Hindered Dialkyl Ether Synthesis with Electrogenerated Carbocations

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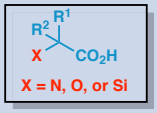
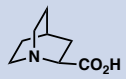
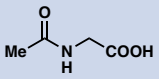
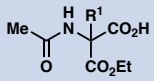




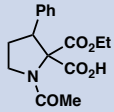
J. Org. Chem., **32**, 480 (1967)
NaOMe/MeOH, Pt(+)/Pt(-), 90 V
reflux, 9 h, N_2, 43% yield



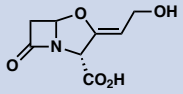
Tetrahedron, **28**, 4497 (1972)
Na/MeOH, Pt(+)/Pt(-), 2.0 A
0.609F, 30% yield



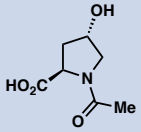
Tetrahedron Lett., **3**, 191 (1976)
Na salt, ROH (R = Me, Et, ^{i}Pr), C(+)/C(-)
250 mA, 130 min, 79-97% yield



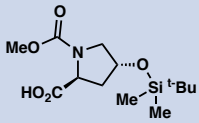
J. Org. Chem., **43**, 335 (1978)
NaOMe/MeOH, C(+)/C(-), 100 mA/cm^2
2.0 F/mol, 98% yield



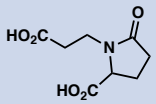
J. Chem. Soc., Perkin. Trans 1., **0**, 2513 (1983)
Et_3N/MeOH, Pt(+)/Pt(-), 200-250 mA/cm^2
- 30 °C, 50 min, 1.2% yield



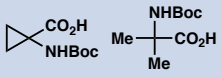
Synthesis, **5**, 424 (1986)
Et_3N/MeOH, Pt(+)/Pt(-), 260 mA/cm^2
2.5 F/mol, 97% yield



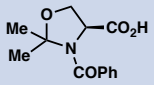
Helv. Chim. Acta, **69**, 1704 (1986)
Et_3N/MeOH, Pt(+)/Pt(-), 275 mA/cm^2
3 F/mol, 89% yield



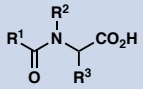
Heterocycles, **29**, 2089 (1989)
NaOAc, CH_3CN/MeOH (3/1)
Pt(+)/Pt(-), 2 F/mol, 75% yield



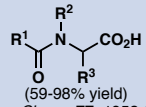
Synlett, **1991**, 737 (1991)
NaOEt/EtOH, Pt(+)/Pt(-), 9 mA/cm^2
0 °C, 79%/73% yield



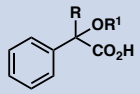
Org. Lett., **2**, 1689 (2000)
NaOMe/MeOH, C(+)/Pt(-), 50 mA
2 F/mol, - 20 °C, 69% yield



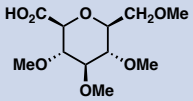
J. Am. Chem. Soc., **129**, 6680 (2007)
silica gel supported piperidine, MeOH,
Pt(+)/Pt(-), 75 mA/cm^2, 3 F/mol, 0 °C, 92-100%



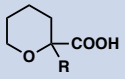
(59-98% yield)
J. Org. Chem., **77**, 1952 (2012)
1) NaOMe/MeOH, Pt(+)/Pt-Ti(-)
1.1 A/dm^2, 3-3.5 F/mol, 0 °C
2) SiO_2-Pip/MeOH, Pt(+)/Pt
0.3 A/dm^2, 2.4-3.75 F/mol, 10 °C



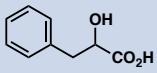
J. Org. Chem., **27**, 281 (1962)
Na/MeOH, Pt(+)/Pt(-)
1.2 A, 62-74% yield



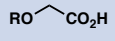
Chem. Pharm. Bull., 28, 3078 (1980)
Et_2NH/MeOH, Pt(+)/Pt(-),160 mA, 2 h
69% yield



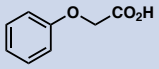
Tetrahedron Lett., **23**, 3987 (1982)
K_2CO_3, Et_4NClO_4/MeOH, Pt(+)/Pt(-)
0.1 A, 67-90% yield, divided cell



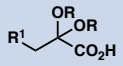
Helv. Chim. Acta, **70**, 292 (1987)
Et_3N/MeOH, Pt(+)/Pt(-), 260 mA/cm^2
2.6 F/mol, 68% yield



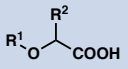
Chem. Ber., **126**, 1623 (1993)
KOH/MeOH or EtOH, Pt(+)/Pt(-)
20 mA/cm^2, 3.0 F/mol
0 °C, 12-66% yield



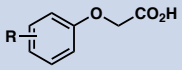
U.P.B. Sci. Bull., Series B, **69**, 3 (2007)
NaOH/Ethylene glycol or Diethylene glycol
C(+)/Pt(-), 0.015 A/cm^2, yield not reported



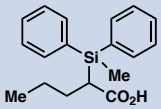
ECS Transactions, **13**, 1 (2008)
MeOH, Pt(+)/Pt(-), >95% yield



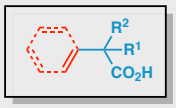
Chem. Commun., **54**, 9969 (2018)
NaOMe/MeOH, C(+)/C(-), 100 mA/cm^2
70 min, 75-93% yield

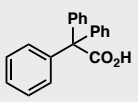


ChemElectroChem. ***6***, xxxx (2019)
NaOMe/MeOH, C(+)/C(-), 20 mA/cm^2
2.5 F/mol, 19-87% yield

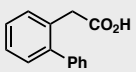


J. Org. Chem., **76**, 4710 (2011)
KOH, CH_3CN/MeOH (3/1), Pt(+)/Pt(-)
250 mA/cm^2, 3 F/mol, 35% yield

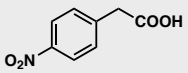




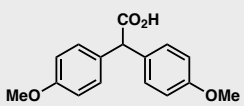
J. Chem. Soc., **0**, 3624 (1952)
NaOMe/MeOH, Pt(+)/Pt(-)
1.5 A, 60% yield



J. Chem. Soc., **0**, 1360 (1962)
Na/MeOH, Pt(+)/Pt(-), 1 A
6 h, 21% yield



J. Chem. Soc., **0**, 1037 (1964)
Na/MeOH, Pt(+)/Pt(-)
1.2 A, 3 h, 16% yield



J. Chem. Soc. B, **0**, 576 (1968)
Na/MeOH, Pt(+)/Pt(-), 1 A
65% yield

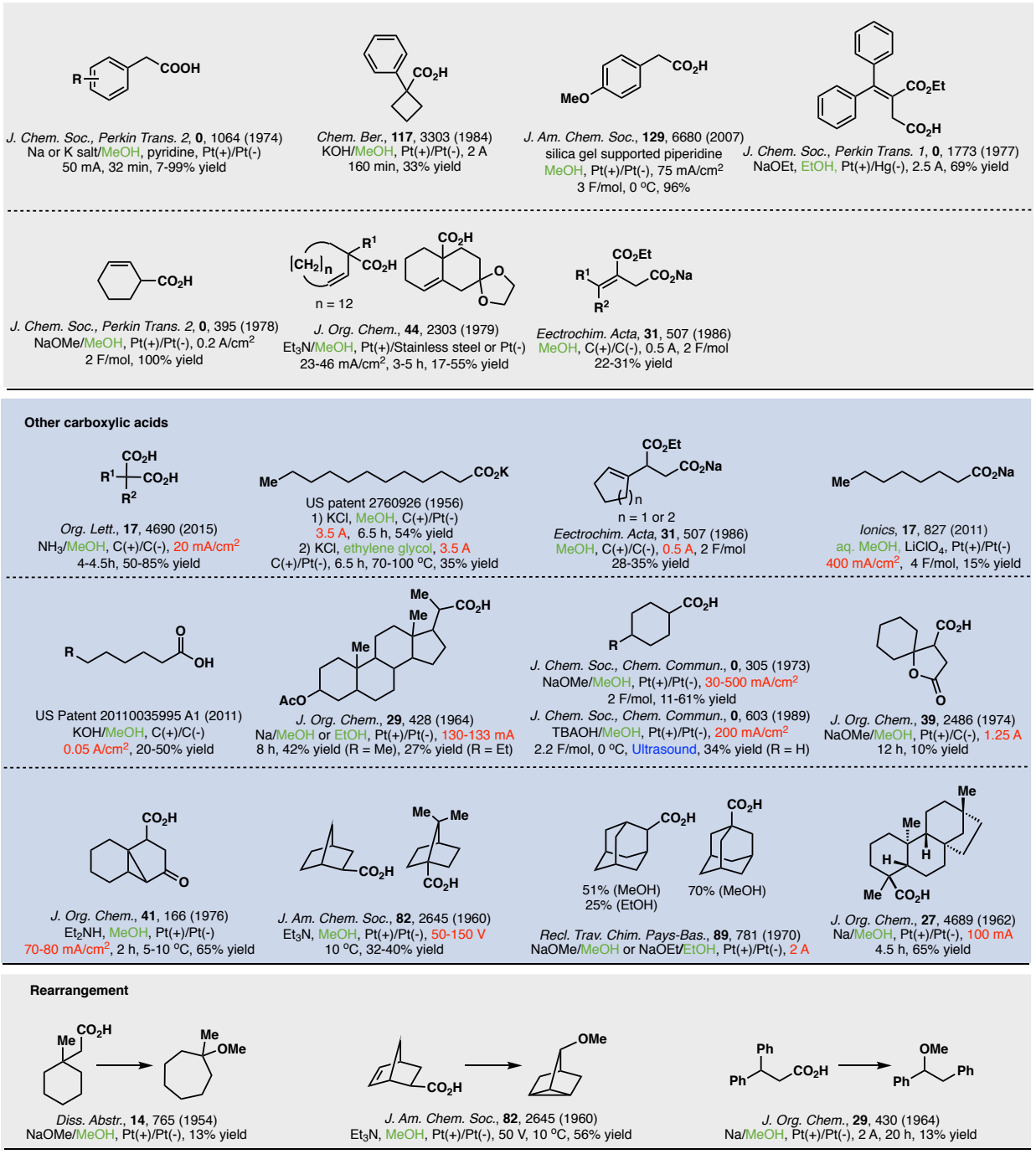
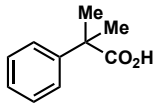


Figure S1: A Survey of Electrochemical Decarboxylative Etherification

General Experimental

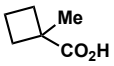
Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF), and acetonitrile (CH_3CN) were obtained by passing the previously degassed solvents through an activated alumina column. $AgPF_6$ was purchase from Alfa Aesar (lot #I17M26). $AgClO_4$ anhydrous was purchase from Alfa Aesar (lot #Y20D047). $AgSbF_6$ was purchase from Oakwood (lot #007268). $^nBu_4NPF_6$ was purchased from Oakwood (lot #A034292920). $^nBu_4NClO_4$ (>98%) was purchased from TCI (Product #T0836). 3Å molecular sieves were purchased from Acros Organics (catalog lot #A034292920) and activated under flame dry for 30 min prior to use. 2,4,6-collidine (99%) was purchased from Sigma-Aldrich (batch # 13925DD). $AgClO_4$ was grinded prior to use. All the other reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material. TLC was performed using 0.25 mm E. Merck Silica plates (60F-254), using short-wave UV light for visualization, and phosphomolybdic acid, $Ce(SO_4)_2$, acidic ethanolic anisaldehyde, or $KMnO_4$ as developing agents upon heating. NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 instruments and are calibrated using residual undeuterated solvent ($CHCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Column chromatography was performed using E. Merck silica gel (60, particle size 0.043–0.063 mm). High-resolution mass spectra (HRMS) were recorded on Waters LC with G2-XS TOF mass spectrometer by electrospray ionization time of flight reflectron experiments. GCMS (EI) was recorded on Agilent 7820A GC systems and 5975 Series MSD. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus and are uncorrected. The enantiomeric excesses were determined with Waters UPC^2 SFC equipped with a photodiode array detector or an Agilent Technologies 1220 Infinity II LC HPLC. Optical rotations were recorded on a Rudolph Research Analytical Autopol III Automatic Polarimeter.

List of Carboxylic Acids Substrates and References for Their Preparation.



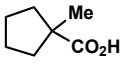
CAS no.: 826-55-1

Ref: *Chem. Commun* 2017, 8316.



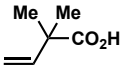
CAS no.: 32936-76-8

Ref: *Chem. Commun* 2006, 4107.



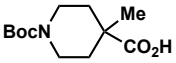
CAS no.: 5217-05-0

Ref: *ACIE* 2014, 53, 4945.



CAS no.: 10276-09-2

Ref: *JACS*, 2018, 140, 16610.



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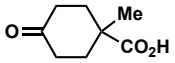
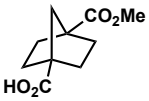
Ref: *J. Med. Chem.* 2017, 60, 4680.



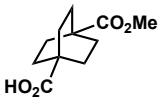
CAS no.: 24463-41-0

Ref: Patent WO 2018086592



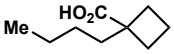
CAS no.: 15448-77-8

Ref: *J. Med. Chem.* 2011, 54, 3480.



CAS no.: 18720-35-9

Ref: *Bioorg. Med. Chem. Lett* 2014, 24, 5731.

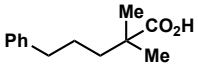


CAS no.: 58148-13-3

Ref: *JACS*, 2014, 136, 8138.

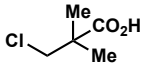
CAS no.: 1510754-94-5

Ref: *Bioorg. Med. Chem. Lett* 2016, 26, 1016.



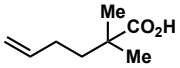
CAS no.: 2840-74-6

Ref: *Helv. Chim. Acta* 2018, 101, e1800049.



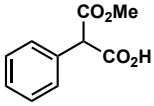
CAS no.: 13511-38-1

Ref: *Org. Lett.* 2017, 19, 4560.



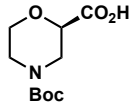
CAS no.: 33315-63-8

Ref: *Eur. J. Org. Chem.*, 2014, 941.



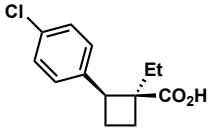
CAS no.: 33315-63-8

Ref: *Adv. Synth. Catal.*, 2018, 360, 2476



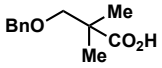
CAS no.: 884512-77-0

Ref: *Bioorg. Med. Chem. Lett* 2011, 21, 4836.



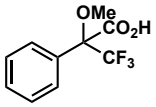
CAS no.: 2271155-09-8

Ref: *ACIE* 2019, 58, 2134.



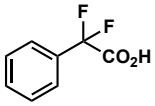
CAS no.: 36881-14-8

Ref: *Eur. J. Org. Chem.*, 2007, 934.



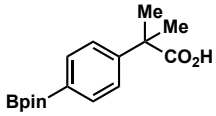
CAS no.: 81655-41-6

Ref: *Syn. Commun*, 1993, 23, 2145.



CAS no.: 360-03-2

Ref: *Eur. J. Org. Chem.*, 2016, 5529.



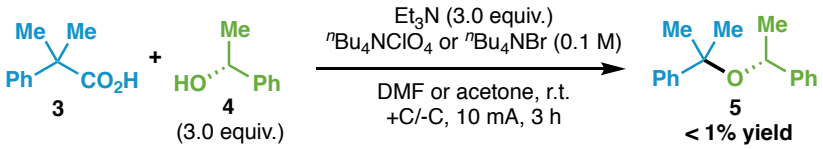
CAS no.: 909187-36-6

Ref: Patent WO 2006094187

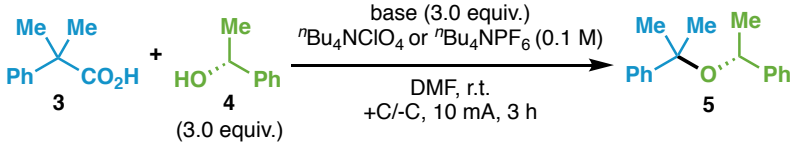
Optimization of Reaction Parameters for Electrochemical Decarboxylative Etherification

All optimization reactions were carried out on 0.20 mmol scale. The crude reaction mixture was analyzed by GC/FID using *n*-dodecane as internal standard.

Starting conditions

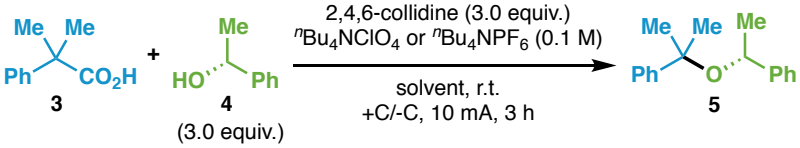


Primary evaluation of bases and electrolyte (**Table S1**)



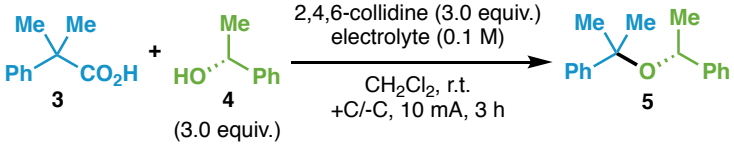
entry	electrolyte	base	yield (%)
1	$^{n}Bu_4NClO_4$	K_2CO_3	<1
2	$^{n}Bu_4NClO_4$	DBU	<1
3	$^{n}Bu_4NClO_4$	2,4,6-collidine	4
4	$^{n}Bu_4NPF_6$	2,4,6-collidine	6

Evaluation of solvents (**Table S2**)



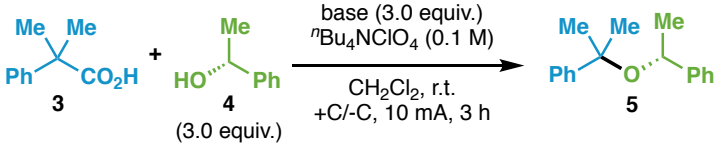
entry	electrolyte	solvent	yield (%)
1	$^{n}Bu_4NClO_4$	CH_3CN	27
2	$^{n}Bu_4NClO_4$	THF	5
3	$^{n}Bu_4NClO_4$	$PhCF_3$	38
4	$^{n}Bu_4NClO_4$	acetone	24
5	*$^{n}Bu_4NClO_4$*	*CH_2Cl_2*	*48*
6	$^{n}Bu_4NClO_4$	$ClCH_2CH_2Cl$	47
7	$^{n}Bu_4NPF_6$	CH_2Cl_2	40
8	$^{n}Bu_4NPF_6$	$ClCH_2CH_2Cl$	42

Further evaluation of electrolytes (**Table S3**)



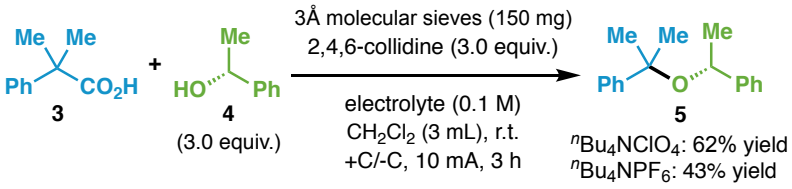
entry	electrolyte	yield (%)
1	$LiClO_4$	16
2	$^{n}Bu_4NOTs$	18
3	Et_4NCl	9

Further evaluation of bases (**Table S4**)

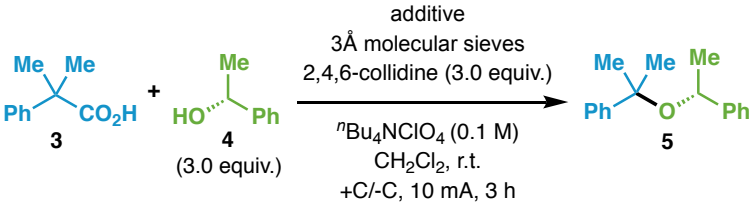


entry	base	yield (%)
1	$^{t}BuOK$	3
2	KOH	9
3	NaOAc	16
4	DBU	15
5	TMG	26
6	2,6-lutidine	46
7	DABCO	<1
8	DMAP	2
9	2,6-di-*tert*-butylpyridine	6

Adding 3Å molecular sieves



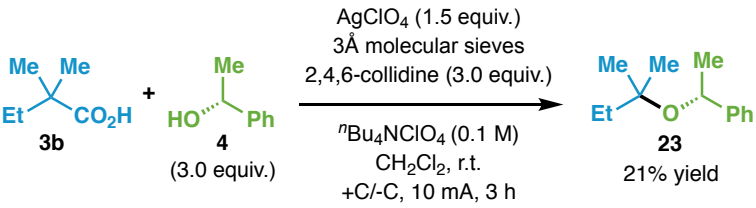
Evaluation of additives (**Table S5**)



entry	additive (1.5 equiv.)	yield (%)
1	$K_3Fe(CN)_6$	53
2	$MnCO_3$	50
3	ZnO	54
4	$KSbF_6$	47
5	Ag_2SO_4	47
6	$AgPF_6$	79
7	$AgBF_4$	72
8	Ag_2O	64
9	*$AgClO_4$*	*81(78)*[a]
10	$AgClO_4$ (0.3 equiv.)	63

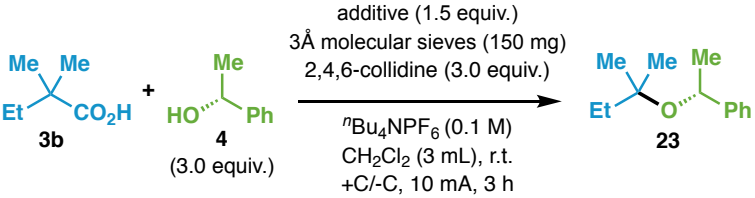
[a] Isolated yield

However, under the aforementioned optimized conditions for 2-methyl-2-phenylpropanoic acid ***3****, decarboxylative etherification of 2,2-dimethylbutanoic acid* ***3b*** *proceeded in low yield.*



In order to identify a more general set of conditions, further optimization efforts were undertaken on 2,2-dimethylbutanoic acid ***3b****.*

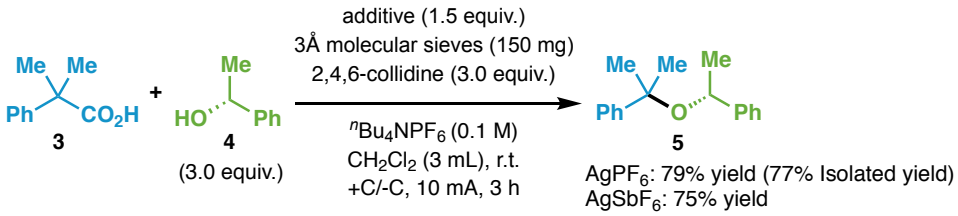
Evaluation of additives using ^{n}Bu$_4$NPF$_6$ as electrolyte (**Table S6**)



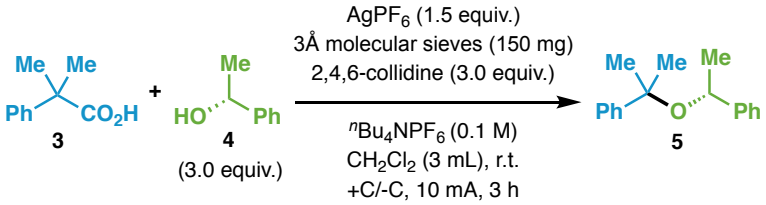
entry	Additive (1.5 equiv.)	yield (%)
1	none	26
2	CH_2Br_2	17
3	$KClO_4$	31
4	KPF_6	47
5	$AgPF_6$	58
6	*$AgSbF_6$*	*62(62)[a]*
7	$KSbF_6$	52
8	$NaSbF_6$	46

[a] Isolated yield

*This optimized set of conditions for the decarboxylative etherification of non-benzylic carboxylic acid **3b** was more general, and was also suitable for 2-methyl-2-phenylpropanoic acid **3**.*

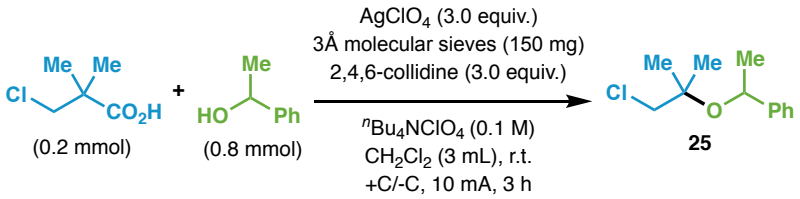


Control experiments (**Table S7**)



entry	Variation from standard conditions	yield (%)
1	No $AgPF_6$	43
2	No 3Å molecular sieves	47
3	No 2,4,6-collidine	0
4	No electric current	0

*Reoptimization for compound **25*** (**Table S8**)



entry	Variation from standard conditions	yield (%)
1	no deviation	24[a]
2	2 mL CH_2Cl_2	32
3	1.5 mL CH_2Cl_2	34
4	1 mL CH_2Cl_2	25
5	*1.5 mL CH_2Cl_2, I = 7.5 mA, 4 h*	*45(43)* [a]
6	1.5 mL CH_2Cl_2, I = 5 mA, 6 h	36

[a] Isolated yield

CH_2Cl_2 Cathodic reduction

Conditions: 0.1 M $^nBu_4NPF_6$, CH_2Cl_2 solvent, GC working /Pt counter electrode, Ag/AgCl reference electrode. Scan rate = 200 mV/s.

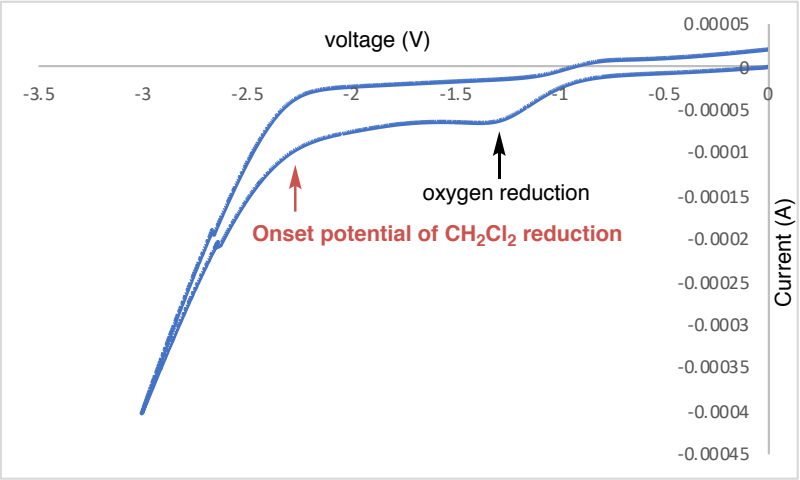
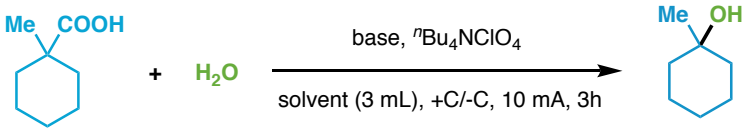


Figure S2: The cathodic potential of the reaction of **3** and **4** was measured as –2.2 V against Ag/AgCl reference electrode, which is in agreement with the reduction of CH_2Cl_2 observed in the cyclic voltammetric study.

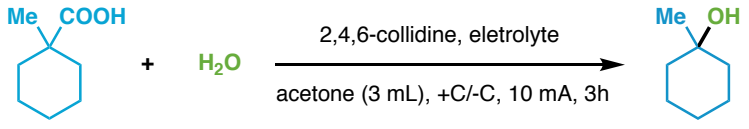
Optimization of Reaction Parameters for Electrochemical Decarboxylative Hydroxylation

All optimization reactions were carried out on 0.20 mmol scale. The crude reaction mixture was analyzed by GC/FID using *n*-dodecane as internal standard.



134

entry	base (3 eq)	[Ag]	H_2O	solvent	yield (%)
1	2,4,6-collidine	-	0.1 mL	CH_2Cl_2 3 mL	21
2	2,4,6-collidine	Ag_2O (1.5 eq)	0.1 mL	CH_2Cl_2 3 mL	24
3	Cs_2CO_3	Ag_2O (1.5 eq)	0.1 mL	CH_2Cl_2 3 mL	15
4	2,4,6-collidine	Ag_2O (1.5 eq)	0.1 mL	MeCN 3 mL	14
5	2,4,6-collidine	Ag_2O (1.5 eq)	0.1 mL	DMF 3 mL	trace
6	2,4,6-collidine	Ag_2O (1.5 eq)	0.1 mL	Dioxane 3 mL	15
7	2,4,6-collidine	Ag_2O (1.5 eq)	0.1 mL	Acetone 3 mL	50
8	*2,4,6-collidine*	-	*0.1 mL*	*Acetone 3 mL*	*65*
9	2,4,6-collidine	$AgClO_4$ (3 eq)	0.1 mL	Acetone 3 mL	39
10	2,4,6-collidine	-	0.5 mL	Acetone 2.5 mL	49

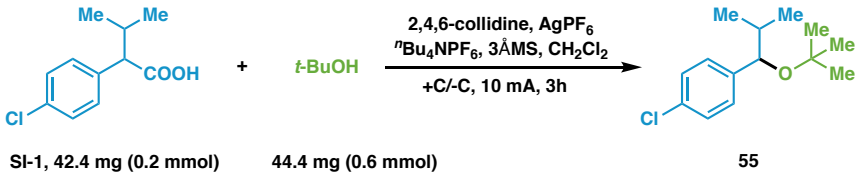


134

entry	base	H_2O	electrolyte	yield (%)
1	2,4,6-collidine (3 eq)	0.2 mL	$^nBu_4NClO_4$	60
2	2,4,6-collidine (3 eq)	0.3 mL	$^nBu_4NClO_4$	59
3	2,4,6-collidine (3 eq)	0.1 mL	$^nBu_4NClO_4$	65
4	2,4,6-collidine (1.5 eq)	0.1 mL	$^nBu_4NClO_4$	71
5	2,4,6-collidine (4.5 eq)	0.1 mL	$^nBu_4NClO4$	64
6	*2,4,6-collidine (1.5 eq)*	*0.1 mL*	*$^nBu_4NPF_6$*	*75(70)[a]*
7	2,4,6-collidine (1.5 eq)	0.1 mL	Et_4NOTs	30
8	2,4,6-collidine (1.5 eq)	0.1 mL	$^nBu_4NF.H_2O$	47

[a] Isolated yield

General Procedure for Electrochemical Decarboxylative Etherification (General Procedure A, Carboxylic Acid as Limiting Reagent):



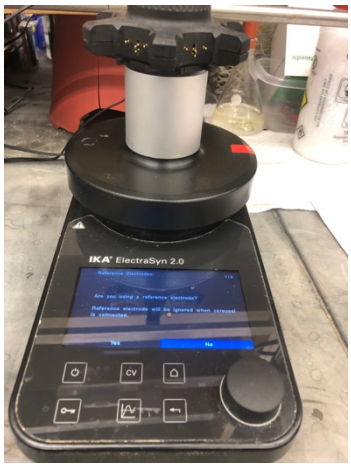
SI-1, 42.4 mg (0.2 mmol) **44.4 mg (0.6 mmol)** **55**

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid (42.4 mg, 0.2 mmol, 1 equiv.), alcohol (44.4 mg, 0.6 mmol, 3 equiv.), 2,4,6-collidine (72.6 mg, 0.6 mmol, 3 equiv.), $^{n}Bu_4NPF_6$ (116 mg, 0.3 mmol, 1.5 equiv.), 3 Å molecular sieves (150 mg), $AgPF_6$ (76 mg, 0.3 mmol, 1.5 equiv.), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. After pre-stirring for 15 minutes, the reaction mixture was electrolyzed at a constant current of 10 mA for 3 hours. The ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with the crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with 2N HCl (20 mL) (for products containing pyridine moiety, washing with 2N HCl is omitted) and $NaHCO_3$ (aq) (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) to furnish the desired product.

Graphical Guide for Electrochemical Decarboxylative Etherification:

Setting Up the ElectraSyn Device

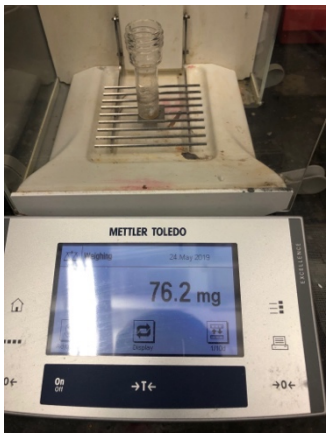
Left: select “New Experiment”. Center: select “Constant Current”. Right: set the current to 10 mA (for a 0.2 mmol scale).

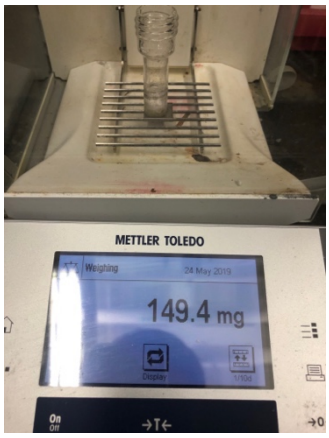


Left: no need to use a reference electrode. Center: choose “Time”. Right: set reaction time to 3h.

Left: 0.2 mmol of carboxylic acid substrate was used. Center: no alternate polarity. Right: Saving data is up to the individual.

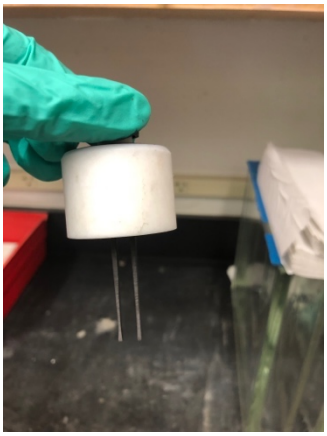

Left: all reagents for this reaction. Center: carboxylic acid (42.4 mg). Right: *t*-BuOH (44.4 mg).





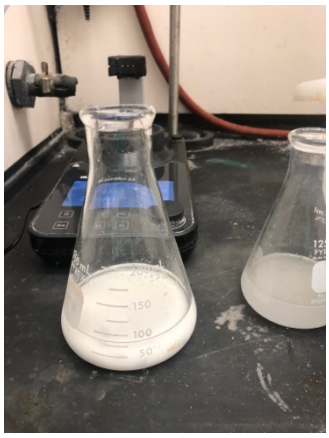
Left: $AgPF_6$ (76 mg). Center: $^nBu_4NPF_6$ (116 mg). Right: 3Å MS (150 mg).

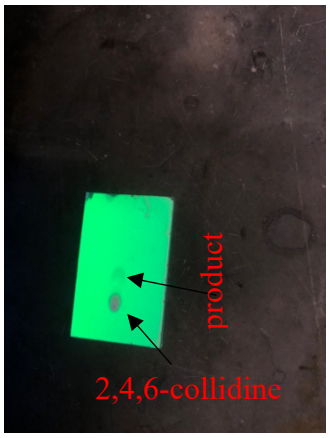

Left: 2,4,6-collidine (72 mg). Center: CH_2Cl_2 from solvent system. Right: CH_2Cl_2 (3 mL).


Left: after adding CH_2Cl_2 to the vial. Center: graphite electrodes. Right: pre-stir for 15 min.

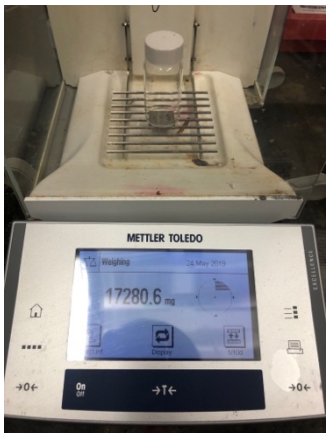
Left: start the reaction on the ElectraSyn 2.0 with a stirring speed of 700 rpm. Center: reaction completed. Right: transfer reaction mixture to a separatory funnel with Et_2O. Then the organic phase was washed with 2N HCl (aq) and sat. $NaHCO_3$ (aq).





Left: dried over Na_2SO_4. Center: filter off Na_2SO_4. Right: crude TLC (Hexanes: Et_2O = 100:1), top spot is the product.

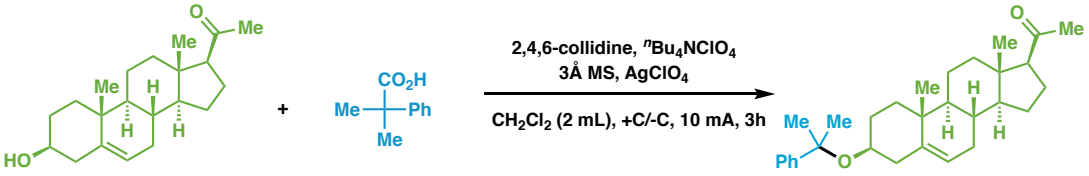




Left: purified by PTLC (Hexanes: Et_2O = 100:1) Center: removal of solvent. Right: weight of vial containing product (31.0 mg, 65% yield).

Note: For volatile ether products, a rotary evaporator was operated over a water bath at 20 °C, and a high vacuum pump was avoided during the whole workup sequence.

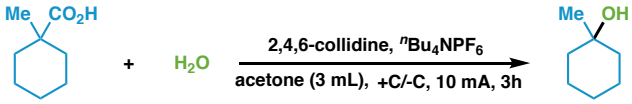
General Procedure for Electrochemical Decarboxylative Etherification (General Procedure B, Alcohol as Limiting Reagent):



SI-2, 48 mg (0.15 mmol) SI-3, 74 mg (0.45 mmol) **51**: 54% yield

Electrochemical Decarboxylative Etherification: With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid **SI-3** (0.45 mmol, 3 equiv.), alcohol **SI-2** (0.15 mmol, 1 equiv.), 2,4,6-collidine (81.6mg, 0.675 mmol, 4.5 equiv.), $^{n}Bu_4NClO_4$ (137 mg, 0.4 mmol, 0.2 M), 3 Å molecular sieves (100 mg), $AgClO_4$ (124 mg, 0.6 mmol, 4 equiv.), and CH_2Cl_2 (2.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. After pre-stirring for 15 minutes, the reaction mixture was electrolyzed under a constant current at 10 mA for 3 hours. The ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with 2N HCl (20 mL) (for products containing pyridine moiety, washing with 2N HCl is omitted) and $NaHCO_3$(aq) (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) to furnish the desired product.

General Procedure for Electrochemical Decarboxylative Hydroxylation: (General Procedure C):

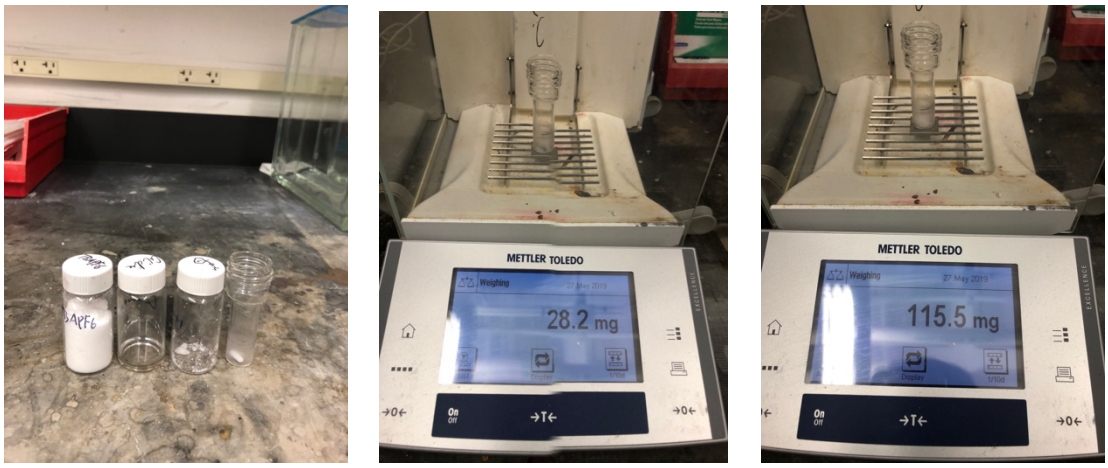


SI-4, 28.4 mg (0.2 mmol) **134**

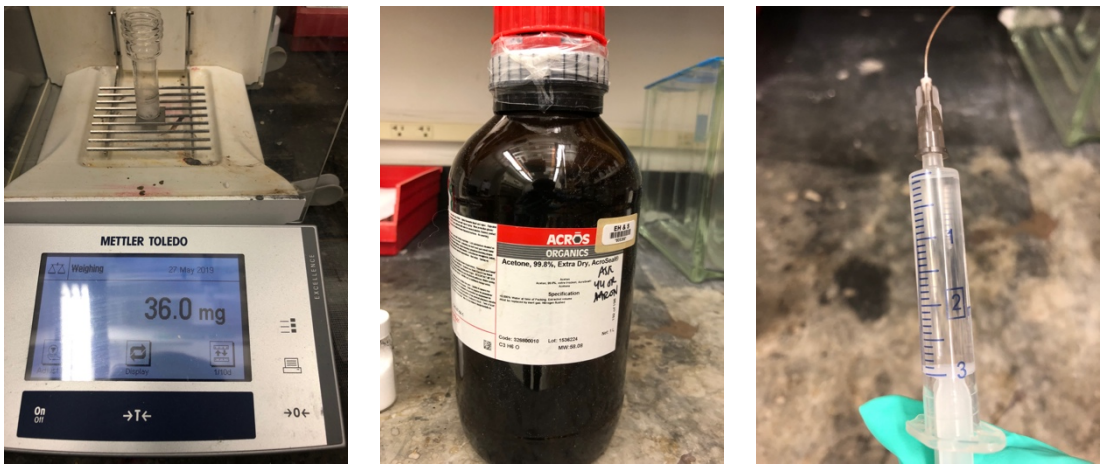
With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid **SI-4** (28.4 mg, 0.2 mmol, 1 equiv.), 2,4,6-collidine (36.3 mg, 0.3 mmol, 1.5 equiv.), $^{n}Bu_4NPF_6$ (114 mg, 0.3 mmol, 0.1M), acetone (3.0 mL), and H_2O (0.1 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted

into the mixture. After pre-stirring for 5 minutes, the reaction mixture was electrolyzed under a constant current of 10 mA for 3 hours. The ElectraSyn vial cap was removed and electrodes were rinsed with Et_2O (2 mL). The resulting solution was diluted with Et_2O (40 mL), and then washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) to furnish the desired product. (Note: an empty balloon is attached for a large scale reaction to balance the pressure resulting from the H_2 generation on the cathode).

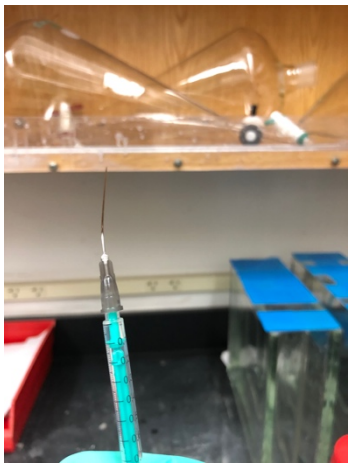
Graphic Procedure for Electrochemical Decarboxylative Hydroxylation:



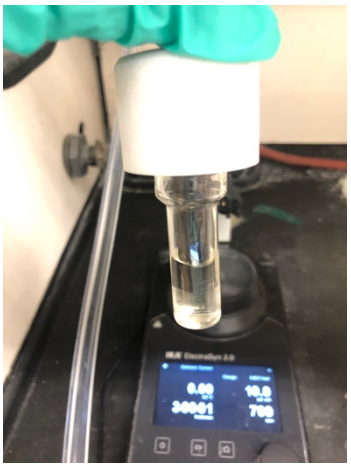
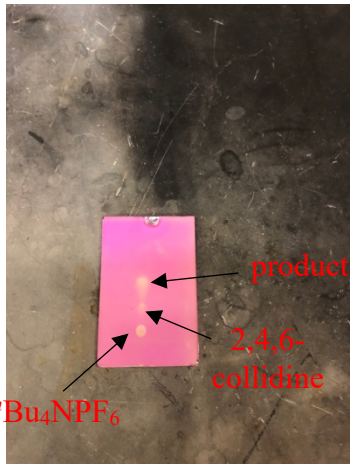
Left: all reagents for hydroxylation reaction. Center: carboxylic acid (28.5 mg, 0.2 mmol). Right: $^{n}Bu_4NPF_6$ (114 mg, 0.3 mmol).



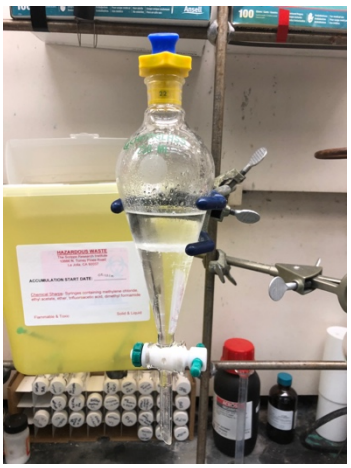
Left: 2,4,6-collidine (36.3 mg, 0.3 mmol). Center: acetone used in this reaction. Right: acetone (3 mL).



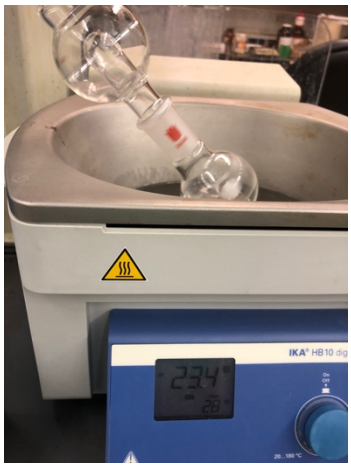
Left: H_2O (0.1 mL). Center: graphite electrode. Right: pre-stir the reaction mixture for 5 min.

Left: start the reaction on the ElectraSyn 2.0. Center: reaction completed. Right: crude TLC (Hexanes: EtOAc = 3:1).

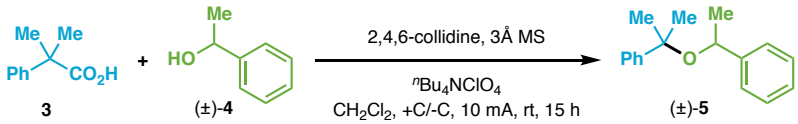




Left: dilute with Et_2O (30 mL) and washed with sat. NH_4Cl (aq). Center: washed with brine. Right: dried over Na_2SO_4 and filtered.



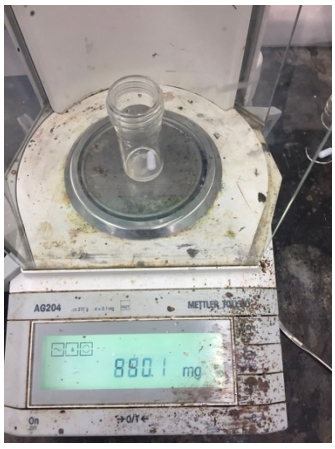

Left: concentrated *in vacuo*. Center: purified by PTLC. Right: weight of vial containing product (16.0 mg, 70% yield).

Experimental Procedure for Gram-Scale Electrochemical Decarboxylative Etherification

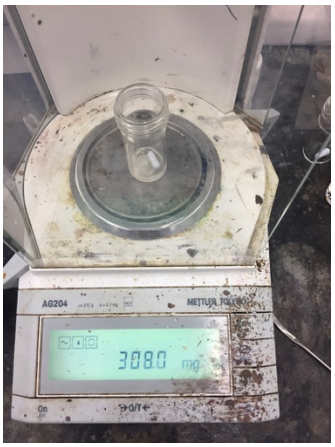


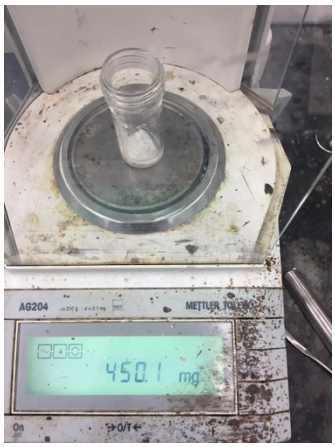


Left: reagents for etherification reaction. Center: ElectraSyn vials (25 mL). Right: Tare of the vial.

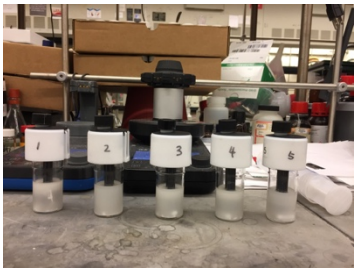


Left: **3** (394 mg, 2.4 mmol). Center: **4** (880 mg, 7.2 mmol). Right: 2,4,6-collidine (436 mg, 3.6 mmol)

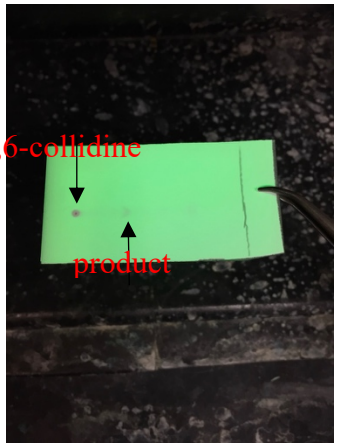




Left: $^{n}Bu_4NClO_4$ (308 mg, 0.9 mmol). Center: 3 Å molecular sieves (450 mg). Right: CH_2Cl_2 (9 mL)



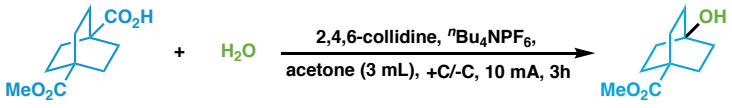

Left: after adding CH_2Cl_2 and equipped with graphite electrodes for 5 reactions. Center: After pre-stirring for 30 minutes, start the reaction on the ElectraSyn device (after 1 min). Right: reaction completed (15h).




Left: crude TLC (Hexanes: Et_2O=30:1). Center: the suspension of 5 reactions was diluted with Et_2O and washed with 1 N HCl. Right: dried over Na_2SO_4.

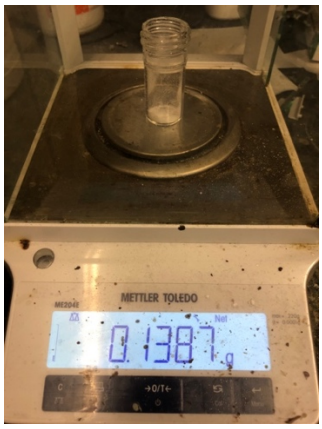
Left: column chromatography purification. Center: weight of empty flask. Right: weight of flask containing product (2.08 g, 72% yield).

Experimental Procedure for Gram-Scale Electrochemical Decarboxylative Hydroxylation

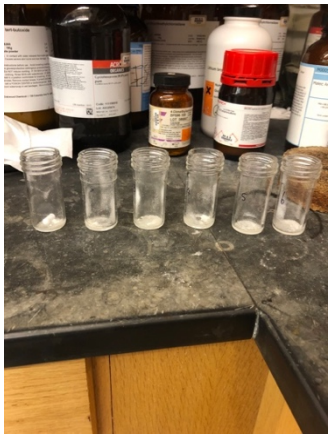
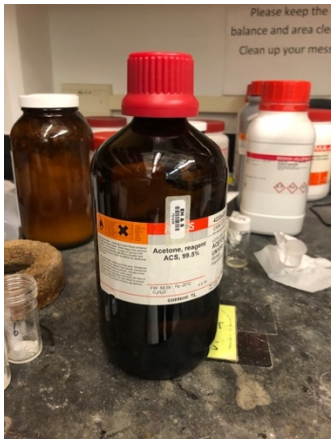


71 81

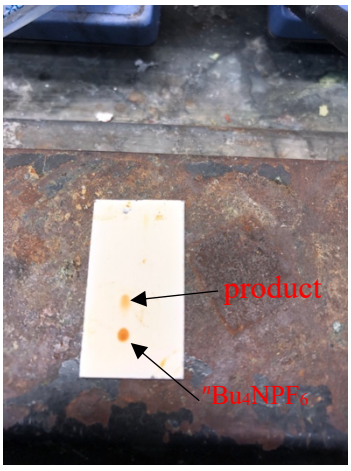
Left: reagents for hydroxylation reaction. Center: ElectraSyn vials (25 mL). Right: Tare of the vial.



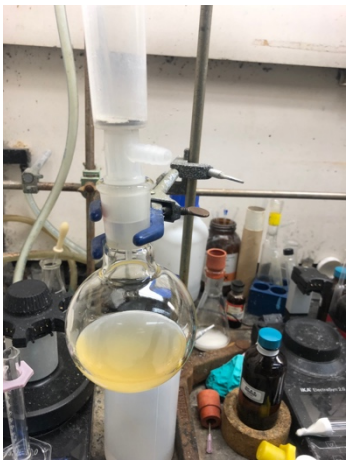
Left: **71** (254 mg, 1.2 mmol). Center: $^{n}Bu_4NPF_6$ (139 mg, 0.36 mmol). Right: 2,4,6-collidine (218 mg, 1.8 mmol)

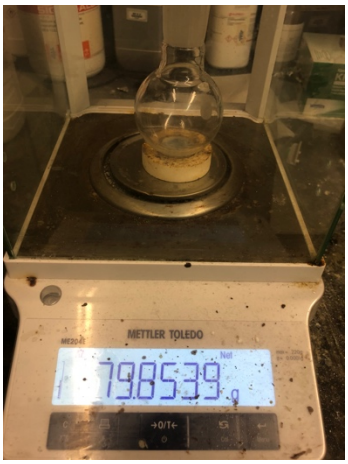



Left: after adding all reagents for 6 reactions. Center: acetone used in this reaction. Right: acetone (9 mL)

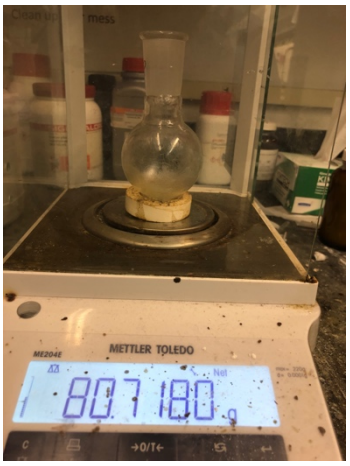



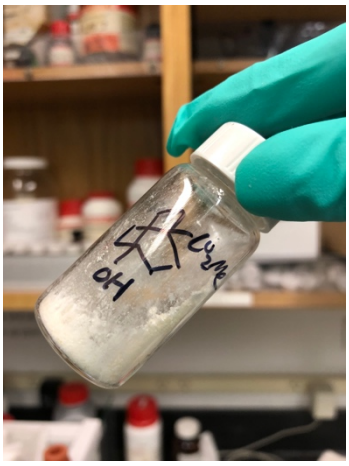
Left: after adding solvent and H_2O, and equipped with graphite electrodes. Center: reaction completed (12h). Right: crude TLC (Hexanes: EtOAc= 4:1).





Left: adding Et_2O to dilute 6 reactions and filtered, rinsed with Et_2O. Center: column chromatography purification. Right: weight of empty flask.





After purification. (864 mg, 65% yield).

Additional Scope for Decarboxylative Etherification and Hydroxylation

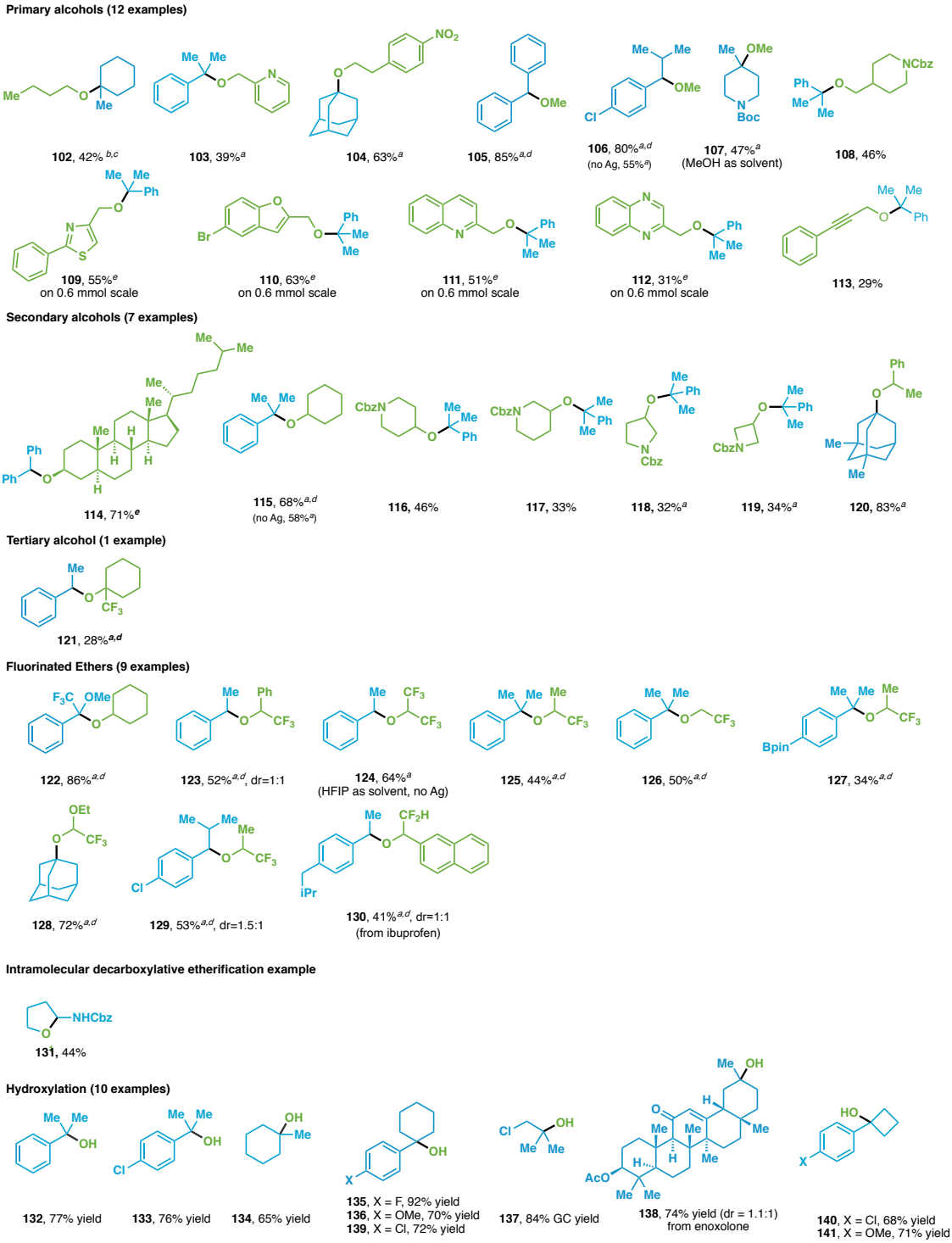


Figure S3: [a]$AgClO_4$ (0.6 mmol) instead of $AgPF_6$, [n]Bu_4NClO_4 (0.1 M) instead of [n]Bu_4NPF_6. [b]$AgSbF_6$ (0.3 mmol) instead of $AgPF_6$. [c]DBU (0.6 mmol) instead of 2,4,6-collidine. [d]4.0 or 6.0 equiv. alcohol. [e]Alcohol as limiting reagent, conditions: alcohol (0.15 mmol), carboxylic acid (0.45 mmol), $AgClO_4$ (0.6 mmol), 2,4,6-collidine (0.675 mmol), [n]Bu_4NClO_4 (0.2 M), 3Å MS (100 mg), CH_2Cl_2 (2 mL), I = 10 mA, 3 h.

Unsuccessful and Challenging Substrates for Decarboxylative Etherification and Hydroxylation

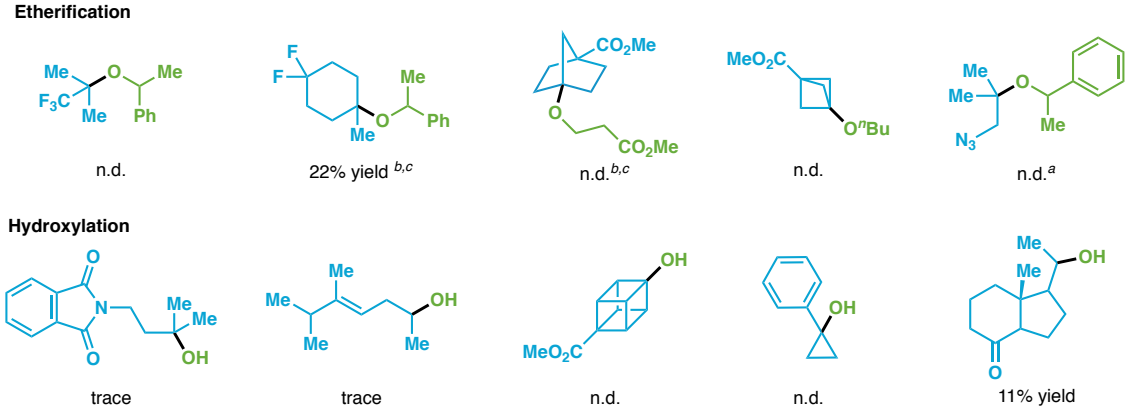


Figure S4: [a]$AgClO_4$ (0.6 mmol) instead of $AgPF_6$, [n]$^nBu_4NClO_4$ (0.1 M) instead of $^nBu_4NPF_6$. [b]$AgSbF_6$ (0.3 mmol) instead of $AgPF_6$. [c]DBU (0.6 mmol) instead of 2,4,6-collidine.

Mechanistic Probes and Kinetic Study Discussion

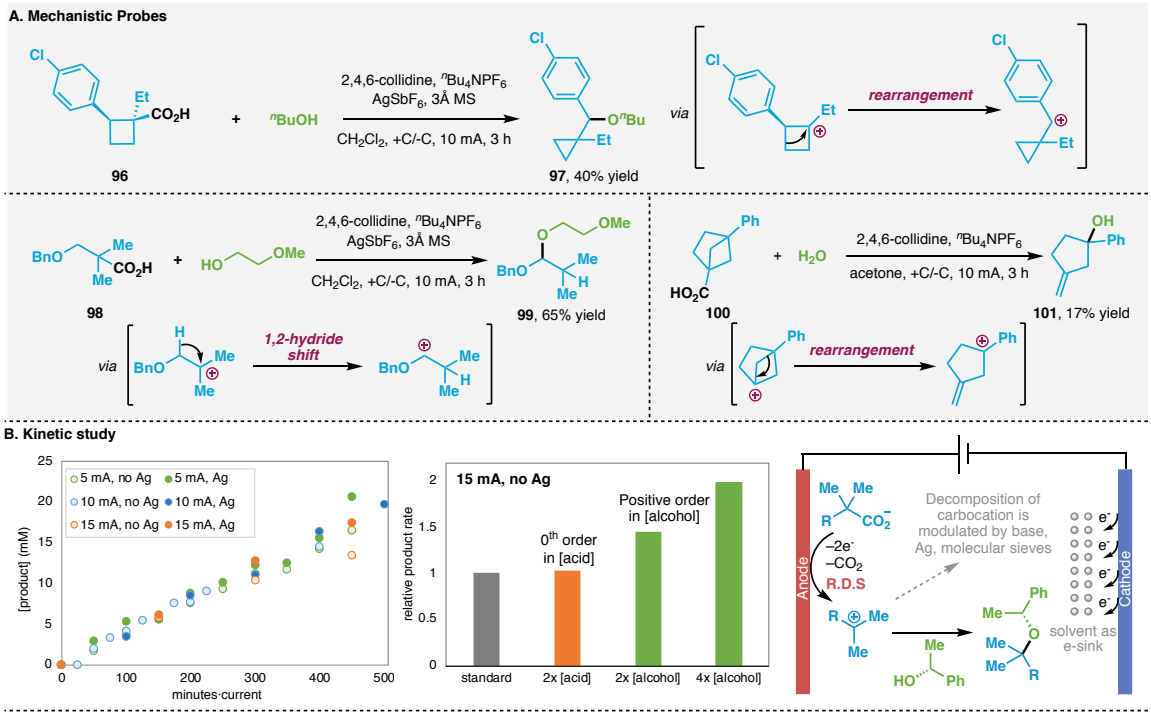


Figure S5. (A) Probe substrates verify the intermediacy of carbocations through well-known rearrangement pathways; and (B) Kinetic and mechanistic analysis of the process, variable time normalization analysis (VTNA) method used to determine first order dependence on current (left).

Subjection of acids containing cyclobutane (**96**), β-alkoxy (**98**), and bridged substituents (**100**) gave rise to products that would be expected from a thermodynamically-favored ring contraction (to **97**), a 1,2-hydride shift (to **99**), and strain release (to **101**), respectively (Figure S5 A). These studies, combined with the scope limitations (*vide supra*) and observation of ^{18}O labeling (Table 2, substrate **81**), confer confidence in the intermediacy of electrogenerated carbocation formation as postulated in Figure S5.

In addition to these probe experiments, a series of kinetic studies was undertaken on the model reaction (Figure 1C) to shed light on the rate-determining step, as well as the role of the silver additive (Figure S5 B). The reaction rate was found to be proportional to the current employed Figure S5 B, left) in the presence or absence of silver salt, indicating that a reaction occurring at the electrode is either involved in, or occurs before, the rate-determining step[1,2]. Accordingly, the rate of product formation exhibits zero-order kinetics in concentrations of both acid and alcohol substrates under the standard conditions of 10 mA current. At higher currents, the reactions on the electrode surface become fast enough, and chemical steps not associated with the electrode begin to contribute to the observed rate of product formation. Hence, at 15 mA, the reaction remains zero-order in [acid] but begins to show positive rate dependence on the concentration of alcohol (Figure S5 B, center), suggesting that carbocation capture contributes to the rate. Regarding the role of silver salt, it appears—consistent with original optimization efforts—that Ag^+ suppresses the formation of elimination (α-methylstyrene **7**) byproducts (See details below for studies investigating the role of silver in the reaction). In summary, the mechanism is likely to be the rate-limiting oxidation of a carboxylate on the anode to generate a carbocation, followed by nucleophilic attack by an alcohol to afford the ether product (Figure S5 B, right).

References:

1. Burés, J. Variable Time Normalization Analysis: General Graphical Elucidation of Reaction Orders from Concentration Profiles. *Angew. Chem. Int. Ed.* **55**, 16084–16087 (2016).

2. Peters, B. K. et al. Scalable and Safe Synthetic Organic Electroreduction Inspired by Li-ion Battery Chemistry. *Science* **363**, 838–845 (2019).

General procedure

To a 10 mL ElectraSyn vial equipped with stir bar was added 2-methyl-2-phenylpropionic acid **3** (32.8 mg, 0.2 mmol), $AgClO_4$ (anhydrous, 124 mg, 0.6 mmol), $^nBu_4NClO_4$ (103 mg, 0.3 mmol)

and 150 mg 3 Å molecular sieves (powder, flame-dried under vacuum). Dichloromethane (dry, 6 mL) was added to the vial, followed by 1-phenylethanol **4** (94 μL, 0.8 mmol) and 2,4,6-collidine (80 µL, 0.6 mmol). The vial cap, equipped with two graphite electrodes, was tightened and the mixture was subjected to 10 mA constant current conditions at a stir speed of 1000 rpm for 90 minutes during which aliquots (20 μL) were removed at indicated times.

Sample preparation

Each aliquot was injected into a filter vial housing and a solution of 4,4'-di-*tert*-butylbiphenyl in acetonitrile (0.5 mL, 1 mM) was added, the filter was inserted and the sample subjected to HPLC analysis.

Analysis

The samples were analyzed on an Agilent 1260 Infinity unit with a UV detector and an Agilent Eclipse Plus C18 column (3.5 µm, 4.6x100 mm). A method based on acetonitrile (A) and 0.1% formic acid in water (B) with a flow of 1 mL/min was used with the following gradient: 60% A for 2 min, 60-95% A over 1 minute, hold 95% A for 13 min, 95-60% A over 10 seconds, hold 60% for 4 minutes.

Data

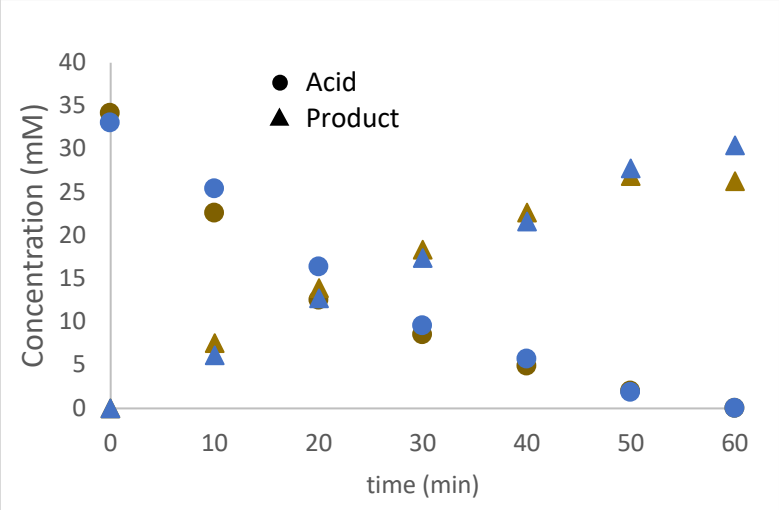


Figure S6: Good reproducibility between two different ElectraSyn Pro instruments

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 mM), 2,4,6-collidine (99.9 mM), $^{n}Bu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 15 mA constant current, graphite electrodes

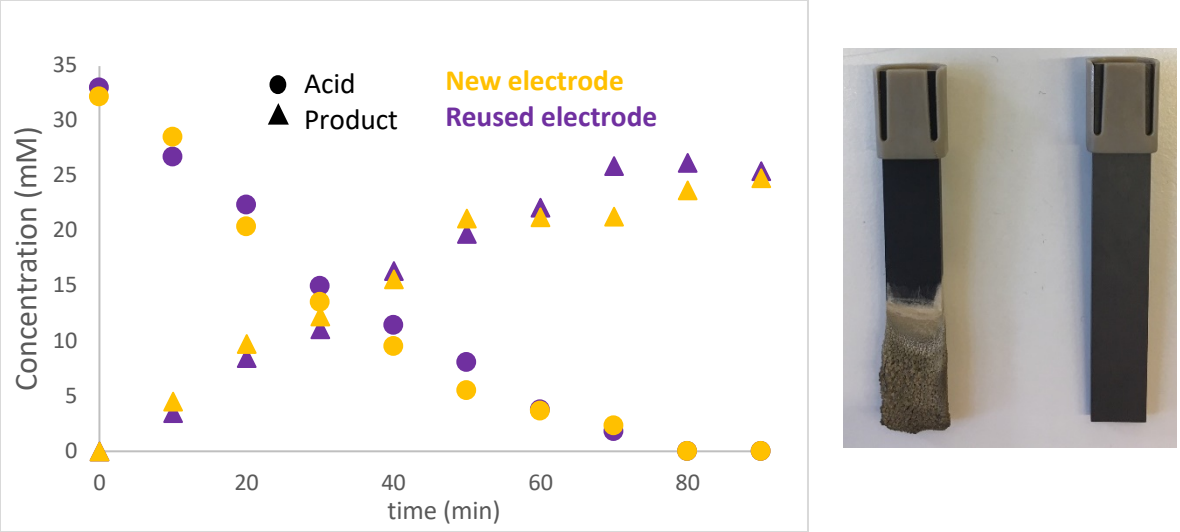


Figure S7: Good reproducibility between new and reused counter electrode (this electrode had been used in 4 reactions with Ag prior to the indicated run).

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 10 mA constant current, graphite electrodes

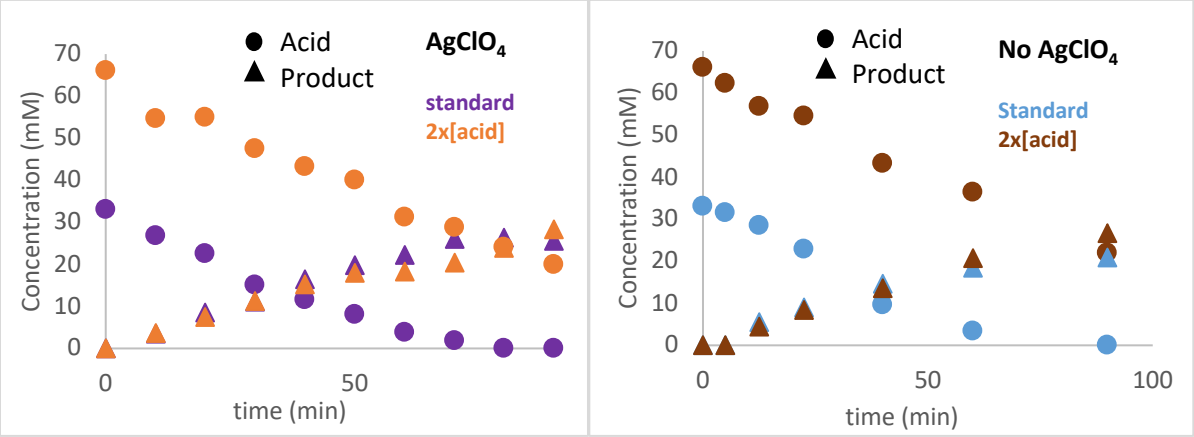


Figure S8: Zero order in [acid] at 10 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 10 mA constant current, graphite electrodes

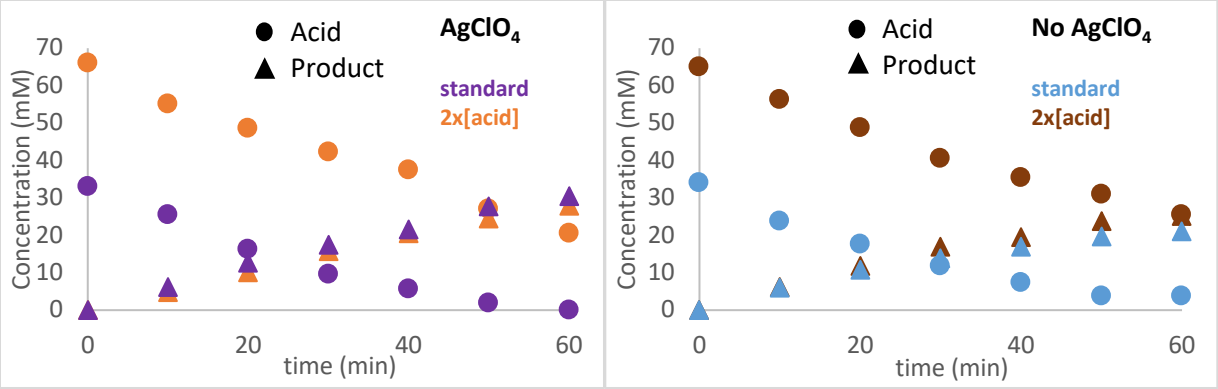


Figure S9: Zero order in [acid] at 15 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 15 mA constant current, graphite electrodes

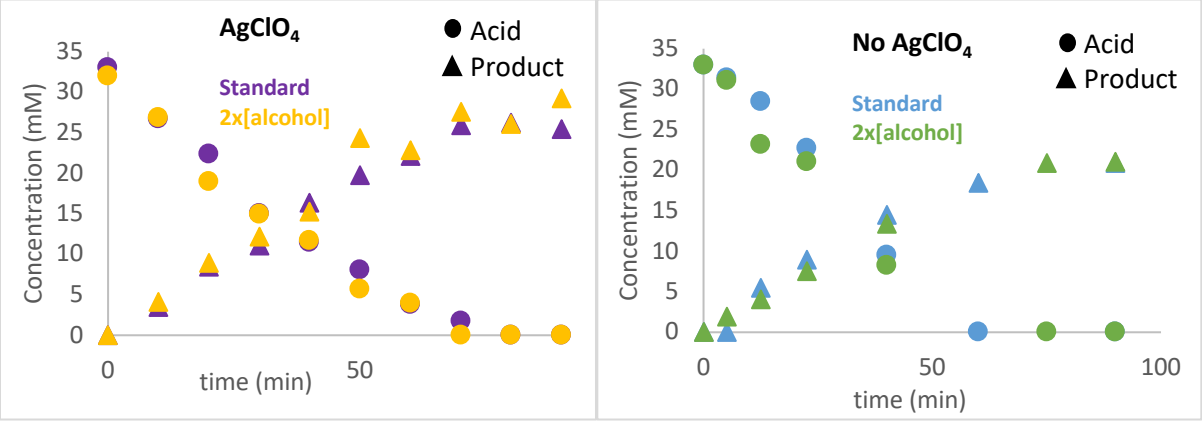


Figure S10: Zero order in [alcohol] at 10 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 10 mA constant current, graphite electrodes

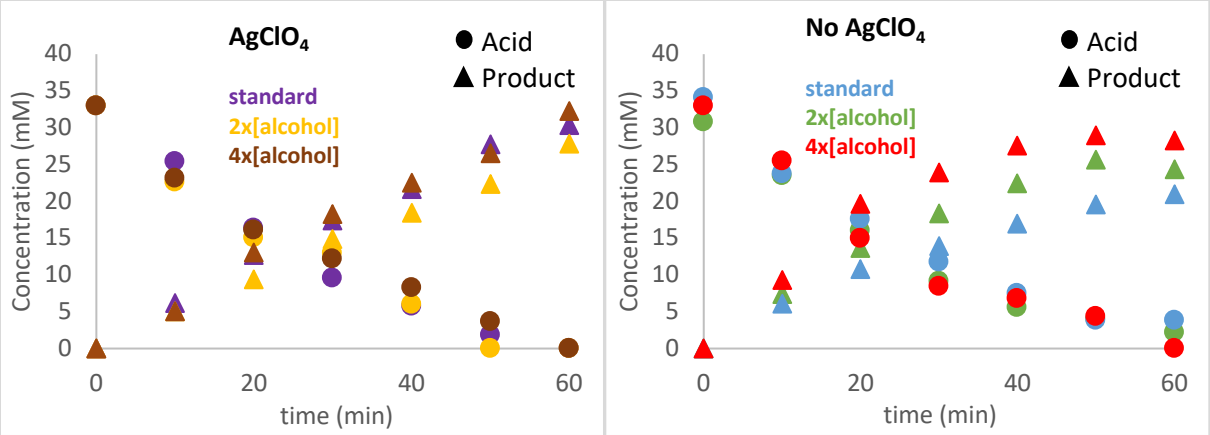


Figure S11: The effect of [alcohol] at 15 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 15 mA constant current, graphite electrodes

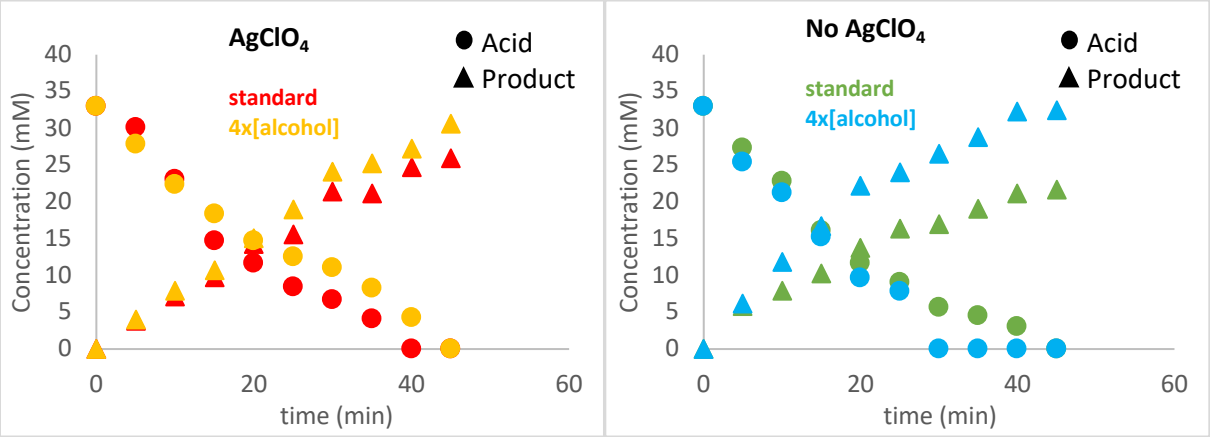


Figure S12: The effect of [alcohol] at 20 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 15 mA constant current, graphite electrodes

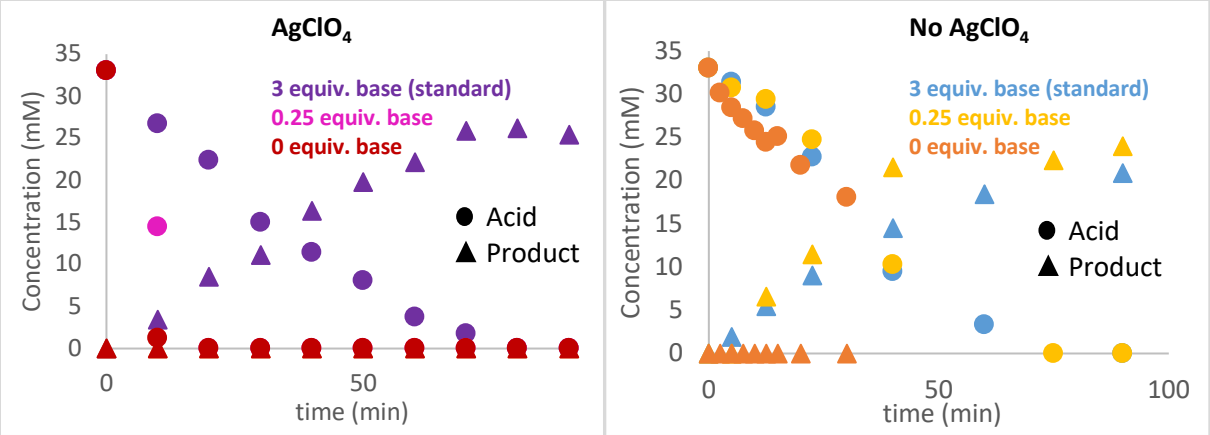


Figure S13: No product formation in absence of base and fast decomposition of acid at low [base] in the presence of Ag

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 10 mA constant current, graphite electrodes

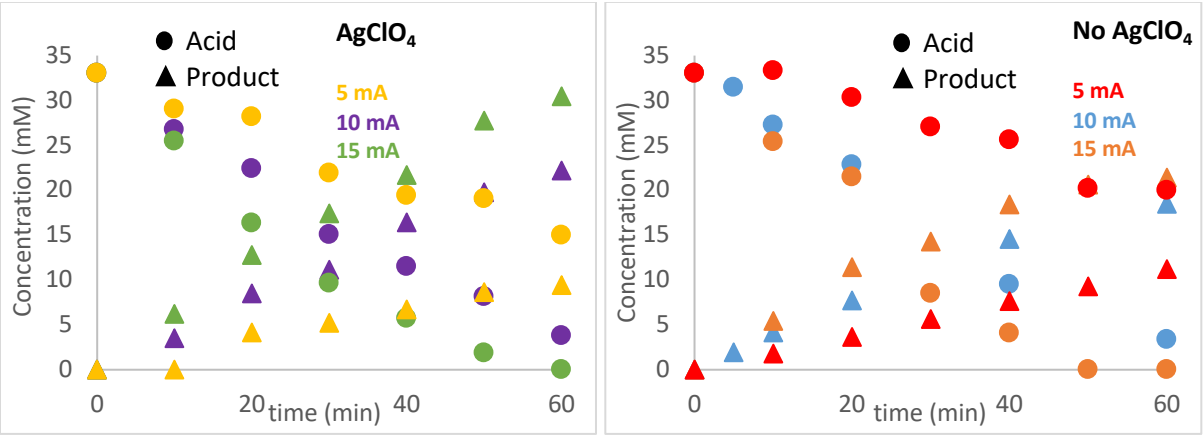


Figure S14: Increased rates with increased current

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, constant current, graphite electrodes

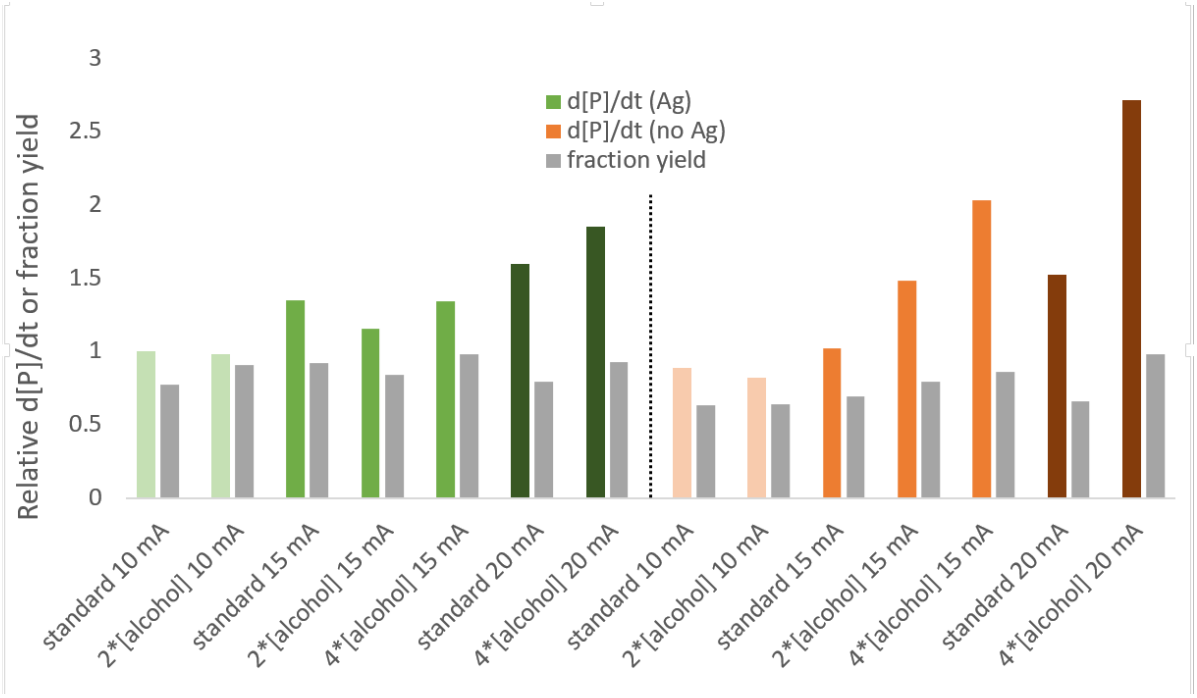


Figure S15: Relative reaction rates under different conditions (normalized to rate for standard conditions with Ag at 10 mA)

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^{n}Bu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, constant current, graphite electrodes

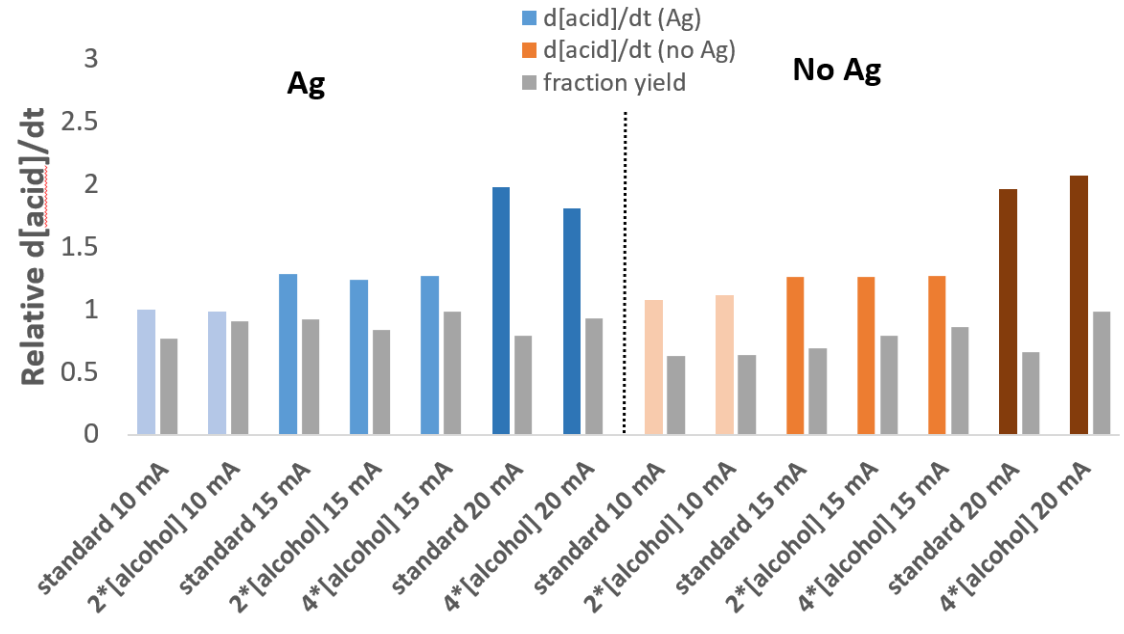


Figure S16: Relative rate of acid disappearance under different conditions (normalized to rate for standard conditions with Ag at 10 mA)

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, constant current, graphite electrodes

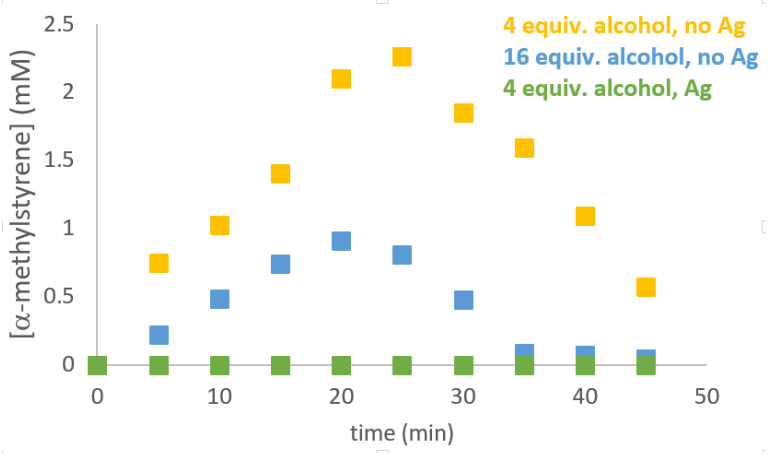


Figure S17: Concentration of α-methylstyrene over time under different conditions at 20 mA

Standard conditions: Alcohol (132 mM), acid (33 mM, 0.2 mmol), $AgClO_4$ (100 or 0 mM), 2,4,6-collidine (99.9 mM), $^nBu_4NClO_4$ (49.5 mM), 3Å MS powder (150 mg), 6 mL CH_2Cl_2 (dry), 1000 rpm, 20 mA constant current, graphite electrodes

Cyclic Voltammetry Analysis

Cyclic voltammetry was recorded with 3 mm disc glassy carbon working electrode, platinum plate counter electrode and aqueous Ag/AgCl reference electrode. Scan rate: 200 mV/s.

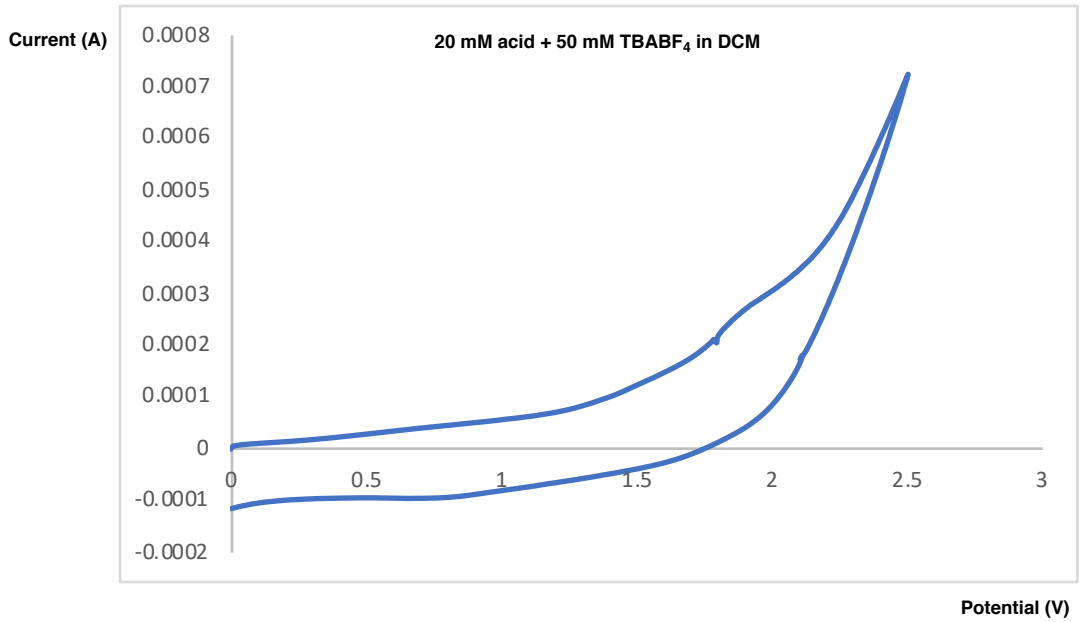


Figure S18: Cyclic voltammograms at 200 mV/s in DCM. Carboxylic acid **3** (20 mM) + $^{n}Bu_4NPF_6$ (50 mM).

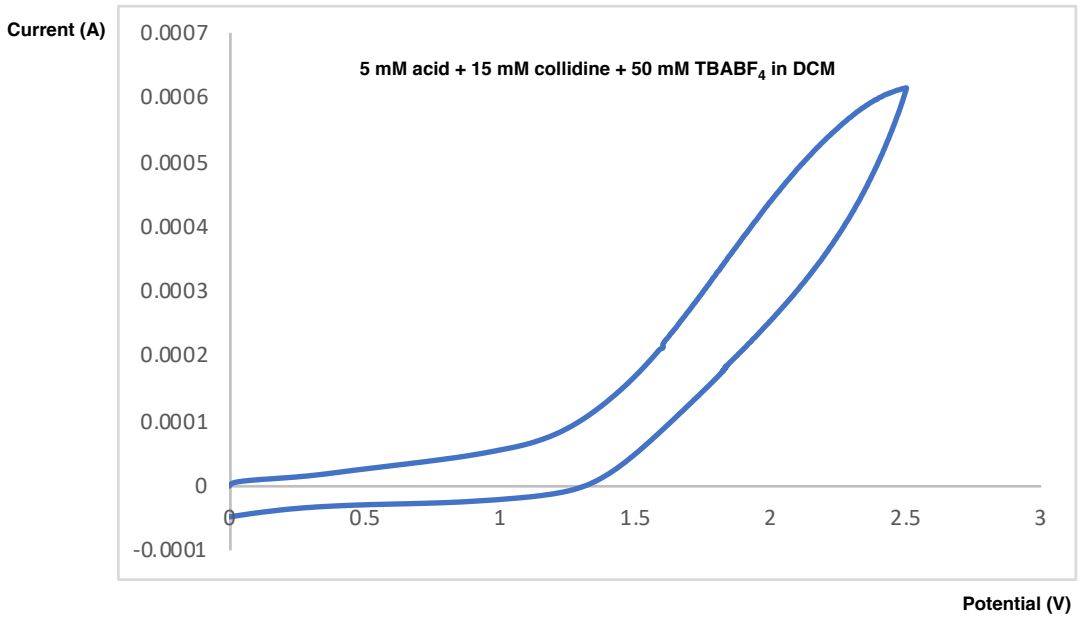


Figure S19: Cyclic voltammograms at 200 mV/s in DCM. Carboxylic acid **3** (5 mM) + 2,4,6-collidine (15 mM) + $^{n}Bu_4NPF_6$ (50 mM).

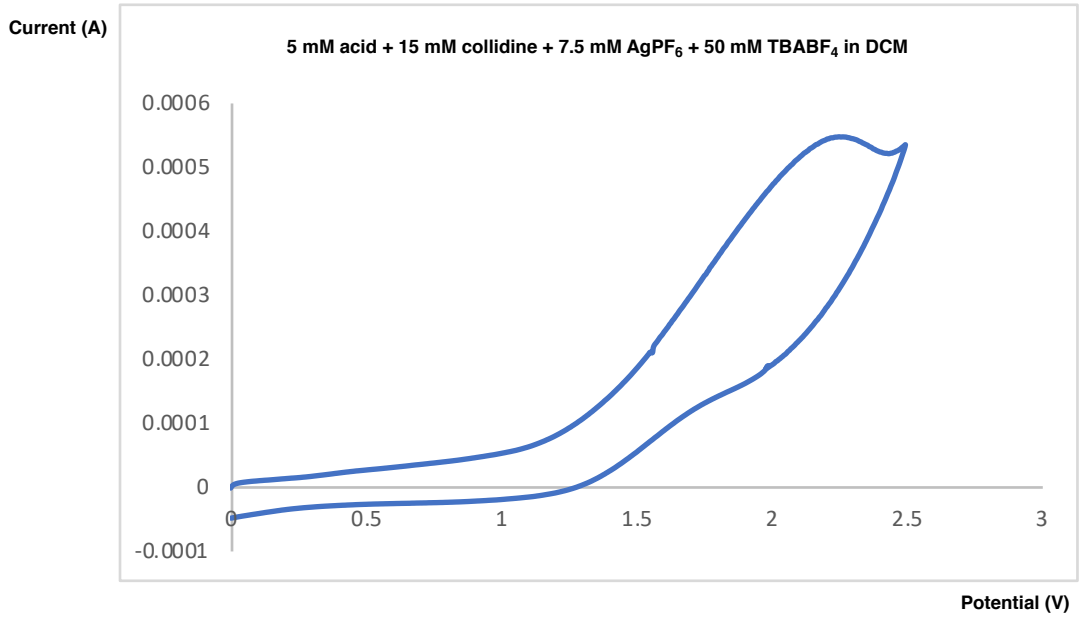


Figure S20: Cyclic voltammograms at 200 mV/s in DCM. Carboxylic acid **3** (5 mM) + 2,4,6-collidine (15 mM) + $^{n}Bu_4NPF_6$ (50 mM) + $AgPF_6$ (7.5 mM).

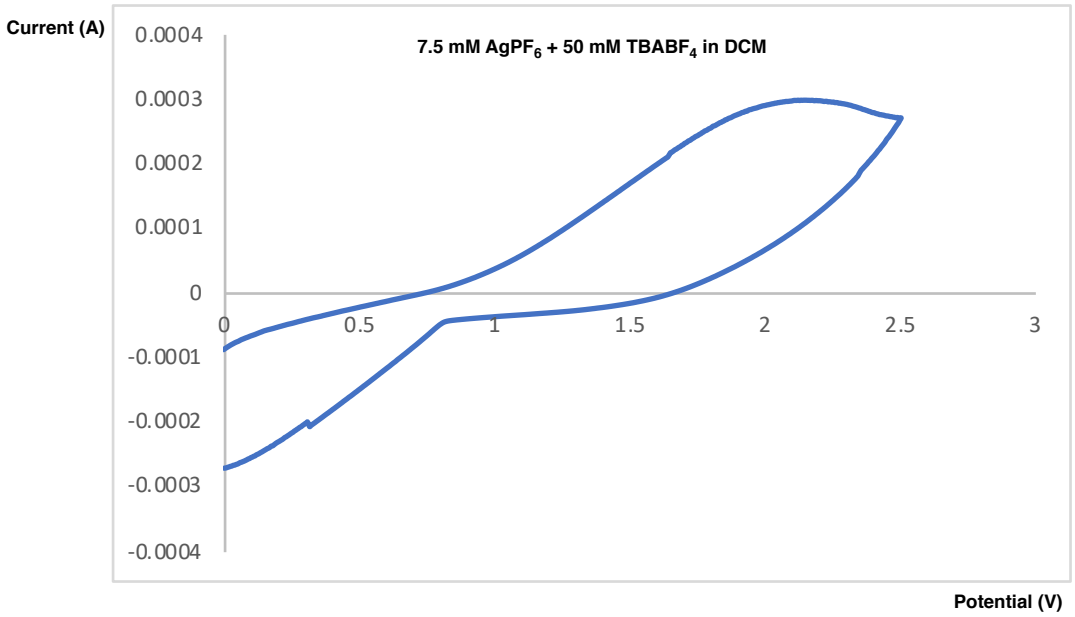
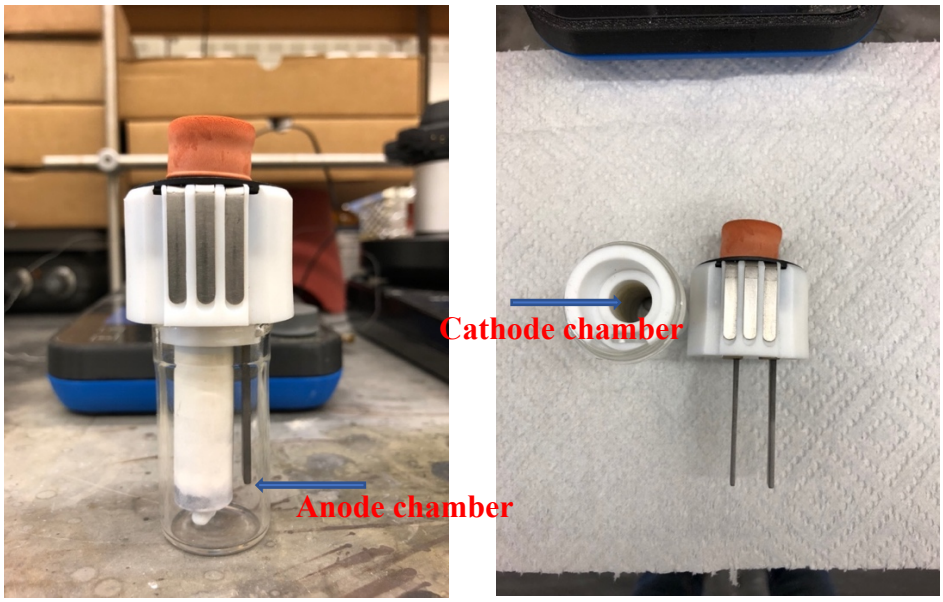


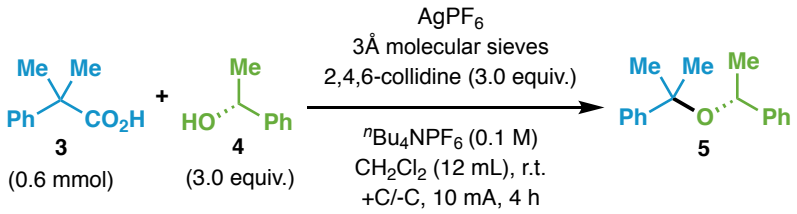
Figure S21: Cyclic voltammograms at 200 mV/s in DCM. $^{n}Bu_4NPF_6$ (50 mM) + $AgPF_6$ (7.5 mM).

Discussion: No clear oxidation of carboxylic acid **3** was observed in the absence nor presence of 2,4,6-collidine, whereas slight change of the cyclic voltammogram was indeed observed after the addition of 2,4,6-collidine. Addition of $AgPF_6$ to the mixture of acid and 2,4,6-collidine led to the appearance of a broad oxidation peak around 2.2 V. However, a similar peak was observed in

the cyclic voltammogram of $AgPF_6$ by itself, indicating that the peak is not likely to be the oxidation of carboxylic acid.

Divided Cell Experiment





Experiment with Ag additive in anodic chamber

Anodic and cathodic chamber are separated by custom-made syrindrical PTFE frit. To the anode chamber (see the picture above) was added compound **3** (66 mg, 0.4 mmol), alcohol **4** (147 mg, 1.2 mmol, 3.0 eq), 2,4,6-collidine (145 mg, 1.2 mmol, 3.0 eq), $^{n}Bu_4NPF_6$ (349 mg, 0.9 mmol), 3 Å molecular sieves (300 mg), $AgPF_6$ (152 mg, 0.3 mmol), and CH_2Cl_2 (9.0 mL). To the cathode chamber was added compound **3** (33 mg, 0.2 mmol), alcohol **4** (73 mg, 0.6 mmol, 3.0 eq), 2,4,6-collidine (73 mg, 0.6 mmol, 3.0 eq), $^{n}Bu_4NPF_6$ (116 mg, 0.3 mmol), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under a constant current at 10 mA for 4 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (3 mL), which was combined with crude mixture. Then, the combined mixture from anode and cathode chamber was further diluted with Et_2O (60 mL). The

resulting mixture was washed with 2N HCl (30 mL) and $NaHCO_3$(aq) (30 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, 50:1 Hexanes: Et_2O) afforded 104.0 mg (72%) of product **5**.

Experiment with Ag additive in cathodic chamber

To the anode chamber was added compound **3** (66 mg, 0.4 mmol), alcohol **4** (147 mg, 1.2 mmol, 3.0 eq), 2,4,6-collidine (145 mg, 1.2 mmol, 3.0 eq), $^nBu_4NPF_6$ (349 mg, 0.9 mmol), 3 Å molecular sieves (300 mg), and CH_2Cl_2 (9.0 mL). To the cathode chamber was added compound **3** (33 mg, 0.2 mmol), alcohol **4** (73 mg, 0.6 mmol, 3.0 eq), 2,4,6-collidine (73 mg, 0.6 mmol, 3.0 eq), $^nBu_4NPF_6$ (116 mg, 0.3 mmol), 3 Å molecular sieves (150 mg), $AgPF_6$ (152 mg, 0.3 mmol), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under a constant current at 10 mA for 4 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (3 mL), which was combined with crude mixture. Then, the combined mixture from anode and cathode chamber was further diluted with Et_2O (60 mL). The resulting mixture was washed with 2N HCl (30 mL) and $NaHCO_3$(aq) (30 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, 50:1 Hexanes: Et_2O) afforded 7.2 mg (5%) of product **5**.

Troubleshooting: Frequently Asked Questions

Question 1:

Are there any precautions that need to be taken for running this reaction?

Answer:

We used all the reagents without any special handling. But the 3Å molecular sieves were flame dried under vacuum for 10 min under vacuum prior to use. The reaction was performed under air without degassing, however, an empty balloon is attached for a large scale reaction of hydroxylation to balance the pressure resulting from the H_2 generation on the cathode.

Question 2:

Is stirring crucial for this reaction?

Answer:

Because the etherification reaction is heterogeneous, stirring is critical—without stirring, the potential of the reaction is high, leading to low yields. Our preferred stirring rate is from 600 to 1000 rpm.

Question 3:

What is the byproduct of this reaction?

Answer:

We have mentioned the common byproducts that we observed for etherification in the manuscript. In addition, one of the major byproducts when using difluorophenylacetic acid as electrophile is *difluoro(phenyl)methyl 2,2-difluoro-2-phenylacetate*, which is resulted from the nucleophilic attack of the difluoro-phenylacetic acid towards the corresponding carbocation.

Question 4:

What can I do if lots of starting materials remain after electrolysis?

Answer:

You can increase the reaction time, use a higher current to get a higher conversion. Alternatively, using more alcohol coupling partners such as 6 equiv. usually helps to get a better yield.

Question 5:

How do I monitor the reaction?

Answer:

We have evaluated the reaction time on the standard substrate, which indicates 3h is enough for full conversion in 0.2 mmol scale. So we chose to leave the reaction for each substrate for 3h without monitoring. But if you want to speed up the process, you can use TLC analysis with UV visualization (254 nm) to see the starting material if it is UV active and I_2 stain for non-UV active substrates.

Question 6:

Does longer reaction time cause decrease of yield?

Answer:

We left the reaction running for 6h during optimization and no significant decrease of yield was observed.

Question 7:

Are the etherification products volatile?

Answer:

Some etherification products that have low molecular weight or no functionalities are volatile. You can use Et_2O for work up and purification and keep the temperature of rotavap water bath below 30 °C.

Question 8:

How to clean up the electrodes after the reaction?

Answer:

Normally, after the reaction, you observe Ag plating on the cathode. To remove Ag plating, you can simply use a blade to scrape the graphite electrode. However, we didn't observe appreciable ill effect to the yield even without removing Ag plating.

Question 9:

This is a heterogeneous reaction. Does the yield drop in a larger scale?

Answer:

We obtained similar yield when scaling up the reaction to gram scale. Larger scale was not tested.

Question 10:

What's the limitation of current decarboxylative C-O bond forming reaction?

Answer:

"Non-activated" (we define "activated" carboxylic acids to be some acid substrates bearing stabilizing elements for the electrogenerated carbon cation such as phenyl group, N, O, Si heteroatom) primary and secondary carboxylic acids without any stabilizing effect for the corresponding carbon cation are generally not compatible probably because the electrogenerated carbocation doesn't have a high enough lifetime to be attacked by the alcohol nucleophile; instead, it undergoes elimination, rearrangement etc. Tertiary alcohols gave low yield when they coupled with tertiary carboxylic acids to generate steric hindered tertiary alkyl-alkyl ethers. Please see "**Unsuccessful or Challenging Substrates in This Study**" section (see page 35) for the problematic substrates we've tried.

Question 11: How do we choose an appropriate conditions for the synthesis of hindered ether?

Answer: General procedure A and B are differentiated by which reagents (acid or alcohol) are used as limiting reagent. The criteria for how to choose conditions is first dependent on the value of the substrates. More specifically, if the carboxylic acid is much more precious, you should choose General procedure A. As for how to choose the [Ag], based on our experience, $AgClO_4$ is suitable for benzylic carboxylic acids, while $AgSbF_6$ is preferred for non-activated carboxylic

acids. $AgPF_6$ is generally effective for all substrates, but yields are slightly lower than using $AgClO_4$ and $AgSbF_6$ respectively. We don't have a clear rule for how to choose the base, but 2,4,6-collidine is proven to be a general base for all types of substrates. Only in a few examples of non-activated carboxylic acids, we found that DBU gave better yields than 2,4,6-collidine.

Question 12: Can we use other electrodes?

Answer: Among a variety of electrodes we have tested for both cathode and anode, we found nickel foam can be used as cathode instead of graphite to give the product in a comparable yield. However, the anode selection is more narrow as we found electrodes such as Pt, RVC, glass carbon etc gave much lower yield than graphite when they were used as anode.

Question 13: How can we scale up these reactions?

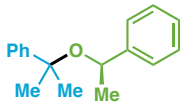
Answer: You can scale up to gram-scale for both of the etherification and hydroxylation according to the procedure we provided (pages 29–33). An even larger scale reaction hasn't been tested. For gram-scale reaction, there are some extra tricks that need to be pointed out. First, the amount of electrolyte and base can be reduced without affecting the yield. Second, we found that double the concentration actually gave a better yield compared to the small scale reaction. Third, the reaction time can be shortened.

Question 14: Why do we need a pre-stir of 15 min before starting the reaction?

Answer: We have not determined the exact role of the pre-stir; we only know for certain that it improves yields relative to omitting this step. It's possible that the pre-stir helps mitigate low kinetic solubility of the reagents, or that it gives the molecular sieves an opportunity to trap adventitious water before the reaction begins.

Experimental Procedures and Characterization Data

Compound 5



(*R*)-(2-(1-phenylethoxy)propan-2-yl)benzene

Following General Procedure **A**. Purification by flash column chromatography (silica, gradient elution, 50:1 Hexanes: Et_2O to 5:1 Hexanes: Et_2O) afforded 37.0 mg (77%) of the title compound **5** and 42.6 mg (58%) of the starting material (*R*)-1-phenylethanol **4**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.26 (m, 5H), 7.23 – 7.18 (m, 1H), 4.31 (q, *J* = 6.5 Hz, 1H), 1.52 (s, 3H), 1.38 (s, 3H), 1.33 (d, *J* = 6.5 Hz, 3H).

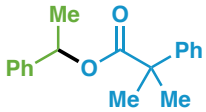
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.6, 147.0, 128.2, 128.1, 127.0, 126.6, 126.2, 125.8, 78.1, 71.9, 31.7, 27.2, 26.6.

GC/MS (EI): m/z (%) 240 (0.003%), 225 (7%), 119 (100%), 105 (100%), 91 (68%).

$[\alpha]_D^{24}$ = 153.6 (*c* = 1.0, $CHCl_3$).

TLC: R_f = 0.3 (50:1 Hexanes: Et_2O).

Compound 10



1-Phenylethyl 2-methyl-2-phenylpropanoate[1]

Following General Procedure **A**, no 2,4,6-collidine. Purification by PTLC (silica, 8:1 Hexanes: Et_2O) afforded 29.0 mg (54%) of the title compound **10**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.21 (m, 8H), 7.19 – 7.14 (m, 2H), 5.86 (q, *J* = 6.6 Hz, 1H), 1.61 (s, 3H), 1.58 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 175.9, 144.7, 141.9, 128.5, 128.4, 127.7, 126.7, 125.90, 125.87, 72.6, 46.7, 26.6, 26.5, 22.3.

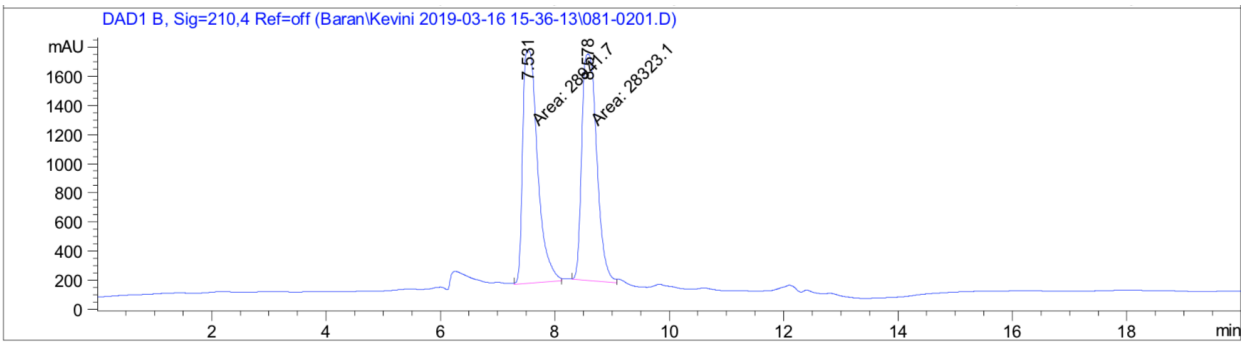
TLC: R_f = 0.40 (8:1 Hexanes:Et_2O).

Note: when using **(*R*)-1-phenylethan-1-ol** as the nucleophile, the product **7** was isolated as racemic (er = 50:50).

Chiral HPLC: Chiralpak IA 4.6 x 250 mm; 5:95 *i*-PrOH : Hexanes, 0.5 mL/min, 212 nm; t_R (minor) = 7.5 min, t_R (major) = 8.5 min, 50:50 er.

(*rac*)-1-phenylethan-1-ol as the nucleophile

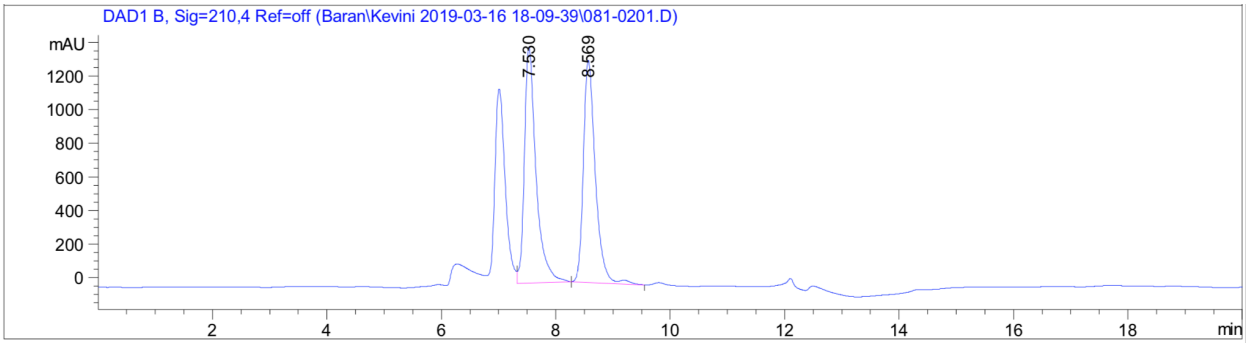
[3] März, M. et al. Azodicarboxylate-free Esterification with Triphenylphosphine Mediated by Flavin and Visible Light: Method Development and Stereoselectivity Control. *Org. Biomol. Chem.*, **16**, 6809–6817 (2018).



Signal 2: DAD1 B, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.531	MM	0.3014	2.89417e4	1600.47656	50.5401
2	8.578	MM	0.3041	2.83231e4	1552.33069	49.4599

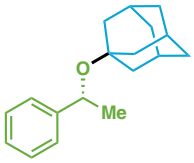
(*R*)-1-phenylethan-1-ol as the nucleophile



Signal 2: DAD1 B, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.530	VB	0.2111	1.98400e4	1402.32031	50.8606
2	8.569	BV R	0.2147	1.91686e4	1321.73340	49.1394

Compound 16



1-((*R*)-1-phenylethoxy)adamantane

Following General Procedure **A**. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 33.4 mg (65%) of the title compound **16**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 4.83 (q, *J* = 6.5 Hz, 1H), 2.08 (s, 3H), 1.72 (q, *J* = 11.5 Hz, 6H), 1.59 – 1.55 (m, 6H), 1.37 (d, *J* = 6.6 Hz, 3H).

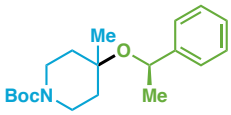
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 128.2, 126.6, 125.7, 73.6, 67.9, 42.7, 36.6, 30.7, 26.9.

GC/MS (EI): m/z (%) 256 (0.03%), 241 (17%), 135 (100%), 105 (89%), 95 (23%).

TLC: R_f = 0.4 (30:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 58.0 (*c* = 0.33, $CHCl_3$).

Compound 17



***tert*-butyl (*R*)-4-methyl-4-(1-phenylethoxy)piperidine-1-carboxylate**

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 28.7 mg (45%) of the title compound **17**.

Physical State: colorless oil.

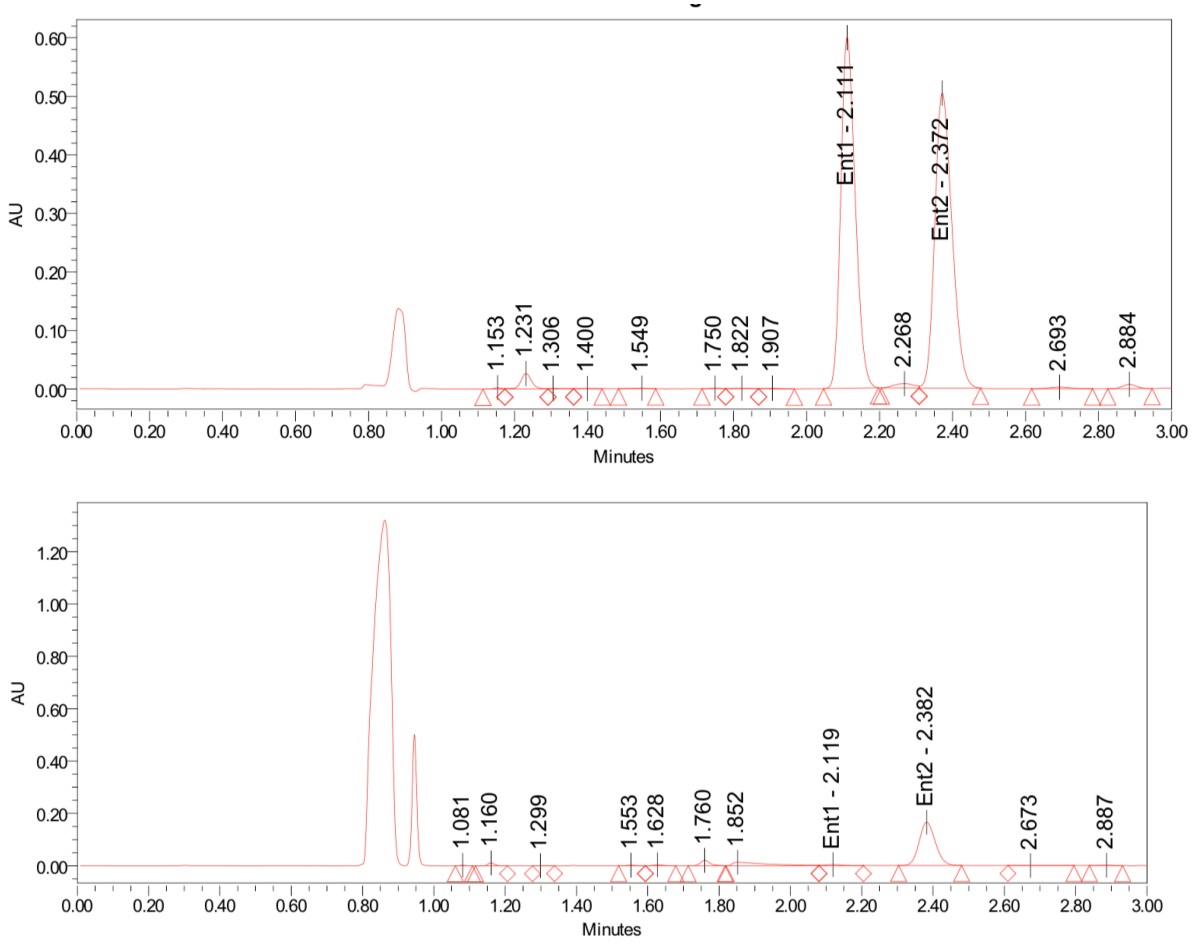
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 3H), 7.24 – 7.19 (m, 1H), 4.61 (q, *J* = 6.5 Hz, 1H), 3.69 (s, 1H), 3.49 (s, 1H), 3.25 (t, *J* = 12.5 Hz, 1H), 2.95 (s, 1H), 1.80 (d, *J* = 13.7 Hz, 1H), 1.63 (d, *J* = 14.0 Hz, 1H), 1.44 – 1.40 (m, 10H), 1.37 (d, *J* = 6.5 Hz, 3H), 1.36 – 1.31 (m, 1H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.0, 147.1, 128.4, 126.9, 125.8, 79.3, 73.3, 69.8, 40.0, 36.6, 28.6, 26.9, 26.0.

HRMS (ESI-TOF): calc'd for $C_{19}H_{29}NNaO_3$ $[M + Na]^+$: 342.2040; found 342.2044.

TLC: R_f = 0.63 (3:1 Hexanes: EtOAc).

Chiral HPLC: Chiralpak IG 4.6 x 250 mm; 5% MeOH/CO_2, 0.5 mL/min, 212 nm; t_R (minor) = 2.11 min, t_R (major) = 2.37 min, 95% *ee*.



SAMPLE INFORMATION

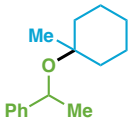
Sample Name:	ms-1-rac, ms-1-chiral	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	Samples_SFC
Vial:	1:A,7, 1:A,8	Acq. Method Set:	G_BAR0275
Injection #:	1	Processing Method	BAR0275
Injection Volume:	2.00 ul	Channel Name:	212nm
Run Time:	3.0 Minutes	Proc. Chnl. Descr.:	PDA Spectrum PDA 212.0 nm

Date Acquired:	3/5/2019 10:14:27 AM PST, 3/5/2019 10:18:22 AM PST
Date Processed:	3/5/2019 10:17:31 AM PST, 3/5/2019 10:21:26 AM PST

Area Summarized by Name

ms-1-rac	49.89	50.11	-0.21	1644012	1650977
ms-1-chiral	2.36	97.64	-95.28	12543	519472

Compound 18



(1-((1-methylcyclohexyl)oxy)ethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 23.6 mg (54%) of the title compound **18**.

Physical State: colorless oil.

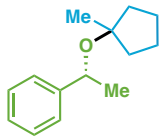
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.35 (m, 2H), 7.32 – 7.28 (m, 2H), 7.22 – 7.19 (m, 1H), 4.66 (q, *J* = 6.5 Hz, 1H), 1.78 – 1.71 (m, 1H), 1.69 – 1.57 (m, 3H), 1.48 – 1.35 (m, 5H), 1.33 – 1.22 (m, 4H), 1.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 128.2, 126.6, 125.9, 75.3, 69.1, 37.7, 37.3, 27.0, 26.0, 25.8, 22.8, 22.6.

GC/MS (EI): m/z 218 (0.5%), 203 (2%), 105 (100%), 77 (15%).

TLC: R_f = 0.56 (20:1 Hexanes: Et_2O).

Compound 19



(*R*)-(1-((1-methylcyclopentyl)oxy)ethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 16.3 mg (40%) of the title compound **19**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 (d, *J* = 6.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 4.59 (q, *J* = 6.6 Hz, 1H), 1.93 – 1.86 (m, 1H), 1.81 – 1.69 (m, 2H), 1.63 – 1.54 (m, 2H), 1.53 – 1.42 (m, 2H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.36 – 1.28 (m, 1H), 1.21 (s, 3H).

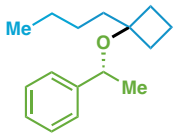
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.6, 128.2, 126.6, 125.7, 85.8, 71.0, 39.1, 38.6, 26.9, 25.0, 24.1, 23.9.

GC/MS (EI): m/z (%) 204 (0.9%), 105 (100%), 99 (3%), 83 (4%), 77 (13%).

TLC: R_f = 0.3 (30:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 57.1 (*c* = 1.0, $CHCl_3$).

Compound 20



(*R*)-(1-(1-butylcyclobutoxy)ethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (pure Hexanes) afforded 24.0 mg (52%) of the title compound **20**.

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 4.52 (q, *J* = 6.5 Hz, 1H), 2.09 (q, *J* = 10.1 Hz, 1H), 1.99 (q, *J* = 10.2 Hz, 1H), 1.91 – 1.82 (m, 1H), 1.76 – 1.69 (m, 1H), 1.69 – 1.61 (m, 2H), 1.56 – 1.43 (m, 2H), 1.40 (d, *J* = 6.5 Hz, 3H), 1.37 – 1.24 (m, 2H), 1.24 – 1.11 (m, 2H), 0.85 (t, *J* = 7.0 Hz, 3H).

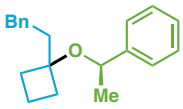
^{13}C NMR (151 MHz, $CDCl_3$): δ 146.8, 128.3, 126.9, 126.1, 80.2, 70.9, 36.7, 33.0, 32.6, 26.0, 25.5, 23.2, 14.2, 13.2.

GC/MS (EI): m/z (%) 232 (0.005%), 127 (4%), 105 (100%), 85 (3%), 77 (8%).

TLC: R_f = 0.4 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 52.4 (*c* = 1.0, $CHCl_3$).

Compound 21



(*R*)-((1-(1-phenethylcyclobutoxy)ethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.) instead of $AgPF_6$. Purification by PTLC (pure Hexanes) afforded 23.0 mg (41%) of the title compound **21**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 7.4 Hz, 2H), 4.57 (q, *J* = 6.5 Hz, 1H), 2.62 (td, *J* = 13.0, 4.8 Hz, 1H), 2.50 (td, *J* = 13.0, 4.8 Hz, 1H), 2.17 (q, *J* = 10.0 Hz, 1H), 2.07 (q, *J* = 10.0 Hz, 1H), 1.97 – 1.80 (m, 4H), 1.77 – 1.67 (m, 1H), 1.55 – 1.49 (m, 1H), 1.45 (d, *J* = 6.5 Hz, 3H).

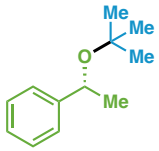
^{13}C NMR (151 MHz, $CDCl_3$): δ 146.6, 143.0, 128.5, 128.5, 128.4, 127.1, 126.2, 125.7, 80.1, 71.3, 39.3, 32.9, 32.6, 30.0, 26.2, 13.2.

GC/MS (EI): m/z (%) 175 (2%), 130 (5%), 105 (100%), 91 (27%), 77 (14%).

TLC: R_f = 0.3 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 55.5 (*c* = 1.0, $CHCl_3$).

Compound 22



(*R*)-(1-(*tert*-butoxy)ethyl)benzene

Following General Procedure **B**. Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 16.4 mg (61%) of the title compound **22**.

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 4.66 (q, *J* = 6.5 Hz, 1H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.16 (s, 9H).

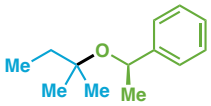
^{13}C NMR (126 MHz, $CDCl_3$): δ 147.7, 128.2, 126.6, 125.7, 74.3, 70.0, 28.7, 26.9.

GC/MS (EI): m/z (%) 178 (0.07%), 163 (30%), 105 (100%), 77 (20%), 57 (30%).

TLC: R_f = 0.4 (Hexanes).

$[\alpha]_D^{24}$ = 65.8 (*c* = 1.0, $CHCl_3$).

Compound 23



(*R*)-(1-(*tert*-pentyloxy)ethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.) instead of $AgPF_6$. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 23.8 mg (62%) of the title compound **23**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 – 7.33 (m, 2H), 7.32 – 7.27 (m, 2H), 7.20 (ddt, *J* = 7.7, 6.7, 1.3 Hz, 1H), 4.64 (q, *J* = 6.5 Hz, 1H), 1.60 – 1.53 (m, 1H), 1.49 – 1.42 (m, 1H), 1.36 (d, *J* = 6.5 Hz, 3H), 1.10 (s, 3H), 1.05 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H).

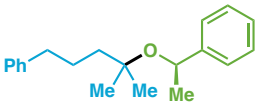
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 128.2, 126.6, 125.7, 76.5, 69.6, 34.2, 26.9, 26.1, 25.8, 8.8.

GC/MS (EI): m/z (%) 177 (1%), 163 (8%), 105 (100%), 77 (13%).

TLC: R_f = 0.50 (20:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = +282.7 (*c* = 1.0, $CHCl_3$).

Compound 24



(*R*)-(4-methyl-4-(1-phenylethoxy)pentyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (pure Hexanes) afforded 19.7 mg (35%) of the title compound **24**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.26 (m, 6H), 7.24 – 7.16 (m, 2H), 7.14 (d, *J* = 7.4 Hz, 2H), 4.61 (q, *J* = 6.4 Hz, 1H), 2.57 – 2.47 (m, 2H), 1.68 – 1.53 (m, 3H), 1.51 – 1.44 (m, 1H), 1.35 (d, *J* = 6.5 Hz, 3H), 1.09 (d, *J* = 20.4 Hz, 6H).

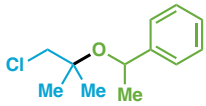
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.7, 142.9, 128.6, 128.4, 128.2, 126.6, 125.8, 125.7, 69.8, 41.4, 36.6, 26.9, 26.5, 26.5, 26.3.

GC/MS (EI): m/z (%) 177 (3%), 159 (9%), 105 (100%), 91 (31%), 77(13%).

TLC: R_f = 0.3 (Hexanes).

$[\alpha]_D^{24}$ = 34.9 (*c* = 1.0, $CHCl_3$).

Compound 25



(1-((1-chloro-2-methylpropan-2-yl)oxy)ethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, the amount of alcohol was 4 equiv., 1.5 mL CH_2Cl_2, I = 7.5 mA, 4 h. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 18.5 mg (43%) of the title compound **25**.

Physical State: colorless oil.

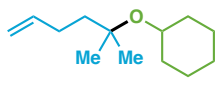
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 – 7.28 (m, 4H), 7.22 (ddt, *J* = 7.6, 6.6, 1.5 Hz, 1H), 4.69 (q, *J* = 6.5 Hz, 1H), 3.49 (d, *J* = 11.1 Hz, 1H), 3.38 (d, *J* = 11.1 Hz, 1H), 1.40 (d, *J* = 6.5 Hz, 3H), 1.23 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 146.9, 128.4, 127.0, 125.7, 76.1, 70.8, 52.7, 26.7, 24.7, 24.4.

GC/MS (EI): m/z (%) 197 (5%), 163 (4%), 105 (100%), 77 (22%).

TLC: R_f = 0.47 (20:1 Hexanes: Et_2O).

Compound 26



((2-methylhex-5-en-2-yl)oxy)cyclohexane

Following General Procedure **A** using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively and the amount of alcohol was 6 equiv. Purification by PTLC (50:1 Hexanes: EtOAc) afforded 16.8 mg (43%) of the title compound **26**.

Physical State: colorless oil.

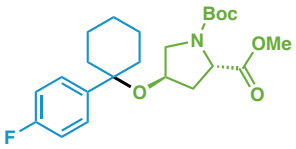
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.84 (ddt, *J* = 16.8, 9.8, 6.6 Hz, 1H), 5.01 (d, *J* = 17.1 Hz, 1H), 4.92 (d, *J* = 10.2 Hz, 1H), 3.39 – 3.28 (m, 1H), 2.11 (q, *J* = 7.5 Hz, 2H), 1.78 – 1.69 (m, 4H), 1.55 – 1.50 (m, 3H), 1.25 (t, *J* = 7.4 Hz, 4H), 1.15 (s, 6H), 1.13 – 1.08 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 139.5, 114.0, 75.0, 69.9, 40.8, 35.7, 28.8, 26.4, 25.8, 25.2.

GC/MS (EI): m/z (%) 181 (0.2%), 141 (18%), 97 (16%), 81 (12%), 59 (100%).

TLC: R_f = 0.3 (50:1 Hexanes: EtOAc).

Compound 27



1-(*tert*-butyl) 2-methyl (2*S*,4*R*)-4-((1-(4-fluorophenyl)cyclohexyl)oxy)pyrrolidine-1,2-dicarboxylate

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (3:1 Hexanes: EtOAc) afforded 39.0 mg (46%) of the title compound **27**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for two rotamers): δ 7.38 – 7.35 (m, 2H), 7.03 – 6.99 (m, 2H), 4.33 – 4.22 (m, 1H), 3.86 – 3.79 (m, 1H), 3.64 (s, 1.21H), 3.62 (s, 1.75H), 3.45 – 3.30 (m, 1H), 3.22 – 3.11 (m, 1H), 2.16 – 1.96 (m, 3H), 1.84 – 1.57 (m, 6H), 1.57 – 1.49 (m, 2H), 1.42 (s, 3.47H), 1.37 (s, 5.82H), 1.30 – 1.20 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$, for two rotamers): δ 173.6, 173.4, 162.89, 162.87, 161.3, 161.2, 154.5, 153.7, 141.53, 141.45, 128.20, 128.15, 115.21, 115.16, 115.1, 115.0, 80.14, 80.11, 77.8, 77.6, 70.3, 69.5, 57.8, 57.4, 52.4, 52.24, 52.21, 52.0, 37.8, 37.1, 36.5, 36.2, 36.1, 28.5, 28.4, 25.7, 22.42, 22.36.

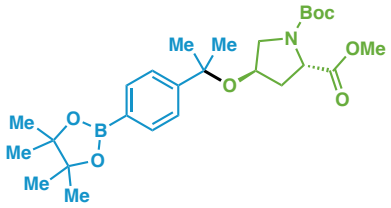
^{19}F NMR (376 MHz, $CDCl_3$, for two rotamers): δ -115.57, -115.67.

HRMS (ESI-TOF): calc'd for $C_{23}H_{32}FNO_5Na$ $[M + Na]^+$: 444.2157; found 444.2165.

TLC: R_f = 0.49 (3:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = -3.5 (*c* = 1.0, $CHCl_3$).

Compound 28



1-(*tert*-butyl) 2-methyl (2*S*,4*R*)-4-((2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) propan-2-yl)oxy)pyrrolidine-1,2-dicarboxylate

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (3:1 Hexanes: EtOAc) afforded 52.9 mg (54%) of the title compound **28**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for two rotamers): δ 7.79 – 7.77 (m, 2H), 7.46 – 7.35 (m, 2H), 4.39 – 4.30 (m, 1H), 4.03 – 3.85 (m, 1H), 3.66 (s, 0.93H), 3.65 (s, 1.75H), 3.60 – 3.51 (m, 1H), 3.37 – 3.23 (m, 1H), 2.28 – 2.12 (m, 1H), 1.99 – 1.94 (m, 1H), 1.54 – 1.49 (m, 6H), 1.44 (s, 4H), 1.39 (s, 5H), 1.34 (s, 12H).

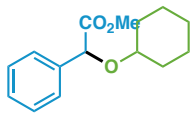
^{13}C NMR (151 MHz, $CDCl_3$, for two rotamers): δ 173.7, 173.4, 154.5, 153.8, 149.6, 149.5, 135.0, 125.32, 125.28, 84.0, 83.9, 80.2, 78.1, 77.9, 71.3, 70.5, 58.0, 57.6, 53.2, 53.1, 52.3, 52.1, 38.3, 37.4, 29.5, 29.1, 28.9, 28.5, 28.4, 25.02, 24.99, 24.97.

HRMS (ESI-TOF): calc'd for $C_{26}H_{40}BNO_7Na$ $[M + Na]^+$: 511.2826; found 511.2841.

TLC: R_f = 0.39 (3:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = +10.2 (*c* = 1.0, $CHCl_3$).

Compound 29



methyl 2-(cyclohexyloxy)-2-phenylacetate

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively and the amount of alcohol was 6 equiv. Purification by PTLC (50:1 Hexanes: EtOAc) afforded 20.4 mg (41%) of the title compound **29**.

Physical State: colorless oil.

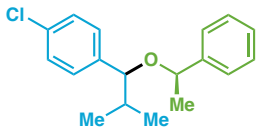
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.33 – 7.30 (m, 1H), 5.05 (s, 1H), 3.71 (s, 3H), 3.35 (td, *J* = 9.7, 9.3, 4.5 Hz, 1H), 1.98 (d, *J* = 11.4 Hz, 1H), 1.88 (d, *J* = 11.9 Hz, 1H), 1.80 – 1.67 (m, 2H), 1.52 (s, 1H), 1.46 – 1.35 (m, 2H), 1.26 – 1.16 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 172.2, 137.5, 128.7, 128.5, 127.2, 78.2, 52.4, 32.3, 32.3, 25.8, 24.3.

GC/MS (EI): m/z (%) 248 (0.02%), 189 (30%), 121 (11%), 107 (100%), 55 (11%).

TLC: R_f = 0.3 (50:1 Hexanes: EtOAc).

Compound 30



1-chloro-4-((1*R*)-2-methyl-1-(1-phenylethoxy)propyl)benzene

Following General Procedure **A**, Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 42.5 mg (74%) of the title compound **30**.

Physical State: colorless oil.

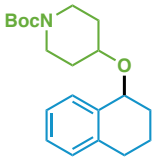
^{1}H NMR (600 MHz, $CDCl_3$, for both diastereomers) (the integration at 4.10 ppm, 3.67 ppm indicated the ratio of the two isomers of **30** to be 1:1): δ 7.38 – 7.26 (m, 5H), 7.26 – 7.24 (m, 4H), 7.24 – 7.19 (m, 5H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 4.35 (q, *J* = 6.3 Hz, 1H), 4.14 (q, *J* = 6.5 Hz, 1H), 4.10 (d, *J* = 6.9 Hz, 1H), 3.67 (d, *J* = 7.6 Hz, 1H), 1.98 – 1.91 (m, 1H), 1.90 – 1.82 (m, 1H), 1.43 (d, *J* = 6.4 Hz, 3H), 1.37 (d, *J* = 6.5 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.62 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, for both diastereomers): δ 144.5, 143.8, 140.5, 133.1, 132.8, 129.1, 128.9, 128.5, 128.4, 128.2, 128.1, 128.0, 127.6, 127.1, 126.9, 126.2, 84.4, 83.6, 75.1, 74.7, 34.9, 34.9, 24.6, 22.1, 19.4, 19.1, 18.9.

GC/MS (EI): m/z (%) 288 (0.02%), 247 (2%), 245 (7%), 125 (8%), 105 (21%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 31



***tert*-butyl 4-((1,2,3,4-tetrahydronaphthalen-1-yl)oxy)piperidine-1-carboxylate**

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (4:1 Hexanes: EtOAc) afforded 45.1 mg (68%) of the title compound **31**.

Physical State: colorless oil.

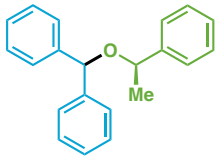
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.31 (m, 1H), 7.19 – 7.14 (m, 2H), 7.10 – 7.06 (m, 1H), 4.53 (t, J = 5.1 Hz, 1H), 3.82 (s, 2H), 3.73 (tt, J = 8.1, 3.7 Hz, 1H), 3.19 – 3.07 (m, 2H), 2.83 (dt, J = 16.7, 5.9 Hz, 1H), 2.71 (ddd, J = 16.7, 7.9, 5.7 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.94 – 1.91 (m, 2H), 1.84 (s, 1H), 1.75 – 1.71 (m, 1H), 1.67 – 1.56 (m, 3H), 1.46 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.0, 137.6, 137.5, 129.1, 127.5, 126.0, 79.6, 72.9, 72.7, 41.4, 32.8, 31.0, 29.3, 29.2, 28.6, 19.2.

HRMS (ESI-TOF): calc'd for $C_{20}H_{29}NO_3Na$ $[M + Na]^+$: 354.2040; found 354.2043.

TLC: R_f = 0.58 (3:1 Hexanes: EtOAc).

Compound 32



((*R*)-((1-phenylethoxy)methylene)dibenzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (50:1 Hexanes: Et_2O) afforded 46.1 mg (80%) of the title compound **32**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.26 (m, 14H), 7.23 – 7.17 (m, 1H), 5.26 (s, 1H), 4.46 (q, J = 6.5 Hz, 1H), 1.49 (d, J = 6.5 Hz, 3H).

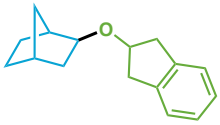
^{13}C NMR (151 MHz, $CDCl_3$): δ 143.8, 143.0, 142.2, 128.6, 128.6, 128.3, 127.7, 127.7, 127.6, 127.2, 127.1, 126.7, 80.1, 75.1, 24.4.

GC/MS (EI): m/z (%) 288 (0.004%), 183 (80%), 167 (100%), 105 (85%), 77 (27%).

TLC: R_f = 0.3 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 79.9 (*c* = 1.0, $CHCl_3$).

Compound 33



2-((bicyclo[2.2.1]heptan-2-yl)oxy)-2,3-dihydro-1*H*-indene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (20:1 Hexanes: Et_2O) afforded 26.0 mg (57%) of the title compound **33**.

Physical State: colorless oil.

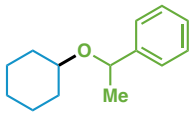
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21 – 7.18 (m, 2H), 7.16 – 7.13 (m, 2H), 4.39 (tt, *J* = 6.9, 5.7 Hz, 1H), 3.51 (dt, *J* = 7.0, 1.7 Hz, 1H), 3.15 (ddd, *J* = 15.9, 13.0, 6.8 Hz, 2H), 2.94 (ddd, *J* = 16.1, 10.8, 5.7 Hz, 2H), 2.33 (d, *J* = 4.9 Hz, 1H), 2.27 – 2.20 (m, 1H), 1.63 – 1.54 (m, 2H), 1.51 (tdd, *J* = 12.1, 4.9, 3.4 Hz, 1H), 1.47 – 1.37 (m, 2H), 1.10 (ddq, *J* = 9.7, 2.9, 1.5 Hz, 1H), 1.08 – 0.97 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 141.3, 141.2, 126.5, 124.8, 124.8, 81.1, 78.0, 41.0, 40.1, 40.1, 39.8, 35.3, 35.0, 28.7, 24.9.

GC/MS (EI): m/z (%) 228 (5%), 117 (67%), 95 (100%), 67 (13%).

TLC: R_f = 0.47 (20:1 Hexanes: Et_2O).

Compound 34



(1-(cyclohexyloxy)ethyl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 20:1 Hexanes: Et_2O) afforded 2.9 mg (7%) of the title compound **34**.

Physical State: colorless oil.

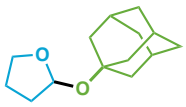
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33– 7.32 (m, 4H), 7.27 – 7.23 (m, 1H), 4.59 (q, *J* = 6.5 Hz, 1H), 3.16 (tt, *J* = 9.7, 3.9 Hz, 1H), 1.97 (d, *J* = 12.4 Hz, 1H), 1.78 – 1.64 (m, 3H), 1.54 – 1.48 (m, 1H), 1.40 (d, *J* = 6.5 Hz, 3H), 1.34 – 1.24 (m, 2H), 1.21 – 1.10 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.3, 128.4, 127.2, 126.2, 75.0, 74.4, 33.6, 32.0, 26.0, 25.0, 24.6, 24.4.

GC/MS (EI): m/z (%) 204 (0.01%), 189 (21%), 105 (100%), 99 (7%), 77 (13%).

TLC: R_f = 0.42 (20:1 Hexanes: Et_2O).

Compound 35



2-((adamantan-1-yl)oxy)tetrahydrofuran

Following General Procedure **A**. Purification by PTLC (silica, 50:1 Hexanes: EtOAc) afforded 25.8 mg (58%) of the title compound **35**.

Physical State: colorless oil.

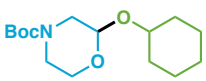
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.54 (dd, *J* = 5.5, 1.8 Hz, 1H), 3.94 (q, *J* = 7.7 Hz, 1H), 3.78 (td, *J* = 7.8, 5.4 Hz, 1H), 2.12 (s, 3H), 2.03 – 1.96 (m, 1H), 1.96 – 1.88 (m, 1H), 1.86 – 1.74 (m, 8H), 1.64 – 1.59 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 97.4, 73.3, 66.7, 43.0, 36.5, 33.6, 30.8, 24.1.

GC/MS (EI): m/z (%) 222 (0.1%), 152 (28%), 135 (48%), 95 (100%), 71 (21%).

TLC: R_f = 0.2 (50:1 Hexanes: EtOAc).

Compound 36



***tert*-butyl 2-(cyclohexyloxy)morpholine-4-carboxylate**

Following General Procedure **A**. Purification by PTLC (silica, 6:1 Hexanes: EtOAc) afforded 31.4 mg (55%) of the title compound **36**.

Physical State: colorless oil.

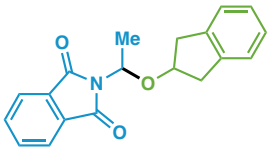
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.63 (s, 1H), 3.93 (s, 1H), 3.75 – 3.56 (m, 2H), 3.52 – 3.44 (m, 2H), 3.39 – 2.93 (m, 2H), 1.87 (s, 2H), 1.73 (s, 2H), 1.53 – 1.48 (m, 1H), 1.45 (s, 9H), 1.41 – 1.35 (m, 1H), 1.29 – 1.18 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.1, 95.2, 94.4, 80.1, 75.4, 61.9, 48.6, 47.1, 43.8, 42.7, 33.7, 31.8, 29.8, 28.5, 25.8, 24.3, 24.1.

GC/MS (EI): m/z (%) 285 (0.6%), 147 (15%), 130 (17%), 102 (80%), 73 (55%), 57 (34%).

TLC: R_f = 0.4 (6:1 Hexanes: EtOAc).

Compound 37



2-(1-((2,3-dihydro-1*H*-inden-2-yl)oxy)ethyl)isoindoline-1,3-dione

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu$_4$NClO$_4$ (0.1 M) instead of $AgPF_6$ and ^{n}Bu$_4$NPF$_6$ respectively. Purification by PTLC (2:1 Hexanes: EtOAc) afforded 50.4 mg (82%) of the title compound **37**.

Physical State: white solid.

m.p.: 124 – 126 °C.

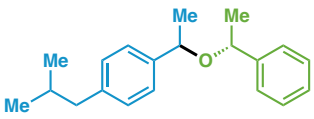
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 – 7.86 (m, 2H), 7.79 – 7.73 (m, 2H), 7.20 – 7.10 (m, 4H), 5.74 (q, *J* = 6.4 Hz, 1H), 4.46 – 4.35 (m, 1H), 3.25 (dd, *J* = 16.0, 6.7 Hz, 1H), 3.10 – 3.00 (m, 2H), 2.94 (dd, *J* = 16.0, 5.6 Hz, 1H), 1.79 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 168.1, 140.8, 140.3, 134.4, 131.9, 126.7, 126.7, 124.8, 124.7, 123.7, 78.5, 76.9, 39.8, 39.0, 19.7.

HRMS (ESI-TOF): calc'd for $C_{19}H_{17}NO_3Na$ $[M + Na]^+$: 330.1101; found 330.1112.

TLC: R_f = 0.47 (3:1 Hexanes: EtOAc).

Compound 38



1-isobutyl-4-((1*R*)-1-(1-phenylethoxy)ethyl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 50.8 mg (90%) of the title compound **38**.

Physical State: colorless oil.

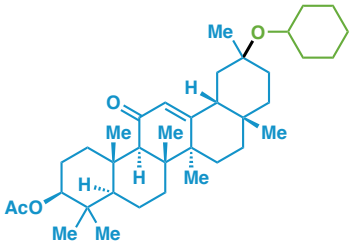
^{1}H NMR (600 MHz, $CDCl_3$, for both diastereomers): (the integration at 1.93 ppm, 1.88 ppm indicated the ratio of the two isomers of **38** to be 1:1): δ 7.40 – 7.34 (m, 2H), 7.34 – 7.27 (m, 7H), 7.27 – 7.17 (m, 5H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 4.59 – 4.51 (m, 2H), 4.32 – 4.21 (m, 2H), 2.51 (d, *J* = 7.2 Hz, 2H), 2.46 (d, *J* = 7.2 Hz, 2H), 1.93 – 1.91 (m, 1H), 1.88 – 1.83 (m, 1H), 1.49 (d, *J* = 6.4 Hz, 6H), 1.40 (d, *J* = 7.7 Hz, 6H), 0.95 (d, *J* = 6.6 Hz, 6H), 0.92 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$, for both diastereomers): δ 144.5, 144.4, 141.5, 141.4, 140.9, 140.7, 129.3, 129.1, 128.6, 128.3, 127.5, 127.2, 126.5, 126.4, 126.2, 126.2, 74.6, 74.5, 74.5, 45.3, 45.3, 30.4, 30.3, 24.9, 24.8, 23.2, 22.9, 22.6, 22.6, 22.5.

GC/MS (EI): m/z (%) 282 (0.04%), 177 (16%), 161 (31%), 105 (100%), 91 (12%).

TLC: R_f = 0.4 (50:1 Hexanes: Et_2O).

Compound 39



(3*S*,4a*R*,6a*R*,6b*S*,8a*S*,12a*R*,14a*R*,14b*S*)-11-(cyclohexyloxy)-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-yl acetate

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (100% CH_2Cl_2) afforded 40.0 mg (35%) of the title compound **39**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$ for two diastereomers) (the integration at 5.62 ppm, 5.59 ppm indicated the ratio of the two isomers of **39** to be 1:1): δ 5.62 (s, 1H), 5.59 (s, 1H), 4.52– 4.49 (m, 2H), 3.44 – 3.28 (m, 2H), 2.81 – 2.77 (m, 2H), 2.41 – 2.31 (m, 3H), 2.12 (td, *J* = 13.8, 4.7 Hz,

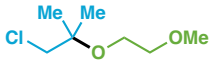
1H), 2.043 (s, 3H), 2.040 (s, 3H), 2.02 – 1.97 (m, 1H), 1.93 (t, J = 13.3 Hz, 1H), 1.86 – 1.77 (m, 2H), 1.74 – 1.67 (m, 10H), 1.67 – 1.61 (m, 6H), 1.61 – 1.53 (m, 5H), 1.52 – 1.47 (m, 3H), 1.45 – 1.38 (m, 7H), 1.38 – 1.35 (m, 4H), 1.33 (s, 3H), 1.32 – 1.21 (m, 9H), 1.20 – 1.14 (m, 13H), 1.14 – 1.10 (m, 9H), 1.09 – 0.95 (m, 5H), 0.87 (s, 12H), 0.843 (s, 3H), 0.836 (s, 3H), 0.80 (d, J = 1.8 Hz, 1H) , 0.78 (d, 1.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$ for two diastereomers): δ 200.4, 200.3, 171.2, 171.1, 170.8, 169.4, 128.3, 128.0, 80.8, 80.7, 75.8, 73.4, 69.62, 69.58, 61.84, 61.81, 55.2, 55.1, 49.1, 46.6, 45.5, 43.49, 43.48, 41.7, 38.9, 38.2, 37.9, 37.1, 36.0, 35.7, 35.6, 35.5, 33.5, 33.4, 32.84, 32.81, 32.7, 31.9, 28.7, 28.4, 28.20, 28.18, 27.7, 26.64, 26.62, 26.5, 26.4, 25.8, 25.7, 25.34, 25.32, 24.9, 24.8, 23.72, 23.69, 23.52, 23.50, 21.4, 21.3, 18.9, 18.8, 17.5, 16.8, 16.5.

HRMS (ESI-TOF): calc'd for $C_{37}H_{59}O_4$ $[M + H]^+$: 567.4408; found 567.4418.

TLC: R_f = 0.66 (3:1 Hexanes: EtOAc).

Compound 40



1-chloro-2-(2-methoxyethoxy)-2-methylpropane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (50:1 Hexanes: Et_2O) afforded 16.0 mg (48%) of the title compound **40**.

Physical State: colorless oil.

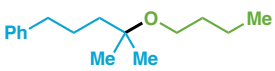
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.56 – 3.50 (m, 4H), 3.48 (s, 2H), 3.38 (s, 3H), 1.28 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 74.8, 72.4, 61.6, 59.3, 51.5, 23.7.

GC/MS (EI): m/z (%) 151 (0.6%), 117 (50%), 91 (30%), 59 (100%), 55 (40%).

TLC: R_f = 0.4 (30:1 Hexanes: Et_2O).

Compound 41



(4-butoxy-4-methylpentyl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 27.6 mg (59%) of the title compound **41**.

Physical State: colorless oil.

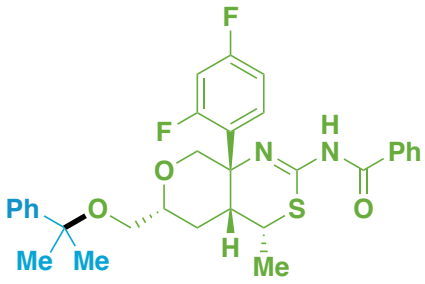
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.15 (m, 3H), 3.26 (t, *J* = 6.6 Hz, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 1.71 – 1.63 (m, 2H), 1.53 – 1.46 (m, 4H), 1.38 – 1.32 (m, 2H), 1.13 (s, 6H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.8, 128.5, 128.4, 125.8, 74.2, 60.9, 40.0, 36.5, 32.9, 25.9, 25.7, 19.6, 14.1.

GC/MS (EI): m/z (%) 219 (1%), 160 (20%), 115 (35%), 104 (100%), 91 (55%), 59 (89%).

TLC: R_f = 0.5 (30:1 Hexanes: Et_2O).

Compound 42



***N*-((4*R*,4a*R*,6*S*,8a*R*)-8a-(2,4-difluorophenyl)-4-methyl-6-(((2-phenylpropan-2-yl)oxy)methyl)-4,4a,5,6,8,8a-hexahydropyrano[3,4-*d*][1,3]thiazin-2-yl)benzamide**

Following General Procedure **B**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 56.0 mg (68%) of the title compound **42**.

Physical State: Pale yellow oil.

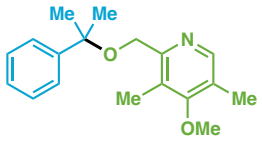
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, *J* = 7.6 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.48 – 7.42 (m, 4H), 7.39 – 7.33 (m, 2H), 7.28 – 7.23 (m, 1H), 6.98 – 6.85 (m, 2H), 4.19 (d, *J* = 12.2 Hz, 1H), 3.86 – 3.80 (m, 2H), 3.39 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.28 (dd, *J* = 7.1, 3.4 Hz, 1H), 3.15 (dd, *J* = 9.6, 5.1 Hz, 1H), 2.97 – 2.90 (m, 1H), 1.75– 1.68 (m, 2H), 1.57 (d, *J* = 2.7 Hz, 6H), 1.27 (d, *J* = 7.0 Hz, 4H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.0 (dd, *J* = 251.5, 12.6 Hz), 158.7 (dd, *J* = 248.4, 11.5 Hz), 145.9, 132.0, 131.1 (dd, *J* = 9.4, 5.6 Hz), 129.3, 128.3, 128.2, 128.1, 127.0, 126.7, 125.8, 124.4, 112.3 (d, *J* = 20.6 Hz), 105.7 (t, J = 26.9 Hz), 73.2, 66.1, 61.2 (d, *J* = 6.9 Hz), 37.7, 36.5, 31.8, 28.7, 27.9, 23.5, 17.1.

HRMS (ESI): calc'd for $C_{31}H_{33}F_2N_2O_3S$ $[M + H]^+$: 551.2174; found 551.2150.

TLC: R_f = 0.72 (1:1, Heptanes: EtOAc).

Compound 43



4-methoxy-3,5-dimethyl-2-(((2-phenylpropan-2-yl)oxy)methyl)pyridine

Following General Procedure **A** without 2N HCl work up, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (3:1 Hexanes: EtOAc) afforded 28.4 mg (50%) of the title compound **43**.

Physical State: colorless oil.

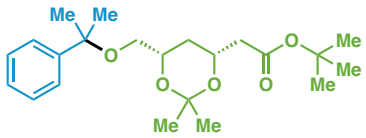
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.26 (m, 1H), 4.31 (s, 2H), 3.75 (s, 3H), 2.24 (s, 3H), 2.23 (s, 3H), 1.65 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 164.3, 156.4, 149.1, 145.9, 128.4, 127.2, 126.1, 125.8, 65.7, 59.9, 28.4, 13.4, 11.1.

GC/MS (EI): m/z (%) 167 (100%), 152 (35%), 138 (51%), 123 (43%), 92 (44%).

TLC: R_f = 0.2 (3:1 Hexanes: EtOAc).

Compound 44



***tert*-butyl 2-((4*R*,6*S*)-2,2-dimethyl-6-(((2-phenylpropan-2-yl)oxy)methyl)-1,3-dioxan-4-yl)acetate**

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (4:1 Hexanes: EtOAc) afforded 39.4 mg (52%) of the title compound **44**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.39 (m, 2H), 7.33 – 7.30 (m, 2H), 7.25 – 7.22 (m, 1H), 4.32 – 4.24 (m, 1H), 4.06 – 3.98 (m, 1H), 3.27 (dd, *J* = 9.1, 5.1 Hz, 1H), 3.02 (dd, *J* = 9.0, 6.7 Hz, 1H), 2.42 (dd, *J* = 15.0, 7.3 Hz, 1H), 2.31 (dd, *J* = 15.0, 5.9 Hz, 1H), 1.74 (dt, *J* = 12.8, 2.5 Hz, 1H), 1.52 (d, *J* = 2.2 Hz, 6H), 1.45 (s, 12H), 1.34 (s, 3H), 1.17 – 1.11 (m, 1H).

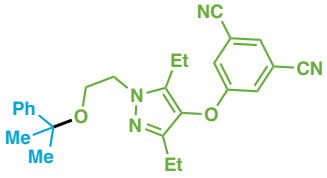
^{13}C NMR (151 MHz, $CDCl_3$): δ 170.4, 146.2, 128.2, 127.0, 126.0, 98.8, 80.7, 76.8, 68.6, 66.8, 66.2, 43.0, 34.3, 30.1, 28.5, 28.24, 28.22, 19.9.

HRMS (ESI-TOF): calc'd for $C_{22}H_{34}O_5Na$ $[M + Na]^+$: 401.2298; found 401.2299.

TLC: R_f = 0.65 (3:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = -6.0 (*c* = 1.0, $CHCl_3$).

Compound 45



5-((3,5-diethyl-1-(2-((2-phenylpropan-2-yl)oxy)ethyl)-1*H*-pyrazol-4-yl)oxy)isophthalonitrile

Following General Procedure **B**. Purification by PTLC (silica, 1:1 heptanes: EtOAc) afforded 27.0 mg (42%) of the title compound **45**.

Physical State: Pale yellow oil.

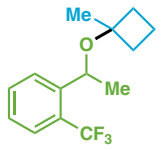
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (t, *J* = 1.4 Hz, 1H), 7.41 (d, *J* = 1.3 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.24 – 7.19 (m, 3H), 4.14 (t, *J* = 5.4 Hz, 2H), 3.53 (t, *J* = 5.4 Hz, 2H), 2.60 (q, *J* = 7.7 Hz, 2H), 2.40 (q, *J* = 7.6 Hz, 2H), 1.48 (s, 6H), 1.16 – 1.06 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.0, 145.6, 144.2, 136.5, 131.3, 128.4, 128.2, 127.0, 125.5, 122.5, 116.3, 115.2, 77.3, 62.1, 50.1, 28.2, 19.0, 16.8, 13.0, 12.9.

HRMS (ESI): calc'd for $C_{26}H_{29}N_4O$ $[M + H]^+$: 429.2285; found 429.2267.

TLC: R_f = 0.6 (1:1 Heptanes: EtOAc).

Compound 46



1-(1-(1-methylcyclobutoxy)ethyl)-2-(trifluoromethyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.) instead of $AgPF_6$. Purification by PTLC (silica, 50:1 Hexanes: EtOAc) afforded 31.1 mg (60%) of the title compound **46**.

Physical State: colorless oil.

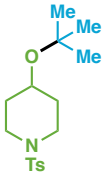
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.48 (d, *J* = 7.9 Hz, 1H), 8.18 (q, *J* = 7.8 Hz, 2H), 7.94 (t, *J* = 7.6 Hz, 1H), 5.58 – 5.53 (m, 1H), 2.75 (q, *J* = 10.1 Hz, 1H), 2.63 (q, *J* = 10.2 Hz, 1H), 2.50 – 2.43 (m, 1H), 2.40 – 2.32 (m, 1H), 2.30 – 2.20 (m, 1H), 2.16 – 2.08 (m, 1H), 2.01 (d, *J* = 6.4 Hz, 3H), 1.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 146.7, 132.2, 128.4, 126.8, 125.7 (q, *J* = 30.2 Hz),125.2 (q, *J* = 5.9 Hz), 124.7 (q, *J* = 271.8 Hz), 77.9, 66.7, 34.7, 34.5, 26.6, 24.6, 12.6.

GC/MS (EI): m/z (%) 258 (0.07%), 230 (15%), 173 (23%), 153 (68%), 133 (54%).

TLC: R_f = 0.3 (50:1 Hexanes: EtOAc).

Compound 47



4-(*tert*-butoxy)-1-tosylpiperidine

Following General Procedure **B**. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 18.2 mg (39%) of the title compound **47**.

Physical State: colorless oil.

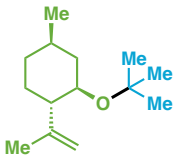
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.45 – 3.36 (m, 3H), 2.71 (t, *J* = 11.8 Hz, 2H), 2.43 (s, 3H), 1.81 – 1.72 (m, 2H), 1.63 – 1.57 (m, 2H), 1.11 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.5, 133.6, 129.7, 127.8, 73.8, 65.9, 44.3, 33.6, 28.4, 21.7.

HRMS (ESI-TOF): calc'd for $C_{16}H_{26}NO_3S$ $[M + H]^+$: 312.1633; found 312.1635.

TLC: R_f = 0.2 (4:1 Hexanes: EtOAc).

Compound 48



(1*S*,2*R*,4*R*)-2-(*tert*-butoxy)-4-methyl-1-(prop-1-en-2-yl)cyclohexane

Following General Procedure **B**. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 10.0 mg (32%) of the title compound **48**.

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.67 (d, *J* = 6.0 Hz, 2H), 3.03 (td, *J* = 10.2, 3.9 Hz, 1H), 2.02 – 1.89 (m, 2H), 1.79 – 1.74 (m, 1H), 1.70 (s, 3H), 1.68 – 1.61 (m, 1H), 1.28 (s, 2H), 1.20 (s, 9H), 1.16 – 1.03 (m, 2H), 0.95 (d, *J* = 6.5 Hz, 3H).

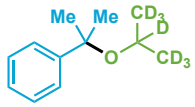
^{13}C NMR (151 MHz, $CDCl_3$): δ 150.2, 108.6, 76.0, 73.4, 44.8, 41.2, 39.0, 34.1, 31.5, 29.2, 20.8, 19.7.

GC/MS (EI): m/z (%) 210 (2%), 154 (14%), 136 (16%), 97 (69%), 57 (100%).

TLC: R_f = 0.3 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = -27.3 (*c* = 0.2, $CHCl_3$).

Compound 49



(2-((propan-2-yl-*d*7)oxy)propan-2-yl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 30.2 mg (82%) of the title compound **49**.

Physical State: colorless oil.

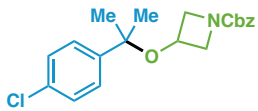
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 1.55 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 147.1, 128.0, 127.0, 126.4, 76.8, 65.0 – 64.7 (m), 29.1, 23.8 (dt, *J* = 38.3, 19.3 Hz).

GC/MS (EI): m/z (%) 185 (0.06%), 170 (49%), 122 (100%), 91 (33%), 77 (17%).

TLC: R_f = 0.39 (20:1 Hexanes: Et_2O).

Compound 50



benzyl 3-((2-(4-chlorophenyl)propan-2-yl)oxy)azetidine-1-carboxylate

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (3:1 Hexanes: EtOAc) afforded 50.1 mg (70%) of the title compound **50**.

Physical State: colorless oil.

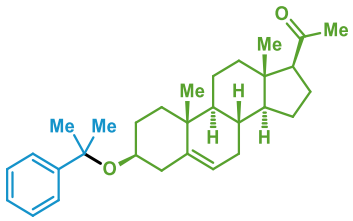
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 – 7.26 (m, 9H), 5.07 (s, 2H), 4.12 – 4.02 (m, 3H), 3.97 – 3.92 (m, 2H), 1.48 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.5, 144.5, 136.8, 133.2, 128.7, 128.6, 128.13, 128.06, 127.2, 78.0, 66.8, 62.5, 58.7, 28.6.

HRMS (ESI-TOF): calc'd for $C_{20}H_{23}ClNO_3$ $[M + H]^+$: 360.1361; found 360.1362.

TLC: R_f = 0.35 (3:1 Hexanes: EtOAc).

Compound 51



1-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-10,13-dimethyl-3-((2-phenylpropan-2-yl)oxy)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)ethenone

Following General Procedure **B**. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 35.2 mg (54%) of the title compound **51**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 5.17 (d, *J* = 5.1 Hz, 1H), 3.10 – 3.03 (m, 1H), 2.49 (t, *J* = 8.9 Hz, 1H), 2.29 (t, *J* = 13.3 Hz, 1H), 2.19 – 2.11 (m, 2H), 2.10 (s, 3H), 2.01 (d, *J* = 11.1 Hz, 1H), 1.93 (d, *J* = 19.5 Hz, 1H), 1.72 (dt, *J* = 13.3, 3.6 Hz, 1H), 1.65 – 1.59 (m, 4H), 1.55 (d, *J* = 12.6 Hz, 6H), 1.45 – 1.30 (m, 4H), 1.22 – 1.05 (m, 3H), 0.97 (s, 3H), 0.91 – 0.83 (m, 2H), 0.60 (s, 3H).

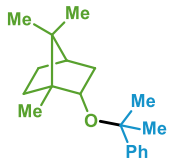
^{13}C NMR (151 MHz, $CDCl_3$): δ 209.6, 147.0, 141.8, 127.9, 127.0, 126.3, 120.8, 76.9, 73.1, 63.8, 57.1, 50.1, 44.1, 41.8, 38.9, 37.7, 36.6, 31.9, 31.9, 31.6, 30.9, 29.5, 28.8, 24.6, 22.9, 21.1, 19.4, 13.3.

HRMS (ESI-TOF): calc'd for $C_{30}H_{43}O_2$ $[M + H]^+$: 435.3263; found 435.3266.

TLC: R_f = 0.2 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = -0.5 (*c* = 1.0, $CHCl_3$).

Compound 52



(2*S*)-1,7,7-trimethyl-2-((2-phenylpropan-2-yl)oxy)bicyclo[2.2.1]heptane

Following General Procedure **B**. Purification by PTLC (silica, pure hexanes) afforded 27.0 mg (66%) of the title compound **52**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 3.61 (dt, *J* = 9.3, 2.5 Hz, 1H), 2.21 – 2.15 (m, 1H), 2.02 – 1.96 (m, 1H), 1.73 – 1.65 (m, 1H), 1.57 (t, *J* = 4.5 Hz, 1H), 1.49 (d, *J* = 11.7 Hz, 6H), 1.30 (s, 1H), 1.20 (d, *J* = 28.5 Hz, 1H), 1.04 (dd, *J* = 13.0, 3.4 Hz, 1H), 0.83 (s, 3H), 0.76 (d, *J* = 10.2 Hz, 6H).

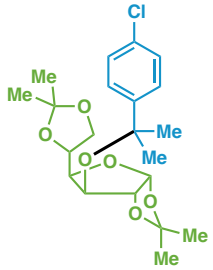
^{13}C NMR (151 MHz, $CDCl_3$): δ 148.4, 127.9, 126.6, 126.1, 77.0, 76.0, 49.5, 47.1, 45.5, 40.0, 29.7, 28.6, 27.9, 26.9, 20.0, 19.0, 14.0.

GC/MS (EI): m/z (%) 272 (0.01%), 153 (44%), 135 (7%), 119 (100%), 109 (81%), 91 (38%).

TLC: R_f = 0.5 (50:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = -22.5 (*c* = 0.5, $CHCl_3$).

Compound 53



(3a*R*,5*R*,6*S*,6a*R*)-6-((2-(4-chlorophenyl)propan-2-yl)oxy)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (4:1 Hexanes: EtOAc) afforded 43.2 mg (52%) of the title compound **53**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.38 (m, 2H), 7.32 – 7.28 (m, 2H), 5.85 (d, *J* = 3.7 Hz, 1H), 4.34 (d, *J* = 3.7 Hz, 1H), 4.33 – 4.28 (m, 1H), 4.13 – 4.09 (m, 2H), 4.06 (d, *J* = 3.3 Hz, 1H), 3.99 (dd, *J* = 8.6, 6.3 Hz, 1H), 1.60 (s, 3H), 1.57 (s, 3H), 1.46 (s, 3H), 1.39 (s, 3H), 1.34 – 1.32 (s, 3H), 1.26 – 1.24 (s, 3H).

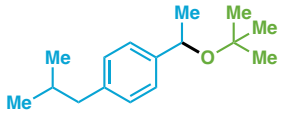
^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 133.2, 128.4, 127.3, 111.8, 109.0, 105.1, 84.9, 81.4, 77.6, 75.7, 72.4, 67.4, 28.3, 27.8, 27.0, 26.8, 26.4, 25.6.

HRMS (ESI-TOF): calc'd for $C_{21}H_{29}ClO_6Na$ $[M + Na]^+$: 435.1545; found 435.1550.

TLC: R_f = 0.54 (3:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = -16.4 (*c* = 1.0, $CHCl_3$).

Compound 54



1-(1-(*tert*-butoxy)ethyl)-4-isobutylbenzene

Following General Procedure **A**, Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 19.5 mg (42%) of the title compound **54**.

Physical State: colorless oil.

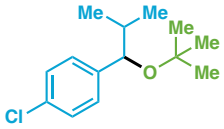
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 4.63 (q, *J* = 6.5 Hz, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.89 – 1.80 (m, 1H), 1.36 (d, *J* = 6.5 Hz, 3H), 1.16 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 139.9, 128.9, 125.5, 74.2, 69.9, 45.3, 30.4, 28.7, 26.8, 22.6.

GC/MS (EI): m/z (%) 234 (4%), 219 (11%), 163 (100%), 161 (25%), 57 (18%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 55



1-(1-(*tert*-butoxy)-2-methylpropyl)-4-chlorobenzene

Following General Procedure **A**. Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 31.0 mg (65%) of the title compound **55**.

Physical State: colorless oil.

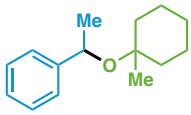
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 4.06 (d, *J* = 6.8 Hz, 1H), 1.75 – 1.66 (m, *J* = 6.6 Hz, 1H), 1.07 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.73 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 144.4, 132.1, 128.5, 127.9, 78.9, 74.1, 36.0, 28.9, 19.3, 19.0.

GC/MS (EI): m/z (%) 240 (0.004%), 197 (18%), 141 (100%), 125 (13%), 57 (51%).

TLC: R_f = 0.3 (100:1 Hexanes: Et_2O).

Compound 56



(1-((1-methylcyclohexyl)oxy)ethyl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 22.7 mg (52%) of the title compound **56**.

Physical State: colorless oil.

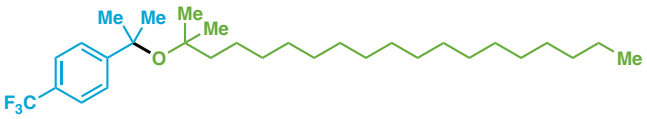
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 4.66 (q, *J* = 6.5 Hz, 1H), 1.79 – 1.72 (m, 1H), 1.62 (d, *J* = 31.1 Hz, 2H), 1.49 – 1.36 (m, 7H), 1.33 – 1.24 (m, 3H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 128.2, 126.6, 125.8, 75.3, 69.1, 37.7, 37.3, 27.0, 26.0, 25.8, 22.8, 22.6.

GC/MS (EI): m/z (%) 218 (0.8%), 203 (3%), 114 (11%), 105 (100%), 77 (10%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 57



1-(2-((2-methylnonadecan-2-yl)oxy)propan-2-yl)-4-(trifluoromethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (10:1 Hexanes: Et_2O) afforded 44.5 mg (46%) of the title compound **57**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 1.45 – 1.41 (m, 2H), 1.40 – 1.36 (m, 2H), 1.27 (d, *J* = 5.8 Hz, 34H), 1.01 (s, 6H), 0.88 (t, *J* = 7.1 Hz, 3H).

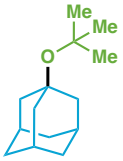
^{13}C NMR (151 MHz, $CDCl_3$): δ 155.1 (q, *J* = 1.3 Hz), 128.7 (q, *J* = 30.2 Hz), 126.0, 124.9 (q, *J* = 4.5 Hz), 124.5 (q, *J* = 271.8 Hz), 77.2, 75.6, 45.40, 32.1, 31.75, 30.41, 29.9, 29.8, 29.5, 28.8, 24.5, 22.9, 14.3.

^{19}F NMR (400 MHz, $CDCl_3$): δ -62.51.

GC/MS (EI): m/z (%) 297 (0.01%), 280 (3%), 187 (100%), 159 (9%), 69 (23%).

TLC: R_f = 0.3 (10:1 Hexanes: Et_2O).

Compound 58



1-(*tert*-butoxy)adamantane

Following General Procedure **A**. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 27.1 mg (65%) of the title compound **58**.

Physical State: white solid.

m.p.: 49 – 51 °C.

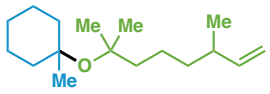
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.09 (s, 3H), 1.87 (d, *J* = 3.1 Hz, 6H), 1.60 (t, *J* = 3.2 Hz, 6H), 1.29 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 74.2, 74.0, 45.4, 36.6, 32.4, 31.2.

GC/MS (EI): m/z (%) 208 (0.2%), 193 (8%), 152 (37%), 135 (82%), 95 (100%).

TLC: R_f = 0.47 (20:1 Hexanes: Et_2O).

Compound 59



1-((2,6-dimethyloct-7-en-2-yl)oxy)-1-methylcyclohexane

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, pure Hexanes) afforded 14.1 mg (28%) of the title compound **59**.

Physical State: colorless oil.

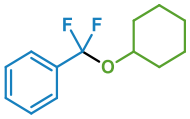
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.71 (ddd, *J* = 17.5, 10.3, 7.5 Hz, 1H), 5.04 – 4.82 (m, 2H), 2.12 (dq, *J* = 13.9, 6.9 Hz, 1H), 1.71 – 1.61 (m, 4H), 1.47 – 1.38 (m, 5H), 1.36 – 1.21 (m, 16H), 0.99 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.2, 112.3, 75.7, 74.8, 45.9, 40.8, 40.7, 37.9, 37.4, 29.4, 29.3, 26.2, 22.9, 22.1, 20.3.

GC/MS (EI): m/z (%) 252 (0.2%), 155 (16%), 114 (20%), 97 (100%), 83 (38%).

TLC: R_f = 0.3 (Hexanes).

Compound 60



((cyclohexyloxy)difluoromethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 6 equiv. Purification by PTLC (neutral aluminum oxide, pure Hexanes) afforded 20.8 mg (46%) of the title compound **60**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62 (d, *J* = 7.2 Hz, 2H), 7.48 – 7.37 (m, 3H), 4.50 – 4.40 (m, 1H), 2.03 – 1.92 (m, 2H), 1.83 – 1.75 (m, 2H), 1.62 – 1.56 (m, 2H), 1.42 – 1.34 (m, 2H), 1.31 – 1.20 (m, 2H).

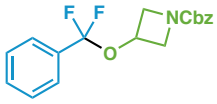
^{13}C NMR (151 MHz, $CDCl_3$): δ 135.2 (t, *J* = 33.1 Hz), 130.4, 128.4, 125.6 (t, *J* = 3.6 Hz), 123.3 (t, *J* = 257.1 Hz), 73.9, 33.5, 25.5, 24.1.

^{19}F NMR (376 MHz, $CDCl_3$): -66.27.

GC/MS (EI): m/z (%) 226 (0.1%), 127 (100%), 99 (29%), 77 (17%), 54 (10%).

TLC: R_f = 0.4 (50:1 Hexanes: Et_2O).

Compound 61



benzyl 3-(difluoro(phenyl)methoxy)azetidine-1-carboxylate

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^{n}Bu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^{n}Bu_4NPF_6$ respectively. Purification by PTLC (neutral aluminum oxide, pure Hexanes) afforded 15.3 mg (23%) of the title compound **61**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 – 7.58 (m, 2H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.38 – 7.30 (m, 5H), 5.19 – 5.13 (m, 1H), 5.11 (s, 2H), 4.38 – 4.31 (m, 2H), 4.15 (dd, *J* = 10.2, 4.5 Hz, 2H).

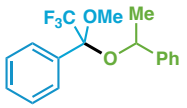
^{13}C NMR (151 MHz, $CDCl_3$): δ 156.4, 136.6, 133.3 (q, *J* = 31.7 Hz), 131.1, 128.7, 128.6, 128.3, 128.2, 125.5 (q, *J* = 4.5 Hz), 123.1 (q, *J* = 261.2 Hz), 67.1, 63.1 (q, *J* =6.0 Hz), 57.3.

^{19}F NMR (400 MHz, $CDCl_3$): δ -68.85.

HRMS (ESI-TOF): calc'd for $C_{18}H_{18}F_2NO_3$ $[M + H]^+$: 334.1255; found 334.1259.

TLC: R_f = 0.2 (Hexanes, aluminum TLC).

Compound 62



(2,2,2-trifluoro-1-methoxy-1-(1-phenylethoxy)ethyl)benzene

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), $^{n}Bu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^{n}Bu_4NPF_6$ respectively,

and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 54.8 mg (88%) of the title compound **62**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for two diastereomers) (the integration at 5.32 ppm, 4.96 ppm indicated the ratio of the two isomers of **62** to be 1:1): δ 7.81 – 7.71 (m, 2H), 7.71 – 7.63 (m, 2H), 7.48 – 7.23 (m, 16H), 5.32 (q, J = 6.4 Hz, 1H), 4.96 (q, J = 6.5 Hz, 1H), 3.13 (s, 3H), 2.97 (s, 3H), 1.60 (d, J = 6.5 Hz, 3H), 1.53 (d, J = 6.5 Hz, 3H).

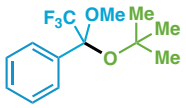
^{13}C NMR (151 MHz, $CDCl_3$, for two diastereomers): δ 145.0, 144.4, 134.9, 134.2, 129.7, 129.6, 128.8, 128.7, 128.5, 128.3, 128.14, 128.10, 127.4, 127.3, 126.3, 125.7, 123.0 (q, J = 290.8 Hz), 122.5 (q, J = 291.1 Hz), 100.0 (q, J = 40.3 Hz), 99.8 (q, J = 40.1 Hz), 72.4, 71.8 (d, J = 1.7 Hz), 52.2, 51.9 (d, J = 1.7 Hz), 25.5, 24.9.

^{19}F NMR (376 MHz, $CDCl_3$, for two diastereomers): δ -76.84, -78.04.

GC/MS (EI): m/z (%) 295 (0.2%), 241 (0.1%), 189 (37%), 105 (100%), 77 (32%).

TLC: R_f = 0.47 (20:1 Hexanes: Et_2O).

Compound 63



(1-(*tert*-butoxy)-2,2,2-trifluoro-1-methoxyethyl)benzene

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu_4NClO_4 (0.1 M) instead of $AgPF_6$ and ^{n}Bu_4NPF_6 respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 22.0 mg (42%) of the title compound **63**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.70 – 7.68 (m, 2H), 7.39 – 7.33 (m, 3H), 3.57 – 3.54 (m, 3H), 1.28 (s, 9H).

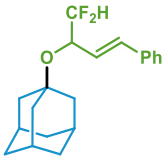
^{13}C NMR (151 MHz, $CDCl_3$): δ 137.2, 129.3, 129.0, 127.6, 122.8 (q, J = 292.2 Hz), 99.3 (q, J = 29.5 Hz), 78.8, 52.0 (d, J = 2.2 Hz), 30.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -76.72.

GC/MS (EI): m/z (%) 189 (84%), 137 (100%), 105 (41%), 77 (35%), 57 (45%).

TLC: R_f = 0.57 (20:1 Hexanes: Et_2O).

Compound 64



1-(((*E*)-1,1-difluoro-4-phenylbut-3-en-2-yl)oxy)adamantane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 32.6 mg (51%) of the title compound **64**.

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 1H), 6.75 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 16.1, 6.0 Hz, 1H), 5.60 (td, *J* = 56.2, 4.3 Hz, 1H), 4.54 – 4.33 (m, 1H), 2.16 (s, 3H), 1.87 – 1.76 (m, 6H), 1.67 – 1.58 (m, 6H).

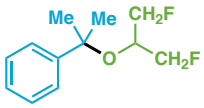
^{13}C NMR (126 MHz, $CDCl_3$): δ 136.5, 133.6, 128.8, 128.1, 126.8, 125.1, 115.91 (t, *J* = 252.0 Hz), 75.1, 70.3 (t, *J* = 25.2 Hz), 42.5, 36.4, 30.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -123.91 (d, *J* = 281.3 Hz), -128.95 (d, *J* = 281.3 Hz).

GC/MS (EI): m/z (%) 318 (0.3%), 267 (15%), 147 (14%), 135 (100%), 93 (10%).

TLC: R_f = 0.4 (30:1 Hexanes: Et_2O).

Compound 65



(2-((1,3-difluoropropan-2-yl)oxy)propan-2-yl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 18.0 mg (42%) of the title compound **65**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 4.40 – 4.33 (m, 2H), 4.33 – 4.24 (m, 2H), 3.71 – 3.62 (m, 1H), 1.61 (s, 6H).

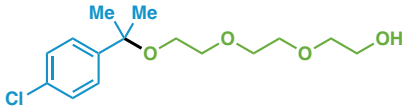
^{13}C NMR (151 MHz, $CDCl_3$): δ 145.1, 128.3, 127.8, 126.3, 82.1 (d, *J* = 166.1 Hz), 82.0 (d, *J* = 166.1 Hz), 78.0, 69.6 (t, *J* = 20.2 Hz), 28.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -231.04.

GC/MS (EI): m/z (%) 199 (100%), 121 (49%), 119 (52%), 91 (47%), 77 (25%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 66



2-(2-(2-((2-(4-chlorophenyl)propan-2-yl)oxy)ethoxy)ethoxy)ethan-1-ol

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^{n}Bu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^{n}Bu_4NPF_6$ respectively. Purification by PTLC (100% Et_2O) afforded 36.0 mg (59%) of the title compound **66**.

Physical State: colorless oil.

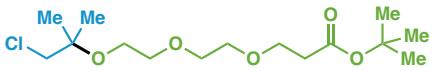
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.33 (m, 2H), 7.30 – 7.26 (m, 2H), 3.73 – 3.71 (m, 2H), 3.69 – 3.65 (m, 2H), 3.65 – 3.57 (m, 6H), 3.31 (t, *J* = 5.8 Hz, 2H), 2.60 (s, 1H), 1.51 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 132.8, 128.4, 127.5, 76.6, 72.6, 71.0, 70.7, 70.5, 62.3, 61.9, 28.4.

HRMS (ESI-TOF): calc'd for $C_{15}H_{23}ClO_4Na$ $[M + Na]^+$: 325.1177; found 325.1188.

TLC: R_f = 0.29 (Et_2O).

Compound 67



***tert*-butyl 3-(2-(2-((1-chloro-2-methylpropan-2-yl)oxy)ethoxy)ethoxy)propanoate**

Following General Procedure **B** without 2N HCl work up (washed twice with H_2O). Purification by PTLC (silica, 1:1 Hexanes: Et_2O) afforded 23.2 mg (48%) of the title compound **67**.

Physical State: colorless oil.

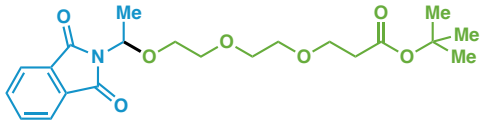
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.71 (t, *J* = 6.6 Hz, 2H), 3.66 – 3.63 (m, 2H), 3.61 – 3.58 (m, 4H), 3.54 – 3.52 (m, 2H), 3.46 (s, 2H), 2.50 (t, *J* = 6.6 Hz, 2H), 1.44 (s, 9H), 1.26 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.1, 80.6, 74.8, 70.9, 70.8, 70.5, 67.1, 61.8, 51.6, 36.4, 28.2, 23.7.

HRMS (ESI-TOF): calc'd for $C_{15}H_{29}ClO_5Na$ $[M + Na]^+$: 347.1596; found 347.1602.

TLC: R_f = 0.39 (3:1 Hexanes: EtOAc).

Compound 68



***tert*-butyl (*R*)-3-(2-(2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)ethoxy)ethoxy)propanoate**

Following General Procedure **B**. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 34.8 mg (57%) of the title compound **68**.

Physical State: colorless oil.

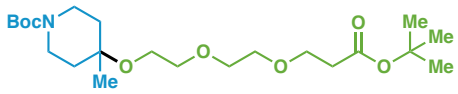
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 5.60 (q, *J* = 6.3 Hz, 1H), 3.69 – 3.48 (m, 10H), 2.46 (t, *J* = 6.6 Hz, 2H), 1.80 (d, *J* = 6.3 Hz, 3H), 1.43 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.0, 168.1, 134.3, 131.9, 123.6, 80.6, 78.8, 70.7, 70.4, 70.3, 68.5, 67.0, 36.4, 28.2, 19.4.

HRMS (ESI-TOF): calc'd for $C_{21}H_{29}NO_7Na$ $[M + Na]^+$: 430.1842; found 430.1842.

TLC: R_f = 0.3 (2:1 Hexanes: EtOAc).

Compound 69



***tert*-butyl 4-(2-(2-(3-(tert-butoxy)-3-oxopropoxy)ethoxy)ethoxy)-4-methylpiperidine-1-carboxylate**

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 21.7 mg (25%) of the title compound **69**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.73 – 3.69 (m, 4H), 3.65 – 3.62 (m, 2H), 3.62 – 3.58 (m, 4H), 3.47 (t, *J* = 5.3 Hz, 2H), 3.13 (s, 2H), 2.50 (t, *J* = 6.6 Hz, 2H), 1.71 (d, *J* = 14.2 Hz, 2H), 1.44 (s, 9H), 1.44 (s, 9H), 1.42 – 1.37 (m, 2H), 1.15 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.1, 155.1, 80.6, 79.4, 71.8, 71.1, 70.8, 70.6, 67.1, 60.6, 39.8, 36.4, 35.7, 28.6, 28.2, 24.6.

HRMS (ESI-TOF): calc'd for $C_{22}H_{42}NO_7$ $[M + H]^+$: 432.2956; found 432.2952.

TLC: R_f = 0.49 (1:1 Hexanes: EtOAc).

Compound 78

2-methyl-5-phenylpentan-2-ol

Following General Procedure **C**. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 18.5 mg (52%) of the title compound **78**.

Physical State: colorless oil.

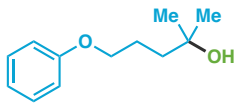
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.15 (m, 3H), 2.63 (t, *J* = 7.7 Hz, 2H), 1.74 – 1.67 (m, 2H), 1.55 – 1.49 (m, 2H), 1.21 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.6, 128.5, 128.4, 125.9, 71.1, 43.6, 36.5, 29.4, 26.4.

GC/MS (EI): m/z (%) 160 (12%), 145 (13%), 104 (100%), 91 (39%), 59 (36%).

TLC: R_f = 0.2 (3:1 Hexanes: EtOAc).

Compound 79



2-methyl-5-phenoxypentan-2-ol

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 25.6 mg (66%) of the title compound **79**.

Physical State: colorless oil.

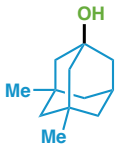
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 (t, *J* = 6.8 Hz, 2H), 6.94 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 2H), 3.99 (t, *J* = 6.4 Hz, 2H), 1.92 – 1.84 (m, 2H), 1.68 – 1.63 (m, 2H), 1.27 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 159.1, 129.6, 120.8, 114.6, 70.8, 68.4, 40.4, 29.5, 24.5.

GC/MS (EI): m/z (%) 194 (2%), 176 (5%), 120 (15%), 94 (100%), 55 (46%).

TLC: R_f = 0.3 (4:1 Hexanes: EtOAc).

Compound 80



3,5-dimethyladamantan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 34.2 mg (95%) of the title compound **80**.

Physical State: colorless oil.

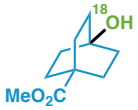
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 – 2.14 (m, 1H), 1.56 (s, 2H), 1.44 (s, 1H), 1.39 – 1.24 (m, 8H), 1.11 (s, 2H), 0.86 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 70.0, 51.6, 50.6, 43.9, 42.6, 33.9, 31.2, 30.0.

GC/MS (EI): m/z (%) 180 (53%), 165 (21%), 123 (100%), 109 (95%), 91 (18%).

TLC: R_f = 0.3 (4:1 Hexanes: EtOAc).

Compound 81



methyl 4-hydroxybicyclo[2.2.2]octane-1-carboxylate

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 22.7 mg (61%) of the title compound **81**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.63 (s, 3H), 1.97 – 1.87 (m, 6H), 1.69 – 1.61 (m, 6H), 1.36 (s, 1H).

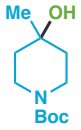
^{13}C NMR (151 MHz, $CDCl_3$): δ 177.9, 69.4, 51.9, 38.5, 33.4, 29.7.

GC/MS (EI): m/z (%) 184 (2%), 155(8%), 124 (100%), 109 (13%), 95 (18%).

GC/MS (EI)(^{18}O): m/z (%) 186 (1%), 155 (9%), 126 (52%), 124 (13%), 115 (22%).

TLC: R_f = 0.3 (4:1 Hexanes: EtOAc).

Compound 82



***tert*-butyl 4-hydroxy-4-methylpiperidine-1-carboxylate**

Following General Procedure **C**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 13.8 mg (32%) of the title compound **82**.

Physical State: colorless oil.

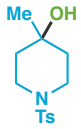
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.69 (s, 2H), 3.23 (s, 2H), 1.54 (q, *J* = 5.0, 4.4 Hz, 4H), 1.45 (s, 9H), 1.26 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.0, 79.5, 68.2, 40.6, 38.6, 30.2, 28.6.

GC/MS (EI): m/z (%) 215 (3%), 141 (34%), 126 (37%), 82 (44%), 57 (100%).

TLC: R_f = 0.2 (2:1 Hexanes: EtOAc).

Compound 83



4-methyl-1-tosylpiperidin-4-ol

Following General Procedure **C**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 37.3 mg (69%) of the title compound **83**.

Physical State: colorless oil.

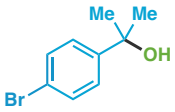
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 3.51 – 3.42 (m, 2H), 2.68 (t, *J* = 13.0 Hz, 2H), 2.42 (s, 3H), 1.71 (t, *J* = 10.5 Hz, 2H), 1.63 – 1.56 (m, 2H), 1.21 (s, 3H), 1.06 (s, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.5, 133.4, 129.8, 127.8, 67.1, 42.5, 38.0, 30.5, 21.6.

HRMS (ESI-TOF): calc'd for $C_{13}H_{20}NO_3S$ $[M + H]^+$: 270.1164; found 270.1167.

TLC: R_f = 0.3 (2:1 Hexanes: EtOAc).

Compound 84



2-(4-bromophenyl)propan-2-ol

Following General Procedure **C**. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 28.5 mg (67%) of the title compound **84**.

Physical State: colorless oil.

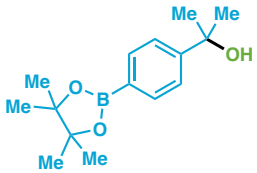
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 1.73 (s, 1H), 1.56 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 148.3, 131.4, 126.5, 120.7, 72.5, 31.9.

GC/MS (EI): m/z (%) 216 (10%), 214 (10%), 201 (94%), 199 (100%), 115 (33%), 91 (23%).

TLC: R_f = 0.5 (3:1 Hexanes: EtOAc).

Compound 85



2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-ol

Following General Procedure **C**. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 28.8 mg (55%) of the title compound **85**.

Physical State: white solid.

m.p.: 118 – 120 °C.

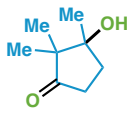
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 1.73 (s, 1H), 1.58 (s, 6H), 1.34 (s, 12H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 152.4, 135.0, 128.4, 123.8, 83.9, 72.8, 31.8, 25.0.

GC/MS (EI): m/z (%) 262 (0.7%), 247 (83%), 158 (87%), 144 (100%), 77 (20%).

TLC: R_f = 0.34 (3:1 Hexanes: EtOAc).

Compound 86



3-hydroxy-2,2,3-trimethylcyclopentanone

Following General Procedure **C**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 15.1 mg (53%) of the title compound **86**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.50 – 2.40 (m, 1H), 2.37 – 2.29 (m, 1H), 2.09 – 1.94 (m, 2H), 1.30 (s, 3H), 1.25 (s, 1H), 1.03 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 221.8, 80.0, 53.1, 33.93, 33.85, 23.0, 21.7, 16.2.

GC/MS (EI): m/z (%) 142 (40%), 127 (3%), 109 (63%), 99 (60%), 71 (100%).

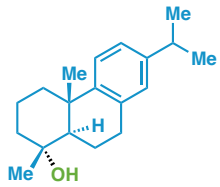
TLC: R_f = 0.19 (3:1 Hexanes: EtOAc).

Compound 87

(4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-ol[2,3]

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 13.1 mg (24%) of compound **87-major** and 4.4 mg (8%) compound **87-minor**.

Compound 87-major



(1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-ol

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.2 Hz, 1H), 7.01 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.92 – 6.90 (m, 1H), 2.98 – 2.87 (m, 2H), 2.86 – 2.81 (m, 1H), 2.30 – 2.23 (m, 1H), 2.11 (ddt, *J* = 12.9, 6.9, 1.9 Hz, 1H), 1.88 (dtd, *J* = 12.5, 3.3, 1.4 Hz, 1H), 1.81 – 1.74 (m, 1H), 1.73 – 1.64 (m, 2H), 1.61 (dd, *J* = 12.6, 1.9 Hz, 1H), 1.49 – 1.36 (m, 2H), 1.24 (s, 6H), 1.23 (s, 3H), 1.16 (s, 3H).

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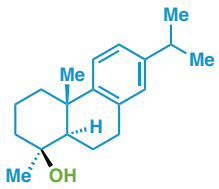
[4] Uyanik, M., Ishihara, K. & Yamamoto, H. Catalytic Diastereoselective Polycyclization of Homo(polyprenyl)arene Analogues Bearing Terminal Siloxyvinyl Groups. *Org. Lett.,* **8**, 5649–5652 (2006).
[5] Lee, C.-K., Fang, J.-M. & Cheng, Y.-S. Norditerpenes from *Juniperus Chinensis*. *Phytochemistry,* **39**, 391–394 (1995).

^{13}C NMR (151 MHz, $CDCl_3$): δ 146.5, 145.8, 134.9, 127.1, 124.7, 124.1, 72.6, 52.6, 42.9, 38.4, 38.1, 33.6, 30.5, 24.7, 24.12, 24.10, 23.1, 20.7, 18.1.

GC/MS (EI): m/z (%) 272 (4%), 257 (4%), 239 (100%), 157 (21%), 91 (19%).

TLC: R_f = 0.42 (3:1 Hexanes: EtOAc).

Compound 87-minor



(1*S*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-ol[2,3]

Physical State: white solid.

m.p.: 64 – 66 °C.

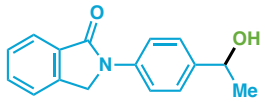
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.2 Hz, 1H), 7.01 – 6.99 (m, 1H), 6.92 – 6.89 (m, 1H), 3.02 – 2.96 (m, 1H), 2.94 – 2.87 (m, 1H), 2.83 (p, *J* = 6.9 Hz, 1H), 2.33 – 2.30 (m, 1H), 2.07 – 1.99 (m, 1H), 1.97 (dt, *J* = 13.8, 3.6 Hz, 1H), 1.95 – 1.84 (m, 1H), 1.76 – 1.72 (m, 1H), 1.64 – 1.60 (m, 1H), 1.48 – 1.40 (m, 3H), 1.31 (d, *J* = 0.9 Hz, 3H), 1.26 (s, 3H), 1.23 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 146.9, 145.8, 134.8, 127.0, 124.1, 124.0, 72.4, 48.8, 40.9, 38.3, 37.3, 33.6, 30.9, 29.6, 24.6, 24.2, 24.1, 18.6, 18.1.

GC/MS (EI): m/z (%) 272 (13%), 257 (19%), 239 (100%), 157 (51%), 91 (20%).

TLC: R_f = 0.58 (3:1 Hexanes: EtOAc).

Compound 88



2-(4-(1-hydroxyethyl)phenyl)isoindolin-1-one

Following General Procedure **C**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 20.1 mg (40%) of the title compound **88**.

Physical State: colorless oil.

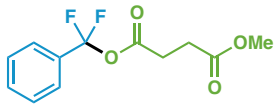
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.86 – 7.82 (m, 2H), 7.62 – 7.57 (m, 1H), 7.52 (d, *J* = 7.7 Hz, 2H), 7.46 – 7.42 (m, 2H), 4.96 – 4.90 (m, 1H), 4.86 (s, 2H), 1.87 (s, 1H), 1.52 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 167.7, 142.1, 140.2, 138.8, 133.3, 132.2, 128.6, 126.4, 124.3, 122.8, 119.7, 70.1, 50.9, 25.3.

HRMS (ESI-TOF): calc'd for $C_{16}H_{16}NO_2$ $[M + H]^+$: 254.1181; found 254.1176.

TLC: R_f = 0.2 (3:1 Hexanes: EtOAc).

Compound 89



difluoro(phenyl)methyl methyl succinate

Following General Procedure **A**, 3 equiv. of 4-methoxy-4-oxobutanoic acid was used as nucleophile, using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu_4NClO_4 (0.1 M) instead of $AgPF_6$ and ^{n}Bu_4NPF_6 respectively. Purification by PTLC (silica, 5:1 Hexanes: EtOAc) afforded 16.0 mg (31%) of the title compound **89**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 – 7.61 (m, 2H), 7.53 – 7.47 (m, 1H), 7.47 – 7.43 (m, 2H), 3.68 (s, 3H), 2.76 (dd, *J* = 7.3, 6.2 Hz, 2H), 2.63 (dd, *J* = 7.4, 6.1 Hz, 2H).

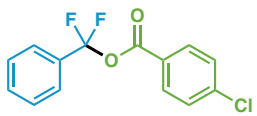
^{13}C NMR (151 MHz, $CDCl_3$): δ 172.1, 167.2, 132.9 (t, *J* = 30.2 Hz), 131.2, 128.6, 125.6 (t, *J* = 4.5 Hz), 121.7 (t, *J* = 265.5 Hz), 52.1 (d, *J* = 2.4 Hz), 29.6, 28.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -69.01.

HRMS (ESI-TOF): calc'd for $C_{12}H_{12}F_2O_4Na$ $[M + Na]^+$: 281.0596; found 281.0599.

TLC: R_f = 0.46 (3:1 Hexanes: EtOAc).

Compound 90



difluoro(phenyl)methyl 4-chlorobenzoate

Following General Procedure **A**, 3 equiv. of 4-chlorobenzoic acid was used as nucleophile, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (silica, 10:1 Hexanes: EtOAc) afforded 20.0 mg (36%) of the title compound **90**.

Physical State: white solid.

m.p.: 61 – 63 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 – 7.96 (m, 2H), 7.71 – 7.69 (m, 2H), 7.55 – 7.50 (m, 1H), 7.50 – 7.42 (m, 4H).

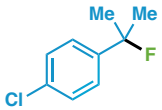
^{13}C NMR (151 MHz, $CDCl_3$): δ 160.6, 141.1, 133.0 (t, J = 30.3 Hz), 131.7, 131.3, 129.3, 128.7, 127.0, 125.6 (t, J = 4.5 Hz), 122.3 (t, J = 265.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -68.73.

GC/MS (EI): m/z (%) 282 (11%), 139 (100%), 127 (47%), 96 (96%), 77 (45%).

TLC: R_f = 0.68 (3:1 Hexanes: EtOAc).

Compound 91



1-chloro-4-(2-fluoropropan-2-yl)benzene

Following General Procedure **A**, KF (42 mg, 3.6 equiv.) was used as nucleophile, $AgClO_4$ (124 mg, 3 equiv.) was used instead of $AgPF_6$ and 18-crown-6 (190 mg, 3.6 equiv.) was used as additive. Purification by PTLC (silica, 100% Hexanes) afforded 11.9 mg (35%) of the title compound **91**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.29 (m, 4H), 1.69 (s, 3H), 1.65 (s, 3H).

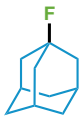
^{13}C NMR (151 MHz, $CDCl_3$): δ 144.5 (d, J = 22.4 Hz), 133.3, 128.5, 125.5 (d, J = 9.1 Hz), 95.4 (d, J = 169.5 Hz), 29.4 (d, J = 25.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -137.65.

GC/MS (EI): m/z (%) 172 (21%), 157 (100%), 137 (23%), 75 (21%).

TLC: R_f = 0.45 (Hexanes).

Compound 92



1-fluoroadamantane

Following General Procedure **A**, KF (42 mg, 3.6 equiv.) was used as nucleophile, $AgClO_4$ (124 mg, 3 equiv.) was used instead of $AgPF_6$ and 18-crown-6 (190 mg, 3.6 equiv.) was used as additive. Purification by PTLC (silica, 100% Hexanes) afforded 18.0 mg (58%) of the title compound **92**.

Physical State: white solid (sublimation at room temperature).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.28 – 2.18 (m, 3H), 1.89 (dd, *J* = 5.7, 3.0 Hz, 6H), 1.68 – 1.56 (m, 6H).

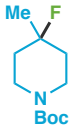
^{13}C NMR (151 MHz, $CDCl_3$): δ 92.7 (d, *J* = 183.2 Hz), 42.9 (d, *J* = 17.0 Hz), 36.0, 31.6 (d, *J* = 9.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -128.70.

GC/MS (EI): m/z (%) 154 (53%), 135 (0.6%), 111 (18%), 97 (100%), 79 (20%).

TLC: R_f = 0.47 (Hexanes).

Compound 93



***tert*-butyl 4-fluoro-4-methylpiperidine-1-carboxylate**

Following General Procedure **A** without 2N HCl work up (washed twice with H_2O), KF (42 mg, 3.6 equiv.) was used as nucleophile, $AgClO_4$ (124 mg, 3 equiv.) was used instead of $AgPF_6$ and 18-crown-6 (190 mg, 3.6 equiv.) was used as additive. Purification by PTLC (silica, 10:1 Hexanes: EtOAc) afforded 7.8 mg (18%) of the title compound **93**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.86 (s, 2H), 3.10 (t, *J* = 12.4 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.64 – 1.54 (m, 2H), 1.45 (s, 9H), 1.36 (d, *J* = 21.4 Hz, 3H).

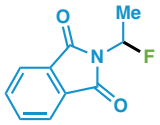
^{13}C NMR (151 MHz, $CDCl_3$): δ 154.9, 92.5 (d, *J* = 168.3 Hz), 79.7, 39.9, 36.4 (d, *J* = 22.0 Hz), 28.6, 27.2 (d, *J* = 24.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -153.97.

GC/MS (EI): m/z (%) 217 (1%), 144 (14%), 116 (11%), 57 (100%).

TLC: R_f = 0.61 (3:1 Hexanes: EtOAc).

Compound 94



2-(1-fluoroethyl)isoindoline-1,3-dione

Following General Procedure **A**, KF (42 mg, 3.6 equiv.) was used as nucleophile, $AgClO_4$ (124 mg, 3 equiv.) was used instead of $AgPF_6$ and 18-crown-6 (190 mg, 3.6 equiv.) was used as additive. Purification by PTLC (silica, 100% CH_2Cl_2) afforded 24.0 mg (62%) of the title compound **94**.

Physical State: white solid.

m.p.: 134 – 136 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 – 7.87 (m, 2H), 7.83 – 7.72 (m, 2H), 6.35 (dq, *J* = 48.2, 6.3 Hz, 1H), 2.00 (dd, *J* = 20.7, 6.3 Hz, 3H).

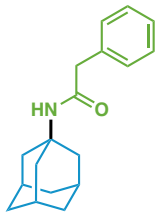
^{13}C NMR (151 MHz, $CDCl_3$): δ 166.9, 134.8, 131.7, 124.0, 87.3 (d, *J* = 198.4 Hz), 18.3 (d, *J* = 28.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -140.04.

GC/MS (EI): m/z (%) 193 (1%), 178 (2%), 173 (100%), 146 (9%), 76 (47%).

TLC: R_f = 0.45 (3:1 Hexanes: EtOAc).

Compound 95



***N*-(adamantan-1-yl)-2-phenylacetamide**

Following General Procedure **A**, 3 equiv. of phenylacetonitrile was used as nucleophile, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively.

Purification by PTLC (silica, 1:1 Hexanes: Et_2O) afforded 7.5 mg (14%) of the title compound **95**.

Physical State: white solid.

m.p.: 172 – 174 °C.

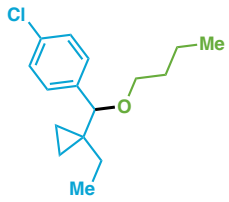
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 – 7.32 (m, 2H), 7.29 – 7.26 (m, 1H), 7.25 – 7.23 (m, 2H), 5.02 (s, 1H), 3.48 (s, 2H), 2.06 – 2.00 (m, 3H), 1.91 (d, *J* = 3.0 Hz, 6H), 1.64 (t, *J* = 3.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 170.2, 135.7, 129.4, 129.0, 127.3, 52.0, 45.2, 41.6, 36.4, 29.5.

HRMS (ESI-TOF): calc'd for $C_{18}H_{24}NO$ $[M + H]^+$: 270.1852; found 270.1863.

TLC: R_f = 0.32 (3:1 Hexanes: EtOAc).

Compound 97



1-(butoxy(1-ethylcyclopropyl)methyl)-4-chlorobenzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.) instead of $AgPF_6$. Purification by PTLC (50:1 Hexanes: Et_2O) afforded 21.3 mg (40%) of the title compound **97**.

Physical State: colorless oil.

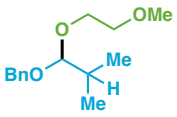
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 – 7.26 (m, 2H), 7.26 – 7.20 (m, 2H), 4.13 (s, 1H), 3.26 (qt, *J* = 9.2, 6.5 Hz, 2H), 1.59 – 1.42 (m, 3H), 1.35 (ddt, *J* = 13.4, 10.0, 6.7 Hz, 2H), 1.13 (dq, *J* = 14.7, 7.4 Hz, 1H), 0.91 – 0.83 (m, 6H), 0.55 (ddd, *J* = 9.5, 4.9, 3.5 Hz, 1H), 0.43 (dt, *J* = 8.5, 4.3 Hz, 1H), 0.32 – 0.23 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 139.9, 129.0, 128.2, 83.7, 69.3, 32.2, 26.9, 25.2, 19.6, 14.1, 10.7, 8.9, 7.8.

GC/MS (EI): m/z (%) 266 (0.1%), 238 (24%), 197 (19%), 182 (44%), 166 (62%), 141(100%).

TLC: R_f = 0.4 (30:1 Hexanes: Et_2O).

Compound 99



((1-(2-methoxyethoxy)-2-methylpropoxy)methyl)benzene

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.) instead of $AgPF_6$. Purification by PTLC (10:1 Hexanes: Et_2O) afforded 31.0 mg (65%) of the title compound **99**.

Physical State: colorless oil.

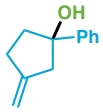
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.31 (m, 4H), 7.30 – 7.26 (m, 1H), 4.69 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.28 (d, *J* = 7.3 Hz, 1H), 3.73 (dt, *J* = 10.8, 4.7 Hz, 1H), 3.66 (ddd, *J* = 10.7, 5.4, 4.1 Hz, 1H), 3.58 – 3.53 (m, 2H), 3.40 (s, 3H), 2.01 (dq, *J* = 13.7, 6.8 Hz, 1H), 0.96 (dd, *J* = 6.8, 4.7 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 128.5, 127.9, 127.6, 107.5, 72.2, 68.1, 64.5, 59.2, 31.1, 18.1, 18.0.

GC/MS (EI): m/z (%) 162 (4%), 131 (5%), 107 (4%), 91 (100%), 59 (13%).

TLC: R_f = 0.3 (10:1 Hexanes: Et_2O).

Compound 101



3-methylene-1-phenylcyclopentan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 5:1 Hexanes: EtOAc) afforded 5.9 mg (17%) of the title compound **101**.

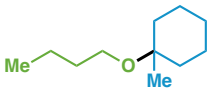
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 5.01 (broad s, 2H), 2.85 (dq, *J* = 16.3, 2.5 Hz, 1H), 2.78-2.64 (m, 2H), 2.85 (dq, *J* = 16.9, 2.5 Hz, 1H), 2.55 (dd, *J* = 16.3, 9.2 Hz, 1H), 2.22-2.07 (m, 2H), 1.70 (broad s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 150.2, 145.9, 128.5, 127.3, 125.3, 107.6, 82.4, 48.8, 41.1, 30.6.

HRMS (ESI-TOF): calc'd for $C_{12}H_{13}$ $[M - OH]^+$: 157.1012, found: 157.1011.

TLC: R_f = 0.4 (5:1 Hexanes: EtOAc).

Compound 102



1-butoxy-1-methylcyclohexane

Following General Procedure **A**, using $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (91.2 mg, 3.0 equiv.) instead of $AgPF_6$ and 2,4,6-collidine respectively. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 14.3 mg (42%) of the title compound **102**.

Physical State: colorless oil.

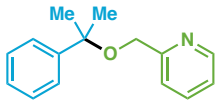
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.29 (t, *J* = 6.6 Hz, 2H), 1.72 – 1.65 (m, 2H), 1.61 – 1.48 (m, 5H), 1.42 – 1.35 (m, 4H), 1.32 – 1.22 (m, 3H), 1.10 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 73.1, 60.1, 36.7, 33.0, 26.0, 24.8, 22.4, 19.8, 14.2.

GC/MS (EI): m/z (%) 170 (6%), 155 (3%), 127 (22%), 71 (100%).

TLC: R_f = 0.47 (20:1 Hexanes: Et_2O).

Compound 103



2-(((2-phenylpropan-2-yl)oxy)methyl)pyridine

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu_4NClO_4 (0.1 M) instead of $AgPF_6$ and ^{n}Bu_4NPF_6 respectively. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 17.7 mg (39%) of the title compound **103**.

Physical State: colorless oil.

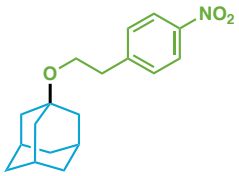
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.51 (d, *J* = 4.9 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.26 (m, 2H), 4.25 (s, 2H), 1.65 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 148.6, 148.2, 145.7, 135.8, 135.3, 128.6, 127.4, 125.9, 123.6, 77.7, 62.8, 28.5.

GC/MS (EI): m/z (%) 212 (17%), 118 (76%), 103 (46%), 92 (100%), 65 (20%).

TLC: R_f = 0.3 (3:1 Hexanes: EtOAc).

Compound 104



1-(4-nitrophenethoxy)adamantane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (silica, 4:1 Hexanes: Et_2O) afforded 38.0 mg (63%) of the title compound **104**.

Physical State: white solid.

m.p.: 50 – 52 °C.

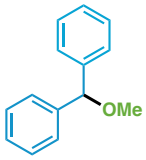
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 – 8.11 (m, 2H), 7.43 – 7.37 (m, 2H), 3.65 (t, J = 6.7 Hz, 2H), 2.91 (t, J = 6.7 Hz, 2H), 2.15 – 2.08 (m, 3H), 1.68 (d, J = 3.0 Hz, 6H), 1.65 – 1.53 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 148.0, 146.6, 130.0, 123.5, 72.5, 60.1, 41.6, 37.3, 36.5, 30.6.

GC/MS (EI): m/z (%) 301 (0.01%), 271 (3%), 150 (5%), 135 (100%), 79 (9%).

TLC: R_f = 0.65 (3:1 Hexanes: EtOAc).

Compound 105



(methoxymethylene)dibenzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively and the amount of MeOH was 6 equiv. Purification by PTLC (silica, pure Hexanes) afforded 33.5 mg (85%) of the title compound **105**.

Physical State: colorless oil.

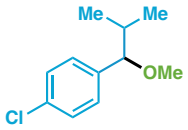
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 7.31 (m, 8H), 7.28 – 7.24 (m, 2H), 5.26 (s, 1H), 3.40 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 142.2, 128.5, 127.6, 127.1, 85.6, 57.2.

GC/MS (EI): m/z (%) 198 (75%), 167 (100%), 121 (74%), 105 (38%), 77 (38%).

TLC: R_f = 0.4 (50:1 Hexanes: Et_2O).

Compound 106



1-chloro-4-(1-methoxy-2-methylpropyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively and the amount of MeOH was 6 equiv. Purification by PTLC (silica, 100:1 Hexanes: Et_2O) afforded 31.7 mg (80%) of the title compound **106**.

Physical State: colorless oil.

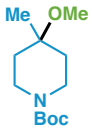
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 3.74 (d, J = 7.1 Hz, 1H), 3.18 (s, 3H), 1.87 (hept, J = 6.8 Hz, 1H), 0.97 (d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 139.8, 133.1, 128.9, 128.4, 89.2, 57.2, 34.8, 18.9.

GC/MS (EI): m/z (%) 198 (0.7%), 157 (32%), 155 (100%), 139 (10%), 91 (15%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 107



***tert*-butyl 4-methoxy-4-methylpiperidine-1-carboxylate**

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and MeOH (3 mL) as solvent. Purification by PTLC (silica, 8:1 Hexanes: EtOAc) afforded 21.5 mg (47%) of the title compound **107**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.69 (d, J = 13.1 Hz, 2H), 3.19 (s, 3H), 3.12 (t, J = 12.2 Hz, 2H), 1.71 (d, J = 13.7 Hz, 2H), 1.45 (s, 9H), 1.44 – 1.38 (m, 2H), 1.15 (s, 3H).

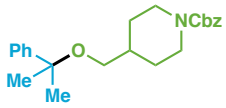
^{13}C NMR (151 MHz, $CDCl_3$): δ 155.1, 79.4, 71.7, 48.8, 40.0, 35.4, 28.6, 23.9.

GC/MS (EI): m/z (%) 229 (2%), 141 (62%), 126 (51%), 82 (58%), 57 (100%).

HRMS (ESI-TOF): calc'd for $C_{12}H_{23}NO_3Na$ $[M + Na]^+$: 252.1576; found 252.1575.

TLC: R_f = 0.3 (8:1 Hexanes: EtOAc).

Compound 108



benzyl 4-[(1-methyl-1-phenylethoxy)methyl]piperidine-1-carboxylate

Following General Procedure **A**. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 31.8 mg (43%) of the title compound **108**.

Physical State: colorless oil.

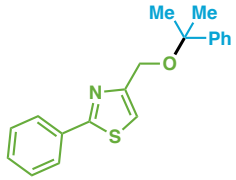
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.11 (m, 10H), 5.03 (s, 2H), 4.08 (broad s, 2H), 2.90 (d, *J* = 6.1 Hz, 2H), 2.69 (broad s, 2H), 1.77 – 1.52 (m, 4H), 1.43 (s, 6H), 1.02 (d, *J* = 13.0 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.4, 146.4, 137.1, 128.6, 128.3, 128.0, 127.9, 127.0, 125.8, 76.25, 67.2, 67.1, 44.1, 36.9, 29.2, 28.4.

HRMS (ESI-TOF): calc'd for $C_{23}H_{30}NO_3$ $[M + H]^+$: 368.2226, found: 368.2244.

TLC: R_f = 0.65 (2:1 Hexanes: EtOAc).

Compound 109



2-phenyl-4-(((2-phenylpropan-2-yl)oxy)methyl)thiazole

Following General Procedure **B** (0.6 mmol scale). Purification by PTLC afforded 102 mg (55%) of the title compound **109**.

Physical State: white solid.

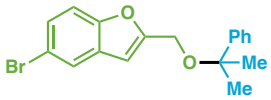
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (m, 2H), 7.45 (m, 2H), 7.35-7.25 (m, 5H), 7.20 (m, 2H), 4.40 (s, 2H), 1.60 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.1, 156.3, 150.0, 133.8, 129.9, 128.9, 128.3, 127.1, 126.5, 125.8, 114.4, 77.6, 62.2, 26.5.

HRMS (ESI-TOF): calc'd for $C_{19}H_{20}NOS$ $[M + H]^+$: 310.1260; found 310.1245.

TLC: R_f = 0.7 (7:3 heptane: MTBE).

Compound 110



5-bromo-2-(((2-phenylpropan-2-yl)oxy)methyl)benzofuran

Following General Procedure **B** (0.6 mmol scale). Purification by PTLC afforded 130 mg (63%) of the title compound **110**.

Physical State: colorless oil.

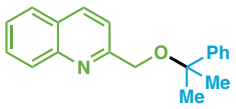
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (m, 1H), 7.55-7.50 (m, 2H), 7.41 (m, 2H), 7.35-725 (m, 3H), 6.57 (m, 1H), 4.32 (s, 2H), 1.66 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 157.1, 153.9, 145.4, 130.4, 128.4, 127.3, 126.9, 125.9, 123.5, 115.7, 112.7, 104.0, 78.1, 58.6, 28.4.

HRMS (ESI-TOF): calc'd for $C_{18}H_{18}BrO_2$ $[M + H]^+$: 345.0490; found 345.0484.

TLC: R_f = 0.8 (7:3 Heptane: MTBE).

Compound 111



2-(((2-phenylpropan-2-yl)oxy)methyl)quinoline

Following General Procedure **B** (0.6 mmol scale). Purification by PTLC afforded 84 mg (51%) of the title compound **111**.

Physical State: colorless oil.

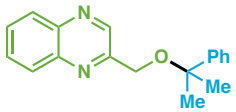
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (m, 1H), 8.01 (m, 1H), 7.82 (m, 1H), 7.77 (m, 1H), 7.69 (m, 1H), 7.60-7.50 (m, 3H), 7.37 (m, 2H), 7.25 (m 1H), 4.59 (s, 2H), 1.70 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.3, 147.4, 145.9, 136.5, 129.4, 128.9, 128.3, 127.6, 127.4, 127.1, 126.0, 125.8, 119.4, 77.7, 67.0, 28.4.

HRMS (ESI-TOF): calc'd for $C_{19}H_{20}NO$ $[M + H]^+$: 278.1539; found 278.1550.

TLC: R_f = 0.4 (7:3 Heptane: MTBE).

Compound 112



2-(((2-phenylpropan-2-yl)oxy)methyl)quinoxaline

Following General Procedure **B** (0.6 mmol scale). Purification by PTLC afforded 52 mg (31%) of the title compound **112**.

Physical State: colorless oil.

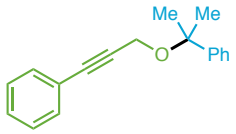
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.12 (s, 1H), 8.12 (m, 1H), 8.01 (m, 1H), 7.75 (m, 2H), 7.53 (m, 2H), 7.39 (m, 2H), 7.29 (m, 1H), 4.61 (s, 2H), 1.71 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 154.4, 145.4, 144.8, 142.0, 141.6, 130.0, 129.4, 129.3, 129.0, 128.5, 127.3, 125.8, 78.1, 65.5, 28.3.

HRMS (ESI-TOF): calc'd for $C_{18}H_{19}N_2O$ $[M + H]^+$: 279.1492; found 279.1501.

TLC: R_f = 0.5 (7:3 Heptane: MTBE).

Compound 113



(2-((3-phenylprop-2-yn-1-yl)oxy)propan-2-yl)benzene

Following General Procedure **A**. Purification by PTLC (silica, 10:1 Hexanes: Et_2O) afforded 14.5 mg (29%) of the title compound **113**.

Physical State: colorless oil.

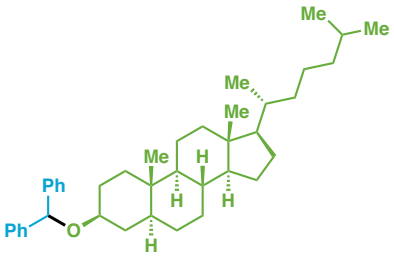
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 – 7.47 (m, 2H), 7.43 (dd, J = 6.7, 2.9 Hz, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.29 (dq, J = 5.9, 2.3, 1.6 Hz, 4H), 4.08 (s, 2H), 1.63 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.5, 131.9, 128.5, 128.3, 128.3, 127.3, 126.0, 123.1, 86.7, 85.1, 78.3, 52.5, 28.6.

GC/MS (EI): m/z (%) 235 (50%), 192 (63%), 115 (100%), 105 (20%), 91 (27%).

TLC: R_f = 0.3 (10:1 Hexanes: Et_2O).

Compound 114



(3*S*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-(benzhydryloxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene

Following General Procedure **B**. Purification by PTLC (40:1 Hexanes: Et_2O) afforded 79.1 mg (71%) of the title compound **114**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.34 (m, 4H), 7.34 – 7.30 (m, 4H), 7.26 – 7.22 (m, 2H), 5.58 (s, 1H), 3.38 – 3.31 (m, 1H), 1.97 (dt, *J* = 12.6, 3.4 Hz, 1H), 1.92 (d, *J* = 10.5 Hz, 1H), 1.85 – 1.77 (m, 1H), 1.74 – 1.63 (m, 3H), 1.58 – 0.96 (m, 24H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.88 (dd, *J* = 6.6, 2.7 Hz, 6H), 0.83 (s, 3H), 0.66 (s, 3H), 0.57 (td, *J* = 12.4, 4.0 Hz, 1H).

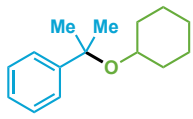
^{13}C NMR (151 MHz, $CDCl_3$): δ 143.2, 128.4, 127.3, 127.2, 80.3, 76.5, 56.6, 56.4, 54.6, 45.0, 42.7, 40.2, 39.7, 37.2, 36.3, 35.9, 35.6, 35.2, 32.3, 29.0, 28.6, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.4, 18.8, 12.5, 12.2.

GC/MS (EI): m/z (%) 491 (1%), 387 (4%), 371 (8%), 215 (10%), 119 (100%), 91 (34%).

TLC: R_f = 0.3 (40:1 Hexanes: Et_2O).

$[\alpha]_D^{24}$ = 8.3 (*c* = 1.0, $CHCl_3$).

Compound 115



(2-(cyclohexyloxy)propan-2-yl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively and the amount of alcohol was 6 equiv. Purification by PTLC (silica, pure Hexanes) afforded 29.6 mg (68%) of the title compound **115**.

Physical State: colorless oil.

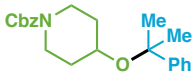
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 3.12 (tt, *J* = 10.1, 4.0 Hz, 1H), 1.77 – 1.68 (m, 2H), 1.68 – 1.62 (m, 2H), 1.55 (s, 6H), 1.47 – 1.42 (m, 1H), 1.31 – 1.22 (m, 2H), 1.15 – 1.03 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 147.4, 127.9, 126.9, 126.3, 76.7, 71.8, 35.3, 29.2, 25.7, 25.0.

GC/MS (EI): m/z (%) 218 (0.3%), 203 (14%), 119 (100%), 91 (30%), 77 (8%).

TLC: R_f = 0.5 (Hexanes).

Compound 116



benzyl 4-(1-methyl-1-phenylethoxy)piperidine-1-carboxylate

Following General Procedure **A**. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 32.7 mg (46%) of the title compound **116**.

Physical State: colorless oil.

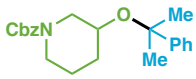
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.45 (m, 2H), 7.37 – 7.24 (m, 8H), 5.11 (s, 2H), 3.88 – 3.78 (broad s, 2H), 3.38 (dt, *J* = 8.4, 4.4 Hz, 1H), 3.03 (ddd, *J* = 13.2, 9.5, 3.5 Hz, 2H), 1.68 – 1.58 (broad m, 2H), 1.55 (s, 6H), 1.53 – 1.41 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.4, 146.8, 137.1, 128.6, 128.1, 128.0, 127.9, 127.2, 126.2, 77.1, 68.4, 67.1, 41.9, 33.7, 29.0.

HRMS (ESI-TOF): calc'd for $C_{22}H_{28}NO_3$ $[M + H]^+$: 354.2069, found: 354.2096.

TLC: R_f = 0.6 (2:1 Hexanes: EtOAc).

Compound 117



benzyl 3-(1-methyl-1-phenylethoxy)piperidine-1-carboxylate

Following General Procedure **A**. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 21.4 mg (30%) of the title compound **117**.

Physical State: colorless oil.

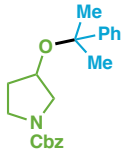
^{1}H NMR (400 MHz, $CDCl_3$, 2 rotamers): δ 7.57 – 7.39 (m, 2H), 7.39 – 7.24 (m, 8H), 5.05 (s, 2H), 4.09 – 3.66 (m, 2H), 3.3 – 2.7 (m, 3H), 1.86 – 1.19 (m, 11H).

^{13}C NMR (151 MHz, $CDCl_3$, 2 rotamers): δ 155.4, 146.6, 137.0, 128.6, 128.1, 128.0, 127.9, 127.2, 126.2, 67.7, 67.1, 50.6, 44.2, 32.9, 30.1, 28.8, 28.7, 23.9, 23.4.

HRMS (ESI-TOF): calc'd for $C_{22}H_{27}NO_3Na$ $[M + Na]^+$: 376.1889, found: 376.1896.

TLC: R_f = 0.59 (2:1 Hexanes: EtOAc).

Compound 118



benzyl 3-(1-methyl-1-phenylethoxy)pyrrolidine-1-carboxylate

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 22.0 mg (32%) of the title compound **118**.

Physical State: colorless oil.

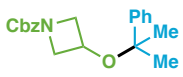
^{1}H NMR (600 MHz, $CDCl_3$, 2 rotamers): δ 7.42 (d, J = 7.9 Hz, 2H), 7.38 – 7.24 (m, 8H), 5.11 (s, 2H), 3.87 – 3.84 (m, 1H), 3.61-3.39 (m, 2H), 3.37 – 3.20 (m, 2H), 1.91-1.85 (m, 2H), 1.55 – 1.53 (4 s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$, 2 rotamers): δ 155.0, 154.9, 146.6, 146.5, 137.2, 137.1, 128.6, 128.4, 128.0, 127.3, 126.1, 126.0, 77.9, 77.7, 72.3, 71.5, 66.8, 66.7, 52.9, 52.5, 44.3, 44.0, 33.5, 32.8, 29.4, 29.2, 29.0, 28.8.

HRMS (ESI-TOF): calc'd for $C_{21}H_{26}NO_3$ $[M + H]^+$: 340.1913, found: 340.1943.

TLC: R_f = 0.56 (2:1 Hexanes: EtOAc).

Compound 119



benzyl 3-(1-methyl-1-phenylethoxy)azetidine-1-carboxylate

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively. Purification by PTLC (silica, 2:1 Hexanes: EtOAc) afforded 22.0 mg (34%) of the title compound **119**.

Physical State: colorless oil.

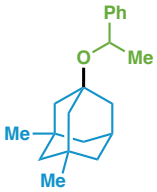
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.27 (m, 10H), 5.07 (s, 2H), 4.16 – 4.08 (m, 1H), 4.04 (dd, *J* = 9.1, 6.7 Hz, 2H), 3.95 (dd, *J* = 9.1, 4.9 Hz, 2H), 1.50 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.5, 145.9, 136.8, 128.6, 128.5, 128.1, 128.0, 127.4, 125.7, 78.4, 66.8, 62.5, 58.8, 28.7.

HRMS (ESI-TOF): calc'd for $C_{20}H_{24}NO_3$ $[M + H]^+$: 326.1756, found: 326.1765.

TLC: R_f = 0.53 (2:1 Hexanes: EtOAc).

Compound 120



1,3-dimethyl-5-(1-phenylethoxy)adamantane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu_4NClO_4 (0.1 M) instead of $AgPF_6$ and ^{n}Bu_4NPF_6 respectively. Purification by PTLC (silica, 1:1 Hexanes: CH_2Cl_2) afforded 47.0 mg (83%) of the title compound **120**.

Physical State: colorless oil.

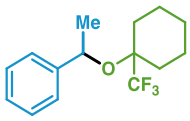
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 4.81 (q, *J* = 6.5 Hz, 1H), 2.12 (p, *J* = 3.2 Hz, 1H), 1.55 (dd, *J* = 10.7, 1.5 Hz, 2H), 1.45 (d, *J* = 10.7, 1H), 1.40 – 1.30 (m, 6H), 1.30 – 1.18 (m, 4H), 1.09 (s, 2H), 0.83 (s, 3H), 0.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 147.7, 128.2, 126.6, 125.7, 75.3, 68.1, 50.9, 49.0, 48.5, 42.9, 41.2, 33.7, 33.6, 31.1, 30.3, 30.3, 26.9.

GC/MS (EI): m/z (%) 269 (7%), 163 (100%), 123 (10%), 105 (60%), 91 (5%), 77 (10%), 55 (5%).

TLC: R_f = 0.59 (1:1 Hexanes: CH_2Cl_2).

Compound 121



(1-((1-(trifluoromethyl)cyclohexyl)oxy)ethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 15.2 mg (28%) of the title compound **121**.

Physical State: colorless oil.

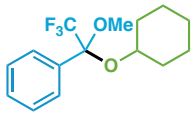
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 – 7.30 (m, 4H), 7.24 (t, *J* = 6.9 Hz, 1H), 4.89 (q, *J* = 6.4 Hz, 1H), 1.95 (t, *J* = 17.5 Hz, 2H), 1.59 – 1.46 (m, 5H), 1.44 (d, *J* = 6.4 Hz, 3H), 1.31 – 1.27 (m, 1H), 1.14 – 1.05 (m, 1H), 0.96 – 0.86 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.9, 128.4, 127.1, 126.8 (q, *J* = 288.4 Hz), 125.8, 77.2 (q, *J* = 25.6 Hz), 72.2, 30.1, 27.0, 26.0, 25.1, 20.6, 20.3.

GC/MS (EI): m/z (%) 272 (0.2%), 257 (26%), 107 (100%), 105 (80%), 79 (27%).

TLC: R_f = 0.5 (40:1 Hexanes: Et_2O).

Compound 122



(1-(cyclohexyloxy)-2,2,2-trifluoro-1-methoxyethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 49.6 mg (86%) of the title compound **122**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.69 – 7.61 (m, 2H), 7.44 – 7.36 (m, 3H), 4.07 – 3.95 (m, 1H), 3.37 (s, 3H), 1.97 – 1.83 (m, 2H), 1.81 – 1.74 (m, 2H), 1.58 – 1.47 (m, 3H), 1.33 – 1.25 (m, 3H).

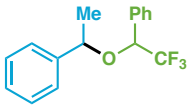
^{13}C NMR (151 MHz, $CDCl_3$): δ 134.9, 129.5, 128.8, 128.0, 122.9 (q, *J* = 291.0 Hz), 99.5 (q, *J* = 29.7 Hz), 72.2, 51.7, 34.1, 33.2, 25.7, 24.4, 24.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -77.32.

GC/MS (EI): m/z (%) 257 (0.06%), 219 (3%), 189 (100%), 137 (70%), 105 (32%).

TLC: R_f = 0.53 (20:1 Hexanes: Et_2O).

Compound 123



(2,2,2-trifluoro-1-(1-phenylethoxy)ethyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 50:1 Hexanes: Et_2O) afforded 29.1 mg (52%) of the title compound **123**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for both diastereomers) (the integration at 4.62 ppm, 4.44 ppm indicated the ratio of the two isomers of **123** to be 1:1): δ 7.47 – 7.27 (m, 15H), 7.25 – 7.13 (m, 5H), 4.83 – 4.75 (m, 1H), 4.62 (q, J = 6.7 Hz, 1H), 4.44 (q, J = 6.8 Hz, 1H), 4.38 – 4.25 (q, J = 6.7 Hz, 1H), 1.54 (d, J = 6.4 Hz, 3H), 1.48 (d, J = 6.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, for both diastereomers): δ 142.4, 141.7, 133.8, 133.0, 129.7, 129.2, 128.9,; 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 127.9, 126.8, 126.5, 124.7 (q, J = 283.9 Hz), 123.9 (q, J = 280.9 Hz), 78.8, 77.2 (q, J = 31.7 Hz), 76.8 (q, J = 31.7 Hz), 75.9, 24.4, 23.4.

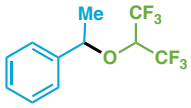
^{19}F NMR (376 MHz, $CDCl_3$, for both diastereomers): δ -76.10, -76.71.

GC/MS (EI) for one diastereomer: m/z (%) 265 (0.2%), 159 (26%), 121 (100%), 105 (100%), 77 (35%).

GC/MS (EI) for the other diastereomer: m/z (%) 265 (15%), 159 (100%), 121 (49%), 105 (75%), 77 (18%).

TLC: R_f = 0.4 (40:1 Hexanes: Et_2O).

Compound 124



(1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)ethyl)benzene

Following General Procedure **A**, HFIP (3 mL) instead of CH_2Cl_2 as solvent, no $AgClO_4$ and 3Å molecular sieves. Purification by PTLC (silica, 30:1 Hexanes: Et_2O) afforded 34.8 mg (64%) of the title compound **124**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.31 (m, 5H), 4.85 (q, *J* = 6.5 Hz, 1H), 3.99 (hept, *J* = 6.0 Hz, 1H), 1.60 (d, *J* = 6.5 Hz, 3H).

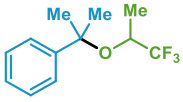
^{13}C NMR (151 MHz, $CDCl_3$): δ 139.6, 129.1, 129.0, 127.3, 123.2 – 120.3 (m), 81.5, 73.0 (p, *J* = 32.1 Hz), 23.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.54 (dq, *J* = 304.6, 9.4 Hz).

GC/MS (EI): m/z (%) 272 (11%), 257 (100%), 105 (69%), 77 (23%).

TLC: R_f = 0.53 (20:1 Hexanes: Et_2O).

Compound 125



(2-((1,1,1-trifluoropropan-2-yl)oxy)propan-2-yl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 40:1 Hexanes: Et_2O) afforded 20.5 mg (44%) of the title compound **125**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 3.80 – 3.71 (m, 1H), 1.62 (s, 3H), 1.59 (s, 3H), 1.12 (d, *J* = 6.4 Hz, 3H).

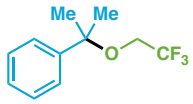
^{13}C NMR (151 MHz, $CDCl_3$): δ 144.8, 128.2, 127.7, 126.5, 125.4 (q, *J* = 282.4 Hz), 78.6, 67.5 (q, *J* = 30.7 Hz), 29.6, 26.8, 16.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -78.47.

GC/MS (EI): m/z (%) 232 (0.2%), 217 (100%), 119 (29%), 91 (24%), 77 (16%).

TLC: R_f = 0.5 (40:1 Hexanes: Et_2O).

Compound 126



(2-(2,2,2-trifluoroethoxy)propan-2-yl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, pure Hexanes) afforded 21.6 mg (50%) of the title compound **126**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 3.52 (q, *J* = 8.7 Hz, 2H), 1.60 (s, 6H).

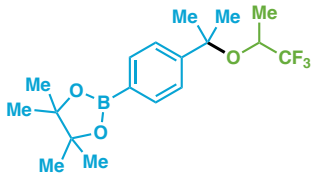
^{13}C NMR (151 MHz, $CDCl_3$): δ 144.4, 128.7, 127.7, 125.9, 123.8 (q, *J* = 277.8 Hz), 78.6, 61.7 (q, *J* = 34.2 Hz), 28.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -74.37.

GC/MS (EI): m/z (%) 218 (0.6%), 203 (100%), 119 (11%), 105 (9%), 91 (13%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 127



4,4,5,5-tetramethyl-2-(4-(2-((1,1,1-trifluoropropan-2-yl)oxy)propan-2-yl)phenyl)-1,3,2-dioxaborolane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^nBu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^nBu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 10:1 Hexanes: Et_2O) afforded 24.4 mg (34%) of the title compound **127**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.81 – 7.79 (m, 2H), 7.50 – 7.48 (m, 2H), 3.73 (p, *J* = 6.5 Hz, 1H), 1.61 (s, 3H), 1.58 (s, 3H), 1.35 (s, 12H), 1.11 (d, *J* = 6.5 Hz, 3H).

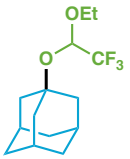
^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 134.7, 133.6, 125.8, 125.3 (q, *J* = 281.9 Hz), 84.0, 78.6, 67.7 (q, *J* = 30.7 Hz), 29.8, 26.7, 25.0 (d, *J* = 5.5 Hz), 16.3 (q, *J* = 2.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -78.45.

GC/MS (EI): m/z (%) 358 (0.2%), 343 (100%), 245 (36%), 145 (52%).

TLC: R_f = 0.26 (20:1 Hexanes: Et_2O).

Compound 128



1-(1-ethoxy-2,2,2-trifluoroethoxy)adamantane

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^{n}Bu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^{n}Bu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (silica, 30:1 hexanes: Et_2O) afforded 40.0 mg (72%) of the title compound **128**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 4.97 (q, *J* = 4.3 Hz, 1H), 3.81 – 3.67 (m, 2H), 2.20 – 2.17 (m, 3H), 1.86 – 1.78 (m, 6H), 1.68 – 1.59 (m, 6H), 1.23 (t, *J* = 7.1 Hz, 3H).

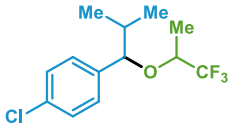
^{13}C NMR (151 MHz, $CDCl_3$): δ 122.4 (q, *J* = 285.5 Hz), 90.4 (q, *J* = 34.6 Hz), 76.0, 62.1, 42.3, 36.2, 30.8, 15.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -80.74.

GC/MS (EI): m/z (%) 278 (0.2%), 209 (2%), 151 (0.5%), 135 (100%), 95 (26%).

TLC: R_f = 0.50 (20:1 Hexanes: Et_2O).

Compound 129



1-chloro-4-(2-methyl-1-((1,1,1-trifluoropropan-2-yl)oxy)propyl)benzene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), $^{n}Bu_4NClO_4$ (0.1 M) instead of $AgPF_6$ and $^{n}Bu_4NPF_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (40:1 Hexanes: Et_2O) afforded 29.6 mg (53%, dr=1.5:1) of the title compound **129**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for both diastereomers) (the integration at 4.12 ppm, 4.00 ppm indicated the ratio of the two isomers of **129** to be 1.7:1): δ 7.32 (t, *J* = 8.2 Hz, 5.3H), 7.21 (d, *J* = 8.3 Hz, 5.4H), 4.12 (d, *J* = 7.9 Hz, 1.0H), 4.00 (d, *J* = 7.2 Hz, 1.7H), 3.65 – 3.55 (m, 2.7H), 1.94 – 1.84 (m, 2.7H), 1.30 (d, *J* = 6.4 Hz, 5.0H), 1.12 (d, *J* = 6.6 Hz, 3.1H), 1.05 (d, *J* = 6.6 Hz, 3.0H), 0.99 (d, *J* = 6.6 Hz, 5.1H), 0.74 (d, *J* = 6.8 Hz, 4.9H), 0.68 (d, *J* = 6.8 Hz, 3.0H).

^{13}C NMR (151 MHz, $CDCl_3$, for both diastereomers): δ 139.3, 138.6, 133.8, 133.7, 129.1, 129.1, 128.6, 128.5, 125.9 (q, *J* = 283.9 Hz), 124.9 (q, *J* = 280.9 Hz), 88.7, 85.4, 71.7 (q, *J* = 30.0 Hz), 71.0 (q, *J* = 31.1 Hz), 35.1, 34.9, 19.0, 19.0, 18.9, 18.9, 15.4 (q, *J* = 2.1 Hz), 12.8 (q, *J* = 2.1 Hz).

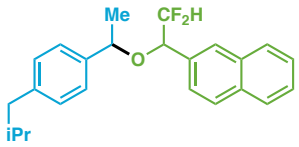
^{19}F NMR (376 MHz, $CDCl_3$, for both diastereomers): δ -78.04, -79.12.

GC/MS (EI) for one diastereomer: m/z (%) 280 (0.5%), 239 (32%), 237 (100%), 141 (35%), 113 (16%).

GC/MS (EI) for the other diastereomer: m/z (%) 280 (0.7%), 239 (33%), 237 (100%), 141 (24%), 113 (10%).

TLC: R_f = 0.4 (100:1 Hexanes: Et_2O).

Compound 130



2-(2,2-difluoro-1-(1-(4-isobutylphenyl)ethoxy)ethyl)naphthalene

Following General Procedure **A**, using $AgClO_4$ (124 mg, 3 equiv.), ^{n}Bu$_4$NClO$_4$ (0.1 M) instead of $AgPF_6$ and ^{n}Bu$_4$NPF$_6$ respectively, and the amount of alcohol was 4 equiv. Purification by PTLC (50:1 Hexanes: Et_2O) afforded 30.2 mg (41%, dr = 1:1) of the title compound **130**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for both diastereomers): the integration at 2.52 ppm, 2.41 ppm indicated the ratio of the two isomers of **130** to be 1:1): δ 7.93 – 7.73 (m, 8H), 7.56 – 7.46 (m, 5H), 7.42 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.23 – 7.12 (m, 6H), 7.05 – 6.99 (m, 2H), 5.89 (td, *J* = 55.8, 28.5 Hz, 1H), 5.88 (td, *J* = 55.8, 28.5 Hz, 1H), 4.76 (q, *J* = 6.4 Hz, 1H), 4.68 (td, *J* = 10.0, 4.9 Hz, 1H), 4.48 (ddd, *J* = 11.6, 10.2, 4.4 Hz, 1H), 4.39 (q, *J* = 6.5 Hz, 1H), 2.52 (d, *J* = 7.3 Hz, 2H), 2.41 (d, *J* = 7.2 Hz, 2H), 1.94 – 1.86 (m, 1H), 1.84 – 1.76 (m, 1H), 1.56 (d, *J* = 6.4 Hz, 3H), 1.49 (d, *J* = 6.5 Hz, 3H), 0.95 (dd, *J* = 6.6, 0.9 Hz, 6H), 0.86 (dd, *J* = 6.6, 3.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): 141.6, 141.2, 140.2, 139.5, 133.8, 133.3, 133.1, 133.0, 132.3, 132.3, 129.5, 129.2, 128.6, 128.3, 128.2, 128.2, 128.2, 127.9, 127.8, 127.6, 126.6, 126.5, 126.5, 126.4, 126.3, 125.5, 125.3, 117.8, 116.2 (t, *J* = 120.8 Hz), 114.5 (t, *J* = 121.8 Hz), 78.5 (t, *J* = 24.2 Hz), 77.9 (t, *J* = 24.2 Hz), 77.6, 75.4, 45.3, 45.2, 30.4, 30.3, 24.5, 22.9, 22.6, 22.5, 22.5.

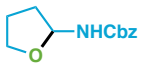
^{19}F NMR (400 MHz, $CDCl_3$): δ -124.91, -125.31, -128.22.

GC/MS (EI) for one diastereomer: m/z (%) 368 (2%), 192 (35%), 177 (23%), 161 (100%), 117 (93%).

GC/MS (EI) for the other diastereomer: m/z (%) 368 (1%), 192 (30%), 177 (17%), 161 (100%), 117 (86%).

TLC: R_f = 0.4 (50:1 Hexanes: Et_2O).

Compound 131

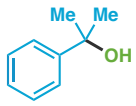


benzyl (tetrahydrofuran-2-yl)carbamate

The title product was synthesized by following General Procedure **A** with 2-(((benzyloxy)carbonyl)amino)-5-hydroxypentanoic acid as staring material[4] (53 mg, 0.2 mmol) to yield the title product as a colorless oil (19 mg, 44%). Spectral data matched those published[5]. ^{1}H NMR data are reported here for convenience:

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.28 (m, 5H), 5.57 (m, 1H), 5.25 – 5.03 (m, 3H), 3.90 (ddd, *J* = 8.4, 7.0, 6.7 Hz, 1H), 3.83 (ddd, *J* = 8.4, 7.0, 6.7 Hz, 1H), 2.19 (m, 1H), 1.93 (m, 2H), 1.68 (m, 1H).

Compound 132



2-phenylpropan-2-ol

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 21.0 mg (77%) of the title compound **132**.

Physical State: colorless oil.

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[6] Synthesized according to the literature procedure: Rosenthal, G. A., Dahlman, D. L., Crooks, P, A., Phuket, S. N. & Trifonov, L. S. Insecticidal Properties of Some Derivatives of L-Canavanine. *J. Agric. Food Chem.*, **43**, 2728–2734 (1995).

[7] Sugiura, M. & Kobayashi, S. Lewis Acid-Catalyzed Ring-Opening Reactions of Semicyclic *N*,*O*-Acetals. *Org. Lett.,* **3**, 477–480 (2001).

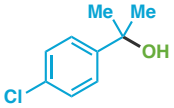
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53 – 7.48 (m, 2H), 7.38 – 7.33 (m, 2H), 7.28 – 7.23 (m, 1H), 1.78 (s, 1H), 1.59 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 149.2, 128.4, 126.8, 124.5, 72.7, 31.9.

GC/MS (EI): m/z (%) 136 (5%), 121 (100%), 91 (9%), 77 (17%).

TLC: R_f = 0.39 (3:1 Hexanes: EtOAc).

Compound 133

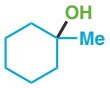


2-(4-chlorophenyl)propan-2-ol

The title product was synthesized by following General Procedure **C** with 2-(4-chlorophenyl)-2-methylpropanoic acid (39.6 mg, 0.2 mmol) to yield the title product as a colorless oil (25.8 mg, 76%). Spectral data matched the one published[6].

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 1.94 (s, 1H), 1.55 (s, 6H).[6]

Compound 134



1-methylcyclohexan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 8:1 Hexanes: EtOAc) afforded 16.0 mg (70%) of the title compound **134**.

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.62 – 1.38 (m, 9H), 1.27 (dq, J = 15.2, 6.1, 4.6 Hz, 1H), 1.18 (s, 3H).

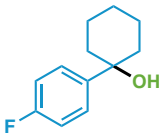
^{13}C NMR (126 MHz, $CDCl_3$): δ 70.0, 39.5, 29.6, 25.7, 22.8.

GC/MS (EI): m/z (%) 114 (5%), 99 (18%), 81 (23%), 71 (100%), 58 (28%).

TLC: R_f = 0.3 (6:1 Hexanes: EtOAc).

[8] Zhang, L. & Hu, X. Room temperature C(sp^2)–H oxidative chlorination via photoredox catalysis. *Chem. Sci.*, **8**, 7009–7013 (2017).

Compound 135



1-(4-fluorophenyl)cyclohexanol

Following General Procedure **C**. Purification by PTLC (silica, 4:1 Hexanes: EtOAc) afforded 36.0 mg (92%) of the title compound **135**.

Physical State: white solid.

m.p.: 72 – 74 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47 (dd, *J* = 8.2, 5.6 Hz, 2H), 7.01 (t, *J* = 8.6 Hz, 2H), 1.86 – 1.70 (m, 7H), 1.68 – 1.59 (m, 3H), 1.34 – 1.23 (m, 1H).

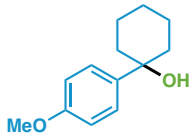
^{13}C NMR (151 MHz, $CDCl_3$): δ 161.8 (d, *J* = 244.8 Hz), 145.3 (d, *J* = 3.3 Hz), 126.5 (d, *J* = 7.9 Hz), 115.0 (d, *J* = 20.9 Hz), 73.0, 39.1, 25.6, 22.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.05.

GC/MS (EI): m/z (%) 194 (17%), 176 (39%), 151 (100%), 109 (36%).

TLC: R_f = 0.58 (3:1 Hexanes: EtOAc).

Compound 136



1-(4-methoxyphenyl)cyclohexanol

Following General Procedure **C**. Purification by PTLC (silica, 3:1 Hexanes: EtOAc) afforded 29.0 mg (70%) of the title compound **136**.

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 1.87 – 1.68 (m, 7H), 1.67 – 1.58 (m, 3H), 1.35 – 1.23 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 158.4, 141.8, 125.9, 113.6, 72.9, 55.4, 39.0, 25.7, 22.4.

HRMS (ESI-TOF): calc'd for $C_{13}H_{19}O_2$ $[M + H]^+$: 207.1380; found 207.1384.

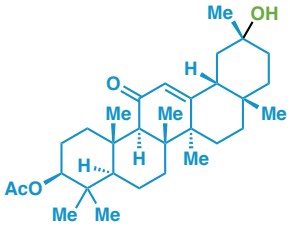
TLC: R_f = 0.47 (3:1 Hexanes:EtOAc).

Compound 137

1-chloro-2-methylpropan-2-ol

Following General Procedure **C**. The yield (84%) was detected by GC-FID.

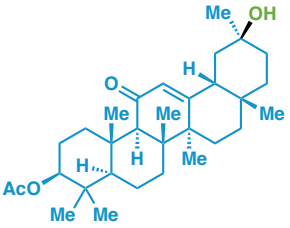
Compound 138



(3*S*,4a*R*,6a*R*,6b*S*,8a*S*,12a*R*,14a*R*,14b*S*)-11-hydroxy-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-yl acetate

Following General Procedure **C**. Purification by PTLC (silica, 1:1 Hexanes: EtOAc) afforded 38.0 mg (39%) of compound **(11*S*)-138** and 34.0 mg (35%) of compound **(11*R*)-138**.

Compound (11*S*)-138



(3*S*,4a*R*,6a*R*,6b*S*,8a*S*,11*S*,12a*R*,14a*R*,14b*S*)-11-hydroxy-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-yl acetate

Physical State: white solid.

m.p.: 242 – 244 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.63 (s, 1H), 4.51 (dd, *J* = 11.8, 4.7 Hz, 1H), 2.78 (dt, *J* = 13.6, 3.7 Hz, 1H), 2.37 (dd, *J* = 13.7, 3.9 Hz, 1H), 2.34 (s, 1H), 2.04 (s, 3H), 2.00 (td, *J* = 13.6, 4.5 Hz, 1H), 1.86 – 1.80 (m, 2H), 1.75 – 1.49 (m, 6H), 1.50 – 1.28 (m, 9H), 1.27 – 1.10 (m, 10H), 1.09 – 0.96 (m, 2H), 0.87 (s, 9H), 0.79 (dd, *J* = 12.0, 1.9 Hz, 1H).

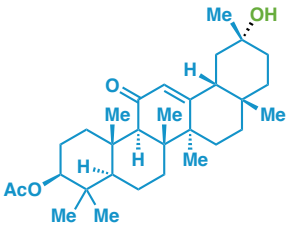
^{13}C NMR (151 MHz, $CDCl_3$): δ 200.2, 171.2, 169.9, 128.3, 80.8, 69.5, 61.8, 55.1, 46.7, 45.6, 44.4, 43.4, 38.9, 38.2, 37.1, 35.6, 34.1, 32.8, 32.0, 31.7, 28.4, 28.2, 26.6, 26.1, 23.7, 23.6, 21.5, 18.8, 17.5, 16.8, 16.5.

HRMS (ESI-TOF): calc'd for $C_{31}H_{49}O_4$ $[M + H]^+$: 485.3625; found 485.3628.

TLC: R_f = 0.41 (1:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = +485.5 (*c* = 1.0, $CHCl_3$).

Compound (11*R*)-138



(3*S*,4a*R*,6a*R*,6b*S*,8a*S*,11*R*,12a*R*,14a*R*,14b*S*)-11-hydroxy-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-3-yl acetate

Physical State: white solid.

m.p.: 279 – 281 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.59 (s, 1H), 4.51 (dd, *J* = 11.8, 4.7 Hz, 1H), 2.78 (dt, *J* = 13.7, 3.7 Hz, 1H), 2.36 (s, 1H), 2.12 (td, *J* = 13.5, 4.4 Hz, 1H), 2.07 – 2.04 (m, 4H), 1.98 (t, *J* = 13.2 Hz, 1H), 1.82 (td, *J* = 13.8, 4.8 Hz, 1H), 1.74 – 1.58 (m, 5H), 1.51 – 1.45 (m, 3H), 1.44 – 1.39 (m, 3H), 1.37 (s, 3H), 1.24 (s, 3H), 1.22 – 1.18 (m, 1H), 1.16 (s, 3H), 1.13 (s, 3H), 1.09 – 0.98 (m, 3H), 0.87 (s, 6H), 0.86 (s, 3H), 0.80 (d, *J* = 11.6 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 200.3, 171.1, 168.8, 128.4, 80.7, 71.5, 61.8, 55.1, 49.6, 45.8, 45.6, 43.5, 38.9, 38.4, 38.2, 37.1, 35.6, 32.8, 32.6, 28.3, 28.2, 26.52, 26.48, 25.3, 23.7, 23.5, 21.4, 18.9, 17.5, 16.8, 16.5.

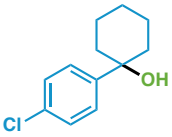
HRMS (ESI-TOF): calc'd for $C_{31}H_{49}O_4$ $[M + H]^+$: 485.3625; found 485.3632.

TLC: R_f = 0.29 (1:1 Hexanes: EtOAc).

$[\alpha]_D^{24}$ = +417.4 (*c* = 1.0, $CHCl_3$).

The structure of **compound (11*R*)-138** was unambiguously determined by an X-ray diffraction analysis (see the CIF file).

Compound 139



1-(4-chlorophenyl)cyclohexan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 5:2 Heptane:EtOAc) afforded 30.1 mg (72%) of the title compound **139**.

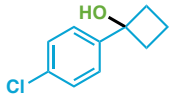
Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.37 (m, 2H), 7.37 – 7.27 (m, 2H), 1.85 – 1.67 (m, 7H), 1.67 – 1.59 (m, 3H), 1.36 – 1.21 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.95, 132.40, 128.23, 126.14, 72.90, 38.79, 25.37, 22.06.

TLC: R_f = 0.6 (3:1 Heptane:EtOAc).

Compound 140



1-(4-chlorophenyl)cyclobutan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 5:3 Heptane:EtOAc) afforded 24.6 mg (68%) of the title compound **140**.

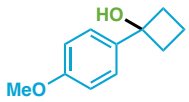
Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.42 (m, 2H), 7.40 – 7.32 (m, 2H), 2.61 – 2.49 (m, 2H), 2.45 – 2.32 (m, 2H), 2.13 – 1.99 (m, 1H), 2.00 (s, 1H), 1.72 (dtt, J = 11.4, 8.8, 7.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.78, 132.99, 128.51, 126.46, 76.60, 37.02, 12.90.

TLC: R_f = 0.5 (3:1 Heptane:EtOAc).

Compound 141



1-(4-methoxyphenyl)cyclobutan-1-ol

Following General Procedure **C**. Purification by PTLC (silica, 2:1 Heptane:EtOAc) afforded 25.3 mg (71%) of the title compound **141**.

Physical State: colorless oil.

^{1}H NMR (400 MHz, Benzene-d_6) δ 7.36 – 7.28 (m, 2H), 6.82 (d, J = 8.8 Hz, 2H), 3.35 (s, 3H), 2.45 – 2.31 (m, 2H), 2.25 – 2.12 (m, 2H), 1.93 – 1.75 (m, 1H), 1.60 – 1.46 (m, 1H).

^{13}C NMR (101 MHz, Benzene-d_6) δ 159.29, 139.44, 126.60, 113.99, 76.59, 54.85, 37.54, 13.32.

TLC: R_f = 0.5 (2:1 Heptane:EtOAc).

Discussion, Experimental Procedures, and Characterization for Applications

In the below section we detail 12 real-world applications in which we used the currently-reported decarboxylative etherification to synthesize 12 molecules of industrial, biomedical, or academic interest. We compare these syntheses to previously-reported literature routes. Because starting materials for respective routes to the same compound differ, comparisons inherently cannot be direct; however, we believe that the dramatic improvements in overall yield, step-count, and reaction time are quite compelling.

The kinase inhibitor intermediate **1** in Figure 1A that was previously accessed in 3.4% overall yield, in 3 steps, over 6 days, can now be prepared in 51% overall yield (63% for ether bond formation), in 2 steps, over 15 hours[9]. Glycogen phosphorylase inhibitors accessed from the hindered ether-containing amino acid **11** were previously prepared in 31% overall yield, in 5 steps, over 2.5 days[10]. Now, they are accessible in 32% yield, in 1 step, over 3 hours. Wipf's elegant synthesis of the anti-tumor marine natural product trunkamide A relied on access to the serine-derived ether **12** which required 7 steps, proceeding in 37% overall yield after >3 days of effort[11]. Alternatively, the same ether could be prepared in a single step, in 3 hours from commercially available Z-Ser-OMe (40% isolated yield). A recent report from Bristol-Meyers Squibb (BMS) on the synthesis of macrocyclic HIV-inhibitors utilized intermediate **13**, which required a 6-step route proceeding in 24% overall yield after 2 days, and necessitated expensive and moisture-sensitive reagents[12]. In stark contrast, **13** can be prepared by our method in a single step (21% yield, 3 h). Cyclohexanone derivatives such as **14**, which have found use as intermediates for the synthesis of liquid crystals, were synthesized through a 4-step sequence in 47% yield over 2 days[13]. Etherification through *via* the carboxylic acid enables a single step, 3-hour preparation in 42% yield. The simple brominated tertiary ether **15** used as an intermediate for the preparation of muscarinic acetylcholine receptor antagonists was accessed through a low-yielding (<2%), 2-step procedure requiring >5 days of reaction time[14]. The same structure can now be accessed in a single step (81% yield, 3 h).

During a recent campaign targeting GPR120 modulators, BMS employed a 7-step route to **72** (involving a variety of labor intensive reactions including the use of mercury) that proceeded in *ca*. 21% overall yield after 4 days[15,16]. In contrast, commercially available **70** could

be subjected to decarboxylative methoxylation to deliver **72** after ester hydrolysis in two steps over 9 hours (56% overall yield). The same starting material could be used to access bridged system **73** in a single decarboxylative step using water as the nucleophile (66% yield, 3 h); this compound was previously prepared in a 9-step process required more than 5 days (*ca*. 15% overall yield)[16]. Signal Pharmaceuticals, in the pursuit of JNK kinase inhibitors, prepared amino-ether **74** in a 7-step process, commencing with **71** proceeding in 12% overall yield after 3 days of reaction time[17]. This simple structure could instead be accessed in 2 intuitive steps (31% overall yield, 24 h) from the same starting material: Electrochemical methoxylation with a basic workup to hydrolyze the resulting ester, followed by Curtius rearrangement. Semi-ester starting materials such as **70** and **71** could also allow us to rapidly access valuable chemical space through decarboxylative hydroxylation. For instance, tertiary alcohol **75** (another GPR120 modulator intermediate) was historically prepared in a 14-step sequence requiring more than 9 days of labor in 5% overall yield by employing a range of inconvenient or expensive reagents including $TMSCHN_2$, BF_3, $LiAlH_4$, Dess-Martin periodinane, and Pd[18]. Striking truncation of this sequence could be achieved by a 2-step sequence (22% overall, 27 h) involving electrochemical hydroxylation (with basic workup to hydrolyze the remaining ester), followed by decarboxylative Giese-type chemistry. The same logic could be applied to alcohol **76**, of use as an intermediate in the liquid-crystal arena, that was previously synthesized in a 7-step sequence (8% overall yield, 62 h)[19]. Thus, a Ni-catalyzed decarboxylative Negishi coupling of **71**, followed by hydrolysis and electrochemical hydroxylation, furnished **76** in only 3 steps (17 % overall). The modularity of the routes to **75** and **76** are notable and, aside from reducing overall step count, the pathways enabled by this electrochemical approach allow for more convenient exploration of diverse chemical space. Finally, studies in the synthesis of steroidal dehydrogenase inhibitors required the semi-synthesis of enoxolone analogs **77**. A 5-step sequence from the natural product (enoxolone) featuring Barton decarboxylative halogenation was required (procedures and diastereomeric ratio were not reported), which could be streamlined in a single step from the same starting material (61% yield, 3 h, 1.1:1 dr)[20].

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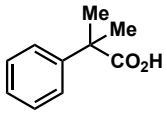
Price of commercial carboxylic acids used in the applications.



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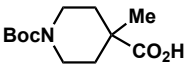
$10/5g (Combi-Blocks Inc)



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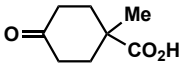

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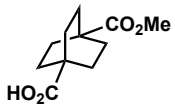

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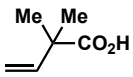

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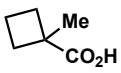

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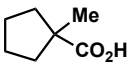
$120/g (Combi-Blocks Inc)



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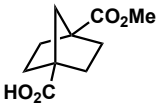
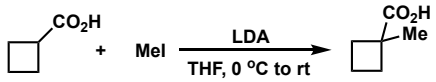
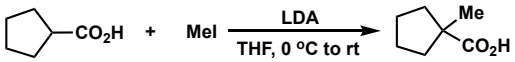


CAS no.: 15448-77-8
$430/g (eNovation Chemicals LLC)

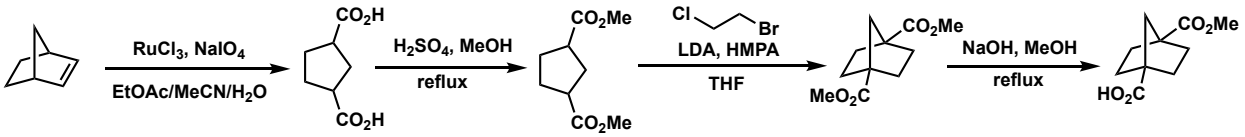
Synthetic routes for the preparation of some expensive carboxylic acids.



ref. *Chem. Commun.* 2006, 39, 4107



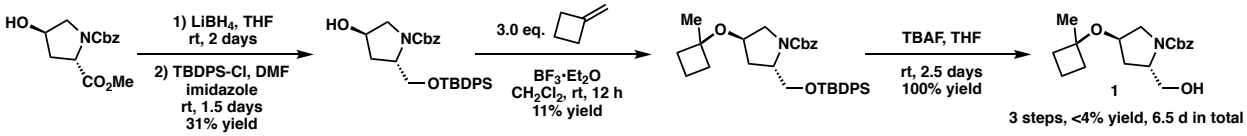
ref. *Angew. Chem. Int. Ed.* 2014, 53, 4945.



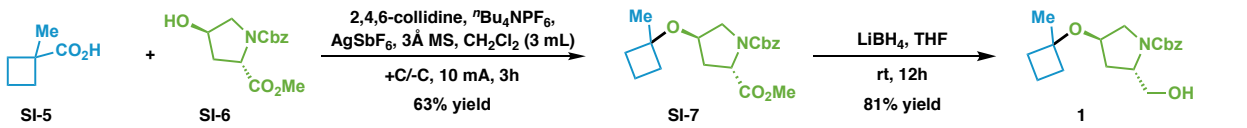
ref. *J. Med. Chem.* 2011, 54, 3480

Application for Etherification No. 1

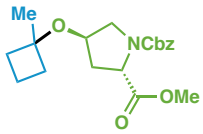
Previous synthesis of intermediate of aurora kinase modulator (compound **1**) (ref. *WO2011088045 A1*).



Scheme for the synthesis of compound **1**



Compound SI-7



1-benzyl 2-methyl (2*S*,4*R*)-4-(1-methylcyclobutoxy)pyrrolidine-1,2-dicarboxylate

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **SI-5** (23 mg, 0.2 mmol, 1 equiv.), **SI-6** (168 mg, 0.6 mmol, 3 equiv.), $AgSbF_6$ (103 mg, 1.5 equiv.), DBU (92.1 mg, 3 equiv.), $^nBu_4NPF_6$ (232 mg, 0.6 mmol), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was pre-stirred for 30 min and electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL).

The resulting mixture was washed with 2N HCl (20 mL) and saturated $NaHCO_3$ aq. (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (3:1 Hexanes:EtOAc, v/v) to give the product **SI-7** as a colorless oil (44.0 mg, 63% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, for two rotamers): δ 7.42 – 7.27 (m, 5H), 5.20 – 5.01 (m, 2H), 4.49 – 4.42 (m, 1H), 4.25 – 4.12 (m, 1H), 3.81 – 3.70 (m, 2.5H), 3.55 (s, 1.5H), 3.51 – 3.34 (m, 1H), 2.33 – 2.15 (m, 1H), 2.14 – 1.99 (m, 3H), 1.92 – 1.81 (m, 2H), 1.76 – 1.66 (m, 1H), 1.65 – 1.50 (m, 2H), 1.37 – 1.29 (m, 3H).

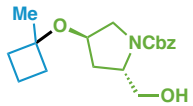
^{13}C NMR (151 MHz, $CDCl_3$, for two rotamers): δ 173.4, 173.3, 155.1, 154.4, 136.7, 136.6, 128.6, 128.5, 128.14, 128.09, 128.06, 128.0, 77.5, 77.4, 70.5, 69.7, 67.3, 67.2, 58.0, 57.8, 53.6, 53.0, 52.5, 52.2, 38.4, 37.4, 34.9, 34.8, 24.3, 12.6.

HRMS (ESI-TOF): calc'd for $C_{19}H_{26}NO_5$ $[M + H]^+$: 348.1805; found 348.1813.

TLC: R_f = 0.27 (3:1 Hexanes:EtOAc).

$[\alpha]_D^{24}$ = -148.7 (*c* = 1.0, $CHCl_3$).

Compound 1



benzyl (2*S*,4*R*)-2-(hydroxymethyl)-4-(1-methylcyclobutoxy)pyrrolidine-1-carboxylate

A solution of ester **SI-7** (18 mg, 0.052 mmol, 1 equiv.) in THF (2 mL) was cooled to 0 °C. 4 M $LiBH_4$ in THF (52 μL, 0.207 mmol, 4 equiv.) was added. After stirring overnight at room temperature the reaction was quenched by adding water (5 mL), and hydrochloric acid (1 N) was added until neutral pH. The aqueous phase was extracted with ethyl acetate (15 mL × 3), the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (1:1 Hexanes: EtOAc, v/v) to give the product as a colorless oil (13.4 mg, 81% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.29 (m, 5H), 5.15 (s, 2H), 4.32 (dd, *J* = 8.6, 2.9 Hz, 1H), 4.23 – 4.14 (m, 1H), 4.10 – 4.07 (m, 1H), 3.73 (ddd, *J* = 10.9, 7.8, 2.8 Hz, 1H), 3.59 (ddd, *J* =

11.1, 7.4, 2.7 Hz, 1H), 3.50 (qd, *J* = 11.6, 4.4 Hz, 2H), 2.14 – 1.98 (m, 3H), 1.89 – 1.83 (m, 2H), 1.77 – 1.67 (m, 2H), 1.60 – 1.50 (m, 1H), 1.32 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 157.3, 136.6, 128.7, 128.2, 128.1, 77.2, 70.0, 67.5, 67.0, 59.7, 54.3, 36.5, 35.0, 24.3, 12.7.

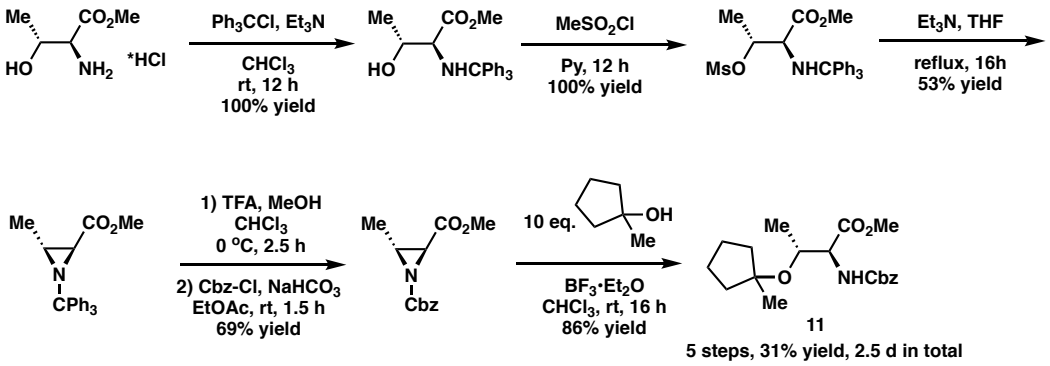
HRMS (ESI-TOF): calc'd for $C_{18}H_{26}NO_4$ $[M + H]^+$: 320.1856; found 320.1860.

TLC: R_f = 0.47 (1:2 Hexanes:EtOAc).

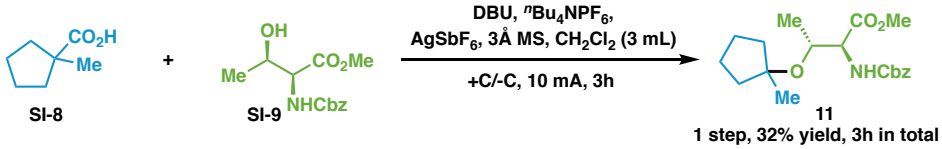
$[\alpha]_D^{24}$ = -97.9 (*c* = 1.0, $CHCl_3$).

Application for Etherification No. 2

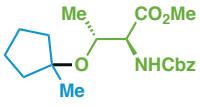
Previous synthesis of intermediate of Glycogen phosphorylase inhibitors (compound **11**) (ref. *WO2006052722 A1*).



Scheme for the synthesis of compound **11**



Compound 11



methyl *N*-((benzyloxy)carbonyl)-*O*-(1-methylcyclopentyl)-*L*-threoninate

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **SI-8** (25.6 mg, 0.2 mmol, 1 equiv.), **SI-9** (160 mg, 0.6 mmol, 3 equiv.), $AgSbF_6$ (103 mg, 0.3 mmol, 1.5 equiv.), DBU (92.1 mg, 0.6 mmol, 3 equiv.), $^nBu_4NPF_6$ (232 mg, 0.6 mmol, 0.2M), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap

equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with 2N HCl (20 mL) and saturated $NaHCO_3$ aq. (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (4:1 Hexanes:EtOAc, v/v) to give the product **11** as a colorless oil (22.3 mg, 32% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 – 7.32 (m, 5H), 5.55 (d, J = 9.6 Hz, 1H), 5.13 (s, 2H), 4.23 (dd, J = 9.6, 1.9 Hz, 1H), 4.19 (qd, J = 6.2, 1.9 Hz, 1H), 3.73 (s, 3H), 1.74 – 1.70 (m, 1H), 1.67 – 1.61 (m, 3H), 1.56 – 1.53 (m, 2H), 1.39 – 1.35 (m, 2H), 1.22 (d, J = 6.2 Hz, 3H), 1.17 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.8, 156.9, 136.5, 128.7, 128.3, 128.3, 85.6, 68.4, 67.2, 60.1, 52.4, 39.2, 38.4, 24.8, 23.8, 23.7, 21.0.

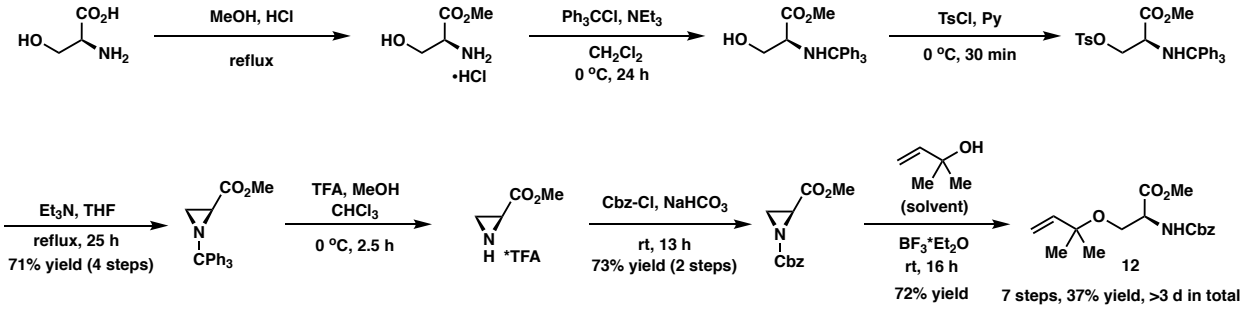
HRMS (ESI-TOF): calc'd for $C_{19}H_{27}NO_5Na$ $[M+Na]^+$: 372.1781, found: 372.1789.

TLC: R_f = 0.3 (4:1 Hexanes:EtOAc).

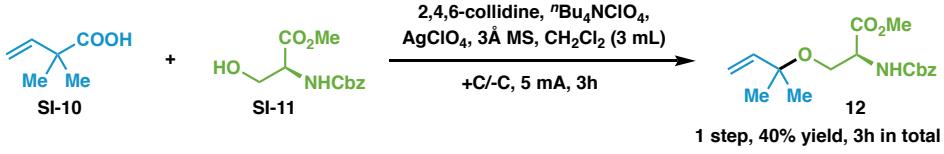
$[\alpha]_D^{24}$ = 5.5 (c = 0.5, $CHCl_3$).

Application for Etherification No. 3

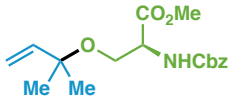
Previous synthesis of anti-tumor marine natural product trunkamide A (compound **12**) (ref. *J. Org. Chem.* **2000**, *65*, 1037–1049).



Scheme for the synthesis of compound **12**



Compound 12



(2*S*)-2-(benzyloxycarbonylamino)-3-(1,1-dimethylallyloxy)propionic acid methyl ester

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **SI-10** (23 mg, 0.2 mmol, 1 equiv.), **SI-11** (152 mg, 0.6 mmol, 3 equiv.), $AgClO_4$ (124 mg, 3 equiv.), 2,4,6-collidine (72.7 mg, 0.6 mmol, 3 equiv.), $^nBu_4NClO_4$ (103 mg, 0.3 mmol, 0.1M), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was pre-stirred for 30 min and electrolyzed under constant current at 5 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with 2N HCl (20 mL) and saturated $NaHCO_3$ aq. (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (4:1 Hexanes:EtOAc, v/v) to give the product **12** as a white solid (26.0 mg, 40% yield).

Physical State: white solid.

m.p.: 42 – 44 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 5H), 5.70 (dd, *J* = 17.9, 10.6 Hz, 1H), 5.61 (d, *J* = 8.9 Hz, 1H), 5.20 – 5.05 (m, 4H), 4.45 (dt, *J* = 8.9, 3.1 Hz, 1H), 3.81 – 3.67 (m, 4H), 3.53 (dd, *J* = 9.2, 3.3 Hz, 1H), 1.21 (s, 3H), 1.20 (s, 3H).

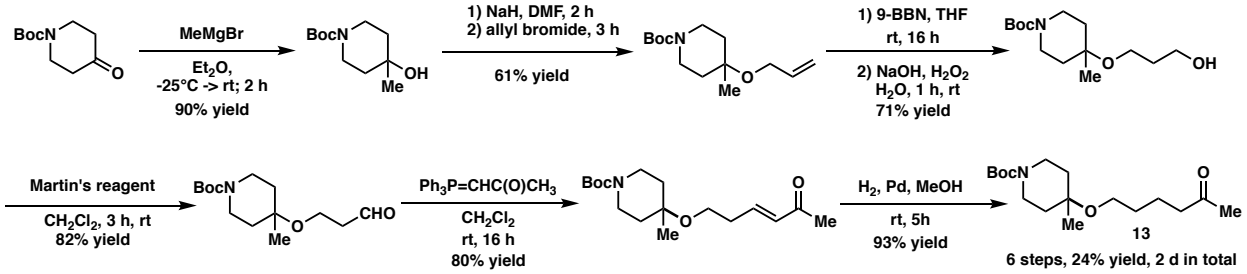
^{13}C NMR (151 MHz, $CDCl_3$): δ 171.2, 156.2, 143.1, 136.4, 128.7, 128.31, 128.28, 114.4, 75.6, 67.1, 62.9, 54.7, 52.5, 25.7, 25.6.

TLC: R_f = 0.25 (CH_2Cl_2).

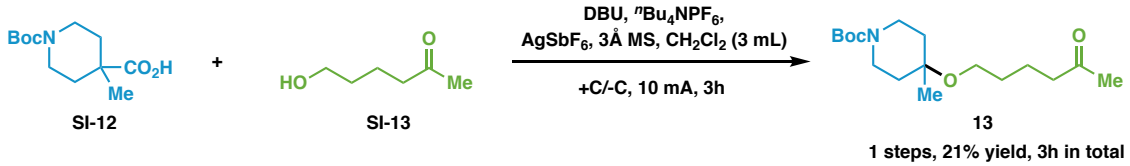
$[\alpha]_D^{24}$ = +9.3 (*c* = 0.95, $CHCl_3$).

Application for Etherification No. 4

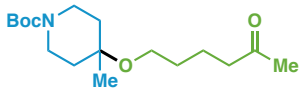
Previous synthesis of the intermediate of macrocyclic HIV-inhibitor (compound **13**) (ref. *US20150232481 A1*).



Scheme for the synthesis of compound **13**



Compound 13



***tert*-butyl 4-methyl-4-((5-oxohexyl)oxy)piperidine-1-carboxylate**

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **SI-12** (49 mg, 0.2 mmol, 1 equiv.), **SI-13** (70 mg, 0.6 mmol, 3 equiv.), $AgSbF_6$ (103 mg, 0.3 mmol, 1.5 equiv.), DBU (92.1 mg, 0.6 mmol, 3 equiv.), $^nBu_4NPF_6$ (232 mg, 0.6 mmol, 0.2 M), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was pre-stirred for 30 min and electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with H_2O (20 mL) twice, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (4:1 Hexanes:EtOAc, v/v) to give the product **13** as a colorless oil (13.2 mg, 21% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.69 (d, *J* = 13.1 Hz, 2H), 3.30 (t, *J* = 6.3 Hz, 2H), 3.10 (t, *J* = 12.1 Hz, 2H), 2.46 (t, *J* = 7.4 Hz, 2H), 2.14 (s, 3H), 1.74 – 1.67 (m, 2H), 1.67 – 1.62 (m, 2H), 1.55 – 1.50 (m, 2H), 1.45 (s, 9H), 1.39 (ddd, *J* = 13.7, 11.5, 4.5 Hz, 2H), 1.14 (s, 3H).

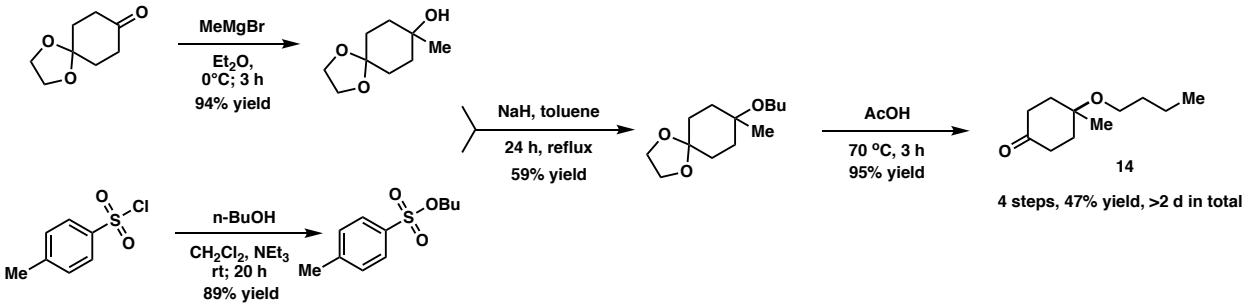
^{13}C NMR (151 MHz, $CDCl_3$): δ 209.1, 155.1, 79.4, 71.3, 60.4, 43.7, 40.0, 35.8, 30.09, 30.05, 28.6, 24.7, 21.0.

HRMS (ESI-TOF): calc'd for $C_{17}H_{31}NO_4Na$ $[M + Na]^+$: 336.2145; found 336.2151.

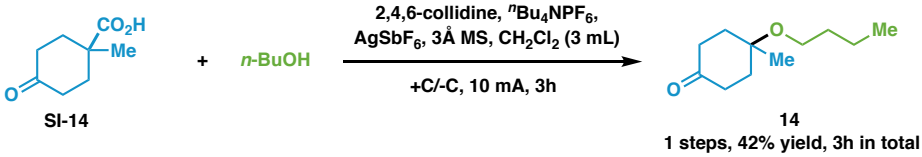
TLC: R_f = 0.21 (3:1 Hexanes:EtOAc).

Application for Etherification No. 5

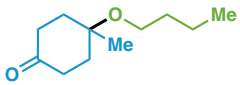
Previous synthesis of intermediate of liquid crystals material (compound **14**) (ref. *WO2017116213 A1*).



Scheme for the synthesis of compound **14**



Compound 14



4-butoxy-4-methylcyclohexan-1-one

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **SI-14** (32 mg, 0.2 mmol, 1 equiv.), *n*-BuOH (360 mg, 4.8 mmol, 24 equiv.), $AgSbF_6$ (103 mg, 0.3 mmol, 1.5 equiv.), 2,4,6-collidine (72.7 mg, 0.6 mmol, 3 equiv.), $^nBu_4NPF_6$ (232 mg, 0.6 mmol, 0.2 M), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was pre-stirred for 30 min and electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with H_2O (20 mL)

twice, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (5:1 Hexanes:EtOAc, v/v) to give the product **14** as a colorless oil (15.6 mg, 42% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.39 (t, *J* = 6.4 Hz, 2H), 2.61 (td, *J* = 14.1, 5.9 Hz, 2H), 2.19 – 2.11 (m, 4H), 1.68 (td, *J* = 14.0, 4.5 Hz, 2H), 1.61 – 1.54 (m, 2H), 1.46 – 1.37 (m, 2H), 1.23 (s, 3H), 0.93 (t, *J* = 7.4 Hz, 3H).

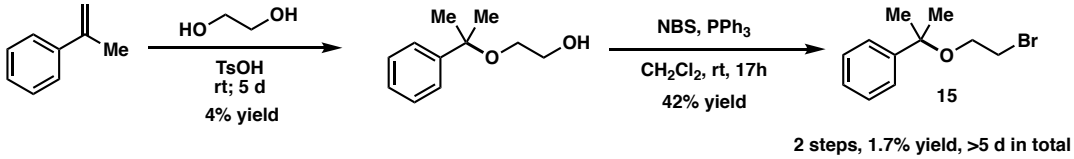
^{13}C NMR (151 MHz, $CDCl_3$): δ 212.5, 71.6, 61.0, 37.1, 36.1, 32.8, 24.3, 19.8, 14.2.

GC/MS (EI): m/z (%) 184 (8%), 169 (0.6%), 127 (74%), 71 (100%), 55 (29%).

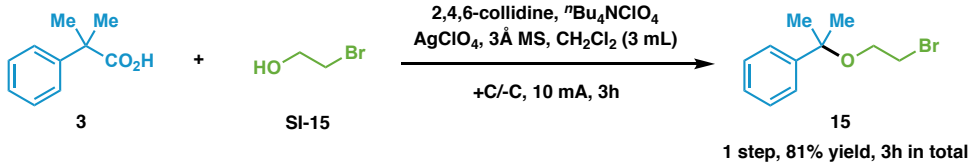
TLC: R_f = 0.54 (3:1 Hexanes:EtOAc).

Application for Etherification No. 6

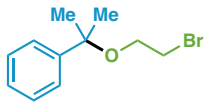
Previous synthesis of the intermediate of muscarinic acetylcholine receptor antagonist (compound **15**) (ref. *WO2005104745 A2*).



Scheme for the synthesis of compound **15**



Compound 15



(2-(2-bromoethoxy)propan-2-yl)benzene

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with **3** (33 mg, 0.2 mmol, 1 equiv.), **SI-15** (75 mg, 0.6 mmol, 3 equiv.), $AgClO_4$ (124 mg, 0.6 mmol, 3.0 equiv.), 2,4,6-collidine (72.7 mg, 0.6 mmol, 3 equiv.), ^{n}Bu$_4$NClO$_4$ (103 mg, 0.3 mmol, 0.1M), 3 Å molecular sieves (150 mg), and CH_2Cl_2 (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The

reaction mixture was pre-stirred for 30 min and electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with Et_2O (2 mL), which was combined with crude mixture. Then, the crude mixture was further diluted with Et_2O (30 mL). The resulting mixture was washed with H_2O (20 mL) twice, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (20:1 Hexanes:Et_2O, v/v) to give the product **15** as a colorless oil (39.5 mg, 81% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47 – 7.42 (m, 2H), 7.38 – 7.33 (m, 2H), 7.29 – 7.24 (m, 1H), 3.49 – 3.46 (m, 2H), 3.43 – 3.40 (m, 2H), 1.57 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.8, 128.4, 127.3, 125.9, 63.4, 31.4, 28.4.

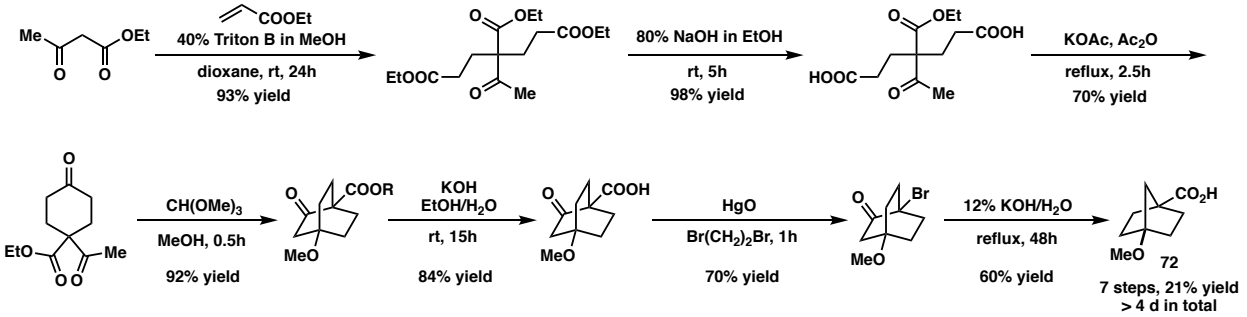
GC/MS (EI): m/z (%) 242 (0.1%), 227 (100%), 118 (63%), 91 (41%), 77 (28%).

TLC: R_f = 0.45 (20:1 Hexanes: Et_2O).

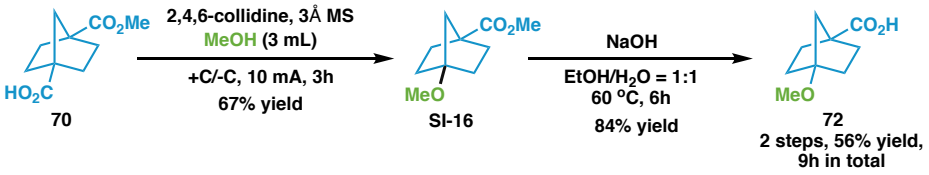
Application for Methoxylation No. 1

Previous synthesis of the intermediate for GPR120 modulator (compound **72**)

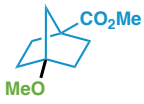
(ref. *WO2014159794 A2*; *J. Org. Chem.*, **1984** *49*, 1387).



Scheme for the synthesis of compound **72**



Compound SI-16



methyl 4-methoxybicyclo[2.2.1]heptane-1-carboxylate

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid **70** (39.6 mg, 0.2 mmol, 1 equiv.), 2,4,6-collidine (72.6 mg, 0.6 mmol, 3 equiv.), 3Å MS (150 mg), MeOH (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under constant current at 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed and electrodes were rinsed with Et_2O (2 mL). The resulting solution was diluted with Et_2O (40 mL), and then washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (30:1 Hexanes:Et_2O, v/v) to furnish the desired product **SI-16** (24.7 mg, 67% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.67 (s, 3H), 3.31 (s, 3H), 2.10 – 2.02 (m, 2H), 1.87 – 1.80 (m, 2H), 1.78 (s, 2H), 1.76 – 1.71 (m, 2H), 1.64 – 1.59 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 176.0, 86.8, 53.0, 51.8, 48.6, 43.2, 32.7, 31.3.

GC/MS (EI): m/z (%) 169 (2%), 155 (21%), 141 (24%), 125 (100%), 109 (18%).

TLC: R_f = 0.3 (30:1 Hexanes: Et_2O).

Compound 72

4-methoxybicyclo[2.2.1]heptane-1-carboxylic acid

In a 25 mL round bottom flask, **SI-16** (36.8 mg, 0.2 mmol, 1.0 eq) and NaOH (32.0 mg, 0.8 mmol, 4.0 eq) was added to a mixture of solvents (6 mL, EtOH/H_2O = 1:1). After stirred for 6 h at 60 °C, the reaction was then poured into 1 M HCl aq. to acidify to pH 1, and the aqueous phase was extracted with EtOAc (3 × 10 mL), washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The desired product **72** (28.6 mg, 84% yield) was purified by preparative thin-layer chromatography (PTLC) (1:1 Hexanes:EtOAc, v/v).

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.31 (s, 3H), 2.10 (td, J = 13.8, 5.7 Hz, 2H), 1.89 – 1.82 (m, 2H), 1.81 (s, 2H), 1.79 – 1.73 (m, 2H), 1.67 – 1.59 (m, 2H).

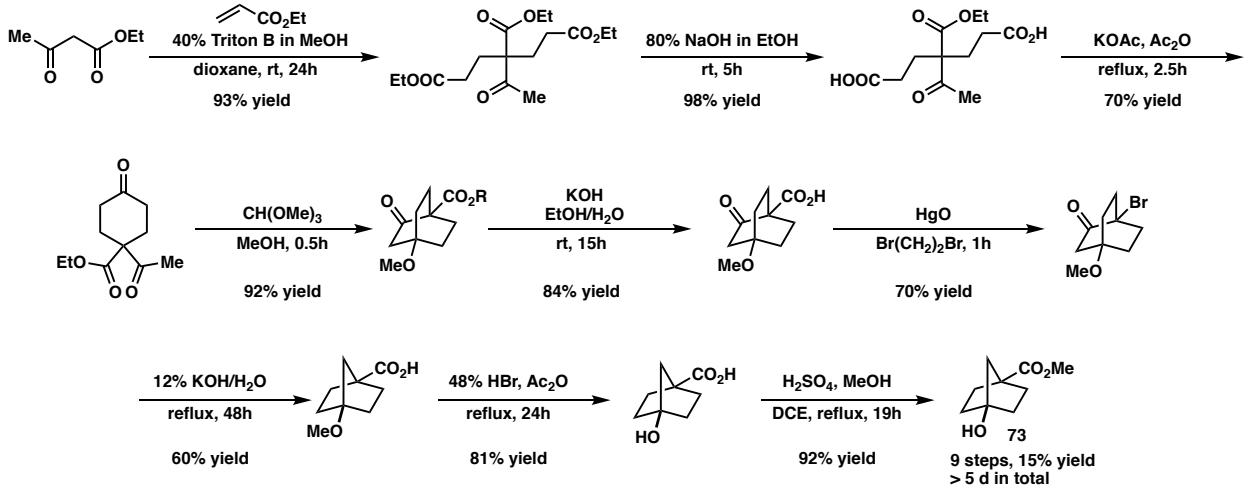
^{13}C NMR (126 MHz, $CDCl_3$): δ 181.9, 87.0, 52.9, 48.4, 43.2, 32.5, 31.3.

GC/MS (EI): m/z (%) 170 (0.3%), 141 (21%), 125 (100%), 97 (20%), 67 (6.4%).

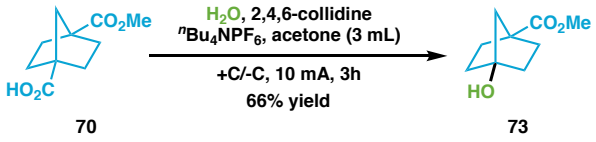
TLC: R_f = 0.2 (1:1 Hexanes: EtOAc).

Application for Hydroxylation No. 1

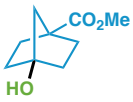
Literature scheme for the synthesis of intermediate for GPR120 modulators (compound **73**) (ref. *J. Org. Chem.*, **1984**, *49*, 1387).



Synthesis of compound **73**, developed herein:



Compound 73



4-methoxybicyclo[2.2.1]heptane-1-carboxylic acid

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with compound **70** (39.6 mg, 0.2 mmol, 1 eq), 2,4,6-collidine (36.3 mg, 0.3 mmol, 1.5 equiv.), $^{n}Bu_4NPF_6$ (116 mg, 0.3 mmol, 0.1M), acetone (3.0 mL), and H_2O (0.1 mL). The ElectraSyn vial cap, equipped with anode (graphite) and cathode (graphite), were inserted into the mixture. The reaction mixture was electrolyzed under a constant current of 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed and electrodes were rinsed with

Et_2O (2 mL). The obtained suspension was diluted with Et_2O (40 mL), and the combined organic phase was washed with saturated aqueous NH_4Cl solution (20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (3:1 Hexanes:EtOAc, v/v) to furnish the desired product **73** (22.4 mg, 66% yield).

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.64 (s, 3H), 2.60 (s, 1H), 2.13 – 1.99 (m, 2H), 1.80 – 1.59 (m, 8H).

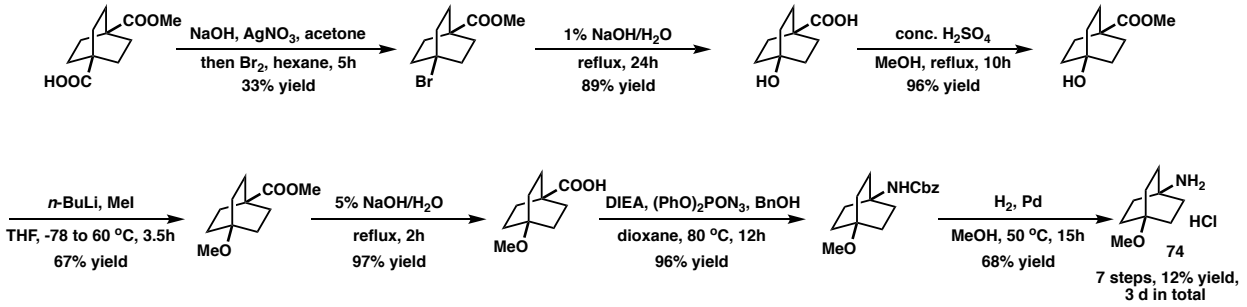
^{13}C NMR (126 MHz, $CDCl_3$): δ 176.0, 81.8, 51.8, 49.1, 46.8, 35.4, 33.0.

GC/MS (EI): m/z (%) 155 (0.2 %), 139 (7%), 127 (16%), 111 (100%), 95 (13%).

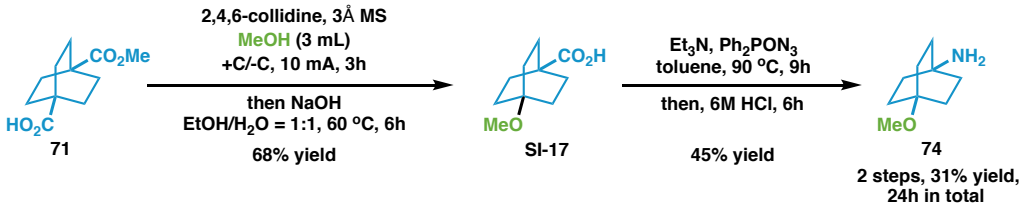
TLC: R_f = 0.2 (1:1 Hexanes: EtOAc).

Application for Methoxylation No. 2

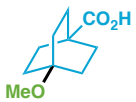
Previous synthesis of the intermediate of JNK protein kinase inhibitors (compound **74**) (ref. *WO2012145569 A1*).



Scheme for the synthesis of compound **74**



Compound SI-17



4-methoxybicyclo[2.2.2]octane-1-carboxylic acid

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid **71** (42.4 mg, 0.2 mmol, 1 equiv.), 2,4,6-collidine (72.6 mg, 0.6 mmol, 3 equiv.), 3Å MS (150 mg), MeOH (3.0 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under constant current at 10 mA for 3 hours. When completion, the reaction mixture was transferred to a 50 mL flask and solvent was removed *in vacuo*. And then NaOH (32mg, 0.8 mmol, 4 equiv.), EtOH (3 mL), H_2O (3 mL) were added to the flask. The reaction mixture was stirred at 60 °C for 6 h. After completion, the mixture was extracted with Et_2O to remove the organic impurities, the aqueous layer was acidified with 2M aq. HCl to pH=1 and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The crude material was purified by preparative thin-layer chromatography (PTLC) (1:1 Hexanes:EtOAc, v/v) to give the desired product **SI-17** (25.0 mg, 68% yield).

Physical State: colorless oil

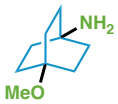
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.18 (s, 3H), 1.97 – 1.91 (m, 6H), 1.72 – 1.66 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 183.0, 73.6, 49.3, 38.2, 29.2, 28.8.

HRMS (ESI-TOF): calc'd for $C_{10}H_{16}O_3Na$ $[M + Na]^+$: 207.0997; found 207.0998.

TLC: R_f = 0.2 (1:1 Hexanes: EtOAc).

Compound 74



4-methoxybicyclo[2.2.2]octan-1-amine

A suspension of **SI-17** (36.8 mg, 0.2 mmol, 1equiv.) in toluene (2 mL) was treated with triethylamine (42 μL, 0.3 mmol, 1.5 eq) and diphenylphosphoryl azide (66 mg, 0.24 mmol, 1.2 equiv.) under argon atmosphere. The solution was slowly and warmed to 90 °C and stirred at 90 °C for 9 h, then concentrated *in vacuo* to remove toluene. The residue was cooled on an ice bath and treated with 6N hydrochloric acid (2 mL). The bath was removed and the mixture was stirred at room temperature for 6h. After completion, the mixture was extracted with Et_2O to remove the organic impurities, the aqueous layer was basified with saturated $NaHCO_3$ (aq), and then extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The crude material was purified by preparative thin-

layer chromatography (PTLC) (1:3 Hexanes:EtOAc, v/v) to give the desired product **74** (13.9 mg, 45% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.16 (s, 3H), 1.86 – 1.68 (m, 6H), 1.68 – 1.59 (m, 6H), 1.55 – 1.14 (m, 2H).

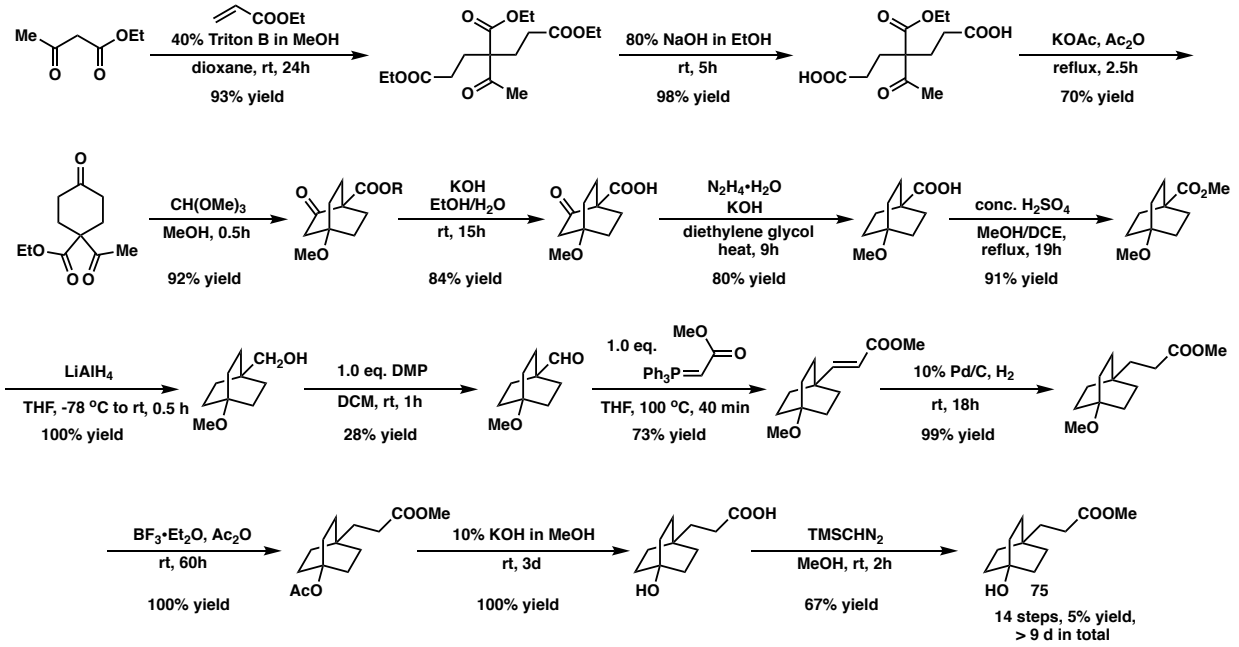
^{13}C NMR (151 MHz, $CDCl_3$): δ 73.0, 49.4, 46.7, 35.6, 29.9.

GC/MS (EI): m/z (%) 155 (5 %), 125 (25%), 112 (32%), 96 (22%), 69 (100%).

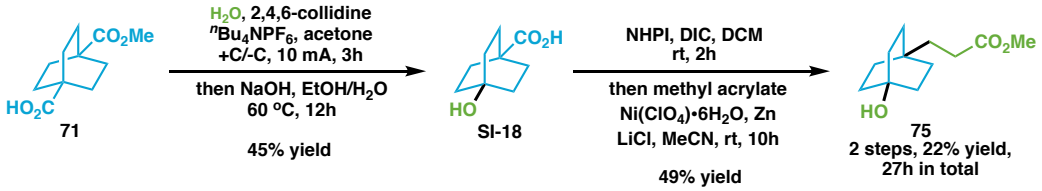
TLC: R_f = 0.1 (2:1 Hexanes:EtOAc).

Application for Hydroxylation No. 2

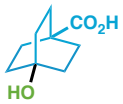
Literature synthesis of compound **75** – an intermediate for the preparation of GPR120 modulator (ref. *J. Org. Chem.,* **1982**, *47*, 2951; *WO2014159802 A1*).



Scheme for the synthesis of compound **75**



Compound SI-18



4-hydroxybicyclo[2.2.2]octane-1-carboxylic acid

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) with a stir bar was charged with carboxylic acid **71** (42.4 mg, 0.2 mmol, 1 equiv.), 2,4,6-collidine (36.3 mg, 0.3 mmol, 1.5 equiv.), $^{n}Bu_4NPF_6$ (114 mg, 0.3 mmol, 0.1M), acetone (3.0 mL), and H_2O (0.1 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) were inserted into the mixture. The reaction mixture was electrolyzed under a constant current of 10 mA for 3 hours. After completion, the reaction mixture was transferred to a 50 mL flask and the solvent was removed under a reduced pressure on a rotary evaporator. A solution of NaOH (32 mg, 0.8 mmol, 4 equiv.) in EtOH (3 mL) and H_2O (3 mL) was added to the residue. The reaction mixture was stirred at 60 °C for 6 h. After completion, the reaction mixture was extracted with Et_2O (3 x 20 mL). Etherial layer was discarded, while the aqueous layer was acidified with 1N aq. HCl to pH = 4. The reaction mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and concentrated *in vacuo.* The crude material was purified by preparative thin-layer chromatography (PTLC) (3:1 Hexanes:EtOAc, v/v) to give the desired product **SI-18** (15.3 mg, 45% yield).

Physical State: colorless oil.

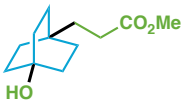
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.02 – 1.92 (m, 6H), 1.75 – 1.66 (m, 6H), 1.58 (s, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 181.7, 69.4, 38.2, 33.3, 29.6.

GC/MS (EI): m/z (%) 170 (6%), 152 (11%), 124 (100%), 109 (14%), 70 (65%).

TLC: R_f = 0.2 (1:1 Hexanes: EtOAc).

Compound 75



methyl 3-(4-hydroxybicyclo[2.2.2]octan-1-yl)propanoate

To a stirred solution of carboxylic acid **SI-18** (36 mg, 0.212 mmol, 1.0 eq), *N*-hydroxyphtalimide (NHPI) (38 mg, 0.23 mmol, 1.1 eq) in anhydrous CH_2Cl_2 (0.5 mL) was added dropwise DIC (36

μL, 0.25 mmol, 1.2 eq). The reaction was monitored by TLC; and usually it was completed within 2 hours. After consumption of the starting material, the solvent was removed under a reduced pressure on a rotary evaporator; and dried on a high-vacuum line (1 ppm) for at least 5 minutes to remove the residual solvents. Dry LiCl (27.6 mg, 0.64 mmol, 3.0 eq), Zn powder (27.6 mg, 0.42 mmol, 2.0 eq), and $Ni(ClO_4)_2 \bullet 6H_2O$ (15.7 mg, 0.042 mmol, 0.2 eq) were added to the residue. Note: due to its hydroscope nature, LiCl can be difficult to weigh on small scale. However, excess LiCl is not detrimental to the success of the reaction were added. A stir bar was added, the culture tube was evacuated and backfilled with argon. Methyl acrylate (38.4 μL, 0.42 mmol, 2.0 eq) was added to the reaction mixture via syringe. Next, MeCN (0.6 mL) was added, and the mixture was stirred at room temperature for overnight. After 12 hours, H_2O (4 mL) and sat. aq. NH_4Cl solution (4 mL) were added. The mixture was extracted with EtOAc (3 x 30 mL), and the combined organic phase dried over $NaSO_4$. Evaporation of the solvent under a reduced pressure afforded a crude material that was purified by preparative thin-layer chromatography (PTLC) (3:1 Hexanes:EtOAc, v/v) to yield the pure product **75** (22.0 mg, 49% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.65 (s, 3H), 2.21 (t, *J* = 6.3 Hz, 3H), 1.64 – 1.59 (m, 6H), 1.53 – 1.47 (m, 6H), 1.47 – 1.42 (m, 2H).

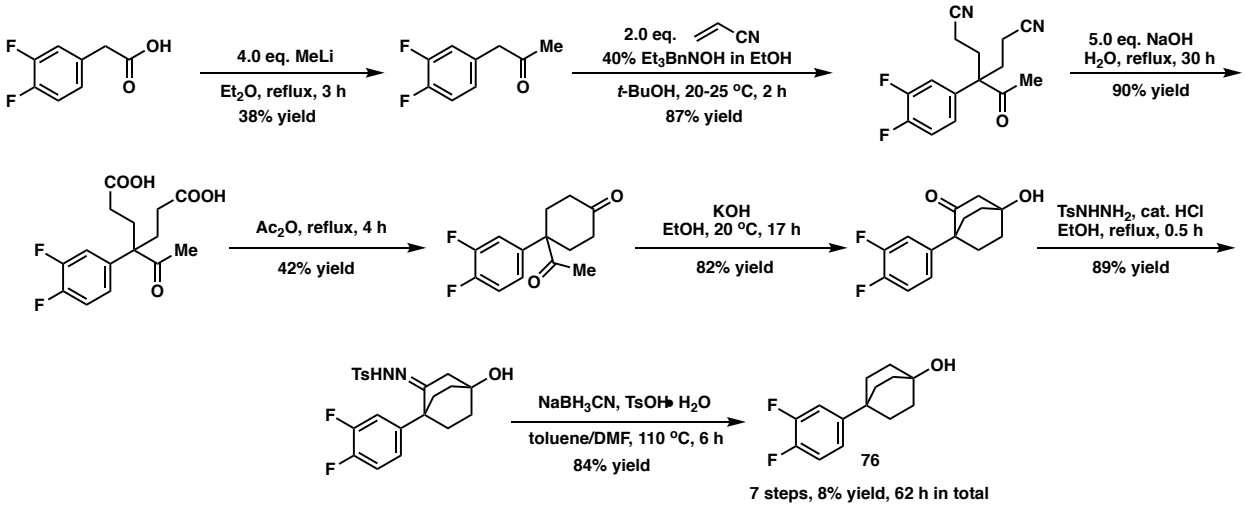
^{13}C NMR (151 MHz, $CDCl_3$): δ 174.8, 69.5, 51.7, 35.4, 34.1, 31.9, 30.1, 29.3.

GC/MS (EI): m/z (%) 212 (4%), 194 (28%), 166 (42%), 143 (40%), 125 (44%), 111 (100%), 95 (27%), 83 (66%).

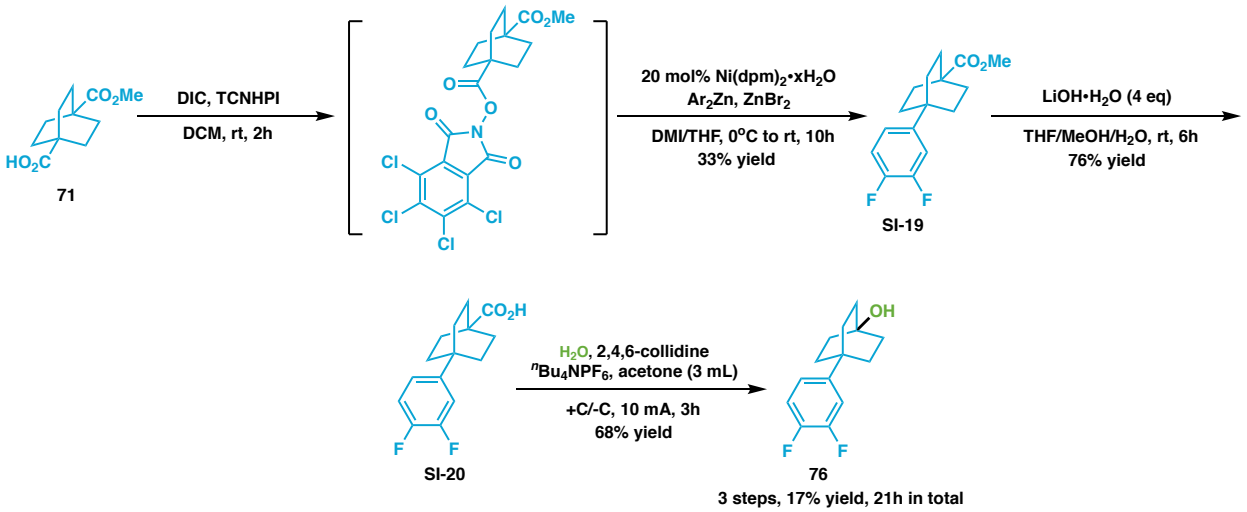
TLC: R_f = 0.3 (3:1 Hexanes:EtOAc).

Application for Hydroxylation No. 3

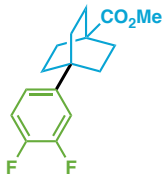
The literature synthesis of compound **76 -** an intermediate in the synthesis of a kinase inhibitor (ref. *Mol. Cryst. Liq. Cryst.*, **2011**, *542*, 106–114).



Synthesis of compound **76**, developed in this work:

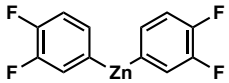


Compound SI-19



methyl 4-(3,4-difluorophenyl)bicyclo[2.2.2]octane-1-carboxylate

preparation of bis(3,4-difluorophenyl)zinc solution in THF



Diarylzinc reagent were prepared in a manner similar to that report by Knochel and coworkers.

LiBr (636.0 mg, 25.0 mmol, 1.25 eq) was added to a 50.0 ml round-bottom flask. The flask was flame-dried under vacuum (to remove water), cooled to a room temperature and backfilled with argon. Magnesium turnings (435.0 mg, 18 mmol, 1.5 equiv.) and THF (anhydrous, 6.0 mL) were added, and the mixture was stirred vigorously for 5 min. DIBAL–H (1.0 M in THF, 0.12 mL, 0.12 mmol, 0.01 eq) was added via syringe, and the mixture was stirred vigorously for another 5 min. The flask was cooled to 0 °C in an ice/water bath, and 4-bromo-1,2-difluorobenzene (2.316 g, 12.0 mmol, 1.0 eq) was added via syringe. After 10 minutes the bath was removed, and the mixture was stirred at room temperature until a full consumption of the starting aryl bromide (as determined by GC/MS spectrum). Titration of the obtained Grignard reagent with I_2 in THF (2 mL) afforded the concentration of 1.28 M.

A Schlenk flask equipped with a stir bar was first flame-dried under vacuum, cooled to a room temperature, and backfilled with nitrogen. $ZnBr_2$ (1.013 g, 4.5 mmol, 1.0 eq) was added. The reaction flask was placed under vacuum again, and heated a heat gun to remove the residual water in $ZnBr_2$. After cooling to a room temperature, the flask was backfilled with nitrogen; and anhydrous THF (8.0 mL) was added. The mixture was vigorously stirred for 5-10 min, until a clear solution was formed. ArMgBr•LiBr (1.28 M, 7.0 ml, 9.0 mmol, 2.0 eq) was added dropwise via a syringe. Often a white precipitate forms during the addition. After addition, the reaction mixture was stirred for another 10 minutes at room temperature to obtain Ar_2Zn reagent (c = 0.38 M, determined by titration).

A flame-dried tube was charged with carboxylic acid **71** (42.4 mg, 0.2 mmol, 1.0 eq), 3,4,5,6-tetrachloro-*N*-hydroxyphthalimide (TCNHPI) (66 mg, 0.22 mmol, 1.1 eq), DMAP (2.4 mg, 0.1 eq), and CH_2Cl_2 (1 mL). DIC (36 μL, 0.24 mmol, 1.2 eq) was added dropwise to a stirred reaction mixture. The reaction was stirred for 2 hours at room temperature, and controlled by TLC. After consumption of the starting material, the solvent was removed under a reduced pressure on a rotary evaporator, and dried on a high-vacuum line (1 ppm) for at least 5 minutes to remove residual solvent. $ZnBr_2$ (45.0 mg, 0.2 mmol, 1.0 eq), $Ni(dpm)_2$•xH_2O (18.6 mg, 0.04 mmol, 0.2 eq) were added at once to the reaction flask. The flask was evacuated and back-filled with argon, followed by an addition of DMI (1.2 mL) via a syringe. The mixture was stirred for 5 minutes at room temperature, and then was was placed into an ice/water bath. The stirring was continued for another 5 minutes. Ar_2Zn in THF (1.6 mL, 0.38 M, 0.6 mmol) was added in one

portion at 0 ºC, and the stirring was continued for 2 min at 0 ºC. The reaction mixture was removed from the ice/water bath and was allowed to stir at room temperature for 10 h. The mixture was diluted with EtOAc or Et_2O (40 mL) and quenched with 1N HCl (to pH = 3). The organic layer was washed with H_2O (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under a reduced pressure. The crude material was purified by preparative thin-layer chromatography (PTLC) (50:1 Hexanes:EtOAc, v/v) to afford the title product **SI-19** (18.5 mg, 33% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.14 – 6.95 (m, 3H), 3.67 (s, 3H), 1.98 – 1.89 (m, 6H), 1.85 – 1.75 (m, 6H)

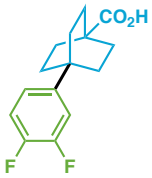
^{13}C NMR (151 MHz, $CDCl_3$): δ 178.3, 150.2 (dd, *J* = 237.1, 12.1 Hz), 148.5 (dd, *J* = 237.1, 12.1 Hz), 146.5 (t, *J* = 4.5 Hz), 121.4 (dd, *J* = 5.8, 3.5 Hz), 116.8 (d, *J* = 16.6 Hz), 114.8 (d, *J* = 16.6Hz), 51.9, 39.1, 34.7, 31.9, 28.8.

^{19}F NMR (400 MHz, $CDCl_3$): δ -138.46 (d, *J* = 21.6 Hz), -142.68 (d, *J* = 21.5 Hz).

GC/MS (EI): m/z (%) 280 (16%), 220 (100%), 205 (6%), 191 (30%), 127 (50%).

TLC: R_f = 0.4 (50:1 Hexanes: EtOAc).

Compound SI-20



4-(3,4-difluorophenyl)bicyclo[2.2.2]octane-1-carboxylic acid

In a 25 mL round bottom flask, **SI-19** (54.0 mg, 1.9 mmol, 1.0 eq) and LiOH•H_2O (40.0 mg, 9.5 mmol, 5.0 eq) were placed. THF (1.5 mL), MeOH (0.75 mL) and water (0.75 mL) were added. The reaction mixture was stirred for 6 h at room temperature. The pH of the reaction mixture was adjusted to 1 by adding aq. HCl dropwise. The reaction mixture was extracted with EtOAc (3 × 10 mL). Water layer was discarded, while the organic phase was washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The obtained crude product was purified by preparative thin-layer chromatography (PTLC) (5:1 Hexanes:EtOAc, v/v) to afford the pure desired product **SI-20** (39.1 mg, 76% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16 – 6.91 (m,3H), 2.00 – 1.89 (m, 6H), 1.87 – 1.78 (m, 6H)

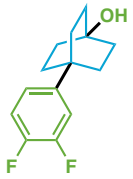
^{13}C NMR (151 MHz, $CDCl_3$): δ 183.6, 150.2 (dd, *J* = 234.05, 13.59 Hz), 148.6 (dd, *J* = 234.05, 12.08 Hz), 146.3 (t, *J* = 4.2 Hz), 121.4 (dd, *J* = 5.9, 3.3 Hz), 116.8 (d, *J* = 16.6 Hz), 114.8 (d, *J* = 17.4 Hz), 38.9, 34.7, 31.8, 28.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -138.37 (d, *J* = 21.6 Hz), -142.56 (d, *J* = 20.9 Hz).

GC/MS (EI): m/z (%) 266 (69%), 237 (48%), 220 (53%), 166 (20%), 127 (82%).

TLC: R_f = 0.2 (1:1 Hexanes: EtOAc).

Compound 76



4-(3,4-difluorophenyl)bicyclo[2.2.2]octan-1-ol

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) was charged with **SI-20** (25.8 mg, 0.1 mmol, 1 eq), 2,4,6-collidine (35.2 mg, 0.3 mmol, 3 eq), $^{n}Bu_4NPF_6$ (116 mg, 0.3 mmol, 0.1 M), acetone (3.0 mL), and H_2O (0.1 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) was inserted into the mixture. The reaction mixture was electrolyzed under a constant current of 10 mA for 3 hours under a stirring. After the reaction, the ElectraSyn vial cap was removed and electrodes were rinsed with Et_2O (2 mL). The resulting suspension was diluted with Et_2O (40 mL), washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (2:1 Hexanes:EtOAc, v/v) to furnish the desired product **76** (15.7 mg, 68% yield).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.13 – 7.01 (m, 2H), 7.01 – 6.96 (m, 1H), 1.97 – 1.86 (m, 6H), 1.82 – 1.73 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 150.1 (dd, *J* = 246.9, 12.1 Hz), 148.5 (dd, *J* = 246.1, 12.1 Hz), 145.9 (t, *J* = 4.4 Hz), 121.4 (dd, *J* = 6.0, 3.3 Hz), 116.7 (d, *J* = 16.6 Hz), 114.8 (d, *J* = 17.5 Hz), 69.7, 34.3, 33.7.

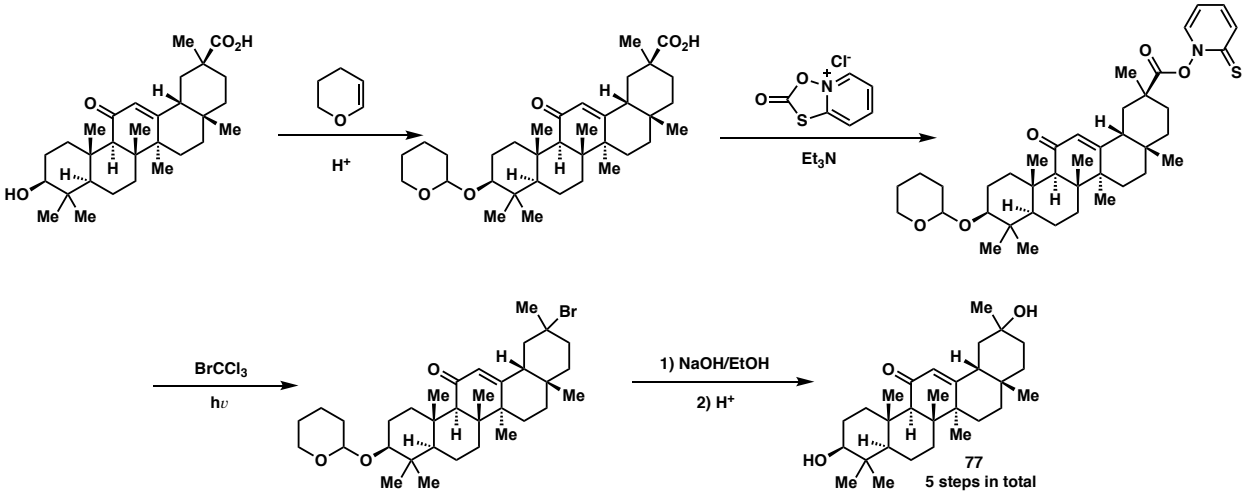
^{19}F NMR (600 MHz, $CDCl_3$): δ -138.46 (d, *J* = 21.7 Hz), -142.64 (d, *J* = 21.6 Hz).

GC/MS (EI): m/z (%) 238 (20%), 220 (7%), 168 (100%), 153 (28%), 127(37%).

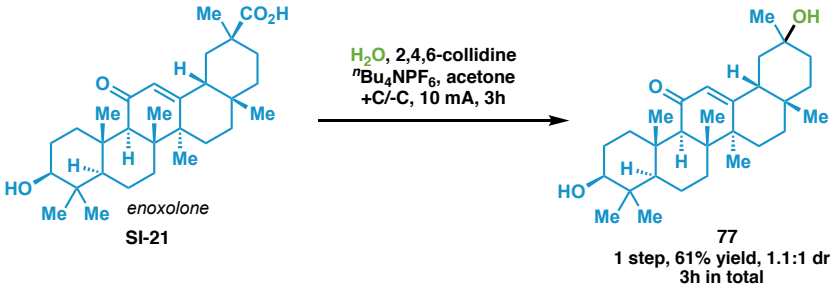
TLC: R_f = 0.3 (2:1 Hexanes:EtOAc).

Application for Hydroxylation No. 4

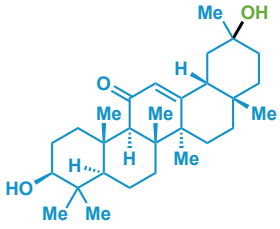
Literature synthesis of 11-*beta*-hydroxysteroid dehydrogenase 1 inhibitor (compound **77**) (ref. *WO2008071169 A2*):



Synthesis of compound **77** developed in this work:



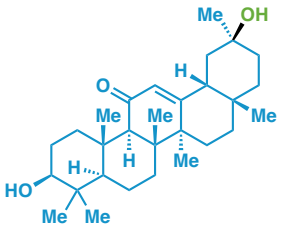
Compound 77



(4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*S*,12b*R*,14b*R*)-2,10-dihydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-1,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,14b-octadecahydropicen-13(2*H*)-one

With no precautions to exclude air or moisture, the ElectraSyn vial (5 mL) was charged with **SI-21** (94 mg, 0.2 mmol, 1 eq), 2,4,6-collidine (35.2 mg, 0.3 mmol, 1.5 eq), $^{n}Bu_4NPF_6$ (116 mg, 0.3 mmol, 1.5 eq), acetone (3.0 mL), and H_2O (0.1 mL). The ElectraSyn vial cap equipped with anode (graphite) and cathode (graphite) was inserted into the mixture. The reaction mixture was electrolyzed under a constant current of 10 mA for 3 hours. After the reaction, the ElectraSyn vial cap was removed, and the electrodes were rinsed with Et_2O (2 mL). The resulting solution was diluted with Et_2O (40 mL). The organic phase was washed with 1N HCl (20 mL), saturated aq. $NaHCO_3$ (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography (PTLC) (1:2 Hexanes:EtOAc, v/v) to furnish the desired products (2*S*)-**77** (25.8 mg, 29% yield) and (2*R*)-**77** (28.4 mg, 32% yield).

Compound (2*S*)-77



(2*S*,4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*S*,12b*R*,14b*R*)-2,10-dihydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-1,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,14b-octadecahydropicen-13(2*H*)-one

Physical State: white solid.

m.p.: > 270 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.63 (s, 1H), 3.22 (dd, *J* = 11.3, 5.0 Hz, 1H), 2.78 (dt, *J* = 13.5, 3.6 Hz, 1H), 2.38 – 2.34 (m, 1H), 2.32 (s, 1H), 2.00 (td, *J* = 13.6, 4.6 Hz, 1H), 1.89 – 1.78 (m, 2H), 1.73 – 1.51 (m, 6H), 1.49 – 1.37 (m, 4H), 1.37 – 1.26 (m, 6H), 1.26 – 1.16 (m, 4H), 1.14 (s, 3H), 1.13 (s, 3H), 1.06 – 0.93 (m, 5H), 0.88 (s, 3H), 0.80 (s, 3H), 0.69 (dt, *J* = 13.9, 3.5 Hz, 1H).

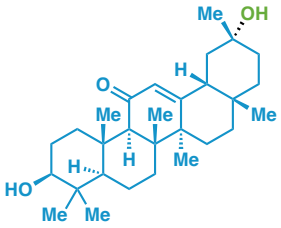
^{13}C NMR (151 MHz, $CDCl_3$): δ 200.4, 169.8, 128.4, 78.9, 69.5, 62.0, 55.1, 46.7, 45.6, 44.4, 43.5, 39.3, 37.2, 35.7, 34.1, 32.9, 32.0, 31.7, 28.4, 28.2, 27.5, 26.6, 26.1, 23.7, 18.9, 17.6, 16.5, 15.7.

HRMS (ESI-TOF): calc'd for $C_{29}H_{47}O_3$ $[M + H]^+$: 443.3520; found 443.3523.

TLC: R_f = 0.39 (2:1, EtOAc:Hexanes).

$[\alpha]_D^{24}$ = +450.9 (*c* = 1.0, $CHCl_3$).

Compound (2*R*)-77



(2*R*,4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*S*,12b*R*,14b*R*)-2,10-dihydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-1,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,14b-octadecahydropicen-13(2*H*)-one

Physical State: white solid.

m.p.: 249 – 251 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.59 (s, 1H), 3.22 (dd, *J* = 11.2, 5.1 Hz, 1H), 2.77 (dt, *J* = 13.5, 3.6 Hz, 1H), 2.33 (s, 1H), 2.12 (td, *J* = 13.6, 4.6 Hz, 1H), 2.07 – 2.03 (m, 1H), 1.97 (t, *J* = 13.3 Hz, 1H), 1.82 (td, *J* = 13.8, 4.8 Hz, 1H), 1.71 – 1.56 (m, 6H), 1.50 – 1.44 (m, 3H), 1.43 – 1.35 (m, 7H), 1.24 (s, 3H), 1.21 – 1.18 (m, 1H), 1.13 (s, 3H), 1.12 (s, 3H), 1.04 – 0.95 (m, 5H), 0.86 (s, 3H), 0.80 (s, 3H), 0.69 (dd, *J* = 11.9, 1.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 200.4, 168.8, 128.4, 78.9, 71.5, 61.9, 55.0, 49.5, 45.8, 45.6, 43.4, 39.3, 38.4, 37.2, 35.6, 32.9, 32.6, 28.3, 28.2, 27.4, 26.53, 26.49, 25.3, 23.6, 18.9, 17.6, 16.5, 15.7.

HRMS (ESI-TOF): calc'd for $C_{29}H_{47}O_3$ $[M + H]^+$: 443.3520; found 443.3514.

TLC: R_f = 0.25 (2:1, EtOAc:Hexanes).

$[\alpha]_D^{24}$ = +370.1 (*c* = 1.0, $CHCl_3$).

X-Ray of Compound (2*R*)-77

CCDC 1918528

The single crystal X-ray diffraction studies were carried out on a Bruker Smart APEX II CCD diffractometer equipped with Cu K_α radiation (λ =1.54178 Å). Crystals of the subject compound were used as received (grown from acetone/hexanes/Et_2O). A 0.2 x 0.2 x 0.2 mm piece of a colorless crystal was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 40 mm and exposure time was 1, 2, 3 seconds depending on the 2θ range per frame using a scan width of 1.00°. Data collection was 100 % complete to 67.679° in θ. A total of 44094 reflections were collected covering the indices, -19<=h<=18, -33<=k<=33, -8<=l<=8. 5820 reflections were found to be symmetry independent, with a R_{int} of 0.0306.

Indexing and unit cell refinement indicated a **P**rimitive, **Orthorhombic** lattice. The space group was found to be ***P*2$_1$2$_1$2**. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table 1.

Notes: Absolute stereochemistry was conclusively assigned (Flack = -0.03(3)). The solvent in the pores was disordered, a total of 214 electrons were squeezed from the unit cell. This is approximately 4 solvent molecules per unit cell.

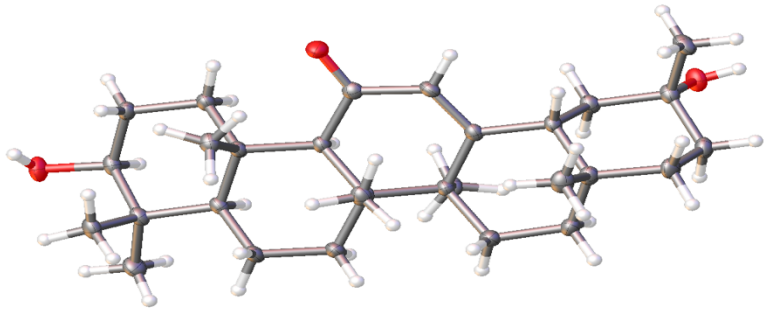


Table 1. Crystal data and structure refinement for **(2*R*)-77**.

Identification code	**(2*R*)-77**	
Empirical formula	C29 H46 O3	
Molecular formula	C29 H46 O3	
Formula weight	442.66	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2$_1$2$_1$2	
Unit cell dimensions	a = 15.6402(8) Å	α= 90°.
	b = 27.8107(15) Å	β= 90°.

	c = 7.0298(4) Å γ = 90°.
Volume	3057.7(3) Å^3
Z	4
Density (calculated)	0.962 Mg/m^3
Absorption coefficient	0.464 mm^{-1}
F(000)	976
Crystal size	0.2 x 0.2 x 0.2 mm^3
Crystal color, habit	clear colourless block
Theta range for data collection	3.178 to 70.292°.
Index ranges	-19<=h<=18, -33<=k<=33, -8<=l<=8
Reflections collected	44094
Independent reflections	5820 [R(int) = 0.0306]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.6664
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5820 / 0 / 298
Goodness-of-fit on F^2	1.043
Final R indices [I>2sigma(I)]	R1 = 0.0280, wR2 = 0.0745
R indices (all data)	R1 = 0.0285, wR2 = 0.0752
Absolute structure parameter	-0.03(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.171 and -0.130 e.Å^{-3}

X-Ray of Compound (11*R*)-138

CCDC 1903823

The single crystal X-ray diffraction studies were carried out on a Bruker Microstar APEX II CCD diffractometer equipped with Cu K_α radiation (λ =1.54178 Å). Crystals of the subject compound were used as received (grown from CH_2Cl_2/Ethyl Acetate). A 0.025 x 0.025 x 0.125 mm piece of a colorless crystal was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 45 mm and exposure time was 4, 10, and 30 seconds depending on the 2θ range per frame using a scan width of 1.20°. Data collection was 98.4 % complete to 67.679° in θ. A total of 16527 reflections were collected covering the indices, -8<=h<=5, -17<=k<=11, -30<=l<=25. 4963 reflections were found to be symmetry independent, with a R_{int} of 0.0265.

Indexing and unit cell refinement indicated a Primitive, Orthorhombic lattice. The space group was found to be $P2_12_12_1$. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table 1.

Absolute Structure Parameter: 0.05(4) (Conclusive)

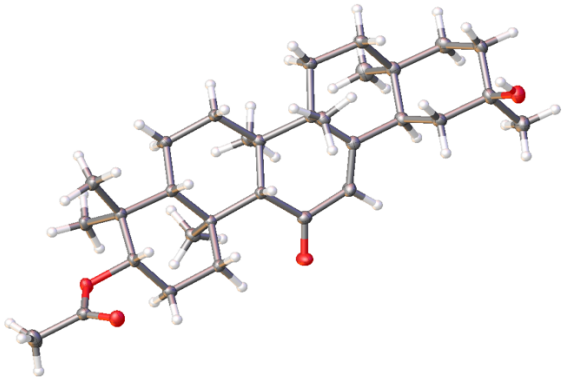


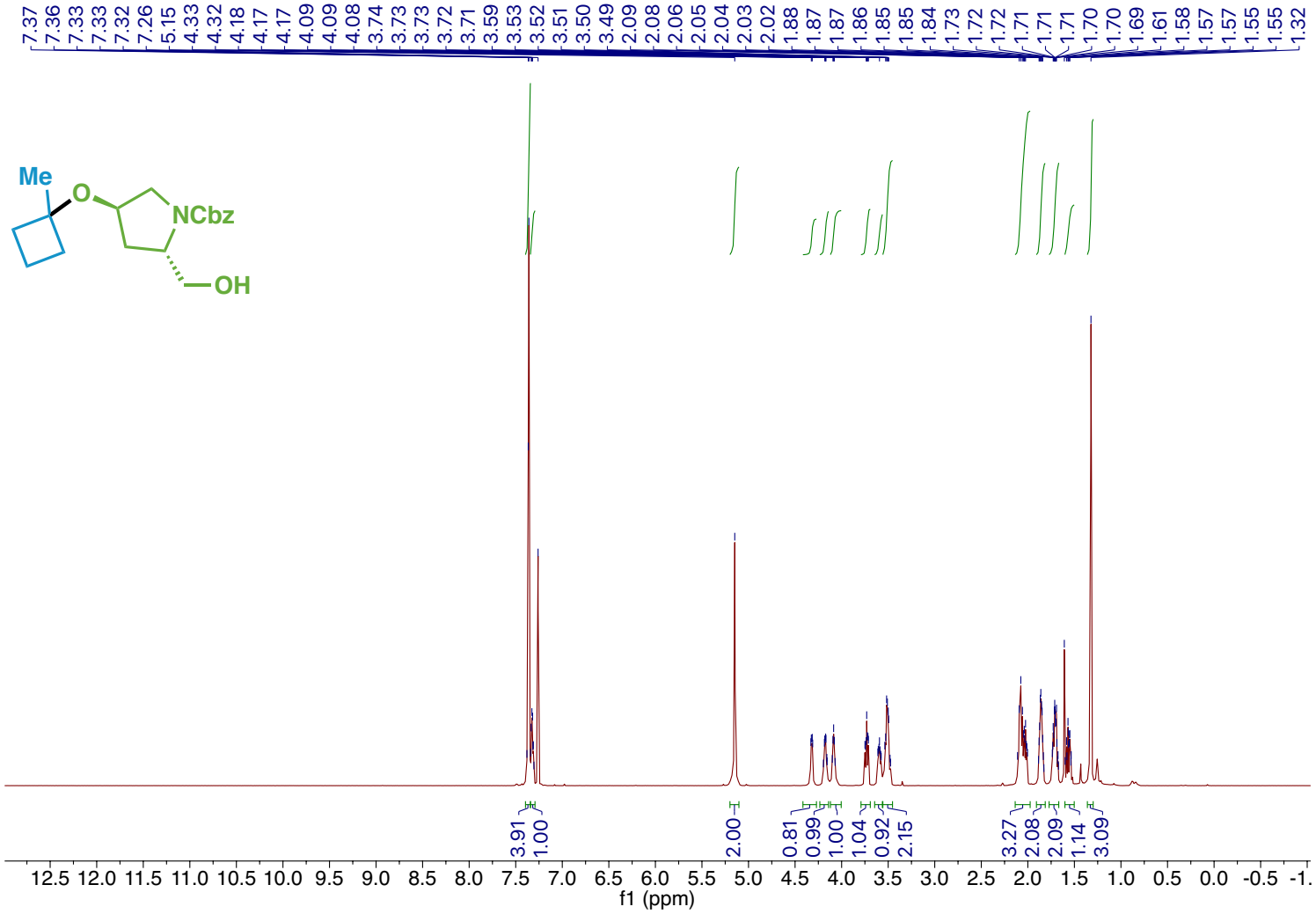
Table 1. Crystal data and structure refinement for **(11*R*)-138**.

Identification code	**(11*R*)-138**	
Empirical formula	C31 H48 O4	
Formula weight	484.69	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.2653(2) Å	α= 90°.
	b = 14.7204(5) Å	β= 90°.
	c = 25.3911(8) Å	γ = 90°.
Volume	2715.53(15) Å^3	
Z	4	
Density (calculated)	1.186 Mg/m^3	

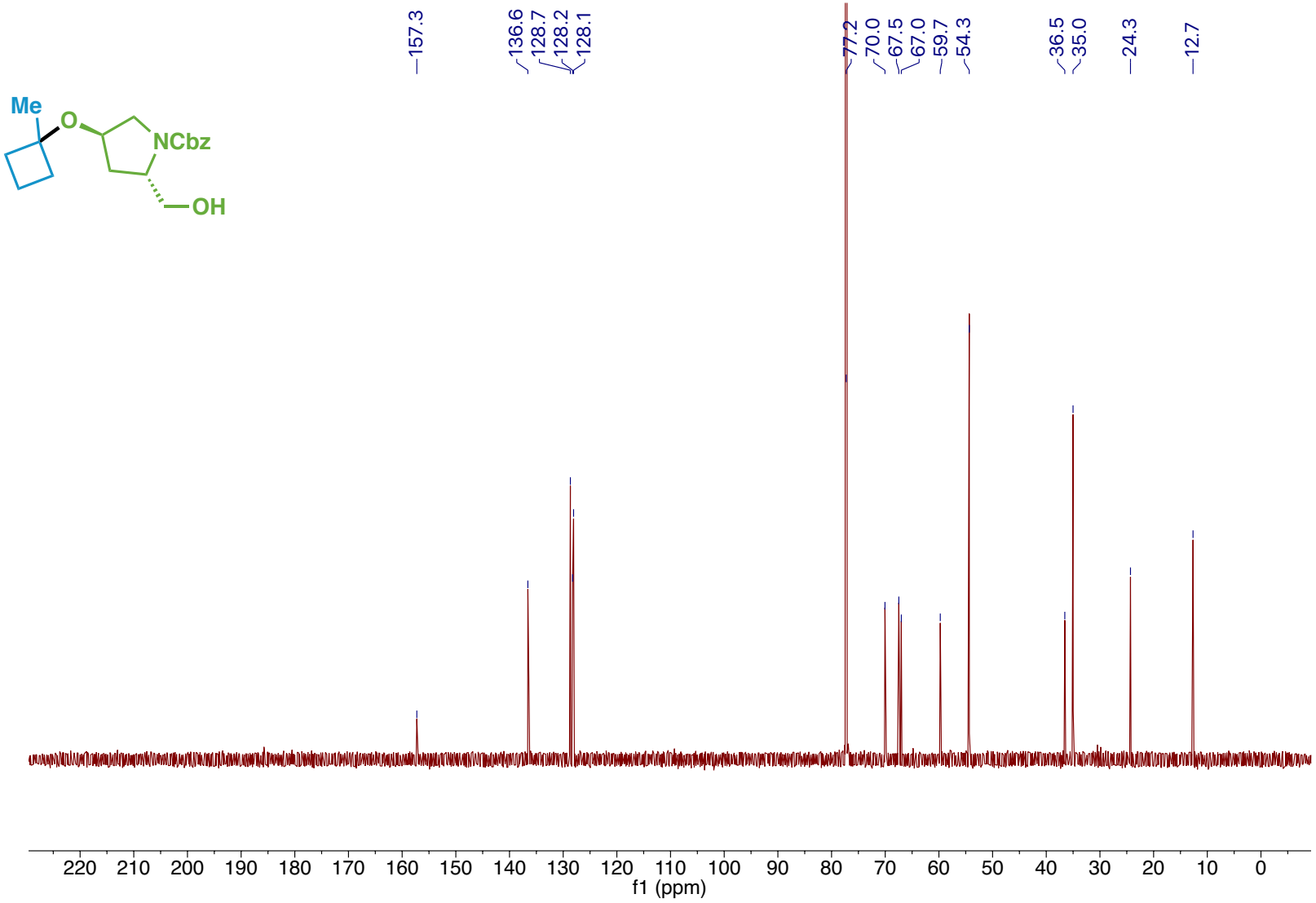
Absorption coefficient	0.594 mm^{-1}
F(000)	1064
Crystal size	0.125 x 0.025 x 0.025 mm^3
Theta range for data collection	3.470 to 69.705°.
Index ranges	-8<=h<=5, -17<=k<=11, -30<=l<=25
Reflections collected	16527
Independent reflections	4963 [R(int) = 0.0265]
Completeness to theta = 67.679°	98.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.6932
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4963 / 0 / 325
Goodness-of-fit on F^2	1.049
Final R indices [I>2sigma(I)]	R1 = 0.0286, wR2 = 0.0764
R indices (all data)	R1 = 0.0289, wR2 = 0.0767
Absolute structure parameter	0.05(4)
Largest diff. peak and hole	0.222 and -0.151 $e.Å^{-3}$

NMR Spectra

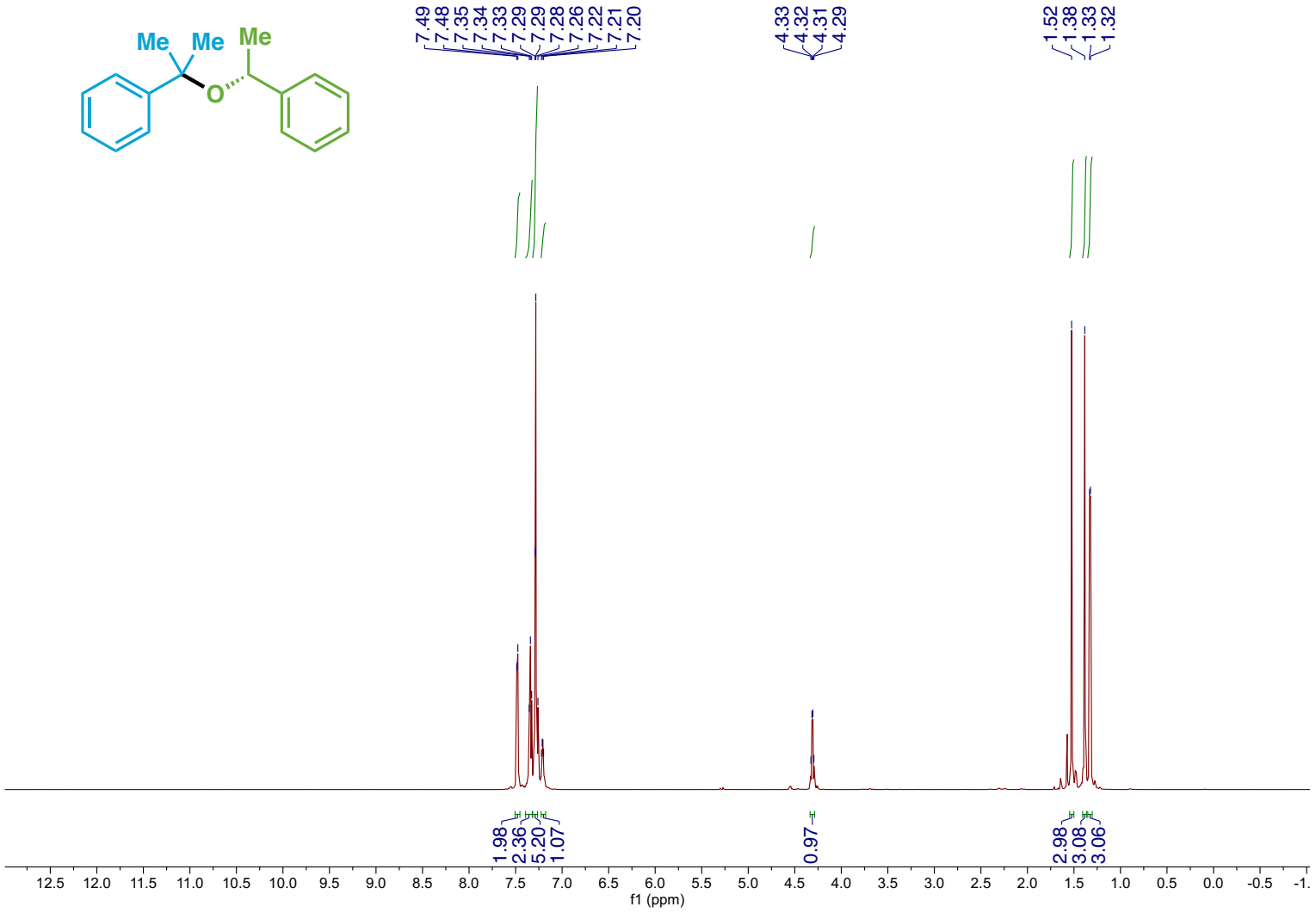
Compound 1 ^{1}H NMR



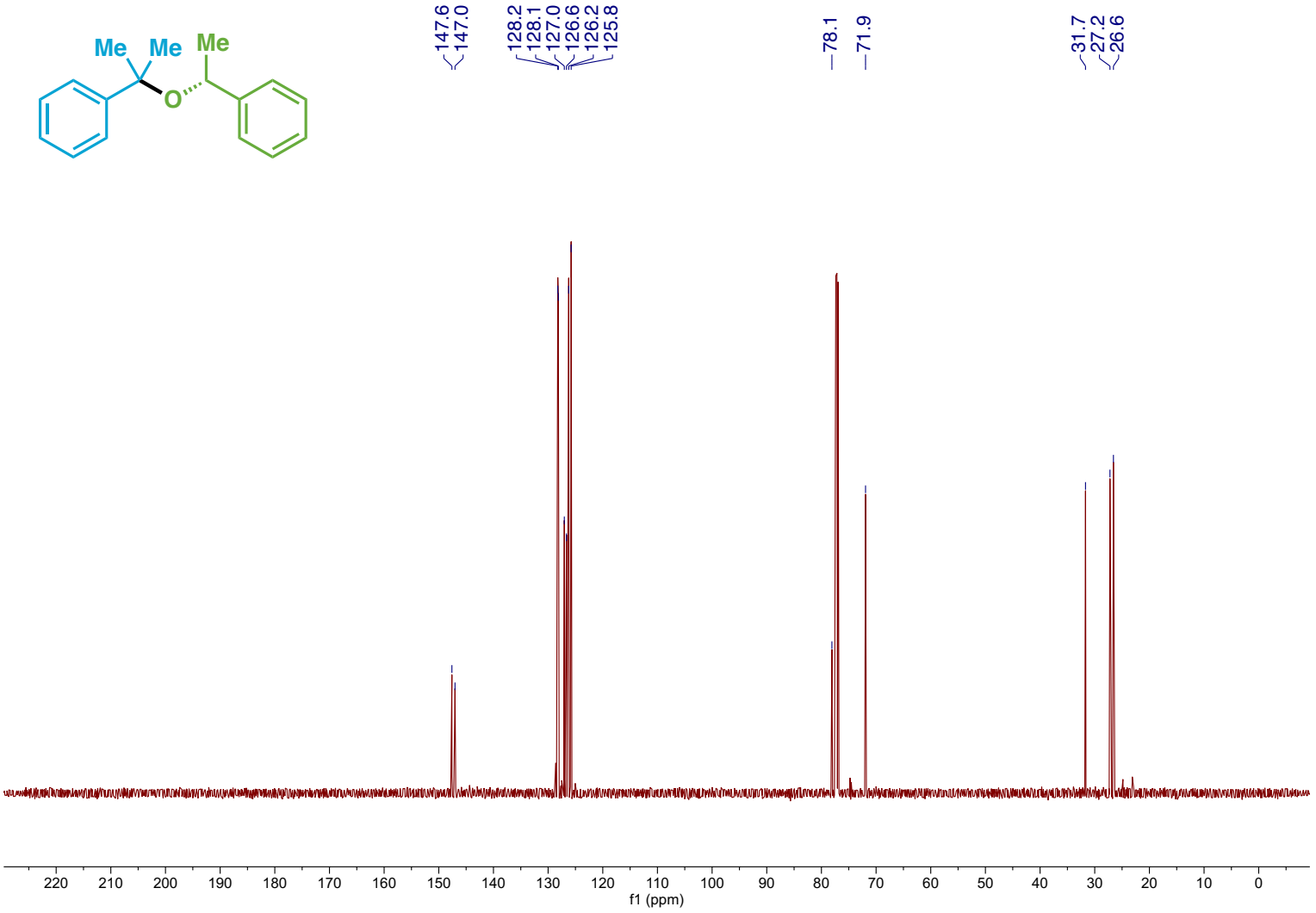
Compound 1 ^{13}C NMR



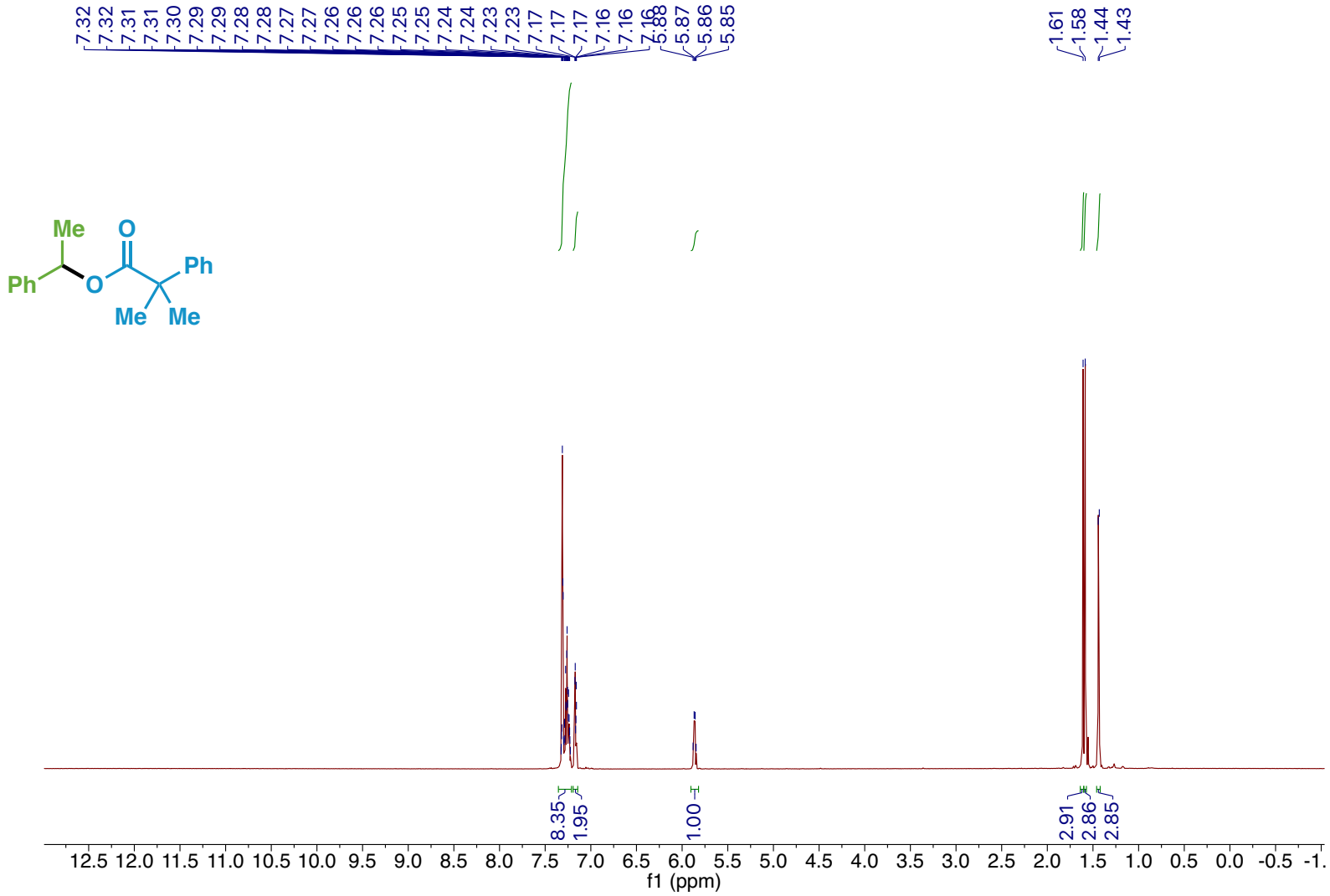
Compound 5 ^{1}H NMR



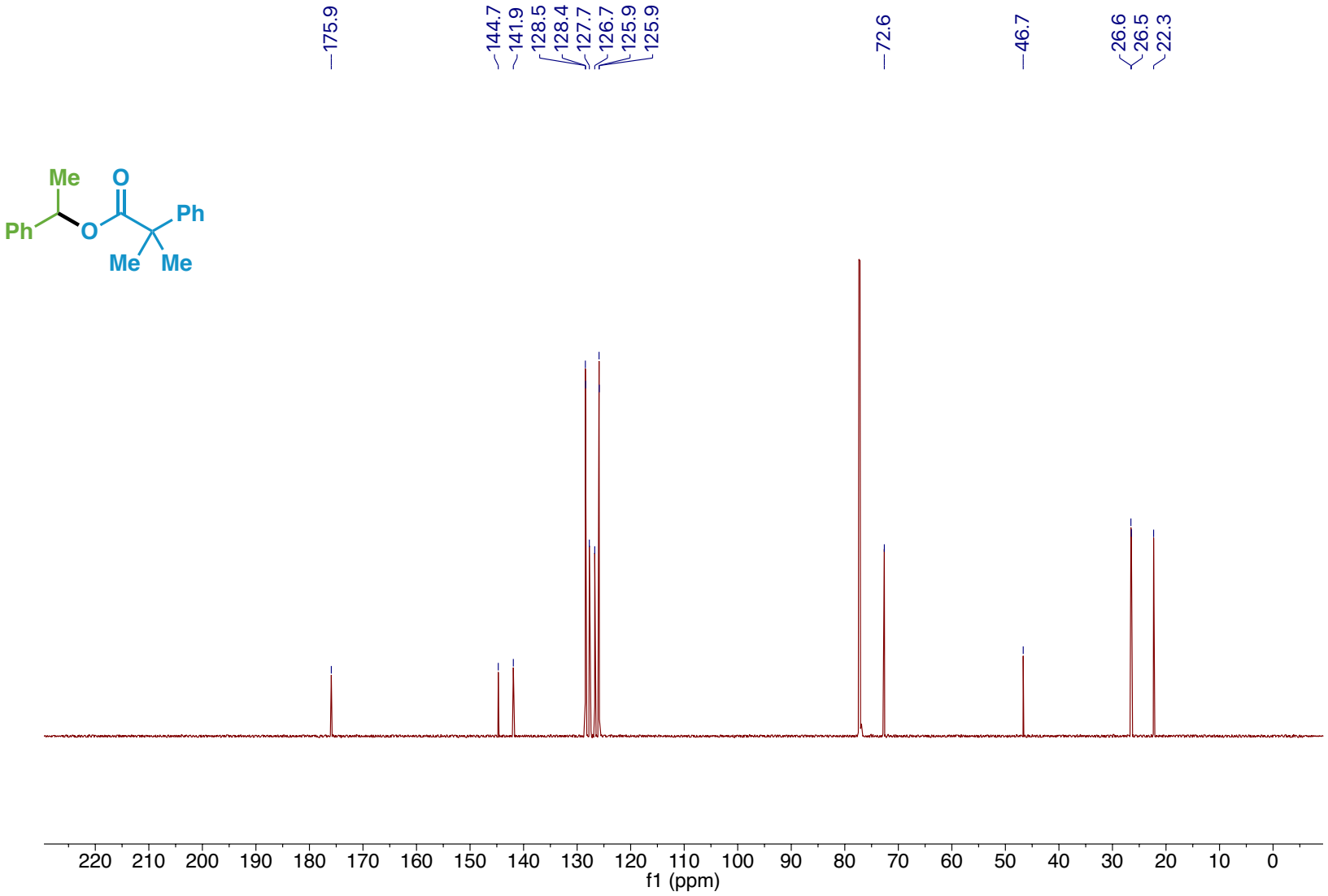
Compound 5 ^{13}C NMR



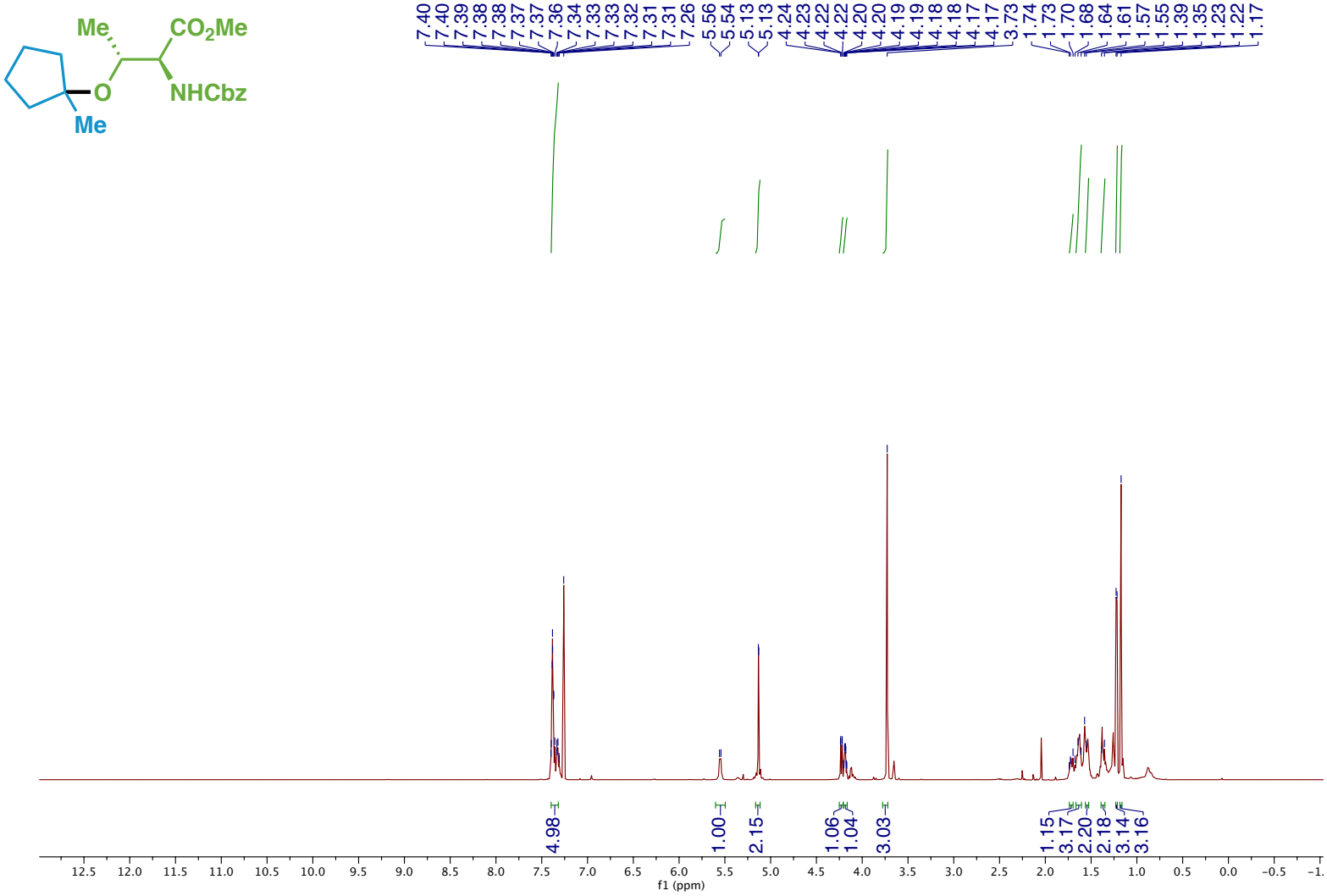
Compound 10 ^{1}H NMR



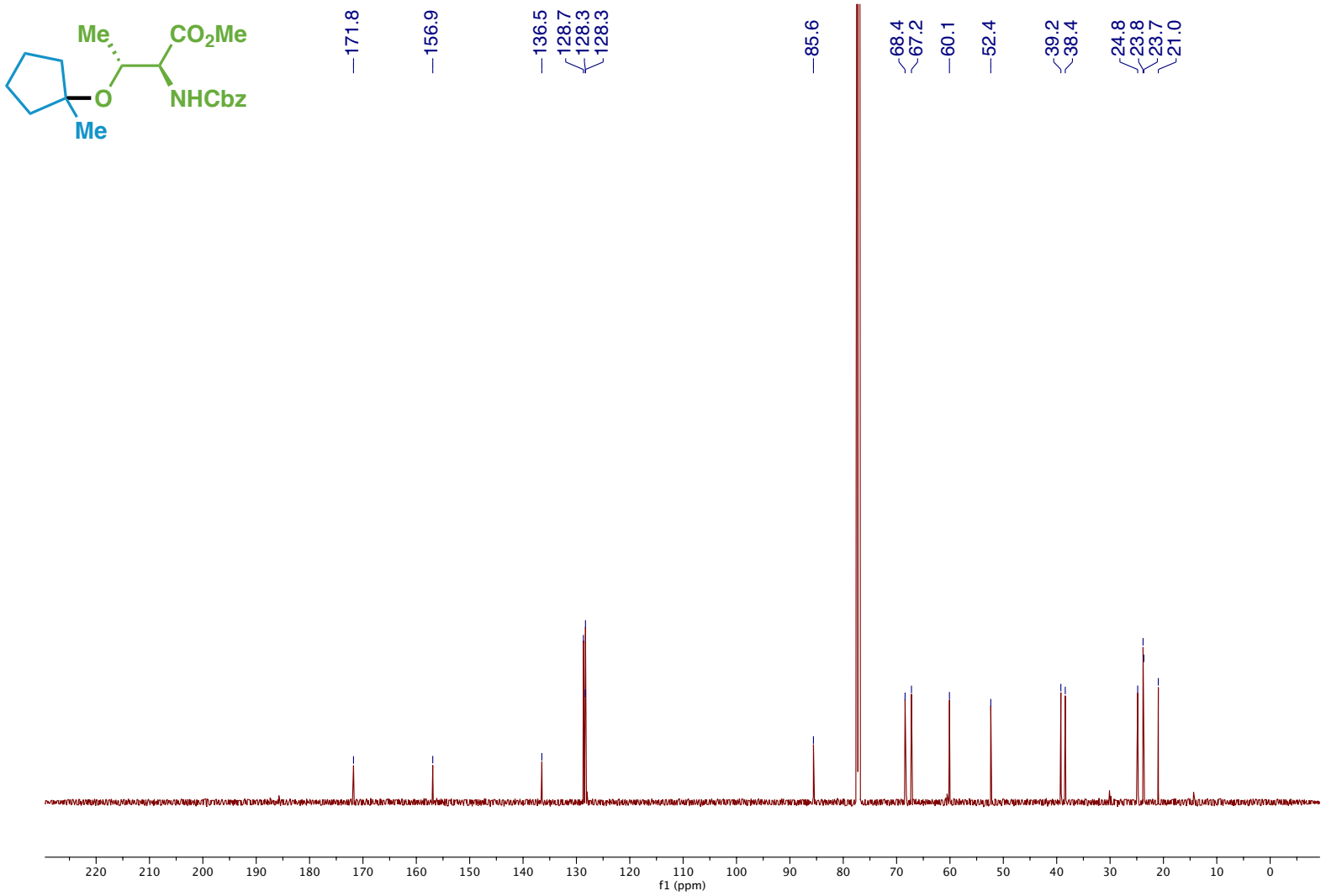
Compound 10 ^{13}C NMR



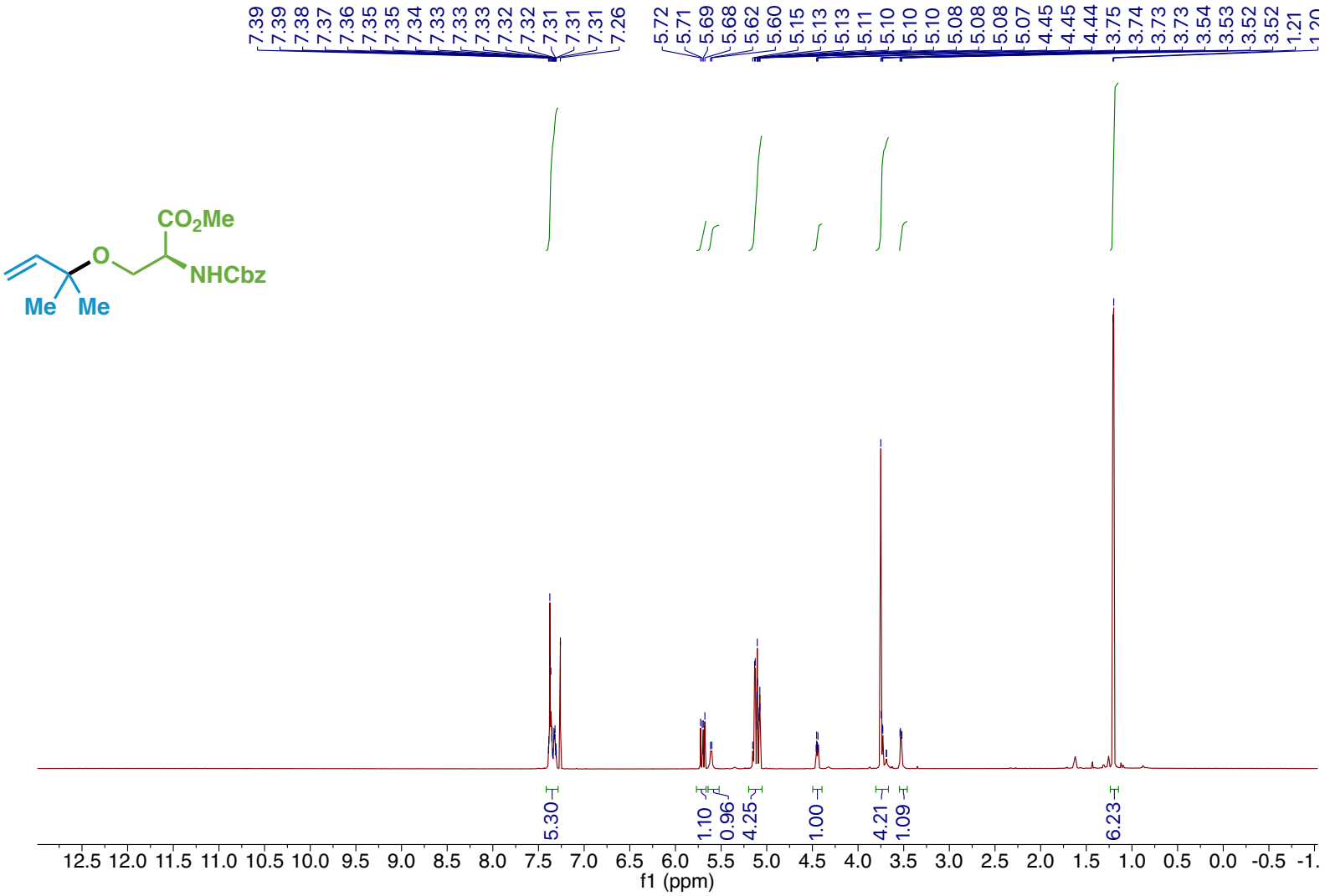
Compound 11 ^{1}H NMR



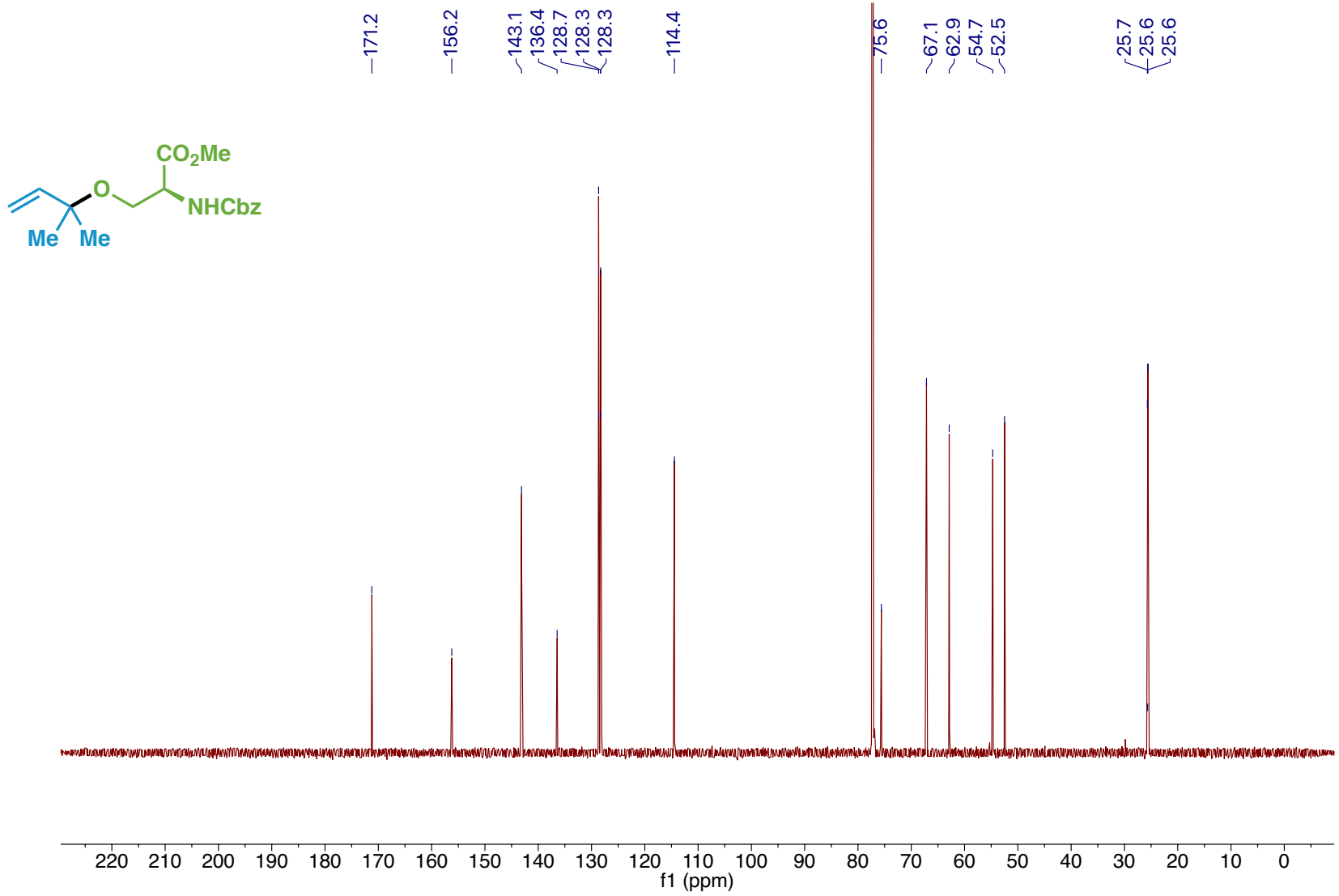
Compound 11 ^{13}C NMR



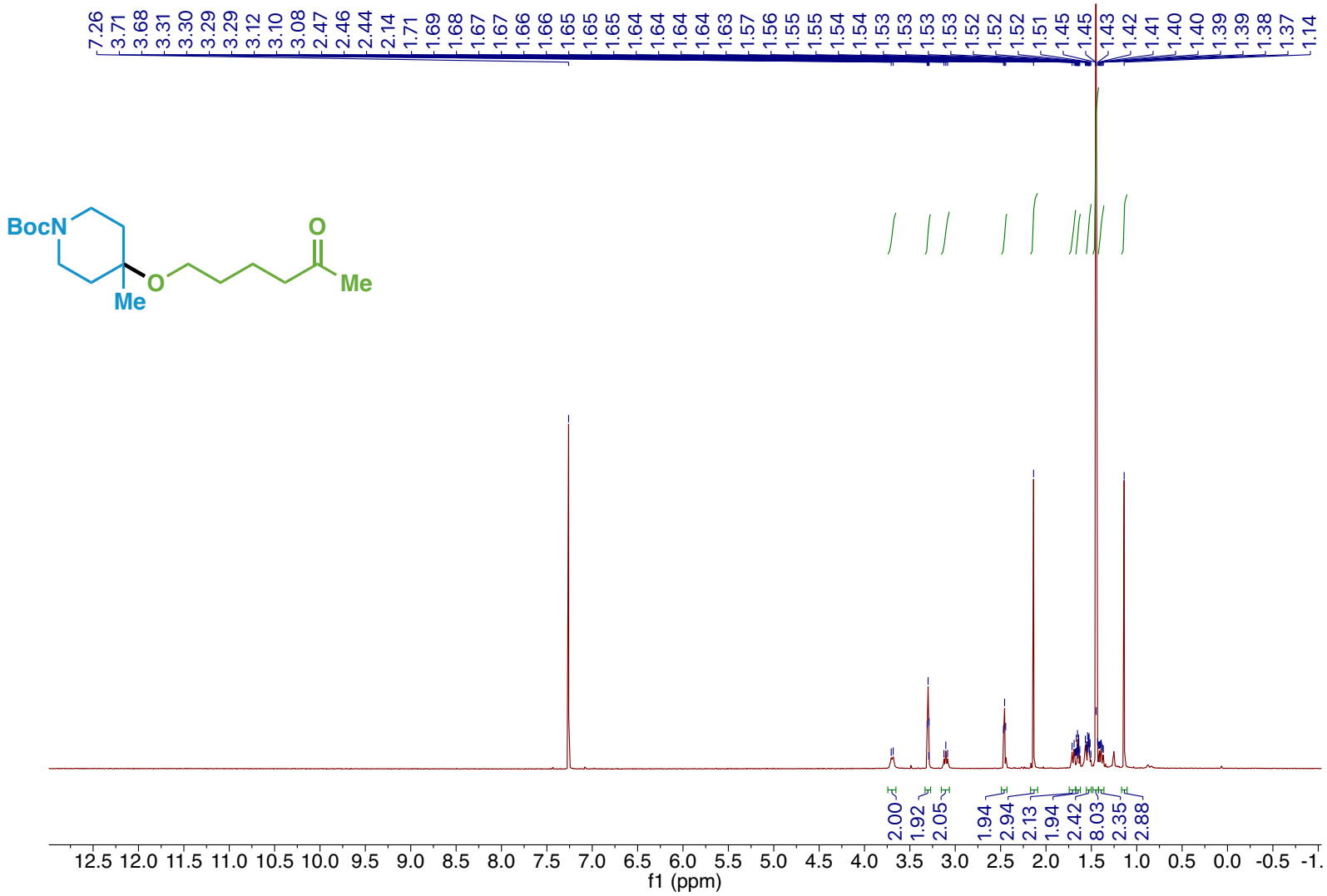
Compound 12 ^{1}H NMR



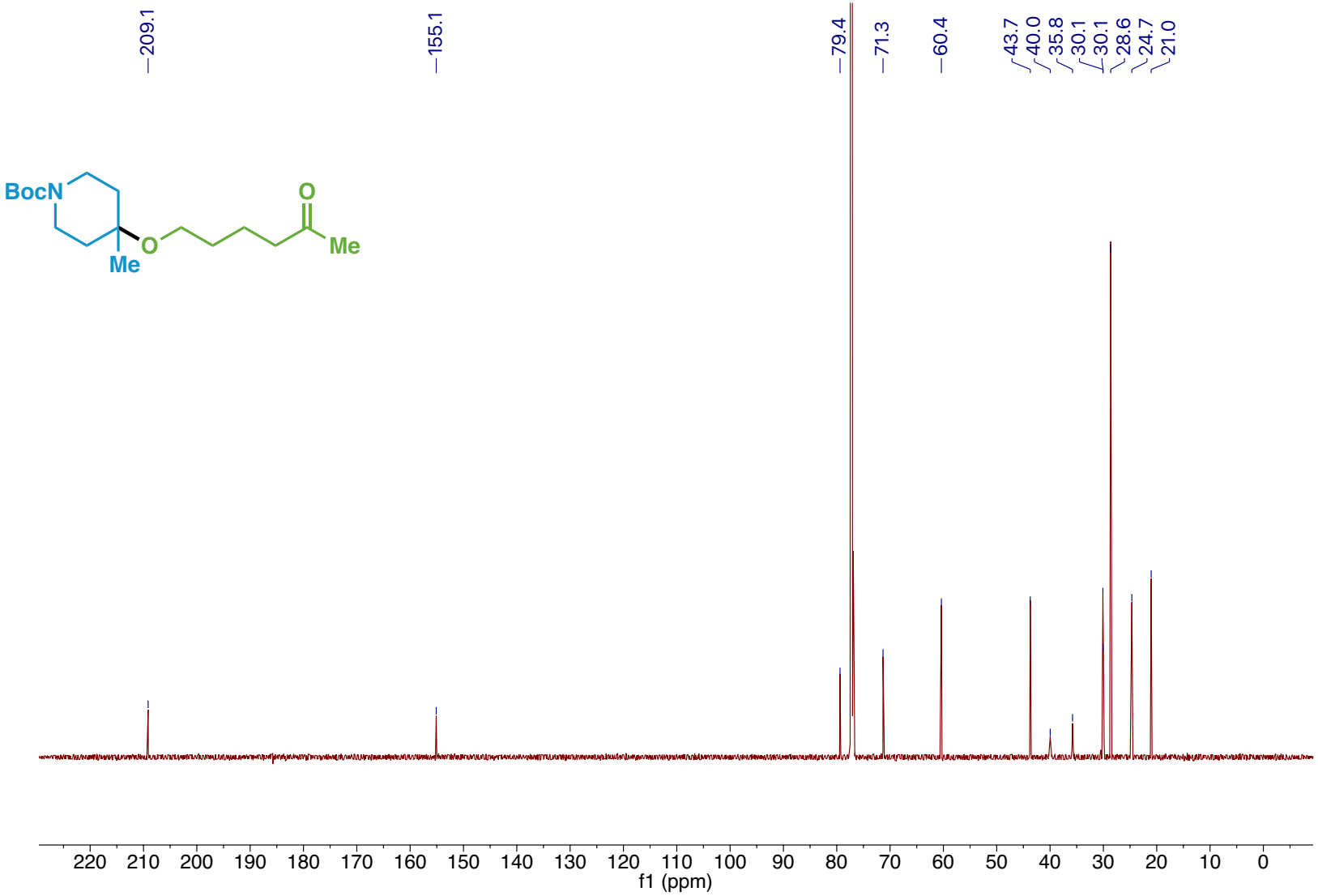
Compound 12 ^{13}C NMR



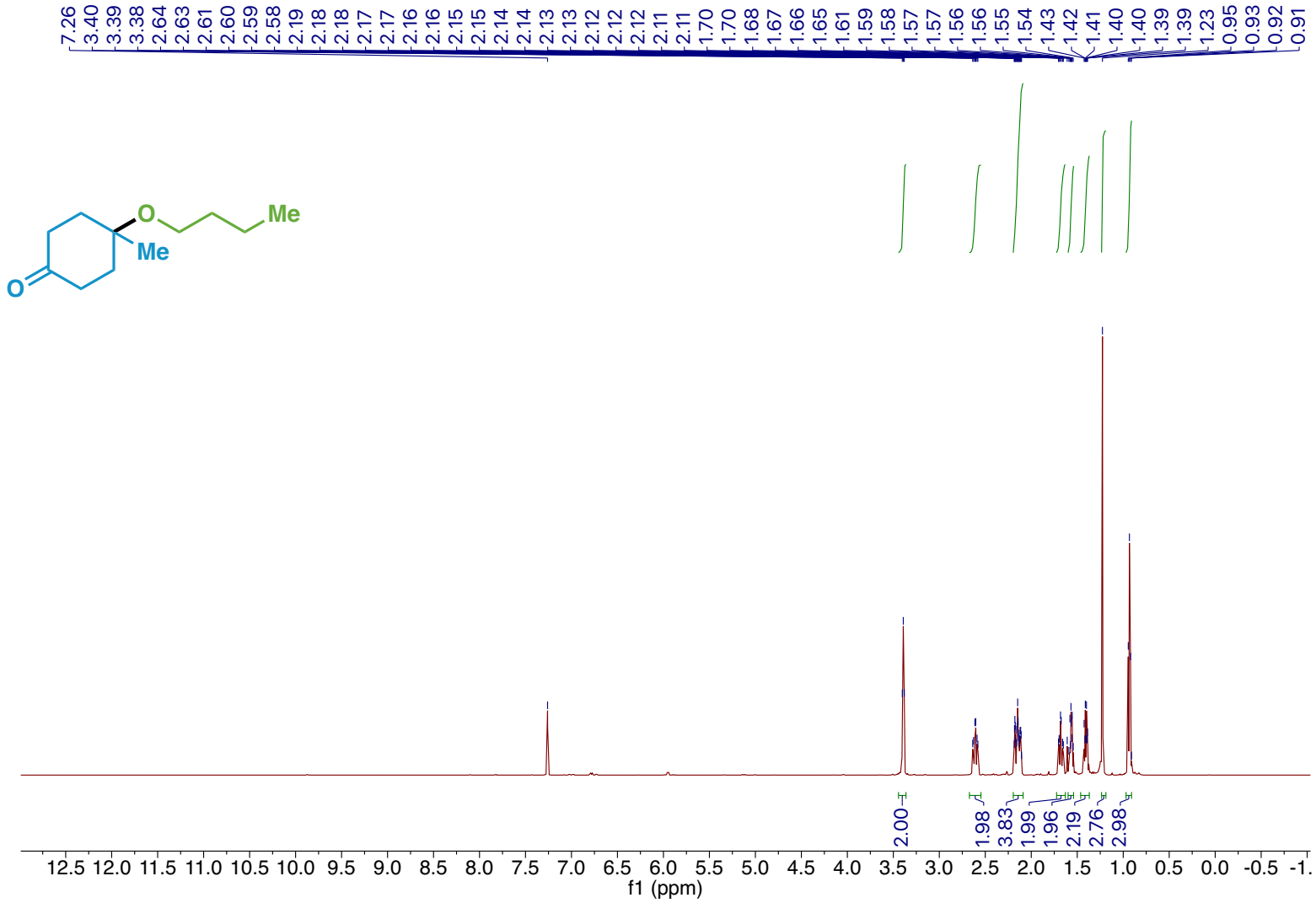
Compound 13 ^{1}H NMR



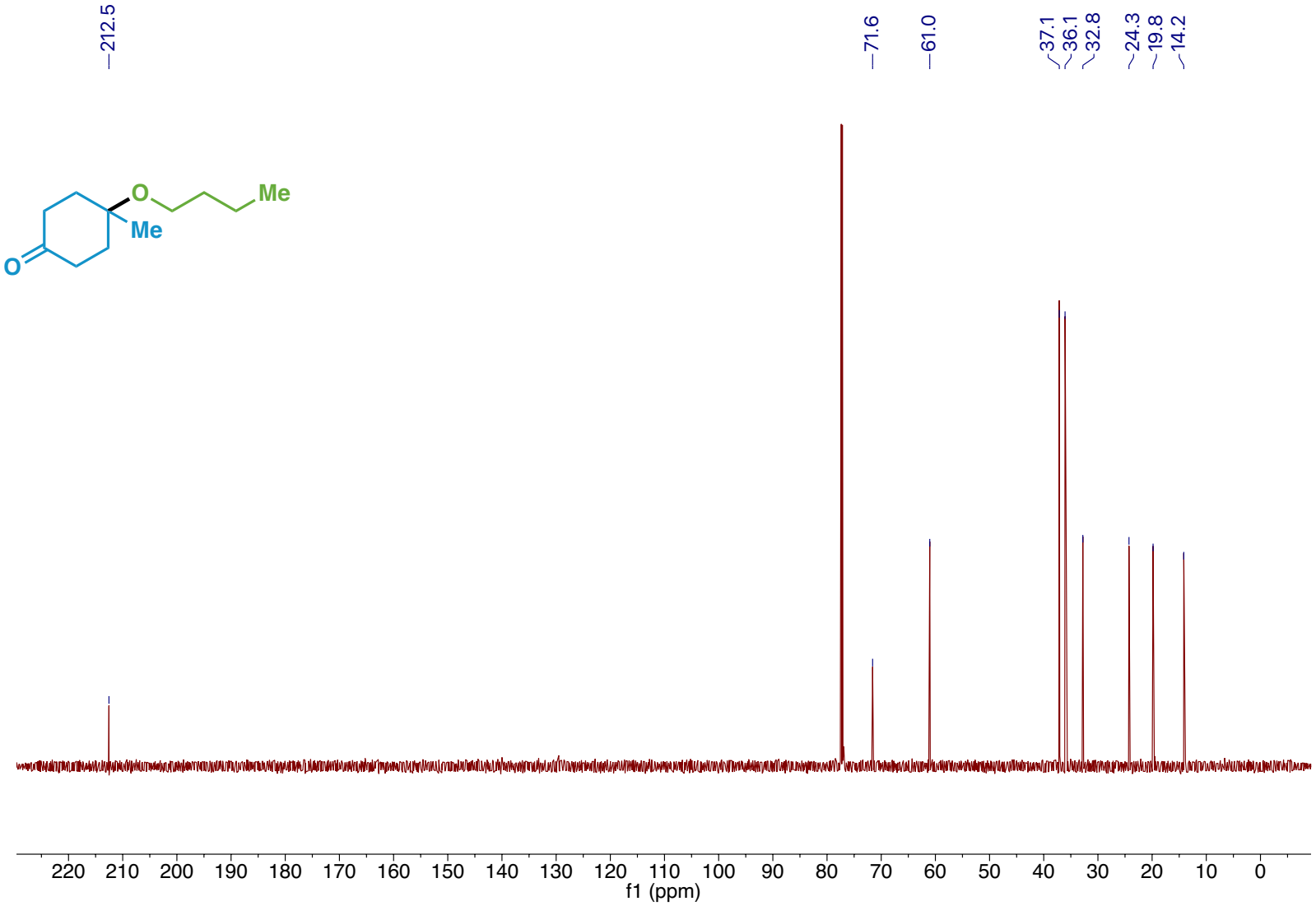
Compound 13 ^{13}C NMR



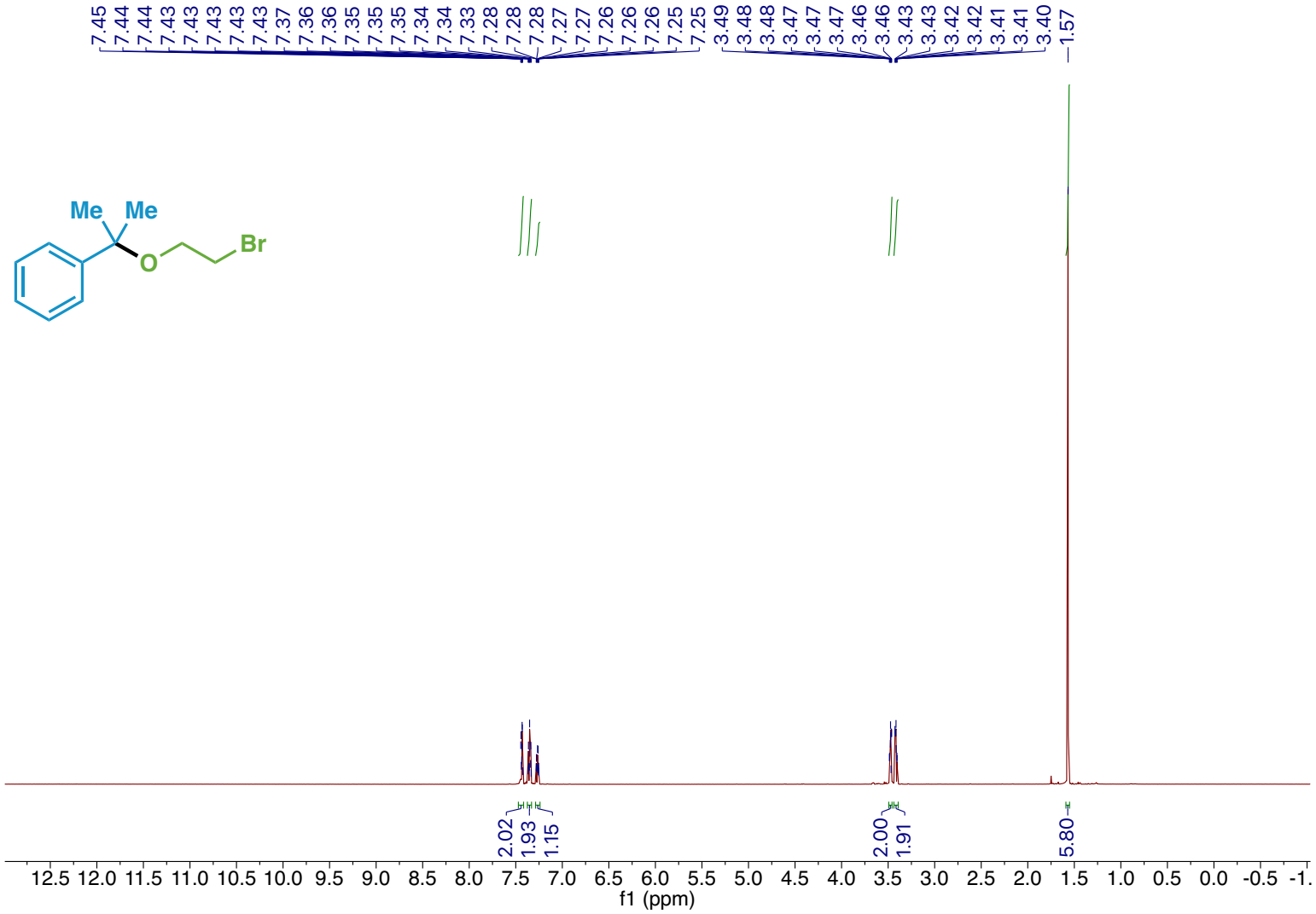
Compound 14 ^{1}H NMR



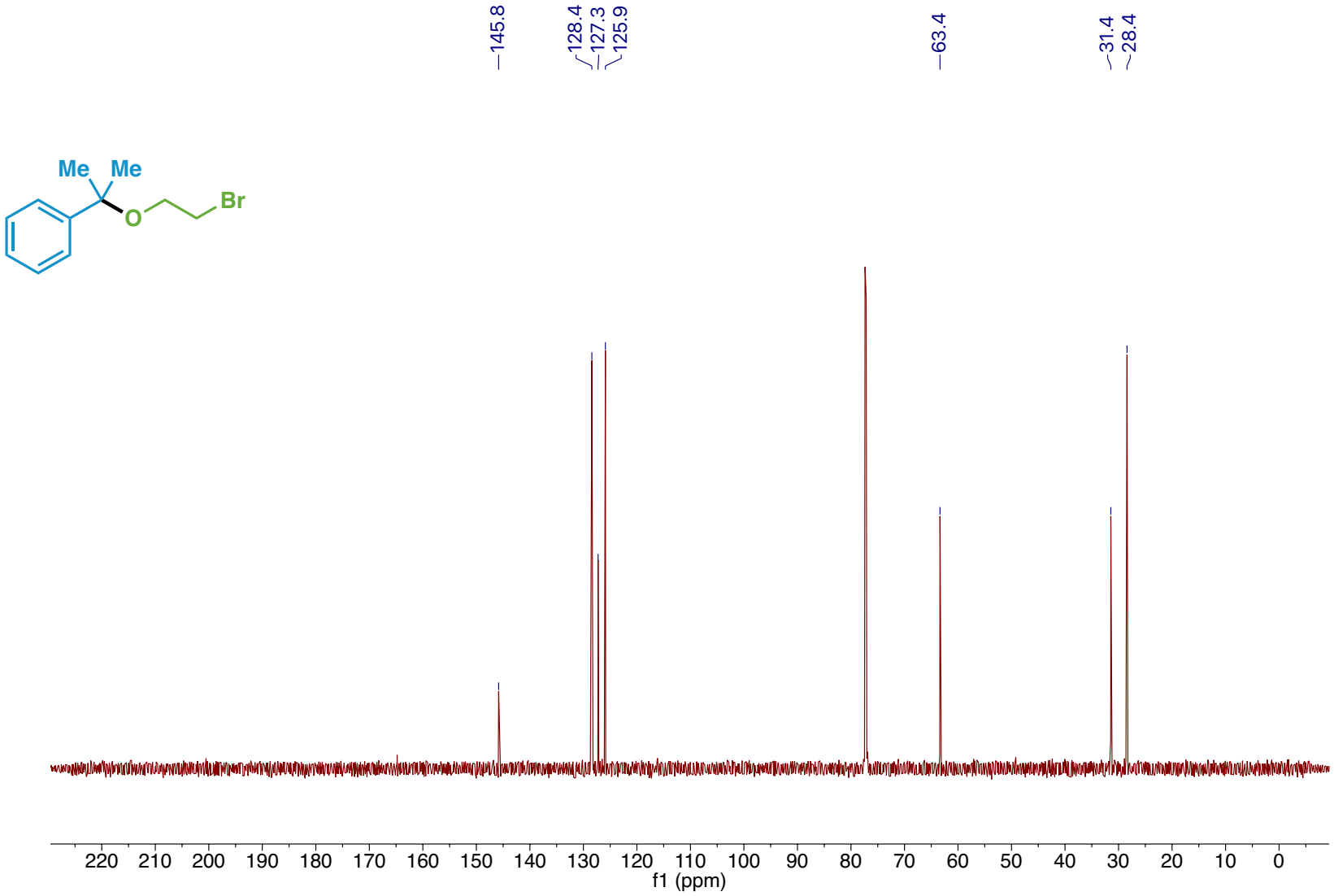
Compound 14 ^{13}C NMR



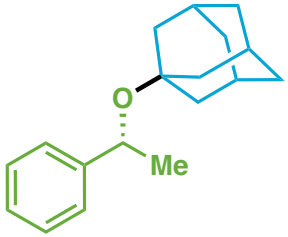
Compound 15 ^{1}H NMR



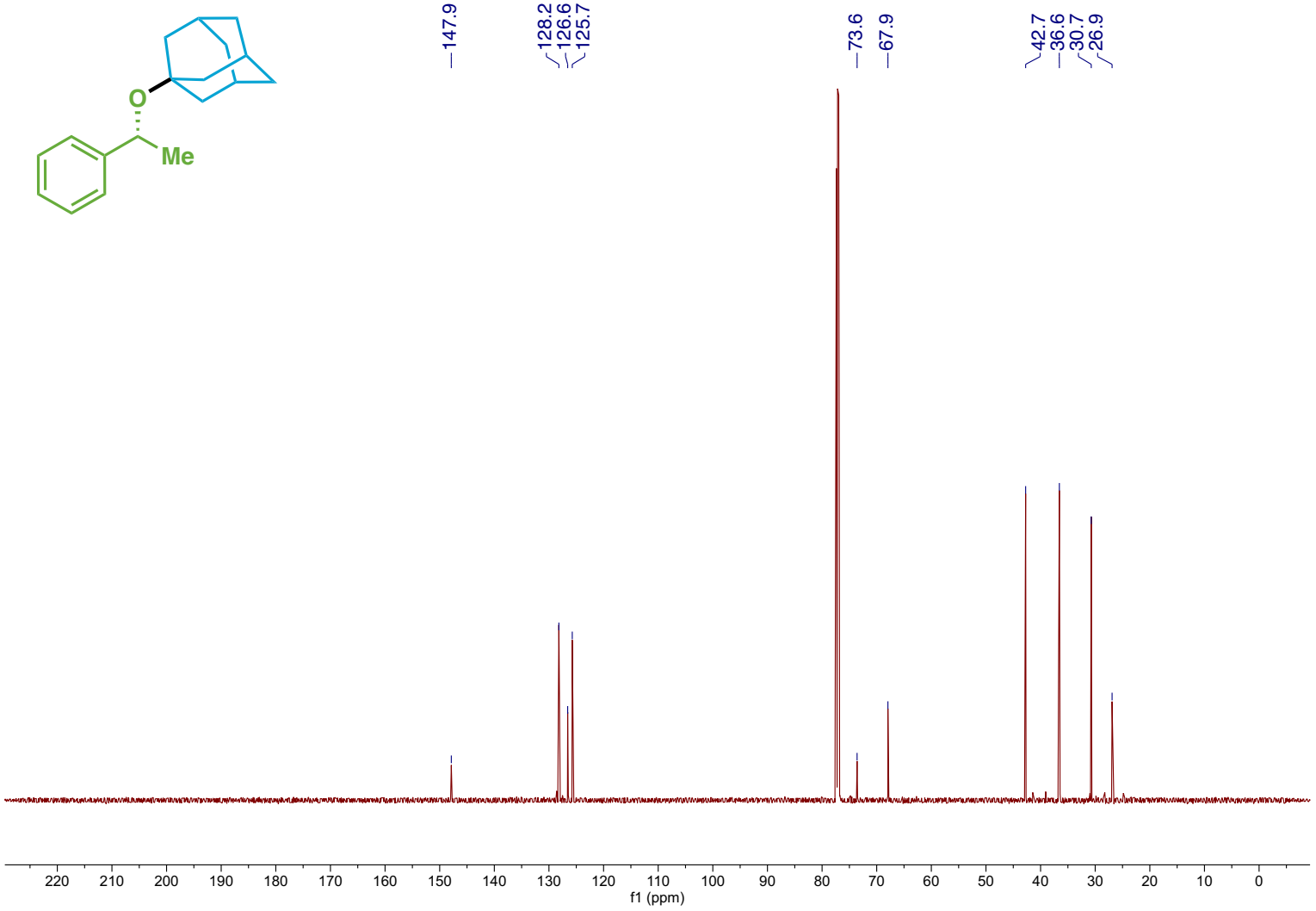
Compound 15 ^{13}C NMR



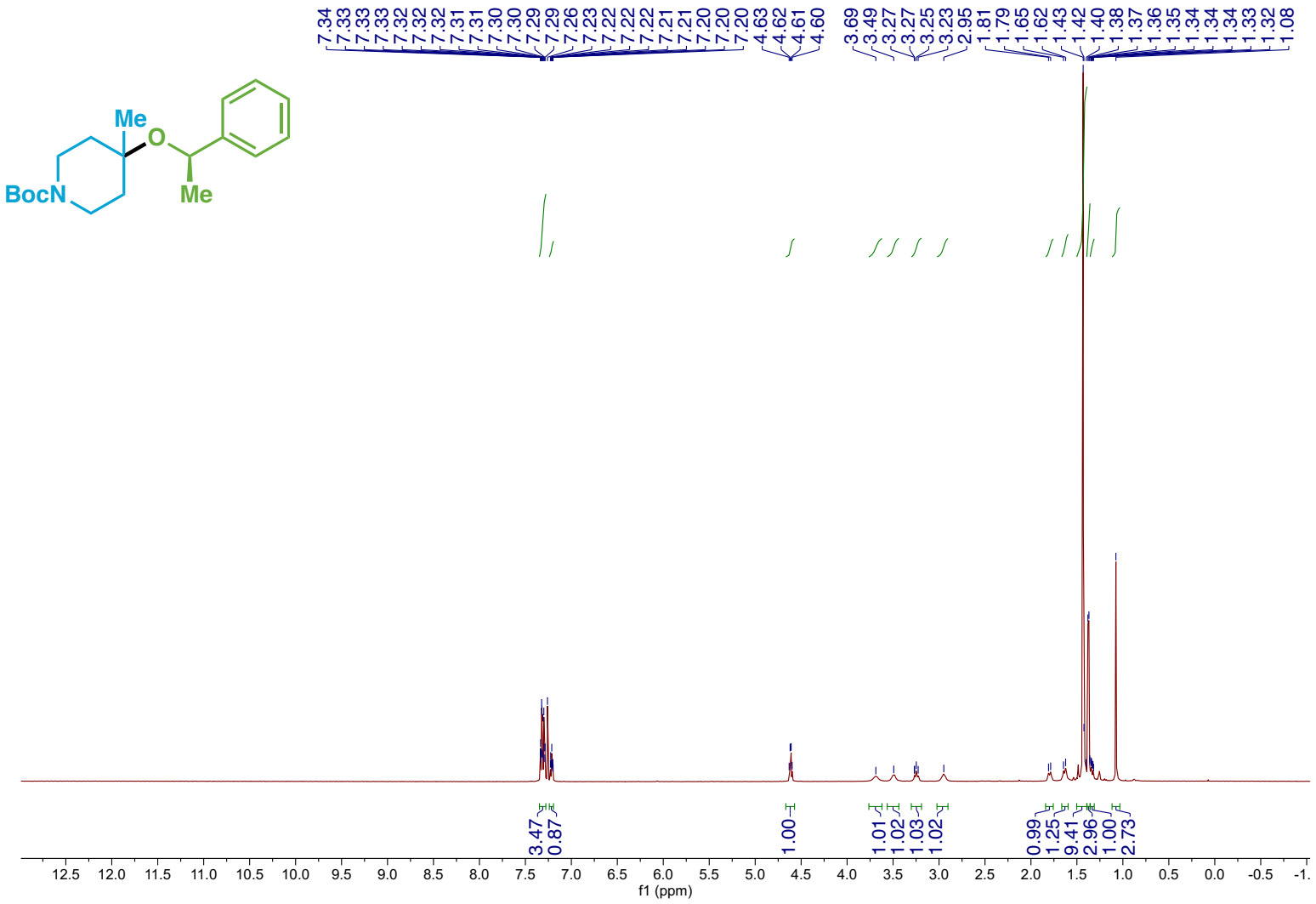
Compound 16 ^{1}H NMR



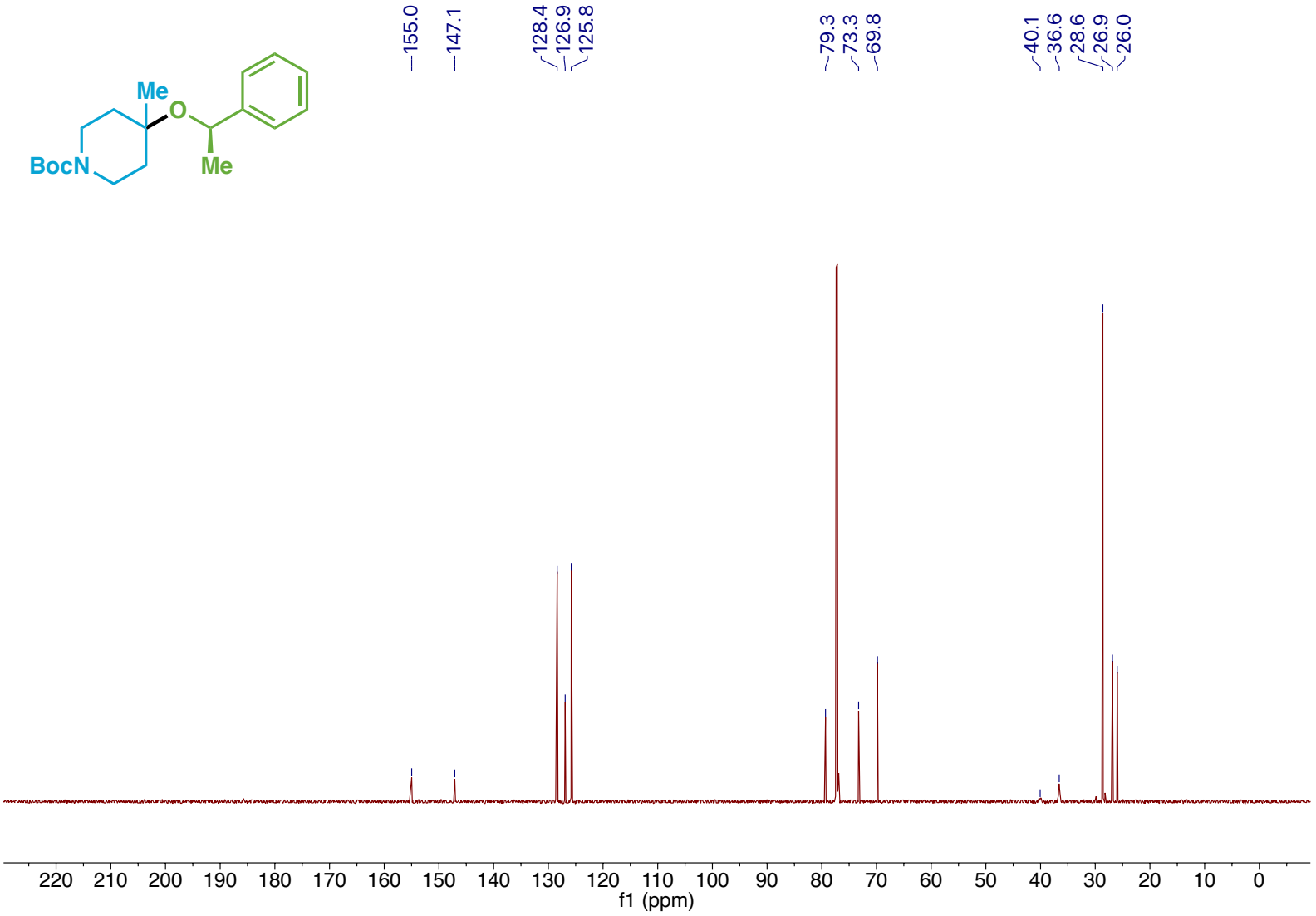
Compound 16 ^{13}C NMR



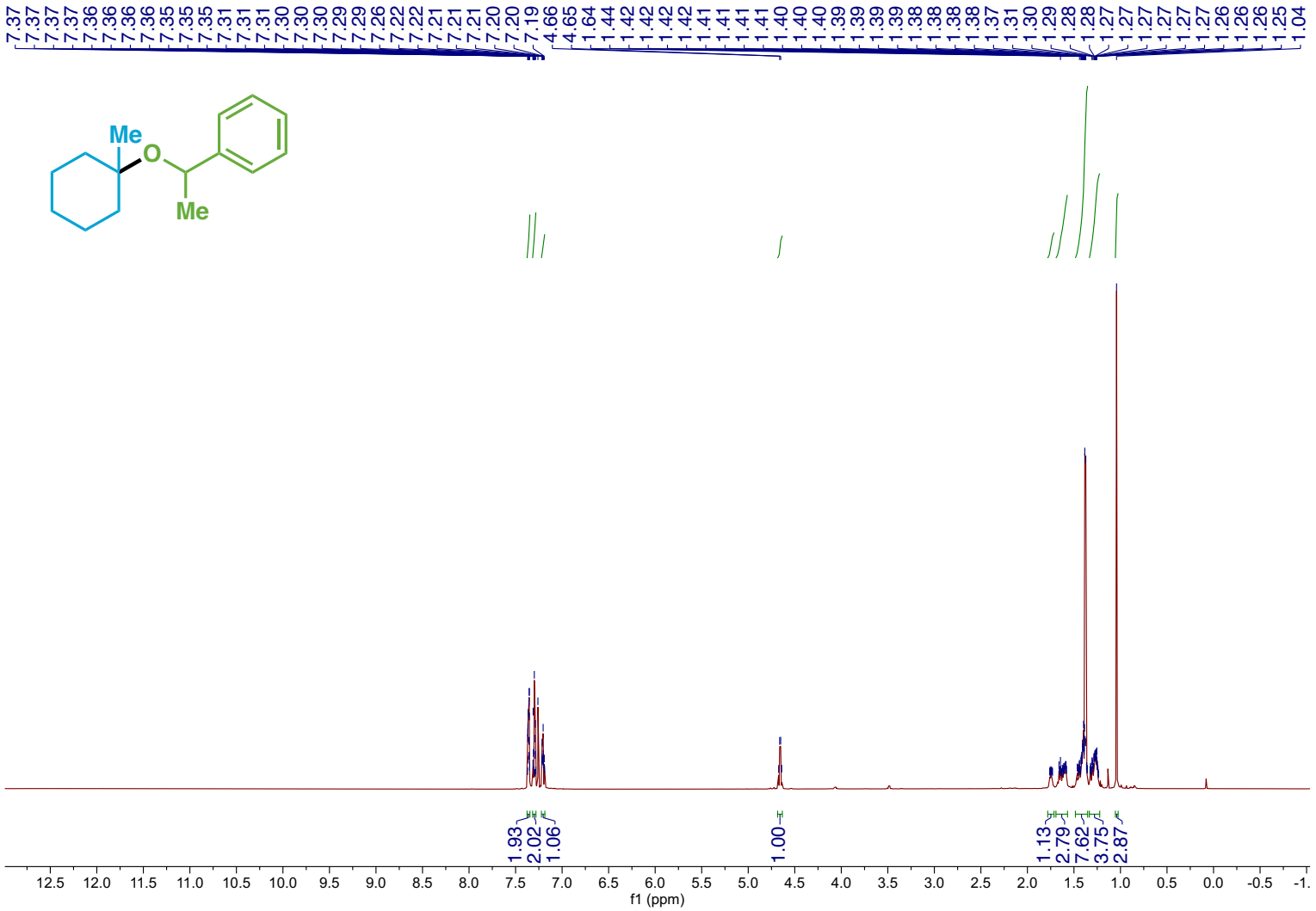
Compound 17 ^{1}H NMR



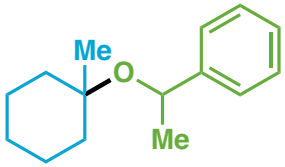
Compound 17 ^{13}C NMR



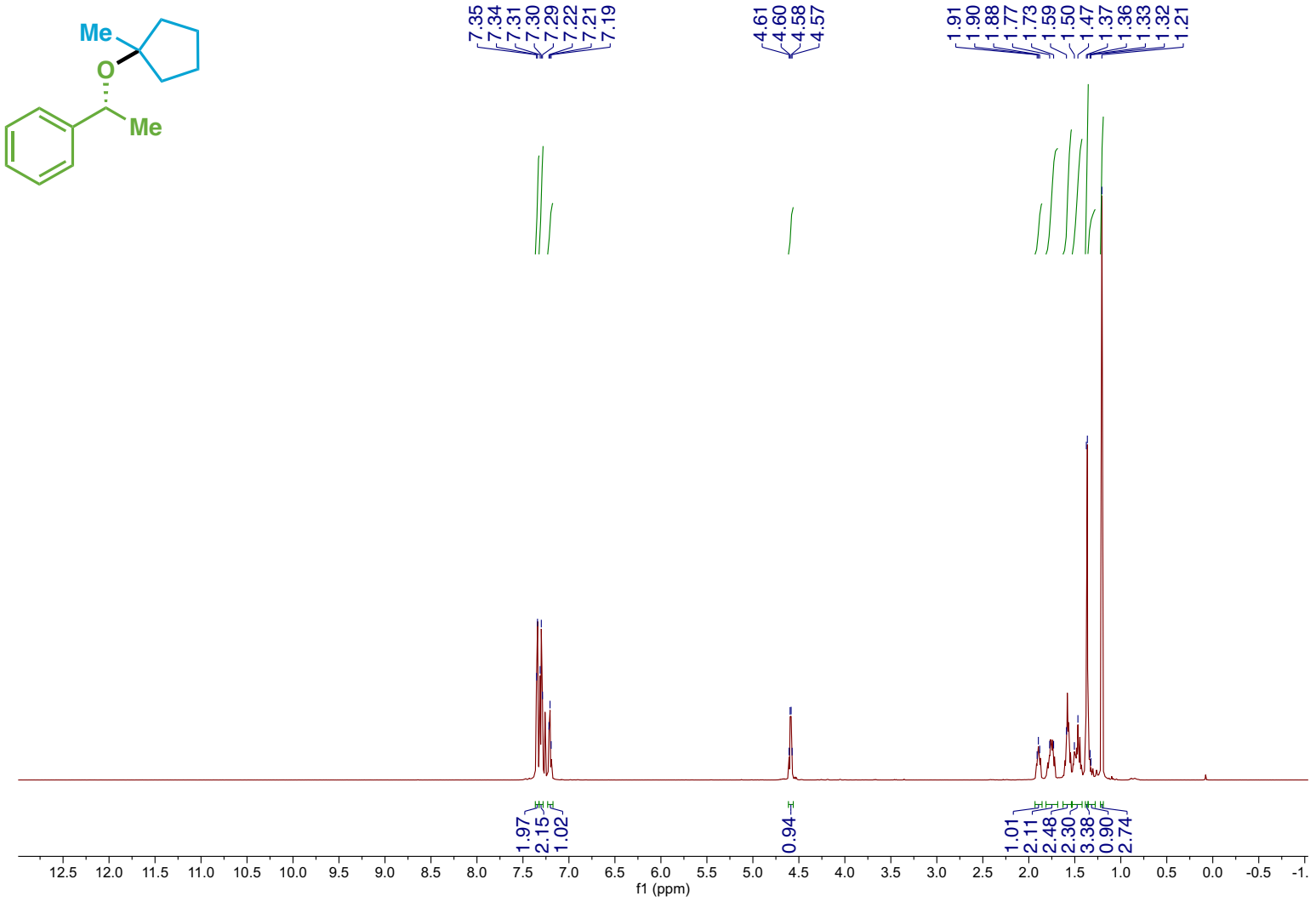
Compound 18 ^{1}H NMR



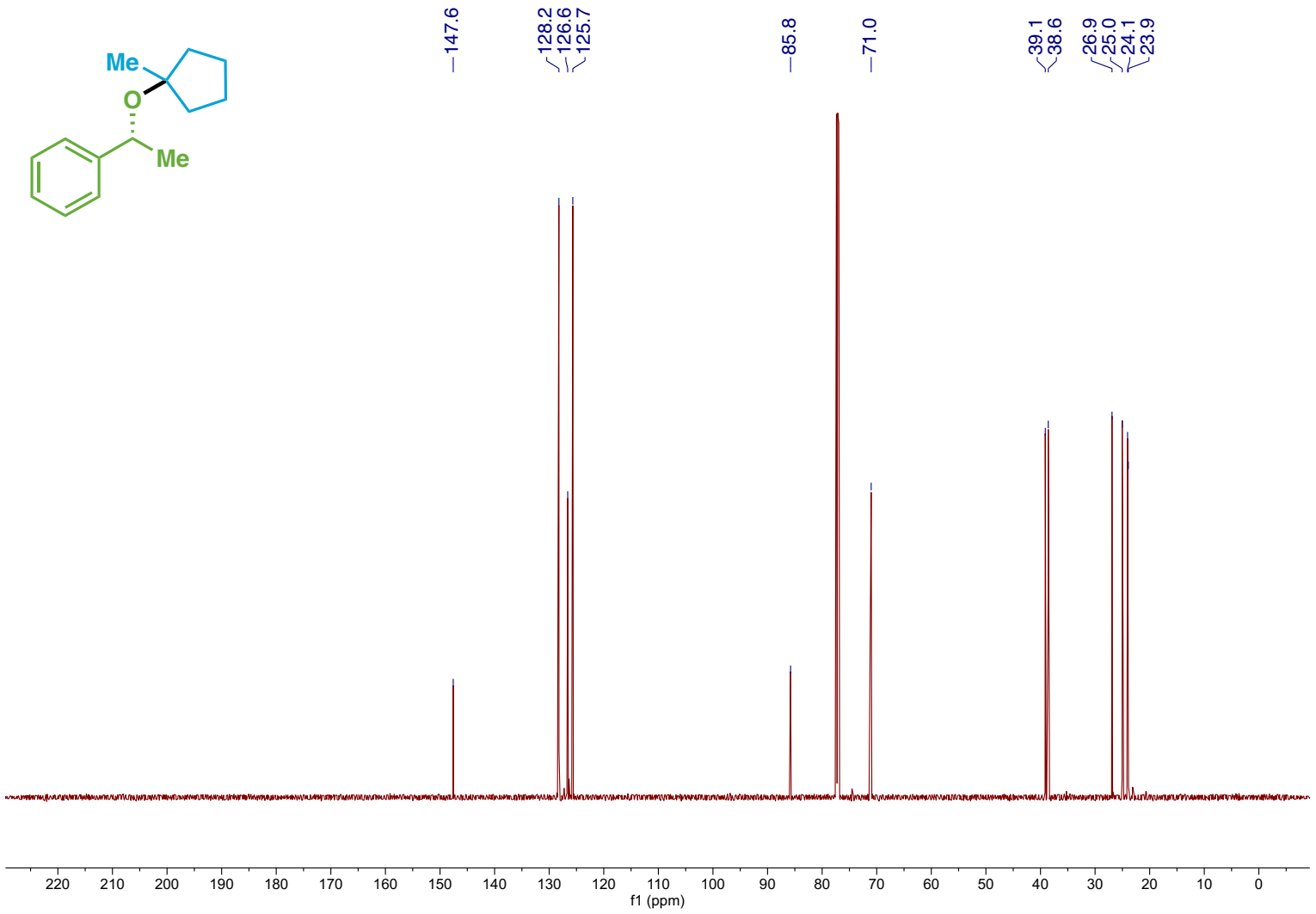
Compound 18 ^{13}C NMR



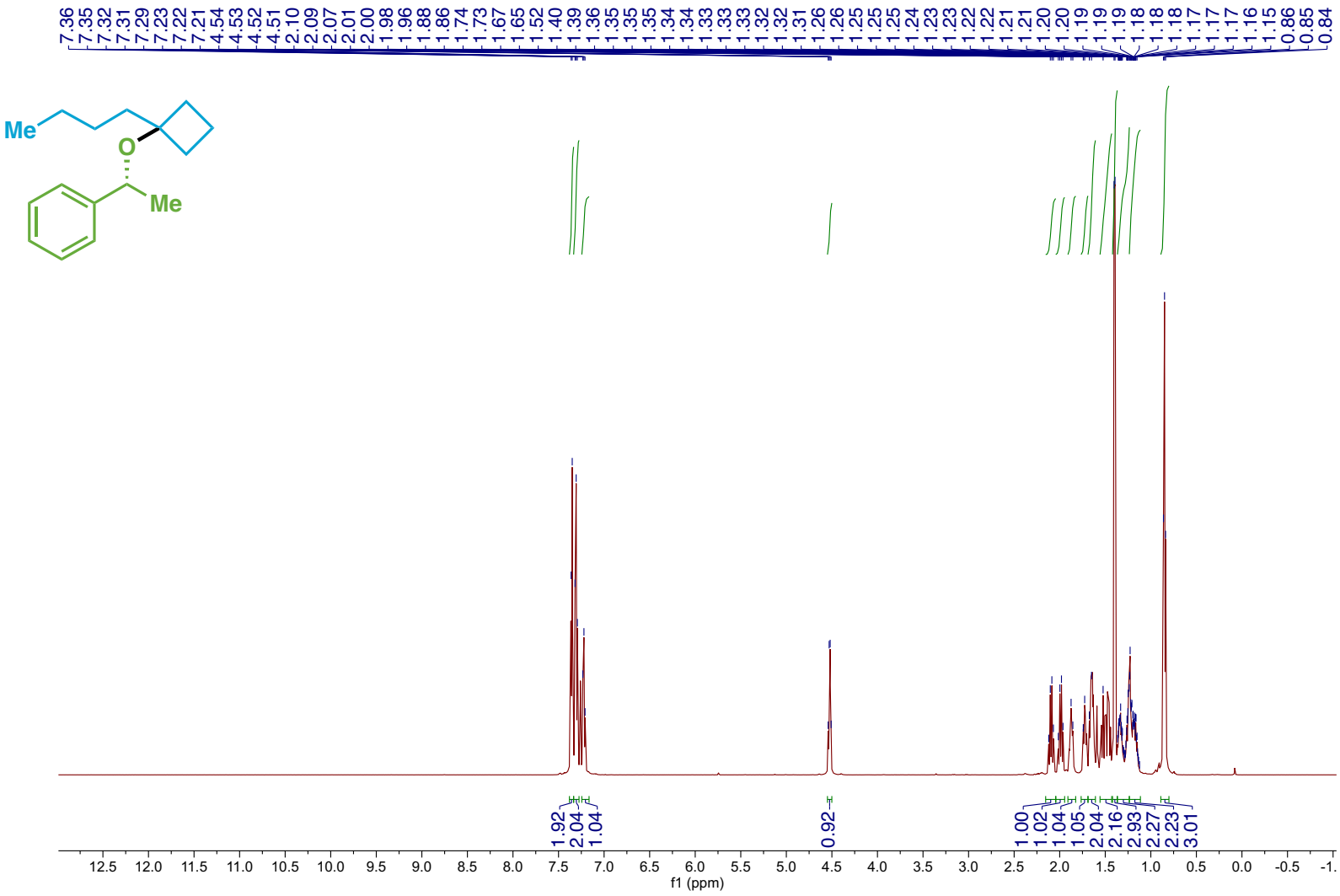
Compound 19 ^{1}H NMR



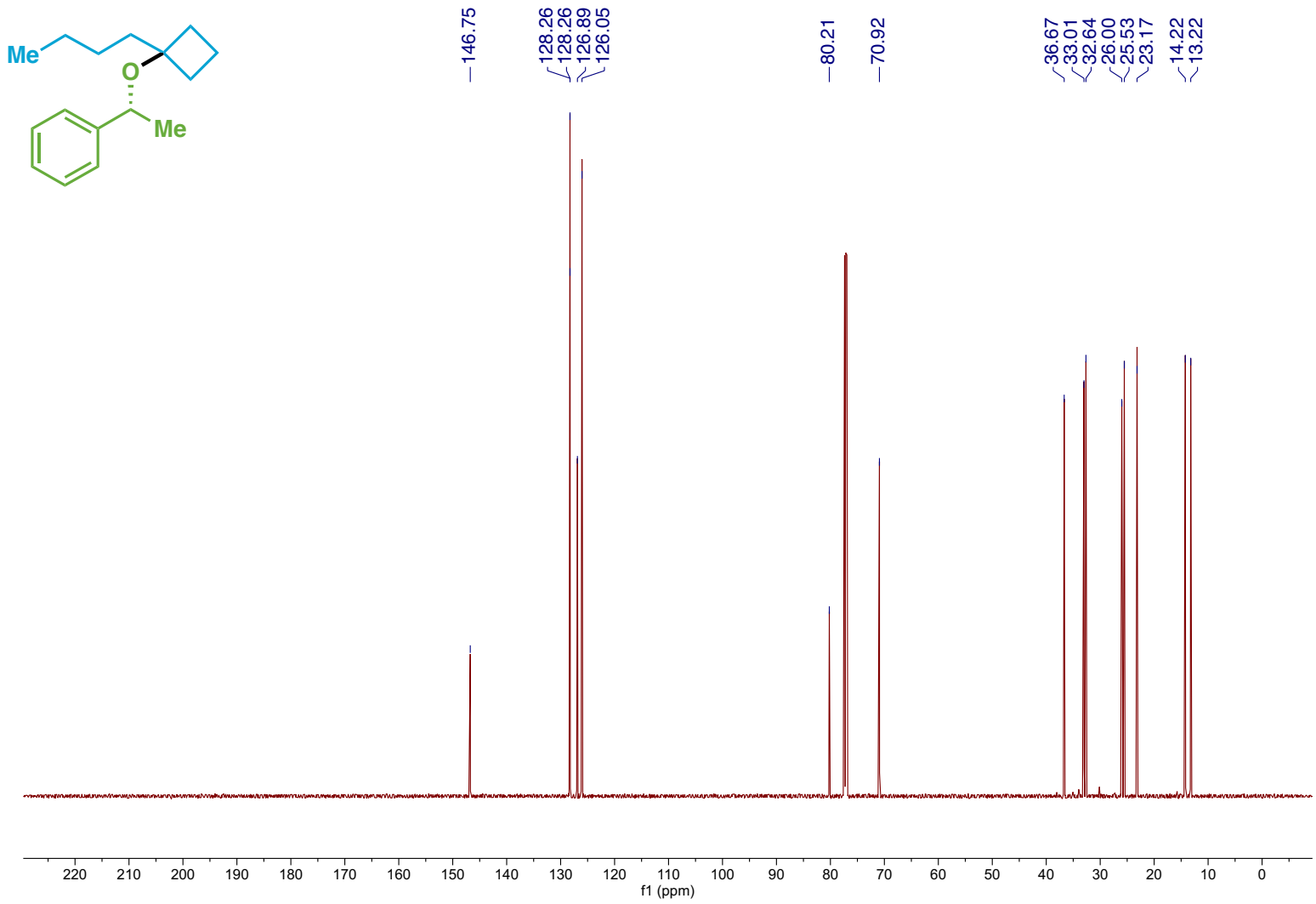
Compound 19 ^{13}C NMR



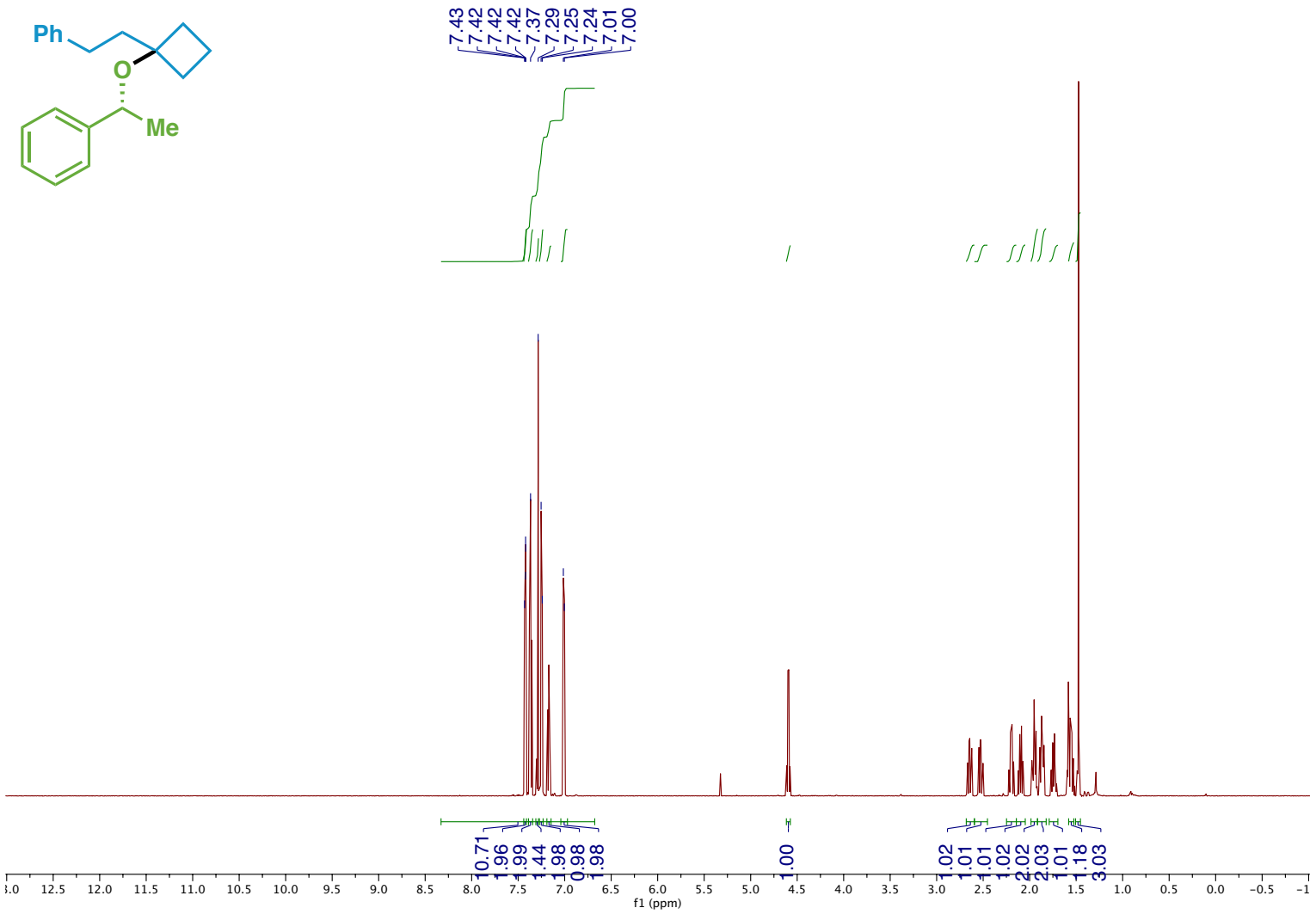
Compound 20 ^{1}H NMR



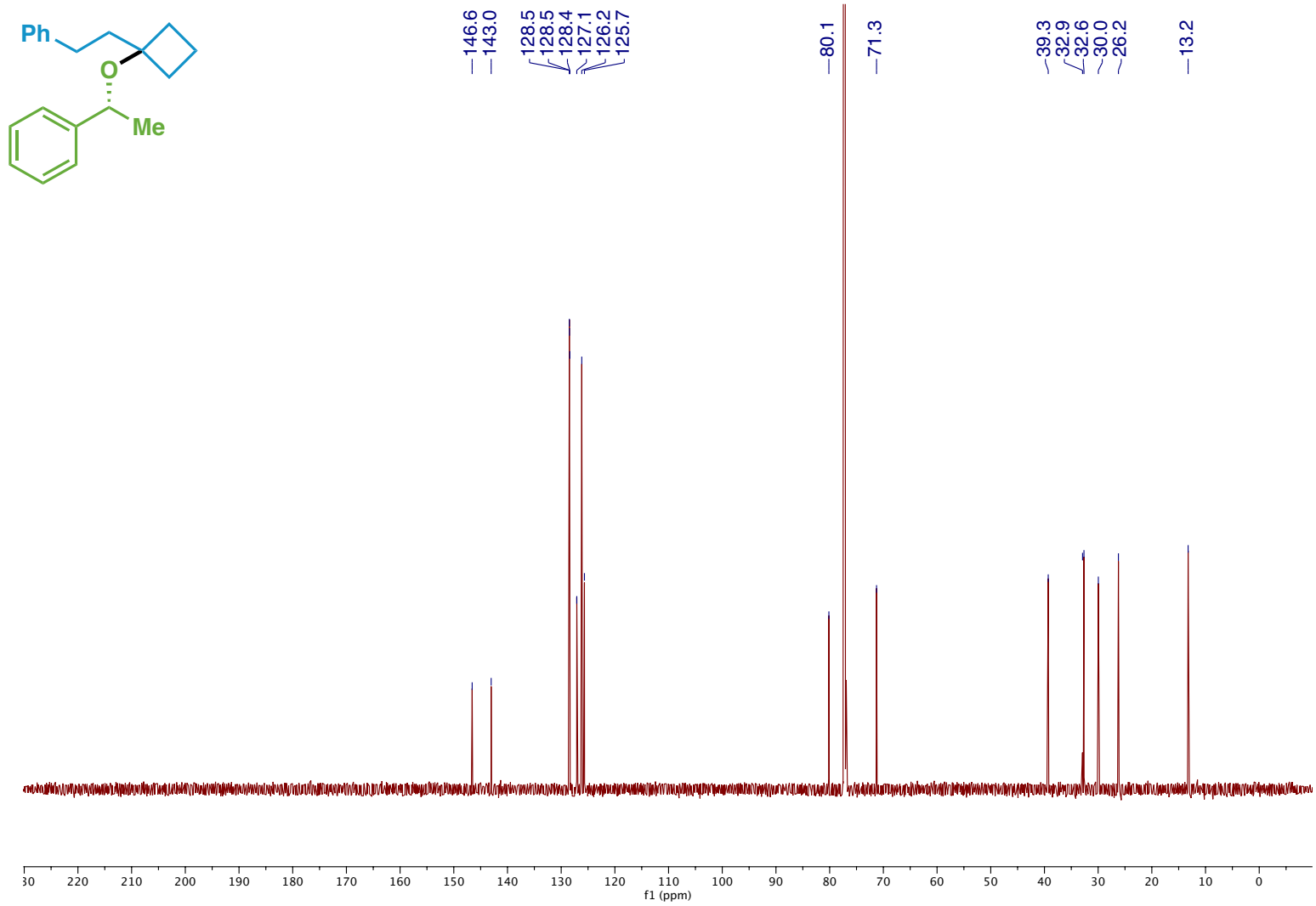
Compound 20 ^{13}C NMR



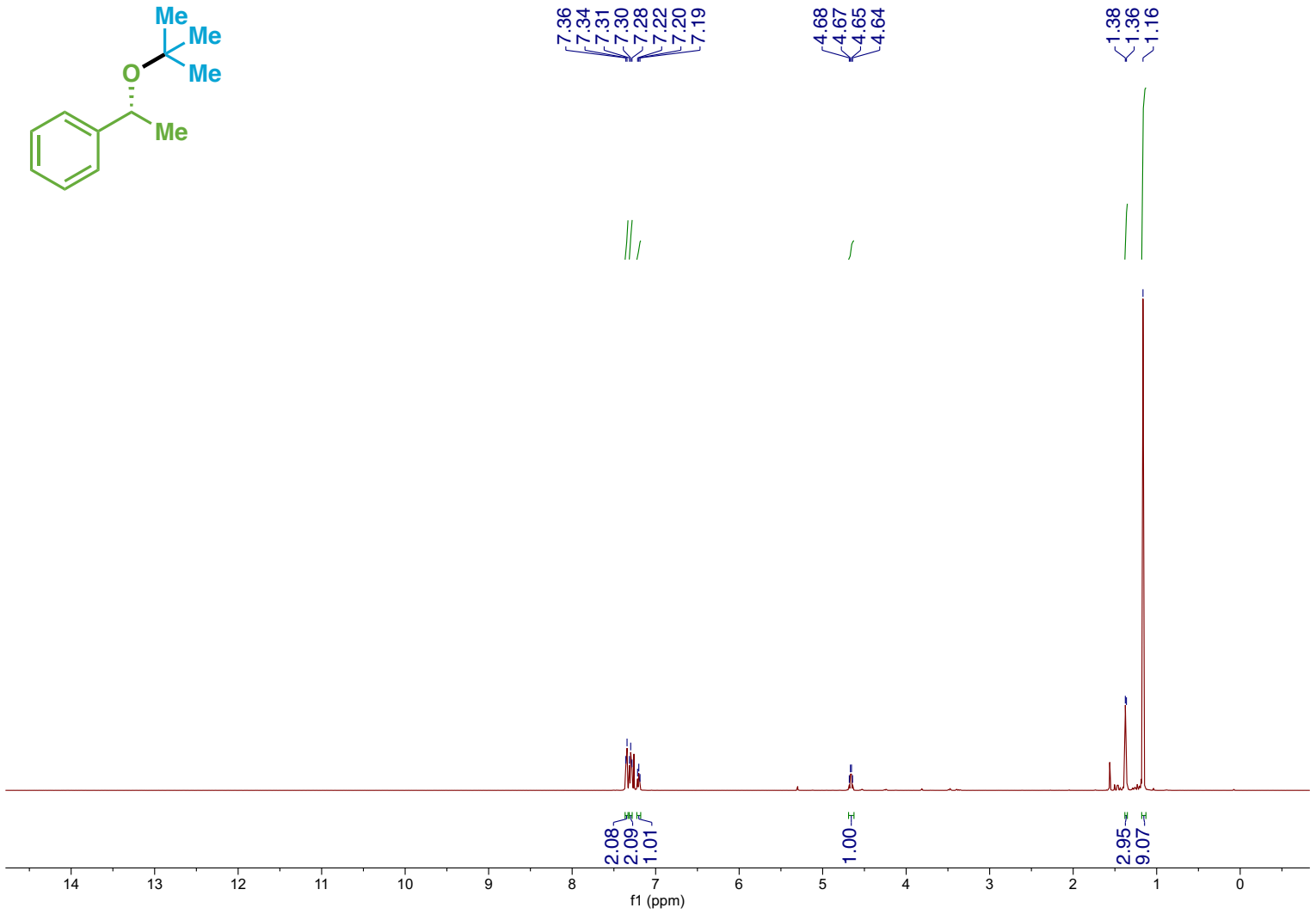
Compound 21 ^{1}H NMR



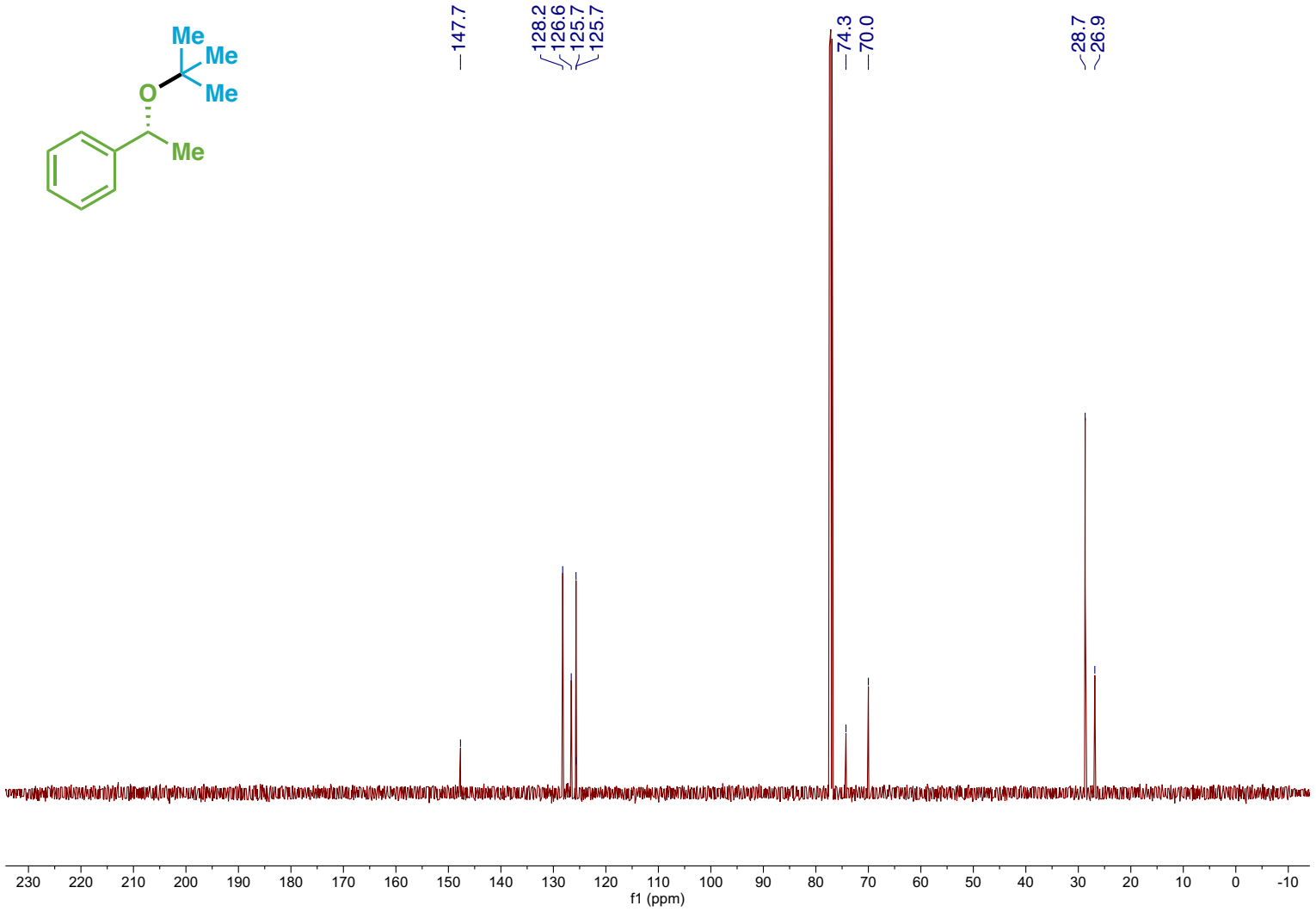
Compound 21 ^{13}C NMR



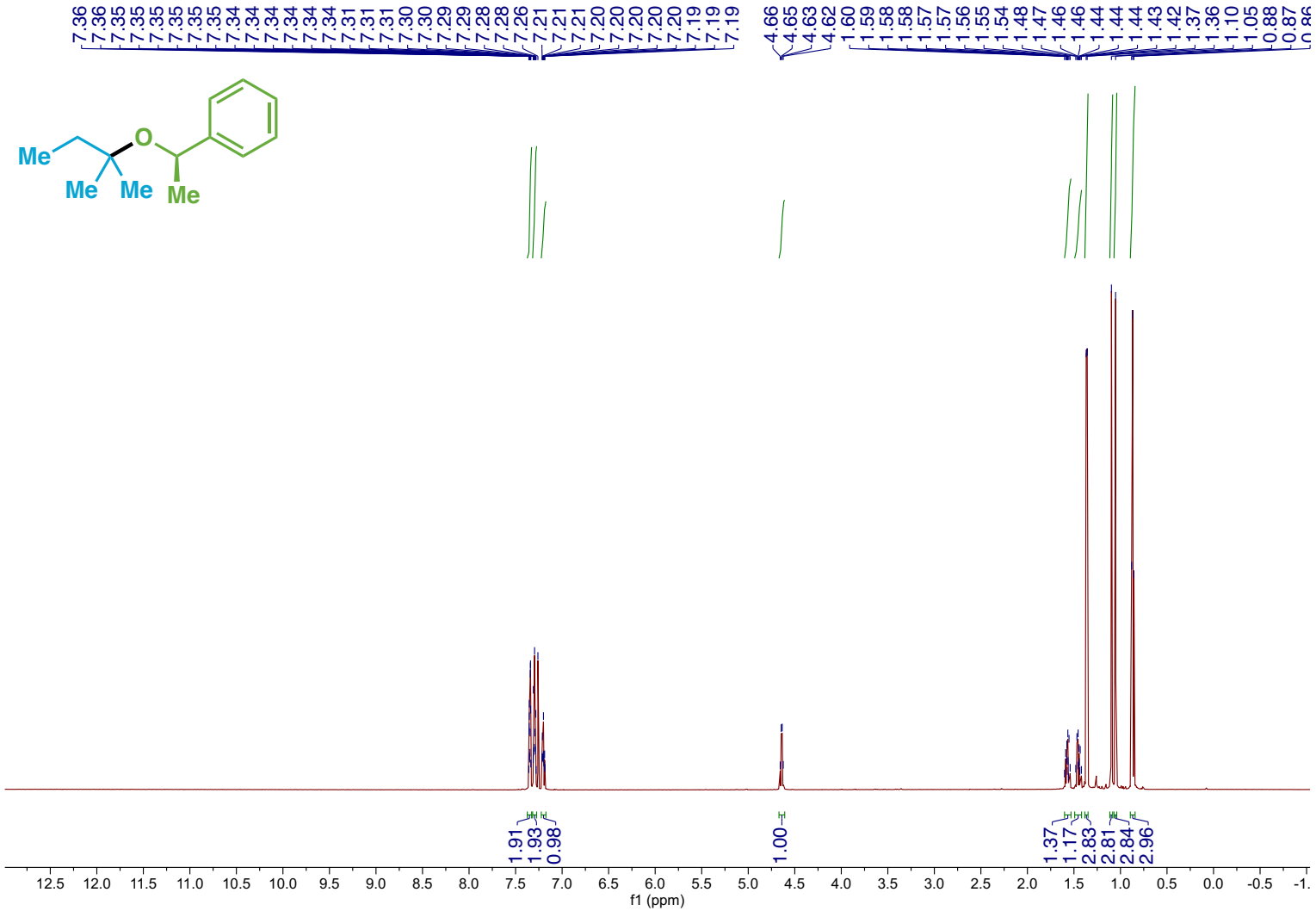
Compound 22 ^{1}H NMR



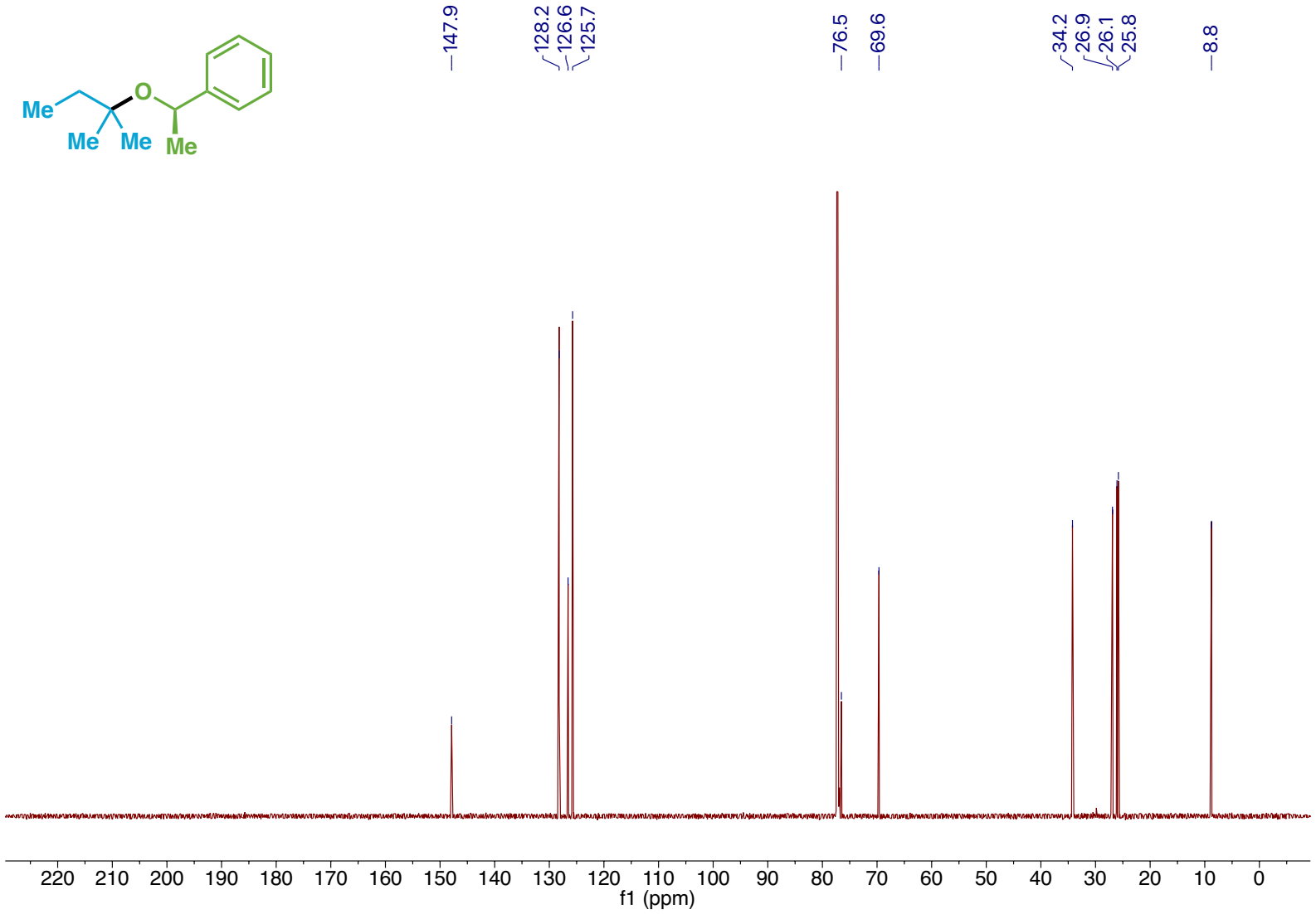
Compound 22 ^{13}C NMR



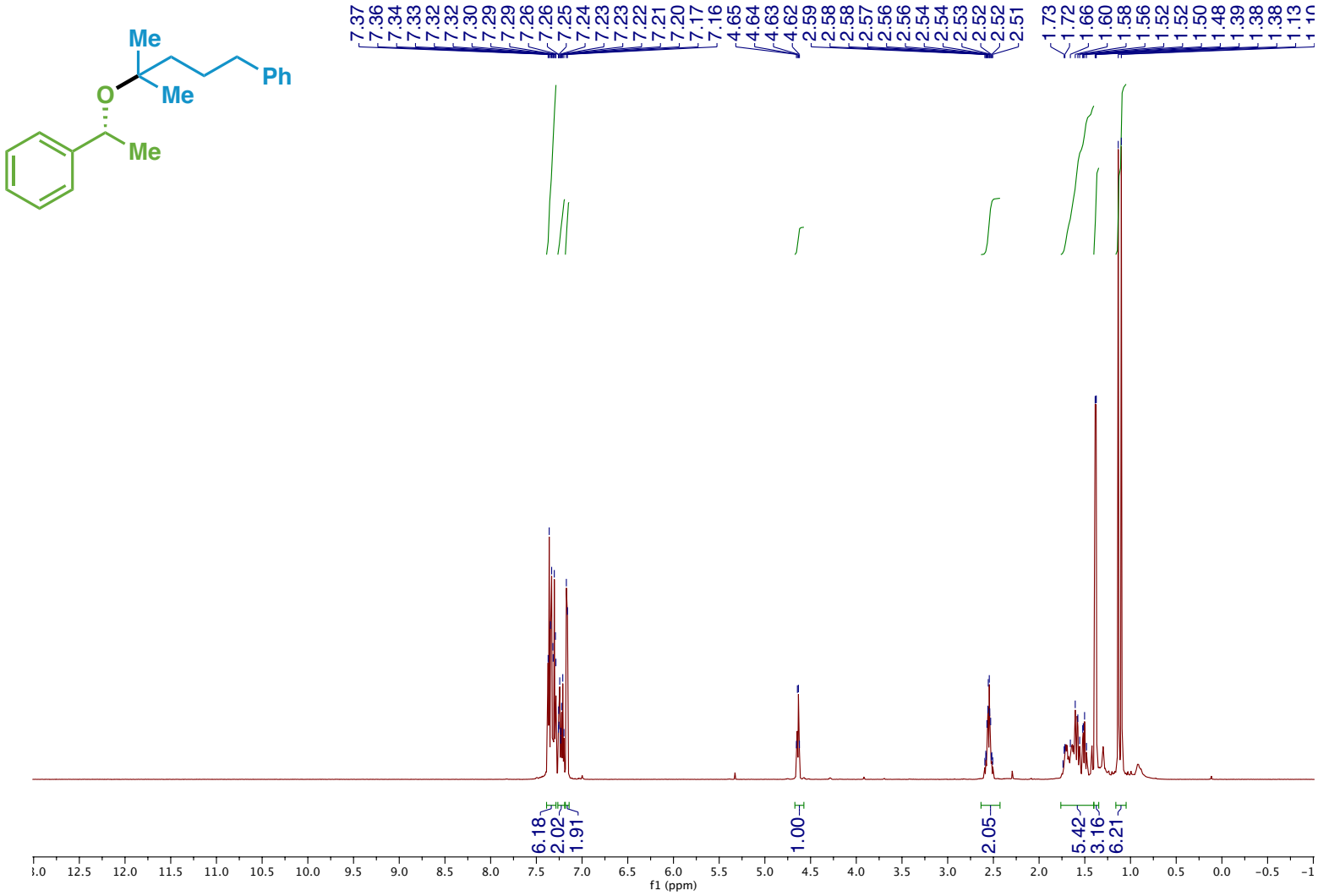
Compound 23 ^{1}H NMR



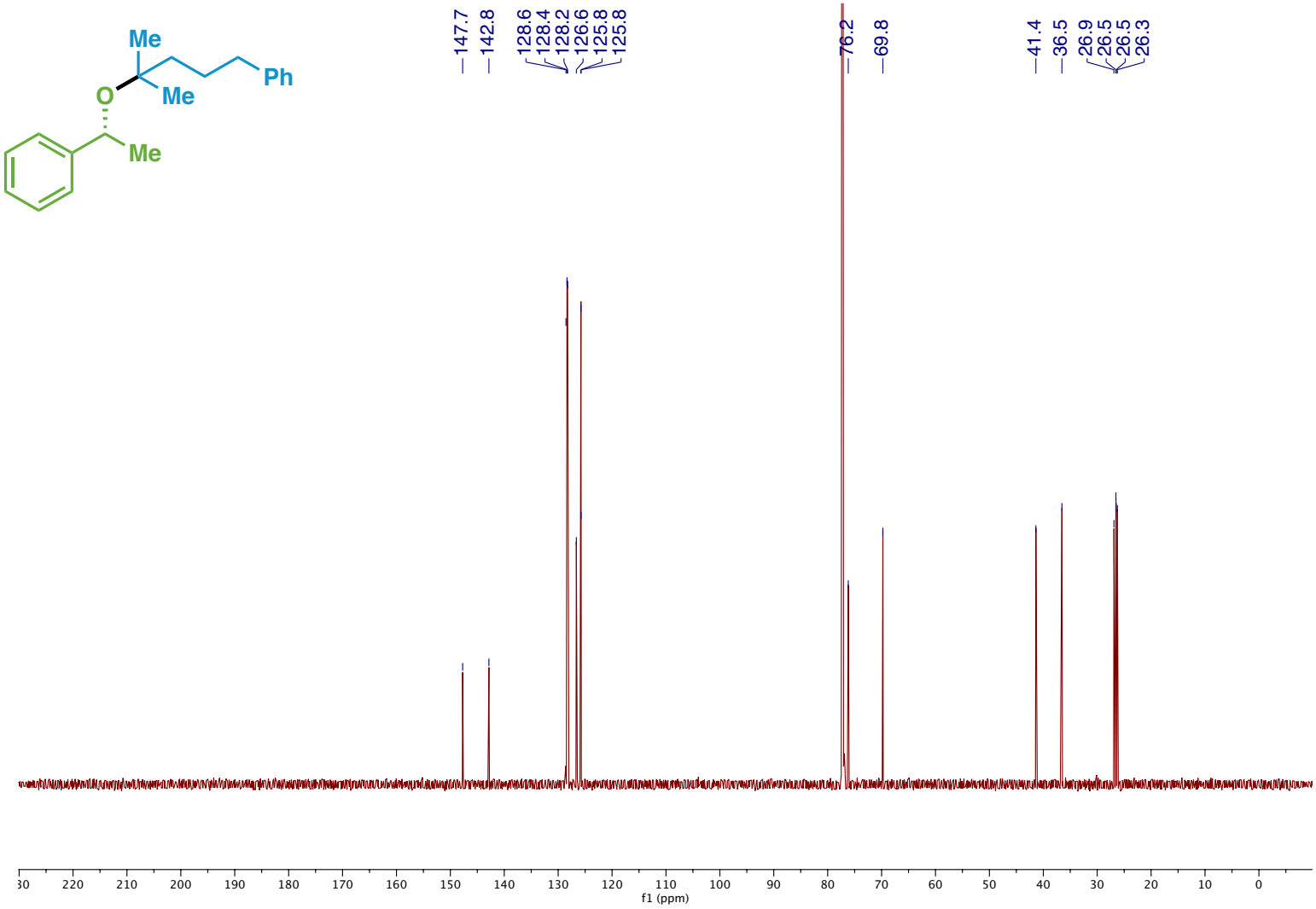
Compound 23 ^{13}C NMR



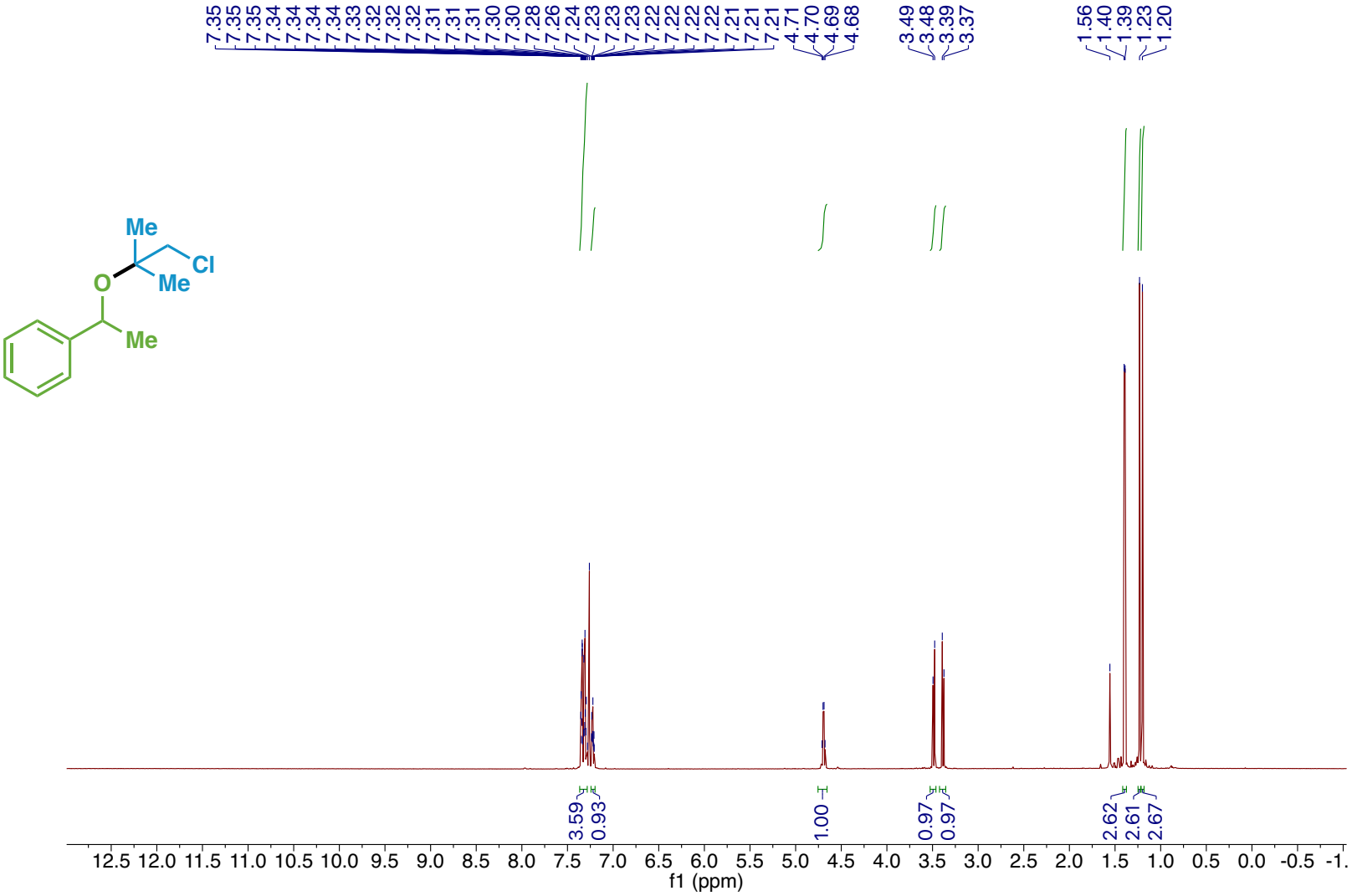
Compound 24 ^{1}H NMR



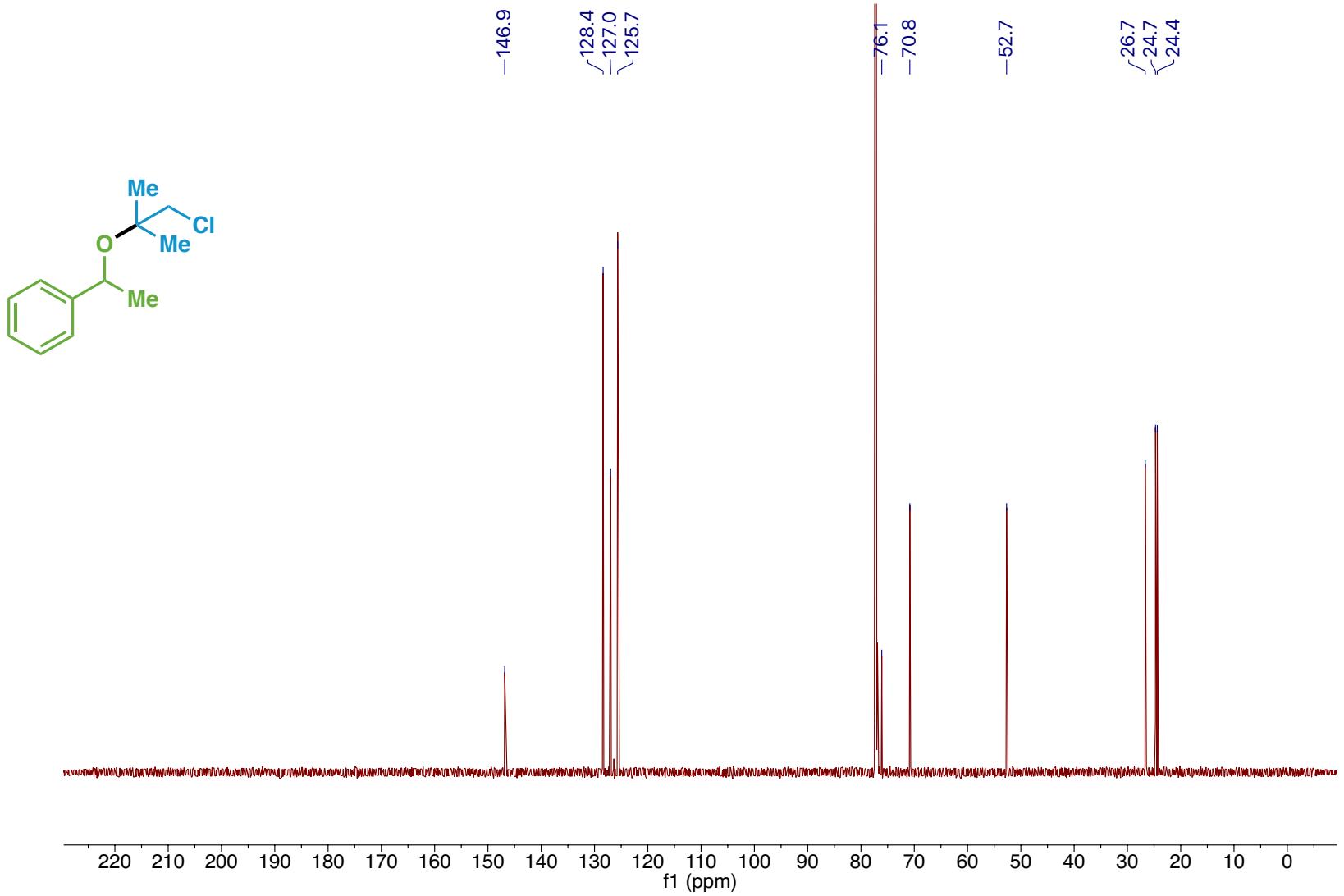
Compound 24 ^{13}C NMR



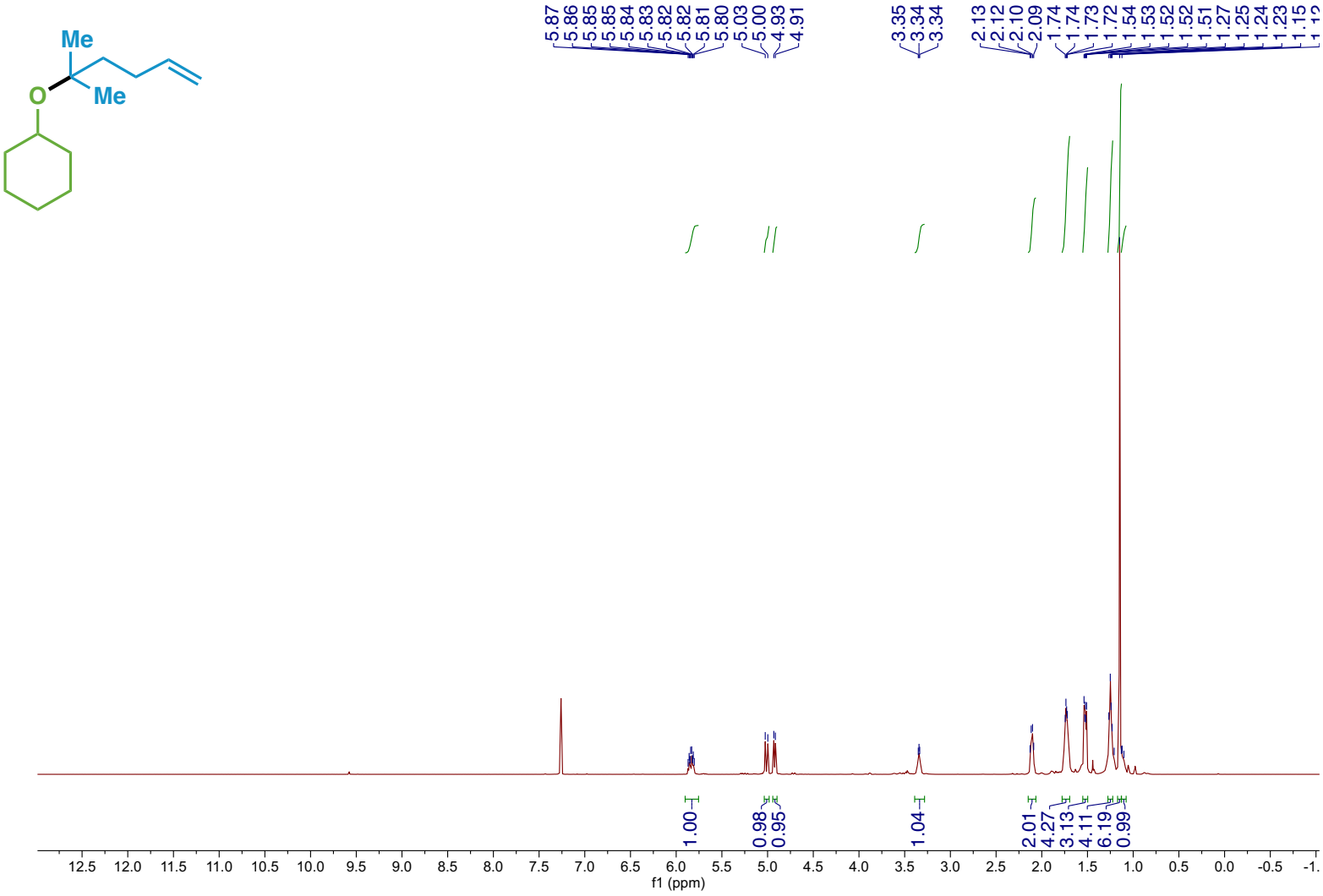
Compound 25 ^{1}H NMR



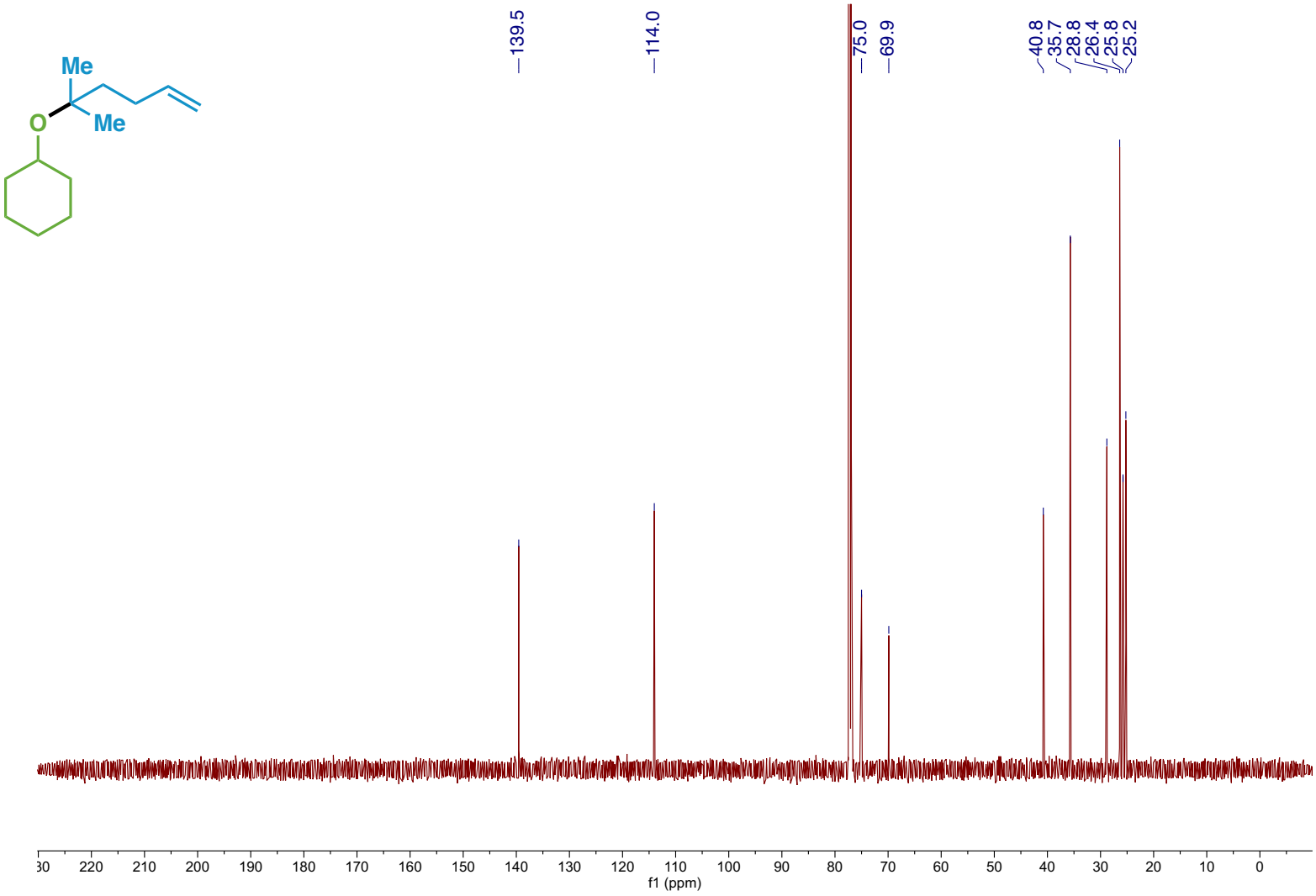
Compound 25 ^{13}C NMR



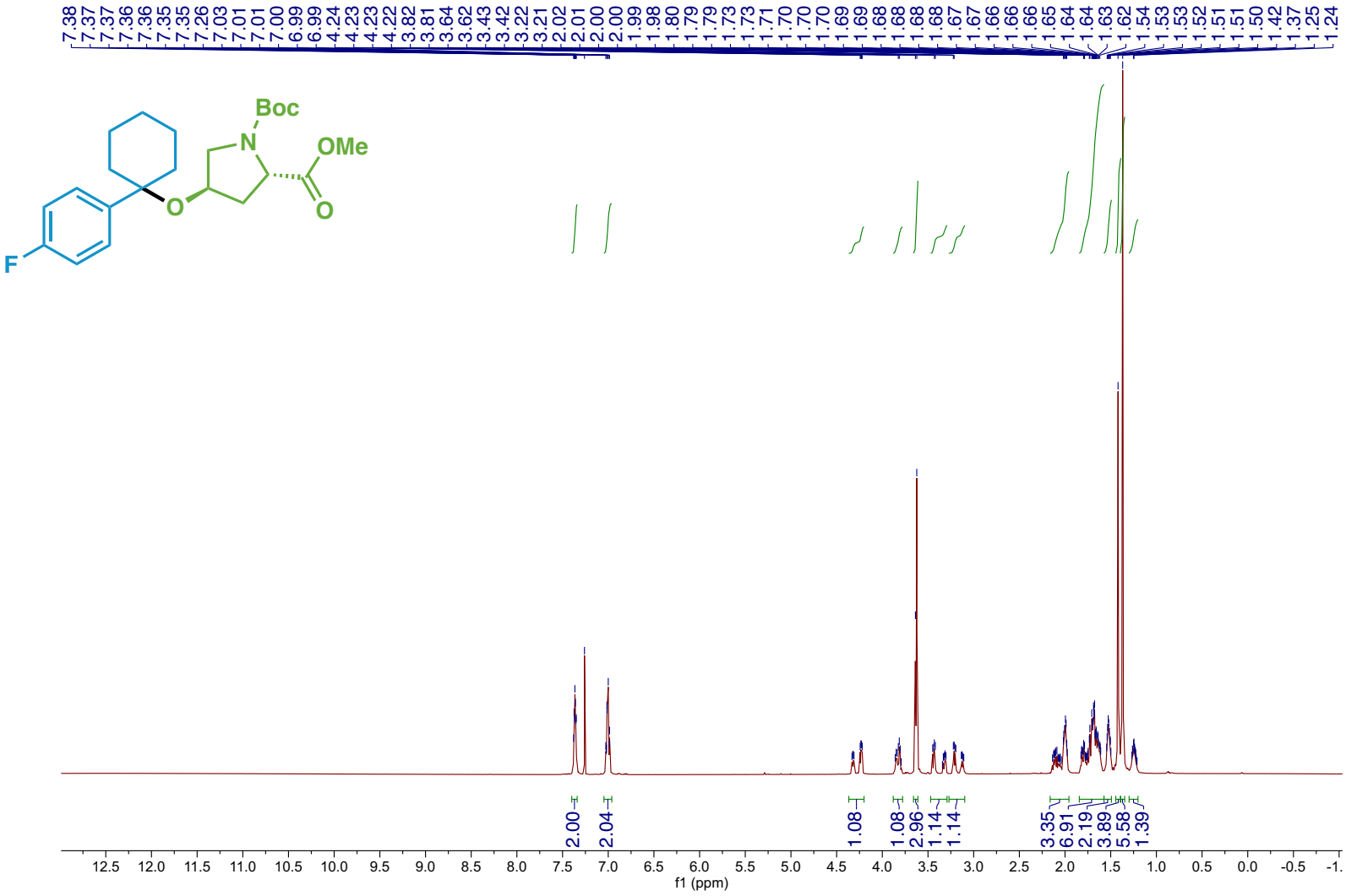
Compound 26 ^{1}H NMR



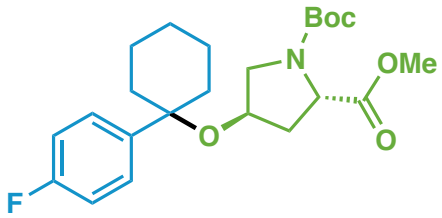
Compound 26 ^{13}C NMR



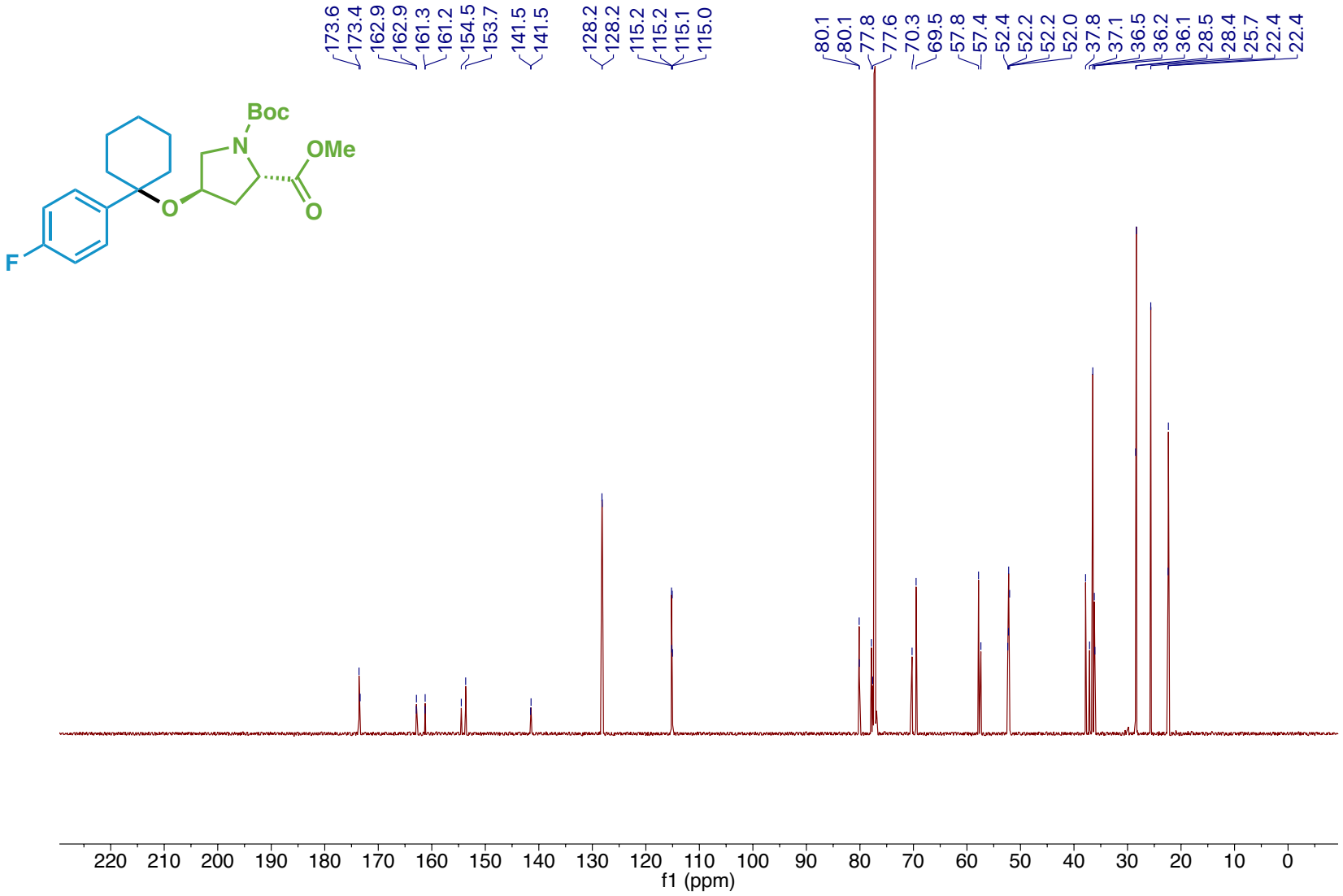
Compound 27 ^{1}H NMR



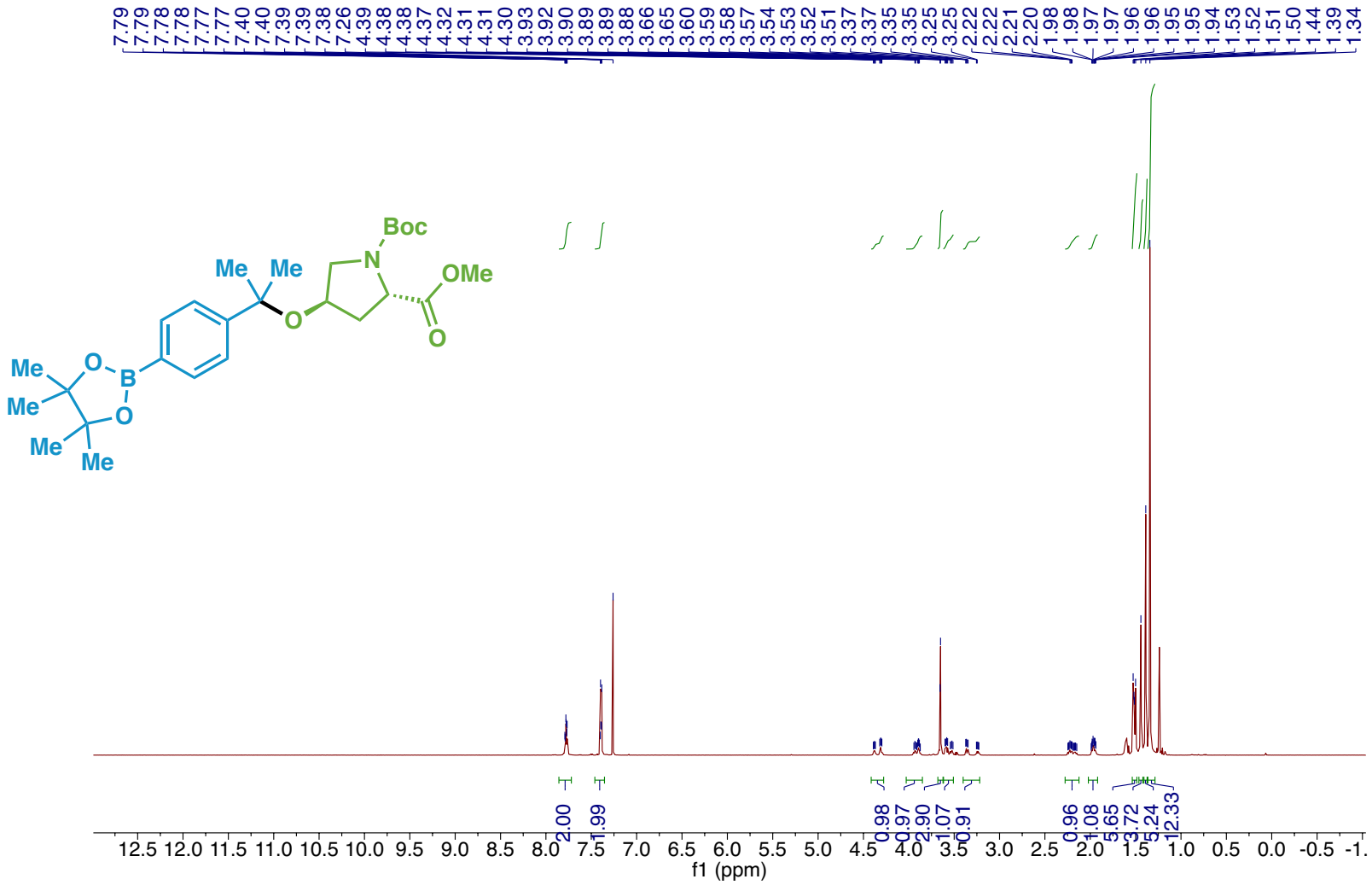
Compound 27 ^{19}F NMR



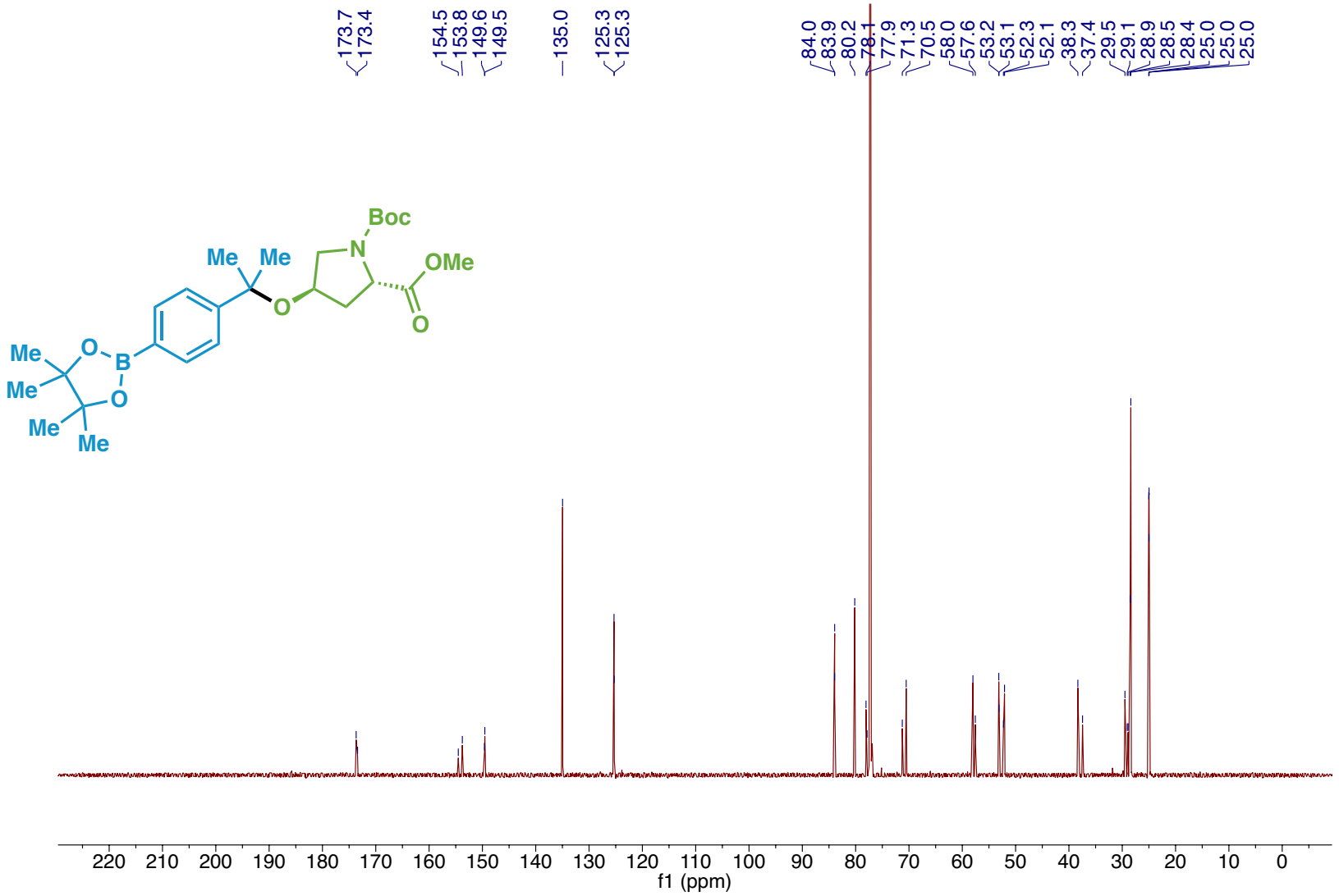
Compound 27 ^{13}C NMR



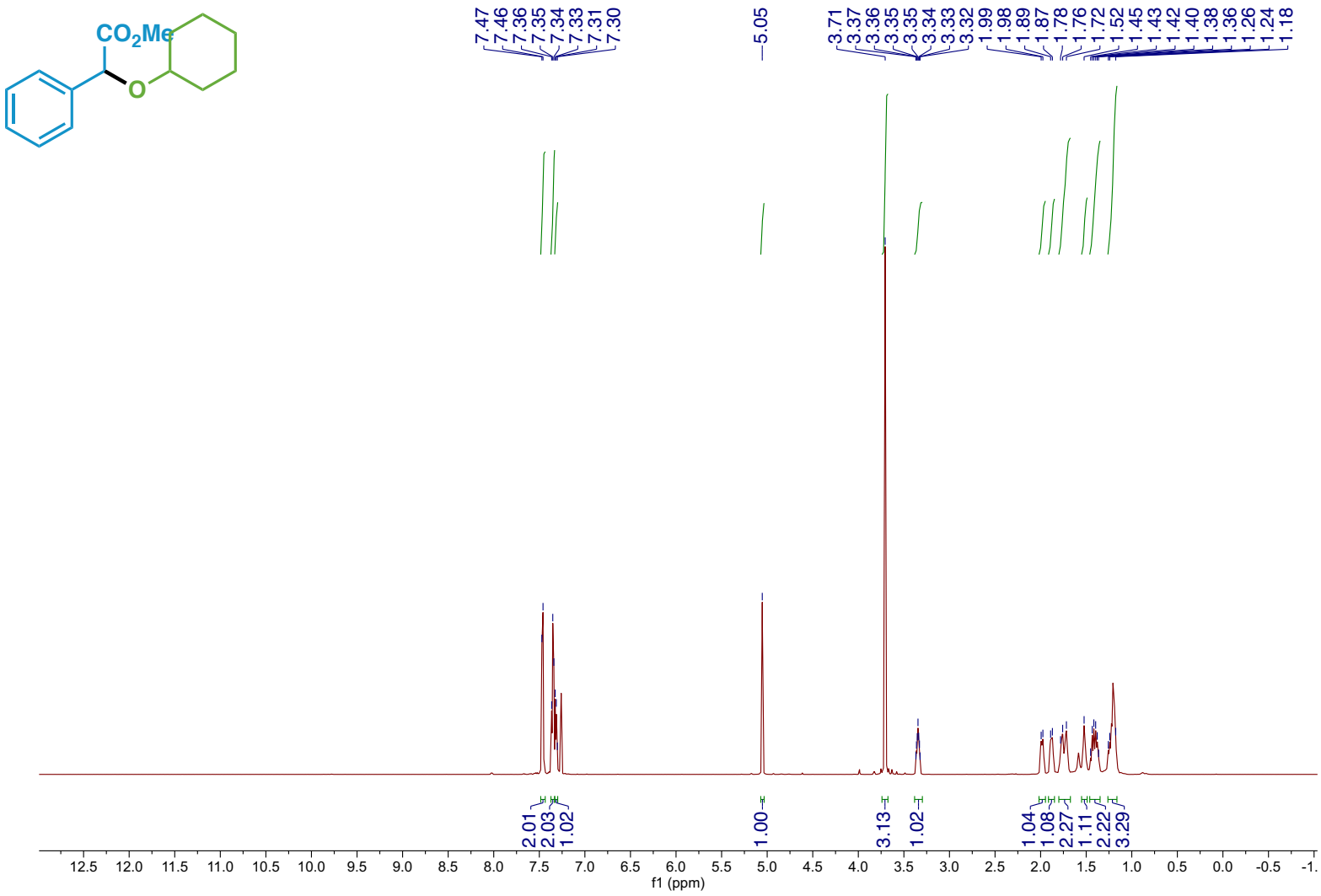
Compound 28 ^{1}H NMR



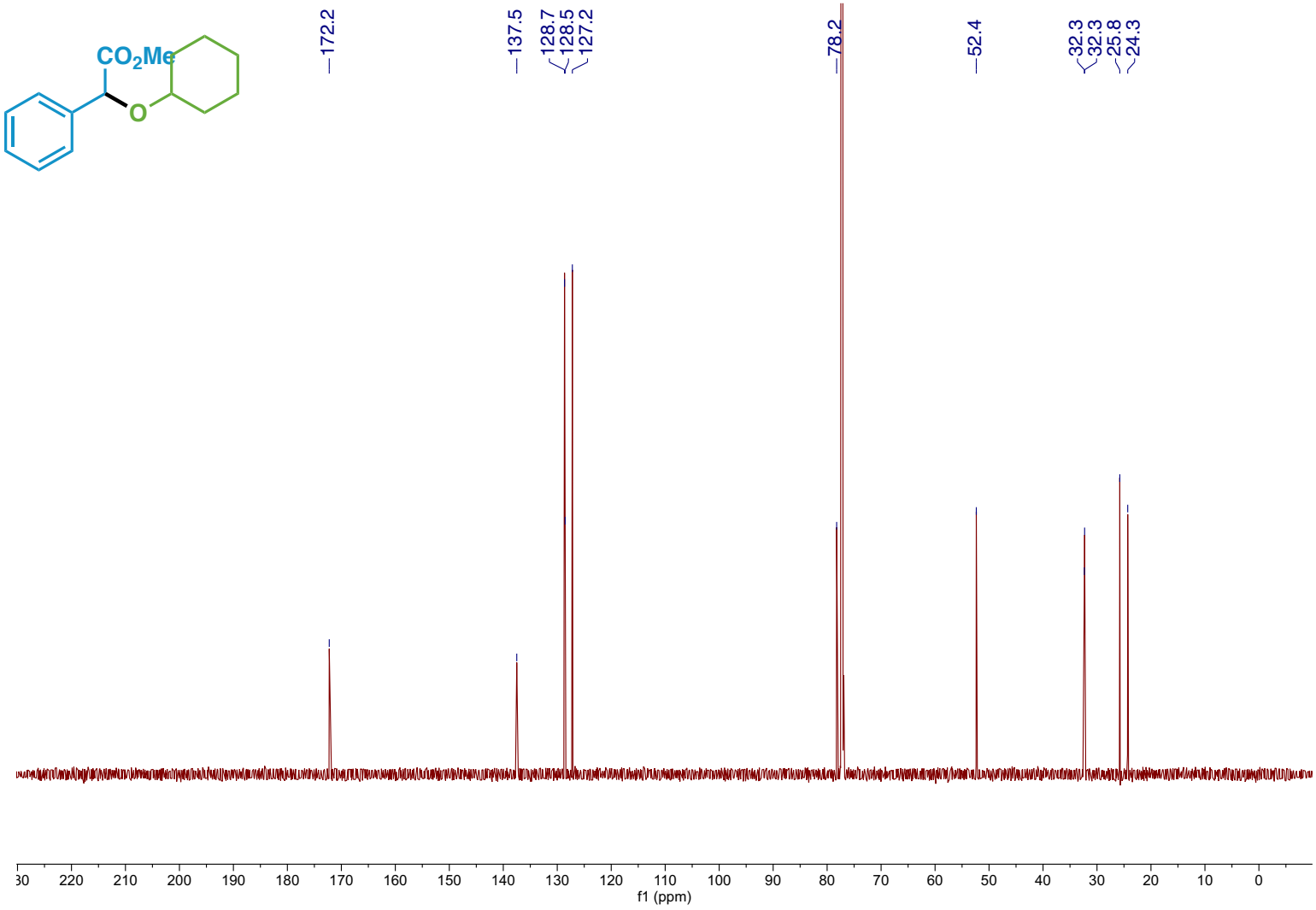
Compound 28 ^{13}C NMR



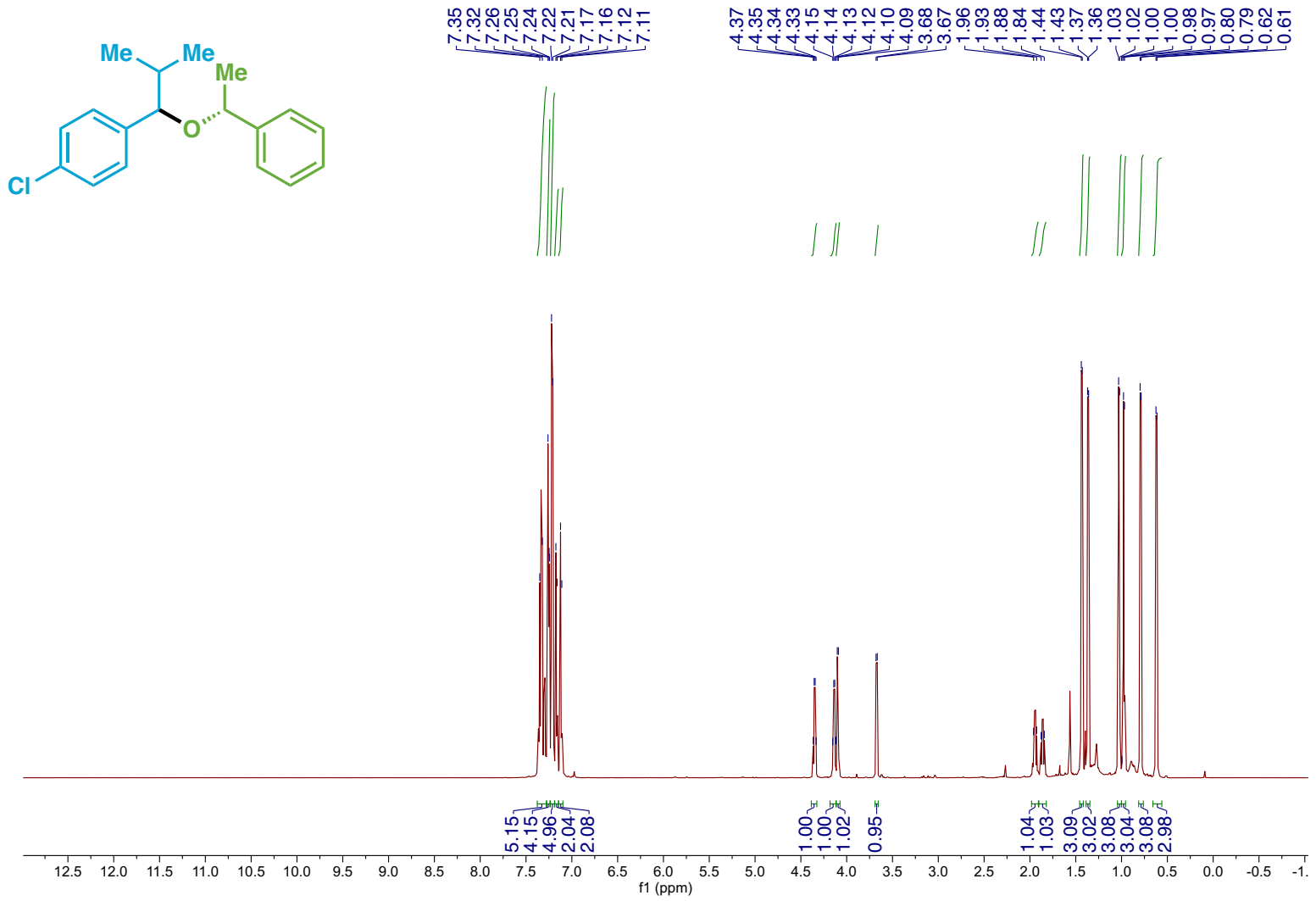
Compound 29 ^{1}H NMR



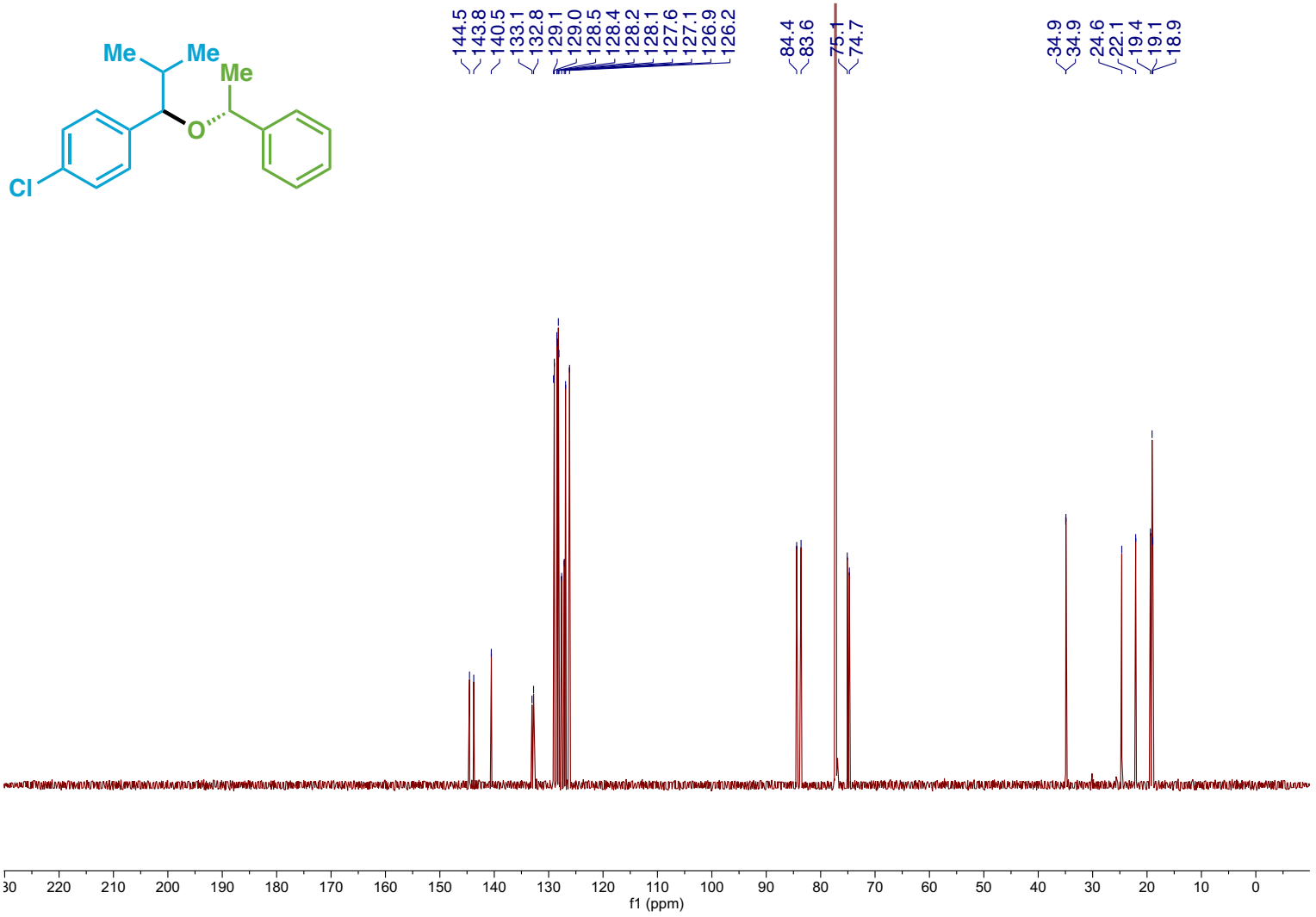
Compound 29 ^{13}C NMR



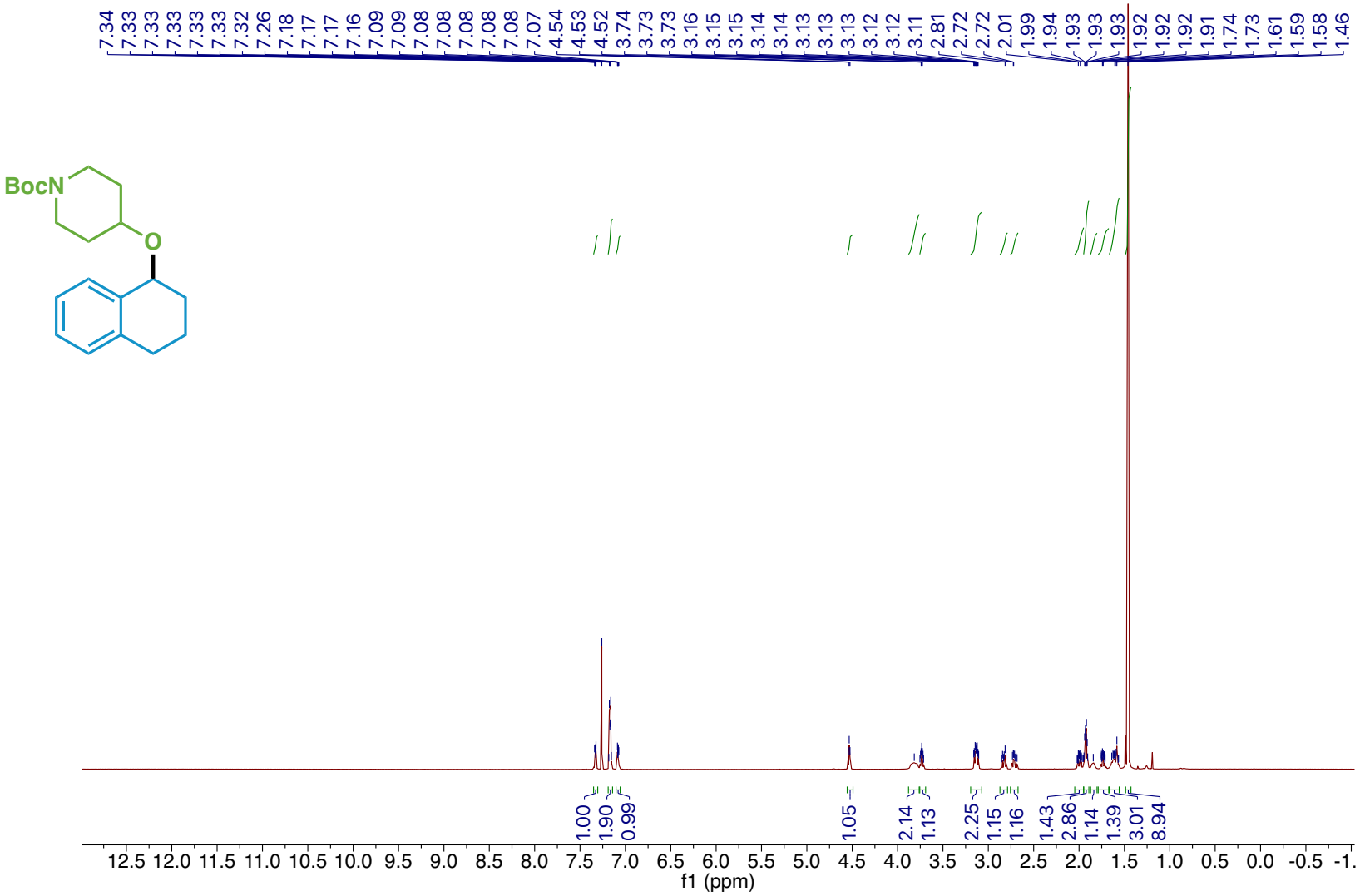
Compound 30 ^{1}H NMR



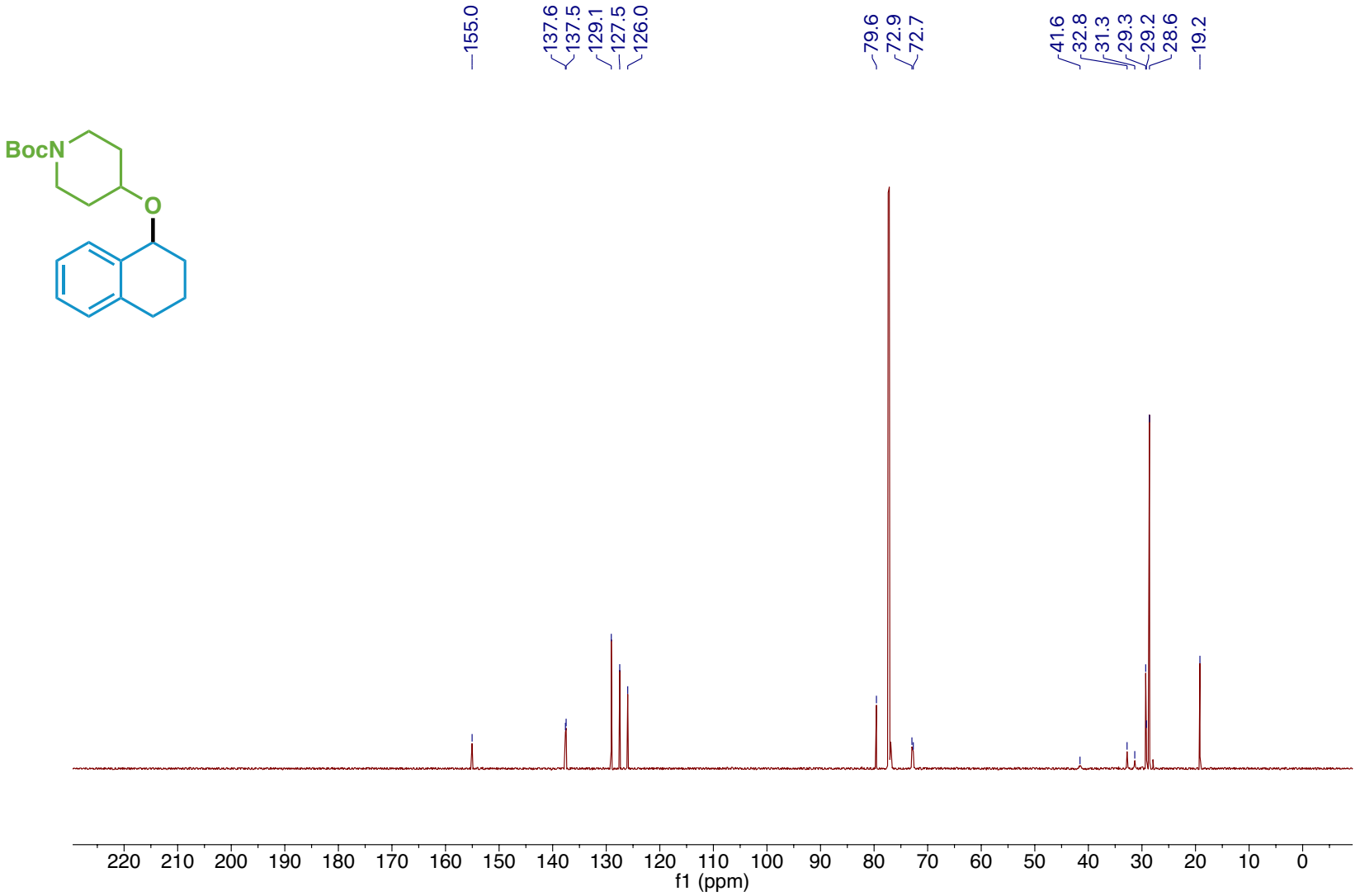
Compound 30 ^{13}C NMR



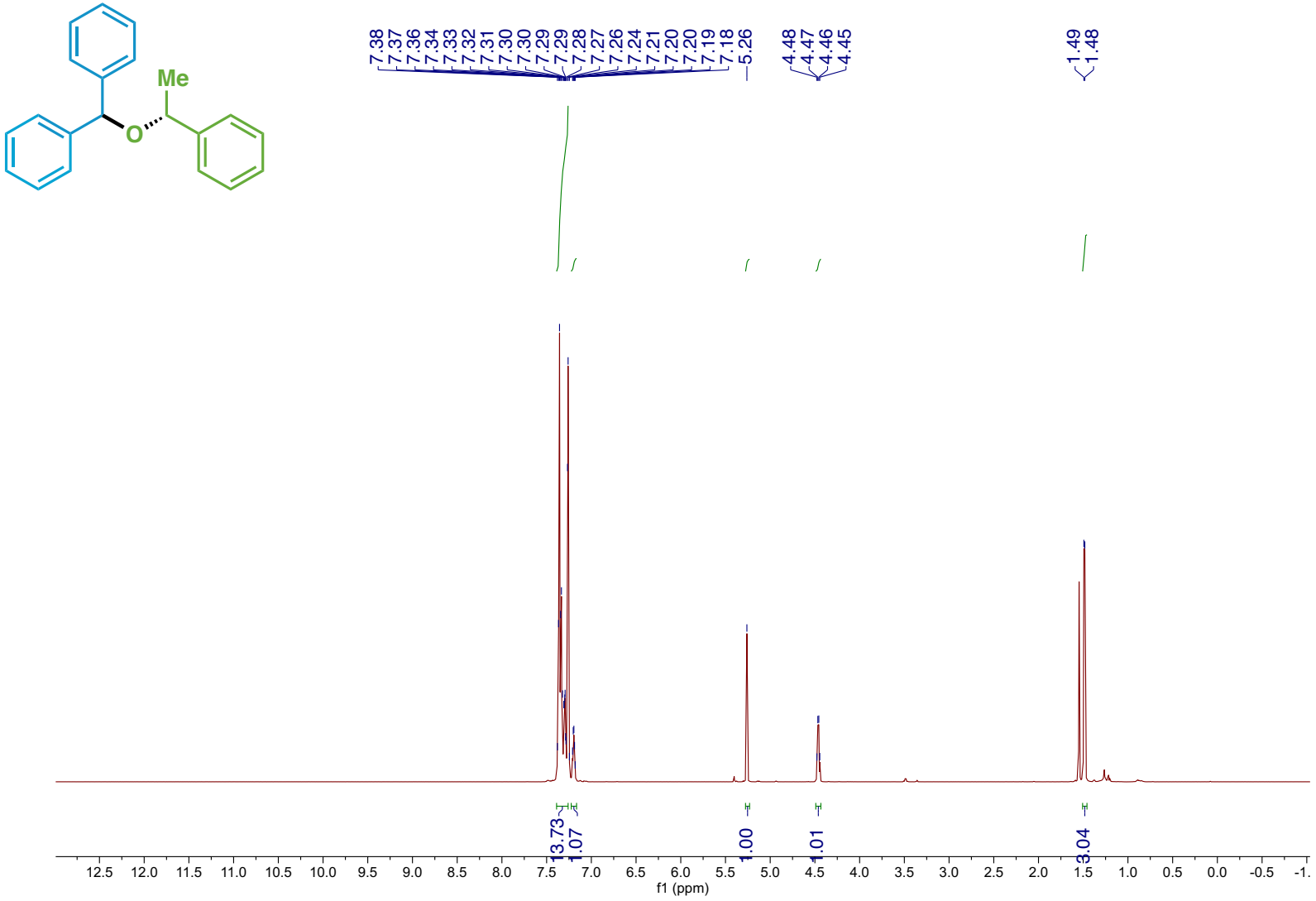
Compound 31 ^{1}H NMR



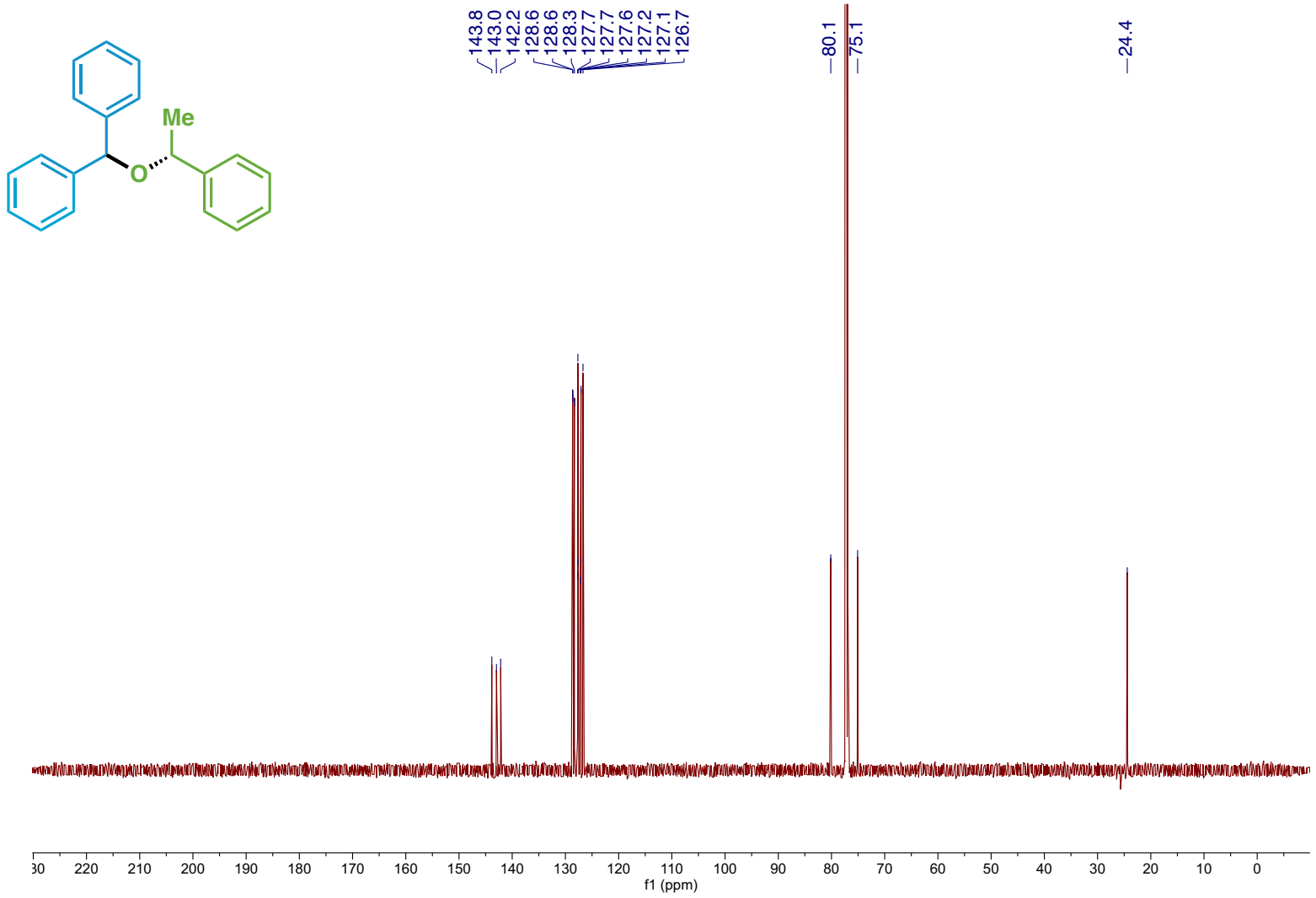
Compound 31 ^{13}C NMR



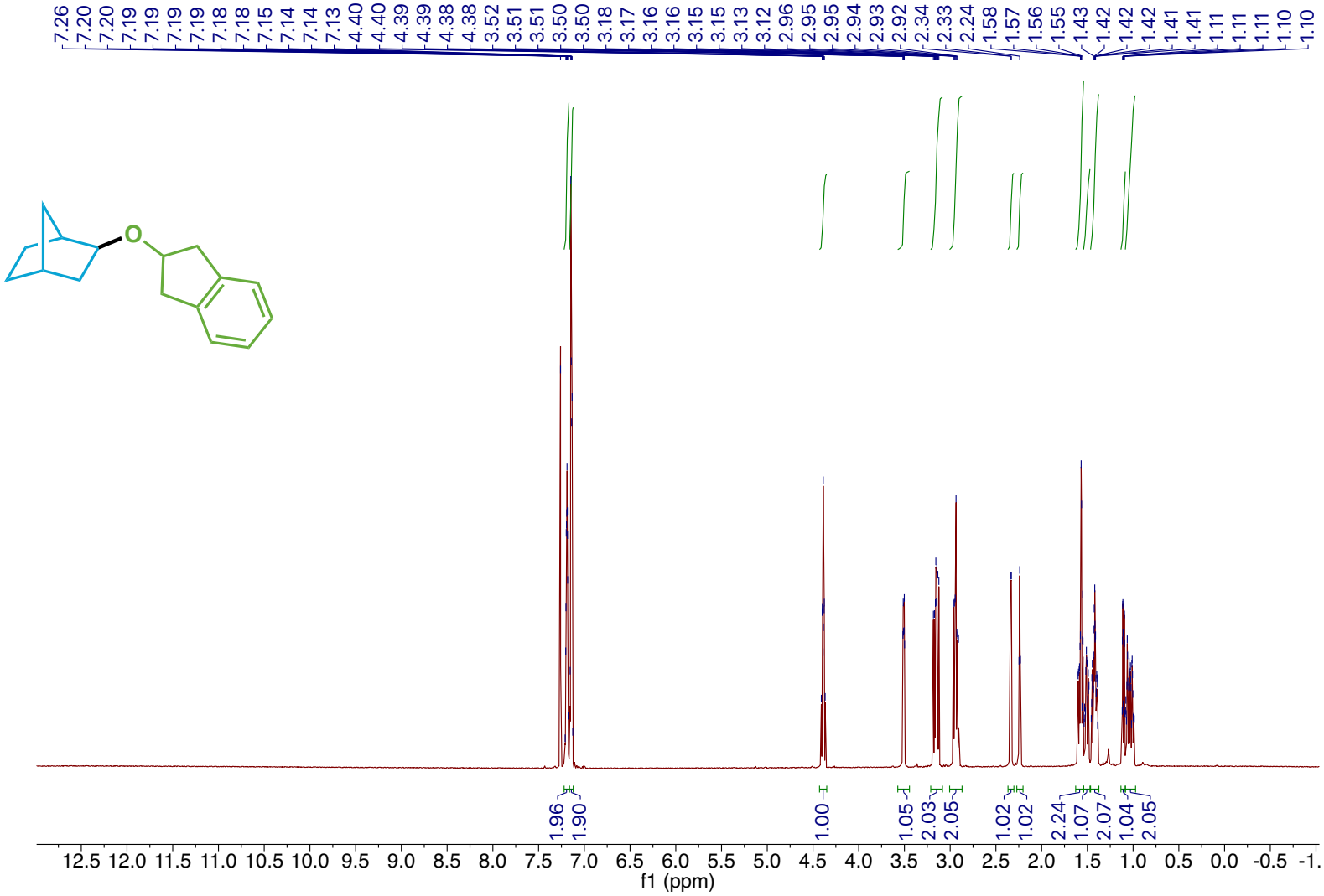
Compound 32 ^{1}H NMR



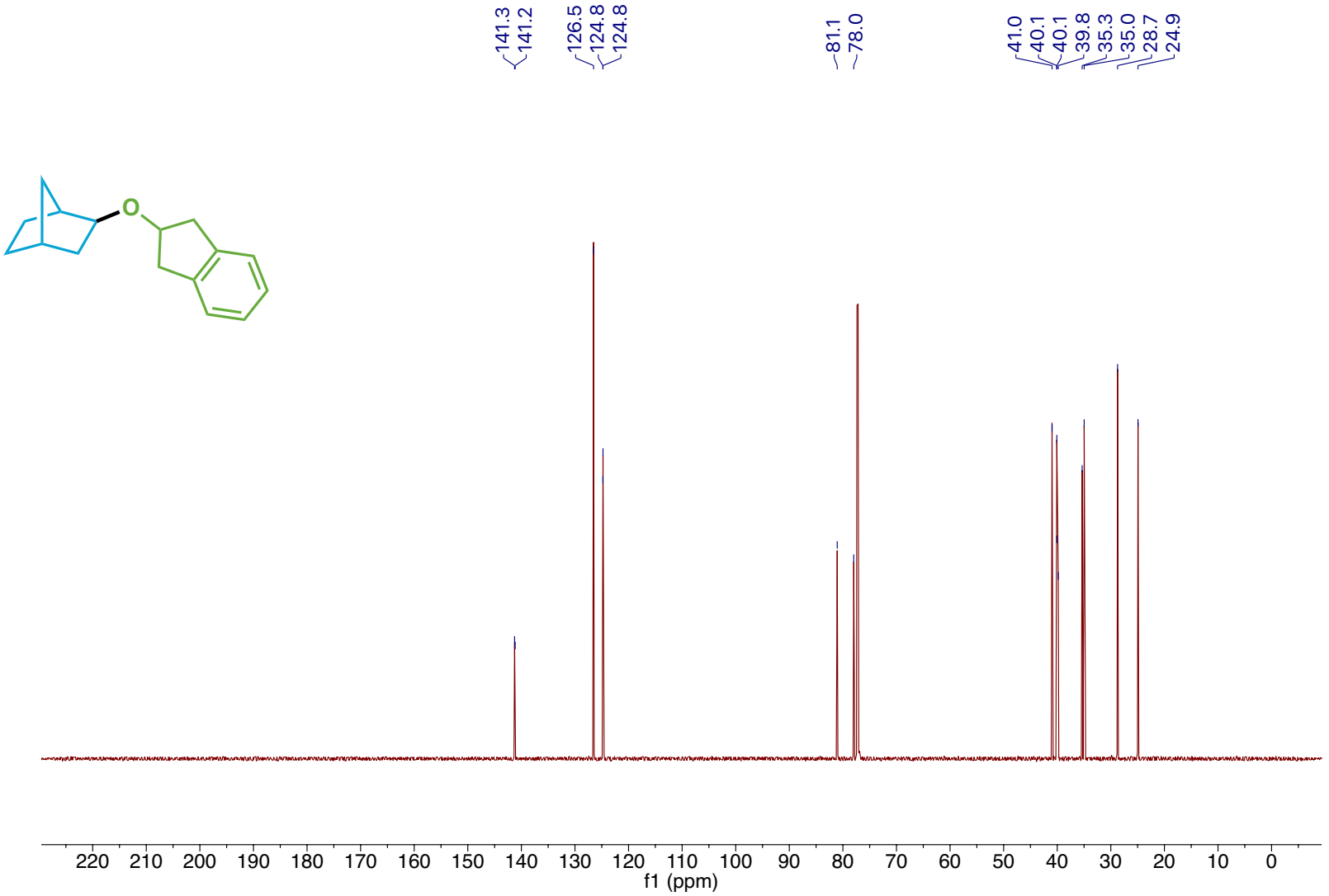
Compound 32 ^{13}C NMR



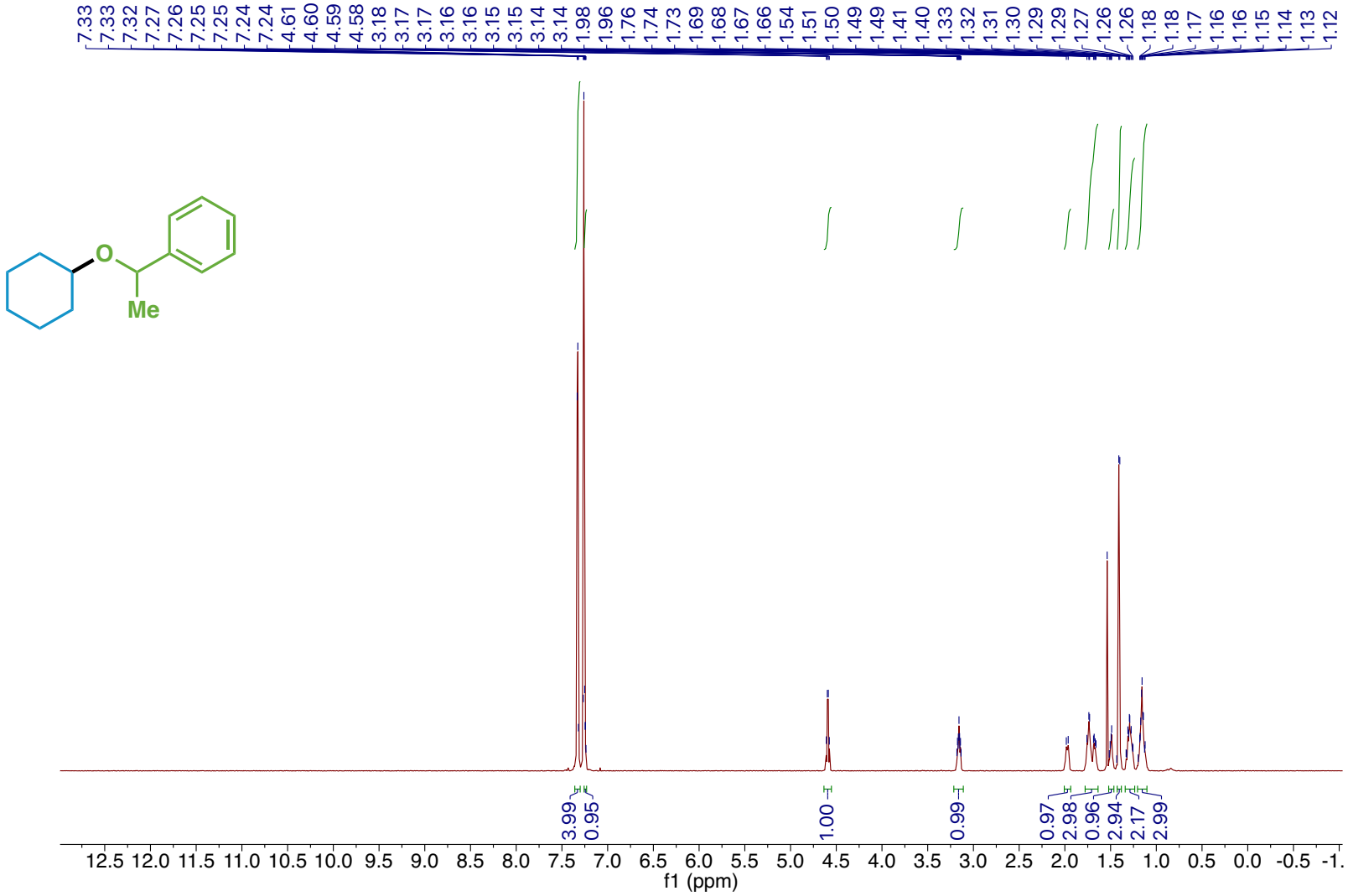
Compound 33 ^{1}H NMR



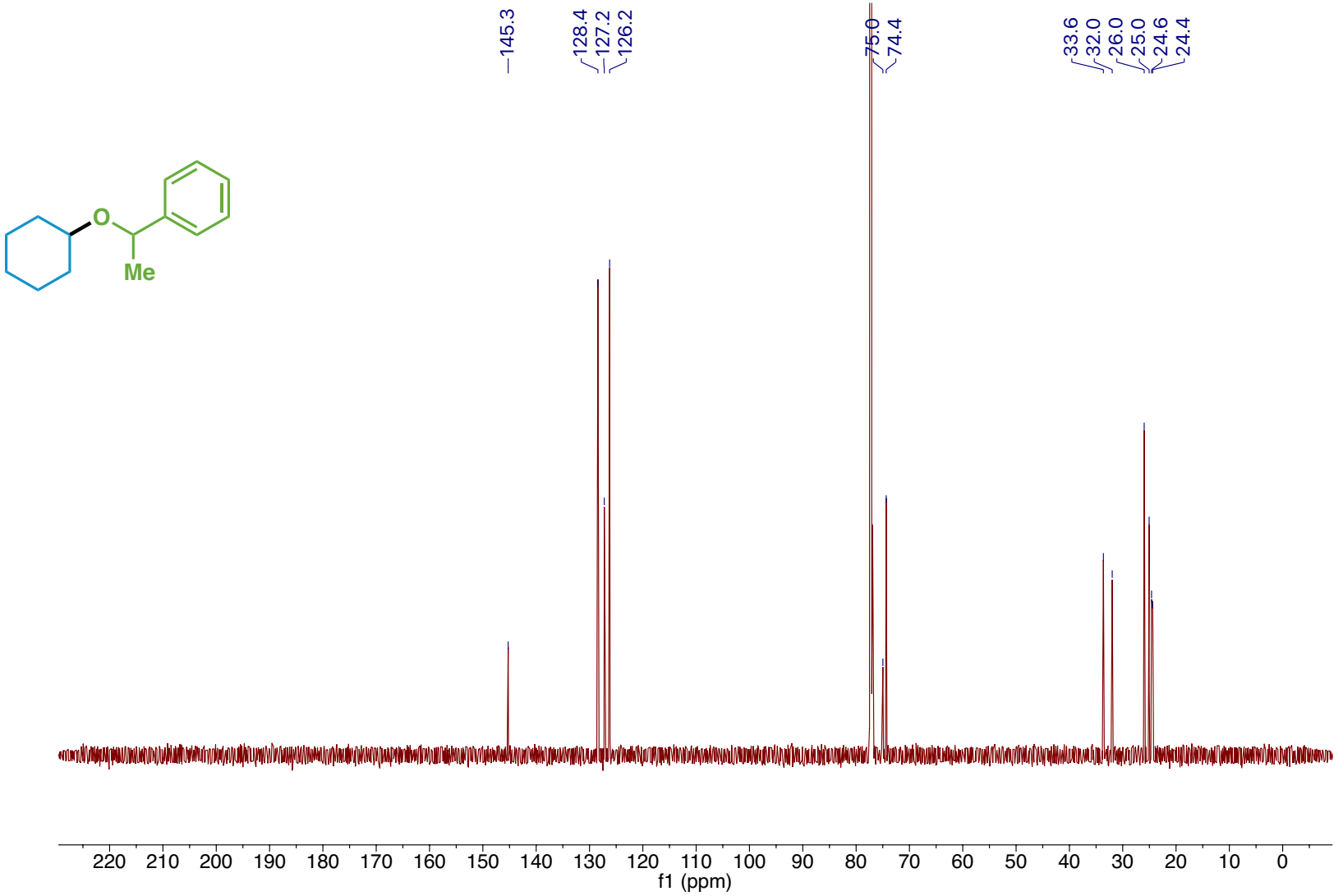
Compound 33 ^{13}C NMR



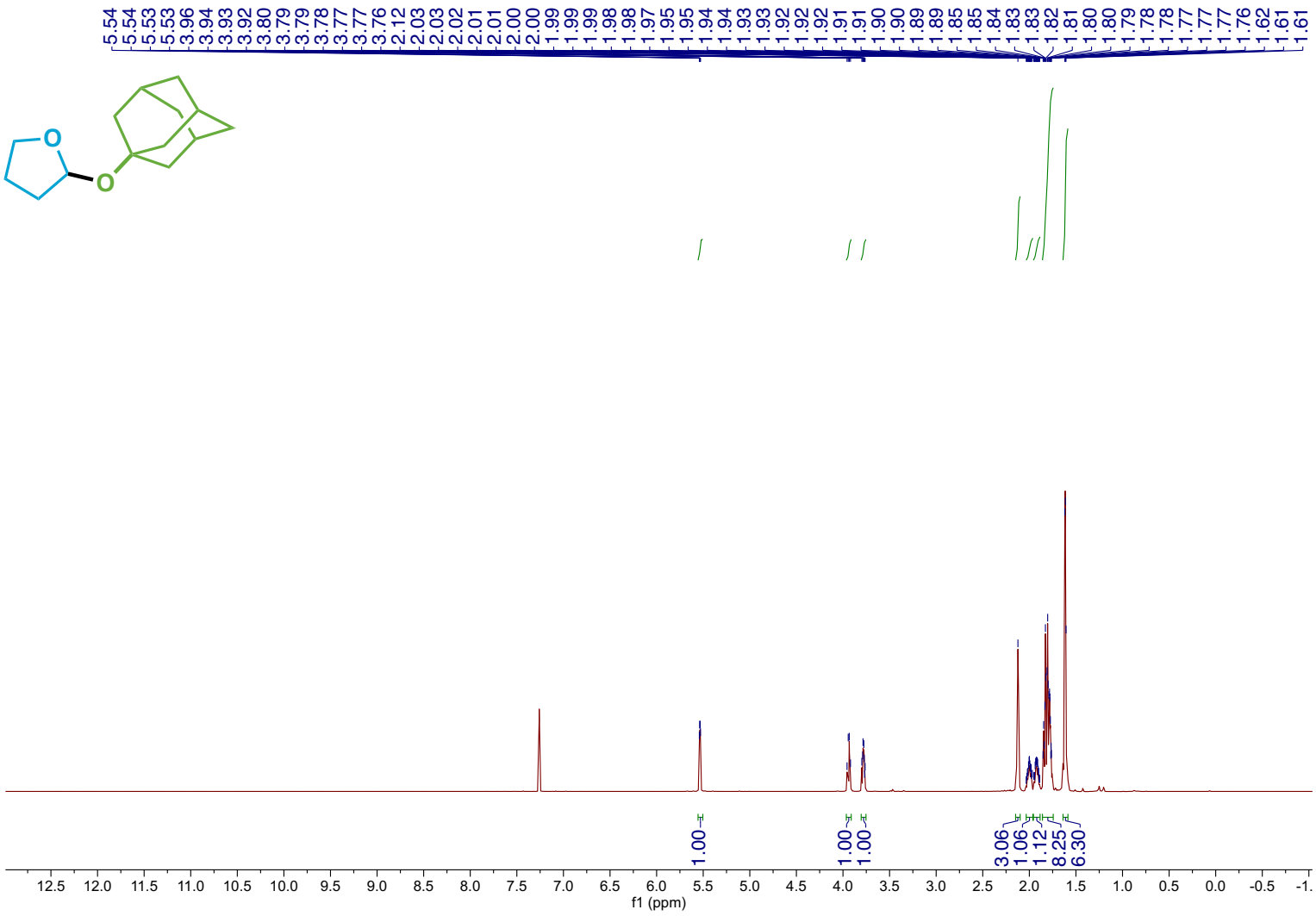
Compound 34 ^{1}H NMR



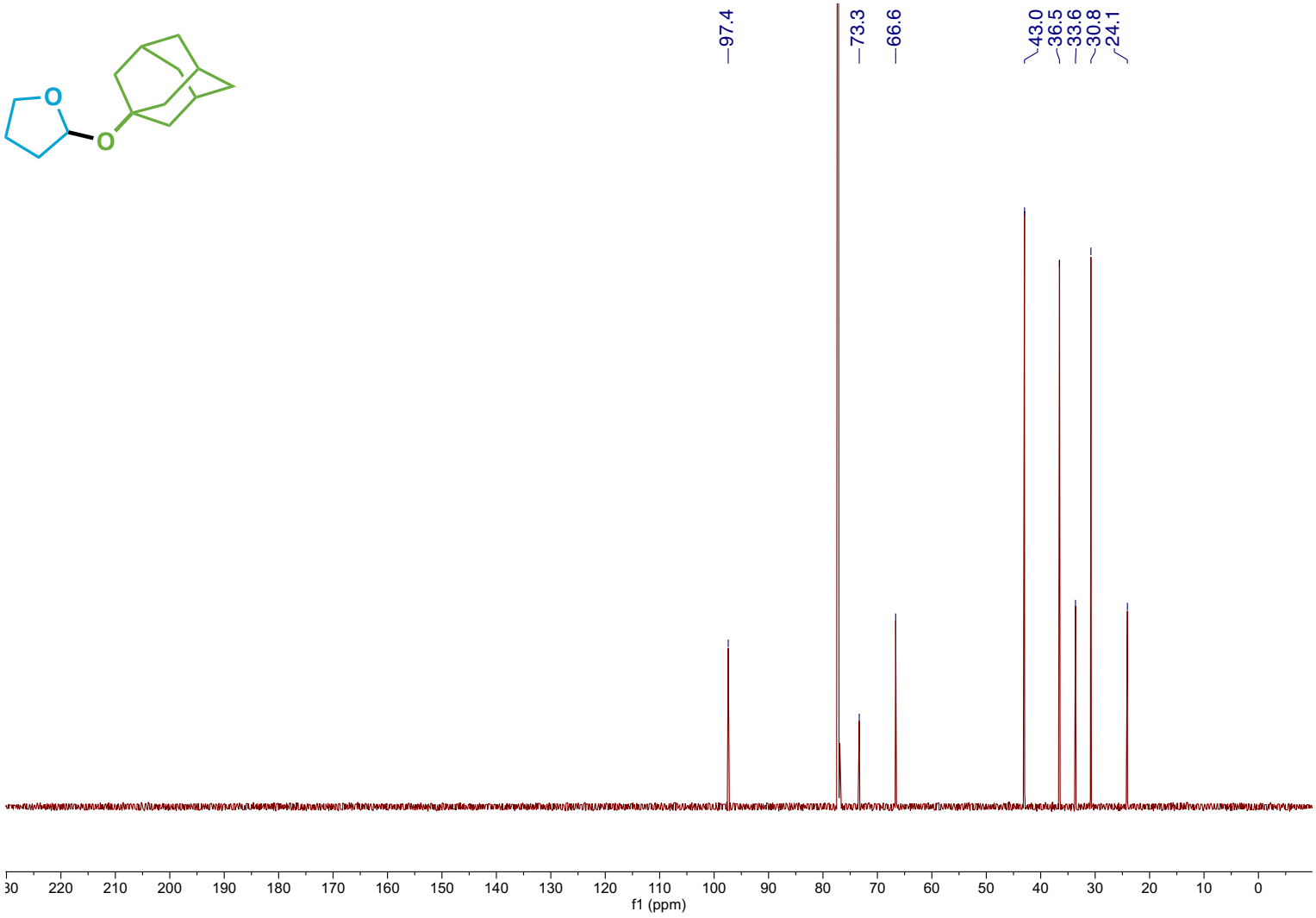
Compound 34 ^{13}C NMR



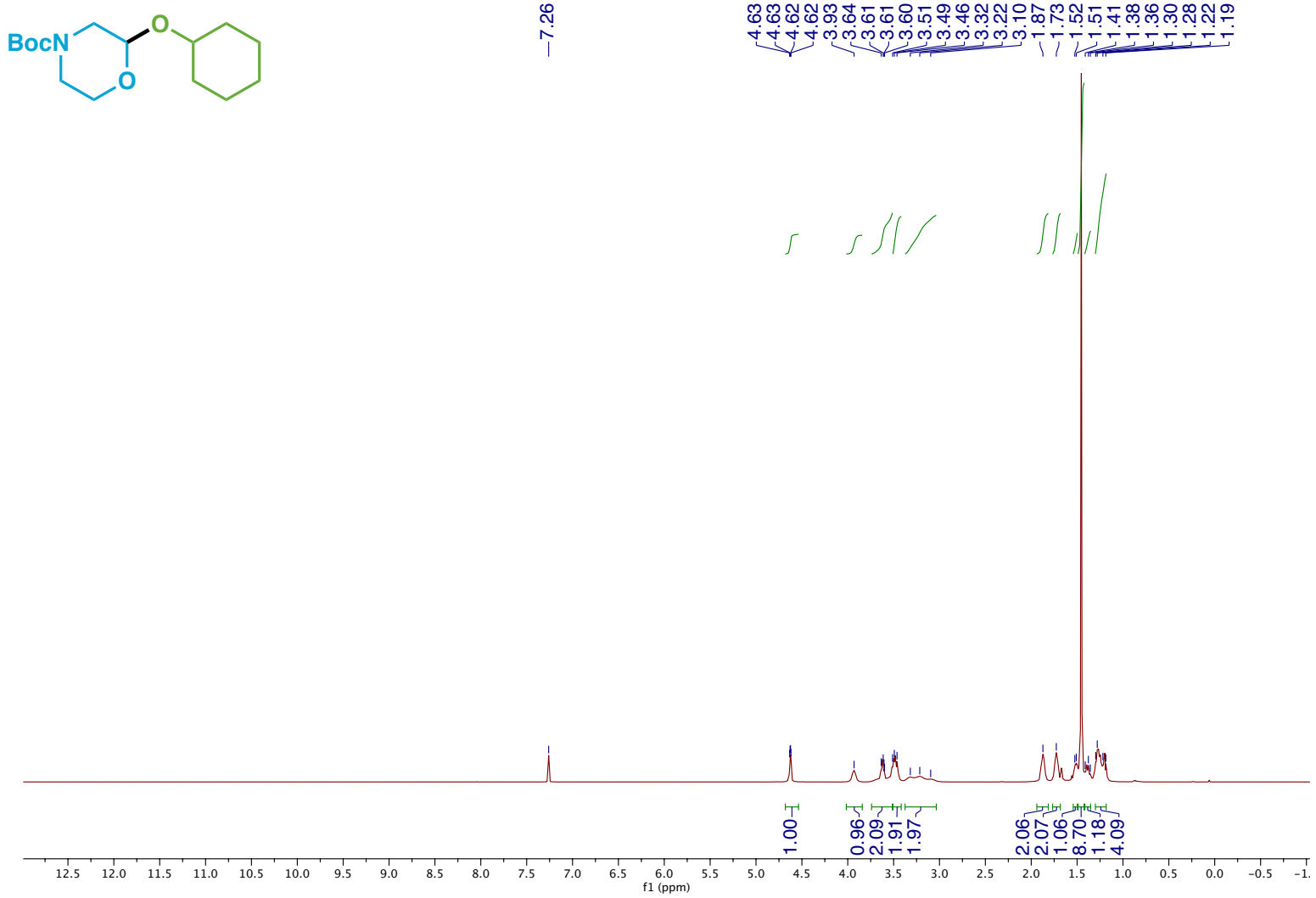
Compound 35 ^{1}H NMR



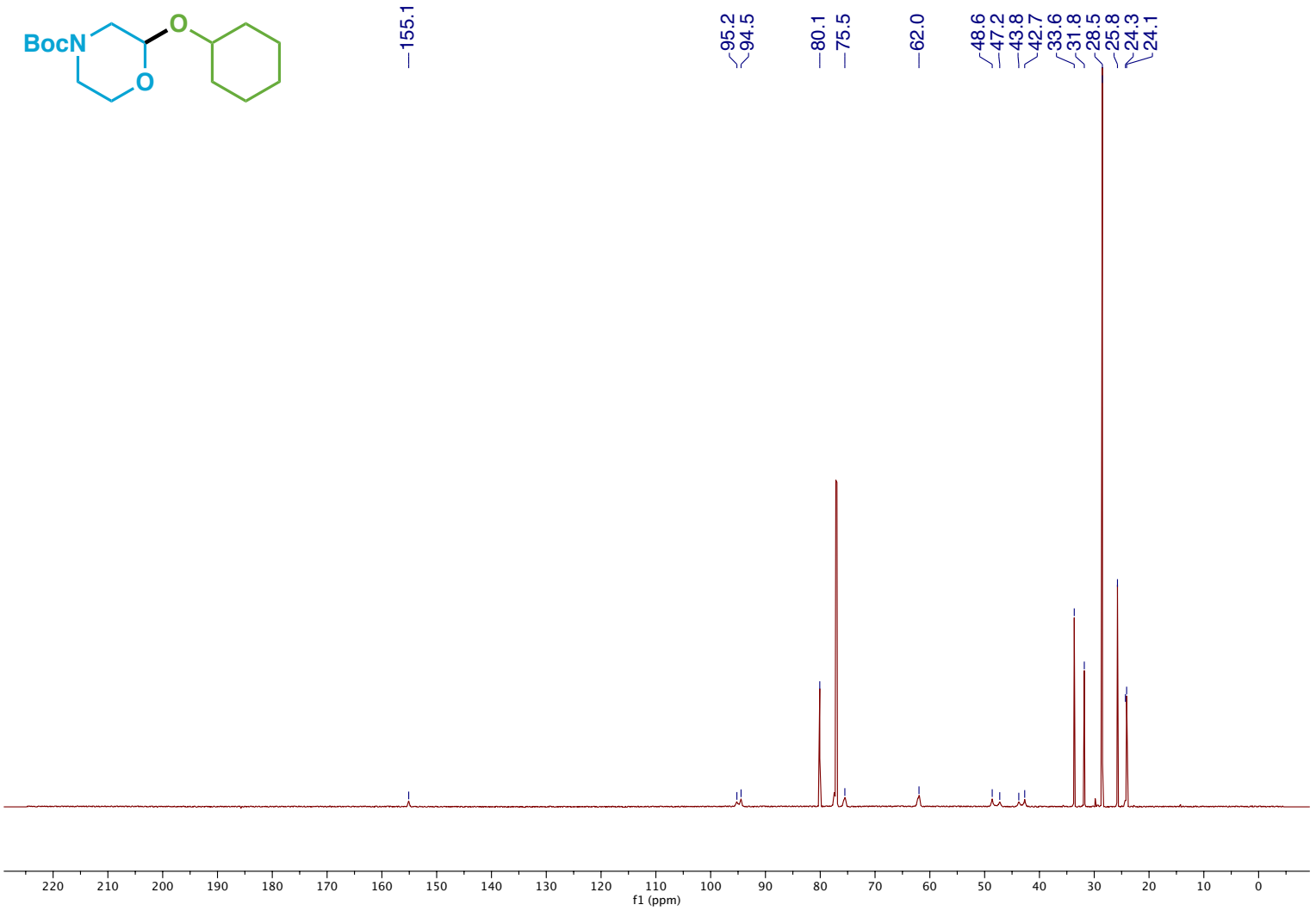
Compound 35 ^{13}C NMR



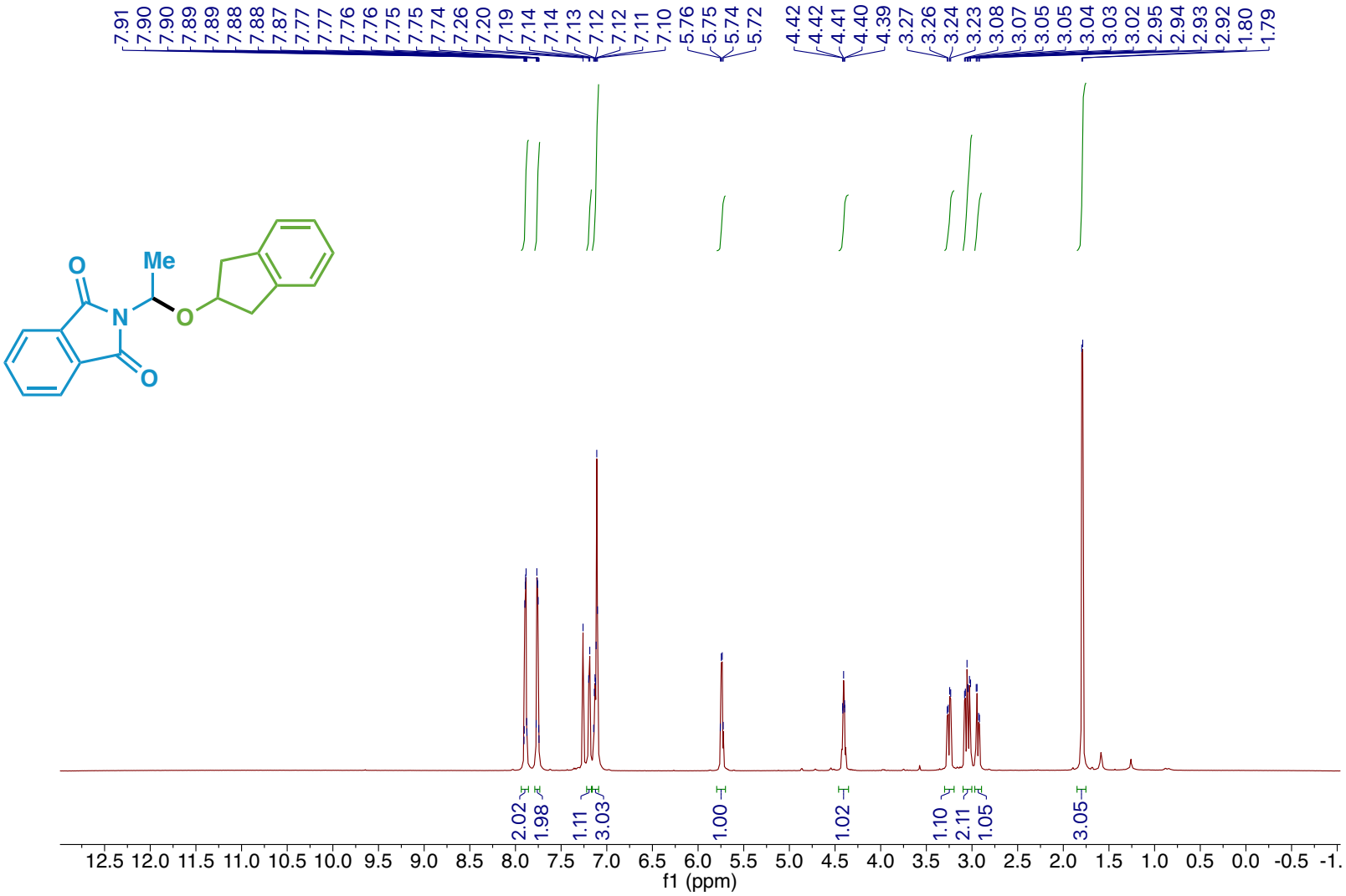
Compound 36 ^{1}H NMR



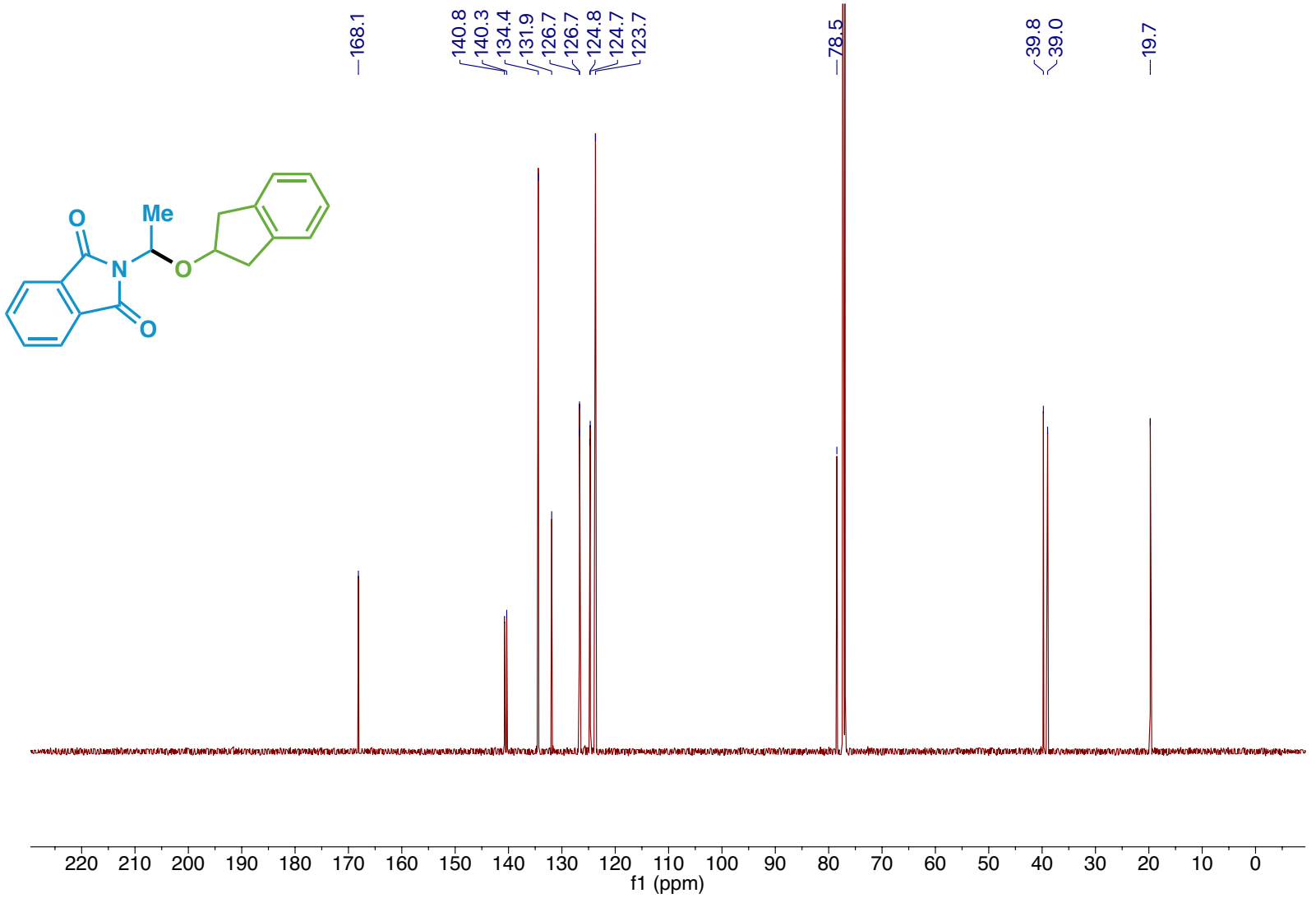
Compound 36 ^{13}C NMR



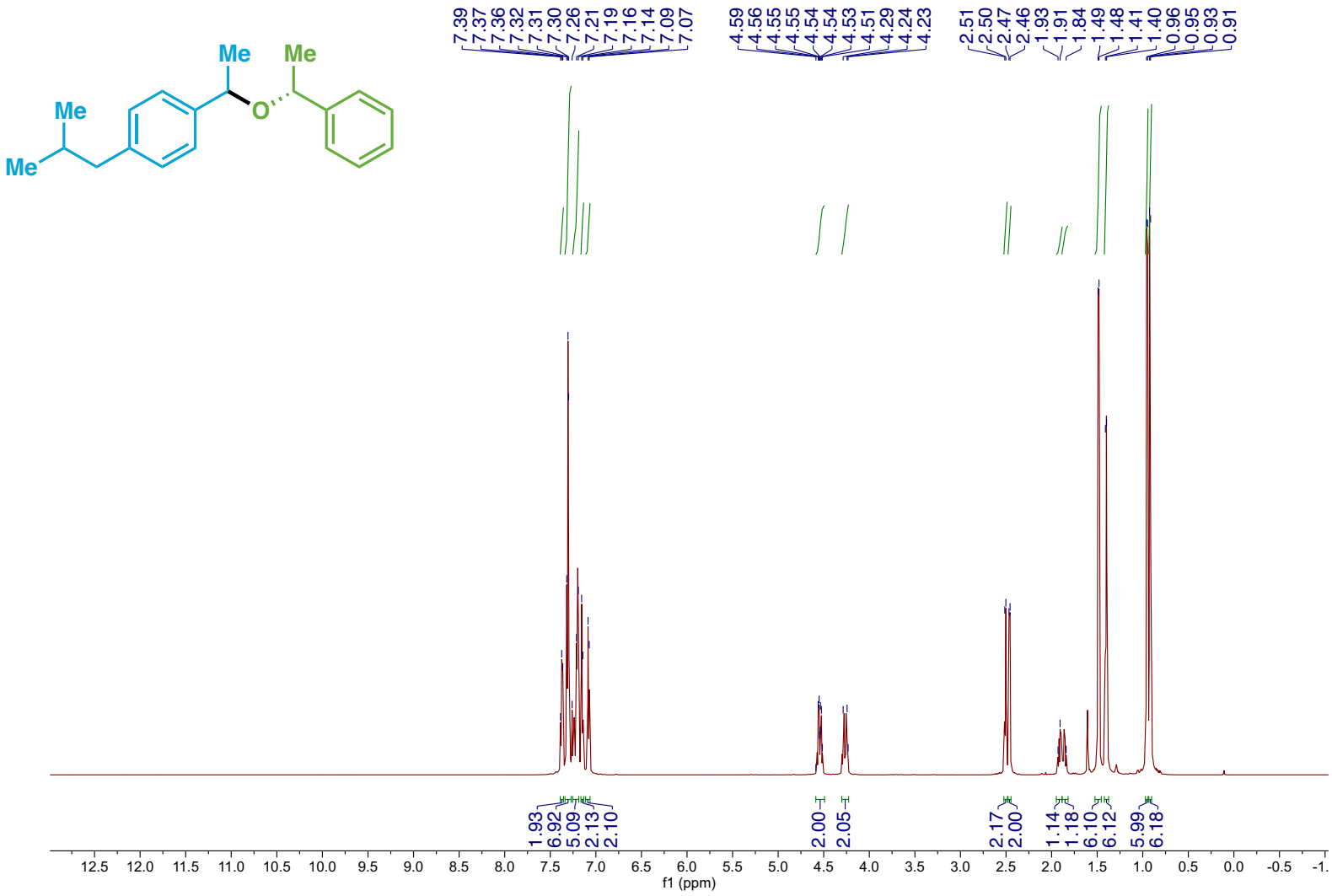
Compound 37 ^{1}H NMR



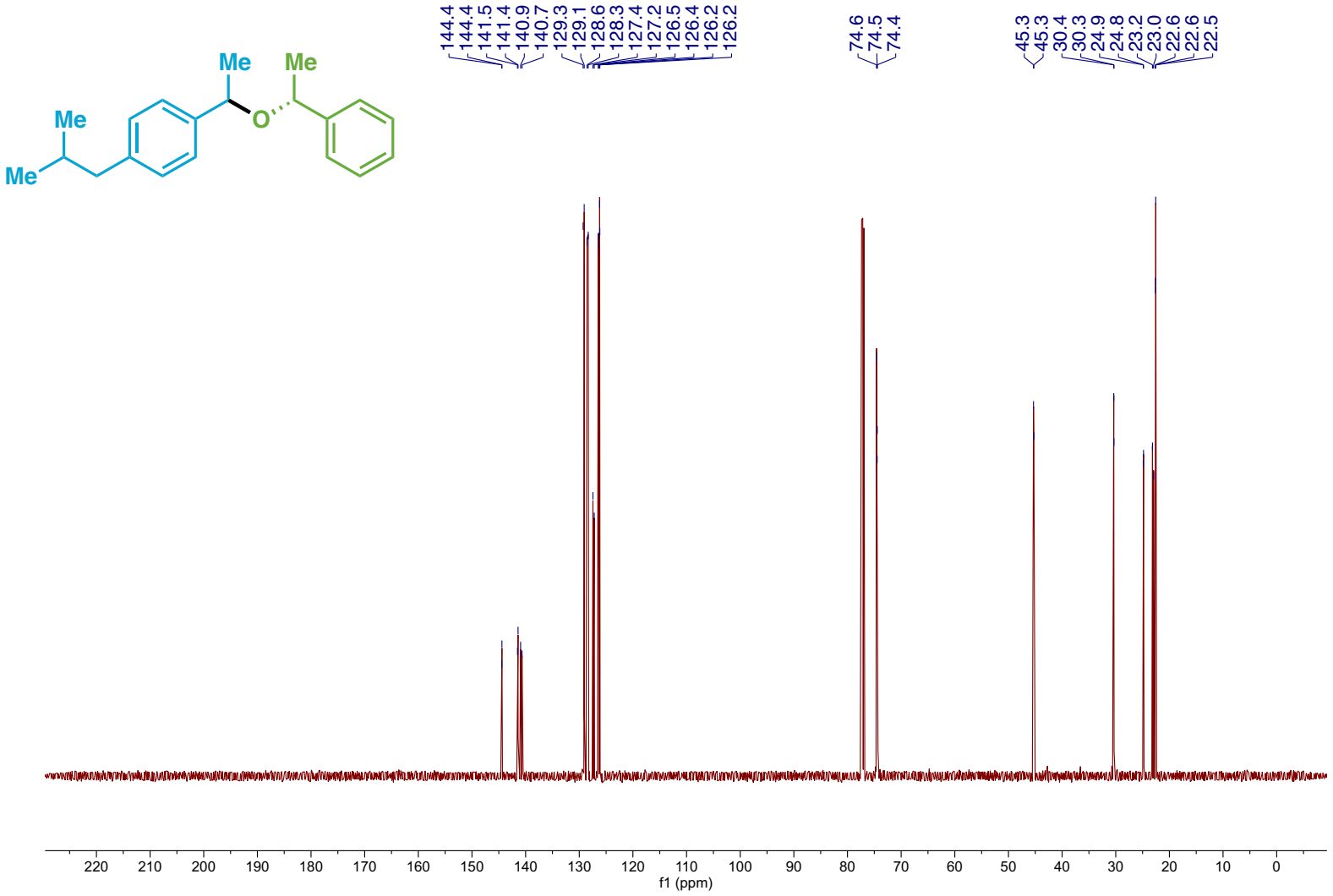
Compound 37 ^{13}C NMR



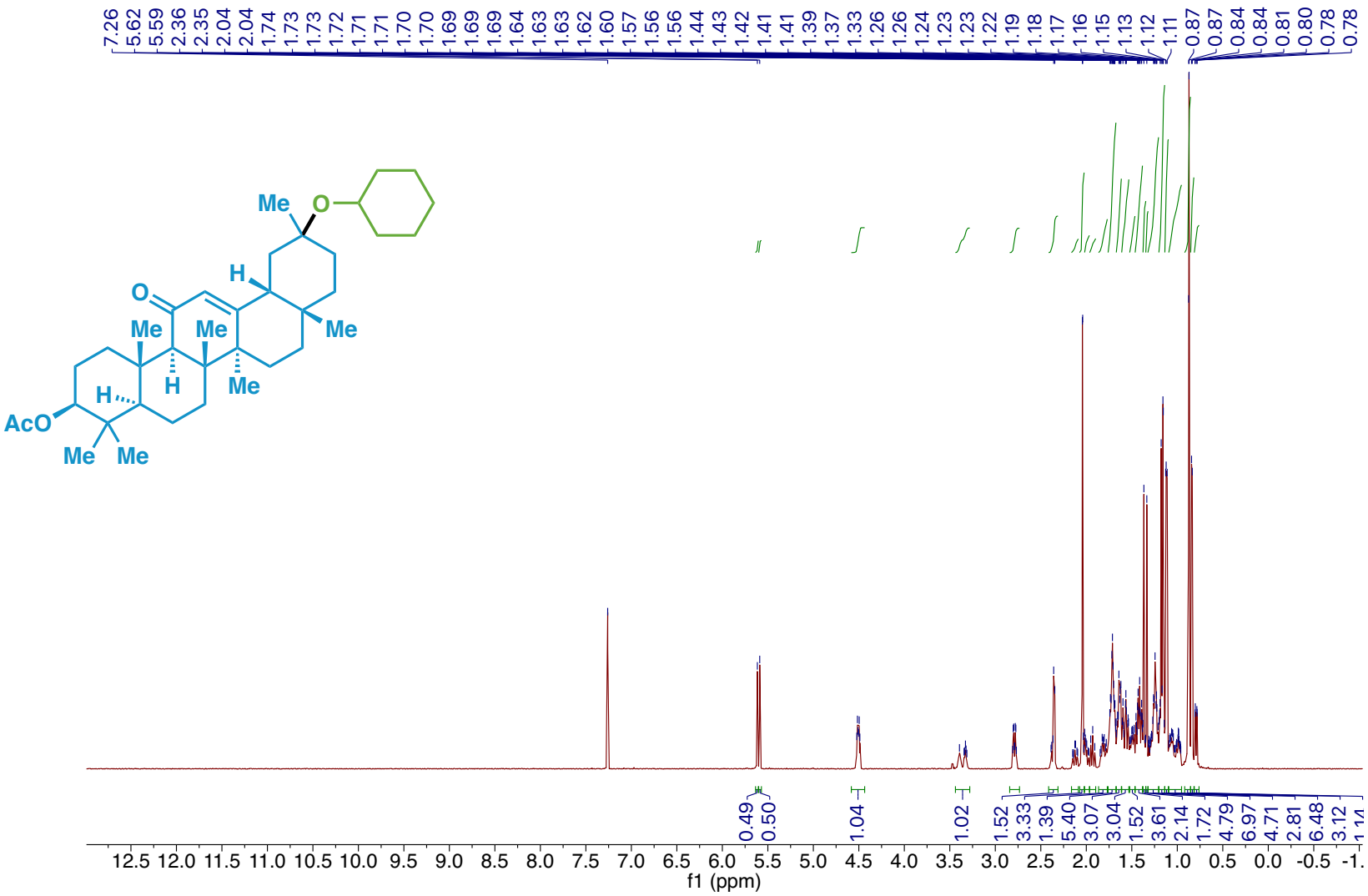
Compound 38 ^{1}H NMR



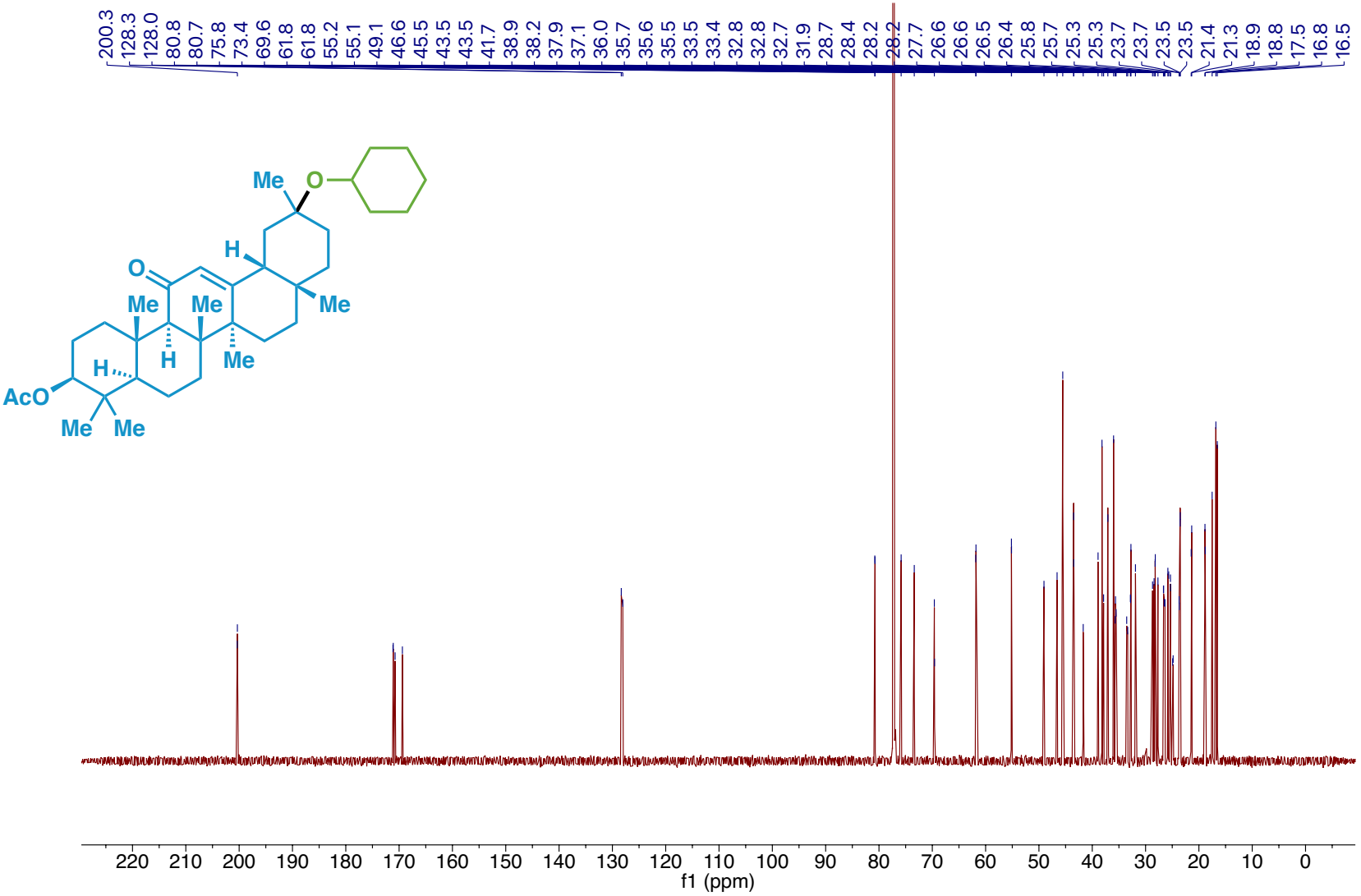
Compound 38 ^{13}C NMR



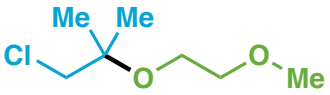
Compound 39 ^{1}H NMR



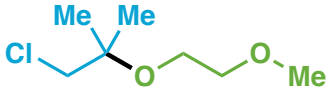
Compound 39 ^{13}C NMR



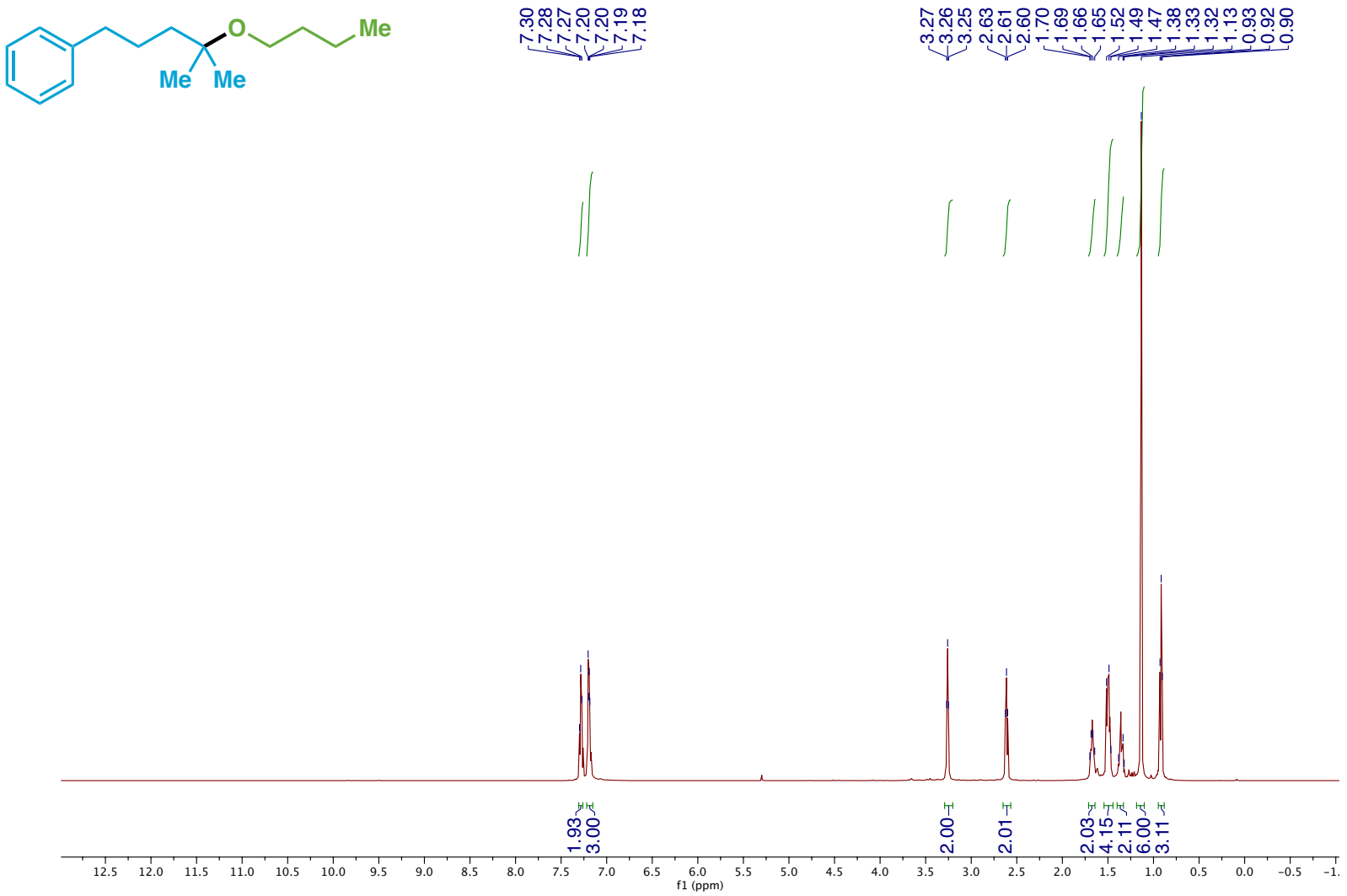
Compound 40 ^{1}H NMR



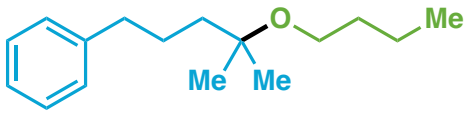
Compound 40 ^{13}C NMR



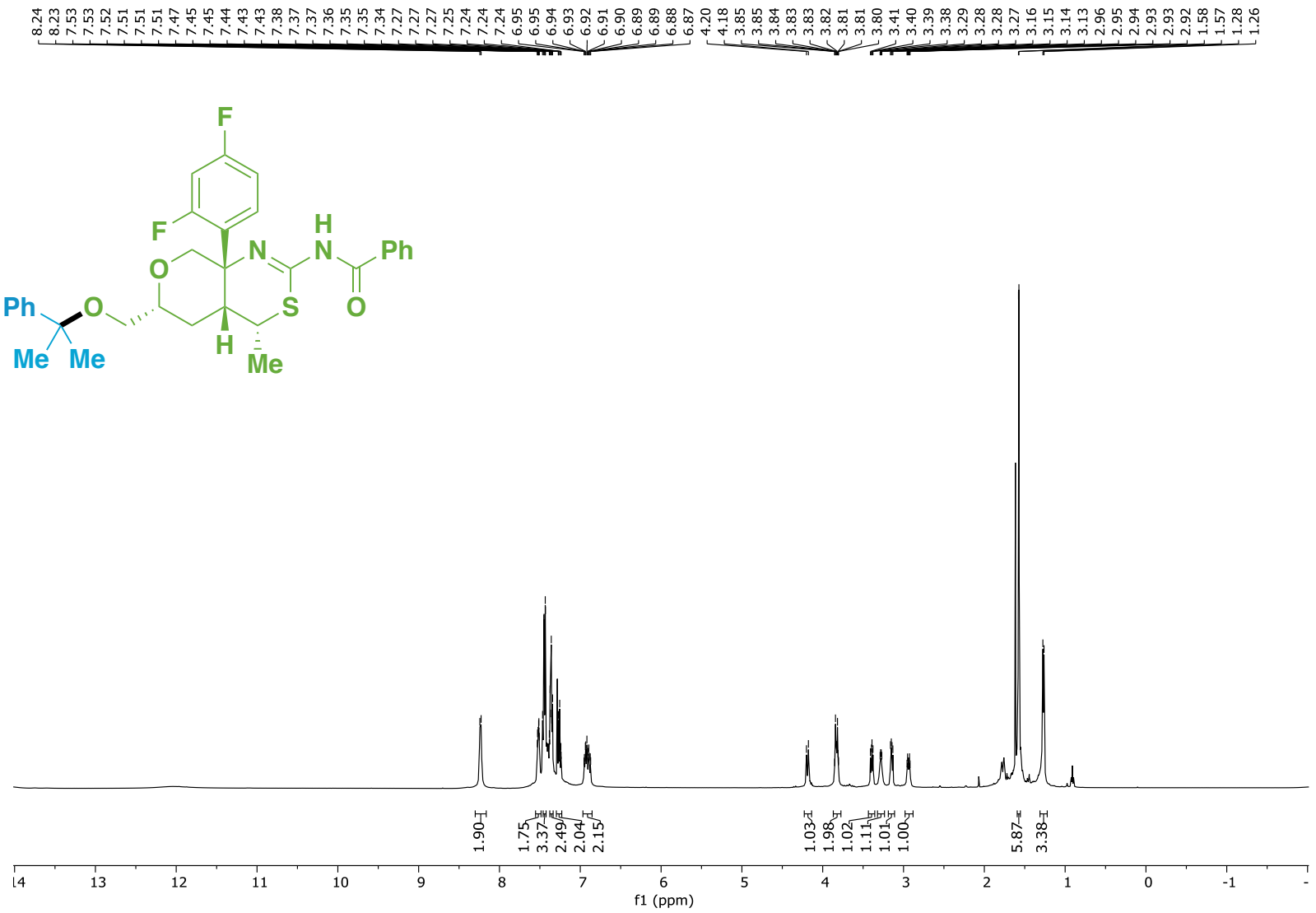
Compound 41 ^{1}H NMR



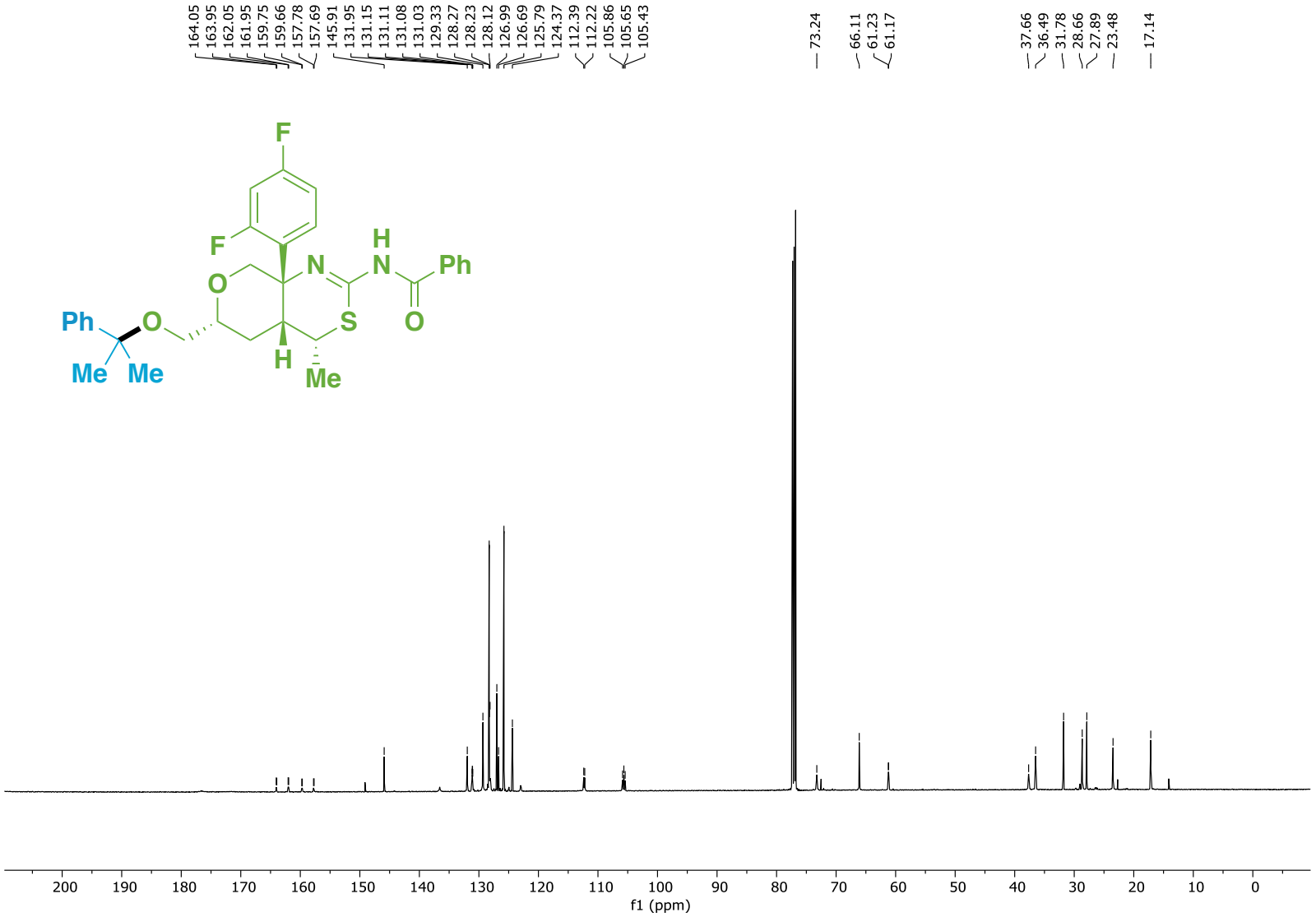
Compound 41 ^{13}C NMR



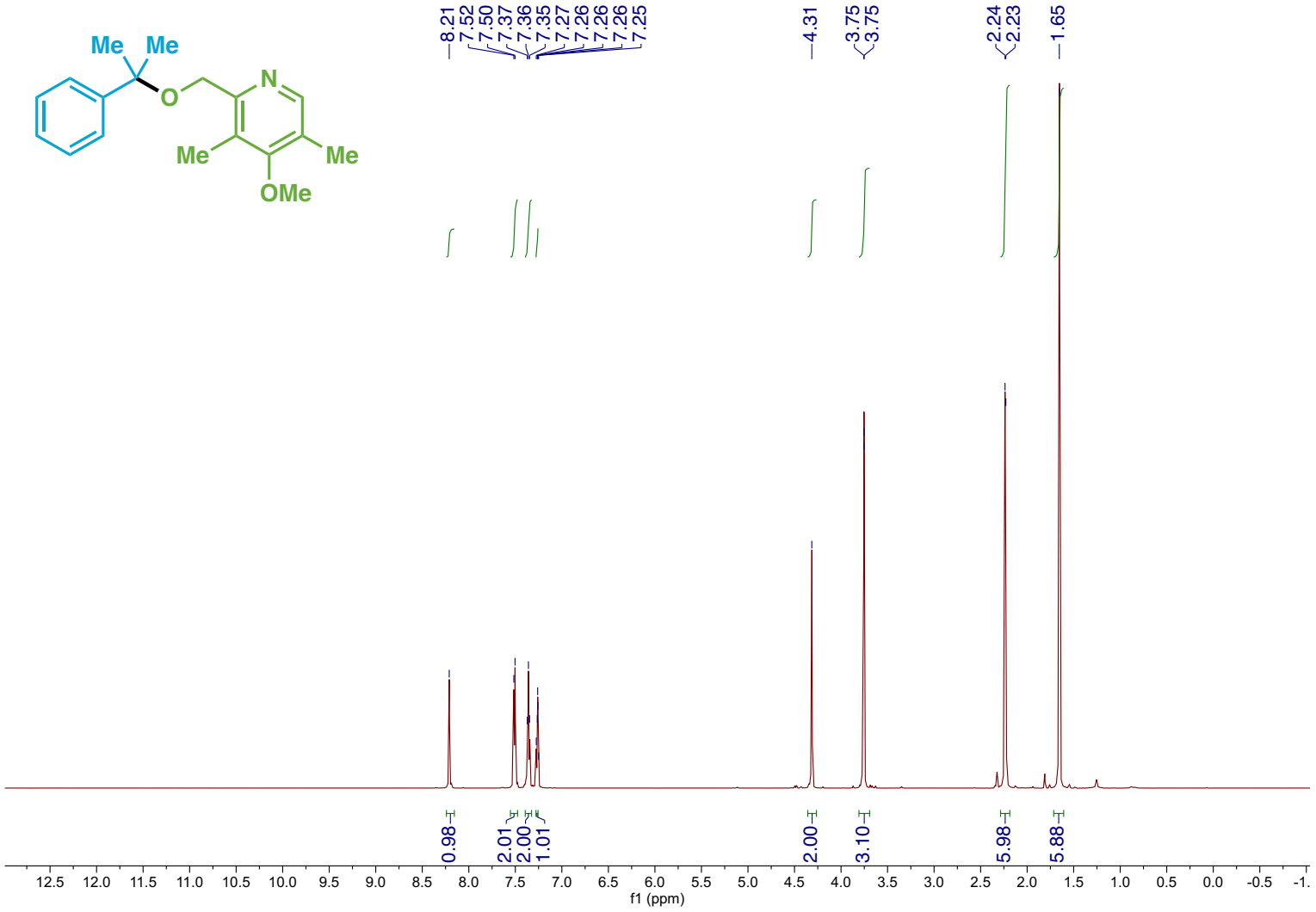
Compound 42 ^{1}H NMR



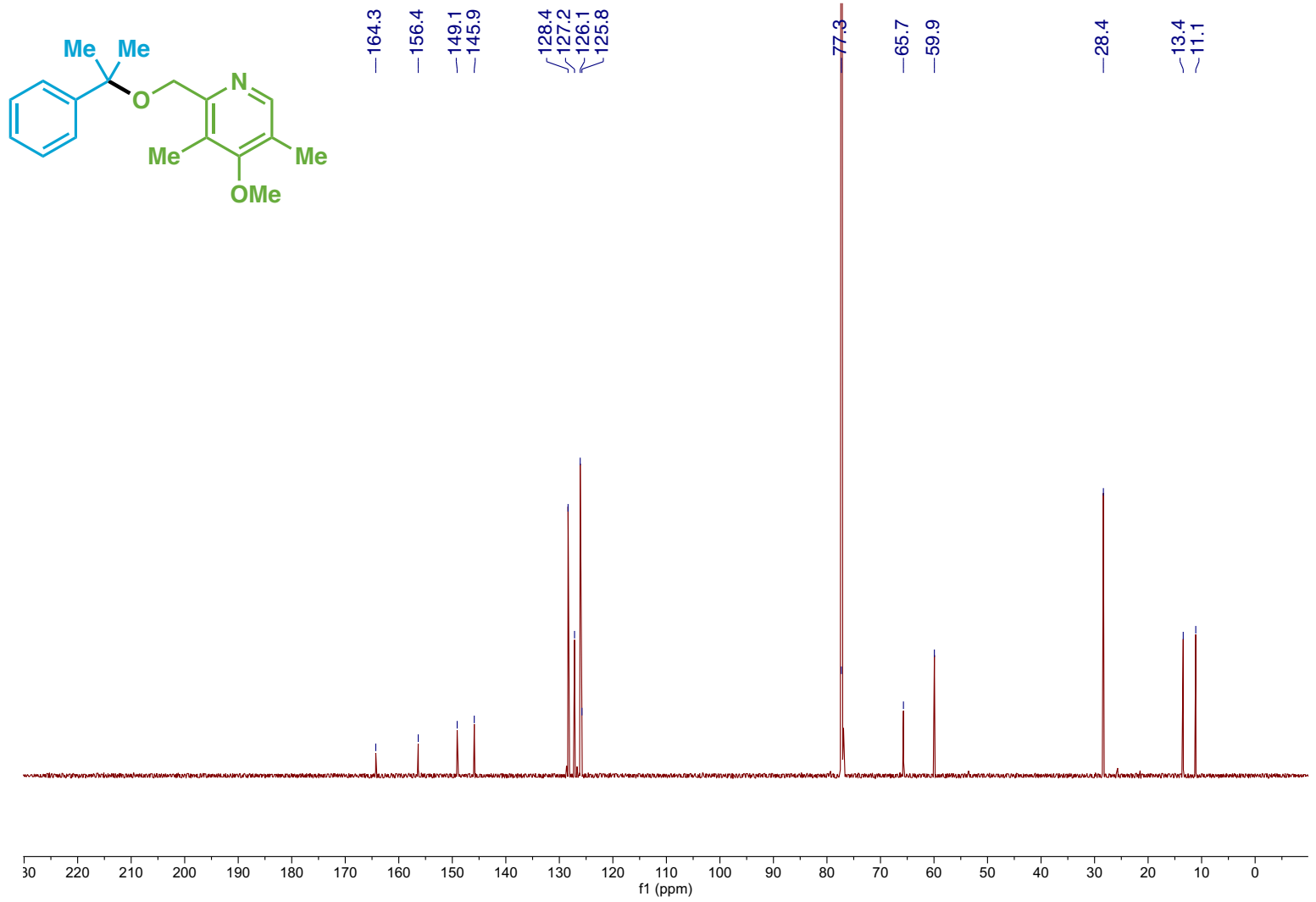
Compound 42 ^{13}C NMR



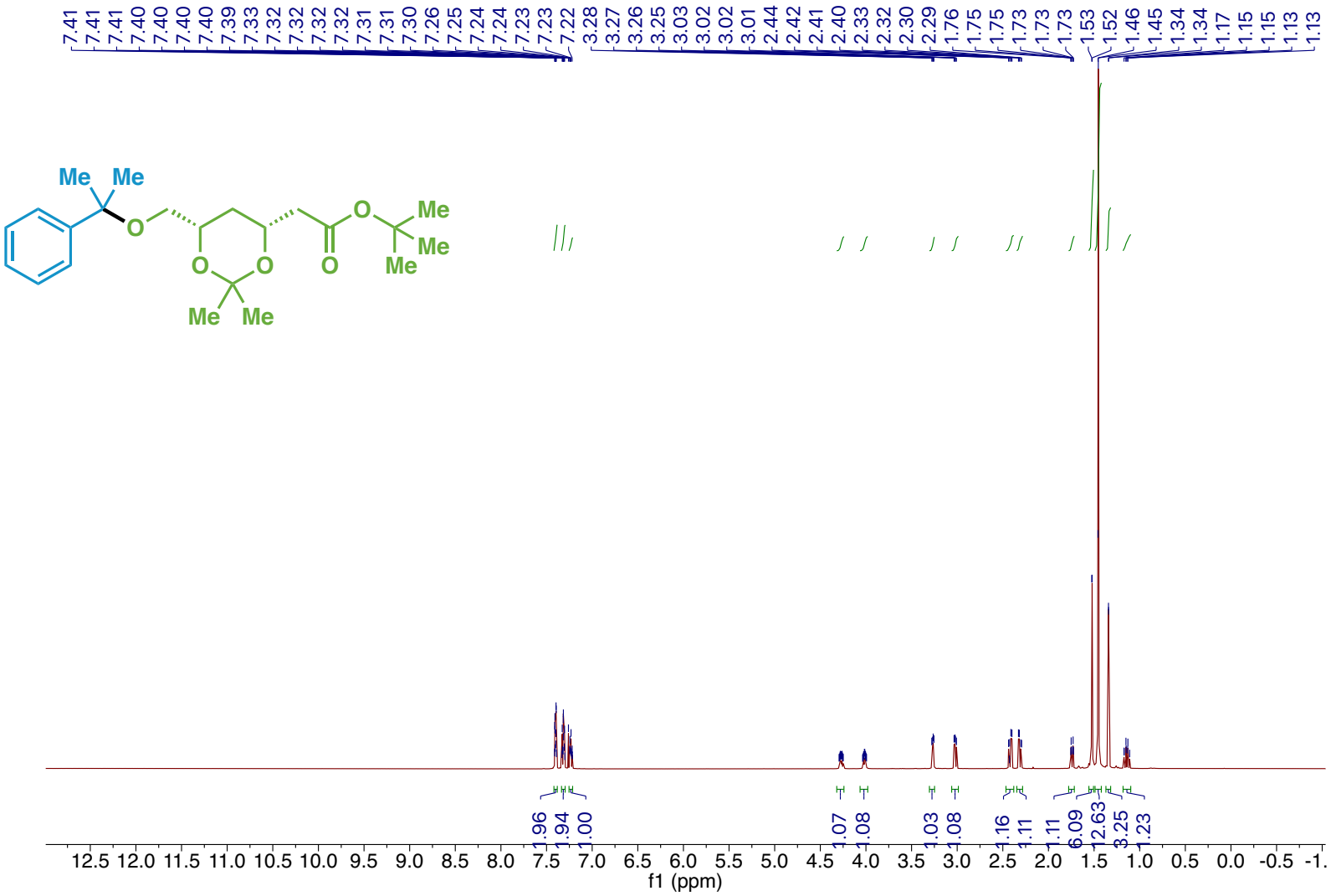
Compound 43 ^{1}H NMR



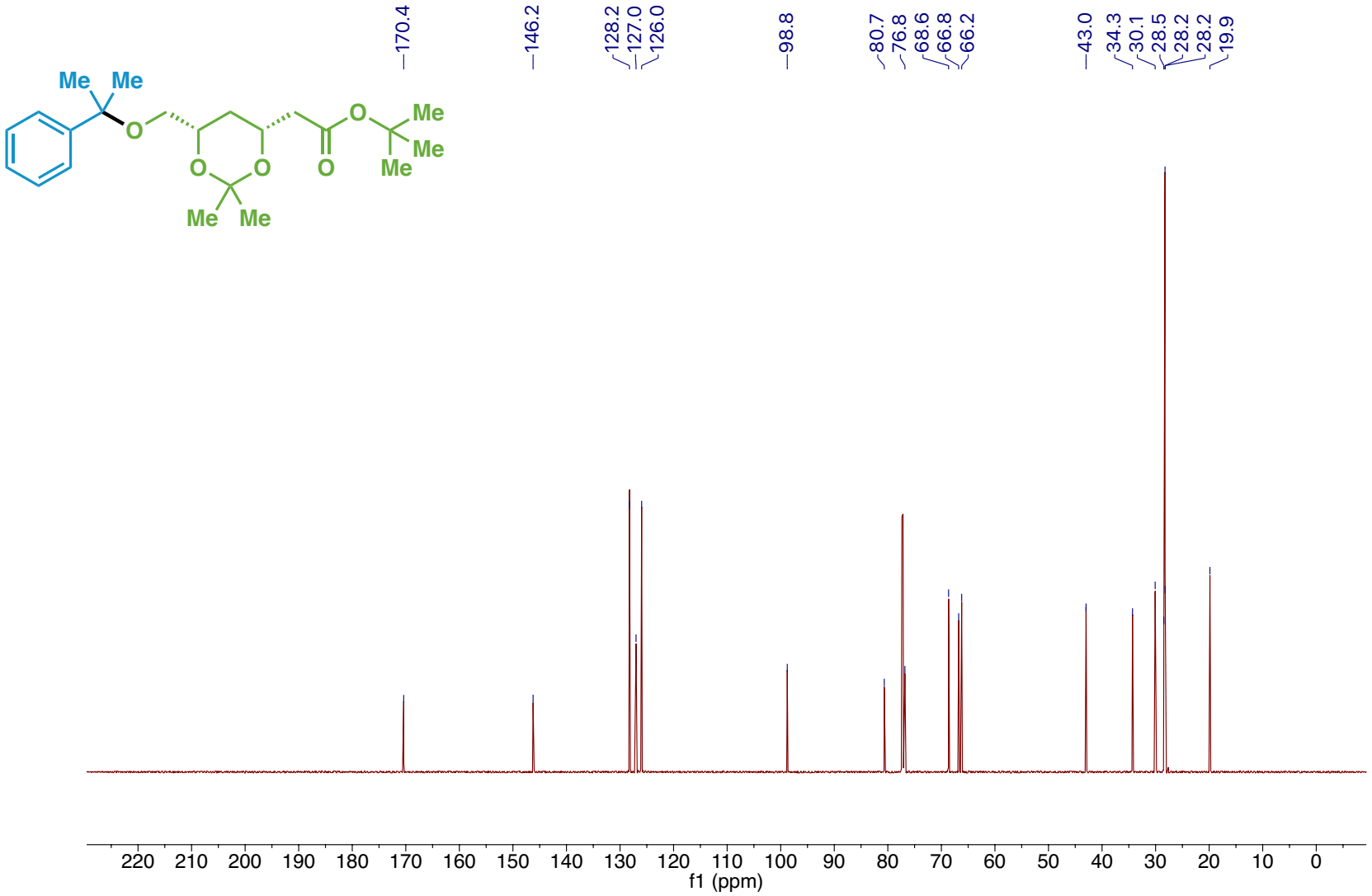
Compound 43 ^{13}C NMR



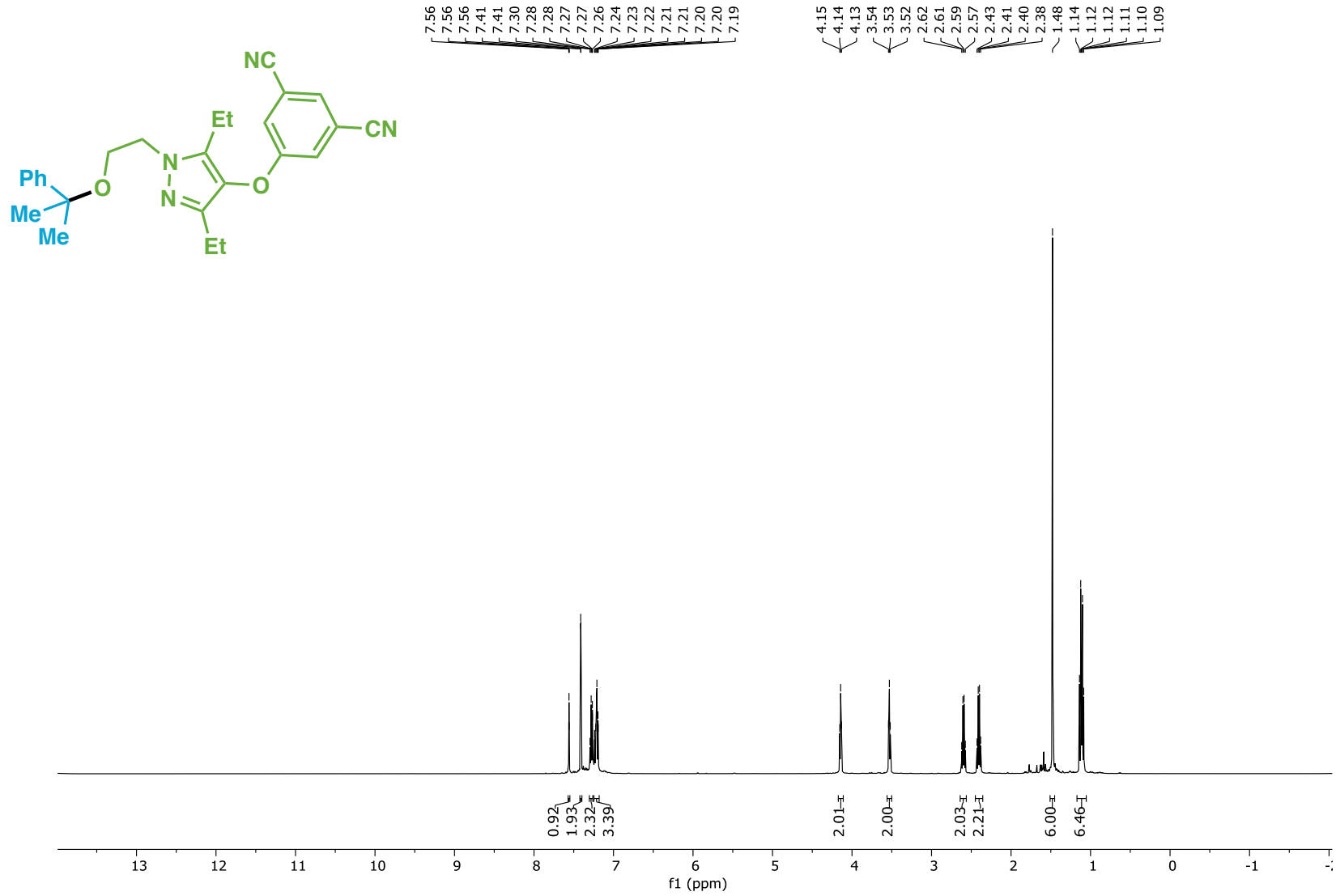
Compound 44 ^{1}H NMR



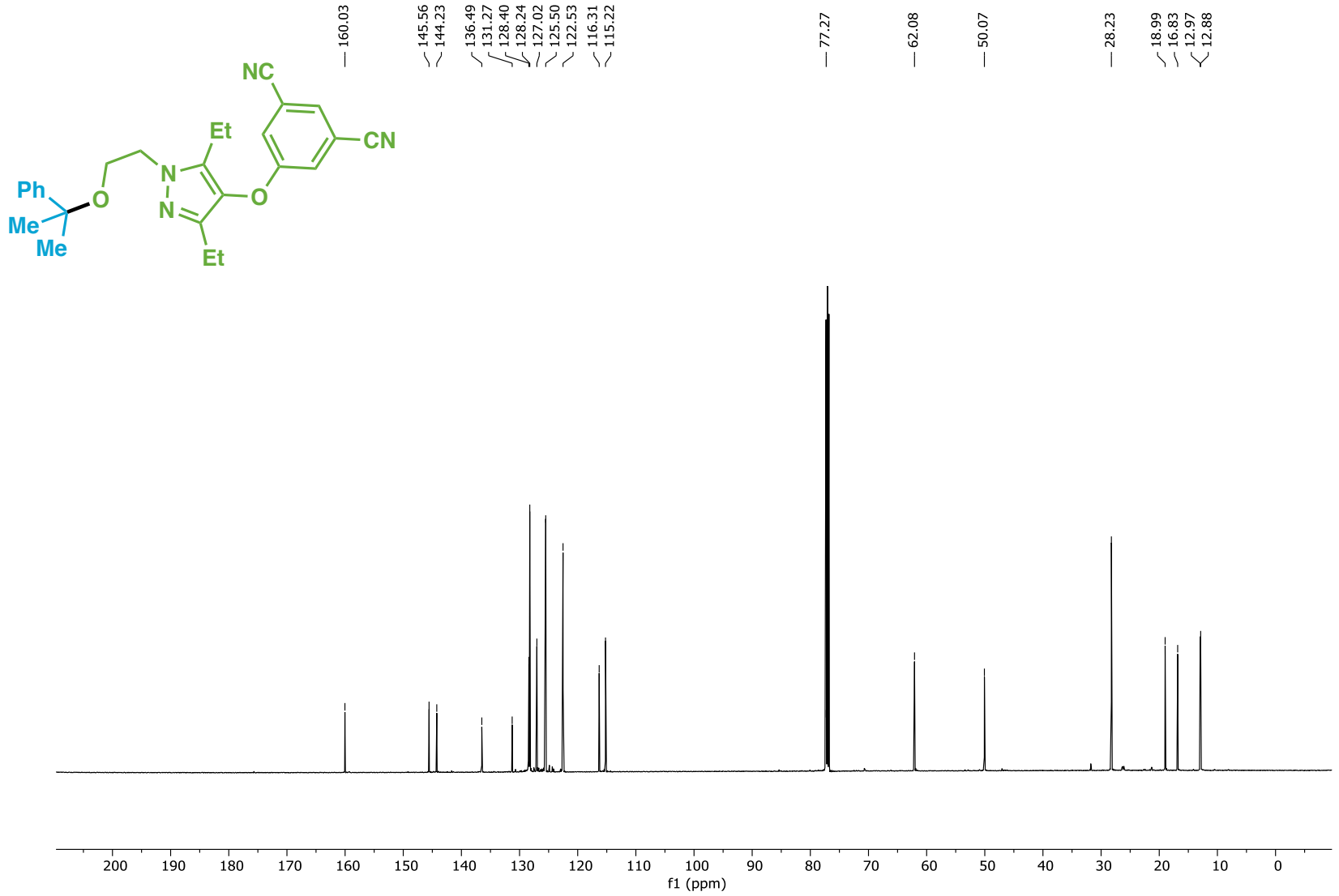
Compound 44 ^{13}C NMR



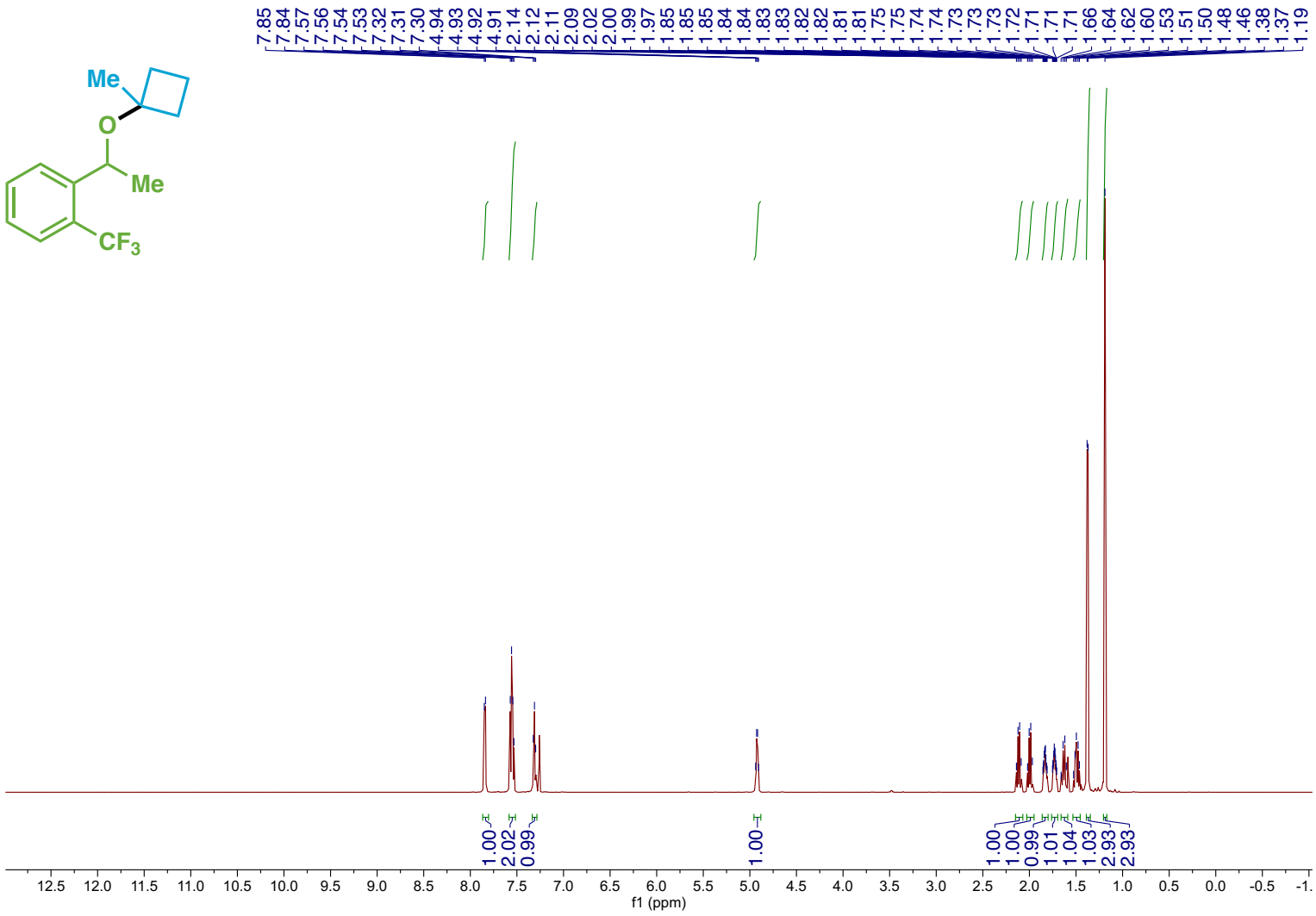
Compound 45 ^{1}H NMR



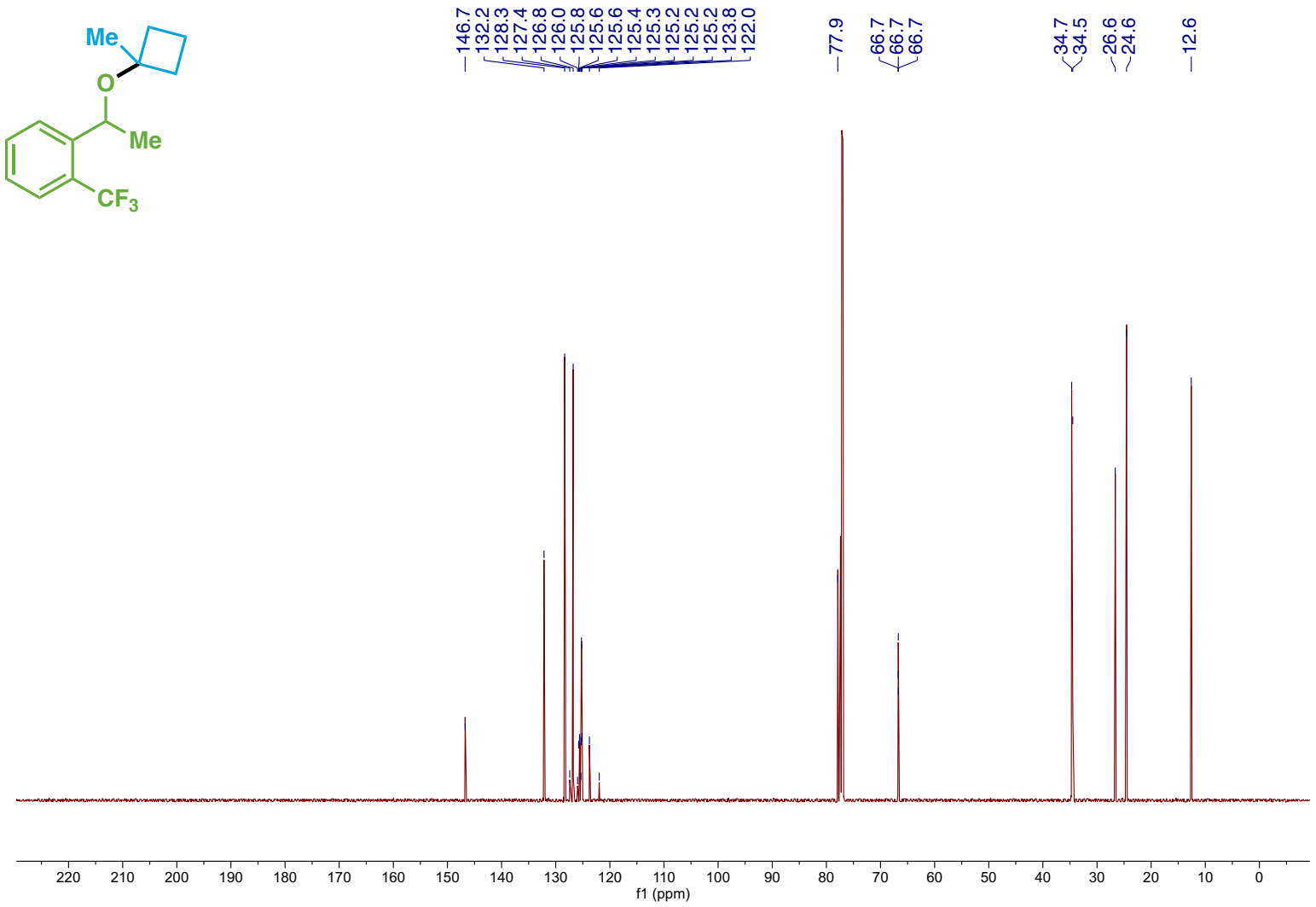
Compound 45 ^{13}C NMR



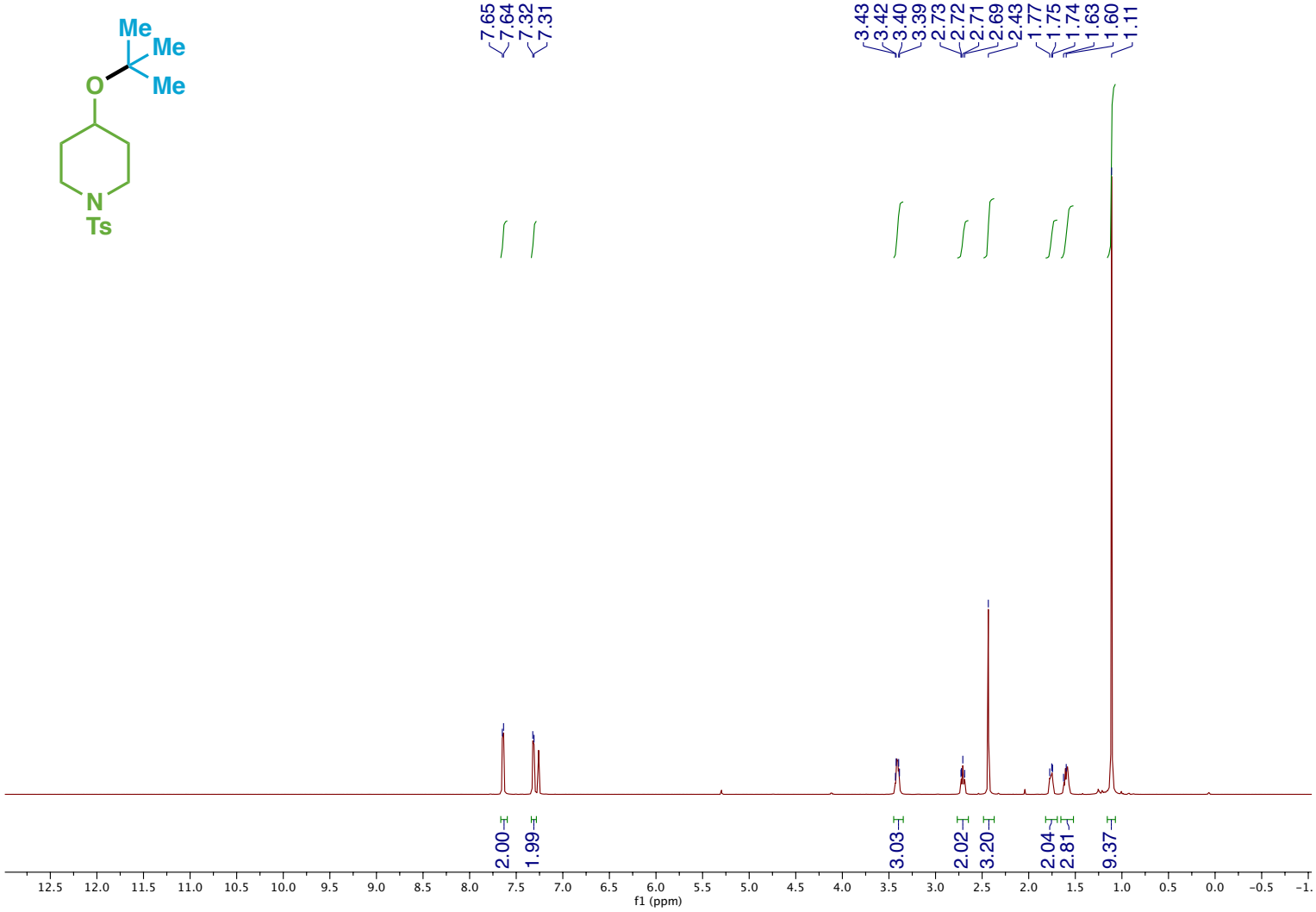
Compound 46 ^{1}H NMR



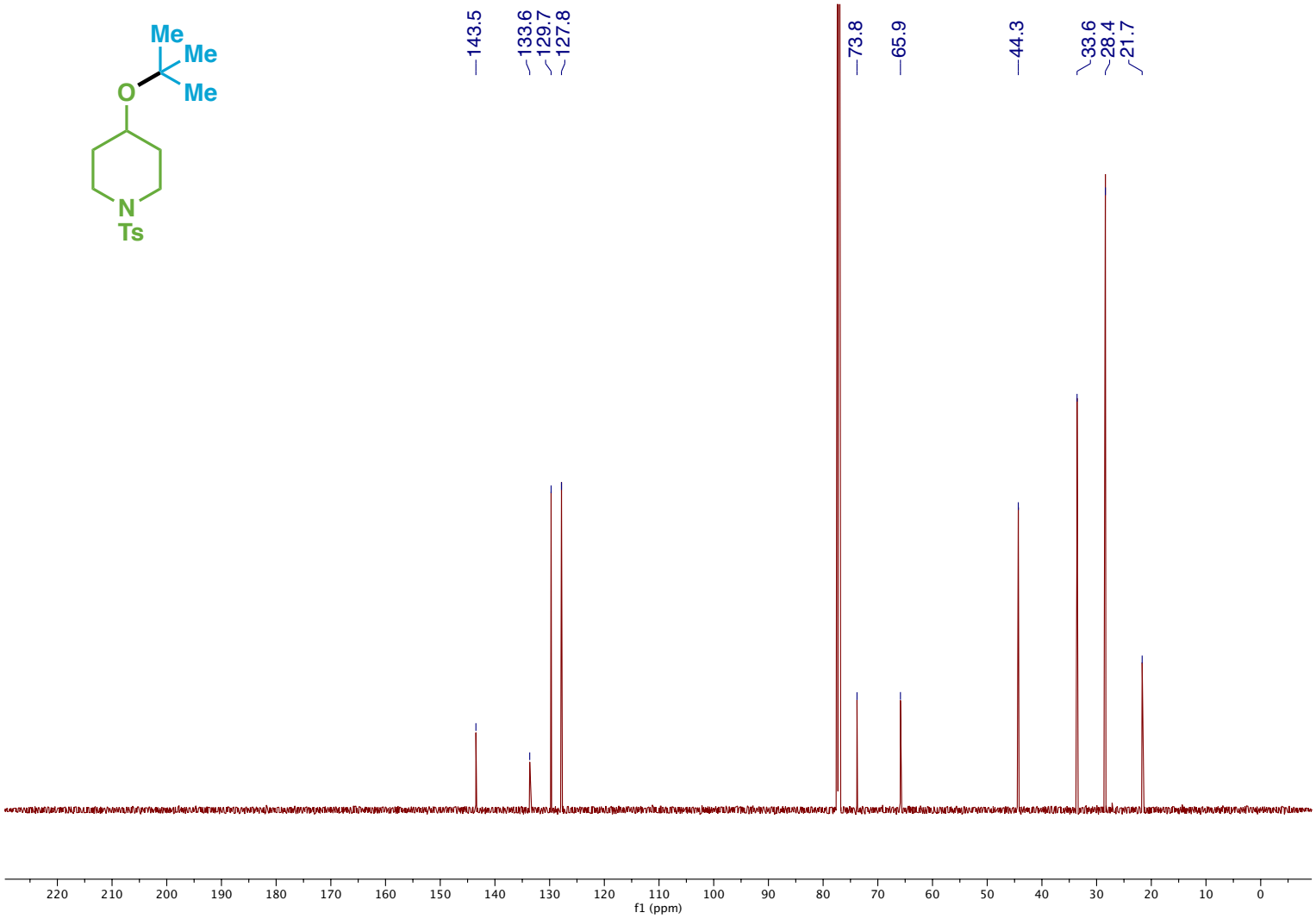
Compound 46 ^{13}C NMR



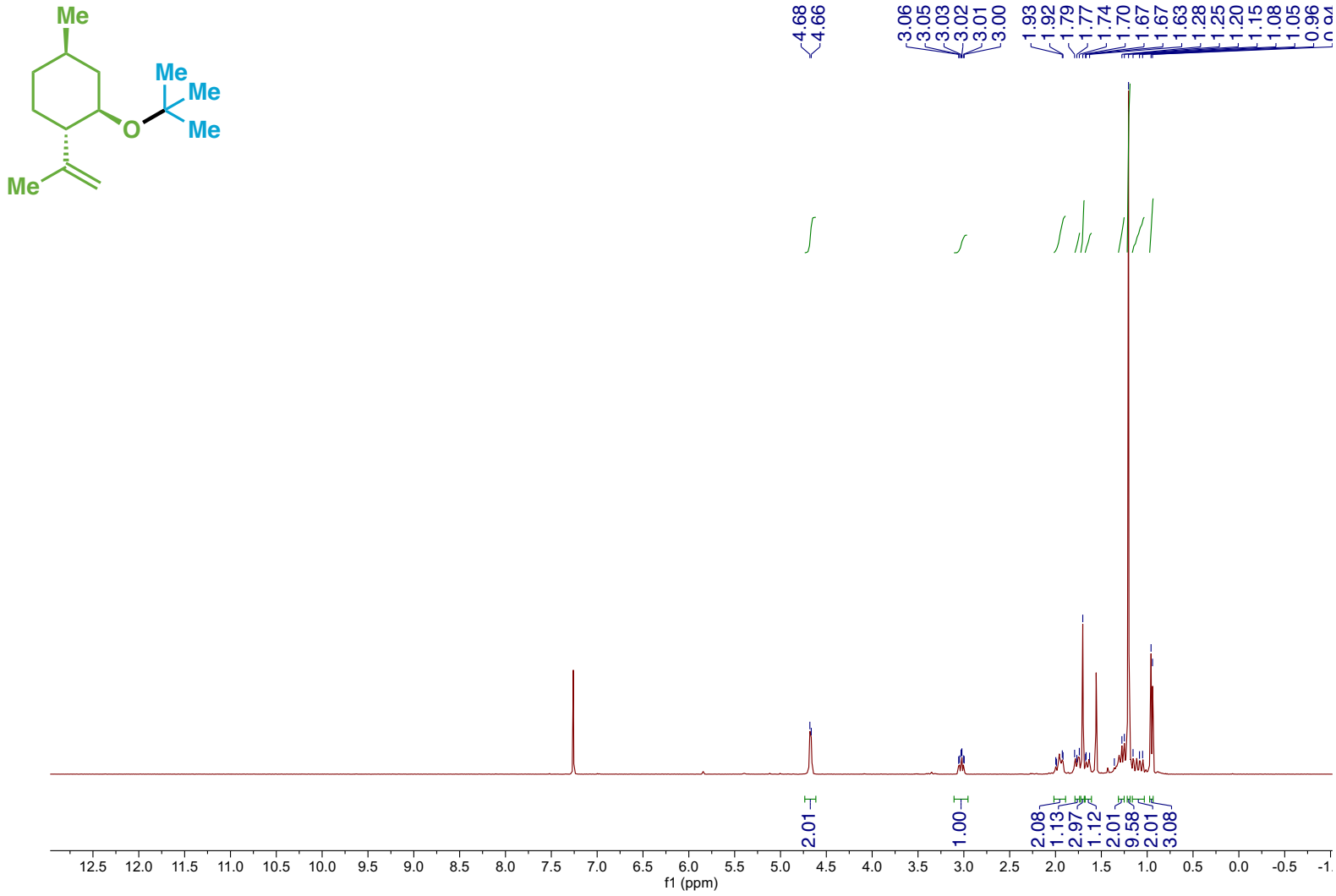
Compound 47 ^{1}H NMR



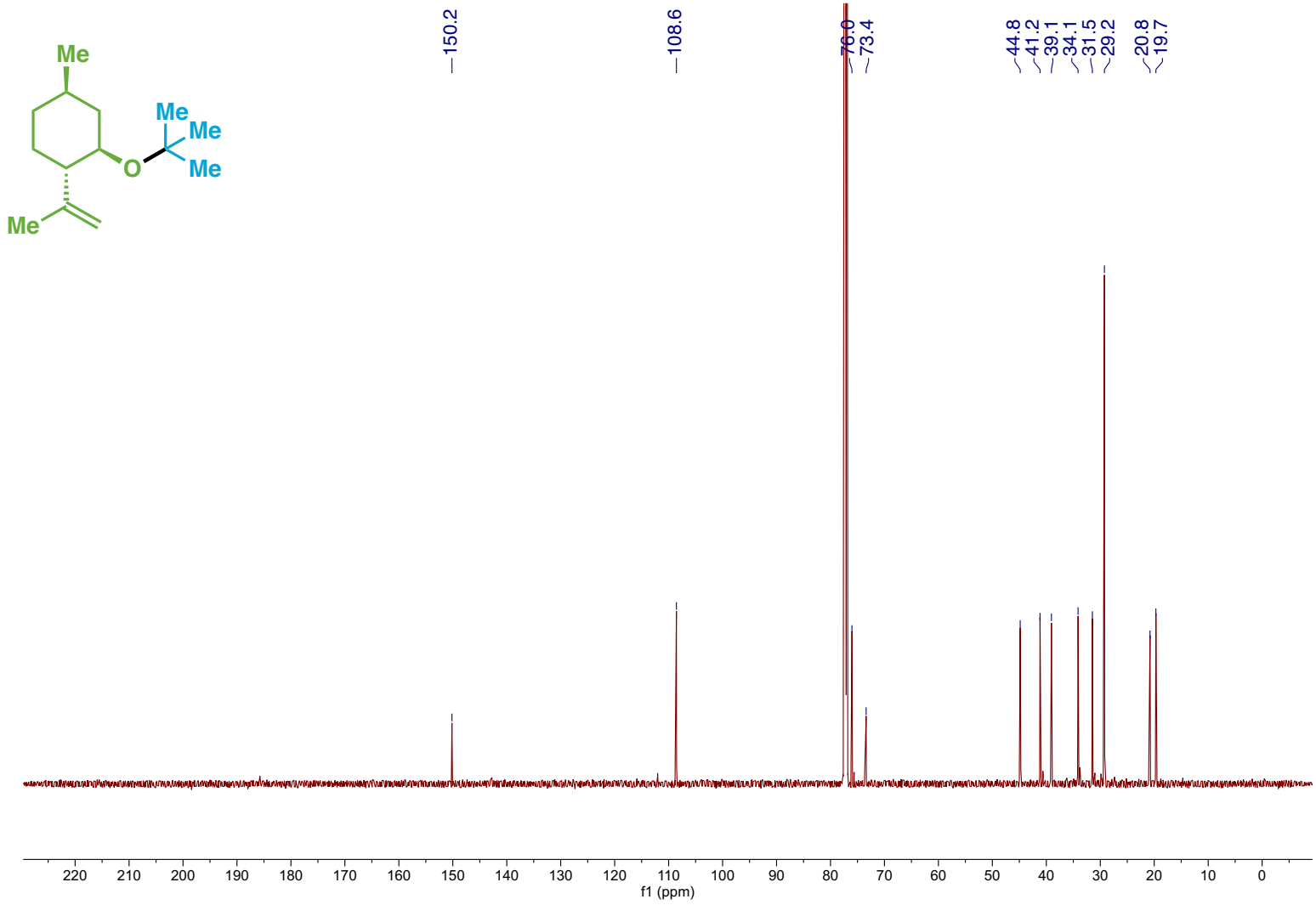
Compound 47 ^{13}C NMR



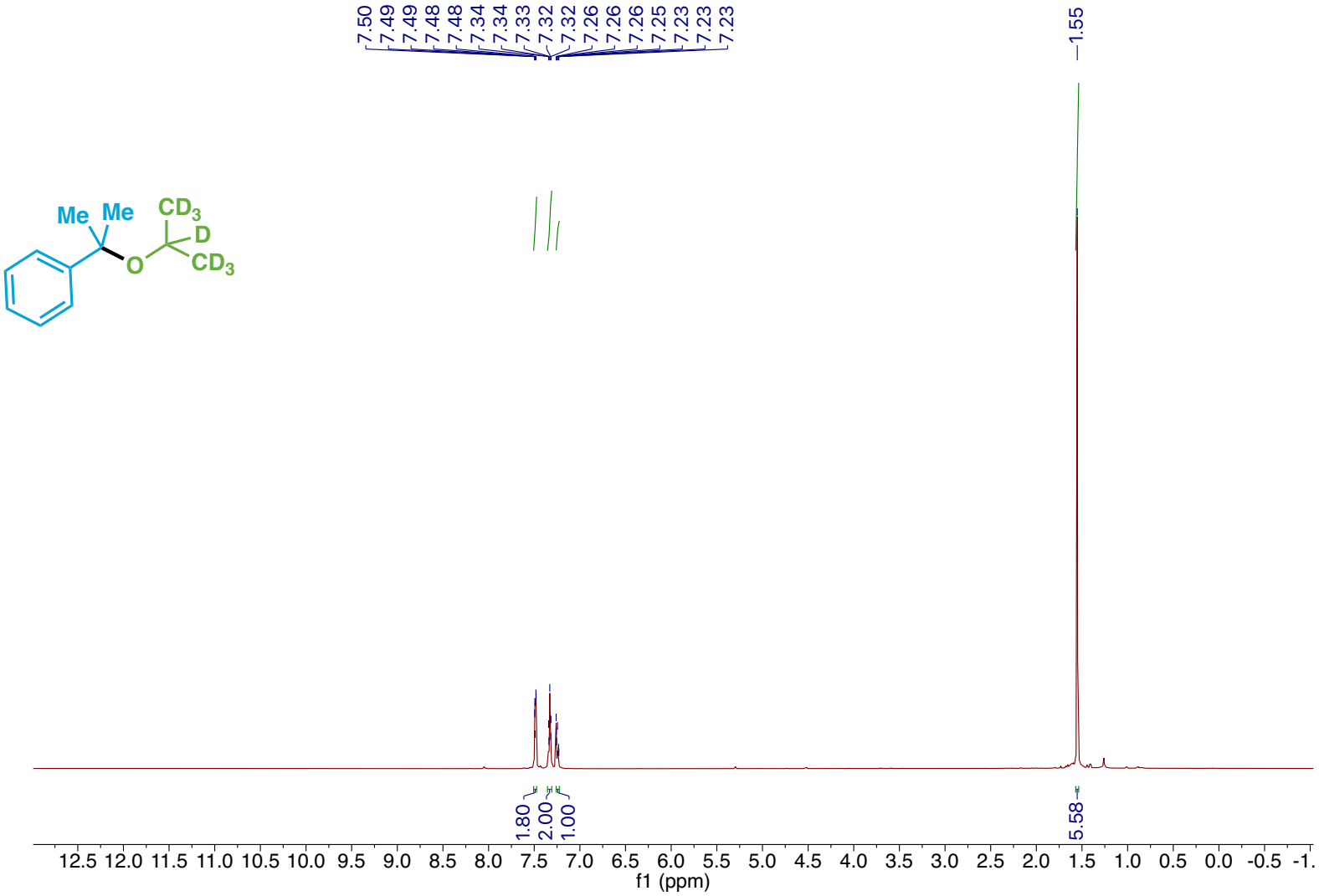
Compound 48 ^{1}H NMR



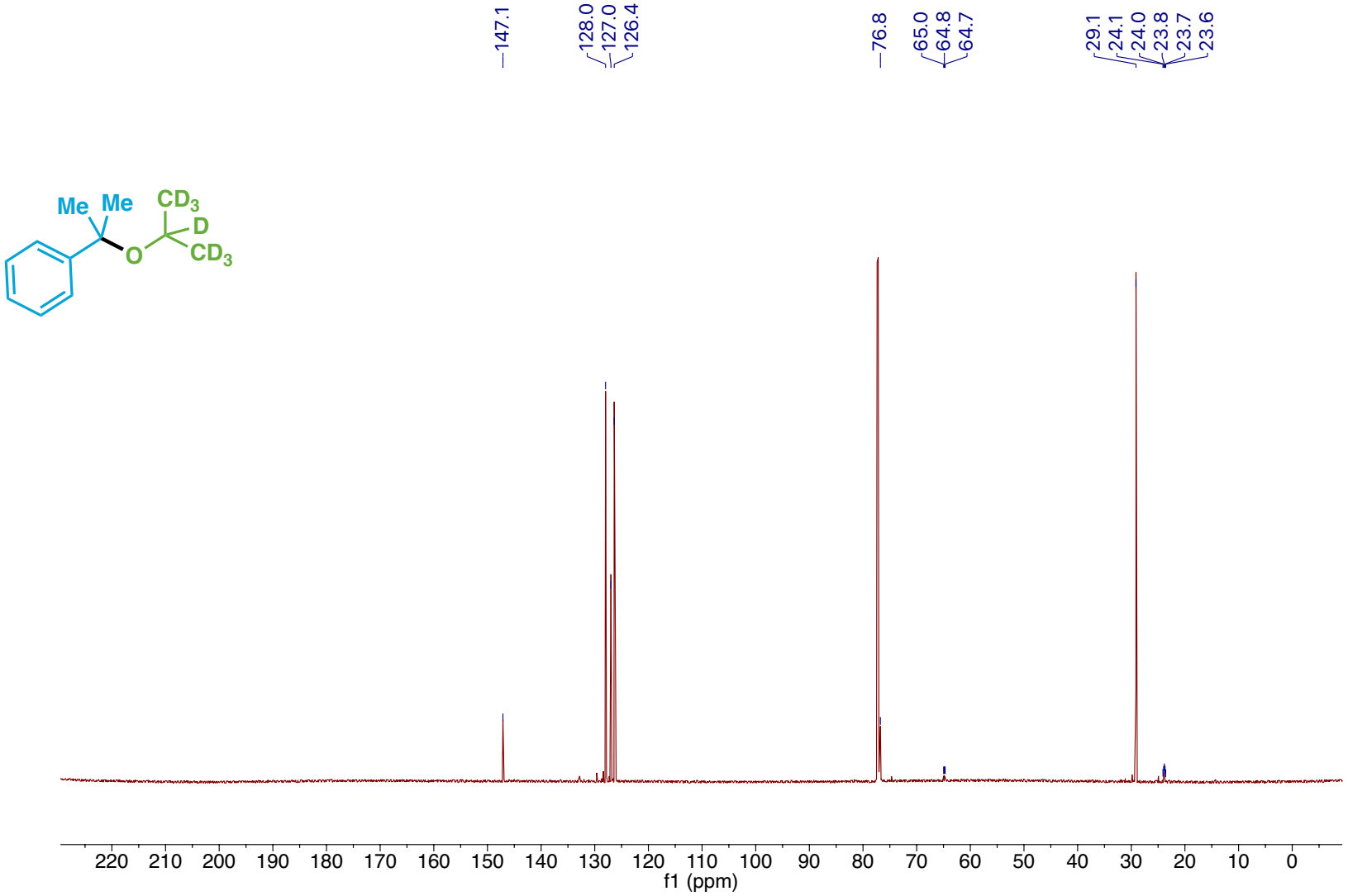
Compound 48 ^{13}C NMR



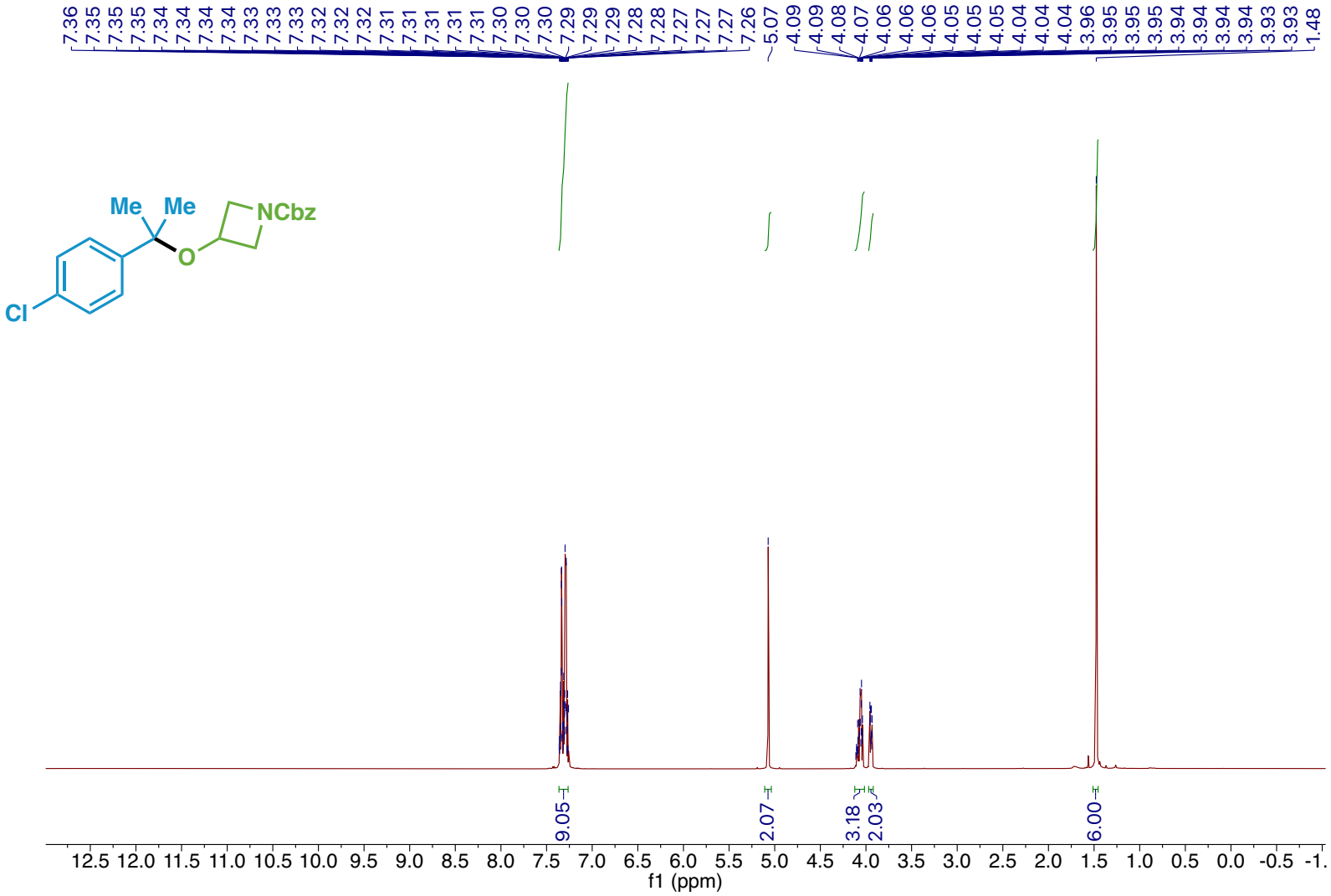
Compound 49 ^{1}H NMR



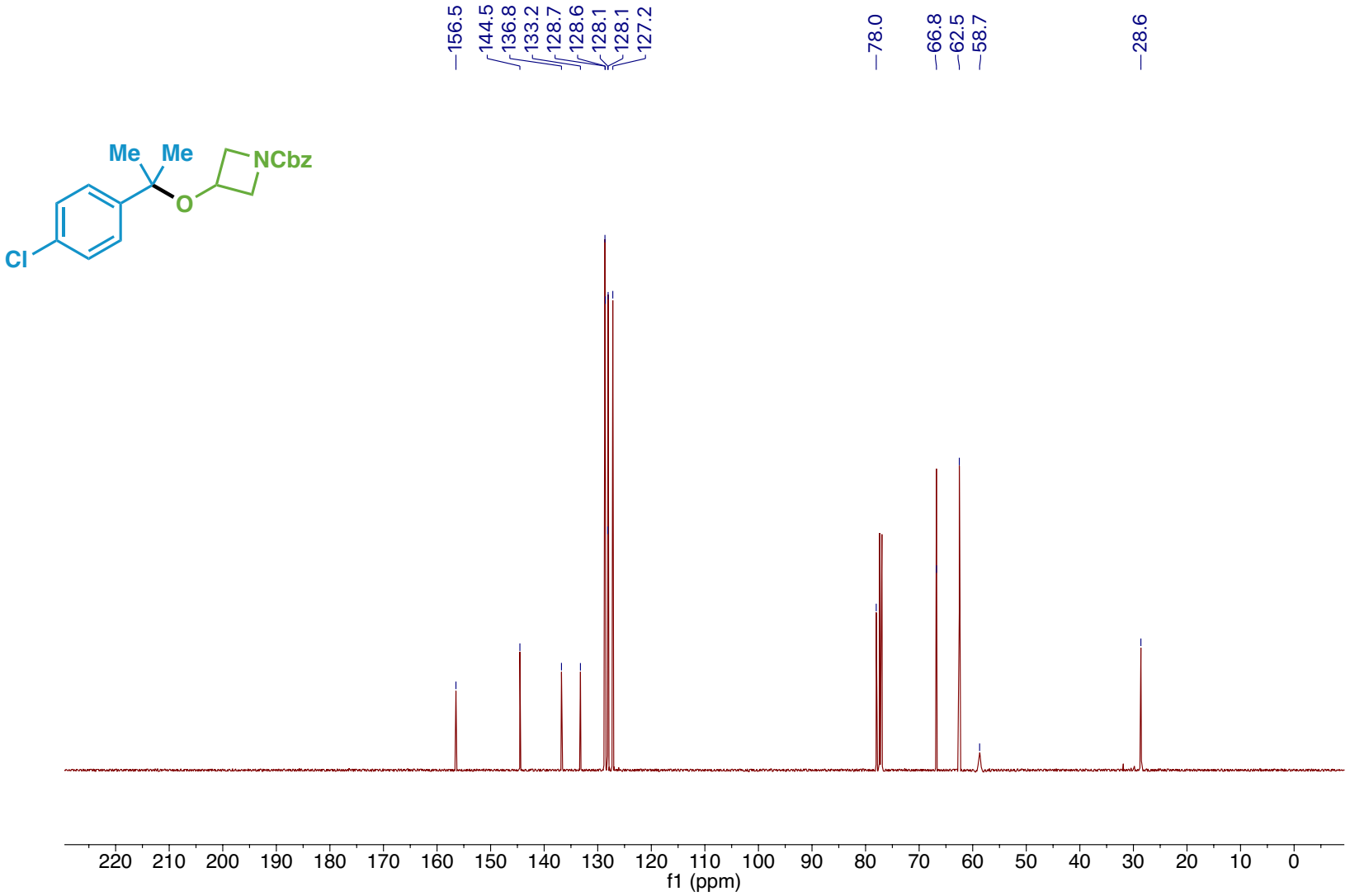
Compound 49 ^{13}C NMR



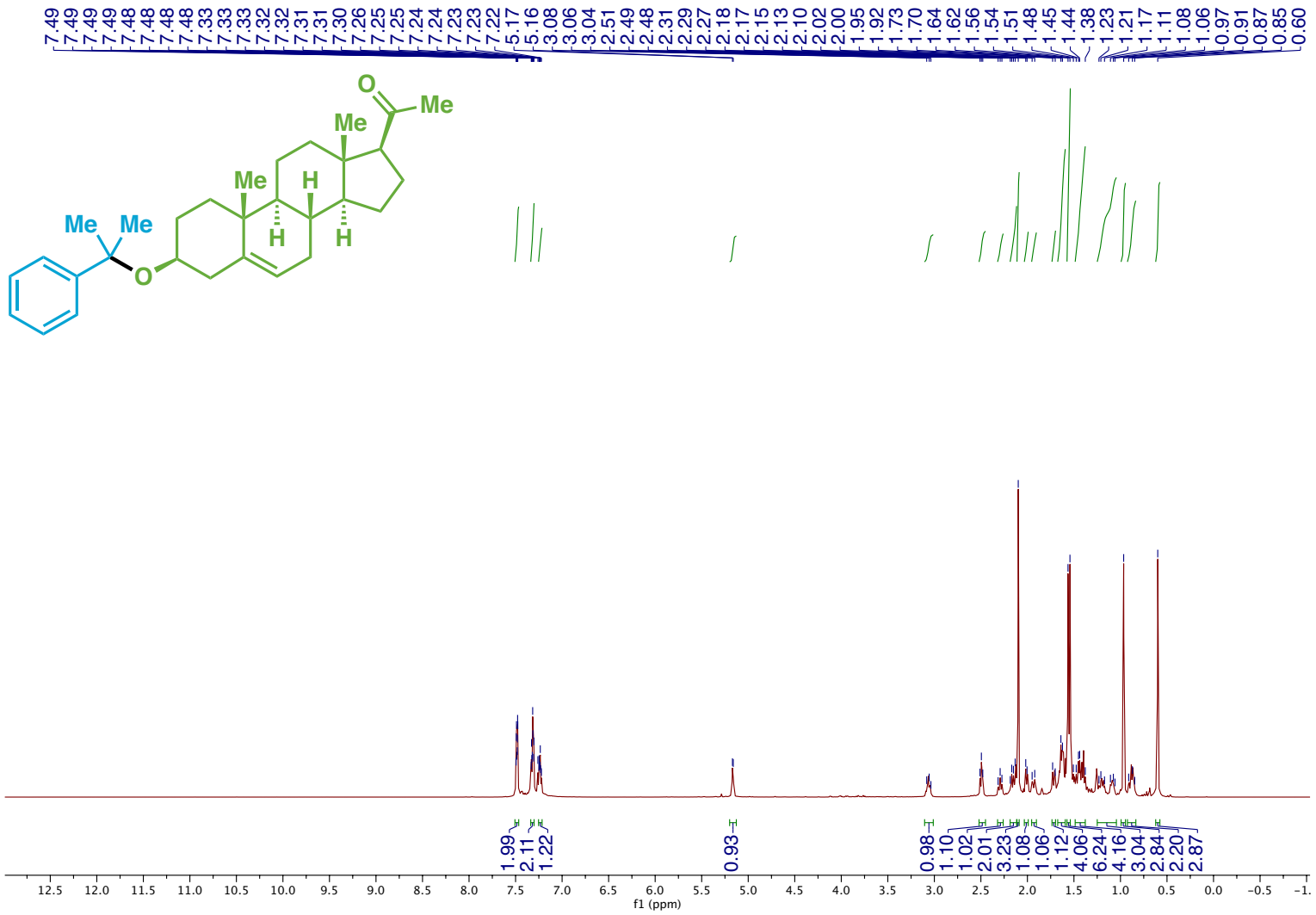
Compound 50 ^{1}H NMR



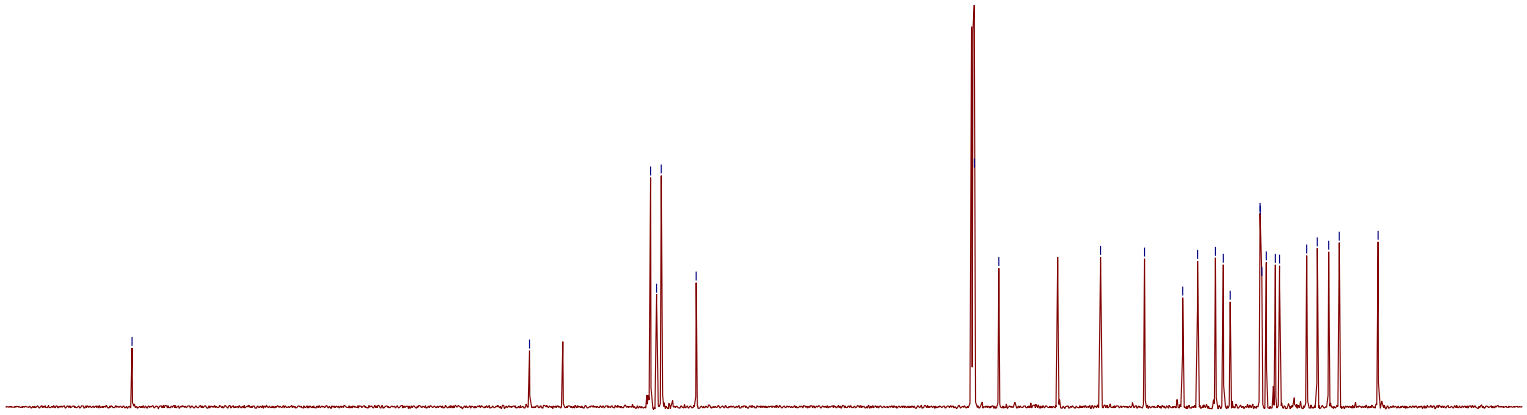
Compound 50 ^{13}C NMR



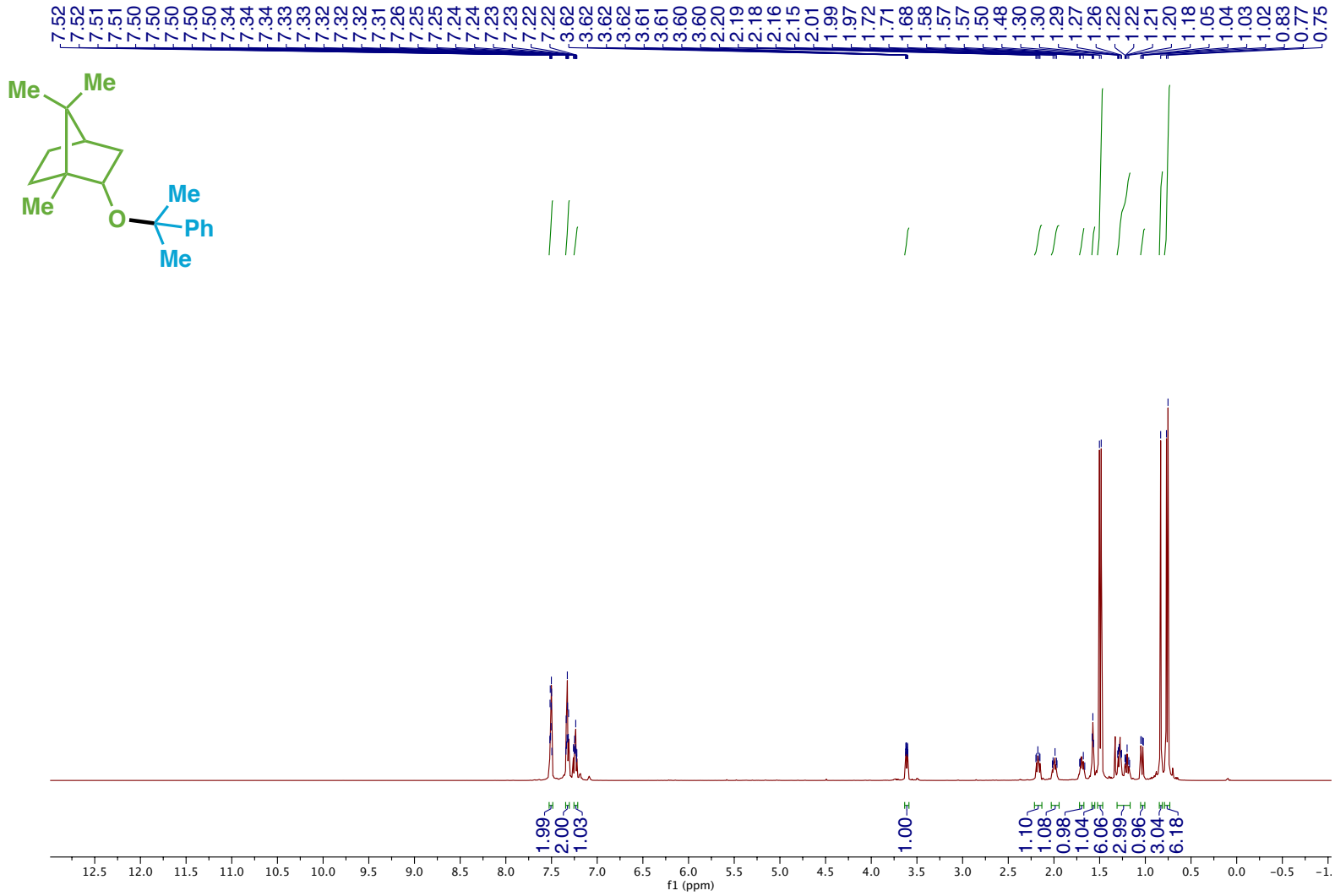
Compound 51 ^{1}H NMR



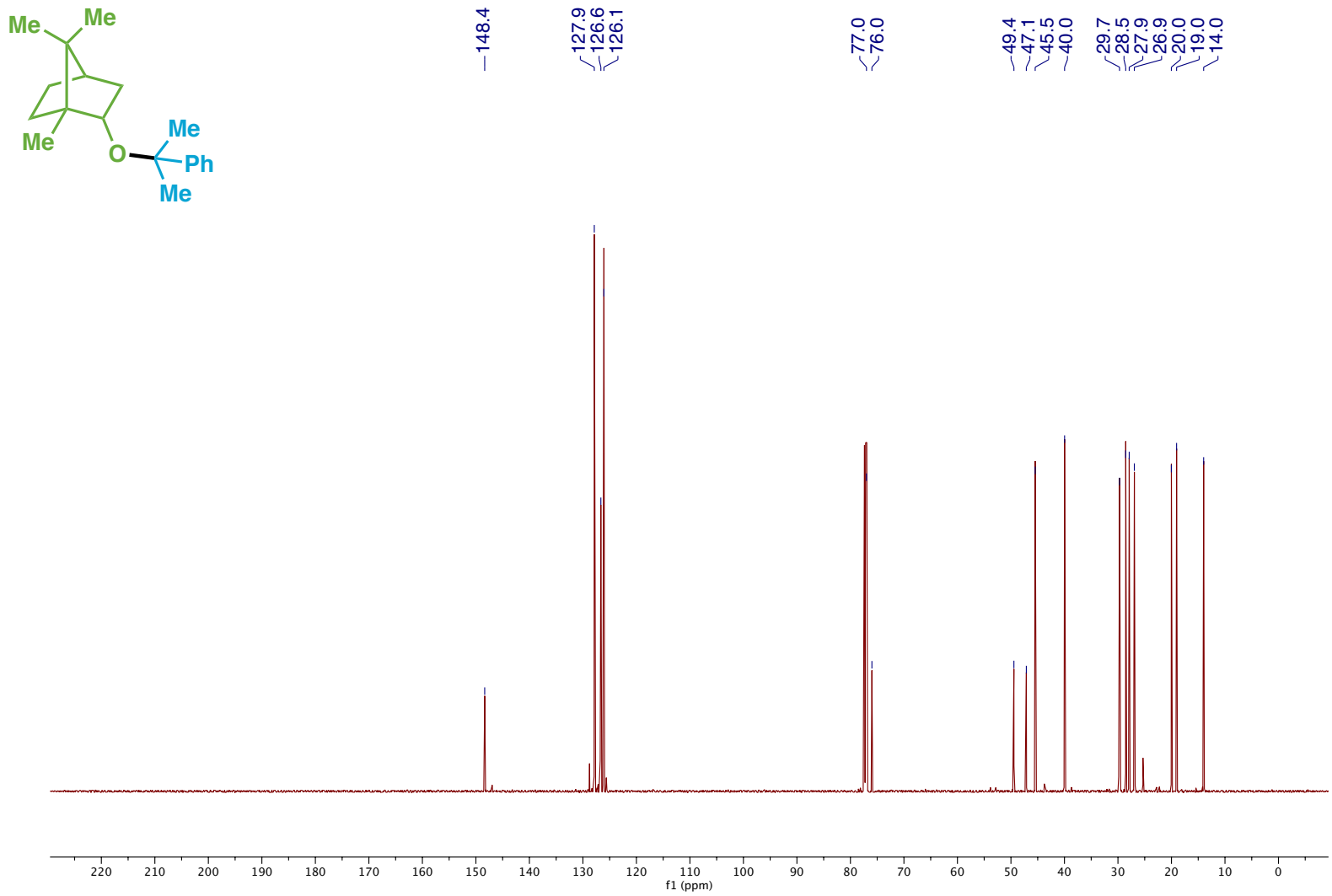
Compound 51 ^{13}C NMR



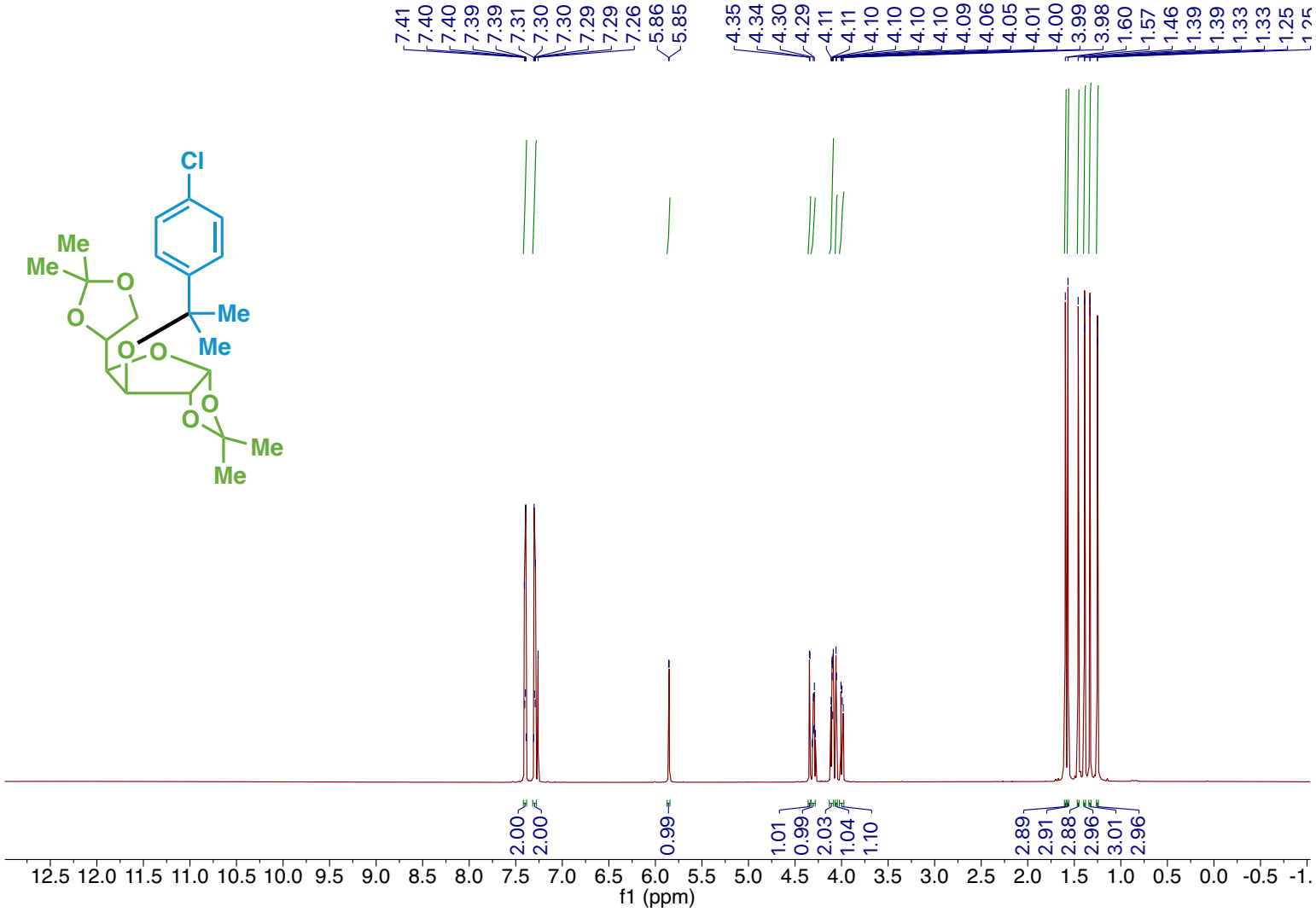
Compound 52 ^{1}H NMR



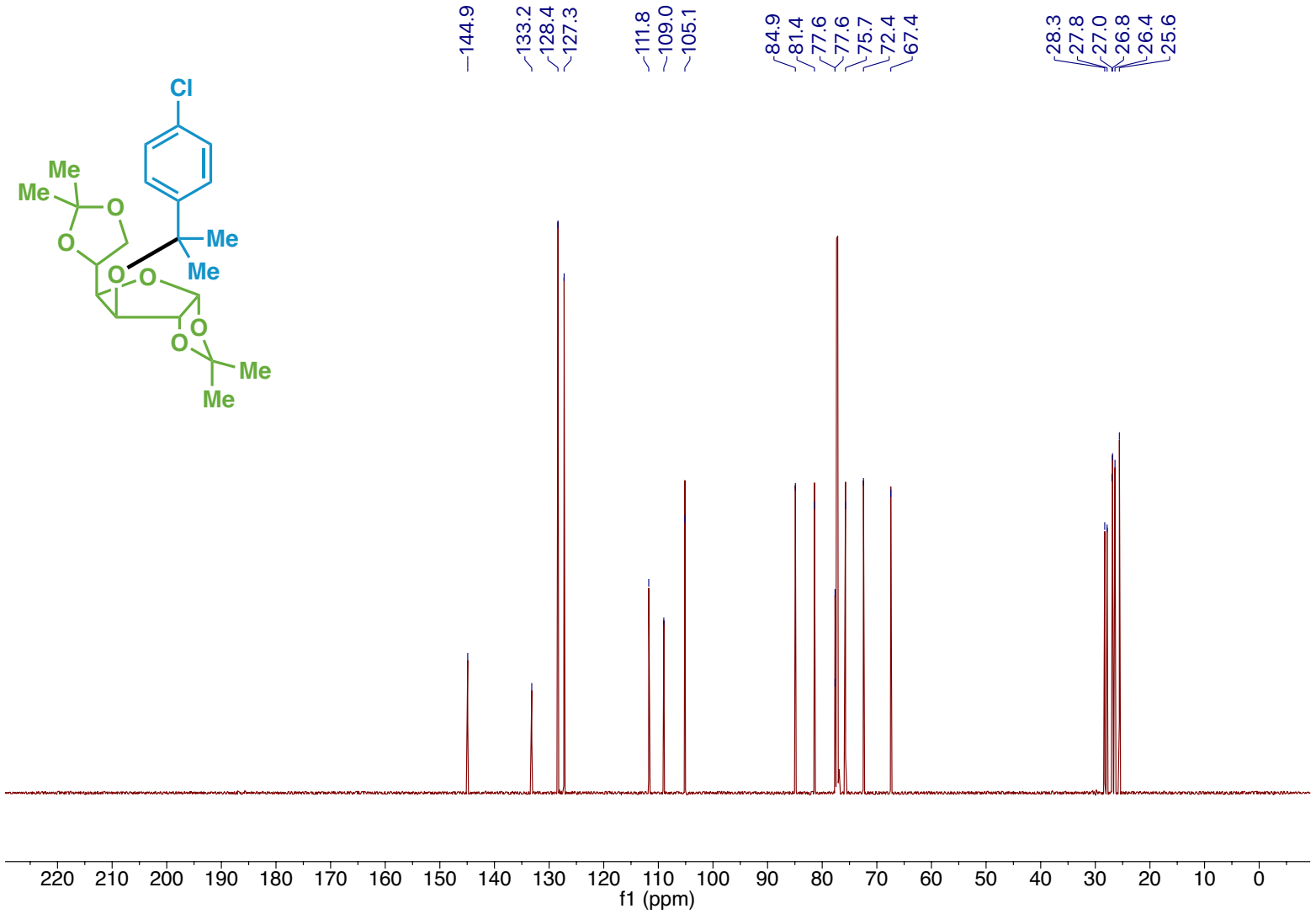
Compound 52 ^{13}C NMR



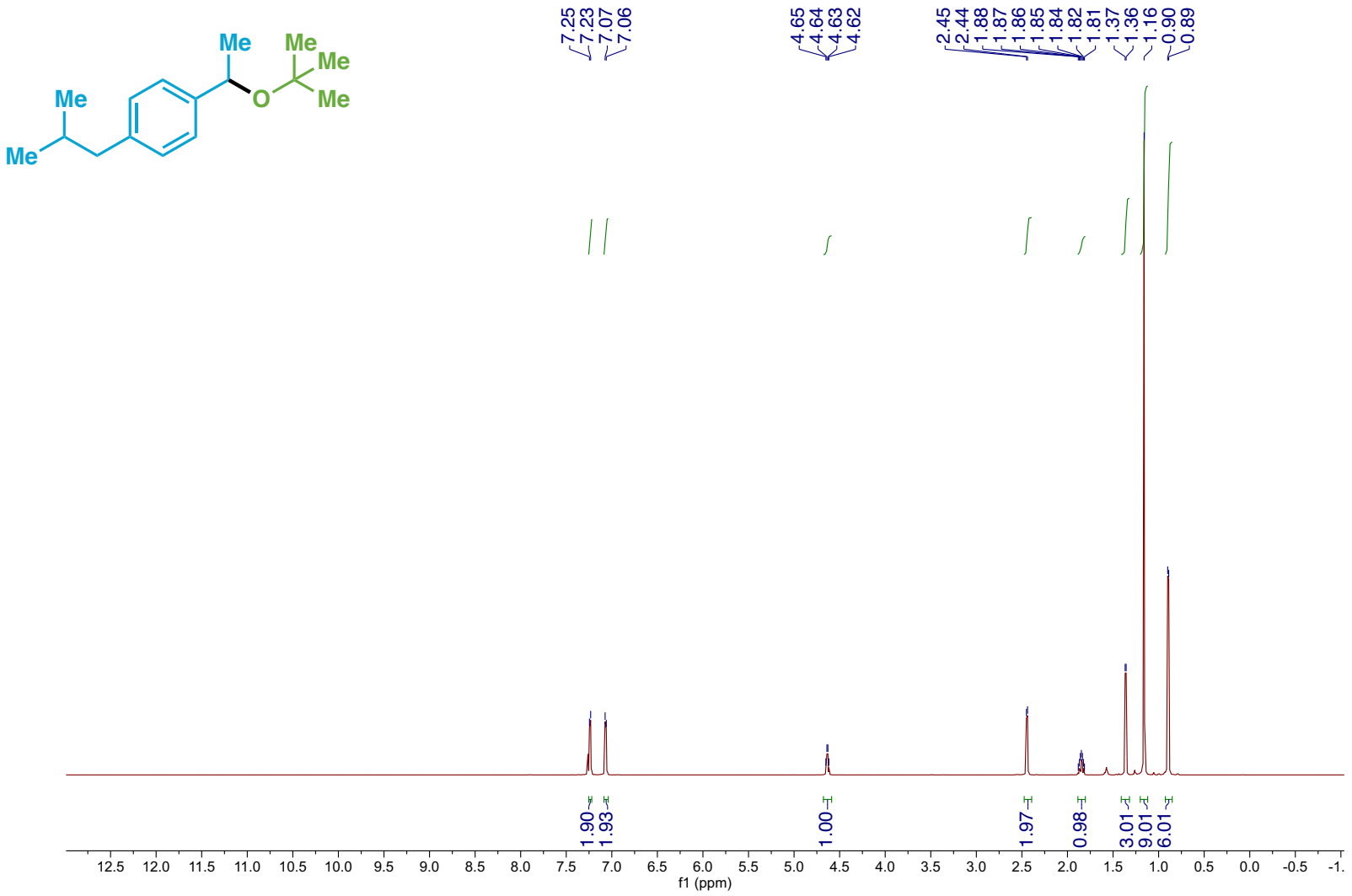
Compound 53 ^{1}H NMR



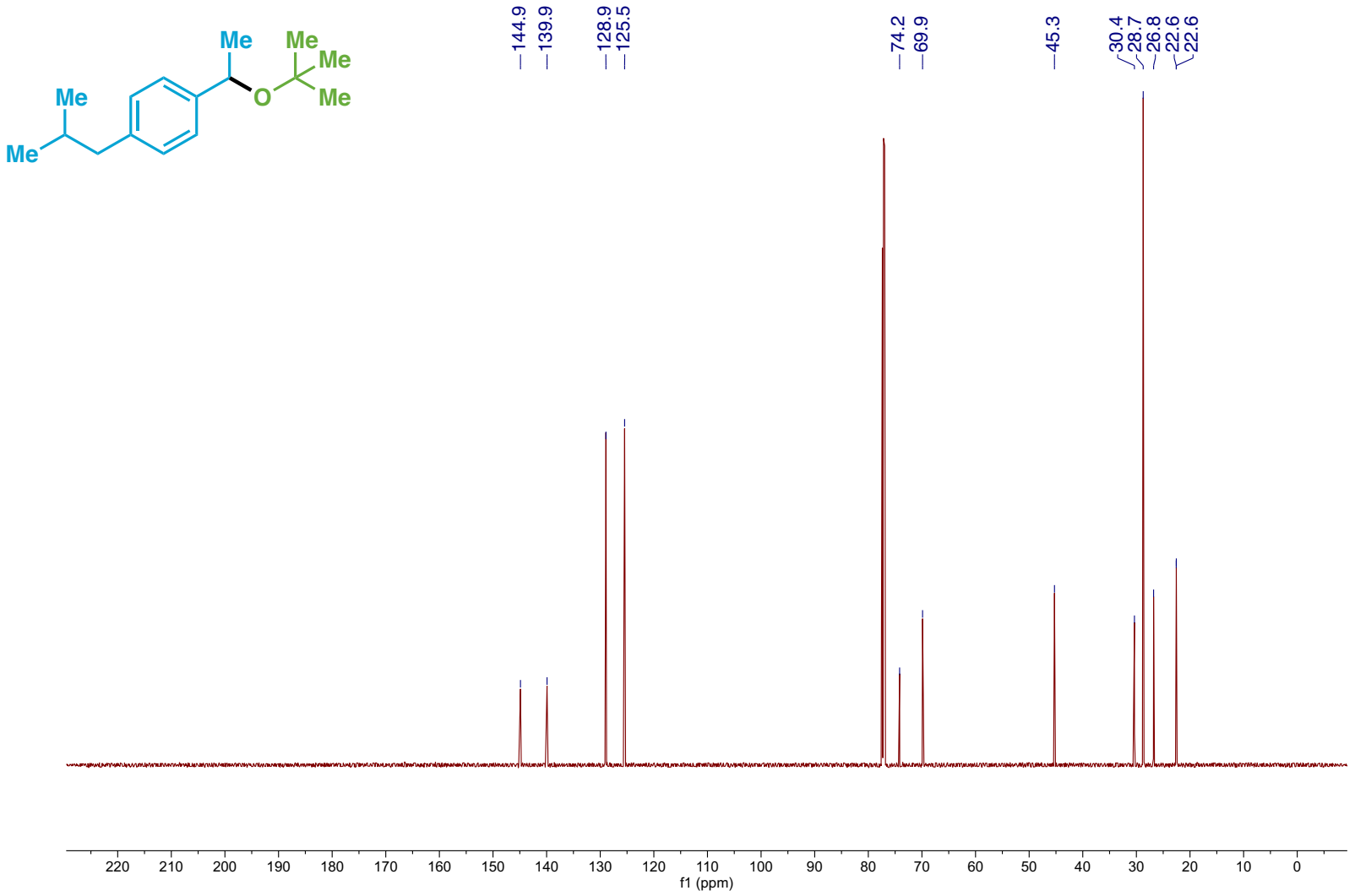
Compound 53 ^{13}C NMR



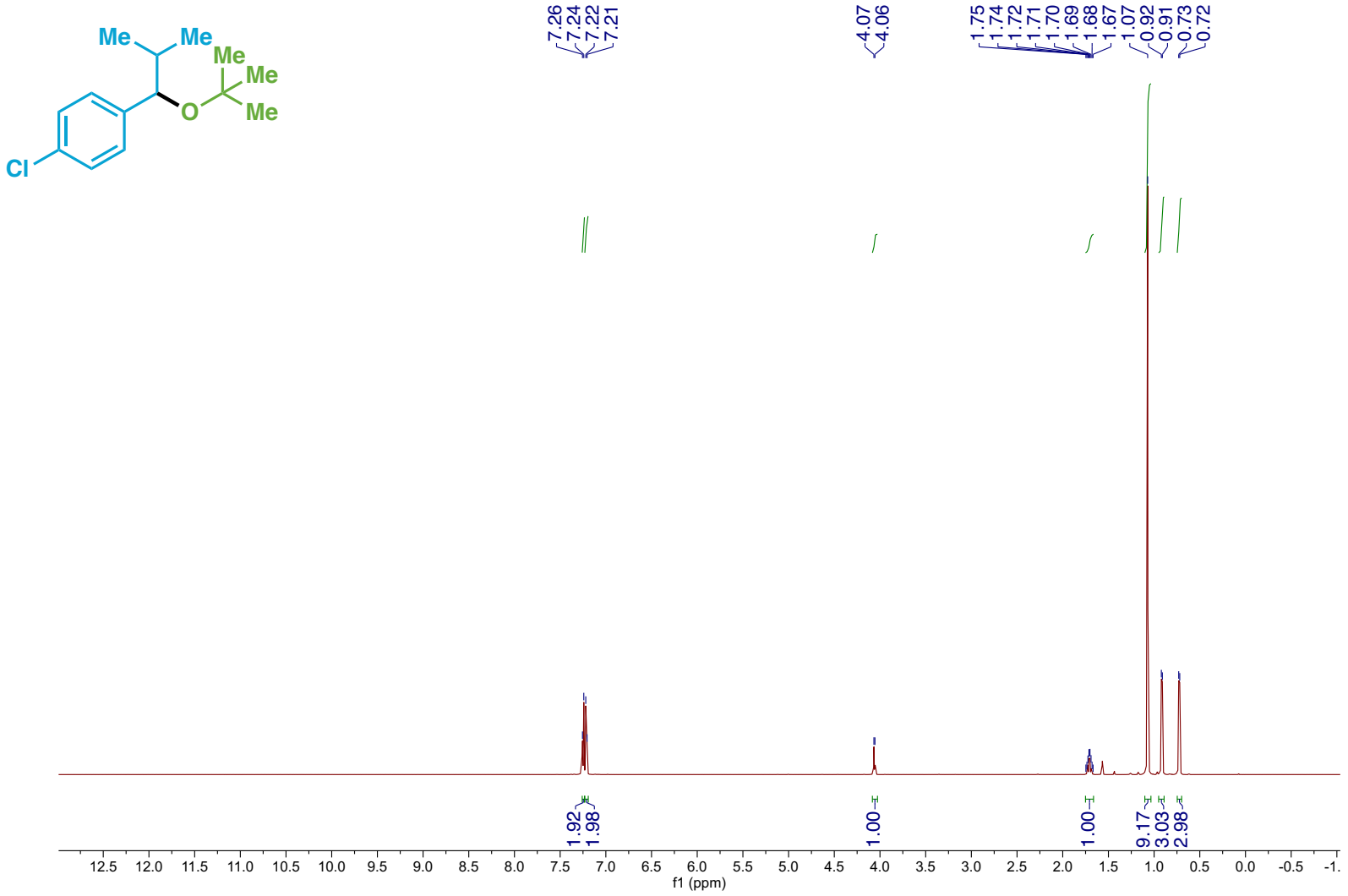
Compound 54 ^{1}H NM



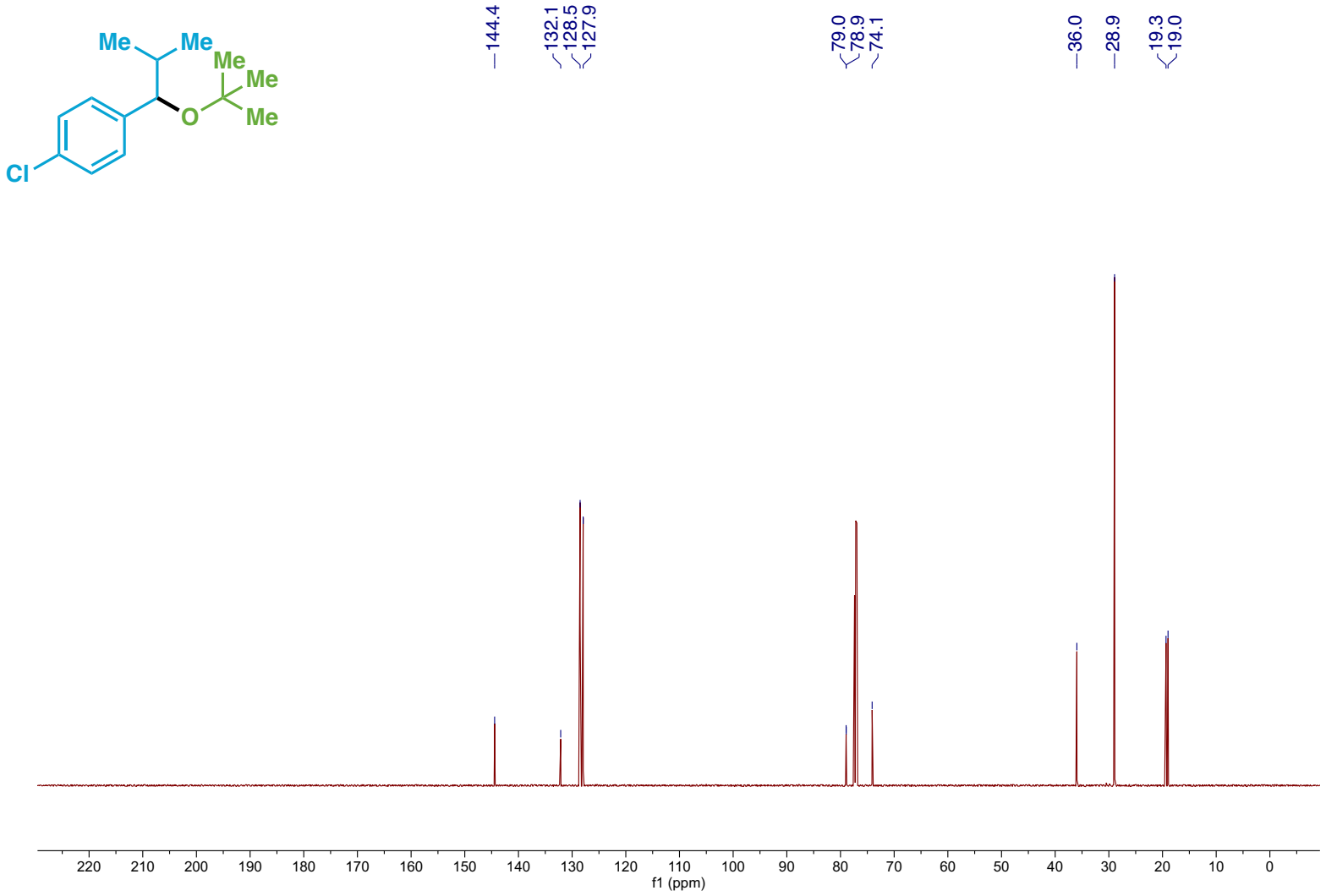
Compound 54 ^{13}C NMR



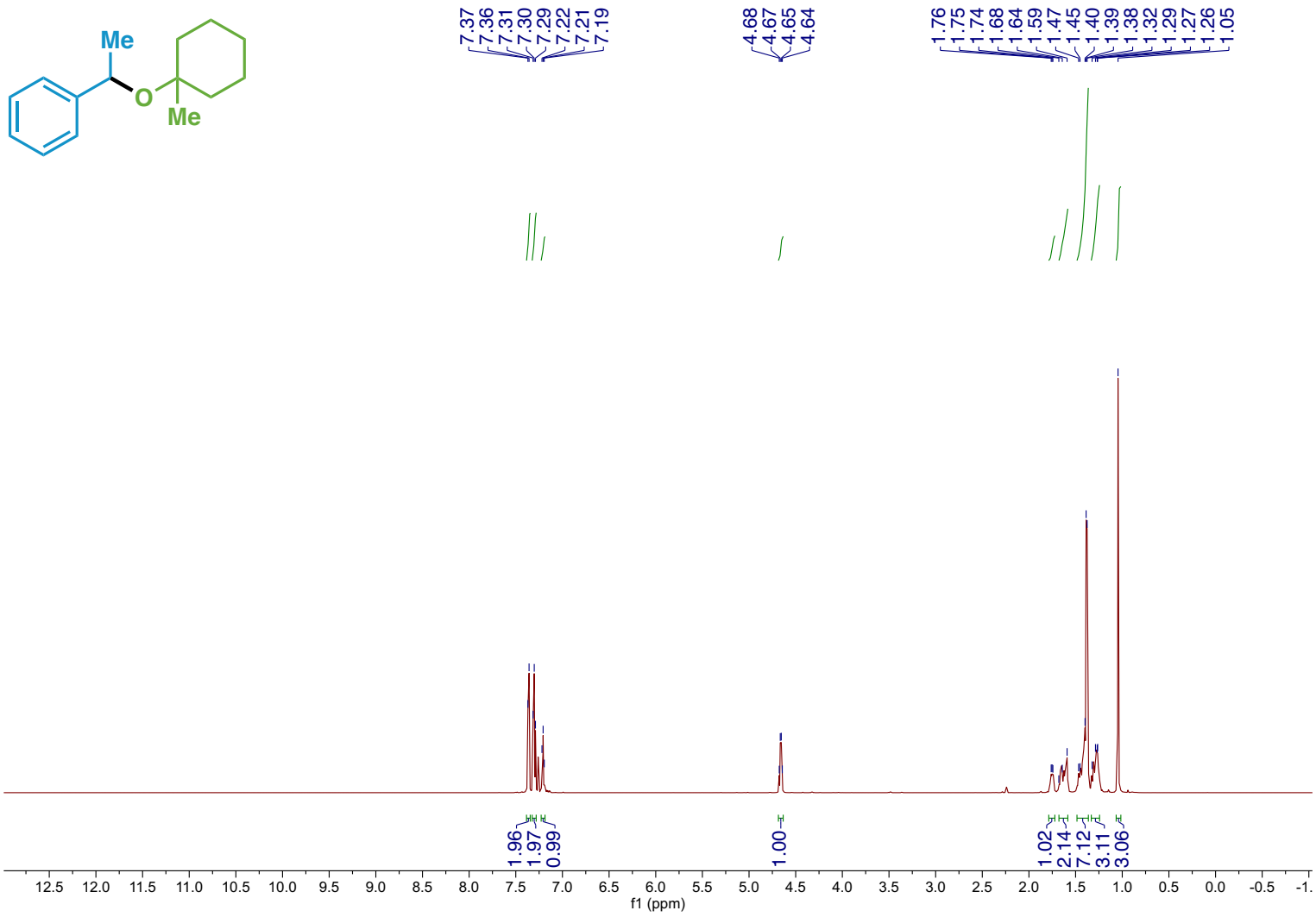
Compound 55 ^{1}H NMR



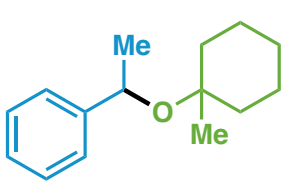
Compound 55 ^{13}C NMR



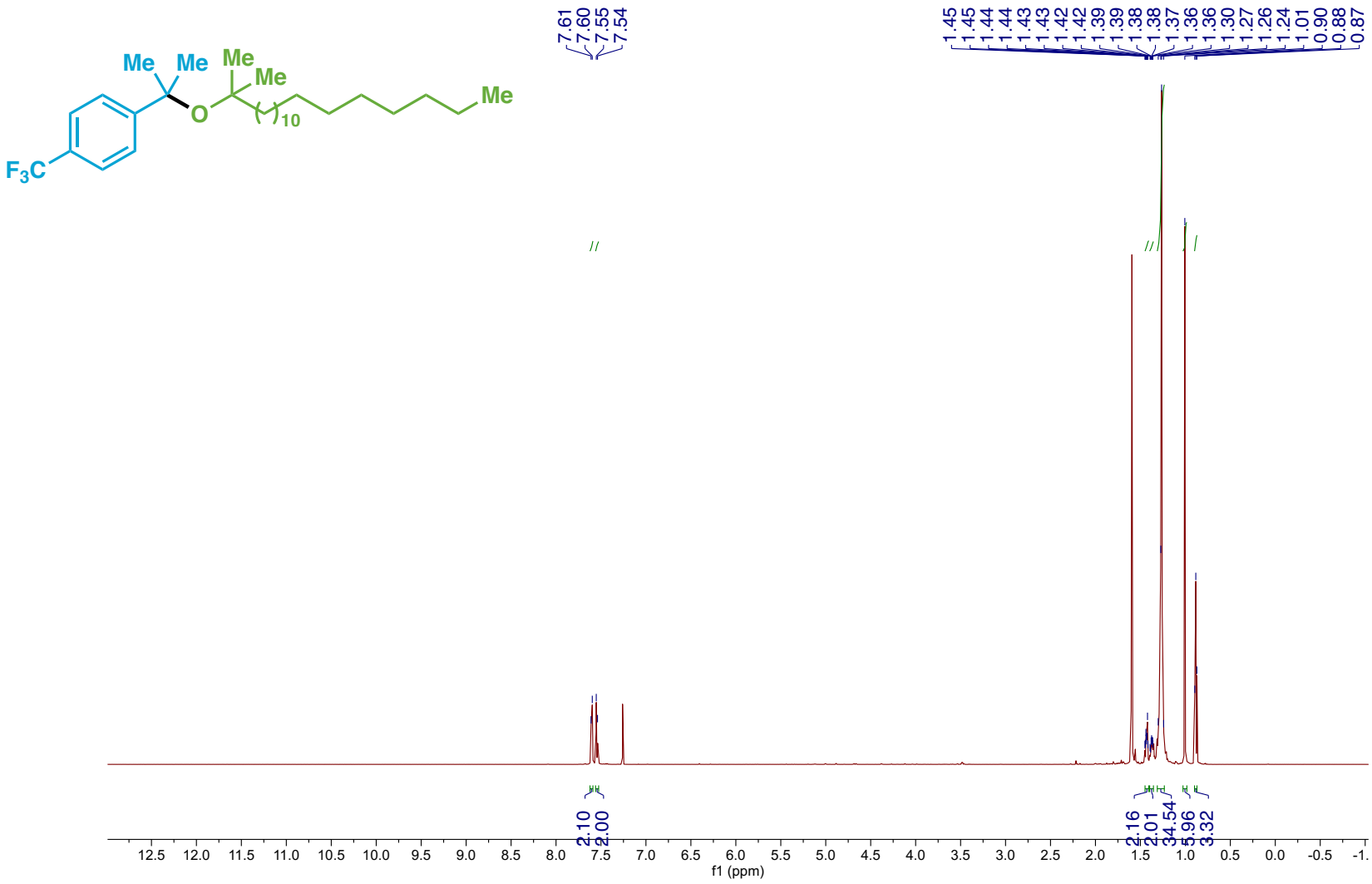
Compound 56 ^{1}H NMR



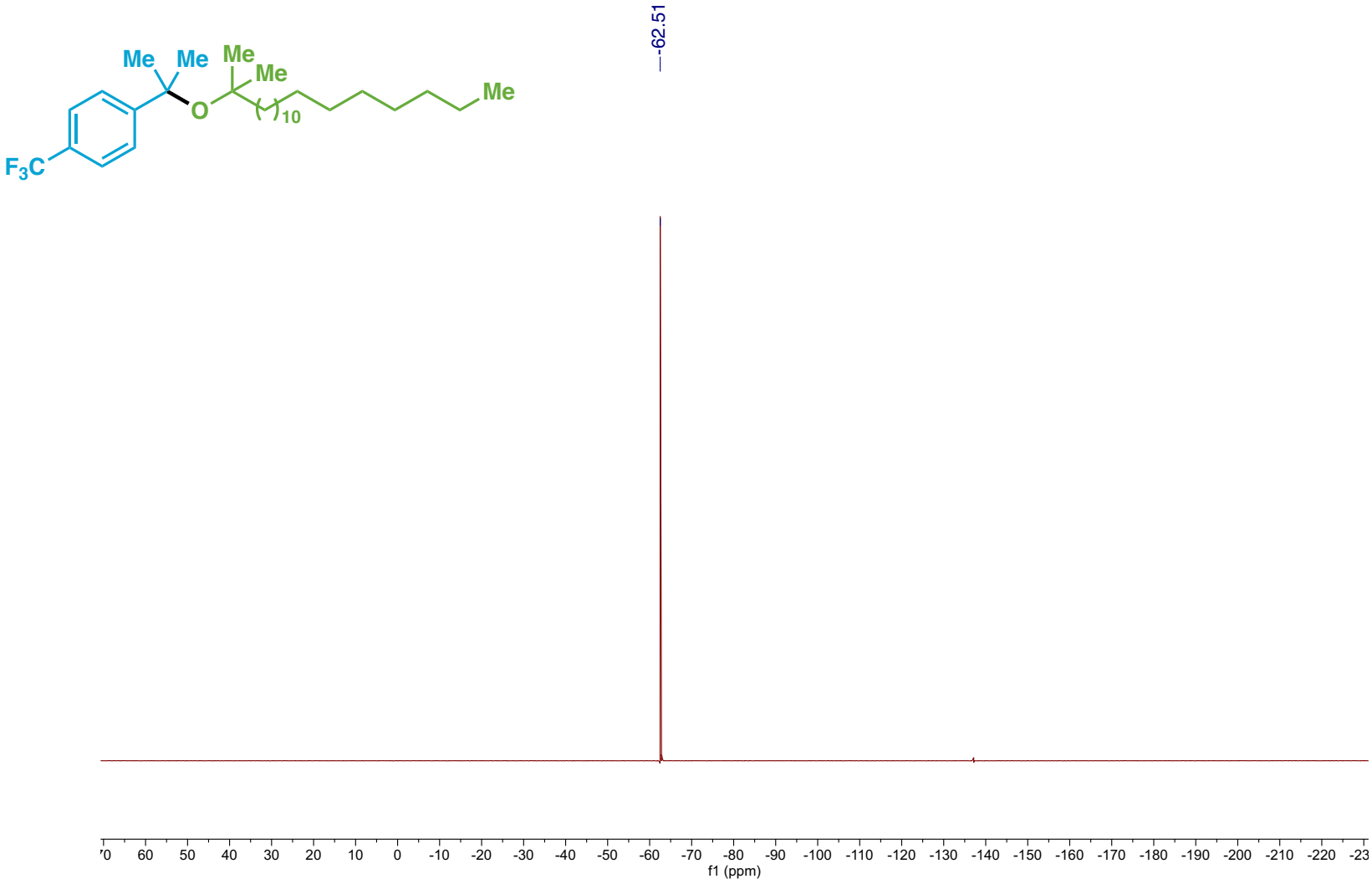
Compound 56 ^{13}C NMR



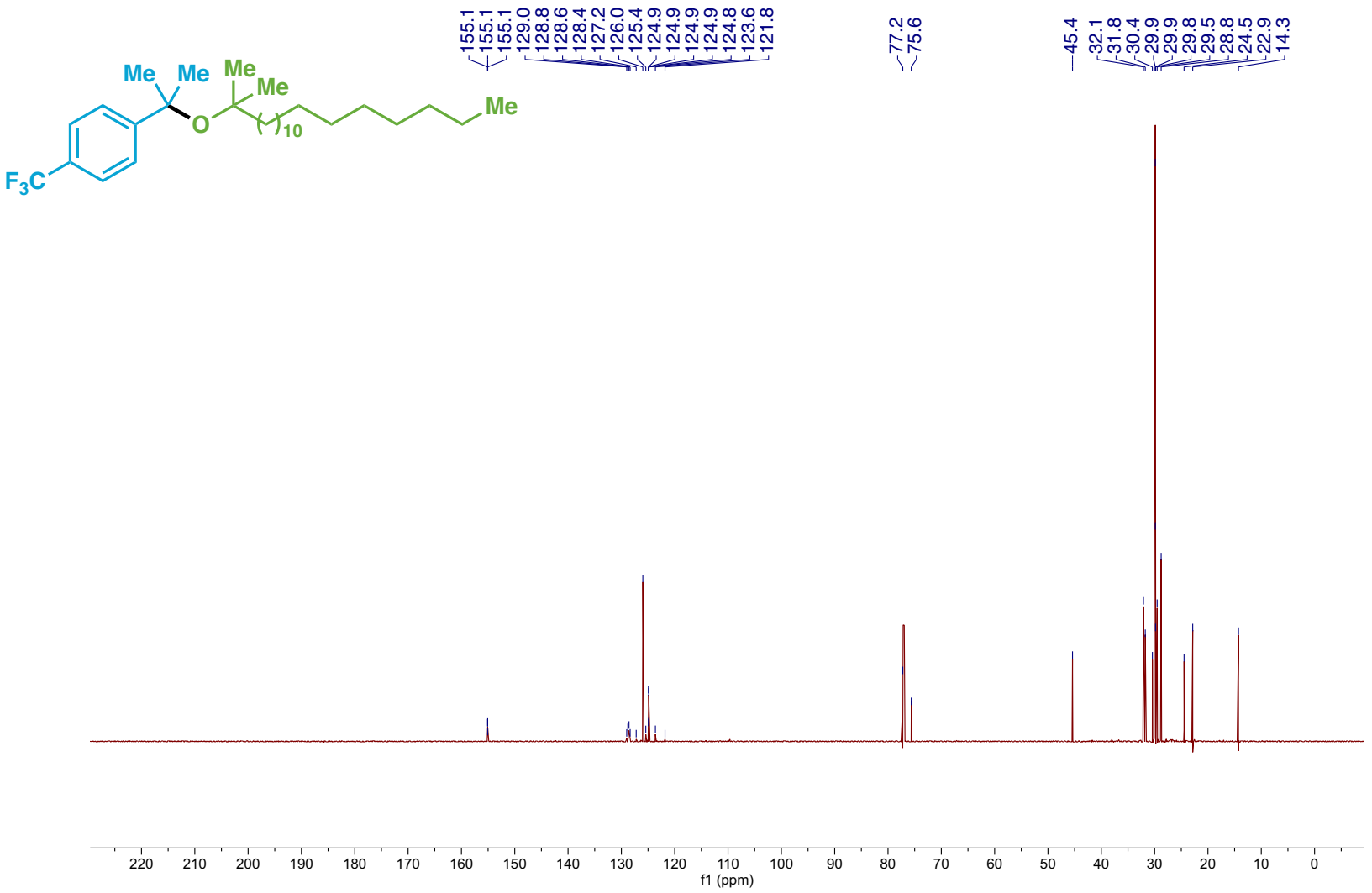
Compound 57 ^{1}H NMR



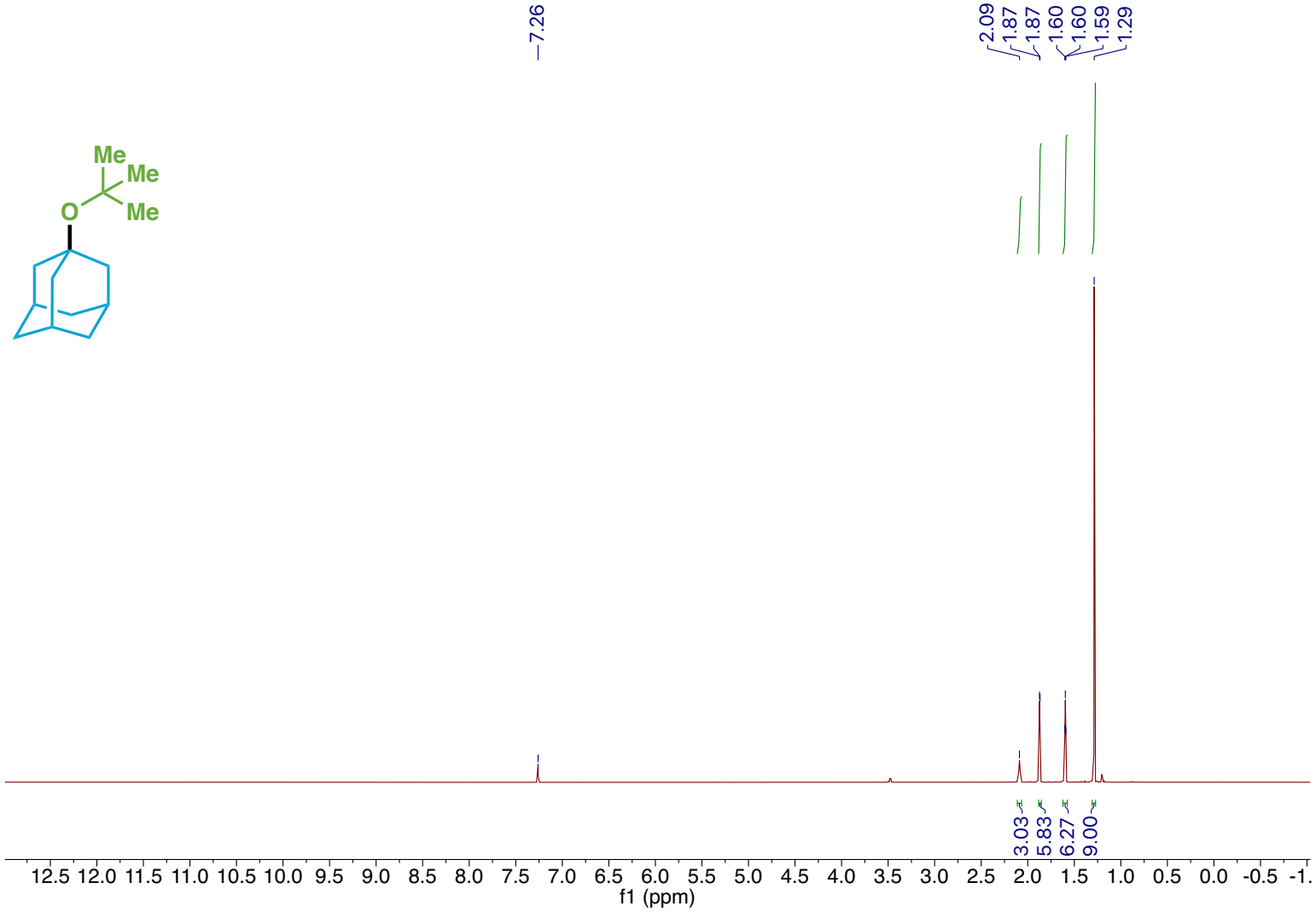
Compound 57 ^{19}F NMR



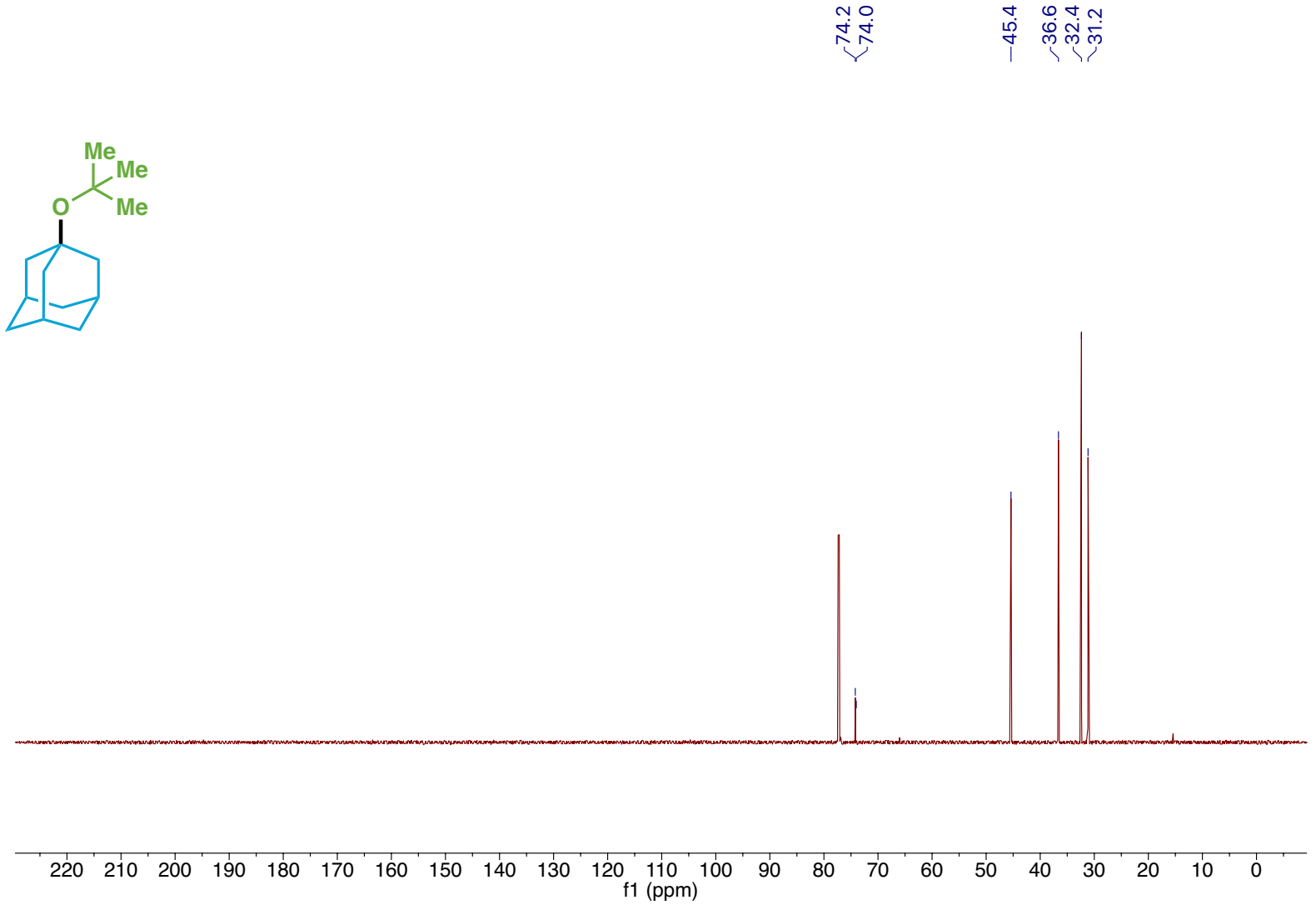
Compound 57 ^{13}C NMR



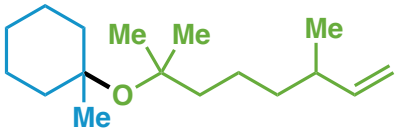
Compound 58 ^{1}H NMR



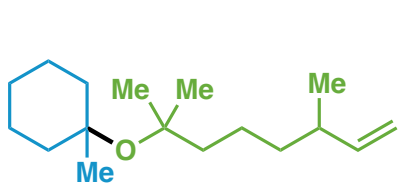
Compound 58 ^{13}C NMR



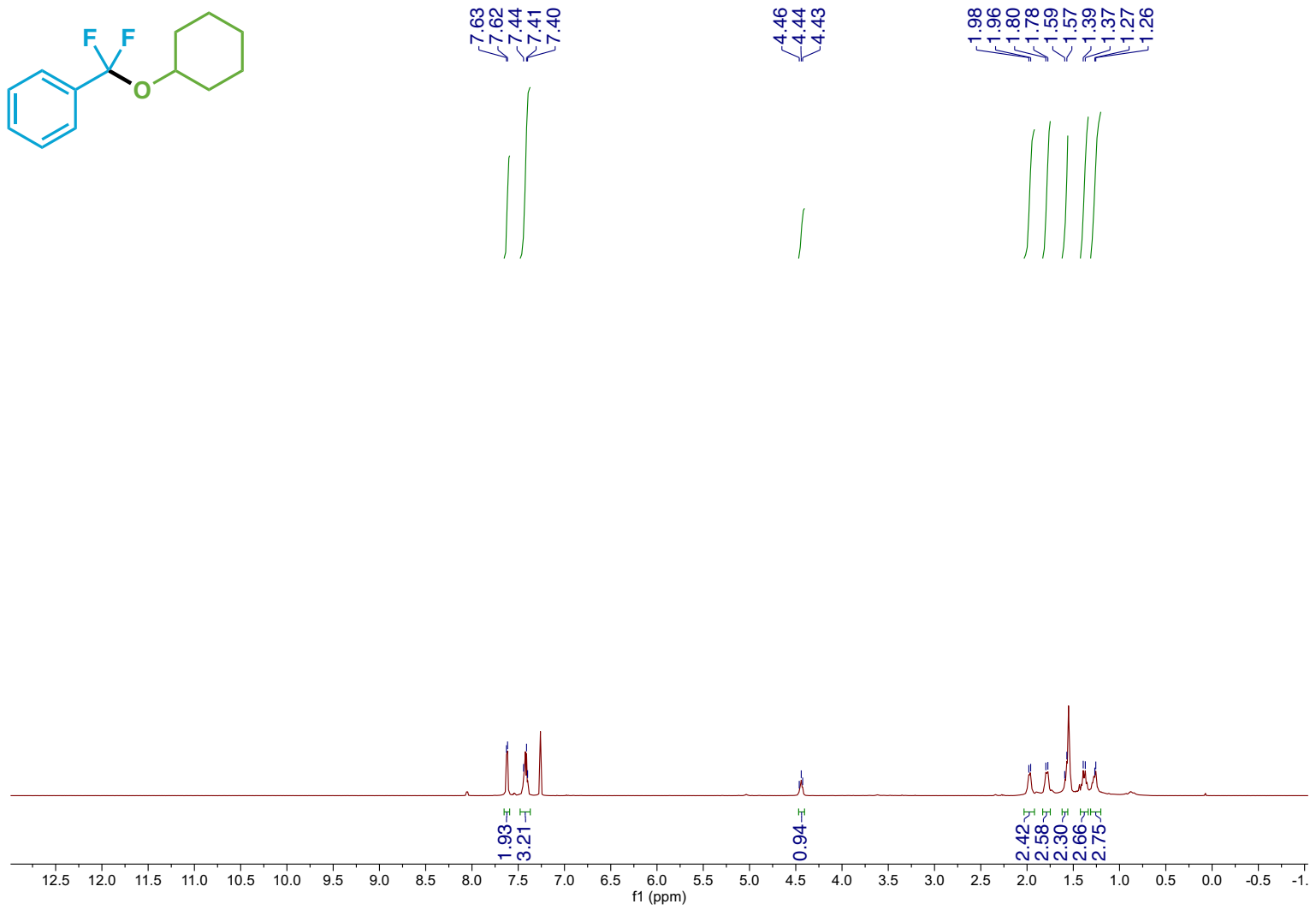
Compound 59 ^{1}H NMR



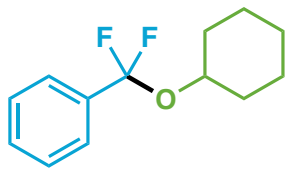
Compound 59 ^{13}C NMR



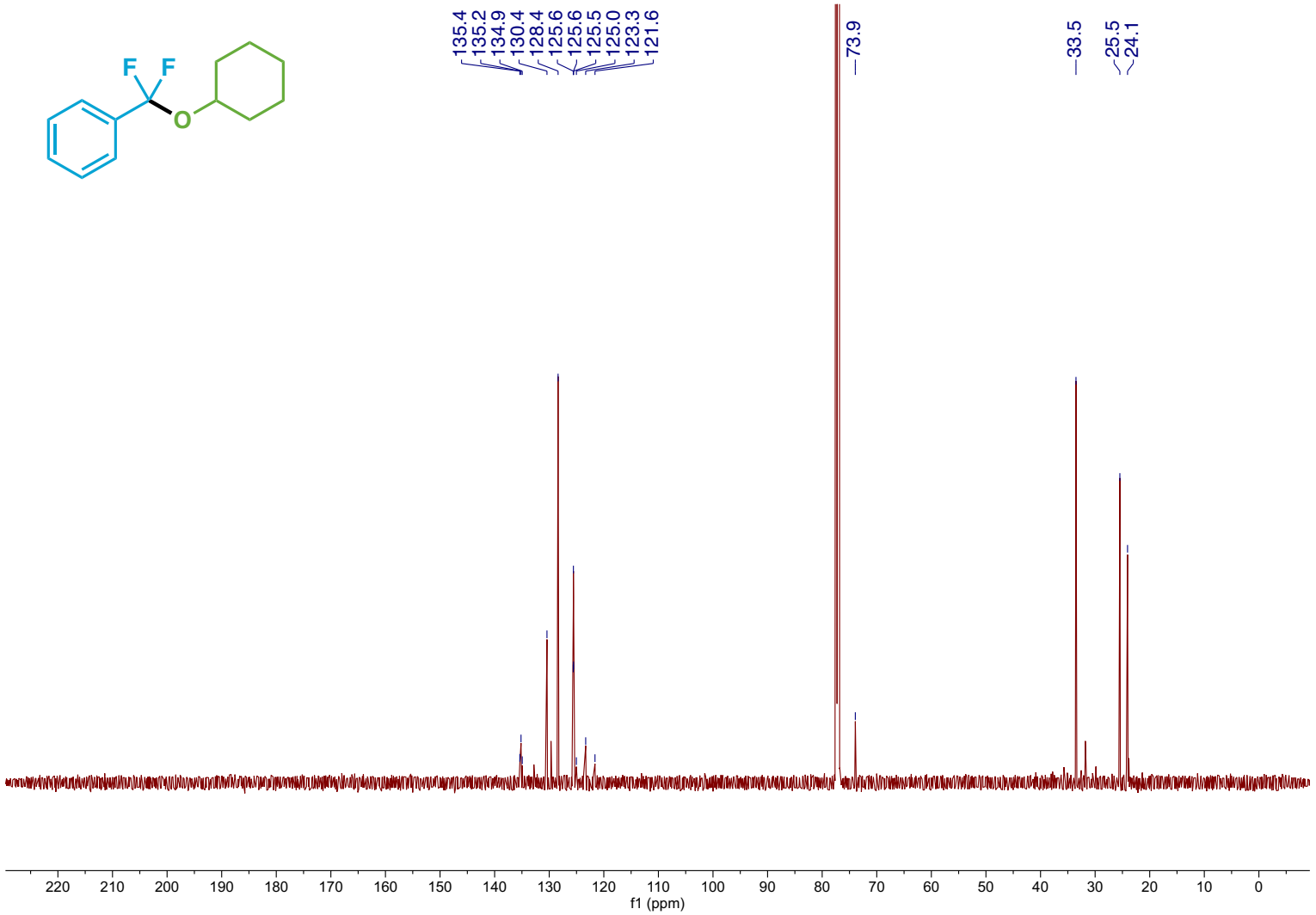
Compound 60 ^{1}H NMR



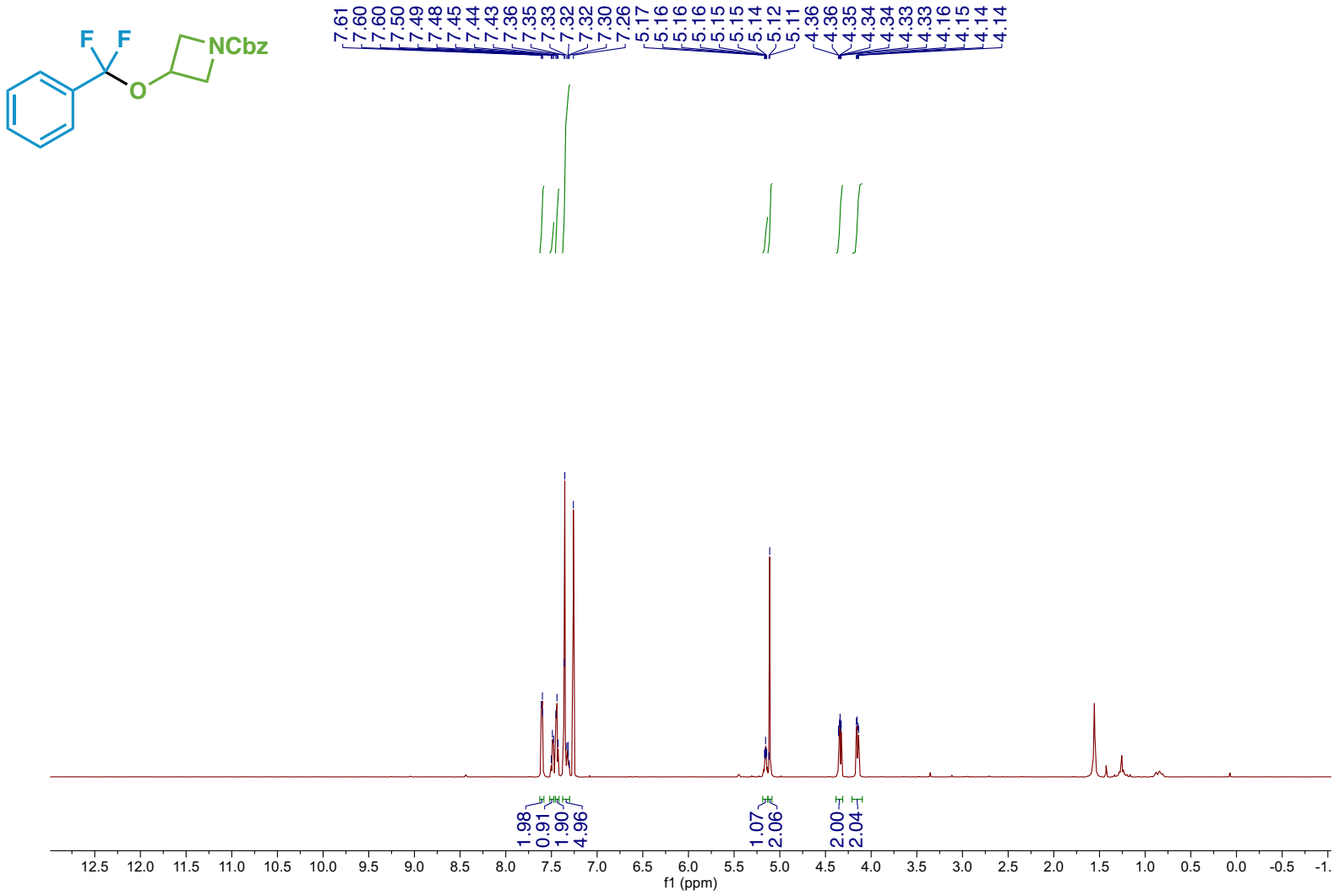
Compound 60 ^{19}F NMR



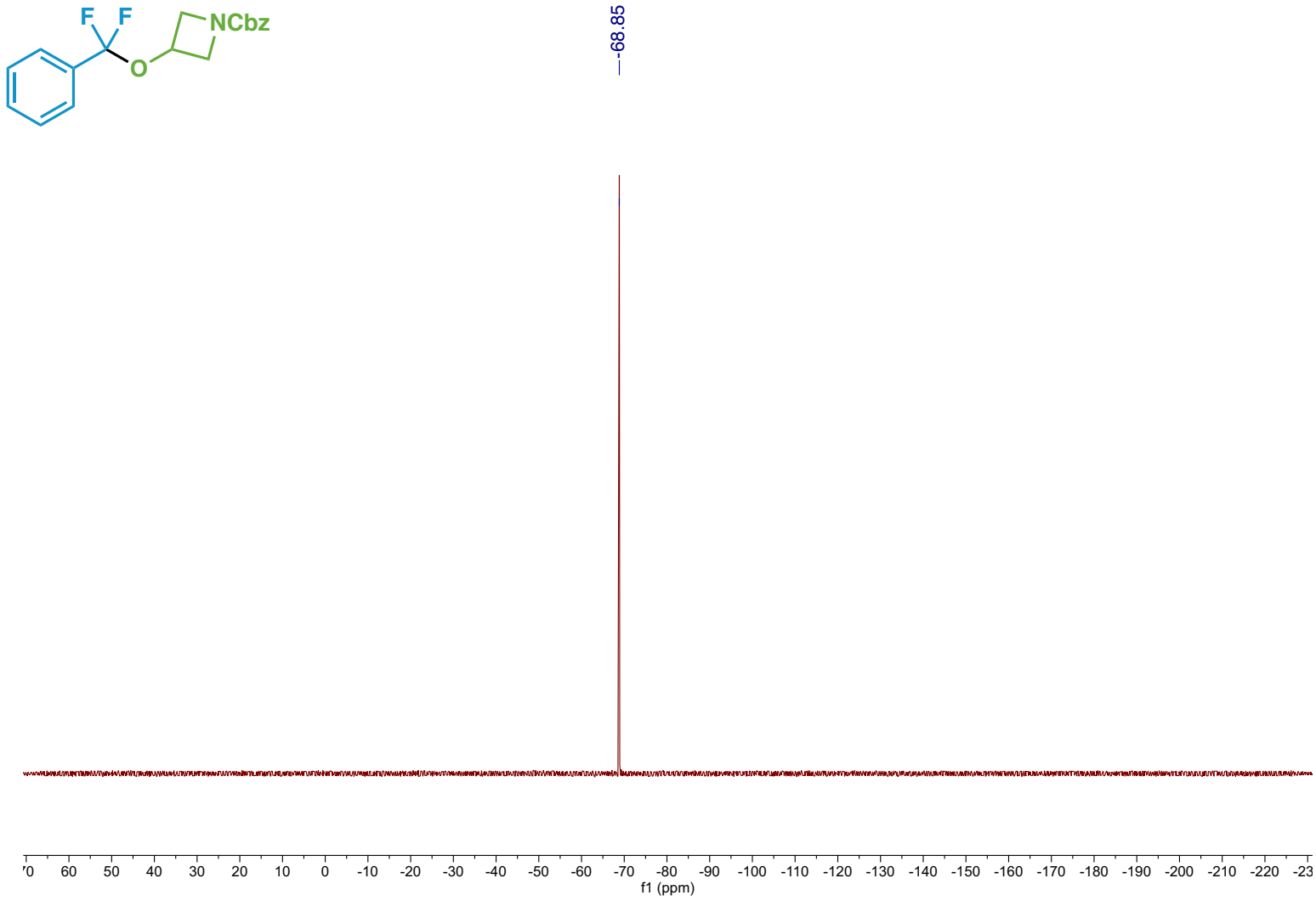
Compound 60 ^{13}C NMR



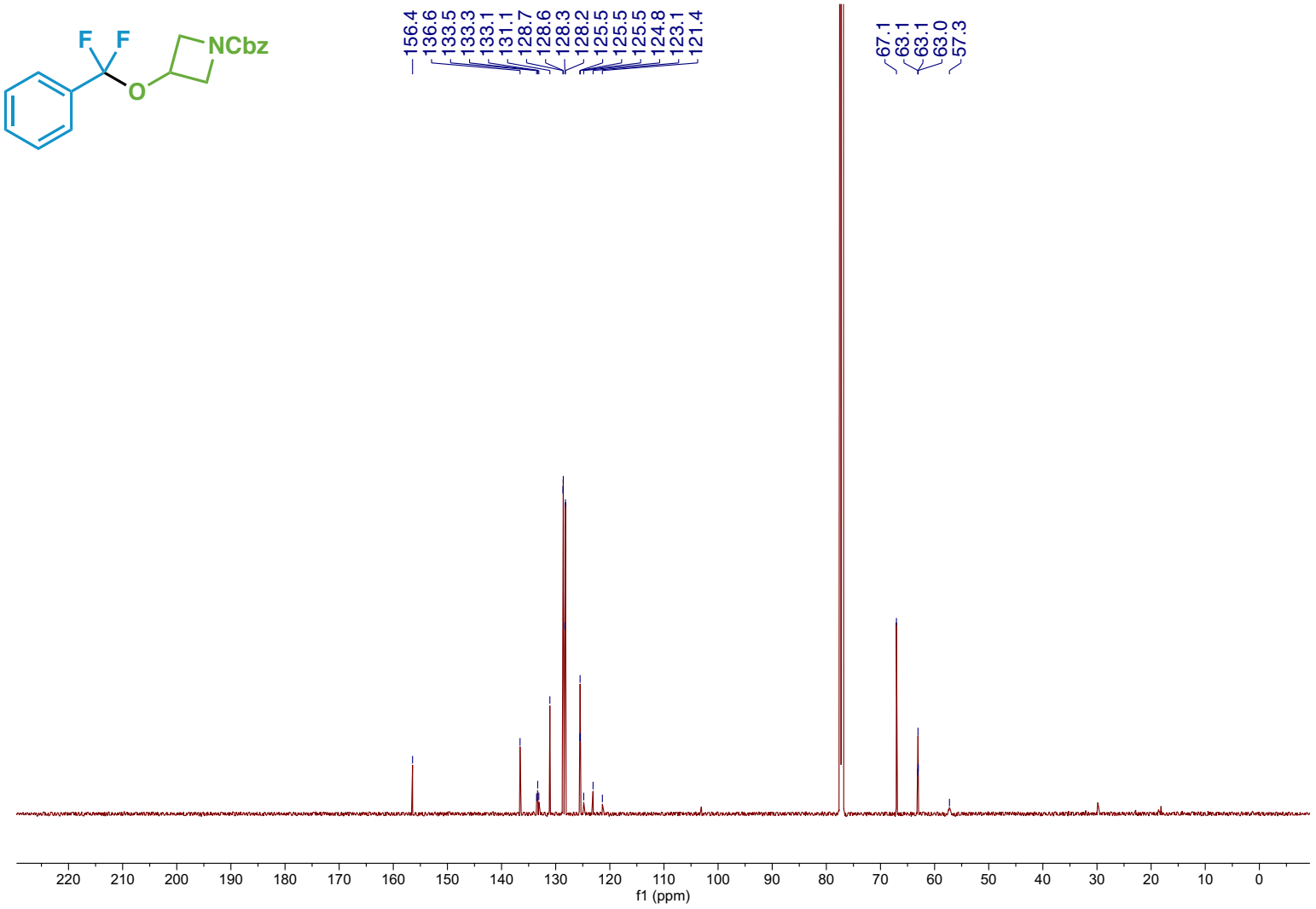
Compound 61 ^{1}H NMR



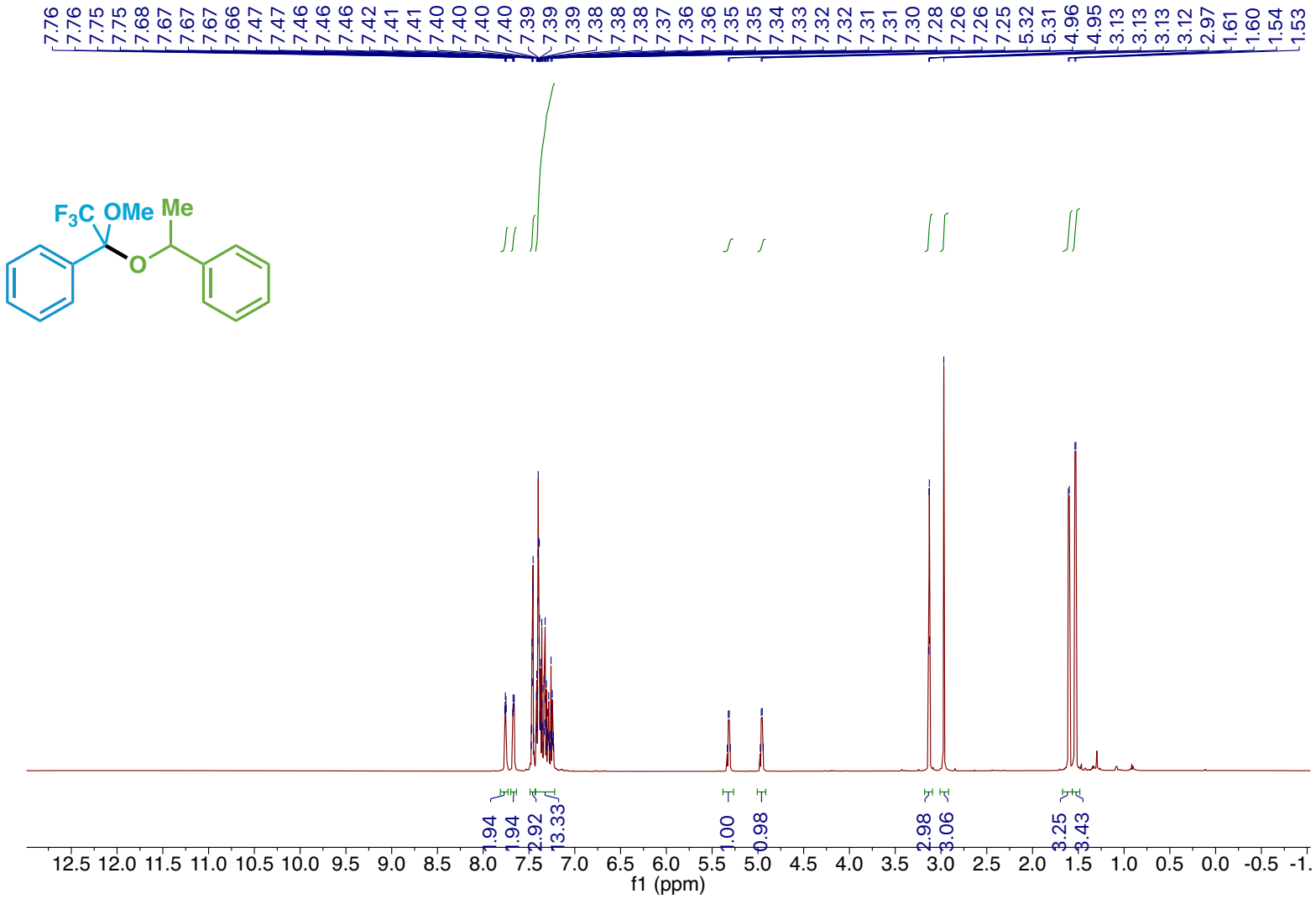
Compound 61 ^{19}F NMR



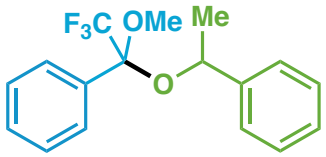
Compound 61 ^{13}C NMR



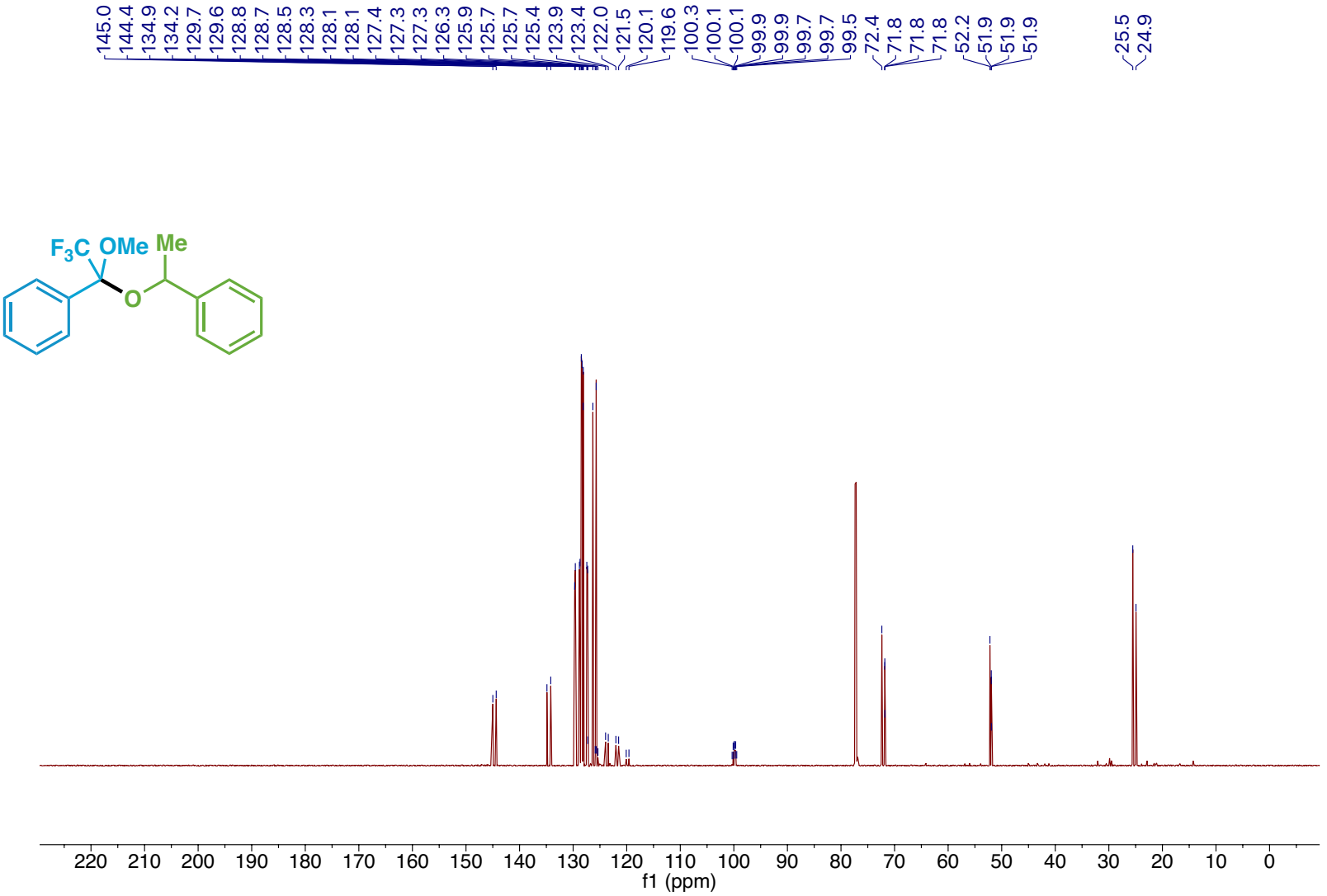
Compound 62 ^{1}H NMR



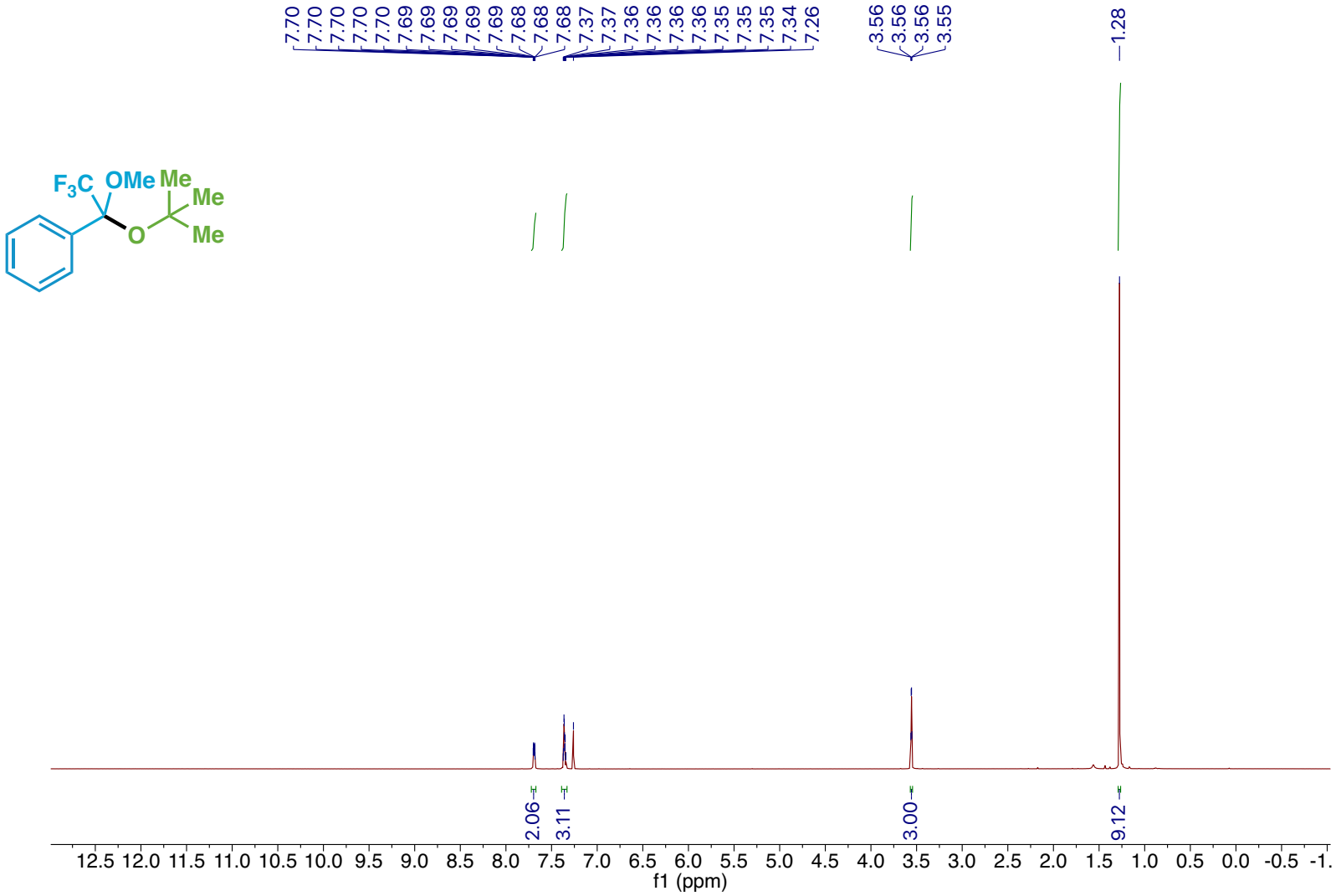
Compound 62 ^{19}F NMR



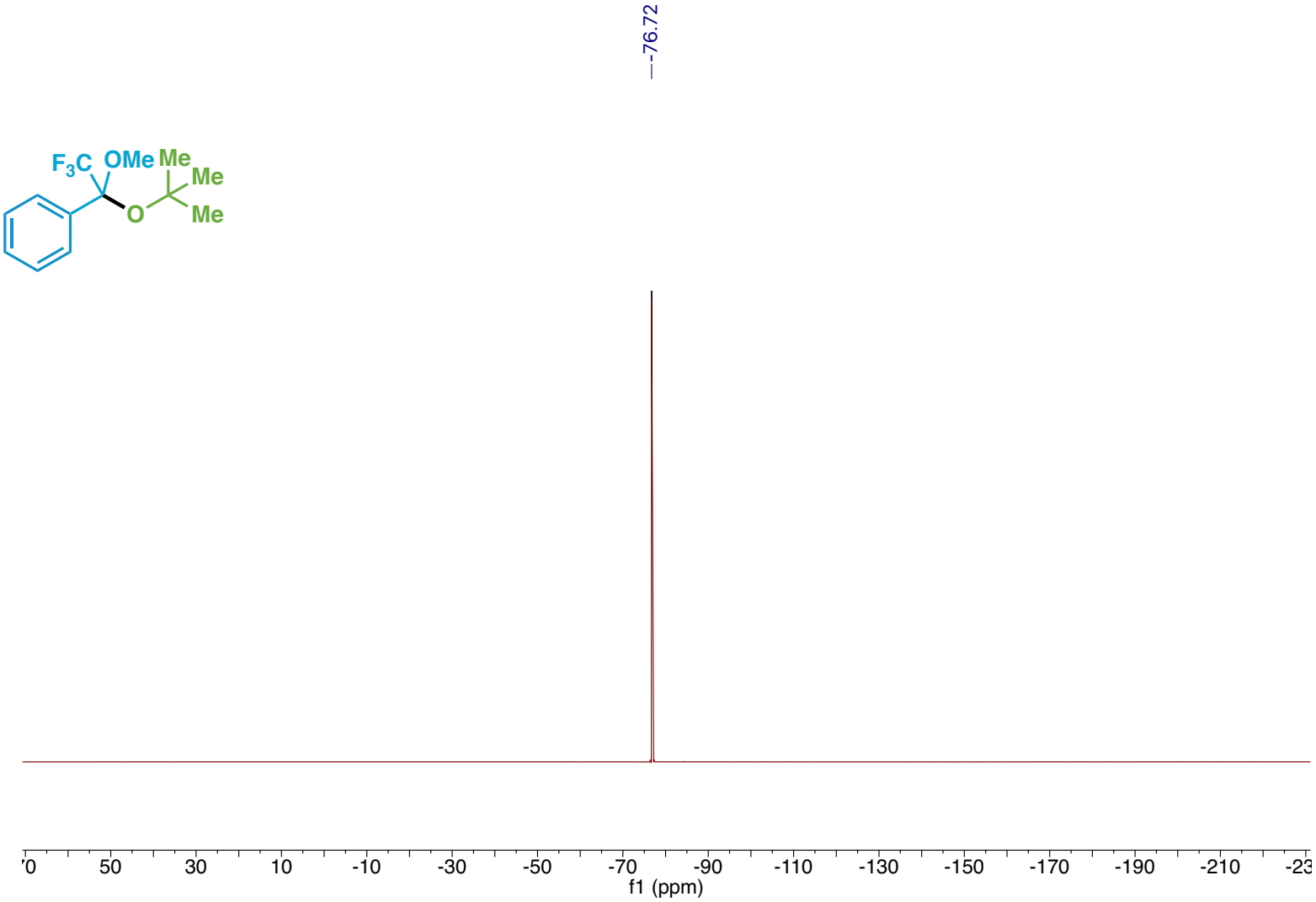
Compound 62 ^{13}C NMR



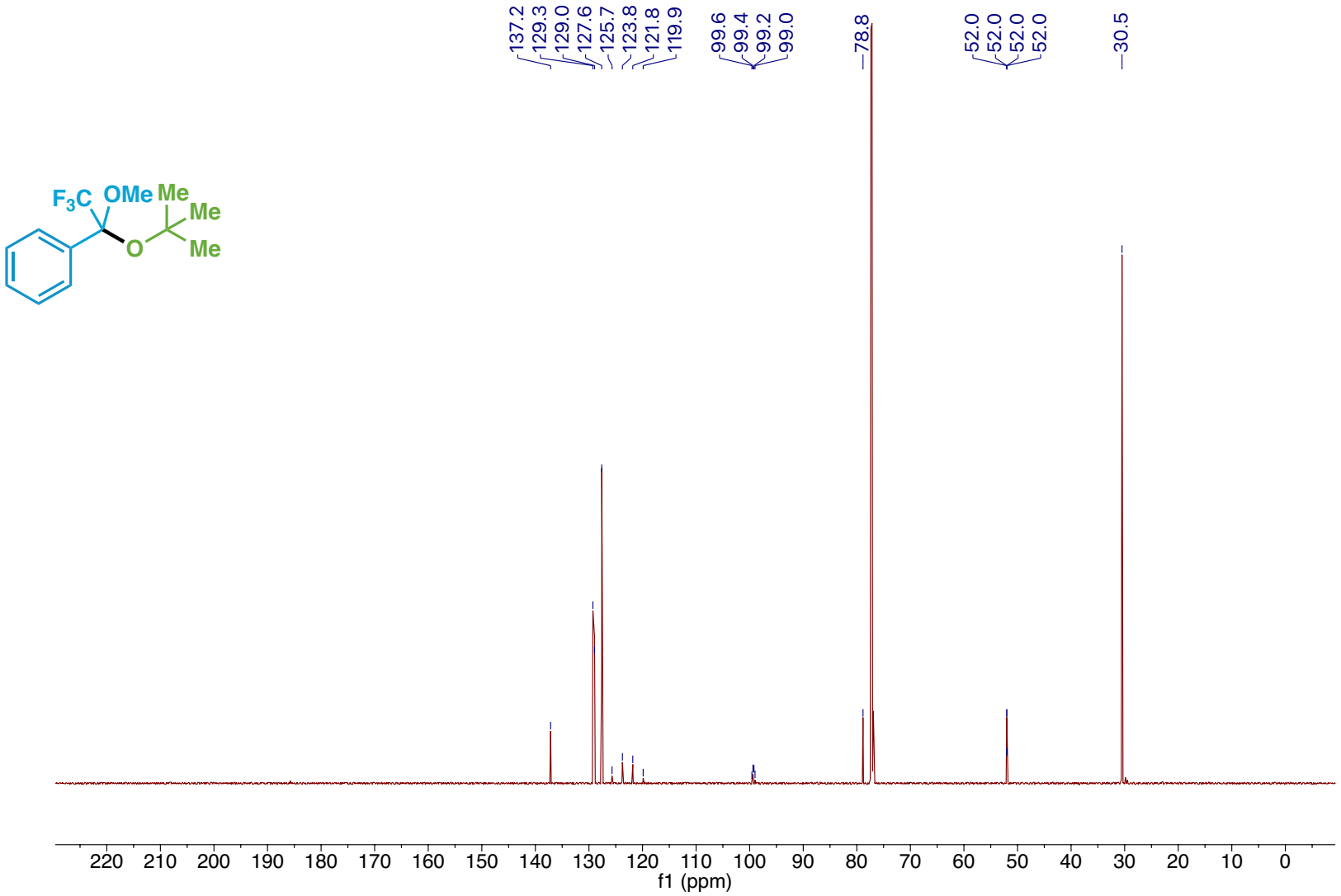
Compound 63 ^{1}H NMR



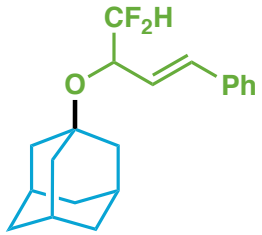
Compound 63 ^{19}F NMR



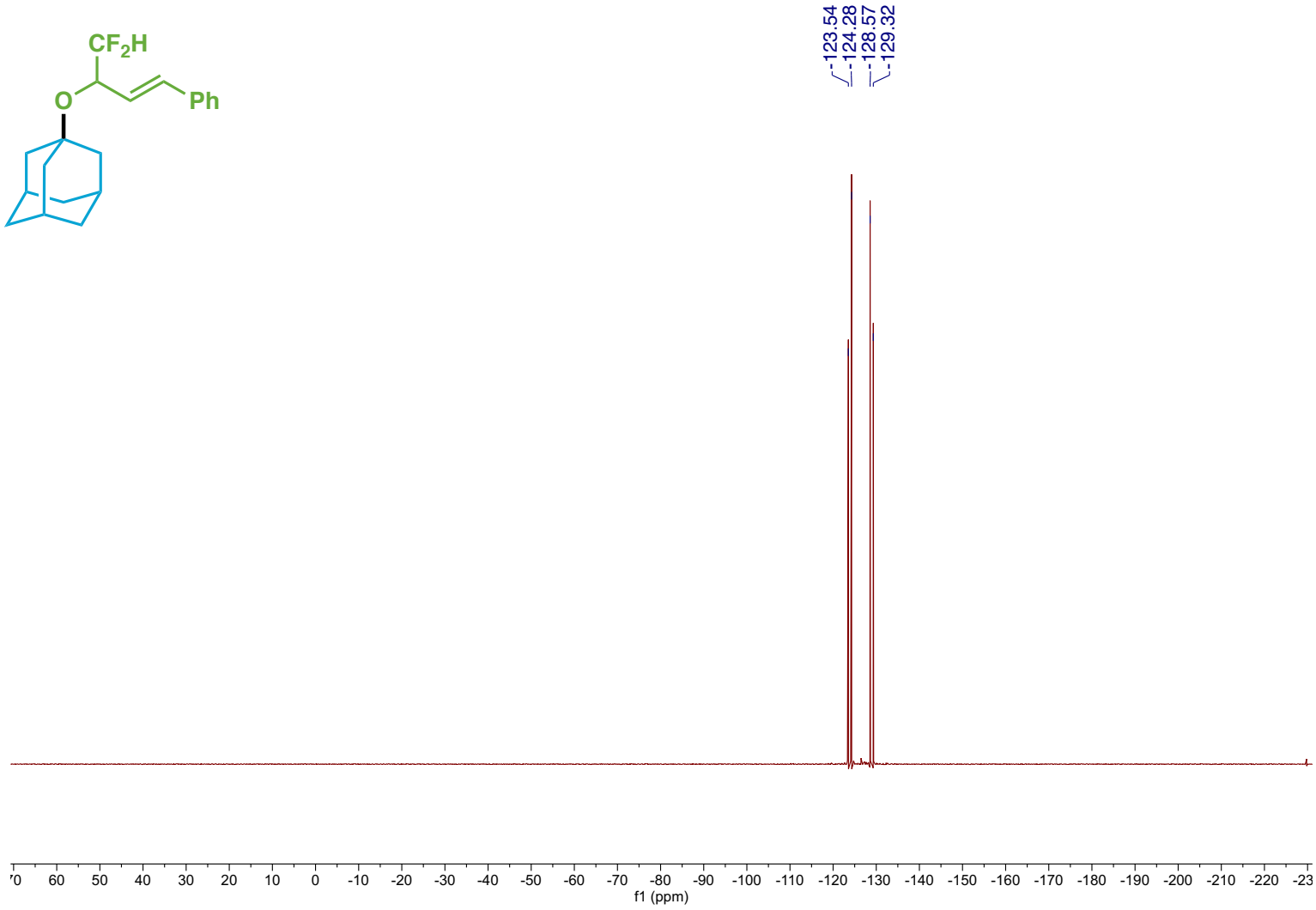
Compound 63 ^{13}C NMR



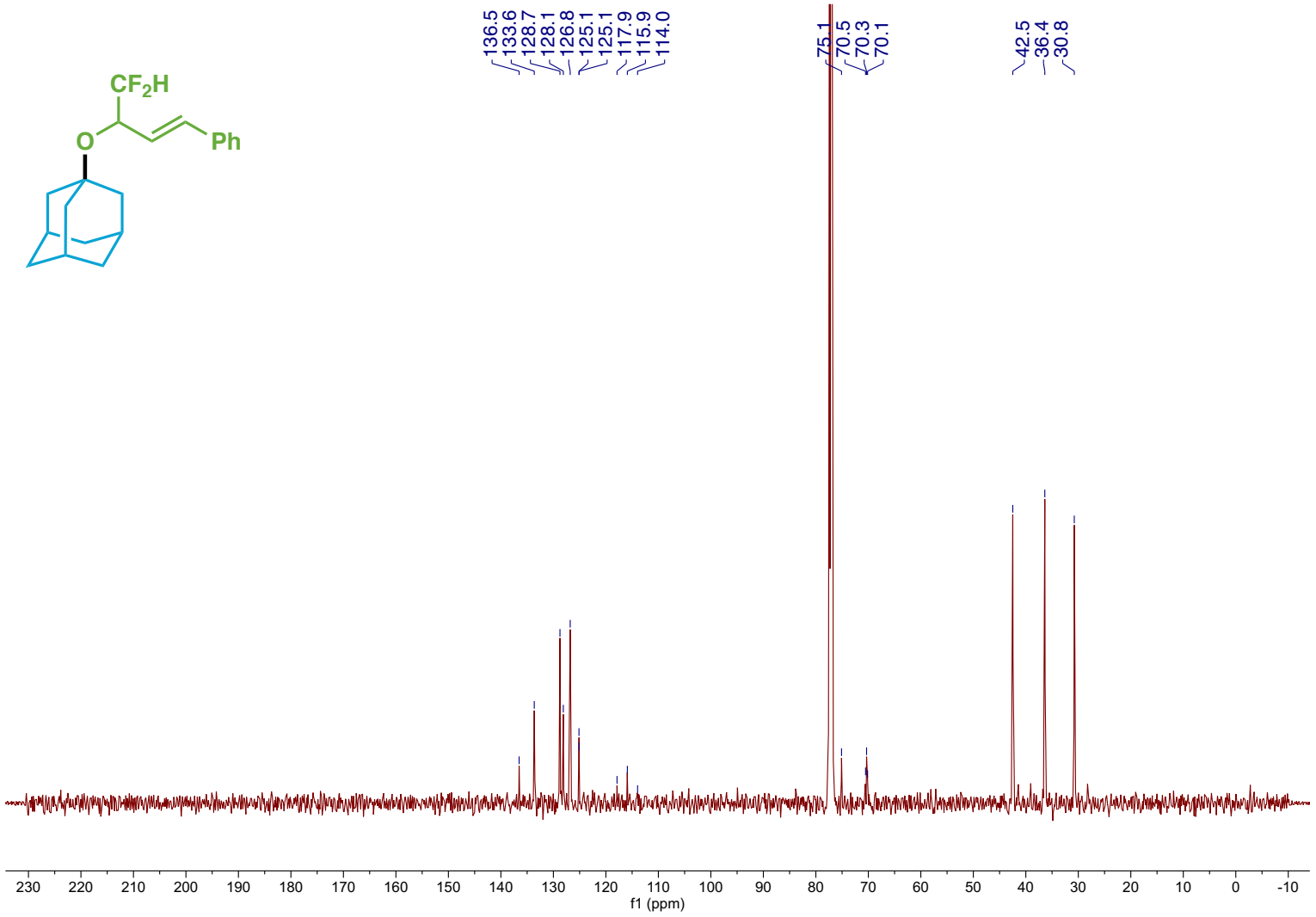
Compound 64 ^{1}H NMR



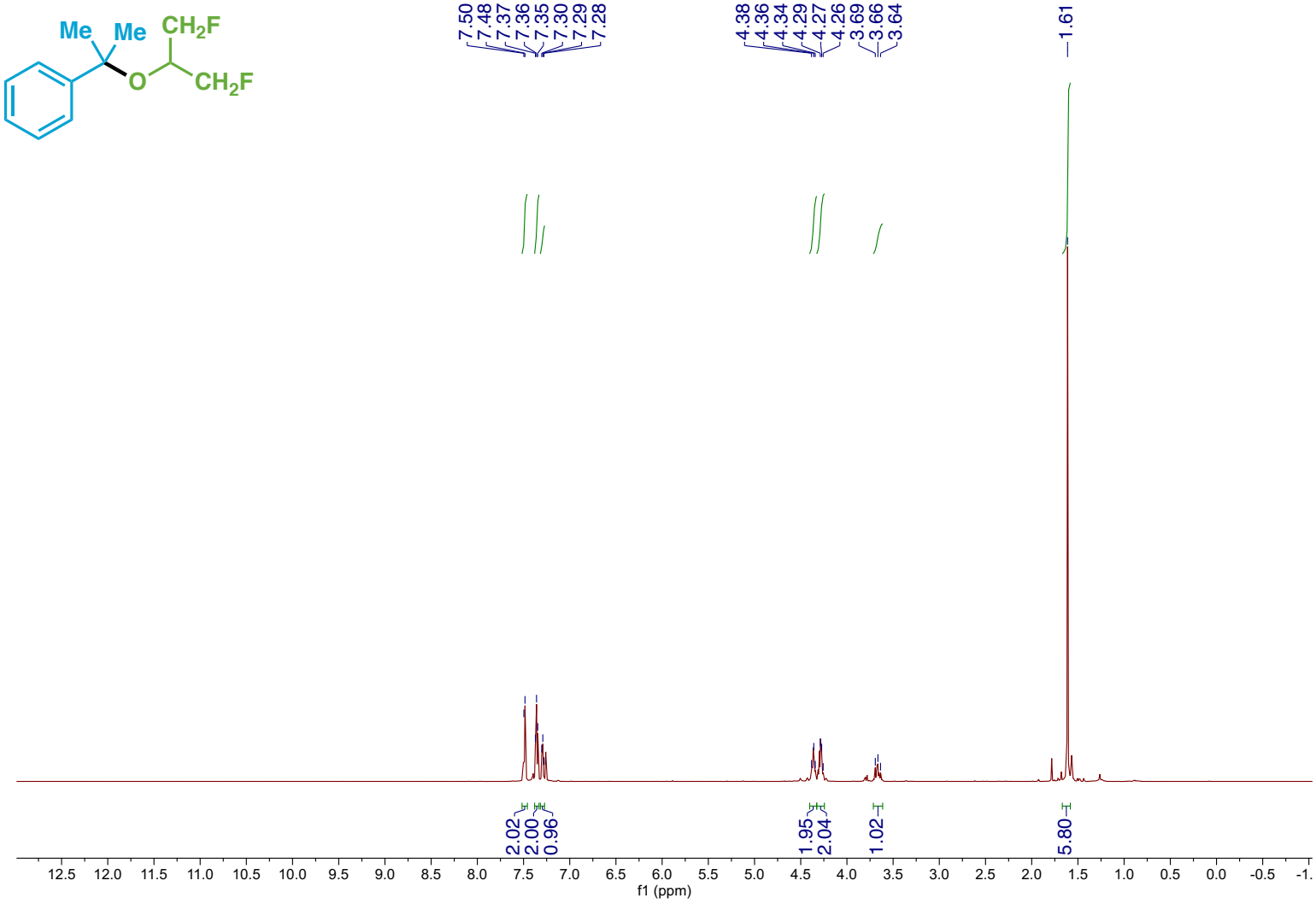
Compound 64 ^{19}F NMR



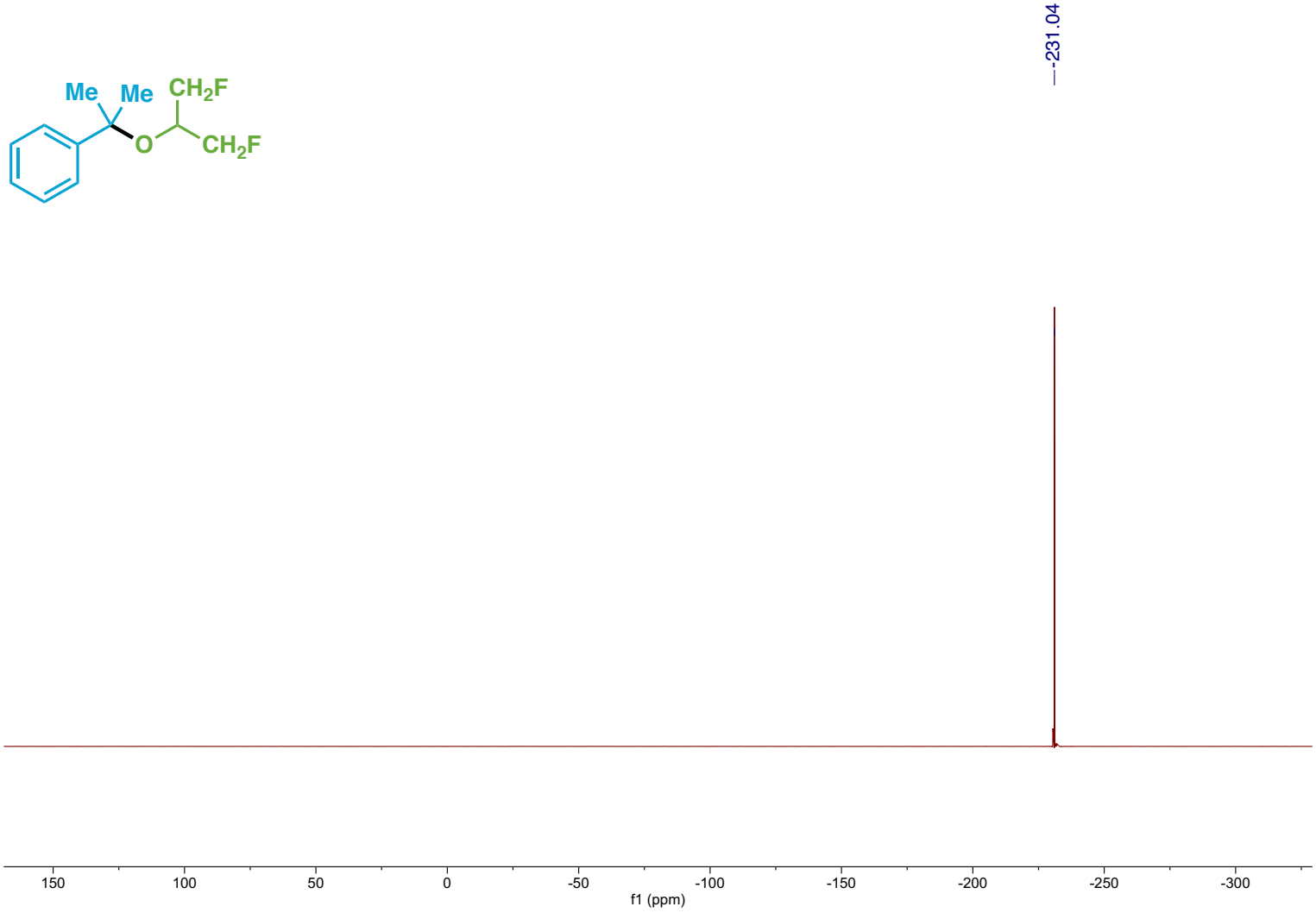
Compound 64 ^{13}C NMR



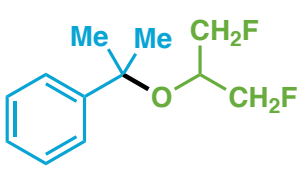
Compound 65 ^{1}H NMR



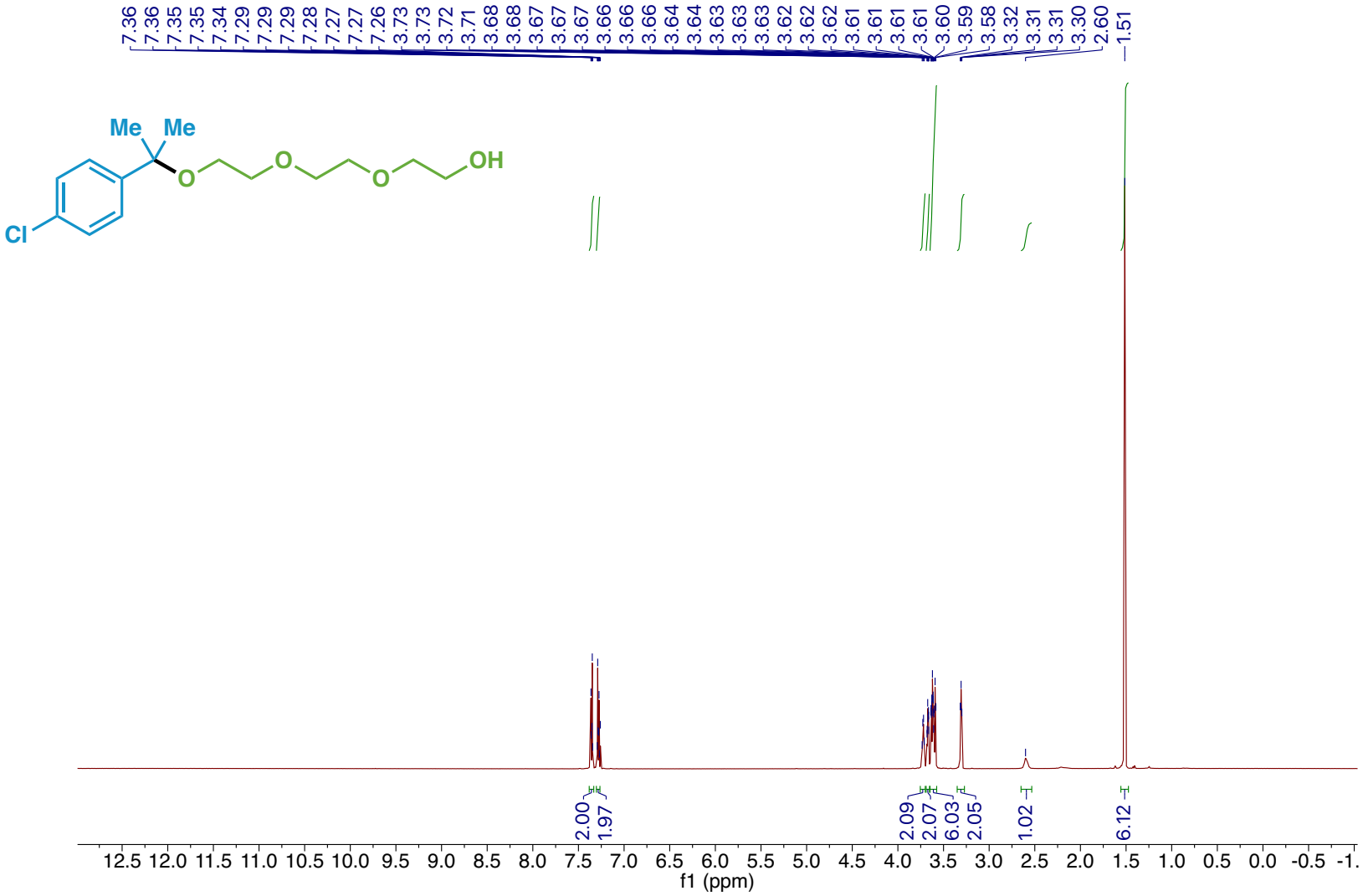
Compound 65 ^{19}F NMR



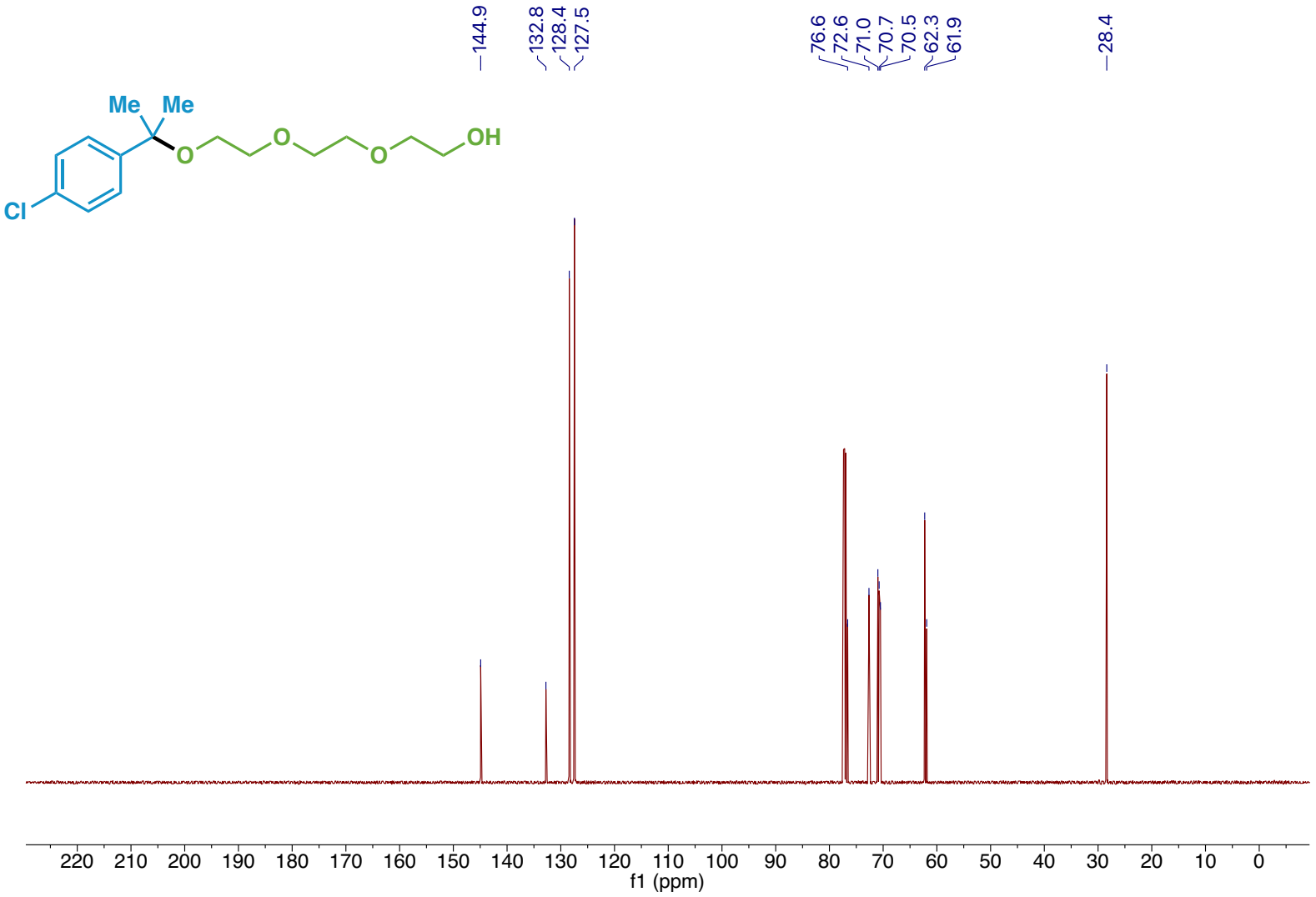
Compound 65 ^{13}C NMR



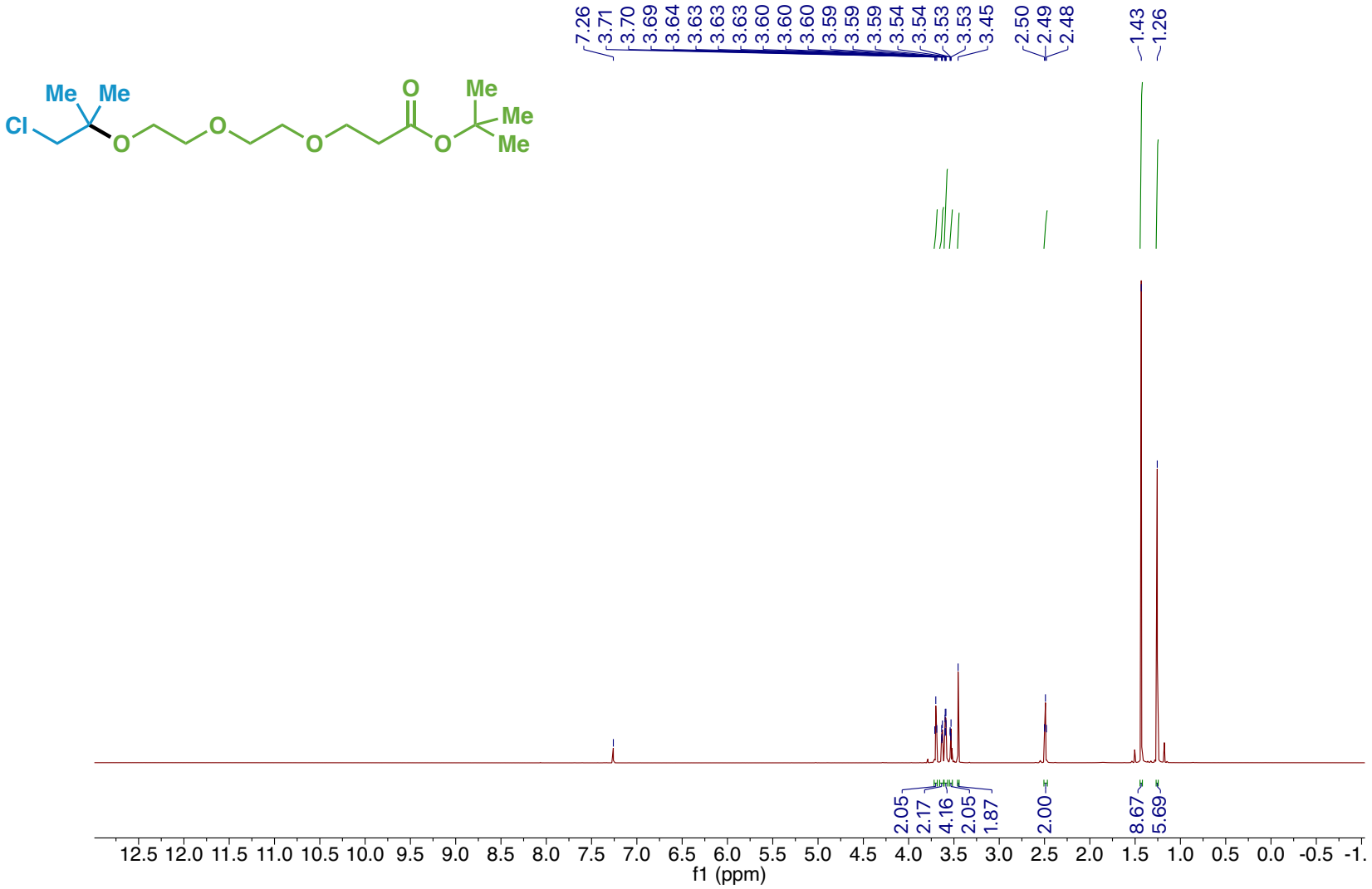
Compound 66 ^{1}H NMR



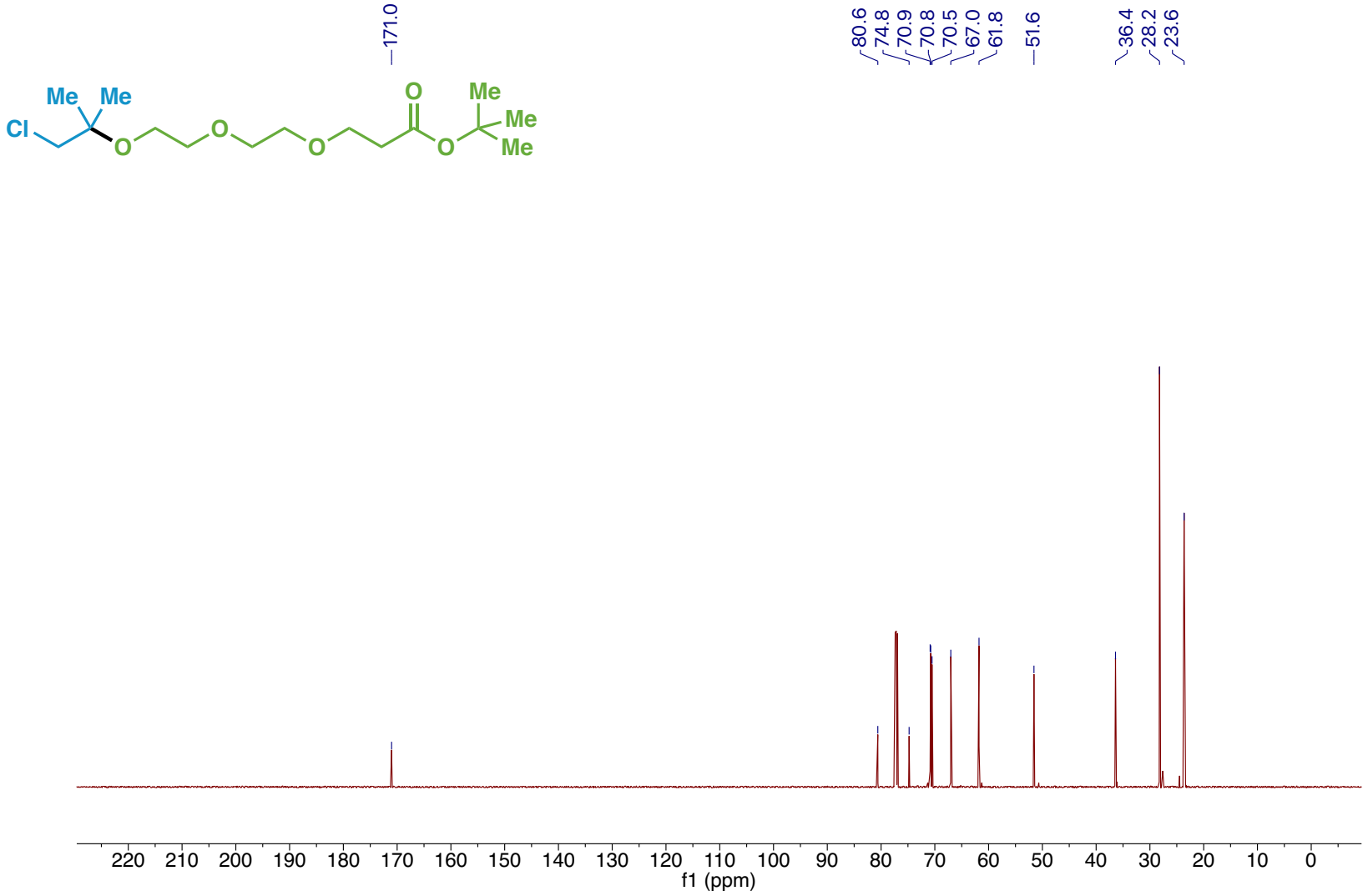
Compound 66 ^{13}C NMR



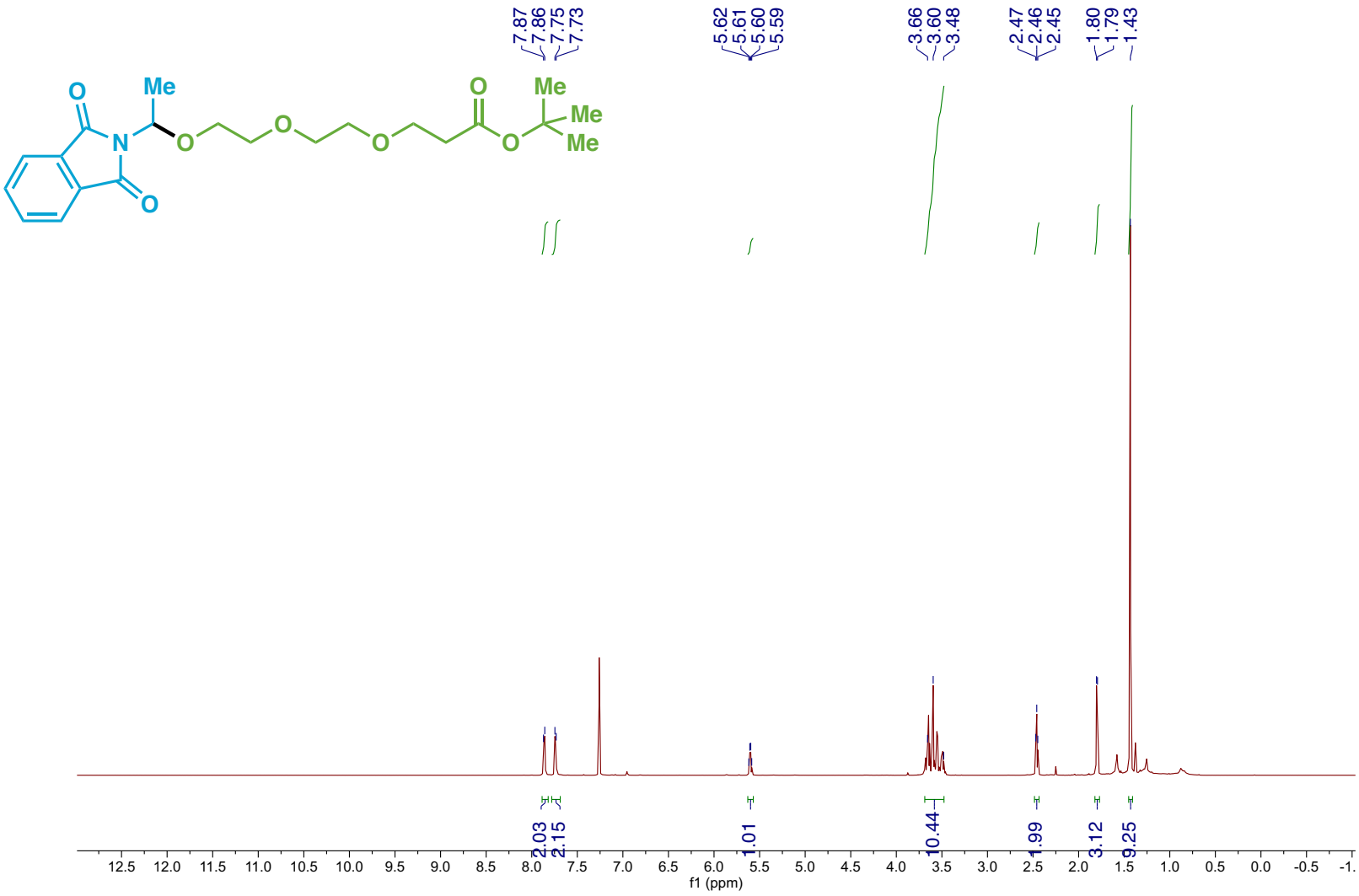
Compound 67 ^{1}H NMR



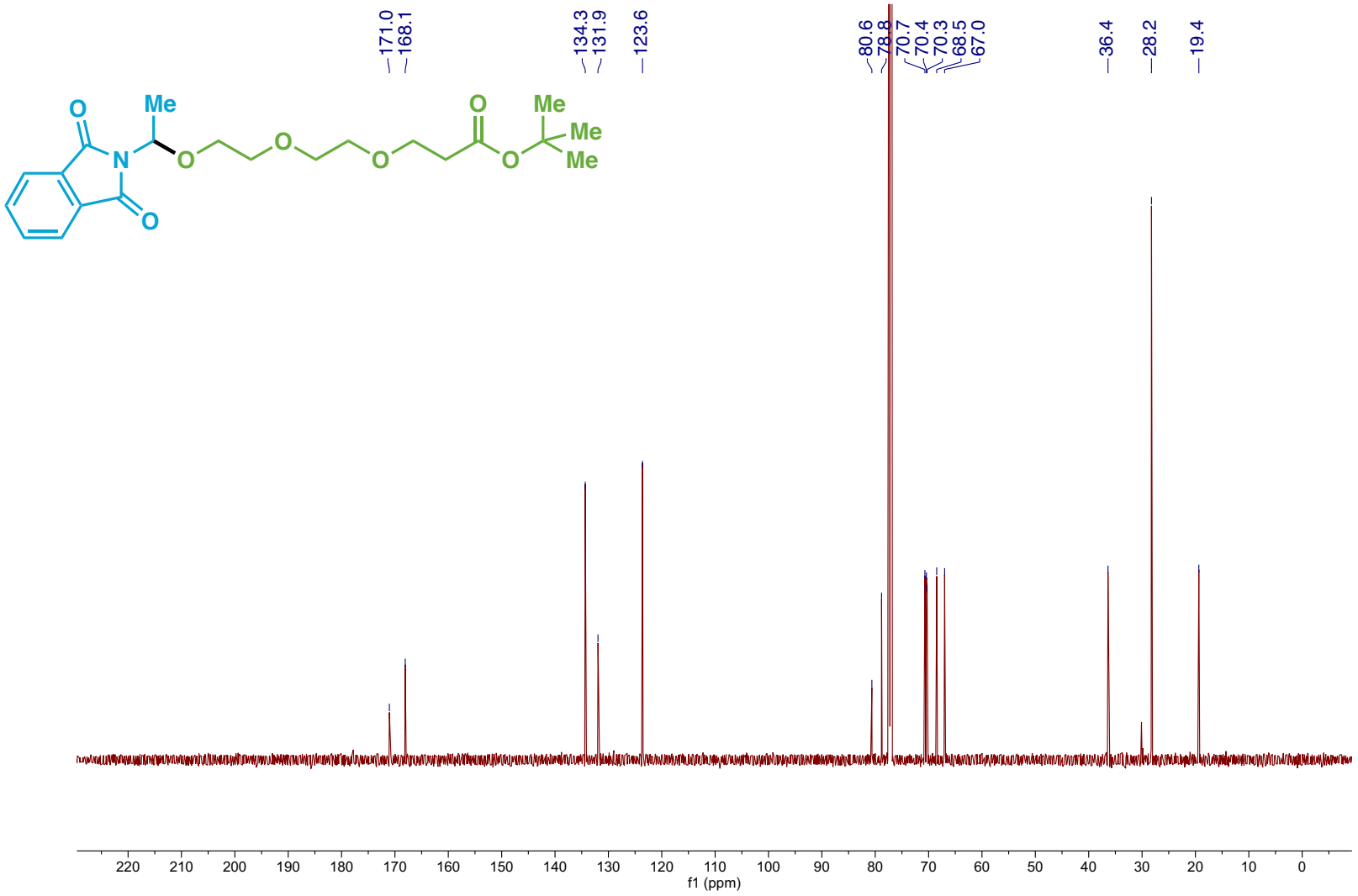
Compound 67 ^{13}C NMR



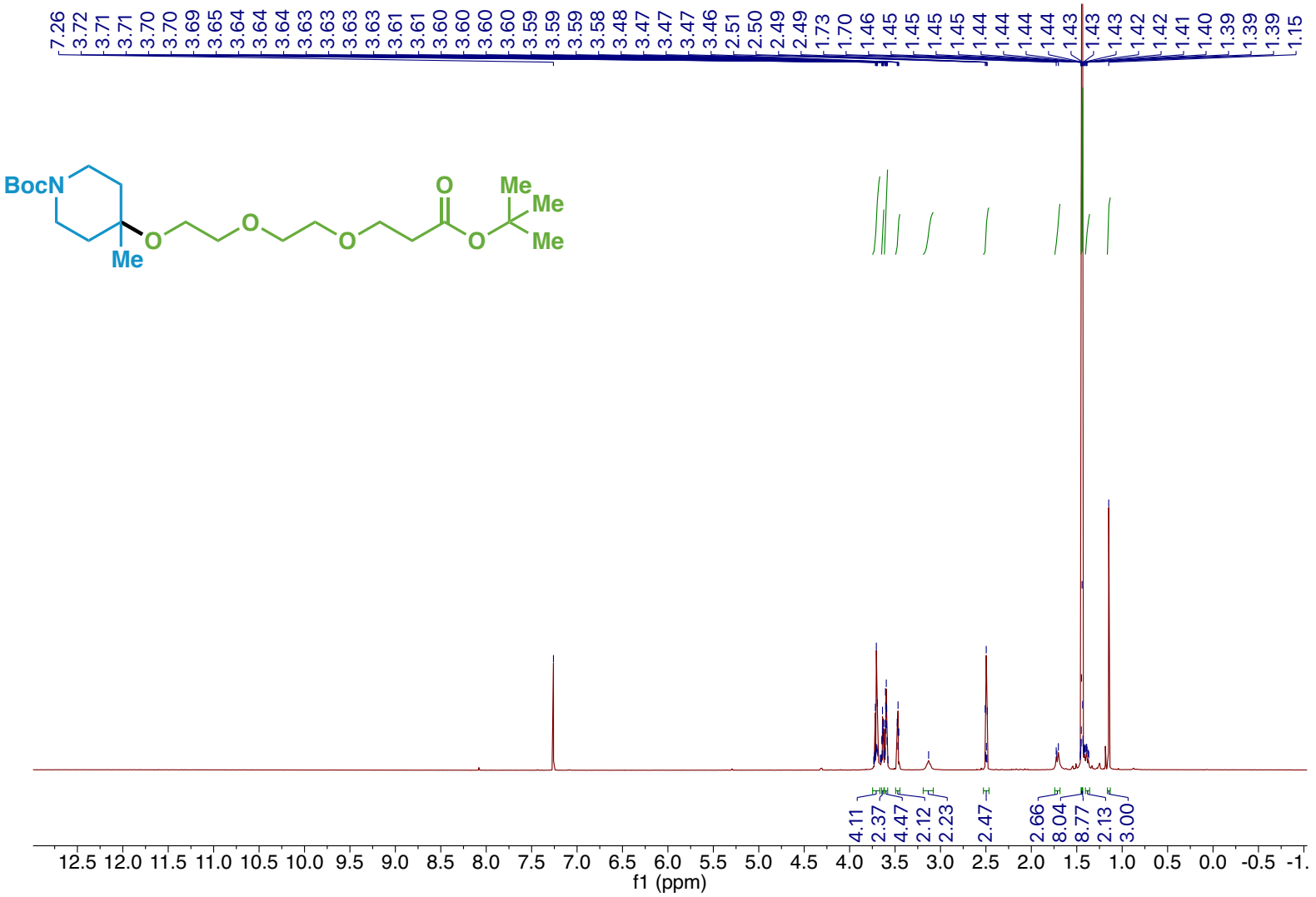
Compound 68 ^{1}H NMR



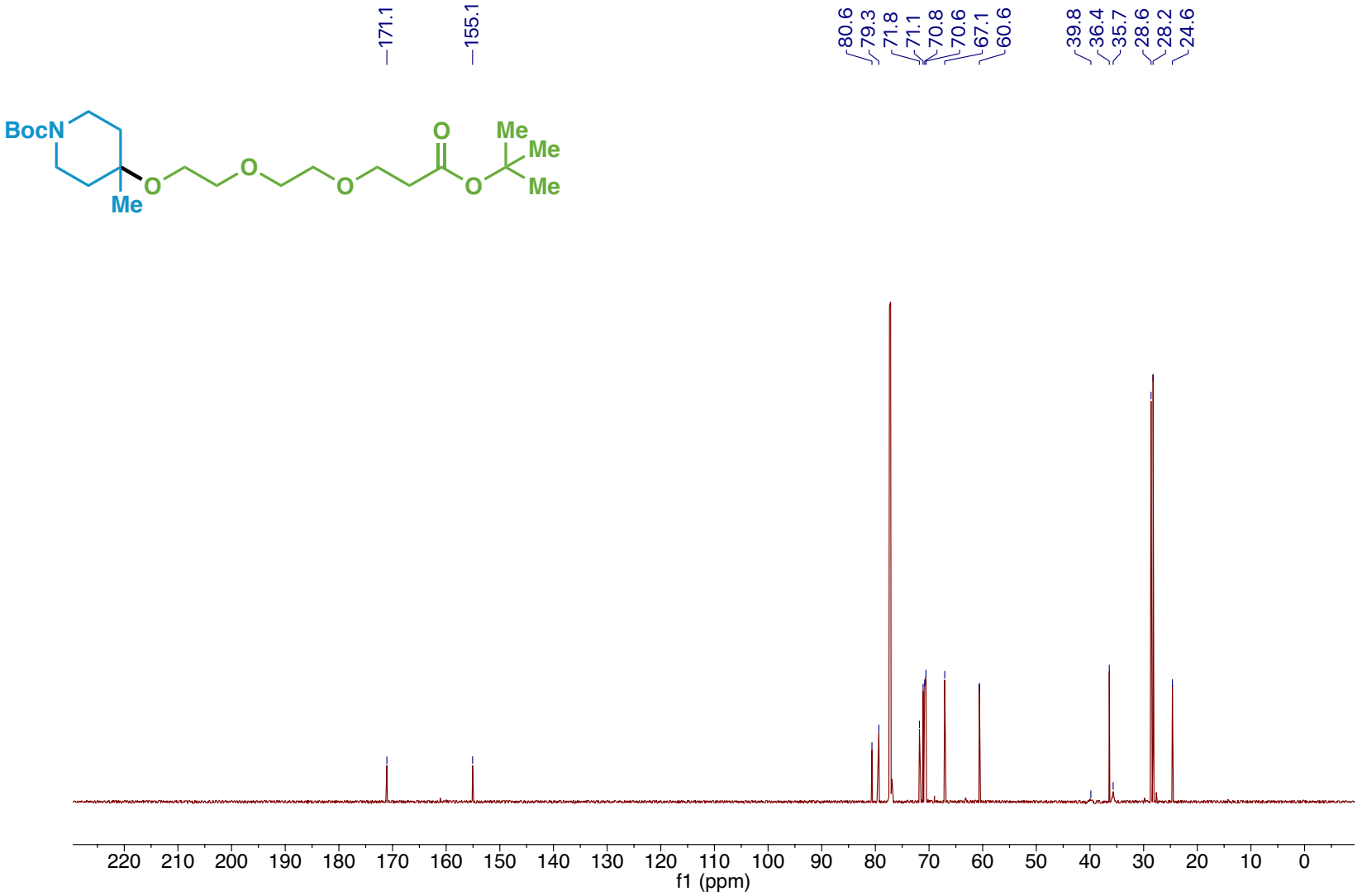
Compound 68 ^{13}C NMR



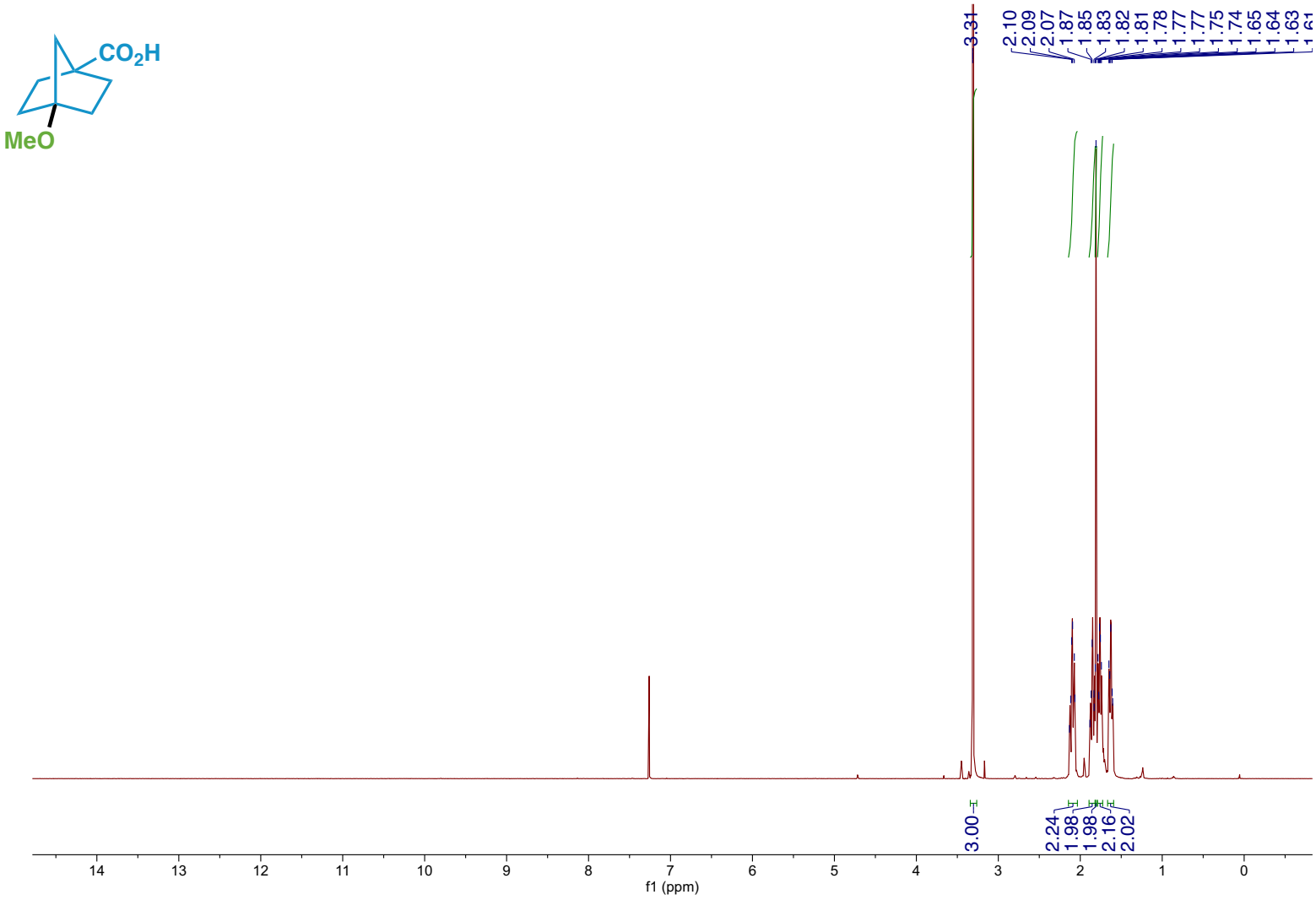
Compound 69 ^{1}H NMR



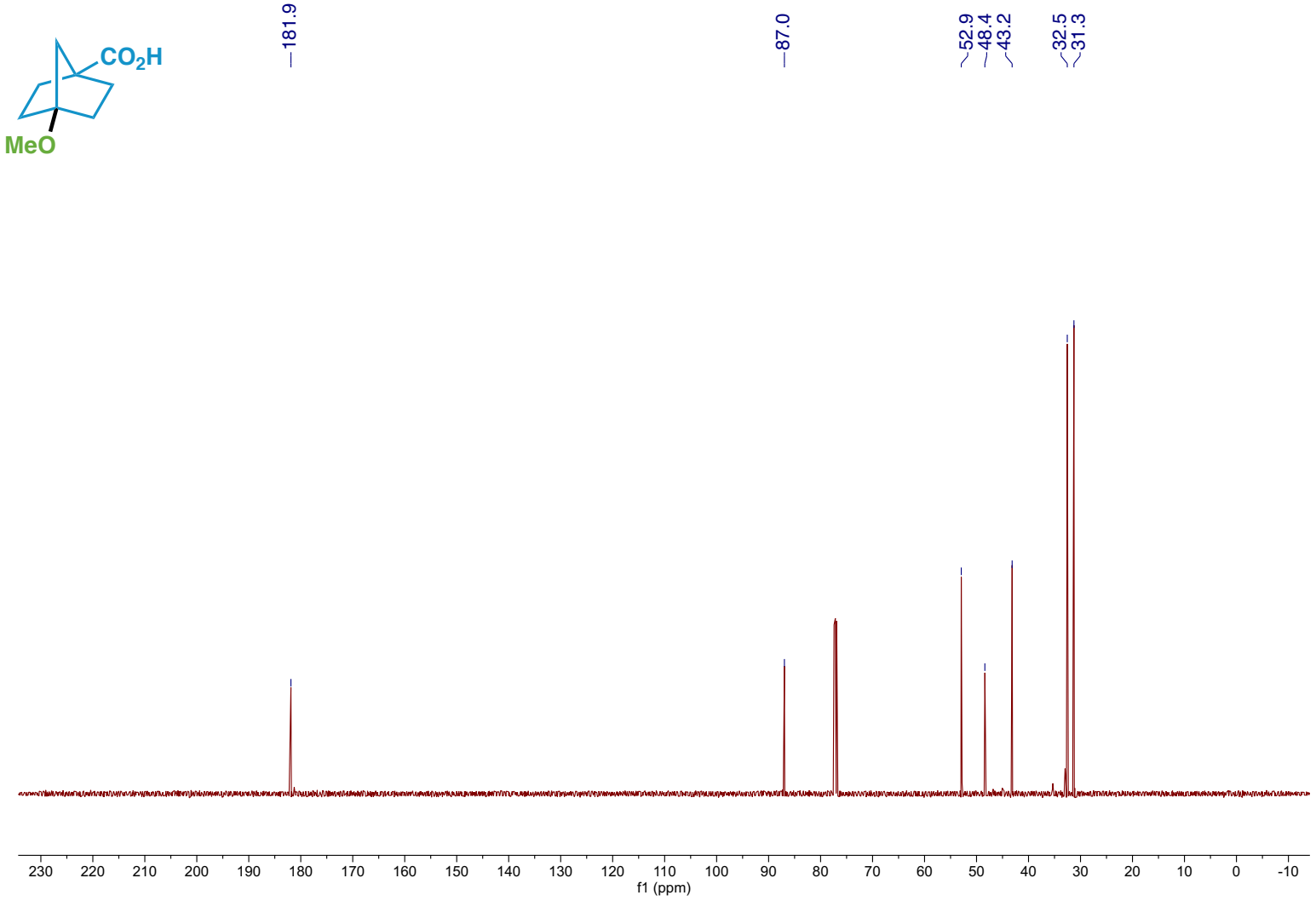
Compound 69 ^{13}C NMR



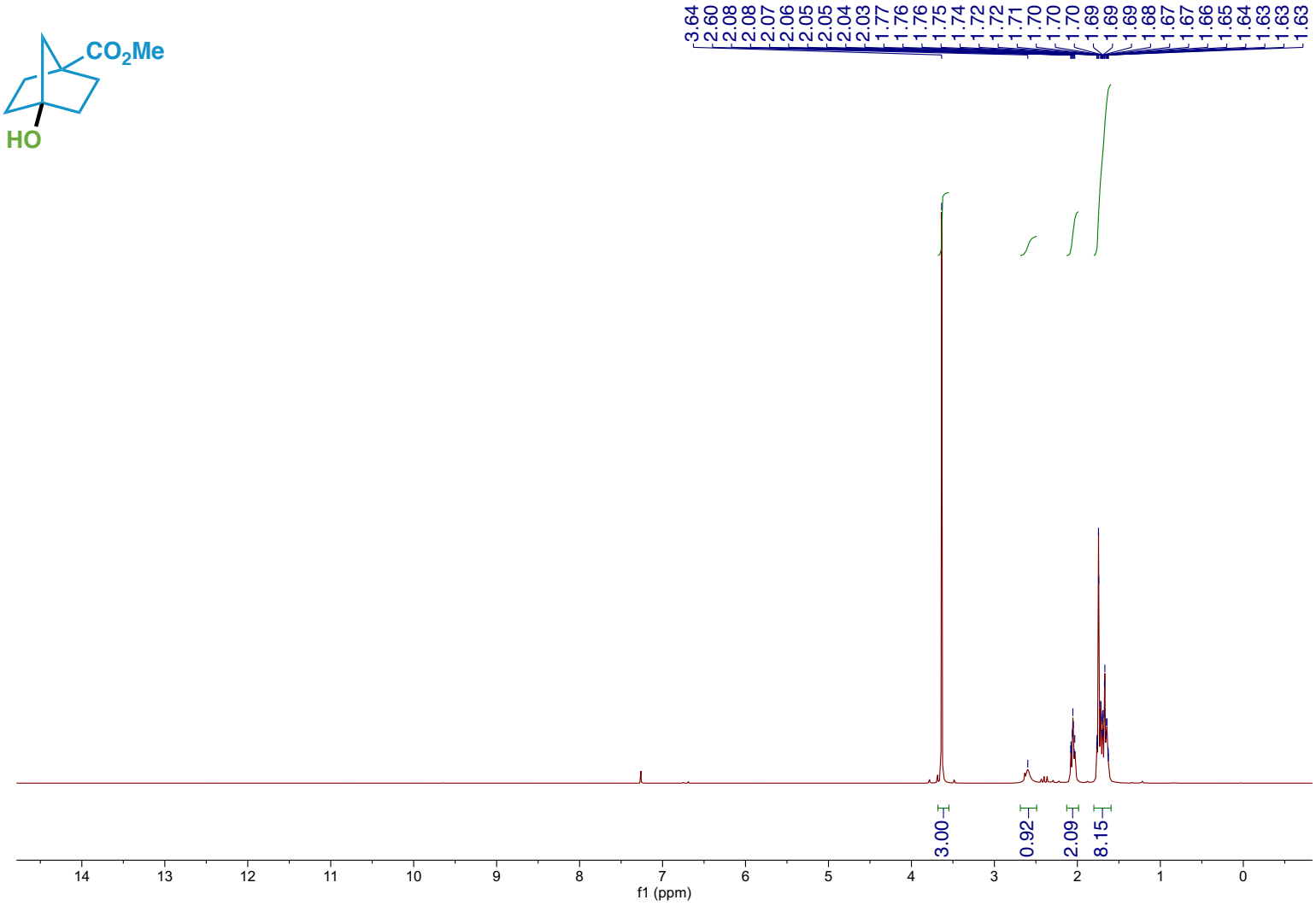
Compound 72 ^{1}H NMR



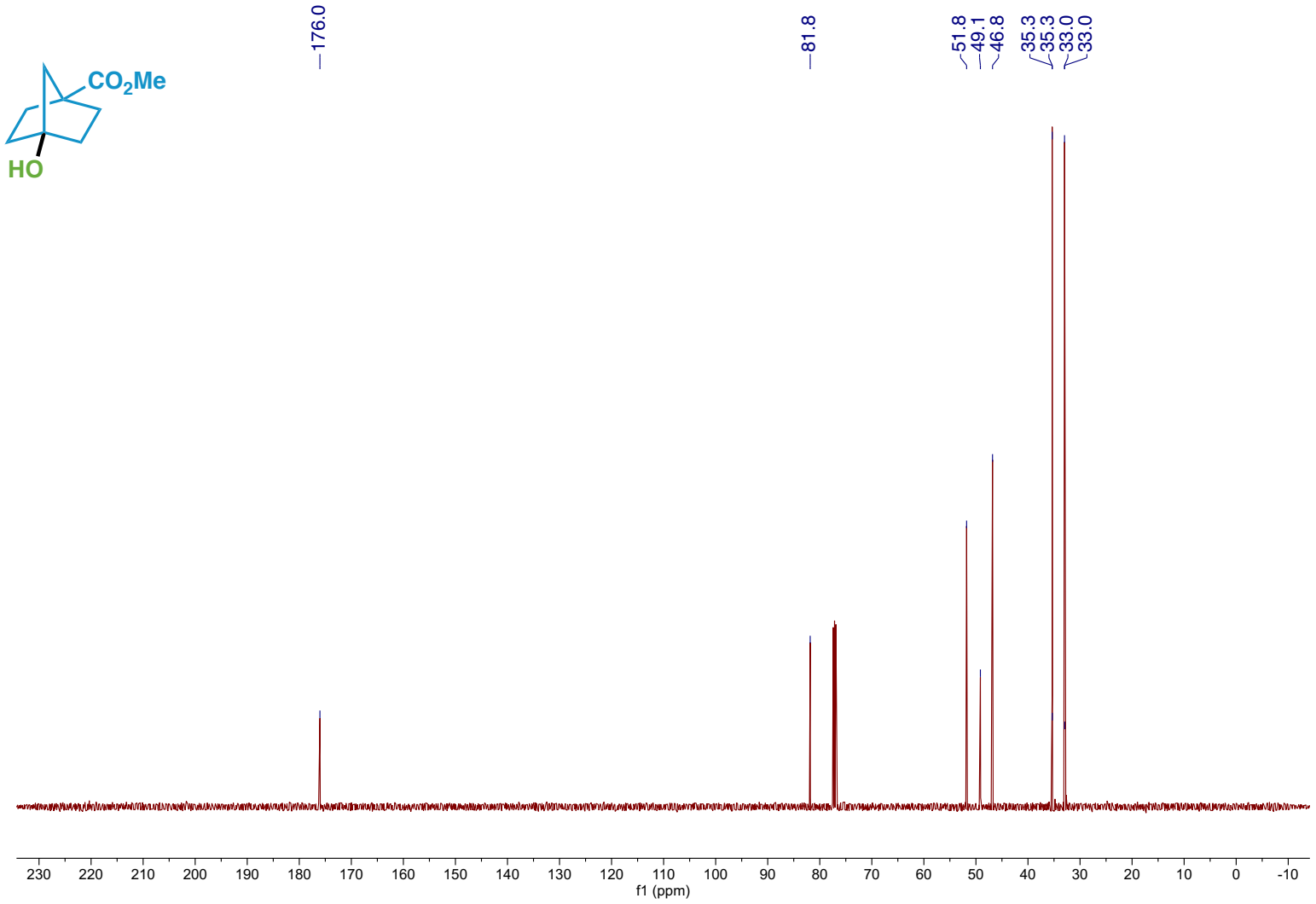
Compound 72 ^{13}C NMR



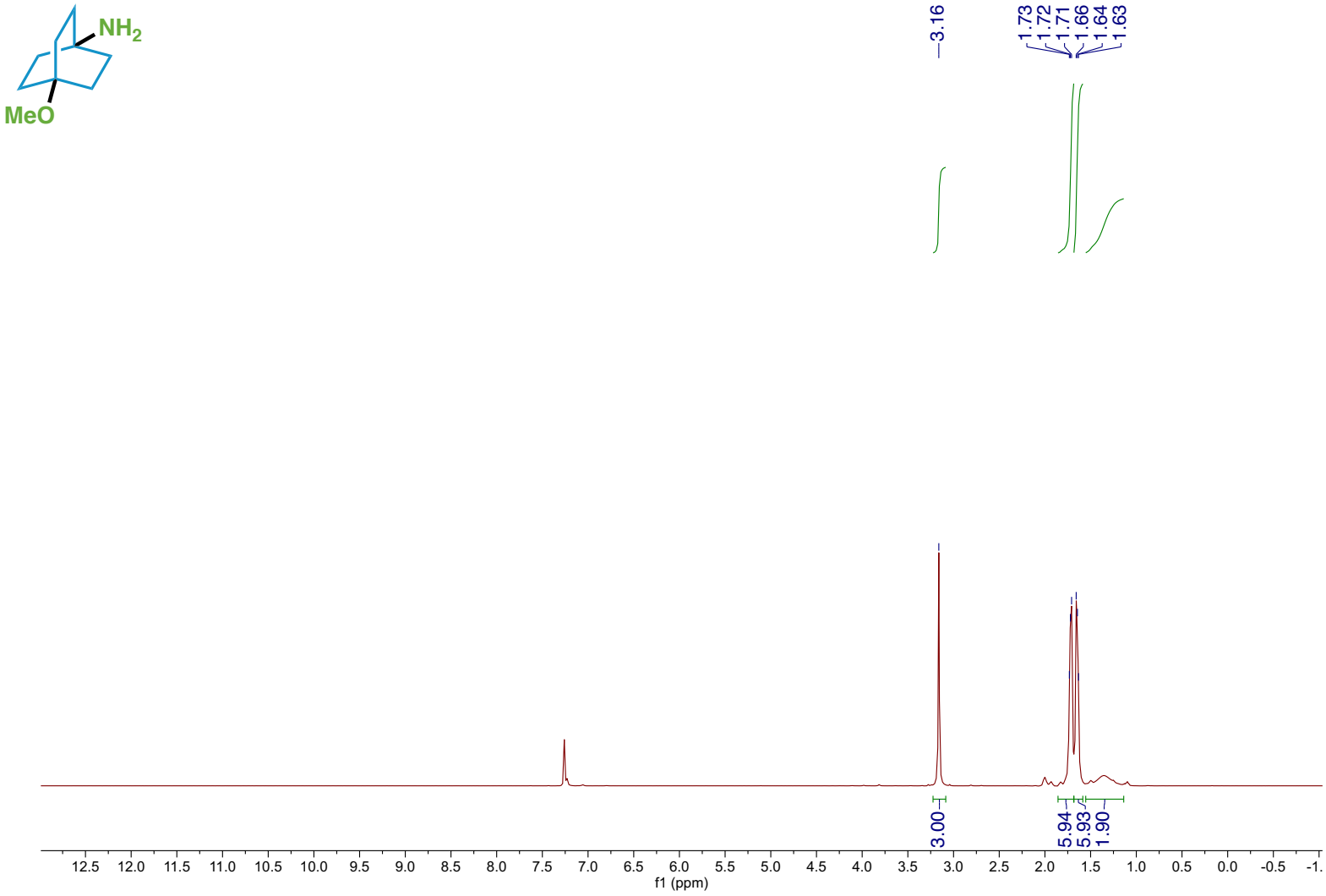
Compound 73 ^{1}H NMR



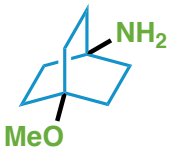
Compound 73 ^{13}C NMR



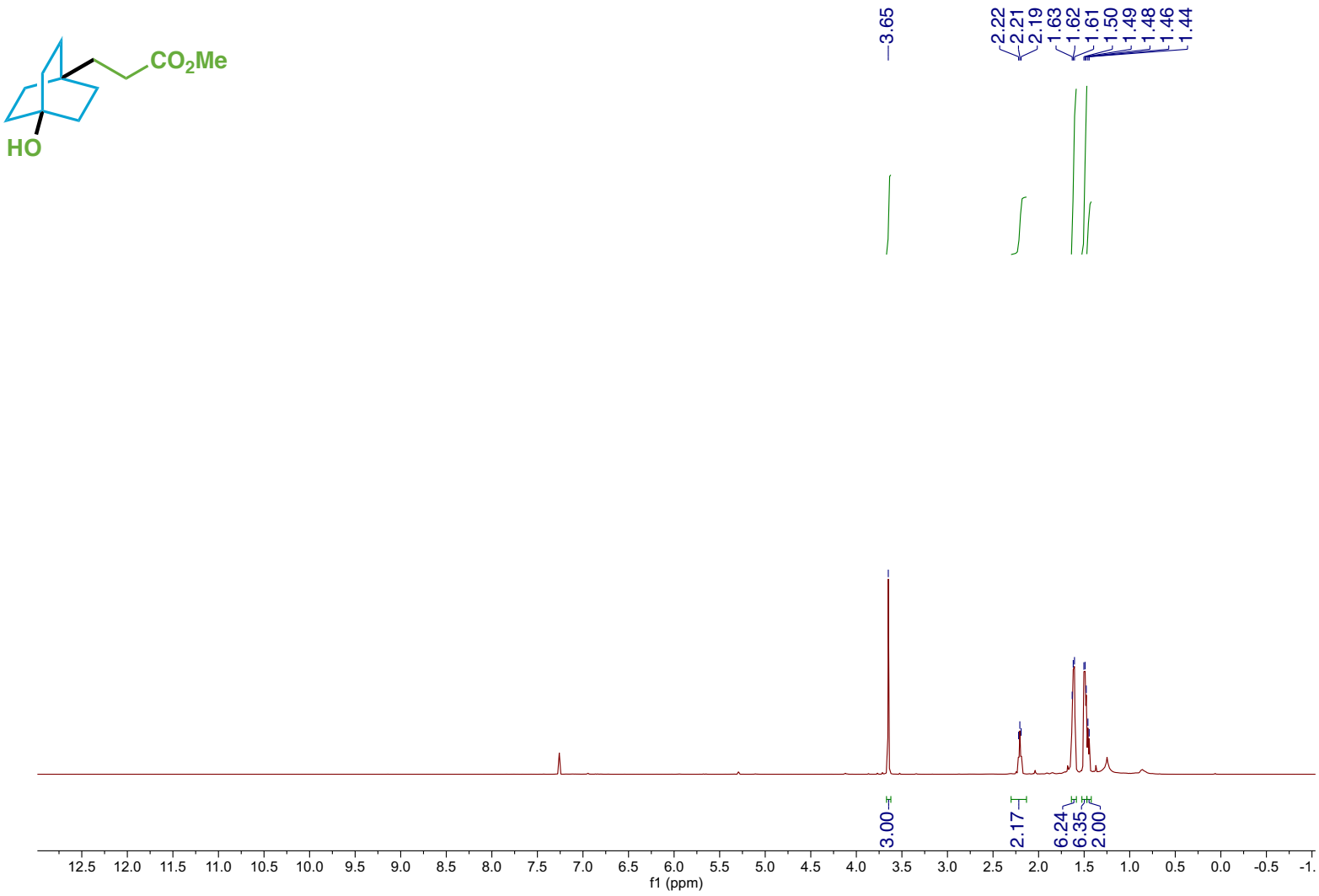
Compound 74 ^{1}H NMR



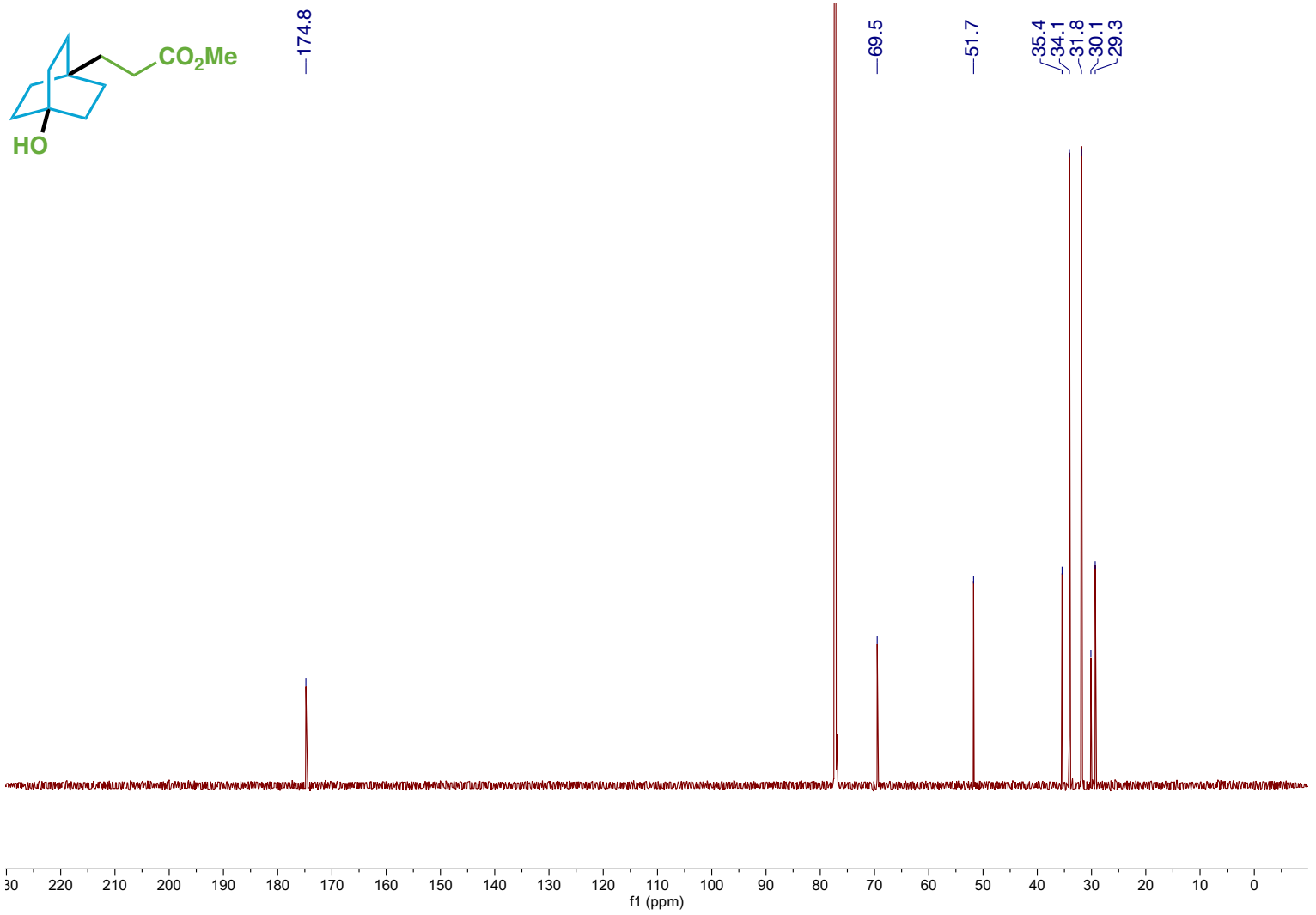
Compound 74 ^{13}C NMR



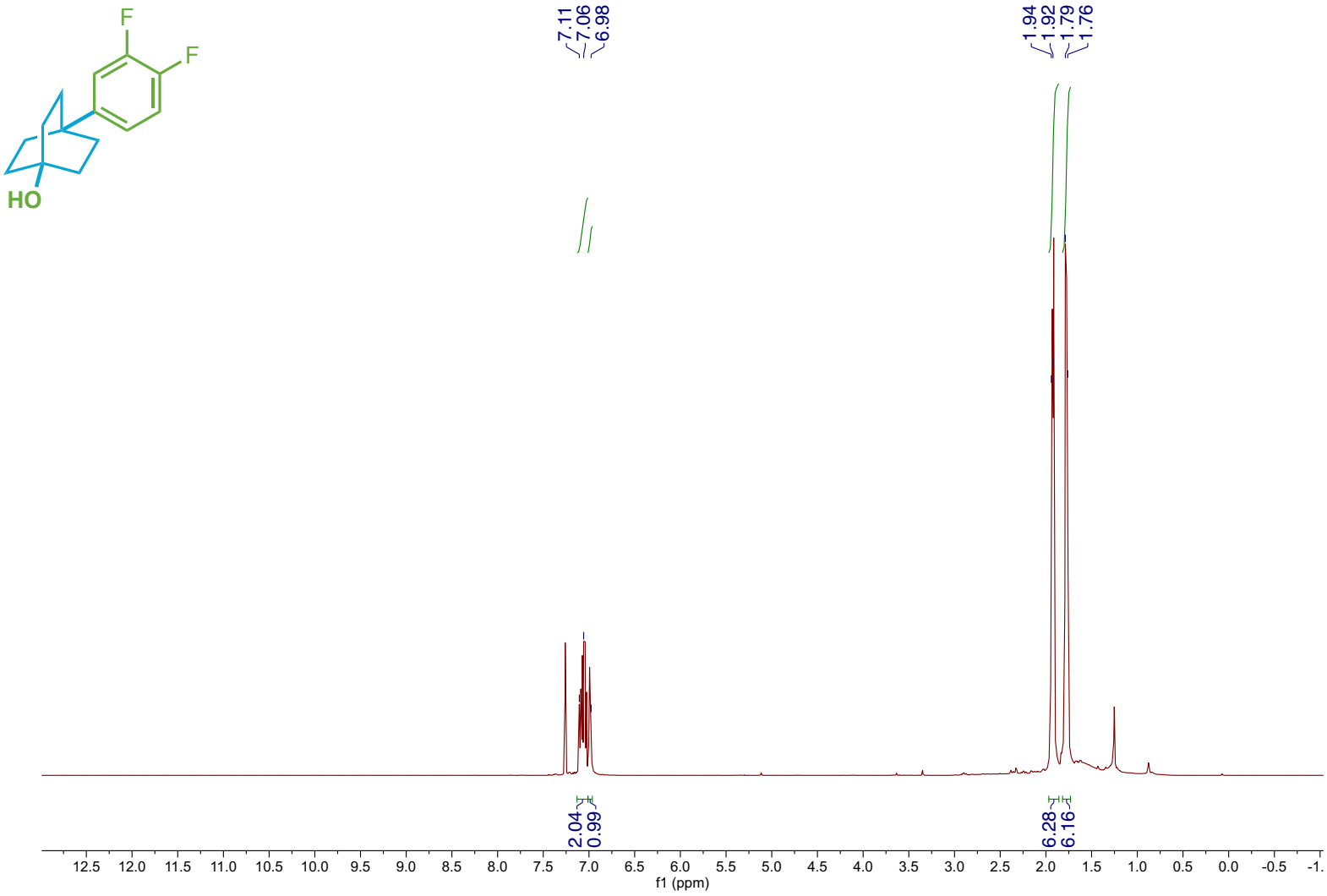
Compound 75 ^{1}H NMR



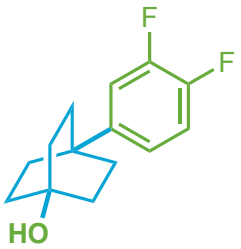
Compound 75 ^{13}C NMR



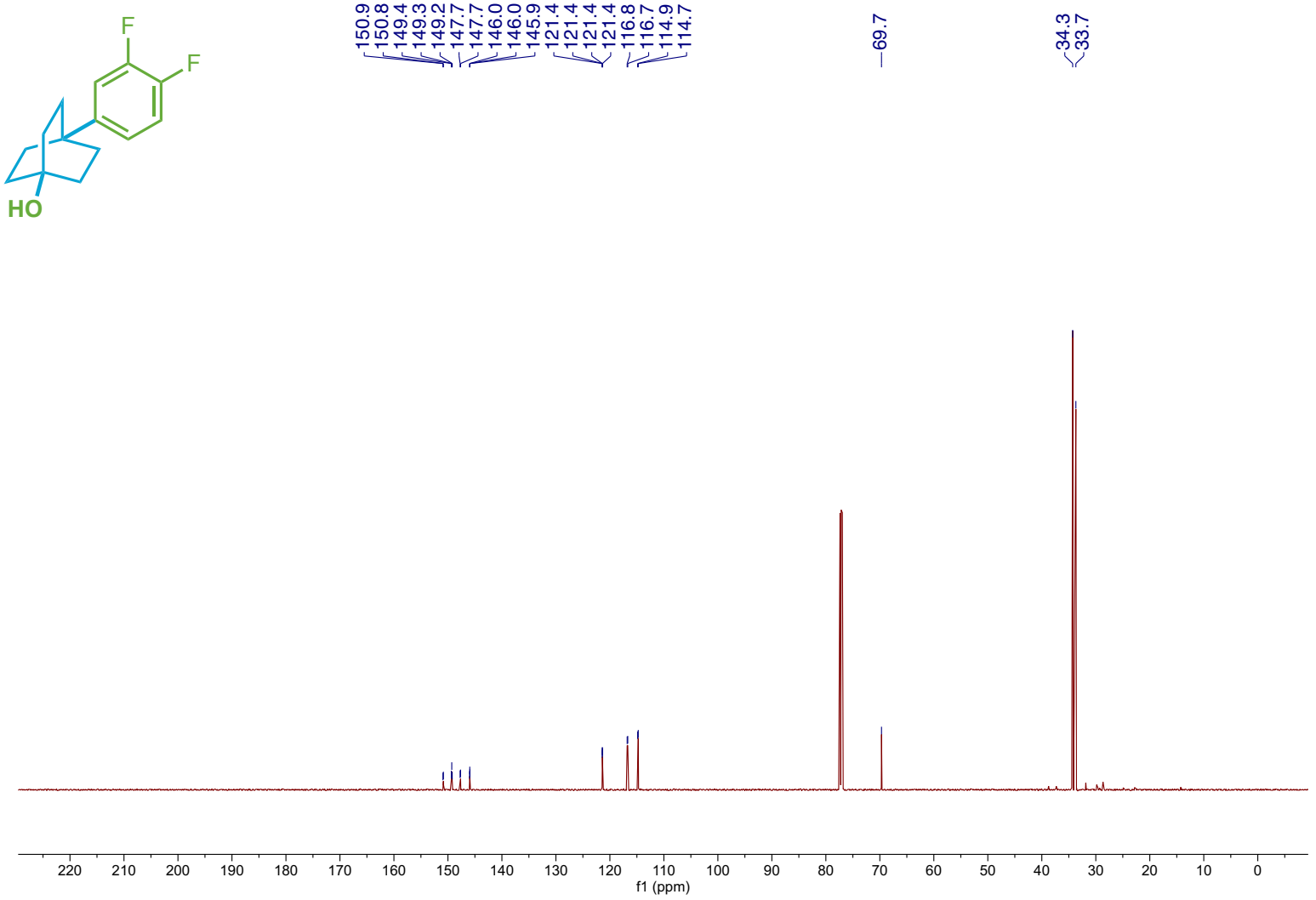
Compound 76 ^{1}H NMR



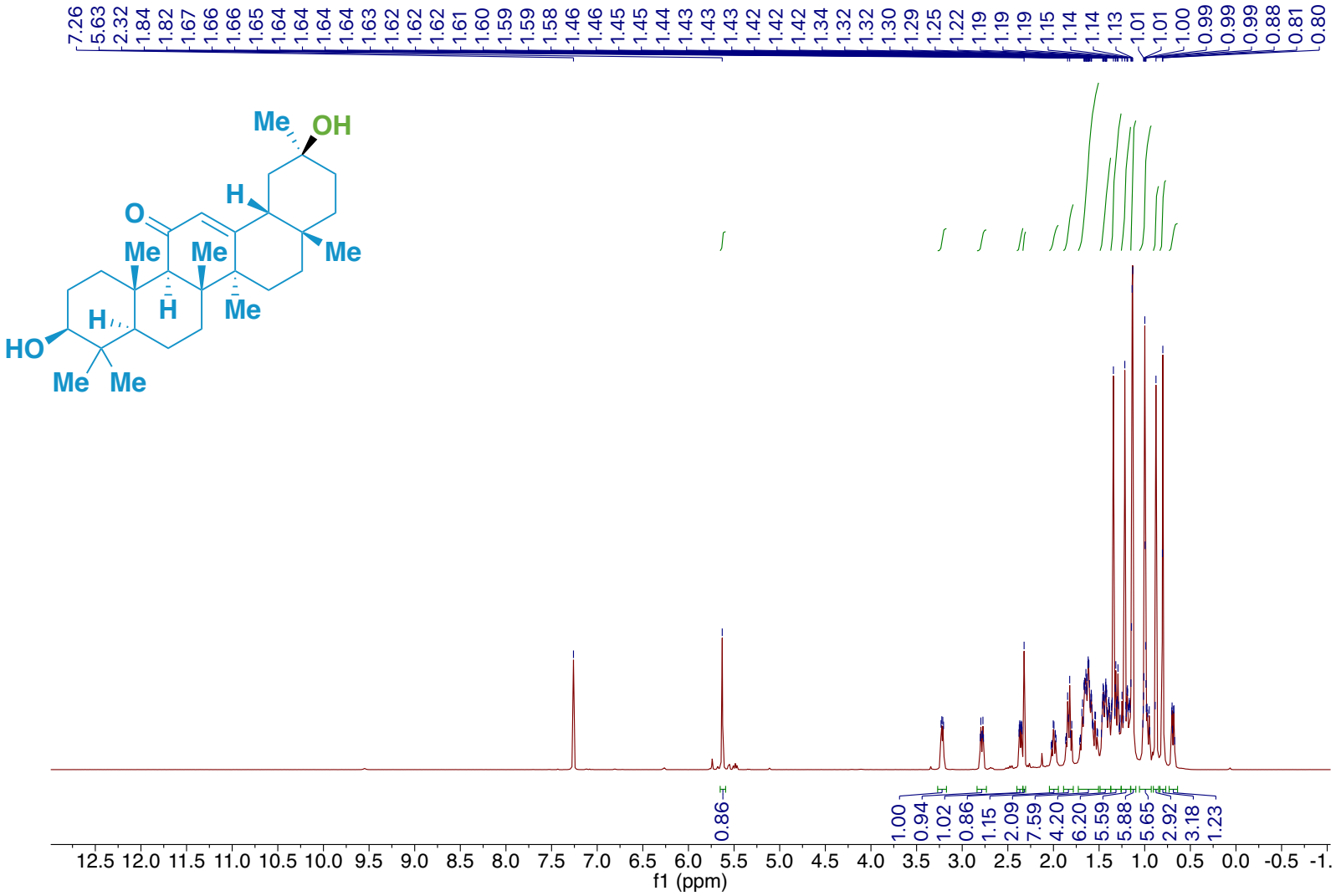
Compound 76 ^{19}F NMR



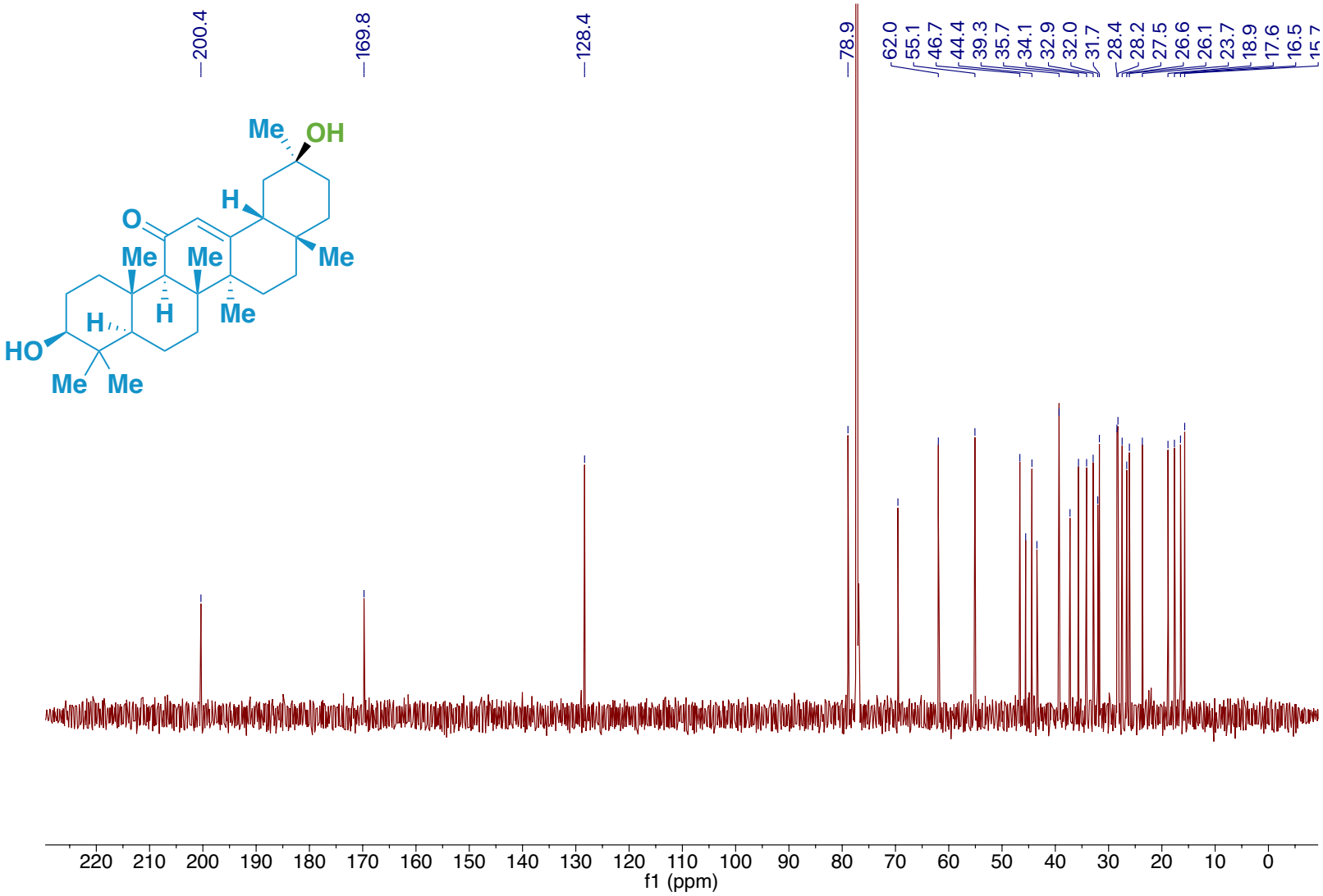
Compound 76 ^{13}C NMR



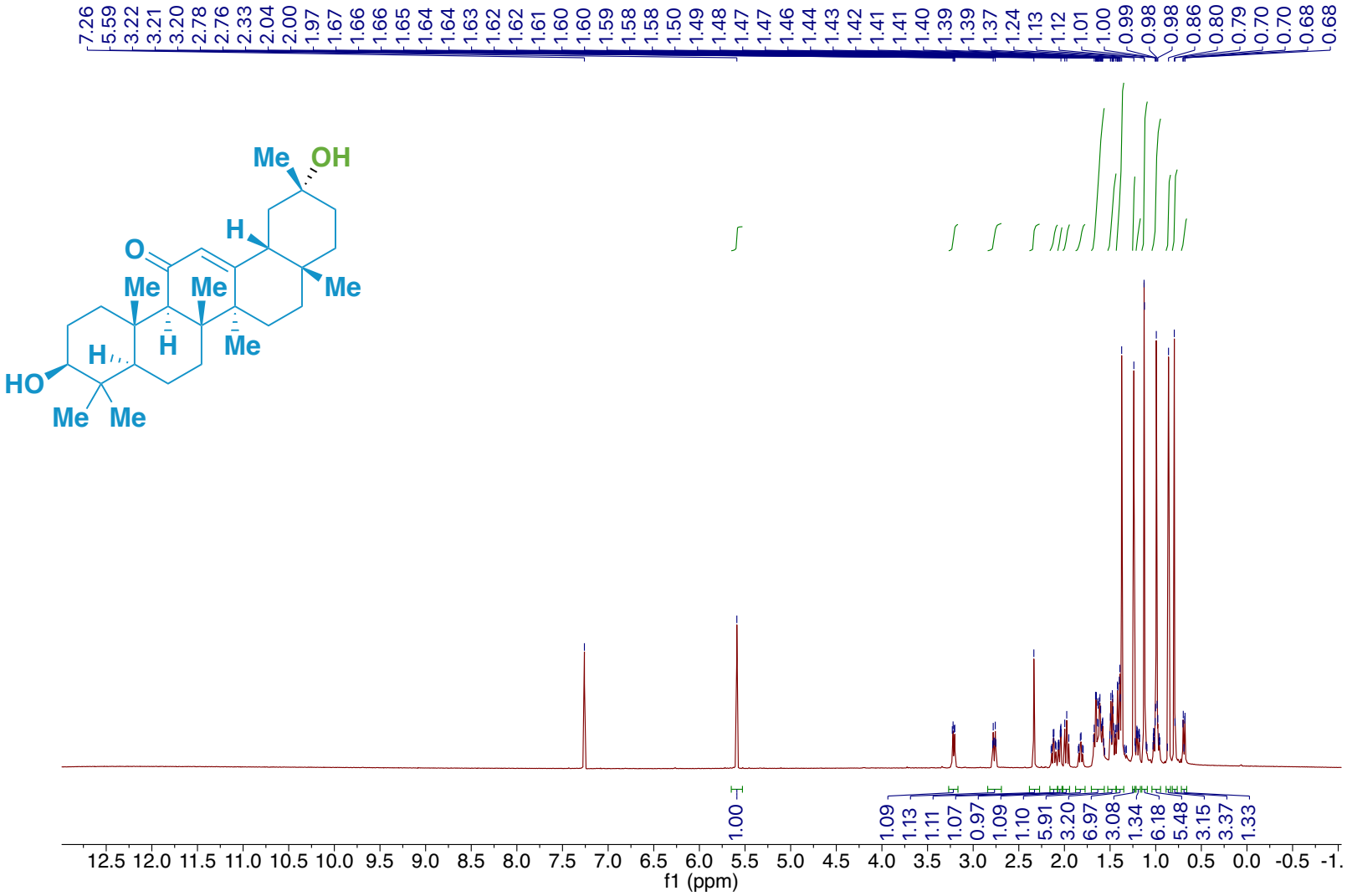
Compound (2*S*)-77 ^{1}H NMR



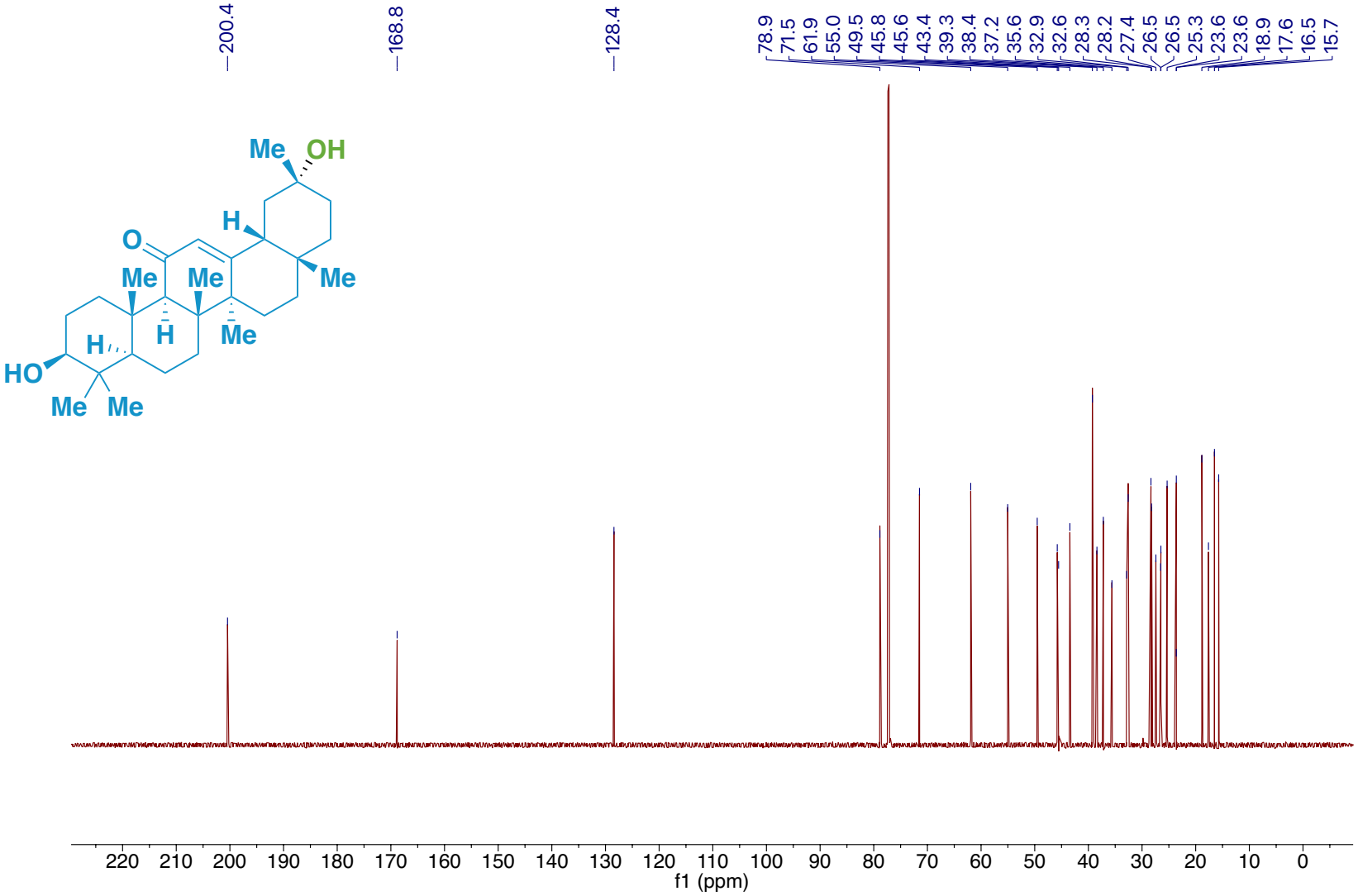
Compound (2*S*)-77 ^{13}C NMR



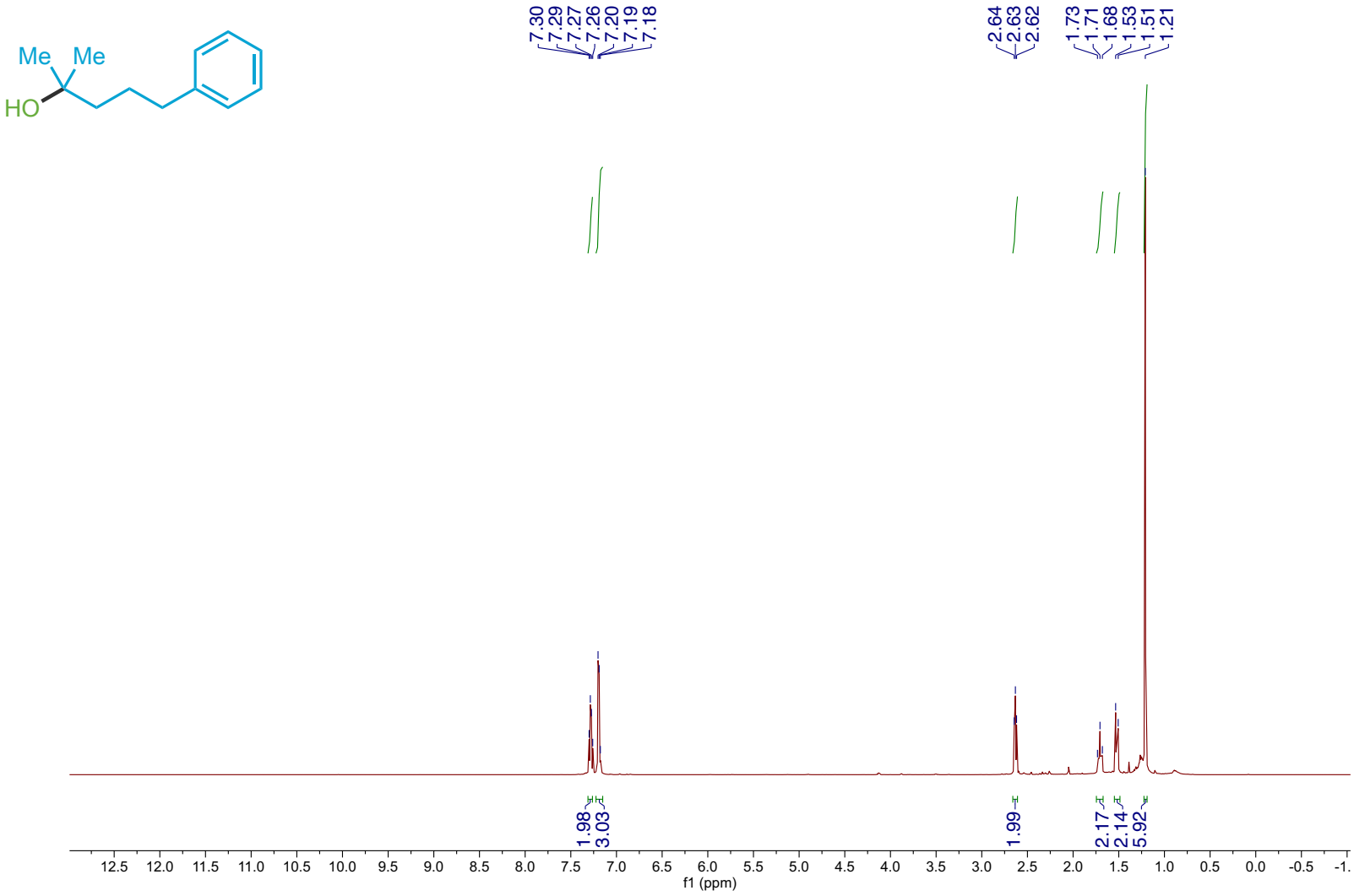
Compound (2*R*)-77 ^{1}H NMR



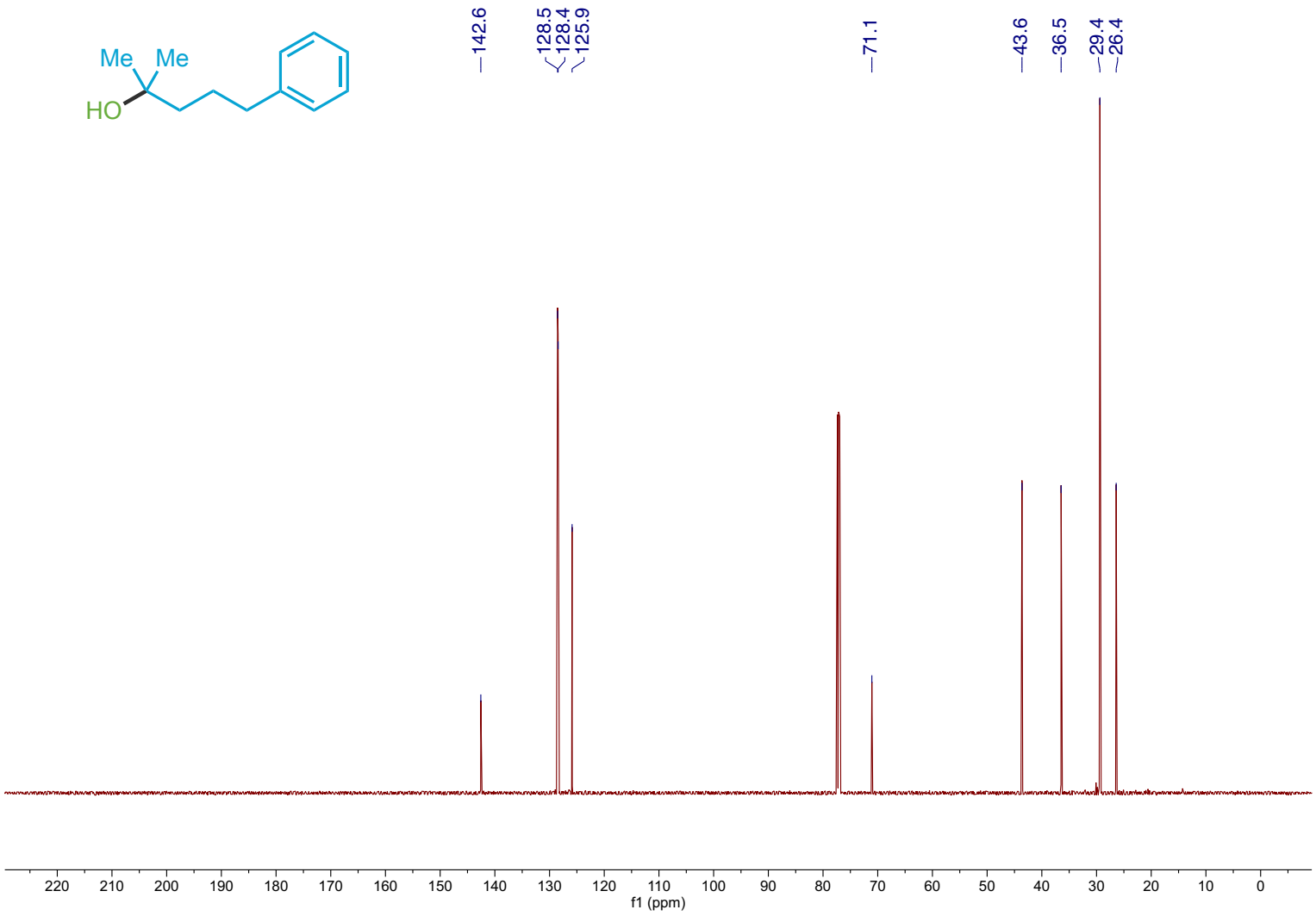
Compound (2*R*)-77 ^{13}C NMR



Compound 78 ^{1}H NMR



Compound 78 ^{13}C NMR



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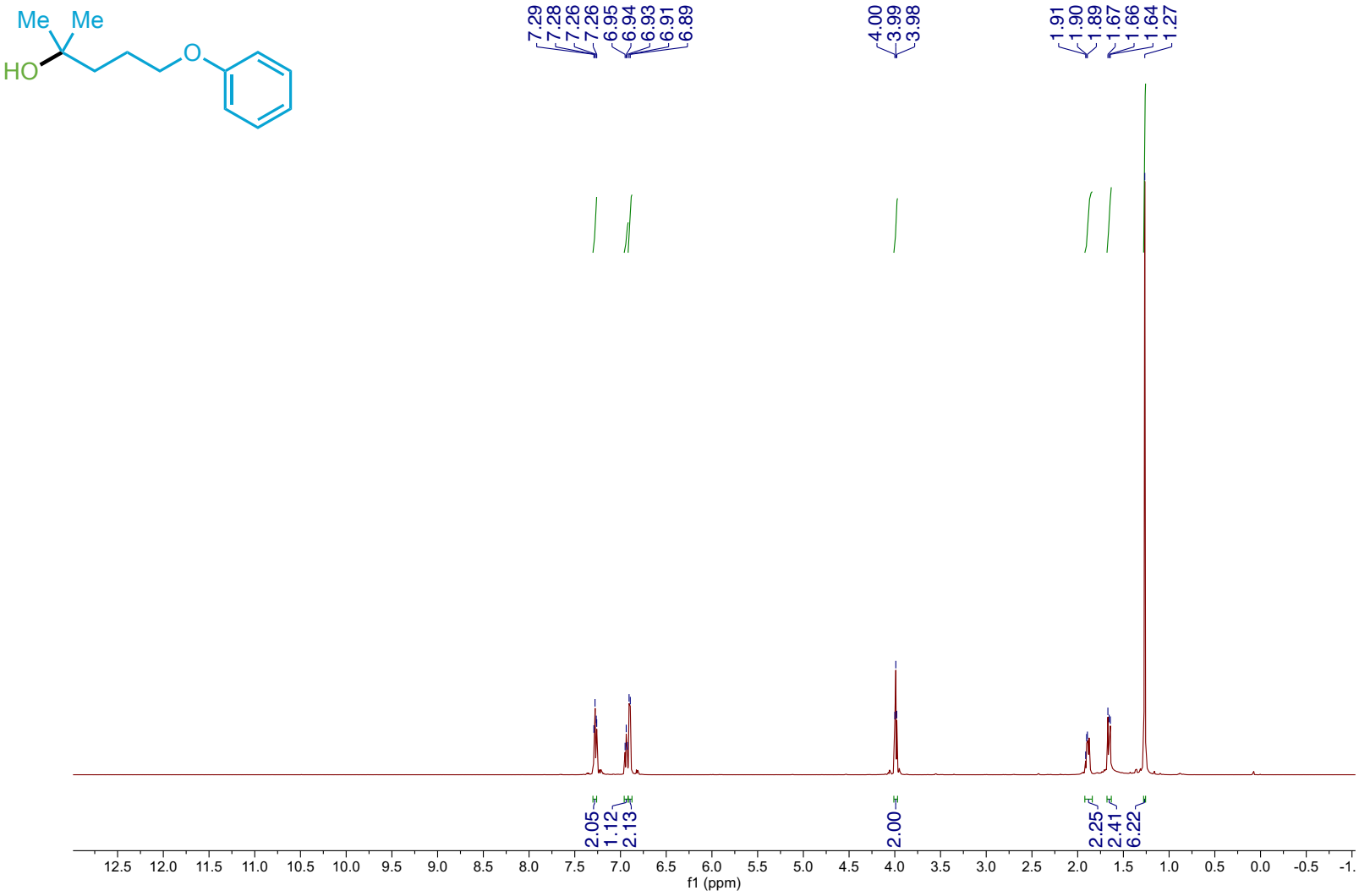
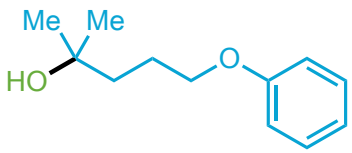
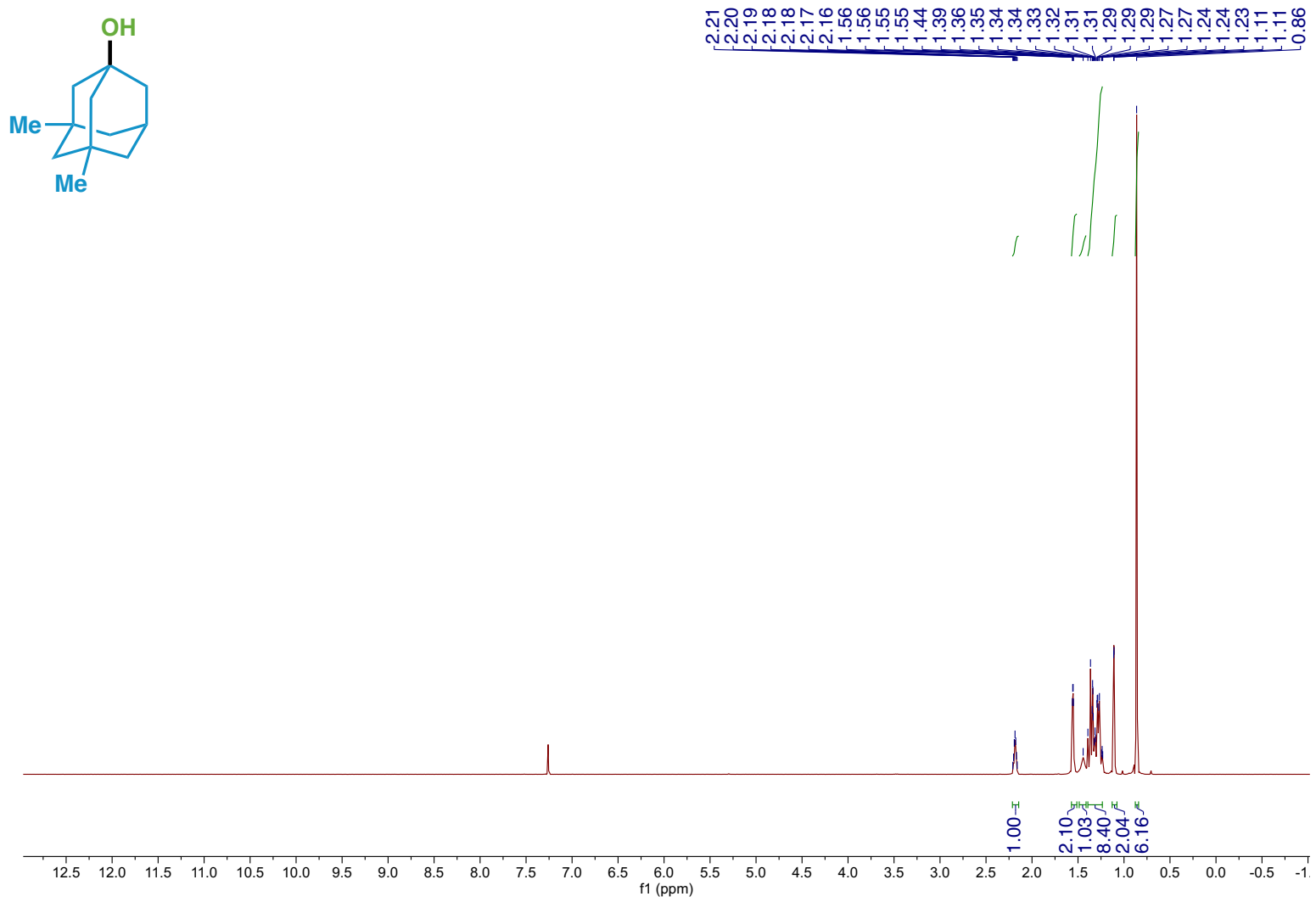


Compound 79 ^{13}C NMR



Compound 80 ^{1}H NMR



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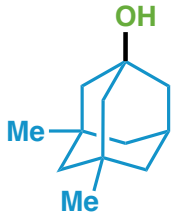
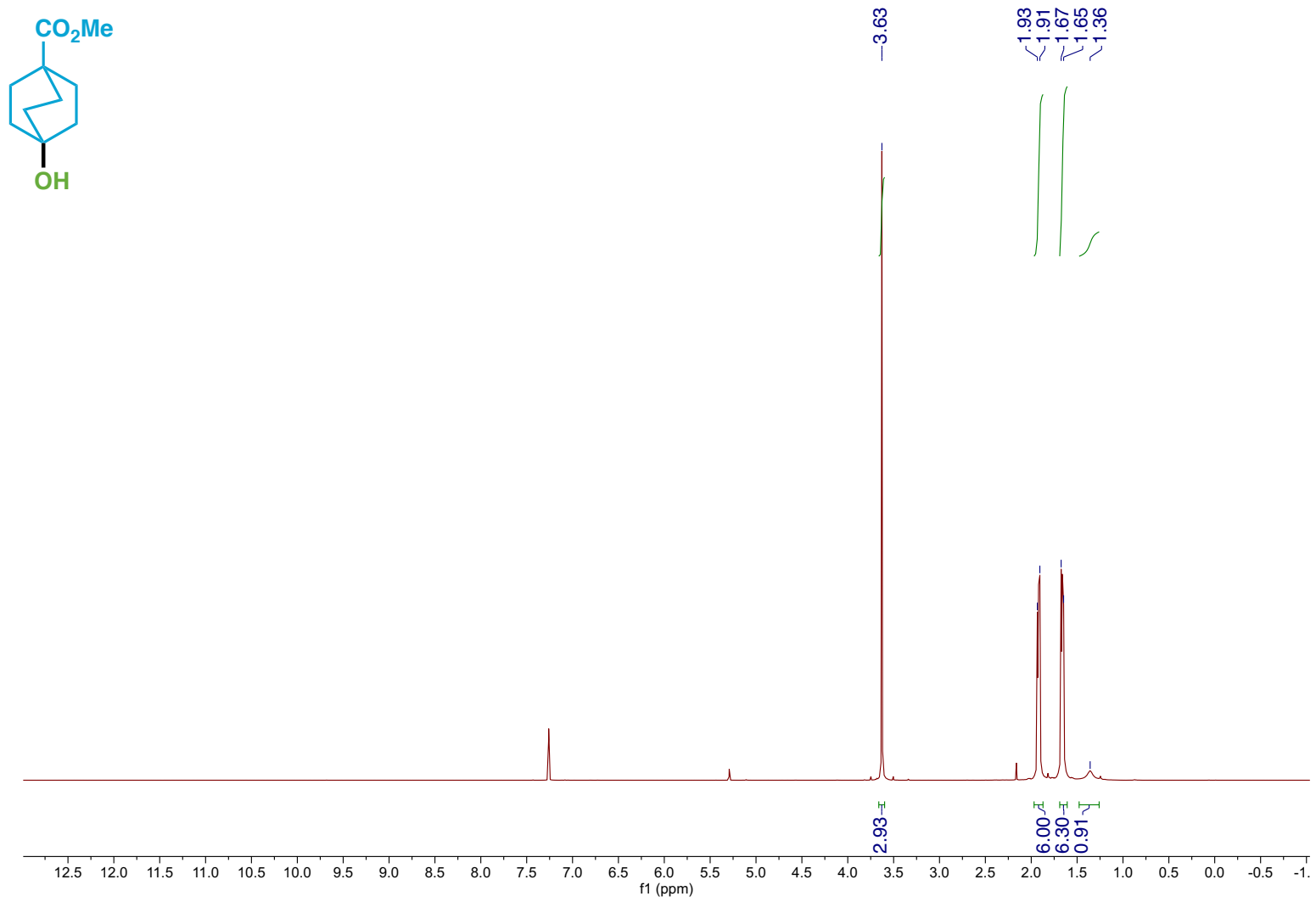


Compound 81 ^{1}H NMR



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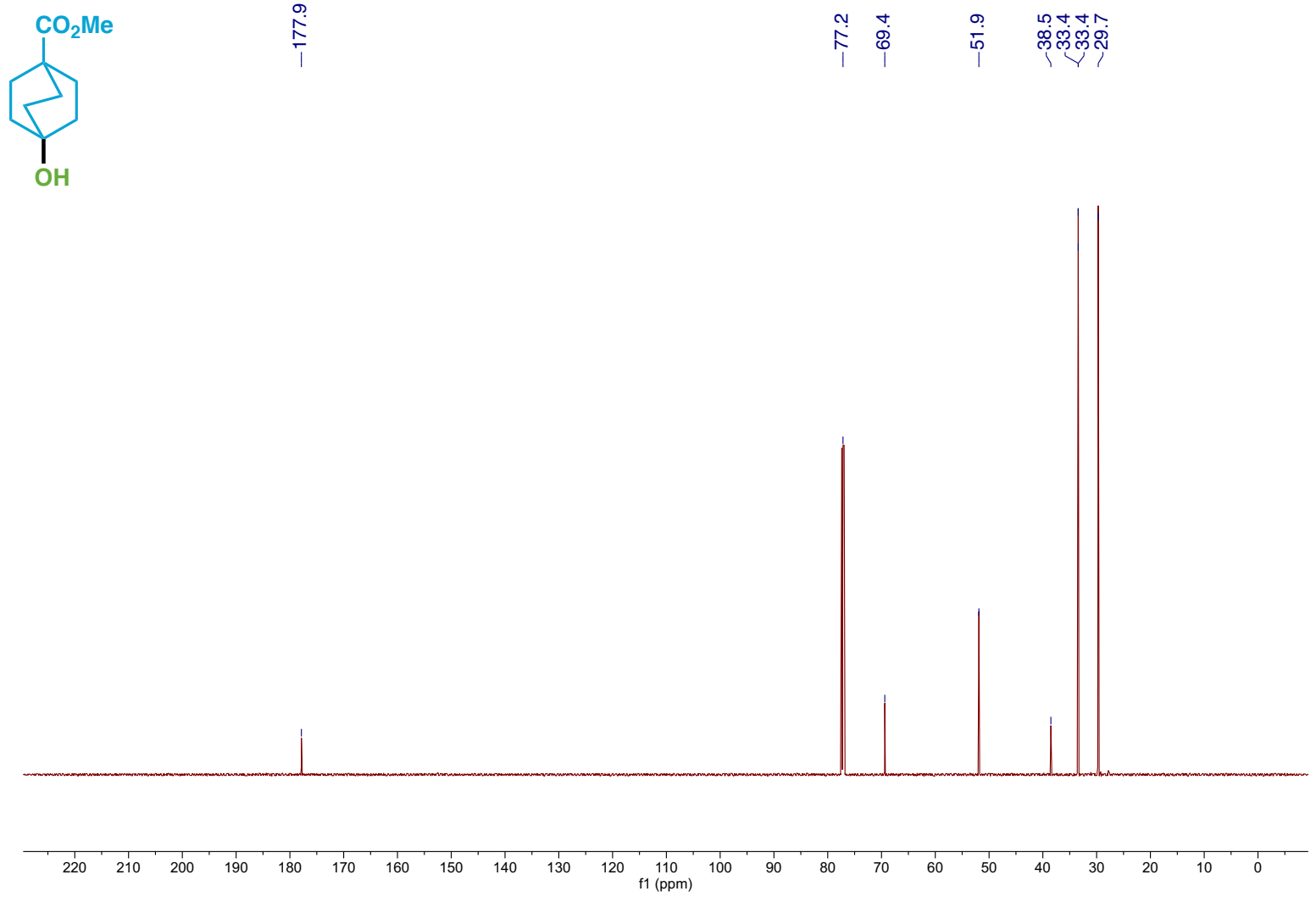

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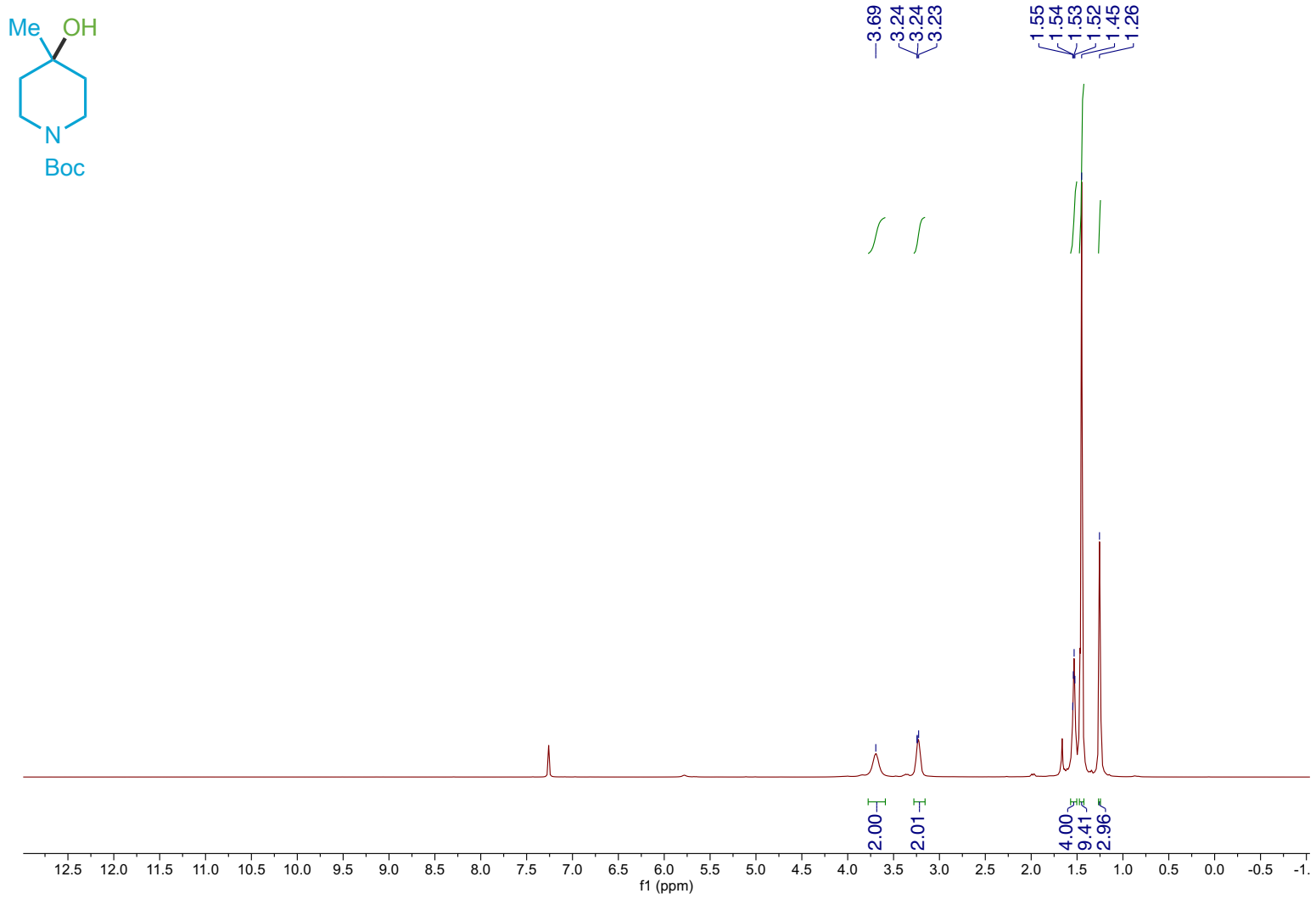

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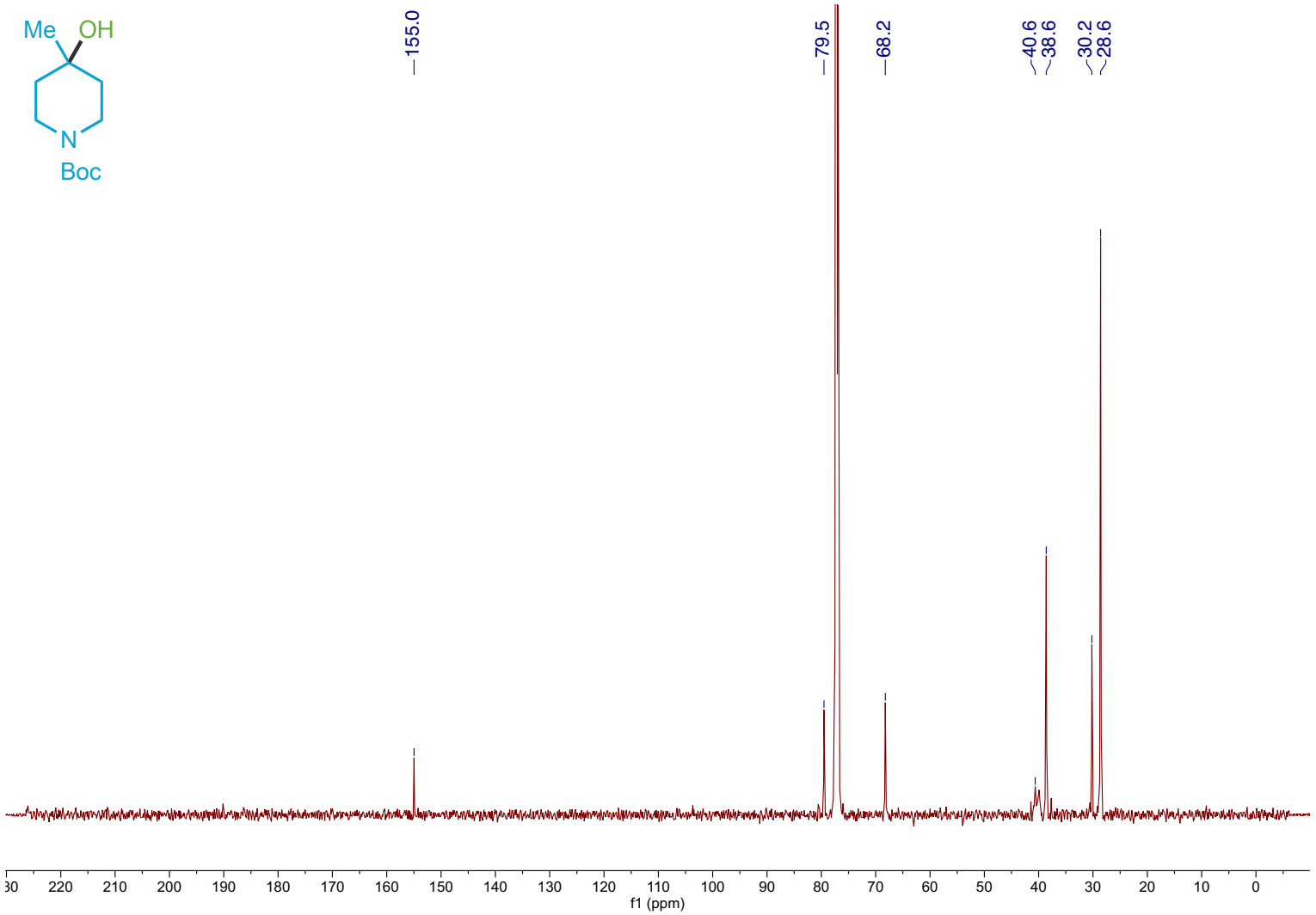

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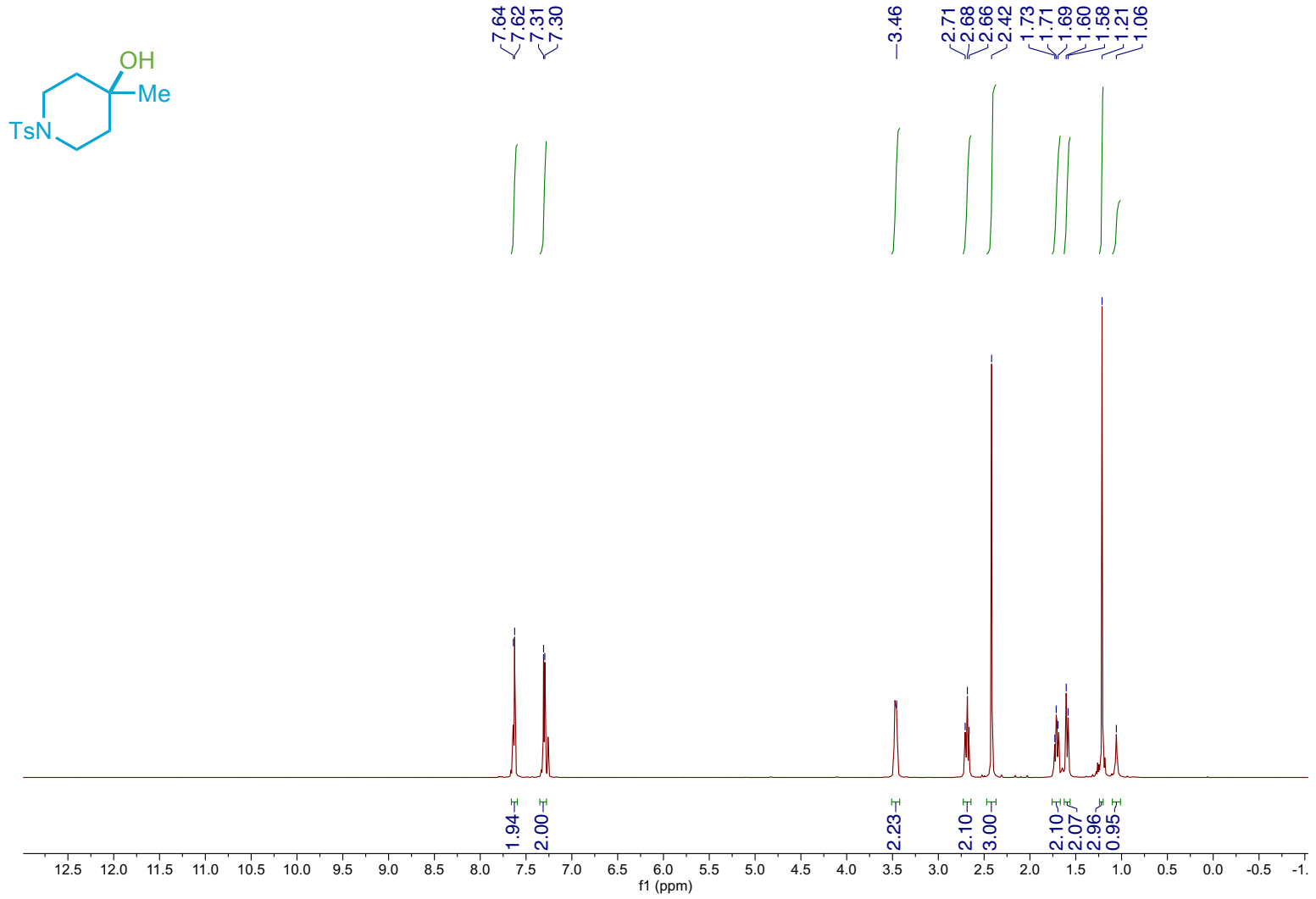
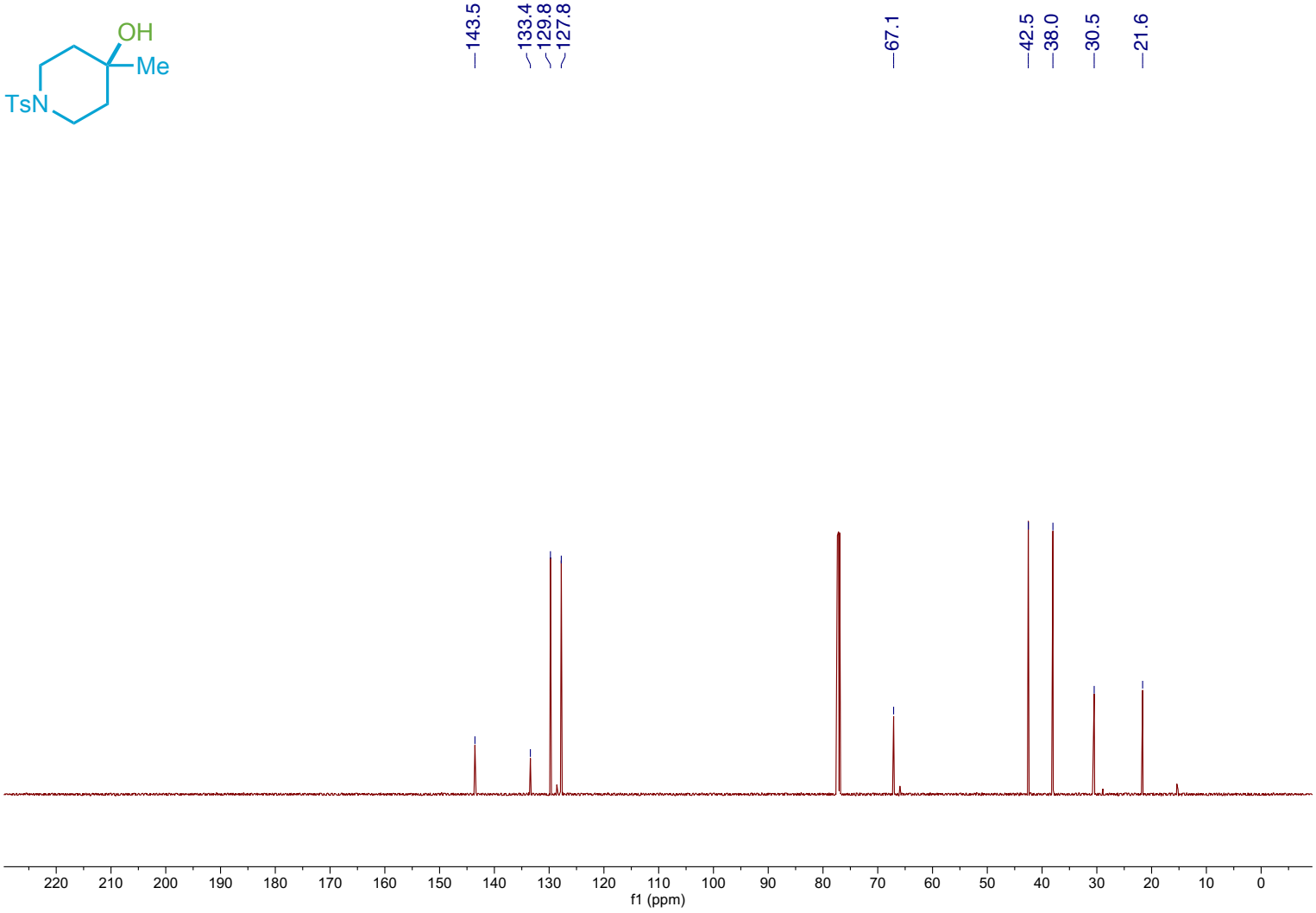


Compound 83 ^{13}C NMR



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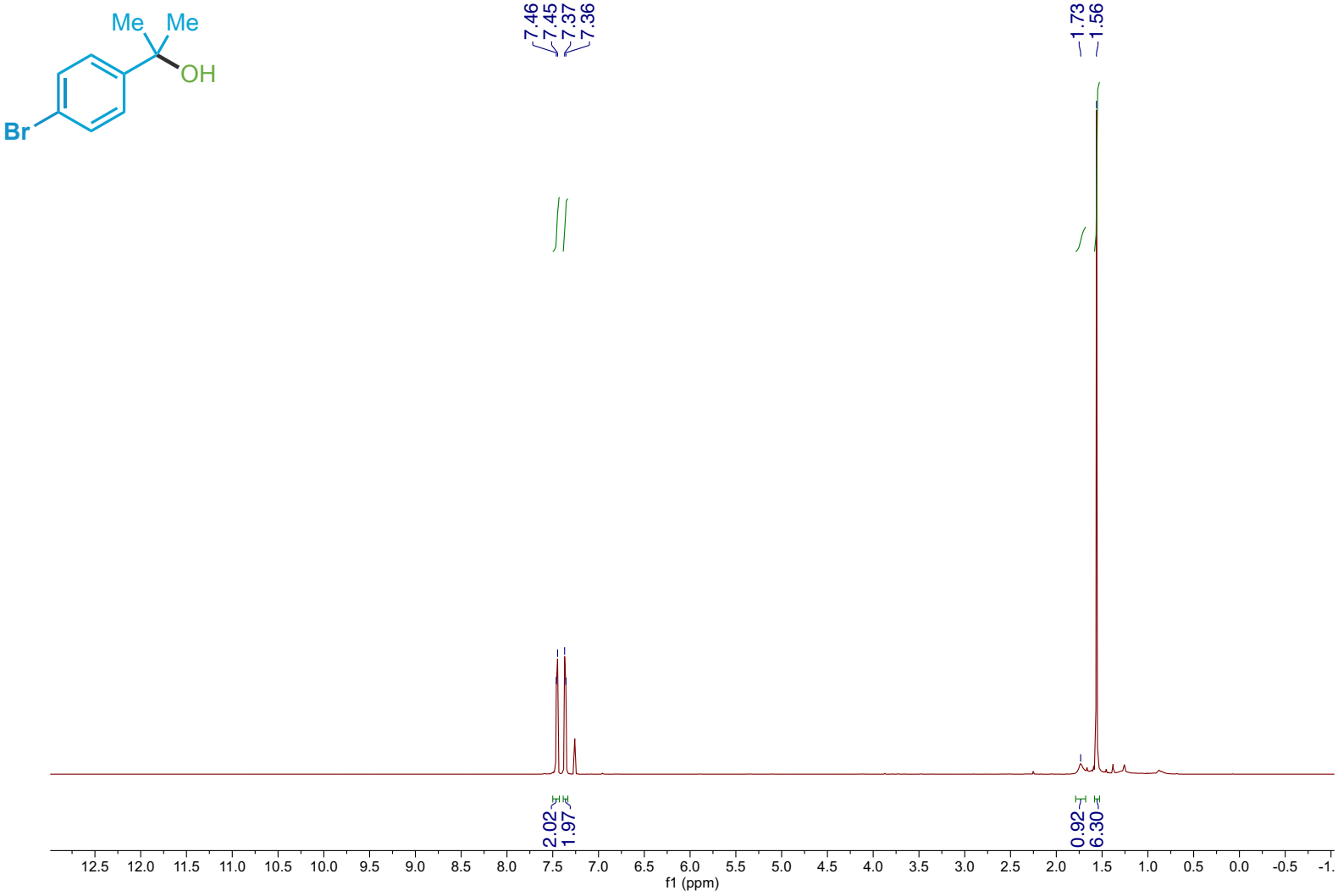

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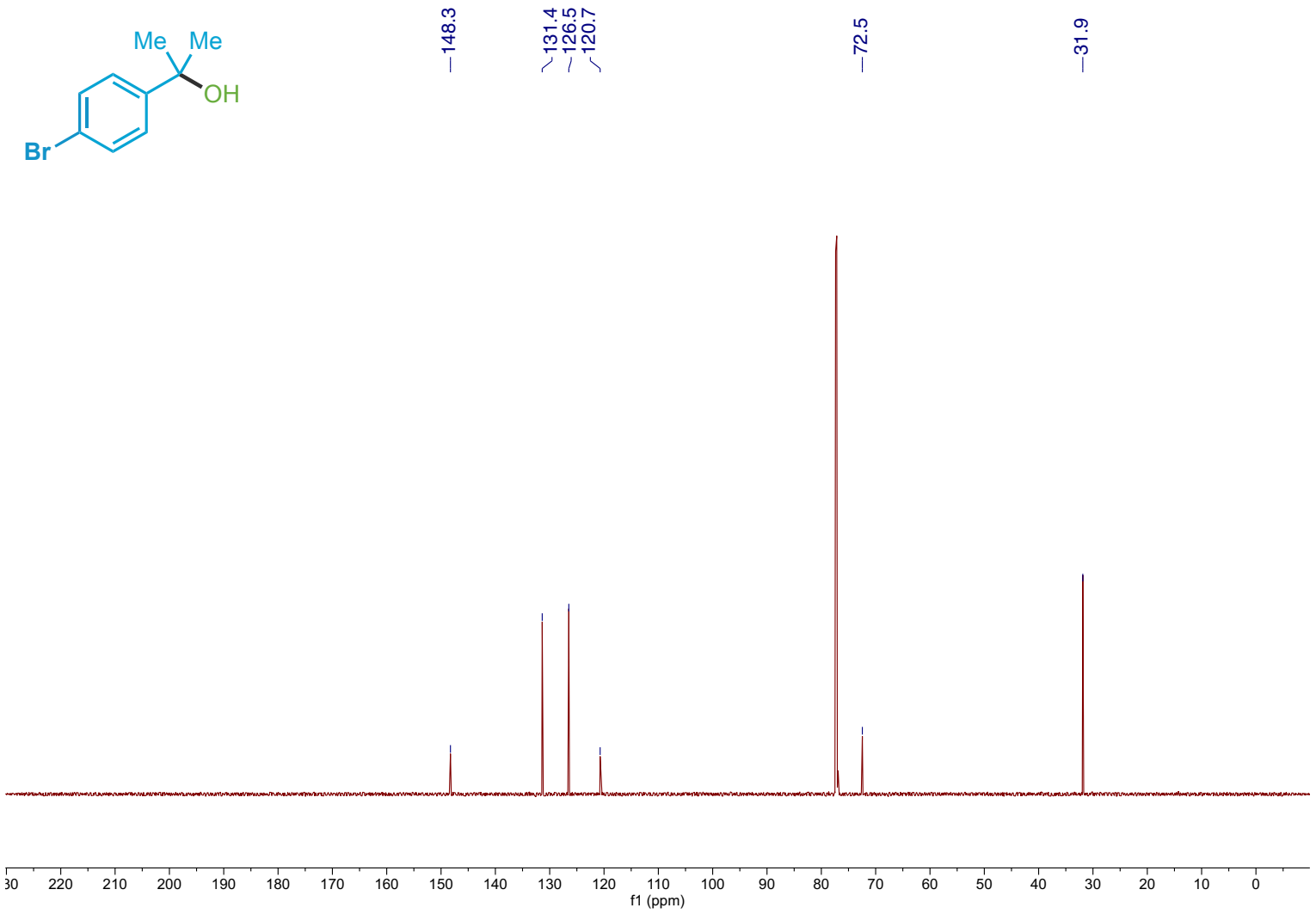
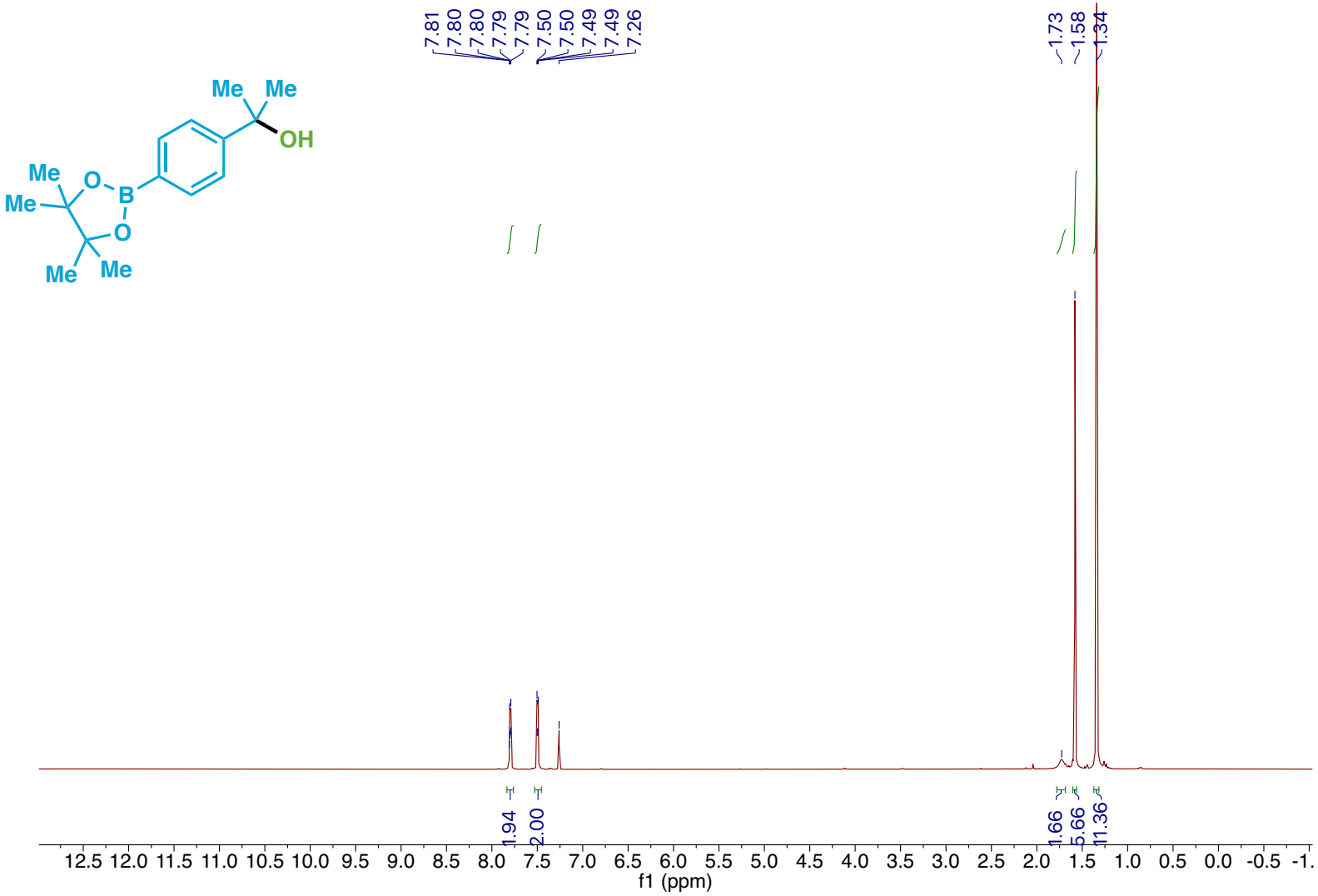


Compound 85 ^{1}H NMR



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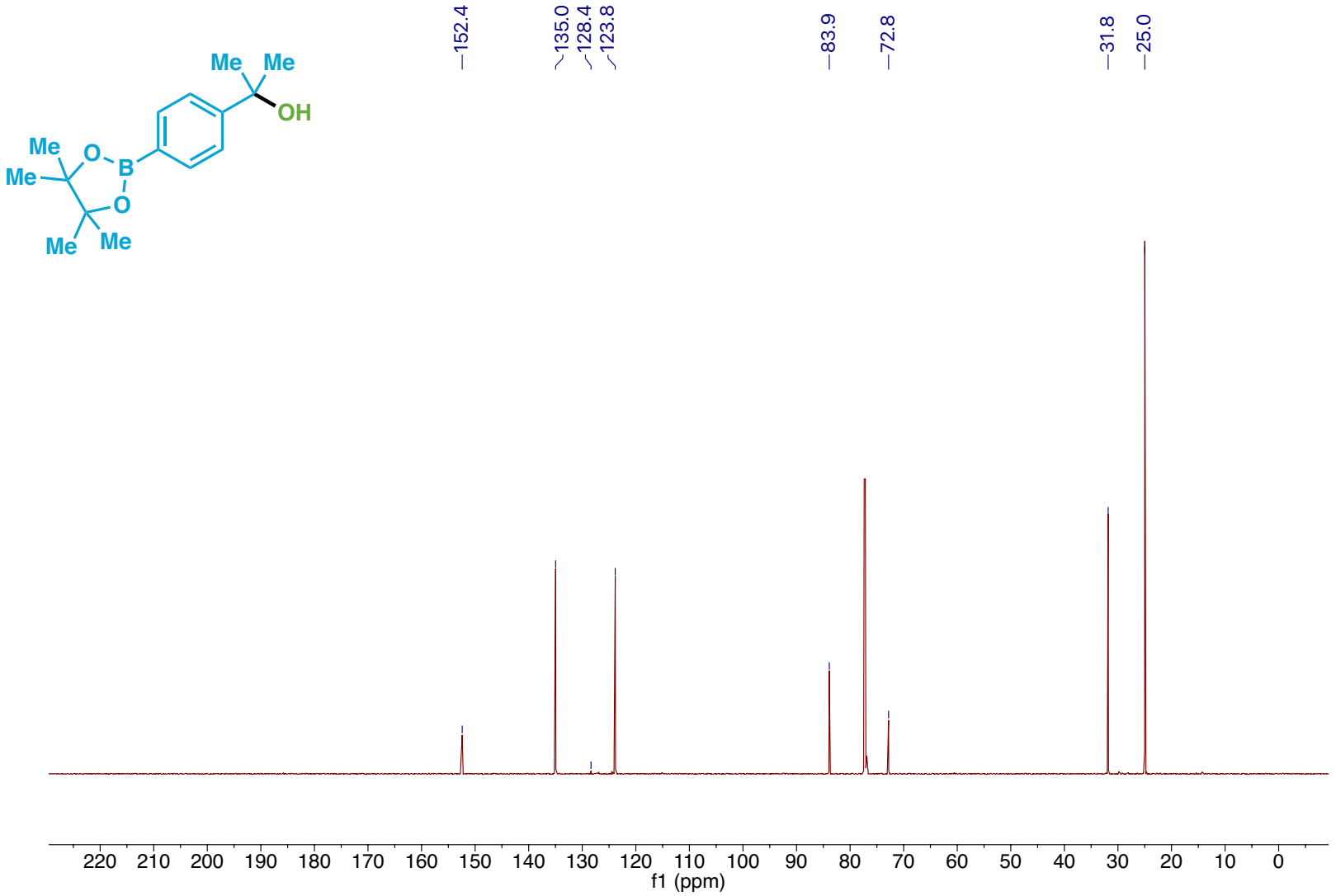

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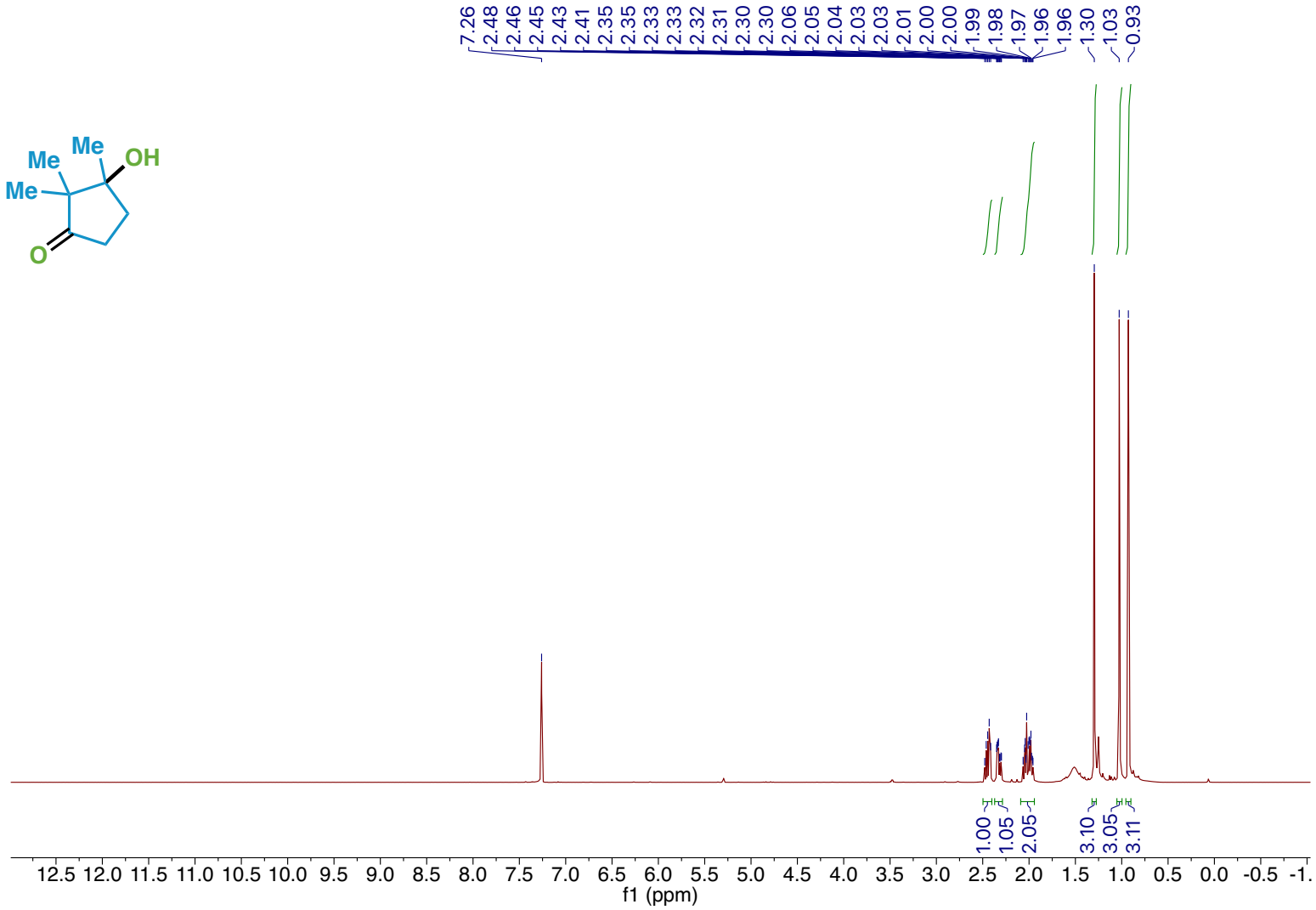

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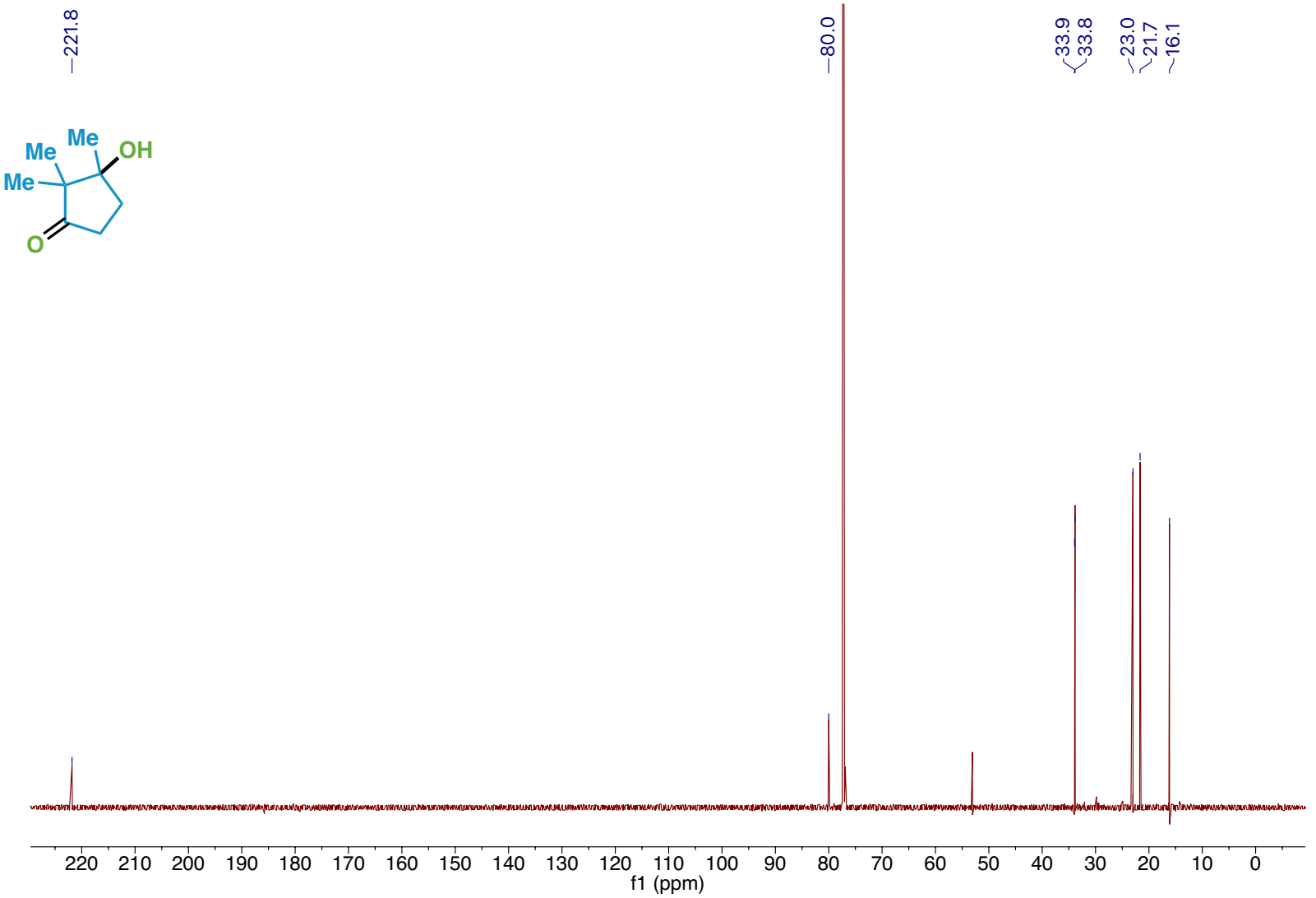

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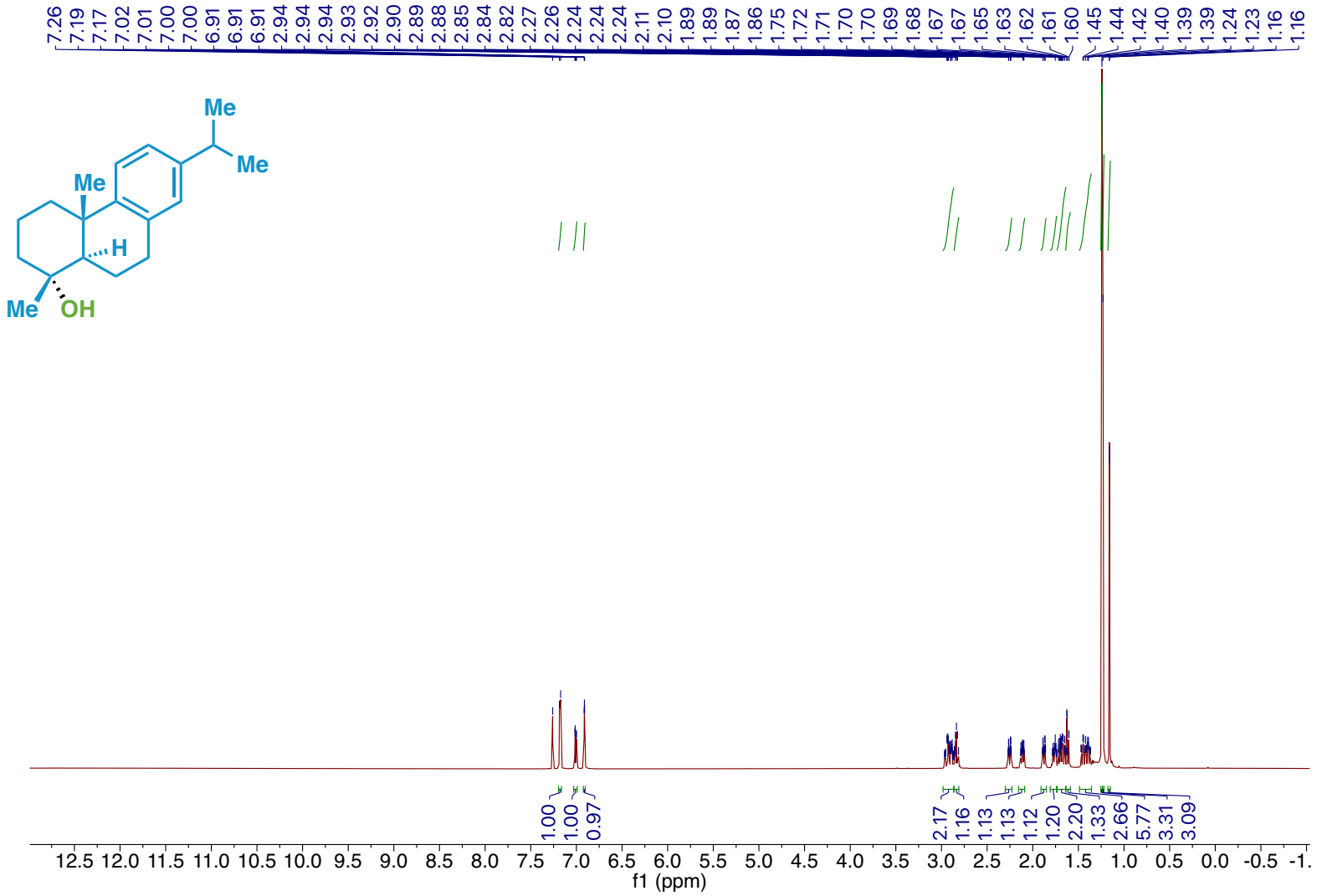

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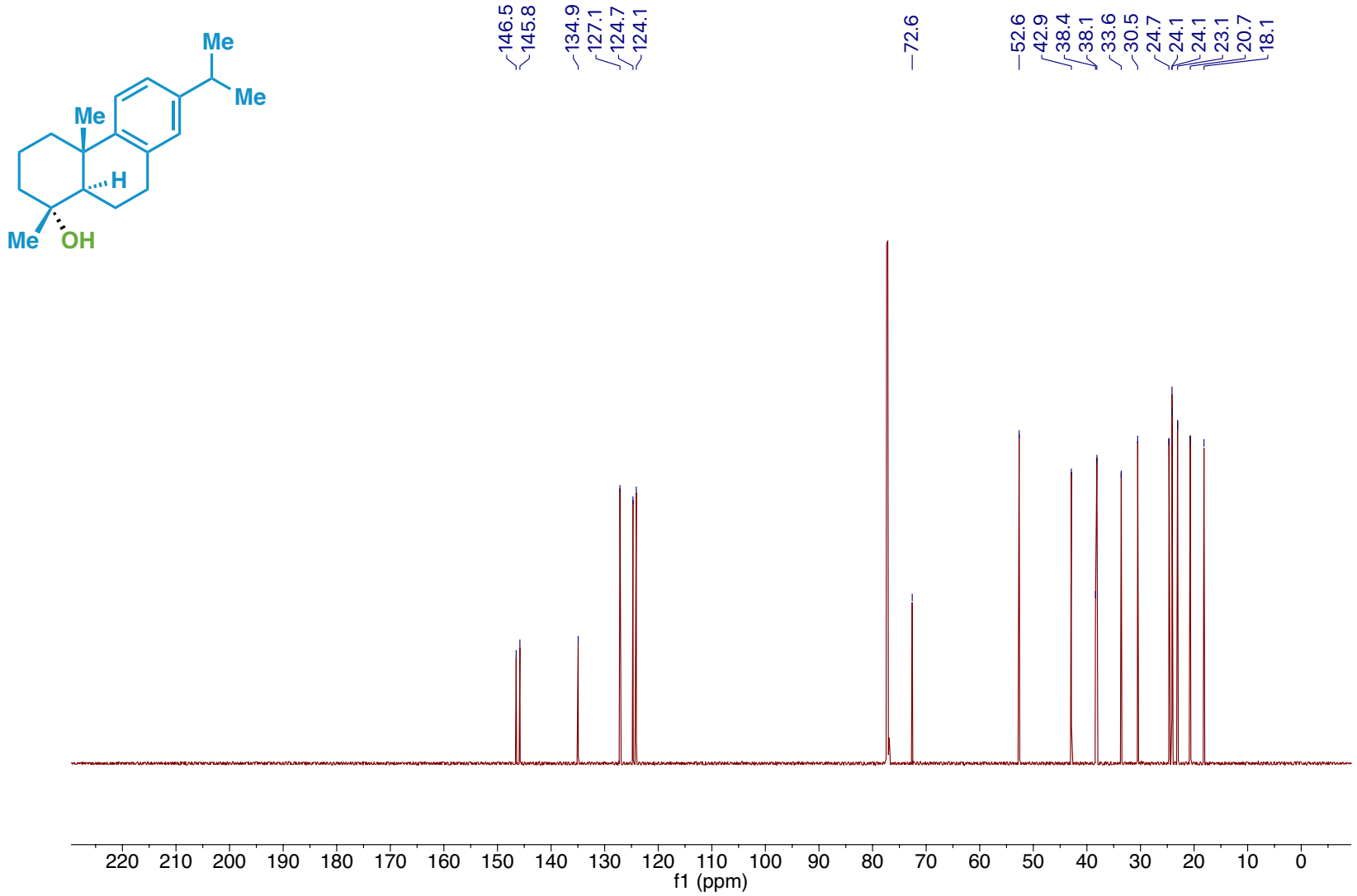

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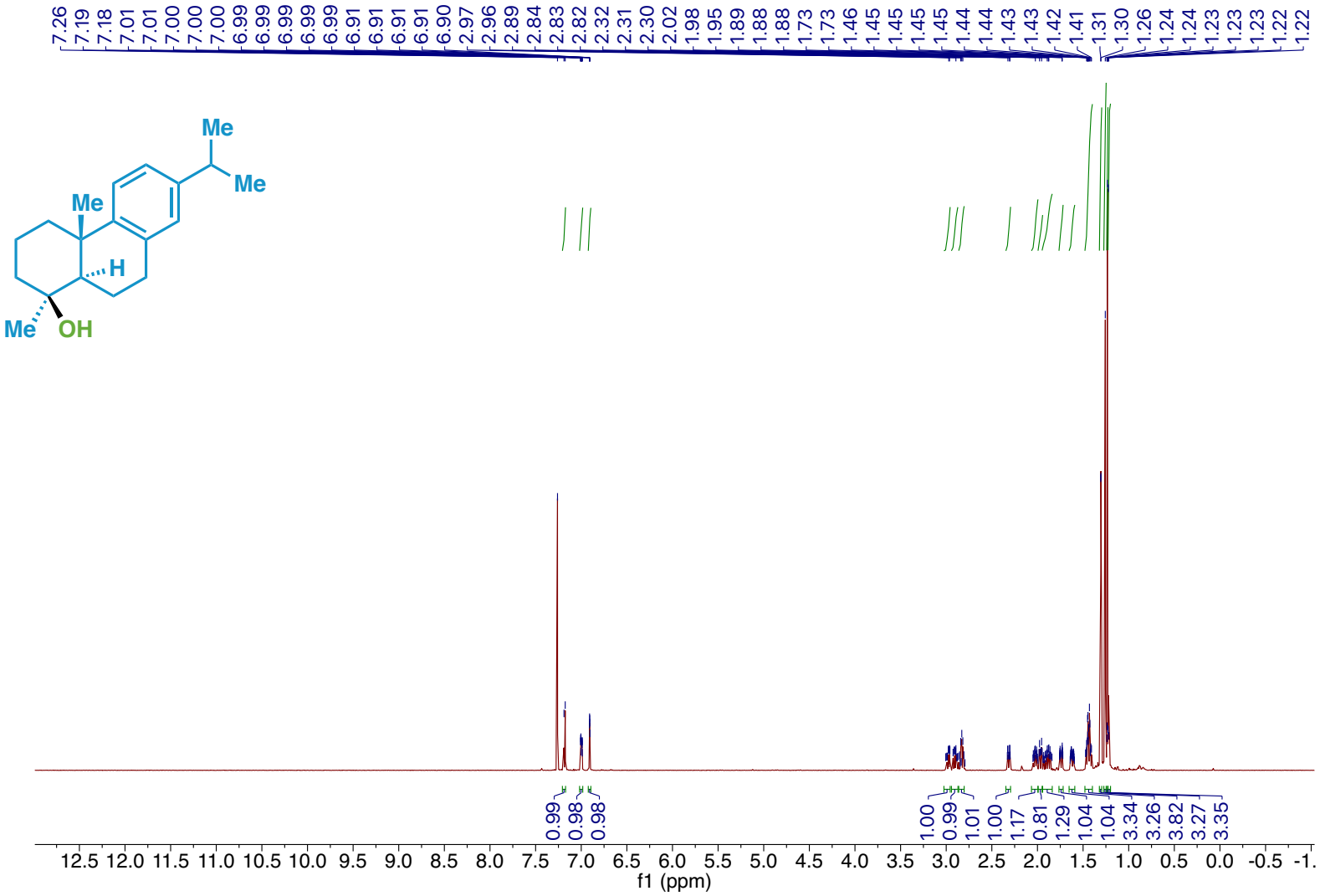

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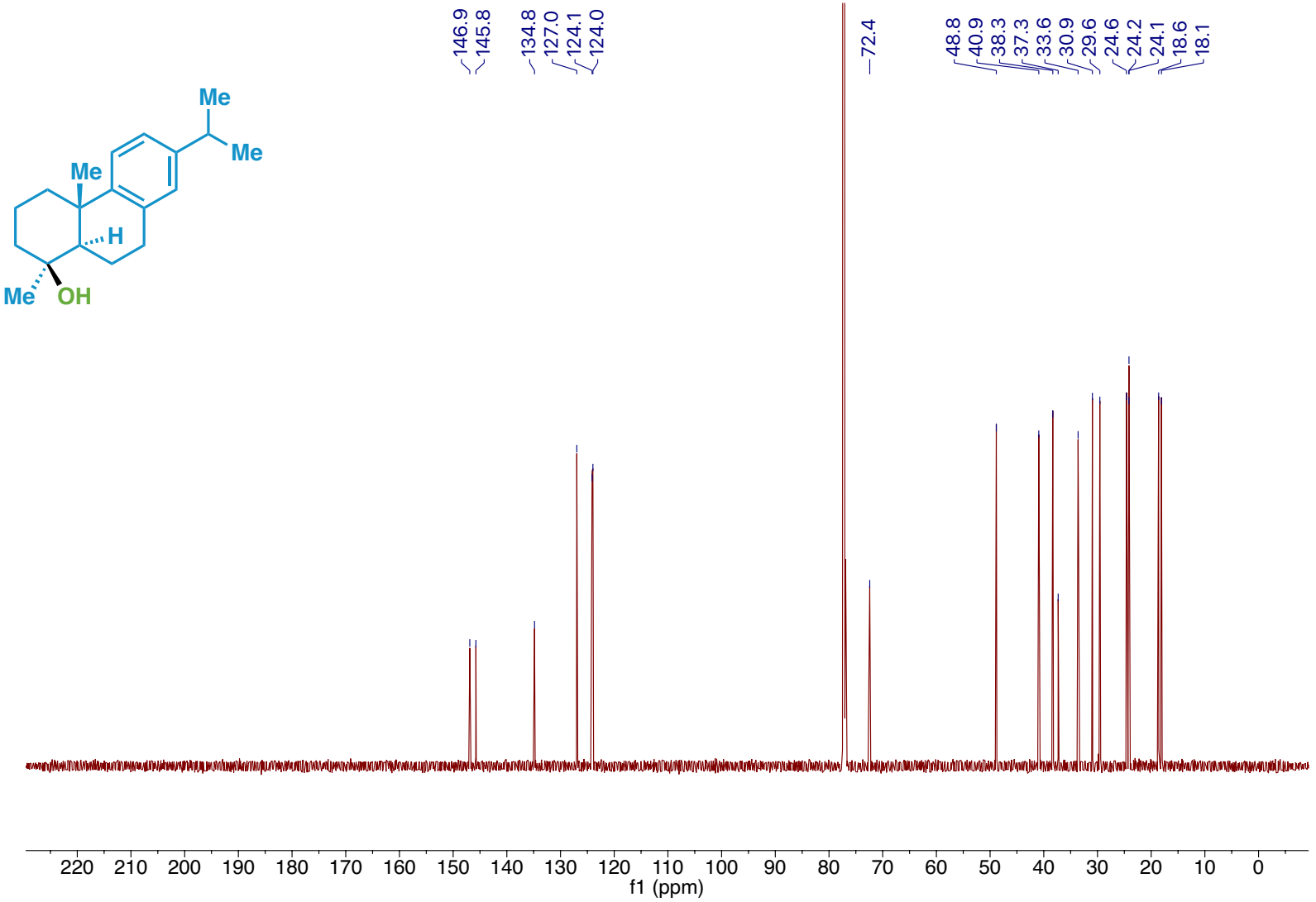
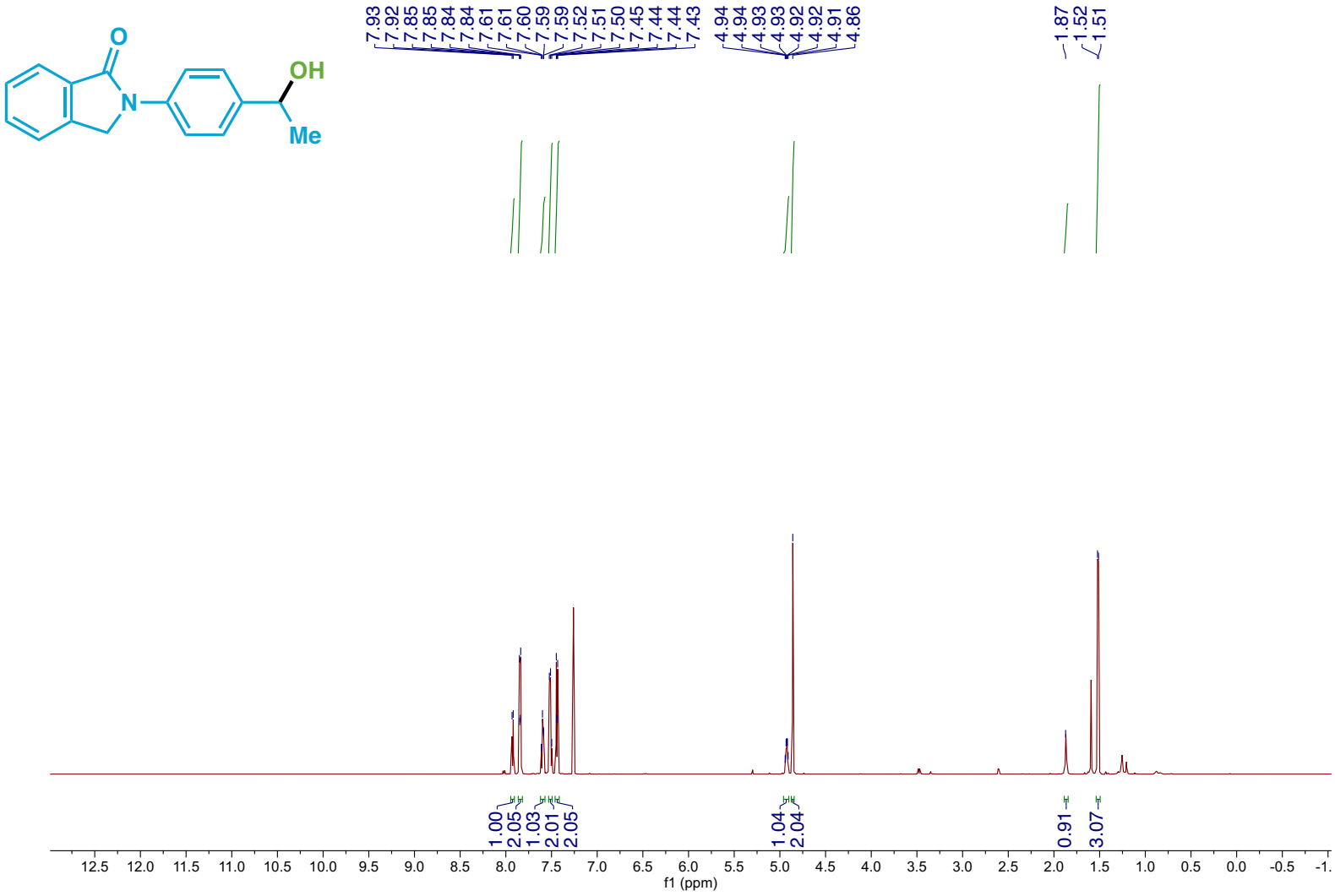


Compound 88 ^{1}H NMR



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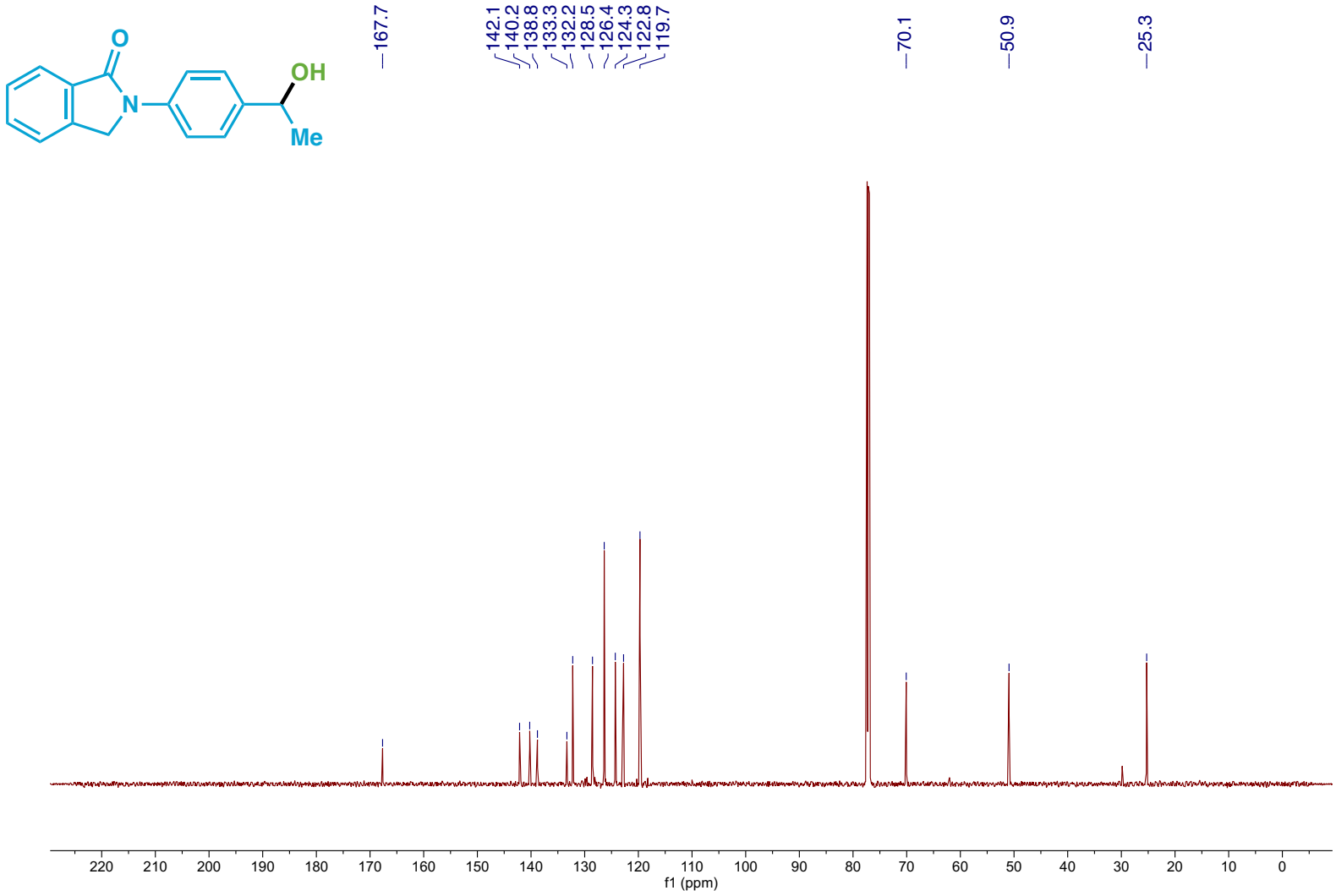
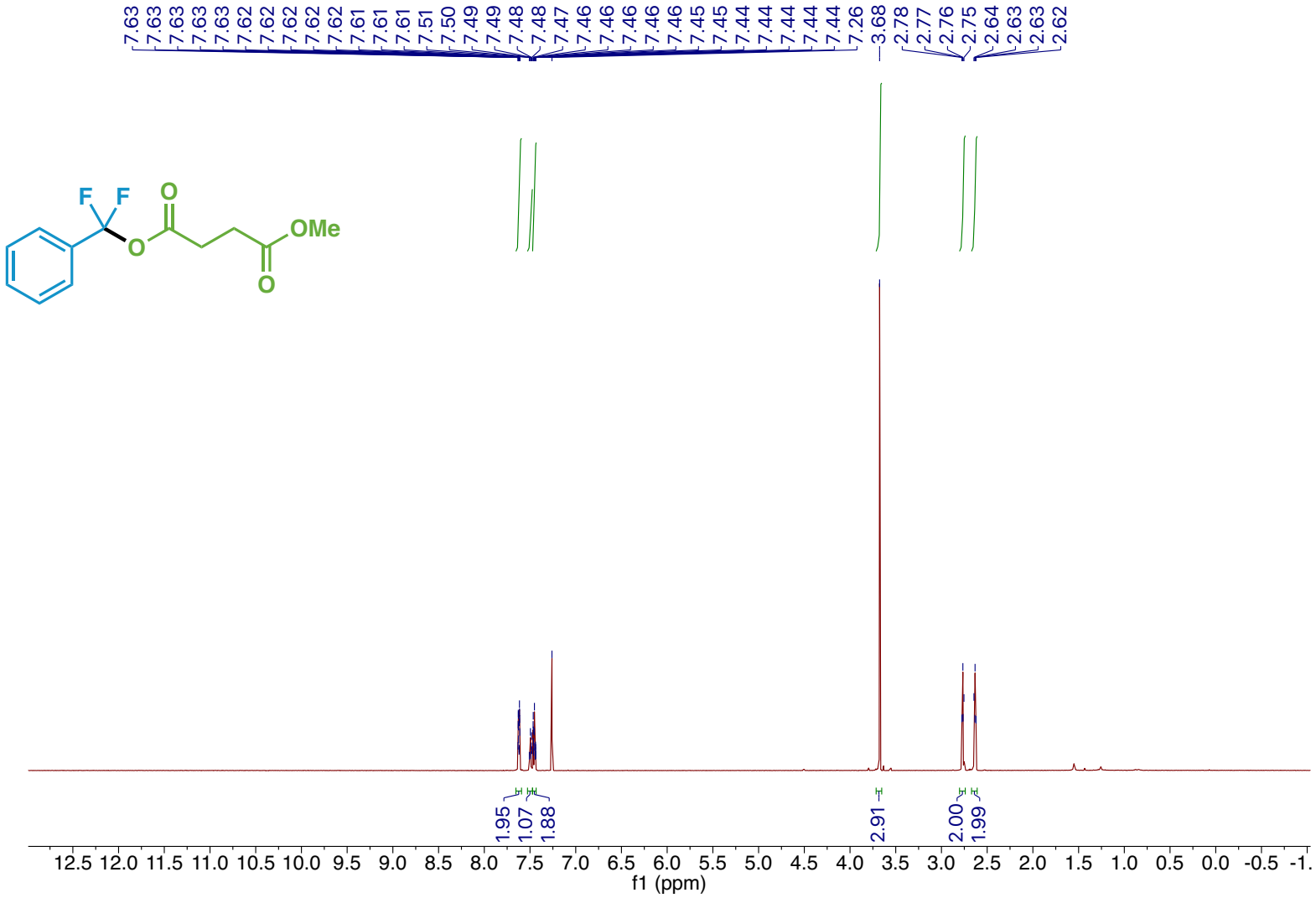
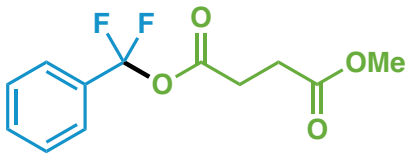


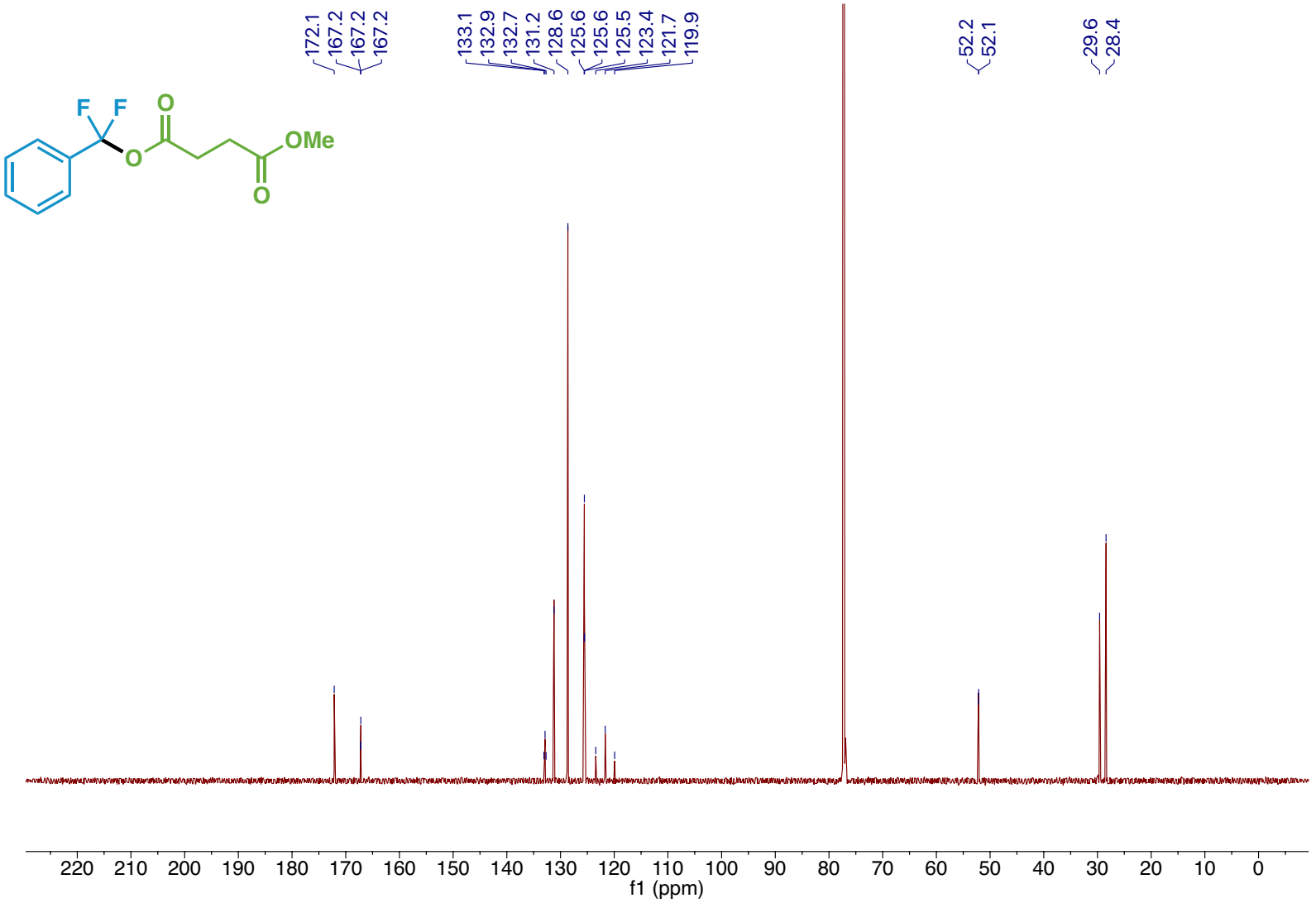
Compound 89 ^{1}H NMR



Compound 89 ^{19}F NMR



Compound 89 ^{13}C NMR



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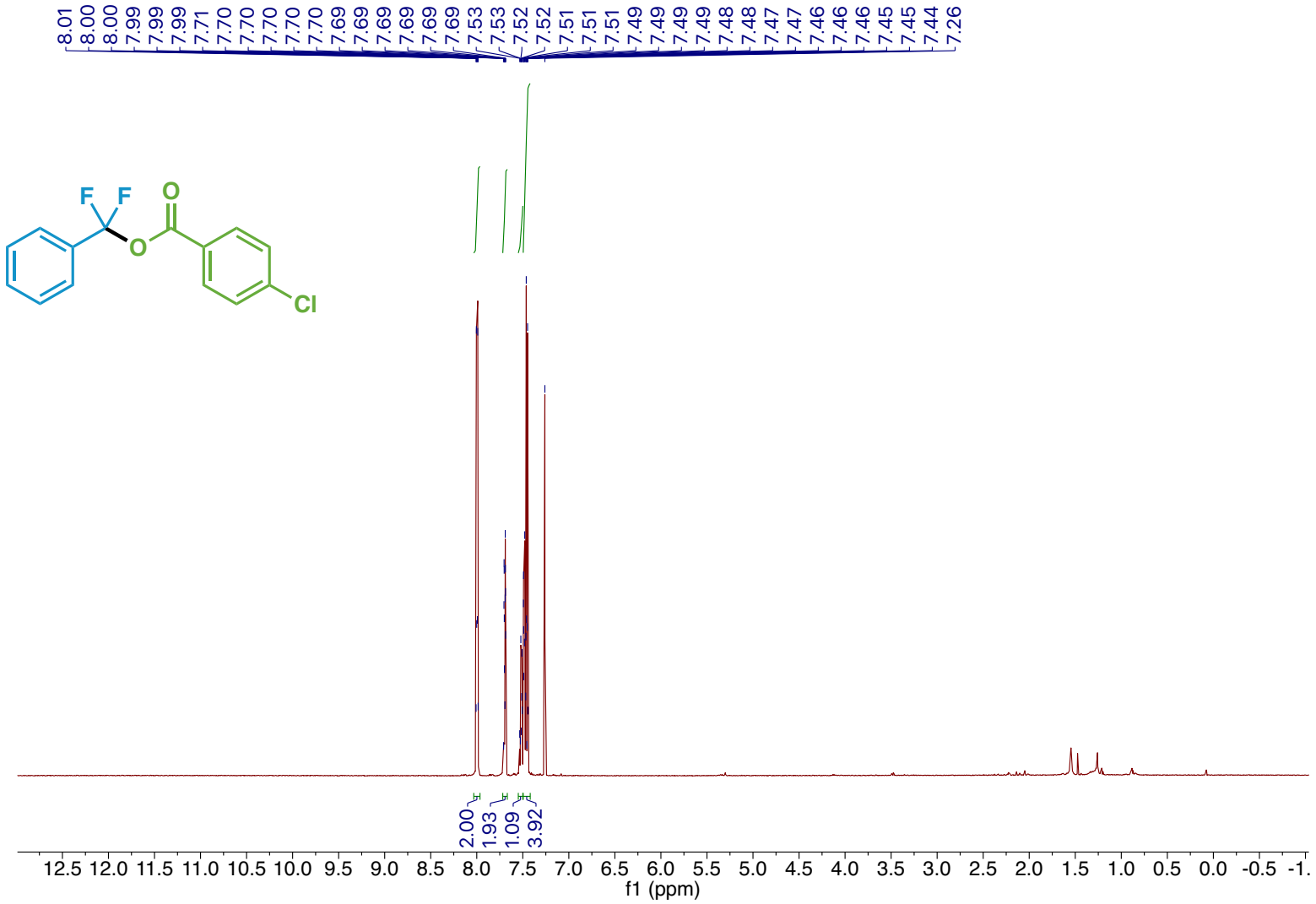
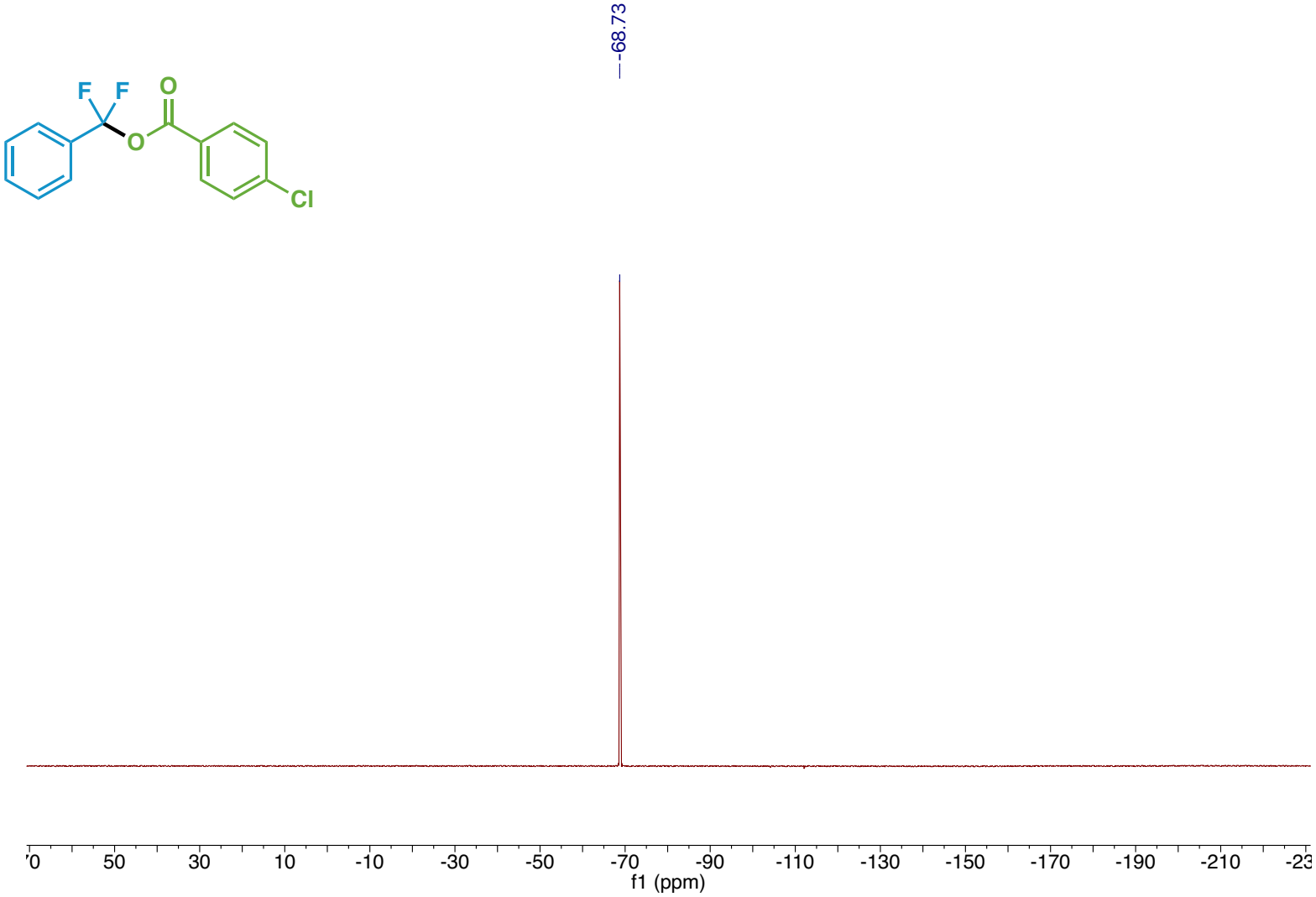
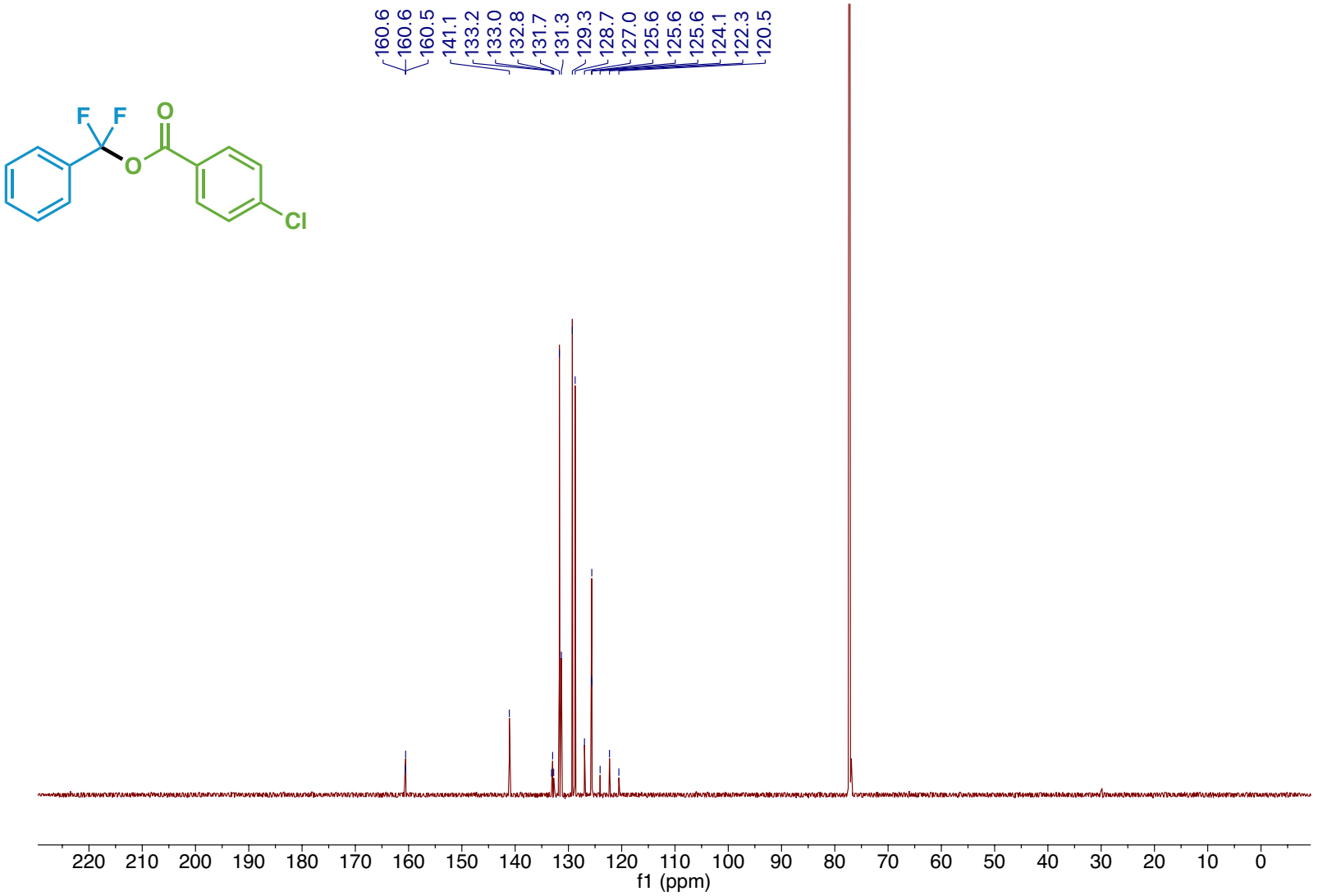


Compound 90 ^{19}F NMR



Compound 90 ^{13}C NMR



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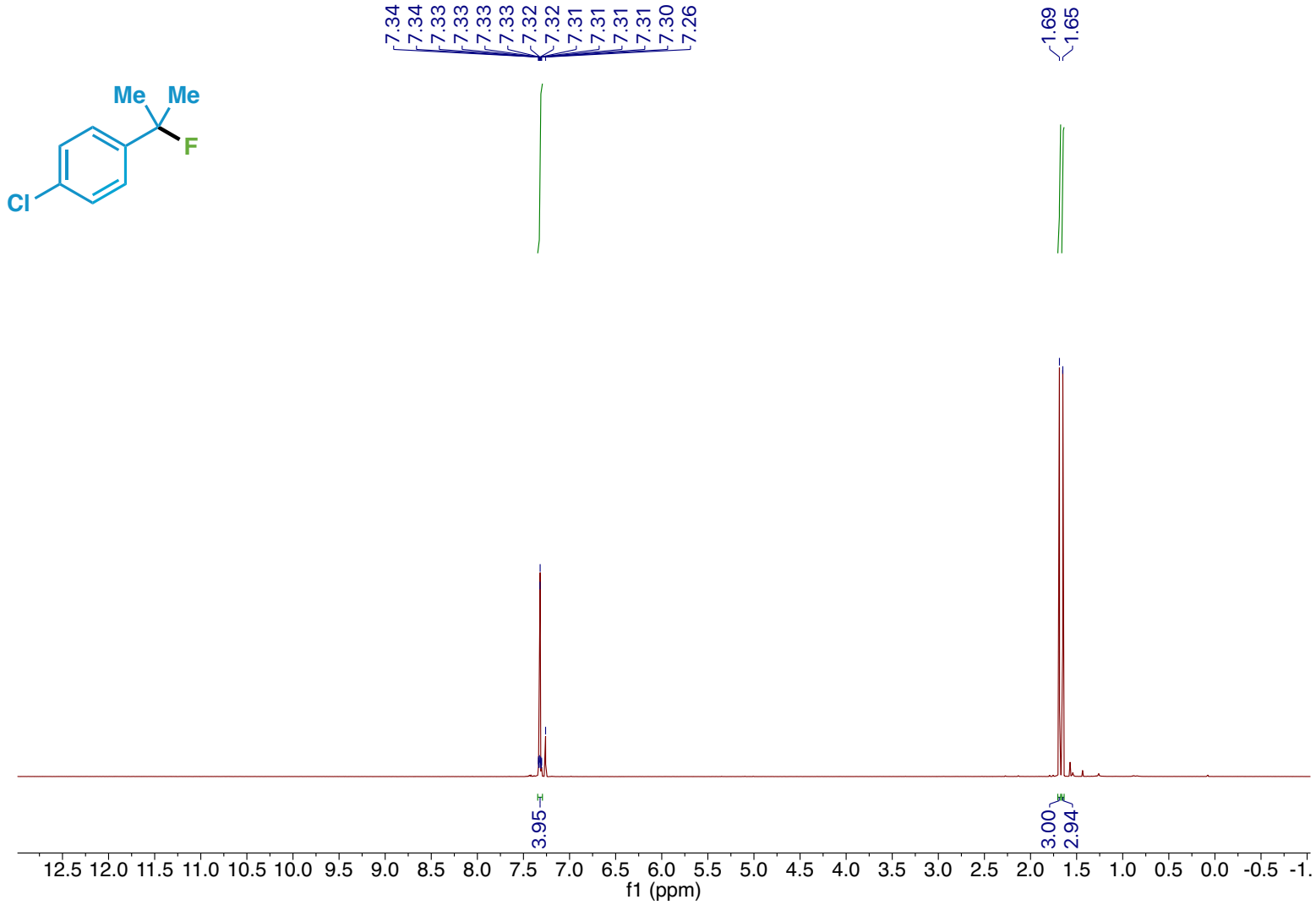

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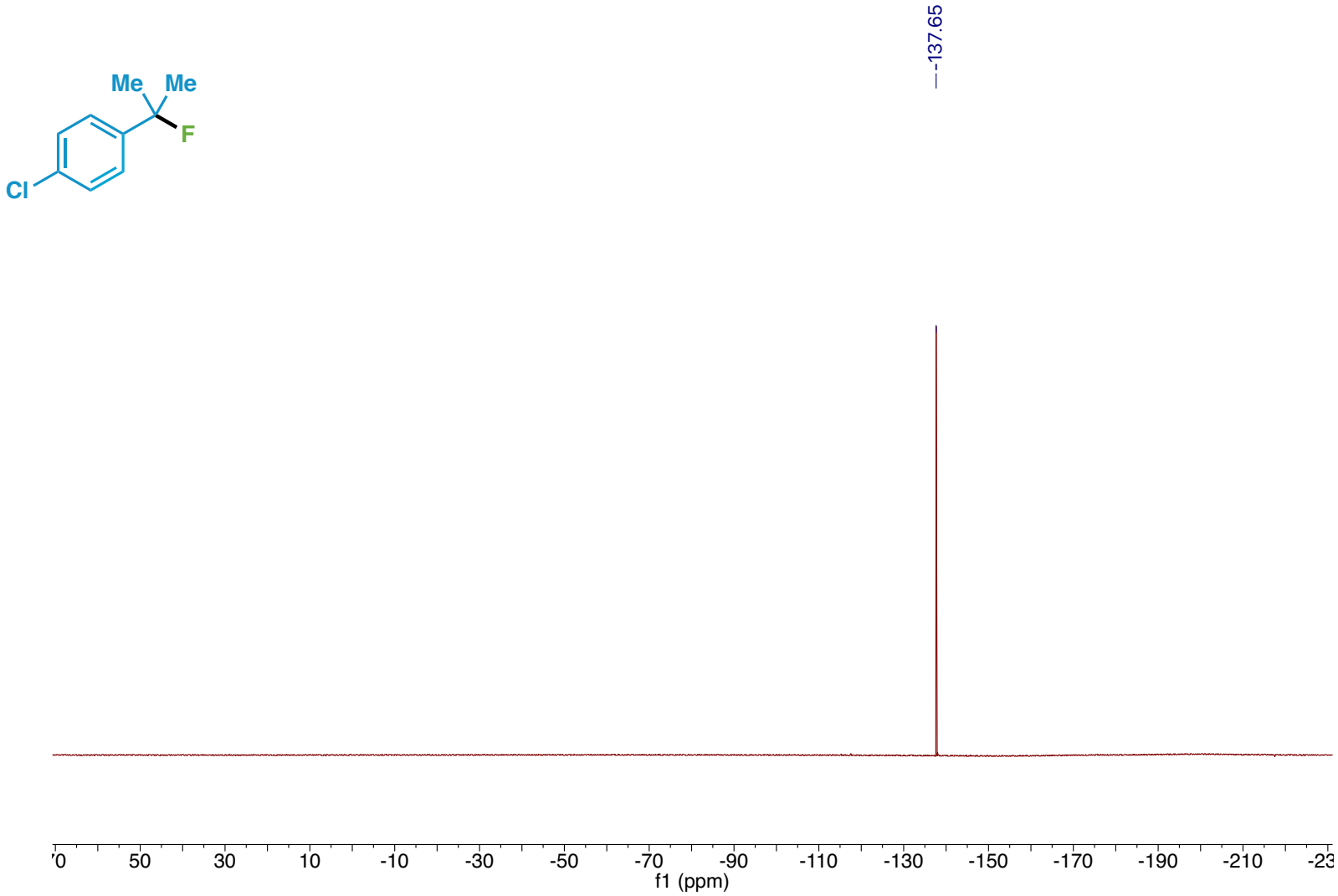
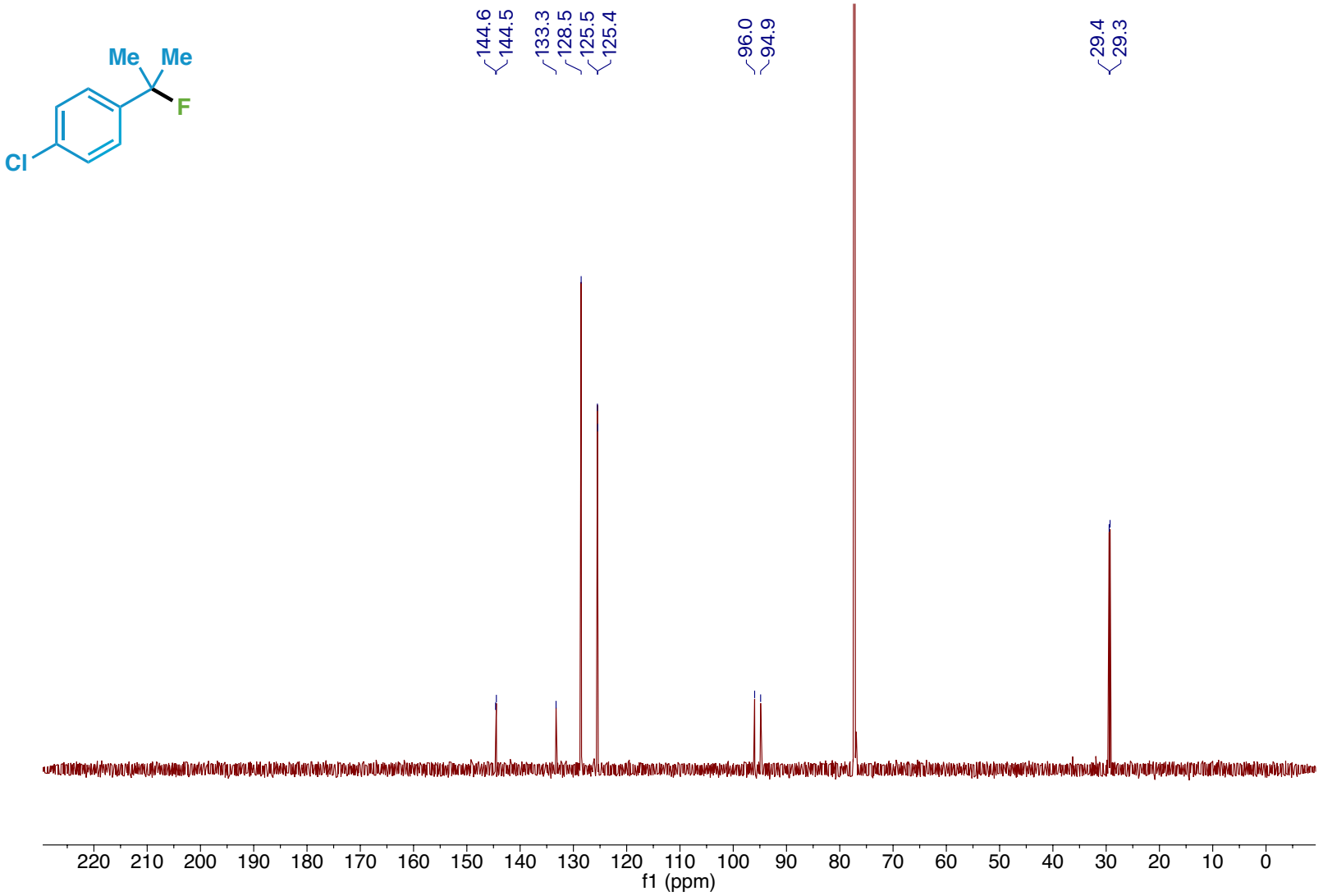


Compound 91 ^{13}C NMR



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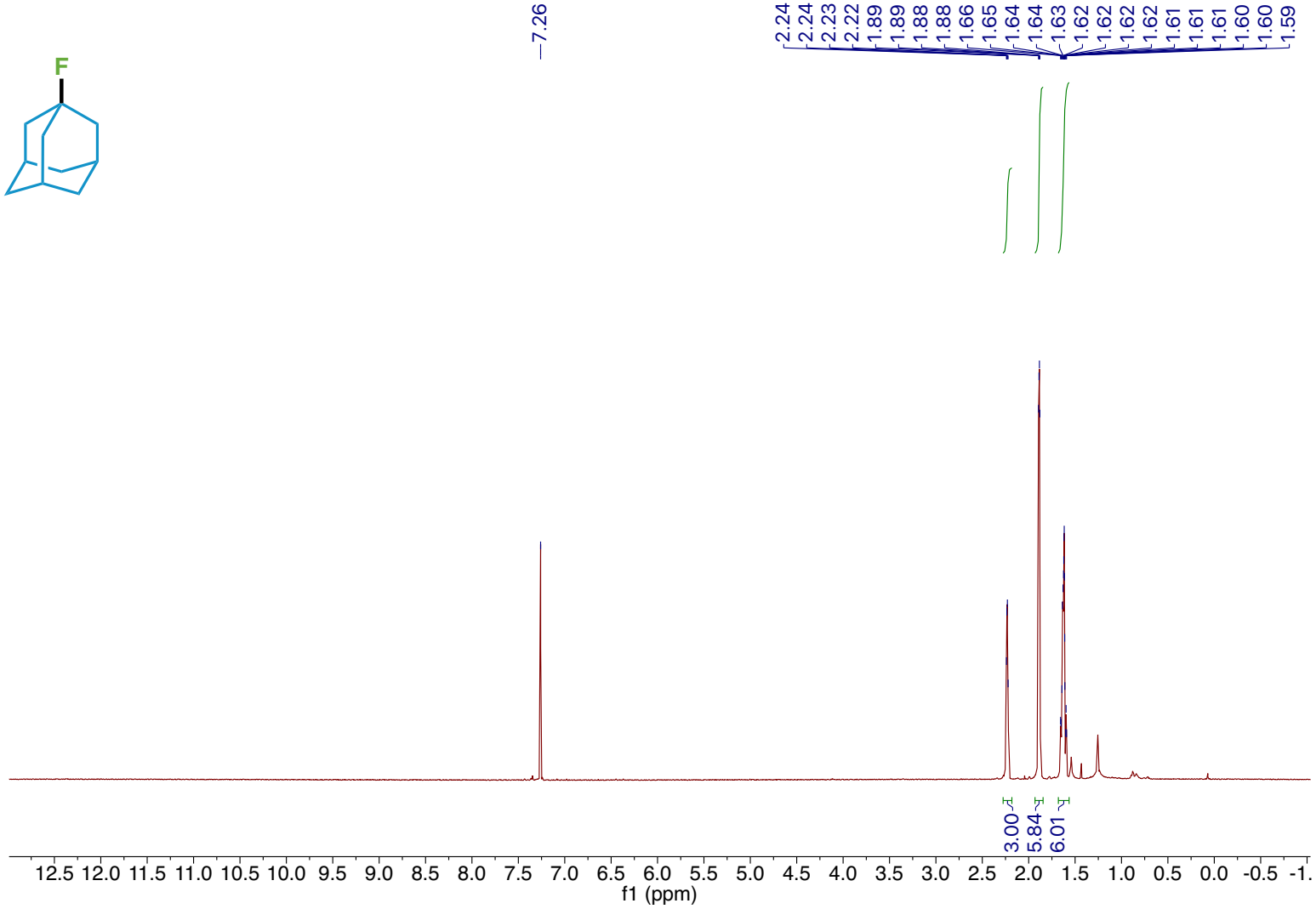
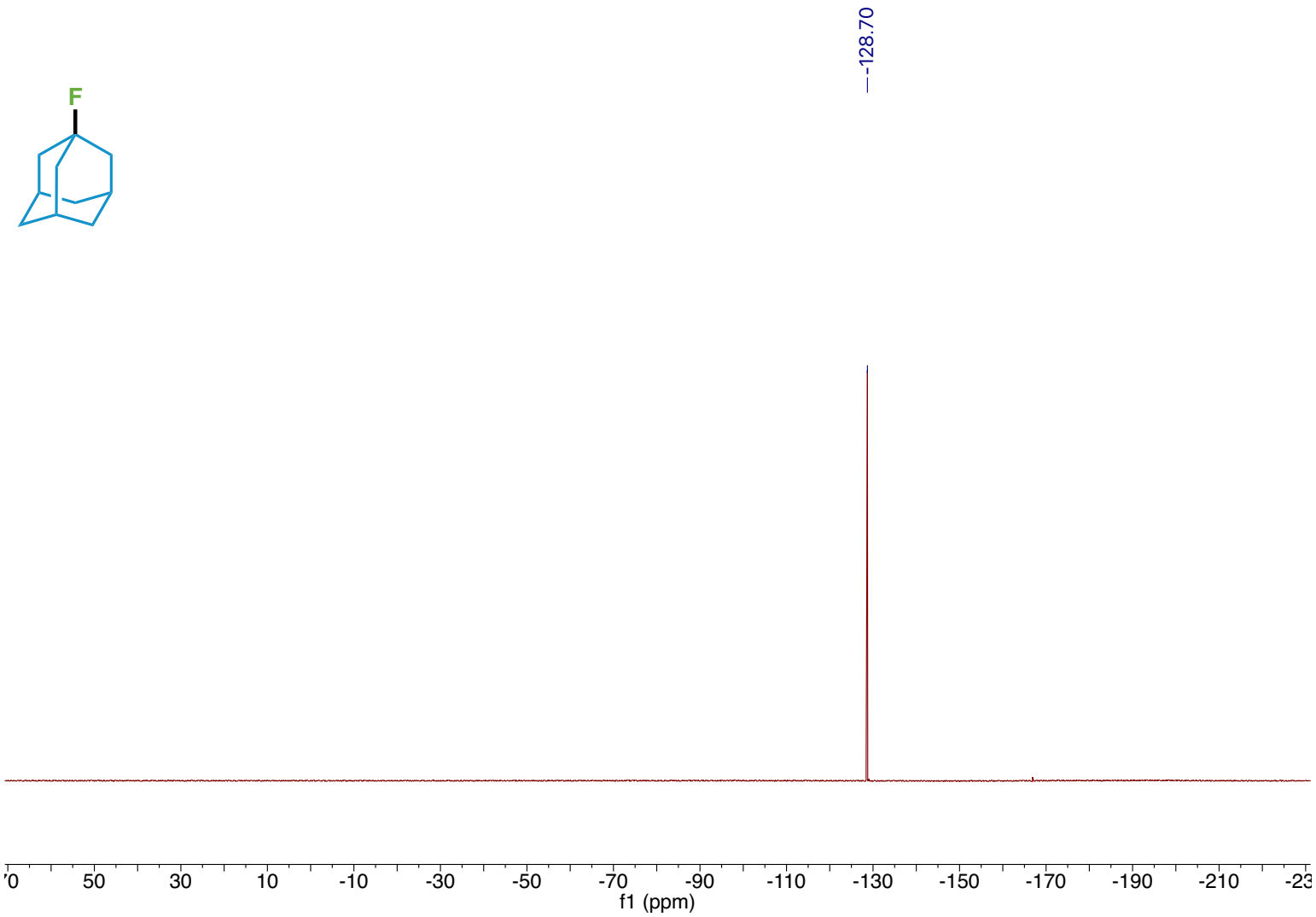
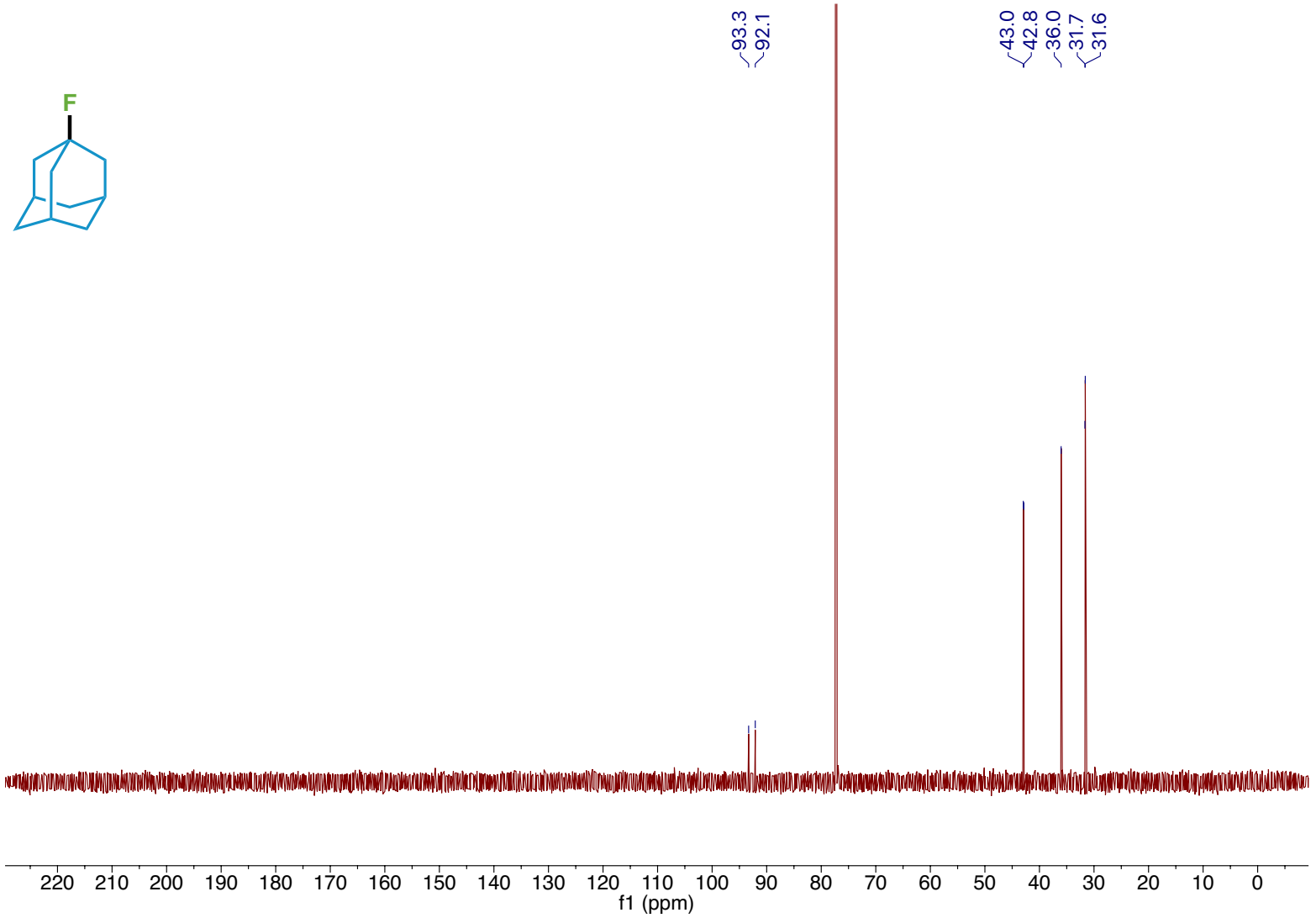


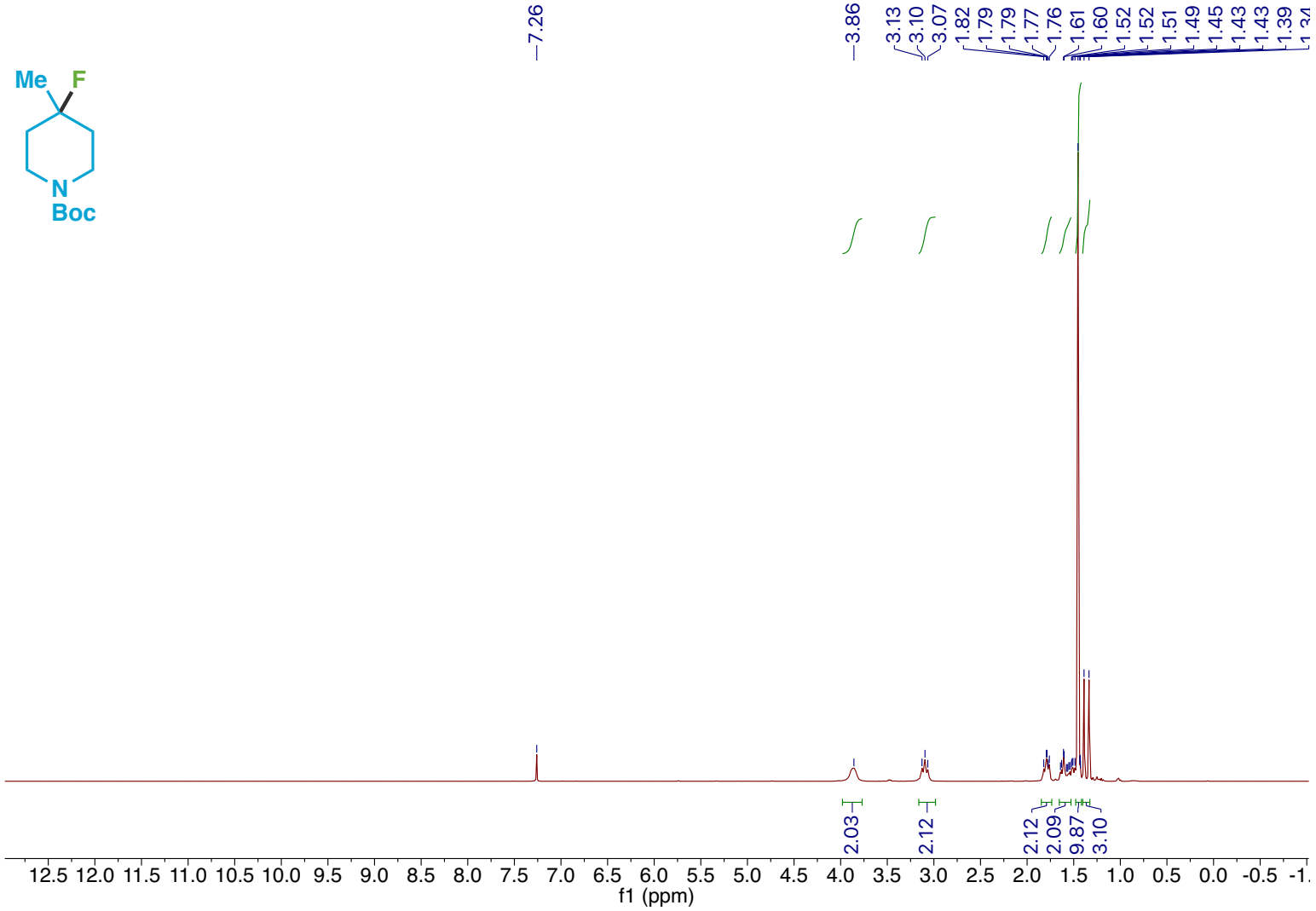
Compound 92 ^{19}F NMR



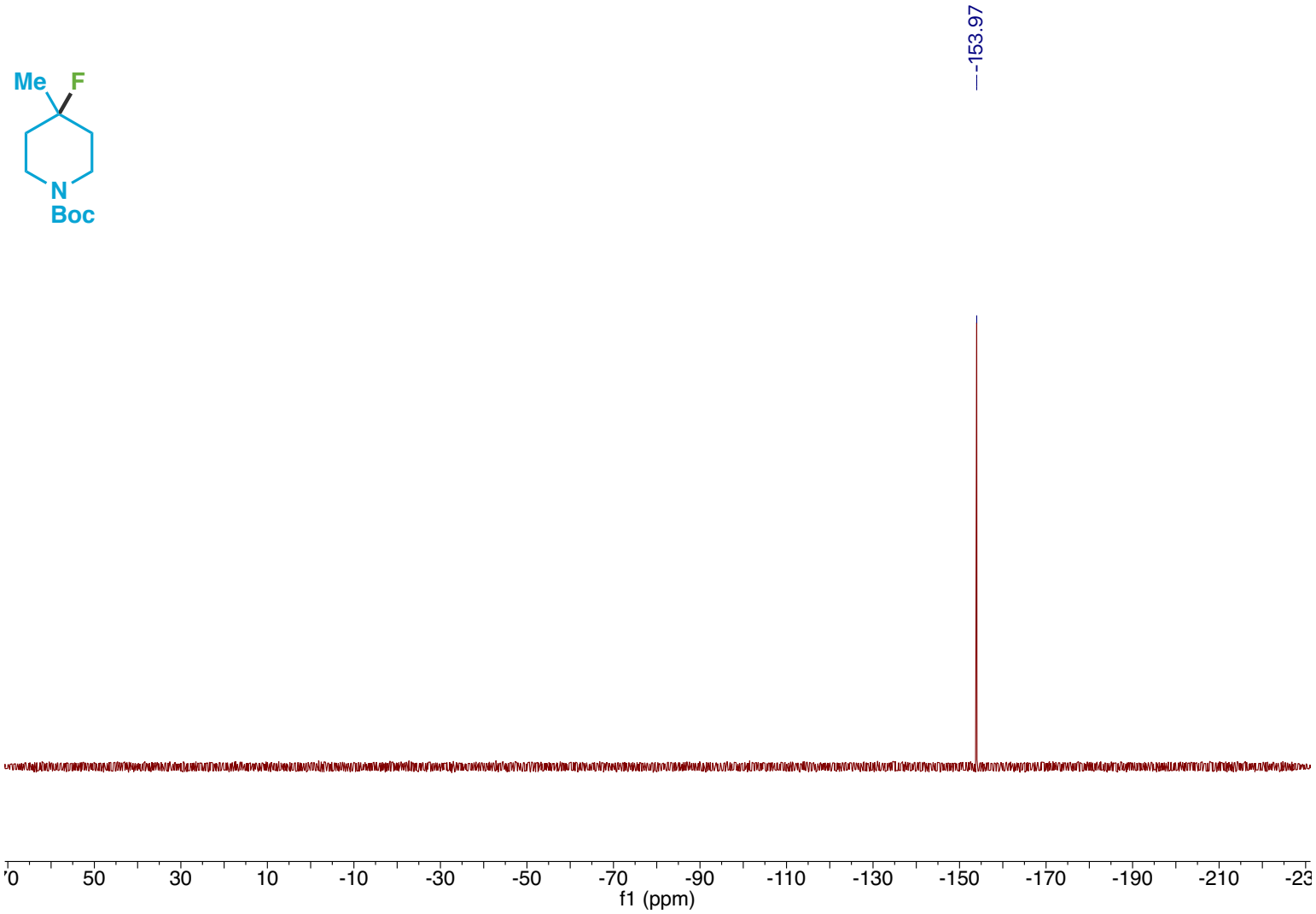
Compound 92 ^{13}C NMR



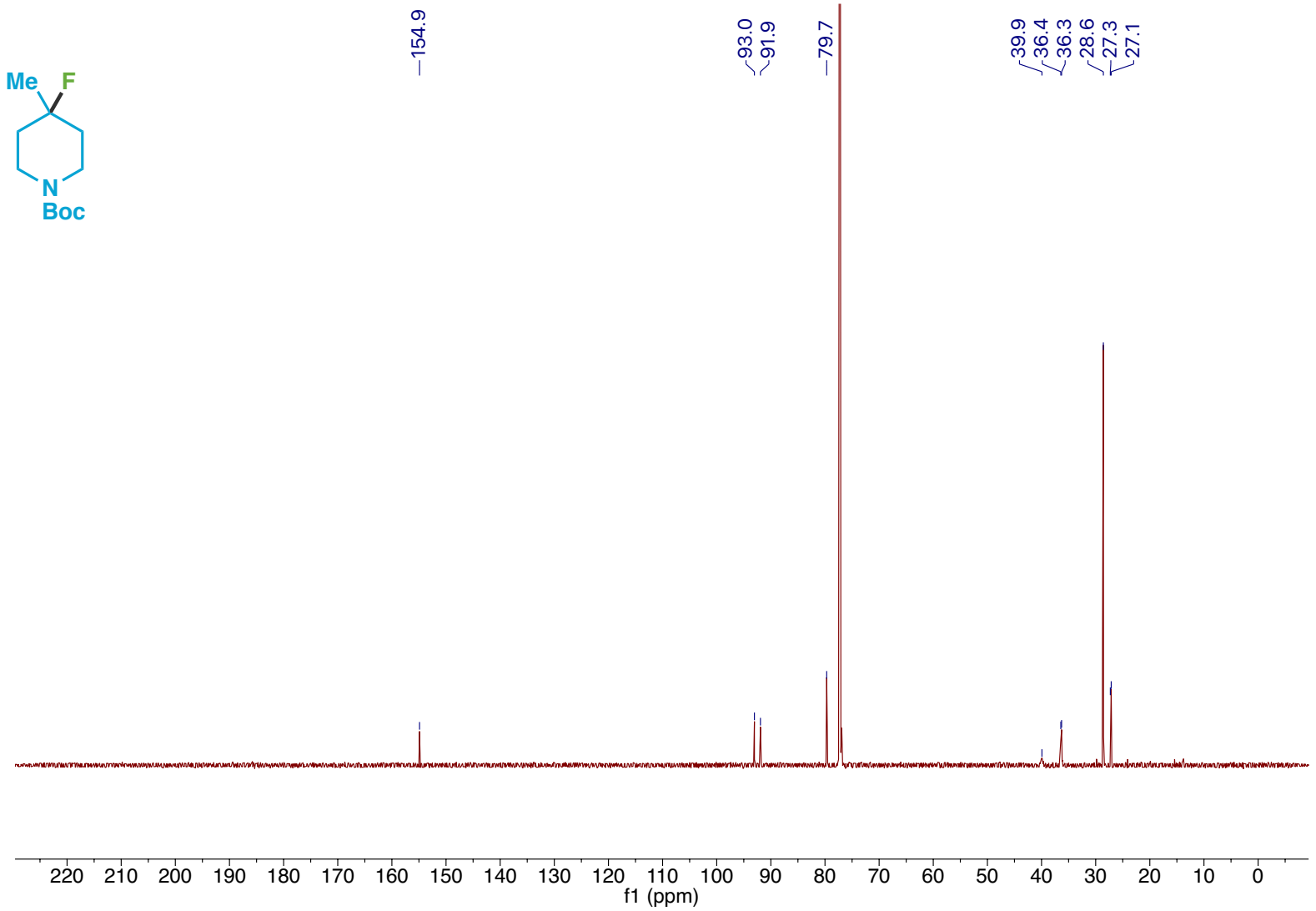
Compound 93 ^{1}H NMR



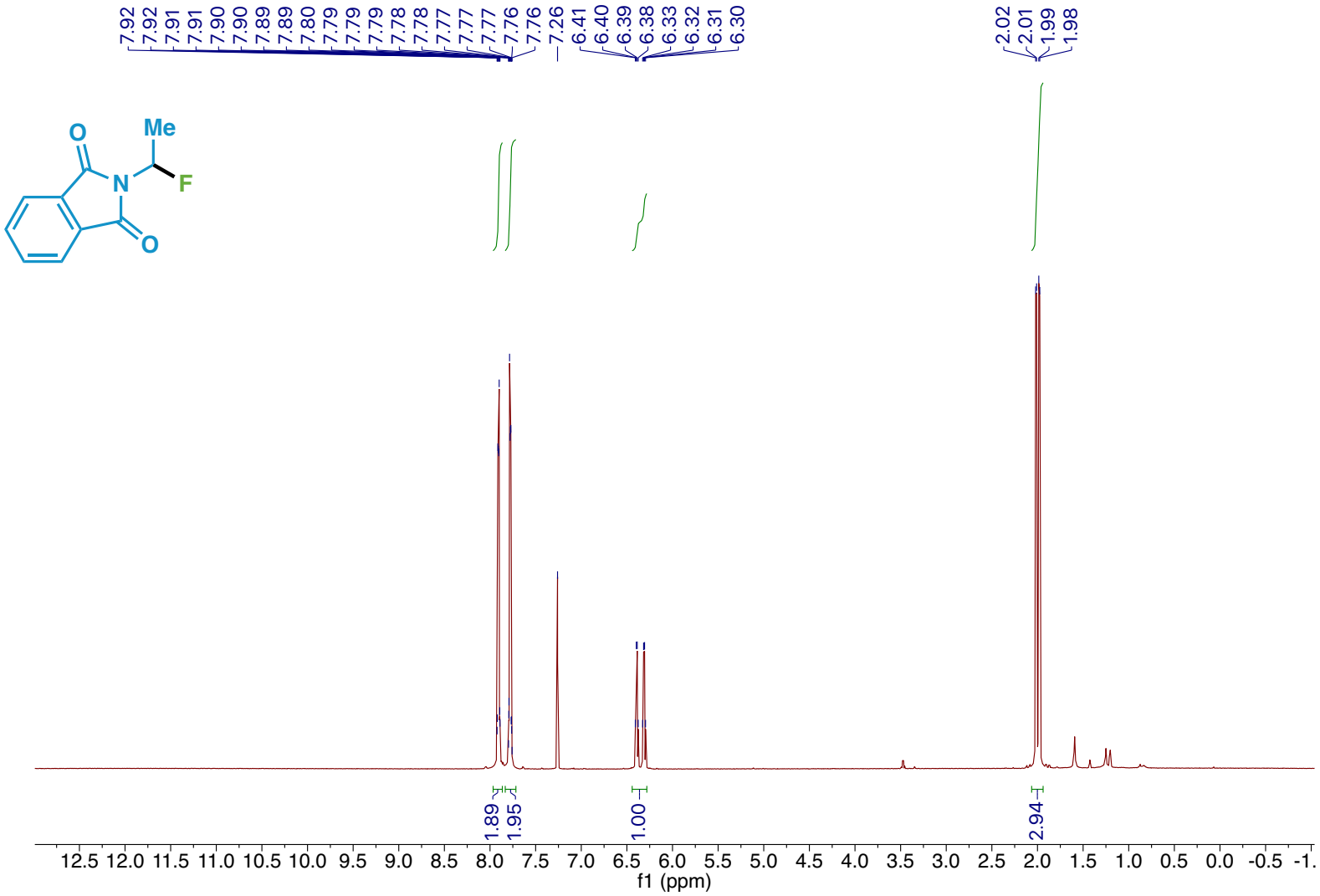
Compound 93 ^{19}F NMR



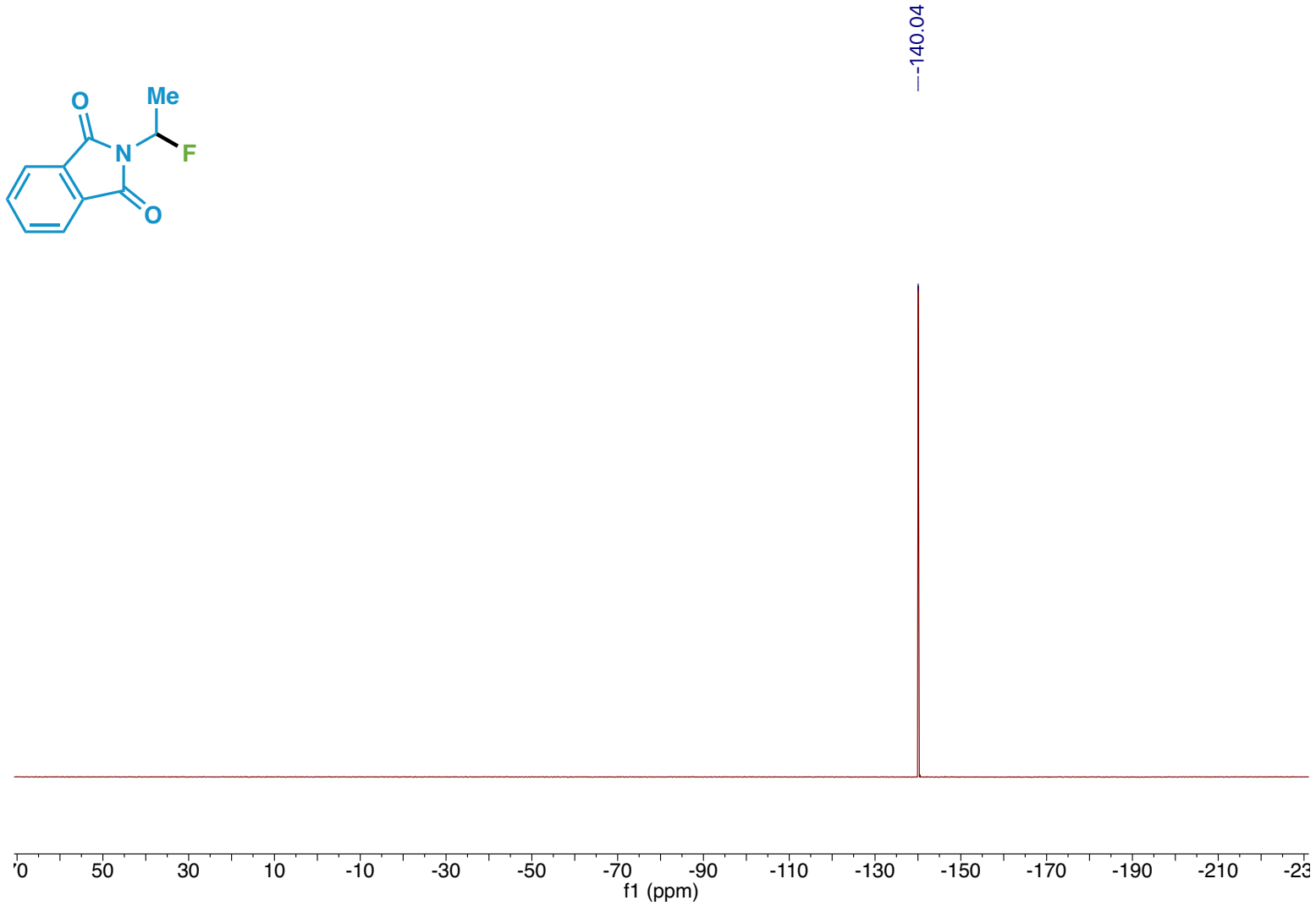
Compound 93 ^{13}C NMR



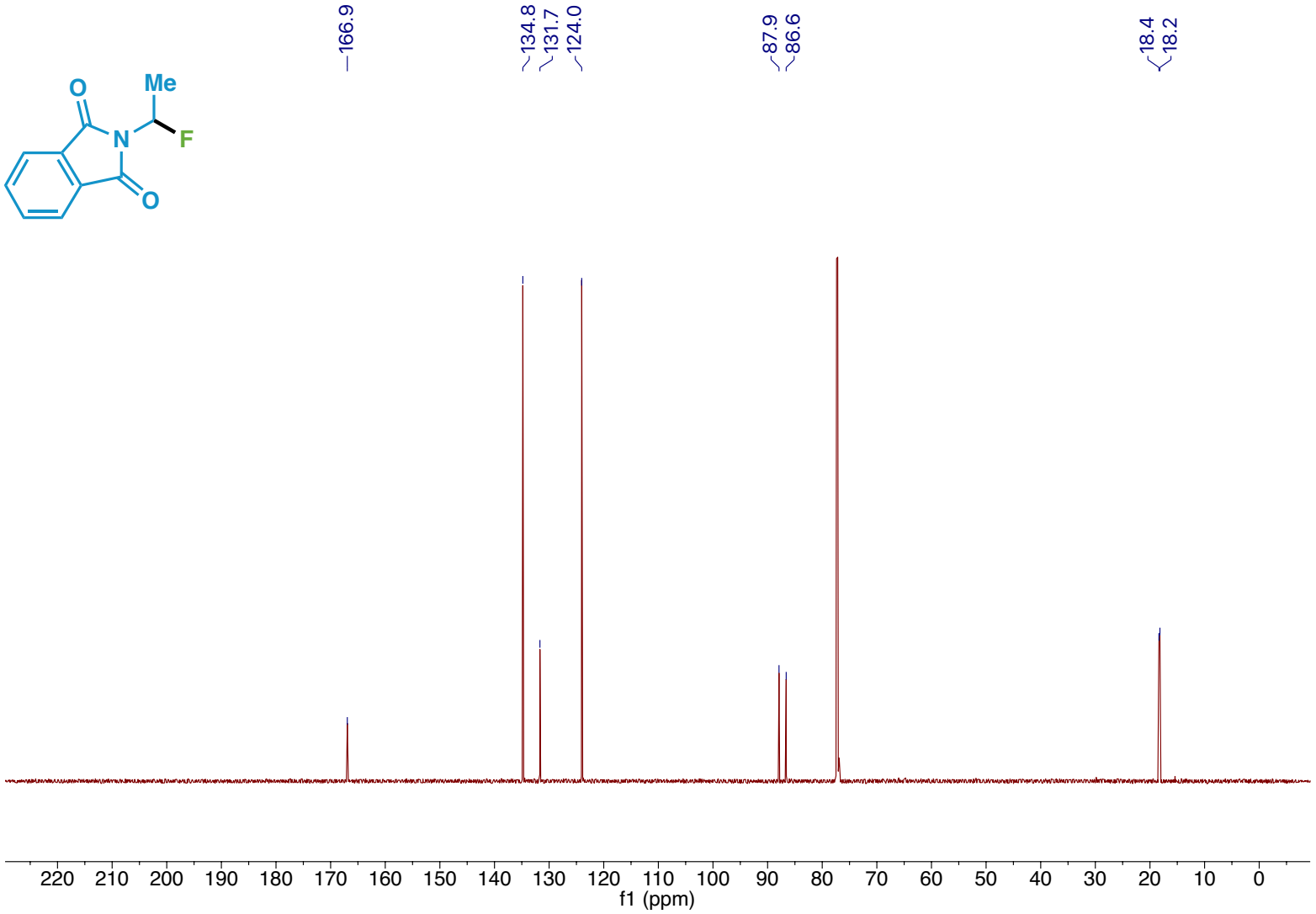
Compound 94 ^{1}H NMR



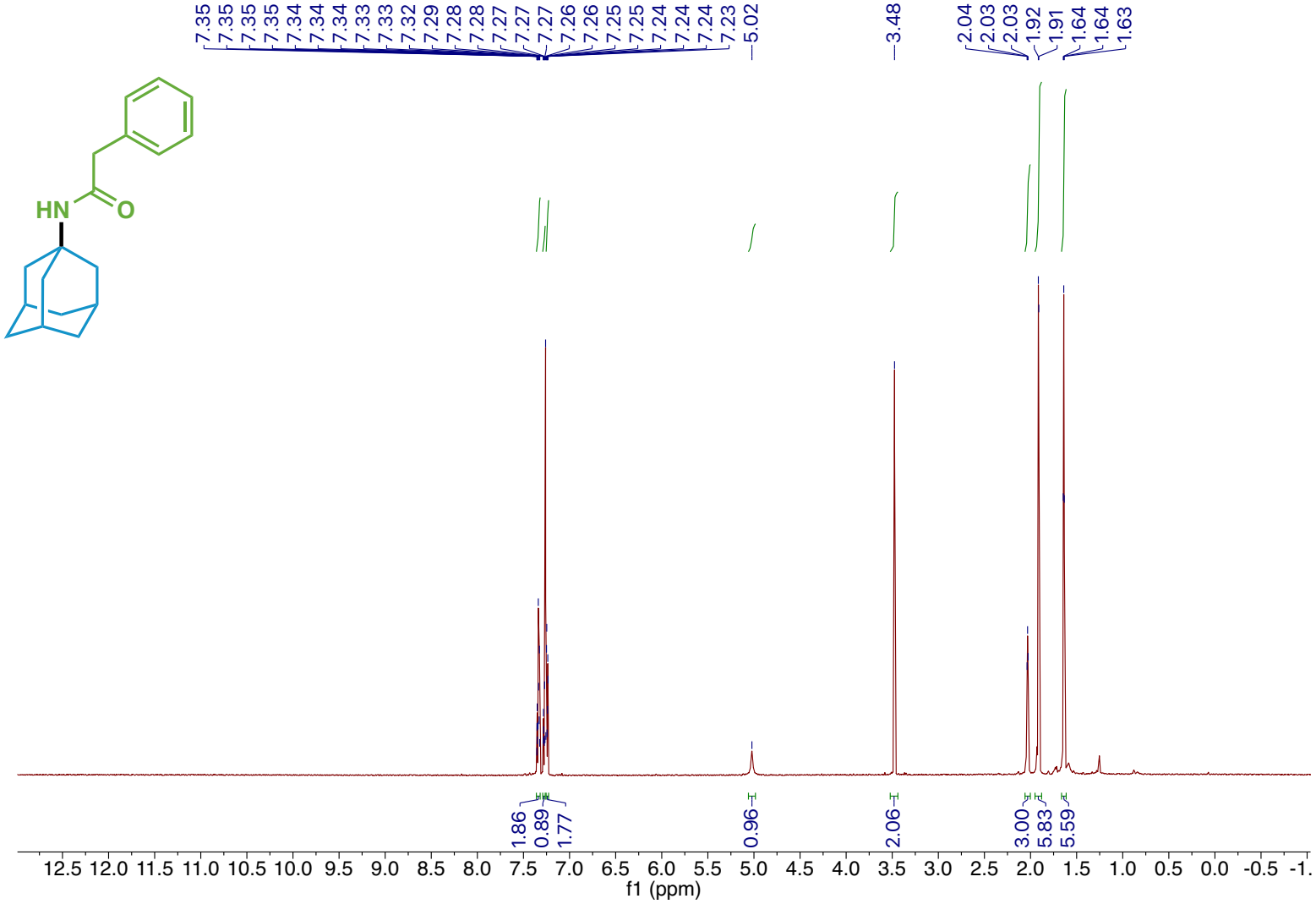
Compound 94 ^{19}F NMR



Compound 94 ^{13}C NMR



Compound 95 ^{1}H NMR



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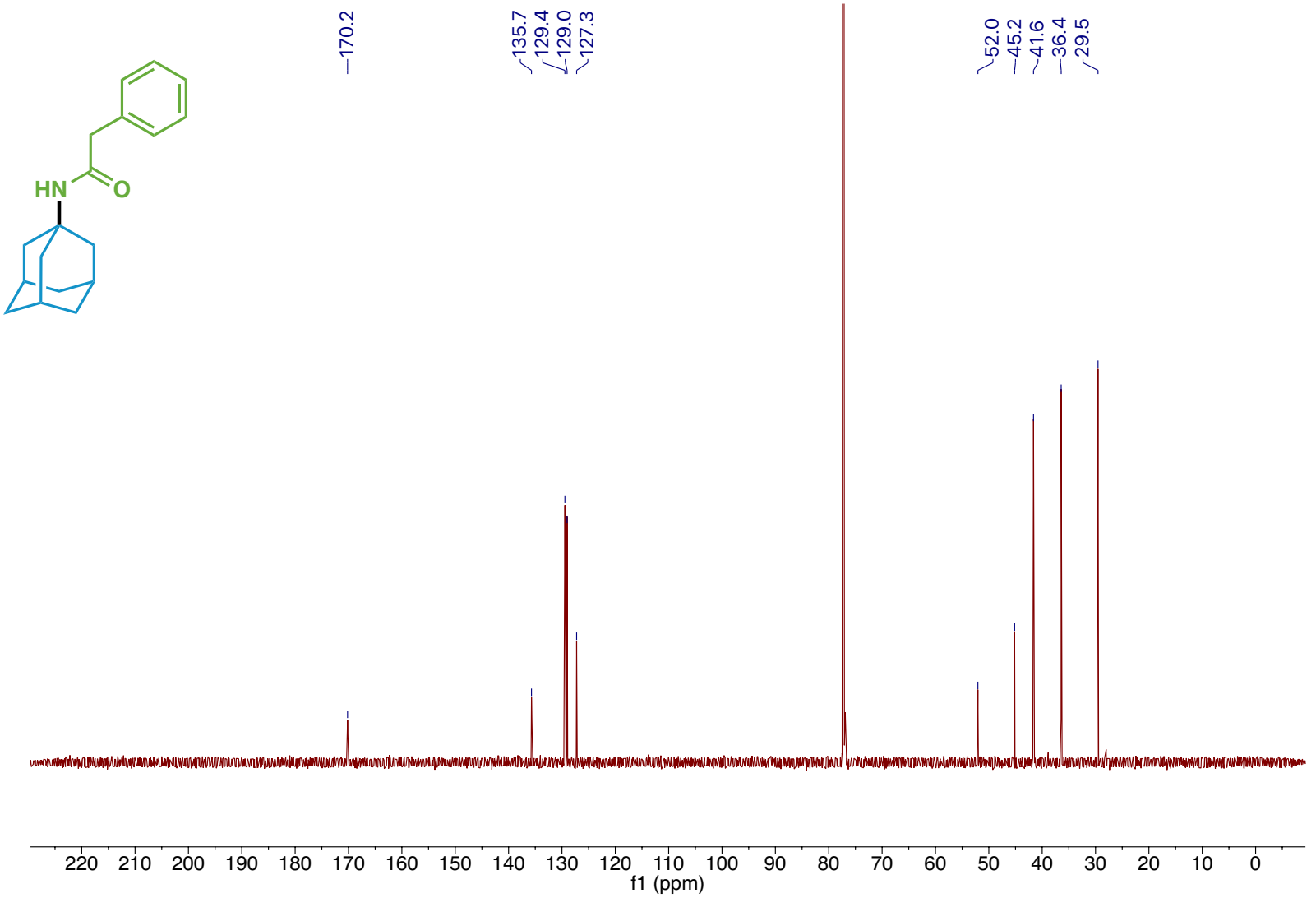

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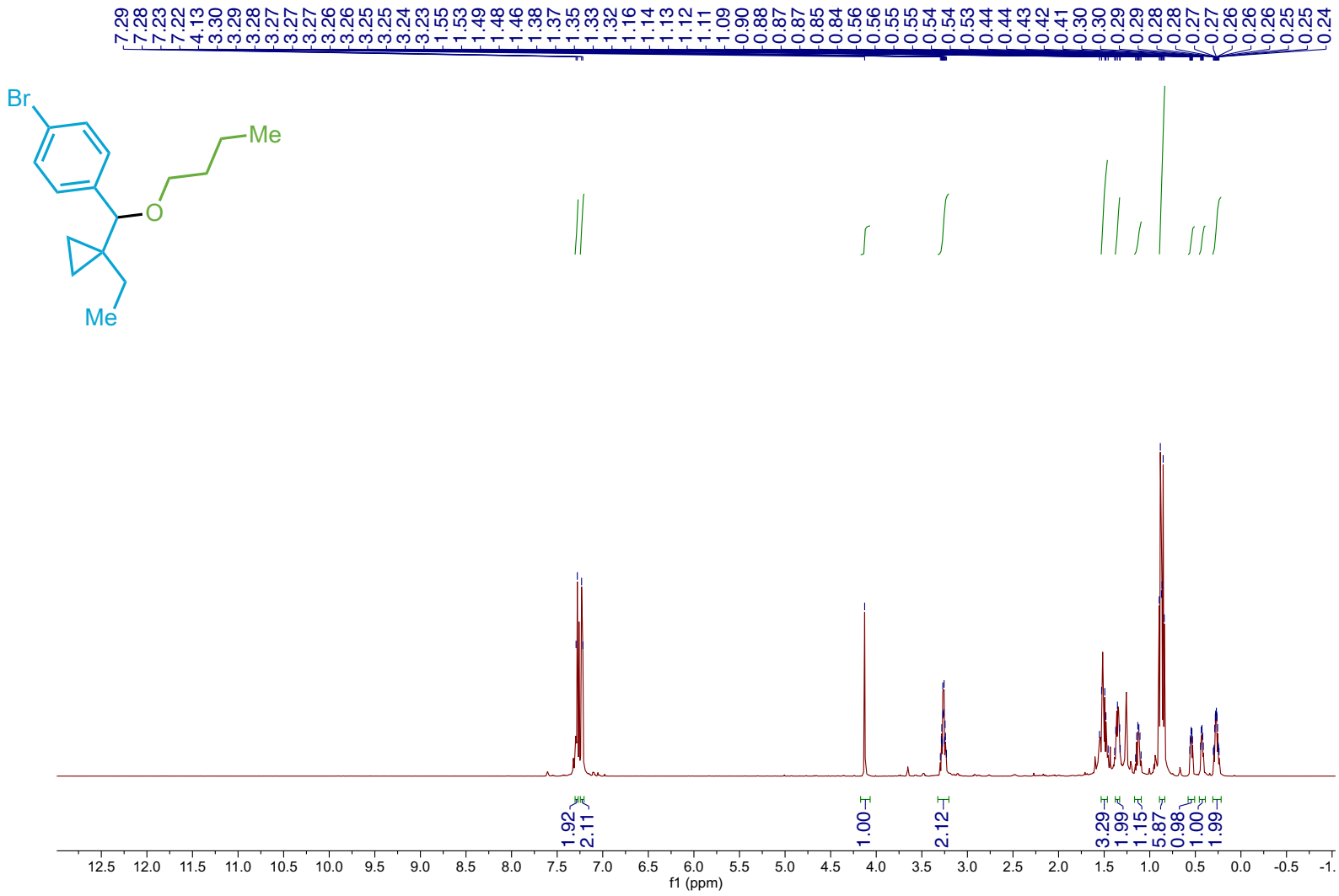

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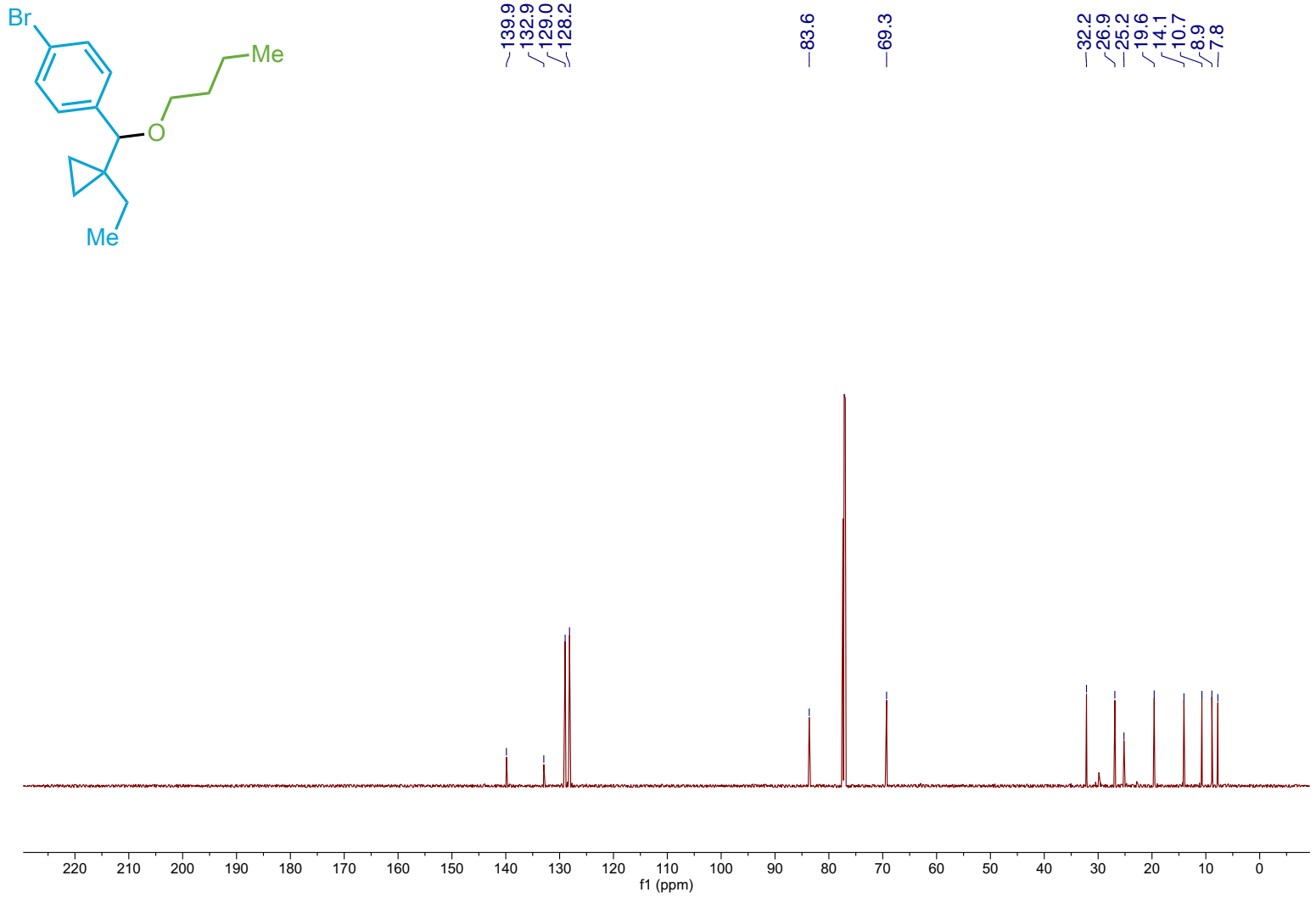

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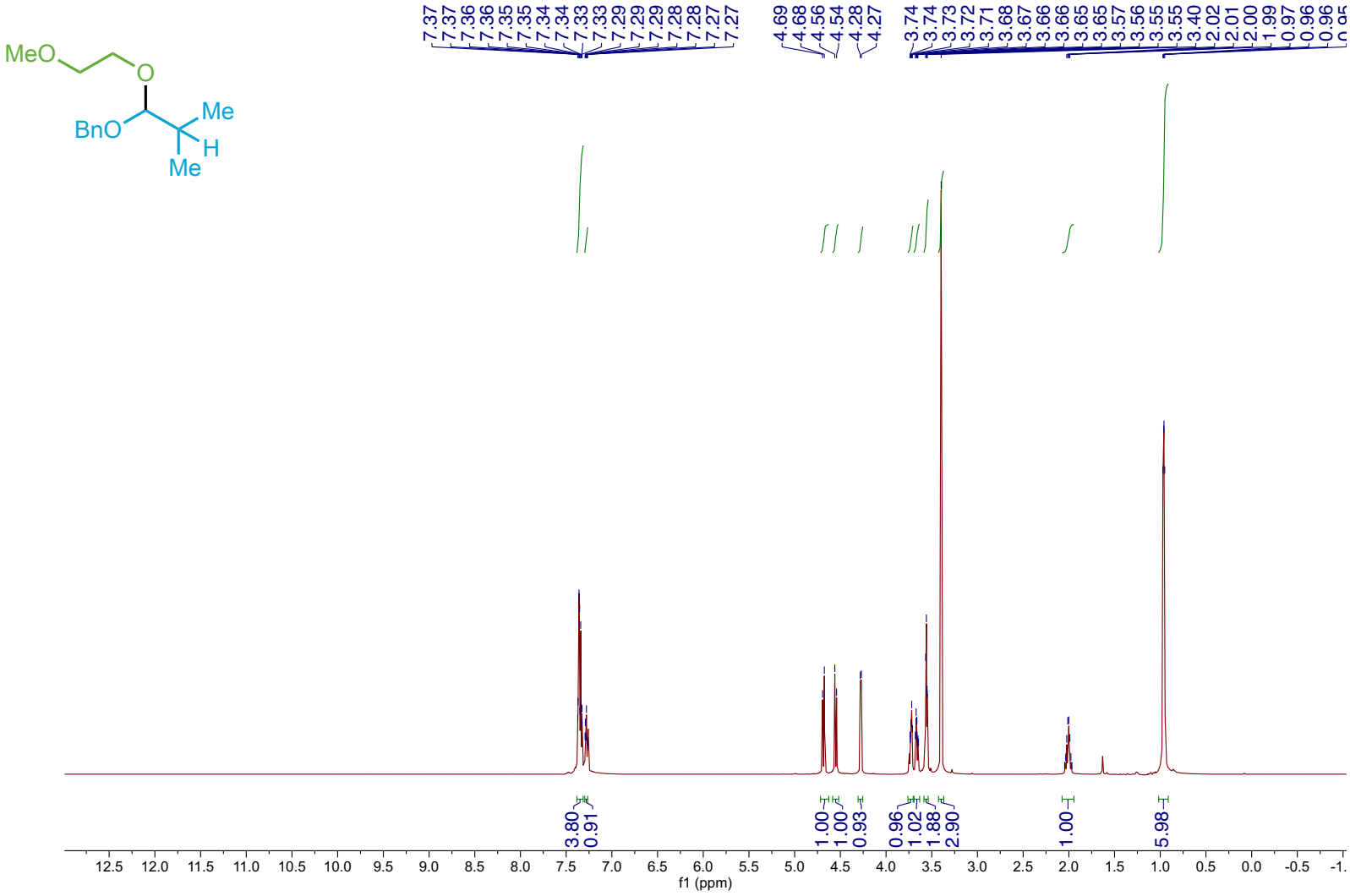

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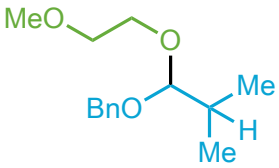
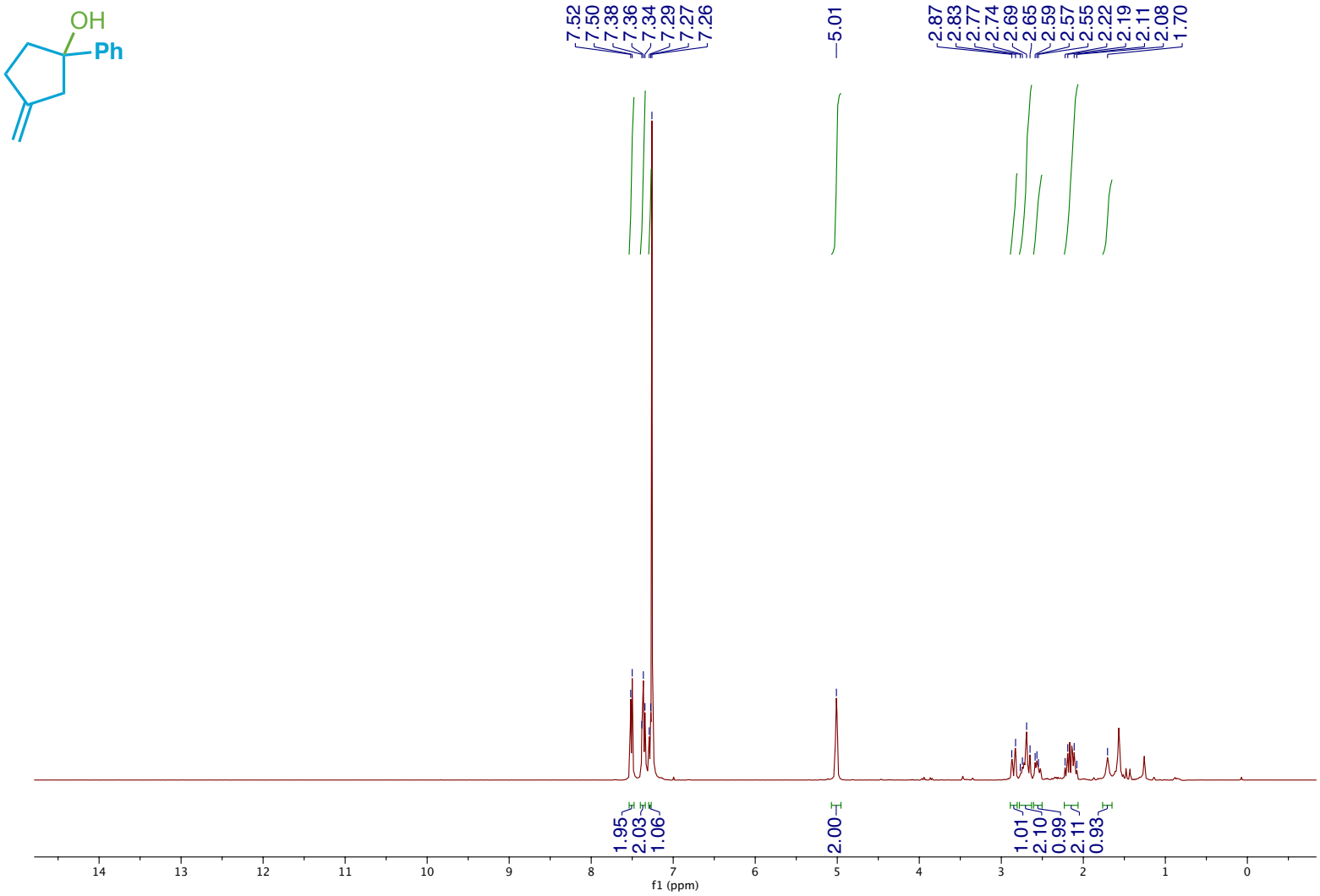
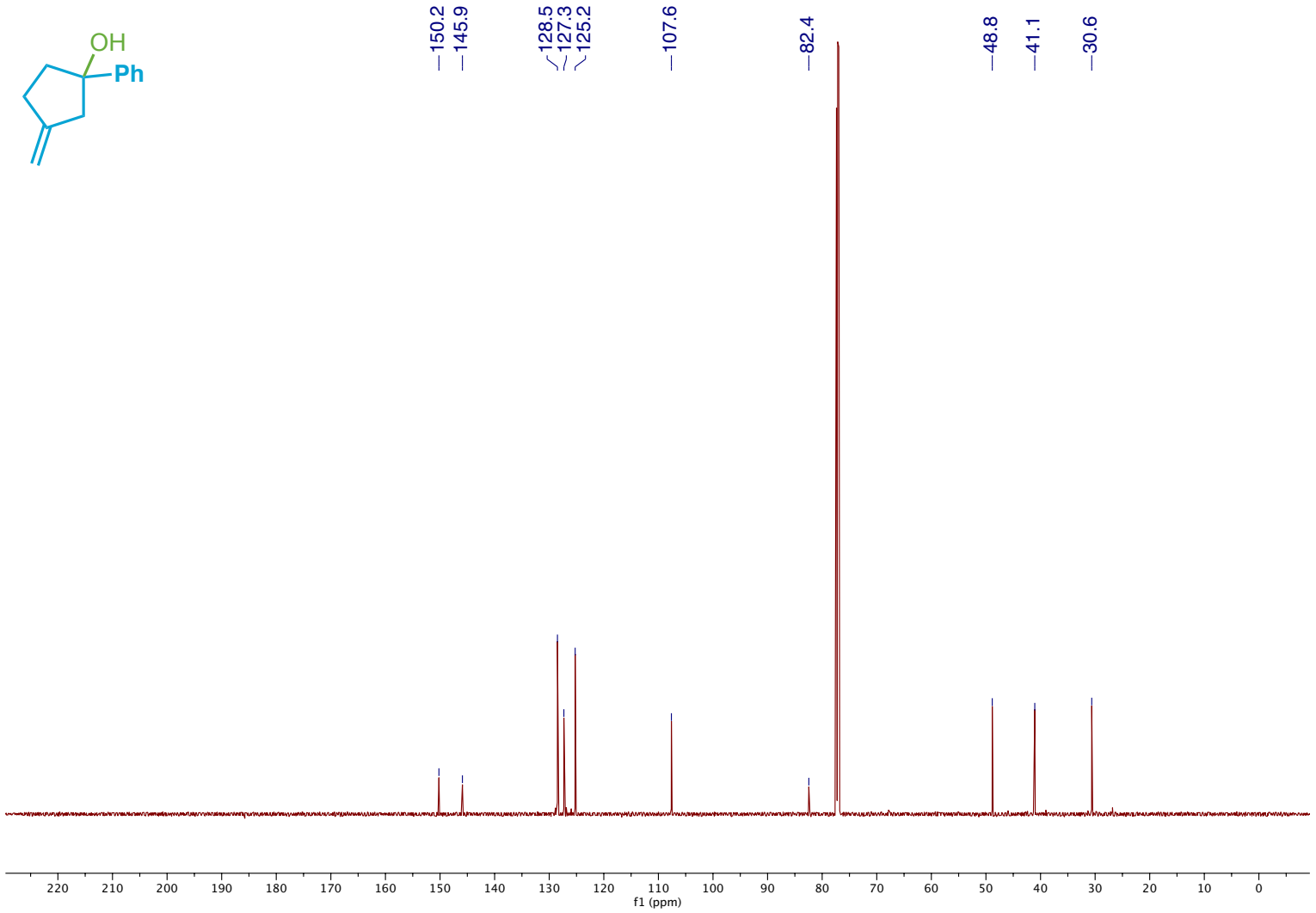


Compound 101 ^{1}H NMR



Compound 101 ^{13}C NMR



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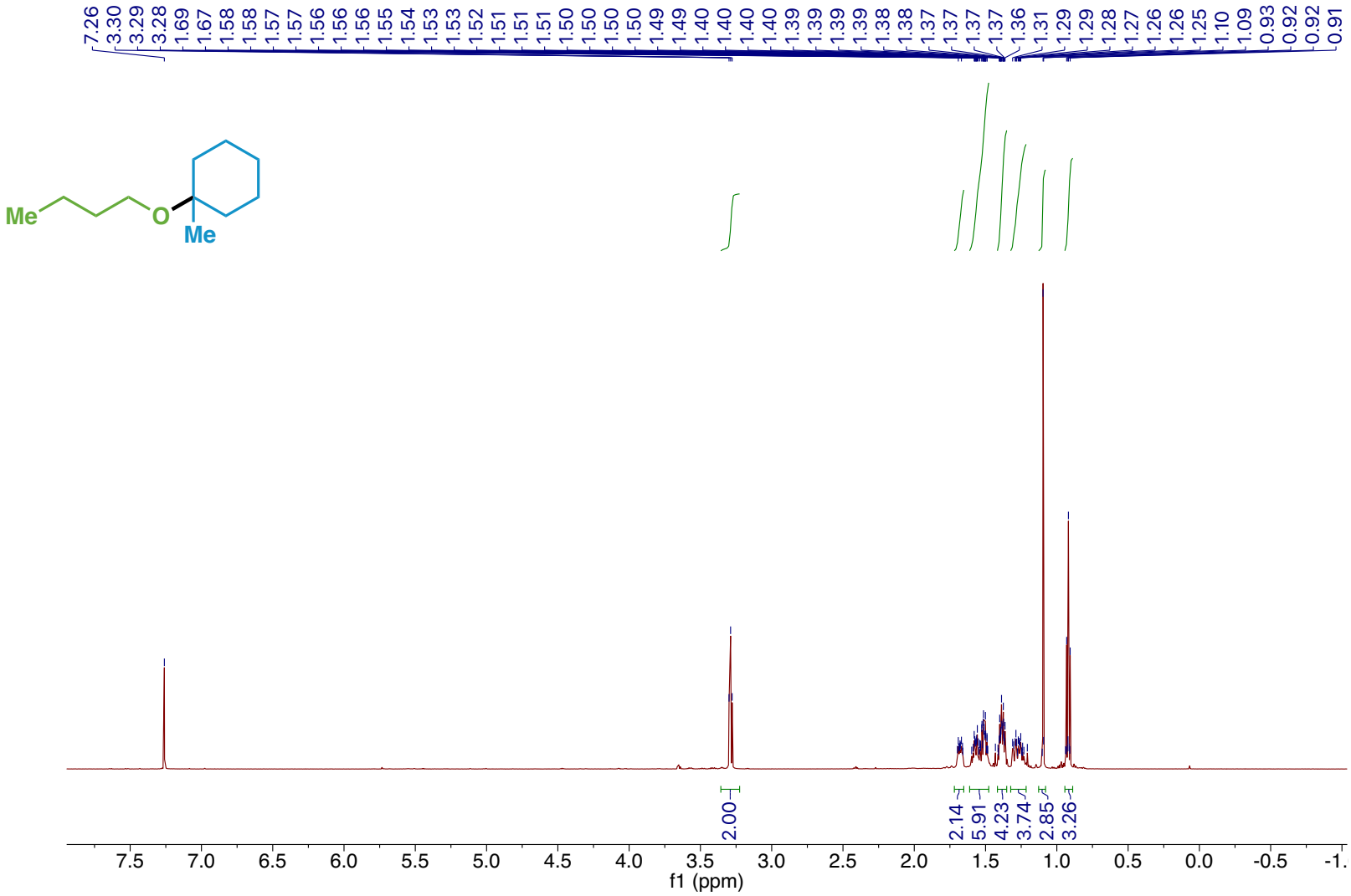
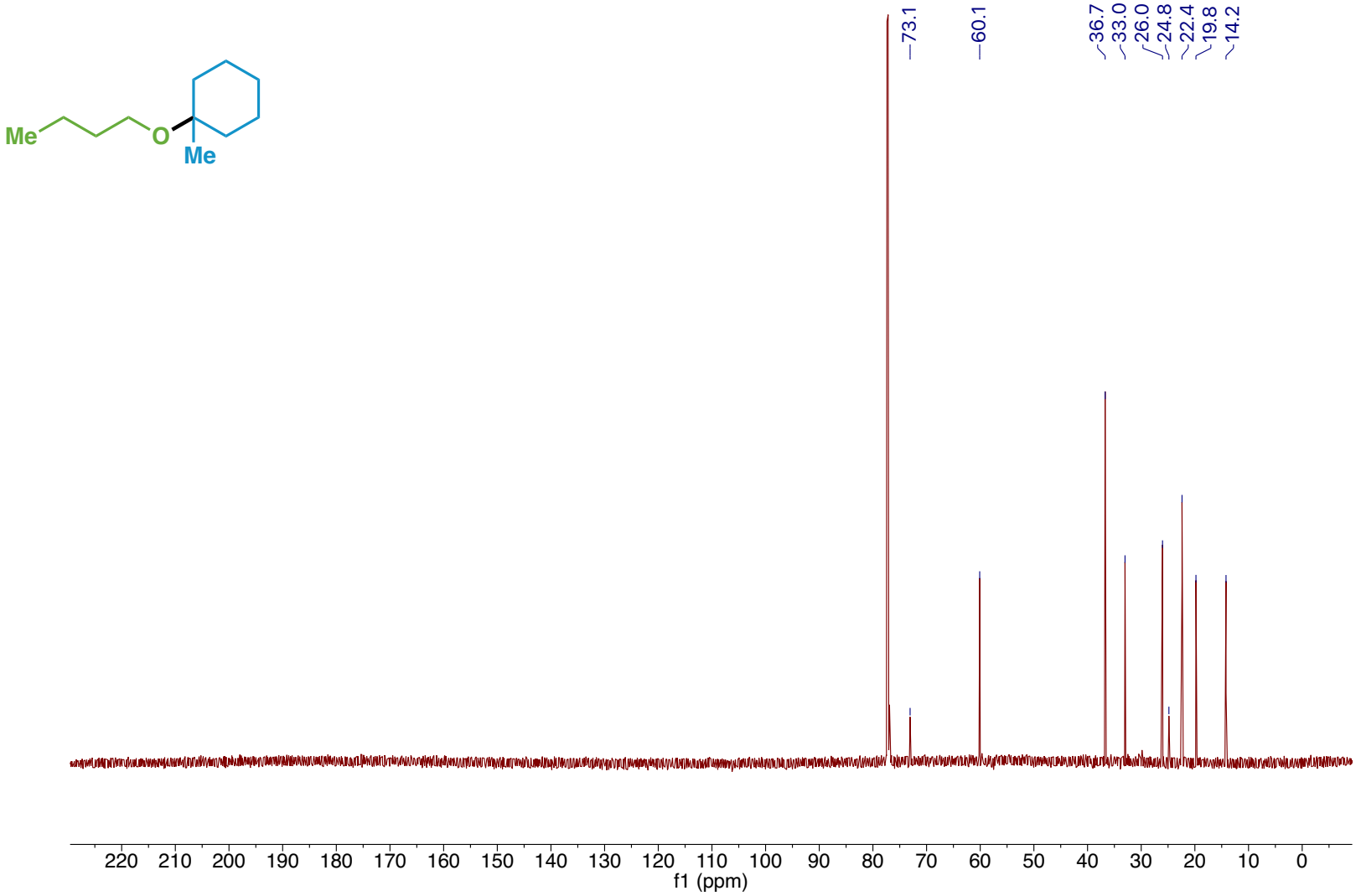
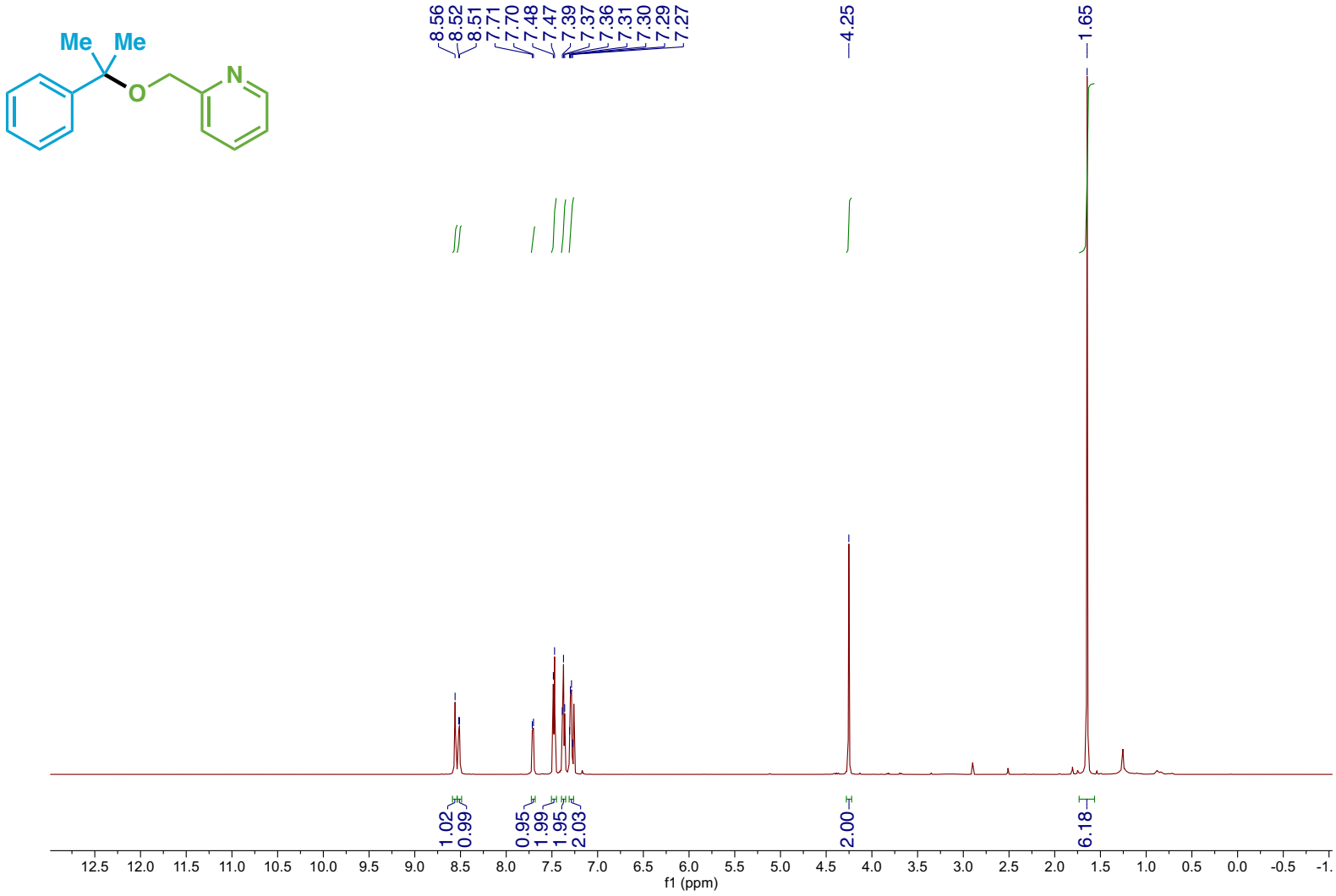


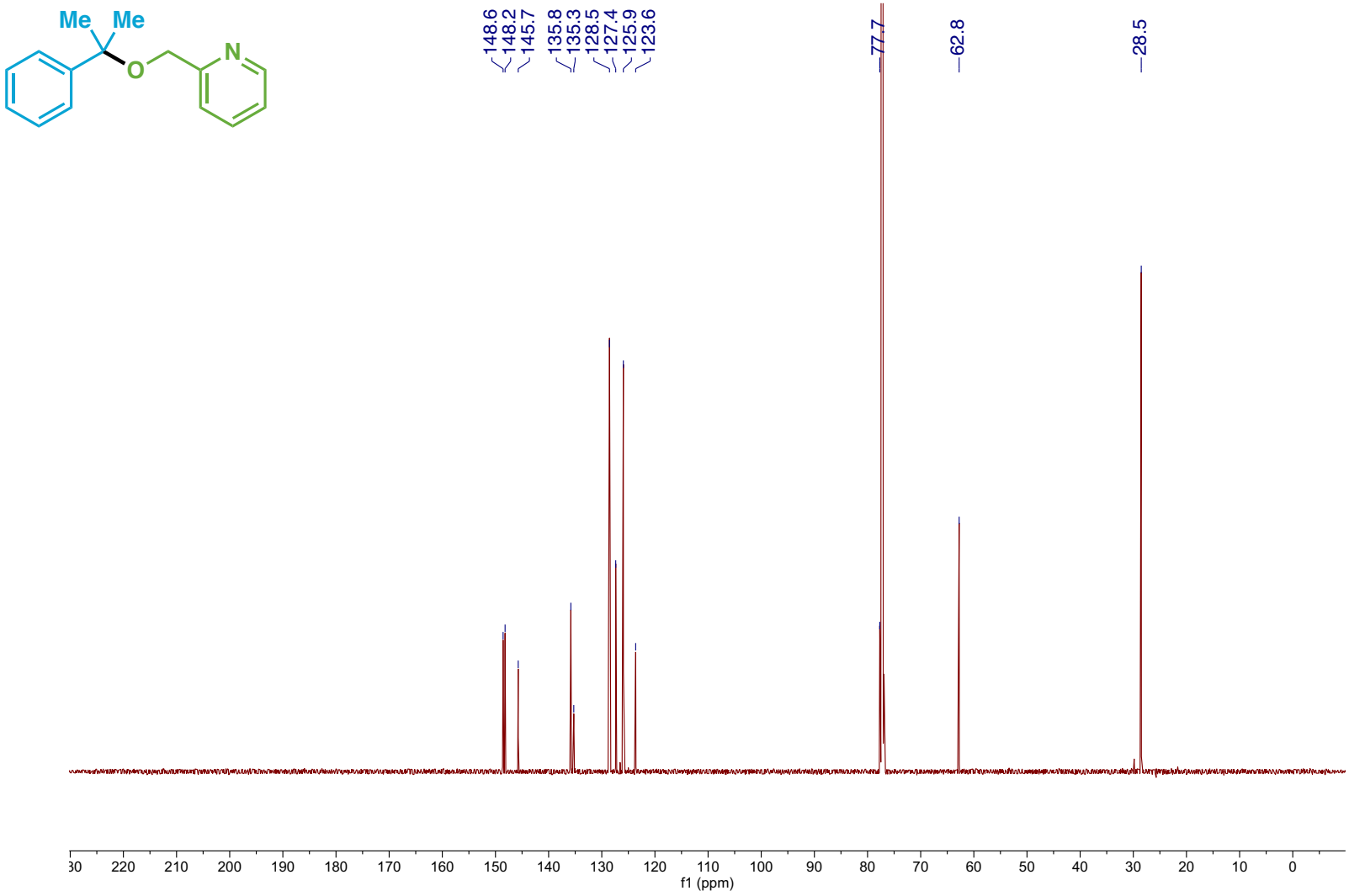
Compound 102 ^{13}C NMR



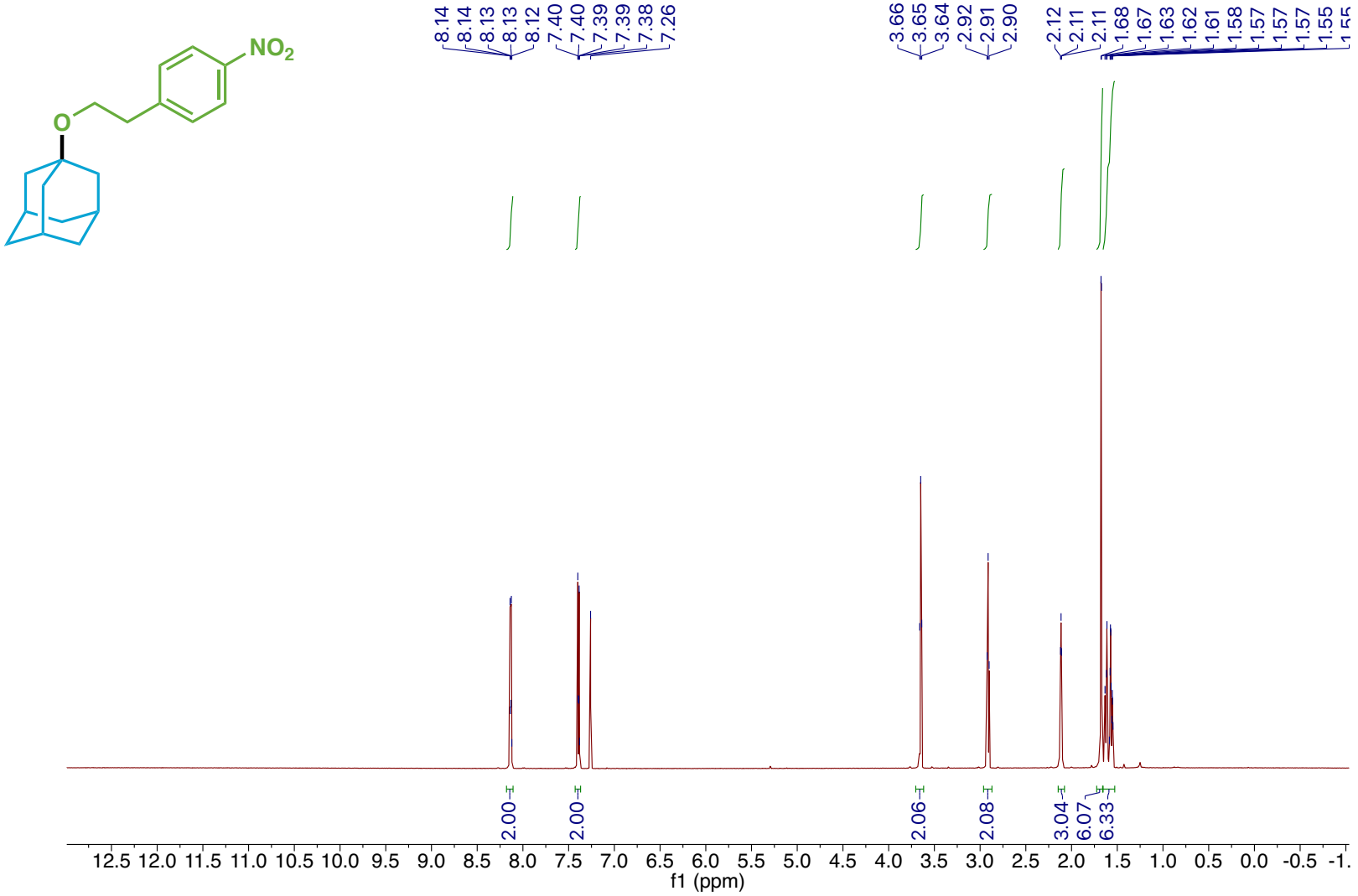
Compound 103 ^{1}H NMR



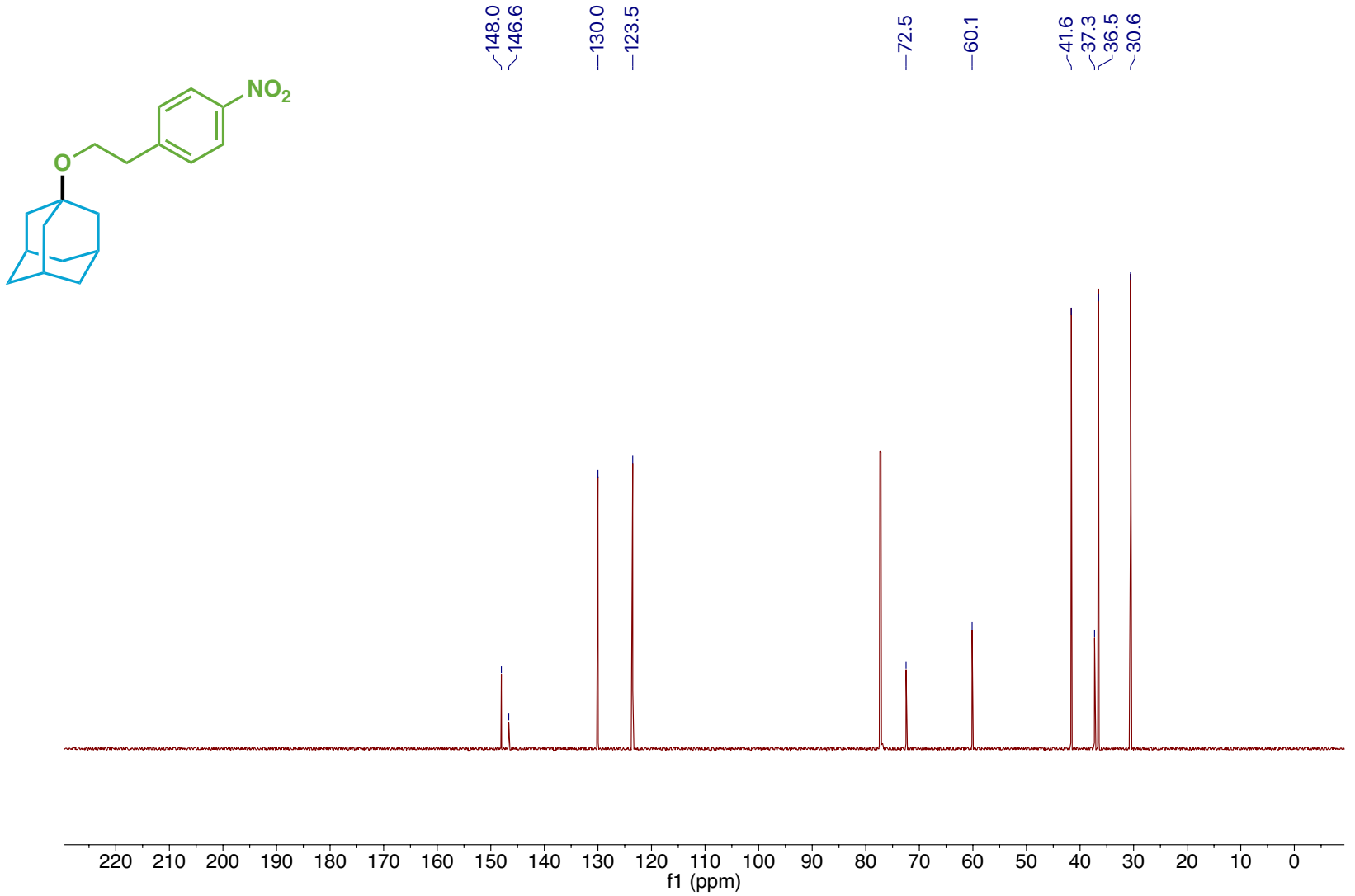
Compound 103 ^{13}C NMR



Compound 104 ^{1}H NMR



Compound 104 ^{13}C NMR



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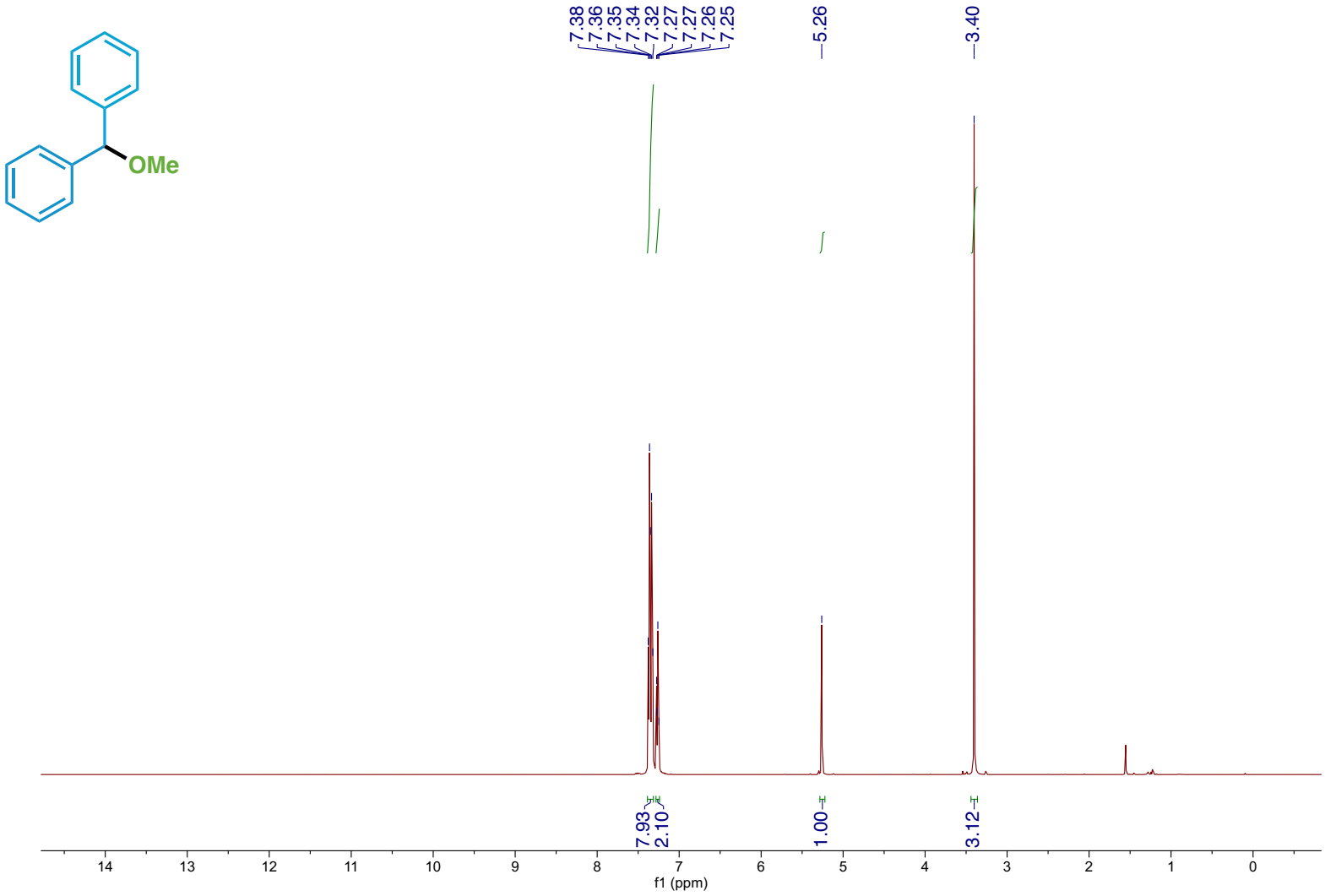

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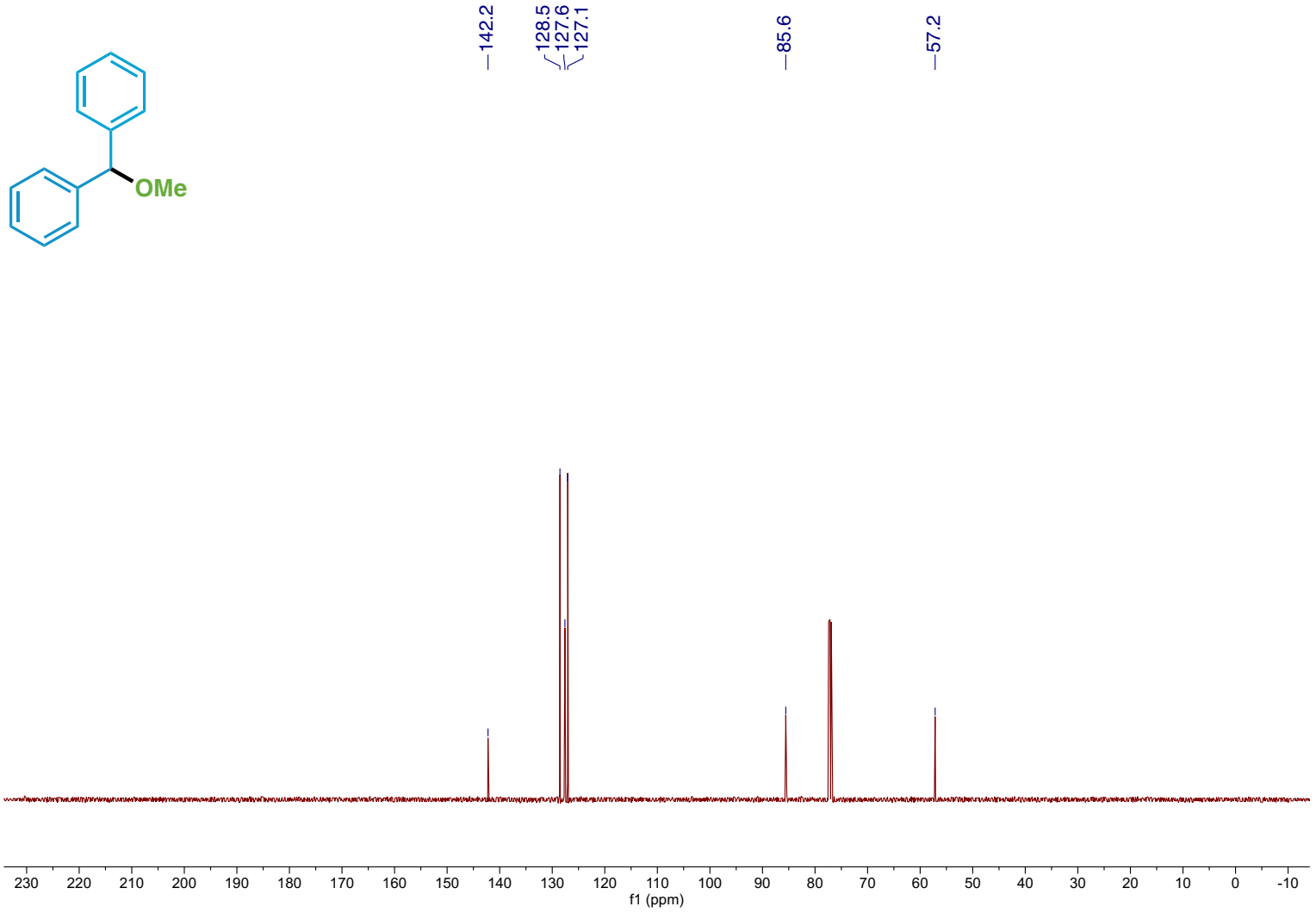

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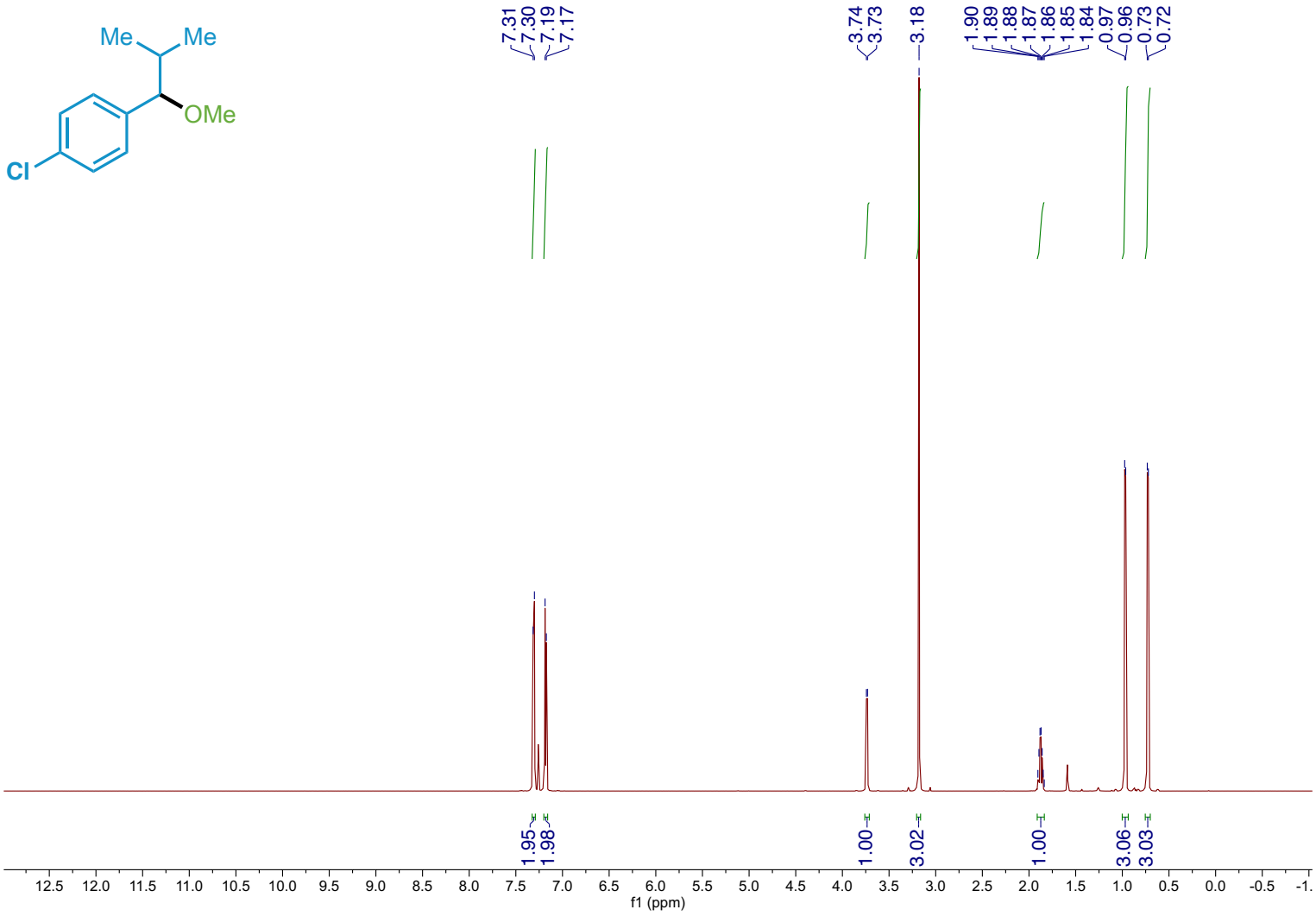
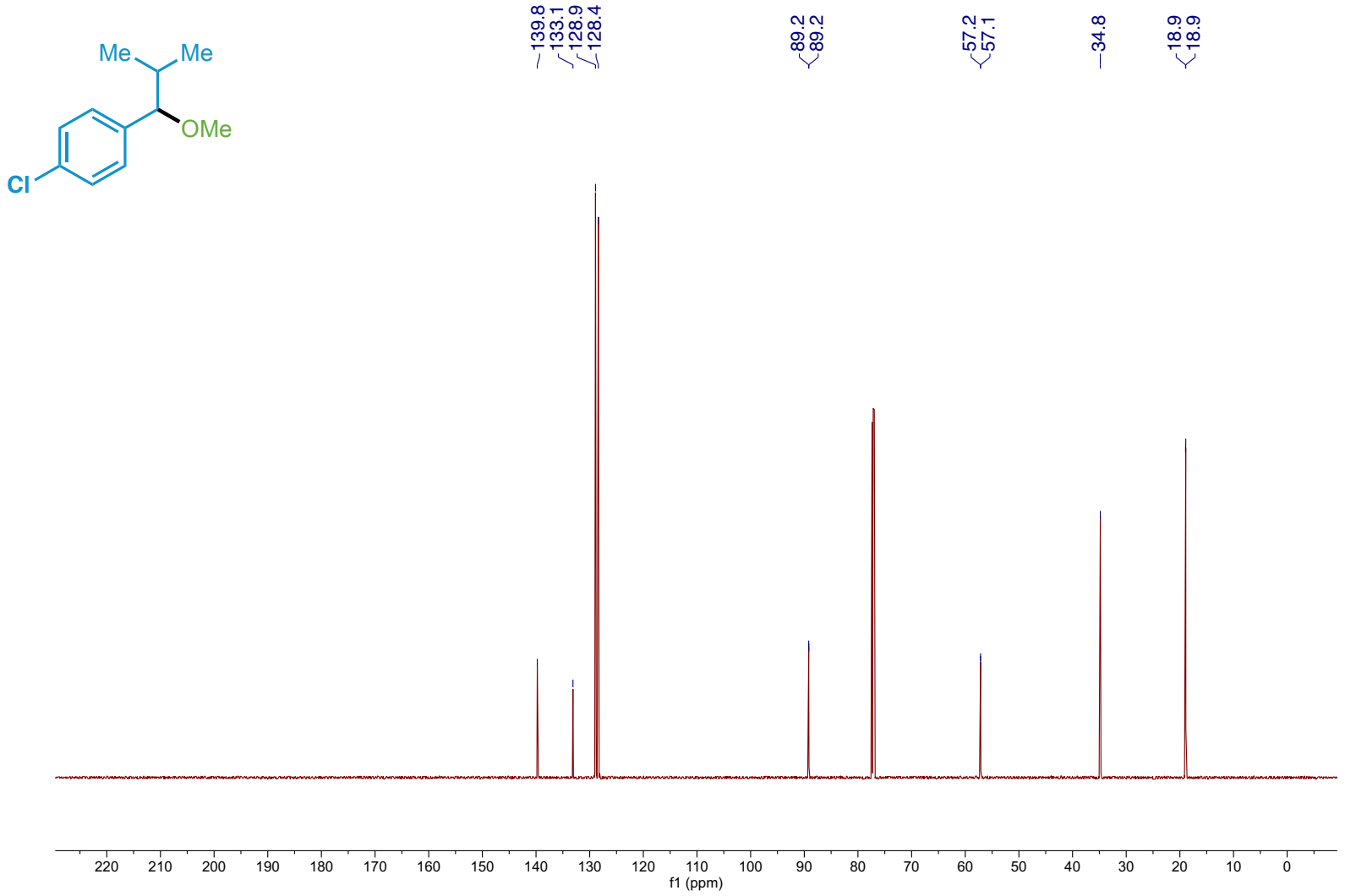
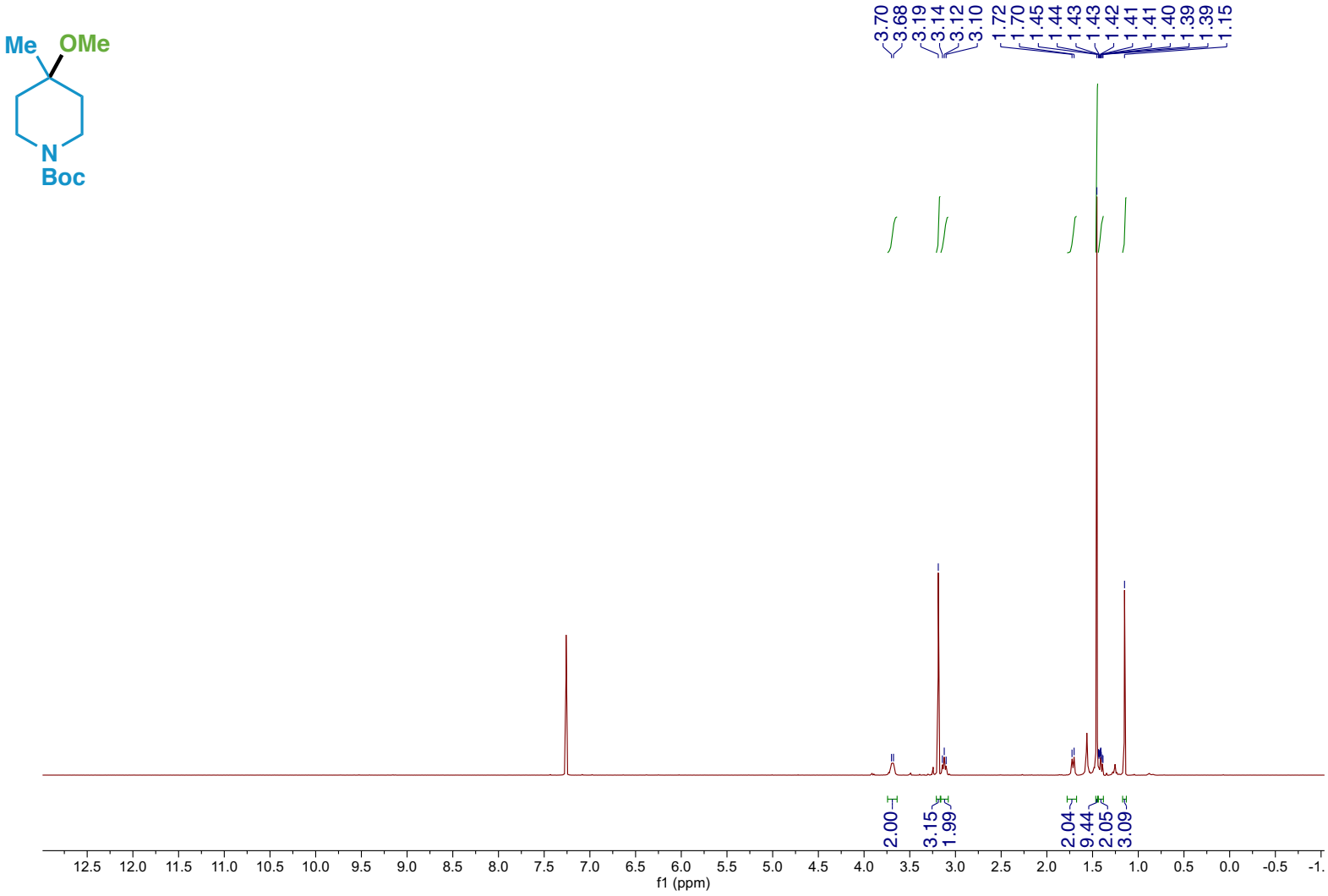


Compound 106 ^{13}C NMR



Compound 107 ^{1}H NMR



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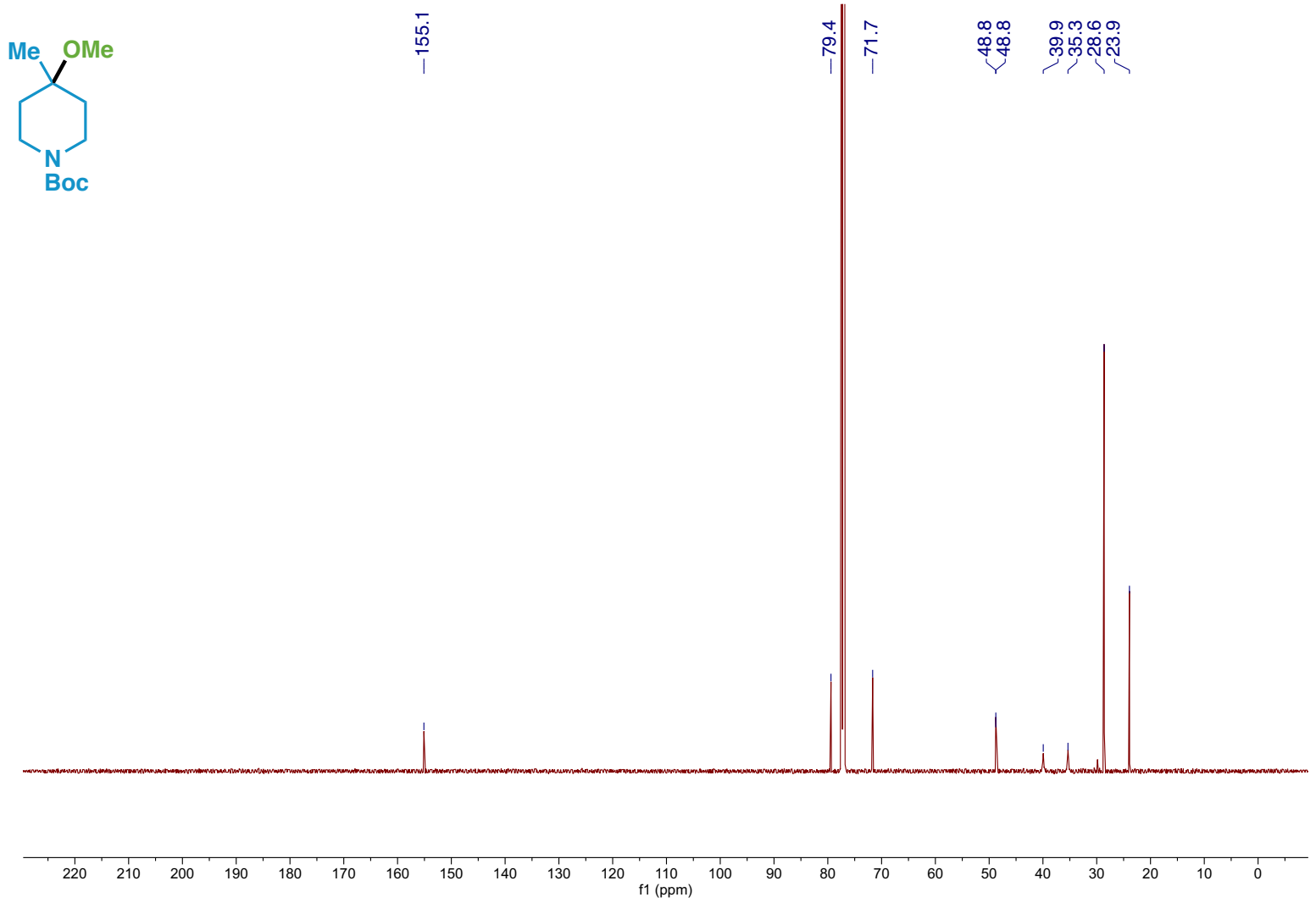

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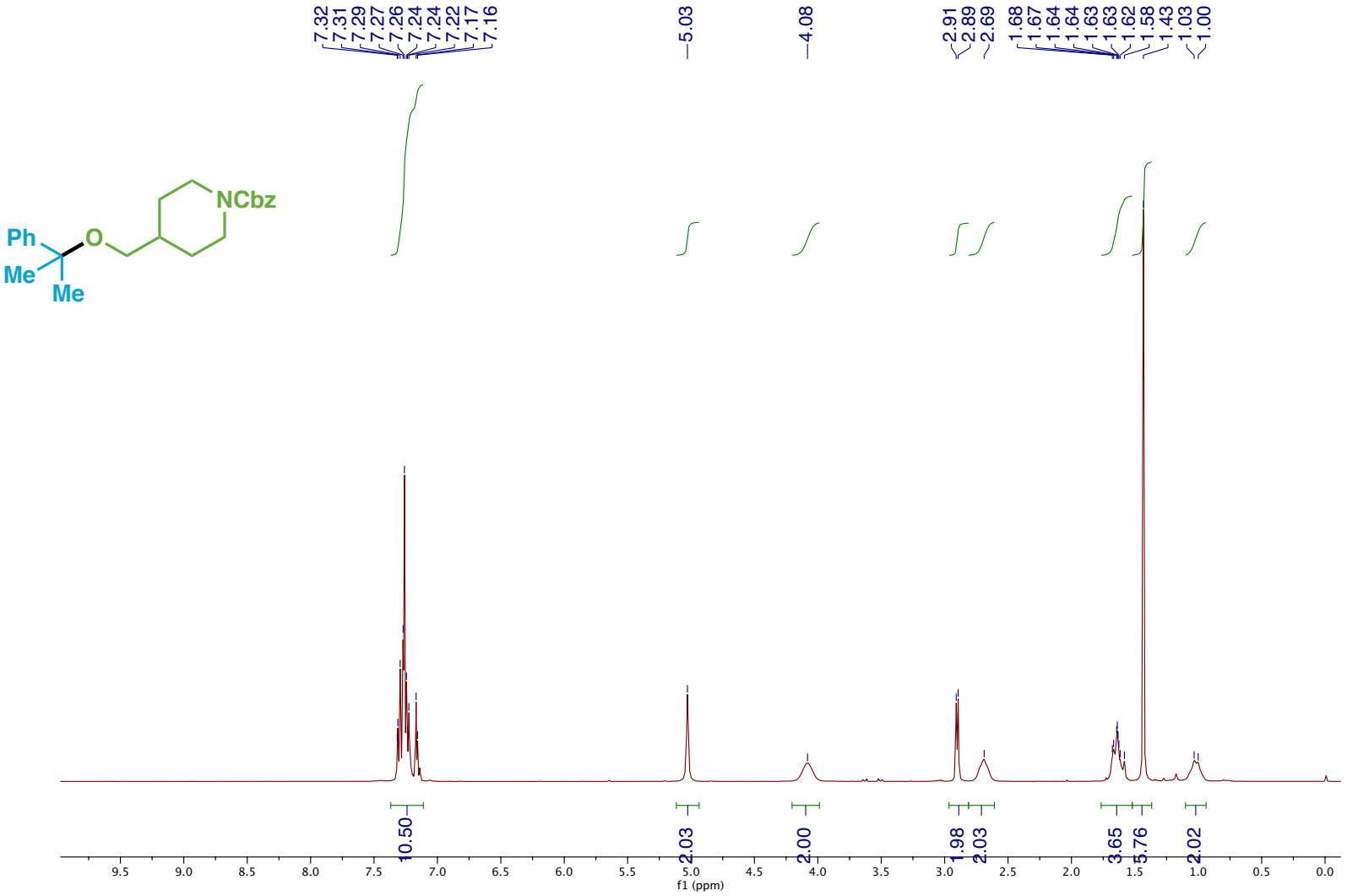

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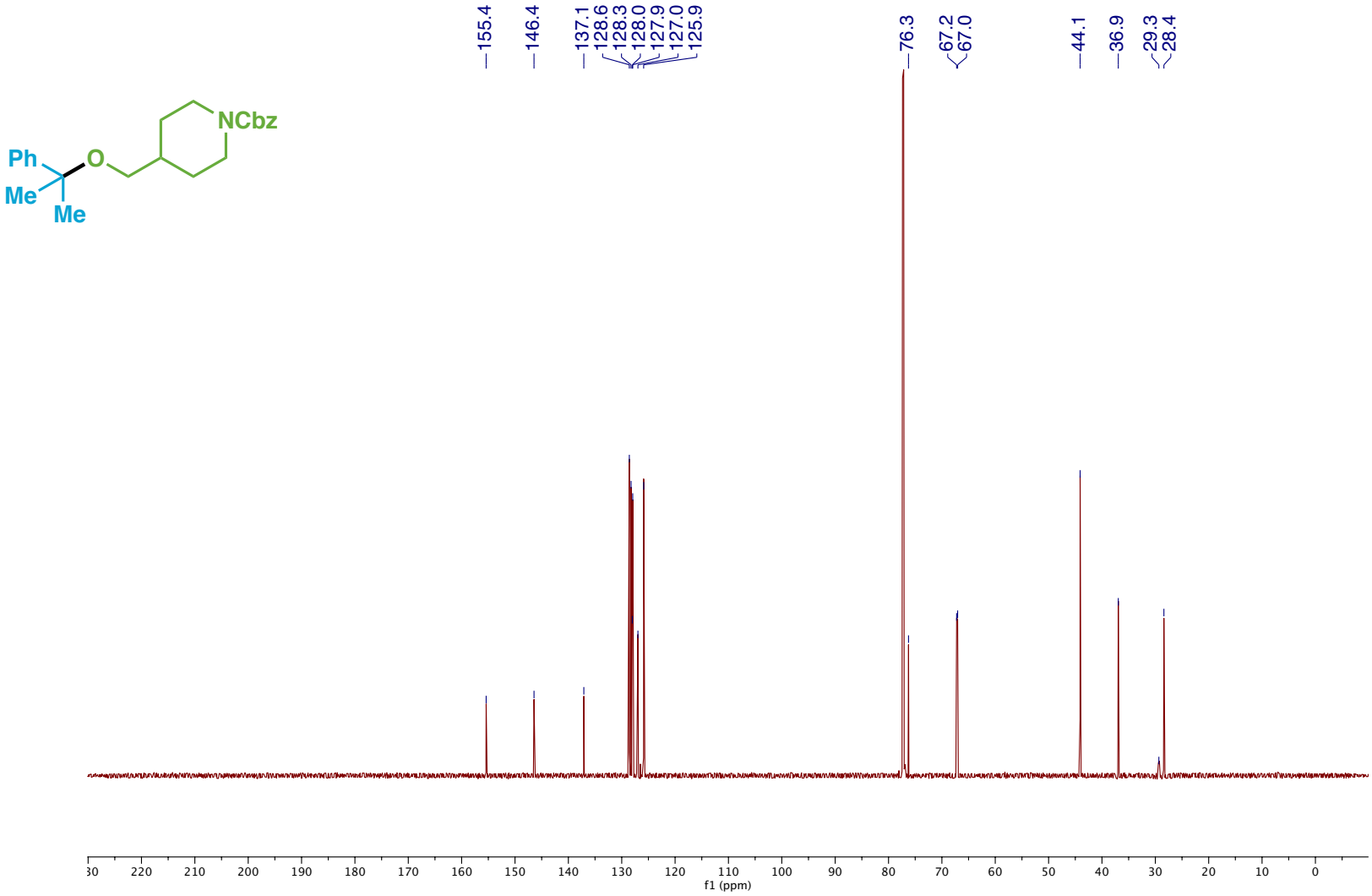

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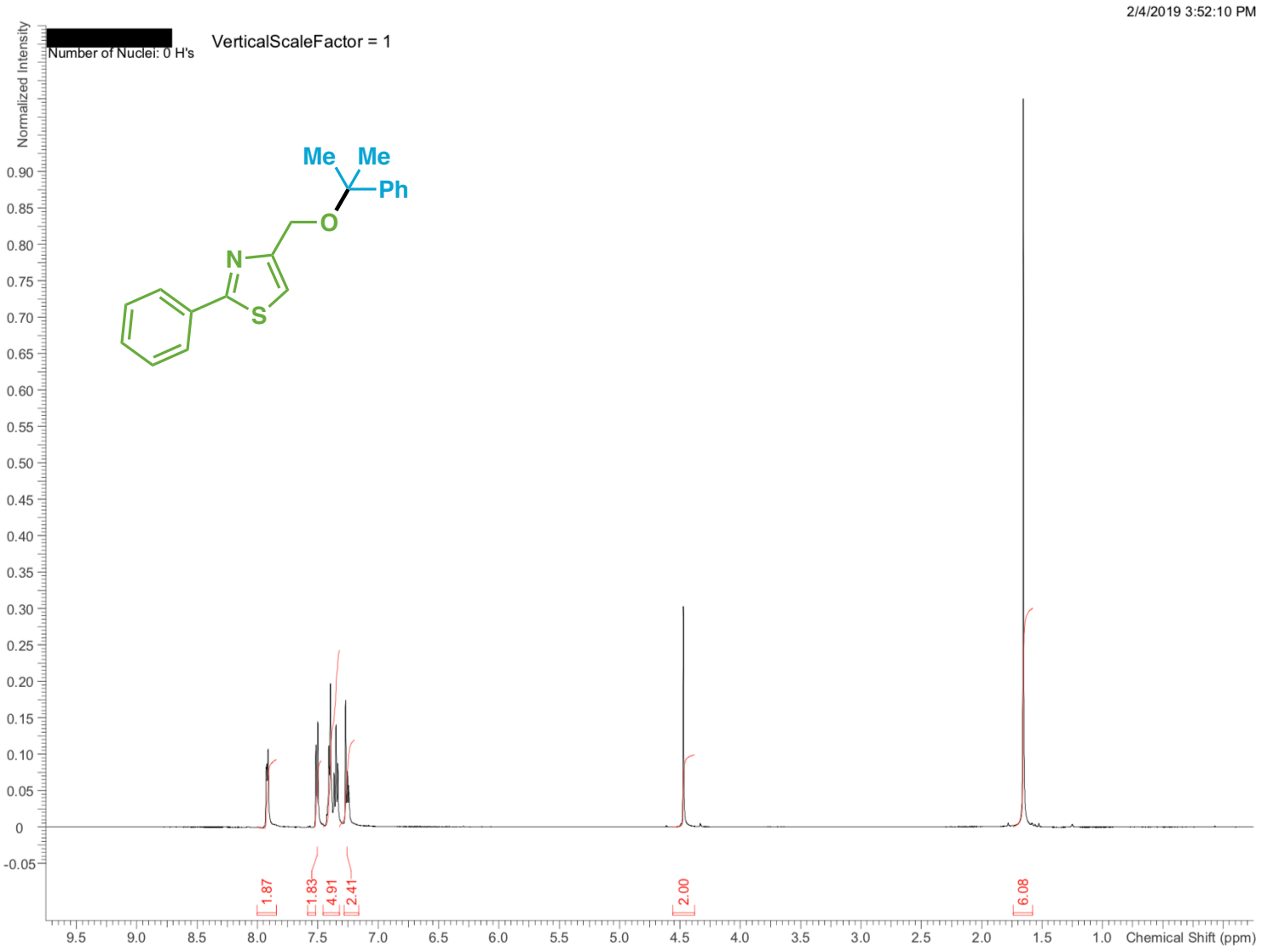

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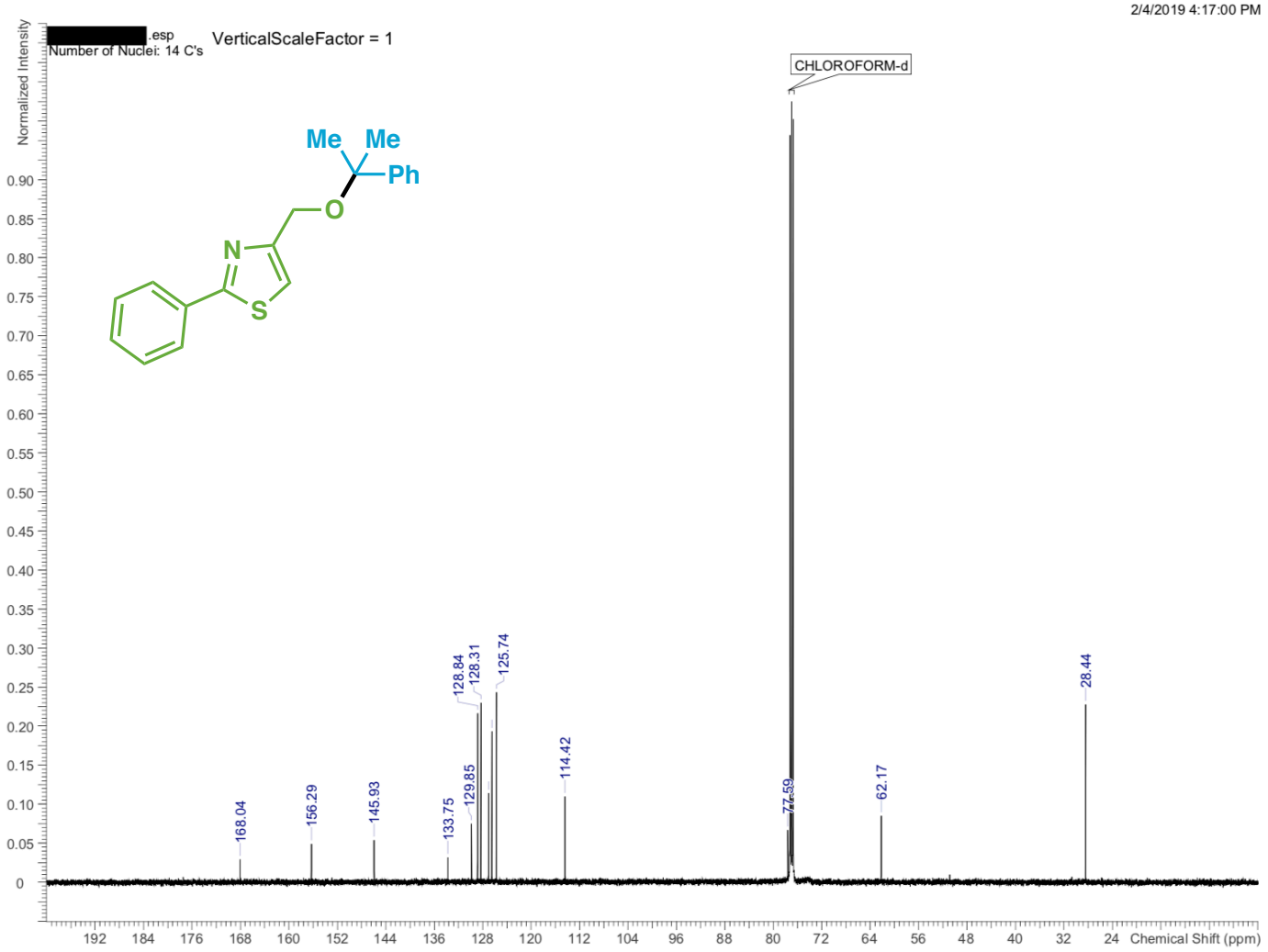

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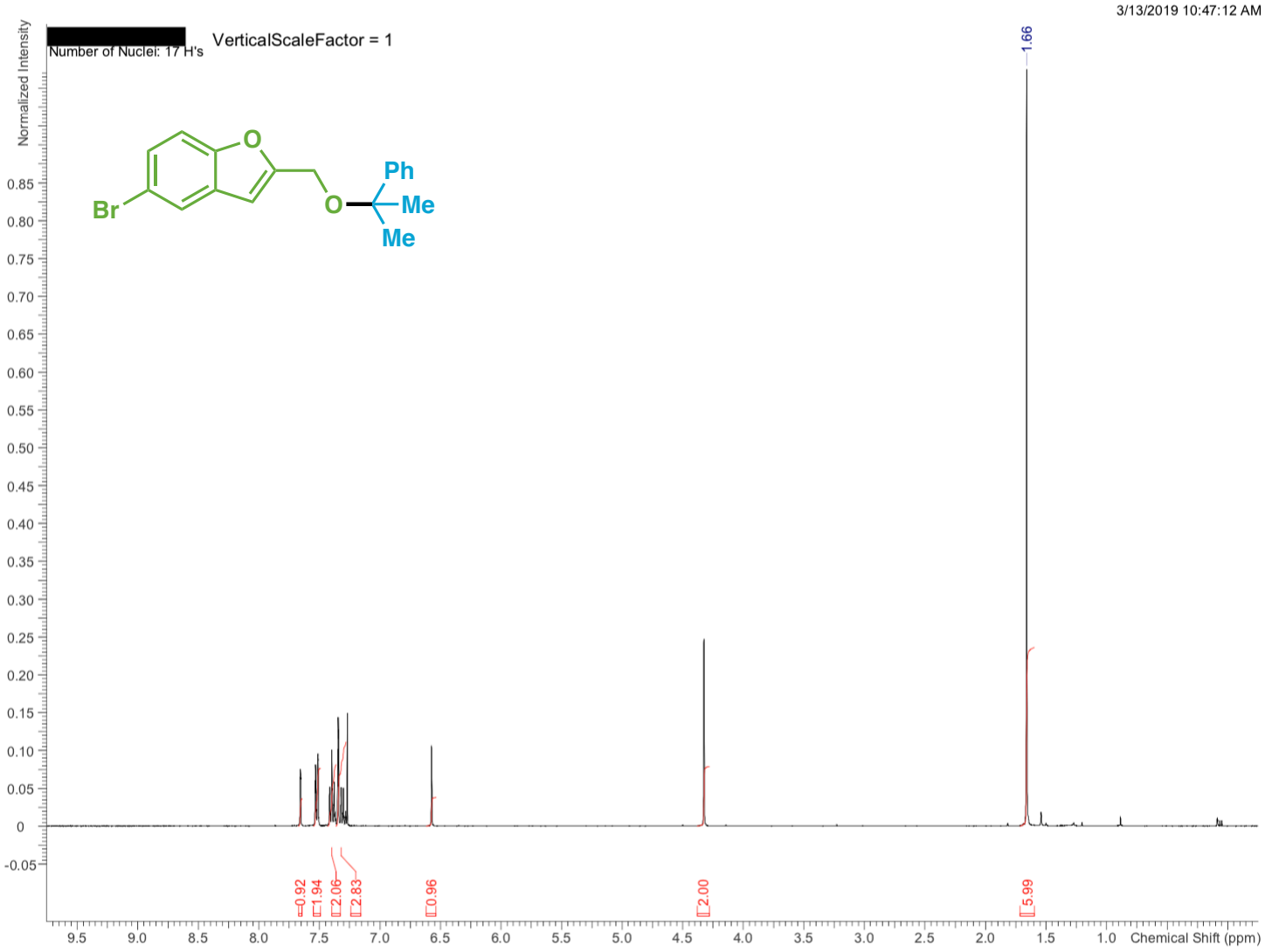

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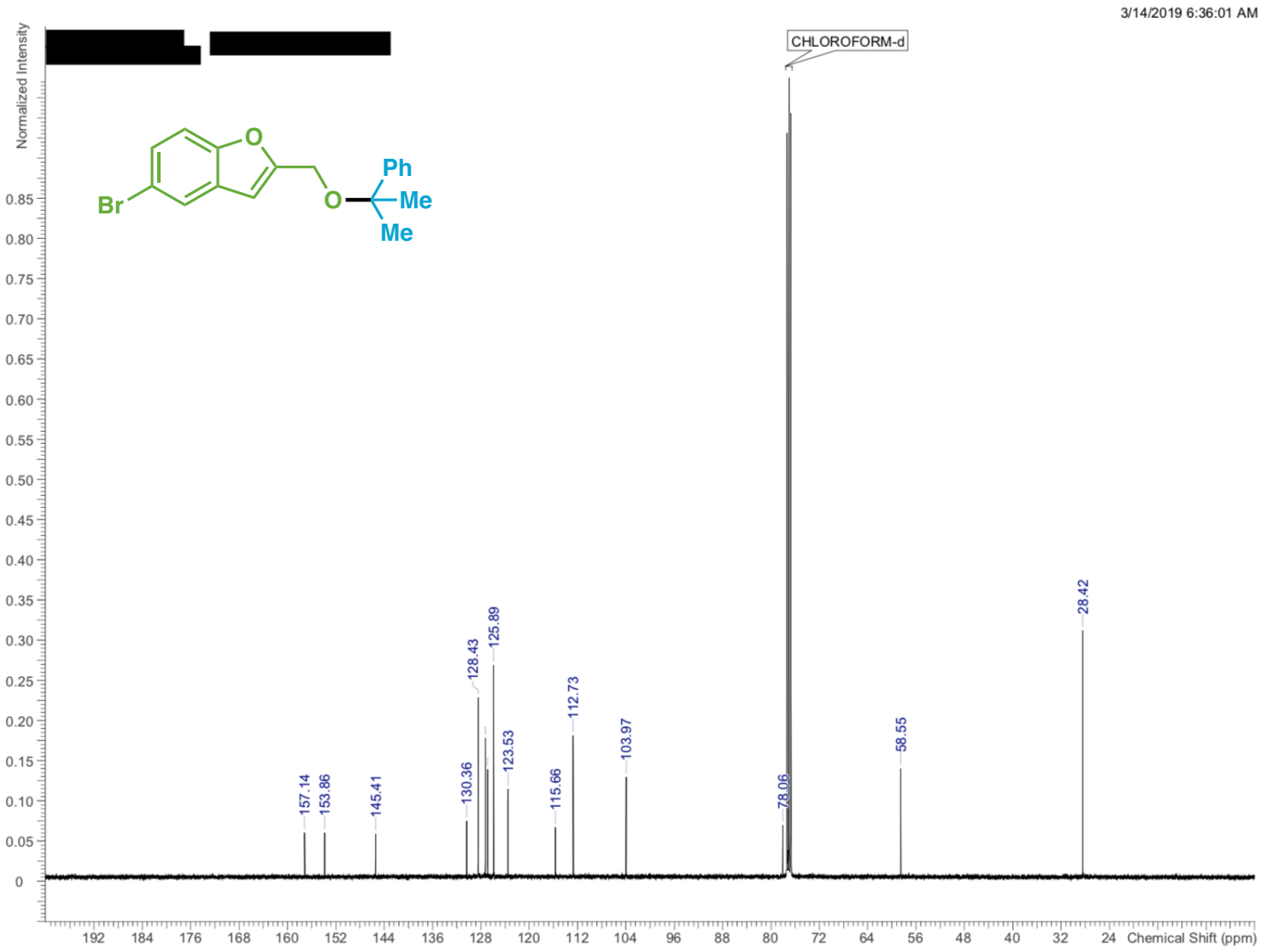

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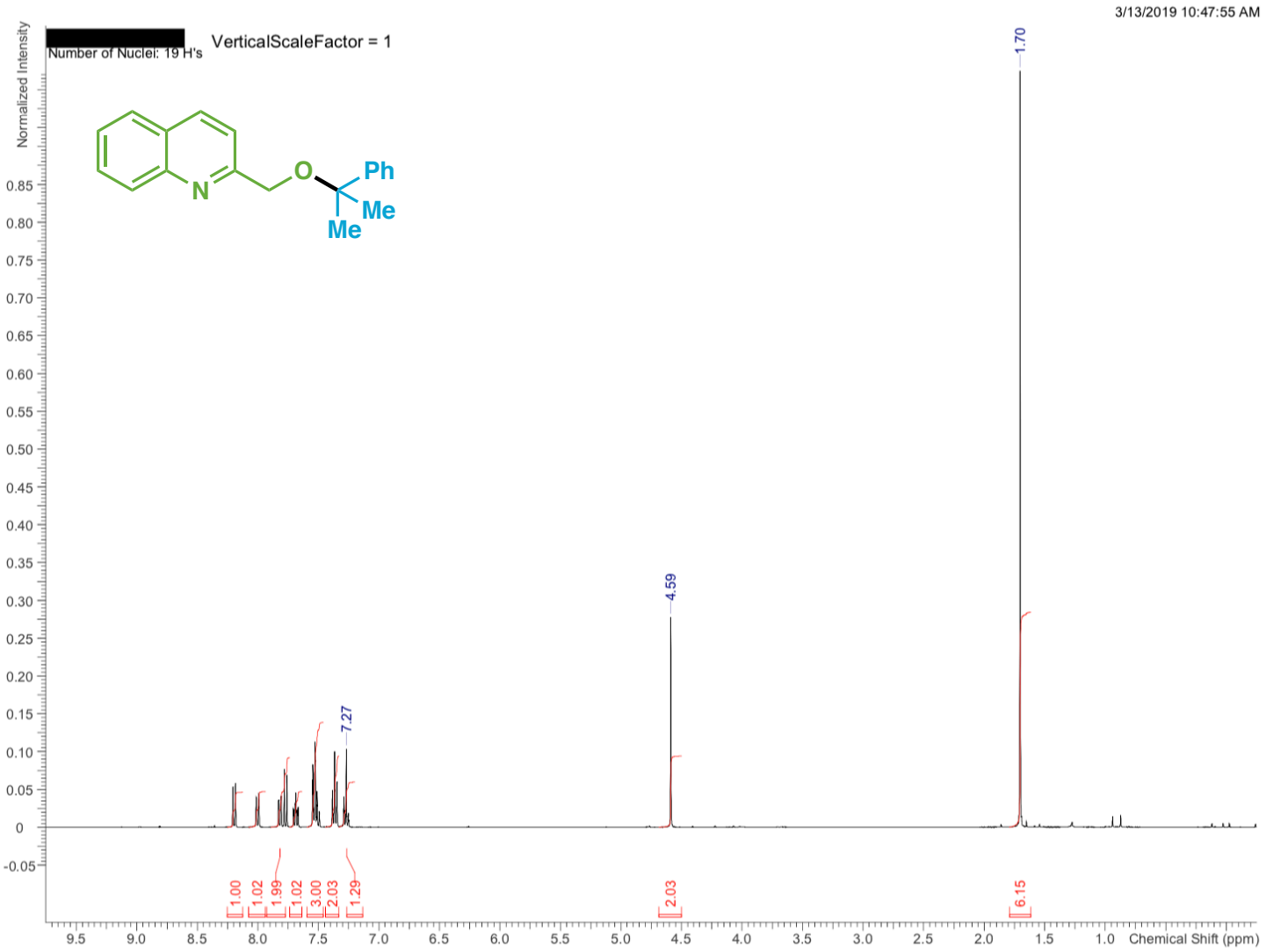

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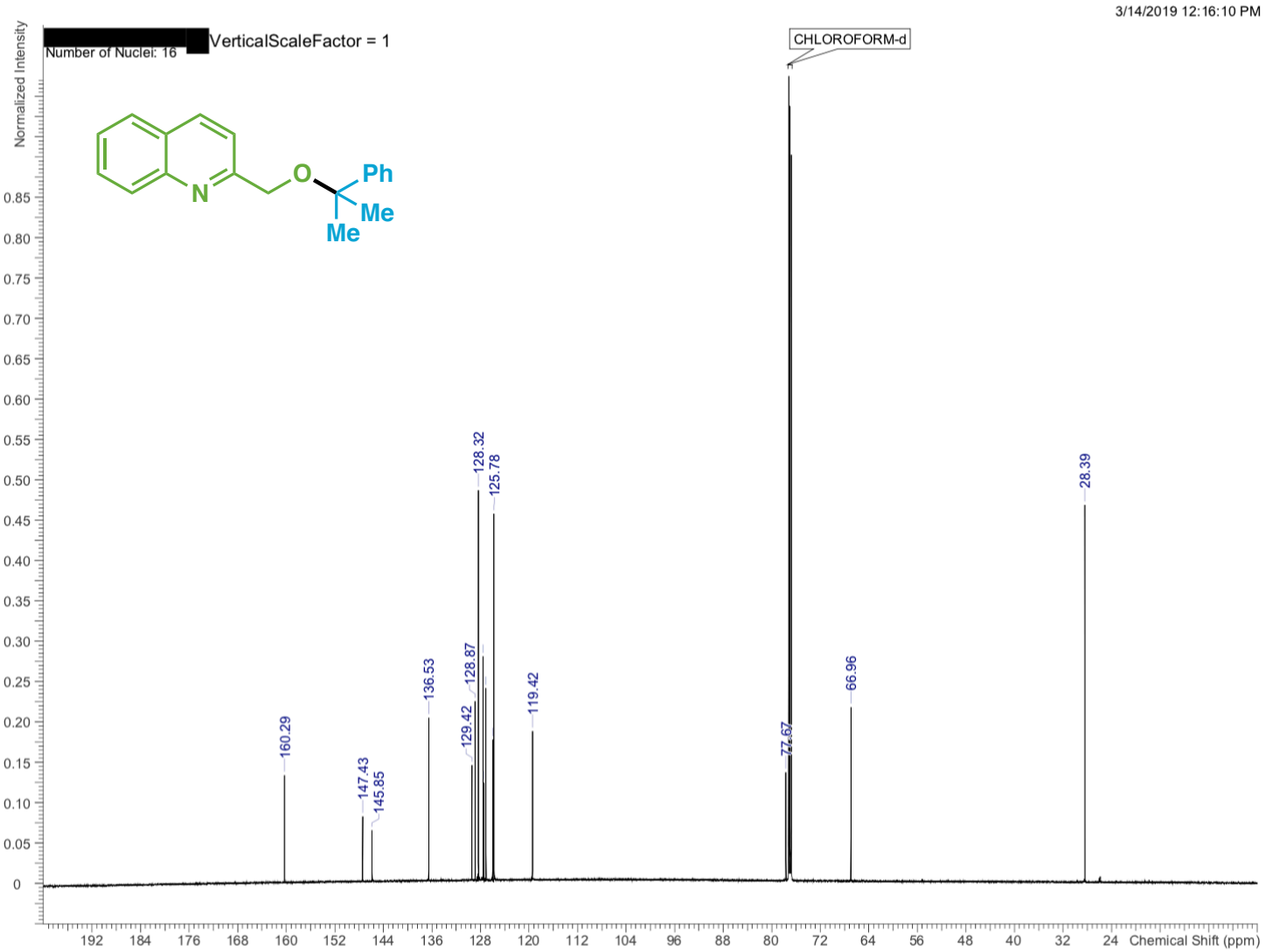
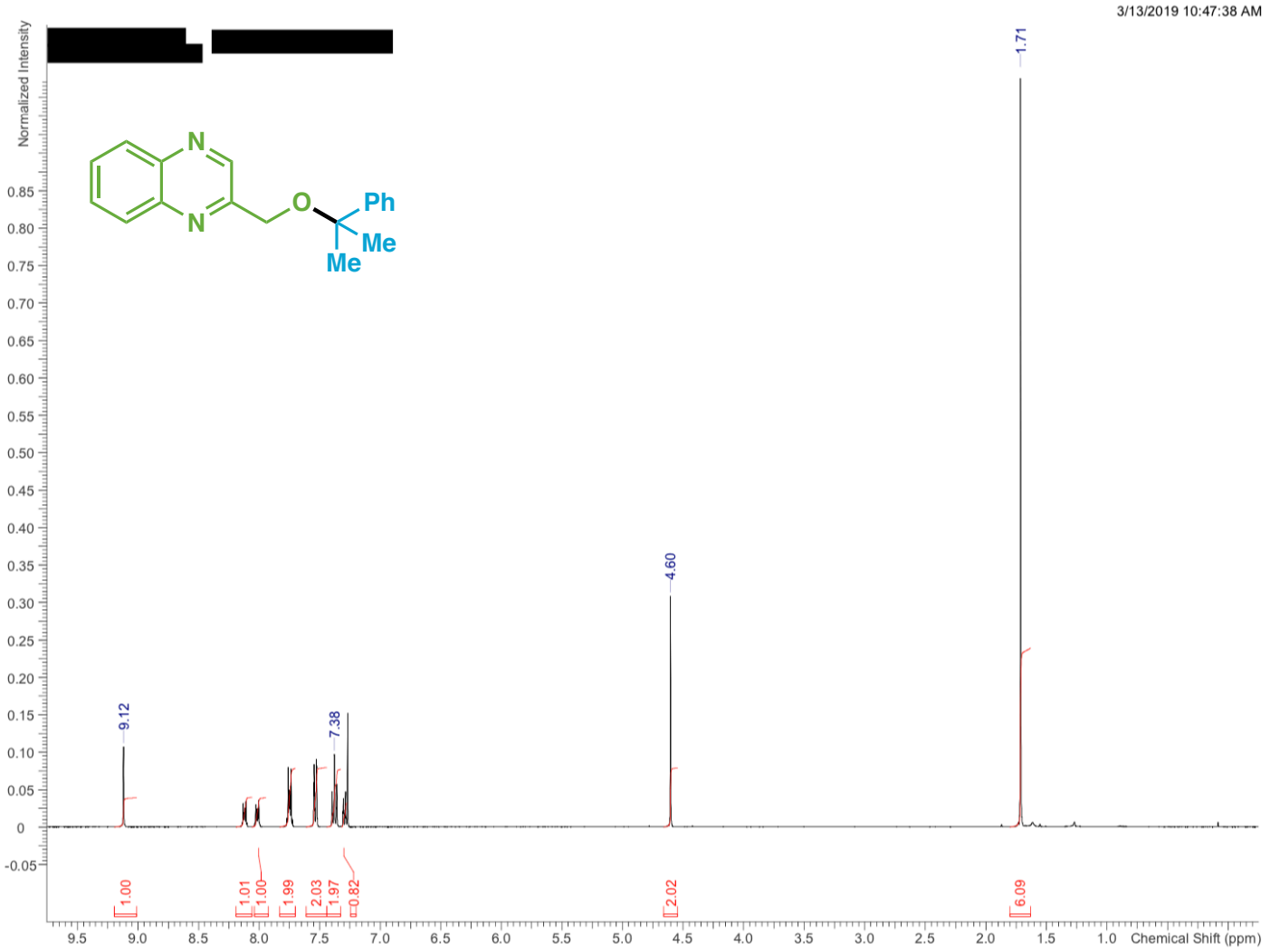
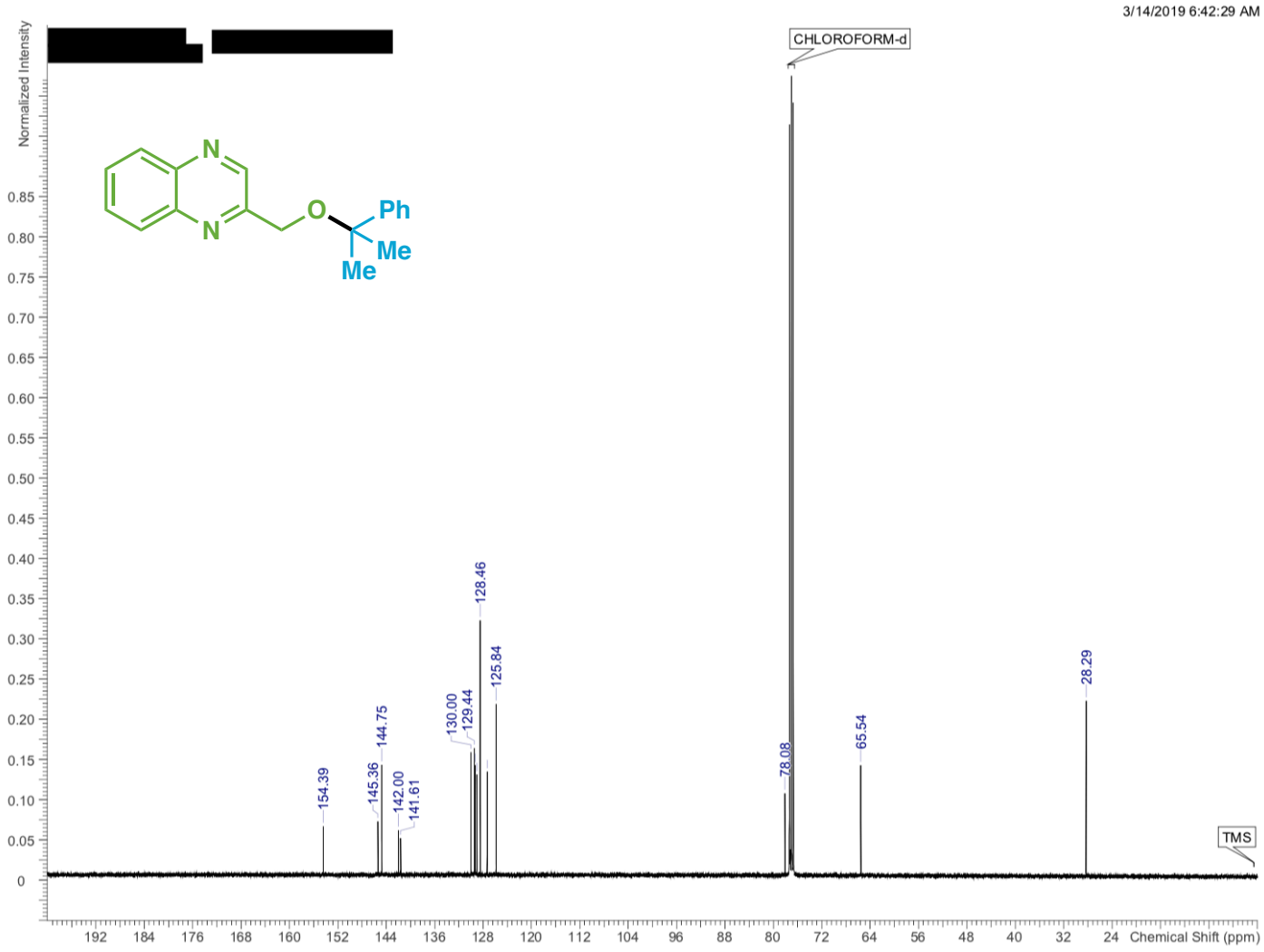


Compound 112 ^{1}H NMR



Compound 112 ^{13}C NMR



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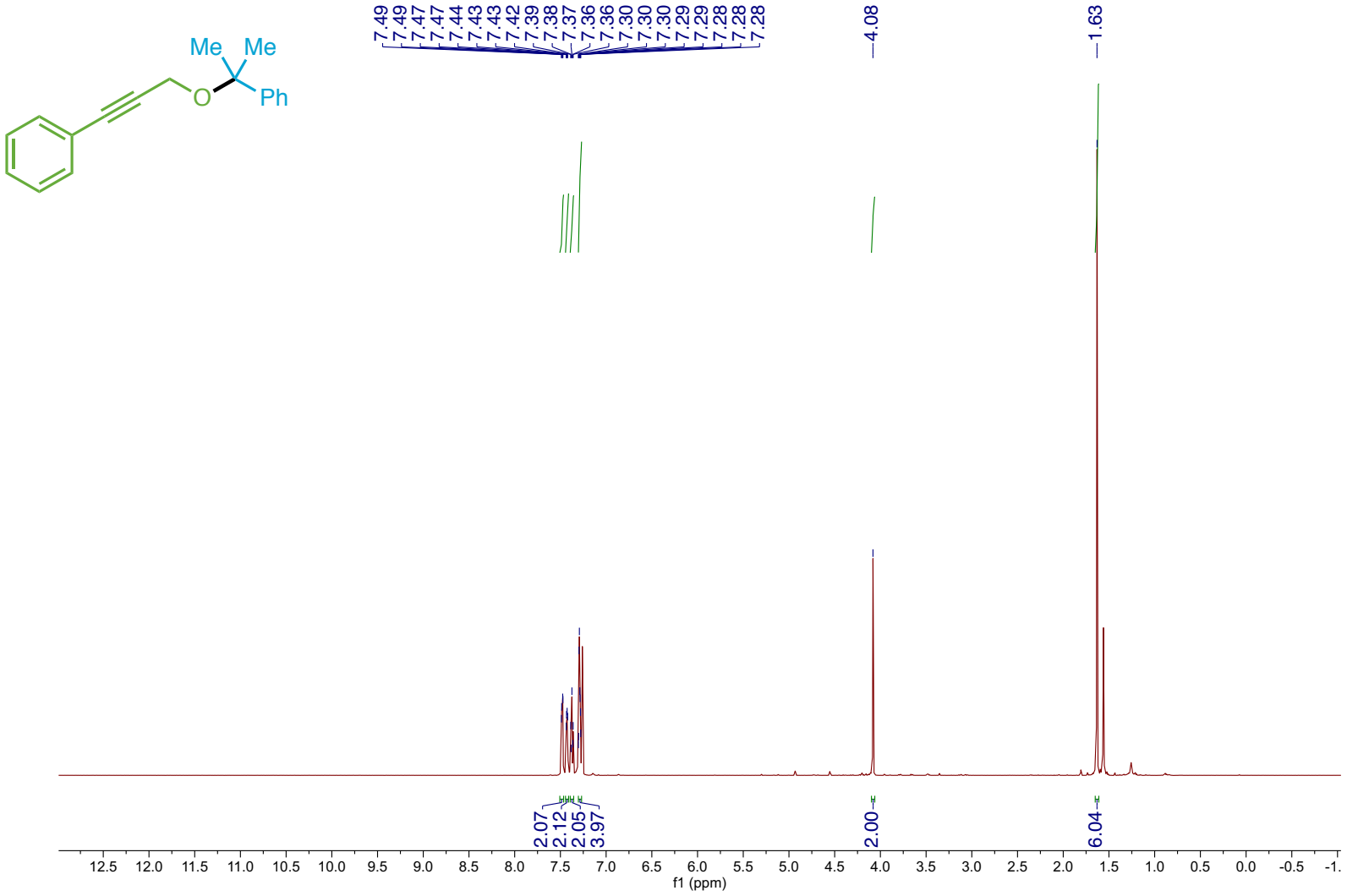

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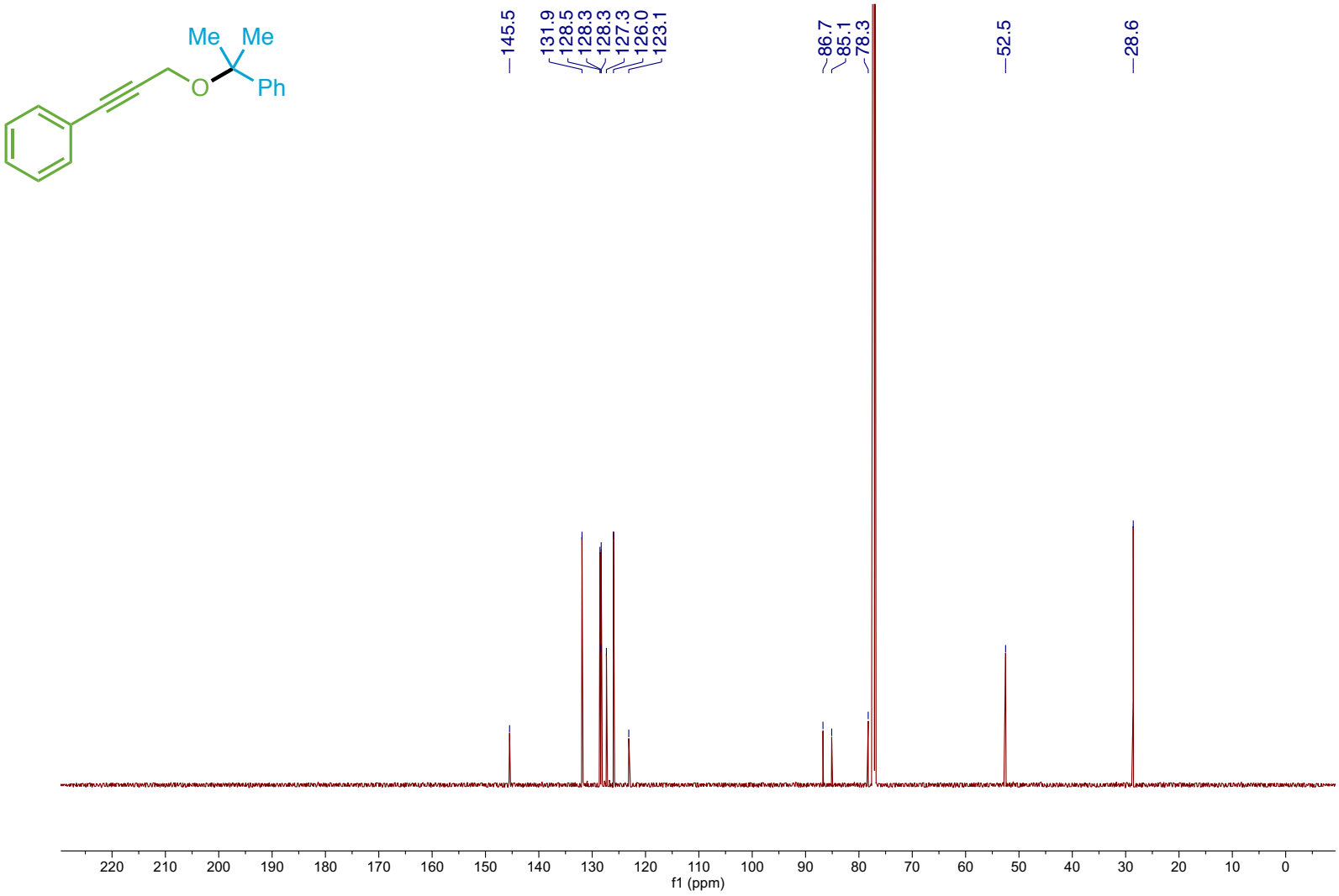

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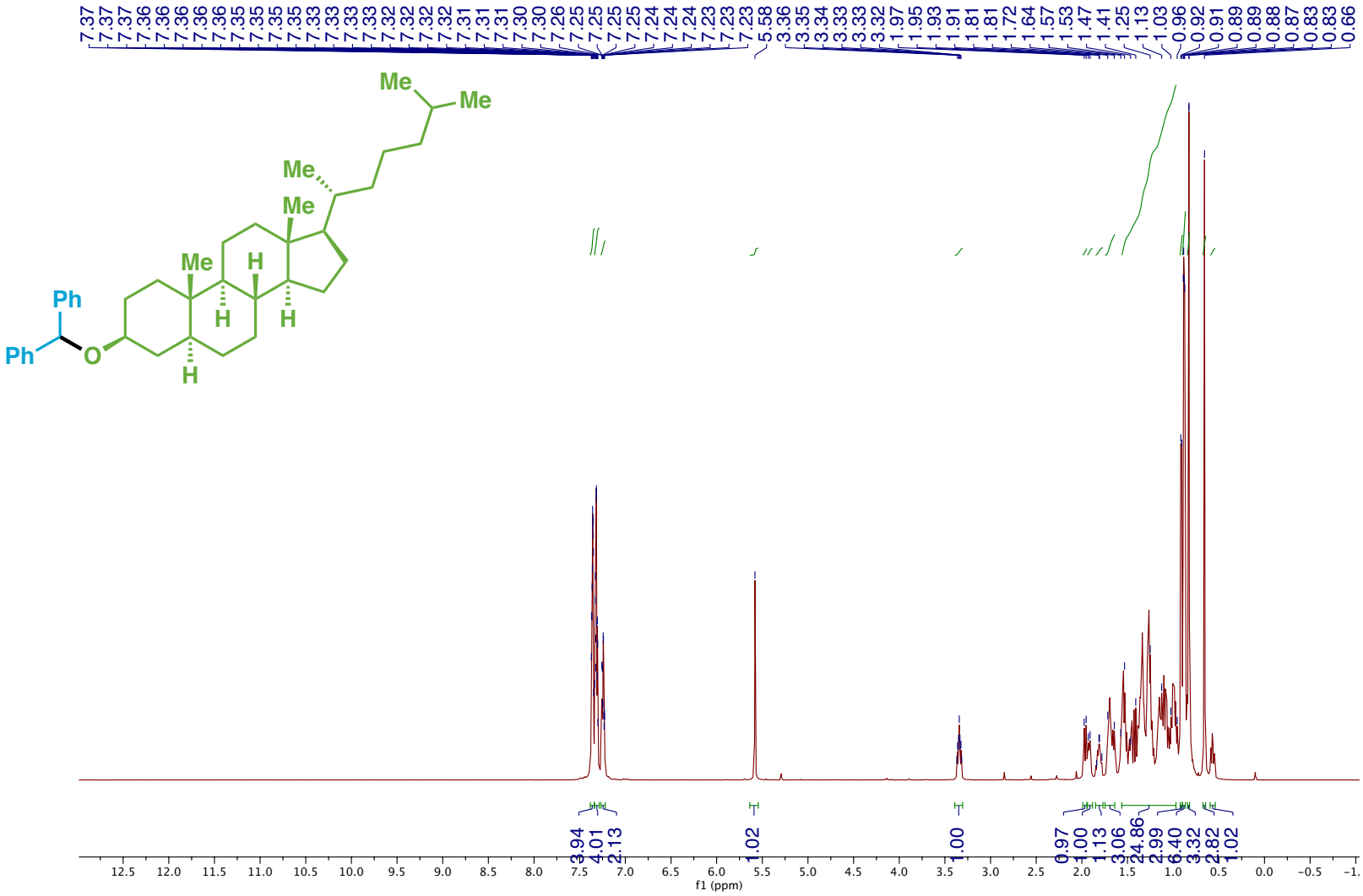

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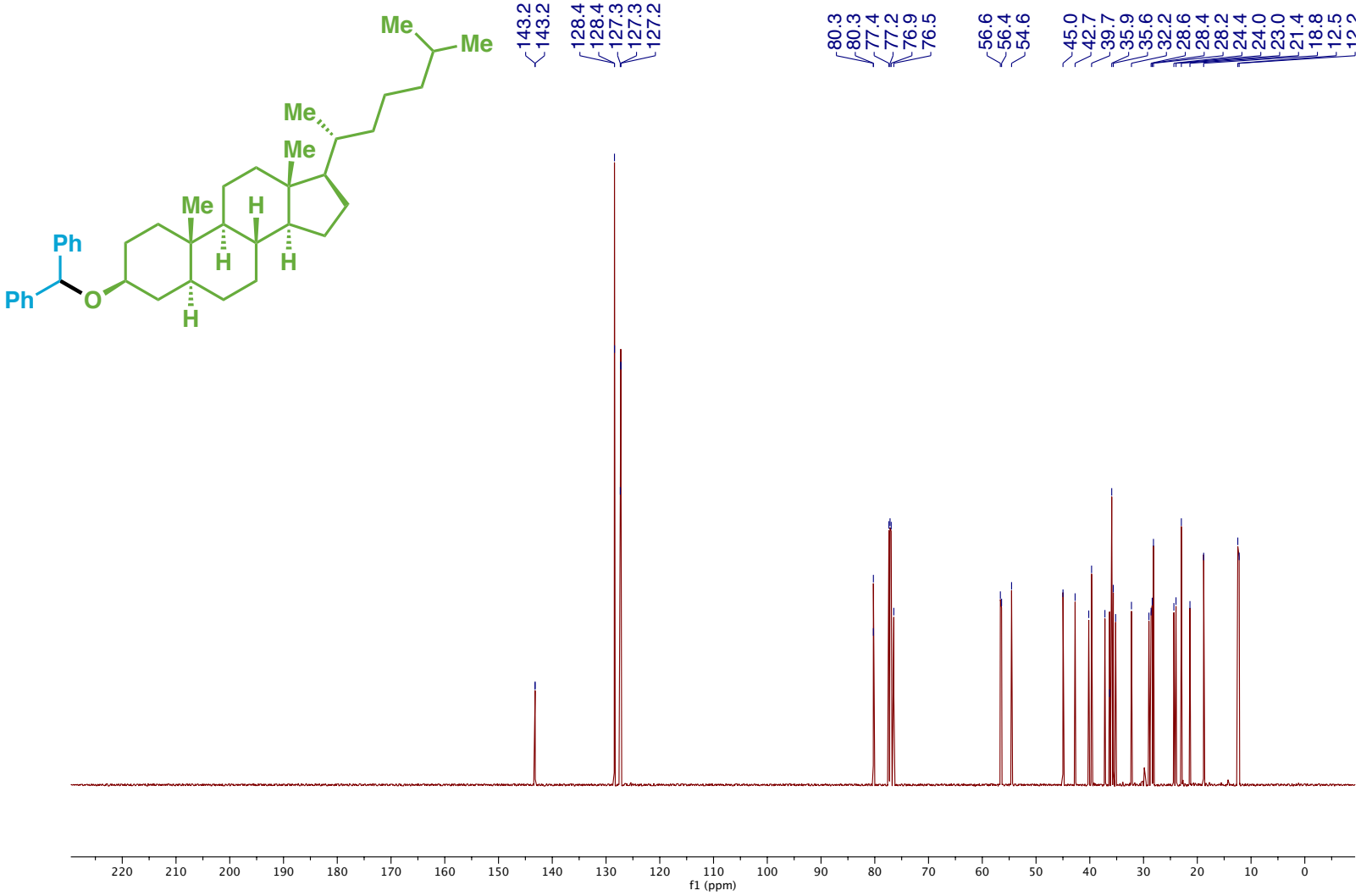
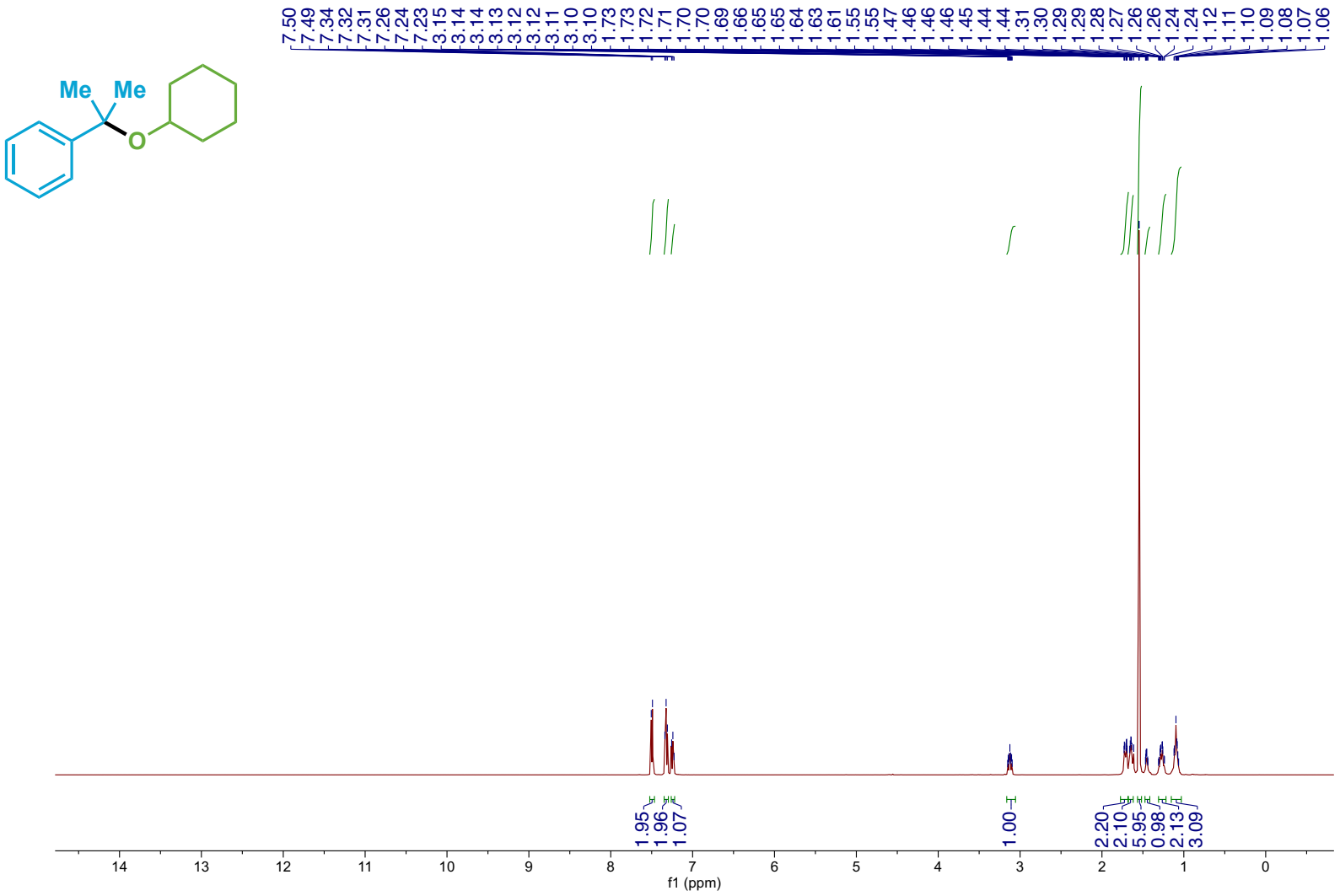


Compound 115 ^{1}H NMR



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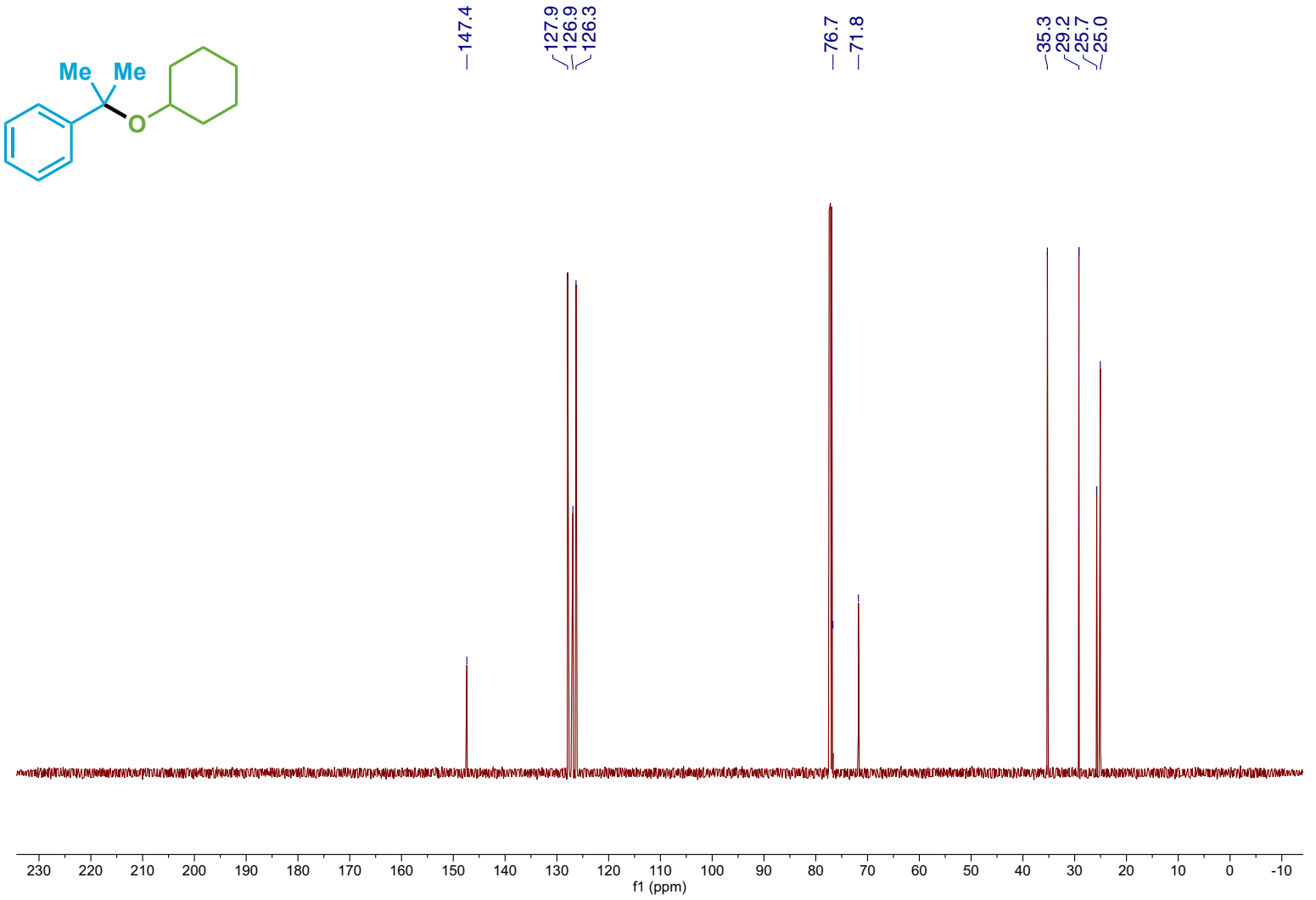
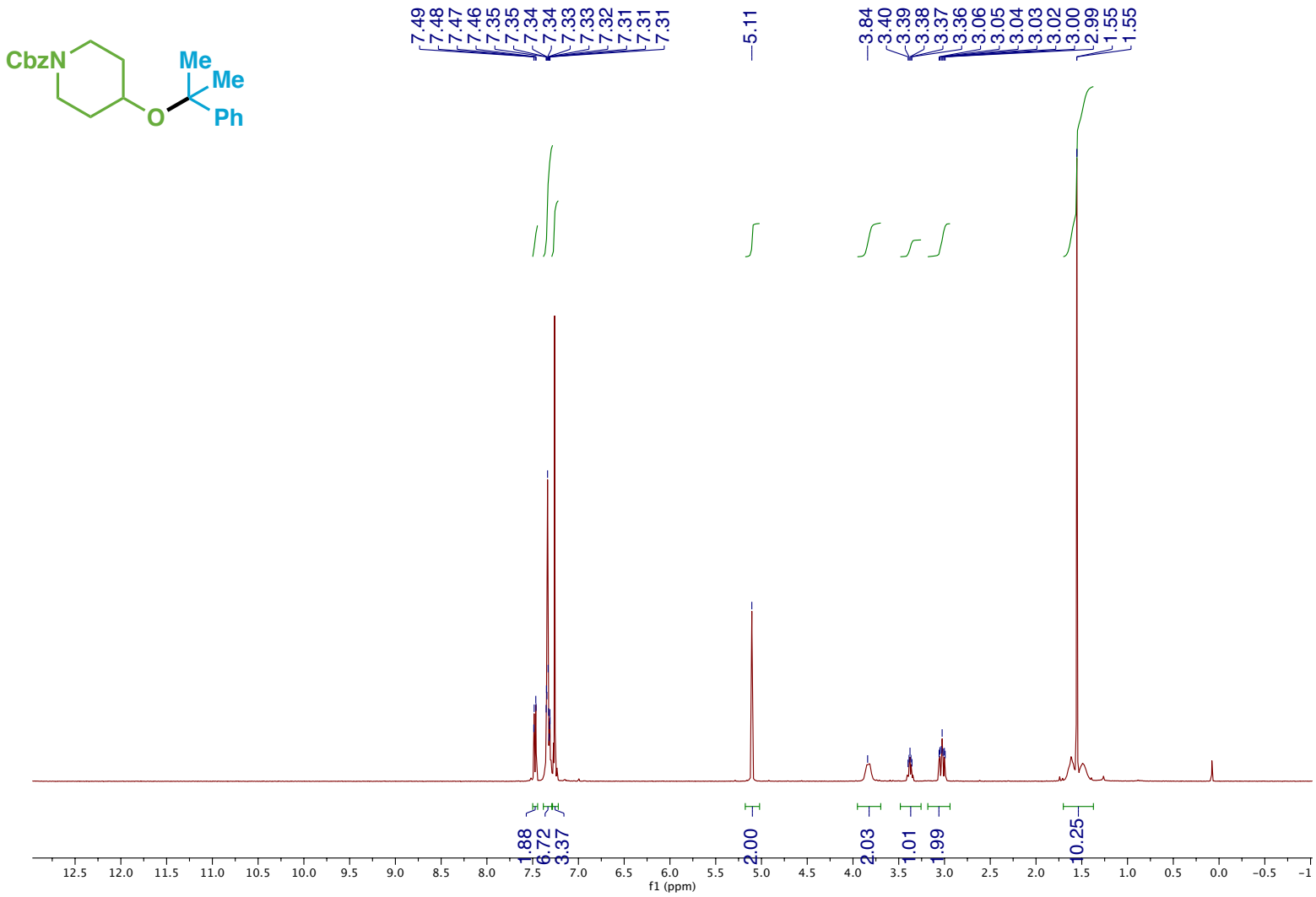


Compound 116 ^{1}H NMR



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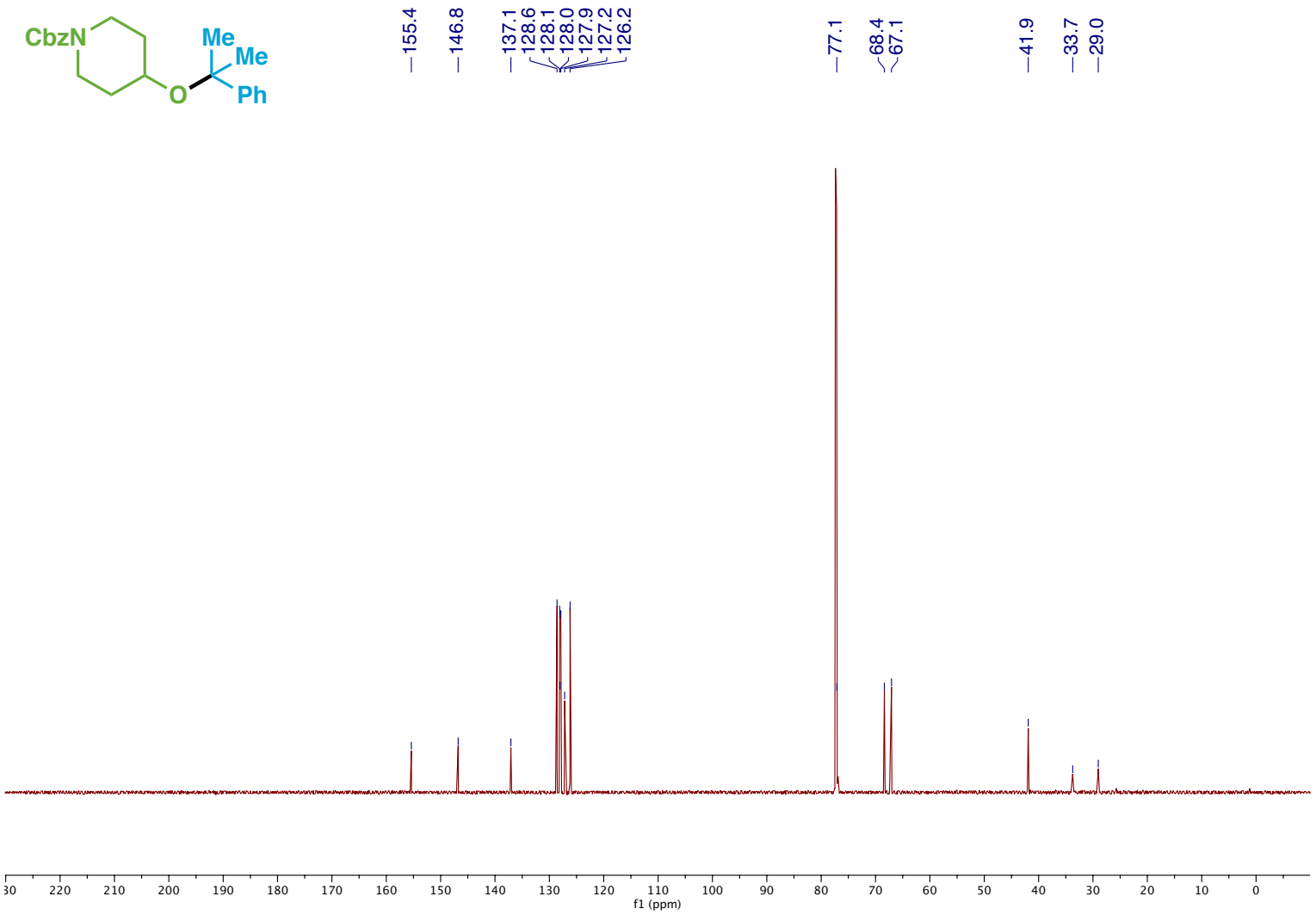

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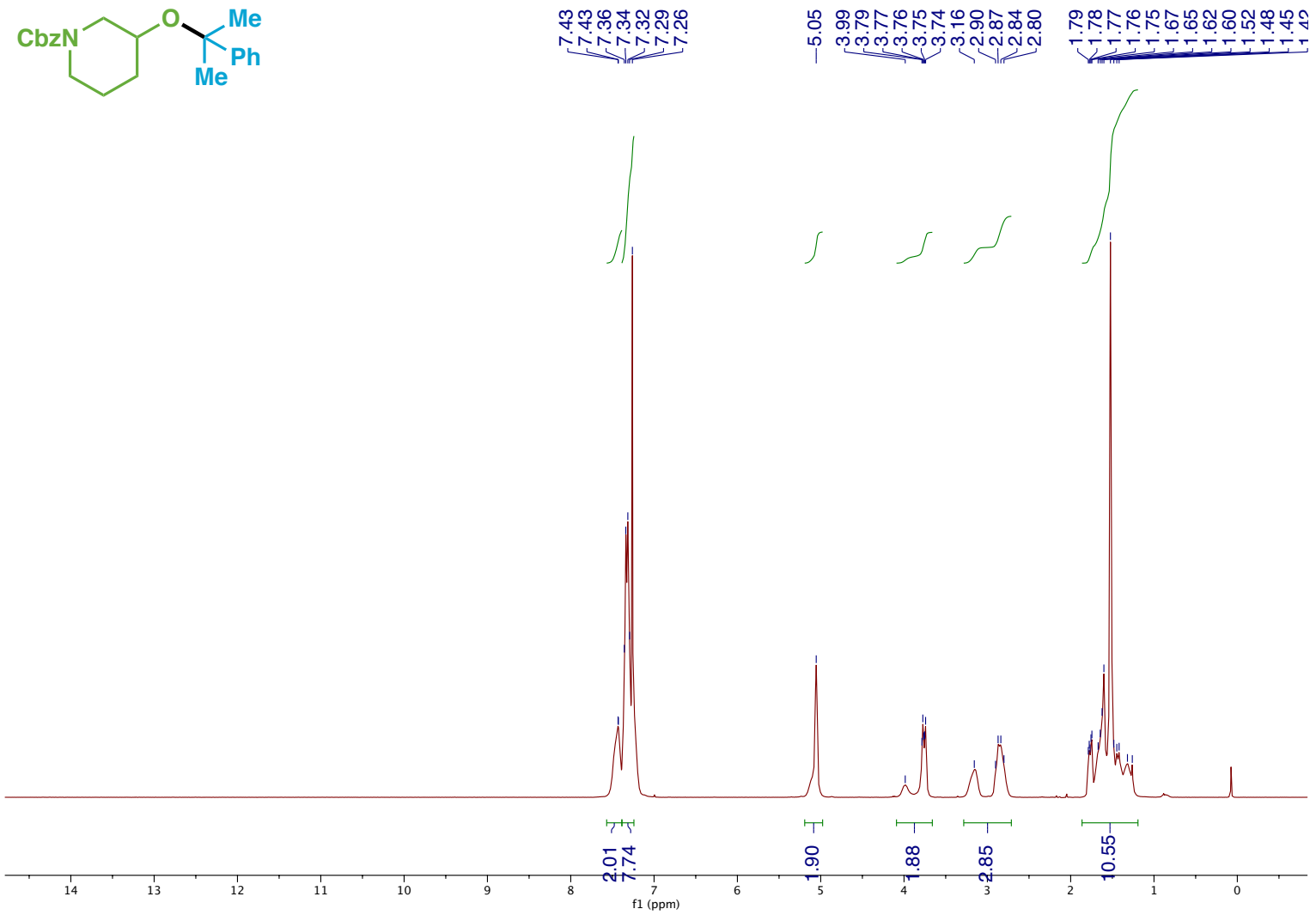

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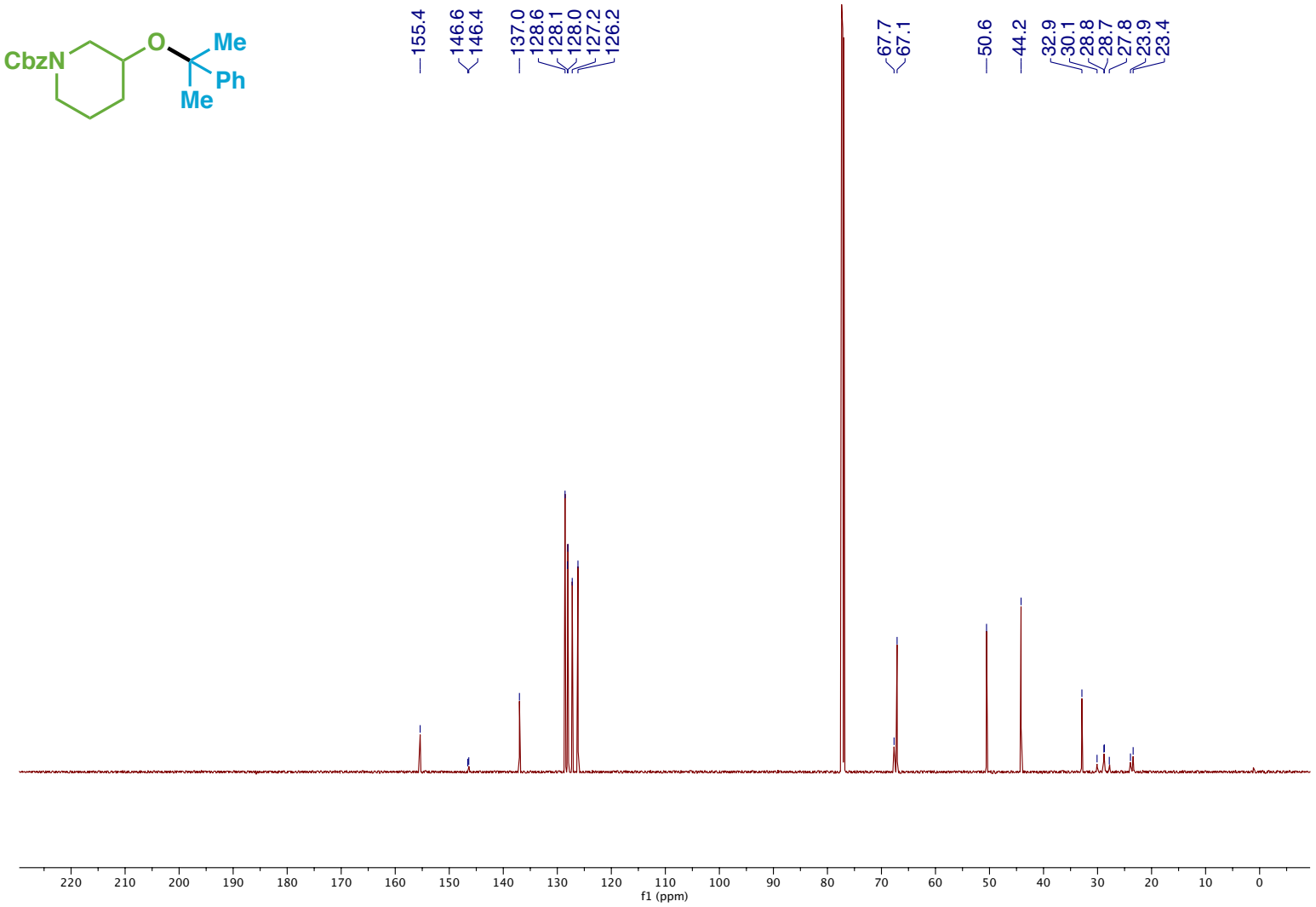
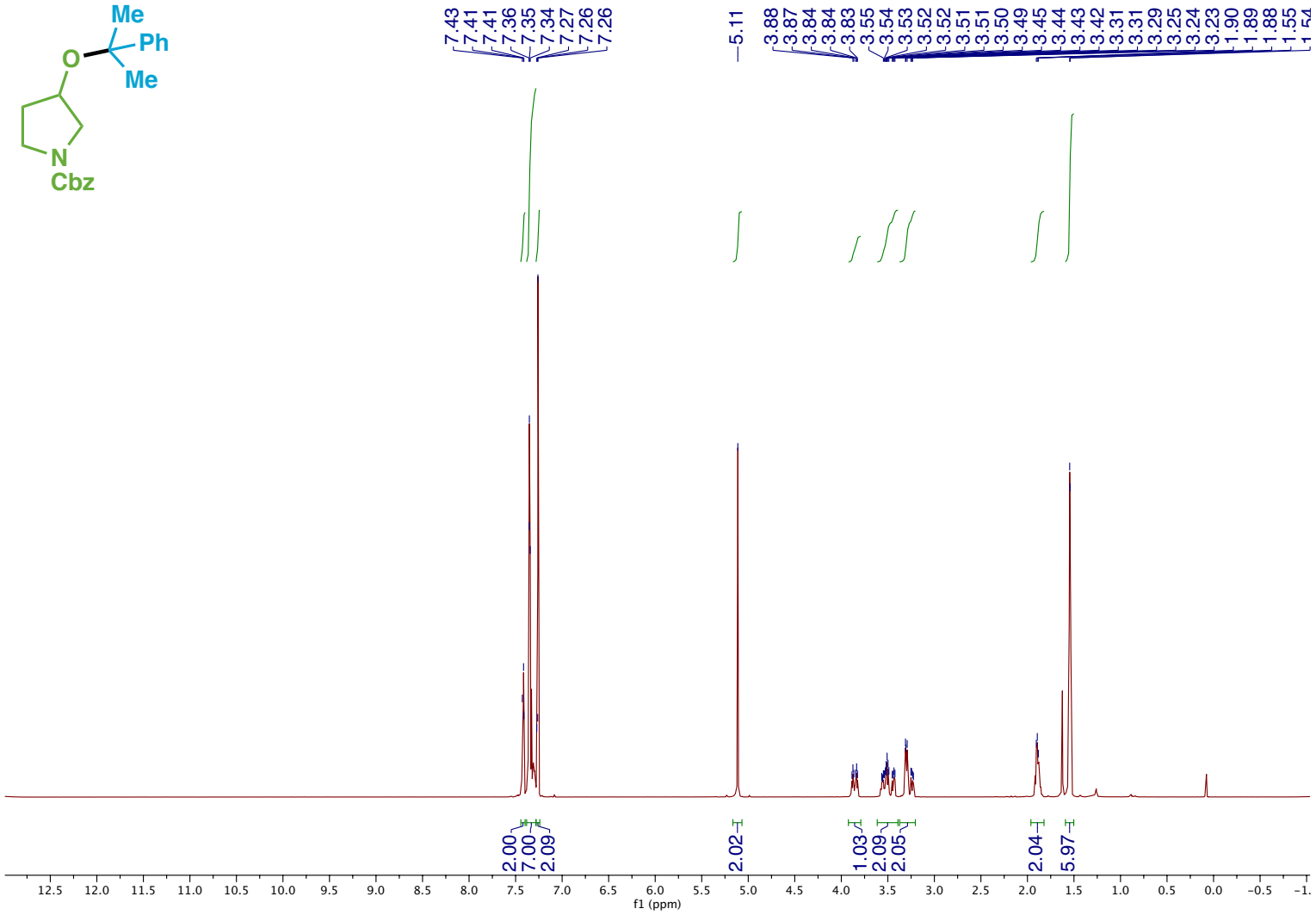
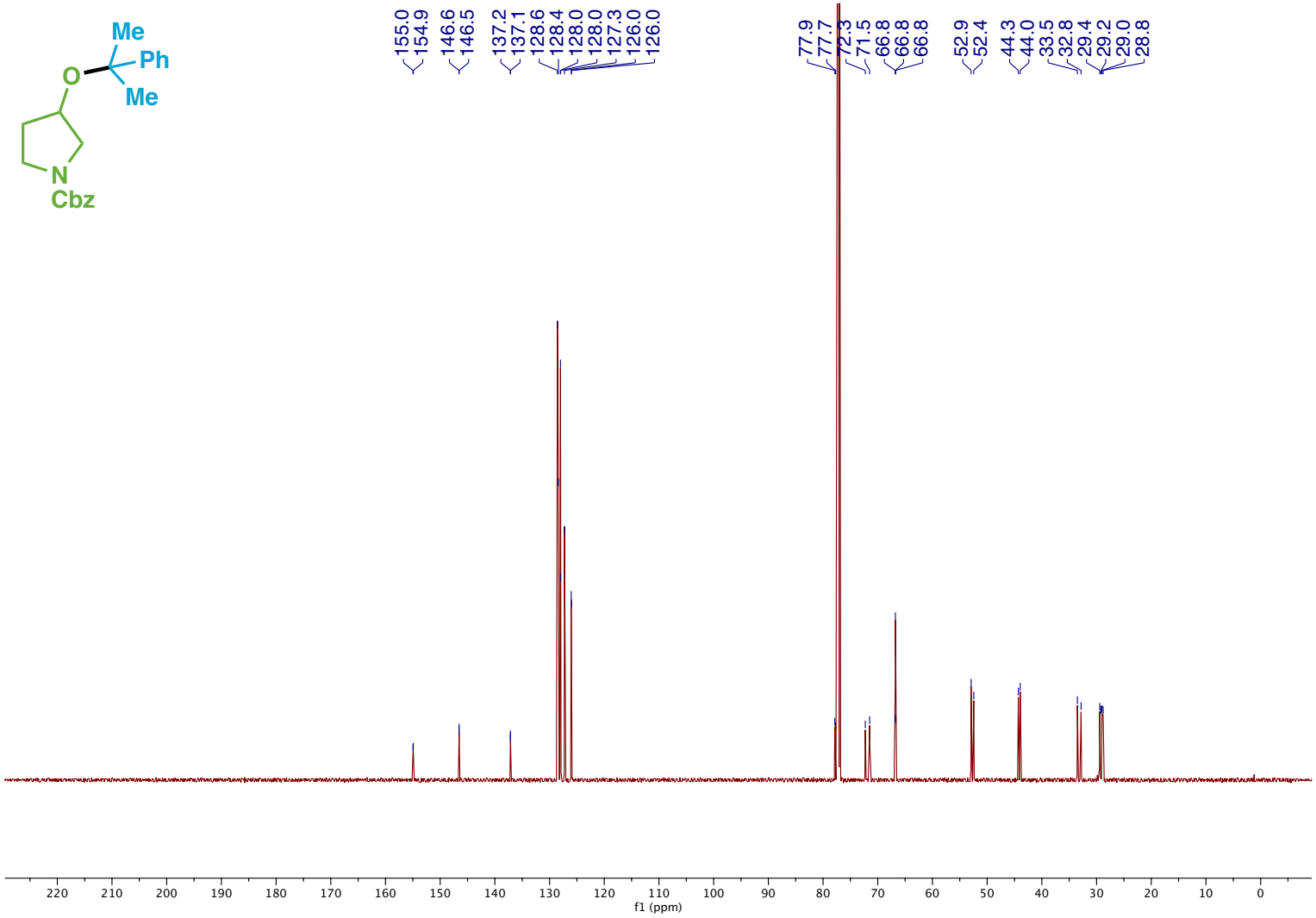


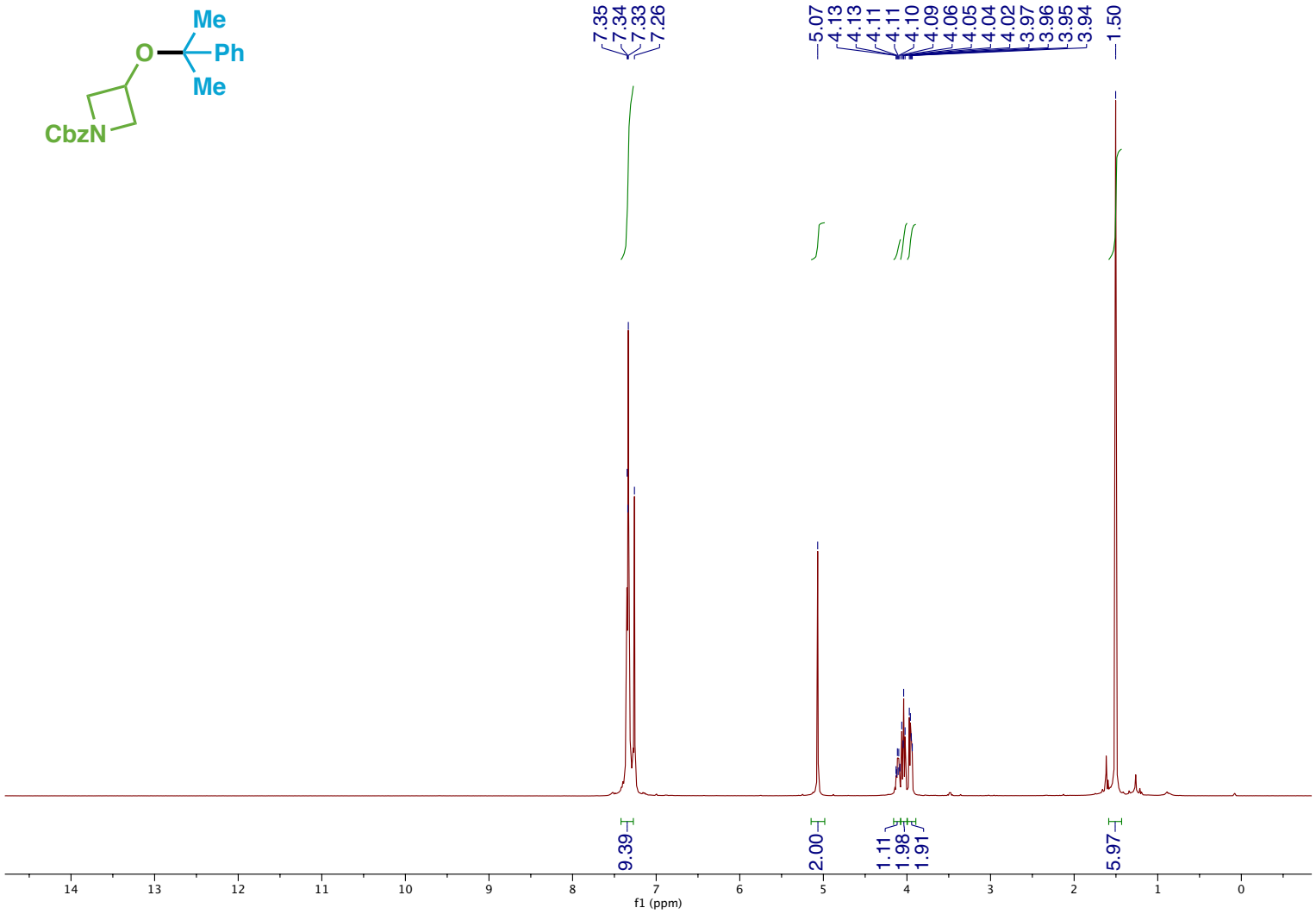
Compound 118 ^{1}H NMR



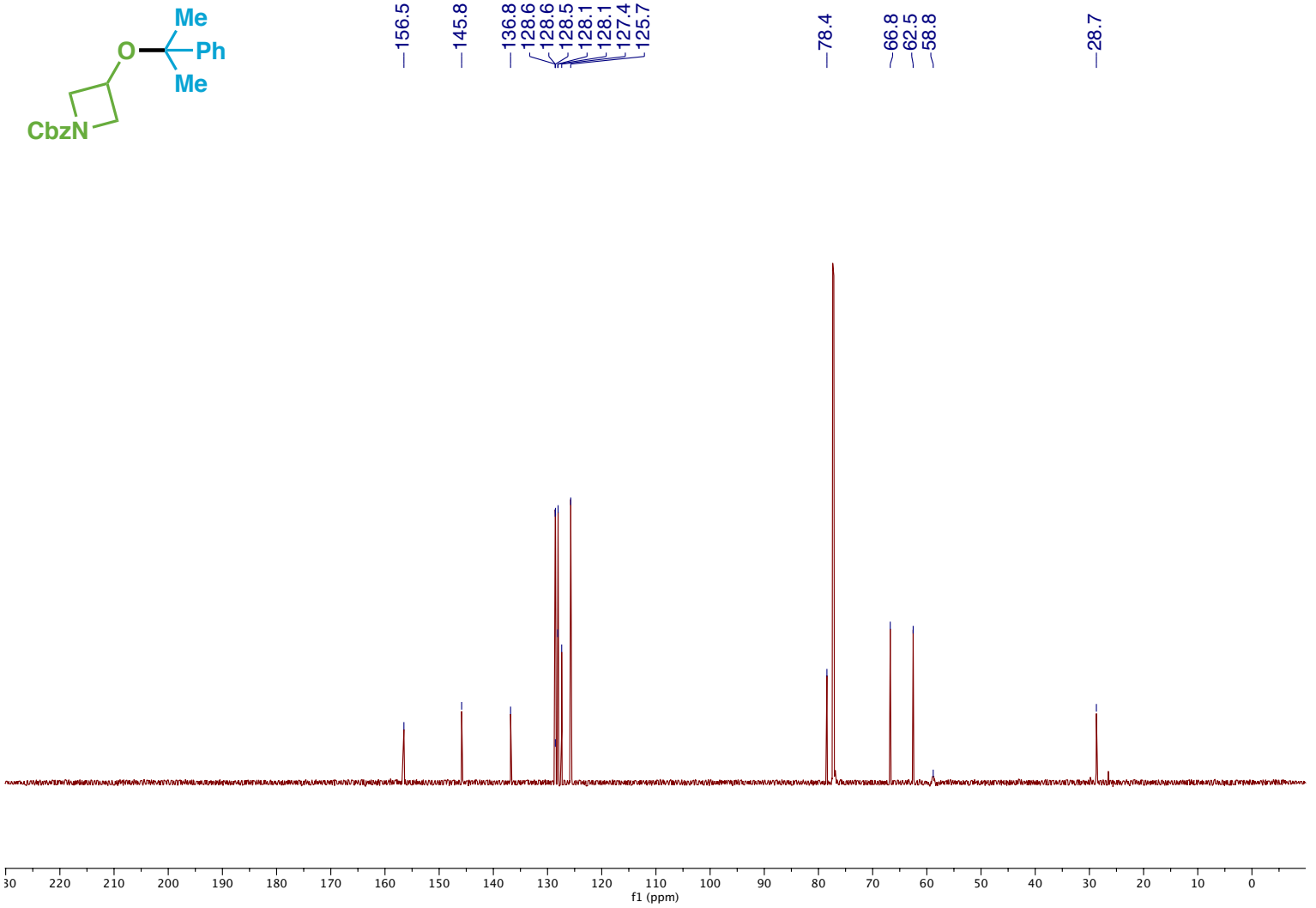
Compound 118 ^{13}C NMR



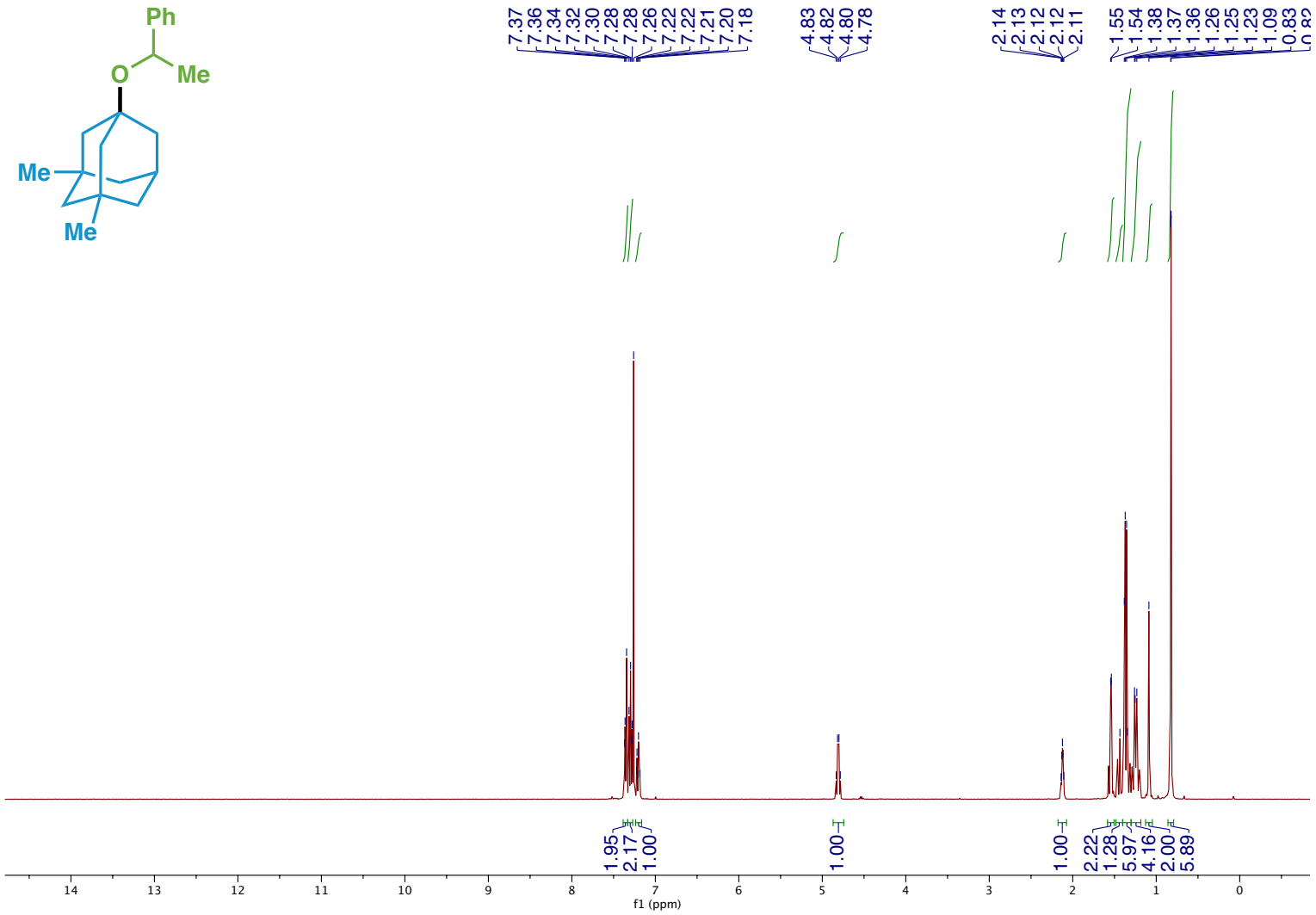
Compound 119 ^{1}H NMR



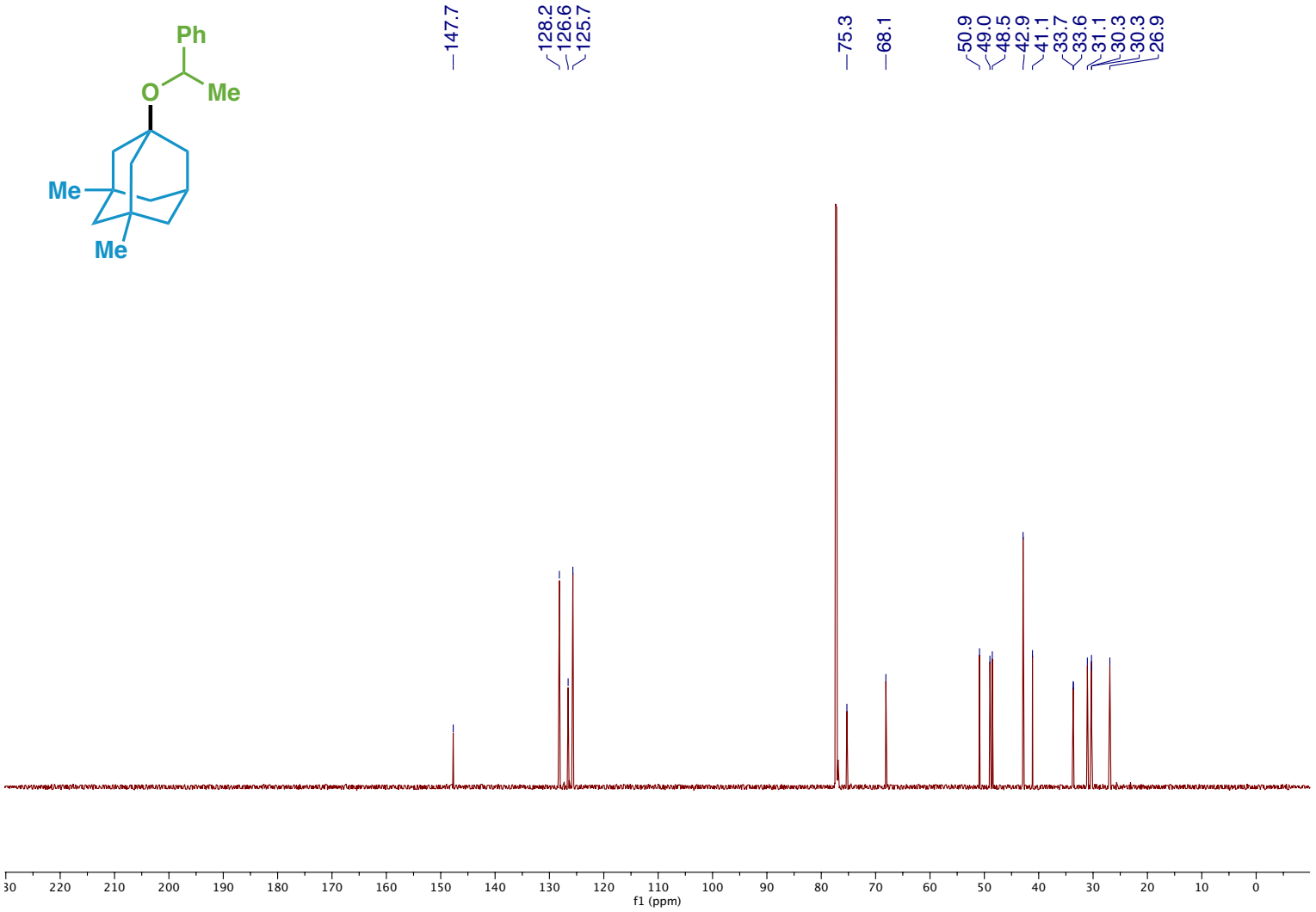
Compound 119 ^{13}C NMR



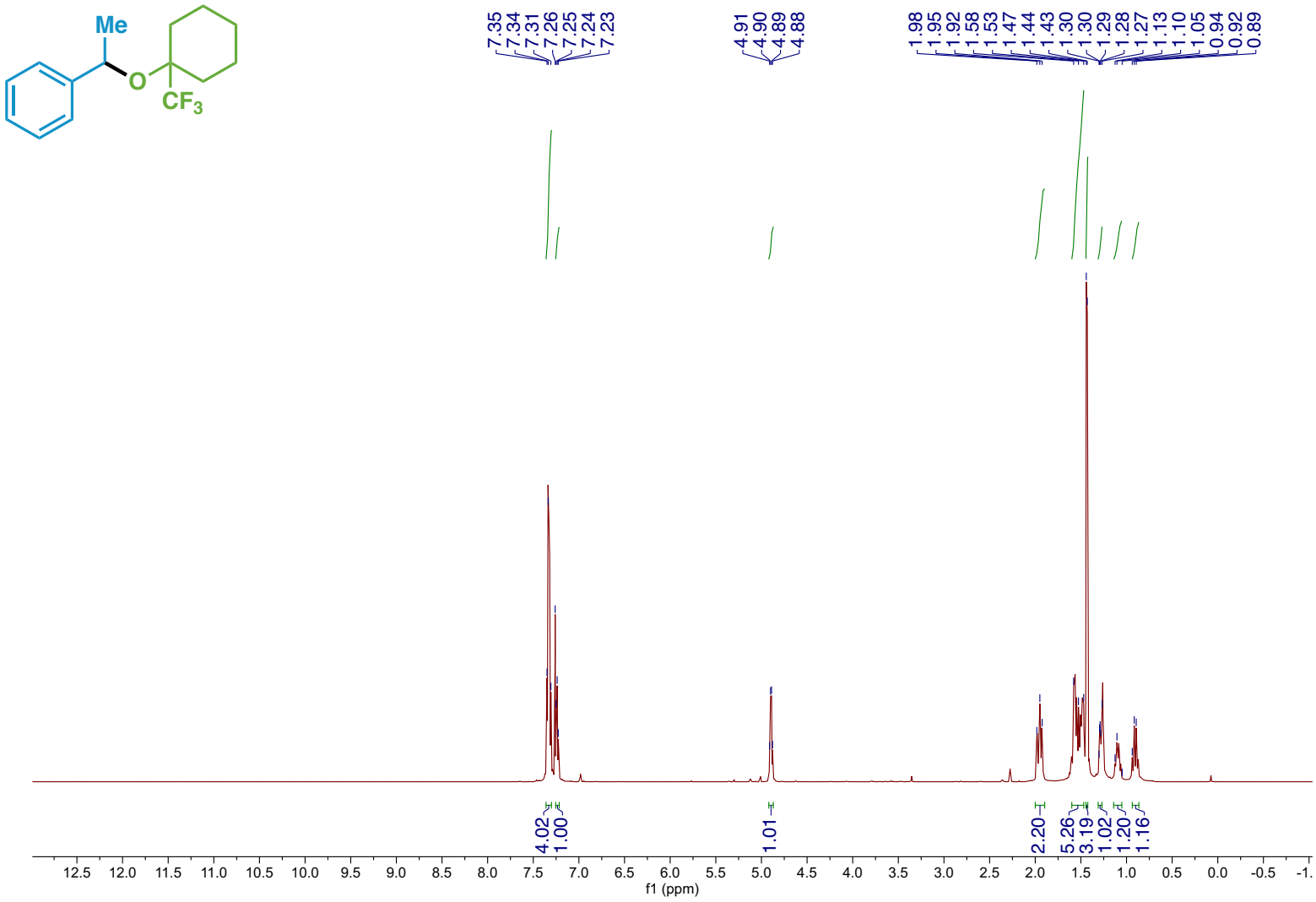
Compound 120 ^{1}H NMR



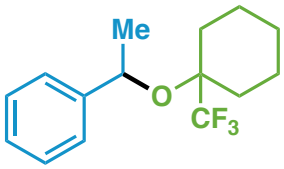
Compound 120 ^{13}C NMR



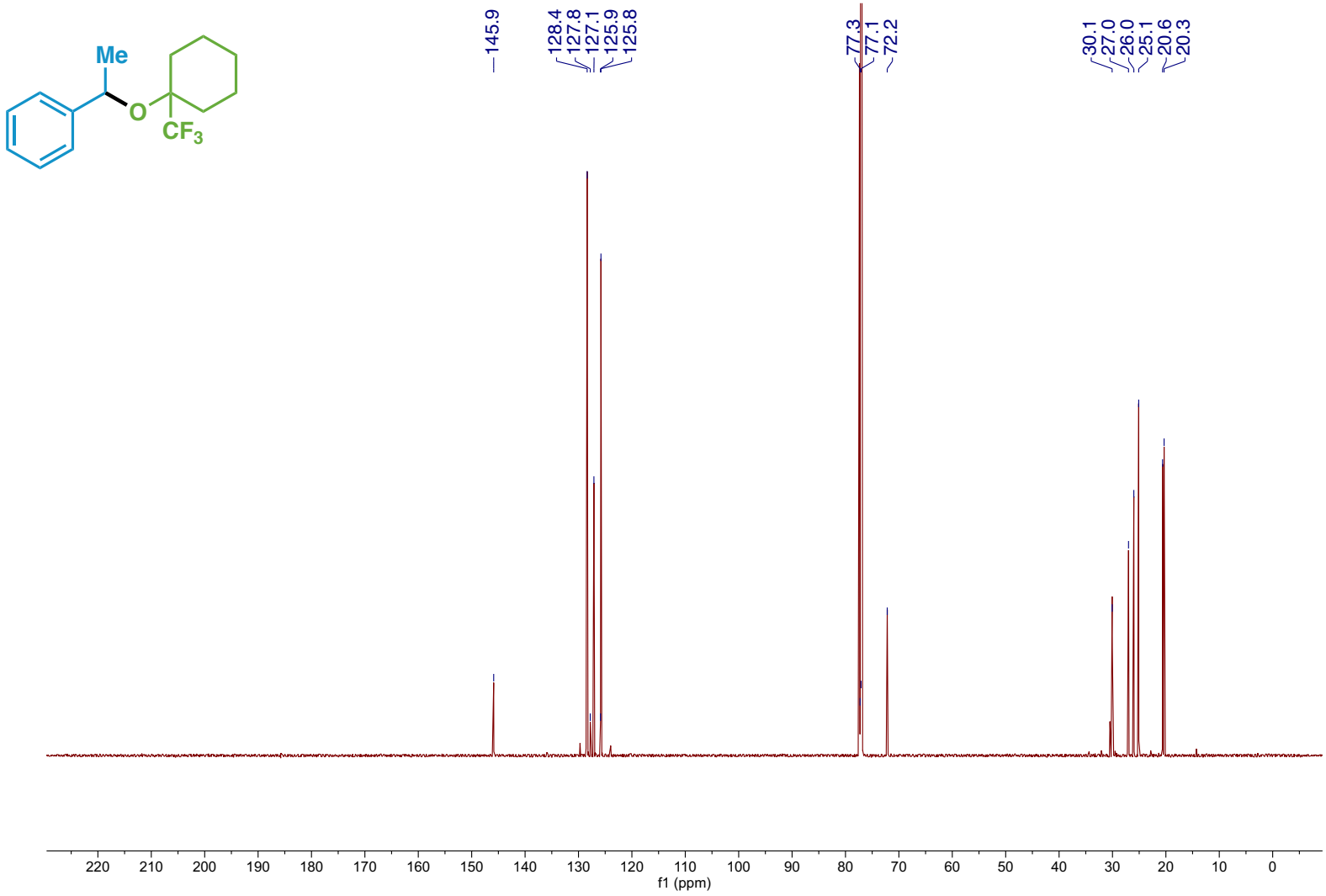
Compound 121 ^{1}H NMR



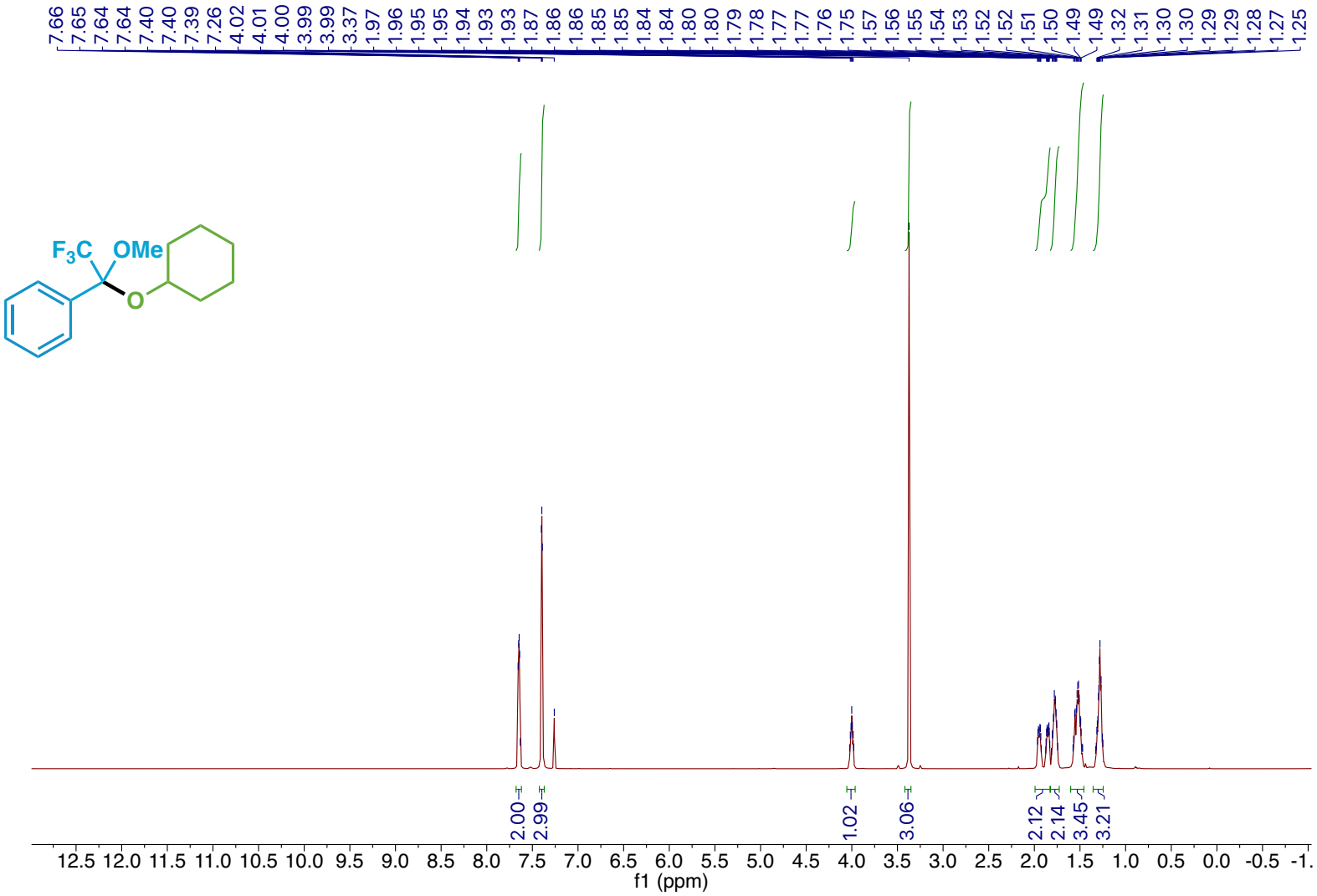
Compound 121 ^{19}F NMR



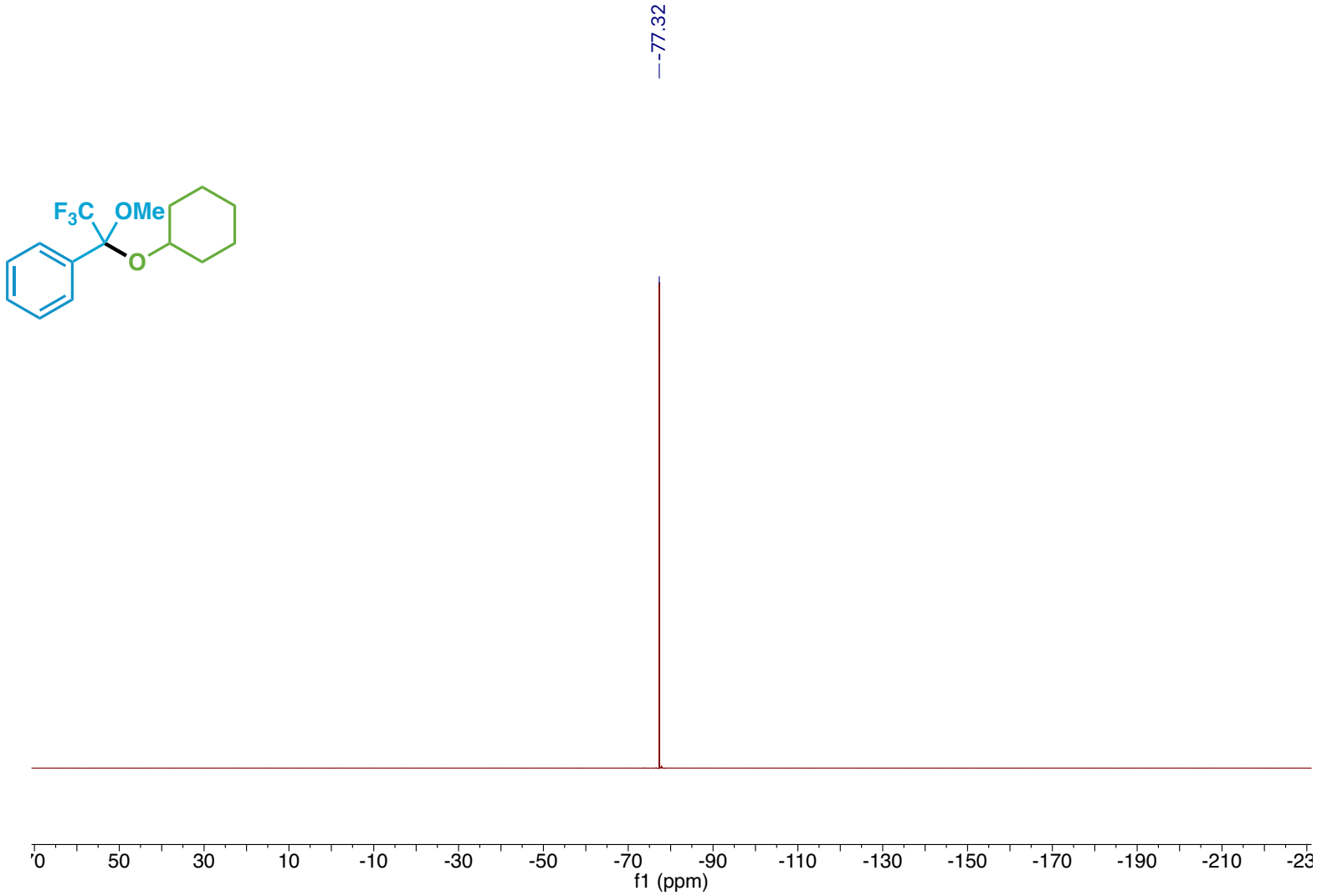
Compound 121 ^{13}C NMR



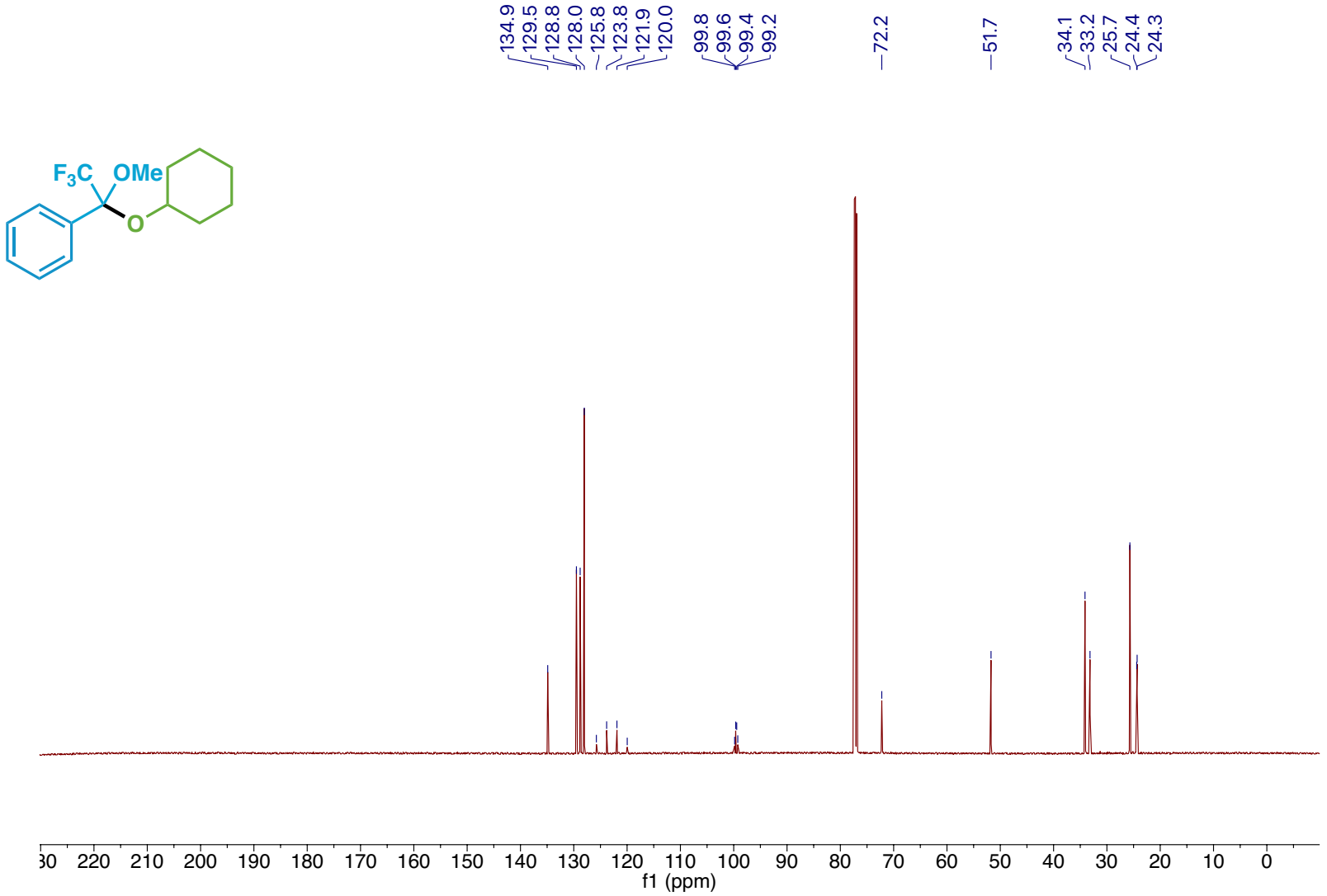
Compound 122 ^{1}H NMR



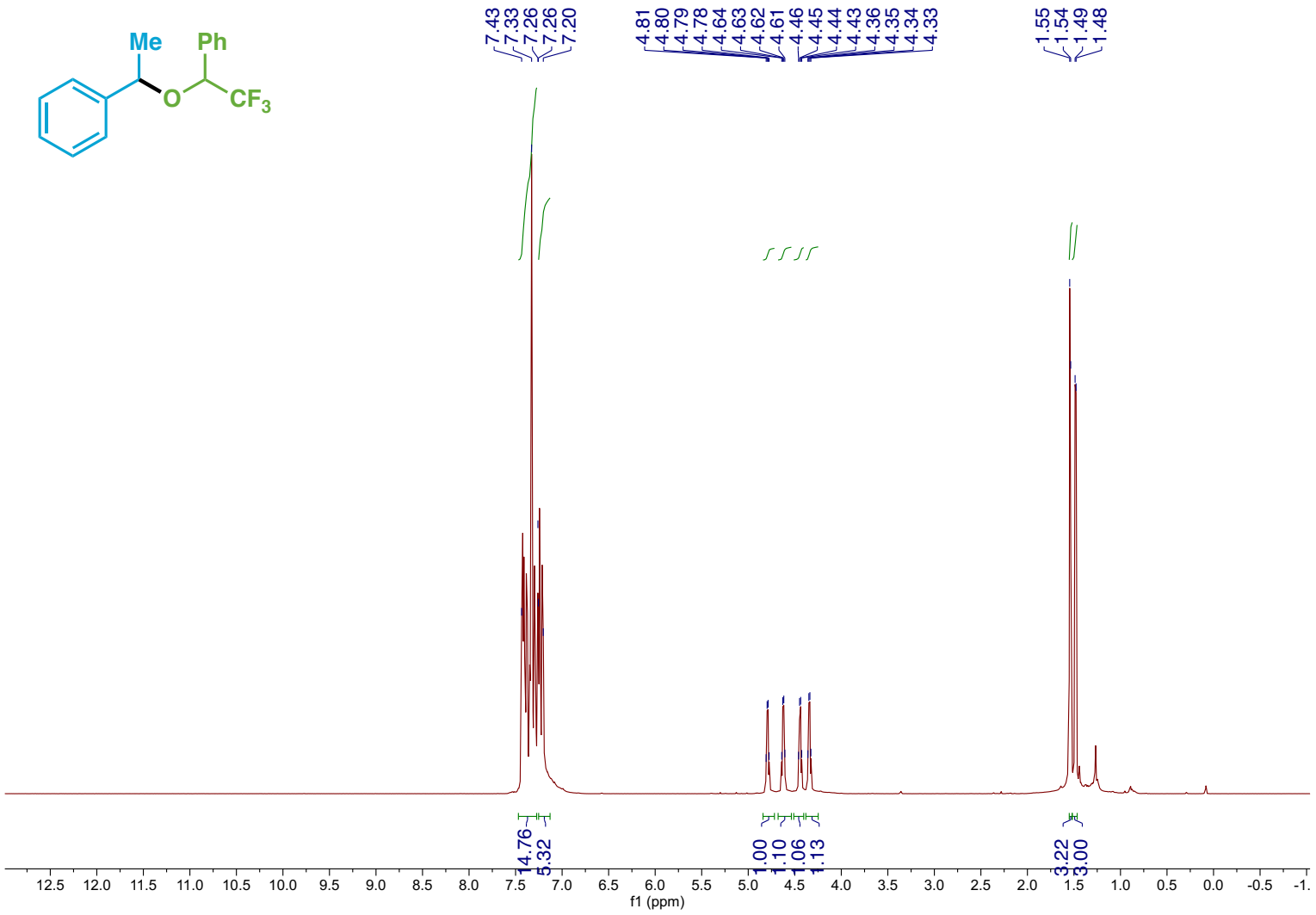
Compound 122 ^{19}F NMR



Compound 122 ^{13}C NMR



Compound 123 ^{1}H NMR



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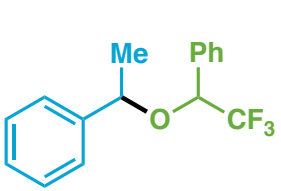
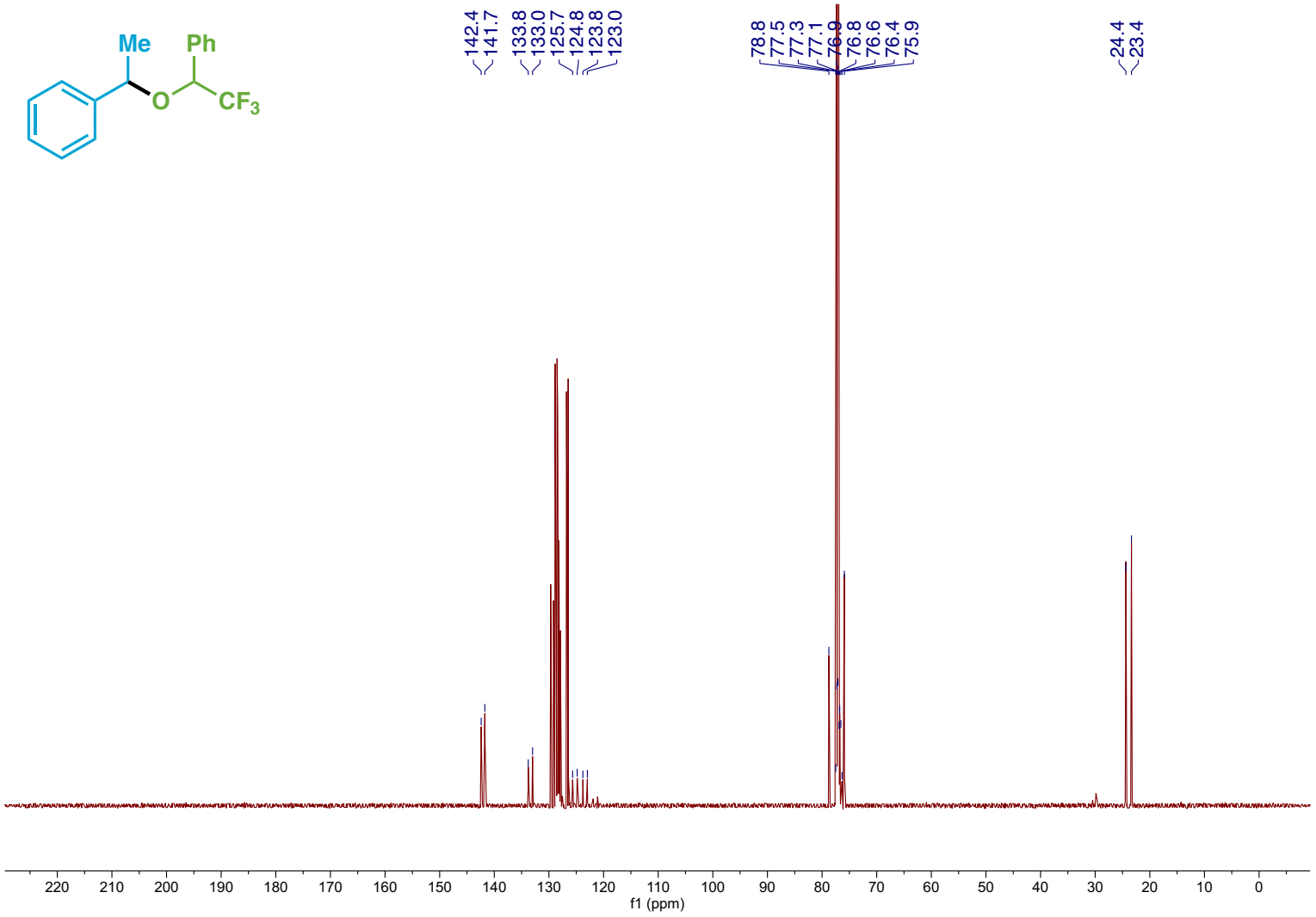
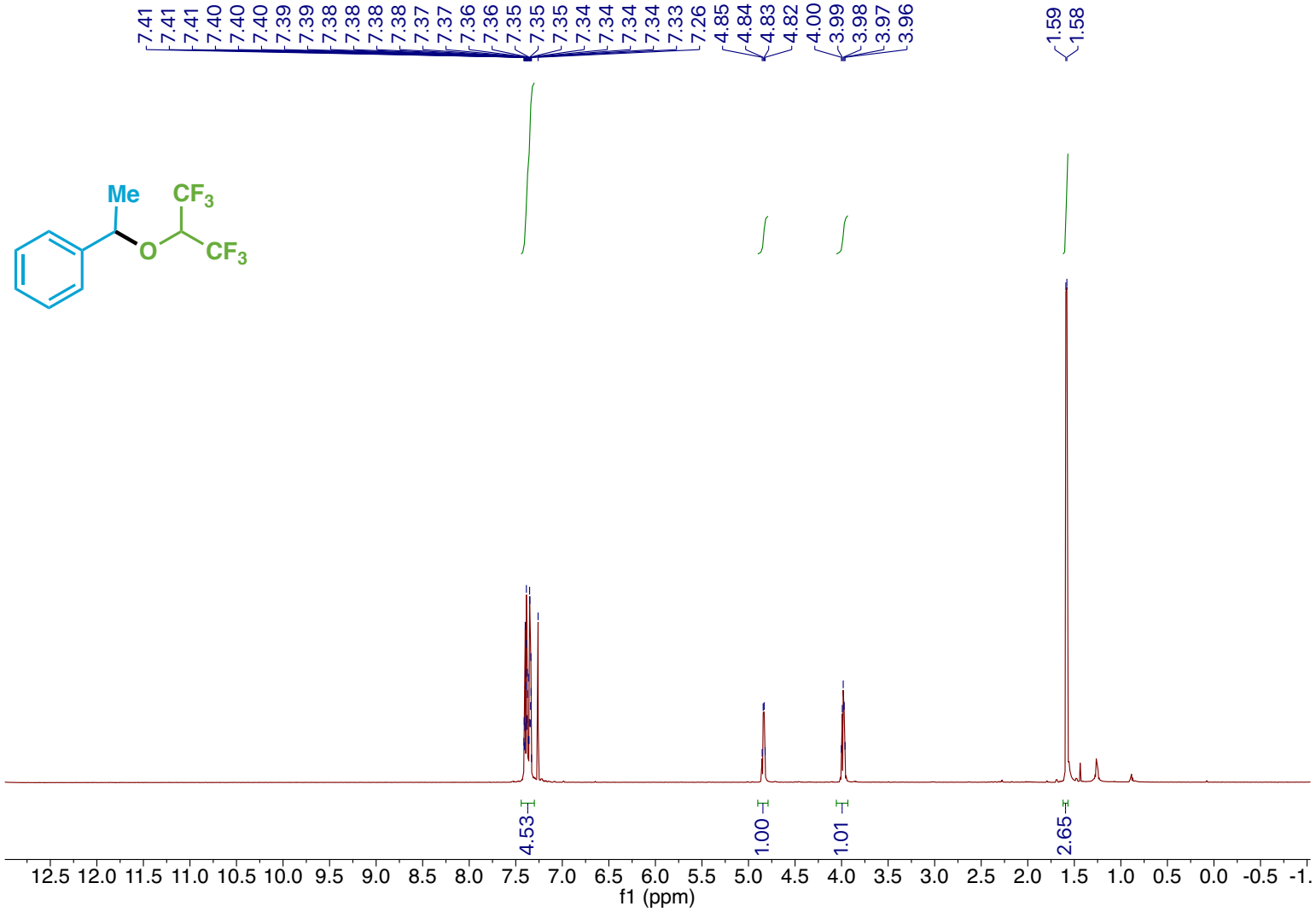


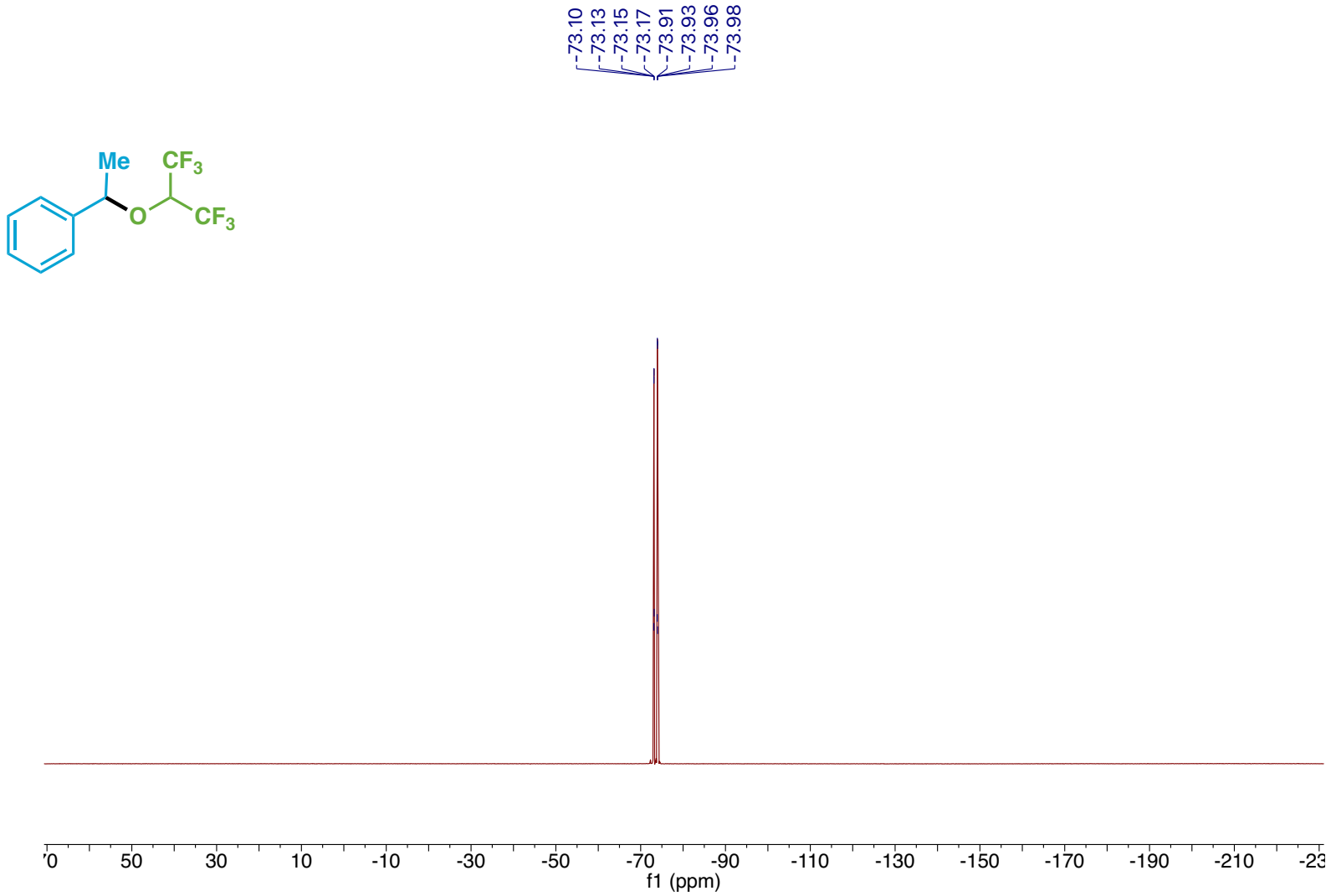
Compound 123 ^{13}C NMR



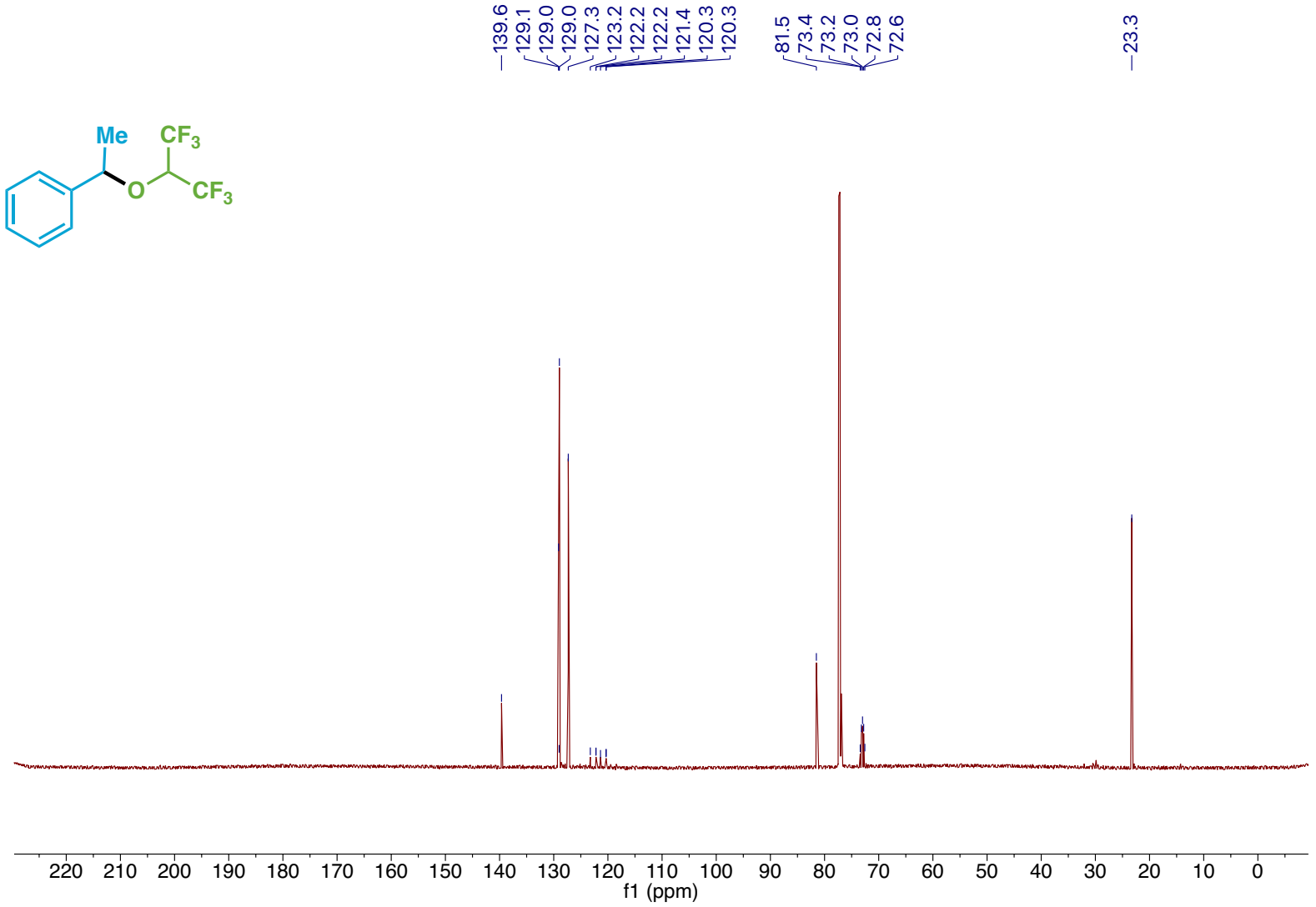
Compound 124 ^{1}H NMR



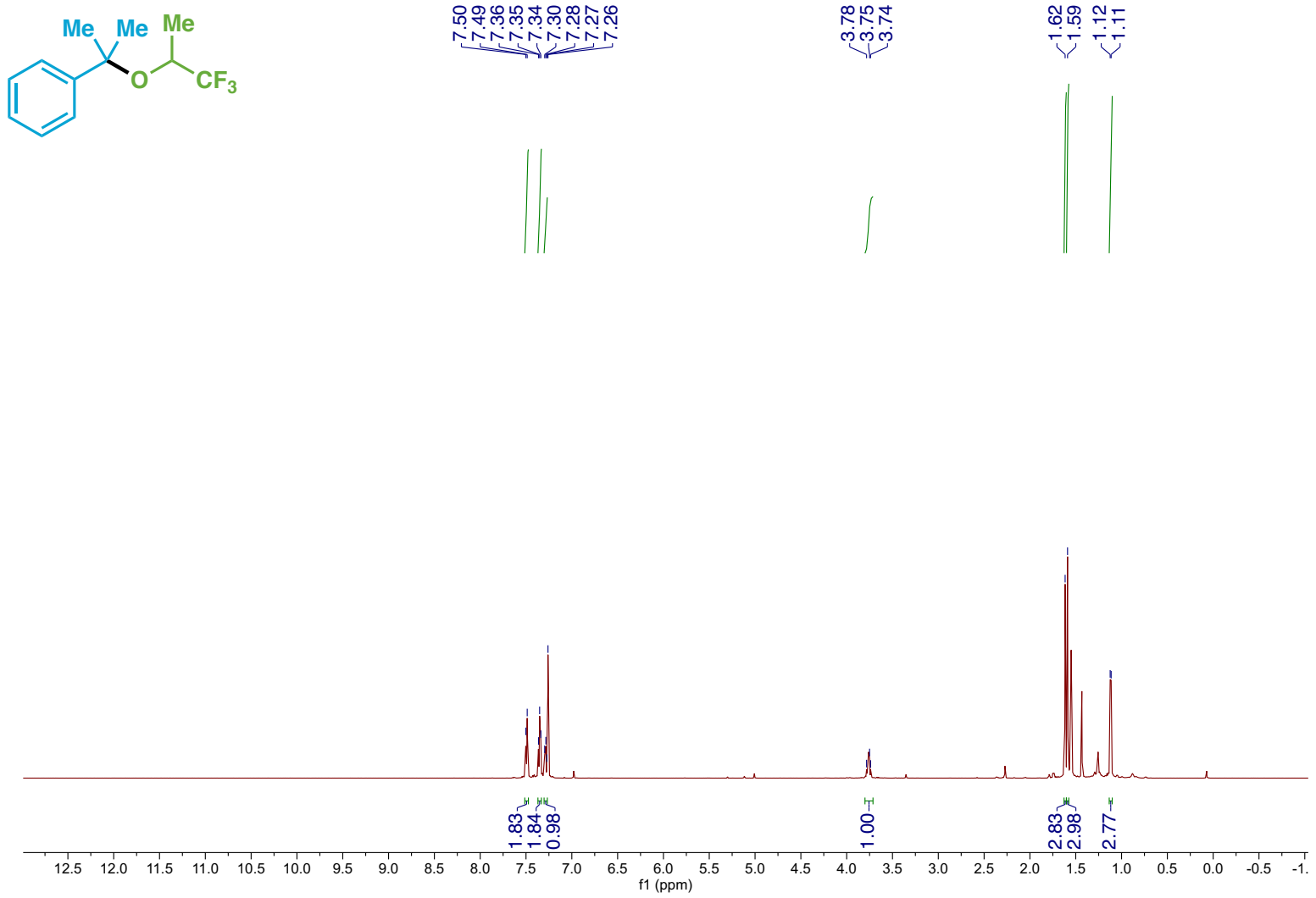
Compound 124 ^{19}F NMR



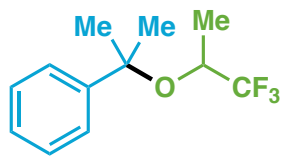
Compound 124 ^{13}C NMR



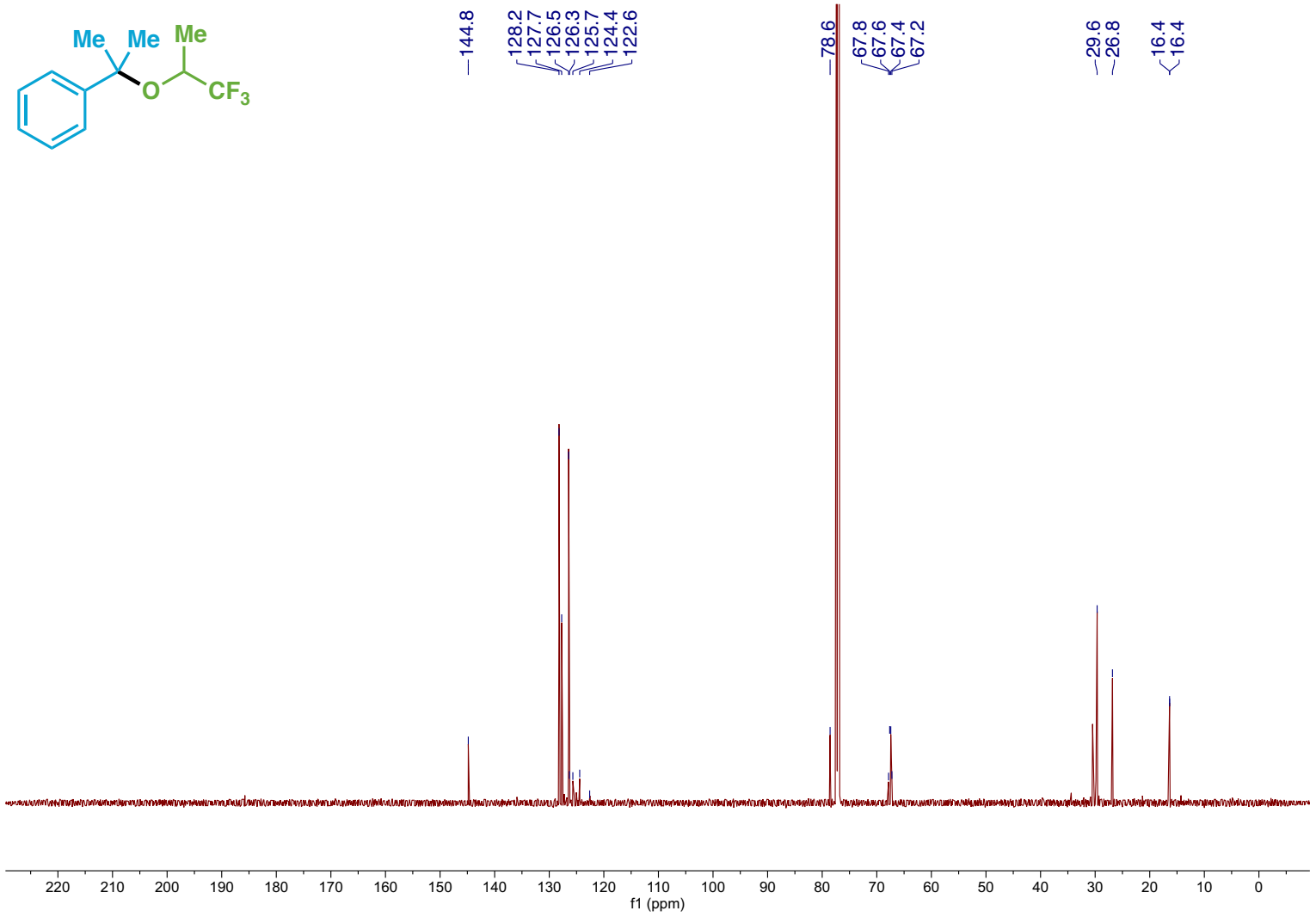
Compound 125 ^{1}H NMR



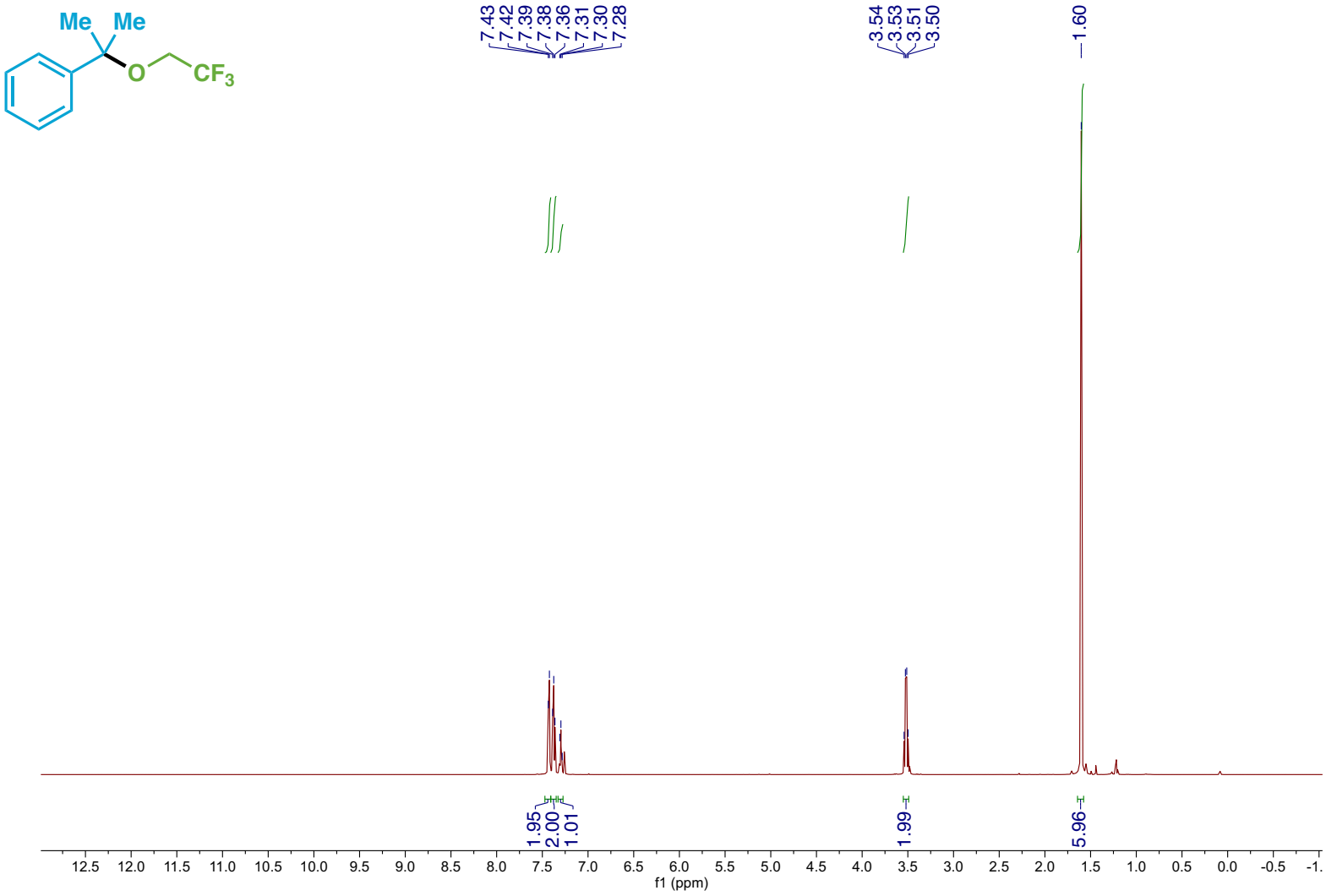
Compound 125 ^{19}F NMR



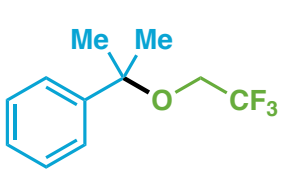
Compound 125 ^{13}C NMR



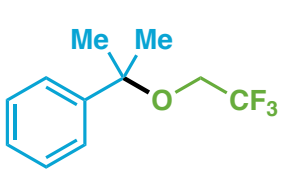
Compound 126 ^{1}H NMR



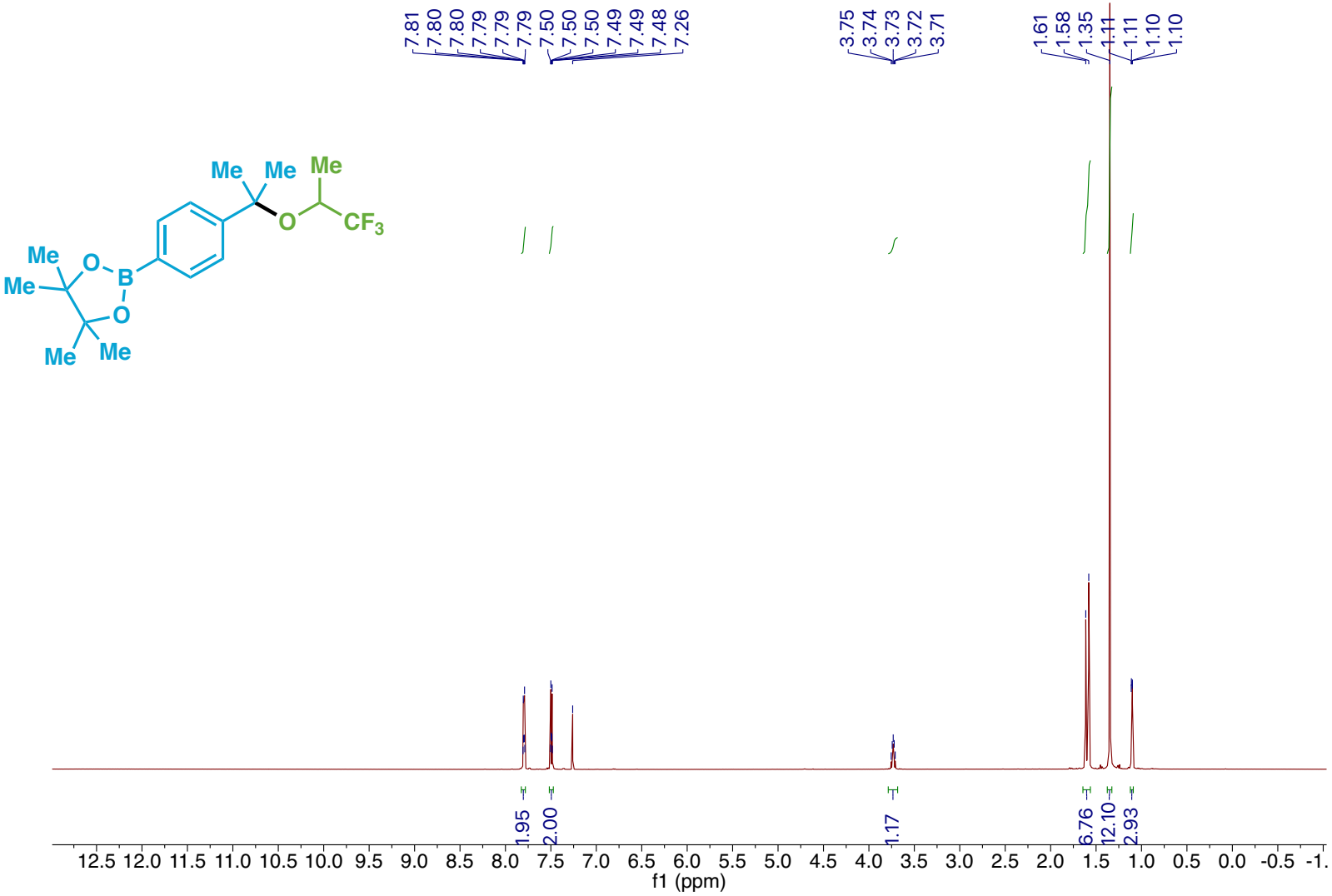
Compound 126 ^{19}F NMR



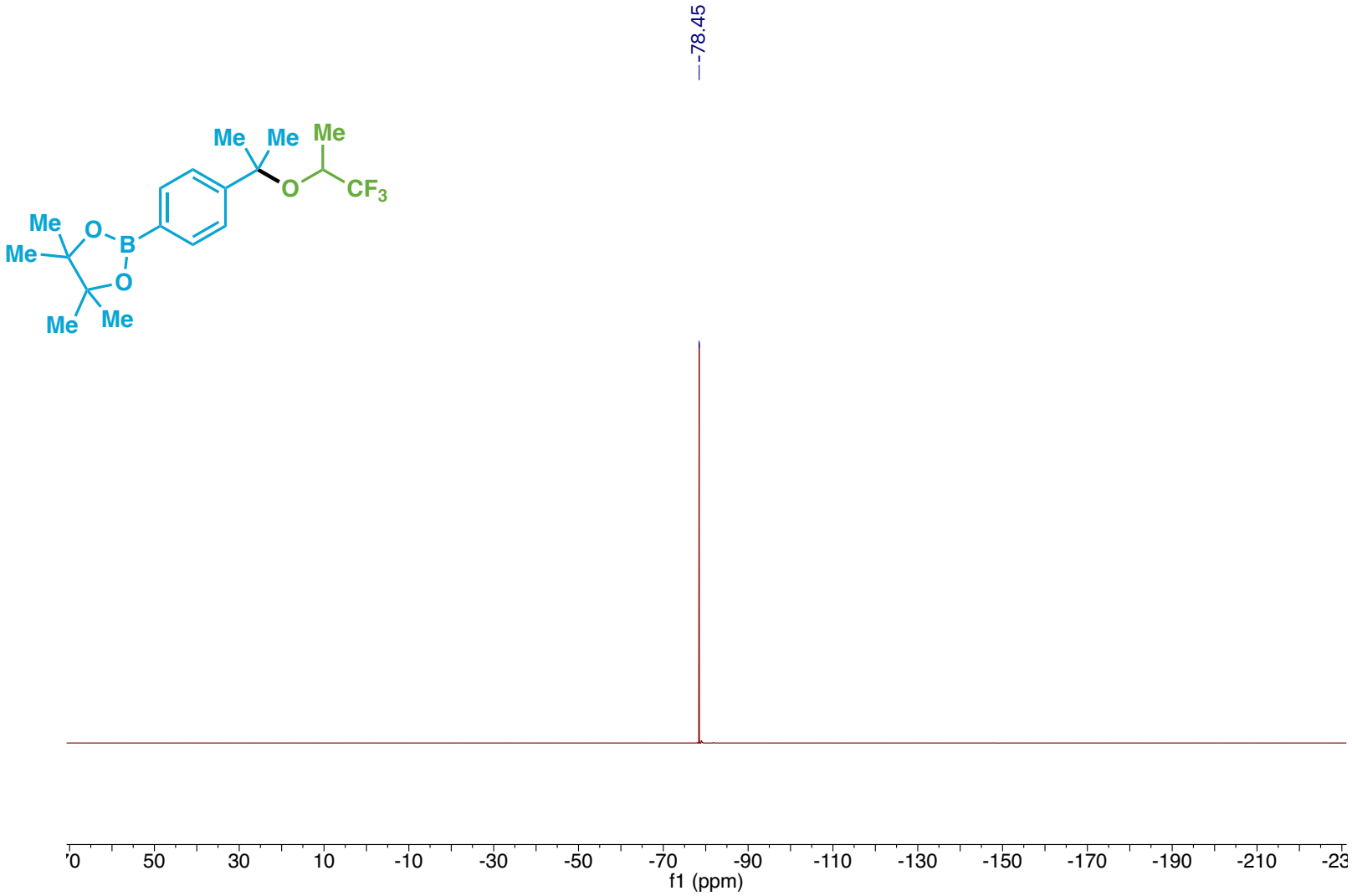
Compound 126 ^{13}C NMR



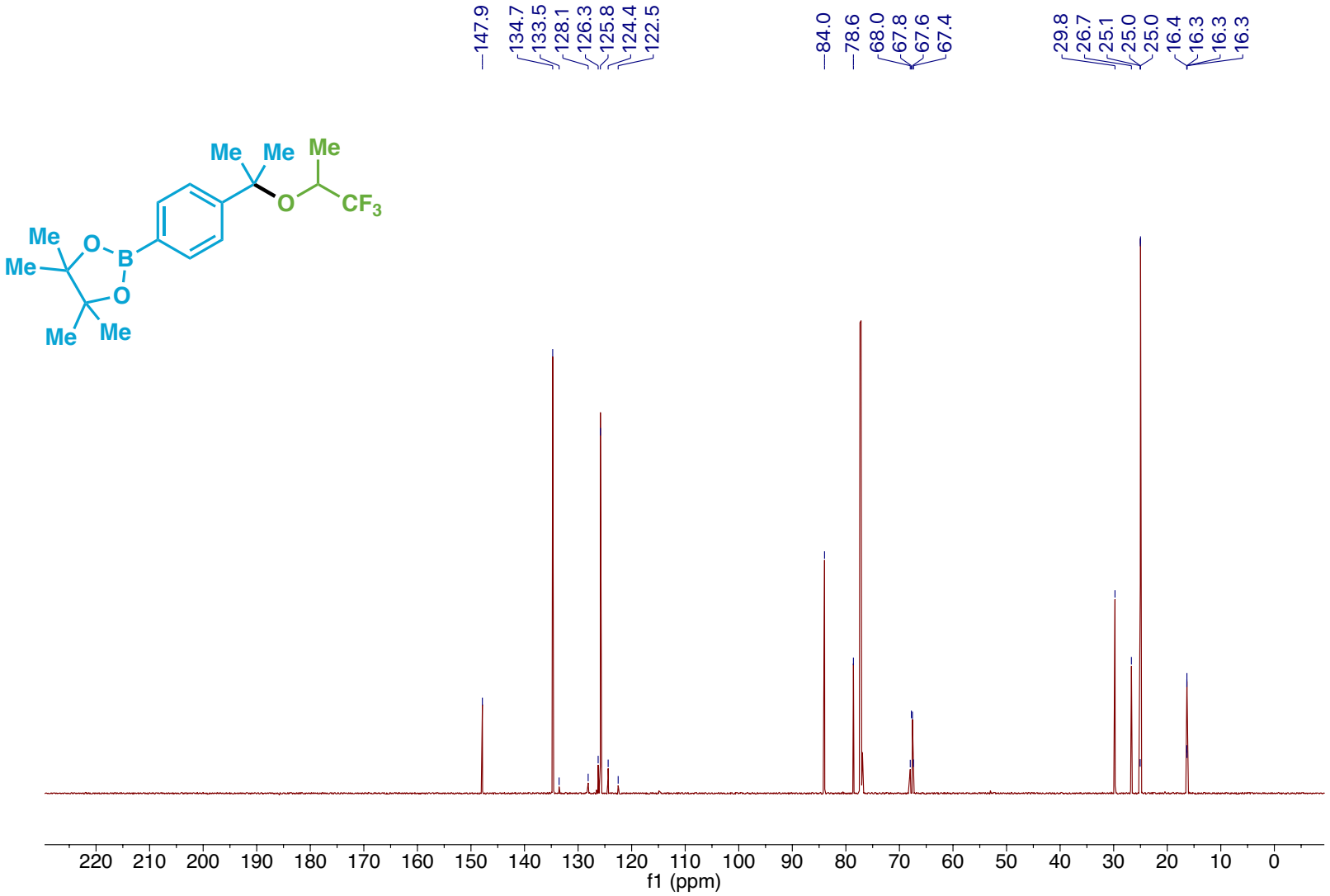
Compound 127 ^{1}H NMR



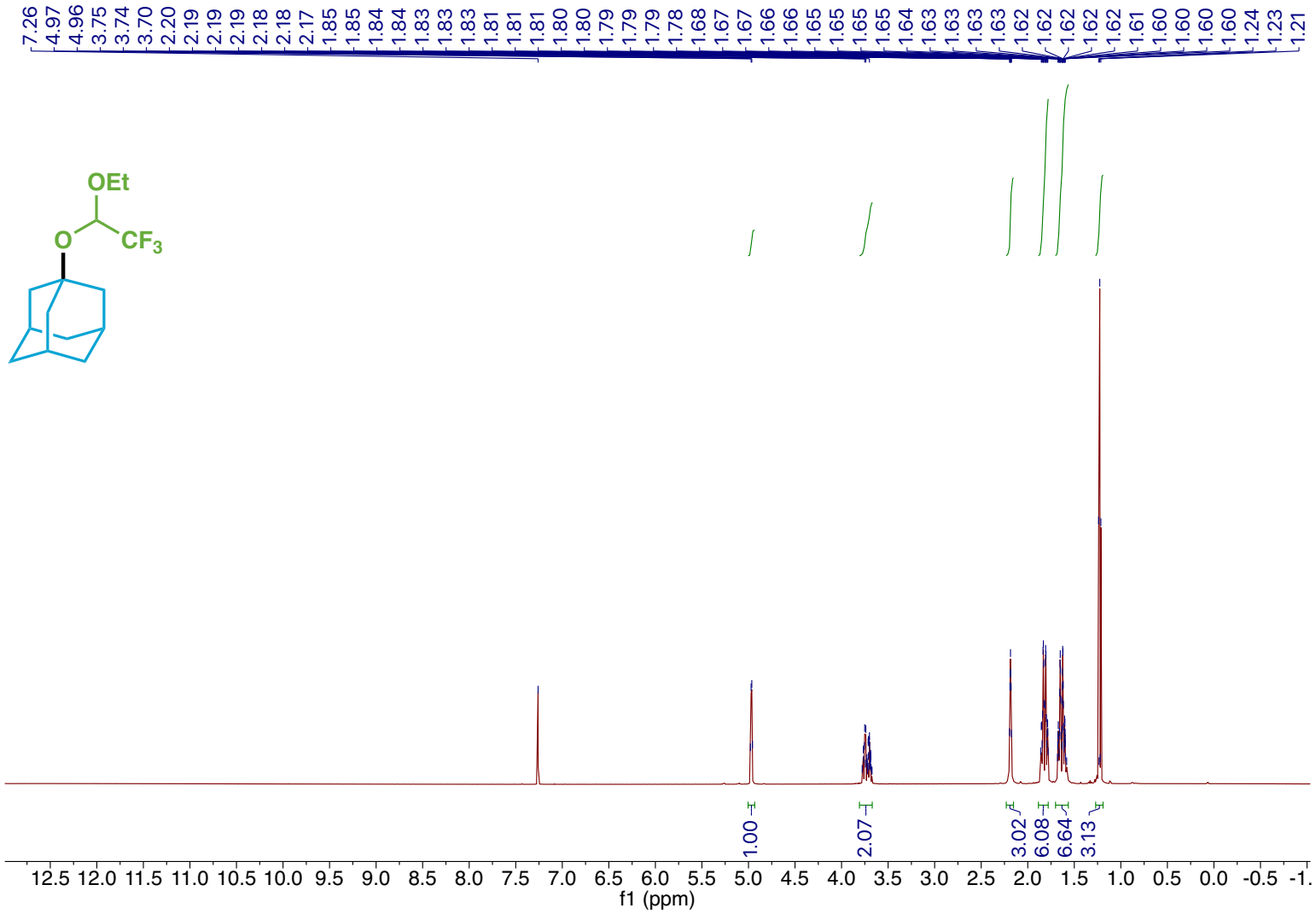
Compound 127 ^{19}F NMR



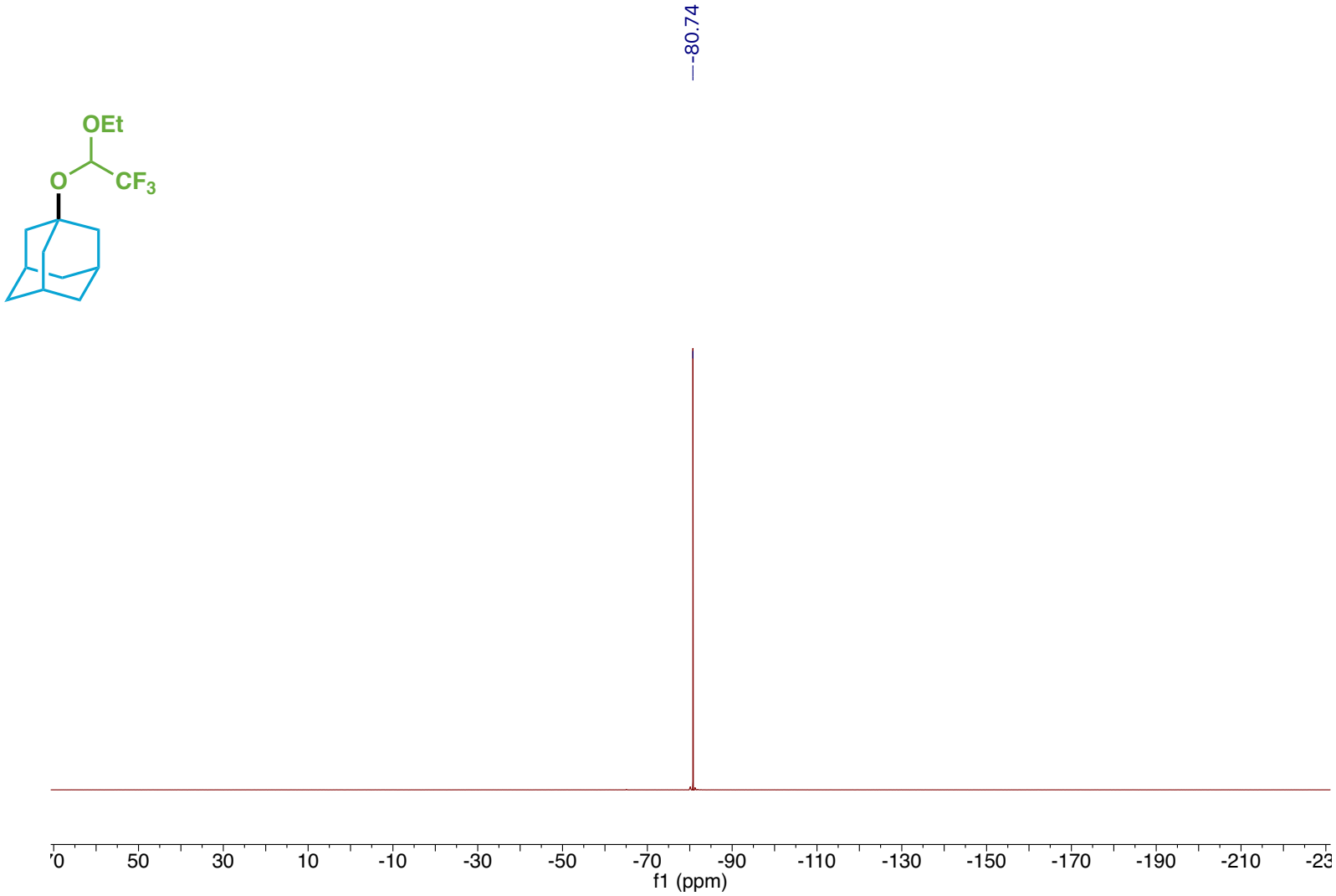
Compound 127 ^{13}C NMR



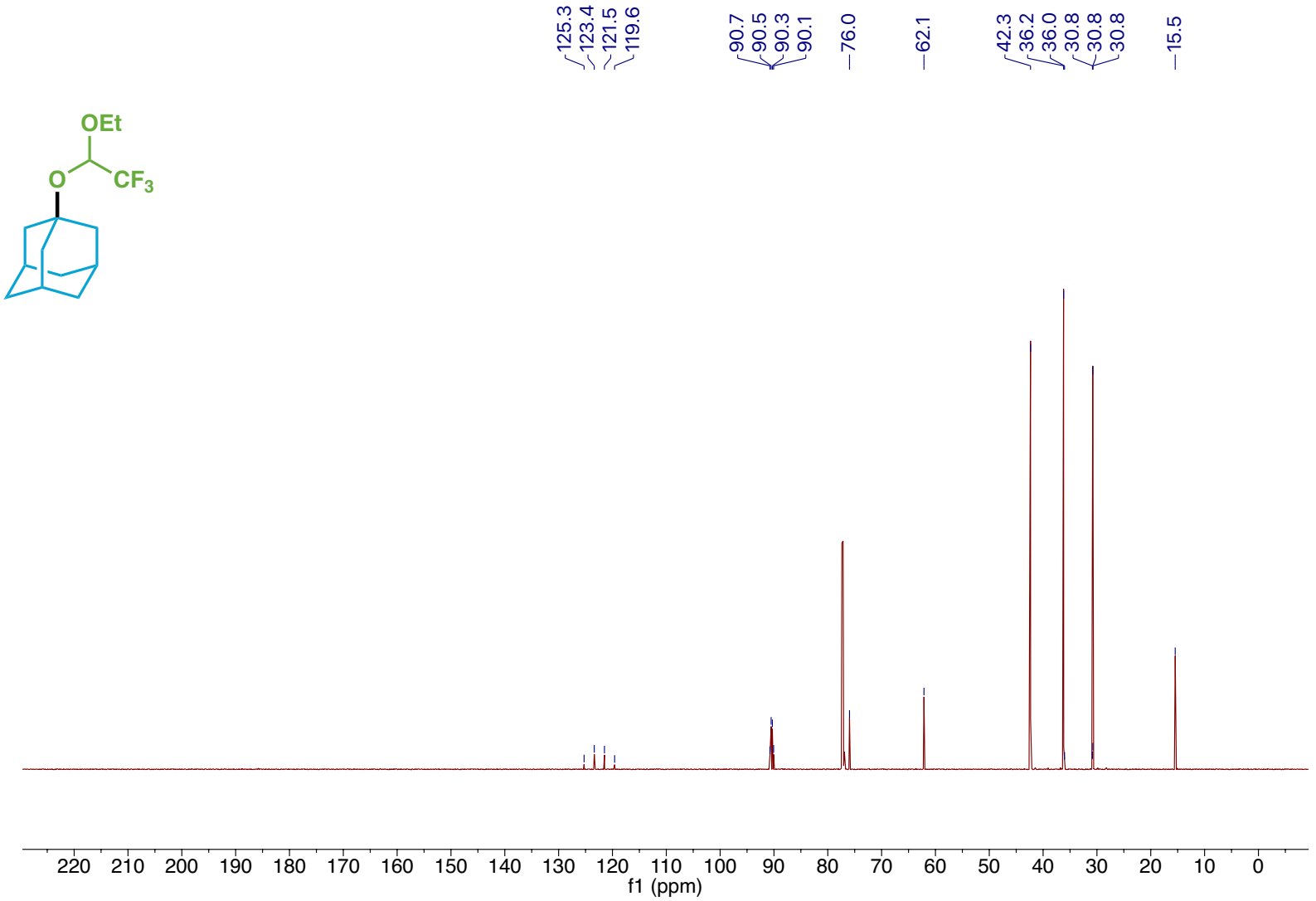
Compound 128 ^{1}H NMR



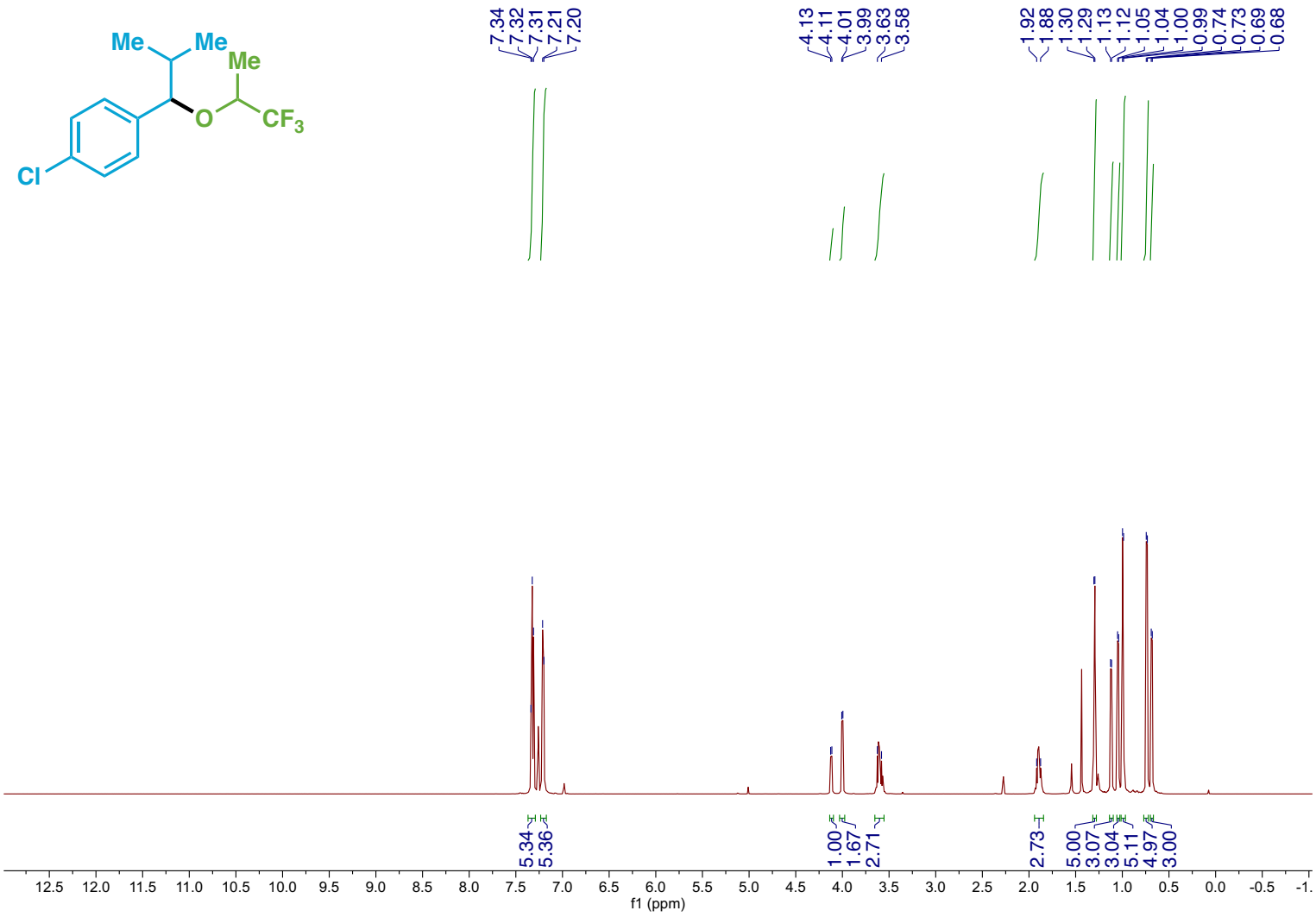
Compound 128 ^{19}F NMR



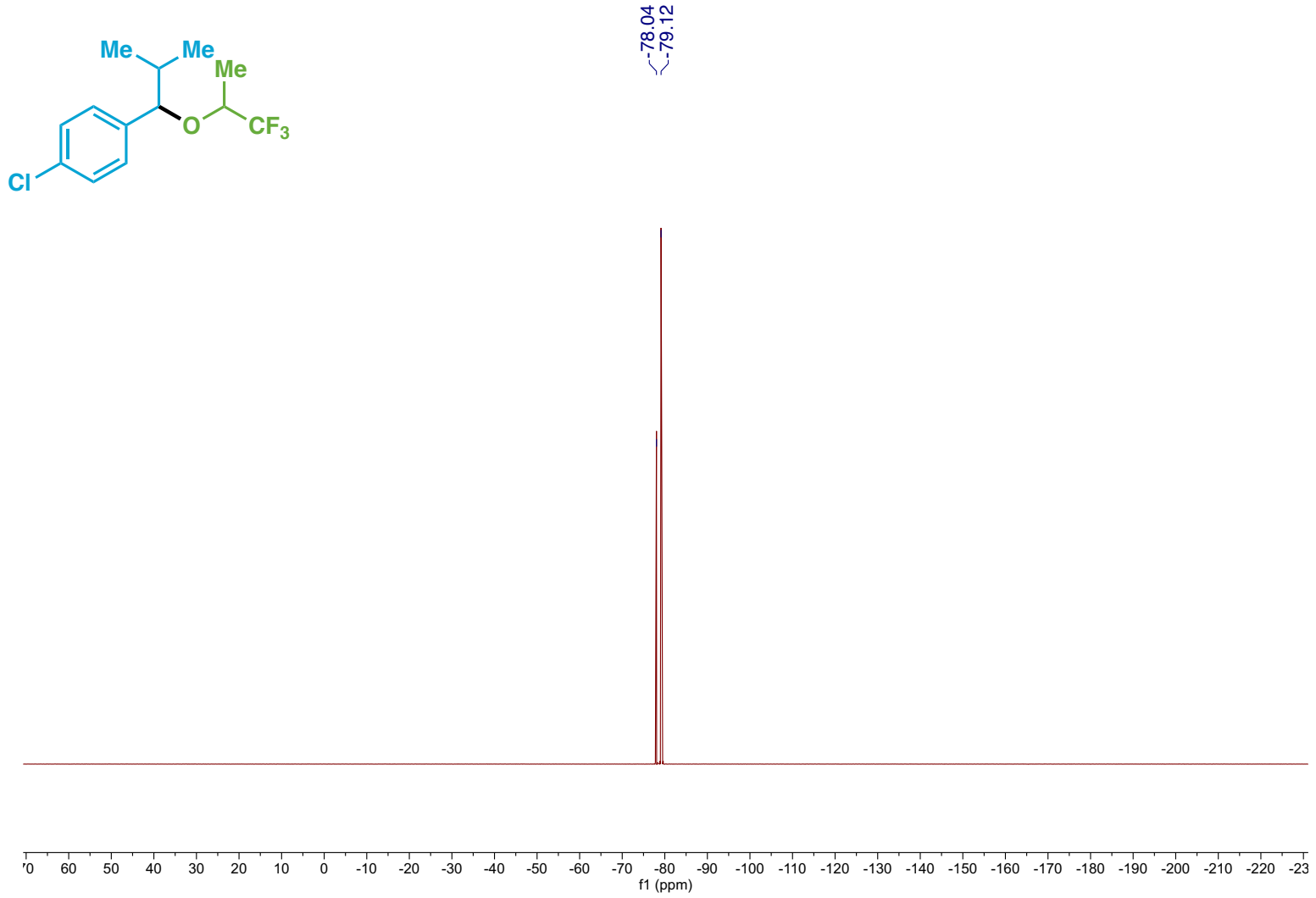
Compound 128 ^{13}C NMR



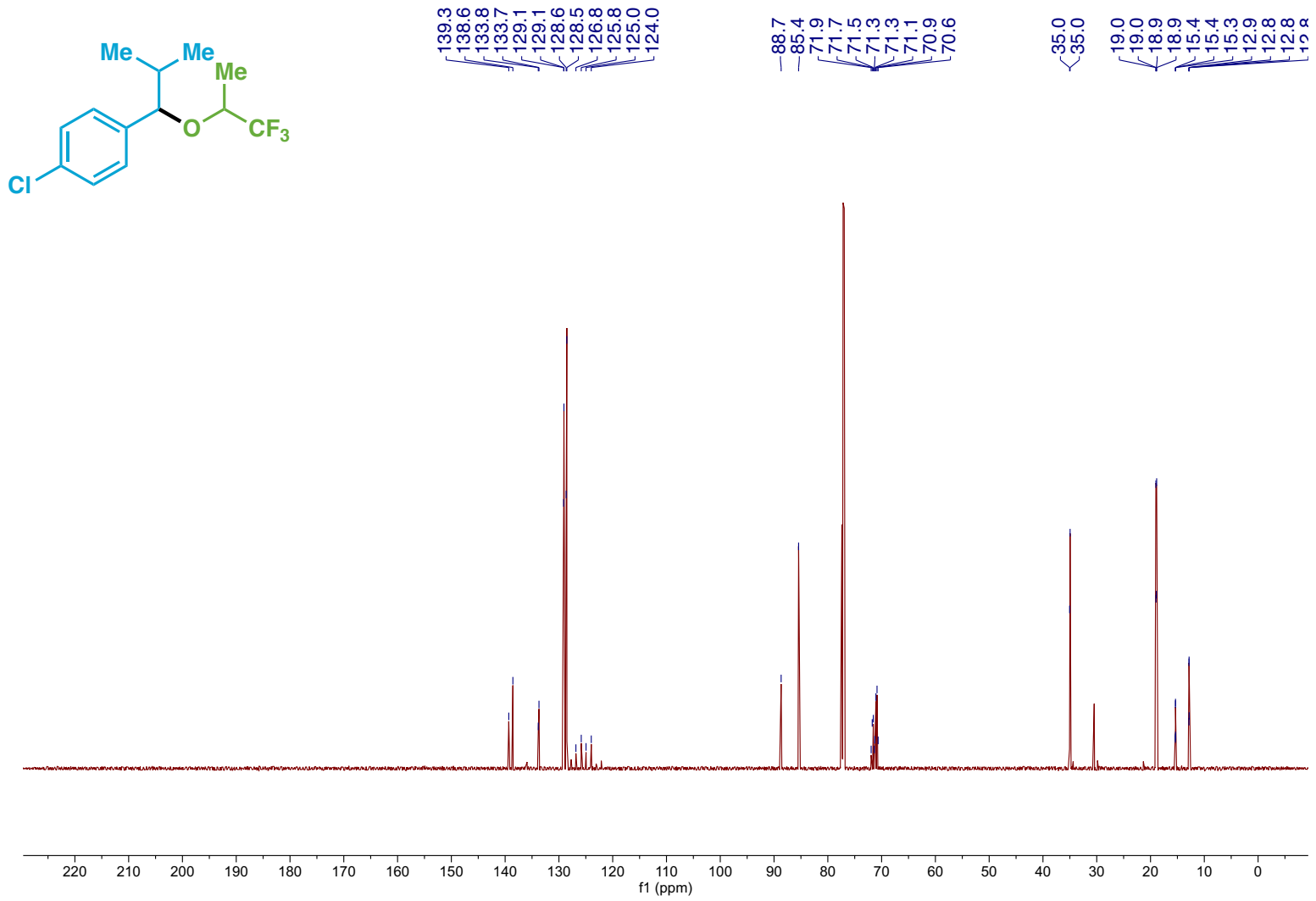
Compound 129 ^{1}H NMR



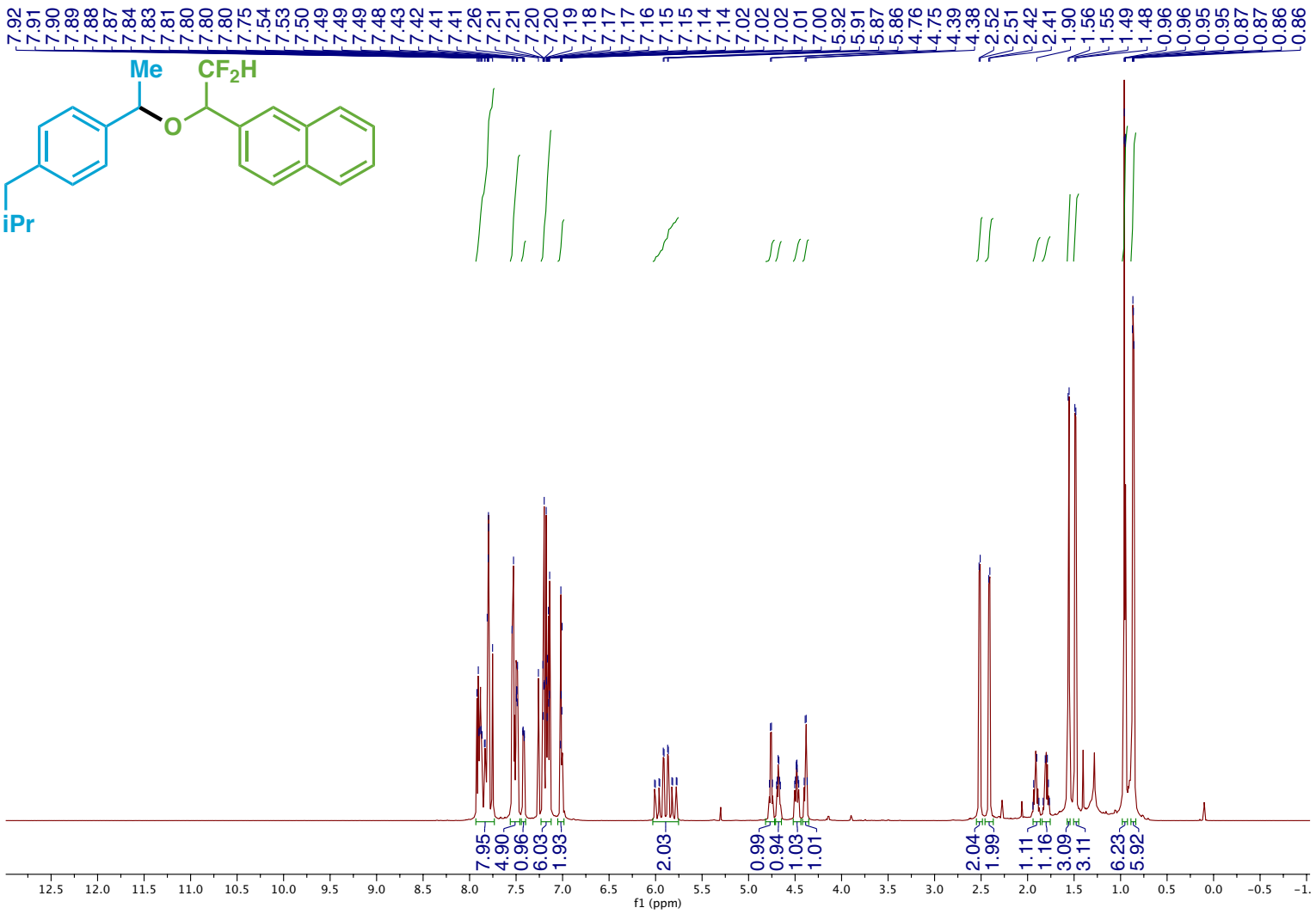
Compound 129 ^{19}F NMR



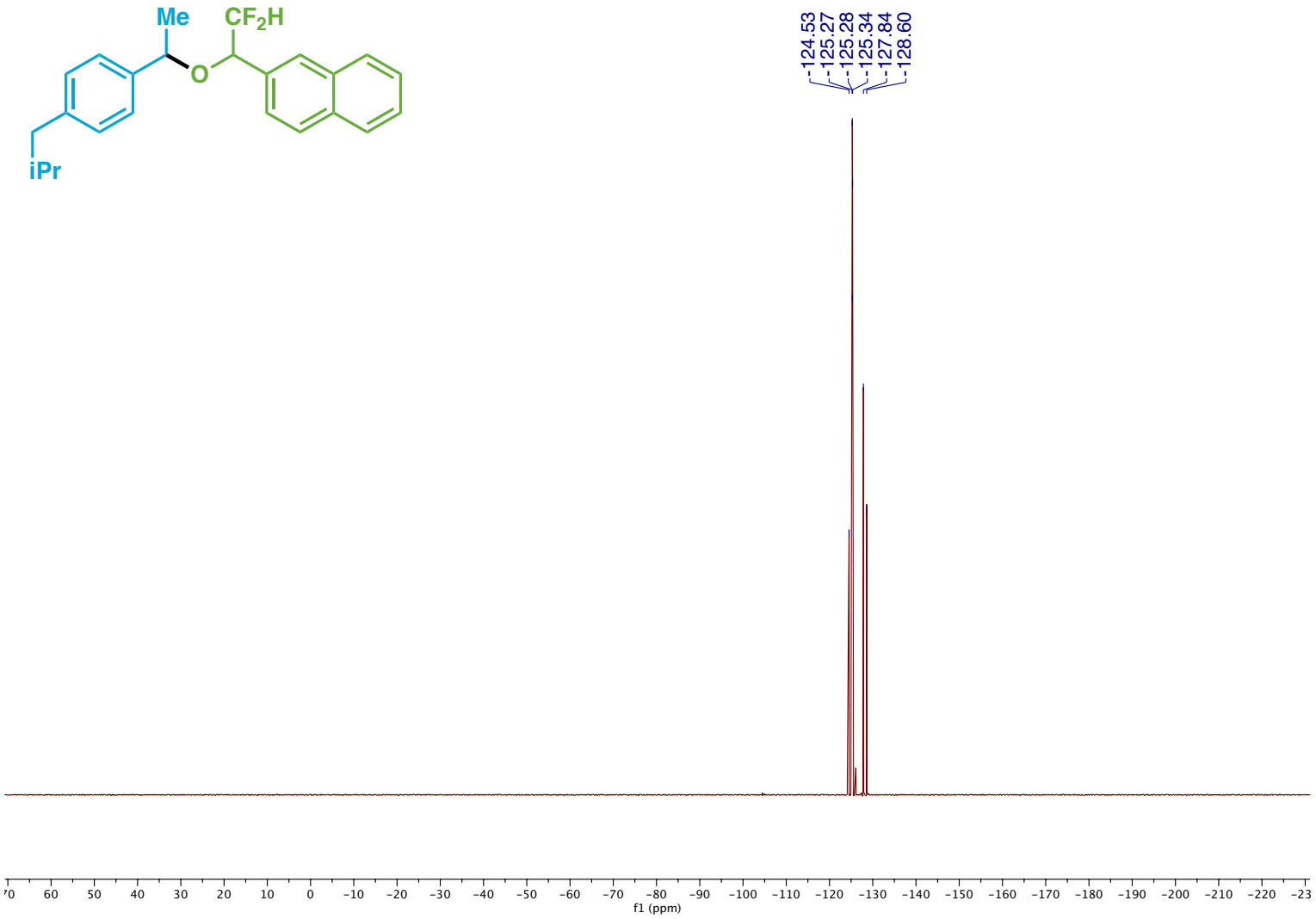
Compound 129 ^{13}C NMR



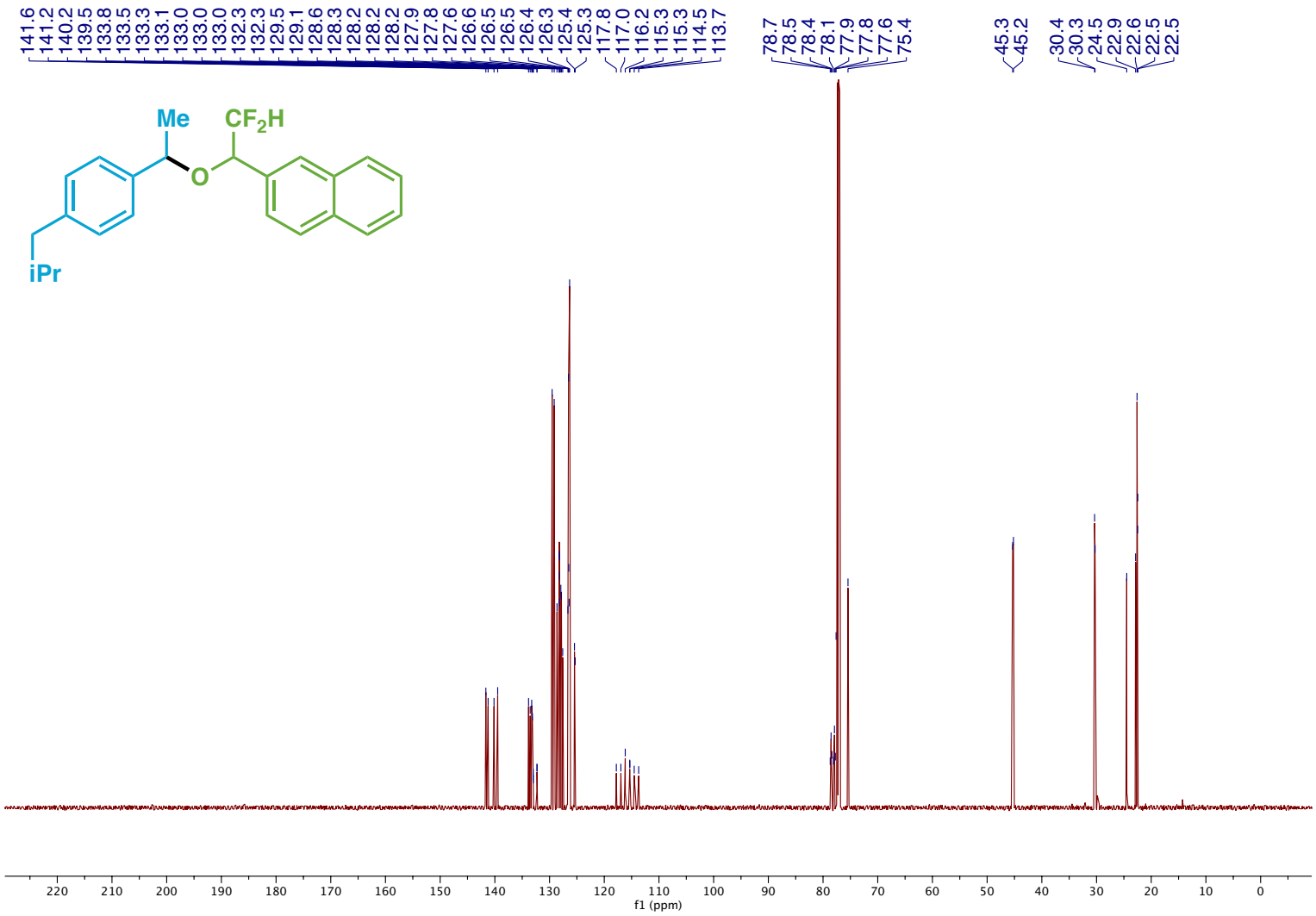
Compound 130 ^{1}H NMR



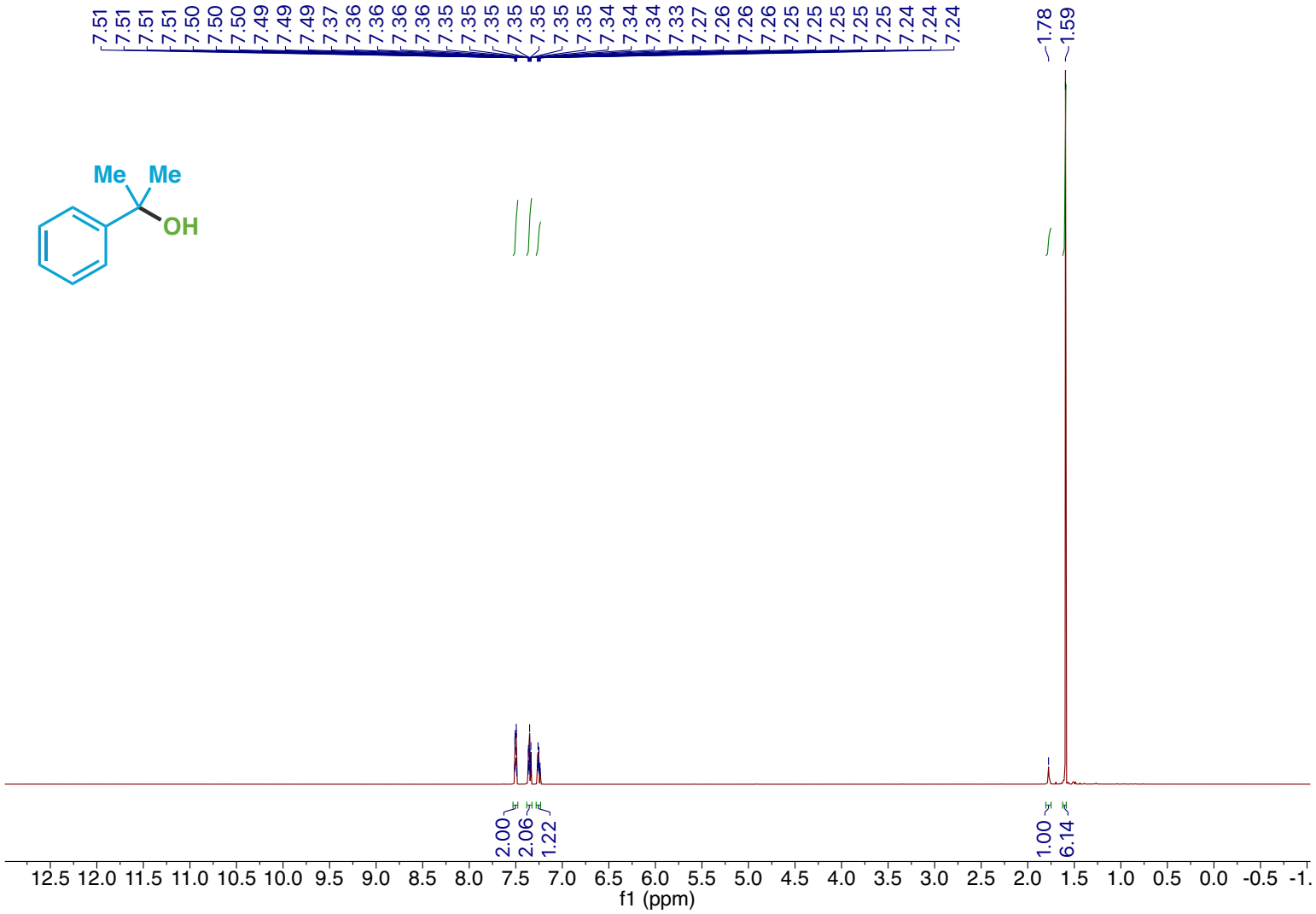
Compound 130 ^{19}F NMR



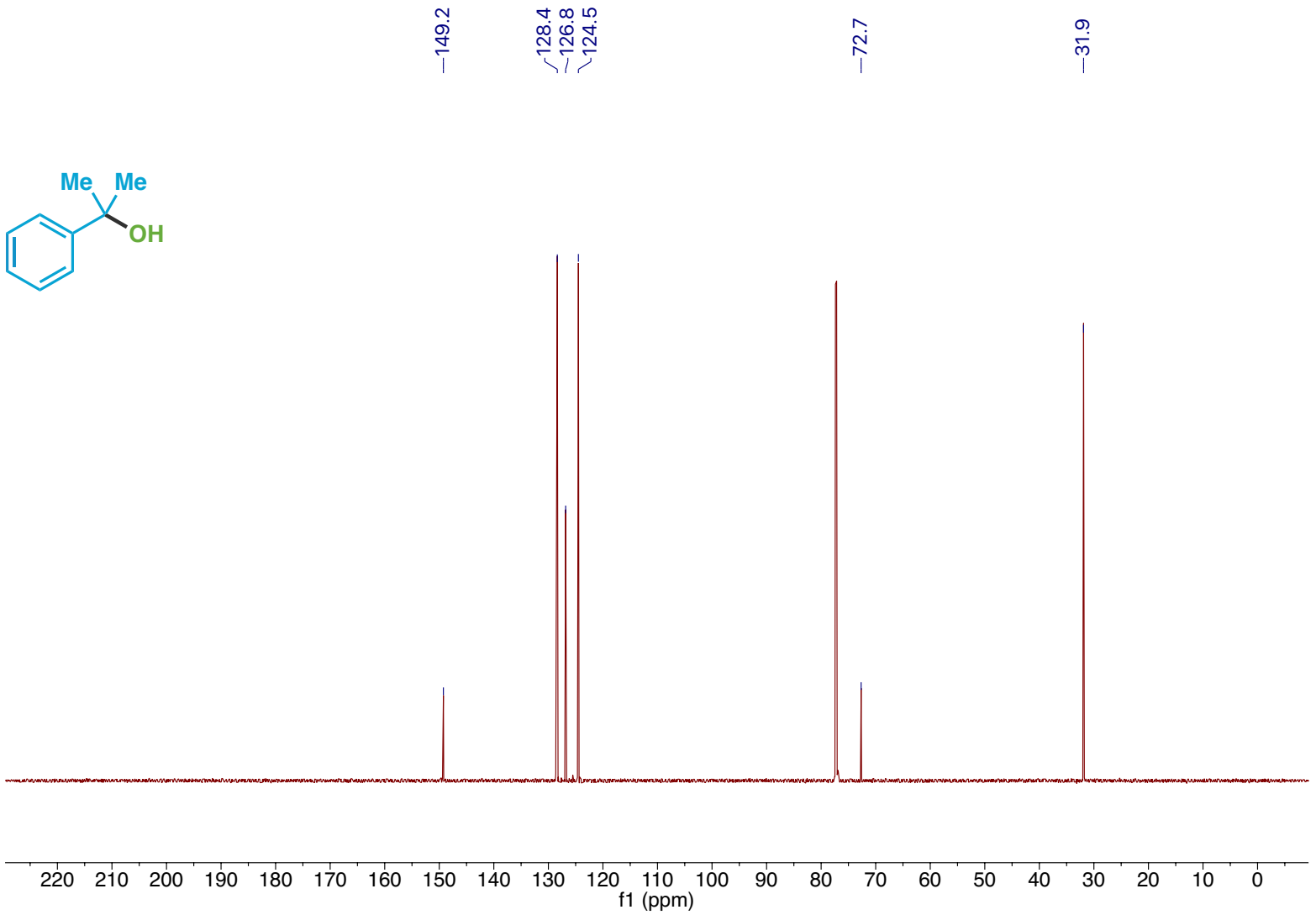
Compound 130 ^{13}C NMR



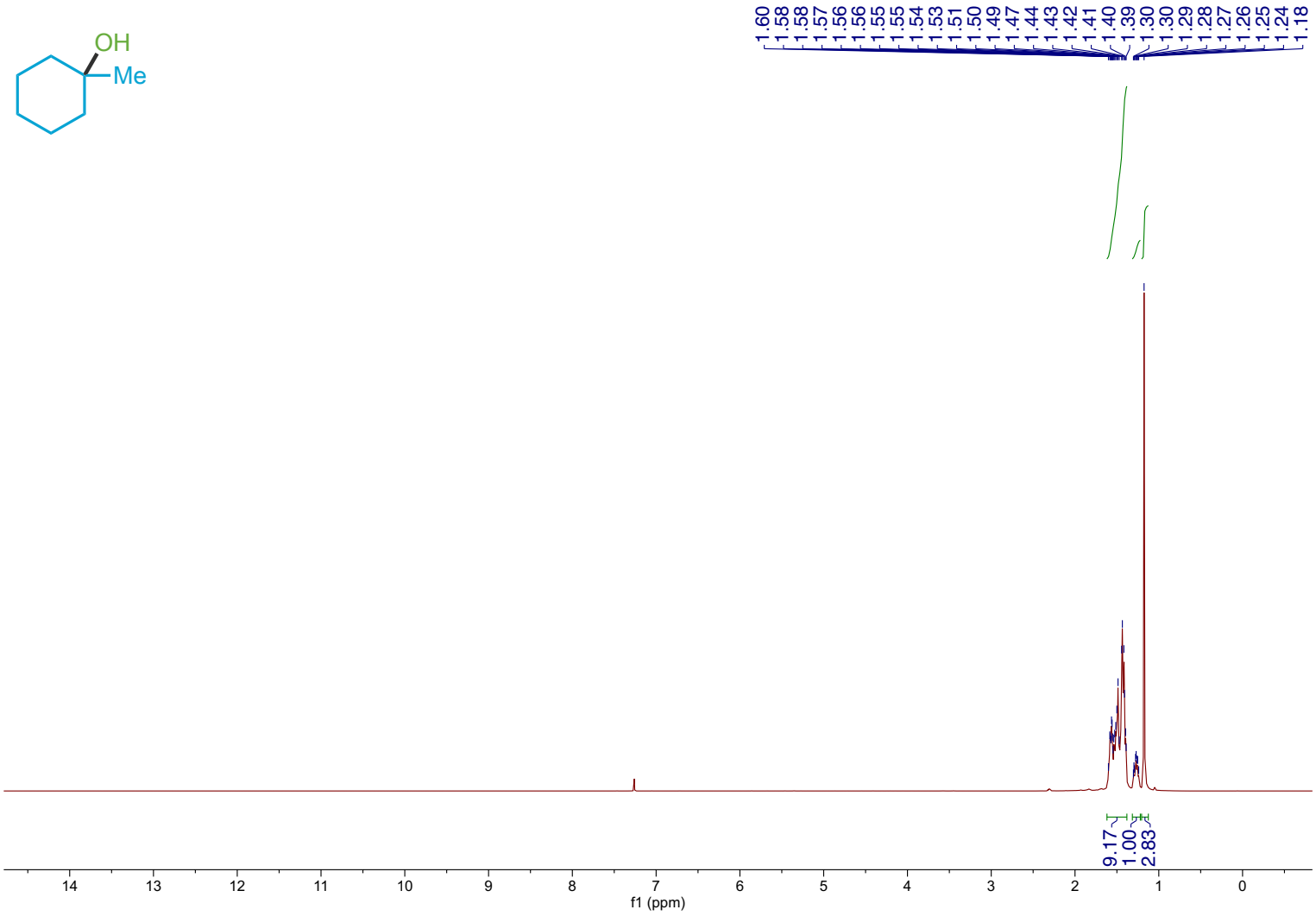
Compound 132 ^{1}H NMR



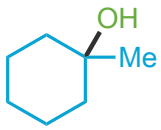
Compound 132 ^{13}C NMR



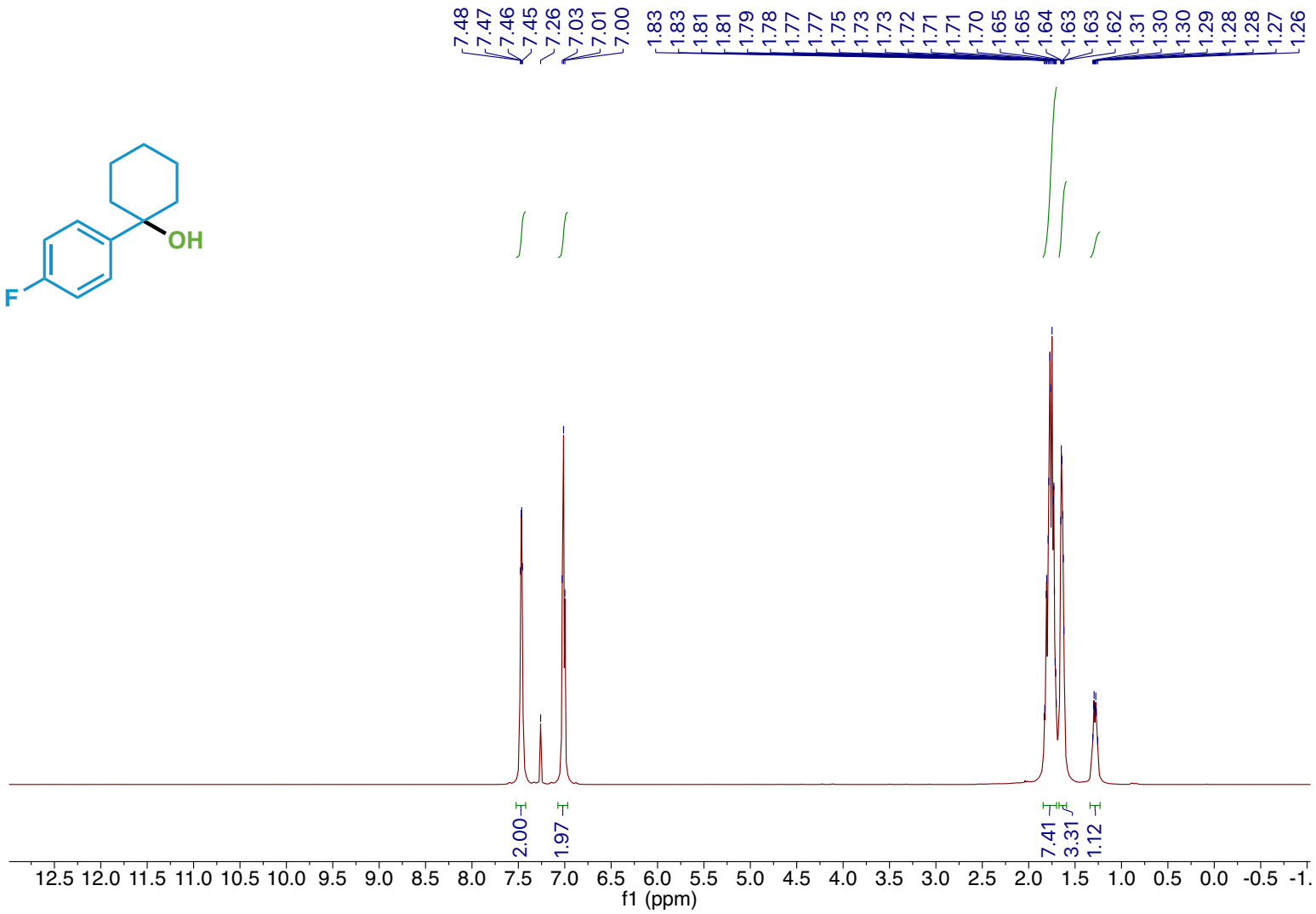
Compound 134 ^{1}H NMR



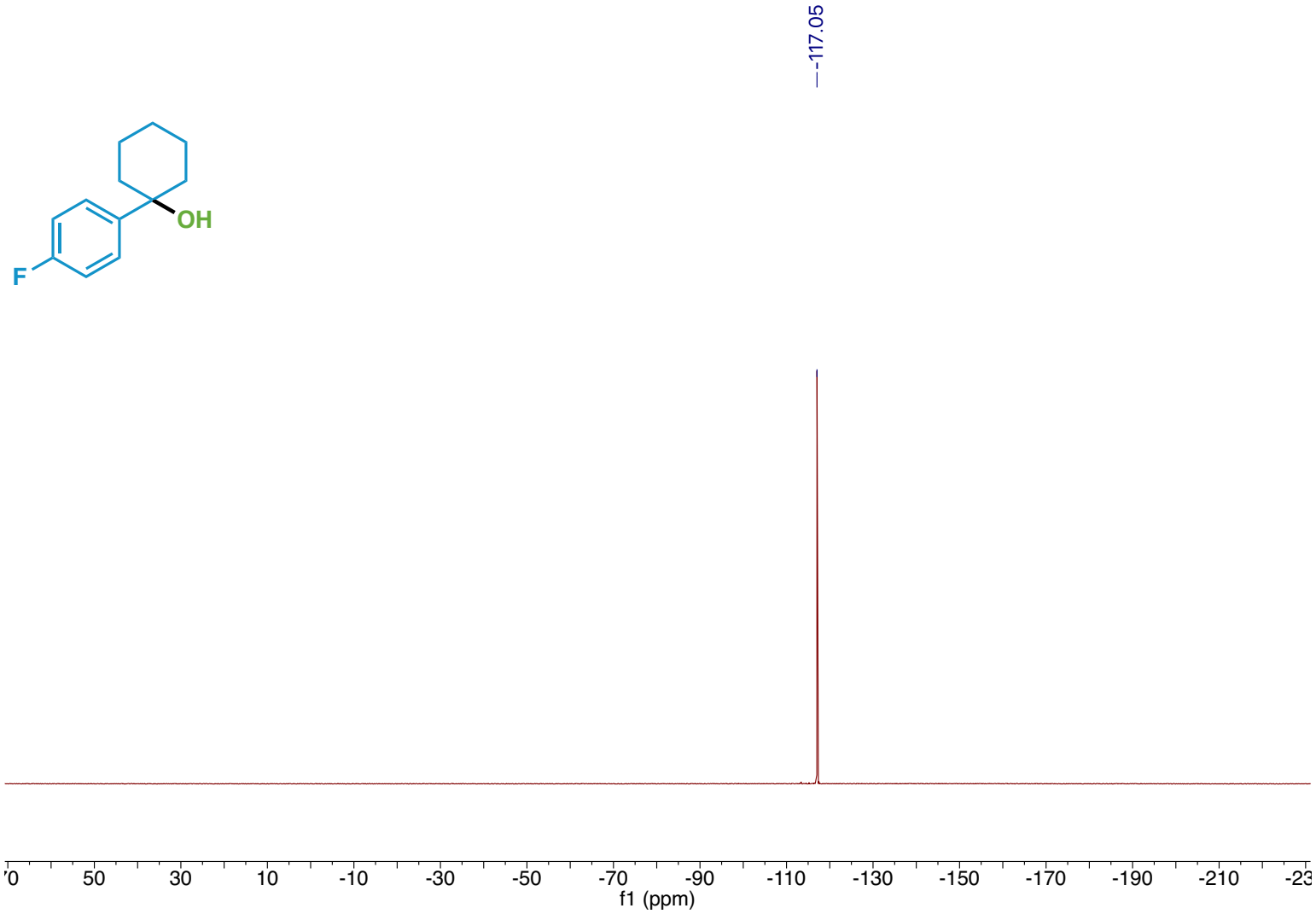
Compound 134 ^{13}C NMR



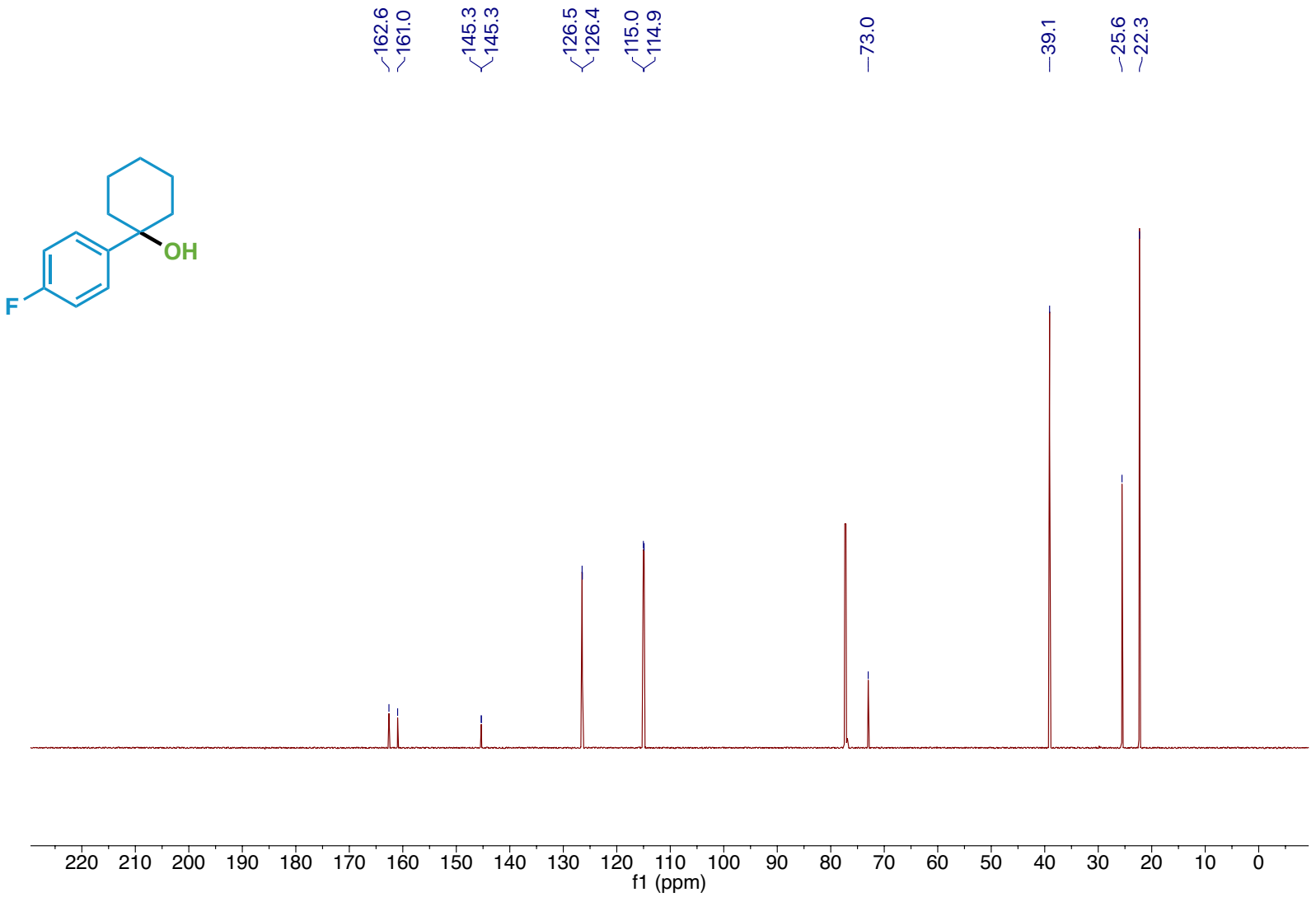
Compound 135 ^{1}H NMR



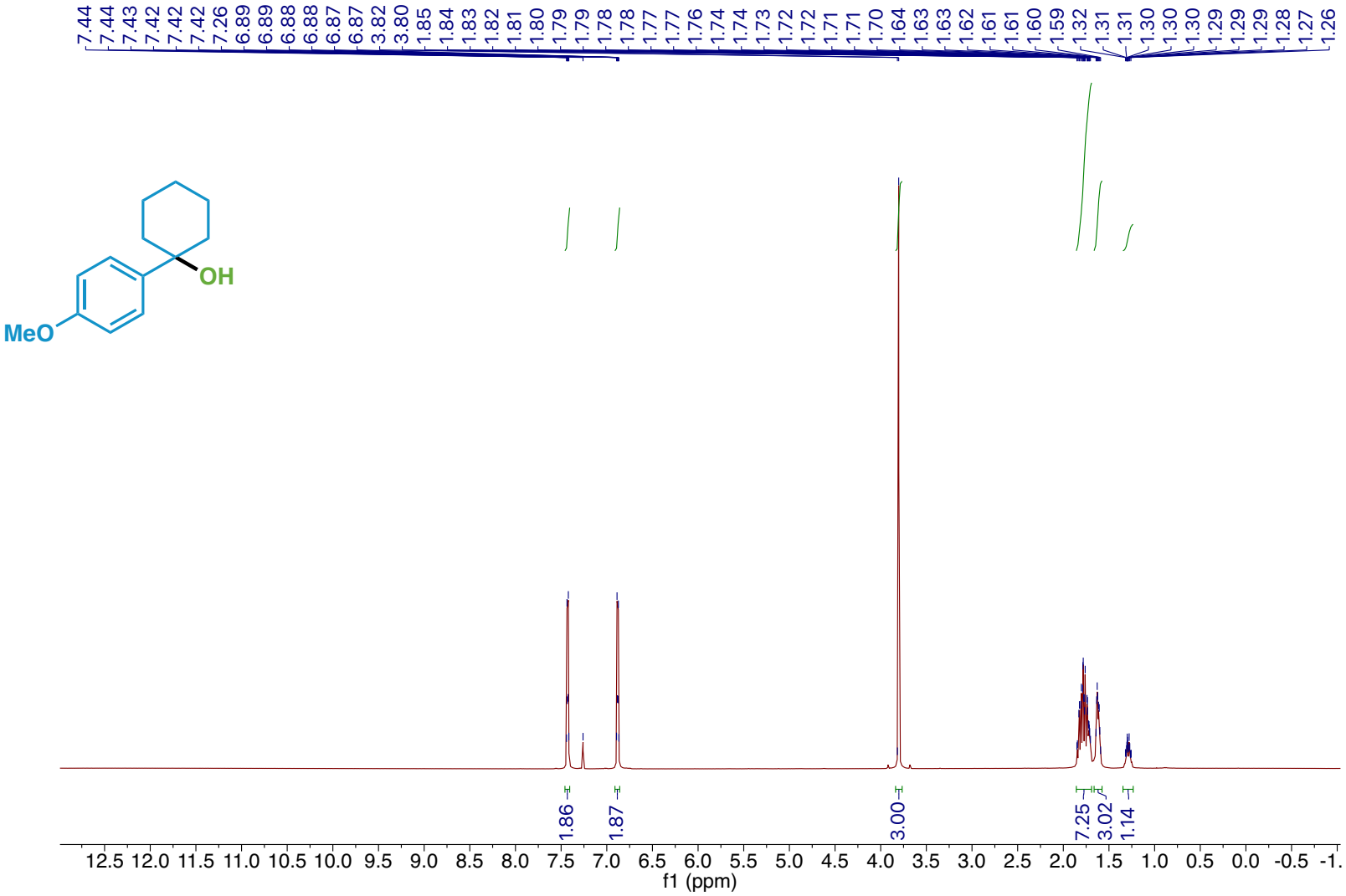
Compound 135 ^{19}F NMR



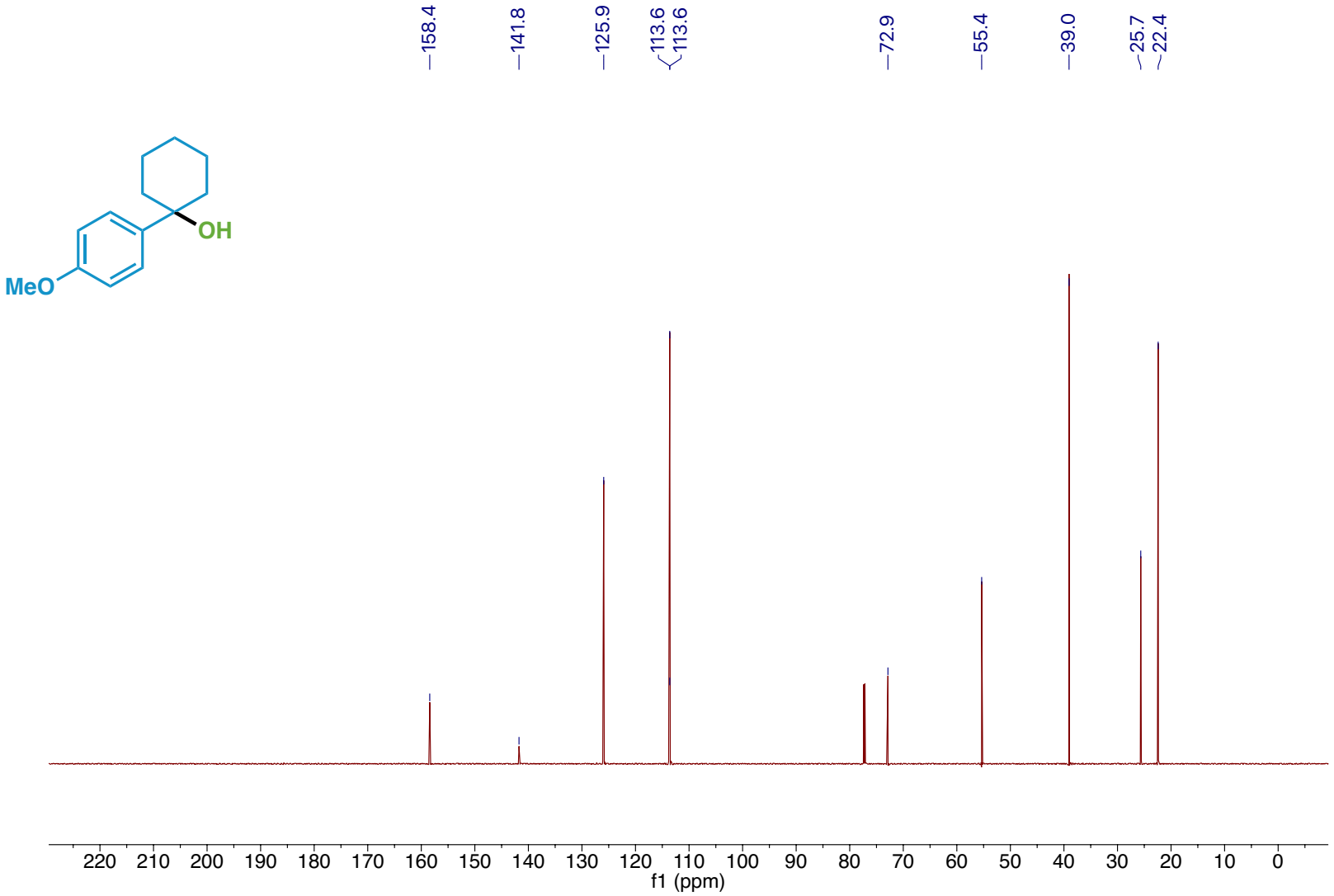
Compound 135 ^{13}C NMR



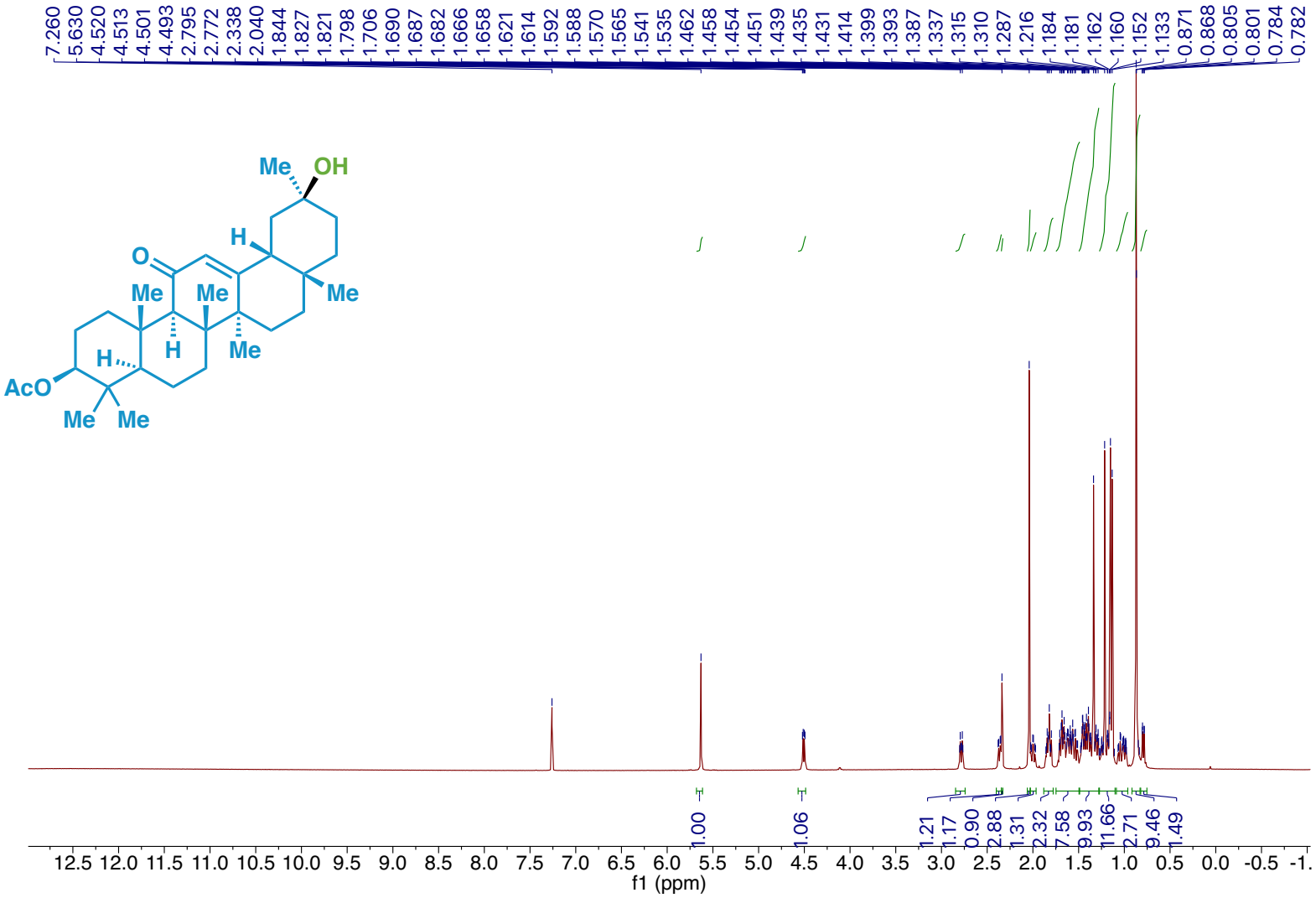
Compound 136 ^{1}H NMR



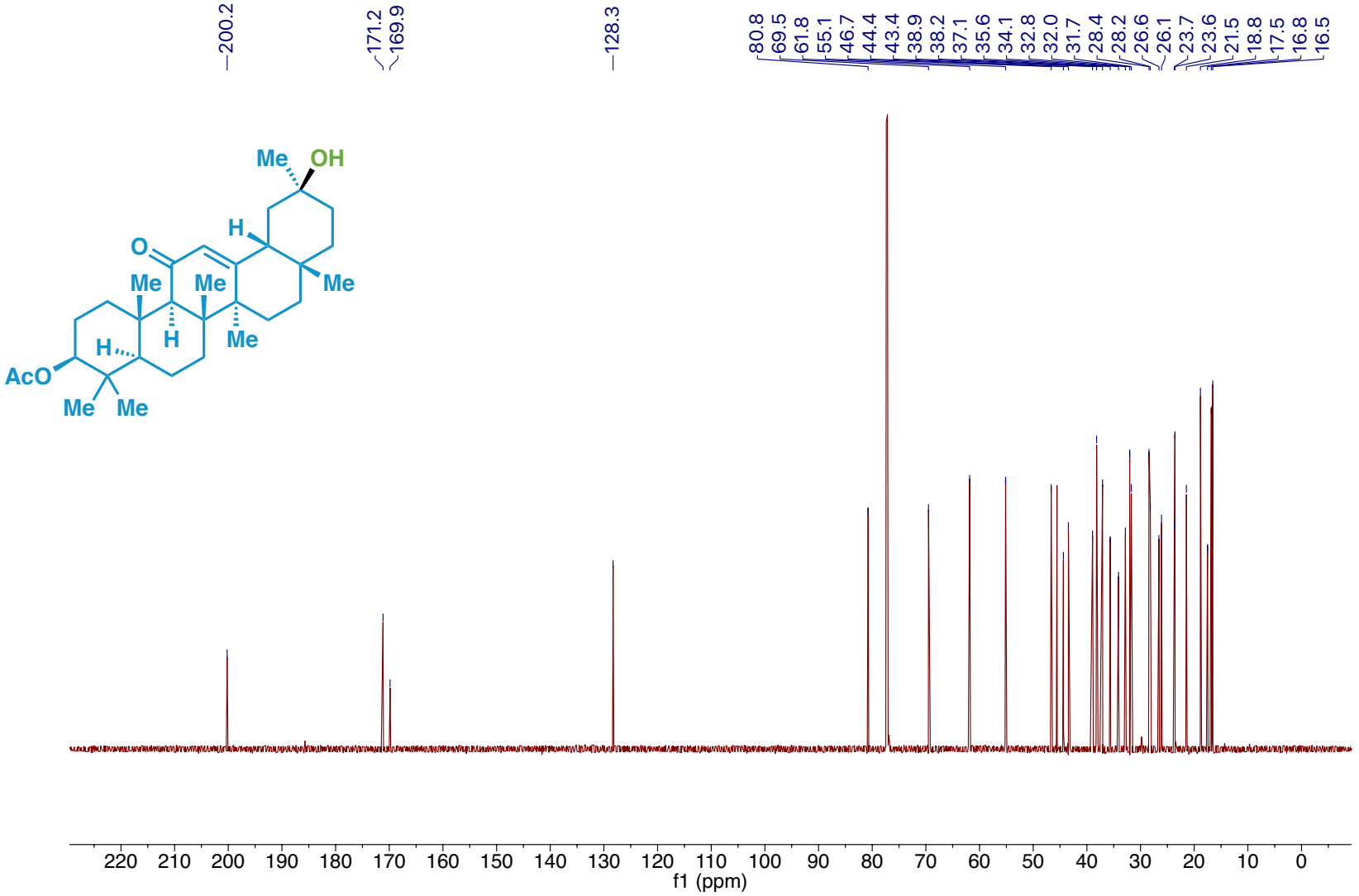
Compound 136 ^{13}C NMR



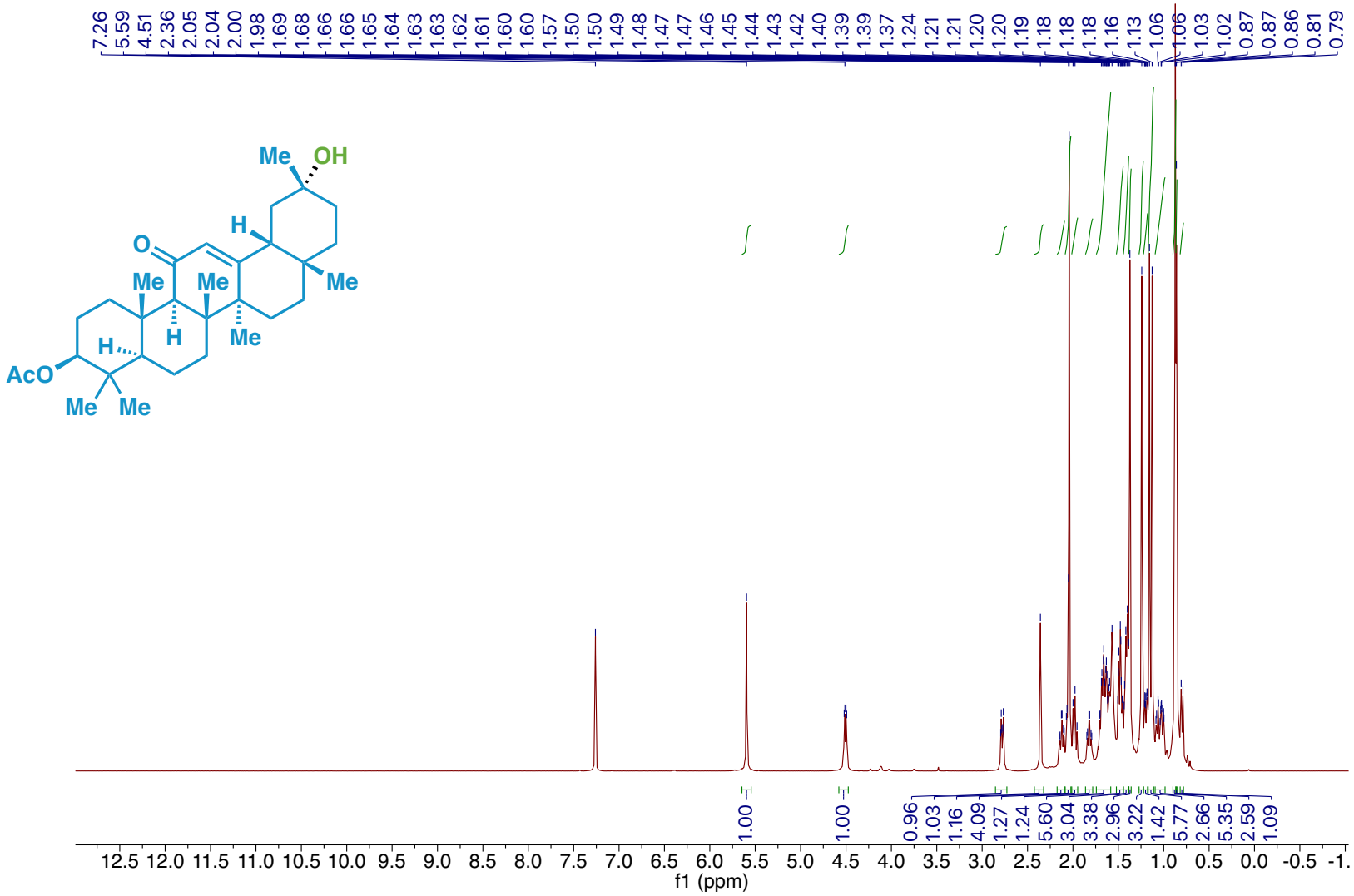
Compound (11*S*)-138 ^{1}H NMR



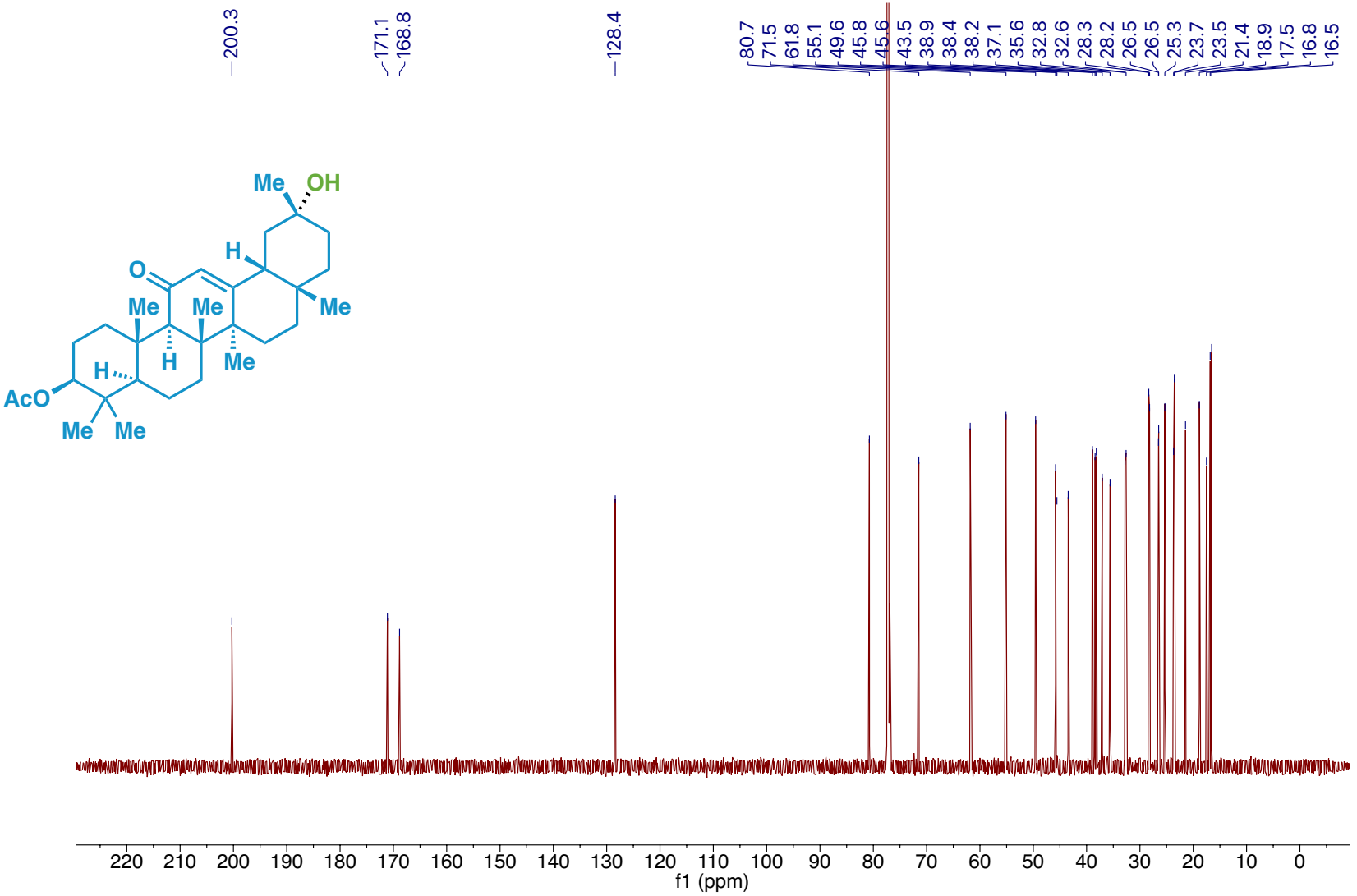
Compound (11*S*)-138 ^{13}C NMR



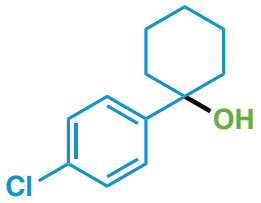
Compound (11*R*)-138 ^{1}H NMR

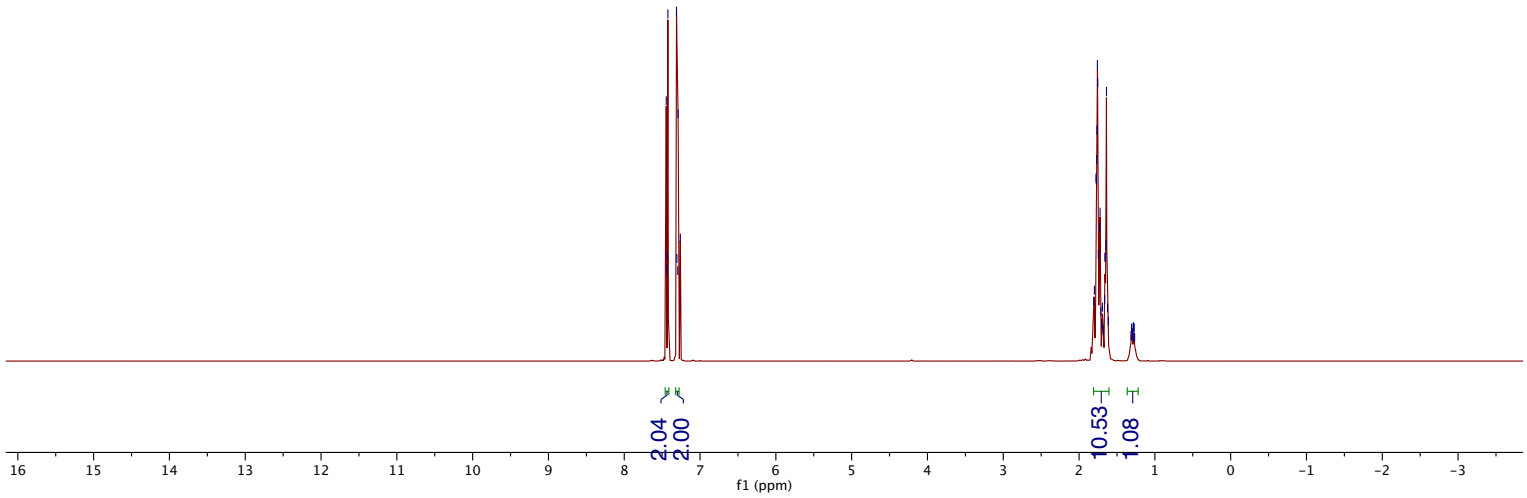


Compound (11*R*)-138 ^{13}C NMR

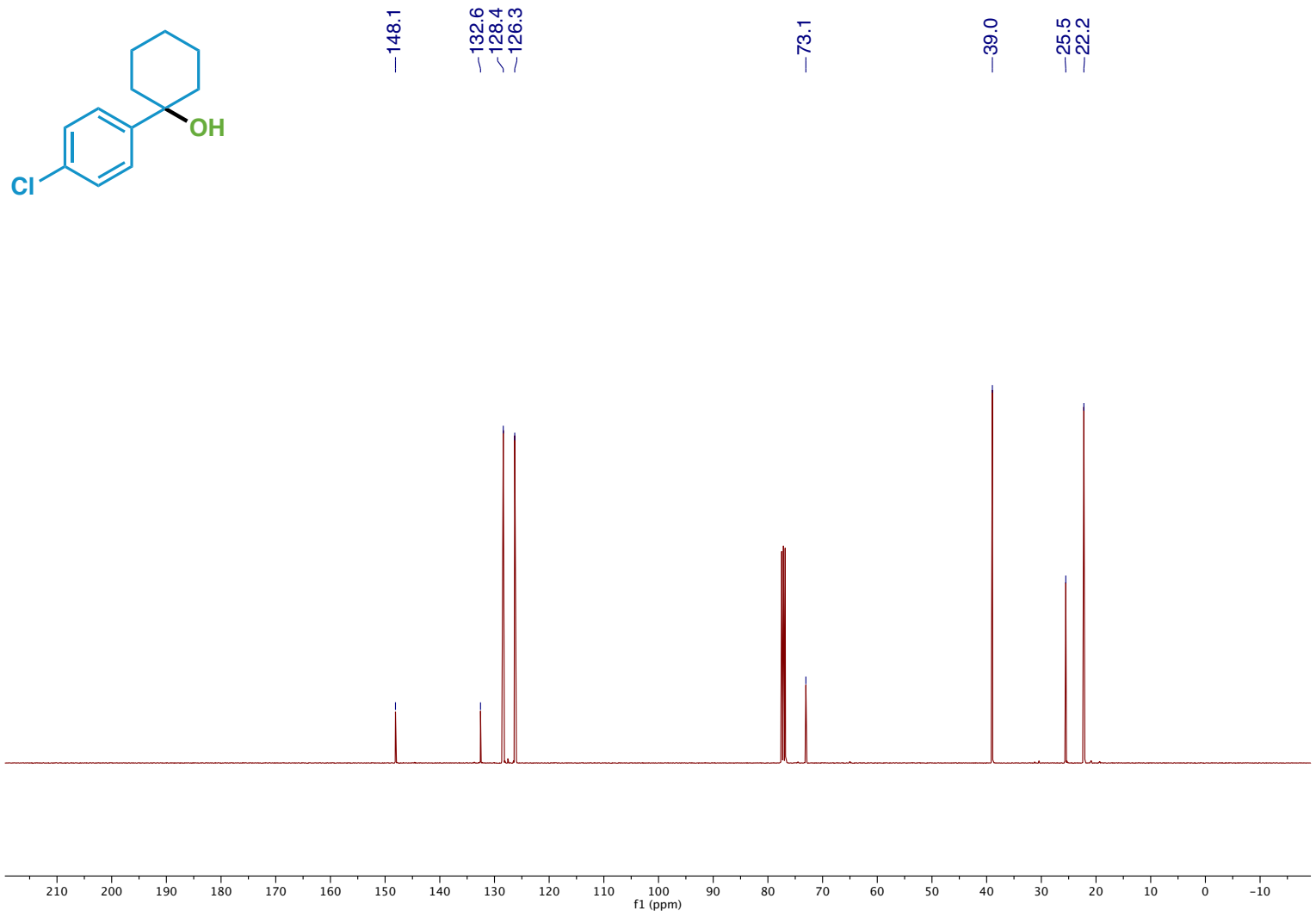


Compound 139 ^{1}H NMR

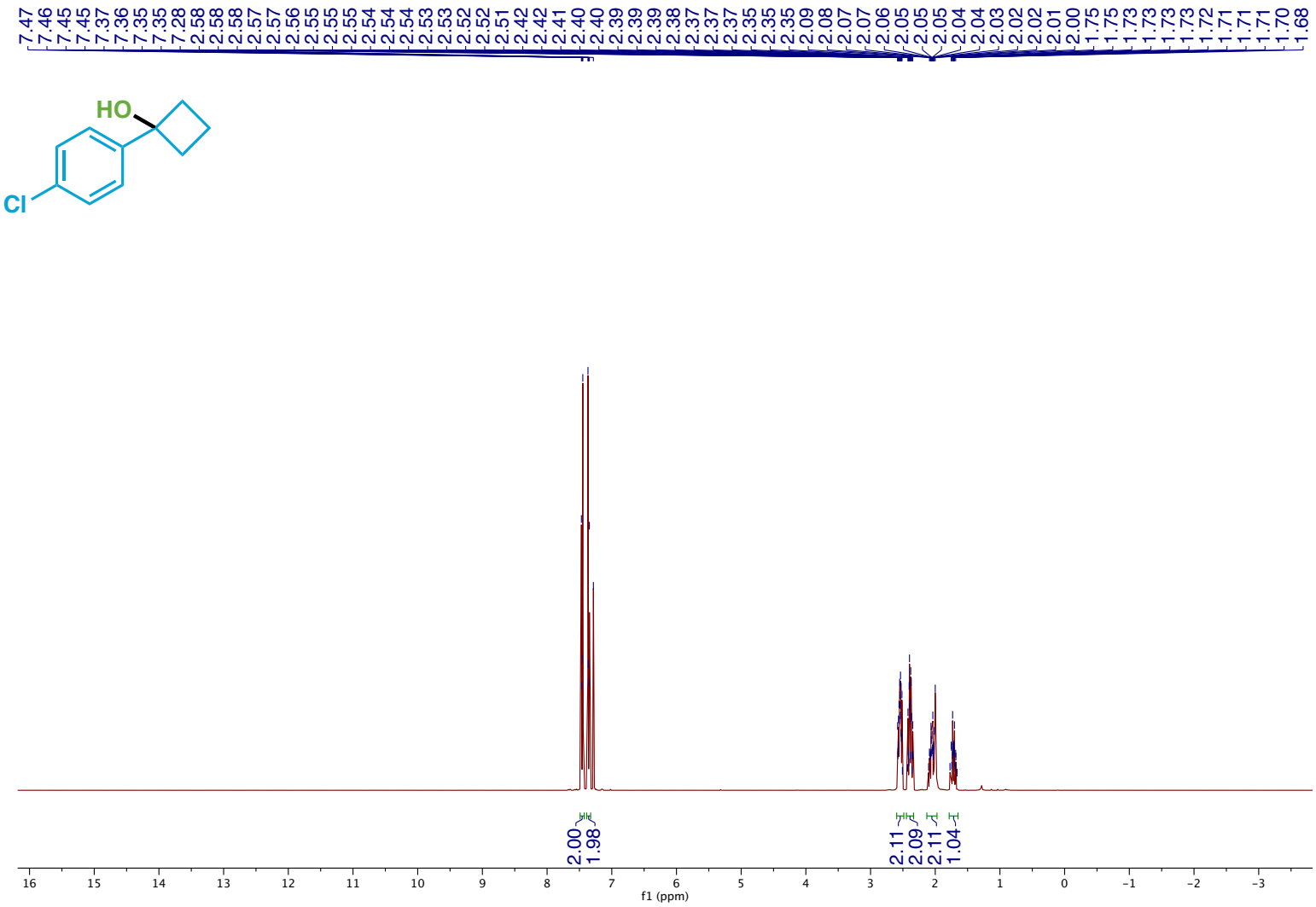




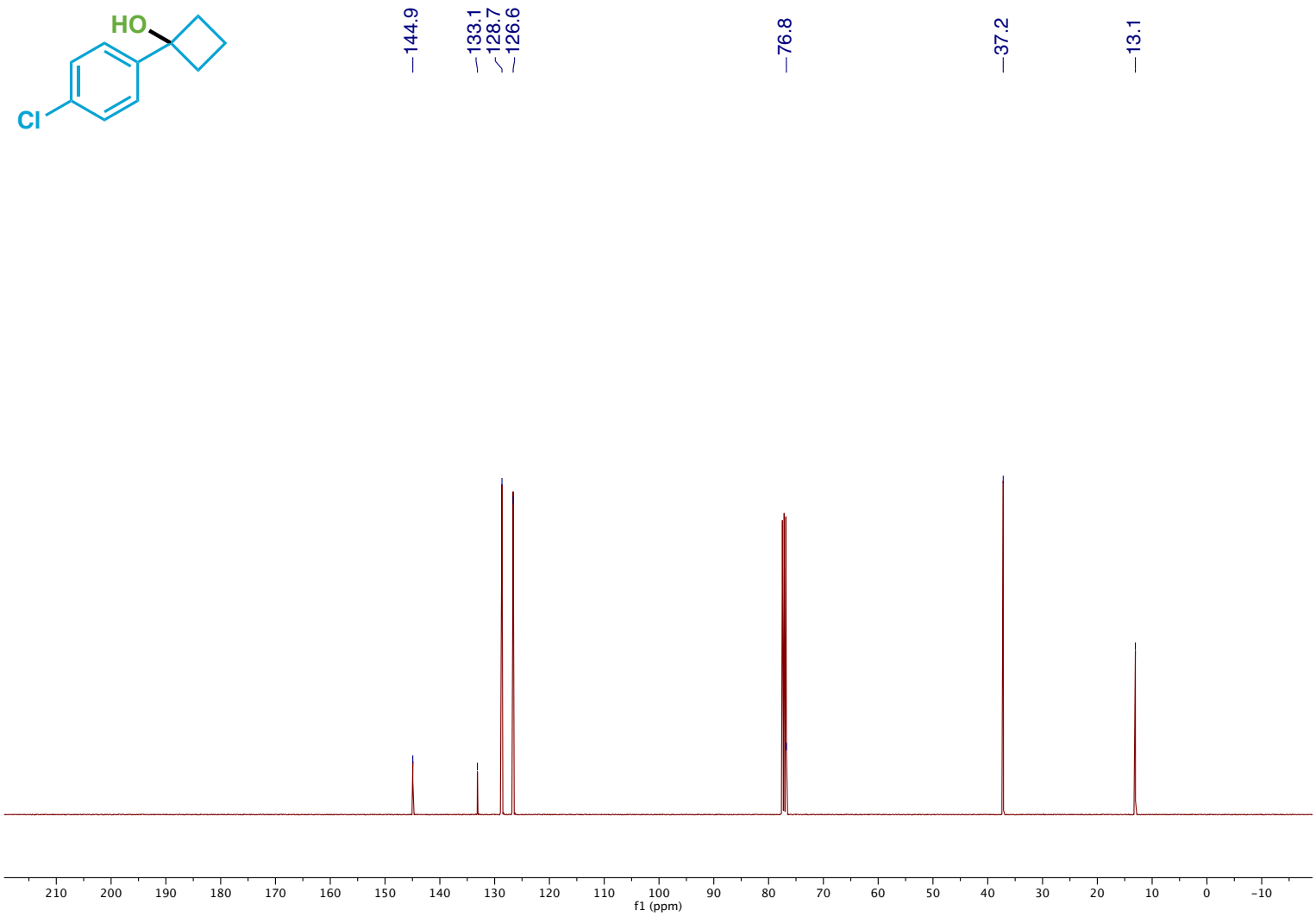
Compound 139 ^{13}C NMR



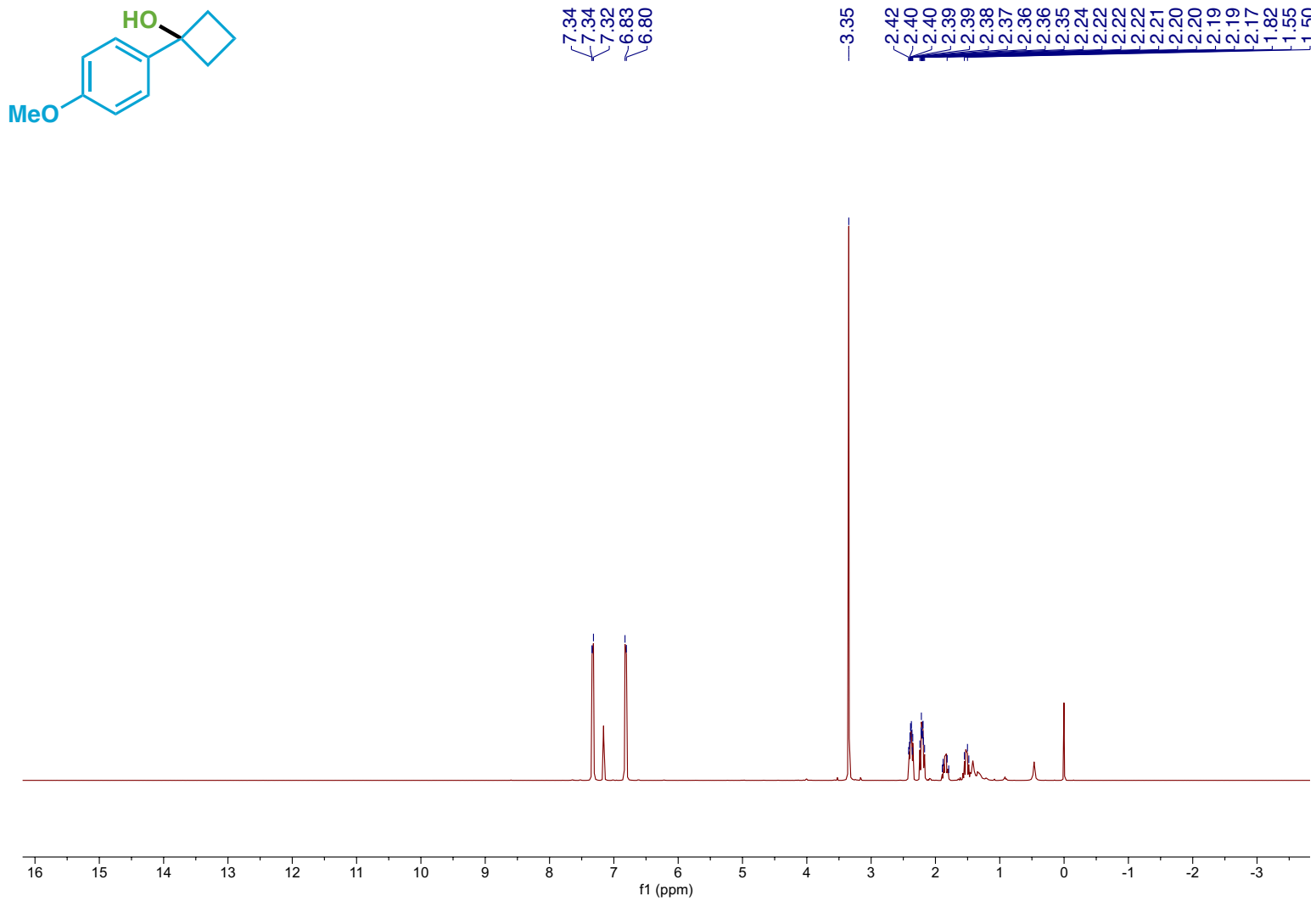
Compound 140 ^{1}H NMR



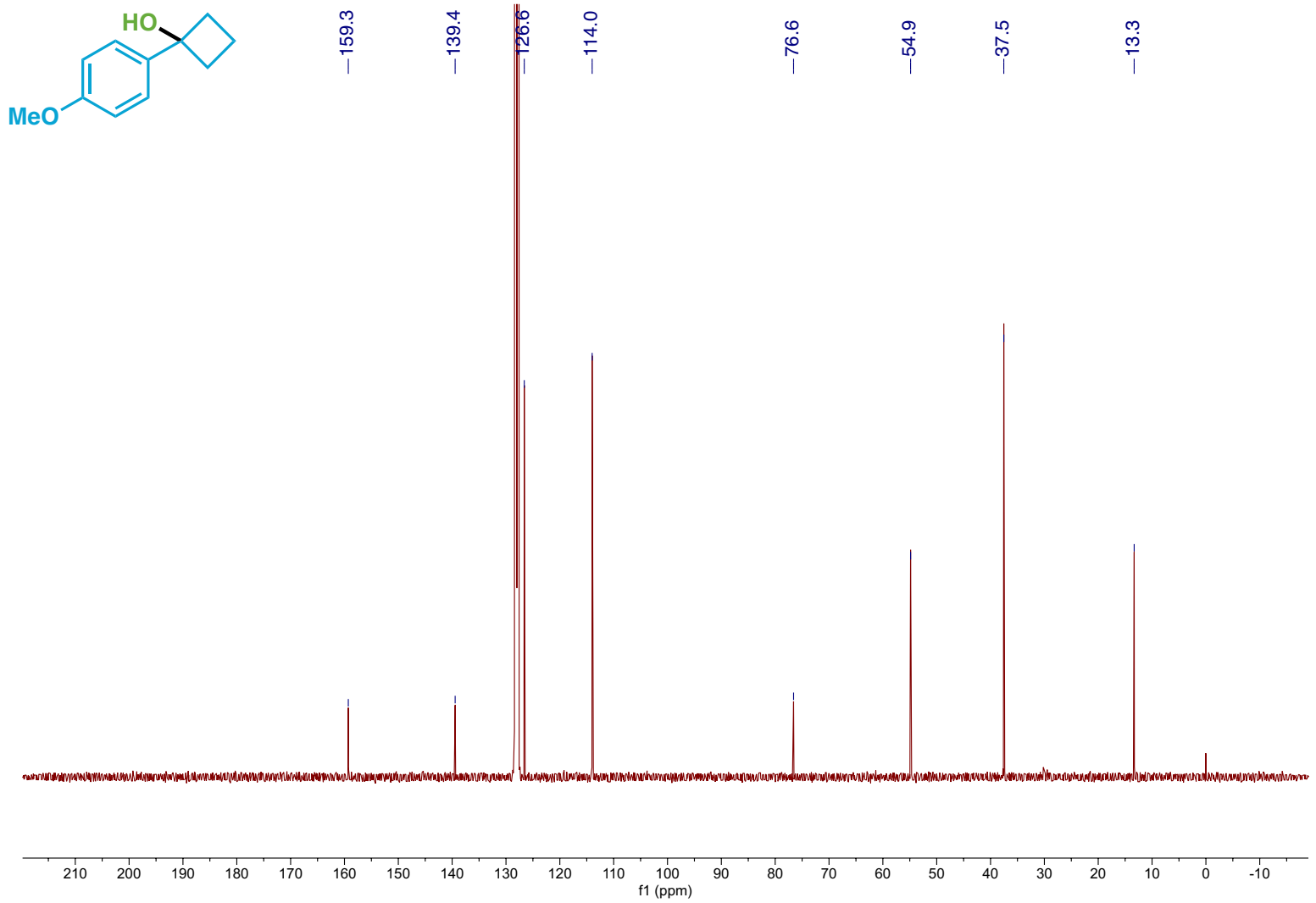
Compound 140 ^{13}C NMR



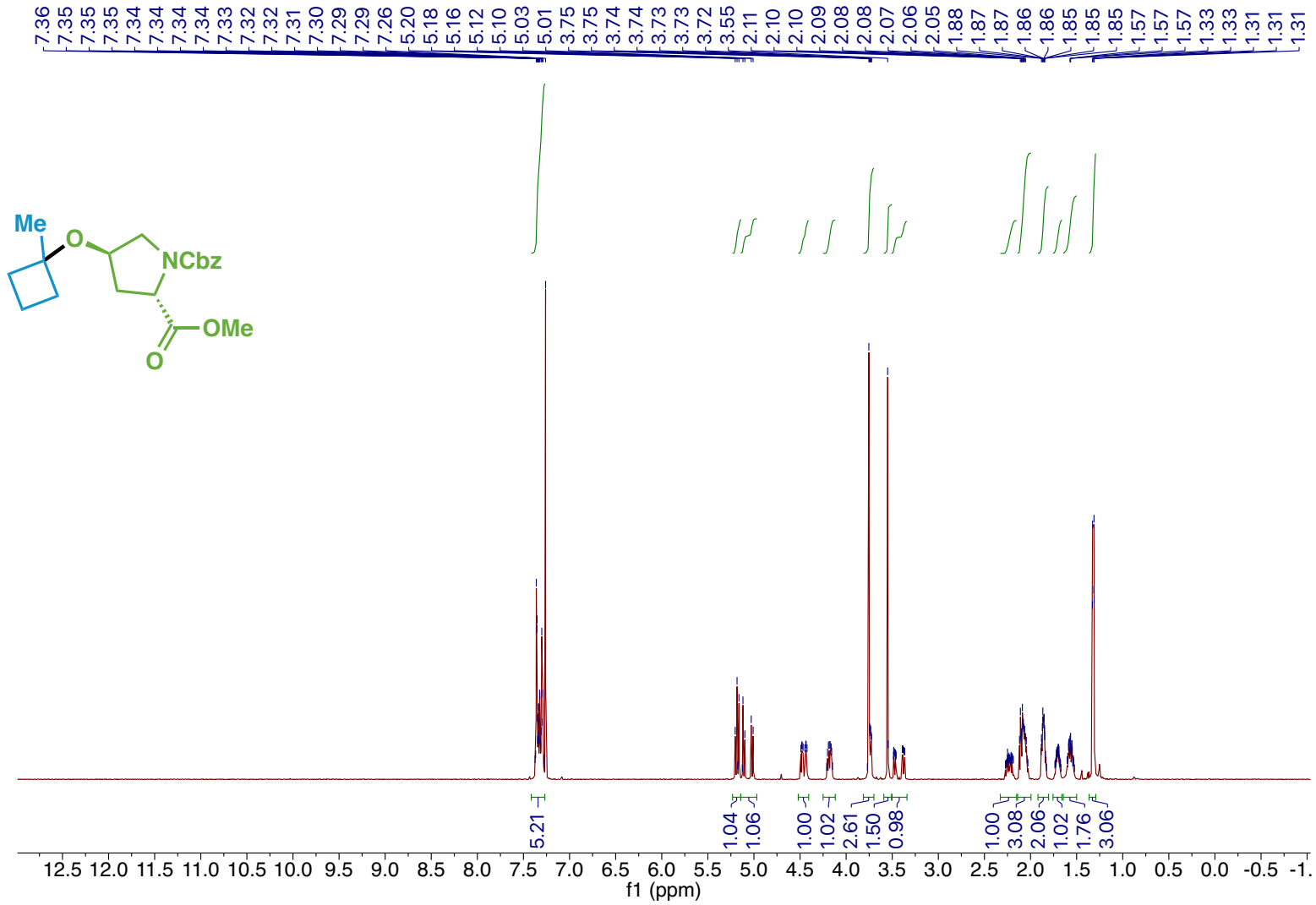
Compound 141 ^{1}H NMR



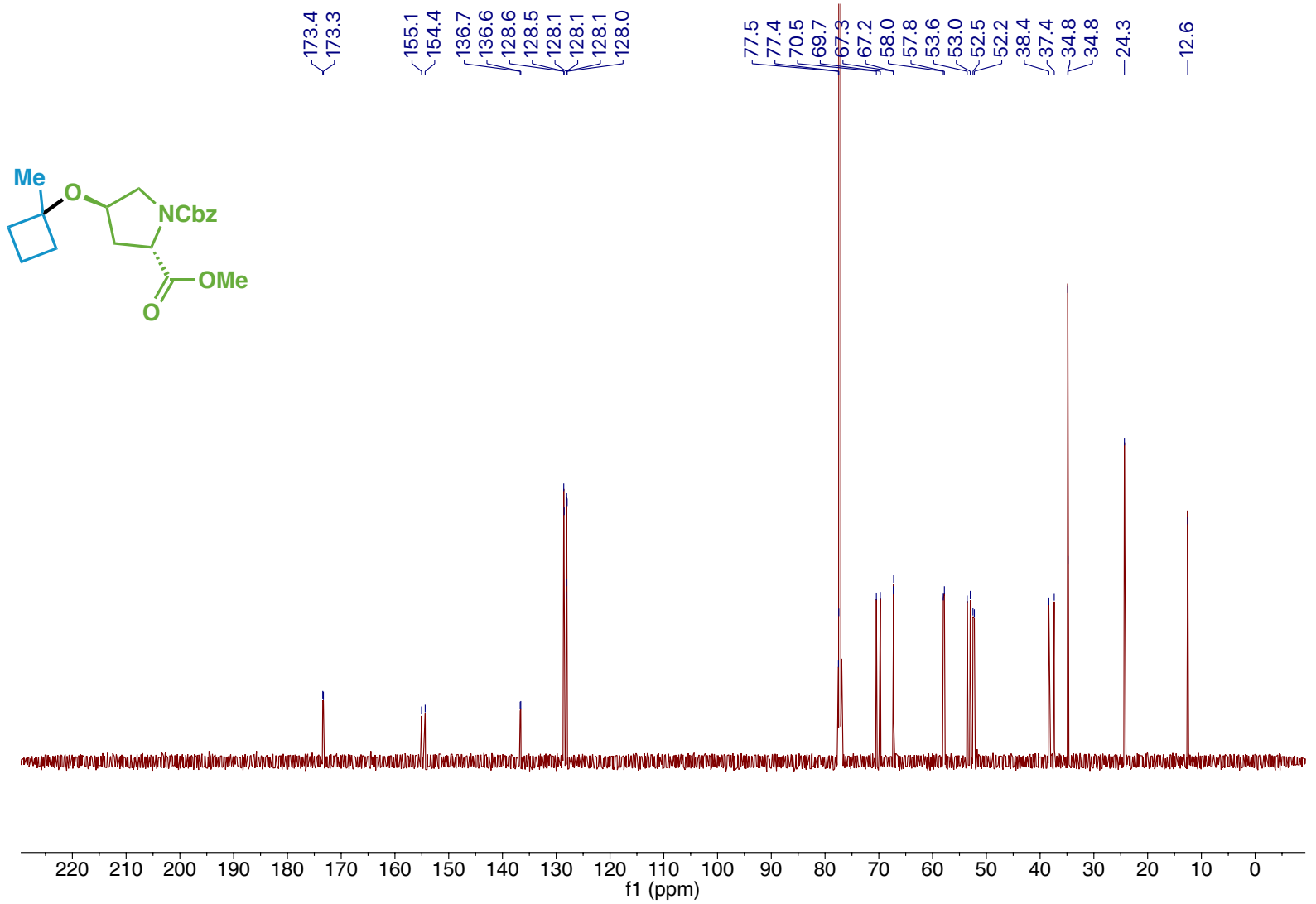
Compound 141 ^{13}C NMR



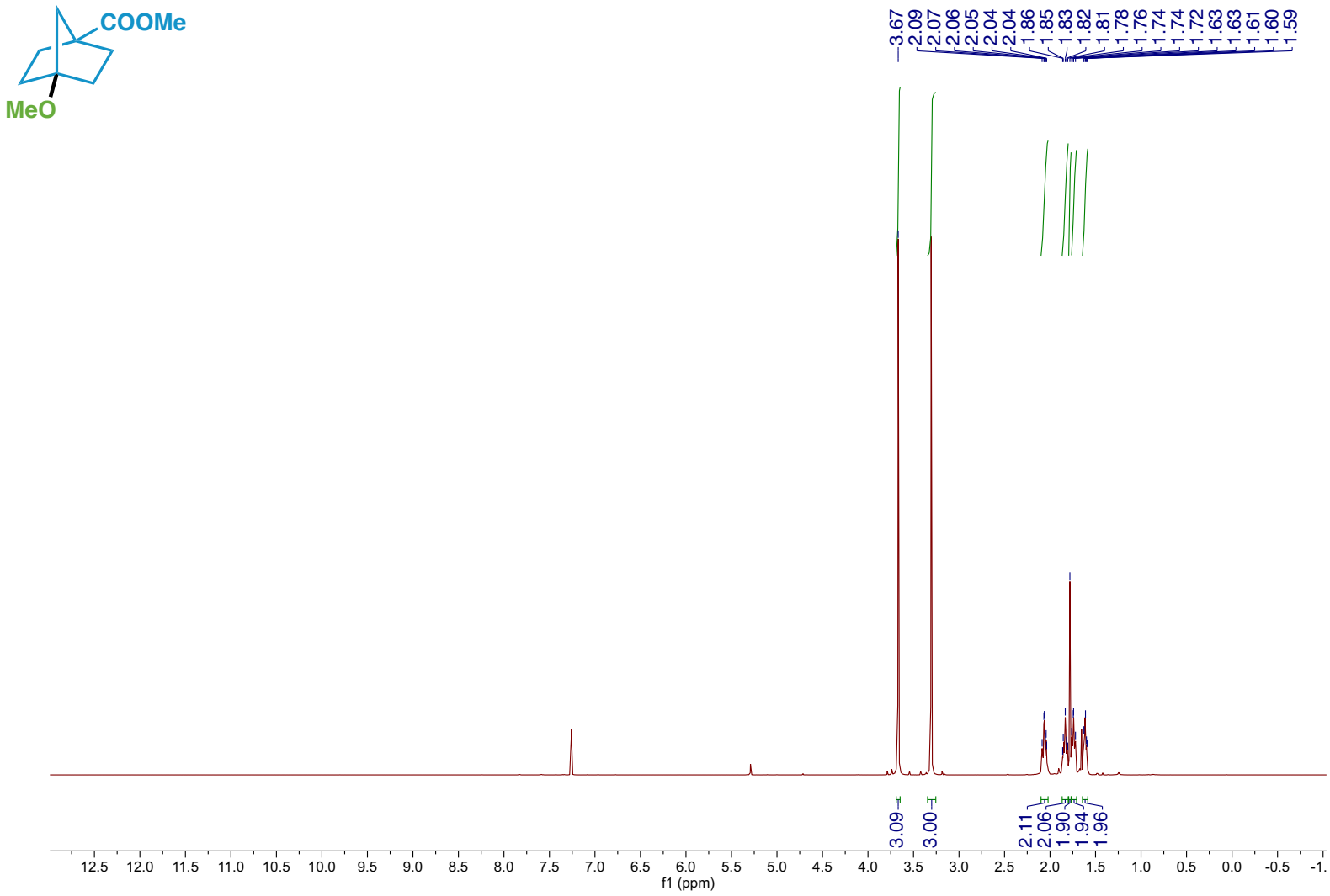
Compound SI-7 ^{1}H NMR



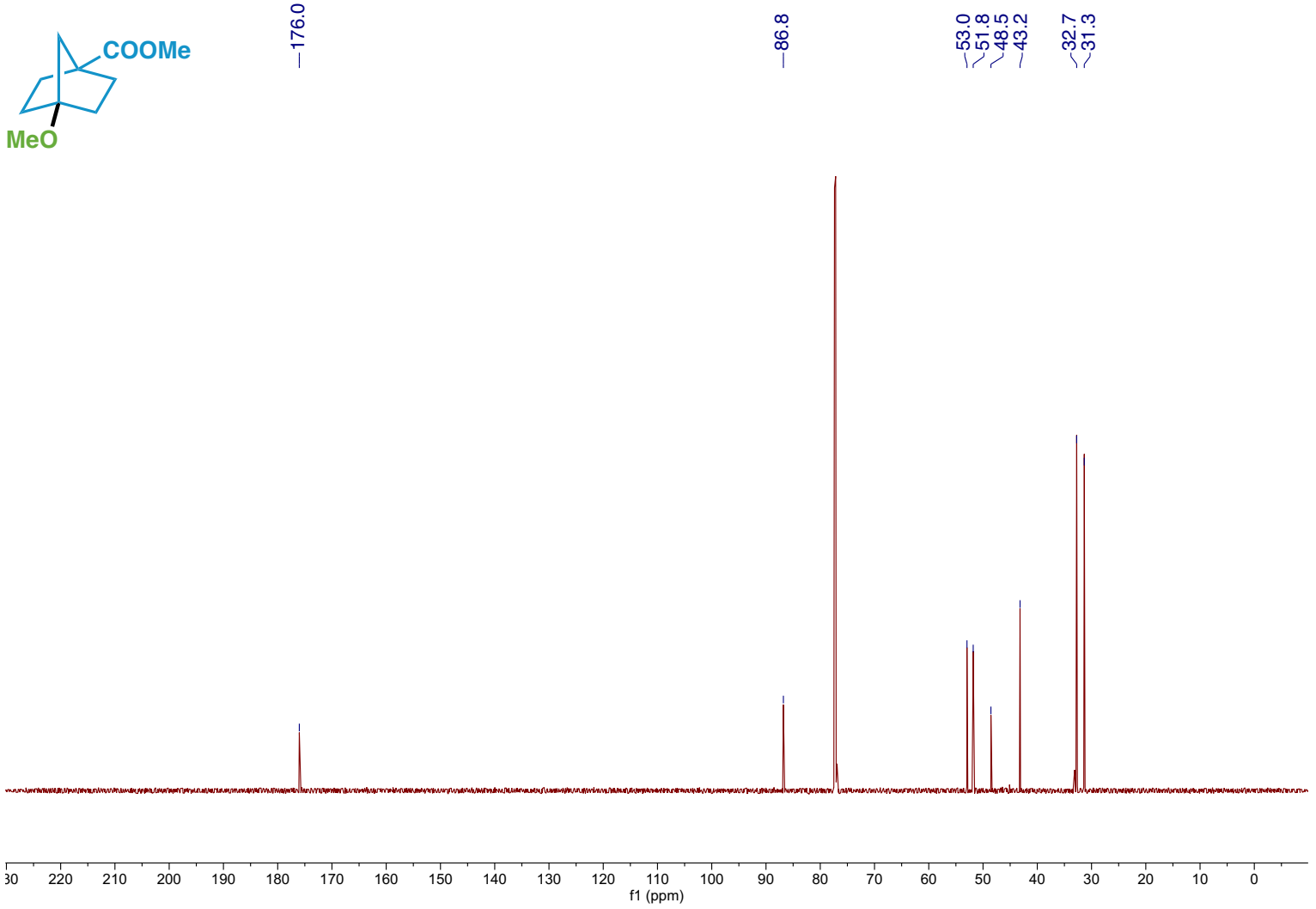
Compound SI-7 ^{13}C NMR



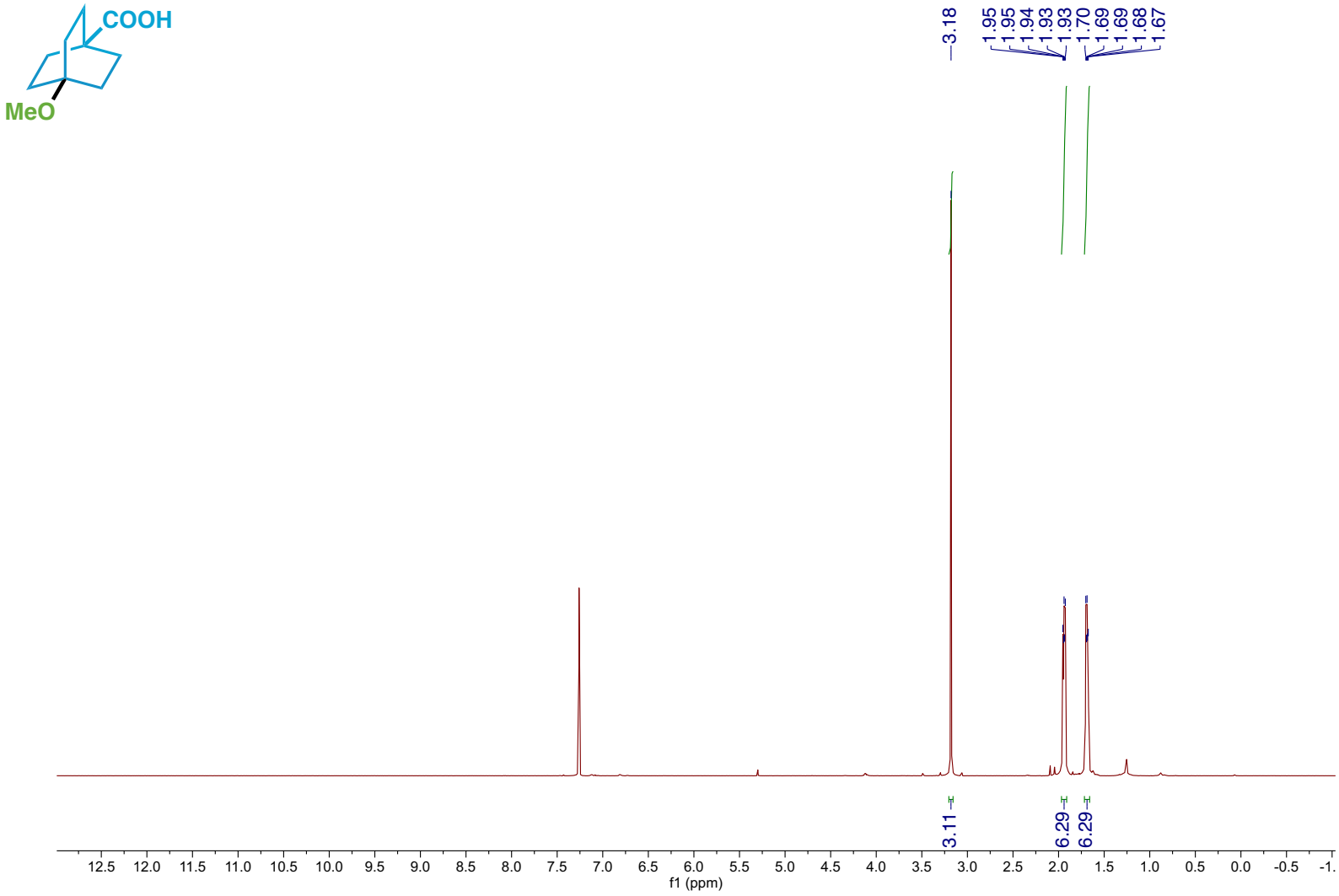
Compound SI-16 ^{1}H NMR



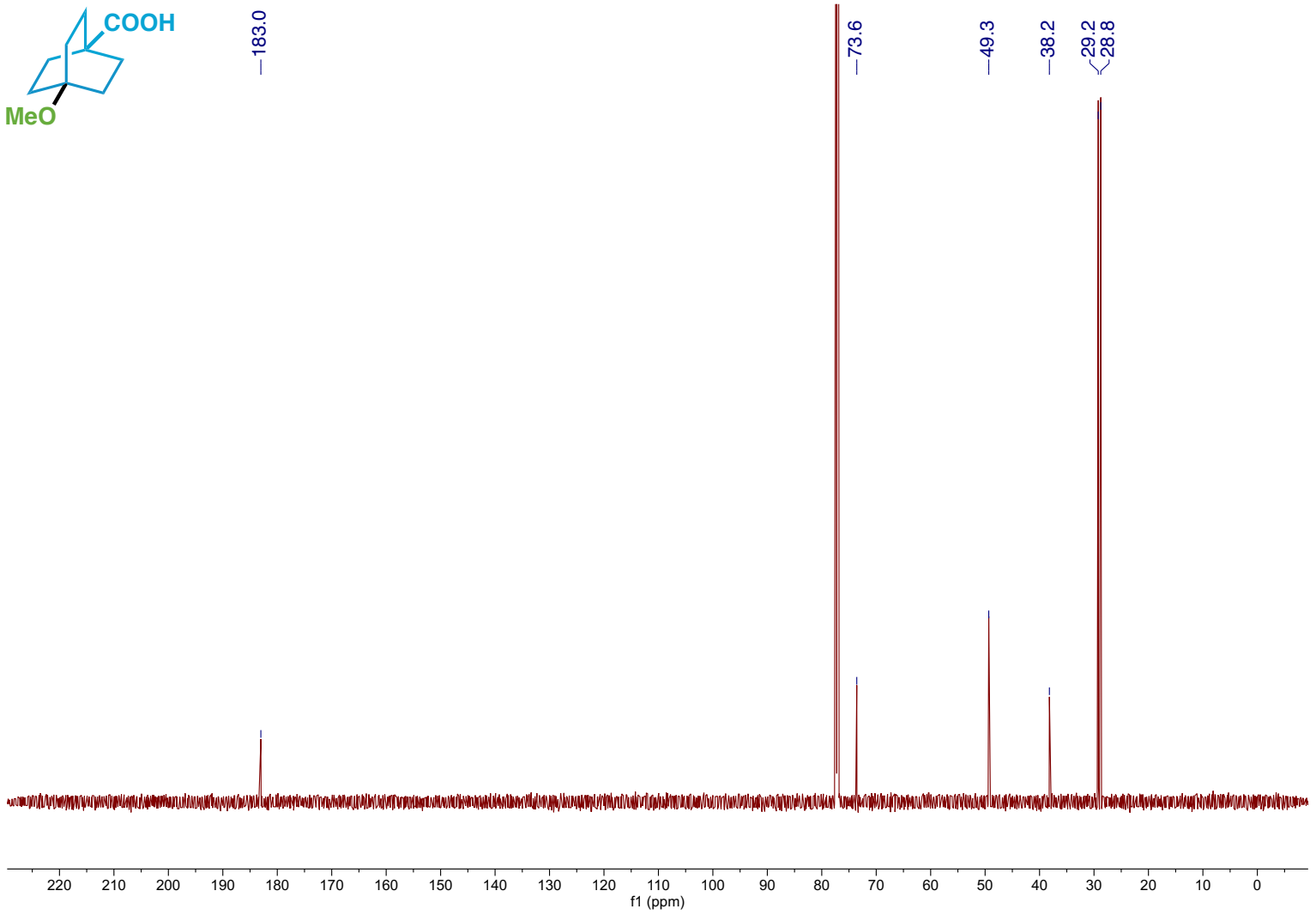
Compound SI-16 ^{13}C NMR



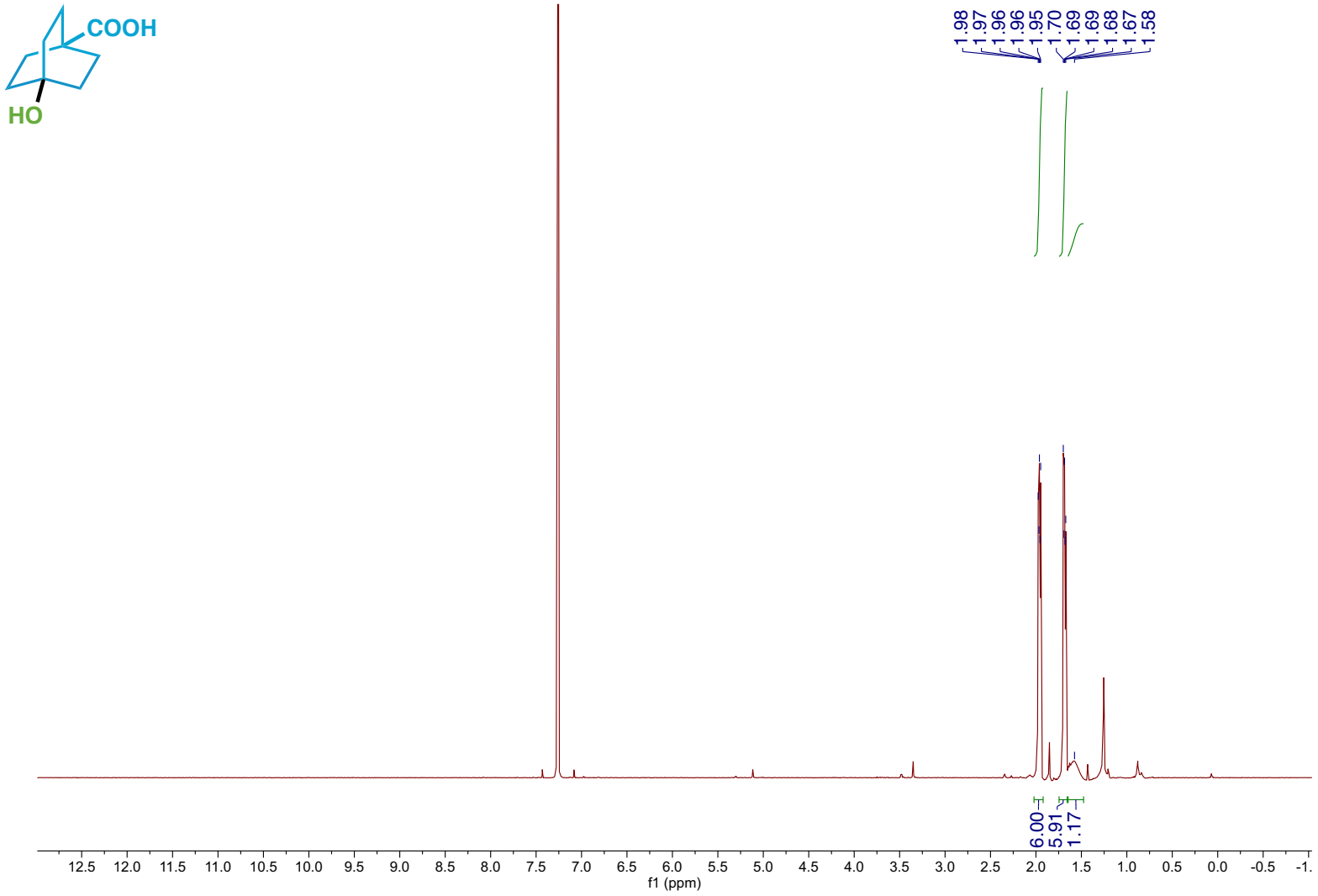
Compound SI-17 ^{1}H NMR



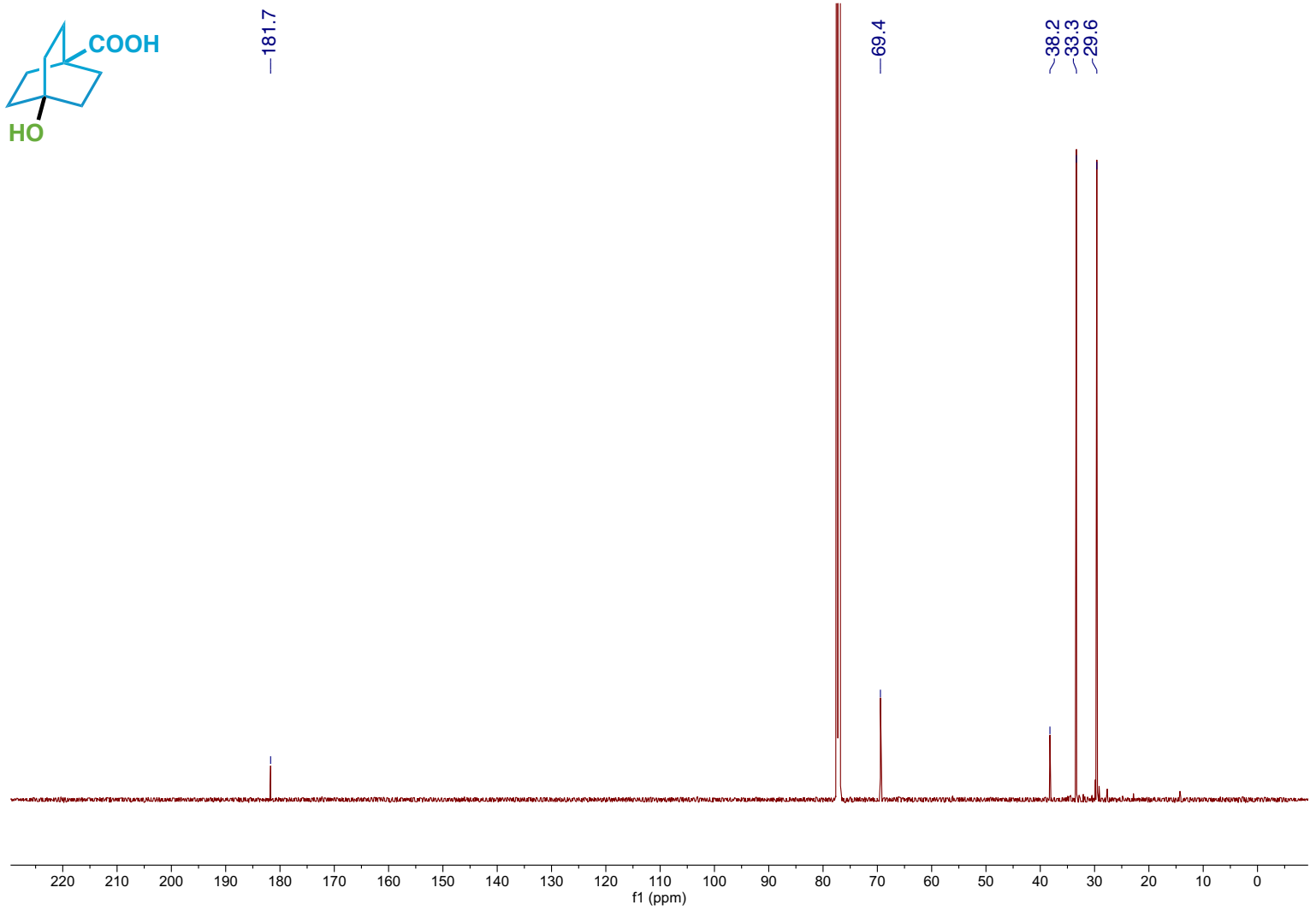
Compound SI-17 ^{13}C NMR



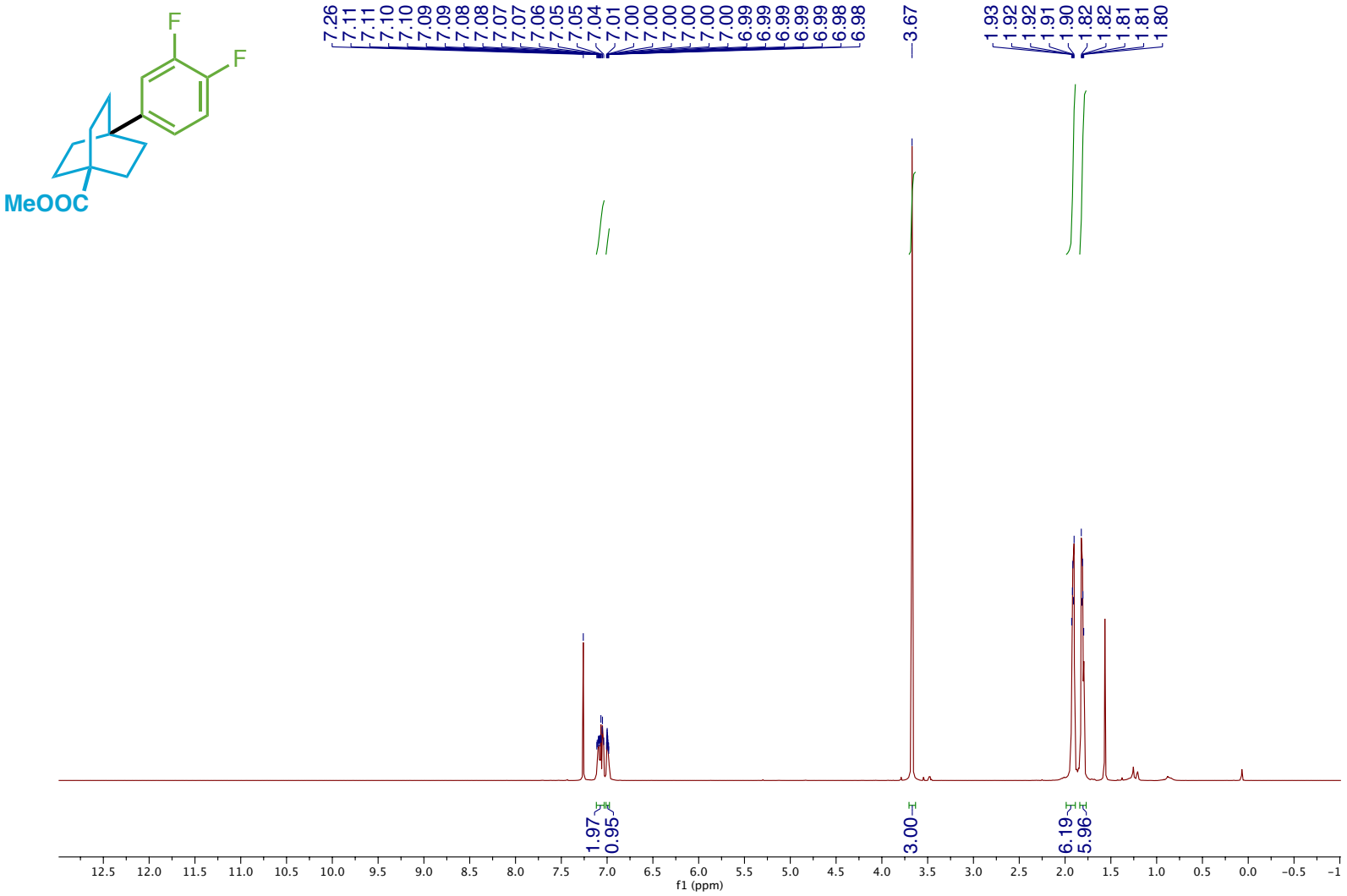
Compound SI-18 ^{1}H NMR



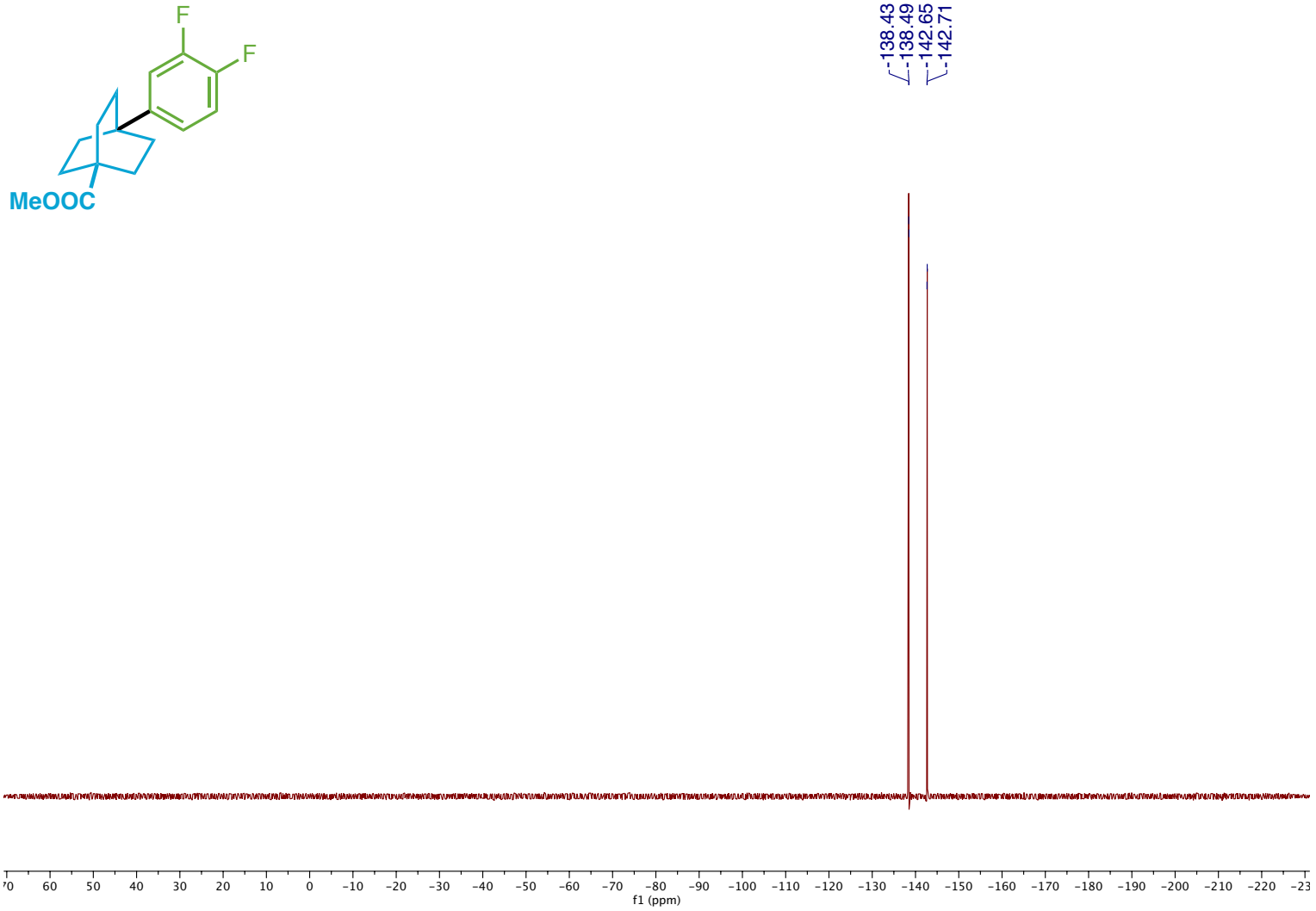
Compound SI-18 ^{13}C NMR



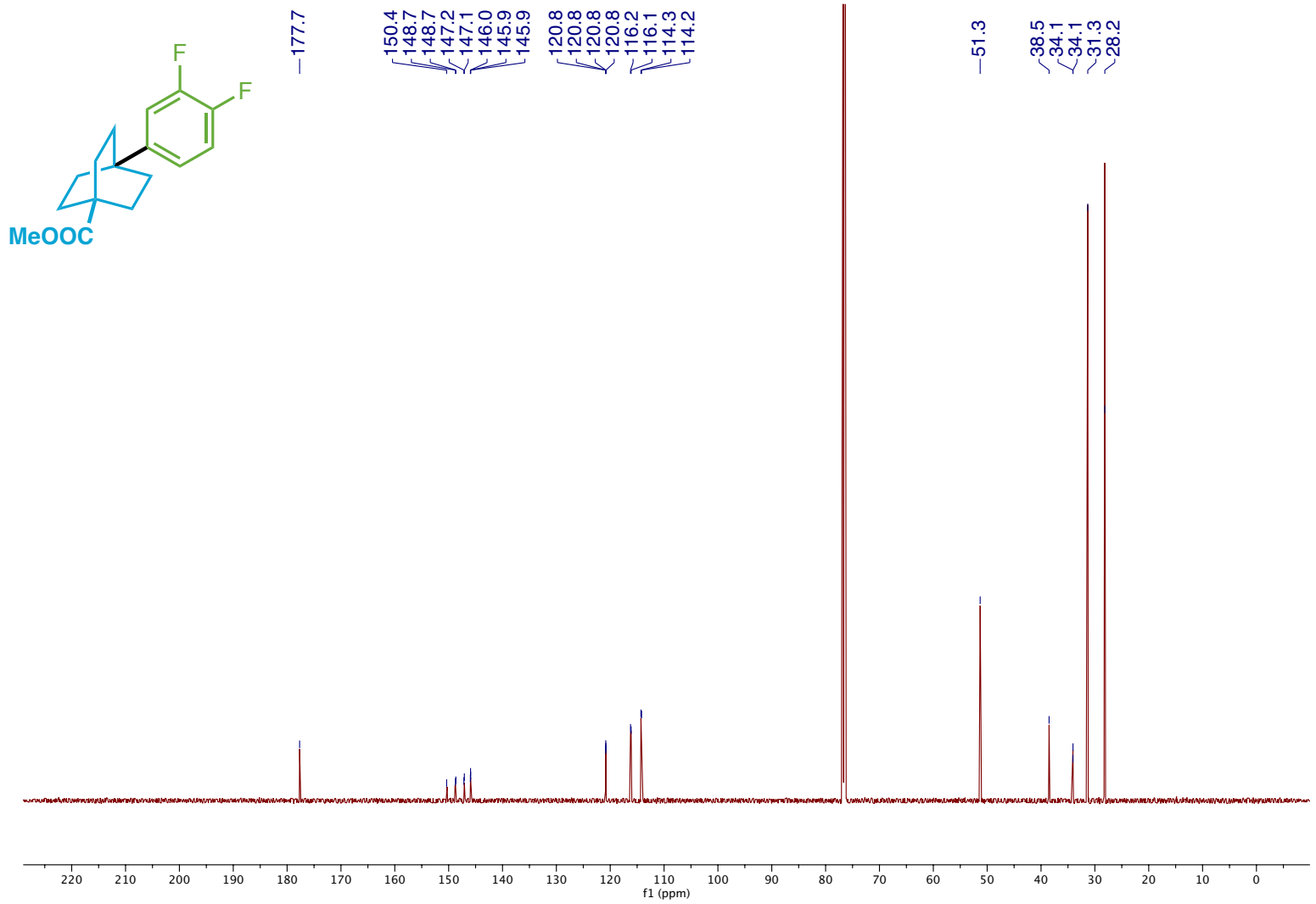
Compound SI-19 ^{1}H NMR



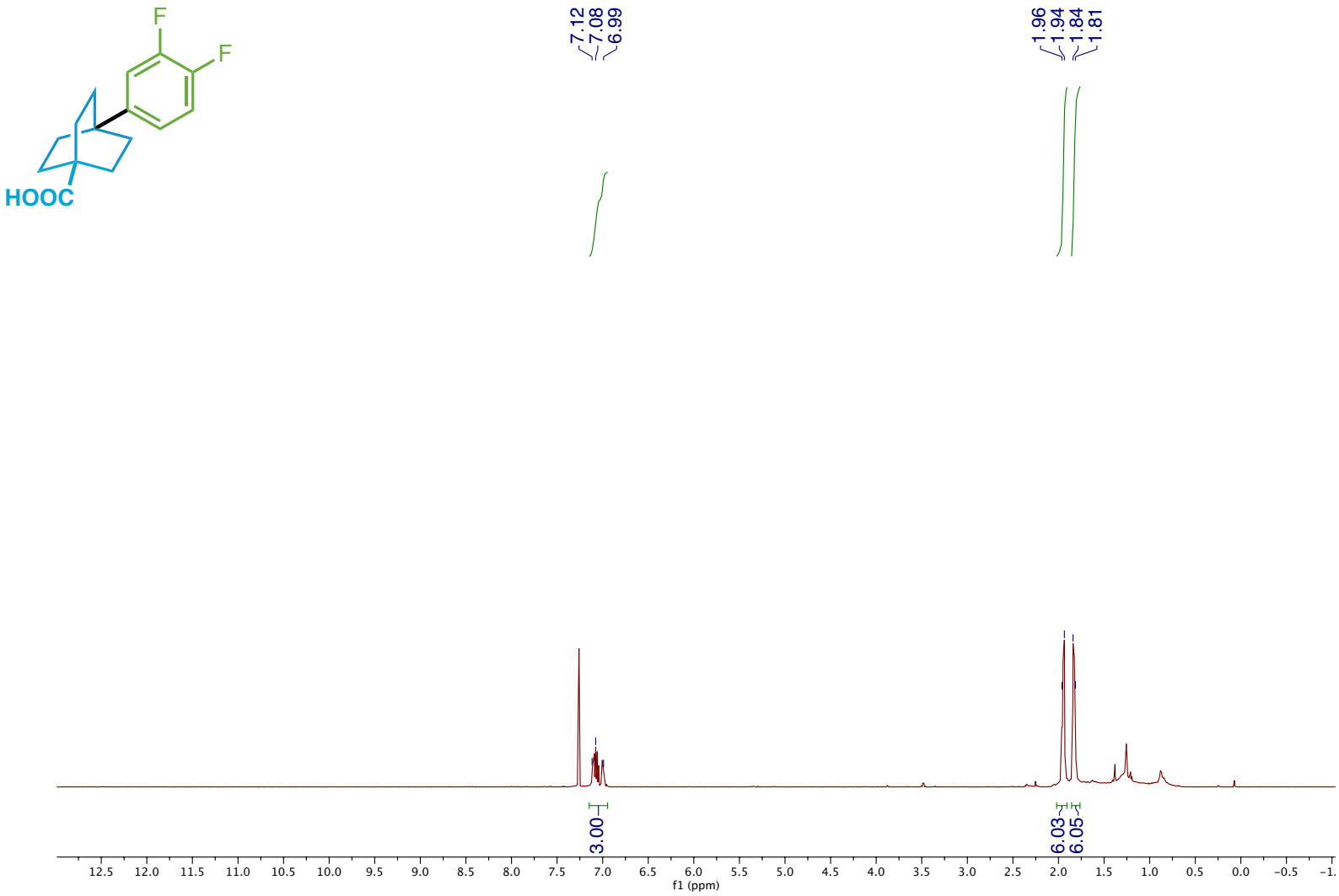
Compound SI-19 ^{19}F NMR



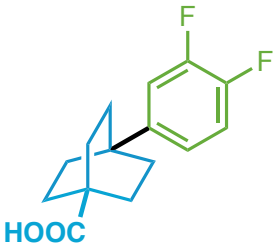
Compound SI-19 ^{13}C NMR



Compound SI-20 ^{1}H NMR



Compound SI-20 ^{19}F NMR



Compound SI-20 ^{13}C NMR