

Deaminative Reductive Cross-Electrophile Couplings of Alkylpyridinium Salts and Aryl Bromides

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[§] These authors made equal contributions.

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General Information

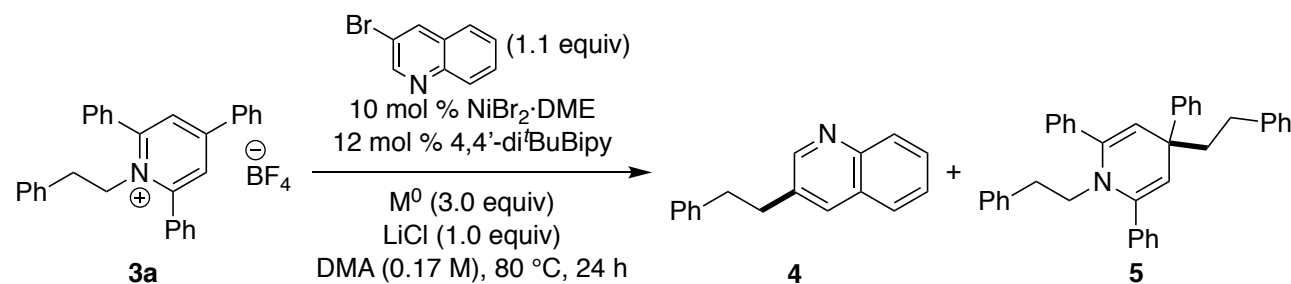
Reactions were performed in oven-dried Schlenk flasks or in oven-dried round-bottomed flasks unless otherwise noted. Round-bottomed flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of N₂. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Silica gel chromatography was performed on silica gel 60 (40–63 μm, 60 Å) unless otherwise noted. Commercial reagents were purchased from Sigma Aldrich, Acros, Fisher, Strem, TCI, Combi Blocks, Alfa Aesar, AK Scientific, Oakwood, or Cambridge Isotopes Laboratories and used as received with the following exceptions: Anhydrous NMP was degassed by sparging with N₂ for 20–30 minutes prior to use in the cross-coupling reactions. CH₂Cl₂ was dried by passing through drying columns.¹ Powdered, activated 4 Å molecular sieves were prepared by heating sieves to ~200°C under high vacuum overnight and then crushing to achieve a fine powder. In some instances oven-dried potassium carbonate was added to CDCl₃ to remove trace acid. Proton nuclear magnetic resonance (¹H NMR) spectra, carbon nuclear magnetic resonance (¹³C NMR) spectra, and fluorine nuclear magnetic resonance spectra (¹⁹F NMR) were recorded on both 400 MHz and 600 MHz spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl₃ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl₃ = δ 77.16). Chemical shifts for fluorine were externally referenced to CFCl₃ in CDCl₃ (CFCl₃ = δ 0). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, dd = doublet of doublets, hept = heptet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using FTIR spectrophotometers with material loaded onto a KBr plate. The mass spectral data were obtained at the University of Delaware mass spectrometry facility. Melting points were taken on a Thomas-Hoover Uni-Melt Capillary Melting Point Apparatus.

Optimization Studies

General Optimization Procedure

In a N₂-filled glovebox: To an oven-dried 1-dram vial was added nickel salt (0.010 mmol, 10 mol %), ligand (0.012 mmol, 12 mol %), additive (0.10 mmol, 1.0 equiv), reductant (0.30 mmol, 3.0 equiv), and pyridinium salt **3a** (50 mg, 0.10 mmol, 1.0 equiv). 3-Bromoquinoline (15 μ L, 0.11 mmol, 1.1 equiv) was then added to the vial followed by solvent. The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. 1,3,5-Trimethoxybenzene (internal standard) and CDCl₃ were added, and the yield was determined by ¹H NMR analysis.

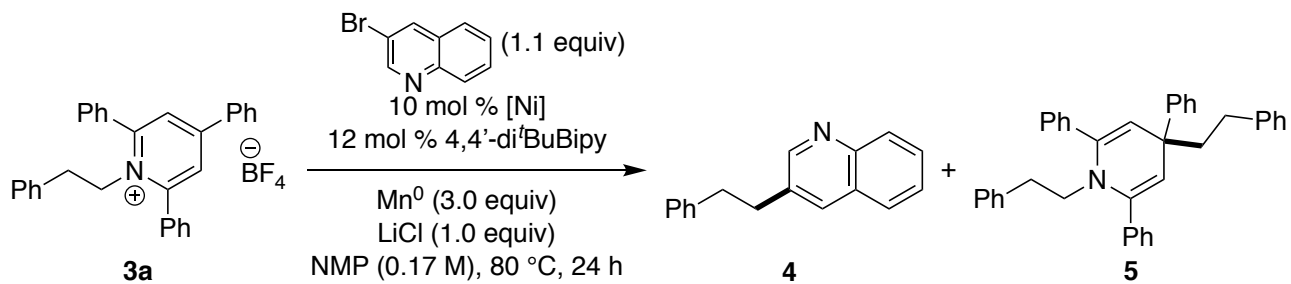
Investigation of Reductants



Entry	M^0	Yield (%) ^a	
		pdt (4)	4-addition (5)
1	Fe ⁰	0	0
2	Cu ⁰	0	0
3	Mg ⁰	20	4
4	Zn ⁰	41	18
5	Mn ⁰	51	5

^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.

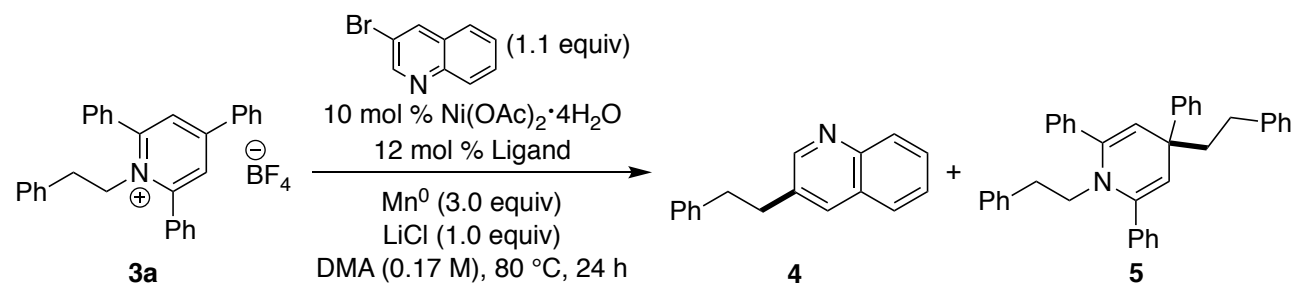
Investigation of Nickel Sources



Entry	[Ni]	Yield (%) ^a	
		pdt (4)	4-addition (5)
1	NiBr ₂ ·DME	58	10
2	NiCl ₂ ·DME	62	10
3	NiI ₂	58	11
4	Ni(OAc) ₂ ·4H ₂ O	47	14
5	Ni(acac) ₂	38	17
6	Ni(hfacac) ₂	39	13
7	Ni(TMHD) ₂	39	16
8	Ni(OTf) ₂	5	27

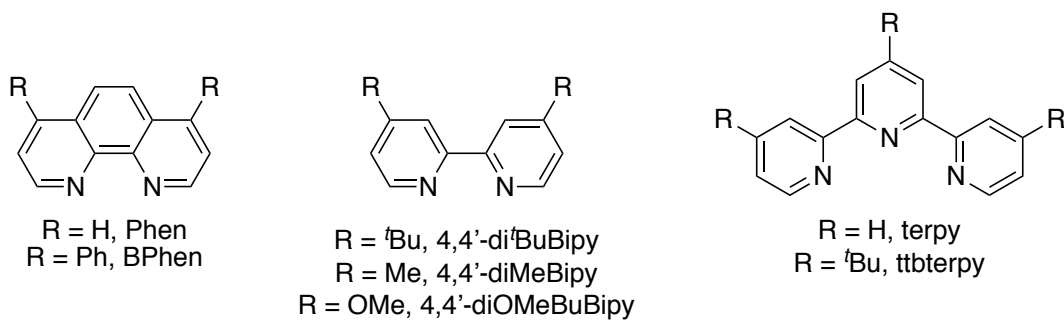
^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.
 TMHD = 2,2,6,6-tetramethyl-3,5-heptanedione.

Investigation of Ligands

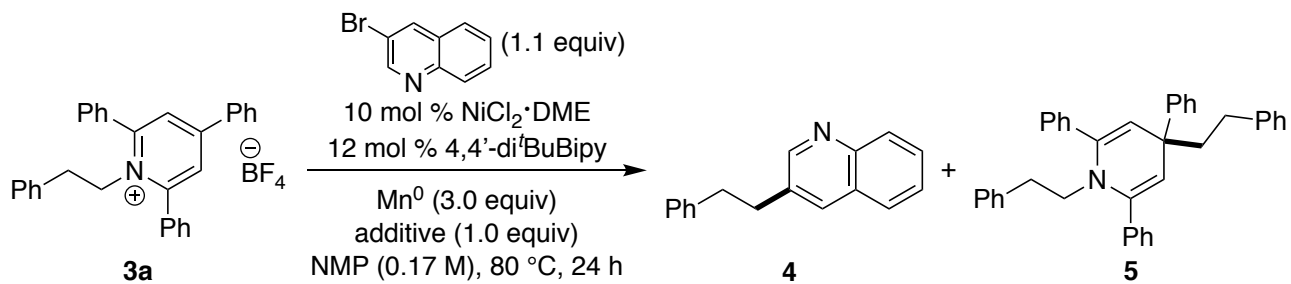


Entry	Ligand	Yield (%) ^a	
		pdt (4)	4-addition (5)
1	Phen	27	20
2	BPhen	42	15
3	4,4'-di ^t BuBipy	57	12
4	4,4'-diMeBipy	57	13
5	4,4'-diOMeBipy	59	14
6	terpy	34	22
7	ttbterpy	38	20

^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.



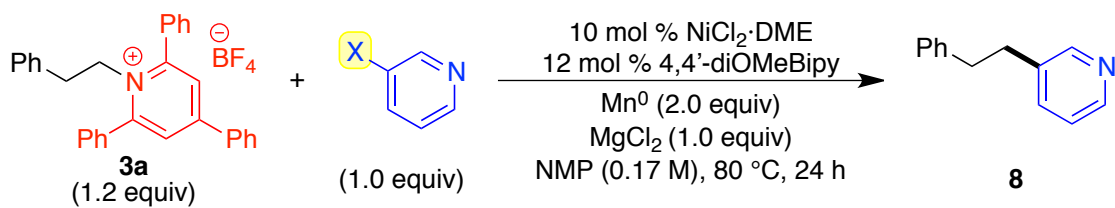
Investigation of Additives



Entry	Additive	Yield (%) ^a	
		pdt (4)	4-addition (5)
1	KBr	57	16
2	KF	52	16
3	NaCl	54	15
4	NaI	55	15
5	LiF	30	21
6	LiCl	60	12
7	MgCl ₂	65	8
8	TBAI	58	14

^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.

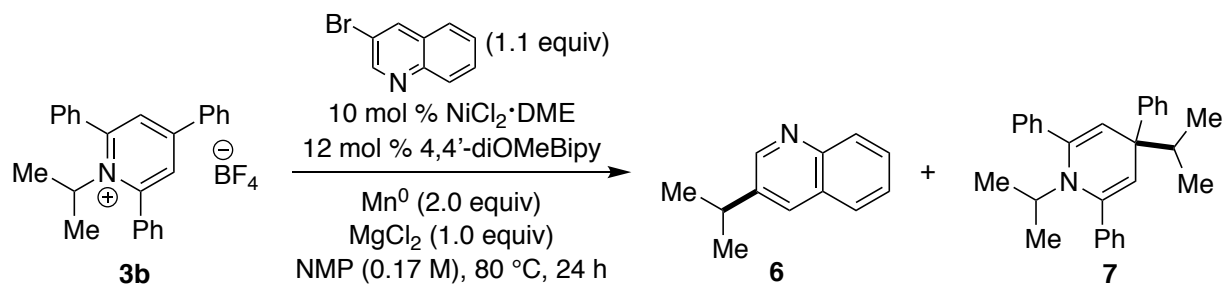
Investigation of Aryl Halides



Entry	X	Yield (%) ^a
1	Br	62 (isolated) ^b
2	I	not detected
3	Cl	8

^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard, unless noted otherwise. ^b Average isolated yield from duplicate reactions performed on 1-mmol scale.

Optimization of Secondary Alkyl Pyridinium Salts

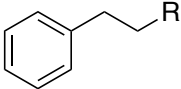
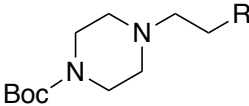
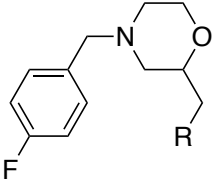
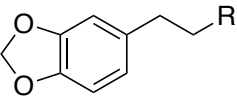


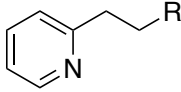
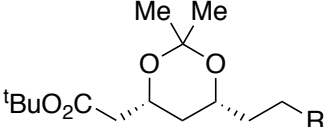
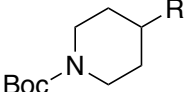
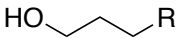
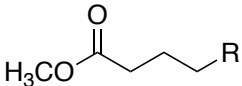
Entry	Reagent(s)	Time (h)	pdt (6)	Yield (%) ^a		
				4-Add'n (7)	Ar–Ar	Ph ₃ Py
1	none	None	19	32	12	70
2	Alk–[N]	1	24	28	28	72
3	Alk–[N]	2	50	3	20	quant.
4	Alk–[N] + ArBr	2	50	14	12	quant.
5	Alk–[N] + ArBr	3	68	9	11	quant.
6	Alk–[N] + ArBr	4	76	8	6	quant.
7	Alk–[N] + ArBr	6	84	2	4	quant.

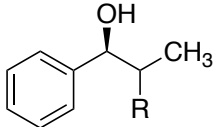
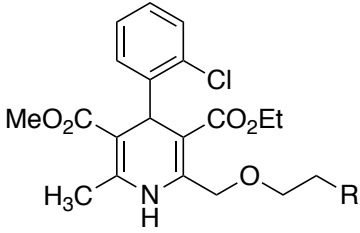
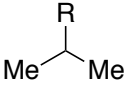
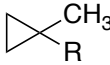
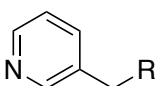
^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.

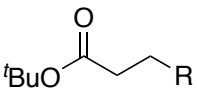
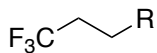
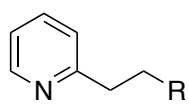
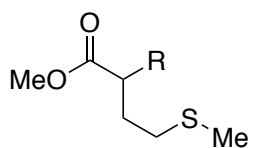
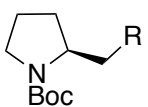
Analysis of Substrate Availability

After our investigations of substrate scope were completed, we retrospectively analyzed the relative availability of our alkyl amine precursors to the analogous bromides and carboxylic acids (see table below). In each case, the least expensive option is highlighted in blue, with the supplier noted in parentheses. In more than half of the examples, the amine is the least expensive. In the remaining cases, the amine is competitively priced.

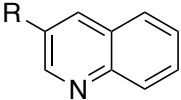
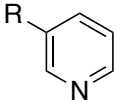
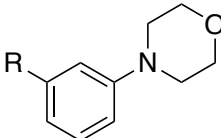
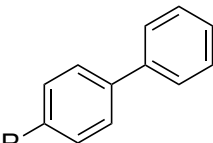
Product	Amine (R = NH ₂)	Bromide (R = Br)	Carboxylic Acid (R = CO ₂ H)
	50mL/\$30.60 (Sigma) 64-04-0	5g/\$10 25g/\$15 100g/\$40 (Combi-Blocks) 103-63-9	5g/\$10 25g/\$15 100g/\$40 (Combi-Blocks) 501-52-0
	1g/\$20 5g/\$75 10g/\$130 25g/\$260 (Combi-Blocks) 192130-34-0	100mg/\$88 250g/\$140 1g/\$350 5g/\$700 (Combi-Blocks) 655225-01-7	1g/\$50 5g/\$200 10g/\$360 25g/\$720 (Combi-Blocks) 242459-97-8
	1g/\$14 5g/\$42 10g/\$63 25g/\$114 (Combi-Blocks) 112914-13-3	Custom Syntheses available 1508657-04-2	Custom Syntheses available 763903-53-3
	1g/\$10 5g/\$24 25g/\$79 100g/\$245 (Combi-Blocks) 1484-85-1	Custom Syntheses available 57587-02-7	1g/\$25 5g/\$75 25g/\$280 100g/\$840 (Combi-Blocks) 2815-95-4

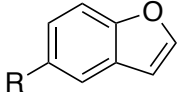
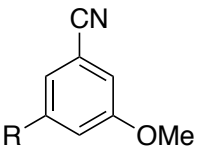
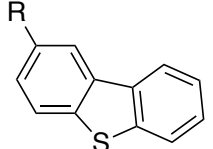
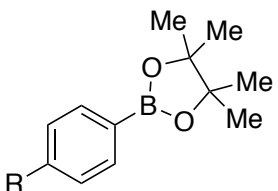
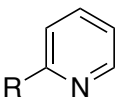
	1g/\$10 5g/\$30 25g/\$95 100g/\$285 (Combi-Blocks) 2706-56-1	1g/\$30 5g/\$95 25g/\$295 100g/\$850 (Combi-Blocks) 72996-65-7 (HBr)	1g/\$84 5g/\$240 10g/\$460 25g/\$920 (Combi-Blocks) 15197-75-8
	1g/\$10 5g/\$15 25g/\$60 100g/\$200 (Combi-Blocks) 125995-13-3	one patent ref 1380521-19-6	Unknown compound
	1g/\$10 5g/\$12 25g/\$35 100g/\$125 (Combi-Blocks) 87120-72-7	1g/\$13 5g/\$30 25g/\$120 4x25g/\$420 (Combi-Blocks) 180695-79-8	5g/\$10 25g/\$20 100g/\$60 500g/\$180 (Combi-Blocks) 84358-13-4
	5 g/\$10 25 g/\$15 100 g/\$40 500 g/\$150 (Combi-Blocks) 156-87-6	5g/\$10 25g/\$14 100g/\$49 (Oakwood) 627-18-9.	Custom Syntheses available (including sodium carboxylate variants) 591-81-1 Methyl Ester Available from Combi 250 mg/\$300 925-57-5
	HCl Salt. 1 g/\$10 5 g/\$18 25 g/\$65 100 g/\$180 (Combi-Blocks) 13031-60-2	5 g/\$10 25 g/\$15 100 g/\$50 500 g/\$200 (Combi-Blocks) 4897-84-1	1 g/\$10 5 g/\$20 25 g/\$80 100 g/\$210 (Combi-Blocks) 1501-27-5

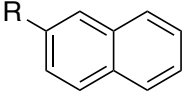
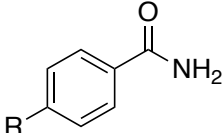
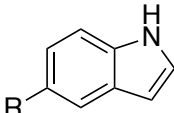
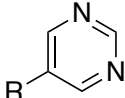
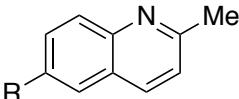
	Discont'd (Sigma) 492-41-1	Custom Syntheses available 1822304-22-2	50 mg/\$53 (Sigma) 76549-02-5
	1g/\$84 5g/\$264 (AK Scientific) 88150-42-9	Unknown compound (including PG variants)	Unknown compound (including PG variants)
	100 mL/\$16 500 mL/\$19 2500 mL/\$61 (Alfa Aesar) 75-31-0	250 mL/\$47 1000 mL/\$175 2500 mL/\$347 5000 mL/\$582 10 L/\$980 (Alfa Aesar) 75-26-3	100 mL/\$21 500 mL/\$25 2500 mL/\$82 (Alfa Aesar) 79-31-2
	HCl Salt 1 g/\$80 5 g/\$240 10 g/\$400 25 g/\$680 (Combi-Blocks) 8887-87-0	1 g/\$1460 5 g/\$4390 (Combi-Blocks) 50915-27-0	1 g/\$24 5 g/\$95 10 g/\$180 25 g/\$310 (Combi-Blocks) 6914-76-7
	5 g/\$10 25 g/\$20 100 g/\$60 (Combi-Blocks) 3731-52-1	HBr Salt 1 g/\$10 5 g/\$35 10 g/\$60 25 g/\$125 100 g/\$375 (Combi-Blocks) 4916-55-6	HCl Salt 5 g/\$10 25 g/\$28 100 g/\$85 500 g/\$340 (Combi-Blocks) 6419-36-9

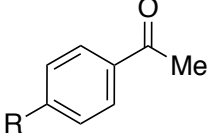
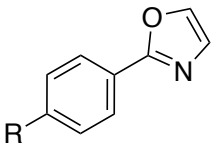
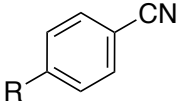
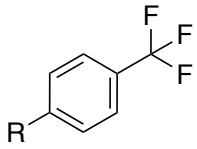
	HCl Salt 5 g/\$20 25 g/\$83 100 g/\$280 500 g/\$960 (Combi-Blocks) 58620-93-2	1 g/\$15 5 g/\$80 10 g/\$150 25 g/\$300 50 g/\$550 (Combi-Blocks) 55666-43-8	1 g/\$10 5 g/\$30 25 g/\$100 100 g/\$300 500 g/\$960 (Combi-Blocks) 15026-17-2
	HCl Salt. 1 g/\$57 (Oakwood) 2968-33-4	Custom Syntheses available 460-32-2	1 g/\$12 5 g/\$17 25 g/\$64 100 g/\$250 (Oakwood) 406-93-9
	1 g/\$10 5 g/\$30 25 g/\$95 100 g/\$285 (Combi-Blocks) 2706-56-1	HBr Salt 1 g/\$30 5 g/\$95 25 g/\$295 100 g/\$850 (Combi-Blocks) 72996-65-7	1 g/\$84 5 g/\$240 10 g/\$460 25 g/\$920 (Combi-Blocks) 15197-75-8
	5 g/\$10 25 g/\$28 100 g/\$80 500 g/\$240 (Combi-Blocks) 2491-18-1	Free Acid Custom Synthesis Available 42990-64-7	Custom Synthesis Available 1601058-89-2 (including diacid)
	1 g/\$25 5 g/\$80 10 g/\$128 25 g/\$307 100 g/\$920 (Combi-Blocks) 119020-01-8	1 g/\$224 5 g/\$748 (Aldrich Partner) 128542-75-6	1 g/\$74 5 g/\$223 10 g/\$415 25 g/\$840 (Combi-Blocks) 56502-01-3

We also retrospectively analyzed the relative availability of our aryl bromides to the analogous boronic acids, (pinacol)boronic esters, and iodides (see table below). In each case, the least expensive option is highlighted in blue, with the supplier noted in parentheses. In almost all cases the aryl bromide is the least expensive option.

	Bromide	Boronic Acid Der.	Bpin	Iodide
	5g/\$10 25g/\$15 100g/\$50 500 g/\$150 (Combi-Blocks) 5332-24-1	1g/\$10 5g/\$23 25g/\$75 100 g/\$225 (Combi-Blocks) 191162-39-7	1 g/\$52 5 g/\$209 (Combi-Blocks) 171364-85-5	1 g/\$640 5 g/\$2010 (Combi-Blocks) 79476-07-6
	1 g/\$9 5 g/\$10 25 g/\$11 100 g/\$38 (Oakwood) 626-55-1	5 g/\$10 25 g/\$40 100 g/\$135 500 g/\$548 (Combi-Blocks) 1692-25-7	1 g/\$10 5 g/\$20 25 g/\$70 100 g/\$225 500 g/\$625 (Combi-Blocks) 329214-79-1	1 g/\$10 5 g/\$15 25 g/\$60 100 g/\$160 500 g/\$640 (Combi-Blocks) 1120-90-7
	1 g/\$22 5 g/\$85 10 g/\$160 25 g/\$320. (Combi-Blocks) 197846-82-5	1 g/\$60 5 g/\$180 10 g/\$290 25 g/\$580 100 g/\$1520 (Combi-Blocks) 863377-22-4	1 g/\$60 5 g/\$205 10 g/\$310 25 g/\$735 (Combi-Blocks) 852227-95-3	1 g/\$569 5 g/\$1651 10 g/\$2448 (Sigma) 291533-82-9
	5 g/\$10 25 g/\$15 100 g/\$40 500 g/\$150 (Combi-Blocks) 92-66-0	5 g/\$10 25 g/\$37 100 g/\$110 500 g/\$420 (Combi-Blocks) 5122-94-1	1 g/\$19 5 g/\$55 10 g/\$90 25 g/\$180 100 g/\$695 (Combi-Blocks) 144432-80-4	1 g/\$10 5 g/\$12 25 g/\$40 100 g/\$103 500 g/\$360 (Combi-Blocks) 1591-31-7

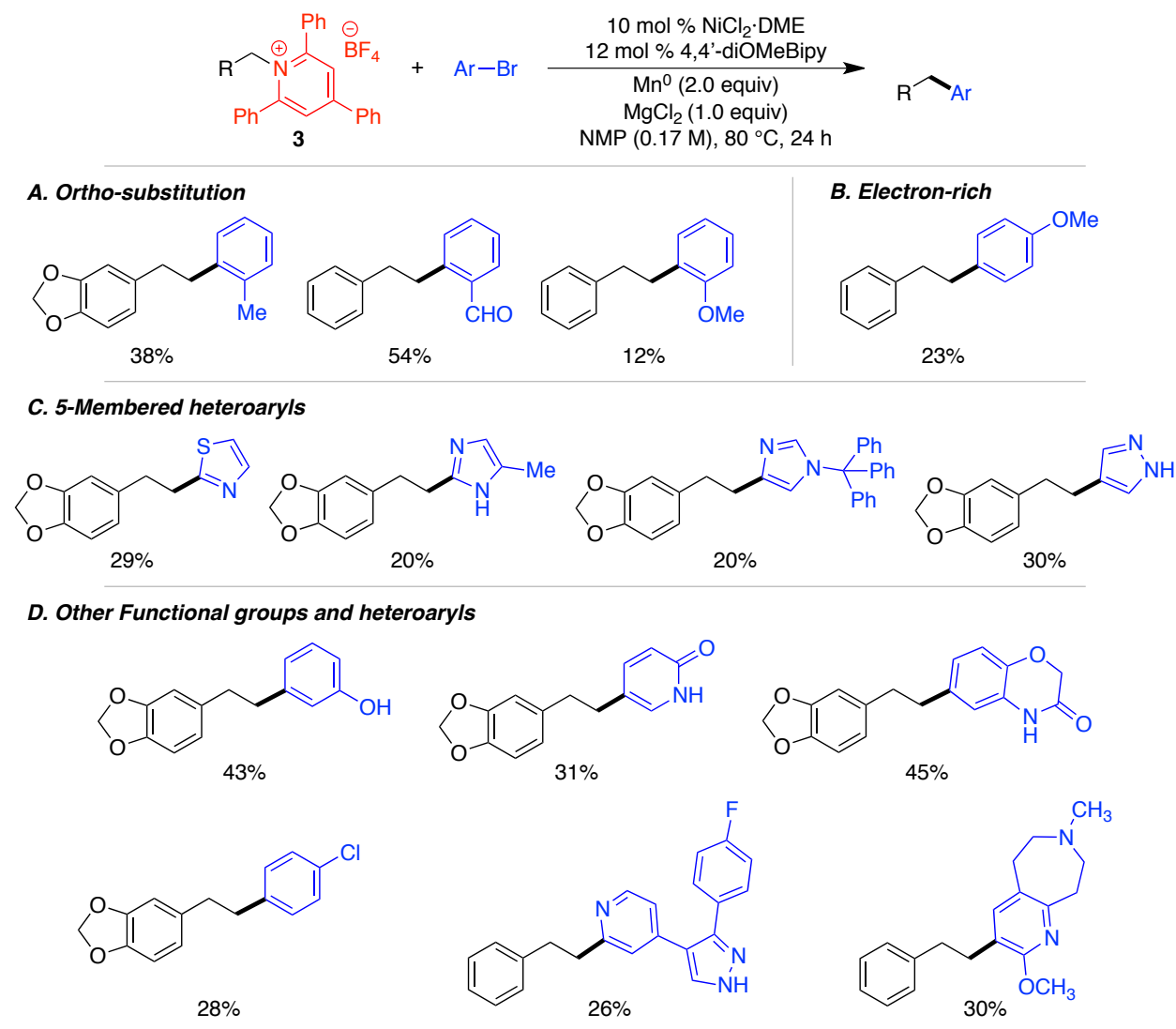
	1 g/\$15 5 g/\$45 10 g/\$75 25 g/\$150 100 g/\$450 (Combi-Blocks) 23145-07-5	1 g/\$60 5 g/\$240 10 g/\$450 25 g/\$960 (Combi-Blocks) 331834-13-0	1 g/\$60 5 g/\$200 10 g/\$350 (Combi-Blocks) 519054-55-8	250 mg/\$176 1 g/\$524 (Sigma) 60770-67-4
	1 g/\$39 5 g/\$100 10 g/\$150 25 g/\$325 100 g/\$875 (Combi-Blocks) 867366-91-4	Custom Synthesis Available 960589-15-5	1 g/\$280 5 g/\$995 (Combi-Blocks) 1035266-33-1	Custom Synthesis Available 269411-72-5
	1 g/\$12 5 g/\$36 10 g/\$60 25 g/\$120 100 g/\$320 (Combi-Blocks) 22439-61-8	1 g/\$30 5 g/\$80 10 g/\$135 25 g/\$250 100 g/\$625 (Combi-Blocks) 668983-97-9	Custom Synthesis Available 890042-21-4	200 mg/\$99 1 g/\$350 (Combi-Blocks) 177586-41-3
	1 g/\$14 5 g/\$28 25 g/\$115 100 g/\$415 (Combi-Blocks) 68716-49-4	Unknown Compound	1 g/\$15 5 g/\$50 10 g/\$80 25 g/\$150 100 g/\$ 360 (Combi-Blocks) 99770-93-1	1 g/\$40 5 g/\$135 25 g/\$520 (Combi-Blocks) 73852-88-7
	1g/\$9.00 5g/\$10.00 25g/\$11.00 100g/\$29.00 500g/\$140.00 (Oakwood) 109-04-6	250 mg/\$57 1g/\$147 (Sigma) 874186-98-8	1 g/\$120 5 g/\$420 25 g/\$1680 (Combi-Blocks) 197958-29-5	1 g/\$10 5 g/\$21 25 g/\$75 100 g/\$290 500 g/\$1250 (Combi-Blocks) 5029-67-4

	5 g/\$10.00 10g/\$12.00 25g/\$19.00 100g/\$59.00 500g/\$199.00 (Oakwood) 580-13-2	5 g/\$10 25 g/\$28 100 g/\$100 500 g/\$480 (Combi-Blocks) 32316-92-0	1 g/\$20 5 g/\$55 10 g/\$105 25 g/\$245 (Combi-Blocks) 256652-04-7	1 g/\$70 5 g/\$250 10 g/\$450 25 g/\$900 100 g/\$2450 (Combi-Blocks) 612-55-5
	1g/\$10.00 5g/\$11.00 25g/\$39.00 100g/\$119.00 (Oakwood) 698-67-9	1 g/\$10 5 g/\$30 25 g/\$90 100 g/\$230 500 g/\$889 (Combi-Blocks) 123088-59-5	1 g/\$59.00 5 g/\$179.00 (Oakwood) 179117-44-3	1g/\$25 5g/\$75 25g/\$250 (Combi-Blocks) 3956-07-8
	5 g/\$10 25 g/\$15 100 g/\$40 500 g/\$150 (Combi-Blocks) 10075-50-0	1 g/\$20 5 g/\$60 10 g/\$100 25 g/\$200 100 g/\$550 (Combi-Blocks) 144104-59-6	1 g/\$33 5 g/\$135 10 g/\$250 25 g/\$450 100 g/\$1200 (Combi-Blocks) 269410-24-4	1 g/\$15 5 g/\$50 25 g/\$200 100 g/\$640 (Combi-Blocks) 16066-91-4
	5 g/\$15 25 g/\$40 100 g/\$120 (Combi-Blocks) 4595-59-9	1 g/\$ 10 5 g/\$27 25 g/\$95 100 g/\$350 (Combi-Blocks) 109299-78-7	1 g/\$20 5 g/\$60 10 g/\$110 25 g/\$200 100 g/\$620 (Combi-Blocks) 321724-19-0	1 g/\$120 5 g/\$360 10 g/\$550 (Combi-Blocks) 31462-58-5
	1 g/\$10 5 g/\$28 25 g/\$85 100 g/\$295 (Combi-Blocks) 877-42-9	1 g/\$330 5 g/\$1133 10 g/\$1936 (Sigma) 1092790-20-9	1 g/\$97 5 g/\$350 (Sigma) 10220-90-86-3	250 mg/\$640 1 g/\$1610 (Combi-Blocks) 1128-62-7

	25g/\$22 100g/\$56 500g/\$232 (Alfa-Aesar) 99-90-1	1 g/\$10 5 g/\$12 25 g/\$45 100 g/\$176 (Combi-Blocks) 149104-90-5	1 g/\$23 5 g/\$85 25 g/\$380 (Combi-Blocks) 171364-81-1	5 g/\$10 25 g/\$20 100 g/\$55 (Combi-Blocks) 13329-40-3
	1 g/\$641 5 g/\$2264 (Aldrich Partner) 176961-50-5	Custom Synthesis Available 1082066-51-0	Custom Synthesis Available 501944-79-2	1 g/\$120 5 g/\$385 10 g/\$595 (Combi-Blocks) 195436-88-5
	5 g/\$10 25 g/\$15 100 g/\$40 500 g/\$150 (Combi-Blocks) 623-00-7	5 g/\$12 25 g/\$50 100 g/\$160 500 g/\$590 (Combi-Blocks) 126747-14-6	1 g/\$15 5 g/\$50 10 g/\$75 25 g/\$155 (Combi-Blocks) 171364-82-2	5 g/\$10 25 g/\$40 100 g/\$140 (Combi-Blocks) 3058-39-7
	1g/\$9.00 5g/\$10.00 25g/\$12.00 100g/\$19.00 500g/\$79.00 (Oakwood) 402-43-7	5g/\$10 25g/\$28 100g/\$75 500g/\$350 (Combi-Blocks) 128796-39-4	1 g/\$35 5 g/\$95 25 g/\$380 (Combi-Blocks) 214360-65-3	1g/\$10.00 5g/\$12.00 25g/\$17.00 100g/\$55.00 500g/\$210.00 (Oakwood) 455-13-0

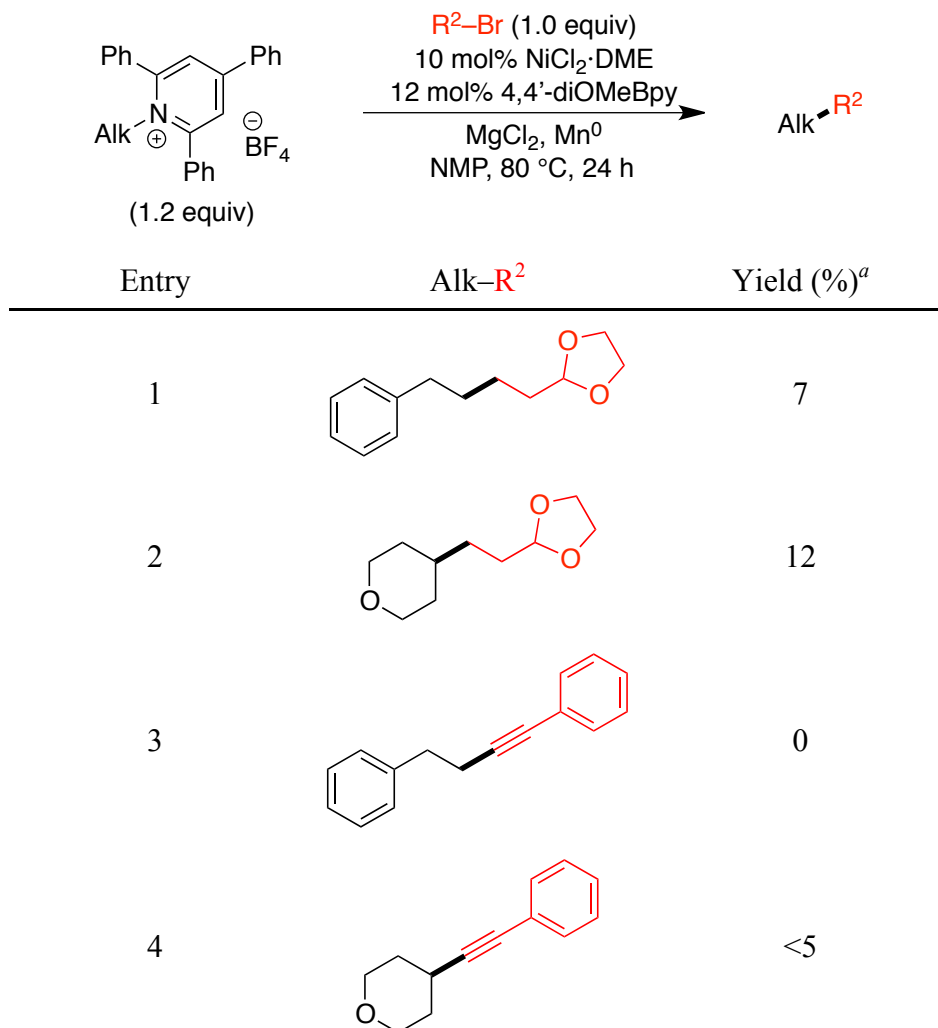
Challenges in Substrate Scope

Lower yields were observed with some classes of aryl bromides (see Scheme below). In particular, aryl bromides with *ortho* substitution, electron-donating substituents, and more complex heteroaryls were challenging. We include these examples to illustrate limitations, but also because these results and yields may be sufficient in certain situations, such as parallel medicinal chemistry efforts.



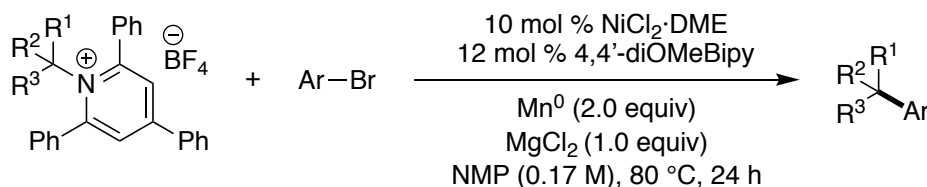
Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as internal standard.

Upon the request of a reviewer, we also investigated our optimized conditions for the cross-coupling of alkylpyridinium salts with alkyl and alkynyl bromides. We saw extremely low yields in these reactions. No attempts at optimization were pursued.



^a Yield determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard.

Reductive Cross-Coupling of Alkyl Pyridinium Salts with Arylbromides



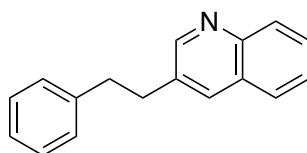
General Procedure A: Cross-Coupling of Primary Pyridinium Salts with Arylbromides

To an oven-dried, 25-mL Schlenk flask was added $\text{NiCl}_2 \cdot \text{DME}$ (22 mg, 0.10 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (26 mg, 0.12 mmol, 12 mol %), magnesium chloride (95 mg, 1.0 mmol, 1.0 equiv), manganese powder (110 mg, 2.0 mmol, 2.0 equiv), alkyl pyridinium salt (1.2 mmol, 1.2 equiv), and arylbromide (1.0 mmol, 1.0 equiv), if solid. The flask was fitted with a rubber septum, sealed with parafilm, and then evacuated and refilled with N_2 (x 3). If the arylbromide was a liquid, it was introduced via syringe at this point. *N*-Methyl-2-pyrrolidone (6.0 mL) was added, and the flask was sealed. The resultant mixture was stirred at 80 °C for 24 h. The mixture was then allowed to cool to room temperature, filtered through a short plug of silica gel, and the filter cake washed with ethyl acetate (4 x 25mL). The filtrate was then washed with sat. NaCl (4 x 25mL). The combined aqueous layers were extracted with ethyl acetate (1 x 25 mL). The combined organic layers were dried with magnesium sulfate and concentrated. The cross-coupled product was then purified via silica gel chromatography.

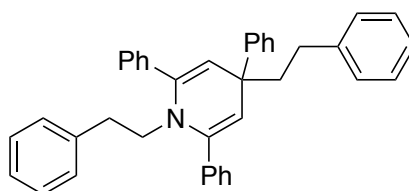
General Procedure B: Cross-Coupling of Secondary Pyridinium Salts with Arylbromides

To an oven-dried, 25-mL Schlenk flask was added $\text{NiCl}_2 \cdot \text{DME}$ (22 mg, 0.10 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (26 mg, 0.12 mmol, 12 mol %), magnesium chloride (95 mg, 1.0 mmol, 1.0 equiv), and manganese powder (110 mg, 2.0 mmol, 2.0 equiv). The flask was fitted with a rubber septum, sealed with parafilm, and then evacuated and refilled with N_2 (x 3). *N*-Methyl-2-pyrrolidone (4.0 mL) was added, and the resultant mixture was heated to 80 °C. To a separate oven-dried, 10-mL Schlenk flask was added alkyl pyridinium salt (1.0 mmol, 1.0 equiv) and arylbromide (1.1 mmol, 1.1 equiv), if solid. The flask was fitted with a rubber septum, sealed with parafilm, and then evacuated and refilled with N_2 (x 3). If the arylbromide was a liquid, it was introduced via syringe at this point. *N*-Methyl-2-pyrrolidone (2.0 mL) was added, and the contents were transferred into a 3-mL nitrogen-purged leur-lock syringe. The solution was added

at a steady rate into the flask containing the catalyst mixture via syringe pump over six hours. The resultant mixture was stirred at 80 °C for an additional 18 hours (24 hours total). The mixture was then allowed to cool to room temperature, filtered through a short plug of silica gel, and the filter cake washed with ethyl acetate (4 x 25mL). The filtrate was then washed with sat. NaCl (4 x 25mL). The combined aqueous layers were extracted with ethyl acetate (1 x 25 mL). The combined organic layers were dried with magnesium sulfate and concentrated. The cross-coupled product was then purified via silica gel chromatography.

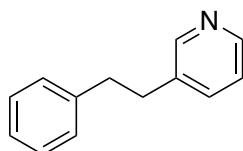


3-Phenethylquinoline (4). Prepared via General Procedure A using 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (10–50% ethyl acetate/hexanes) to give **4** (run 1: 201 mg, 86%; run 2: 195 mg, 84%) as a pale yellow oil: ¹H NMR (600 MHz, CDCl₃) δ 8.75 (d, *J* = 2.2 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.88 – 7.85 (m, 1H), 7.77 – 7.72 (m, 1H), 7.69 – 7.63 (m, 1H), 7.55 – 7.49 (m, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.14 (m, 3H), 3.13 (t, *J* = 7.8 Hz, 2H), 3.03 (t, *J* = 7.8 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 152.0, 146.9, 140.8, 134.4, 134.2, 129.2, 128.7, 128.5, 128.1, 127.3, 126.6, 126.2, 37.5, 35.1. The spectral data matches that reported in the literature.²

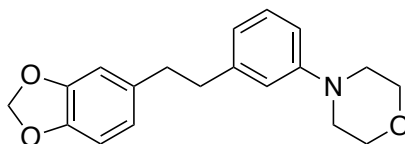


1,4-Diphenethyl-2,4,6-triphenyl-1,4-dihydropyridine (5). In a N₂-filled glovebox: To an oven-dried 1-dram vial was added magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **3a** (50 mg, 0.10 mmol, 1.0 equiv). *N*-Methyl-2-pyrrolidone (0.6 mL) was then added. The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. The 4-addition byproduct (**5**) was then isolated by preparative thin layer chromatography: ¹H NMR

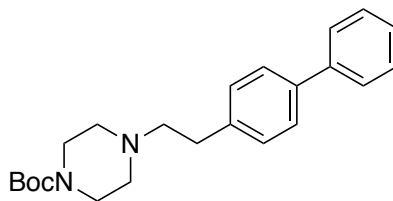
(400 MHz, CDCl₃) δ 7.57 (s, 6H), 7.44 – 7.35 (m, 8H), 7.25 – 7.11 (m, 6H), 7.04 – 6.95 (m, 3H), 6.51 – 6.44 (m, 2H), 5.18 (s, 2H), 3.29 – 3.20 (m, 2H), 2.72 – 2.63 (m, 2H), 2.37 – 2.28 (m, 2H), 2.20 – 2.11 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 151.4, 143.1, 143.0, 139.1, 138.0, 128.42, 128.39, 128.37, 128.35, 128.3, 128.11, 128.08, 128.00, 126.4, 125.8, 125.6, 125.5, 113.3, 50.0, 46.7, 43.8, 34.7, 32.7; FTIR (neat) 3024, 1600, 1494, 1388, 756, 698 cm⁻¹; HRMS (ESI+) [M+H]⁺ calculated for C₃₉H₃₆N: 518.2842, found 518.2823.



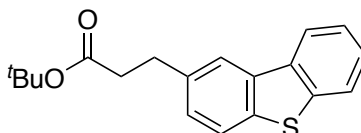
3-Phenethylpyridine (8). Prepared via General Procedure A using 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (5–60% ether/hexanes w/ 1% Et₃N) to give **8** (run 1: 115 mg, 63%; run 2: 110 mg, 60%) as a pale yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 8.45 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.44 – 8.41 (m, 1H), 7.43 (dt, *J* = 7.8, 2.0 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.23 – 7.13 (m, 4H), 2.93 (s, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 150.2, 147.6, 141.0, 136.9, 136.0, 128.59, 128.57, 126.3, 123.3, 37.6, 35.1. The spectral data matches that reported in the literature.³



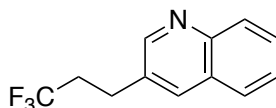
4-(3-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)phenyl)morpholine (9). Prepared via General Procedure A using 1-(2-(benzo[d][1,3]dioxol-5-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (5–20% ethyl acetate/hexanes) to give **9** (run 1: 164 mg, 53%; run 2: 181 mg, 58%) as an off-white solid (mp 44–46 °C): ¹H NMR (600 MHz, CDCl₃) δ 7.20 (t, *J* = 7.8 Hz, 1H), 6.76 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.74 – 6.70 (m, 3H), 6.68 (d, *J* = 1.6 Hz, 1H), 6.63 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.92 (s, 2H), 3.88 – 3.83 (m, 4H), 3.16 – 3.11 (m, 4H), 2.83 (s, 4H); ¹³C NMR (151 MHz, CDCl₃) δ 151.4, 147.5, 145.6, 142.7, 135.7, 129.1, 121.2, 120.3, 116.1, 113.4, 109.0, 108.1, 100.8, 67.0, 49.5, 38.6, 37.7; FTIR (neat) 2853, 1600, 1489, 1443, 1242, 1121, 928, 696 cm⁻¹; HRMS (ESI+) [M+H]⁺ calculated for C₁₉H₂₂NO₃: 312.1594, found 312.1590.



tert-Butyl 4-(2-([1,1'-biphenyl]-4-yl)ethyl)piperazine-1-carboxylate (10). Prepared via General Procedure A using 1-(2-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (10–20% ethyl acetate/hexanes) to give **10** (run 1: 268 mg, 73%; run 2: 275 mg, 75%) as a white solid (mp 85–89 °C): ^1H NMR (400 MHz, CDCl_3) δ 7.61 – 7.55 (m, 2H), 7.55 – 7.48 (m, 2H), 7.48 – 7.39 (m, 2H), 7.38 – 7.31 (m, 1H), 7.31 – 7.27 (m, 2H), 3.52 – 3.44 (m, 4H), 2.90 – 2.81 (m, 2H), 2.69 – 2.60 (m, 2H), 2.52 – 2.46 (m, 4H), 1.47 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 154.8, 141.0, 139.2, 139.1, 129.1, 128.8, 127.2, 127.1, 127.0, 79.7, 60.5, 53.0, 43.7 (br), 33.2, 28.5; FTIR (neat) 2929, 2807, 1695, 1420, 1247, 1171, 1003, 761 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{31}\text{N}_2\text{O}_2$: 367.2380, found 367.2376.

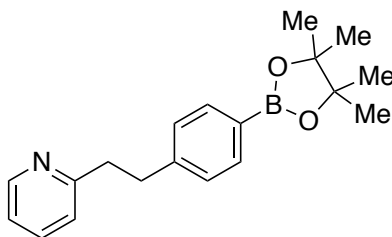


tert-Butyl 3-(dibenzo[*b,d*]thiophen-2-yl)propanoate (11). Prepared via General Procedure A using 1-(3-(*tert*-butoxy)-3-oxopropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (2–10% diethyl ether/hexanes) to give **11** (run 1: 200 mg, 64%; run 2: 199 mg, 64%) as a white solid (mp 53–55 °C): ^1H NMR (600 MHz, CDCl_3) δ 8.19 – 8.13 (m, 1H), 8.02 (s, 1H), 7.90 – 7.84 (m, 1H), 7.79 (d, $J = 8.2$ Hz, 1H), 7.50 – 7.44 (m, 2H), 7.37 – 7.32 (m, 1H), 3.12 (t, $J = 7.8$ Hz, 2H), 2.67 (t, $J = 7.8$ Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.2, 139.8, 137.23, 137.21, 135.8, 135.4, 127.5, 126.6, 124.3, 122.9, 122.7, 121.5, 121.2, 80.5, 37.5, 31.2, 28.1; FTIR (neat) 2976, 2930, 1726, 1366, 1150, 764 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{19}\text{H}_{21}\text{O}_2\text{S}$: 313.1257, found 313.1245.

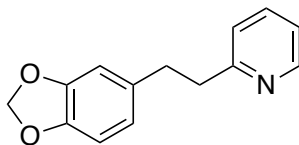


3-(3,3,3-Trifluoropropyl)quinoline (12). Prepared via General Procedure A using 2,4,6-triphenyl-1-(3,3,3-trifluoropropyl)pyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (10–40% ethyl acetate/hexanes) to give **12** (run 1: 188 mg,

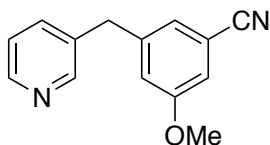
84%; run 2: 173 mg, 77%) as a pale yellow solid (mp 54–55 °C): ^1H NMR (400 MHz, CDCl_3) δ 8.80 (d, $J = 2.3$ Hz, 1H), 8.10 (d, $J = 8.5$ Hz, 1H), 7.97 (d, $J = 1.3$ Hz, 1H), 7.83 – 7.75 (m, 1H), 7.75 – 7.66 (m, 1H), 7.60 – 7.51 (m, 1H), 3.14 – 3.05 (m, 2H), 2.60 – 2.43 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 151.3, 147.2, 134.5, 131.5, 129.3, 129.2, 127.9, 127.4, 127.0, 126.4 (q, $J_{\text{C-F}} = 276.9$ Hz), 35.3 (q, $J_{\text{C-F}} = 28.8$ Hz), 25.7 (q, $J_{\text{C-F}} = 3.3$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ –66.43; FTIR (neat) 2955, 1496, 1235, 1143, 1097, 976, 756 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{12}\text{H}_{11}\text{F}_3\text{N}$: 226.0838, found 266.0838.



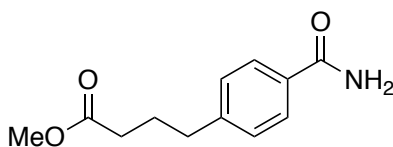
2-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenethyl)pyridine (13). Prepared via General Procedure A using 2,4,6-triphenyl-1-(2-(pyridin-2-yl)ethyl)pyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (2–10% ethyl acetate/hexanes) to give **13** (run 1: 183 mg, 59%; run 2: 203 mg, 66%) as a white solid (mp 95–96 °C): ^1H NMR (400 MHz, CDCl_3) δ 8.59 – 8.52 (m, 1H), 7.72 (d, $J = 8.0$ Hz, 2H), 7.55 (td, $J = 7.7, 1.9$ Hz, 1H), 7.21 (d, $J = 7.9$ Hz, 2H), 7.13 – 7.08 (m, 1H), 7.08 – 7.01 (m, 1H), 3.13 – 3.02 (m, 4H), 1.33 (s, 12H); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$) δ 161.9, 150.13, 150.11, 146.2, 137.0, 135.6, 128.8, 123.7, 122.0, 84.4, 40.5, 36.5, 25.2; FTIR (neat) 2978, 1361, 1144, 1090, 659 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{19}\text{H}_{25}\text{BNO}_2$: 310.1973, found 310.1972.



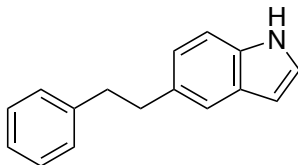
2-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)pyridine (14). Prepared via General Procedure A using 1-(2-(benzo[d][1,3]dioxol-5-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (5–40% ether/hexanes) to give **14** (run 1: 83 mg, 36%; run 2: 77 mg, 34%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 8.56 (ddd, $J = 4.9, 1.9, 0.9$ Hz, 1H), 7.57 (td, $J = 7.7, 1.9$ Hz, 1H), 7.16 – 7.09 (m, 1H), 7.09 – 7.03 (m, 1H), 6.74 – 6.67 (m, 2H), 6.63 (dd, $J = 7.9, 1.7$ Hz, 1H), 5.92 (s, 2H), 3.09 – 3.01 (m, 2H), 3.01 – 2.92 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.2, 149.5, 147.6, 145.8, 136.4, 135.5, 123.2, 121.4, 121.3, 109.1, 108.3, 100.9, 40.7, 35.9. The spectral data matches that reported in the literature.⁴



3-Methoxy-5-(pyridin-3-ylmethyl)benzonitrile (15). Prepared via General Procedure B using 2,4,6-triphenyl-1-(pyridin-3-ylmethyl)pyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (20–60% ethyl acetate/hexanes) to give **15** (run 1: 129 mg, 58%; run 2: 127 mg, 57%) as an off-white solid (mp 74–78 °C): ^1H NMR (400 MHz, CDCl_3) δ 8.54 – 8.46 (m, 2H), 7.49 – 7.41 (m, 1H), 7.26 – 7.23 (m, 1H), 7.08 – 7.04 (m, 1H), 7.03 – 6.98 (m, 1H), 6.95 – 6.90 (m, 1H), 3.97 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.9, 150.1, 148.3, 142.8, 136.3, 134.8, 124.8, 123.7, 120.0, 118.6, 114.8, 113.4, 55.6, 38.6; FTIR (neat) 3029, 2923, 2841, 2228, 1591, 1292, 1059, 718 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}$: 225.1022, found 255.1021.

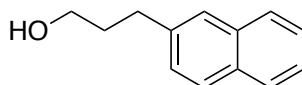


Methyl 4-(4-carbamoylphenyl)butanoate (16). Prepared via General Procedure A using 1-(4-methoxy-4-oxobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (50–100% ethyl acetate/hexanes) to give **16** (run 1: 103 mg, 46%; run 2: 125 mg, 56%) as a light pink solid (mp 100–101 °C): ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H, *overlaps with* CHCl_3), 6.06 (s, br, 1H), 5.69 (s, br, 1H), 3.67 (s, 3H), 2.70 (t, J = 7.6 Hz, 2H), 2.33 (t, J = 7.4 Hz, 2H), 1.97 (p, J = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.7, 169.2, 145.9, 131.1, 128.8, 127.6, 51.6, 35.0, 33.3, 26.2; FTIR (neat) 3406, 3192, 1740, 1645, 1172 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{12}\text{H}_{16}\text{NO}_3$: 222.1125, found 222.1124.

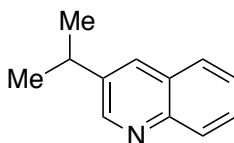


5-Phenethyl-1H-indole (17). Prepared via General Procedure B using 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (5–60 % diethyl ether/hexanes) to give **17** (run 1: 105 mg, 47%; run 2: 110 mg, 50%) as a white solid: ^1H NMR (400 MHz, CDCl_3) δ 8.09 (s, br, 1H), 7.51 – 7.45 (m, 1H), 7.35

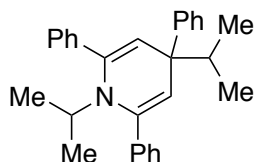
– 7.27 (m, 3H), 7.25 – 7.16 (m, 4H), 7.06 (dd, $J = 8.3, 1.7$ Hz, 1H), 6.54 – 6.47 (m, 1H), 3.07 – 2.92 (m, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 142.3, 134.4, 133.3, 128.5, 128.3, 128.1, 125.8, 124.3, 123.0, 119.9, 110.8, 102.3, 38.9, 38.2. The spectral data matches that reported in the literature.⁵



3-(Naphthalen-2-yl)propan-1-ol (18). Prepared via General Procedure A using 1-(3-hydroxypropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (10–40% ethyl acetate/hexanes) to give **18** (run 1: 145 mg, 78%; run 2: 137 mg, 74%) as a white solid: ^1H NMR (600 MHz, CDCl_3) δ 7.73 (d, $J = 8.0$ Hz, 1H), 7.72 – 7.68 (m, 2H), 7.57 (s, 1H), 7.40 – 7.33 (m, 2H), 7.30 – 7.26 (m, 1H), 3.64 (t, $J = 6.4$ Hz, 2H), 2.84 – 2.78 (m, 2H), 1.96 – 1.88 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 139.5, 133.8, 132.19, 128.12, 127.8, 127.6, 127.4, 126.6, 129.1, 125.3, 62.4, 34.3, 32.4. The spectral data matches that reported in the literature.⁶

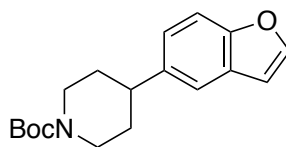


3-Isopropylquinoline (6). Prepared via General Procedure B using 1-isopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (5–15% ethyl acetate/hexanes) to give **6** (run 1: 119 mg, 70%; run 2: 118 mg, 69%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 8.84 (d, $J = 2.3$ Hz, 1H), 8.07 (d, $J = 8.5$ Hz, 1H), 7.93 (d, $J = 2.2$ Hz, 1H), 7.82 – 7.75 (m, 1H), 7.70 – 7.61 (m, 1H), 7.56 – 7.47 (m, 1H), 3.14 (hept, $J = 7.0$ Hz, 1H), 1.38 (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 151.3, 146.9, 141.1, 131.8, 129.1, 128.5, 128.2, 127.5, 126.5, 31.9, 23.7. The spectral data matches that reported in the literature.⁷

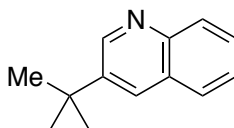


1,4-Diisopropyl-2,4,6-triphenyl-1,4-dihydropyridine (7). In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **3b** (44 mg, 0.10 mmol, 1.0 equiv).

N-Methyl-2-pyrrolidone (0.6 mL) was then added. The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. The 4-addition byproduct (**7**) was then isolated by preparative thin layer chromatography: ¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.60 (m, 4H), 7.50 – 7.43 (m, 2H), 7.42 – 7.29 (m, 8H), 7.20 – 7.12 (m, 1H), 5.29 (s, 2H), 3.30 (hept, *J* = 6.9 Hz, 1H), 2.01 (hept, *J* = 6.8 Hz, 1H), 0.78 (d, *J* = 6.8 Hz, 6H), 0.58 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 151.7, 145.2, 140.9, 128.2, 128.0, 127.9, 127.7, 126.8, 125.1, 115.3, 53.6, 47.0, 39.5, 22.6, 18.4; FTIR (neat) 2966, 1658, 1445, 1156, 748, 699 cm⁻¹; HRMS (ESI+) [*M*+*H*]⁺ calculated for C₂₉H₃₂N: 394.2529, found 394.2513.

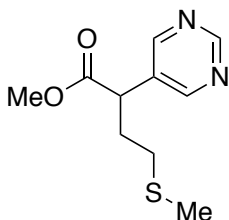


tert-Butyl 4-(benzofuran-5-yl)piperidine-1-carboxylate (19). Prepared via General Procedure B using 1-(1-(*tert*-butoxycarbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (2–10% ethyl acetate/hexanes) to give **19** (run 1: 218 mg, 72%; run 2: 210 mg, 70%) as a white solid: ¹H NMR (600 MHz, CDCl₃) δ 7.62 – 7.58 (m, 1H), 7.44 – 7.40 (m, 2H), 7.17 – 7.12 (m, 1H), 6.73 (s, 1H), 4.37 – 4.17 (br m, 2H), 2.92 – 2.77 (m, 2H), 2.74 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.89 – 1.83 (m, 2H), 1.73 – 1.62 (m, 2H), 1.49 (s, 9H); ¹³C NMR (151 MHz, CDCl₃) δ 154.9, 153.7, 145.3, 140.5, 127.6, 123.4, 118.7, 111.2, 106.5, 79.4, 44.5 (br), 42.7, 33.8, 28.5. The spectral data matches that reported in the literature.⁸

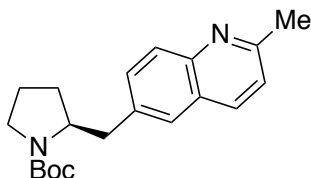


3-(1-Methylcyclopropyl)quinoline (20). Prepared via General Procedure B using 1-(1-methylcyclopropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (5–20% ethyl acetate/hexanes) to give **20** (run 1: 61 mg, 33%; run 2: 65 mg, 36%) as a yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 8.84 (d, *J* = 2.3 Hz,

1H), 8.06 (d, $J = 8.4$ Hz, 1H), 7.99 – 7.93 (m, 1H), 7.76 (d, $J = 8.1$ Hz, 1H), 7.69 – 7.60 (m, 1H), 7.56 – 7.47 (m, 1H), 1.51 (s, 3H), 1.00 (t, $J = 5.4$ Hz, 2H), 0.87 (t, $J = 5.4$ Hz, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 151.0, 146.5, 139.6, 132.9, 129.1, 128.5, 127.9, 127.3, 126.6, 25.6, 18.4, 15.0; FTIR (neat) 3076, 3001, 2958, 2925, 2870, 1492, 1016, 750 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{13}\text{H}_{14}\text{N}$: 184.1121; found 184.1116.

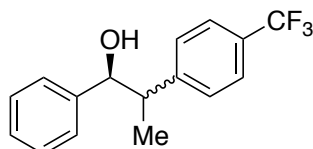


Methyl 4-(methylthio)-2-(pyrimidin-5-yl)butanoate (21). Prepared via General Procedure B using 1-(1-methoxy-4-(methylthio)-1-oxobutan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (5–30% ethyl acetate/hexanes) to give **21** (run 1: 113 mg, 50%; run 2: 116 mg, 51%) as a pale yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 9.15 (s, 1H), 8.71 (s, 2H), 3.87 – 3.82 (m, 1H), 3.71 (s, 3H), 2.54 – 2.34 (m, 3H), 2.12 – 2.01 (m, 1H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.6, 158.1, 156.7, 132.1, 52.8, 45.4, 31.9, 31.6, 15.4; FTIR (neat) 2917, 1736, 1561, 1412, 1203, 728 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{10}\text{H}_{15}\text{N}_2\text{O}_2\text{S}$: 227.0849, found 227.0851.



tert-Butyl (S)-2-((2-methylquinolin-6-yl)methyl)pyrrolidine-1-carboxylate (22). Prepared via General Procedure B using (S)-1-((1-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)methyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (10–50% ethyl acetate/hexanes) to give **22** (run 1: 191 mg, 59%; run 2: 182 mg, 56%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3 , mixture of rotamers) δ 8.03 – 7.92 (m, br, 2H), 7.62 – 7.49 (m, br, 2H), 7.31 – 7.26 (m, br, 1H, *overlaps with CHCl₃*), 4.16 – 4.02 (m, br, 1H), 3.44 – 3.15 (m, br, 3H), 2.80 – 2.65 (m, br, 1H), 2.74 (s, br, 3H), 1.81 – 1.70 (m, br, 4H), 1.51 (s, br, 9H); ^{13}C NMR (101 MHz, CDCl_3 , mixture of rotamers) δ 158.5 (major), 158.3 (minor), 154.6 (minor), 154.6 (major), 146.6, 136.8 (minor), 135.9 (major), 132.0 (minor), 131.4 (major), 128.5 (major), 128.2 (minor), 127.4, 127.3, 126.5, 122.2 (major), 122.0 (minor), 79.4

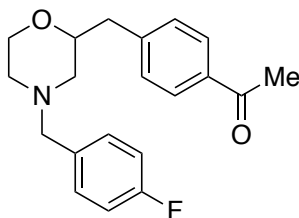
(major), 79.2 (minor), 58.7, 46.9 (minor), 46.3 (major), 40.5 (major), 39.5 (minor), 29.8 (major), 29.0 (minor), 28.6, 25.3, 23.5 (minor), 22.7 (major); FTIR (neat) 2972, 2875, 1691, 1395, 1170, 1116, 772 cm^{-1} ; HRMS (ESI+) $[M+H]^+$ calculated for $\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_2$: 327.2067, found 327.2066. The enantiomeric excess was determined to be >99% by chiral HPLC analysis (CHIRALPAK IA, 0.2 mL/min, 2% *i*-PrOH/hexanes, $\lambda=210$ nm); $t_R(\text{major}) = 103.75$ min, $t_R(\text{minor}) = 111.85$ min.



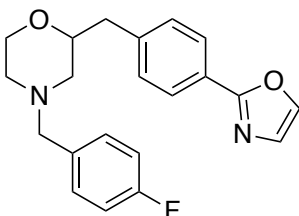
(S)-1-Phenyl-2-(4-(trifluoromethyl)phenyl)propan-1-ol (23). Prepared via General Procedure B using 1-((1*R*,2*S*)-1-hydroxy-1-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (5–20% Diethyl ether/hexanes) to give **23** as a 1:1 mixture of diastereomers (run 1: 111 mg, 39%; run 2: 132 mg, 47%) as a white solid (mp 132–134 °C): The diastereomers of **23** were then separated using preparatory SFC with a chiral stationary phase to give analytically pure samples for characterization.

Diastereomer A: ^1H NMR (600 MHz, CDCl_3) δ 7.48 (d, $J = 8.0$ Hz, 2H), 7.35 – 7.21 (m, 5H, *overlaps with CHCl₃*), 7.20 – 7.12 (m, 2H), 4.81 (dd, $J = 6.0, 3.3$ Hz, 1H), 3.17 (p, $J = 6.8$ Hz, 1H), 1.85 (d, $J = 3.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 147.7, 142.4, 128.6 (q, $J_{\text{C-F}} = 37.4$ Hz), 128.5, 128.2, 127.6, 126.3, 125.8 (q, $J_{\text{C-F}} = 38.4$ Hz), 125.0 (q, $J_{\text{C-F}} = 4.0$ Hz), 78.6, 47.2, 15.3; ^{19}F NMR (376 MHz, CDCl_3) δ –62.34; FTIR (neat) 3740, 1384, 1329, 1110, 1022 cm^{-1} .

Diastereomer B: ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.0$ Hz, 2H), 7.50 – 7.30 (m, 7H), 4.74 (dd, $J = 8.4, 2.2$ Hz, 1H), 3.14 (p, $J = 7.3$ Hz, 1H), 1.87 (d, $J = 2.6$ Hz, 1H), 1.14 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 147.84 (q, $J_{\text{C-F}} = 1.01$ Hz), 142.4, 129.0 (q, $J_{\text{C-F}} = 32.3$ Hz), 128.5, 128.4, 128.1, 126.8, 125.4 (q, $J_{\text{C-F}} = 4.0$ Hz), 124.3 (q, $J_{\text{C-F}} = 272.7$ Hz), 79.4, 47.8, 18.3; ^{19}F NMR (376 MHz, CDCl_3) δ –62.32; FTIR (neat) 3368, 2972, 1329, 1162, 1112, 1071, 700 cm^{-1} ; HRMS (ESI+) $[M-\text{H}_2\text{O}+H]^+$ calculated for $\text{C}_{16}\text{H}_{14}\text{F}_3$: 263.1048, found 263.1044.

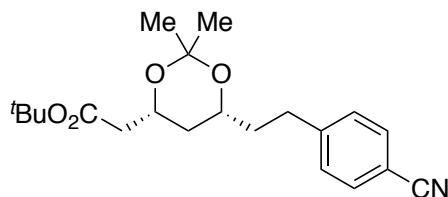


1-(4-((4-(4-Fluorobenzyl)morpholin-2-yl)methyl)phenyl)ethan-1-one (24). Prepared via General Procedure A using 1-((4-(4-fluorobenzyl)morpholin-2-yl)methyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified by silica gel chromatography (20–75% ethyl acetate/hexanes w/ 1% Et₃N) to give **24** (run 1: 244 mg, 77%; run 2: 258 mg, 82%) as a pale yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.85 (m, 2H), 7.33 – 7.28 (m, 2H), 7.28 – 7.21 (m, 2H, *overlaps with CHCl₃*), 7.04 – 6.94 (m, 2H), 3.88 – 3.80 (m, 1H), 3.80 – 3.71 (m, 1H), 3.59 (td, *J* = 11.3, 2.5 Hz, 1H), 3.51 – 3.35 (m, 2H), 2.86 (dd, *J* = 13.9, 7.7 Hz, 1H), 2.78 – 2.66 (m, 2H), 2.65 – 2.55 (m, 1H), 2.58 (s, 3H), 2.13 (td, *J* = 11.3, 3.3 Hz, 1H), 1.99 – 1.89 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 198.0, 162.2 (d, *J*_{C-F} = 245.1 Hz), 144.2, 135.52, 133.46 (d, *J*_{C-F} = 3.1 Hz), 130.7 (d, *J*_{C-F} = 8.0 Hz), 129.6, 128.6, 115.2 (d, *J*_{C-F} = 21.2 Hz), 76.2, 67.0, 62.5, 58.4, 52.8, 40.3, 26.8; ¹⁹F NMR (376 MHz, CDCl₃) δ –115.59; FTIR (neat) 2935, 2805, 1682, 1268, 842 cm⁻¹; HRMS (ESI+) [*M*+H]⁺ calculated for C₂₀H₂₃FN₂O₂: 328.1707, found 328.1703.



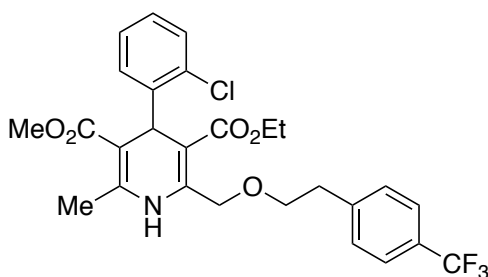
4-(4-Fluorobenzyl)-2-(4-(oxazol-2-yl)benzyl)morpholine (25). Prepared via General Procedure A using 1-((4-(4-fluorobenzyl)morpholin-2-yl)methyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate on a 4.0 mmol scale. The crude mixture was purified by silica gel chromatography (10–15% ethyl acetate/hexanes) to give **25** (1.04 g, 74%) as a pale yellow oil: ¹H NMR (600 MHz, CDCl₃) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.69 (s, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.23 (m, 2H, *overlaps with CHCl₃*), 7.22 (s, 1H), 6.99 (t, *J* = 8.7 Hz, 2H), 3.87 – 3.81 (m, 1H), 3.81 – 3.74 (m, 1H), 3.65 – 3.57 (m, 1H), 3.48 (d, *J* = 13.0 Hz, 1H), 3.39 (d, *J* = 13.0 Hz, 1H), 2.87 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.76 – 2.69 (m, 2H), 2.60 (d, *J* = 11.2 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.95 (t, *J* = 10.5 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 162.05 (d, *J*_{C-F} = 244.9 Hz),

162.04, 140.8, 138.3, 133.4 (d, $J_{C-F} = 3.2$ Hz), 130.5 (d, $J_{C-F} = 7.9$ Hz), 129.7, 128.4, 126.4, 125.7, 115.1 (d, $J_{C-F} = 21.2$ Hz), 76.2, 66.9, 62.4, 58.3, 52.7, 40.1; ^{19}F NMR (565 MHz, CDCl_3) δ -115.72; FTIR (neat) 3125, 3040, 2935, 2856, 2805, 1921, 1509, 1221, 1112, 846, 715 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{21}\text{H}_{22}\text{FN}_2\text{O}_2$: 353.1660, found 353.1654.



tert-Butyl 2-((4R,6R)-6-(4-cyanophenethyl)-2,2-dimethyl-1,3-dioxan-4-yl)acetate (26).

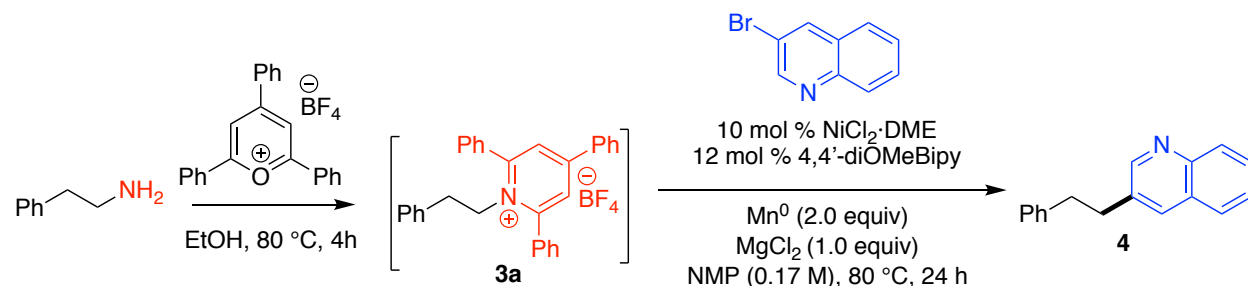
Prepared via General Procedure B using 1-(2-((4R,6R)-6-(2-(*tert*-butoxy)-2-oxoethyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (5–60% ether/hexanes) to give **26** (run 1: 191 mg, 53%; run 2: 219 mg, 61%) as a clear oil: ^1H NMR (400 MHz, CDCl_3) δ 7.59 (d, $J = 8.2$ Hz, 2H), 7.30 (d, $J = 8.2$ Hz, 2H), 4.23 (dtd, $J = 11.5, 6.5, 2.5$ Hz, 1H), 3.86 – 3.74 (m, 1H), 2.91 – 2.65 (m, 2H), 2.45 (dd, $J = 15.2, 6.9$ Hz, 1H), 2.31 (dd, $J = 15.2, 6.3$ Hz, 1H), 1.90 – 1.76 (m, 1H), 1.78 – 1.64 (m, 1H), 1.56 (dt, $J = 12.7, 2.4$ Hz, 1H), 1.46 (s, 9H), 1.43 (s, 3H), 1.41 (s, 3H), 1.29 – 1.19 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.3, 147.8, 132.2, 129.3, 119.1, 109.7, 98.8, 80.7, 67.5, 66.2, 42.6, 37.3, 36.5, 31.4, 30.1, 28.1, 19.8; FTIR (neat) 2980, 2227, 1729, 1368, 1159, 845 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{21}\text{H}_{30}\text{NO}_4$: 360.2169, found 360.2167.



3-Ethyl 5-methyl 4-(2-chlorophenyl)-6-methyl-2-((4-(trifluoromethyl)phenethoxy)methyl)-1,4-dihydropyridine-3,5-dicarboxylate (27). Prepared via General Procedure A using 1-(2-((4-(2-chlorophenyl)-3-(ethoxycarbonyl)-5-(methoxycarbonyl)-6-methyl-1,4-dihydropyridin-2-yl)methoxy)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate. The crude mixture was purified via silica gel chromatography (5–40% ethyl acetate/hexanes) to give **27** (run 1: 326 mg, 61%; run 2: 357 mg, 67%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, $J = 7.7$ Hz,

2H), 7.43 – 7.35 (m, 2H), 7.31 (dd, $J = 7.7, 1.7$ Hz, 1H), 7.22 (dd, $J = 8.0, 1.4$ Hz, 1H), 7.16 – 7.07 (m, 1H), 7.08 – 6.99 (m, 1H), 6.68 (s, 1H), 5.36 (s, 1H), 4.79 – 4.62 (m, 2H), 4.10 – 3.97 (m, 2H), 3.88 – 3.73 (m, 2H), 3.60 (s, 3H), 3.02 (t, $J = 6.3$ Hz, 2H), 2.08 (s, 3H), 1.17 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 167.9, 167.1, 145.6, 145.1, 143.6, 143.0, 132.4, 131.5, 129.28, 129.27, 129.0 (q, $J_{\text{C-F}} = 32.5$ Hz), 127.4, 126.8, 125.6 (q, $J_{\text{C-F}} = 3.7$ Hz), 123.7 (q, $J_{\text{C-F}} = 271.7$ Hz), 103.9, 101.4, 71.4, 67.7, 59.8, 50.8, 37.2, 36.0, 19.3, 14.3; ^{19}F NMR (376 MHz, CDCl_3) δ –62.43; FTIR (neat) 3393, 2948, 1693, 1483, 1326, 1210, 1115, 756 cm^{-1} ; HRMS (ESI+) $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{27}\text{H}_{28}\text{ClF}_3\text{NO}_5$: 538.1603, found 538.1590.

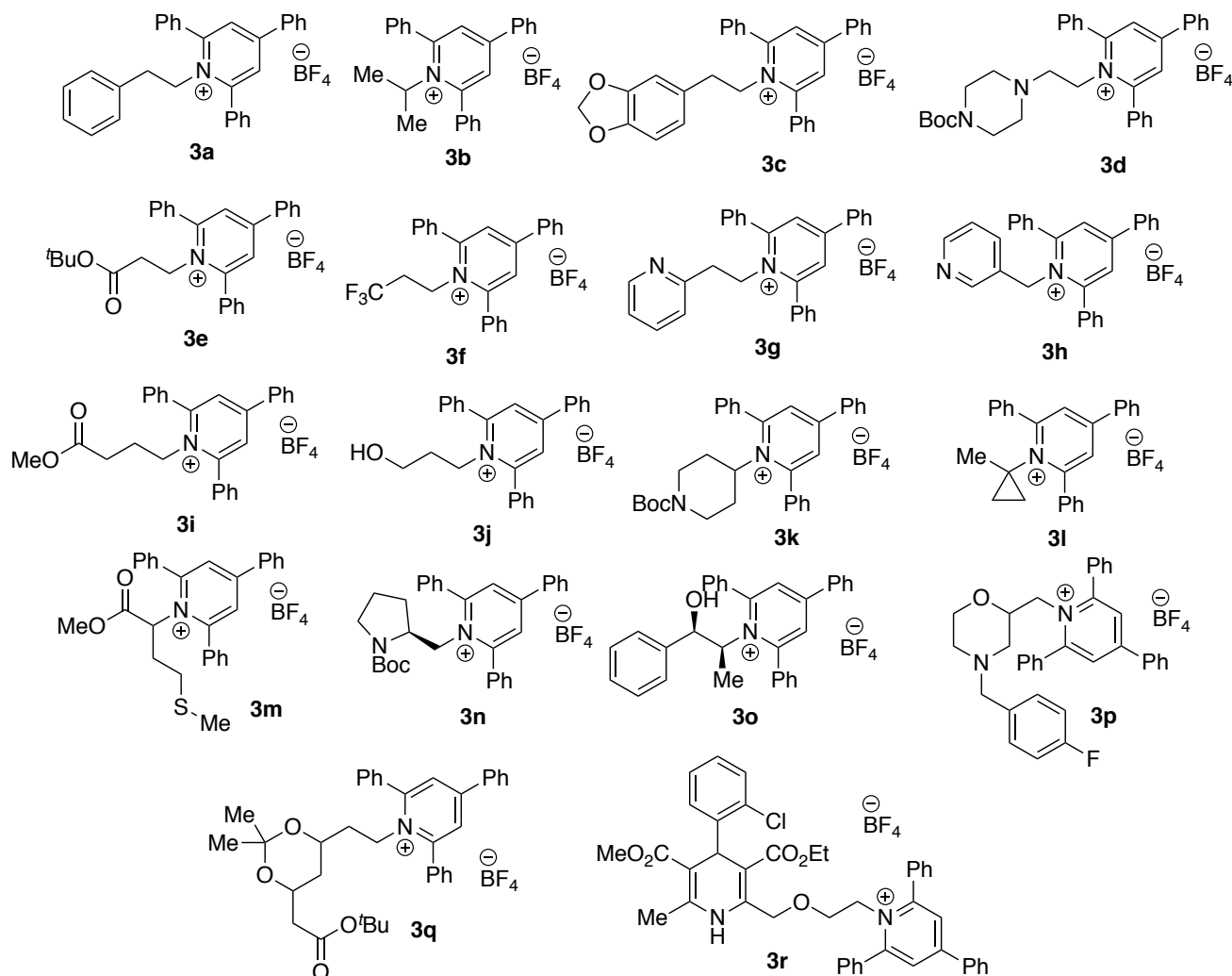
Cross-Coupling with In Situ Pyridinium Salt Formation



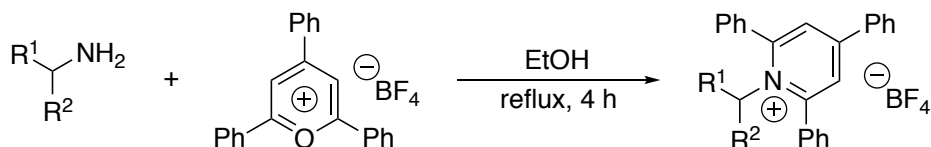
Product **4** was formed via a procedure adapted from General Procedure C and A. The amine (0.15 mL, 1.2 mmol, 1.2 equiv) was added to a suspension of 2,4,6-triphenylpyrillium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv) and EtOH (1.0M) in a round-bottomed flask. The flask was fitted with a reflux condenser. The mixture was stirred and heated at reflux in an oil bath at 80–85 °C for 4 h. The mixture was allowed to cool to room temperature and concentrated. To the flask was added NiCl₂·DME (22 mg, 0.10 mmol, 10 mol %), 4,4' - dimethoxy-2,2'-bipyridine (26 mg, 0.12 mmol, 12 mol %), magnesium chloride (95 mg, 1.0 mmol, 1.0 equiv), manganese powder (110 mg, 2.0 mmol, 2.0 equiv) and aryl bromide (0.14 mL, 1.0 mmol, 1.0 equiv). N-Methyl-2-pyrrolidone (6.0 mL) was added, and the mixture was stirred at 80 °C for 24 h. The mixture was then allowed to cool to room temperature and filtered through a short plug of silica gel. The silica gel was washed with ethyl acetate (4 x 25 mL). The filtrate was then washed with sat. NaCl (4 x 25 mL). The combined aqueous layers were extracted with ethyl acetate (1 x 25 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. The crude mixture was purified by silica gel chromatography (1–50% ethyl acetate/hexanes) to give **4** (116 mg, 50%).

Preparation of Alkyl Pyridinium Salts

Pyridinium salts **3a**, **3c**, **3d**, **3k**, **3n**, **3p**, and **3q** were all synthesized as described previously,⁹ as was **3g**,¹⁰ **3h**,¹¹ and **3l**.¹²



General Procedure C: Conversion of Amines to Pyridinium Salts⁹

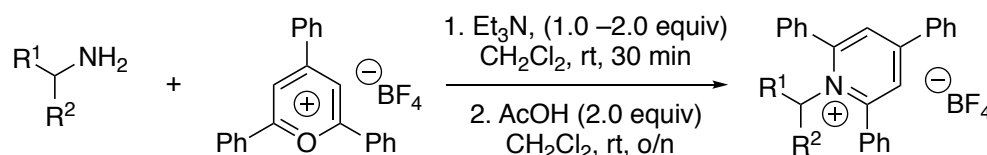


The amine (1.2 equiv) was added to a suspension of 2,4,6-triphenylpyridinium tetrafluoroborate (1.0 equiv) and EtOH (1.0 M) in a round-bottomed flask. The flask was fitted with a reflux condenser. The mixture was stirred and heated at reflux in an oil bath at 80–85 °C for 4 h. The mixture was then allowed to cool to room temperature. If product precipitation occurred during reflux, the solid was filtered, washed with EtOH (3 x 25 mL) and then Et₂O (3 x

25 mL), and dried under high vacuum. If product precipitation did not occur during reflux, the solution was diluted with Et₂O (2–3x volume of EtOH used) and vigorously stirred for 1 h to induce trituration. The resulting solid pyridinium salt was filtered and washed with Et₂O (3 x 25 mL). If the pyridinium salt failed to precipitate at this point, the flask containing the reaction mixture and Et₂O was sealed with parafilm and stored in a –27 °C freezer for 1–3 days (or until precipitation occurred). The cold mixture was quickly filtered and washed with Et₂O (3 x 25 mL) to give the corresponding analytically pure pyridinium salt. If the salt still did not precipitate, it was subjected to silica gel chromatography with acetone/DCM.

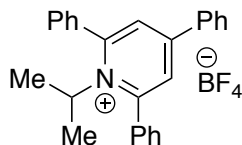
The corresponding amine hydrochloride salts can also be used following a modified procedure: Et₃N (1.2 equiv) was added to a mixture of the corresponding alkyl ammonium hydrochloride salt (1.2 equiv) and EtOH (1.0 M). After stirring the mixture for 30 min at room temperature, 2,4,6-triphenylpyrylium tetrafluoroborate (1 equiv) was added. From this point forward, the same procedure was followed as for alkyl amines described above; however prior to washing the solid product with EtOH and/or Et₂O, the mixture was washed with water (3 x 25 mL) to remove Et₃N·HCl.

General Procedure D: Conversion of Amines to Pyridinium Salts¹⁰

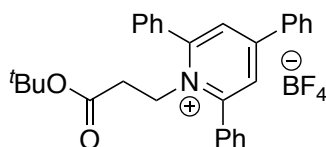


The amine (1.0 equiv) was added to a suspension of 2,4,6-triphenylpyrylium tetrafluoroborate (1.0 equiv), powdered activated 4Å molecular sieves (~500 mg/mmol), and CH₂Cl₂ (0.5 M) in a round-bottomed flask equipped with a stirbar. The flask was fitted with a septum and a vent needle. The mixture was stirred as Et₃N (1.0 equiv for free base amines; 2.0 equiv for amine hydrochloride salts) was added by syringe. The vent needle was removed, and the mixture was stirred at rt for 30 min. The vent needle was reinserted before the addition of acetic acid (2.0 equiv). The needle was again removed, and the mixture was stirred at rt overnight. The mixture was then filtered through a short pad of Celite using CH₂Cl₂ to rinse the flask and Celite pad. The filtrate was then washed successively with aq. HCl (1.0 M, 2 x 30 mL), aq. NaHCO₃ (sat. 2 x 30 mL), and sat. NaCl (2 x 30 mL), dried (MgSO₄), filtered, and concentrated. Et₂O (ca. 100 mL) was added to the solid to precipitate the pyridinium salt, which

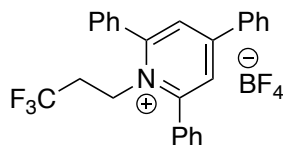
was then isolated by filtration. If the salt still did not precipitate, it was purified by silica gel chromatography with acetone/CH₂Cl₂ as the eluent.



1-Isopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3b). Prepared via General Procedure C on a 10.0 mmol scale with commercially available isopropylamine to give **3b** (3.11 g, 71%) as a white powder: ¹H NMR (400 MHz, CDCl₃) δ 7.81 (s, 2H), 7.79 – 7.71 (m, 6H), 7.65 – 7.51 (m, 6H), 7.55 – 7.42 (m, 3H), 5.12 (hept, *J* = 7.0 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 157.0, 155.2, 134.0, 133.9, 131.9, 130.8, 129.6, 129.5, 128.9, 128.32, 128.27, 62.6, 23.4; ¹⁹F NMR (376 MHz, CDCl₃) δ –153.34 (minor, ¹¹BF₄), –153.39 (major, ¹⁰BF₄). The spectral data matches that reported in the literature.¹³

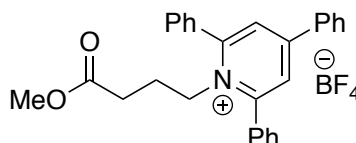


1-(3-(*tert*-Butoxy)-3-oxopropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3e). Prepared via General Procedure C on a 5.0 mmol scale with commercially available *tert*-butyl 3-aminopropanoate hydrochloride to give **3e** (2.00 g, 76%) as a white powder (mp 203–205 °C): ¹H NMR (400 MHz, CDCl₃) δ 7.87 (s, 2H), 7.83 – 7.72 (m, 6H), 7.64 – 7.58 (m, 6H), 7.57 – 7.45 (m, 3H), 4.66 (t, *J* = 7.9 Hz, 2H), 2.44 (t, *J* = 7.9 Hz, 2H), 1.22 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 168.0, 156.7, 156.4, 134.2, 132.6, 132.1, 131.2, 129.7, 129.5, 129.0, 128.2, 126.9, 81.9, 50.3, 34.4, 27.8; ¹⁹F NMR (376 MHz, CDCl₃) δ –153.14 (minor, ¹¹BF₄), –153.19 (major, ¹⁰BF₄); FTIR (neat) 2980, 1726, 1625, 1153, 1055, 768, 703 cm^{–1}; HRMS (ESI+) [*M*–BF₄]⁺ calculated for C₃₀H₃₀NO₂: 436.2271, found 436.2264.

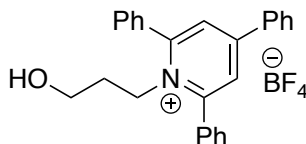


2,4,6-Triphenyl-1-(3,3,3-trifluoropropyl)pyridin-1-ium tetrafluoroborate (3f). Prepared via General Procedure C on a 5.0 mmol scale with commercially available (3,3,3-trifluoropropyl)amine hydrochloride to give **3f** (2.26 g, 92%) as a white powder (mp 213–215 °C): ¹H NMR (400 MHz, CDCl₃) δ 7.89 (s, 2H), 7.87 – 7.80 (m, 4H), 7.79 – 7.71 (m, 2H), 7.69 –

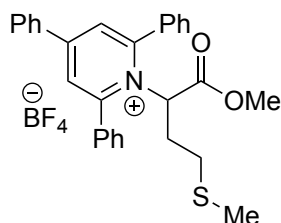
7.55 (m, 7H), 7.54 – 7.46 (m, 2H), 4.75 – 4.66 (m, 2H), 2.45 – 2.28 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 156.9, 156.7, 134.0, 132.3, 132.1, 131.5, 129.7, 129.6, 128.9, 128.3, 127.1, 124.3 (q, $J_{\text{C-F}} = 277.2$ Hz), 47.7 (q, $J_{\text{C-F}} = 3.1$ Hz), 32.8 (q, $J_{\text{C-F}} = 29.8$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ –66.09, –152.78 (minor, $^{11}\text{BF}_4$), –152.83 (major, $^{10}\text{BF}_4$); FTIR (neat) 3018, 1625, 1256, 1144, 1055, 765, 705 cm^{-1} ; HRMS (ESI+) $[\text{M-BF}_4]^+$ calculated for $\text{C}_{26}\text{H}_{21}\text{F}_3\text{N}$: 404.1621, found 404.1604.



1-(4-Methoxy-4-oxobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3i). Prepared via General Procedure C on a 10.0 mmol scale with commercially available methyl 4-aminobutyrate hydrochloride to give **3i** (3.74 g, 76%) as a white powder (mp 230–232 $^{\circ}\text{C}$): ^1H NMR (400 MHz, CDCl_3) δ 7.93 – 7.85 (m, 2H), 7.85 – 7.79 (m, 4H), 7.79 – 7.74 (m, 2H), 7.65 – 7.59 (m, 6H), 7.59 – 7.48 (m, 3H), 4.56 – 4.48 (m, 2H), 3.43 (s, 3H), 1.86 – 1.72 (m, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.7, 156.6, 156.0, 134.0, 132.6, 132.2, 131.1, 129.7, 129.4, 129.1, 128.2, 126.8, 54.0, 51.8, 30.6, 24.8; ^{19}F NMR (565 MHz, CDCl_3) δ –153.29 (minor, $^{11}\text{BF}_4$), –153.35 (major, $^{10}\text{BF}_4$); FTIR (neat) 3061, 1733, 1623, 1055, 768, 704 cm^{-1} ; HRMS (ESI+) $[\text{M-BF}_4]^+$ calculated for $\text{C}_{28}\text{H}_{26}\text{NO}_2$: 408.1958, found 408.1958.

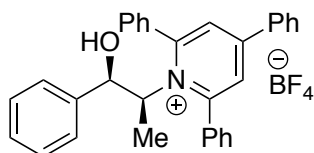


1-(3-Hydroxypropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3j). Prepared via General Procedure C on a 10.0 mmol scale with commercially available 3-amino-1-propanol to give **3j** (3.74 g, 83%) as a white powder (mp 122–124 $^{\circ}\text{C}$): ^1H NMR (600 MHz, CDCl_3) δ 7.91 (s, 2H), 7.83 – 7.75 (m, 6H), 7.66 – 7.60 (m, 6H), 7.60 – 7.51 (m, 3H), 4.72 – 4.55 (m, 2H), 3.17 (q, $J = 5.5$ Hz, 2H), 1.72 – 1.63 (m, 2H), 1.51 (t, $J = 5.4$ Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 157.1, 156.0, 134.1, 132.8, 132.3, 131.3, 129.9, 129.6, 129.2, 128.3, 126.9, 59.1, 53.3, 32.3; ^{19}F NMR (565 MHz, CDCl_3) δ –153.17 (minor, $^{11}\text{BF}_4$), –153.22 (major, $^{10}\text{BF}_4$); FTIR (neat) 3547, 1623, 1565, 1058, 767, 702 cm^{-1} ; HRMS (ESI+) $[\text{M-BF}_4]^+$ calculated for $\text{C}_{26}\text{H}_{24}\text{NO}$: 366.1852, found 366.1849.



1-(1-methoxy-4-(methylthio)-1-oxobutan-2-yl)-2,4,6-triphenylpyridin-1-ium

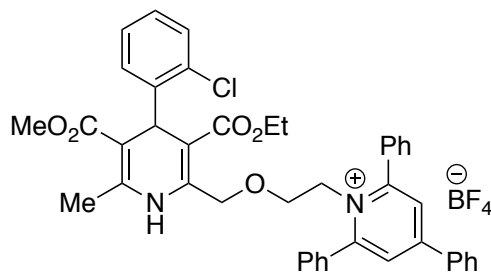
tetrafluoroborate (3m). Prepared via General Procedure D on a 5.0 mmol scale with commercially available methionine methyl ester. The crude material was purified via column chromatography (5→15% acetone/CH₂Cl₂) to give pyridinium salt **3m** (1.86 g, 69%) as a light yellow solid: ¹H NMR (400 MHz, CDCl₃) δ 7.97 – 7.90 (m, 2H), 7.85 – 7.80 (m, 3H), 7.70 – 7.47 (m, 12H), 6.04 (dt, *J* = 9.4, 2.5 Hz, 1H), 3.73 (s, 3H), 2.43 – 2.20 (m, 3H), 1.90 – 1.80 (m, 1H), 1.87 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 169.2, 157.2, 134.2, 132.8, 132.3, 131.5, 129.8, 129.2, 128.7, 66.7, 53.8, 31.7, 30.6, 14.8 (3 carbons missing due to signal broadening as stated in the literature); ¹⁹F NMR (376 MHz, CDCl₃) δ –152.85 (minor, ¹¹BF₄), –152.91 (major, ¹⁰BF₄). The spectral data matches that of the literature.¹³



1-((1R,2S)-1-Hydroxy-1-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate

(3o). Prepared according to a procedure adapted from the literature:¹⁴ (1R,2S)-(-)-Norephedrine (1.51 g, 10 mmol, 1.0 equiv) was added to a suspension of 2,4,6-triphenylpyrylium tetrafluoroborate (3.96 g, 10 mmol, 1.0 equiv) and CH₂Cl₂ (300 mL, 0.33 M) in a round-bottomed flask. The resulting mixture was stirred at room temperature overnight. The crude reaction was concentrated and triturated with Et₂O. The resulting solid was filtered and washed with Et₂O to give **3o** (2.52 g, 47%) as a yellow solid (mp 111–119 °C): ¹H NMR (600 MHz, CDCl₃) δ 7.91 – 7.77 (m, 2H), 7.74 (s, 2H), 7.73 – 7.68 (m, 2H), 7.64 – 7.48 (m, 9H), 7.48 – 7.45 (m, 2H), 7.18 – 7.13 (m, 1H), 7.13 – 7.07 (m, 2H), 6.66 – 6.61 (m, 2H), 5.40 – 5.32 (m, 1H), 5.03 (t, *J* = 5.6 Hz, 1H), 3.41 (d, *J* = 5.5 Hz, 1H), 1.18 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, (CD₃)₂CO) δ 164.2, 160.2, 145.3, 139.4, 138.5, 137.8, 136.5, 136.3, 134.9, 134.7, 134.1, 133.8, 133.7, 132.7, 131.2, 79.5, 77.4, 24.9; ¹⁹F NMR (565 MHz, CDCl₃) δ –152.99 (minor, ¹¹BF₄), –

153.04 (major, $^{10}\text{BF}_4$); FTIR (neat) 3503, 3062, 1617, 1056, 1028, 770, 702 cm^{-1} ; HRMS (ESI+) $[\text{M} - \text{BF}_4]^+$ calculated for $\text{C}_{32}\text{H}_{28}\text{NO}$: 442.2165, found 442.2170.

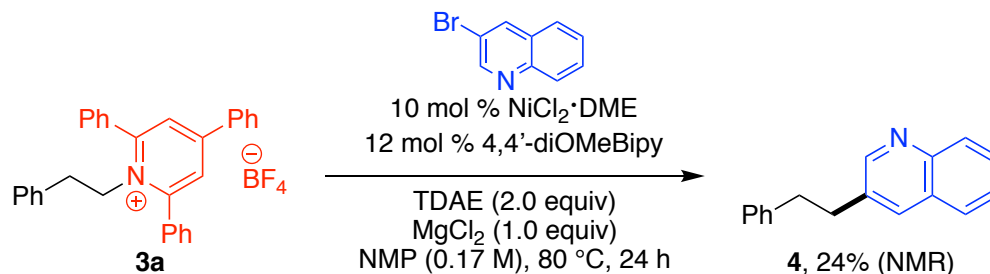


1-(2-((4-(2-Chlorophenyl)-3-(ethoxycarbonyl)-5-(methoxycarbonyl)-6-methyl-1,4-dihydropyridin-2-yl)methoxy)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3r).

Prepared via General Procedure D on a 6.0 mmol scale with commercially available 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-1,4-dihydropyridine (Amlodipine) to give **3r** (3.71 g, 79%) as a yellow solid (mp 129–134 °C): ^1H NMR (600 MHz, CDCl_3) δ 7.89 (s, 2H), 7.83 – 7.74 (m, 6H), 7.60 – 7.54 (m, 6H), 7.54 – 7.49 (m, 2H), 7.33 – 7.28 (m, 1H), 7.22 – 7.18 (m, 1H), 7.11 – 7.04 (m, 2H), 7.03 – 6.98 (m, 1H), 5.35 (s, 1H), 4.91 – 4.80 (m, 2H), 4.30 (d, $J = 13.5$ Hz, 1H), 4.16 (d, $J = 13.5$ Hz, 1H), 3.98 – 3.86 (m, 2H), 3.60 (s, 3H), 3.52 – 3.45 (m, 1H), 3.43 – 3.36 (m, 1H), 2.22 (s, 3H), 1.10 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ 167.9, 166.8, 157.4, 156.3, 145.7, 145.0, 143.6, 133.9, 132.9, 132.3, 132.1, 131.4, 131.2, 129.8, 129.5, 129.4, 129.2, 128.2, 127.4, 127.0, 126.9, 103.4, 103.2, 68.0, 67.5, 59.8, 54.0, 50.8, 37.0, 19.0, 14.2; ^{19}F NMR (565 MHz, CDCl_3) δ –151.92 (minor, $^{11}\text{BF}_4$), –151.98 (major, $^{10}\text{BF}_4$); FTIR (neat) 3061, 1693, 1622, 1497, 1208, 1098, 762 cm^{-1} ; HRMS (ESI+) $[\text{M} - \text{BF}_4]^+$ calculated for $\text{C}_{43}\text{H}_{40}\text{ClN}_2\text{O}_5$: 699.2620, found 699.2616.

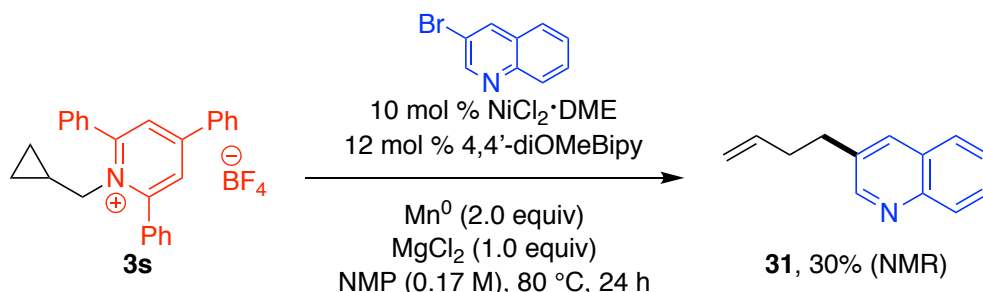
Mechanistic Experiments

Organic Reductant (TDAE)



In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{NiCl}_2 \cdot \text{DME}$ (2.2 mg, 0.010 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (2.6 mg, 0.012 mmol, 12 mol %), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), and pyridinium salt **3a** (60 mg, 0.12 mmol, 1.2 equiv). 3-Bromoquinoline (14 μL , 0.10 mmol, 1.0 equiv) and tetrakis(dimethylamino)ethylene (TDAE) (40 μL , 0.20 mmol, 2.0 equiv) were then added to the vial followed by *N*-methyl-2-pyrrolidone (0.6 mL). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO_4), and concentrated. The yield of the product (**4**) was determined to be 24% by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

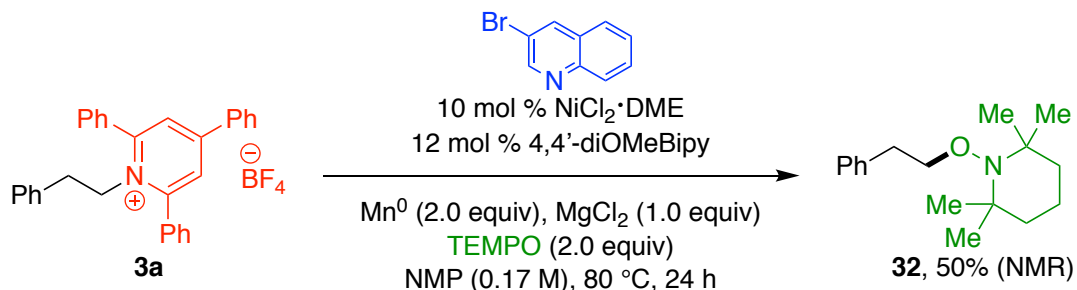
Radical Clock Experiment



In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{NiCl}_2 \cdot \text{DME}$ (2.2 mg, 0.010 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (2.6 mg, 0.012 mmol, 12 mol %), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **3s** (54 mg, 0.10 mmol, 1.0 equiv). 3-Bromoquinoline (15 μL , 0.11 mmol, 1.1 equiv) was then added to the vial followed by *N*-methyl-2-pyrrolidone (0.6 mL). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox.

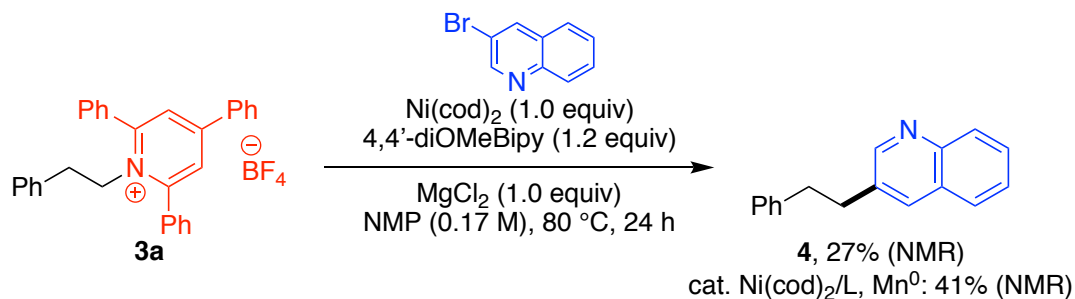
The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. The yield of the ring-opened product (**31**) was determined to be 30% by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

Radical Trap Experiment



In a N₂-filled glovebox: To an oven-dried 1-dram vial was added NiCl₂·DME (2.2 mg, 0.010 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (2.6 mg, 0.012 mmol, 12 mol %), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO, 31 mg, 0.20 mmol, 2.0 equiv) and pyridinium salt **3a** (60 mg, 0.12 mmol, 1.2 equiv). 3-Bromoquinoline (14 μL, 0.10 mmol, 1.0 equiv) was then added to the vial followed by *N*-methyl-2-pyrrolidone (0.6 mL). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. The yield of known TEMPO adduct (**32**)⁹ was determined to be 50% by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. No cross-coupled product was observed.

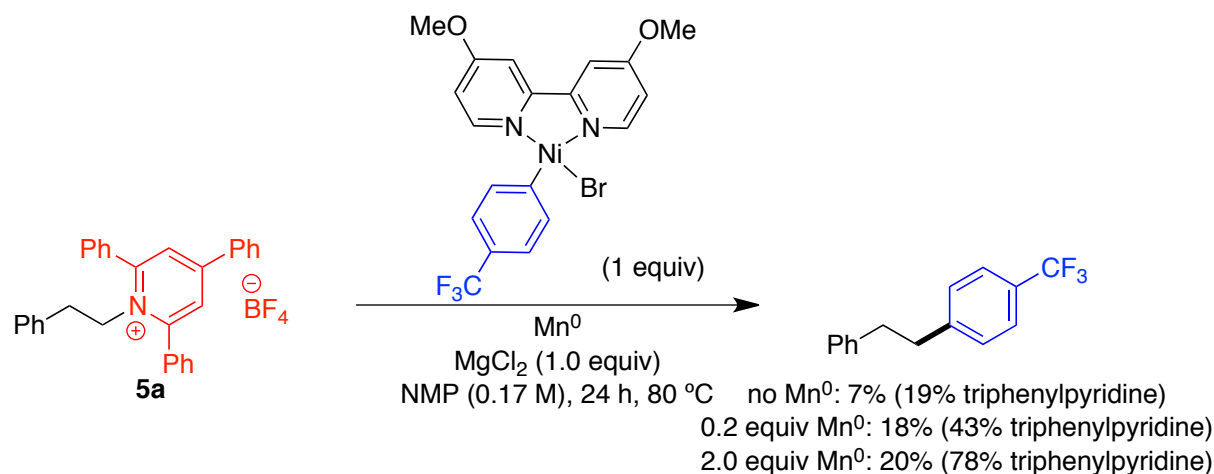
Catalytic and Stoichiometric Ni(0) Studies



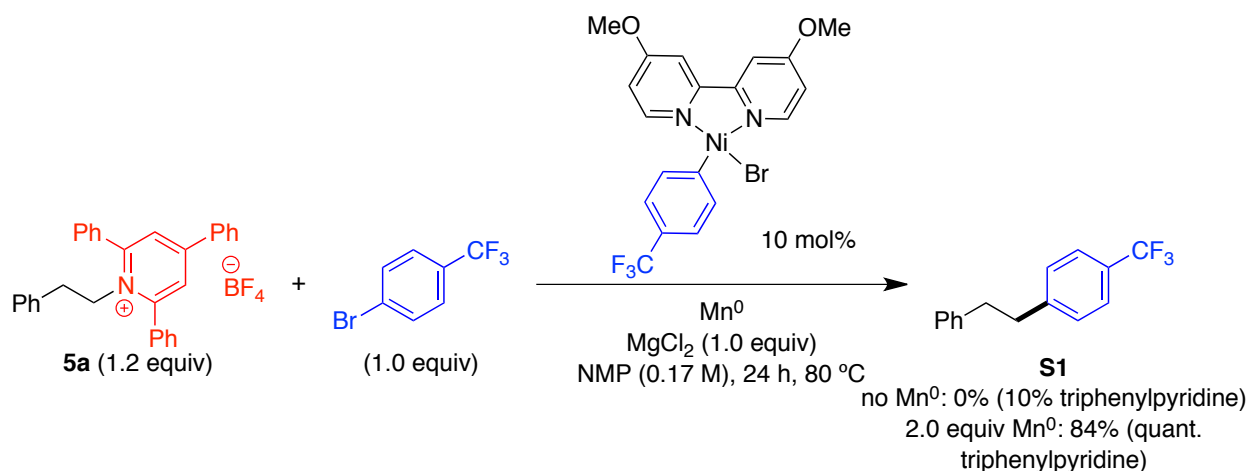
In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{Ni}(\text{cod})_2$ (27.5 mg, 0.10 mmol, 1.0 equiv), 4,4'-dimethoxy-2,2'-bipyridine (26 mg, 0.12 mmol, 1.2 equiv), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **3a** (60 mg, 0.12 mmol, 1.2 equiv). 3-Bromoquinoline (14 μL , 0.10 mmol, 1.0 equiv) was then added to the vial followed by *N*-methyl-2-pyrrolidone (0.6 mL). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO_4), and concentrated. The yield of the product (**4**) was determined to be 27% by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{Ni}(\text{cod})_2$ (2.8 mg, 0.010 mmol, 10 mol %), 4,4'-dimethoxy-2,2'-bipyridine (2.6 mg, 0.012 mmol, 12 mol %), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **3a** (60 mg, 0.12 mmol, 1.2 equiv). 3-Bromoquinoline (14 μL , 0.10 mmol, 1.2 equiv) was then added to the vial followed by *N*-methyl-2-pyrrolidone (0.6 mL). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with EtOAc (1.5 mL), filtered through a short plug of silica gel, and the filter cake was washed with EtOAc (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO_4), and concentrated. The yield of the product (**4**) was determined to be 41% by ^1H NMR spectroscopic analysis using 1,3,5-trimethoxybenzene as an internal standard.

Catalytic and Stoichiometric Ni(II) Studies



In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{Ni}(4,4'\text{-diOMeBipy})(p\text{-CF}_3\text{C}_6\text{H}_4)\text{Br}^{15}$ (50 mg, 0.10 mmol, 1.0 equiv), magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (if used), and pyridinium salt **5a** (60 mg, 0.12 mmol, 1.2 equiv). The vial was then equipped with a stir bar, capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 °C for 24 h. The mixture was then diluted with Et_2O (1.5 mL), filtered through a short plug of celite, and the filter cake was washed with Et_2O (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO_4), and concentrated. 1,3,5-Trimethoxybenzene (internal standard) and CDCl_3 were added, and the yield was determined by ^1H NMR analysis.

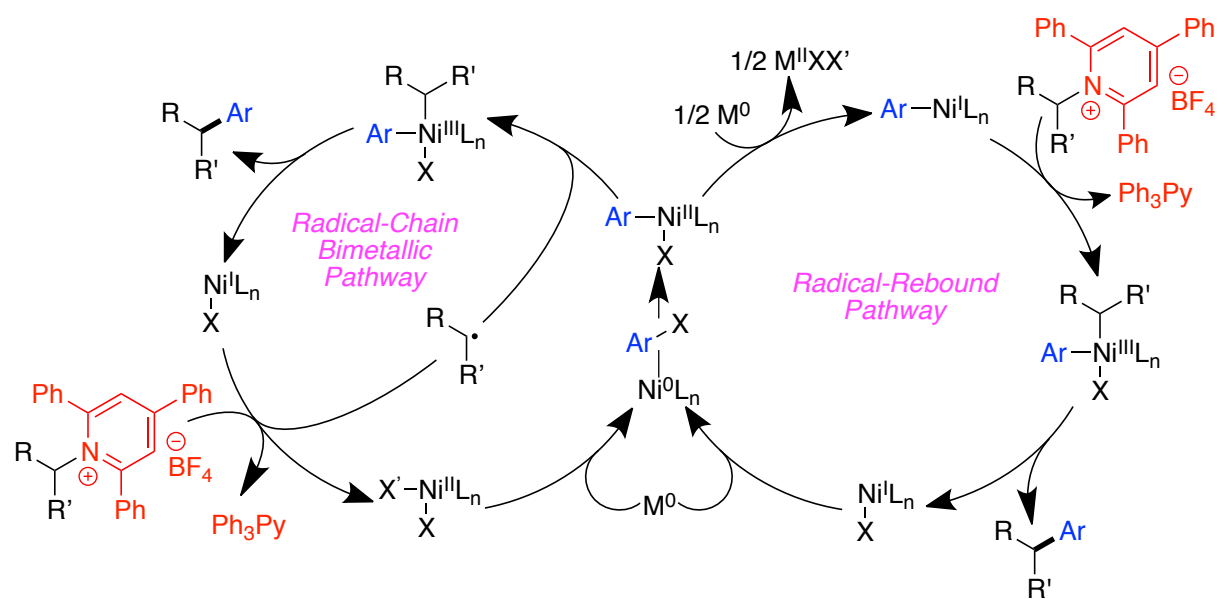


In a N_2 -filled glovebox: To an oven-dried 1-dram vial was added $\text{Ni}(4,4'\text{-diOMeBipy})(p\text{-CF}_3\text{C}_6\text{H}_4)\text{Br}^{15}$ (5.0 mg, 0.010 mmol, 1.0 equiv) magnesium chloride (9.5 mg, 0.10 mmol, 1.0 equiv), manganese powder (11 mg, 0.20 mmol, 2.0 equiv), and pyridinium salt **5a** (60 mg, 0.12

mmol, 1.2 equiv). 4-Bromobenzotrifluoride (14 μ L, 0.10 mmol, 1.0 equiv) was then added to the vial followed by 0.6 mL NMP. The vial was then equipped with a stir bar, and charged with capped with a Teflon-coated cap, and removed from the glovebox. The resulting mixture was stirred vigorously at 80 $^{\circ}$ C for 24 h. The mixture was then diluted with Et₂O (1.5 mL), filtered through a short plug of celite, and the filter cake was washed with Et₂O (10 mL). The filtrate was then washed with sat. NaCl (2 x 5 mL), dried (MgSO₄), and concentrated. 1,3,5-Trimethoxybenzene (internal standard) and CDCl₃ were added. The yield of the crude product was determined to be 76% by ¹H NMR spectroscopic analysis using 1,3,5-trimethoxybenzene as an internal standard.

Additional Mechanism Discussion

As discussed in the communication, we cannot distinguish between a radical-chain bimetallic pathway and a radical-rebound pathway. These are depicted below. The key difference between them is the role of Mn⁰. In the radical-chain bimetallic pathway, Mn⁰ completes the catalytic cycle by reducing a nickel(II) intermediate to a nickel(0) species. In the radical-rebound pathway, Mn⁰ acts at two steps of the catalytic cycle, first reducing an arylnickel(II) species to the required arylnickel(I) intermediate, and then reducing a nickel(I) intermediate to a nickel(0) species to complete the cycle. Both mechanisms proceed via oxidative addition of the aryl bromide and the single-electron transfer (SET) of the alkyl pyridinium salt to form an alkyl radical, consistent with our experiments. When stoichiometric Ni(cod)₂/4,4'-diOMeBipy was used, product **4** was formed in 27% yield (NMR, see above). At first glance, this result seems to suggest a radical-chain bimetallic pathway is operating. However, the stoichiometric Ni(0) may in fact be acting as a reductant to turn over a radical-rebound pathway. We also tested stoichiometric arylnickel(II) bromide (see above). In the absence of Mn⁰, only 7% yield is observed. Although this increases to 18% yield with 0.2 equiv of Mn⁰, it remains at 20% with even 2.0 equiv of Mn⁰, making interpretation difficult. We have confirmed that this arylnickel(II) bromide is catalytically competent (see above).

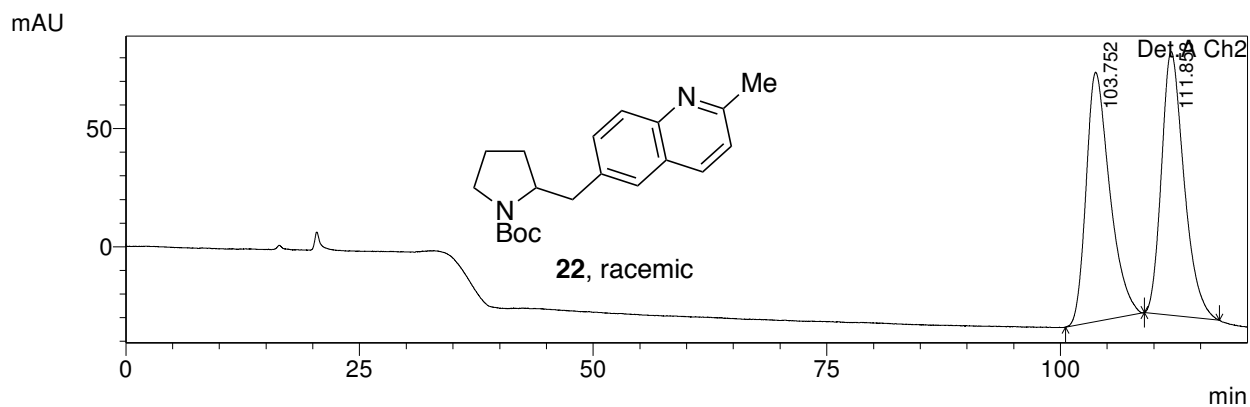


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HPLC Spectra

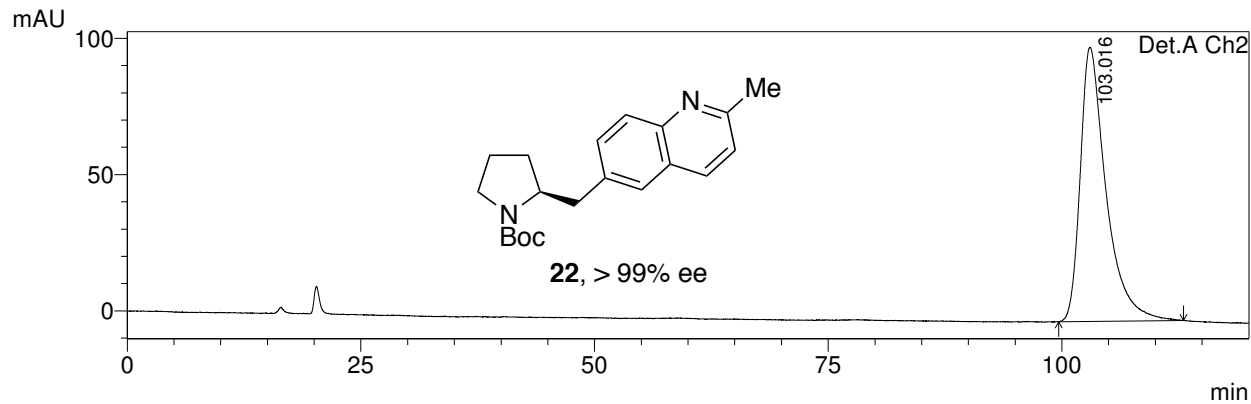
Compound 22, racemic (210 nm)



Detector A Ch2 210nm

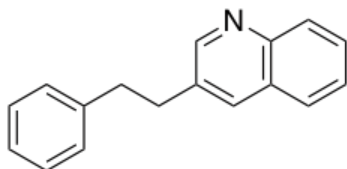
Peak#	Ret. Time	Area	Height	Area %	Height %
1	103.752	18566299	105683	49.739	48.610
2	111.853	18761296	111728	50.261	51.390
Total		37327594	217412	100.000	100.000

Compound 22, >99% ee (210 nm)



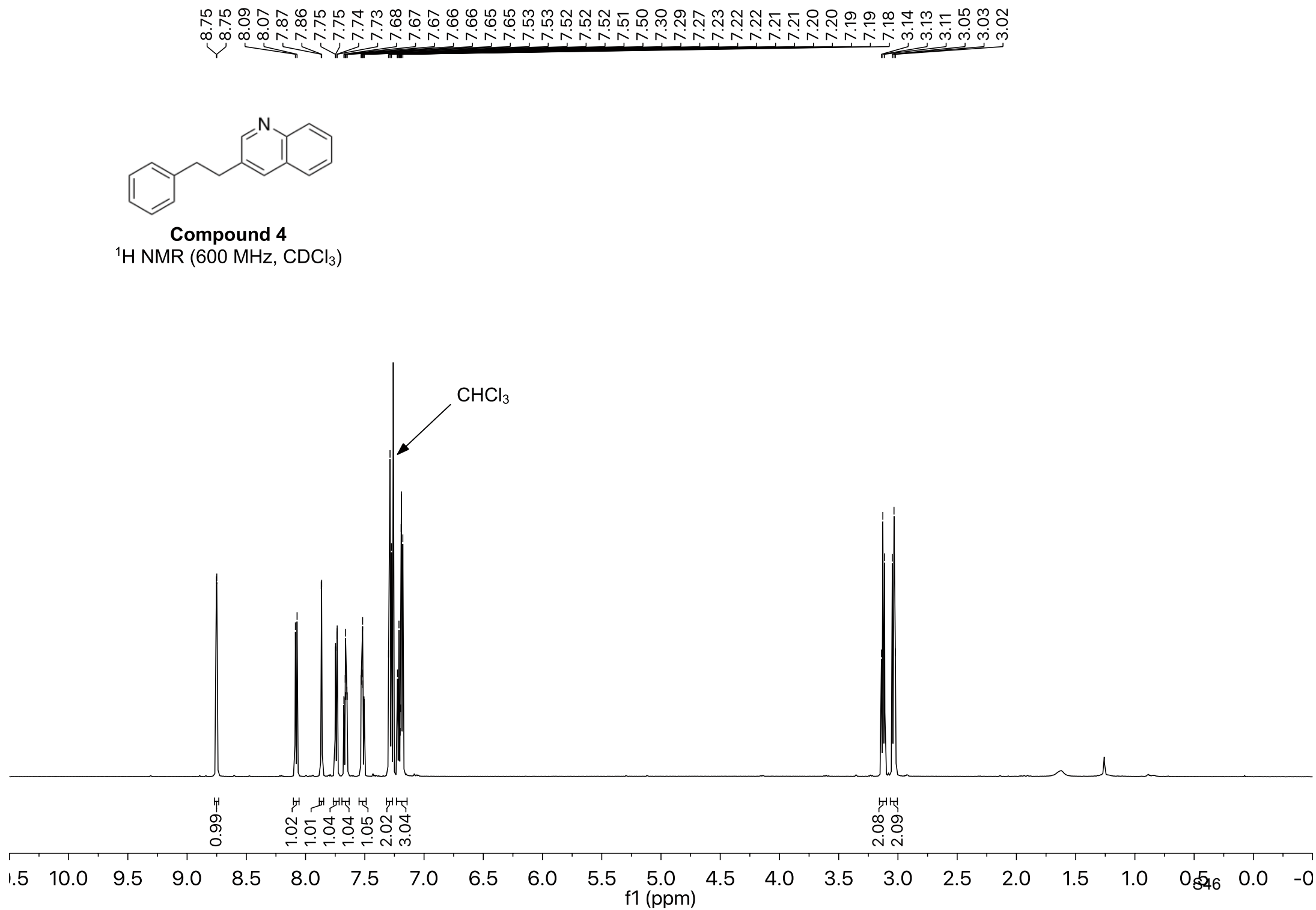
Detector A Ch2 210nm

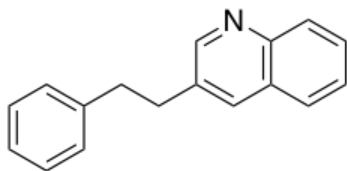
Peak#	Ret. Time	Area	Height	Area %	Height %
1	103.016	19309963	100587	100.000	100.000
Total		19309963	100587	100.000	100.000



Compound 4

^1H NMR (600 MHz, CDCl_3)





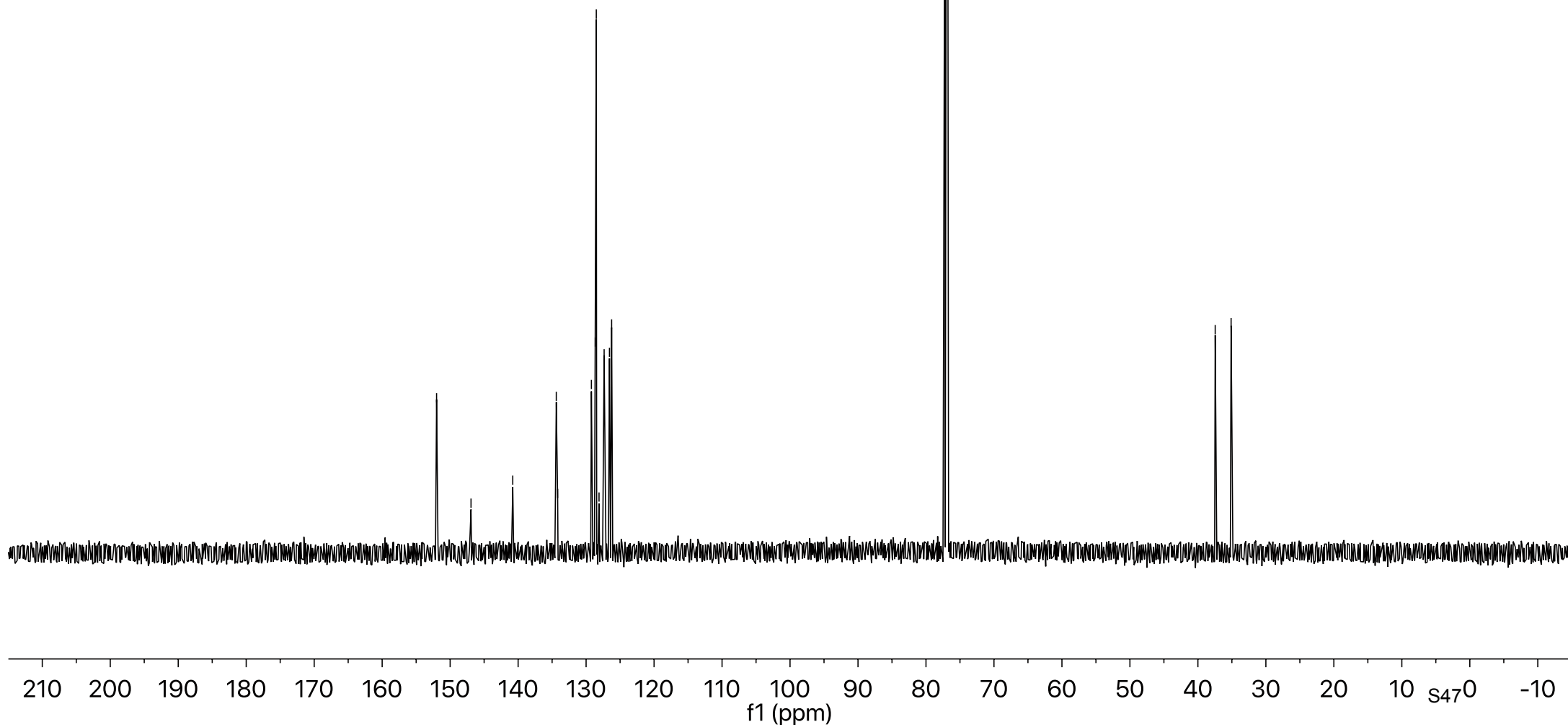
Compound 4

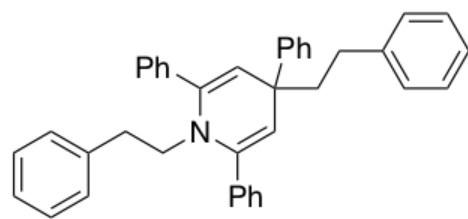
^{13}C NMR (151 MHz, CDCl_3)

151.99
146.93
140.79
134.39
134.18
129.22
128.65
128.50
128.10
127.35
126.56
126.24

~37.46
~35.12

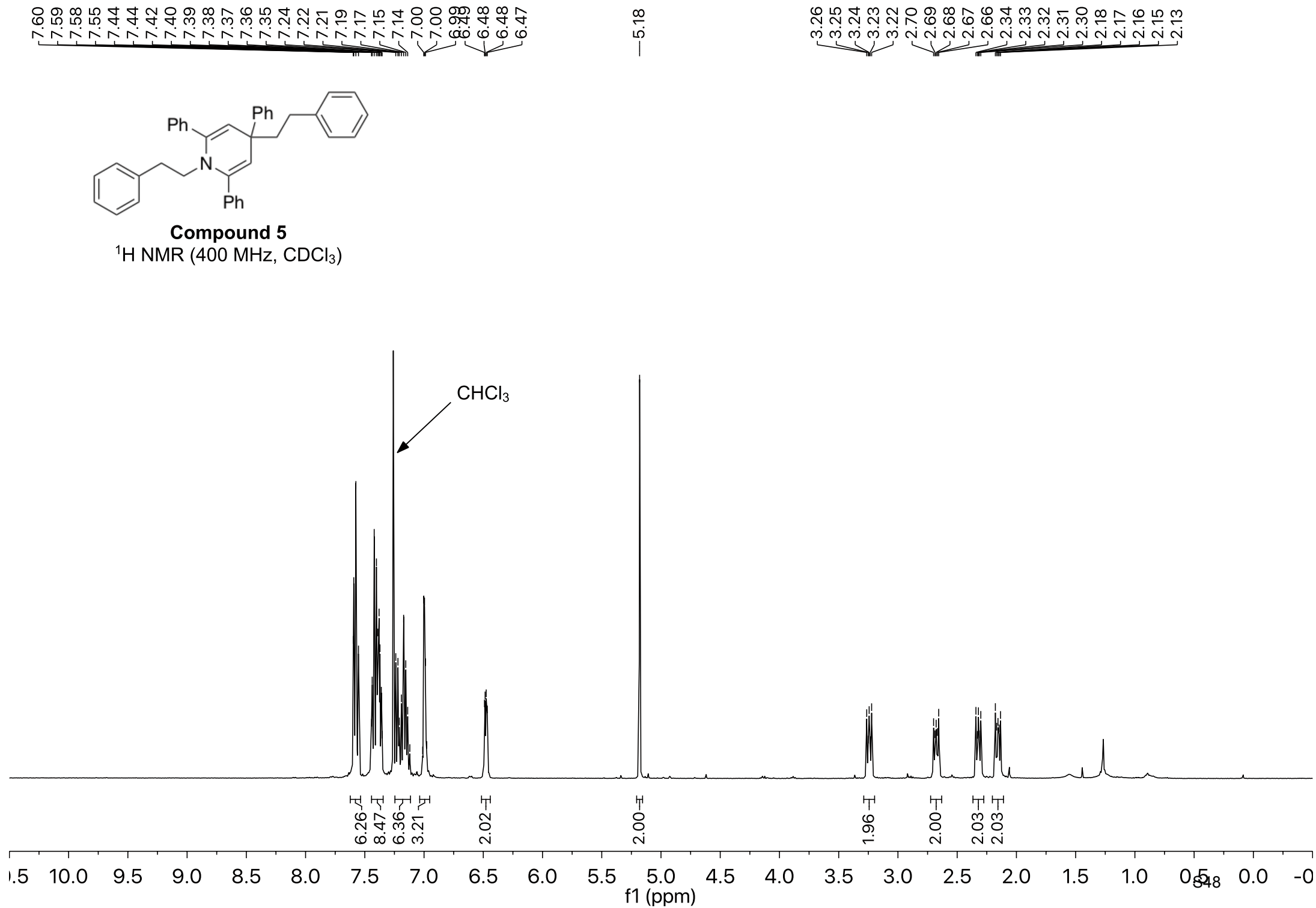
CDCl_3

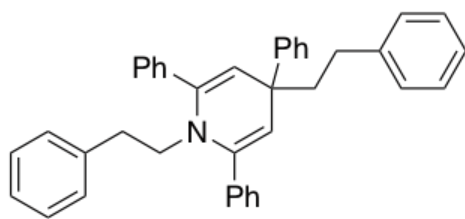




Compound 5

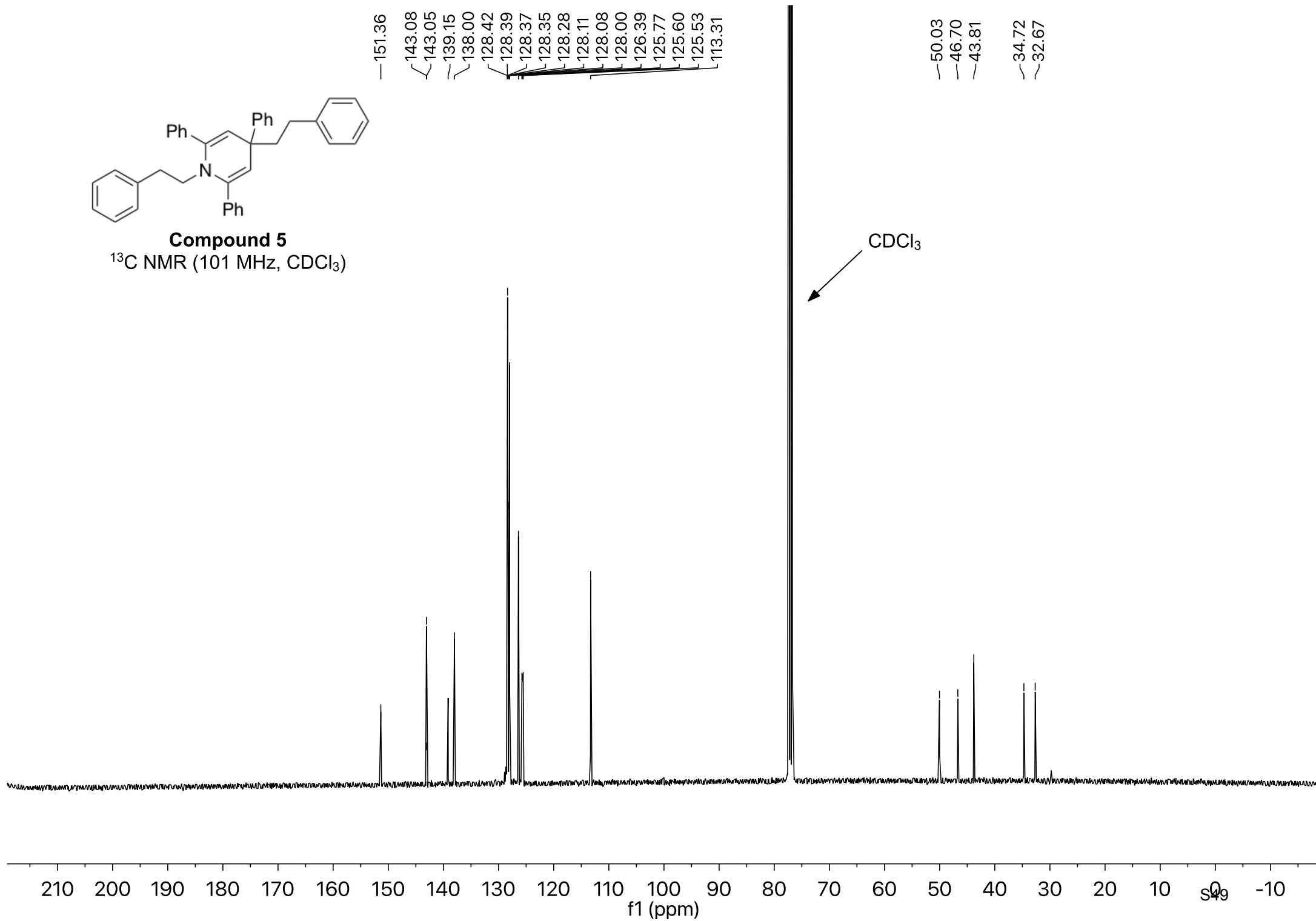
^1H NMR (400 MHz, CDCl_3)

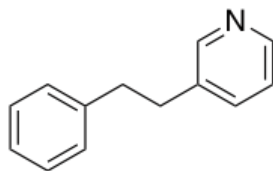




Compound 5

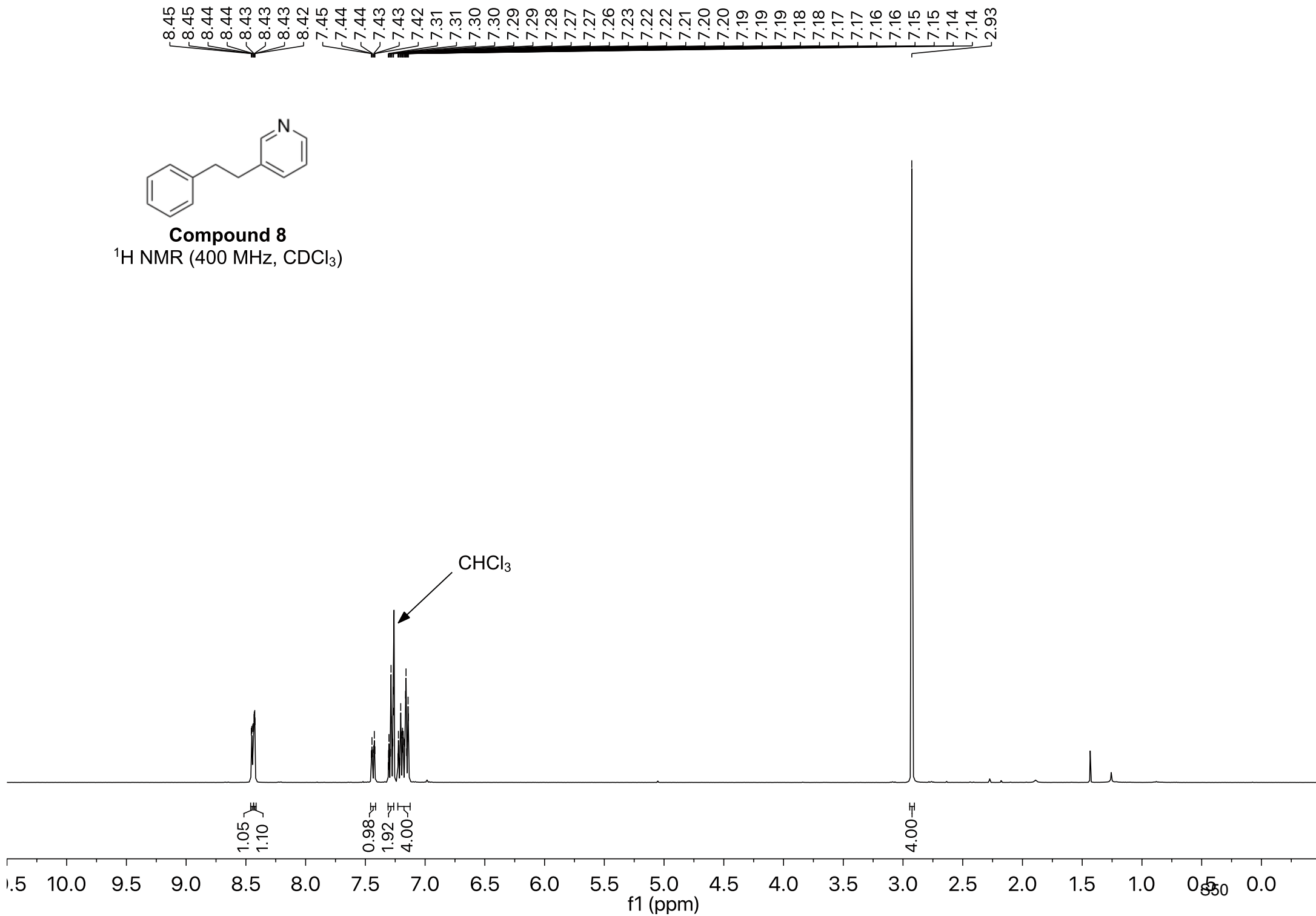
^{13}C NMR (101 MHz, CDCl_3)

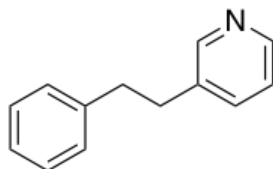




Compound 8

^1H NMR (400 MHz, CDCl_3)





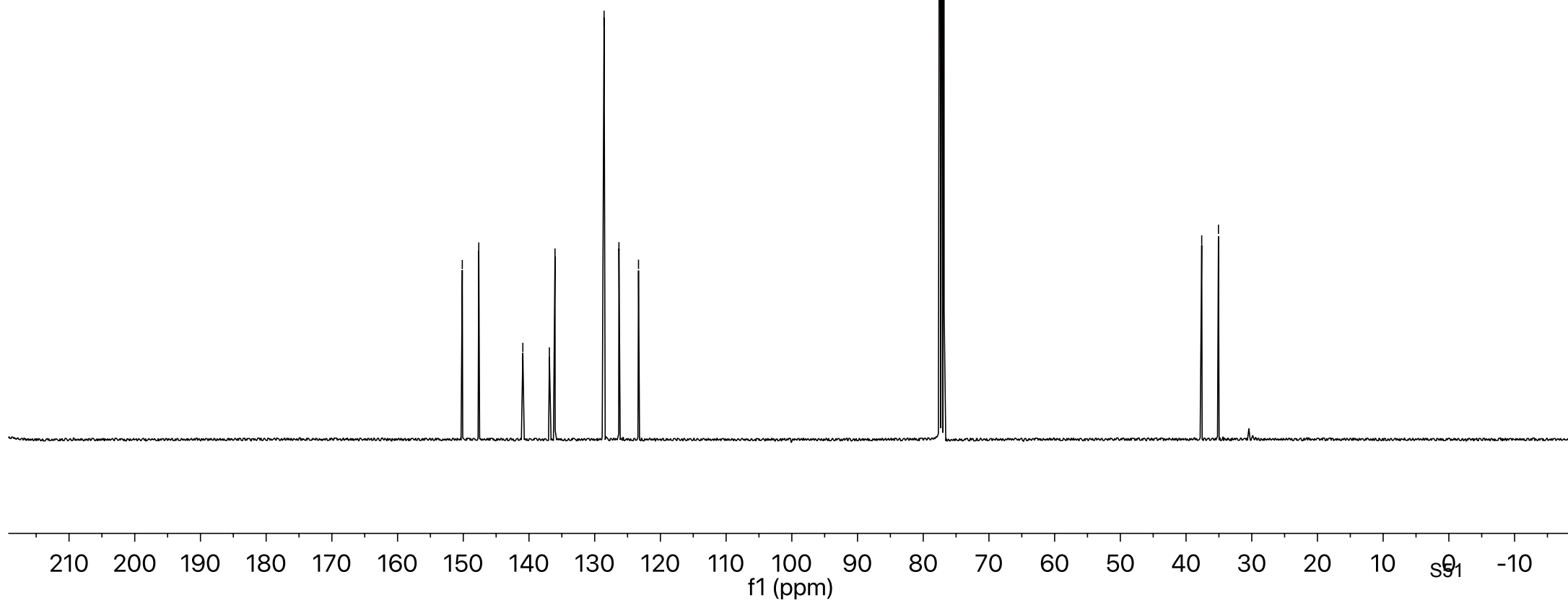
Compound 8

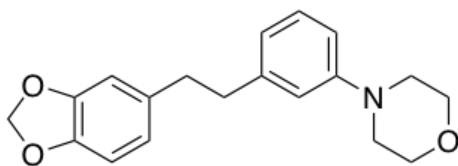
^{13}C NMR (101 MHz, CDCl_3)

150.15
147.64
140.94
136.90
136.04
128.59
128.57
126.31
123.33

37.61
35.07

CDCl_3





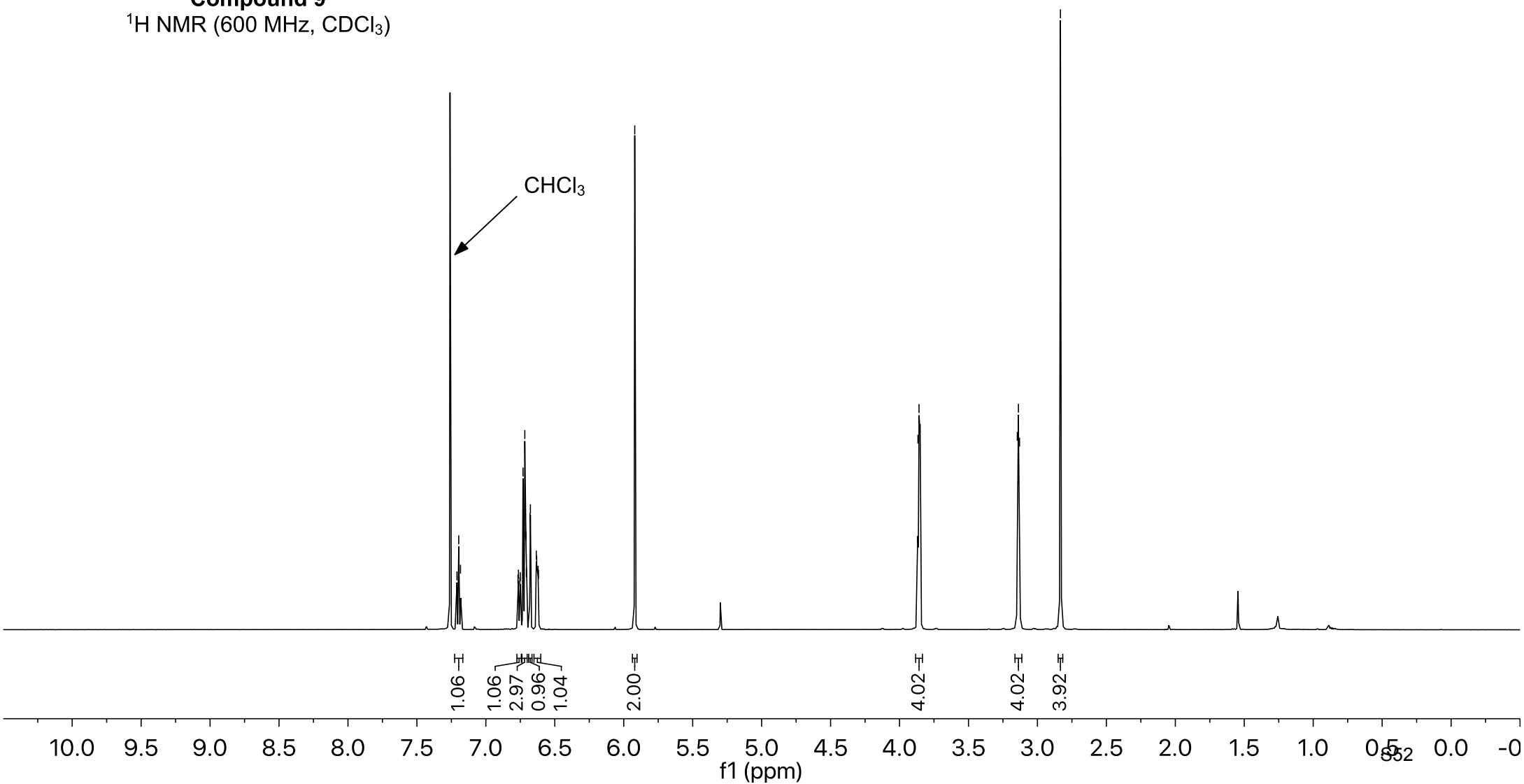
Compound 9

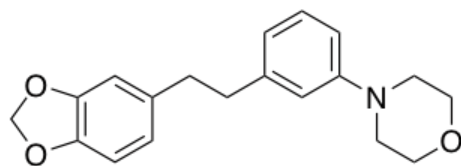
^1H NMR (600 MHz, CDCl_3)

7.21
7.20
7.18
6.77
6.76
6.75
6.75
6.73
6.72
6.71
6.71
6.68
6.68
6.63
6.63
6.62
6.62
5.92

3.87
3.86
3.85

3.15
3.14
3.13
2.83

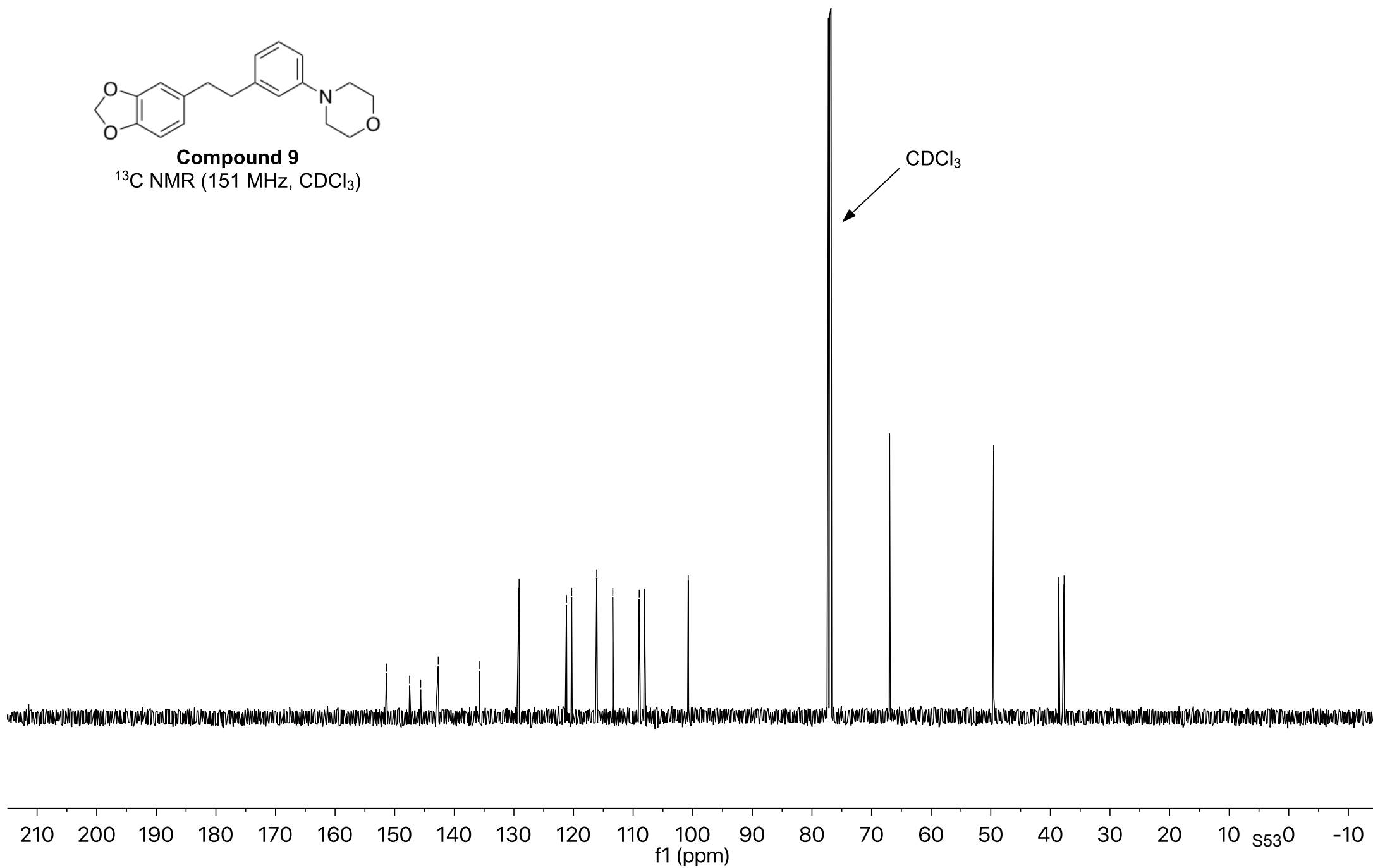


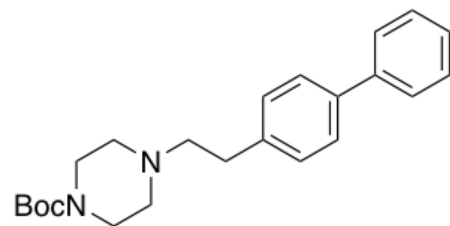


Compound 9

^{13}C NMR (151 MHz, CDCl_3)

\sim 151.38
 \sim 147.49
 \sim 145.64
 \sim 142.69
 —135.72
 —129.13
 \sim 121.18
 \sim 120.31
 \sim 116.10
 \sim 113.41
 \sim 108.97
 \sim 108.11
 —100.75
 —66.98
 —49.52
 \sim 38.59
 \sim 37.69



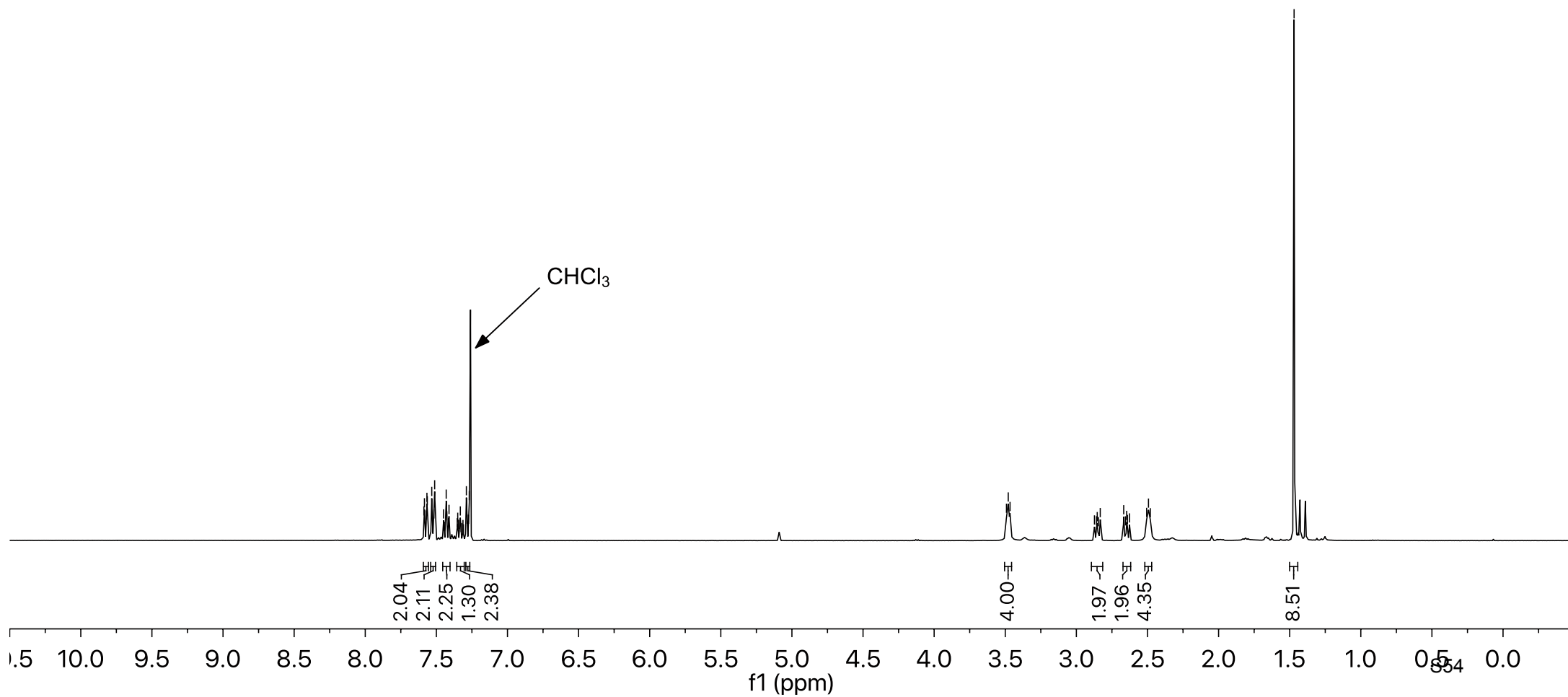


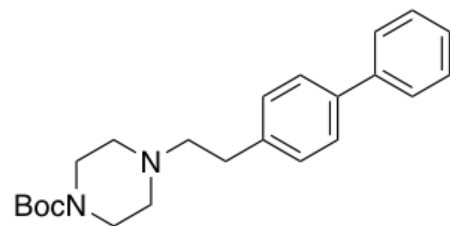
Compound 10

^1H NMR (400 MHz, CDCl_3)

7.59, 7.58, 7.57, 7.57, 7.56, 7.53, 7.52, 7.51, 7.45, 7.44, 7.43, 7.43, 7.41, 7.41, 7.35, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.31, 7.31, 7.29, 7.28, 7.27, 7.27

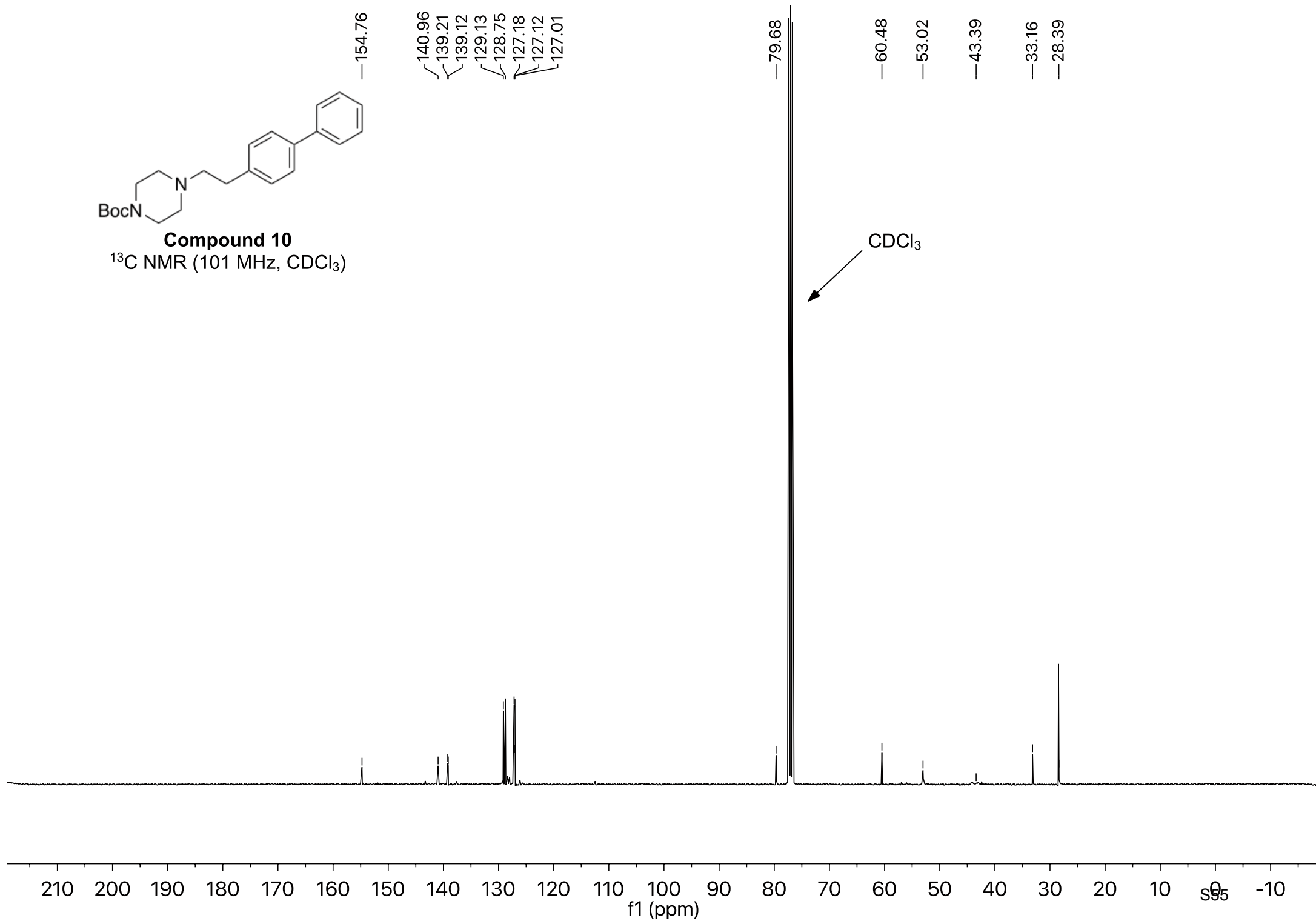
3.49, 3.48, 3.47, 2.87, 2.86, 2.85, 2.84, 2.83, 2.67, 2.65, 2.65, 2.64, 2.63, 2.51, 2.49, 2.48, 1.47

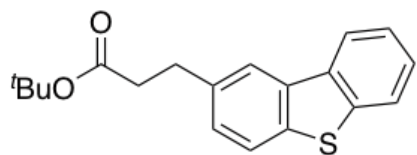




Compound 10

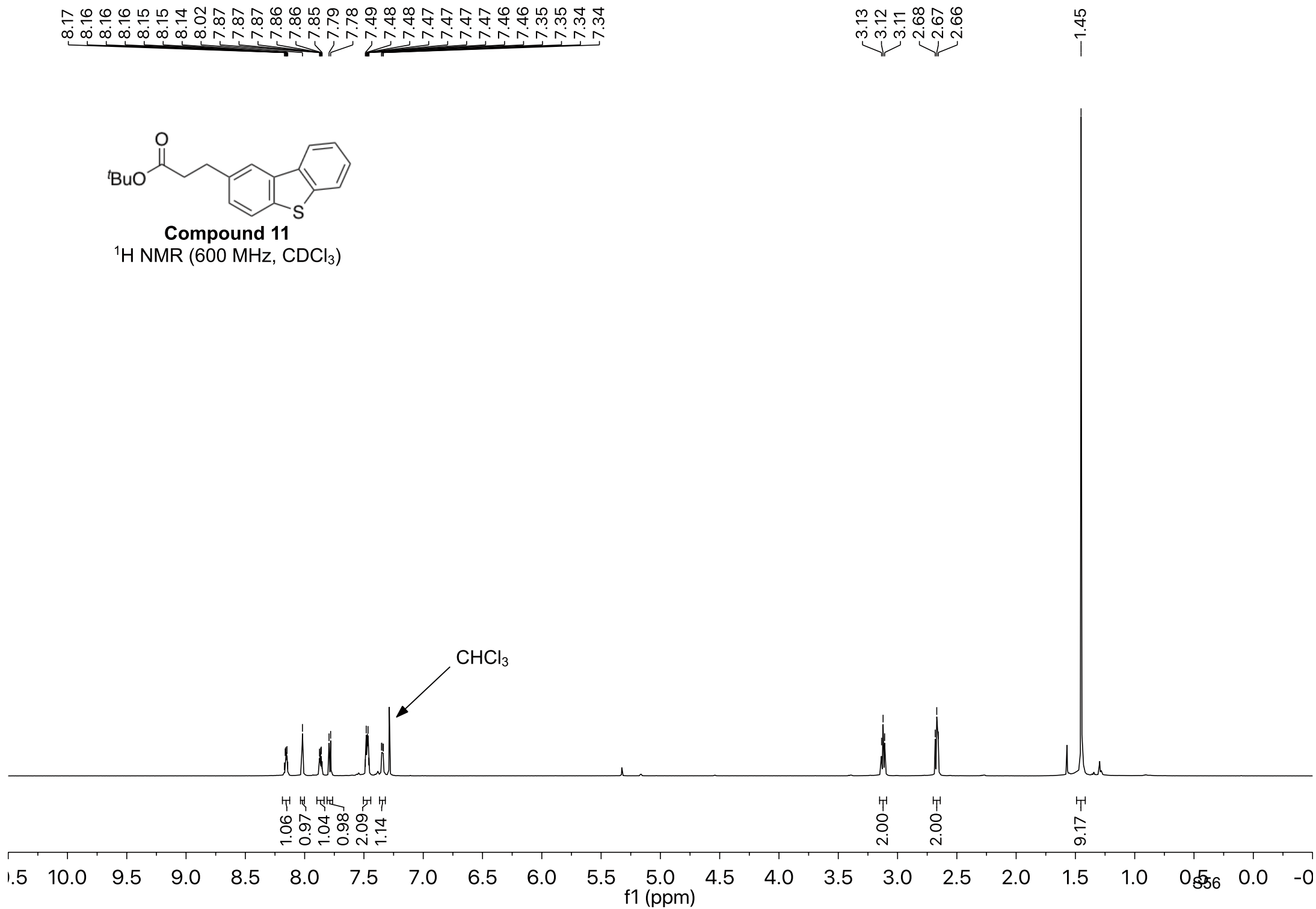
^{13}C NMR (101 MHz, CDCl_3)

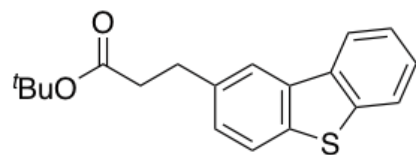




Compound 11

^1H NMR (600 MHz, CDCl_3)





Compound 11

^{13}C NMR (151 MHz, CDCl_3)

—172.20

139.83

137.23

137.21

135.76

135.42

127.46

126.62

124.28

122.86

122.67

121.48

121.19

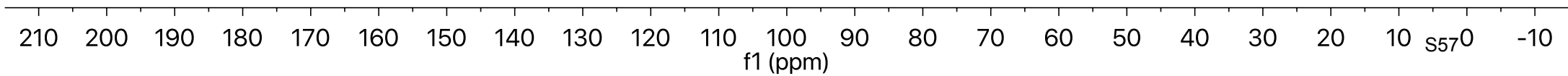
—80.49

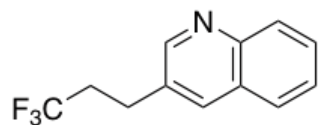
37.49

31.19

28.12

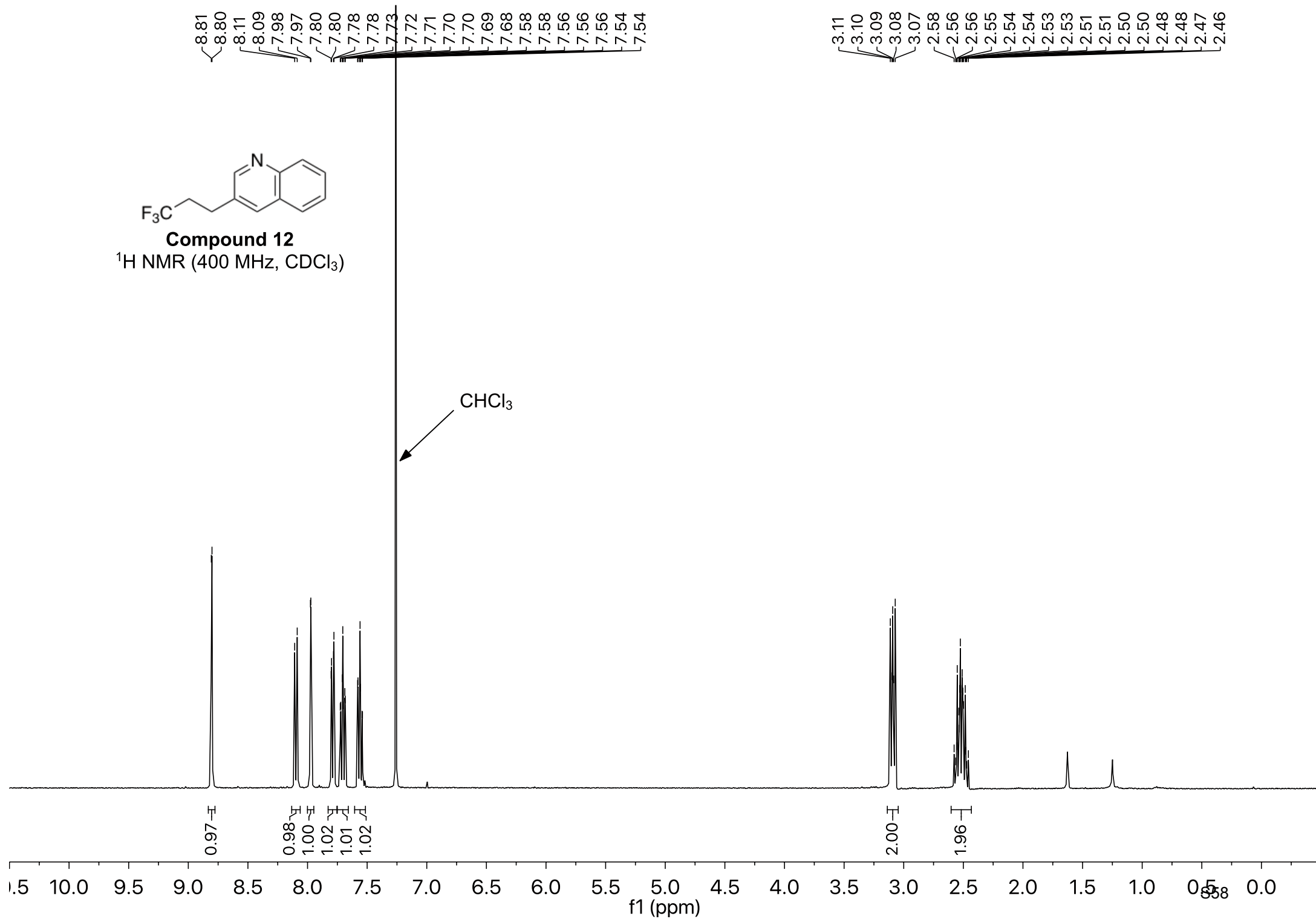
CDCl_3

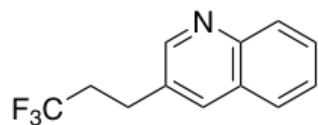




Compound 12

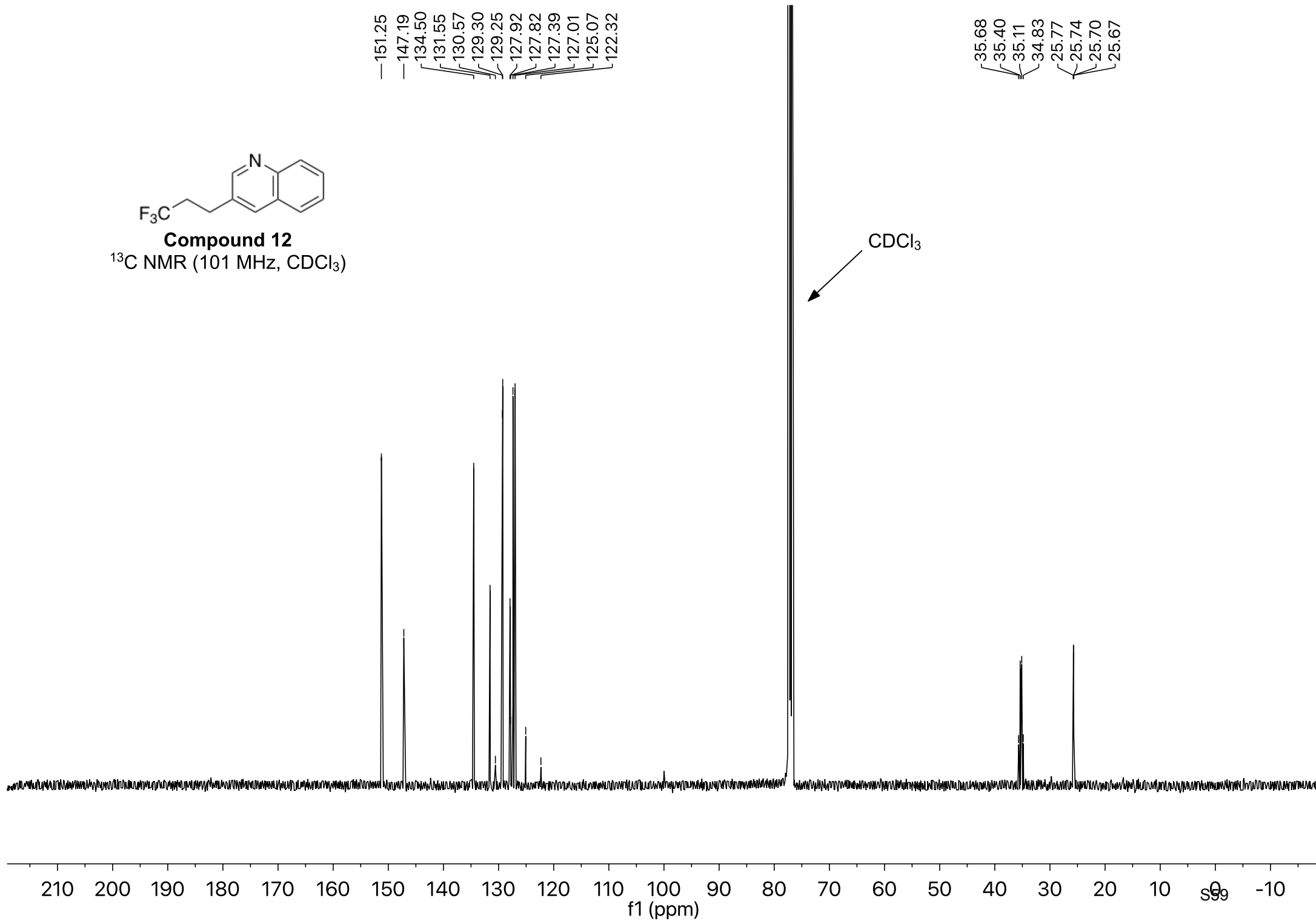
^1H NMR (400 MHz, CDCl_3)

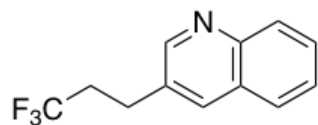




Compound 12

^{13}C NMR (101 MHz, CDCl_3)

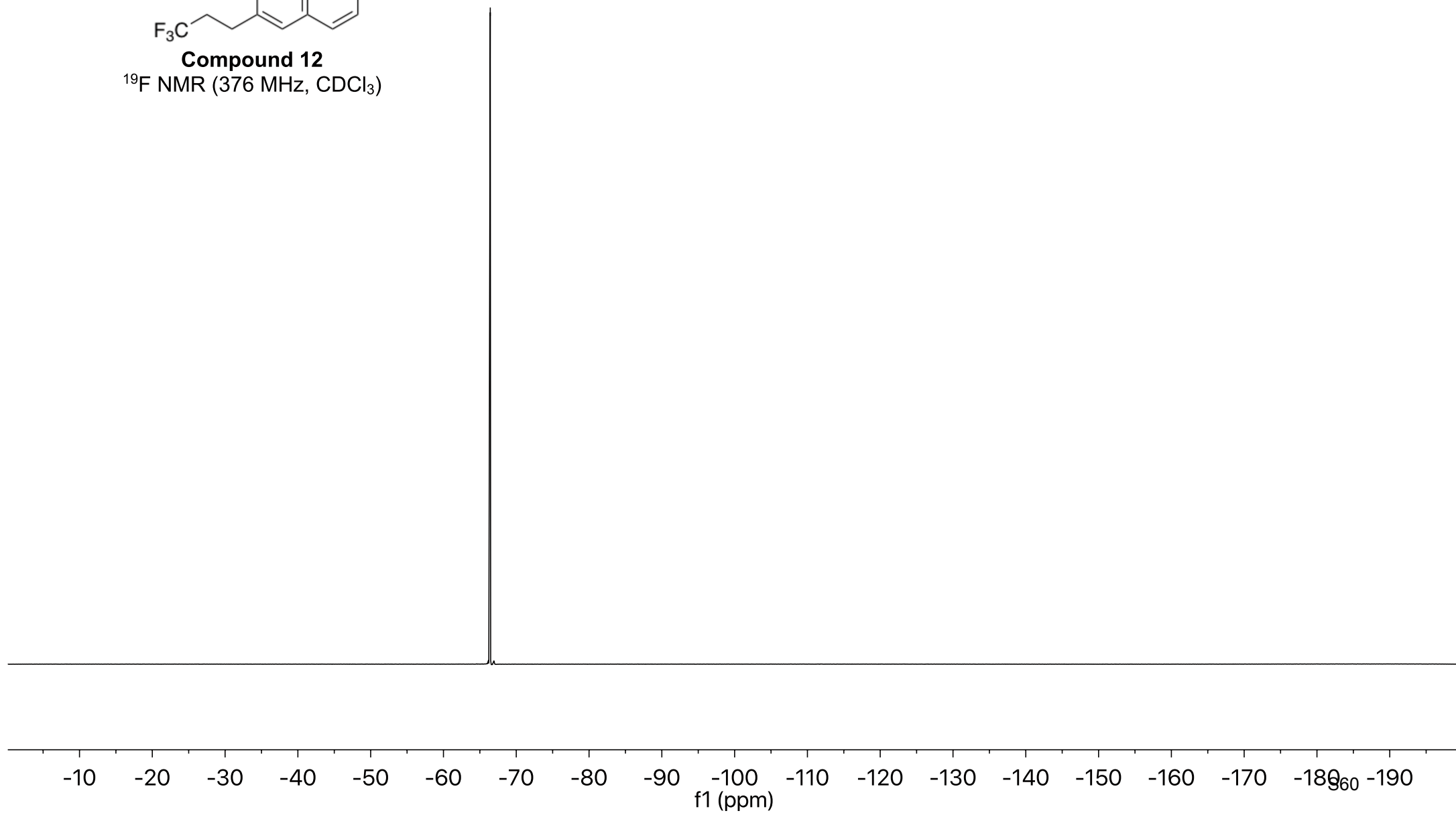


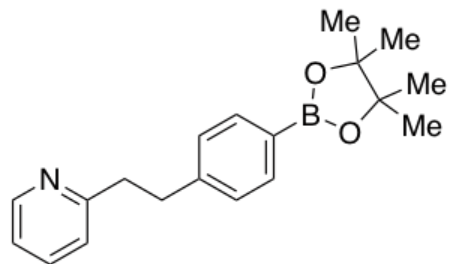


Compound 12

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

---66.43





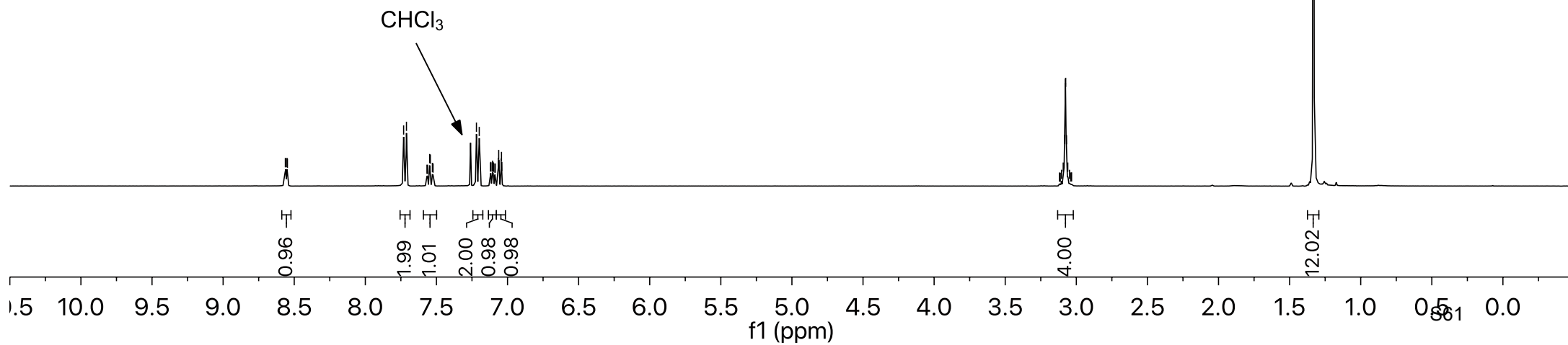
Compound 13

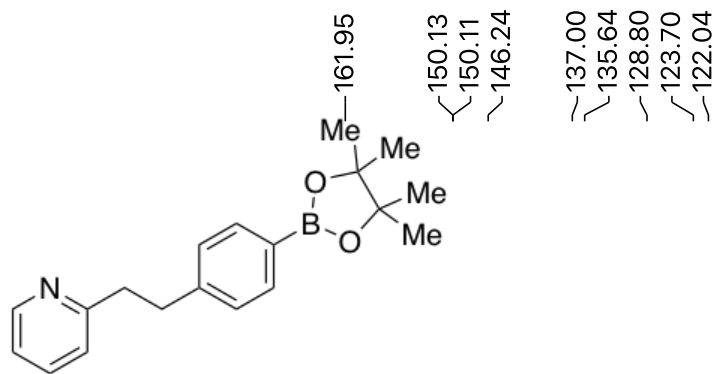
^1H NMR (400 MHz, CDCl_3)

8.56
8.56
8.55
8.55
7.73
7.71
7.57
7.56
7.55
7.54
7.53
7.52
7.22
7.20
7.12
7.12
7.11
7.11
7.10
7.10
7.09
7.09
7.06
7.06
7.06
7.05
7.04
7.04

3.12
3.11
3.10
3.09
3.08
3.08
3.07
3.07
3.06
3.05
3.04
3.03

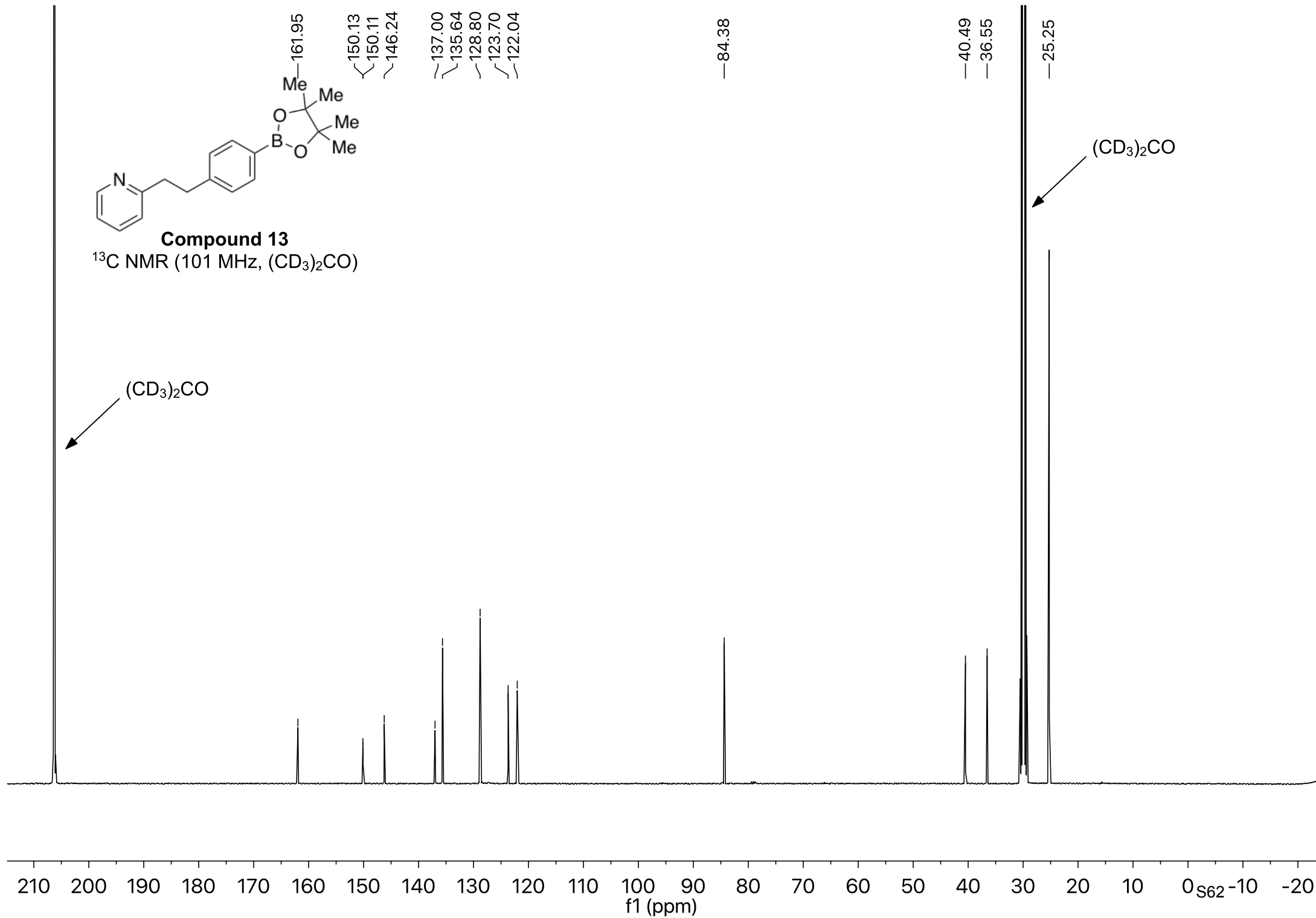
—1.33

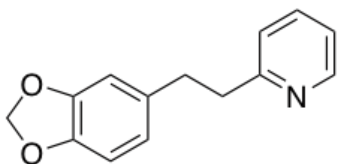




Compound 13

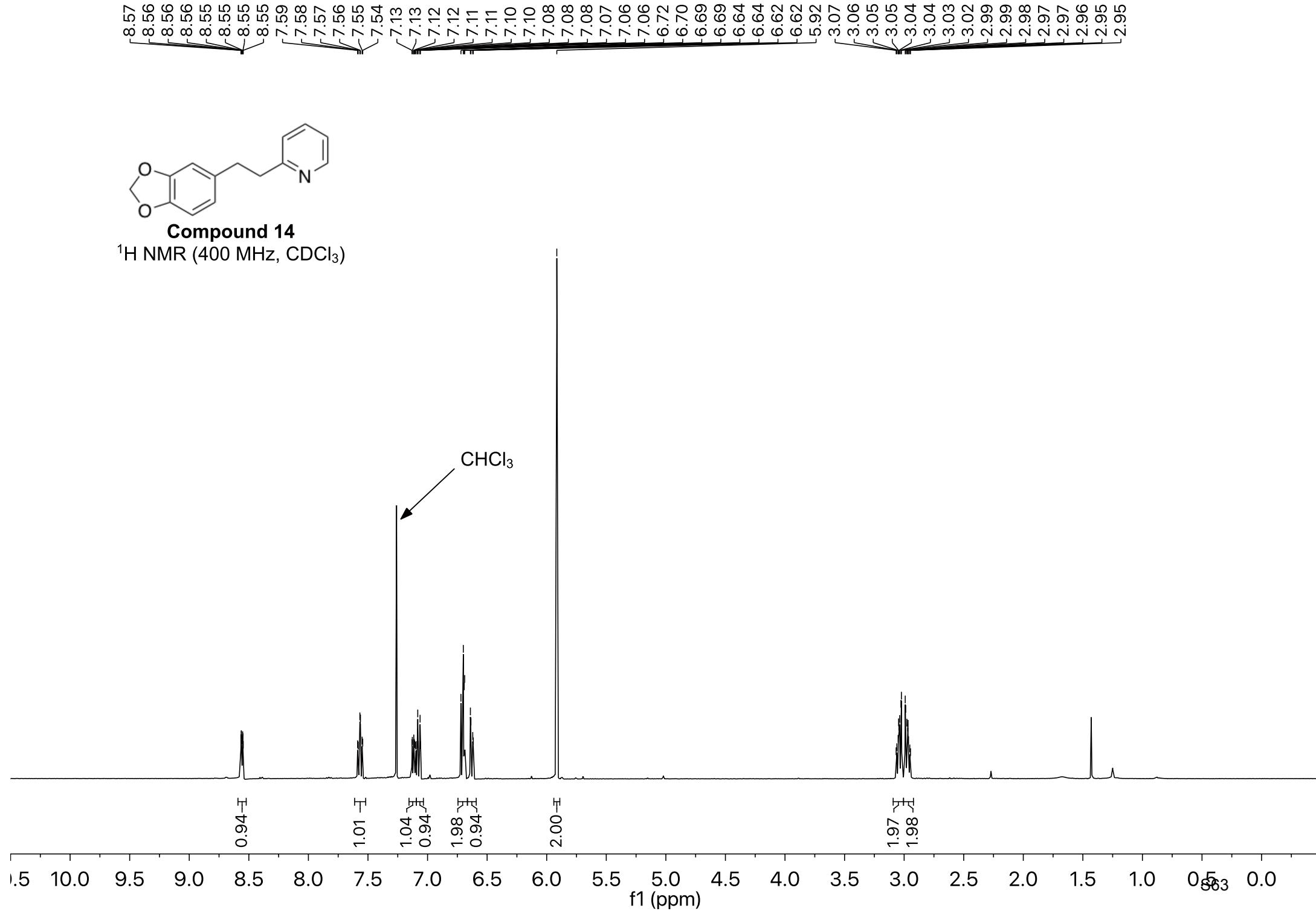
^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$)

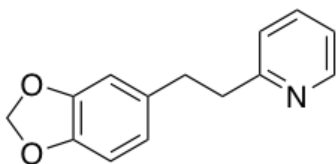




Compound 14

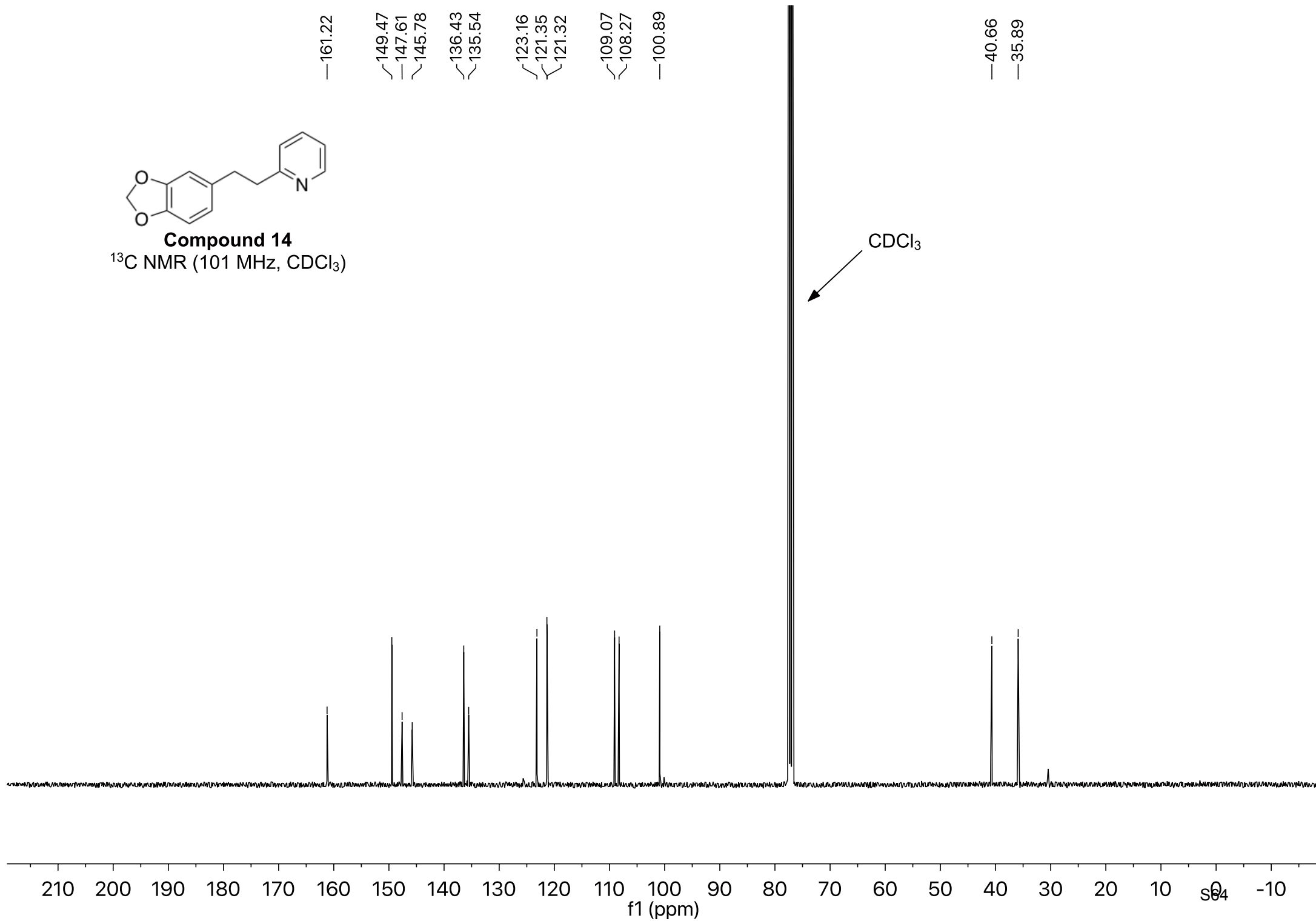
^1H NMR (400 MHz, CDCl_3)

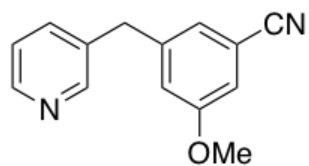




Compound 14

^{13}C NMR (101 MHz, CDCl_3)

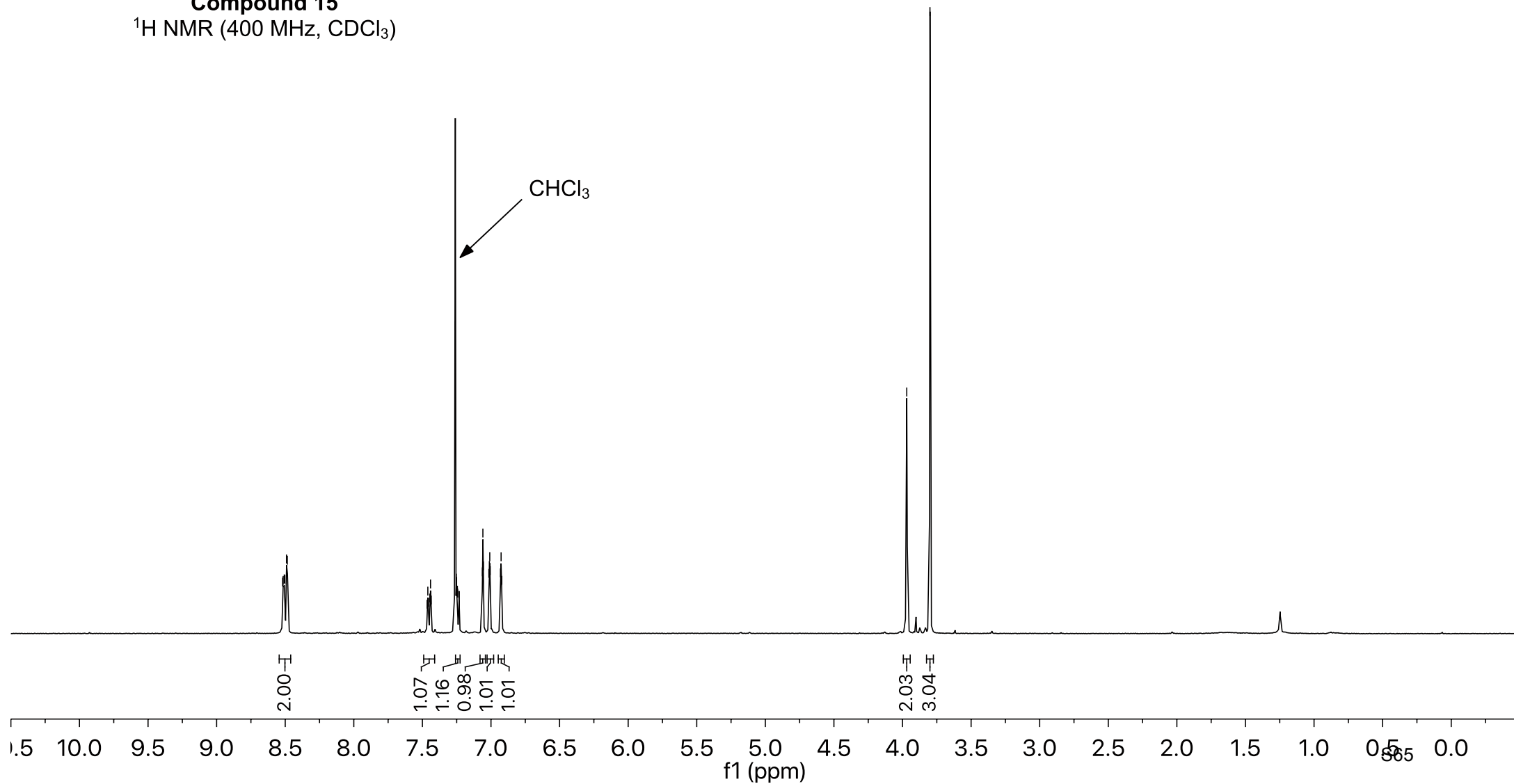


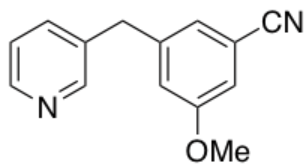


Compound 15

^1H NMR (400 MHz, CDCl_3)

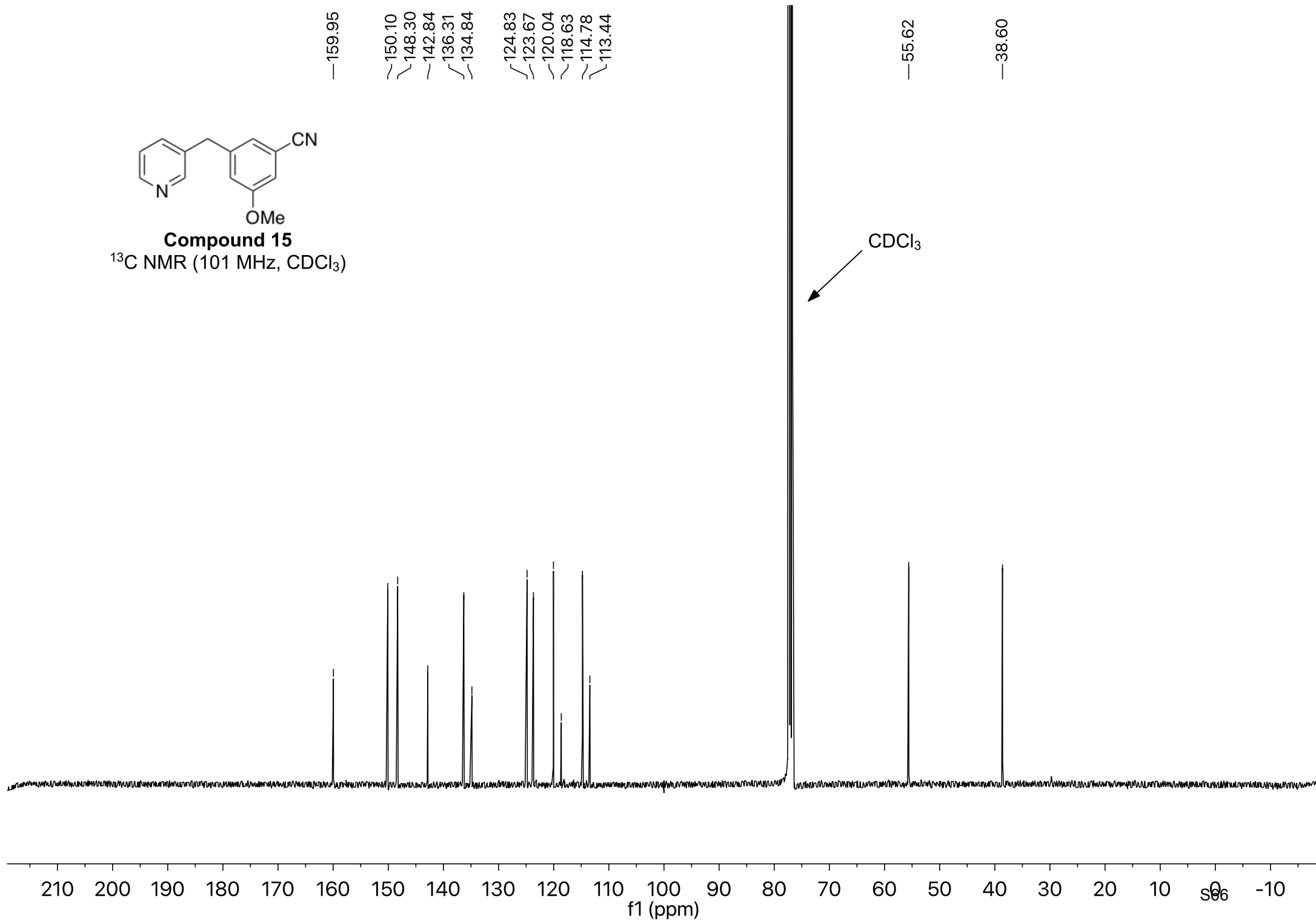
8.52, 8.51, 8.51, 8.50, 8.49, 8.48, 7.47, 7.46, 7.46, 7.45, 7.44, 7.44, 7.26, 7.25, 7.25, 7.25, 7.24, 7.23, 7.23, 7.06, 7.06, 7.06, 7.02, 7.01, 7.01, 7.01, 6.93, 6.93, 6.92, 3.97, 3.80

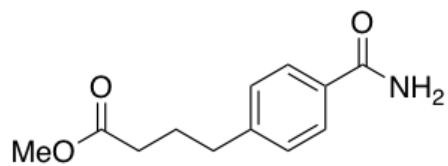




Compound 15

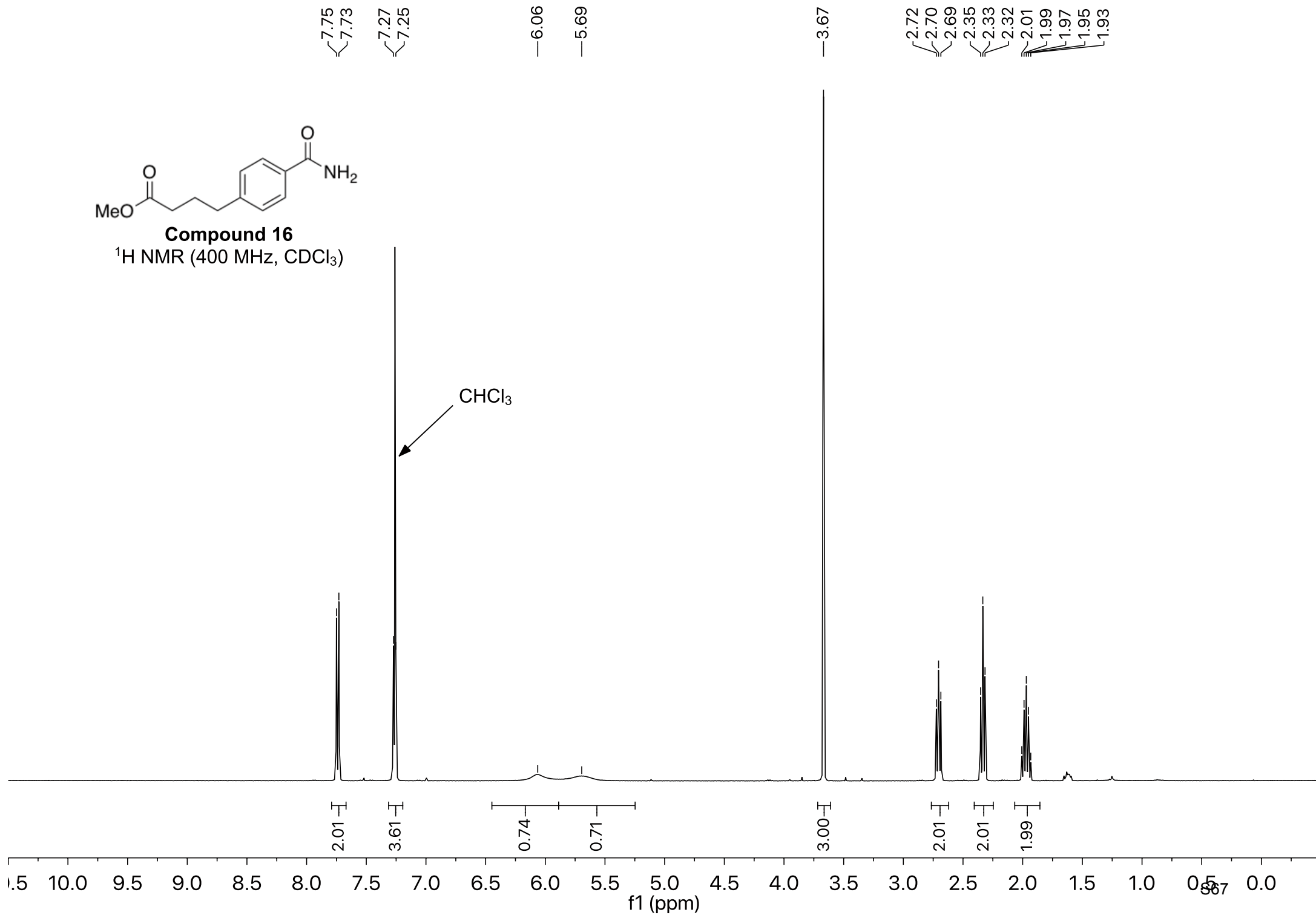
^{13}C NMR (101 MHz, CDCl_3)

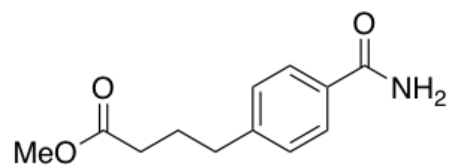




Compound 16

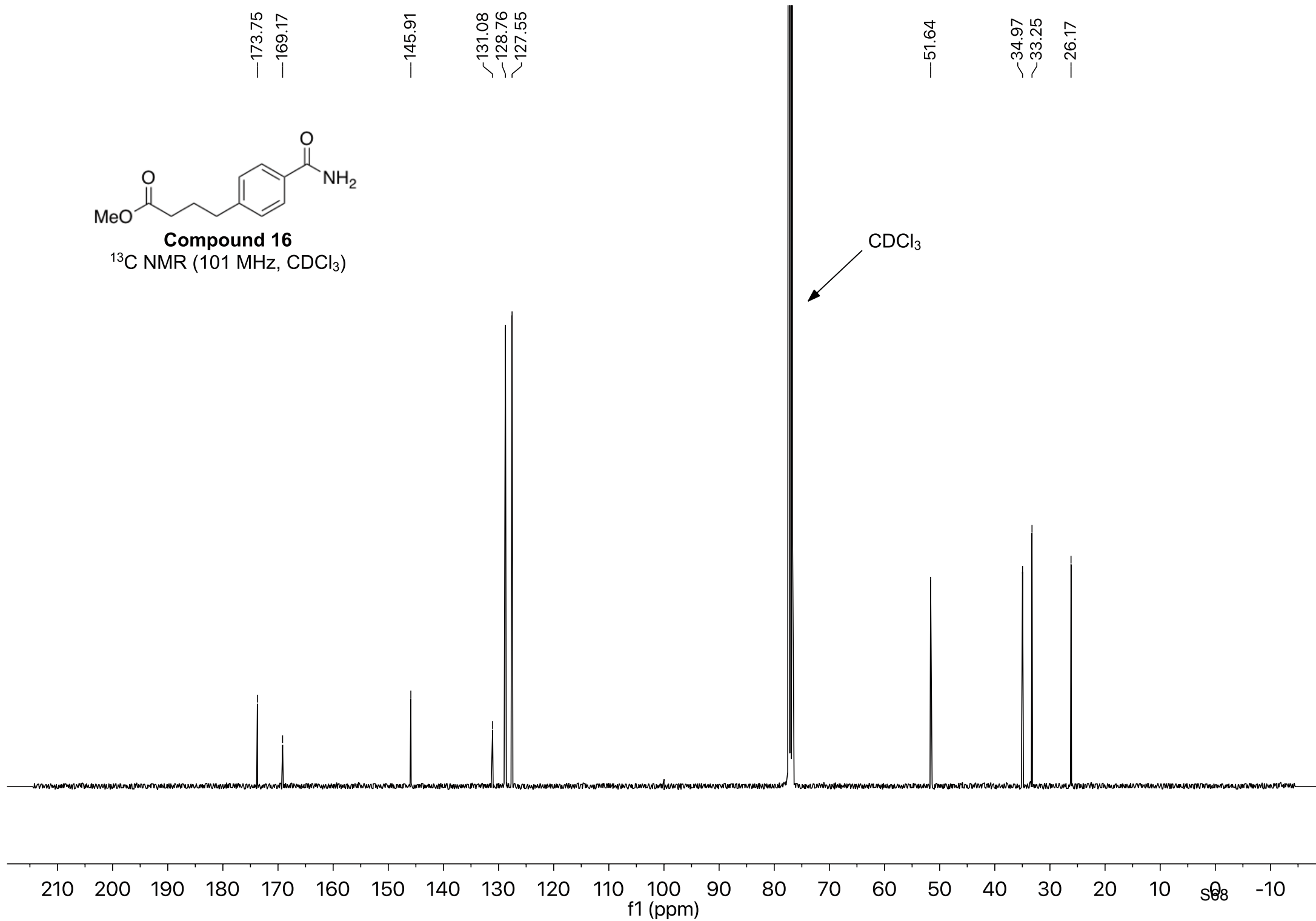
^1H NMR (400 MHz, CDCl_3)

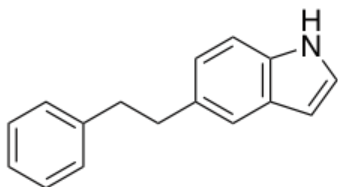




Compound 16

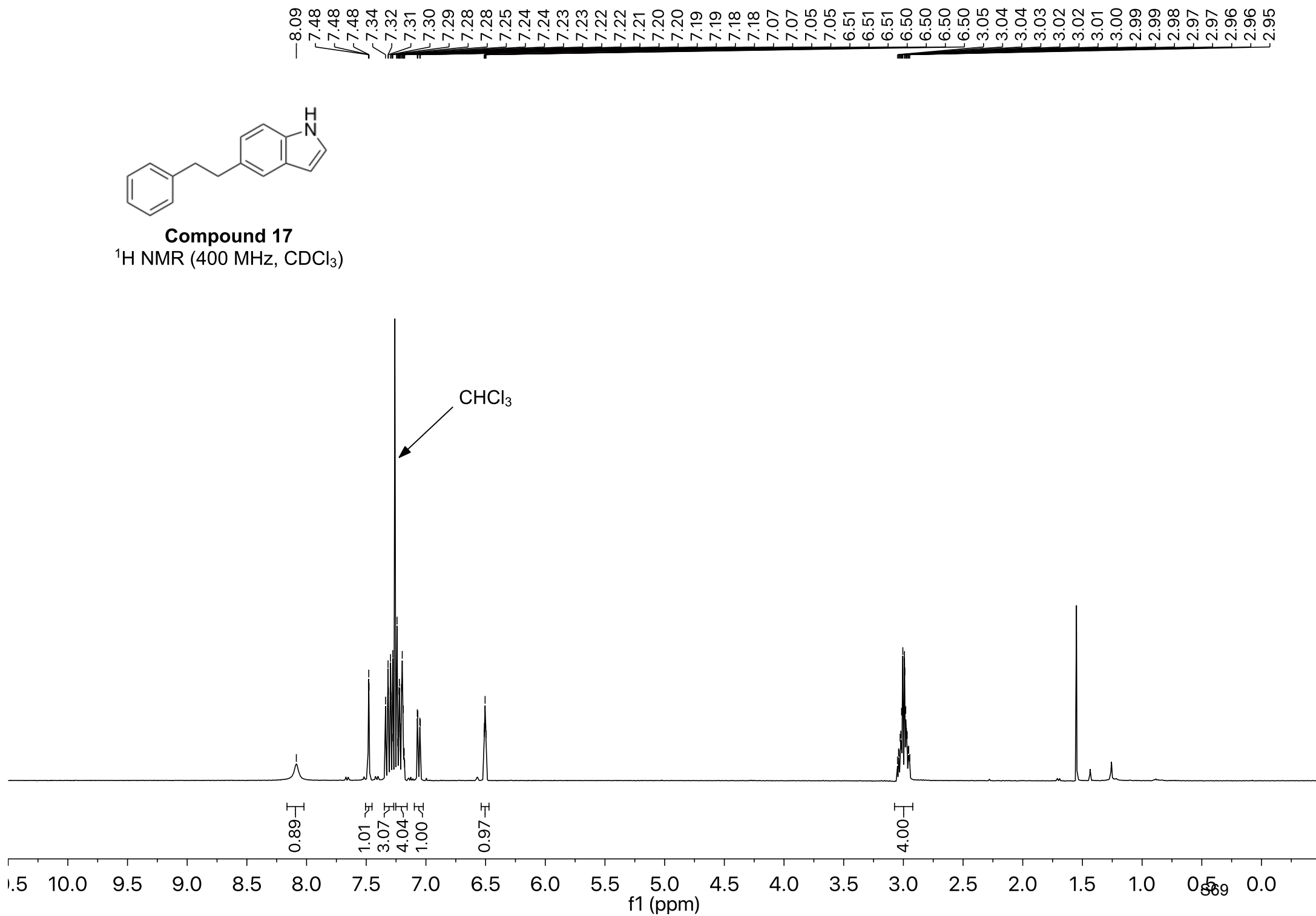
^{13}C NMR (101 MHz, CDCl_3)

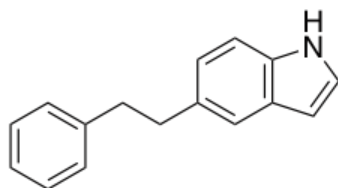




Compound 17

^1H NMR (400 MHz, CDCl_3)





Compound 17

^{13}C NMR (101 MHz, CDCl_3)

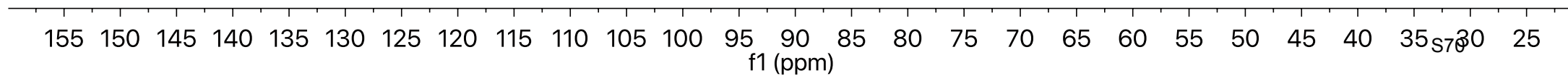
—142.31
 ~134.39
 ~133.30
 ~128.50
 ~128.31
 ~128.06
 ~125.79
 ~124.32
 ~123.04
 ~119.88

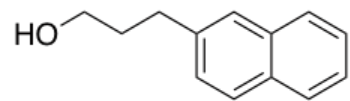
—110.78

—102.33

~38.91
 ~38.19

CDCl_3





Compound 18

^1H NMR (600 MHz, CDCl_3)

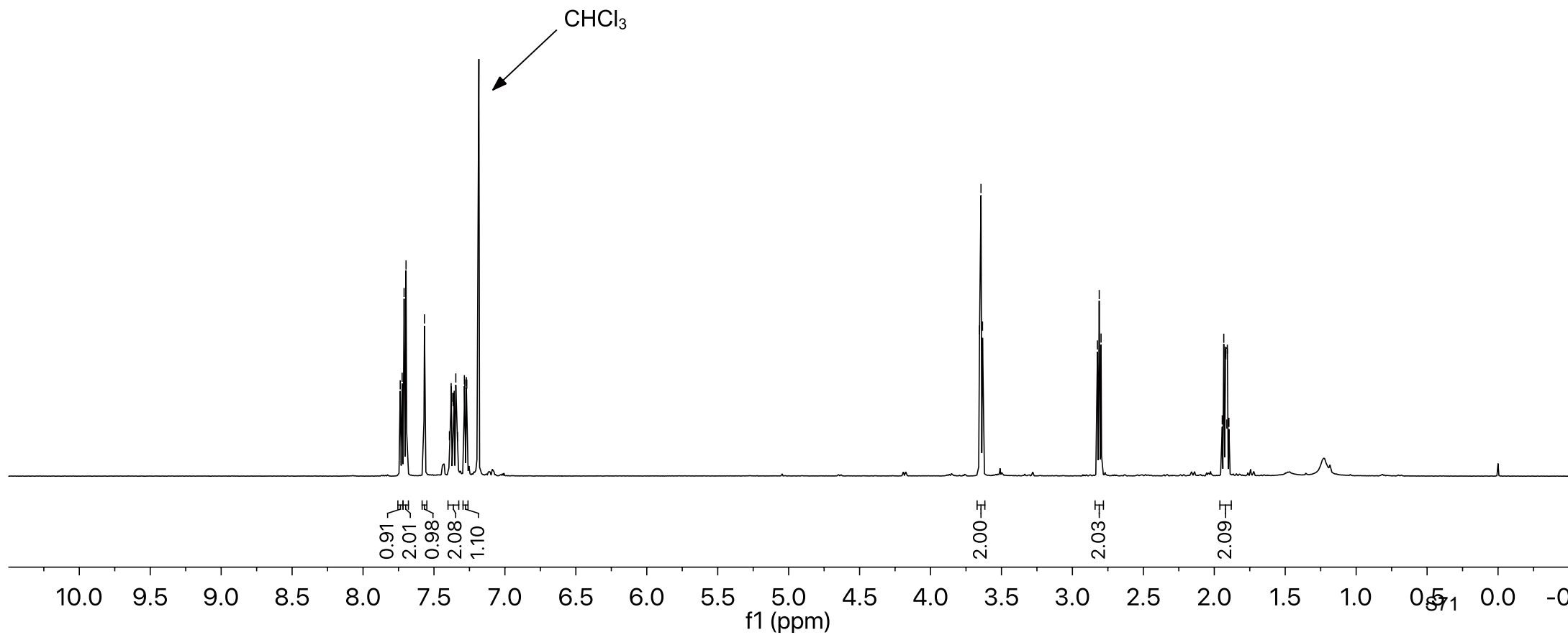
7.74
7.72
7.71
7.71
7.70
7.57
7.39
7.38
7.37
7.36
7.36
7.36
7.35
7.33
7.29
7.28
7.27
7.27

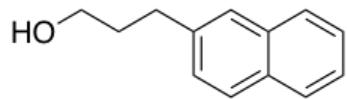
3.66
3.64
3.63

2.82
2.81
2.80

1.94
1.93
1.93
1.92
1.92
1.91
1.91
1.90

CHCl_3





Compound 18

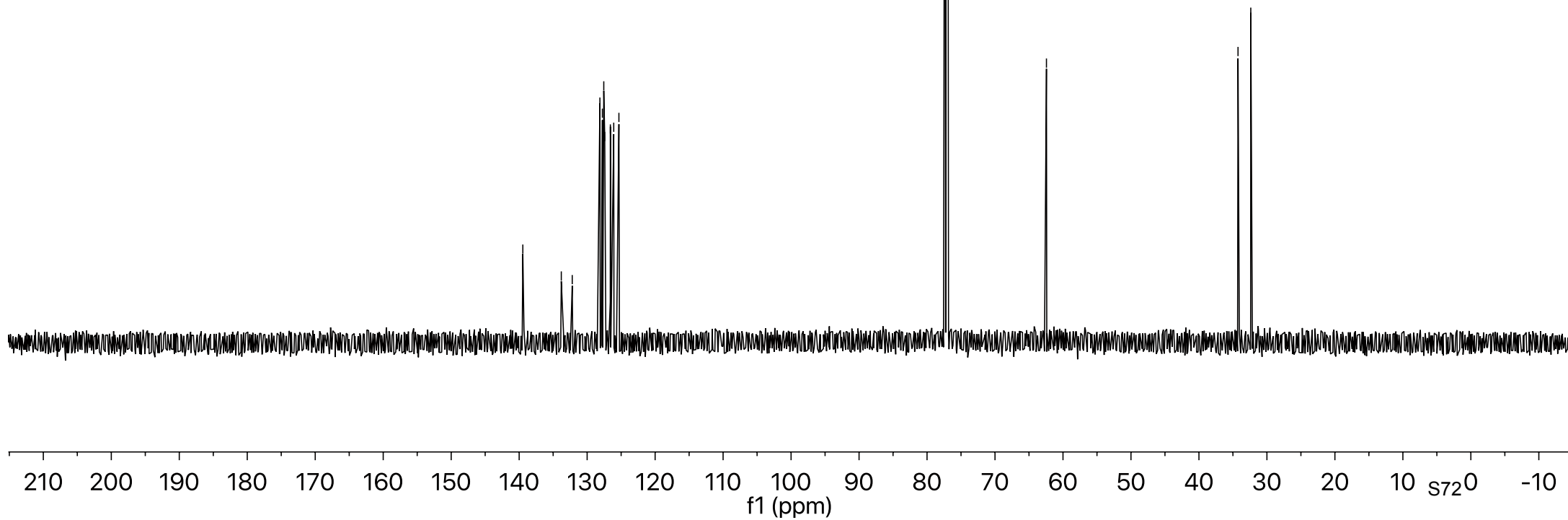
^{13}C NMR (151 MHz, CDCl_3)

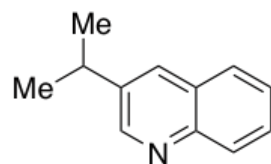
139.46
133.80
132.19
128.12
127.76
127.55
127.41
126.58
126.09
125.33

—62.43

~34.25
~32.37

CDCl_3





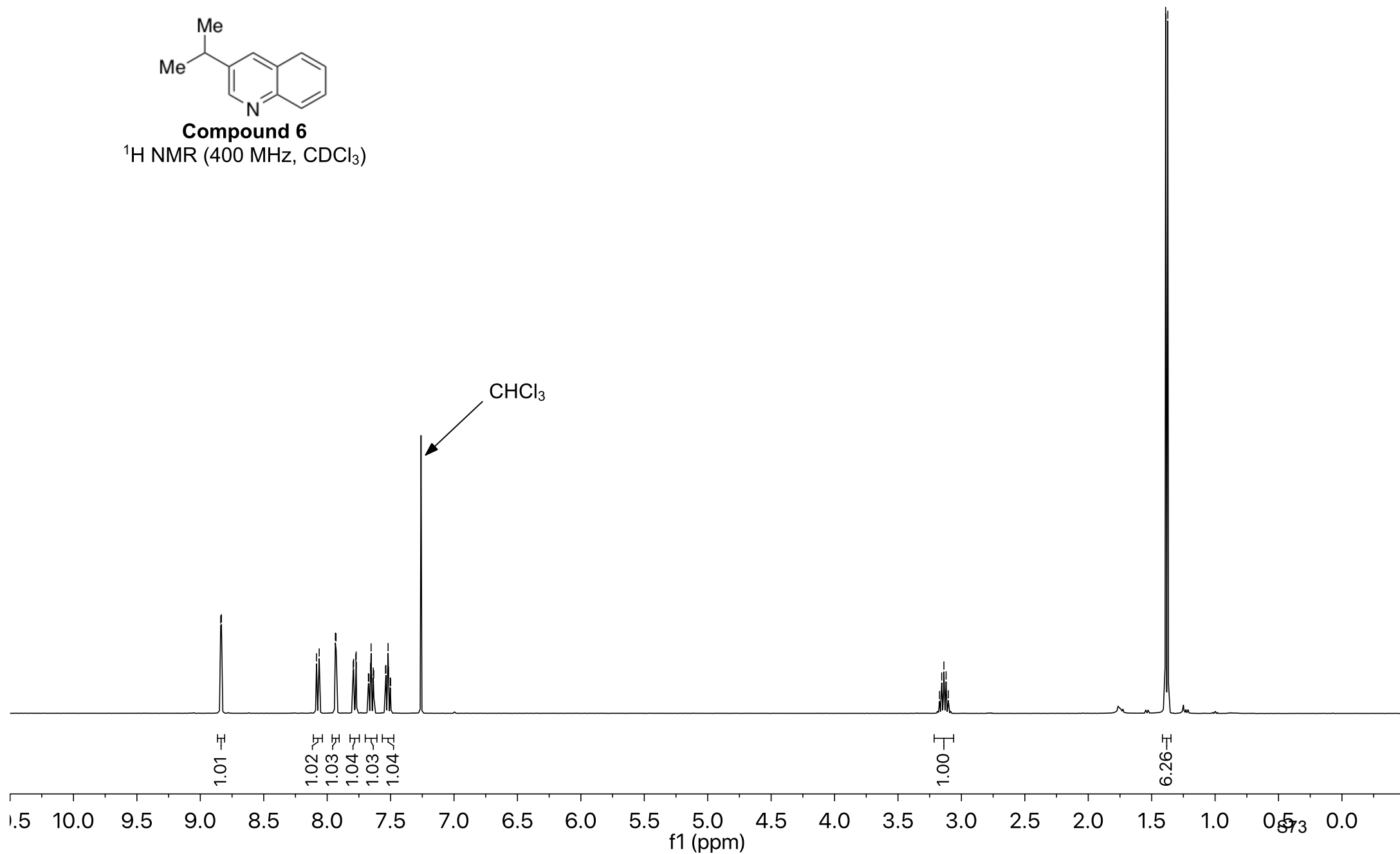
Compound 6

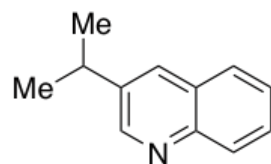
^1H NMR (400 MHz, CDCl_3)

8.84
8.83
8.08
8.06
7.94
7.93
7.79
7.79
7.77
7.77
7.67
7.67
7.66
7.65
7.65
7.64
7.63
7.54
7.54
7.52
7.52
7.52
7.50
7.50

3.17
3.16
3.14
3.12
3.10

1.39
1.37





Compound 6

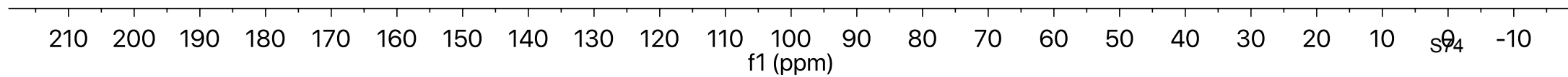
^{13}C NMR (101 MHz, CDCl_3)

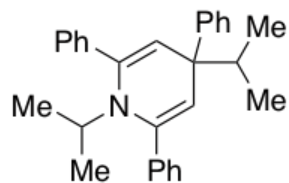
151.28
146.90
141.12
131.78
129.11
128.53
128.23
127.47
126.50

31.87

23.69

CDCl_3





Compound 7

^1H NMR (400 MHz, CDCl_3)

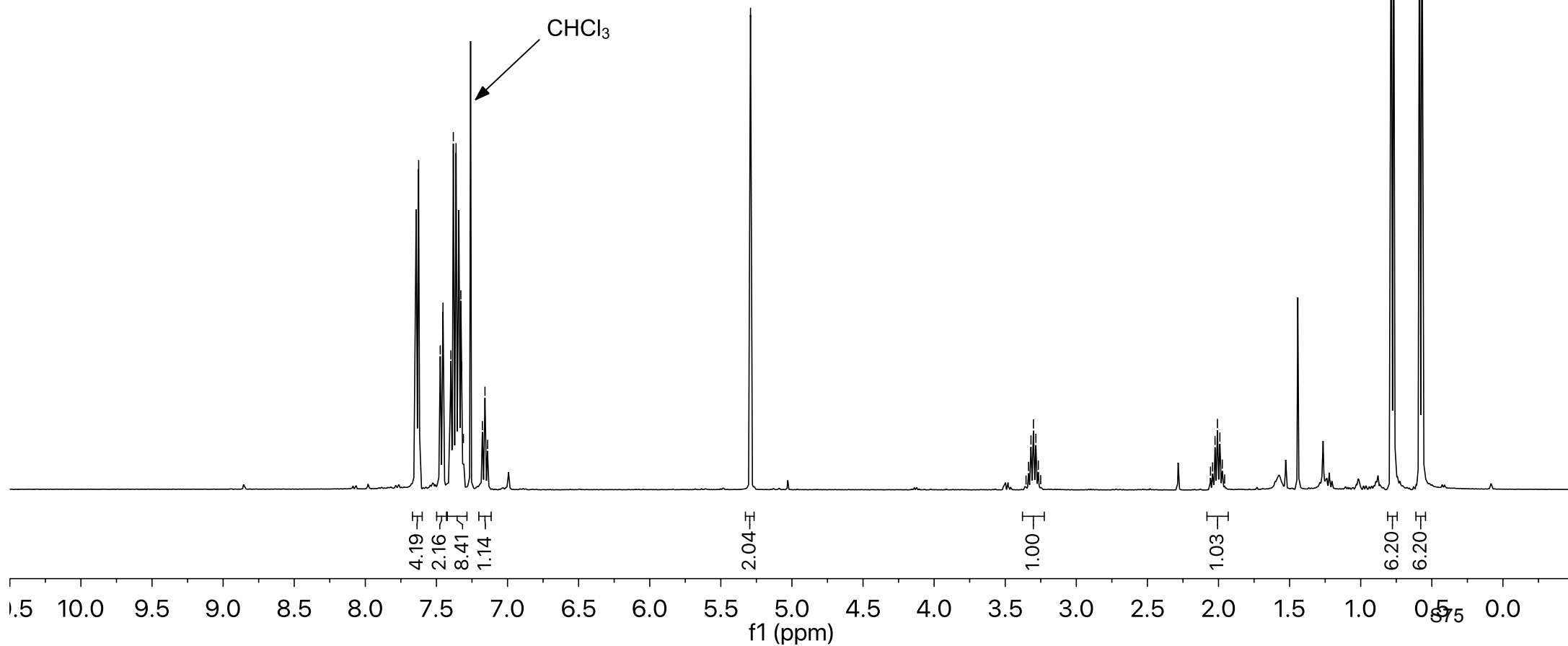
7.64
7.62
7.47
7.45
7.40
7.38
7.36
7.34
7.33
7.32
7.31
7.18
7.16
7.14

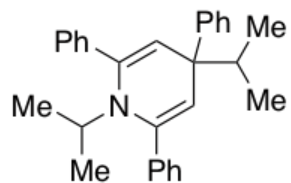
5.29

3.35
3.34
3.32
3.30
3.28
3.27
3.25

2.06
2.04
2.02
2.01
1.99
1.97
1.96

0.79
0.77
0.59
0.57





Compound 7

^{13}C NMR (101 MHz, CDCl_3)

151.66
145.25
140.87
128.17
127.96
127.89
127.66
126.83
125.05
115.30

53.59

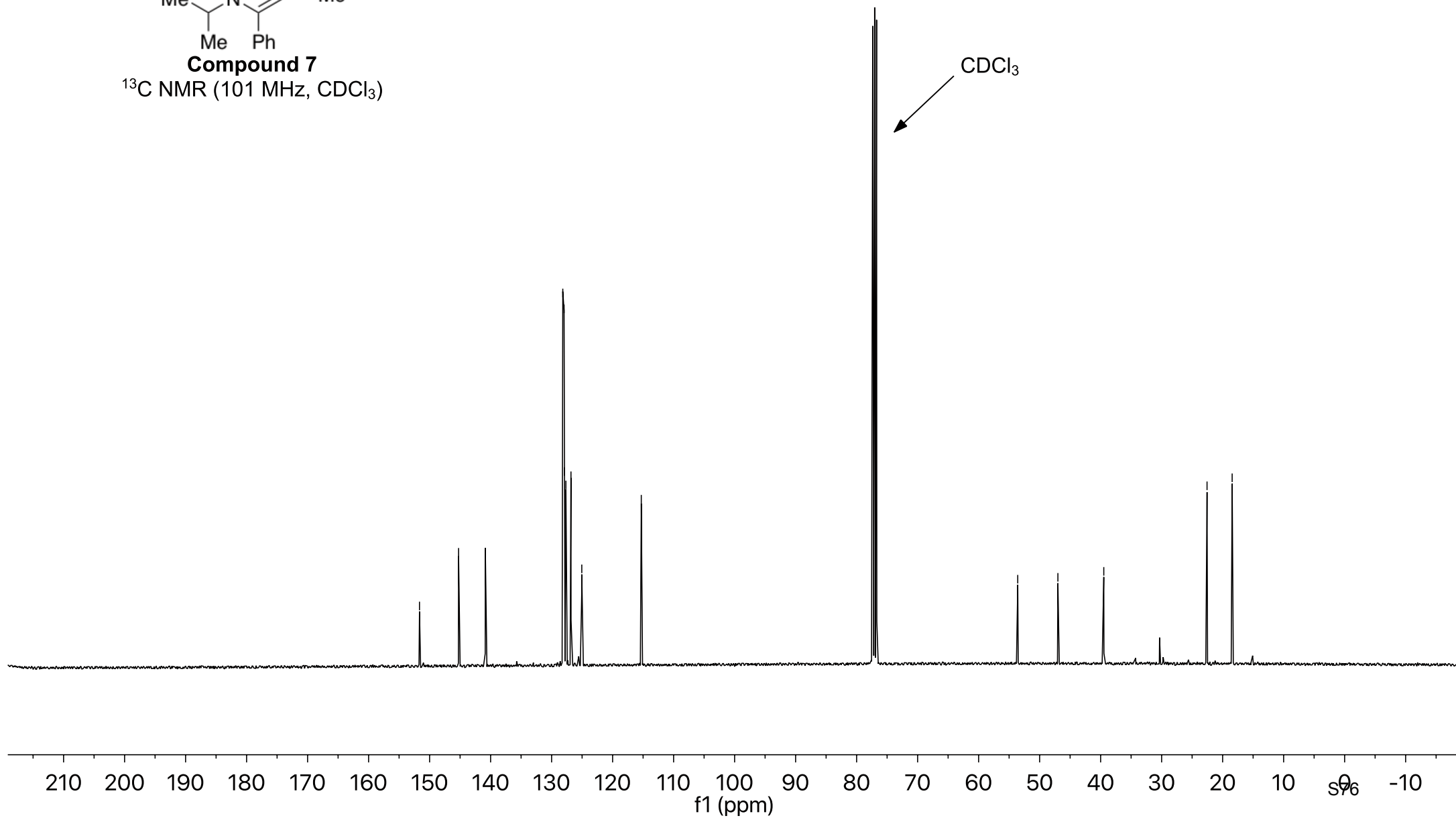
47.00

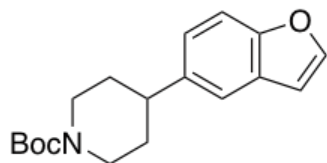
39.48

22.56

18.44

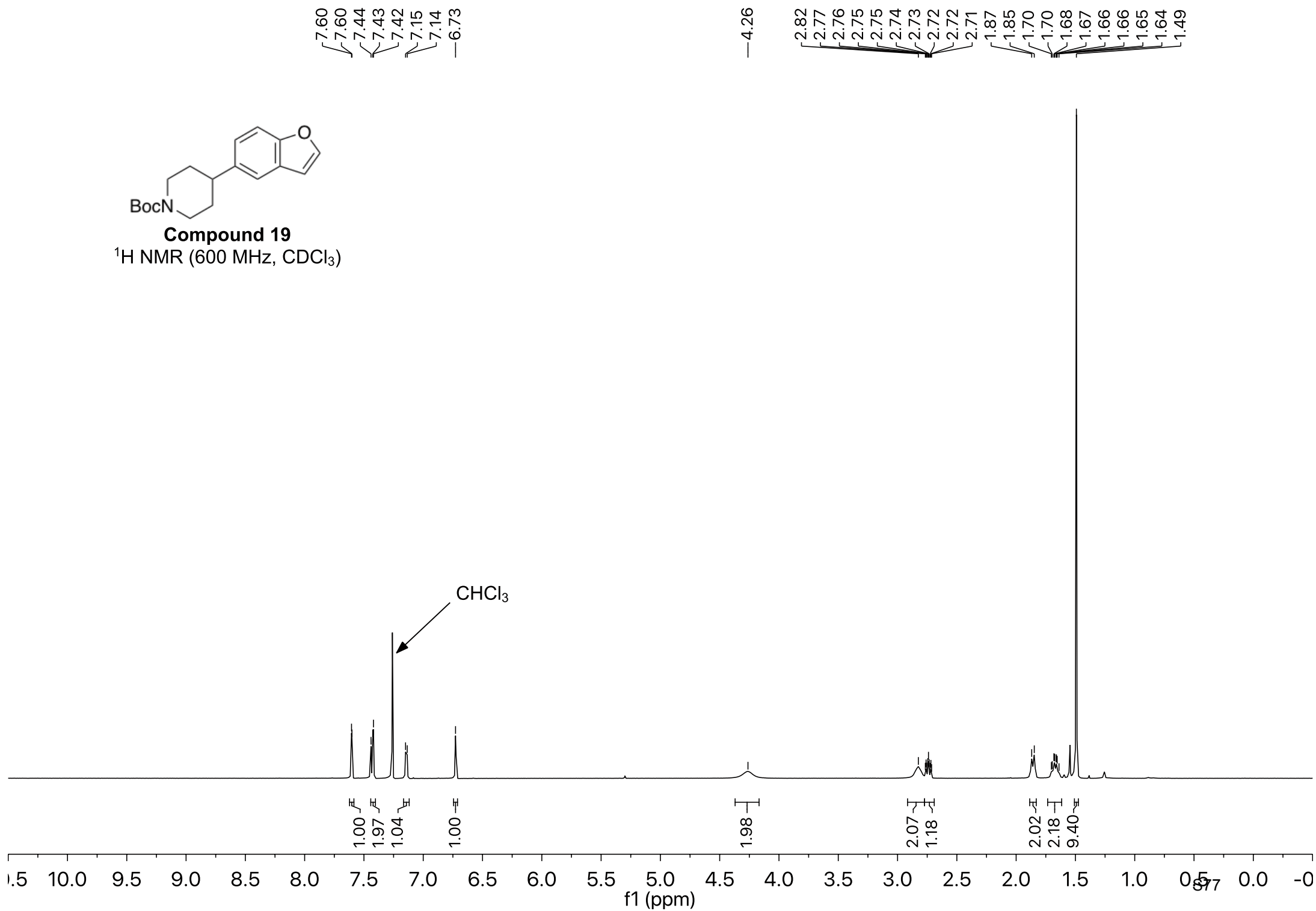
CDCl_3

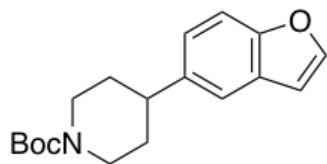




Compound 19

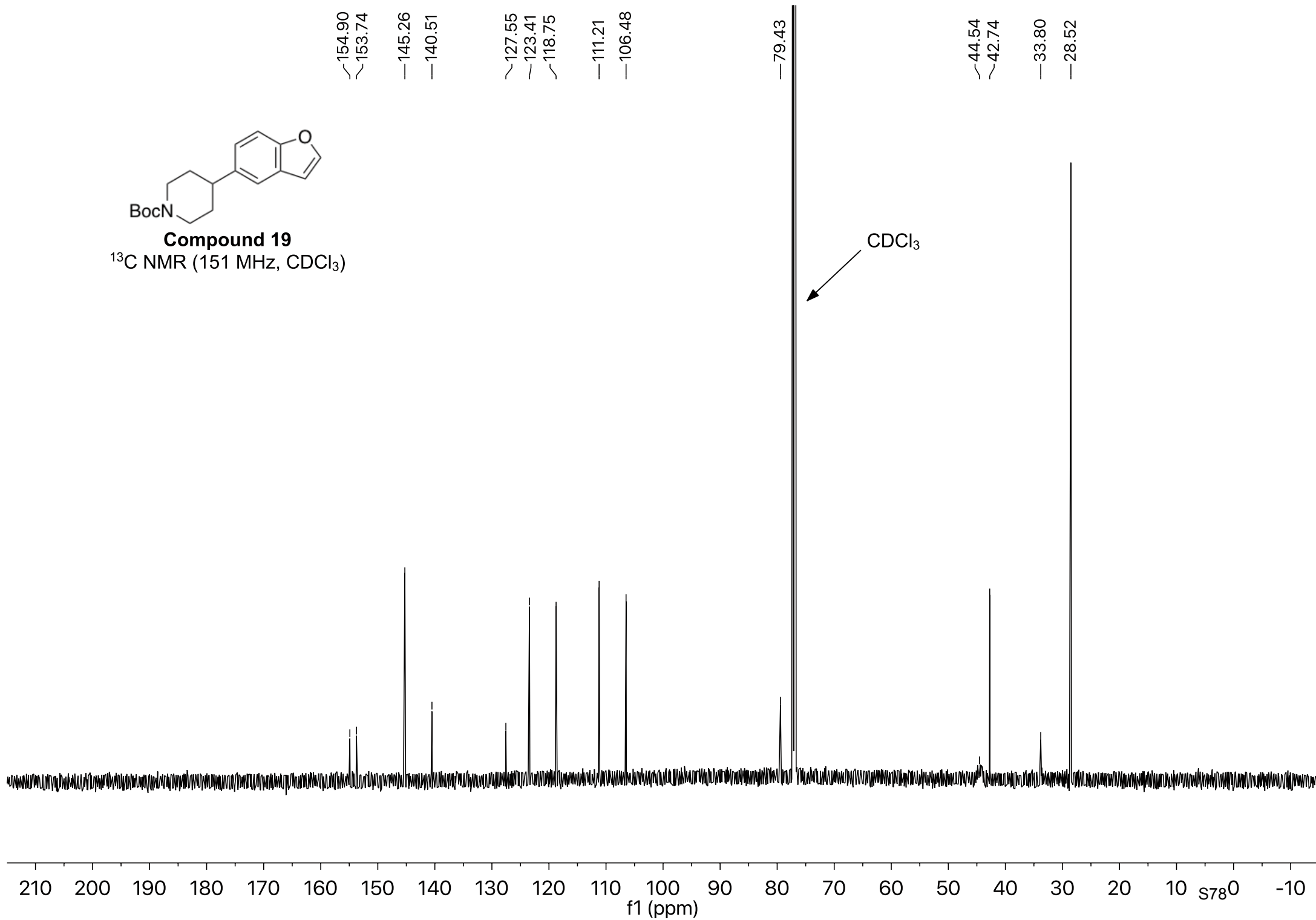
^1H NMR (600 MHz, CDCl_3)

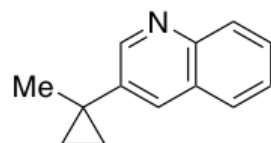




Compound 19

^{13}C NMR (151 MHz, CDCl_3)



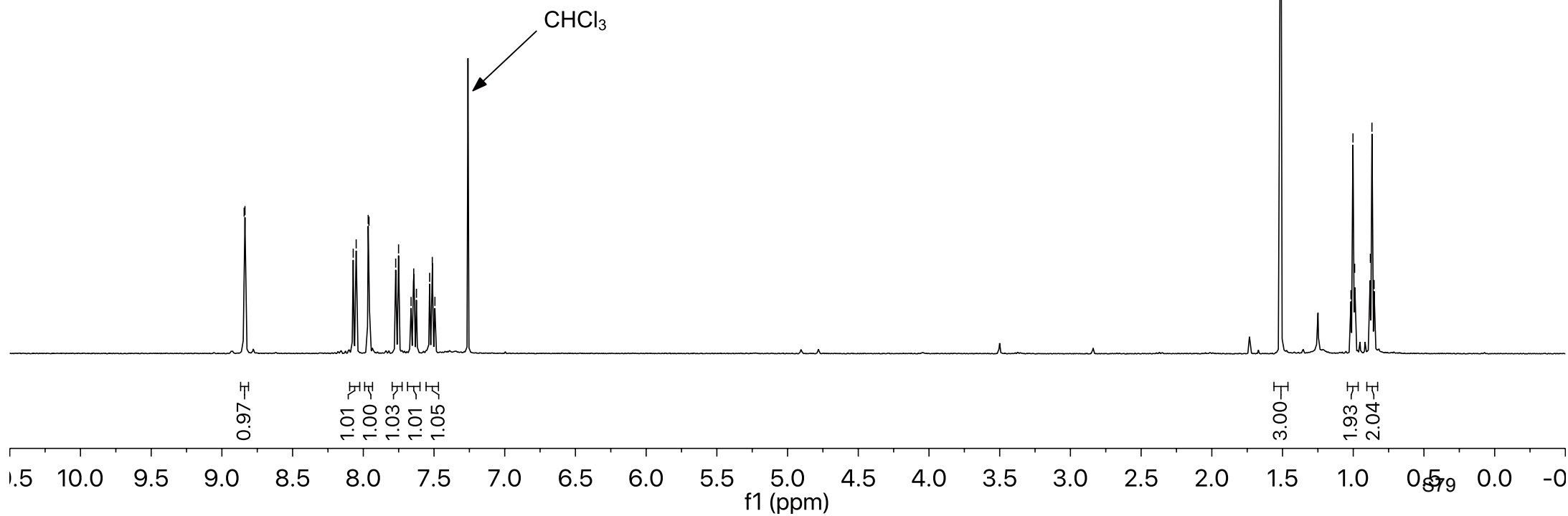


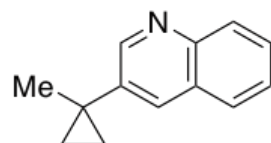
Compound 20

^1H NMR (400 MHz, CDCl_3)

8.84
8.84
8.07
8.05
7.97
7.96
7.77
7.75
7.66
7.64
7.62
7.53
7.51
7.49

1.51
1.02
1.00
0.99
0.88
0.87
0.85





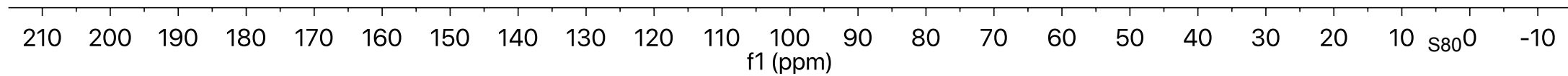
Compound 20

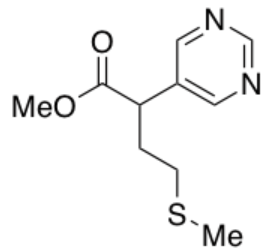
^{13}C NMR (151 MHz, CDCl_3)

— 151.02
— 146.55
— 139.58
— 132.91
— 129.09
— 128.54
— 127.95
— 127.35
— 126.56

— 25.58
— 18.40
— 15.03

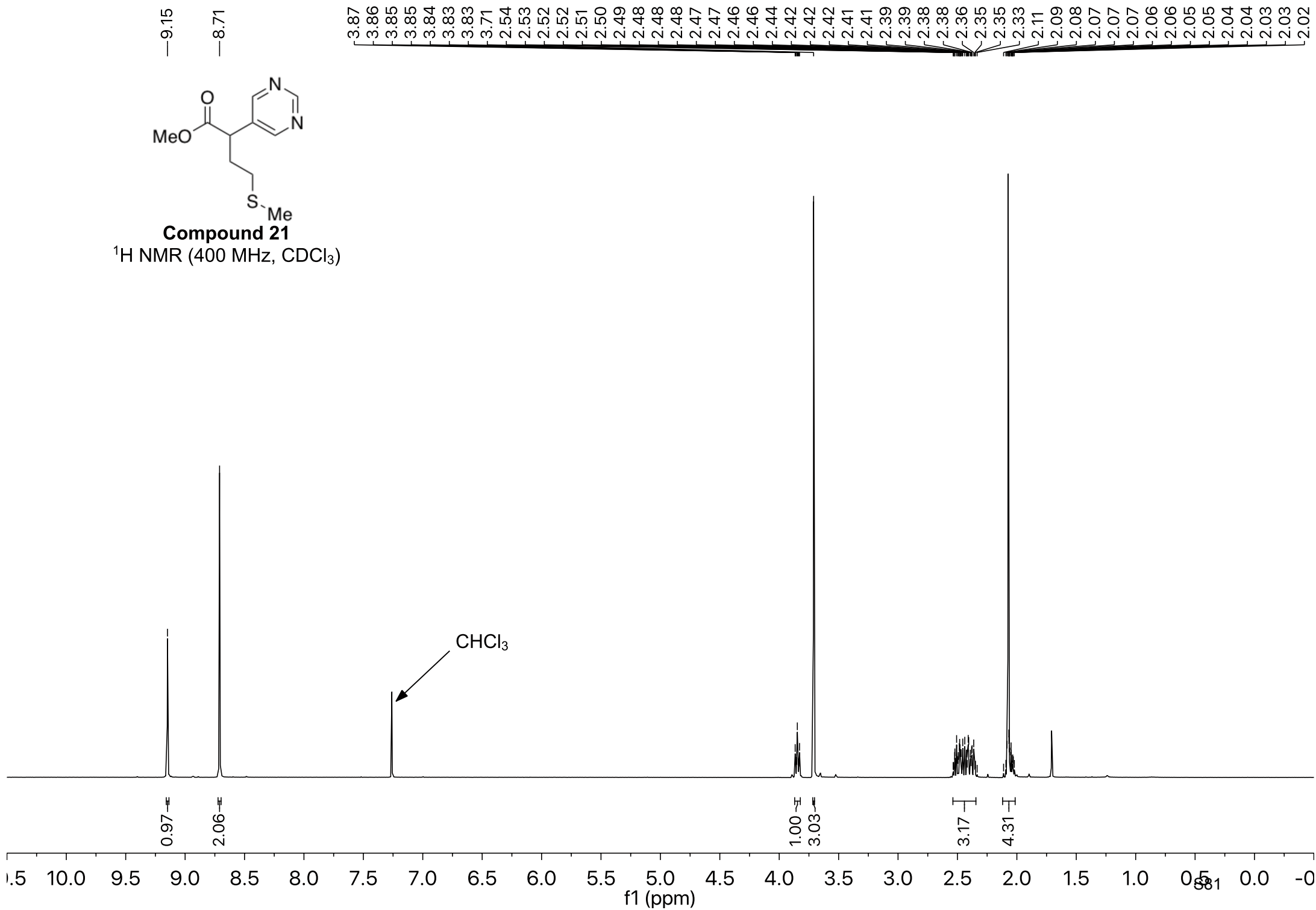
CDCl_3

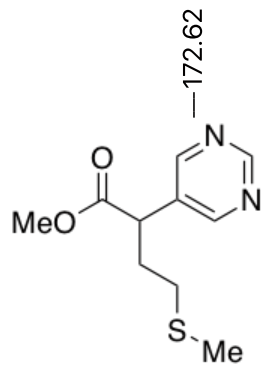




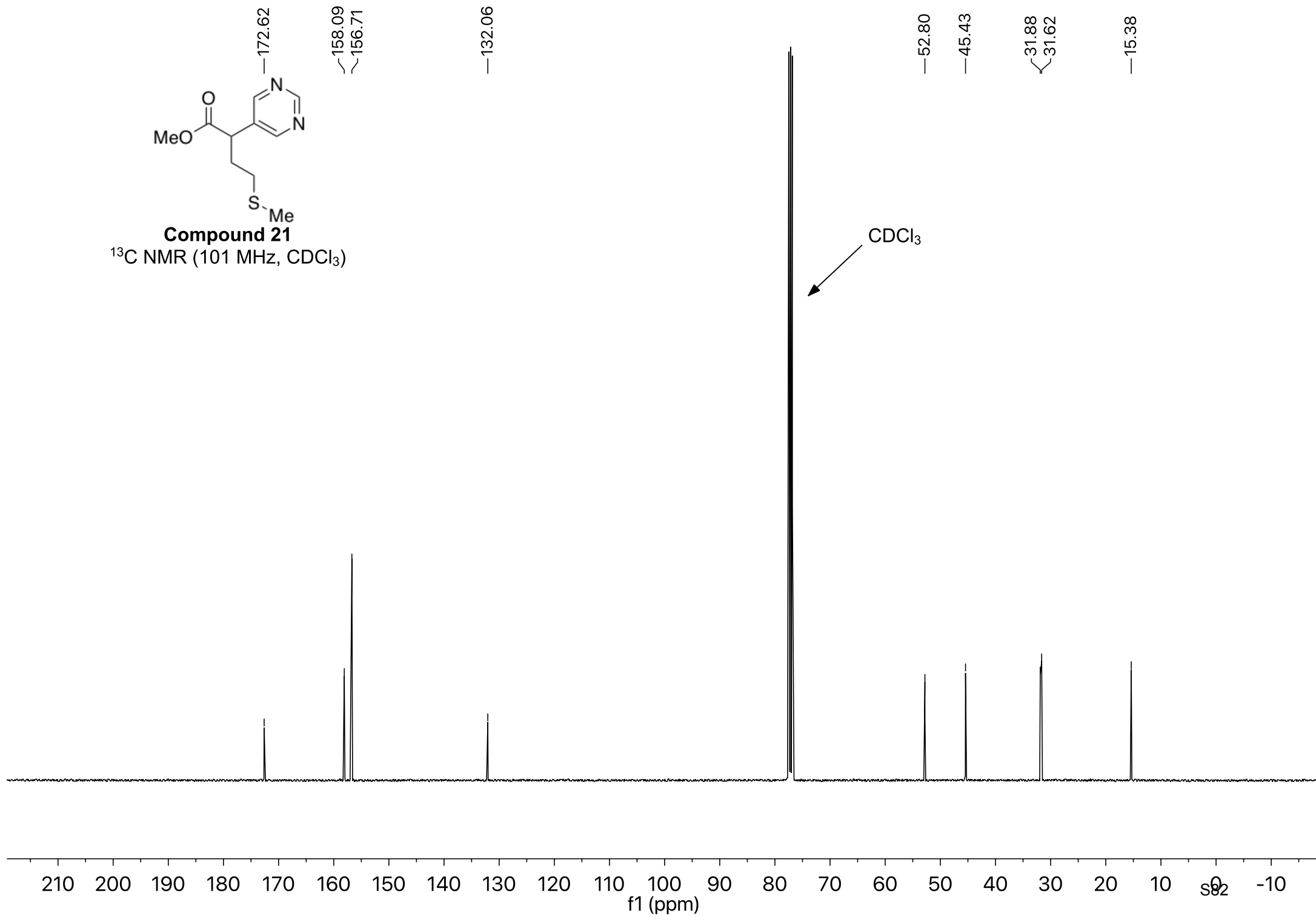
Compound 21

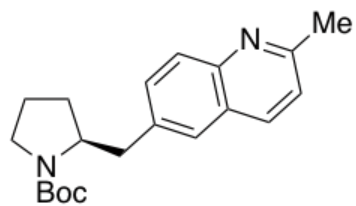
^1H NMR (400 MHz, CDCl_3)





Compound 21
 ^{13}C NMR (101 MHz, CDCl_3)



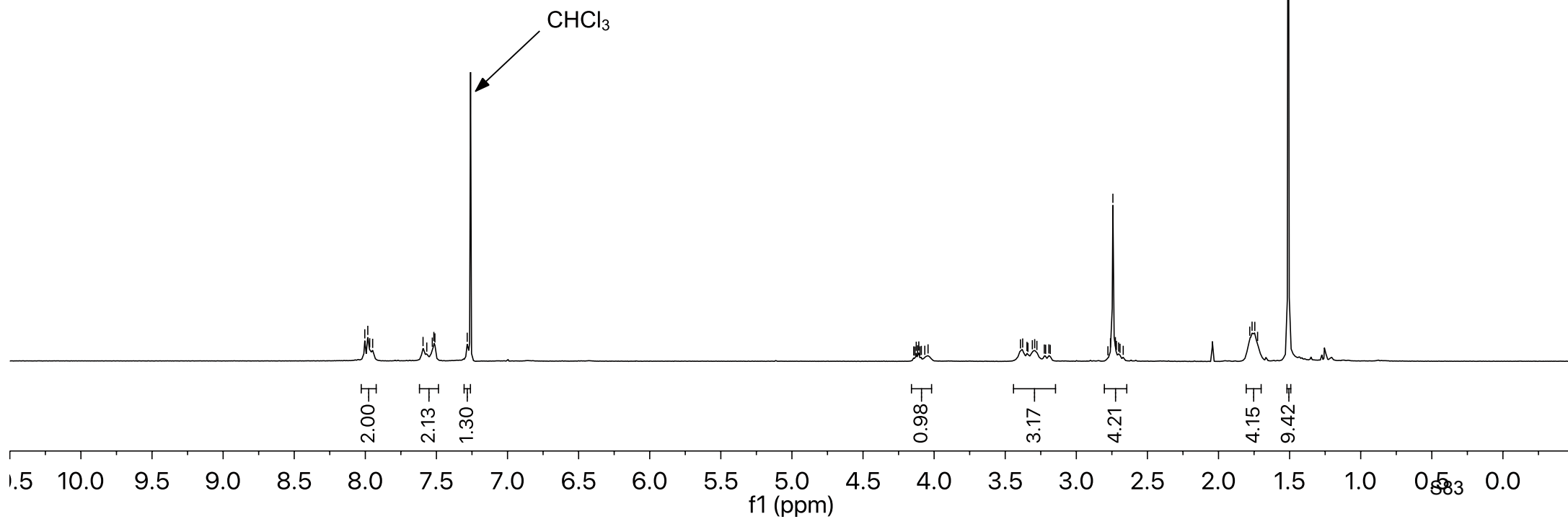


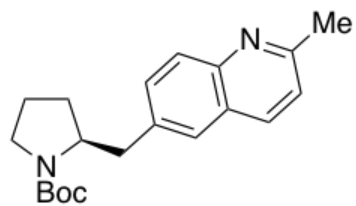
Compound 22

^1H NMR (400 MHz, CDCl_3)

8.00
7.98
7.97
7.95
7.59
7.57
7.53
7.52
7.51
7.28

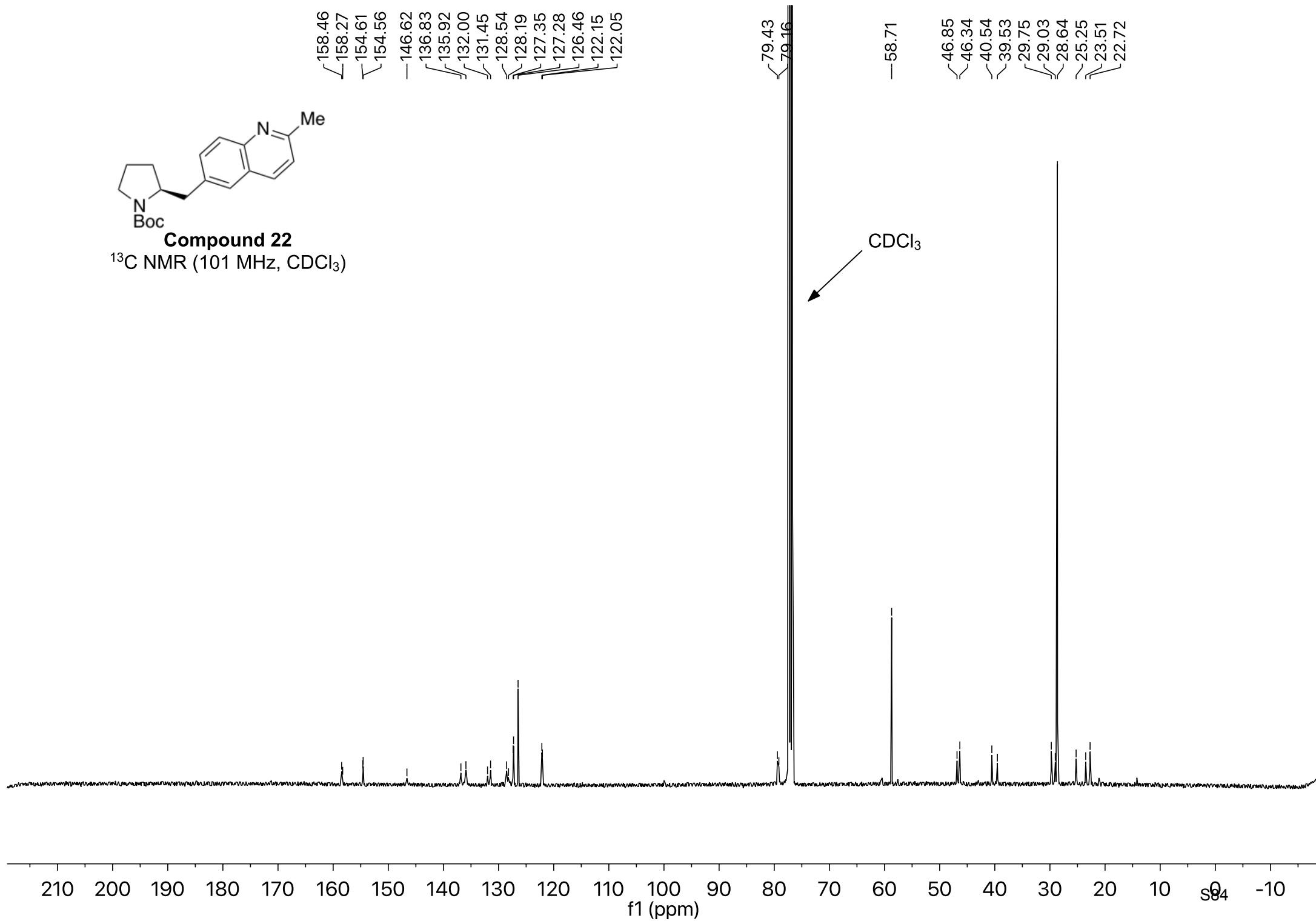
4.14
4.13
4.13
4.12
4.11
4.10
4.09
4.07
4.04
3.39
3.38
3.35
3.34
3.31
3.29
3.28
3.23
3.22
3.19
3.18
2.78
2.76
2.74
2.73
2.72
2.70
2.69
2.67
1.78
1.76
1.74
1.73
1.51

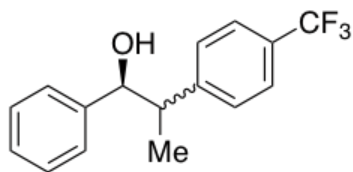




Compound 22

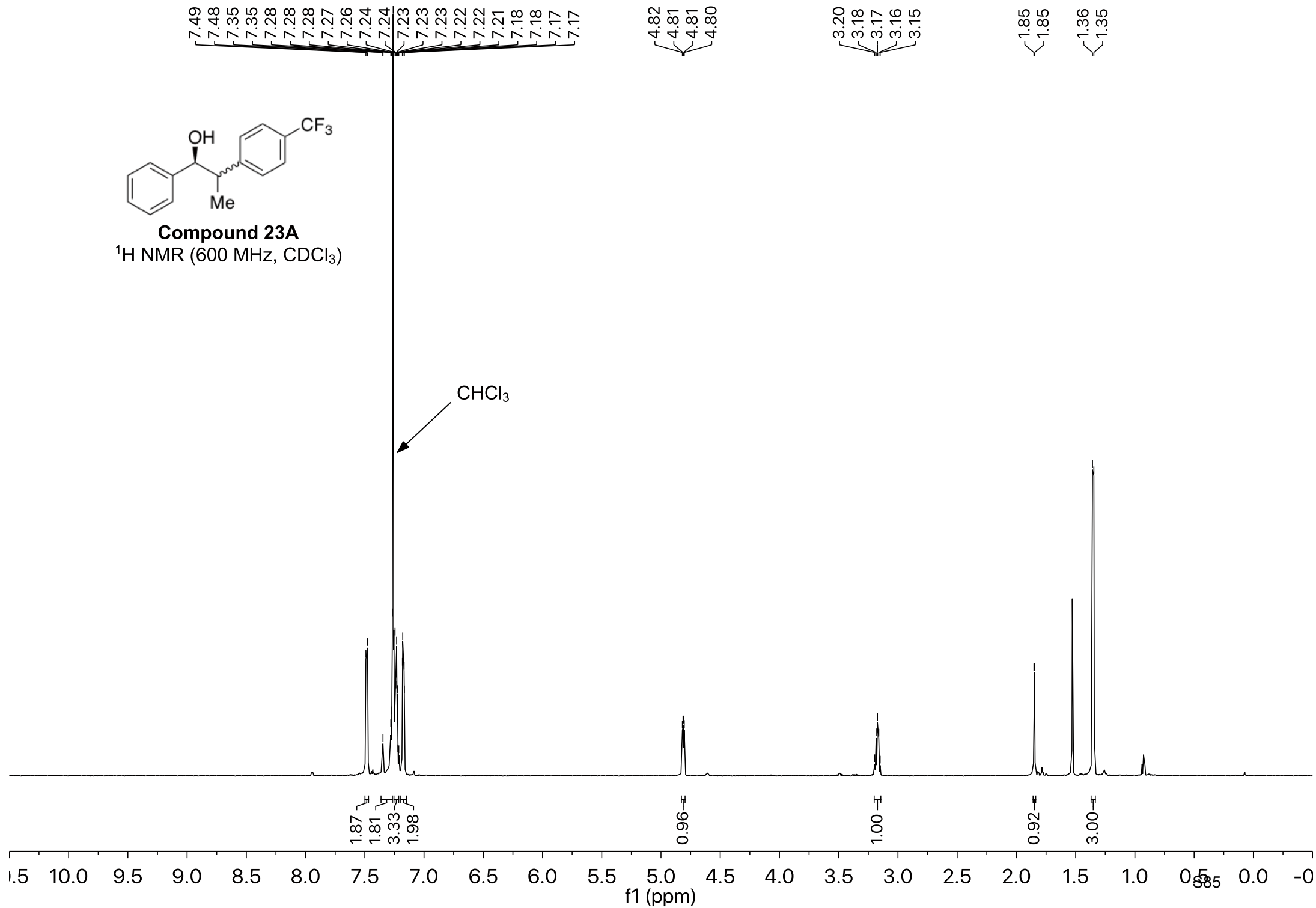
^{13}C NMR (101 MHz, CDCl_3)

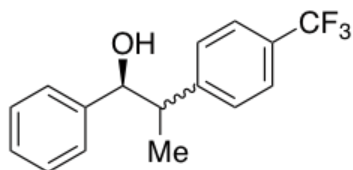




Compound 23A

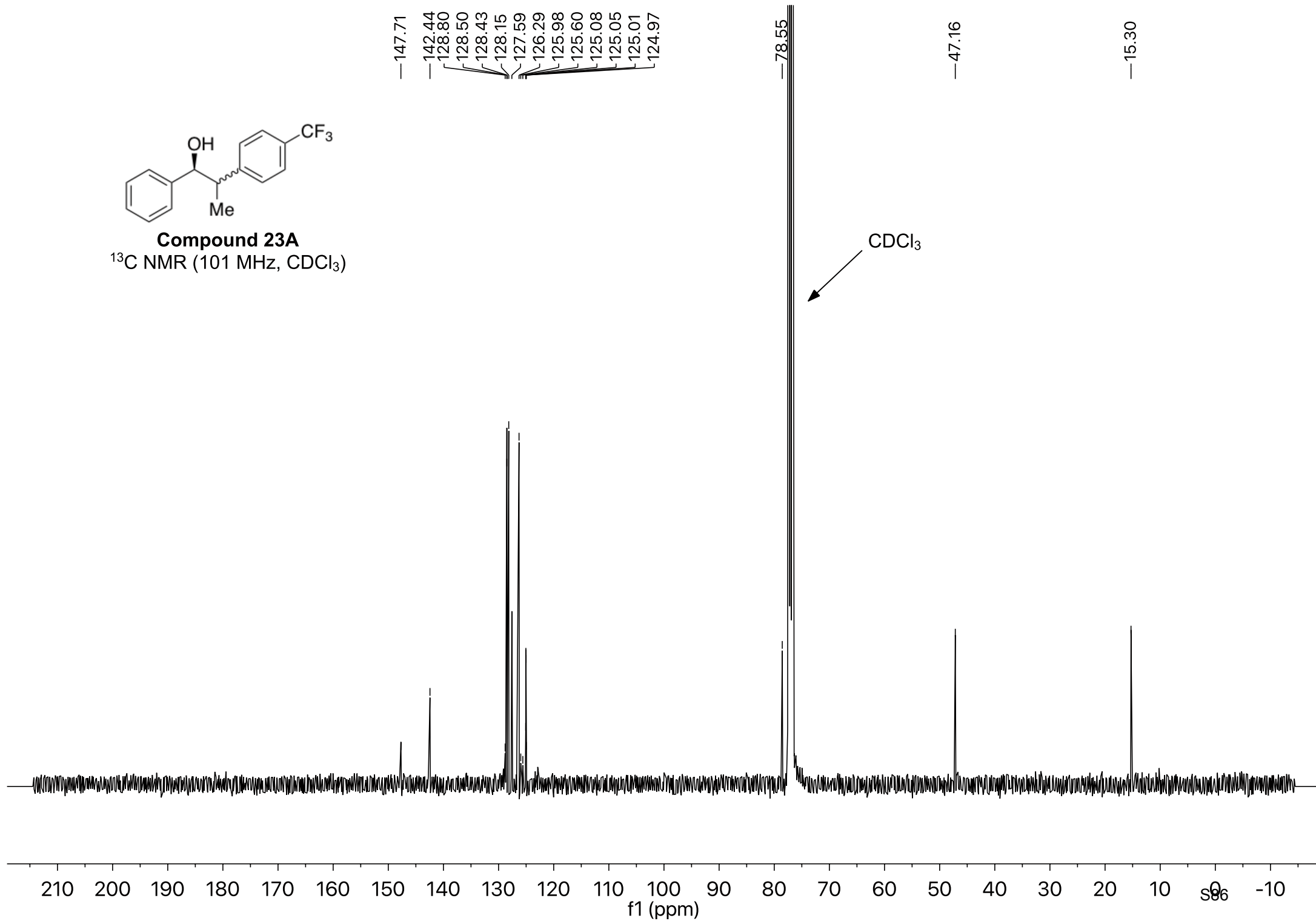
^1H NMR (600 MHz, CDCl_3)

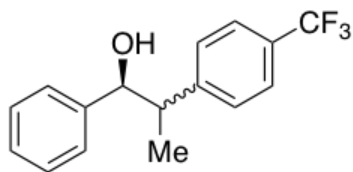




Compound 23A

^{13}C NMR (101 MHz, CDCl_3)

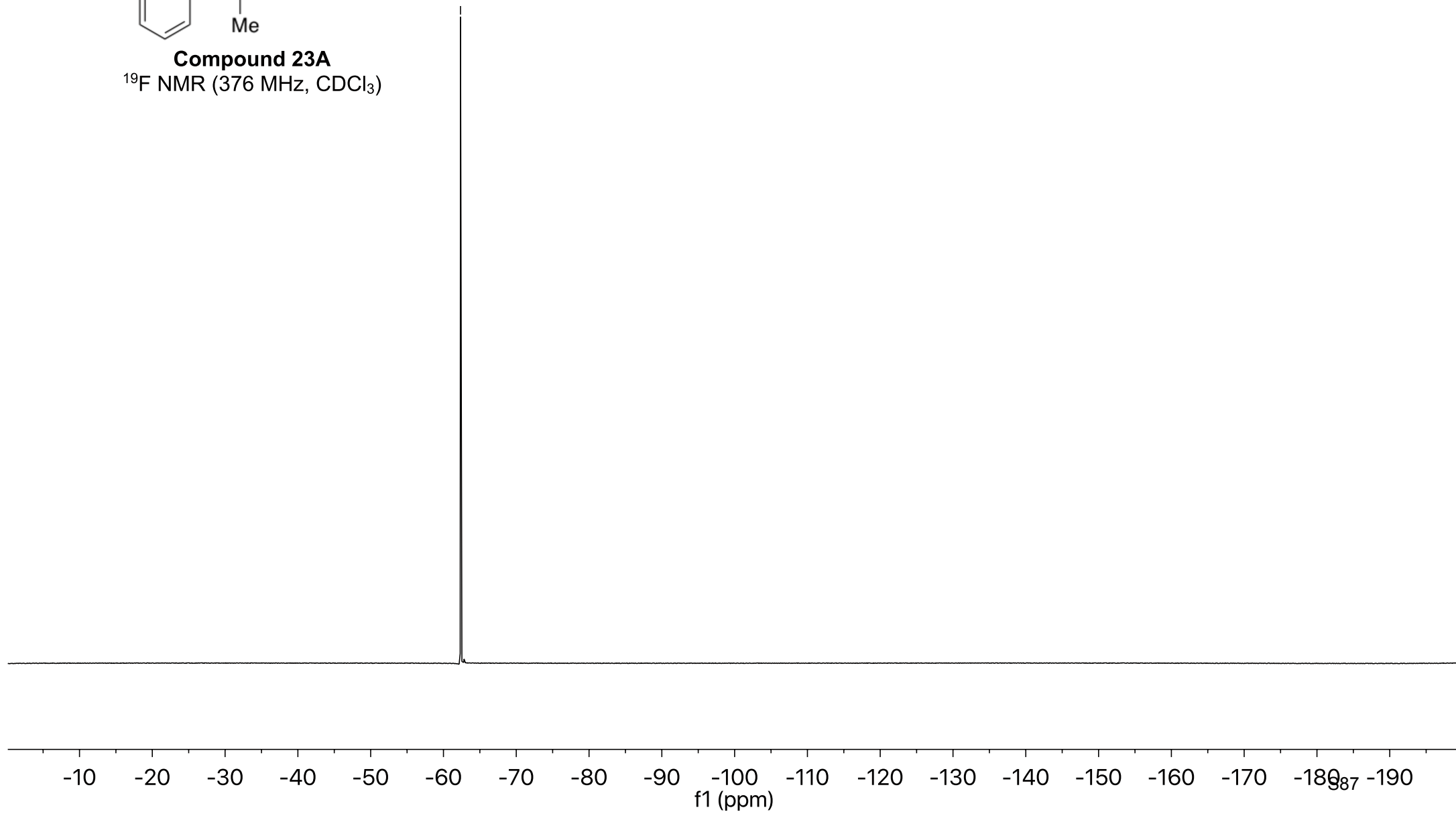


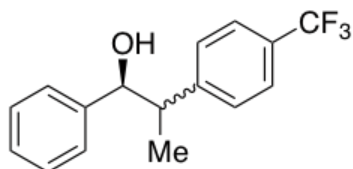


Compound 23A

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

62.34





Compound 23B

^1H NMR (400 MHz, CDCl_3)

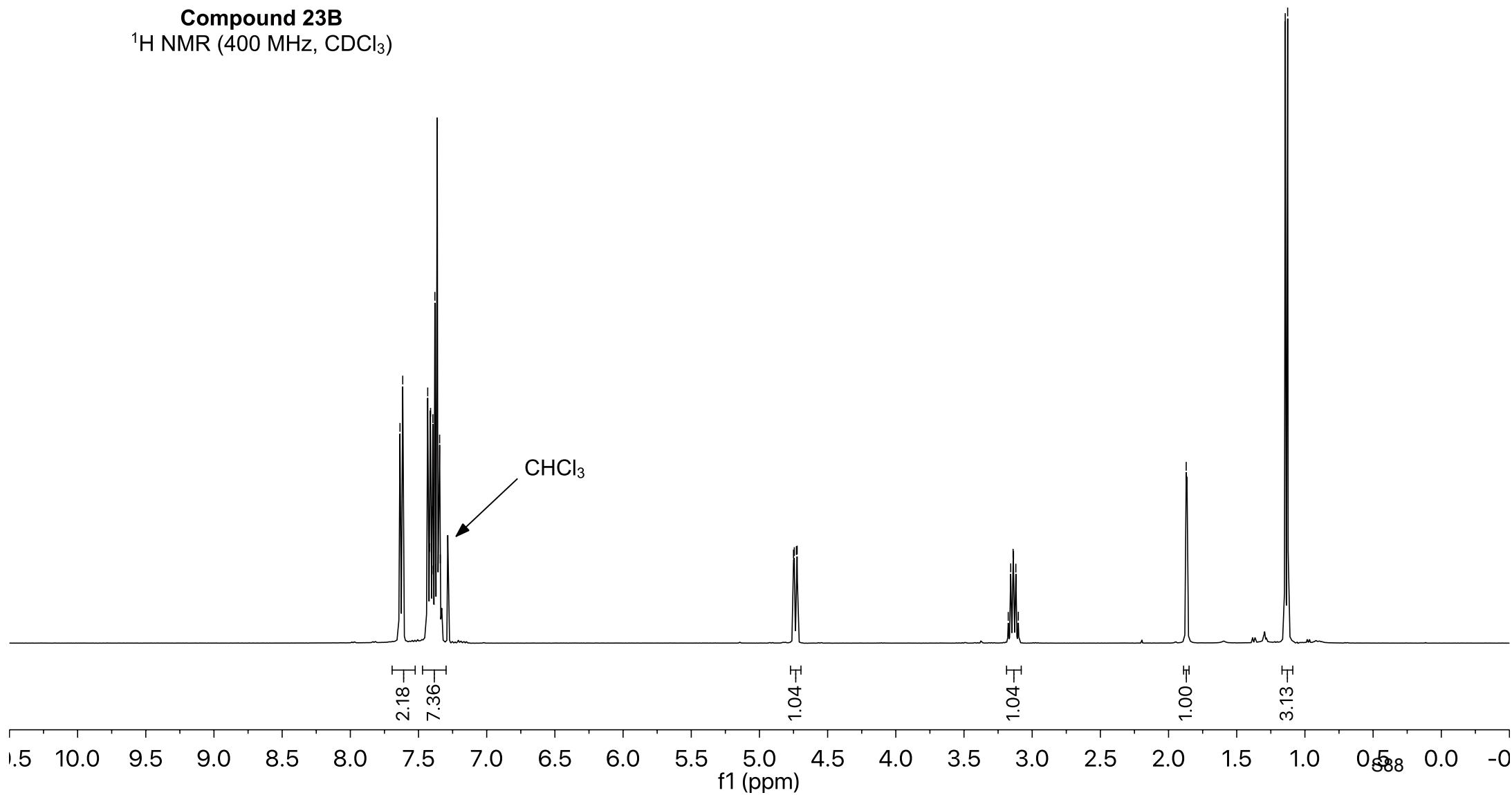
7.64
7.62
7.43
7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.38
7.37
7.36
7.36
7.35
7.35
7.35
7.34

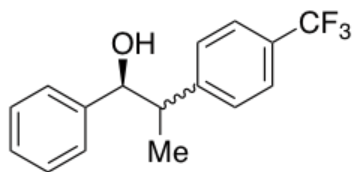
4.75
4.74
4.73
4.72

3.18
3.16
3.14
3.14
3.12
3.10

1.87
1.86

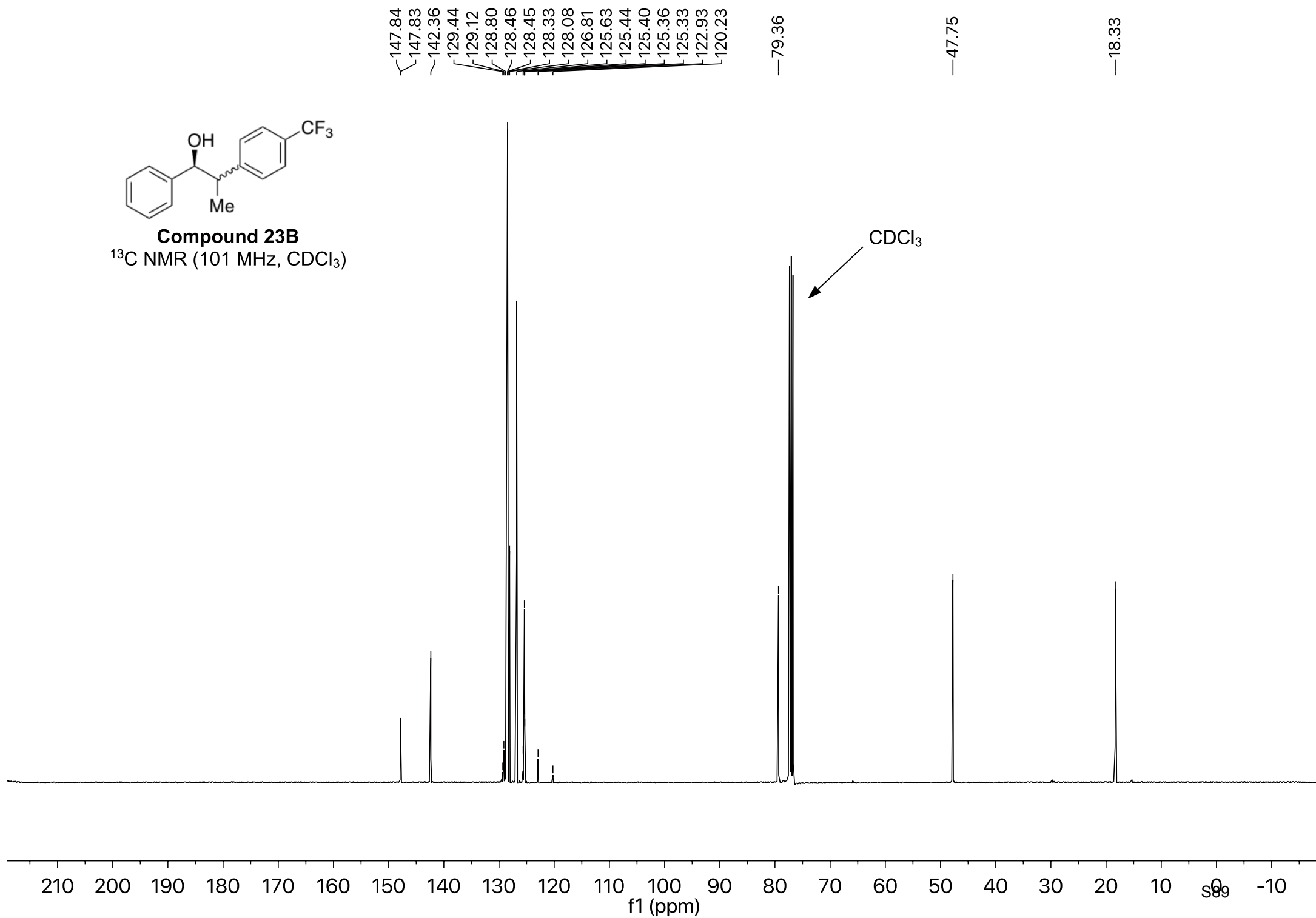
1.14
1.13

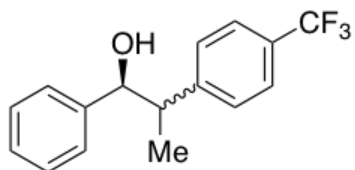




Compound 23B

^{13}C NMR (101 MHz, CDCl_3)



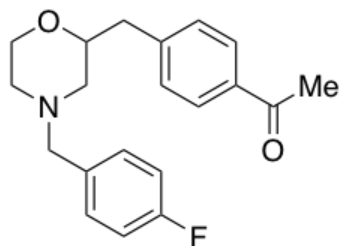


Compound 23B

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

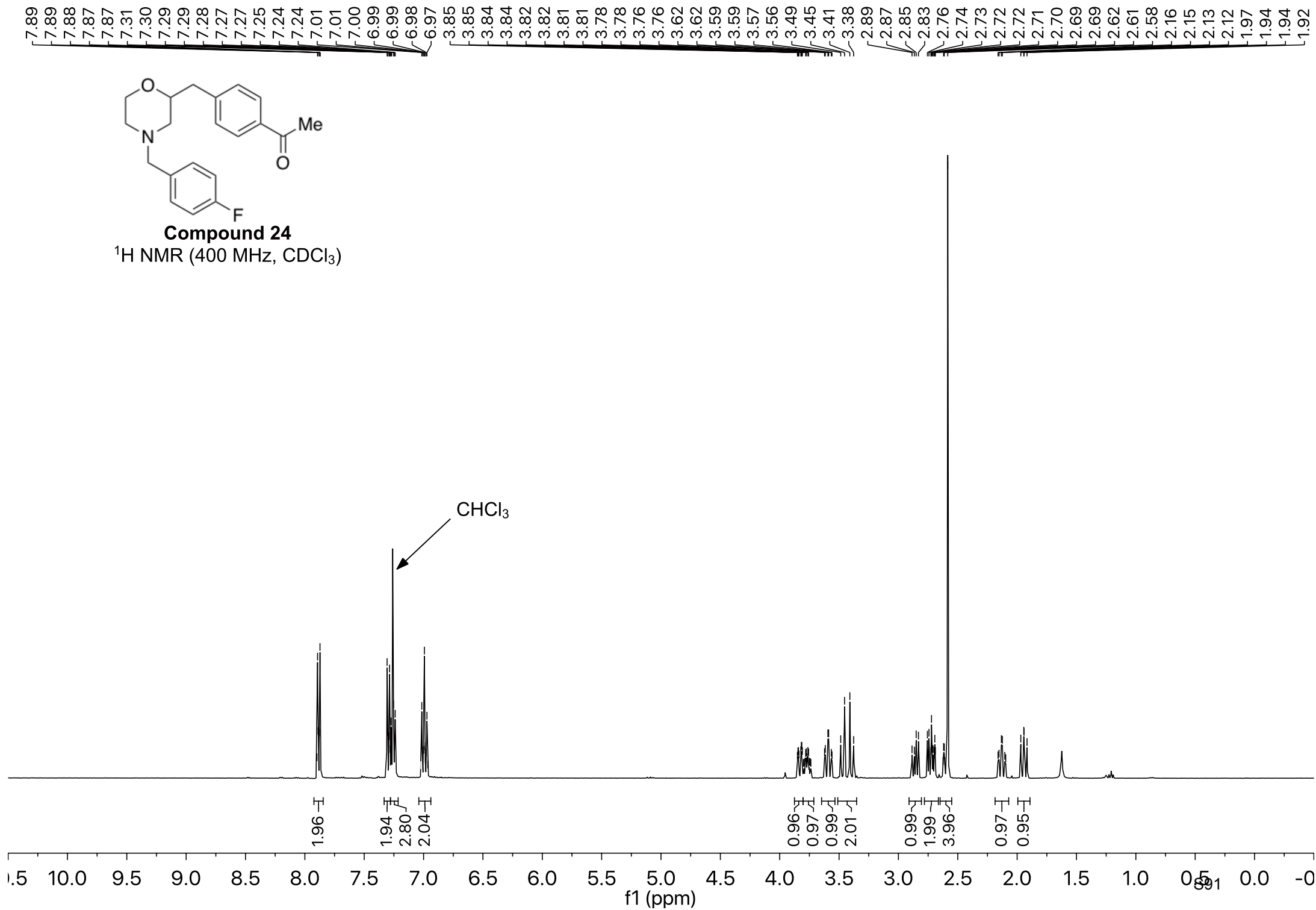
62.32

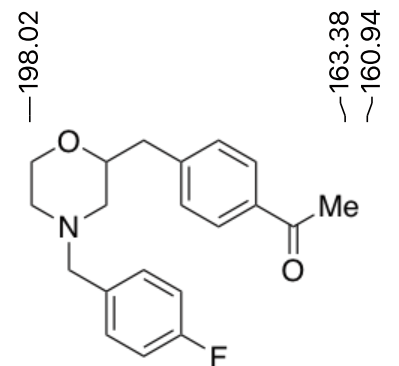
f1 (ppm)



Compound 24

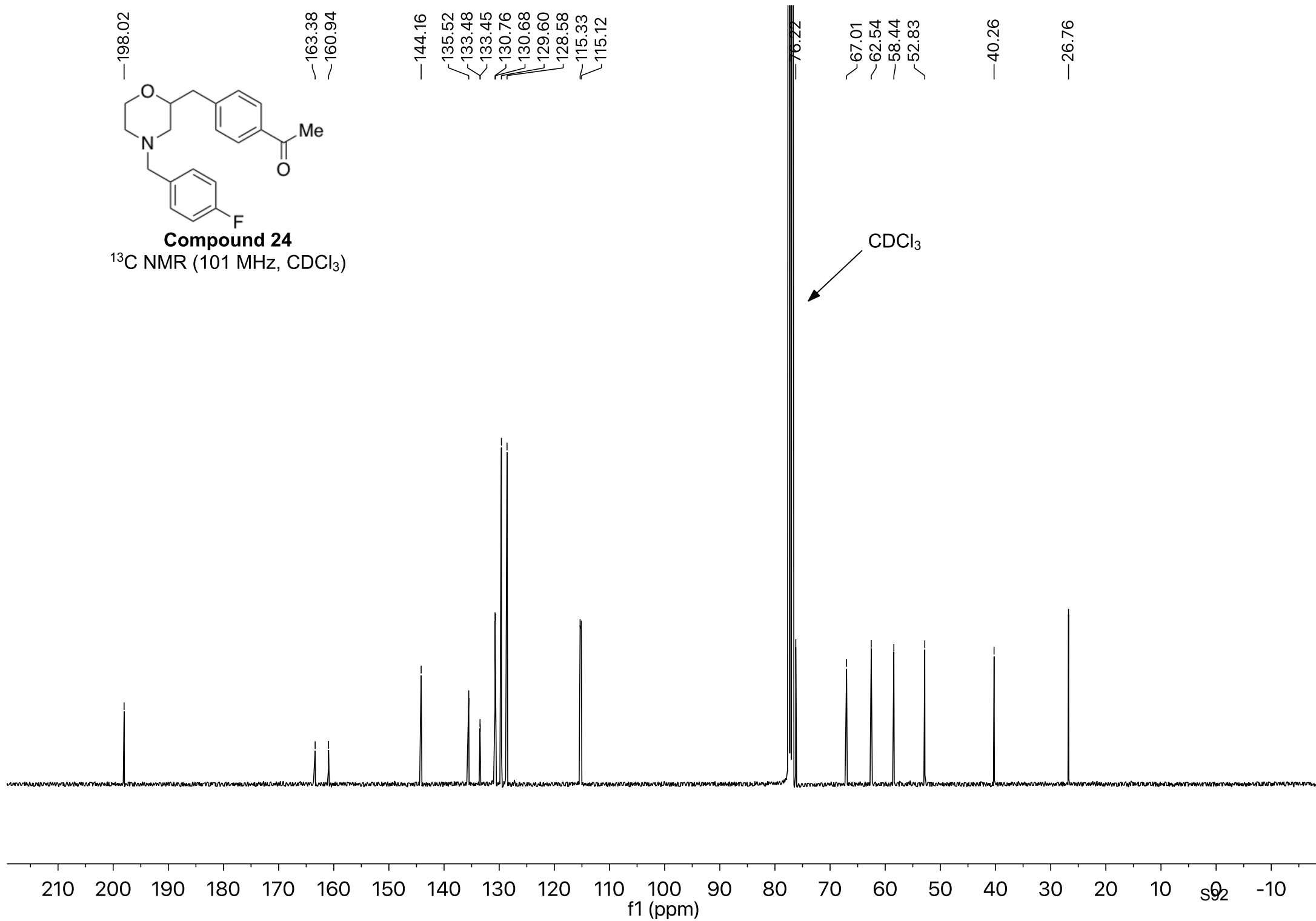
^1H NMR (400 MHz, CDCl_3)

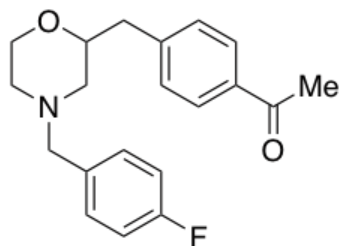




Compound 24

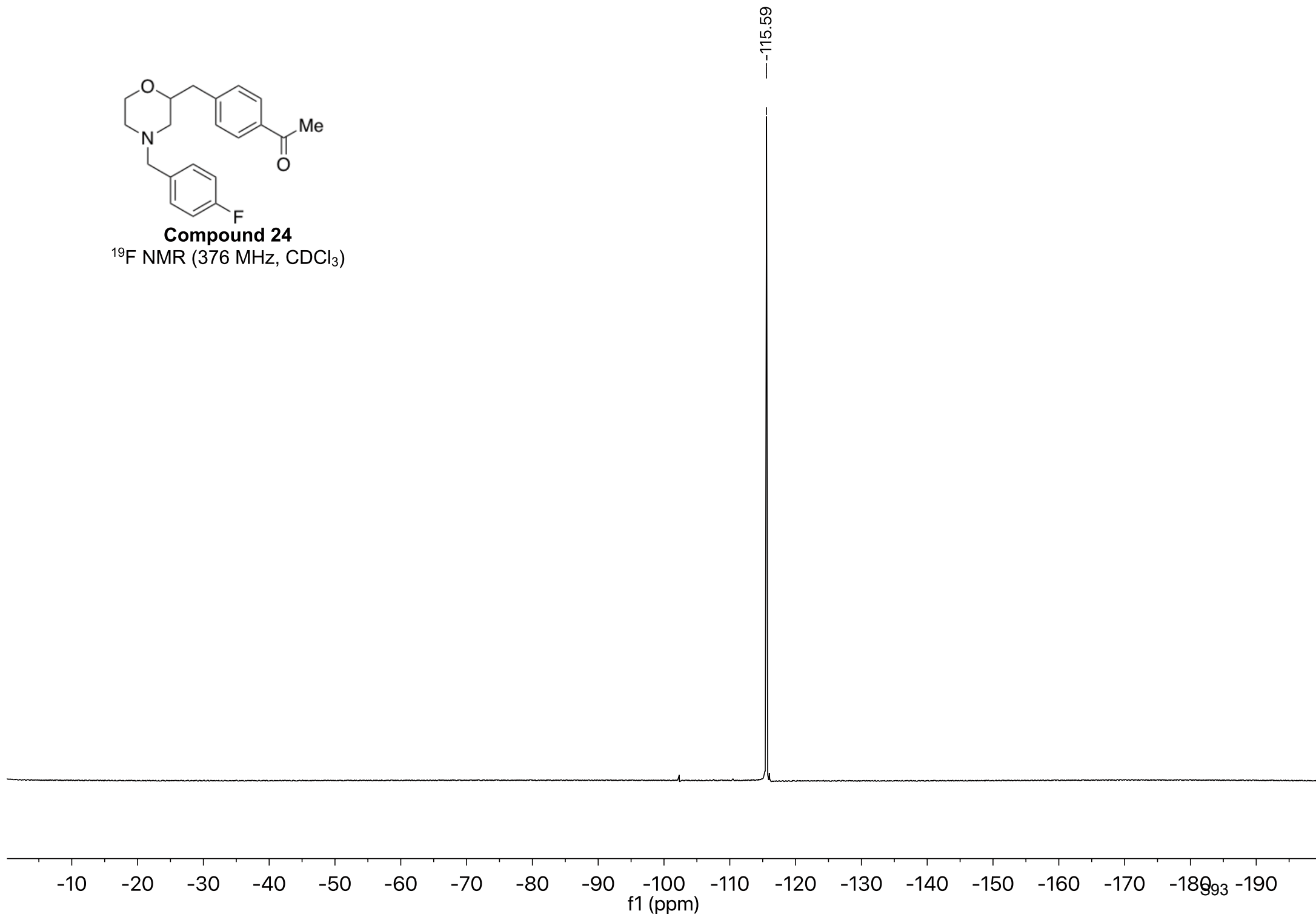
^{13}C NMR (101 MHz, CDCl_3)

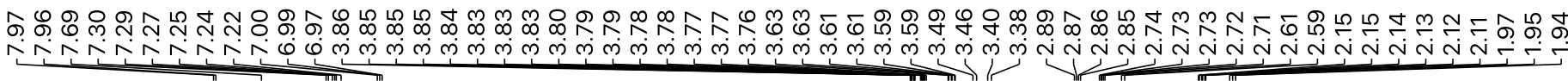
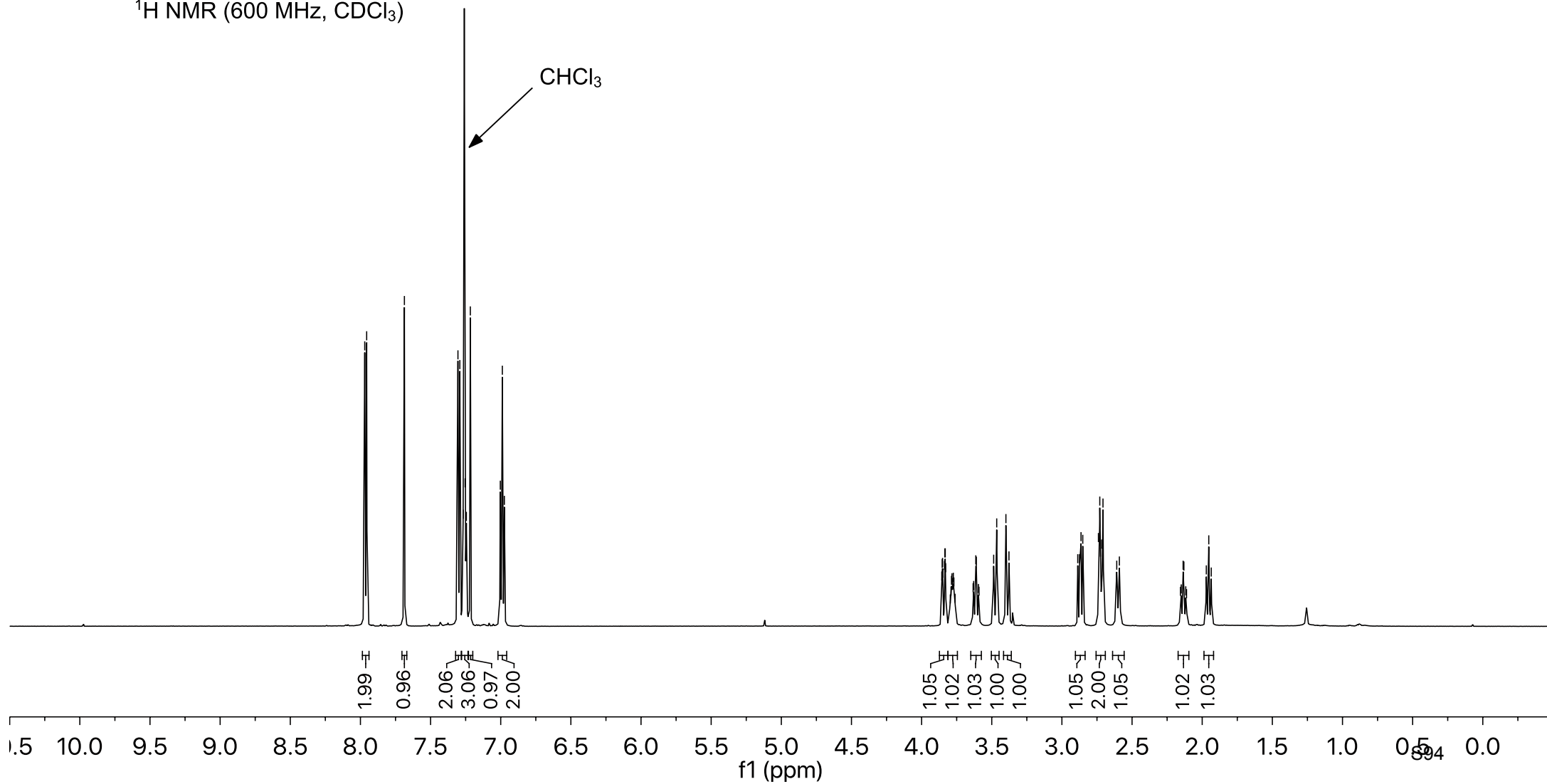


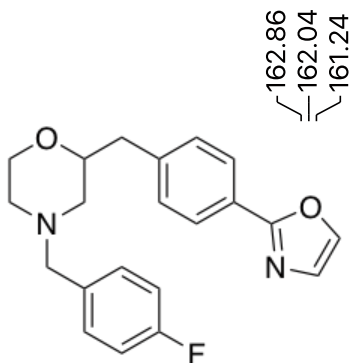


Compound 24

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

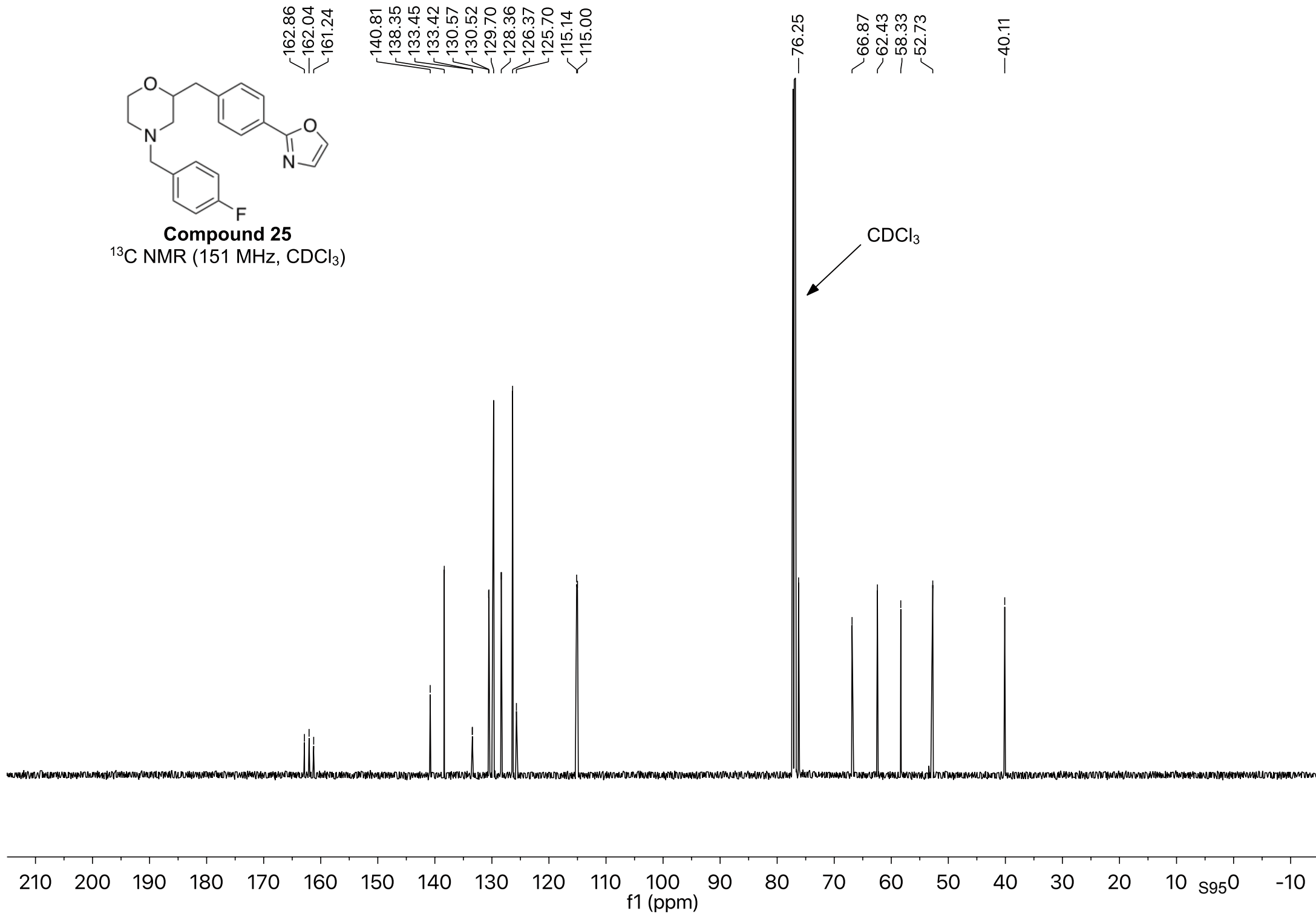


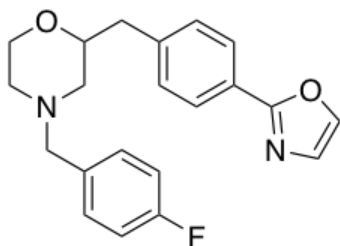
¹H NMR (600 MHz, CDCl₃)



Compound 25

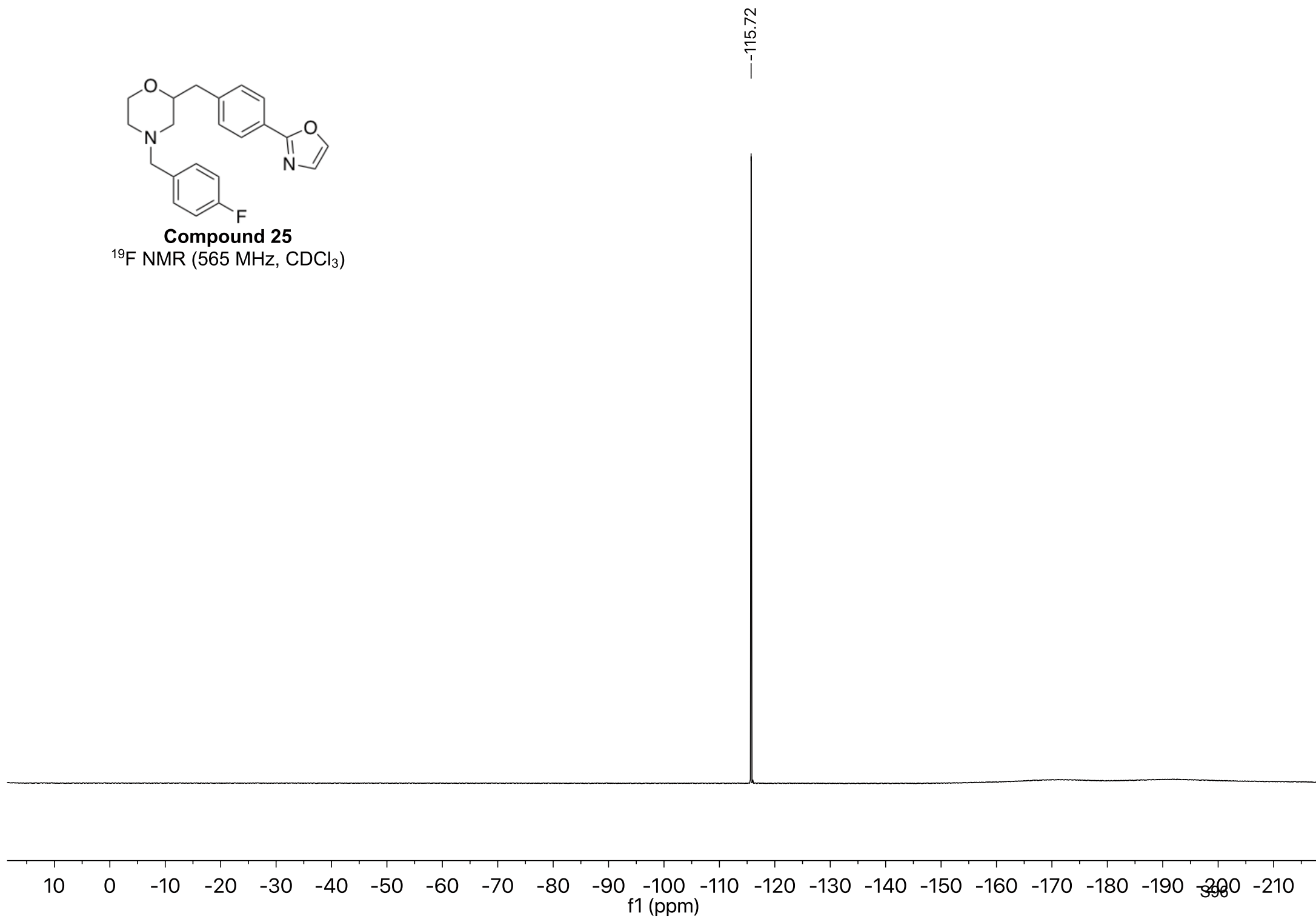
^{13}C NMR (151 MHz, CDCl_3)

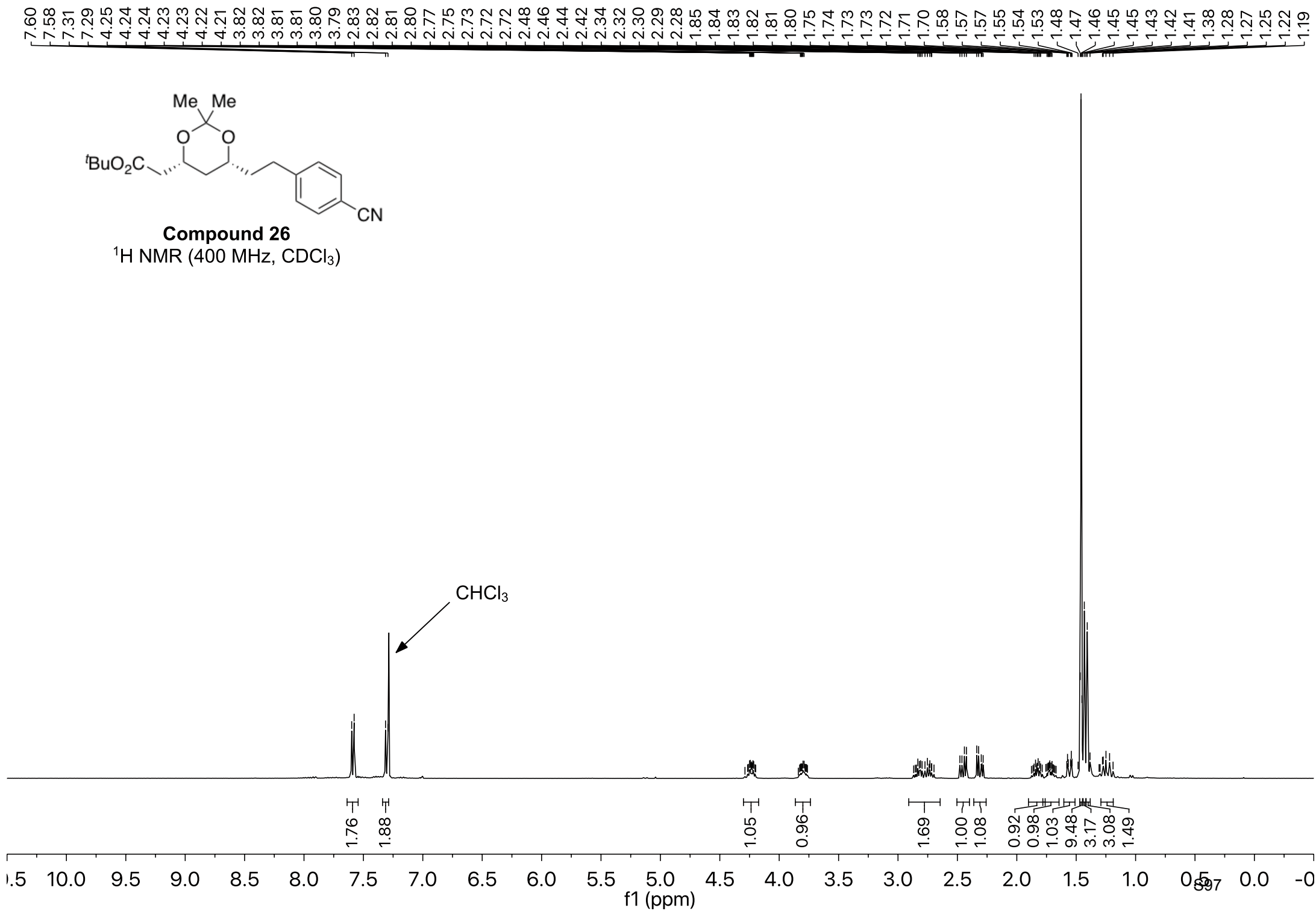


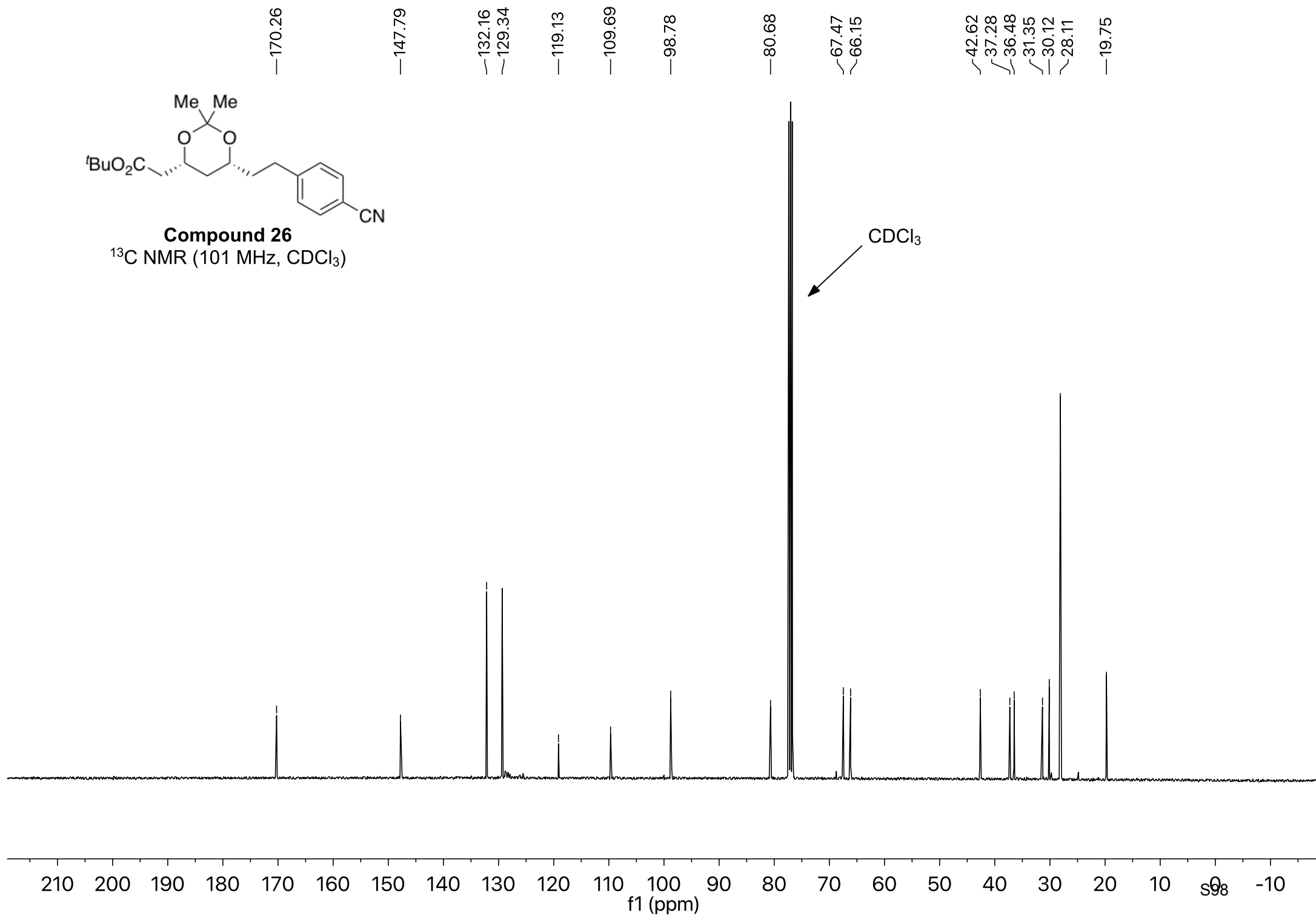


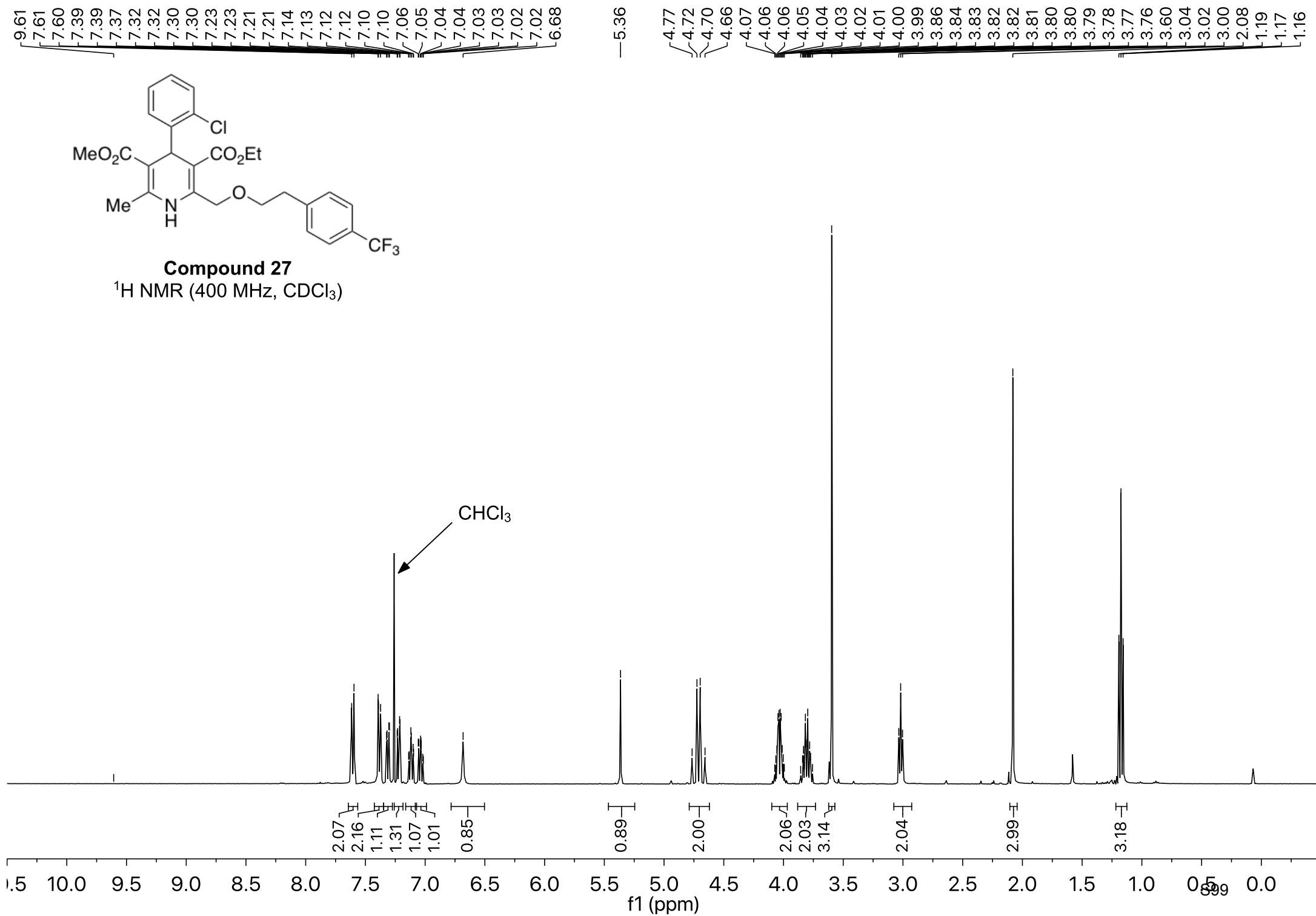
Compound 25

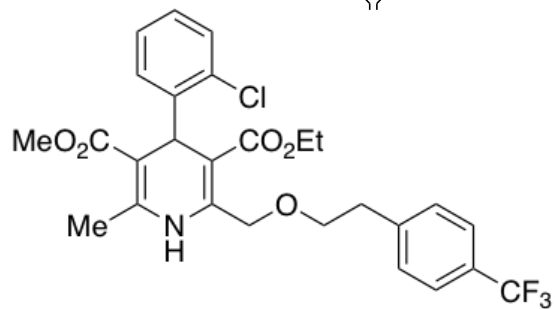
^{19}F NMR (565 MHz, CDCl_3)





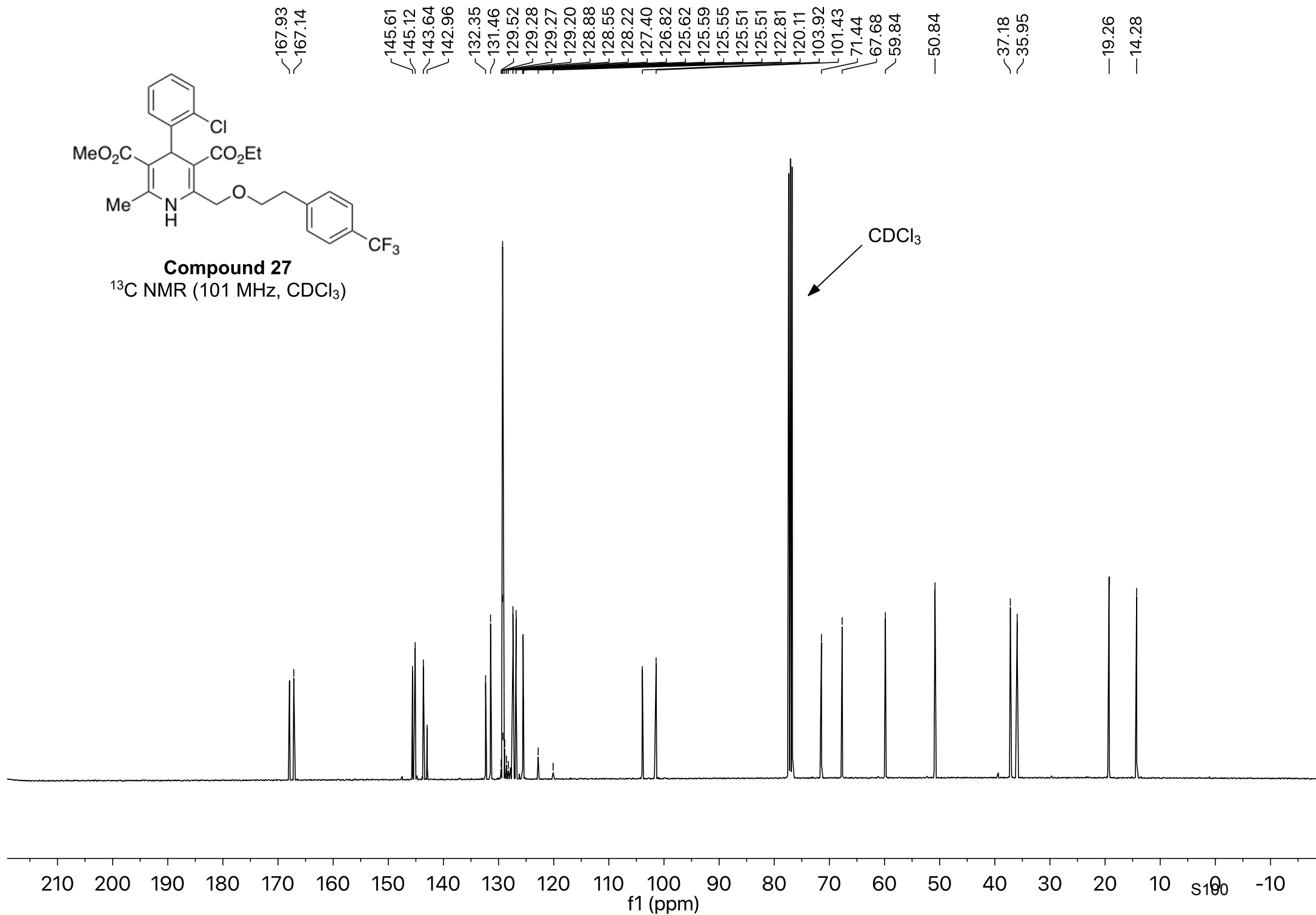


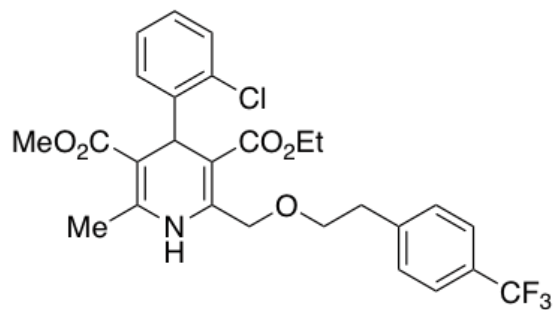




Compound 27

^{13}C NMR (101 MHz, CDCl_3)





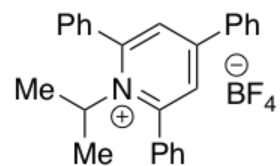
Compound 27

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

-62.43

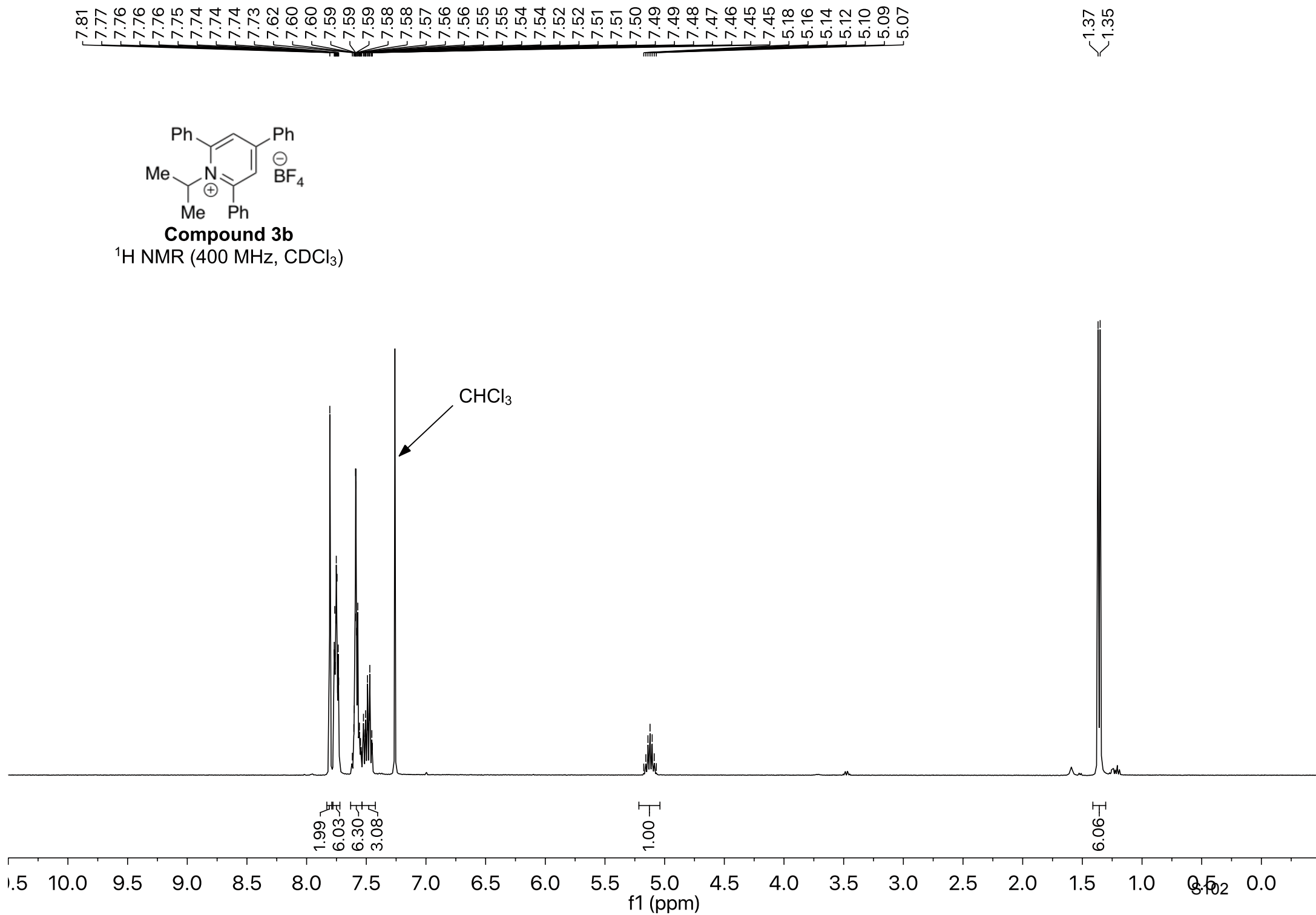
f1 (ppm)

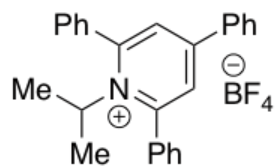
8401



Compound 3b

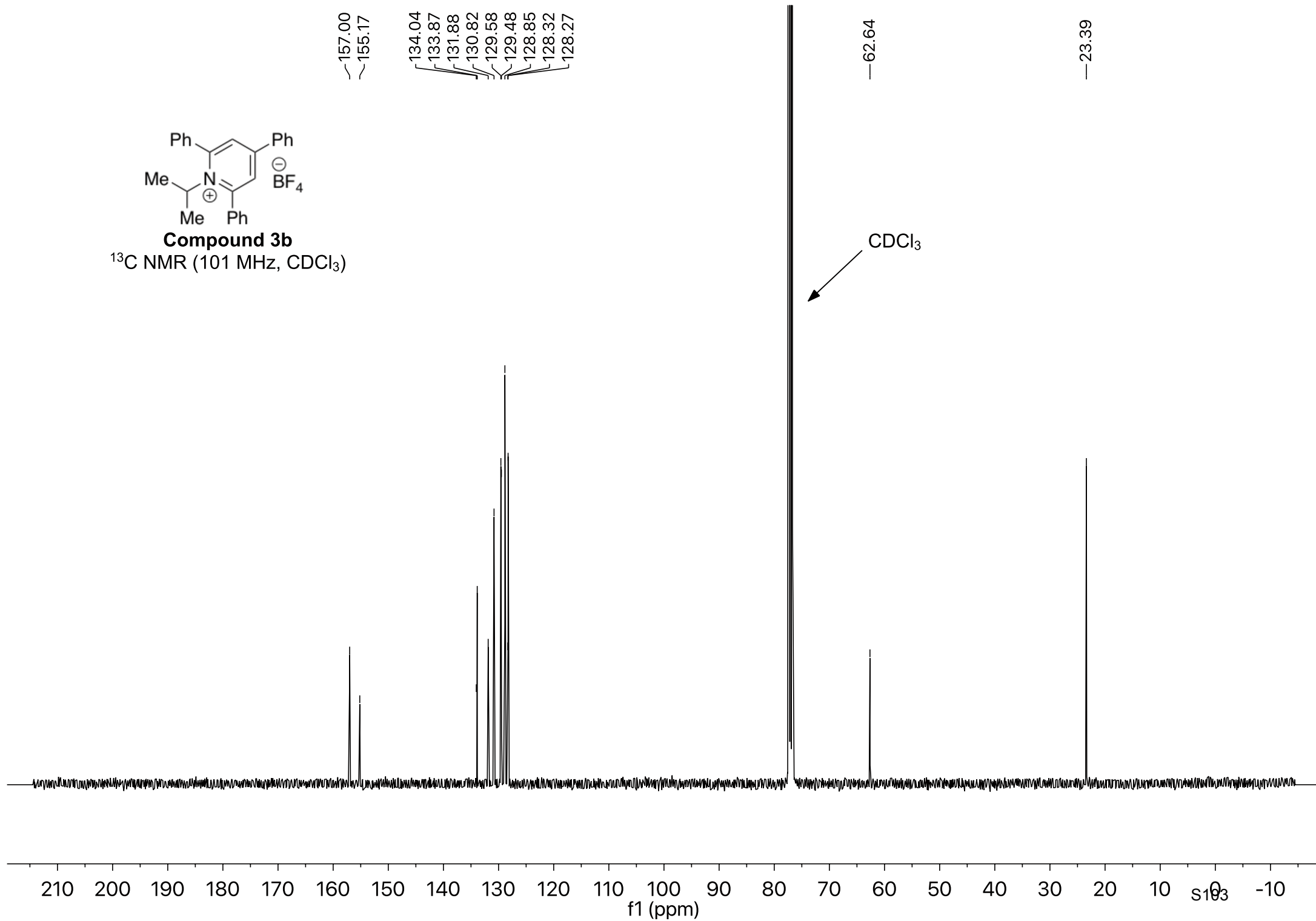
^1H NMR (400 MHz, CDCl_3)

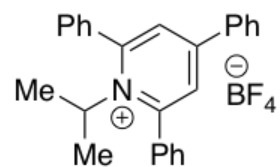




Compound 3b

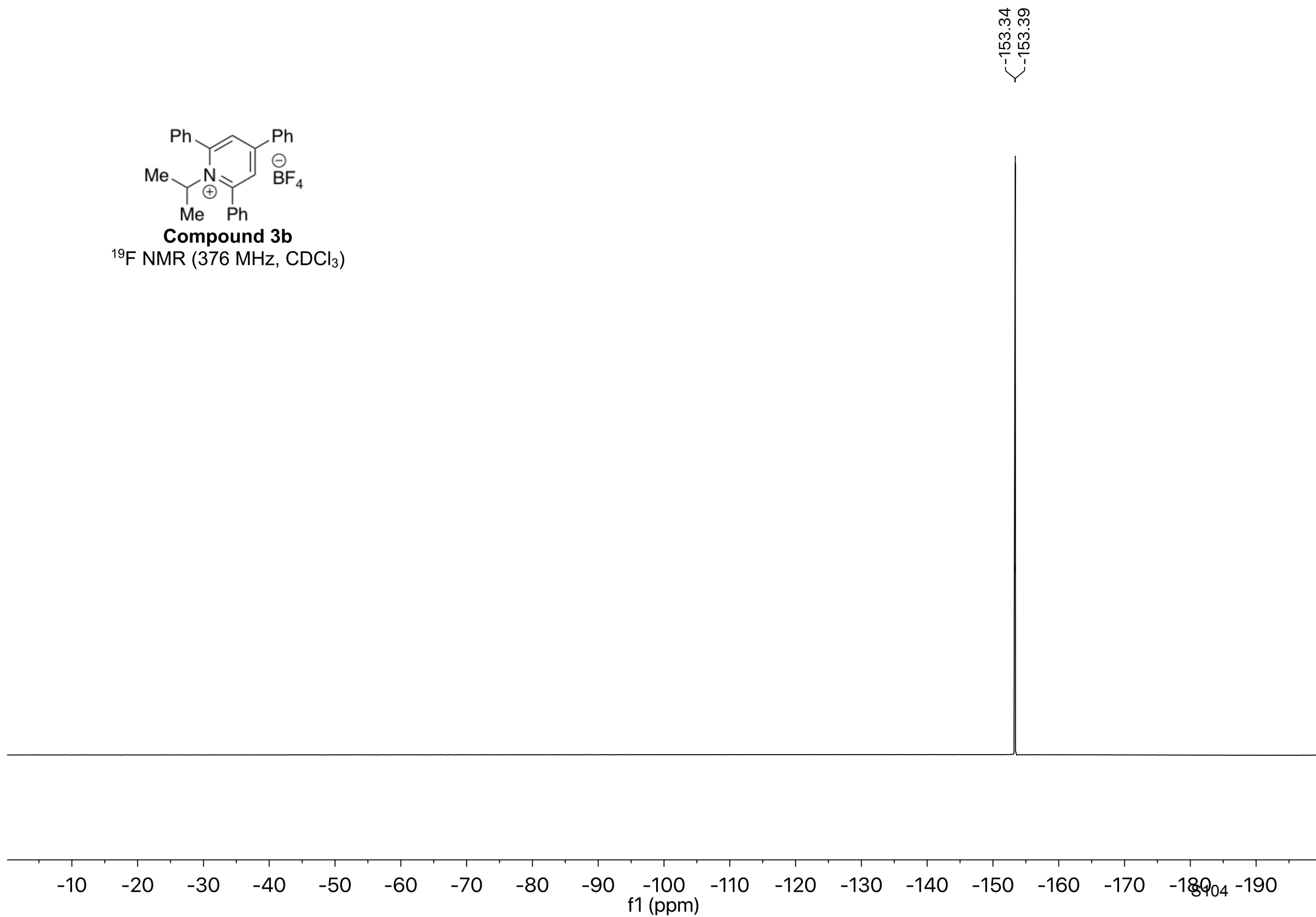
^{13}C NMR (101 MHz, CDCl_3)

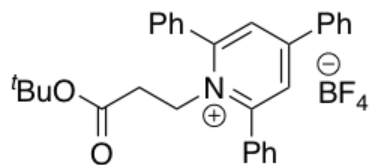




Compound 3b

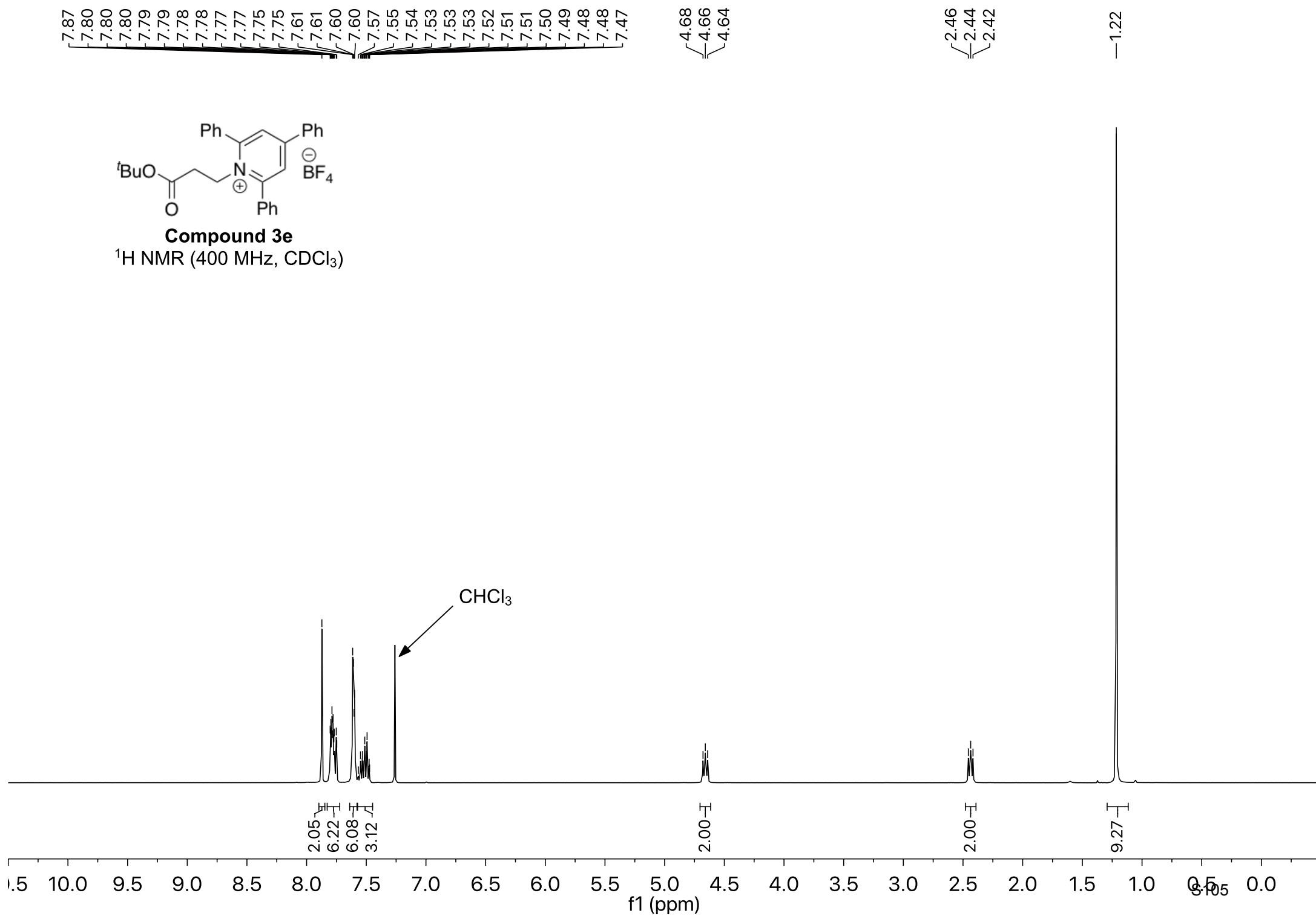
^{19}F NMR (376 MHz, CDCl_3)

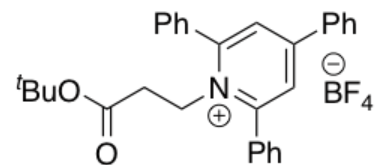




Compound 3e

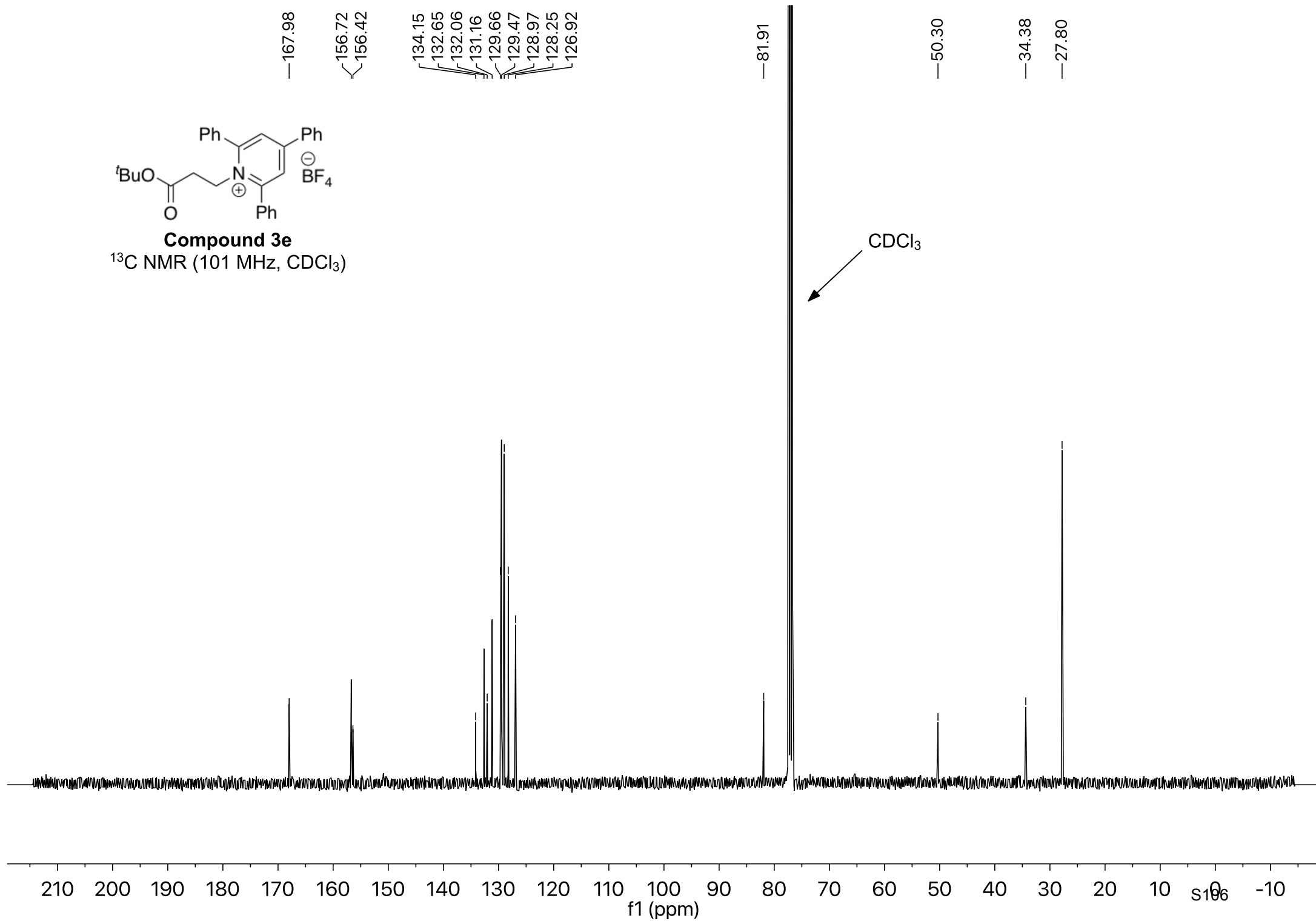
^1H NMR (400 MHz, CDCl_3)

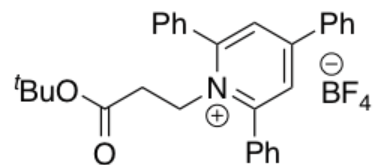




Compound 3e

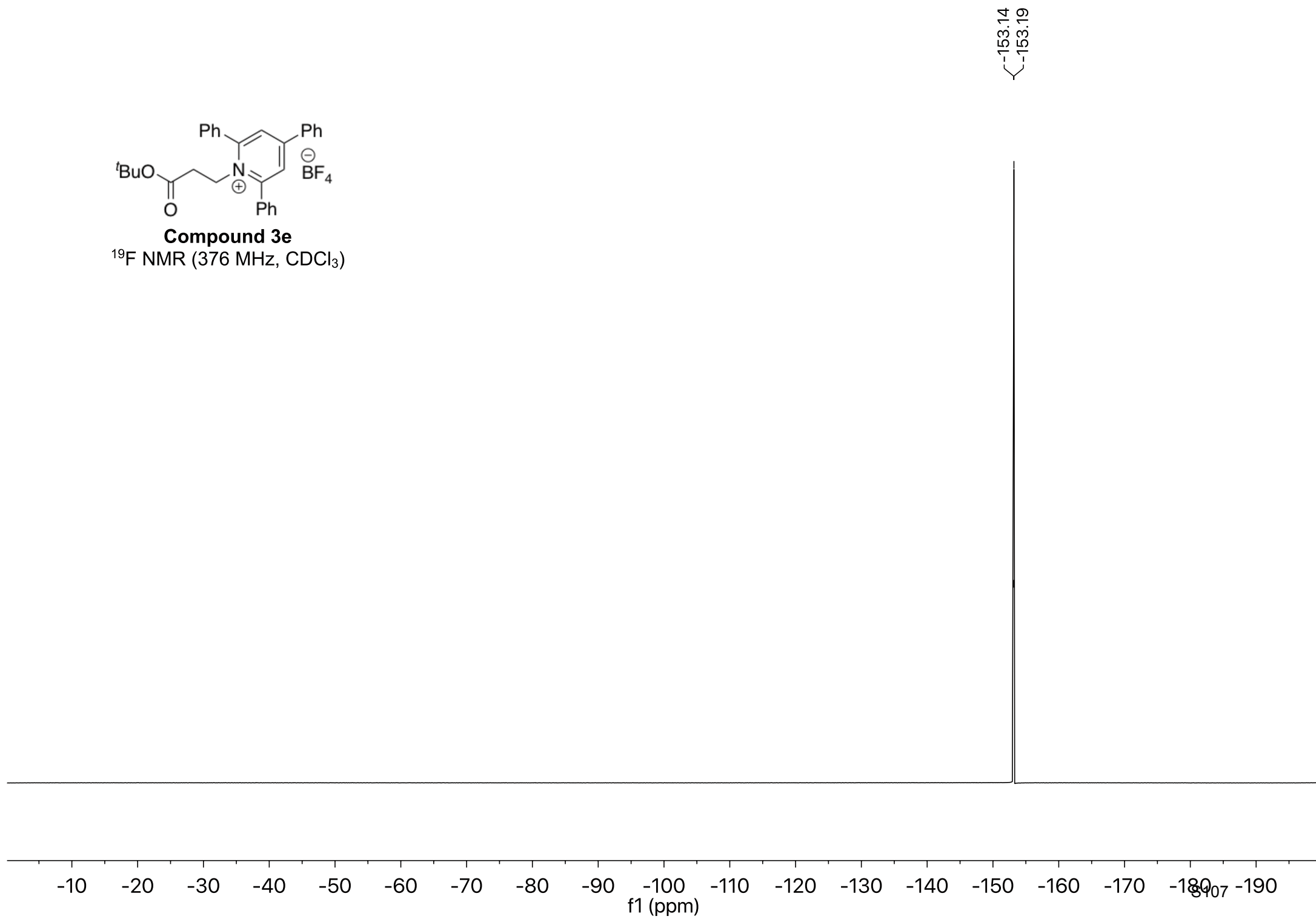
^{13}C NMR (101 MHz, CDCl_3)

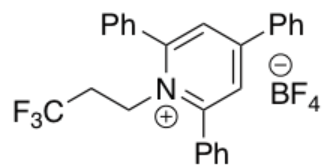




Compound 3e

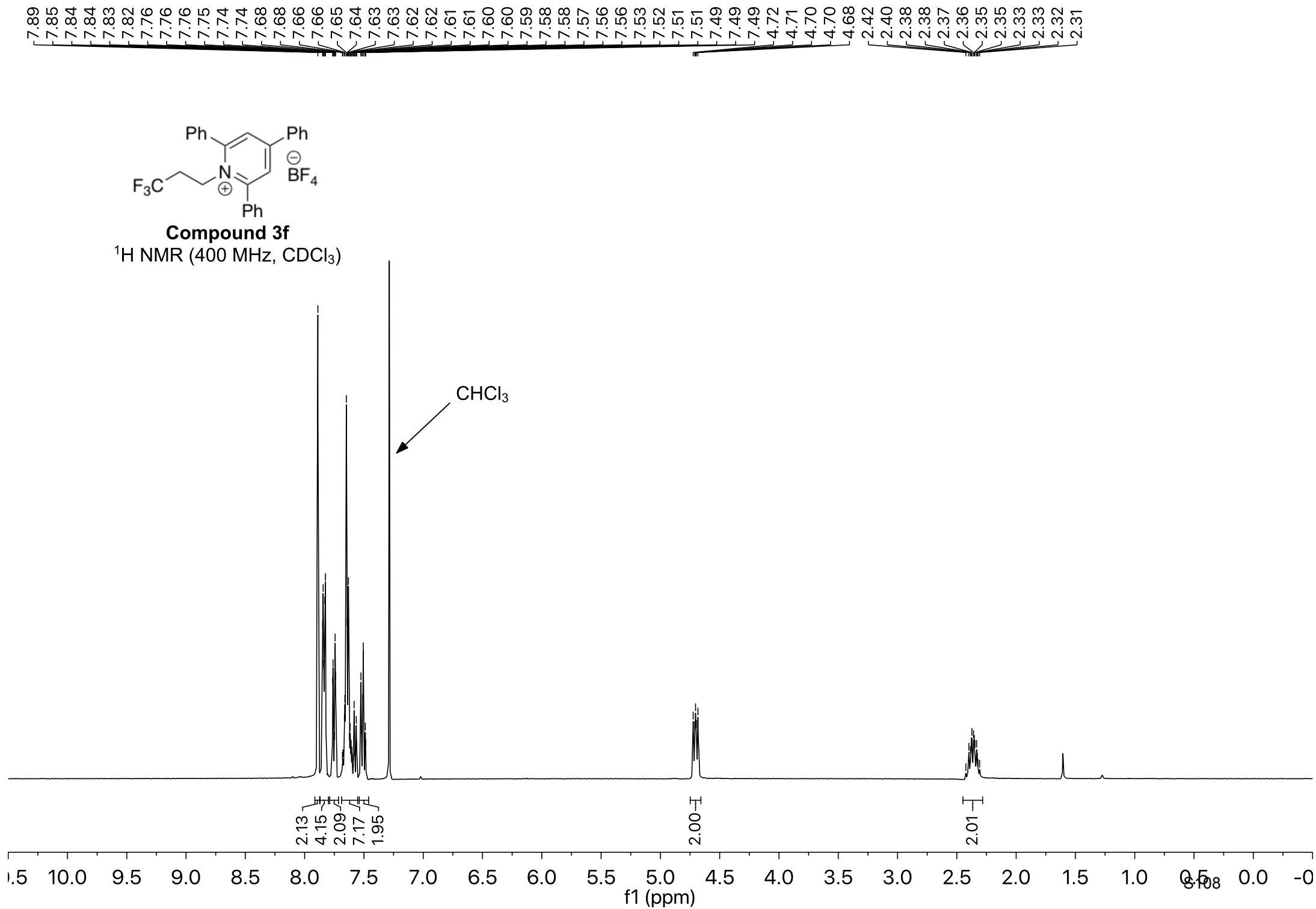
¹⁹F NMR (376 MHz, CDCl₃)

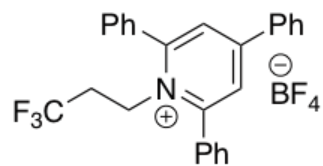




Compound 3f

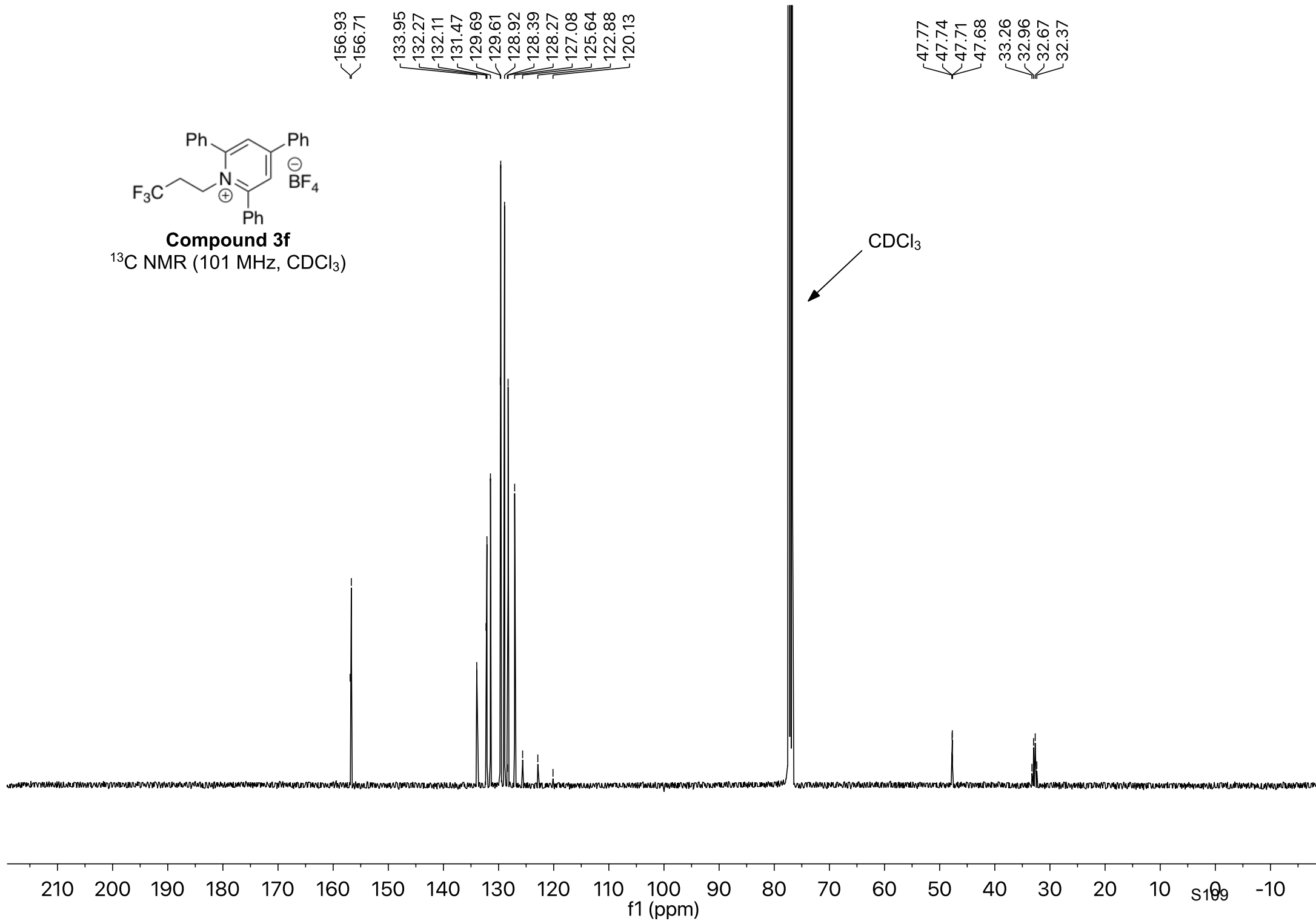
^1H NMR (400 MHz, CDCl_3)

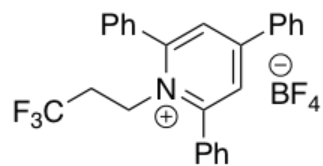




Compound 3f

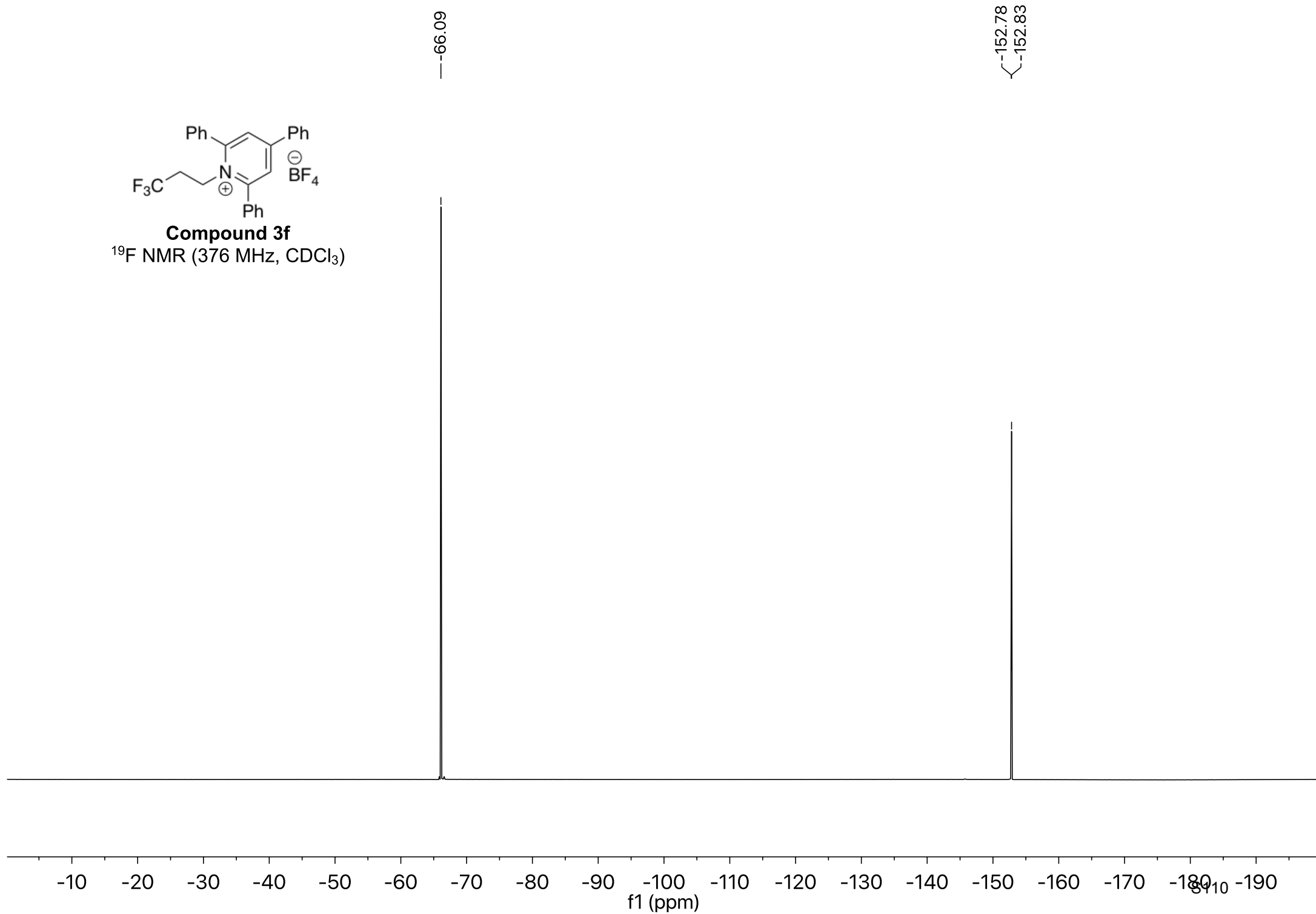
^{13}C NMR (101 MHz, CDCl_3)

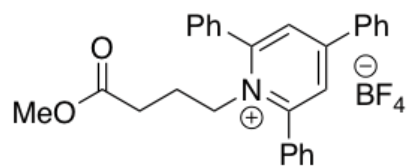




Compound 3f

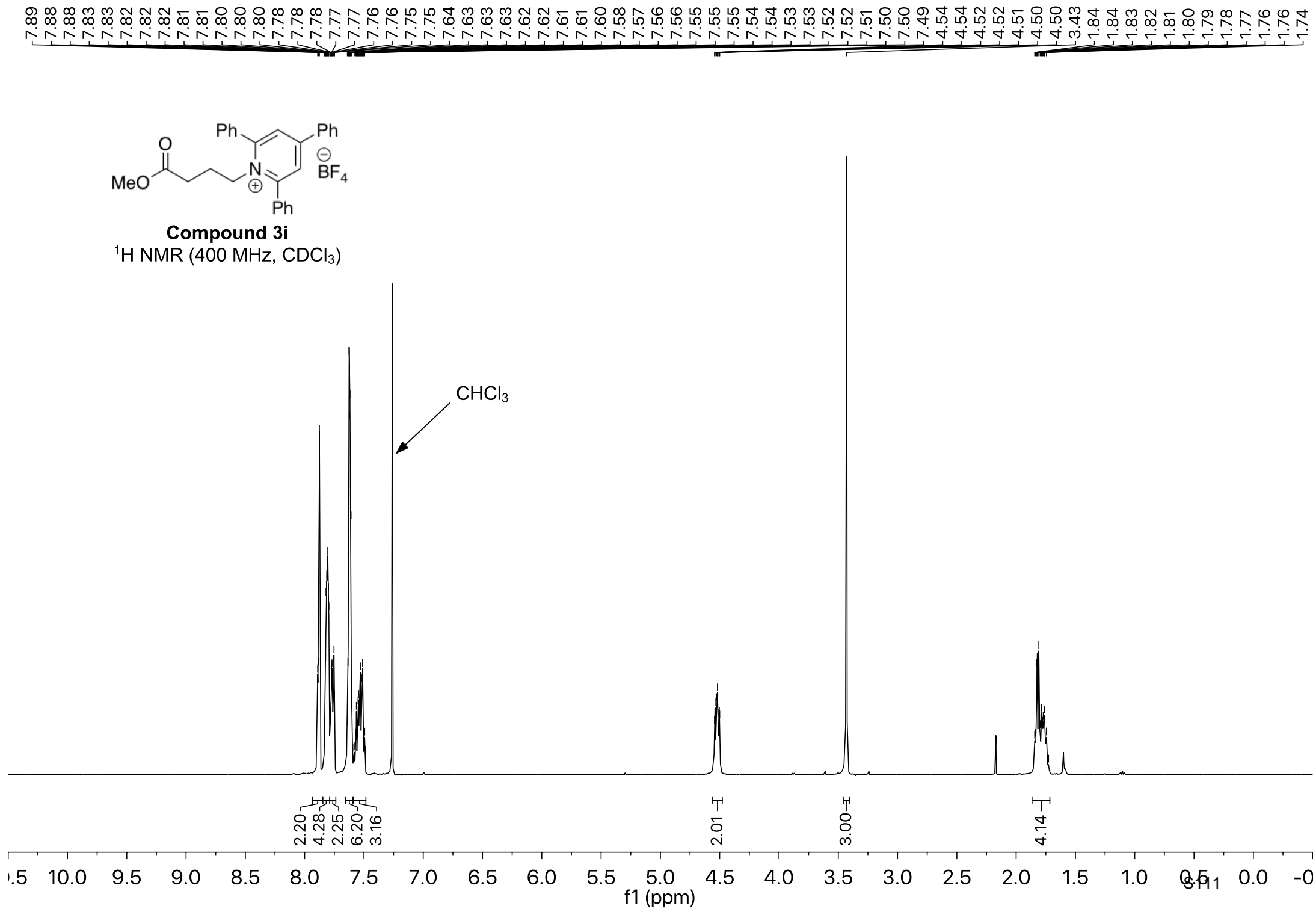
^{19}F NMR (376 MHz, CDCl_3)

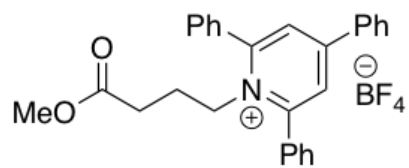




Compound 3i

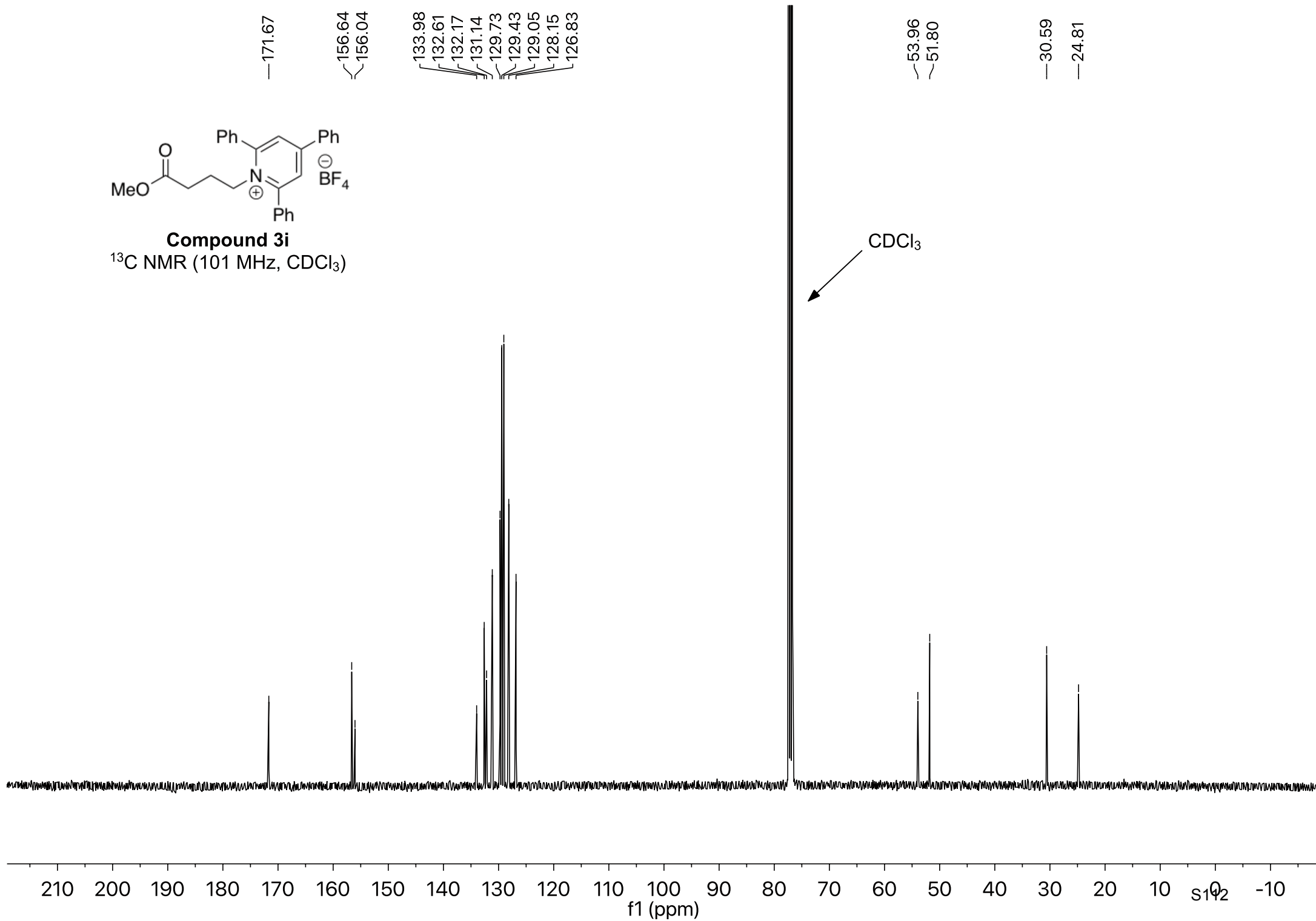
^1H NMR (400 MHz, CDCl_3)

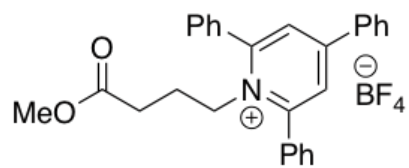




Compound 3i

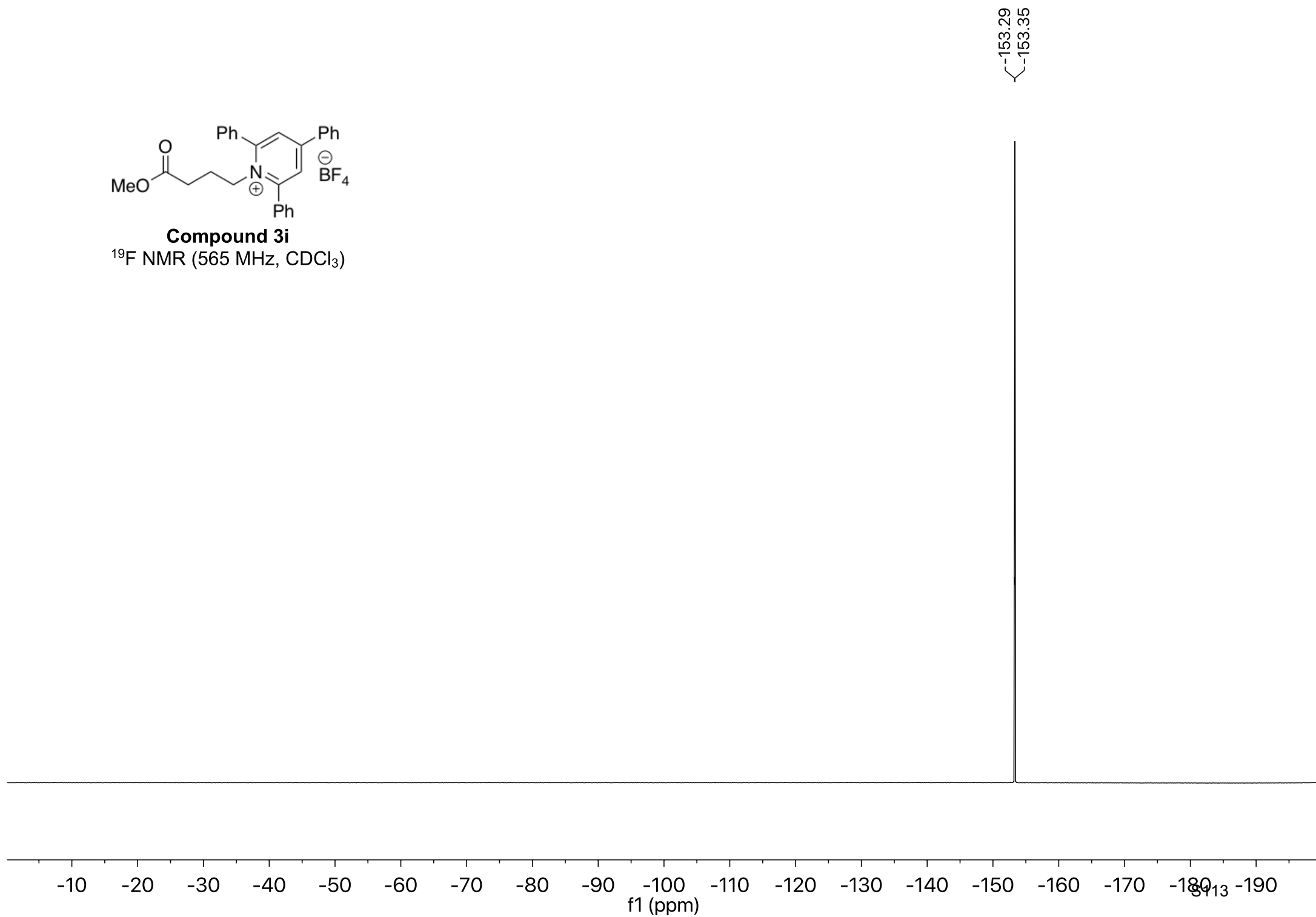
^{13}C NMR (101 MHz, CDCl_3)

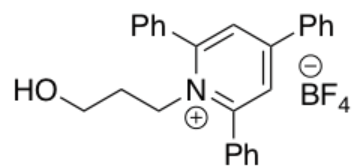




Compound 3i

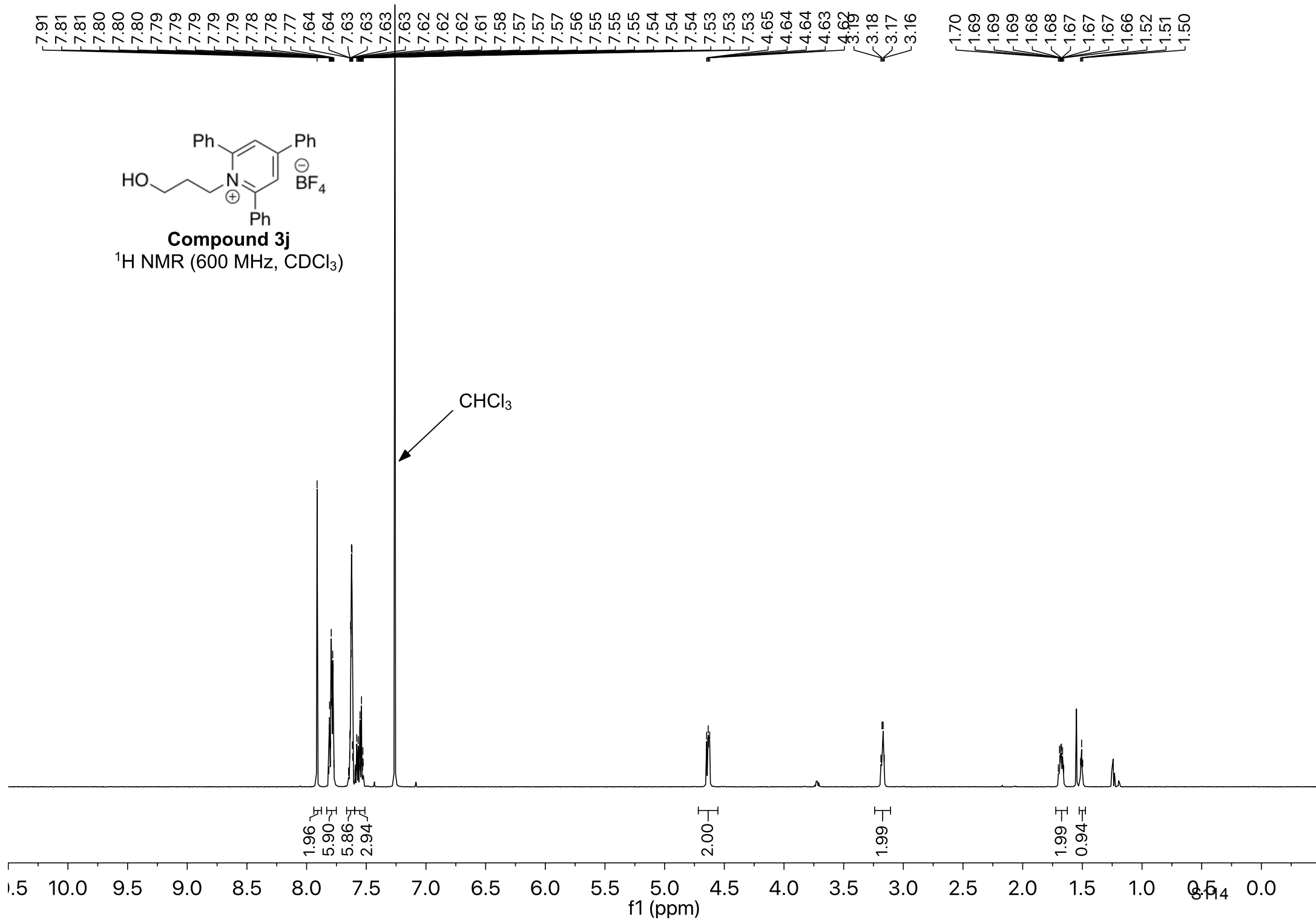
^{19}F NMR (565 MHz, CDCl_3)

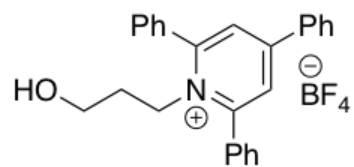




Compound 3j

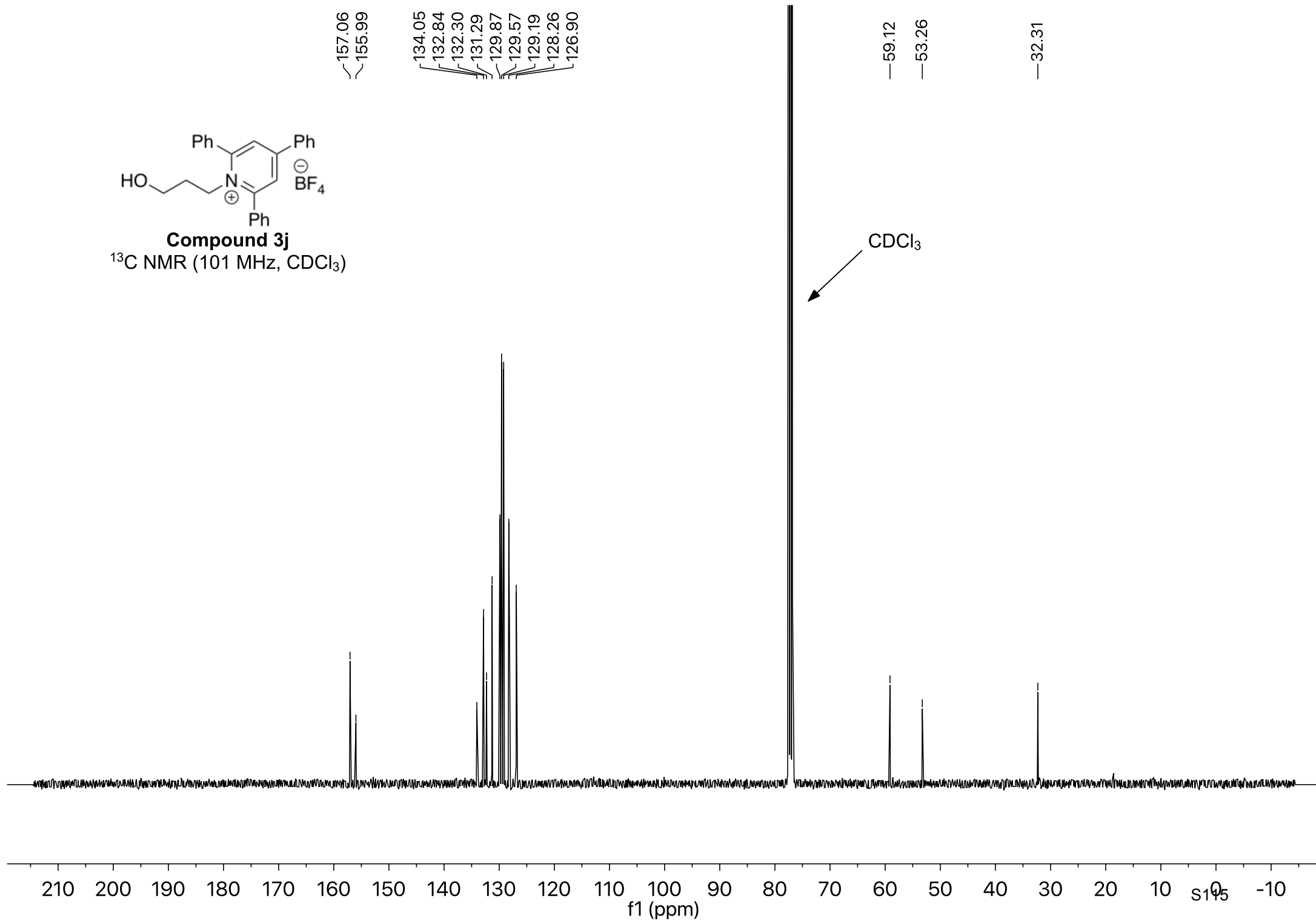
^1H NMR (600 MHz, CDCl_3)

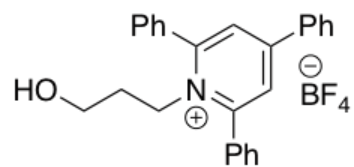




Compound 3j

^{13}C NMR (101 MHz, CDCl_3)

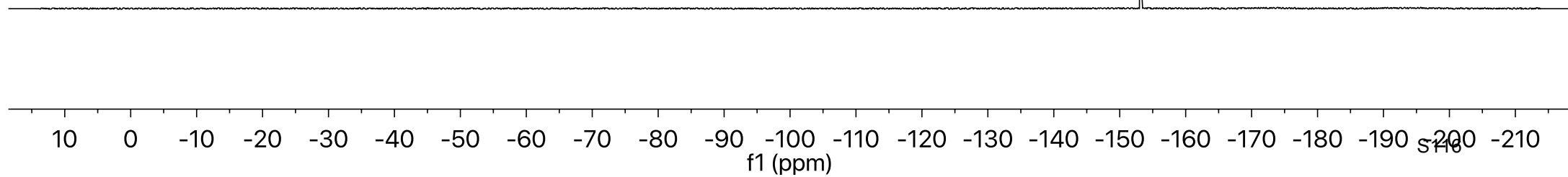


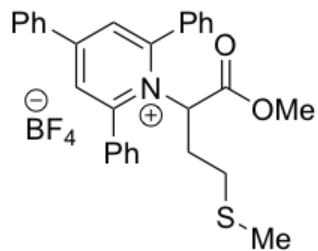


Compound 3j

^{19}F NMR (565 MHz, CDCl_3)

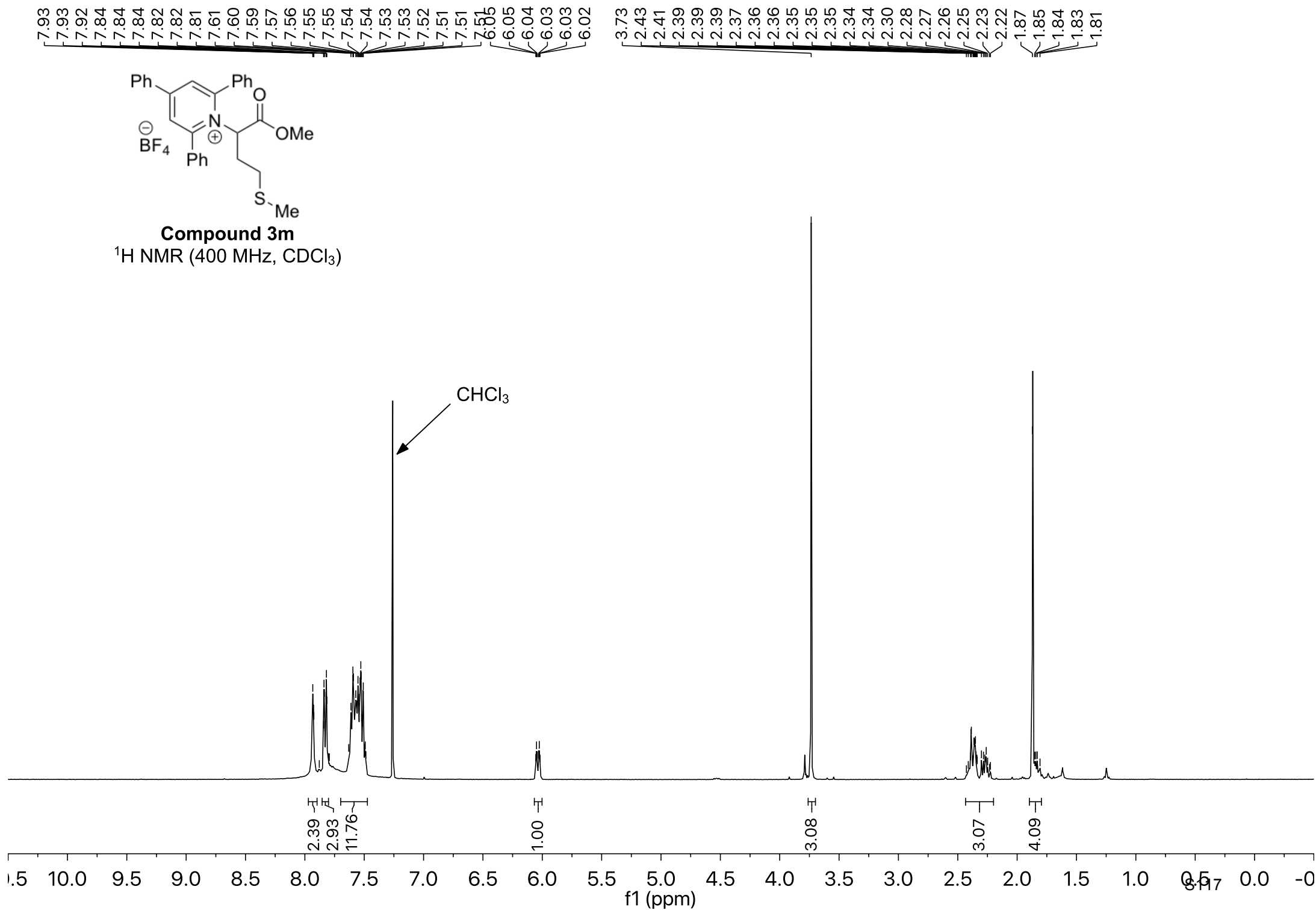
-153.17
-153.22

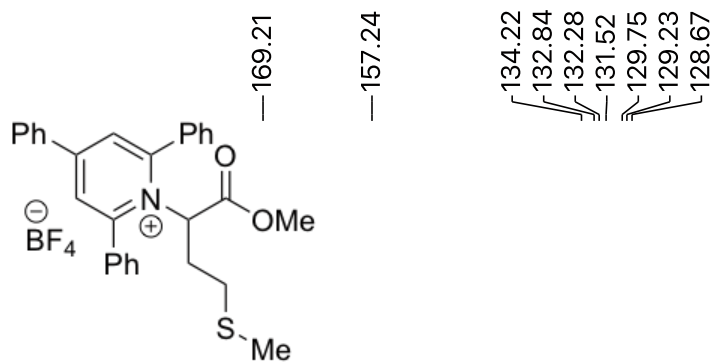




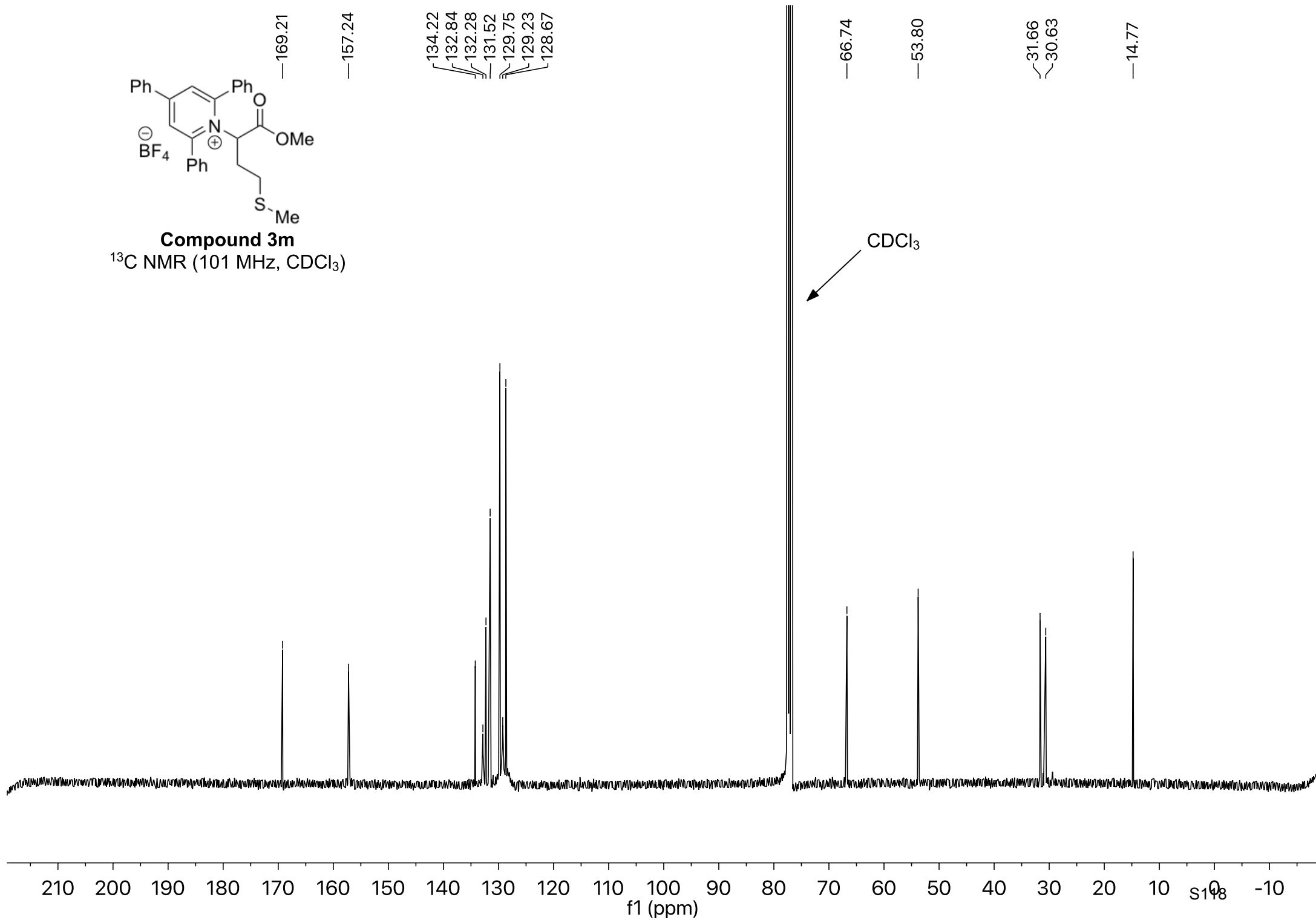
Compound 3m

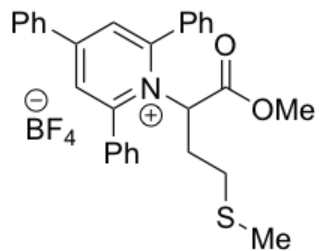
^1H NMR (400 MHz, CDCl_3)





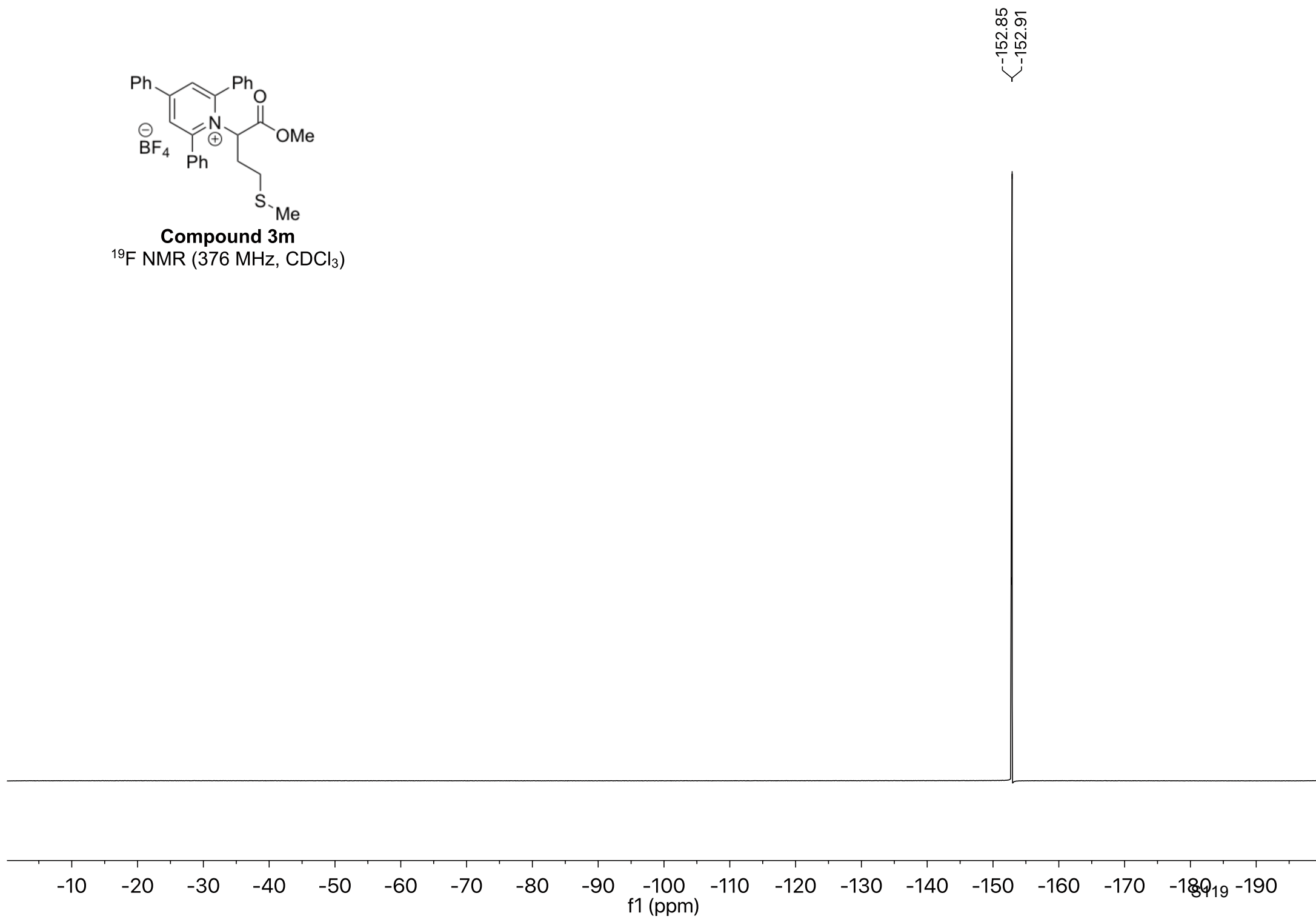
Compound 3m
 ^{13}C NMR (101 MHz, CDCl_3)

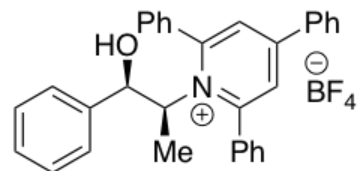




Compound 3m

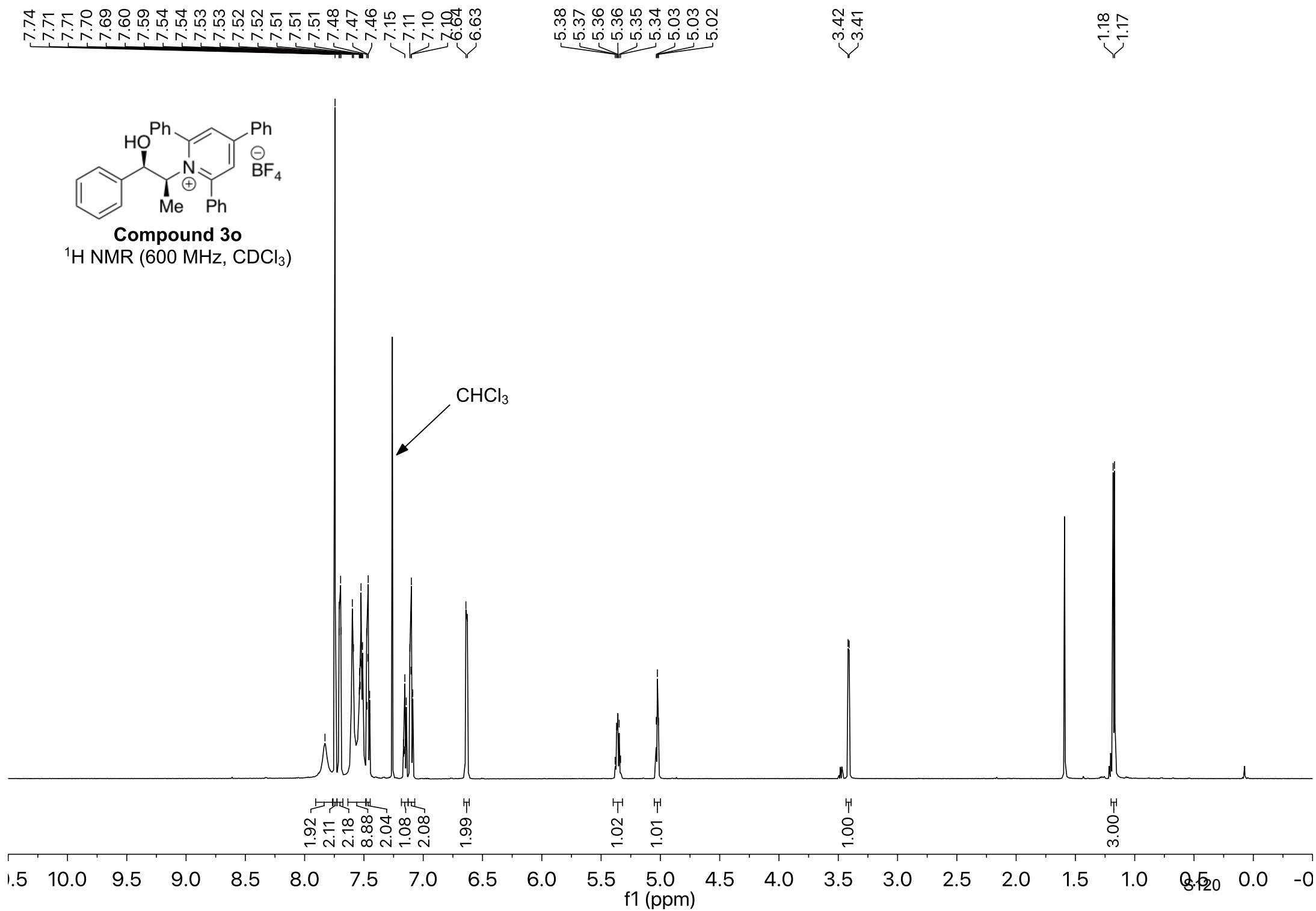
¹⁹F NMR (376 MHz, CDCl₃)

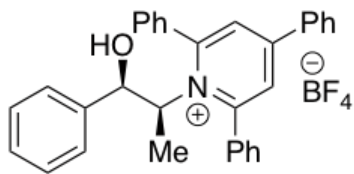




Compound 3o

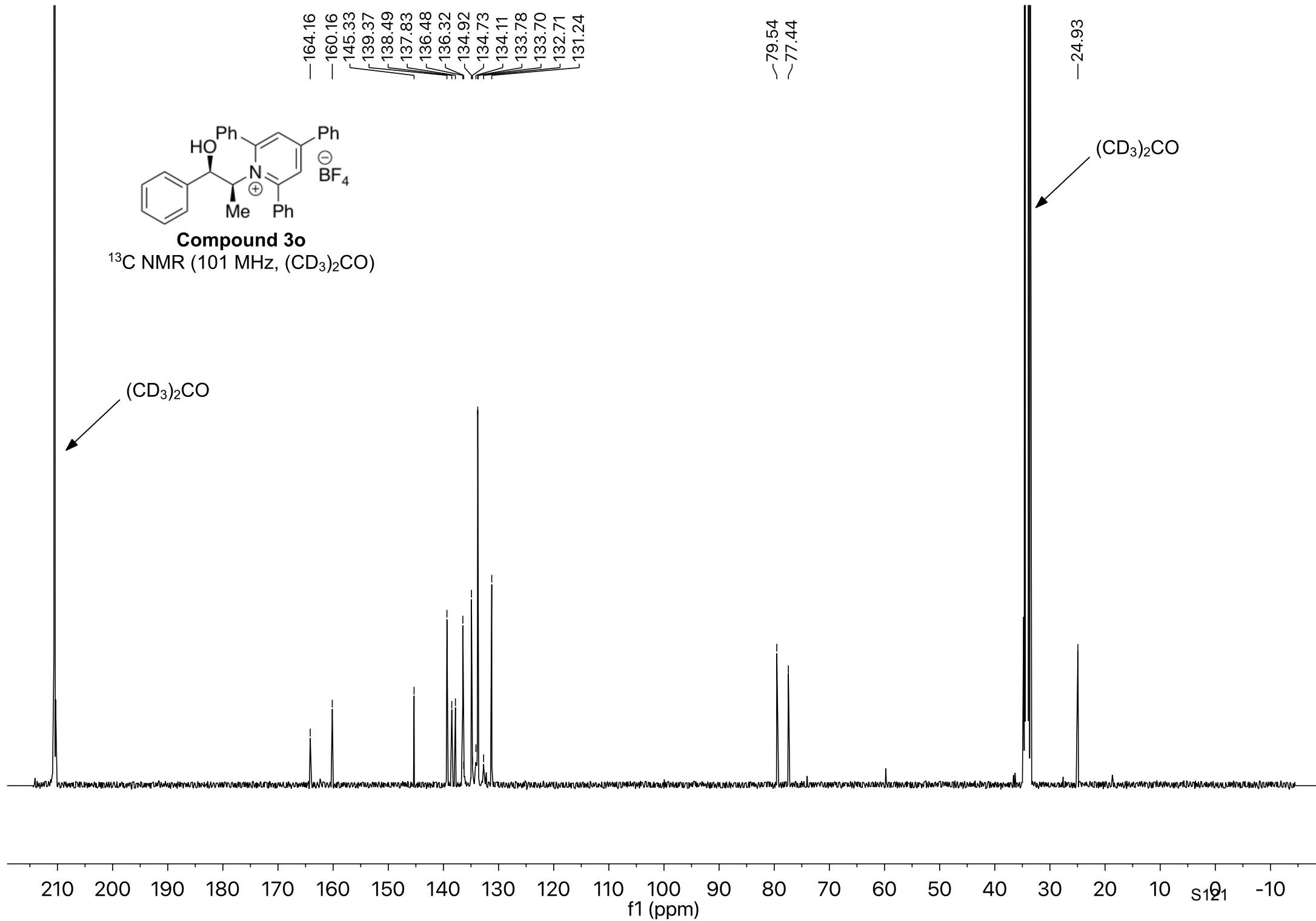
^1H NMR (600 MHz, CDCl_3)

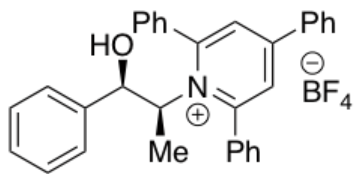




Compound 3o

^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$)

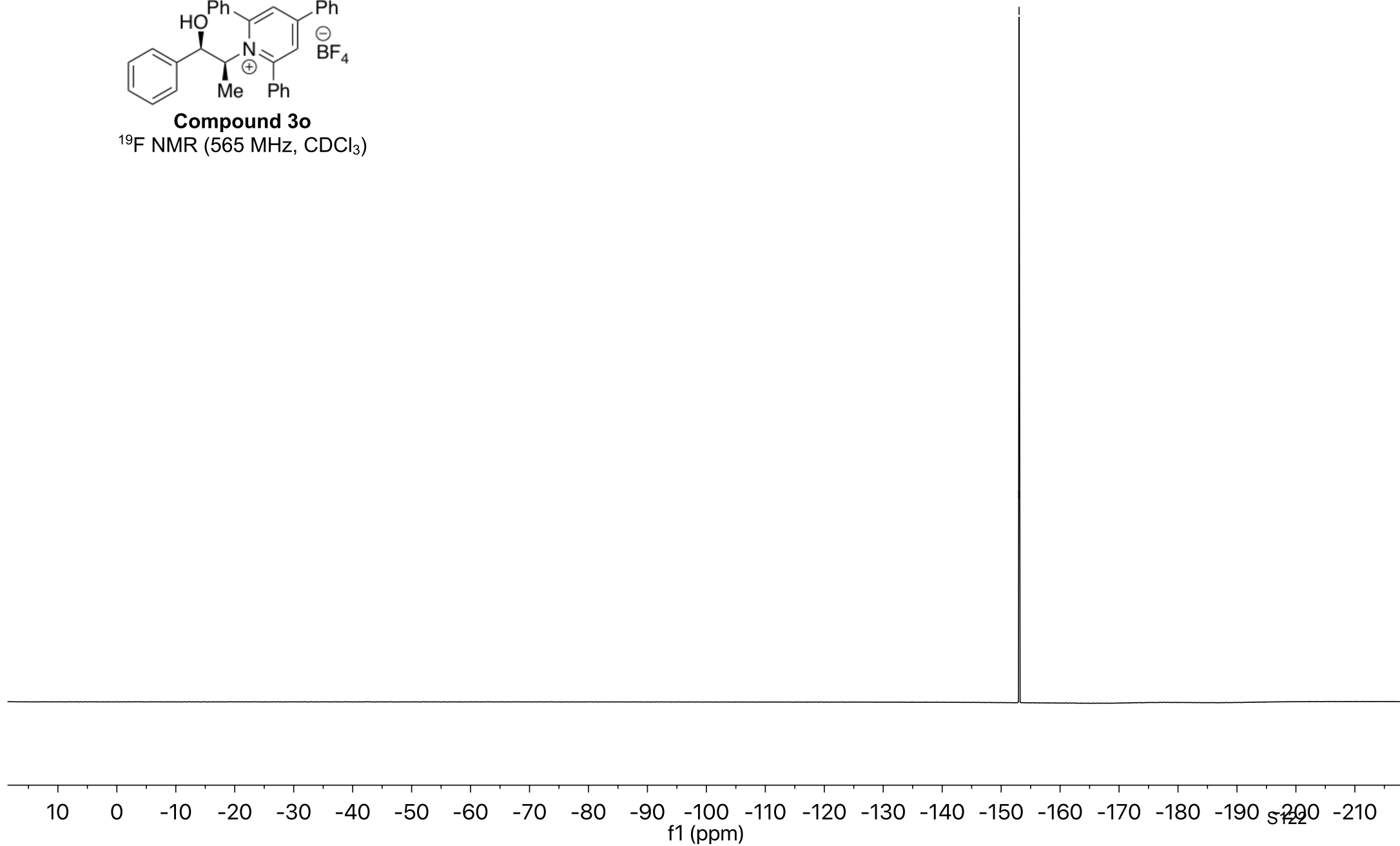


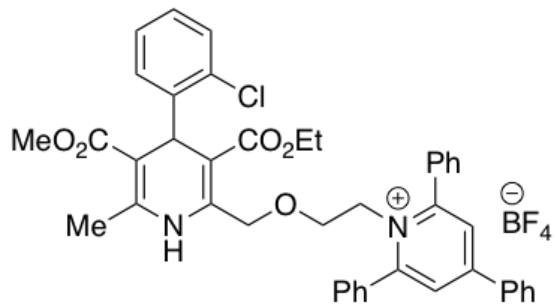


Compound 3o

^{19}F NMR (565 MHz, CDCl_3)

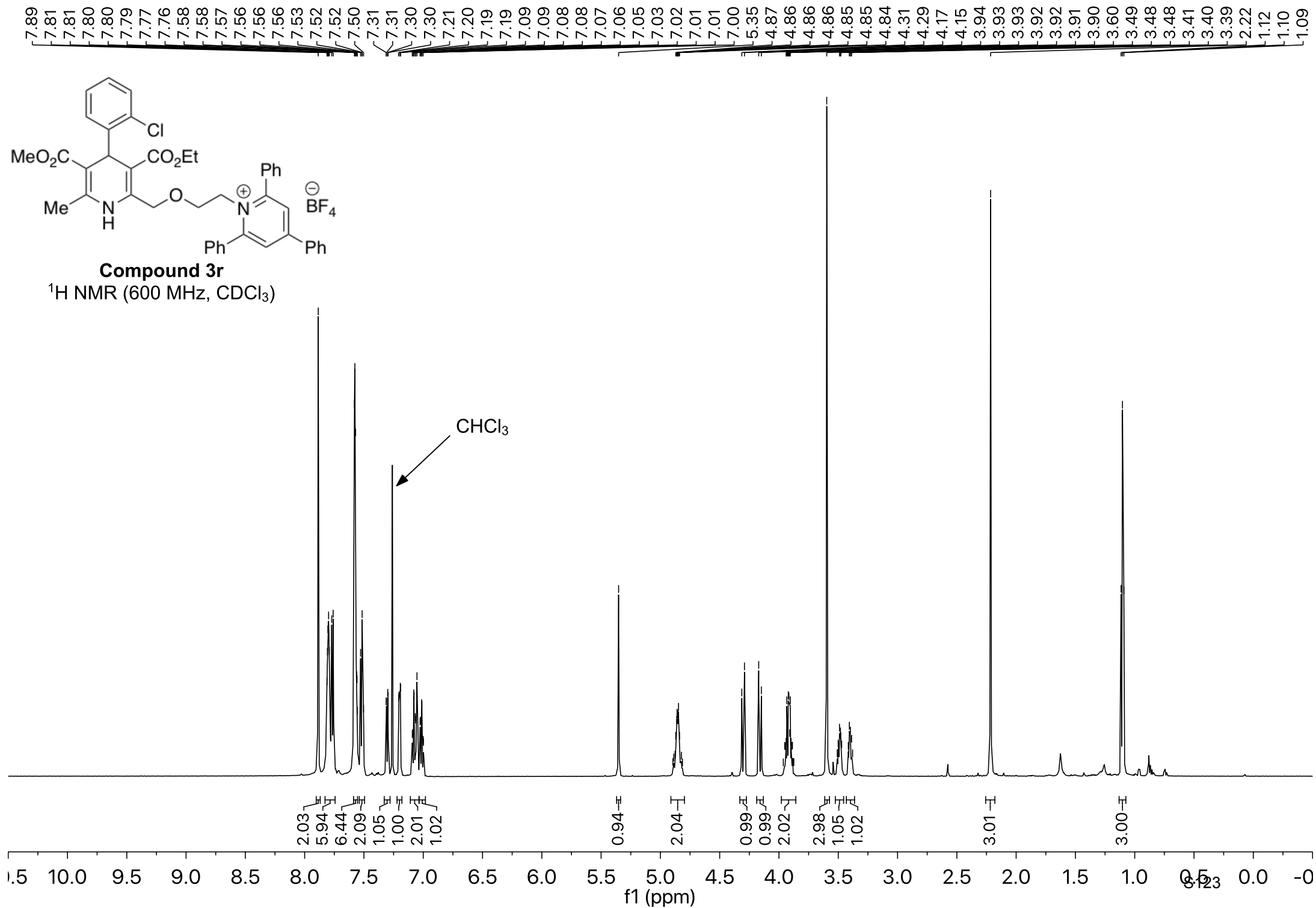
-152.99
-153.04

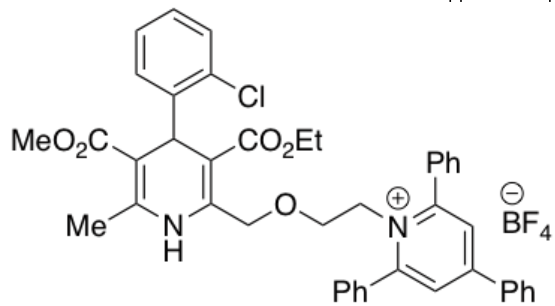




Compound 3r

^1H NMR (600 MHz, CDCl_3)





Compound 3r

^{13}C NMR (151 MHz, CDCl_3)

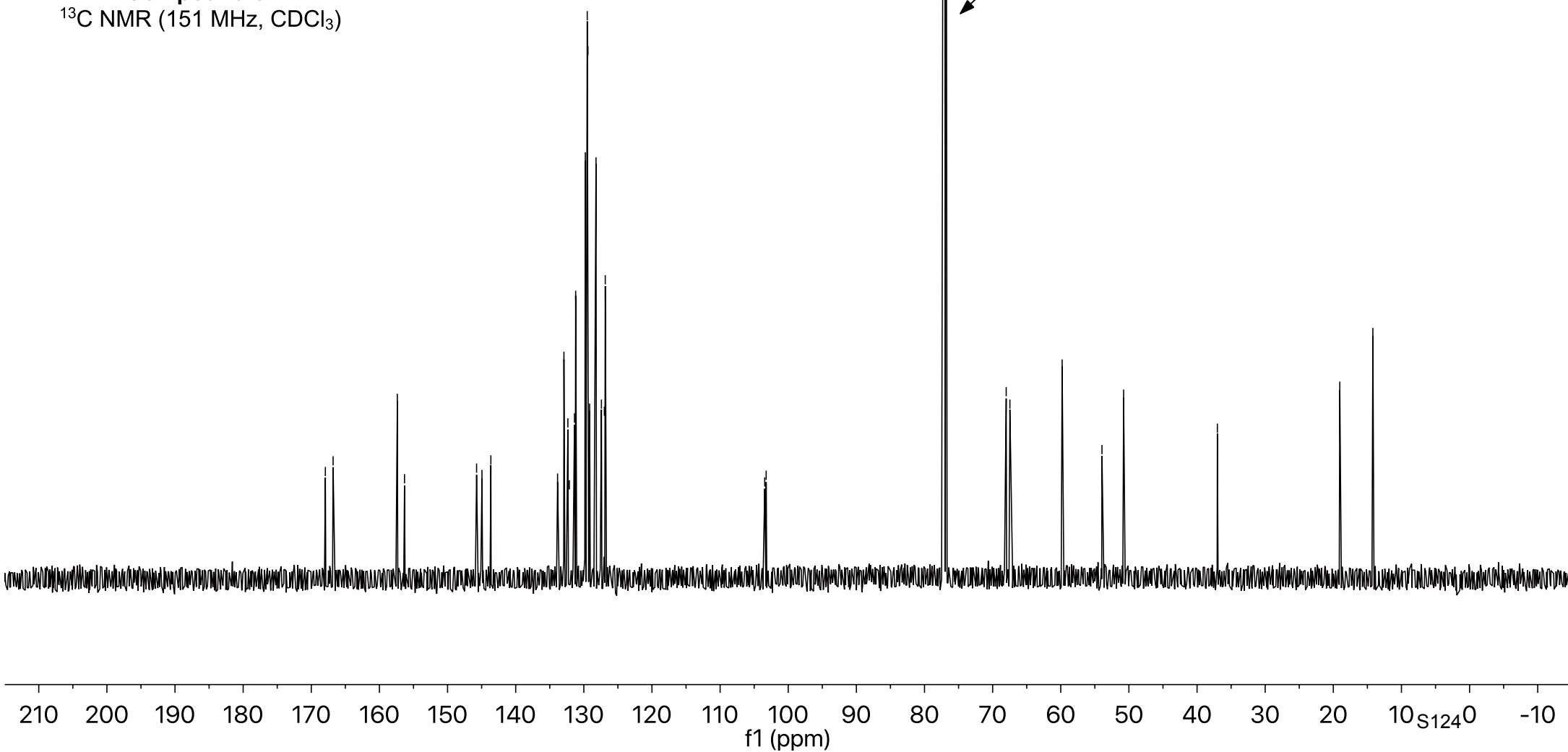
167.94
166.80
157.37
156.32
145.74
144.95
143.64
133.85
132.92
132.34
132.12
131.37
131.20
129.78
129.50
129.40
129.15
128.21
127.42
126.98
126.85
103.45
103.24

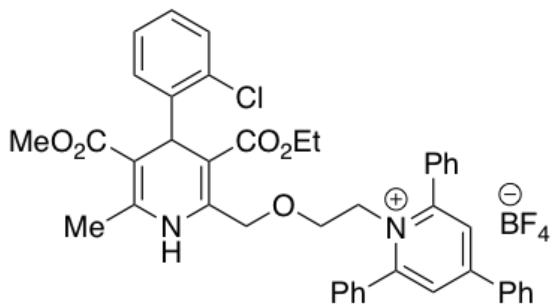
68.01
67.47
59.80
53.96
50.77

37.02

19.05
14.19

CDCl_3





Compound 3r

¹⁹F NMR (565 MHz, CDCl₃)

