Zinc-Free, Scalable Reductive Cross-Electrophile Coupling Driven by Electrochemistry in an Undivided Cell

Mareena C. Franke[†], Victoria R. Longley[†], Mohammad Rafiee[‡], Shannon S. Stahl[†], Eric C. Hansen,[§] Daniel J. Weix*[†]*

[†]Department of Chemistry, University of Wisconsin–Madison, Madison, WI 53706 USA.

[‡]Department of Chemistry, University of Missouri−Kansas City, Kansas City, MO 64110 USA.

[§]Chemical Research and Development, Pfizer, Inc., Eastern Point Road, Groton, CT 06340 USA.

Corresponding Authors

*dweix@wisc.edu

*eric.hansen@pfizer.com

Supporting Information

1. General Information

1.1 Reagents and materials

Metals

Nickel(II) dibromide trihydrate ($NiBr_2$•$3H_2O$), nickel(II) dibromide 2-methoxyethyl ether complex ($NiBr_2$•diglyme), nickel(II) dichloride 2-methoxyethyl ether complex ($NiCl_2$•diglyme), and nickel(II) chloride ethylene glycol dimethyl ether complex ($NiCl_2$•dme) were purchased from Sigma Aldrich.

Ligands

4,4',4"-tri-*tert*-butyl-2,2':6',2"-terpyridine (**L1**) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (**L2**) were purchased from Sigma Aldrich. 4,4',4"-trimethyl-2,2':6',2"-terpyridine (**L3**) and 4,4′-dimethyl-2,2′-bipyridine (**L4**) were synthesized according to reported procedure.[1]

Substrates

Preparation and characterization of starting materials **2g**, **2h**, **2p**, are described below in the synthesis of starting materials. All other starting materials were purchased from commercial suppliers and were used as received.

Other Reagents

N,*N*-diisopropylethylamine (DIPEA) was purchased from Sigma Aldrich. Tetrabutylammonium hexafluorophosphate ($TBAPF_6$) was purchased from Oakwood. Anhydrous acetonitrile (MeCN) was purchased from Sigma Aldrich.

Electrochemical Equipment

Nickel foam with 1.6 mm thickness and a surface density of 350 g/m^2 (80-110 pores per inch, average hole diameters about 0.25 mm) was purchased from MTI corporation (Part number EQ-bcnf-16m) and was cut to size.
Graphite rods with 0.125" diameter, grade: GR008G were purchased from Graphitestore.com (Part number NC001295) and cut into 10 cm pieces.
Nickel plate electrode was purchased from Electrocell (part number 4-40005-02).
Graphite plate, 0.125" thickness, grade: G347B was purchased from MWI Carbon and Graphite Solutions (Part number G347b-311-Custom) and was machined to make four electrode plates.
WaveNow^{xv} potentiostat from Pine Research (Part number WN70-XV).
LowProfile Silver Wire Pseudo-Reference Electrode from Pine Research (Part number RREF0153).
Glassy Carbon Electrode, 3.0mm diameter, from BASi (Part number MF-2012).
Teflon cap from BASi (Part number MR-1065).
Platinum auxiliary electrode, 99.95% pure, 0.5 mm diameter, from BASi (Part number MW-4130).
Glass vial from BASi (Part number MR-5255).
Reference Electrode Glass Body and CoralPor® Membrane from BASi (Part number MF-2042).
Replacement CoralPor® for Reference Electrodes from BASi (Part number MF-2064).

Tubing
Peristaltic pump tubing: Masterflex® L/S® Precision Pump Tubing, PharMed® BPT, size 14 and size 16, and Masterflex L/S® Precision Pump Tubing, Gore® STA-PURE® PFL-Series size 16 tubing were purchased from Cole Parmer. Teflon tubing (1/16" inner diameter, 1/8" outer diameter) was purchased from Thermo Scientific. The tubing was connected using Masterflex® Fittings, Polypropylene (PP), Straight Hose Barb Unions, 1/16" ID from Cole Parmer.

Cost of Flow Setup

Dr Meter DC Bench Power Supply × 2	$ 134
Masterflex L/S® Easy-Load® II Pump Head, 2-Channel	$ 498
Masterflex L/S® Analog Variable-Speed Console Drive	$ 948
Masterflex® L/S® Precision Pump Tubing, PharMed® BPT, size 14	$ 161
ElectroCell Micro Flow Cell Base Unit × 2	$3,590
MWI Graphite plate: grade G347B (0.125" × 4.3" × 7.5")	$ 235
MTI Nickel foam (1 m × 300 mm × 1.6 mm)	$ 298
Fisherbrand™ Fiberglass Insulated Cloth Heating Tape × 2	$ 140
General glassware and other supplies	$ 250
Total	$6,254

1.2 Methods

NMR Spectroscopy
NMR spectra were recorded on Avance Bruker NMR spectrometers operating at either 400 MHz or 500 MHz and data analysis was performed with MestReNova. ^{1}H nuclear magnetic resonance (NMR) spectroscopy chemical shifts are referenced to tetramethylsilane (TMS) in $CDCl_3$ ($\delta = 0.00$ ppm) or to the residual CH_2Cl_2 solvent peak ($\delta = 5.33$ ppm) when in CD_2Cl_2. ^{13}C NMR chemical shifts are referenced to the residual $CDCl_3$ solvent peak ($\delta = 77.2$ ppm). Chemical shifts are reported in parts per million (ppm), multiplicities are indicated by singlet (s), doublet (d), triplet (t), quartet (q), heptet (hept), multiplet (m) and broad (br). Coupling constants (J) are reported in Hertz (Hz).

Gas Chromatography
GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m × 180 μm × 0.18 μm), dual FID detectors, and hydrogen as the carrier gas. A sample volume of 1 μL was injected at a temperature of 300 °C and a 100:1 split ratio. The initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. The initial oven temperature of 50 °C was held for 0.46 min followed by a temperature ramp of 65 °C/min up to 300 °C. The total run time was 5.0 min and the FID temperature was 325 °C.

Chromatography
Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques, on a Teledyne Isco Rf-200 (detection at 210 nm and 280 nm), or on a Biotage Isolera One (detection at 210 nm and 400 nm, on KPsil columns). Products were visualized by UV or PMA stain.

Elemental Analysis

Analytical data were obtained from the CENTC Elemental Analysis Facility at the University of Rochester, funded by NSF CHE-0650456. Microanalysis samples were weighed with a PerkinElmer Model AD6000 Autobalance and their compositions were determined with a PerkinElmer 2400 Series II Analyzer. Air-sensitive samples were handled in a VAC Atmospheres glovebox. Samples were transferred under argon and was combusted in a tin capsule that was crimp-sealed with a die apparatus.

Infrared Spectroscopy

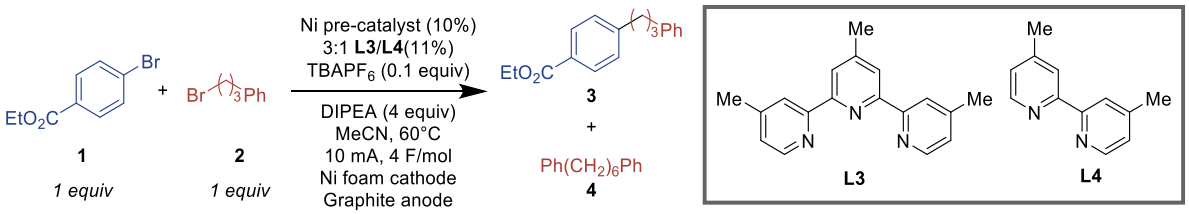
Infrared (IR) spectra were recorded on a Bruker Alpha Platinum FT-IR spectrometer in ATR mode and are reported in wavenumbers (cm^{-1}).

High Resolution Mass Spectrometry

Mass spectrometry data was collected on a Thermo Q Exactive Plus (thermofisher.com) via flow injection with electrospray ionization or via ASAP-MS (asap-ms.com) by the chemistry mass spectrometry facility at the University of Wisconsin-Madison. The purchase of the Thermo Q Exactive Plus in 2015 was funded by NIH Award 1S10 OD020022 to the Department of Chemistry.

2. Supplemental Data

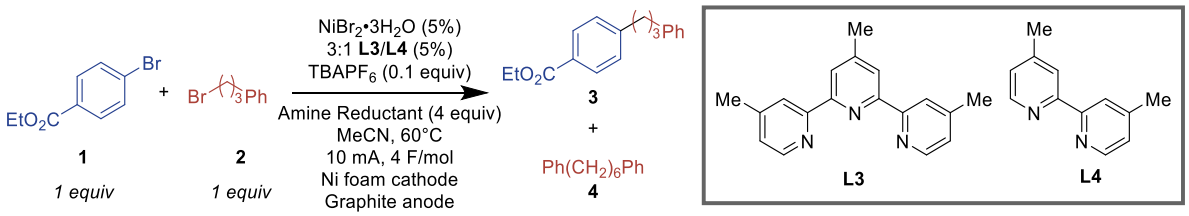
2.1 Figure S1. Nickel Pre-catalyst Screen in Batch



Entry	Ni pre-catalyst	Yield (%)[a]			
		1	**2**	**3**	**4**
1	$NiBr_2•3H_2O$	0	0	**69**	16
2	$NiBr_2$•diglyme	0	1	**69**	13
3	$NiCl_2$•diglyme	0	11	**72**	8
4	$NiCl_2$•dme	43	20	**42**	16

[a]Corrected GC yield vs dodecane.

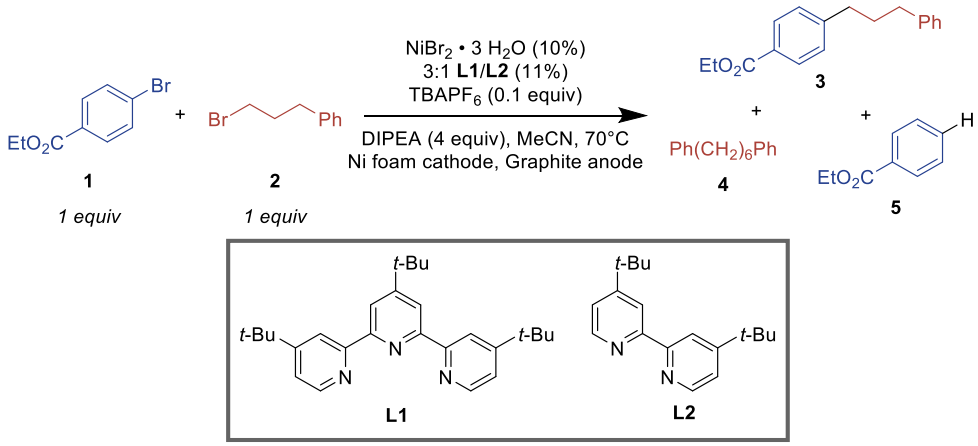
2.2 Figure S2. Amine Reductant Screen in Batch



Entry	Amine Reductant	Yield (%)[a]			
		1	**2**	**3**	**4**
1	Triethylamine	2	4	**59**	15
2	DIPEA	2	0	**74**	11

[a]Corrected GC yield vs dodecane.

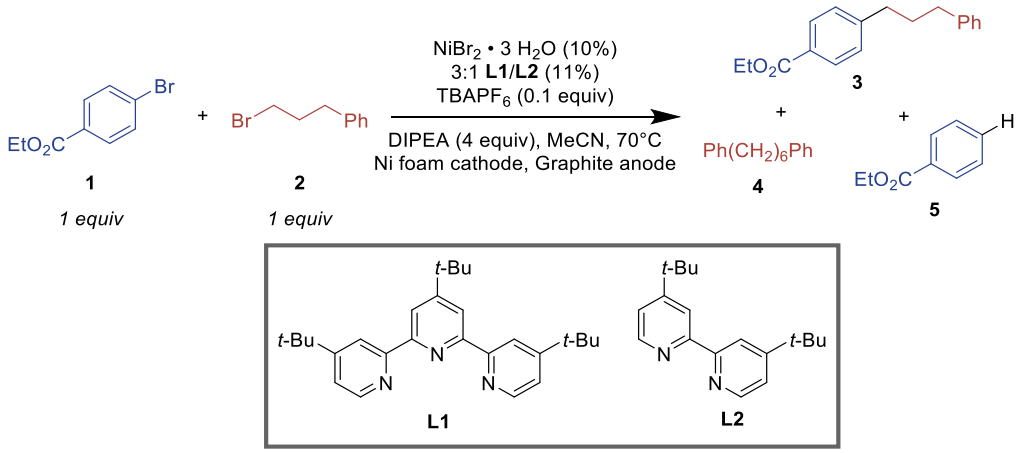
2.3 Figure S3. Air and Water Tolerance in Batch[a]



Entry	Description	Yield (%)[b]				
		1	**2**	**3**	**4**	**5**
1	Glovebox procedure	0	3	**96**	5	4
2	Glovebox procedure, then opened to air	0	0	**93**	10	6
3	Benchtop procedure	0	1	**88**	7	8

[a]Reactions were conducted in an undivided cell and run on 0.4 mmol scale in MeCN (2 mL).
[b]Yields were determined by NMR using CH_2Br_2 as an internal standard.

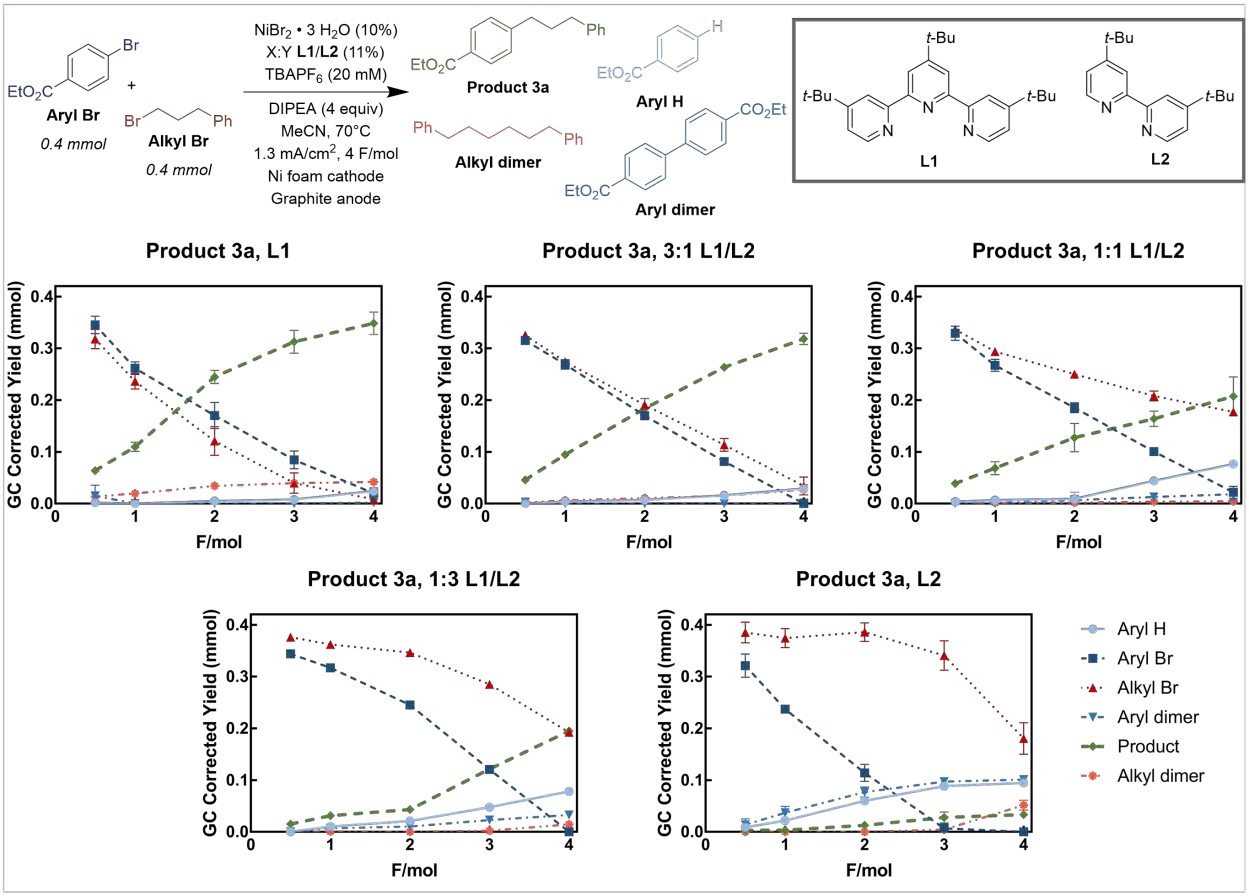
2.4 Figure S4. Current Density in Batch[a]



Entry	Current Density (mA/cm^2)	F/mol	Yield (%)[b]				
			1	**2**	**3**	**4**	**5**
1	1.33	2	43	40	**50**	2	0
2	1.33	4	3	5	**89**	3	4
3	2.67	2	37	7	**56**	12	4
4	2.67	4	0	0	**59**	12	14
5	5.33	2	53	13	**32**	14	5
6	5.33	4	11	0	**44**	16	20

[a]Reactions were conducted in an undivided cell and run on 0.4 mmol scale in MeCN (2 mL).
[b]Corrected GC yield vs dodecane.

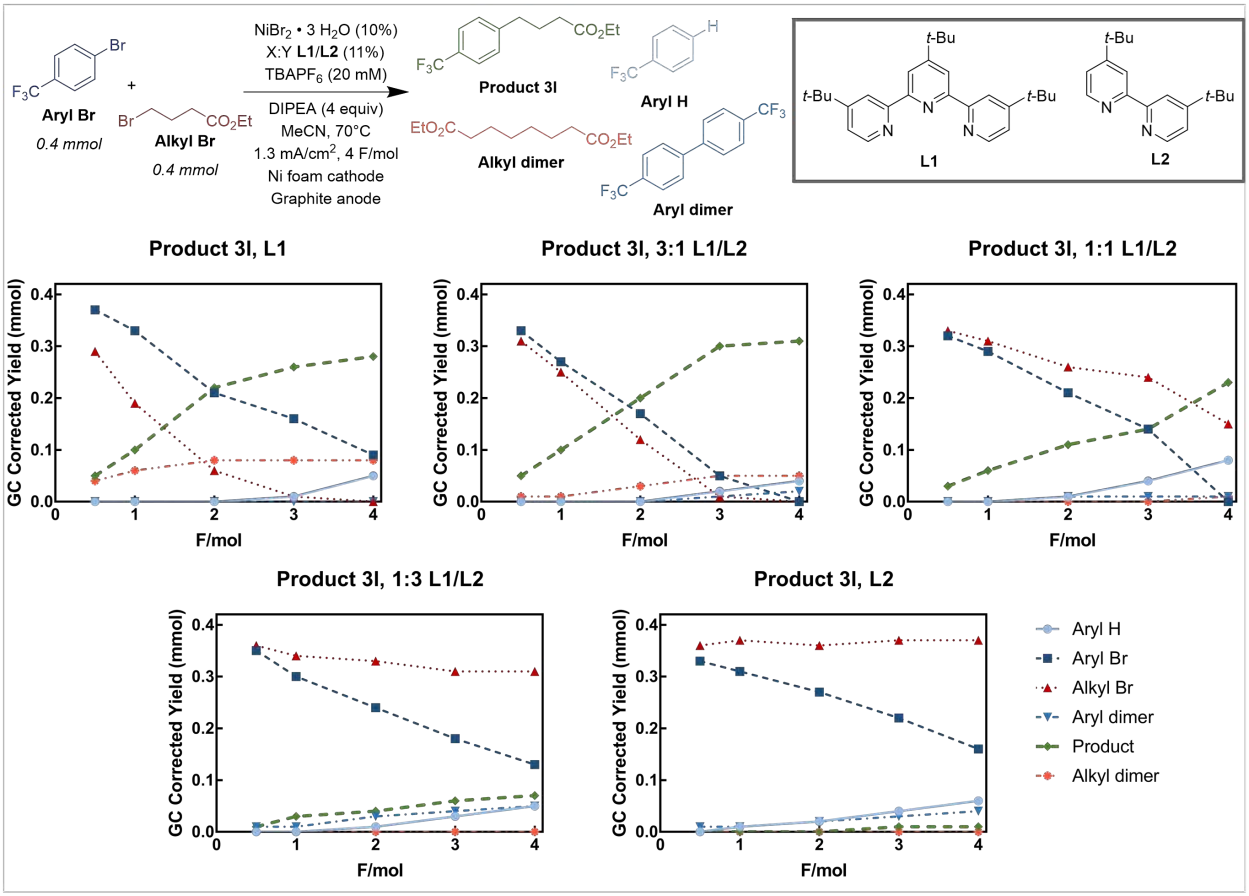
2.5 Figure S5. Time Courses of Varying Ligand Ratios for Product 3a[a]



[a]Reactions were conducted in duplicate. The average data is shown with standard deviation error bars, except for 1:3 **L1**/**L2** which only has one data set.

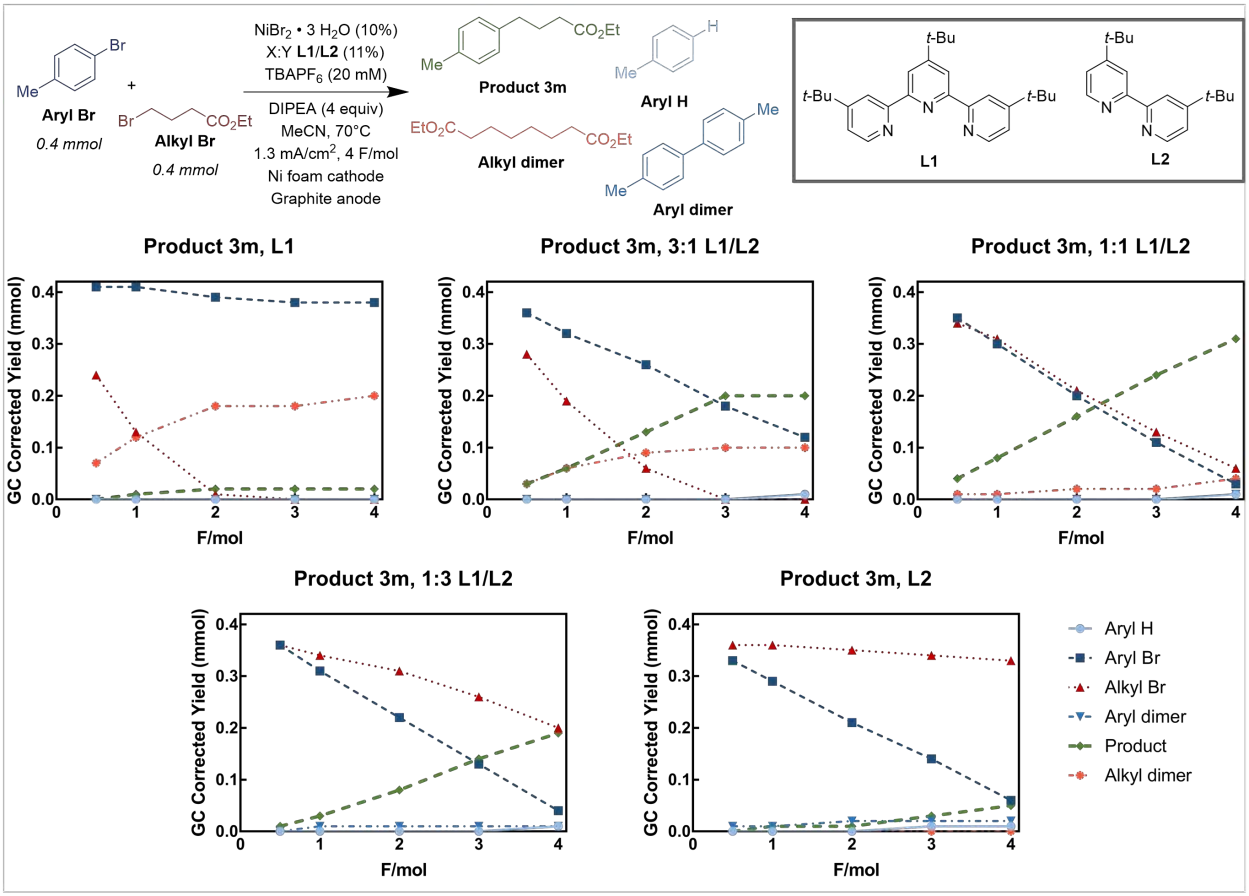
See 4.3 Ligand Ratio Time Course Procedure for the procedure and method of analysis.

2.6 Figure S6. Time Courses of Varying Ligand Ratios for Product 3l



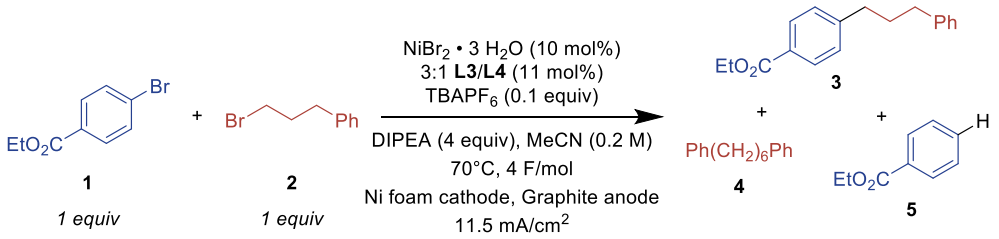
See 4.3 Ligand Ratio Time Course Procedure for the procedure and method of analysis.

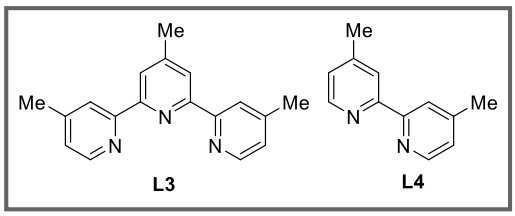
2.7 Figure S7. Time Courses of Varying Ligand Ratios for Product 3m



See 4.3 Ligand Ratio Time Course Procedure for the procedure and method of analysis.

2.8 Figure S8. Current Density Optimization in Batch[a]

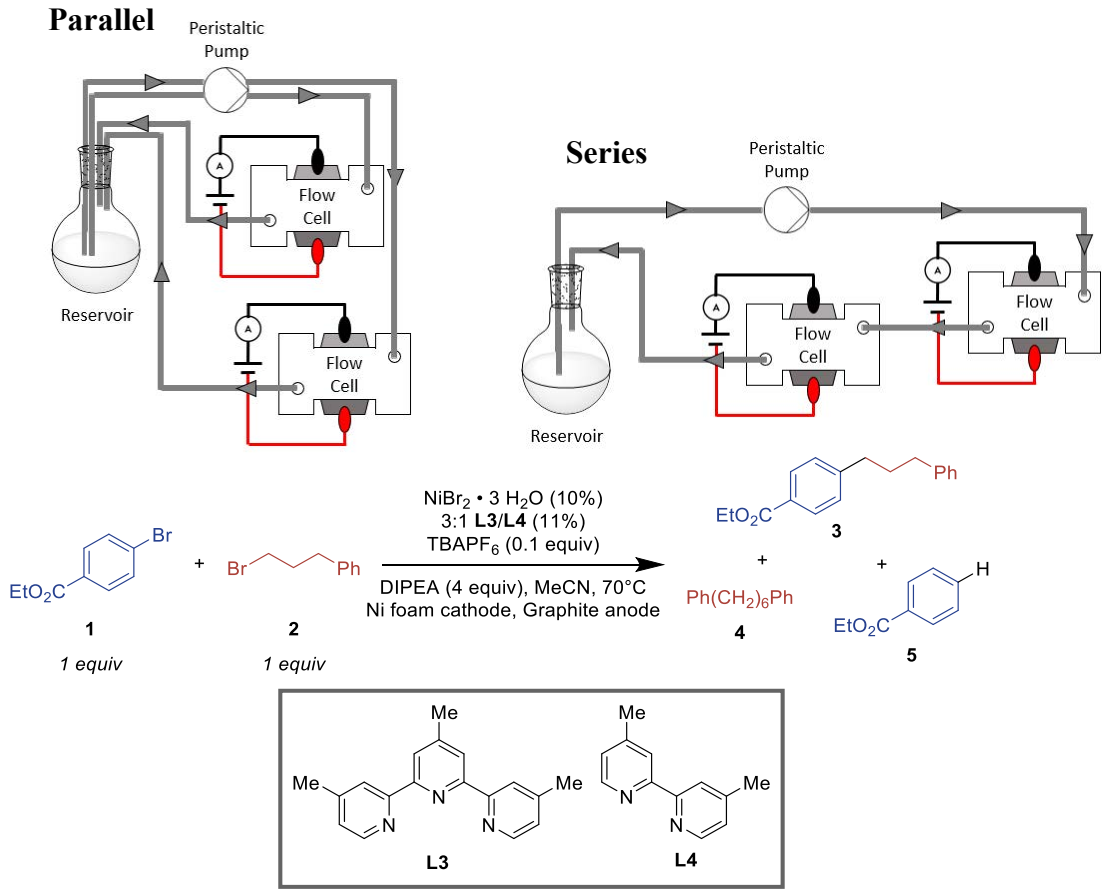




Entry	Deviation from above conditions	Yield (%)[b]				
		1	**2**	**3**	**4**	**5**
1	None	0	0	**59**	9	10
2	1.2 equiv of **1** instead of 1.0 equiv	0	0	**60**	12	10
3	1.2 equiv of **2** instead of 1.0 equiv	0	0	**57**	9	14
4	0.2 equiv of $TBAPF_6$ instead of 0.1 equiv	0	0	**59**	10	12
5	15 mol% ligands instead of 11 mol%	0	0	**50**	12	34
6	20 mol% ligands instead of 11 mol%	0	0	**34**	16	48
7	11 mol% Ni instead of 10 mol%	3	3	**62**	8	10
8	8 mol% Ni instead of 10 mol%	0	0	**47**	13	30
9	5.5 mol% Ni instead of 10 mol%	13	0	**14**	23	56
10	0.2 equiv phthalimide	15	2	**36**	14	30
11	0.2 equiv potassium phthalimide	6	0	**45**	12	31
12	0.2 equiv 4-ethylpyridine	0	0	**58**	10	16
13	60 °C instead of 70 °C	32	2	**26**	15	21
14	80 °C instead of 70 °C	0	0	**52**	10	17

[a]Reactions were conducted in an undivided cell and run on 0.4 mmol scale in MeCN (2 mL).
[b]Corrected GC yield vs dodecane.

2.9 Figure S9. Two Flow Cells in Parallel vs Series



Setup[a]	Reaction Time (h)	Efficiency (mmol/h/cm^2)	Yield 3 (%)[b]
One flow cell	5.4	0.053	**75**
Two flow cells in parallel	3.1	0.046	**72**
Two flow cells in series	3.4	0.042	**64**

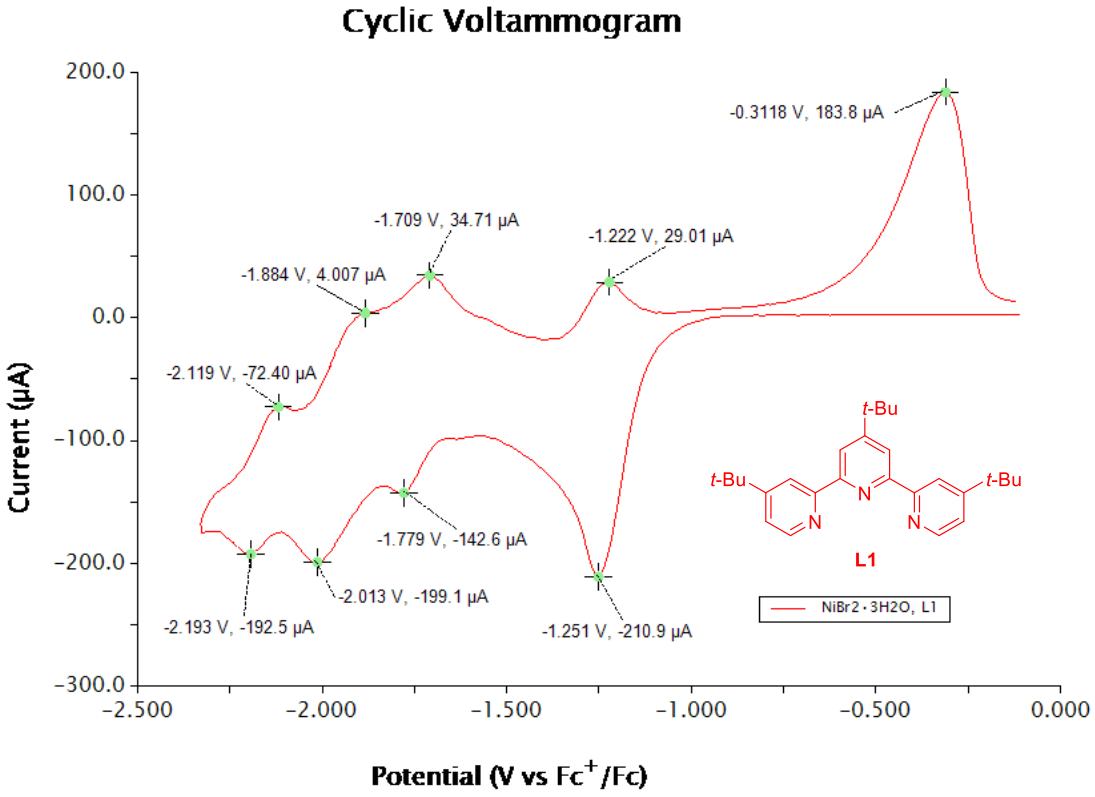
[a]Reactions in recirculation flow with an undivided flow cell(s) and run on 3 mmol scale in MeCN (15 mL).
[b]Corrected GC yield vs 1,3,5-trimethoxybenzene.

3. Cyclic Voltammetry Data

Cyclic voltammograms (CVs) were conducted at room temperature in a N_2 filled glovebox. Electrodes used include: a $Ag/AgNO_3$ reference electrode, a glassy carbon working electrode, and a Pt wire counter electrode. The reference electrode was filled with 10 mM $AgNO_3$, 100 mM $TBAPF_6$ in MeCN. First a ferrocene standard (10 mM ferrocene, 100 mM $TBAPF_6$ in MeCN) was analyzed. The CVs of subsequent complexes were referenced to the $E_{1/2}$ of the ferrocene standard.

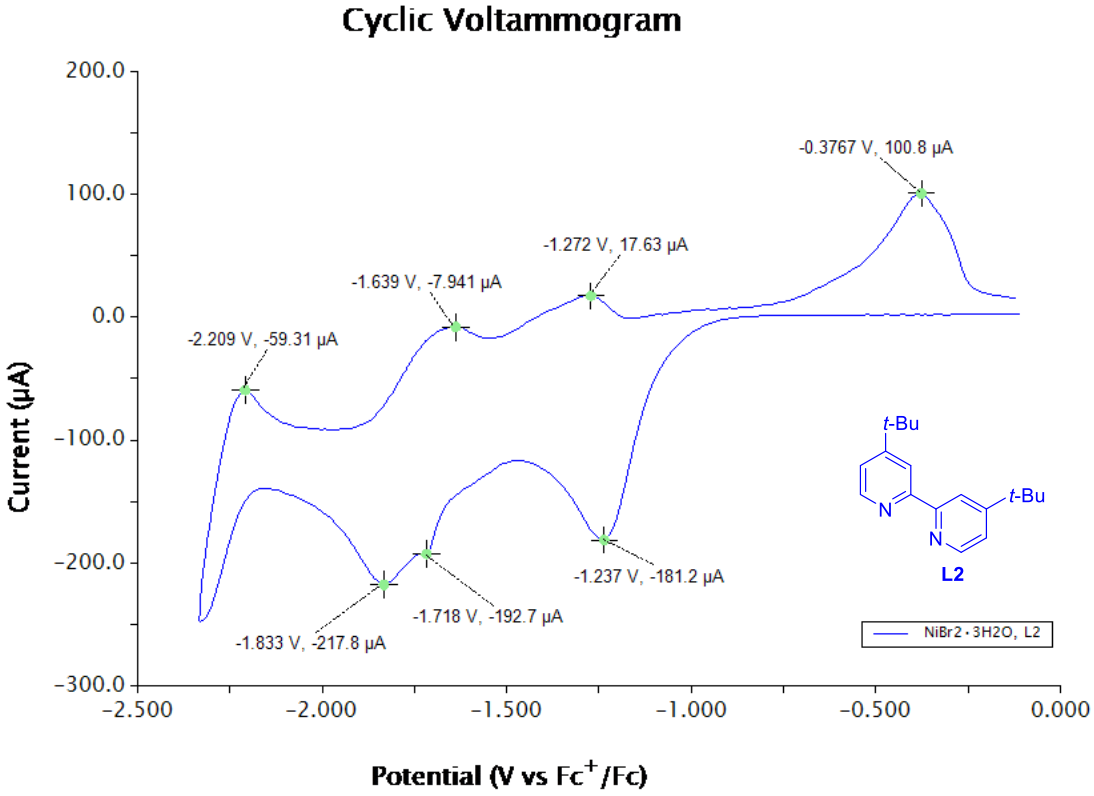
3.1 Figure S10. CV of $NiB_2•3H_2O$ + L1

10 mM $NiBr_2•3H_2O$, 10 mM **L1**, 100 mM $TBAPF_6$ in MeCN



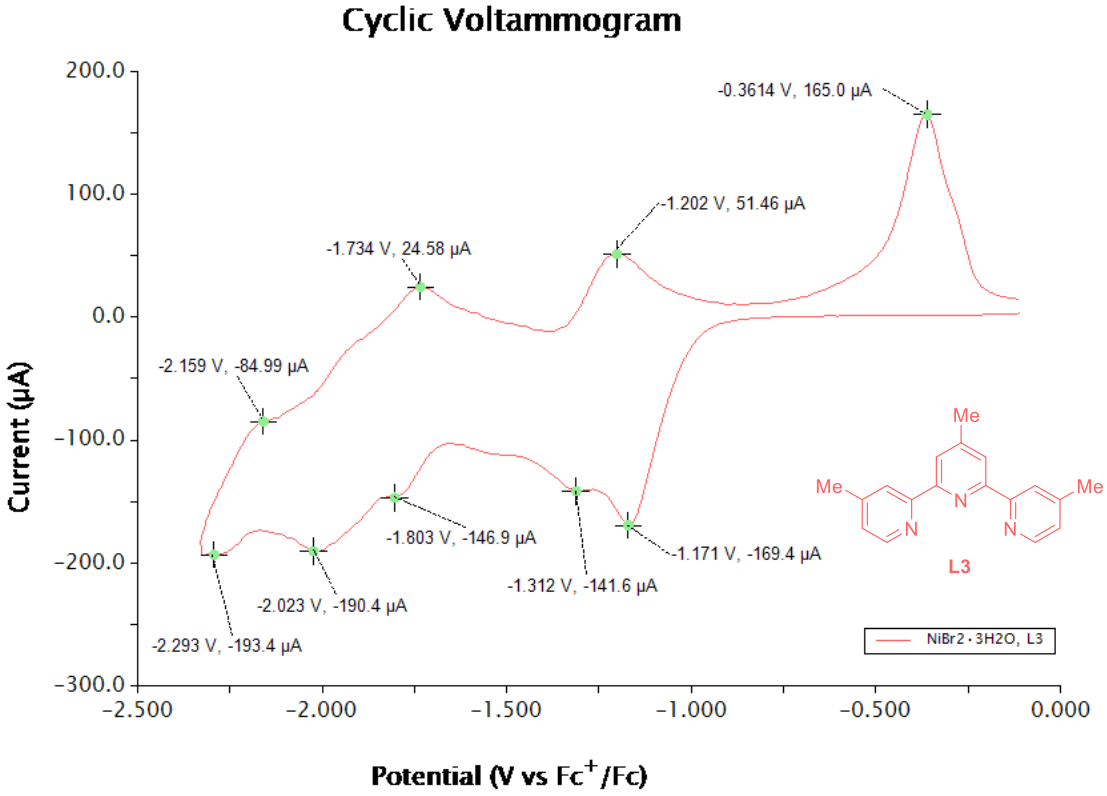
3.2 Figure S11. CV of $NiB_2•3H_2O$ + L2

10 mM $NiBr_2•3H_2O$, 10 mM **L2**, 100 mM $TBAPF_6$ in MeCN



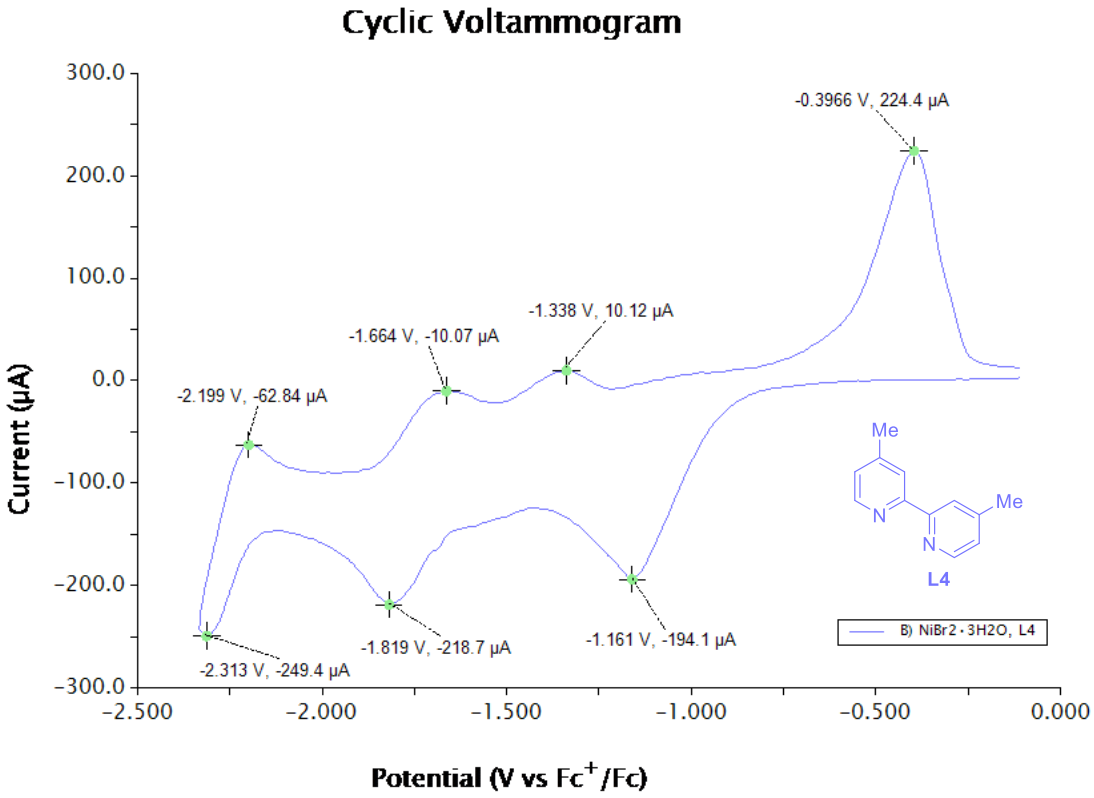
3.3 Figure S12. CV of $NiB_2•3H_2O$ + L3

10 mM $NiBr_2•3H_2O$, 10 mM **L3**, 100 mM $TBAPF_6$ in MeCN



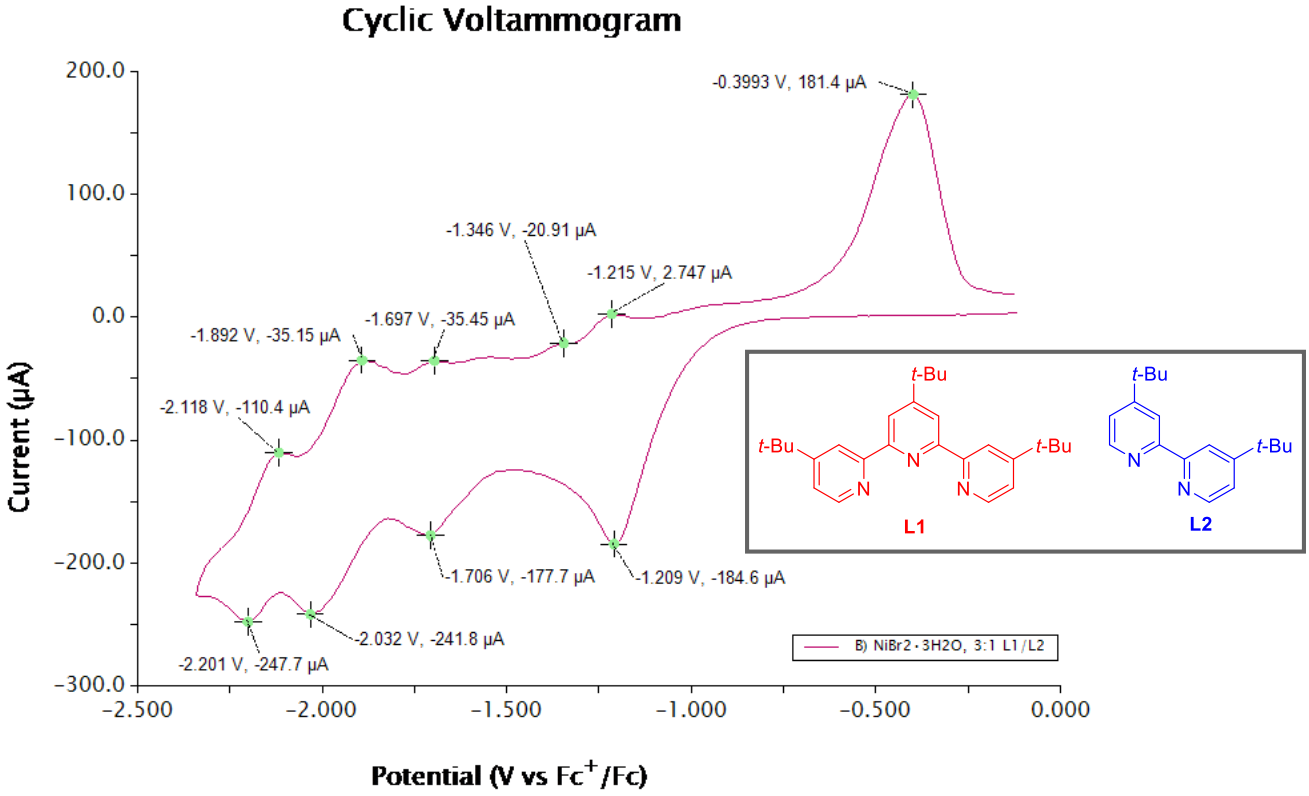
3.4 Figure S13. CV of $NiB_2•3H_2O$ + L4

10 mM $NiBr_2•3H_2O$, 10 mM **L4**, 100 mM $TBAPF_6$ in MeCN



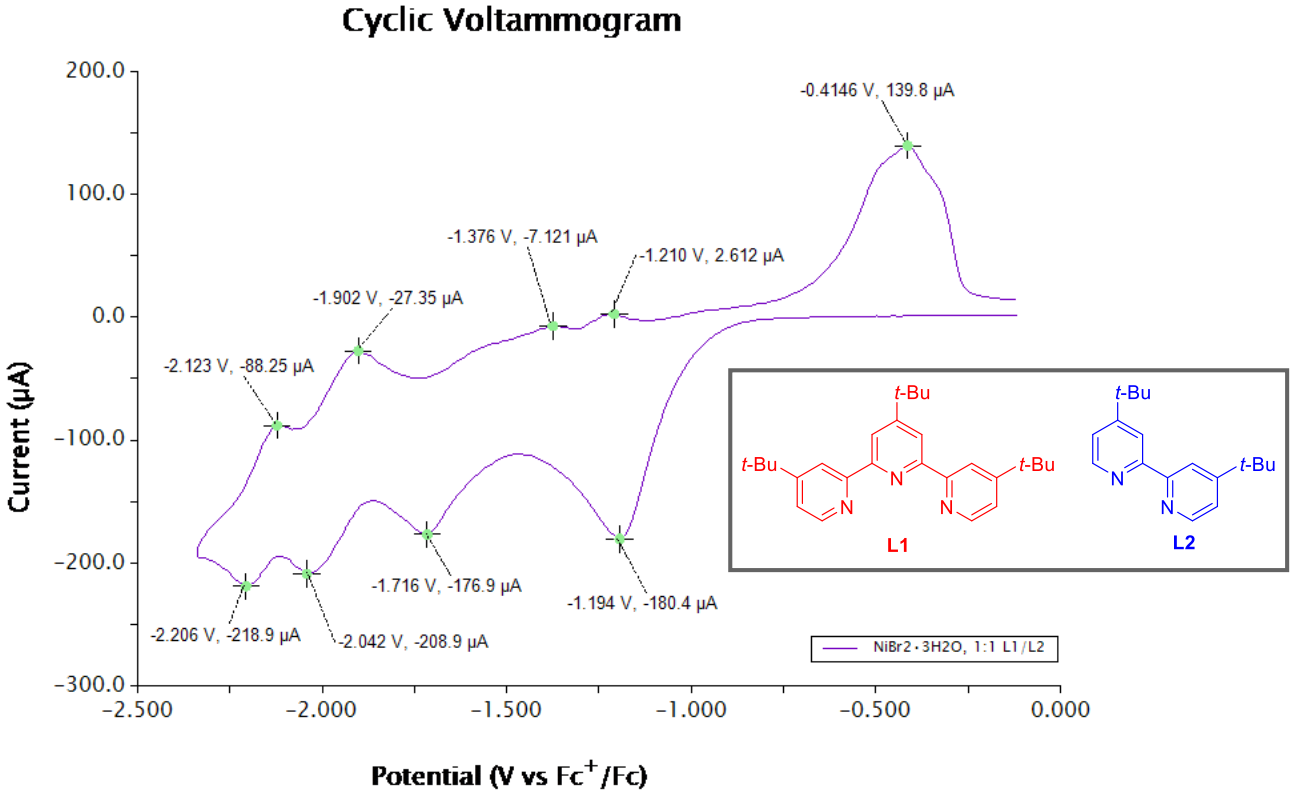
3.5 Figure S14. CV of NiB_2•$3H_2O$ + 3:1 L1/L2

10 mM $NiBr_2$•$3H_2O$, 7.5 mM **L1**, 2.5 mM **L2**, 100 mM $TBAPF_6$ in MeCN



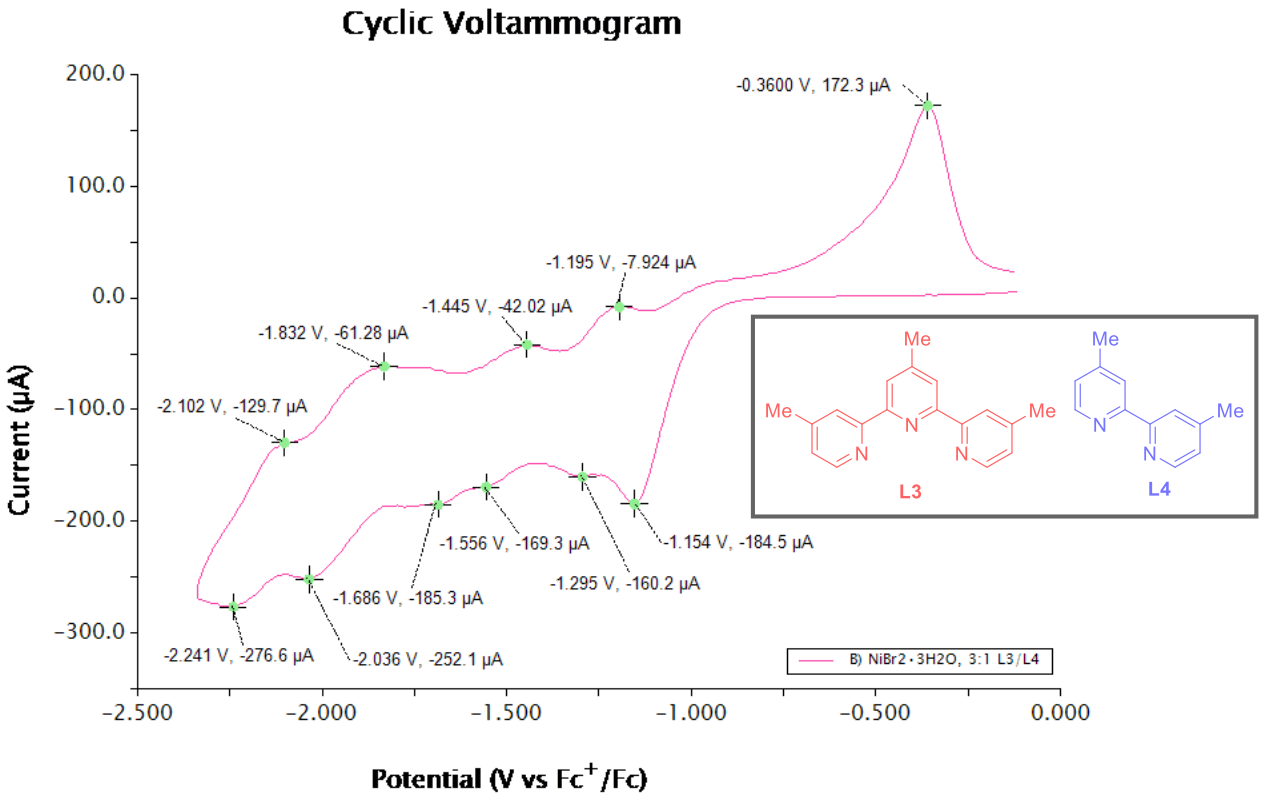
3.6 Figure S15. CV of $NiB_2•3H_2O$ + 1:1 L1/L2

10 mM $NiBr_2•3H_2O$, 5 mM **L1**, 5 mM **L2**, 100 mM $TBAPF_6$ in MeCN



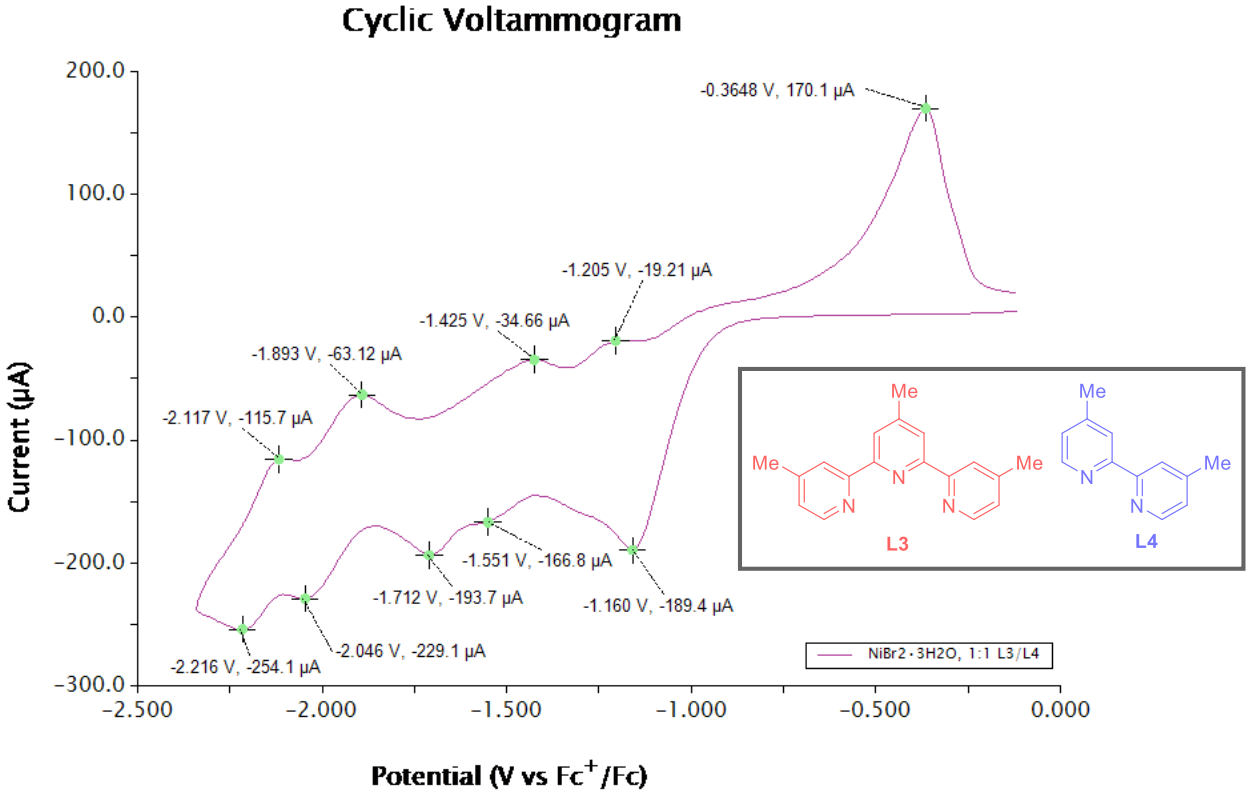
3.7 Figure S16. CV of $NiB_2•3H_2O$ + 3:1 L3/L4

10 mM $NiBr_2•3H_2O$, 7.5 mM **L3**, 2.5 mM **L4**, 100 mM $TBAPF_6$ in MeCN

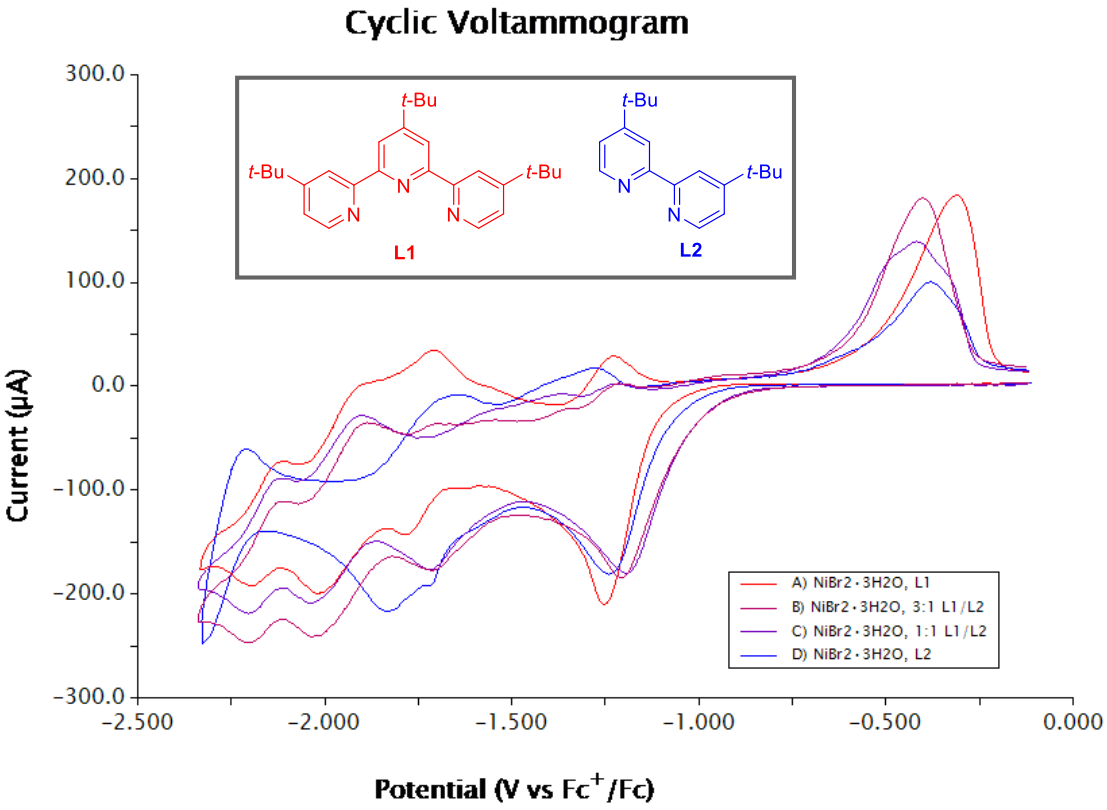


3.8 Figure S17. CV of $NiB_2•3H_2O$ + 1:1 L3/L4

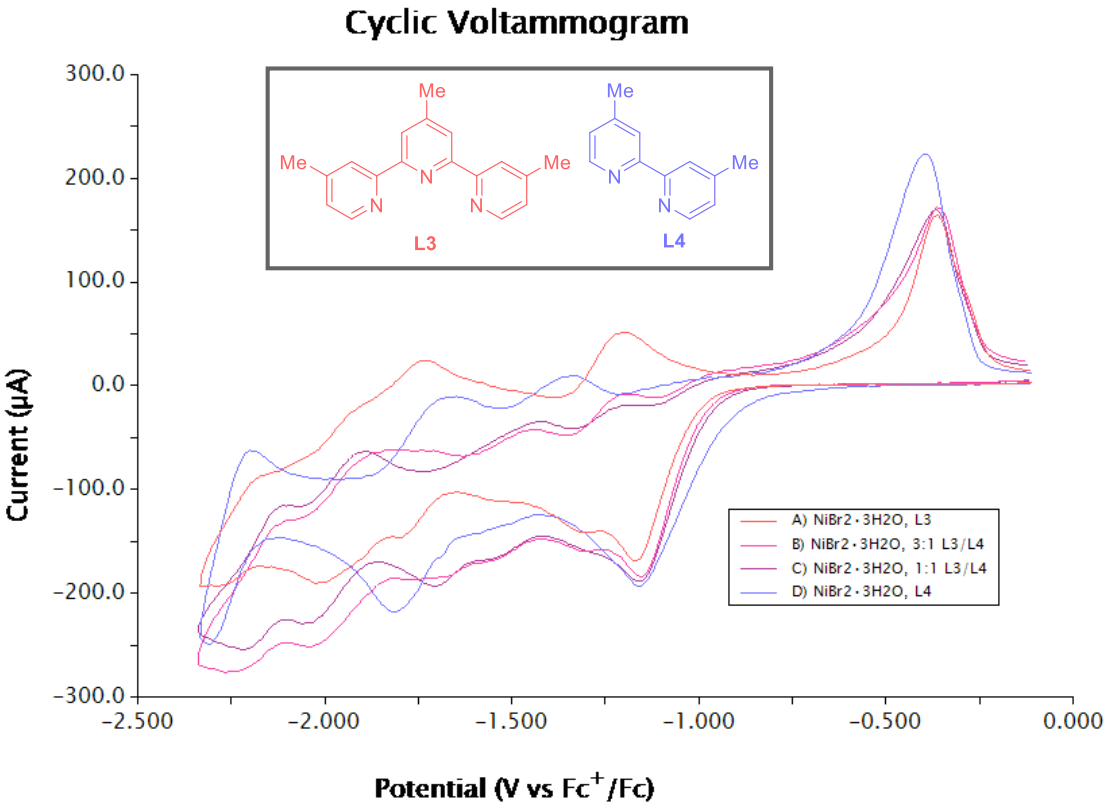
10 mM $NiBr_2•3H_2O$, 5 mM **L3**, 5 mM **L4**, 100 mM $TBAPF_6$ in MeCN



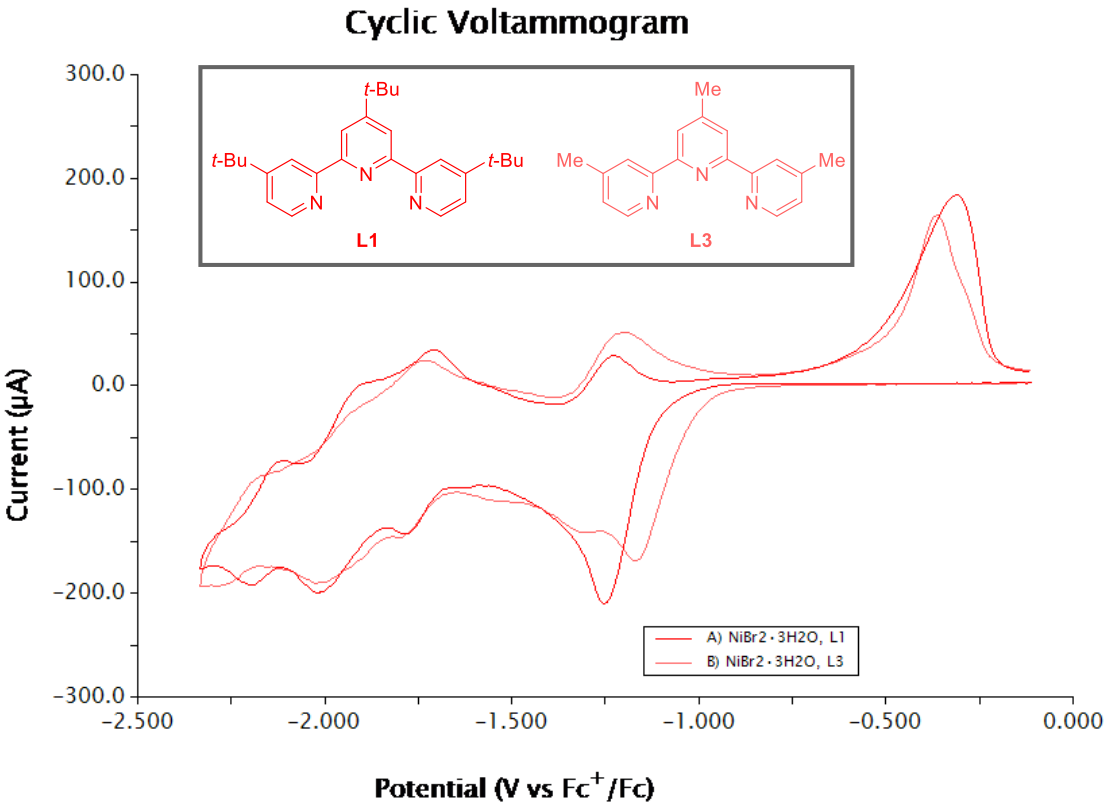
3.9 Figure S18. Stacked CVs of Figures S10,11,14,15; NiB_2•$3H_2O$ + varying ratios of L1/L2



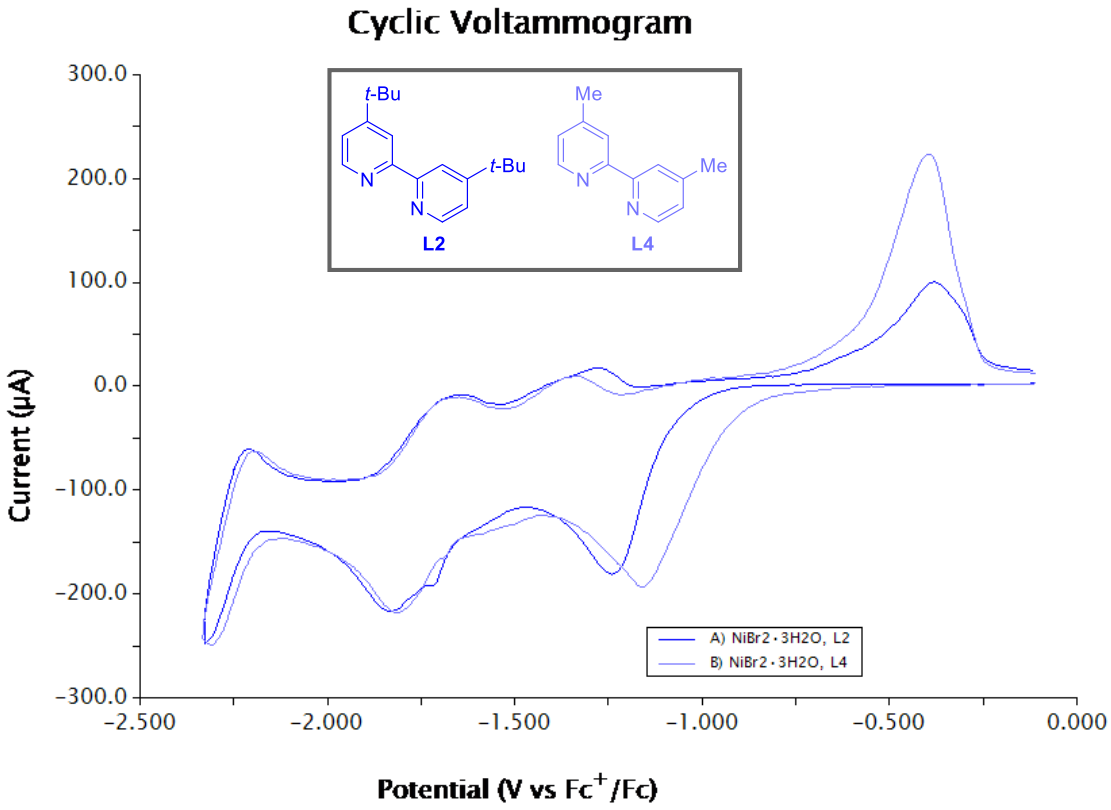
3.10 Figure S19. Stacked CVs of Figures S12,13,16,17; NiB_2•$3H_2O$ + varying ratios of L3/L4



3.11 Figure S20. Stacked CVs of Figures S10,12; $NiB_2•3H_2O$ + terpyridine ligands



3.12 Figure S21. Stacked CVs of Figures S11,13; $NiB_2•3H_2O$ + bipyridine ligands



4. General Reaction Procedures

4.1 General Batch Procedure

Assembly of the electrode cap

A graphite rod was inserted through a 14/20 rubber septum. Two thin slices of polyethylene tubing were threaded onto the middle and bottom of the graphite rod to separate the electrodes and prevent short circuiting. Nickel foam cut into a 3 × 2.5 cm rectangle was curled into a cylinder and attached to a copper wire paperclip. The copper wire was inserted through the septum.

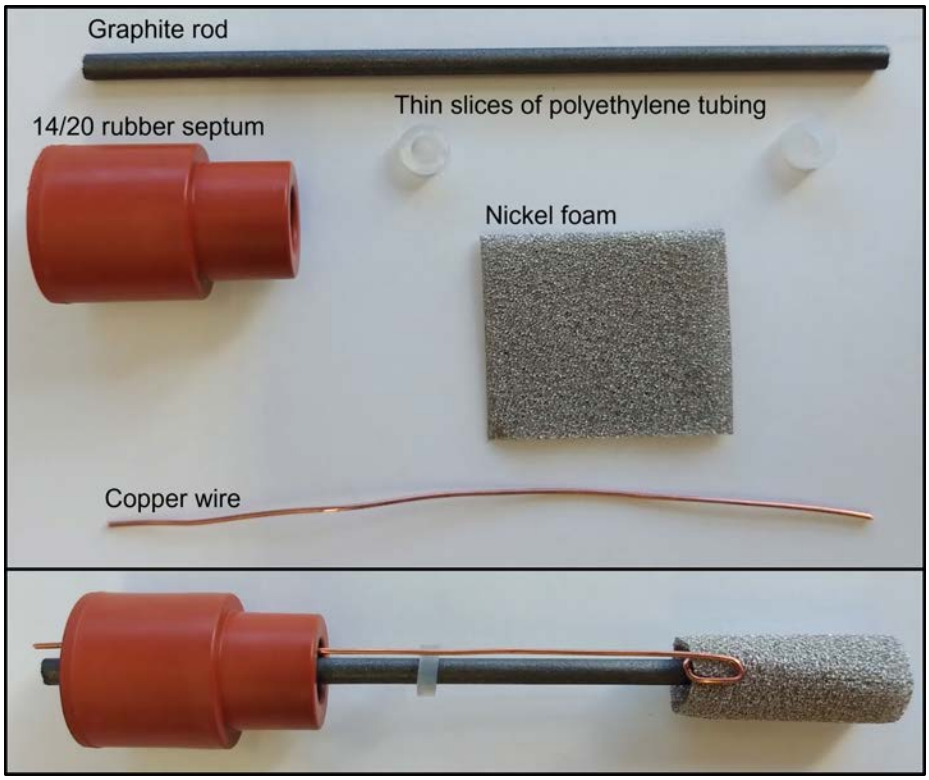


Image 1. Electrode components and assembled electrode cap for batch reactions.

Reactions were set up in a N_2 filled glove box. For a benchtop procedure, see **4.2. Batch Benchtop Procedure**.

Preparation of the 3:1 **L1**/**L2** catalyst stock solution (0.02 M with respect to Ni)

In a N_2 filled glovebox, $NiBr_2 \cdot 3H_2O$ (55.1 mg, 0.20 mmol, 0.1 equiv), **L1** (66.9 mg, 0.17 mmol, 0.08 equiv), **L2** (15.9 mg, 0.056 mmol, 0.03 equiv), $TBAPF_6$ (78.3 mg, 0.20 mmol, 0.1 equiv), MeCN (10.1 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for 10 min to afford a homogeneous emerald green solution.

Preparation of the 1:1 **L1**/**L2** catalyst stock solution (0.02 M with respect to Ni)

In a N_2 filled glovebox, $NiBr_2 \cdot 3H_2O$ (55.1 mg, 0.20 mmol, 0.1 equiv), **L1** (44.6 mg, 0.11 mmol, 0.055 equiv), **L2** (31.8 mg, 0.11 mmol, 0.055 equiv), $TBAPF_6$ (78.3 mg, 0.20 mmol, 0.1 equiv), MeCN (10.1 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for 10 min to afford a homogeneous emerald green solution.

Preparation and assembly of the batch reaction

In a N_2 filled glovebox, catalyst stock solution (2 mL, 0.04 mmol Ni, 10 mol% Ni), alkyl bromide (0.40 mmol, 1.0 equiv), aryl bromide (0.40 mmol. 1.0 equiv), DIPEA (278.7 µL, 1.6 mmol, 4.0 equiv), and a stir bar were added to an oven-dried glass test tube (15 × 85 mm). The solution turned cloudy yellow with the addition of DIPEA. The test tube was sealed with the electrode cap. The reaction was removed from the glovebox and placed in an aluminum reaction block preheated to 70 °C. Alligator clips connected to the power supply were attached to the graphite rod as the anode and copper wire attached to the Ni foam as the cathode. The reactions were stirred for 10 min to reach the reaction temperature. Constant current (10 mA) was then applied for 4 F/mol (4.3 h).

Image 2. Electrochemical batch reaction setup.

GC Analysis

An aliquot of the reaction mixture (30 µL) was removed using a 50 µL gas-tight syringe, the aliquot was added to a dram vial and the syringe was rinsed into the dram vial with Et_2O (2 mL). The organic solution was extracted with H_2O (0.2 mL) and the organic layer was then filtered through a 2-cm silica plug in a Pasteur pipette into a GC vial. The resulting solution was analyzed by GC and yields were determined based on the peak area of the analyte compared to dodecane as an internal standard.

Isolation and Purification

The electrodes were rinsed with EtOAc (10 mL) into the test tube and the reaction solution was filtered through a short plug of silica (2 cm thick × 3 cm diameter) into a round bottom flask. The silica plug was rinsed with additional EtOAc (10 mL) and the filtrate collected in the round bottom flask. The filtrate was concentrated under reduced pressure by rotary evaporation and the resulting residue was purified by column chromatography to afford the cross-coupled product.

4.2 Batch Benchtop Procedure

The following procedures were performed on the bench using standard Schlenk techniques and N_2 as the inert gas.

Preparation of nickel catalyst stock solution

$NiBr_2 \bullet 3H_2O$ (43.7 mg, 0.16 mmol, 0.1 equiv), **L1** (53.0 mg, 0.13 mmol, 0.08 equiv), **L2** (12.5 mg, 0.044 mmol, 0.03 equiv), $TBAPF_6$ (65.0 mg, 0.16 mmol, 0.1 equiv), and a PTFE-coated stir-bar were added to a 20 mL scintillation vial which was then capped with a screw cap fitted with a PTFE-faced silicone septum. The vial was connected to a Schlenk line via needle through the septum. A second venting needle (open to air) was added, and the vial was purged with N_2 for 15 min. MeCN (8 mL) was added via syringe through the septum cap. The venting needle was removed, and the mixture was stirred under positive N_2 pressure at rt for ~10 min to afford a homogeneous emerald green solution.

Electrochemical catalytic reaction setup

An oven-dried glass test tube (15 × 85 mm) equipped with a PTFE-coated stir-bar was sealed with the electrode cap. The test tube was connected to a Schlenk line via a needle through the septum. A second venting needle (open to air) was added, and the vial was purged with N_2 for 10 min. Then, catalyst stock solution (2 mL, 0.04 mmol Ni, 10 mol% Ni), alkyl bromide (0.40 mmol, 1.0 equiv), aryl bromide (0.40 mmol. 1.0 equiv), and DIPEA (279 µL, 1.6 mmol, 4.0 equiv) were added via syringe to the test tube. The venting needle was removed, alligator clips connected to the power supply were attached to the electrodes, and the mixture was stirred under positive N_2 pressure in the aluminum heating block preheated to 70 °C. After 10 min to allow the temperature to equilibrate, constant current (10 mA) was applied for 4 F/mol (4.3 h).

NMR Analysis

The electrodes were rinsed with EtOAc (10 mL) into the test tube and the reaction solution was filtered through a short plug of silica (2 cm thick × 3 cm diameter), the silica plug was washed with additional EtOAc (10 mL). The filtrate was concentrated by rotary evaporation. CH_2Br_2 (14 µL, 0.2 mmol) was added.

4.3 Ligand Ratio Time Course Procedure

See 4.1 General Batch Procedure for assembly of the electrode cap.

Preparation of the **L1** catalyst stock solution (0.02 M with respect to Ni)

In a N_2 filled glovebox, $NiBr_2$•$3H_2O$ (27.8 mg, 0.10 mmol, 0.10 equiv), **L1** (45.1 mg, 0.11 mmol, 0.11 equiv), $TBAPF_6$ (39.5 mg, 0.10 mmol, 0.10 equiv), MeCN (5.1 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for 10 min to afford a homogeneous green solution.

Preparation of the **L2** catalyst stock solution (0.02 M with respect to Ni)

In a N_2 filled glovebox, $NiBr_2$•$3H_2O$ (27.8 mg, 0.10 mmol, 0.10 equiv), **L2** (30.1 mg, 0.11 mmol, 0.11 equiv), $TBAPF_6$ (39.5 mg, 0.10 mmol, 0.10 equiv), MeCN (5.1 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for 10 min to afford a homogeneous teal solution.

Preparation and assembly of the batch reaction

In a N_2 filled glovebox, alkyl bromide (0.40 mmol, 1.0 equiv), aryl bromide (0.40 mmol. 1.0 equiv), a variable amount of the catalyst stock solutions: **L1** stock solution (mL)/**L2** stock solution (mL) = 2:0, 1.5:0.5, 1:1, 0.5:1.5, 2:0) for a total of 2 mL of catalyst stock solution (0.04 mmol Ni, 10 mol% Ni), DIPEA (278.7 µL, 1.6 mmol, 4.0 equiv), and a stir bar were added to five oven-dried glass test tubes (15 × 85 mm). The solutions turned cloudy yellow with the addition of DIPEA. The test tubes were sealed with the electrode caps. The reactions were removed from the glovebox and placed in an aluminum reaction block preheated to 70 °C. Alligator clips connected to the power supply were attached to the graphite rod as the anode and copper wire attached to the Ni

foam as the cathode. The reactions were stirred for 10 min to reach the reaction temperature. Constant current (10 mA) was then applied for 4 F/mol (4.3 h). Time points were taken at 0.5, 1.0, 2.0, 3.0, and 4.0 F/mol and analyzed by GC.

GC Analysis

An aliquot of the reaction mixture (30 µL) was removed using a 50 µL gas-tight syringe, the aliquot was added to a dram vial and the syringe was rinsed into the dram vial with Et_2O (2 mL). The organic solution was extracted with H_2O (0.2 mL) and the organic layer was then filtered through a 2-cm silica plug in a Pasteur pipette into a GC vial. The resulting solution was analyzed by GC and yields were determined based on the peak area of the analyte compared to dodecane as an internal standard.

4.4 Single Pass Flow Procedure

Preparation of reaction solution

In a N_2 filled glovebox, $NiBr_2 \cdot 3H_2O$ (81.8 mg, 0.3 mmol, 0.1 equiv), 4:1 **L3**/**L4** (84.9 mg, 0.33 mmol, 0.11 equiv), $TBAPF_6$ (116.2 mg, 0.3 mmol, 0.1 equiv), MeCN (15 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for ~10 min until it turned from yellow to emerald green. Then 1-bromo-3-phenylpropane (456 µL, 3.0 mmol, 1.0 equiv), ethyl 4-bromobenzoate (490 µL, 3.0 mmol. 1.0 equiv), and DIPEA (2090 µL, 12 mmol, 4.0 equiv) were added to the vial. The solution turned cloudy yellow with the addition of DIPEA. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum and removed from the glovebox.

Single pass flow setup

Flow cell assembly: The ElectroCell Micro Flow Cell was assembled (pictured below) using a stainless steel endplate, PTFE frame, Ni plate, PFTE spacer with Ni foam (9.4 cm^2) and PFTE turbulence mesh inlaid, graphite plate, PTFE frame, stainless steel endplate with EPDM gaskets in between each layer. The flow cell was screwed together tightly with 6 bolts (hex head, 2 1/2" length). Teflon tubing (1/16" inner diameter, 1/8" outer diameter) was connected to the outgoing and incoming holes. The flow cell was connected to a Dr Meter DC Bench Power Supply with alligator clips: positive (red) lead attached to the graphite plate (anode), negative (black) lead attached to the Ni plate (cathode). The flow cell was placed in a sand bath and covered with an insulating blanket and heated to ~85 °C.

Reaction assembly: The scintillation vial containing the reaction solution was connected to a Schlenk line via a needle through the septum. The reaction solution was transferred to a syringe which was then connected to the ingoing Teflon tubing. The syringe was placed in a KDS 220 Multi-Syringe Infusion Pump. The outgoing Teflon tubing was placed in a collection vial. The system was purged with N_2 for 15 min. The syringe pump was turned on until the reaction solution filled the flow cell, then was set to the desired flow rate and constant current was applied. Fractions (0.5 mL) were collected.

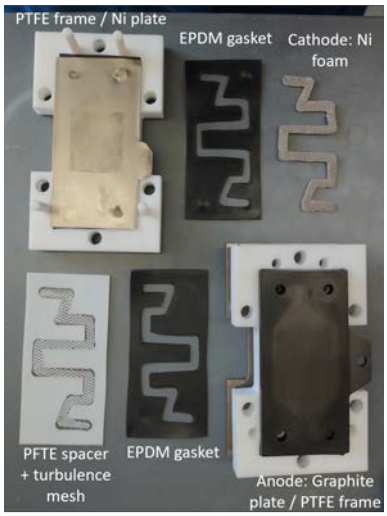


Image 3. Flow cell parts for single pass method.

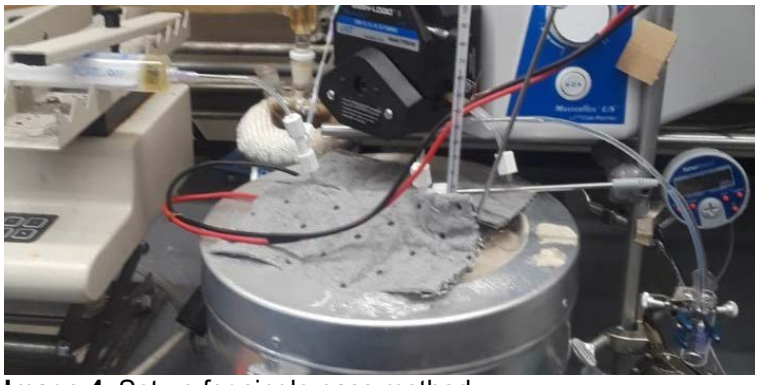


Image 4. Set up for single pass method.

GC Analysis

An aliquot of the reaction mixture (~30 µL) was removed using a 50 µL gas-tight syringe, the aliquot was added to a dram vial and the syringe was rinsed into the dram vial with Et_2O (2 mL). The organic solution was extracted with H_2O (0.2 mL) and the organic layer was then filtered through a 2-cm silica plug in a Pasteur pipette into a GC vial. The resulting solution was analyzed by GC and yields were determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard. (Dodecane was determined to be an inaccurate internal standard for the flow reactions, since the EPDM gaskets have an unsatisfactory compatibility with alkanes.)

4.5 Recirculation Flow Procedure

Preparation of reaction solution

In a N_2 filled glovebox, $NiBr_2 \bullet 3H_2O$ (81.8 mg, 0.3 mmol, 0.1 equiv), 4:1 **L3**/**L4** (84.9 mg, 0.33 mmol, 0.11 equiv), $TBAPF_6$ (116.2 mg, 0.3 mmol, 0.1 equiv), MeCN (15 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for ~10 min until it turned from yellow to emerald green. Then 1-bromo-3-phenylpropane (456 µL, 3.0 mmol, 1.0 equiv), ethyl 4-bromobenzoate (490 µL, 3.0 mmol. 1.0 equiv), and DIPEA (2090 µL, 12 mmol, 4.0 equiv) were added to the vial. The solution turned cloudy yellow with the addition of DIPEA. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum and removed from the glovebox.

Recirculation flow setup

Flow cell assembly: The ElectroCell Micro Flow Cell was assembled (pictured below) using a stainless steel endplate, PTFE frame, Ni plate, PFTE spacer with Ni foam (3 × 3.5 cm) and PP turbulence mesh inlaid, graphite plate, PTFE frame, stainless steel endplate with EPDM gaskets

in between each layer. The flow cell was screwed together tightly with 6 bolts (hex head, 2 1/2" length). Teflon tubing (1/16" inner diameter, 1/8" outer diameter) was connected to the outgoing and incoming holes. The flow cell was wrapped with Fisherbrand™ Fiberglass Insulated Cloth Heating Tape. The flow cell was connected to a Dr Meter DC Bench Power Supply with alligator clips: positive (red) lead attached to the graphite plate (anode), negative (black) lead attached to the Ni plate (cathode).

Peristaltic pump assembly: The incoming Teflon tubing was fitted to the peristaltic tubing (Masterflex L/S® Precision Pump Tubing, Gore® STA-PURE® PFL-Series) which was inserted through the peristaltic pump (Masterflex L/S® Easy-Load® II Pump Head, 2-Channel, Masterflex L/S® Analog Variable-Speed Console Drive) and attached to another piece of Teflon tubing.

Reservoir flask assembly: A 3-neck flask was used at the reservoir. In the right neck, the incoming and outgoing Teflon tubing were connected through a rubber septum. In the left neck, a thermometer inserted through a rubber septum was connected. In the middle neck, a condenser was attached. The top of the condenser was attach to a N_2 line and the system was purged with N_2 for 20 min, and then kept under positive N_2 pressure for the duration of the reaction.

Pre-heat and leak check: Via syringe, MeCN (~15 mL) was added to the flask and the pump was turned on. The heating mantle under the reservoir flask and the heating tape around the flow cell were also turned on. Solvent was recirculated while the system pre-heated (~1 h). The solvent level was monitored to ensure there were no leaks before proceeding with the reaction. The pump was reversed to flow all the MeCN pre-heat solution into the flask. Via syringe, the pre-heat solution was removed.

Reaction setup: The vial containing the reaction solution was connected to a Schlenk line via a needle through the septum. Via syringe, the reaction solution was transferred to the reservoir flask. The pump was turned on in the forward direction and the solution recirculated until equilibrium temperature (75 °C) was established. Constant current was applied for 4 F/mol.

GC Analysis

An aliquot of the reaction mixture (30 μL) was removed using a 50 μL gas-tight syringe, the aliquot was added to a dram vial and the syringe was rinsed into the dram vial with Et_2O (2 mL). The organic solution was extracted with H_2O (0.2 mL) and the organic layer was then filtered through a 2-cm silica plug in a Pasteur pipette into a GC vial. The resulting solution was analyzed by GC and yields were determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard. (Dodecane was determined to be an inaccurate internal standard for the flow reactions, since the EPDM gaskets have an unsatisfactory compatibility with alkanes.)

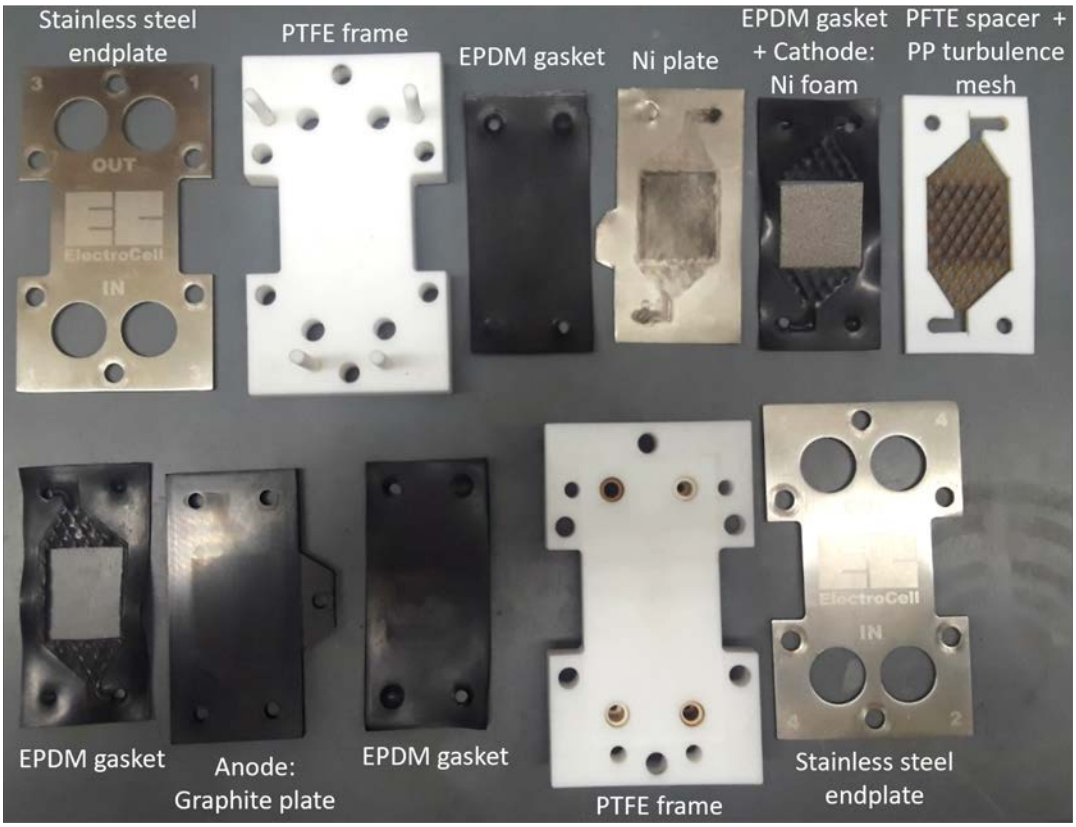


Image 5. Interior of flow cell for recirculation method.

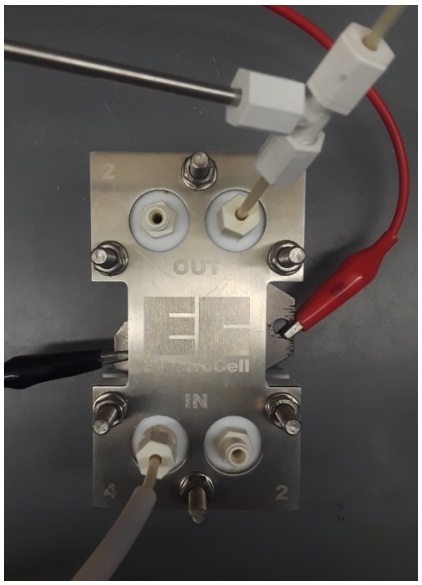


Image 6. Assembled flow cell for recirculation method.

Image 7. Set up for recirculation method.

4.6 Large Scale (12 mmol) Recirculation Flow Procedure

Flow cell assembly: Two ElectroCell Micro Flow Cells were assembled as above. Each flow cell was wrapped with Fisherbrand™ Fiberglass Insulated Cloth Heating Tape and covered in aluminum foil. The two flow cells were connected to two Dr Meter DC Bench Power Supplies with alligator clips: positive (red) lead attached to the graphite plate (anode), negative (black) lead attached to the Ni plate (cathode).

Peristaltic pump assembly: The incoming pieces of Teflon tubing were connected with PP hose barb unions, 1/16" ID, to two pieces of peristaltic tubing (Masterflex® L/S® Precision Pump Tubing, PharMed® BPT, size 14, cut to 18 cm). Both lines were inserted through the peristaltic pump (Masterflex L/S® Easy-Load® II Pump Head, 2-Channel, Masterflex L/S® Analog Variable-Speed Console Drive) and each were attached to another piece of Teflon tubing using PP hose barb unions, 1/16" ID. One flow cell had a PP Compression Union Tee, 1/8" OD, attached to the outgoing line with a Fisherbrand™ Traceable™ Full-Scale Plus Thermometer inserted in the perpendicular port. The tubing was wrapped with glass wool and covered with aluminum foil.

Reservoir flask assembly: A 250 mL 3-neck flask was used at the reservoir. In the right neck, the incoming and outgoing Teflon tubing were connected through a 14/20 rubber septum. In the left neck, a thermometer inserted through a 14/20 rubber septum was connected. In the middle neck, a condenser was attached. The top of the condenser was attach to a N_2 line and the system was purged with N_2 for 20 min, and then kept under positive N_2 pressure for the duration of the reaction.

Pre-heat and leak check: Via syringe, MeCN (40 mL) was added to the flask and the pump was turned on. The oil bath under the reservoir flask and the heating tapes around each flow cell were also turned on. Solvent was recirculated while the system pre-heated (~1 h). The solvent level was monitored to ensure there were no leaks before proceeding with the reaction. The pump was reversed to flow all the MeCN pre-heat solution into the flask. Via syringe, the pre-heat solution was removed.

Reaction setup: $NiBr_2$•$3H_2O$ (0.328 g, 1.2 mmol, 0.1 equiv), **L3** (0.220 g, 0.80 mmol, 0.07 equiv), **L4** (0.074 g, 0.40 mmol, 0.03 equiv), $TBAPF_6$ (0.4669 g, 1.2 mmol, 0.1 equiv), MeCN (40 mL), and a PTFE-coated stir-bar were added to the reservoir flask. The solution was stirred for ~15 min until it turned from yellow to emerald green. Then 1-Boc-4-bromopiperdine (12.0 mmol, 1.0 equiv), ethyl 4-bromobenzoate (12.0 mmol, 1.0 equiv), and DIPEA (8.4 mL, 48 mmol, 4.0 equiv) were added to the vial. The solution turned cloudy yellow with the addition of DIPEA. The pump was turned on in the forward direction and the solution recirculated until equilibrium temperature (70 °C) was established. Constant current was applied for 4 F/mol.

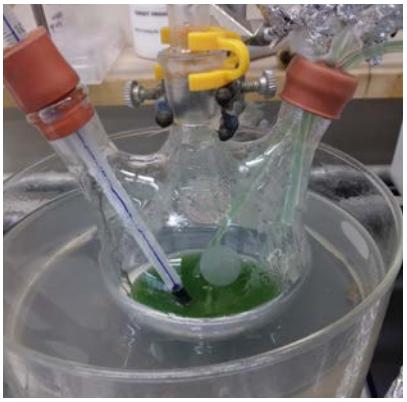


Image 8. Catalyst pre-stir.

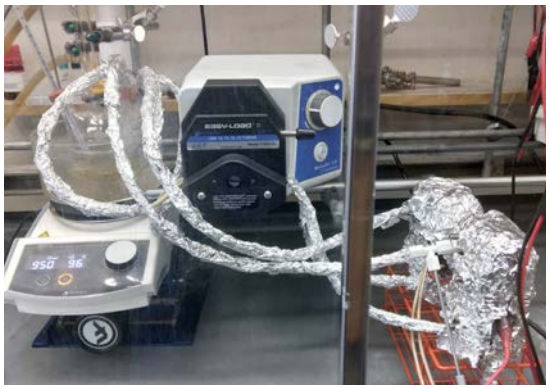


Image 9. Large scale flow setup.

Isolation and Purification

The reaction solution was transferred to a round bottom flask. MeCN (2 × 25 mL) was added to the reservoir flask and recirculated for a few min, then transferred to the round bottom flask. The reaction solution was concentrated under reduced pressure by rotary evaporation, then was transferred to a 500 mL separatory funnel using EtOAc.

EtOAc (20 mL) was added to the reservoir flask and recirculated for a few min, then transferred to the separatory funnel. H_2O (20 mL) was added to the reservoir flask and recirculated for a few min, then transferred to the separatory funnel. EtOAc (20 mL) was added to the reservoir flask and recirculated for a few min, then transferred to the separatory funnel. Additional EtOAc and H_2O were added to the separatory funnel so there was ~200 mL of EtOAc and ~100 mL of H_2O. The aqueous layer was removed. Brine (2 x ~100 mL) was added and aqueous layers were removed. EtOAc (2 x 100 mL) was added to the combined aqueous layers and the aqueous layers were removed.

The combined organic layers were dried over sodium sulfate, and filtered through a short plug of silica (2 cm thick × 3 cm diameter) into a round bottom flask. The silica plug was rinsed with additional EtOAc (20 mL) and the filtrate collected in the round bottom flask. The filtrate was concentrated under reduced pressure by rotary evaporation and the resulting residue was purified by silica gel chromatography (50 g silica column, Gradient 0-->20% ethyl acetate in hexanes).

Large Scale (12 mmol) at 11.4 mA/cm^2

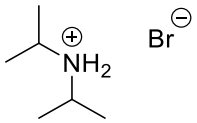
Reaction setup was followed with 1-Boc-4-bromopiperdine (3.1769 g, 12.0 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (2.7482 g, 12.0 mmol, 1.0 equiv). The current was set to 120 mA for each flow cell, 240 mA total. Isolation and purification yielded the product (2.364 g, 59% yield) as a viscous yellow oil. Characterization data matched those reported in the literature.[5]

Large Scale (12 mmol) at 5.7 mA/cm^2

Reaction setup was followed with 1-Boc-4-bromopiperdine (3.1720 g, 12.0 mmol, 1.0 equiv) and ethyl 4-bromobenzoate (2.7504 g, 12.0 mmol, 1.0 equiv). The current was set to 60 mA for each flow cell, 120 mA total. Isolation and purification yielded the product (2.921 g, 73% yield) as a viscous yellow oil. Characterization data matched those reported in the literature.[5]

Amine reductant byproduct formation

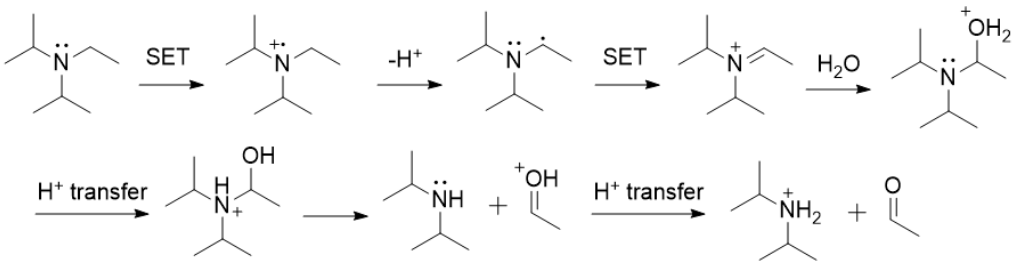
Diisopropylamine•HBr



Insoluble colorless crystals formed during the initial concentration of the crude reaction mixture were collected and rinsed with EtOAc. ^{1}H-NMR data is consistent with those reported in the literature (in DMSO-d6).[7]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, br, 2H), 3.50 (hept, *J* = 6.5 Hz, 2H), 1.54 (d, *J* = 6.5 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 48.1, 19.4.

We propose the formation of an iminium ion[8] followed by hydrolysis to form a secondary amine.



4.7 Practical considerations for flow reactions

- Low quality graphite will be too porous and the organic solvent will leak out. Resin-filled graphite prevents leaks, but we have found that it is more breakable, so we recommend grade G347B graphite.

- It is important to have high quality peristaltic pump tubing that is compatible with the pump head to prevent leaks. In addition, we recommend using hose barb unions to securely connect the peristaltic pump tubing to the Teflon tubing.

- Temperature control is important for these reactions. To ensure minimal heat loss, we recommend insulating the Teflon tubing with glass wool and wrapping the tubing and flow cells with aluminum foil.

- Gasket material. We used EPDM gaskets. Although they work well to prevent leaks, EPDM gaskets appear to absorb hydrocarbons (such as dodecane). Alternative gaskets might be needed for some applications.

5. Chronopotentiometry

5.1 Reaction setup

Assembly of the electrode cap

A graphite rod was inserted through screw cap fitted with a PTFE-faced silicone septum. Two thin slices of polyethylene tubing were threaded onto the middle and bottom of the graphite rod to separate the electrodes and prevent short circuiting. Nickel foam cut into a 3 × 2.5 cm rectangle was curled into a cylinder and attached to a copper wire paperclip. The copper wire was inserted through the septum.

Preparation of reaction solution

In a N_2 filled glovebox, $NiBr_2$•$3H_2O$ (43.6 mg, 0.16 mmol, 0.1 equiv), **L1** (53.0 mg, 0.13 mmol, 0.83 equiv), **L2** (12.2 mg, 0.45 mmol, 0.028 equiv), $TBAPF_6$ (62.0 mg, 0.16 mmol, 0.1 equiv), MeCN (8 mL), and a PTFE-coated stir-bar were added to an oven-dried 20 mL scintillation vial. The solution was stirred for ~10 min until it turned from yellow to emerald green. Then 1-bromo-3-phenylpropane (322.0 mg, 1.62 mmol, 1.0 equiv), ethyl 4-bromobenzoate (367.4 mg, 1.60 mmol. 1.0 equiv), and DIPEA (1115 µL, 6.4 mmol, 4.0 equiv) were added to the vial. The solution turned cloudy yellow with the addition of DIPEA. The vial was capped with the electrode cap and removed from the glovebox.

Reference electrode

To slow diffusion into the reference electrode during the 17.2 h chronopotentiometry experiment, it was placed in an additional capillary filled with electrolyte solution. To monitor if there was a potential drift during the chronopotentiometry experiment, the reference electrode (without the secondary capillary) was used to take a CV of a ferrocene standard before and after the experiment.

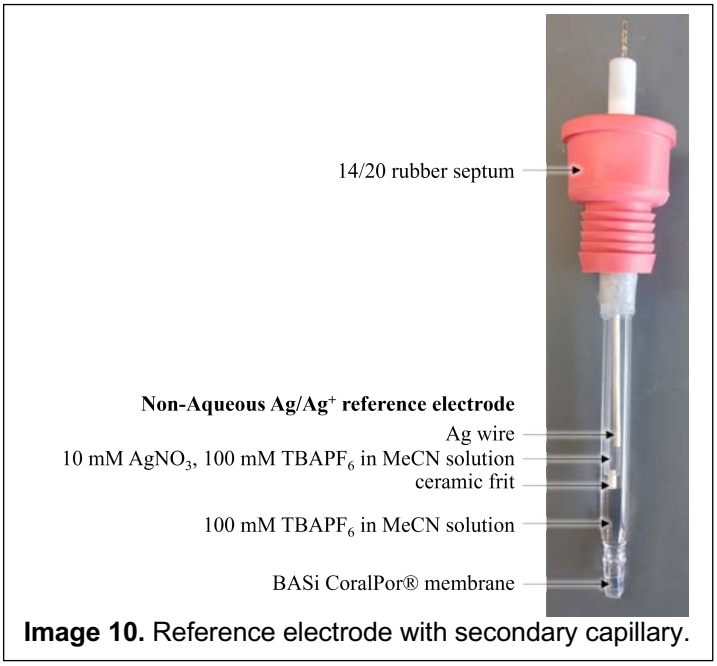


Image 10. Reference electrode with secondary capillary.

Reaction setup

The vial with the electrode cap was pierced with a needle and the reference electrode inside the secondary capillary was inserted through the septum. The vial was placed in an oil bath set to 70 °C. The reaction was stirred for 15 min to reach the reaction temperature. The electrodes were connected to the potentiostat via alligator clips (Ni foam = working electrode, Graphite rod = counter electrode, $Ag/AgNO_3$ = reference electrode). Constant current (-10 mA) was then applied for 4 F/mol (17.2 h).

GC Analysis

An aliquot of the reaction mixture (30 µL) was removed using a 50 µL gas-tight syringe, the aliquot was added to a dram vial and the syringe was rinsed into the dram vial with Et_2O (2 mL). The organic solution was extracted with H_2O (0.2 mL) and the organic layer was then filtered through a 2-cm silica plug in a Pasteur pipette into a GC vial. The resulting solution was analyzed by GC and yields were determined based on the peak area of the analyte compared to dodecane as an internal standard.

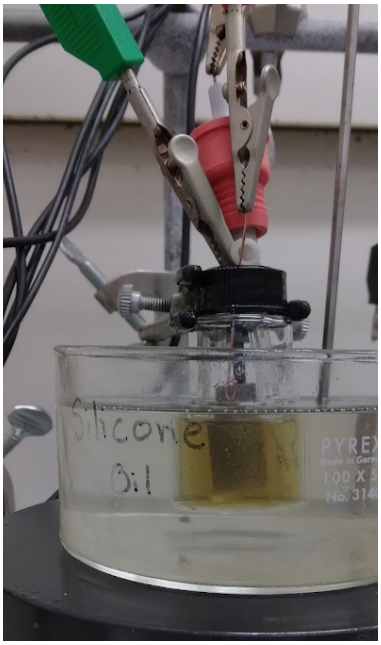
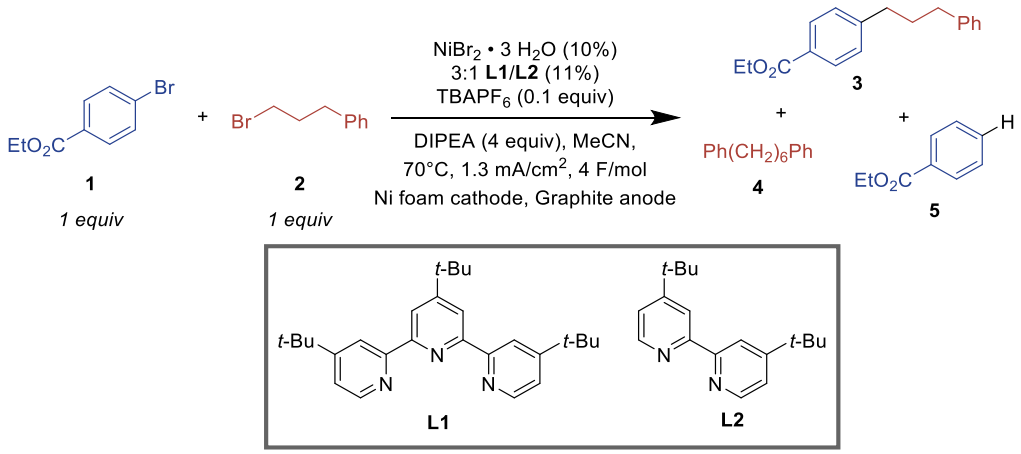


Image 11. Chronopotentiometry setup.

5.2 Figure S22: Chronopotentiometry GC Results



Entry	Description	Scale (mmol)	Yield (%)[a]				
			1	2	3	4	5
1	2-electrode setup[b]	0.4	0	5	**81**	4	7
2	Chronopotentiometry, 3-electrode setup	1.6	0	0	**73**	6	12

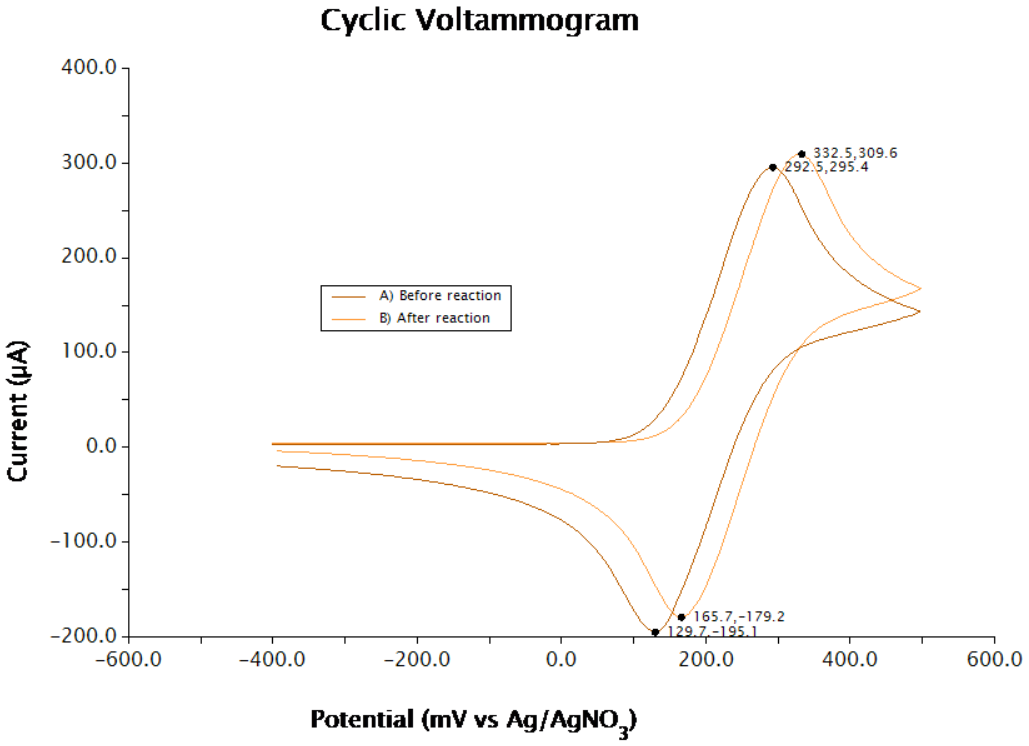
[a]Corrected GC yield vs dodecane. [b]Reaction set up without a reference electrode, using a power supply instead of a potentiostat.

5.3 Figure S23: Stacked CVs of ferrocene taken before and after the reaction

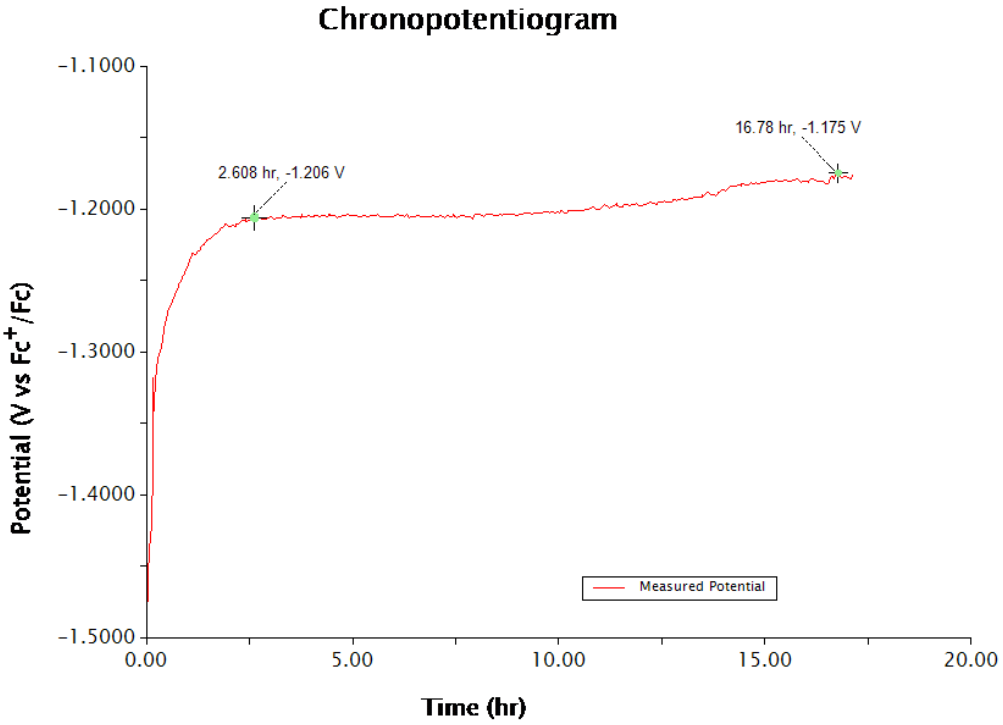
A ferrocene standard (10 mM ferrocene, 100 mM $TBAPF_6$ in MeCN) was sparged with N_2 for 10 min, then a CV was taken at room temperature. Electrodes used include: a $Ag/AgNO_3$ reference electrode, a glassy carbon working electrode, and a Pt wire counter electrode. The reference electrode was filled with 10 mM $AgNO_3$, 100 mM $TBAPF_6$ in MeCN.

$E_{1/2}$ of ferrocene before the reaction = 211.1 mV vs $AgNO_3$
$E_{1/2}$ of ferrocene after the reaction = 249.1 mV vs $AgNO_3$
Difference = 38 mV

The average $E_{1/2}$ (230 mV vs $AgNO_3$) was used to reference the chronopotentiogram.

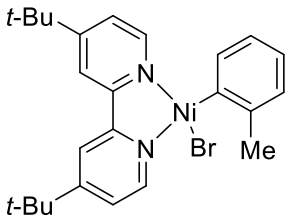


5.4 Figure S24: Chronopotentiogram



6. Ligand Exchange

6.1 Synthesis of Ni complex and Characterization



Ni(L2)(o-tolyl)Br

Synthesized from a reported procedure.[6]

In a glovebox, a scintillation vial was charged with $Ni(cod)_2$ (275.1 mg, 1.0 mmol), **L2** (268.4 mg, 1.0 mmol), and THF (3 mL) at room temperature. The reaction mixture turned dark royal indigo. After stirring for 2 h, *o*-tolyl-bromide (500 µL, 4.15 mmol) was added to the indigo solution causing a color change to dark red within 3 min. After stirring for 20 min, pentane (~12 mL) was added to the solution, causing a red precipitate. The resulting solution was filtered through a disposable flared top filter funnel using vacuum filtration and a filter flask. After washing with excess pentane, the orange powder was transferred to a scintillation vial and dried on high vac overnight. Removed from high vac, orange powder (449.0 mg, 90% yield), was stored in the glovebox freezer electrical taped closed. Characterization data matched those reported in the literature.[6]

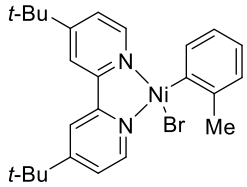
^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.26 (d, J = 5.9 Hz, 1H), 7.86 (d, J = 1.9 Hz, 1H), 7.82 (d, J = 2.2 Hz, 1H), 7.53 (ddd, J = 8.5, 6.4, 1.8 Hz, 2H), 7.13 (dd, J = 6.1, 2.1 Hz, 1H), 7.04 (d, J = 6.2 Hz, 1H), 6.85 – 6.71 (m, 3H), 3.03 (s, 3H), 1.42 (s, 9H), 1.35 (s, 9H).

Elemental Analysis Calculated: C, 60.28%; H, 6.27%; N, 5.62%. Measured: C, 60.348%; H, 6.185%; N, 5.521%. Confirmed purity (≥99.5% pure).

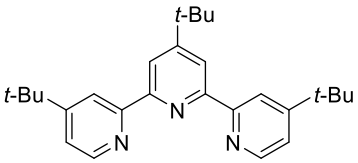
6.2 Ligand Exchange NMR Experiment

In a N_2 filled glovebox, a 0.02 M Ni(**L2**)(*o*-tolyl)Br stock solution was made by adding Ni(**L2**)(*o*-tolyl)Br (19.9 mg, 0.04 mmol) to a 2 mL volumetric flask, filling with CD_2Cl_2, and mixing well resulting in a homogenous dark orange solution. A 0.02 M **L1** stock solution was made by adding **L1** (16.1 mg, 0.04 mmol) to a 2 mL volumetric flask, filling with CD_2Cl_2, and mixing well resulting in a homogenous colorless solution. Using a Hamilton syringe, Ni(**L2**)(*o*-tolyl)Br stock solution (300 µL) was added to each NMR tube. Using a Hamilton syringe, **L1** stock solution (0, 60, 120, 180, 240, 300 µL) was added to the NMR tubes. Using a Hamilton syringe, CD_2Cl_2 (300, 240, 180, 120, 60, 0 µL) was added to the NMR tubes. Each sample is 0.01 M with respect to Ni. The NMR tubes were capped and mixed well for 10 min. The full stacked NMR spectra can be found in section **10. NMR Spectra**.

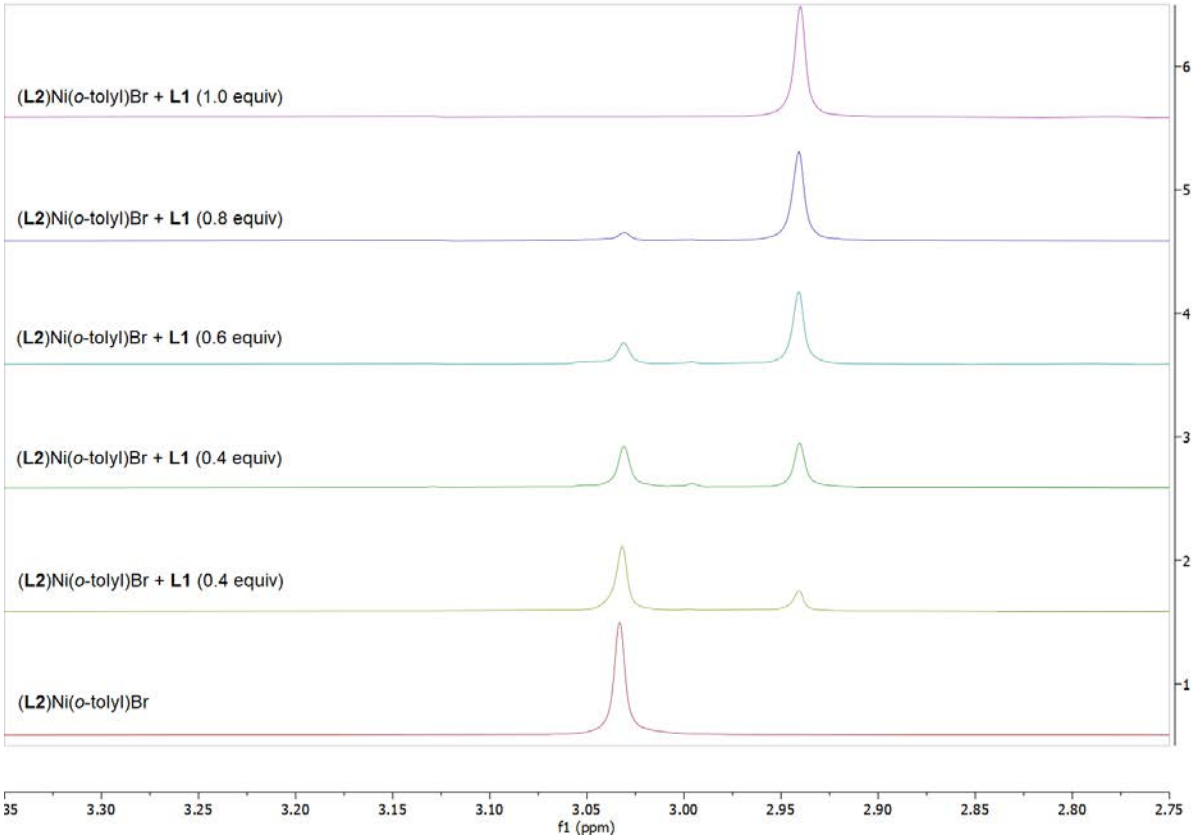
Shown in the expansion of stacked NMR spectra below, as more **L1** is added, the methyl peak for Ni(**L2**)(*o*-tolyl)Br begins to disappear and a new methyl peak grows in that we ascribe to Ni(**L1**)(*o*-tolyl)Br.



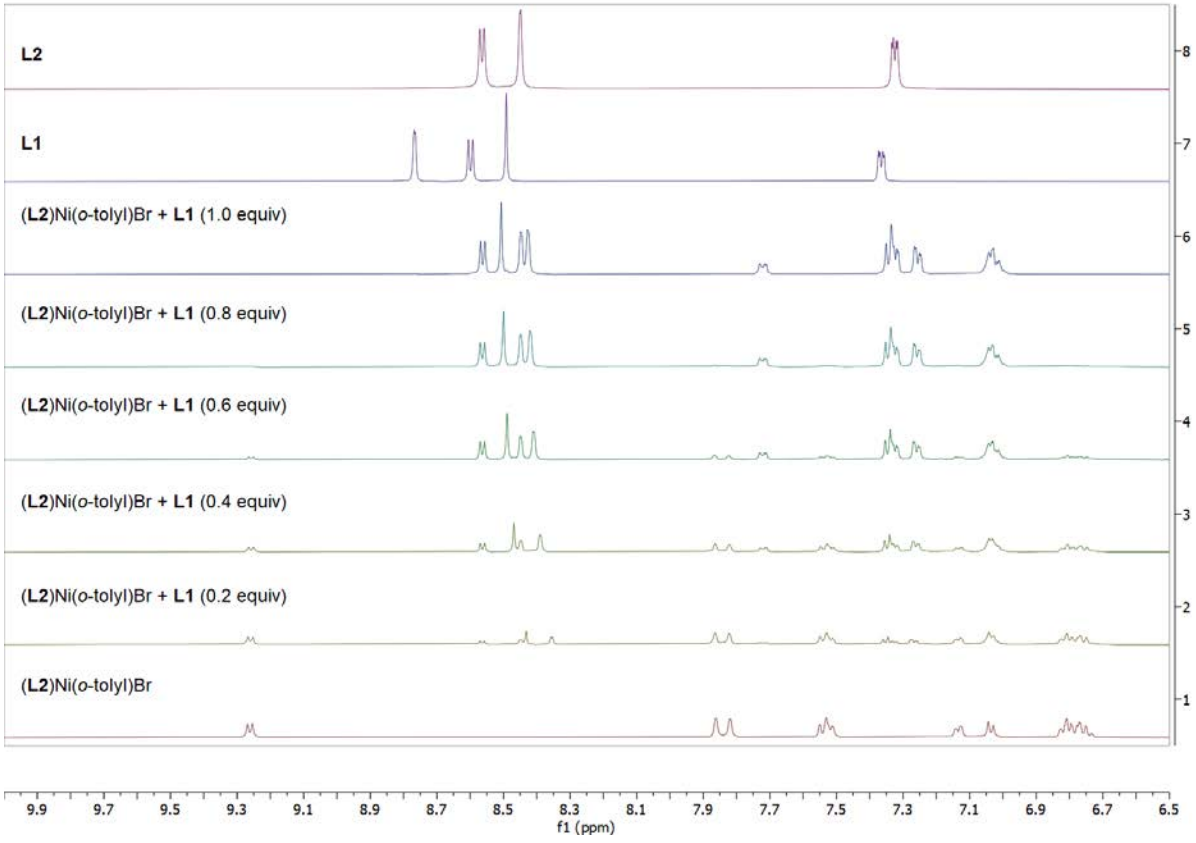
Ni(**L2**)(o-tolyl)Br



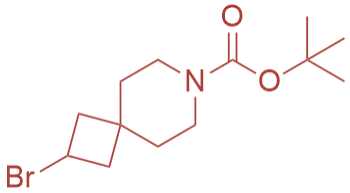
L1



Additionally, shown in another expansion of stacked NMR spectra below, as more **L1** is added, there is no evidence of free **L1** and the peaks corresponding to free **L2** grows in, indicating that **L1** is replacing **L2** on the Ni.



7. Synthesis of Starting Materials and Characterization



***tert*-Butyl 2-bromo-7-azaspiro[3.5]nonan-7-carboxylate (2g) [CAS: 1225276-07-2]**

To a flame-dried flask, *tert*-butyl 2-oxo-7-azaspiro[3.5]nonane-7-carboxylate (15.00 g, 62.5 mmol, 1 equiv), MeOH (190 mL), and a PTFE-coated stir-bar were added, then cooled in an ice bath. $NaBH_4$ (2.41 g, 62.5 mmol, 1 equiv) was added and the reaction mixture stirred overnight and was allowed to warm to room temperature. The reaction mixture was concentrated in vacuo and purified by silica gel chromatography to yield 2-hydroxy-7-azaspiro[3.5]nonane-7-carboxylic acid *tert*-butyl ester. This intermediate (10.38 g, 42.7 mmol, 1.0 equiv) was then dissolved in THF (130 mL) and cooled in an ice bath. PPh_3 (13.61 g, 51.2 mmol, 1.2 equiv) and CBr_4 (17.13 g, 51.2 mmol, 1.2 equiv) were added and the reaction stirred for 30 min, then was allowed to warm to room temperature. The reaction mixture was concentrated in vacuo and purified by silica gel chromatography to yield **2g** as a white solid (6.4 g, 21.0 mmol, 49% yield). ^{1}HNMR data matched that reported in the literature.[2] ^{13}C NMR data was not previously reported in the literature.

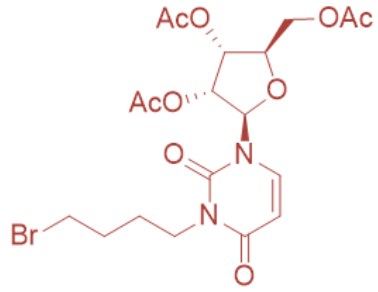
^{1}H NMR (500 MHz, CDCl3) δ 4.48 (p, J = 7.9 Hz, 1H), 3.36 – 3.26 (m, 4H), 2.64 – 2.56 (m, 2H), 2.33 – 2.25 (m, 2H), 1.67 – 1.61 (m, 2H), 1.56 – 1.50 (m, 2H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, CDCl3) δ 154.8, 79.4, 44.8, 40.6 (br), 39.4, 38.0, 36.3, 35.5, 28.4.

HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{13}H_{23}BrNO_2^+$ = 304.0907, found = 304.0902.

IR (cm^{-1}) 2973, 2927, 2856, 1678, 1419, 1361, 1251, 1155, 987, 853, 820, 772, 651, 527, 470.

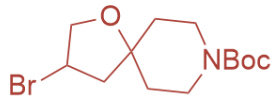
Melting point range (°C) 91.6–92.9.



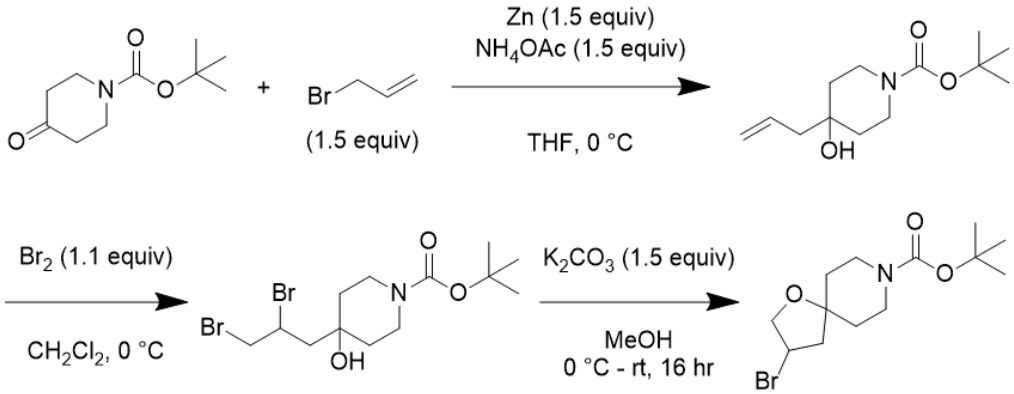
(2R,3R,4R,5R)-2-(acetoxymethyl)-5-(3-(4-bromobutyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3,4-diyl diacetate (2h)

To a flame-dried flask, 2',3',5'-triacetyluridine (10.13 g, 27.4 mmol, 1.0 equiv) and DMF (75 mL) were added and heated to 60 °C. Then, 1,4-dibromobutane (4.9 mL, 41 mmol, 1.5 equiv) and K_2CO_3 (5.63 g, 41 mmol, 1.5 equiv) were added and the reaction mixture stirred overnight, and was allowed to cool to room temperature. The reaction mixture was transferred to a separatory funnel and was washed with H_2O (300 mL). The organic layer was extracted with EtOAc (200 mL × 3). The combined organic layers were washed with brine (300 mL) then concentrated in vacuo and purified by silica gel chromatography to yield **2h** (9.52 g, 18.9 mmol, 69% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 1H), 6.01 (d, *J* = 4.8 Hz, 1H), 5.81 (d, *J* = 8.1 Hz, 1H), 5.37 (dd, *J* = 5.8, 4.8 Hz, 1H), 5.35 – 5.31 (m, 1H), 4.36 (s, 3H), 3.95 (td, *J* = 7.1, 2.0 Hz, 2H), 3.44 (t, *J* = 6.7 Hz, 2H), 2.17 (s, 9H), 2.14 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H), 1.95 – 1.85 (m, 2H), 1.84 – 1.74 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 206.9, 170.1, 169.6, 162.2, 150.8, 137.3, 102.8, 88.8, 79.8, 73.0, 70.0, 63.0, 40.2, 33.0, 30.9, 30.0, 26.3, 20.8, 20.48, 20.46.
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{19}H_{26}BrN_2O_9^+$ = 505.0816, found = 505.0812.
IR (cm^{-1}) 2963, 1744, 1710, 1664, 1456, 1371, 1212, 1093, 1043, 956, 902, 807, 766, 718, 641, 600, 560, 422.



***tert*-butyl 3-bromo-1-oxa-8-azaspiro[4.5]decane-8-carboxylate (2p)**
Adapted from reported procedures.[3]



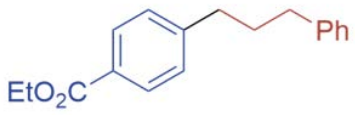
To a flame-dried 500 mL round-bottom flask, *N*-Boc-4-piperidone (9.971 g), Zn flakes (4.903), NH_4OAc (5.783 g) were added under N_2. THF (~200 mL) was added. The reaction stirred while being cooled in an ice bath. Allyl bromide (6.5 mL) was added dropwise. After stirring for 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (100 mL) and allowed to warm to room temperature. The mixture was then transferred to a separatory funnel with EtOAc (100 mL) and H_2O (100 mL) and then extracted with EtOAc (3 × 100 mL). The organic layers were combined, washed with sat. aq. NaCl solution (2 × 100 mL), dried over Na_2SO_4, and evaporated under reduced pressure to yield *tert*-butyl 4-hydroxy- 4-(prop-2-en-1-yl)piperidine-1-carboxylate as a pale yellow oil.

A solution of *tert*-butyl 4-hydroxy- 4-(prop-2-en-1-yl)piperidine-1-carboxylate in CH_2Cl_2 (70 mL) was cooled in an ice bath. A solution of Br_2 (2.8 mL) in CH_2Cl_2 (15 mL) was added dropwise and the solution turned bright orange. The reaction stirred for 1 h, then sat. aq. $Na_2S_2O_3$ and $NaHCO_3$ was slowly added, and the solution turned pale yellow. The mixture was then transferred to a separatory funnel with CH_2Cl_2 (100 mL) and H_2O (100 mL) and was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with sat. aq. NaCl solution (2 × 100 mL), dried over sodium sulfate, gravity filtered, and evaporated under reduced pressure to yield a pale yellow viscous oil.

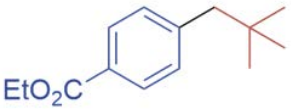
A solution of *tert*-butyl 4-(2,3-dibromopropyl)-4-hydroxypiperidine-1-carboxylate in MeOH (125 mL) was cooled in an ice bath. K_2CO_3 (10.381 g) was added and the reaction was stirred overnight and allowed to warm to room temperature. The reaction mixture was gravity

filtered and concentrated in vacuo. The reaction mixture was transferred to a separatory funnel with CH_2Cl_2 (50 mL) and was washed with H_2O (2 × 50 mL). The organic layers were extracted from the aqueous layers with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over $NaSO_4$, gravity filtered, concentrated in vacuo, and purified by silica gel chromatography (Gradient: 0% to 25% ethyl acetate in hexanes) to yield **2p** as a white solid (8.7652 g).
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.40 (dq, *J* = 9.9, 5.1 Hz, 1H), 4.19 (dd, *J* = 10.3, 5.4 Hz, 1H), 4.01 (dd, *J* = 10.3, 5.0 Hz, 1H), 3.64 (s, br, 2H), 3.38 – 3.25 (m, 2H), 2.36 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.17 (dd, *J* = 14.1, 4.8 Hz, 1H), 1.91 (d, br, *J* = 13.4 Hz, 1H), 1.70 (ddd, *J* = 13.7, 10.3, 4.2 Hz, 1H), 1.62 – 1.49 (m, 2H), 1.46 (s, 9H).
^{13}C NMR (126 MHz, CDCl3) δ 154.8, 80.9, 79.5, 74.5, 47.8, 44.7, 40.7 (br), 36.9, 36.5, 28.5.
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{13}H_{23}BrNO_3^+$ = 320.0856, found = 320.0850.
IR (cm^{-1}) 2973, 2923, 2861, 1676, 1420, 1361, 1243, 1178, 1139, 1093, 1044, 981, 914, 860, 766, 734, 553, 518.
Melting point range (°C) 67.8–69.9.

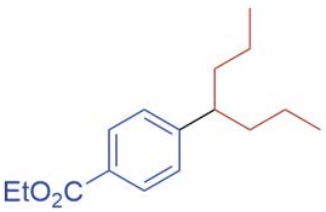
8. Specific Procedures and Product Characterization



Ethyl 4-(3-phenylpropyl)benzoate (3a) [CAS: 959023-25-7]
General Procedure A was followed with 1-bromo-3-phenylpropane (79.6 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (0.101 g, 94% yield) as a pale yellow oil. Characterization data matched those reported in the literature.[4] Contains <1% aryl dimer and <2% alkyl dimer that was inseparable.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.32 – 7.18 (m, 5H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.65 (dt, *J* = 18.7, 7.7 Hz, 4H), 1.95 (p, *J* = 7.7 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 147.8, 142.0, 129.7, 128.5, 128.4, 128.2, 125.9, 60.8, 35.5, 35.4, 32.7, 14.4.

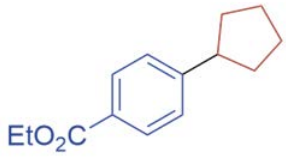


Ethyl 4-(2,2-dimethylpropyl)benzoate (3b) [CAS: 2419964-55-7]
General Procedure A was followed with neopentyl bromide (60.4 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (35.7 mg, 41% yield) as a colorless oil. Characterization data matched those reported in the literature.[5]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.54 (s, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 0.91 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 145.2, 130.4, 128.9, 128.1, 60.8, 50.2, 31.9, 29.4, 14.4.

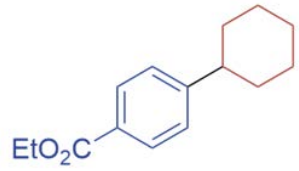


Ethyl 4-(1-propylbutyl)benzoate (3c)
General Procedure A was followed with 4-bromoheptane (71.3 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (81.8 mg, 83% yield) as a orange-yellow oil.

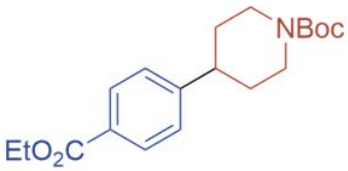
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.59 (tt, *J* = 9.5, 5.3 Hz, 1H), 1.66 – 1.48 (m, 4H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.22 – 1.05 (m, 4H), 0.83 (t, *J* = 7.4 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 151.9, 129.6, 128.2, 127.7, 60.7, 45.6, 39.0, 20.6, 14.4, 14.1.
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{16}H_{25}O_2^+$ = 249.1849, found = 249.1849.
IR (cm^{-1}) 2924, 2866, 1716, 1609, 1458, 1372, 1270, 1176, 1104, 1021, 853, 772, 707.



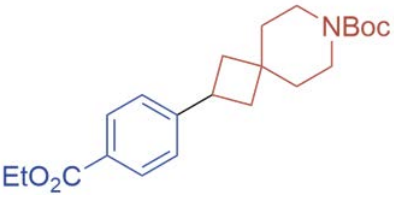
Ethyl 4-cyclopentylbenzoate (3d) [CAS: 1448351-68-5]
General Procedure A was followed with bromocyclopentane (59.6 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (71.0 mg, 81% yield) as a colorless oil. Characterization data matched those reported in the literature.[9]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.03 (tt, *J* = 9.6, 7.6 Hz, 1H), 2.14 – 2.02 (m, 2H), 1.88 – 1.76 (m, 2H), 1.75 – 1.64 (m, 2H), 1.66 – 1.52 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 152.1, 129.6, 128.0, 127.1, 60.7, 46.0, 34.5, 25.6, 14.4.



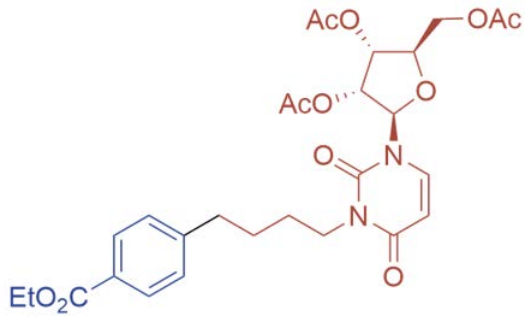
Ethyl 4-cyclohexylbenzoate (3e) [CAS: 959141-01-6]
General Procedure A was followed with bromocyclohexane (65.2 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (57.8 mg, 62% yield) as a white solid. Characterization data matched those reported in the literature.[4]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.61 – 2.49 (m, 1H), 1.92 – 1.80 (m, 4H), 1.75 (d, br, *J* = 11.9 Hz, 1H), 1.49 – 1.33 (m, 7H), 1.31 – 1.20 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 153.4, 129.7, 128.1, 126.8, 60.7, 44.7, 34.2, 26.8, 26.1, 14.4.



***tert*-Butyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate (3f) [CAS: 206446-48-2]**
General Procedure A was followed with N-Boc-4-bromopiperidine (105.7 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (91.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->20% ethyl acetate in hexanes) to yield the product (0.1025 g, 77% yield) as a colorless oil. Characterization data matched those reported in the literature.[5]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.26 (s, br, 2H), 2.81 (t, *J* = 12.8 Hz, 2H), 2.71 (tt, *J* = 12.1, 3.6 Hz, 1H), 1.82 (d, br, *J* = 12.8 Hz, 2H), 1.63 (qd, *J* = 12.7, 4.3 Hz, 2H), 1.49 (s, 9H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 154.8, 150.9, 129.8, 128.7, 126.8, 79.5, 60.8, 42.8, 32.9, 28.5, 14.4.



7-Azaspiro[3.5]nonane-7-carboxylic acid, 2-(4-(ethoxycarbonyl)phenyl)-, *tert*-butyl ester (3g)
General Procedure A was followed with 2-bromo-7-azaspiro[3.5]nonane-7-carboxylic acid *tert*-butyl ester (121.8 mg, 0.40 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (92.6 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->20% ethyl acetate in hexanes) to yield the product (118.2 mg, 79% yield) as a white solid.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.56 (p, *J* = 9.1 Hz, 1H), 3.42 (dd, *J* = 6.2, 4.0 Hz, 2H), 3.30 (dd, *J* = 6.2, 4.0 Hz, 2H), 2.32 (td, *J* = 9.1, 2.5 Hz, 2H), 1.91 (td, *J* = 9.5, 2.5 Hz, 2H), 1.71 (dd, *J* = 6.7, 4.5 Hz, 2H), 1.51 (dd, *J* = 6.7, 4.5 Hz, 2H), 1.46 (s, 9H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 155.0, 151.4, 129.6, 128.1, 126.3, 79.3, 60.8, 40.8 (br), 39.1, 38.9, 35.8, 34.0, 33.5, 28.5, 14.4.
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{22}H_{32}NO_4^+$ = 374.2326, found = 374.2322.
IR (cm^{-1}) 2968, 2919, 2857, 1690, 1605, 1409, 1369, 1273, 1241, 1175, 1107, 1013, 863, 764, 701, 576.
Melting point range (°C) 93.7–95.8.



(2R,3R,4R,5R)-2-(acetoxymethyl)-5-(3-(4-(4-(ethoxycarbonyl)phenyl)butyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3,4-diyl diacetate (3h)

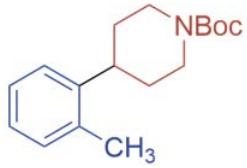
General Procedure A was followed with **2h** (206.8 mg, 0.41 mmol, 1.0 equiv) and ethyl-4-bromobenzoate (93.1 mg, 0.41 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->20% ethyl acetate in hexanes) to yield the product (189.8 mg, 81% yield) as a light yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 2H), 6.00 (d, *J* = 4.7 Hz, 1H), 5.80 (d, *J* = 8.1 Hz, 1H), 5.39 (dd, *J* = 5.8, 4.7 Hz, 1H), 5.36 – 5.30 (m, 1H), 4.40 – 4.31 (m, 5H), 3.98 – 3.89 (m, 2H), 2.74 – 2.67 (m, 2H), 2.12 (d, *J* = 6.5 Hz, 6H), 2.07 (s, 3H), 1.67 (p, *J* = 3.7 Hz, 4H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 169.5, 169.5, 166.6, 162.1, 150.7, 147.6, 137.3, 129.6, 128.4, 128.1, 102.7, 88.8, 79.6, 77.4, 77.2, 76.9, 73.0, 69.9, 62.9, 60.6, 40.9, 35.5, 28.3, 27.0, 20.7, 20.4, 20.3, 14.3.

HRMS (ESI) m/z calcd for $[M+Na]^+$ $C_{28}H_{35}N_2O_{11}^+$ = 597.2055, found = 597.2050.

IR (cm^{-1}) 2939, 1746, 1709, 1664, 1455, 1367, 1274, 1213, 1178, 1102, 1045, 1021, 902, 806, 764, 705, 599, 422.



***tert*-Butyl 4-(2-methylphenyl)-1-piperidinecarboxylate (3i) [CAS: 651053-90-6]**

General Procedure A was followed with N-Boc-4-bromopiperidine (106.0 mg, 0.40 mmol, 1.0 equiv) and 2-bromotoluene (68.4 mg, 0.40 mmol, 1.0 equiv) using 1:3 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->15% ethyl acetate in hexanes) to yield the product (67.9 mg, 62% yield) as a colorless oil. Characterization data matched those reported in the literature.[10]

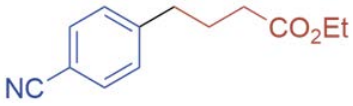
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.06 (m, 4H), 4.26 (s, br, 2H), 2.92 – 2.71 (m, 3H), 2.35 (s, 3H), 1.74 (dt, J = 13.6, 2.5 Hz, 2H), 1.61 (qd, J = 12.6, 4.3 Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 143.6, 135.1, 130.4, 126.3, 126.0, 125.4, 79.4, 44.7 (br), 38.4, 32.4, 28.5, 19.4.

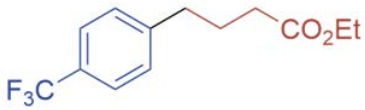
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{17}H_{26}NO_2^+$ = 276.1958, found = 276.1953.

IR (cm^{-1}) 2974, 2932, 2852, 1688, 1419, 1364, 1321, 1279, 1230, 1161, 1127, 1106, 1012, 933, 886, 862, 751, 725, 528, 448.

***tert*-Butyl 4-(2-(methoxycarbonyl)phenyl)-1-piperidinecarboxylate (3j) [CAS: 732275-95-5]**
General Procedure A was followed with N-Boc-4-bromopiperidine (105.8 mg, 0.40 mmol, 1.0 equiv) and methyl-2-bromobenzoate (86.3 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (10 g silica column, Gradient 0-->25% ethyl acetate in hexanes) to yield the product (47.0 mg, 37% yield) as a pale yellow oil. Characterization data matched those reported in the literature.[11]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.47 (td, *J* = 7.6, 1.5 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.25 (td, *J* = 7.8, 1.4 Hz, 1H), 4.25 (s, br, 2H), 3.90 (s, 3H), 3.55 (tt, *J* = 12.0, 3.4 Hz, 1H), 2.84 (t, br, 2H), 1.83 (d, br, *J* = 12.9 Hz, 1H), 1.62 (qd, *J* = 12.6, 4.2 Hz, 2H), 1.49 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 154.9, 146.8, 132.0, 130.3, 129.7, 126.8, 126.0, 79.4, 52.0, 44.5 (br), 38.4, 33.1, 28.5.
HRMS (ESI) m/z calcd for $[M+Na]^+$ $C_{18}H_{25}NNaO_4^+$ = 342.1676, found = 342.1670.
IR (cm^{-1}) 2937, 2854, 1687, 1419, 1372, 1242, 1166, 1107, 1063, 1014, 948, 875, 812, 757.

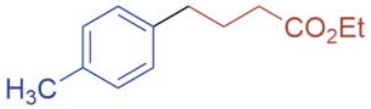


Ethyl 4-(4-cyanophenyl)butanoate (3k) [CAS: 131379-33-4]
General Procedure A was followed with ethyl-4-bromobutyrate (78.0 mg, 0.40 mmol, 1.0 equiv) and 4-bromobenzonitrile (73.5 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->15% ethyl acetate in hexanes) to yield the product (56.9 mg, 65% yield) as a colorless oil. Characterization data matched those reported in the literature.[4] Contains <2% alkyl dimer that was inseparable from the title compound.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.72 (dd, *J* = 7.5 Hz, 2H), 2.33 (dd, *J* = 7.4 Hz, 2H), 1.96 (p, *J* = 7.5 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 147.2, 132.2, 129.3, 119.0, 109.9, 60.4, 35.2, 33.4, 26.0, 14.2.

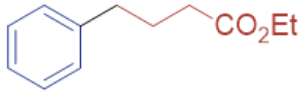


Ethyl 4-[4-(trifluoromethyl)phenyl]butanoate (3l) [CAS: 1235271-20-1]
General Procedure A was followed with ethyl 4-bromobutyrate (78.0 mg, 0.40 mmol, 1.0 equiv) and 4-bromobenzotrifluoride (90.0 mg, 0.40 mmol, 1.0 equiv). After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->20% ethyl acetate in hexanes) to yield the product (64.5 mg, 62% yield) as a colorless oil. Characterization data matched those reported in the literature.[4]

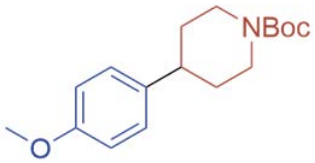
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.71 (t, *J* = 7.7 Hz, 2H), 2.32 (t, *J* = 7.4 Hz, 2H), 1.97 (p, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 145.6 (d, *J* = 1.36 Hz), 128.8, 128.4 (q, *J* = 32.9 Hz), 125.3 (q, *J* = 3.8), 124.3 (q, *J* = 271.6 Hz), 60.4, 35.0, 33.5, 26.2, 14.3.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.8.



Ethyl 4-(4-methylphenyl)butanoate (3m) [CAS: 36440-63-8]
General Procedure A was followed with ethyl 4-bromobutyrate (78.0 mg, 0.40 mmol, 1.0 equiv) and 4-bromotoluene (68.5 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (42.8 mg, 52% yield) as a colorless oil. Characterization data matched those reported in the literature.[13]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 – 7.03 (m, 4H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.31 (s, 3H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.93 (p, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 138.4, 135.4, 129.1, 128.4, 60.2, 34.7, 33.7, 26.7, 21.0, 14.5.

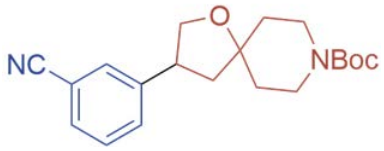


Ethyl 4-phenylbutanoate (3n) [CAS: 10031-93-3]
General Procedure A was followed with ethyl 4-bromobutyrate (78.2 mg, 0.40 mmol, 1.0 equiv) and bromobenzene (63.2 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->10% ethyl acetate in hexanes) to yield the product (41.9 mg, 54% yield) as a yellow oil. Characterization data matched those reported in the literature.[12]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.65 (t, *J* = 7.4 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.95 (p, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 141.5, 128.5, 128.4, 126.0, 60.3, 35.2, 33.7, 26.6, 14.3.



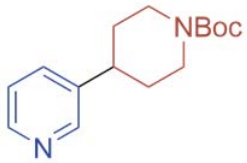
***tert*-Butyl 4-(4-methoxyphenyl)-1-piperidinecarboxylate (3o) [CAS: 303975-71-5]**
General Procedure A was followed with N-Boc-4-bromopiperidine (105.7 mg, 0.40 mmol, 1.0 equiv) and 4-bromoanisole (74.8 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->15% ethyl acetate in

hexanes) to yield the product (77.7 mg, 67% yield) as a colorless oil. Characterization data matched those reported in the literature.[14]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.23 (s, br, 2H), 3.78 (s, 3H), 2.78 (t, br, *J* = 13.1 Hz, 2H), 2.58 (tt, *J* = 12.3, 3.7 Hz, 1H), 1.79 (d, br, *J* = 13.4 Hz, 2H), 1.57 (qd, *J* = 12.6, 4.6 Hz, 2H), 1.48 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 154.9, 138.0, 127.6, 113.9, 79.4, 55.2, 44.4 (br), 41.8, 33.4, 28.5.



***tert*-butyl 3-(3-cyanophenyl)-1-oxa-8-azaspiro[4.5]decane-8-carboxylate (3p)**
General Procedure A was followed with *tert*-butyl 3-bromo-1-oxa-8-azaspiro[4.5]decane-8-carboxylate (128.2 mg, 0.40 mmol, 1.0 equiv) and 3-bromobenzonitrile (73.8 mg, 0.41 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 10-->30% ethyl acetate in hexanes) to yield the product (107.4 mg, 78% yield) as a colorless oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dt, *J* = 6.3, 1.6 Hz, 2H), 7.49 (dt, *J* = 7.9, 1.7 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 4.23 (dd, *J* = 8.9, 7.4 Hz, 1H), 3.78 (t, *J* = 8.7 Hz, 1H), 3.65 (s, br, 2H), 3.54 (p, *J* = 8.5 Hz, 1H), 3.41 – 3.28 (m, 2H), 2.29 (dd, *J* = 12.7, 8.2 Hz, 1H), 1.78 (dd, *J* = 12.7, 9.8 Hz, 1H), 1.76 – 1.64 (m, 3H), 1.58 (ddd, *J* = 13.7, 10.0, 4.2 Hz, 1H), 1.47 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 143.4, 131.8, 130.9, 130.4, 129.5, 118.7, 112.7, 81.1, 79.5, 72.7, 45.4, 44.3, 41.0 (br), 37.0, 36.3, 28.5.
HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{20}H_{27}N_2O_3^+$ = 343.2016, found = 343.2011.
IR (cm^{-1}) 2973, 2931, 2869, 2229, 1683, 1480, 1420, 1365, 1266, 1242, 1172, 1146, 1055, 966, 861, 799, 768, 693, 552, 487.

Ethyl 4-(pyridin-2-yl)butanoate (3q) [CAS: 84199-93-9]
General Procedure A was followed with ethyl 4-bromobutyrate (78.0 mg, 0.40 mmol, 1.0 equiv) and 2-bromopyridine (63.2 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->25% ethyl acetate in hexanes) to yield the product (23.6 mg, 31% yield). Characterization data matched those reported in the literature.[15]
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.59 (td, *J* = 7.7, 1.9 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.11 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.83 (dd, *J* = 8.4, 6.9 Hz, 2H), 2.36 (dd, *J* = 7.5 Hz, 2H), 2.08 (p, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 161.2, 149.3, 136.4, 122.9, 121.2, 60.3, 37.4, 33.7, 24.9, 14.3.

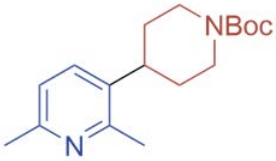


***tert*-butyl 4-(pyridin-3-yl)piperidine-1-carboxylate (3r) [CAS: 550371-77-2]**

General Procedure A was followed with N-Boc-4-bromopiperidine (107.1 mg, 0.41 mmol, 1.0 equiv) and 3-bromopyridine (63.6 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (10 g silica column, Gradient 20-->60% ethyl acetate in hexanes) to yield the product (52.8 mg, 50% yield) as a light orange oil. Characterization data matched those reported in the literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 – 8.45 (m, 2H), 7.51 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.24 (ddd, *J* = 7.9, 4.8, 0.8 Hz, 1H), 4.27 (s, br, 2H), 2.82 (t, br, *J* = 11.7 Hz, 2H), 2.68 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.83 (d, br, *J* = 13.9 Hz, 2H), 1.63 (qd, *J* = 12.5, 4.4 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 148.8, 147.9, 140.8, 134.1, 123.5, 79.6, 44.2 (br), 40.2, 32.9, 28.5.



***tert*-butyl 4-(2,6-dimethylpyridin-3-yl)piperidine-1-carboxylate (3s)**

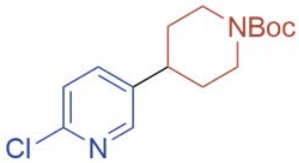
General Procedure A was followed with N-Boc-4-bromopiperidine (106.3 mg, 0.40 mmol, 1.0 equiv) and 3-bromo-2,6-dimethylpyridine (75.0 mg, 0.40 mmol, 1.0 equiv) using 1:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (10 g silica column, Gradient 20-->50% ethyl acetate in hexanes) to yield the product (87.3 mg, 75% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 4.26 (s, br, 2H), 2.81 (tt, *J* = 12.2, 3.2 Hz, 3H), 2.54 (s, 3H), 2.47 (s, 3H), 1.73 (d, br, *J* = 12.7 Hz, 2H), 1.55 (qt, *J* = 12.8, 5.3 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 154.9, 154.8, 135.4, 133.5, 121.0, 79.5, 44.5 (br), 37.8, 32.2, 28.5, 24.0, 22.1.

HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{17}H_{27}N_2O_2^+$ = 291.2067, found = 291.2063.

IR (cm^{-1}) 2929, 2855, 1688, 1582, 1456, 1418, 1371, 1309, 1234, 1164, 1121, 1015, 934.



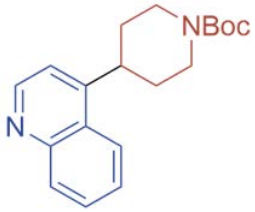
***tert*-butyl 4-(6-chloropyridin-3-yl)piperidine-1-carboxylate (3t)**

General Procedure A was followed with N-Boc-4-bromopiperidine (105.7 mg, 0.40 mmol, 1.0 equiv) and 5-bromo-2-chloropyridine (77.0 mg, 0.40 mmol, 1.0 equiv) using 5:1 **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->15% ethyl acetate in

hexanes) to yield the product (67.2 mg, 62% yield) as a pale yellow oil. Characterization data matched those reported in the literature.[17]

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 2.5 Hz, 1H), 7.49 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 4.27 (s, br, 2H), 2.81 (t, br, *J* = 13.0 Hz, 2H), 2.69 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.82 (d, br, *J* = 13.7 Hz, 2H), 1.60 (qd, *J* = 12.7, 4.4 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 149.5, 148.5, 139.8, 137.0, 124.1, 79.7, 44.1 (br), 39.6, 32.8, 28.4.



***tert*-butyl 4-(4-quinolinyl)piperidine-1-carboxylate (3u) [CAS: 2128285-30-1]**

General Procedure A was followed with N-Boc-4-bromopiperidine (105.7 mg, 0.40 mmol, 1.0 equiv) and 4-bromoquinoline (83.2 mg, 0.40 mmol, 1.0 equiv) using **L1**/**L2** catalyst stock solution. After 4.3 h, (4 F/mol) the current and heat were turned off. The crude material was purified by silica gel chromatography (12 g silica column, Gradient 0-->15% ethyl acetate in hexanes) to yield the product (73.7 mg, 59% yield) as a tan solid. ^{1}H and ^{13}C NMR data matched those reported in the literature.[18]

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.6 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.3 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.71 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.58 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.25 (d, *J* = 4.6 Hz, 1H), 4.34 (s, br, 2H), 3.48 (tt, *J* = 12.0, 3.4 Hz, 1H), 2.95 (t, br, *J* = 14.3 Hz, 2H), 1.97 (dt, *J* = 13.3, 2.8 Hz, 2H), 1.75 (qd, *J* = 12.6, 4.3 Hz, 2H), 1.50 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 151.1, 150.4, 148.4, 130.6, 129.0, 126.6, 126.5, 122.6, 117.5, 79.7, 44.3 (br), 37.2, 32.3, 28.5.

HRMS (ESI) m/z calcd for $[M+H]^+$ $C_{19}H_{25}N_2O_2^+$ = 313.1911, found = 313.1907.

IR (cm^{-1}) 2974, 2930, 2860, 1675, 1585, 1426, 1365, 1240, 1171, 1114, 989, 860, 754.

Melting point range (°C) 115.8–118.0.

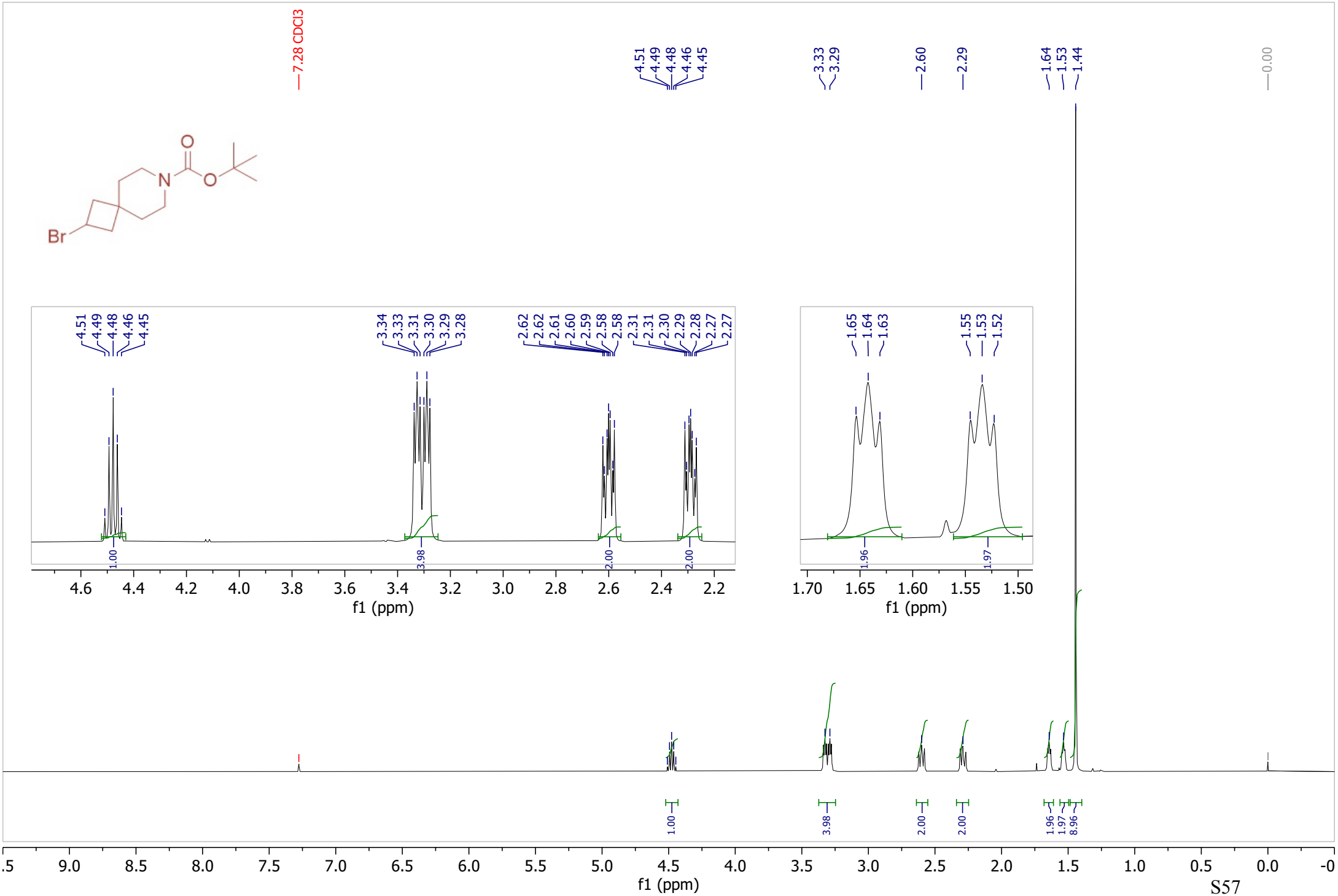
9. References

1. Robo, M. T.; Prinsell, M. R.; Weix, D. J. 4,4′,4″-Trimethyl-2,2′:6′,2″-Terpyridine by Oxidative Coupling of 4-Picoline. *J. Org. Chem.* **2014**, *79*, 10624–10628. https://doi.org/10.1021/jo501925s.
2. Long, S. a; Meyers, M. J.; Pelc, M. J.; Schweitzer, B. a; Thorarensen, A.; Wang, J. L. 7-Azaspiro[3.5]Nonane-7-Carboxamide Compounds. US2010113465 (A1), May 6, 2010.
3. Weires, N. A.; Slutskyy, Y.; Overman, L. E. Facile Preparation of Spirolactones by an Alkoxycarbonyl Radical Cyclization–Cross-Coupling Cascade. *Angew. Chem. Int. Ed.* **2019**, *58*, 8561–8565. https://doi.org/10.1002/anie.201903353.
4. Amatore, M.; Gosmini, C. Direct Method for Carbon–Carbon Bond Formation: The Functional Group Tolerant Cobalt-Catalyzed Alkylation of Aryl Halides. *Chem. – Eur. J.* **2010**, *16*, 5848–5852. https://doi.org/10.1002/chem.201000178.
5. Biswas, S.; Qu, B.; Desrosiers, J.-N.; Choi, Y.; Haddad, N.; Yee, N. K.; Song, J. J.; Senanayake, C. H. Nickel-Catalyzed Cross-Electrophile Reductive Couplings of Neopentyl Bromides with Aryl Bromides. *J. Org. Chem.* **2020**, *85*, 8214–8220. https://doi.org/10.1021/acs.joc.0c00549.
6. Shields, B. J.; Kudisch, B.; Scholes, G. D.; Doyle, A. G. Long-Lived Charge-Transfer States of Nickel(II) Aryl Halide Complexes Facilitate Bimolecular Photoinduced Electron Transfer. *J. Am. Chem. Soc.* **2018**, *140*, 3035–3039. https://doi.org/10.1021/jacs.7b13281.
7. Wang, L.-S.; Lu, Y.; Máille, G. M. Ó.; Anthony, S. P.; Nolan, D.; Draper, S. M. Sonogashira Cross-Coupling as a Route to Tunable Hybrid Organic–Inorganic Rods with a Polyoxometalate Backbone. *Inorg. Chem.* **2016**, *55*, 9497–9500. https://doi.org/10.1021/acs.inorgchem.6b01395.
8. Barham, J. P.; John, M. P.; Murphy, J. A. Contra-Thermodynamic Hydrogen Atom Abstraction in the Selective C–H Functionalization of Trialkylamine N-CH3 Groups. *J. Am. Chem. Soc.* **2016**, *138*, 15482–15487. https://doi.org/10.1021/jacs.6b09690.
9. Liu, Z.; Dong, N.; Xu, M.; Sun, Z.; Tu, T. Mild Negishi Cross-Coupling Reactions Catalyzed by Acenaphthoimidazolylidene Palladium Complexes at Low Catalyst Loadings. *J. Org. Chem.* **2013**, *78*, 7436–7444. https://doi.org/10.1021/jo400803s.
10. Gonnard, L.; Guérinot, A.; Cossy, J. Cobalt-Catalyzed Cross-Coupling of 3- and 4-Iodopiperidines with Grignard Reagents. *Chem. Eur. J.* **2015**, *21*, 12797–12803. https://doi.org/10.1002/chem.201501543.
11. Corley, E. G.; Conrad, K.; Murry, J. A.; Savarin, C.; Holko, J.; Boice, G. Direct Synthesis of 4-Arylpiperidines via Palladium/Copper(I)-Cocatalyzed Negishi Coupling of a 4-Piperidylzinc Iodide with Aromatic Halides and Triflates. *J. Org. Chem.* **2004**, *69*, 5120–5123. https://doi.org/10.1021/jo049647i.
12. Everson, D. A.; Jones, B. A.; Weix, D. J. Replacing Conventional Carbon Nucleophiles with Electrophiles: Nickel-Catalyzed Reductive Alkylation of Aryl Bromides and Chlorides. *J. Am. Chem. Soc.* **2012**, *134*, 6146–6159. https://doi.org/10.1021/ja301769r.
13. Nani, R. R.; Reisman, S. E. α-Diazo-β-Ketonitriles: Uniquely Reactive Substrates for Arene and Alkene Cyclopropanation. *J. Am. Chem. Soc.* **2013**, *135*, 7304–7311. https://doi.org/10.1021/ja401610p.
14. Allwood, D. M.; Blakemore, D. C.; Brown, A. D.; Ley, S. V. Metal-Free Coupling of Saturated Heterocyclic Sulfonylhydrazones with Boronic Acids. *J. Org. Chem.* **2014**, *79*, 328–338. https://doi.org/10.1021/jo402526z.

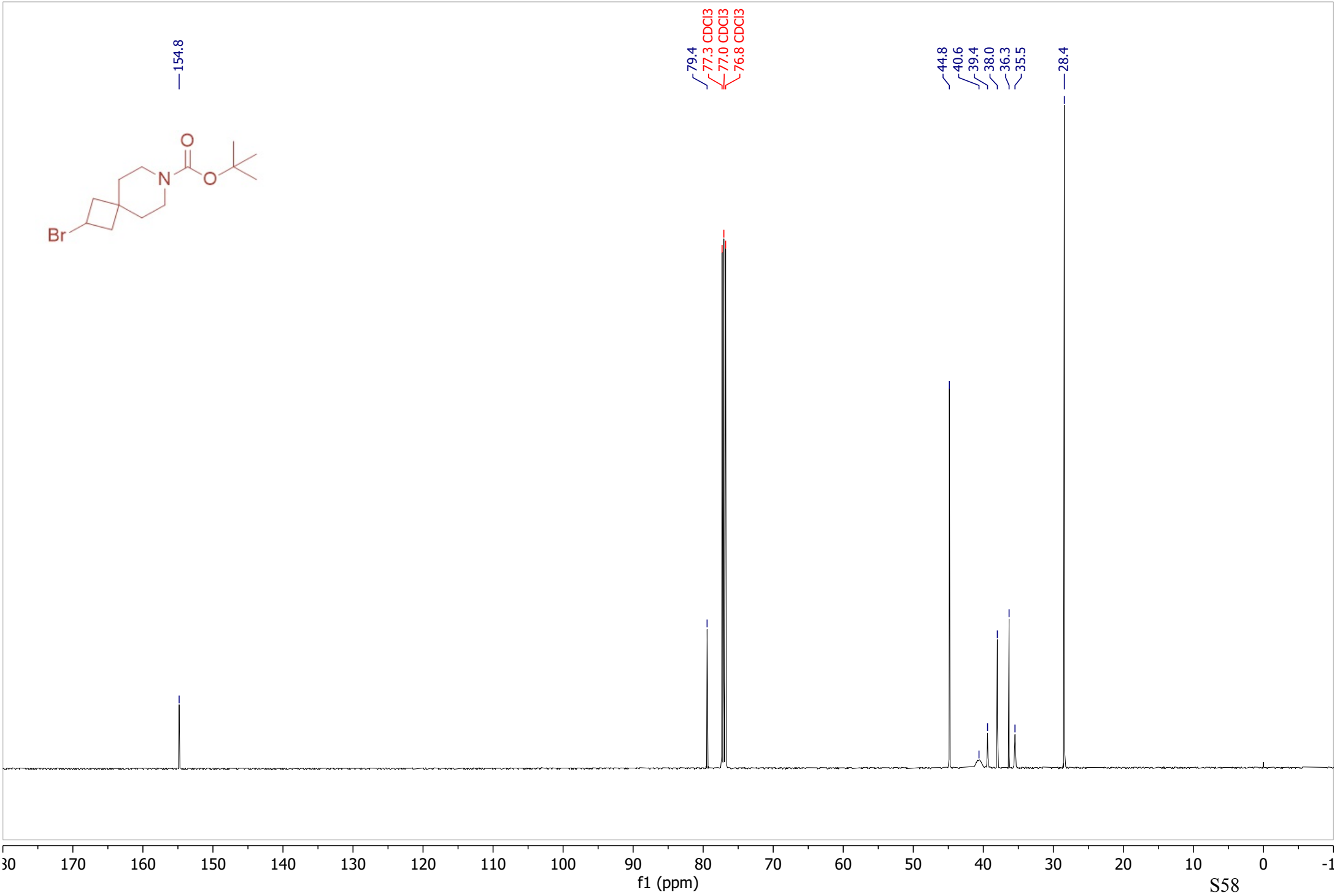
15. Everson, D. A.; Buonomo, J. A.; Weix, D. J. Nickel-Catalyzed Cross-Electrophile Coupling of 2-Chloropyridines with Alkyl Bromides. *Synlett* **2014**, *25*, 233–238. https://doi.org/10.1055/s-0033-1340151.
16. Molander, G. A.; Traister, K. M.; O'Neill, B. T. Reductive Cross-Coupling of Nonaromatic, Heterocyclic Bromides with Aryl and Heteroaryl Bromides. *J. Org. Chem.* **2014**, *79*, 5771–5780. https://doi.org/10.1021/jo500905m.
17. Wang, J.; Qin, T.; Chen, T.-G.; Wimmer, L.; Edwards, J. T.; Cornella, J.; Vokits, B.; Shaw, S. A.; Baran, P. S. Nickel-Catalyzed Cross-Coupling of Redox-Active Esters with Boronic Acids. *Angew. Chem. Int. Ed.* **2016**, *55*, 9676–9679. https://doi.org/10.1002/anie.201605463.
18. Speckmeier, E.; Maier, T. C. ART─An Amino Radical Transfer Strategy for C(Sp^2)–C(Sp^3) Coupling Reactions, Enabled by Dual Photo/Nickel Catalysis. *J. Am. Chem. Soc.* **2022**, *144*, 9997–10005. https://doi.org/10.1021/jacs.2c03220.

10. NMR Spectra

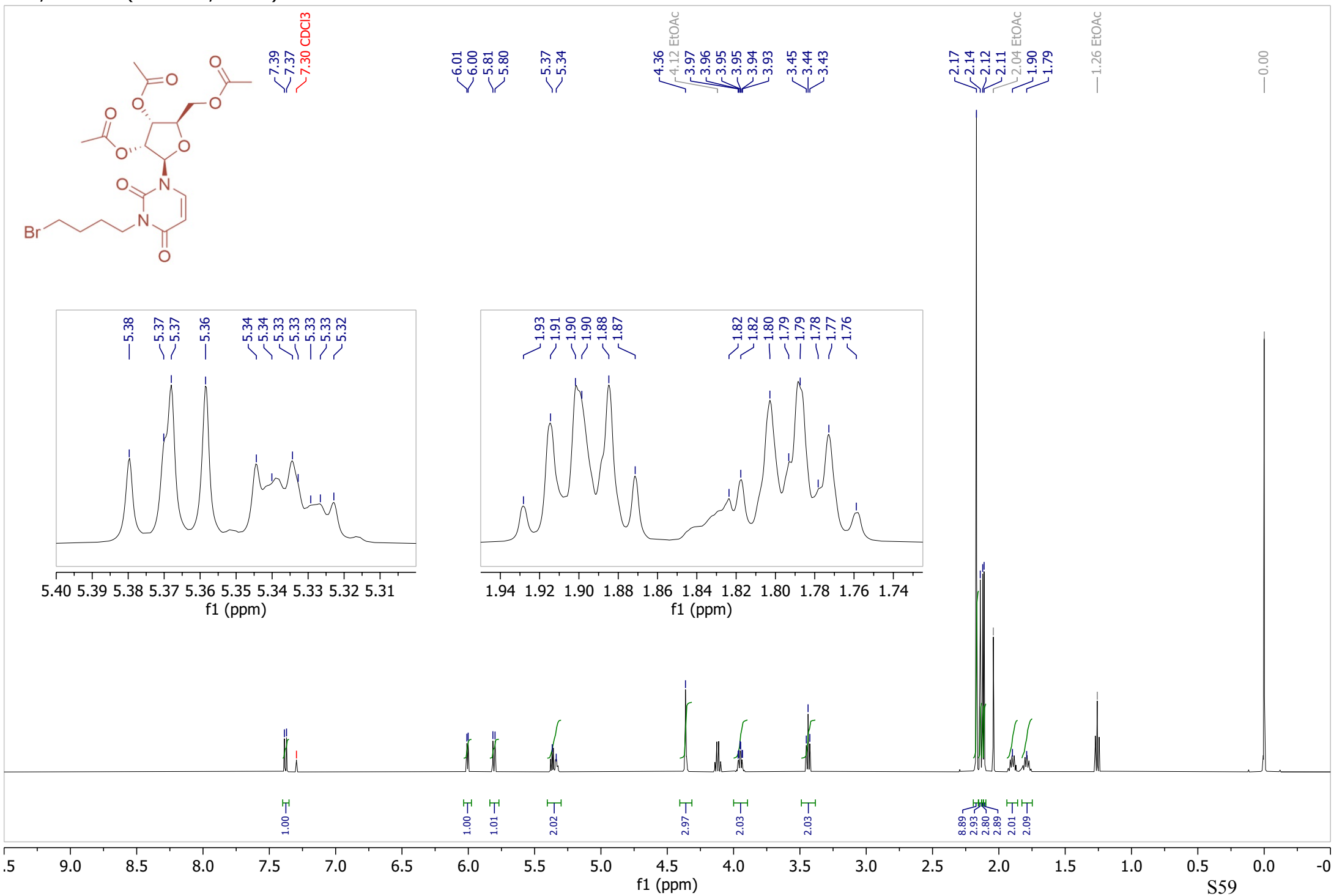
2g, ^{1}H NMR (500 MHz, CDCl3)



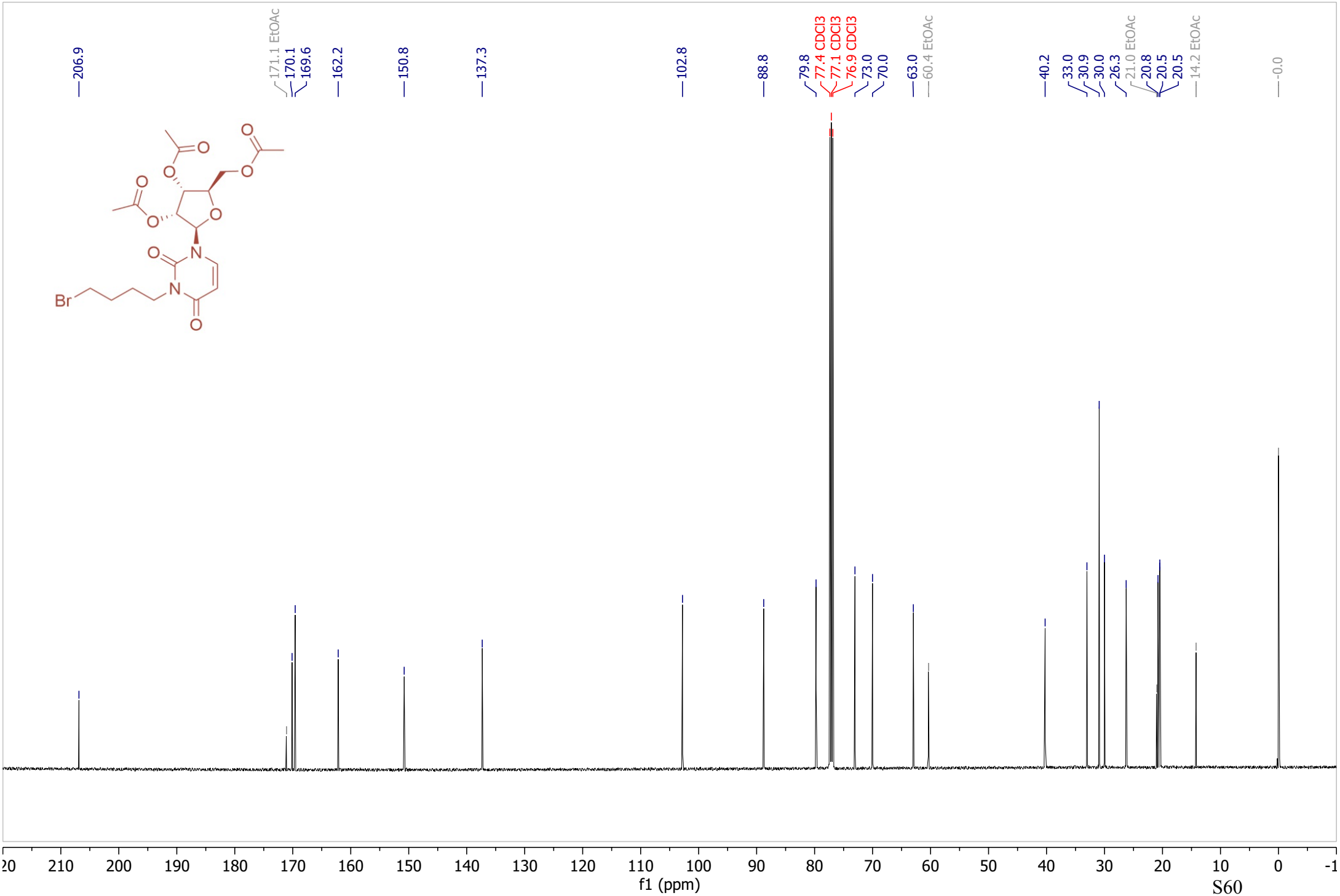
2g, ^{13}C NMR (126 MHz, CDCl3)



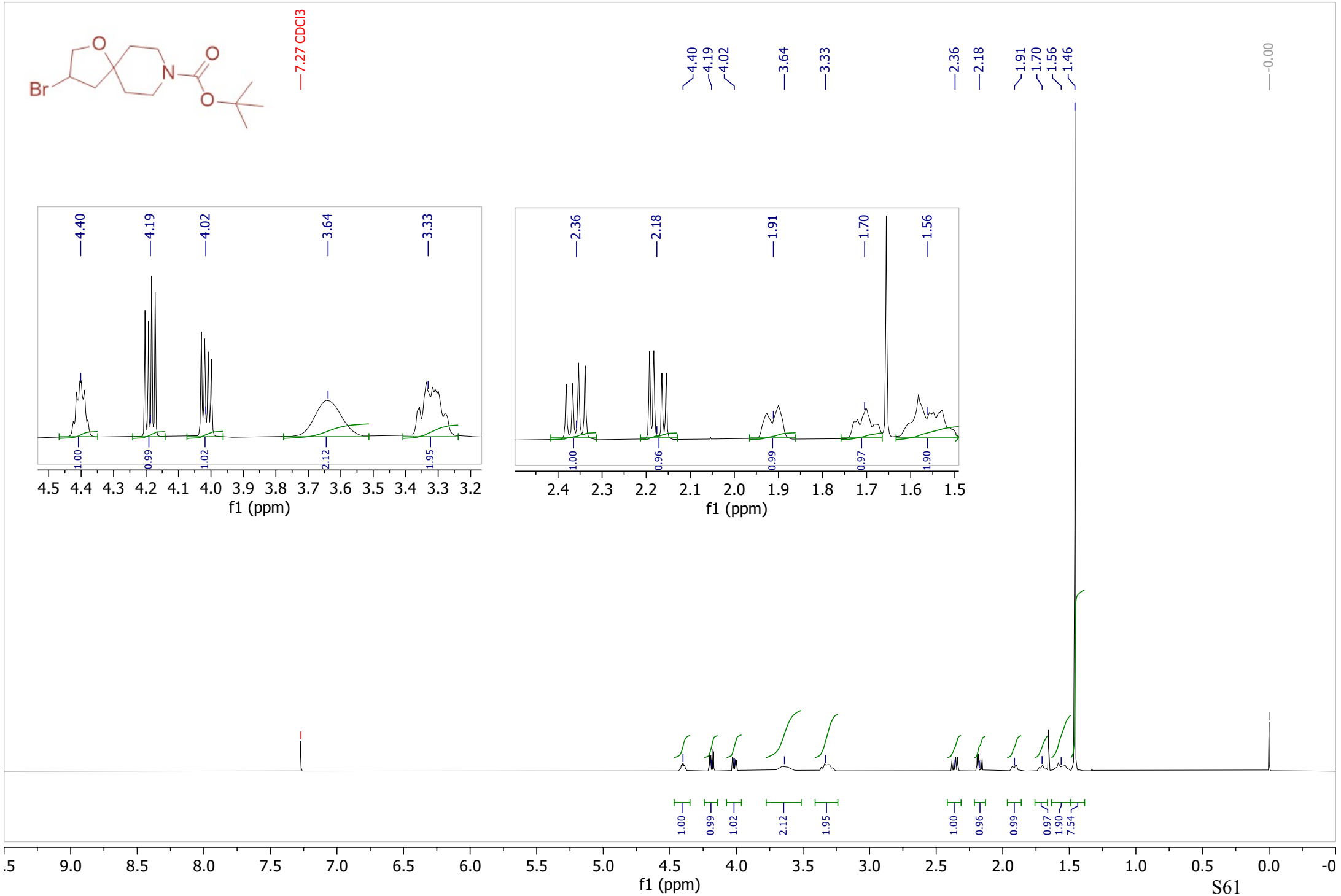
2h, ^{1}H NMR (500 MHz, CDCl3)



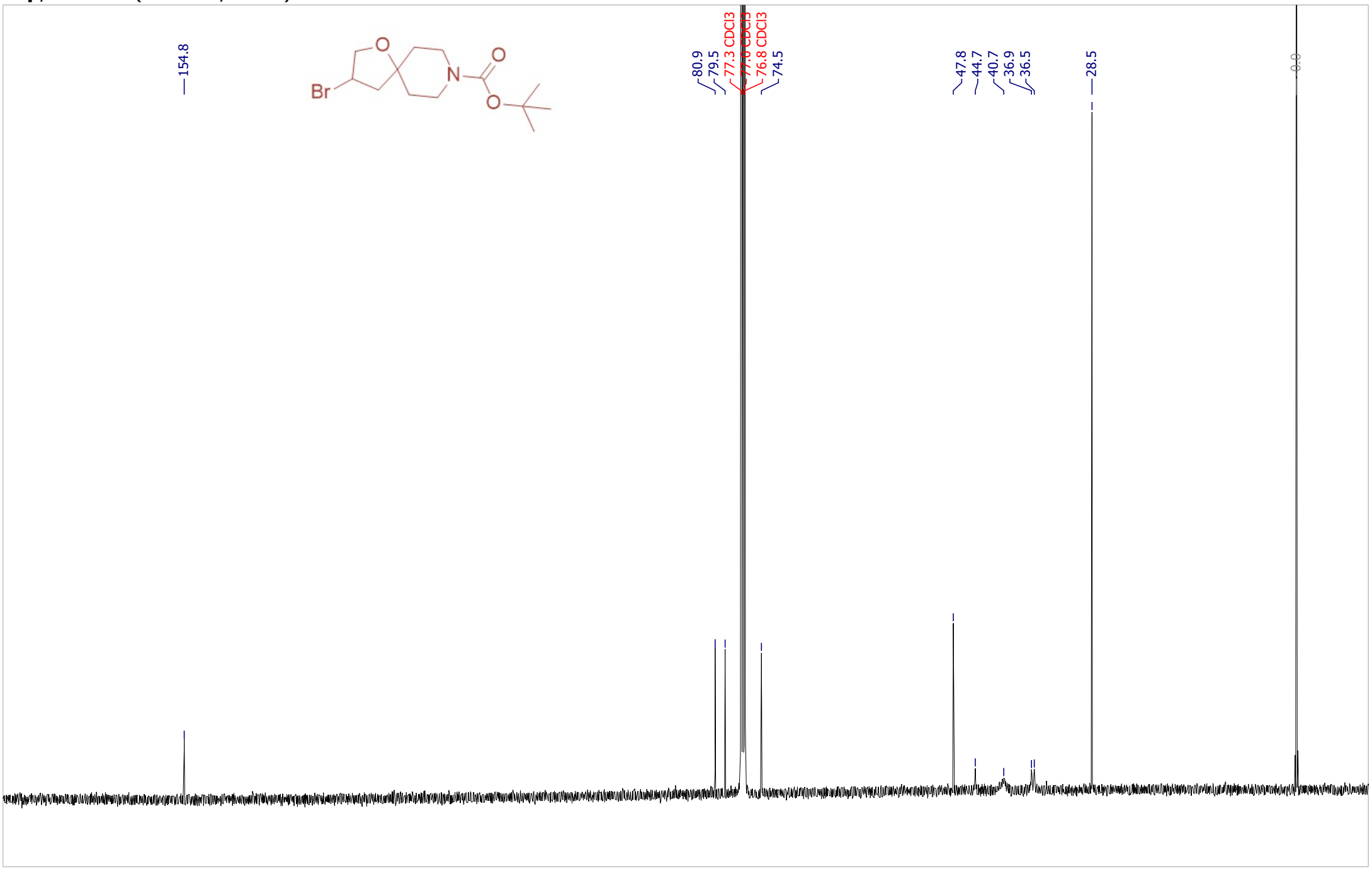
2h, ^{13}C NMR (126 MHz, CDCl3)



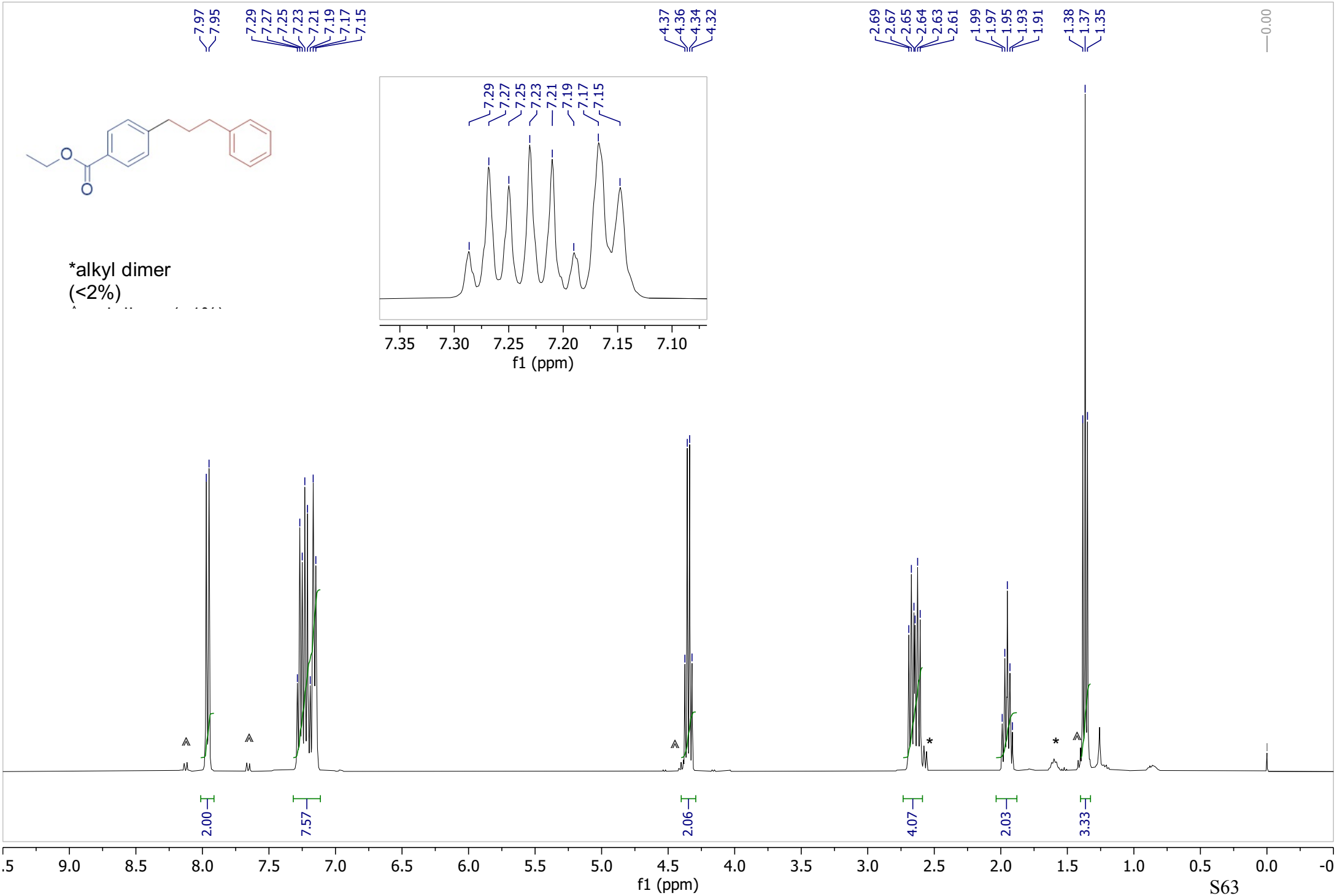
2p, ^{1}H NMR (500 MHz, CDCl3)



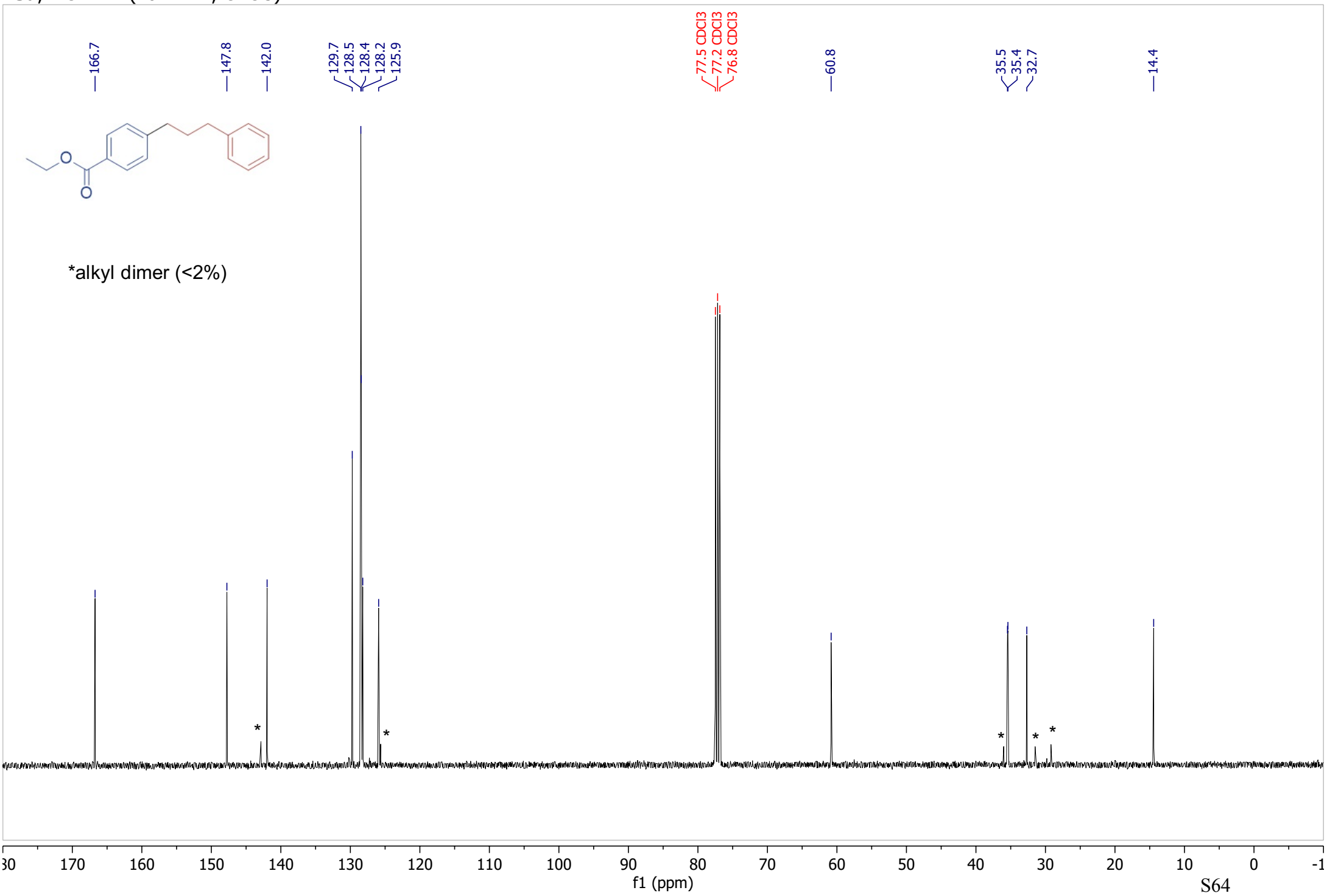
2p, ^{13}C NMR (126 MHz, CDCl3)



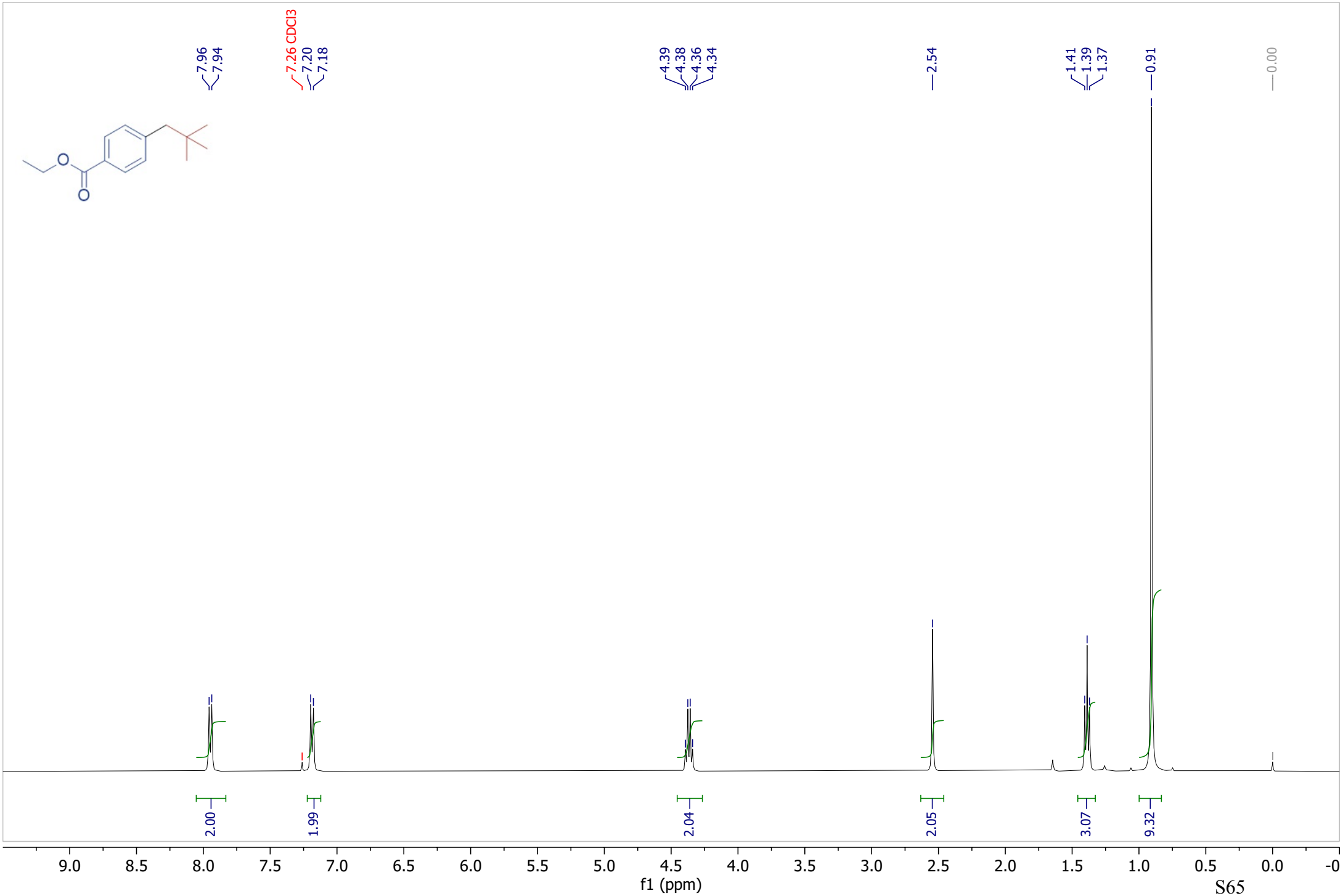
3a, ^{1}H NMR (400 MHz, CDCl3)



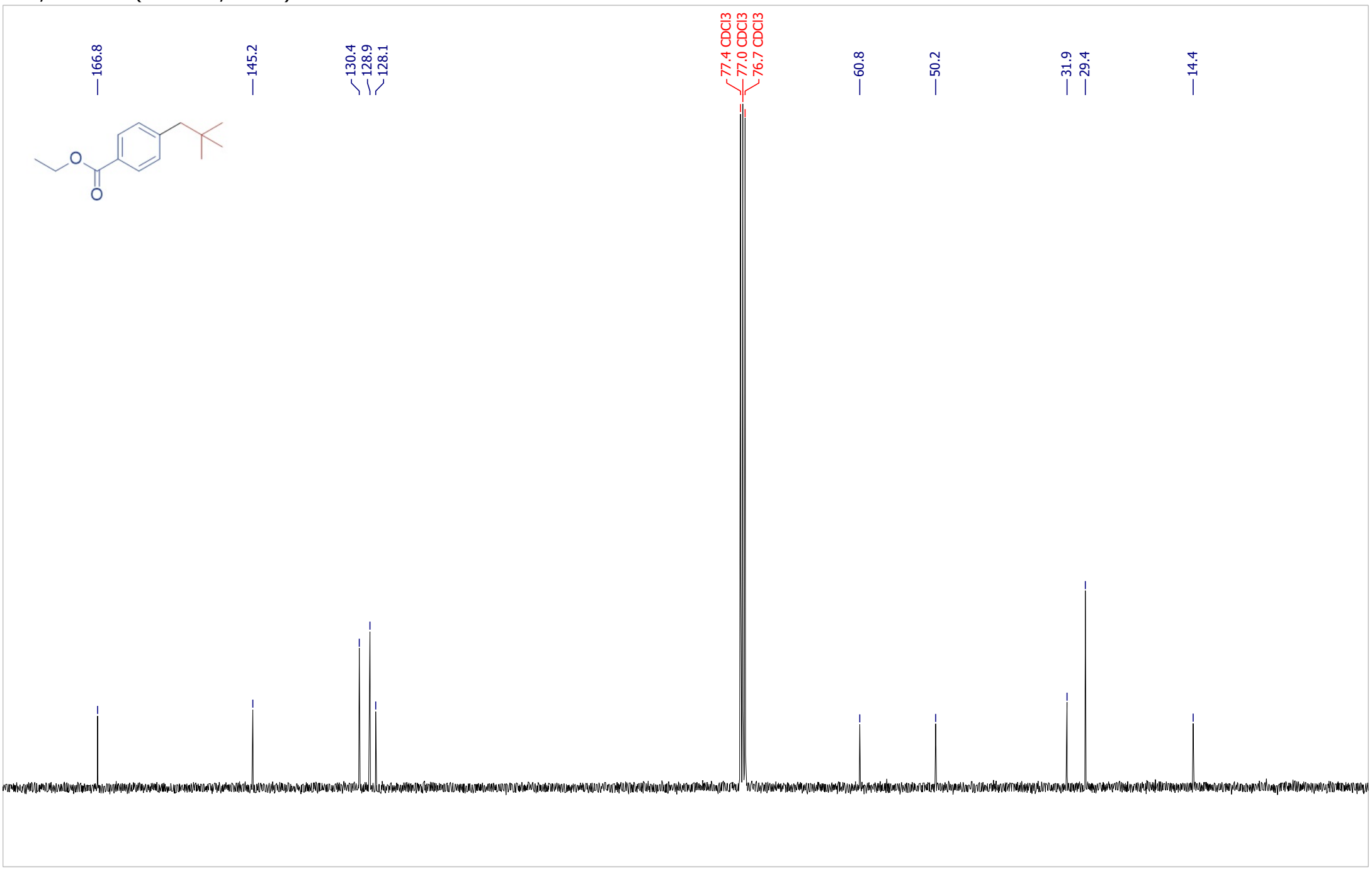
3a, ^{13}C NMR (101 MHz, CDCl3)



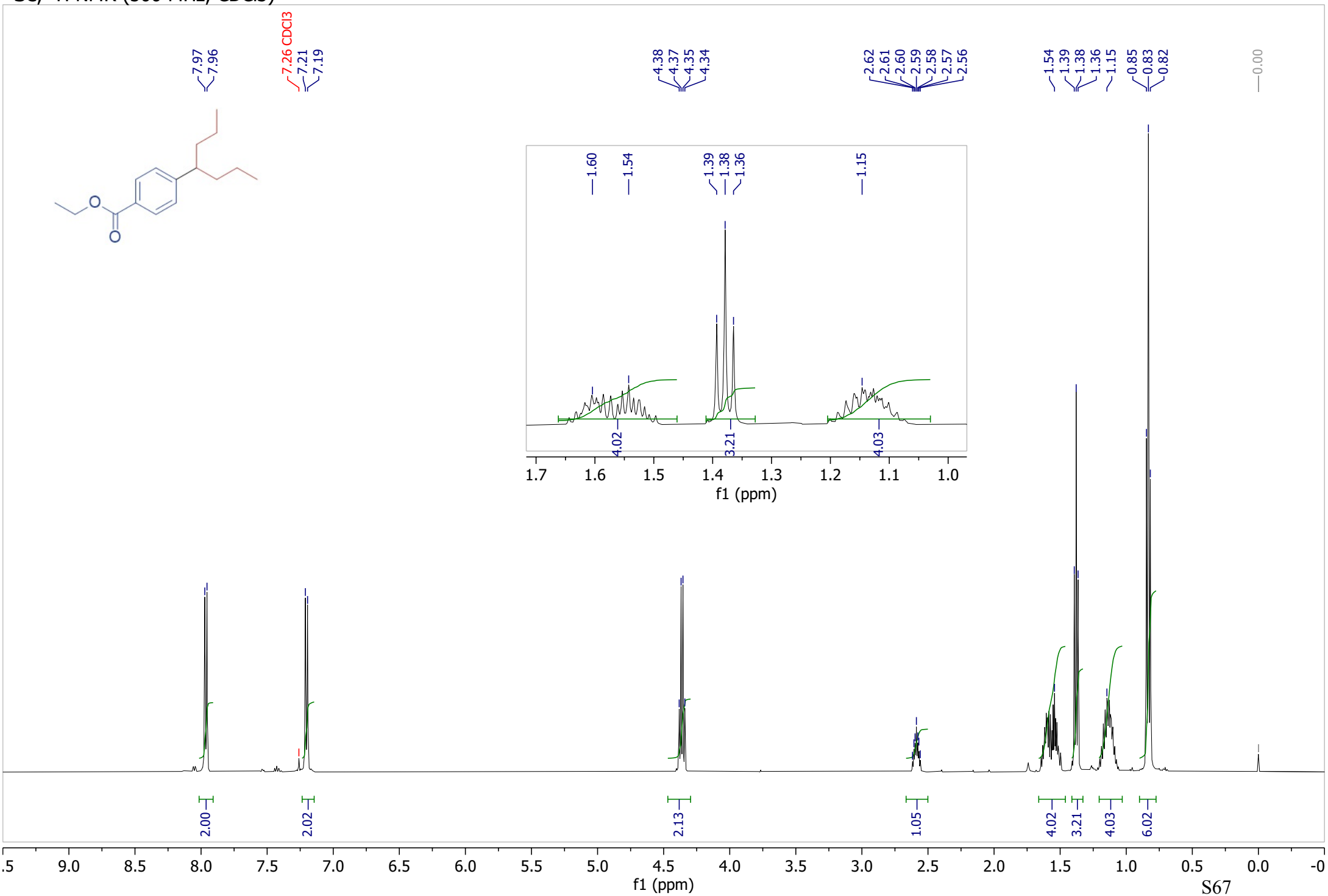
3b, ^{1}H NMR (400 MHz, CDCl3)



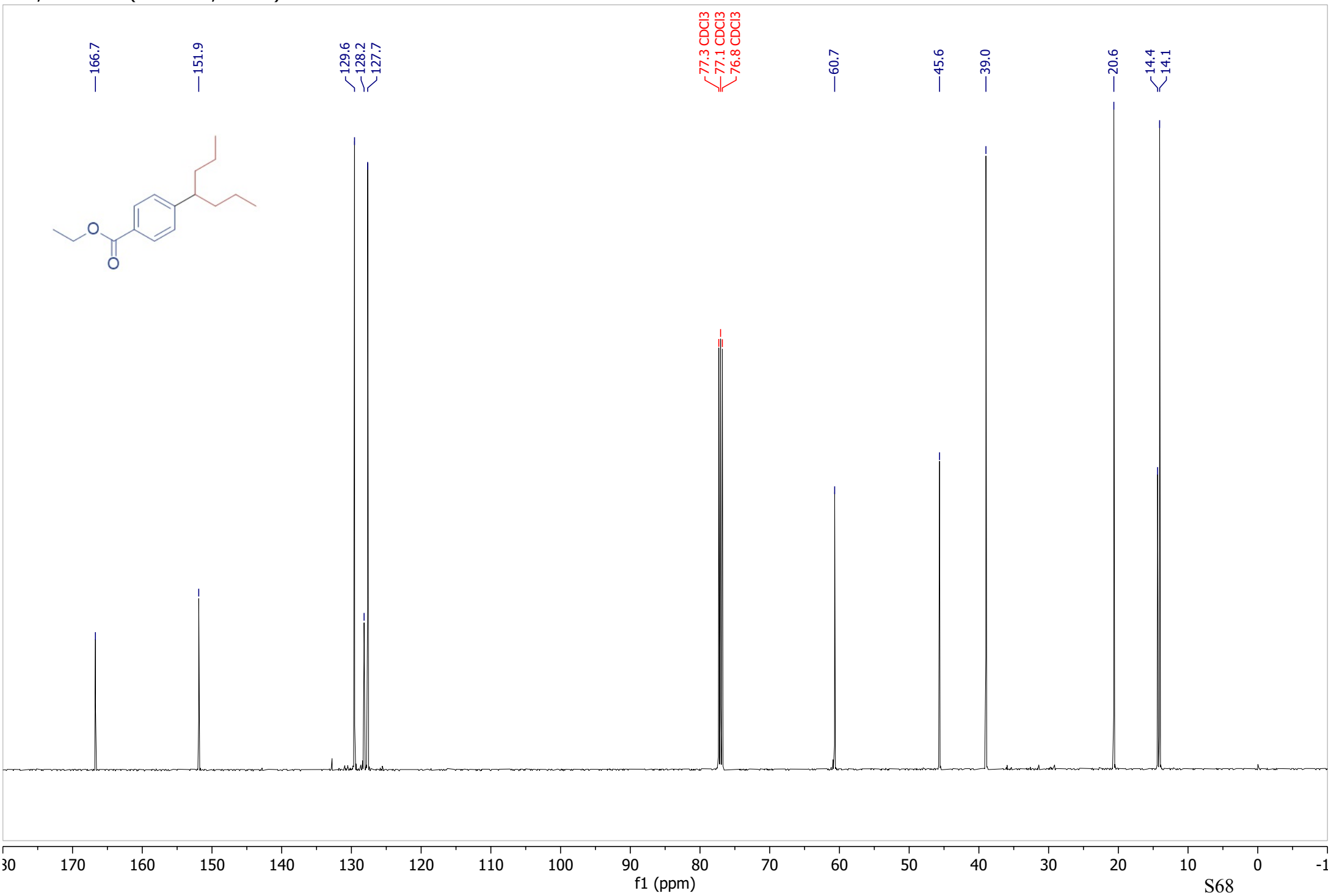
3b, ^{13}C NMR (101 MHz, CDCl3)



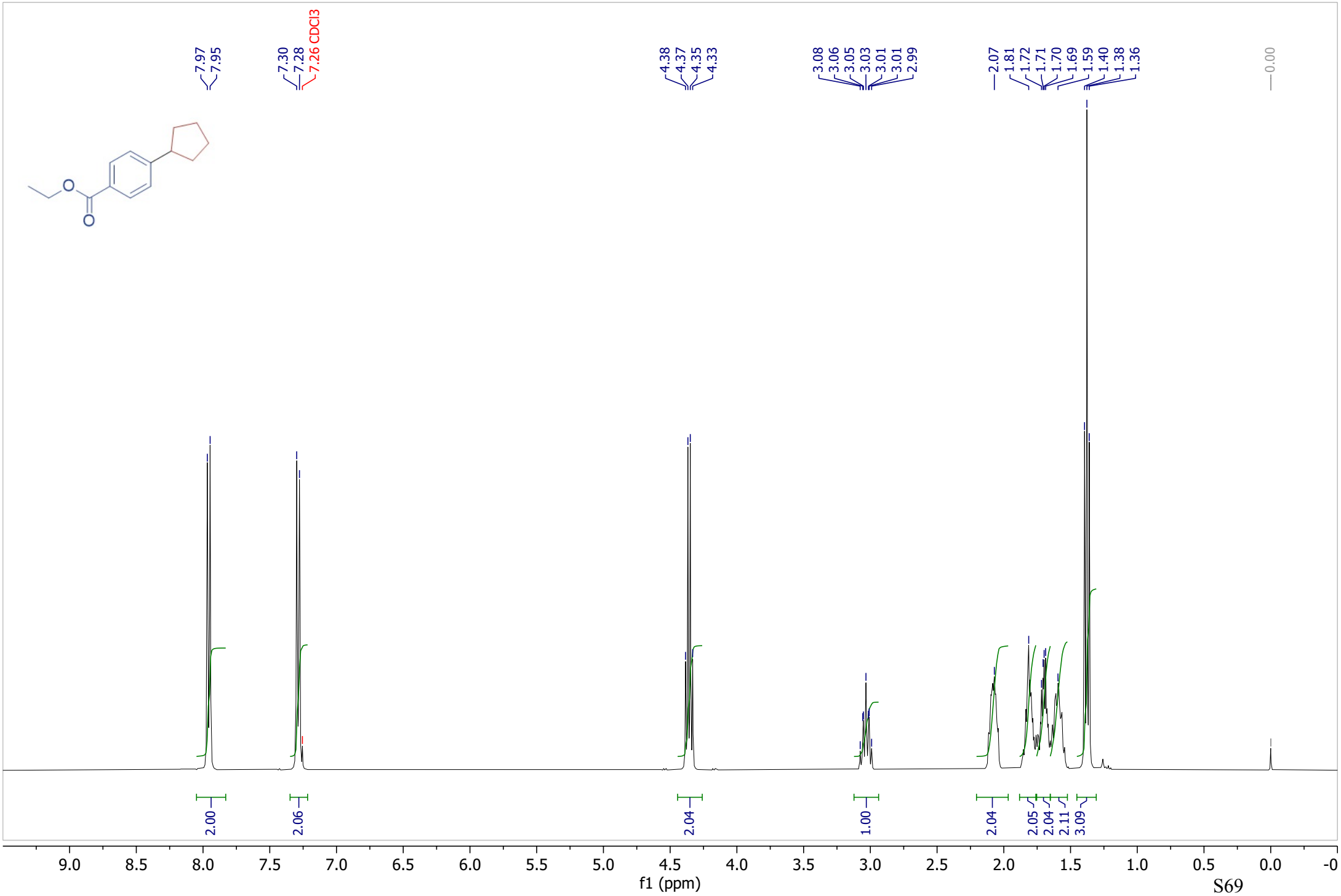
3c, ^{1}H NMR (500 MHz, CDCl3)



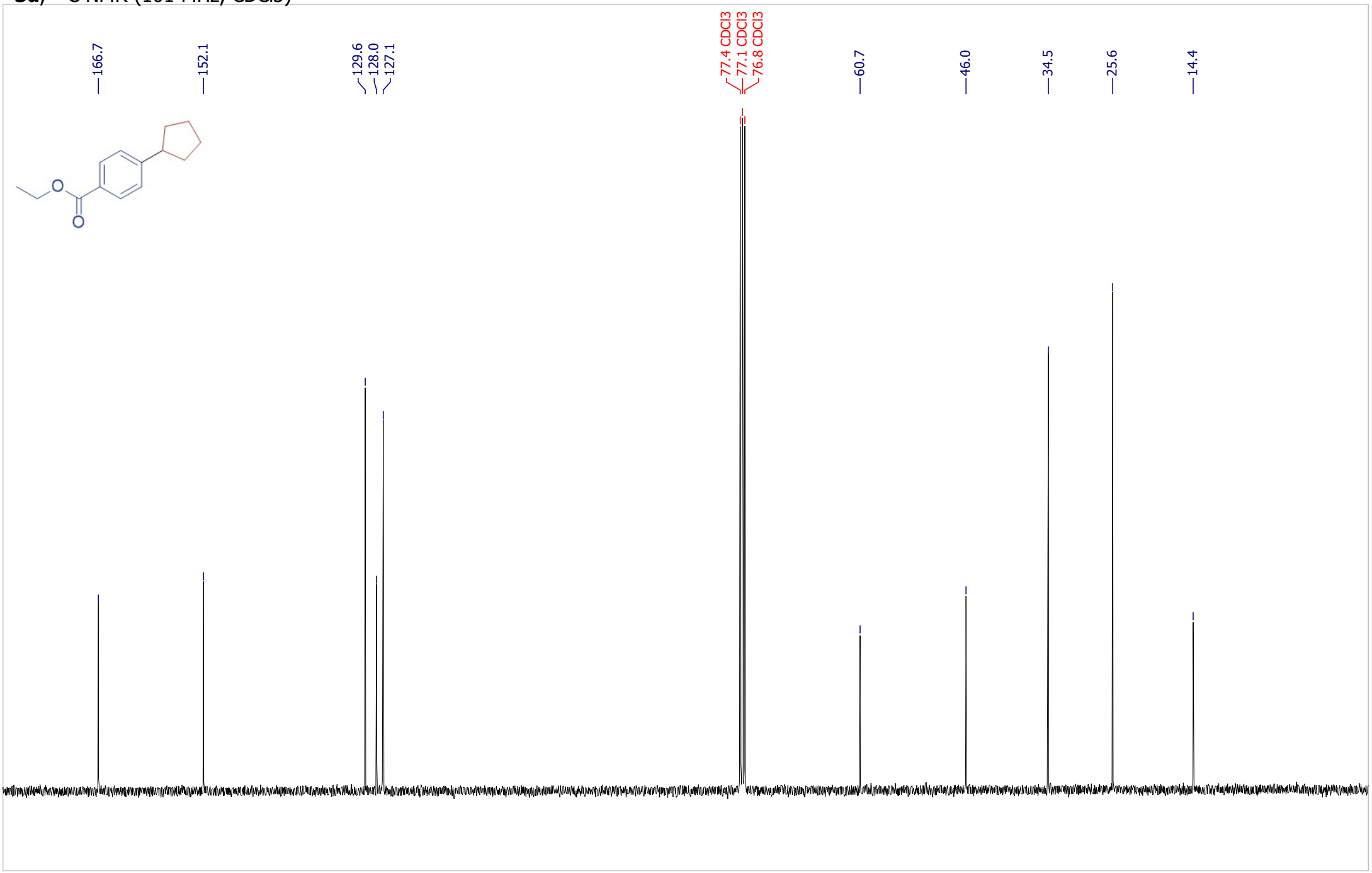
3c, ^{13}C NMR (126 MHz, CDCl3)



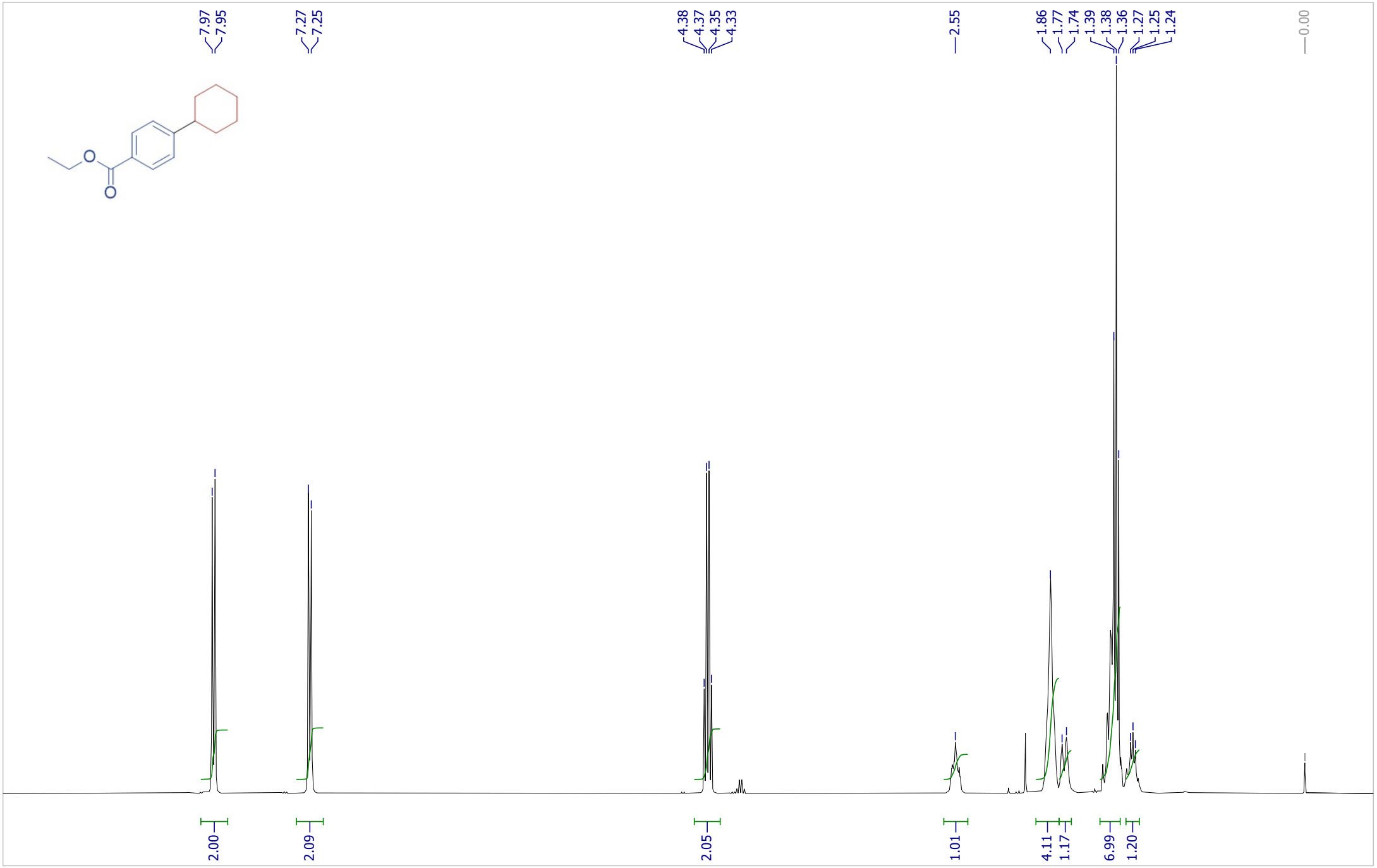
3d, ^{1}H NMR (400 MHz, CDCl3)



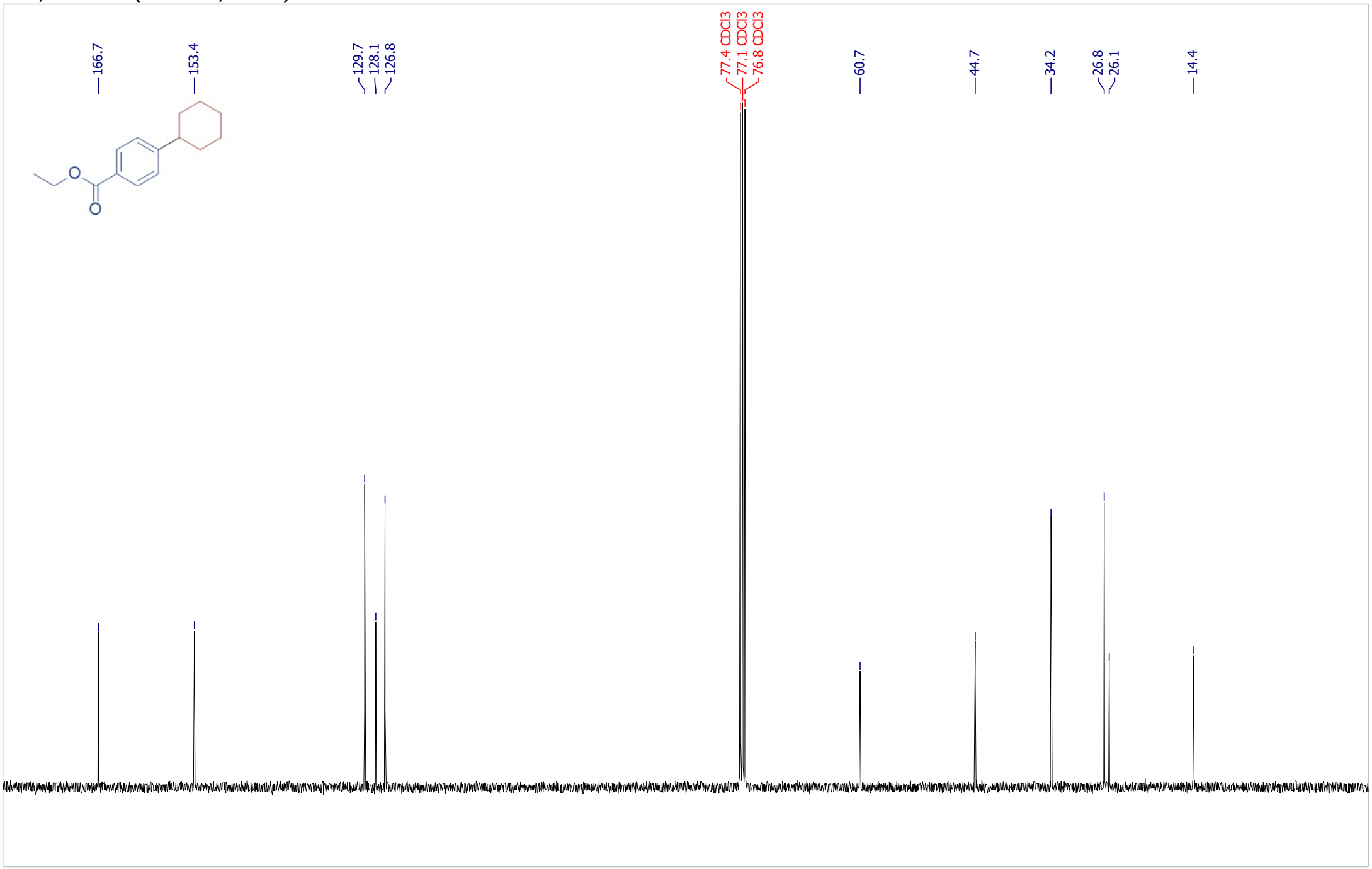
3d, ^{13}C NMR (101 MHz, CDCl3)



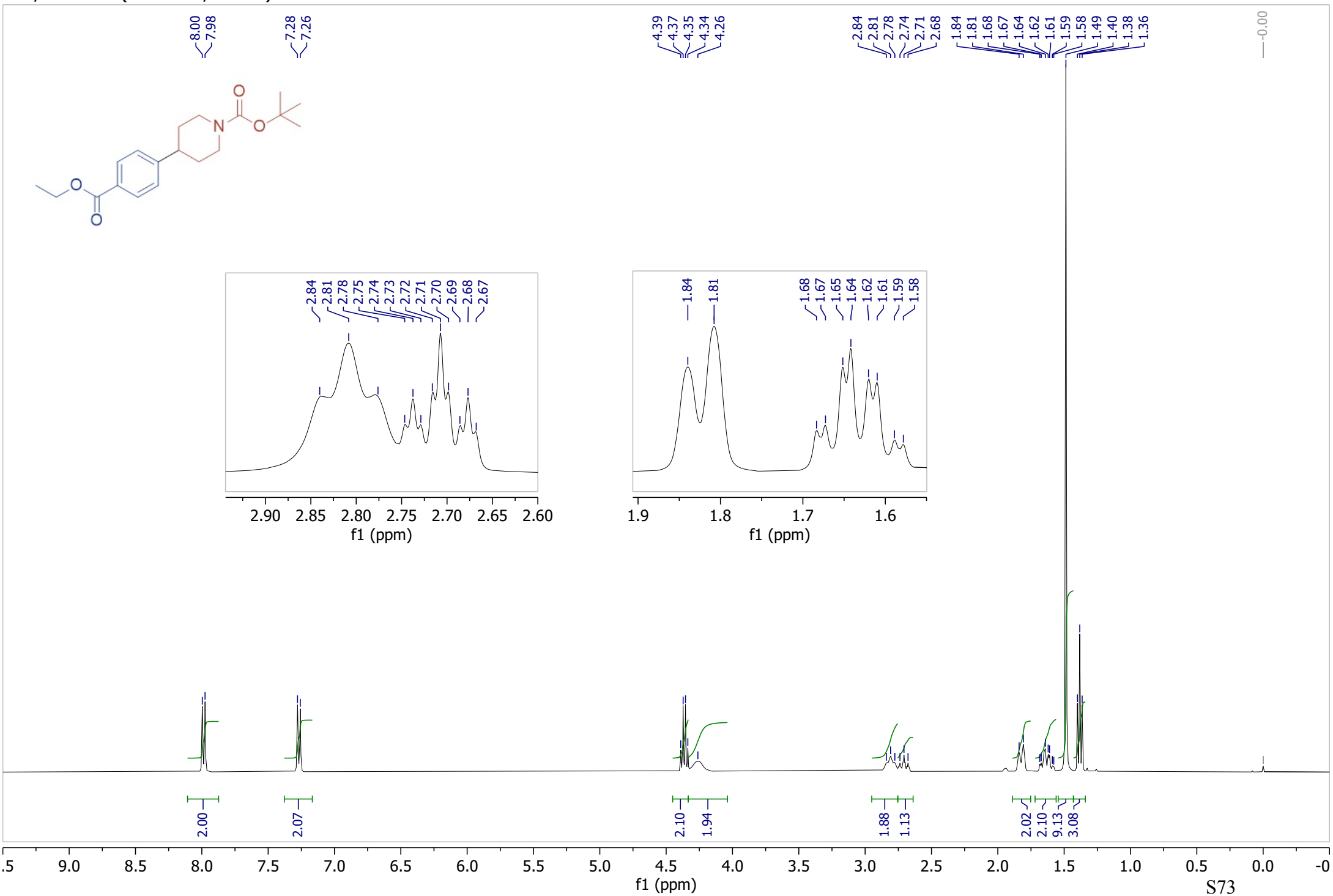
3e, ^{1}H NMR (400 MHz, CDCl3)



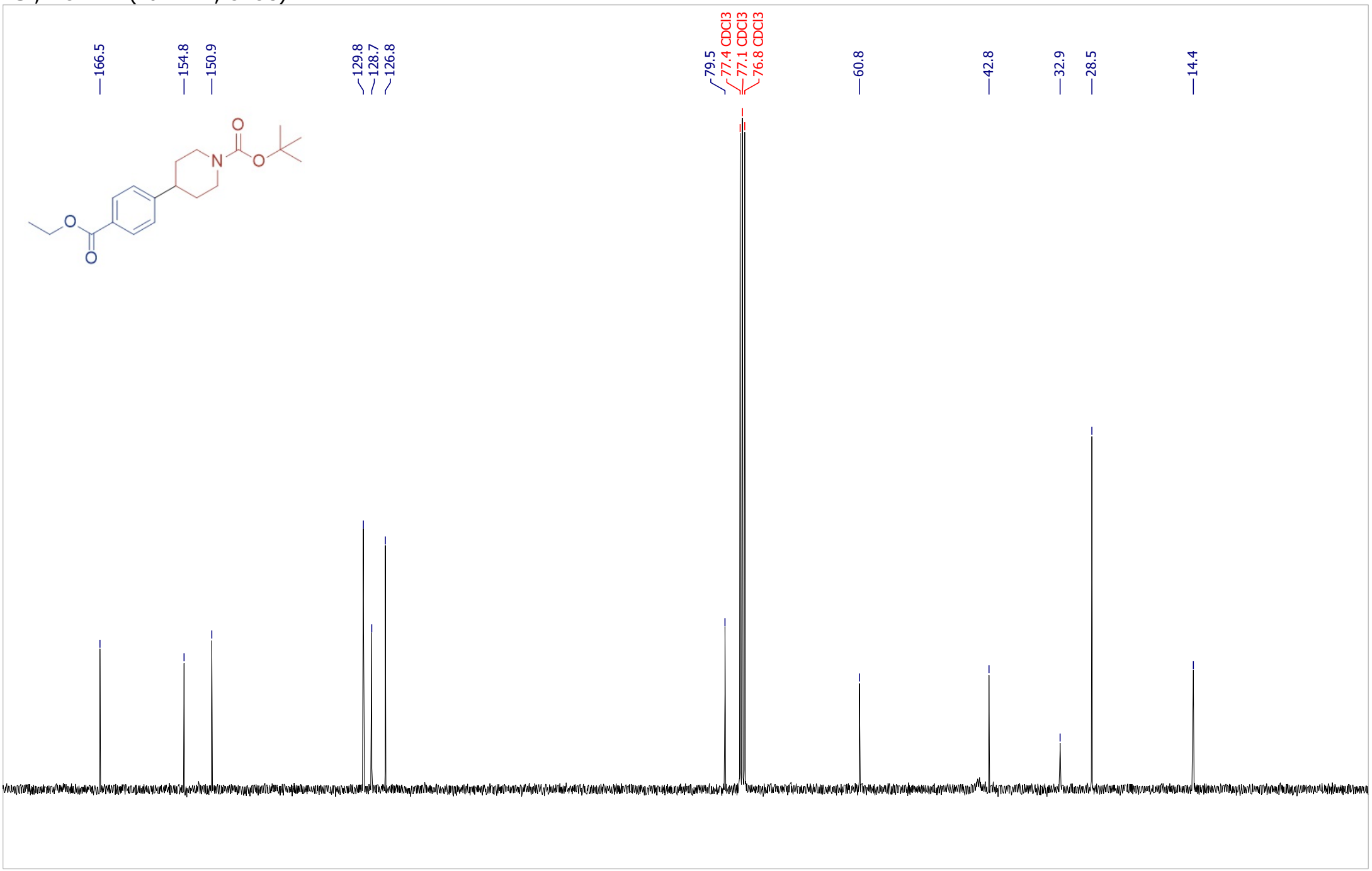
3e, ^{13}C NMR (101 MHz, CDCl3)



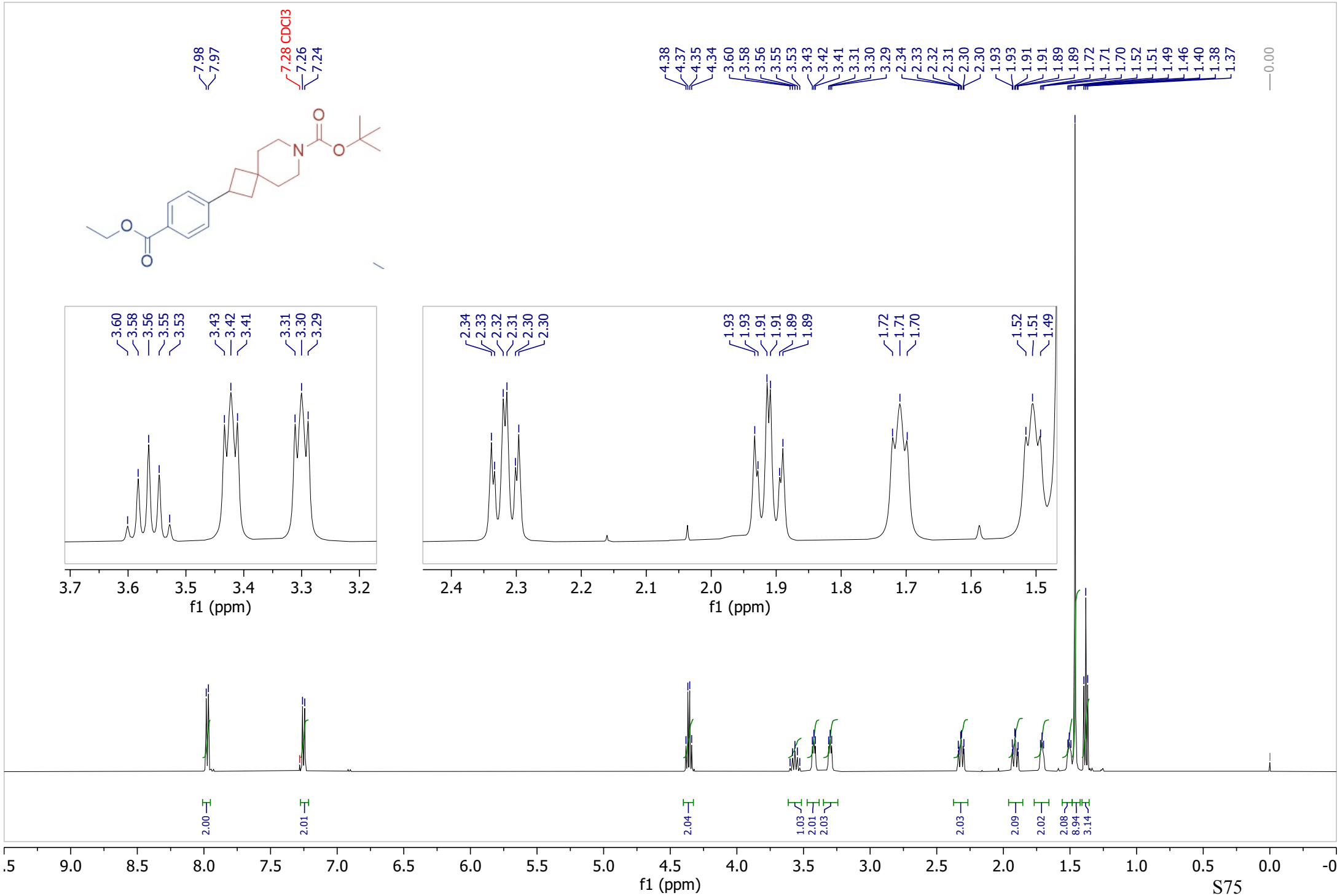
3f, ^{1}H NMR (400 MHz, CDCl3)



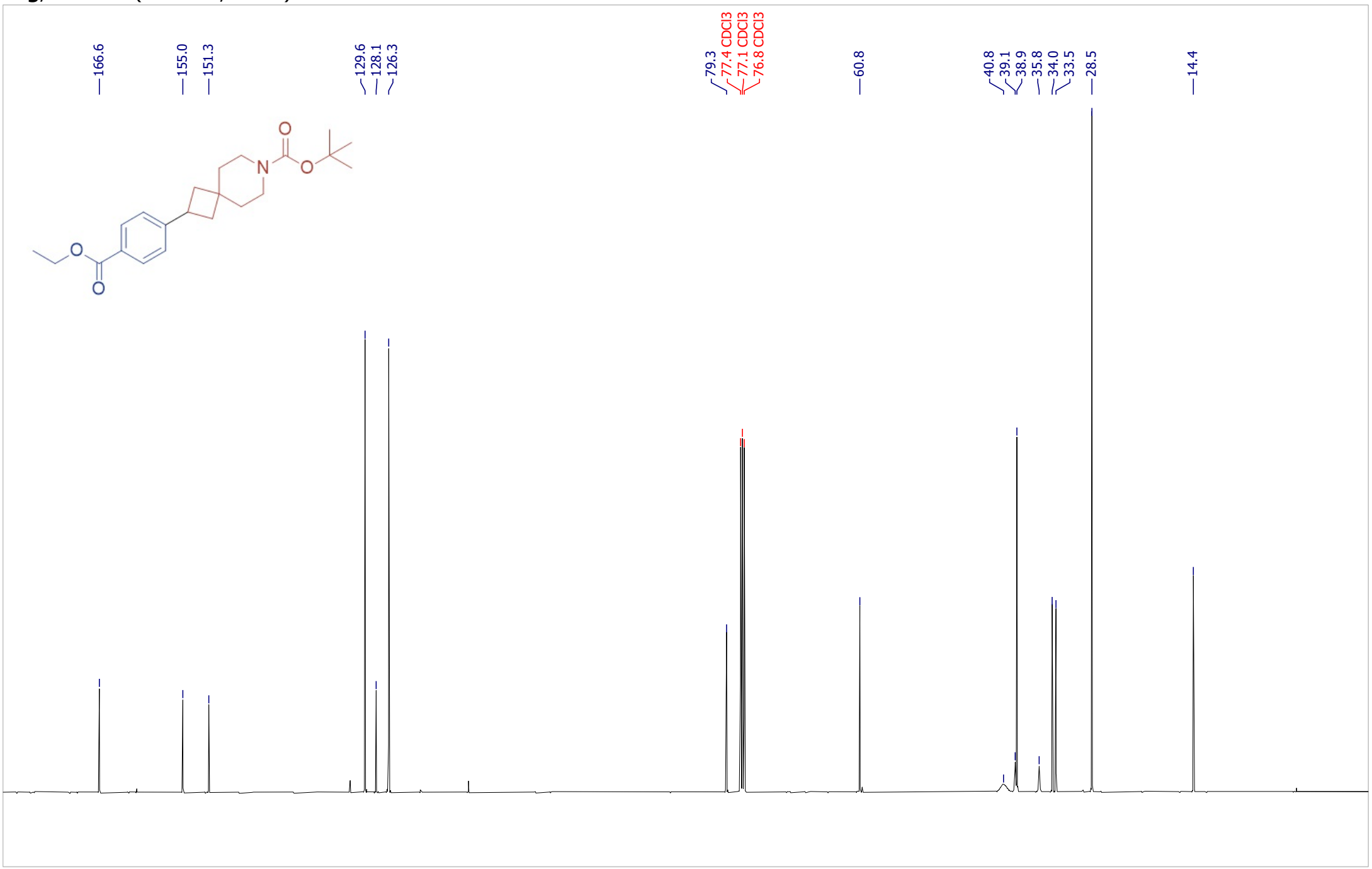
3f, ^{13}C NMR (101 MHz, CDCl3)



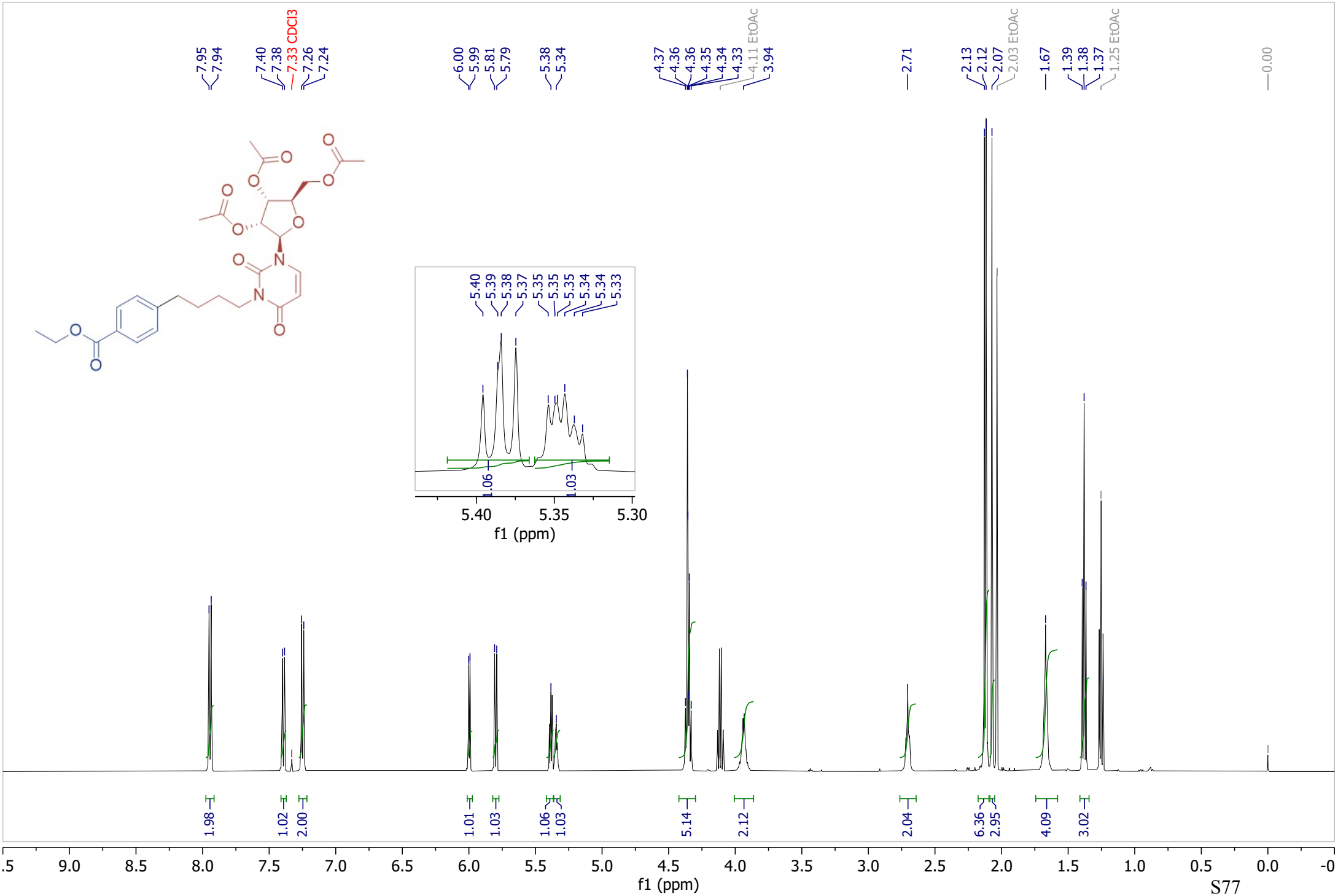
3g, ^{1}H NMR (500 MHz, CDCl3)



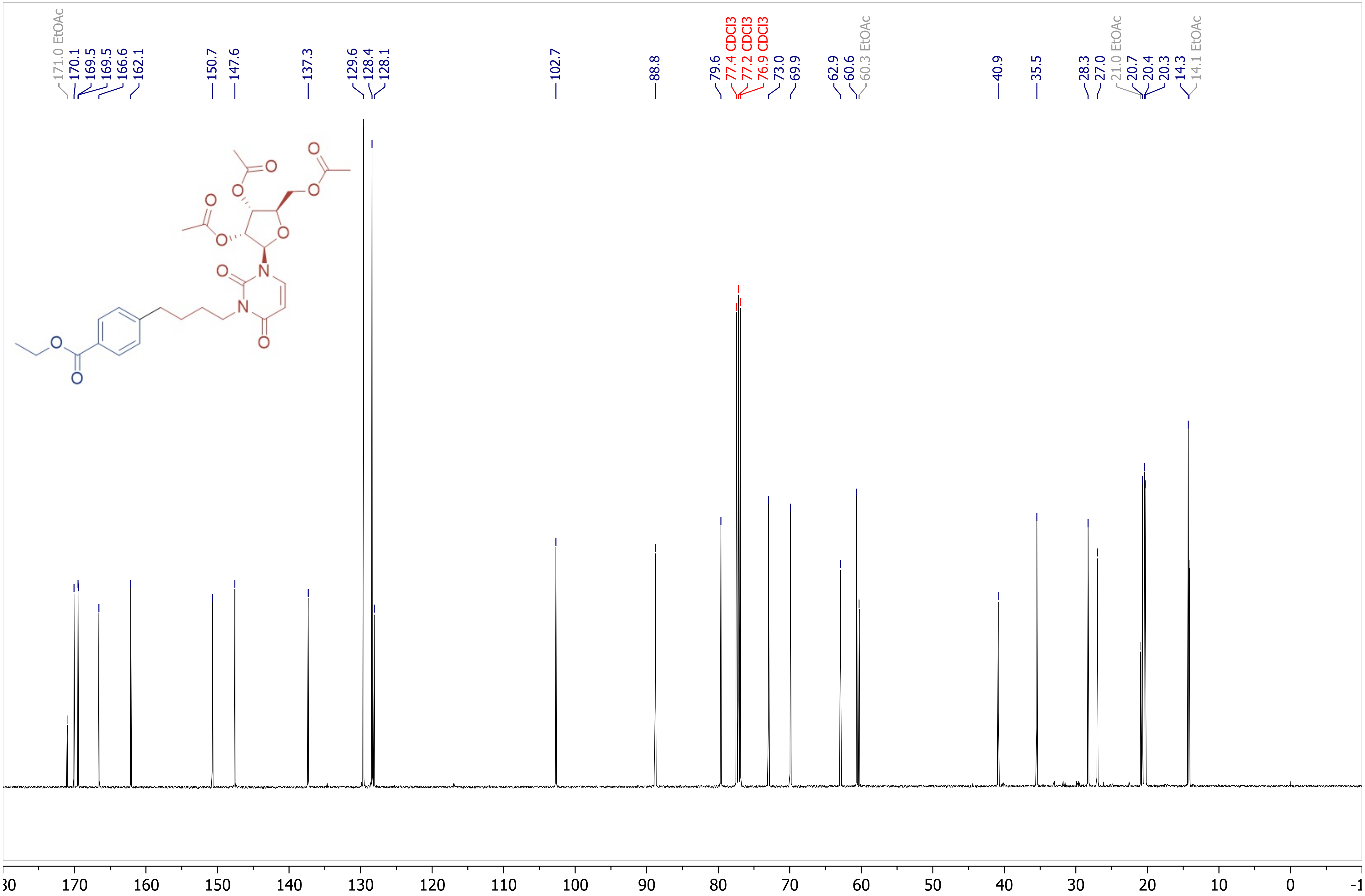
3g, ^{13}C NMR (126 MHz, CDCl3)



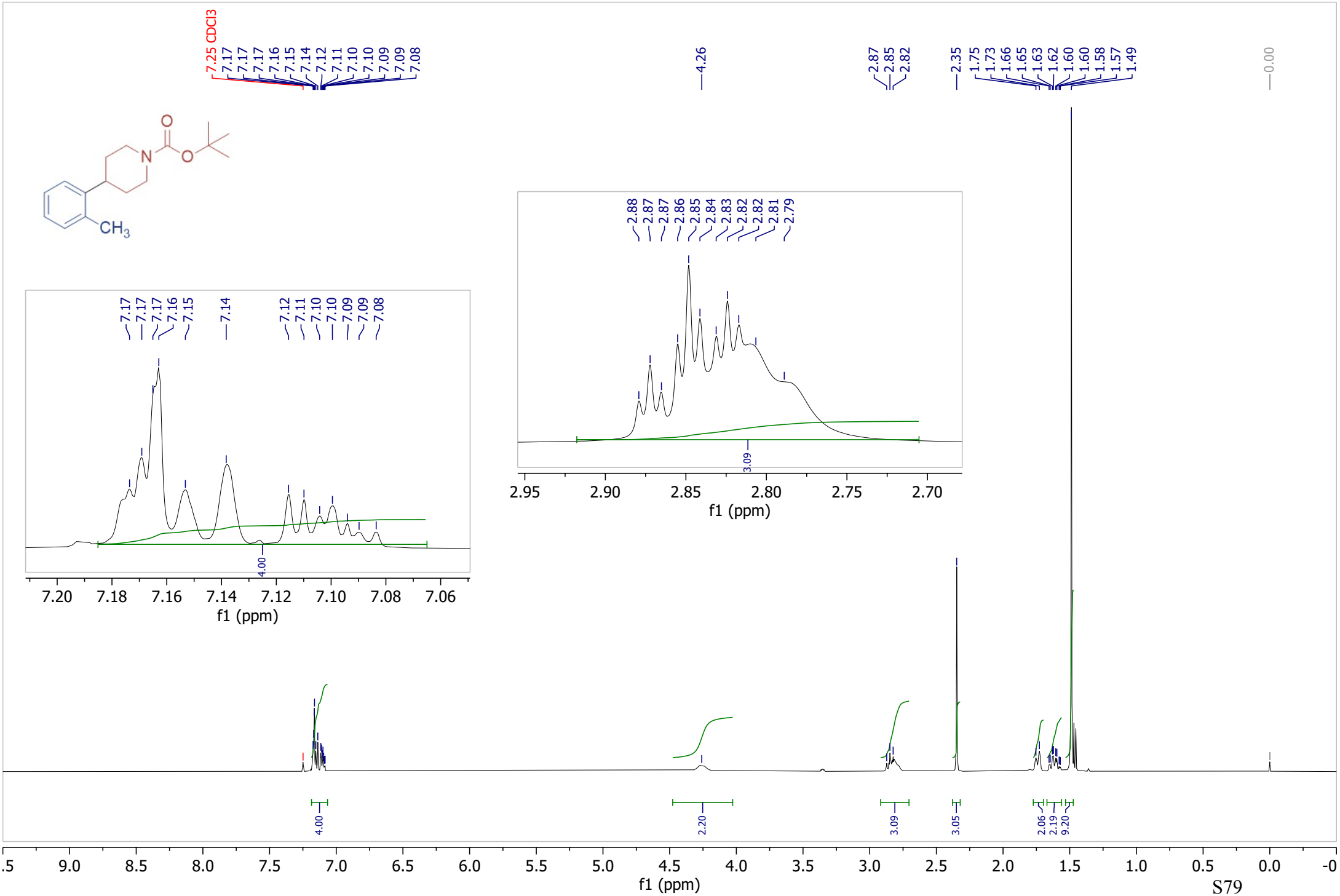
3h, ^{1}H NMR (500 MHz, CDCl3)



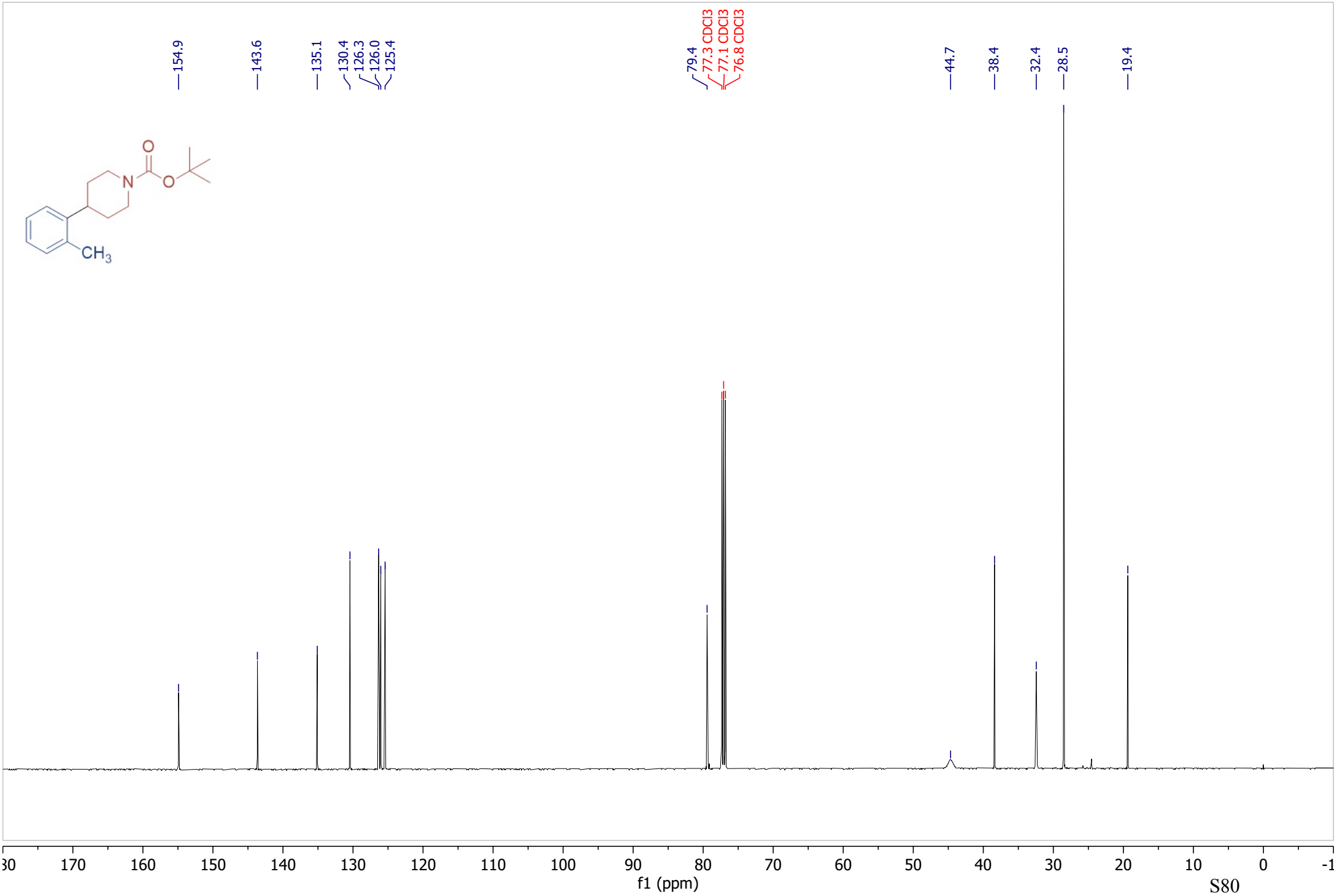
3h, ^{13}C NMR (126 MHz, CDCl3)



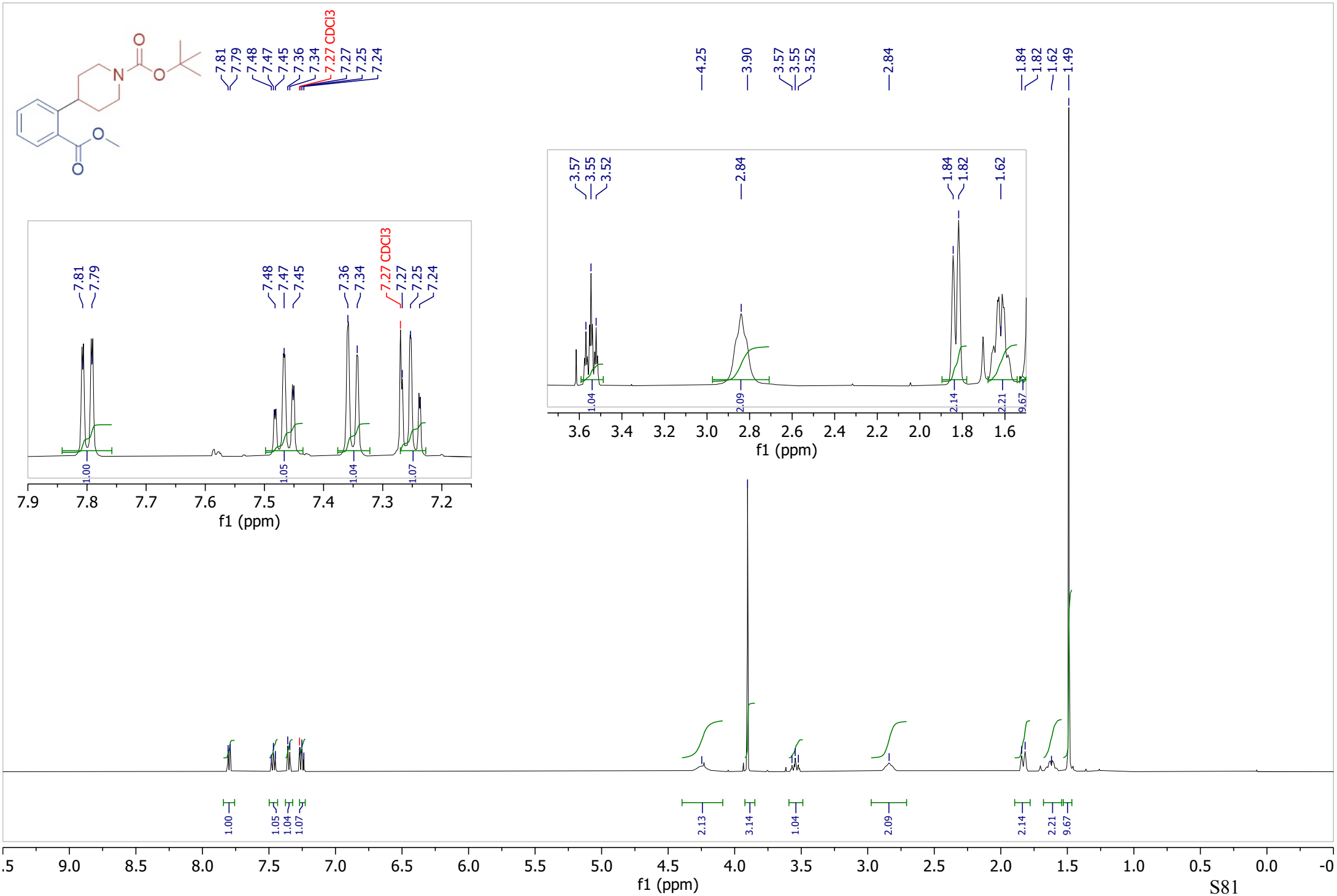
3i, ^{1}H NMR (500 MHz, CDCl3)



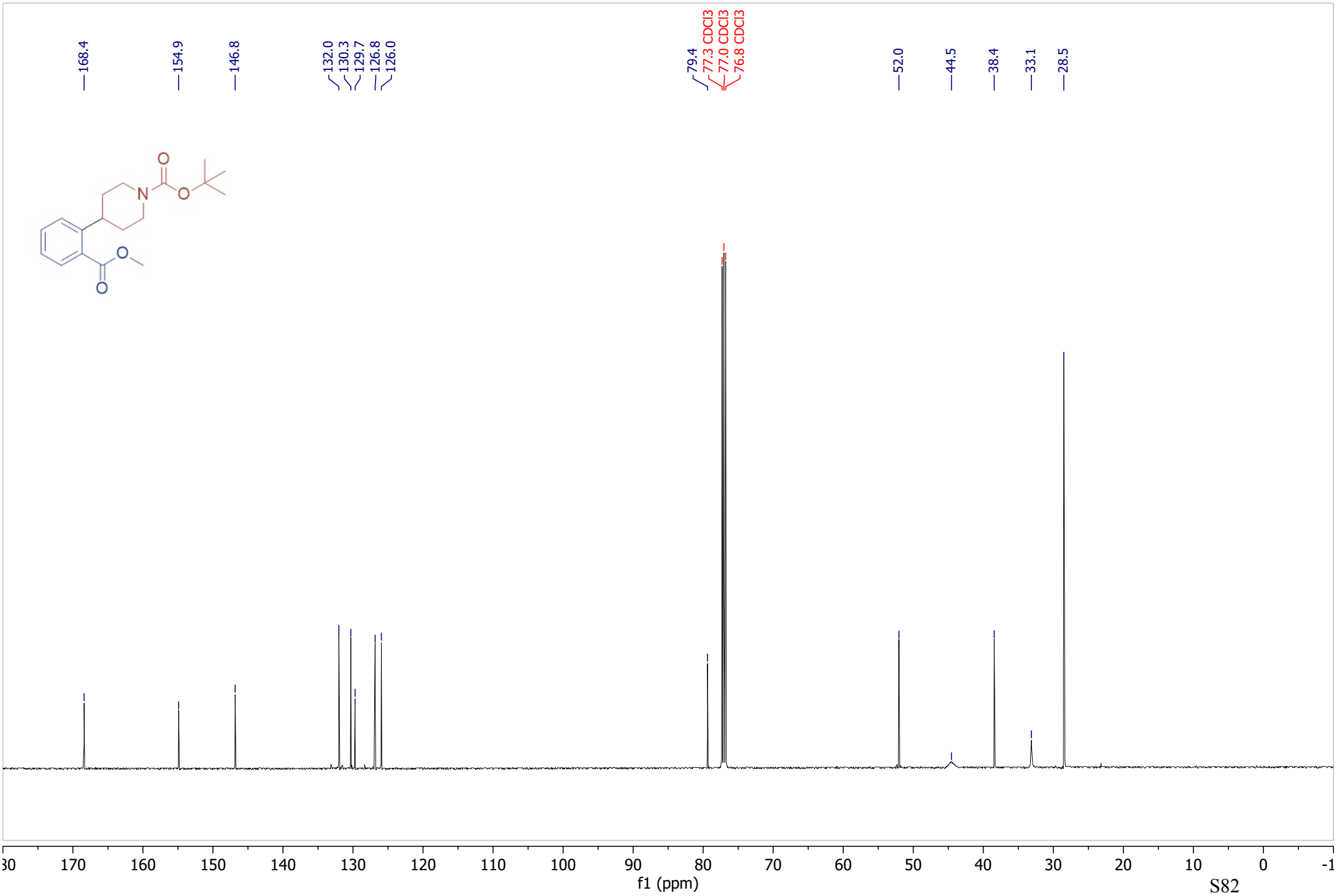
3i, ^{13}C NMR (126 MHz, CDCl3)



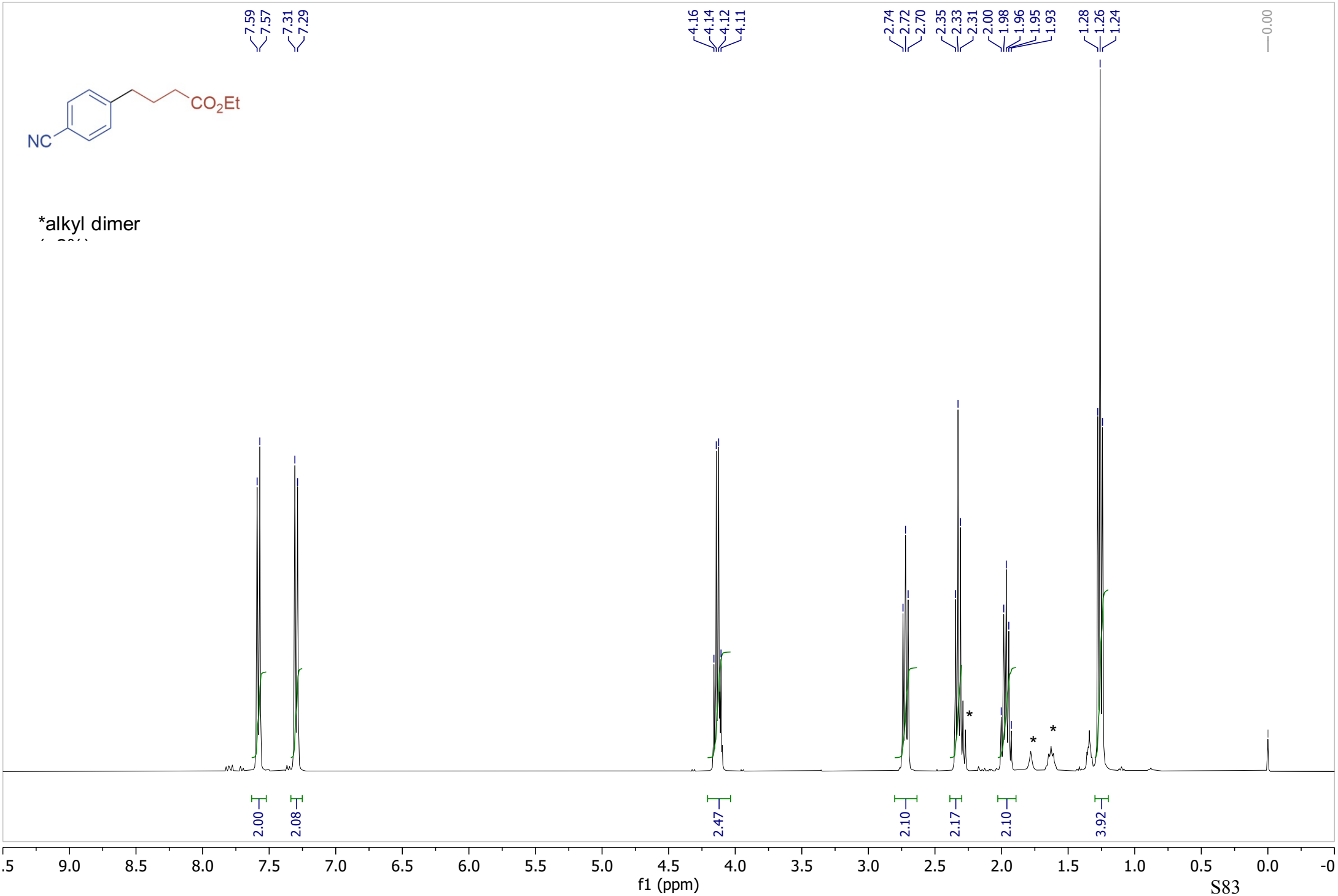
3j, ^{1}H NMR (500 MHz, CDCl3)



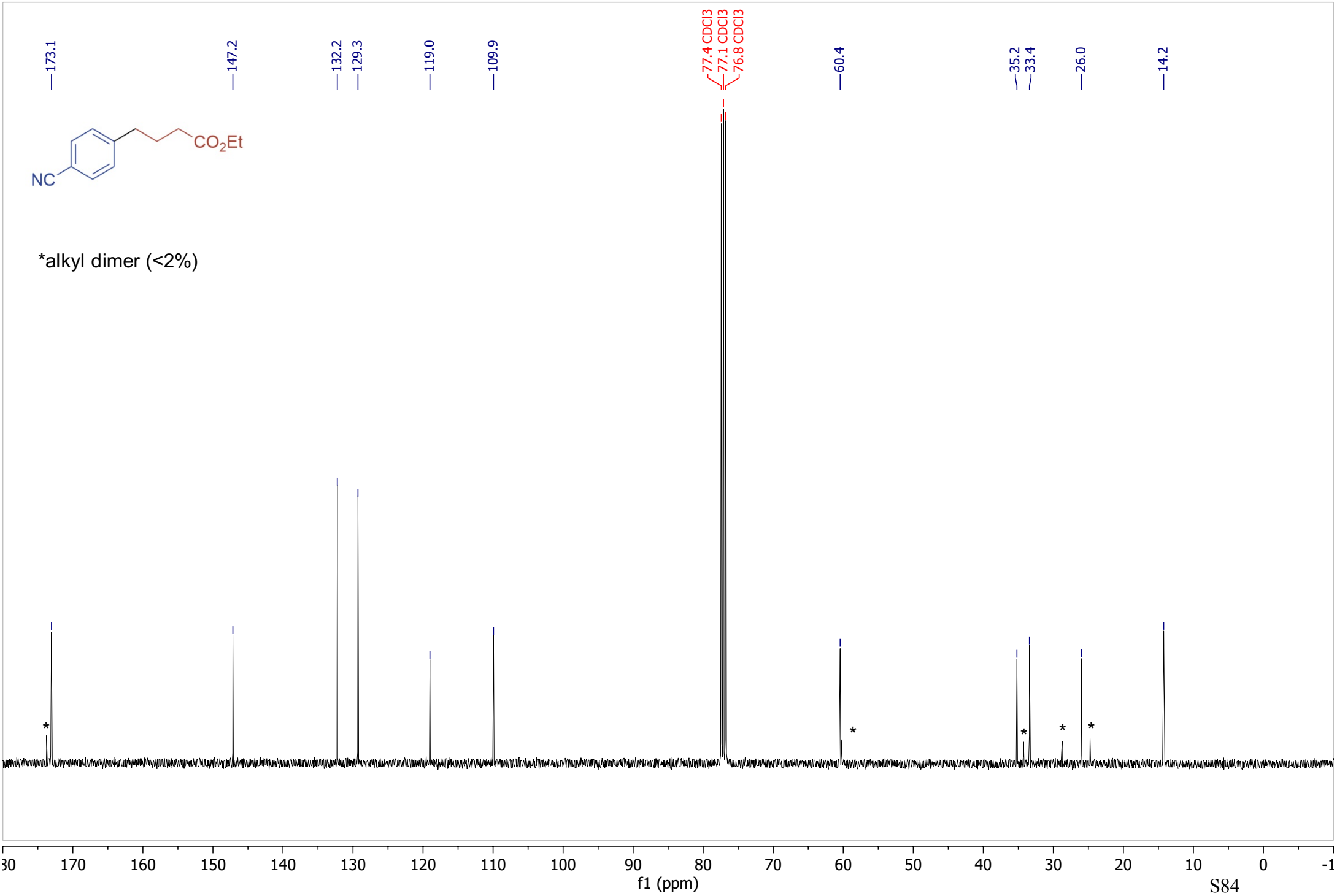
3j, ^{13}C NMR (126 MHz, CDCl3)



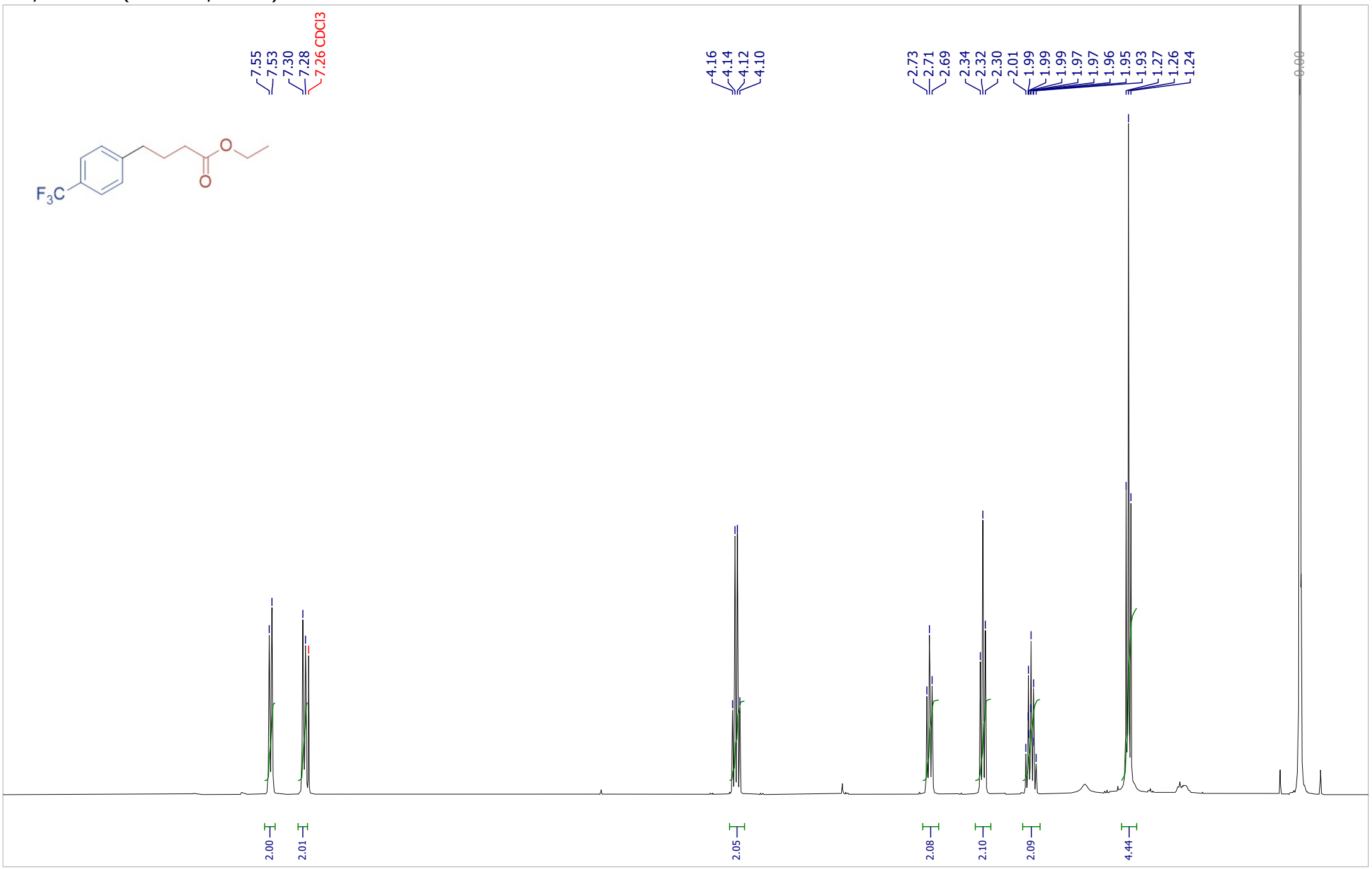
3k, ^{1}H NMR (400 MHz, CDCl3)



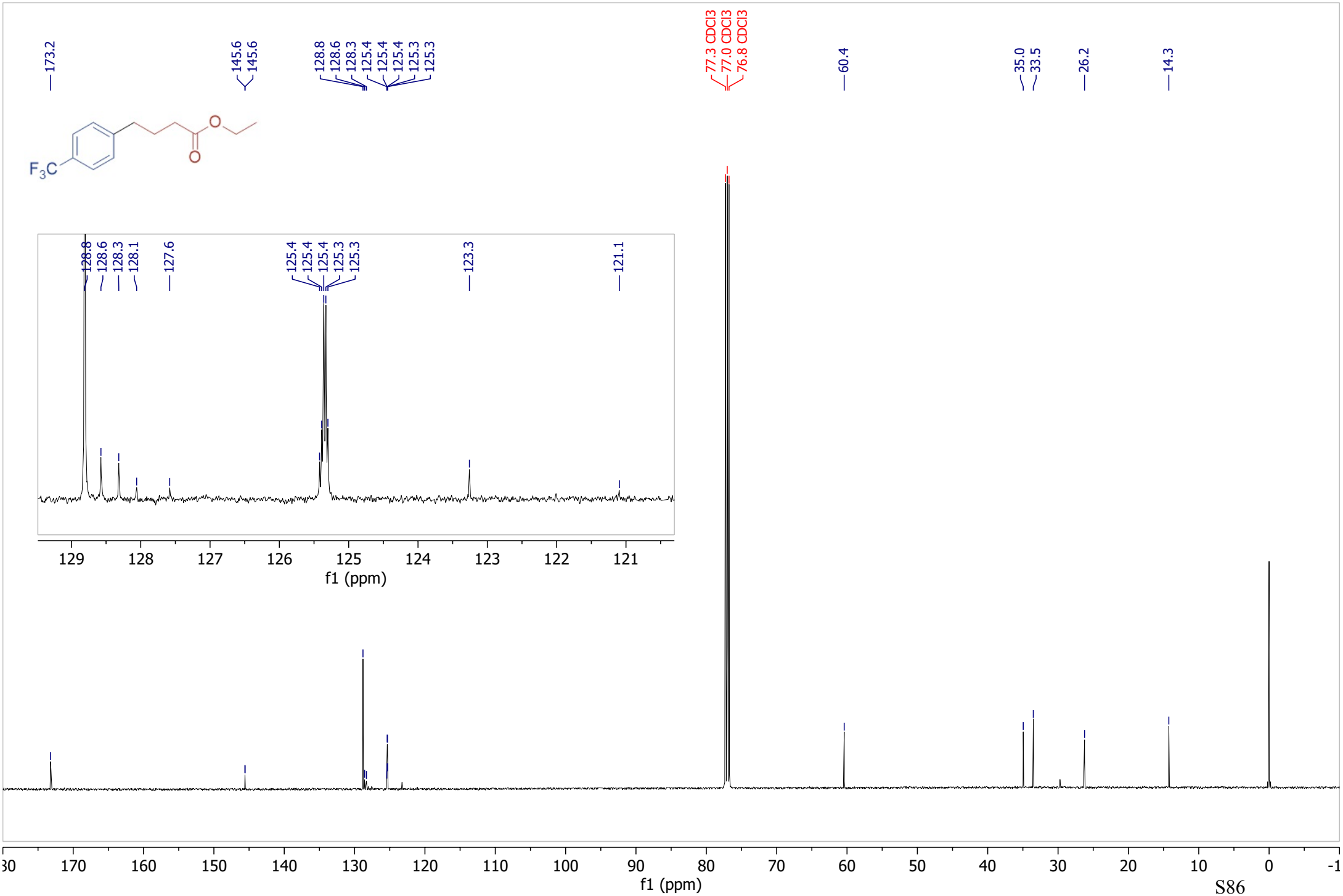
3k, ^{13}C NMR (101 MHz, CDCl3)



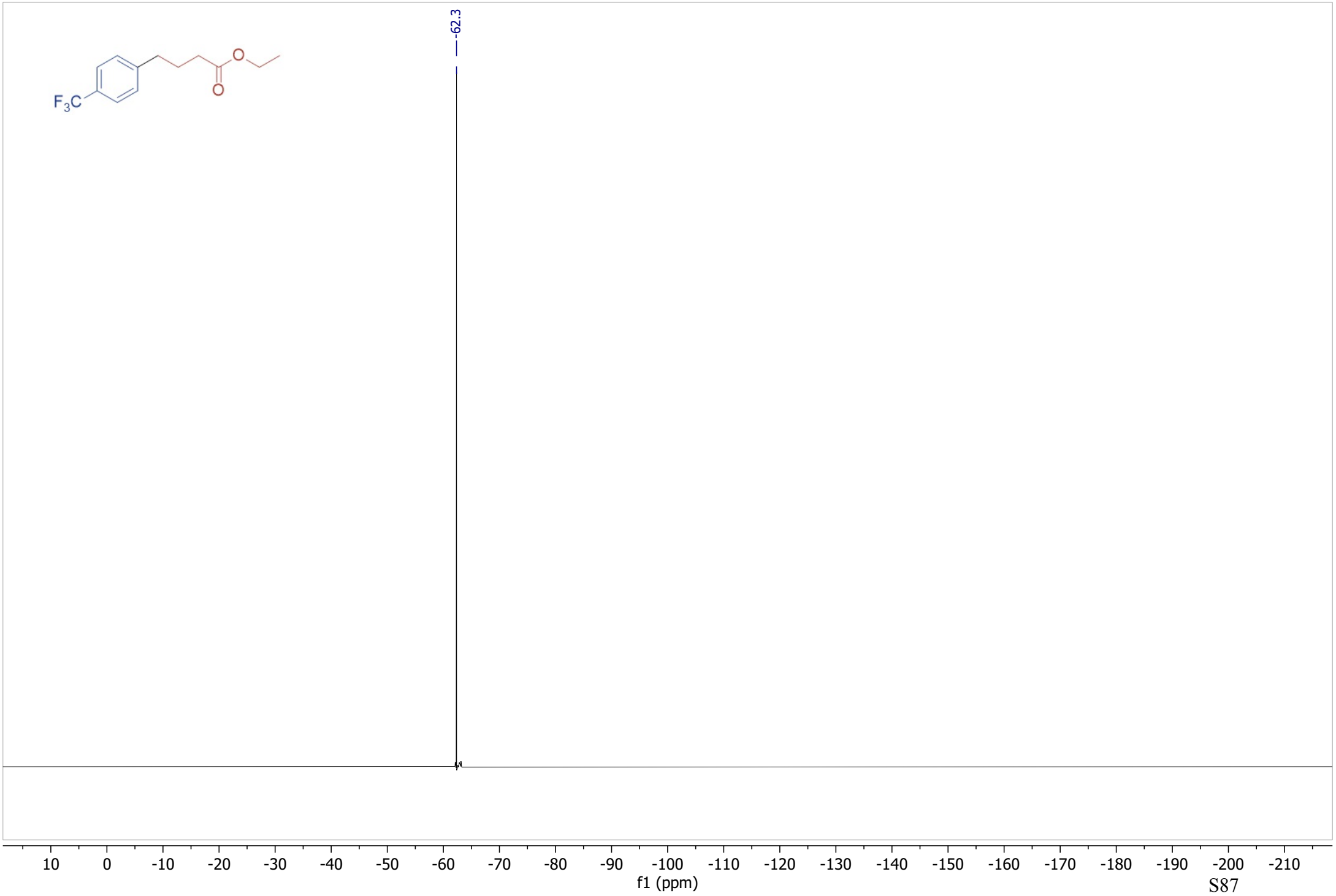
3l, ^{1}H NMR (400 MHz, CDCl3)



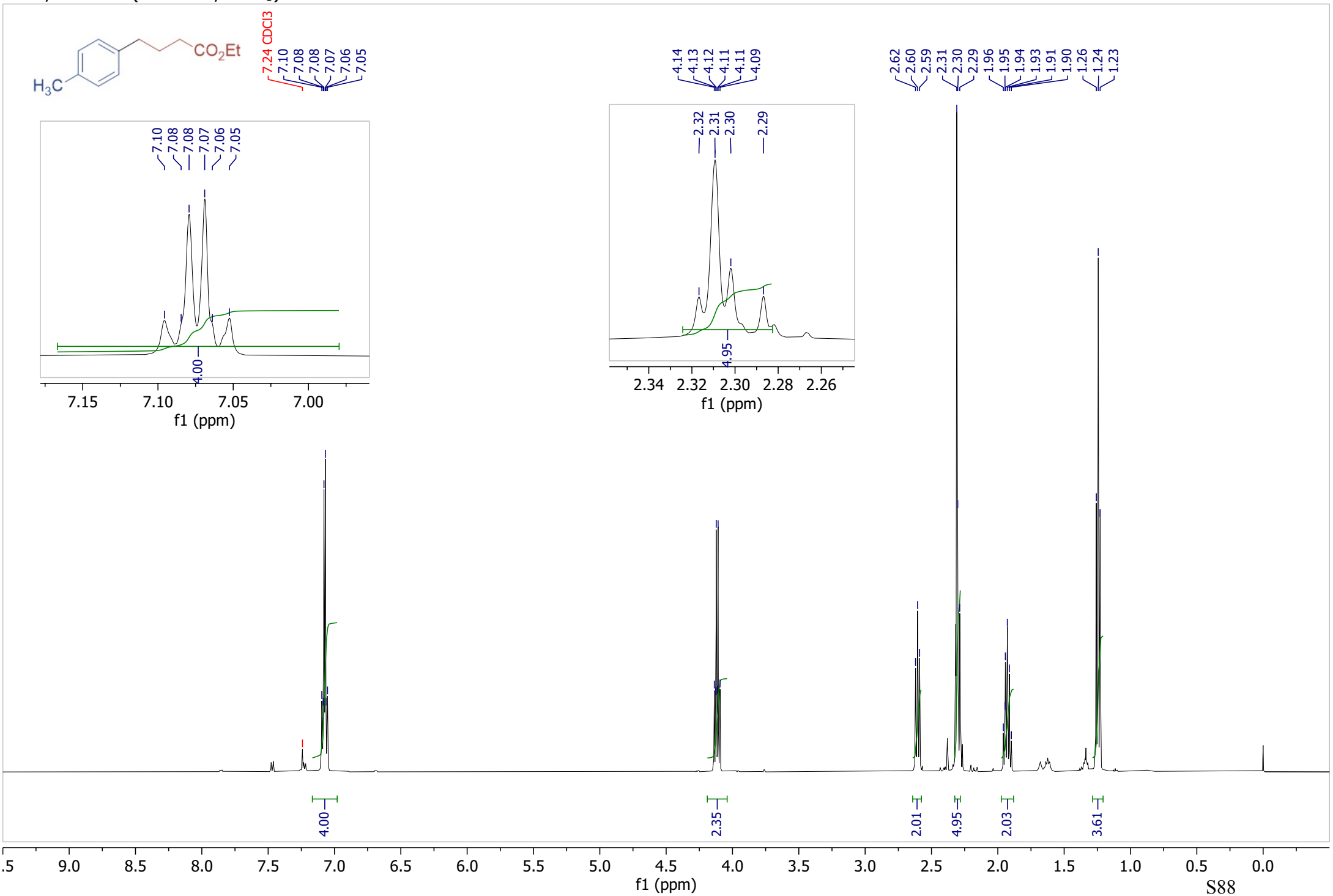
3l, ^{13}C NMR (126 MHz, CDCl3)



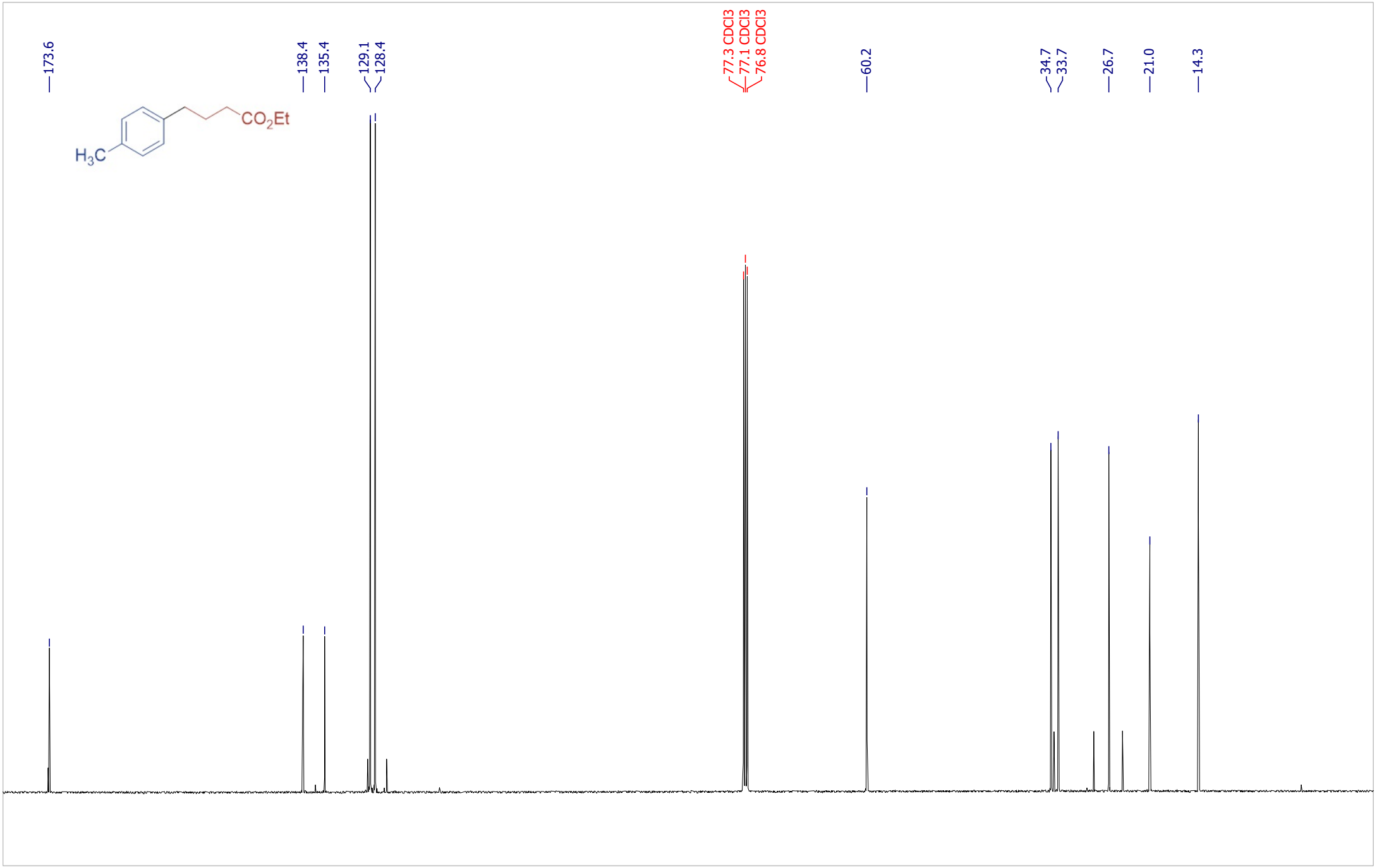
3l, ^{19}F NMR (126 MHz, CDCl3)



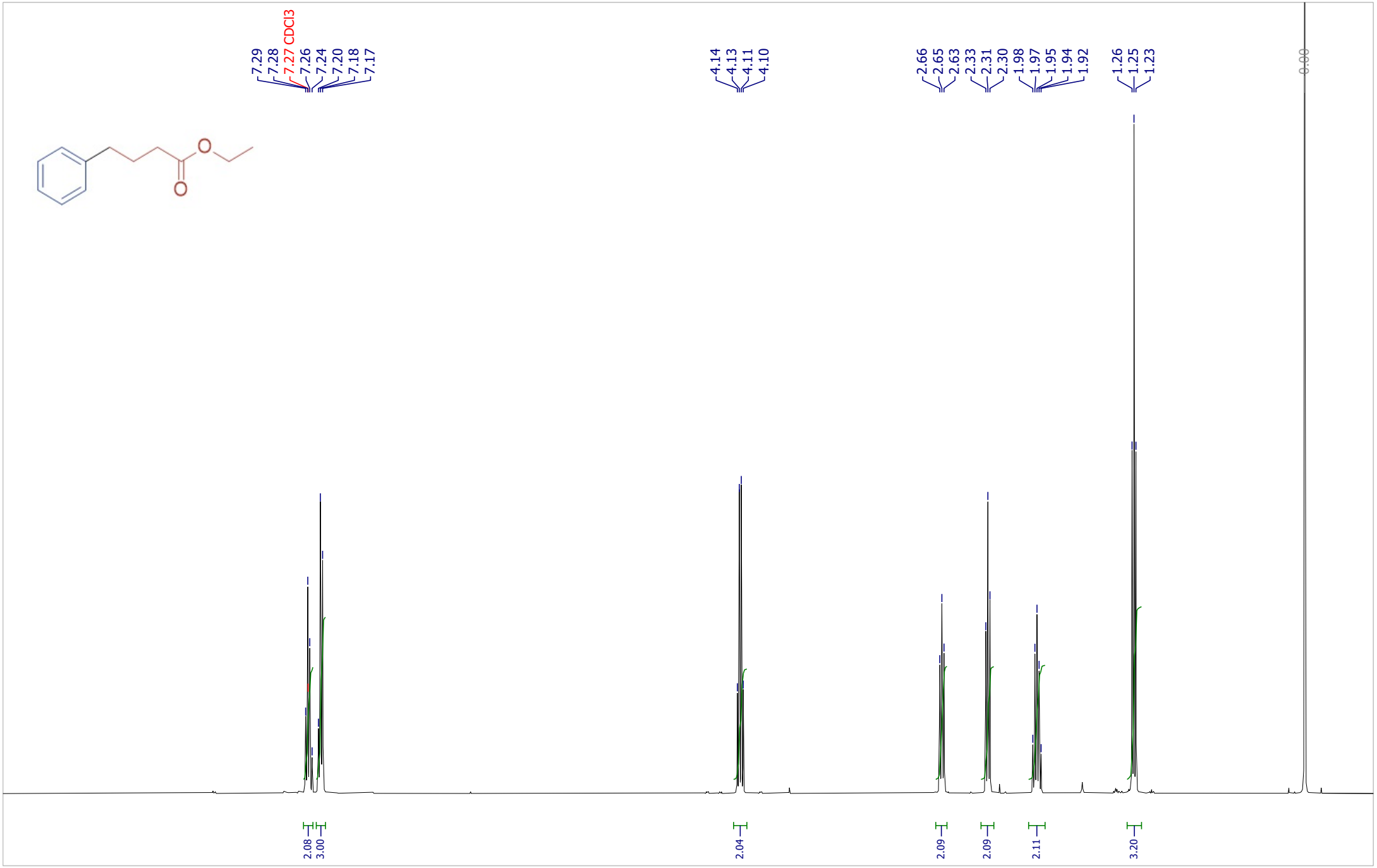
3m, ^{1}H NMR (500 MHz, $CDCl_3$)



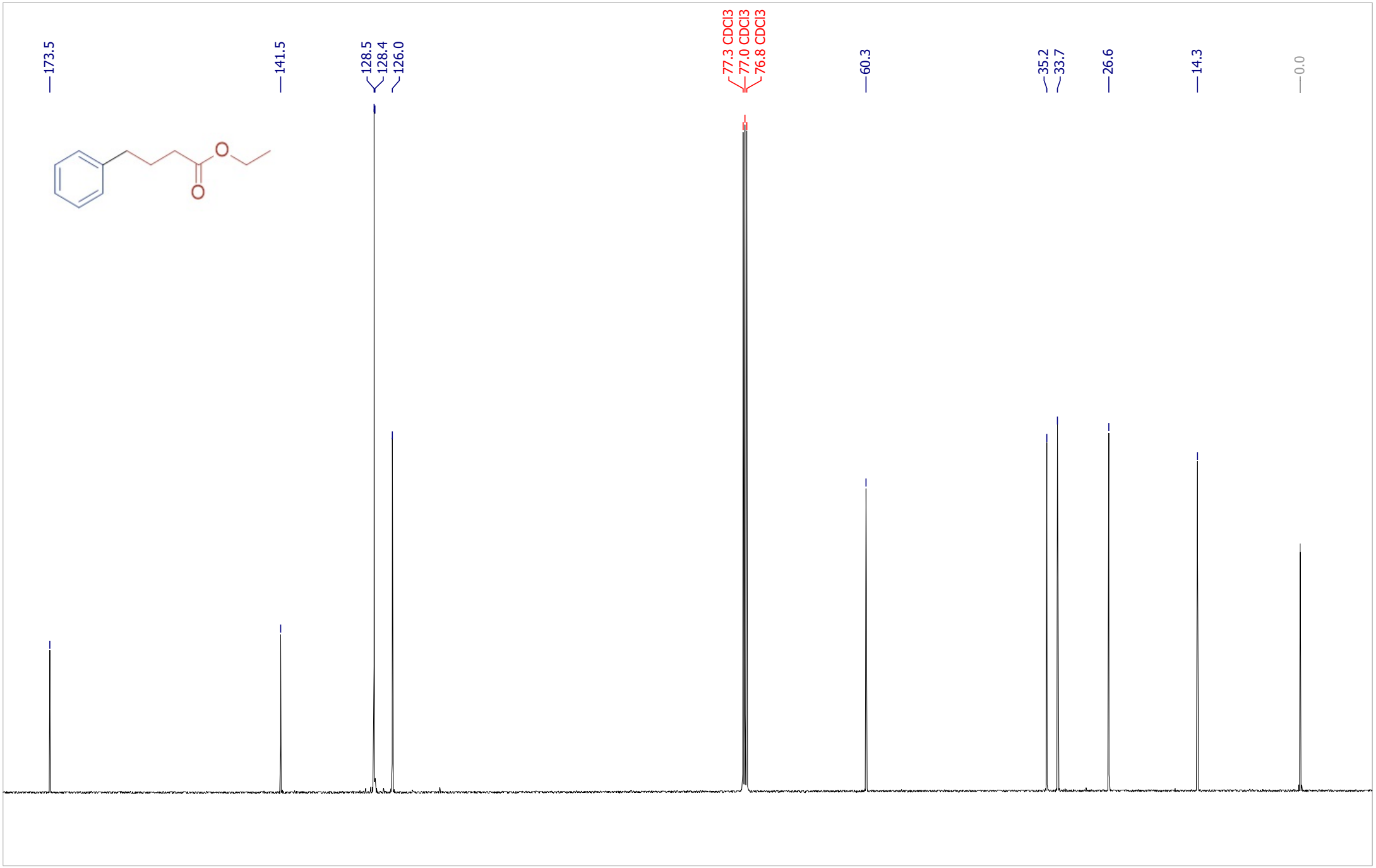
3m, ^{13}C NMR (126 MHz, $CDCl_3$)



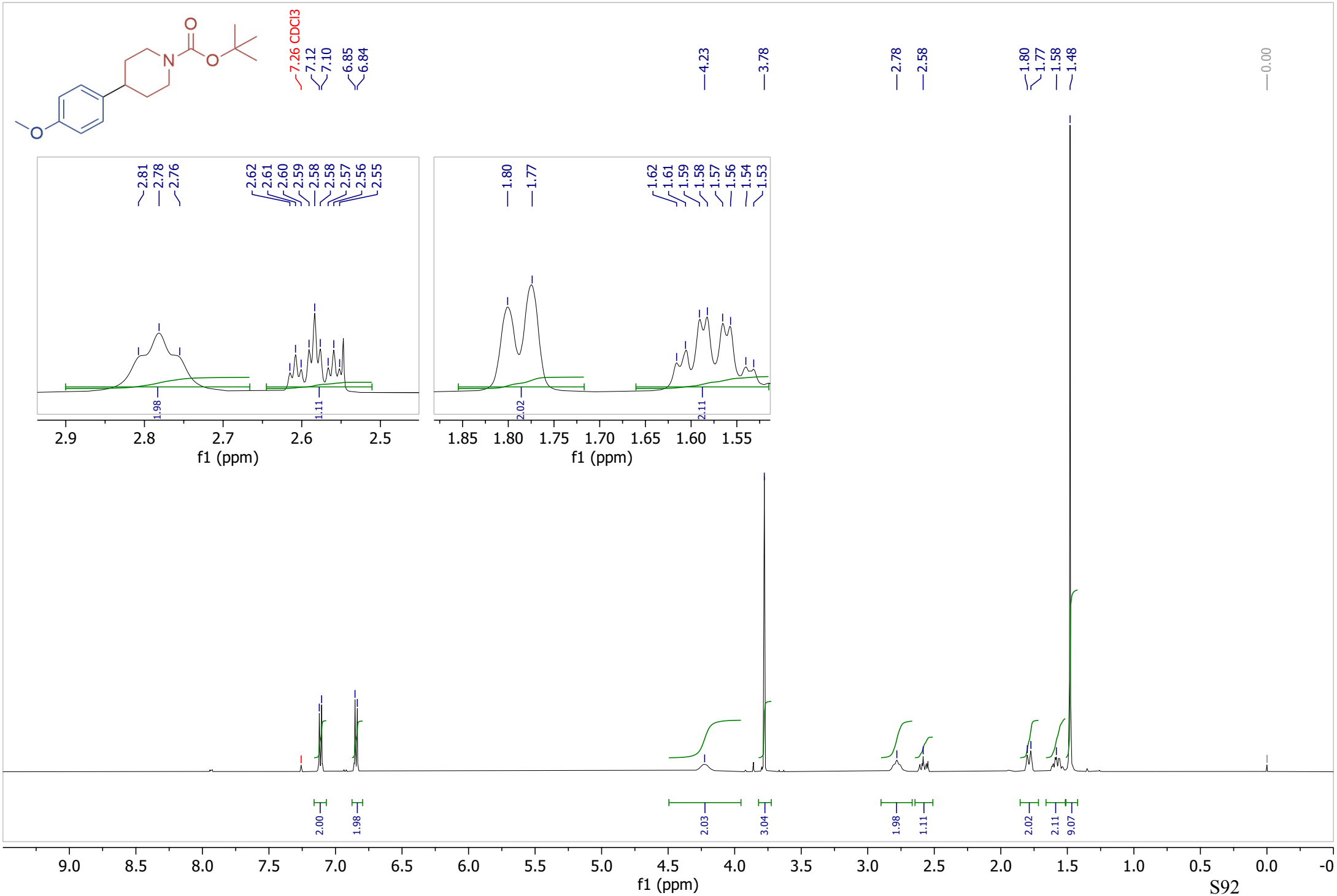
3n, ^{1}H NMR (500 MHz, $CDCl_3$)



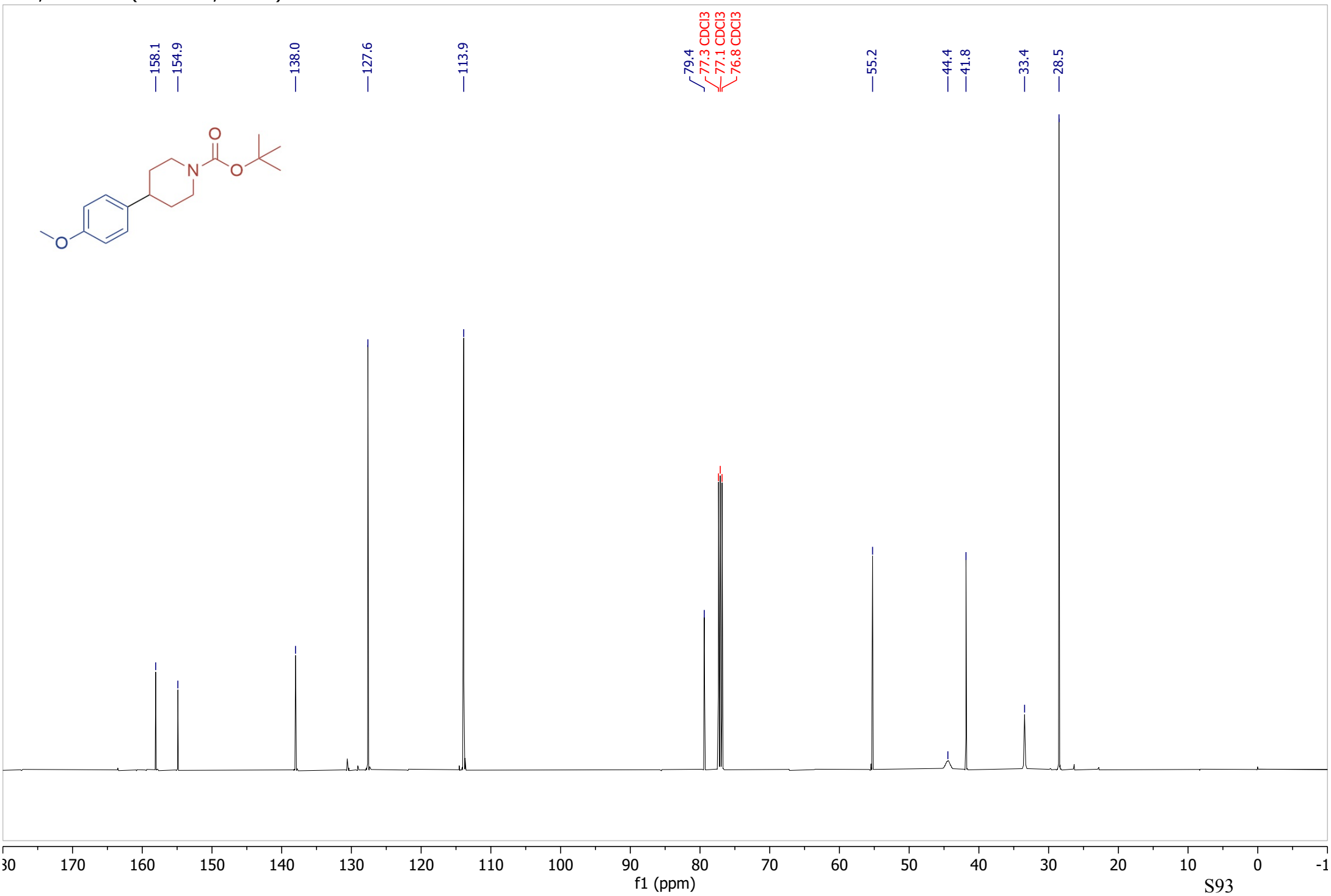
3n, ^{13}C NMR (126 MHz, CDCl3)



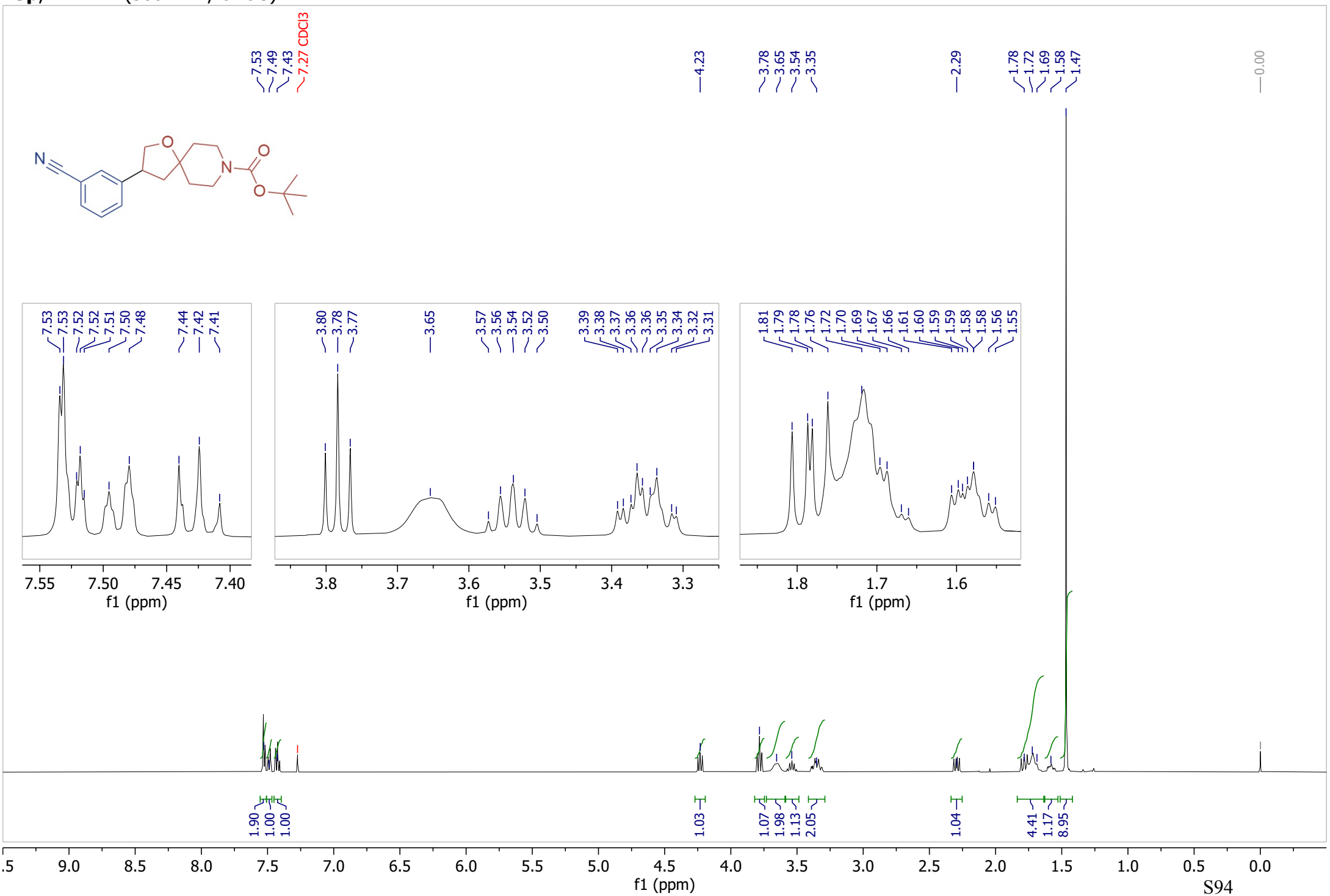
3o, ^{1}H NMR (500 MHz, $CDCl_3$)



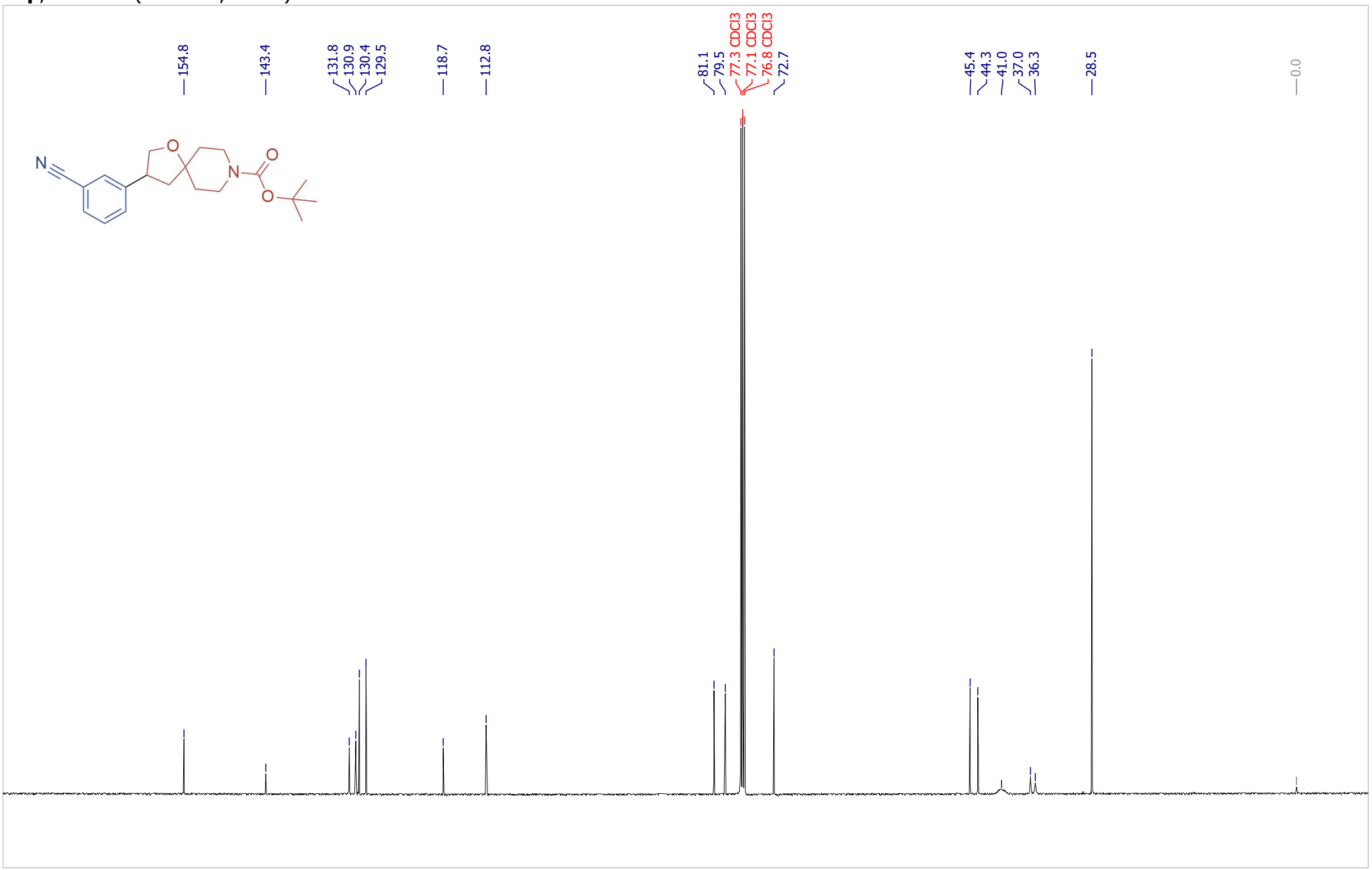
3o, ^{13}C NMR (126 MHz, CDCl3)



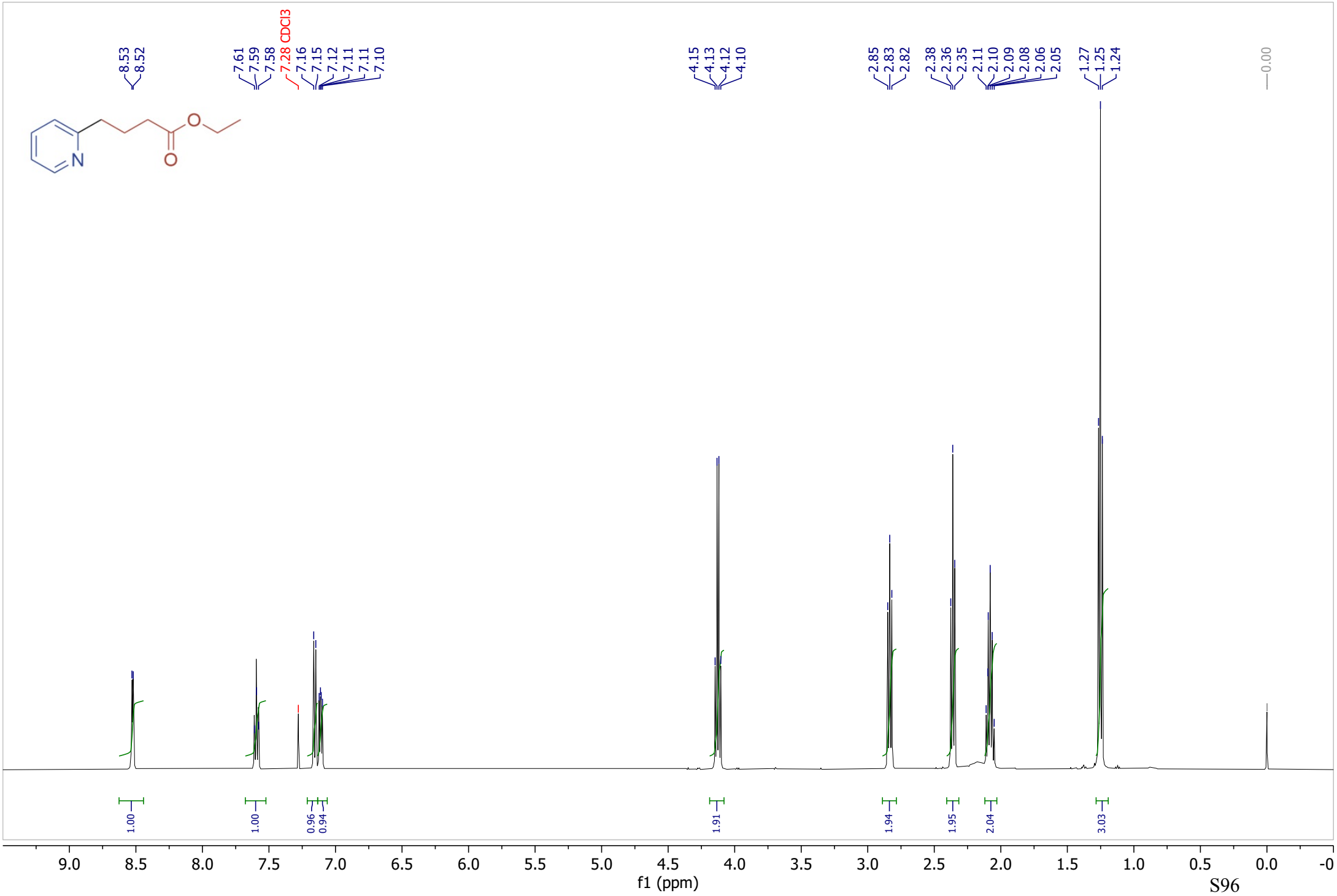
3p, ^{1}H NMR (500 MHz, CDCl3)



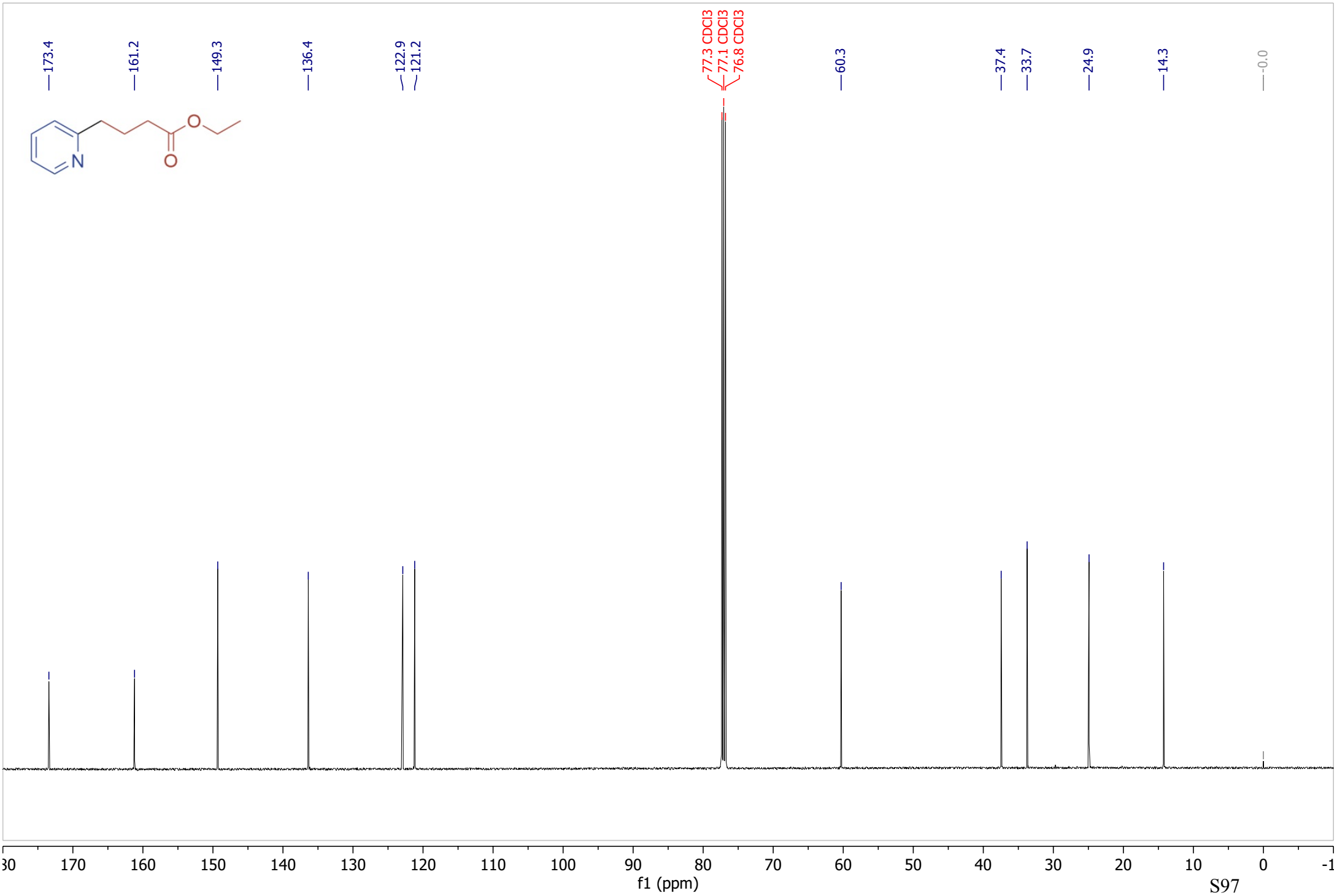
3p, ^{13}C NMR (126 MHz, CDCl3)



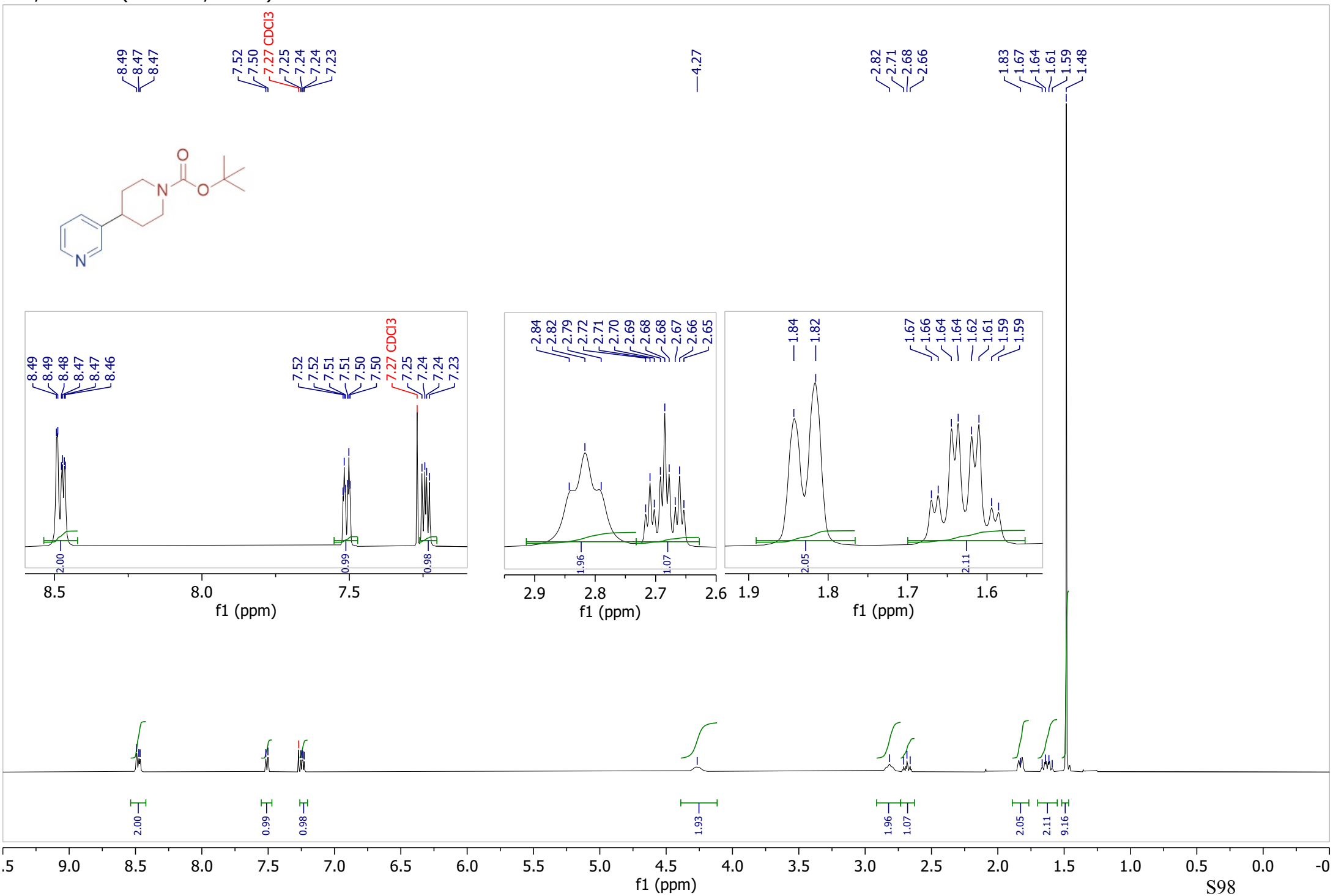
3q, ^{1}H NMR (500 MHz, CDCl3)



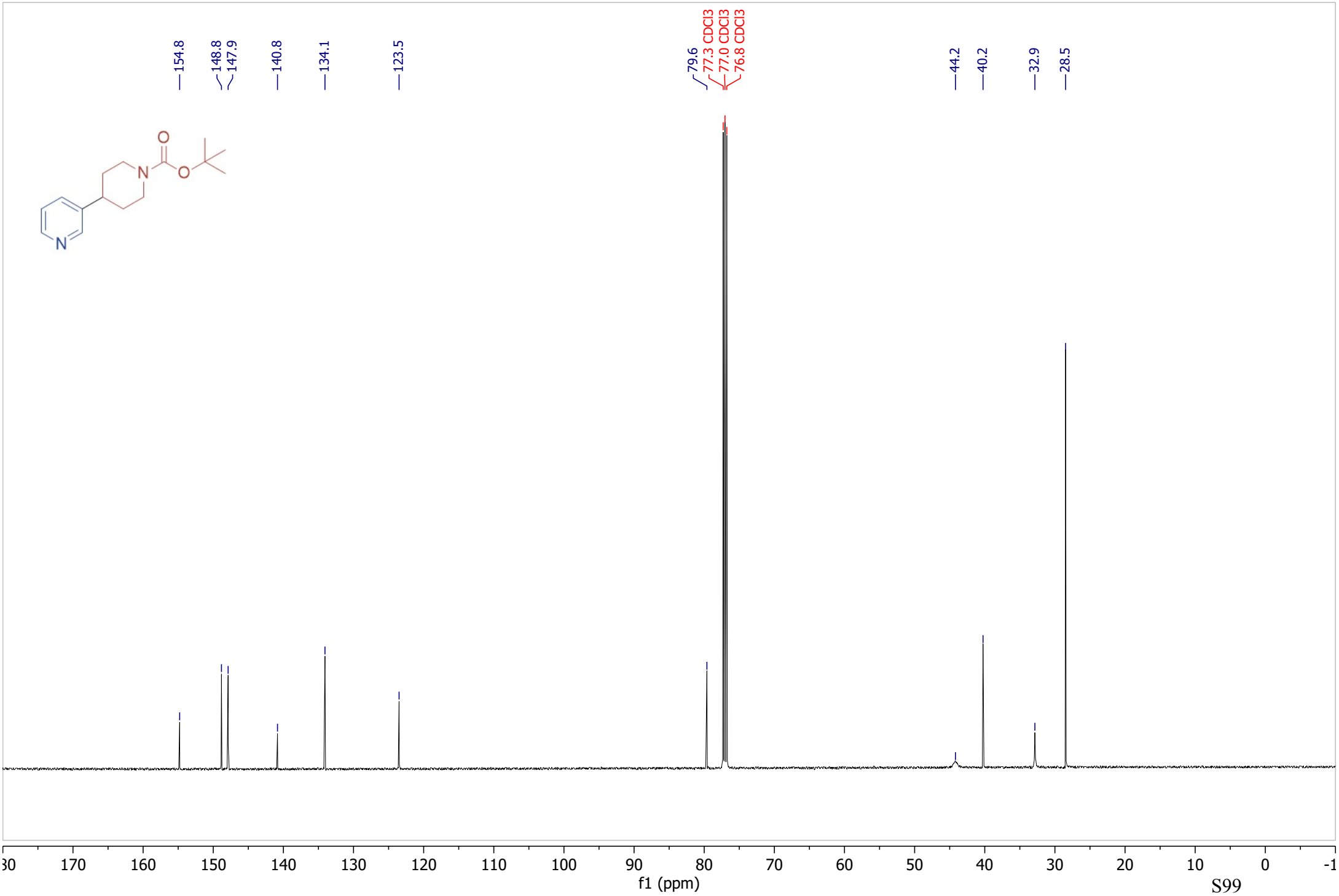
3q, ^{13}C NMR (126 MHz, CDCl3)



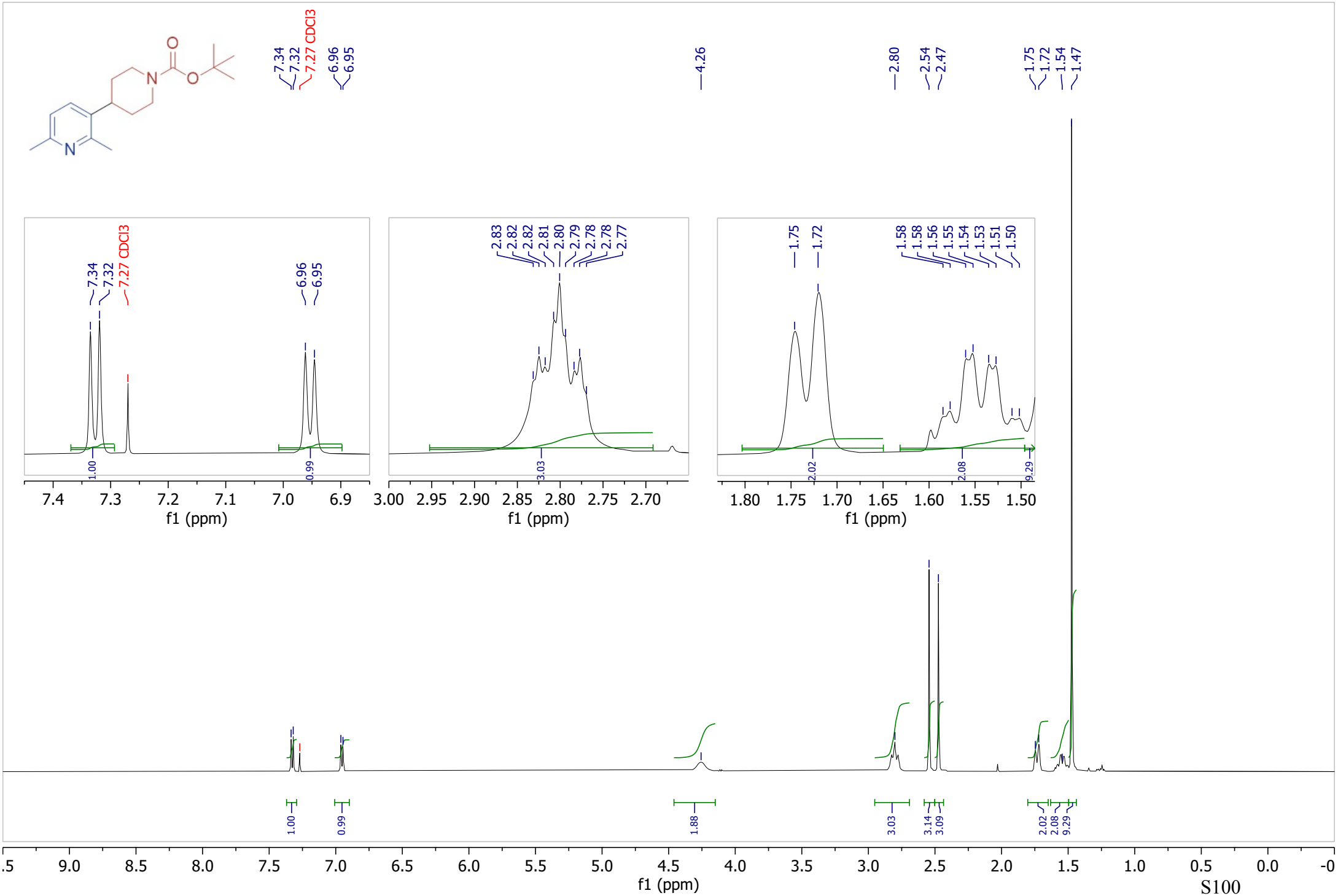
3r, ^{1}H NMR (500 MHz, CDCl3)



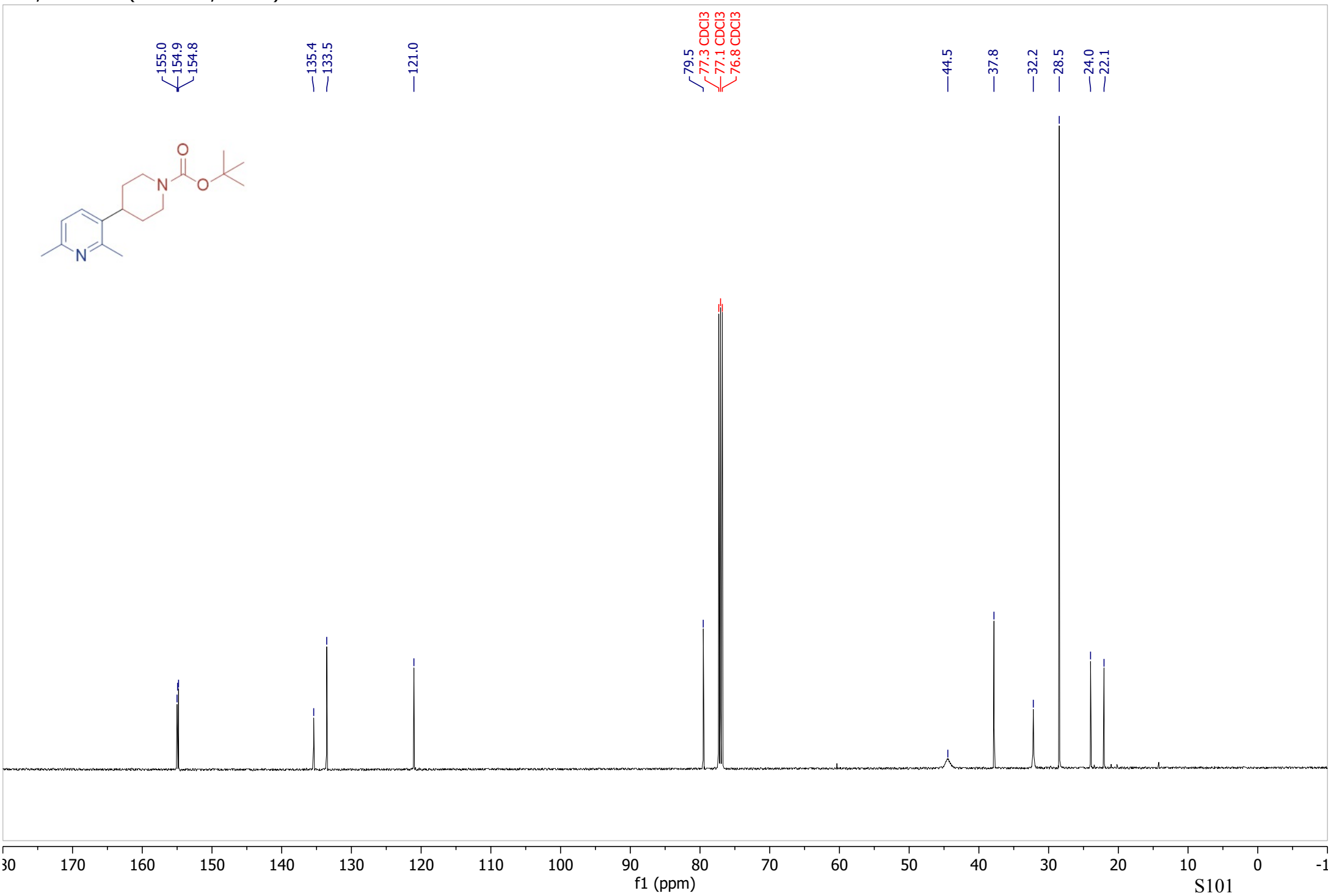
3r, ^{13}C NMR (126 MHz, CDCl3)



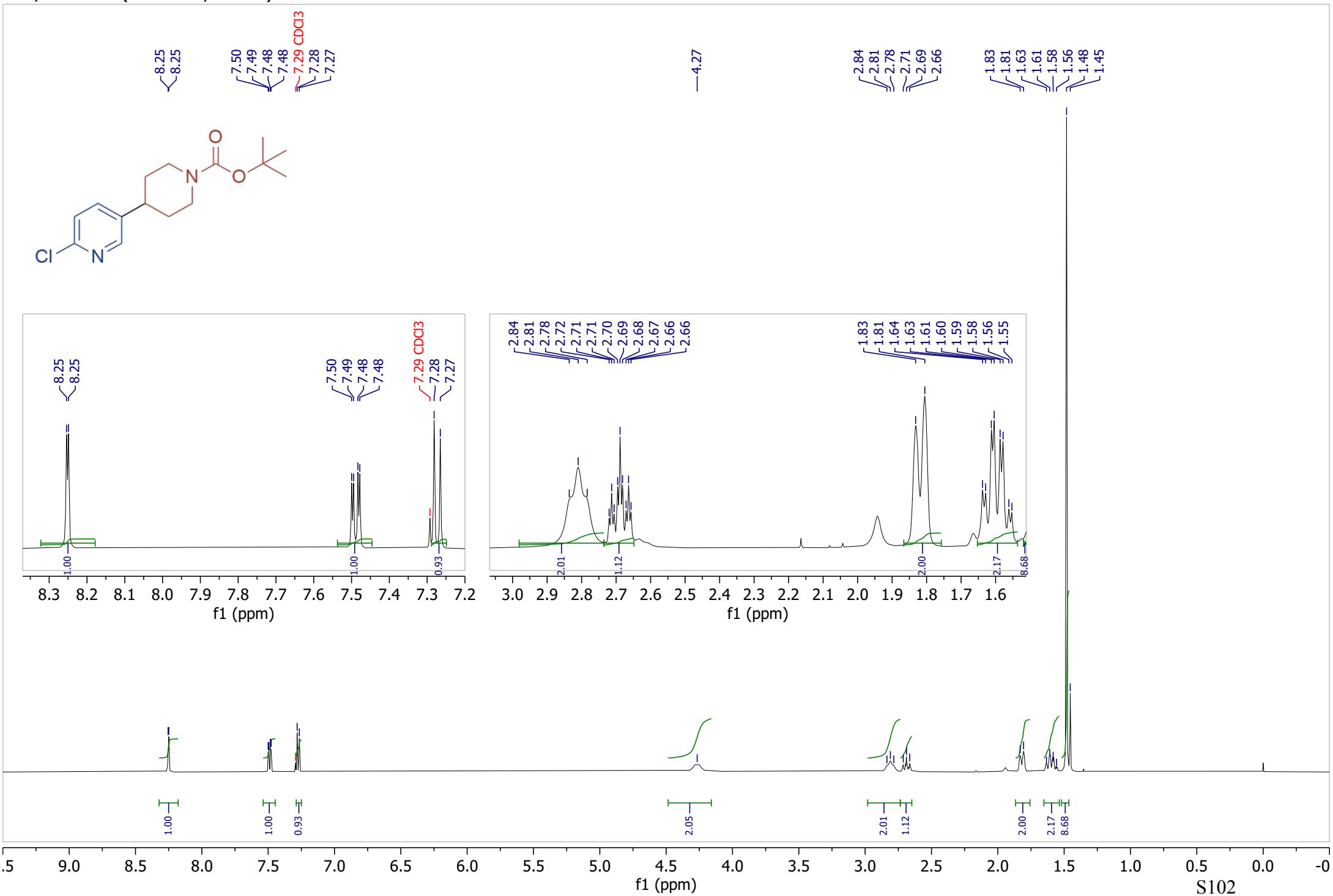
3s, ^{1}H NMR (500 MHz, CDCl3)



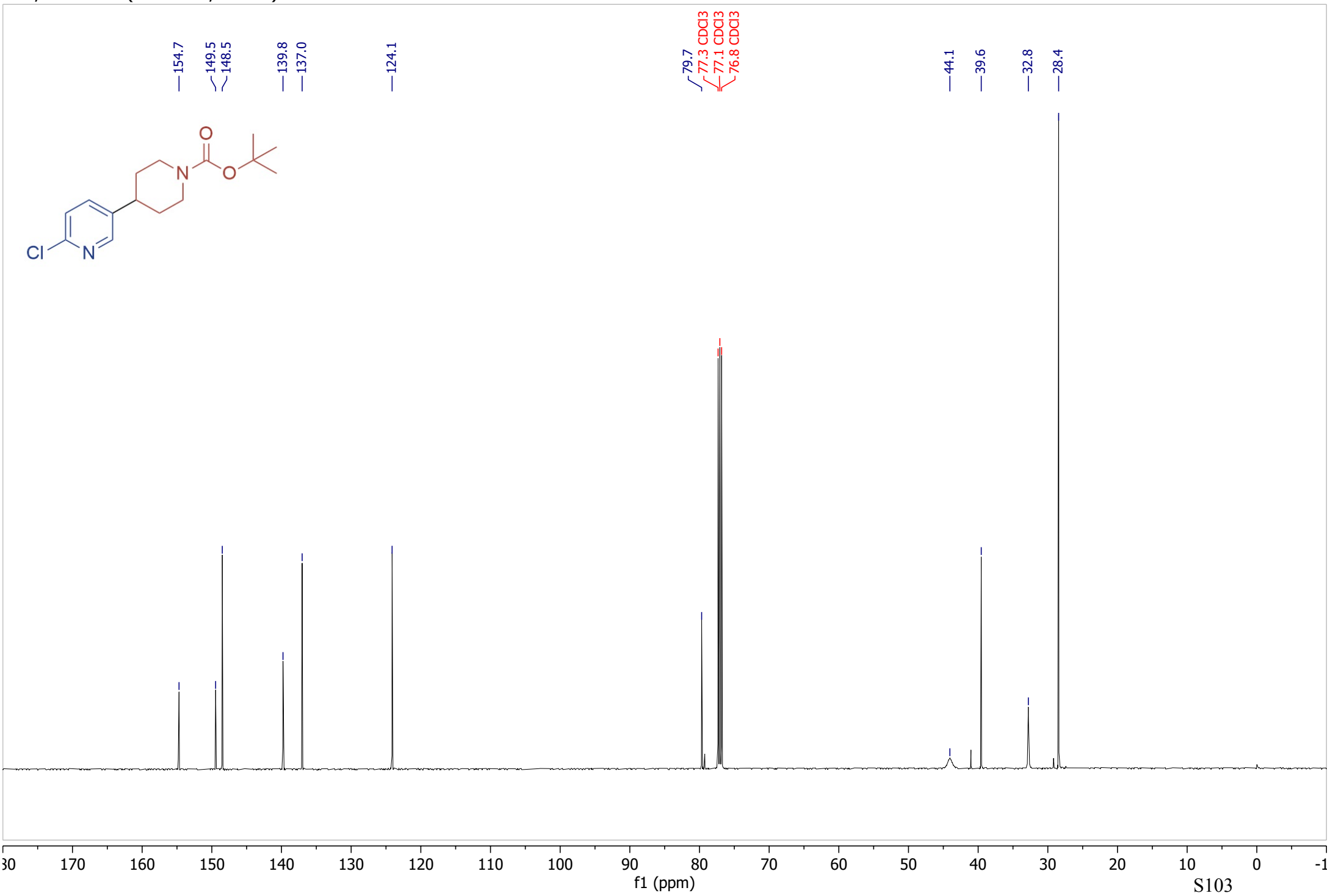
3s, ^{13}C NMR (126 MHz, CDCl3)



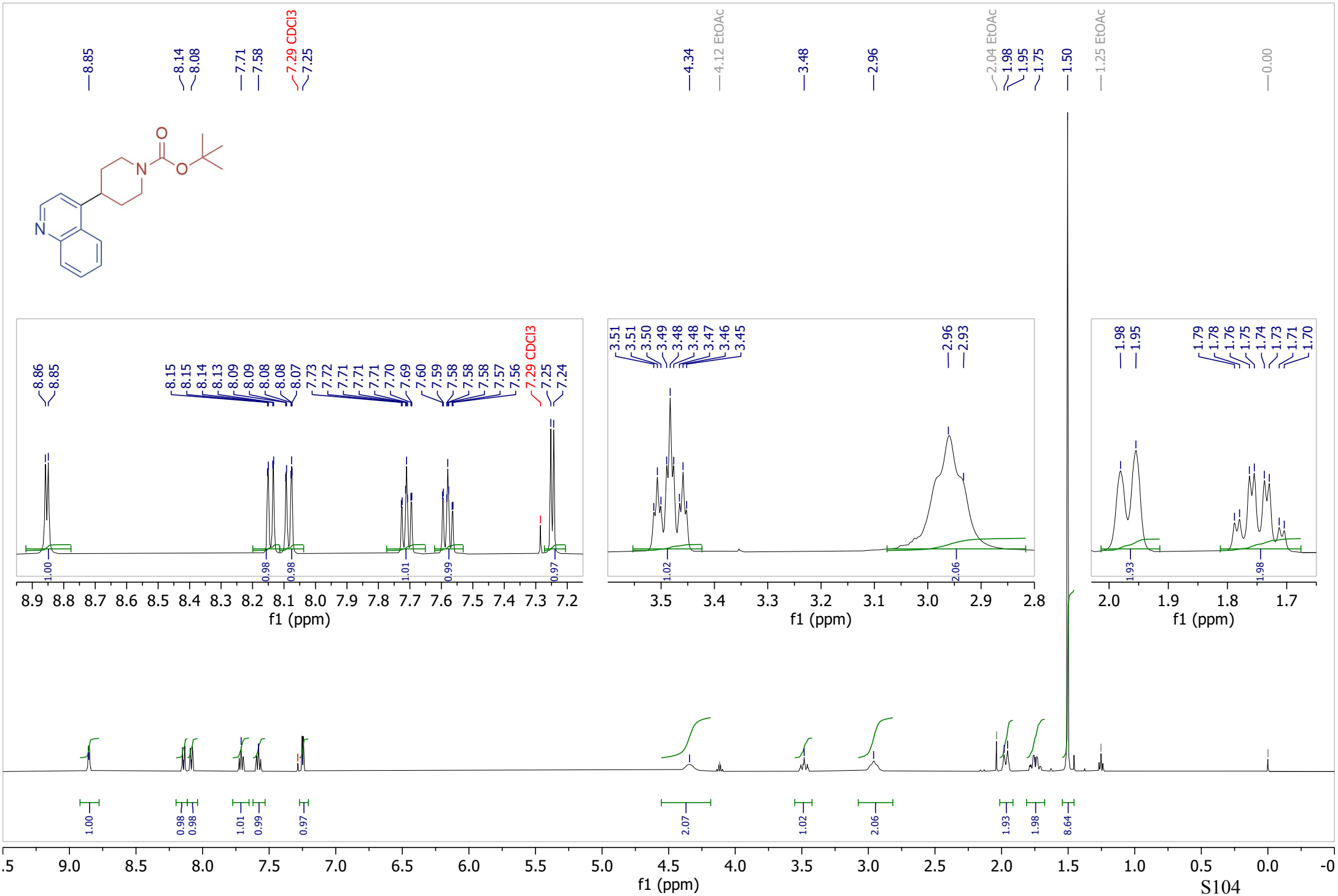
3t, ^{1}H NMR (500 MHz, CDCl3)



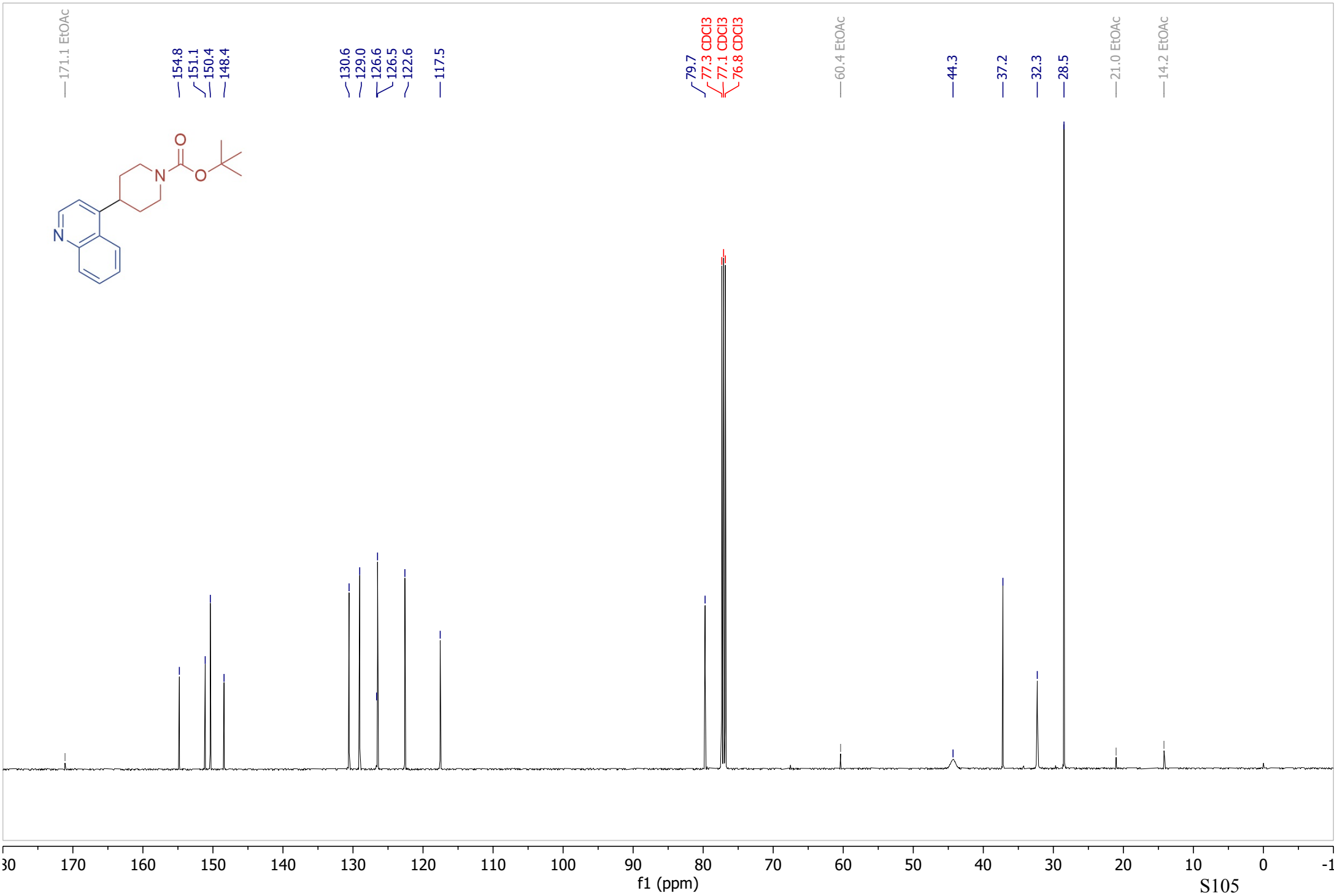
3t, ^{13}C NMR (126 MHz, CDCl3)



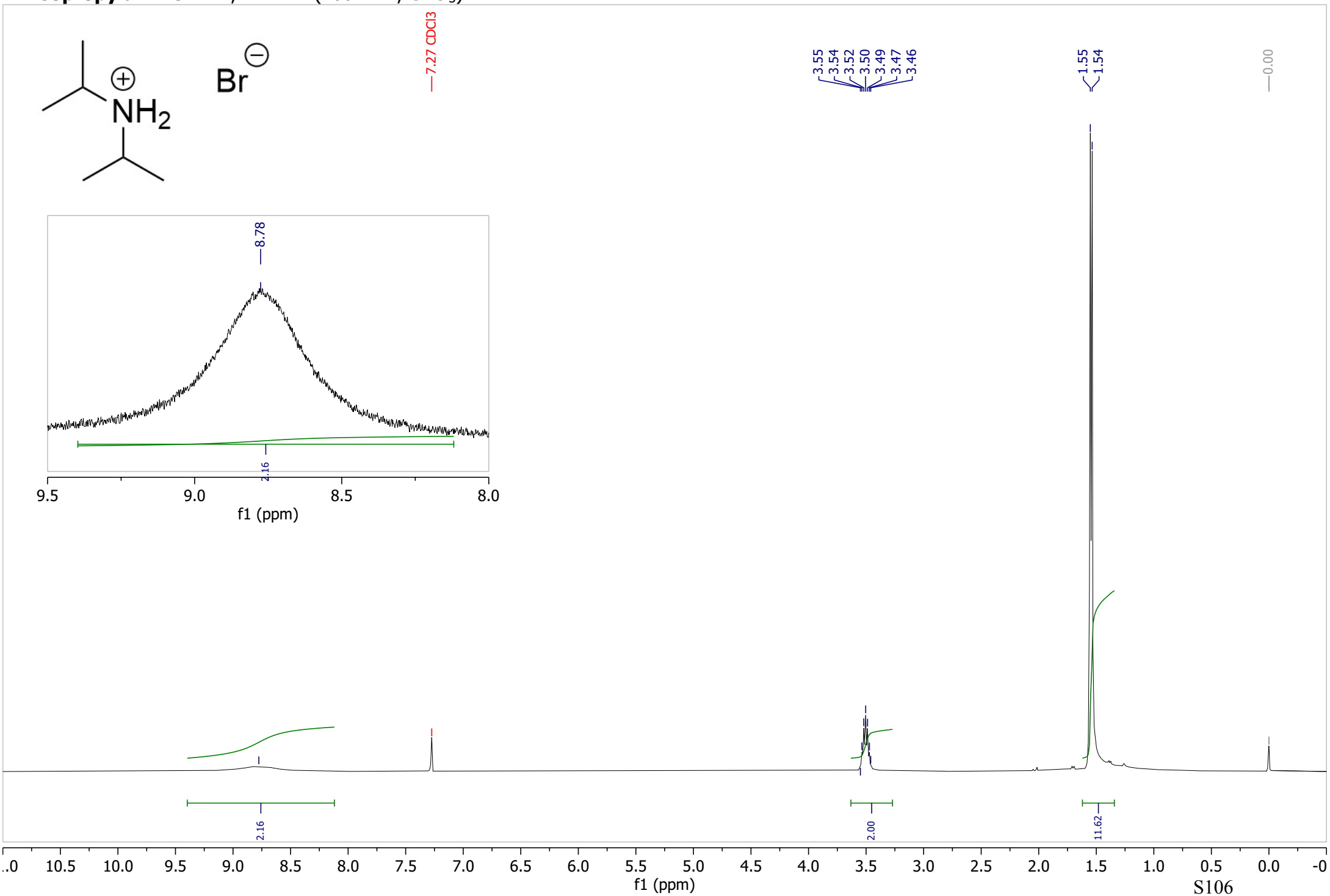
3u, ^{1}H NMR (500 MHz, CDCl3)



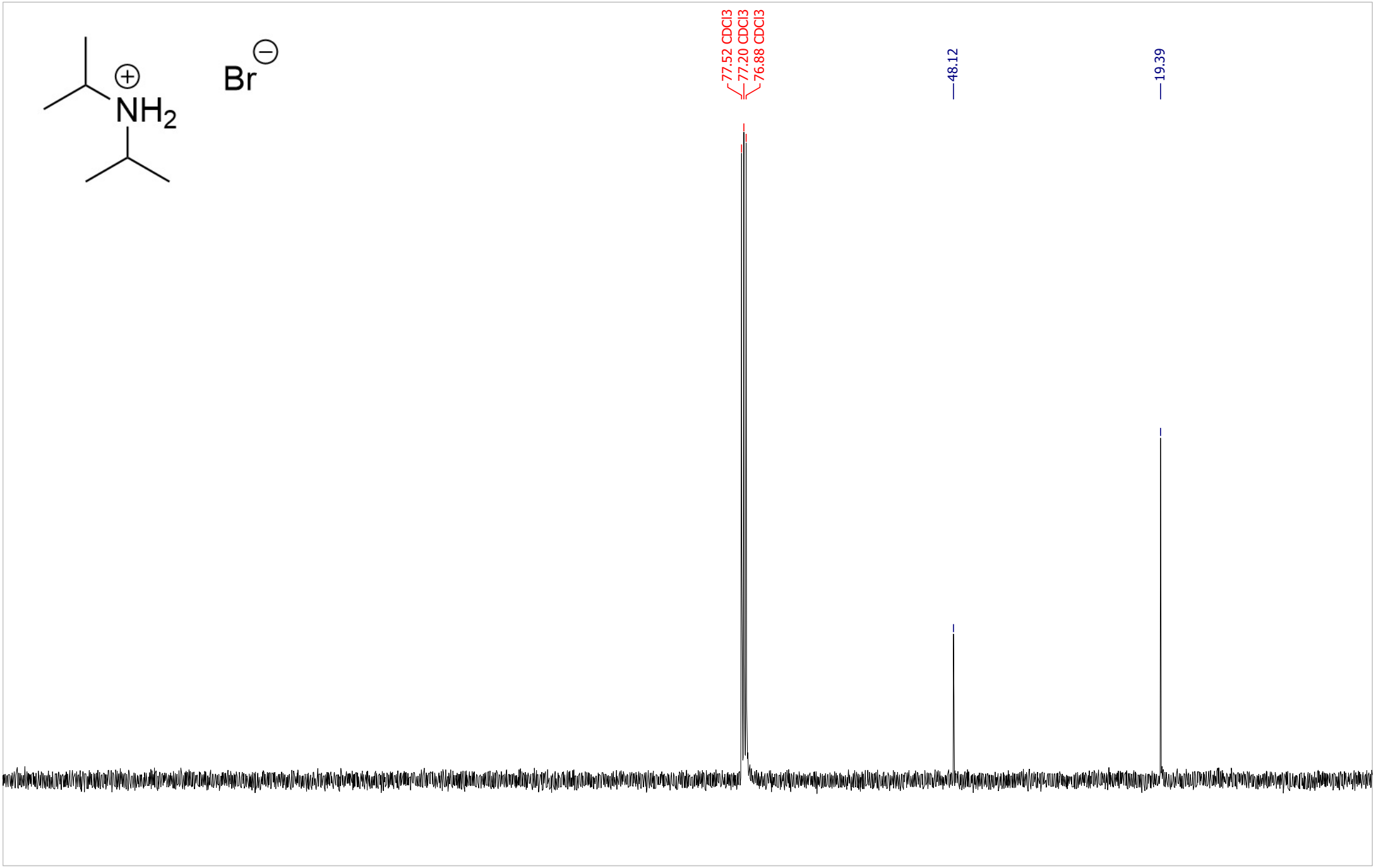
3u, ^{13}C NMR (126 MHz, CDCl3)



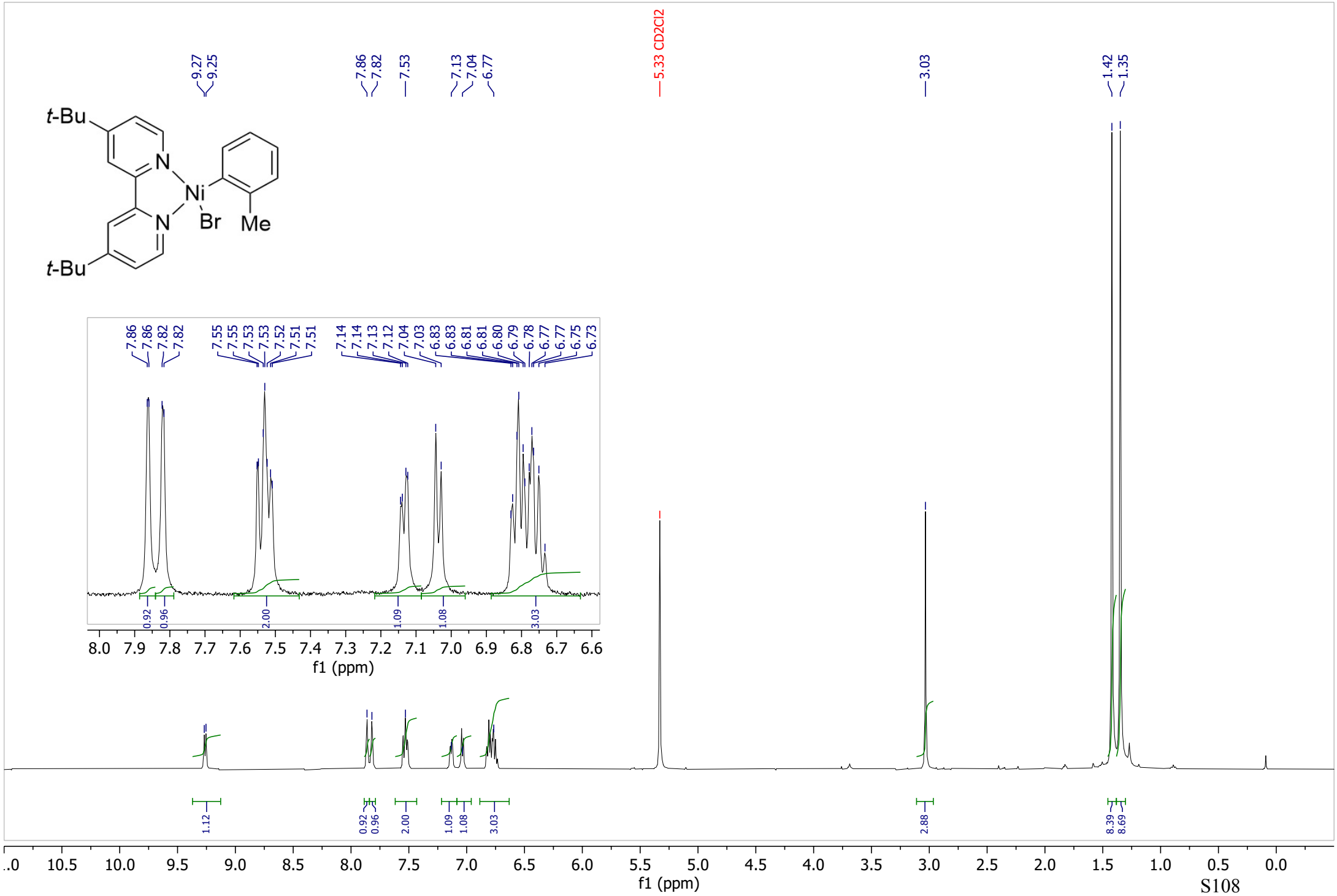
Diisopropylamine•HBr, ^{1}H NMR (400 MHz, $CDCl_3$)



Diisopropylamine•HBr, ^{13}C NMR (101 MHz, $CDCl_3$)



Ni(L2)(*o*-tolyl)Br, ^{1}H NMR (400 MHz, CD_2Cl_2)



Stacked Free Ligand and Ligand Exchange Studies, ^{1}H NMR (400 MHz, CD_2Cl_2)