

3.1.3. [^{14}C]JNJ-40355003 analogue

[^{14}C] 4-(4-(4-chlorophenoxy)benzyl)-*N*-(pyridin-3-yl)piperazine-1-carboxamide **([^{14}C]39)**

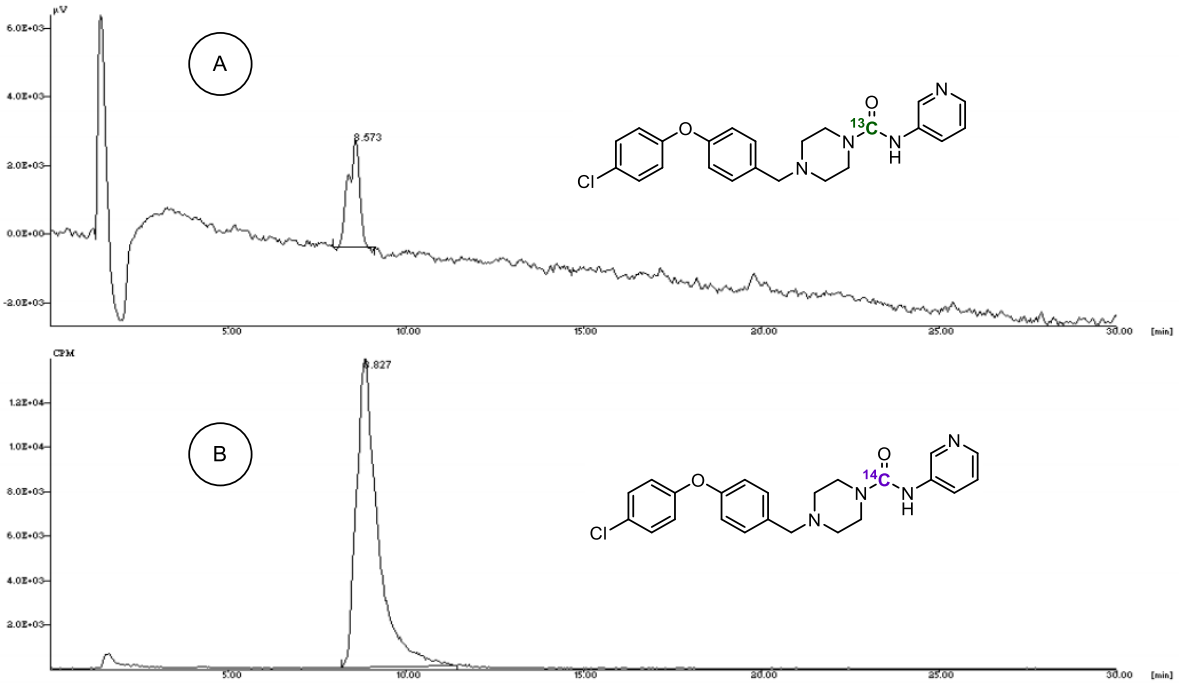


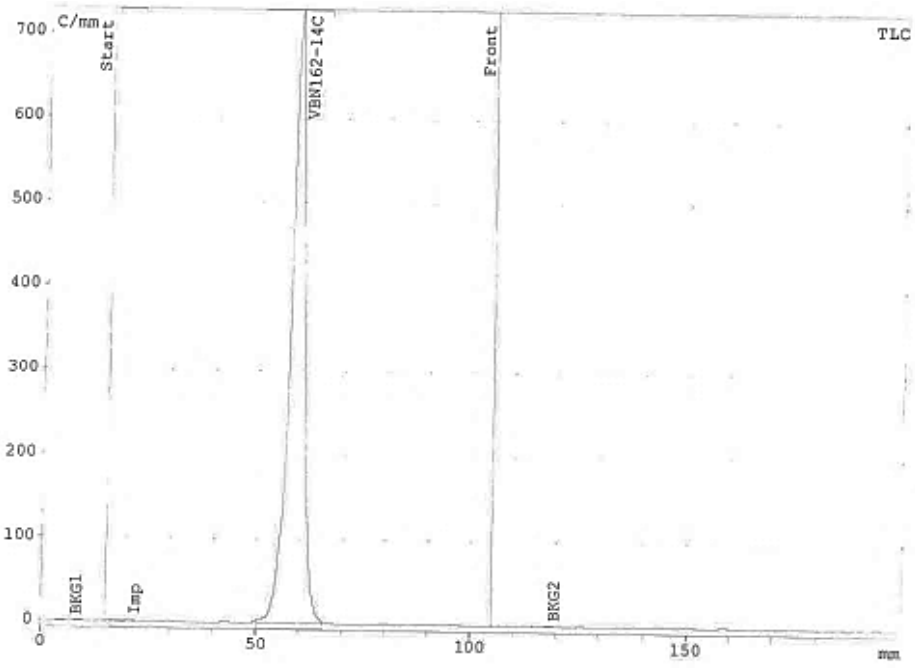
$C_{22}{}^{14}CH_{24}ClN_4O_2$
MW: 424.15 g.mol^{-1}
RCY: 76%

The [^{14}C] 4-(4-(4-chlorophenoxy)benzyl)-*N*-(pyridin-3-yl)piperazine-1-carboxamide **[^{14}C]39** was prepared accordingly to the general procedure **GP4**, using $PPhMe_2$ (0.10 mmol, 14.4 µL), 3-azidopyridine **S7** (0.1 mmol, 12.0 mg), 1-(4-(4-chlorophenoxy)benzyl)piperazine **S35** (33.3 mg, 0.11 mmol) and $^{14}CO_2$ (0.103 mmol, 223.72 MBq (6.05 mCi)) in CH_3CN for 5 minutes at 25 °C. The crude mixture was purified by flash chromatography on SiO_2 gel using CH_2Cl_2/MeOH (100/0 to 95/5) as eluent affording the expected compound (147.63 MBq, 0.076 mmol, 76%)

$^{14}CO_2$ molar activity: 2.172 GBq.mmol^{-1}
Molar activity of XX (MS (ESI)): 1.944 GBq.mmol^{-1}
TLC (silicagel 60F254, CH_2Cl_2/MeOH (95/5)): Rf = 0.49
Radiochemical purity (TLC): 99.7%

A: UV chromatogram / B: Radiochromatogram





Description de l'échantillon

Etude:	OLIVIER		
Mesure:	VBN162-14C-Pur.rta, commencé:		24/09/2019 17:08
Méthode:	C14		
Origine:	15 mm	Front 105 mm	
Meas. time:	0,2 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		

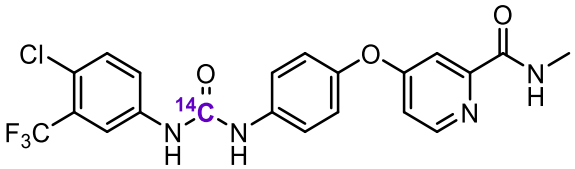
VBN162-14C-Pur
Silicagel Merck 60F254 - CH2Cl2 95 - MeOH 5
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

Substance	R/F	Type	Aire	%Aire
			Counts	%
Imp	0,069	DD	6,687	0,24
VBN162-14C	0,490	DD	2812,264	99,76
Sum in ROI			2818,951	
Aire totale			2836,789	
Aire RF			2830,115	
BKG1			0,2372	
BKG2			0,1049	
Remainder RF			11,16	0,39
Remainder (Tot)			17,84	0,63

3.1.4. [^{14}C]Sorafenib

[^{14}C] *N*-[4-Chloro-3-(trifluoromethyl)phenyl]- ({4-[2-(*N*-methyl-carbamoyl)(4-pyridyloxy)] phenyl}amino)-carboxamide **([^{14}C]41)**



$C_{20}{}^{14}CH_{16}ClF_3N_4O_3$
MW: 466.06 g.mol^{-1}
RCY: 26%

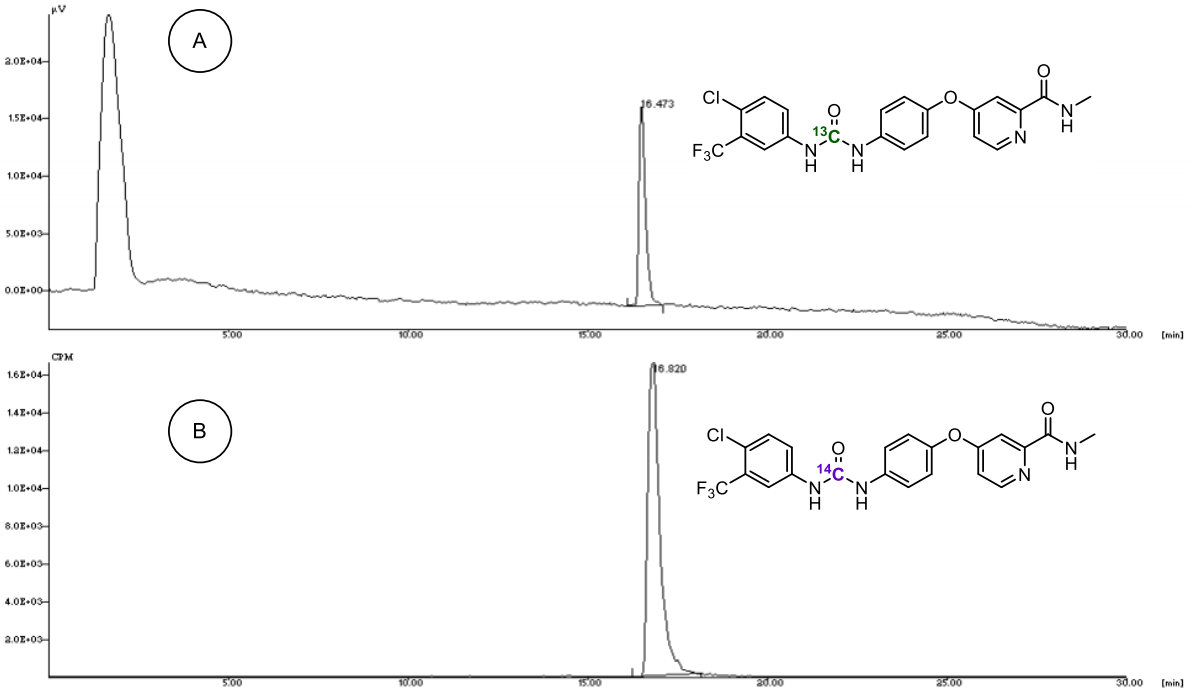
The [^{14}C] *N*-[4-Chloro-3-(trifluoromethyl)phenyl]- ({4-[2-(N-methyl-carbamoyl)(4-pyridyloxy)] phenyl}amino)-carboxamide **[^{14}C]41** was prepared accordingly to general procedure **GP4**, using $PPhMe_2$ (14.4 µL, 0.10 mmol), 4-(4-aminophenoxy)-*N*-methylpicolinamide (48.6 mg, 0.20 mmol), 4-azido-1-chloro-2-(trifluoromethyl)benzene **S26** (22.1 mg, 0.10 mmol), *N*-methylimidazole (16.0 µL, 0.20 mmol) and $^{14}CO_2$ (0.114 mmol, 247.53 MBq (6.69 mCi)) in DMF for 120 minutes at 80 °C. The crude mixture was first purified by RP-HPLC using the conditions described below:

Column: Hypurity C18 (250 x 10 mm) from Thermo
Solvent of injection: H_2O/CH_3CN 45/55 (700 µL / 22.2 MBq (600 µCi) per injection)
Detection: UV (254 nm) and radioactive
Gradient: t=0 (H_2O/CH_3CN/HCOOH 95/5/0.1), t=15 mn (H_2O/CH_3CN/HCOOH 80/20/0.1), t=40mn (H_2O/CH_3CN/HCOOH 20/80/0.1), t=50 mn (CH_3CN 100), t=60 mn (end)

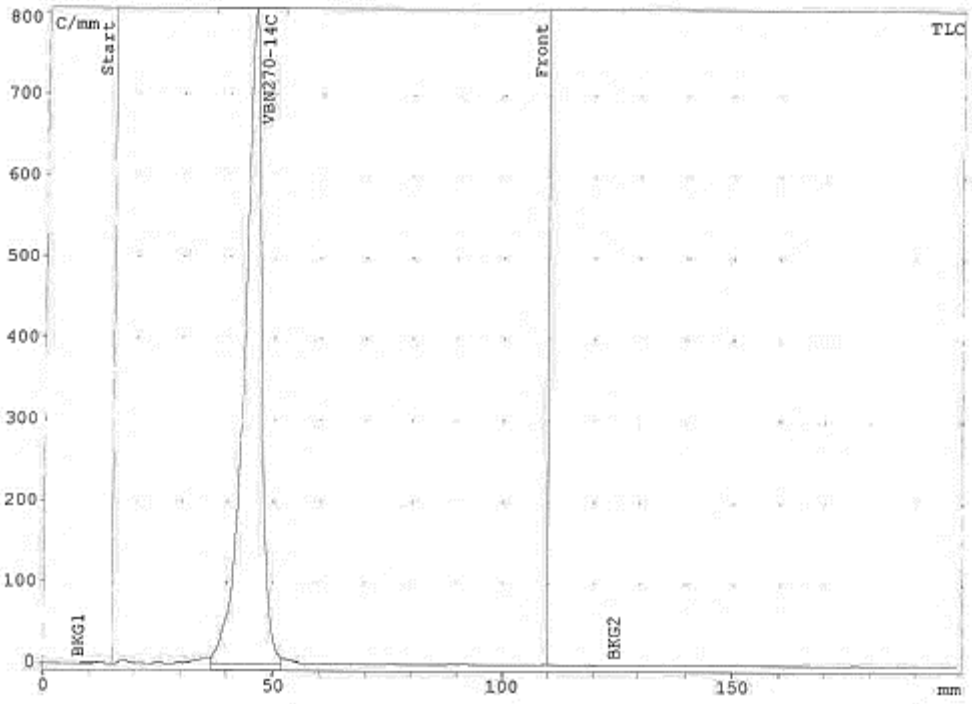
A second purification by flash chromatography on SiO_2 gel using CH_2Cl_2/MeOH 100/4 afforded the expected compound **[^{14}C]50** in a pure form (54.34 MBq, 0.026 mmol, 36%).

$^{14}CO_2$ molar activity: 2.172 GBq.mmol^{-1}
Molar activity of XX (MS (ESI)): 2.069 GBq.mmol^{-1}
TLC (silicagel 60F254, CH_2Cl_2/MeOH (100/4)): Rf = 0.32
Radiochemical purity: >99%

A: UV chromatogram / B: Radiochromatogram


A
μV
2.0E+04
1.5E+04
1.0E+04
5.0E+03
0.0E+00
16.473
5.00
10.00
15.00
20.00
25.00
30.00
[min]
Cl
F3C
O
13C
N
H
O
N
H
N
O
N
H

B
CPM
1.6E+04
1.4E+04
1.2E+04
1.0E+04
8.0E+03
6.0E+03
4.0E+03
2.0E+03
16.820
5.00
10.00
15.00
20.00
25.00
30.00
[min]
Cl
F3C
O
14C
N
H
O
N
H
N
O
N
H



Description de l'échantillon

Etude:	OLIVIER		
Mesure:	VBN270-14C Purif C.rta, commencé:		26/08/2020 14:24
Méthode:	C14		
Origine:	15 mm	Front 110 mm	
Meas. time:	0,1 min	Résolution: 0,4 mm	
Haute tension:	1620,0 V		

VBN270-14C Purifié
Silicagel Merck 60F254 - CH2Cl2 100 MeOH 4
Détecteur de radioactivité: raytest RITA
Autre Square flow cell #0
Cell volume 0 ul

Intégration TLC

Substance	R/F	Type	Aire	%Aire
			Counts	%
VBN270-14C	0,320	DD	3505,159	100,00
Sum in ROI			3505,159	
Aire totale			3551,095	
Aire RF			3550,393	
BKG1			0,1299	
BKG2			0,0974	
Remainder RF			45,23	1,27
Remainder (Tot)			45,94	1,29

3.2. Synthesis of ^{11}C-labeled drug derivatives

General procedure for ^{11}C radiolabeling

Automated radiosynthesis with carbon-11 was performed using a MeI$_{plus}$ research synthesizer (Synthra GmbH, Germany) with modifications to undergo direct bubbling of [^{11}C]CO_2 into the reaction vessel (Figure S4). No carrier-added [^{11}C]CO_2 (3.5-18 GBq) was produced via the ^{14}N(p, α)^{11}C nuclear reaction by irradiation of a [^{14}N]N_2 target containing 0.15-0.5% of O_2 on a cyclone 18/9 cyclotron (18 MeV, IBA, Belgium) and trapped at -180 °C. [^{11}C]CO_2 was then released at 50 °C under a stream of helium (8 mL.min^{-1}) to bubble for 10 s into the reaction vessel containing a solution of the azide precursor (1 mg), the amine precursor (10 mg) and dimethylphenyl phosphine (15 µL) in DMF (250 µL) at -50 °C. After 5 min at room temperature, the reaction was hydrolyzed with a mixture of CH_3CN/H_2O/TFA (1 mL, 30/70/0.1 v/v/v).

Quality control was performed by HPLC using a 717$_{plus}$ Autosampler system equipped with a 1525 binary pump and a 2996 photodiode array detector (Waters, USA) and a Flowstar LB 513 (Berthold, France) gamma detector. The system was monitored with the Empower 3 (Waters, USA) software. HPLC were realized on a reverse phase analytical Symmetry C18 (50 x 3.9 mm, 5 µm, Waters, USA) column using a mixture of H_2O/CH_3CN/PicB7® (proportions depending on the compound, 2 mL/min) as eluent. UV detection was performed at the maximum absorbance of the compound. Identification of the peak was assessed by comparing the retention time of carbon-11 labeled compound with the retention time of the non-radioactive reference (t_R^{ref}). For acceptance, the retention time must be within the t_R^{ref} ± 10% range. Radiochemical purity (RCP) was calculated as the ratio of the area under the curve (AUC) of the peak over the sum of the AUCs of all other peaks on gamma chromatograms. Radiochemical purity is the mean value of three consecutive runs. The radiochemical yield (RCY) of the labeling reaction was calculated as the ratio of the decay-corrected activity at the end of the synthesis (A_{EOS}), measured in an ionization chamber (Capintec®, Berthold, France) over the starting activity of [^{11}C]CO_2 (A_{CO2}) measured by the calibrated detector of the synthesizer. This ratio was corrected for the radiochemical purity following the equation: RCY = (A_{EOS} / A_{CO2}) x RCP. Molar activity was calculated as the ratio of the activity of the collected peak of the radioactive product measured in an ionization chamber (Capintec®, Berthold, France) over the molar quantity of the compound determined using calibration curves. Molar activity was calculated as the mean value of three consecutive runs.

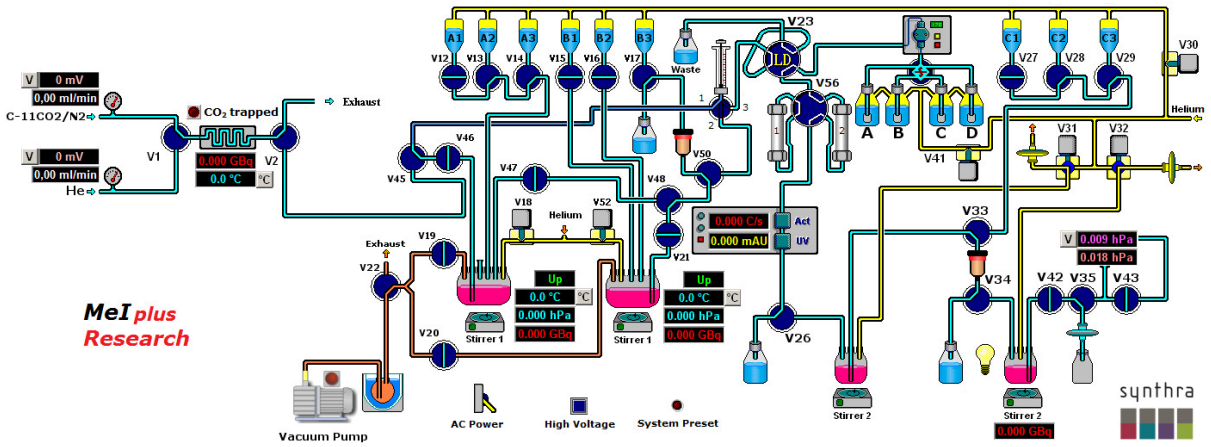
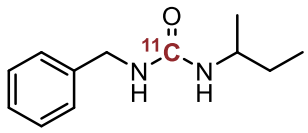


Figure S4 Modified MeI$_{plus}$ Research module for direct CO_2 labeling.

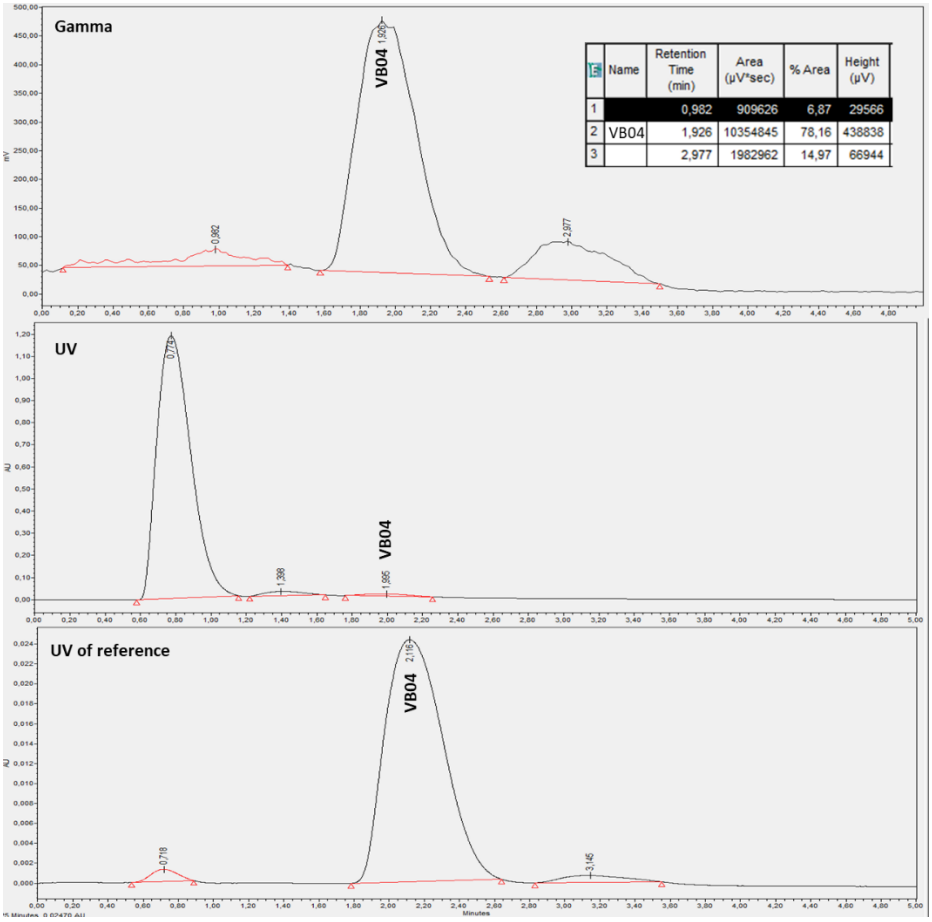
3.2.1. 1-benzyl-3-(sec-butyl)urea ([^{11}C]1)

[^{11}C] 1-benzyl-3-(sec-butyl)urea **([^{11}C]6)**



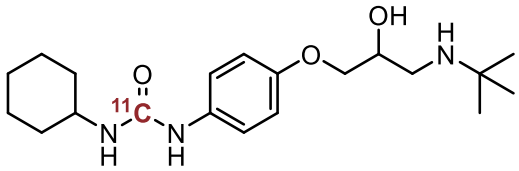
$C_{11}{}^{11}CH_{18}N_2O$
MW: 205.15 g.mol^{-1}
RCY = 63 %

The [^{11}C] 1-benzyl-3-(sec-butyl)urea **[^{11}C]1** (2.1 GBq) was synthesized according to the general procedure within 15 minutes in 63% RCY and 78% RCP as calculated after analysis by HPLC (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 220 nm).



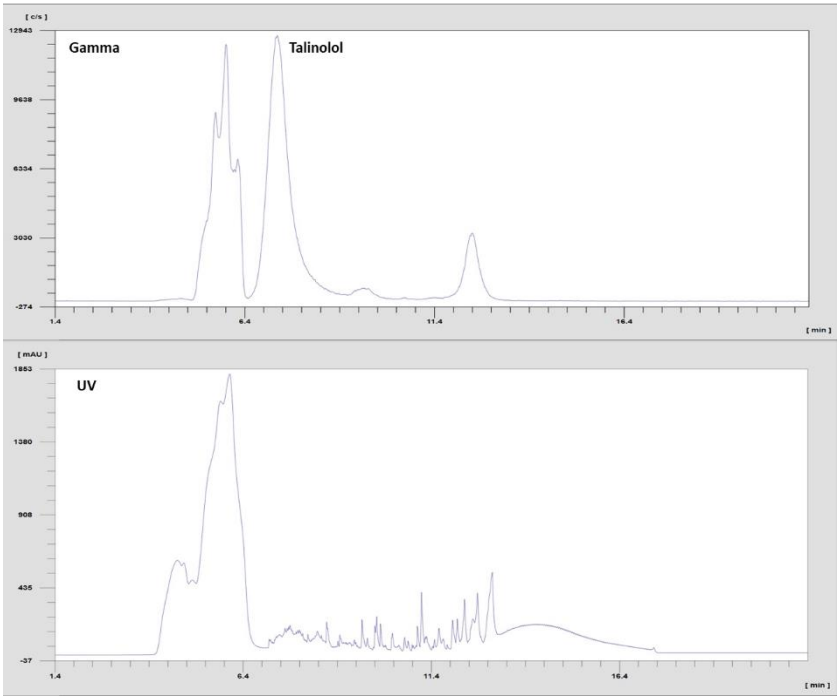
3.2.2. [^{11}C] Talinolol ([^{11}C]37)

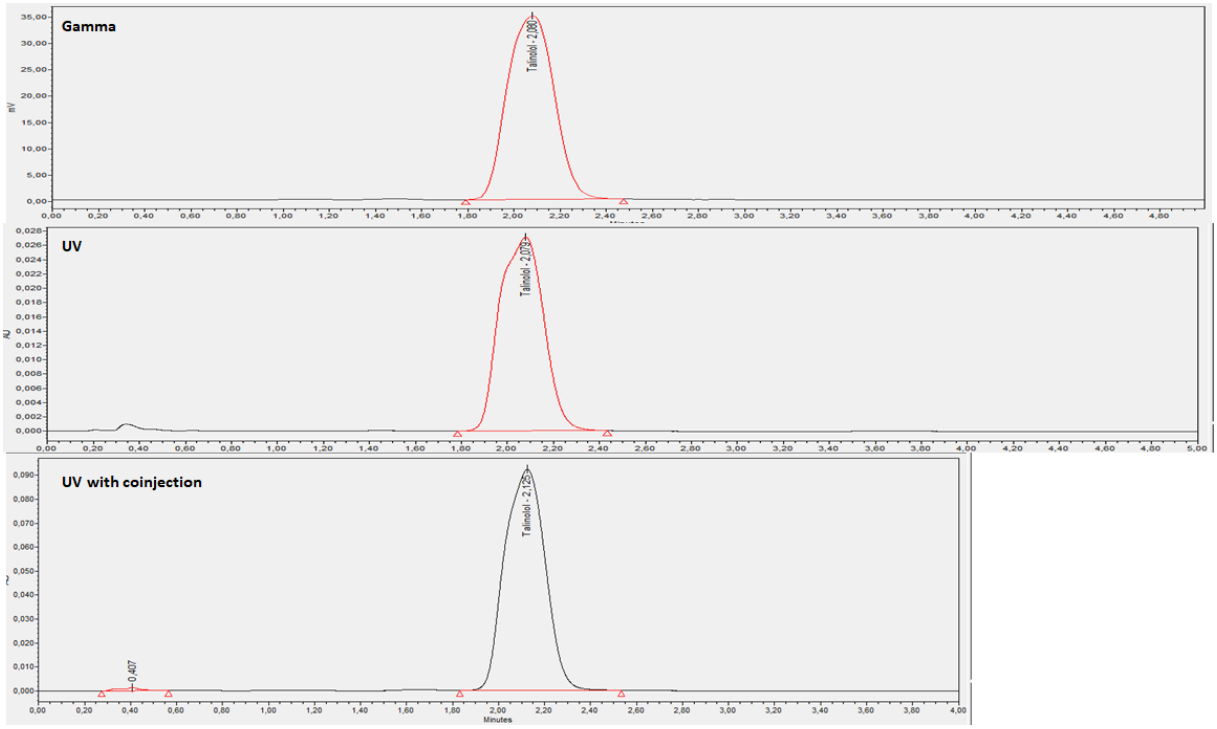
[^{11}C] 1-(4-(3-(tert-butylamino)-2-hydroxypropoxy)phenyl)-3-cyclohexylurea **([^{11}C]37)**



$C_{19}{}^{11}CH_{33}N_3O_3$
MW: 362.26 g.mol^{-1}
RCY: 26 %

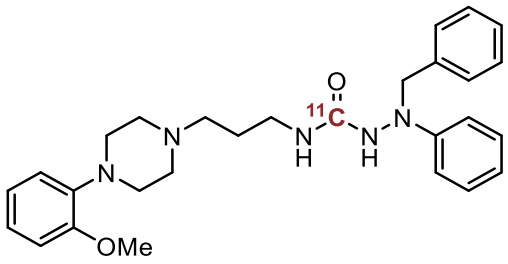
The crude product was synthesized following the general procedure using azide **S31** and cyclohexylamine as precursors. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (60/40/0.1 v/v/v, 5 mL/min) as eluent with gamma and UV (λ = 245 nm) detection. The collected peak (t_R = 6.5-8.0 min) of [^{11}C]Talinolol was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]Talinolol (0.9 ± 0.2 GBq) was obtained within 30 min from end of beam in 26 ± 6% RCY and 55 ± 10 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure (H_2O/CH_3CN/PicB7® 70/30/0.2 v/v/v, 2 mL/min, λ = 245 nm).





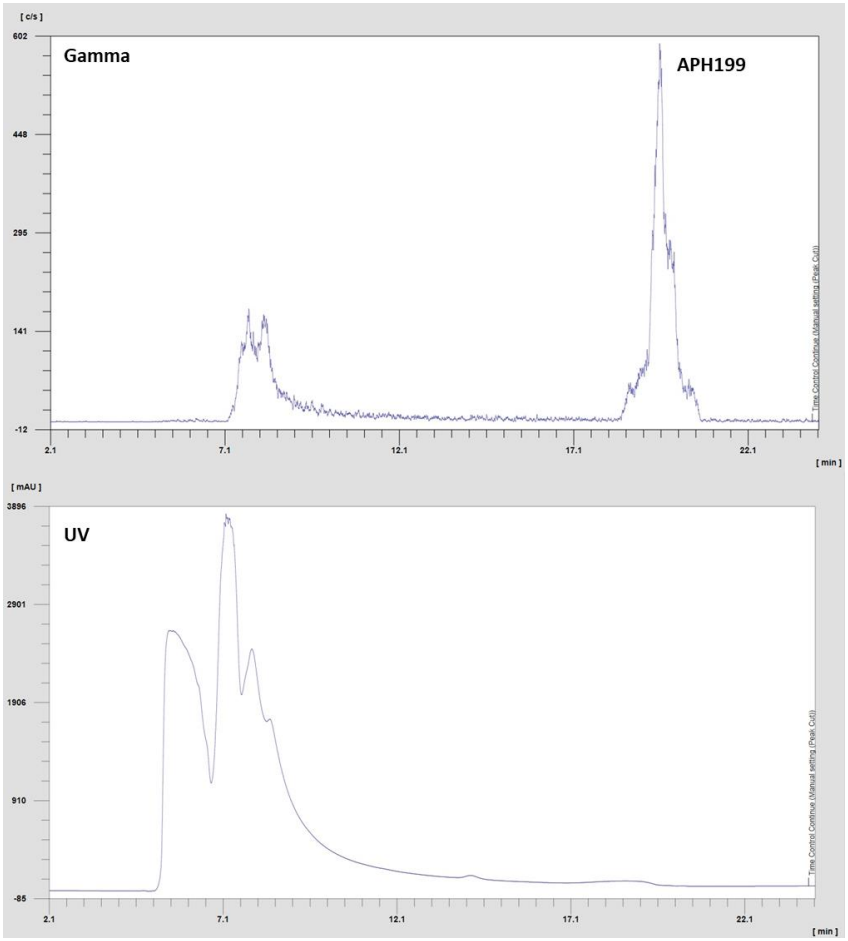
3.2.3. [^{11}C] APH199 ([^{11}C]42)

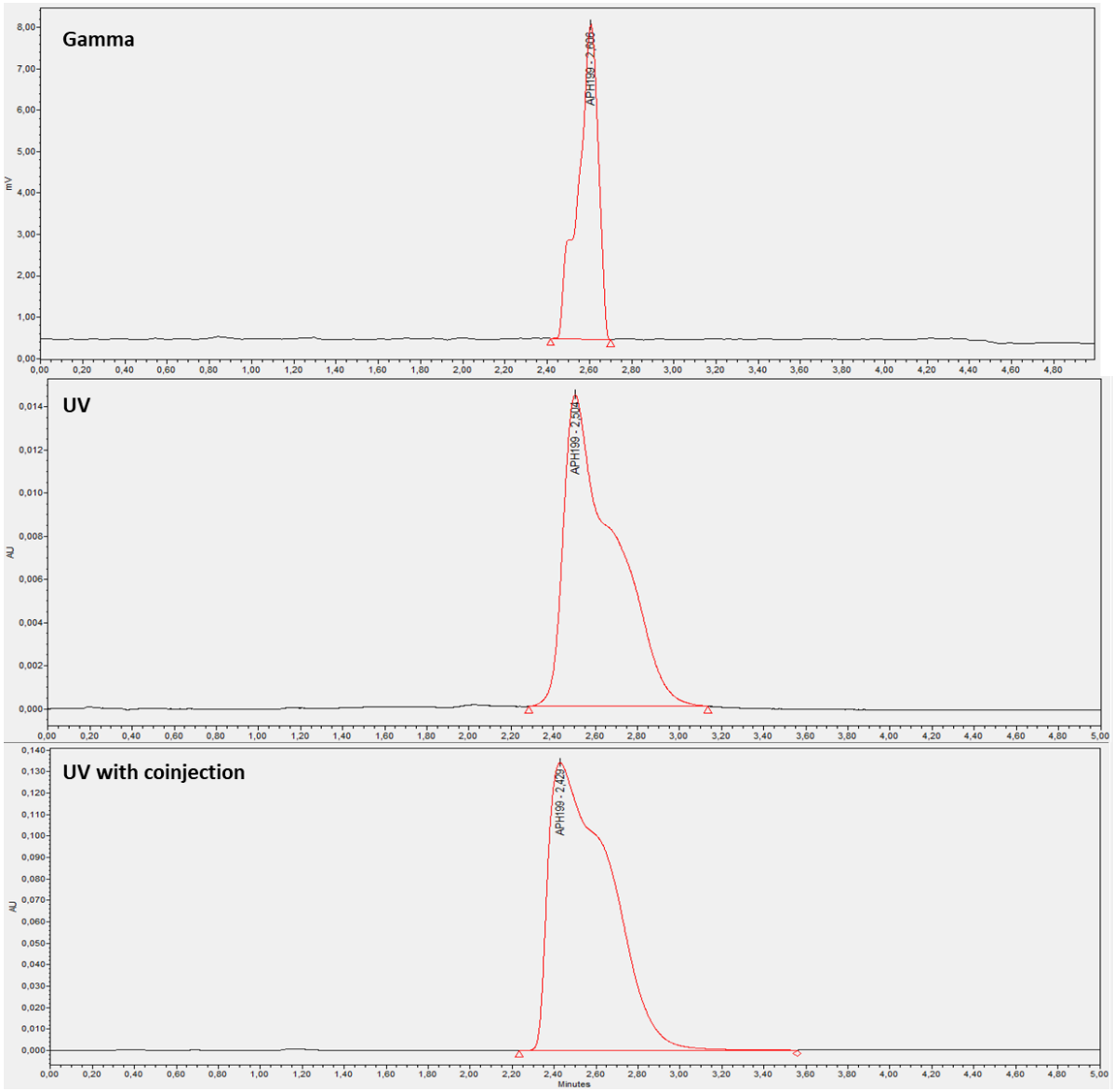
[^{11}C] 2-benzyl-*N*-(3-(4-(2-methoxyphenyl)piperazin-1-yl)propyl)-2-phenylhydrazine-1-carboxamide **([^{11}C]42)**



$C_{27}{}^{11}CH_{35}N_5O_2$
MW: 472.29 g.mol^{-1}
RCY: 31 %

The crude product was synthesized following the general procedure using azide **S37** and *N*-benzyl-*N*-phenylhydrazine as precursors. Purification by semi-preparative HPLC was performed on a reverse phase Symmetry C18 column (250 x 4.6 mm, 5 µm, Waters, USA) using a mixture of H_2O/CH_3CN/TFA (70/30/0.1 v/v/v, 4 mL/min) as eluent with gamma and UV (λ = 245 nm) detection. The collected peak (t_R = 19.0-20.5 min) of [^{11}C]APH199 was diluted with water (20 mL) and loaded on a C18 cartridge (Sep-Pak C18, Waters, USA). The cartridge was rinsed with water (10 mL) and the product was eluted with ethanol (2 mL) and further diluted with aq. 0.9 % NaCl (18 mL). Ready-to-inject [^{11}C]APH199 (0.4 ± 0.1 GBq) was obtained within 45 min from end of beam in 31 ± 4% RCY and 70 ± 8 GBq/µmol molar activity (n = 2). Quality control was performed following the general procedure (H_2O/CH_3CN/PicB7® 65/35/0.2 v/v/v, 2 mL/min, λ = 245 nm).


[c/s]
602
448
295
141
-12
Gamma
APH199
2.1
7.1
12.1
17.1
22.1
[min]
[mAU]
3896
2901
1906
910
-85
UV
2.1
7.1
12.1
17.1
22.1
[min]

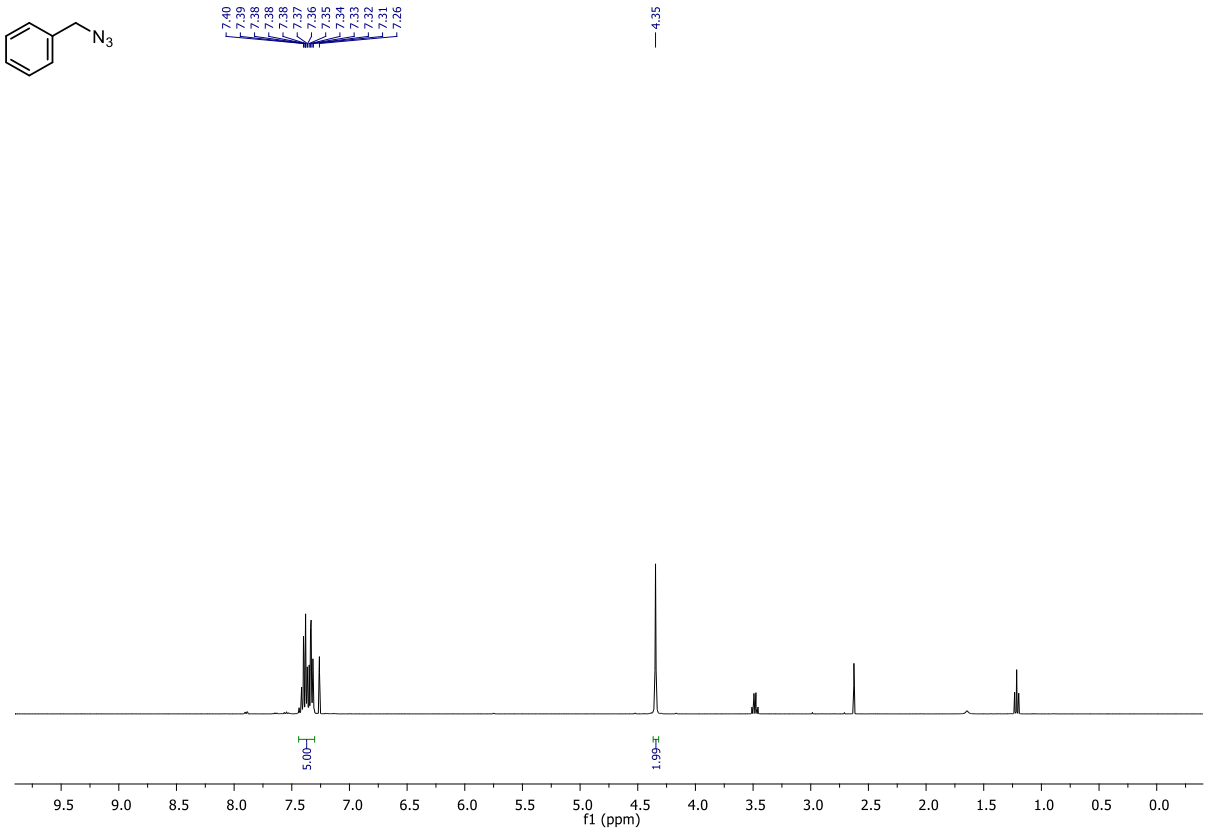

Gamma
APH199 - 2,608
mV
UV
APH199 - 2,504
AU
UV with coinjection
APH199 - 2,429
AU
Minutes

4. NMR Spectra

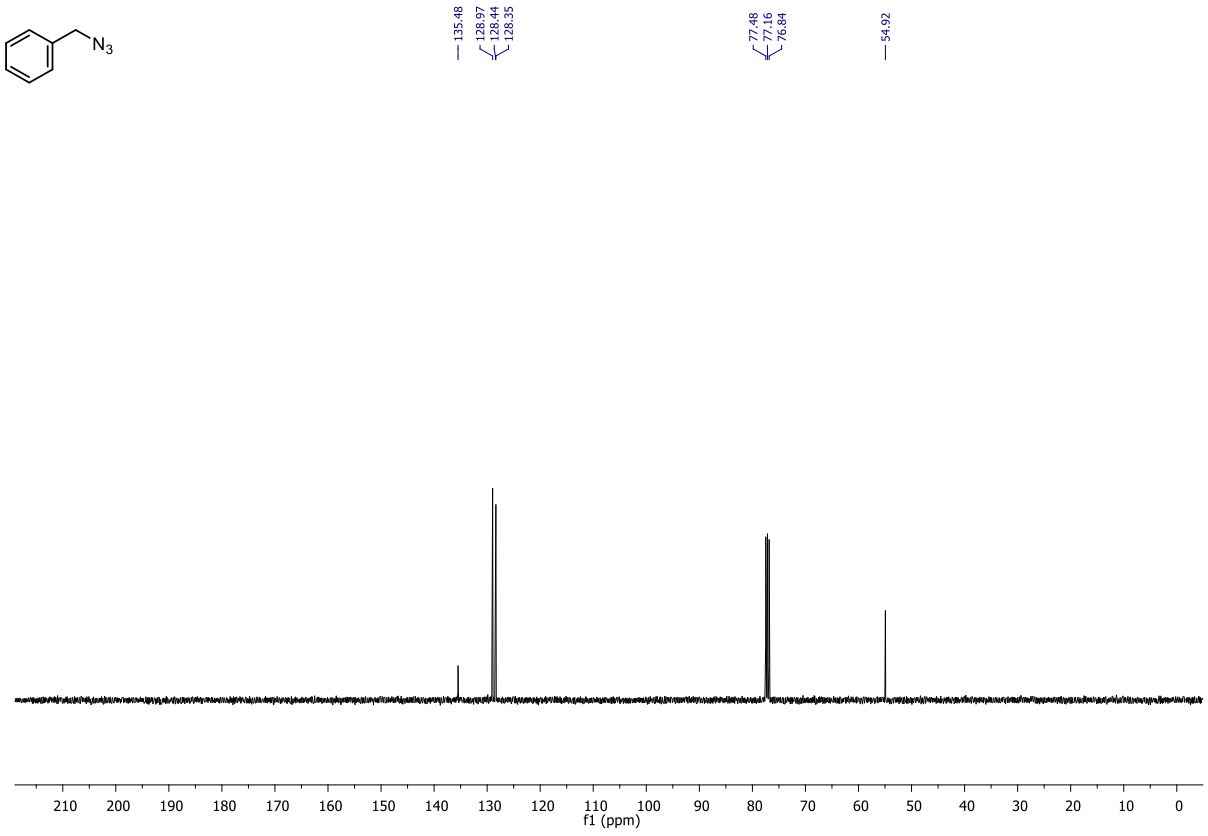
Note: Due to low boiling point of some of the described azides, solvent residual peaks from the reaction medium or the following treatment could appear in ^{1}H NMR spectra.
Thus, according to the literature,[29] contaminations by the following solvent could be observed:

- Diethyl ether in $CDCl_3$: δ = 3.48 (q), 1.21 (t)
- DMSO in $CDCl_3$: δ = 2.62 (s)
- H_2O in $CDCl_3$: δ = 1.56 (s)
- Acetonitrile: δ = 2.10 (s)

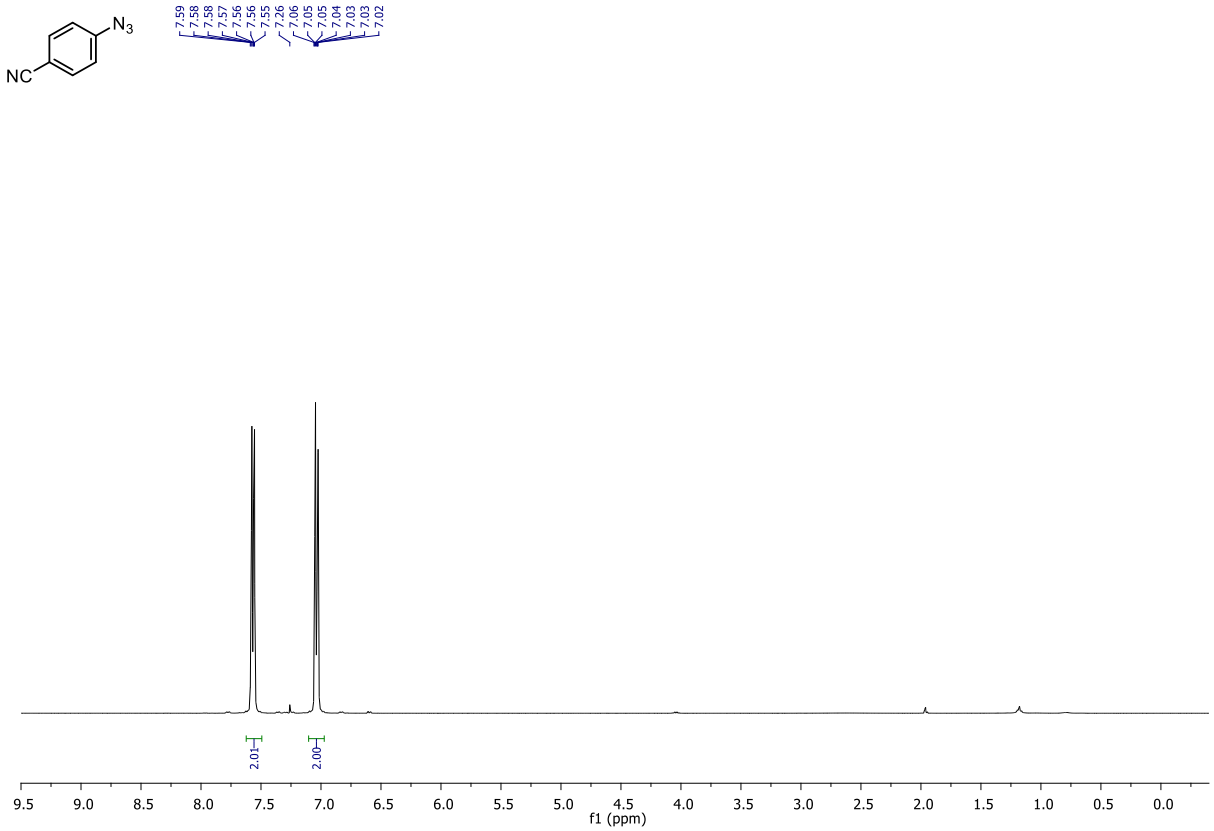
^{1}H NMR (400 MHz, $CDCl_3$) **S1**:



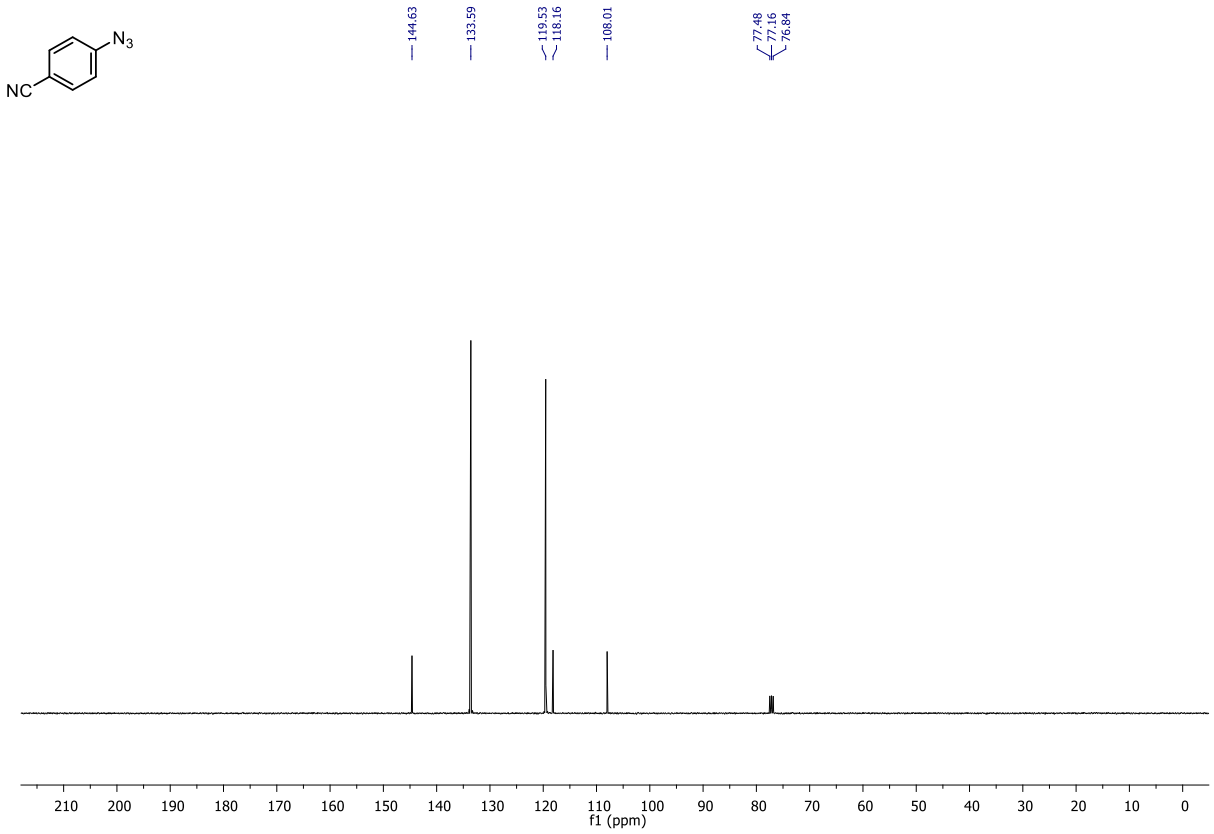
^{13}C NMR (100 MHz, $CDCl_3$) **S1**:



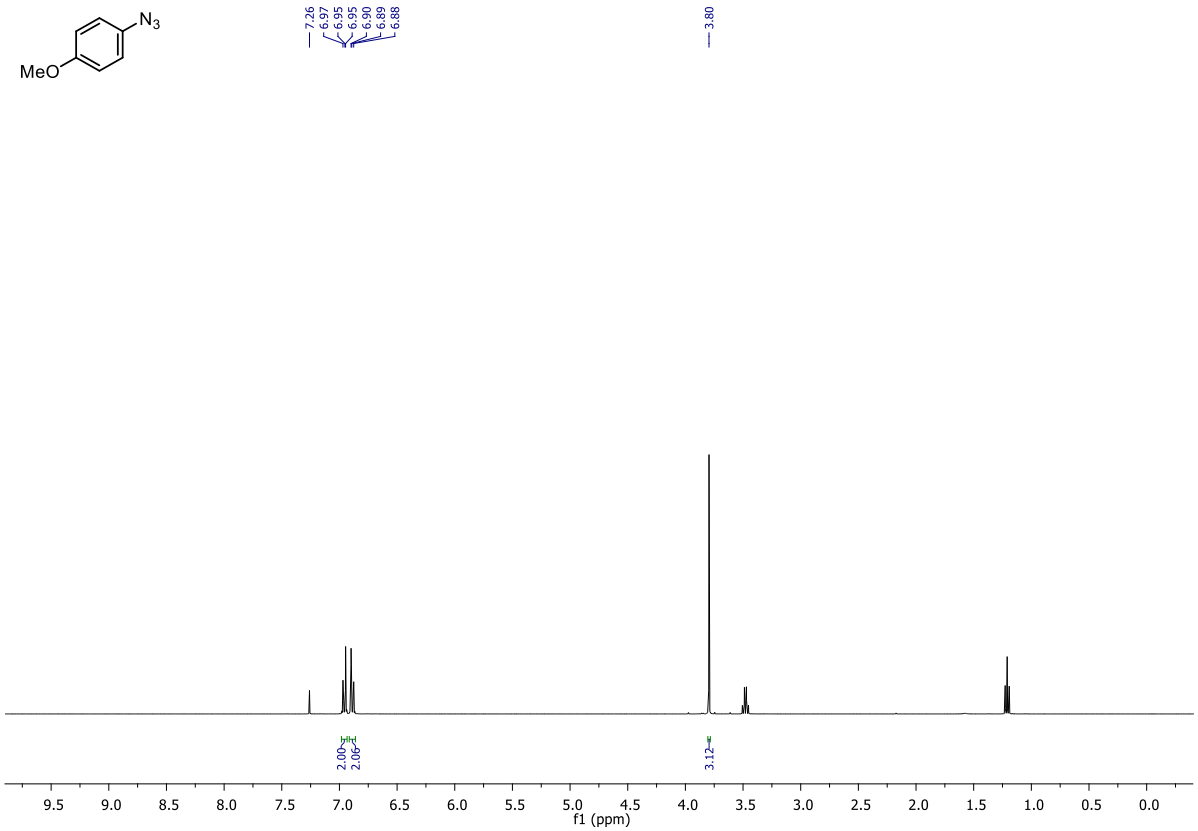
^{1}H NMR (400 MHz, $CDCl_3$) **S2**:



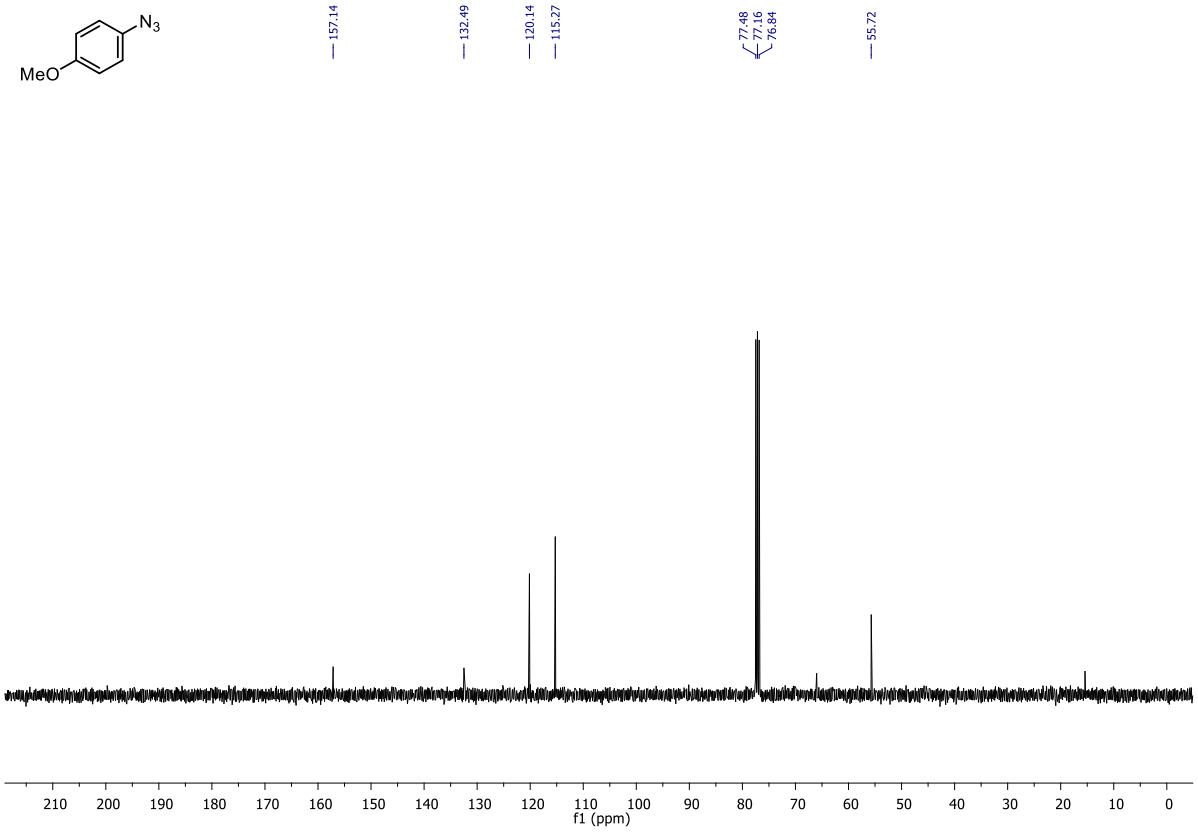
^{13}C NMR (100 MHz, $CDCl_3$) **S2**:



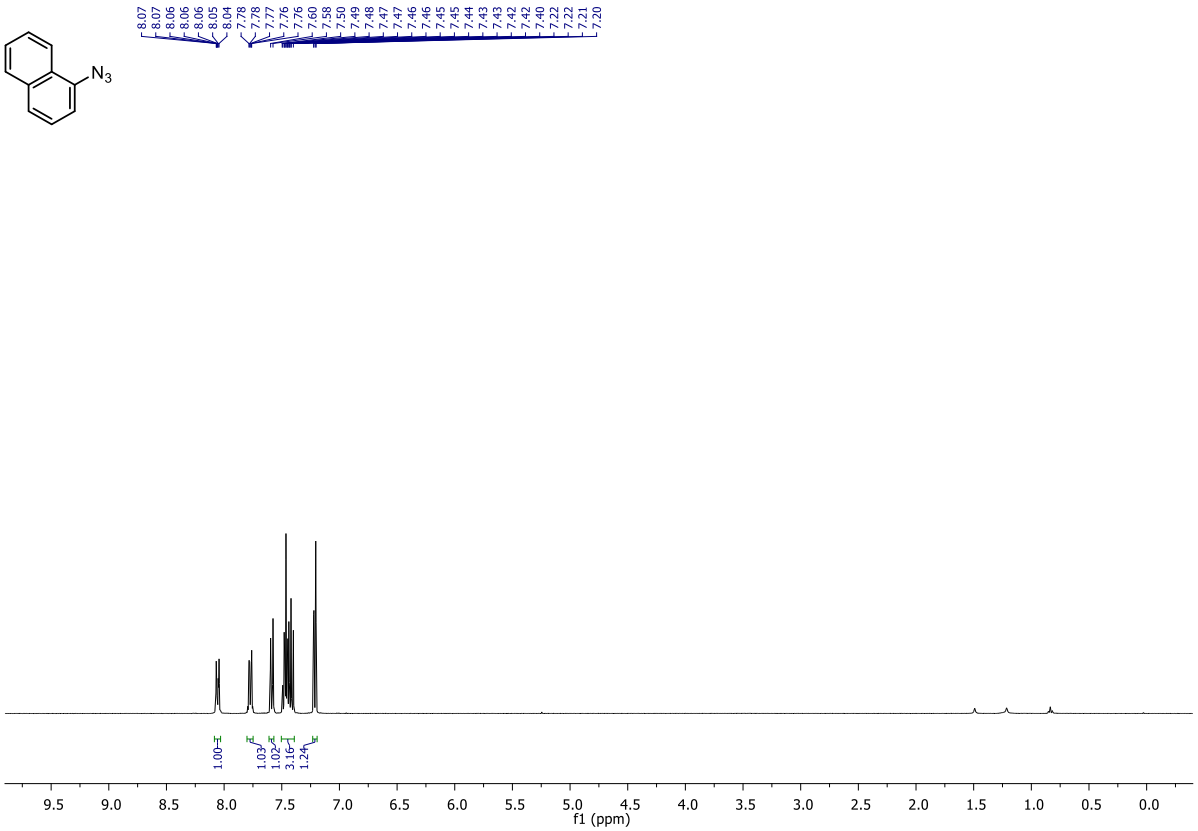
^{1}H NMR (400 MHz, $CDCl_3$) **S3**:



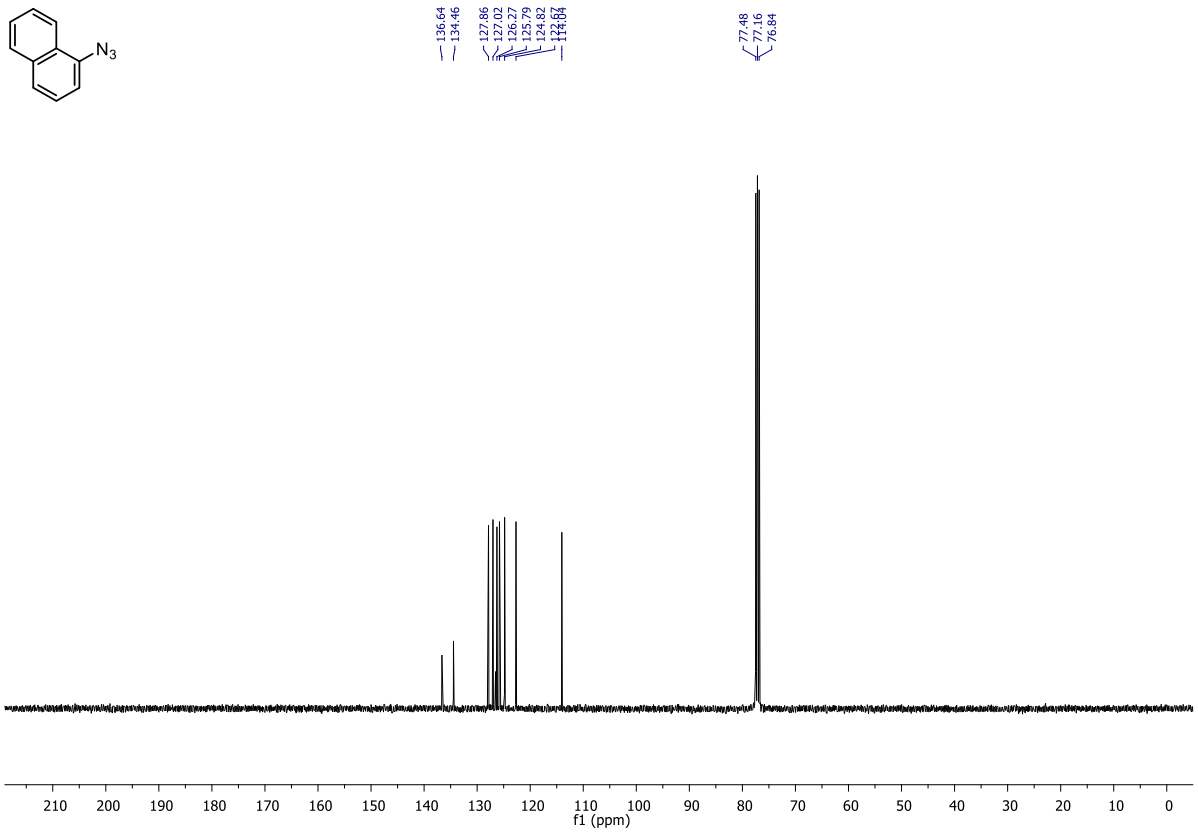
^{13}C NMR (100 MHz, $CDCl_3$) **S3**:



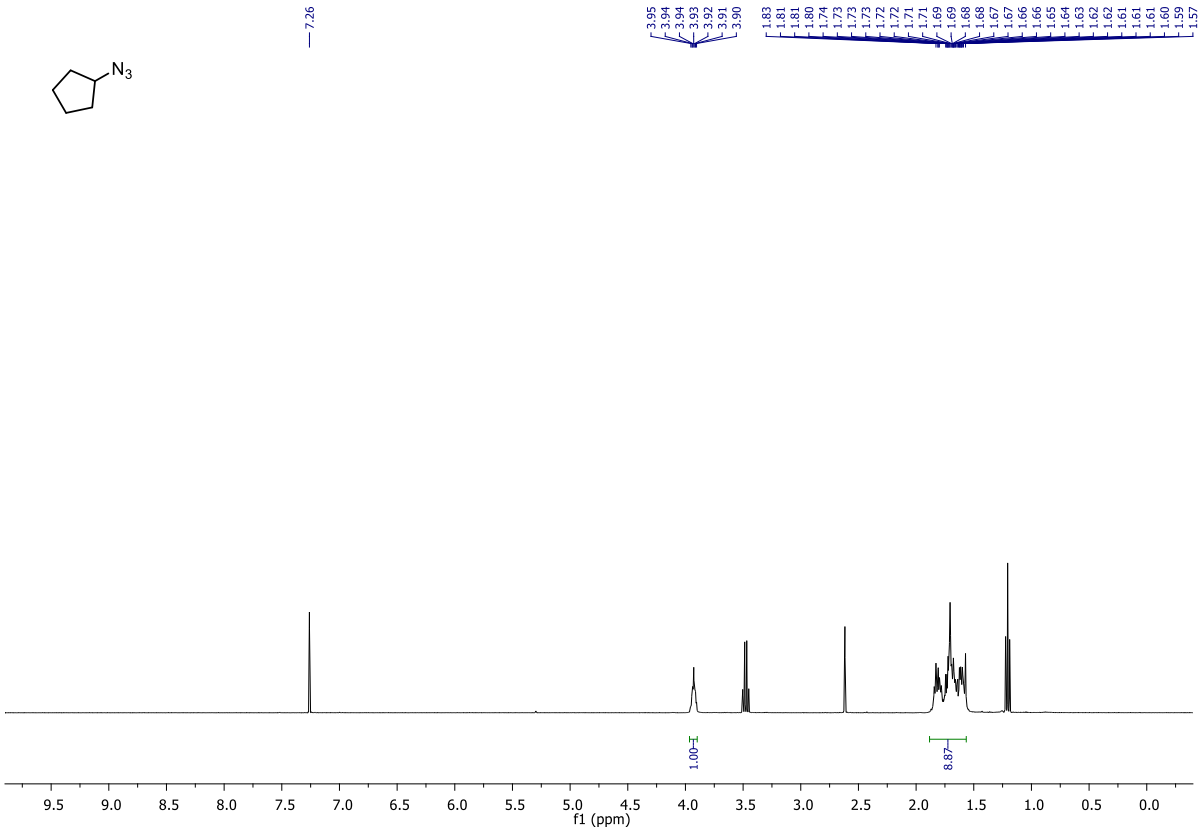
^{1}H NMR (400 MHz, $CDCl_3$) **S4**:



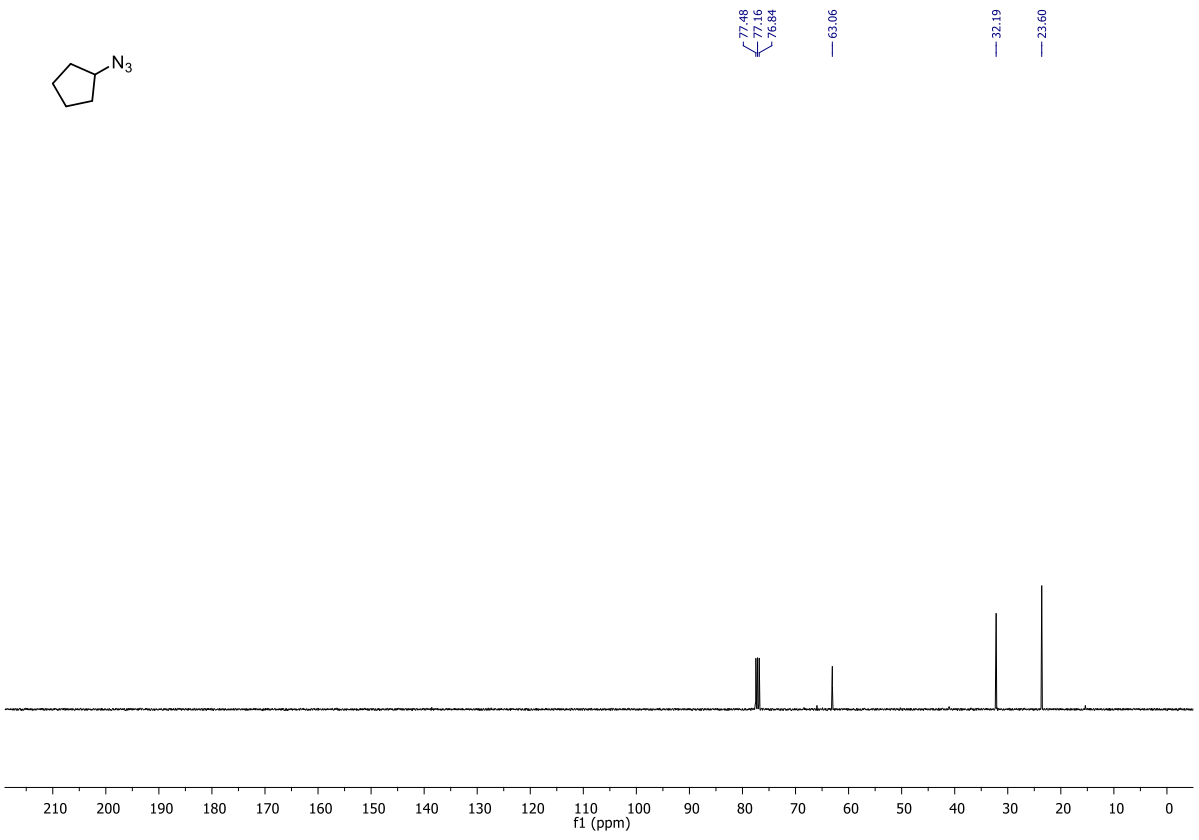
^{13}C NMR (100 MHz, $CDCl_3$) **S4**:



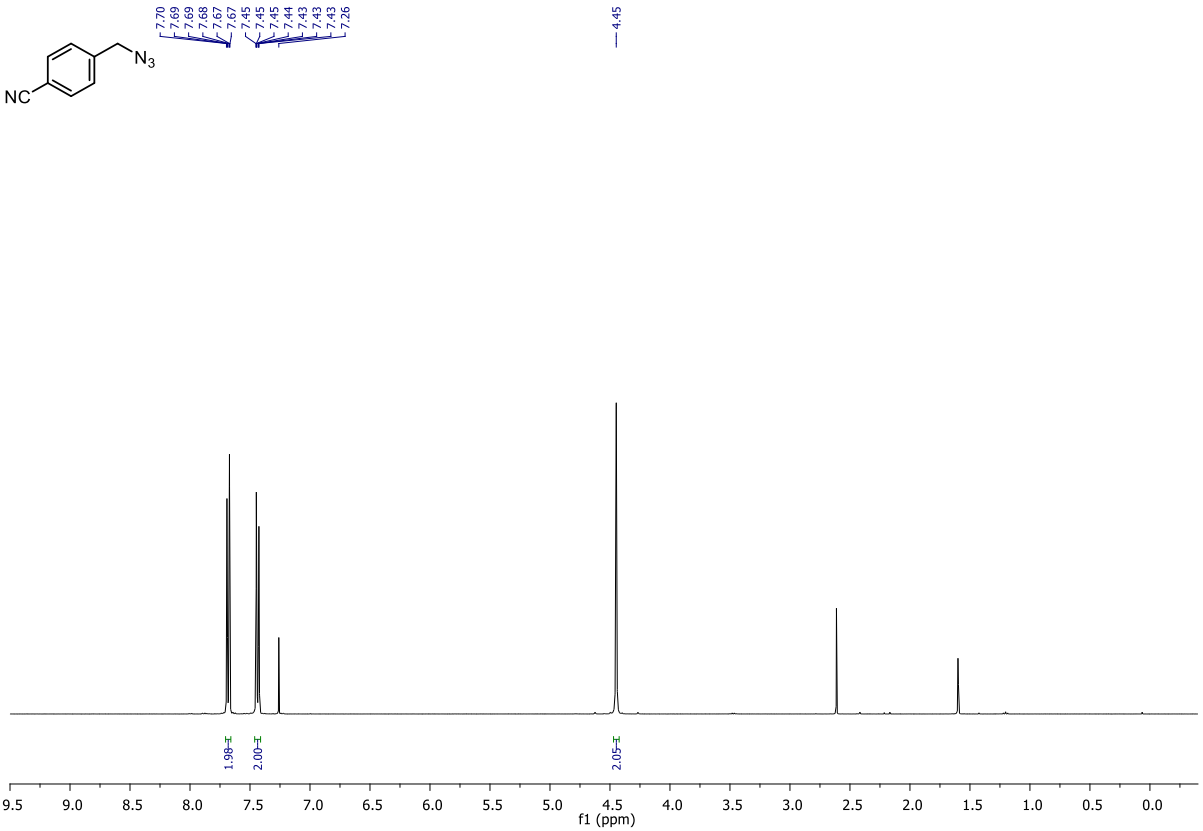
^{1}H NMR (400 MHz, $CDCl_3$) **S5**:



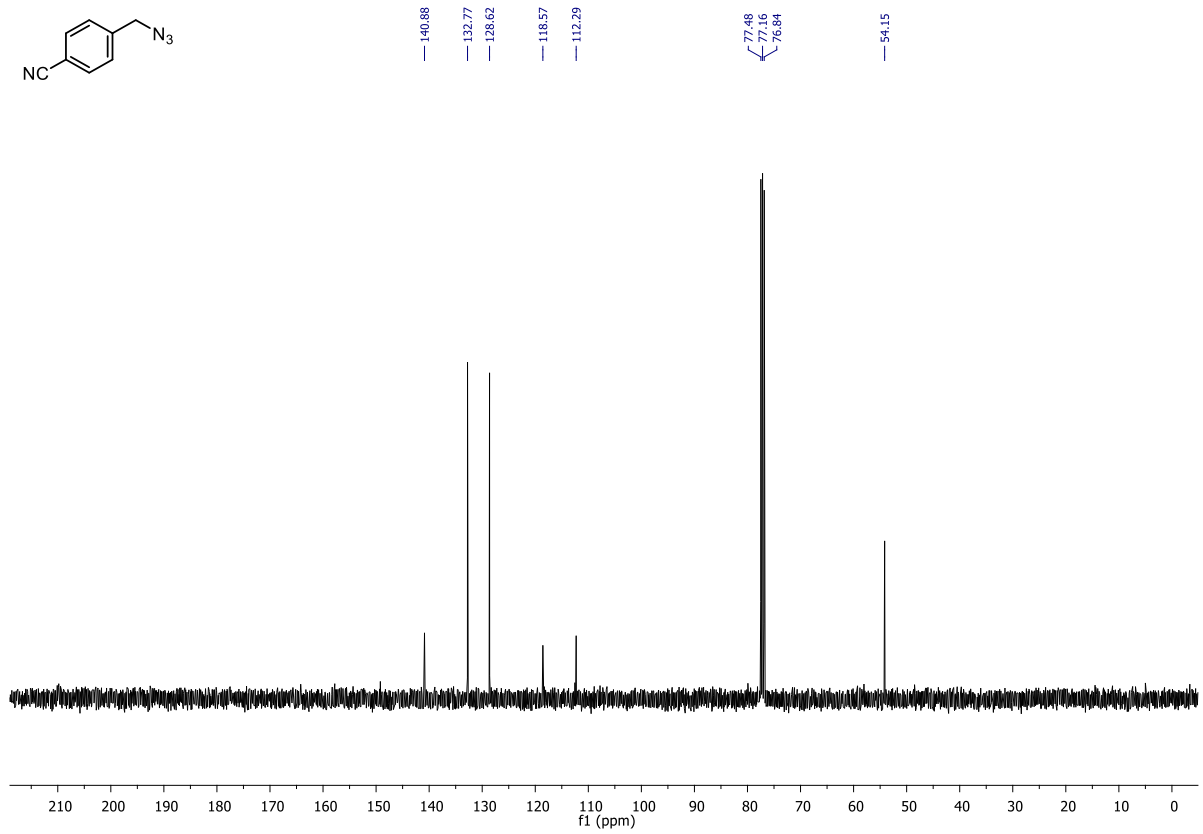
^{13}C NMR (100 MHz, $CDCl_3$) **S5**:



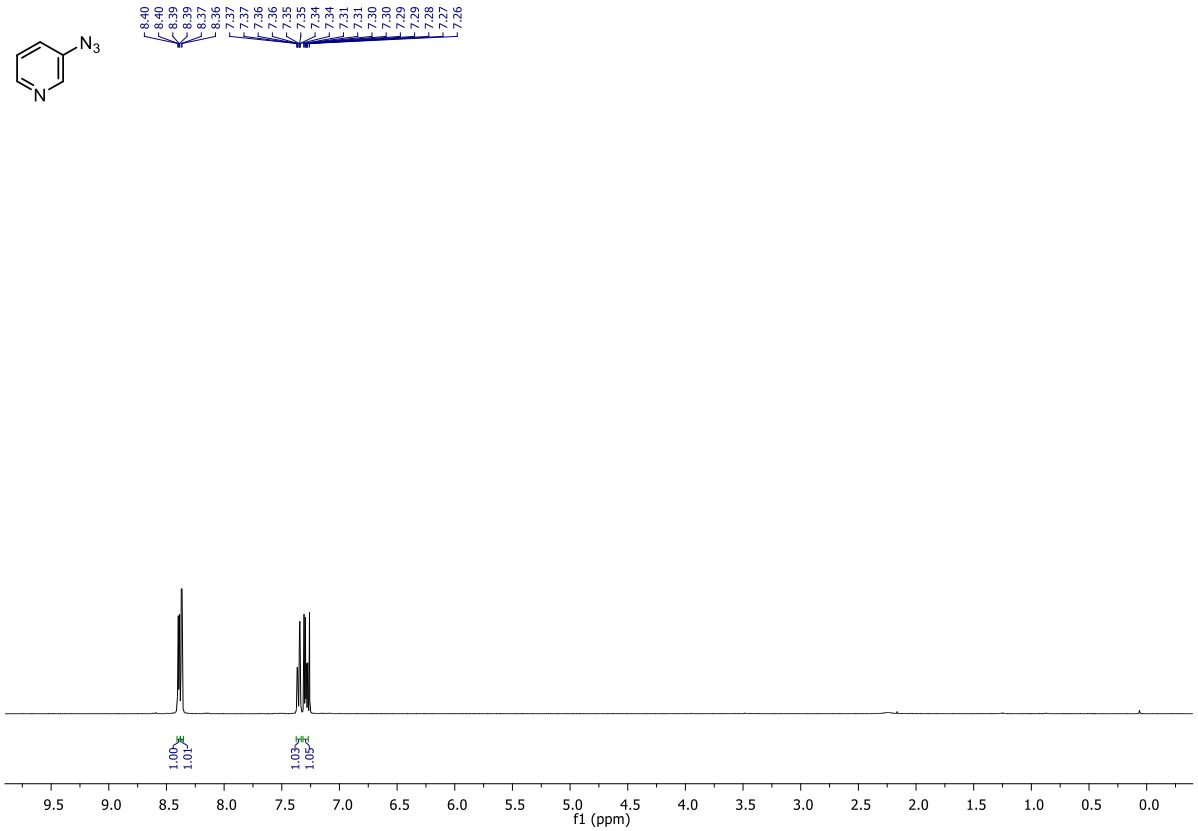
^{1}H NMR (400 MHz, $CDCl_3$) **S6**:



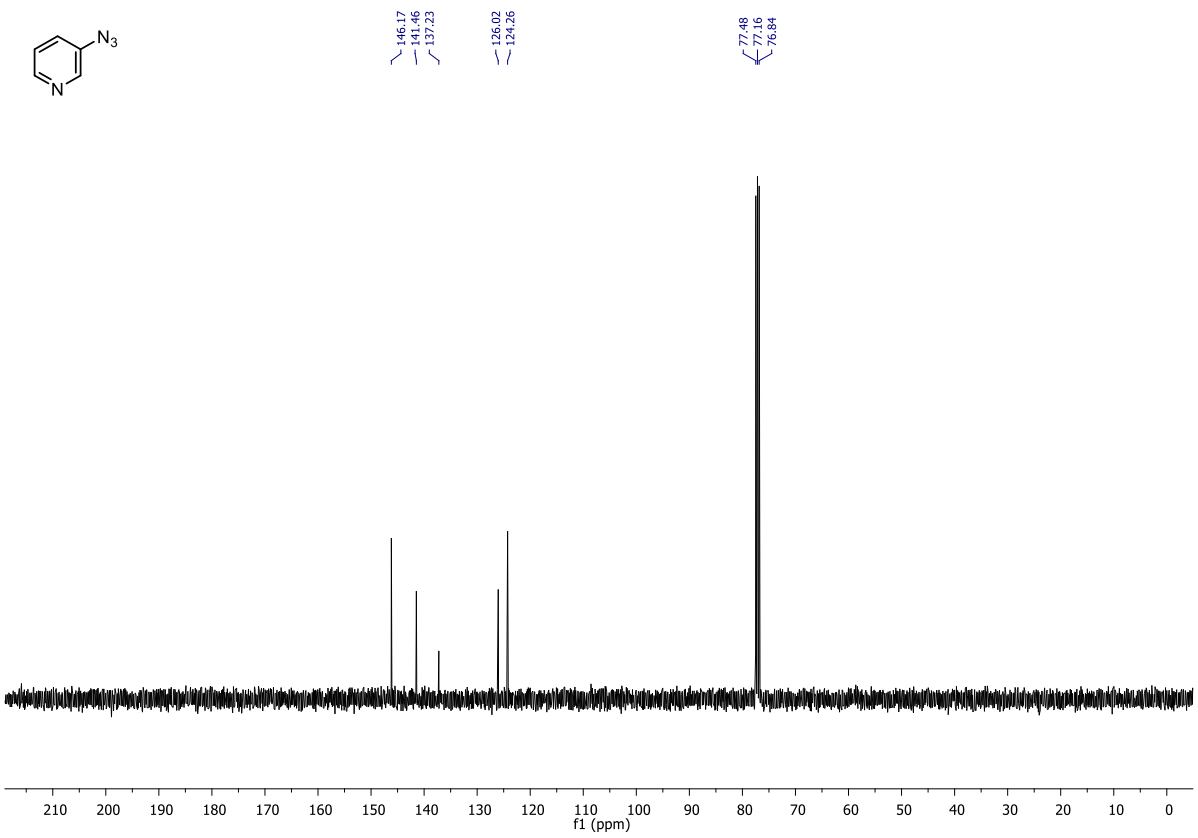
^{13}C NMR (100 MHz, $CDCl_3$) **S6**:



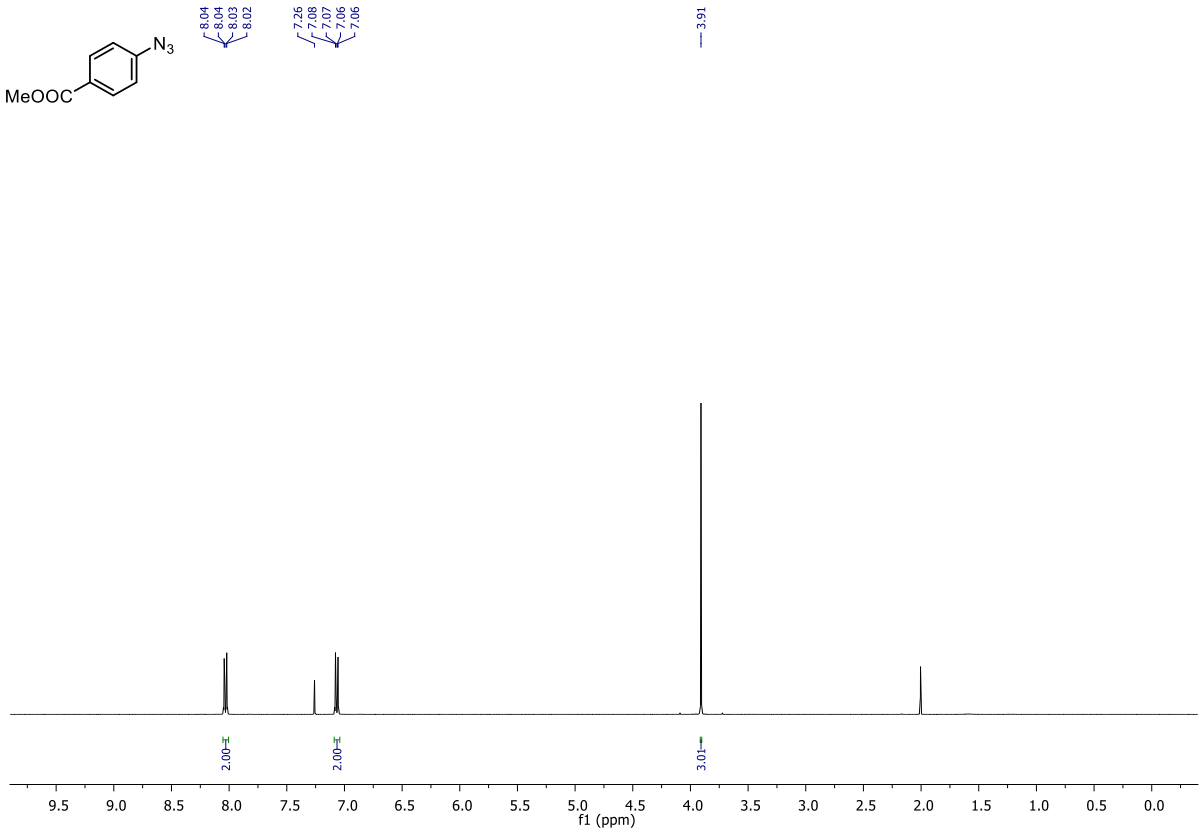
^{1}H NMR (400 MHz, $CDCl_3$) **S7**:



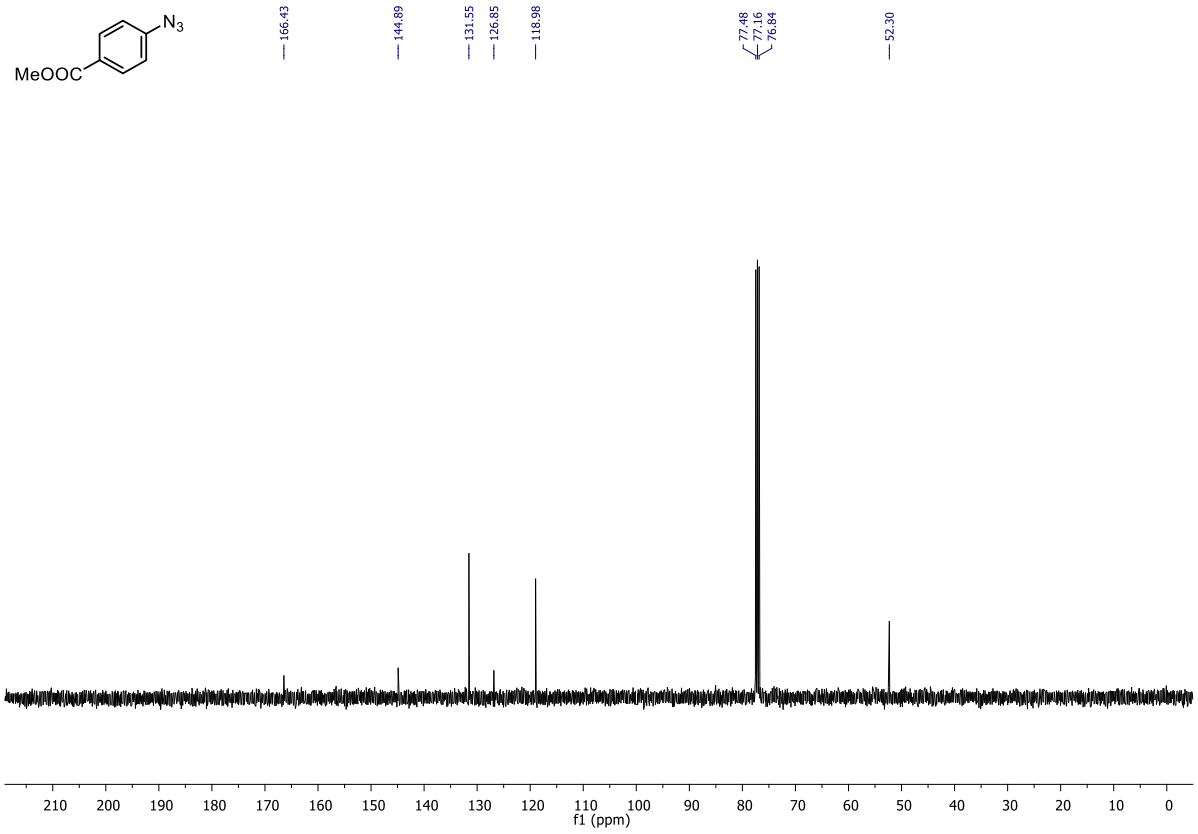
^{13}C NMR (100 MHz, $CDCl_3$) **S7**:



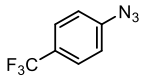
^{1}H NMR (400 MHz, $CDCl_3$) **S8**:

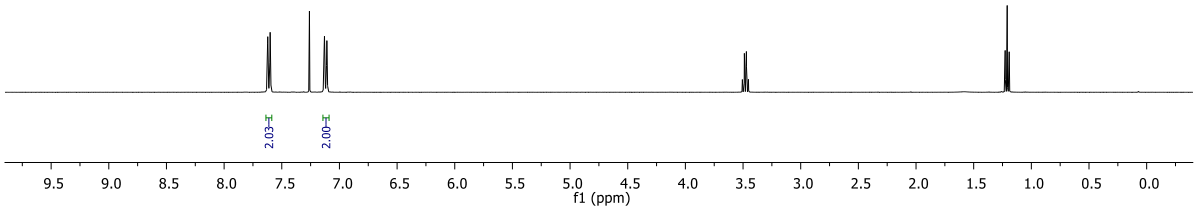


^{13}C NMR (100 MHz, $CDCl_3$) **S8**:

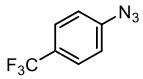


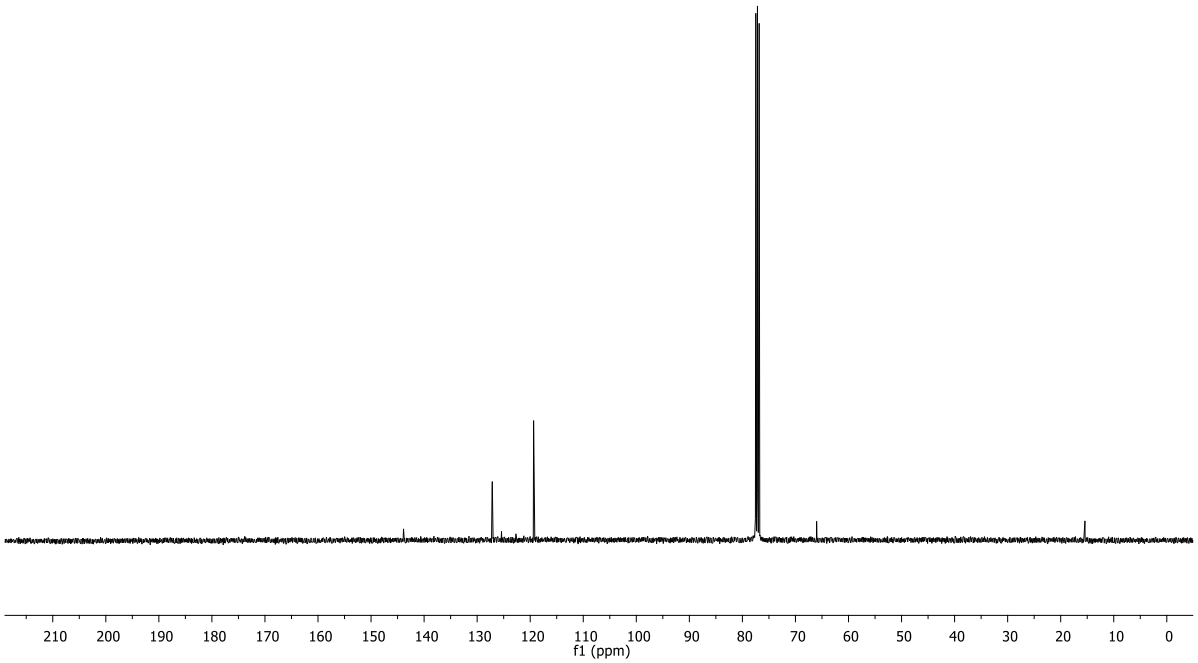
^{1}H NMR (400 MHz, $CDCl_3$) **S9**:



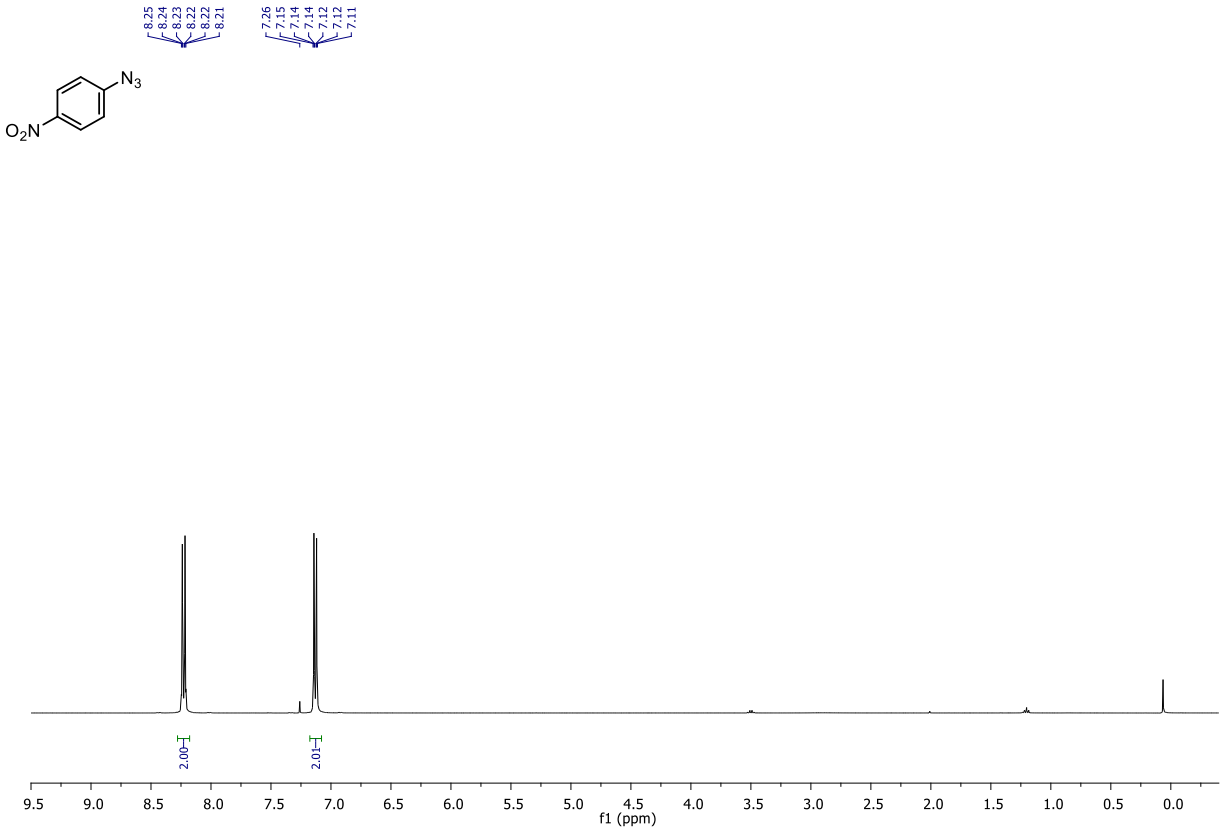


^{13}C NMR (100 MHz, $CDCl_3$) **S9**:

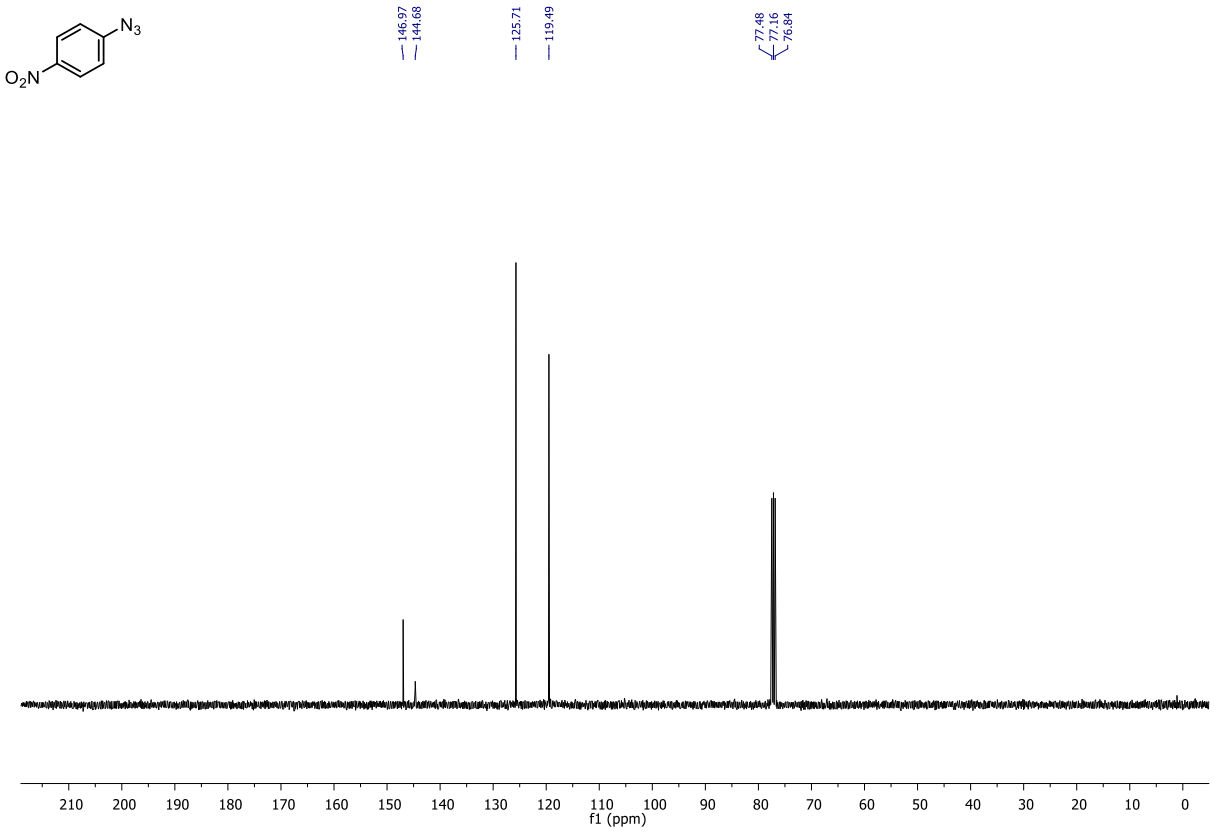




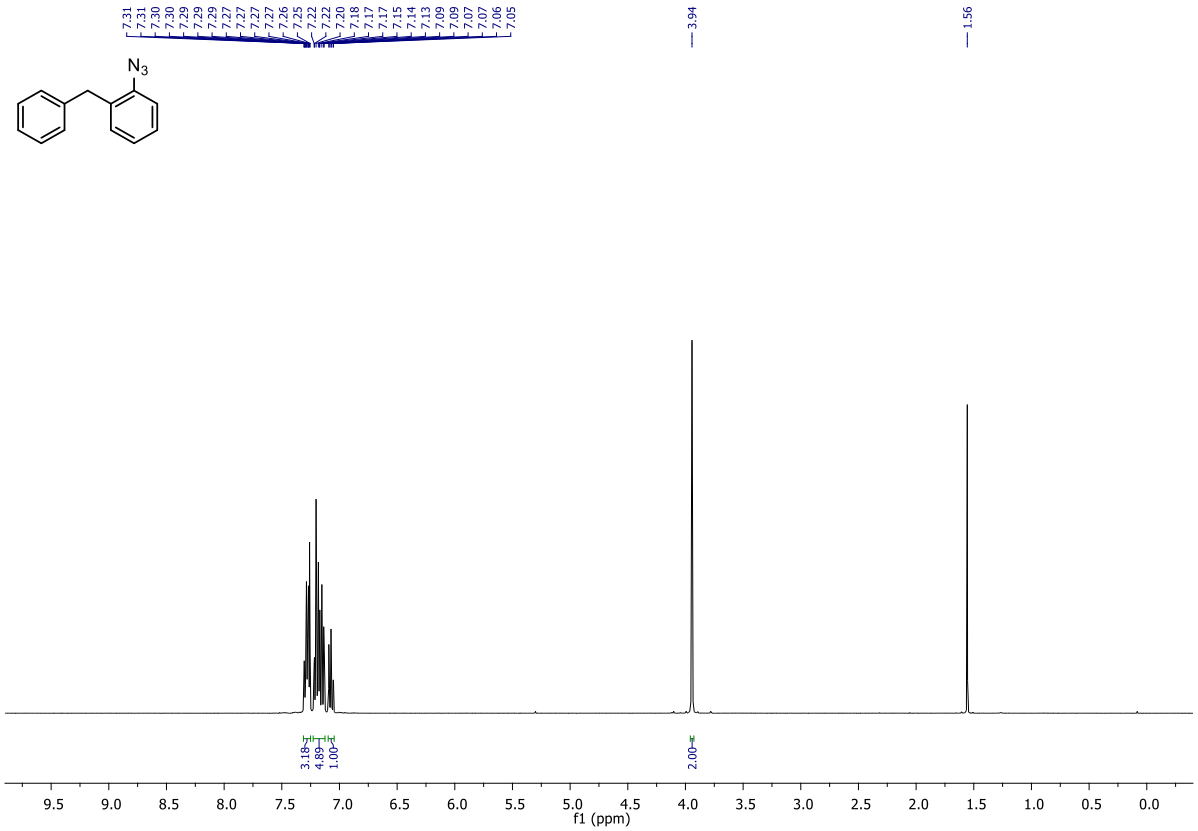
^{1}H NMR (400 MHz, $CDCl_3$) **S10**:



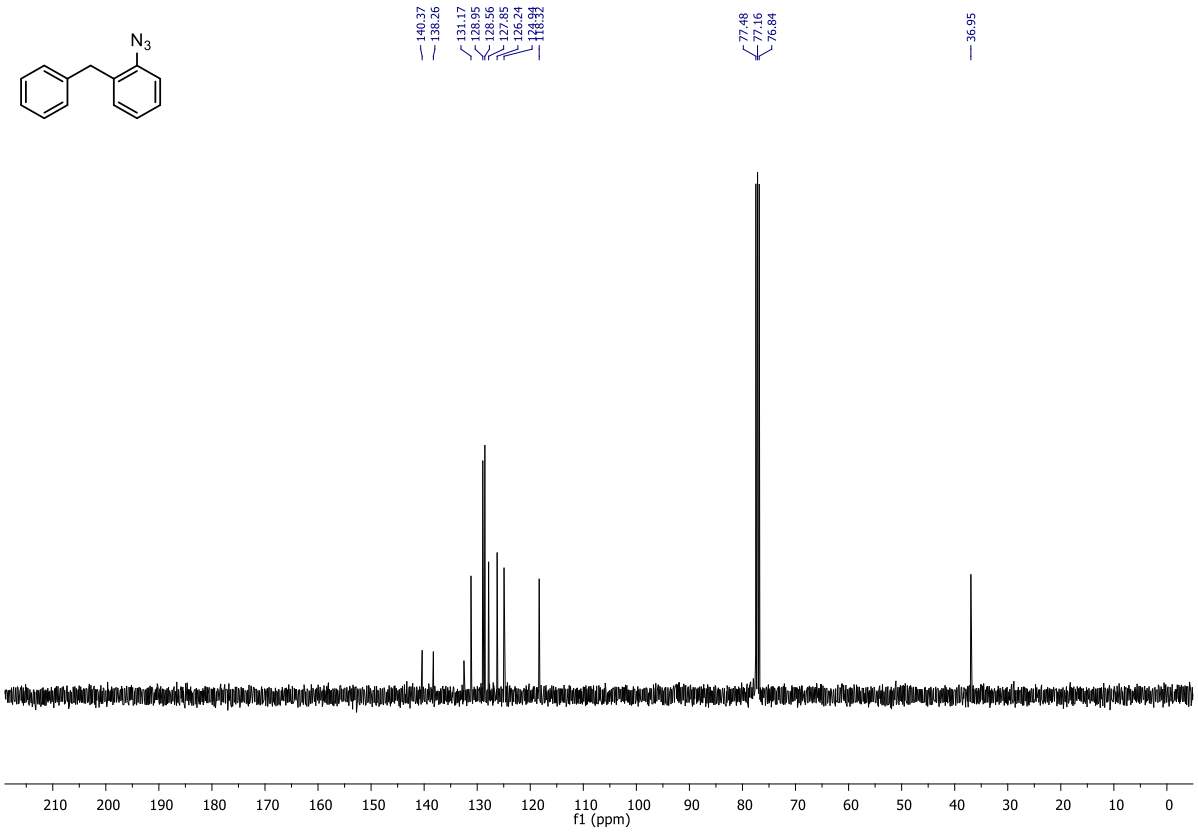
^{13}C NMR (100 MHz, $CDCl_3$) **S10**:



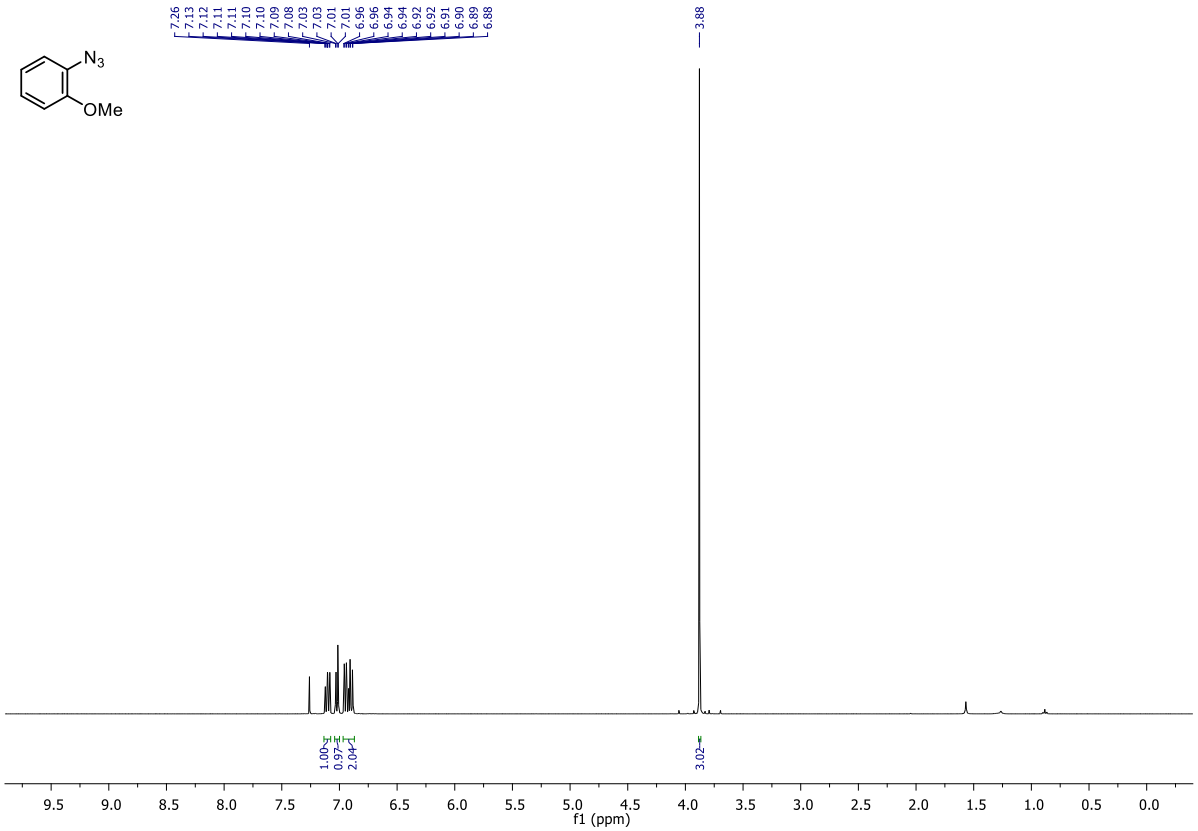
^{1}H NMR (400 MHz, $CDCl_3$) **S11**:



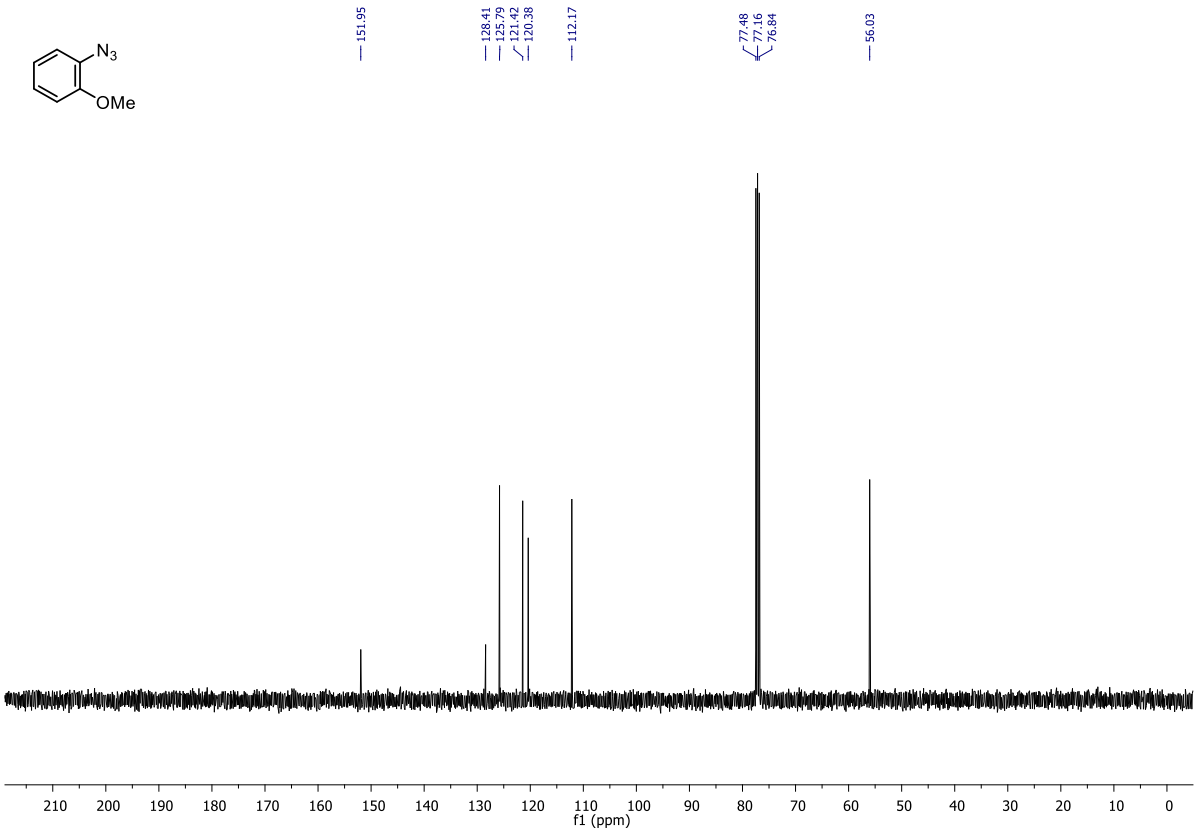
^{13}C NMR (100 MHz, $CDCl_3$) **S11**:



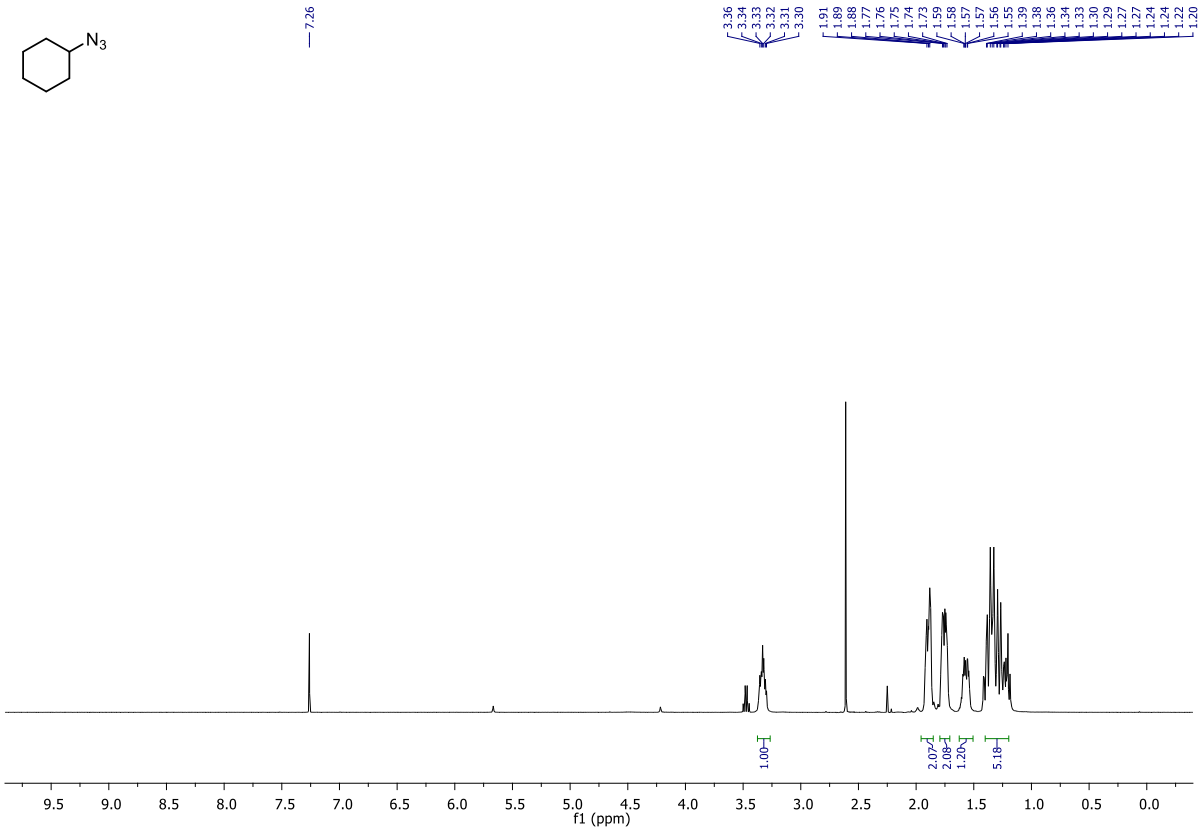
^{1}H NMR (400 MHz, $CDCl_3$) **S12**:



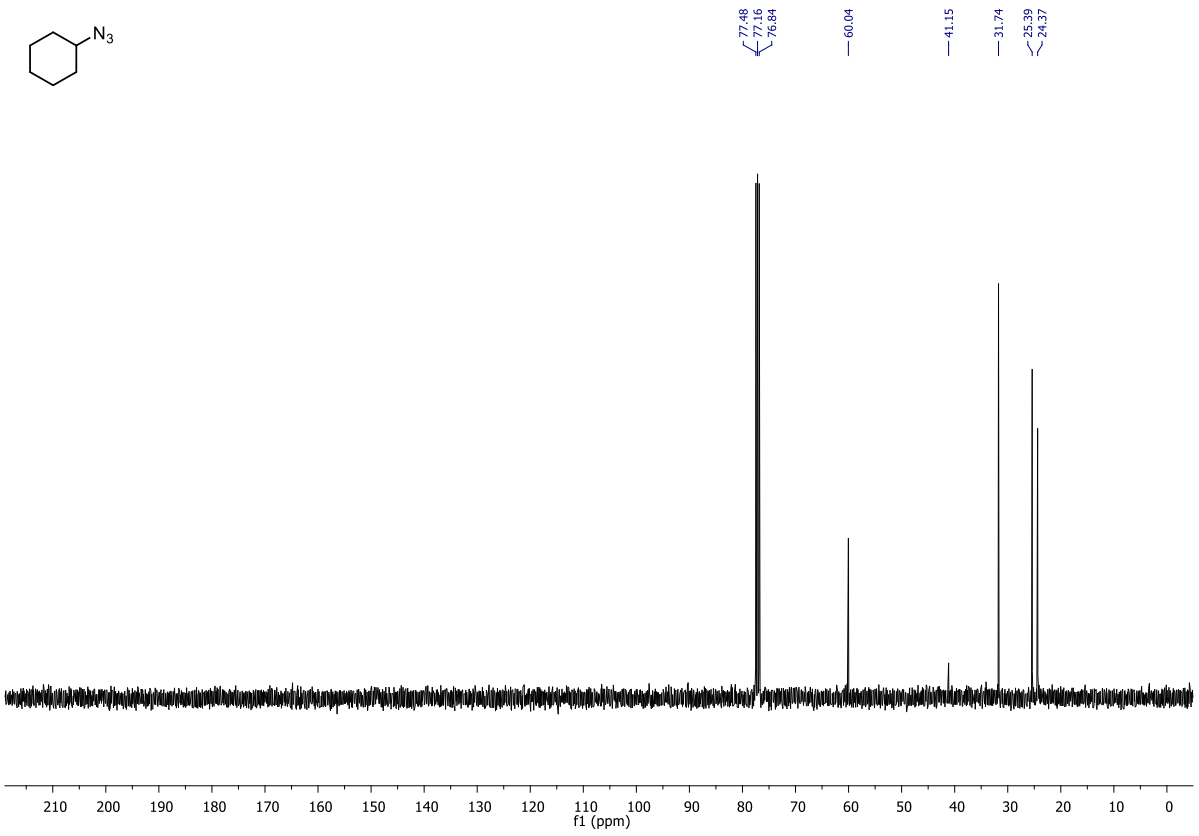
^{13}C NMR (100 MHz, $CDCl_3$) **S12**:



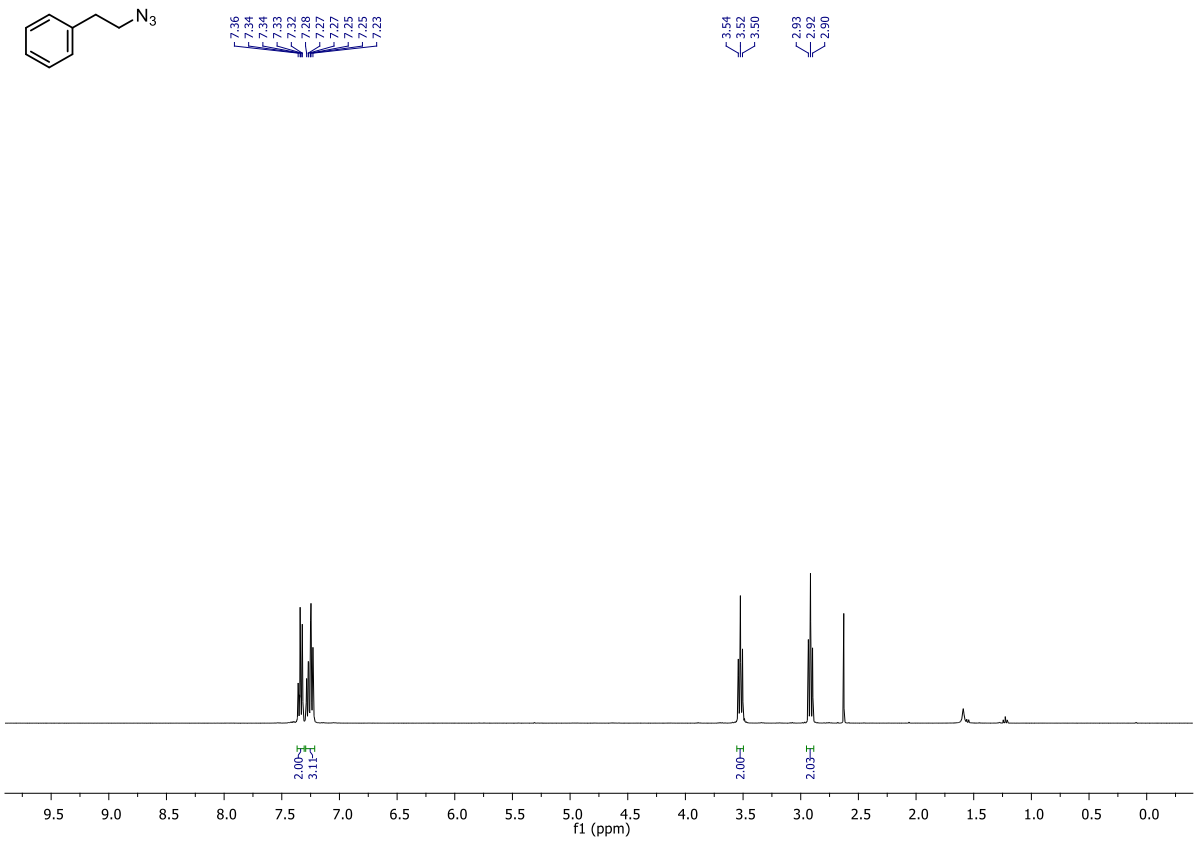
^{1}H NMR (400 MHz, $CDCl_3$) **S13**:



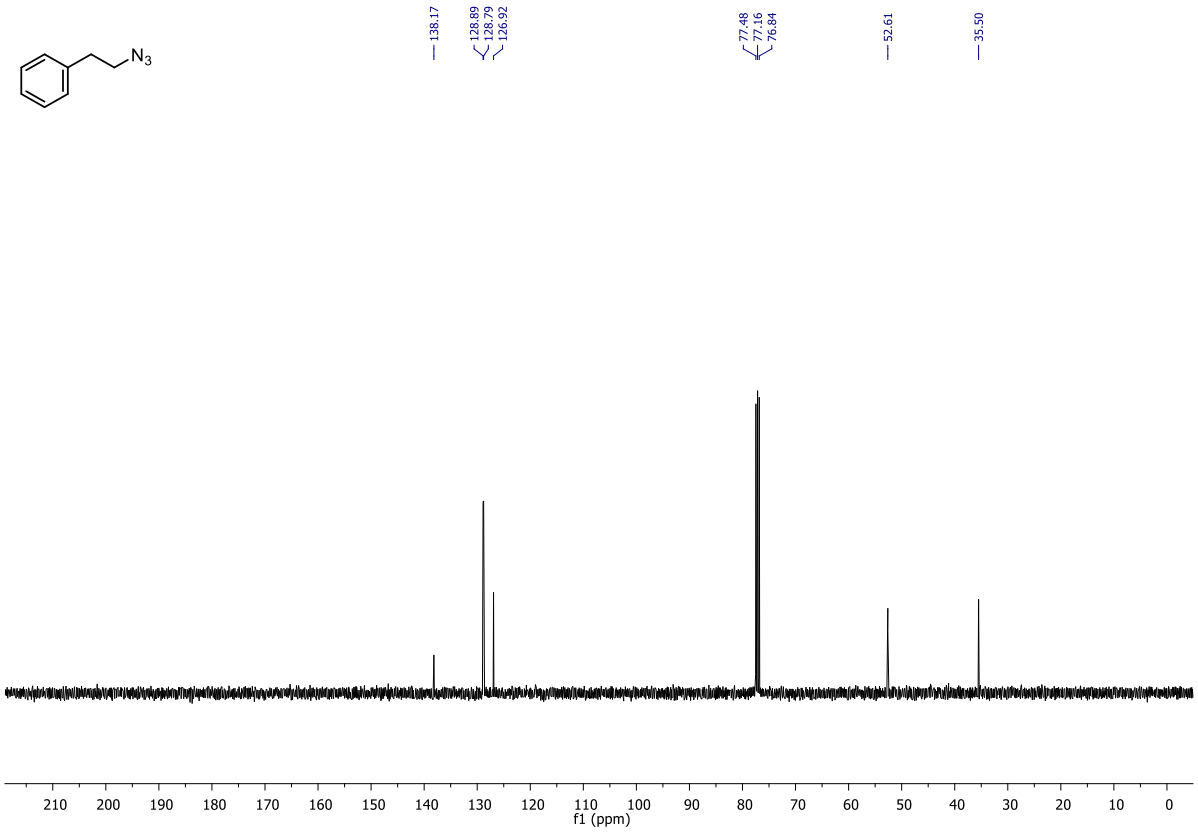
^{13}C NMR (100 MHz, $CDCl_3$) **S13**:



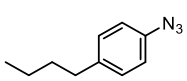
^{1}H NMR (400 MHz, $CDCl_3$) **S14**:

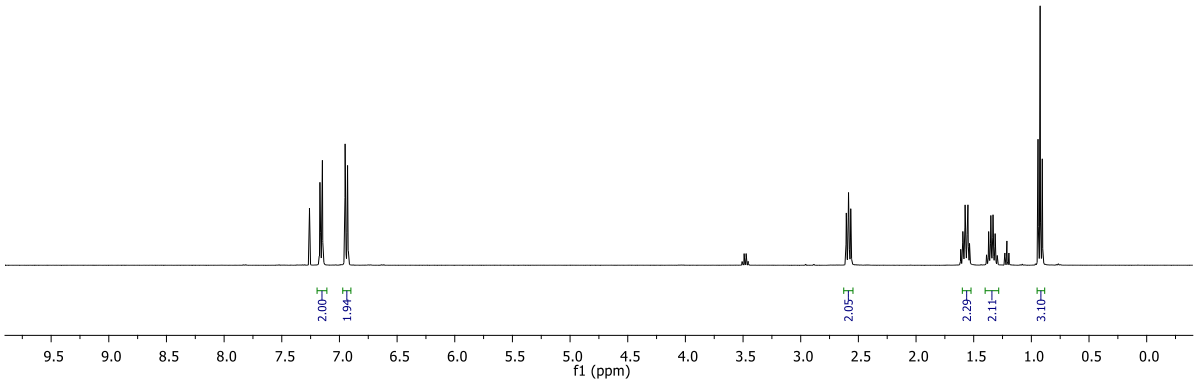


^{13}C NMR (100 MHz, $CDCl_3$) **S14**:

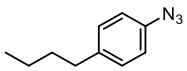


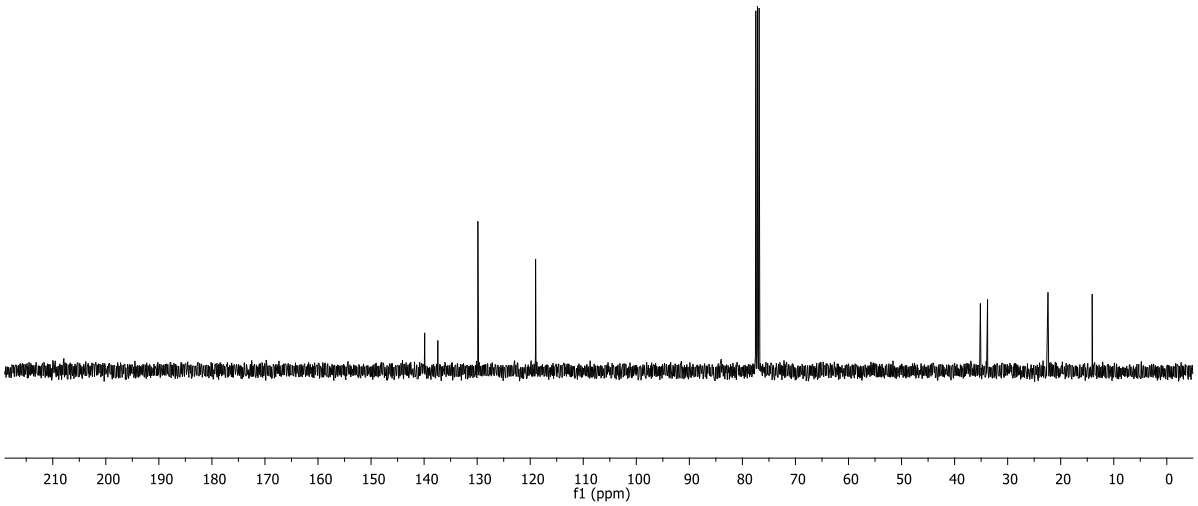
^{1}H NMR (400 MHz, $CDCl_3$) **S15**:



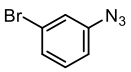


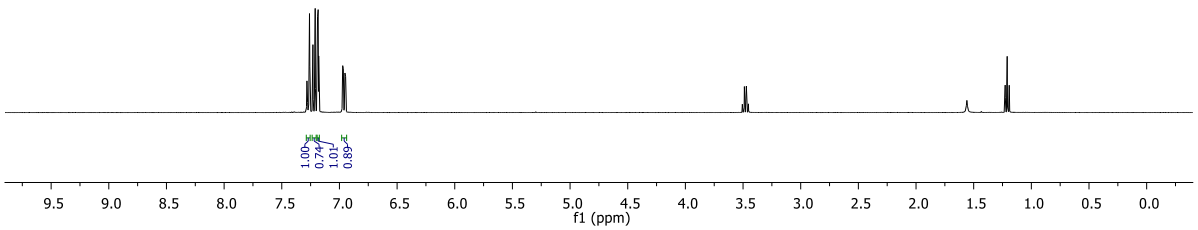
^{13}C NMR (100 MHz, $CDCl_3$) **S15**:



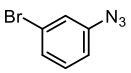


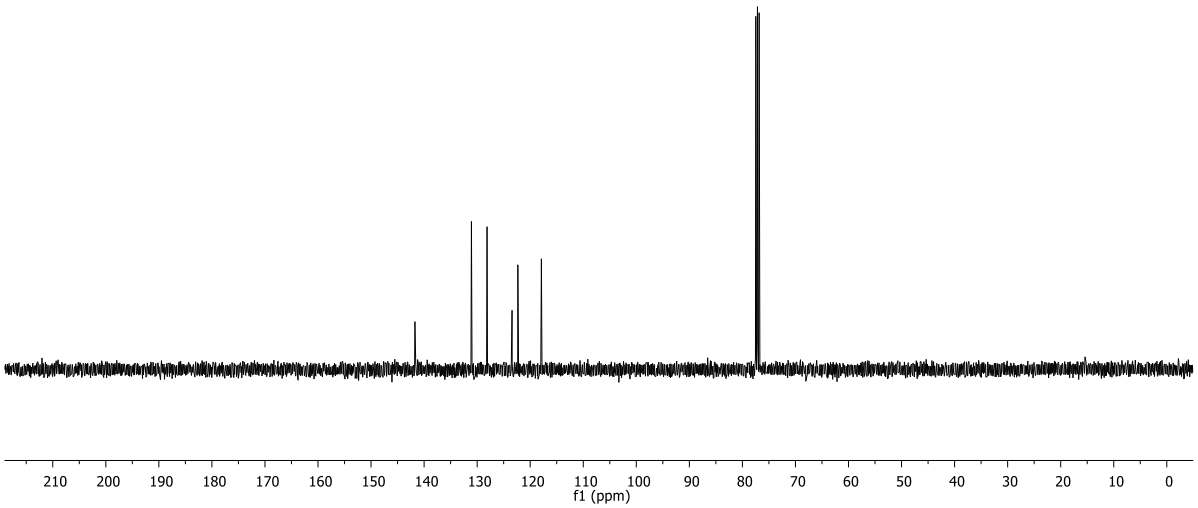
^{1}H NMR (400 MHz, $CDCl_3$) **S16**:



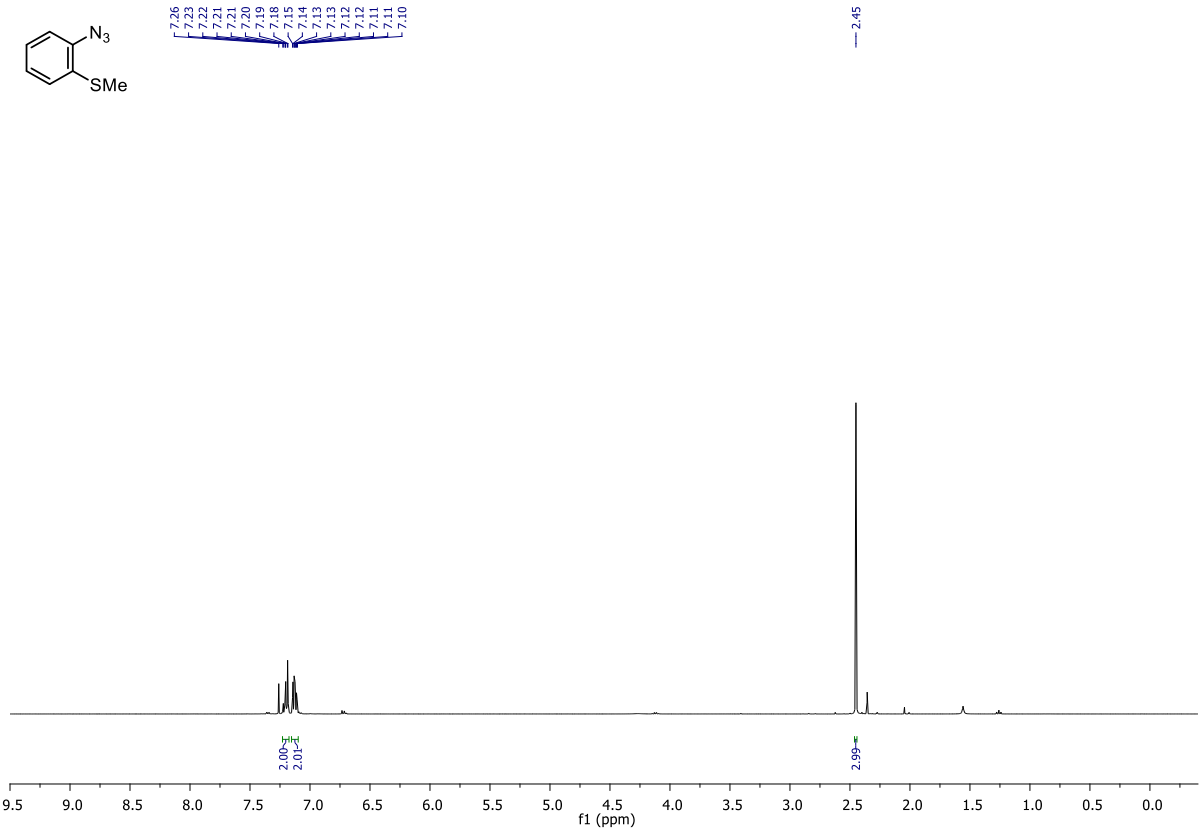


^{13}C NMR (100 MHz, $CDCl_3$) **S16**:

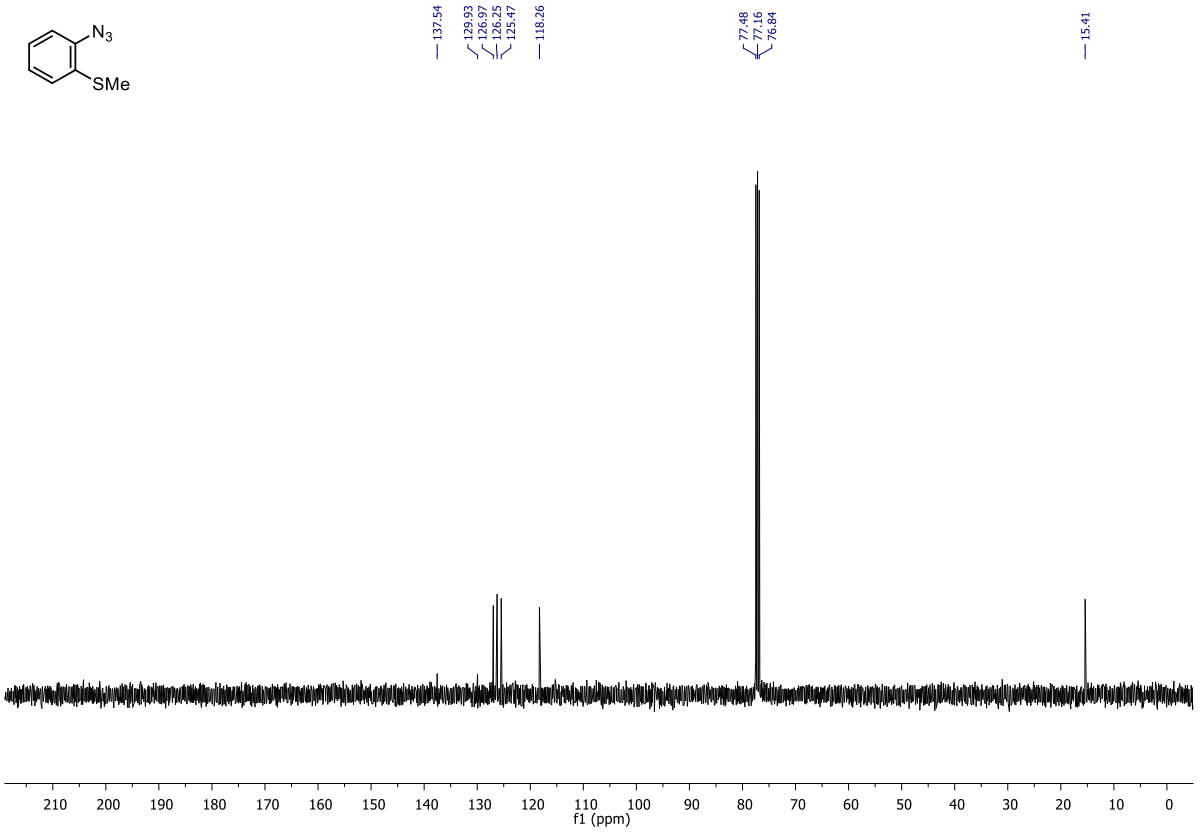




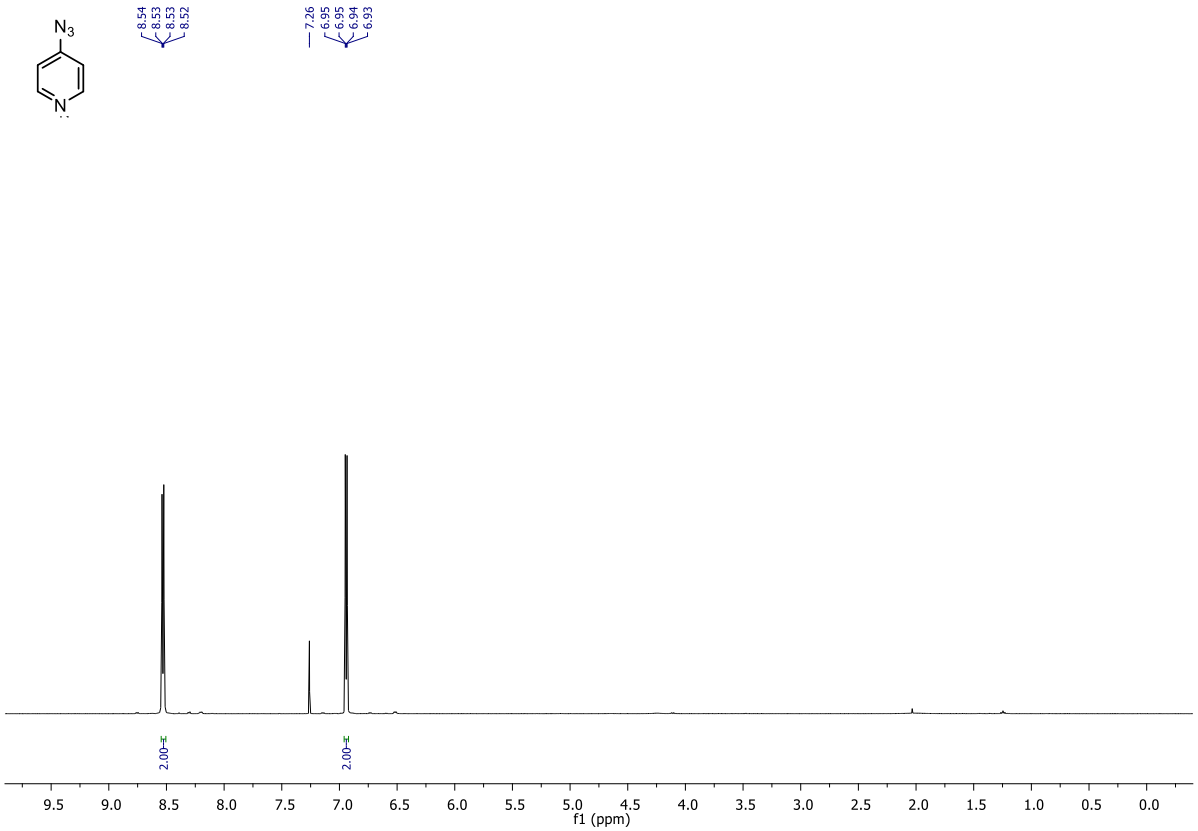
^{1}H NMR (400 MHz, $CDCl_3$) **S17**:



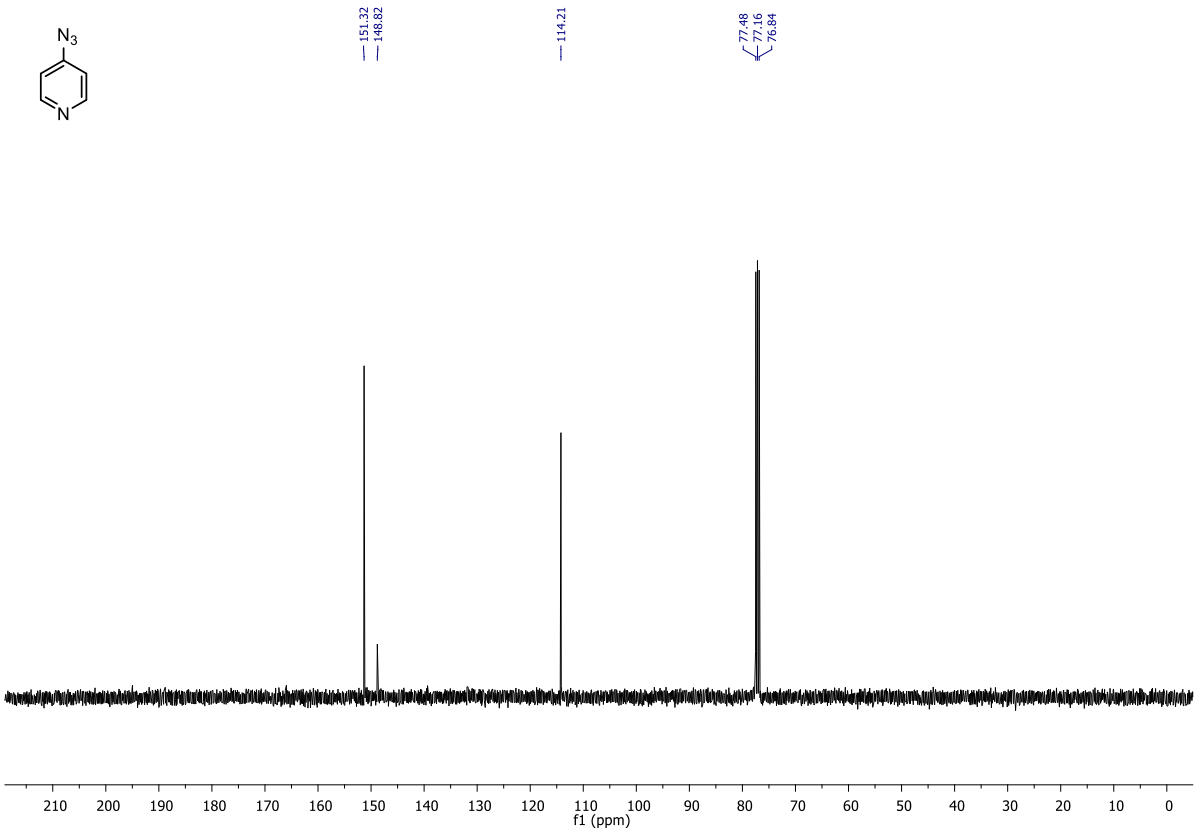
^{13}C NMR (100 MHz, $CDCl_3$) **S17**:



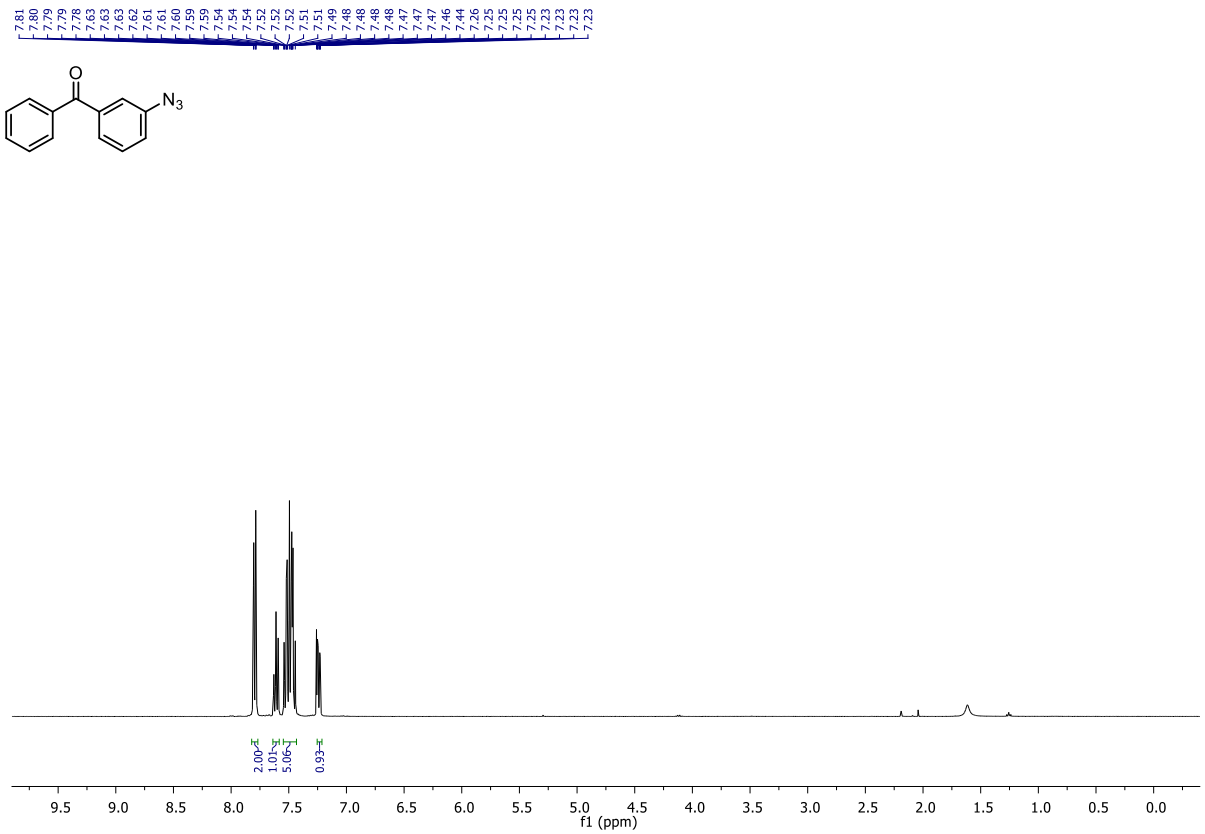
^{1}H NMR (400 MHz, $CDCl_3$) **S18**:



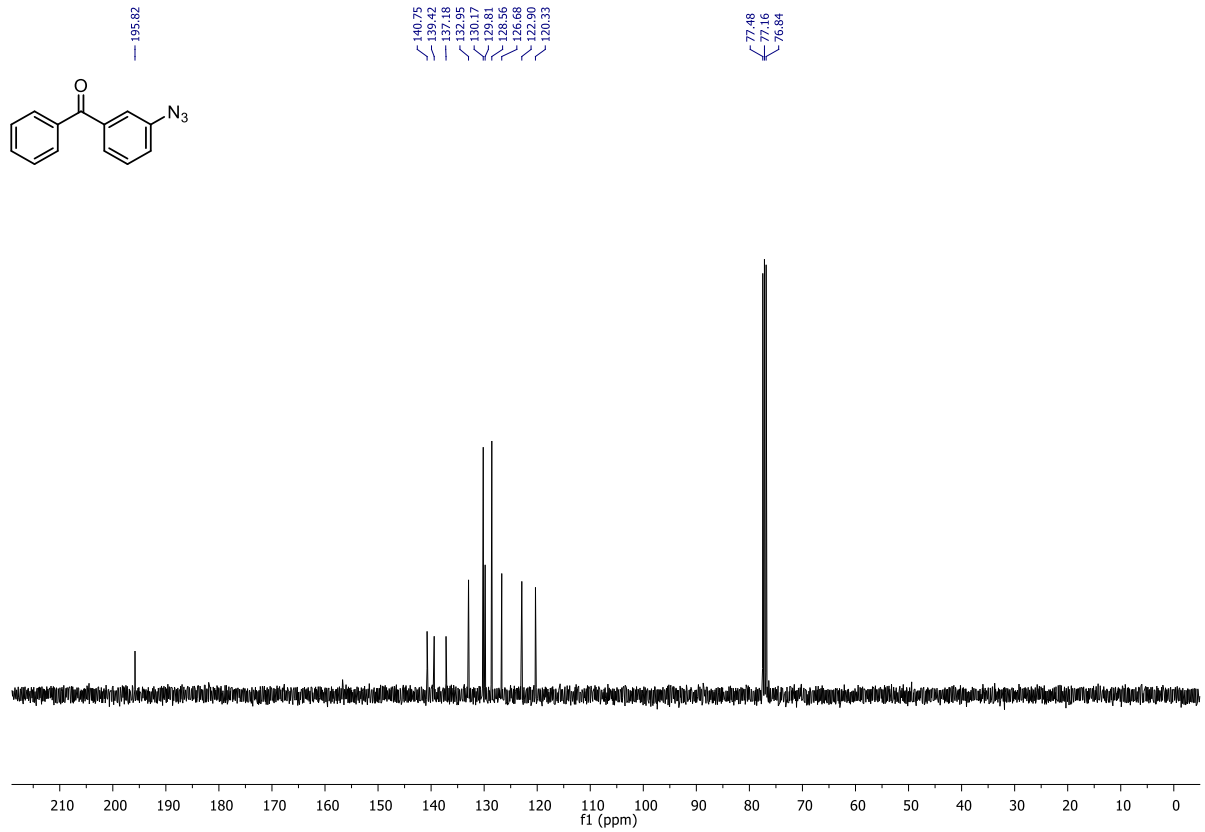
^{13}C NMR (100 MHz, $CDCl_3$) **S18**:



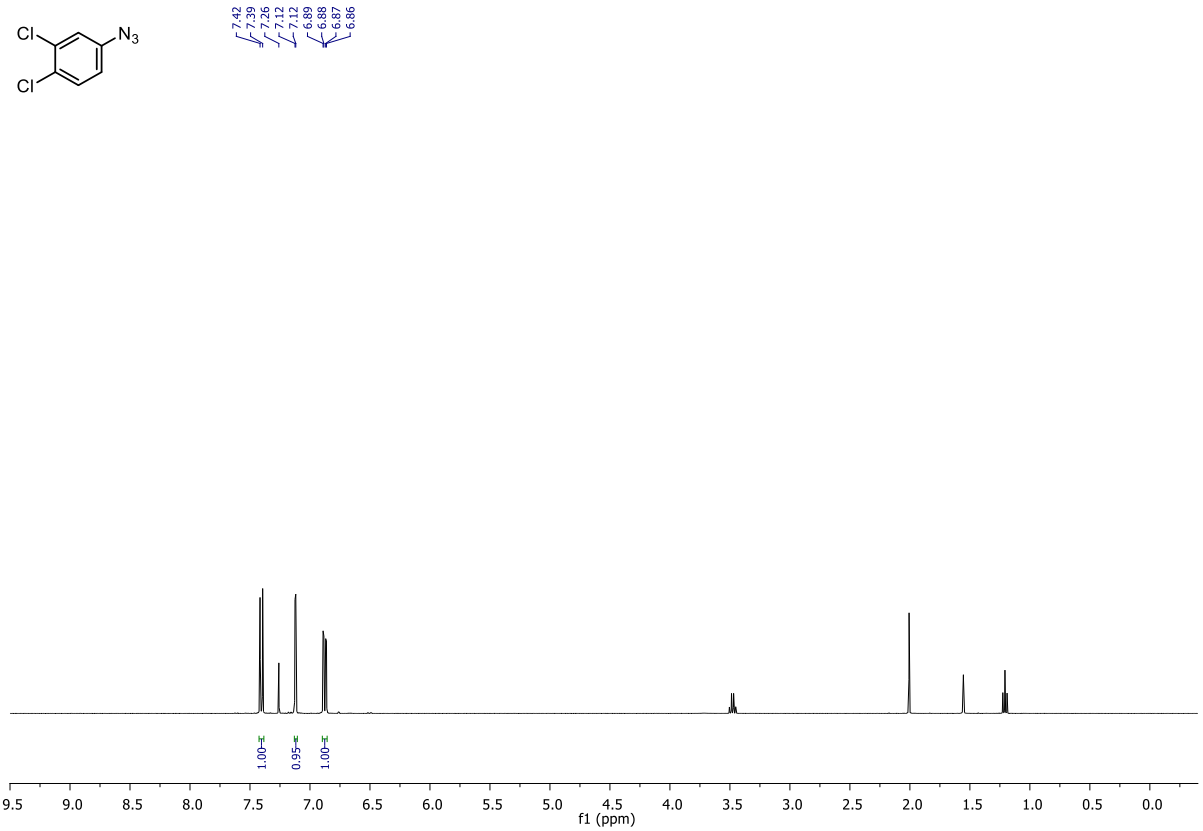
^{1}H NMR (400 MHz, $CDCl_3$) **S19**:



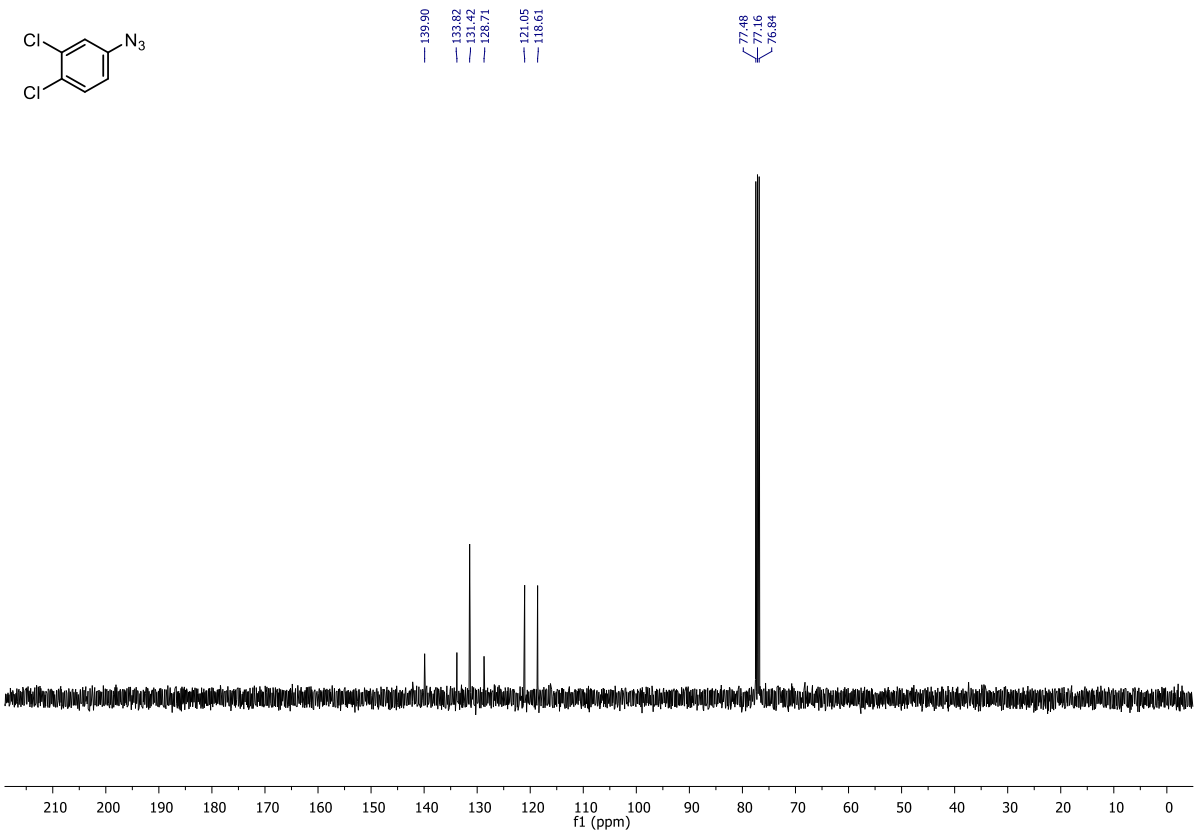
^{13}C NMR (100 MHz, $CDCl_3$) **S19**:



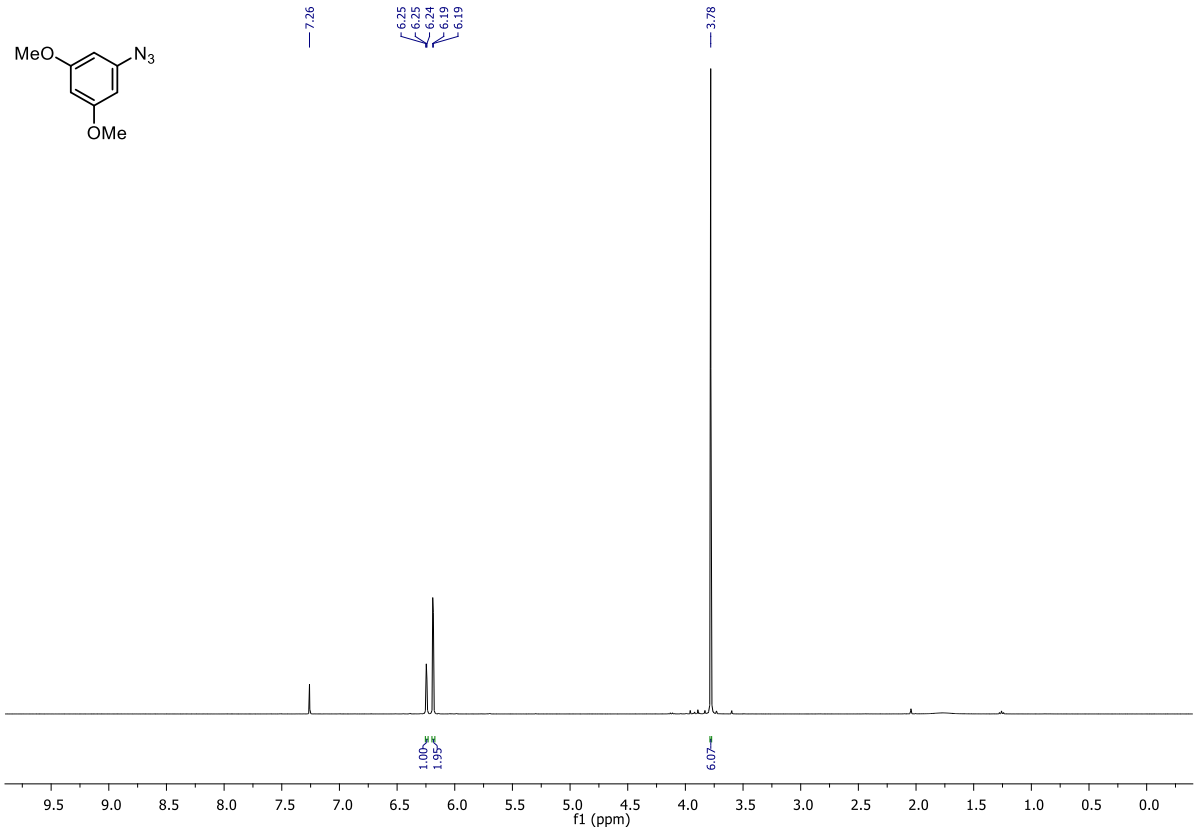
^{1}H NMR (400 MHz, $CDCl_3$) **S20**:



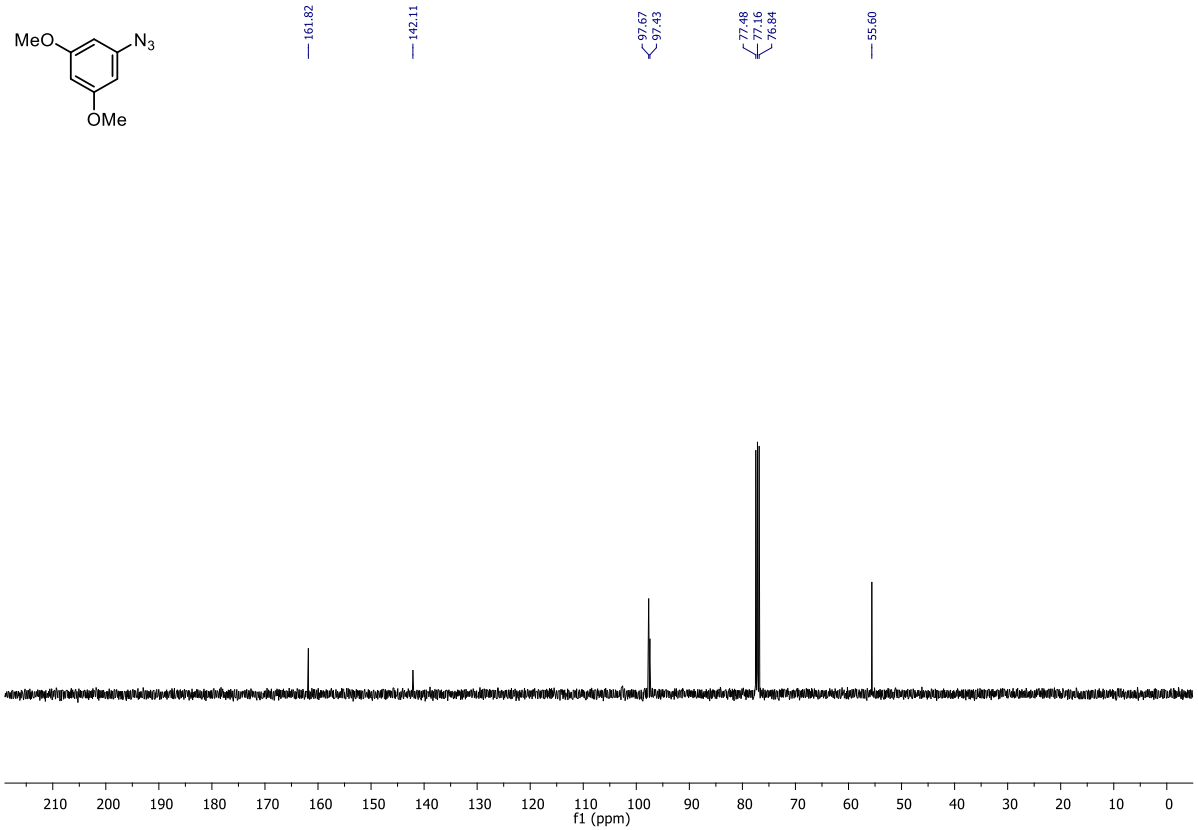
^{13}C NMR (100 MHz, $CDCl_3$) **S20**:



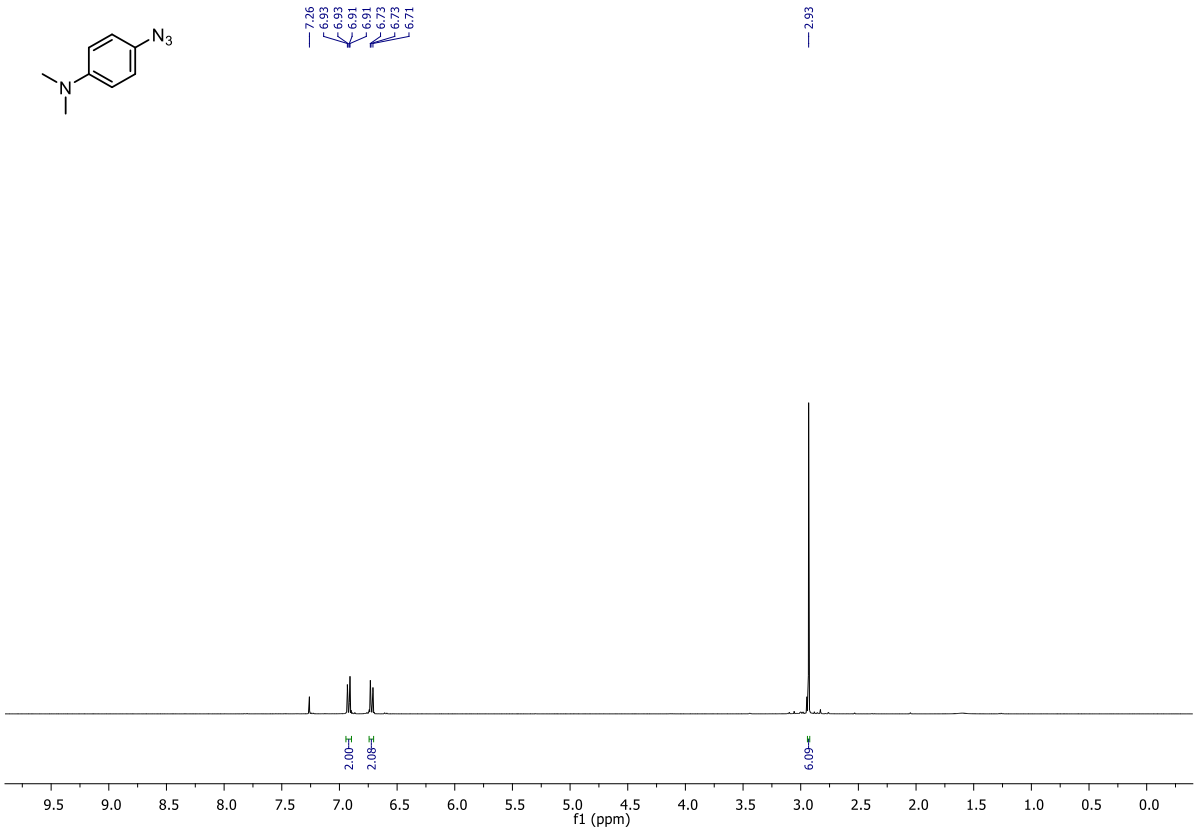
^{1}H NMR (400 MHz, $CDCl_3$) **S21**:



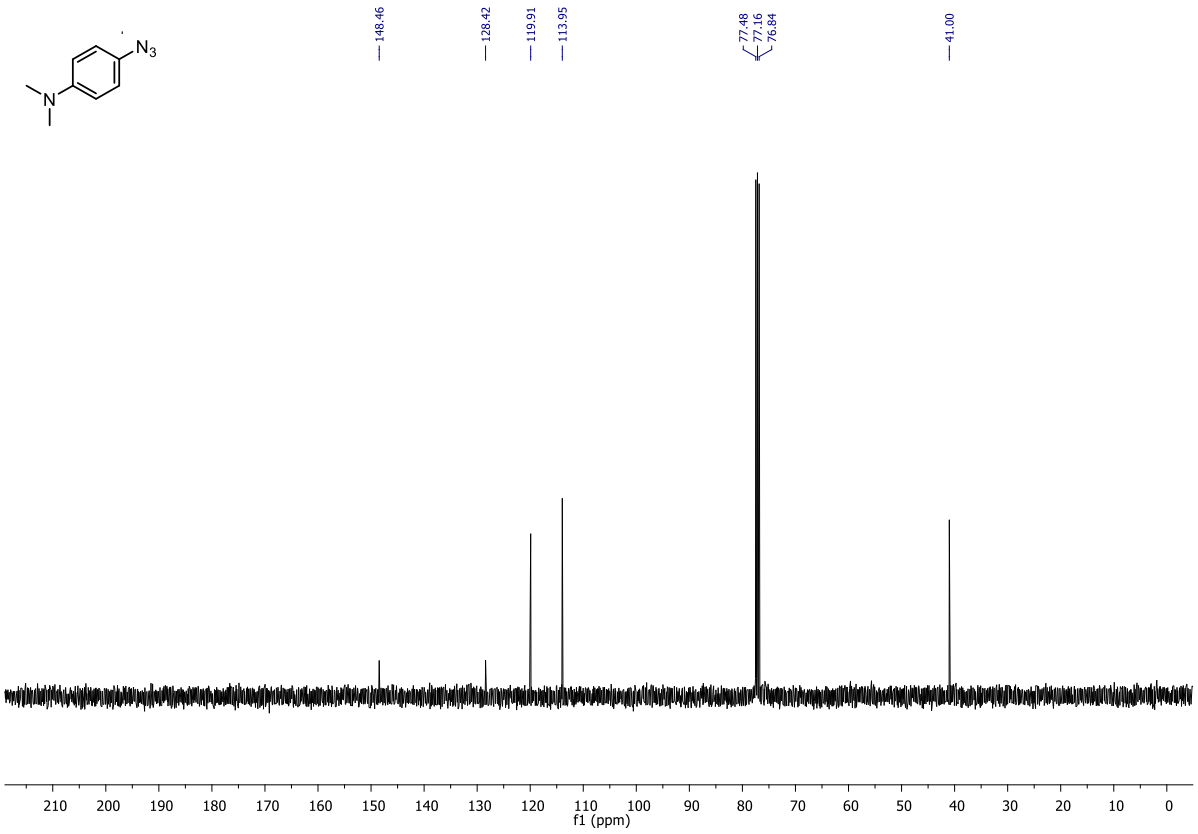
^{13}C NMR (100 MHz, $CDCl_3$) **S21**:



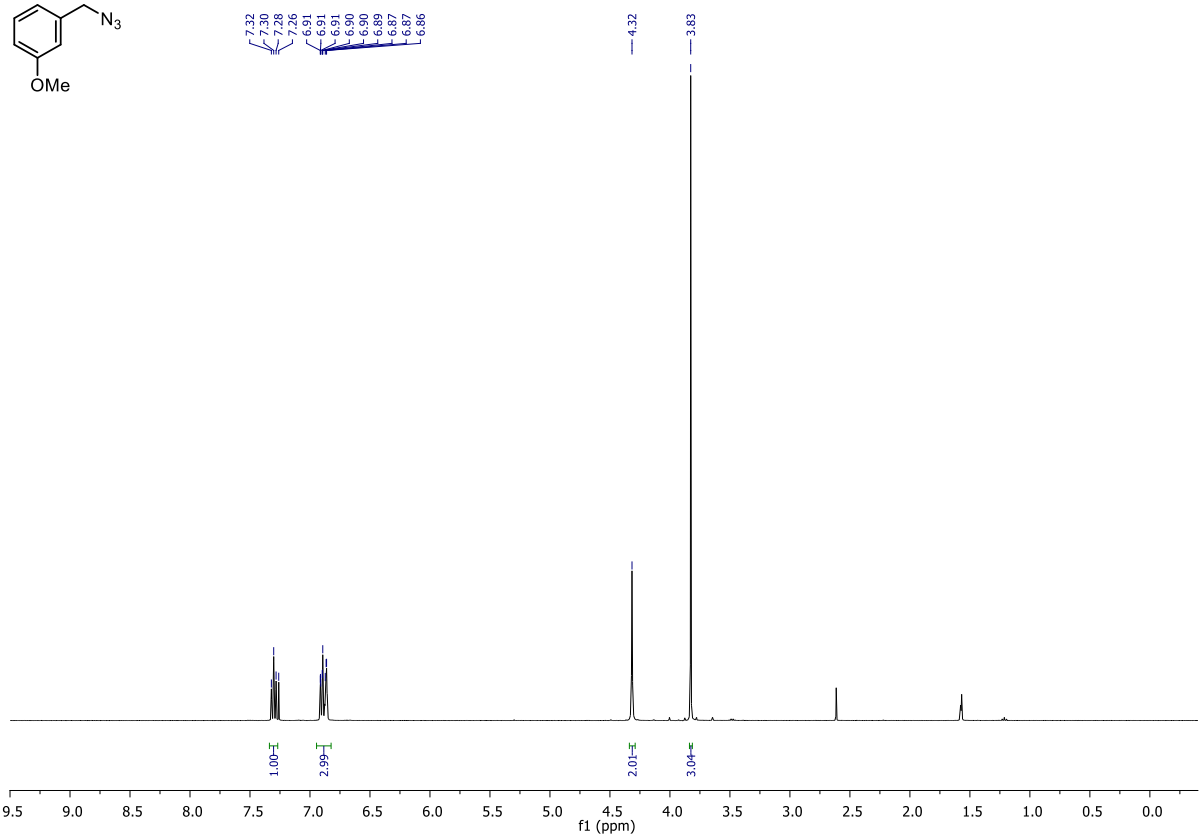
^{1}H NMR (400 MHz, $CDCl_3$) **S22**:



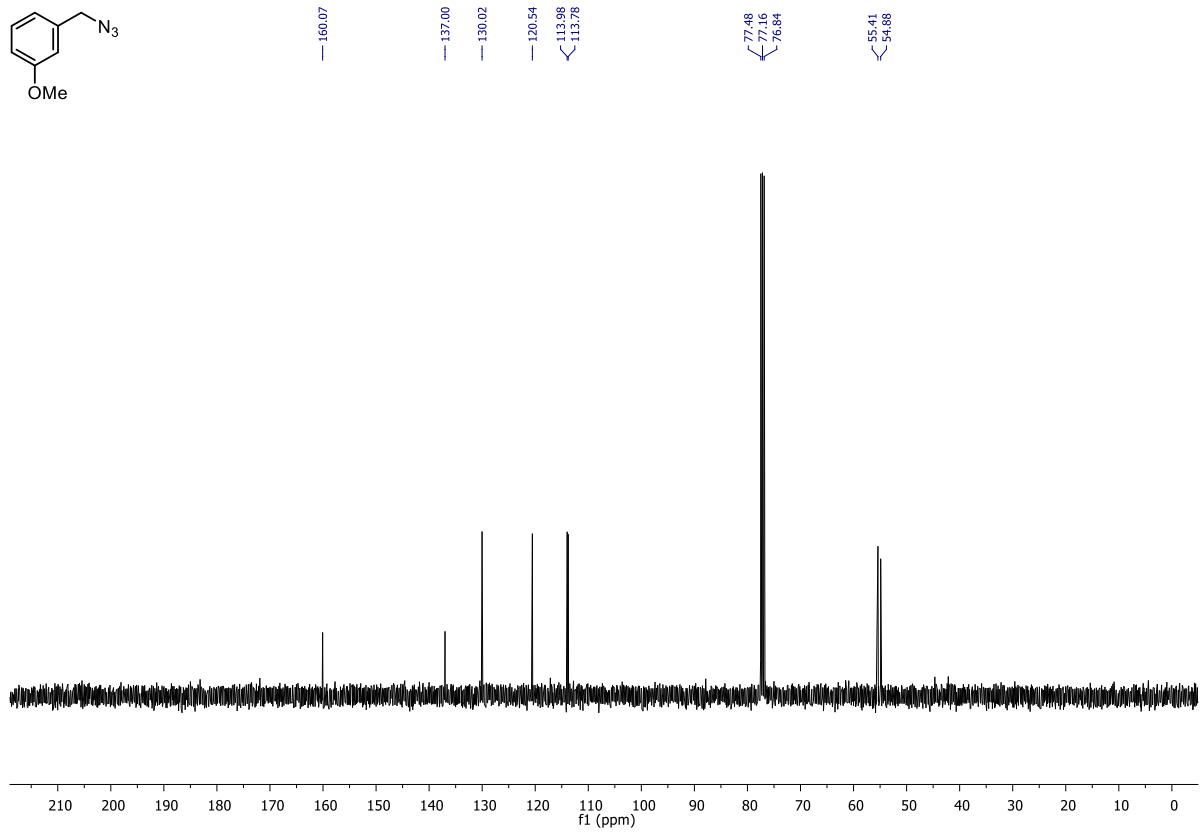
^{13}C NMR (100 MHz, $CDCl_3$) **S22**:



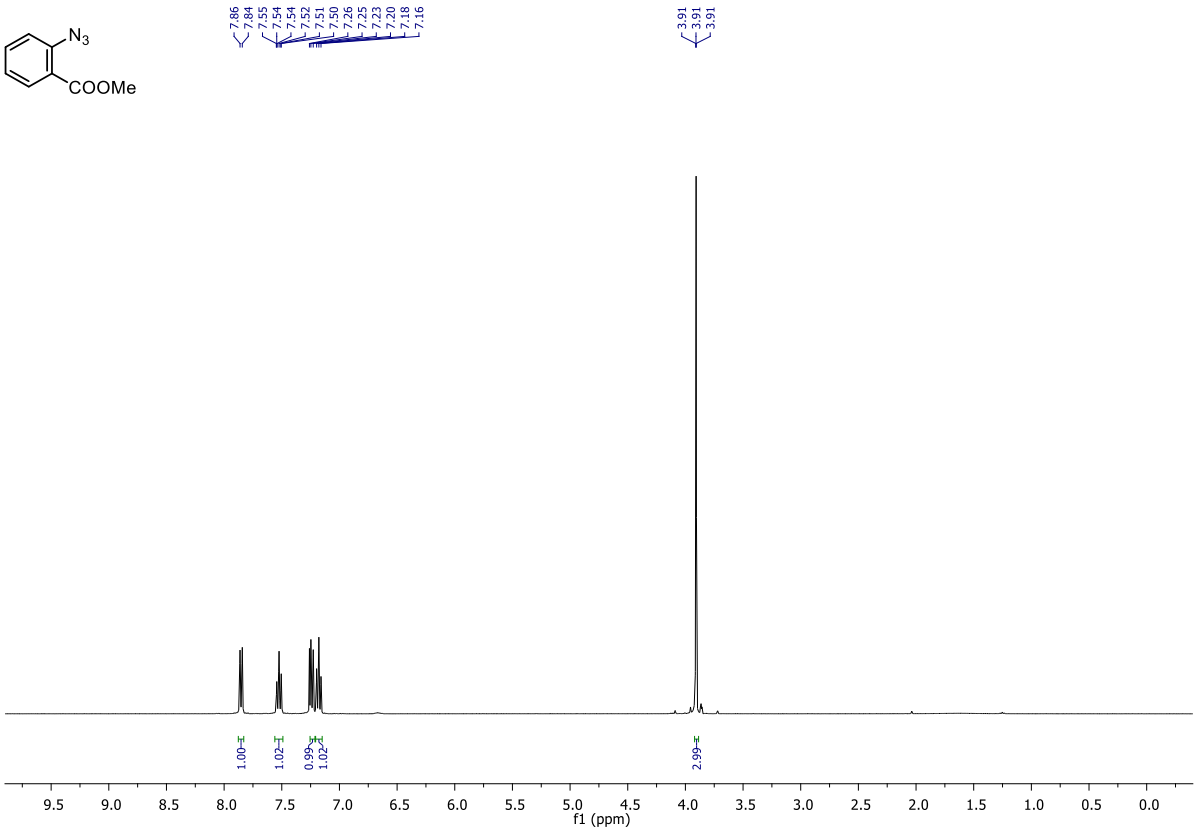
^{1}H NMR (400 MHz, $CDCl_3$) **S23**:



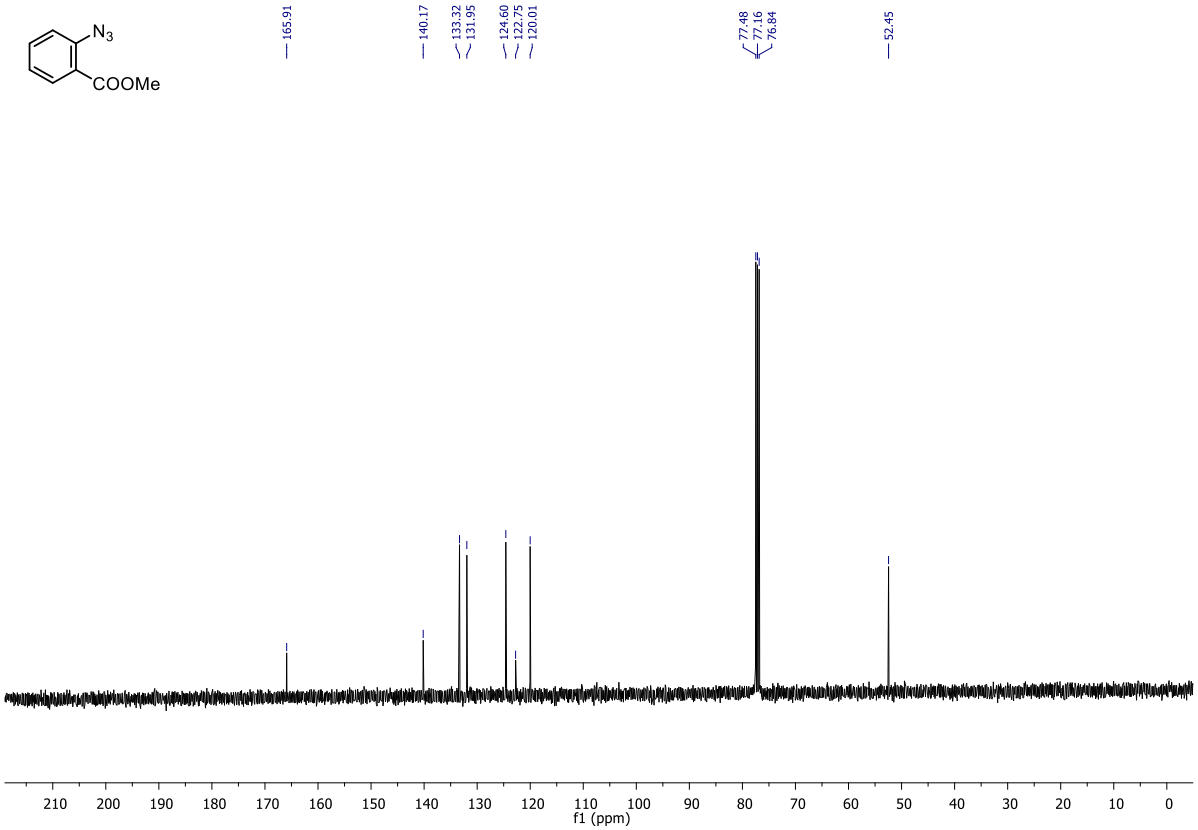
^{13}C NMR (100 MHz, $CDCl_3$) **S23**:



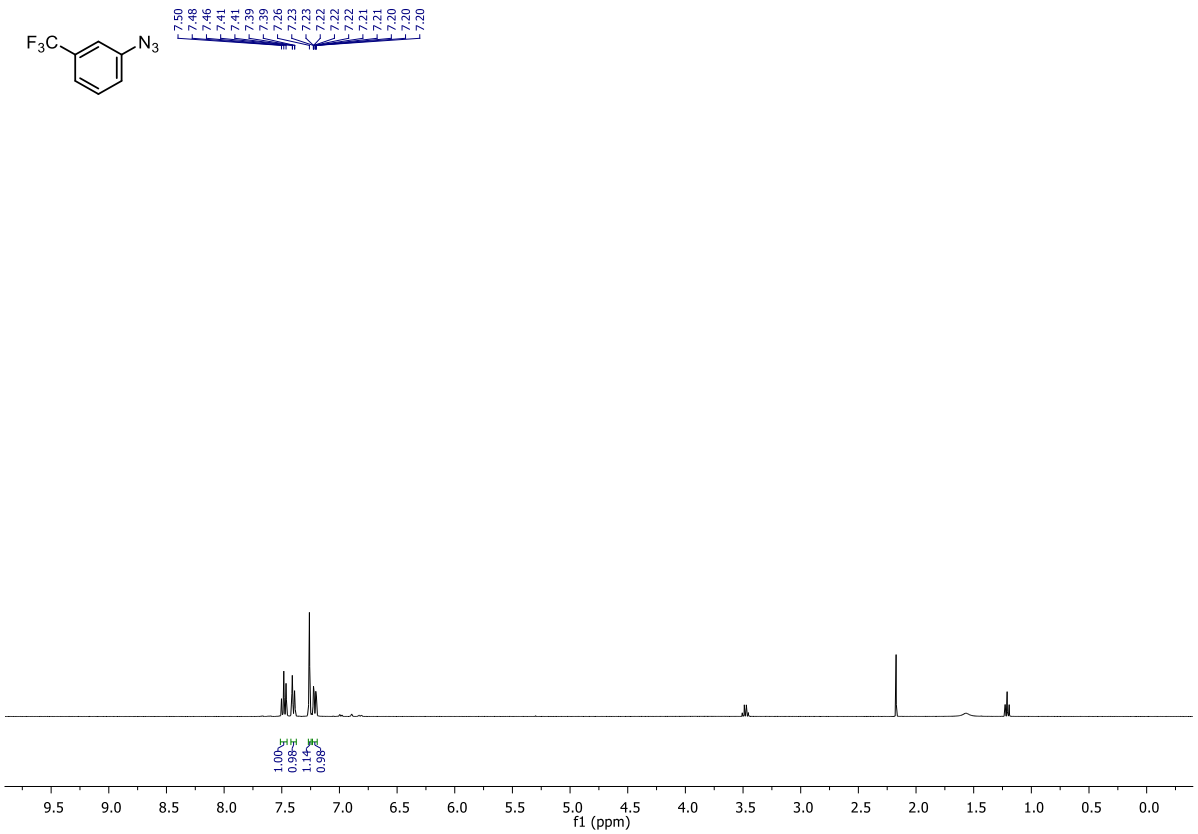
^{1}H NMR (400 MHz, $CDCl_3$) **S24**:



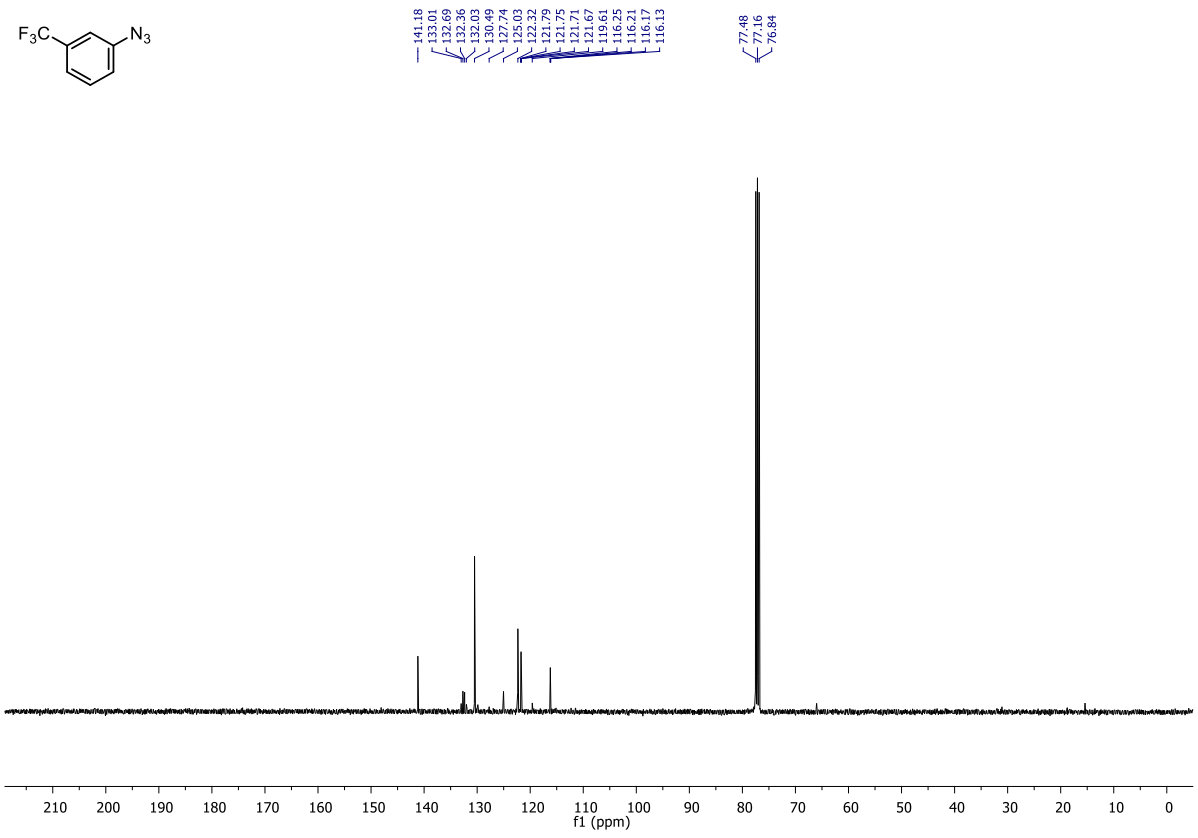
^{13}C NMR (100 MHz, $CDCl_3$) **S24**:



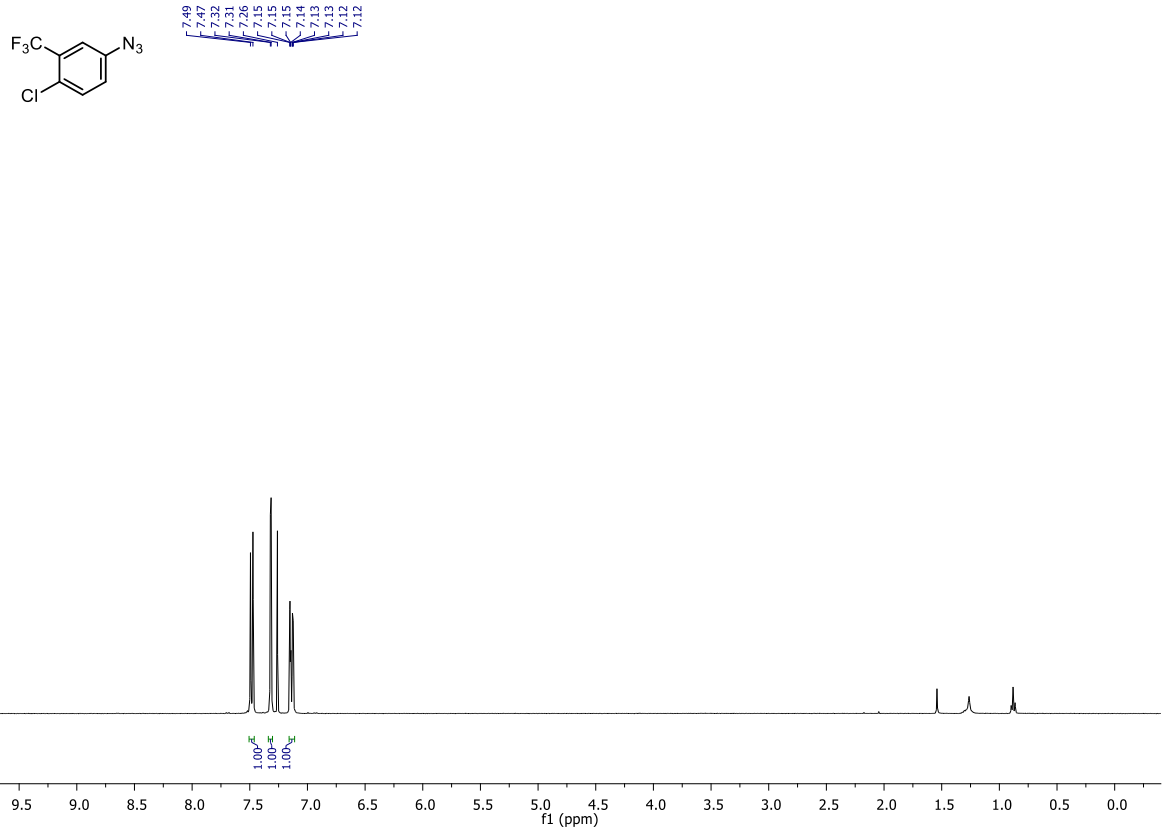
^{1}H NMR (400 MHz, $CDCl_3$) **S25**:



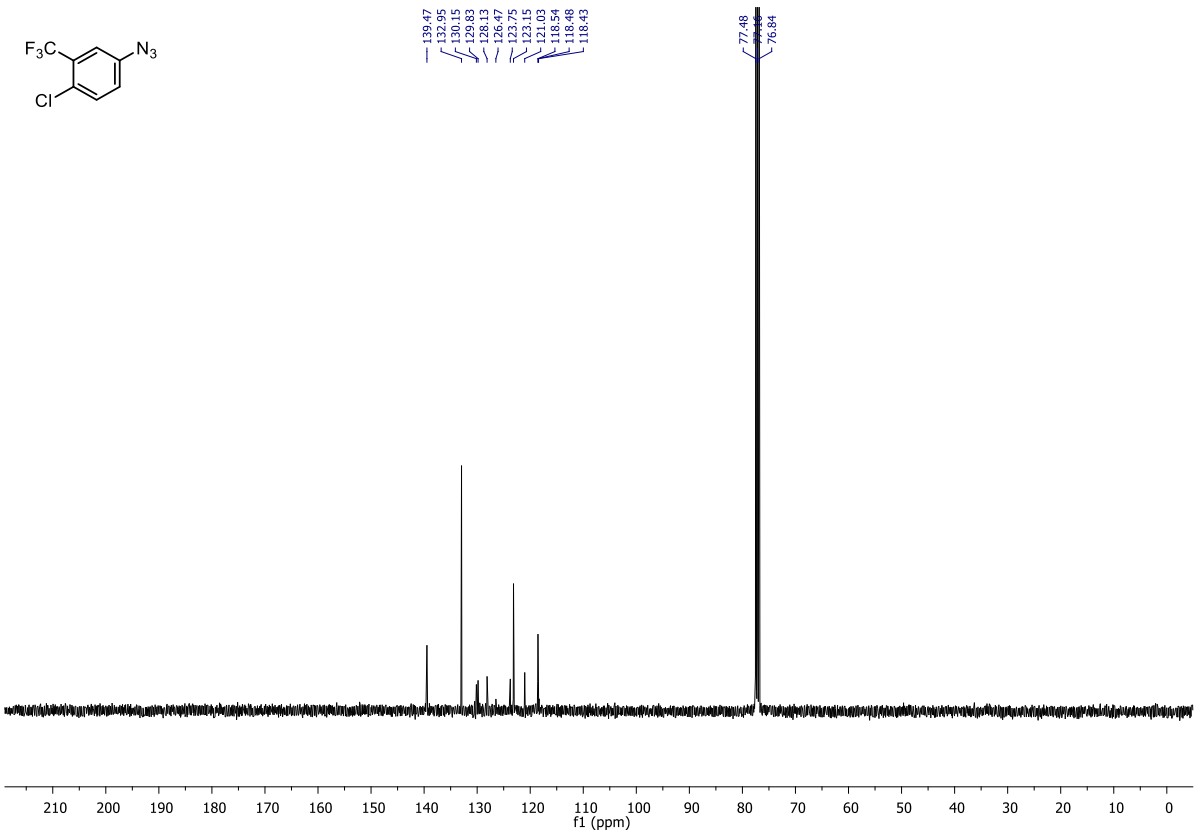
^{13}C NMR (100 MHz, $CDCl_3$) **S25**:



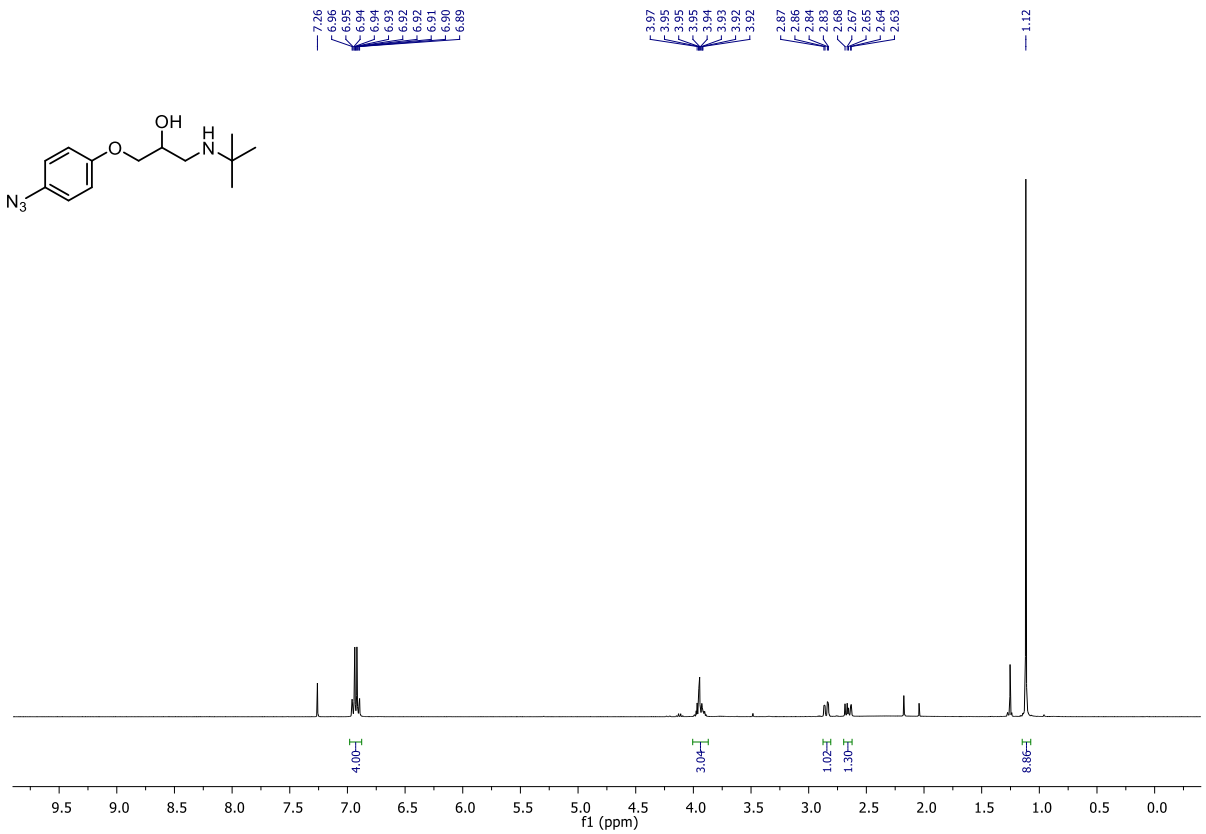
^{1}H NMR (400 MHz, $CDCl_3$) **S26**:



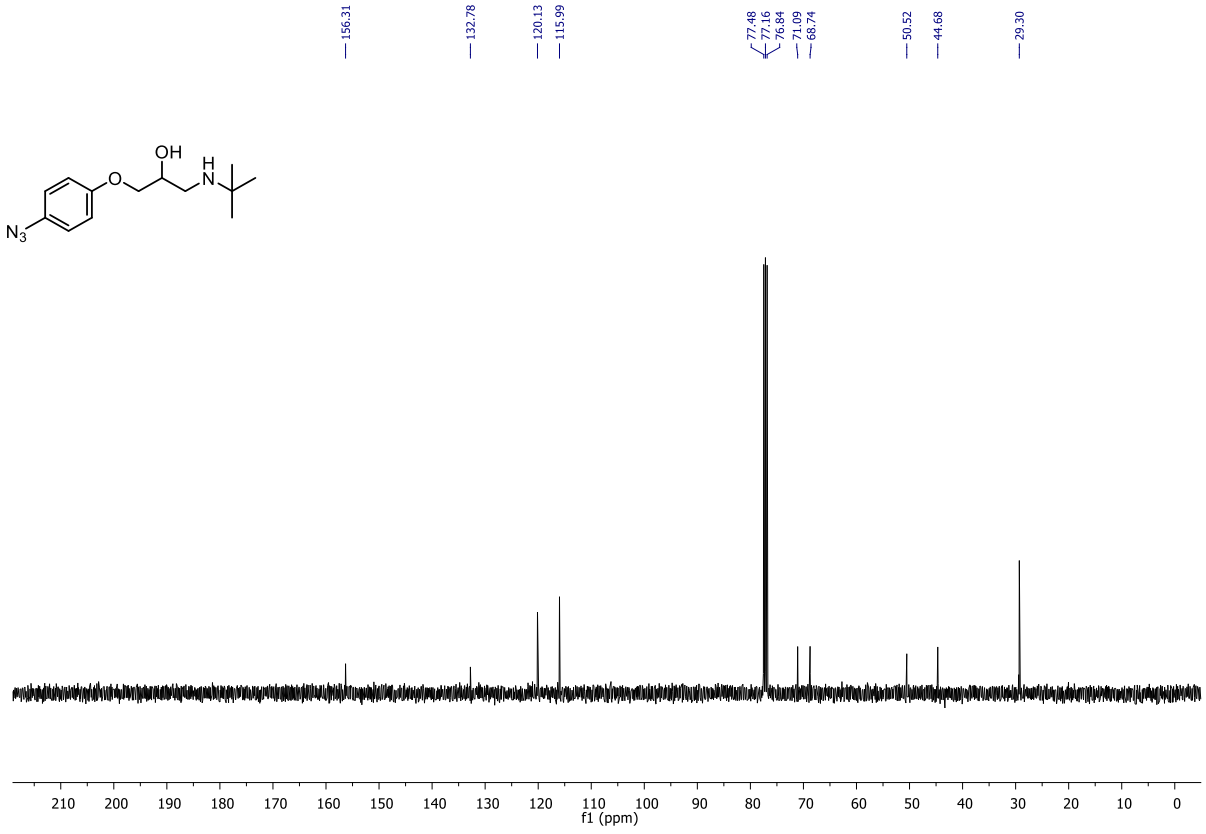
^{13}C NMR (100 MHz, $CDCl_3$) **S26**:



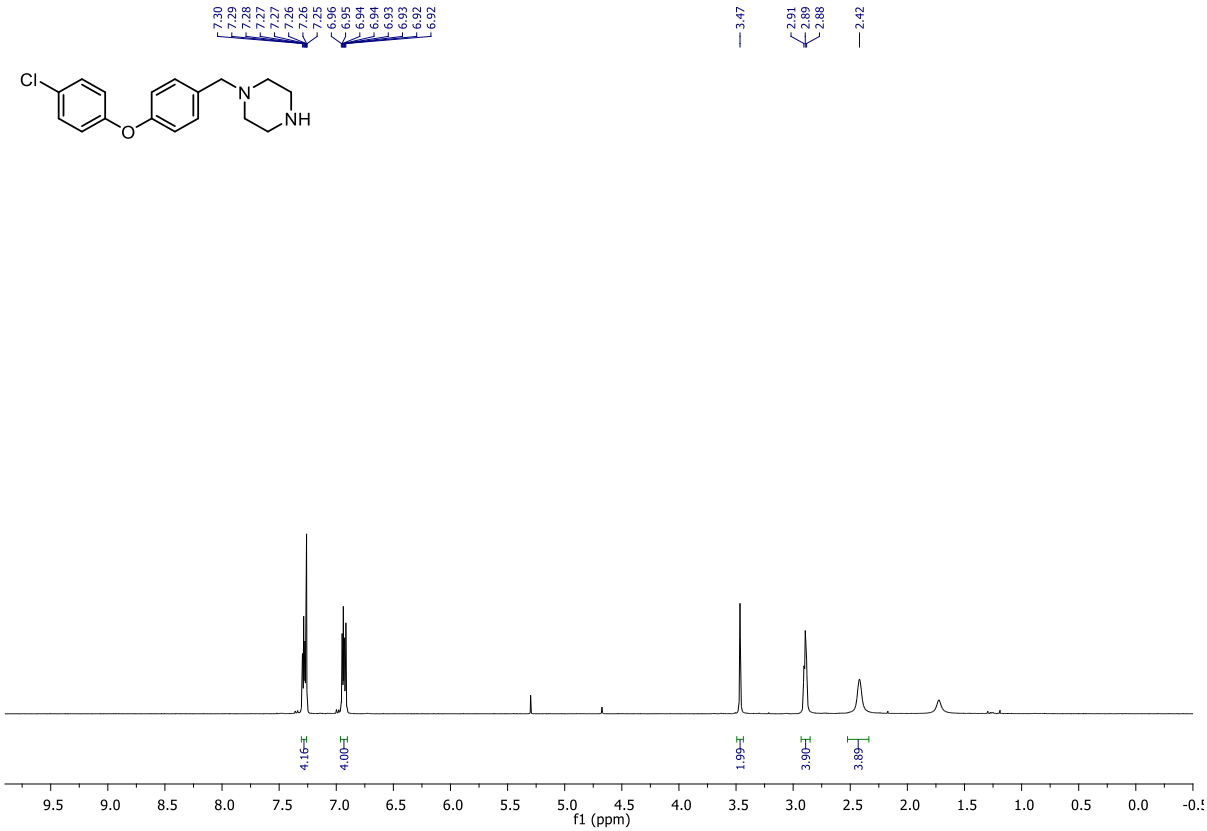
^{1}H NMR (400 MHz, $CDCl_3$) **S31**:



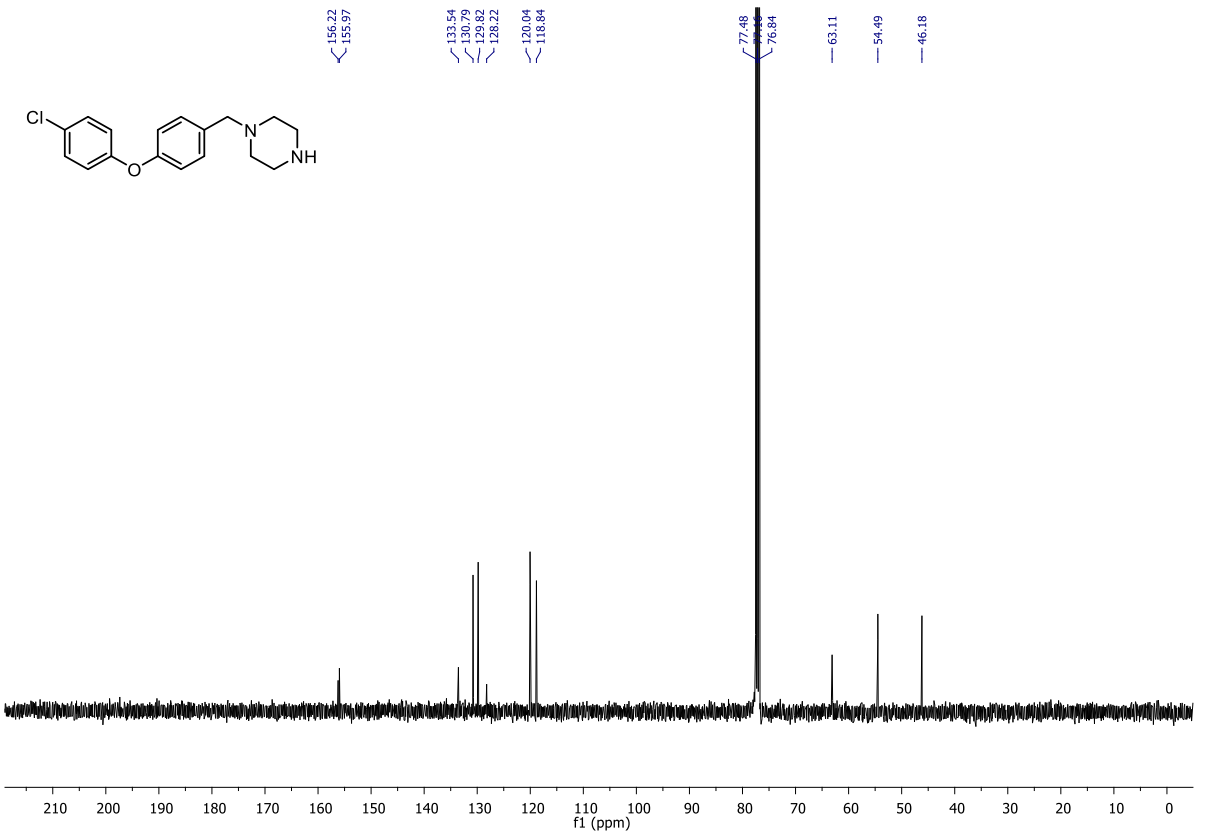
^{13}C NMR (100 MHz, $CDCl_3$) **S31**:



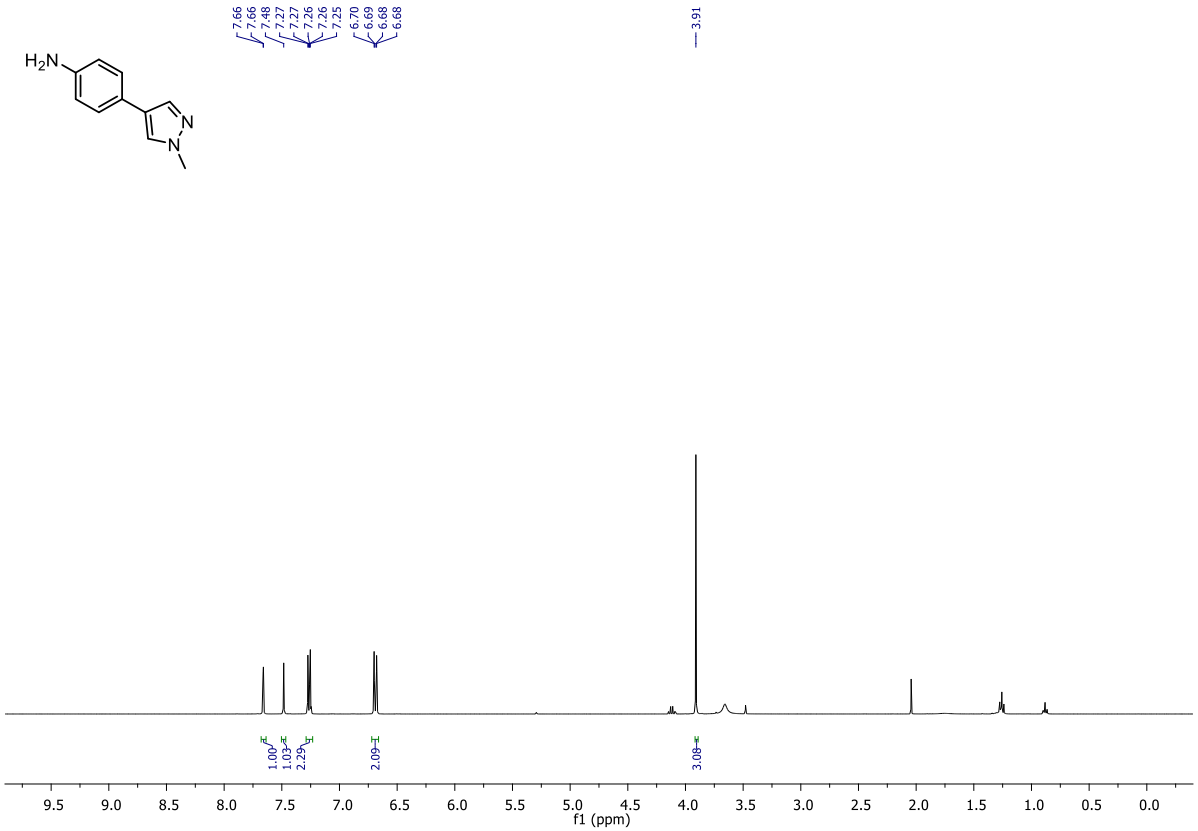
^{1}H NMR (400 MHz, $CDCl_3$) **S32**:



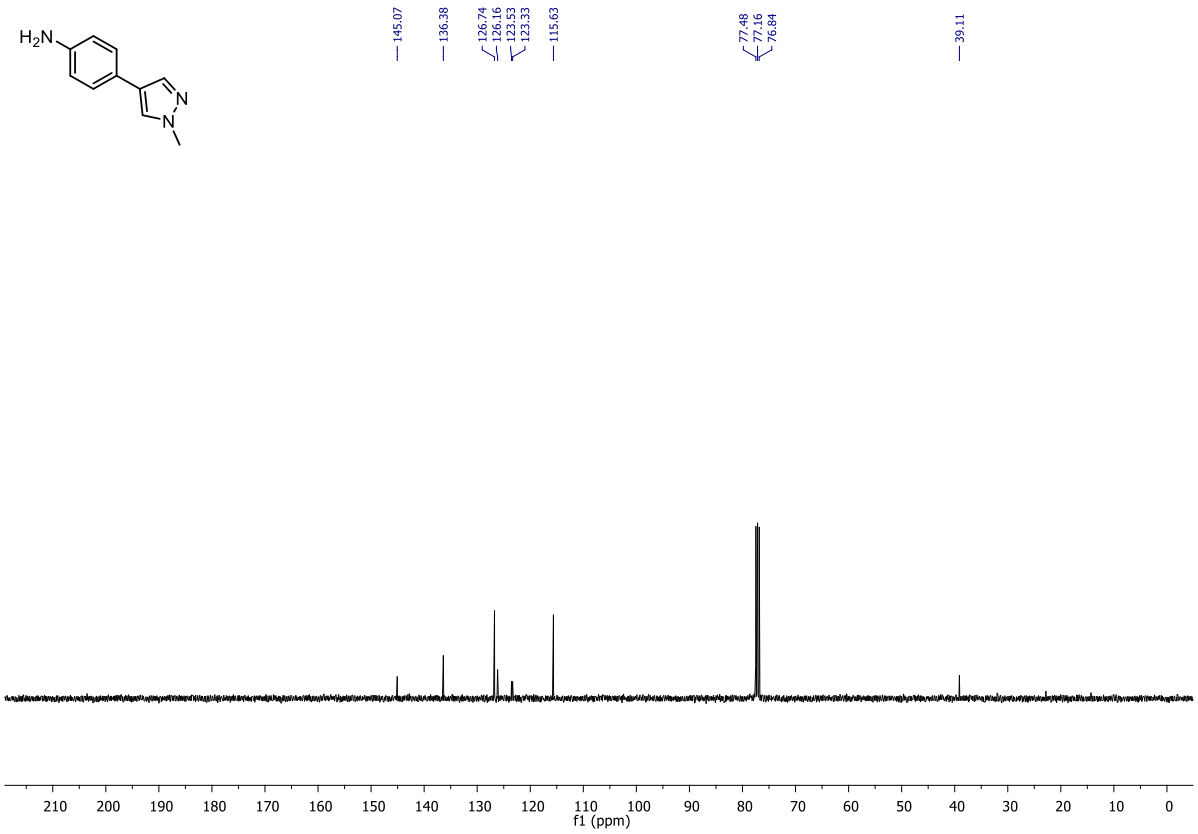
^{13}C NMR (100 MHz, $CDCl_3$) **S32**:



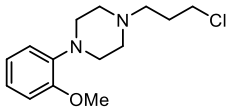
^{1}H NMR (400 MHz, $CDCl_3$) **S35**:

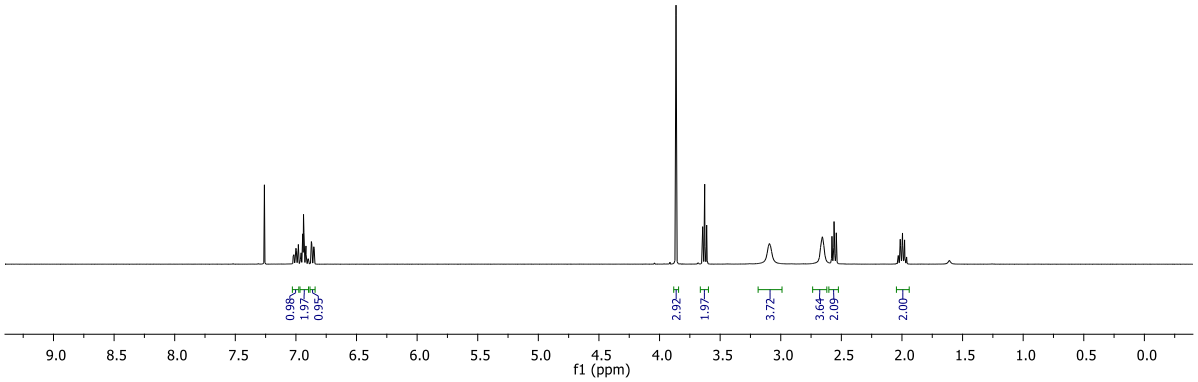


^{13}C NMR (100 MHz, $CDCl_3$) **S35**:

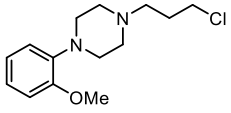


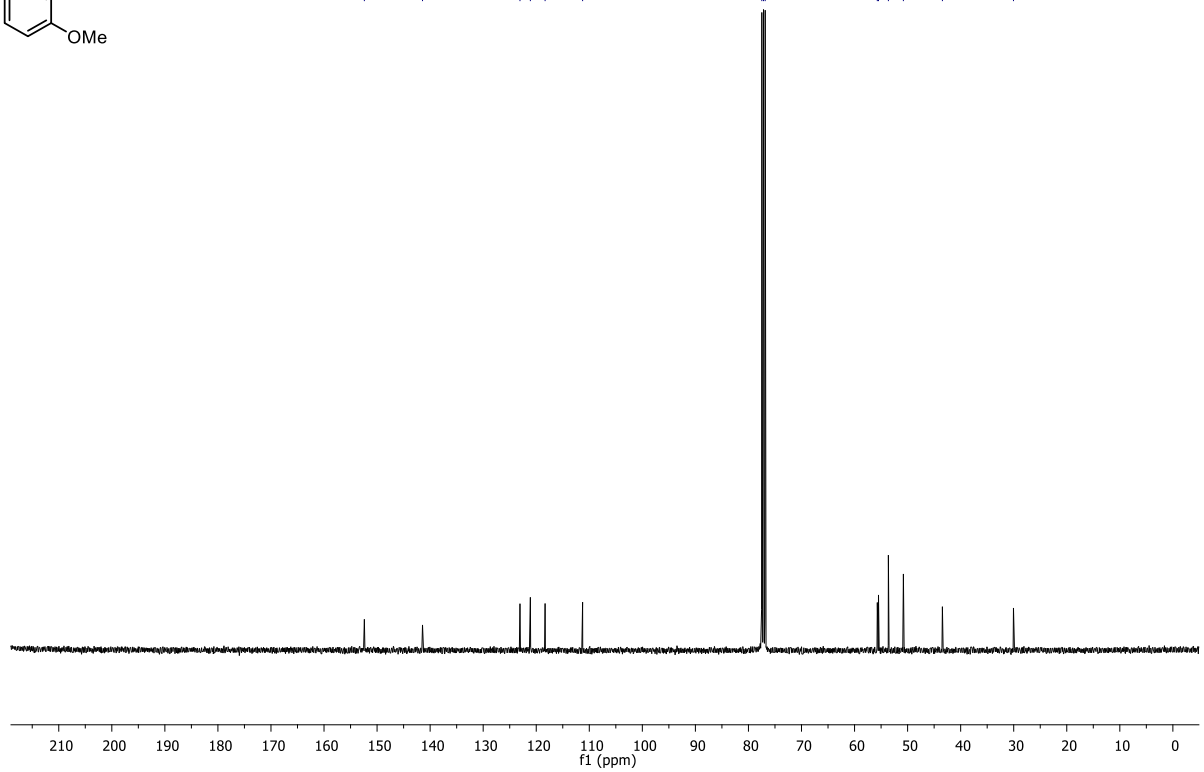
^{1}H NMR (400 MHz, $CDCl_3$) **S36**:



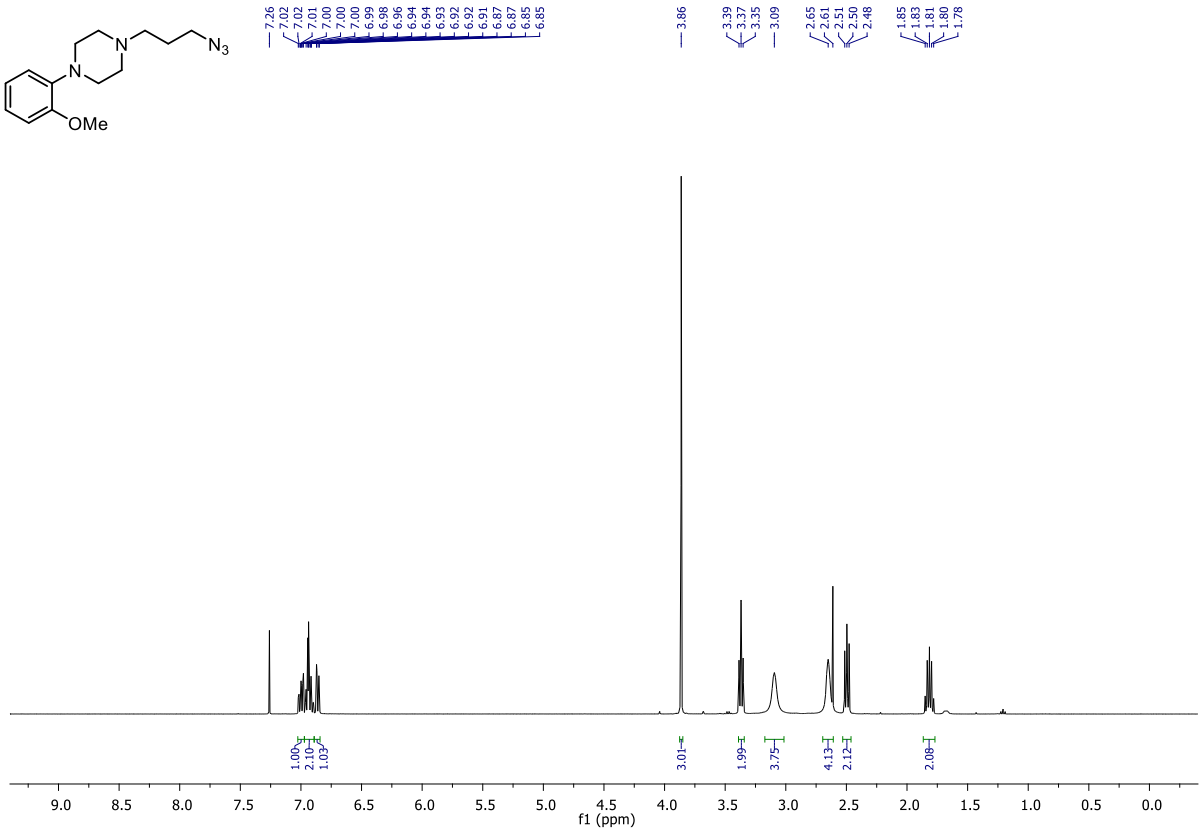


^{13}C NMR (100 MHz, $CDCl_3$) **S36**:

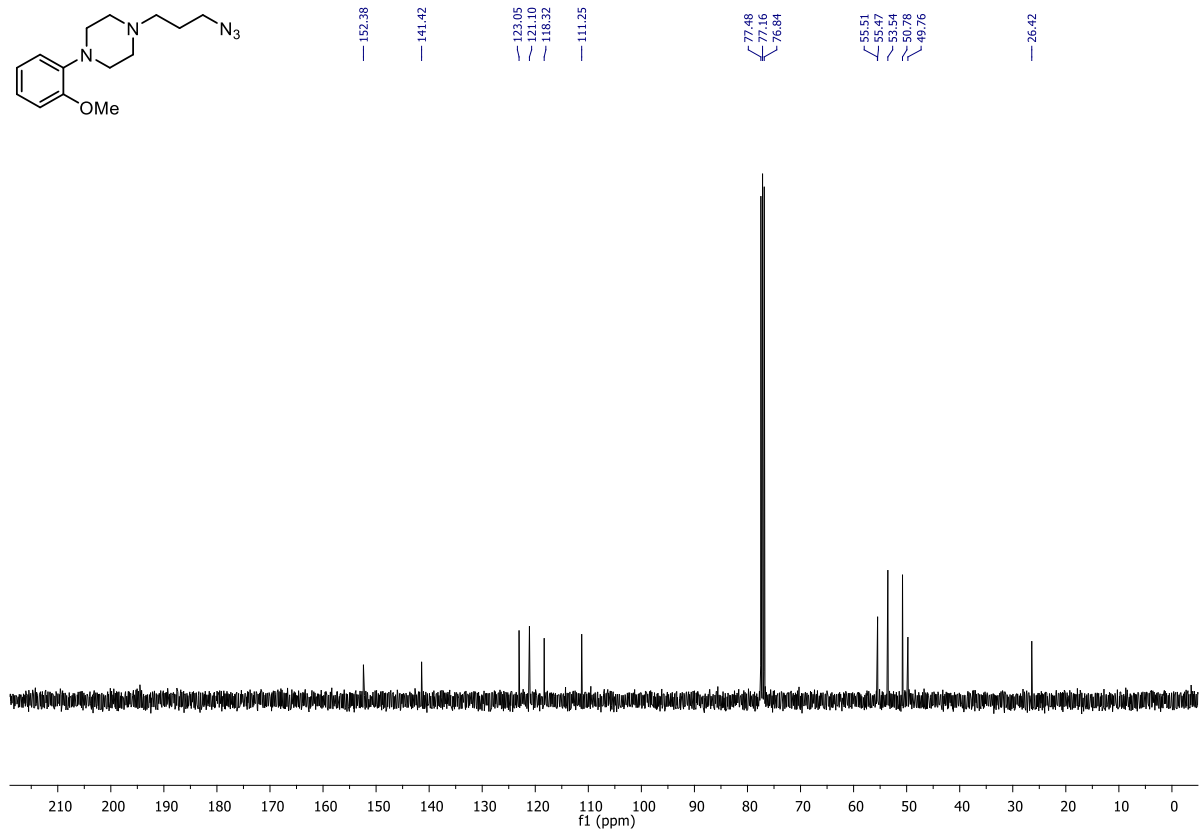




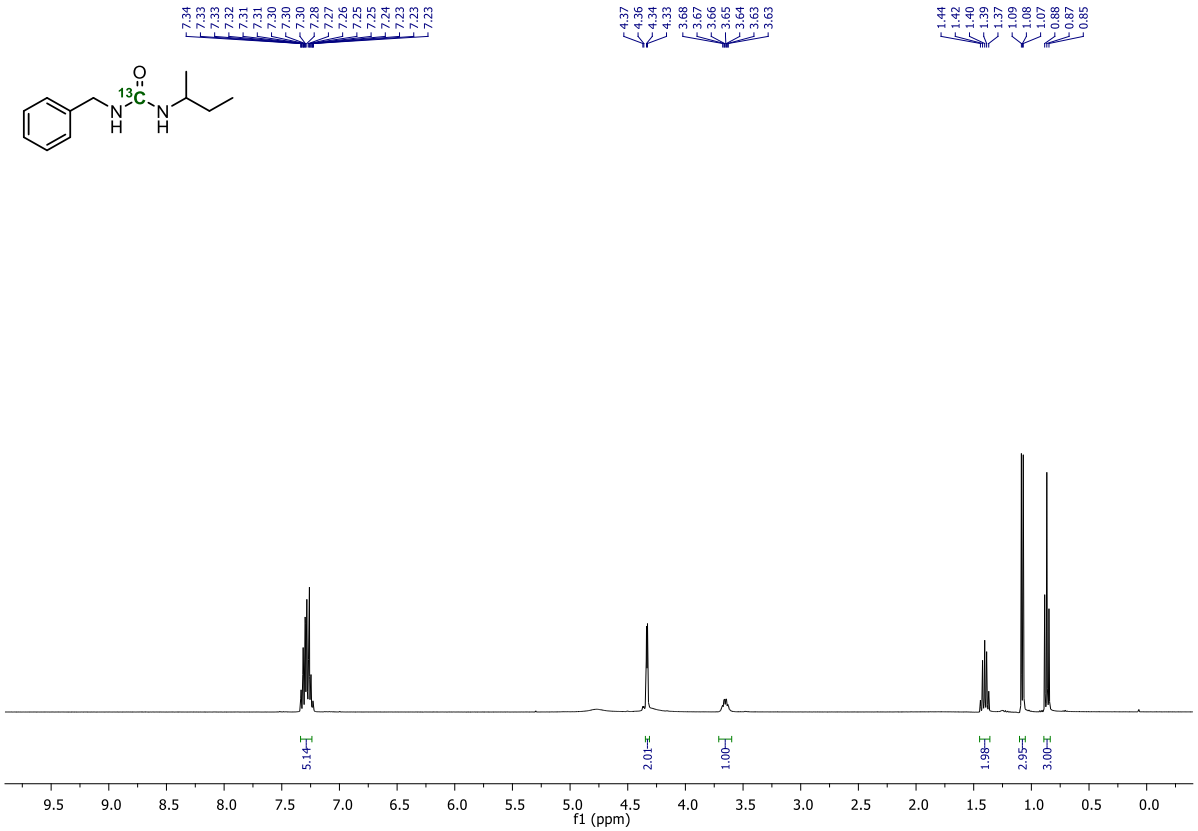
^{1}H NMR (400 MHz, $CDCl_3$) **S37**:



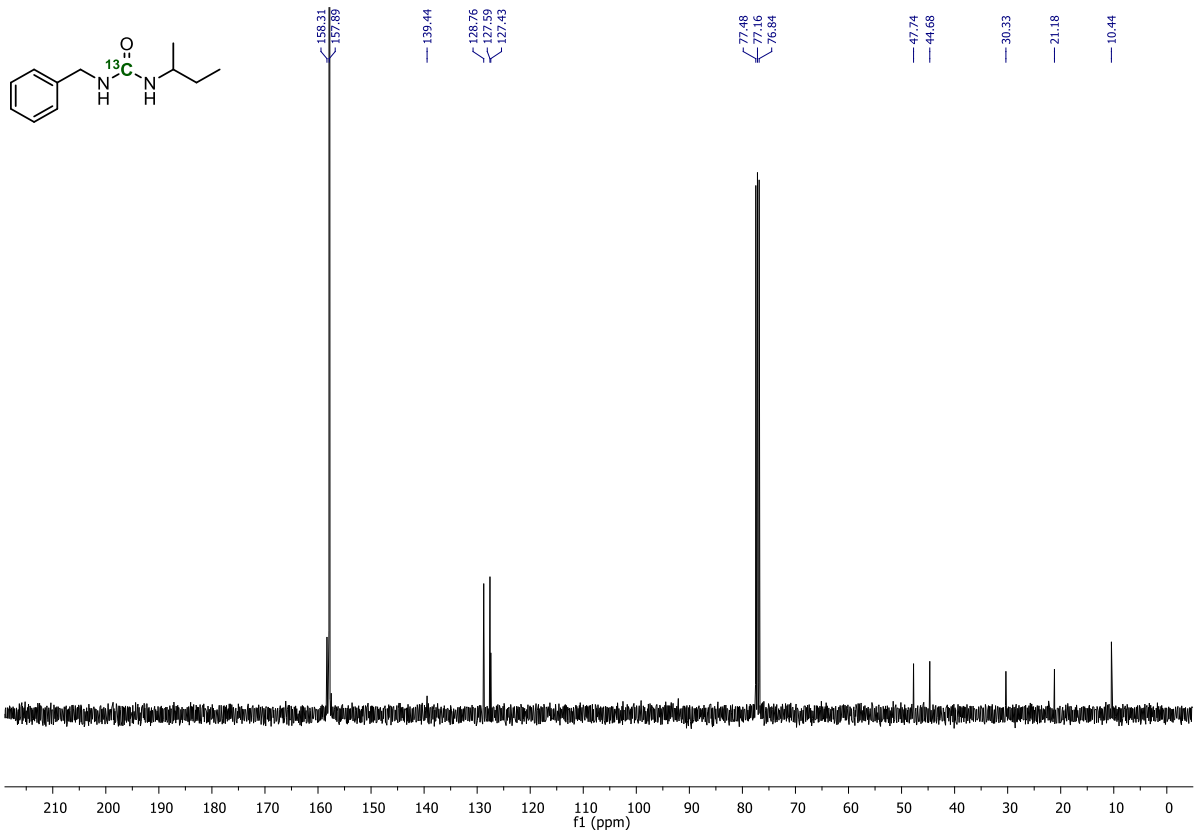
^{13}C NMR (100 MHz, $CDCl_3$) **S37**:



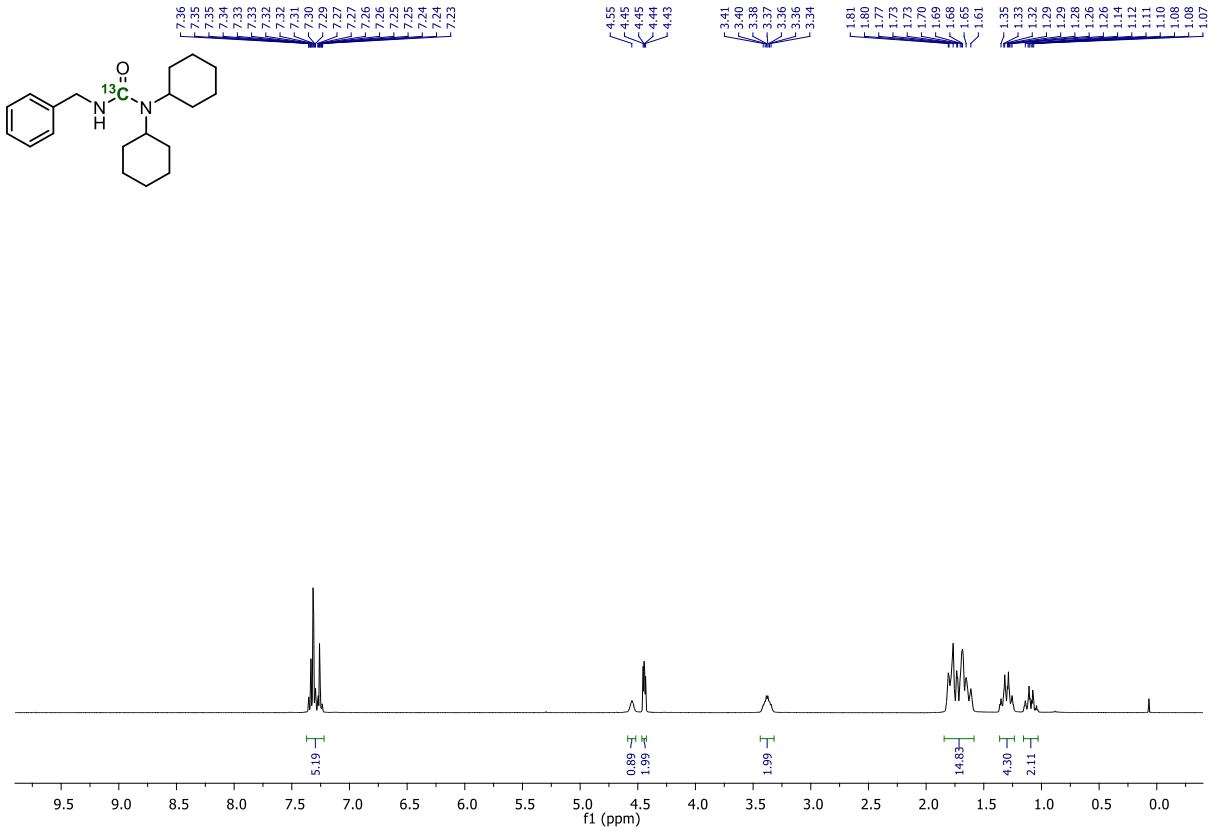
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]1**:



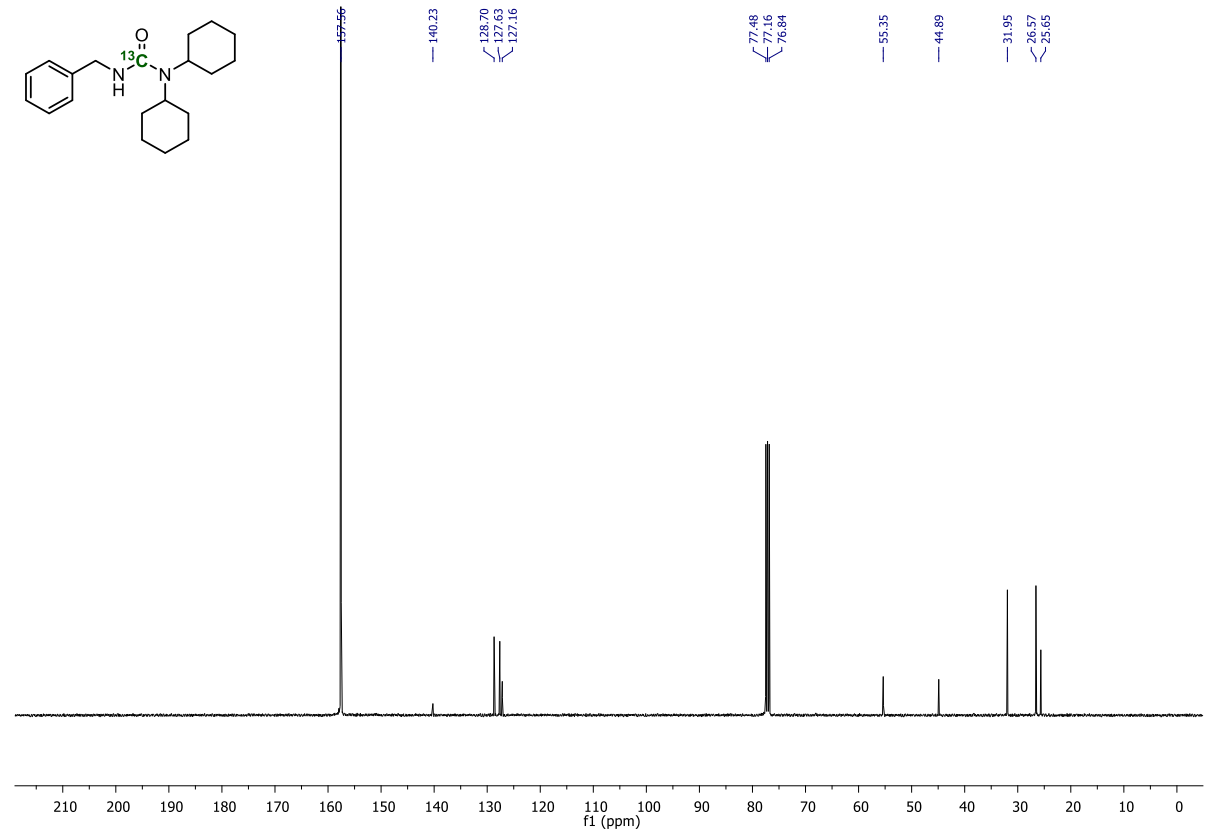
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]1**:



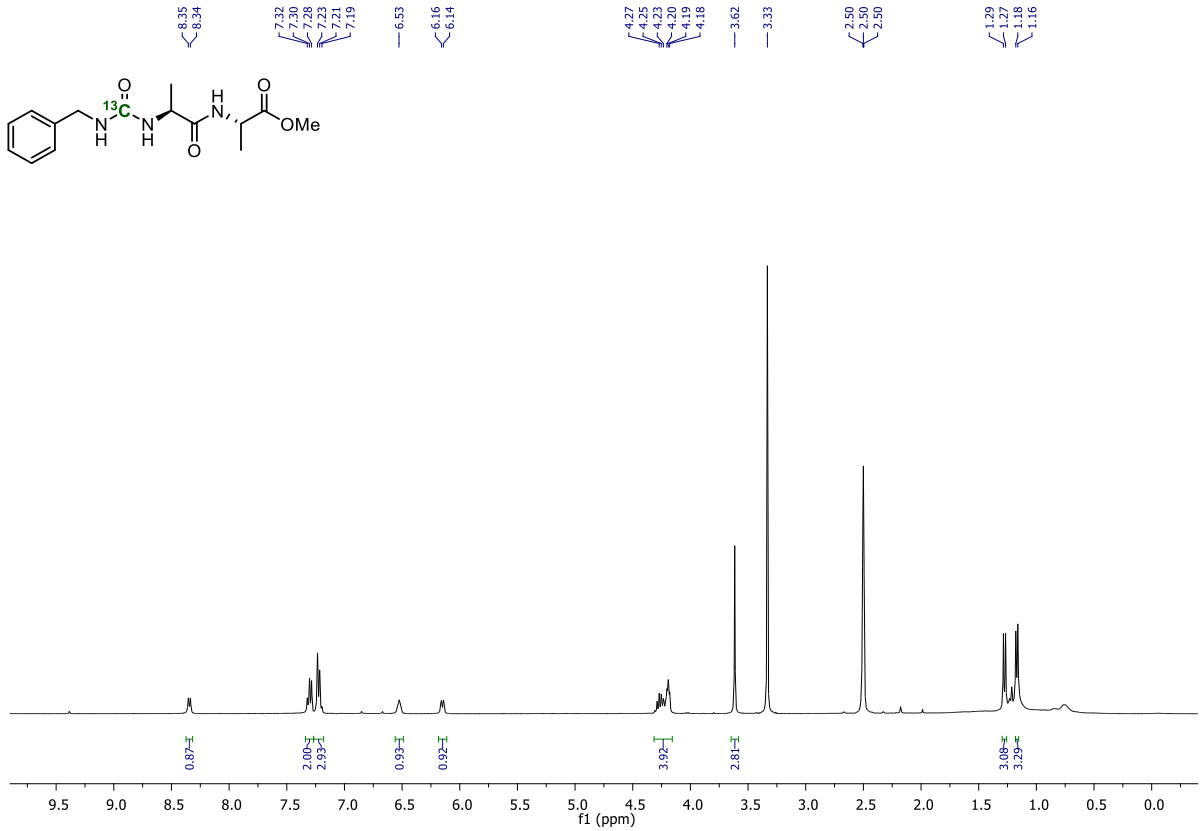
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]2**:



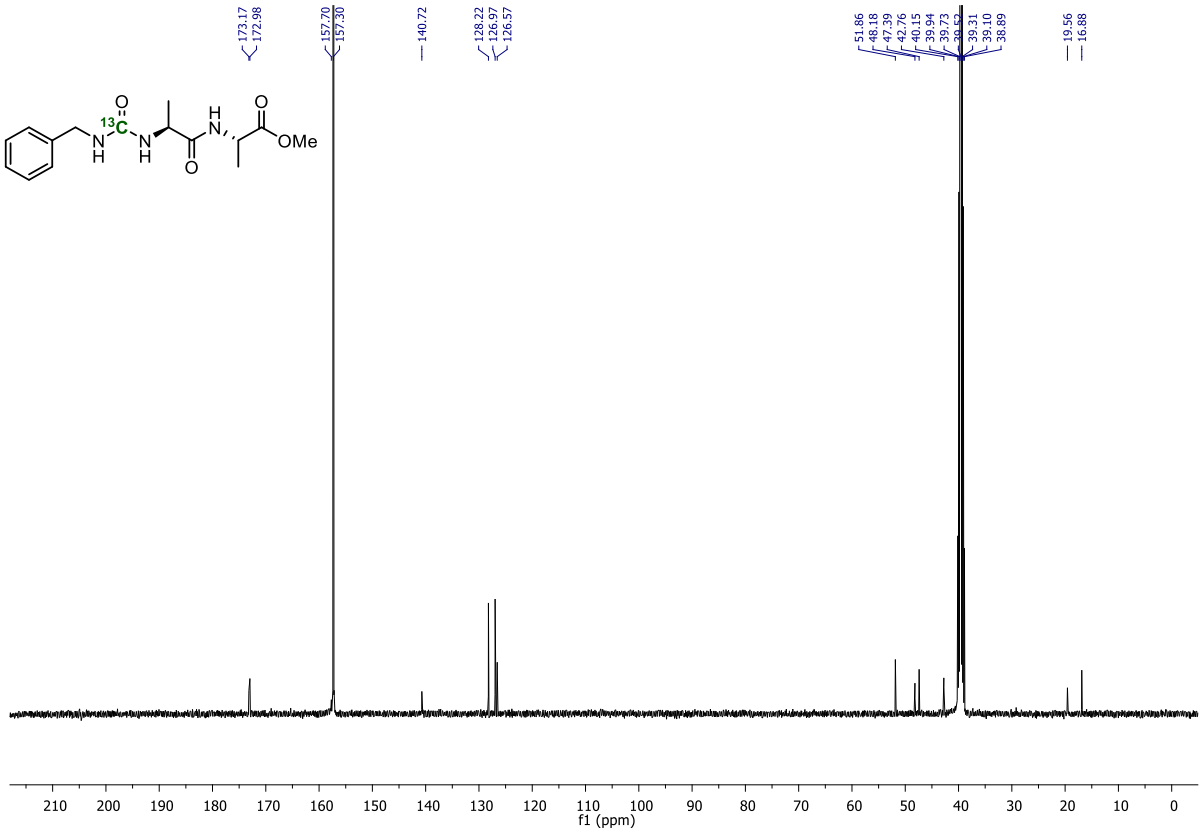
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]2**:



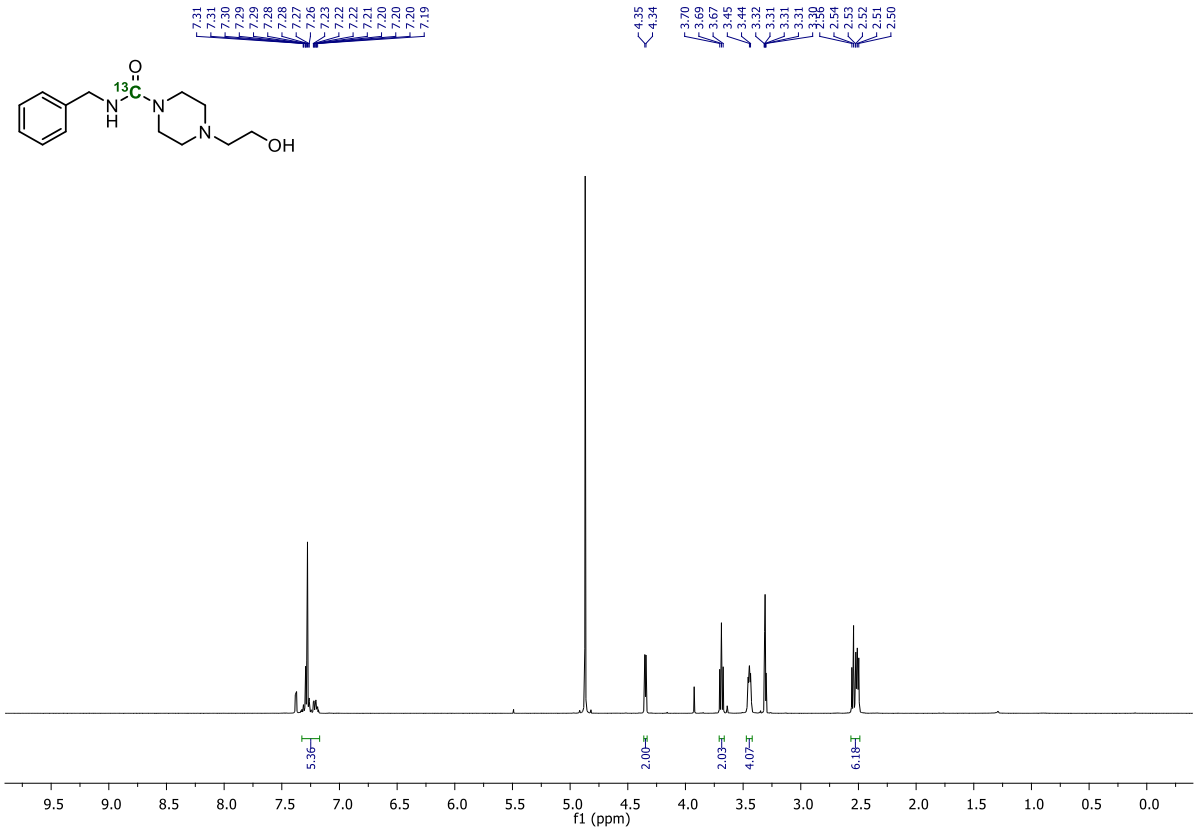
^{1}H NMR (400 MHz, DMSO-d$_6$) **[^{13}C]3**:



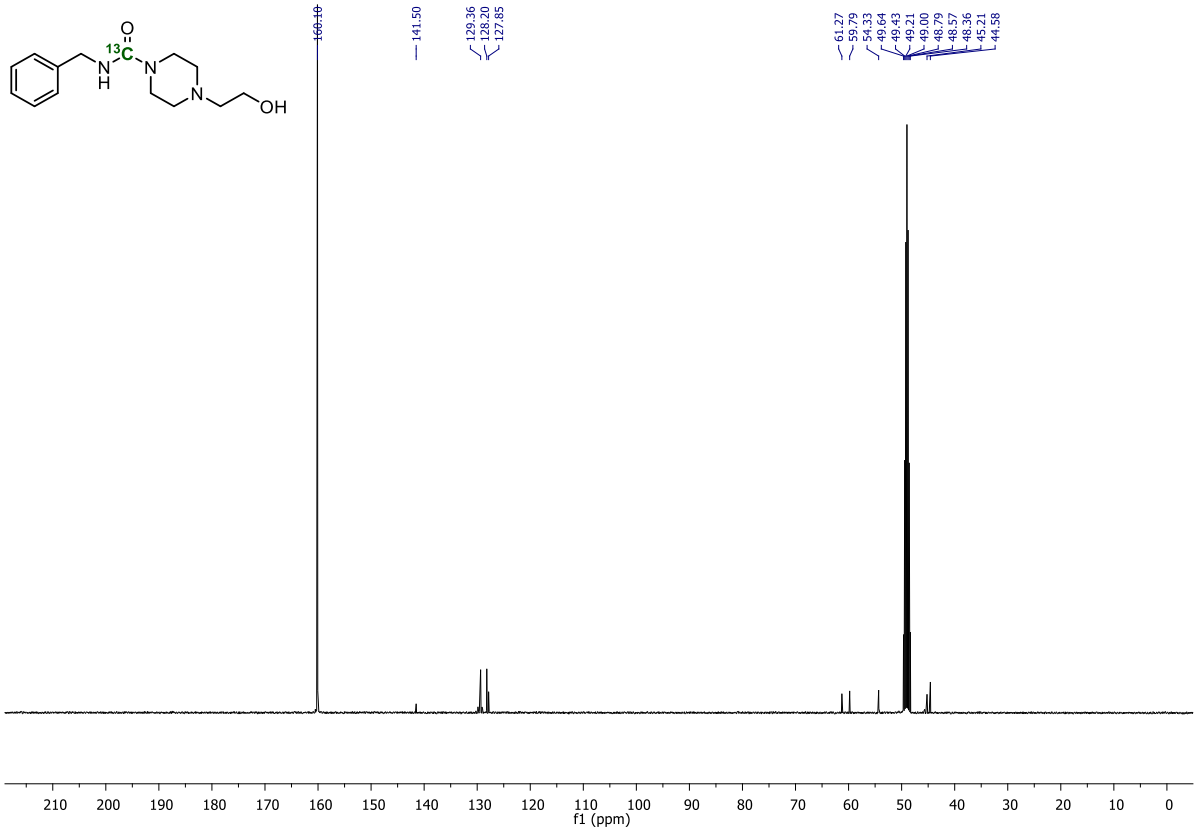
^{13}C NMR (100 MHz, DMSO-d$_6$) **[^{13}C]3**:



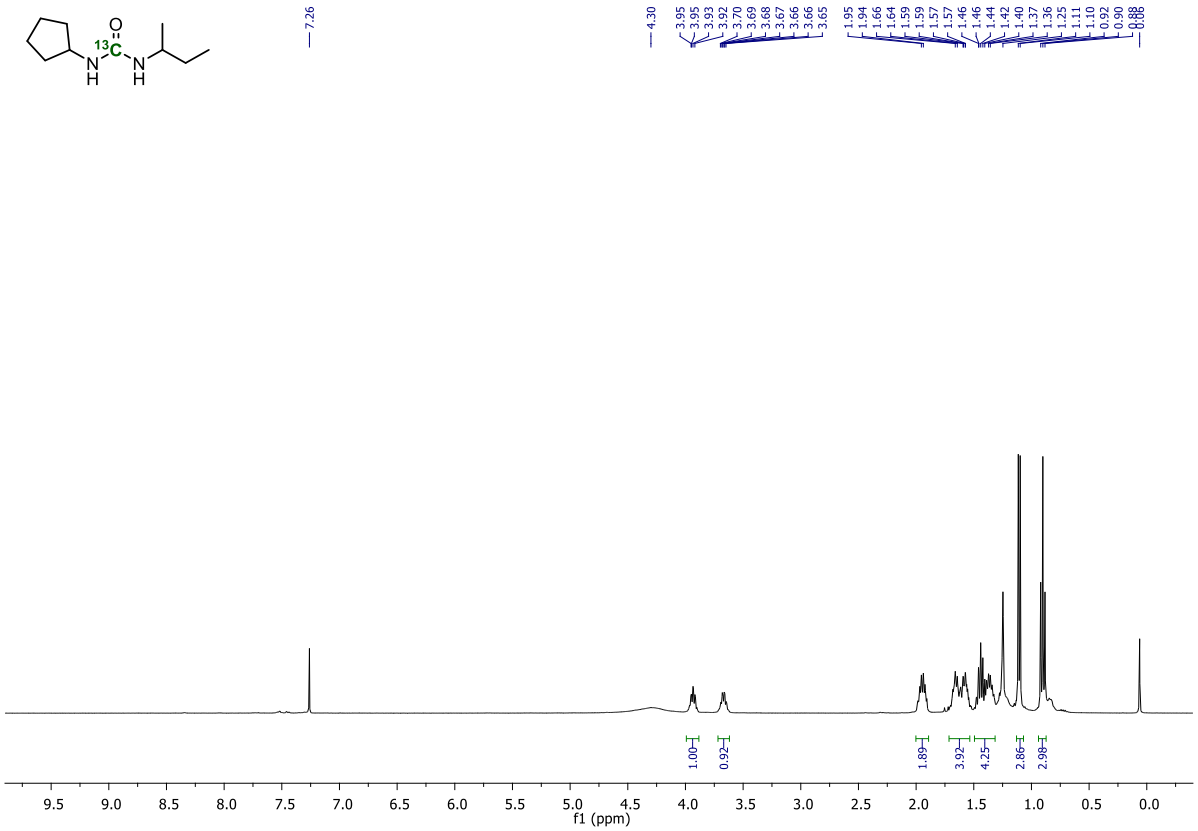
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]4**:



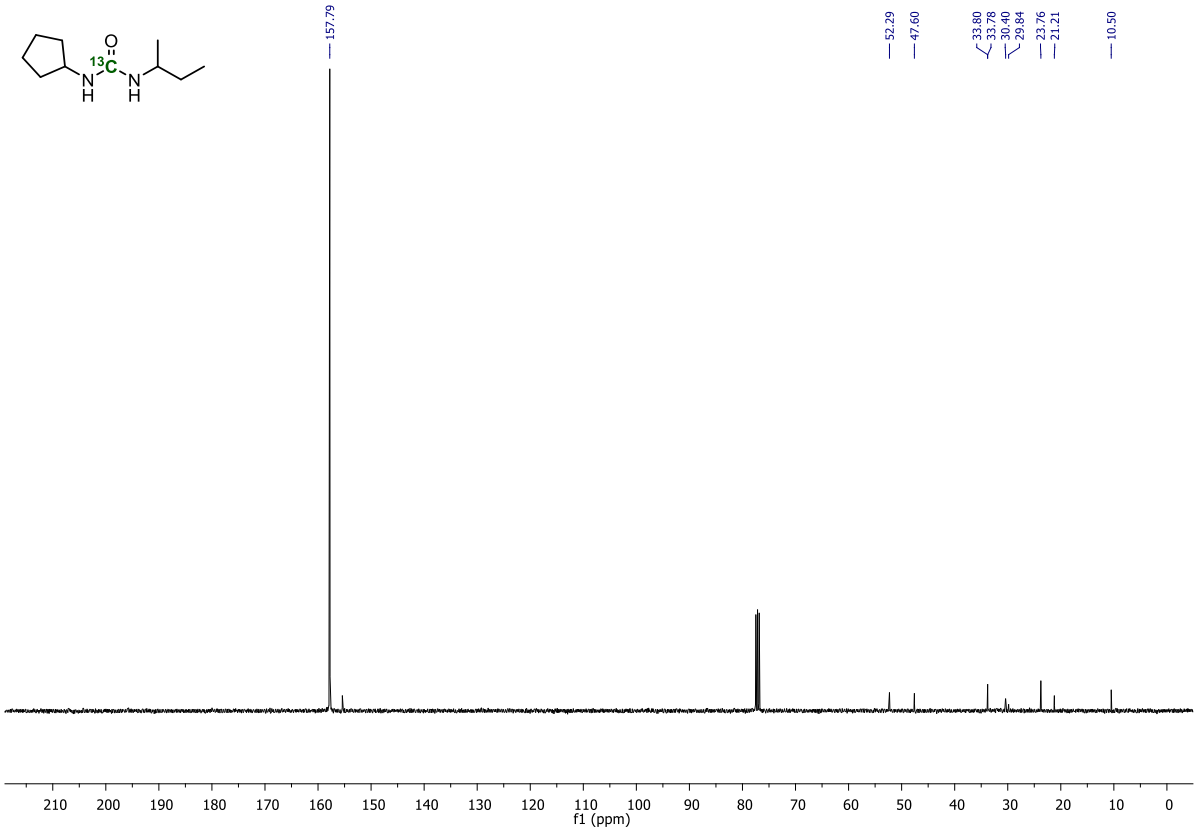
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]4**:



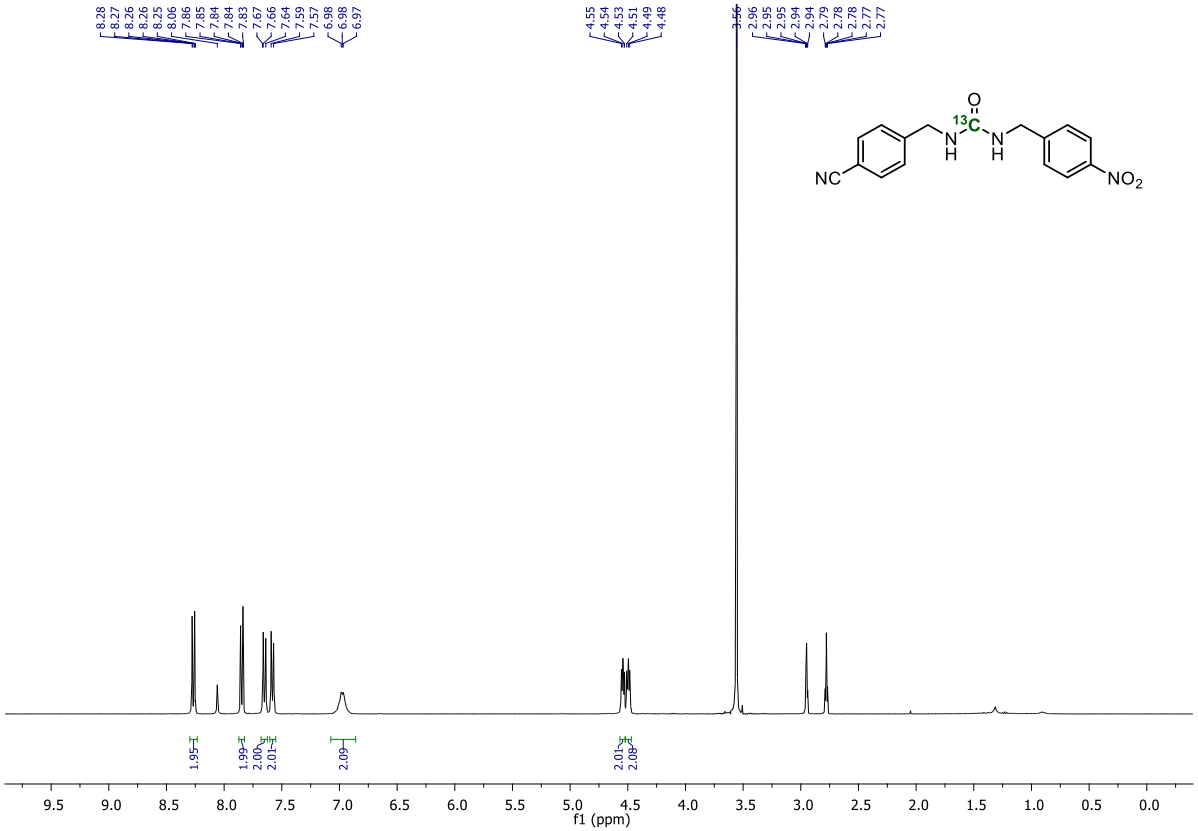
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]5**:



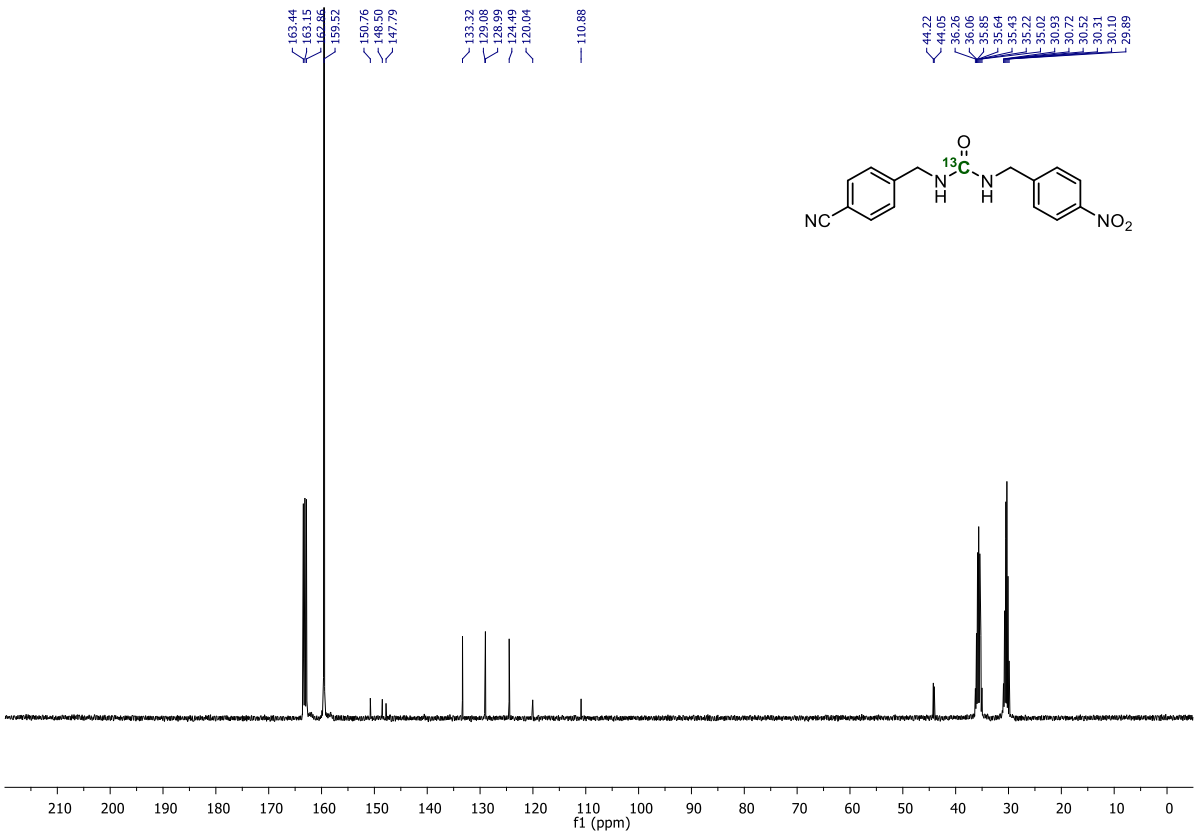
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]5**:



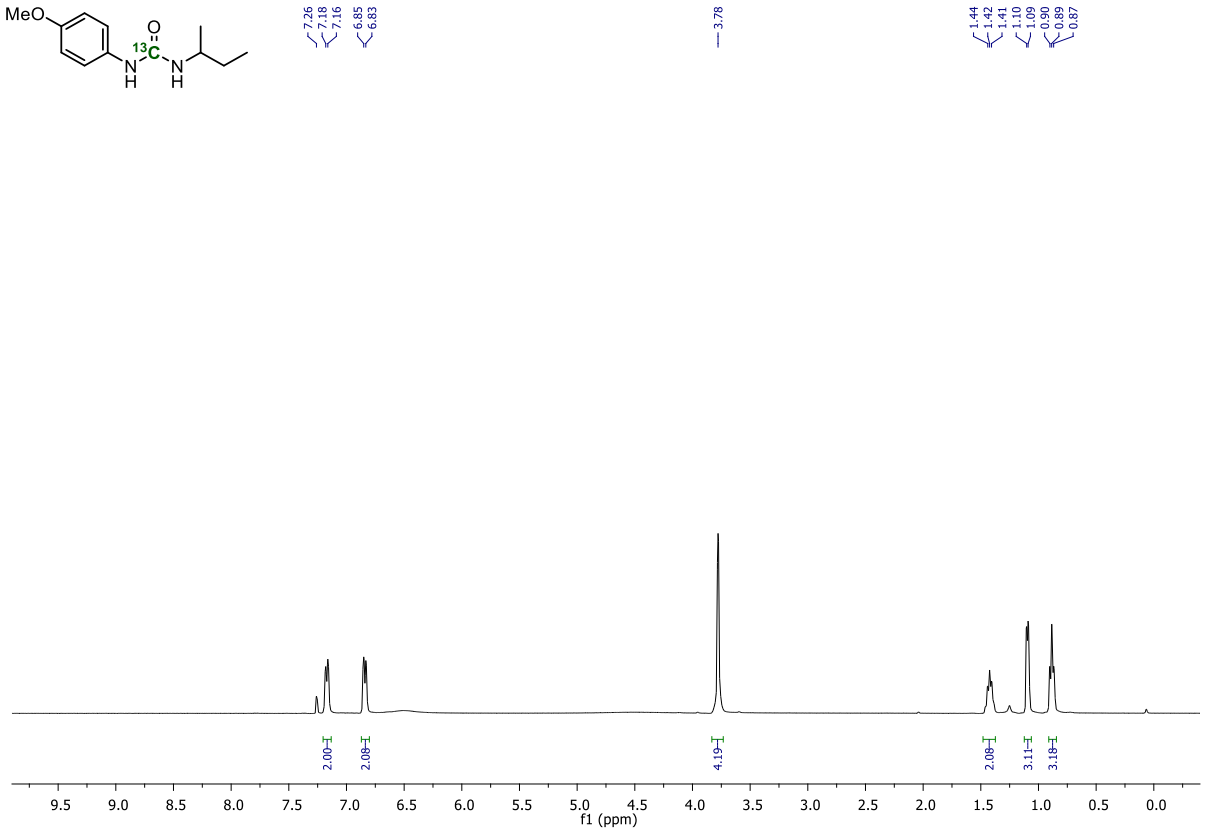
^{1}H NMR (400 MHz, DMF-d_7) **[^{13}C]6**:



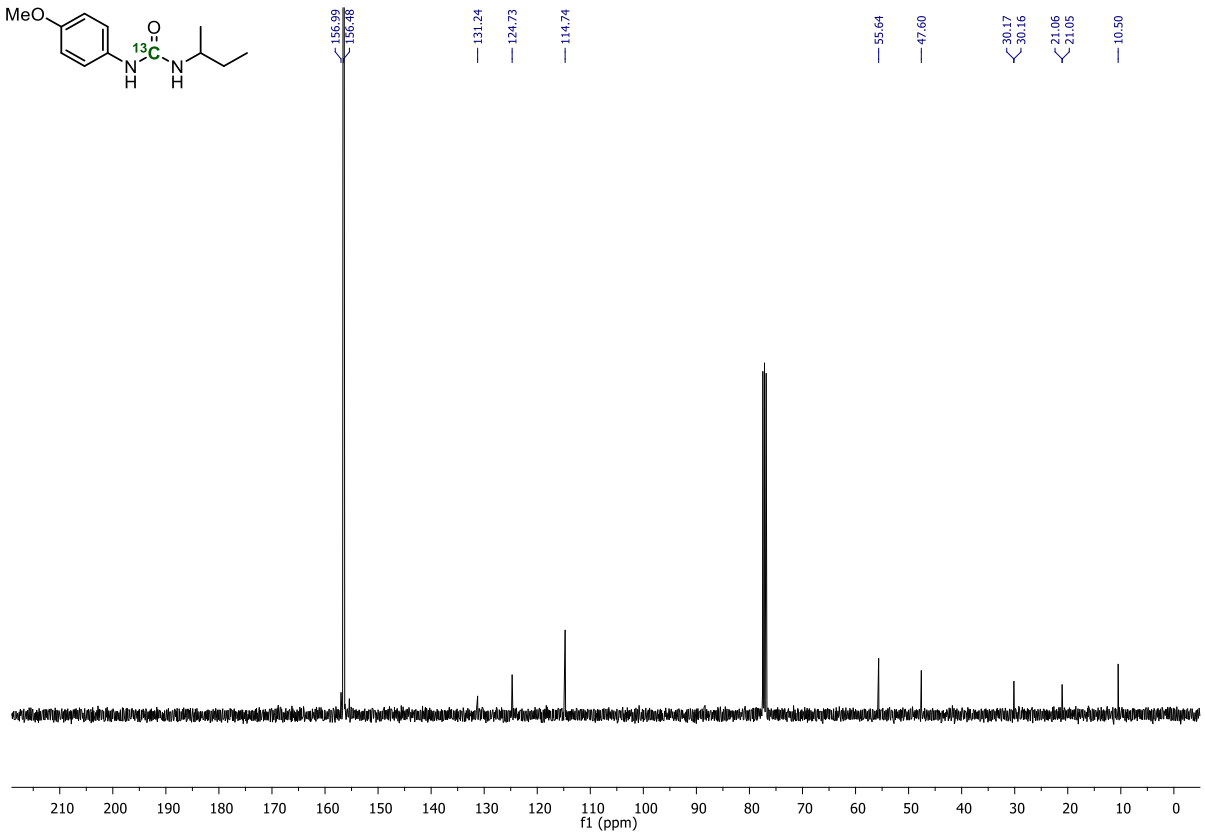
^{13}C NMR (100 MHz, DMF-d_7) **[^{13}C]6**:



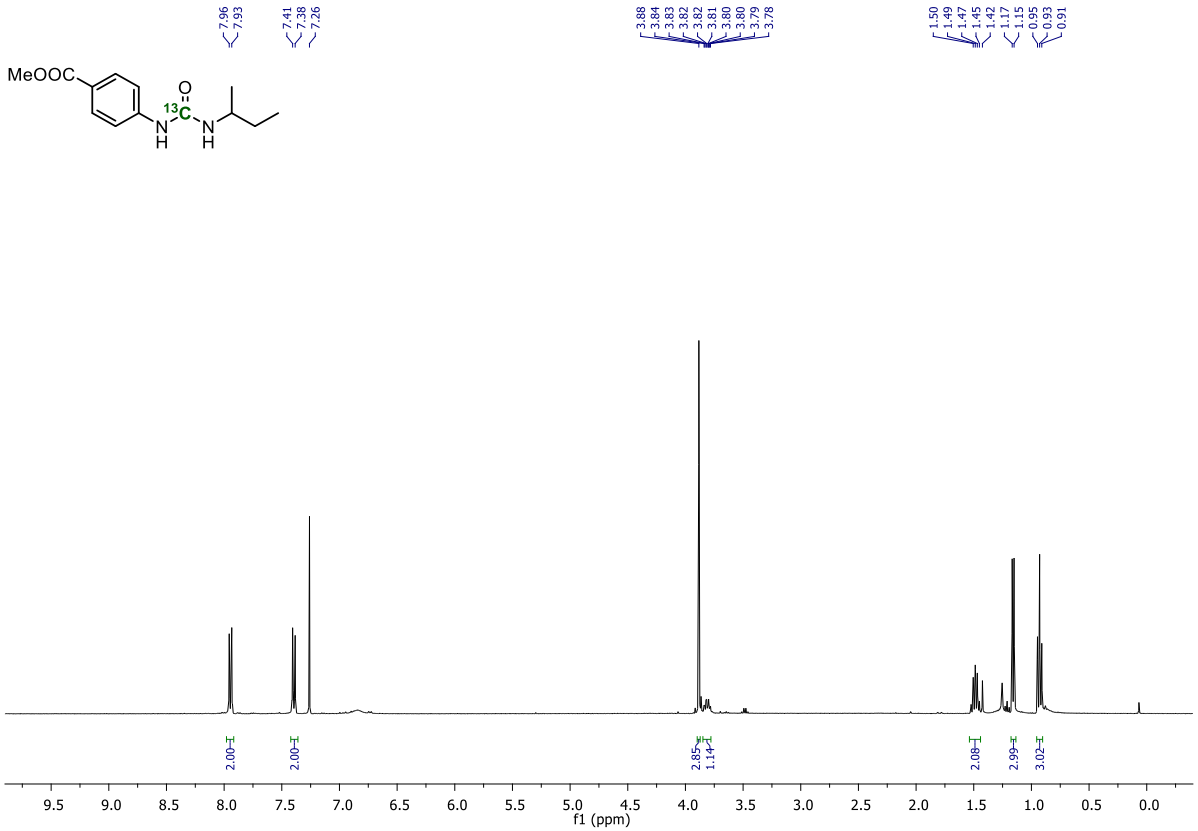
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]7**:



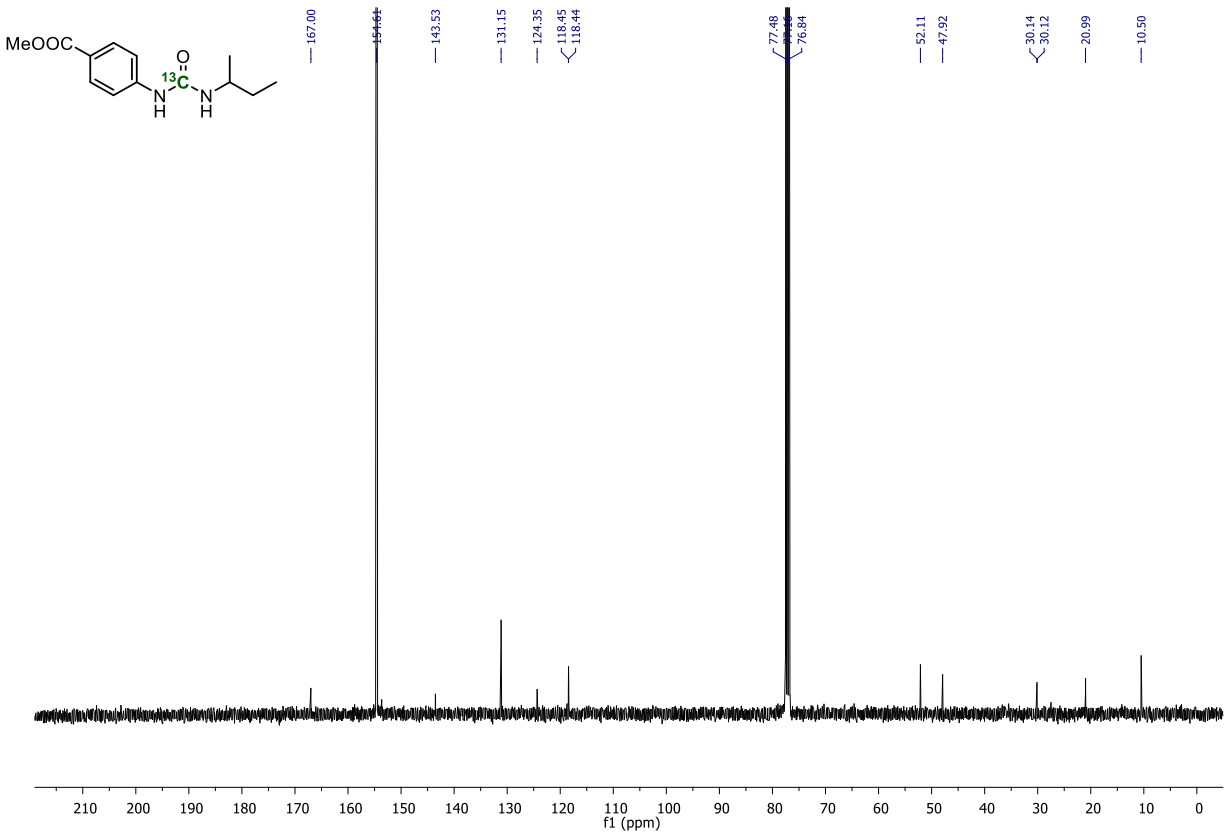
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]7**:



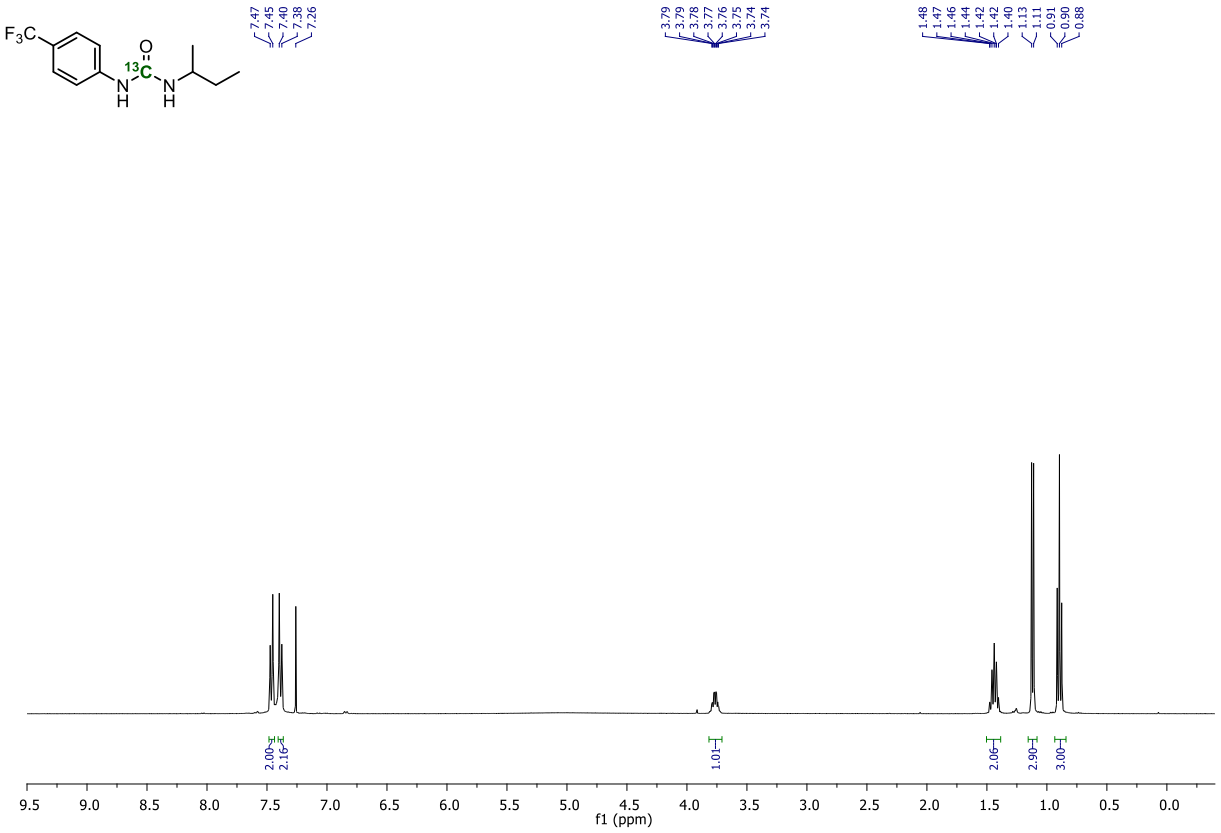
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]8**:



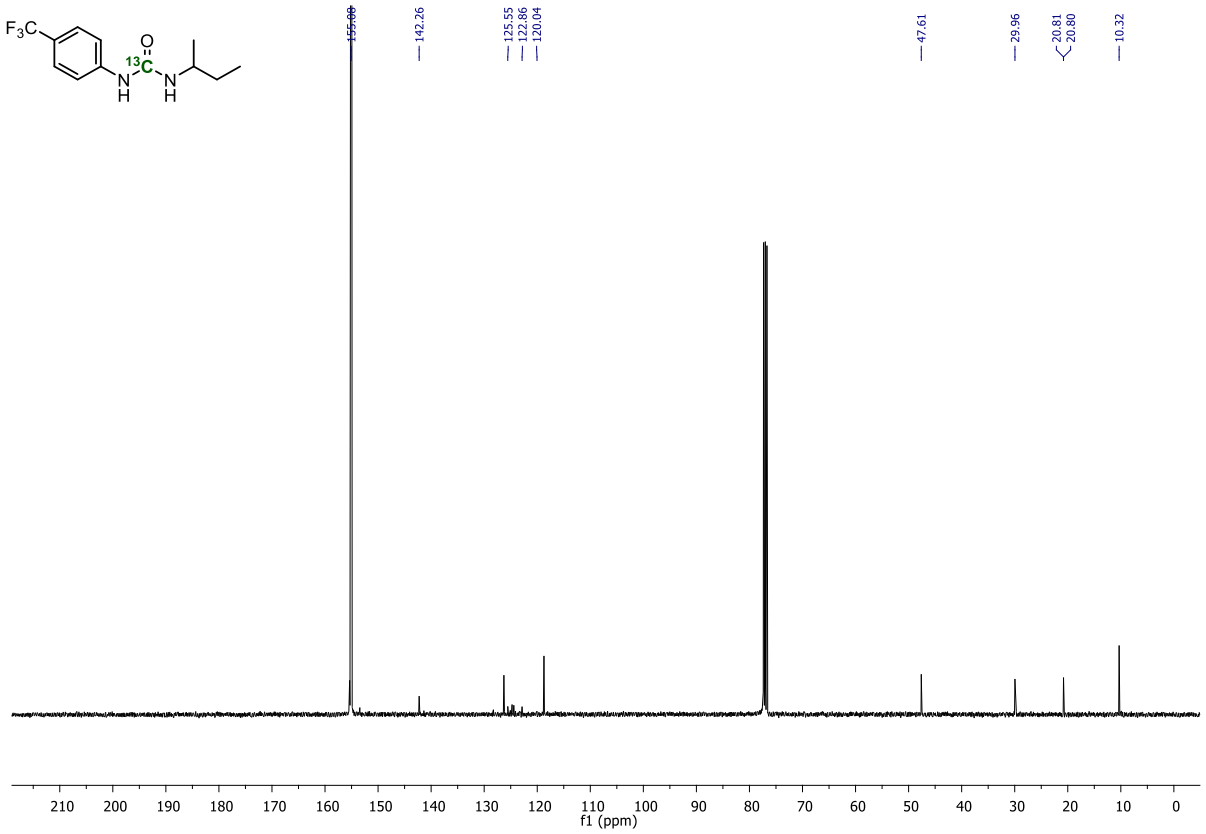
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]8**:



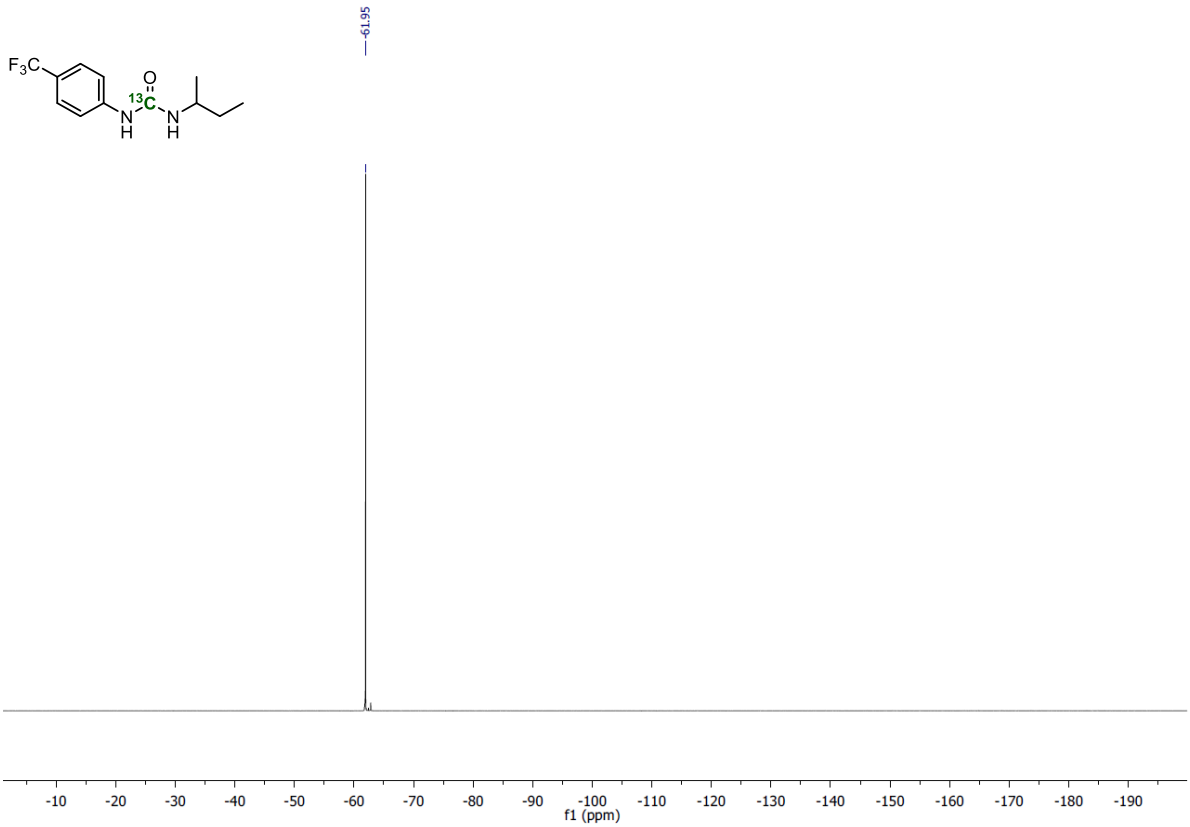
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]9**:



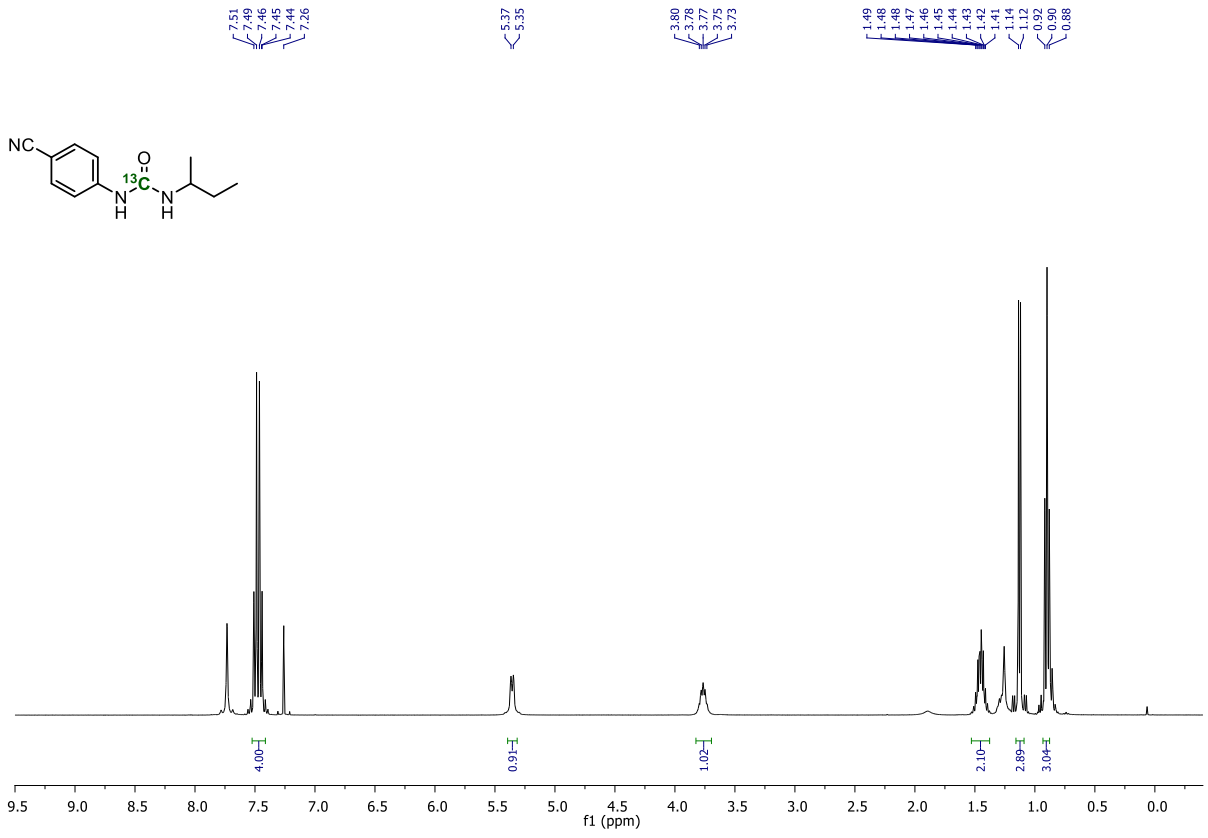
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]9**:



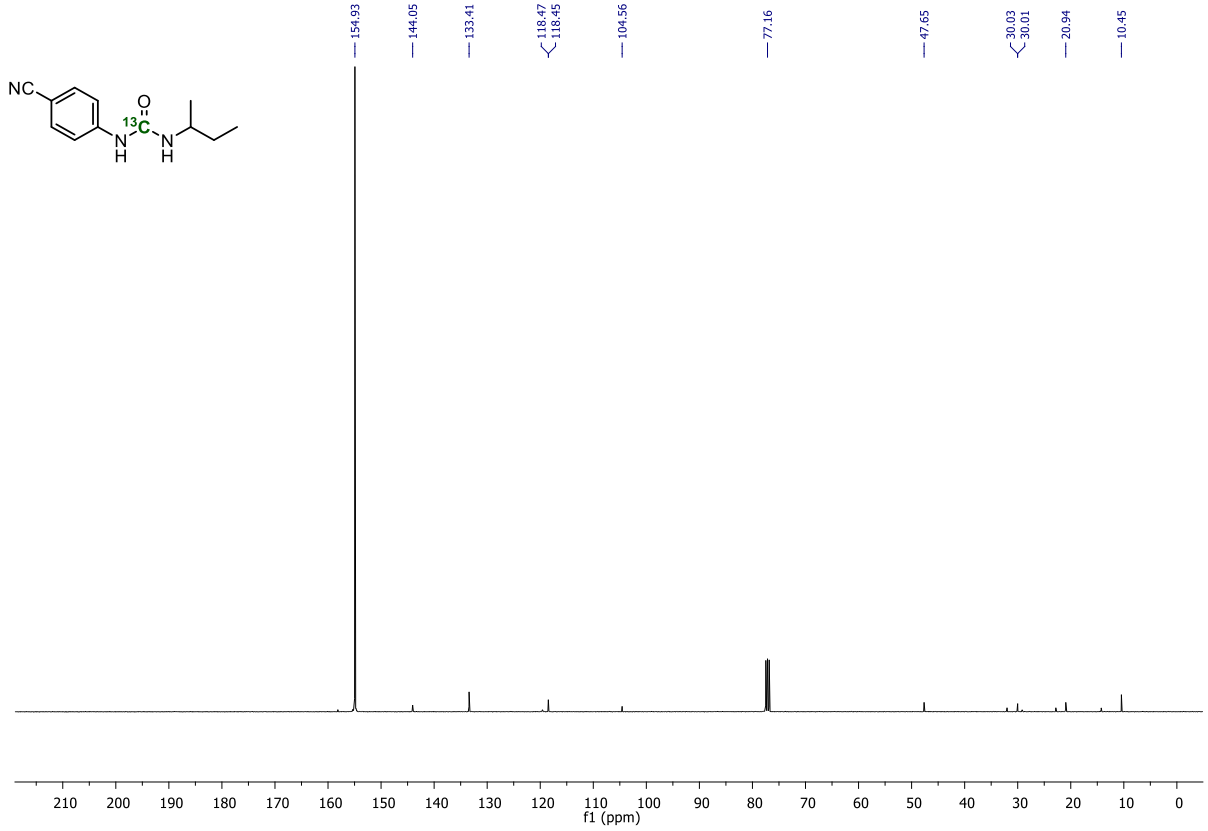
^{19}F NMR (376 MHz, $CDCl_3$) **[^{13}C]9**



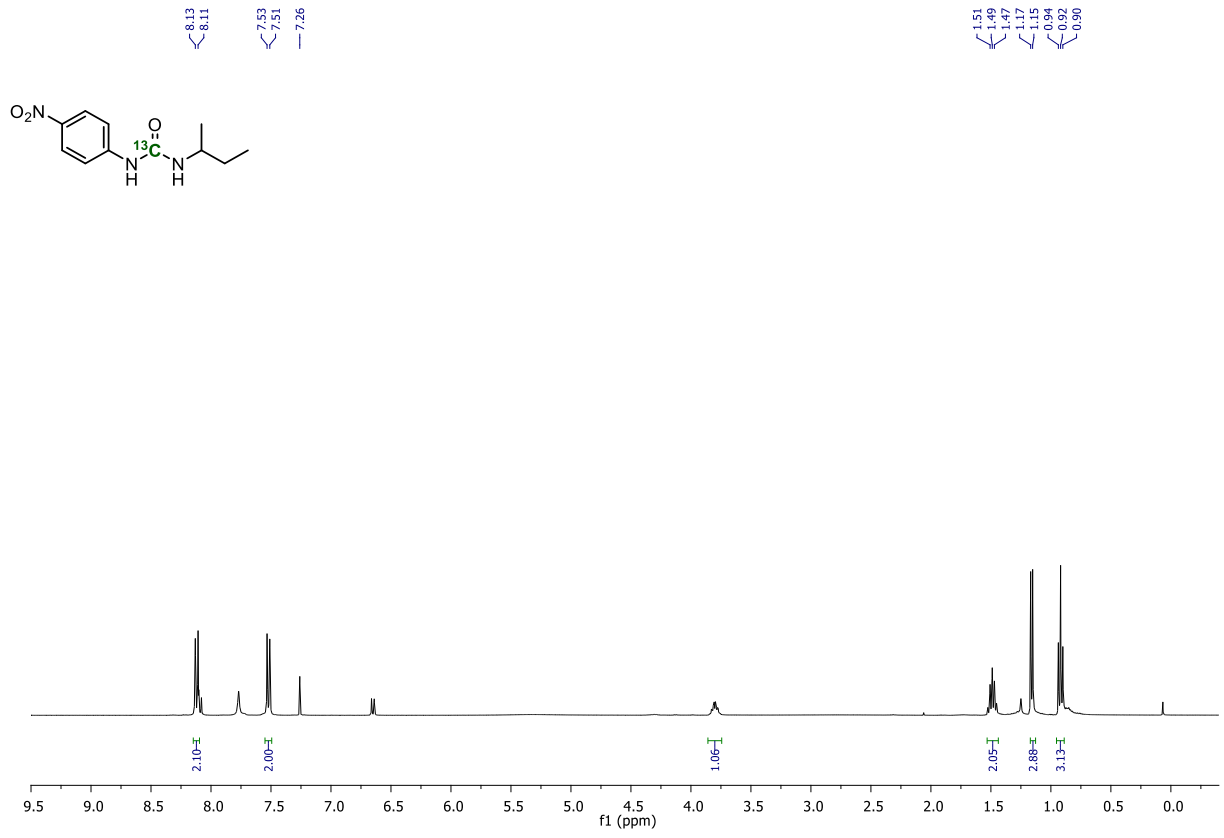
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]10**:



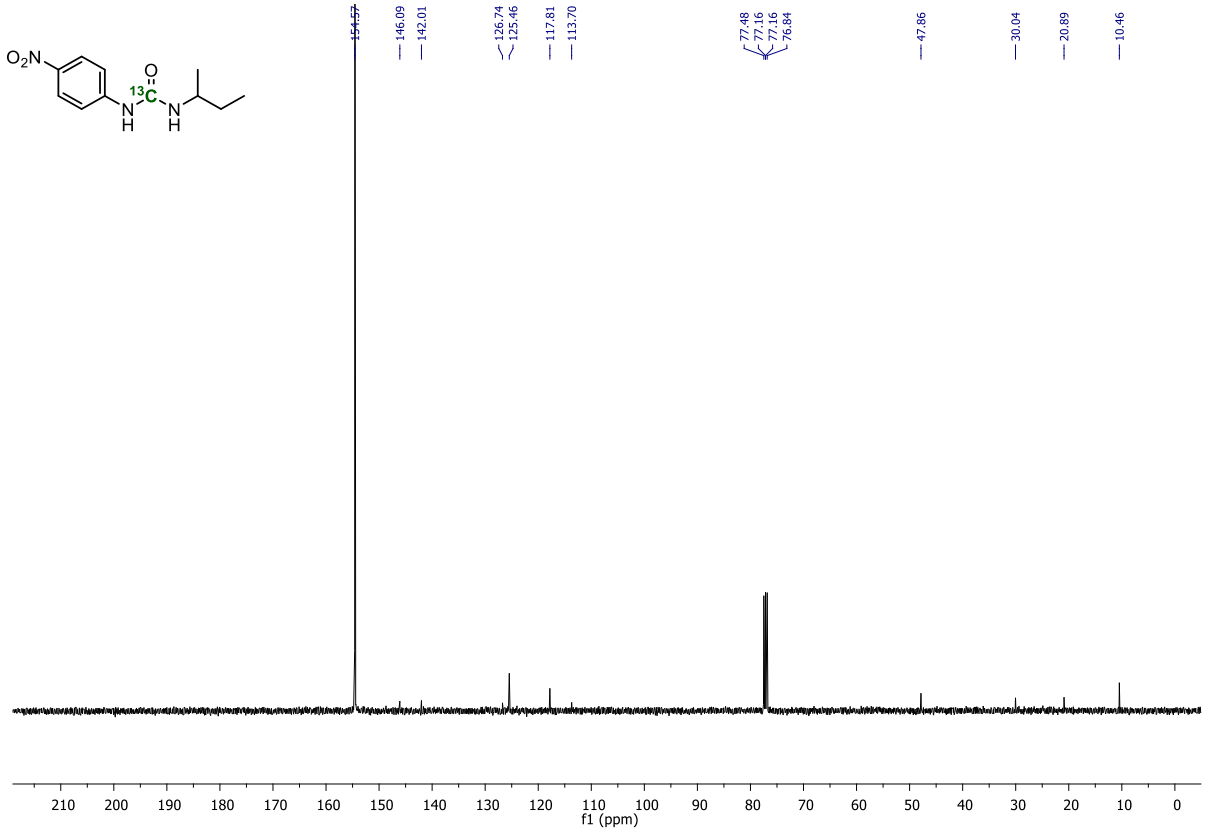
^{13}C NMR (400 MHz, $CDCl_3$) **[^{13}C]10**:



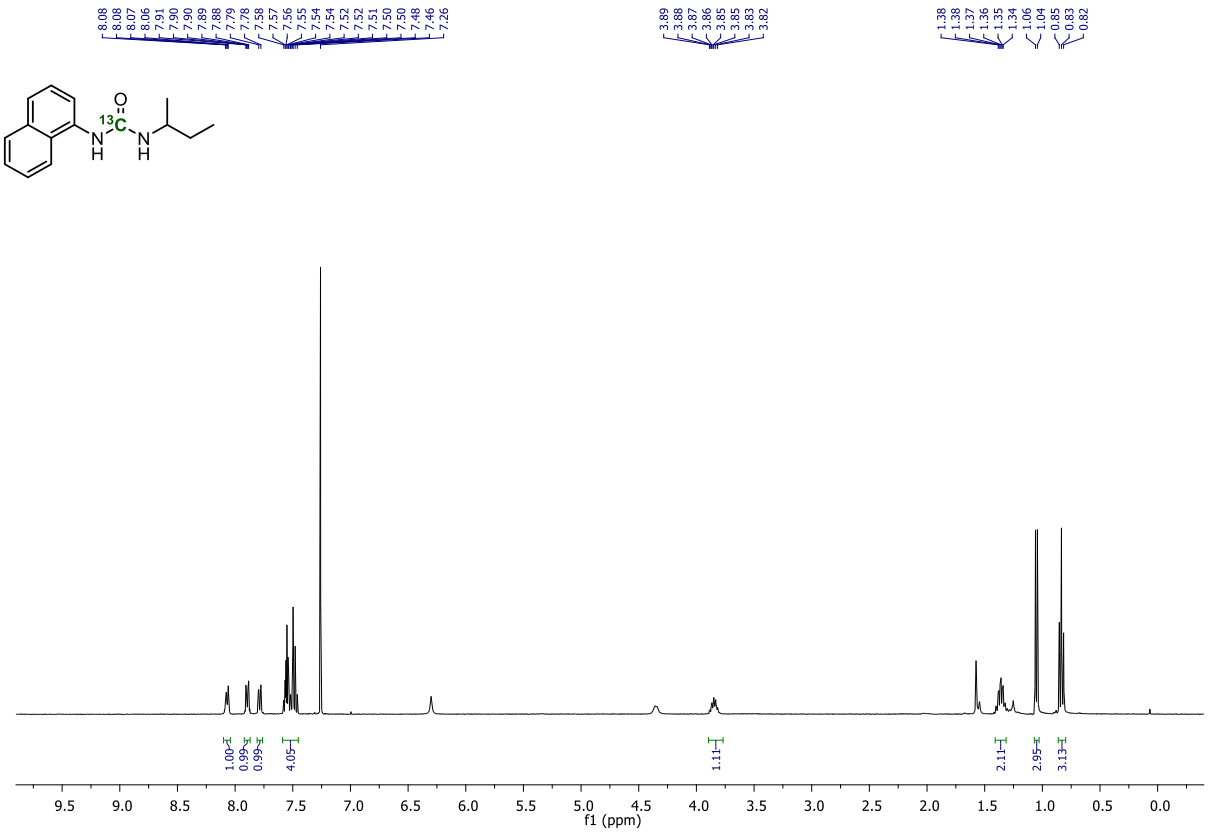
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]11**:



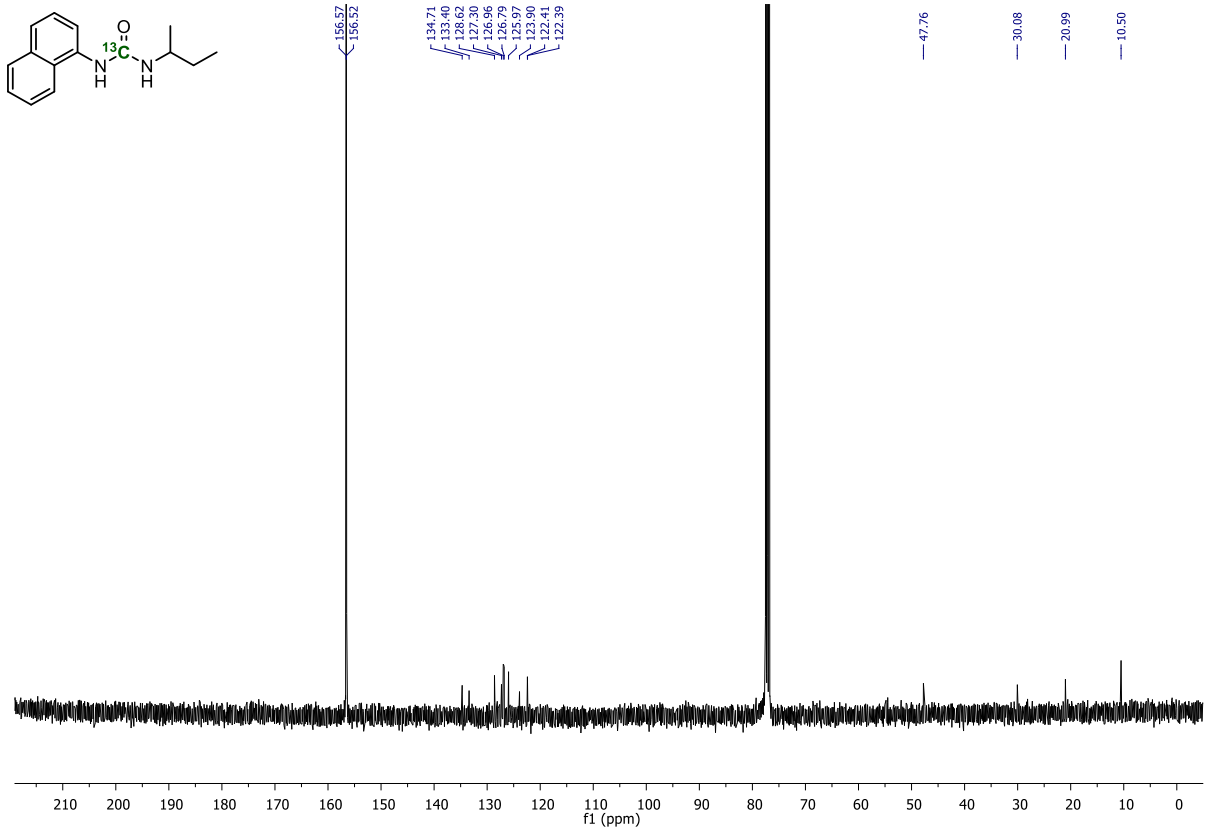
^{13}C NMR (400 MHz, $CDCl_3$) **[^{13}C]11**:



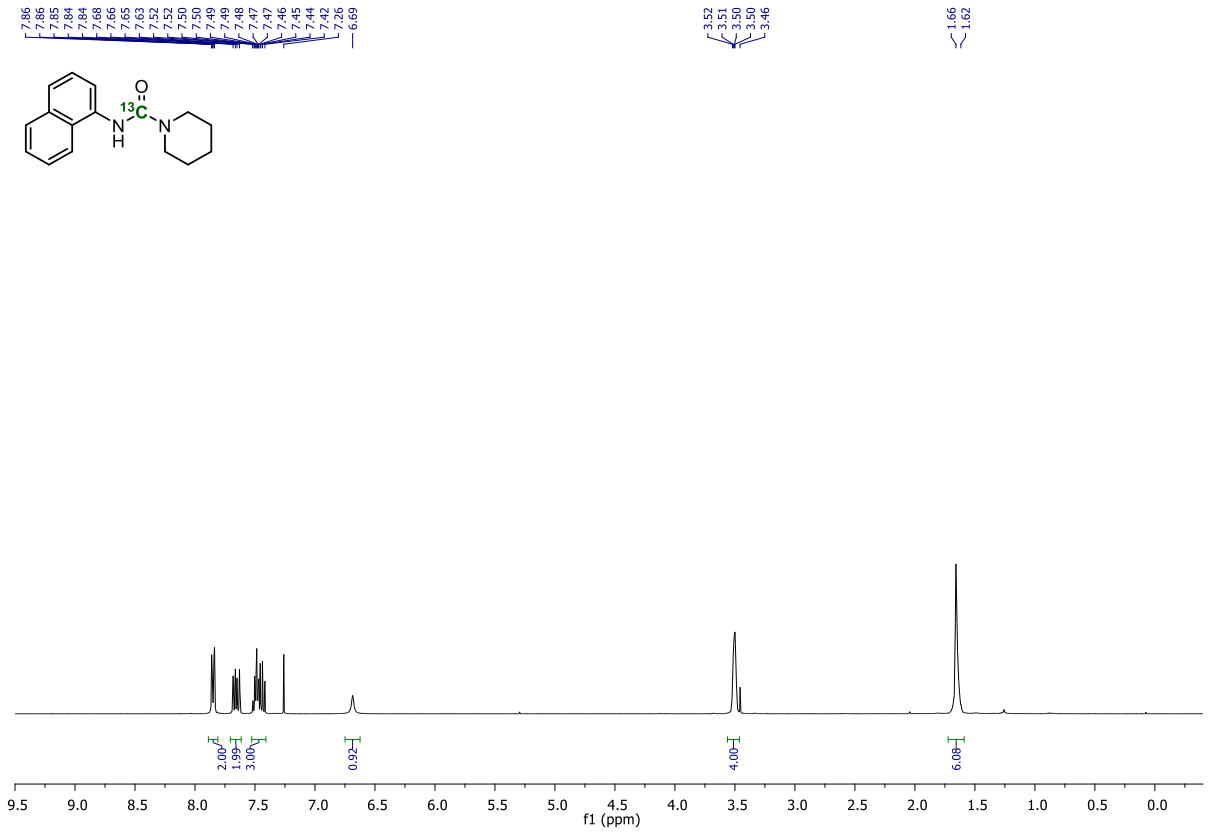
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]12**:



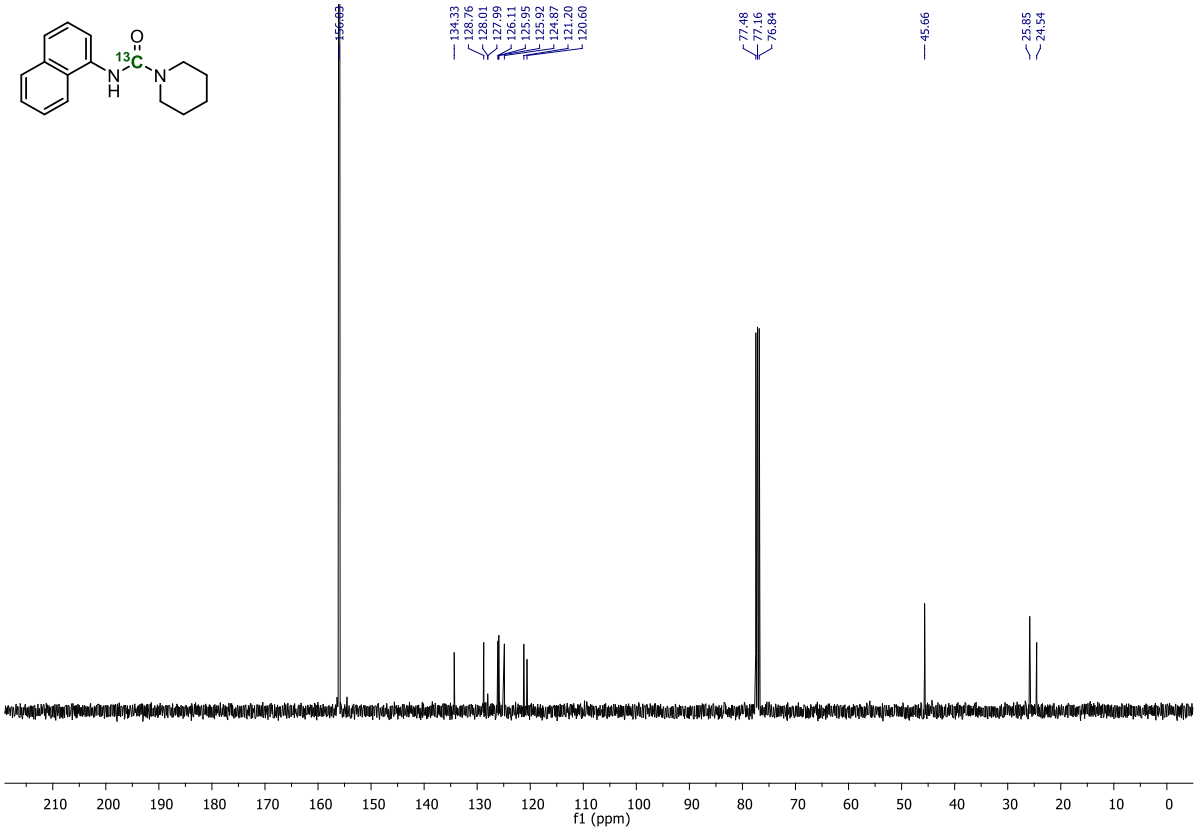
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]12**:



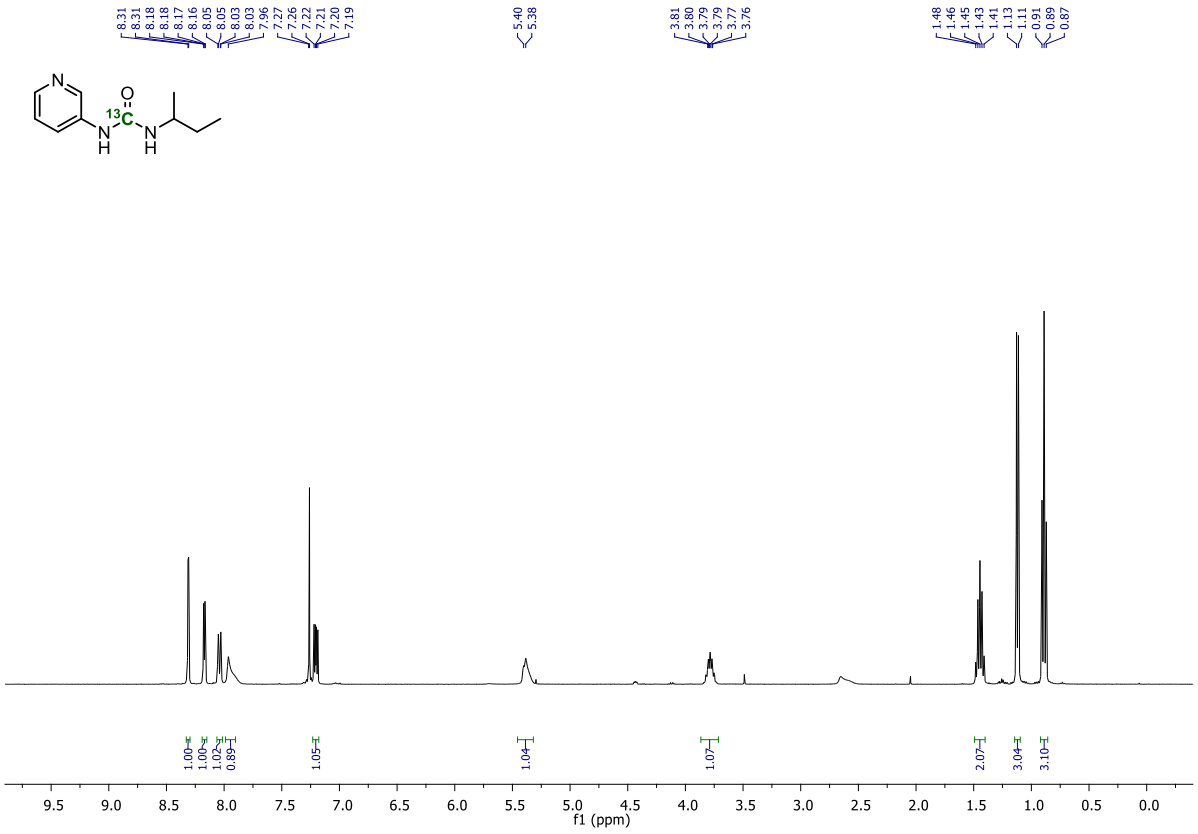
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]13**:



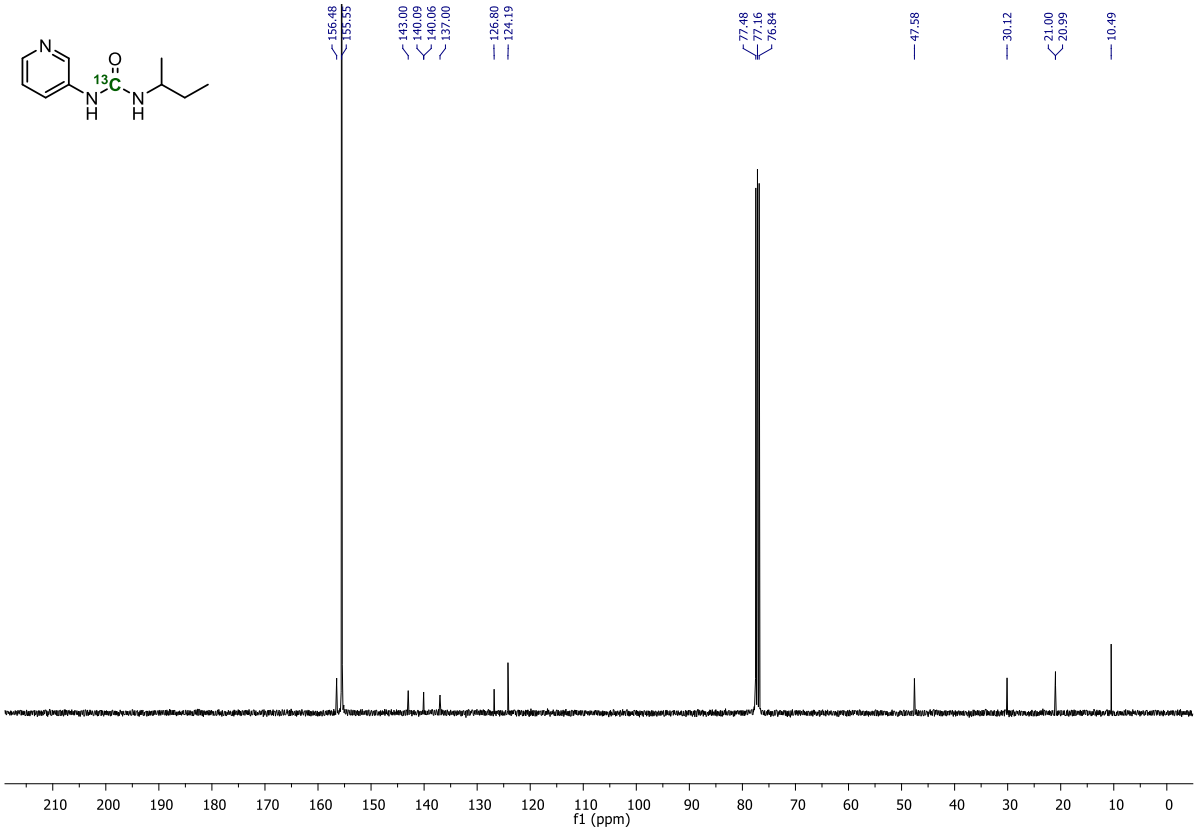
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]13**:



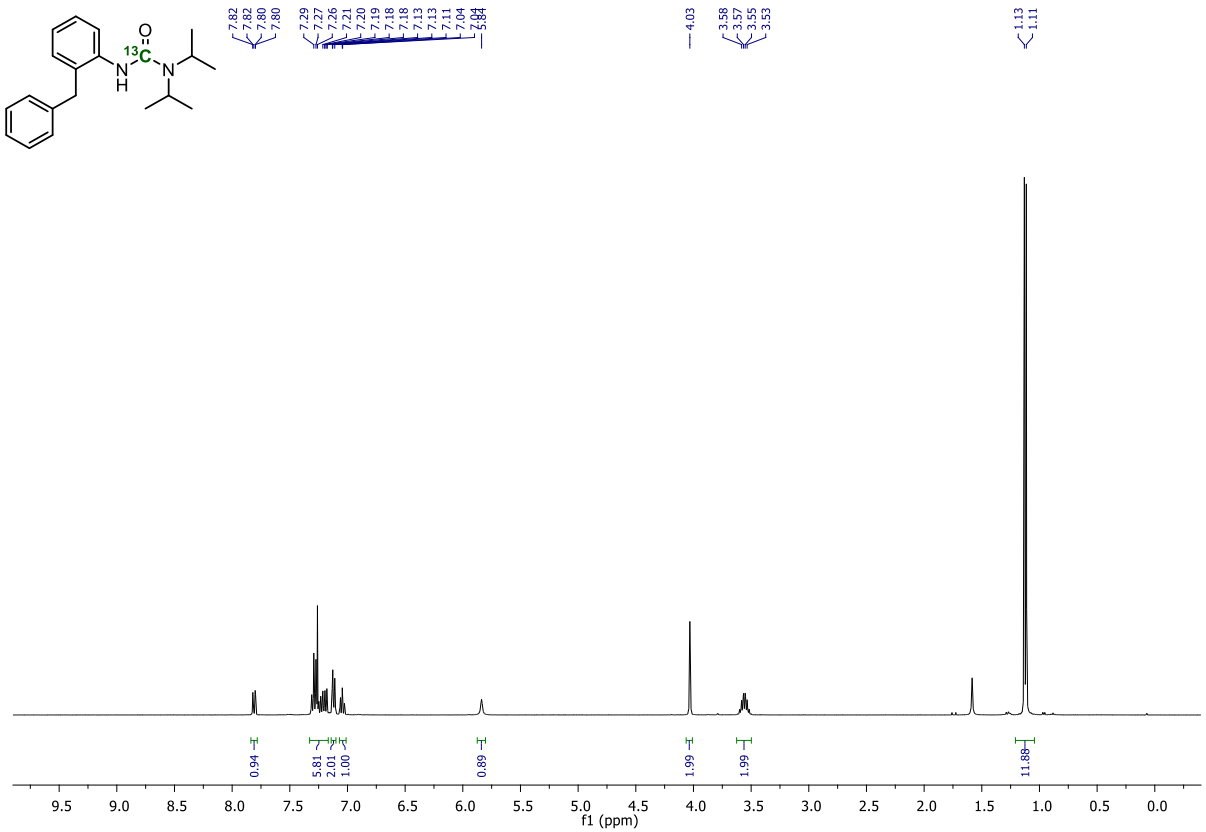
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]14**:



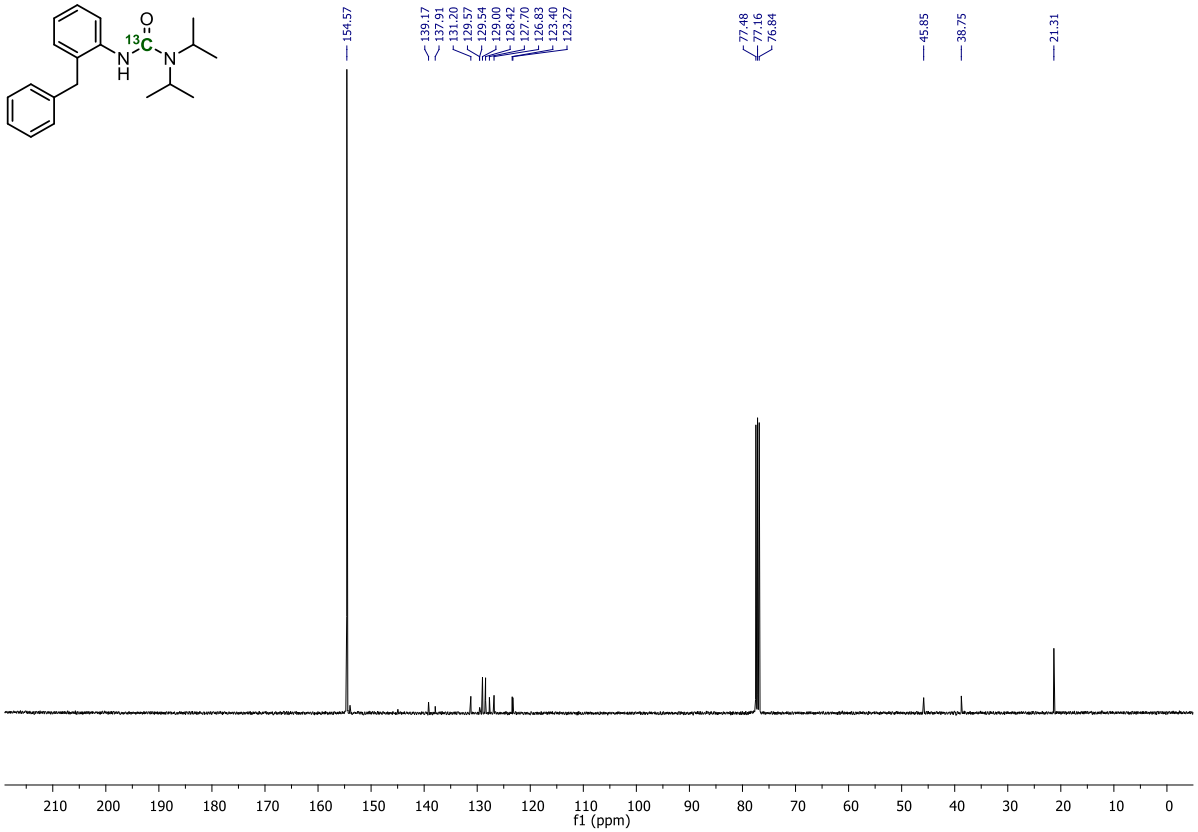
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]14**:



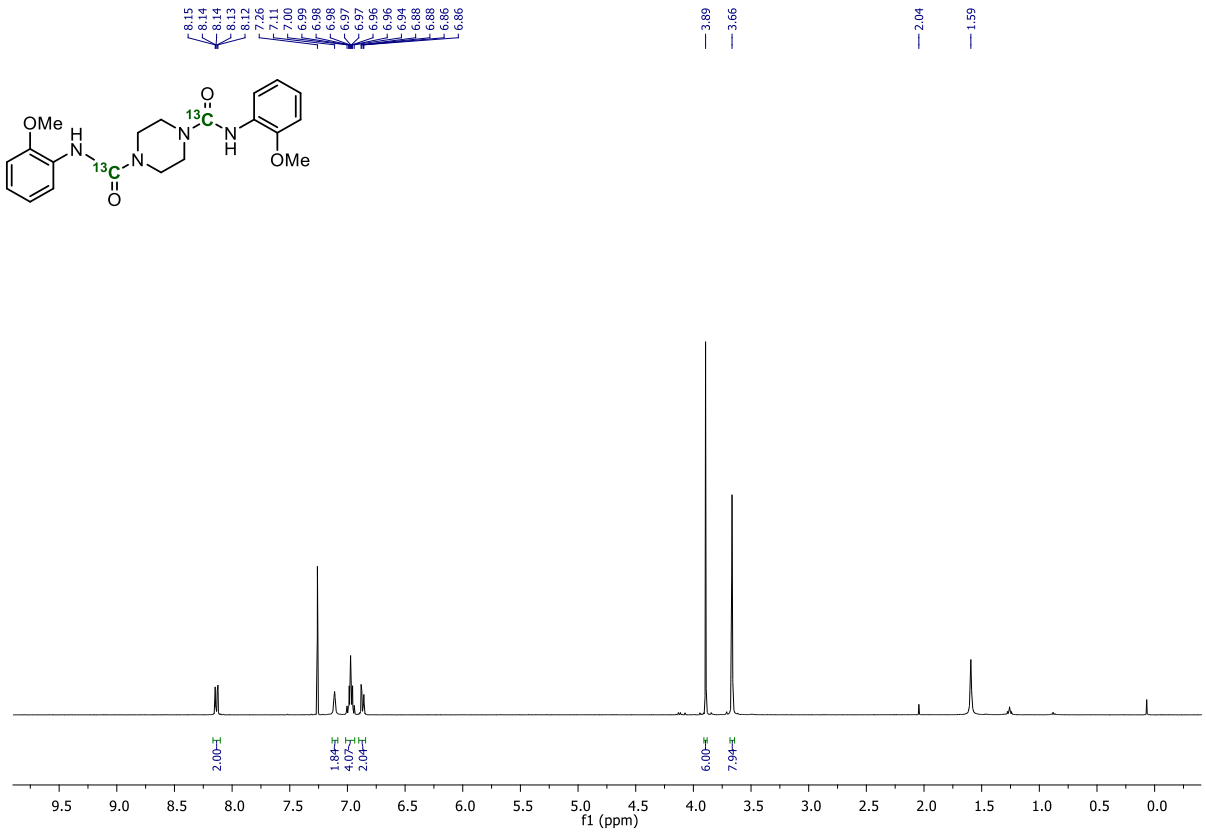
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]15**:



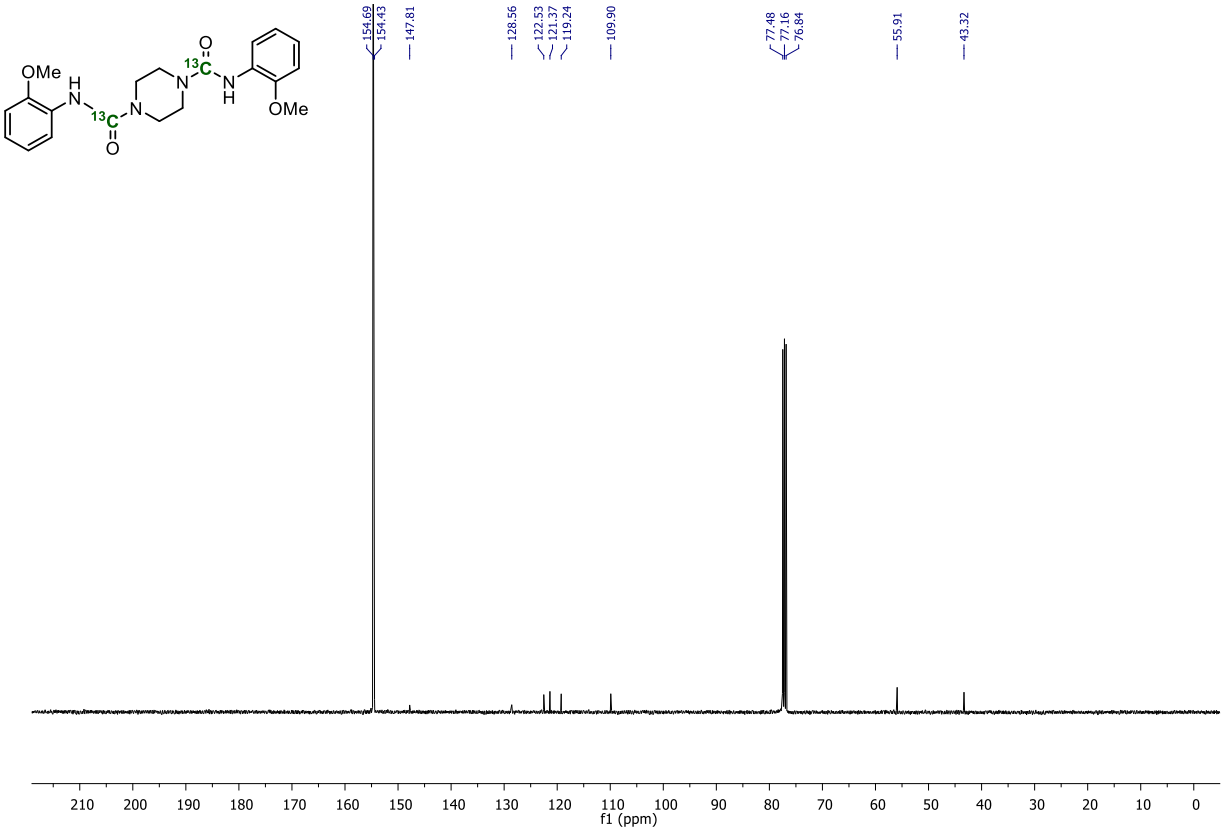
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]15**:



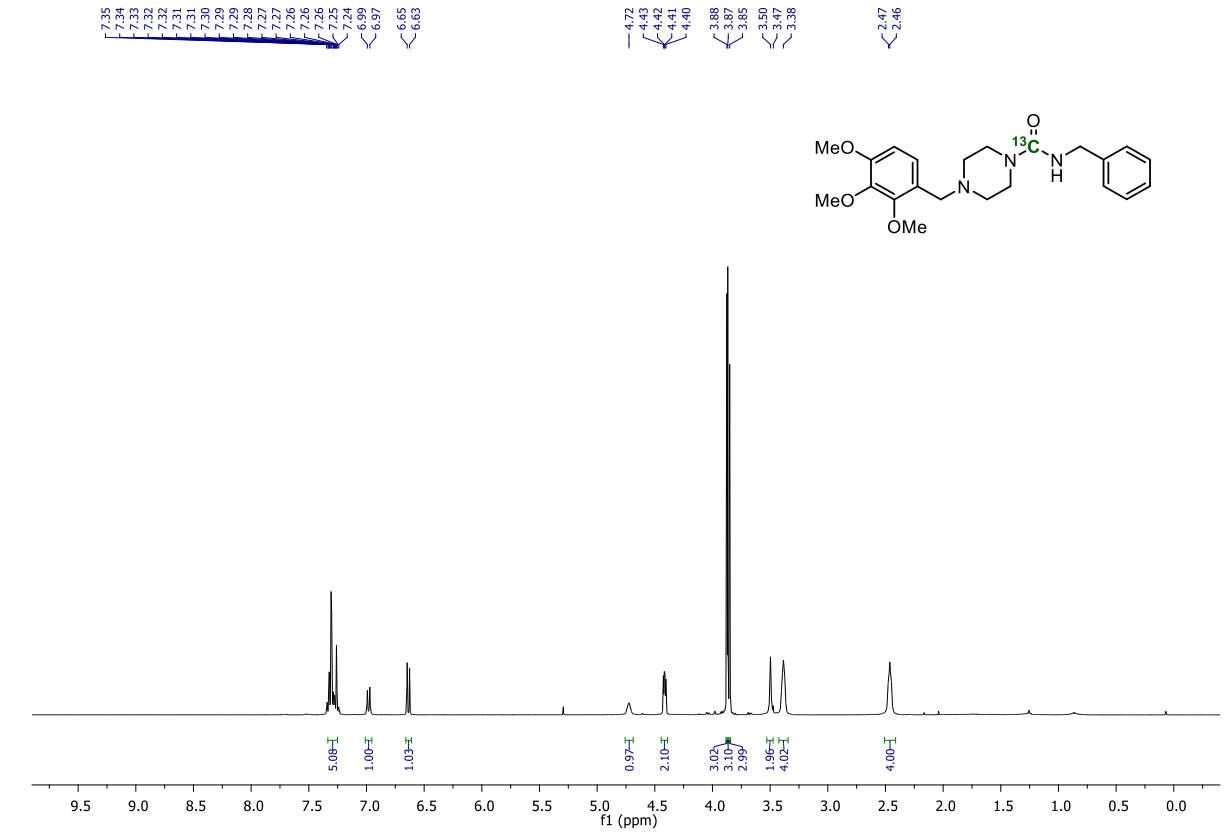
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]16**:



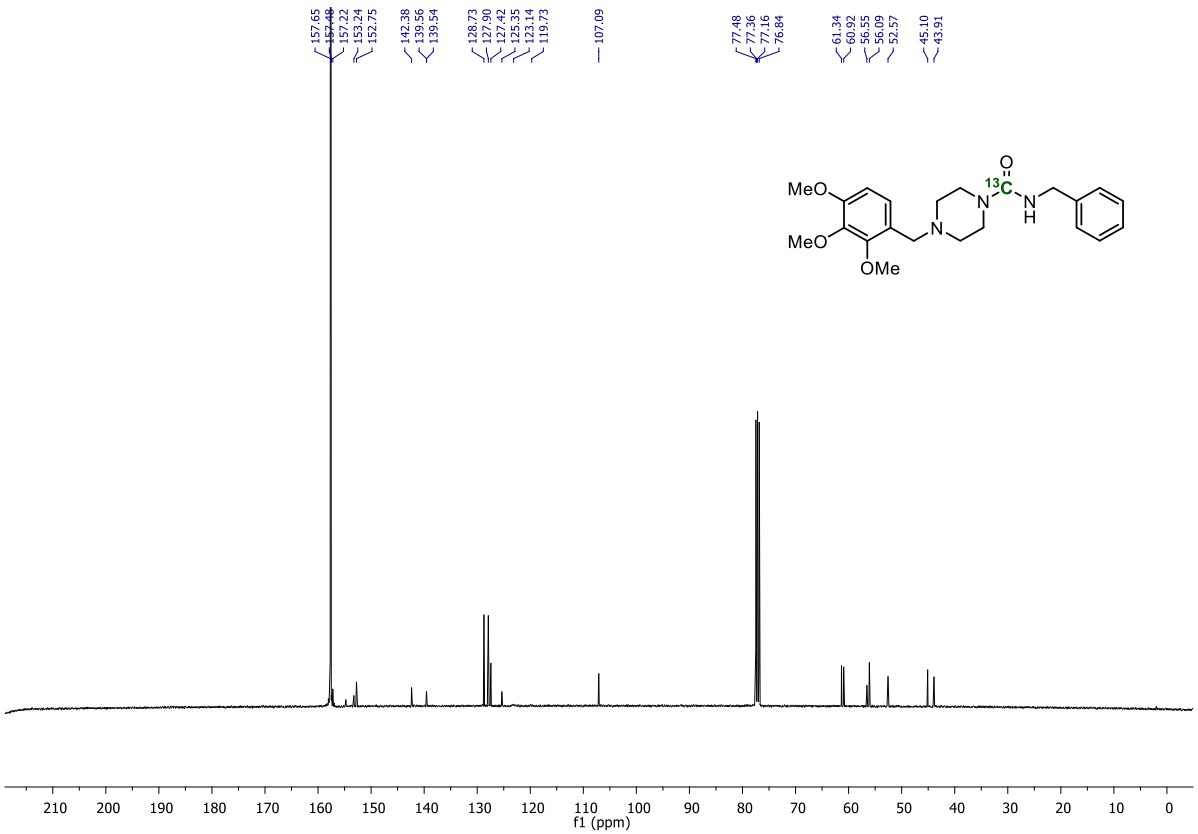
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]16**:



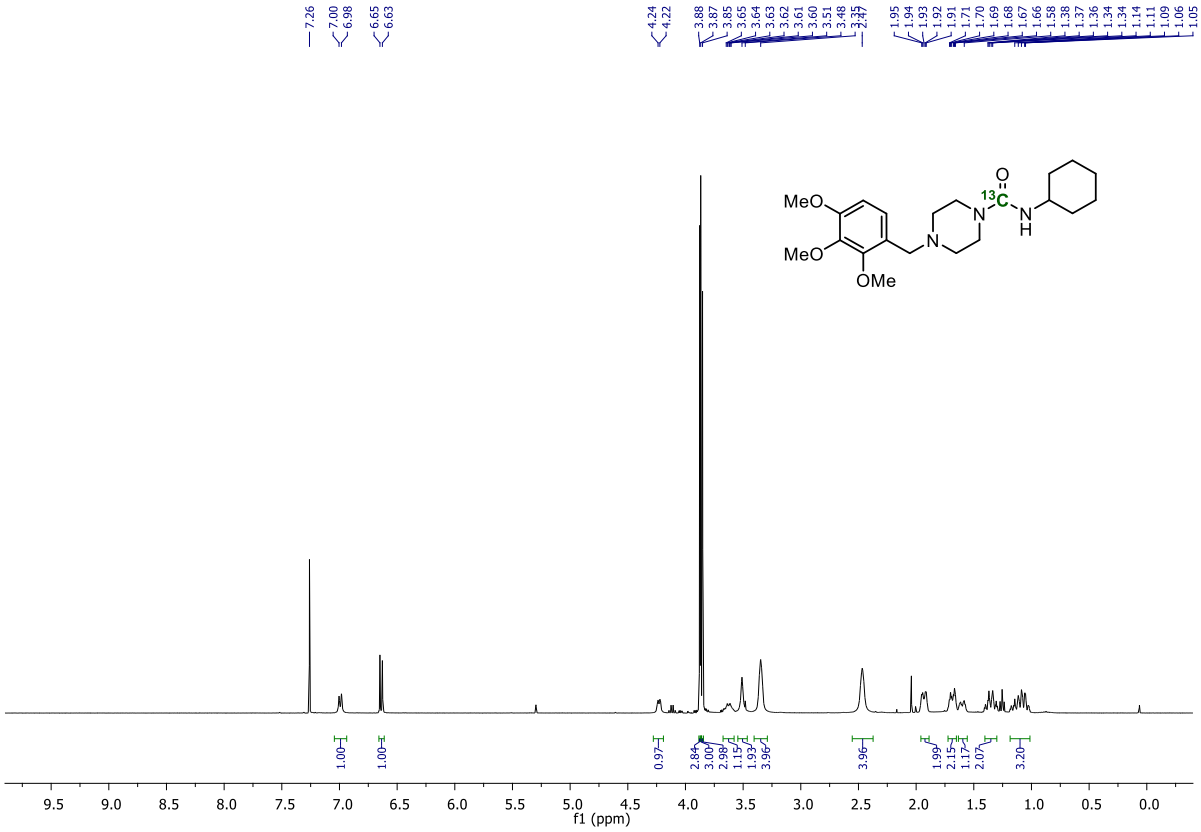
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]17**:



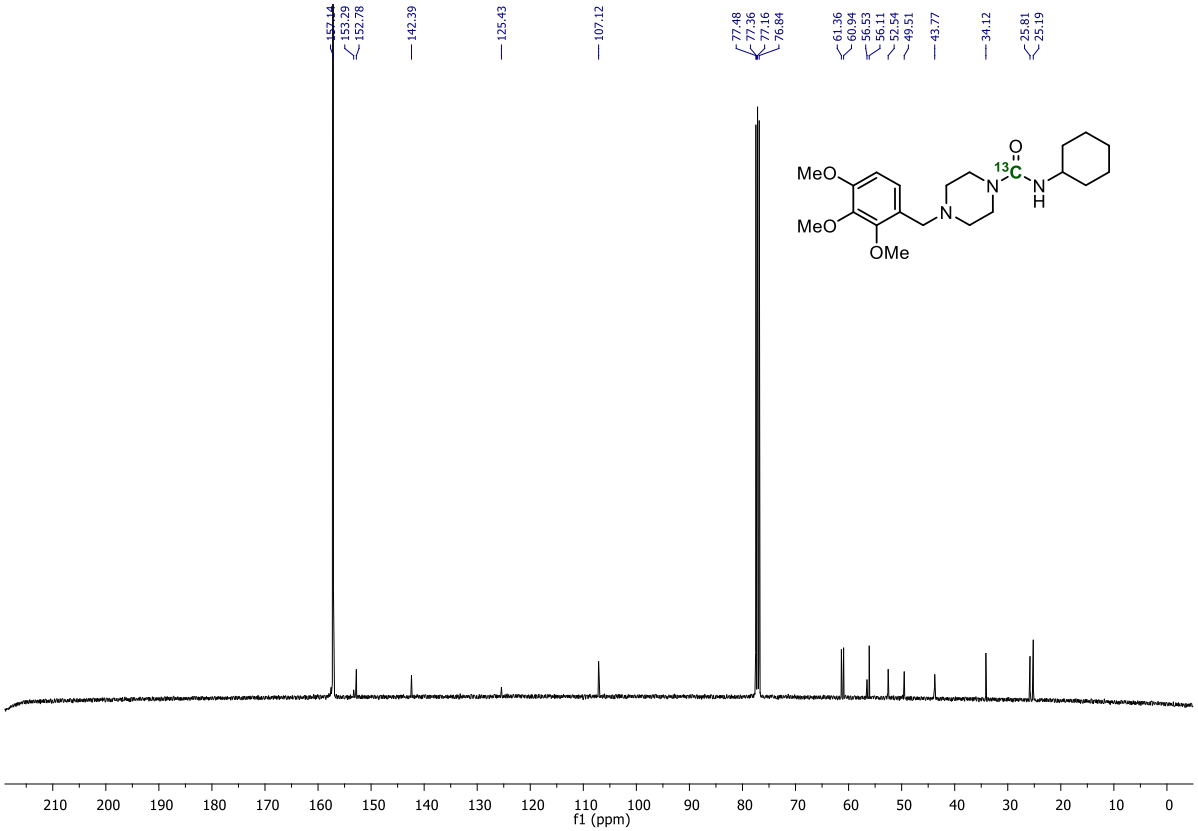
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]17**:



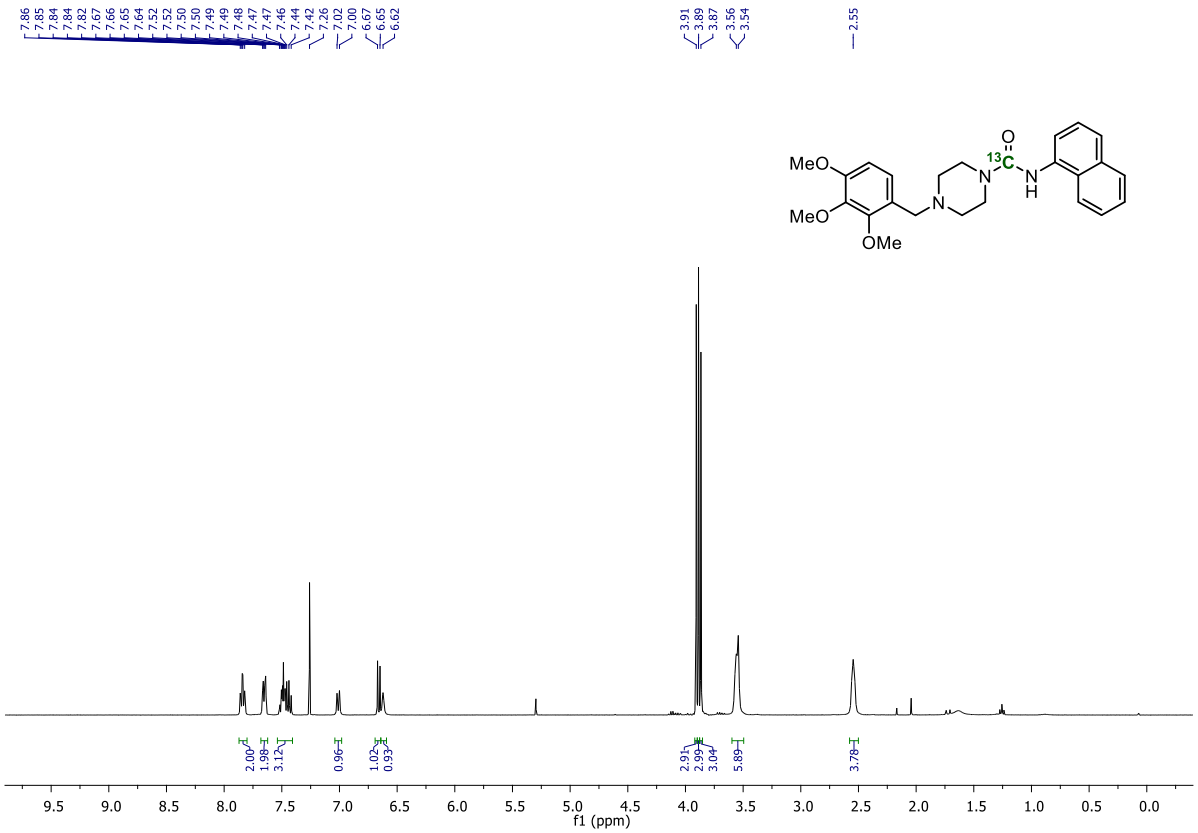
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]18**:



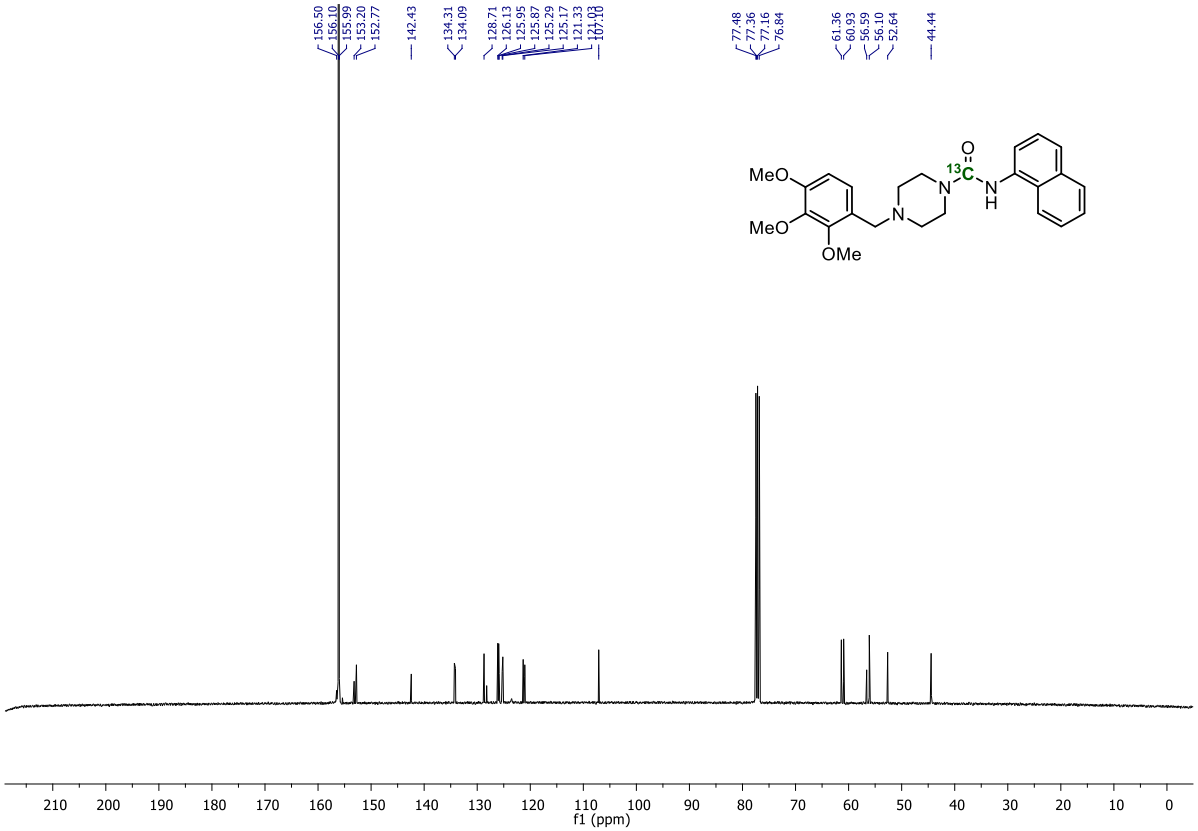
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]18**:



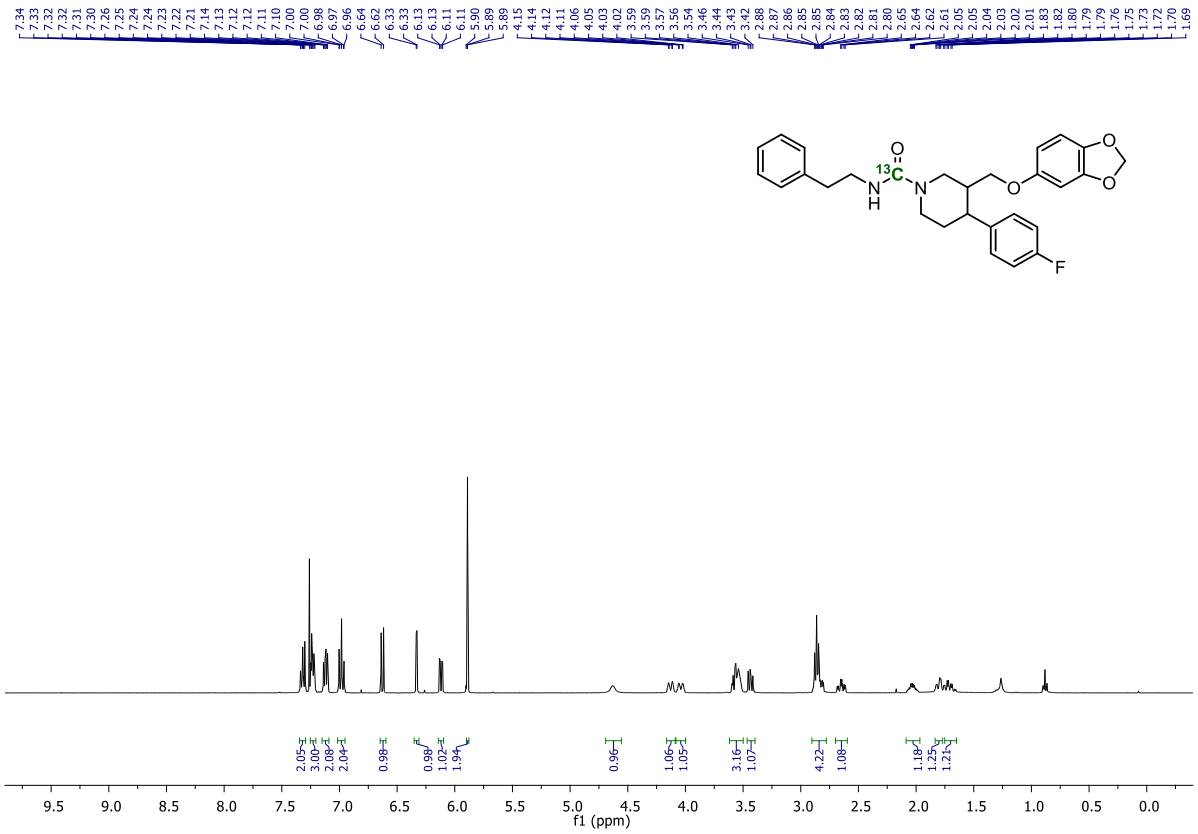
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]19**:



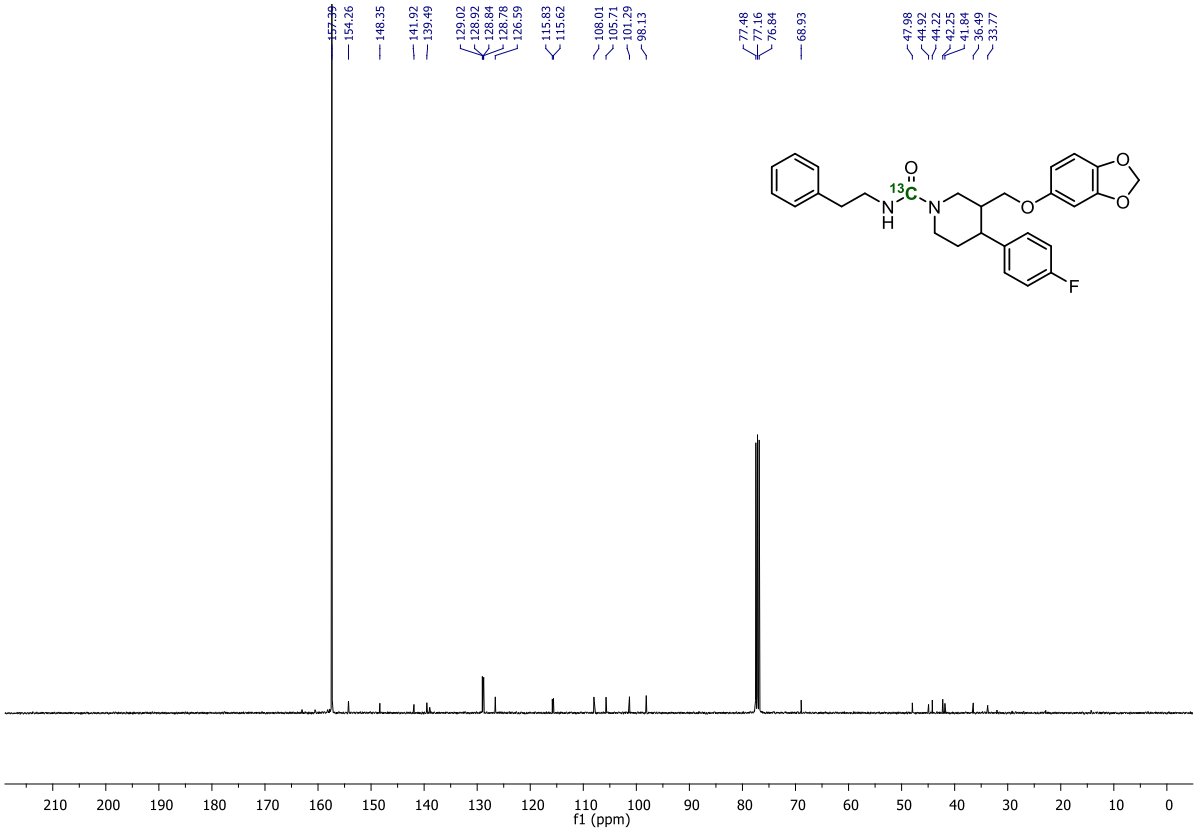
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]19**:



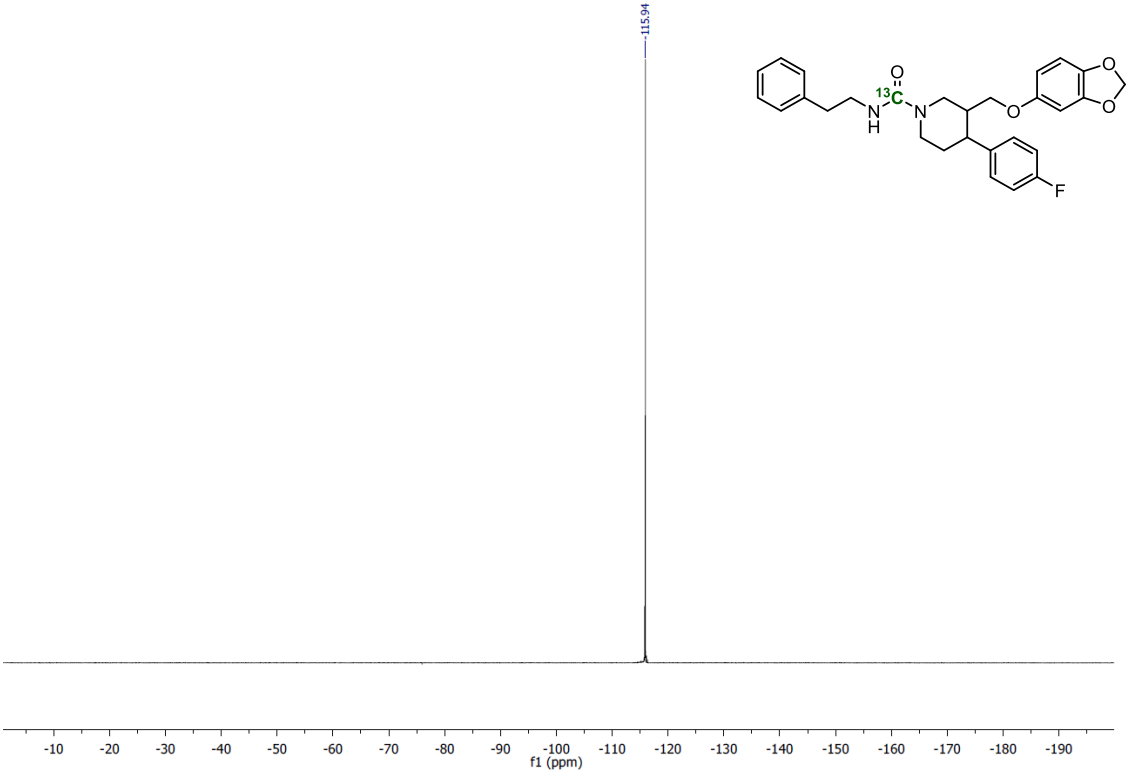
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]20**:



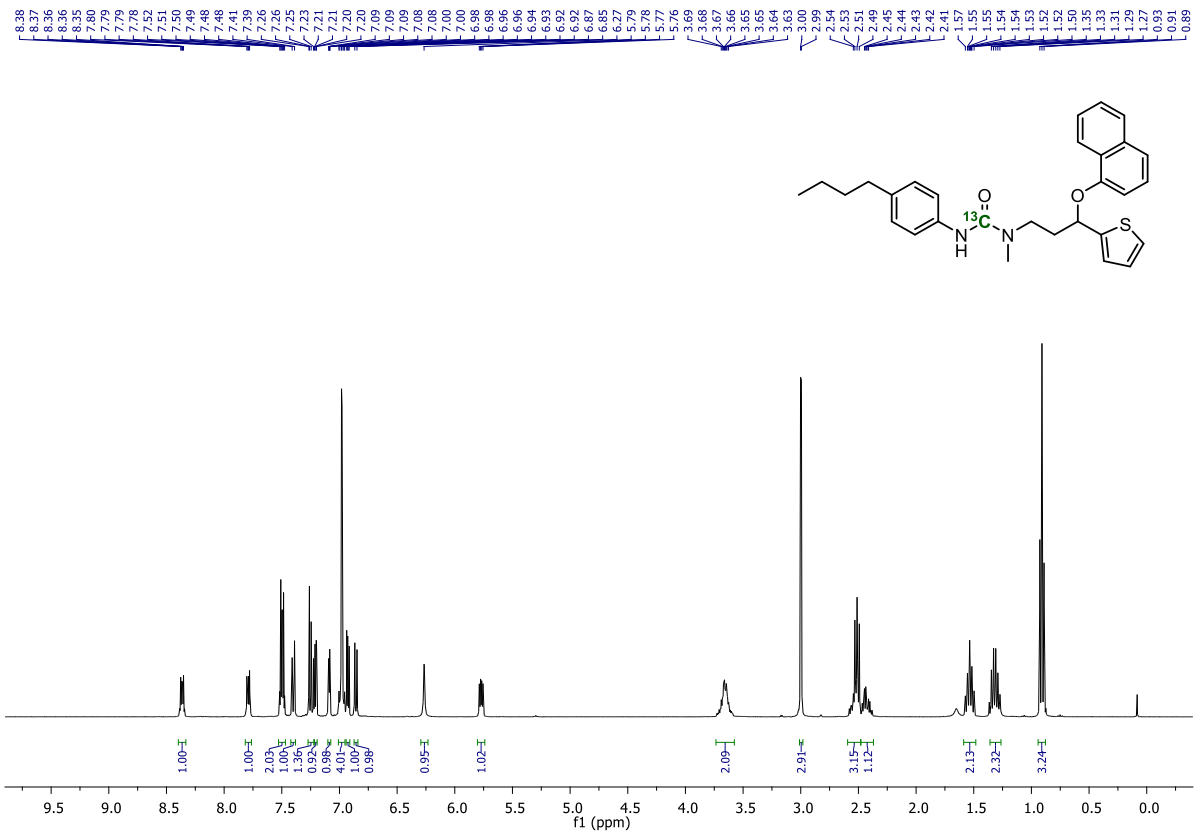
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]20**:



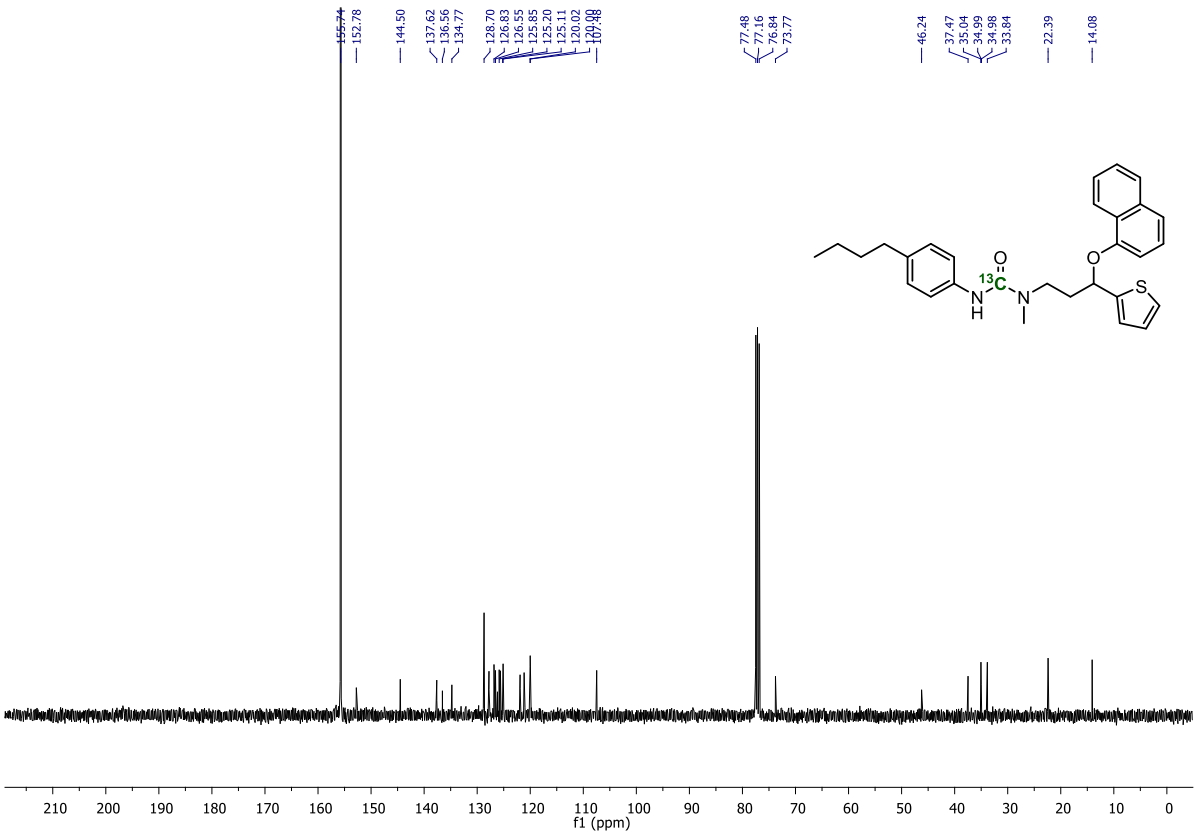
^{19}F NMR (376 MHz, $CDCl_3$) **[^{13}C]20**



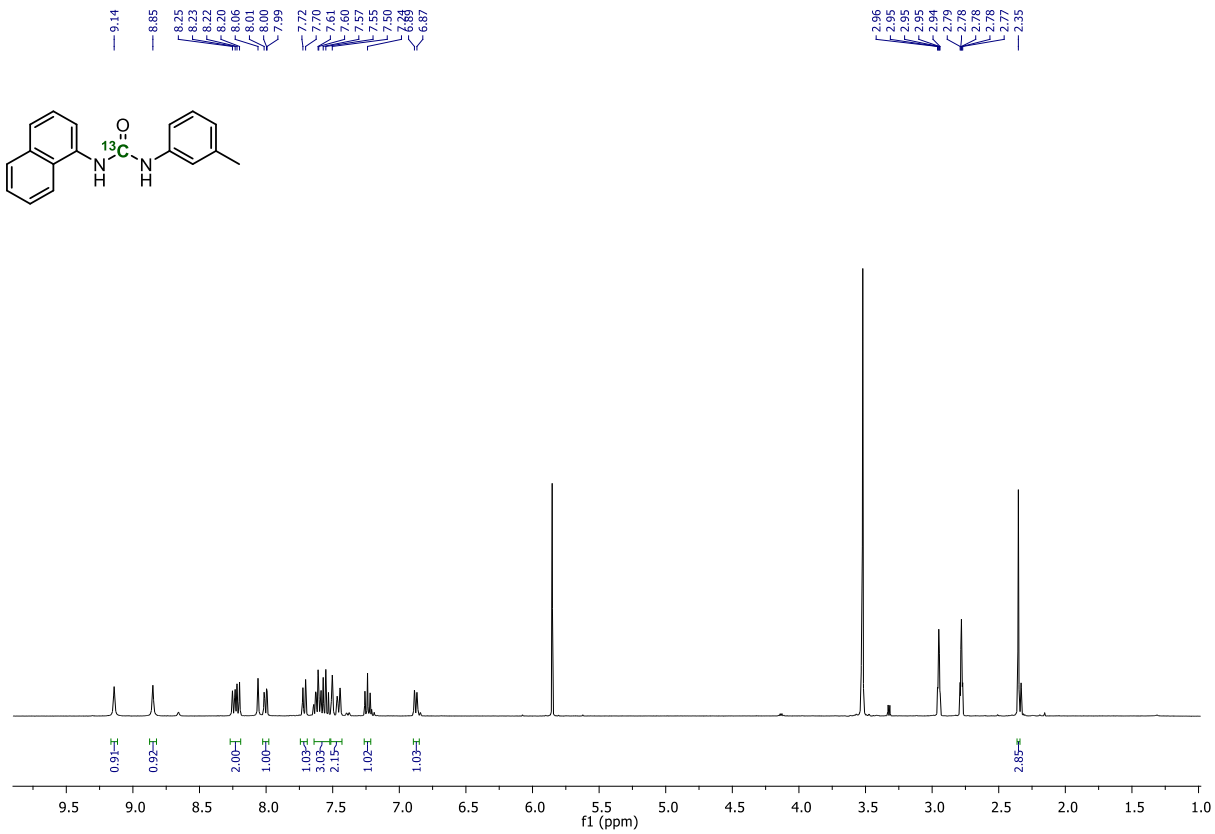
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]21**:



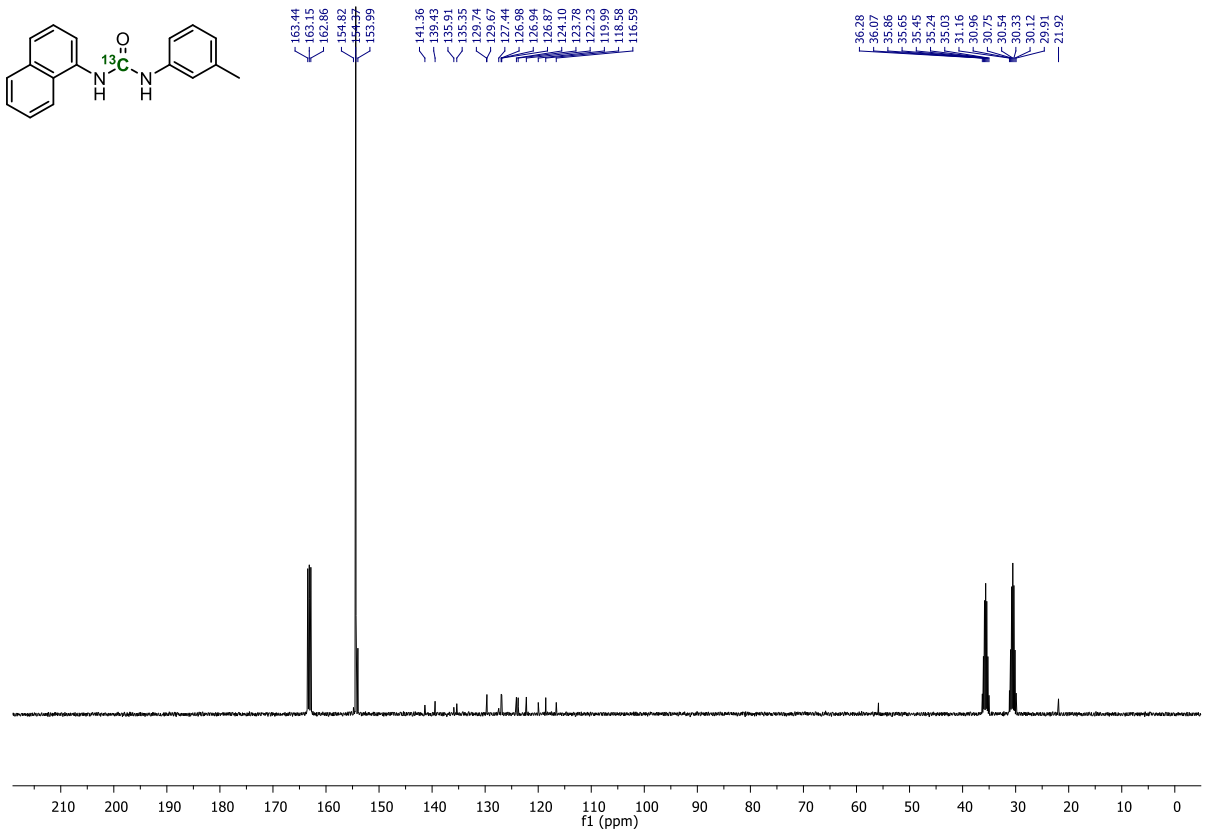
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]21**:



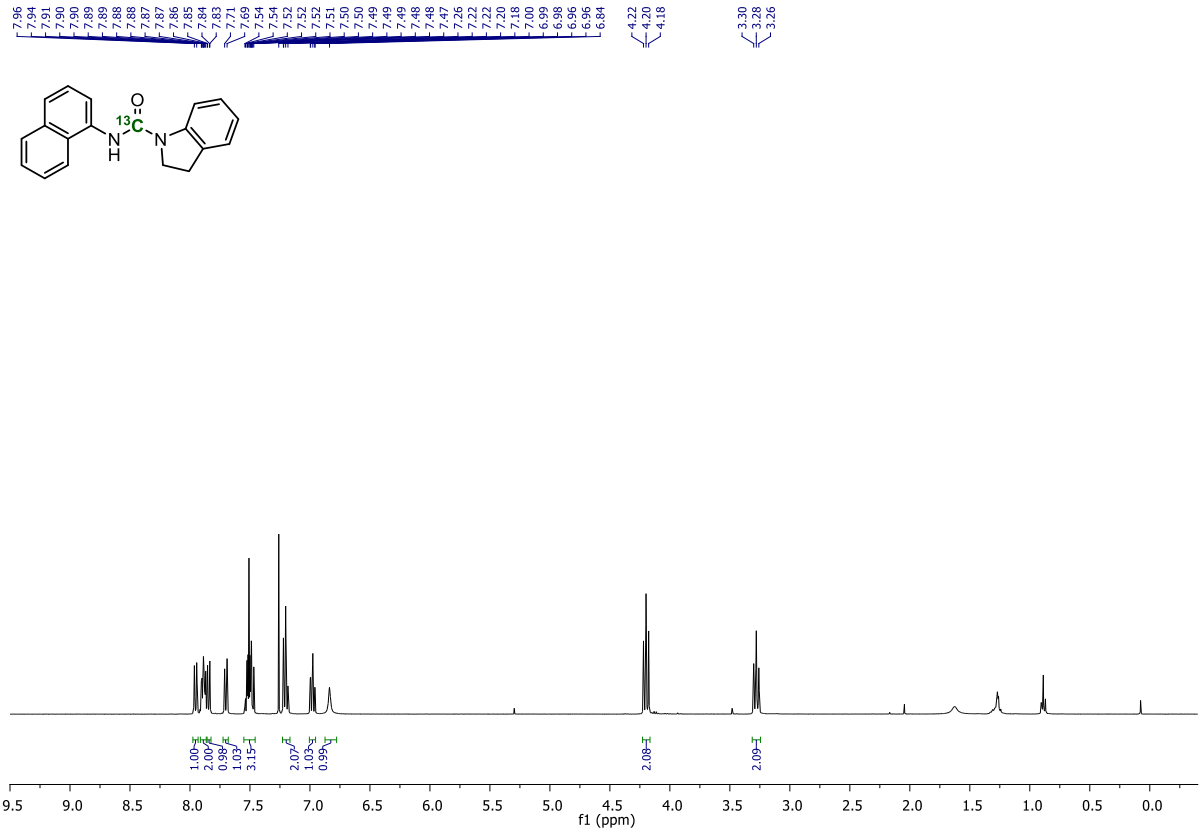
^{1}H NMR (400 MHz, DMF-d_7) **[^{13}C]22**:



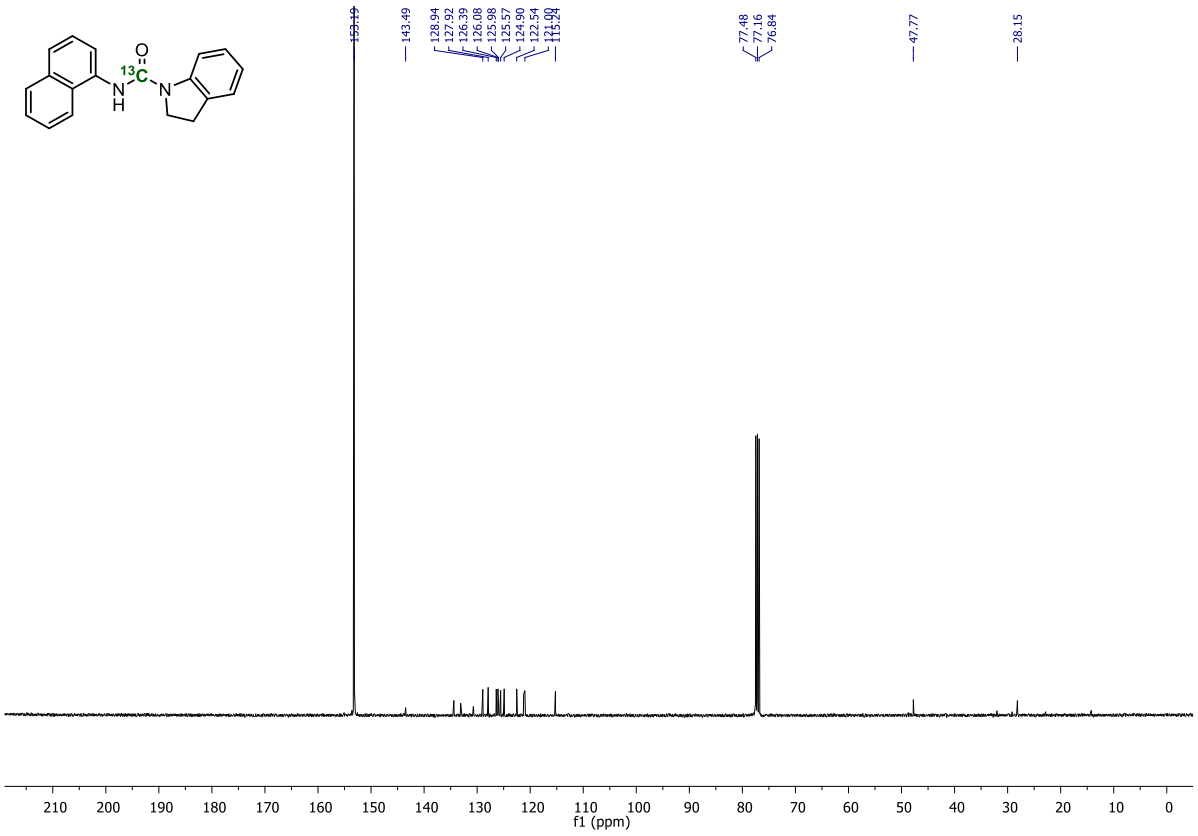
^{13}C NMR (100 MHz, DMF-d_7) **[^{13}C]22**:



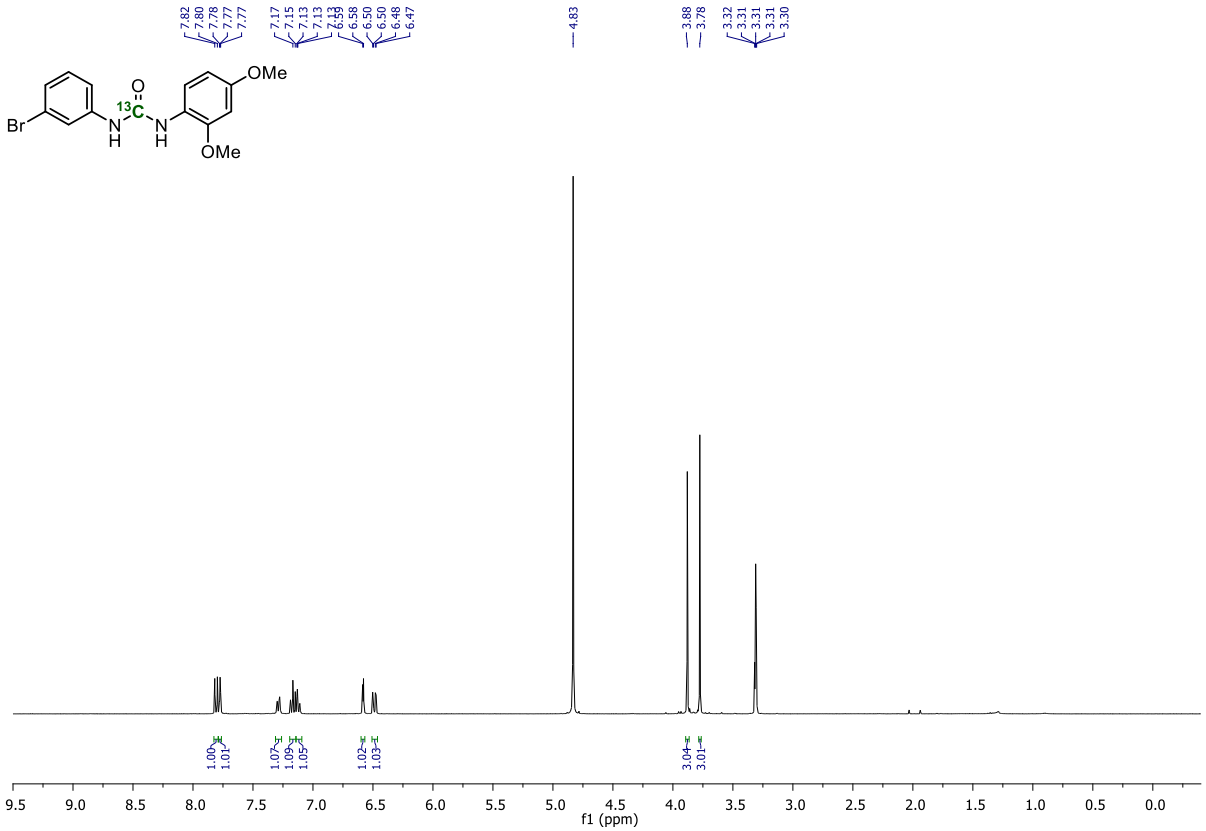
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]23**:



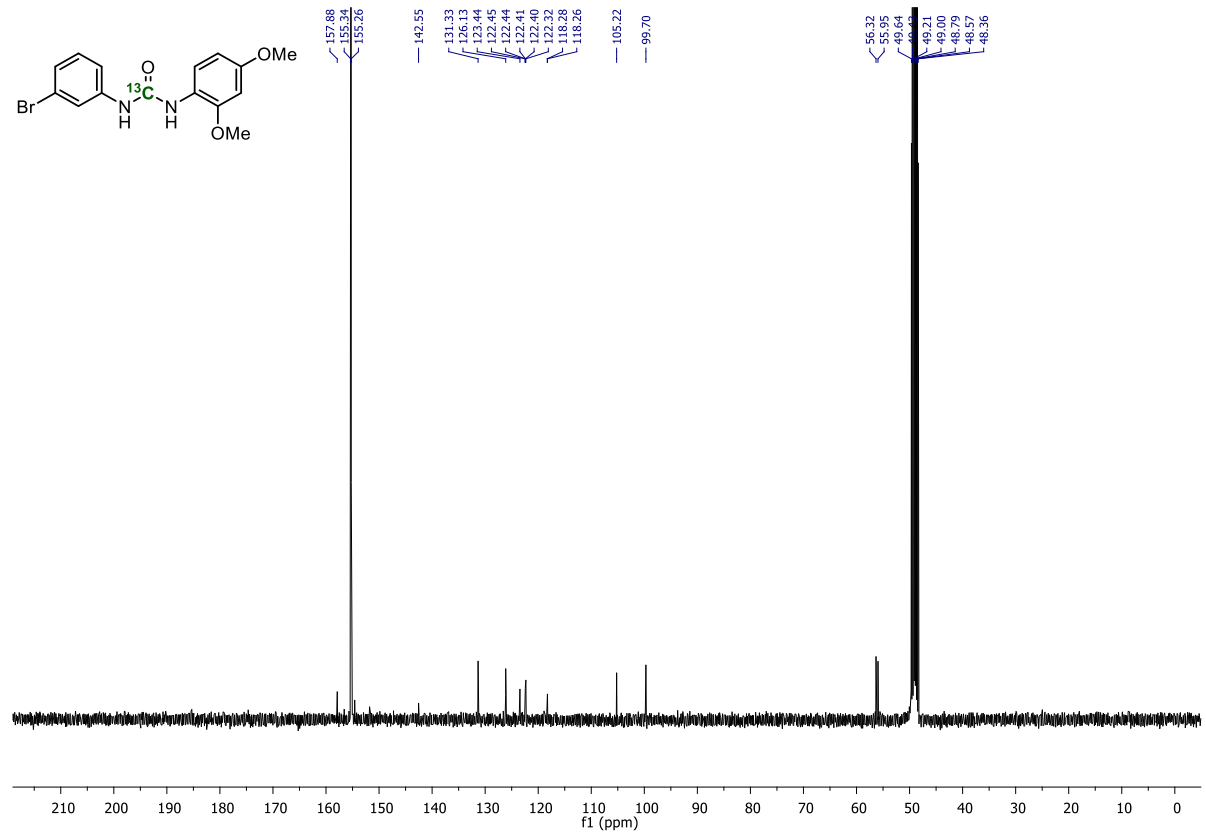
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]23**:



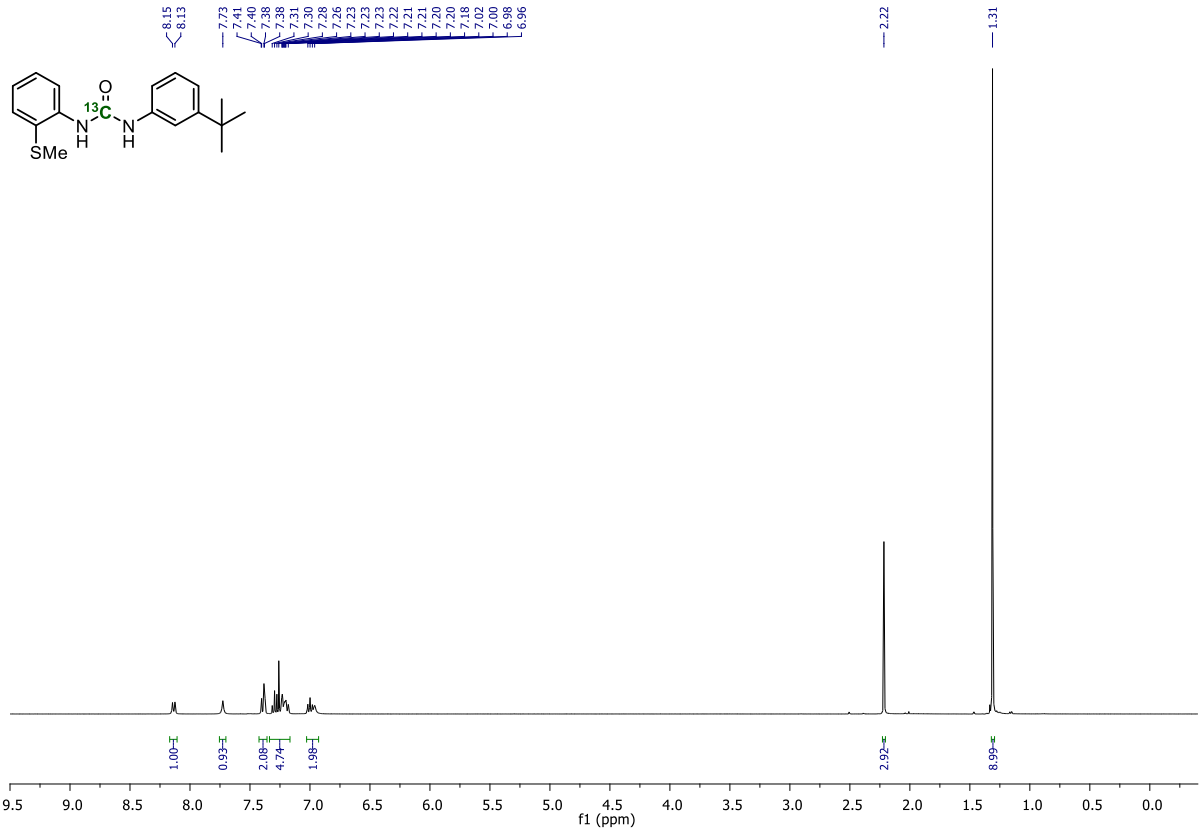
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]24**:



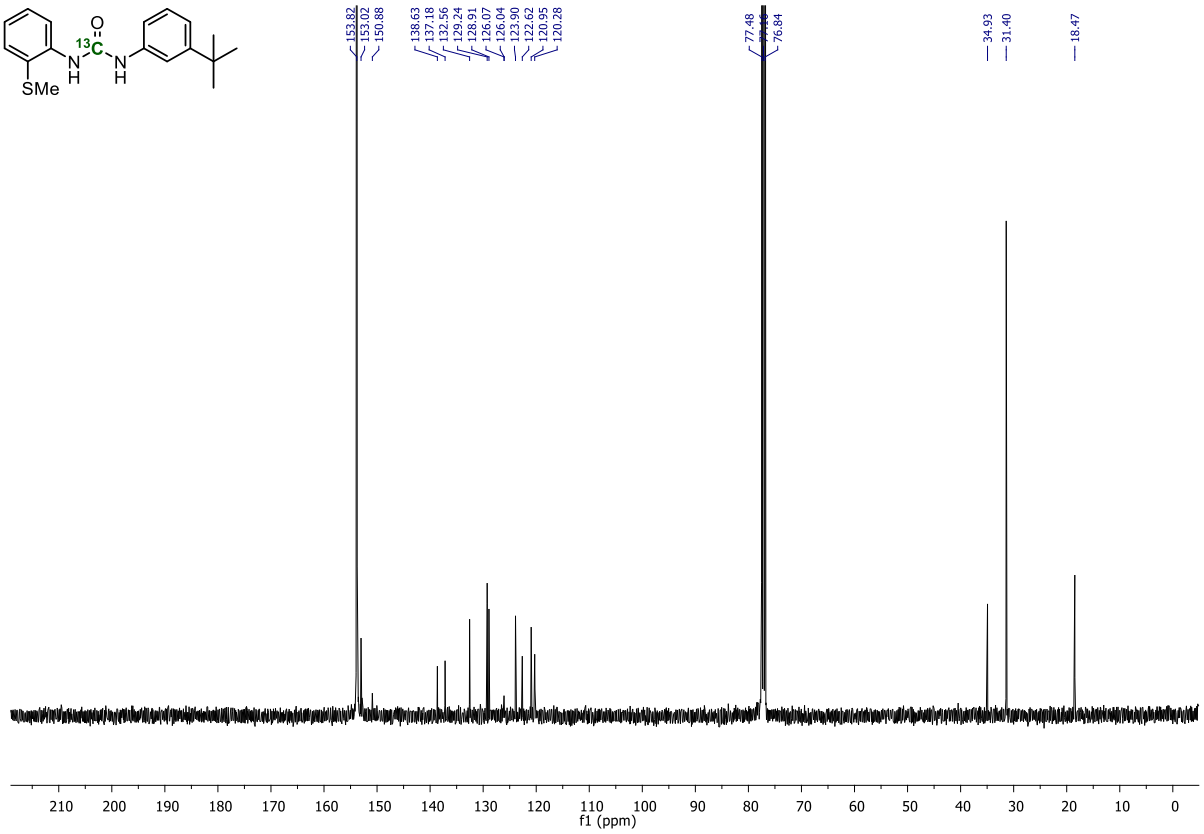
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]24**



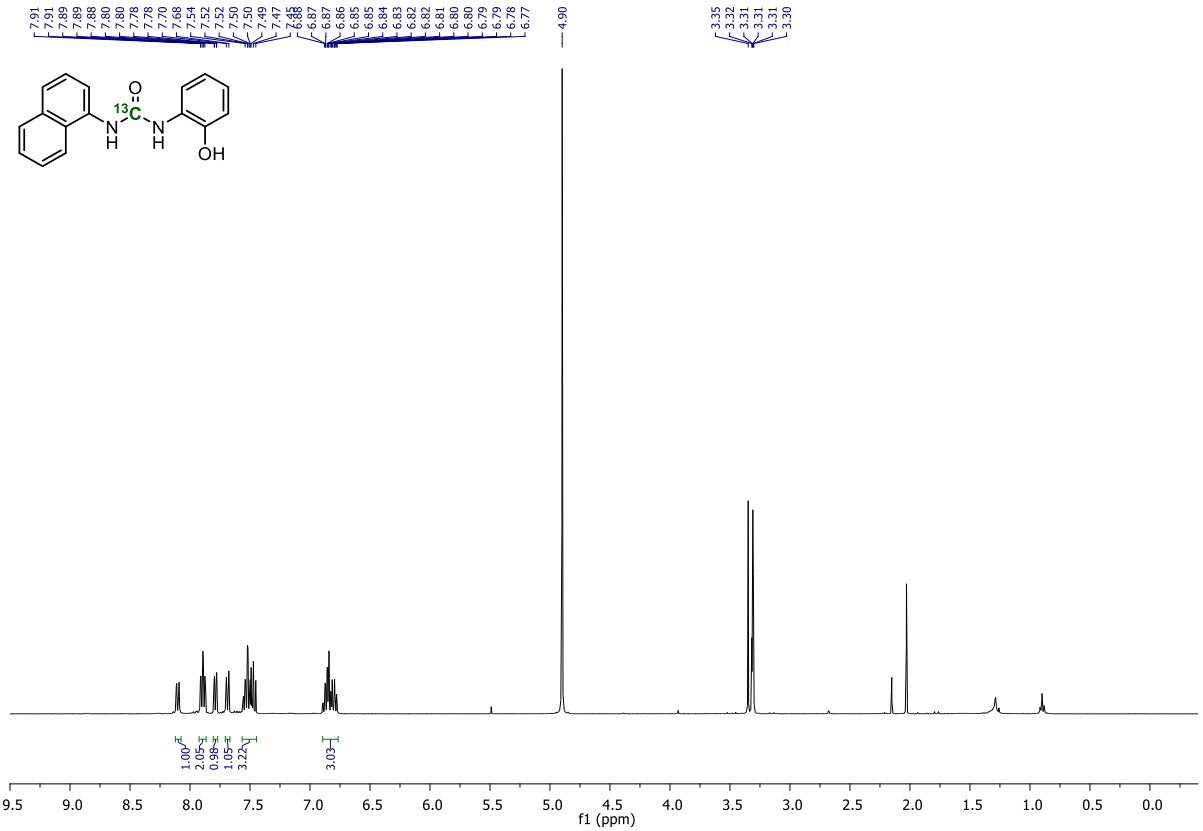
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]25**:



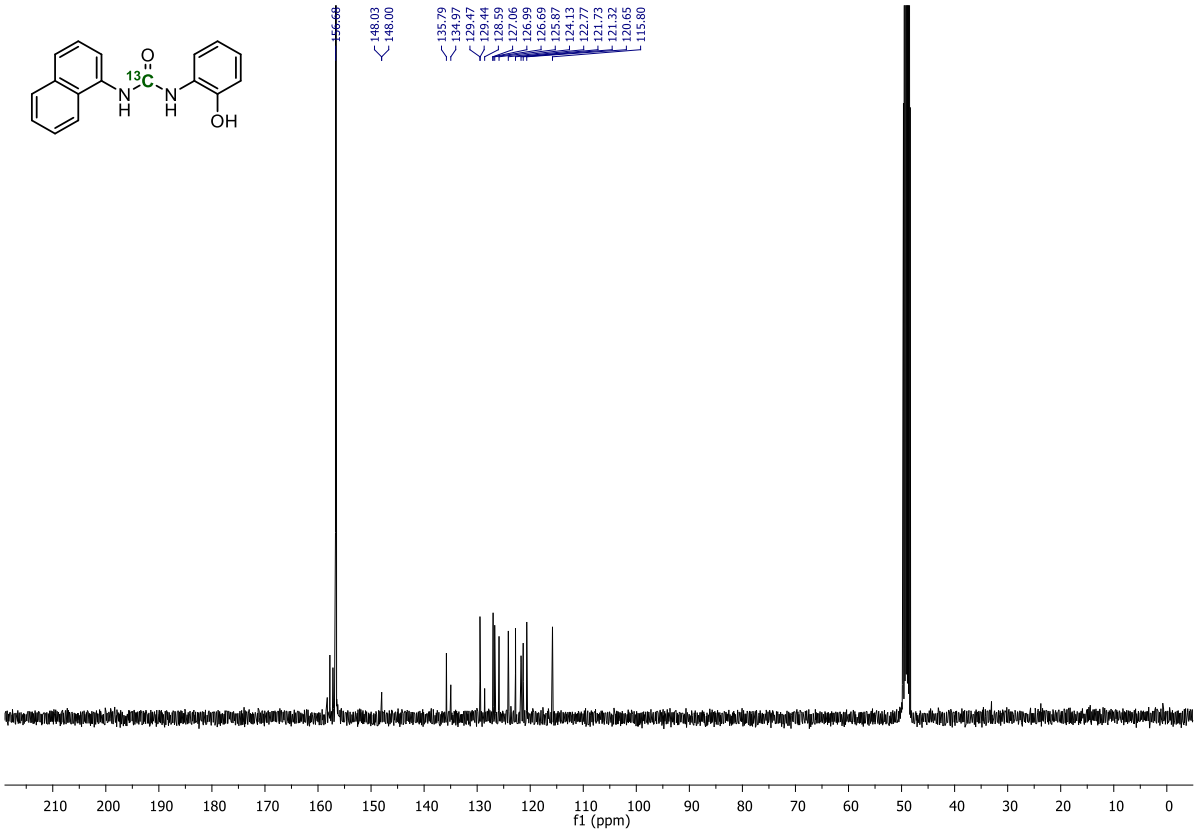
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]25**:



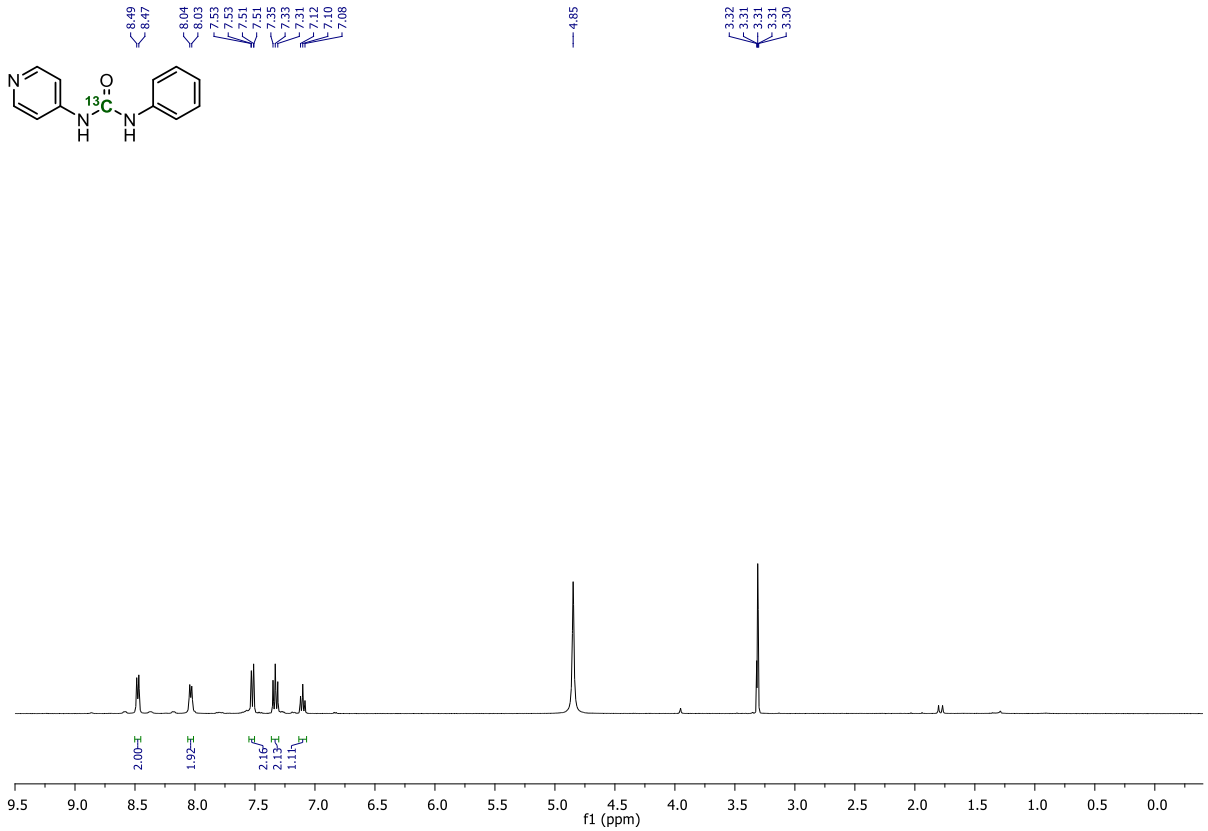
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]26**:



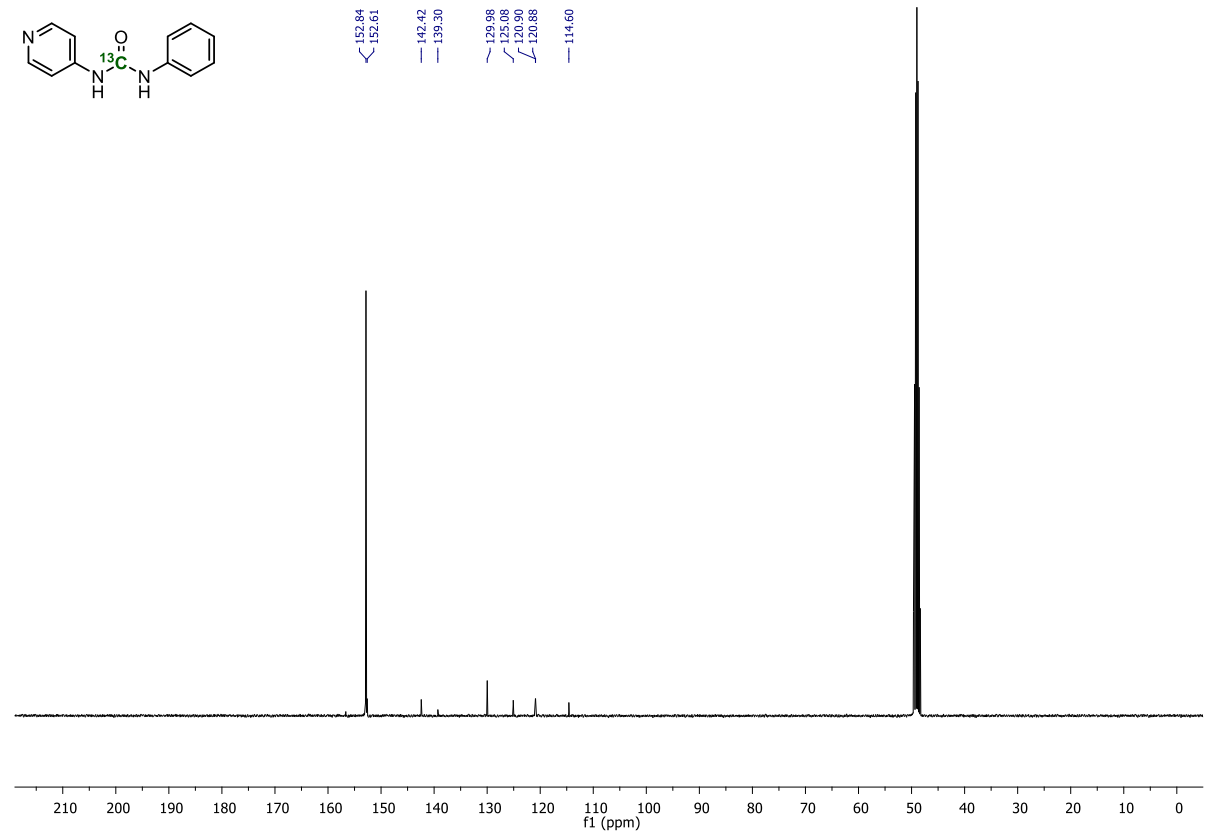
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]26**:



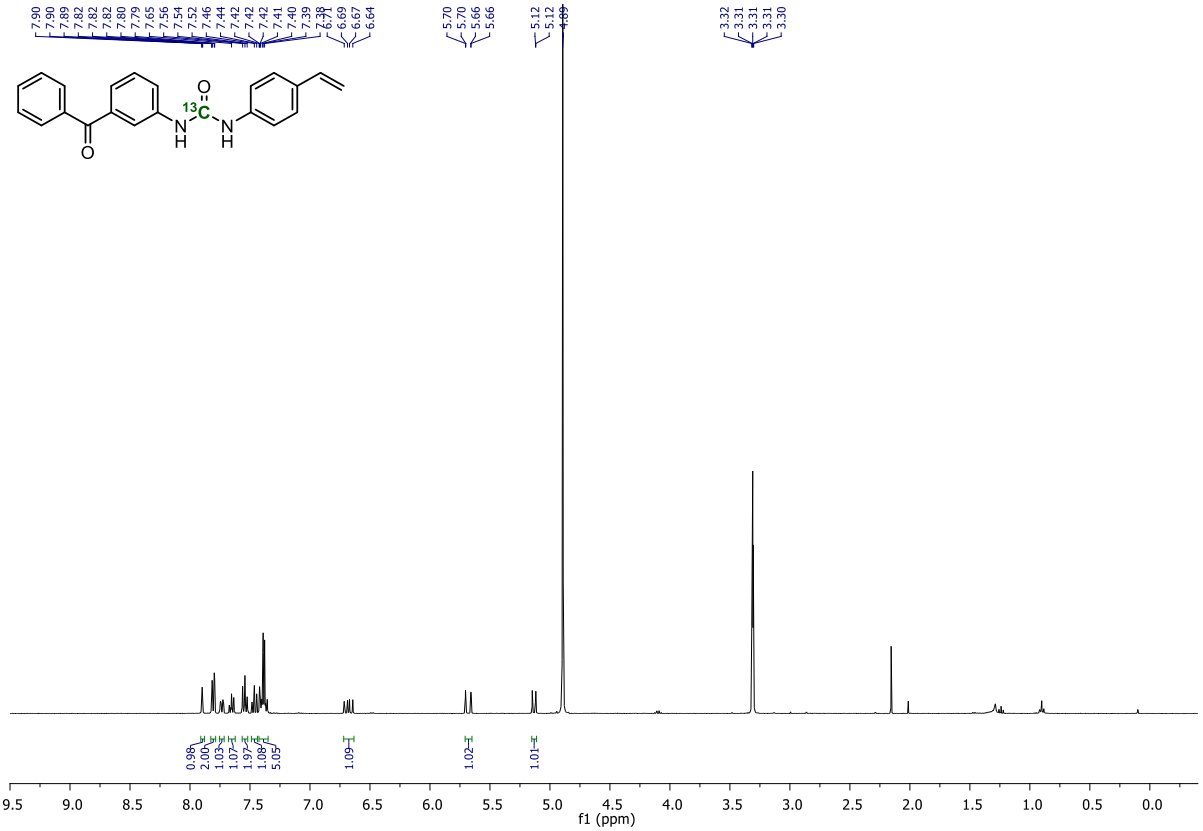
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]27**:



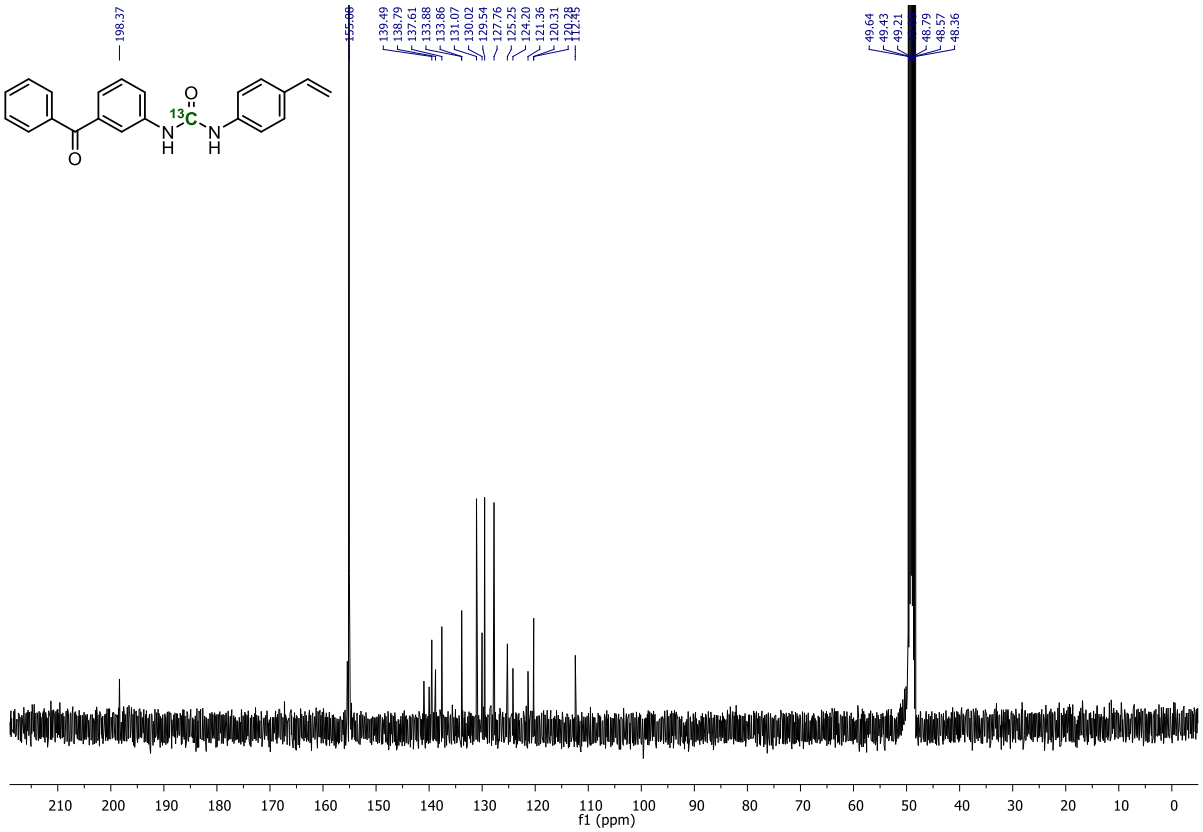
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]27**:



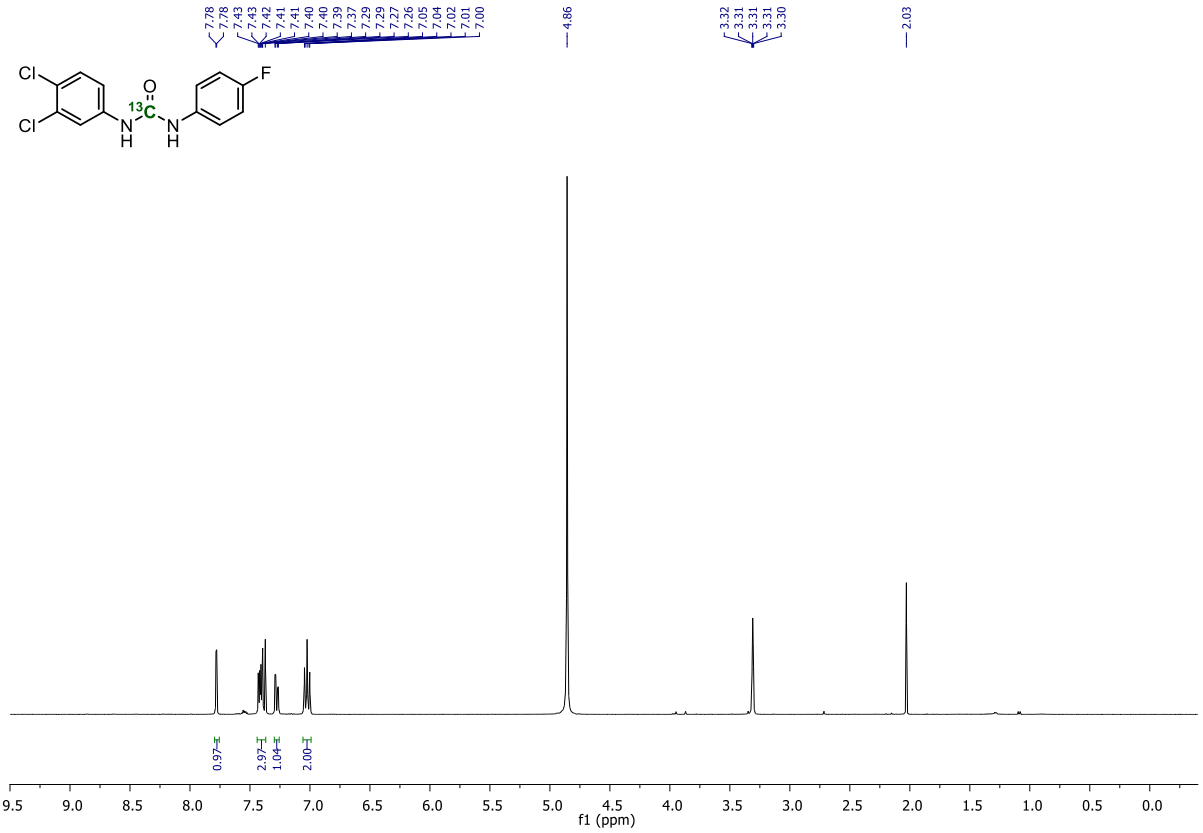
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]28**:



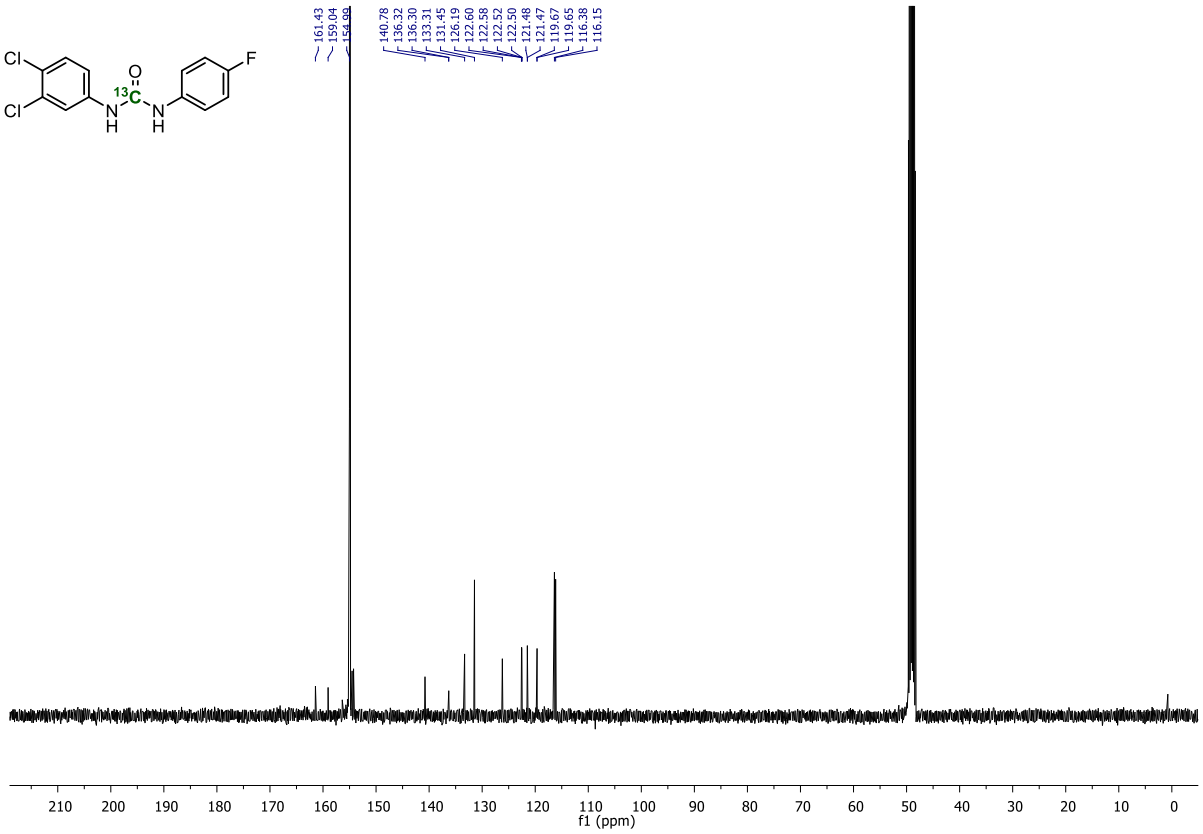
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]28**:



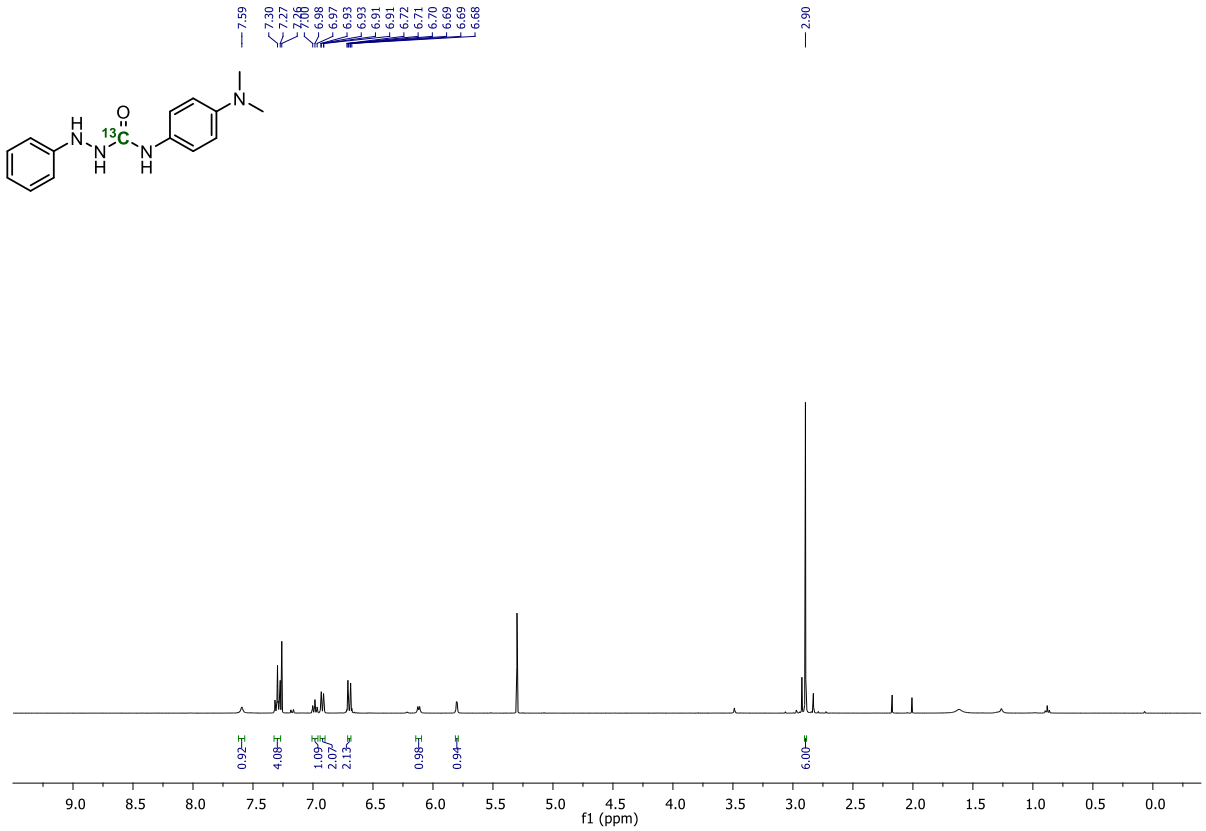
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]29**:



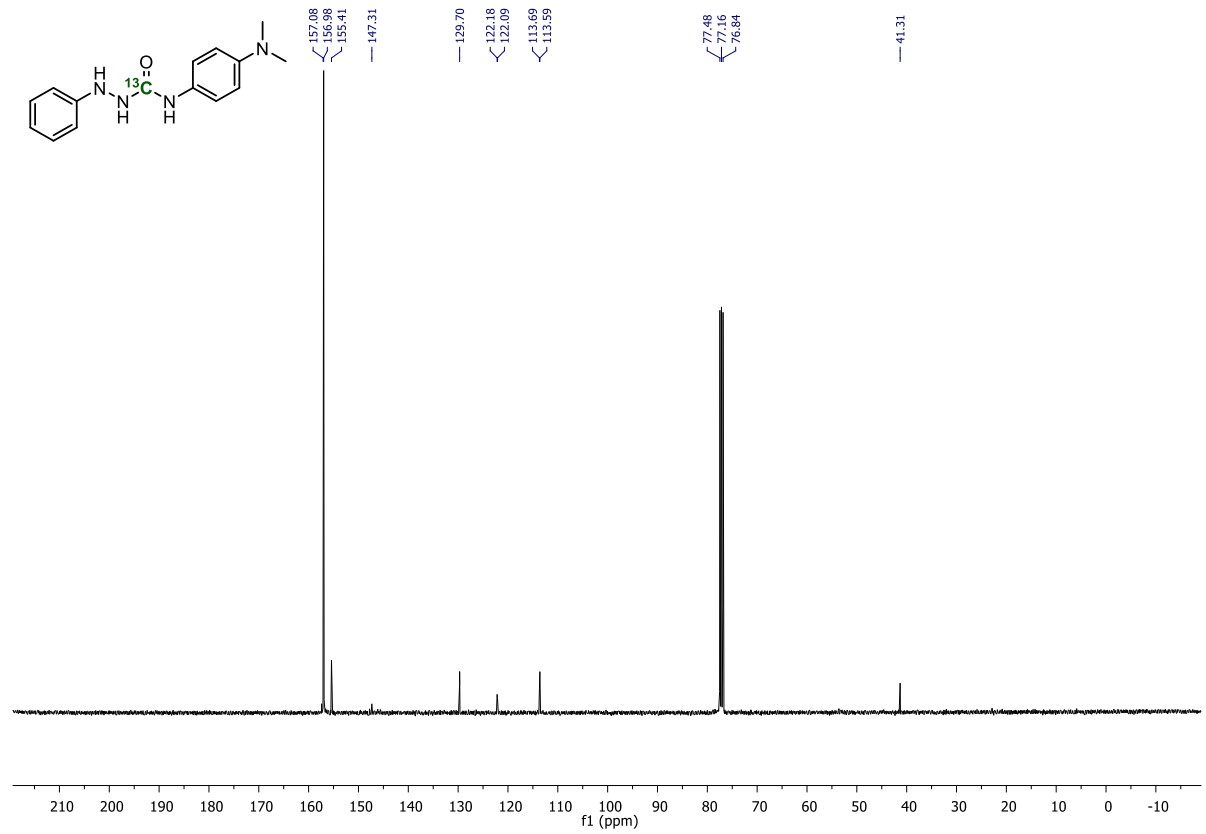
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]29**:



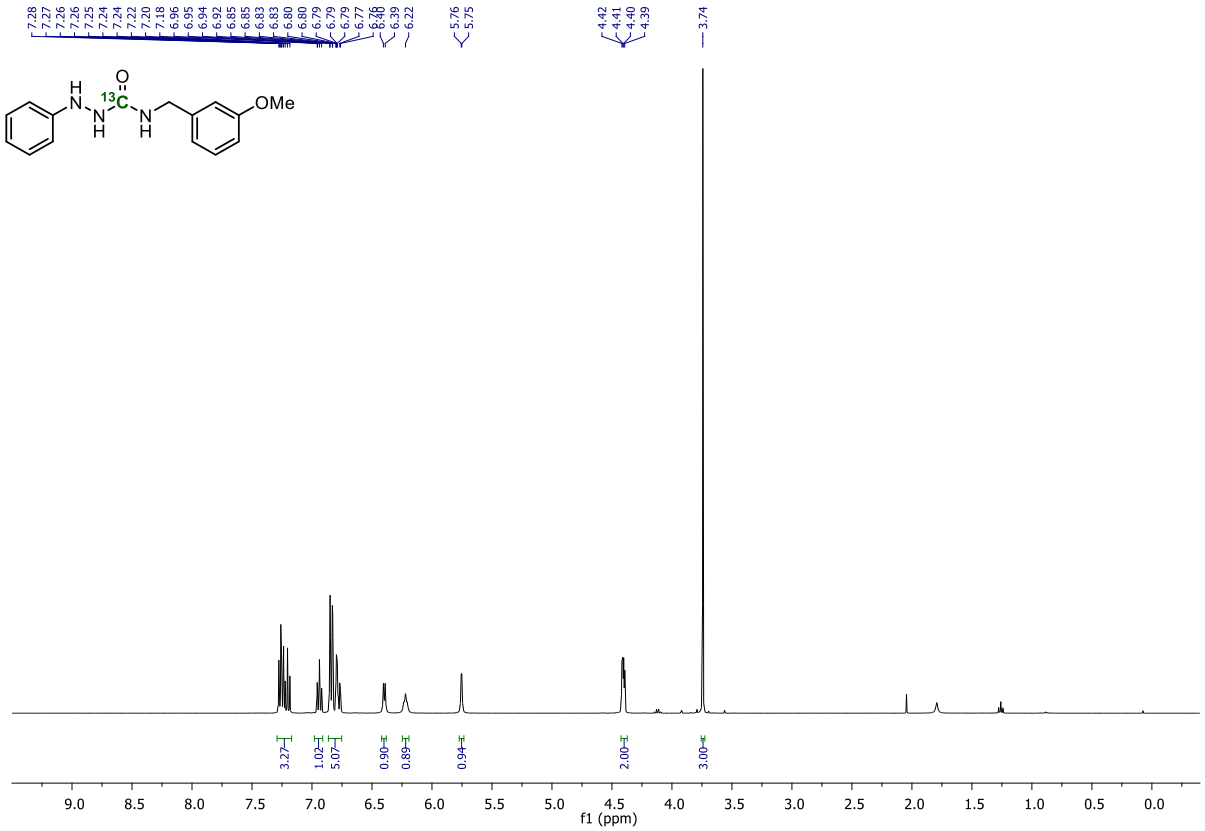
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]31**:



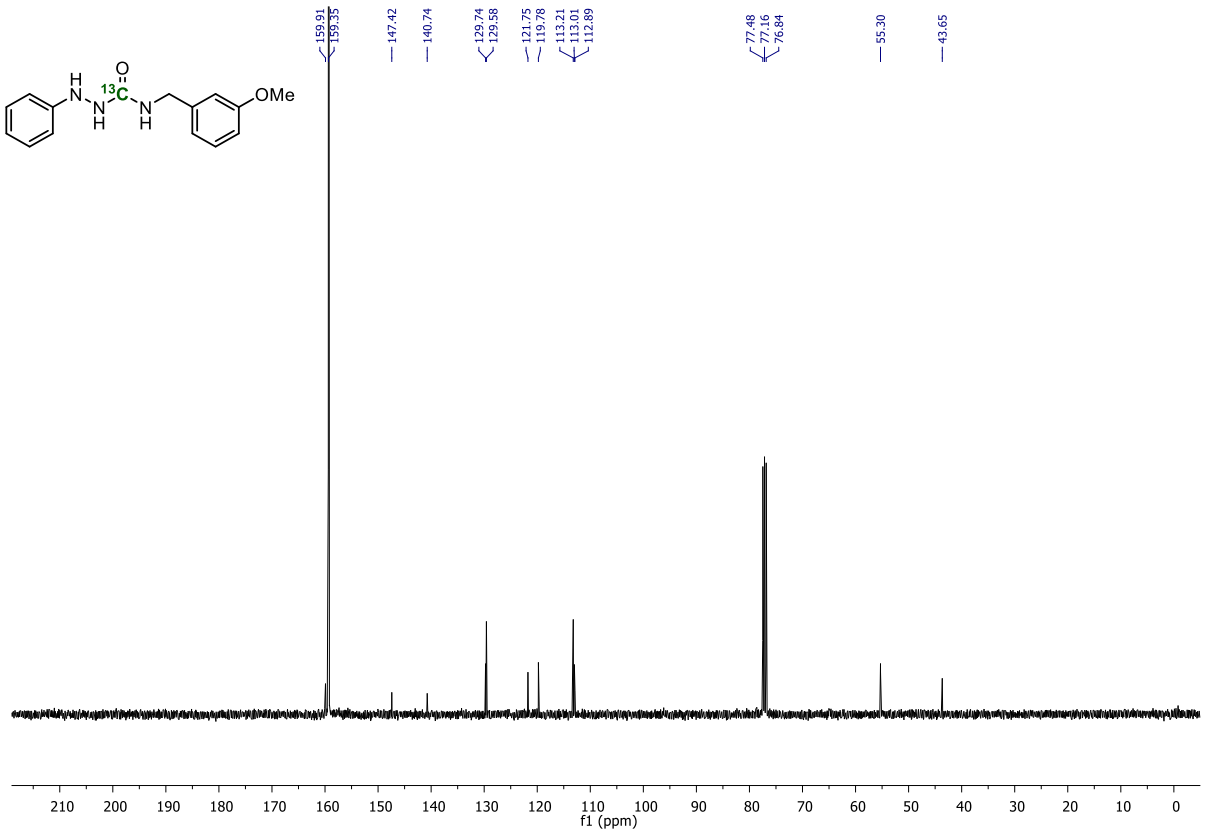
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]31**:



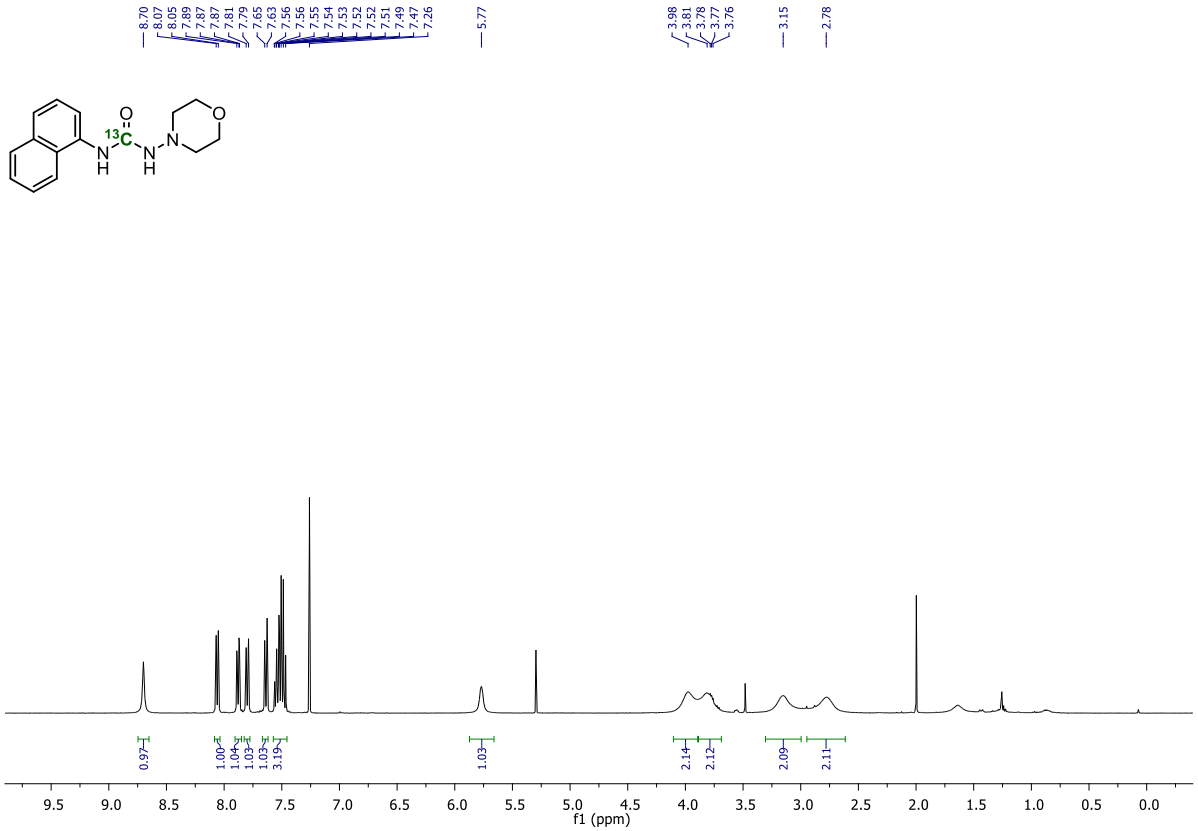
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]32**:



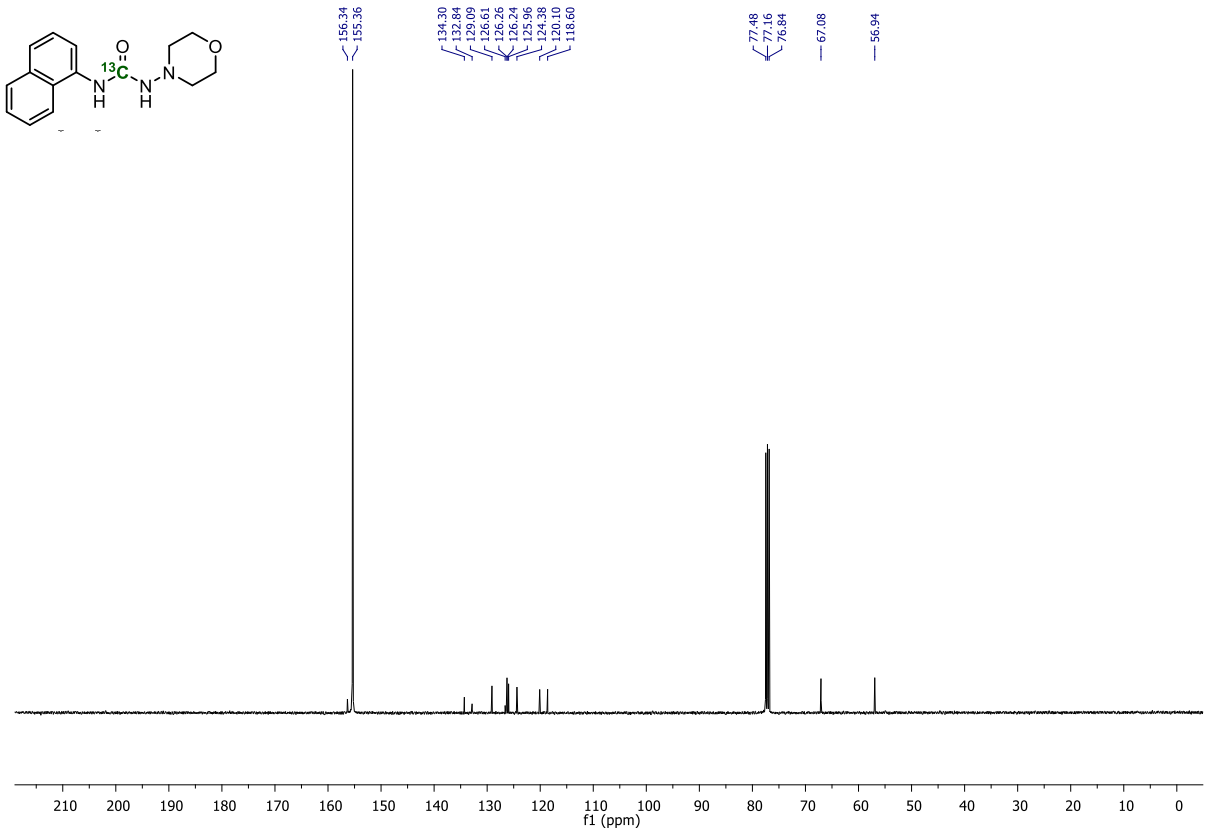
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]32**:



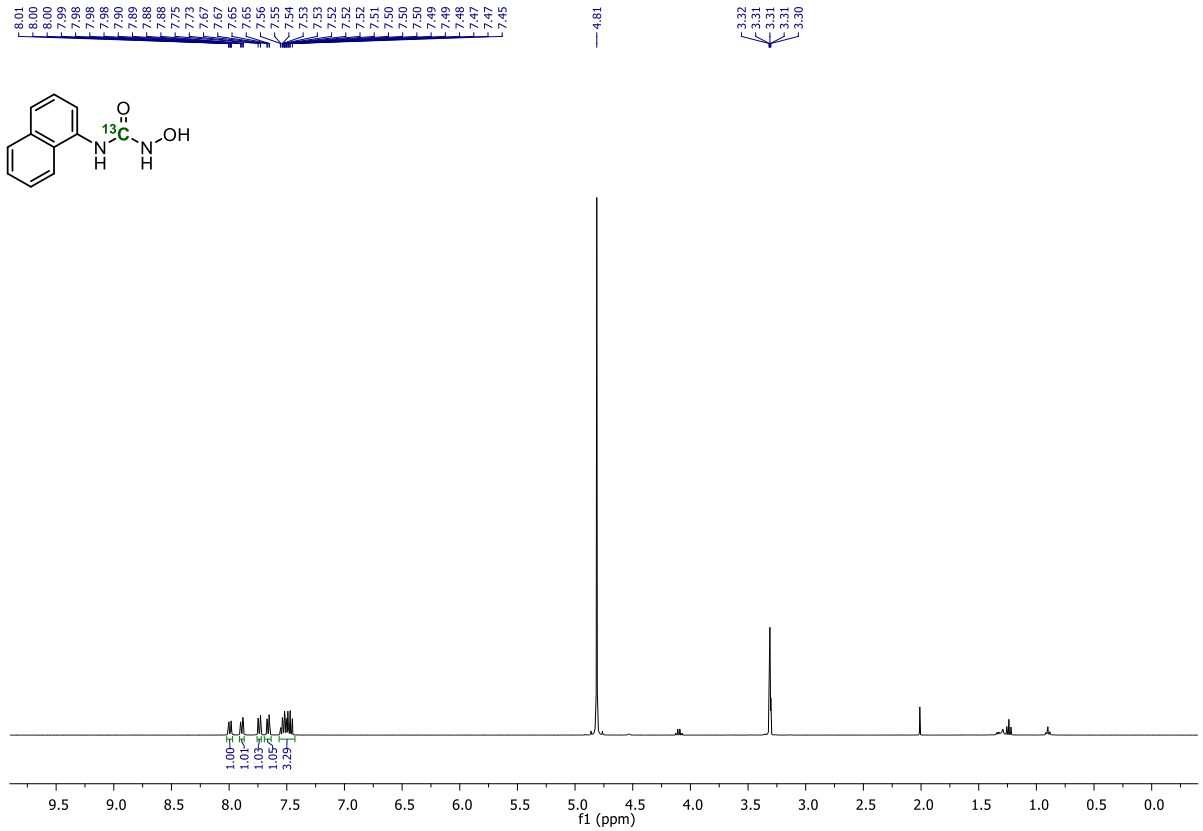
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]33**:



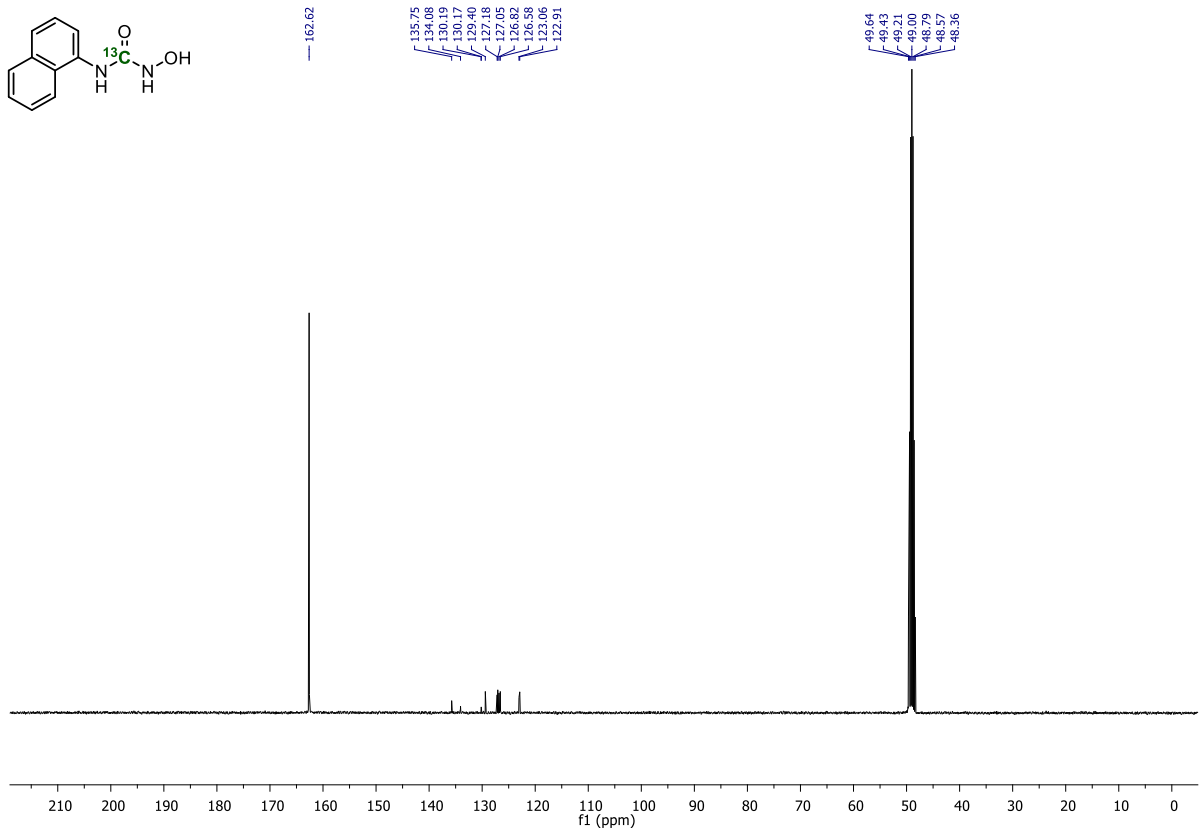
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]33**:



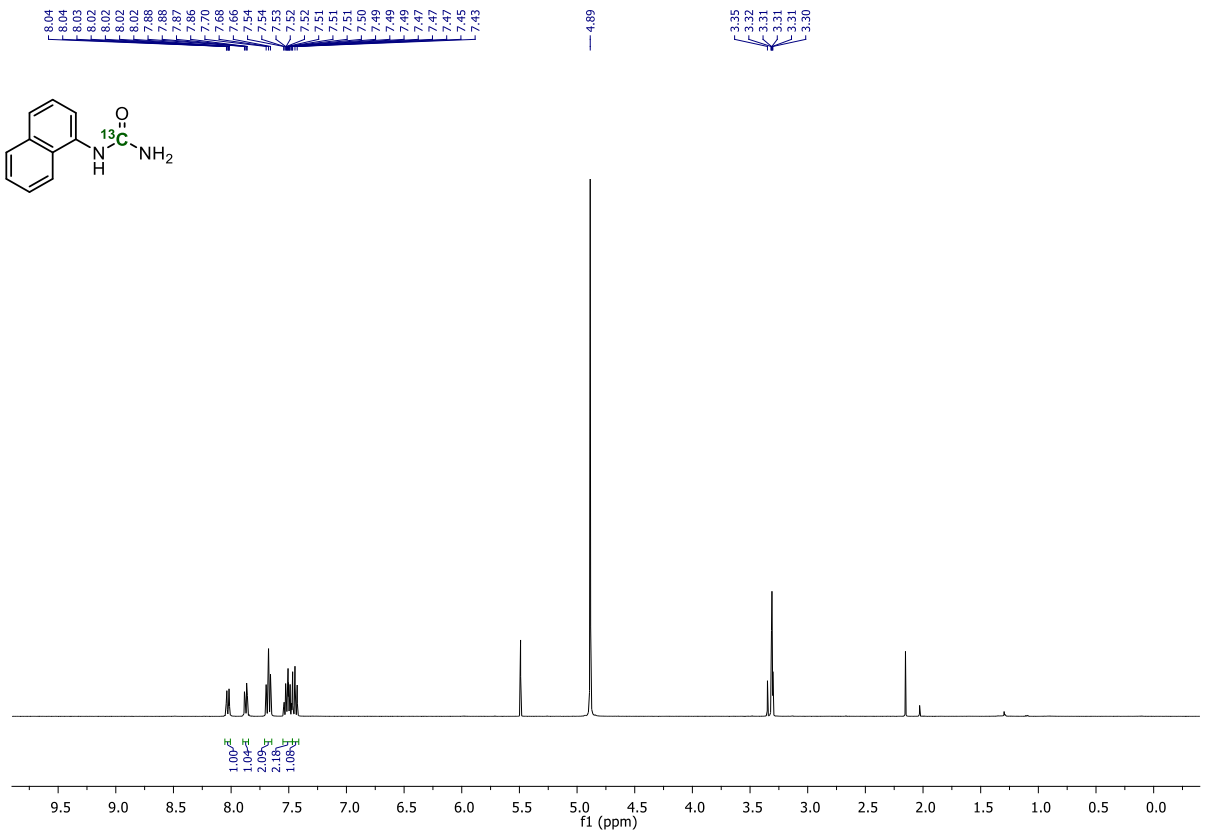
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]34**:



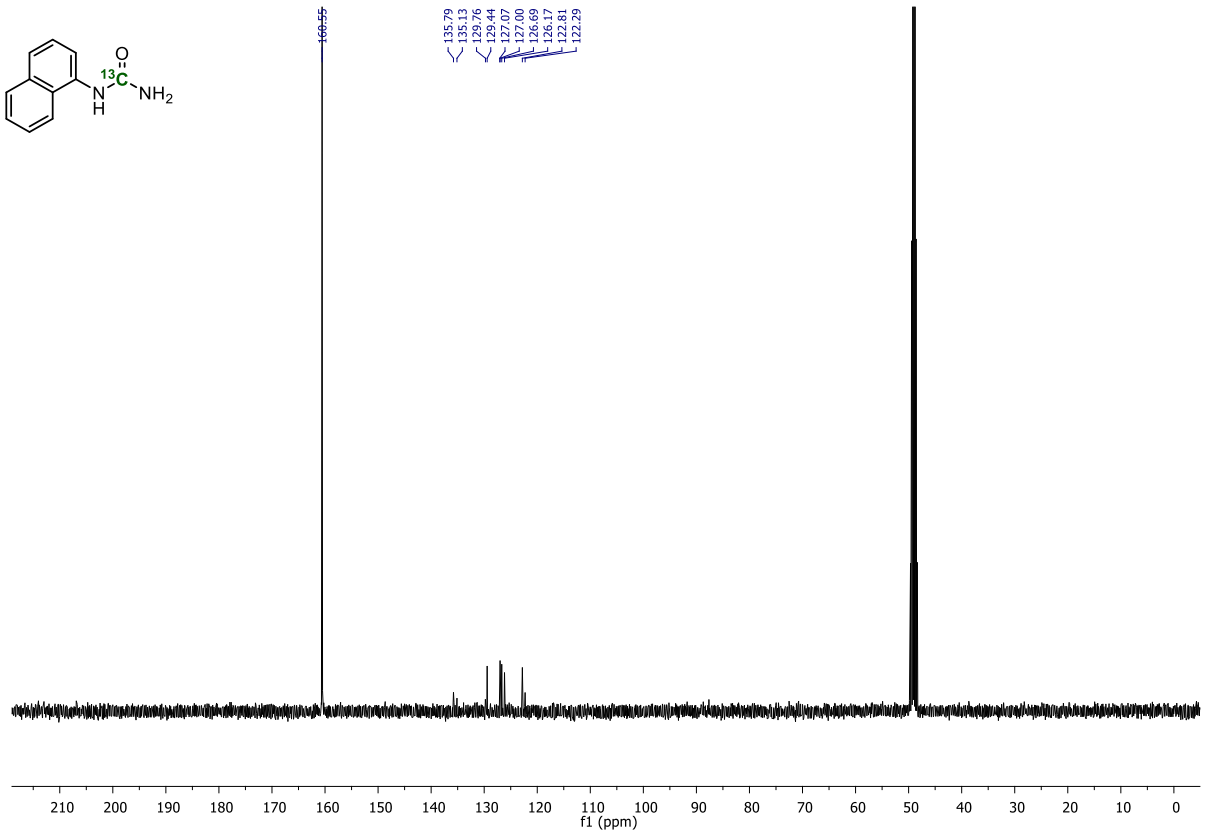
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]34**:



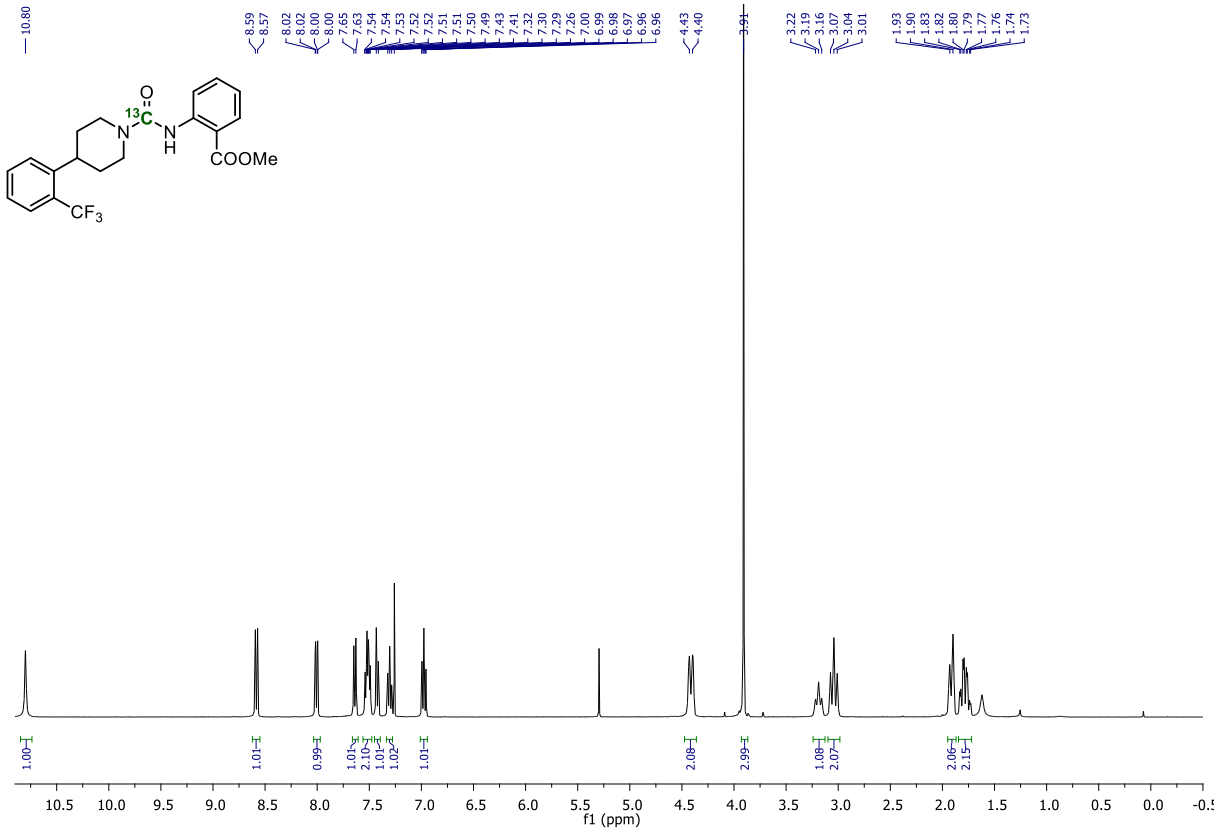
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]35**:



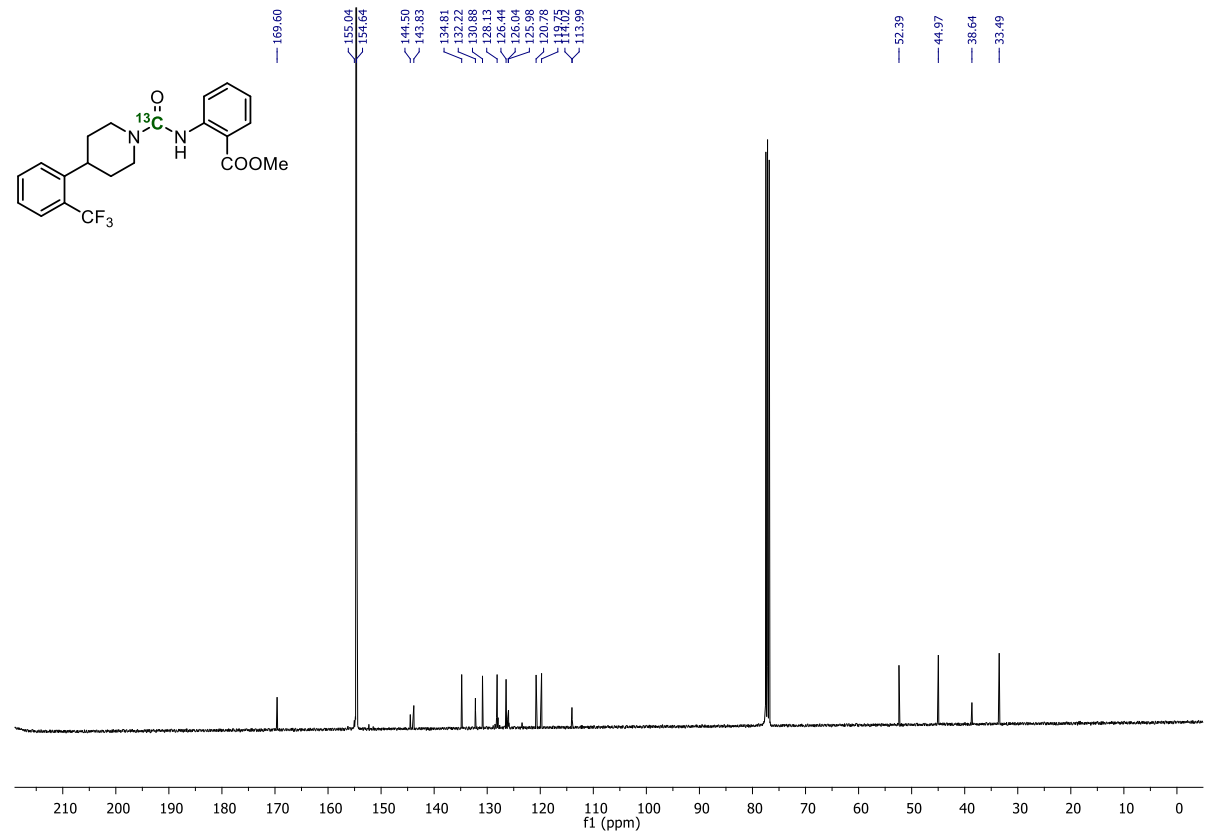
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]35**:



^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]36**:

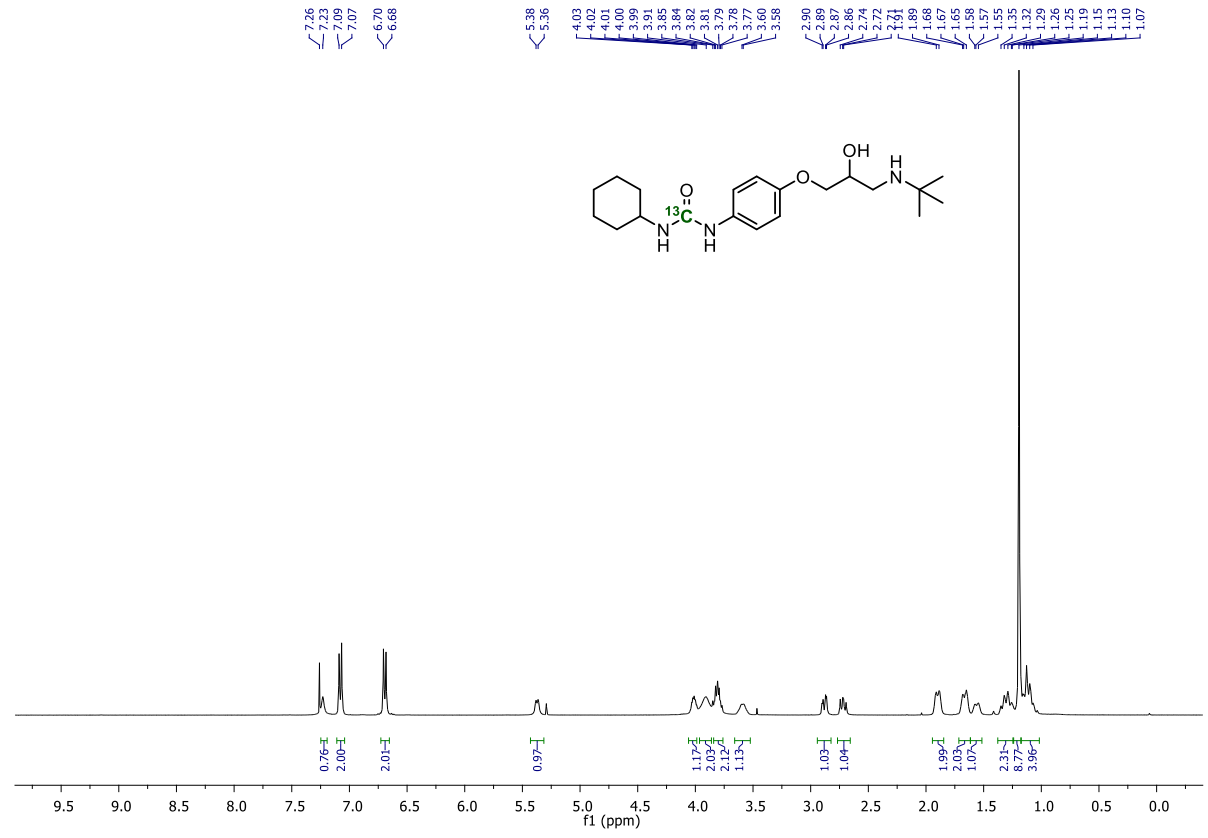


^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]36**:

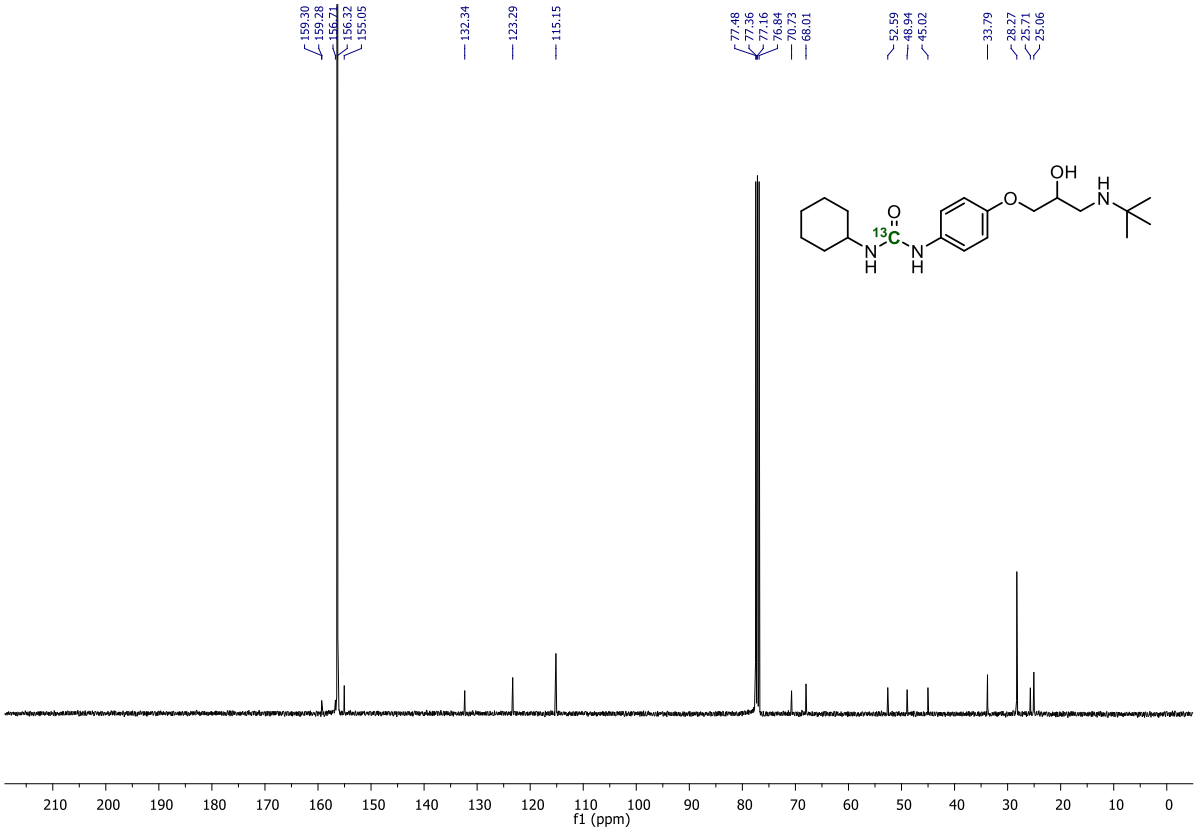


^{19}F NMR (376 MHz, $CDCl_3$) **[^{13}C]36**

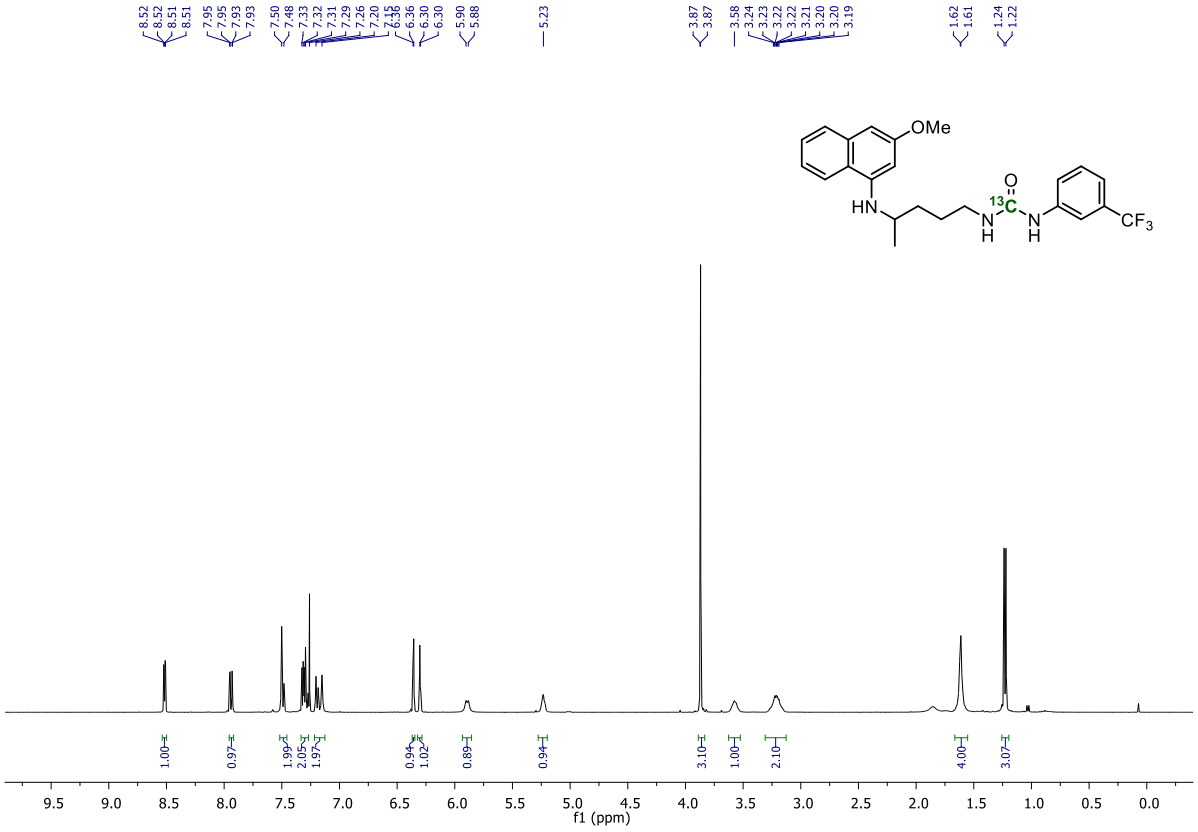
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]37**:



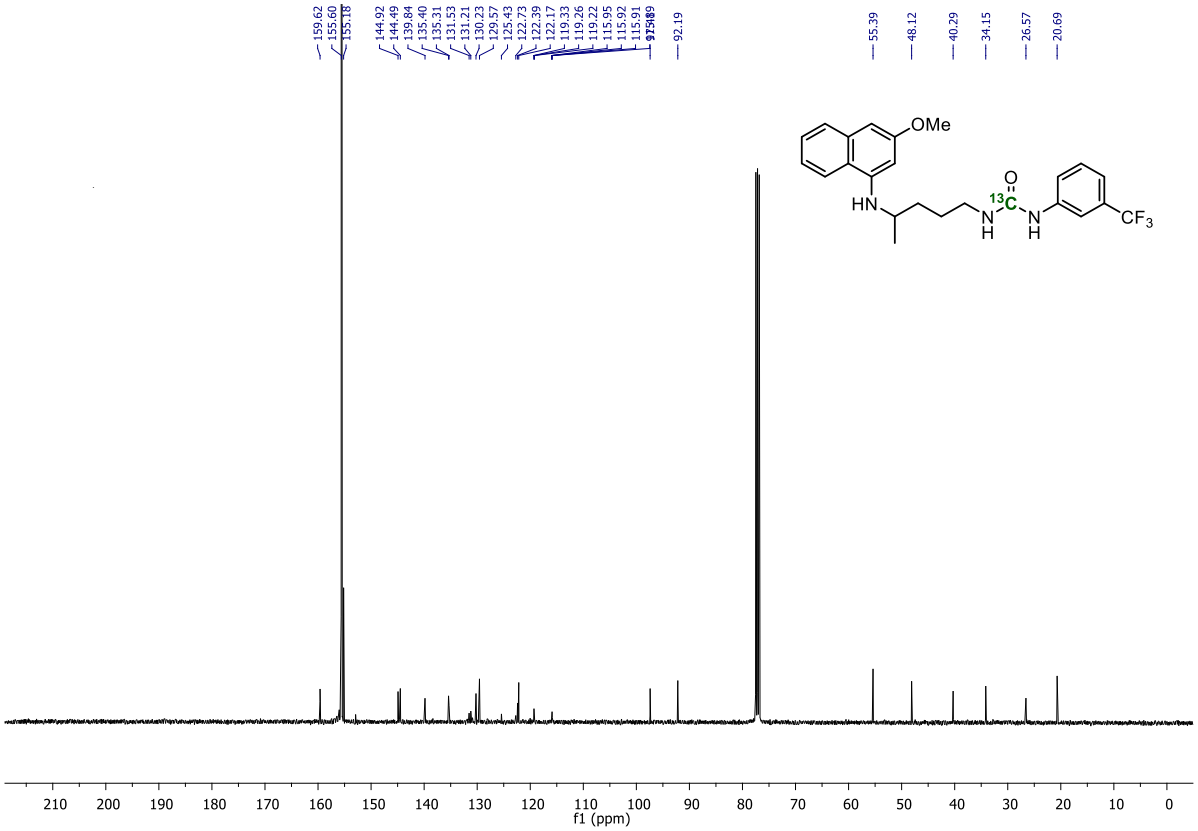
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]37**:



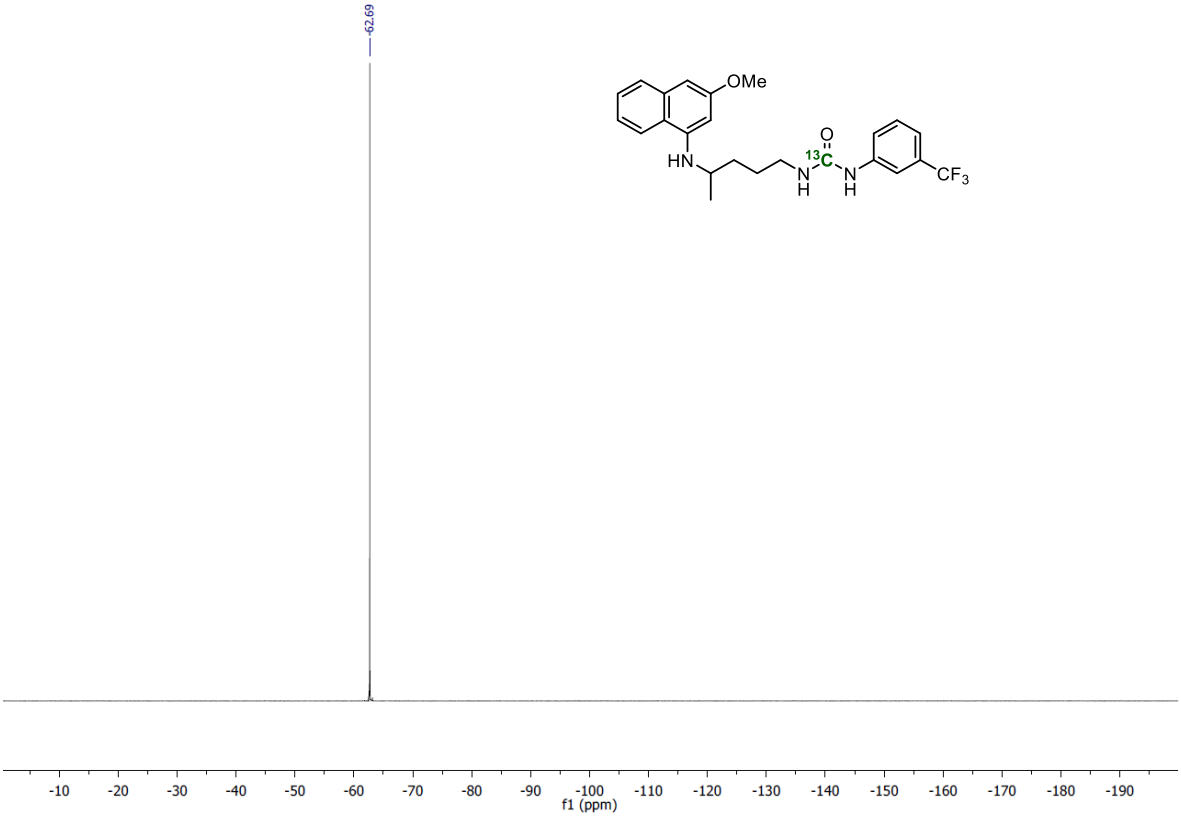
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]38**:



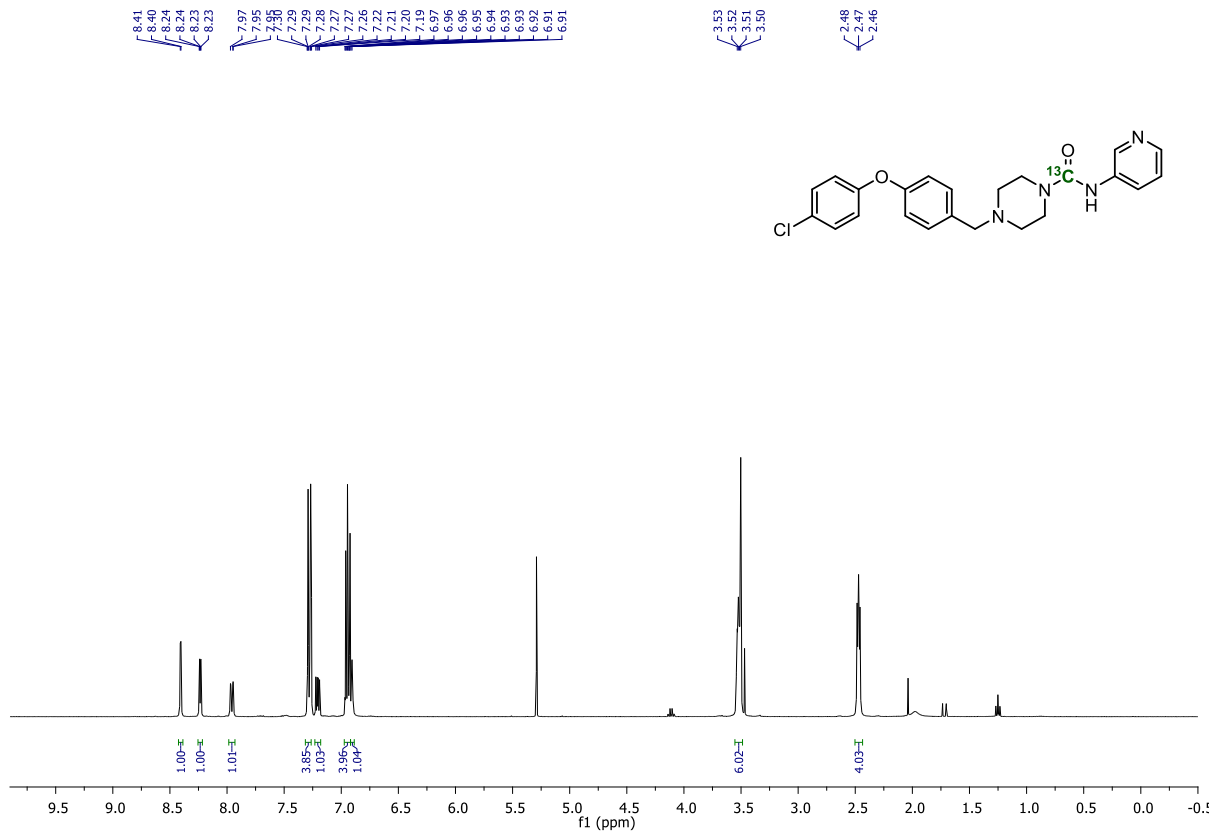
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]38**:



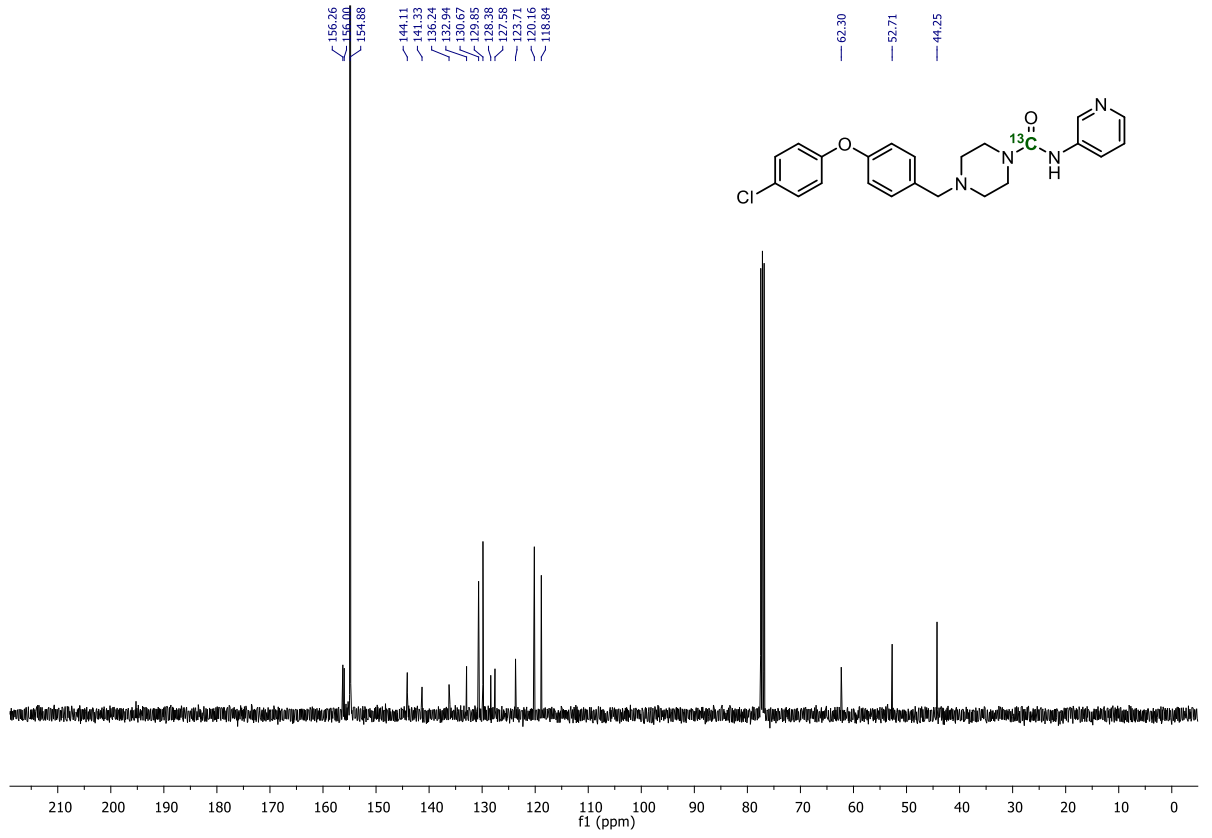
^{19}F NMR (376 MHz, $CDCl_3$) **[^{13}C]38:**



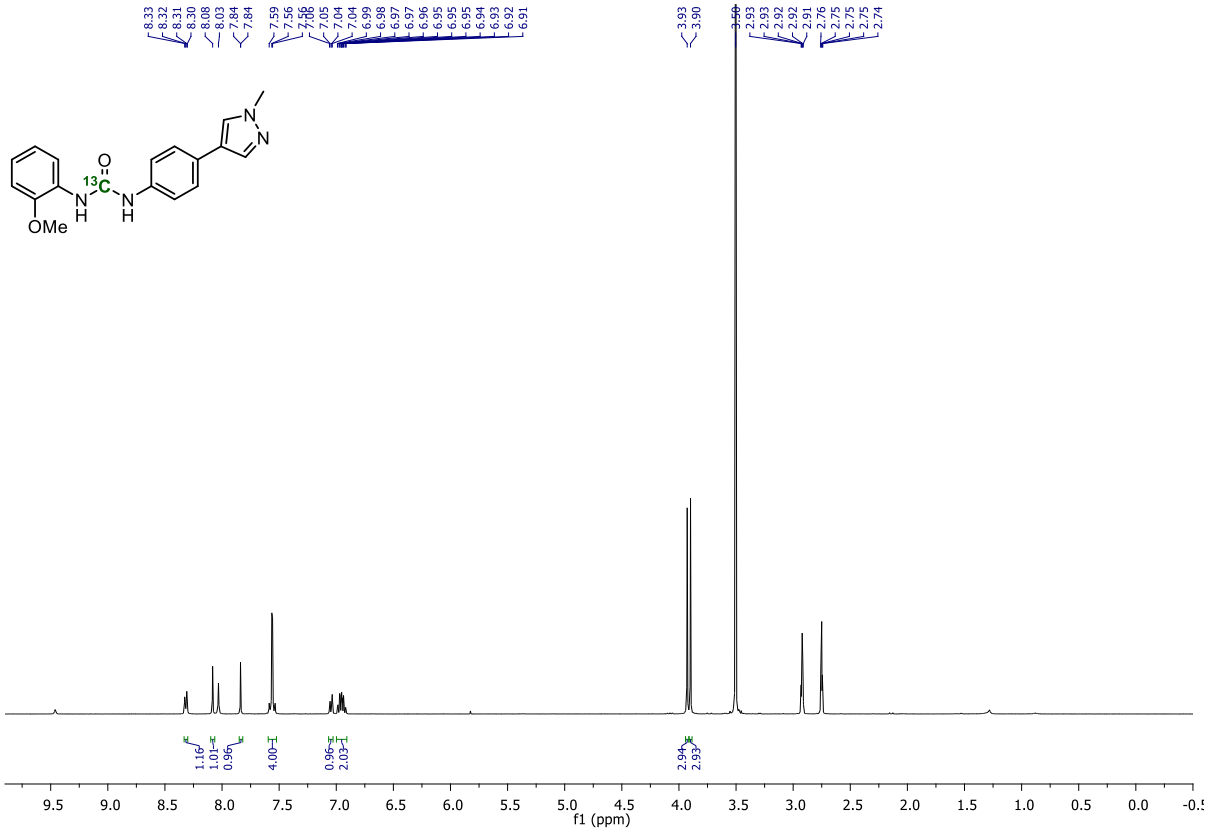
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]39**:



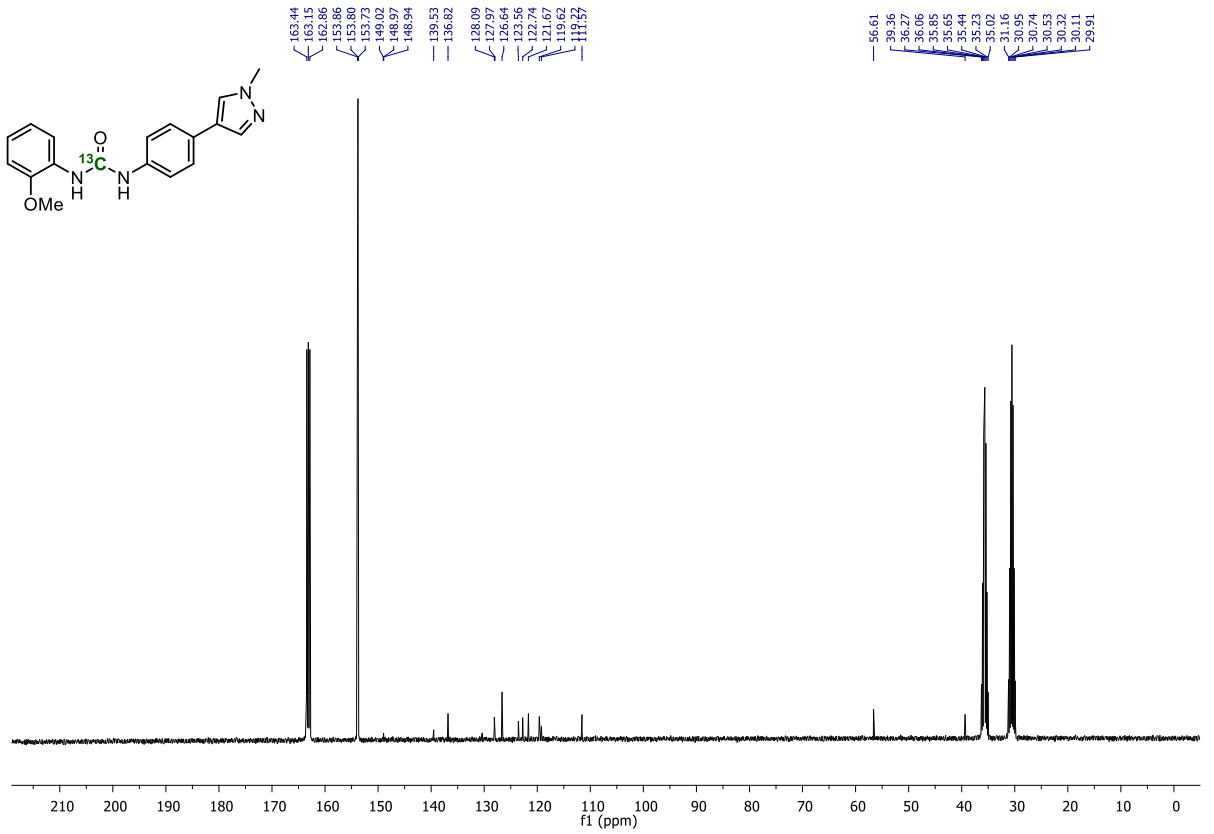
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]39**:



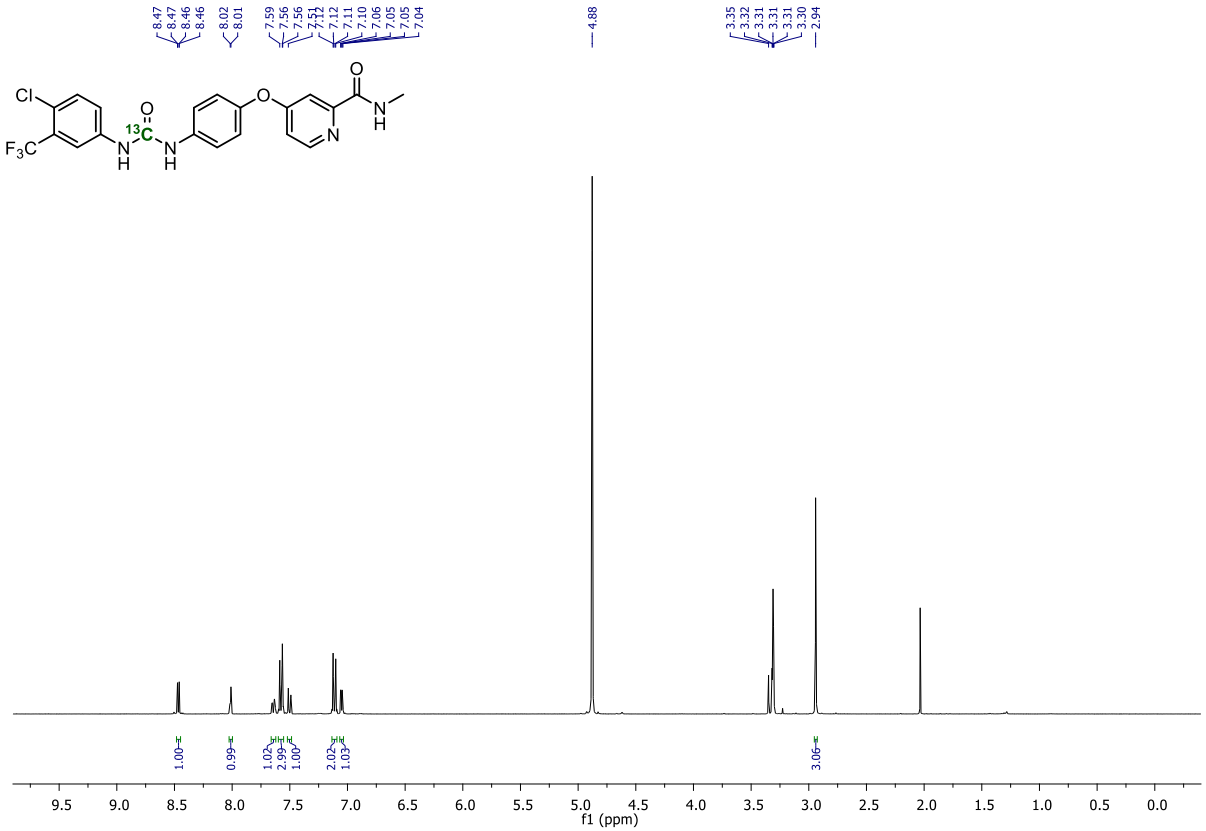
^{1}H NMR (400 MHz, DMF-d_7) **[^{13}C]40**:



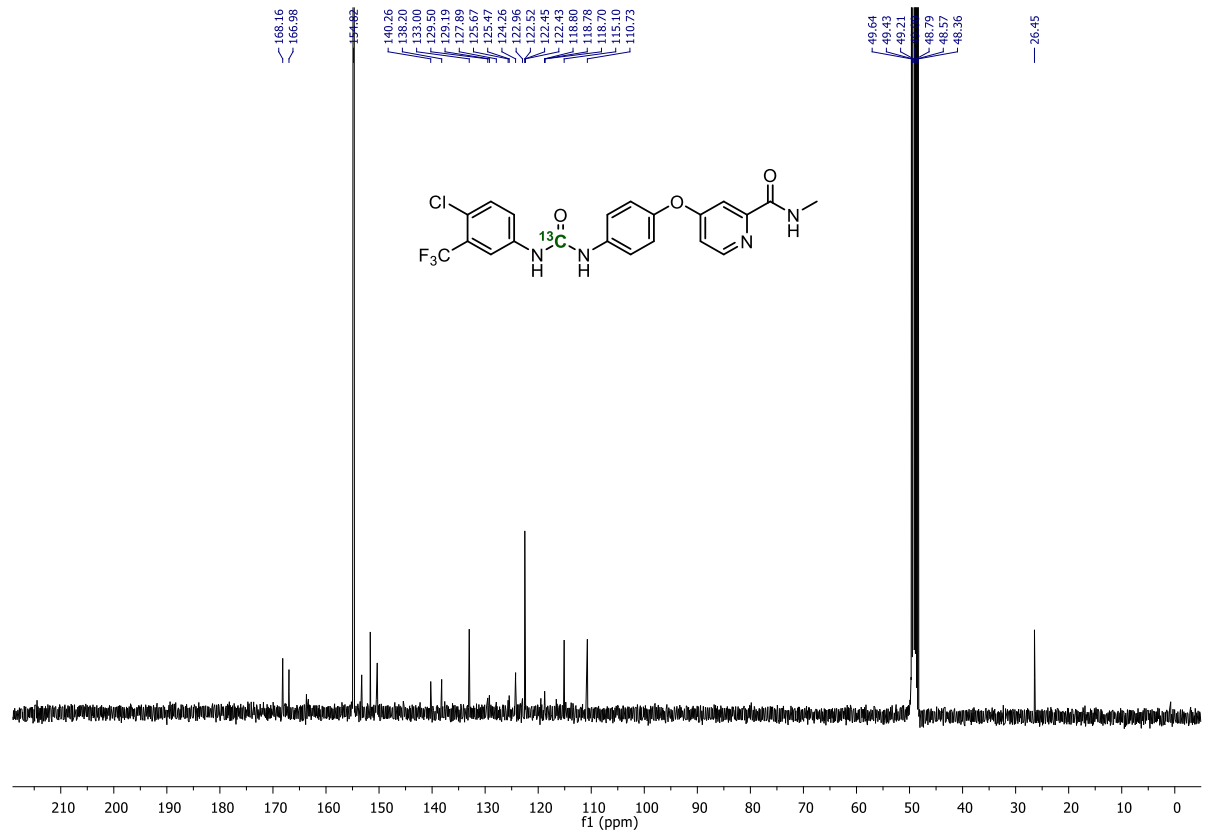
^{13}C NMR (100 MHz, DMF-d_7) **[^{13}C]40**:



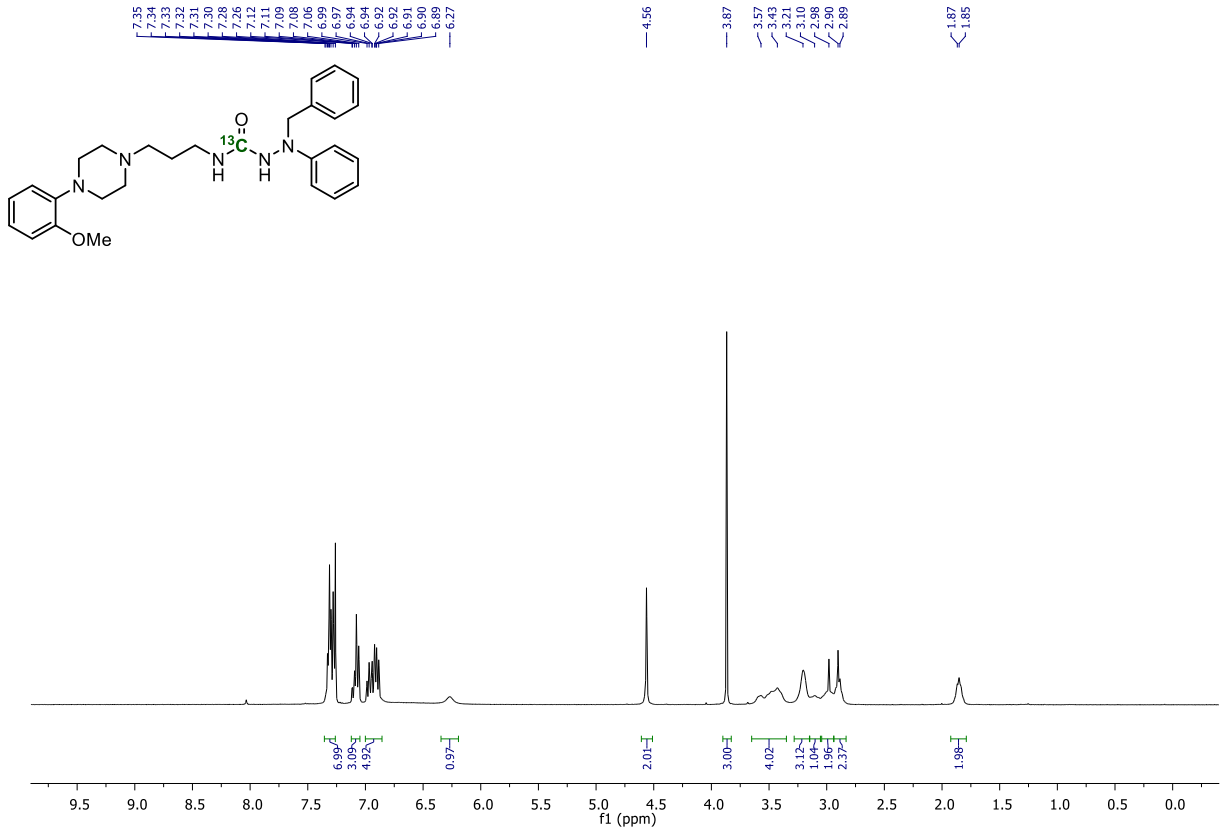
^{1}H NMR (400 MHz, CD_3OD) **[^{13}C]41**:



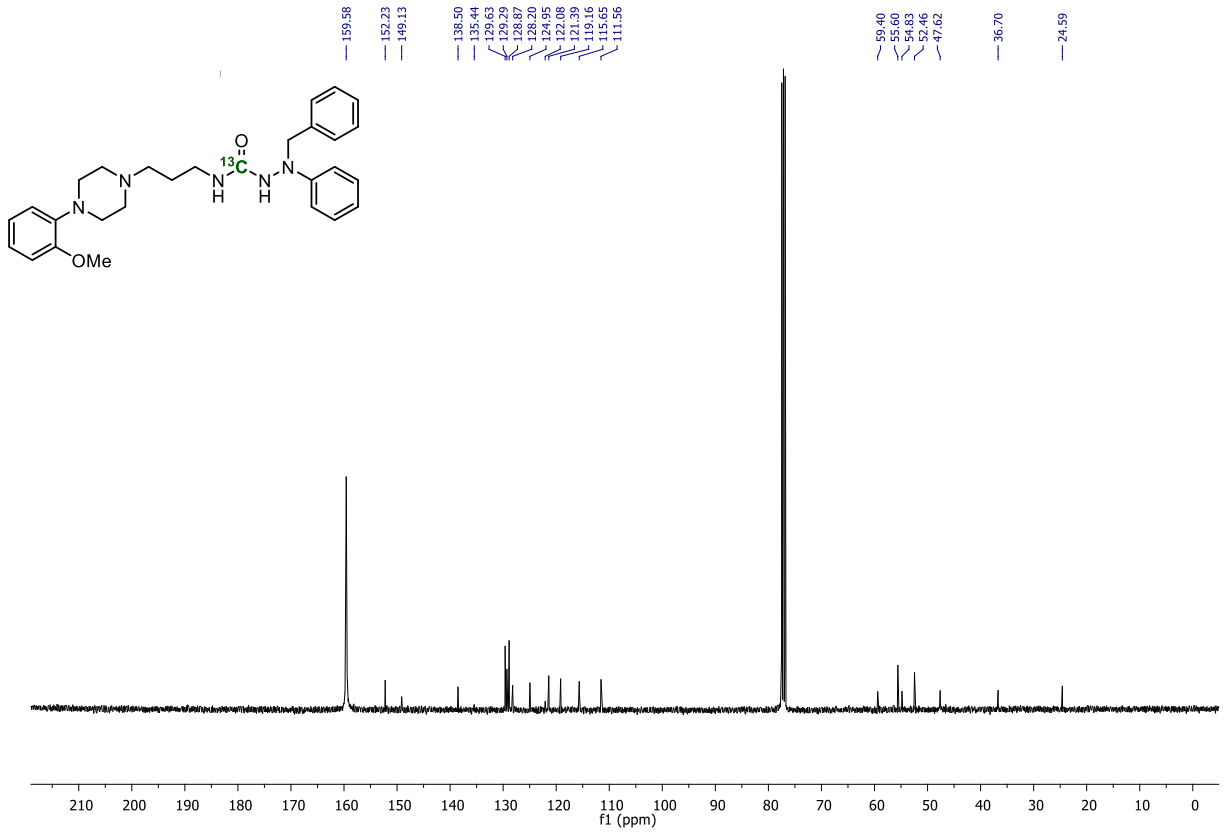
^{13}C NMR (100 MHz, CD_3OD) **[^{13}C]41**:



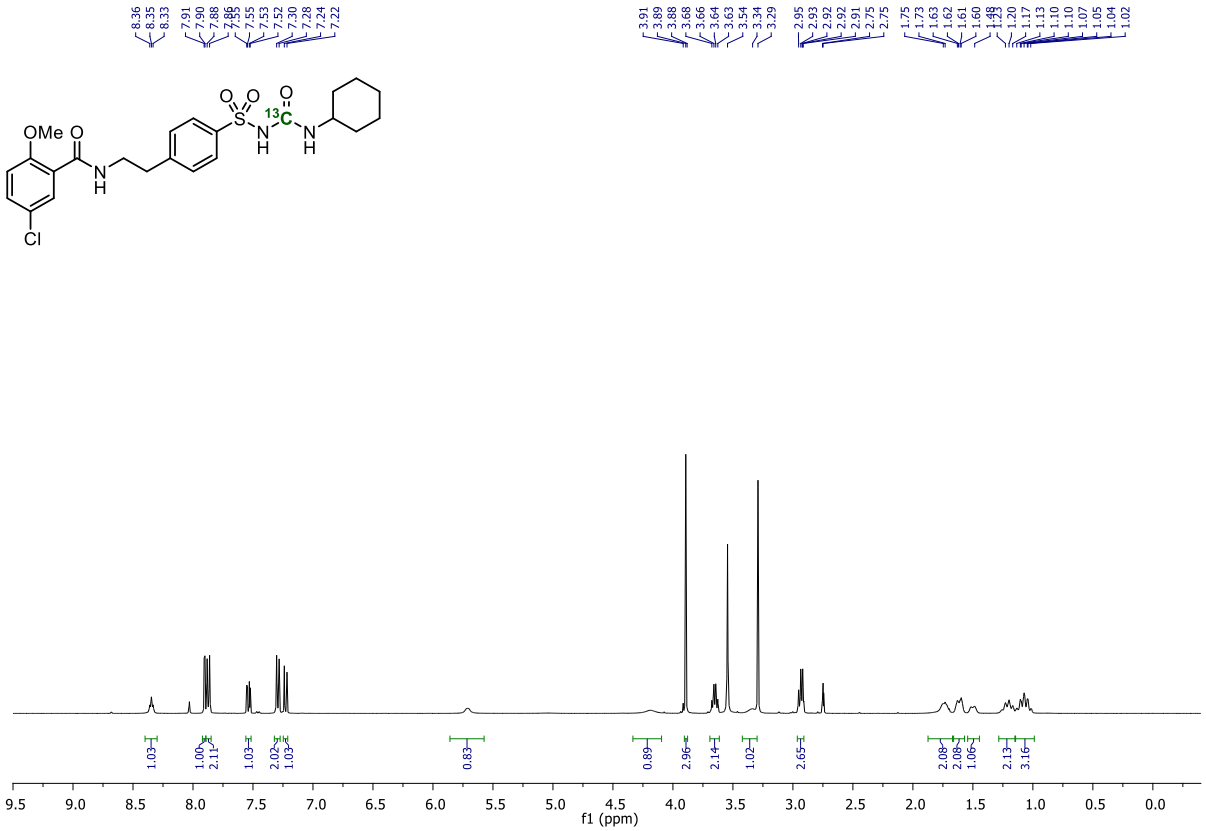
^{1}H NMR (400 MHz, $CDCl_3$) **[^{13}C]42**:



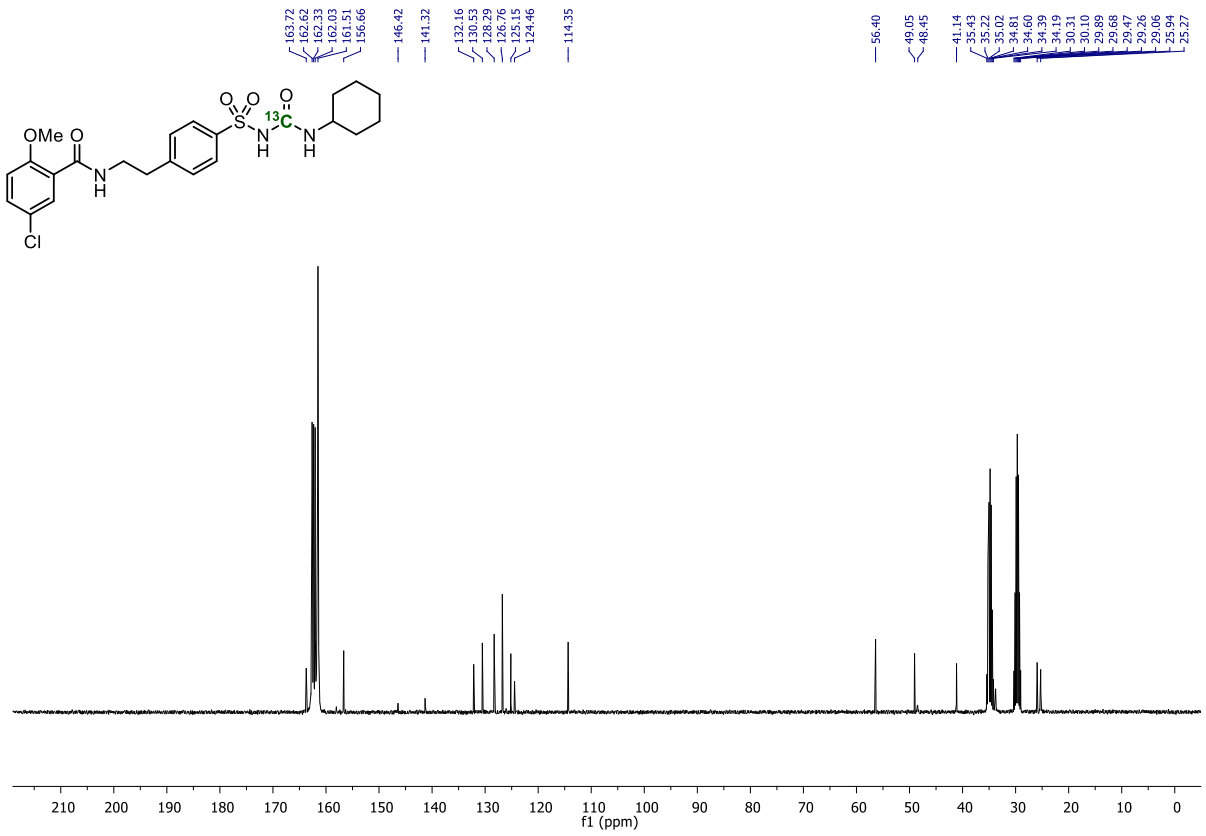
^{13}C NMR (100 MHz, $CDCl_3$) **[^{13}C]42**:



^{1}H NMR (400 MHz, DMF-d_7) **[^{13}C]43**:



^{13}C NMR (100 MHz, DMF-d_7) **[^{13}C]43**:



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