Synthesis of o-Chlorophenols via an Unexpected Nucleophilic Chlorination of Quinone Monoketals Mediated by N, N'-Dimethylhydrazine Dihydrochloride

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General Information:

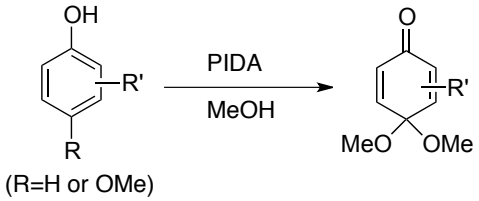
Anhydrous acetonitrile was distilled from $CaCl_2$ under an atmosphere of argon. All reagents were purchased from commercial sources or synthesized using literature methods. Microwave reactions are done in a CEM microwave reactor, Discover® SP System. ^{1}H and ^{13}C NMR spectra were recorded on BRUKE 500 MHz spectrometers; ^{19}F NMR spectra were done on a Bruke 400 MHz spectrometer. ^{1}H and ^{13}C NMR Chemical shifts (δ values) were reported in ppm from downfield using internal standard TMS (^{1}H NMR) or CDCl3 (^{13}C NMR), respectively; ^{19}F NMR were reported from down field using hexafluorobenzene as internal standard. All mass spectra were run by Dr. Cliff Soll at the Hunter College Mass Spectrometry Facility and taken on an Agilent 6520A Q-TOF using electrospray ionization and Dr. Lijia Yang at City College on an Applied Biosystems 4000 QTRAP spectrometer. X-ray crystallography was performed on a Bruker AXS SMART APEXII Single Crystal Diffractometer by Dr. Chunhua Hu at Department of Chemistry of New York University. All infrared spectra were taken on a Thermo Nicolet IR100 spectrometer. Column chromatography was performed over silica with a porosity of 60 Å and a particle size of 40-63 μm.

Experimental:

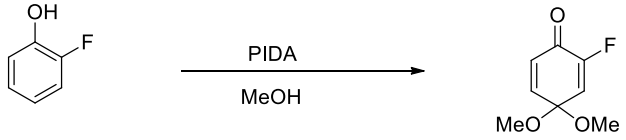
1. Preparation of Quinone Monoketals

Quinone monoketals were made from oxidation of phenols by phenyliodoso diacetate (PIDA) following general procedures of Tamura,[1] Pelter [2] and Taylor,[3] and verified by ^{1}H and ^{13}C NMR. General scheme as follow:

Scheme 1. Synthesis of Quinone Monoketals from Commercial Phenols



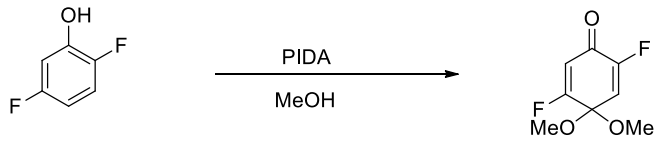
Note: All the fluoro quinone monoketals are unstable (except **2p**); they should be freshly prepared and used right away.



2e

2-fluoro-4,4-dimethoxycyclohexa-2,5-dienone (**2e**): 1 g 2-fluoro-phenol(8.92 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0°C for 10 min. To this solution, 6.3 g PIDA (19.63 mmol, 2.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc: Hexane, 1:4) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:10 to 1:4) to give product **2e** as a liquid 0.49 g. (Note: **2e** is very unstable and it must be freshly prepared and used right away; when exposed to air, product became dark in 5 minutes)

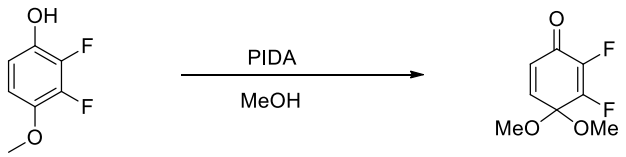
32 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (dd, J = 10.5 Hz, J = 3.0 Hz, 1 H), 6.42 (dd, J = 13.0 Hz, J = 3.0 Hz, 1 H), 6.27 (dd, J = 10.5 Hz, J = 7.0 Hz, 1 H), 3.39 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.03 (d, J = 23.8 Hz), 153.58 (d, J = 270.0 Hz), 144.46 (d, J = 2.5 Hz), 127.92 (d, J = 3.8 Hz), 118.96 (d, J = 11.3 Hz), 95.77 (d, J = 11.3 Hz), 50.54; ^{19}F NMR (377 MHz, $CDCl_3$) δ -129.88.



2o

2,5-difluoro-4,4-dimethoxycyclohexa-2,5-dienone(**2o**): 1 g 2,5-difluorophenol (7.69 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0˚C for 10 min. To this solution, 5.5 g PIDA (16.91 mmol, 2.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc: Hexane, 1:4) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:10 to 1:4) to give product **2o** as a liquid 0.43 g.

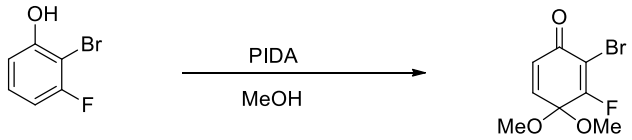
29 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (dd, J = 11.5 Hz, J = 8.5 Hz, 1 H), 6.00 (dd, J = 13.5 Hz, J = 6.0 Hz, 1 H), 3.45 (d, J = 3.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.43 (dd, J = 25.0 Hz, J = 17.5 Hz), 171.13 (dd, J = 301.3 Hz, J = 2.5 Hz), 153.29 (dd, J = 271.3 Hz, J = 1.3 Hz), 116.36 (dd, J = 13.8 Hz, J = 5.0 Hz), 109.25 (dd, J = 11.3 Hz, J = 5.0 Hz), 95.36 (dd, J = 22.5 Hz, J = 12.5 Hz), 51.71 (d, J = 1.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.45, -129.44. LRMS: m/z 212.8 $[M+Na]^+$



2p

2,3-difluoro-4,4-dimethoxycyclohexa-2,5-dienone(**2p**): 1 g 2,3-difluoro-4-methoxy-phenol(6.25 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0˚C for 10 min. To this solution, 2.41 g PIDA (7.49 mmol, 1.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc: Hexane, 1:4) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:10 to 1:4) to give product **2p** as a white solid 1.01 g.

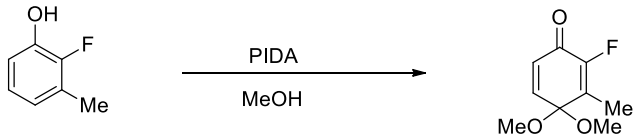
85 % yield; m. p. = 35 – 37°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (dd, J = 10.0 Hz, J = 4.0 Hz, 1 H), 6.28 (dd, J = 10.5 Hz, J = 6.5 Hz, 1 H), 3.46 (d, J = 3.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.75 (dd, J = 22.2 Hz, J = 7.5 Hz), 153.31 (dd, J = 295.0 Hz, J = 6.3 Hz), 141.20 (t, J = 2.5 Hz), 140.67 (dd, J = 265.0 Hz, J = 5.0 Hz), 127.64 (t, J = 2.5 Hz), 96.20 (dd, J = 18.8 Hz, J = 3.8 Hz), 51.79 (d, J = 1.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -134.15 (d, J = 7.9 Hz), -159.14 (d, J = 8.3 Hz). LRMS: m/z 212.8 $[M+Na]^+$



2q

2-bromo-3-fluoro-4,4-dimethoxycyclohexa-2,5-dienone(**2q**): 1 g 2-bromo-3-fluorophenol (5.24 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0°C for 10 min. To this solution, 3.71 g PIDA (11.52 mmol, 2.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc: Hexane, 1:4) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:10 to 1:4) to give product **2q** as a liquid 0.08 g.

6 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (t, J = 10.0 Hz, 1 H), 6.45 (d, J = 10.0 Hz, 1 H), 3.44 (d, J = 1.5 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.20 (d, J = 7.5 Hz), 167.57 (d, J = 298.8 Hz), 140.85 (d, J = 5.0 Hz), 128.77 (d, J = 2.5 Hz), 107.63 (d, J = 11.3 Hz), 94.41 (d, J = 21.3 Hz), 51.88; ^{19}F NMR (377 MHz, $CDCl_3$) δ -90.57. LRMS: 272.7 $[M+Na]^+$

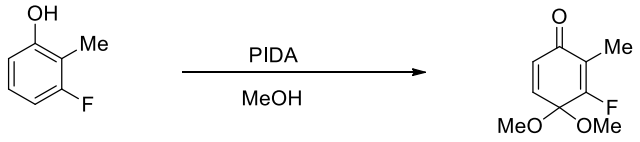


2r

2-fluoro-4,4-dimethoxy-3-methylcyclohexa-2,5-dienone(**2r**): 1 g 2-fluoro-3-methylphenol (7.93 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0°C for 10 min. To this solution, 5.62 g PIDA (17.44 mmol, 2.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc:

Hexane, 1:10) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:20 to 1:10) to give product **2s** as a liquid 0.55 g.

37 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (d, J = 10.0 Hz, 1 H), 6.41 (d, J = 10.5 Hz, J = 7.0 Hz, 1 H), 3.25 (s, 6 H), 1.90 (d, J = 3.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.29 (d, J = 23.8 Hz), 152.13 (d, J = 325.5 Hz), 144.95 (d, J = 2.5 Hz), 132.06 (d, J = 8.8 Hz), 130.34 (d, J = 3.8 Hz), 98.01 (d, J = 10.0 Hz), 51.16, 8.35 (d, J = 3.8 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -108.79. LRMS: 208.8 $[M+Na]^+$



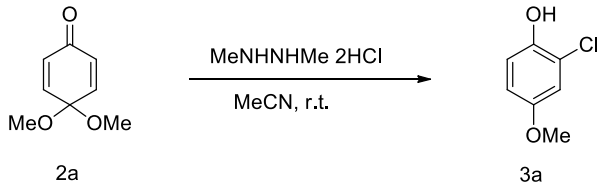
2s

3-fluoro-4,4-dimethoxy-2-methylcyclohexa-2,5-dienone(**2s**): 1 g 3-fluoro-2-methylphenol (7.93 mmol, 1 eqv) was dissolved in 20 mL MeOH and stirred at 0°C for 10 min. To this solution, 5.62 g PIDA (17.44 mmol, 2.2 eqv) was slowly added in small portions. TLC monitoring (EtOAc: Hexane, 1:10) shows reaction complete in 1 hr and hence the reaction was quenched with saturated $NaHCO_3$, extracted with DCM for 3 times. The organic layer was washed with brine water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash chromatography (EtOAc: Hexane, 1:20 to 1:10) to give product **2s** as a liquid 0.24 g.

16 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (t, J = 10.0 Hz, 1 H), 6.33 (d, J = 10.5 Hz, 1 H), 3.41 (d, J = 1.5 Hz, 6 H), 1.87 (d, J = 3.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.55 (d, J = 13.8 Hz), 165.62 (d, J = 287.5 Hz), 140.19 (d, J = 5.0 Hz), 130.17 (d, J = 2.5 Hz), 118.77 (d, J = 7.5 Hz), 93.20 (d, J = 22.5 Hz), 51.61, 6.53 (d, J = 5.0 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -108.79; HRMS m/z Calcd $C_9H_{12}FO_3^+$ $(M+H)^+$: 187.0770, Found: 187.0759.

2 Preparation of 2-chloro phenol Derivatives

2.1 Discovery of 2-chlorination of Quinone Monoketals by N, N'-Dimethylhydrazine Dihydrochloride



2a 3a

Entry	MeNHNHMe•2HCl	DBU	Temperature (℃)	Yield(%)
1	1.2 eqv (added before DBU)	3 eqv	25	2
2	1.2 eqv (added after DBU)	3 eqv	25	0
3	1.2 eqv (added after DBU)	3 eqv	reflux	0
4	1.2 eqv (added before DBU)	0 eqv	25	82

Table 1. Discovery of chlorination of QMK

Entry 1: To a stirred solution of 2a (150 mg, 0.973 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (155 mg, 1.168 mmol, 1.2 eqv) following by adding DBU (450 ul, 3 eqv) at room temperature. Reaction was stirred for 1 hr and TLC monitoring (EtOAc: Hexane, 1:10) shows no new product underneath UV while CAM stain gives a spot above starting material. Reaction was concentrated under reduced pressure and the mixture was purified by flash column to give starting material **2a** and a solid product 3 mg. This product was characterized by ^{1}H and ^{13}C NMR to be **3a**. [4] Its structure was confirmed by comparison of the TLC and spectra of an authentic compound.

2 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, J = 9.0 Hz, 1 H), 6.87 (d, J = 3.0 Hz, 1 H), 6.47 (dd, J = 9.0 Hz, J = 3.0 Hz, 1 H), 5.25 (s, 1 H), 3.74 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.64, 145.49, 119.86, 116.58, 114.51, 114.08, 55.93.

From the above table 1, **3a** is not formed when DBU is added before MeNHNHMe•2HCl and reaction gives a 82 % yield in the absence of DBU. Subsequently we deduced the reaction is a acid mediated reaction and thus screened a number of different chloride regents.

2.2 Screening of Chloride Sources

entry	chloride source	temp	time	yield(%)	description
1	1a	25	1hr	82	
2	1b	25	1hr	80	
3	1c	25	1hr	62	
4	1d	25	1hr	56	

5	HCl(1M)	25	1hr	55	
6	1a	reflux	20 min	99	
7	Pyr HCl	reflux	1hr	83	
8	TMSCl	reflux	1hr	32	
9	TBDMSCl	reflux	1hr	67	
10	Et3N HCl	reflux	1hr	0	no rxn
11	TBAC	reflux	1hr	0	no rxn
12	ZnCl2	reflux	1hr	0	QMK decompose
13	CuCl2	reflux	1hr	0	QMK decompose

Table 2. Screening of chloride sources

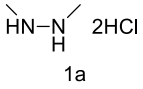
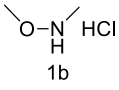
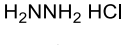
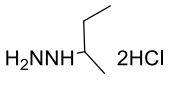
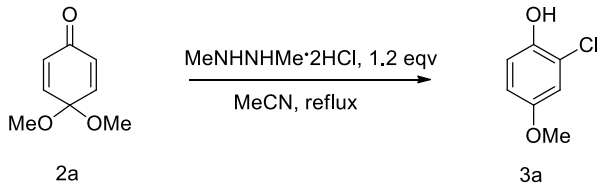
	1a	**1b**	**1c**	**1d**
Structure	 1a	 1b	 1c	 1d

Table 3. Structure for Hydrochloride Salt 1a, 1b, 1c and 1d

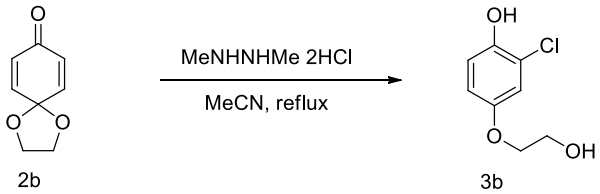
2.3 Synthesized chlorophenol Products

General protocol follows **3a**: reactions in this section were carried out on a scale of 100 – 300 mg; MeNHNHMe•2HCl (1.2 eqv) was added to a solution of QMK in MeCN, and reaction was then refluxed and monitored by TLC with CAM stain. Structures were confirmed by ^{1}H NMR and ^{13}C NMR; known compounds were compared and confirmed with literature reported data, while many of the first time synthesized phenols were further confirmed by HRMS.



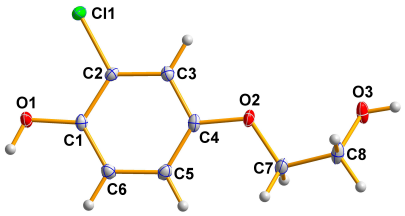
2a 3a

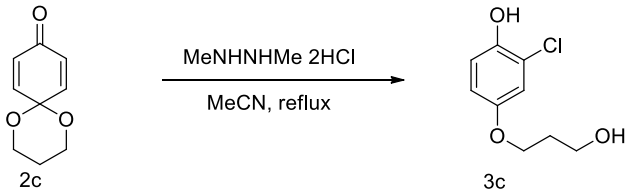
2-chloro-4-methoxyphenol(**3a**)[4]: To a stirred solution of 2a (203 mg, 1.317 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (210 mg, 1.580 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product 207 mg. 99 % yield



4-(2-hydroxyethoxy)phenol(**3b**)[5]: To a stirred solution of 2b (110 mg, 0.723 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (115 mg, 0.868 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 1 hr, TLC monitoring (EtOAc: Hexane, 1:1) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:2 to 1:1) to give solid product 105 mg.
77 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (d, J = 9.0 Hz, 1 H), 6.91 (d, J = 3.0 Hz, 1 H), 6.78 (dd, J = 9.0 Hz, J = 3.0 Hz, 1 H), 5.28 (s, 1 H), 4.02 (t, J = 4.5 Hz, 2 H), 3.94 (t, J = 5.0 Hz, 2 H), 2.05 (t, J = 5.8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.61, 145.92, 119.91, 116.64, 115.21, 115.08, 70.10, 61.43.

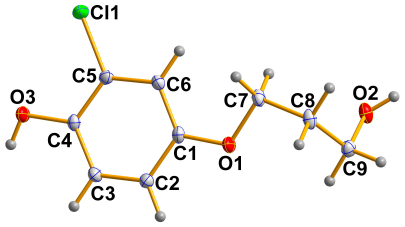
2b was subject to Winterfeldt conditions (HCl, THF/H2O; Baesler, S.; Brunck, A.; Jautelat, R.; Winterfeld, E. *Helv. Chim. Acta* **2000**, *83*, 1854.) and still led to formation **3b** and chlorohydroquinone. The structure was determined by X-ray crystallographic analysis using **3b** recrystallized from hexane/EtOAc. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 971456). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html

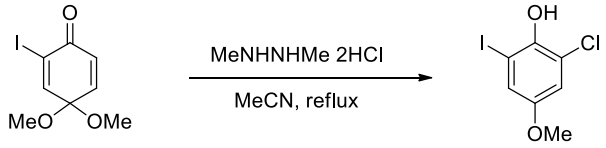




2-chloro-4-(3-hydroxypropoxy)phenol(**3c**): reaction procedure refer to **3b**.
75% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, J = 8.5 Hz, 1 H), 6.90 (d, J = 3.0 Hz, 1 H), 6.75 (dd, J = 9.0 Hz, J = 3.0 Hz, 1 H), 5.32 (s, 1 H), 4.05 (t, J = 6.0 Hz, 2 H), 3.86 (t, J = 6.0 Hz, 2 H), 2.02 (qnt, J = 6.0 Hz, 2 H), 1.77(s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.78, 145.72, 119.89, 116.59, 115.12, 114.93, 66.59, 60.41, 31.92; HRMS m/z Calcd $C_9H_{12}ClO_3^+$ $(M+H)^+$: 203.0475, Found: 203.0472.

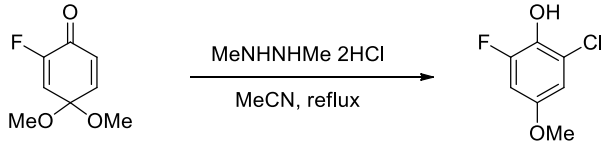
The structure was confirmed by X-ray crystallographic analysis using **3c** recrystallized from hexane/EtOAc. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 921686). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html





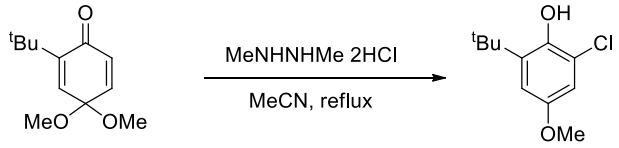
2d 3d

2-chloro-6-iodo-4-methoxyphenol(**3d**): reaction procedure refer to **3a**.
78 % yield; mp 54 - 55 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, J = 3.0 Hz, 1 H), 6.91 (d, J = 3.0 Hz, 1 H), 5.55 (s, 1 H), 3.74 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.80, 145.23, 123.17, 118.83, 115.65, 83.04, 56.08.



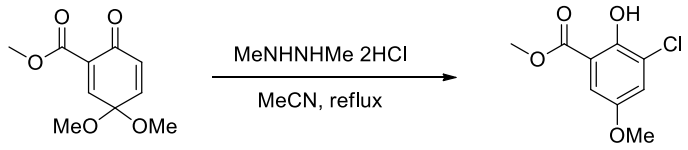
2e 3e

2-chloro-6-fluoro-4-methoxyphenol(**3e**): **2e** must be freshly prepared and used right away; reaction procedure refer to **3a**.
87 % yield; mp 67-68 °C; 1H NMR (500 MHz, CDCl3) δ 6.68 (dd, J = 2.8 Hz, J = 2.3 Hz, 1 H), 6.63 (dd, J = 11.8 Hz, J = 2.8 Hz, 1 H), 5.23 (s, 1 H), 3.74 (s, 3 H); 13C NMR (125 MHz, CDCl3) δ 152.82 (d, J = 11.3 Hz), 151.44 (d, J = 242.5 Hz), 134.68 (d, J = 15.0 Hz), 121.57 (J = 5.0 Hz), 109.88 (d, J = 2.5 Hz), 102.25 (d, J = 21.3 Hz), 56.01; ^{19}F NMR (377 MHz, $CDCl_3$) δ -135.72.



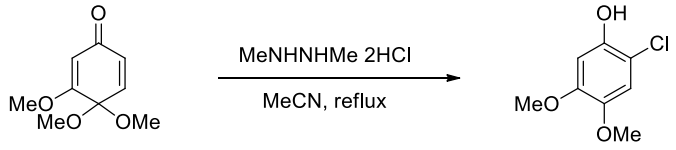
2f 3f

2-(tert-butyl)-6-chloro-4-methoxyphenol(**3f**): reaction procedure refer to **3a**.
88 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (d, J = 3.0 Hz, 1 H), 6.74 (d, J = 3.0 Hz, 1 H), 5.48 (s, 1 H), 3.74 (s, 3 H), 1.38 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.85, 143.30, 137.78, 119.78, 112.82, 109.56, 55.09, 34.67, 28.52; HRMS m/z Calcd $C_{11}H_{16}ClO_2^+$(M+H)$^+$: 215.0839, Found: 215.0836.



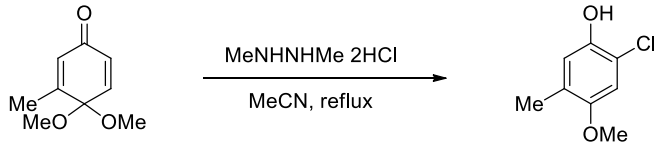
2g 3g

methyl 3-chloro-2-hydroxy-5-methoxybenzoate(**3g**)[6]: reaction procedure refer to **3a**.
84 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.85 (s, 1 H), 7.23 (d, J = 3.0 Hz, 1 H), 7.16 (d, J = 3.5 Hz, 1 H), 3.95 (s, 3 H), 3.75 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.00, 151.80, 151.54, 123.62, 122.62, 112.95, 111.46, 56.01, 52.77.



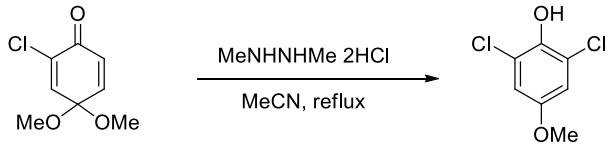
2h 3h

2-chloro-4, 5-dimethoxyphenol(**3h**)[7]: reaction procedure refer to **3a**.
85 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (s, 1 H), 6.61 (s, 1 H), 5.24 (s, 1 H), 3.84 (s, 3 H), 3.82 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.19, 145.57, 143.35, 111.87, 109.30, 100.53, 56.63, 56.11.



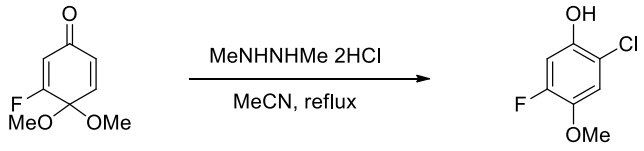
2i 3i

2-chloro-4-methoxy-5-methylphenol(**3i**): reaction procedure refer to **3a**.
81 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (s, 1 H), 6.74 (s, 1 H), 5.17 (s, 1 H), 3.75 (s, 3 H), 2.15 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.85, 144.88, 127.35, 118.15, 116.15, 110.74, 56.01, 15.94; HRMS m/z Calcd $C_8H_8ClO_2^-$ $(M-H)^-$: 171.0213, Found: 171.0214.



2j 3j

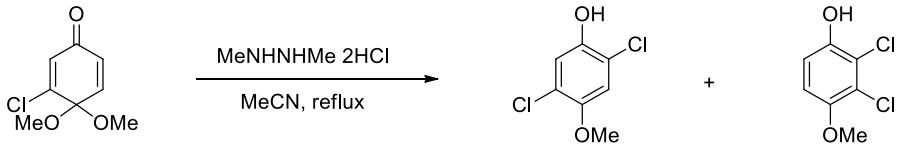
2,6-dichloro-4-methoxyphenol(**3j**)[8]: reaction procedure refer to **3a**.
99 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (s, 2 H), 5.47 (s, 1 H), 3.75 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.97, 142.09, 121.17, 114.20, 56.02.



2k 3k

2-chloro-5-fluoro-4-methoxyphenol(**3k**): **2k** need to be freshly prepared; reaction procedure refer to **3a**.

88 % yield; mp 64 - 69°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (d, J = 8.5 Hz, 1 H), 6.81 (d, J = 11.5 Hz, 1 H), 5.32 (s, 1 H), 3.83(s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.86 (d, J = 245.0 Hz), 145.49 (d, J = 11.3 Hz), 141.95 (d, J = 12.5 Hz), 114.20 (d, J = 3.8 Hz), 113.74 (d, J = 3.8 Hz), 104.97 (d, J = 22.5 Hz), 57.20; ^{19}F NMR (377 MHz, $CDCl_3$) δ -136.15; HRMS m/z Calcd $C_7H_5ClFO_2^-$(M-H)$^-$: 174.9962, Found: 174.9940.

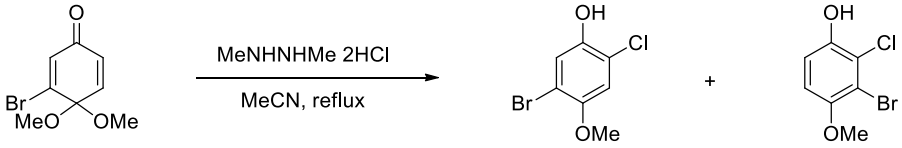


2l 3l 3l'

To a stirred solution of **2l** (270 mg, 1.432 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (229 mg, 1.718 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete (Rf: **2l** = 0.35; **3l** = 0.4; **3l'** = 0.2). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product **3l** 204 mg and **3l'** 43 mg.

2,5-dichloro-4-methoxyphenol(**3l**)[8]:74 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 1 H), 6.92 (s , 1 H), 5.21 (s, 1 H), 3.87 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.34, 145.52, 122.22, 117.89, 117.85, 112.74, 56.91.

2,3-dichloro-4-methoxyphenol(**3l'**)[8]:16 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (d, J = 9.0 Hz, 1 H), 6.81 (d, J = 9.5 Hz, 1 H), 5.36 (s, 1 H), 3.86 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.12, 146.38, 121.42, 120.17, 113.56, 111.55, 56.99.

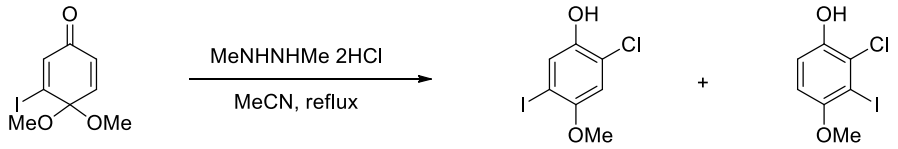


2m 3m 3m'

To a stirred solution of **2m** (50 mg, 0.214 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (34 mg, 0.257 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete (Rf: **2m** = 0.35; **3m** = 0.4; **3m'** = 0.2). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product **3m** 30 mg and **3m'** 9 mg.

5-bromo-2-chloro-4-methoxyphenol(**3m**): 59 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (s, 1 H), 6.86 (s , 1 H), 5.24 (s, 1 H), 3.84 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.25, 145.81, 120.72, 118.72, 112.51, 110.85, 56.99; HRMS m/z Calcd $C_7H_5BrClO_2^-$(M-H)$^-$: 234.9161, Found: 234.9139.

3-bromo-2-chloro-4-methoxyphenol(**3m'**): 18 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (d, J = 9.0 Hz, 1 H), 6.80 (d, J = 9.0 Hz, 1 H), 5.30 (s, 1 H), 3.86 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.19, 146.40, 121.94, 114.44, 112.24, 111.54, 57.09; HRMS m/z Calcd $C_7H_5BrClO_2^-$(M-H)$^-$: 234.9161, Found: 234.9160.

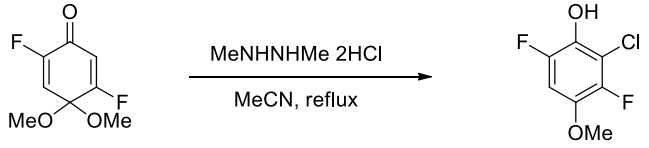


2n 3n 3n'

To a stirred solution of **2n** (150 mg, 0.536 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (85 mg, 0.643 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete (Rf: **2n** = 0.35; **3n** = 0.4; **3n'** = 0.3). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:20 to 1:10) to give solid product **3n** 104 mg and **3n'** 46 mg.

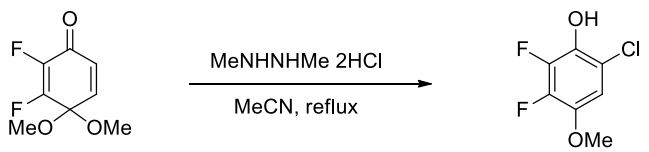
2-chloro-5-iodo-4-methoxyphenol(**3n**): 68 % yield; mp 112 - 114 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (s, 1 H), 6.77 (s , 1 H), 5.27 (s, 1 H), 3.82 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.63, 146.09, 126.44, 119.88, 111.27, 84.34, 57.11; HRMS m/z Calcd $C_7H_5ClIO_2^-$(M-H)$^-$: 282.9023, Found: 282.9019.

2-chloro-3-iodo-4-methoxyphenol(**3n'**): 30 % yield; mp 66- 71°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (d, J = 9.0 Hz, 1 H), 6.74 (d, J = 9.0 Hz, 1 H), 5.26 (s, 1 H), 3.85 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.76, 145.88, 125.49, 115.71, 110.79, 90.28, 57.25; HRMS m/z Calcd $C_7H_5ClIO_2^-$(M-H)$^-$: 282.9023, Found: 282.9015.



2o 3o

2-chloro-3,6-difluoro-4-methoxyphenol(3o): **2o** need to be freshly prepared; reaction procedure refer to **3a**.
90 % yield; mp 76 - 80 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (dd, J = 6.5 Hz, J = 2.5 Hz, 1 H), 5.21 (s , 1 H), 3.84 (s , 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.42 (dd, J = 238.6 Hz, J = 4.8 Hz), 145.54 (dd, J = 249.4 Hz, J = 10.0 Hz), 141.21 (dd, J = 12.5 Hz, J = 10.0 Hz), 134.61 (d, J = 1.6 Hz), 111.05 (dd, J = 18.8 Hz, J = 5.0 Hz), 101.10 (dd, J = 23.1 Hz, J = 1.9 Hz), 57.32; ^{19}F NMR (377 MHz, $CDCl_3$) δ -142.51 (d, J = 11.3 Hz), -142.70 (d, J = 11.3 Hz)); HRMS m/z Calcd $C_7H_4ClF_2O_2^-$(M-H)$^-$: 192.9868, Found: 192.9841.

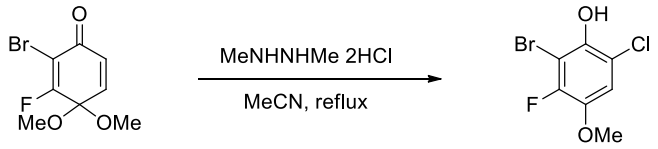


2p 3p

6-chloro-2,3-difluoro-4-methoxyphenol(**3p**): **2p** can be stored under Argon in fridge; reaction procedure refer to **3a** (note: 3p has almost identical Rf as 2p (Rf: 2p = 0.3, 3p =0.32), while TLC upon CAM stain, 3p gives a darker spot).

92 % yield; mp 70 - 73 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (dd, J = 7.5 Hz, J = 2.5 Hz, 1 H),

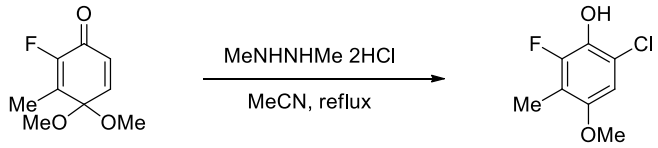
5.40 (s , 1 H), 3.85 (s , 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.21(dd, J = 8.8 Hz, J = 2.5 Hz), 141.38 (dd, J = 245.0 Hz, J = 13.8 Hz), 141.18 (dd, J = 247.5 Hz, J = 12.5 Hz), 135.74 (dd, J = 11.3 Hz, J = 1.3 Hz), 114.73 (t, J = 4.4 Hz), 108.41 (d, J = 2.5 Hz), 57.23; ^{19}F NMR (377 MHz, $CDCl_3$) δ -158.59 (d, J = 19.6 Hz), -160.28 (d, J = 19.3 Hz); HRMS m/z Calcd $C_7H_4ClF_2O_2^-$(M-H)$^-$: 192.9868, Found: 192.9875.



2q 3q

2-bromo-6-chloro-3-fluoro-4-methoxyphenol(**3q**): **2q** need to be freshly prepared; reaction procedure refer to **3a**.

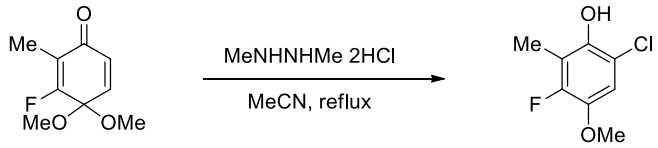
92 % yield; mp 82- 84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, J = 8.5 Hz, 1 H), 5.59 (s , 1 H), 3.85 (s , 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.12 (d, J = 246.3 Hz), 143.39 (d, J = 2.5 Hz), 142.09 (d, J = 12.5 Hz), 114.21 (d, J = 3.8 Hz), 113.68 (d, J = 2.5 Hz), 99.71 (d, J = 22.5 Hz), 57.38; ^{19}F NMR (377 MHz, $CDCl_3$) δ -128.15); HRMS m/z Calcd $C_7H_4BrClFO_2^-$(M-H)$^-$: 252.9067, Found: 252.9058.



2r 3r

6-chloro-2-fluoro-4-methoxy-3-methylphenol(**3r**): **2r** need to be freshly prepared; reaction procedure refer to **3a**.

98 % yield; mp 96 - 99 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (d, J = 2.5 Hz, 1 H), 5.22 (s , 1 H), 3.76 (s , 3 H), 2.10 (d, J = 2.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.24 (d, J = 8.8 Hz), 150.20 (d, J = 238.8 Hz), 134.74 (d, J = 16.3 Hz), 117.28 (d, J = 5.0 Hz), 114.10 (d, J = 17.5 Hz), 106.32 (d, J = 2.5 Hz), 56.15, 7.85 (d, J = 3.8 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -139.80); HRMS m/z Calcd $C_8H_7ClFO_2^-$(M-H)$^-$: 189.0119, Found: 189.0117.

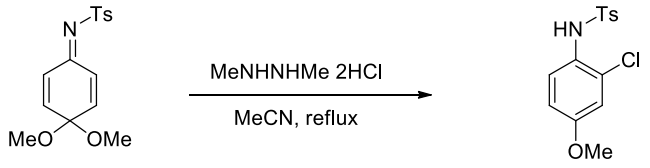


2s 3s

6-chloro-3-fluoro-4-methoxy-2-methylphenol(**3s**): **2s** need to be freshly prepared; reaction procedure refer to **3a**.

89 % yield; mp 65 - 66 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (d, J = 8.0 Hz, 1 H), 5.30 (s , 1 H), 3.81 (s , 3 H), 2.21 (d, J = 2.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.40 (d, J = 241.3 Hz), 144.07 (d, J = 7.5 Hz), 141.68 (d, J = 13.8 Hz), 114.59 (d, J = 18.8 Hz), 112.98 (d, J = 3.8 Hz), 110.61 (d ,J = 2.5 Hz), 57.02, 8.62 (d, J = 6.3 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -140.25); HRMS m/z Calcd $C_8H_7ClFO_2^-$(M-H)$^-$: 189.0119, Found: 189.0125.

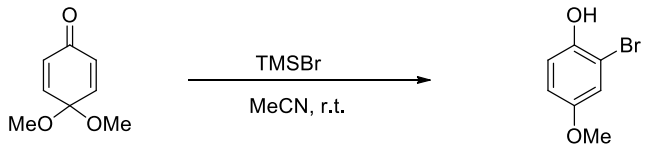
3. Quinone imine ketal and miscellaneous nucleophiles



4

N-(2-chloro-4-methoxyphenyl)-4-methylbenzenesulfonamide(**4**): To a stirred solution of N-Ts imine ketal (200 mg, 0.651 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (104 mg, 0.781 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 1 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product 198 mg. (The structure was confirmed by tosylation of commercial 2-chloro-4-methoxyaniline)

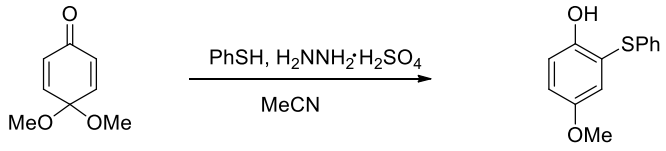
98 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 2 H), 7.55 (d, J = 9.0 Hz, 1 H), 7.18 (d, J = 8.0 Hz, 2 H), 6.85 (s, 1 H), 6.78 (dd, J =4.0 Hz, J = 2.5 Hz, 1 H), 6.75 (d, J = 3.0 Hz, 1 H), 3.72 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.80, 143.95, 135.93, 129.52, 127.99, 127.26, 126.11, 114.56, 113.55, 55.62, 21.52.



2a 5

2-bromo-4-methoxyphenol(**5**)[9]: To a stirred solution of **2a** (120 mg, 0.778 mmol, 1 eqv) in 3 ml MeCN, add TMSBr (123 ul, 0.934 mmol, 1.2 eqv) at room temperature. The reaction was stirred for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:20 to 1:10) to give product 110 mg.

70 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, J = 3.0 Hz, 1 H), 6.94 (d, J = 9.0 Hz, 1 H), 6.79 (d, J = 9.0 Hz, J = 3.0 Hz, 1 H), 5.17 (s , 1 H), 3.74 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.83, 146.50, 116.83, 116.32, 115.35, 109.92, 55.98.

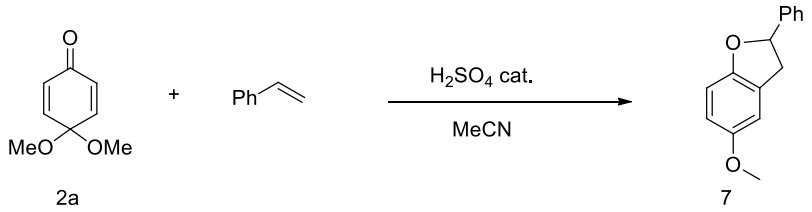


2a 6

4-methoxy-2-(phenylthio)phenol(**6**)[10]: To a stirred solution of **2a** (50 mg, 0.324 mmol, 1 eqv) in 3 ml MeCN, add PhSH (43 mg, 0.389 mmol, 1.2 eqv) and H_2NNH_2•H_2SO_4 (50 mg, 0.389 mmol, 1.2 eqv) at room temperature. The reaction was stirred for 1 hr, TLC monitoring (EtOAc: Hexane, 1:4) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10 to 1:4) to give product 52 mg.

69 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.09 (m, 5 H), 7.05 (d, J = 3.0 Hz, 1 H), 7.00

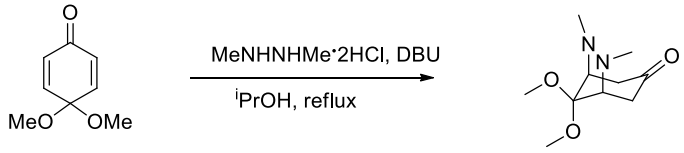
(d, J = 9.0 Hz, 1 H), 6.95 (dd, J = 9.0 Hz, J = 3.0 Hz, 1 H), 6.12 (s, 1 H), 3.75 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.52, 151.40, 135.70, 129.23, 126.91, 126.17, 120.31, 118.88, 116.29, 116.12, 55.88.



2a 7

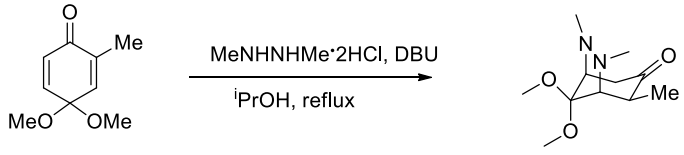
5-methoxy-2-phenyl-2,3-dihydrobenzofuran(**7**)[11]: To a stirred solution of **2a** (70 mg, 0.454 mmol, 1 eqv) in 3 ml MeCN, add styrene (96 mg, 0.908 mmol, 2 eqv) and 50 ul H_2SO_4 acetonitrile solution(solution was prepared by diluting 0.5 ml concentrated H_2SO_4 in 10 ml acetonitrile) at room temperature. The reaction was stirred for 1 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete. Acid was neutralized by small amount of Li_2CO_3 and solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give product 36 mg.
35 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.22 (m, 5 H), 6.70 (m, 2 H), 6.63 (dd, J = 8.5 Hz, J = 3.0 Hz, 1 H), 5.66 (t, J = 9.0 Hz, 1 H), 3.67 (s, 3 H), 3.52 (dd, J = 15.5 Hz, J = 9.5 Hz, 1 H), 3.12 (dd, J = 15.5 Hz, J = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.30, 153.78, 142.02, 128.66, 128.03, 127.53, 125.80, 112.99, 111.20, 109.22, 84.26, 56.05, 38.90.

4. Preparation of N,N-double Michael addition Derivatives



2a 8

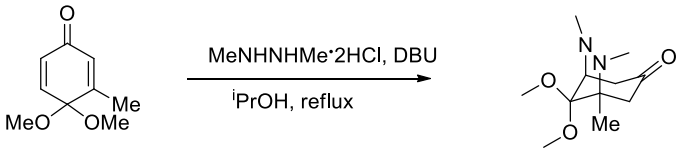
8,8-dimethoxy-6,7-dimethyl-6,7-diazabicyclo[3.2.1]octan-3-one(**8**): To a solution of **2a** (120 mg, 0.778 mmol, 1 eqv) in 5 ml ^{i}PrOH add MeNHNHMe•2HCl (124 mg, 0.934 mmol, 1.2 eqv)and DBU (443 mg, 2.907 mmol, 4 eqv). Reaction was refluxed for 3 hr; product **8** is very polar; TLC monitoring (EtOAc: Hexane, 1:4; Rf(**2a**) = 0.4, Rf (**8**) = 0)/ (EtOAc: MeOH, 1:4; Rf(**2a**) = 1, Rf (**8**) = 0.5) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (pure EtOAC to EtOAc: MeOH,1: 10) to give product as a liquid 154 mg.
94 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.40 (s, 3 H), 3.36 (d, J = 2.0 Hz, 2 H), 3.35 (s, 3 H), 2.70 – 2.57 (m, 4 H), 2.54 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.17, 106.46, 61.92, 50.68, 49.15, 42.80, 41.45.



9

8,8-dimethoxy-2,6,7-trimethyl-6,7-diazabicyclo[3.2.1]octan-3-one(**9**): reaction procedure refer to

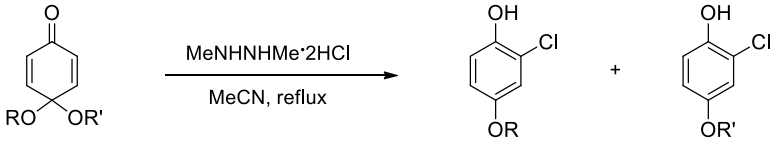
8.
26 % yield; mp 57 - 60 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (dd, J = 5.0 Hz, J = 3.0 Hz, 1 H), 3.39 (s, 3H), 3.36 (s, 3 H), 2.86 (t, J = 2.0 Hz, 1 H), 2.78 (dd, J = 17.0 Hz, J = 3.0 Hz, 1 H), 2.62 (q, J = 6.5 Hz, 1 H), 2.56 (s, 3 H), 2.51 (m, 1 H), 2.40 (s, 3 H), 1.11 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.40, 106.25, 68.76, 61.86, 50.64, 49.04, 46.94, 44.89, 39.46, 38.36, 12.24.



2i 10

8,8-dimethoxy-1,6,7-trimethyl-6,7-diazabicyclo[3.2.1]octan-3-one(**10**): reaction procedure refer to **8**.
56 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.43 (s, 3 H), 3.42 (s, 3 H), 3.20 (t, J = 3.0 Hz, 1 H), 2.74 (dd, J = 17.0 Hz, J = 8.0 Hz, 1 H), 2.62 (dd, J = 17.5 Hz, J = 2.5 Hz, 1 H), 2.58 (s, 3 H), 2.52 (dt, J = 16.5 Hz, J = 2.5 Hz, 1 H), 2.46 (d, J = 17.5 Hz, 1 H), 2.36 (s, 3 H), 1.22 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.27, 105.06, 66.34, 61.17, 49.89, 49.61, 46.58, 46.48, 43.86, 35.69, 18.73.

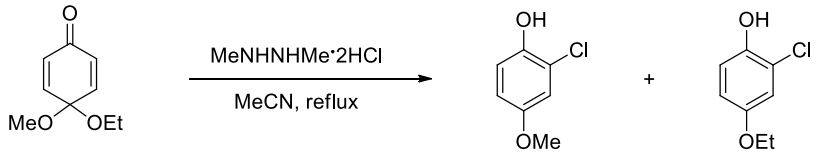
5. Chlorination of Mixed Quinone Monoketals



2 3

Entry	QMK	Yield	Ratio	Description
1	**2t** (R = Me, R' = Et)	85%	**3a** (R = Me) : **3t** (R' = Et) 1 : 3.5	inseparable mixture ratio calculated from ^{1}H NMR
2	**2u** (R = Me, R' = ^{i}Pr)	85%	**3a** (R = Me) : **3u** (R' = ^{i}Pr) 1 : 7.5	inseparable mixture ratio calculated from ^{1}H NMR
3	**2v** (R = Me, R' = propargyl)	81%	**3a** is the only product	
4	**2t** (R = Me, R' = TBS)	**3a** (25%); **3w** (46%) (seperated yield)	**3a** (R = Me) : **3w** (R' = TBS) 1 : 1.6	ratio calculated from ^{1}H NMR of the crude product before column chromatography

Entry 1:

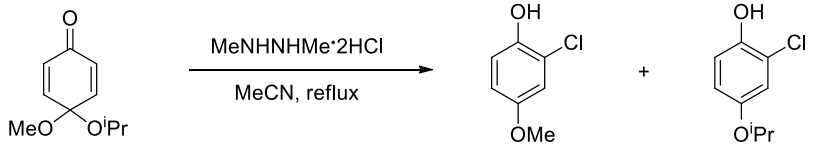


2t 3a 3t

ratio 1 : 3.5

To a stirred solution of **2t** (28 mg, 0.166 mmol, 1 eqv) in 3 ml MeCN, add MeNHNHMe•2HCl (27 mg, 0.200 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete (Rf: **2t** = 0.3; **3a = 3t =** 0.4). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product **24** mg. ^{1}H NMR (refer to attached spectra) showed mixture of **3a** and **3t**, and the ratio of **3a**: **3t** is 1: 3.5.

Entry 2:



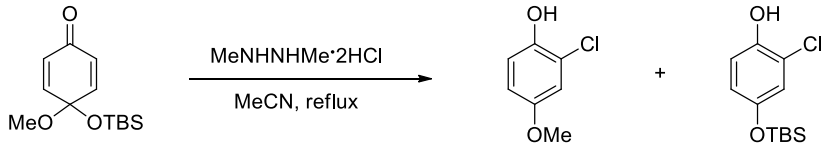
2u 3a 3u

ratio 1 : 7.5

To a stirred solution of **2u** (80 mg, 0.439 mmol, 1 eqv) in 3 ml MeCN, add MeNHNHMe•2HCl (44 mg, 0.527 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete (Rf: **2u** = 0.3; **3a = 3u =** 0.4). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product **65** mg. ^{1}H NMR (refer to attached spectra) showed mixture of **3a** and **3u**, and the ratio of **3a**: **3u** is 1: 7.5.

Entry 3: To a stirred solution of **2v** (75 mg, 0.421 mmol, 1 eqv) in 3 ml MeCN, add MeNHNHMe•2HCl (67 mg, 0.505 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete (Rf: **2v** = 0.3; **3a =** 0.4). Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:10) to give solid product 54 mg. ^{1}H NMR (refer to attached spectra) showed **3a** as the only product, yield 81 %.

Entry 4:



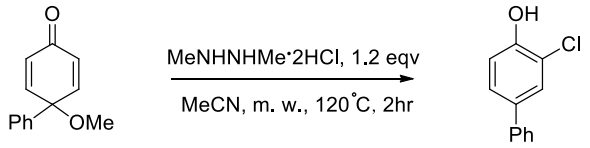
2w 3a 3w

4-((tert-butyldimethylsilyl)oxy)-2-chlorophenol(**3w**): To a stirred solution of **2w** (170 mg, 0.669 mmol, 1 eqv) in 5 ml MeCN, add MeNHNHMe•2HCl (107 mg, 0.803 mmol, 1.2 eqv) at room temperature. The reaction was then refluxed for 0.5 hr, TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete (Rf: **2w** = 0.55; **3w** = 0.45; **3a** = 0.3). Solvent was removed under reduced pressure and a ^{1}H NMR spectra (refer to the attached spectra) was taken for the crude product (ratio of **3a**: **3w** = 1: 1.6). Then the mixture was purified via flash chromatography (EtOAc: Hexane, 1:40 to 1:20) to give solid product **3w** 80 mg (yield 46%) and

3a 27 mg (yield 25 %).

3w, 46 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (d, J = 9.0 Hz, 1 H), 6.82 (d, J = 3.0 Hz, 1 H), 6.67 (dd, J = 9.0 Hz, J = 3.0 Hz, 1 H), 5.24 (s, 1 H), 0.97 (s, 9 H), 0.17 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.29, 145.94, 120.24, 120.02, 119.52, 116.27, 25.63, 18.13, -4.57; HRMS m/z Calcd $C_{12}H_{18}ClO_2Si^-$ $(M-H)^-$: 57.0765, Found: 257.0756.

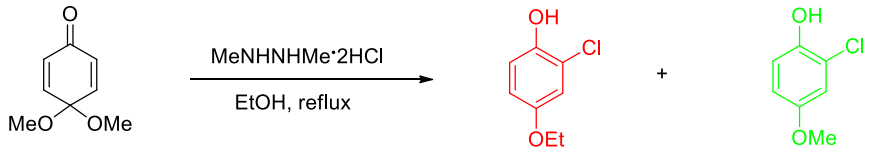
6. Mechanism Study: synthesis of 14 and scrambling experiments



13 14

3-chloro-[1, 1'-biphenyl]-4-ol(**14**):[12] To a solution of 13 (100 mg, 0.500 mmol, 1 eqv) in 3 ml MeCN in a CEM microwave tube add MeNHNHMe•2HCl (80 mg, 0.600 mmol, 1.2 eqv). Set reaction parameter as 120 °C, 120 min; TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane, 1:20 to 1:10) to give product 82 mg.

80 % yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 2.0 Hz, 1 H), 7.49 – 7.48 (m, 2 H), 7.41 – 7.37 (m, 3 H), 7.32 – 7.29 (m, 1 H), 7.06 (d, J = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.71, 139.52, 134.94, 128.84, 127.47, 127.23, 127.11, 126.68, 120.24, 116.48.



2a 3t 3a

ratio 4.3 : 1

To a solution of **2a** (100 mg, 0.649 mmol, 1 eqv) in 3 ml MeCN add MeNHNHMe•2HCl (104 mg, 0.779 mmol, 1.2 eqv). Reaction was refluxed for 1 hr; TLC monitoring (EtOAc: Hexane, 1:10) with CAM stain showed reaction complete. Solvent was removed under reduced pressure and the mixture was purified via flash chromatography (EtOAc: Hexane,1: 10) to give product as a inseparable mixture of **3a** and **3t**, 62 mg. The ratio of **3a**: **3t** on ^{1}H NMR is 1: 4.3.

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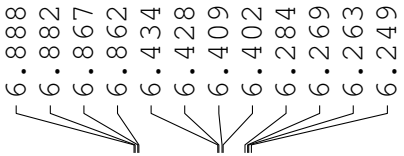
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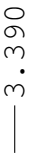
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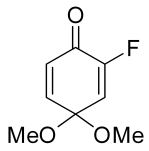
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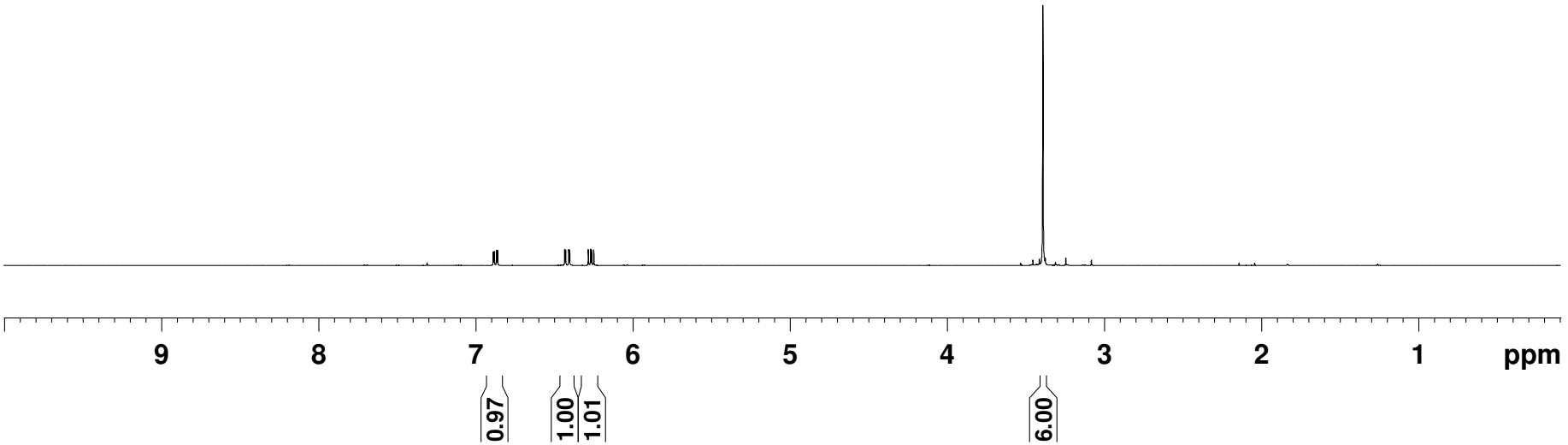
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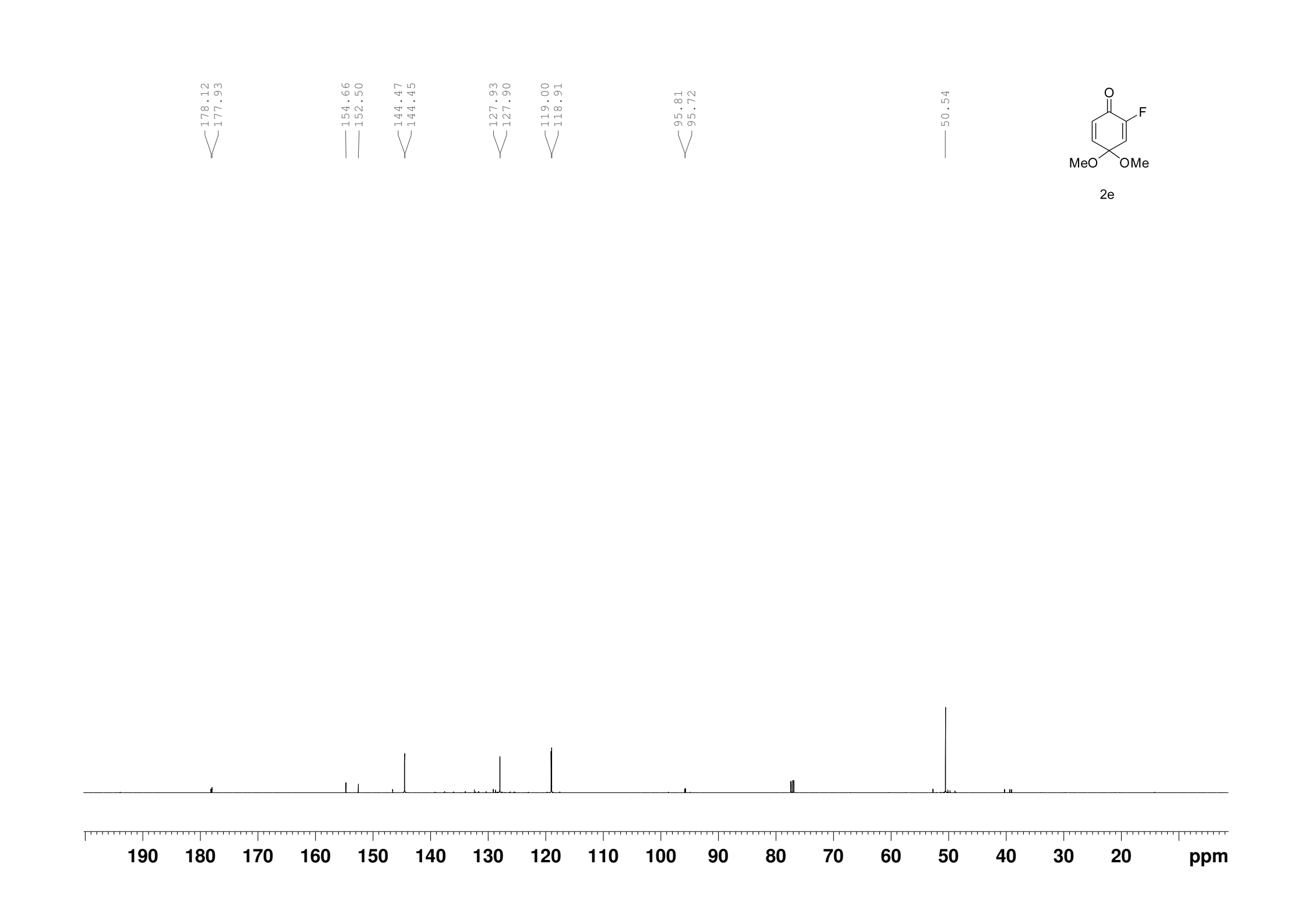
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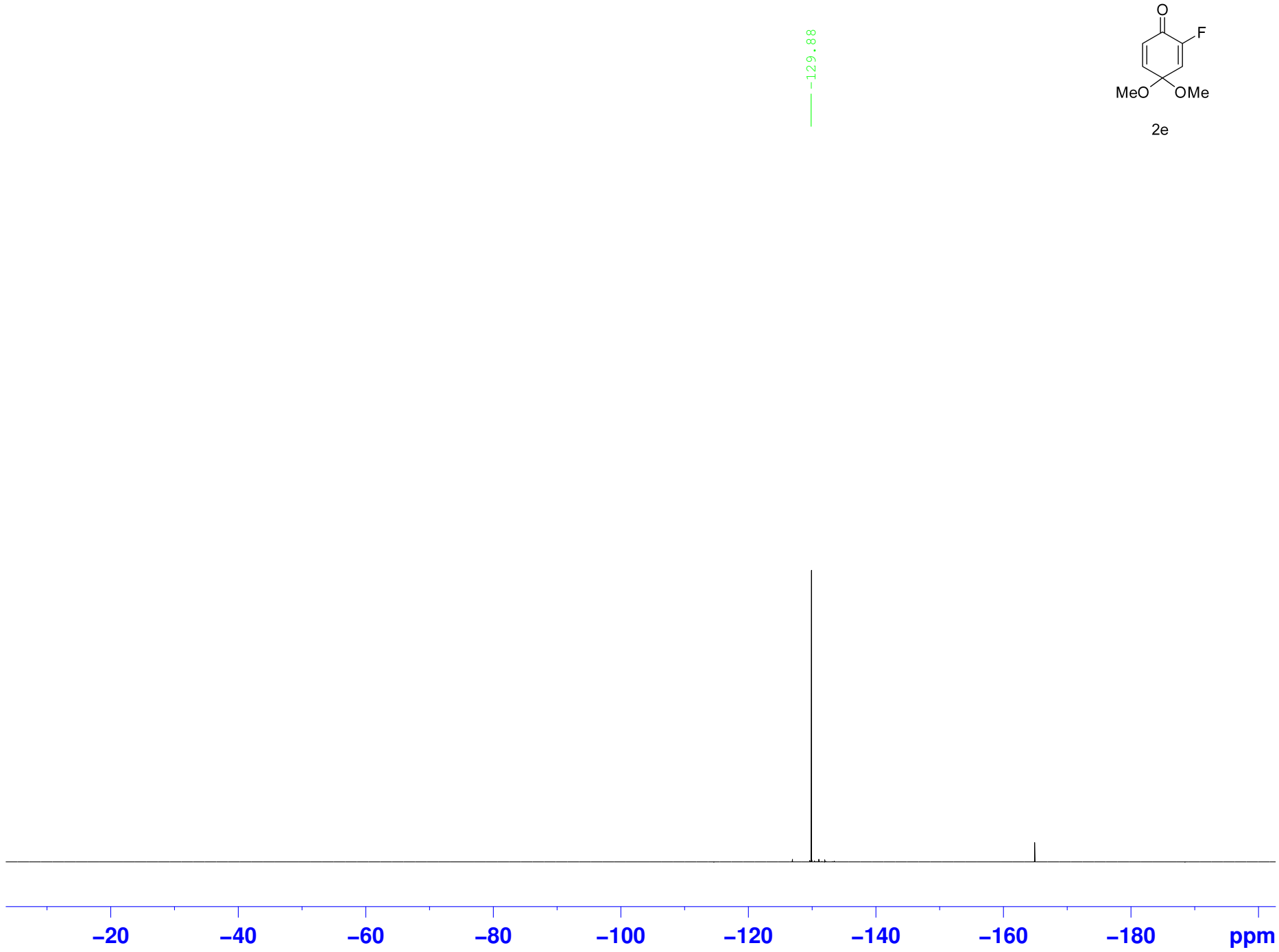
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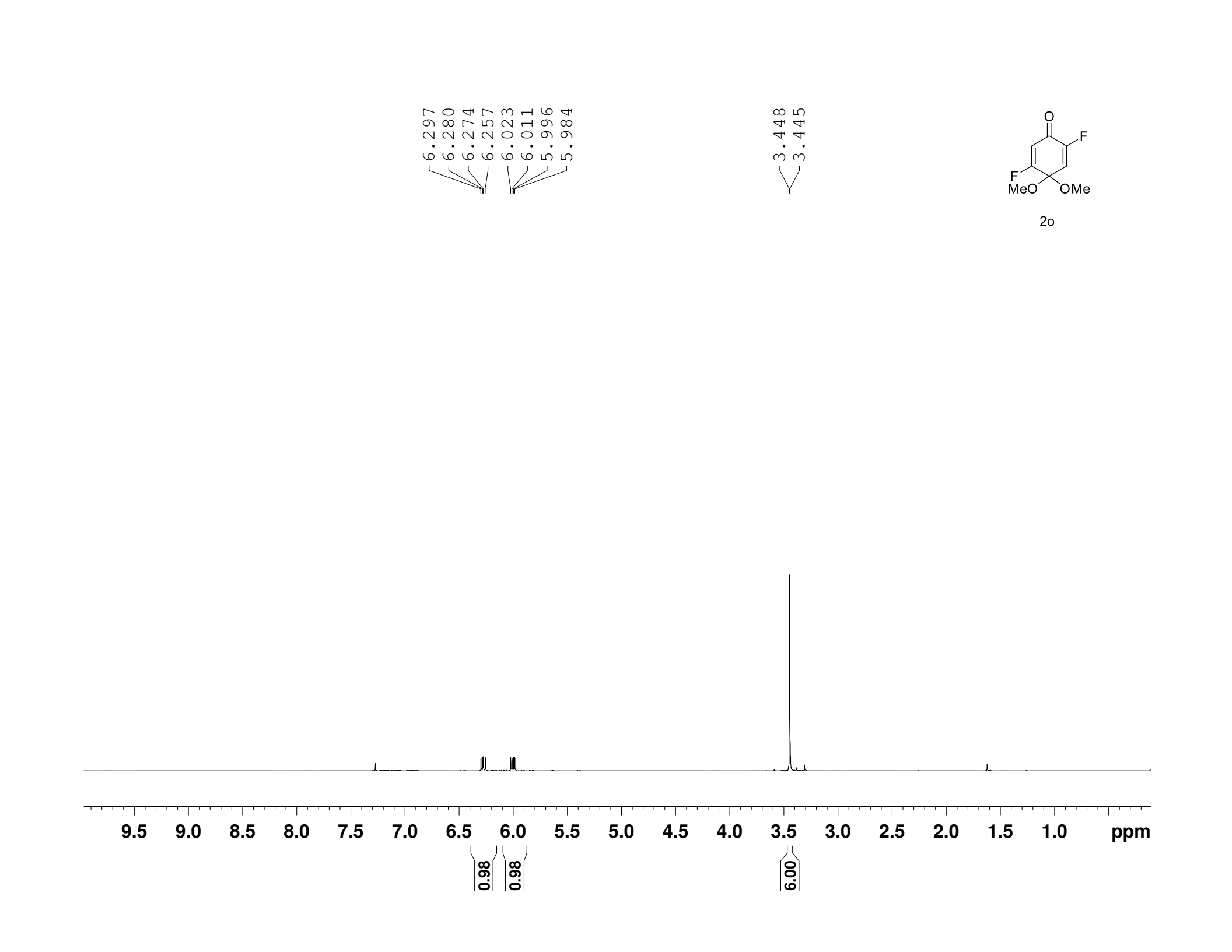
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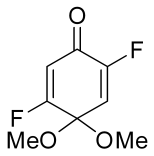

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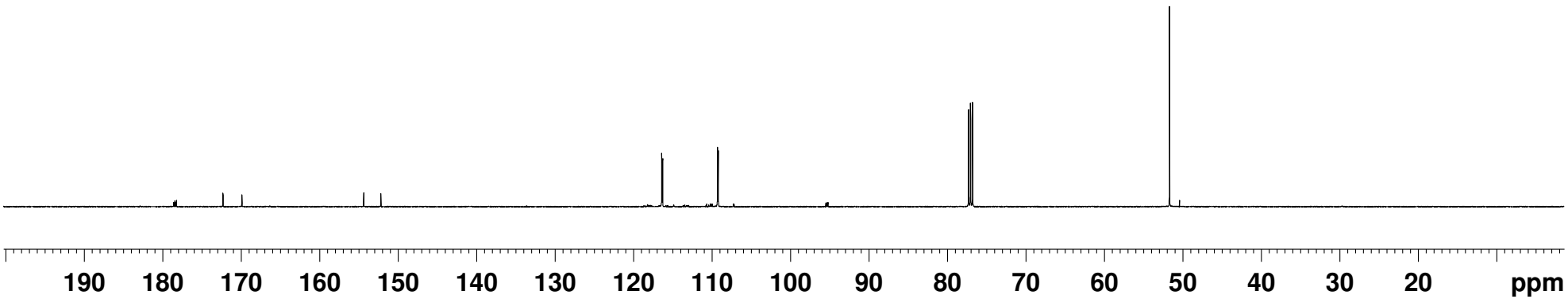

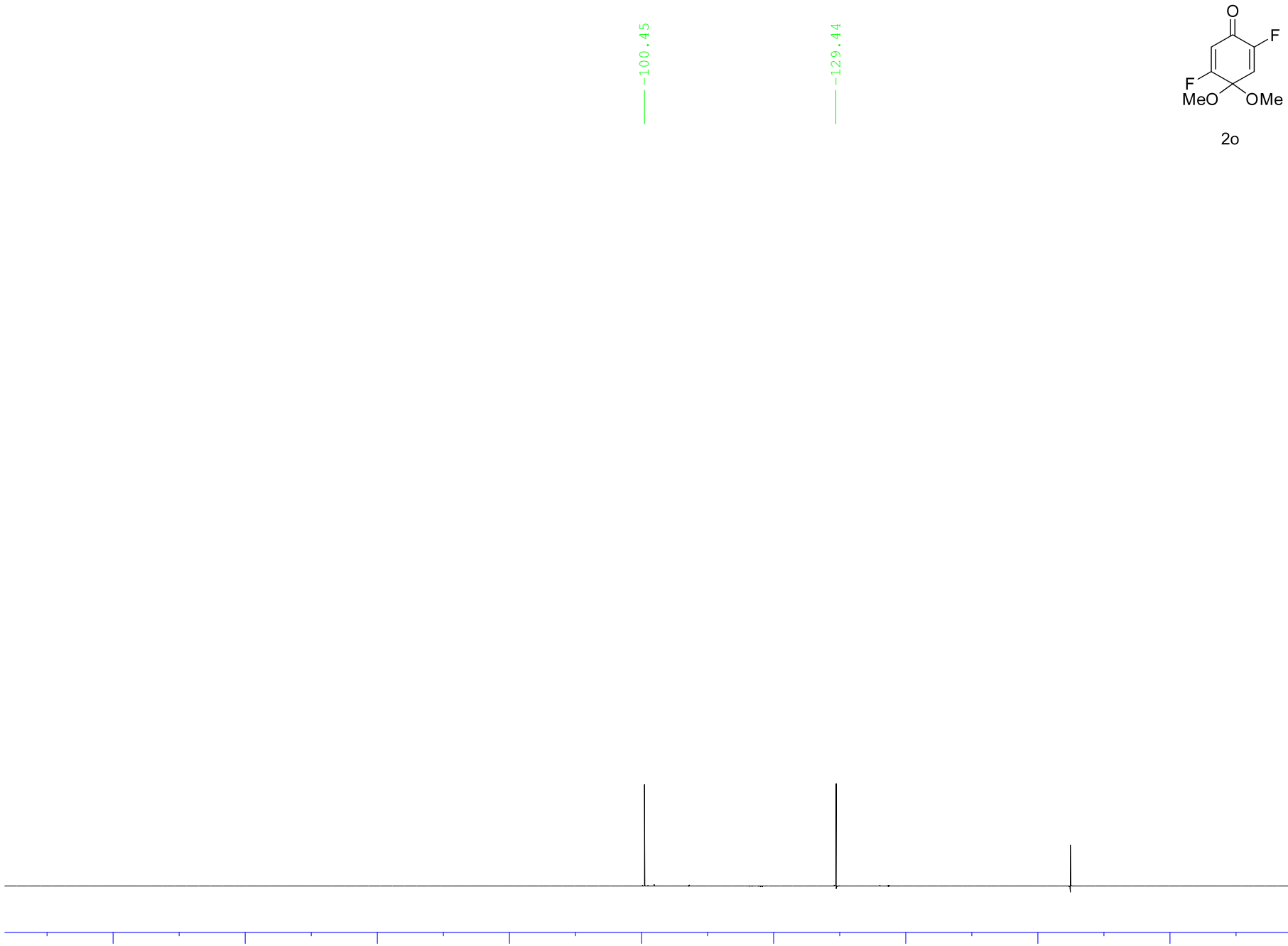

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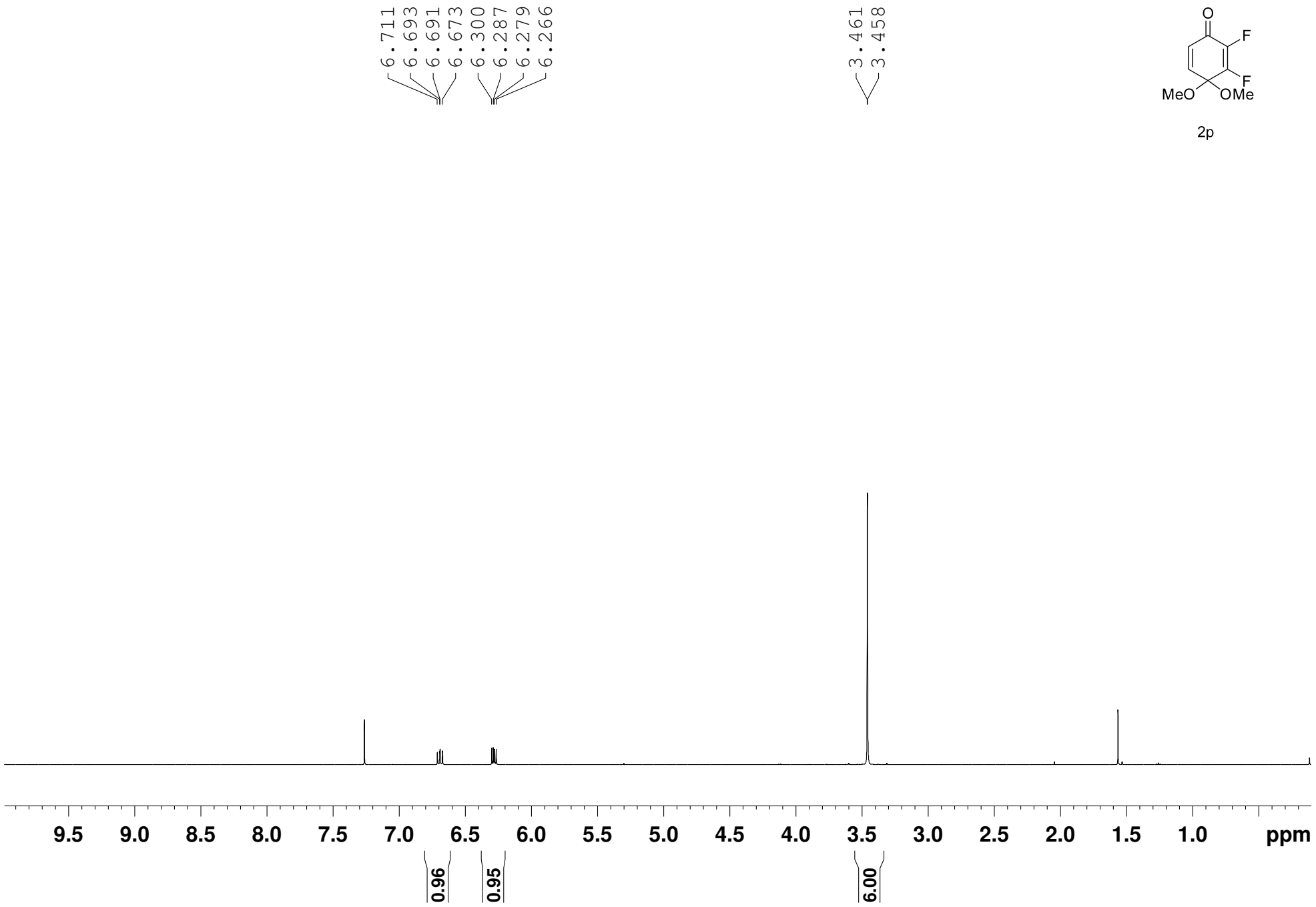
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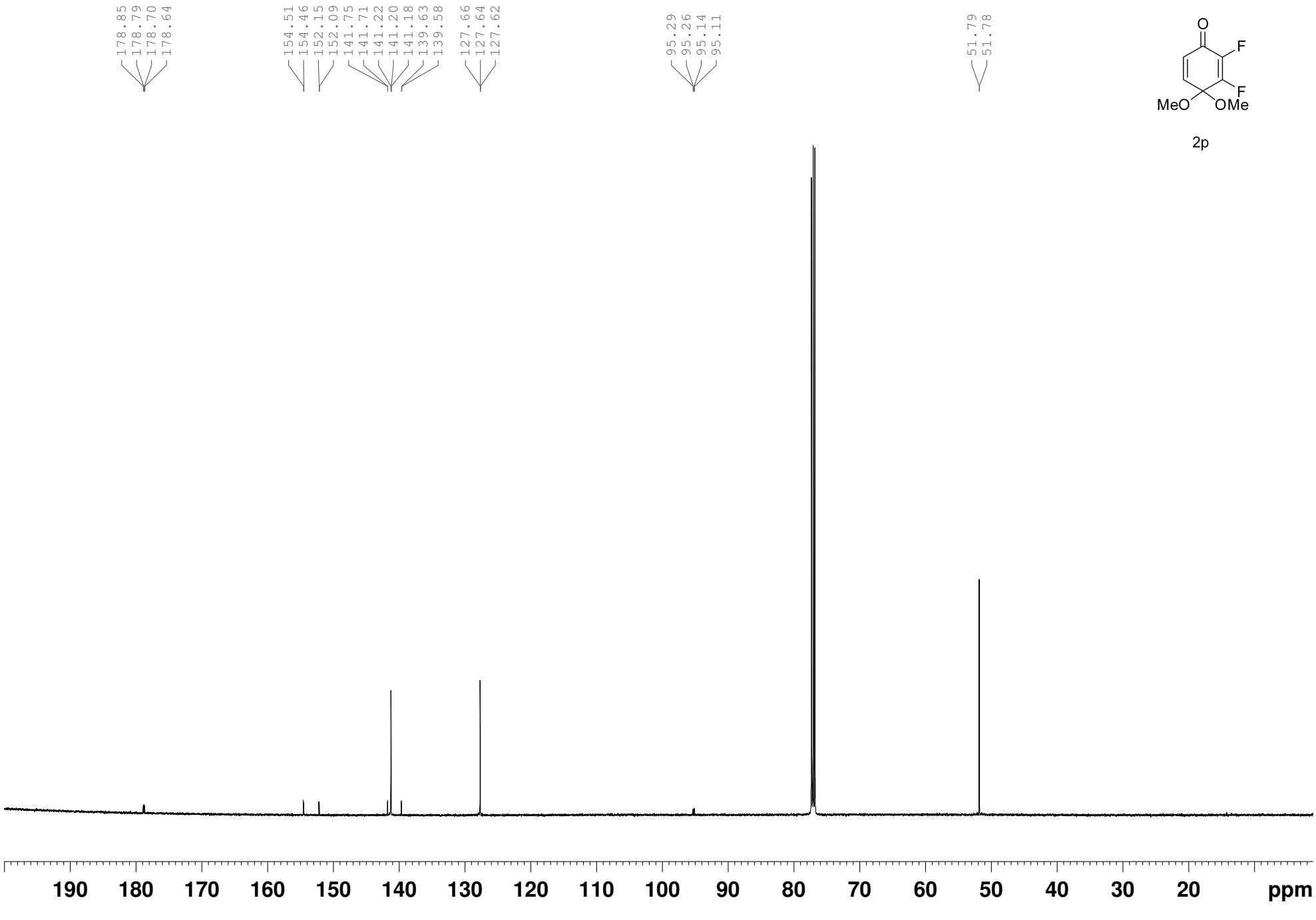
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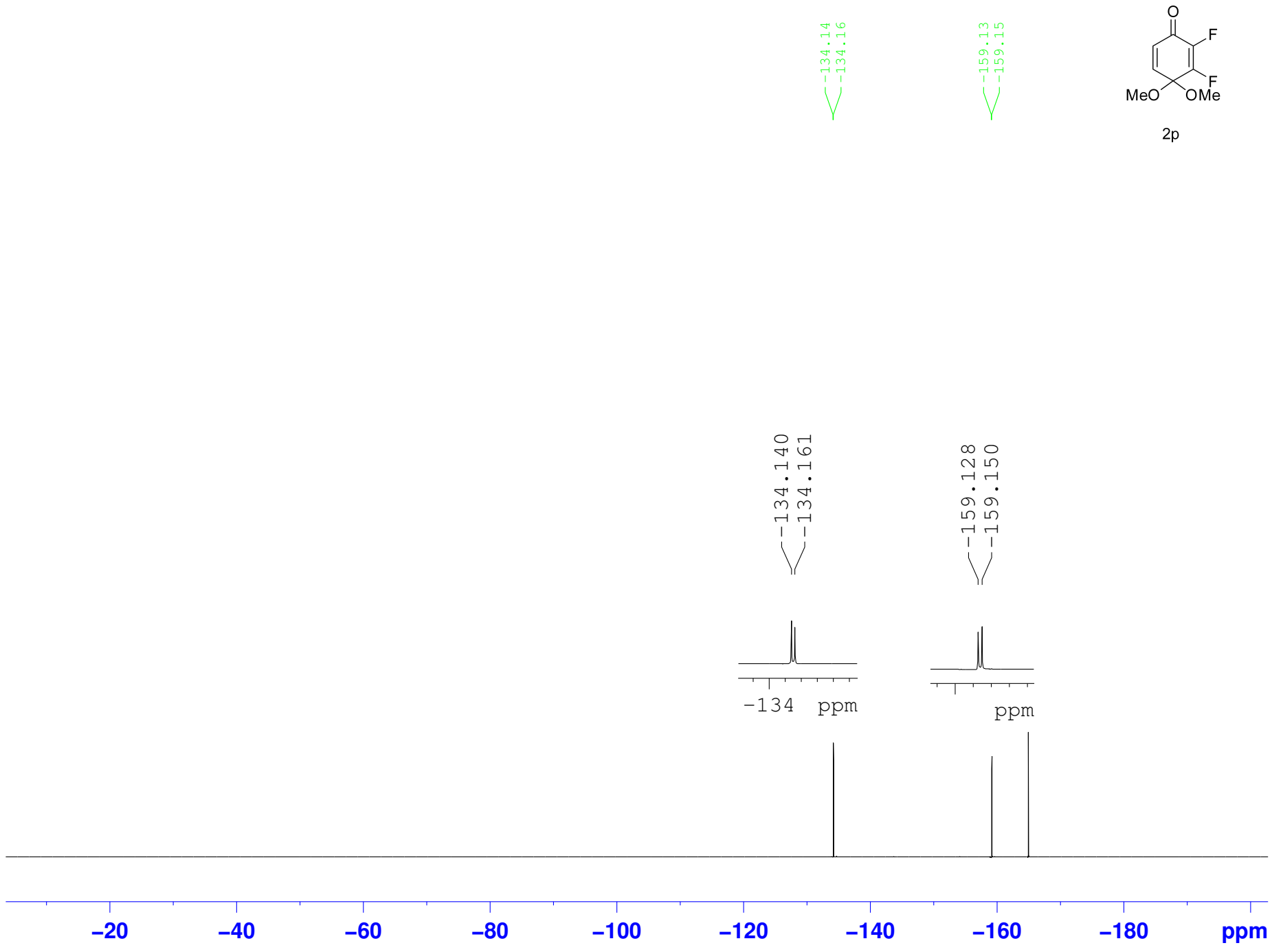
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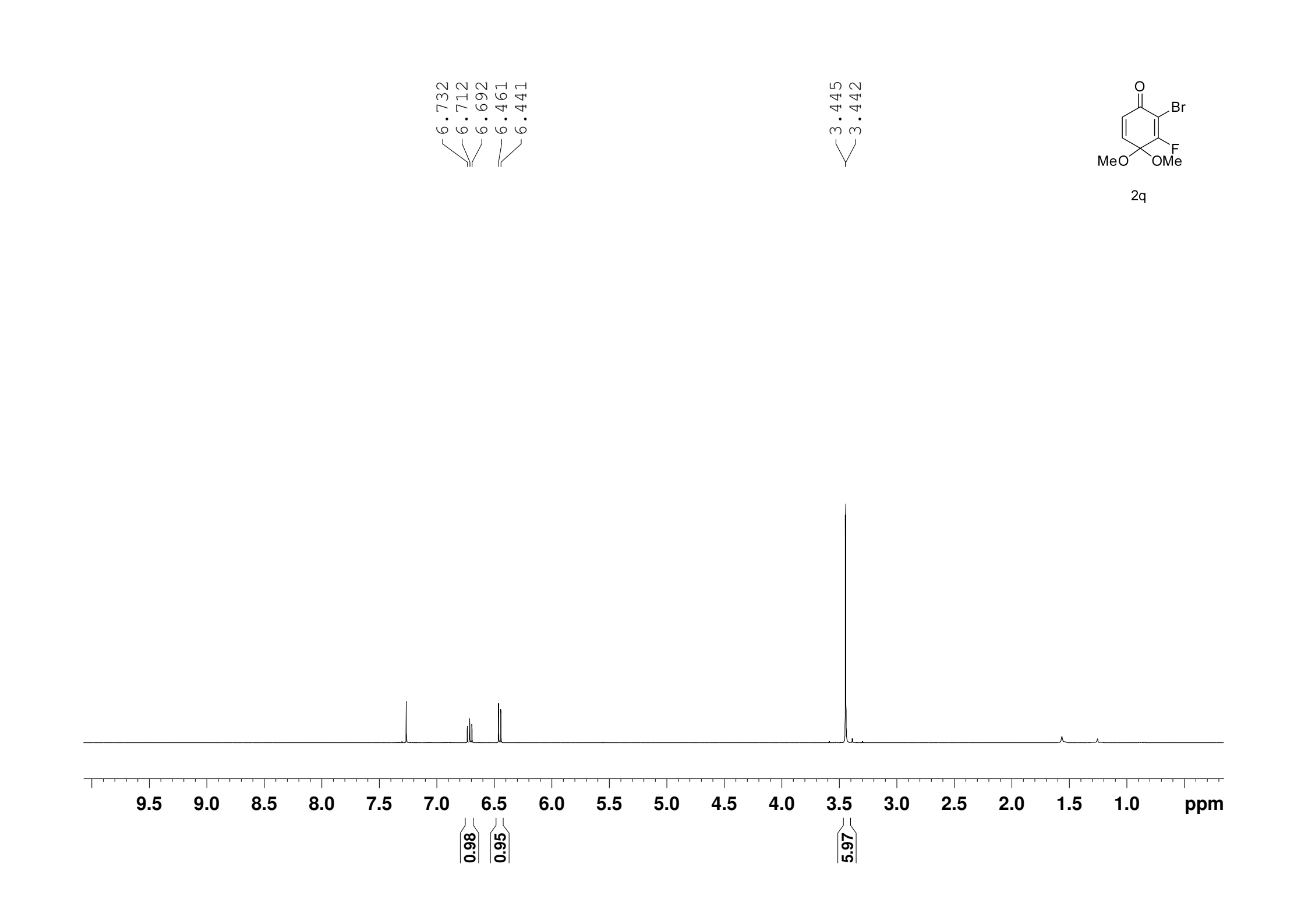
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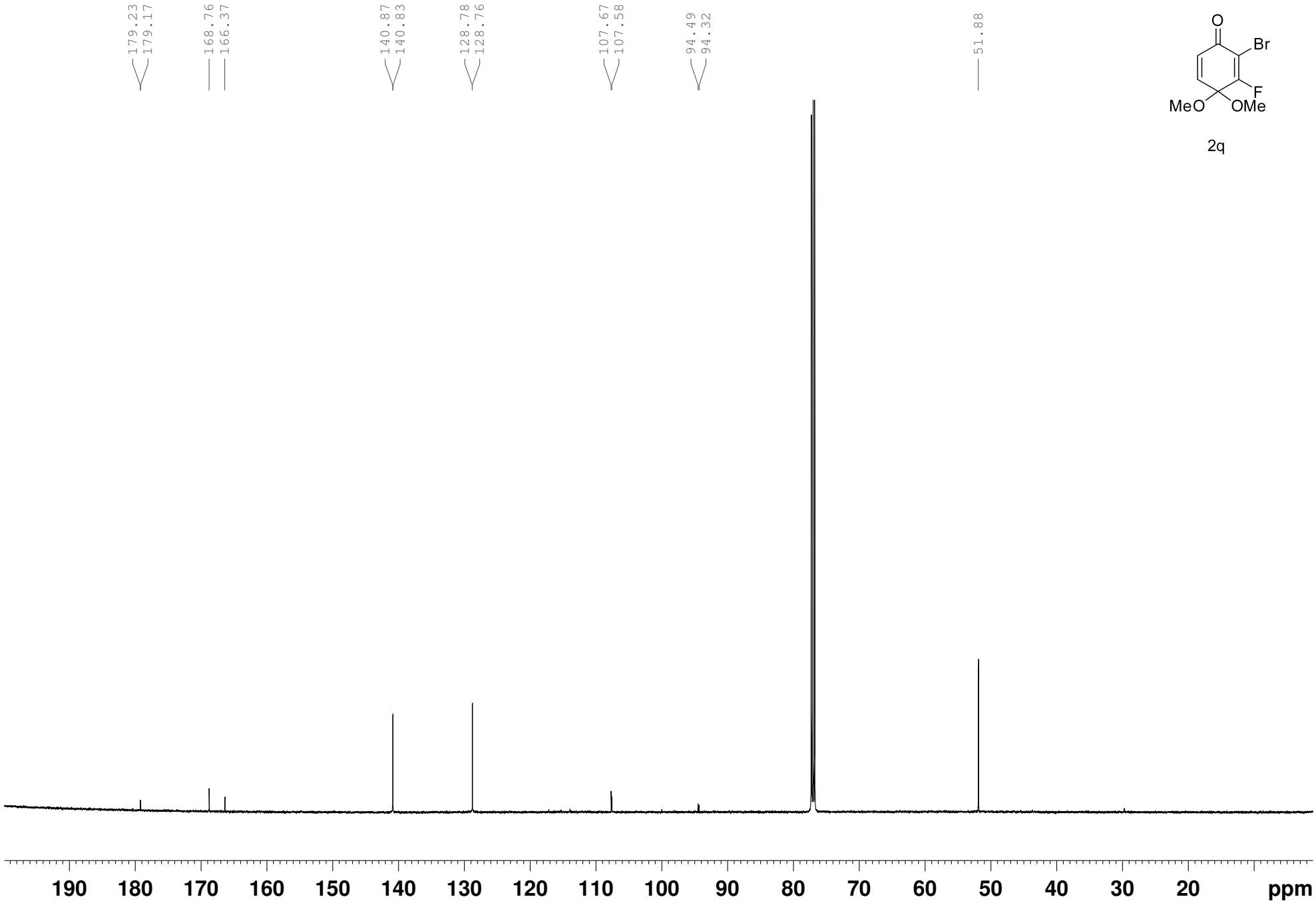
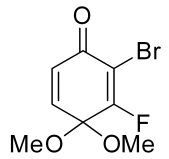
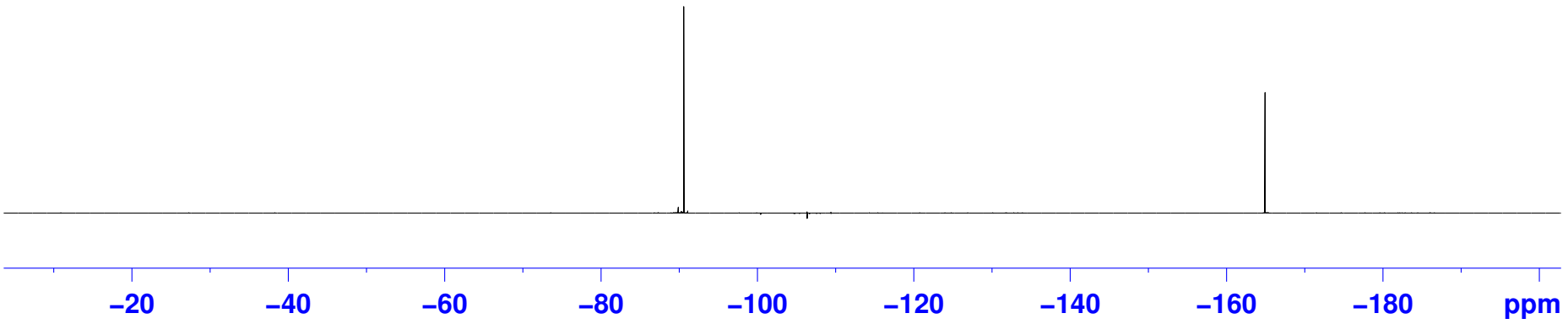
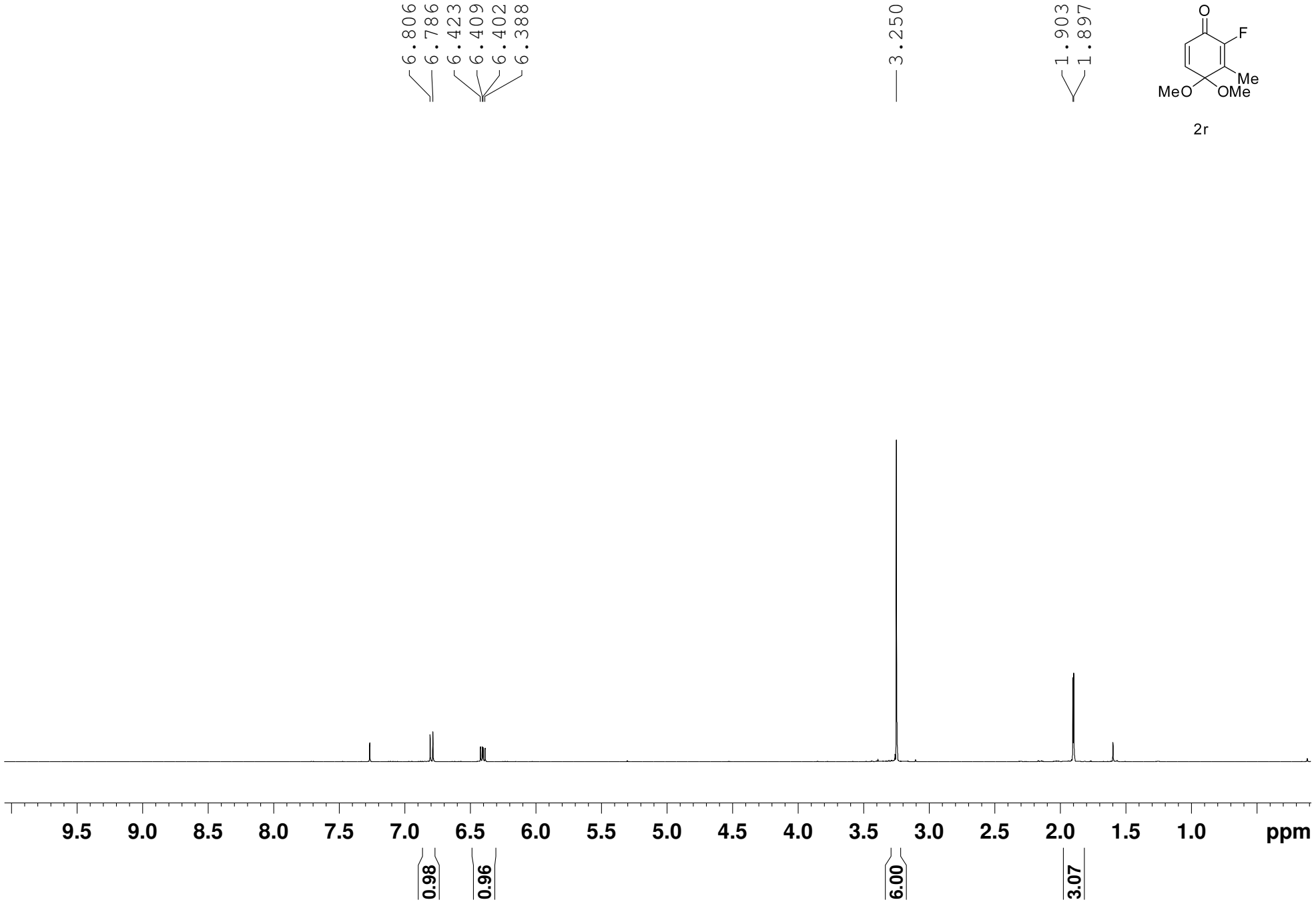
5.97

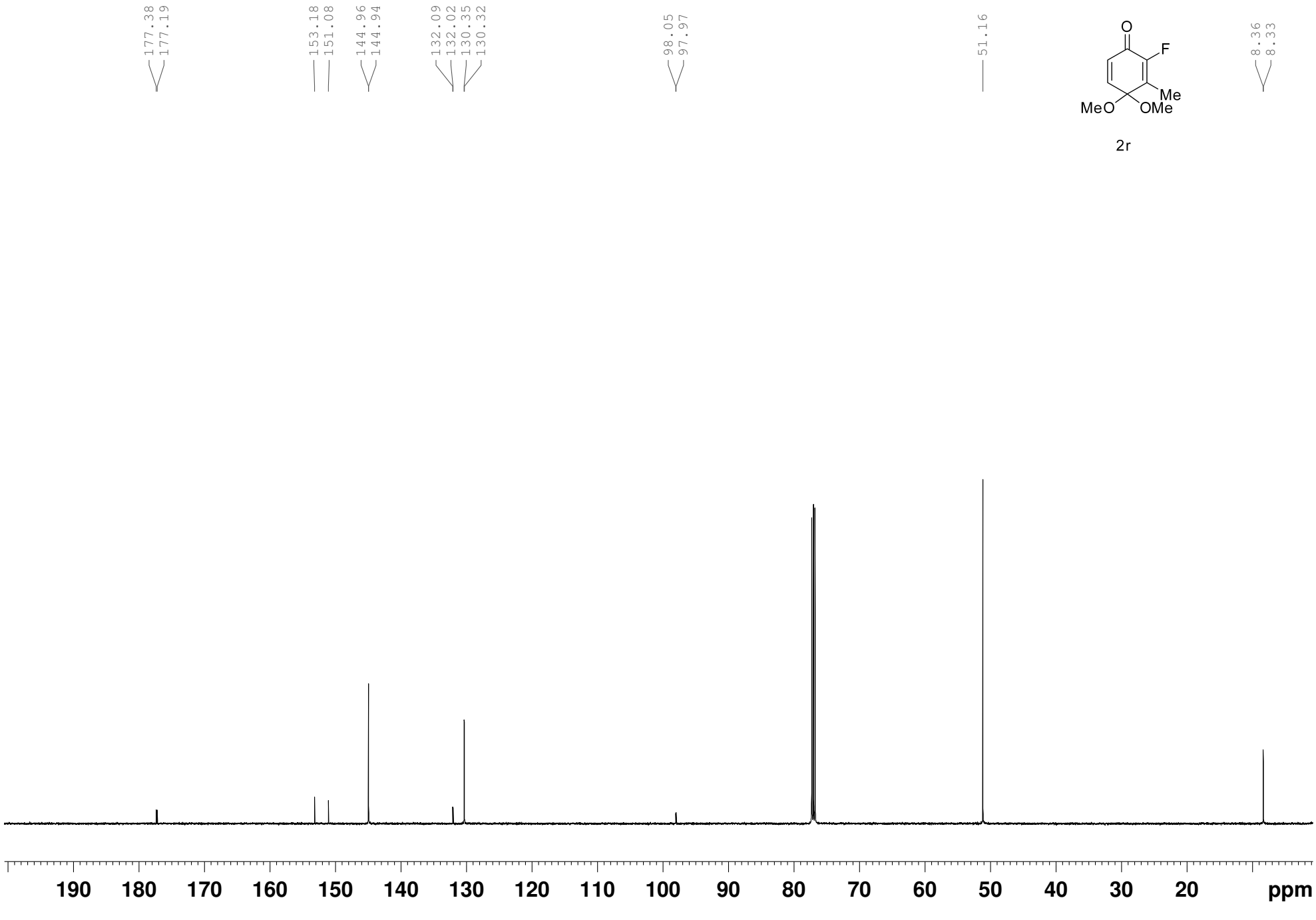

179.23
179.17
168.76
166.37
140.87
140.83
128.78
128.76
107.67
107.58
94.49
94.32
51.88
O
Br
F
MeO
OMe
2q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



2q




6.806
6.786
6.423
6.409
6.402
6.388
3.250
1.903
1.897
O
F
Me
MeO
OMe
2r
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.98
0.96
6.00
3.07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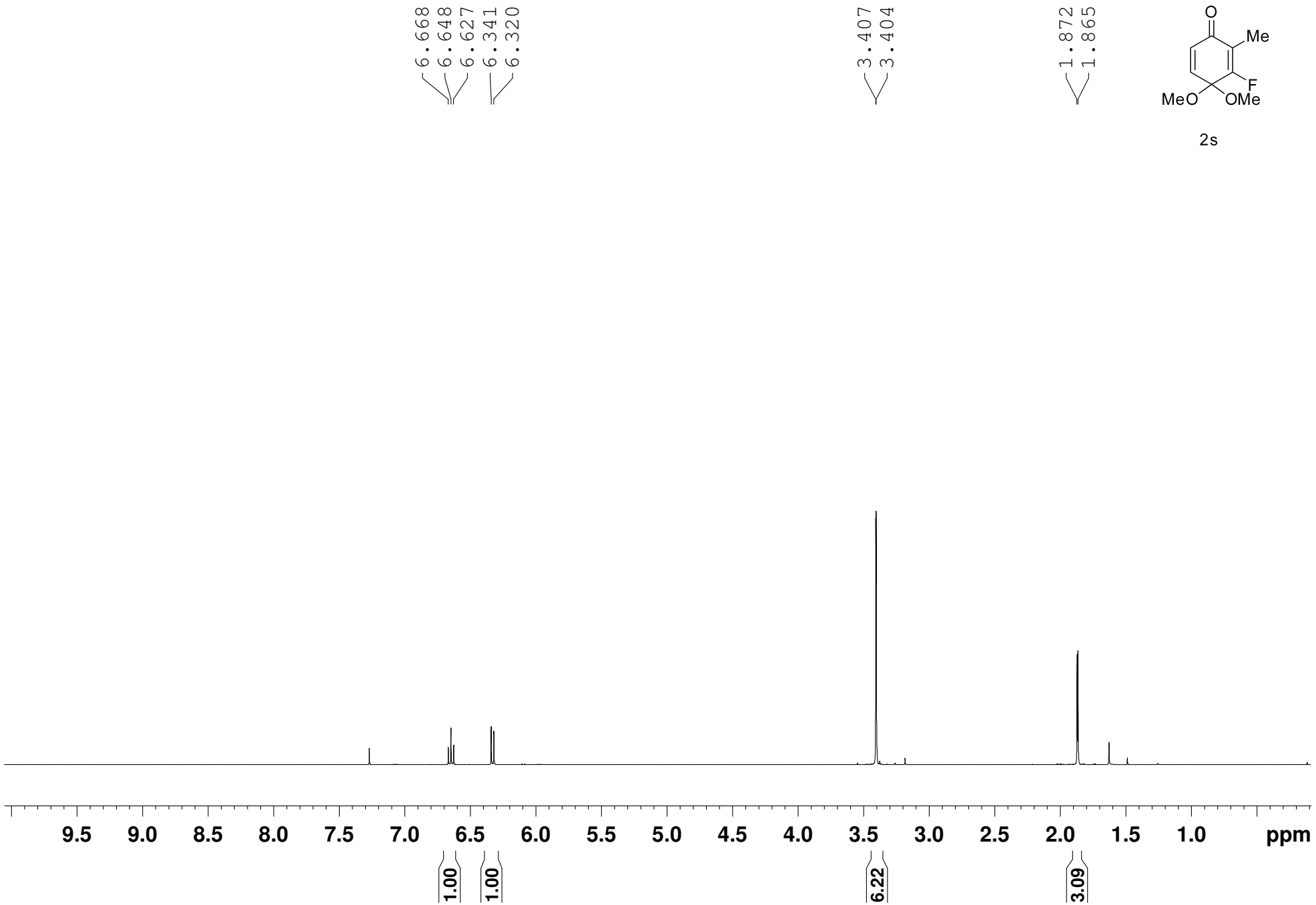
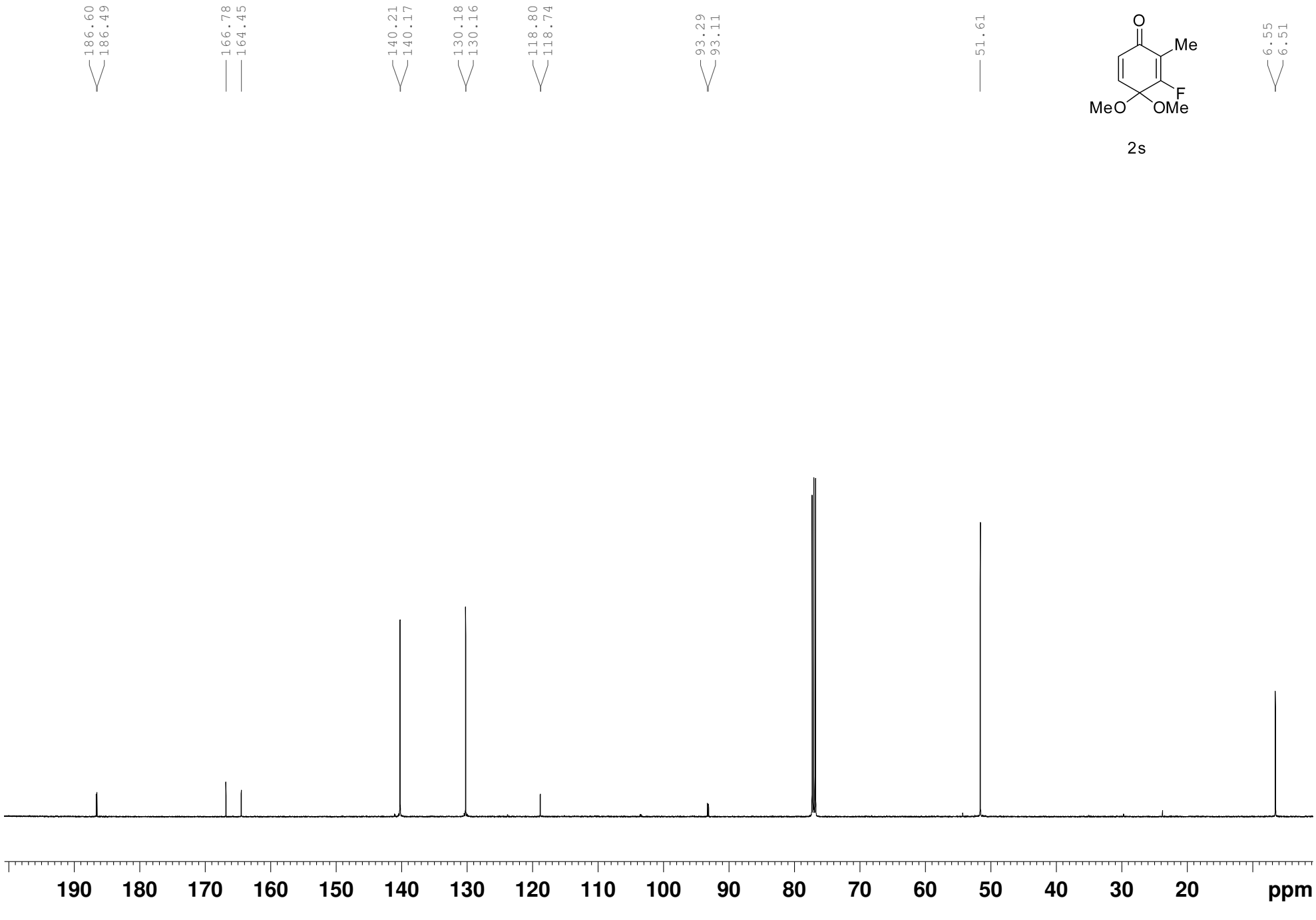
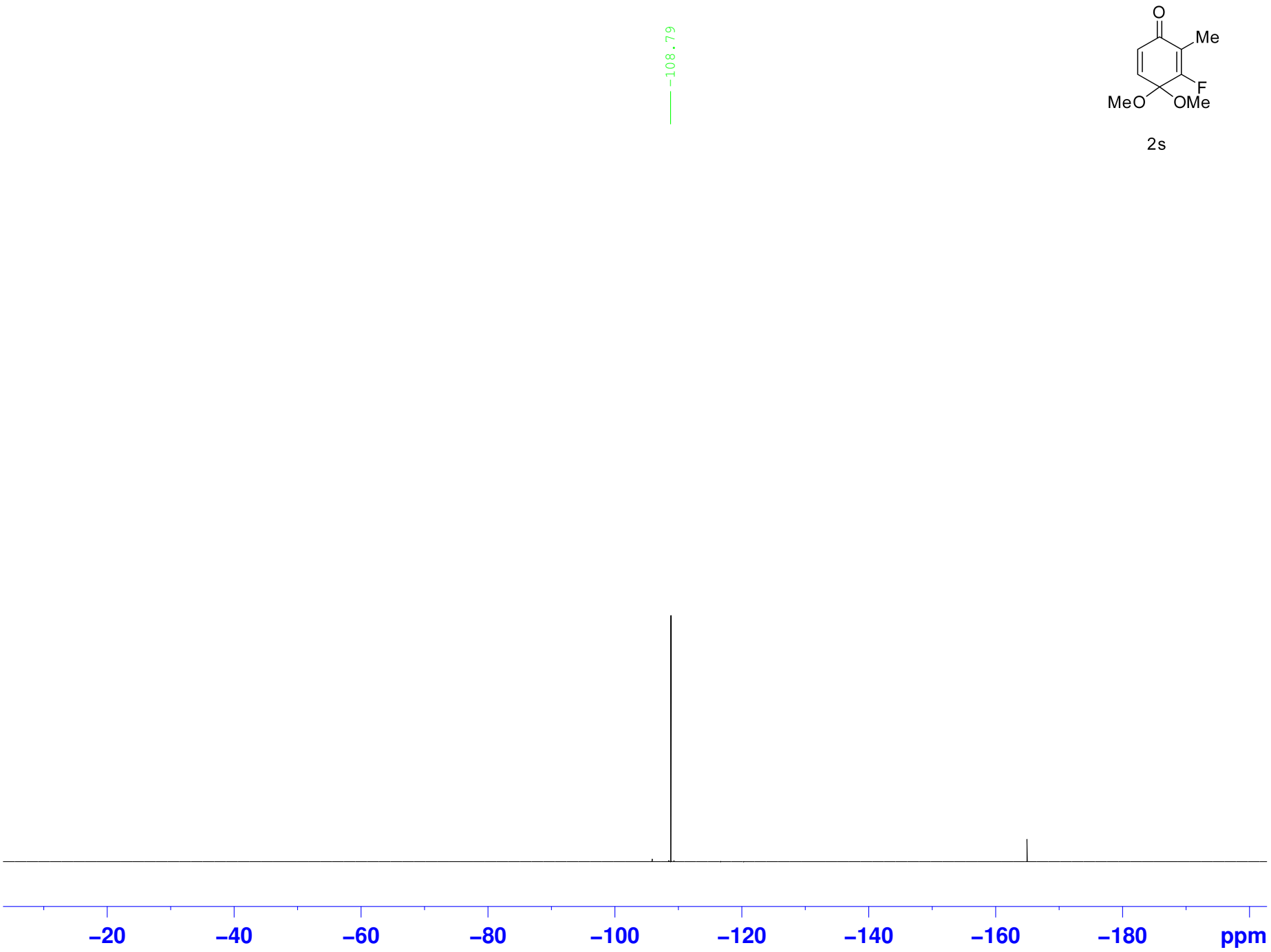
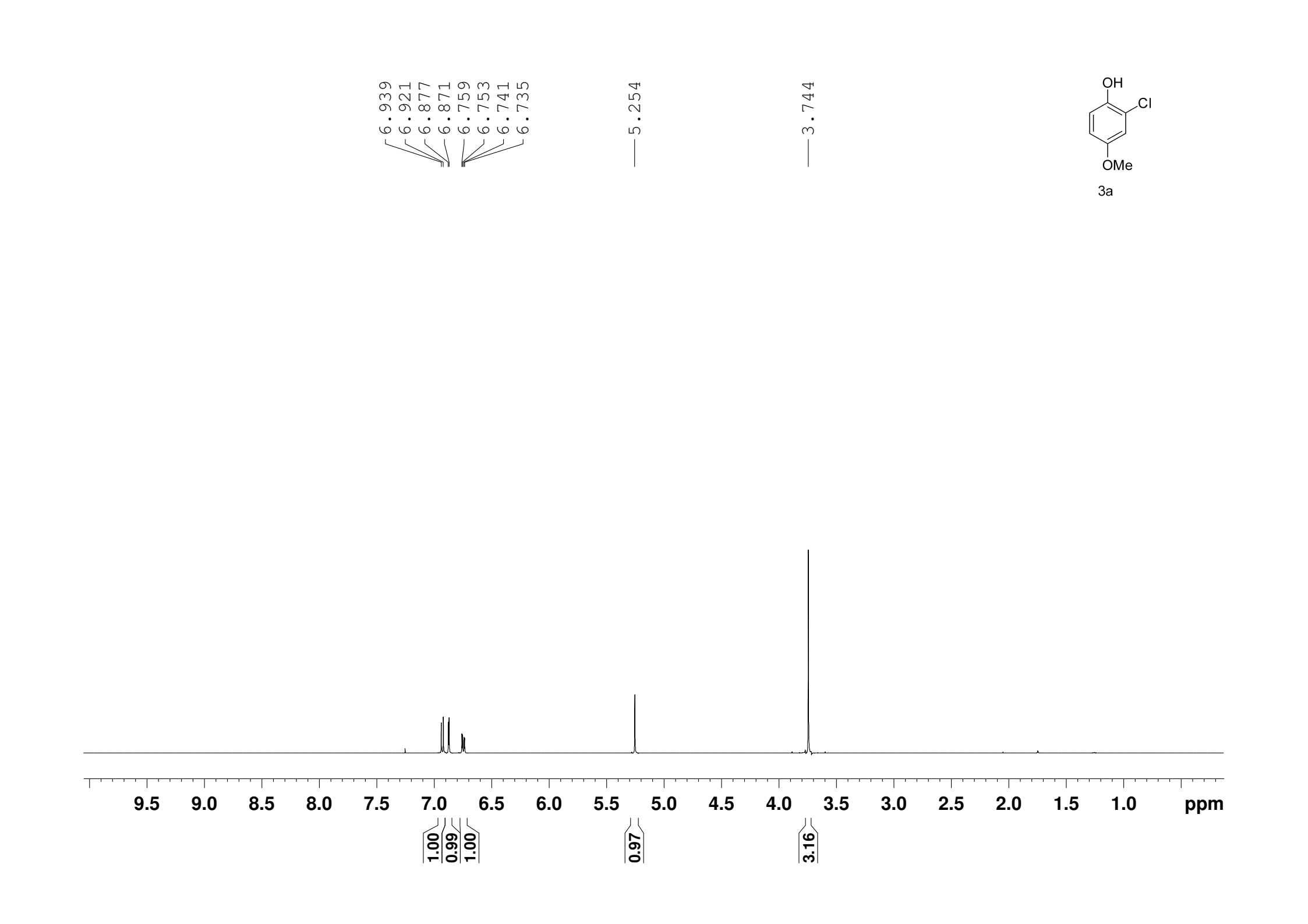
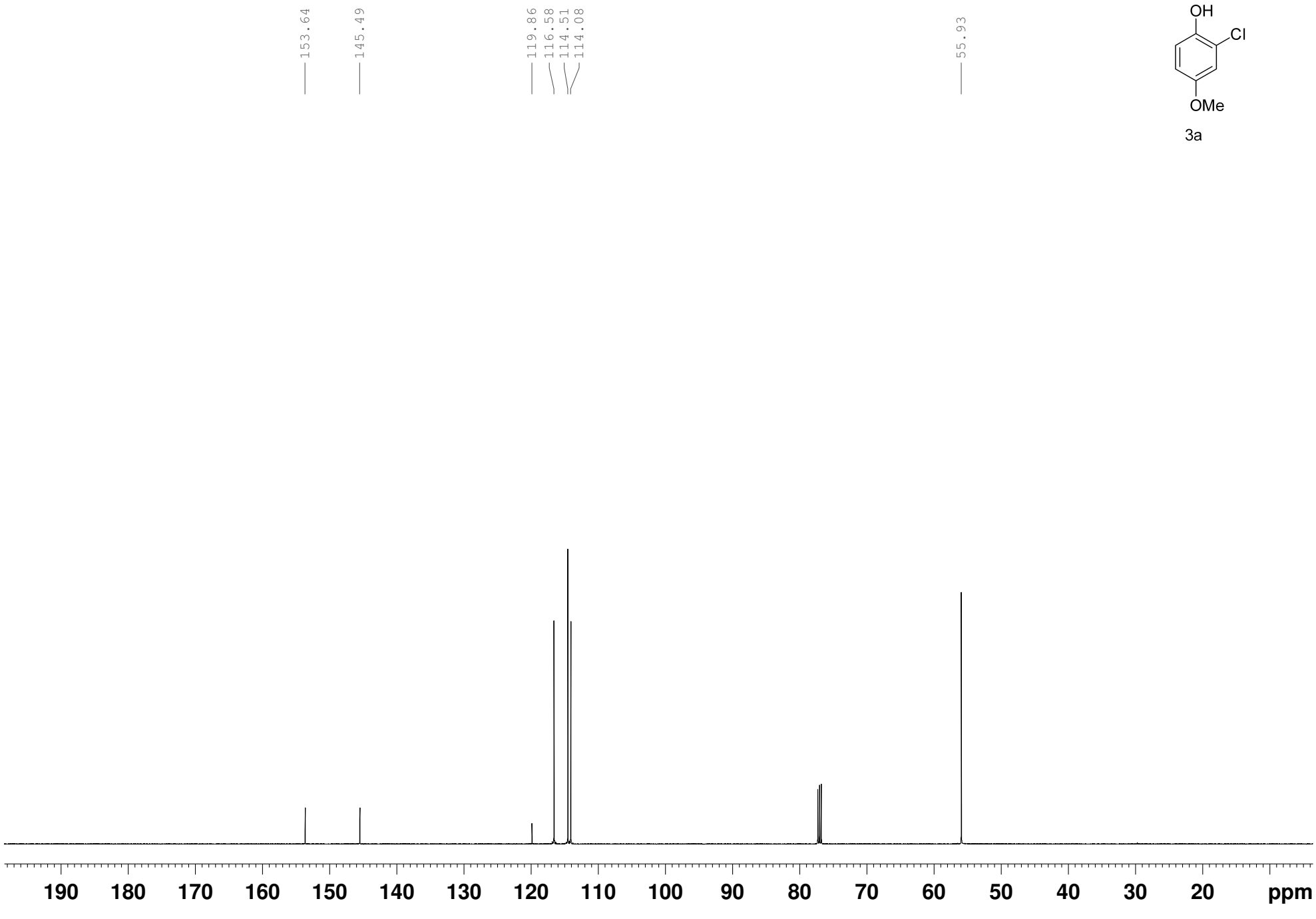
177.19
153.18
151.08
144.96
144.94
132.09
132.02
130.35
130.32
98.05
97.97
51.16
8.36
8.33
O
F
Me
MeO
OMe
2r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

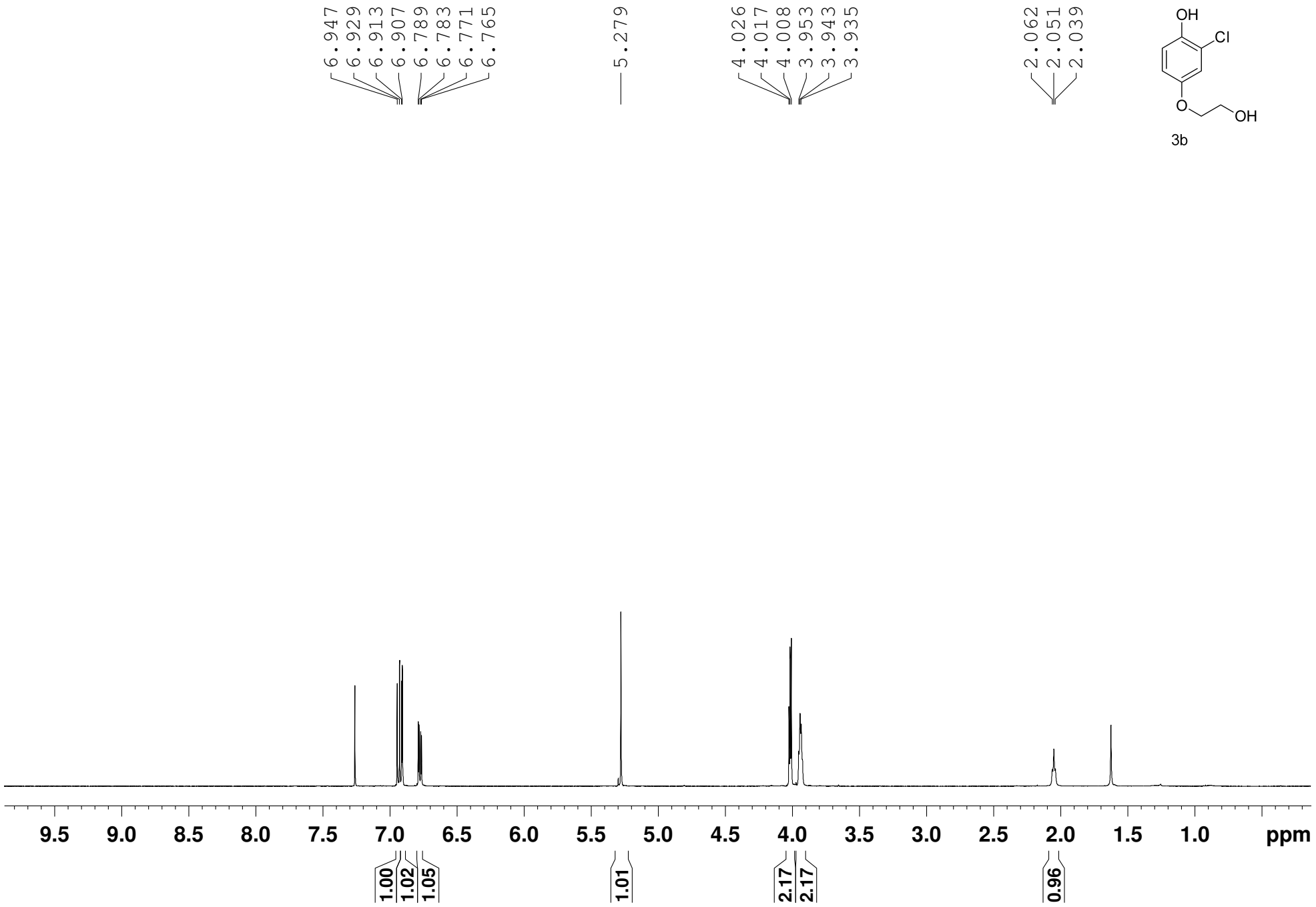

6.668
6.648
6.627
6.341
6.320
3.407
3.404
1.872
1.865
O
Me
F
MeO
OMe
2s
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.00
6.22
3.09

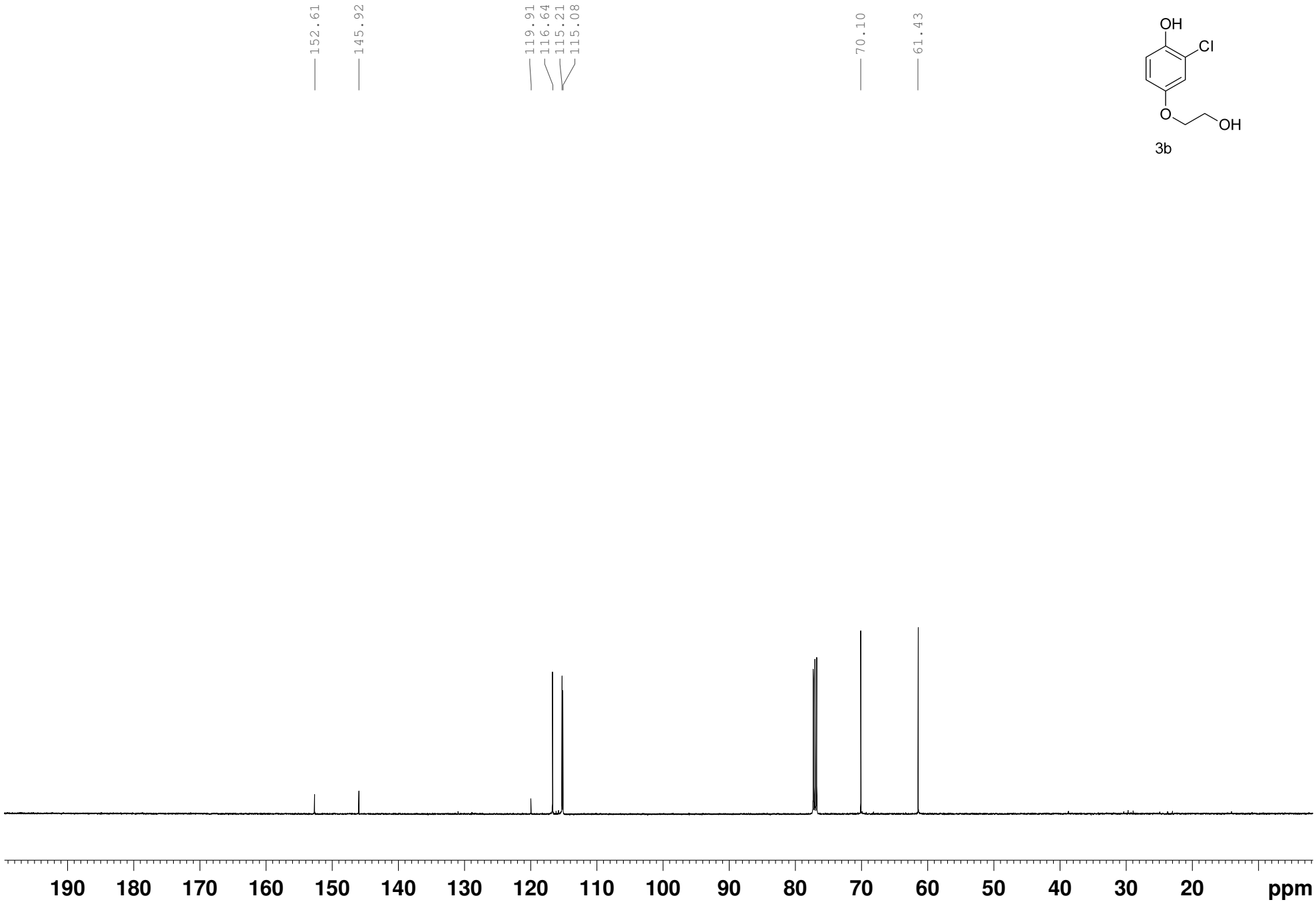

186.60
186.49
166.78
164.45
140.21
140.17
130.18
130.16
118.80
118.74
93.29
93.11
51.61
6.55
6.51
O
Me
F
MeO
OMe
2s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

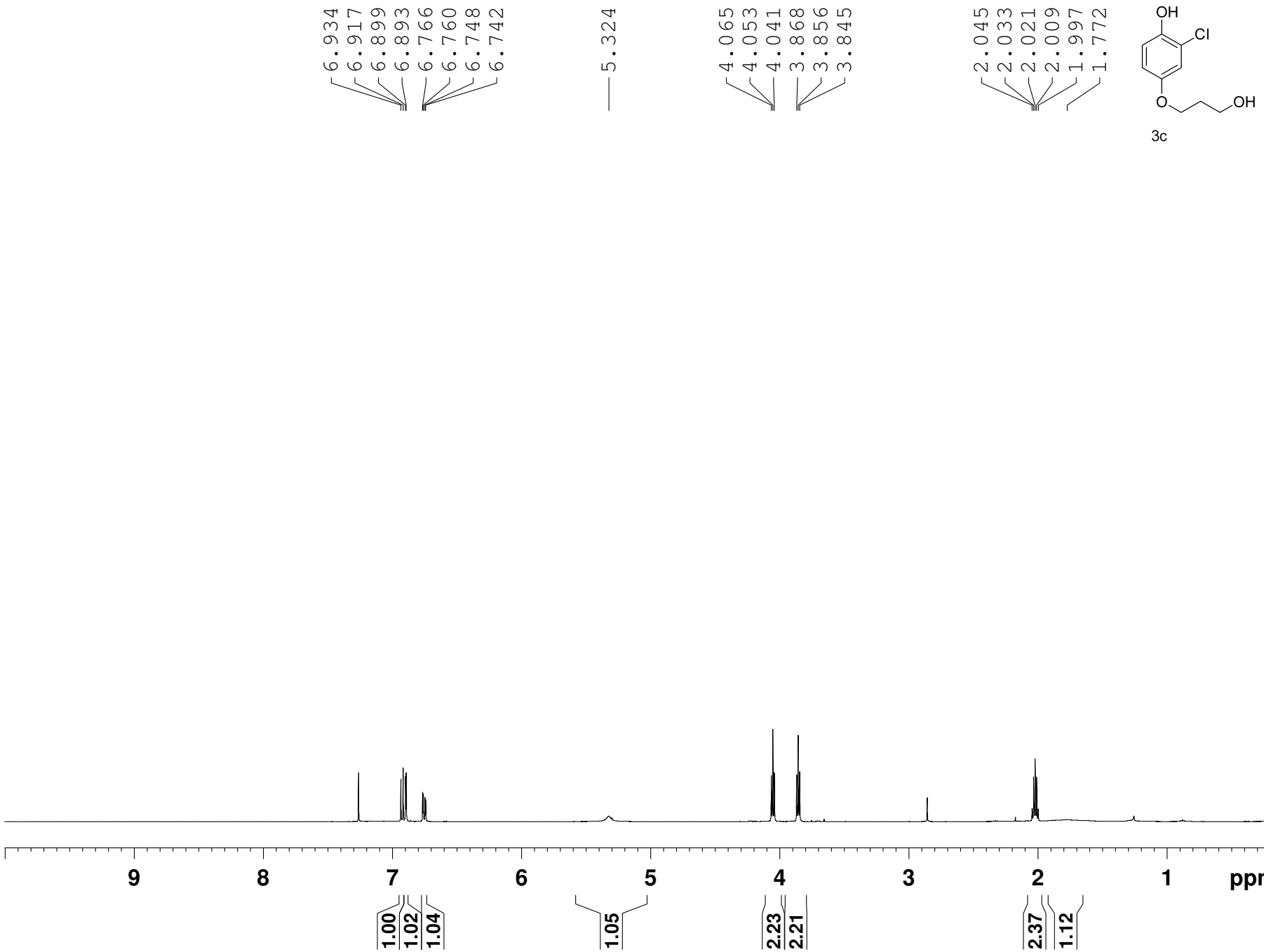

-108.79
O
Me
F
MeO
OMe
2s
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm


6.939
6.921
6.877
6.871
6.759
6.753
6.741
6.735
5.254
3.744
OH
Cl
OMe
3a
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
0.99
1.00
0.97
3.16


153.64
145.49
119.86
116.58
114.51
114.08
55.93
OH
Cl
OMe
3a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

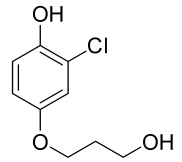

6.947
6.929
6.913
6.907
6.789
6.783
6.771
6.765
5.279
4.026
4.017
4.008
3.953
3.943
3.935
2.062
2.051
2.039
OH
Cl
O
OH
3b
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.02
1.05
1.01
2.17
2.17
0.96


152.61
145.92
119.91
116.64
115.21
115.08
70.10
61.43
OH
Cl
O
OH
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

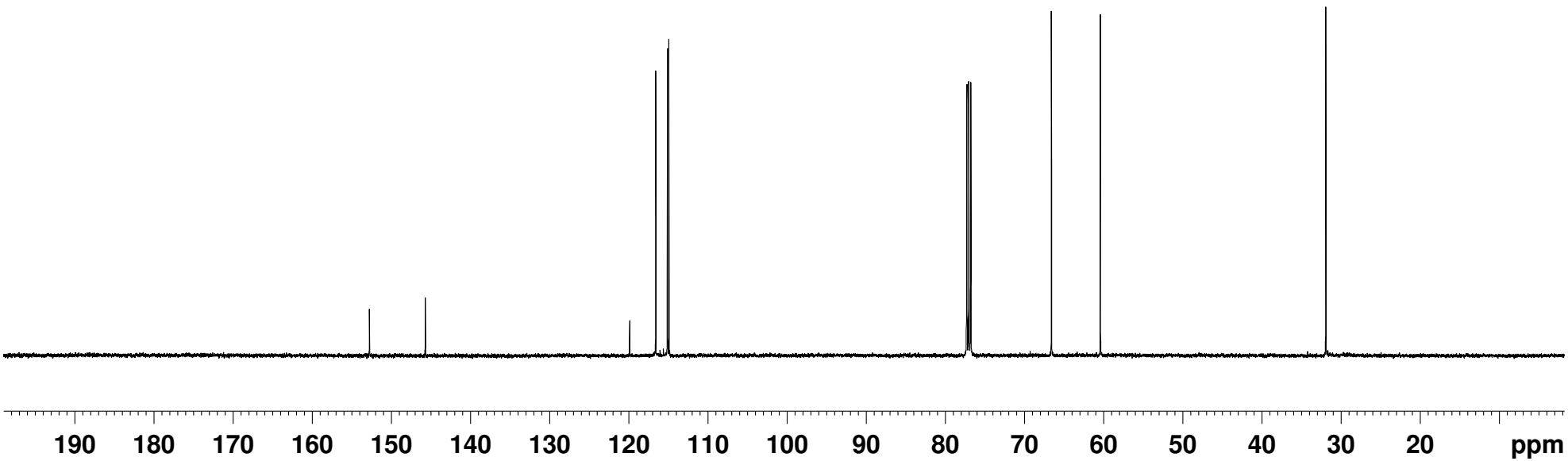

6.934
6.917
6.899
6.893
6.766
6.760
6.748
6.742
5.324
4.065
4.053
4.041
3.868
3.856
3.845
2.045
2.033
2.021
2.009
1.997
1.772
OH
Cl
O
OH
3c
9
8
7
6
5
4
3
2
1
ppm
1.00
1.02
1.04
1.05
2.23
2.21
2.37
1.12

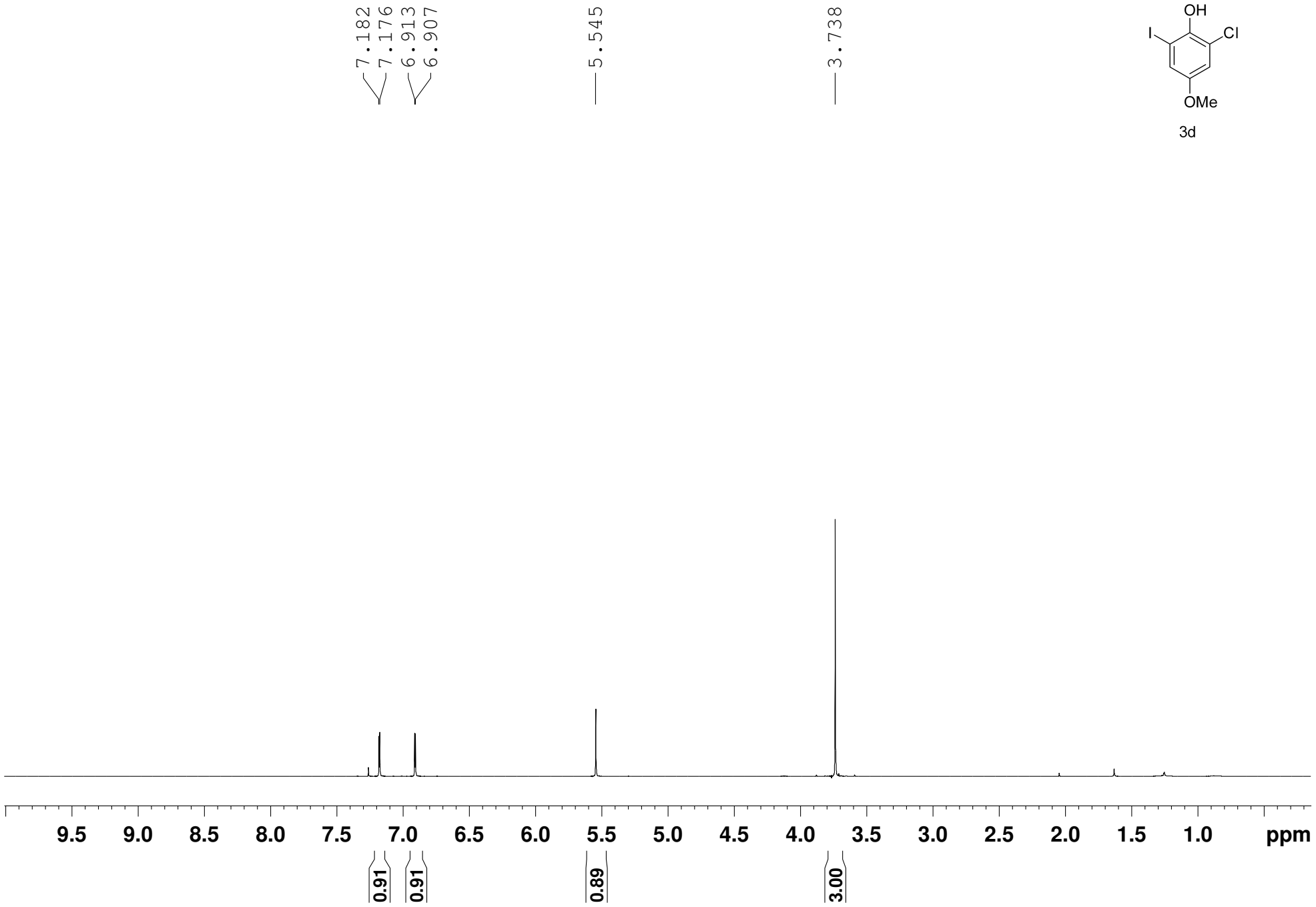
DEPT

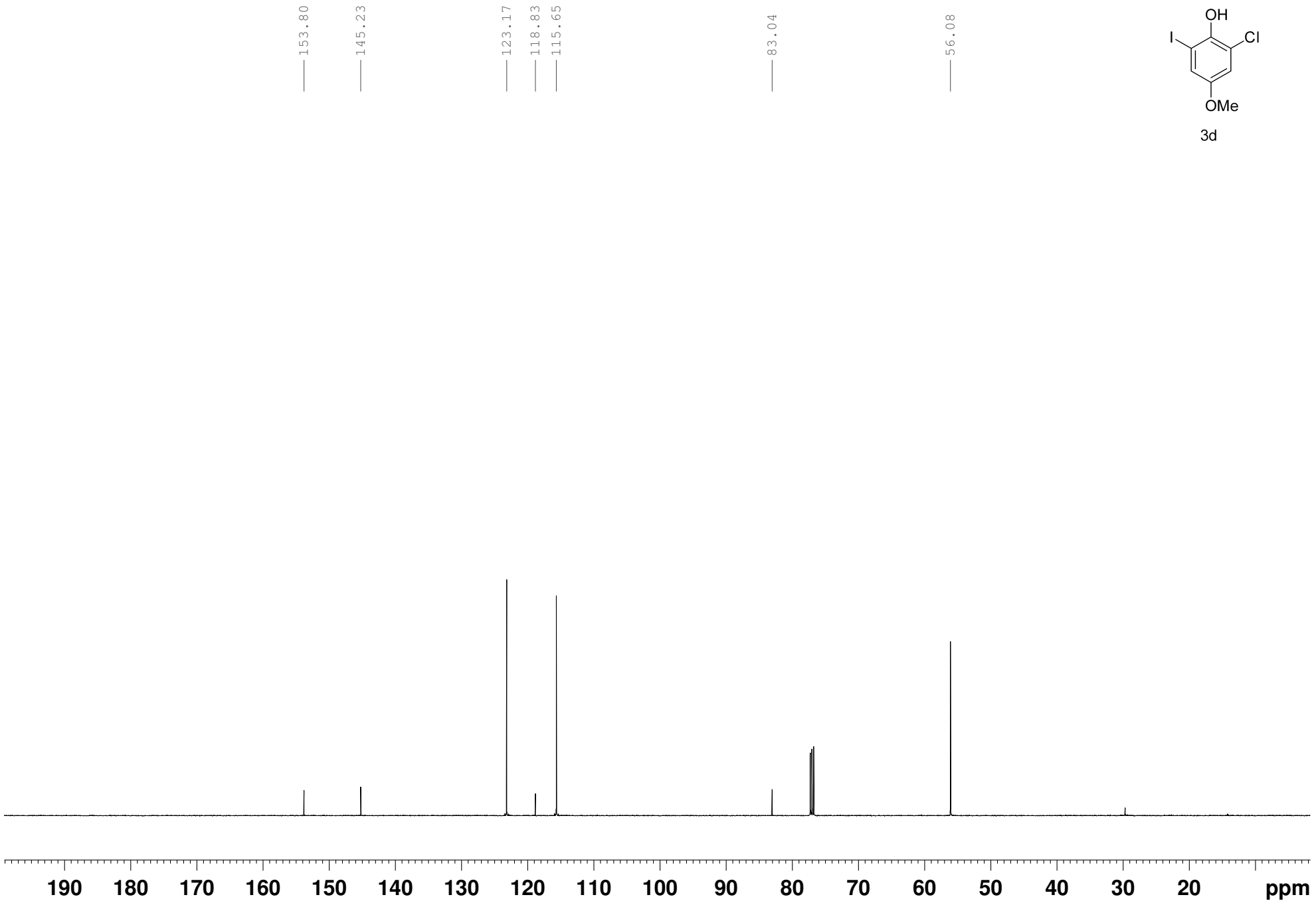
152.78
145.72
119.89
116.59
115.12
114.93
66.59
60.41
31.92

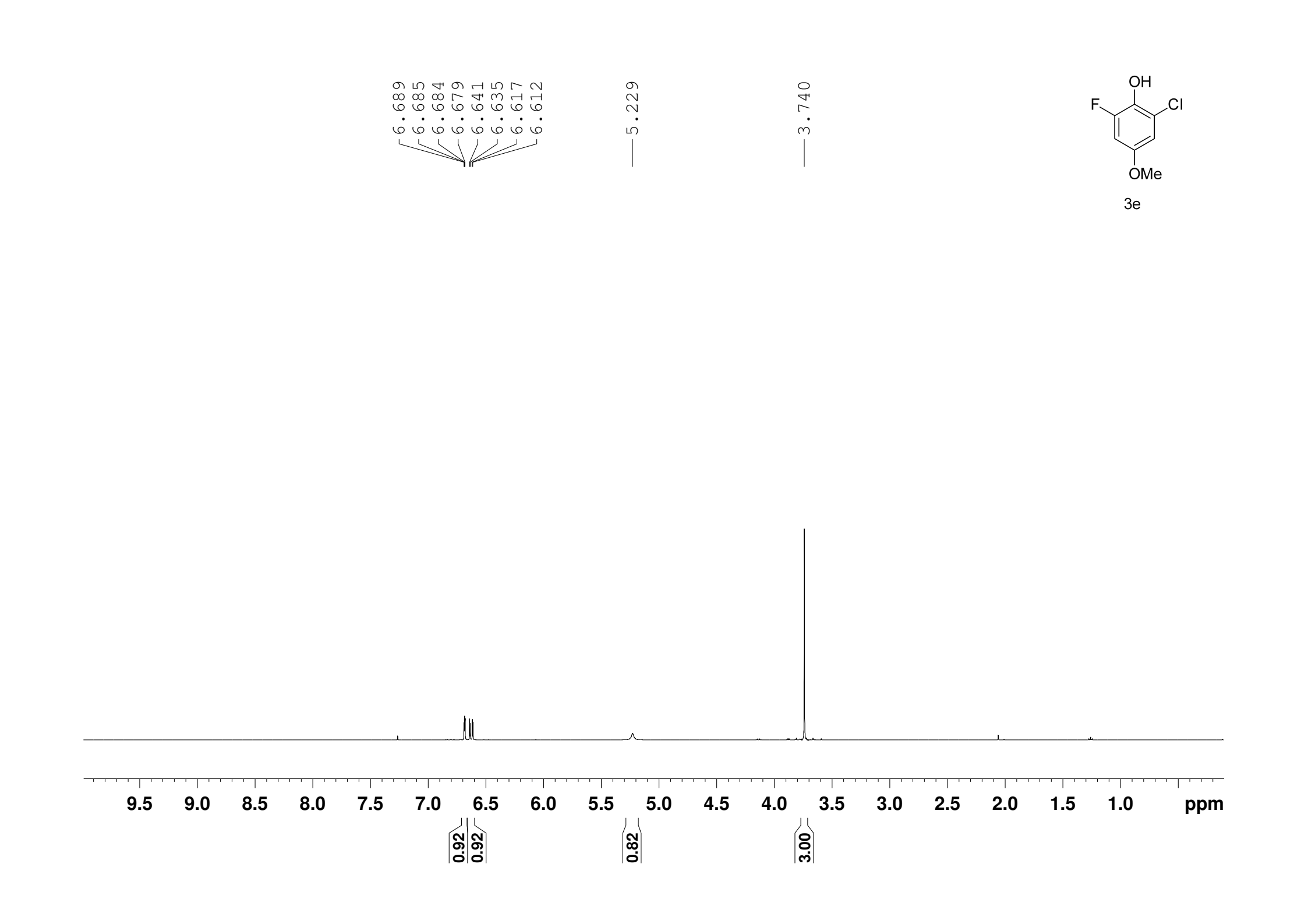


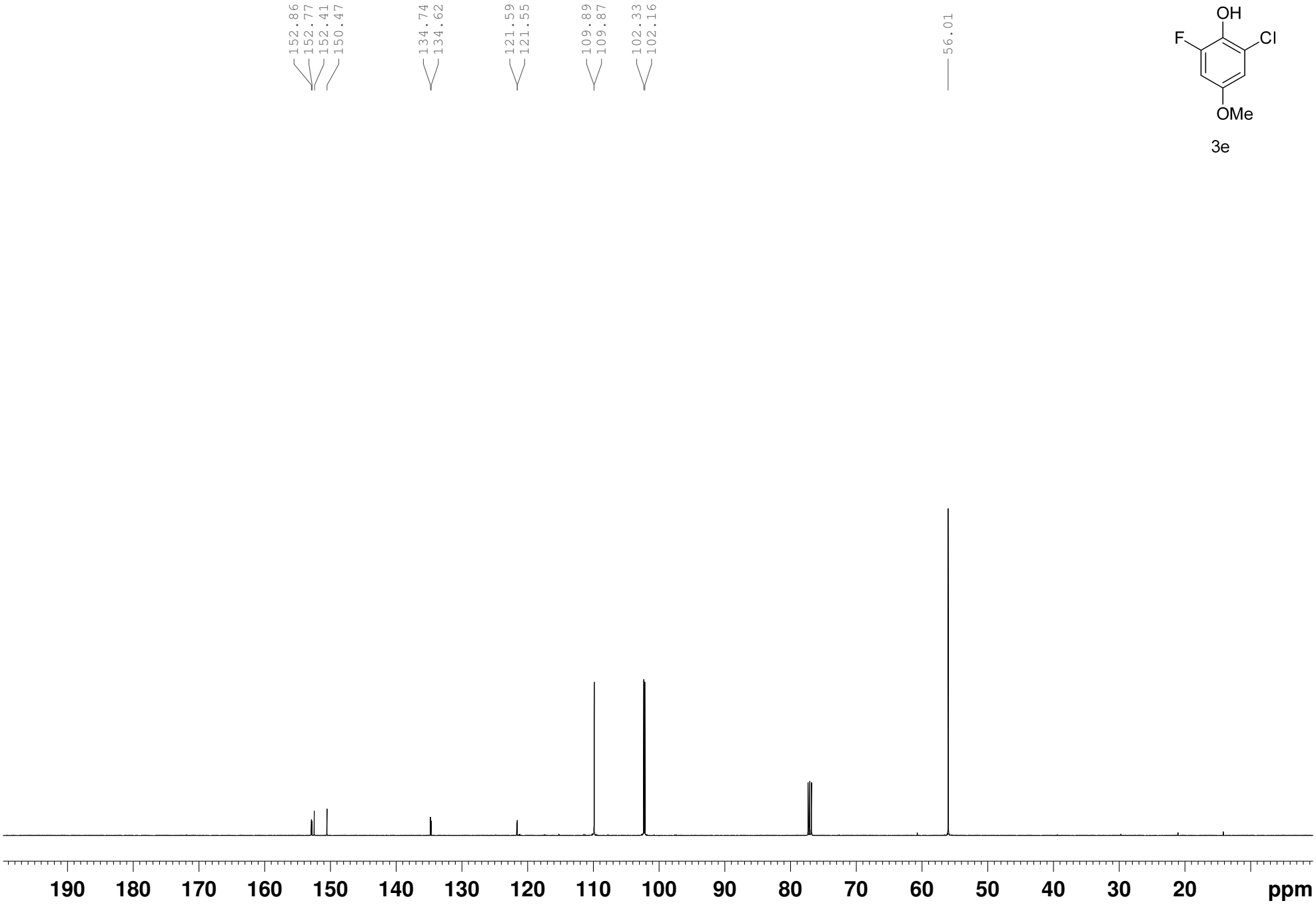
3c

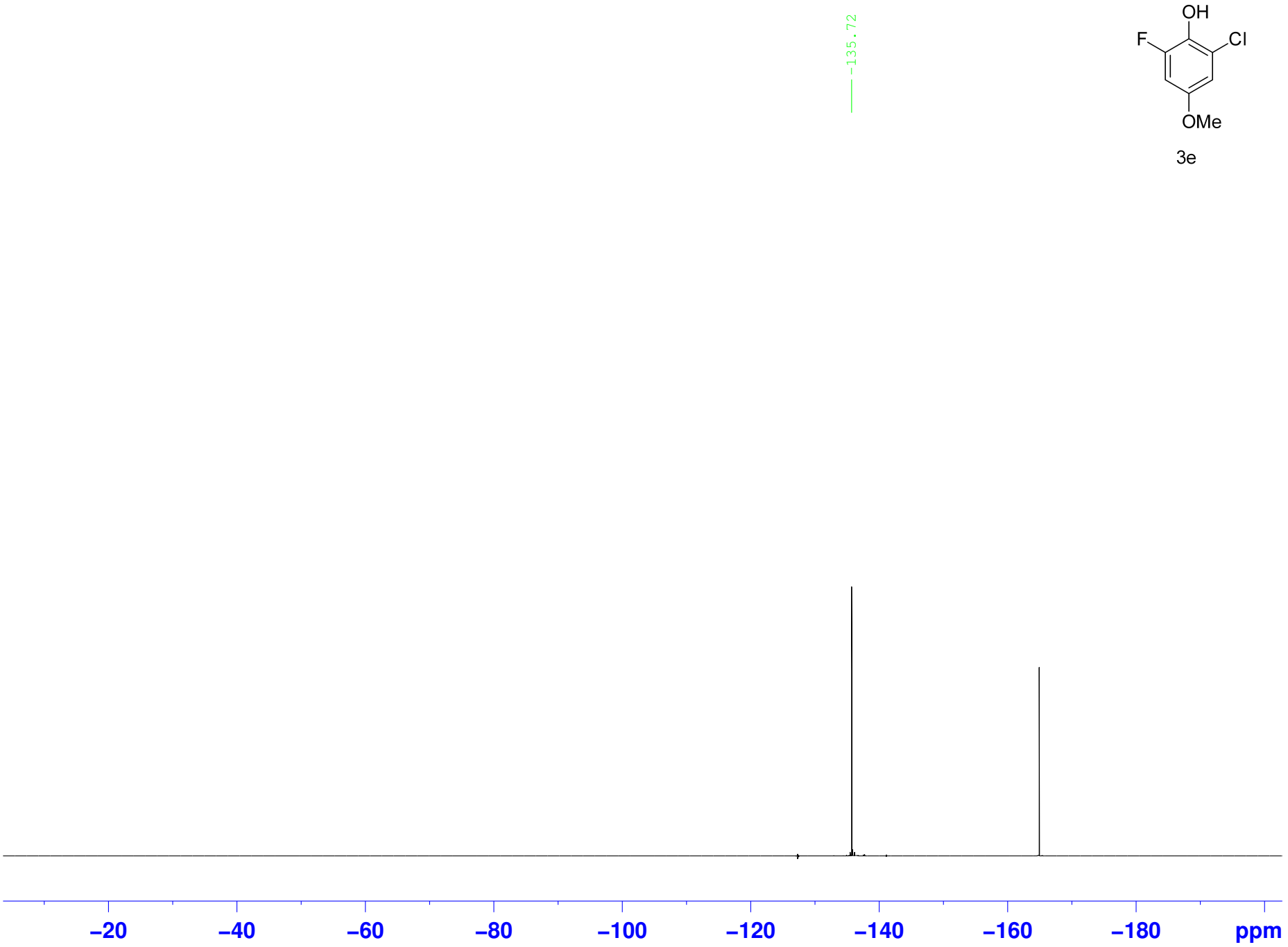


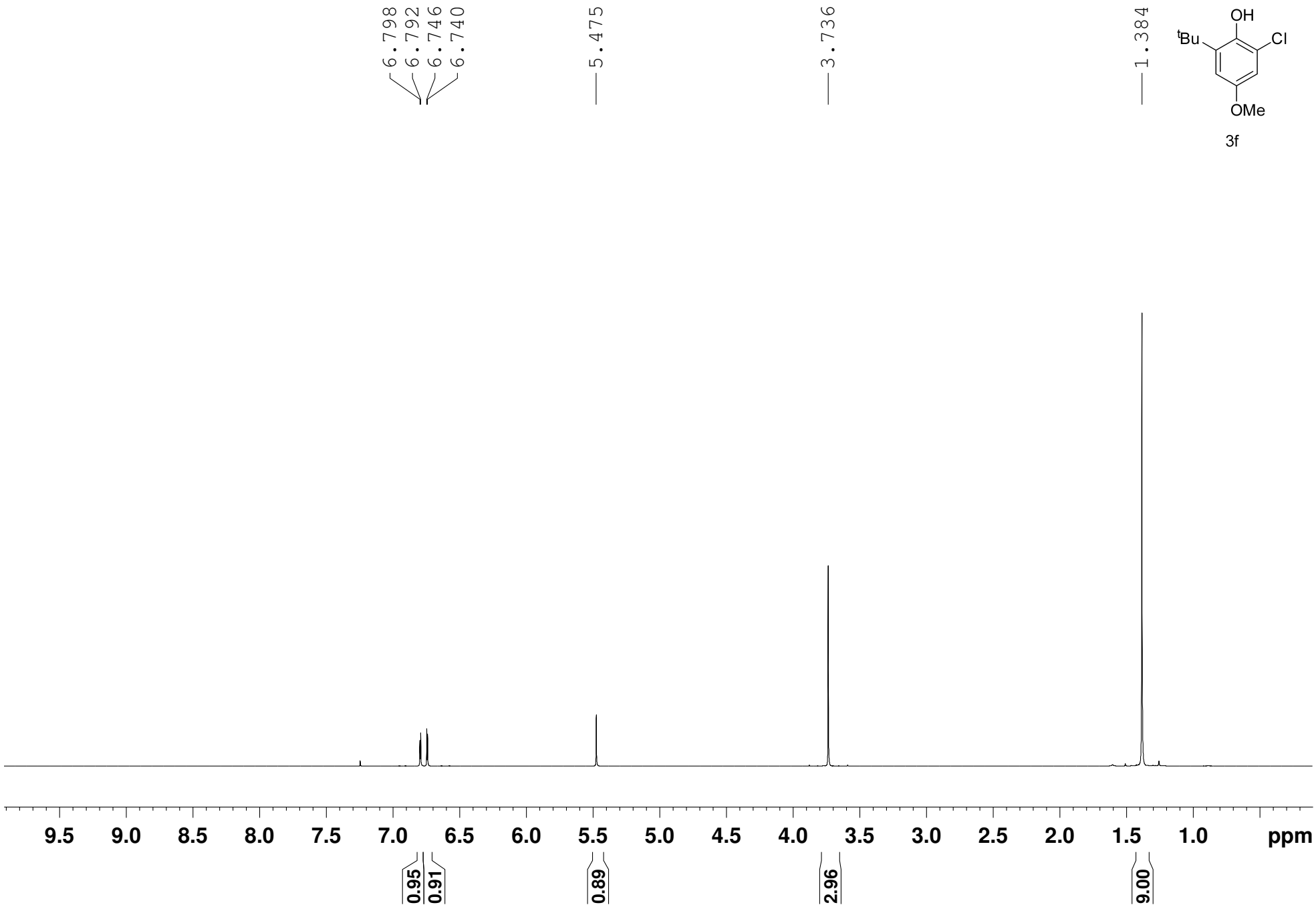

7.182
7.176
6.913
6.907
5.545
3.738
OH
I
Cl
OMe
3d
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.91
0.91
0.89
3.00

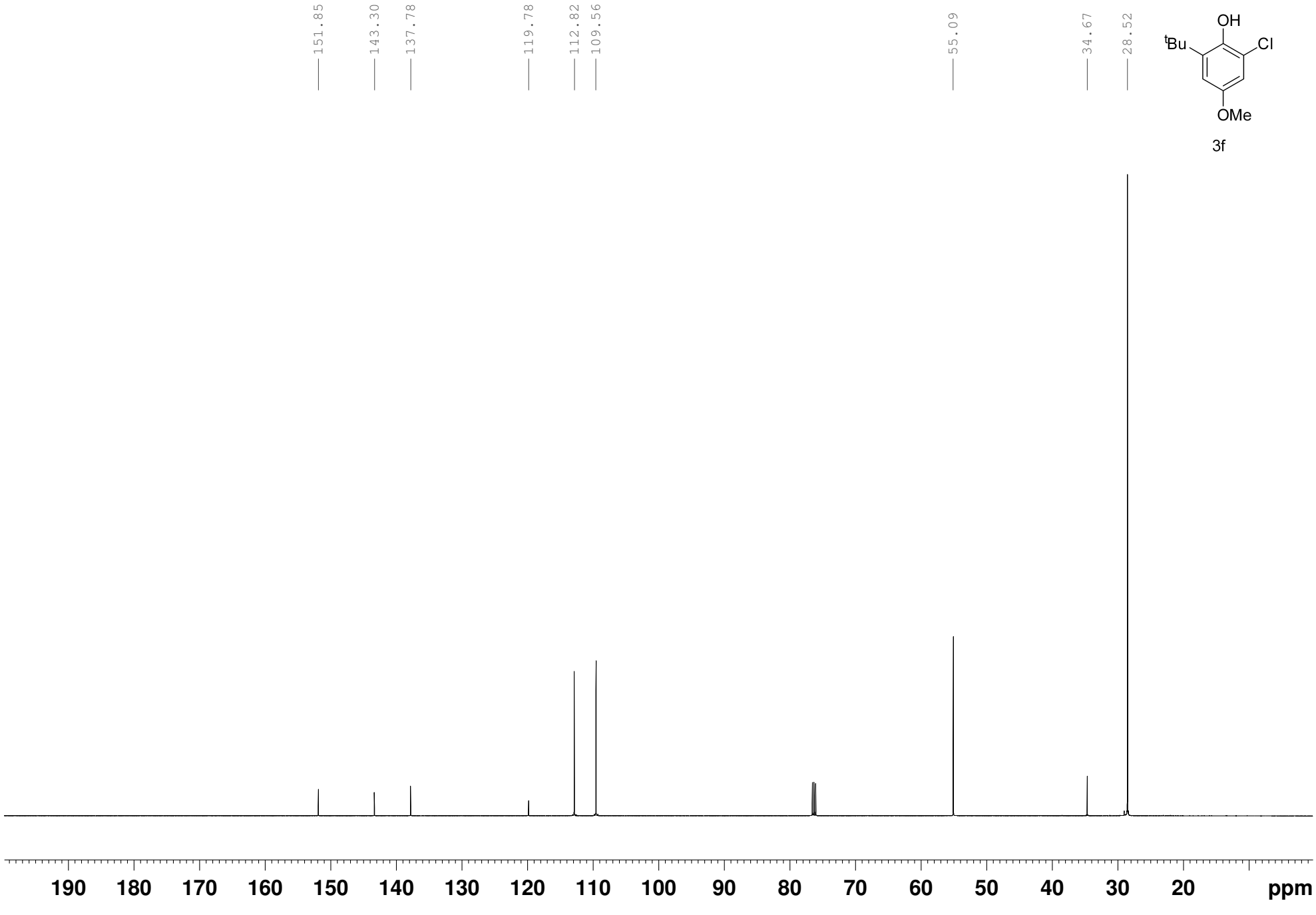

153.80
145.23
123.17
118.83
115.65
83.04
56.08
OH
I
Cl
OMe
3d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

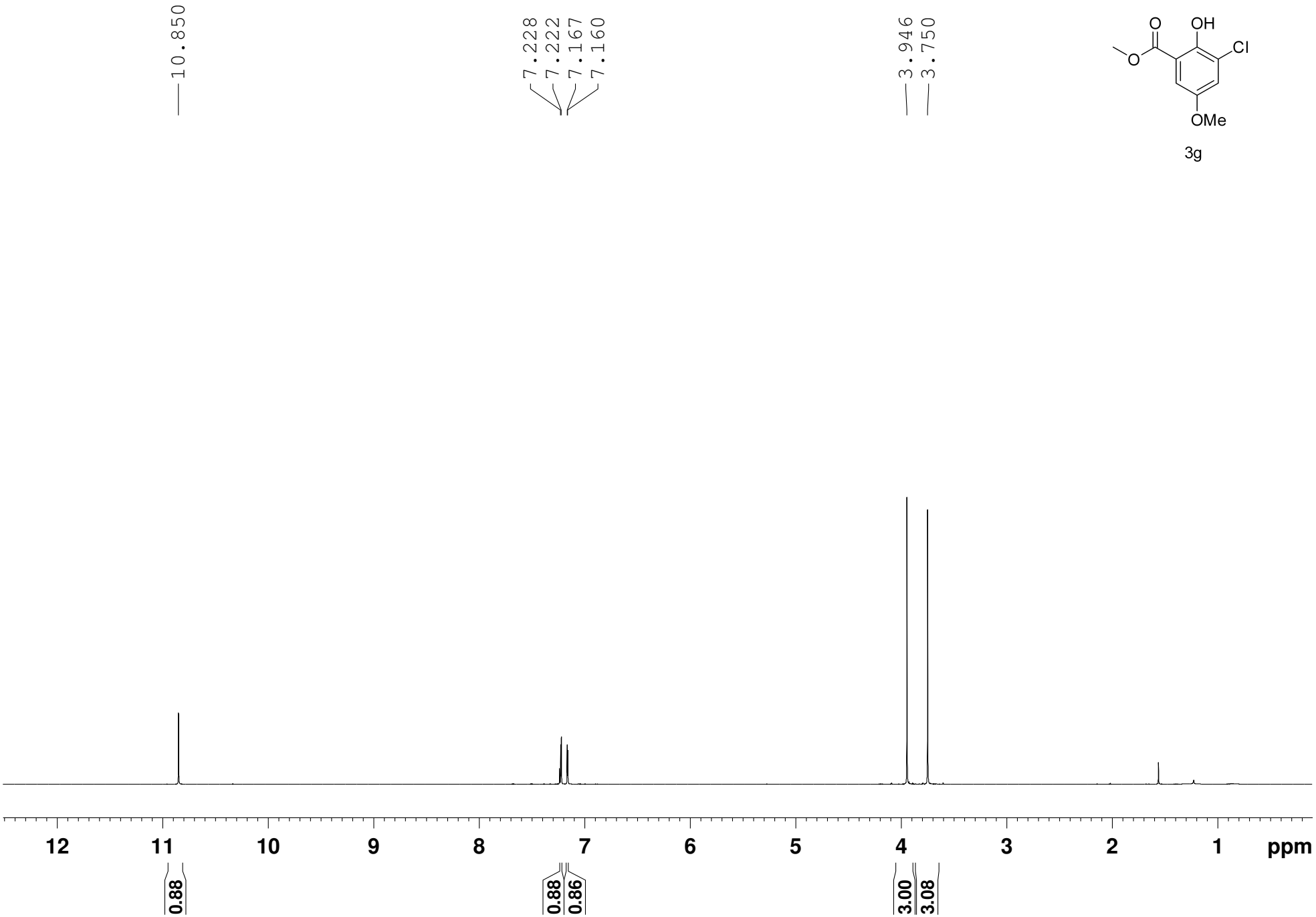

6.689
6.685
6.684
6.679
6.641
6.635
6.617
6.612
5.229
3.740
OH
F
Cl
OMe
3e
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.92
0.92
0.82
3.00

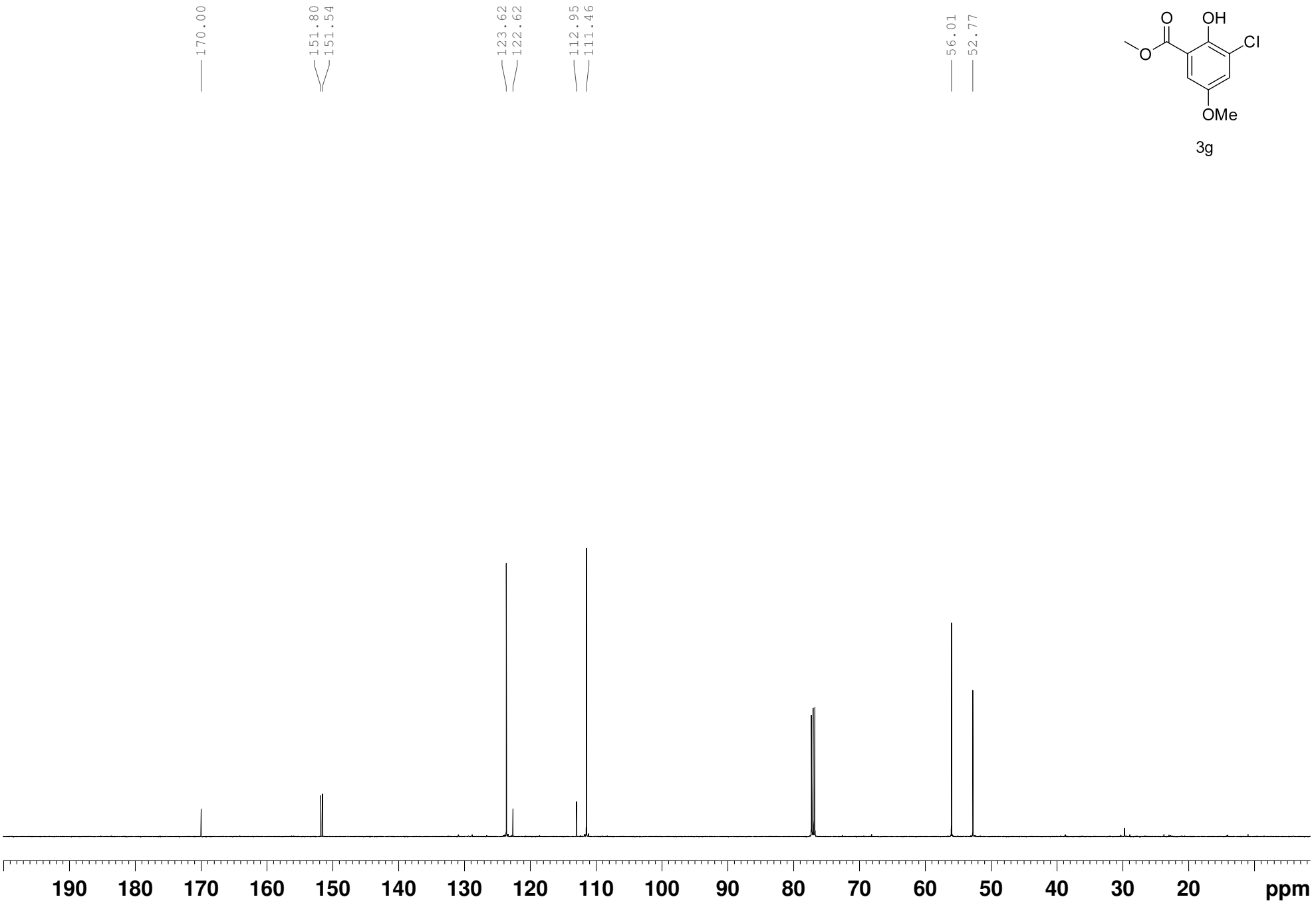

152.86
152.77
152.41
150.47
134.74
134.62
121.59
121.55
109.89
109.87
102.33
102.16
56.01
OH
F
Cl
OMe
3e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

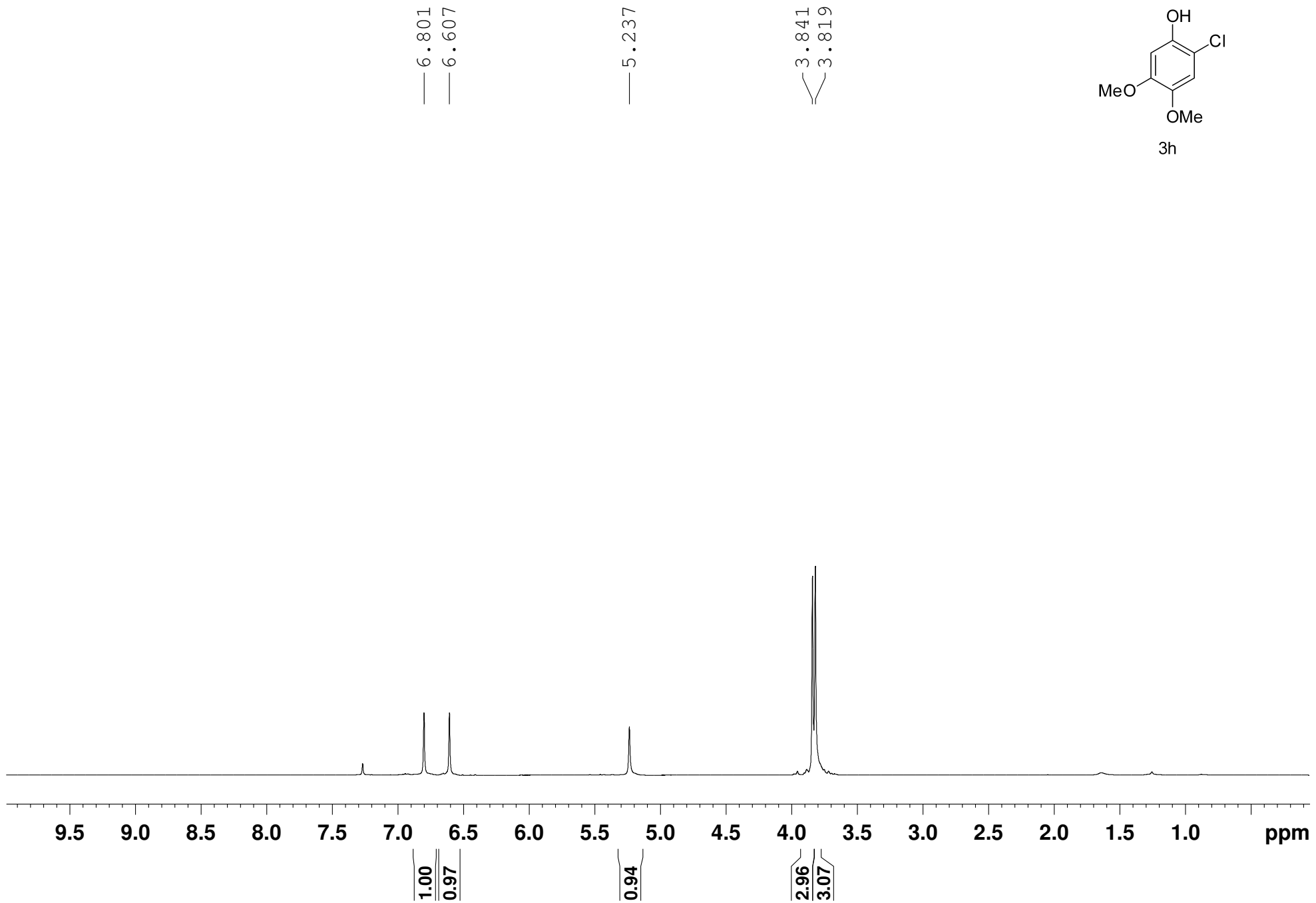

-135.72
OH
F
Cl
OMe
3e
–20
–40
–60
–80
–100
–120
–140
–160
–180
ppm

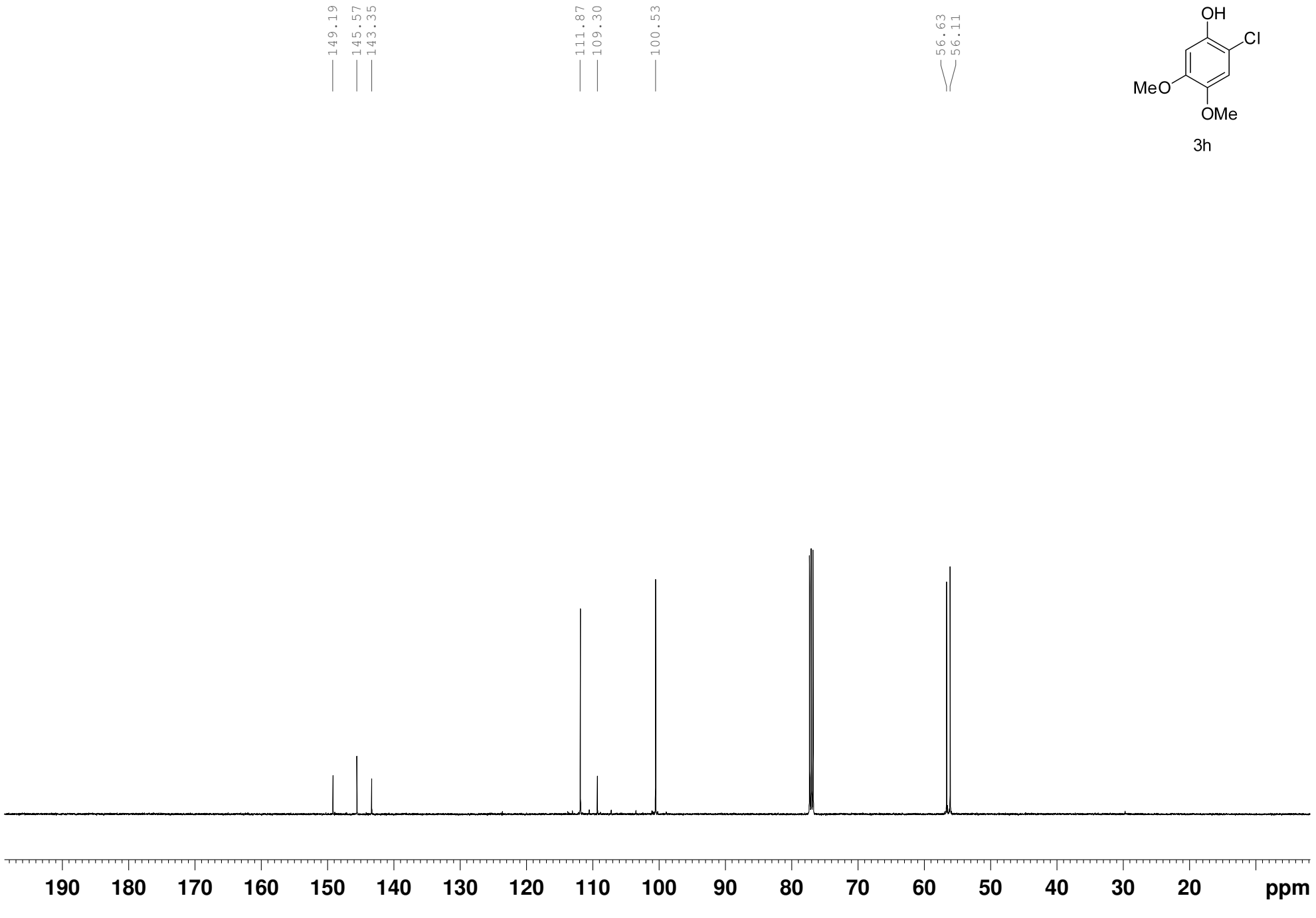

6.798
6.792
6.746
6.740
5.475
3.736
1.384
OH
tBu
Cl
OMe
3f
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.95
0.91
0.89
2.96
9.00

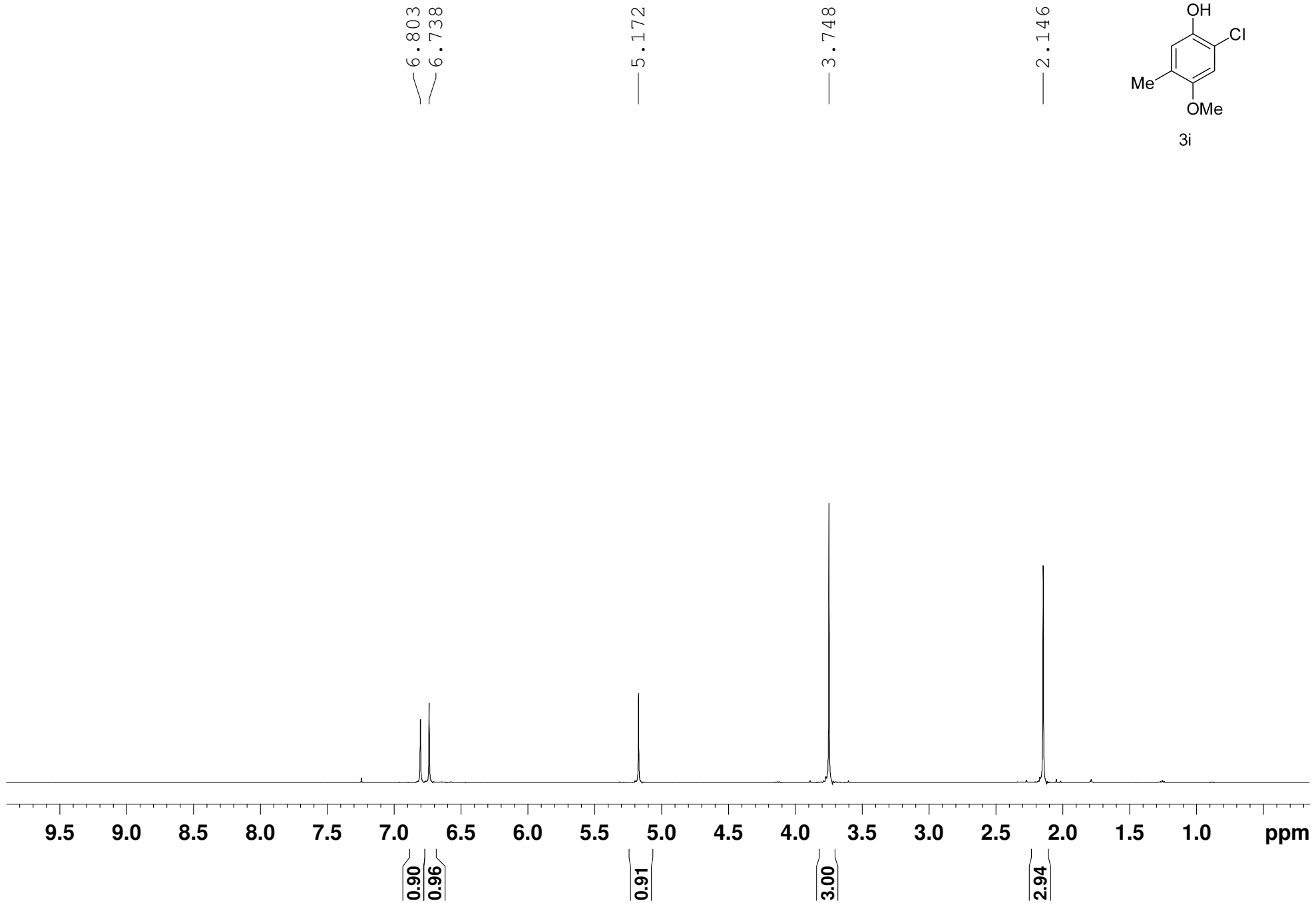

151.85
143.30
137.78
119.78
112.82
109.56
55.09
34.67
28.52
OH
tBu
Cl
OMe
3f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

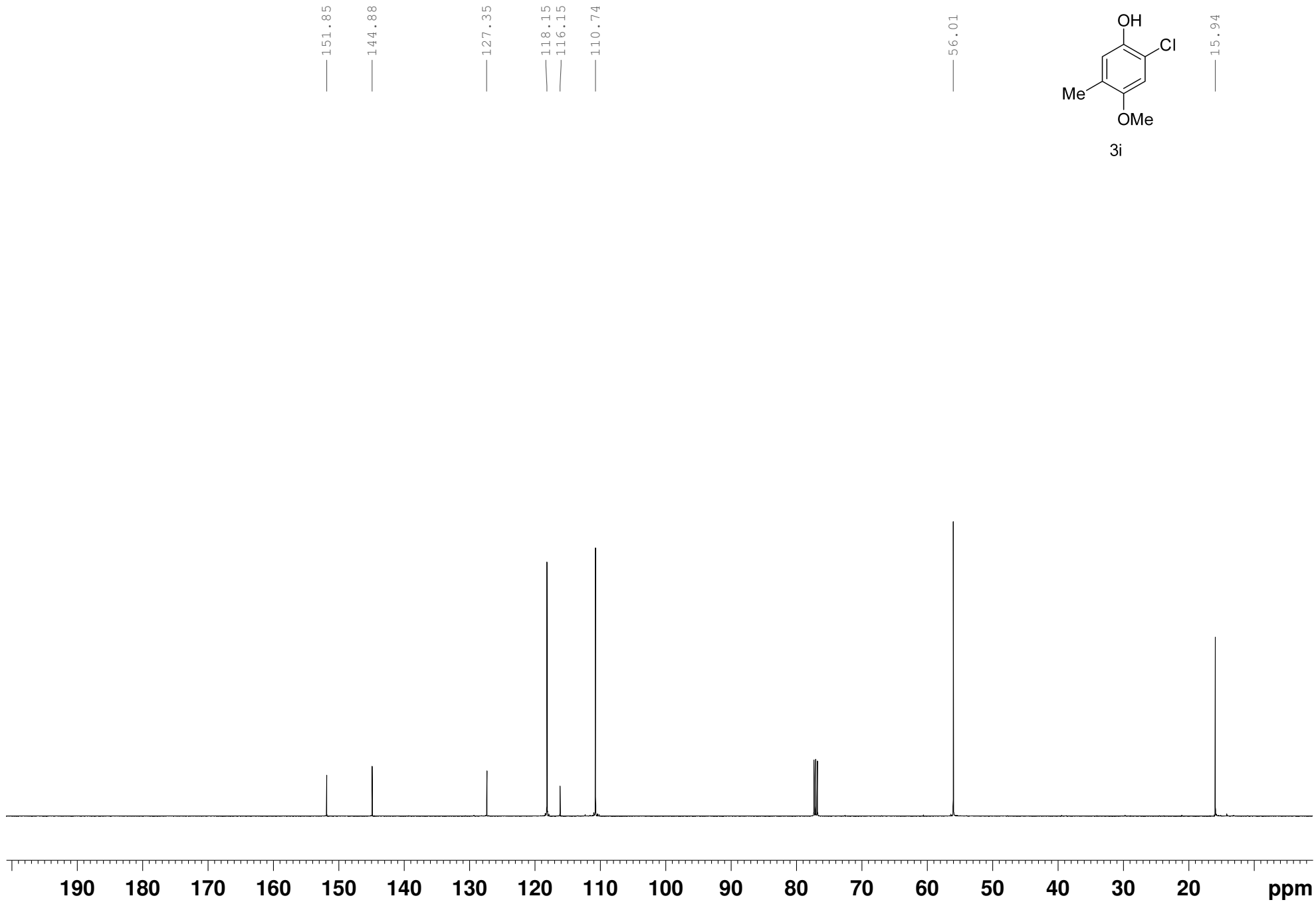

10.850
7.228
7.222
7.167
7.160
3.946
3.750
O
OH
Cl
O
OMe
3g
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.88
0.88
0.86
3.00
3.08

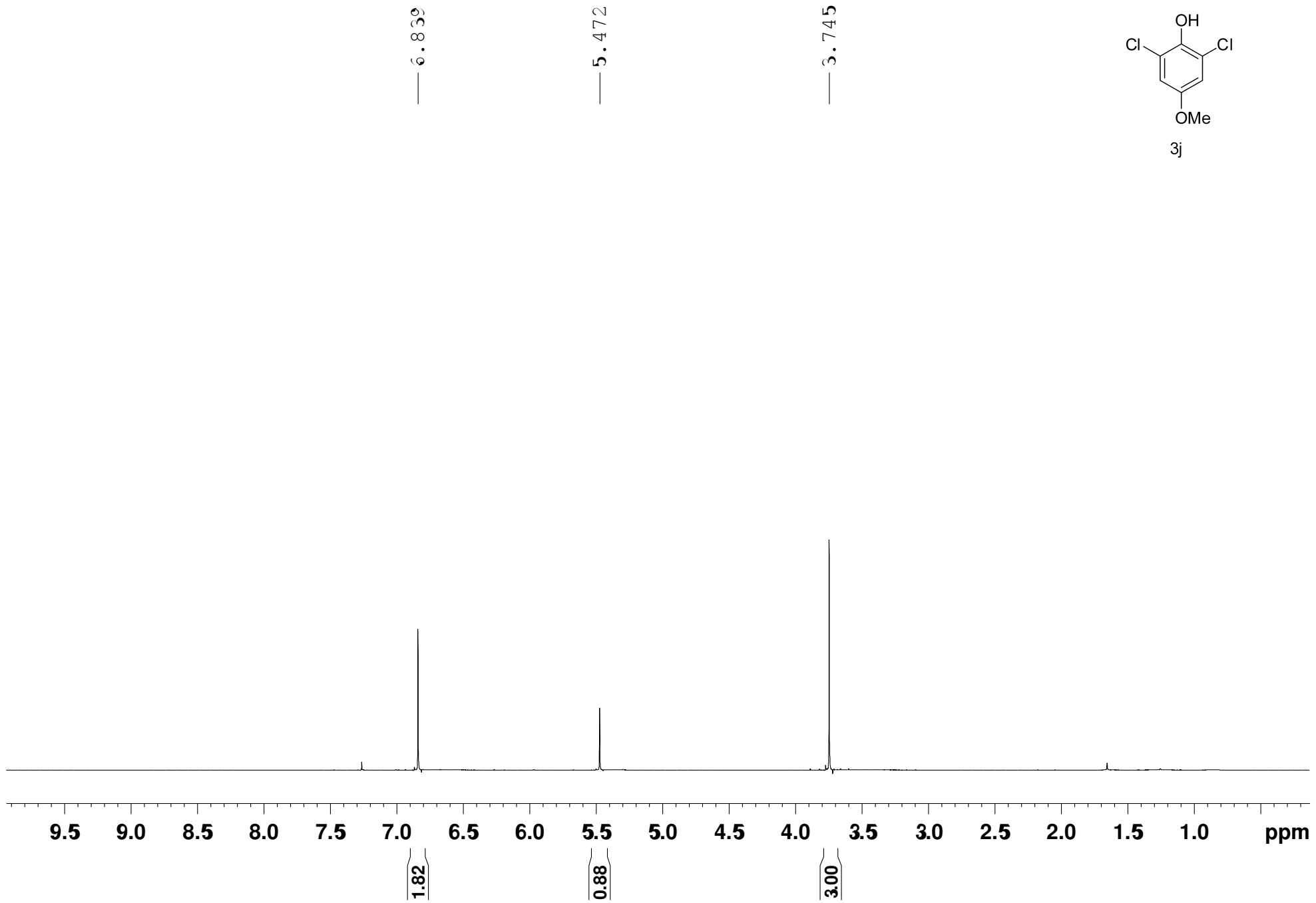

170.00
151.80
151.54
123.62
122.62
112.95
111.46
56.01
52.77
O
OH
Cl
O
OMe
3g
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

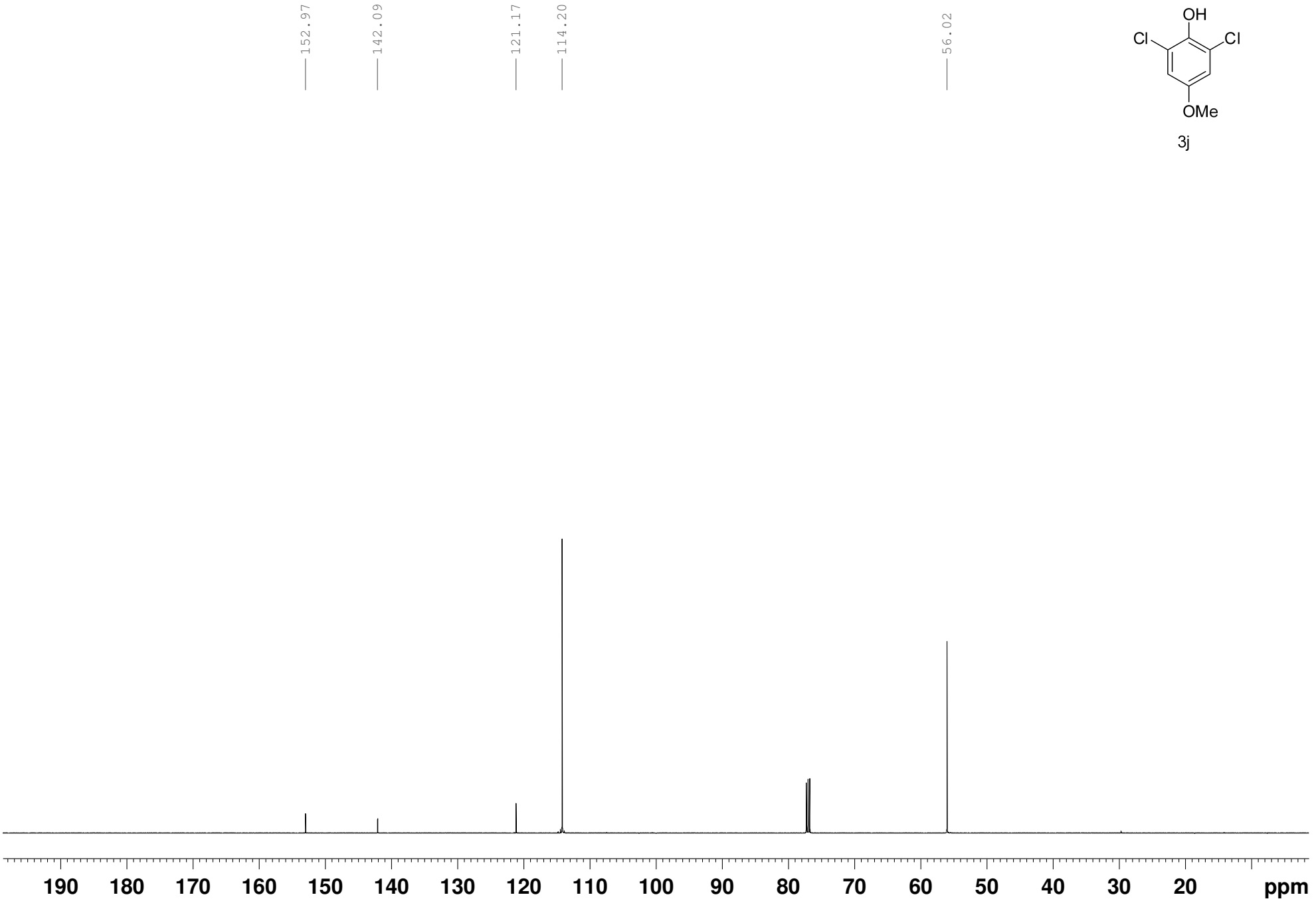

6.801
6.607
5.237
3.841
3.819
OH
Cl
MeO
OMe
3h
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
0.97
0.94
2.96
3.07

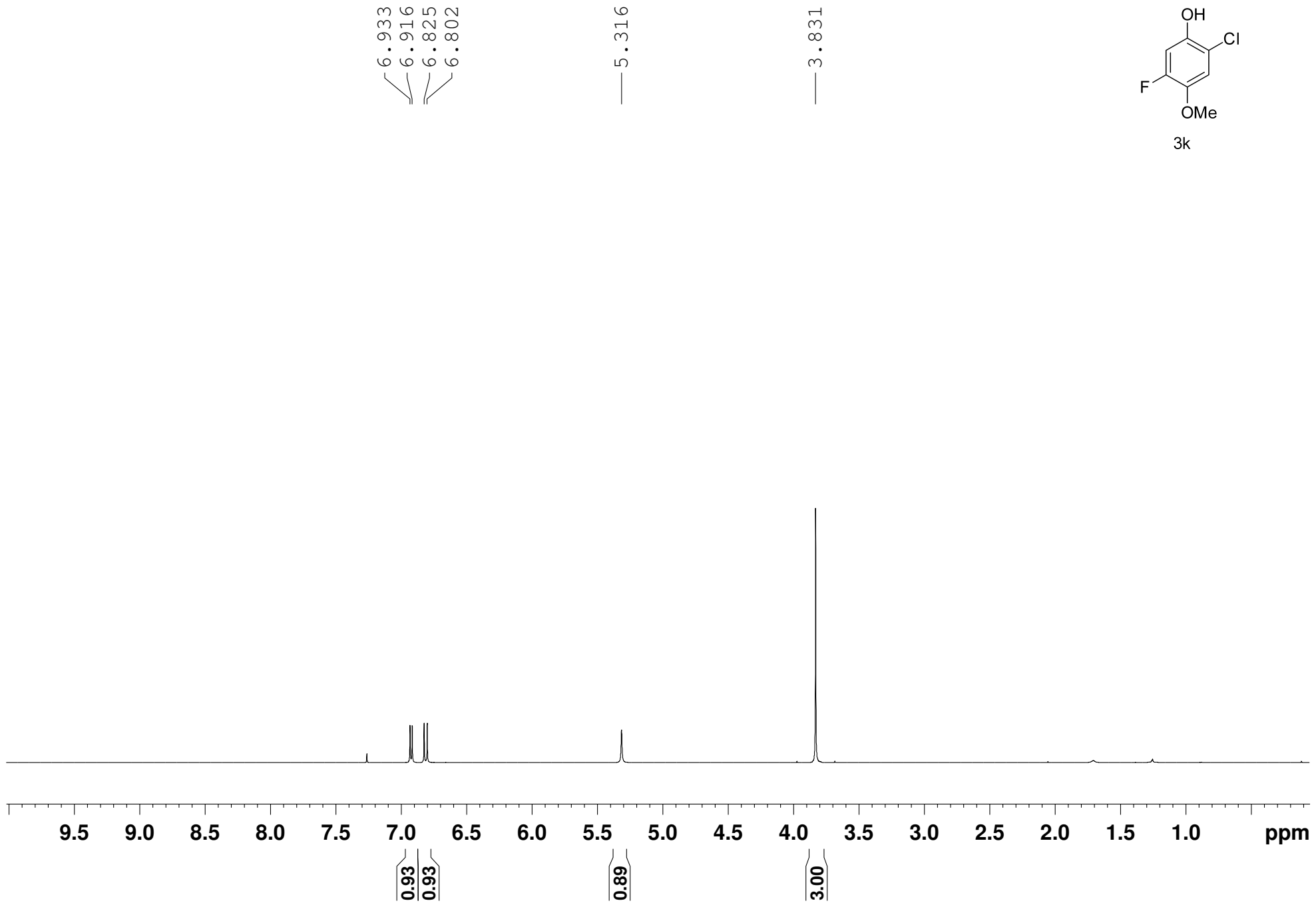

149.19
145.57
143.35
111.87
109.30
100.53
56.63
56.11
OH
Cl
MeO
OMe
3h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

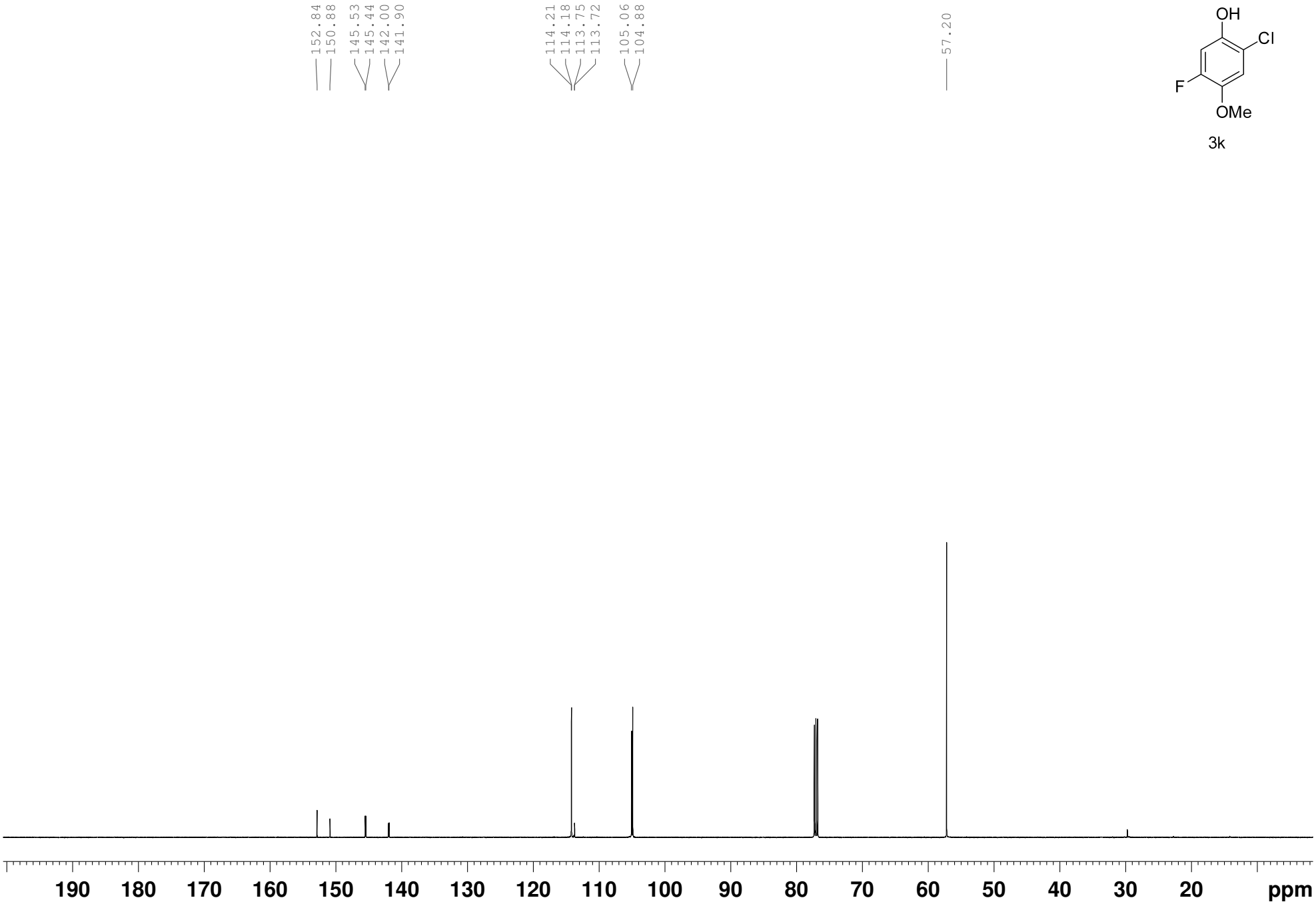

6.803
6.738
5.172
3.748
2.146
OH
Cl
Me
OMe
3i
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.90
0.96
0.91
3.00
2.94

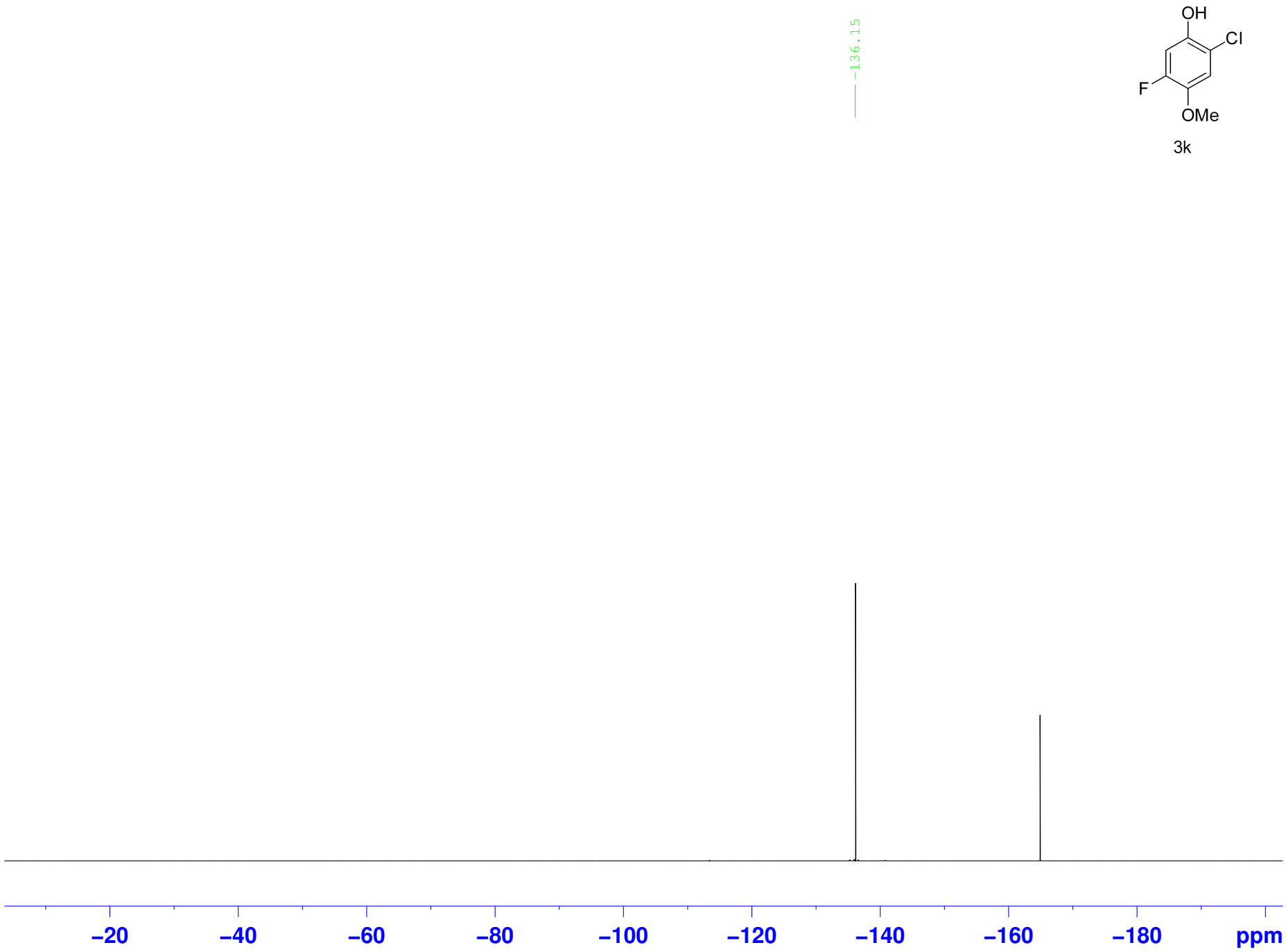

151.85
144.88
127.35
118.15
116.15
110.74
56.01
15.94
OH
Cl
Me
OMe
3i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

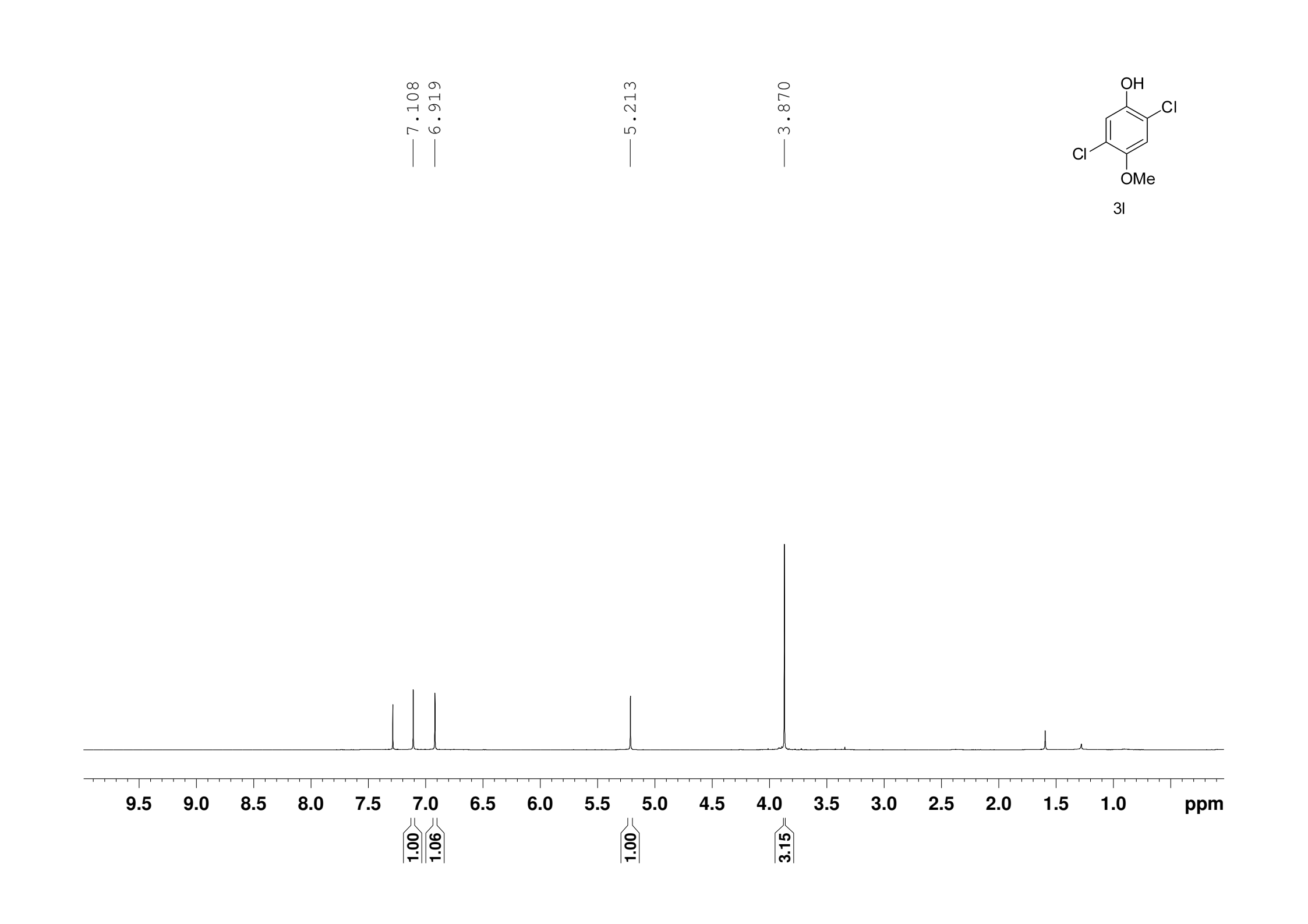

6.839
5.472
3.745
OH
Cl
Cl
OMe
3j
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.82
0.88
3.00

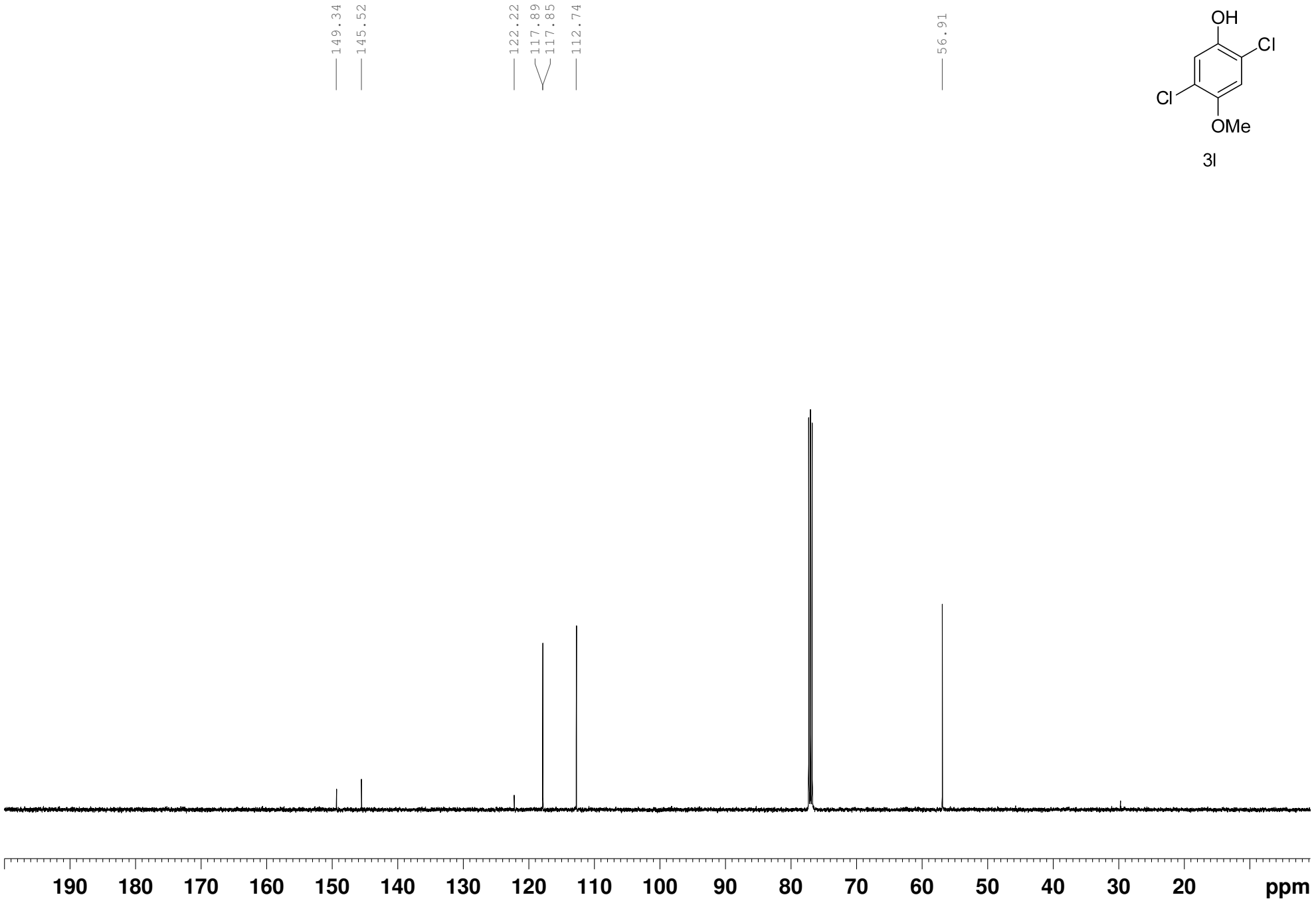

152.97
142.09
121.17
114.20
56.02
OH
Cl
Cl
OMe
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

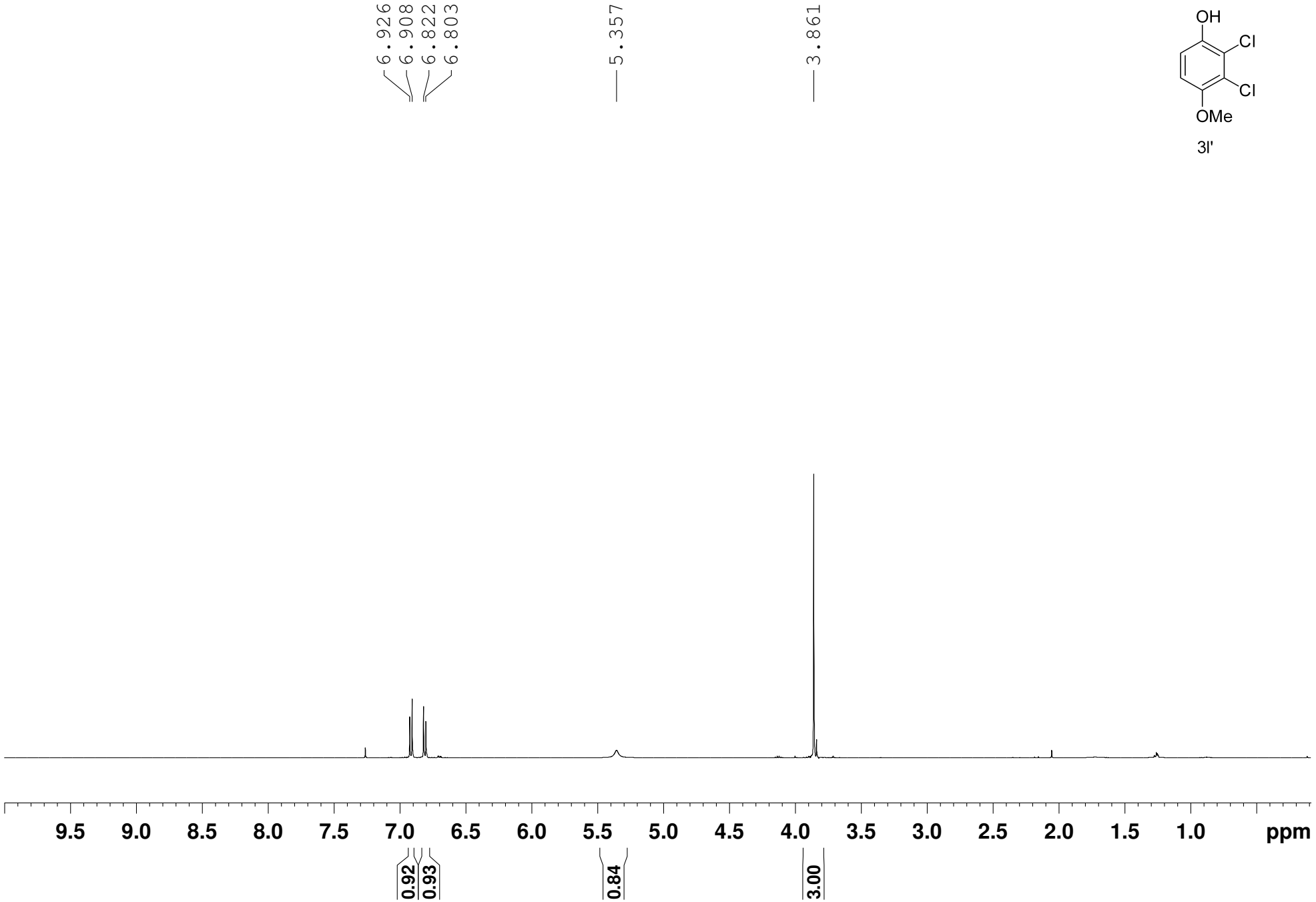

6.933
6.916
6.825
6.802
5.316
3.831
OH
Cl
F
OMe
3k
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.93
0.93
0.89
3.00

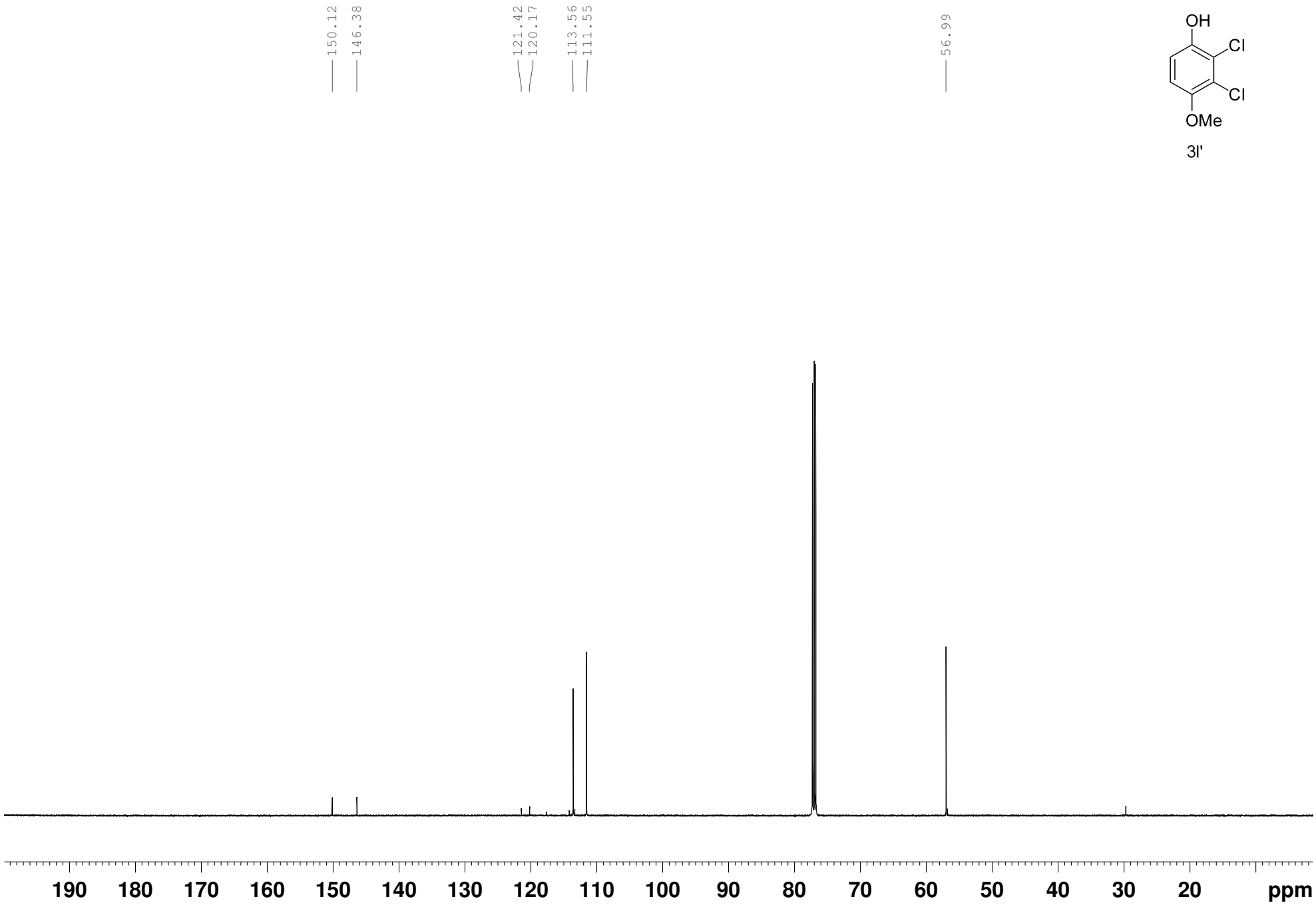

152.84
150.88
145.53
145.44
142.00
141.90
114.21
114.18
113.75
113.72
105.06
104.88
57.20
OH
Cl
F
OMe
3k
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

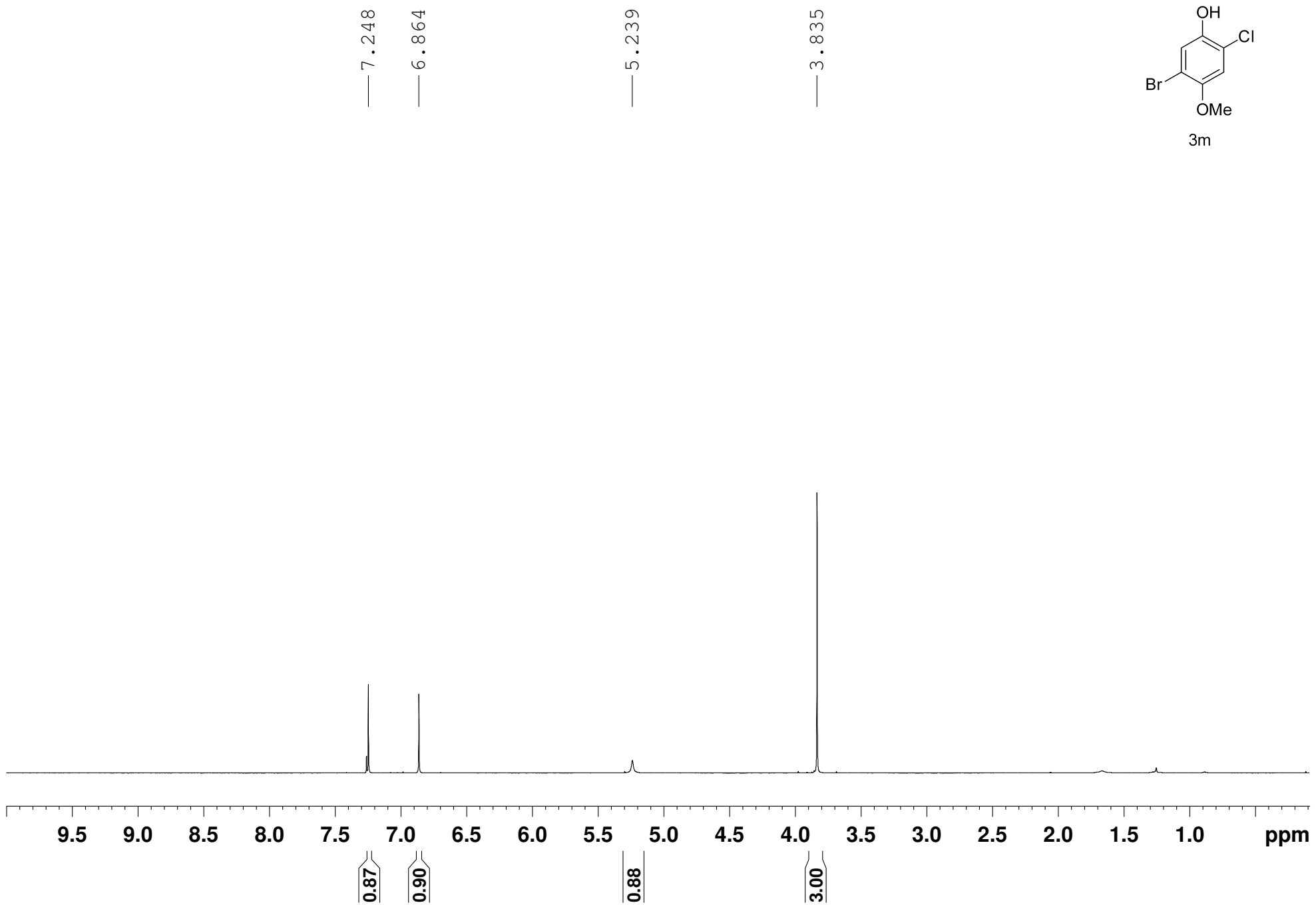

-136.15
OH
Cl
F
OMe
3k
–20
–40
–60
–80
–100
–120
–140
–160
–180
ppm

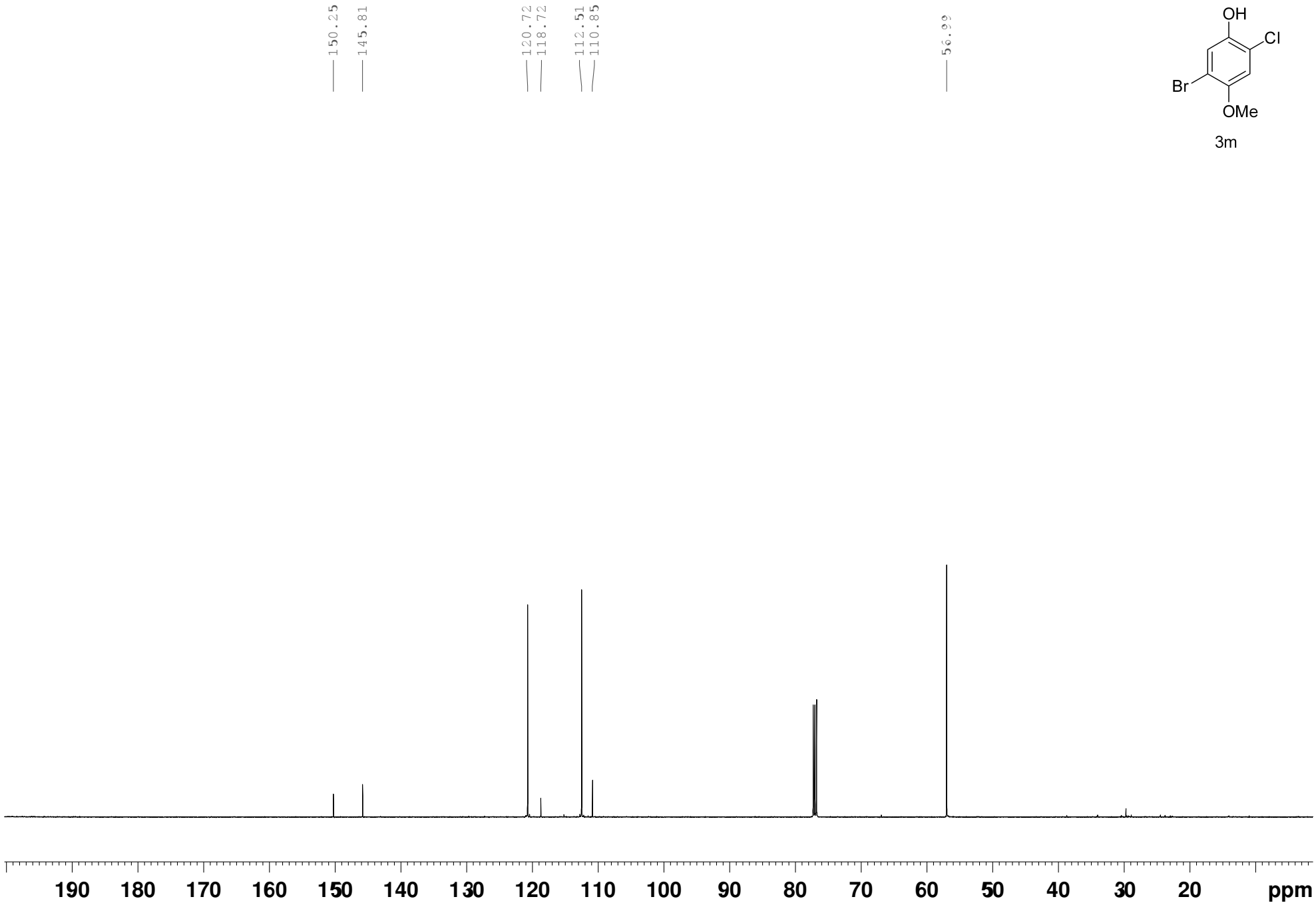

7.108
6.919
5.213
3.870
OH
Cl
Cl
OMe
3l
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.06
1.00
3.15

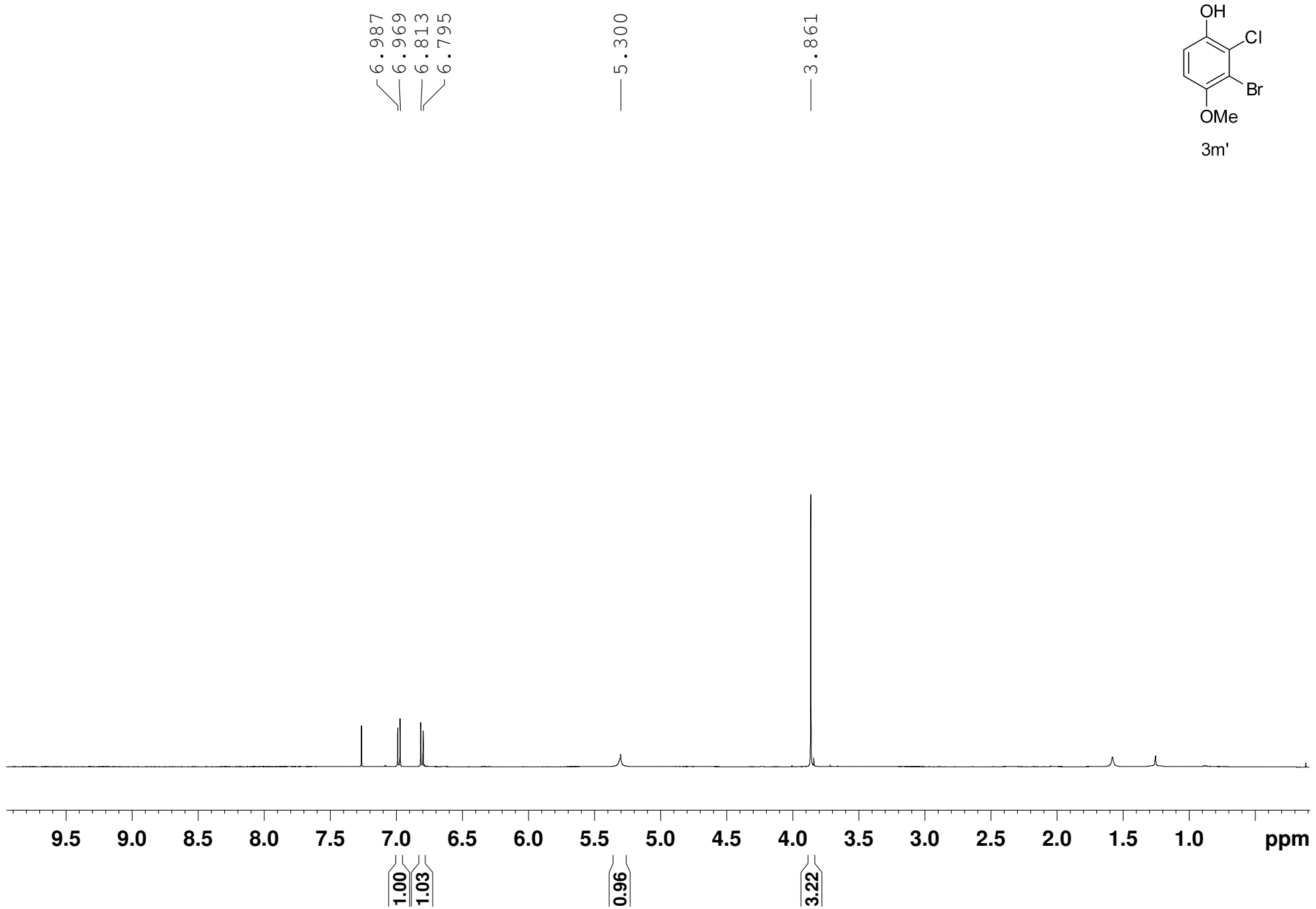

149.34
145.52
122.22
117.89
117.85
112.74
56.91
OH
Cl
Cl
OMe
3l
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

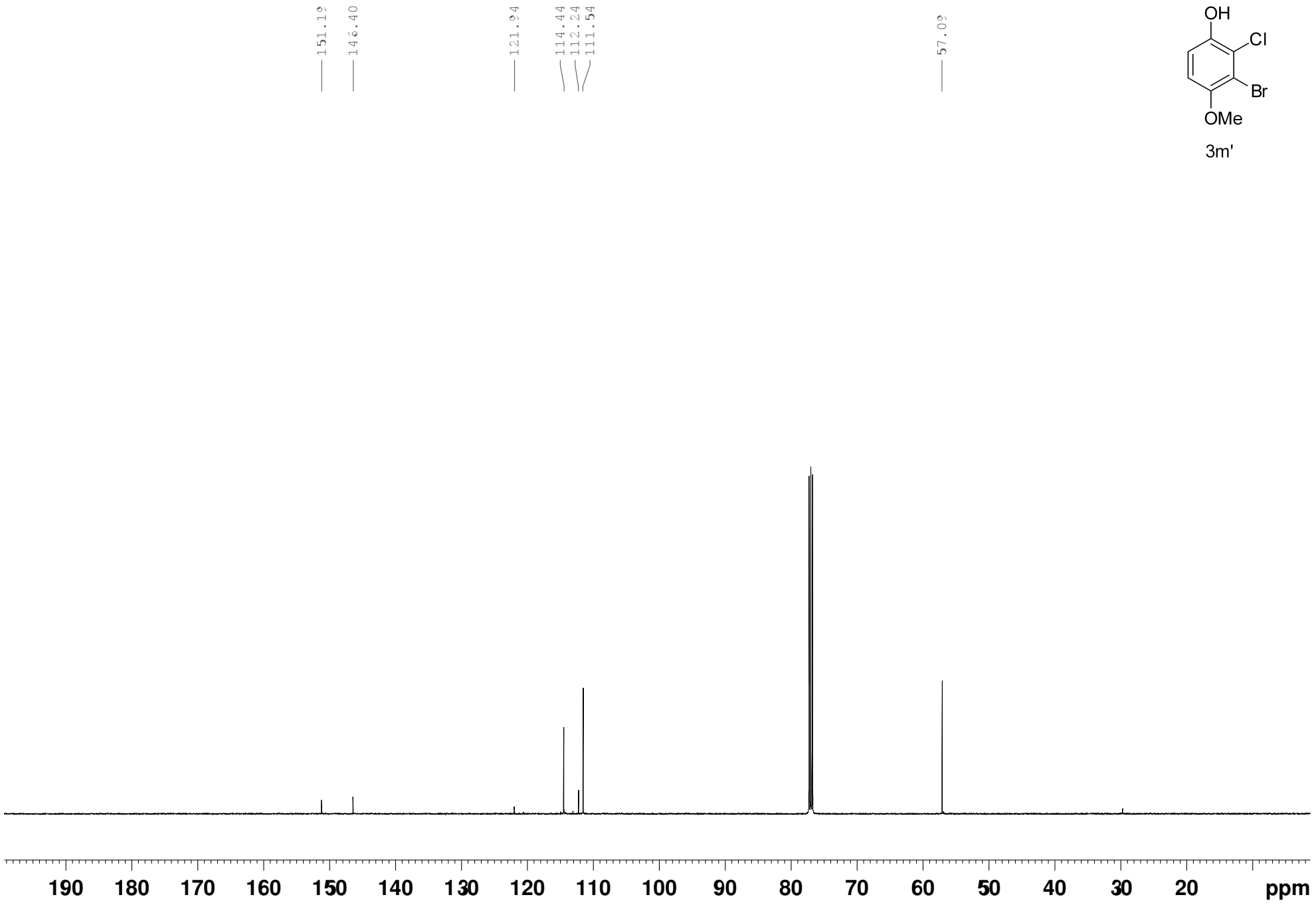

6.926
6.908
6.822
6.803
5.357
3.861
OH
Cl
Cl
OMe
3l'
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.92
0.93
0.84
3.00

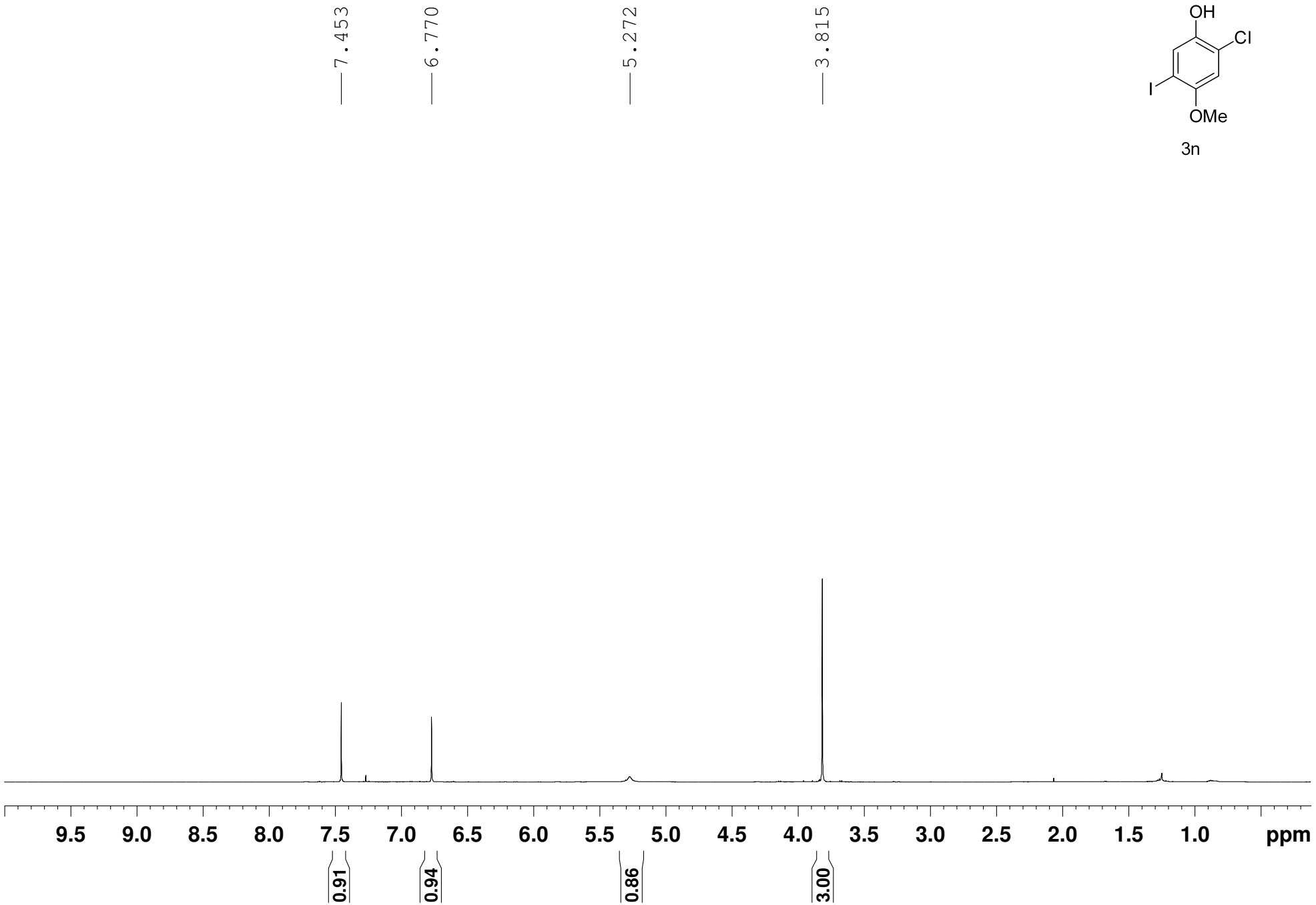

150.12
146.38
121.42
120.17
113.56
111.55
56.99
OH
Cl
Cl
OMe
3l'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

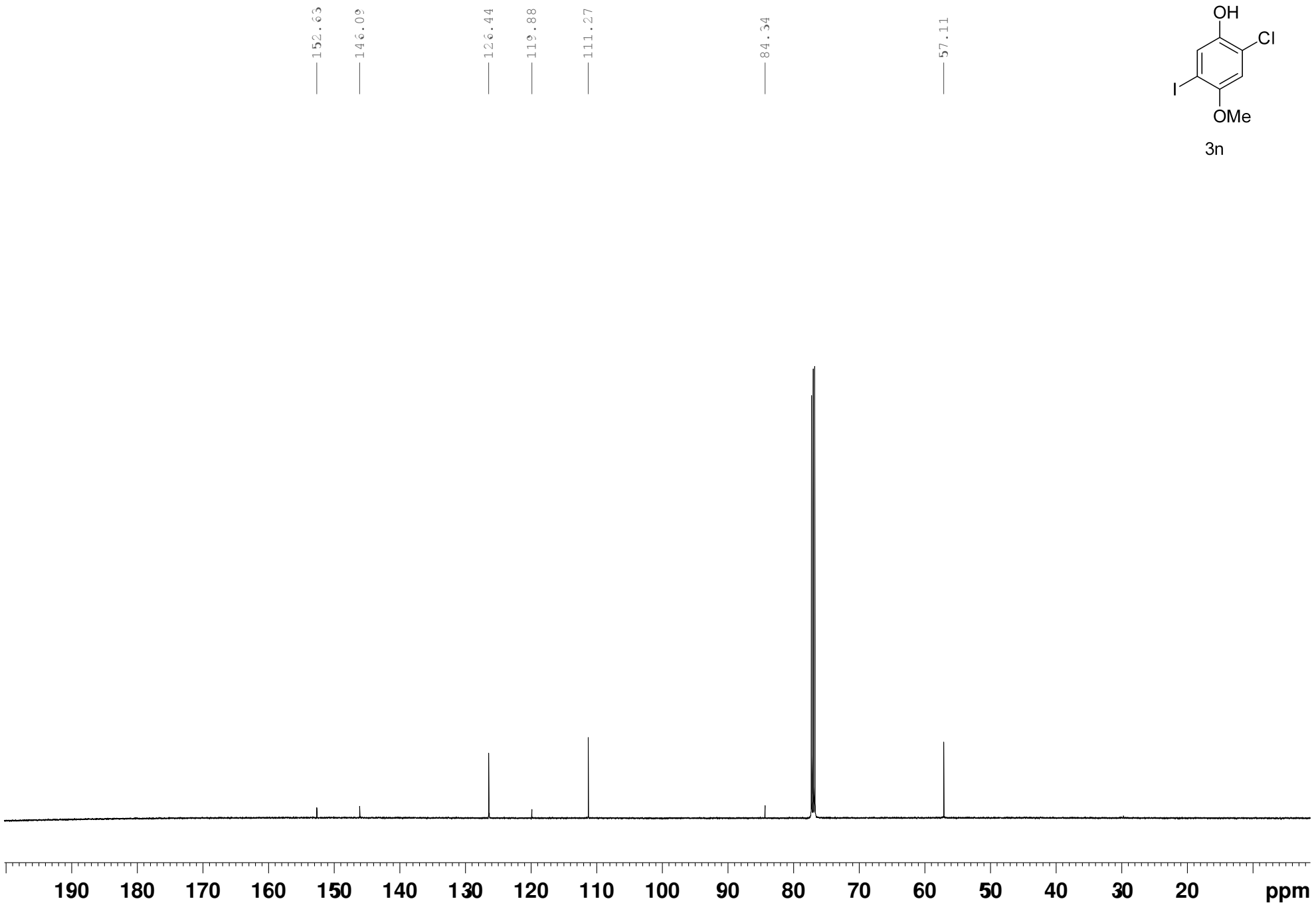

7.248
6.864
5.239
3.835
OH
Cl
Br
OMe
3m
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.87
0.90
0.88
3.00

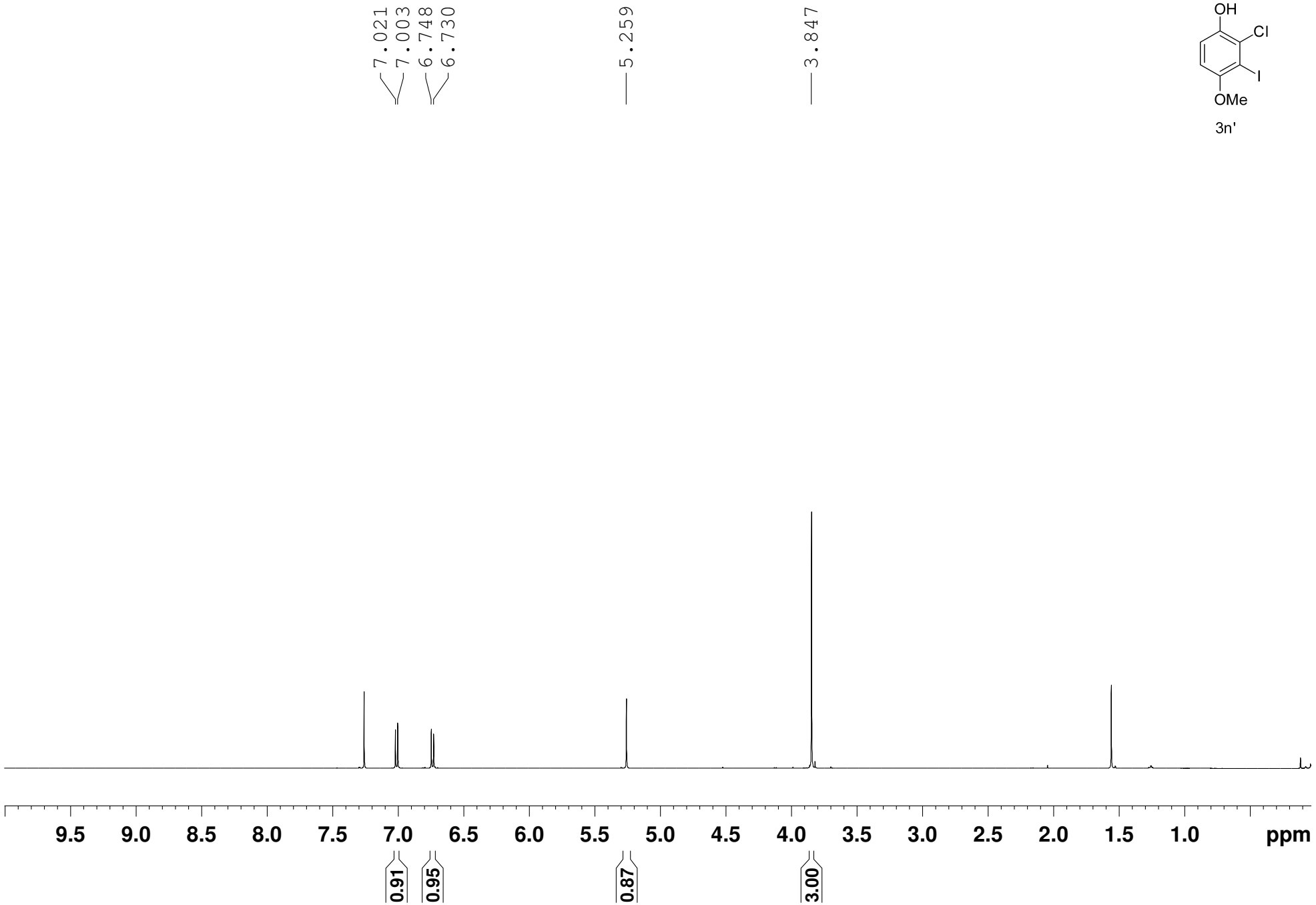

150.25
145.81
120.72
118.72
112.51
110.85
56.99
OH
Cl
Br
OMe
3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

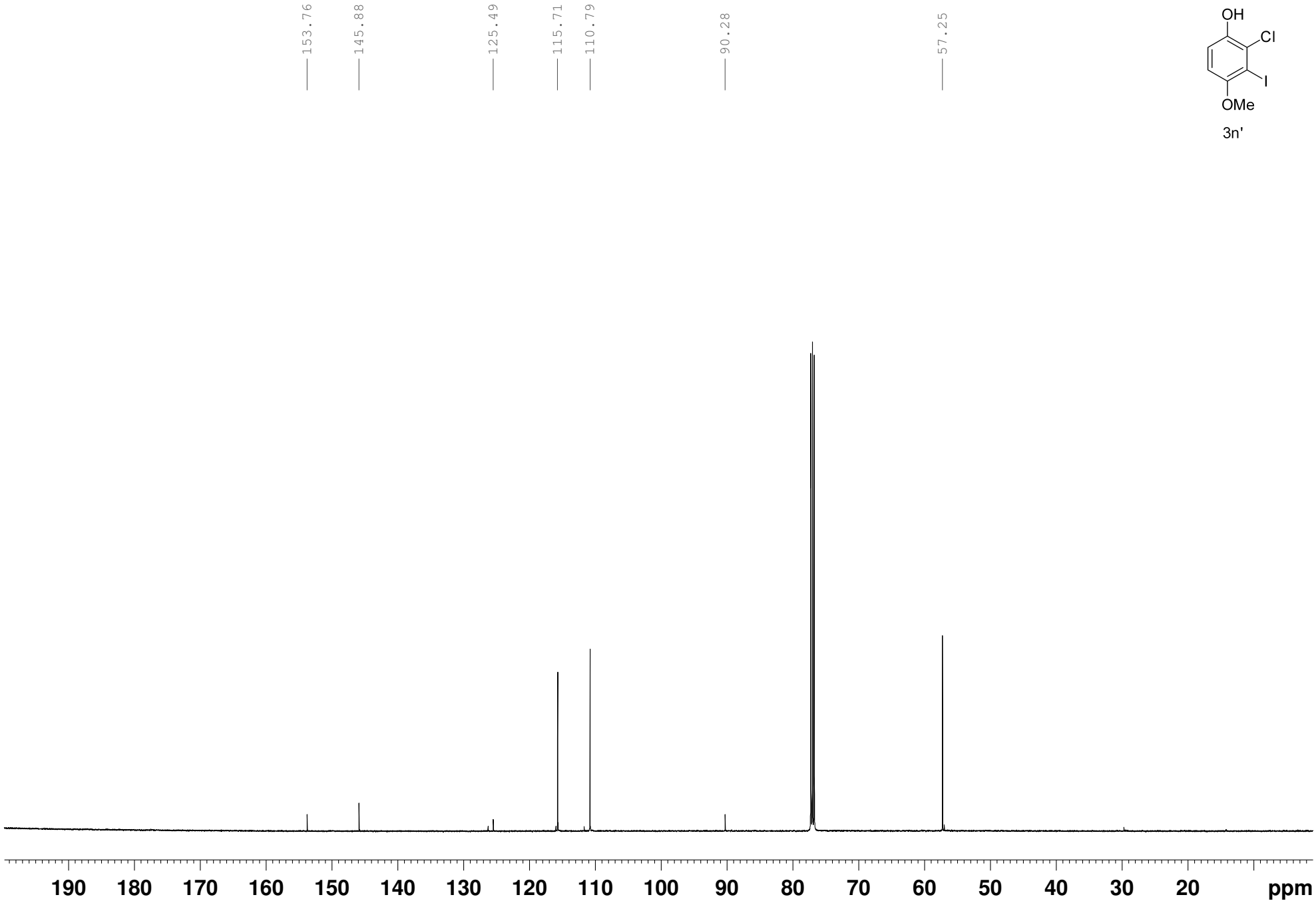

6.987
6.969
6.813
6.795
5.300
3.861
OH
Cl
Br
OMe
3m'
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.03
0.96
3.22

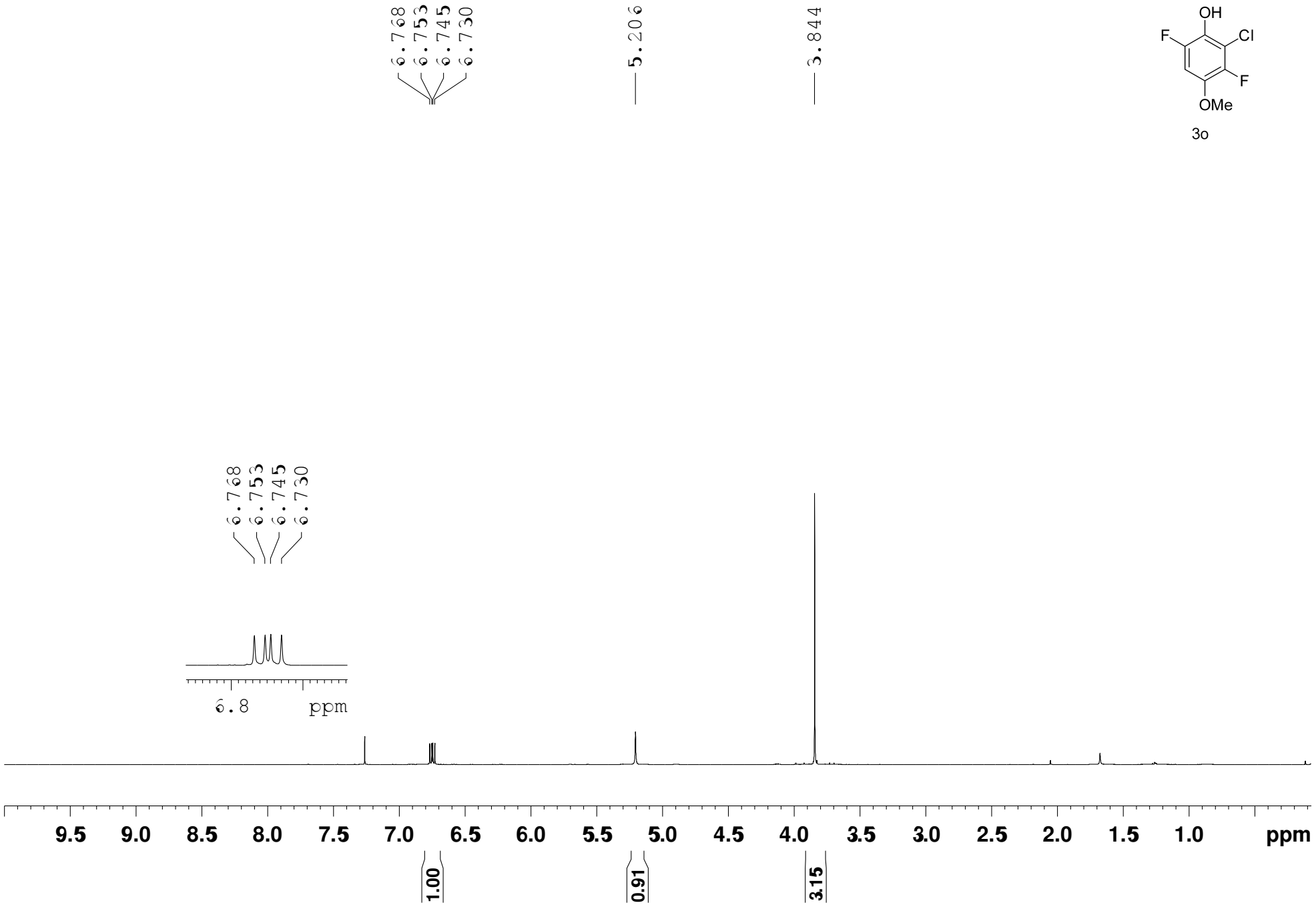

151.19
146.40
121.94
114.44
112.24
111.54
57.09
OH
Cl
Br
OMe
3m'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

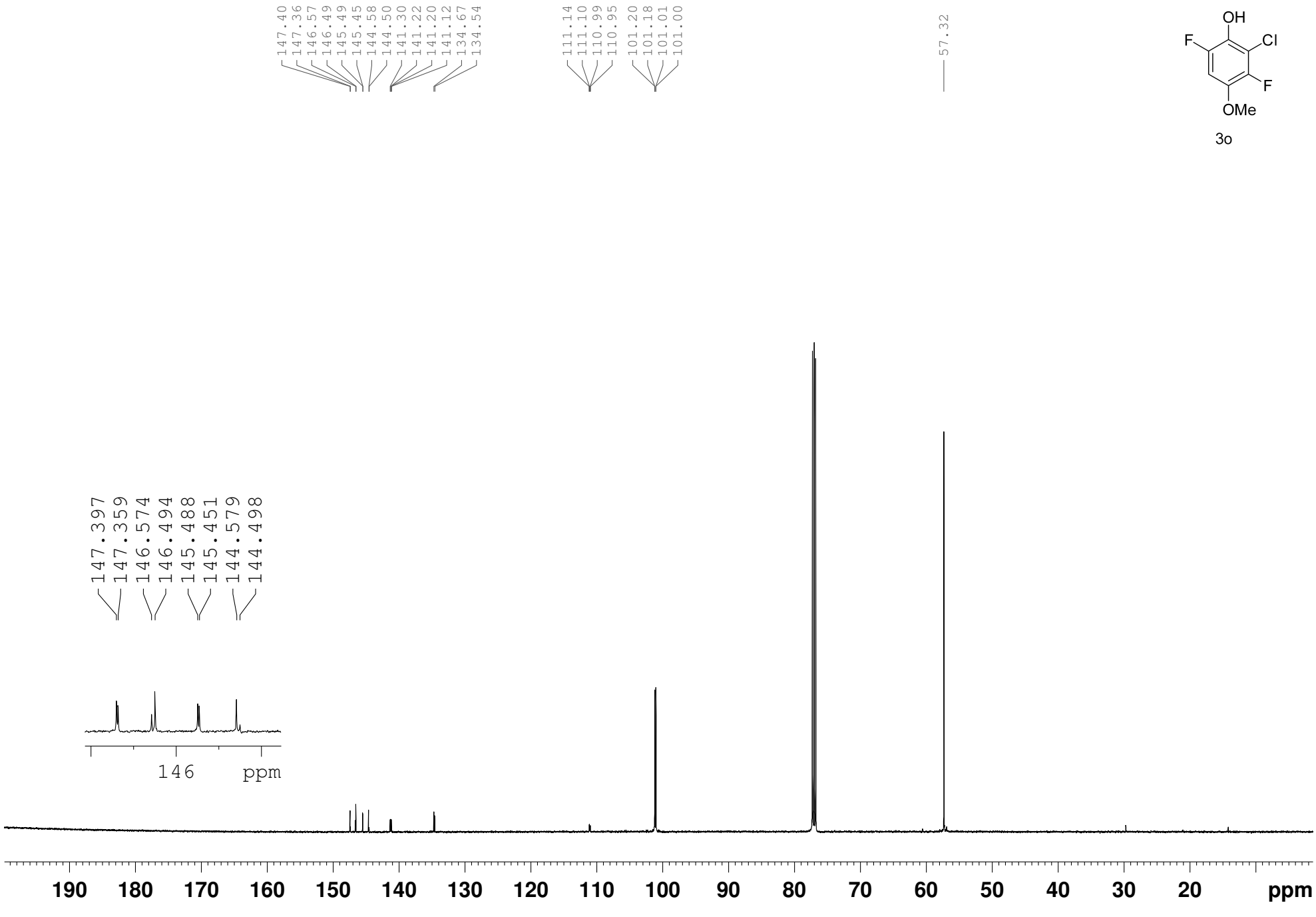

7.453
6.770
5.272
3.815
OH
Cl
I
OMe
3n
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.91
0.94
0.86
3.00

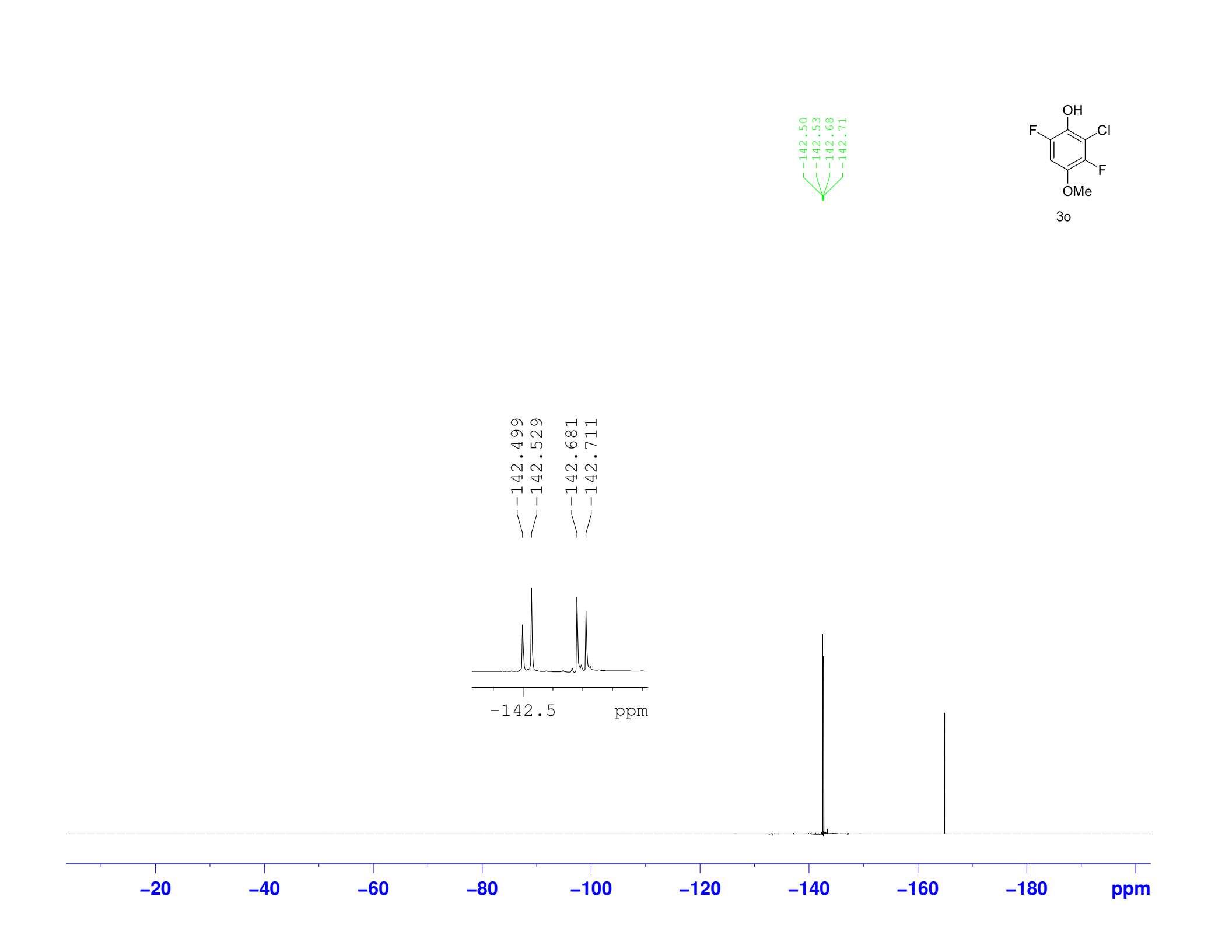

152.63
146.09
126.44
119.88
111.27
84.34
57.11
OH
Cl
I
OMe
3n
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

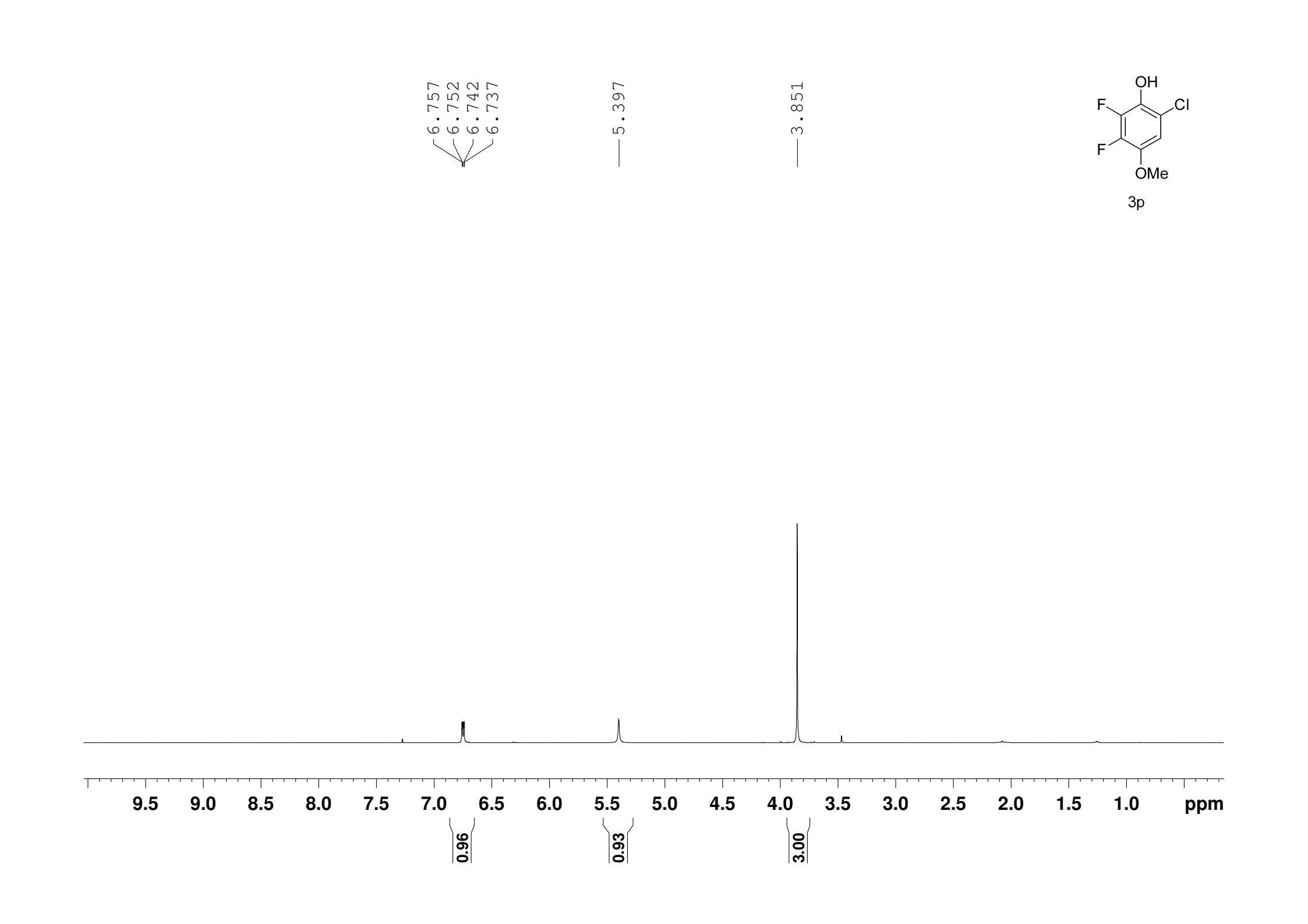

7.021
7.003
6.748
6.730
5.259
3.847
OH
Cl
I
OMe
3n'
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.91
0.95
0.87
3.00

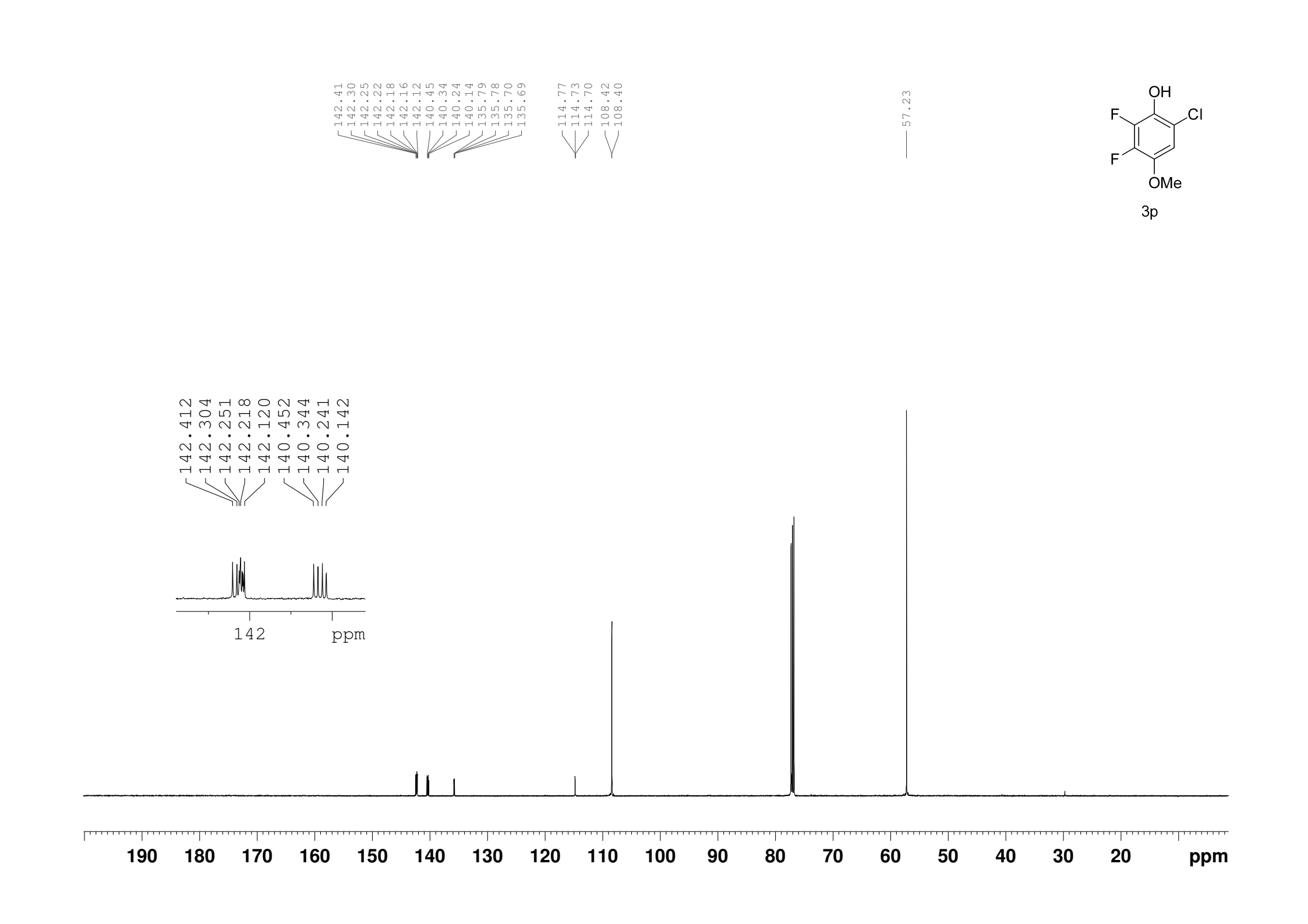

153.76
145.88
125.49
115.71
110.79
90.28
57.25
OH
Cl
I
OMe
3n'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

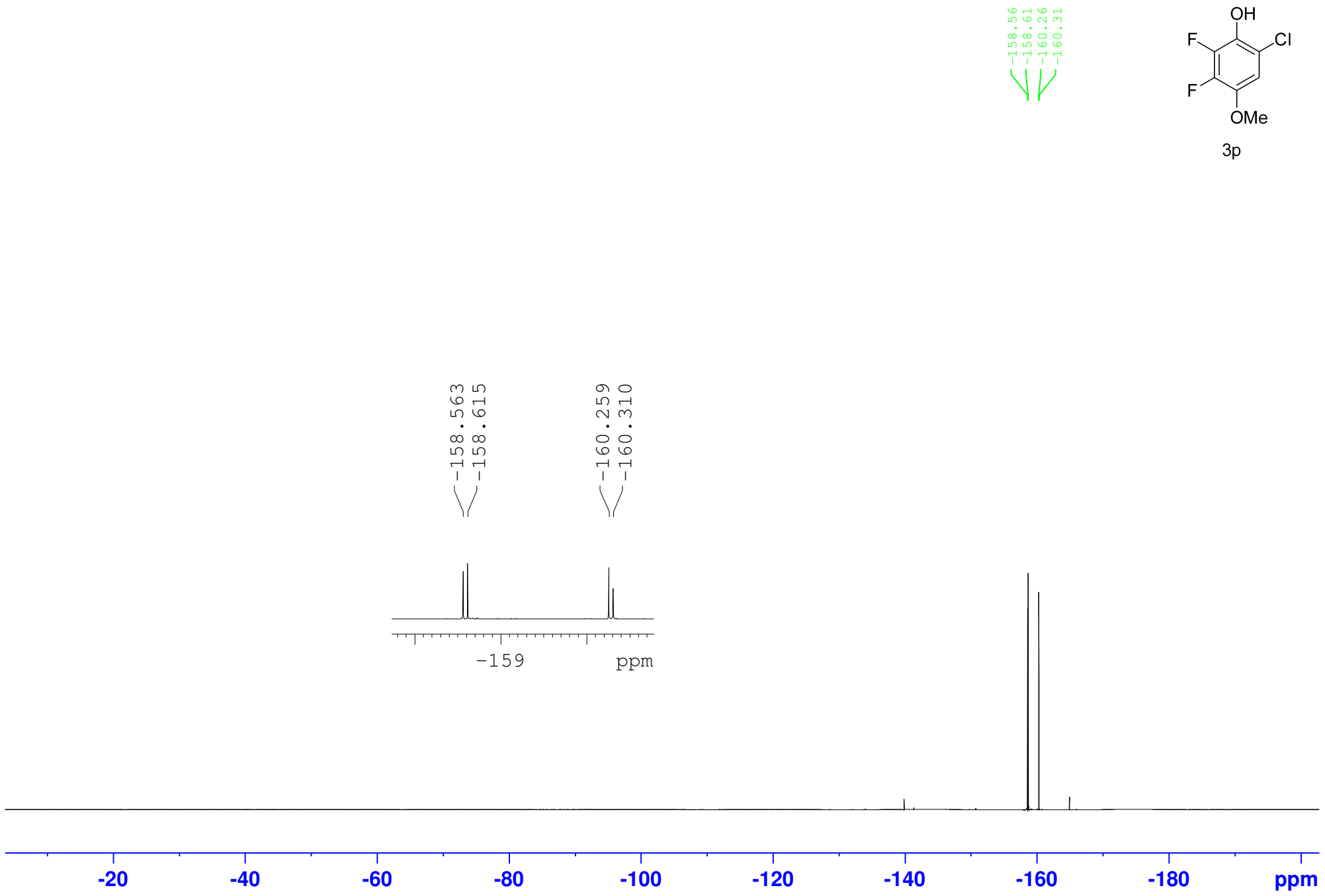

6.768
6.753
6.745
6.730
5.206
3.844
OH
F
Cl
F
OMe
3o
6.8
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
0.91
3.15

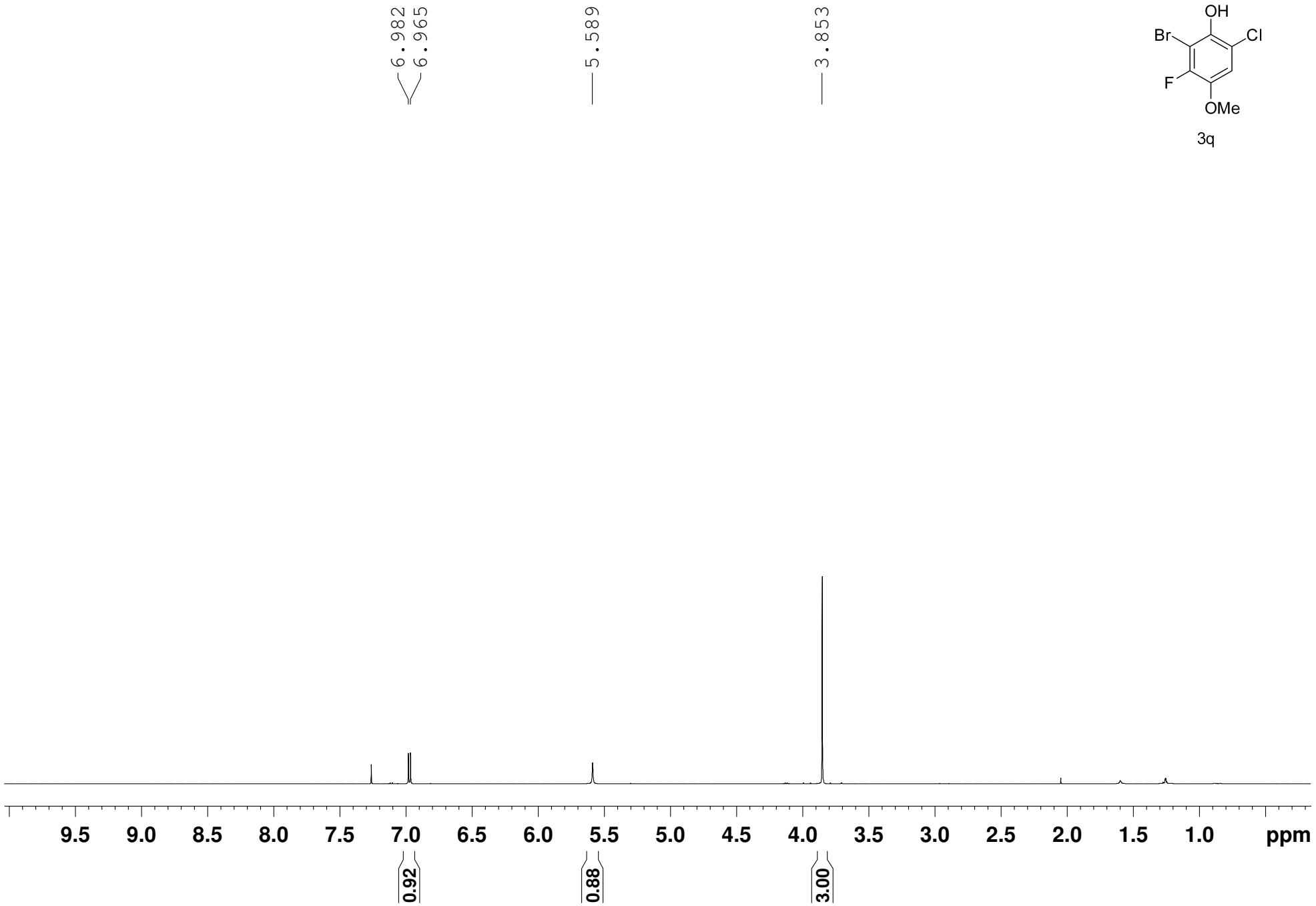

147.40
147.36
146.57
146.49
145.49
145.45
144.58
144.50
141.30
141.22
141.20
141.12
134.67
134.54
111.14
111.10
110.99
110.95
101.20
101.18
101.01
101.00
57.32
OH
F
Cl
F
OMe
3o
147.397
147.359
146.574
146.494
145.488
145.451
144.579
144.498
146
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

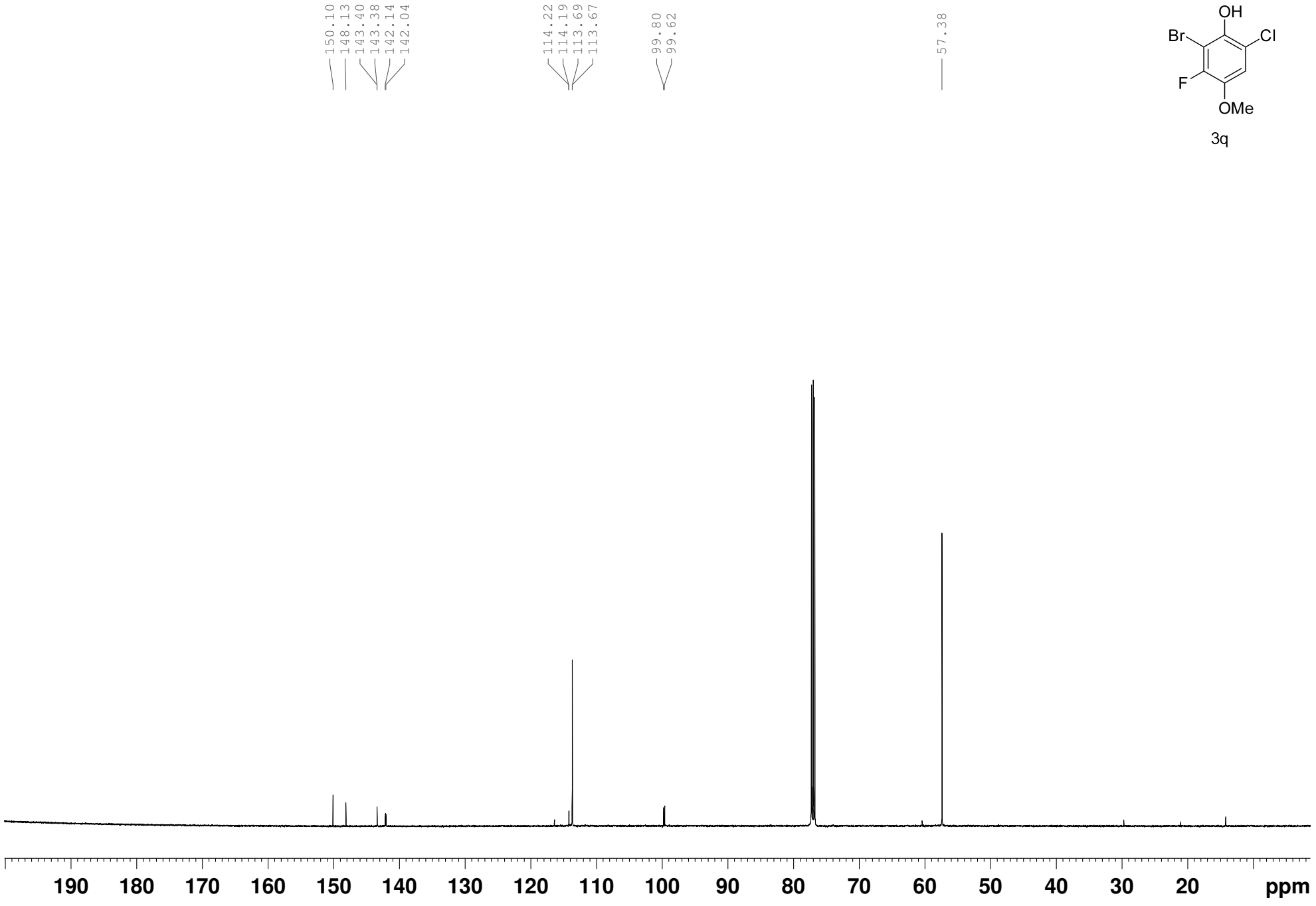

-142.50
-142.53
-142.68
-142.71
OH
F
Cl
F
OMe
3o
-142.499
-142.529
-142.681
-142.711
-142.5
ppm
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

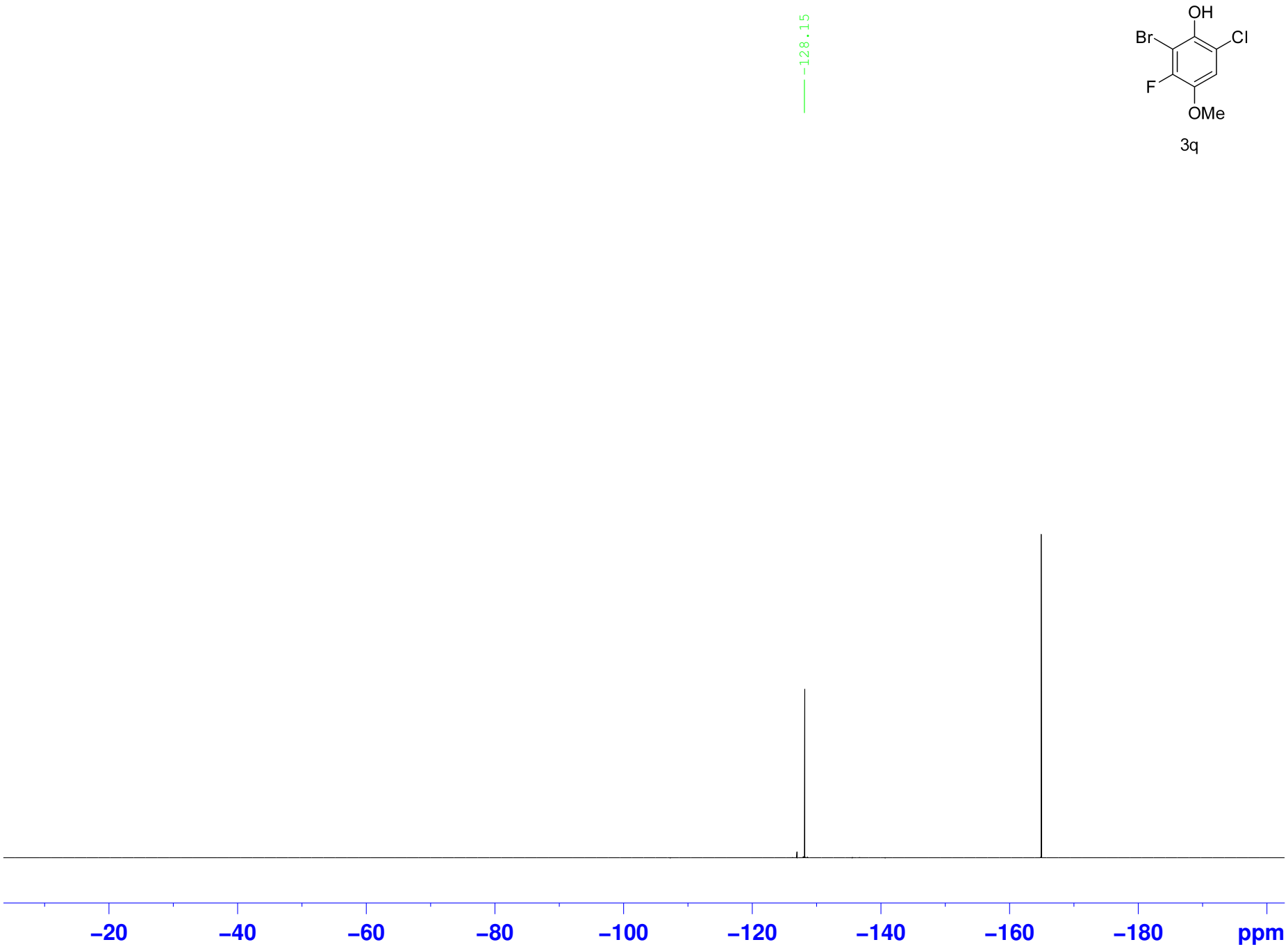

6.757
6.752
6.742
6.737
5.397
3.851
OH
F
Cl
F
OMe
3p
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
0.93
3.00

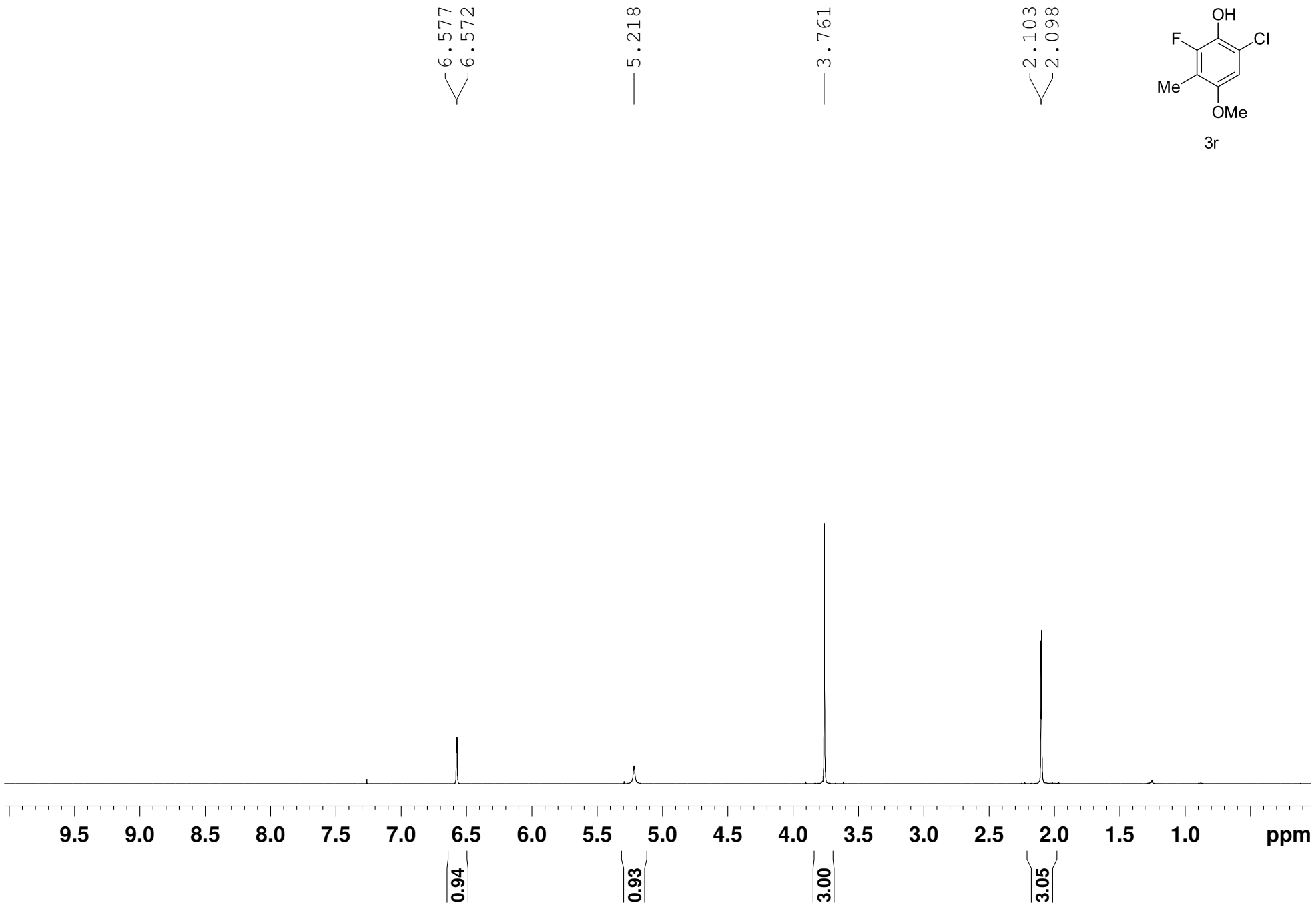

142.41
142.30
142.25
142.22
142.18
142.16
142.12
140.45
140.34
140.24
140.14
135.79
135.78
135.70
135.69
114.77
114.73
114.70
108.42
108.40
57.23
OH
F
Cl
F
OMe
3p
142.412
142.304
142.251
142.218
142.120
140.452
140.344
140.241
140.142
142
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

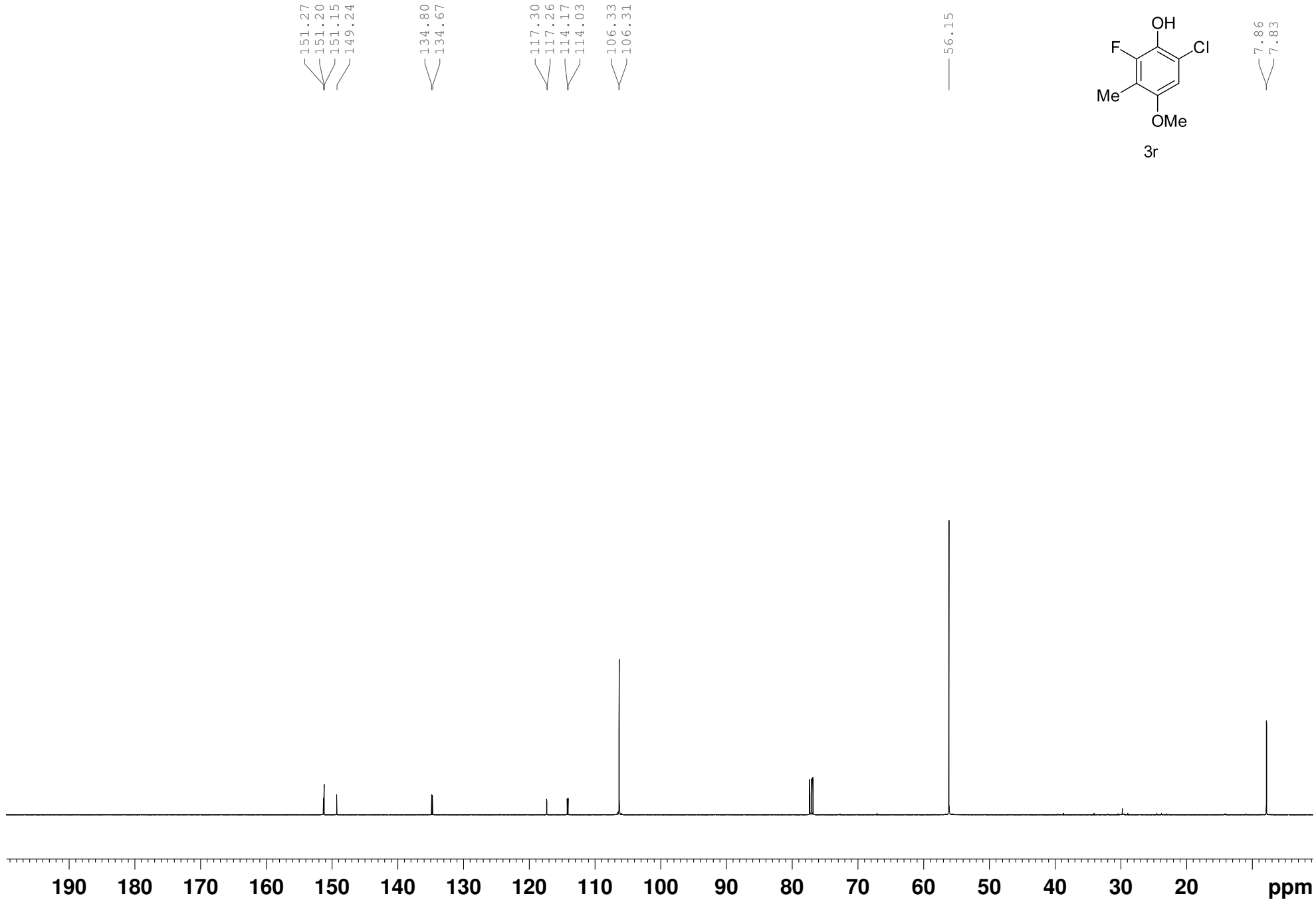

-158.56
-158.61
-160.26
-160.31
OH
F
Cl
F
OMe
3p
-158.563
-158.615
-160.259
-160.310
-159
ppm
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


6.982
6.965
5.589
3.853
OH
Br
Cl
F
OMe
3q
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.92
0.88
3.00

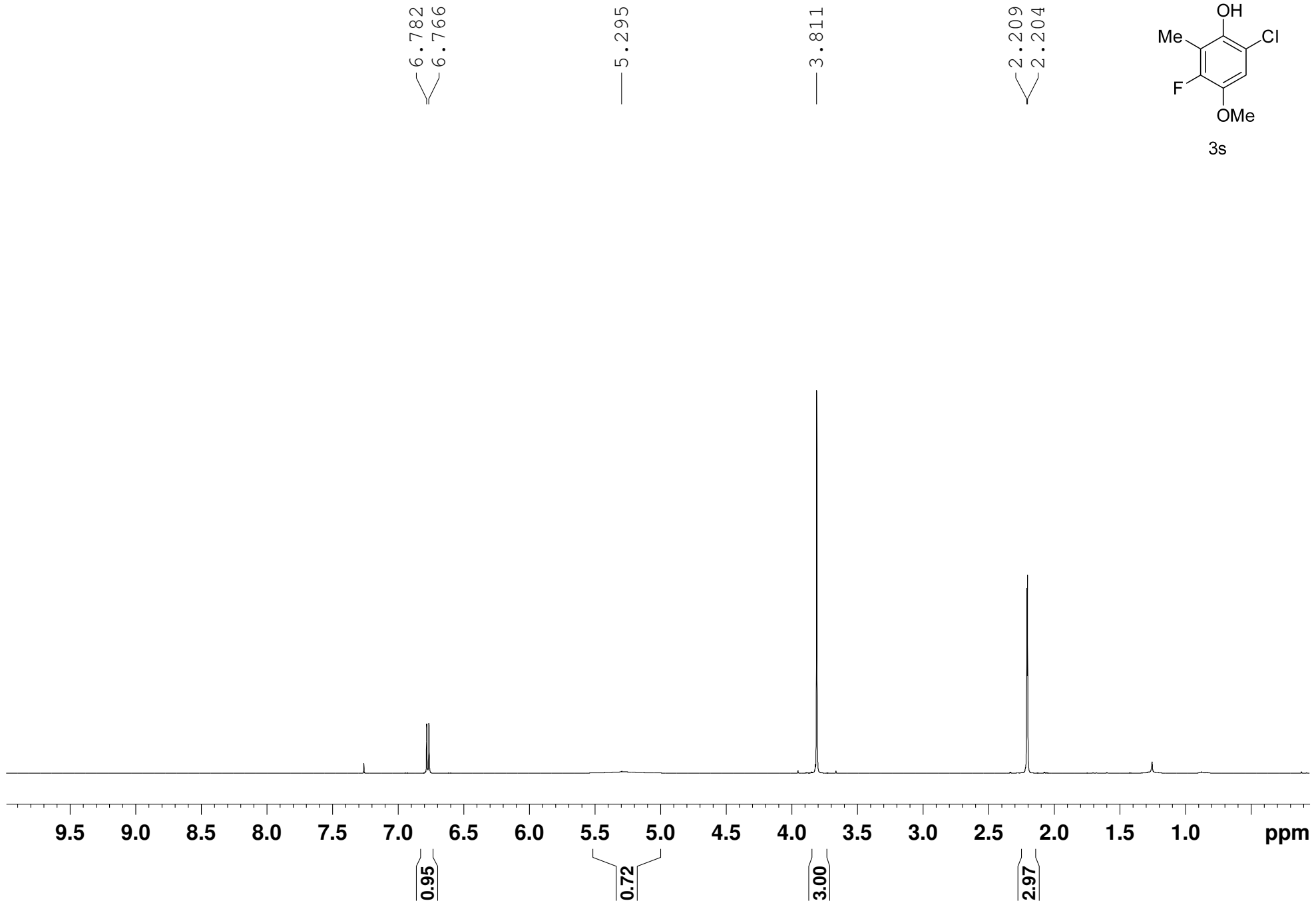

150.10
148.13
143.40
143.38
142.14
142.04
114.22
114.19
113.69
113.67
99.80
99.62
57.38
OH
Br
Cl
F
OMe
3q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-128.15
OH
Br
Cl
F
OMe
3q
–20
–40
–60
–80
–100
–120
–140
–160
–180
ppm


6.577
6.572
5.218
3.761
2.103
2.098
OH
F
Cl
Me
OMe
3r
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.94
0.93
3.00
3.05


151.27
151.20
151.15
149.24
134.80
134.67
117.30
117.26
114.17
114.03
106.33
106.31
56.15
7.86
7.83
OH
F
Cl
Me
OMe
3r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-139.80
OH
F
Cl
Me
OMe
3r
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm


6.782
6.766
5.295
3.811
2.209
2.204
OH
Me
Cl
F
OMe
3s
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
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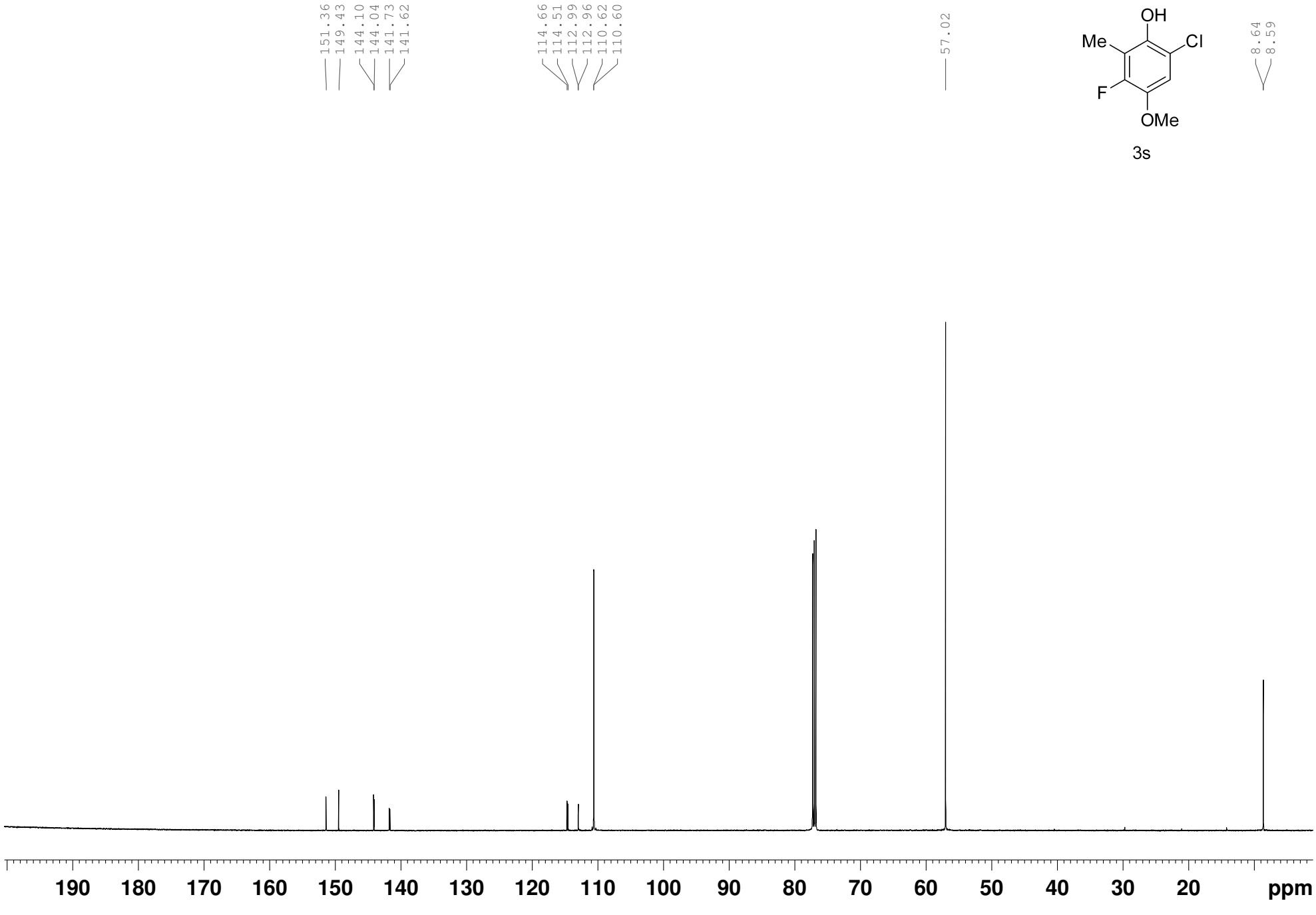
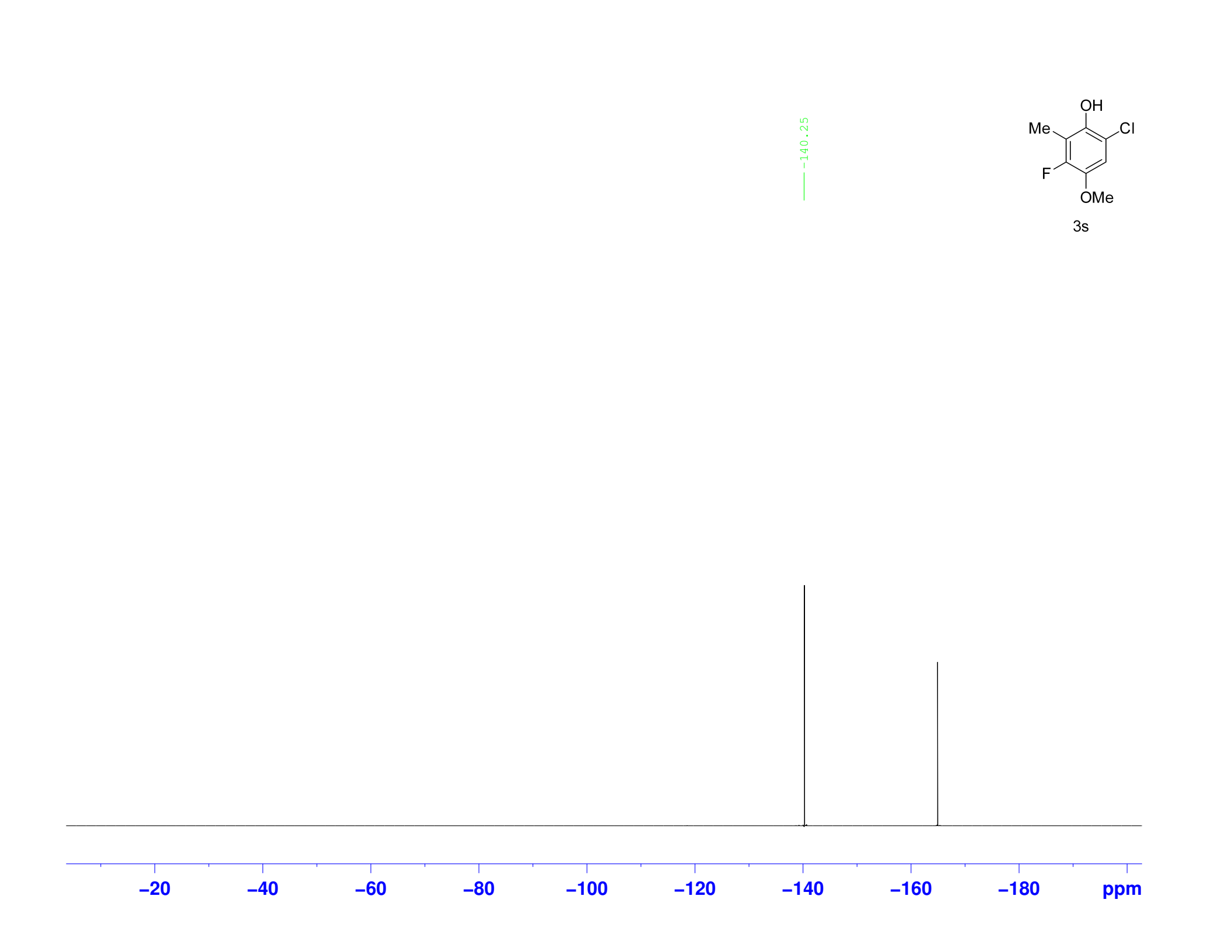
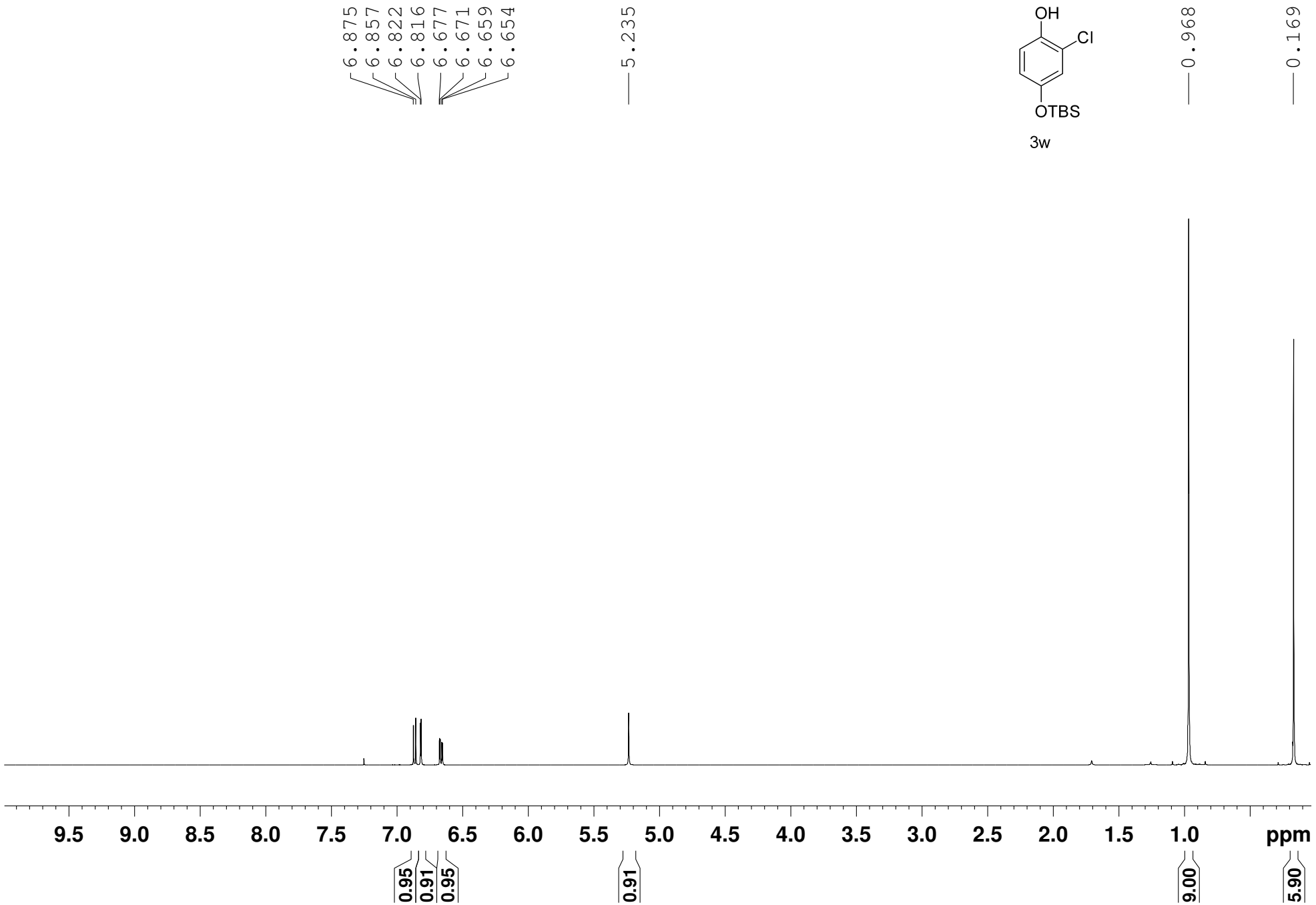
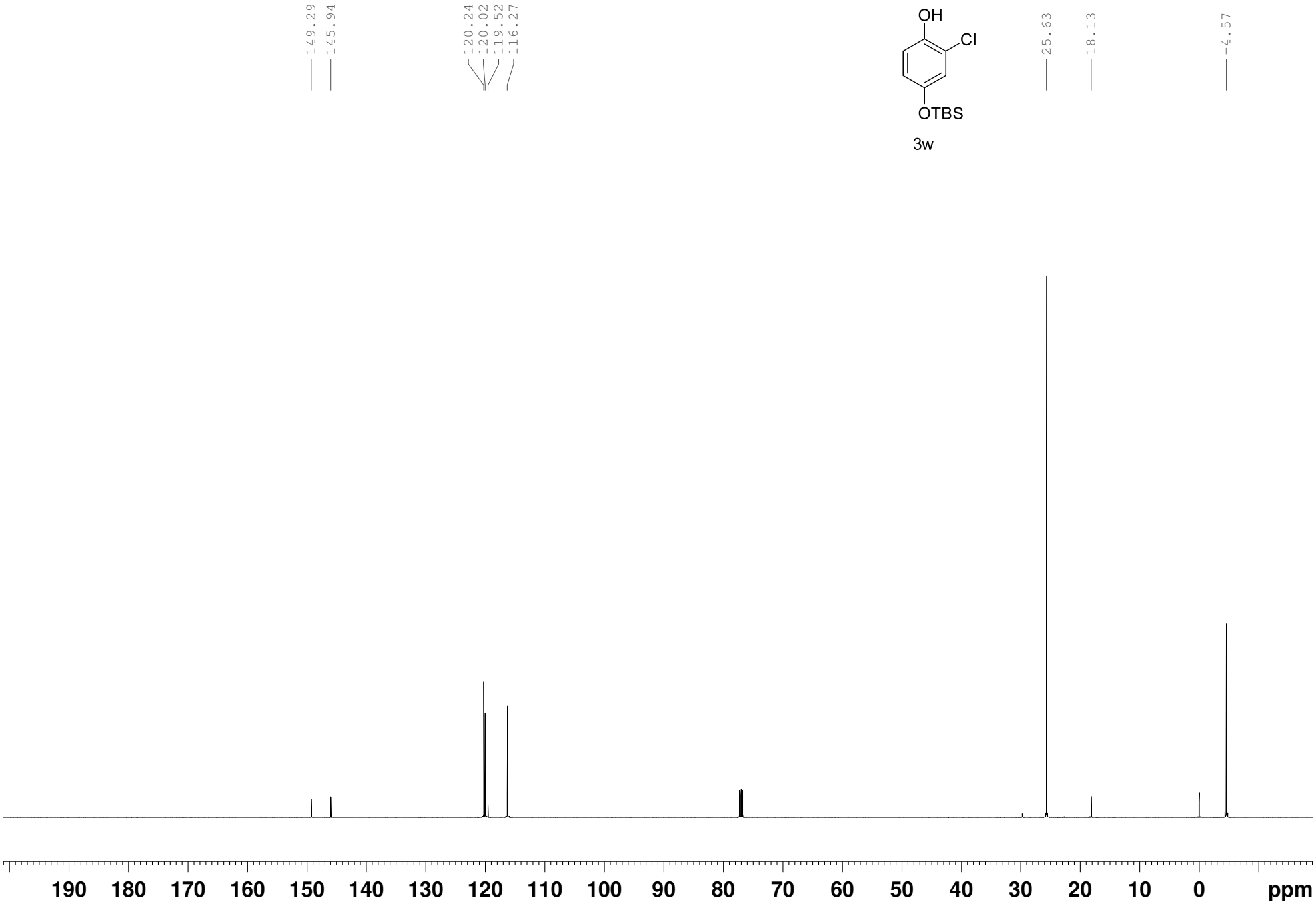
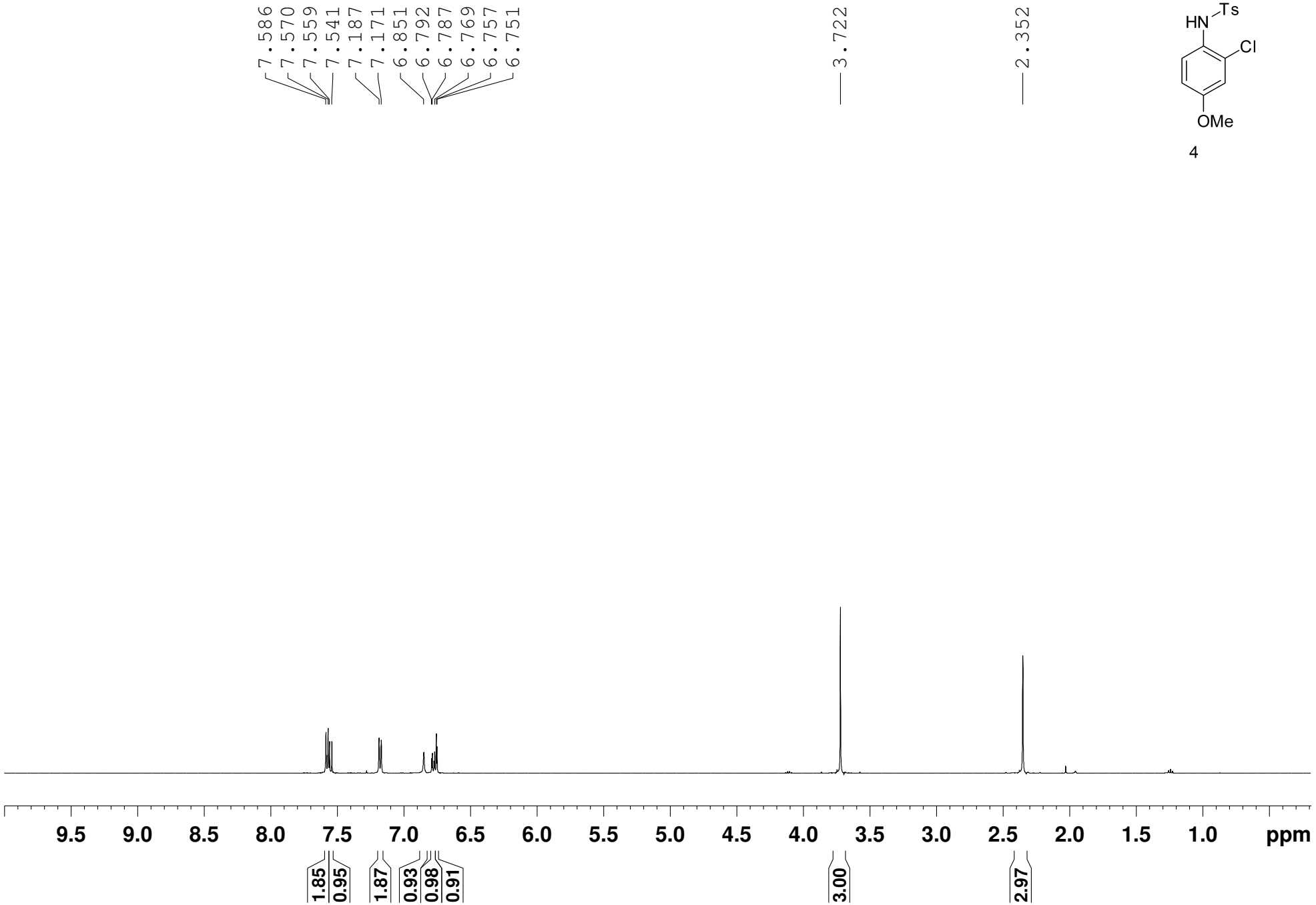
0.72
3.00
2.97

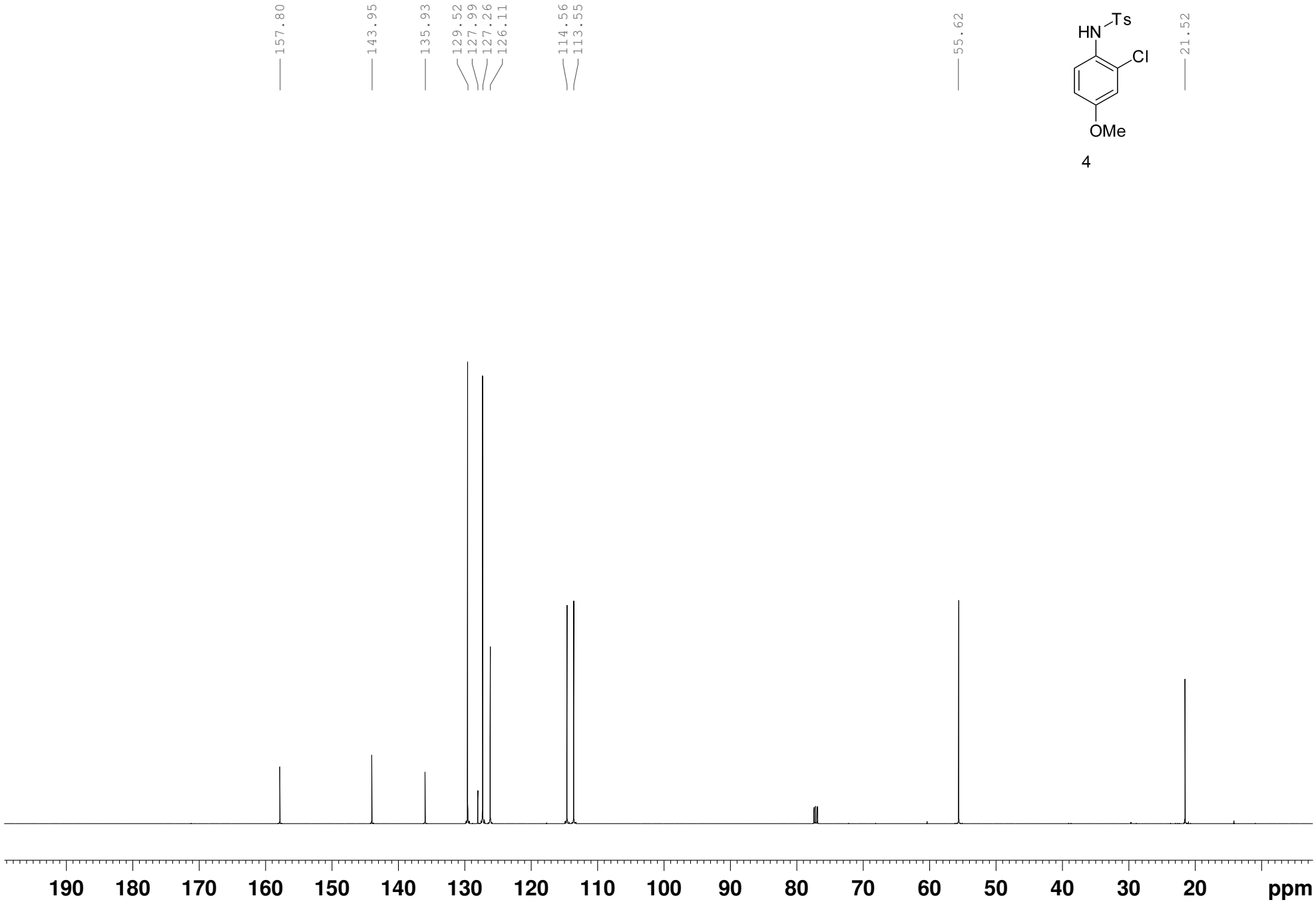

151.36
149.43
144.10
144.04
141.73
141.62
114.66
114.51
112.99
112.96
110.62
110.60
57.02
8.64
8.59
OH
Me
Cl
F
OMe
3s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

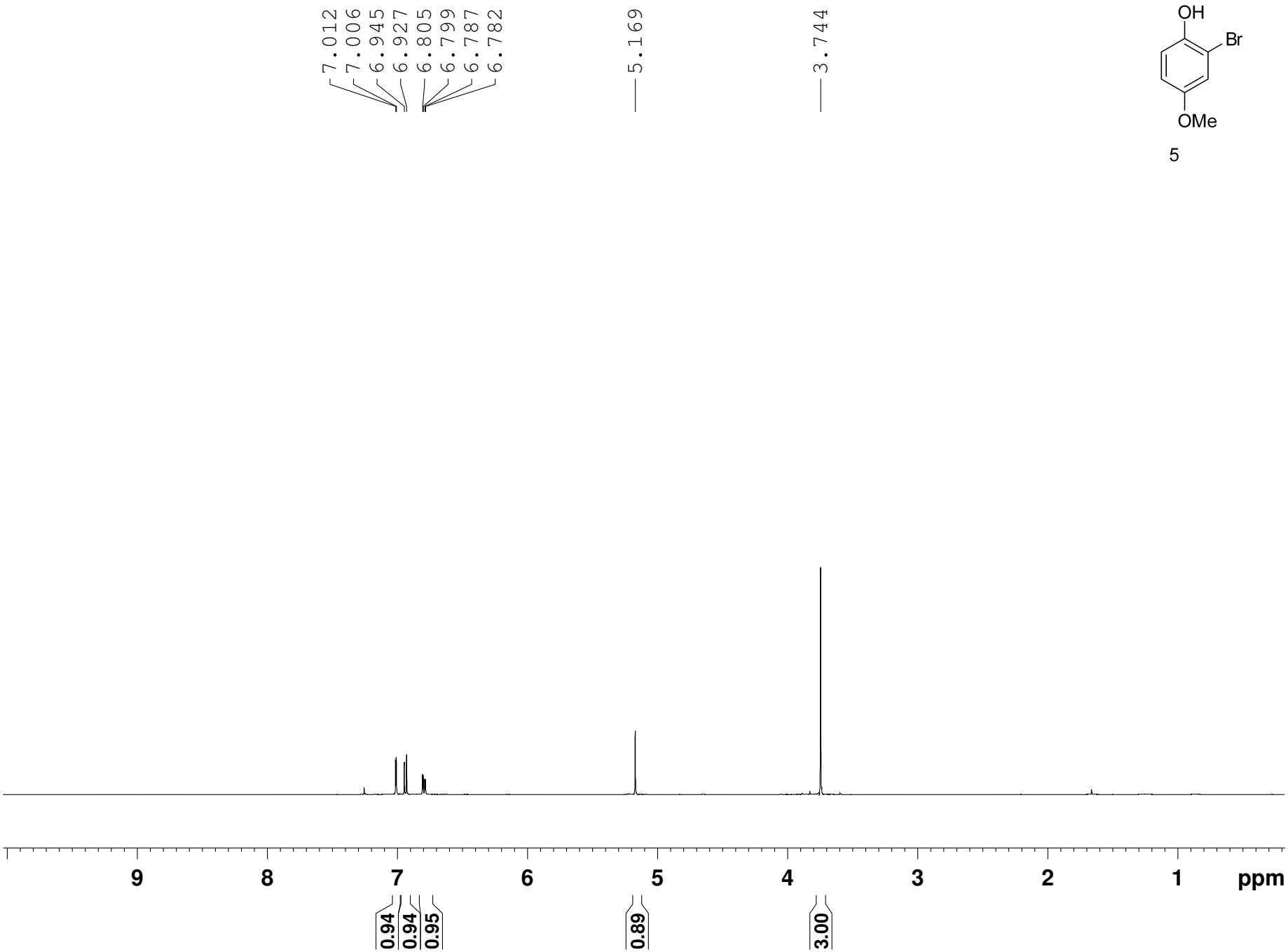

-140.25
OH
Me
Cl
F
OMe
3s
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm

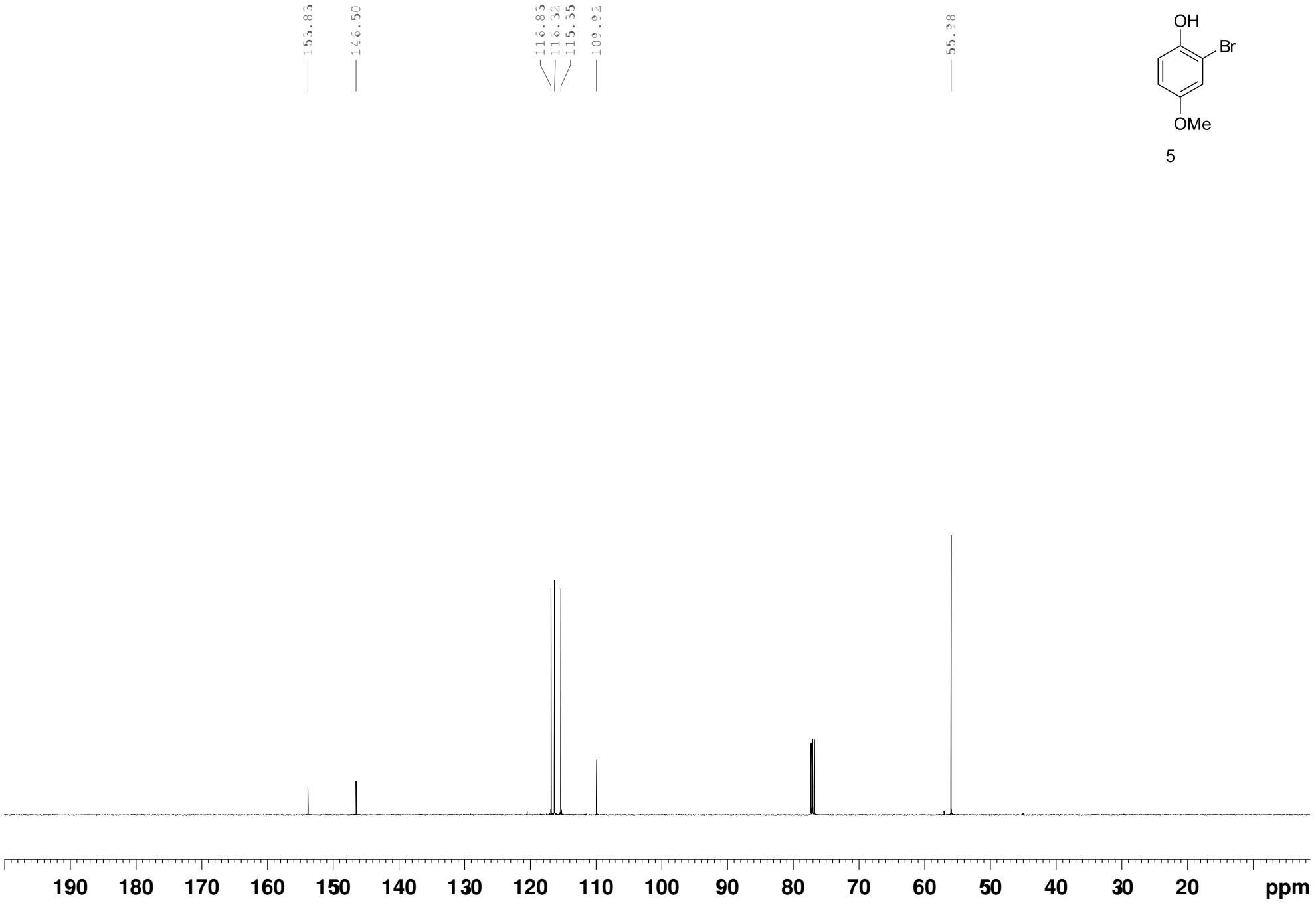

6.875
6.857
6.822
6.816
6.677
6.671
6.659
6.654
5.235
OH
Cl
OTBS
3w
0.968
0.169
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.95
0.91
0.95
0.91
9.00
5.90


149.29
145.94
120.24
120.02
119.52
116.27
OH
Cl
OTBS
25.63
18.13
-4.57
3w
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

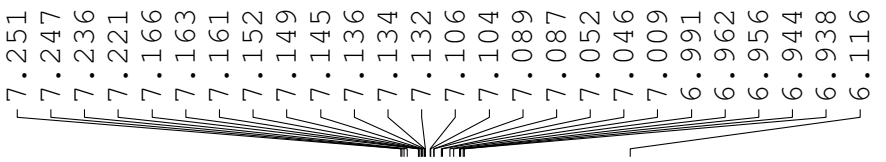

7.586
7.570
7.559
7.541
7.187
7.171
6.851
6.792
6.787
6.769
6.757
6.751
3.722
2.352
HN
Ts
Cl
OMe
4
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.85
0.95
1.87
0.93
0.98
0.91
3.00
2.97

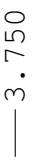

157.80
143.95
135.93
129.52
127.99
127.26
126.11
114.56
113.55
55.62
21.52
HN
Ts
Cl
OMe
4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

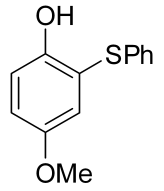

7.012
7.006
6.945
6.927
6.805
6.799
6.787
6.782
5.169
3.744
OH
Br
OMe
5
9
8
7
6
5
4
3
2
1
ppm
0.94
0.94
0.95
0.89
3.00


153.83
146.50
116.83
116.32
115.35
109.92
55.98
OH
Br
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

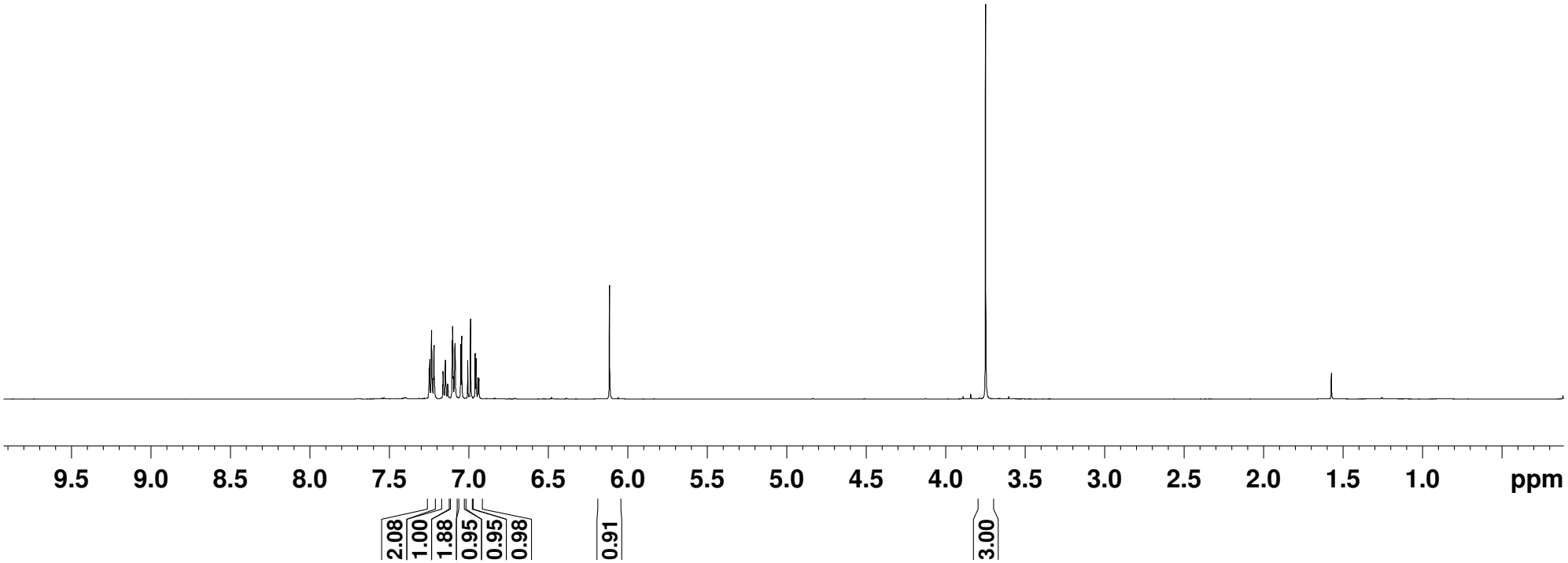
5

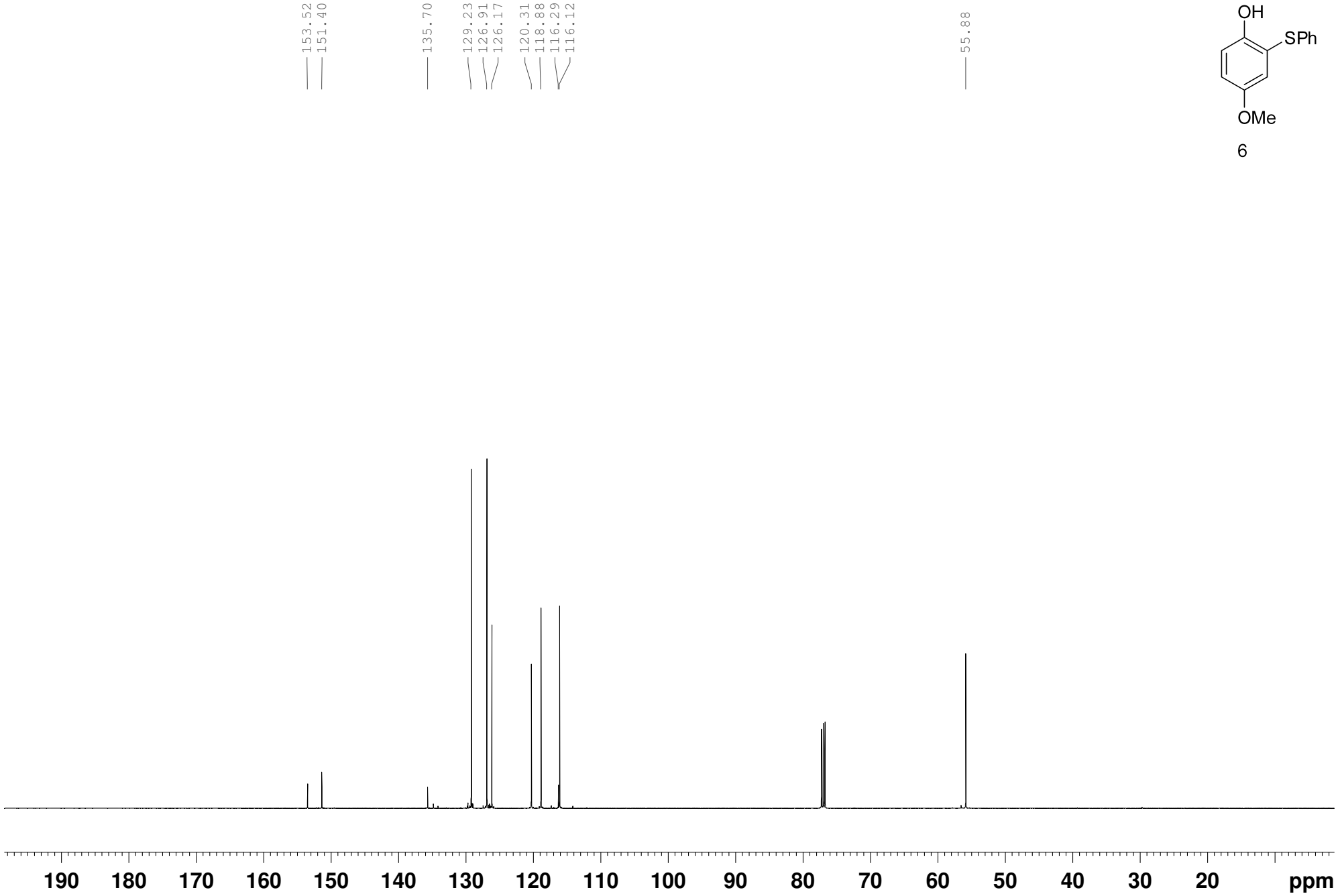

7.251
7.247
7.236
7.221
7.166
7.163
7.161
7.152
7.149
7.145
7.136
7.134
7.132
7.106
7.104
7.089
7.087
7.052
7.046
7.009
6.991
6.962
6.956
6.944
6.938
6.116

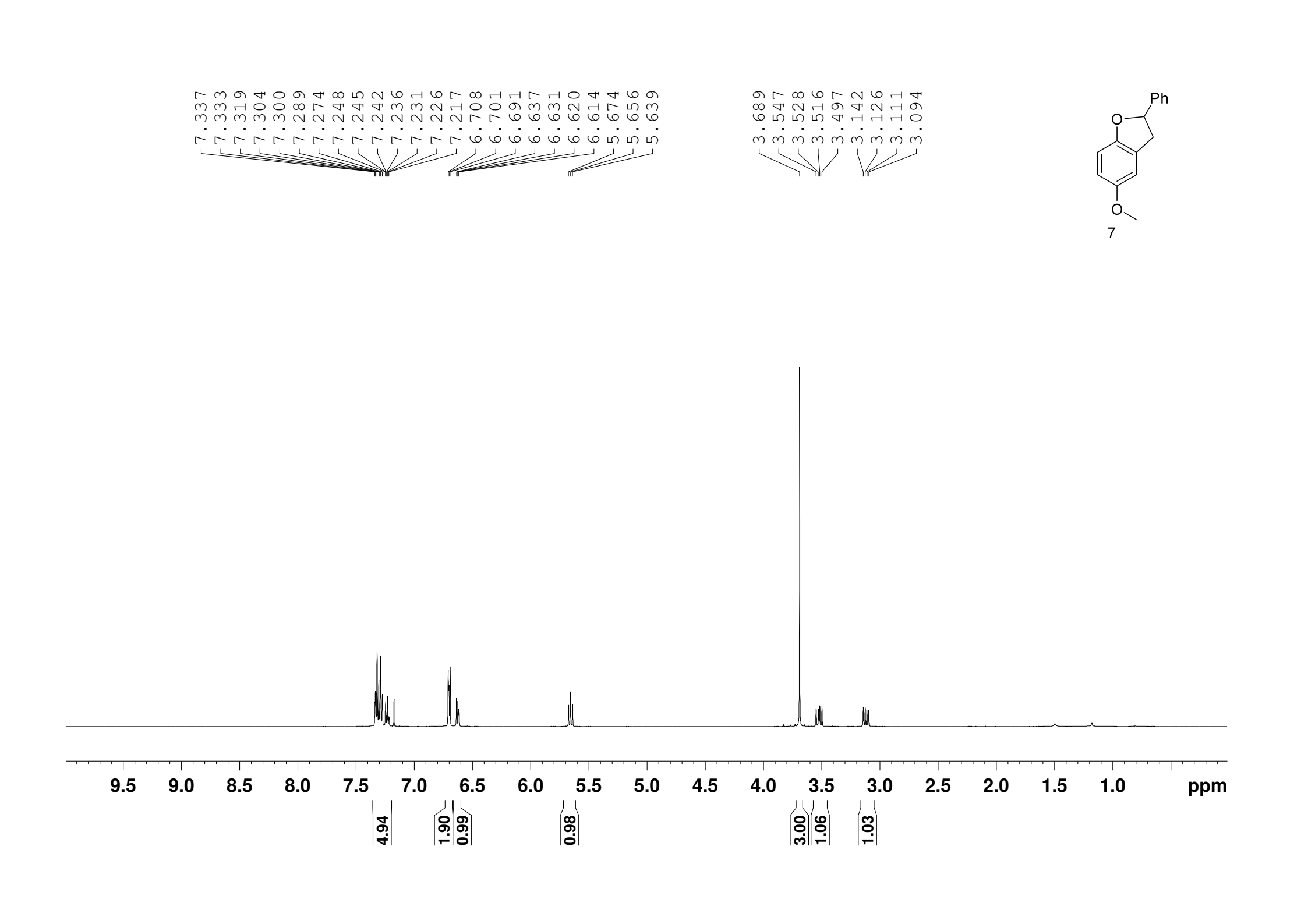

3.750

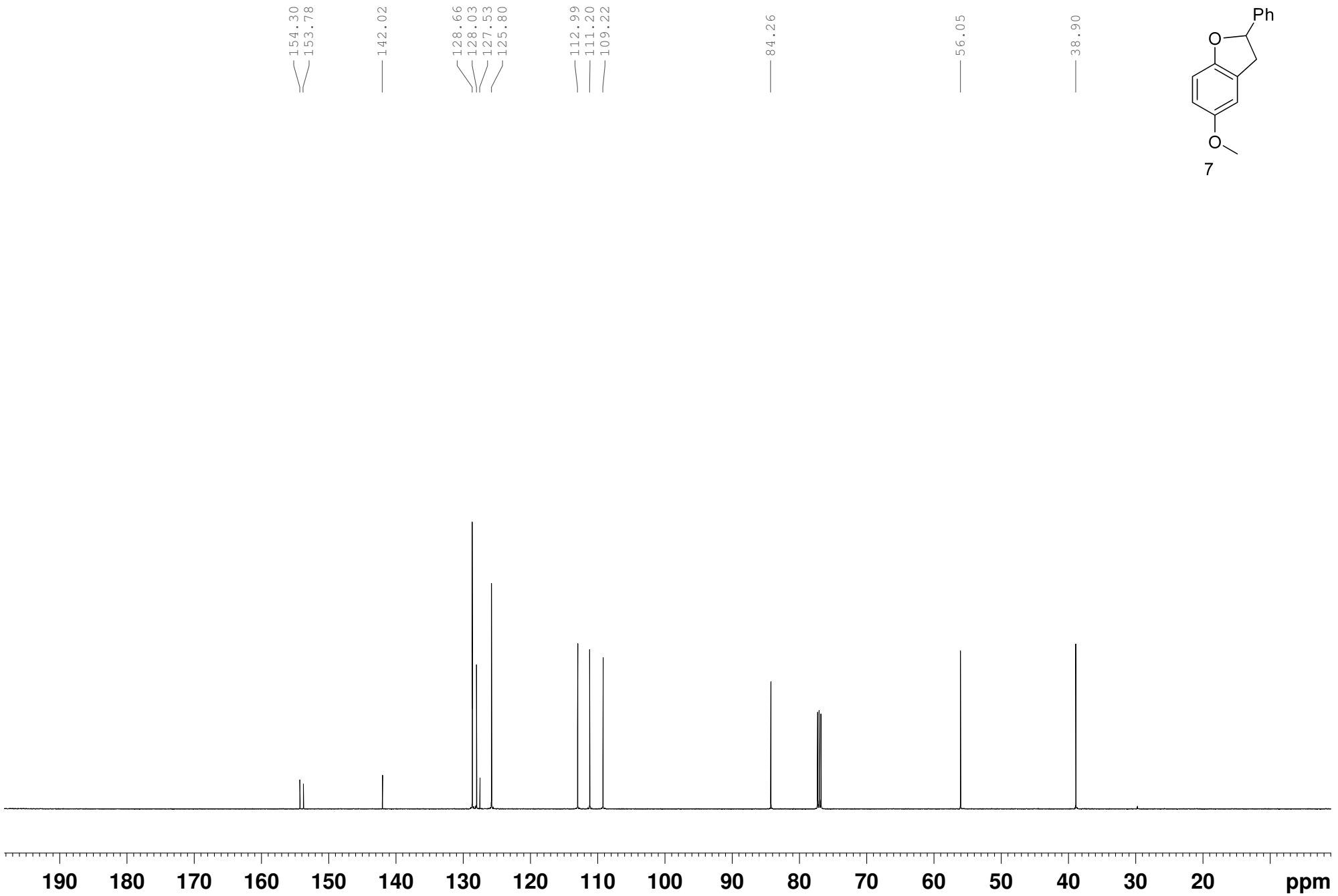

OH
SPh
OMe

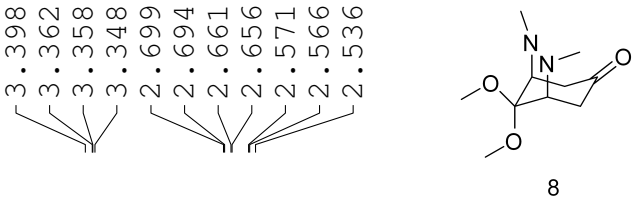
6


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.08
1.00
1.88
0.95
0.95
0.98
0.91
3.00

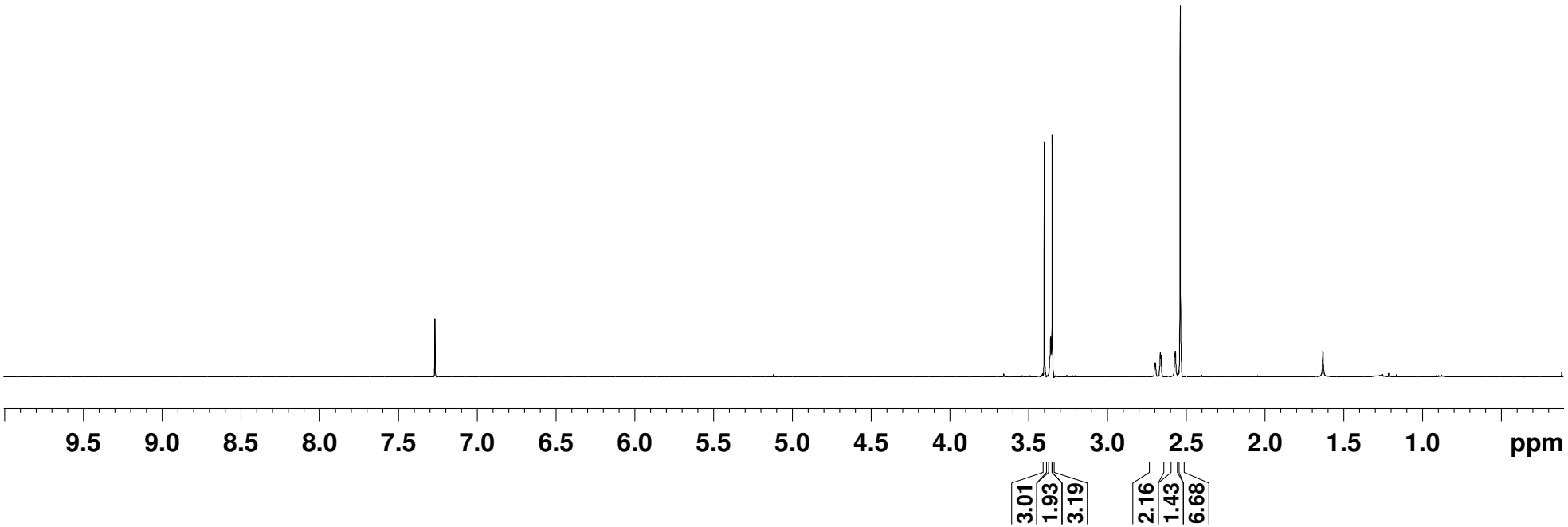

153.52
151.40
135.70
129.23
126.91
126.17
120.31
118.88
116.29
116.12
55.88
OH
SPh
OMe
6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

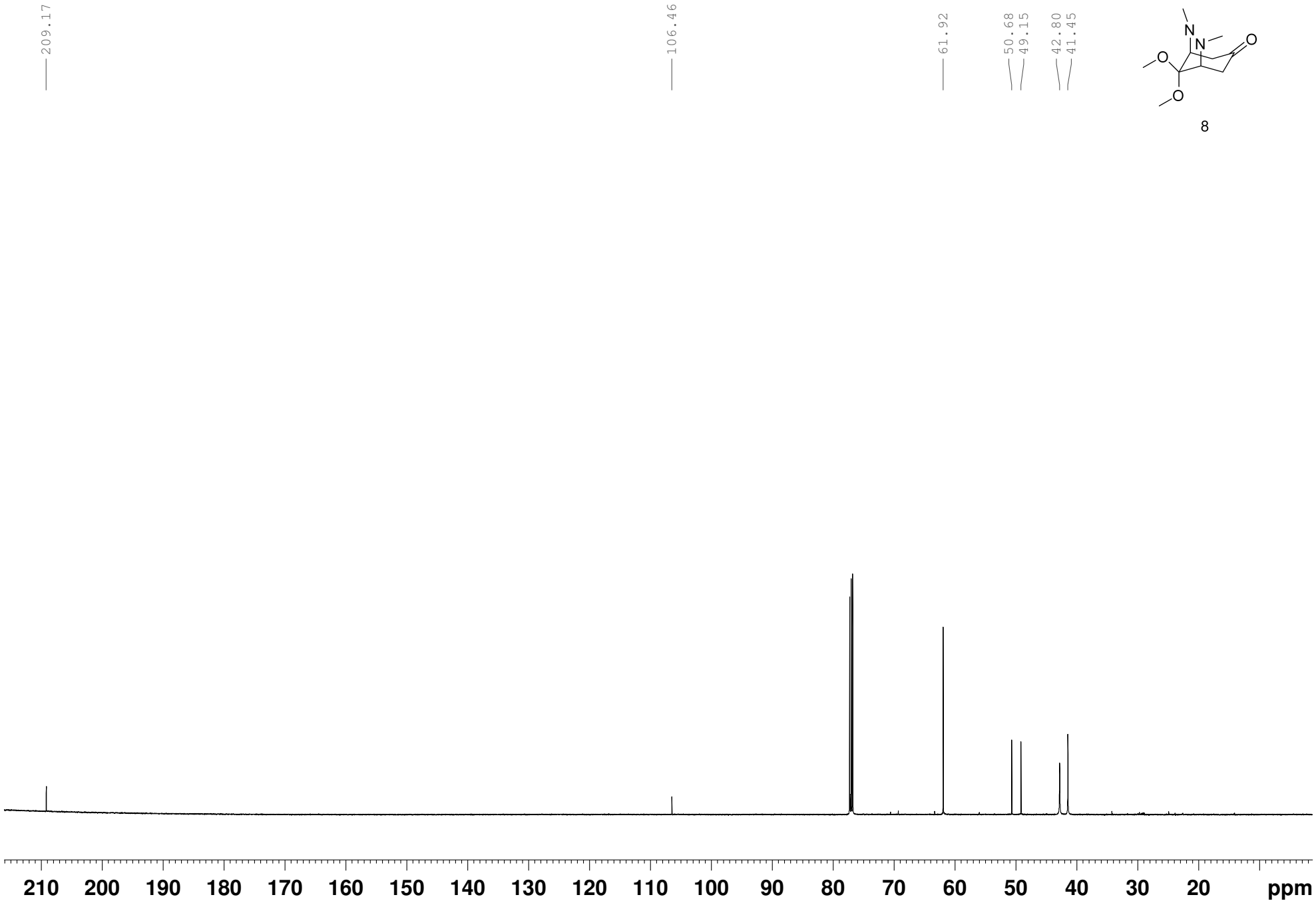

7.337
7.333
7.319
7.304
7.300
7.289
7.274
7.248
7.245
7.242
7.236
7.231
7.226
7.217
6.708
6.701
6.691
6.637
6.631
6.620
6.614
5.674
5.656
5.639
3.689
3.547
3.528
3.516
3.497
3.142
3.126
3.111
3.094
Ph
O
O
7
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
4.94
1.90
0.99
0.98
3.00
1.06
1.03

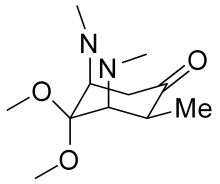

154.30
153.78
142.02
128.66
128.03
127.53
125.80
112.99
111.20
109.22
84.26
56.05
38.90
Ph
O
O
7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


3.398
3.362
3.358
3.348
2.699
2.694
2.661
2.656
2.571
2.566
2.536
N
N
O
O
O

8

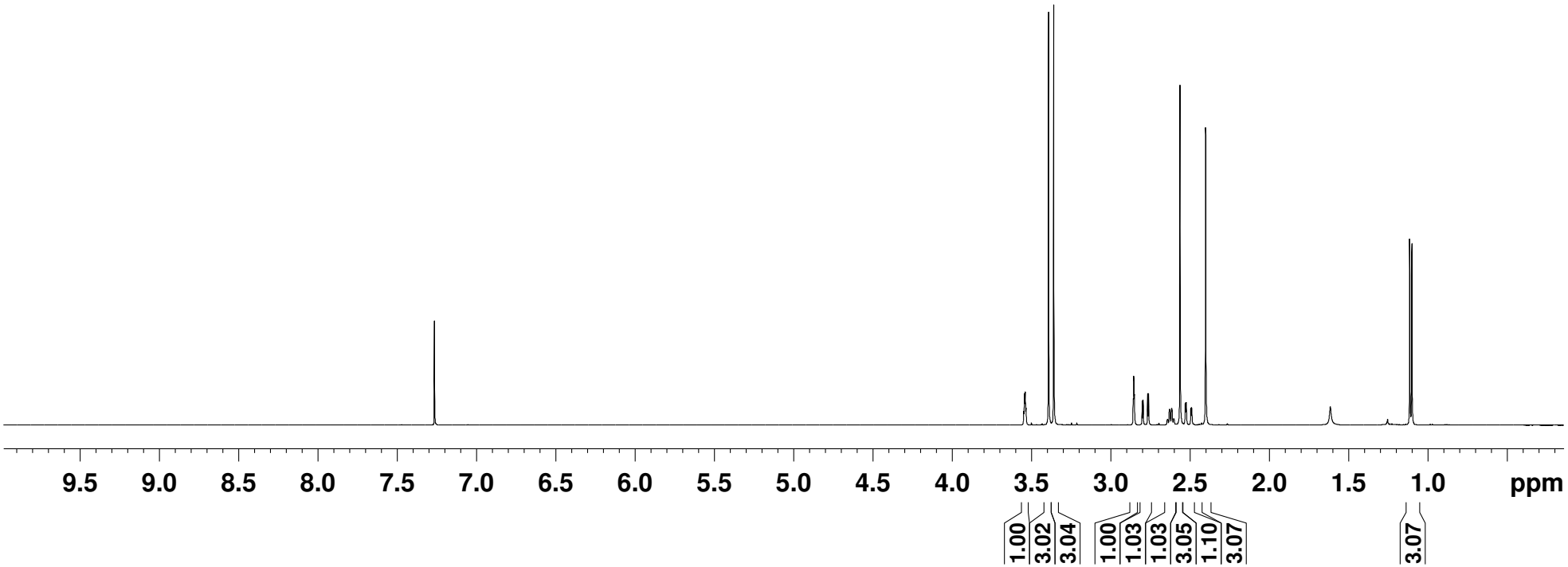

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
3.01
1.93
3.19
2.16
1.43
6.68

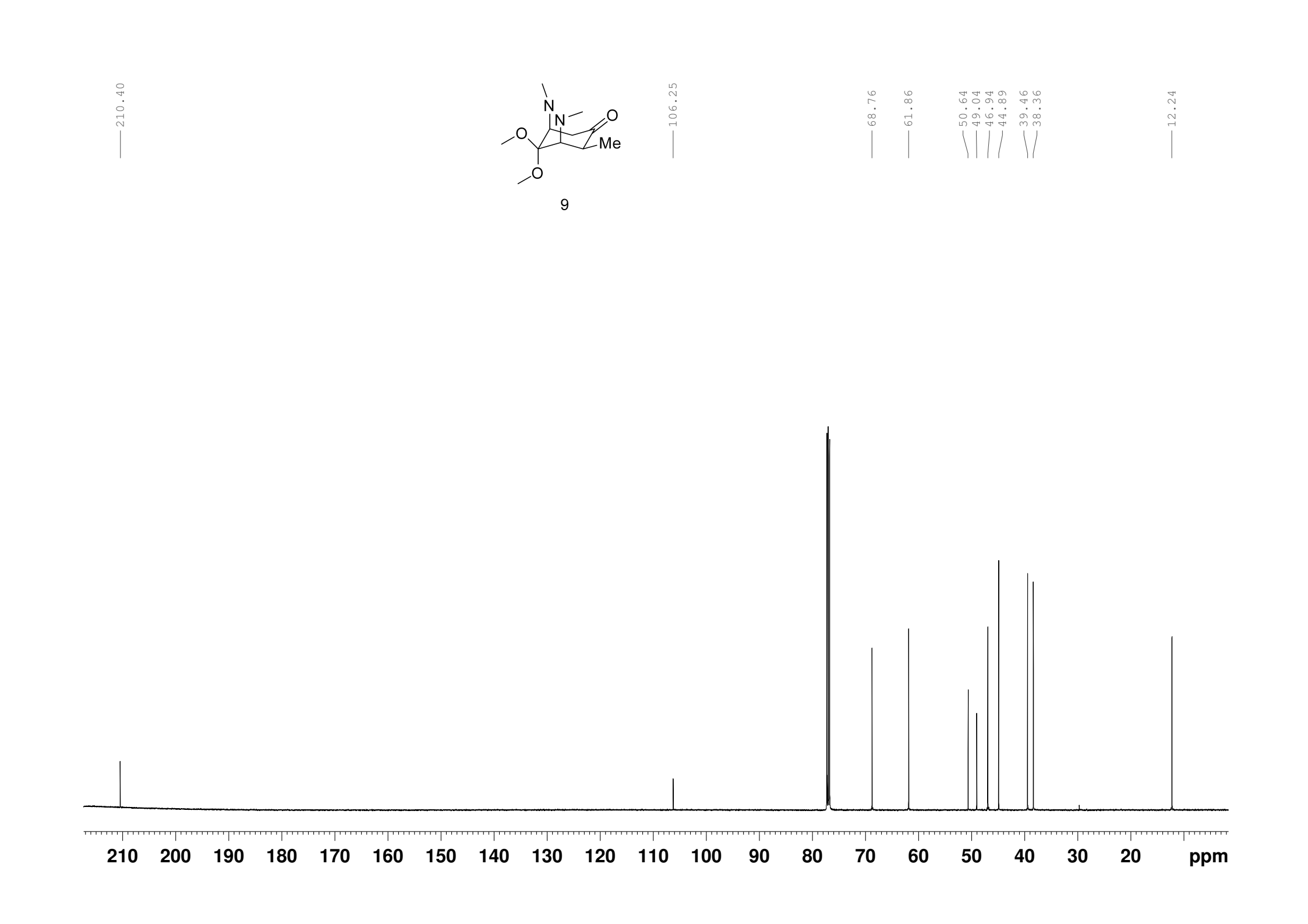

209.17
106.46
61.92
50.68
49.15
42.80
41.45
N
N
O
O
O
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

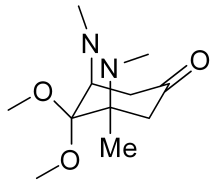


9

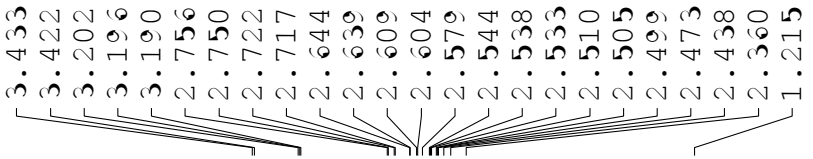
3.549
3.544
3.540
3.534
3.393
3.360
2.858
2.855
2.851
2.802
2.796
2.768
2.762
2.643
2.629
2.616
2.603
2.564
2.530
2.529
2.525
2.523
2.496
2.494
2.490
2.489
2.402
1.115
1.101

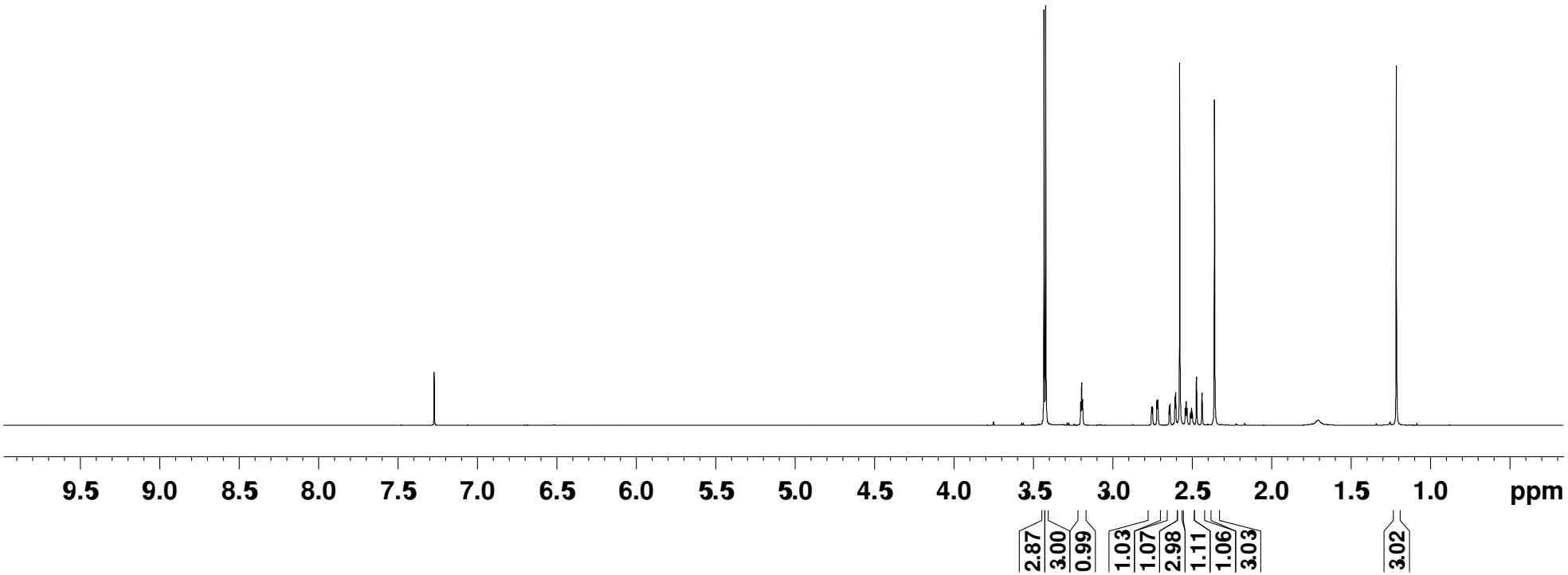



210.40
106.25
68.76
61.86
50.64
49.04
46.94
44.89
39.46
38.36
12.24
N
N
O
O
O
Me
9
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

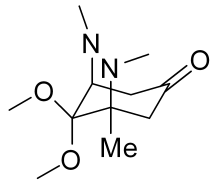

N
N
O
O
O
Me

10


3.433
3.422
3.202
3.196
3.190
2.756
2.750
2.722
2.717
2.644
2.639
2.609
2.604
2.579
2.544
2.538
2.533
2.510
2.505
2.499
2.473
2.438
2.360
1.215


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.87
3.00
0.99
1.03
1.07
2.98
1.11
1.06
3.03
3.02

209.27



10

105.06

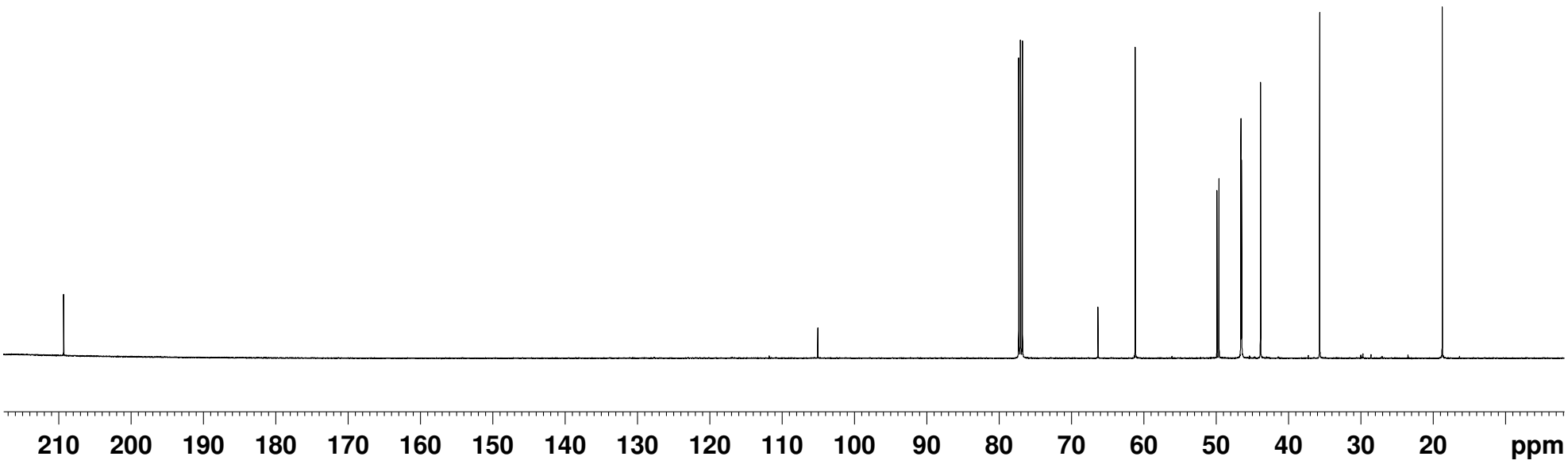
66.34

61.17

49.89
49.61
46.58
46.48
43.86

35.69

18.73



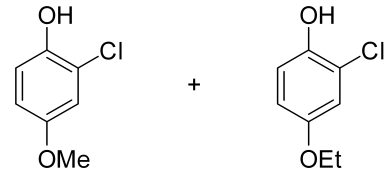
DEPT

6.931 6.913 6.874 6.869 6.755 6.750 6.738 6.732

5.180

3.974 3.961 3.947 3.933 3.751

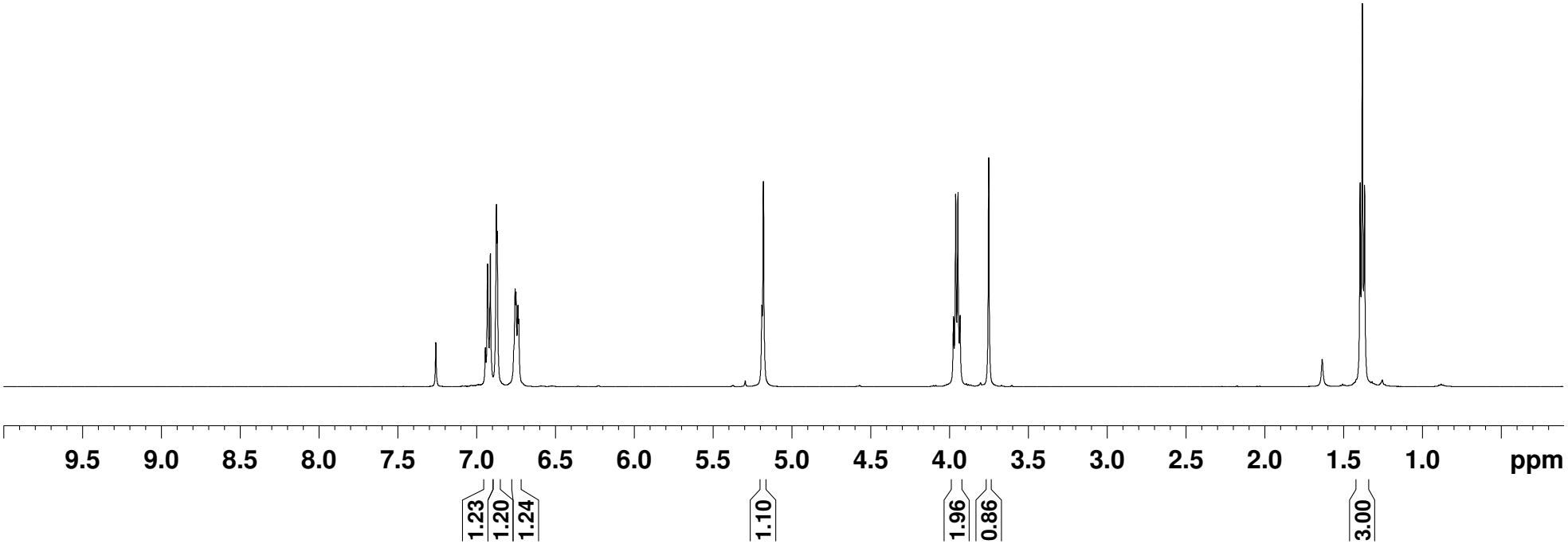
1.395 1.381 1.367



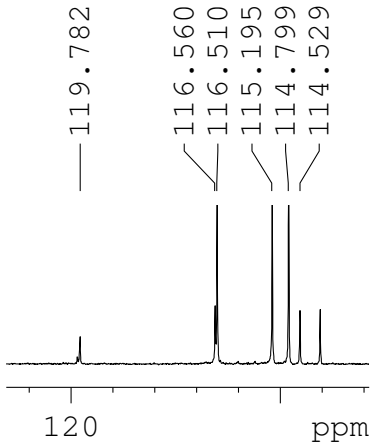
+

3a 3t

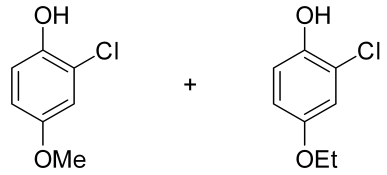
ratio 1 : 3.5



DEPT

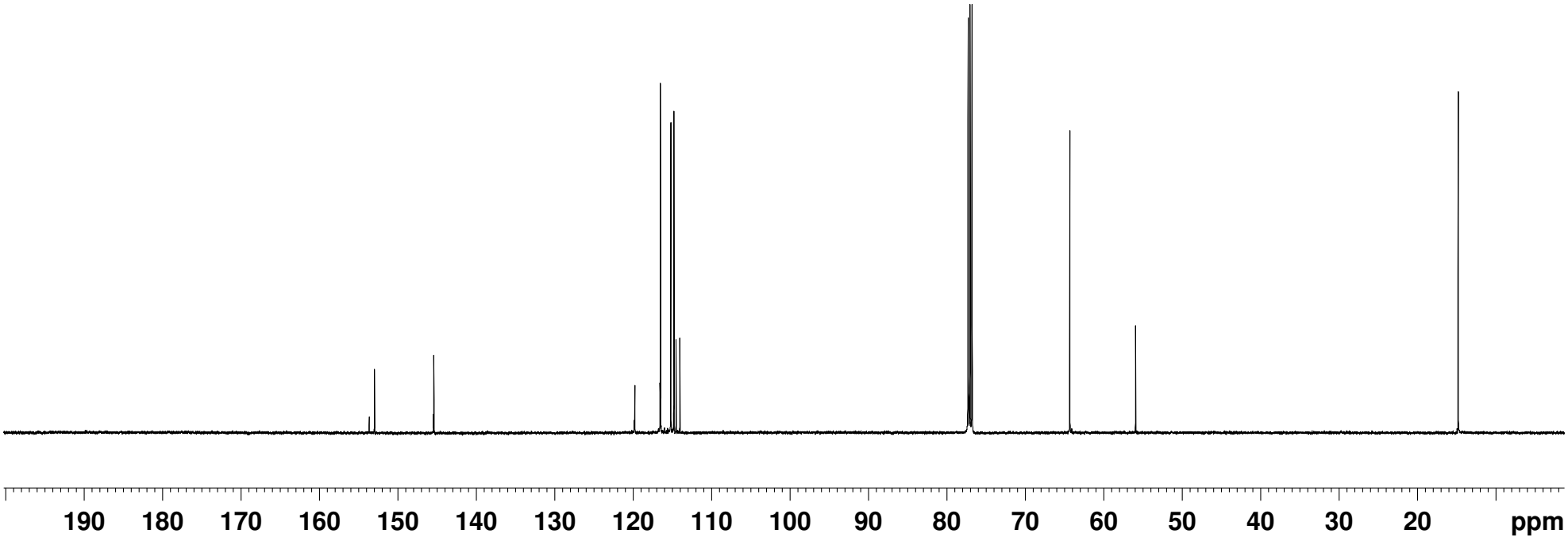


153.66
152.98
145.48
145.41
119.78
116.56
116.51
115.20
114.80
114.53
114.05
64.33
55.94
14.81

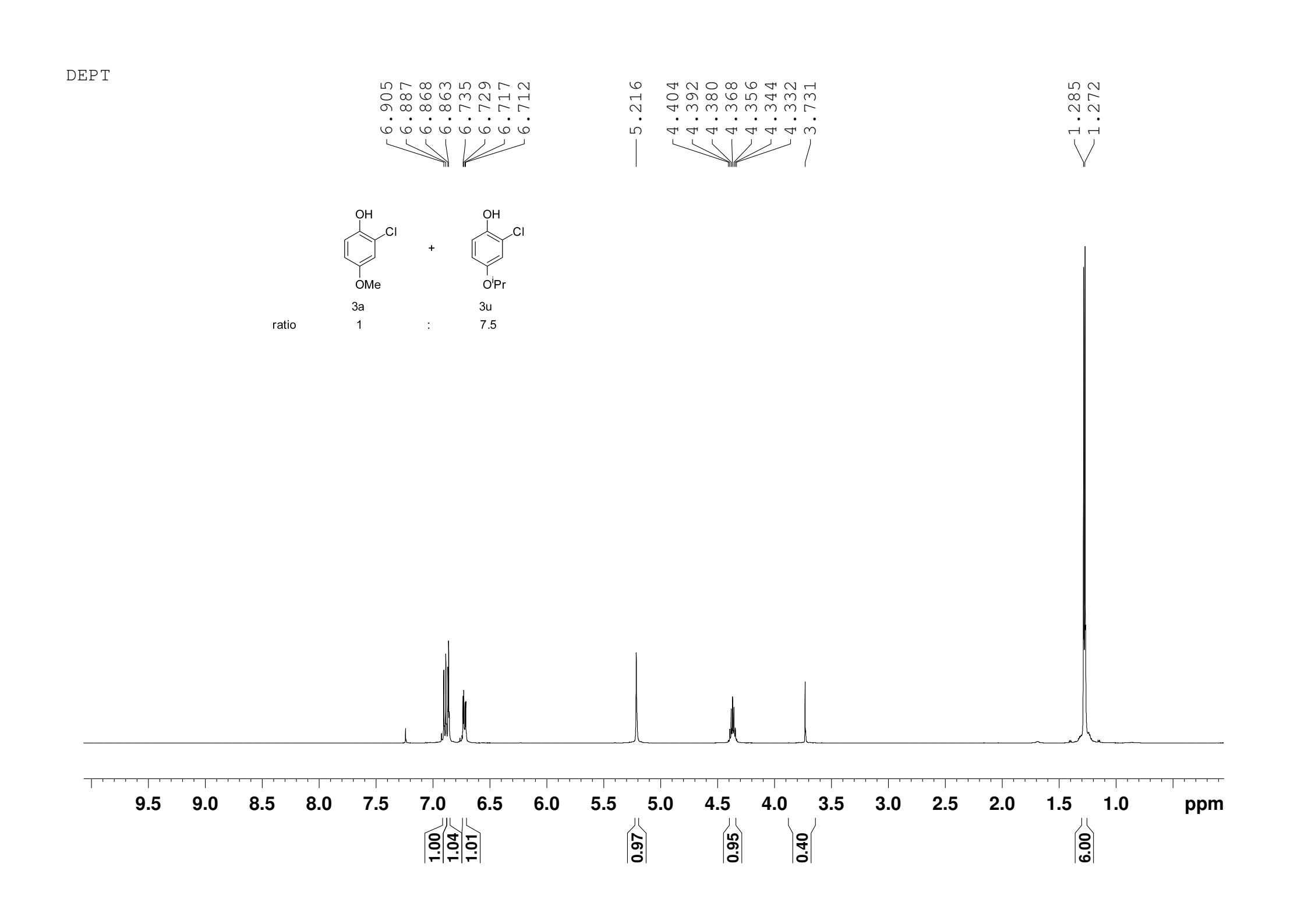


3a 3t

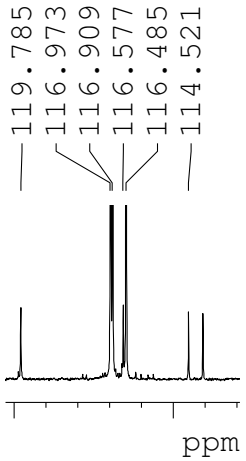
ratio 1 : 3.5



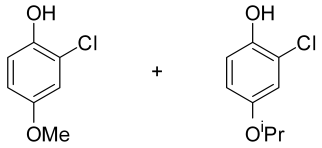
DEPT


6.905
6.887
6.868
6.863
6.735
6.729
6.717
6.712
5.216
4.404
4.392
4.380
4.368
4.356
4.344
4.332
3.731
1.285
1.272
OH
Cl
OMe
+
OH
Cl
O^iPr
3a
3u
ratio
1
:
7.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.04
1.01
0.97
0.95
0.40
6.00

DEPT

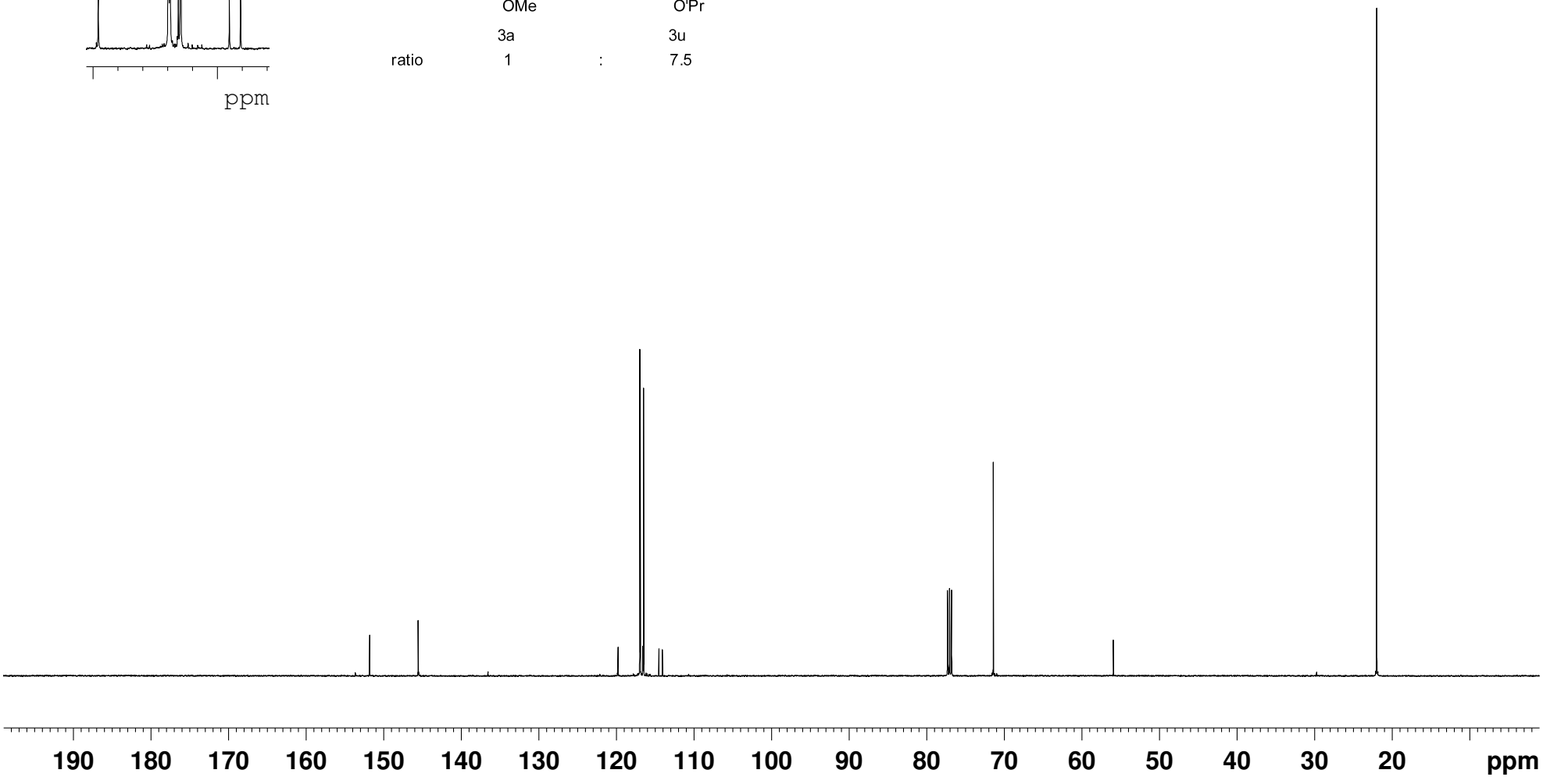


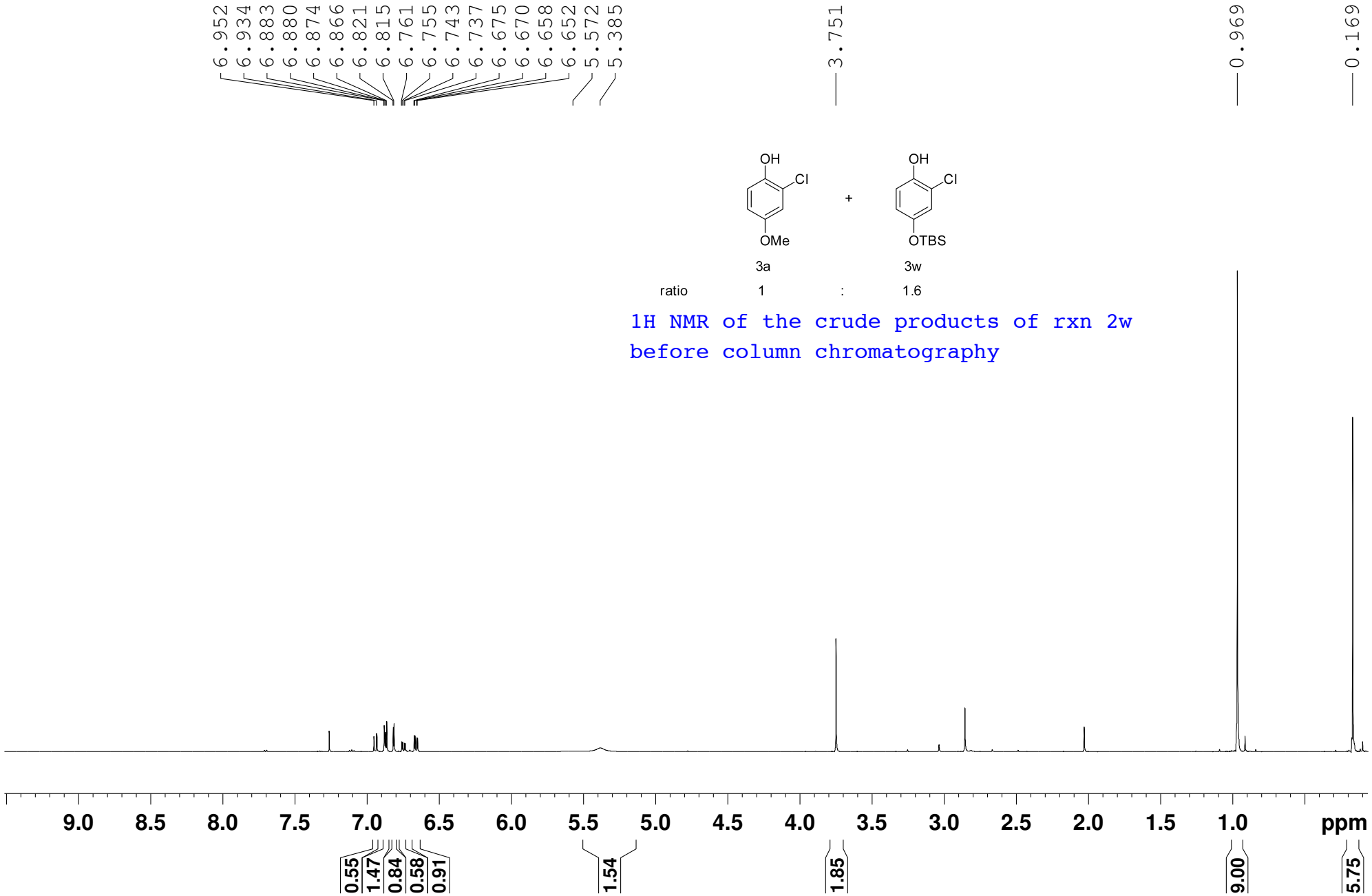
151.81
145.56
119.79
116.97
116.91
116.58
116.48
114.52
114.07
71.40
55.94
22.00

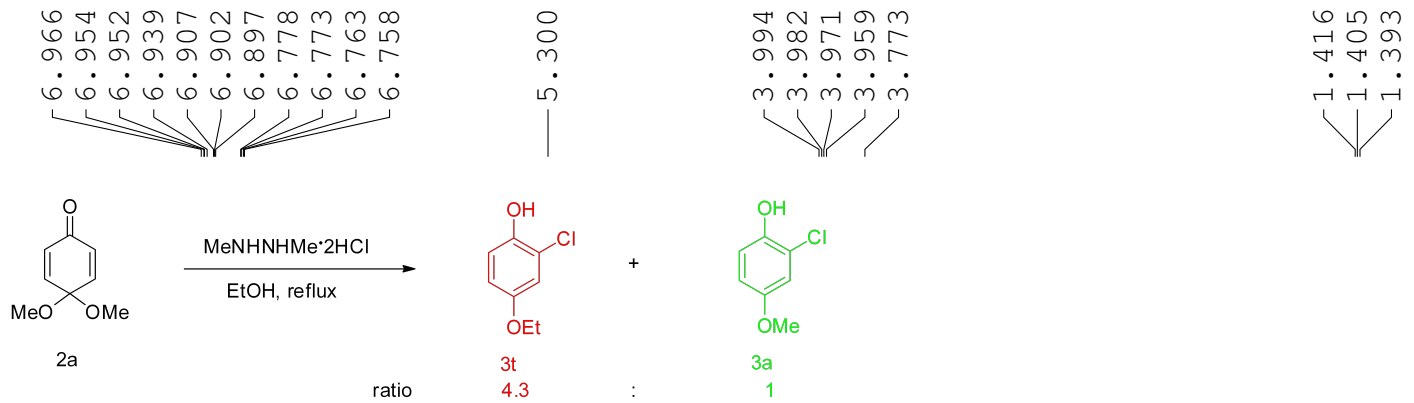


3a : 3u

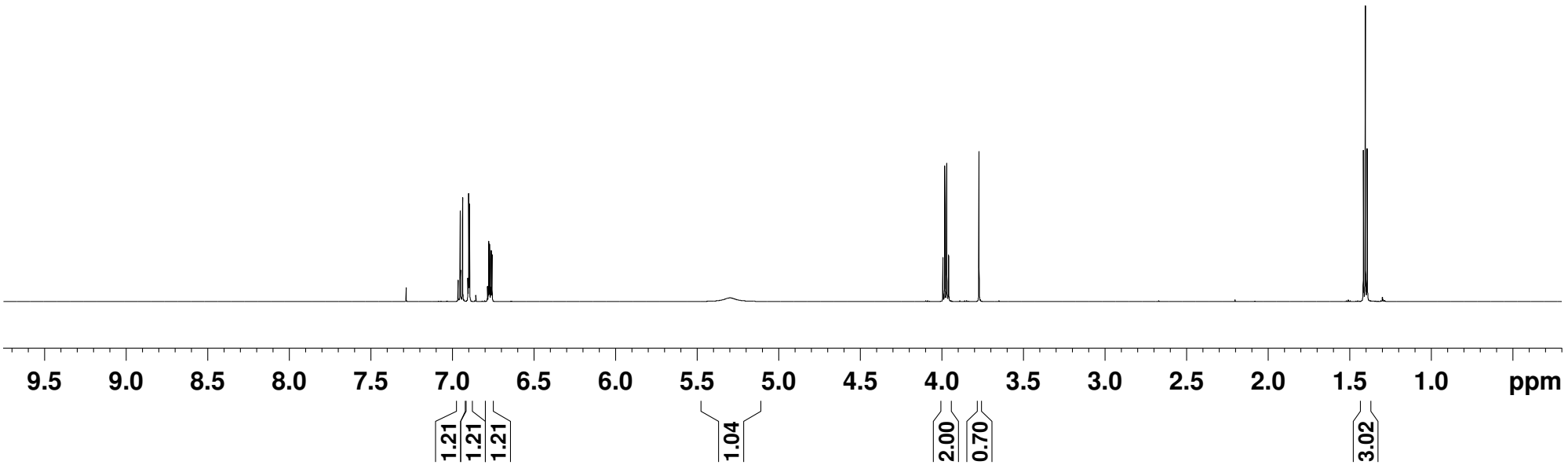
ratio 1 : 7.5

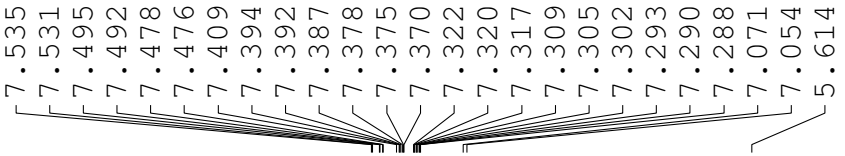



6.952
6.934
6.883
6.880
6.874
6.866
6.821
6.815
6.761
6.755
6.743
6.737
6.675
6.670
6.658
6.652
5.572
5.385
3.751
0.969
0.169
OH
Cl
OMe
+
OH
Cl
OTBS
3a
3w
ratio
1
:
1.6
1H NMR of the crude products of rxn 2w
before column chromatography
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.55
1.47
0.84
0.58
0.91
1.54
1.85
9.00
5.75



solvent scrambling




7.535
7.531
7.495
7.492
7.478
7.476
7.409
7.394
7.392
7.387
7.378
7.375
7.370
7.322
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7.309
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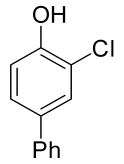
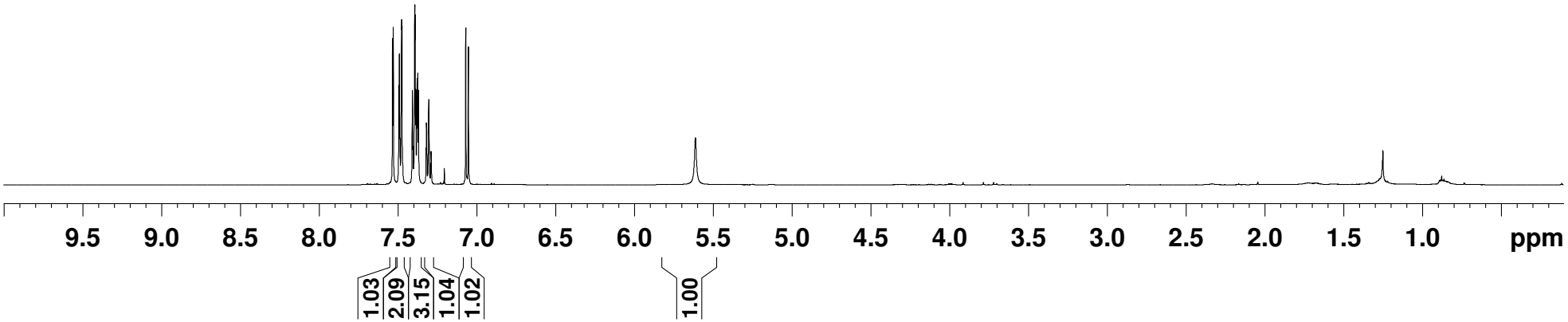
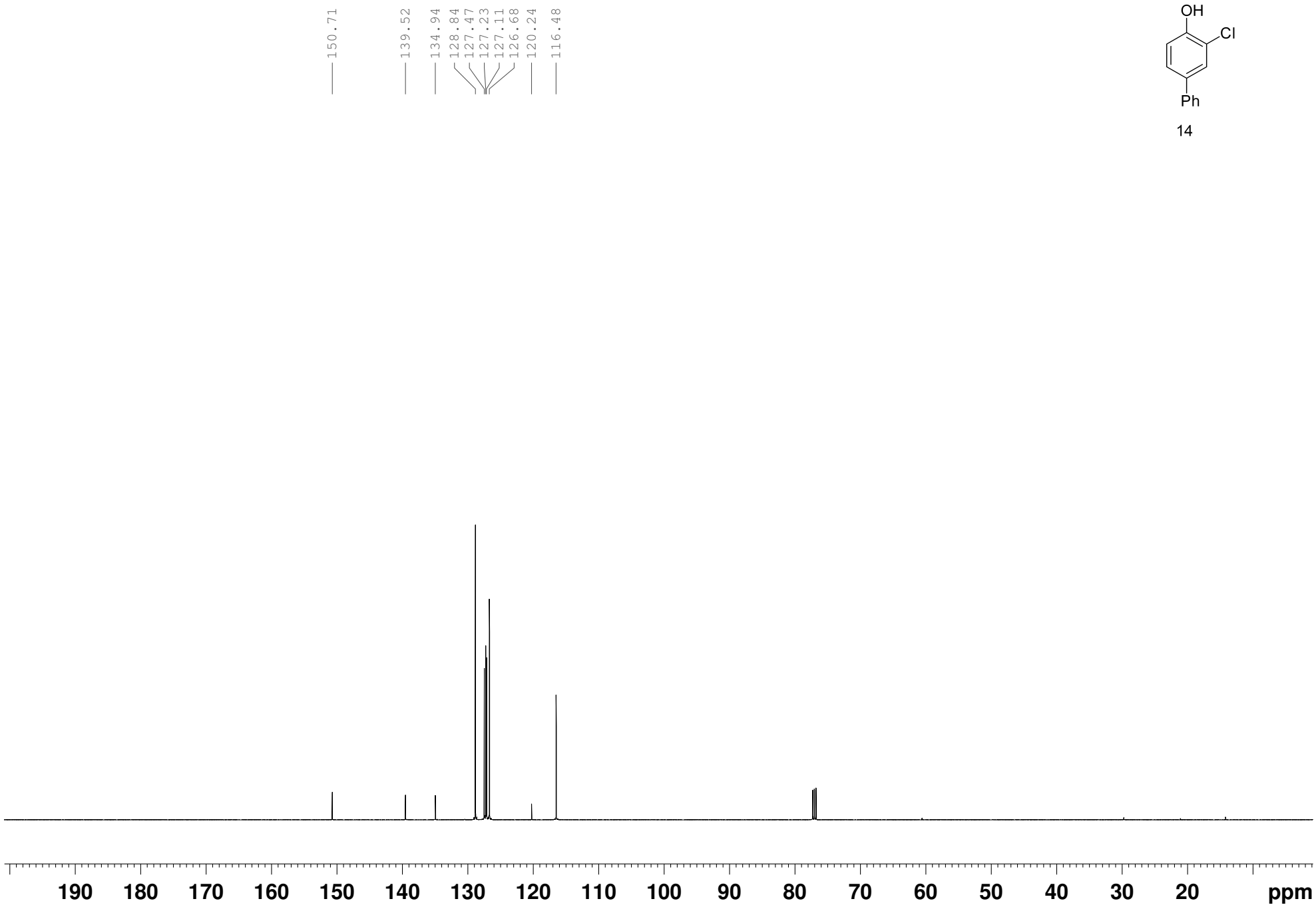
7.302
7.293
7.290
7.288
7.071
7.054
5.614


OH
Cl
Ph

14


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.03
2.09
3.15
1.04
1.02
1.00


150.71
139.52
134.94
128.84
127.47
127.23
127.11
126.68
120.24
116.48
OH
Cl
Ph
14
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm