

Iodonium based cross-linking tool for tyrosine conjugation

Electronic Supplementary Information

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1. General remarks

Unless otherwise indicated, starting materials were obtained from commercial suppliers, and were used without further purification. Analytical thin-layer chromatography (TLC) was performed on MerckDC pre-coated TLC plates with 0.25 mm Kieselgel 60 F₂₅₄. Visualization was performed with a 254 nm UV lamp and KMnO₄ stain.

All melting points were measured on Büchi 501 apparatus.

The ¹H, ¹³C and ¹⁹F NMR spectra were recorded on Bruker Avance-400 spectrometer in CDCl₃. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards (CDCl₃: δ 7.26 for ¹H, δ 77.16 for ¹³C). Coupling constants (J) are reported in Hertz (Hz). Splitting patterns are designated as s (singlet), bs (broad singlet), d (doublet), dd (doublet doublet), t (triplet), q (quartet), dq (doublet quartet), qd (quartet doublet), m (multiplet).

Conversions determined by gas chromatography. This, and low-resolution mass spectrometry was obtained on an Agilent 6890N Gas Chromatograph (30 m x 0.25 mm column with 0.25 μm HP-5MS coating, He carrier gas) and Agilent 5973 Mass Spectrometer (Ion source: EI+, 70eV, 230°C interface 300°C). GC-MS conversion was calculated from the chromatogram using the integral of the peak belonging to the starting material (ISM) and the integral of the peak belonging to the products (IP):

$$conversion(\%) = \frac{IP_y}{\sum_{x=1}^n IP_x + ISM} \cdot 100$$

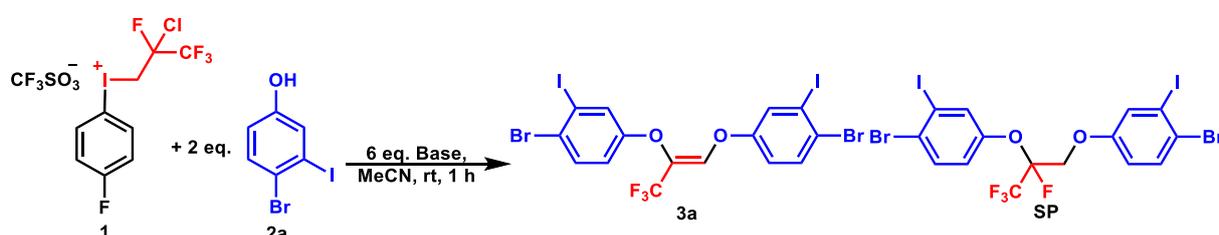
High-resolution mass spectra were acquired on an Agilent 6230 time-of-flight mass spectrometer equipped with a Jet Stream electrospray ion source in positive ion mode. Injections of 0.1-0.3 μl were directed to the mass spectrometer at a flow rate 0.5 ml/min (70% acetonitrile-water mixture, 0.1 % formic acid), using an Agilent 1260 Infinity HPLC system. Jet Stream parameters: drying gas (N₂) flow and temperature: 10.0 l/min and 325 °C, respectively; nebulizer gas (N₂) pressure: 10 psi; capillary voltage: 4000V; sheath gas flow and temperature: 325°C and 7.5 l/min; TOFMS parameters: fragmentor voltage: 120 V; skimmer potential: 120 V; OCT 1 RF Vpp: 750 V. Full-scan mass spectra were acquired over the m/z range 100-2500 at an acquisition rate of 250 ms/spectrum and processed by Agilent MassHunter B.03.01 software.

2. Optimization of the reaction conditions

2.1. Examination of the reaction conditions of the diaryloxy-ethene synthesis

Base screen

Different bases (0.6 mmol), 4-bromo-3-iodophenol (58 mg, 0.2 mmol) and MeCN (0.28 mL) were measured into a screw cap vial. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature, then analyzed by GC-MS and by NMR spectroscopy using 1-chloro-2-(trifluoromethyl)benzene as internal standard.

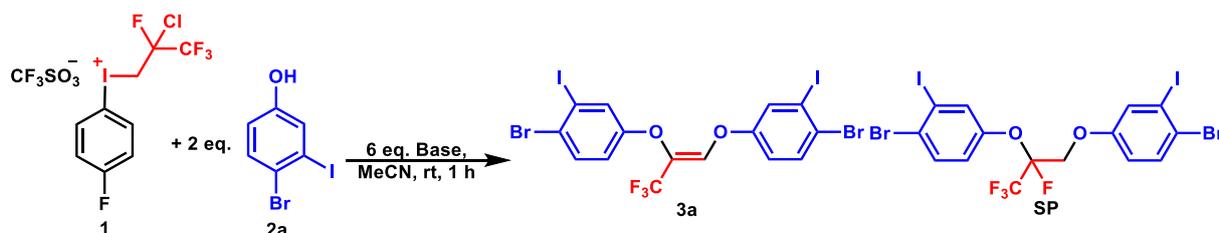


Entry	Base	3a ¹⁹ F-NMR yield ^a	SP ¹⁹ F-NMR yield ^a
1	K ₃ PO ₄	80	20
2	Pyridine	0	0
3	Collidine	0	0
4	DIPEA	0	0
5	TEA	0	0
6	Me ₂ NH	15	3
7	Piperidine	13	16
8	Pyrrolidine	7	1
9	TMG	85	0
10	DBU	58	0
11	TBD	2	0
12	K ₂ HPO ₄	18	16
13	d ^t BuPy	0	0
14	Li ₂ CO ₃	0	0
15	Na ₂ CO ₃	2	0
16	K ₂ CO ₃	65	0
17	Cs ₂ CO ₃	63	0
18	NaOH	61	0
19	NaH (60%)	45	0
20	LiO ^t Bu	30	0
21	NaO ^t Bu	32	0
22	KO ^t Bu	30	0

^aThe yields were measured after 60 minutes of reaction time by NMR spectroscopy using 1-chloro-2-(trifluoromethyl)benzene as internal standard.

Base mixture screen

A mixture of K_3PO_4 and different bases (0.6 mmol), 4-bromo-3-iodophenol (58 mg, 0.2 mmol) and MeCN (0.28 mL) were measured into a screw cap vial. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature, then analyzed by GC-MS and by NMR spectroscopy using 1-chloro-2-(trifluoromethyl)benzene as internal standard.

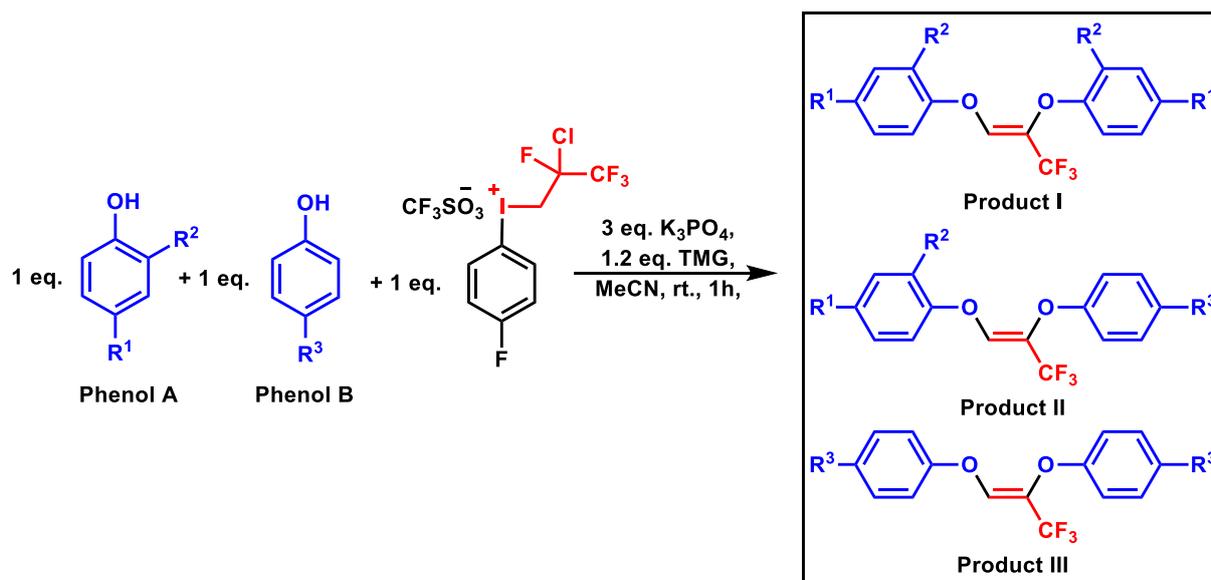


Entry	Base mixture (mmol:mmol)	3a ¹⁹ F-NMR yield ^a	SP ¹⁹ F-NMR yield ^a
1	K_3PO_4 :DBU = 0.3:0.3	63	0
2	K_3PO_4 :DBU = 0.57:0.03	90	3
3	K_3PO_4 :TMG = 0.3:0.3	87	0
4	K_3PO_4 :TMG = 0.36:0.24	92	0
5	K_3PO_4 :TMG = 0.42:0.18	93	0
6	K_3PO_4 :TMG = 0.48:0.12	96	0
7	K_3PO_4 :TMG = 0.54:0.06	95	1
8	K_3PO_4 :TMG = 0.42:0.12	96	1
9	K_3PO_4 :TMG = 0.36:0.12	85	1
10	K_3PO_4 :TMG = 0.3:0.12	96	0
11	K_3PO_4 :TMG = 0.24:0.12	89	1

^aThe yields were measured after 60 minutes of reaction time by NMR spectroscopy using 1-chloro-2-(trifluoromethyl)benzene as internal standard.

2.2. Examination of the hetero diaryloxy-ethene synthesis

Different phenols (A and B, 0.1 mmol), and K_3PO_4 (63.7 mg, 0.3 mmol), were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (13.8216 mg, 0.12 mmol, 15.2 μ l) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl)(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at an ambient temperature, then analyzed by GC-MS spectroscopy.

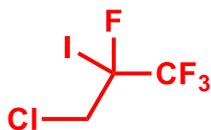


Entry	R^1	R^2	R^3	Product I (GC-MS%)	Product II (GC-MS%)	Product III (GC-MS%)
1	-Br	-H	-I	30	45	25
2	-COOEt	-H	-I	26	45	29
3	-NO ₂	-H	-Me	18	15	67
4	-NO ₂	-NO ₂	-I	0	0	100

Results indicate that in the first two cases the formation of a statistical mixture occurs when employing two different phenols with the same reactivity in the diaryloxy-ethene formation reaction. In the third case the balance shifts towards the formation of product III since phenol A is more acidic thus the formation of products I and II is slightly less favorable. Finally, when one of the two phenols that were used in the transformation is a limitation of the diaryloxy-ethene synthesis, then the acquired product consists of the diaryloxy-ethene formed by the other phenol, as shown in entry nr. 4.

3. Synthesis of the starting materials

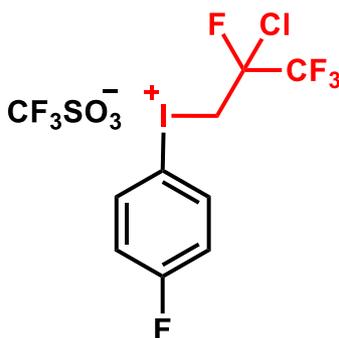
3-Chloro-1,1,1,2-tetrafluoro-2-iodopropane



A 250 mL pressure flask was tared with the Teflon bottlecap and stirring bar. The flask was evacuated and refilled with HFO gas three times. 2,3,3,3-Tetrafluoroprop-1-ene (HFO-1234yf) gas was condensed and filled the flask about half (155.52 g, 1.364 mol) using liquid nitrogen bath then closed with the bottlecap. After the flask warmed up to room temperature the weight was measured and the required ICl amount was calculated. The flask was cooled down again using liquid nitrogen bath and the ICl (56.7 mL, 183.8 g, 1.132 mol) was added. The pressure flask was heated up to 50 °C using an oil bath for 3 hours. The reaction mixture cooled down until the next day to room temperature. The flask was cooled down again using liquid nitrogen bath then the bottlecap has been removed and the mixture was allowed to warm to room temperature. The dark oil was washed three times with 1:1 mixture of saturated NaHCO₃ and Na₂SO₃ (using no organic solvent). The organic phase was washed twice with 50 mL cc. NaCl and dried by pushing through a plug of MgSO₄ using positive pressure. The addition reaction produces 5-7% regioisomer. The product was stored in a dark vial on copper shavings and refrigerated.^[1-2]

Yield: 217.5 g (0.787 mol, 70%) colorless oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 4.55 (dd, *J* = 19.0, 13.5 Hz, 1H), 4.39 (dd, *J* = 19.5, 13.5 Hz, 1H). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -74.7 (d, *J* = 11.8 Hz), -139.0 (q, *J* = 11.8 Hz). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 121.5 (qd, *J* = 283.2, 29.2 Hz), 78.1 (dq, *J* = 255.6, 34.4 Hz), 48.4 (d, *J* = 22.1 Hz). MS (EI, 70 eV): *m/z* (%): 278 (13), 276 (41, [M⁺]), 177 (10), 162 (12), 151 (32), 149 (100), 148 (12), 127 (33), 113 (9), 95 (15), 69 (41). Spectral data is in accordance with data given in literature.^[1-2]

(2-chloro-2,3,3,3-tetrafluoropropyl)(4-fluorophenyl)iodonium trifluoromethanesulfonate (1)

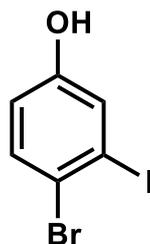


A screw cap vial with a stirrer bar was evacuated and refilled with argon three times. Trifluoroacetic anhydride (49.42 g, 32.7 mL, 235 mmol) and catalytic amount of trifluoroacetic acid (0.75 g, 0.5 mL, 7 mmol) was added through syringe. The mixture was cooled to -10 °C, then hydrogen-peroxide (50 w/w% in water) (3.74 g, 3.2 mL, 55 mmol) was added dropwise within two minutes. 3-Chloro-1,1,1,2-tetrafluoro-2-iodopropane (13.82 g, 6.5 mL, 50 mmol) was added dropwise through syringe. The resulting reaction mixture was stirred for 16 hours at 35 °C. After that, the mixture was cooled to -20 °C, then freshly distilled dichloromethane (32.5

mL) was added to the mixture. Fluorobenzene (5.05 g, 5.0 mL, 52.5 mmol) was added dropwise to the reaction mixture, followed by the addition of trifluoromethanesulfonic acid (7.50 g, 4.5 mL, 50 mmol). The reaction mixture was kept between 0 °C and 4 °C for 16 hours. After that, all volatiles were removed under reduced pressure at 0 °C protected from light. The dark oil was shaken with cold (-20 °C) diethyl ether, getting white precipitate. The suspension was kept at -20 °C for 2 hours, then the white precipitate was filtered and washed with cold diethyl ether three times.^[2]

Yield: 12.317 g (24 mmol, 47%) white solid. **Mp.** 129-130 °C. **MS** (EI, 70 eV): m/z (%): Compound decomposes in injector. **¹H NMR** (400 MHz, Acetonitrile-*d*₃) δ 8.22 (dd, *J* = 8.9, 4.8 Hz, 2H), 7.33 (t, *J* = 8.8 Hz, 2H), 5.09 (dd, *J* = 13.1, 8.7 Hz, 1H), 4.93 (dd, *J* = 28.1, 13.2 Hz, 1H). **¹⁹F NMR** (376 MHz, Acetonitrile-*d*₃) δ -79.3, -80.9 (d, *J* = 6.2 Hz), -104.9, -118.3 (q, *J* = 6.2 Hz). **¹³C NMR** (101 MHz, Acetonitrile-*d*₃) δ 166.6 (d, *J* = 254.8 Hz), 141.4 (d, *J* = 9.6 Hz), 121.7 (q, *J* = 320.0 Hz), 120.8 (d, *J* = 23.6 Hz), 119.9 (qd, *J* = 285.4, 31.2 Hz), 104.7 (dq, *J* = 254.7, 38.4 Hz), 103.8 (d, *J* = 3.3 Hz), 41.7 (d, *J* = 21.9 Hz). **IR** (solid, ATR) 1581, 1484, 1275, 1231, 1182, 1163, 1126, 1022, 1003, 929, 832, 813 cm⁻¹. **HRMS** (ESI) [M - OTf]⁺ calculated for C₉H₆ClF₅I⁺: 370.9123, found: 370.9120. Spectral data is in accordance with data given in literature.^[4]

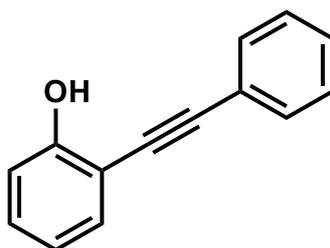
4-bromo-3-iodophenol (2a)¹⁻²



To a solution of 3-iodophenol (20 mmol, 4.4g) in 50 mL of acetic acid was added bromine (25 mmol, 3995.25 mg, 1.30 mL). The reaction mixture was stirred at room temperature overnight and a saturated solution of Na₂S₂O₃ was added. The layers were separated, the aqueous layer was neutralized with NaHCO₃ and extracted then twice with CH₂Cl₂. The combined organic layers were washed with water, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (CH₂Cl₂) to afford the desired 4-bromo-3-iodophenol.

Yield: 3.3 g (11.2 mmol, 56%) orange solid. **R_f** = 0.6 in CH₂Cl₂. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 8.7 Hz, 1H), 7.37 (d, *J* = 2.9 Hz, 1H), 6.71 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.89 (s, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 154.8, 133.0, 127.2, 120.6, 117.3, 101.2. Spectral data is in accordance with data given in the literature.^[1-2]

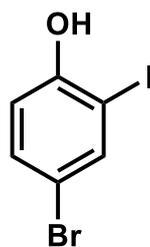
2-(phenylethynyl)phenol (2e)³



2-iodophenol (330 mg, 1.5 mmol), bis- (triphenylphosphine)palladium(II) dichloride (31.6 mg, 0.045 mmol) and copper(I) iodide (25.7 mg, 0.135 mmol) were all measured into a screw cap vial after which the vial was evacuated and subsequently filled with nitrogen three times. Benzene (7.5 ml) was added via syringe and upon continuous stirring ethynylbenzene (0.25 ml, 2.25 mmol), and diisopropylamine (0.22 ml, 1.5 mmol) were added to the reaction mixture. The resulting solution was stirred at room temperature for 2 hours. The mixture was passed through a short pad of celite and the solvent was removed in vacuo. The residue was dissolved in ethyl acetate (20 ml) and the solution was washed with water (40 ml), dried (Na₂SO₄), and concentrated to Celite under reduced pressure. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate = 9:1) to provide either *o*-phenylethynylphenol.

Yield: 222 mg (1.14 mmol, 76%) orange solid. **R_f** = 0.58 in Hex:EtOAc = 4:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.63 – 7.55 (m, 2H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.45 – 7.37 (m, 3H), 7.36 – 7.27 (m, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 5.90 (s, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 156.6, 131.8, 131.7, 130.6, 129.0, 128.6, 122.5, 120.6, 114.9, 109.7, 96.5, 83.2. Spectral data is in accordance with data given in the literature^[3].

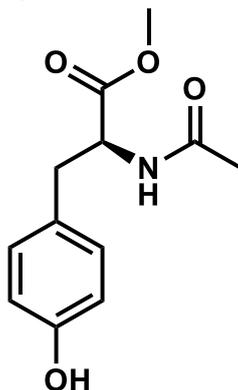
4-bromo-2-iodophenol (2r)⁴



4-Bromophenol (3270 mg, 18.9 mmol) and N-iodosuccinimide (4252.4 mg., 18.9 mmol) were combined in acetic acid (25 mL). The mixture was stirred briefly, treated with concentrated sulfuric acid (5.67 mmol, 556.137 mg, 0.3 ml) and stirred at about 22°C. overnight. The mixture was poured into water (about 40 mL) with stirring to precipitate the product. The suspension was stirred for about 1 hour and filtered. The crude product was washed with water (80 mL, 3x) and purified by flash chromatography on silica gel (Hex:EtOAc = 7:3) to afford the desired 4-bromo-2-iodophenol.

Yield: 2.9 g (9.8 mmol, 52%) white solid. **R_f** = 0.21 in Hex:EtOAc = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 1H), 5.27 (s, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 154.3, 139.9, 133.2, 116.4, 113.2, 86.3. Spectral data is in accordance with data given in the literature.^[4]

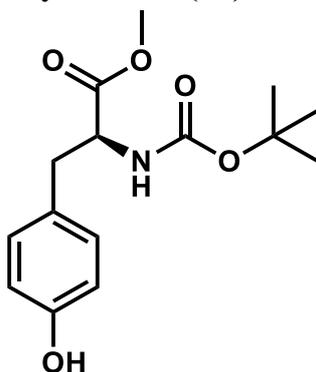
Methyl (*S*)-*N*-acetyltyrosinate (2w)⁵



To a mixture of acetic anhydride (41.5 mmol, 4.0 mL) and pyridine (47.5 mmol, 4.0 mL) at 0° C methyl (*S*)-tyrosinate hydrochloride (5 mmol, 1.2 g) was added. The reaction mixture was stirred under cooling up to the complete solution of methyl (*S*)-tyrosinate hydrochloride and the yellowish colouring of the solution. After the addition of sulfuric acid (1 M, 31 mL) the reaction mixture was extracted with ethyl acetate (3 × 23 mL). The combined organic phases were washed with a saturated aqueous sodium chloride solution and dried over sodium sulfate. After removal of the solvent under reduced pressure, the residue was dissolved in methanol (35 mL) and diluted with an aqueous potassium carbonate solution (25 mmol, 3.5 g in 23 mL water). The mixture was stirred for 30 minutes and afterwards extracted with ethyl acetate (3 × 20 mL), washed with a saturated aqueous sodium chloride solution and dried over sodium sulfate. After removal of the solvent methyl (*S*)-*N*-acetyltyrosinate (1.95 mmol, 458.9 mg, 39%) was obtained as white solid.

Yield: 458.9 mg (1.95 mmol, 39%) white solid. $R_f = 0.31$ in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 20:1$. $^1\text{H NMR}$ (400 MHz, Methanol- d_4) δ 7.00 (d, $J = 8.5$ Hz, 2H), 6.70 (d, $J = 8.5$ Hz, 2H), 4.58 (dd, $J = 8.7, 5.8$ Hz, 1H), 3.67 (s, 3H), 3.02 (dd, $J = 13.9, 5.8$ Hz, 1H), 2.84 (dd, $J = 13.9, 8.7$ Hz, 1H), 1.91 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, Methanol- d_4) δ 173.7, 173.1, 157.4, 131.1, 128.7, 116.2, 55.6, 52.6, 37.7, 22.2. Spectral data is in accordance with data given in the literature^[5].

Methyl (*tert*-butoxycarbonyl) *L*-tyrosinate (4a)⁶⁻⁷



To a solution of methyl *L*-tyrosinate hydrochloride (10 mmol, 2316.8 mg) in methanol (40 mL) was added di-*tert*-butyl dicarbonate (20 mmol, 4365 mg) and triethylamine (40 mmol, 4047.6 mg, 5.6 mL). The reaction mixture was heated to refluxing and stirred for 3 h at the same temperature, and concentrated under reduced pressure. The residue was diluted with water (20 mL), adjusted to pH 2.0–3.0 with 2 M HCl at 0–5 °C, and then extracted with ethyl acetate (25 mL × 3). The combined extracts were washed with saturated brine (30 mL), dried over anhydrous Na_2SO_4 , and then concentrated under reduced pressure. The crude product was

chromatographically purified on silica gel column eluting with CH₂Cl₂/MeOH (10:1 v/v) to provide methyl (tert-butoxycarbonyl) tyrosinate.

Yield: 2322.2 mg (7.9 mmol, 79%) white foam. $R_f = 0.27$ in CH₂Cl₂. ¹H NMR (400 MHz, Chloroform-d) δ 6.95 (d, J = 7.9 Hz, 2H), 6.72 (d, J = 8.0 Hz, 2H), 6.36 (s, 1H), 5.04 (d, J = 8.4 Hz, 1H), 4.53 (q, J = 6.7 Hz, 1H), 3.70 (s, 3H), 2.99 (tt, J = 14.0, 6.7 Hz, 2H), 1.41 (s, 9H). ¹³C NMR (101 MHz, Chloroform-d) δ 172.8, 155.5, 155.3, 130.5, 127.5, 115.6, 80.4, 54.8, 52.4, 37.7, 28.4. Spectral data is in accordance with data given in the literature^[6-7].

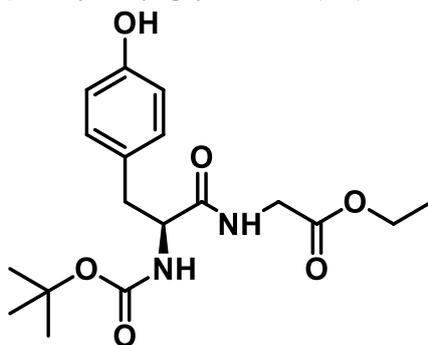
General procedure A for the amide bond formation⁸

Methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg) and the other *L*-amino acid, (2 mmol) were dissolved in 10 mL of anhydrous DMF. To this solution was added 1-Hydroxybenzotriazole hydrate (HOBt) (2.0 mmol, 270.2 mg) and Et₃N (6.6 mmol, 667.9 mg, 0.92 ml). After stirring the resultant solution for 5 minutes, it was cooled to 0°C, and 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride (EDC) (3 mmol, 573.5 mg) was added at once. The reaction mixture was allowed to warm to room temperature while stirring. The reaction was stirred for 18 hours. The resulting mixture was partitioned between EtOAc(20 ml) and water(30 ml). The two phases were separated and the aqueous phase was extracted three times with EtOAc(15 ml). The organic layers were combined and sequentially washed with sat. NaHCO₃ (aq., 40 ml), sat. NH₄Cl (aq., 40 ml), and brine(40 ml). The organic layer was dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was chromatographically purified on silica gel column eluting with CH₂Cl₂/MeOH to yield the desired products.

General procedure B for the amide bond formation⁸

(*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg) and the other *L*-amino acid hydrochloride, (2 mmol) were dissolved in 10 mL of anhydrous DMF. To this solution was added 1-Hydroxybenzotriazole hydrate (HOBt) (2.0 mmol, 270.2 mg) and Et₃N (6.6 mmol, 667.9 mg, 0.92 ml). After stirring the resultant solution for 5 minutes, it was cooled to 0°C, and 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride (EDC) (3 mmol, 573.5 mg) was added at once. The reaction mixture was allowed to warm to room temperature while stirring. The reaction was stirred for 18 hours. The resulting mixture was partitioned between EtOAc(20 ml) and water(30 ml). The two phases were separated and the aqueous phase was extracted three times with EtOAc(15 ml). The organic layers were combined and sequentially washed with sat. NaHCO₃ (aq., 40 ml), sat. NH₄Cl (aq., 40 ml), and brine(40 ml). The organic layer was dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was chromatographically purified on silica gel column eluting with CH₂Cl₂/MeOH to yield the desired products.

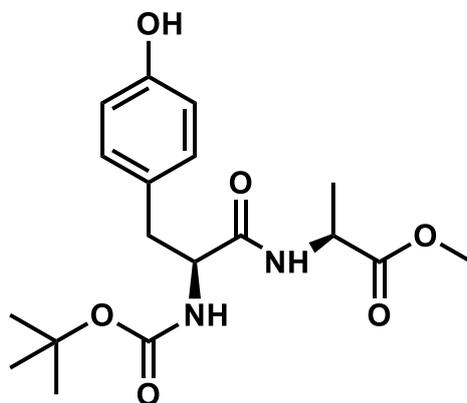
Ethyl (*tert*-butoxycarbonyl)-*L*-tyrosylglycinate (4b)^{8,9}



According to the general procedure B using (*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg), ethyl glycinate hydrochloride (2 mmol, 279.2 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 406.4 mg (1.11 mmol, 55%) white solid. $R_f = 0.46$ in CH₂Cl₂:MeOH = 8:2. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.01 (d, $J = 8.5$ Hz, 2H), 6.72 (d, $J = 8.5$ Hz, 2H), 6.65 (t, $J = 5.4$ Hz, 1H), 5.19 (s, 1H), 4.36 (s, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.01 (dd, $J = 18.1, 5.4$ Hz, 1H), 3.91 (dd, $J = 18.2, 5.0$ Hz, 1H), 3.00 (d, $J = 7.3$ Hz, 2H), 1.40 (s, 9H), 1.25 (t, $J = 7.1$ Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 172.1, 169.7, 155.8, 155.4, 130.5, 127.9, 115.7, 80.6, 61.8, 55.9, 41.5, 37.7, 28.4, 14.2. Spectral data is in accordance with data given in the literature^[9].

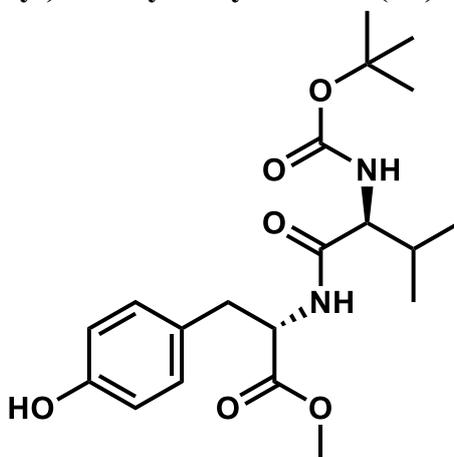
Methyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-alaninate (4c)^{7,10}



According to the general procedure B using (*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg), methyl *L*-alaninate hydrochloride (2 mmol, 279.3 mg), HOBt (2 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.8 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 167.1 mg (0.46 mmol, 23%) white solid. $R_f = 0.46$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 (s, 1H), 6.97 (d, $J = 8.0$ Hz, 2H), 6.92 (s, 1H), 6.71 (d, $J = 8.0$ Hz, 2H), 5.29 (d, $J = 8.1$ Hz, 1H), 4.54 – 4.42 (m, 1H), 4.41 – 4.28 (m, 1H), 3.66 (s, 3H), 3.05 – 2.83 (m, 2H), 1.37 (s, 9H), 1.30 (d, $J = 7.2$ Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 172.9, 171.8, 155.8, 155.5, 130.4, 127.5, 115.7, 80.5, 55.8, 52.5, 48.2, 37.6, 28.3, 18.0. Spectral data is in accordance with data given in the literature^[10].

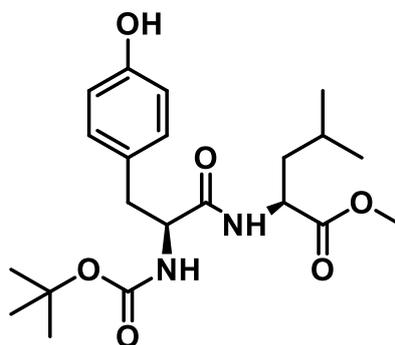
Methyl (*tert*-butoxycarbonyl)-*L*-valyl-*L*-tyrosinate (4d)^{8,11}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*-valine (2 mmol, 434.5 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 541.9 mg (1.38 mmol, 69%) white solid. **R_f** = 0.36 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.19 (s, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.1 Hz, 2H), 5.47 (d, *J* = 9.0 Hz, 1H), 4.71 (q, *J* = 6.7 Hz, 1H), 3.93 (t, *J* = 8.2 Hz, 1H), 3.56 (s, 3H), 2.94 – 2.88 (m, 2H), 1.96 (h, *J* = 6.5 Hz, 1H), 1.35 (s, 9H), 0.87 – 0.73 (m, 6H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 171.8, 155.9, 155.7, 130.0, 126.5, 115.4, 79.8, 59.7, 53.5, 52.0, 36.9, 30.8, 28.1, 18.9, 17.8. Spectral data is in accordance with data given in the literature^[11].

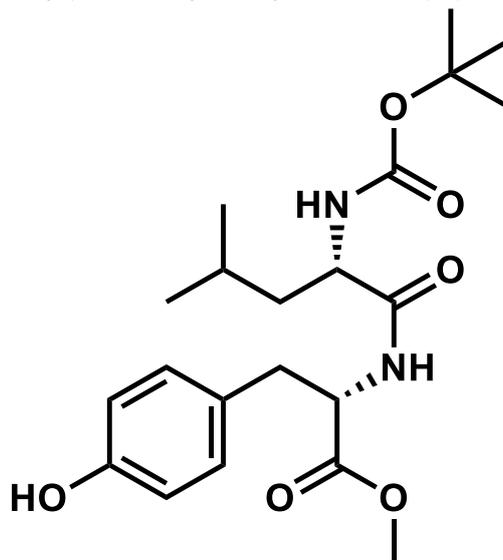
Methyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-leucinate (**4e**)^{8,12}



According to the general procedure B using (*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg), methyl *L*-leucinate hydrochloride (2 mmol, 363.4 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 600.7 mg (1.47 mmol, 74%) white solid. **R_f** = 0.57 in CH₂Cl₂:MeOH = 9:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.02 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 2H), 6.63 (s, 1H), 6.35 (d, *J* = 8.2 Hz, 1H), 5.10 (s, 1H), 4.56 (td, *J* = 8.3, 4.4 Hz, 1H), 4.28 (d, *J* = 8.2 Hz, 1H), 3.68 (s, 3H), 2.96 (d, *J* = 6.9 Hz, 2H), 1.67 – 1.55 (m, 2H), 1.47 (dd, *J* = 9.1, 7.5 Hz, 1H), 1.42 (s, 9H), 0.89 (t, *J* = 5.9 Hz, 6H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 173.9, 173.0, 171.4, 170.4, 155.7, 155.4, 130.6, 128.0, 115.7, 80.6, 56.0, 52.4, 50.9, 41.7, 37.5, 28.4, 24.8, 22.9, 22.0. Spectral data is in accordance with data given in the literature^[12].

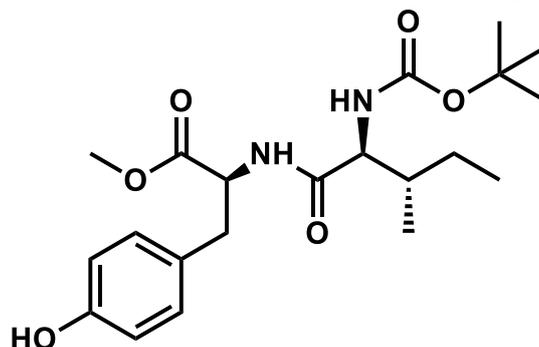
Methyl (*tert*-butoxycarbonyl)-*L*-leucyl-*L*-tyrosinate (4f)^{8,13}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*-leucine (2 mmol, 462.6 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 620.7 mg (1.56 mmol, 78%) white solid. $R_f = 0.66$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 6.90 (d, $J = 8.2$ Hz, 2H), 6.78 (s, 1H), 6.72 (d, $J = 7.4$ Hz, 1H), 6.67 (d, $J = 8.0$ Hz, 2H), 4.96 (d, $J = 8.5$ Hz, 1H), 4.83 (dt, $J = 8.0, 5.5$ Hz, 1H), 4.11 (s, 1H), 3.73 (s, 3H), 3.12 – 2.97 (m, 2H), 1.69 – 1.55 (m, 2H), 1.45 (s, 10H), 0.90 (t, $J = 6.4$ Hz, 6H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 172.4, 171.9, 156.0, 155.5, 130.5, 127.0, 115.6, 80.5, 53.5, 53.1, 52.5, 41.3, 37.2, 28.5, 24.8, 22.9, 22.1. Spectral data is in accordance with data given in the literature^[13].

Methyl (*tert*-butoxycarbonyl)-*L*-isoleucyl-*L*-tyrosinate (4g)^{8,14}

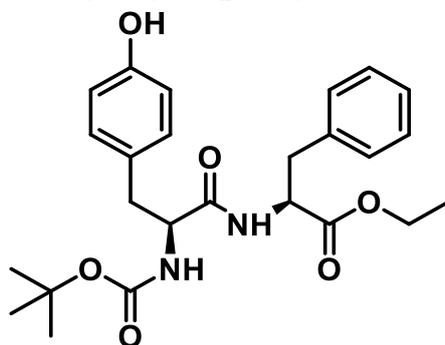


According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*-isoleucine (2 mmol, 462.6 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 554.3 mg (1.36 mmol, 68%) white solid. $R_f = 0.43$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 6.96 – 6.86 (m, 3H), 6.68 (d, $J = 8.0$ Hz, 2H), 6.56 (d, $J = 8.1$ Hz, 1H), 5.12 (d, $J = 9.1$ Hz, 1H), 4.85 (dt, $J = 8.1, 5.6$ Hz, 1H), 3.91 (t, $J = 8.2$ Hz, 1H), 3.73 (s, 3H), 3.08 – 2.96 (m, 2H), 1.83 – 1.71 (m, 1H), 1.46 (s, 9H), 1.36 – 0.99 (m, 2H), 0.94 – 0.78 (m, 6H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.9, 171.6, 156.1, 155.6, 130.5, 126.9, 115.7,

80.4, 59.3, 53.4, 52.5, 37.3, 28.5, 24.8, 15.5, 11.4. Spectral data is in accordance with data given in the literature^[14].

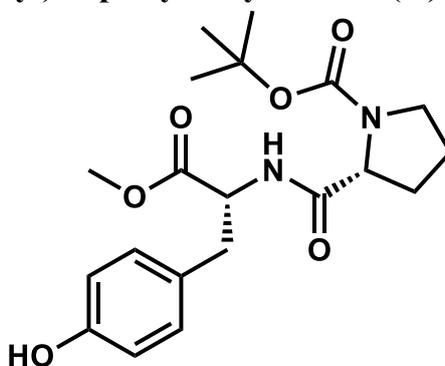
Ethyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-phenylalaninate (**4h**)^{8,15}



According to the general procedure B using (*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg), ethyl *L*-phenylalaninate hydrochloride (2 mmol, 459.4 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 688.5 mg (1.51 mmol, 75%) white solid. $R_f = 0.49$ in CH₂Cl₂:MeOH = 9:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.05 (dd, $J = 7.5, 1.9$ Hz, 4H), 7.01 (d, $J = 7.6$ Hz, 4H), 6.74 (d, $J = 8.4$ Hz, 2H), 6.45 (s, 1H), 5.07 (s, 1H), 4.76 (d, $J = 6.9$ Hz, 1H), 4.30 (s, 1H), 4.12 (dd, $J = 7.2, 4.1$ Hz, 2H), 3.07 (dd, $J = 6.0, 1.7$ Hz, 2H), 3.01 – 2.90 (m, 2H), 1.42 (s, 9H), 1.20 (t, $J = 7.1$ Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.3, 171.1, 155.6, 155.4, 135.8, 130.5, 129.4, 128.6, 127.2, 115.8, 80.5, 61.7, 56.1, 53.5, 38.2, 37.7, 28.4, 14.2. According to the literature^[15].

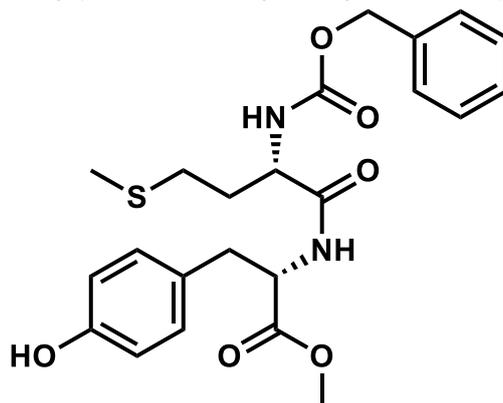
Methyl (*tert*-butoxycarbonyl)-*L*-prolyl-*L*-tyrosinate (**4i**)^{8,16}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl) *L*-proline (2 mmol, 430.5 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 689 mg (1.7 mmol, 88%) colorless oil. $R_f = 0.39$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 6.99 (d, $J = 8.2$ Hz, 2H), 6.66 (d, $J = 8.0$ Hz, 2H), 4.64 – 4.53 (m, 1H), 4.22 – 4.06 (m, 1H), 3.65 (s, 3H), 3.45 – 3.36 (m, 1H), 3.30 – 3.26 (m, 1H), 3.10 – 2.96 (m, 1H), 2.95 – 2.76 (m, 1H), 2.17 – 1.99 (m, 1H), 1.84 – 1.65 (m, 3H), 1.27 (s, 9H). ¹³C NMR (101 MHz, Methanol-*d*₄) δ 175.6, 173.4, 157.5, 156.0, 131.1, 128.7, 116.3, 81.5, 61.5, 55.3, 52.6, 47.8, 37.4, 32.2, 28.5, 24.3. Spectral data is in accordance with data given in the literature^[16].

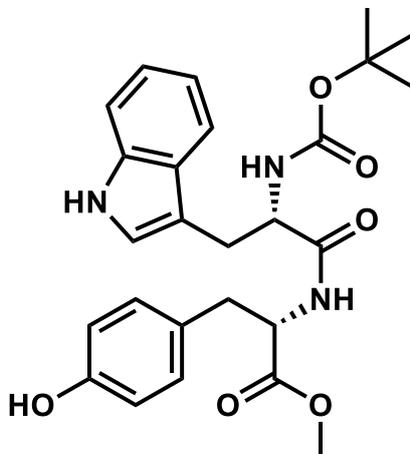
Methyl ((benzyloxy)carbonyl)-*L*-methionyl-*L*-tyrosinate (4j)^{8,17}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), ((benzyloxy)carbonyl)-*L*-methionine (2 mmol, 566.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 792 mg (1.7 mmol, 86%) white solid. $R_f = 0.44$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.28 (m, 6H), 6.93 (d, $J = 8.0$ Hz, 2H), 6.75 – 6.59 (m, 3H), 5.99 (s, 1H), 5.55 (d, $J = 8.3$ Hz, 1H), 5.16 – 5.02 (m, 2H), 4.81 (q, $J = 6.0$ Hz, 1H), 4.36 (q, $J = 7.3$ Hz, 1H), 3.72 (s, 3H), 3.13 – 2.97 (m, 2H), 2.52 (t, $J = 7.2$ Hz, 2H), 2.14 – 2.06 (m, 1H), 2.03 (s, 3H), 1.93 (td, $J = 14.3, 7.1$ Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.8, 171.4, 156.3, 155.7, 136.1, 130.3, 128.5, 128.2, 128.2, 128.1, 126.7, 115.7, 67.2, 53.7, 53.5, 52.4, 36.9, 31.8, 29.9, 15.1. According to the literature^[17].

Methyl (*tert*-butoxycarbonyl)-*L*-tryptophyl-*L*-tyrosinate (4k)^{8,18}

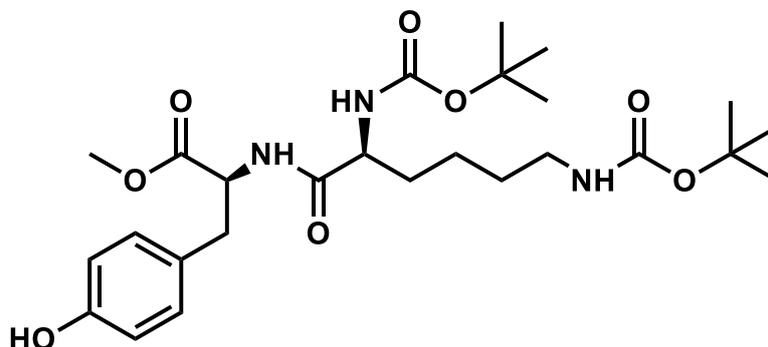


According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*-tryptophan (2 mmol, 608.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 711.8 mg (1.5 mmol, 74%) white solid. $R_f = 0.39$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.42 (s, 1H), 7.60 (d, $J = 7.9$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.21 – 7.12 (m, 1H), 7.08 (t, $J = 7.4$ Hz, 1H), 6.84 (s, 1H), 6.64 (d, $J = 8.8$ Hz, 2H), 6.61 (d, $J = 8.6$ Hz, 2H), 6.38 (d, $J = 7.8$ Hz, 1H), 5.22 (s, 1H), 4.71 (d, $J = 6.6$ Hz, 1H), 4.43 (s, 1H), 3.60 (s, 3H), 3.25 (dd, 1H), 3.11 (dd, $J = 14.5, 7.0$ Hz, 1H), 2.82 (dd, $J = 14.0, 6.1$ Hz, 3H), 1.41 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 171.7, 155.8, 155.5, 136.4, 130.4, 127.6, 127.0, 123.5, 122.3,

119.8, 118.9, 115.6, 111.4, 110.2, 80.6, 55.5, 53.5, 52.4, 37.2, 34.6, 28.4, 28.3. Spectral data is in accordance with data given in the literature^[18].

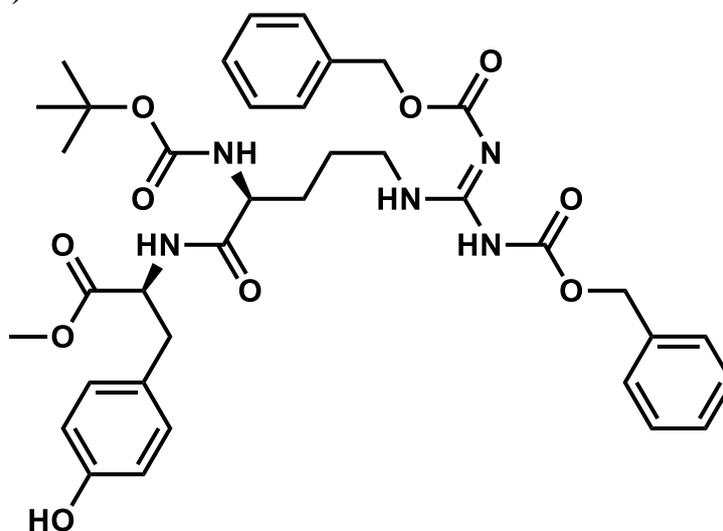
Methyl N²,N⁶-bis(*tert*-butoxycarbonyl)-*L*-lysyl-*L*-tyrosinate (4l)⁸



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), N², N⁶-bis(*tert*-butoxycarbonyl)-*L*-lysine dicyclohexylamine salt (2 mmol, 692.8 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 304.1 mg (1.15 mmol, 57%) white solid. **Mp.** 54-57 °C. **R_f** = 0.45 in CH₂Cl₂:MeOH = 8.5:1.5. **¹H NMR** (400 MHz, Chloroform-*d*) δ 6.93 (d, *J* = 8.1 Hz, 2H), 6.74 (d, *J* = 7.9 Hz, 2H), 6.69 (d, *J* = 7.5 Hz, 1H), 5.18 (d, *J* = 7.3 Hz, 1H), 4.79 (s, 2H), 4.01 (s, 1H), 3.71 (s, 3H), 3.08 (s, 1H), 3.01 (s, 2H), 1.59 (s, 2H), 1.43 (s, 22H), 1.16 (s, 2H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.1, 172.0, 156.6, 155.9, 155.8, 130.4, 126.9, 115.8, 54.8, 53.2, 52.5, 40.2, 37.3, 32.1, 29.8, 28.6, 28.4, 22.5. **HRMS** (ESI) [M + Na]⁺ calculated for C₂₆H₄₁N₃O₈Na⁺: 546.2791, found 546.2792.

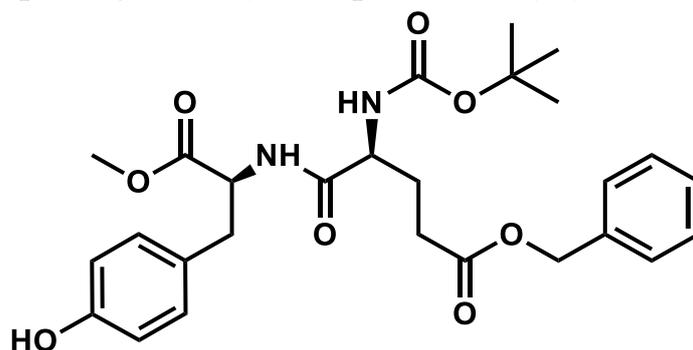
Methyl (*E*)-N^ω,N^{ω'}-bis((benzyloxy)carbonyl)-N²-(*tert*-butoxycarbonyl)-*L*-arginyl-*L*-tyrosinate (4m)⁸



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*E*)-N^ω,N^{ω'}-bis((benzyloxy)carbonyl)-N²-(*tert*-butoxycarbonyl)-*L*-arginine (2 mmol, 1085.2 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 1029.3 mg (1.68 mmol, 84%) white solid. **Mp.** 88-91 °C. **R_f** = 0.64 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 9.42 (s, 1H), 9.29 (s, 1H), 7.42 – 7.27 (m, 11H), 6.94 – 6.86 (m, 1H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.66 (d, *J* = 8.2 Hz, 2H), 5.63 (d, *J* = 8.5 Hz, 1H), 5.20 (s, 2H), 5.16 – 5.07 (m, 2H), 4.79 – 4.69 (m, 1H), 4.25 – 4.12 (m, 1H), 3.85 (p, *J* = 8.5, 7.5 Hz, 2H), 3.63 (s, 3H), 2.99 – 2.93 (m, 1H), 2.77 (dd, *J* = 14.4, 6.9 Hz, 1H), 1.71 – 1.50 (m, 4H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 171.7, 163.6, 160.7, 155.8, 155.5, 136.7, 134.6, 130.2, 128.9, 128.8, 128.5, 128.4, 128.0, 127.9, 127.0, 115.5, 80.1, 69.0, 67.1, 54.2, 53.4, 52.3, 44.1, 36.9, 28.5, 28.3, 24.8. **HRMS** (ESI) [M + H]⁺ calculated for C₃₇H₄₆N₅O₁₀⁺: 720.3245, found 720.3253.

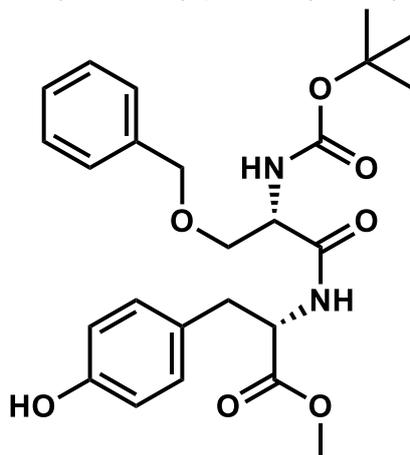
Benzyl (S)-4-((*tert*-butoxycarbonyl)amino)-5-(((S)-3-(4-hydroxyphenyl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentanoate (4n)⁸



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (S)-5-(benzyloxy)-2-((*tert*-butoxycarbonyl)amino)-5-oxopentanoic acid (2 mmol, 674.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 572.5 mg (1.11 mmol, 56%) colorless viscous liquid. **Mp.** 99-102 °C. **R_f** = 0.45 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 5H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.77 (s, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.34 (d, *J* = 8.2 Hz, 1H), 5.09 (s, 2H), 4.80 (dt, *J* = 8.0, 5.8 Hz, 1H), 4.18 (q, *J* = 8.2, 7.4 Hz, 1H), 3.70 (s, 3H), 3.05 (dd, *J* = 14.1, 5.4 Hz, 1H), 2.99 (d, *J* = 6.2 Hz, 1H), 2.42 (h, *J* = 7.0 Hz, 2H), 2.07 (dq, *J* = 11.8, 7.0 Hz, 1H), 1.89 (dd, *J* = 14.6, 7.5 Hz, 1H), 1.43 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 173.2, 171.8, 171.4, 162.9, 155.9, 155.5, 135.8, 130.4, 128.7, 128.4, 127.1, 115.7, 80.5, 66.7, 53.7, 53.6, 52.5, 37.1, 30.5, 28.4, 28.0. **HRMS** (ESI) [M + Na]⁺ calculated for C₂₇H₃₄N₂O₈Na⁺: 537.2213, found 537.2213.

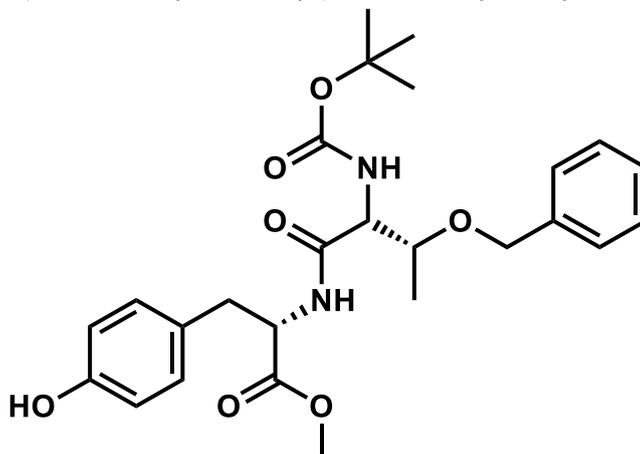
Methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-seryl-*L*-tyrosinate (4o)^{8,19}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-serine (2 mmol, 590.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 661.5 mg (1.4 mmol, 70%) white solid. **R_f** = 0.57 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.41 – 7.22 (m, 5H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 6.46 (s, 1H), 5.43 (d, *J* = 7.1 Hz, 1H), 4.82 (q, *J* = 6.2 Hz, 1H), 4.65 – 4.41 (m, 2H), 4.31 (s, 1H), 3.91 (dd, *J* = 9.4, 3.9 Hz, 1H), 3.69 (s, 3H), 3.57 (dd, *J* = 9.3, 6.4 Hz, 1H), 3.02 (qd, 2H), 1.45 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.7, 170.3, 155.4, 137.4, 130.5, 128.6, 128.1, 128.0, 127.2, 115.6, 80.6, 73.6, 69.9, 54.0, 53.8, 52.4, 37.2, 28.4. Spectral data is in accordance with data given in the literature^[19].

Methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-threonyl-*L*-tyrosinate (4p)⁸

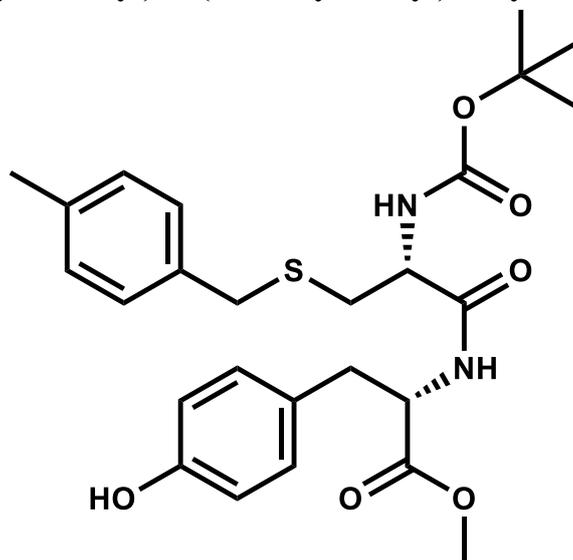


According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-threonine (2 mmol, 618.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 679.1 mg (1.4 mmol, 70%) white solid. **Mp.** 83-86 °C. **R_f** = 0.47 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.34 – 7.25 (m, 5H), 7.23 (d, *J* = 11.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.58 (d, *J* = 7.2 Hz, 1H), 4.76 (q, *J* = 6.5 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.49 (d, *J* = 11.4 Hz, 1H), 4.36 – 4.29 (m, 1H), 4.19

– 4.10 (m, 1H), 3.63 (s, 3H), 3.03 – 2.89 (m, 2H), 1.45 (s, 9H), 1.21 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 171.6, 169.9, 155.8, 155.7, 137.7, 130.1, 128.3, 127.8, 127.7, 126.6, 115.5, 80.3, 74.6, 71.3, 57.5, 53.8, 52.1, 37.1, 28.2, 14.9. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_7\text{Na}^+$: 509.2264, found 509.2262.

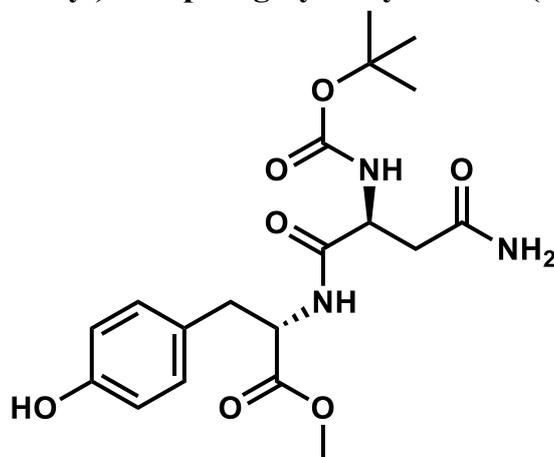
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(4-methylbenzyl)-*L*-cysteinyl-*L*-tyrosinate (4q)⁸



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), *N*-(ethoxycarbonyl)-*S*-(4-methylbenzyl)cysteine (2 mmol, 650.9 mg), HOBt (2.0 mmol, 270.2 mg), Et_3N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 995.2 mg (1.98 mmol, 99%) white solid. **Mp.** 94-97 °C. $R_f = 0.72$ in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 20:1$. ^1H NMR (400 MHz, Chloroform- d) δ 7.66 (s, 1H), 7.18 (d, $J = 7.7$ Hz, 2H), 7.08 (d, $J = 7.8$ Hz, 3H), 6.92 (d, $J = 8.0$ Hz, 2H), 6.72 (d, $J = 8.0$ Hz, 2H), 5.45 (d, $J = 8.0$ Hz, 1H), 4.80 (q, $J = 6.2$ Hz, 1H), 4.37 – 4.10 (m, 1H), 3.68 (s, 3H), 3.66 (s, 2H), 3.08 – 2.96 (m, 2H), 2.79 – 2.55 (m, 2H), 2.30 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, Chloroform- d) δ 171.6, 170.7, 155.6, 136.8, 134.6, 130.3, 129.3, 128.9, 126.6, 115.6, 80.6, 53.7, 52.3, 37.0, 36.0, 33.4, 28.3, 21.1. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_6\text{SNa}^+$: 525.2035, found 525.2039.

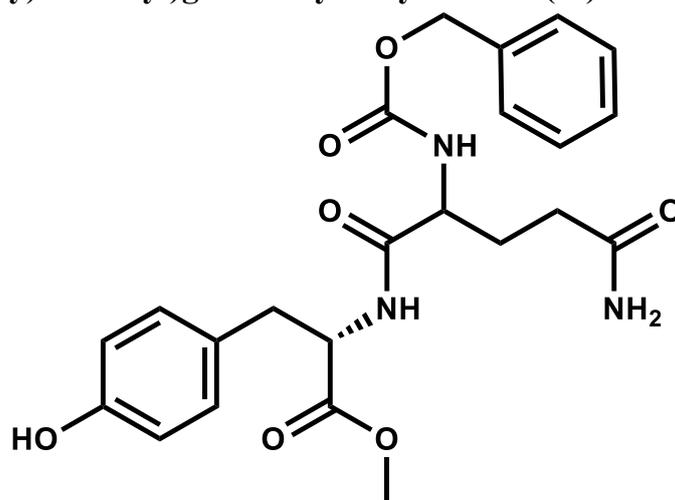
Methyl (*tert*-butoxycarbonyl)-*L*-asparaginyl-*L*-tyrosinate (4r)^{8,20}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*- asparagine (2 mmol, 464.5 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 330.0 mg (0.80 mmol, 40%) white solid. $R_f = 0.42$ in CH₂Cl₂:MeOH = 10:1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.22 (s, 1H), 7.98 (d, *J* = 7.5 Hz, 1H), 7.26 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 9.9 Hz, 2H), 6.65 (d, *J* = 7.9 Hz, 2H), 4.37 (q, *J* = 7.0 Hz, 1H), 4.27 (td, *J* = 8.5, 4.9 Hz, 1H), 3.57 (s, 3H), 2.95 – 2.77 (m, 2H), 2.44 – 2.26 (m, 2H), 1.36 (s, 9H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.8, 171.7, 171.5, 156.1, 155.1, 130.1, 126.8, 115.1, 78.3, 53.9, 51.8, 51.1, 37.2, 36.0, 28.2. According to the literature^[20].

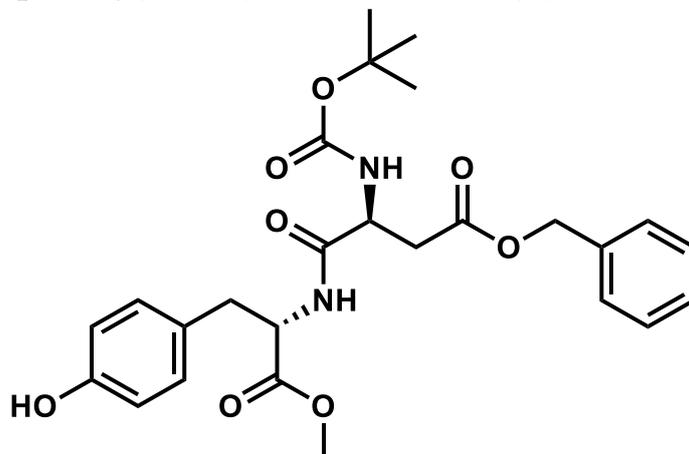
Methyl ((benzyloxy)carbonyl)glutaminy-*L*-tyrosinate (4s)^{8,21}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), ((benzyloxy)carbonyl)glutamine (2 mmol, 560.6 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 798.4 mg (1.74 mmol, 87%) white solid. $R_f = 0.33$ in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.22 (s, 1H), 8.21 (dd, *J* = 16.6, 7.6 Hz, 1H), 7.36 (s, 5H), 7.33 – 7.30 (m, 1H), 7.22 (d, *J* = 18.7 Hz, 1H), 7.02 – 6.93 (m, 2H), 6.75 (d, *J* = 7.2 Hz, 1H), 6.68 – 6.61 (m, 2H), 5.01 (s, 2H), 4.38 (dp, *J* = 11.8, 4.2, 3.7 Hz, 1H), 4.01 (dt, *J* = 8.7, 4.8 Hz, 1H), 3.57 (s, 3H), 2.94 – 2.89 (m, 1H), 2.87 – 2.78 (m, 1H), 2.18 – 1.96 (m, 2H), 1.93 – 1.74 (m, 1H), 1.73 – 1.57 (m, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 173.8, 172.0, 171.6, 156.0, 155.8, 137.0, 130.0, 128.4, 127.8, 127.7, 126.9, 115.1, 65.5, 54.3, 53.8, 51.8, 35.9, 31.4, 27.8. According to the literature^[21].

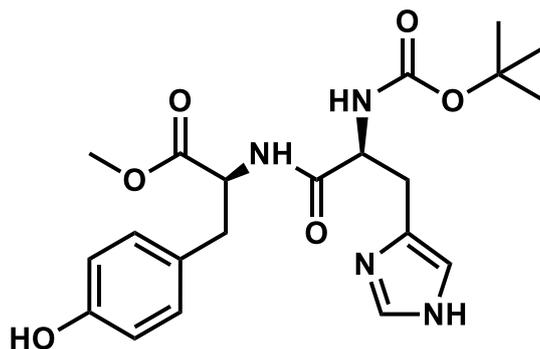
Benzyl (*S*)-3-((*tert*-butoxycarbonyl)amino)-4-(((*S*)-3-(4-hydroxyphenyl)-1-methoxy-1-oxopropan-2-yl)amino)-4-oxobutanoate (4t**)⁸**



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*S*)-4-(benzyloxy)-2-((*tert*-butoxycarbonyl)amino)-4-oxobutanoic acid (2 mmol, 646.7 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 663.2 mg (1.32 mmol, 66%) white solid. **Mp.** 60-63 °C. **R_f** = 0.43 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 6.6 Hz, 1H), 7.29 (s, 5H), 7.20 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 8.1 Hz, 2H), 5.91 (d, *J* = 8.7 Hz, 1H), 5.22 – 4.96 (m, 2H), 4.74 (q, *J* = 6.5 Hz, 1H), 4.60 (d, *J* = 8.2 Hz, 1H), 3.61 (s, 3H), 2.98 (d, *J* = 5.8 Hz, 2H), 2.96 – 2.88 (m, 1H), 2.80 – 2.71 (m, 1H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.4, 171.1, 170.6, 155.6, 155.4, 135.2, 130.1, 128.3, 128.1, 128.0, 126.3, 115.4, 80.4, 66.6, 53.6, 52.0, 50.5, 36.7, 35.9, 28.0. **HRMS** (ESI) [M + Na]⁺ calculated for C₂₆H₃₂N₂O₈Na⁺: 523.2056, found 523.2054.

Methyl (*tert*-butoxycarbonyl)-*L*-histidyl-*L*-tyrosinate (4u**)^{8,22}**

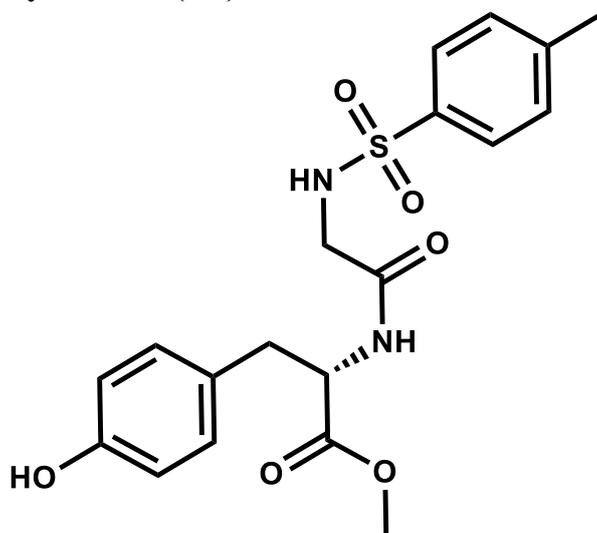


According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), (*tert*-butoxycarbonyl)-*L*-histidine (2 mmol, 510.5 mg), HOBt (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 319.1 mg (0.74 mmol, 37%) white solid. **R_f** = 0.22 in CH₂Cl₂:MeOH = 10:1. **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.64 (d, *J* = 2.6 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 35.5 Hz, 1H), 6.69 (dd, *J* = 8.6, 2.6 Hz, 2H), 4.95 (s, 5H), 4.60 (t, *J* = 6.6 Hz, 1H), 4.30 (dd, *J* = 8.9, 5.2 Hz, 1H), 3.67 (d, *J* = 12.6 Hz, 3H), 3.11 – 2.88 (m, 3H), 2.78 (ddd, *J* = 28.2, 14.8, 9.0 Hz, 1H), 1.39 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 174.0, 173.3, 157.5, 136.1, 134.3, 131.3

(d, $J = 3.6$ Hz), 128.3, 118.5, 116.3 (d, $J = 3.9$ Hz), 80.7, 55.9, 55.3, 52.7, 37.6, 30.5, 28.6, 14.5. Spectral data is in accordance with data given in the literature^[22].

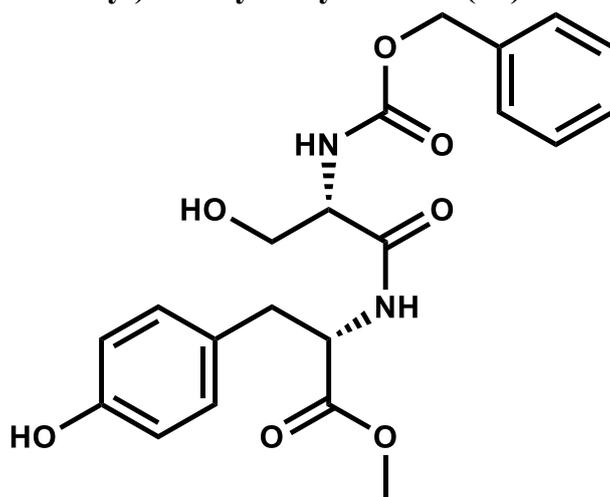
Methyl tosylglycyl-*L*-tyrosinate (4w)⁸



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), tosylglycine (2 mmol, 458.5 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 713.1 mg (1.76 mmol, 88%) white solid. **Mp.** 108-111 °C. **R_f** = 0.54 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.63 (d, $J = 7.9$ Hz, 2H), 7.47 (s, 1H), 7.20 (d, $J = 8.2$ Hz, 3H), 6.89 (d, $J = 8.1$ Hz, 2H), 6.66 (d, $J = 8.0$ Hz, 2H), 6.23 – 6.10 (m, 1H), 4.70 (q, $J = 6.4$ Hz, 1H), 3.62 (s, 3H), 3.50 (s, 2H), 2.94 (t, $J = 5.5$ Hz, 2H), 2.32 (s, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 168.8, 155.4, 144.1, 135.6, 130.4, 129.9, 127.1, 126.8, 115.7, 53.6, 52.6, 45.5, 36.7, 21.5. **HRMS** (ESI) [M + Na]⁺ calculated for C₁₉H₂₂N₂O₆SNa⁺: 429.1096, found 429.1094.

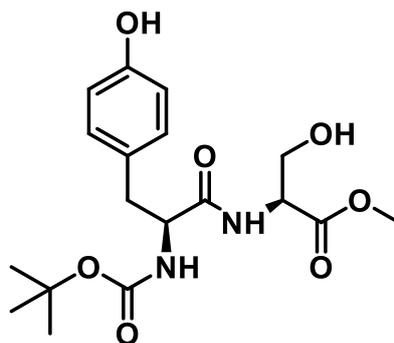
Methyl ((benzyloxy)carbonyl)-*L*-seryl-*L*-tyrosinate (4x)^{8,17}



According to the general procedure A using methyl *L*-tyrosinate hydrochloride (2 mmol, 463.4 mg), ((benzyloxy)carbonyl)serine (2 mmol, 478.5 mg), HOBT (2.0 mmol, 270.2 mg), Et₃N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 673.9 mg (1.62 mmol, 81%) white solid. $R_f = 0.7$ in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 20:1$. $^1\text{H NMR}$ (400 MHz, Chloroform- d) δ 7.82 (s, 1H), 7.43 (s, 1H), 7.30 (s, 5H), 6.91 (d, $J = 8.0$ Hz, 2H), 6.71 (d, $J = 8.0$ Hz, 2H), 6.31 (d, $J = 7.6$ Hz, 1H), 5.15 – 4.97 (m, 2H), 4.79 (q, $J = 6.6$ Hz, 1H), 4.35 (s, 1H), 4.02 (s, 1H), 3.84 (d, $J = 9.7$ Hz, 1H), 3.63 (s, 4H), 3.07 – 2.98 (m, 1H), 2.97 – 2.87 (m, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform- d) δ 172.1, 170.8, 156.7, 155.5, 135.9, 130.3, 128.5, 128.2, 128.0, 126.7, 115.5, 67.3, 62.5, 56.0, 53.8, 52.4, 36.6. According to the literature^[8].

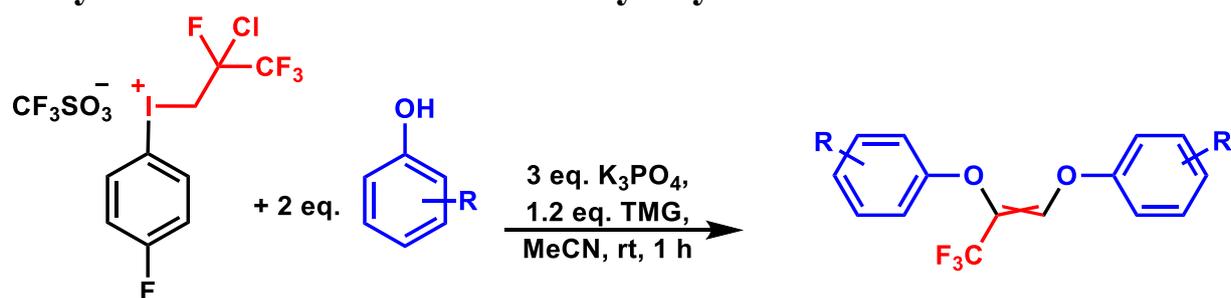
Methyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-serinate (4y)^{8,23}



According to the general procedure B using (*tert*-butoxycarbonyl)-*L*-tyrosine (2 mmol, 562.6 mg), methyl *L*-serinate hydrochloride (2 mmol, 311.2 mg), HOBt (2.0 mmol, 270.2 mg), Et_3N (6.6 mmol, 667.9 mg, 0.92 ml), EDC (3 mmol, 573.5 mg), and anhydrous DMF (10 ml).

Yield: 323.2 mg (0.85 mmol, 42%) white solid. $R_f = 0.30$ in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 9:1$. $^1\text{H NMR}$ (400 MHz, Methanol- d_4) δ 7.06 (d, $J = 8.4$ Hz, 2H), 6.70 (d, $J = 8.5$ Hz, 2H), 4.52 (t, $J = 4.3$ Hz, 1H), 4.29 (dd, $J = 9.4, 5.2$ Hz, 1H), 3.89 (dd, $J = 11.3, 4.5$ Hz, 1H), 3.79 (dd, $J = 11.3, 4.2$ Hz, 1H), 3.72 (s, 3H), 3.03 (dd, $J = 13.9, 5.4$ Hz, 1H), 2.74 (dd, $J = 13.9, 9.1$ Hz, 1H), 1.38 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, Methanol- d_4) δ 174.6, 171.9, 157.7, 157.2, 131.4, 129.1, 116.1, 80.7, 62.9, 57.5, 56.1, 52.8, 38.4, 28.6. Spectral data is in accordance with data given in the literature^[23].

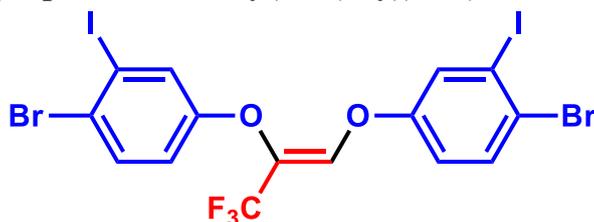
4. Synthesis of trifluorinated diaryloxy-ethenes



General procedure

Different phenols (0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol) and MeCN (0.85 mL) were measured into a screw cap vial. After the formation of a suspension 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l) was added in one portion by Hamilton syringe. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) in 2.15 mL MeCN was dosed over 30 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature (monitored by gas chromatography and TLC), after which the reaction mixture was concentrated to Celite under reduced pressure. The crude product was purified by column chromatography using Hex:EtOAc or CH_2Cl_2 :MeOH as eluent.

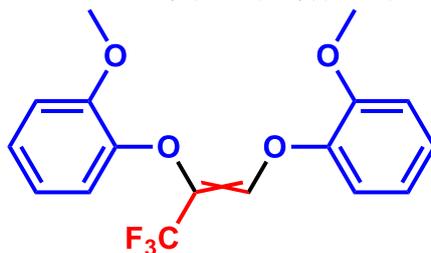
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(1-bromo-2-iodobenzene) (3a)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-bromo-3-iodophenol (179.3 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 190.0 mg (0.28 mmol, 92%) white solid. **E/Z ratio**: 2:98. **Mp.** 105-107 $^{\circ}C$. **R_f** = 0.76 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 692(16), 691(7), 690(30), 688(16), 392(15), 390(14), 346(5), 345(8), 344(5), 312(9), 300(17), 299(5), 298(17), 297(5), 283(25), 282(7), 281(25), 280(7), 277(6), 276(29), 271(8), 269(7), 267(5), 266(51), 265(7), 264(53), 247(5), 185(7), 179(5), 173(8), 172(8), 170(7), 157(10), 156(43), 155(8), 154(42), 151(5), 150(12), 144(5), 142(5), 137(5), 76(12), 75(100), 74(30), 73(5). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.55 – 7.55 (m, 1H), 7.54 (d, J = 2.9 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.47 (d, J = 2.9 Hz, 1H), 7.11 (s, 1H), 6.92 (dd, J = 8.8, 3.0 Hz, 1H), 6.85 (dd, J = 8.8, 2.9 Hz, 1H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -69.0. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 155.3, 154.6, 136.9 (q, J = 5.0 Hz), 133.3, 132.9, 128.6, 127.3, 127.2 (q, J = 36.1 Hz), 125.6, 123.4, 121.0 (q, J = 272.0 Hz), 118.3, 116.9, 101.8, 101.2. **HRMS** (EI) $[M]^+$ calculated for $C_{15}H_7Br_2F_3I_2O_2^+$: 687.68543, found 687.68523.

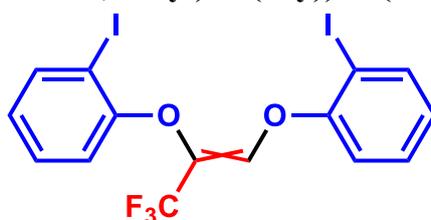
2,2'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(methoxybenzene) (3b)



Synthesized according to the general procedure at the beginning of chapter 3 using 2-methoxyphenol (74.484 mg, 0.6 mmol, 55.5 μ l), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 18.8 mg (0.06 mmol, 19%) yellow oil. *E/Z* ratio: 3:97. R_f = 0.80 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 341(13), 340(75), 217(16), 216(10), 202(8), 197(11), 189(18), 170(7), 159(7), 149(5), 148(13), 139(11), 135(9), 124(29), 123(17), 122(35), 121(41), 119(13), 109(24), 107(5), 105(5), 96(5), 95(36), 93(8), 92(60), 91(14), 81(5), 80(11), 79(8), 78(11), 77(100), 76(5), 67(7), 65(25), 64(23), 63(18), 53(5), 52(25), 51(21), 50(8). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (dd, J = 8.0, 1.6 Hz, 1H), 7.11 (td, J = 7.8, 1.7 Hz, 1H), 7.03 (s, 1H), 7.02 – 6.99 (m, 1H), 6.97 (dd, J = 8.0, 1.7 Hz, 1H), 6.95 – 6.93 (m, 1H), 6.93 – 6.92 (m, 1H), 6.91 – 6.89 (m, 1H), 6.90 – 6.87 (m, 1H), 3.90 (s, 3H), 3.81 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -68.6. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 150.5, 149.4, 146.2, 145.9, 140.3 (q, J = 5.1 Hz), 126.0, 125.0 (q, J = 35.2 Hz), 123.4, 121.9 (q, J = 272.0 Hz), 121.1, 120.7, 120.2, 115.1, 113.3, 112.9, 56.3, 56.2. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{17}H_{15}F_3O_4Na^+$: 363.0820, found 363.0820.

2,2'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(iodobenzene) (3c)

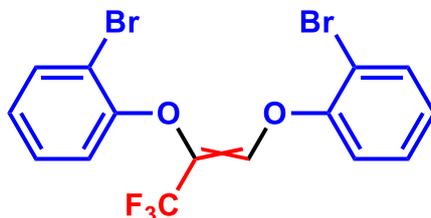


Synthesized according to the general procedure at the beginning of chapter 3 using 2-iodophenol (132.0 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 129.1 mg (0.24 mmol, 81%) yellow oil. *E/Z* ratio: 27:73. R_f = 0.54 in Hex:EtOAc = 10:1. **MS** (EI, 70 eV): m/z (%): 533(13), 532(85), 312(12), 278(8), 258(11), 239(6), 220(28), 219(15), 203(71), 202(29), 191(12), 186(47), 181(17), 167(5), 158(5), 157(5), 153(6), 152(18), 151(6), 136(6), 108(6), 93(5), 92(45), 89(5), 77(18), 76(100), 75(23), 74(13). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.86 – 7.79 (m, 1.33H), 7.77 – 7.74 (m, 0.72H), 7.38 – 7.28 (m, 2H), 7.16 – 7.12 (m, 1H), 7.11 (s, 0.73H), 7.01 – 6.97 (m, 1H), 6.94 – 6.86 (m, 1.3H), 6.85 (s, 0.24H), 6.84 – 6.79 (m, 0.71H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -68.9. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.0, 155.9, 155.8, 155.6, 141.5 (q, J = 2.3 Hz), 140.2, 140.2, 140.2,

139.8, 137.1 (q, $J = 5.0$ Hz), 131.0 (q, $J = 37.0$ Hz), 130.0, 129.9, 129.9, 129.6, 127.7 (q, $J = 35.9$ Hz), 126.6, 126.4, 125.5, 125.1, 121.3 (q, $J = 272.1$ Hz), 120.6 (q, $J = 275.4$ Hz), 116.6, 116.4, 115.0, 114.8, 86.7, 85.8. **HRMS** (EI) $[M]^+$ calculated for $C_{15}H_9F_3I_2O_2^+$: 531.86440, found 531.86528.

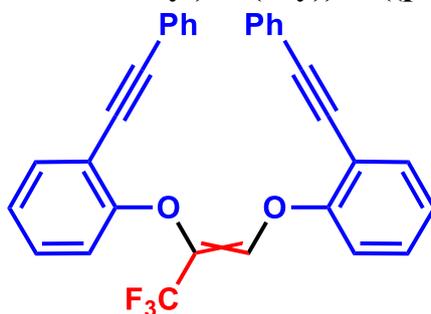
2,2'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(bromobenzene) (3d)



Synthesized according to the general procedure at the beginning of chapter 3 using 2-bromophenol (103.8 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 116.0 mg (0.26 mmol, 88%) yellow oil. **E/Z ratio**: 14:86. $R_f = 0.88$ in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 440(16), 439(6), 438(32), 436(16), 266(9), 264(9), 202(25), 187(13), 186(100), 183(5), 181(14), 174(20), 173(9), 172(20), 171(7), 167(8), 158(12), 157(70), 156(5), 155(66), 153(5), 152(18), 151(5), 145(24), 143(24), 136(8), 119(8), 117(7), 92(8), 89(6), 77(17), 76(54), 75(62), 74(15), 64(16), 63(30), 62(6), 51(9), 50(27). **1H NMR** (400 MHz, Chloroform- d) δ 7.50 (t, $J = 2.1$ Hz, 0.16H), 7.46 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.42 (dd, $J = 7.9, 1.6$ Hz, 0.84H), 7.21 – 7.17 (m, 1H), 7.17 – 7.13 (m, 1H), 7.08 (dd, $J = 8.3, 1.6$ Hz, 1H), 6.98 (s, 0.84H), 6.95 – 6.93 (m, 0.86H), 6.93 – 6.91 (m, 1H), 6.90 – 6.88 (m, 0.28H), 6.84 (td, $J = 7.7, 1.6$ Hz, 0.89H), 6.73 (s, 0.16H). **^{19}F NMR** (376 MHz, Chloroform- d) δ -64.8, -69.0. **^{13}C NMR** (101 MHz, Chloroform- d) δ 154.4, 153.4, 153.4, 153.2, 141.4 (q, $J = 2.2$ Hz), 137.5 (q, $J = 5.0$ Hz), 134.2, 134.1, 134.1, 133.8, 131.0 (q, $J = 37.1$ Hz), 129.0, 129.0, 128.9, 128.5, 127.3 (q, $J = 35.9$ Hz), 126.3, 126.1, 125.1, 124.6, 121.3 (q, $J = 272.1$ Hz), 120.7 (q, $J = 275.1$ Hz), 118.2, 117.6, 116.2, 115.8, 113.4, 113.3, 112.4, 112.2. **HRMS** (EI) $[M]^+$ calculated for $C_{15}H_9Br_2F_3O_2^+$: 435.89214, found 435.89107.

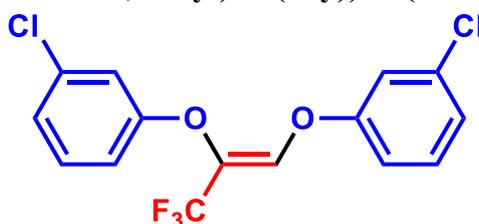
2,2'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis((phenylethynyl)benzene) (3e)



Synthesized according to the general procedure at the beginning of chapter 3 using 2-(phenylethynyl)phenol (116.5 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 104.3 mg (0.22 mmol, 72%) yellow solid. **E/Z ratio**: 9:91. **Mp.** 91-93 °C. **R_f** = 0.57 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 481(15), 480(46), 479(6), 461(5), 460(12), 459(8), 440(8), 439(19), 419(5), 413(7), 412(33), 411(100), 410(19), 409(6), 404(5), 403(16), 402(6), 397(5), 396(7), 395(15), 394(21), 393(28), 392(23), 391(5), 387(6), 386(8), 384(15), 383(42), 382(13), 381(20), 379(10), 376(6), 375(13), 374(5), 369(6), 368(11), 367(9), 366(10), 365(17), 364(19), 363(36), 356(5), 355(12), 354(5), 353(8), 352(7), 351(6), 350(10), 339(7), 335(11), 334(36), 333(11), 326(7), 319(7), 318(27), 317(5), 310(5), 307(7), 306(21), 305(56), 294(6), 292(5), 290(5), 289(15), 288(5), 287(20), 286(23), 282(5), 281(19), 278(5), 277(10), 276(16), 275(5), 268(7), 267(34), 265(8), 263(5), 259(10), 252(6), 240(6), 239(31), 238(31), 237(5), 236(6), 220(7), 219(11), 218(42), 210(5), 209(9), 207(10), 206(12), 205(23), 196(13), 194(10), 193(5), 191(8), 190(32), 189(66), 187(6), 184(6), 183(10), 182(9), 178(16), 177(23), 176(77), 175(19), 174(9), 169(11), 166(9), 165(55), 164(26), 163(27), 162(6), 152(13), 151(39), 150(32), 149(5), 139(21), 138(7), 137(7), 127(8), 126(13), 115(11), 113(5), 105(15), 89(5), 88(6), 87(5), 77(18), 76(5), 75(7), 63(7), 51(6). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.41 (m, 2H), 7.40 – 7.35 (m, 2H), 7.33 (d, *J* = 7.1 Hz, 2H), 7.23 – 7.12 (m, 8H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.92 (t, *J* = 8.0 Hz, 2H), 6.82 (t, *J* = 7.5 Hz, 1H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -68.6. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 157.0, 156.7, 138.8 (q, *J* = 5.0 Hz), 133.9, 133.5, 131.8, 131.7, 129.9, 129.5, 128.8, 128.5, 128.4, 128.3, 126.0 (q, *J* = 35.4 Hz), 125.0, 123.6, 122.9, 122.8, 121.7 (q, *J* = 272.3 Hz), 117.9, 114.8, 114.3, 113.5, 95.5, 94.3, 84.9, 83.9. **HRMS** (ESI) [M + Na]⁺ calculated for C₃₁H₁₉F₃O₂Na⁺: 503.1235, found 503.1232.

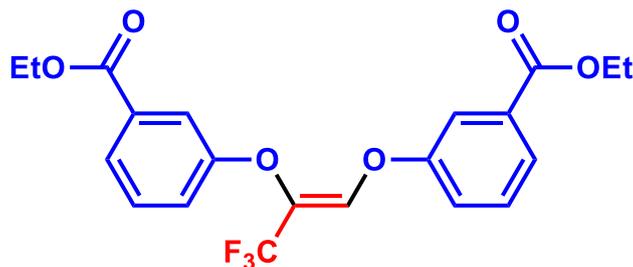
3,3'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(chlorobenzene) (3f)



Synthesized according to the general procedure at the beginning of chapter 3 using 3-chlorophenol (77.1 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 91.4 mg (0.26 mmol, 87%) yellow oil. **E/Z ratio**: 3:97. **R_f** = 0.80 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 350(22), 349(6), 348(35), 223(11), 222(25), 221(32), 220(67), 203(5), 202(7), 201(15), 195(10), 193(32), 186(9), 152(21), 145(7), 143(21), 139(8), 130(10), 128(30), 113(32), 112(10), 111(100), 101(6), 100(6), 99(16), 85(8), 77(7), 76(23), 75(84), 74(13), 73(11), 64(7), 63(17), 62(5), 51(9), 50(17). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.06 (s, 1H), 7.05 – 7.02 (m, 1H), 7.00 – 6.98 (m, 1H), 6.97 – 6.94 (m, 1H), 6.90 – 6.89 (m, 1H), 6.88 – 6.85 (m, 1H), 6.77 (dd, *J* = 8.3, 2.6 Hz, 1H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -69.1. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 157.3, 156.6, 137.3 (q, *J* = 5.0 Hz), 135.6, 135.1, 130.9, 130.5, 127.1 (q, *J* = 35.8 Hz), 125.2, 123.6, 121.3 (q, *J* = 272.2 Hz), 117.8, 116.3, 115.2, 113.8. **HRMS** (EI) [M]⁺ calculated for C₁₅H₉Cl₂F₃O₂⁺: 347.99317, found 347.99250.

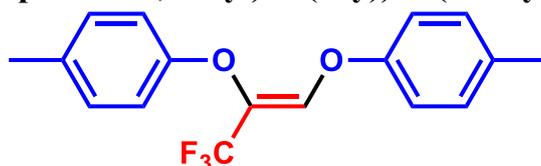
Diethyl 3,3'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))dibenzoate (3g)



Synthesized according to the general procedure at the beginning of chapter 3 using ethyl 3-hydroxybenzoate (99.7 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 87.0 mg (0.2 mmol, 68%) colorless oil. ***E/Z* ratio**: 1:99. **R_f** = 0.62 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 425(22), 424(100), 380(11), 379(52), 352(5), 351(14), 336(9), 335(53), 323(11), 307(5), 249(5), 243(7), 239(14), 231(24), 230(45), 214(8), 213(42), 211(8), 209(9), 203(10), 201(10), 199(7), 197(5), 191(8), 188(5), 187(48), 186(25), 185(7), 183(8), 182(6), 181(23), 180(12), 179(5), 176(9), 169(6), 168(10), 167(54), 166(13), 165(6), 159(16), 158(5), 155(5), 153(20), 152(40), 151(26), 149(5), 145(7), 141(10), 139(12), 138(66), 133(17), 127(10), 122(13), 121(61), 120(13), 119(5), 115(6), 110(5), 109(9), 105(13), 104(29), 103(21), 94(12), 93(17), 92(29), 91(5), 81(7), 77(28), 76(93), 75(30), 74(7), 66(6), 65(62), 64(22), 63(19), 51(8), 50(20). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.74 (d, J = 7.8 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.66 – 7.66 (m, 1H), 7.59 – 7.52 (m, 1H), 7.30 (t, J = 7.9 Hz, 1H), 7.29 (t, J = 8.1 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.16 (s, 1H), 7.07 (dd, J = 8.2, 2.7 Hz, 1H), 4.32 – 4.23 (m, 4H), 1.34 – 1.22 (m, 6H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -69.1. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 166.0, 165.5, 156.6, 156.1, 137.5 (q, J = 5.0 Hz), 132.7, 132.3, 130.1, 129.6, 127.0 (q, J = 35.7 Hz), 125.9, 124.4, 121.7, 121.4 (q, J = 270.2 Hz), 120.1, 117.7, 116.4, 61.5, 61.3, 14.3. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{21}H_{19}F_3O_6Na^+$: 447.1031, found 447.1027.

4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(methylbenzene) (3h)

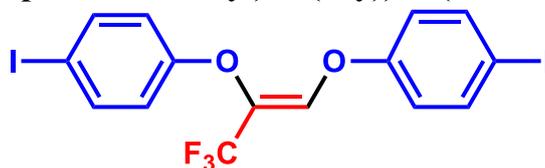


Synthesized according to the general procedure at the beginning of chapter 3 using 4-hydroxytoluene (64.9 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 50.7 mg (0.17 mmol, 55%) colorless oil. ***E/Z* ratio**: 1:99. **R_f** = 0.79 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 309(9), 308(51), 201(24), 200(26), 199(7), 181(9), 173(17), 153(7), 133(5), 132(6), 131(5), 123(11), 119(7), 109(8), 108(66), 107(13), 103(5), 92(9), 91(100), 90(9), 89(20), 80(13), 79(12), 78(11), 77(31), 65(53), 63(10), 51(6). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.14 (d, J = 8.6 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 7.11 (s, 1H), 7.01 (d, J = 8.5 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 3H). **^{19}F NMR** (376 MHz,

Chloroform-*d*) δ -64.7, -68.8. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.8, 154.6, 138.3 (q, J = 4.9 Hz), 134.4, 132.4, 130.4, 130.0, 126.4 (q, J = 34.9 Hz), 121.8 (q, J = 272.1 Hz), 117.0, 115.3, 20.8, 20.7. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_2\text{Na}^+$: 331.0922, found 331.0924.

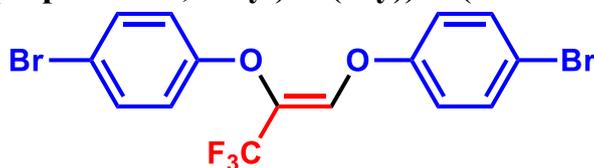
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(iodobenzene) (3i)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-iodophenol (132.0 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 146.6 mg (0.28 mmol, 92%) white solid. *E/Z* ratio: 2:98. **Mp.** 105-107 $^\circ\text{C}$. R_f = 0.39 in hexane. **MS** (EI, 70 eV): m/z (%): 533(9), 532(55), 312(14), 220(33), 219(6), 203(33), 191(9), 187(6), 186(65), 181(12), 153(7), 152(20), 93(6), 92(14), 77(12), 76(100), 75(19), 74(14). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 8.9 Hz, 2H), 7.12 (s, 1H), 6.84 (d, J = 8.9 Hz, 2H), 6.75 (d, J = 8.9 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.7, -69.1. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.7, 156.1, 139.1, 138.6, 137.2 (q, J = 5.0 Hz), 127.0 (q, J = 35.7 Hz), 121.3 (q, J = 272.3 Hz), 119.1, 117.8, 88.1, 85.9. HRMS (EI) $[\text{M}]^+$ calculated for $\text{C}_{15}\text{H}_9\text{F}_3\text{I}_2\text{O}_2^+$: 531.86440, found 531.86363.

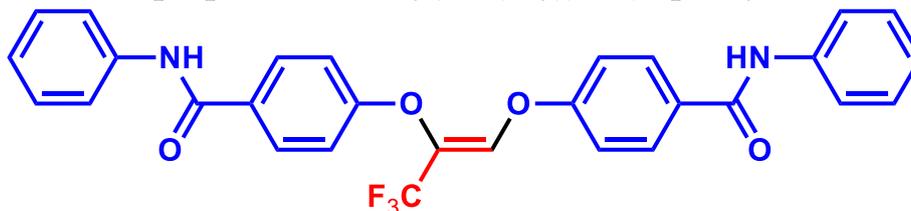
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(bromobenzene) (3j)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-bromophenol (103.8 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 122.7 mg (0.28 mmol, 93%) white solid. *E/Z* ratio: 2:98. **Mp.** 56-59 $^\circ\text{C}$. R_f = 0.90 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 440(18), 439(6), 438(37), 436(20), 266(11), 264(12), 202(19), 187(14), 186(100), 185(5), 181(9), 174(20), 173(5), 172(21), 158(9), 157(60), 156(5), 155(56), 153(6), 152(22), 145(20), 143(20), 119(6), 117(6), 77(12), 76(50), 75(48), 74(14), 64(13), 63(25), 62(6), 51(6), 50(24). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.33 (d, J = 9.0 Hz, 2H), 7.30 (d, J = 9.2 Hz, 2H), 7.02 (s, 1H), 6.86 (d, J = 9.0 Hz, 2H), 6.75 (d, J = 8.9 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -64.6, -69.0. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.8, 155.2, 137.3 (q, J = 4.9 Hz), 133.1, 132.6, 127.1 (q, J = 35.7 Hz), 121.4 (q, J = 272.2 Hz), 118.7, 117.7, 117.4, 115.7. HRMS (EI) $[\text{M}]^+$ calculated for $\text{C}_{15}\text{H}_9\text{Br}_2\text{F}_3\text{O}_2^+$: 435.89214, found 435.89217.

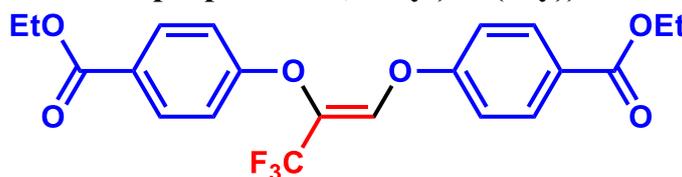
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(*N*-phenylbenzamide) (3k)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-hydroxy-*N*-phenylbenzamide (127.9 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 136.9 mg (0.26 mmol, 88%) colorless solid. ***E/Z* ratio**: 2:98. **Mp.** decomposes after 215 °C. **R_f** = 0.92 in CH₂Cl₂:MeOH = 10:1. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.23 (s, 1H), 10.20 (s, 1H), 8.04 – 7.99 (m, 4H), 7.99 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 4H), 7.44 – 7.24 (m, 8H), 7.14 – 7.02 (m, 2H). **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -63.3, -67.6. **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.7, 164.4, 158.5, 157.5, 139.3 (q, *J* = 5.0 Hz), 139.2, 139.1, 131.0, 129.9, 129.8, 128.6, 124.5 (q, *J* = 35.7 Hz), 123.7, 123.6, 121.2 (q, *J* = 271.5 Hz), 120.4, 120.3, 116.6, 114.6. **HRMS** (ESI) [M + Na]⁺ calculated for C₂₉H₂₁F₃N₂O₄Na⁺: 541.1351, found 541.1347.

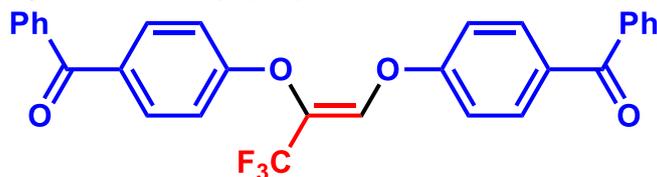
Diethyl 4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))dibenzoate (3l)



Synthesized according to the general procedure at the beginning of chapter 3 using ethyl 4-hydroxybenzoate (99.7 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 113.4 mg (0.27 mmol, 89%) white solid. ***E/Z* ratio**: 3:97. **Mp.** 47-49 °C. **R_f** = 0.62 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): *m/z* (%): 425(14), 424(62), 380(20), 379(100), 352(8), 351(33), 335(14), 323(7), 307(11), 306(30), 239(9), 231(8), 230(23), 213(17), 201(5), 187(19), 186(12), 183(5), 181(7), 176(9), 167(44), 159(7), 153(10), 152(24), 151(10), 145(8), 141(5), 139(5), 138(27), 133(14), 122(5), 121(28), 120(9), 109(10), 105(10), 104(26), 103(13), 93(8), 92(21), 81(6), 77(14), 76(35), 75(16), 65(27), 64(11), 63(10), 51(5), 50(10). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 8.9 Hz, 4H), 7.20 (s, 1H), 7.01 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.25 (q, *J* = 7.0 Hz, 2H), 4.25 (q, *J* = 7.0 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -69.2. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 165.9, 165.6, 160.0, 159.0, 136.7 (q, *J* = 5.0 Hz), 131.9, 131.6, 127.2 (q, *J* = 36.0 Hz), 127.1, 125.6, 121.2 (q, *J* = 272.2 Hz), 116.4, 115.1, 61.2, 60.9, 14.4, 14.3. **HRMS** (ESI) [M + Na]⁺ calculated for C₂₁H₁₉F₃O₆Na⁺: 447.1031, found 447.1033.

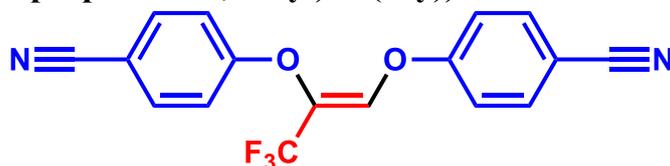
(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(phenylmethanone) (3m)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-hydroxybenzophenone (118.9 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 108.7 mg (0.22 mmol, 74%) yellow oil. **E/Z ratio:** 4:96. **R_f** = 0.43 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 489(15), 488(49), 412(25), 411(100), 228(10), 213(5), 181(10), 152(11), 151(5), 106(5), 105(60), 104(6), 77(42), 76(7), 51(5). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (t, J = 7.9 Hz, 4H), 7.74 (t, J = 7.3 Hz, 4H), 7.62 – 7.52 (m, 2H), 7.51 – 7.41 (m, 4H), 7.37 (s, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -69.0. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 195.4, 195.1, 159.8, 158.7, 137.8, 137.4, 136.8 (q, J = 4.9 Hz), 134.1, 132.7, 132.6, 132.5, 132.4, 132.3, 129.9, 129.9, 128.4, 128.4, 127.2 (q, J = 36.0 Hz), 121.2 (q, J = 272.2 Hz), 116.4, 115.1. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{29}H_{19}F_3O_4Na^+$: 511.1133, found 511.1129.

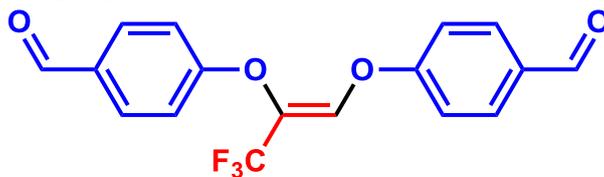
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))dibenzonitrile (3n)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-cyanophenol (71.5 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 82.1 mg (0.25 mmol, 83%) white solid. **E/Z ratio:** 2:98. **Mp.** 98-100 °C. **R_f** = 0.75 in Hex:EtOAc = 2:1. **MS** (EI, 70 eV): m/z (%): 331(19), 330(100), 212(26), 211(30), 192(12), 184(31), 164(6), 143(6), 134(24), 130(8), 119(19), 103(11), 102(84), 90(9), 76(16), 75(25), 64(7), 63(7), 51(12). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.65 (d, J = 9.1 Hz, 2H), 7.62 (d, J = 9.4 Hz, 2H), 7.30 (s, 1H), 7.14 (d, J = 8.9 Hz, 2H), 7.07 (d, J = 8.9 Hz, 2H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.6, -69.2. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 159.5, 158.3, 136.3 (q, J = 5.0 Hz), 134.5, 134.2, 127.5 (q, J = 36.4 Hz), 120.8 (q, J = 272.4 Hz), 118.4, 118.0, 117.5, 116.2, 108.8, 107.1. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{17}H_9F_3N_2O_2Na^+$: 353.0514, found 353.0507.

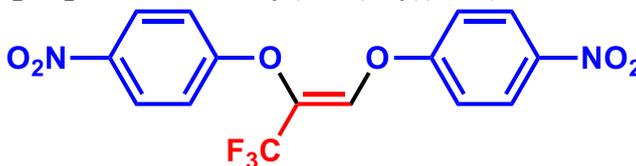
(Z)-4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))dibenzaldehyde (3o)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-hydroxybenzaldehyde (73.3 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 45.3 mg (0.14 mmol, 45%) yellow solid. **E/Z ratio:** 0:100. **Mp.** 87-89 °C. **R_f** = 0.81 in Hex:EtOAc = 1:1. **MS** (EI, 70 eV): m/z (%): 336(30), 335(22), 309(7), 308(39), 307(11), 214(5), 213(17), 195(6), 187(29), 186(40), 183(7), 167(28), 159(22), 155(7), 153(8), 152(14), 139(5), 133(6), 127(5), 122(5), 121(16), 118(8), 109(21), 105(26), 104(17), 95(5), 94(22), 93(6), 92(11), 78(10), 77(100), 76(26), 75(15), 74(7), 66(9), 65(16), 64(8), 63(13), 51(28). **¹H NMR** (400 MHz, Chloroform-*d*) δ 9.86 (s, 1H), 9.85 (s, 1H), 7.81 (d, J = 8.6 Hz, 2H), 7.80 (d, J = 8.7 Hz, 2H), 7.27 (s, 1H), 7.13 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 8.7 Hz, 2H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -69.2. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 190.8, 190.5, 161.1, 159.9, 136.4 (q, J = 4.9 Hz), 133.2, 132.2, 132.0, 127.6 (q, J = 36.3 Hz), 121.0 (q, J = 272.2 Hz), 117.1, 115.9. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{17}H_{11}F_3O_4Na^+$: 359.0507, found 359.0504.

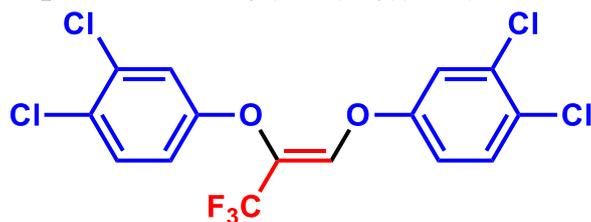
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(nitrobenzene) (3p)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-nitrophenol (83.5 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 95.0 mg (0.26 mmol, 86%) yellowish solid. **E/Z ratio:** 6:94. **Mp.** 107-108 °C. **R_f** = 0.53 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 371(23), 370(100), 354(7), 305(6), 243(5), 232(5), 231(17), 215(10), 212(6), 207(5), 202(7), 201(11), 197(5), 187(8), 186(73), 185(11), 173(6), 169(6), 168(11), 167(7), 152(9), 151(5), 145(8), 141(10), 139(16), 136(6), 127(6), 122(14), 115(5), 109(17), 108(5), 105(12), 102(6), 93(5), 92(27), 89(5), 80(5), 79(7), 77(20), 76(72), 75(53), 74(16), 65(6), 64(27), 63(29), 51(5), 50(27). **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.16 (d, J = 9.2 Hz, 2H), 8.15 (d, J = 9.3 Hz, 2H), 7.31 (s, 1H), 7.11 (d, J = 9.2 Hz, 2H), 7.05 (d, J = 9.2 Hz, 2H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.6, -69.3. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 161.0, 159.7, 144.6, 143.6, 136.4 (q, J = 4.9 Hz), 127.9 (q, J = 36.6 Hz), 126.2, 126.0, 120.8 (q, J = 272.4 Hz), 117.0, 115.7. **HRMS** (EI) $[M]^+$ calculated for $C_{15}H_9F_3N_2O_6^+$: 370.04127, found 370.04033.

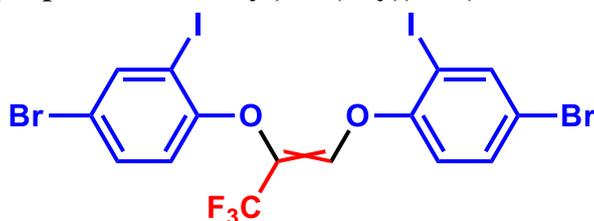
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(1,2-dichlorobenzene) (3q)



Synthesized according to the general procedure at the beginning of chapter 3 using 3,4-dichlorophenol (97.8 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 95.4 mg (0.23 mmol, 76%) colorless oil. **E/Z ratio**: 3:97. R_f = 0.79 in Hex:EtOAc = 10:1. **MS** (EI, 70 eV): m/z (%): 420(16), 419(6), 418(35), 417(5), 416(29), 258(5), 257(11), 256(22), 255(16), 254(32), 238(5), 237(7), 236(13), 235(10), 229(19), 227(31), 222(16), 221(6), 220(38), 191(5), 188(6), 186(11), 179(14), 177(24), 175(6), 173(9), 166(5), 164(26), 163(5), 162(42), 161(5), 149(11), 148(7), 147(62), 146(11), 145(100), 137(5), 135(22), 134(6), 133(34), 123(5), 112(8), 111(36), 110(24), 109(94), 107(7), 99(6), 98(6), 97(10), 87(5), 85(11), 84(12), 75(62), 74(43), 73(16), 72(6), 69(5), 63(32), 62(13), 61(6), 50(8). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.42 (d, J = 8.9 Hz, 1H), 7.38 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 2.9 Hz, 1H), 7.12 (d, J = 2.8 Hz, 1H), 7.11 (s, 1H), 6.92 (dd, J = 8.9, 2.9 Hz, 1H), 6.86 (dd, J = 8.8, 2.9 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -69.2. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.4, 154.6, 137.1 (q, J = 4.9 Hz), 133.9, 133.4, 131.5, 131.0, 129.0, 127.5 (q, J = 36.3 Hz), 127.0, 121.1 (q, J = 272.3 Hz), 119.3, 117.8, 116.5, 115.2. **HRMS** (EI) $[M]^+$ calculated for $C_{15}H_7Cl_4F_3O_2^+$: 415.91522, found 415.91411.

4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(1-bromo-3-iodobenzene) (3r)

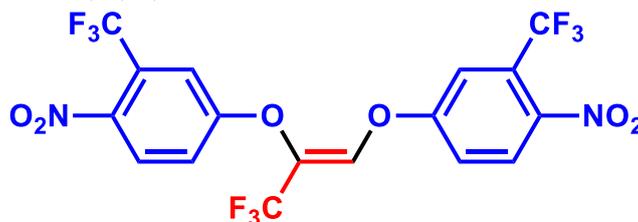


Synthesized according to the general procedure at the beginning of chapter 3 using 4-bromo-2-iodophenol (179.3 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 176.3 mg (0.25 mmol, 85%) white solid. **E/Z ratio**: 31:69. **Mp.** 81-83 °C. R_f = 0.55 in Hex:EtOAc = 20:1. **MS** (EI, 70 eV): m/z (%): 692(21), 691(8), 690(45), 688(23), 345(9), 339(9), 337(5), 328(6), 312(8), 300(18), 299(28), 298(19), 297(28), 283(46), 282(31), 281(49), 280(29), 276(11), 271(23), 269(23), 267(5), 266(49), 265(6), 264(50), 260(5), 247(7), 245(5), 237(5), 235(5), 218(5), 202(5), 201(6), 185(11), 179(5), 173(7), 172(38), 171(5), 170(40), 157(15), 156(65), 155(11), 154(65), 151(8), 150(20), 145(7), 144(13), 142(12), 137(10), 76(12), 75(100), 74(44), 73(5). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.95 (dd, J = 7.2, 2.4 Hz, 0.7H), 7.92 – 7.87 (m, 1.3H), 7.47 – 7.43 (m, 1.3H), 7.41 (dd, J = 8.8, 2.2 Hz, 0.7H), 7.05 (s,

0.7H), 6.97 (d, $J = 8.8$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.82 (s, 0.35H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.4, -69.1. ^{13}C NMR (101 MHz, Chloroform- d) δ 156.2, 155.3, 155.0, 154.7, 142.1, 142.1, 142.0, 141.7, 141.2 (q, $J = 2.0$ Hz), 136.6 (q, $J = 5.0$ Hz), 132.8, 132.8, 132.7, 132.5 – 132.3 (m), 131.3 (q, $J = 37.3$ Hz), 128.2 (q, $J = 36.2$ Hz), 121.0 (q, $J = 272.2$ Hz), 120.3 (q, $J = 275.5$ Hz), 118.4, 118.2, 117.4, 117.3, 117.1, 116.5, 116.0, 116.0, 87.6, 87.5, 86.7, 86.6. HRMS (EI) $[\text{M}]^+$ calculated for $\text{C}_{15}\text{H}_7\text{Br}_2\text{F}_3\text{I}_2\text{O}_2^+$: 687.68543, found 687.68528.

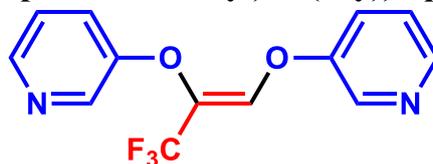
4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(1-nitro-2-(trifluoromethyl)benzene) (3s)



Synthesized according to the general procedure at the beginning of chapter 3 using 4-nitro-3-(trifluoromethyl)phenol (124.3 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 104.2 mg (0.21 mmol, 69%) yellow oil. *E/Z* ratio: 7:93. $R_f = 0.43$ in Hex:EtOAc = 4:1. MS (EI, 70 eV): m/z (%): 507(19), 506(100), 490(6), 487(12), 476(15), 269(9), 254(7), 253(6), 235(7), 219(14), 185(8), 163(8), 145(8), 144(29), 143(21), 132(13), 125(21), 94(8), 75(23), 74(5), 69(7), 63(15). ^1H NMR (400 MHz, Chloroform- d) δ 8.03 (d, $J = 2.4$ Hz, 1H), 8.01 (d, $J = 2.4$ Hz, 1H), 7.50 (d, $J = 2.8$ Hz, 1H), 7.42 (d, $J = 2.7$ Hz, 1H), 7.40 (d, $J = 1.3$ Hz, 1H), 7.36 (dd, $J = 2.8, 1.5$ Hz, 1H), 7.33 (dd, $J = 2.8, 1.4$ Hz, 1H). ^{19}F NMR (376 MHz, Chloroform- d) δ -60.3, -60.3, -64.5, -69.2. ^{13}C NMR (101 MHz, Chloroform- d) δ 158.7, 157.5, 144.5, 143.4, 136.5 (q, $J = 4.8$ Hz), 128.3 (q, $J = 37.1$ Hz), 128.3, 128.2, 126.8 (q, $J = 35.1$ Hz), 126.6 (q, $J = 34.8$ Hz), 121.5 (q, $J = 273.8$ Hz), 121.3 (q, $J = 274.2$ Hz), 120.5 (q, $J = 272.6$ Hz), 120.1, 118.4, 116.9 (q, $J = 5.6$ Hz), 115.6 (q, $J = 5.7$ Hz). HRMS (EI) $[\text{M}]^+$ calculated for $\text{C}_{17}\text{H}_7\text{F}_9\text{N}_2\text{O}_6^+$: 506.01604, found 506.01642.

(*Z*)-3,3'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))dipyridine (3t)

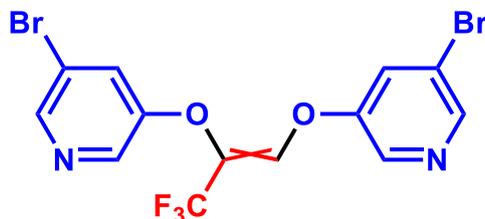


Synthesized according to the general procedure at the beginning of chapter 3 using 3-hydroxypyridine (57.1 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 59.5 mg (0.21 mmol, 70%) beige solid. *E/Z* ratio: 0:100. **Mp.** 38-41 $^\circ\text{C}$. $R_f = 0.56$ in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 10:1$. MS (EI, 70 eV): m/z (%): 283(5), 282(32), 281(20), 253(5), 213(9), 188(11), 185(29), 168(8), 156(19), 155(17), 95(11), 79(12), 78(100), 67(5), 52(8), 51(53),

50(5). ¹H NMR (400 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 8.39 (s, 1H), 8.37 – 8.28 (m, 2H), 7.36 (d, *J* = 6.9 Hz, 1H), 7.31 – 7.21 (m, 3H), 7.19 (s, 1H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -69.3. ¹³C NMR (101 MHz, Chloroform-*d*) δ 153.1, 152.5, 146.3, 144.7, 139.5, 138.7, 137.0 (q, *J* = 5.0 Hz), 127.6 (q, *J* = 36.1 Hz), 124.3, 124.2, 124.0, 122.6, 121.1 (q, *J* = 272.1 Hz). HRMS (EI) [M]⁺ calculated for C₁₃H₉F₃N₂O₂⁺: 282.06161, found 282.06209.

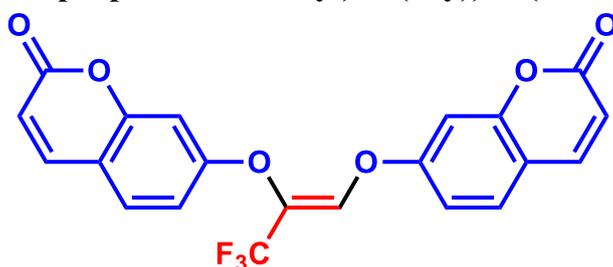
5,5'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(3-bromopyridine) (3u)



Synthesized according to the general procedure at the beginning of chapter 3 using 3-bromo-5-hydroxypyridine (104.4 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 123.1 mg (0.28 mmol, 93%) orange solid. *E/Z* ratio: 3:97. **Mp.** 92-95 °C. **R_f** = 0.86 in CH₂Cl₂:MeOH = 20:1. **MS** (EI, 70 eV): *m/z* (%): 443(5), 442(36), 441(19), 440(74), 439(23), 438(38), 361(5), 359(5), 345(14), 343(28), 341(16), 333(5), 331(5), 316(8), 314(15), 312(8), 268(17), 267(8), 266(18), 265(7), 248(13), 246(13), 235(17), 233(17), 187(13), 186(8), 175(11), 173(11), 159(13), 158(97), 156(100), 154(5), 147(5), 146(7), 145(5), 144(7), 131(25), 129(25), 127(5), 119(17), 117(17), 78(7), 77(30), 76(70), 75(9), 66(6), 65(8), 51(9). ¹H NMR (400 MHz, Chloroform-*d*) δ 8.48 (d, *J* = 1.9 Hz, 1H), 8.40 (d, *J* = 1.8 Hz, 1H), 8.37 (d, *J* = 2.6 Hz, 1H), 8.29 (d, *J* = 2.6 Hz, 1H), 7.52 (t, *J* = 2.2 Hz, 1H), 7.50 (t, *J* = 2.2 Hz, 1H), 7.21 (q, *J* = 1.1 Hz, 2H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -64.7, -69.2. ¹³C NMR (101 MHz, Chloroform-*d*) δ 152.9, 152.1, 147.6, 145.9, 137.6, 136.7, 136.7 (q, *J* = 4.5 Hz), 127.9 (q, *J* = 36.6 Hz), 125.6, 120.7 (q, *J* = 272.4 Hz), 120.6, 120.4. HRMS (EI) [M]⁺ calculated for C₁₃H₇Br₂F₃N₂O₂⁺: 437.88264, found 437.88058.

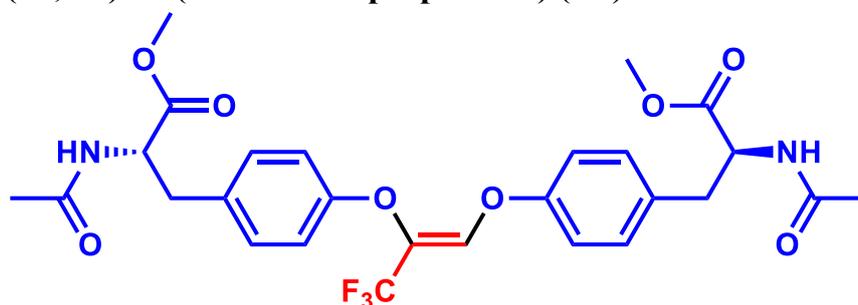
(*Z*)-7,7'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(2*H*-chromen-2-one) (3v)



Synthesized according to the general procedure at the beginning of chapter 3 using 7-hydroxycoumarin (97.3 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 39.4 mg (0.1 mmol, 32%) white solid. ***E/Z* ratio**: 2:98. **Mp.** 143-146 °C. **R_f** = 0.59 in Hex:EtOAc = 1:1. **MS** (EI, 70 eV): *m/z* (%): 417(23), 416(100), 255(33), 254(16), 235(14), 227(28), 226(30), 200(6), 199(52), 186(6), 180(10), 162(21), 158(5), 151(7), 149(6), 145(6), 134(33), 133(11), 117(13), 105(7), 90(7), 89(69), 77(11), 63(29), 62(6), 51(11). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 9.3 Hz, 0H), 7.65 (d, *J* = 9.4 Hz, 3H), 7.46 (d, *J* = 7.7 Hz, 3H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.31 (s, 1H), 7.05 – 6.98 (m, 3H), 6.96 – 6.87 (m, 3H), 6.35 (d, *J* = 9.7 Hz, 1H), 6.31 (d, *J* = 9.6 Hz, 1H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -69.1. **¹³C NMR** (101 MHz, CDCl₃) δ 160.6, 160.1, 159.2, 158.0, 155.5, 155.4, 143.1, 142.7, 136.9 (q, *J* = 5.0 Hz), 129.6, 129.3, 127.5 (q, *J* = 36.4 Hz), 121.0 (q, *J* = 272.6 Hz), 116.0, 115.8, 114.8, 113.4, 112.8, 105.1, 103.4. **HRMS** (ESI) [*M* + Na]⁺ calculated for C₂₁H₁₁F₃O₆Na⁺: 439.0405, found 439.0396.

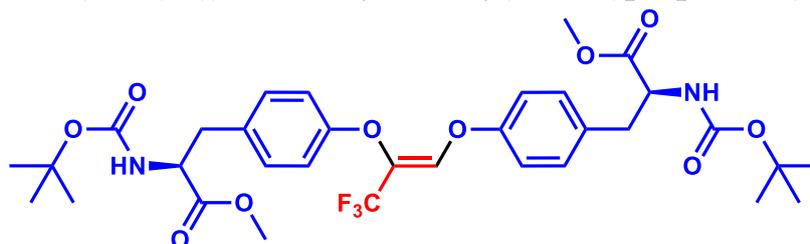
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-acetamidopropanoate) (3w)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl acetyl-*L*-tyrosinate (142.4 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 141.7 mg (0.25 mmol, 83%) colorless solid. ***E/Z* ratio**: 1:99. **Mp.** 155-158 °C. **R_f** = 0.39 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.42 (s, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.66 – 4.59 (m, 2H), 3.68 (s, 3H), 3.64 (s, 1H), 3.17 – 3.05 (m, 2H), 2.97 – 2.85 (m, 2H), 1.89 (s, 3H), 1.88 (s, 3H). **¹⁹F NMR** (376 MHz, Methanol-*d*₄) δ -65.9, -70.5. **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 173.5, 173.3, 173.1, 157.1, 156.6, 139.4 (q, *J* = 4.8 Hz), 134.7, 132.7, 131.8, 131.3, 127.3 (q, *J* = 35.4 Hz), 123.1 (q, *J* = 270.8 Hz), 117.8, 116.3, 55.3, 55.2, 52.7, 52.6, 37.6, 37.6, 22.2, 22.2. **HRMS** (ESI) [*M* + Na]⁺ calculated for C₂₇H₂₉F₃N₂O₈Na⁺: 589.1774, found 589.1779.

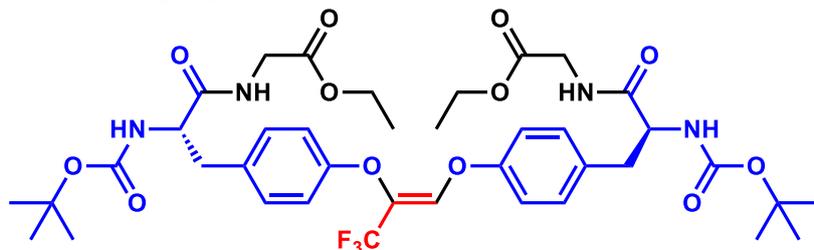
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*tert*-butoxycarbonyl)amino)propanoate) (5a)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl) *L*-tyrosinate (177.2 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 187 mg (0.27 mmol, 91%) yellowish solid. ***E/Z* ratio**: 1:99. **Mp.** 52-54 °C. **R_f** = 0.85 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.12 (s, 1H), 7.09 – 7.02 (m, 4H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.1 Hz, 2H), 5.06 (d, *J* = 8.5 Hz, 2H), 4.52 (s, 2H), 3.67 (s, 3H), 3.63 (s, 3H), 3.11 – 3.01 (m, 2H), 3.00 – 2.91 (m, 2H), 1.37 (s, 18H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.9, -68.9. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.3, 172.1, 155.8, 155.3, 155.1, 155.1, 137.7 (q, *J* = 3.3 Hz), 132.6, 130.8, 130.7, 130.4, 126.4 (q, *J* = 35.5 Hz), 121.5 (q, *J* = 272.1 Hz), 117.0, 115.5, 80.0, 79.9, 54.5, 54.4, 52.3, 52.1, 37.5, 37.5, 28.3. **HRMS** (ESI) [M + Na]⁺ calculated for C₃₃H₄₁F₃N₂O₁₀Na⁺: 705.2611, found 705.2623.

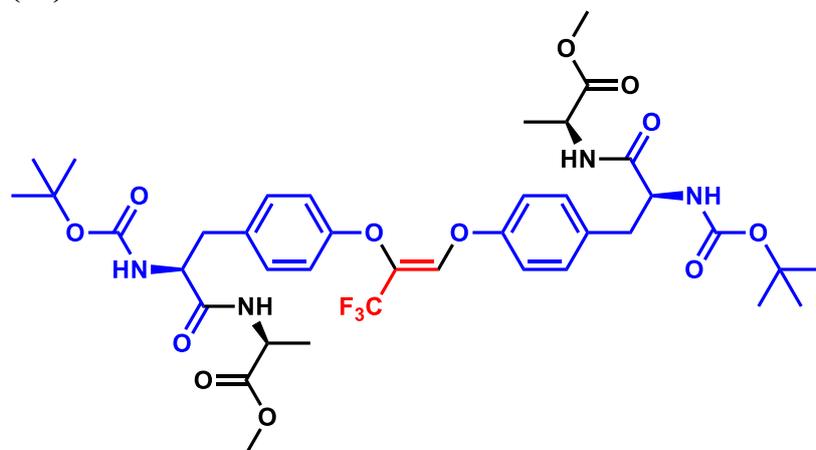
Diethyl 2,2'-(((2*S*,2'*S*)-3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(2-((*tert*-butoxycarbonyl)amino)propanoyl))bis(azanediyl))diacetate (5b)



Synthesized according to the general procedure at the beginning of chapter 3 using ethyl (*tert*-butoxycarbonyl)-*L*-tyrosylglycinate (219.8 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 192.7 mg (0.23 mmol, 78%) yellow solid. ***E/Z* ratio**: 6:94. **Mp.** 68-72 °C. **R_f** = 0.49 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.15 (s, 1H), 7.12 (d, *J* = 9.6 Hz, 3.35H), 7.02 (d, *J* = 8.0 Hz, 0.65H), 6.96 (d, *J* = 8.3 Hz, 1.6H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.80 – 6.64 (m, 2H), 6.70 – 6.64 (m, 0.4H), 5.25 – 5.13 (m, 2H), 4.45 – 4.32 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 4H), 4.04 – 3.83 (m, 4H), 3.07 (dd, *J* = 14.2, 6.2 Hz, 2H), 3.00 – 2.88 (m, 2H), 1.37 (s, 9H), 1.35 (s, 9H), 1.24 (t, *J* = 7.3 Hz, 3H), 1.24 (t, *J* = 7.2 Hz, 3H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.9, -68.9. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 171.9, 171.7, 169.6, 169.6, 155.7, 155.3, 137.9 (q, *J* = 4.7 Hz), 133.3, 131.3, 130.9, 130.5, 130.5, 126.6 (q, *J* = 34.8 Hz), 121.6 (q, *J* = 272.1 Hz), 117.2, 115.7, 115.6, 80.4, 80.4, 61.6, 61.6, 55.7, 55.6, 41.4, 41.4, 37.8, 37.7, 28.3, 28.3, 14.2. **HRMS** (ESI) [M + Na]⁺ calculated for C₃₉H₅₁F₃N₄O₁₂Na⁺: 847.3353, found 847.3340.

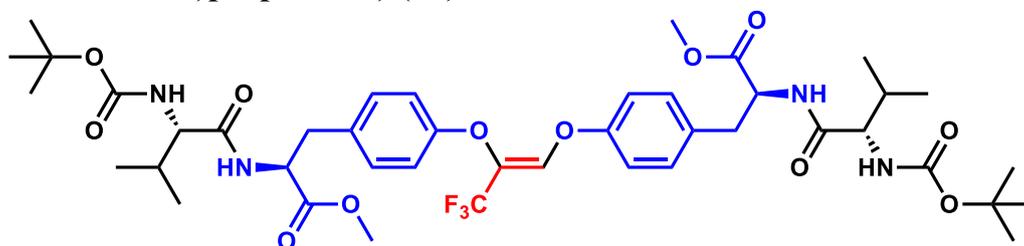
Dimethyl 2,2'-(((2*S*,2'*S*)-3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(2-((*tert*-butoxycarbonyl)amino)propanoyl))bis(azanediy))((2*S*,2'*S*)-dipropionate (5c)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-alaninate (105.3 mg, 0.29 mmol), K₃PO₄ (91.5 mg, 0.43 mmol), 1,1,3,3-tetramethylguanidine (TMG) (19.86 mg, 1.8 mmol, 21.8 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (74.8 mg, 0.14 mmol) and MeCN (1.5 ml).

Yield: 56.0 mg (0.07 mmol, 49%) white solid. *E/Z* ratio: 1:99. **Mp.** 126-129 °C. **R_f** = 0.65 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.13 (s, 1H), 7.10 (d, *J* = 6.8 Hz, 4H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.88 – 6.78 (m, 4H), 5.42 – 5.09 (m, 2H), 4.55 – 4.41 (m, 2H), 4.41 – 4.24 (m, 2H), 3.67 (s, 6H), 3.00 (dd, *J* = 13.8, 5.8 Hz, 2H), 2.92 (dd, *J* = 13.9, 7.6 Hz, 2H), 1.38 (s, 9H), 1.36 (s, 9H), 1.32 (d, *J* = 7.7 Hz, 3H), 1.30 (d, *J* = 7.9 Hz, 3H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -69.0. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 173.0, 172.9, 171.2, 170.9, 155.8, 155.6, 155.3, 137.4 (q, *J* = 3.8 Hz), 133.3, 131.4, 130.9, 130.5, 127.0 (q, *J* = 38.0 Hz), 121.5 (q, *J* = 272.1 Hz), 117.0, 115.6, 80.3, 55.8, 55.7, 52.5, 52.5, 48.1, 48.1, 37.9, 37.7, 28.3, 28.3, 18.2, 18.1. **HRMS** (ESI) [M + Na]⁺ calculated for C₃₉H₅₁F₃N₄O₁₂Na⁺: 847.3353, found 847.3362.

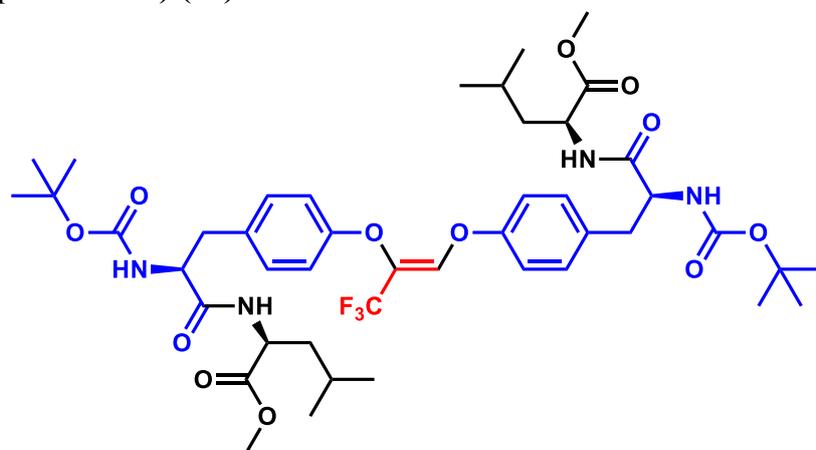
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))((2*S*,2'*S*)-bis(2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)propanoate) (5d)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-valyl-*L*-tyrosinate (236.7 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 156.7 mg (0.18 mmol, 59%) yellow solid. **E/Z ratio:** 5:95. **Mp.** 104-106 °C. **R_f** = 0.71 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.11 (s, 1H), 7.09 – 7.02 (m, 4H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.54 – 6.45 (m, 2H), 5.09 (d, *J* = 8.7 Hz, 2H), 4.85 – 4.75 (m, 2H), 3.95 – 3.83 (m, 2H), 3.68 (s, 3H), 3.64 (s, 3H), 3.13 – 2.96 (m, 4H), 2.12 – 1.97 (m, 2H), 1.41 (s, 18H), 0.93 – 0.80 (m, 12H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.9, -68.9. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.7, 171.5, 171.4, 171.4, 155.8, 155.8, 155.4, 137.5 (q, *J* = 4.3 Hz), 132.3, 130.8, 130.3, 130.3, 126.5 (q, *J* = 34.2 Hz), 121.5 (q, *J* = 272.2 Hz), 117.1, 115.6, 79.9, 60.0, 60.0, 53.2, 53.1, 52.4, 52.2, 37.2, 37.2, 30.8, 28.3, 19.2, 19.2, 17.8, 17.7. **HRMS** (ESI) [M + Na]⁺ calculated for C₄₃H₅₉F₃N₄O₁₂Na⁺: 903.3979, found 903.3998.

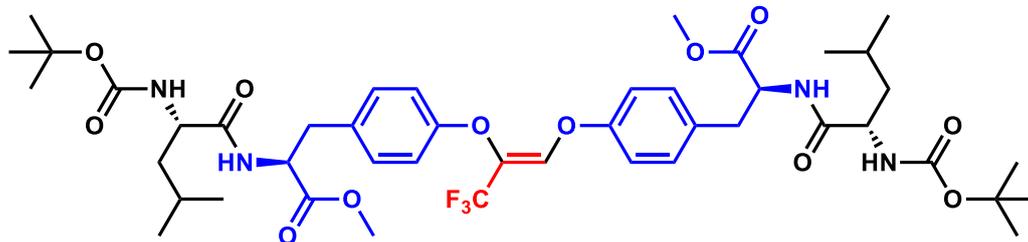
Dimethyl 2,2'-(((2*S*,2'*S*)-3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(2-((*tert*-butoxycarbonyl)amino)propanoyl))bis(azanediyl))(2*S*,2'*S*)-bis(4-methylpentanoate) (5e)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-leucinate (283.5 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 242.5 mg (0.27 mmol, 89%) yellow solid. **E/Z ratio:** 7:93. **Mp.** 78-80 °C. **R_f** = 0.74 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.14 (s, 1H), 7.13 – 7.09 (m, 4H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.46 (d, *J* = 8.2 Hz, 2H), 5.17 – 5.04 (m, 2H), 4.57 – 4.48 (m, 2H), 4.31 (q, *J* = 7.5 Hz, 2H), 3.66 (s, 3H), 3.65 (s, 3H), 3.06 – 2.90 (m, 4H), 1.64 – 1.54 (m, 4H), 1.50 – 1.42 (m, 2H), 1.38 (s, 9H), 1.38 (s, 9H), 0.94 – 0.82 (m, 12H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.9, -68.9. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 174.0, 173.0, 173.0, 171.2, 170.9, 170.0, 155.8, 155.5, 155.5, 155.3, 137.9 (q, *J* = 8.2 Hz), 133.3, 131.3, 130.9, 130.5, 130.4, 126.5 (q, *J* = 35.1 Hz), 121.6 (q, *J* = 272.2 Hz), 117.2, 115.5, 80.3, 55.7, 55.7, 52.3, 52.3, 50.9, 50.8, 41.6, 41.5, 37.6, 37.4, 28.3, 24.8, 22.8, 22.8, 22.0, 21.9. **HRMS** (ESI) [M + Na]⁺ calculated for C₄₅H₆₃F₃N₄O₁₂Na⁺: 931.4292, found 931.4294.

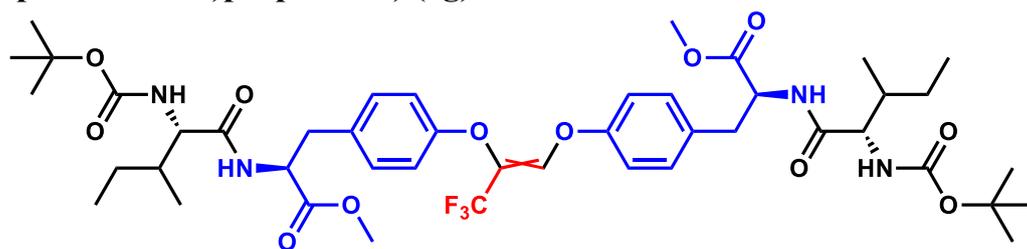
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)propanoate) (5f)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-leucyl-*L*-tyrosinate (245.1 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl)(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 234.5 mg (0.26 mmol, 86%) yellow solid. *E/Z* ratio: 7:93. **Mp.** 84-86 °C. **R_f** = 0.86 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.11 (s, 1H), 7.06 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.65 (d, *J* = 7.8 Hz, 2H), 4.96 (s, 2H), 4.82 – 4.73 (m, 2H), 4.14 – 3.99 (m, 2H), 3.68 (s, 3H), 3.63 (s, 3H), 3.15 – 2.95 (m, 4H), 1.70 – 1.50 (m, 4H), 1.40 (s, 20H), 0.88 (t, *J* = 5.3 Hz, 12H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.9, -68.9. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 172.4, 172.4, 171.7, 171.6, 155.9, 155.7, 155.4, 137.6 (q, *J* = 5.1 Hz), 132.4, 130.9, 130.5, 130.4, 126.6 (q, *J* = 35.3 Hz), 121.6 (q, *J* = 272.1 Hz), 117.1, 115.6, 112.1, 80.1, 53.4, 53.2, 52.4, 52.3, 41.2, 37.2, 37.2, 28.3, 24.7, 22.9, 22.0. **HRMS** (ESI) [M + Na]⁺ calculated for C₄₅H₆₃F₃N₄O₁₂Na⁺: 931.4292, found 931.4284.

Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((2*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)propanoate) (5g)

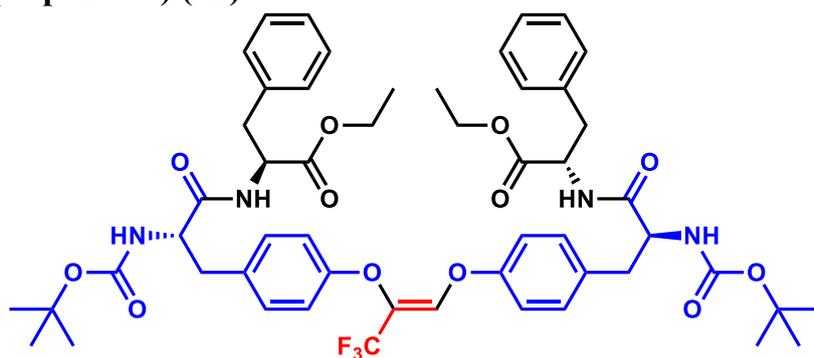


Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-isoleucyl-*L*-tyrosinate (245.1 mg, 0.6 mmol), 1,1,3,3-tetramethylguanidine (TMG) (207.3 mg, 1.8 mmol, 0.23 ml), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl)(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 215.3 mg (0.24 mmol, 79%) yellow solid. *E/Z* ratio: 22:78. **Mp.** 172-175 °C. **R_f** = 0.92 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.50 – 7.41 (m, 0.53H), 7.11 (s, 1H), 7.09 – 7.02 (m, 3.47H), 6.97 (d, *J* = 8.4 Hz, 1.7H), 6.93 (d, *J* = 8.3 Hz, 0.3H), 6.87 (d, *J* = 8.1 Hz, 1.7H), 6.74 (d, *J* = 8.1 Hz, 0.3H), 6.49 – 6.40 (m, 2H), 5.05 (d, *J* = 9.6 Hz, 2H), 4.86 – 4.78 (m, 2H), 3.98 – 3.86 (m, 2H), 3.70 (s, 0.7H), 3.69 (s, 2.3H), 3.67 (s, 0.7H), 3.65 (s,

2.3H), 3.13 – 2.98 (m, 4H), 1.90 – 1.70 (m, 2H), 1.42 (s, 20H), 1.17 – 0.95 (m, 2H), 0.88 – 0.87 (m, 6H), 0.86 – 0.84 (m, 6H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -64.9, -68.9. ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.7, 171.7, 171.6, 171.5, 171.4, 156.0, 155.8, 155.5, 137.6 (q, *J* = 5.0 Hz), 132.4, 131.8, 130.9, 130.4, 128.4, 126.9 (q, *J* = 20.2 Hz), 126.4, 122.0 (q, *J* = 253.8 Hz), 121.6 (q, *J* = 272.0 Hz), 117.2, 115.7, 112.2, 108.2, 108.1, 80.0, 59.4, 53.4, 53.3, 53.2, 52.5, 52.5, 52.4, 52.3, 37.3, 37.2, 37.2, 37.1, 28.4, 24.8, 15.5, 15.5, 11.5, 11.5, 11.4, 11.4. HRMS (ESI) [M + Na]⁺ calculated for C₄₅H₆₃F₃N₄O₁₂Na⁺: 931.4292, found 931.4293.

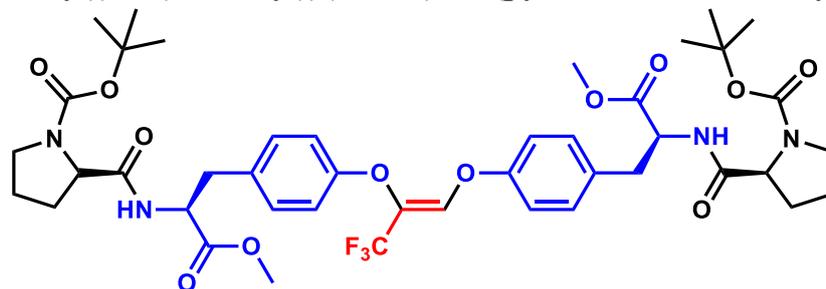
Diethyl 2,2'-(((2*S*,2'*S*)-3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(2-((*tert*-butoxycarbonyl)amino)propanoyl))bis(azanediyl))(2*S*,2'*S*)-bis(3-phenylpropanoate) (5h)



Synthesized according to the general procedure at the beginning of chapter 3 using ethyl (*tert*-butoxycarbonyl)-*L*-tyrosyl-*L*-phenylalaninate (273.9 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 213.1 mg (0.21 mmol, 71%) yellow solid. *E/Z* ratio: 1:99. **Mp.** 112-115 °C. **R_f** = 0.86 in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.18 (m, 6H), 7.14 – 7.08 (m, 4H), 7.05 – 6.71 (m, 9H), 6.48 – 6.33 (m, 2H), 5.14 – 4.95 (m, 2H), 4.74 (q, *J* = 6.6 Hz, 2H), 4.39 – 4.23 (m, 2H), 4.14 – 4.06 (m, 4H), 3.07 – 2.89 (m, 8H), 1.39 (s, 9H), 1.38 (s, 9H), 1.18 (t, *J* = 7.2 Hz, 6H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -64.7, -68.8. ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.8, 171.1, 171.0, 170.9, 170.7, 169.9, 155.8, 155.6, 155.4, 155.3, 138.1 (q, *J* = 1.8 Hz), 136.0, 135.8, 135.8, 135.7, 133.2, 131.1, 130.9, 130.5, 130.5, 129.4, 129.4, 128.6, 127.2, 127.2, 127.1, 126.3 (q, *J* = 34.6 Hz), 121.6 (q, *J* = 272.3 Hz), 117.3, 115.7, 115.5, 80.3, 80.3, 61.6, 61.6, 61.6, 61.6, 55.7, 53.4, 53.4, 53.3, 53.3, 38.1, 38.0, 37.7, 37.6, 28.3, 28.3, 14.2, 14.1. HRMS (ESI) [M + Na]⁺ calculated for C₅₃H₆₃F₃N₄O₁₂Na⁺: 1027.4292, found 1027.4291.

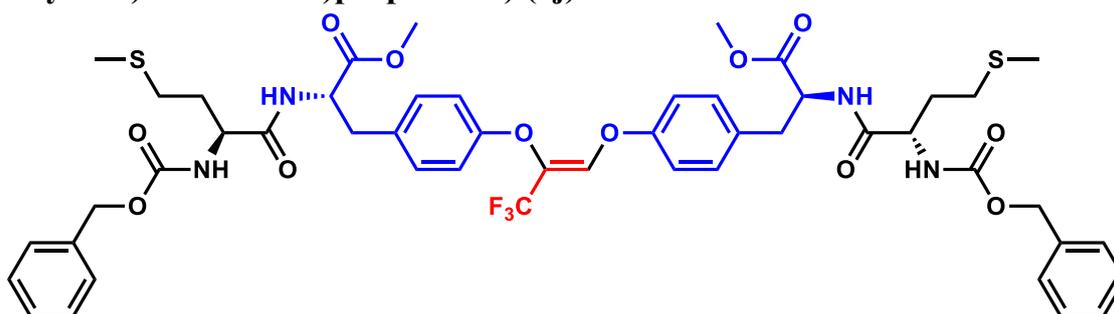
Di-tert-butyl 2,2'-(((2*S*,2'*S*)-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(3-methoxy-3-oxopropane-1,2-diyl))bis(azanediy))bis(carbonyl))(2*S*,2'*S*)-bis(pyrrolidine-1-carboxylate) (5i)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-prolyl-*L*-tyrosinate (235.5 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 229.6 mg (0.26 mmol, 87%) yellowish solid. *E/Z* ratio: 5:95. **Mp.** 73-76 °C. **R_f** = 0.69 in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.12 (s, 1H), 7.08 – 7.01 (m, 4H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.48 (d, *J* = 29.2 Hz, 1H), 4.81 (s, 2H), 4.23 (s, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.34 – 3.21 (m, 4H), 3.18 – 3.08 (m, 2H), 3.02 – 2.95 (m, 2H), 2.31 – 1.61 (m, 9H), 1.41 (s, 18H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -64.9, -68.8. ¹³C NMR (101 MHz, Chloroform-*d*) δ 172.2, 171.9, 171.8, 171.5, 155.8, 155.4, 154.6, 154.4, 138.0 (q, *J* = 3.5 Hz), 132.7 (q, *J* = 35.6 Hz), 130.8, 130.3, 121.5 (q, *J* = 272.4 Hz), 117.1, 115.4, 80.8, 80.5, 61.0, 59.9, 53.3, 52.7, 52.4, 52.3, 47.0, 37.3, 30.6, 28.3, 24.5, 23.6. **HRMS** (ESI) [M + Na]⁺ calculated for C₄₃H₅₅F₃N₄O₁₂Na⁺: 899.3666, found 899.3676.

Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-2-(((benzyloxy)carbonyl)amino)-4-(methylthio)butanamido)propanoate) (5j)

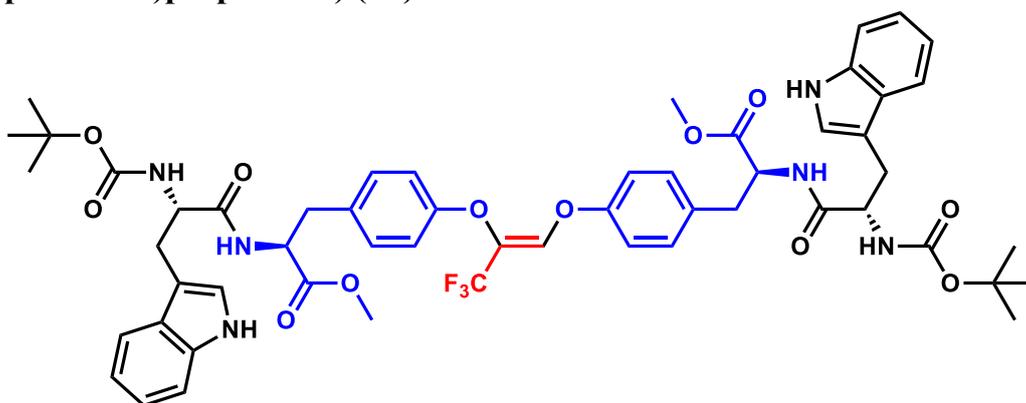


Synthesized according to the general procedure at the beginning of chapter 3 using methyl ((benzyloxy)carbonyl)-*L*-methionyl-*L*-tyrosinate (301.6 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 240.1 mg (0.24 mmol, 80%) white solid. *E/Z* ratio: 3:97. **Mp.** 112-115 °C. **R_f** = 0.96 in CH₂Cl₂:MeOH = 20:1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 (s, 10H), 7.09 (s, 1H), 7.02 (d, *J* = 5.8 Hz, 4H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 7.8 Hz, 2H),

5.58 (t, $J = 7.4$ Hz, 2H), 5.13 – 4.99 (m, 4H), 4.81 (t, $J = 6.2$ Hz, 2H), 4.35 (t, $J = 7.2$ Hz, 2H), 3.71 (s, 3H), 3.67 (s, 3H), 3.15 – 2.92 (m, 4H), 2.51 (t, $J = 7.1$ Hz, 4H), 2.03 (s, 3H), 2.01 (s, 3H), 2.00 – 1.83 (m, 4H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.8, -68.9. ^{13}C NMR (101 MHz, Chloroform- d) δ 171.7, 171.5, 171.0, 170.9, 156.1, 156.0, 155.4, 137.5 (q, $J = 4.8$ Hz), 136.2, 132.2, 130.9, 130.4, 130.3, 128.7, 128.7, 128.4, 128.3, 128.1, 126.7 (q, $J = 35.8$ Hz), 121.6 (q, $J = 271.9$ Hz), 117.2, 115.8, 67.2, 53.7, 53.7, 53.4, 53.3, 52.6, 52.5, 37.1, 31.6, 30.0, 15.2, 15.1. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{49}\text{H}_{55}\text{F}_3\text{N}_4\text{O}_{12}\text{S}_2\text{Na}^+$: 1035.3108, found 1035.3112.

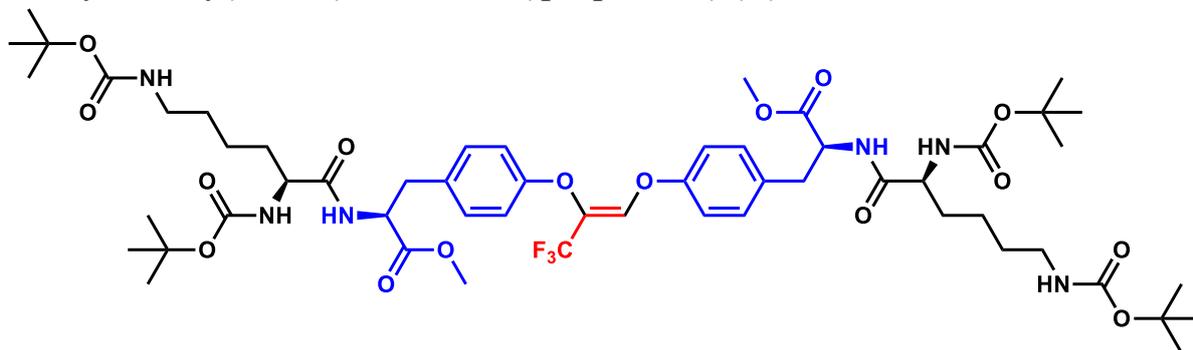
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(1*H*-indol-3-yl)propanamido)propanoate) (5k)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-tryptophyl-*L*-tyrosinate (288.9 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 146.0 mg (0.14 mmol, 46%) yellow solid. ***E/Z* ratio**: 1:99. **Mp.** 100-103 °C. **R_f** = 0.46 in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 20:1$. ^1H NMR (400 MHz, Chloroform- d) δ 8.42 (s, 1H), 8.38 (s, 1H), 7.63 (d, $J = 7.8$ Hz, 2H), 7.29 (t, $J = 8.4$ Hz, 2H), 7.19 – 7.13 (m, 2H), 7.11 (d, $J = 7.5$ Hz, 2H), 7.07 (d, $J = 5.1$ Hz, 1H), 6.97 – 6.93 (m, 1H), 6.88 (s, 1H), 6.84 (d, $J = 8.2$ Hz, 2H), 6.74 (d, $J = 8.2$ Hz, 2H), 6.63 (d, $J = 6.1$ Hz, 4H), 6.31 – 6.25 (m, 1H), 6.22 (d, $J = 8.2$ Hz, 1H), 5.16 (s, 2H), 4.70 (dt, $J = 14.7, 7.0$ Hz, 2H), 4.43 (s, 2H), 3.60 (s, 3H), 3.58 (s, 3H), 3.38 – 3.23 (m, 1H), 3.09 (dd, $J = 14.7, 7.1$ Hz, 1H), 2.98 – 2.79 (m, 4H), 1.42 (s, 18H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.9, -68.9. ^{13}C NMR (101 MHz, Chloroform- d) δ 171.4, 171.4, 171.2, 155.8, 155.2, 137.6 (q, $J = 4.4$ Hz), 136.4, 136.3, 132.2, 130.8, 130.4, 127.5, 127.5, 126.5 (q, $J = 35.1$ Hz), 123.6, 123.5, 122.4, 122.3, 121.6 (q, $J = 272.5$ Hz), 119.9, 119.0, 118.9, 116.9, 115.4, 111.4, 111.4, 110.3, 80.4, 55.3, 53.3, 53.2, 52.4, 52.3, 37.1, 37.0, 29.8, 28.4, 28.3. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{55}\text{H}_{61}\text{F}_3\text{N}_6\text{O}_{12}\text{Na}^+$: 1077.4197, found 1077.4200.

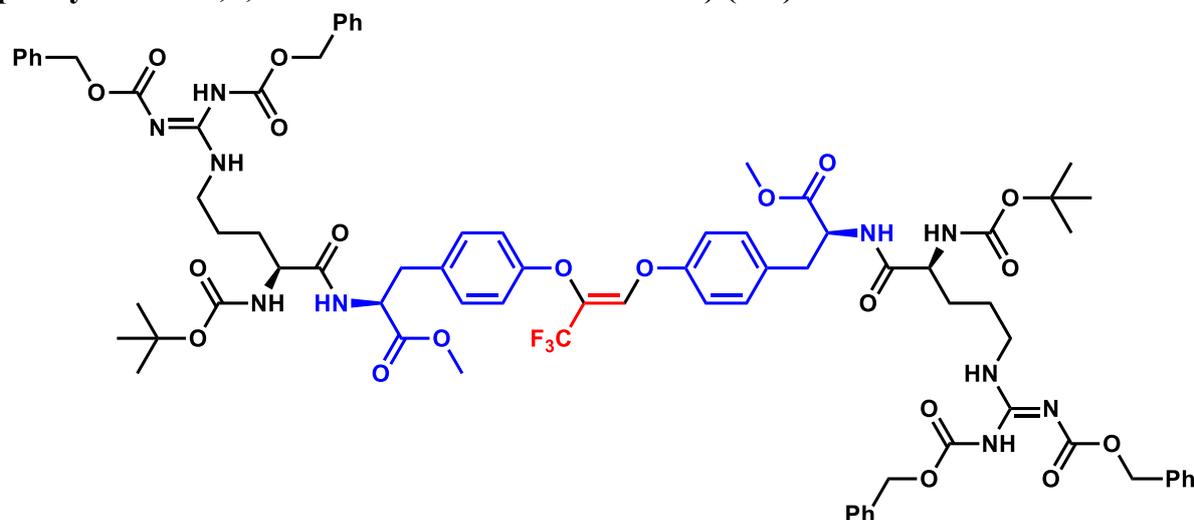
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-2,6-bis(*tert*-butoxycarbonyl)amino)hexanamido)propanoate) (5l)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl N^2, N^6 -bis(*tert*-butoxycarbonyl)-*L*-lysyl-*L*-tyrosinate (314.2 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 219.8 mg (0.19 mmol, 64%) yellow solid. ***E/Z* ratio:** 1:99. **Mp.** 82-84 °C. **R_f** = 0.78 in $CH_2Cl_2:MeOH = 20:1$. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.09 (s, 1H), 7.04 (d, $J = 8.6$ Hz, 2H), 7.01 (d, $J = 8.7$ Hz, 2H), 6.93 (d, $J = 8.7$ Hz, 2H), 6.83 (d, $J = 8.4$ Hz, 2H), 6.78 – 6.71 (m, 2H), 5.35 – 5.18 (m, 2H), 4.84 – 4.67 (m, 4H), 4.10 – 3.92 (m, 2H), 3.65 (s, 3H), 3.61 (s, 3H), 3.10 – 2.94 (m, 8H), 1.77 – 1.65 (m, 2H), 1.60 – 1.49 (m, 2H), 1.47 – 1.41 (m, 4H), 1.38 (s, 18H), 1.37 (s, 18H), 1.32 – 1.23 (m, 4H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.6, -68.9. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.1, 172.0, 171.8, 171.6, 156.2, 155.8, 155.7, 155.3, 137.6 (q, $J = 4.8$ Hz), 132.5, 130.8, 130.5, 130.3, 126.5 (q, $J = 35.5$ Hz), 121.5 (q, $J = 272.1$ Hz), 117.0, 115.6, 79.9, 79.0, 54.4, 53.3, 53.2, 52.4, 52.3, 40.4, 39.8, 38.6, 37.1, 37.0, 31.9, 29.6, 29.6, 28.4, 28.3, 22.5. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{55}H_{81}F_3N_6O_{16}Na^+$: 1161.5559, found 1161.5549.

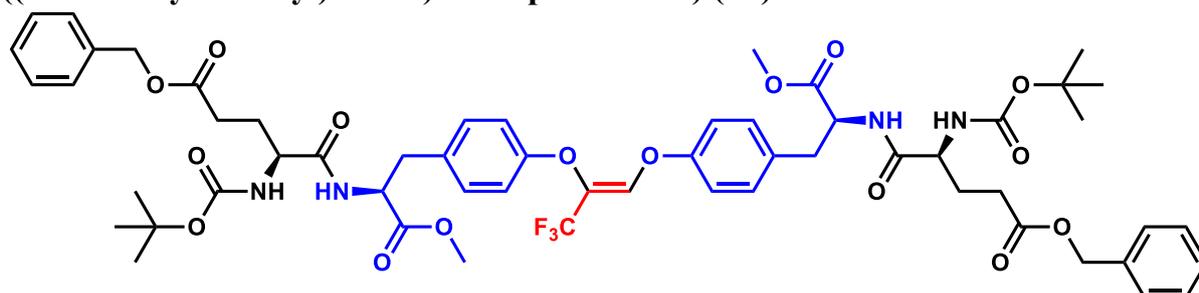
Dimethyl 13,13'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(methylene))(4*Z*,4'*Z*,10*S*,10'*S*,13*S*,13'*S*)-bis(5-(((benzyloxy)carbonyl)amino)-10-((*tert*-butoxycarbonyl)amino)-3,11-dioxo-1-phenyl-2-oxa-4,6,12-triazatetradec-4-en-14-oate) (5m)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*E*)-*N*^ω,*N*^{ω'}-bis((benzyloxy)carbonyl)-*N*²-(*tert*-butoxycarbonyl)-*L*-arginyl-*L*-tyrosinate (431.9 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 345.8 mg (0.22 mmol, 75%) orange solid. ***E/Z* ratio:** 11:89. **Mp.** 93-95 °C. **R_f** = 0.89 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 9.42 (s, 2H), 9.26 (s, 2H), 7.45 – 7.27 (m, 22H), 7.09 (s, 1H), 6.98 (s, 2H), 6.95 (d, *J* = 9.4 Hz, 4H), 6.87 – 6.76 (m, 4H), 5.62 (t, *J* = 7.9 Hz, 2H), 5.21 (s, 4H), 5.16 – 5.00 (m, 4H), 4.74 – 4.64 (m, 2H), 4.21 (s, 2H), 3.98 – 3.87 (m, 2H), 3.87 – 3.78 (m, 2H), 3.63 (s, 3H), 3.58 (s, 3H), 3.01 – 2.89 (m, 2H), 2.82 – 2.70 (m, 2H), 1.77 – 1.51 (m, 8H), 1.40 (s, 18H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.7, -68.7. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 171.8, 171.6, 171.4, 163.6, 163.6, 160.7, 160.7, 155.8, 155.8, 155.7, 155.7, 155.7, 155.2, 137.7 (q, *J* = 5.0 Hz), 136.8, 136.8, 134.7, 134.6, 132.6, 130.7, 130.7, 130.2, 128.9, 128.9, 128.8, 128.8, 128.5, 128.5, 128.4, 128.4, 128.0, 127.9, 126.3 (q, *J* = 35.0 Hz), 121.6 (q, *J* = 272.6 Hz), 116.8, 115.4, 79.8, 69.0, 69.0, 67.0, 67.0, 54.1, 53.3, 53.2, 52.3, 52.2, 44.1, 44.0, 37.0, 36.8, 28.3, 24.7. **HRMS** (ESI) [M + H]⁺ calculated for C₇₇H₉₀F₃N₁₀O₂₀⁺: 1531.6285, found 1531.6316.

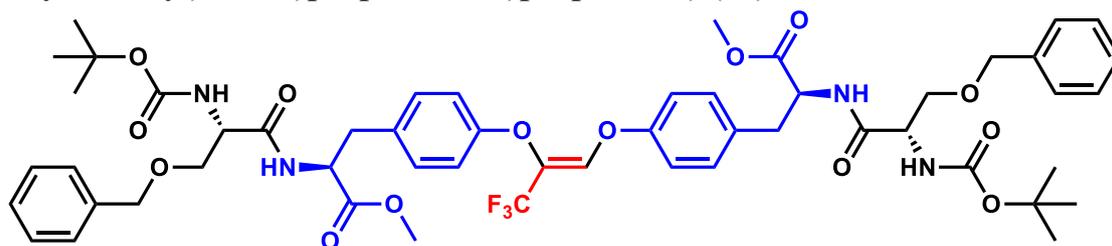
Dibenzyl 5,5'-(((2*S*,2'*S*)-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))bis(3-methoxy-3-oxopropane-1,2-diyl))bis(azanediy)))(4*S*,4'*S*)-bis(4-((*tert*-butoxycarbonyl)amino)-5-oxopentanoate) (5n)



Synthesized according to the general procedure at the beginning of chapter 3 using benzyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-5-(((*S*)-3-(4-hydroxyphenyl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentanoate (308.7 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 145.5 mg (0.13 mmol, 43%) orange viscous oil. ***E/Z* ratio**: 12:88. **R_f** = 0.92 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 10H), 7.12 (s, 1H), 7.09 – 7.02 (m, 4H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 4H), 5.36 (d, *J* = 8.0 Hz, 2H), 5.09 (s, 4H), 4.84 – 4.72 (m, 2H), 4.23 – 4.12 (m, 2H), 3.67 (s, 3H), 3.63 (s, 3H), 3.15 – 2.93 (m, 4H), 2.52 – 2.37 (m, 4H), 2.14 – 2.02 (m, 2H), 1.95 – 1.82 (m, 2H), 1.40 (s, 18H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.8, -68.8. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 173.1, 173.1, 171.6, 171.5, 171.4, 171.4, 155.9, 155.6, 155.3, 137.6 (q, *J* = 4.0 Hz), 135.8, 135.7, 132.4, 130.8, 130.4, 130.3, 128.6, 128.6, 128.3, 128.3, 128.3, 126.5 (q, *J* = 35.2 Hz), 121.5 (q, *J* = 272.1 Hz), 117.1, 115.6, 80.1, 66.6, 66.6, 53.7, 53.5, 53.3, 52.4, 52.3, 37.1, 37.1, 30.4, 28.3, 27.9, 27.8. **HRMS** (ESI) [M + Na]⁺ calculated for C₅₇H₆₇F₃N₄O₁₆Na⁺: 1143.4402, found 1143.4415.

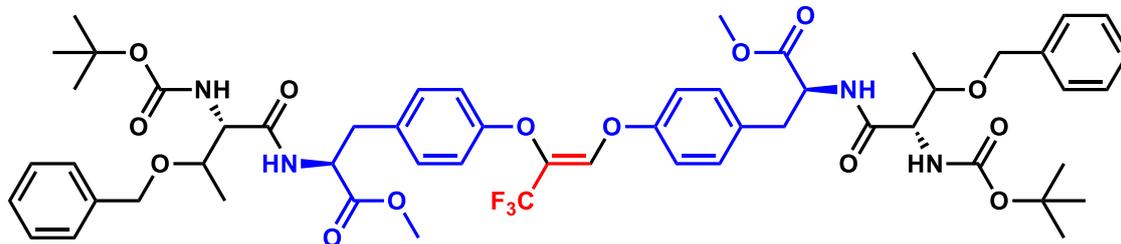
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-3-(benzyloxy)-2-((*tert*-butoxycarbonyl)amino)propanamido)propanoate) (5o)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-seryl-*L*-tyrosinate (283.5 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 189.3 mg (0.18 mmol, 61%) yellow solid. ***E/Z* ratio**: 1:99. **Mp.** 61-64 °C. **R_f** = 0.81 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.14 (m, 10H), 7.02 – 6.96 (m, 3H), 6.92 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.58 (d, *J* = 8.1 Hz, 2H), 5.39 – 5.14 (m, 2H), 4.79 – 4.67 (m, 2H), 4.51 – 4.38 (m, 4H), 4.21 (s, 2H), 3.92 (dd, *J* = 9.1, 3.4 Hz, 1H), 3.88 – 3.80 (m, 1H), 3.61 (s, 3H), 3.56 (s, 3H), 3.54 – 3.43 (m, 2H), 3.11 – 2.89 (m, 4H), 1.36 (s, 9H), 1.36 (s, 9H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.6, -68.8. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.5, 171.3, 170.1, 155.9, 155.6, 155.4, 137.8 (q, *J* = 4.9 Hz), 137.4, 131.0, 130.5, 130.4, 128.7, 128.6, 128.2, 128.2, 128.1, 128.1, 128.0, 126.4 (q, *J* = 35.5 Hz), 121.6 (q, *J* = 272.5 Hz), 117.0, 115.6, 80.6, 80.5, 73.8, 73.6, 70.2, 69.9, 53.7, 53.6, 52.5, 52.3, 37.2, 36.9, 28.4. **HRMS** (ESI) [M + Na]⁺ calculated for C₅₃H₆₃F₃N₄O₁₄Na⁺: 1059.4191, found 1059.4197.

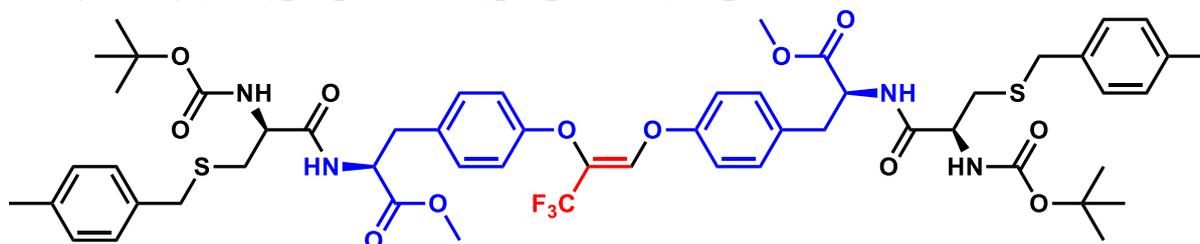
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((2*S*)-3-(benzyloxy)-2-((*tert*-butoxycarbonyl)amino)butanamido)propanoate) (5p)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl *O*-benzyl-*N*-(*tert*-butoxycarbonyl)-*L*-threonyl-*L*-tyrosinate (291.9 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 210.7 mg (0.2 mmol, 66%) yellow solid. ***E/Z* ratio:** 1:99. **Mp.** 150-152 °C. **R_f** = 0.86 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.20 (s, 10H), 7.11 – 7.00 (m, 2H), 6.94 (s, 1H), 6.86 – 6.73 (m, 6H), 6.56 (d, *J* = 8.1 Hz, 2H), 5.45 – 5.28 (m, 2H), 4.73 – 4.62 (m, 2H), 4.52 (t, *J* = 9.6 Hz, 2H), 4.42 (d, *J* = 11.5 Hz, 2H), 4.25 – 4.17 (m, 2H), 4.14 – 4.00 (m, 2H), 3.58 (s, 3H), 3.52 (s, 3H), 3.05 – 2.78 (m, 4H), 1.35 (s, 18H), 1.18 – 1.05 (m, 6H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.6, -68.8. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 171.4, 171.2, 169.7, 169.6, 155.7, 155.2, 137.9, 137.8, 137.6 (q, *J* = 4.7 Hz), 132.2, 130.6, 130.3, 130.2, 128.4, 128.4, 127.8, 127.8, 127.8, 127.7, 126.2 (q, *J* = 35.3 Hz), 121.5 (q, *J* = 272.2 Hz), 116.9, 115.5, 80.2, 80.0, 74.8, 74.7, 71.4, 71.3, 57.5, 57.3, 53.6, 53.4, 52.3, 52.1, 37.1, 36.9, 28.2, 14.8, 14.8. **HRMS** (ESI) [M + Na]⁺ calculated for C₅₅H₆₇F₃N₄O₁₄Na⁺: 1087.4504, found 1087.4519.

Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*)-bis(2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-((4-methylbenzyl)thio)propanamido)propanoate) (5q)

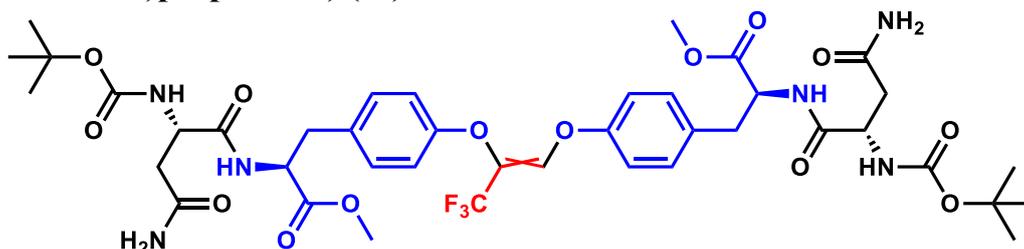


Synthesized according to the general procedure at the beginning of chapter 3 using methyl *N*-(ethoxycarbonyl)-*S*-(4-methylbenzyl)-*L*-cysteinyl-*L*-tyrosinate (301.6 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 125.6 mg (0.12 mmol, 40%) yellow solid. ***E/Z* ratio:** 7:93. **Mp.** 70-72 °C. **R_f** = 0.87 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 7.8 Hz, 4H), 7.12 (s, 1H), 7.09 (d, *J* = 8.4 Hz, 4H), 7.05 (d, *J* = 7.4 Hz, 4H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* =

8.5 Hz, 2H), 6.81 (d, $J = 7.5$ Hz, 2H), 5.23 (s, 2H), 4.78 (q, $J = 6.1$ Hz, 2H), 4.20 (s, 2H), 3.70 (s, 4H), 3.67 (s, 3H), 3.65 (s, 3H), 3.18 – 3.01 (m, 4H), 2.80 (dd, $J = 13.9, 6.0$ Hz, 2H), 2.70 (dd, $J = 13.9, 6.4$ Hz, 2H), 2.31 (s, 6H), 1.43 (s, 18H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.8, -68.8. ^{13}C NMR (101 MHz, Chloroform- d) δ 171.5, 171.3, 170.5, 170.5, 156.0, 155.5, 137.7 (q, $J = 4.2$ Hz), 137.0, 137.0, 134.8, 134.7, 132.4, 130.9, 130.5, 130.4, 129.4, 129.4, 129.0, 126.6 (q, $J = 35.1$ Hz), 121.6 (q, $J = 272.3$ Hz), 117.2, 115.7, 80.5, 53.8, 53.8, 53.6, 53.5, 52.5, 52.4, 37.2, 37.2, 36.3, 36.2, 33.5, 28.3, 21.2. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{55}\text{H}_{67}\text{F}_3\text{N}_4\text{O}_{12}\text{S}_2\text{Na}^+$: 1119.4058, found 1119.4047.

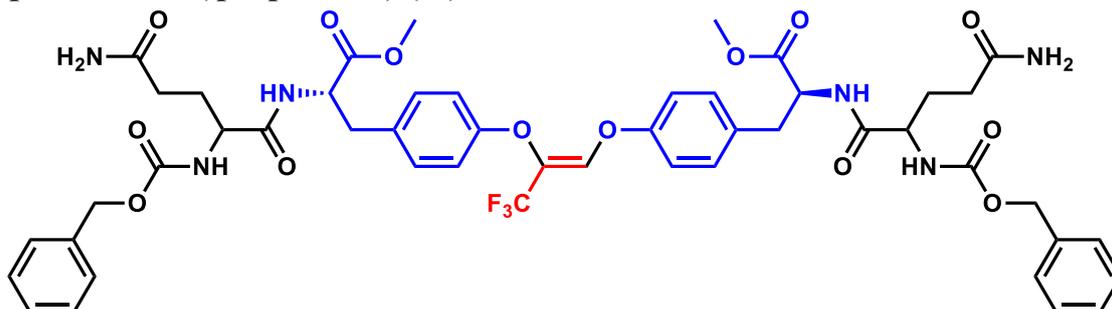
Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*')-bis(2-((*S*)-4-amino-2-((*tert*-butoxycarbonyl)amino)-4-oxobutanamido)propanoate) (5r)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl (*tert*-butoxycarbonyl)-*L*-asparaginyl-*L*-tyrosinate (245.7 mg, 0.6 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

Yield: 123.5 mg (0.13 mmol, 45%) white solid. *E/Z* ratio: 38:62. **Mp.** 182-185 °C. **R_f** = 0.34 in $\text{CH}_2\text{Cl}_2:\text{MeOH} = 10:1$. ^1H NMR (400 MHz, DMSO- d_6) δ 8.13 (t, $J = 7.3$ Hz, 2H), 7.71 (s, 1H), 7.25 (s, 2H), 7.23 – 7.14 (m, 4H), 7.06 (d, $J = 8.2$ Hz, 2H), 7.01 (d, $J = 8.1$ Hz, 2H), 6.94 – 6.82 (m, 4H), 4.41 (q, $J = 7.3$ Hz, 2H), 4.25 (p, $J = 7.8, 7.3$ Hz, 2H), 3.58 (s, 3H), 3.53 (s, 3H), 3.05 – 2.90 (m, 4H), 2.41 – 2.23 (m, 4H), 1.34 (s, 18H). ^{19}F NMR (376 MHz, DMSO- d_6) δ -67.5, -77.8. ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.8, 171.7, 171.7, 171.4, 161.0, 156.1, 155.1 (q, $J = 3.4$ Hz), 155.0, 154.4, 139.5, 133.4, 131.6, 130.7, 130.5, 130.1, 126.8, 125.5, 124.2 (q, $J = 34.4$ Hz), 122.3, 121.7 (q, $J = 271.8$ Hz), 119.1, 116.8, 115.9, 115.1, 114.7, 78.3, 78.2, 53.9, 53.6, 53.6, 51.9, 51.8, 51.2, 51.2, 37.2, 35.8, 28.2. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{41}\text{H}_{53}\text{F}_3\text{N}_6\text{O}_{14}\text{Na}^+$: 933.3470, found 933.3480.

Dimethyl 3,3'-(((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))bis(4,1-phenylene))(2*S*,2'*S*')-bis(2-(5-amino-2-(((benzyloxy)carbonyl)amino)-5-oxopentanamido)propanoate) (5s)



Synthesized according to the general procedure at the beginning of chapter 3 using methyl ((benzyloxy)carbonyl)glutaminy-*L*-tyrosinate (274.5 mg, 0.6 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (3 ml).

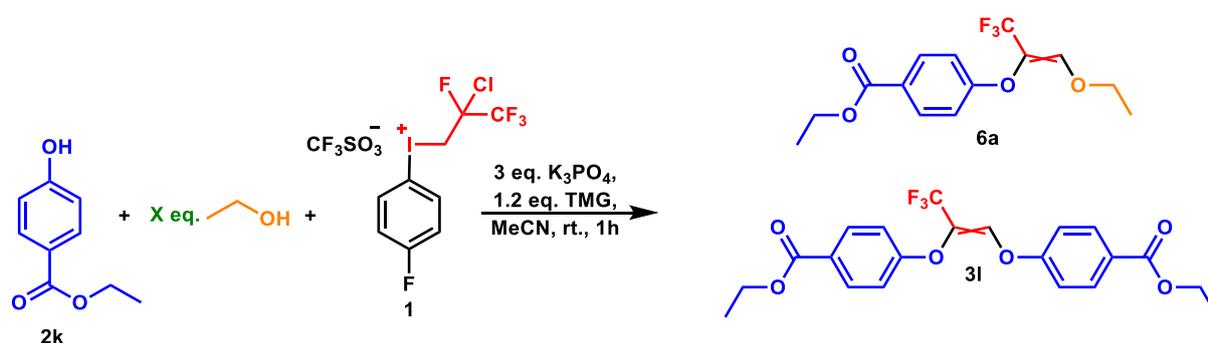
Yield: 180.6 mg (0.18 mmol, 60%) white solid. ***E/Z* ratio**: 1:99. **Mp.** 82-84 °C. **R_f** = 0.48 in CH₂Cl₂:MeOH = 20:1. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 8.38 – 8.27 (m, 1H), 8.26 – 8.16 (m, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.37 – 7.33 (m, 10H), 7.27 – 7.12 (m, 4H), 7.09 – 6.93 (m, 4H), 6.76 (s, 2H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.01 (s, 4H), 4.42 (dp, *J* = 13.8, 6.9 Hz, 2H), 4.00 (dp, *J* = 12.8, 4.3 Hz, 2H), 3.65 – 3.46 (m, 6H), 3.07 – 2.78 (m, 4H), 2.20 – 1.95 (m, 4H), 1.90 – 1.75 (m, 2H), 1.74 – 1.56 (m, 2H). **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -63.2, -67.4. **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 173.8, 173.7, 172.0, 172.0, 171.9, 171.8 (q, *J* = 1.6 Hz), 171.7, 156.1, 155.9, 155.0, 154.4, 139.7, 137.0, 133.5, 131.6, 131.6, 130.7, 130.7, 130.5, 130.5, 130.1, 130.1, 128.4, 128.4, 127.9, 127.8, 127.8, 127.7, 127.0, 124.2 (q, *J* = 34.6 Hz), 121.7 (q, *J* = 272.4 Hz), 116.8, 115.1, 114.7, 65.5, 65.5, 54.3, 54.1, 53.8, 53.4, 51.9, 51.9, 36.2, 35.8, 31.5, 31.4, 27.8, 27.8. **HRMS** (ESI) [M + Na]⁺ calculated for C₄₉H₅₃F₃N₆O₁₄Na⁺: 1029.347, found 1029.3477.

5. Synthesis of trifluorinated alkoxy-aryloxy-ethenes

5.1. Examination of the reaction conditions of the aryloxy-alkoxy-ethene synthesis

The stoichiometry of the reaction

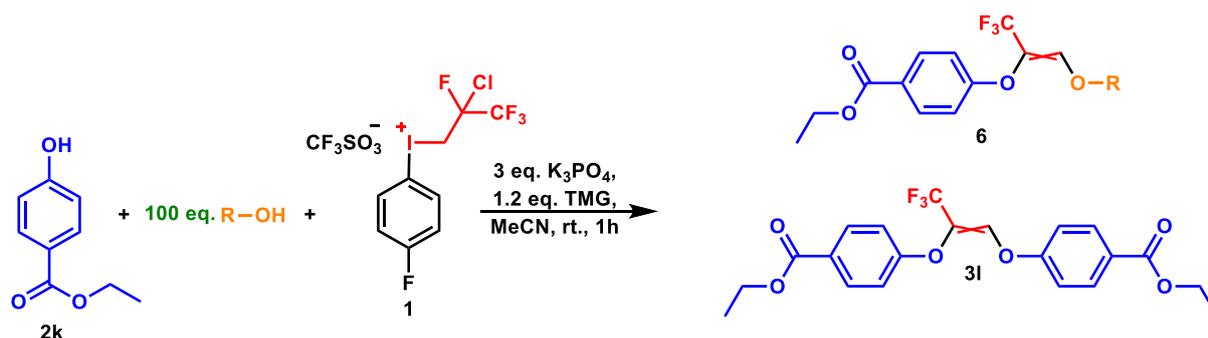
4-hydroxybenzoate (16.6 mg, 0.1 mmol), K_3PO_4 (63.7 mg, 0.3 mmol), and EtOH were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (13.8216 mg, 0.12 mmol, 15.2 μ l) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at an ambient temperature, then analyzed by GC-MS spectroscopy.



Entry	X eq. EtOH	7a (GC-MS%)	3l (GC-MS%)
1	1	0	100
2	5	32	68
3	10	53	47
4	25	95	5
5	30	95	5
6	35	97	3
7	40	96	4
8	45	98	2
9	50	98	2
10	75	99	1
11	100	100	0

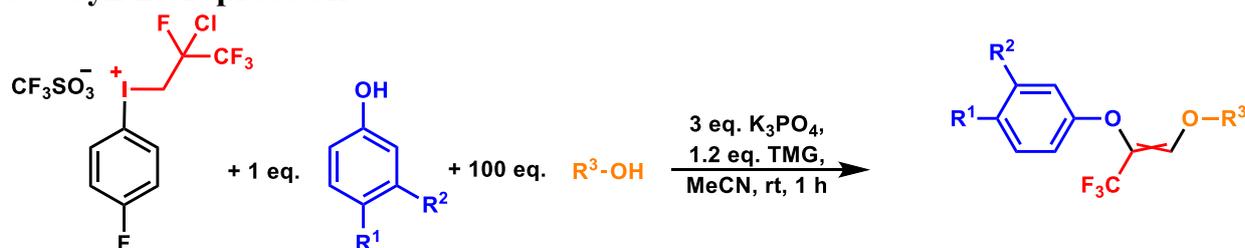
5.2 The scope and the limitations of the reaction

4-hydroxybenzoate (16.6 mg, 0.1 mmol), K_3PO_4 (63.7 mg, 0.3 mmol), and several aliphatic alcohols were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (13.8216 mg, 0.12 mmol, 15.2 μ l) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at an ambient temperature, then analyzed by GC-MS spectroscopy.



Entry	Alcohol	6 (GC-MS%)	31 (GC-MS%)
1	Methanol	46	0
2	Ethanol	100	0
3	1-Propanol	92	8
4	1-Buthanol	82	18
5	2-Propanol	79	21
6	<i>tert</i> -Butyl alcohol	8	92
7	Cyclohexanol	40	60
8	1-Decanol	53	47
9	2-Chloroethanol	85	15
10	Allyl alcohol	94	6
11	1-Aziridineethanol	0	6
12	1,4-Butanediol	0	6
13	2-Methoxyethanol	54	0
14	2-Dimethylaminoethanol	4	60
15	3-Hydroxypropionitrile	16	20
16	Glycidol	5	95
17	Propargyl alcohol	5	0

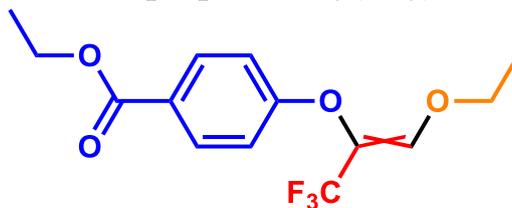
5.3. Synthetic procedures



General procedure

Phenol (0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), and the respective alcohol derivative were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) in 2.15 mL MeCN was dosed over 30 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature (monitored by gas chromatography and TLC), after which the reaction mixture was concentrated to Celite under reduced pressure. The crude product was purified by column chromatography using Hex:EtOAc as eluent.

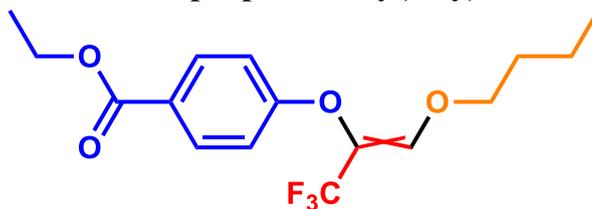
Ethyl 4-((1-ethoxy-3,3,3-trifluoroprop-1-en-2-yl)oxy)benzoate (6a)



Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-hydroxybenzoate (49.8 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), ethanol (1382.07 mg, 30 mmol, 1.75 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 64.8 mg (0.21 mmol, 71%) colorless oil. *E/Z* ratio: 26:74. R_f = 0.60 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 305(11), 304(61), 276(7), 260(6), 259(46), 248(36), 232(13), 231(100), 219(11), 211(12), 203(5), 179(10), 164(6), 151(28), 149(5), 133(20), 127(14), 121(8), 119(5), 109(9), 107(9), 105(26), 104(25), 103(12), 93(5), 92(12), 91(7), 79(10), 77(18), 76(34), 75(16), 74(5), 65(13), 64(5), 63(5). **1H NMR** (400 MHz, Chloroform-*d*) δ 8.00 (d, J = 8.9 Hz, 2H), 7.08 – 6.98 (m, 2H), 6.78 (s, 0.7H), 6.65 (s, 0.3H), 4.34 (q, J = 7.1 Hz, 2H), 4.00 (q, J = 7.1 Hz, 0.5H), 3.97 (q, J = 7.1 Hz, 1.5H), 1.37 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.4, -68.6. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 166.2, 166.1, 162.8, 160.4, 147.5 (q, J = 2.3 Hz), 141.9 (q, J = 4.7 Hz), 131.7, 131.5, 125.2, 125.0, 124.5 (q, J = 36.8 Hz), 122.2 (q, J = 35.5 Hz), 121.9 (q, J = 270.9 Hz), 121.3 (q, J = 274.1 Hz), 115.0, 114.9, 71.0, 70.8, 60.9, 60.9, 15.3, 15.2, 14.4. **HRMS** (ESI) $[M + Na]^+$ calculated for $C_{14}H_{15}F_3O_4Na^+$: 327.0820, found 327.0830.

Ethyl 4-((1-butoxy-3,3,3-trifluoroprop-1-en-2-yl)oxy)benzoate (6b)

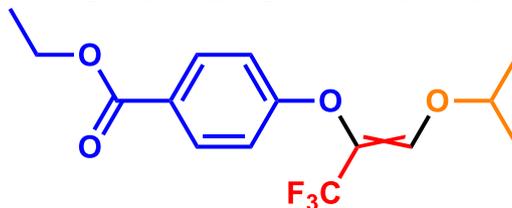


Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-hydroxybenzoate (49.8 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), 1-butanol (2223.6 mg, 30 mmol, 2.7 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 45.2 mg (0.13 mmol, 45%) colorless oil. *E/Z* ratio: 20:80. R_f = 0.57 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 333(9), 332(50), 288(9), 287(46), 277(11), 276(60), 257(8), 249(9), 248(72), 247(13), 232(19), 231(100), 230(8), 229(5), 219(33), 211(14), 204(6), 203(8), 201(10), 183(9), 180(14), 179(75), 165(5), 164(9), 152(9), 151(94), 149(13), 135(7), 133(33), 127(16), 123(5), 122(10), 121(16), 120(5), 119(5), 109(8), 107(12), 105(42), 104(43), 103(20), 93(8), 92(15), 91(13), 81(7), 79(19), 78(5), 77(27), 76(49), 75(17), 65(18), 64(7), 63(8), 57(23), 50(15). **1H NMR** (400 MHz, Chloroform-*d*) δ 8.00 (d, J = 8.9 Hz, 2H), 7.10 – 6.97 (m, 2H), 6.77 (s, 0.8H), 6.66 (s, 0.2H), 4.35 (q, J = 7.1 Hz, 2H), 3.97 – 3.88 (m, 2H), 1.69 (p, J = 6.6 Hz, 0.5H), 1.54 (p, J = 6.7 Hz, 1.5H), 1.37 (t, J = 7.2 Hz, 3H), 1.23 (h, J = 7.4 Hz, 2H), 0.96 (t, J =

7.4 Hz, 0.7H), 0.84 (t, $J = 7.4$ Hz, 2.3H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.5, -68.6. ^{13}C NMR (101 MHz, Chloroform- d) δ 166.1, 166.0, 162.8, 160.4, 147.8 (q, $J = 2.1$ Hz), 142.0 (q, $J = 4.7$ Hz), 131.6, 131.4, 125.0, 124.9, 124.2 (q, $J = 36.4$ Hz), 122.0 (q, $J = 35.5$ Hz), 121.8 (q, $J = 270.7$ Hz), 121.2 (q, $J = 271.5$ Hz), 114.9, 114.8, 75.1, 74.9, 60.8, 60.8, 31.6, 31.6, 18.7, 18.6, 14.3, 13.6, 13.5. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{16}\text{H}_{19}\text{F}_3\text{O}_4\text{Na}^+$: 355.1133, found 355.1137.

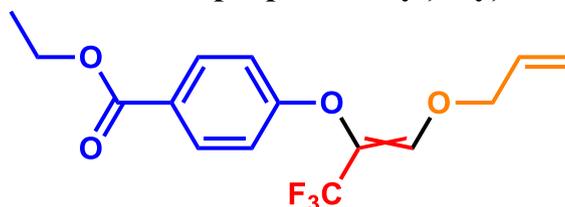
Ethyl 4-((3,3,3-trifluoro-1-isopropoxyprop-1-en-2-yl)oxy)benzoate (6c)



Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-hydroxybenzoate (49.8 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), 2-propanol (1803 mg, 30 mmol, 2.3 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 32.4 mg (0.1 mmol, 34%) white solid. **E/Z ratio:** 8:92. **Mp.** 38-40 $^\circ\text{C}$. **R_f** = 0.66 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 318(16), 277(11), 276(76), 274(5), 273(28), 257(7), 249(5), 248(38), 247(11), 232(13), 231(100), 219(31), 211(11), 203(5), 201(8), 183(8), 180(5), 179(46), 165(6), 164(5), 152(7), 151(63), 149(7), 133(25), 127(23), 123(6), 122(6), 121(12), 120(5), 107(9), 105(31), 104(25), 103(14), 94(5), 93(7), 92(14), 91(6), 79(14), 78(10), 77(20), 76(39), 75(16), 65(15), 64(6), 63(6), 50(6). ^1H NMR (400 MHz, Chloroform- d) δ 8.00 (d, $J = 8.9$ Hz, 2H), 7.03 (d, $J = 9.0$ Hz, 2H), 6.82 (s, 0.9H), 6.68 (s, 0.1H), 4.35 (q, $J = 7.1$ Hz, 2H), 4.12 (hept, $J = 6.1$ Hz, 1H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.34 (s, 0.3H), 1.32 (s, 0.3H), 1.22 (s, 2.7H), 1.20 (s, 2.7H). ^{19}F NMR (376 MHz, Chloroform- d) δ -64.3, -68.6. ^{13}C NMR (101 MHz, Chloroform- d) δ 166.3, 166.1, 163.0, 160.5, 146.4 (q, $J = 2.4$ Hz), 140.6 (q, $J = 4.6$ Hz), 131.8, 131.4, 125.1, 125.0, 122.1 (q, $J = 35.5$ Hz), 122.0 (q, $J = 270.8$ Hz), 115.1, 114.9, 78.2, 78.1, 61.0, 60.9, 22.4, 22.3, 14.5. HRMS (ESI) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{15}\text{H}_{17}\text{F}_3\text{O}_4\text{Na}^+$: 341.0977, found 341.0974.

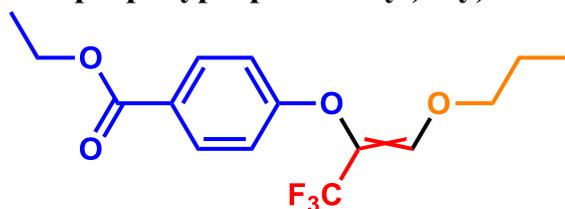
Ethyl 4-((1-(allyloxy)-3,3,3-trifluoroprop-1-en-2-yl)oxy)benzoate (6d)



Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-hydroxybenzoate (49.8 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), allyl alcohol (1742.4 mg, 30 mmol, 2.1 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 40.8 mg (0.13 mmol, 43%) colorless oil. ***E/Z* ratio**: 19:81. ***R_f*** = 0.62 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): *m/z* (%): 316(28), 298(6), 288(9), 287(19), 272(11), 271(49), 270(6), 259(10), 249(5), 244(5), 243(25), 242(5), 241(13), 225(6), 223(6), 219(6), 216(9), 215(47), 214(5), 203(10), 202(7), 201(8), 199(6), 195(9), 193(5), 187(24), 180(8), 177(8), 176(5), 175(16), 174(6), 167(13), 166(13), 165(9), 159(5), 151(13), 149(9), 147(19), 146(6), 145(16), 144(7), 139(5), 138(24), 135(6), 133(12), 132(7), 131(14), 129(5), 128(6), 127(10), 123(6), 122(15), 121(100), 120(11), 119(7), 117(18), 115(13), 110(12), 109(30), 107(5), 105(13), 104(44), 103(62), 102(8), 101(12), 99(5), 95(6), 94(10), 93(54), 92(49), 91(17), 89(5), 87(5), 83(24), 81(22), 79(6), 77(36), 76(43), 75(28), 74(8), 71(5), 69(13), 67(5), 66(10), 65(55), 64(23), 63(21), 62(6), 53(12), 51(9), 50(10). **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.79 (s, 0.8H), 6.66 (s, 0.2H), 5.94 (ddt, *J* = 16.2, 10.8, 5.5 Hz, 0.2H), 5.82 (ddt, *J* = 16.5, 11.1, 5.7 Hz, 0.8H), 5.42 – 5.32 (m, 0.4H), 5.31 – 5.22 (m, 1.6H), 4.45 (d, *J* = 5.5 Hz, 0.4H), 4.39 (d, *J* = 5.7 Hz, 1.6H), 4.35 (q, *J* = 7.3 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -68.7. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 166.2, 166.1, 162.7, 160.4, 147.1 (q, *J* = 2.1 Hz), 141.2 (q, *J* = 4.7 Hz), 132.2, 132.0, 131.8, 131.6, 125.2, 125.1, 124.8 (q, *J* = 36.5 Hz), 122.6 (q, *J* = 35.7 Hz), 121.8 (q, *J* = 271.0 Hz), 121.3 (q, *J* = 274.1 Hz), 119.8, 119.7, 115.0, 114.9, 75.2, 75.0, 61.0, 60.9, 14.5. **HRMS** (ESI) [*M* + Na]⁺ calculated for C₁₅H₁₅F₃O₄Na⁺: 339.082, found 339.0822.

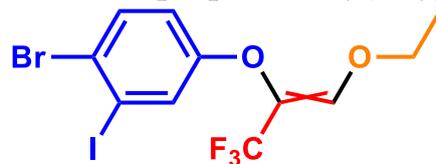
Ethyl 4-((3,3,3-trifluoro-1-propoxyprop-1-en-2-yl)oxy)benzoate (6e)



Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-hydroxybenzoate (49.8 mg, 0.3 mmol), K₃PO₄ (191 mg, 0.9 mmol), 1-propanol (1803 mg, 30 mmol, 2.2 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μl), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 56.5 mg (0.18 mmol, 59%) colorless oil. ***E/Z* ratio**: 16:84. ***R_f*** = 0.59 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): *m/z* (%): 319(11), 318(64), 277(5), 276(36), 274(6), 273(42), 257(6), 249(5), 248(43), 247(8), 232(15), 231(100), 219(20), 211(8), 201(5), 179(23), 151(43), 149(5), 133(18), 127(10), 122(7), 121(11), 109(8), 107(8), 105(39), 104(47), 103(28), 93(11), 92(18), 91(12), 81(5), 79(15), 78(9), 77(33), 76(60), 75(23), 74(6), 65(37), 64(12), 63(12). **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.03 – 7.97 (m, 2H), 7.10 – 6.99 (m, 2H), 6.77 (q, *J* = 1.2 Hz, 0.8H), 6.66 (s, 0.2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.93 – 3.78 (m, 2H), 1.72 (h, *J* = 7.2 Hz, 0.4H), 1.58 (h, *J* = 7.2 Hz, 1.6H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 0.6H), 0.81 (t, *J* = 7.4 Hz, 2.4H). **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -64.5, -68.7. **¹³C NMR** (101 MHz, Chloroform-*d*) δ 166.2, 166.1, 162.9, 160.5, 147.9 (q, *J* = 2.3 Hz), 142.1 (q, *J* = 4.7 Hz), 131.7, 131.5, 125.2, 125.0, 124.3 (q, *J* = 36.7 Hz), 122.1 (q, *J* = 35.6 Hz), 121.9 (q, *J* = 270.8 Hz), 121.4 (q, *J* = 274.0 Hz), 115.0, 114.9, 76.9, 76.7, 61.0, 60.9, 23.1, 23.1, 14.4, 10.0, 9.9. **HRMS** (EI) [*M*]⁺ calculated for C₁₅H₁₇F₃O₄⁺: 318.10789, found 318.10639.

1-bromo-4-((1-ethoxy-3,3,3-trifluoroprop-1-en-2-yl)oxy)-2-iodobenzene (6f)



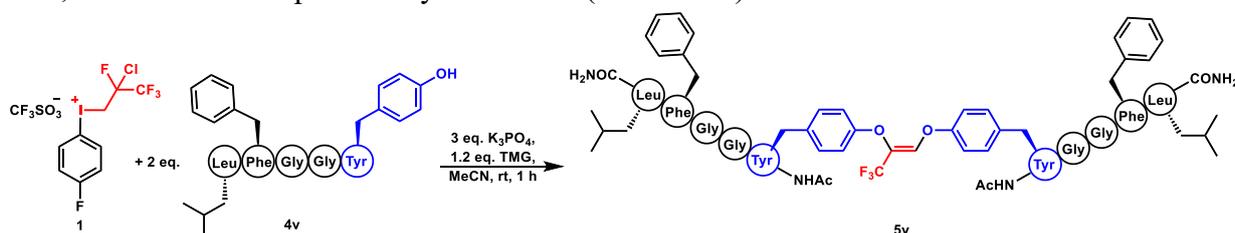
Synthesized according to the general procedure at the beginning of chapter 4 using ethyl 4-bromo-3-iodophenol (89.7 mg, 0.3 mmol), K_3PO_4 (191 mg, 0.9 mmol), ethanol (1382.07 mg, 30 mmol, 1.75 ml), 1,1,3,3-tetramethylguanidine (TMG) (41.4648 mg, 0.36 mmol, 45.6 μ l), 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.3 mmol) and MeCN (2.15 ml).

Yield: 96.4 mg (0.22 mmol, 74%) yellowish oil. ***E/Z* ratio**: 20:80. **R_f** = 0.68 in Hex:EtOAc = 4:1. **MS** (EI, 70 eV): m/z (%): 439(5), 438(44), 437(6), 436(46), 410(18), 408(19), 284(6), 283(13), 282(9), 281(14), 203(8), 202(29), 186(11), 157(6), 156(14), 155(7), 154(13), 104(6), 91(5), 77(6), 76(14), 75(100), 74(38), 73(5), 63(29), 62(11). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.53 – 7.46 (m, 2H), 6.95 – 6.83 (m, 2H), 6.76 (q, J = 0.9 Hz, 0.8H), 6.64 (s, 0.2H), 4.01 (q, J = 7.1 Hz, 0.4H), 4.00 (q, J = 7.1 Hz, 1.6H), 1.35 (t, J = 7.1 Hz, 0.6H), 1.26 (t, J = 7.1 Hz, 2.5H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.3, -68.6. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 158.2, 155.8, 147.6 (q, J = 2.2 Hz), 141.9 (q, J = 4.6 Hz), 133.0, 132.7, 127.1, 124.5 (q, J = 36.8 Hz), 122.8, 122.5, 122.3 (q, J = 35.5 Hz), 121.8 (q, J = 270.9 Hz), 121.2 (q, J = 274.0 Hz), 117.0, 116.8, 101.3, 100.9, 71.1, 71.0, 15.4, 15.2. **HRMS** (EI) $[M]^+$ calculated for $C_{11}H_9BrF_3IO_2^+$: 435.87827, found 435.87730.

6. Cross-linking of Leu-enkephalin derivative

In order to prove that the developed methodology can be applied as a peptide cross-linking tool, we performed the functionalization of an enkephalin derivative which is a well-known pentapeptide.

Peptide was synthesized manually by solid-phase peptide synthesis on Fmoc-Rink amide MBHA resin (0.3 g, 0.74 mmol/g capacity) using the standard protocol of Fmoc / ^tBu strategy. The Fmoc-group was removed with 2 % DBU and 2 % piperidine in DMF (four times; 2, 2, 5, 10 min, respectively). For the coupling of the following amino acid derivatives, DIC-Oxyma-pure (3-3 equiv.) were applied in DMF for 60 min. The peptides were removed from the resin by cleavage with 5 mL TFA, containing 0.125 mL distilled water and 0.125 mL TIS (as scavengers). The crude product was precipitated by dry diethyl ether, dissolved in 10 % acetic acid, freeze-dried and purified by RP-HPLC (Gradient I).



General procedure

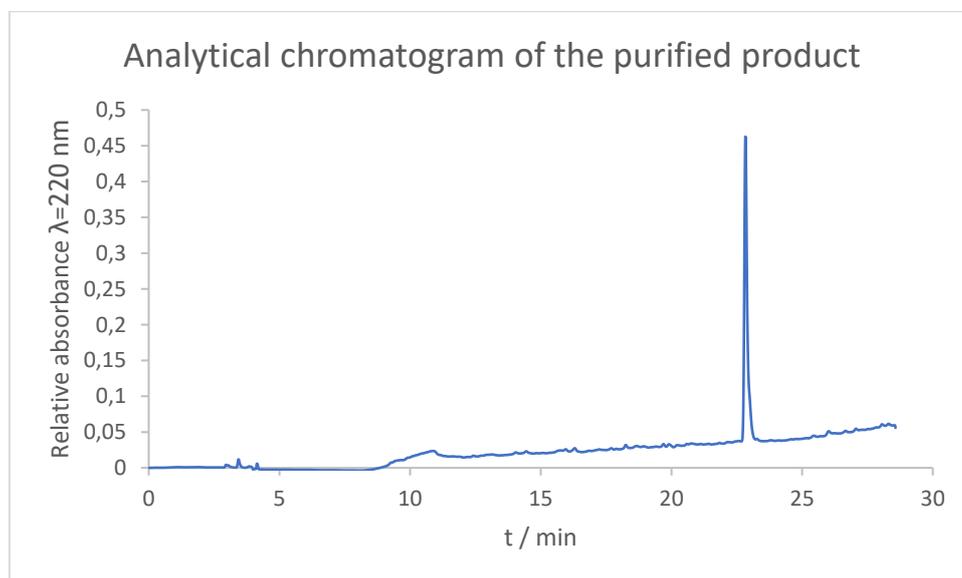
Enkephalin derivative **4v** (59.7 mg, 0.1 mmol), K₃PO₄ (31.8 mg, 0.15 mmol) and MeCN (0.14 mL) were measured into a screw cap vial. After the formation of a suspension 1,1,3,3-tetramethylguanidine (TMG) (6.9108 mg, 0.06 mmol, 7.6 μ l) was added in one portion by syringe. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (26 mg, 0.05 mmol) in 0.36 mL MeCN was dosed over 5 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature, after which the reaction mixture was filtered and then analyzed by NMR spectroscopy. ¹⁹F-NMR spectroscopy showed the formation of the desired product (**5v**) in 74% yield.

Reverse phase high-performance liquid chromatography (RP-HPLC)

The purification of the crude peptide (I) and the isolated conjugate (II) was carried out by RP-HPLC using KNAUER 2501 HPLC system (Bad Homburg, Germany) using Phenomenex Jupiter (Torrance, CA, USA) C18 column (250 x 21.2 mm I.D.) filled with 10 μ m silica (100 Å pore size) and Phenomenex Jupiter (Torrance, CA, USA) C4 column (250 x 21.2 mm I.D.) filled with 10 μ m silica (300 Å pore size). Latter was used for repurification of the product containing fraction. The isolation methods were achieved at a flow rate of 9 mL/min (I) and 4 mL/min (II) at RT. Linear gradient elution was applied using eluents 0.1 % TFA in d.i. water (A) and 0.1 % TFA in CH₃CN-water (80:20, v/v) (B). Gradients used for the separation were as follows; gradient I: 0 min 20 % (B), 5 min 20 % (B), 50 min 70 % (B) and gradient II: 0 min 20 % (B), 5 min 20 % (B), 50 min. 70 % (B), 60 min 100 % (B). Peaks were detected at λ = 220 nm wavelength.

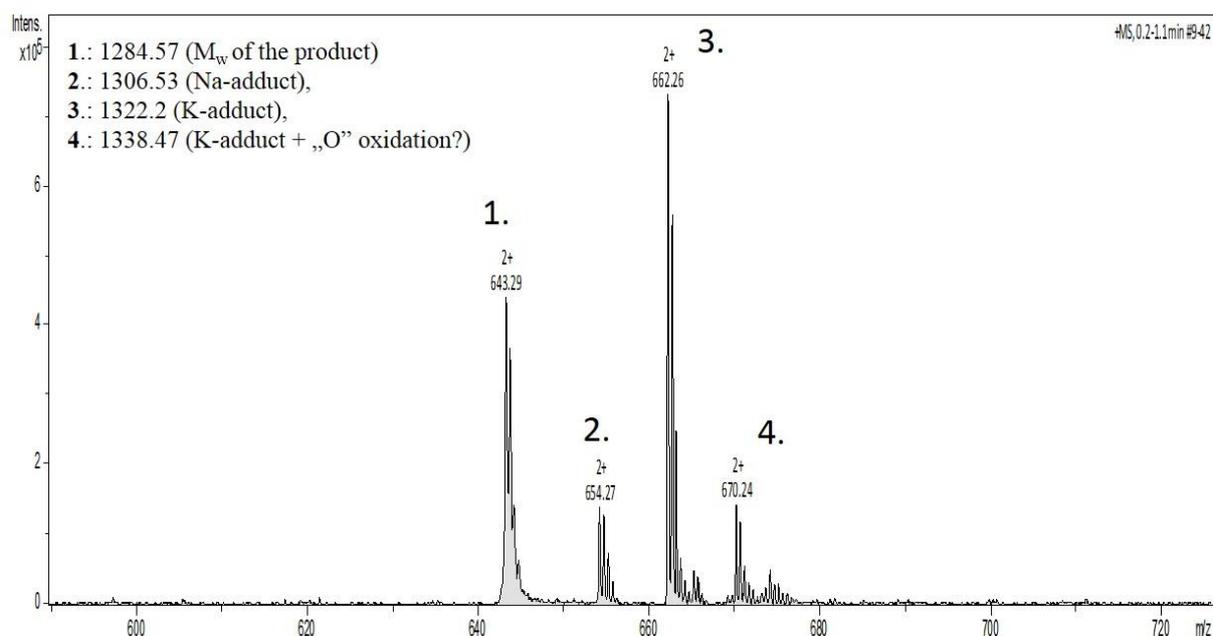
Analytical RP-HPLC was performed on a EC Nucleosil (Macherey-Nagel GmbH & Co. KG) C18 column (150x4.5mm) with 5 μ m silica (100 Å pore size) as a stationary phase. A

linear gradient elution was developed: 0 min 2 % (B); 2 min 2 % (B); 30 min 90 % (B) using the same eluent systems as was mentioned above with a flow rate of 1 mL/min at ambient temperature. Samples were dissolved in eluent (A) and 20 μ L was injected for the analysis. Peaks were detected also at $\lambda = 220$ nm.

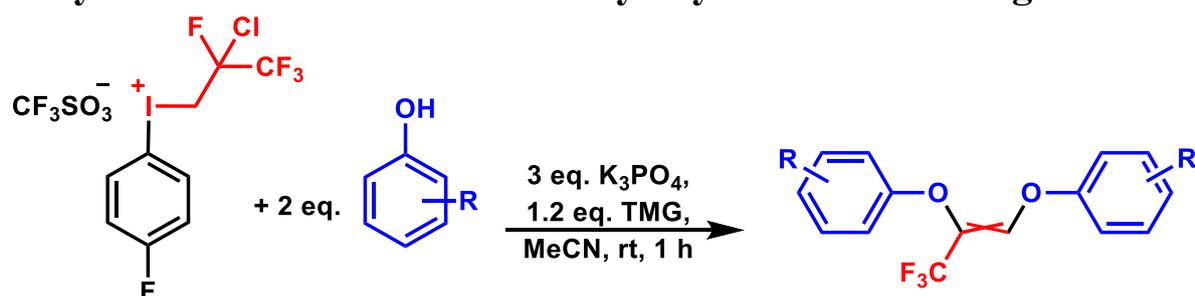


Mass spectrometry (MS)

The identification of the peptide derivatives and conjugates was carried out by electrospray ionization mass spectrometry (ESI-MS) on a Bruker Amazon (Bremen, Germany) ion trap mass spectrometer, operating in continuous sample injection at 4 μ L/min flow rate. Samples were dissolved in CH₃CN -water (50:50 v/v) mixture containing 0.1 v/v formic acid. Mass spectra were recorded in positive ion mode in the m/z 50-1200 range.

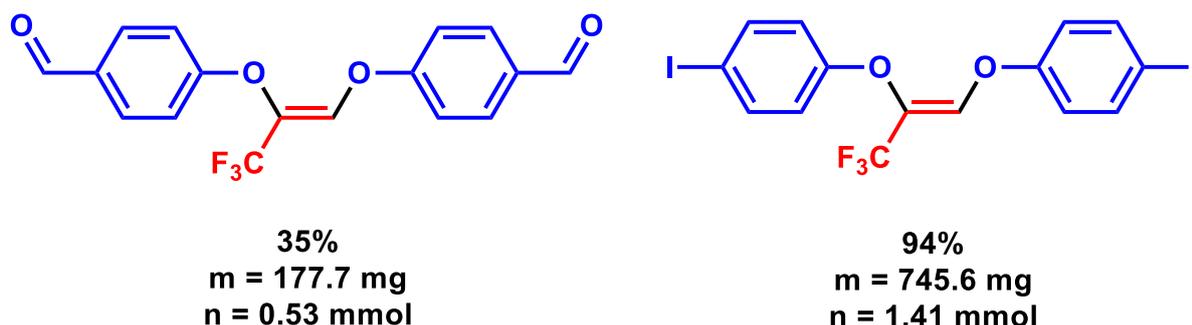


7. Synthesis of trifluorinated diaryloxy ethenes on a larger scale

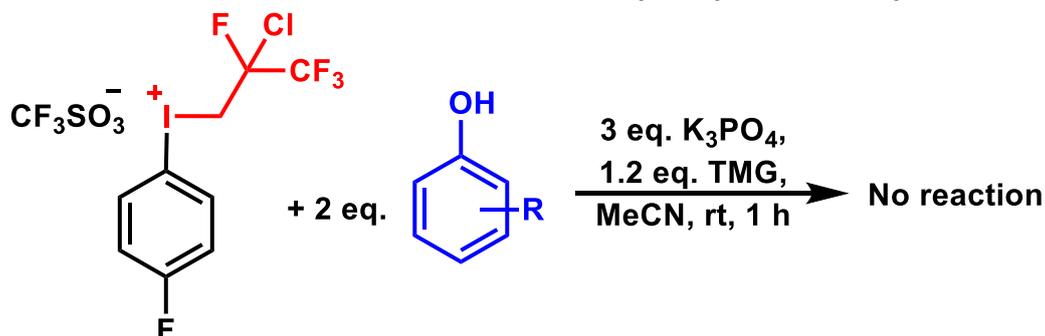


General procedure

Different phenols (3 mmol), K_3PO_4 (955.2 mg, 4.5 mmol) and MeCN (4.25 mL) were measured into a screw cap vial. After the formation of a suspension 1,1,3,3-tetramethylguanidine (TMG) (207.324 mg, 1.8 mmol, 0.23 ml) was added in one portion by syringe. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (780.8 mg, 1.5 mmol) in 10.75 mL MeCN was dosed over 150 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature (monitored by gas chromatography and TLC), after which the reaction mixture was concentrated to Celite under reduced pressure. The crude product was purified by column chromatography using Hex:EtOAc as eluent.

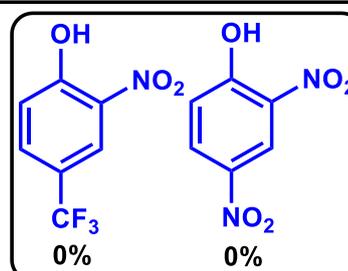
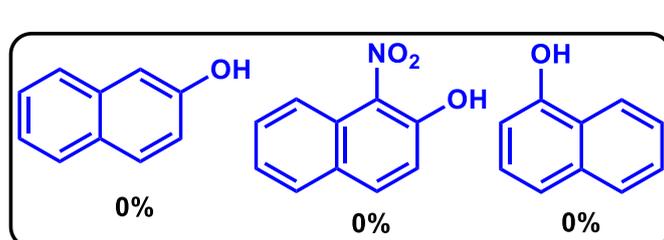
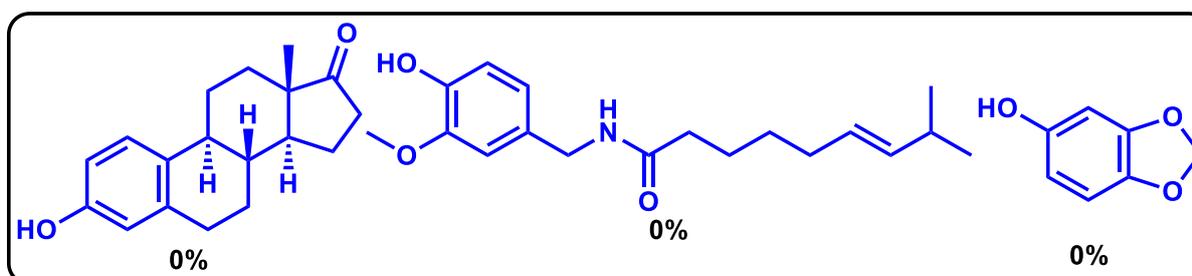
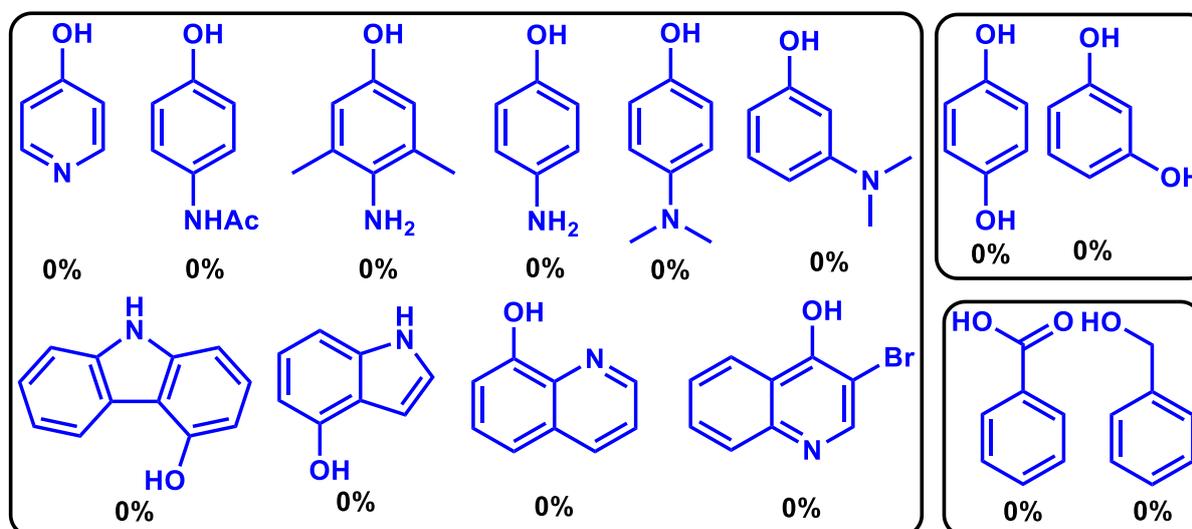
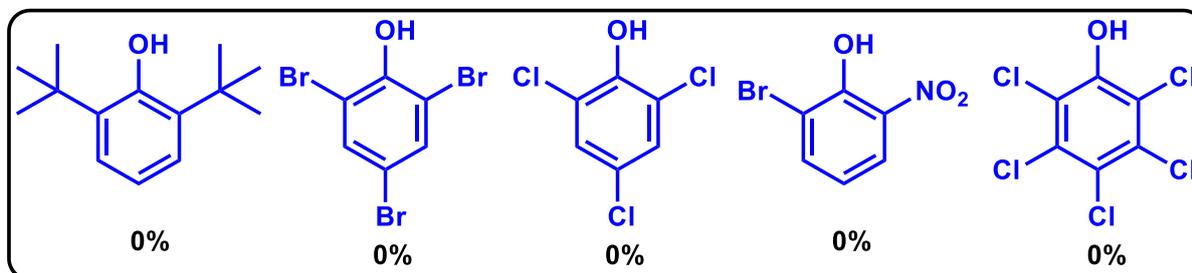


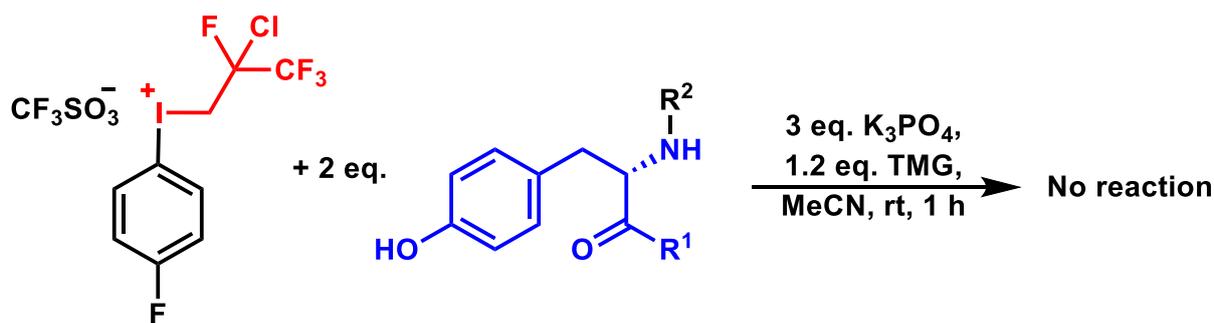
8. Limitations of the trifluorinated diaryloxy ethene synthesis



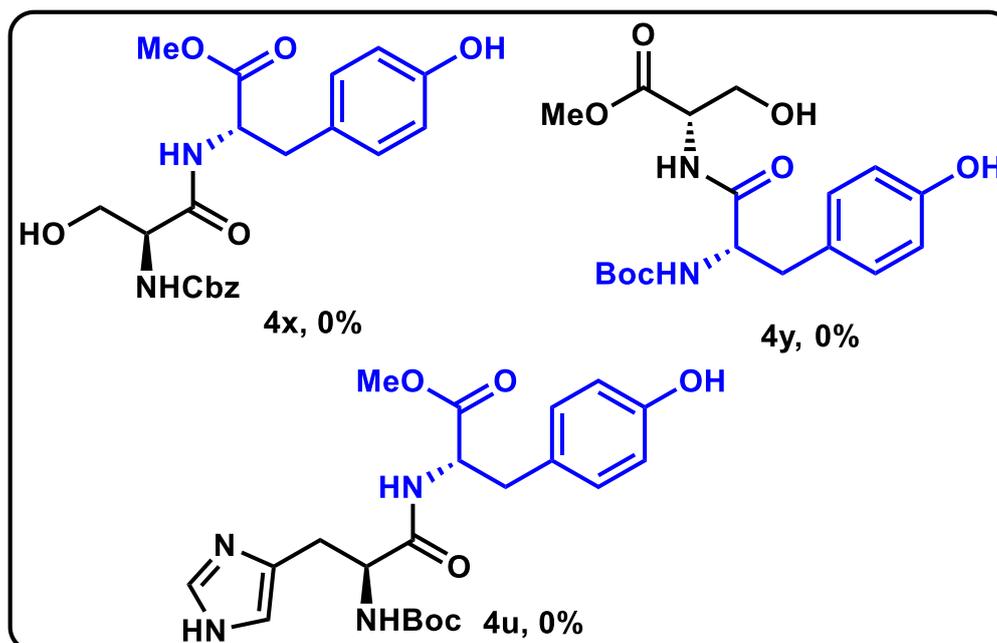
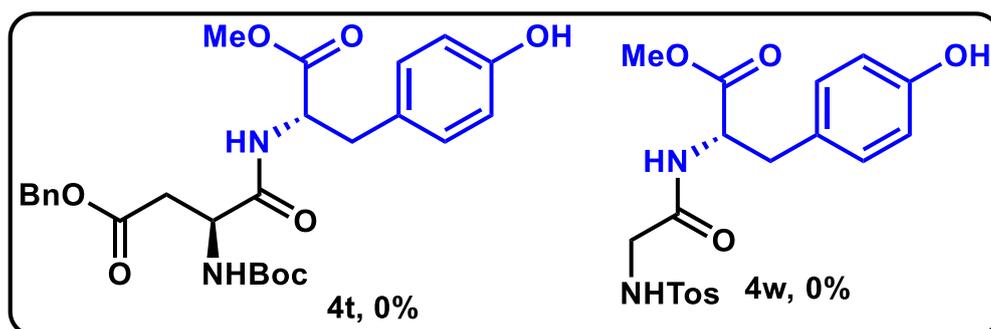
Different phenols (0.2 mmol), K_3PO_4 (63.7 mg, 0.3 mmol), and MeCN (0.28 mL) were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (13.8216 mg, 0.12 mmol, 15.2 μ l) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at

ambient temperature, then analyzed by GC-MS and ^{19}F -NMR spectroscopy. No reaction occurred. Based on the GC-MS measurement, only the phenol and 1-fluoro-4-iodobenzene could be identified in the reaction mixture. Based on ^{19}F -NMR measurement, only the degradation of the iodonium reagent occurred, thus only the peaks of the byproducts (1-fluoro-4-iodobenzene, triflate ion) were detected.



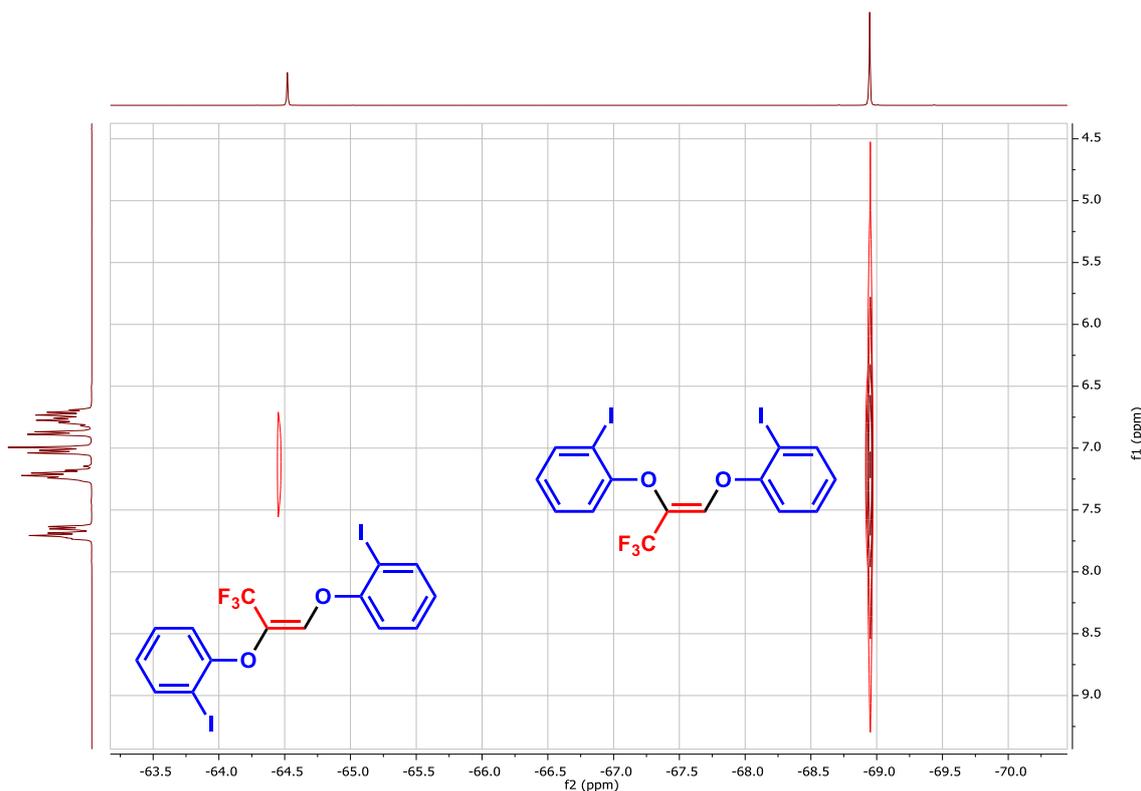


Different tyrosine-based dipeptides (0.2 mmol), K_3PO_4 (63.7 mg, 0.3 mmol), and MeCN (0.28 mL) were measured into a screw cap vial. 1,1,3,3-tetramethylguanidine (TMG) (13.8216 mg, 0.12 mmol, 15.2 μl) was added in one portion to the reaction mixture. Finally, upon continuous stirring, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (52.1 mg, 0.1 mmol) in 0.72 mL MeCN was dosed over 10 minutes at ambient temperature using syringe pump. The resulting mixture was stirred for 1 hour at ambient temperature, then analyzed by ^{19}F -NMR spectroscopy. No reaction occurred. Based on ^{19}F -NMR measurement, only the degradation of the iodonium reagent occurred, thus only the peaks of the byproducts (1-fluoro-4-iodobenzene, triflate ion) were detected.



9. Determination of the diastereomers using ^{19}F - ^1H HOESY NMR measurements

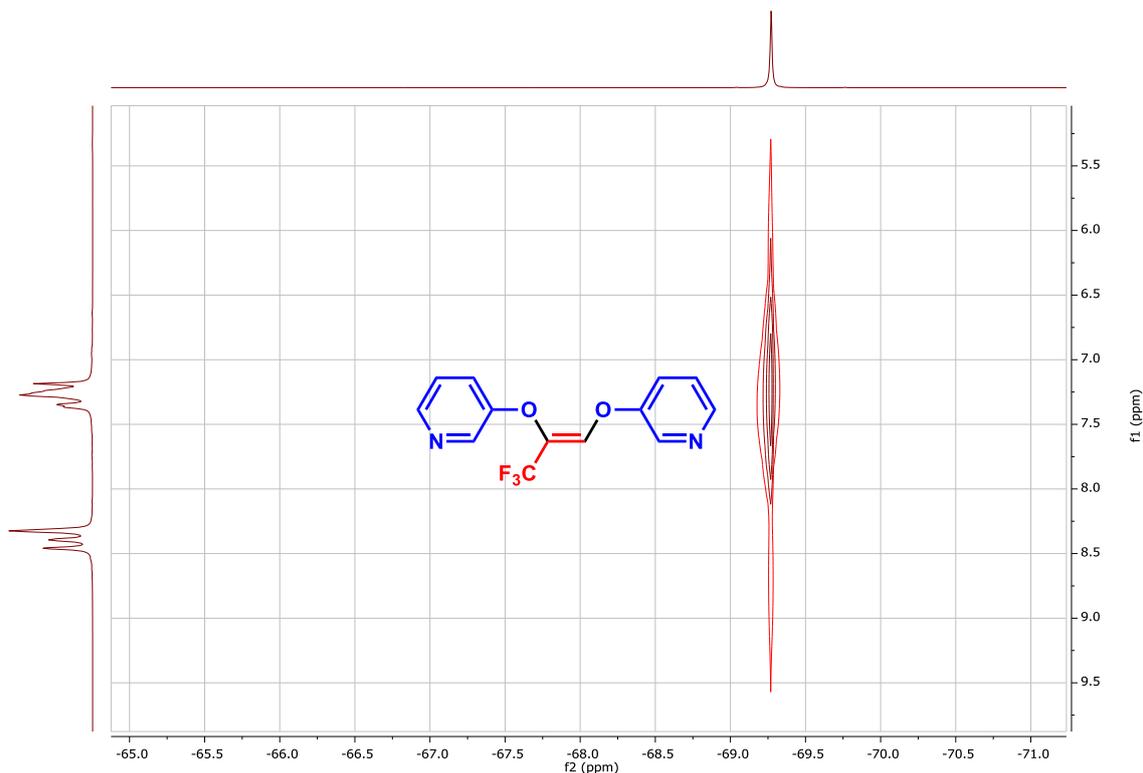
In order to assess a certain configuration of the isomers, we used a 2D ^{19}F - ^1H HOESY NMR measurements. This technique is a dipolar coupling-based experiment. If there are a proton and a fluorine close to each other (usually the distance $< 5 \text{ \AA}$), there will be a cross peak in the 2D HOESY spectra. The peak intensity indicates the distance between two atoms, which helps determining the structure of the diastereomer. For these measurements, we used isomeric mixture of product **3c**, and the single isomer obtained in the formation of product **3t**.



The ^{19}F - ^1H HOESY NMR spectra of product **3c**.

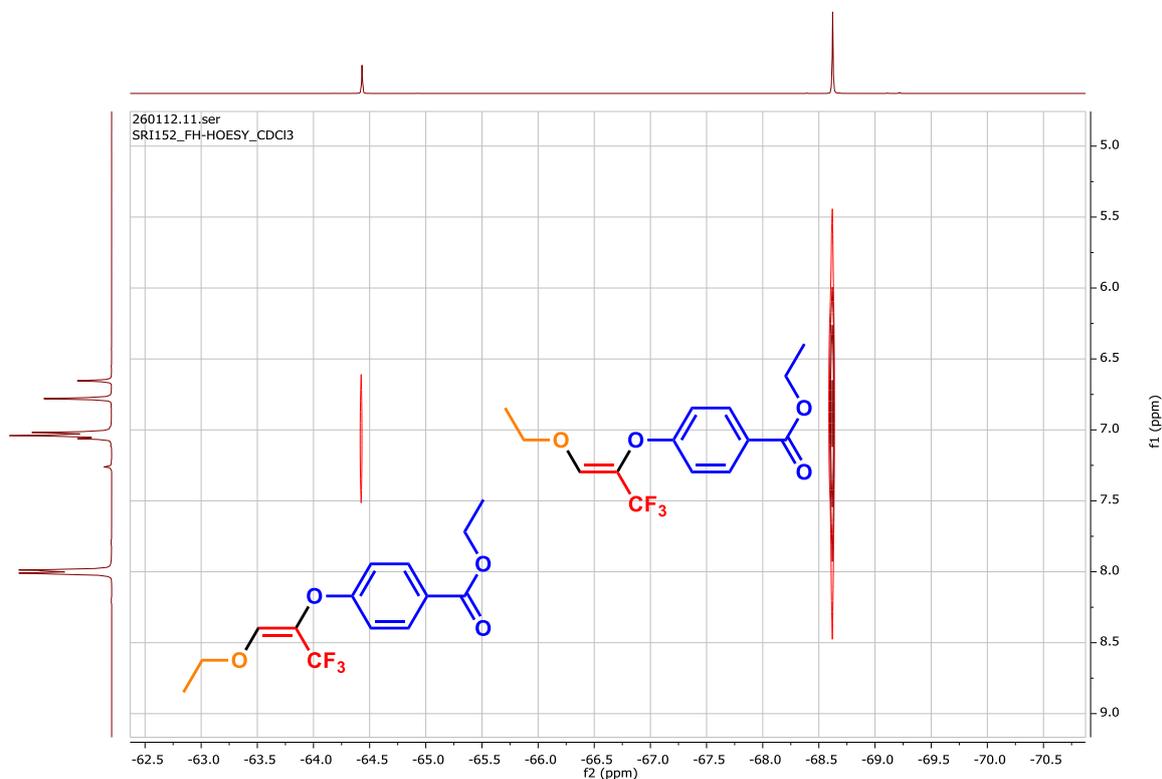
The results indicate that in the case of the *E* isomer a far less intensive cross peak is acquired, since the vinyl proton and the CF_3 group are farther apart. In contrast in the case of the *Z* isomer a more intensive cross peak is present in the HOESY map, since in this case the vinyl proton and the CF_3 are closer to each other.

On the other hand, the results indicate that in the case of the isomer pure product **3t** an intensive cross peak is present in the HOESY map. This shows that the vinyl proton and the CF_3 are closer to each other, thus it is safe to assume that the *Z* isomer of the product was formed.



The ^{19}F - ^1H HOESY NMR spectra of product **3t**.

The results indicate that in the case of the *E* isomer of product **6a** a far less intensive cross peak is acquired, since the vinyl proton and the CF_3 group are farther apart. In contrast in the case of the *Z* isomer a more intensive cross peak is present in the HOESY map, since in this case the vinyl proton and the CF_3 are closer to each other.



The ^{19}F - ^1H HOESY NMR spectra of product **6a**.

11. Determination of the diastereomers using X-ray crystallography measurements

In order to be perfectly sure that the assessed configuration of the isomers is adequate, we used X-ray crystallography measurements on products **3a** and **3o**.

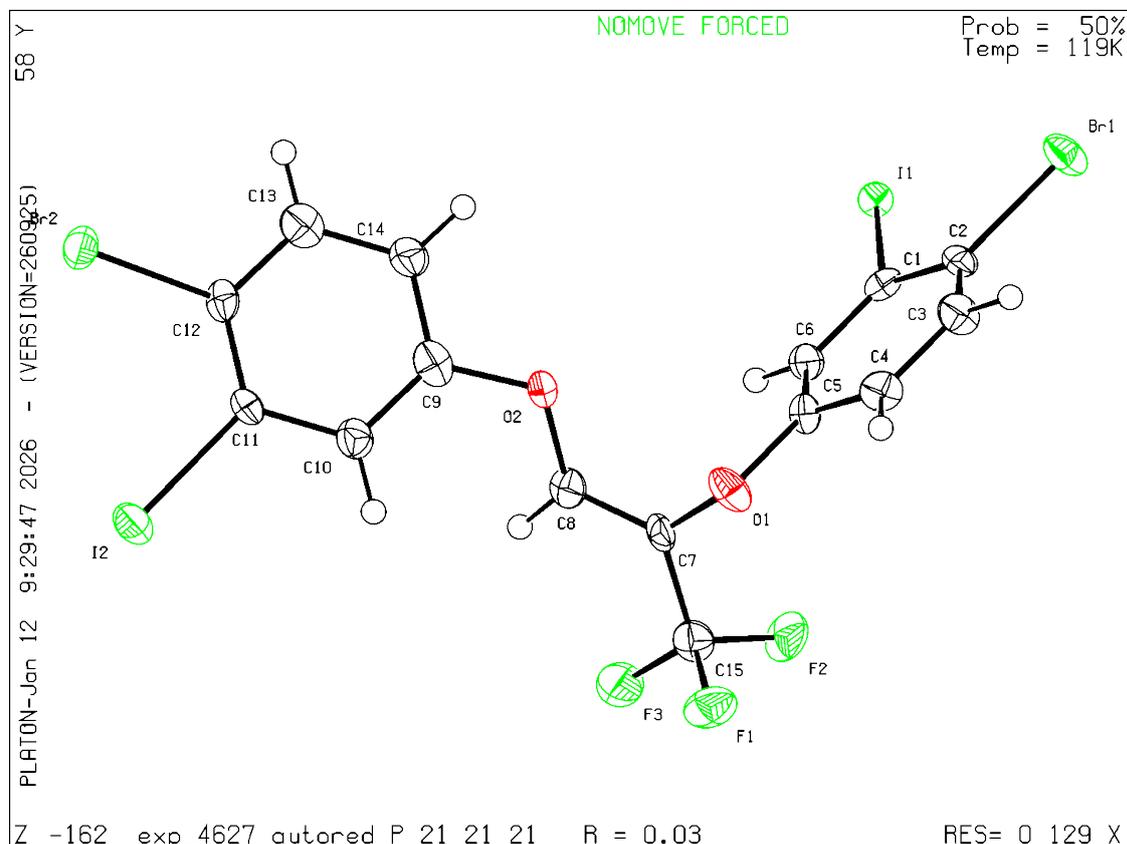


Table 1 Crystal data and structure refinement for **3a**.

Identification code	3a
Empirical formula	C ₁₅ H ₇ Br ₂ F ₃ I ₂ O ₂
Formula weight	689.83
Temperature/K	119.15
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	4.80194(5)
b/Å	13.41159(17)
c/Å	27.6655(3)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	1781.70(3)
Z	4
ρ _{calc} /cm ³	2.572
μ/mm ⁻¹	33.329

F(000)	1264.0
Crystal size/mm ³	0.34 × 0.09 × 0.03
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/ $^{\circ}$	6.39 to 151.168
Index ranges	-4 \leq h \leq 5, -16 \leq k \leq 16, -34 \leq l \leq 34
Reflections collected	16331
Independent reflections	3549 [R _{int} = 0.0334, R _{sigma} = 0.0206]
Data/restraints/parameters	3549/0/217
Goodness-of-fit on F ²	1.188
Final R indexes [$I \geq 2\sigma(I)$]	R ₁ = 0.0250, wR ₂ = 0.0722
Final R indexes [all data]	R ₁ = 0.0255, wR ₂ = 0.0724
Largest diff. peak/hole / e \AA^{-3}	0.93/-0.95
Flack parameter	-0.008(5)

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
I2	-2446.1 (12)	6439.4 (4)	4877.2 (2)	18.84 (13)
I1	12187.3 (14)	5909.5 (4)	7787.3 (2)	28.80 (15)
Br2	-320 (2)	5241.9 (8)	3818.0 (3)	30.1 (2)
Br1	13465 (2)	8289.9 (8)	7282.3 (3)	28.2 (2)
F1	3344 (13)	2292 (4)	6361 (2)	36.6 (14)
F2	-369 (12)	3037 (5)	6128 (2)	37.3 (14)
O2	4667 (14)	3732 (5)	5681 (2)	27.2 (14)
F3	1431 (14)	3381 (5)	6825 (2)	40.0 (15)
O1	5909 (14)	5526 (5)	6162 (2)	25.3 (14)
C9	3356 (16)	4113 (7)	5276 (3)	18.4 (17)
C1	10448 (18)	6452 (7)	7148 (3)	19.3 (17)
C8	3760 (19)	3972 (7)	6139 (3)	21.6 (18)
C14	4154 (19)	3680 (7)	4843 (3)	23.9 (19)
C5	7530 (20)	6143 (7)	6457 (3)	26.0 (18)
C15	2060 (20)	3167 (7)	6367 (3)	27 (2)
C7	4481 (18)	4799 (7)	6381 (3)	23.6 (18)
C2	10998 (17)	7387 (7)	6970 (3)	21.6 (19)
C4	7990 (20)	7093 (7)	6282 (3)	29 (2)
C6	8700 (20)	5816 (7)	6885 (3)	25.4 (19)
C13	3040 (20)	4021 (7)	4412 (3)	27 (2)
C11	289 (17)	5218 (6)	4854 (3)	18.7 (16)
C3	9810 (20)	7711 (8)	6539 (3)	29 (2)
C12	1060 (20)	4792 (7)	4420 (3)	21.8 (19)
C10	1370 (20)	4873 (7)	5287 (3)	24.0 (19)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
I2	18.4 (2)	18.4 (2)	19.7 (2)	-0.50 (18)	0.5 (2)	2.1 (2)
I1	34.4 (3)	31.4 (3)	20.7 (3)	1.9 (2)	-4.8 (2)	4.1 (3)
Br2	43.0 (6)	31.4 (5)	15.9 (4)	0.5 (4)	0.3 (4)	10.6 (5)
Br1	29.6 (5)	30.8 (5)	24.3 (4)	-5.0 (4)	0.4 (4)	-9.2 (4)
F1	37 (3)	22 (3)	51 (4)	6 (3)	-2 (3)	4 (2)
F2	22 (3)	36 (3)	54 (4)	2 (3)	-15 (3)	-7 (3)
O2	28 (3)	32 (4)	21 (3)	1 (3)	-4 (3)	16 (3)
F3	52 (4)	40 (3)	28 (3)	0 (3)	6 (3)	-11 (3)
O1	31 (4)	28 (3)	17 (3)	1 (3)	-7 (3)	-9 (3)
C9	8 (3)	25 (4)	22 (4)	-2 (4)	-4 (3)	3 (3)
C1	20 (4)	25 (4)	13 (4)	0 (3)	0 (3)	2 (4)
C8	22 (4)	24 (4)	18 (4)	0 (4)	-10 (3)	2 (4)
C14	26 (5)	19 (4)	27 (5)	-3 (4)	4 (4)	9 (3)
C5	25 (4)	31 (4)	22 (4)	-5 (3)	0 (4)	10 (4)
C15	27 (5)	24 (4)	29 (4)	0 (4)	-4 (4)	7 (4)
C7	12 (4)	31 (5)	27 (4)	3 (4)	-5 (3)	-2 (4)
C2	12 (4)	31 (5)	22 (4)	-3 (4)	-1 (3)	-2 (3)
C4	39 (6)	27 (5)	20 (4)	-1 (4)	0 (4)	-1 (4)
C6	30 (5)	25 (5)	21 (4)	-3 (4)	-1 (4)	1 (4)
C13	37 (6)	23 (4)	21 (4)	-4 (4)	2 (4)	9 (4)
C11	15 (4)	14 (4)	27 (4)	0 (4)	2 (3)	-1 (3)
C3	33 (5)	29 (5)	26 (4)	-3 (4)	2 (4)	8 (4)
C12	32 (5)	21 (4)	13 (4)	2 (3)	1 (3)	-2 (4)
C10	33 (5)	21 (4)	17 (4)	-3 (4)	1 (3)	-2 (4)

Table 4 Bond Lengths for 3a.

Atom Atom	Length/ \AA	Atom Atom	Length/ \AA
I2 C11	2.101 (8)	C1 C2	1.372 (13)
I1 C1	2.088 (8)	C1 C6	1.400 (13)
Br2 C12	1.890 (9)	C8 C15	1.493 (13)
Br1 C2	1.901 (9)	C8 C7	1.340 (13)
F1 C15	1.325 (10)	C14 C13	1.384 (13)
F2 C15	1.353 (11)	C5 C4	1.379 (13)
O2 C9	1.382 (10)	C5 C6	1.383 (13)
O2 C8	1.379 (11)	C2 C3	1.392 (13)
F3 C15	1.334 (11)	C4 C3	1.399 (14)
O1 C5	1.399 (11)	C13 C12	1.404 (13)
O1 C7	1.338 (11)	C11 C12	1.380 (12)
C9 C14	1.386 (12)	C11 C10	1.385 (12)
C9 C10	1.398 (13)		

Table 5 Bond Angles for 3a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	O2	C9	121.0 (7)	F2	C15	C8	110.9 (7)
C7	O1	C5	116.9 (7)	F3	C15	F2	107.2 (8)
O2	C9	C14	114.8 (7)	F3	C15	C8	111.8 (8)
O2	C9	C10	124.3 (8)	O1	C7	C8	120.7 (9)
C14	C9	C10	120.9 (8)	C1	C2	Br1	122.7 (7)
C2	C1	I1	123.0 (6)	C1	C2	C3	120.8 (9)
C2	C1	C6	119.2 (8)	C3	C2	Br1	116.5 (8)
C6	C1	I1	117.8 (7)	C5	C4	C3	118.1 (9)
O2	C8	C15	113.1 (8)	C5	C6	C1	119.6 (9)
C7	C8	O2	124.8 (9)	C14	C13	C12	119.5 (8)
C7	C8	C15	121.9 (9)	C12	C11	I2	121.1 (7)
C13	C14	C9	119.9 (8)	C12	C11	C10	121.1 (8)
C4	C5	O1	115.6 (8)	C10	C11	I2	117.8 (7)
C4	C5	C6	121.8 (9)	C2	C3	C4	120.4 (10)
C6	C5	O1	122.5 (8)	C13	C12	Br2	117.3 (6)
F1	C15	F2	106.2 (8)	C11	C12	Br2	122.8 (7)
F1	C15	F3	108.0 (8)	C11	C12	C13	119.9 (8)
F1	C15	C8	112.4 (8)	C11	C10	C9	118.6 (8)

Table 6 Torsion Angles for 3a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
I2	C11	C12	Br2	-1.4 (11)	C14	C9	C10	C11	-2.7 (14)
I2	C11	C12	C13	175.6 (7)	C14	C13	C12	Br2	178.6 (7)
I2	C11	C10	C9	-175.0 (7)	C14	C13	C12	C11	1.5 (14)
I1	C1	C2	Br1	1.1 (11)	C5	O1	C7	C8	-154.7 (9)
I1	C1	C2	C3	179.3 (7)	C5	C4	C3	C2	-3.1 (15)
I1	C1	C6	C5	-179.2 (7)	C15	C8	C7	O1	-177.4 (8)
Br1	C2	C3	C4	179.4 (8)	C7	O1	C5	C4	-153.3 (9)
O2	C9	C14	C13	-178.2 (9)	C7	O1	C5	C6	29.2 (13)
O2	C9	C10	C11	177.4 (8)	C7	C8	C15	F1	-122.2 (10)
O2	C8	C15	F1	52.6 (10)	C7	C8	C15	F2	119.0 (9)
O2	C8	C15	F2	-66.2 (10)	C7	C8	C15	F3	-0.5 (12)
O2	C8	C15	F3	174.3 (7)	C2	C1	C6	C5	-0.7 (13)
O2	C8	C7	O1	8.4 (14)	C4	C5	C6	C1	-1.4 (15)
O1	C5	C4	C3	-174.1 (8)	C6	C1	C2	Br1	-177.3 (7)
O1	C5	C6	C1	175.9 (8)	C6	C1	C2	C3	0.9 (13)
C9	O2	C8	C15	101.7 (9)	C6	C5	C4	C3	3.3 (15)
C9	O2	C8	C7	-83.7 (11)	C12	C11	C10	C9	3.0 (13)
C9	C14	C13	C12	-1.2 (14)	C10	C9	C14	C13	1.9 (14)

Table 6 Torsion Angles for 3a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C1	C2	C3	C4	1.1 (14)	C10	C11	C12	Br2	-179.3 (7)
C8	O2	C9	C14	-169.3 (8)	C10	C11	C12	C13	-2.4 (13)
C8	O2	C9	C10	10.6 (13)					

Table 7 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a.

Atom	x	y	z	U(eq)
H14	5466.61	3150.56	4841.14	29
H7	3973.03	4868.78	6710.72	28
H4	7100.39	7319.58	5996.27	35
H6	8312.06	5163.85	7001.02	30
H13	3603.52	3736.11	4113.77	32
H3	10238.2	8356.66	6418.7	35
H10	765.54	5148.41	5586.2	29

Experimental

Single crystals of $\text{C}_{15}\text{H}_7\text{Br}_2\text{F}_3\text{I}_2\text{O}_2$ **3a** were **obtained by crystallization from dichlormethane-pentane**. A suitable crystal was selected mounted on a MD 0.08x0.3 elliptical loop with Mitegen's LV CryoOil™ and measured on a XtaLAB Synergy R, HyPix diffractometer. The crystal was kept at 119.15 K during data collection. Using Olex2²⁴, the structure was solved with the SHELXT²⁵ structure solution program using Intrinsic Phasing and refined with the SHELXL²⁶ refinement package using Least Squares minimisation.

Crystal structure determination of 3a

Crystal Data for $\text{C}_{15}\text{H}_7\text{Br}_2\text{F}_3\text{I}_2\text{O}_2$ ($M = 689.83$ g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 4.80194(5)$ Å, $b = 13.41159(17)$ Å, $c = 27.6655(3)$ Å, $V = 1781.70(3)$ Å³, $Z = 4$, $T = 119.15$ K, $\mu(\text{CuK}\alpha) = 33.329$ mm⁻¹, $D_{\text{calc}} = 2.572$ g/cm³, 16331 reflections measured ($6.39^\circ \leq 2\theta \leq 151.168^\circ$), 3549 unique ($R_{\text{int}} = 0.0334$, $R_{\text{sigma}} = 0.0206$) which were used in all calculations. The final R_1 was 0.0250 ($I > 2\sigma(I)$) and wR_2 was 0.0724 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:

1. Fixed Uiso

At 1.2 times of:

All C(H) groups

2.a Aromatic/amide H refined with riding coordinates:

C14(H14), C7(H7), C4(H4), C6(H6), C13(H13), C3(H3), C10(H10)

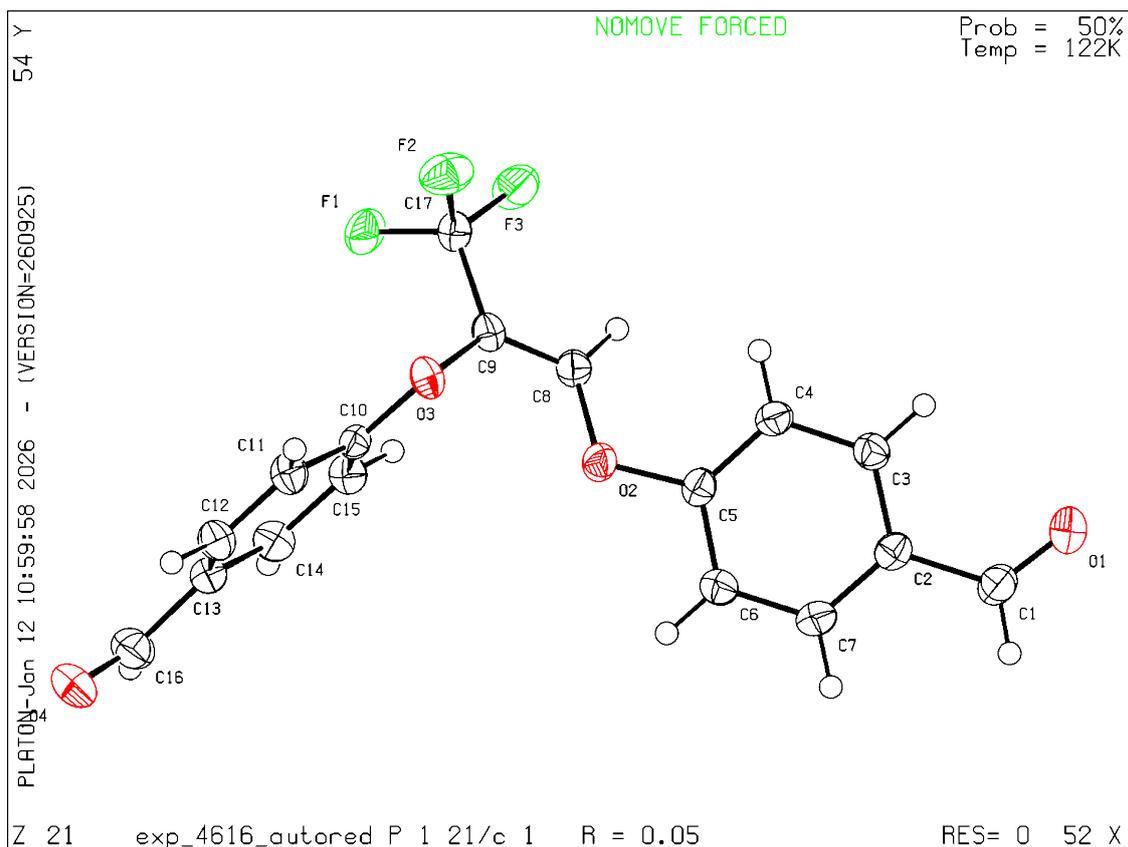


Table 1 Crystal data and structure refinement for 3o.

Identification code	3o
Empirical formula	C ₁₇ H ₁₁ F ₃ O ₄
Formula weight	336.26
Temperature/K	122.15
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	4.76959(7)
b/Å	22.6319(4)
c/Å	13.6112(2)
α/°	90
β/°	94.9419(15)
γ/°	90
Volume/Å ³	1463.80(4)
Z	4
ρ _{calc} /cm ³	1.526
μ/mm ⁻¹	1.160
F(000)	688.0
Crystal size/mm ³	0.432 × 0.226 × 0.145
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	7.6 to 150.926
Index ranges	-4 ≤ h ≤ 5, -28 ≤ k ≤ 27, -17 ≤ l ≤ 16

Reflections collected 26677
 Independent reflections 2970 [$R_{\text{int}} = 0.0569$, $R_{\text{sigma}} = 0.0229$]
 Data/restraints/parameters 2970/0/218
 Goodness-of-fit on F^2 1.168
 Final R indexes [$I \geq 2\sigma(I)$] $R_1 = 0.0451$, $wR_2 = 0.1482$
 Final R indexes [all data] $R_1 = 0.0472$, $wR_2 = 0.1497$
 Largest diff. peak/hole / $e \text{ \AA}^{-3}$ 0.28/-0.25

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3o. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
O3	1295 (3)	7271.3 (6)	1145.0 (10)	26.7 (3)
F1	-3427 (3)	7641.9 (6)	2114.9 (10)	39.1 (4)
F2	485 (3)	7825.7 (7)	2930.5 (10)	43.8 (4)
O2	2377 (3)	8144.2 (6)	-216.3 (11)	28.8 (3)
F3	-1844 (4)	8528.6 (6)	2171.8 (11)	51.1 (4)
O4	-4113 (4)	5052.9 (7)	-1225.9 (13)	43.9 (4)
O1	9877 (4)	10265.3 (7)	-1662.5 (13)	45.1 (5)
C8	1083 (4)	8277.8 (8)	607.6 (15)	25.5 (4)
C13	-3195 (4)	6016.9 (9)	-562.4 (15)	28.2 (4)
C7	6198 (4)	8880.6 (9)	-2049.3 (15)	30.2 (5)
C3	6744 (4)	9456.7 (9)	-564.9 (15)	26.8 (4)
C15	-2632 (4)	7039.2 (8)	-59.1 (15)	26.8 (4)
C5	3965 (4)	8579.6 (8)	-627.7 (15)	24.6 (4)
C4	5079 (4)	9059.9 (9)	-99.3 (14)	26.1 (4)
C2	7300 (4)	9372.8 (9)	-1541.5 (14)	25.9 (4)
C11	529 (4)	6290.5 (9)	658.5 (15)	28.1 (4)
C6	4503 (4)	8484.1 (9)	-1601.5 (15)	29.4 (4)
C9	421 (4)	7850.3 (8)	1208.8 (15)	24.8 (4)
C10	-338 (4)	6875.7 (8)	568.4 (14)	22.5 (4)
C1	9059 (5)	9802.7 (10)	-2027.2 (16)	32.8 (5)
C14	-4051 (4)	6603.5 (9)	-623.3 (16)	30.8 (5)
C12	-899 (5)	5865.0 (9)	91.2 (16)	30.4 (5)
C17	-1092 (4)	7967.2 (9)	2100.9 (15)	26.5 (4)
C16	-4708 (5)	5571.3 (10)	-1192.9 (17)	36.6 (5)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3o. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O3	24.9 (7)	19.9 (7)	34.4 (8)	0.4 (5)	-1.9 (6)	-0.2 (5)
F1	26.8 (7)	50.9 (8)	40.6 (7)	-0.7 (6)	8.6 (5)	-12.5 (5)
F2	35.5 (7)	66.2 (10)	29.0 (7)	-1.7 (6)	-1.2 (5)	-0.4 (6)
O2	32.4 (8)	21.5 (7)	33.9 (8)	-0.3 (5)	11.5 (6)	-0.8 (5)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3o. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F3	79.4 (11)	26.9 (7)	52.1 (9)	2.3 (6)	35.8 (8)	7.7 (7)
O4	52.9 (11)	33.3 (9)	45.6 (10)	-12.2 (7)	4.4 (8)	-5.9 (7)
O1	58.1 (11)	35.7 (9)	43.1 (10)	1.4 (7)	12.4 (8)	-15.3 (8)
C8	23.8 (9)	22.8 (9)	30.6 (10)	-1.3 (7)	5.6 (7)	0.4 (7)
C13	29.6 (10)	28.2 (10)	27.5 (10)	-2.6 (8)	6.4 (8)	-2.9 (8)
C7	31.9 (11)	33.9 (11)	25.9 (10)	-2.2 (8)	8.0 (8)	-0.4 (8)
C3	26.7 (10)	25.0 (9)	29.1 (10)	-1.9 (7)	4.2 (8)	-0.3 (7)
C15	25.3 (10)	23.7 (9)	31.2 (10)	1.7 (7)	1.5 (8)	4.0 (7)
C5	23.7 (9)	20.8 (9)	29.9 (10)	3.5 (7)	6.4 (7)	3.2 (7)
C4	27.3 (10)	27.7 (10)	23.7 (9)	0.0 (7)	5.2 (7)	1.0 (7)
C2	23.7 (9)	26.6 (9)	27.7 (10)	2.6 (7)	4.5 (7)	2.8 (7)
C11	29.2 (10)	23.5 (9)	31.2 (10)	3.5 (7)	-0.8 (8)	2.0 (7)
C6	31.6 (11)	27.5 (10)	29.6 (10)	-4.8 (8)	6.1 (8)	-1.6 (8)
C9	23.8 (9)	20.0 (9)	30.4 (10)	-0.1 (7)	1.7 (7)	-0.4 (7)
C10	21.8 (9)	22.3 (9)	23.9 (9)	0.8 (7)	5.5 (7)	-2.2 (7)
C1	34.7 (11)	33.4 (11)	31.3 (11)	3.6 (8)	8.0 (9)	-1.3 (8)
C14	27.9 (10)	32.8 (11)	30.9 (10)	-0.4 (8)	-1.3 (8)	1.4 (8)
C12	35.9 (11)	22.2 (9)	33.3 (11)	-0.1 (8)	4.3 (8)	1.1 (8)
C17	23.8 (10)	24.8 (9)	31.0 (10)	2.1 (7)	3.3 (8)	-2.2 (7)
C16	37.6 (12)	36.5 (12)	35.3 (11)	-7.0 (9)	1.6 (9)	-4.1 (9)

Table 4 Bond Lengths for 3o.

Atom Atom	Length/ \AA	Atom Atom	Length/ \AA
O3 C9	1.380 (2)	C7 C2	1.390 (3)
O3 C10	1.385 (2)	C7 C6	1.384 (3)
F1 C17	1.336 (2)	C3 C4	1.387 (3)
F2 C17	1.340 (2)	C3 C2	1.391 (3)
O2 C8	1.360 (2)	C15 C10	1.379 (3)
O2 C5	1.390 (2)	C15 C14	1.390 (3)
F3 C17	1.326 (2)	C5 C4	1.384 (3)
O4 C16	1.209 (3)	C5 C6	1.388 (3)
O1 C1	1.209 (3)	C2 C1	1.478 (3)
C8 C9	1.323 (3)	C11 C10	1.390 (3)
C13 C14	1.389 (3)	C11 C12	1.377 (3)
C13 C12	1.393 (3)	C9 C17	1.489 (3)
C13 C16	1.472 (3)		

Table 5 Bond Angles for 3o.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C9	O3	C10	119.42 (15)	C7	C6	C5	118.84 (19)
C8	O2	C5	118.46 (15)	O3	C9	C17	112.97 (16)
C9	C8	O2	119.82 (17)	C8	C9	O3	124.46 (18)
C14	C13	C12	118.99 (19)	C8	C9	C17	122.22 (18)
C14	C13	C16	119.5 (2)	O3	C10	C11	114.68 (17)
C12	C13	C16	121.47 (19)	C15	C10	O3	123.69 (17)
C6	C7	C2	120.71 (18)	C15	C10	C11	121.63 (18)
C4	C3	C2	120.80 (18)	O1	C1	C2	124.2 (2)
C10	C15	C14	118.33 (18)	C13	C14	C15	121.23 (19)
C4	C5	O2	123.07 (17)	C11	C12	C13	120.60 (19)
C4	C5	C6	121.61 (18)	F1	C17	F2	105.33 (16)
C6	C5	O2	115.22 (17)	F1	C17	C9	112.14 (16)
C5	C4	C3	118.70 (18)	F2	C17	C9	111.62 (16)
C7	C2	C3	119.32 (18)	F3	C17	F1	107.20 (17)
C7	C2	C1	120.67 (18)	F3	C17	F2	107.65 (17)
C3	C2	C1	120.02 (18)	F3	C17	C9	112.50 (16)
C12	C11	C10	119.20 (19)	O4	C16	C13	125.6 (2)

Table 6 Torsion Angles for 3o.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O3	C9	C17	F1	-61.1 (2)	C6	C7	C2	C3	1.7 (3)
O3	C9	C17	F2	56.8 (2)	C6	C7	C2	C1	178.65 (19)
O3	C9	C17	F3	177.99 (17)	C6	C5	C4	C3	0.8 (3)
O2	C8	C9	O3	9.6 (3)	C9	O3	C10	C15	8.9 (3)
O2	C8	C9	C17	177.65 (17)	C9	O3	C10	C11	171.80 (17)
O2	C5	C4	C3	177.10 (17)	C10	O3	C9	C8	-89.7 (2)
O2	C5	C6	C7	176.54 (18)	C10	O3	C9	C17	96.94 (19)
C8	O2	C5	C4	22.2 (3)	C10	C15	C14	C13	-0.1 (3)
C8	O2	C5	C6	161.25 (18)	C10	C11	C12	C13	-0.3 (3)
C8	C9	C17	F1	125.4 (2)	C14	C13	C12	C11	-1.0 (3)
C8	C9	C17	F2	-116.6 (2)	C14	C13	C16	O4	177.8 (2)
C8	C9	C17	F3	4.5 (3)	C14	C15	C10	O3	177.99 (17)
C7	C2	C1	O1	173.2 (2)	C14	C15	C10	C11	-1.3 (3)
C3	C2	C1	O1	-7.2 (3)	C12	C13	C14	C15	1.2 (3)
C5	O2	C8	C9	156.28 (18)	C12	C13	C16	O4	-1.6 (4)
C4	C3	C2	C7	-0.8 (3)	C12	C11	C10	O3	177.86 (18)
C4	C3	C2	C1	179.51 (18)	C12	C11	C10	C15	1.5 (3)

Table 6 Torsion Angles for 3o.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C4	C5	C6	C7	0.1 (3)	C16	C13	C14	C15	178.30 (19)
C2	C7	C6	C5	-1.3 (3)	C16	C13	C12	C11	178.5 (2)
C2	C3	C4	C5	-0.4 (3)					

Table 7 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3o.

Atom	x	y	z	U(eq)
H8	656.76	8676.91	751.07	31
H7	6613.82	8815.63	-2710.86	36
H3	7512.67	9789.68	-212.32	32
H15	-3226.15	7439.64	-104.38	32
H4	4710.72	9116.86	569.01	31
H11	2088.15	6185.29	1105.91	34
H6	3720.16	8152.38	-1954.25	35
H1	9579.51	9709.69	-2667.36	39
H14	-5636.71	6708.66	-1058.67	37
H12	-313.73	5464.24	146.24	36
H16	-6286.05	5702.46	-1609.42	44

Experimental

Single crystals of $\text{C}_{17}\text{H}_{11}\text{F}_3\text{O}_4$ **3o** were obtained by crystallization from dichloromethane-pentane. A suitable crystal was selected mounted on a MD 0.2 loop with Mitegen's LV CryoOil™, and measured on a XtaLAB Synergy R, HyPix diffractometer. The crystal was kept at 122.15 K during data collection. Using Olex2²⁴, the structure was solved with the SHELXS²⁷ structure solution program using Direct Methods and refined with the SHELXL²⁶ refinement package using Least Squares minimisation.

Crystal structure determination of 3o

Crystal Data for $\text{C}_{17}\text{H}_{11}\text{F}_3\text{O}_4$ ($M = 336.26$ g/mol): monoclinic, space group $P2_1/c$ (no. 14), $a = 4.76959(7)$ Å, $b = 22.6319(4)$ Å, $c = 13.6112(2)$ Å, $\beta = 94.9419(15)^\circ$, $V = 1463.80(4)$ Å³, $Z = 4$, $T = 122.15$ K, $\mu(\text{CuK}\alpha) = 1.160$ mm⁻¹, $D_{\text{calc}} = 1.526$ g/cm³, 26677 reflections measured ($7.6^\circ \leq 2\theta \leq 150.926^\circ$), 2970 unique ($R_{\text{int}} = 0.0569$, $R_{\text{sigma}} = 0.0229$) which were used in all calculations. The final R_1 was 0.0451 ($I > 2\sigma(I)$) and wR_2 was 0.1497 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:

1. Fixed Uiso

At 1.2 times of:

All C(H) groups

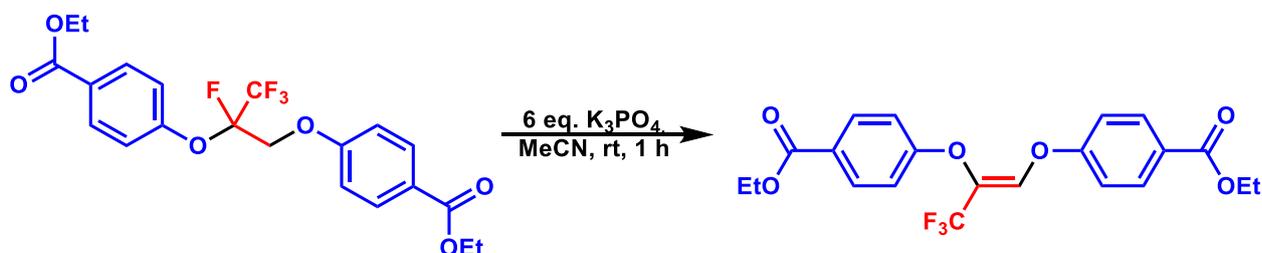
2.a Aromatic/amide H refined with riding coordinates:

C8 (H8), C10 (H10), C11 (H11), C12 (H12), C14 (H14),
C16 (H16), C17 (H17), C20 (H20), C21 (H21), C22 (H22), C24 (H24)

10. Mechanistical studies and proposed mechanistic route

HF elimination during the vinyl-ether synthesis

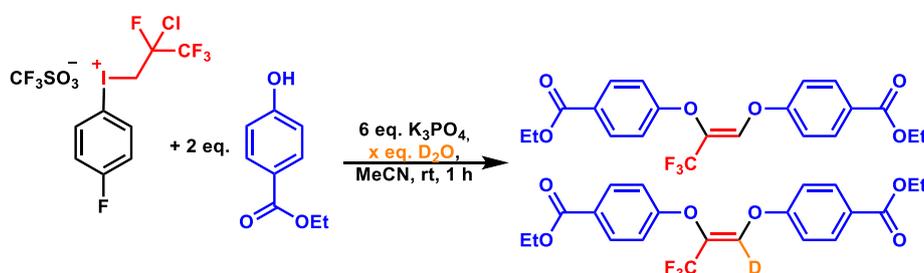
K₃PO₄ (190.1 mg, 0.90 mmol), a previously prepared mixture of diethyl 4,4'-((2,3,3,3-tetrafluoropropane-1,2-diyl)bis(oxy))dibenzoate (**SP**) and diethyl 4,4'-((3,3,3-trifluoroprop-1-ene-1,2-diyl)bis(oxy))(Z)-dibenzoate (**31**) (61.9 mg, the ratio of **SP**:**31** is 31:69 measured by ¹⁹F NMR) and MeCN (1.5 mL) was measured into a screw cap vial. The mixture was stirred for 2 hours at ambient temperature, then analyzed by GC-MS.



Formation of further vinyl-ether (**31**) was not observed, measured by ¹⁹F-NMR.

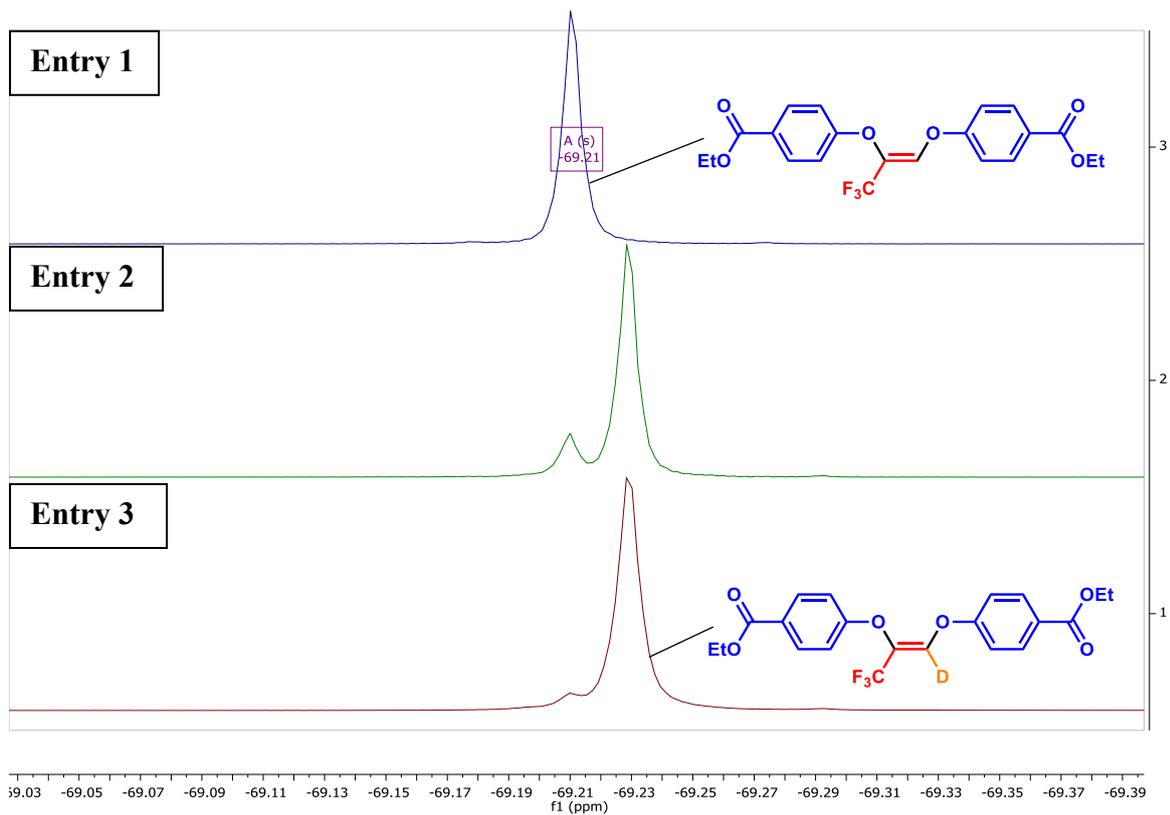
Deuteration of the vinyl-ether compound

Dried K₃PO₄ (380.3 mg, 1.80 mmol), ethyl 4-hydroxybenzoate (99.7 mg, 0.60 mmol), freshly distilled MeCN (0.85 mL) and D₂O was measured into a screw cap vial. While the mixture was stirred at ambient temperature, the solution of 3-chloro-1,1,1,2-tetrafluoropropan-2-yl(4-fluorophenyl)iodonium trifluoromethanesulfonate (156.2 mg, 0.30 mmol) in 2.15 mL MeCN was added in 30 minutes using syringe pump and stirring the reaction mixture for further 1 hour. The solvent was evaporated under reduced pressure to Celite and the crude product was purified by column chromatography using hexanes-ethyl acetate as eluent.

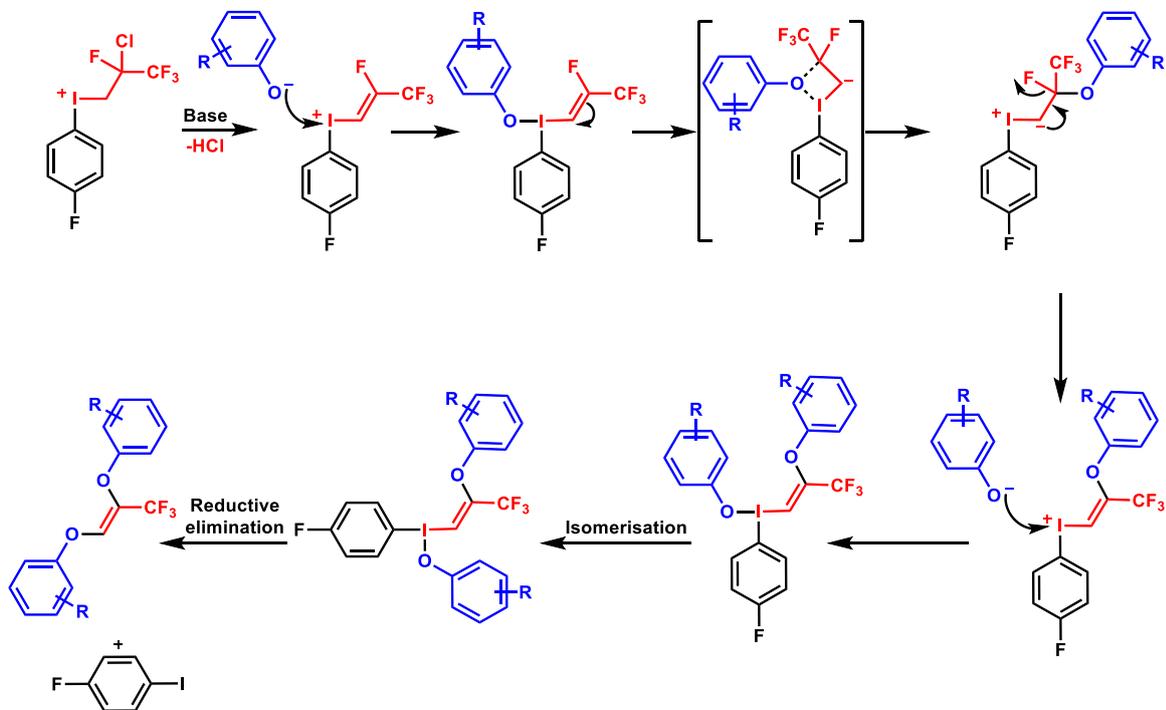


Entry	D ₂ O	D _{NMR} ^a	Theo ^b	Yield ^c
1	0 eq.	0%	0%	89%
2	20 eq.	84%	91%	87%
3	50 eq.	92%	96%	88%

^aEffectivity of the deuteration, calculated from ¹⁹F NMR measurements. ^bTheoretical deuteration from probability. ^cIsolated yield.



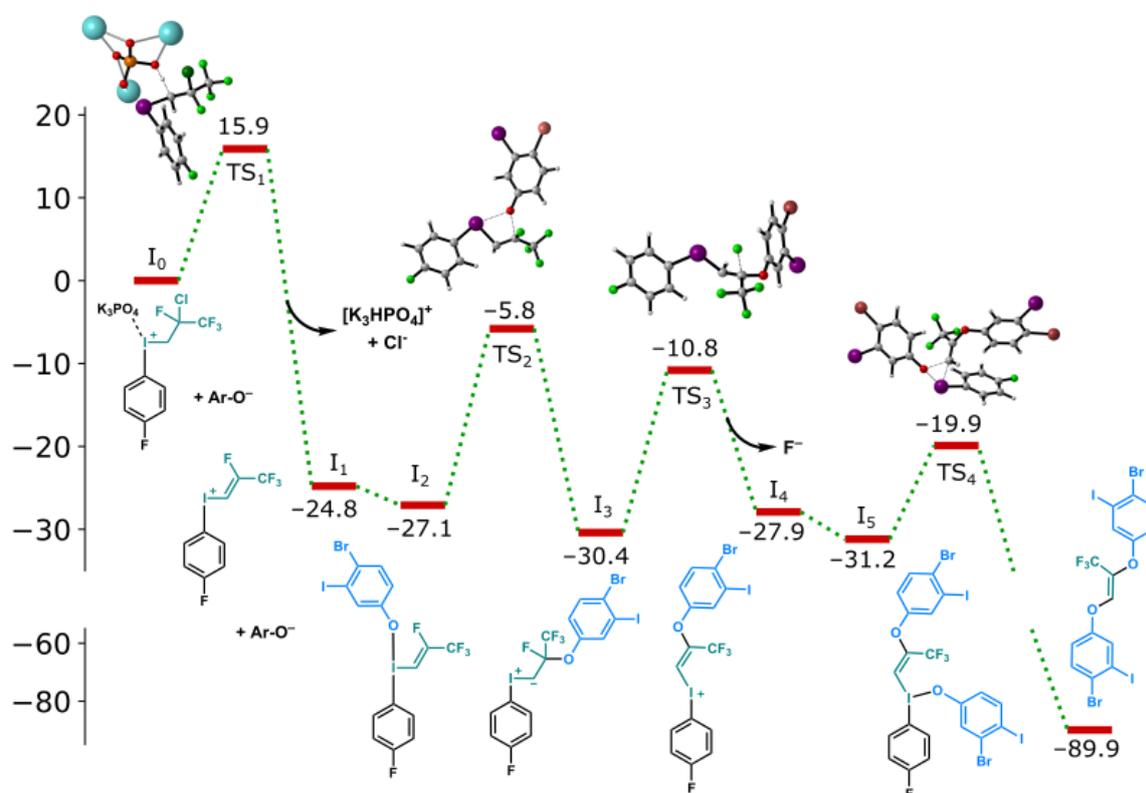
The proposed mechanistical route



11. Computational details

The Gaussian16 software was utilized for all computational chemistry work²⁸. Geometries were optimized and their vibrational frequencies were characterized with the range-separated hybrid density functional ω B97XD²⁹. Element-specific basis sets were employed: the 6-31G* basis set was used for the majority of atoms, whereas the LANL2DZ effective core potential, supplemented with polarization functions from the aug-cc-pVDZ-PP set, was applied for bromine and iodine^{30,31,32}. After optimization, more accurate electronic energies were determined via single-point calculations on the obtained structures employing the SMD implicit solvation model³³. For these, an expanded basis set was chosen: LanL08d (with added diffuse and polarization functions from aug-cc-pVTZ-PP) for bromine and iodine and the 6-311++G(3df,3pd) basis set for all other elements. Gibbs free energies were estimated based on the harmonic oscillator, rigid rotor, and ideal gas model. The final reported Gibbs free energies represent a composite of the high-level electronic energies and the Gibbs free energy corrections derived from the lower-level frequency calculations. The nature of each stationary point was verified by vibrational frequency analysis, confirming minima (zero imaginary frequencies) or transition states (a single imaginary frequency). Furthermore, combined intrinsic reaction coordinate (IRC) and optimizations were carried out to verify that the located transition states indeed link the corresponding two intermediate structures. The presented free energy values also take into account that formation of the intermediates is accompanied by the stabilization of the counter ions in the most favorable salt formation. TS structures were drawn by the CYLview software³⁴.

Gibbs free energy profil for the formation of the E isomer of product **3a**.



Gibbs free energy profile for the reaction of 4-bromo-3-iodophenol leading to the formation of the E isomer. Energy values are given in kcal/mol. Color code for the TS structures: C, grey, H: white, O: red, F: light green, Cl: dark green, Br: brown, I: purple, P: orange, K: blue.

Cartesian coordinates

Reactants and general byproducts:

iodoniumsalt.xyz

30

E (Hartree): -2278.94279572
I 0.243064 -1.056212 -0.754197
C -1.927571 -1.166219 -0.756284
C -2.489759 -1.734220 0.531952
C -4.035269 -1.633983 0.561425
F -2.050207 -1.012497 1.603041
Cl -1.996480 -3.431262 0.757304
F -4.533835 -2.125927 1.686257
F -4.380211 -0.343789 0.471036
F -4.561350 -2.285328 -0.476514
H -2.219492 -1.786668 -1.604420
H -2.295608 -0.149388 -0.907084
C 0.185785 1.050081 -0.631618
C 0.913004 1.778848 -1.567147
C 0.882292 3.166184 -1.495350
C 0.132523 3.774910 -0.497708
C -0.587656 3.045619 0.438120
C -0.555765 1.656570 0.376354
H 1.508576 1.285592 -2.324836
H 1.435577 3.774184 -2.201638
F 0.103529 5.106994 -0.435336
H -1.151467 3.560280 1.207527
H -1.104779 1.071318 1.104791
O 2.606236 -0.532472 -0.799906
S 3.424234 -1.623262 -1.462412
C 3.559367 -0.939124 -3.171126
O 2.631114 -2.843953 -1.616321
O 4.781092 -1.714515 -0.968304
F 4.201562 -1.777263 -3.972318
F 2.326612 -0.730914 -3.674498
F 4.193467 0.231502 -3.161554

FPhI.xyz

12

E (Hartree): -342.285037300
C -0.005101 0.000000 -0.002945
C -0.028946 0.000000 1.383643
C 1.176809 0.000000 2.078191
C 2.379334 0.000000 1.373709
C 2.388170 0.000000 -0.019949
C 1.183797 0.000000 -0.716890
H -0.978973 0.000000 1.906212
H 1.172061 0.000000 3.162565

I 4.200963 0.000000 2.425427
H 3.324892 0.000000 -0.566248
H 1.161341 0.000000 -1.800922
F -1.165311 0.000000 -0.672793

triflate_anion.xyz

8

E (Hartree): -961.721032016
O 0.007877 0.032611 -0.012152
S 0.015049 0.022445 1.456312
O 1.342926 -0.018960 2.082126
C -0.659763 -1.654605 1.845468
F -0.735066 -1.867416 3.170498
F -1.897397 -1.822891 1.348793
F 0.106452 -2.632663 1.332597
O -0.960136 0.912087 2.099910

f_opt.xyz

1

E (Hartree): -99.9957443875
F 0.000000 0.000000 0.000000

Br-I-phenolate_opt.xyz

12

E= -330.364463501
O 0.026410 0.123849 0.097113
C 0.018130 0.081574 1.347393
C -1.052843 0.659860 2.142808
C -1.063100 0.613871 3.521659
C -0.031848 0.000985 4.247251
C 1.021423 -0.569770 3.518848
C 1.055792 -0.537526 2.141369
H -1.859399 1.138381 1.597203
I -2.725216 1.520910 4.501831
Br 0.028025 -0.104961 6.161914
H 1.828331 -1.048650 4.068548
H 1.888354 -0.990276 1.607990

Br-I-phenol_opt.xyz

13

E= -330.850394493
O -0.022151 0.151799 0.087266
C 0.019111 0.077555 1.439598
H 0.758046 -0.277265 -0.284423
C -1.041738 0.653760 2.137333
C -1.069645 0.617334 3.528402

C -0.029171 0.000004 4.232815
C 1.025762 -0.572483 3.525653
C 1.056654 -0.537894 2.138293
H -1.837637 1.126860 1.574224
I -2.709100 1.512525 4.481973
Br 0.020117 -0.099318 6.131076
H 1.832067 -1.050847 4.070198
H 1.889789 -0.991049 1.607097

k3hpo4_opt.xyz

9

E= -2442.94617441

P 0.046268 -0.155431 -0.439833
O -0.633945 -0.398101 0.912975
O 1.538241 0.201982 -0.322104
O -0.053292 -1.661309 -1.128594
O -0.721940 0.820750 -1.347708
K -2.956961 0.105996 -0.132801
K 1.628313 -1.147365 1.946839
K 1.359240 2.268642 -1.873441
H 0.343677 -1.664063 -2.008436

K-Br-I-phenolate_opt.xyz

13

E= -930.237278909

O 0.041152 0.091187 0.048892
C -0.000421 0.008555 1.326783
C -1.068615 0.592792 2.083237
C -1.064895 0.629058 3.477305
C -0.017079 0.065493 4.199470
C 1.021611 -0.555123 3.486624
C 1.039061 -0.587606 2.108524
H -1.944294 0.945660 1.541304
I -2.699354 1.587675 4.410061
Br 0.088885 0.088624 6.103837
H 1.832122 -1.012175 4.046278
H 1.854997 -1.073821 1.581575
K -0.011240 2.526158 -0.035865

kcl_opt.xyz

2

E= -1060.25404385

Cl 0.000000 0.000000 -0.314979
K 0.000000 0.000000 2.414979

kf_opt.xyz

2

E= -699.867269109

F 0.000000 0.000000 -0.033038
K 0.000000 0.000000 2.133038

k_opt.xyz

1

E= -599.845012643

K 1.922027 -1.109683 1.292217

ktriflat_opt.xyz

9

E= -1561.59025247

O -0.114511 -0.246037 -0.331603
S -0.009253 -0.038585 1.098227
O 1.355729 0.059042 1.671665
C -0.627435 -1.585799 1.887248
F -0.547978 -1.439018 3.237811
F -1.896793 -1.825766 1.583969
F 0.105643 -2.640733 1.554766
O -0.903421 0.978438 1.704584
K 0.607076 1.379964 3.771100

Common intermediates product and TS- s:

I0.xyz

30

E= -3759.69907310

C -0.389668 0.445033 -1.101027
H 0.057943 0.425282 -2.095606
H -1.489728 0.370479 -1.163405
C 0.048770 1.730597 -0.424749
C -0.664579 2.945319 -1.084751
F -0.475409 2.903330 -2.402293
F -1.989763 2.906712 -0.854343
F -0.190239 4.087073 -0.615310
F 1.370173 1.957980 -0.582979
Cl -0.318800 1.775614 1.334745
I 0.155316 -1.418538 -0.170970
C 3.854105 0.003364 1.739359
C 4.766692 -0.012831 0.693794
C 4.412435 -0.400081 -0.592357
C 3.097477 -0.778746 -0.834895
C 2.156907 -0.752993 0.196493
C 2.539209 -0.370569 1.482642
H 4.176900 0.306187 2.729083
H 5.161357 -0.406784 -1.376317
H 2.813437 -1.092931 -1.835796
H 1.815739 -0.355120 2.292626
F 6.027784 0.350510 0.932376
O -1.926802 -1.977236 -0.825389
P -3.273609 -1.339826 -0.231105

O -4.393926 -2.347188 -0.578105
O -3.163607 -1.110448 1.297157
O -3.460520 0.011268 -0.990037
K -3.902042 -1.688001 -3.054462
K -4.461555 -3.319116 1.772283
K -3.648675 1.441583 1.122348

I1.xyz

20

E= -856.362260874
C -1.784991 -1.236935 -0.868909
H -2.255843 -1.513698 -1.802100
C -2.349446 -1.398886 0.322082
C -3.737143 -1.997130 0.532337
F -4.509089 -1.100664 1.135295
F -4.270526 -2.328244 -0.639806
F -3.635518 -3.075523 1.297521
F -1.769033 -1.046981 1.450399
I 0.115682 -0.392197 -1.005942
C -0.701999 3.471362 0.760916
C -0.935519 4.268141 -0.356908
C -0.880074 3.771069 -1.656222
C -0.582938 2.429537 -1.852146
C -0.352851 1.640556 -0.725496
C -0.401347 2.128701 0.580291
H -0.753548 3.905960 1.752562
H -1.066865 4.432305 -2.494521
H -0.533343 2.026214 -2.857452
H -0.214541 1.493582 1.438813
F -1.219350 5.545838 -0.177570

I2.xyz

32

E= -1186.75379644
C -0.632358 0.777216 0.889527
H -0.578224 1.206447 1.879164
C -0.279150 1.447211 -0.193071
C 0.175711 2.890208 -0.193998
F -0.669576 3.636535 -0.913583
F 0.212929 3.371880 1.050550
F 1.386171 2.995850 -0.735103
F -0.285389 0.928472 -1.415610
I -1.089954 -1.253090 0.810558
C -4.459159 -0.327479 -1.871533
C -5.529170 -0.220260 -0.993574
C -5.383289 -0.389899 0.376083
C -4.118322 -0.673733 0.881047
C -3.027307 -0.782839 0.018041
C -3.199354 -0.614324 -1.357032
H -4.620216 -0.188830 -2.934774

H -6.247591 -0.298864 1.024414
H -3.992218 -0.807776 1.951859
H -2.355162 -0.697073 -2.034414
F -6.741944 0.054103 -1.484301
O 0.960019 -1.346405 1.743070
C 1.952208 -0.609625 1.267336
C 2.285642 -0.598204 -0.099734
C 3.261251 0.259659 -0.601896
C 3.965774 1.100919 0.260715
C 3.673660 1.064953 1.626602
C 2.682362 0.236135 2.123309
H 1.753125 -1.260815 -0.774254
I 3.564979 0.247775 -2.680874
Br 5.300383 2.321060 -0.334215
H 4.224552 1.713938 2.299164
H 2.445772 0.230930 3.182495

I3.xyz

32

E= -1186.76138654
C 1.131332 -0.302686 -0.646821
O -0.005501 -1.017320 -0.382750
C -1.184615 -0.314767 -0.205140
C -2.313370 -1.111923 -0.057598
C -3.559646 -0.521970 0.134739
C -3.664427 0.872850 0.172944
C -2.518677 1.650804 0.021936
C -1.268750 1.074102 -0.166407
H -2.203250 -2.189277 -0.095772
I -5.209149 -1.795964 0.362527
Br -5.318848 1.773920 0.431106
H -2.602335 2.731126 0.055278
H -0.393630 1.711672 -0.257189
F 1.700351 2.847264 0.015063
C 1.452952 -0.366563 -2.123847
F 2.498314 0.393362 -2.478208
F 1.742080 -1.628890 -2.467247
F 0.396531 0.026787 -2.836594
C 1.778679 0.285856 0.349029
I 3.363780 1.622794 0.225948
C 4.715464 -0.020884 0.543464
C 4.837989 -1.050332 -0.391640
C 5.742698 -2.084434 -0.182094
C 6.524249 -2.064418 0.965636
C 6.426191 -1.052083 1.907896
C 5.509328 -0.026497 1.690385
H 4.226122 -1.059474 -1.288500
H 5.852188 -2.896066 -0.892846
F 7.399349 -3.056192 1.168688
H 7.052016 -1.077743 2.793051

H 5.416640 0.765473 2.429005
H 1.374464 0.200330 1.350845

I4-E.xyz

31

E= -1086.74442640

C -2.186697 -1.829263 0.839557
O -1.755627 -1.253464 -0.286364
C -0.400119 -0.912510 -0.417281
C 0.256301 -0.204658 0.576562
C 1.584260 0.143222 0.366350
C 2.234379 -0.200487 -0.819405
C 1.545820 -0.904909 -1.817909
C 0.213742 -1.261877 -1.606854
H -0.249716 0.083617 1.491801
H 2.123741 0.695668 1.126850
Br 4.044488 0.322544 -1.007634
I 2.425207 -1.474997 -3.624119
H -0.344362 -1.811807 -2.355425
C -1.352511 -2.967049 1.439865
F -0.573644 -2.527138 2.425864
F -0.620214 -3.564343 0.521808
F -2.187374 -3.894174 1.977521
C -3.359806 -1.421036 1.335744
I -4.366178 -2.326320 2.931383
C -5.546753 -0.668607 3.428097
C -5.036901 0.268878 4.327639
C -5.828297 1.359859 4.657500
C -7.093617 1.472635 4.087682
C -7.599958 0.530873 3.196806
C -6.816789 -0.564339 2.859131
H -4.051043 0.162018 4.766682
H -5.480623 2.117404 5.350386
F -7.843489 2.513446 4.407135
H -8.593297 0.660366 2.782916
H -7.198127 -1.310716 2.170677
H -3.933228 -0.612545 0.897558

I4-Z.xyz

31

E= -1086.75876269

C -3.484311 -1.621182 0.938577
H -4.113730 -1.892768 1.775601
C -2.250908 -2.078592 0.714977
C -1.592946 -3.033077 1.724569
F -2.532787 -3.714404 2.378900
F -0.799618 -3.876505 1.080543
F -0.871378 -2.356546 2.621470
I -4.358176 -0.283020 -0.411468
C -0.966256 1.921381 -1.943725

C -0.709342 2.828542 -0.921009
C -1.496603 2.908597 0.224885
C -2.567982 2.037829 0.369878
C -2.801034 1.115351 -0.648578
C -2.029574 1.040410 -1.806969
H -0.324378 1.895154 -2.816986
H -1.265550 3.644948 0.986067
H -3.191882 2.086104 1.255568
H -2.224669 0.303287 -2.577620
F 0.324184 3.644875 -1.039069
O -1.597703 -1.799231 -0.416764
C -0.329666 -1.210127 -0.411527
C 0.415510 -1.404995 -1.561523
C 1.612252 -0.707923 -1.729516
C 2.048244 0.162717 -0.720581
C 1.288501 0.313840 0.439975
C 0.084826 -0.359013 0.600764
H 0.048753 -2.079767 -2.326521
I 2.648993 -0.988519 -3.520510
Br 3.634226 1.184261 -0.869963
H 1.635920 0.983988 1.218049
H -0.512006 -0.198971 1.490767

I5-E.xyz

43

E= -1417.14041368

C -0.111786 0.549886 -0.788860
C -0.161543 0.010428 0.423734
C -1.029999 0.356418 1.616623
F -1.948304 1.293464 1.353246
F -1.649456 -0.728783 2.065148
F -0.246265 0.830310 2.601560
I -1.052385 2.284665 -1.473550
C 0.539696 3.290785 -0.418946
O 0.690087 -0.999631 0.770386
C 2.043044 -0.772669 0.597179
C 2.802070 -1.827592 0.115705
C 4.180369 -1.671183 -0.046279
C 4.777634 -0.446945 0.269465
C 3.993569 0.600923 0.755726
C 2.627558 0.446924 0.927680
H 2.311020 -2.762376 -0.128114
I 5.257547 -3.308697 -0.782819
Br 6.638993 -0.126794 0.066345
H 4.461624 1.545341 1.009861
H 2.031055 1.265084 1.316118
O -2.382657 0.832757 -2.504771
C -2.880177 -0.192391 -1.819881
C -2.492706 -1.508894 -2.123255
C -2.967389 -2.576302 -1.379110

C -3.830840 -2.371504 -0.300812
C -4.236752 -1.070484 0.006071
C -3.776867 0.000416 -0.755754
H -1.809155 -1.672299 -2.950365
H -2.658687 -3.587578 -1.621605
Br -4.394070 -3.896423 0.689995
I -5.509466 -0.625294 1.616986
H -4.100077 1.009825 -0.525629
C 1.775131 3.450580 -1.047502
C 2.860339 3.965662 -0.344688
C 2.684022 4.310967 0.987573
C 1.461350 4.174731 1.632254
C 0.382978 3.660308 0.918051
H 1.907442 3.162325 -2.086794
H 3.831759 4.091305 -0.810066
F 3.729682 4.782624 1.675671
H 1.367199 4.462416 2.673535
H -0.570193 3.529770 1.420715
H 0.578112 0.144693 -1.519851

I5-Z.xyz

43

E= -1417.15465859

C 2.746563 -2.270941 -0.098716
H 2.830413 -3.263027 -0.516702
C 2.653121 -2.073887 1.212084
C 2.736658 -3.251202 2.165628
F 2.908268 -4.408984 1.518167
F 3.749155 -3.094840 3.021709
F 1.603380 -3.332691 2.873222
I 2.520311 -0.872759 -1.621626
C 3.864686 0.527419 -0.701227
O 2.535601 -0.912004 1.889733
C 1.456549 -0.071890 1.662627
C 1.724270 1.287014 1.725231
C 0.685795 2.199100 1.550125
C -0.614560 1.732903 1.325058
C -0.858374 0.360276 1.281523
C 0.172750 -0.554433 1.447705
H 2.742253 1.616434 1.896632
I 1.174306 4.235513 1.616701
Br -2.091045 2.899640 1.079842
H -1.869235 0.002384 1.123657
H -0.031411 -1.619087 1.410799
O 1.151730 -2.553482 -2.265414
C -0.005741 -2.617401 -1.623069
C -0.244942 -3.594364 -0.637005
C -1.437984 -3.614172 0.068467
C -2.434423 -2.666891 -0.178910
C -2.228832 -1.709939 -1.177768

C -1.031728 -1.690187 -1.886491
H 0.520859 -4.335417 -0.430287
H -1.604497 -4.367374 0.831461
Br -4.013498 -2.737508 0.883424
I -3.656824 -0.244944 -1.659138
H -0.869369 -0.952506 -2.665051
C 4.973897 0.147610 0.049644
C 5.796083 1.119121 0.611110
C 5.498703 2.457752 0.391222
C 4.406416 2.856165 -0.365567
C 3.579567 1.876316 -0.906530
H 5.199345 -0.900952 0.219009
H 6.659398 0.852226 1.210315
F 6.289853 3.391389 0.928935
H 4.198608 3.911012 -0.503300
H 2.698475 2.183589 -1.465106

TS1.xyz

30

E= -3759.68517695

C -0.492160 0.425269 -0.959135
H -0.079334 0.407866 -1.971145
H -1.926547 0.222497 -0.971131
C -0.034601 1.698819 -0.322925
C -0.748836 2.909057 -0.988771
F -0.590858 2.851548 -2.309874
F -2.075243 2.893971 -0.734402
F -0.263271 4.059042 -0.547880
F 1.294863 1.973614 -0.455011
Cl -0.393100 1.778178 1.454683
I 0.271396 -1.347045 -0.038797
C 4.050156 0.097936 1.631089
C 4.915668 0.019941 0.548637
C 4.503470 -0.431716 -0.698495
C 3.177981 -0.814961 -0.864358
C 2.290890 -0.733765 0.208949
C 2.724470 -0.282614 1.455353
H 4.416447 0.454230 2.587205
H 5.215986 -0.480997 -1.514102
H 2.845101 -1.173231 -1.834140
H 2.035439 -0.216614 2.291647
F 6.187024 0.388044 0.711612
O -1.983877 -2.173015 -0.472026
P -3.318149 -1.405803 -0.211817
O -4.471129 -2.145569 -0.915709
O -3.645371 -1.120047 1.266096
O -3.082883 0.011369 -0.967787
K -3.034629 -2.021142 -3.075344
K -5.449618 -3.013156 1.295710
K -3.633962 1.458214 1.180880

TS2.xyz

32

E= -1186.71854902

C -1.510521 1.589530 1.065884
H -1.862826 1.601047 2.087642
C -0.381548 2.281926 0.738571
C 0.062620 3.475691 1.576208
F -0.611440 4.567560 1.185500
F -0.191564 3.268670 2.866894
F 1.360025 3.720449 1.423091
F 0.040857 2.388622 -0.518806
I -1.317387 -0.325461 0.316046
C -5.262119 0.453347 -1.391769
C -5.781320 -0.825017 -1.546805
C -5.076603 -1.960374 -1.172157
C -3.807377 -1.810027 -0.622104
C -3.279612 -0.531309 -0.470723
C -3.990445 0.601969 -0.848992
H -5.849135 1.312839 -1.695232
H -5.522313 -2.939632 -1.304371
H -3.251866 -2.691720 -0.314971
H -3.564930 1.591664 -0.710070
F -7.002417 -0.967072 -2.069840
O 0.887357 0.792295 1.198518
C 2.107400 0.471240 0.782488
C 2.600854 -0.813266 1.075857
C 3.855654 -1.224291 0.637640
C 4.661239 -0.351217 -0.097478
C 4.181794 0.928276 -0.380167
C 2.927807 1.339267 0.042028
H 1.980928 -1.479463 1.666677
I 4.457373 -3.177682 1.133581
Br 6.392034 -0.818506 -0.740543
H 4.805654 1.609685 -0.948839
H 2.577982 2.335037 -0.197789

TS3-E.xyz

32

E= -1186.73043705

C 0.738268 -0.081880 1.644077
O -0.572259 0.151307 1.513394
C -1.198734 -0.149463 0.314352
C -1.918099 0.860246 -0.301061
C -2.625136 0.580801 -1.472949
C -2.589488 -0.711335 -2.004676
C -1.856198 -1.711228 -1.360134
C -1.157642 -1.442902 -0.193650
H -1.925142 1.851800 0.136088
I -3.691902 2.152501 -2.356185

Br -3.509623 -1.189234 -3.597661

H -1.842002 -2.710894 -1.779169

H -0.575615 -2.194929 0.327777

F 1.045376 -1.973619 1.773973

C 1.073620 0.109947 3.127991

F 2.349123 -0.167145 3.412716

F 0.874911 1.409010 3.414763

F 0.290323 -0.605811 3.921832

C 1.619356 0.201236 0.601444

I 3.070472 -1.276819 0.606907

C 4.597549 -0.109581 -0.286872

C 4.620925 1.265989 -0.077919

C 5.641279 2.024473 -0.641475

C 6.616829 1.384405 -1.393600

C 6.603603 0.013765 -1.608177

C 5.576204 -0.740904 -1.049819

H 3.838337 1.742717 0.505771

H 5.687912 3.098823 -0.502933

F 7.599316 2.113565 -1.934583

H 7.380502 -0.445070 -2.209193

H 5.548732 -1.813091 -1.223809

H 1.201123 0.295376 -0.394333

TS3-Z

43

E= -1417.15465859

C 2.746563 -2.270941 -0.098716

H 2.830413 -3.263027 -0.516702

C 2.653121 -2.073887 1.212084

C 2.736658 -3.251202 2.165628

F 2.908268 -4.408984 1.518167

F 3.749155 -3.094840 3.021709

F 1.603380 -3.332691 2.873222

I 2.520311 -0.872759 -1.621626

C 3.864686 0.527419 -0.701227

O 2.535601 -0.912004 1.889733

C 1.456549 -0.071890 1.662627

C 1.724270 1.287014 1.725231

C 0.685795 2.199100 1.550125

C -0.614560 1.732903 1.325058

C -0.858374 0.360276 1.281523

C 0.172750 -0.554433 1.447705

H 2.742253 1.616434 1.896632

I 1.174306 4.235513 1.616701

Br -2.091045 2.899640 1.079842

H -1.869235 0.002384 1.123657

H -0.031411 -1.619087 1.410799

O 1.151730 -2.553482 -2.265414

C -0.005741 -2.617401 -1.623069

C -0.244942 -3.594364 -0.637005

C -1.437984 -3.614172 0.068467
C -2.434423 -2.666891 -0.178910
C -2.228832 -1.709939 -1.177768
C -1.031728 -1.690187 -1.886491
H 0.520859 -4.335417 -0.430287
H -1.604497 -4.367374 0.831461
Br -4.013498 -2.737508 0.883424
I -3.656824 -0.244944 -1.659138
H -0.869369 -0.952506 -2.665051
C 4.973897 0.147610 0.049644
C 5.796083 1.119121 0.611110
C 5.498703 2.457752 0.391222
C 4.406416 2.856165 -0.365567
C 3.579567 1.876316 -0.906530
H 5.199345 -0.900952 0.219009
H 6.659398 0.852226 1.210315
F 6.289853 3.391389 0.928935
H 4.198608 3.911012 -0.503300
H 2.698475 2.183589 -1.465106

TS4-E.xyz

43

E= -1417.12231046

C -0.053619 0.045017 -0.050007
C -0.021677 0.014868 1.292764
C 0.260245 1.110911 2.270117
F 0.457778 2.295694 1.660800
F -0.730925 1.257734 3.150222
F 1.378626 0.858413 2.991899
I 1.179895 1.355255 -1.265100
C 3.014773 0.642706 -0.523748
O -0.411647 -1.166805 1.910999
C 0.523644 -2.155697 2.080933
C 0.016643 -3.391015 2.475305
C 0.872998 -4.470788 2.674606
C 2.248889 -4.310980 2.474253
C 2.741329 -3.067681 2.084399
C 1.891419 -1.988772 1.883884
H -1.052747 -3.491138 2.620035
I 0.012805 -6.290388 3.259811
Br 3.500266 -5.722999 2.708050
H 3.809068 -2.939297 1.943422
H 2.299581 -1.029615 1.595844
O -1.286122 1.144106 -1.086446
C -2.040066 1.927467 -0.320048
C -2.884170 1.380064 0.659289
C -3.626039 2.210000 1.485488
C -3.561786 3.597178 1.356542
C -2.734809 4.153234 0.375485
C -1.977985 3.324225 -0.445991

H -2.949132 0.302835 0.764901
H -4.268284 1.779954 2.246148
Br -4.619214 4.648974 2.539380
I -2.555741 6.225900 0.078451
H -1.335030 3.751282 -1.208424
C 3.577517 -0.506299 -1.080624
C 4.682428 -1.089816 -0.473246
C 5.192235 -0.510170 0.681609
C 4.650486 0.640428 1.239175
C 3.545012 1.223021 0.629162
H 3.153166 -0.959460 -1.970560
H 5.137869 -1.989692 -0.870593
F 6.230082 -1.092307 1.284835
H 5.078552 1.054450 2.144801
H 3.086192 2.098753 1.074186
H -0.271372 -0.869549 -0.584675

TS4-Z

43

E= -1417.15465859

C 2.746563 -2.270941 -0.098716
H 2.830413 -3.263027 -0.516702
C 2.653121 -2.073887 1.212084
C 2.736658 -3.251202 2.165628
F 2.908268 -4.408984 1.518167
F 3.749155 -3.094840 3.021709
F 1.603380 -3.332691 2.873222
I 2.520311 -0.872759 -1.621626
C 3.864686 0.527419 -0.701227
O 2.535601 -0.912004 1.889733
C 1.456549 -0.071890 1.662627
C 1.724270 1.287014 1.725231
C 0.685795 2.199100 1.550125
C -0.614560 1.732903 1.325058
C -0.858374 0.360276 1.281523
C 0.172750 -0.554433 1.447705
H 2.742253 1.616434 1.896632
I 1.174306 4.235513 1.616701
Br -2.091045 2.899640 1.079842
H -1.869235 0.002384 1.123657
H -0.031411 -1.619087 1.410799
O 1.151730 -2.553482 -2.265414
C -0.005741 -2.617401 -1.623069
C -0.244942 -3.594364 -0.637005
C -1.437984 -3.614172 0.068467
C -2.434423 -2.666891 -0.178910
C -2.228832 -1.709939 -1.177768
C -1.031728 -1.690187 -1.886491
H 0.520859 -4.335417 -0.430287

H -1.604497 -4.367374 0.831461
Br -4.013498 -2.737508 0.883424
I -3.656824 -0.244944 -1.659138
H -0.869369 -0.952506 -2.665051
C 4.973897 0.147610 0.049644
C 5.796083 1.119121 0.611110
C 5.498703 2.457752 0.391222
C 4.406416 2.856165 -0.365567
C 3.579567 1.876316 -0.906530
H 5.199345 -0.900952 0.219009
H 6.659398 0.852226 1.210315
F 6.289853 3.391389 0.928935
H 4.198608 3.911012 -0.503300
H 2.698475 2.183589 -1.465106

Product 3a, E isomer

31
E= -1074.92918622
C -1.368290 -0.612410 1.152537
O -1.247889 -0.686932 -0.215324
C -1.408666 0.501267 -0.898192
C -2.459518 1.371318 -0.614667
C -0.486869 0.796749 -1.890770
C -0.595270 1.991224 -2.607344
C -1.626900 2.885356 -2.308801
C -2.555522 2.562431 -1.316556
C -2.435160 -1.532350 1.677959
F -2.478842 -1.557984 3.009020
C -0.602984 0.230472 1.844485
O -0.658566 0.400861 3.189103
C -0.732834 1.703372 3.616325
C -0.361231 1.962883 4.932172
C -0.436114 3.260884 5.409587
C -0.869470 4.306537 4.588541
C -1.244970 4.035641 3.272124
C -1.184346 2.726769 2.790328
Br -1.835939 4.551354 -3.196392
H 0.315175 0.095535 -2.089462
Br -0.920660 6.053284 5.333007
H -1.504023 2.515472 1.776215
F -2.241118 -2.780071 1.236937
F -3.643781 -1.135586 1.231293
H -3.362554 3.252734 -1.098721
H -3.190753 1.117473 0.144528
I 0.850902 2.367496 -4.074885
H 0.112549 0.857354 1.313385
H -0.018308 1.150660 5.562964
H -0.148225 3.476420 6.432264
I -1.911968 5.503924 1.932755

Product 3a, Z isomer

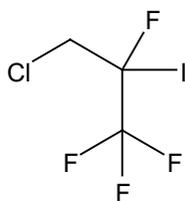
31
E= -1074.93536638
C -0.361993 2.887828 -0.124597
O -1.451808 2.485495 0.594362
C -2.359430 1.636336 0.005391
C -2.591402 1.600265 -1.364719
C -3.077497 0.822375 0.871770
C -4.039540 -0.051424 0.369523
C -4.272541 -0.106322 -1.008600
C -3.545651 0.723812 -1.861285
C -0.331348 4.359814 -0.405939
F 0.811761 4.718160 -1.011744
C 0.601797 2.062102 -0.533190
O 0.472469 0.729757 -0.349713
C 1.603109 -0.047153 -0.340690
C 1.468409 -1.351023 -0.806106
C 2.571784 -2.187821 -0.793713
C 3.808518 -1.735353 -0.326055
C 3.930963 -0.427839 0.149394
C 2.817595 0.416389 0.148624
Br -5.550039 -1.275833 -1.791969
H -2.869071 0.877334 1.933628
Br 5.263740 -2.955603 -0.364309
H 2.898136 1.419539 0.552466
F -0.448636 5.074748 0.717118
F -1.349736 4.713637 -1.210563
H -3.736924 0.686226 -2.927755
H -2.044135 2.251673 -2.036038
I -5.065949 -1.249835 1.749168
H 1.472228 2.414380 -1.077322
H 0.506440 -1.691587 -1.172067
H 2.482361 -3.205287 -1.156747
I 5.724053 0.350152 0.903078

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13. NMR spectra

¹H NMR (400 MHz, DMSO-*d*₆)

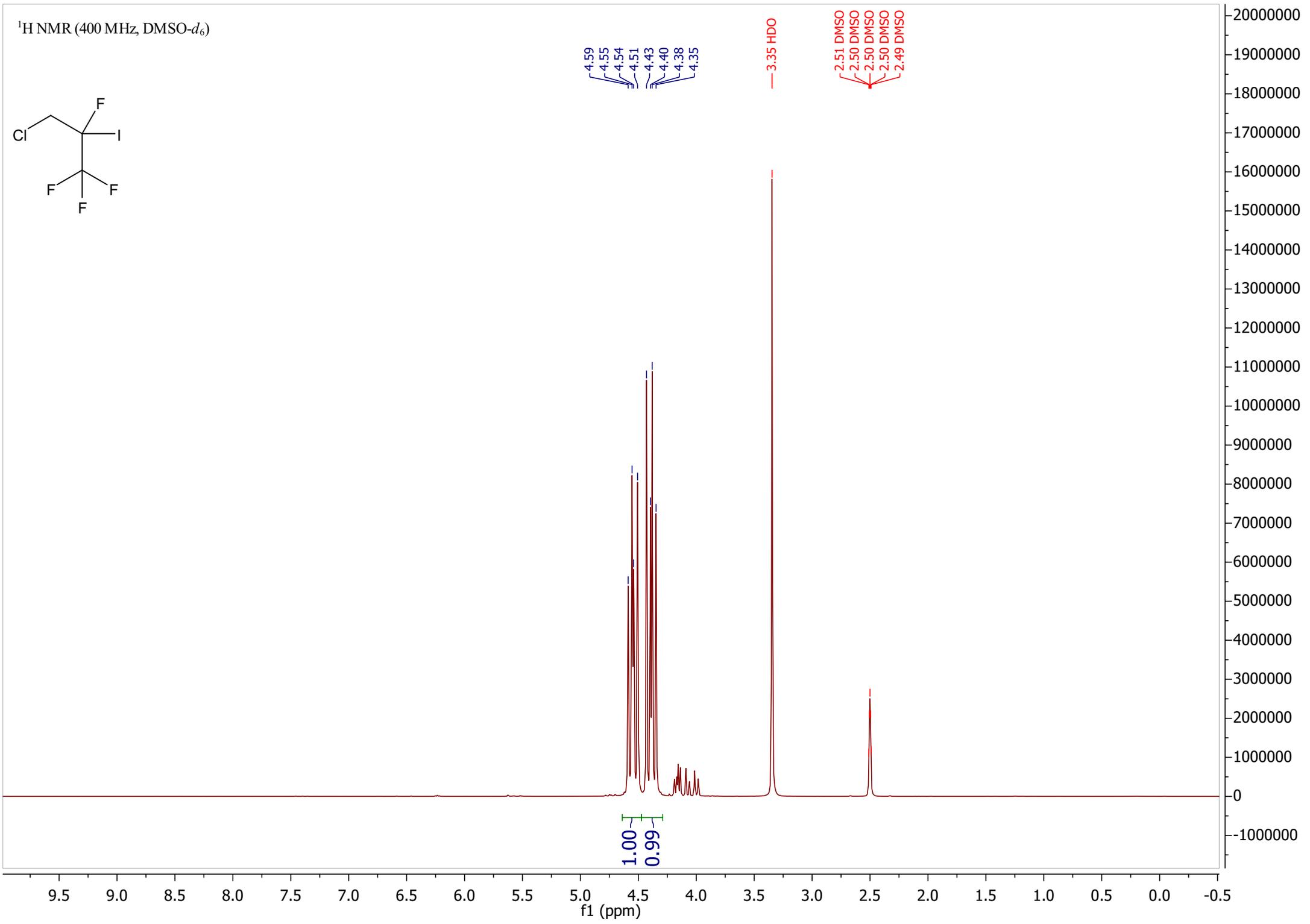


4.59
4.55
4.54
4.51
4.43
4.40
4.38
4.35

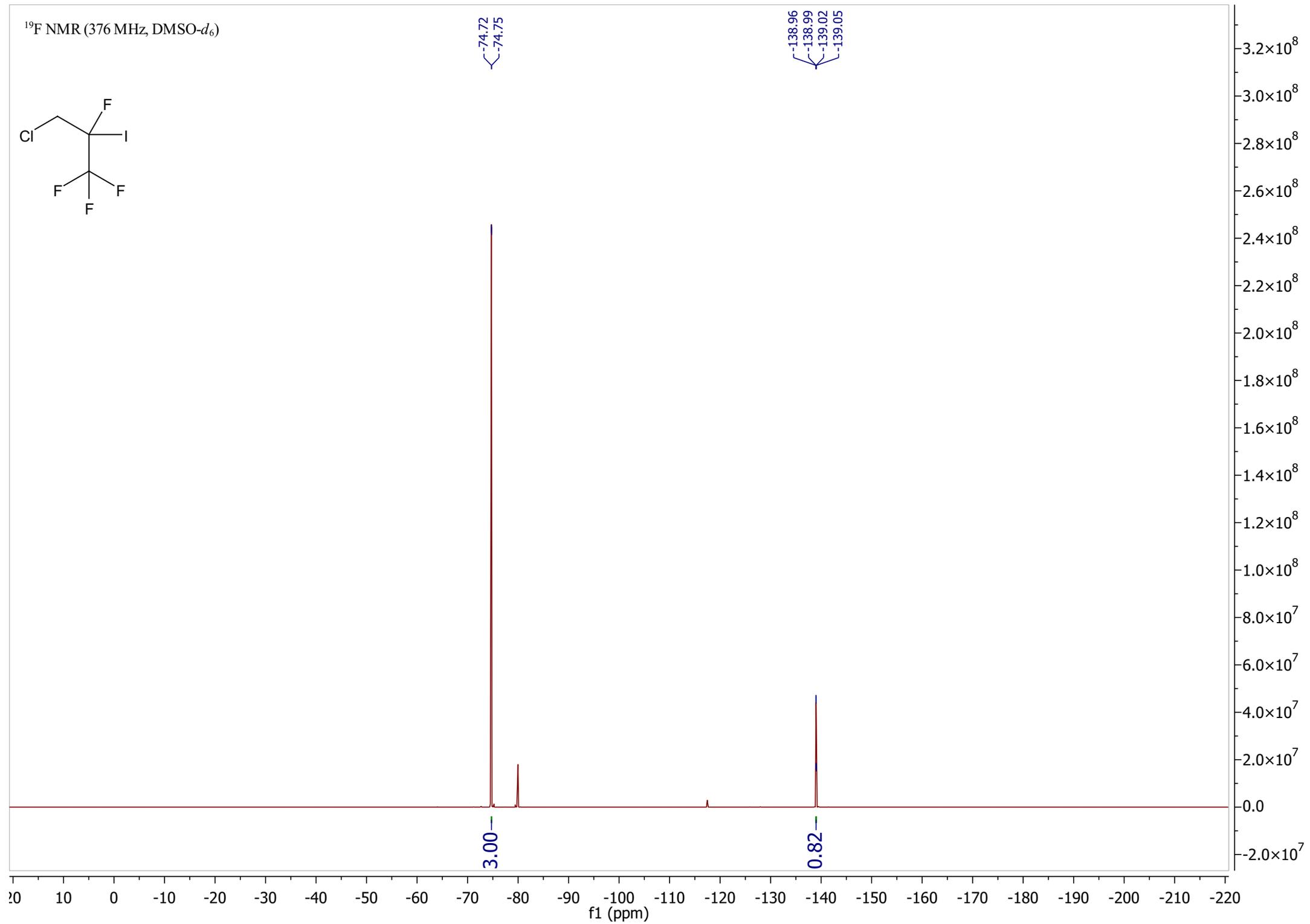
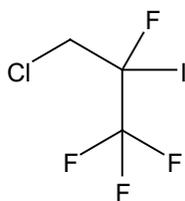
3.35 H₂O

2.51 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO

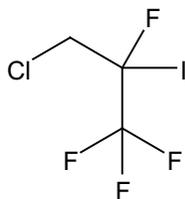
1.00
0.99



^{19}F NMR (376 MHz, $\text{DMSO-}d_6$)



¹³C NMR (101 MHz, DMSO-*d*₆)



125.84
125.55
123.03
122.74
120.21
119.92
117.40
117.11

79.90
79.56
79.22
78.88
77.36
77.02
76.68
76.34

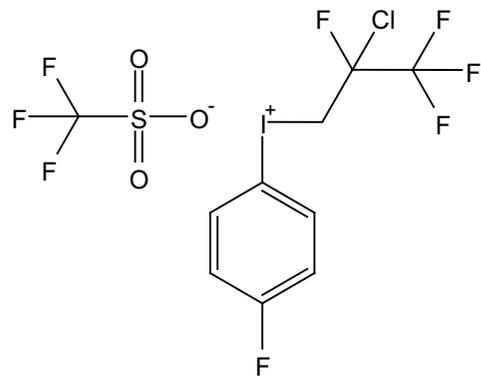
48.49
48.27
40.15 DMSO
39.99 DMSO
39.94 DMSO
39.78 DMSO
39.73 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
38.90 DMSO

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0

¹H NMR (400 MHz, Acetonitrile-*d*₃)



8.23
8.22
8.21
8.20

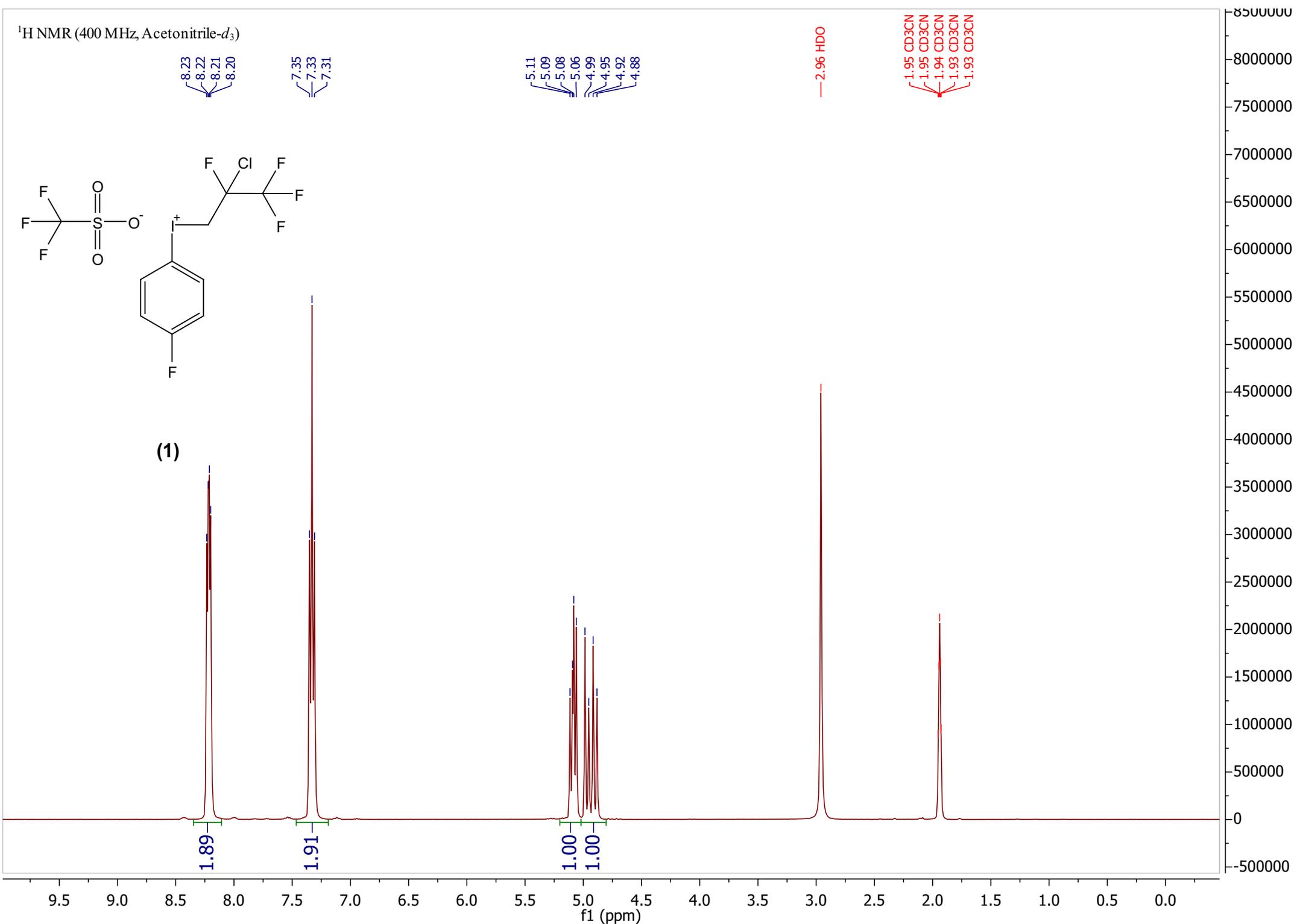
7.35
7.33
7.31

5.11
5.09
5.08
5.06
4.99
4.95
4.92
4.88

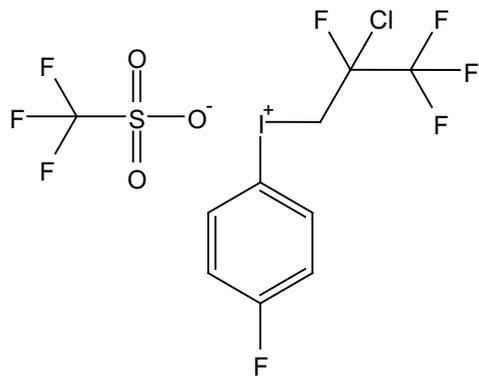
2.96 HDO

1.95 CD3CN
1.95 CD3CN
1.94 CD3CN
1.93 CD3CN
1.93 CD3CN

(1)



^{19}F NMR (376 MHz, Acetonitrile- d_3)



-79.32
-80.93
-80.95

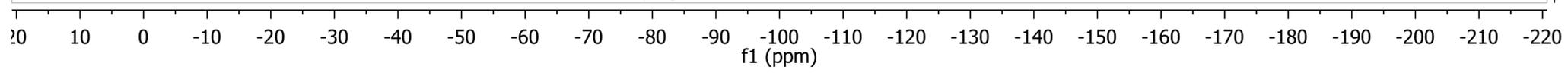
-104.91

-118.32
-118.33
-118.35
-118.37

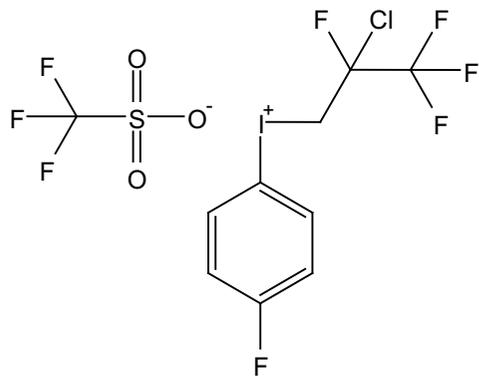
2.98
3.02

1.02

1.00



¹³C NMR (101 MHz, Acetonitrile-*d*₃)

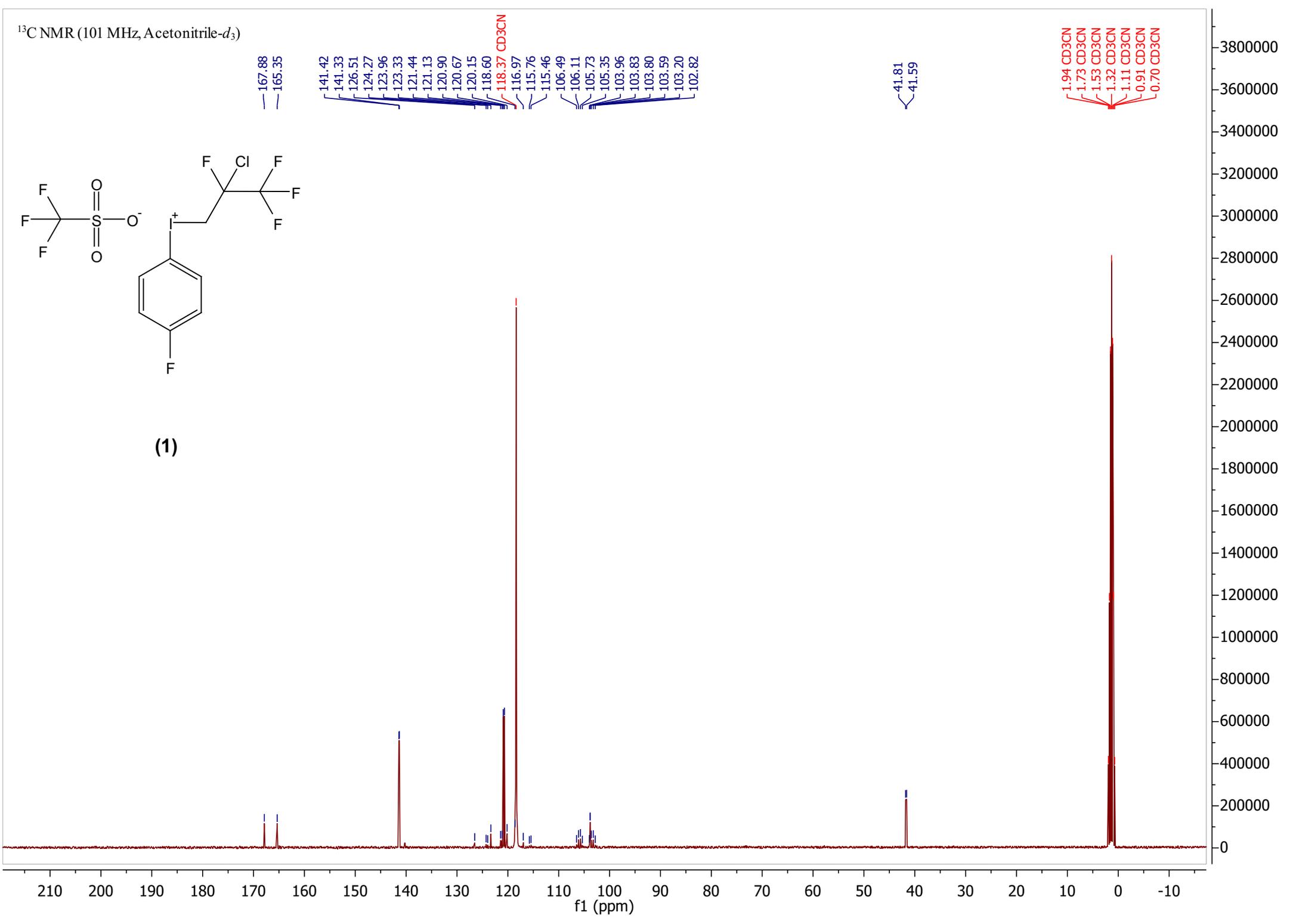


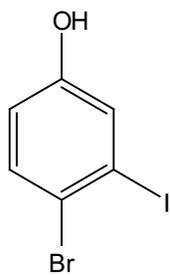
167.88
165.35

141.42
141.33
126.51
124.27
123.96
123.33
121.44
121.13
120.90
120.67
120.15
118.60
118.37 CD3CN
116.97
115.76
115.46
106.49
106.11
105.73
105.35
103.96
103.83
103.80
103.59
103.20
102.82

41.81
41.59

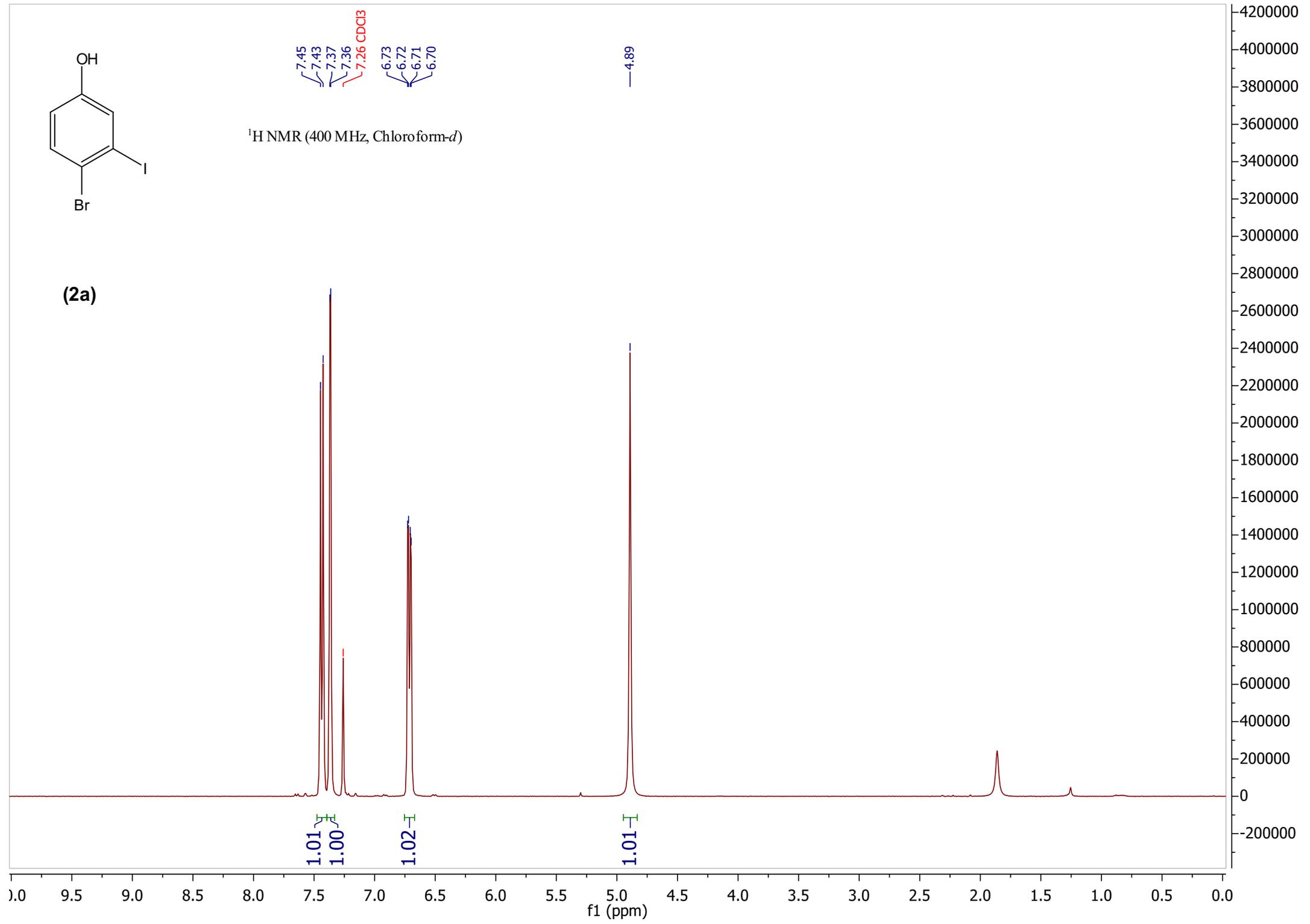
1.94 CD3CN
1.73 CD3CN
1.53 CD3CN
1.32 CD3CN
1.11 CD3CN
0.91 CD3CN
0.70 CD3CN

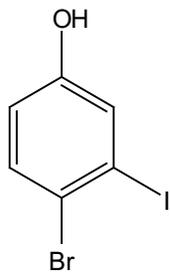




(2a)

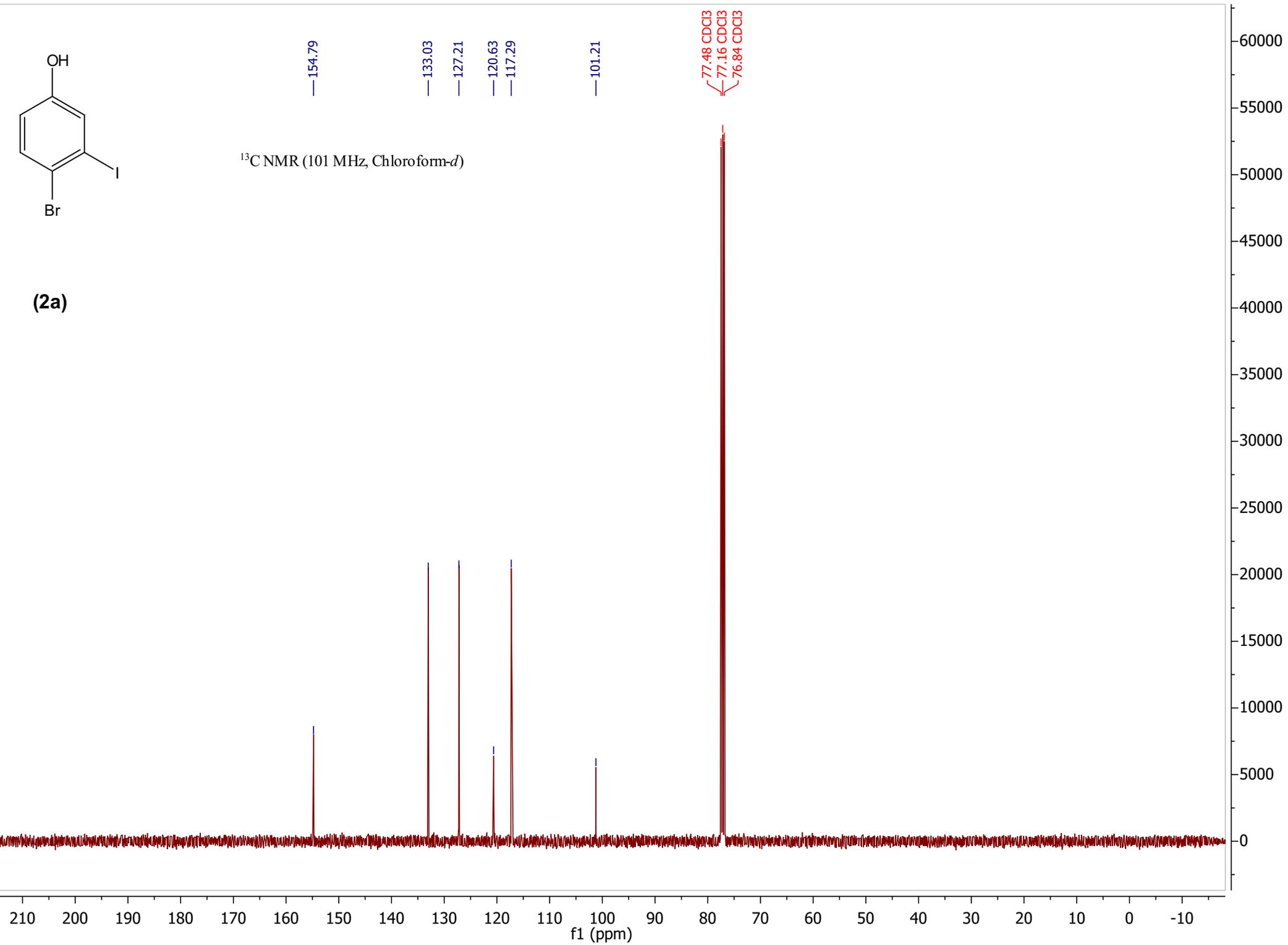
¹H NMR (400 MHz, Chloroform-*d*)

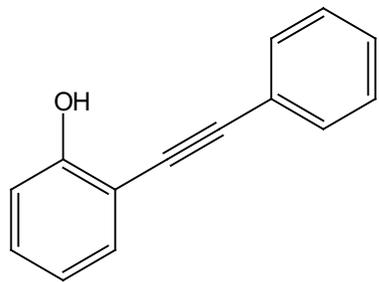




(2a)

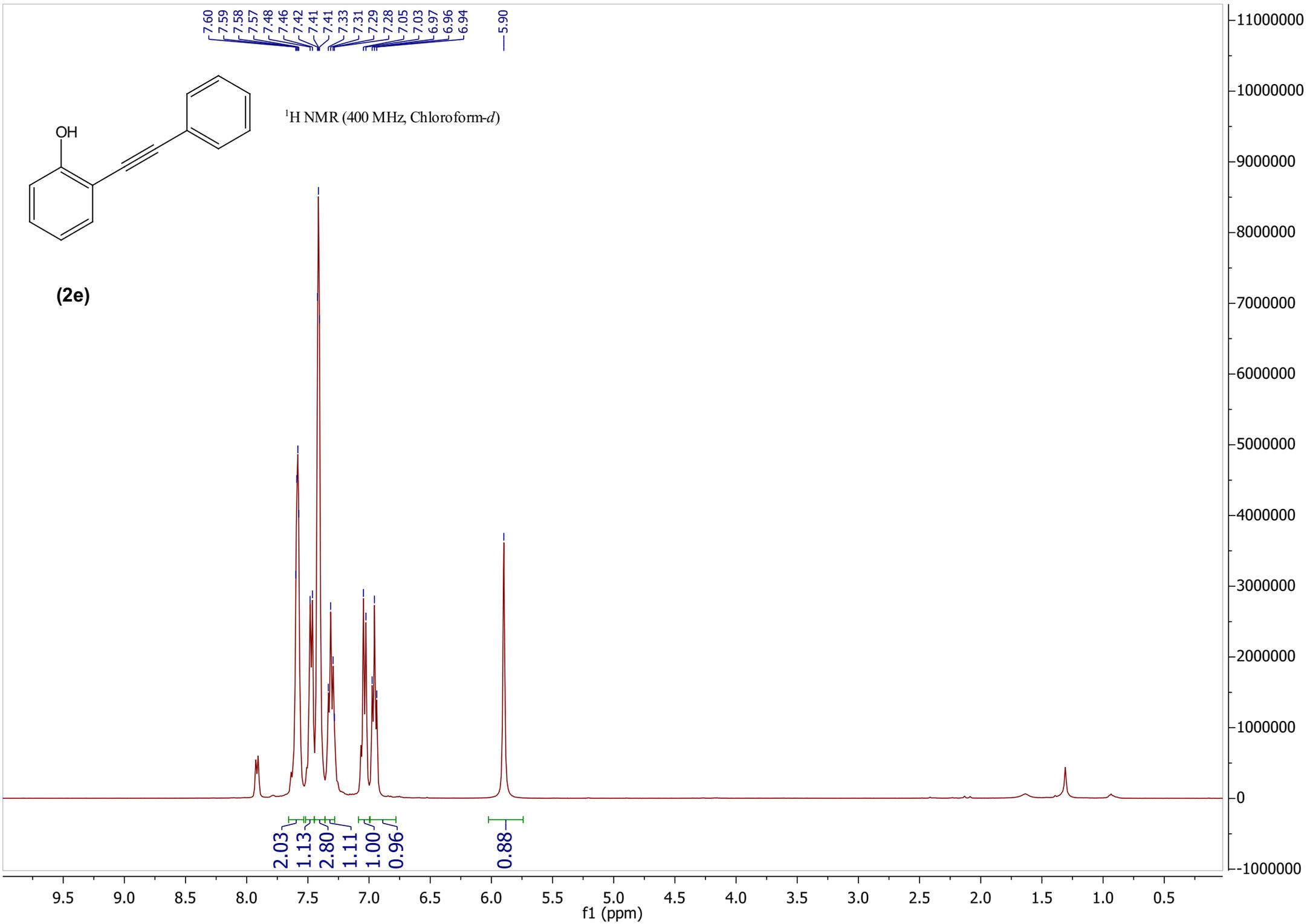
^{13}C NMR (101 MHz, Chloroform-*d*)

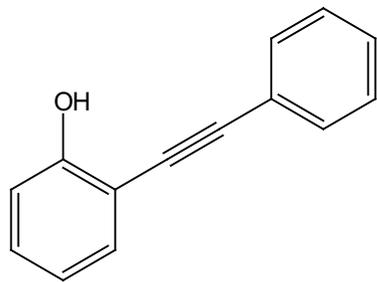




(2e)

¹H NMR (400 MHz, Chloroform-*d*)





(2e)

^{13}C NMR (101 MHz, Chloroform-*d*)

156.63

131.80

131.74

130.63

128.96

128.63

122.51

120.57

114.87

109.71

96.51

83.15

77.48 CDCl₃

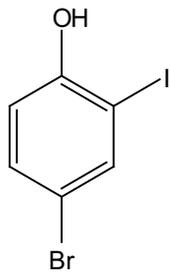
77.16 CDCl₃

76.84 CDCl₃

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

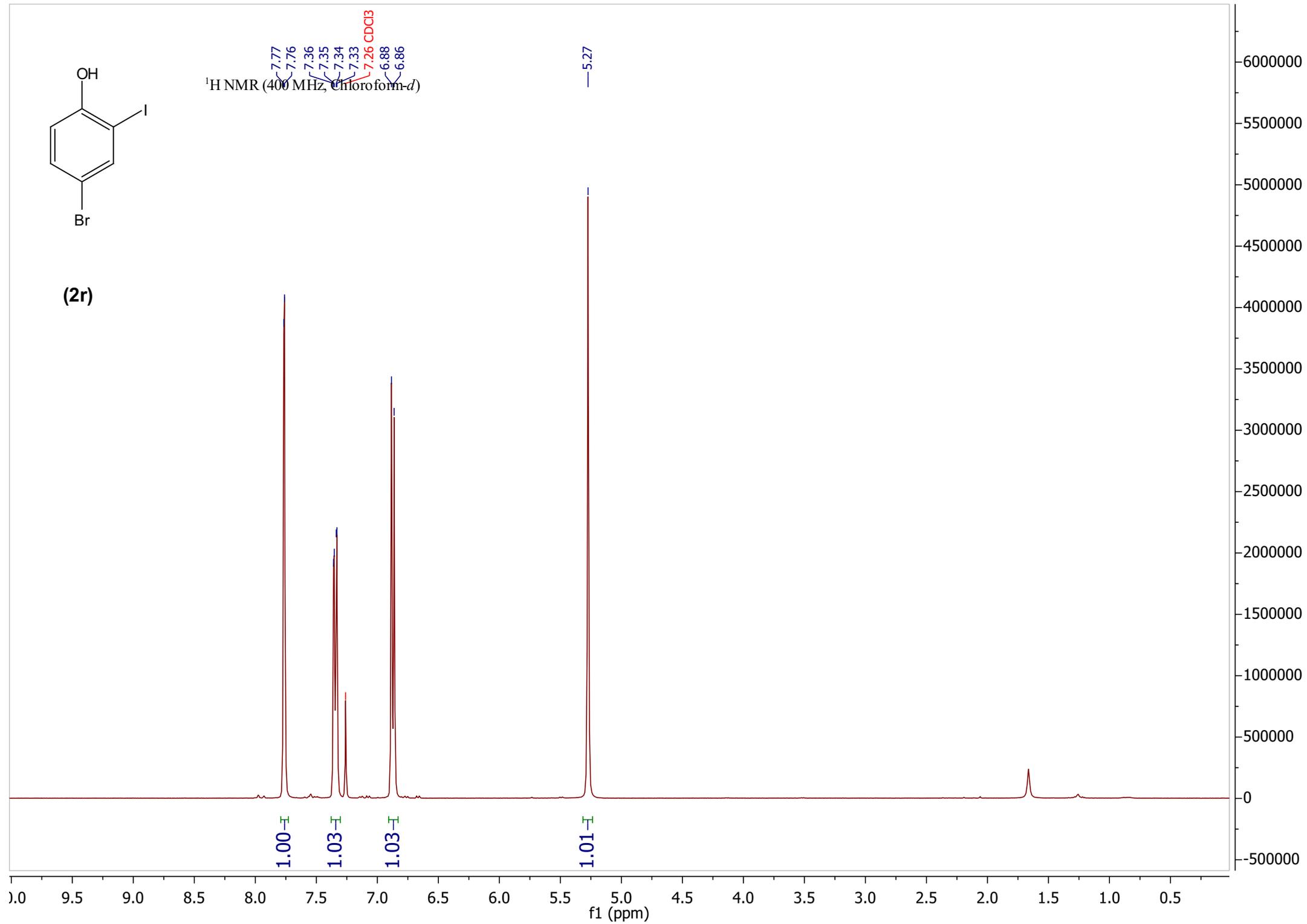
f1 (ppm)

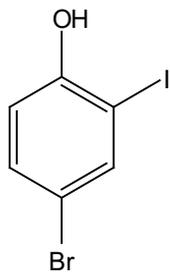
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
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90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000



(2r)

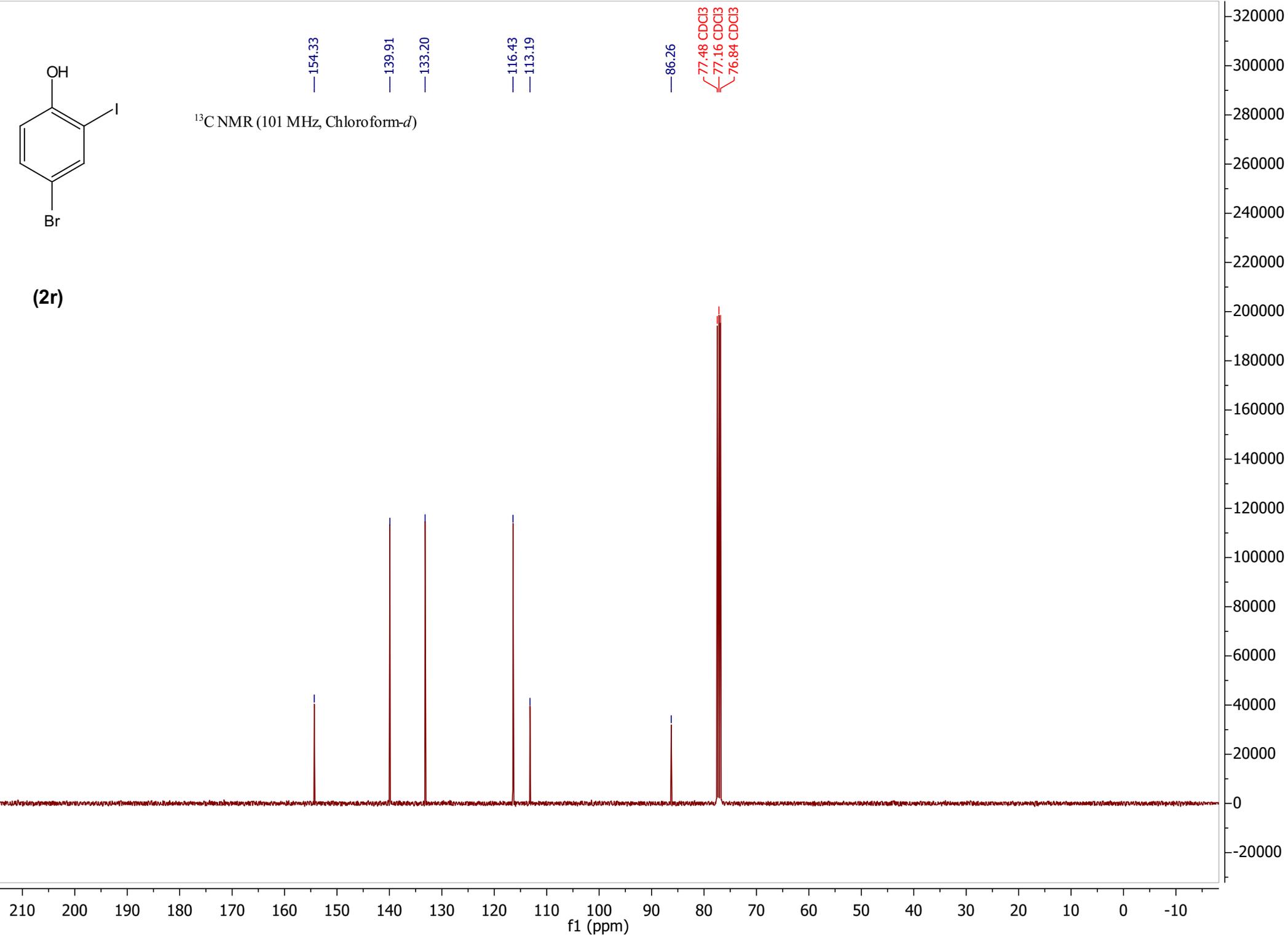
¹H NMR (400 MHz, Chloroform-*d*)

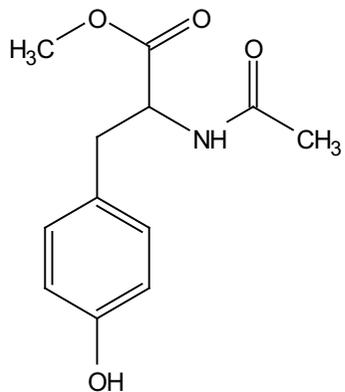




(2r)

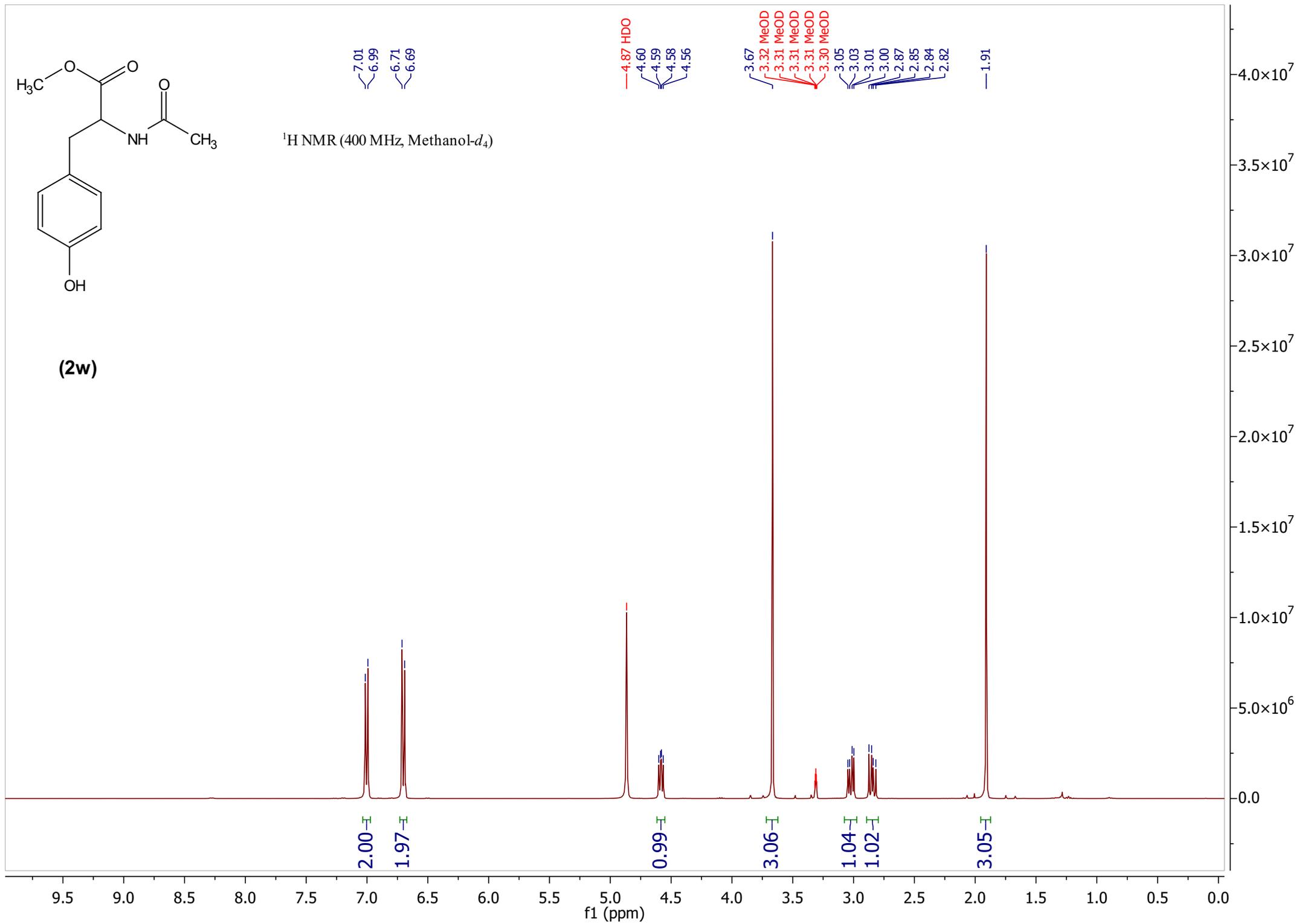
^{13}C NMR (101 MHz, Chloroform-*d*)

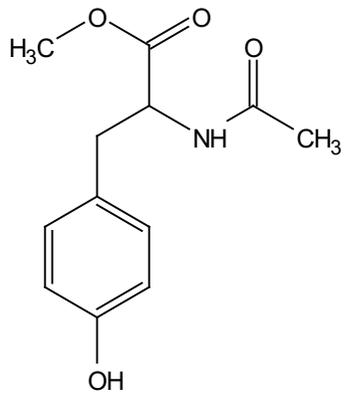




(2w)

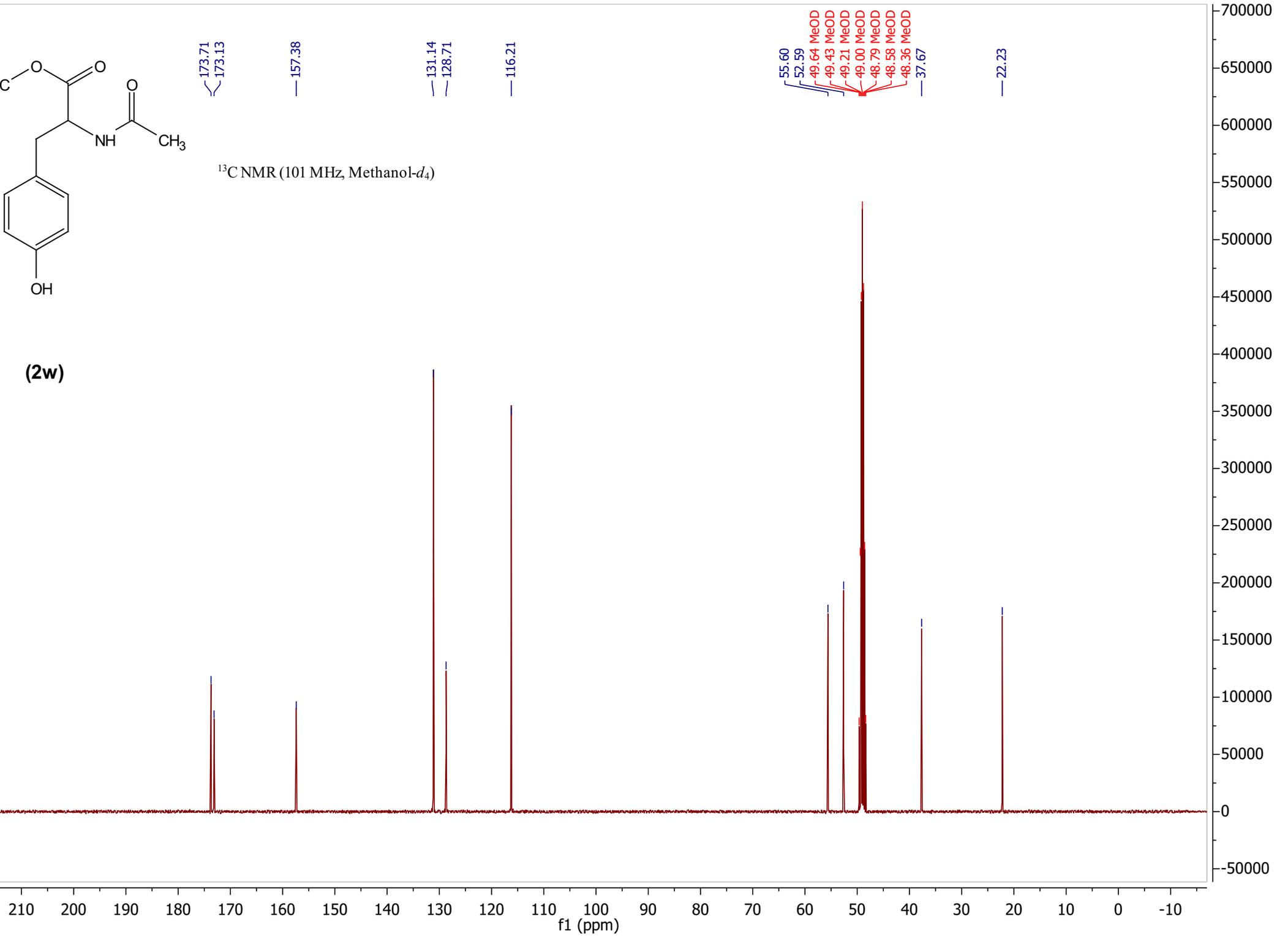
¹H NMR (400 MHz, Methanol-*d*₄)

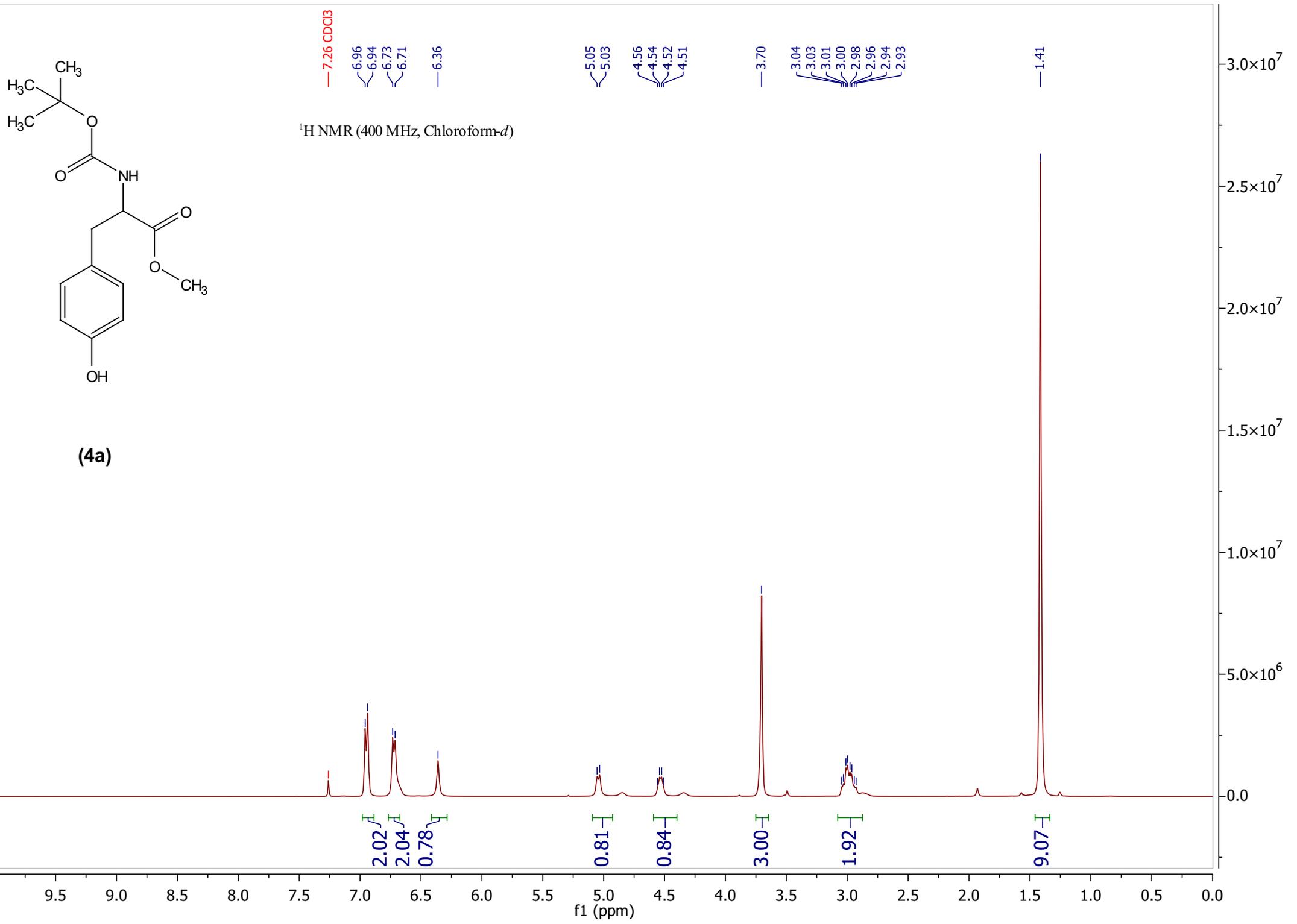


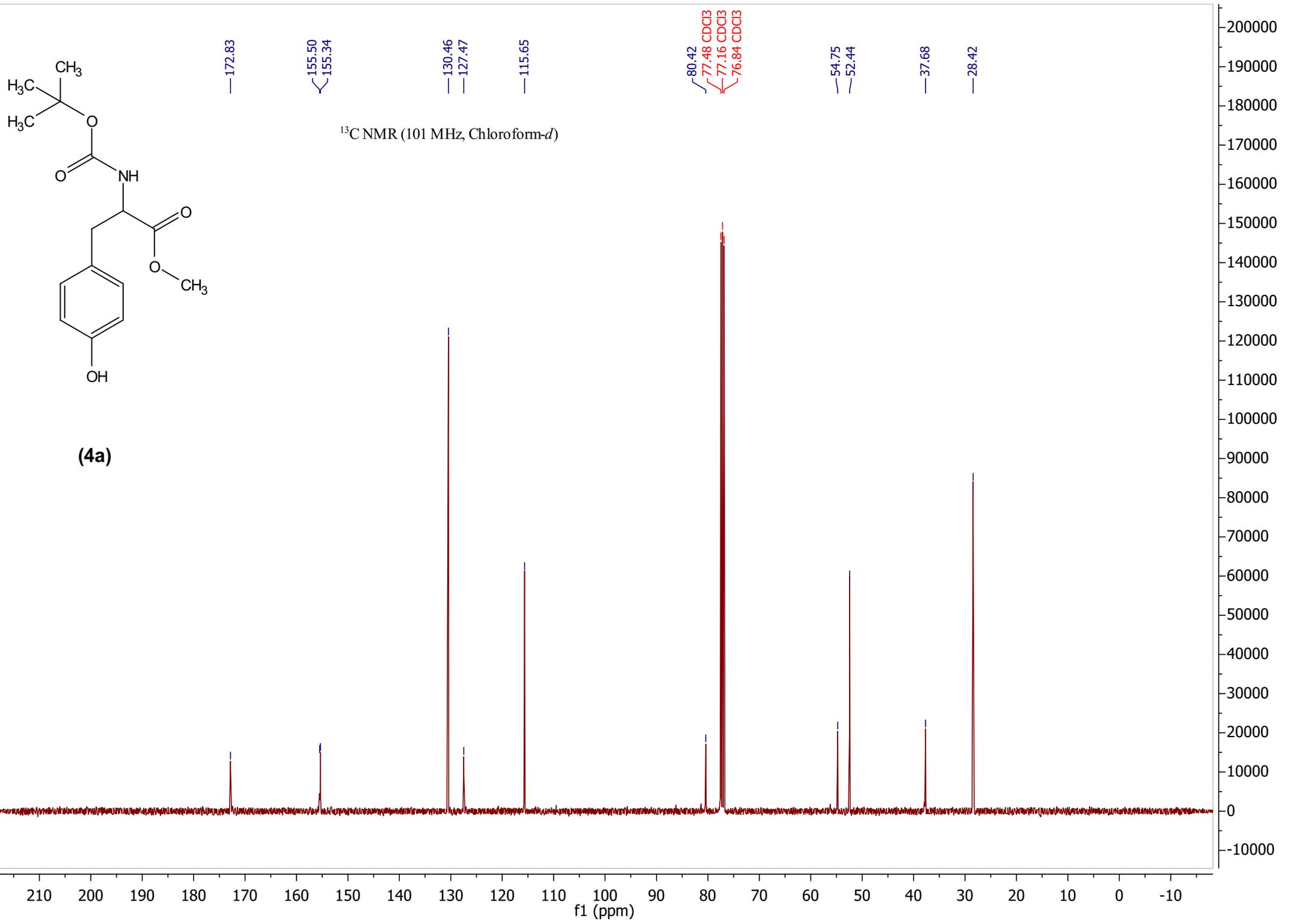


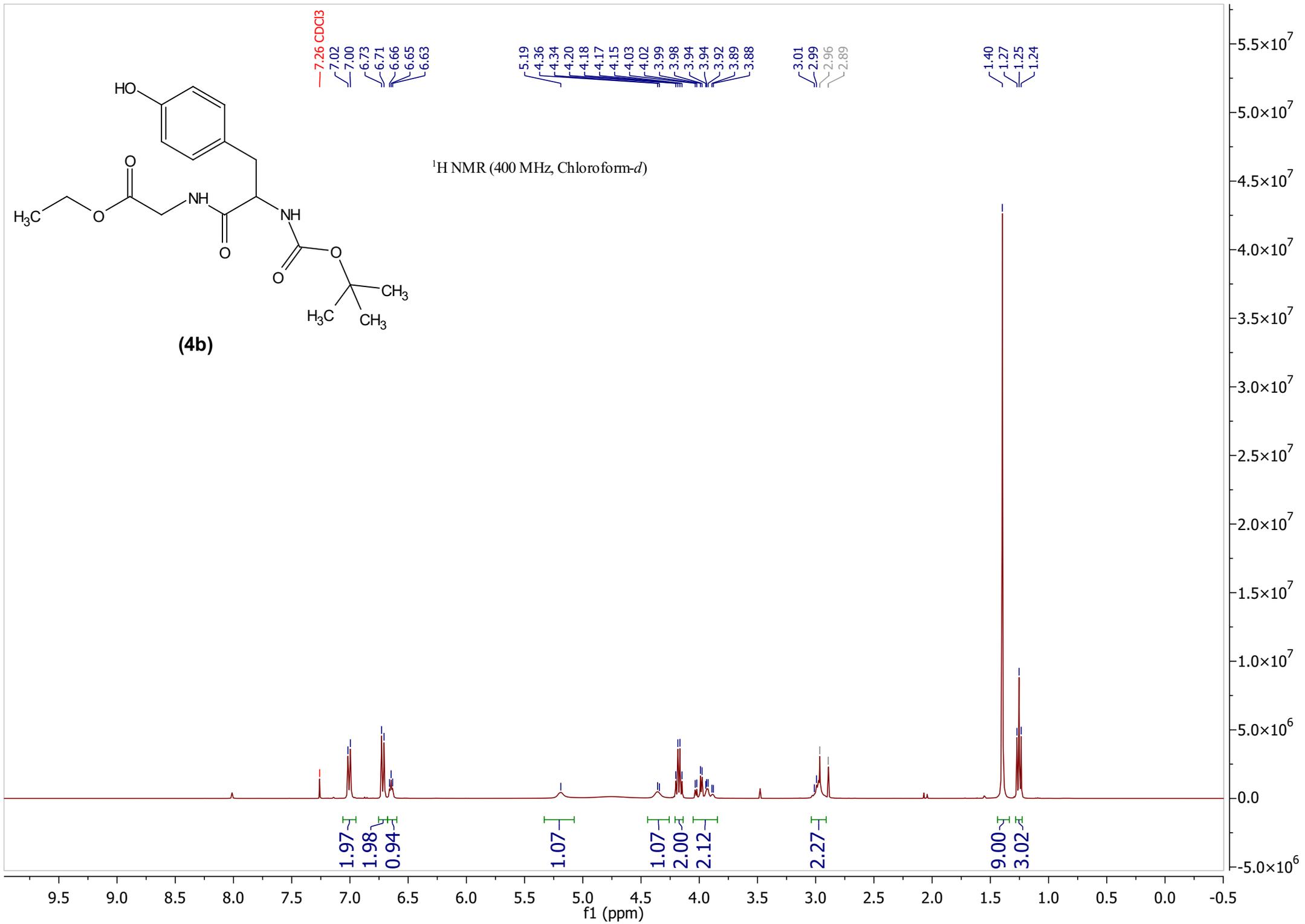
(2w)

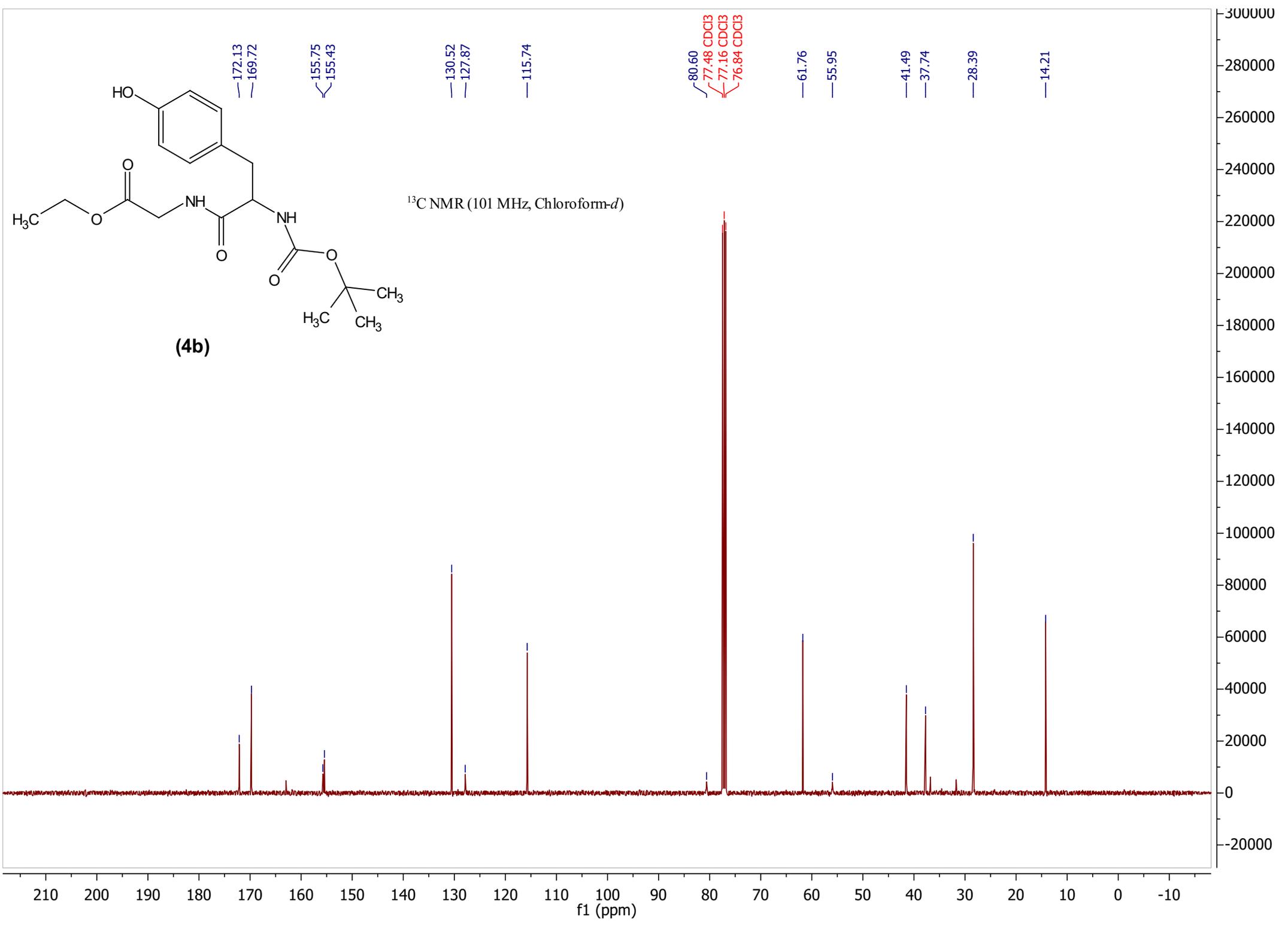
¹³C NMR (101 MHz, Methanol-*d*₄)

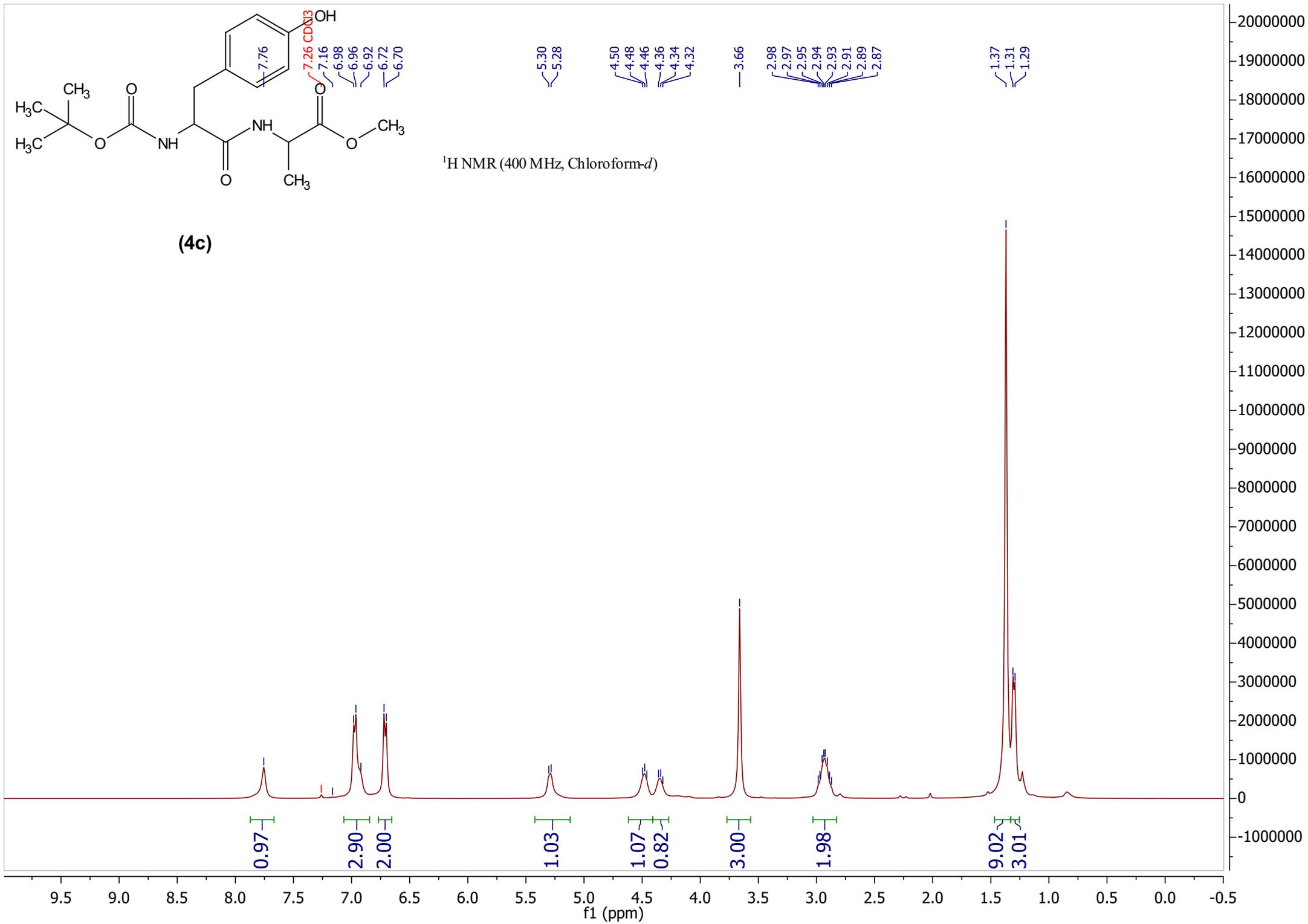


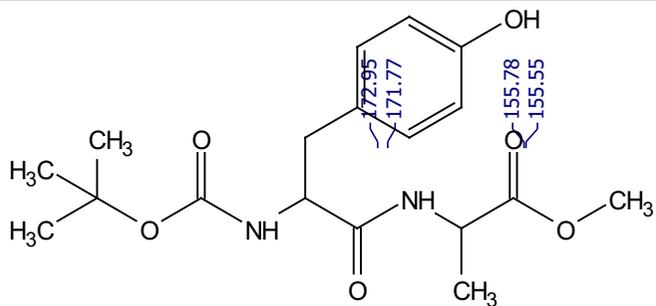






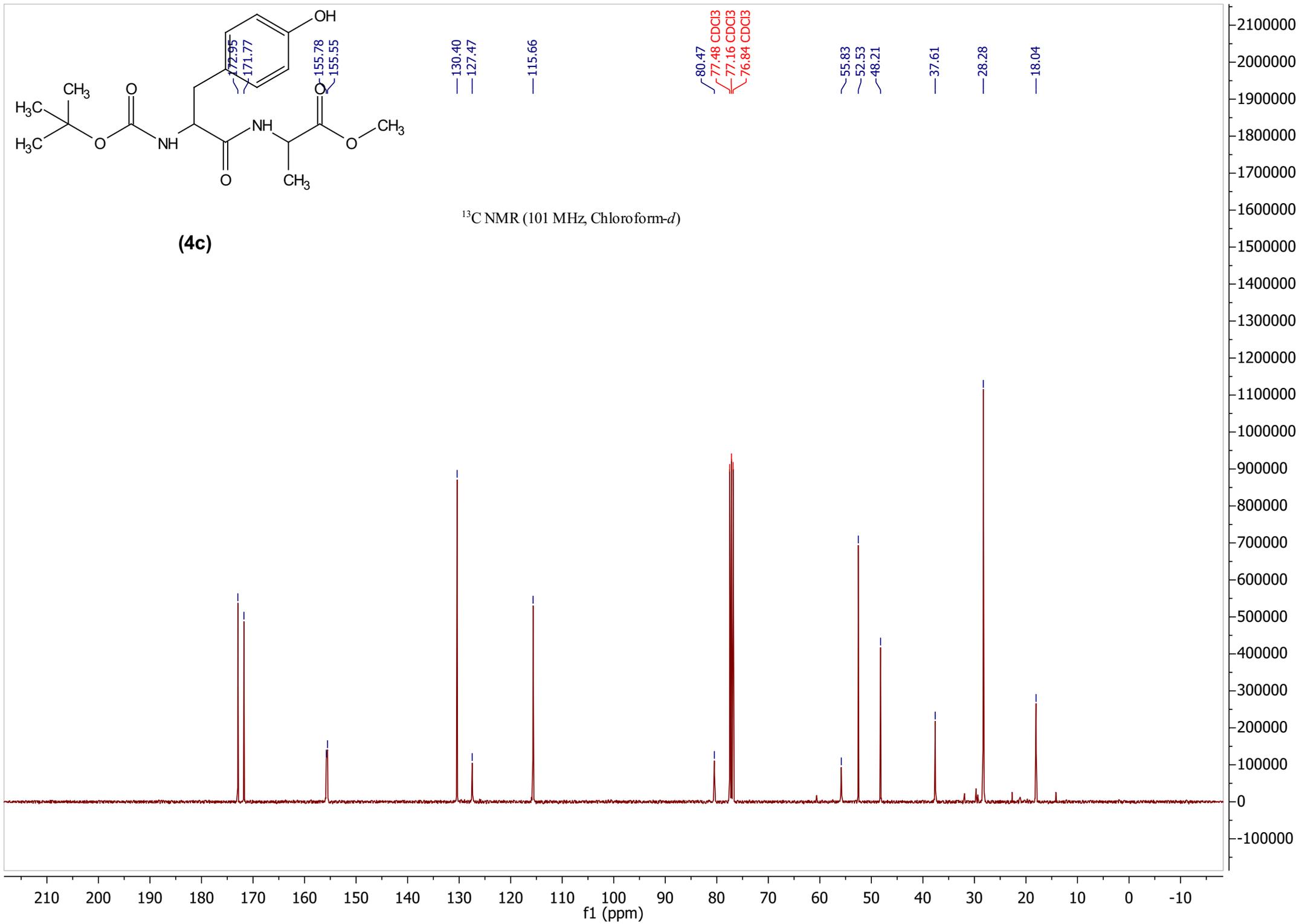


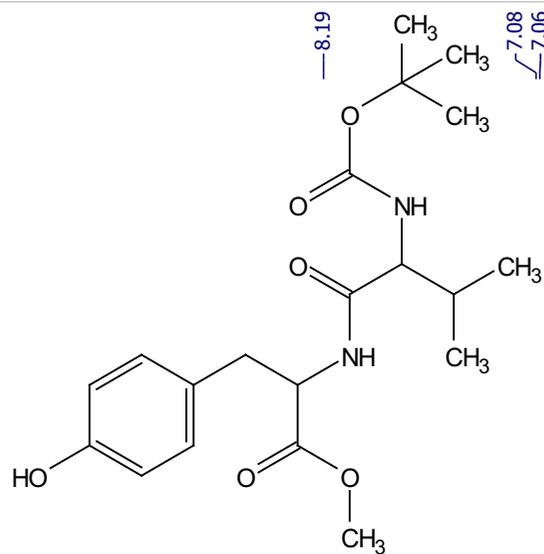




(4c)

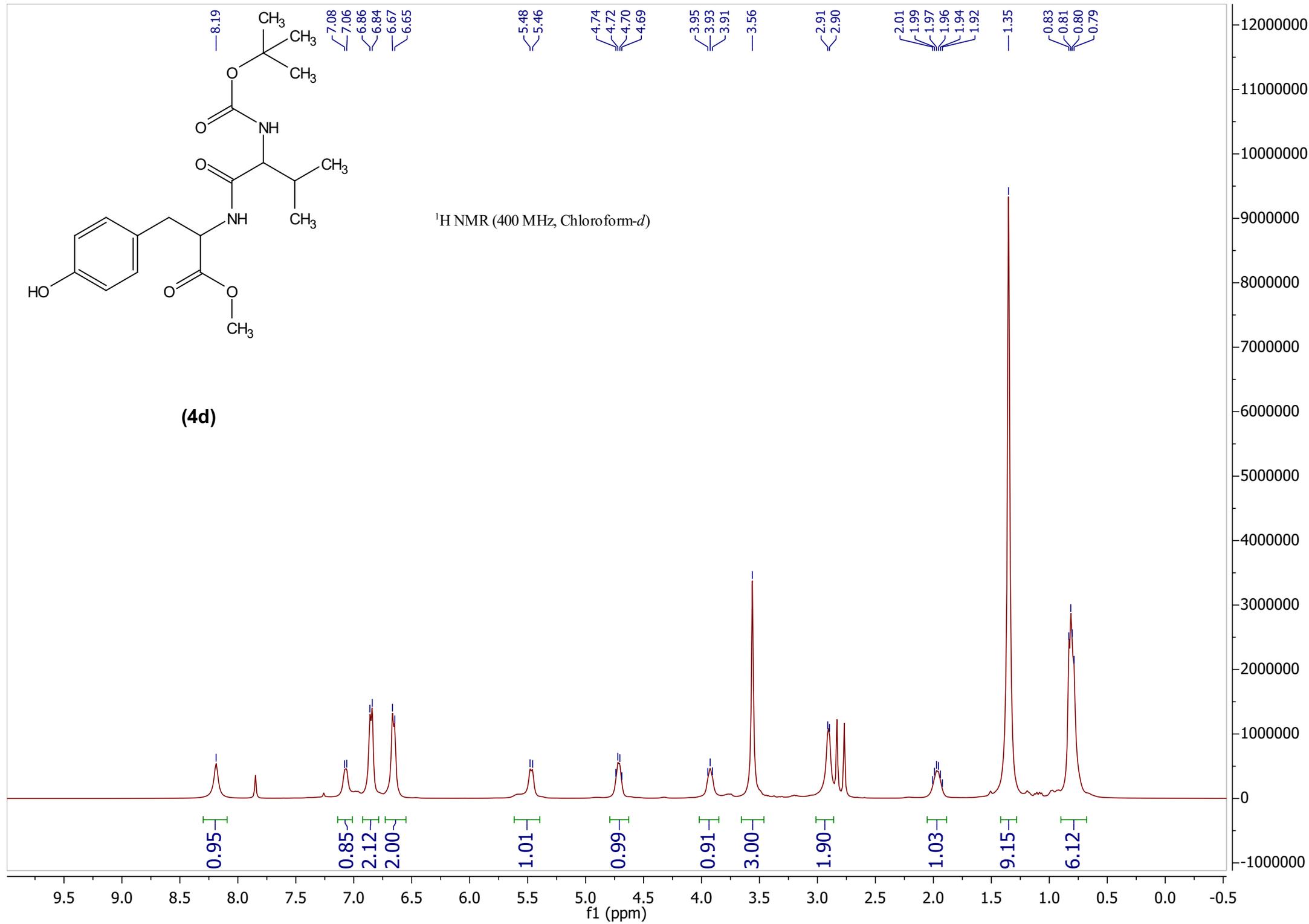
¹³C NMR (101 MHz, Chloroform-*d*)

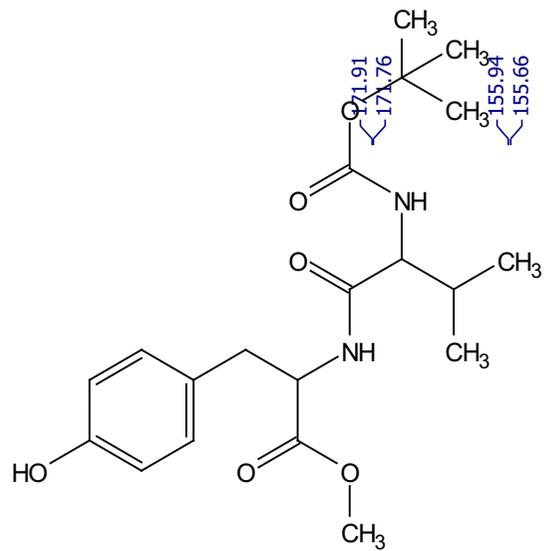




(4d)

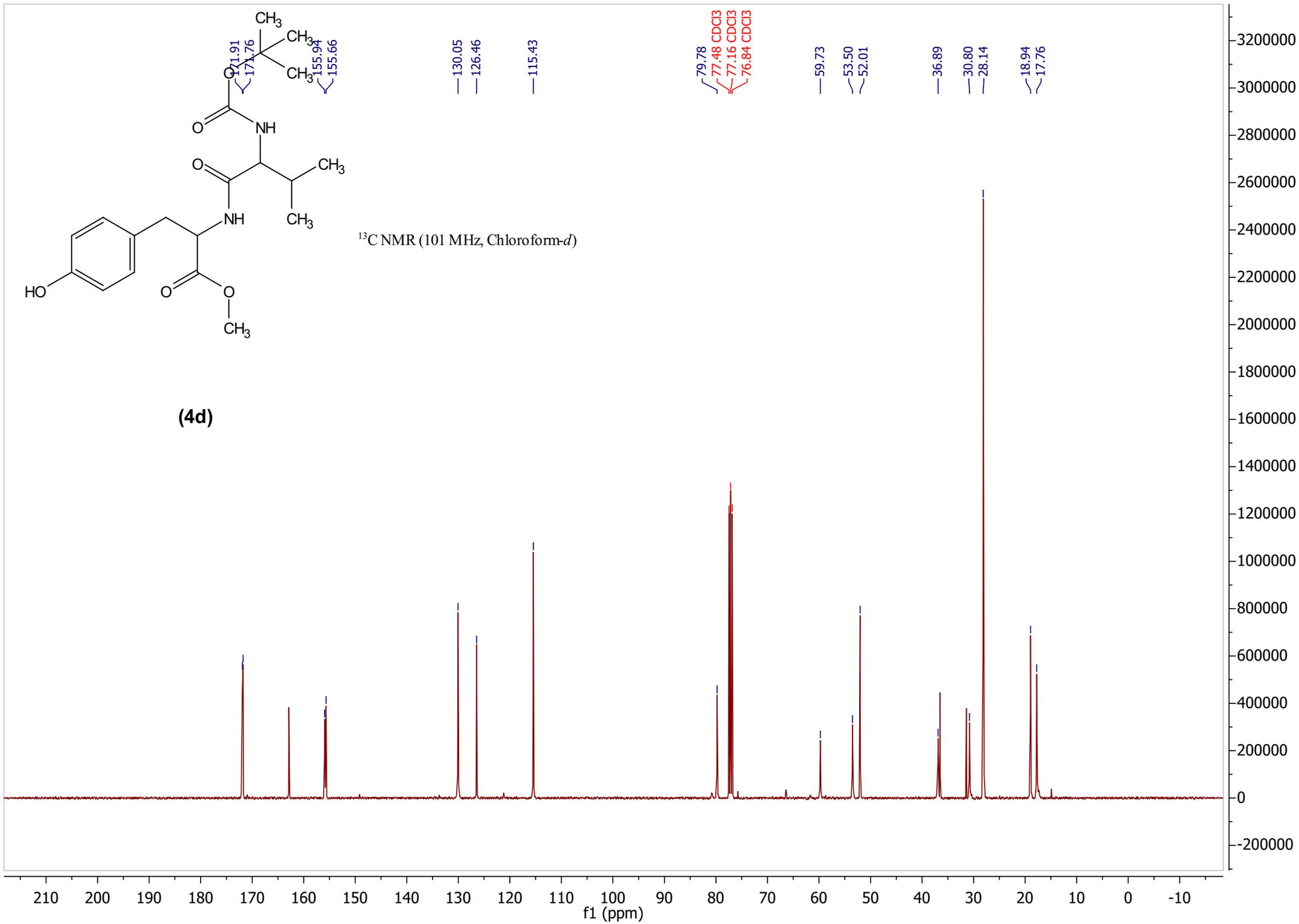
¹H NMR (400 MHz, Chloroform-*d*)

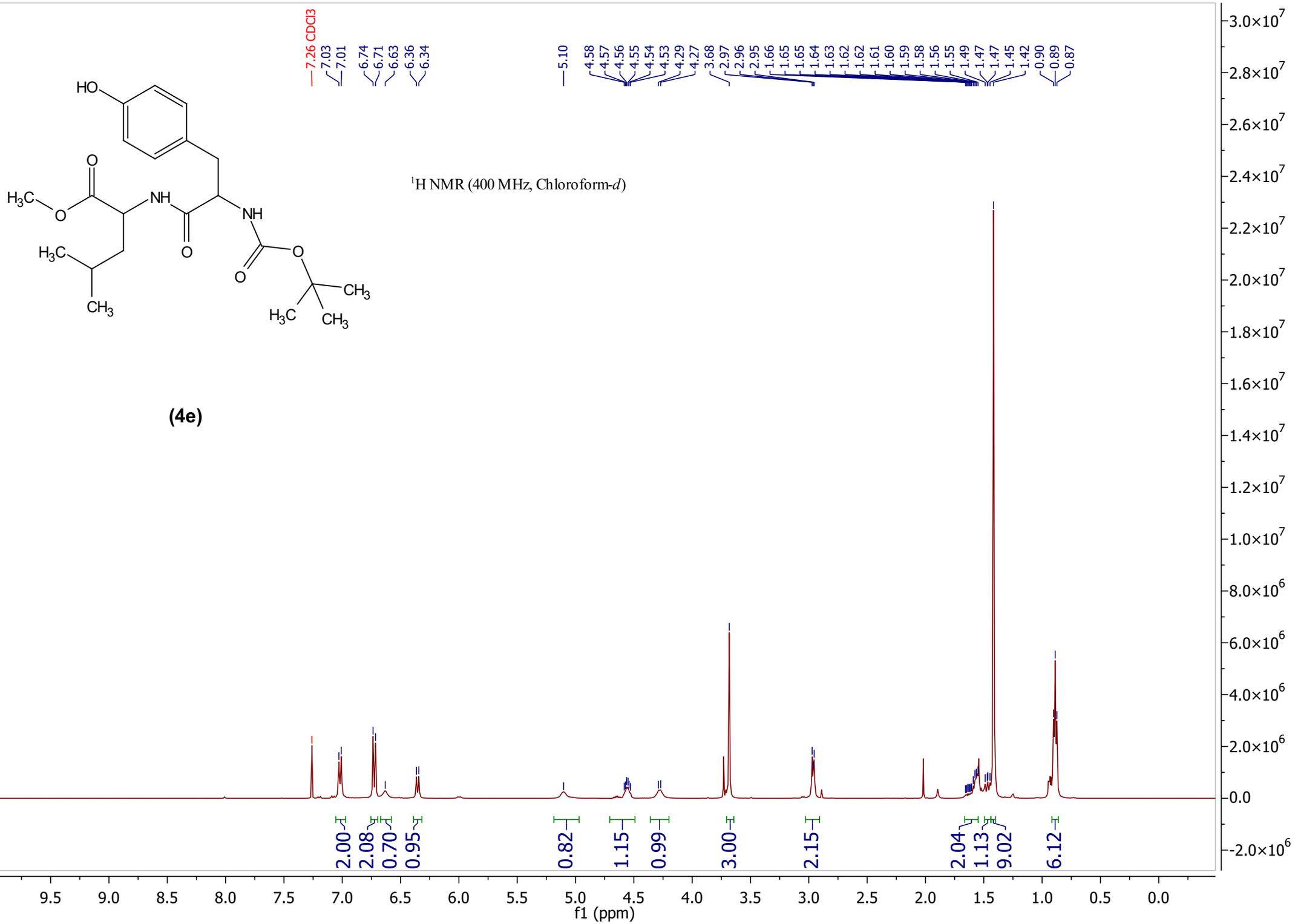


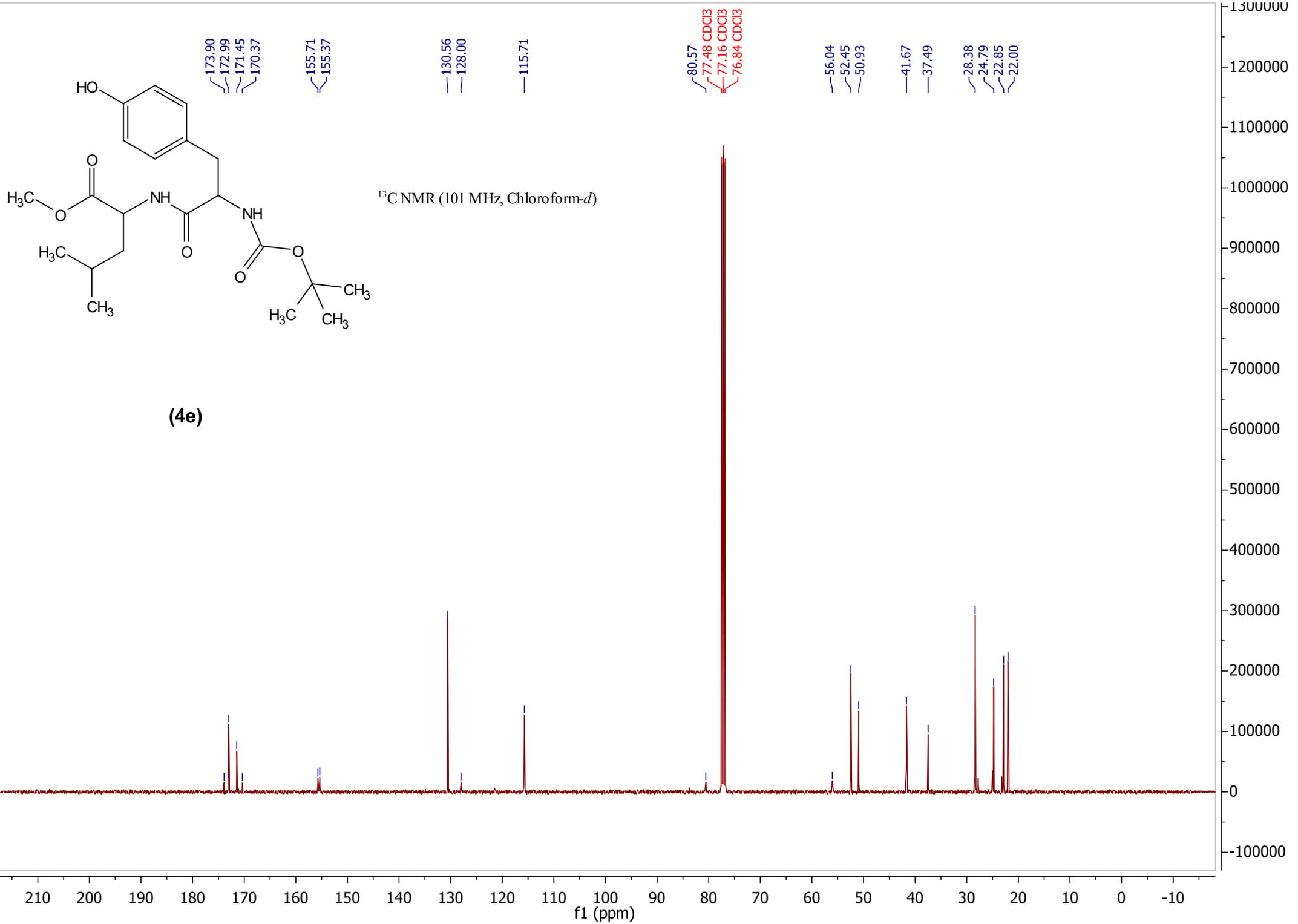


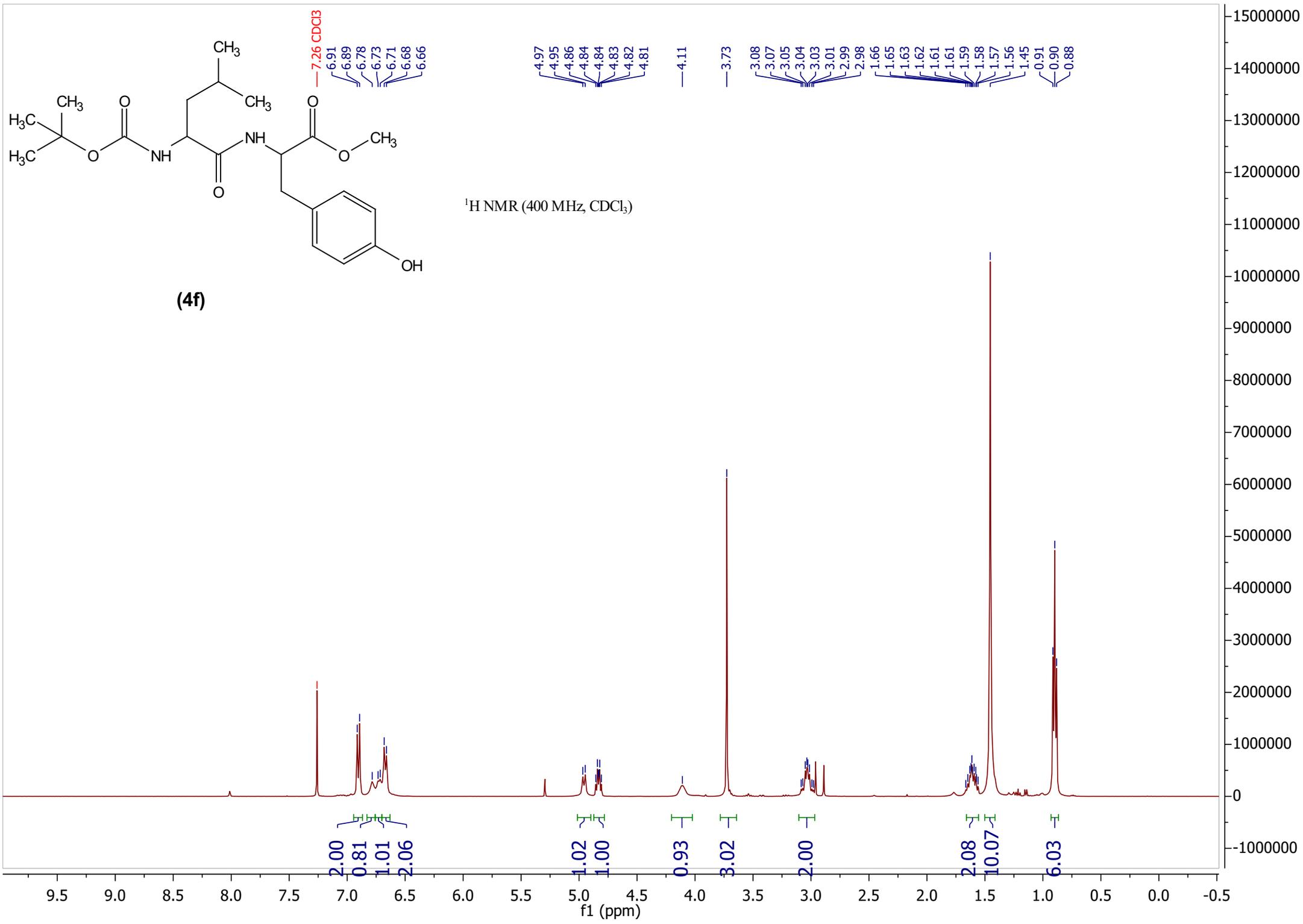
(4d)

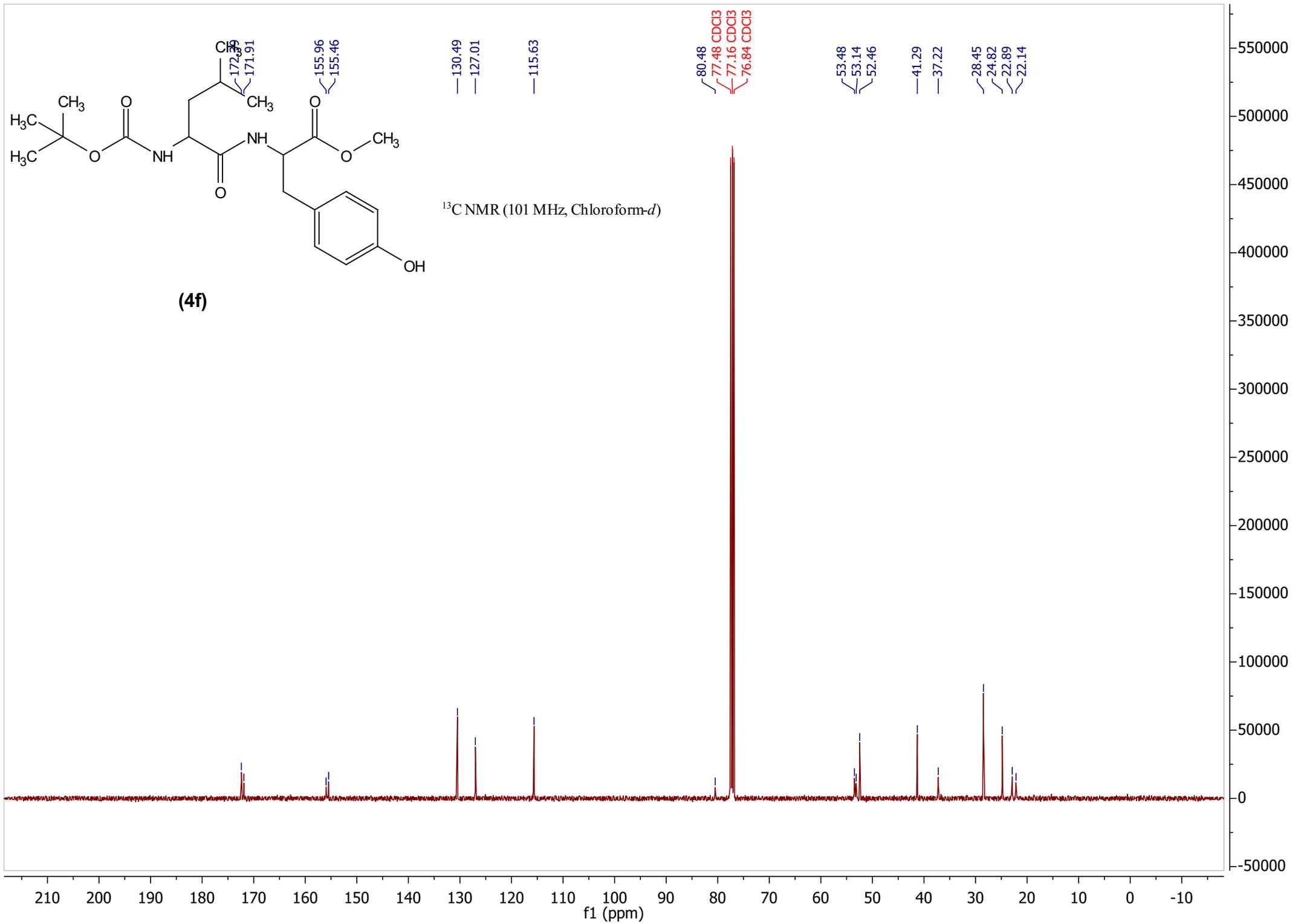
¹³C NMR (101 MHz, Chloroform-*d*)

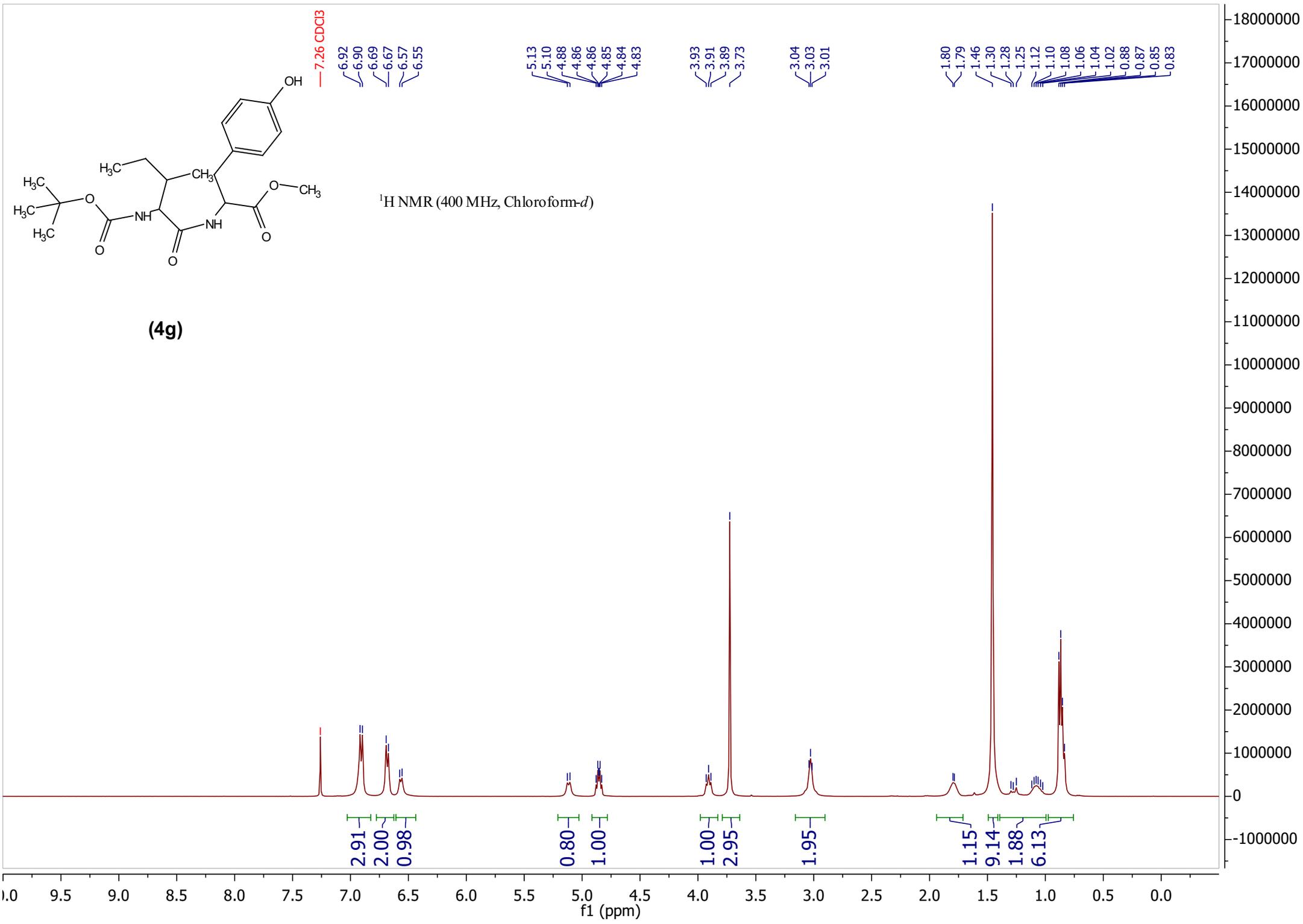


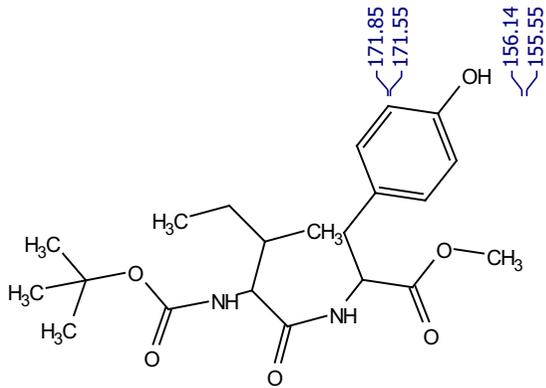






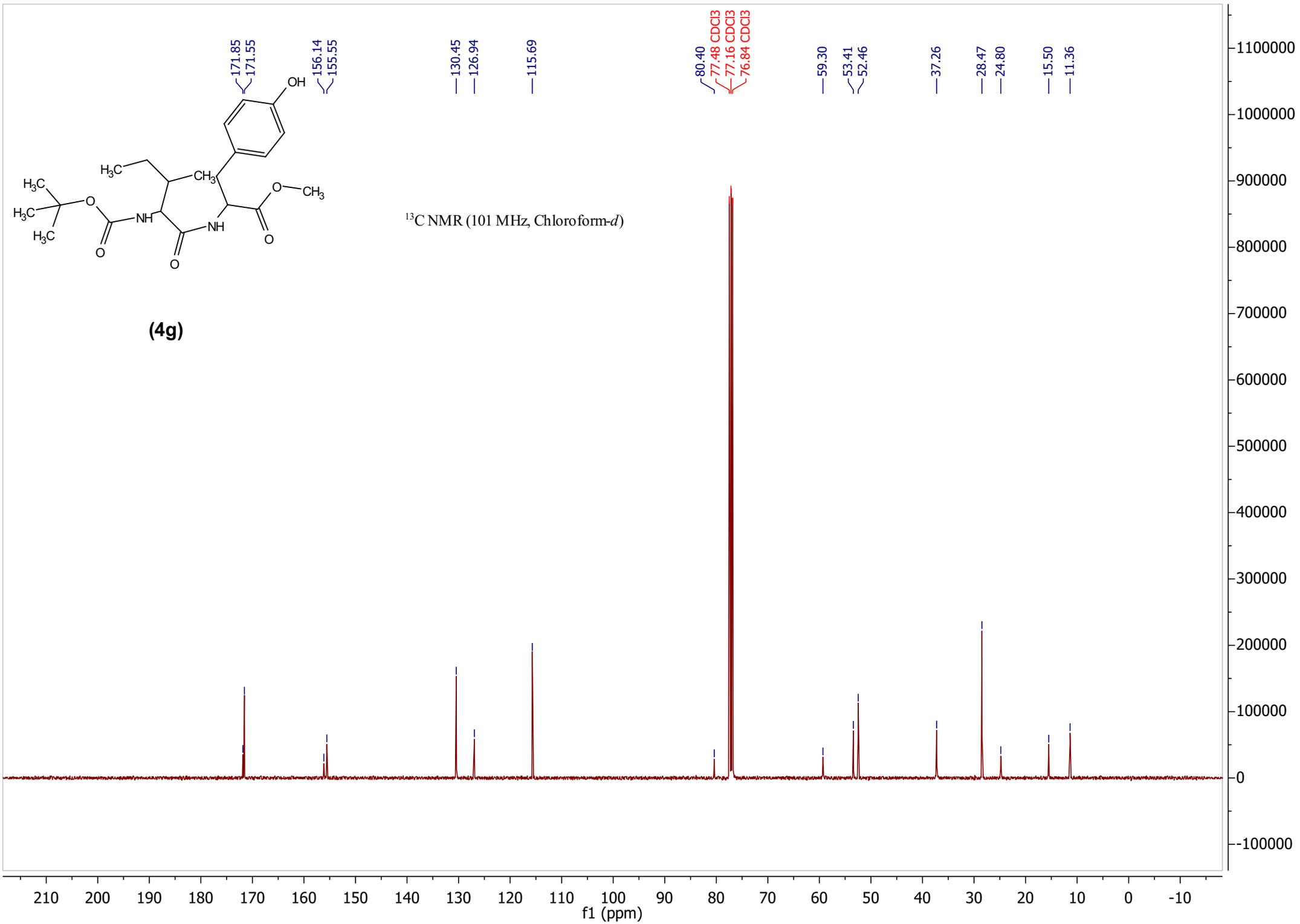


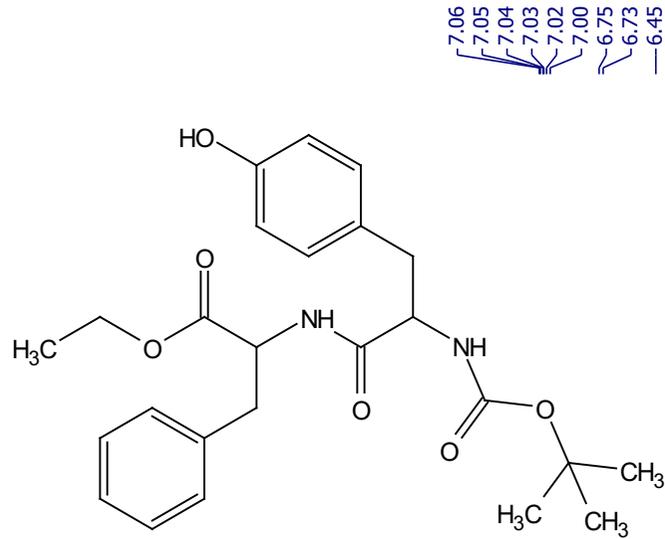




(4g)

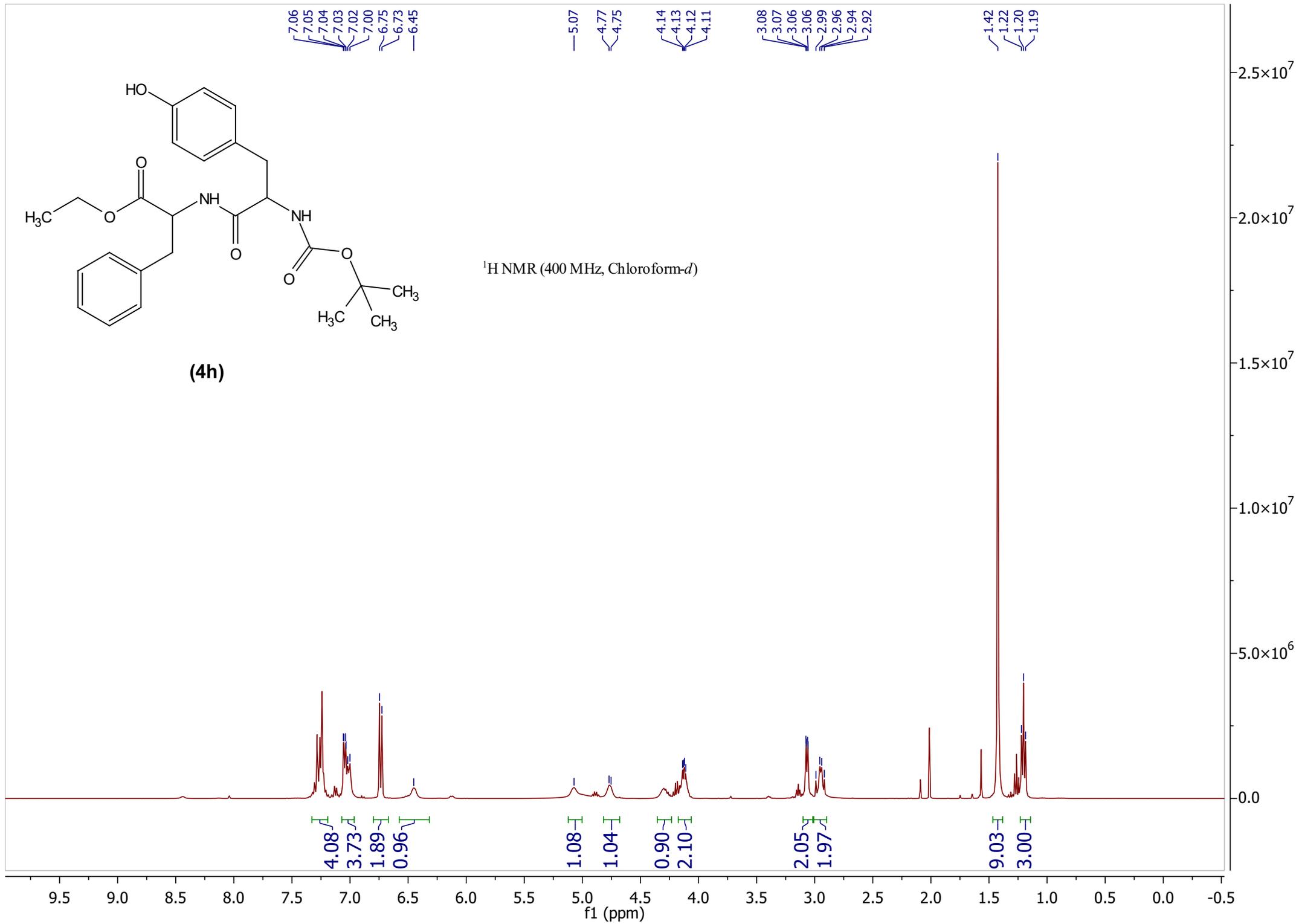
¹³C NMR (101 MHz, Chloroform-*d*)

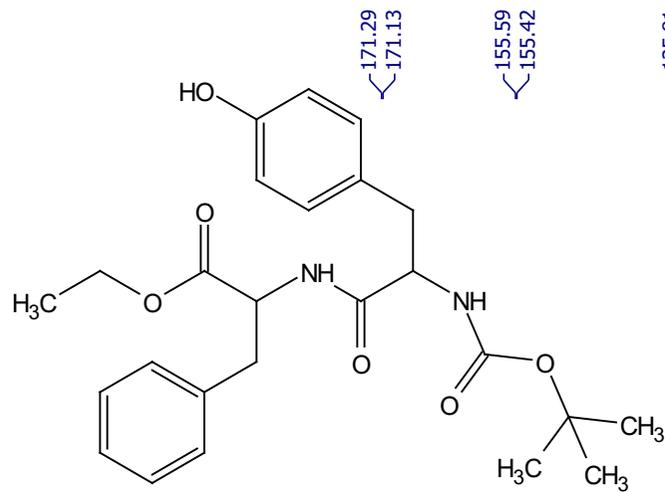




(4h)

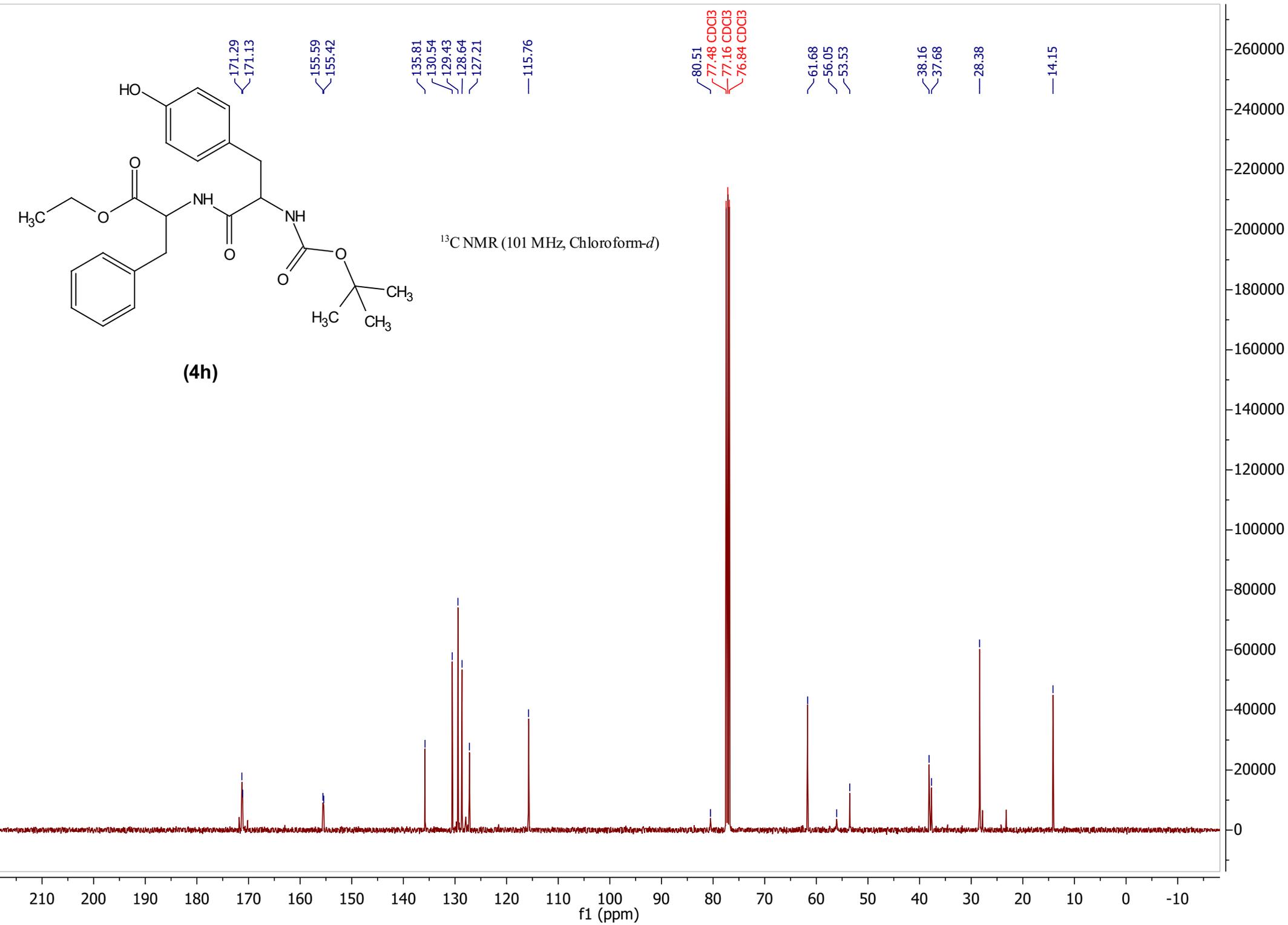
¹H NMR (400 MHz, Chloroform-*d*)



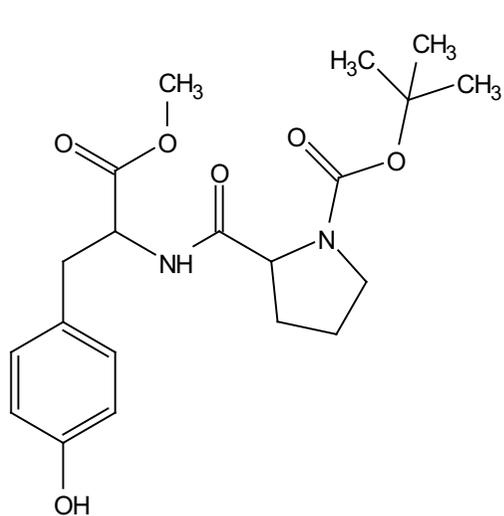


(4h)

^{13}C NMR (101 MHz, Chloroform-*d*)



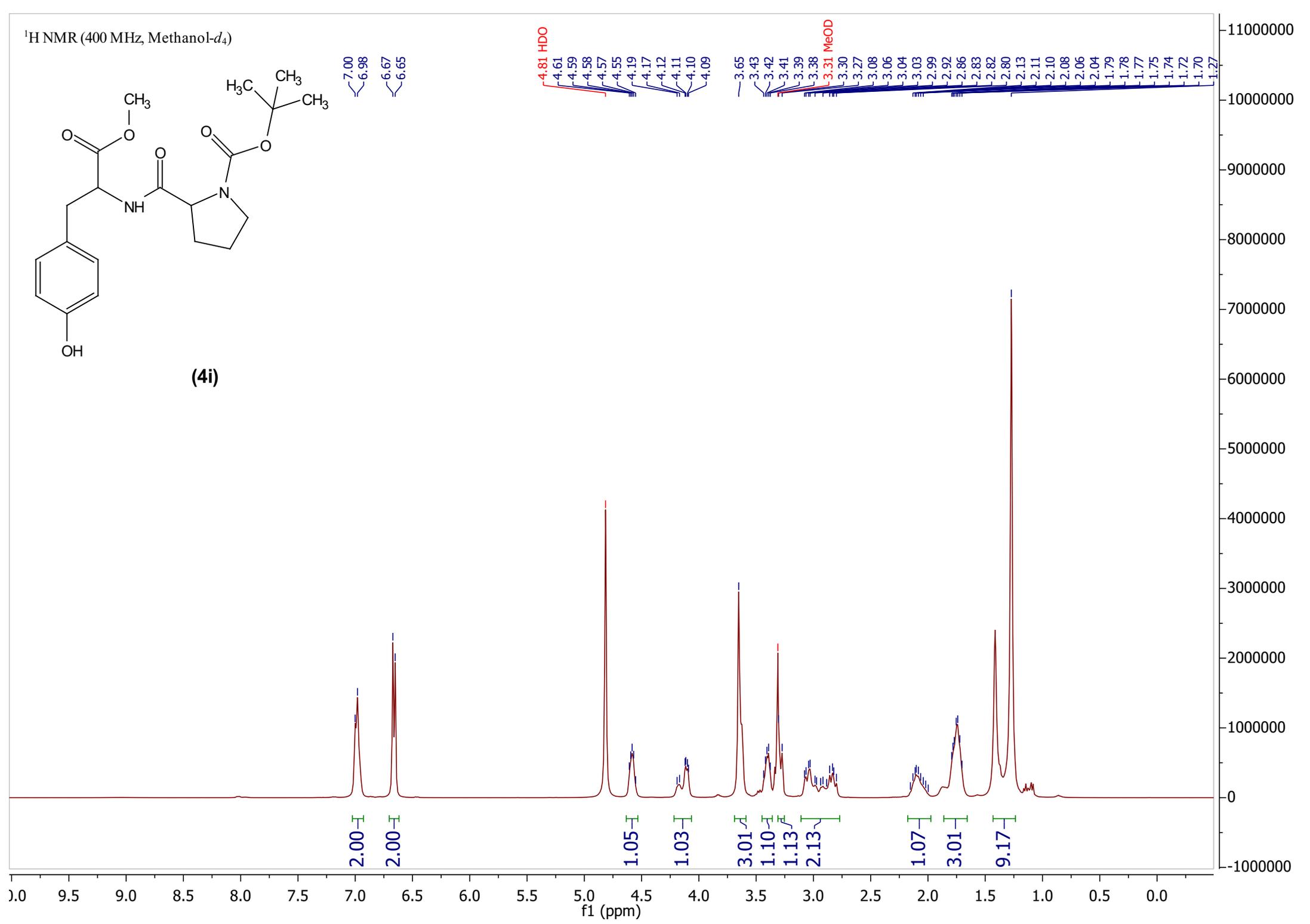
¹H NMR (400 MHz, Methanol-*d*₄)



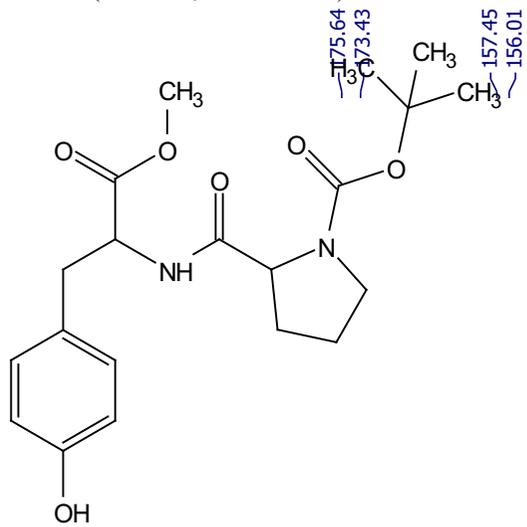
7.00
6.98
6.67
6.65

4.81 H₂O
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4.17
4.12
4.11
4.10
4.09

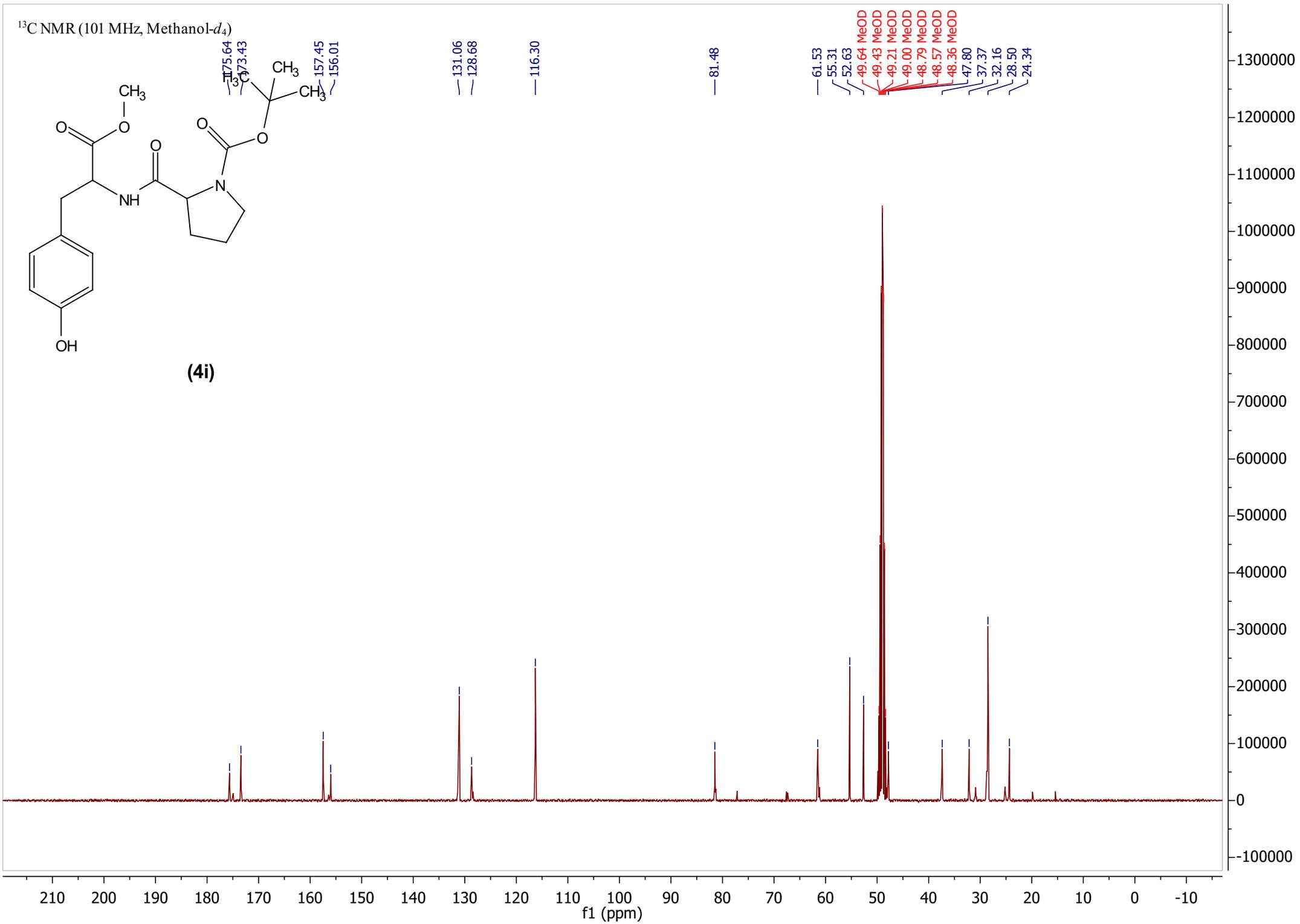
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3.03
2.99
2.92
2.86
2.83
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2.80
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1.75
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1.72
1.70
1.27



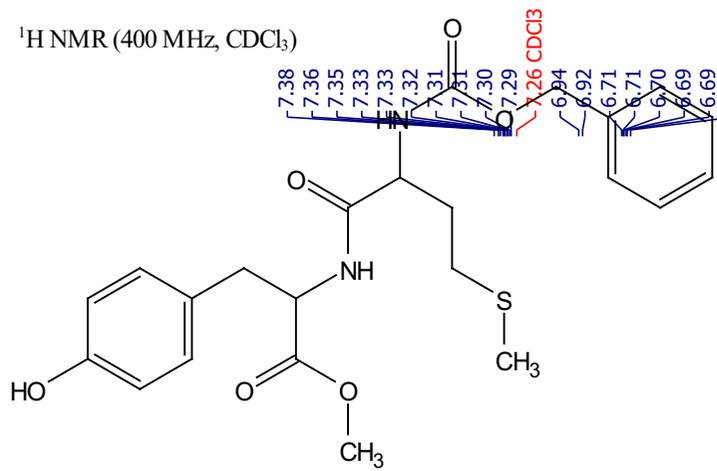
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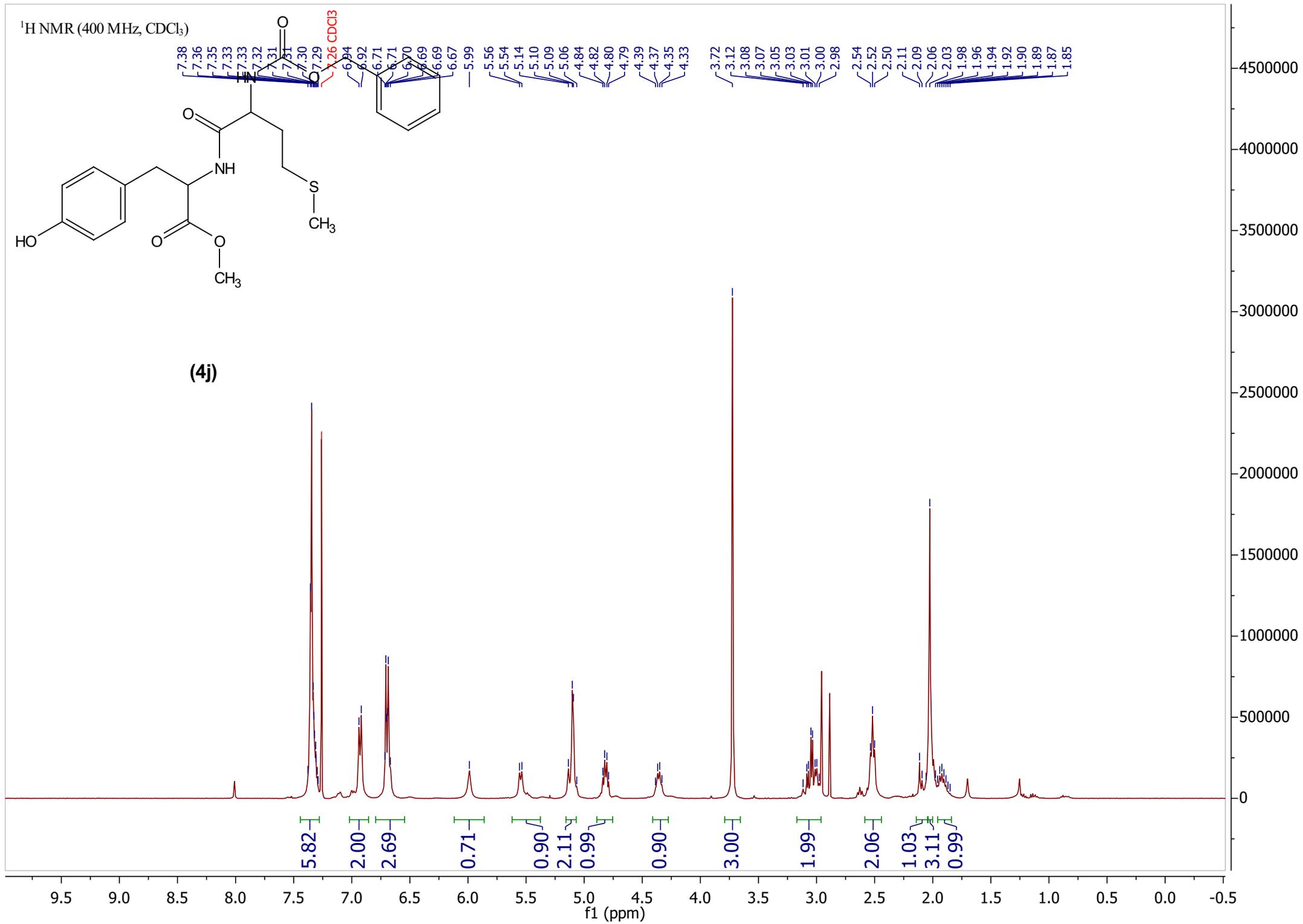
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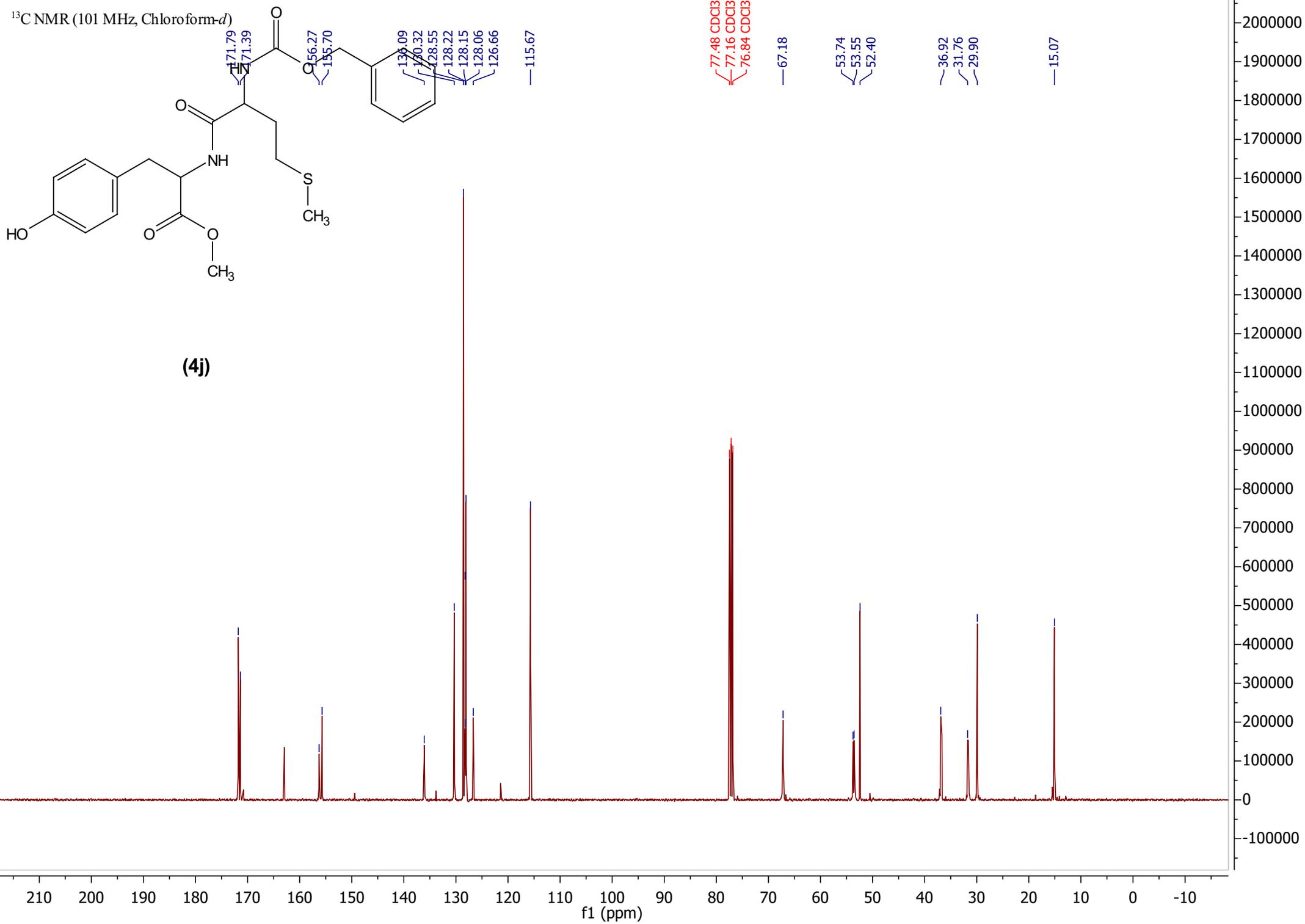
¹H NMR (400 MHz, CDCl₃)

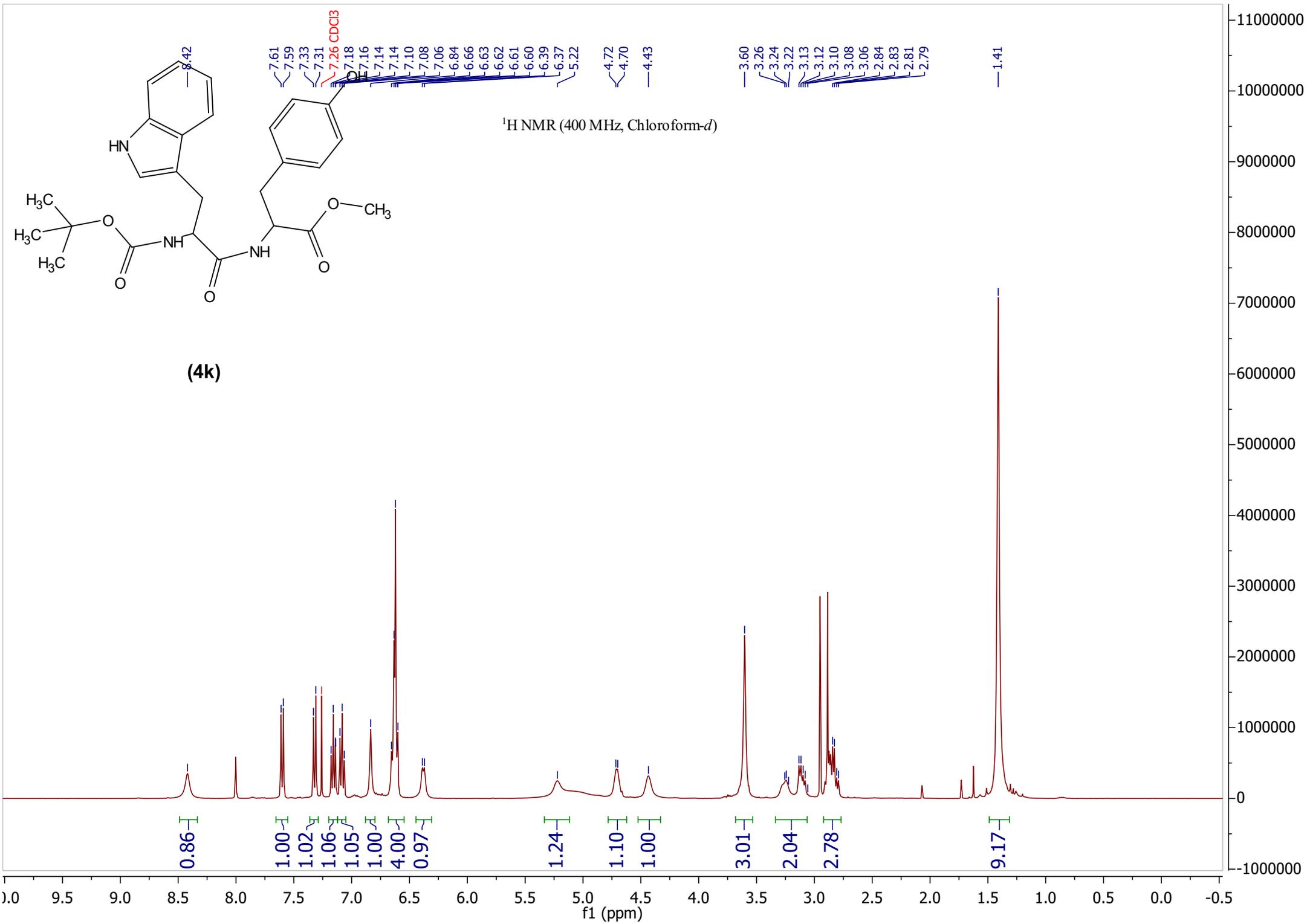


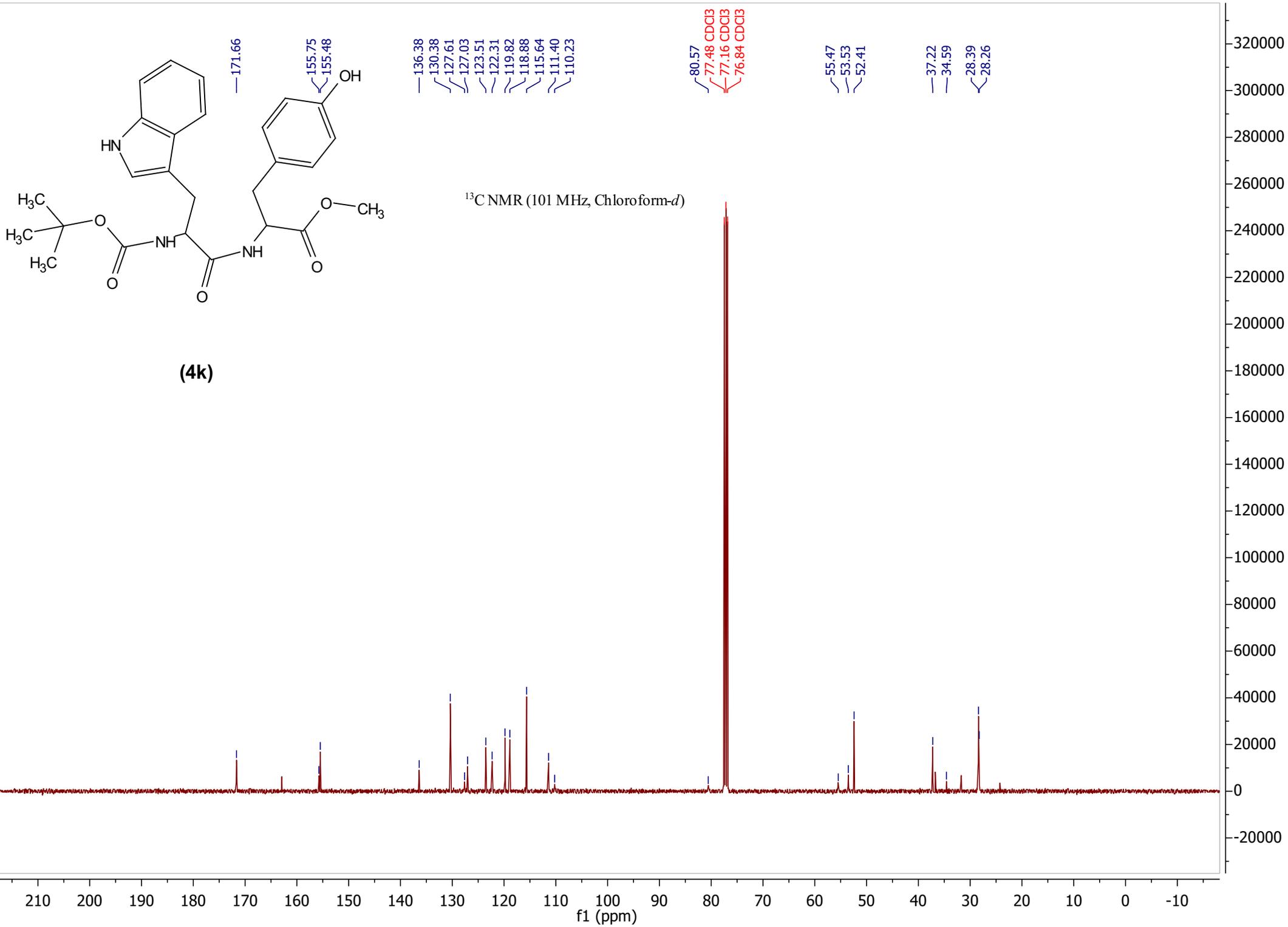
(4j)

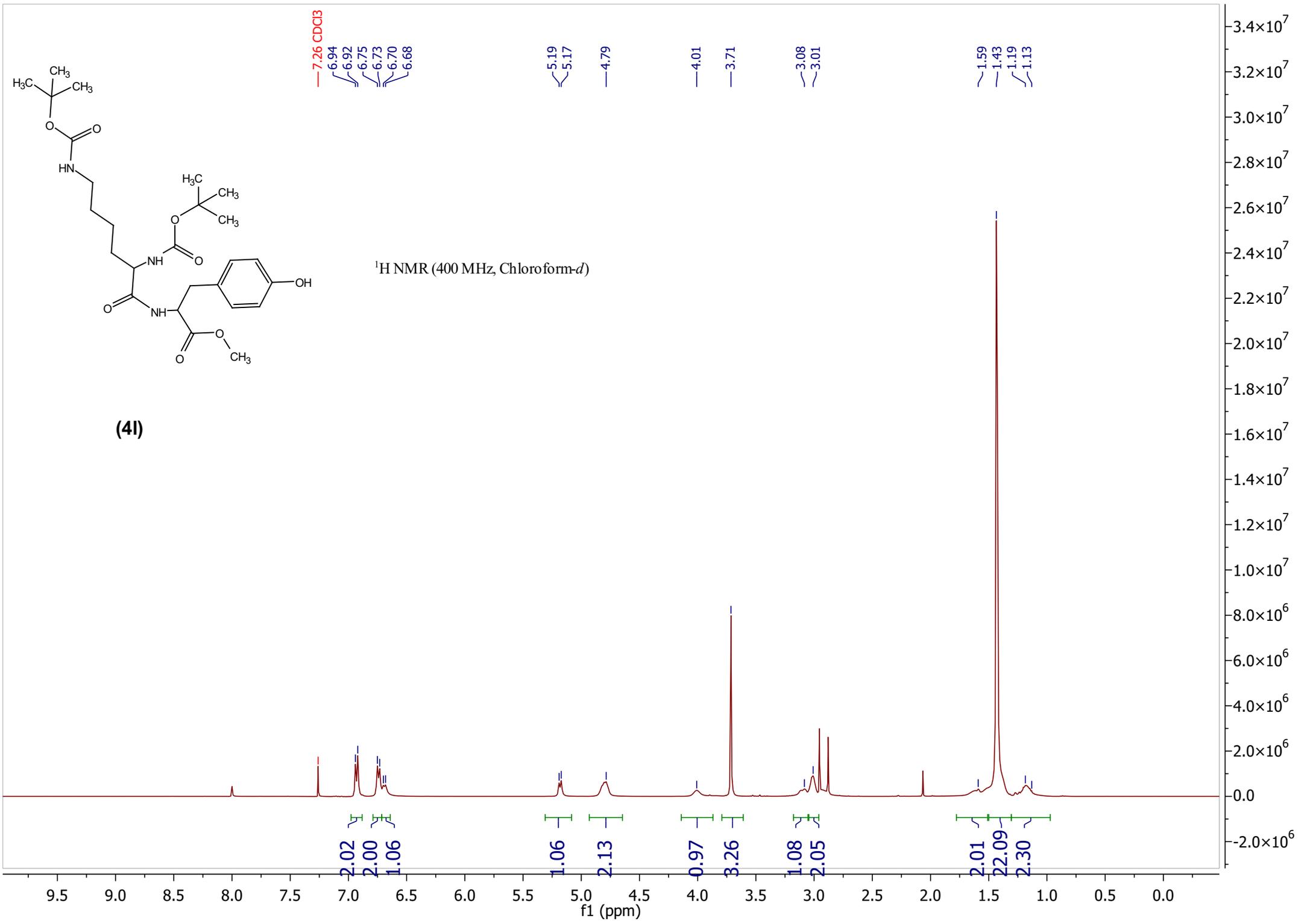


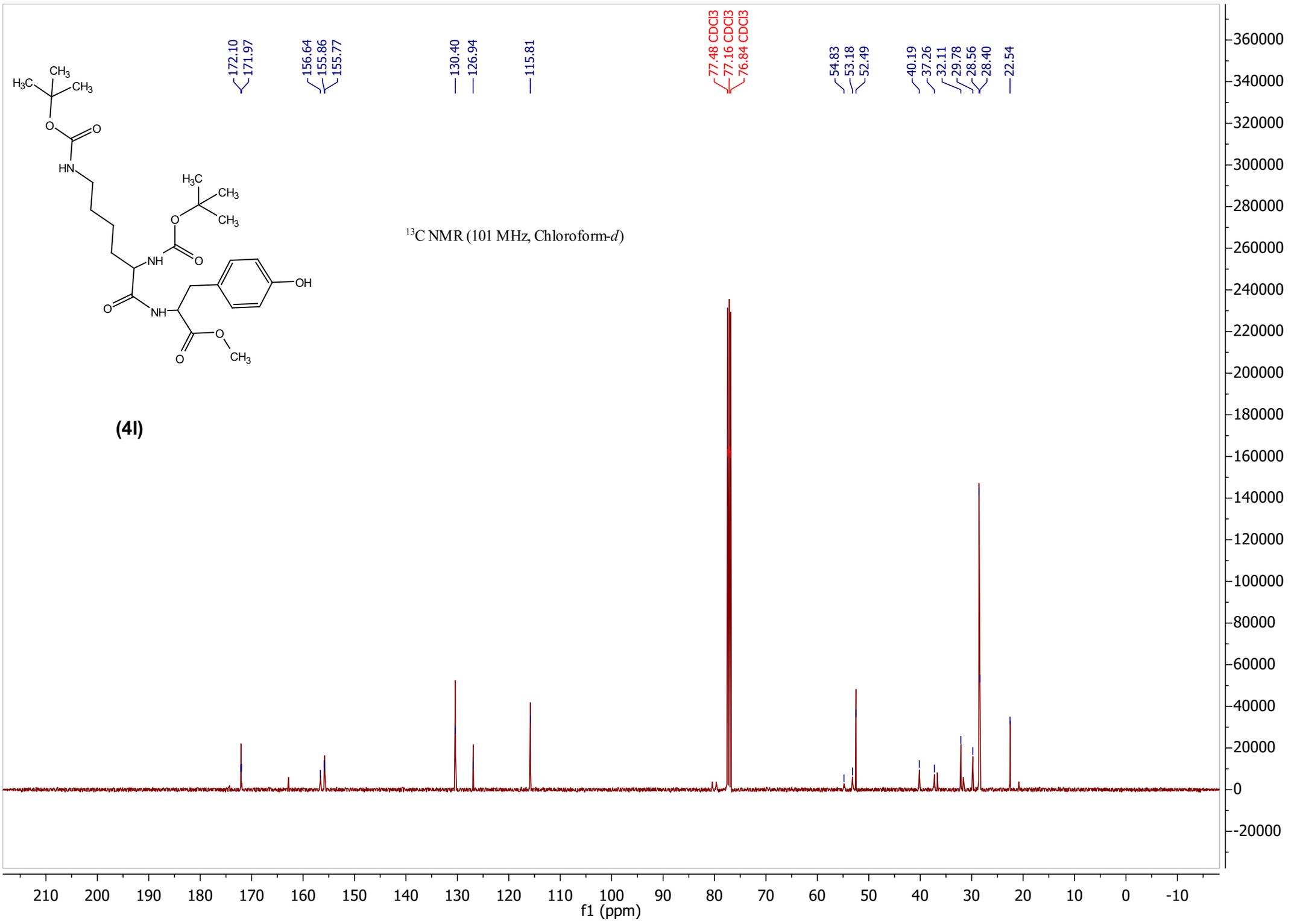
¹³C NMR (101 MHz, Chloroform-*d*)

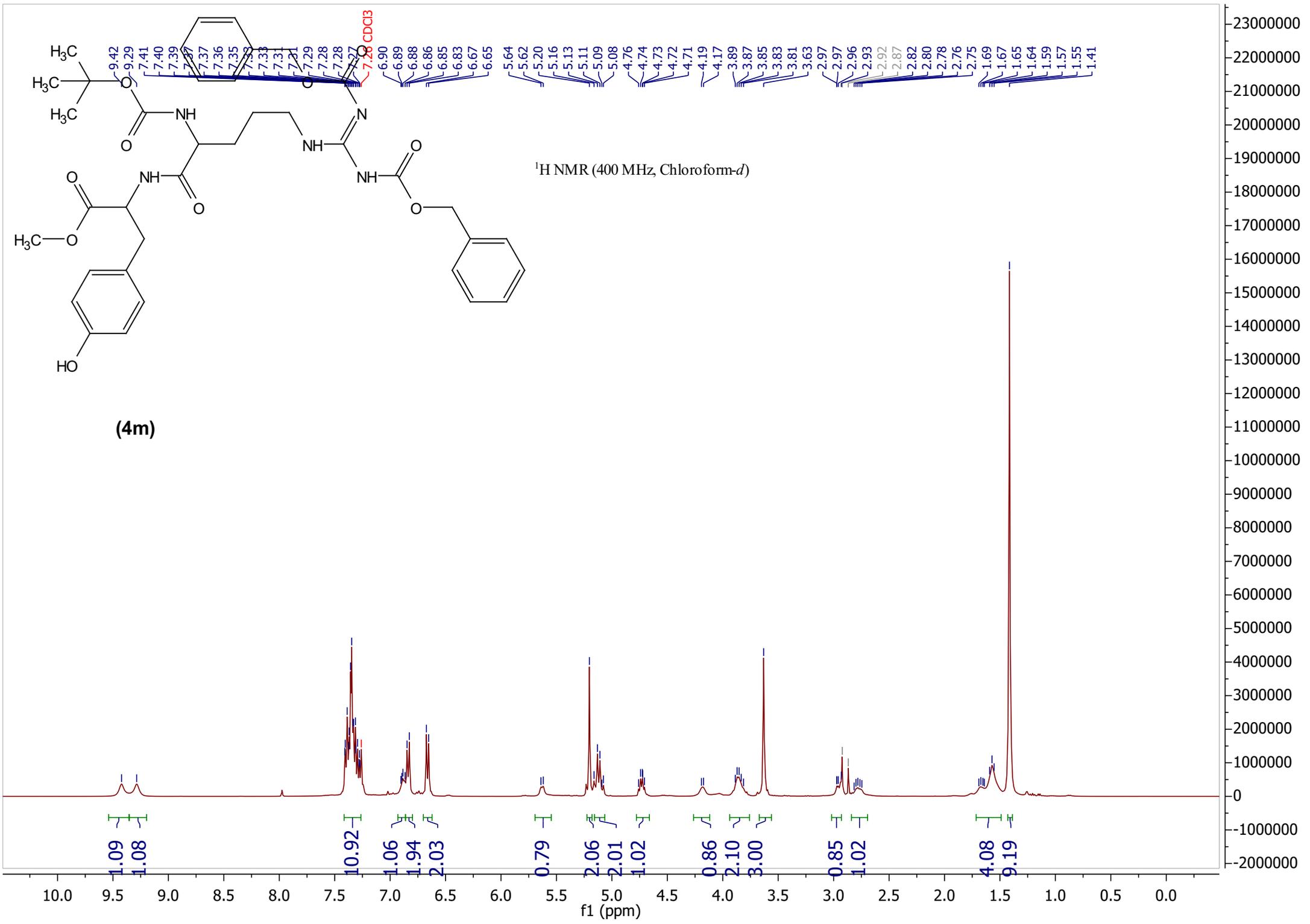


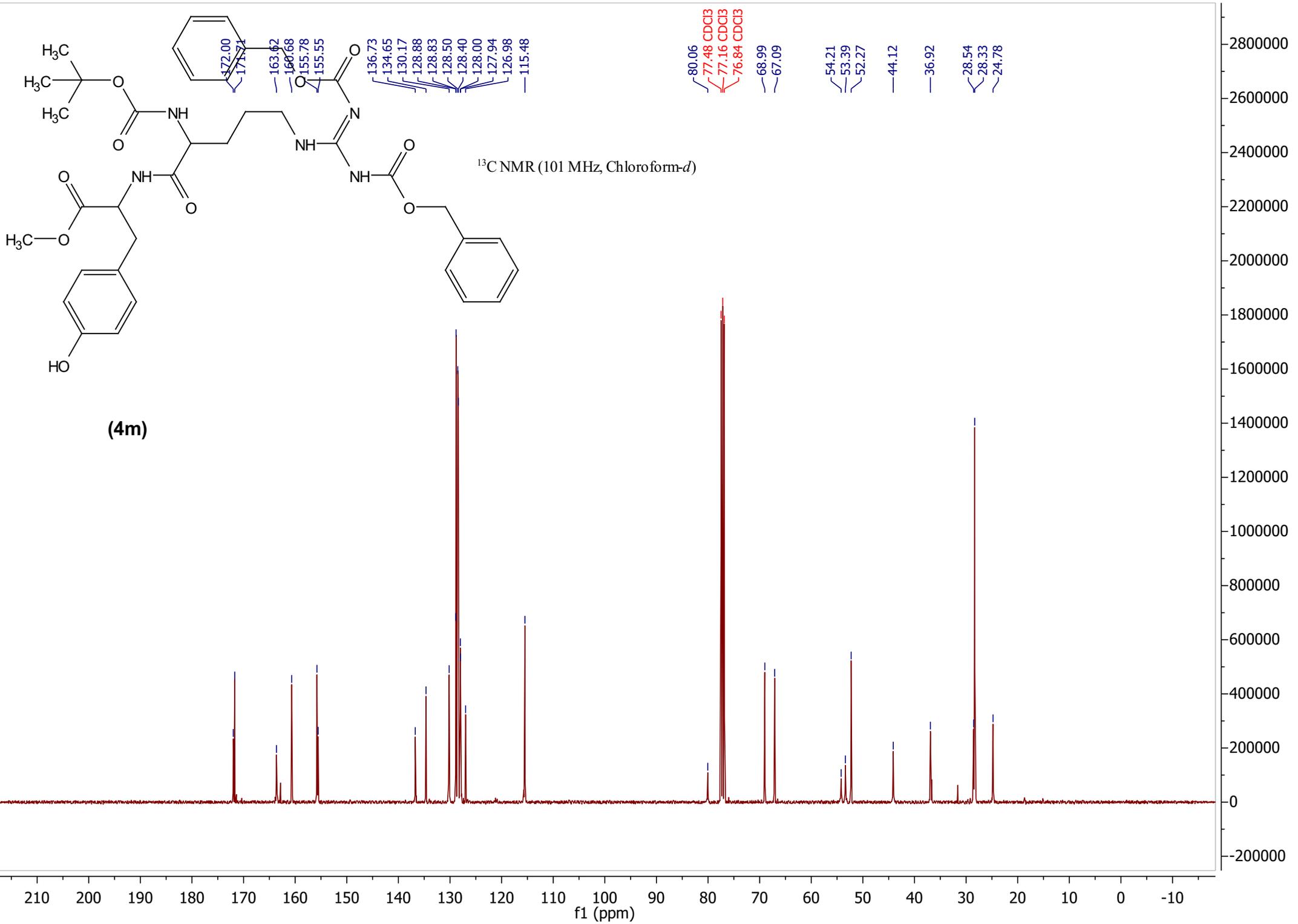


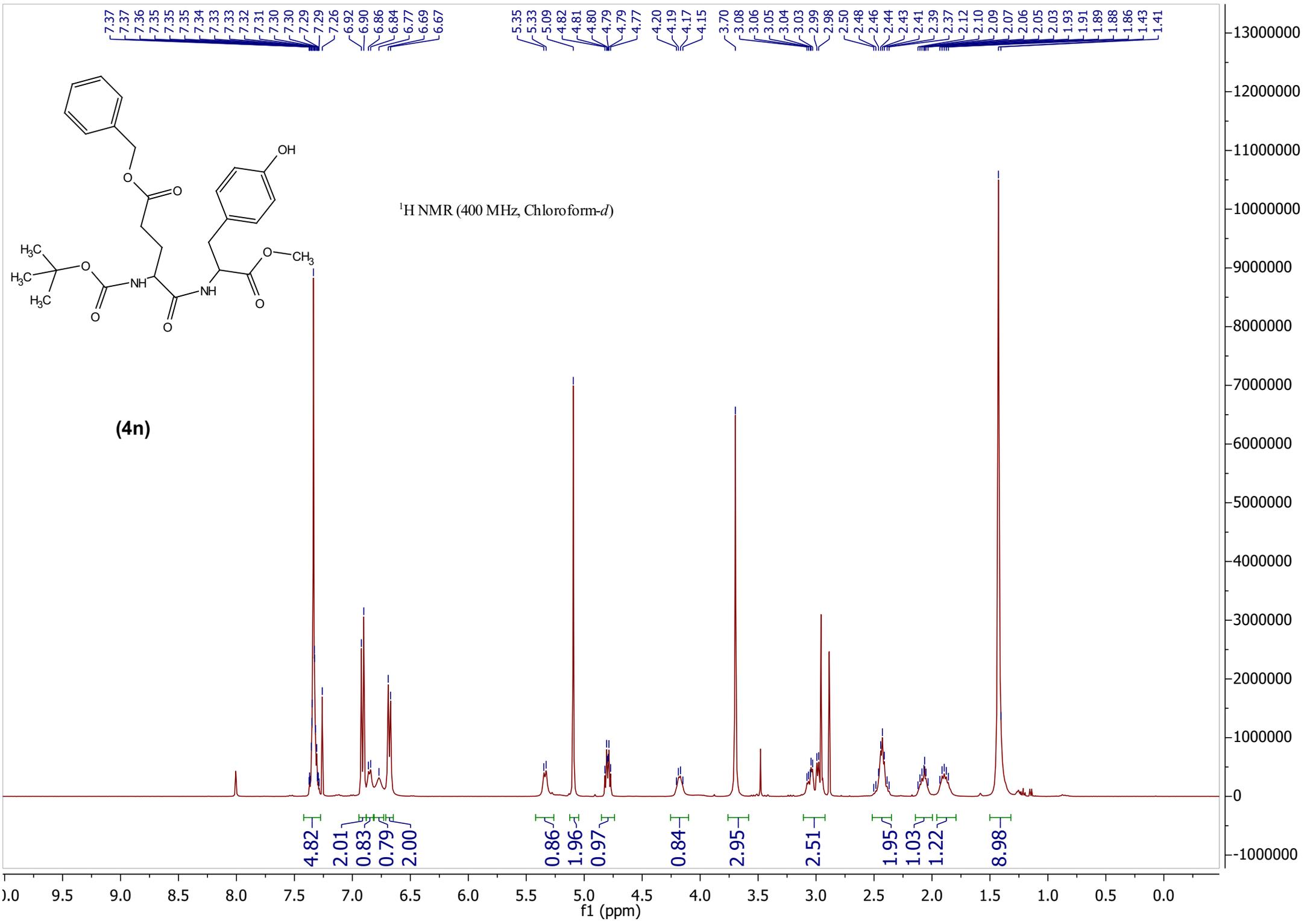


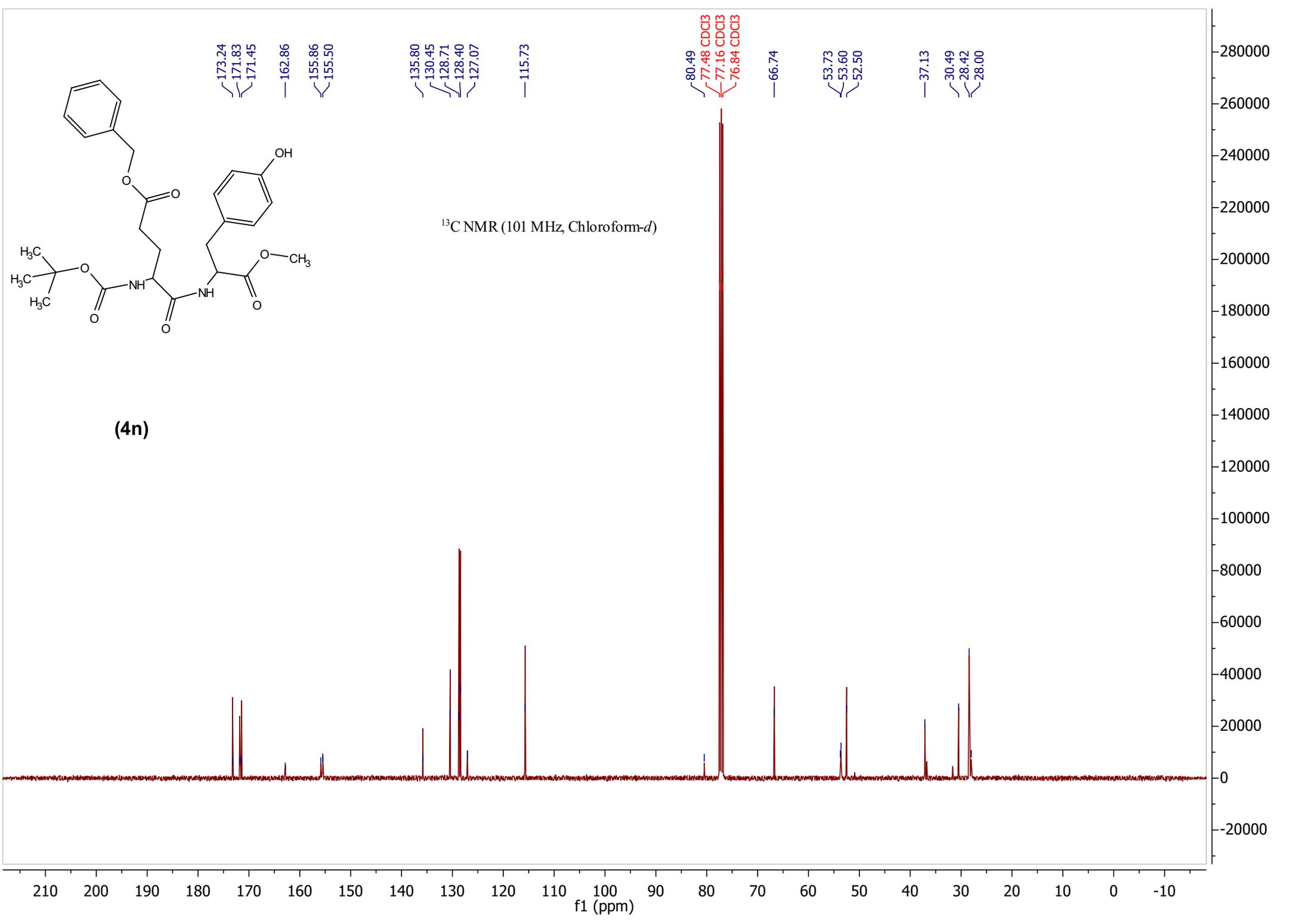


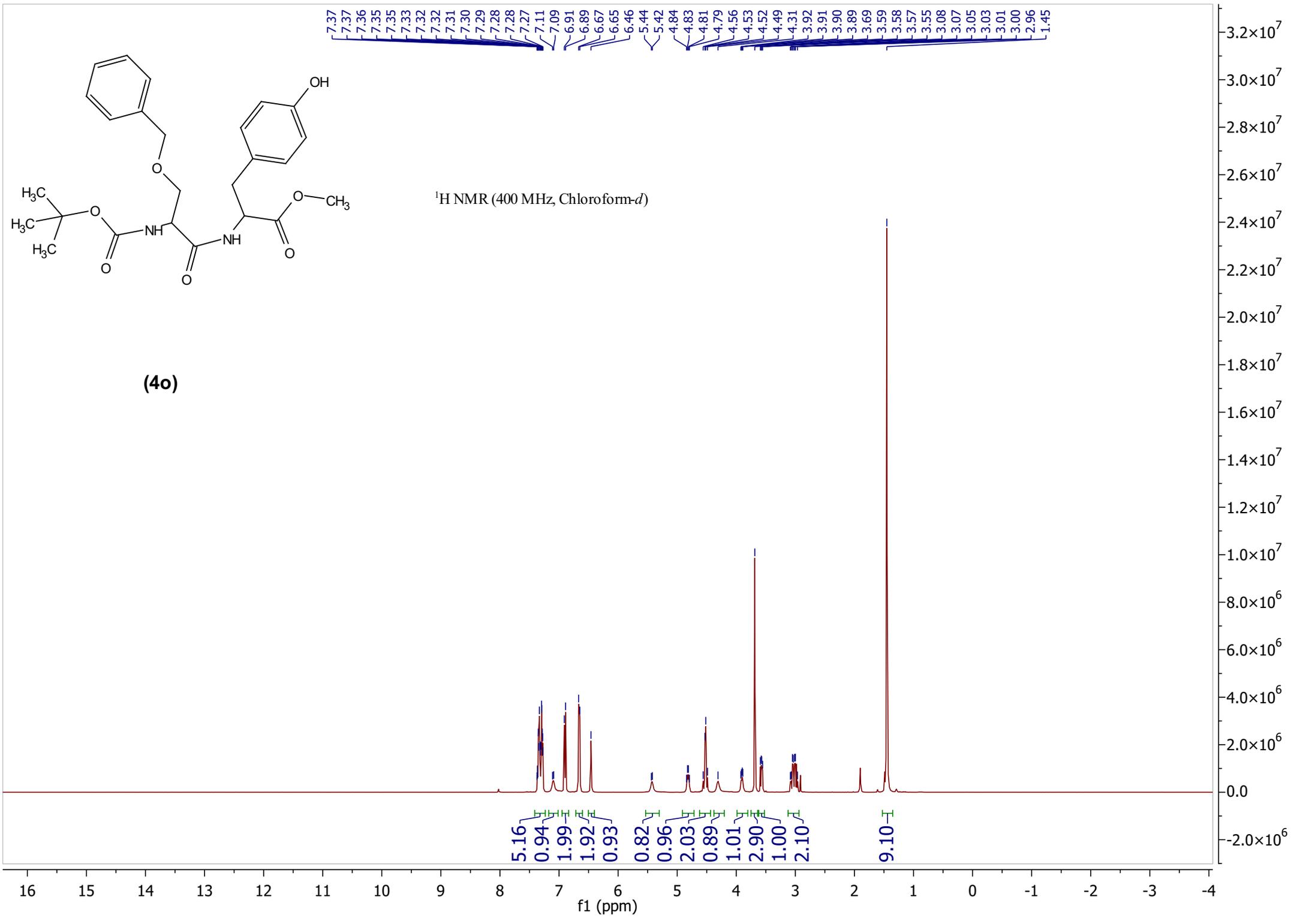


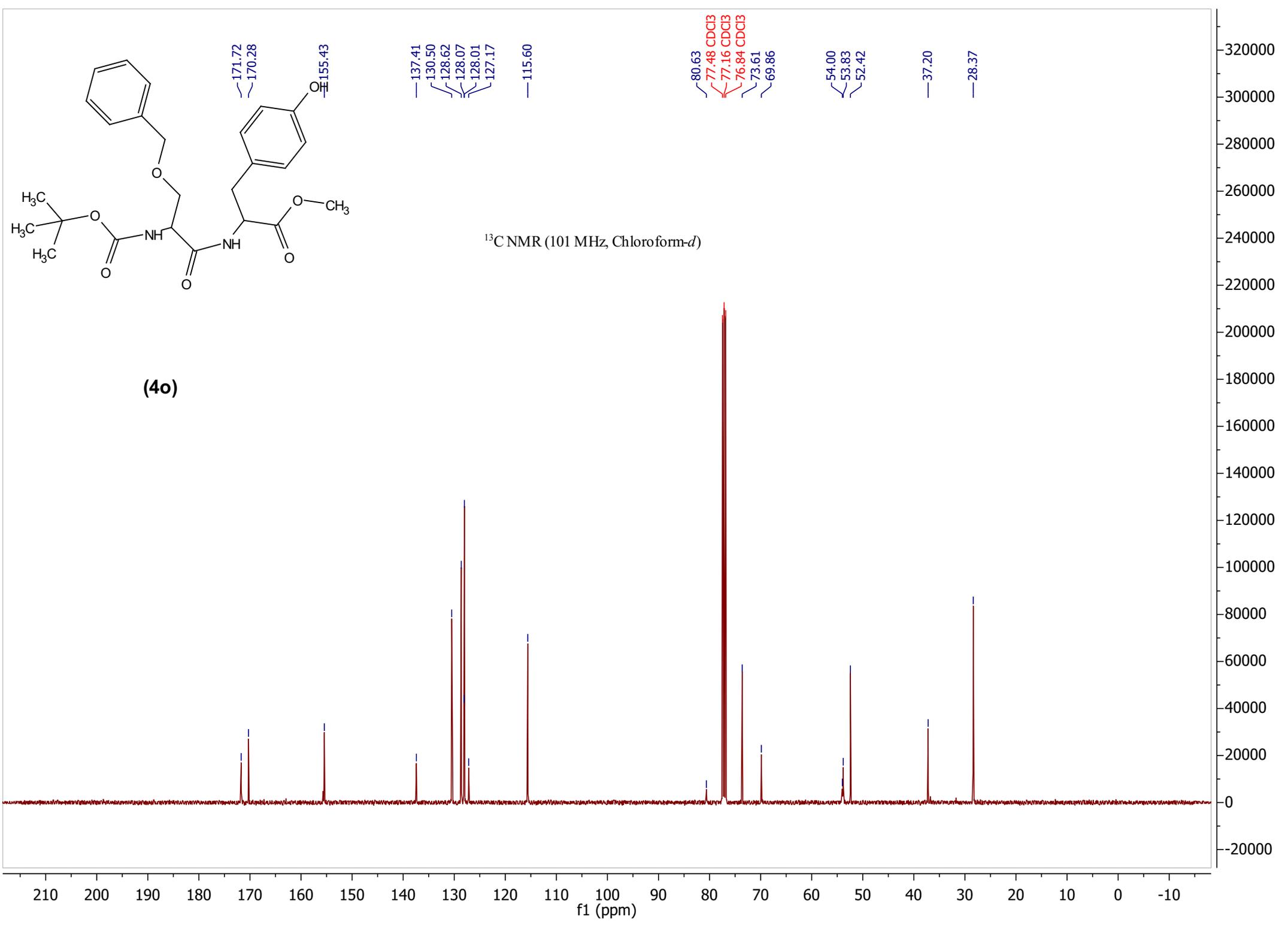




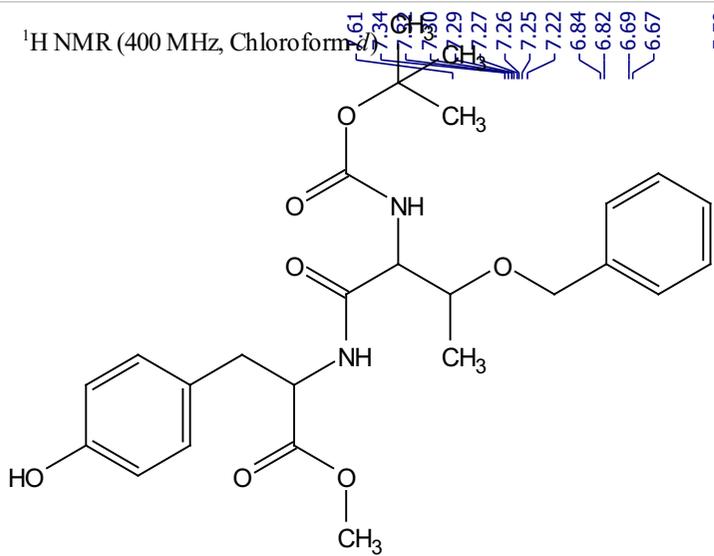




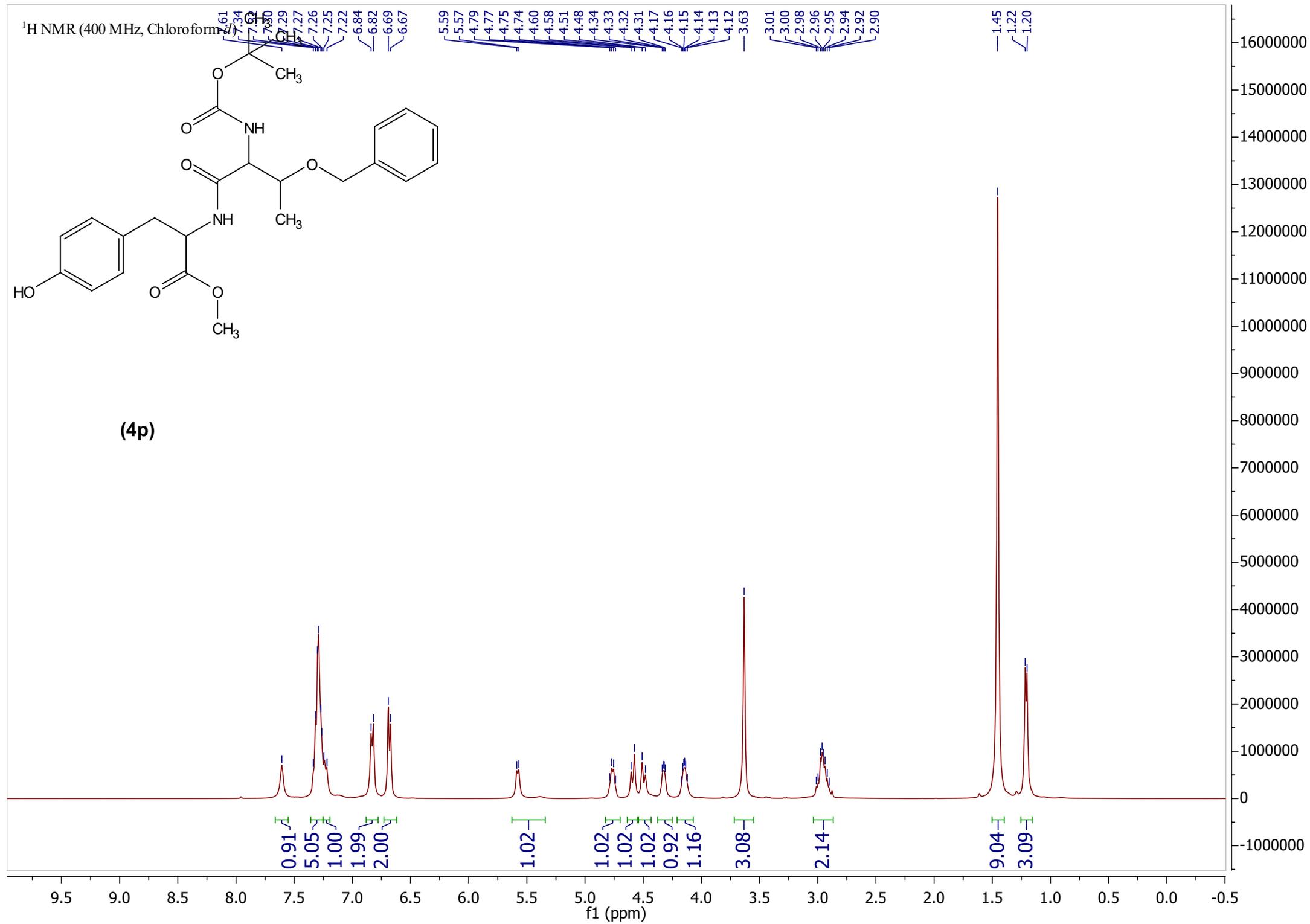




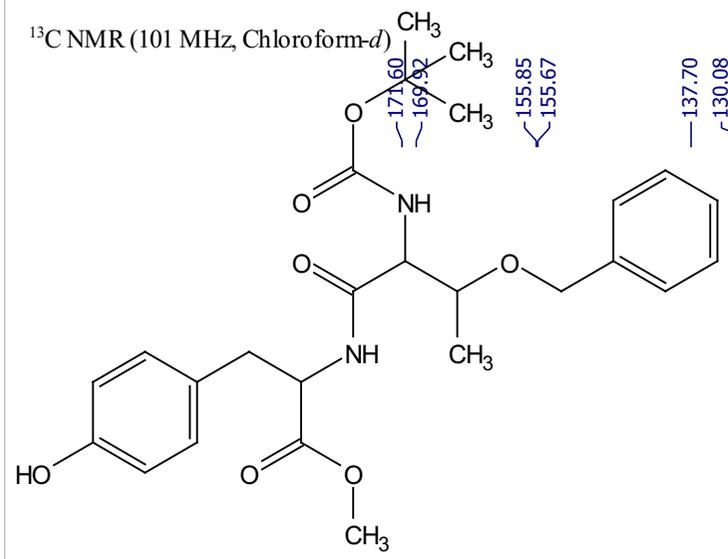
¹H NMR (400 MHz, Chloroform-d)



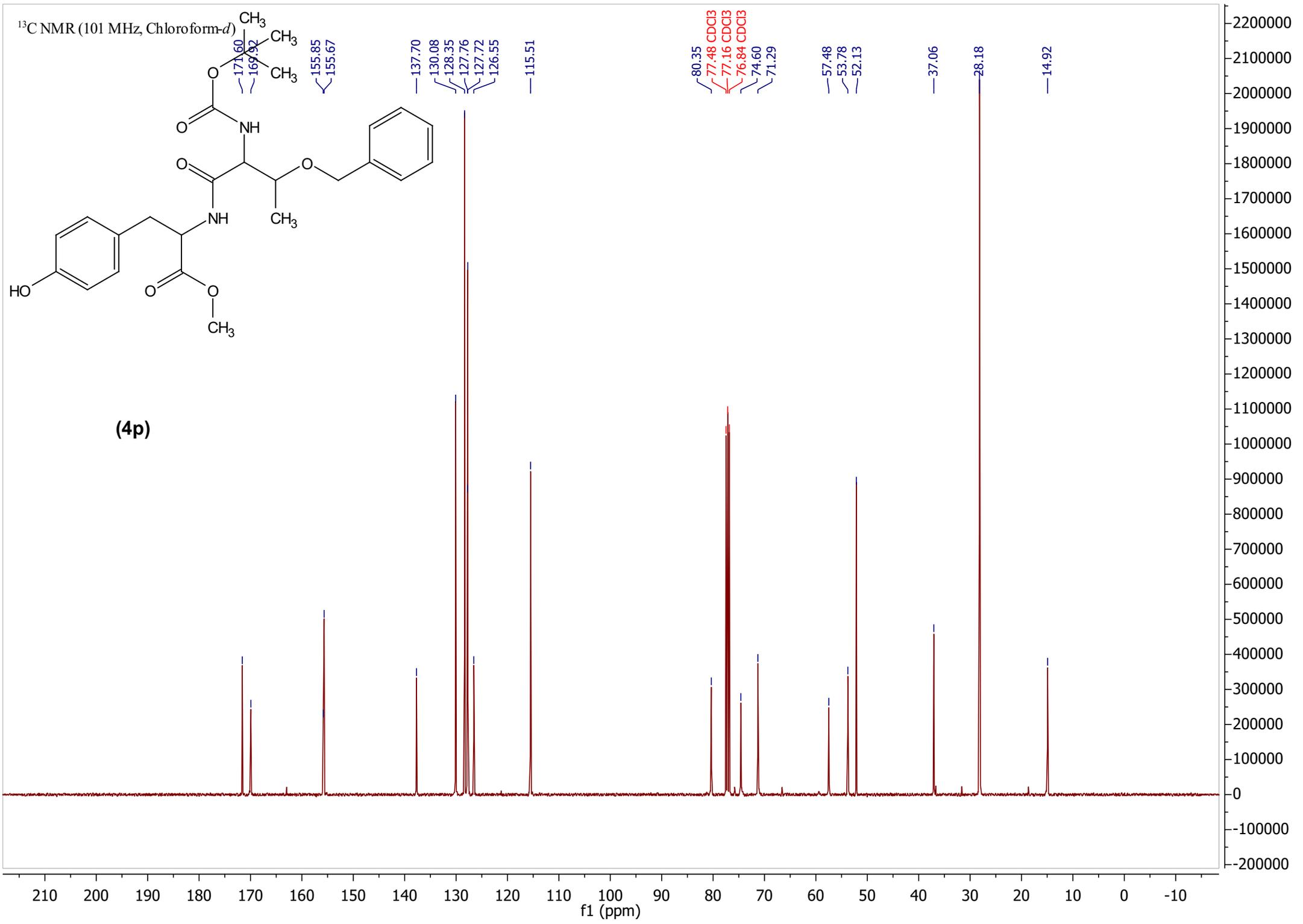
(4p)

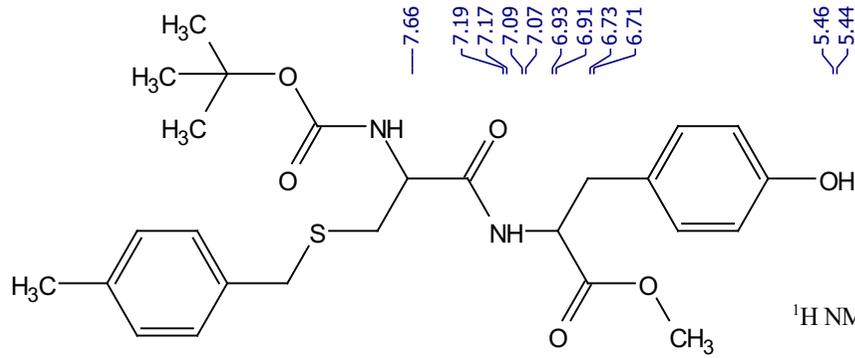


¹³C NMR (101 MHz, Chloroform-*d*)



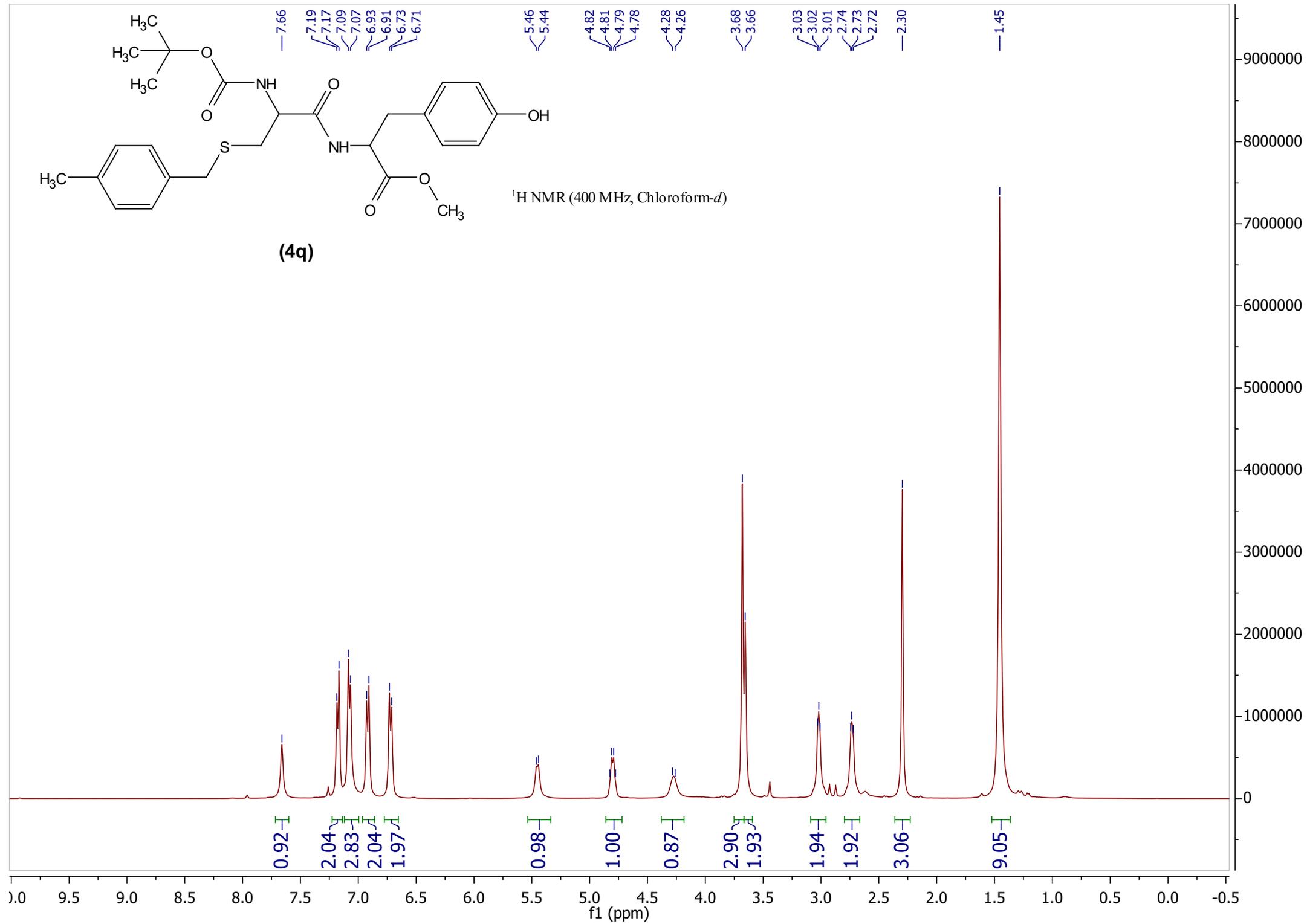
(4p)

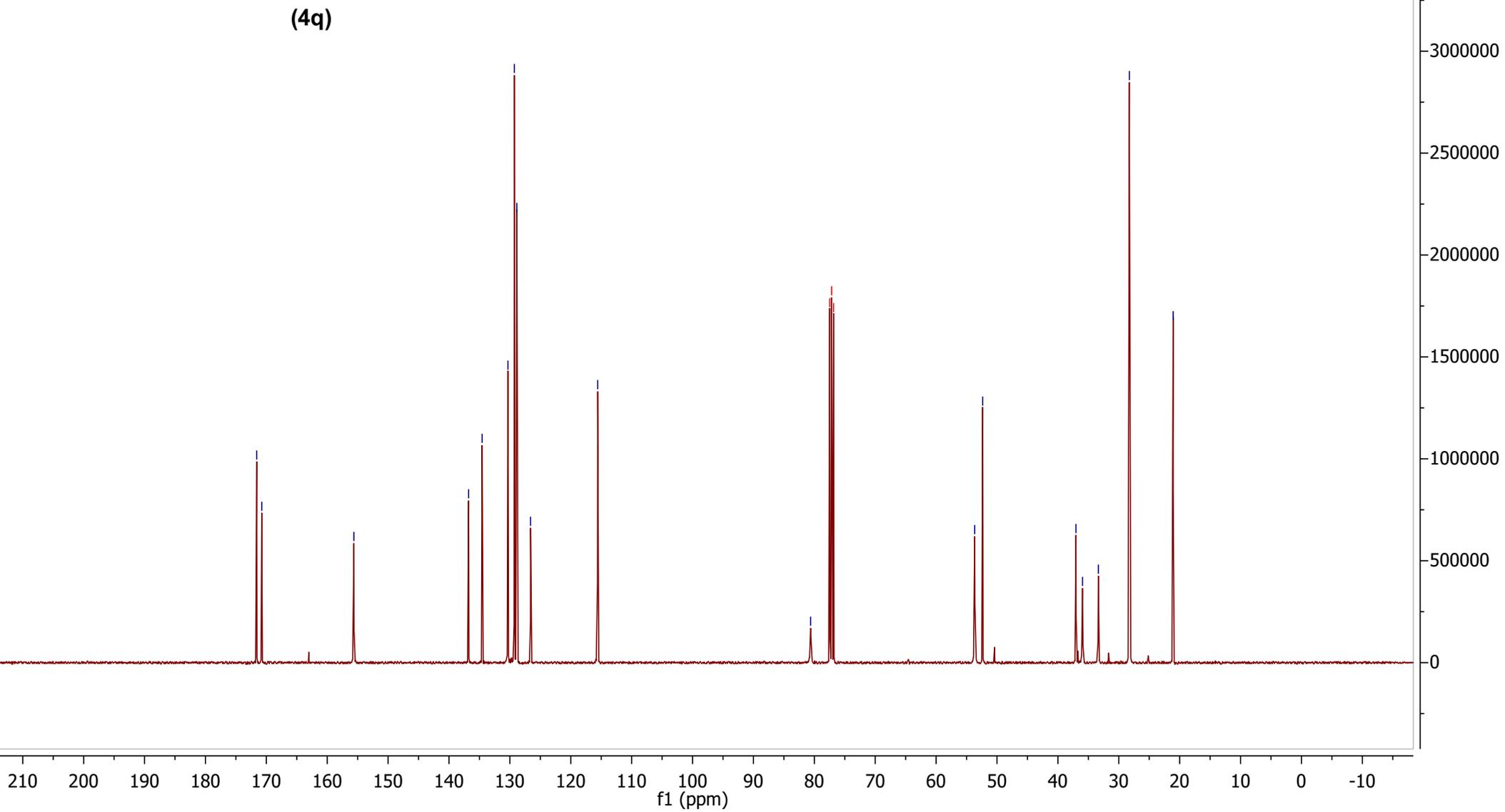
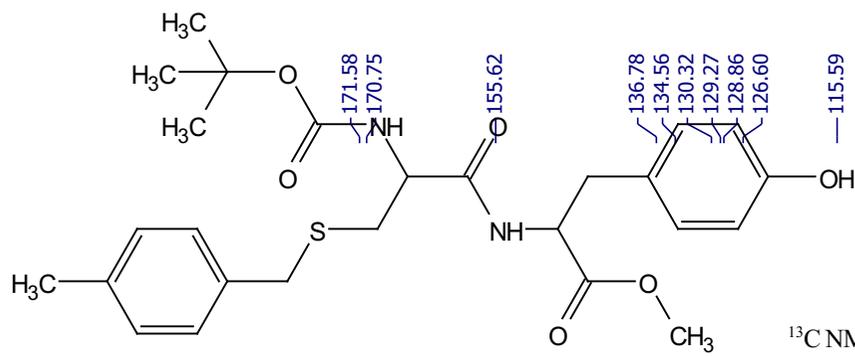




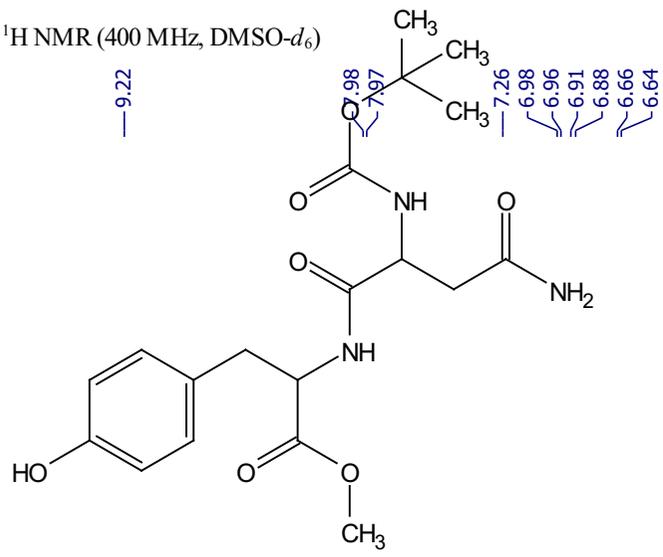
(4q)

¹H NMR (400 MHz, Chloroform-*d*)

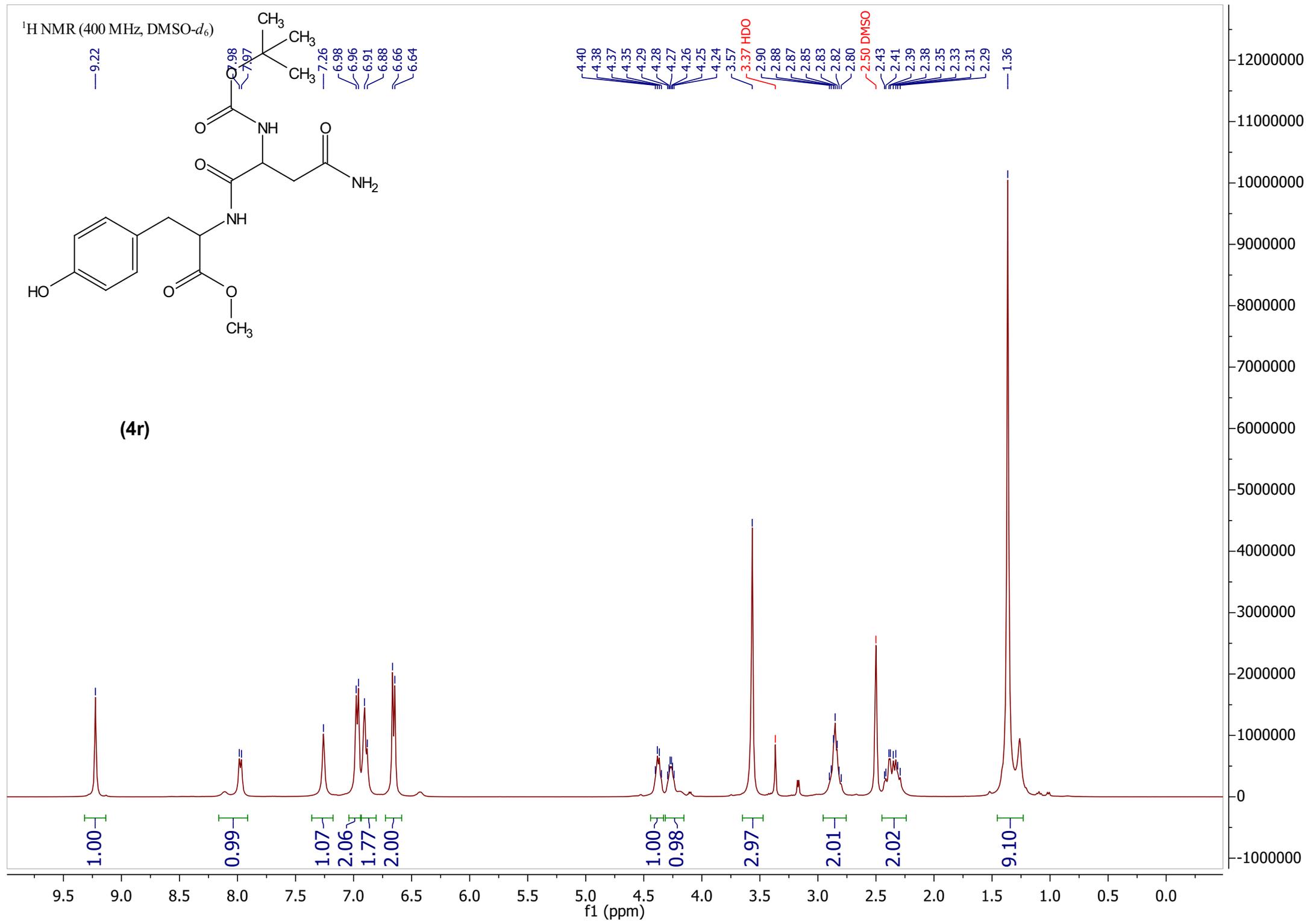




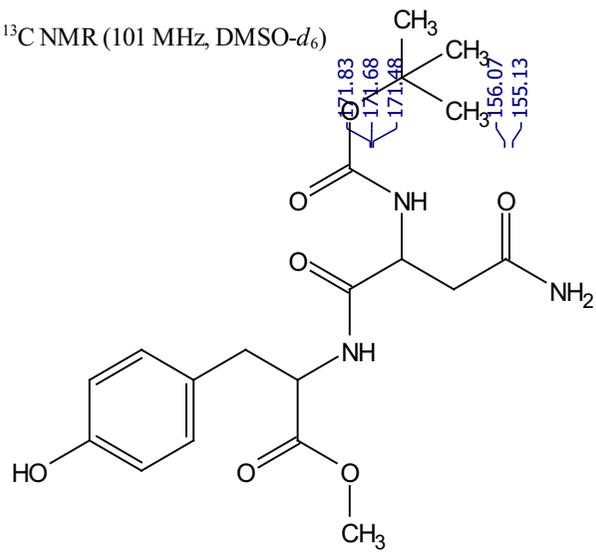
¹H NMR (400 MHz, DMSO-*d*₆)



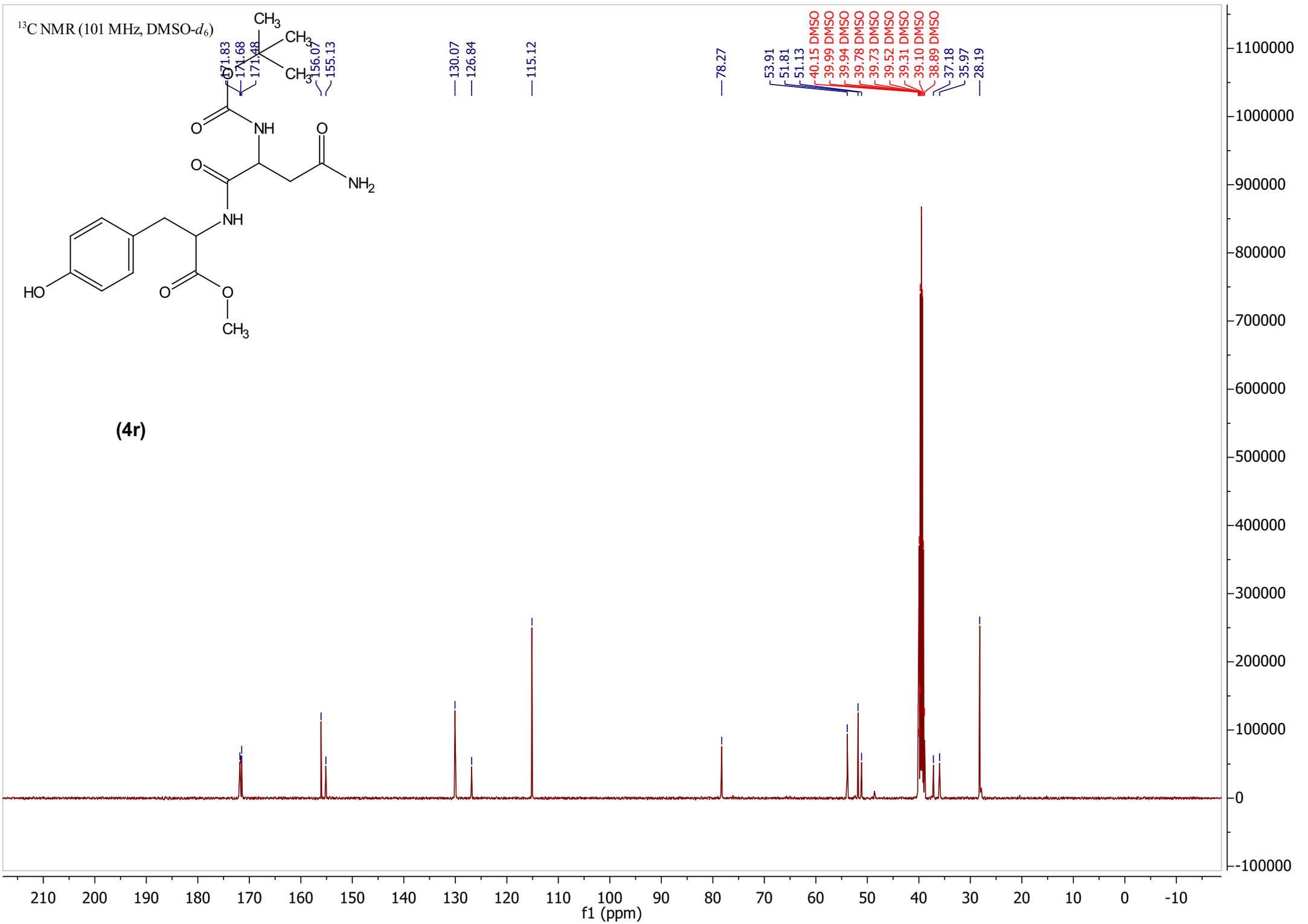
(4r)



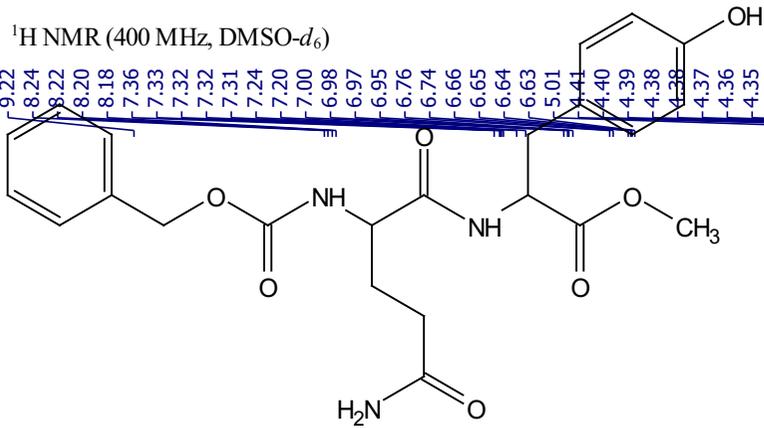
¹³C NMR (101 MHz, DMSO-*d*₆)



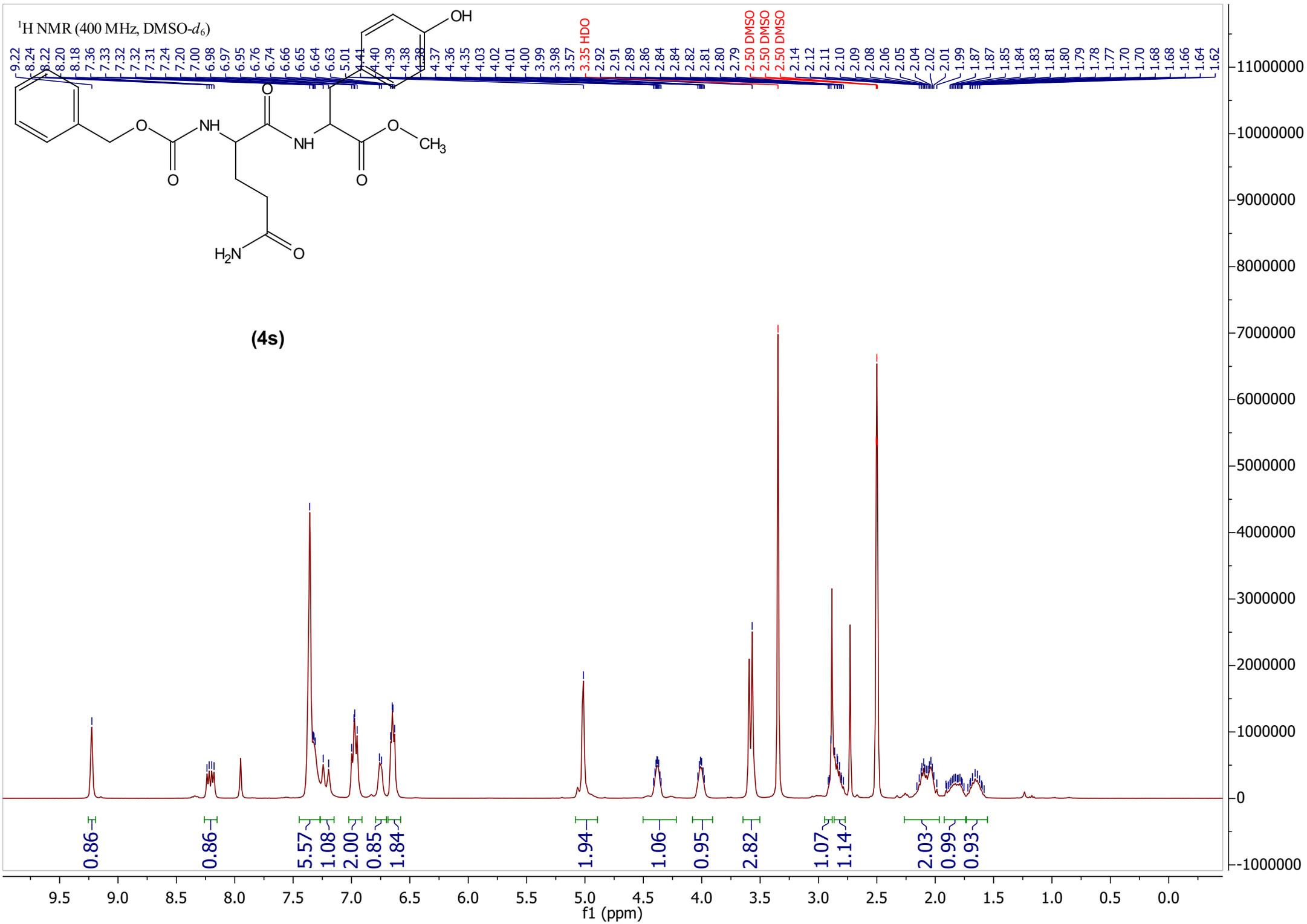
(4r)



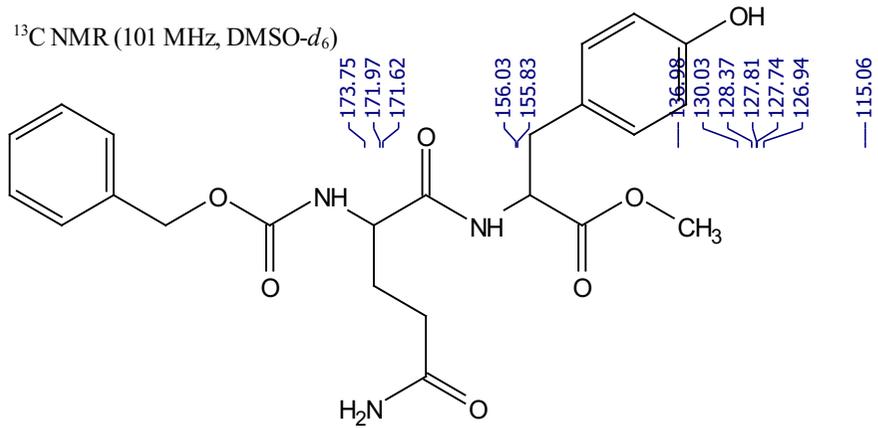
¹H NMR (400 MHz, DMSO-d₆)



(4s)



¹³C NMR (101 MHz, DMSO-*d*₆)



(4s)

65.46

54.28

53.79

51.77

40.15 DMSO

39.99 DMSO

39.94 DMSO

39.78 DMSO

39.52 DMSO

39.31 DMSO

39.10 DMSO

38.89 DMSO

35.95

31.40

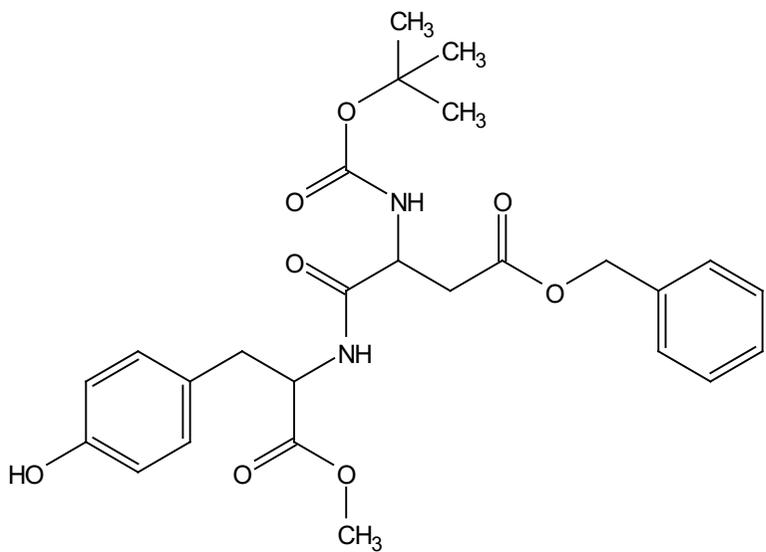
27.77

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

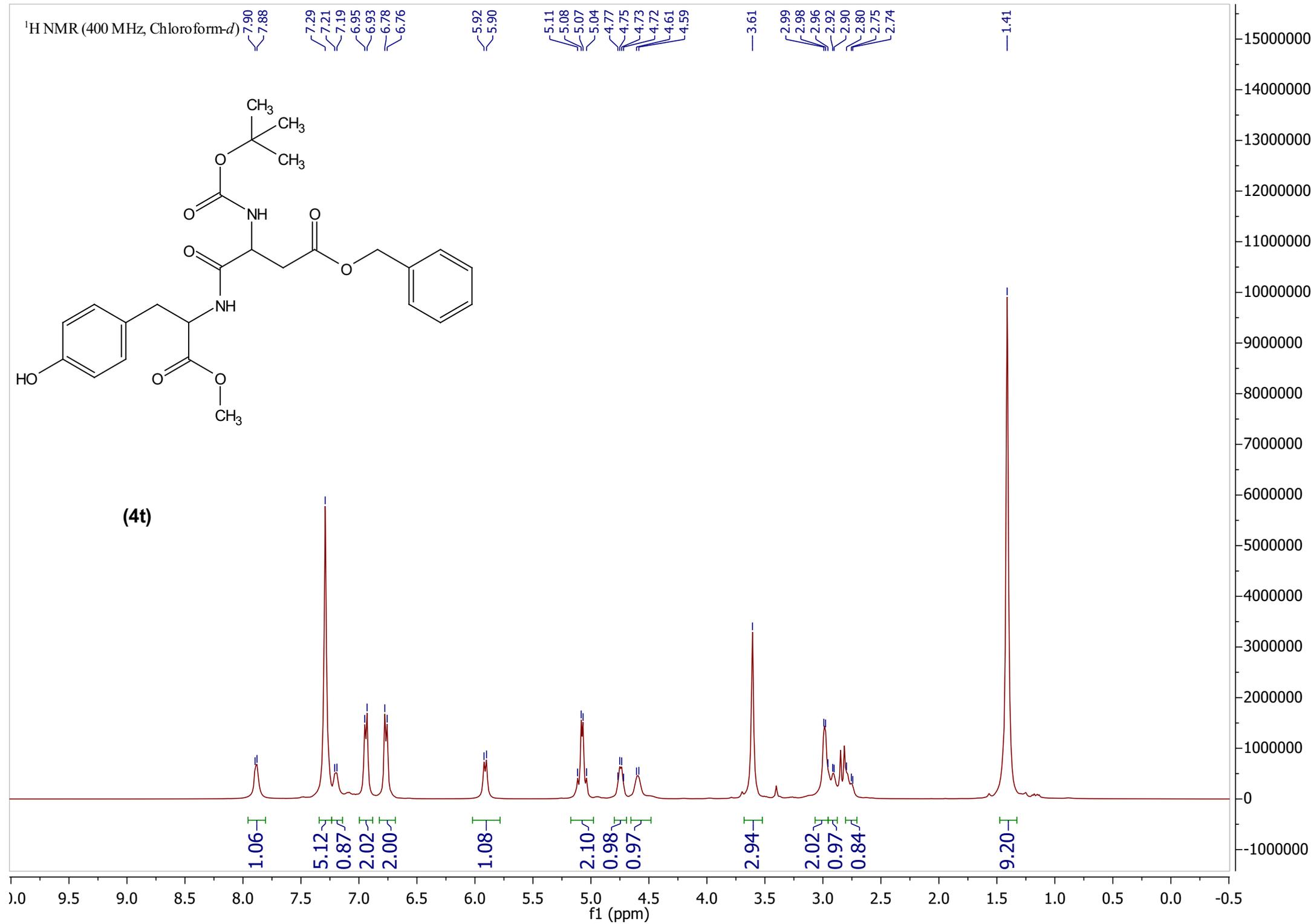
f1 (ppm)

500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0

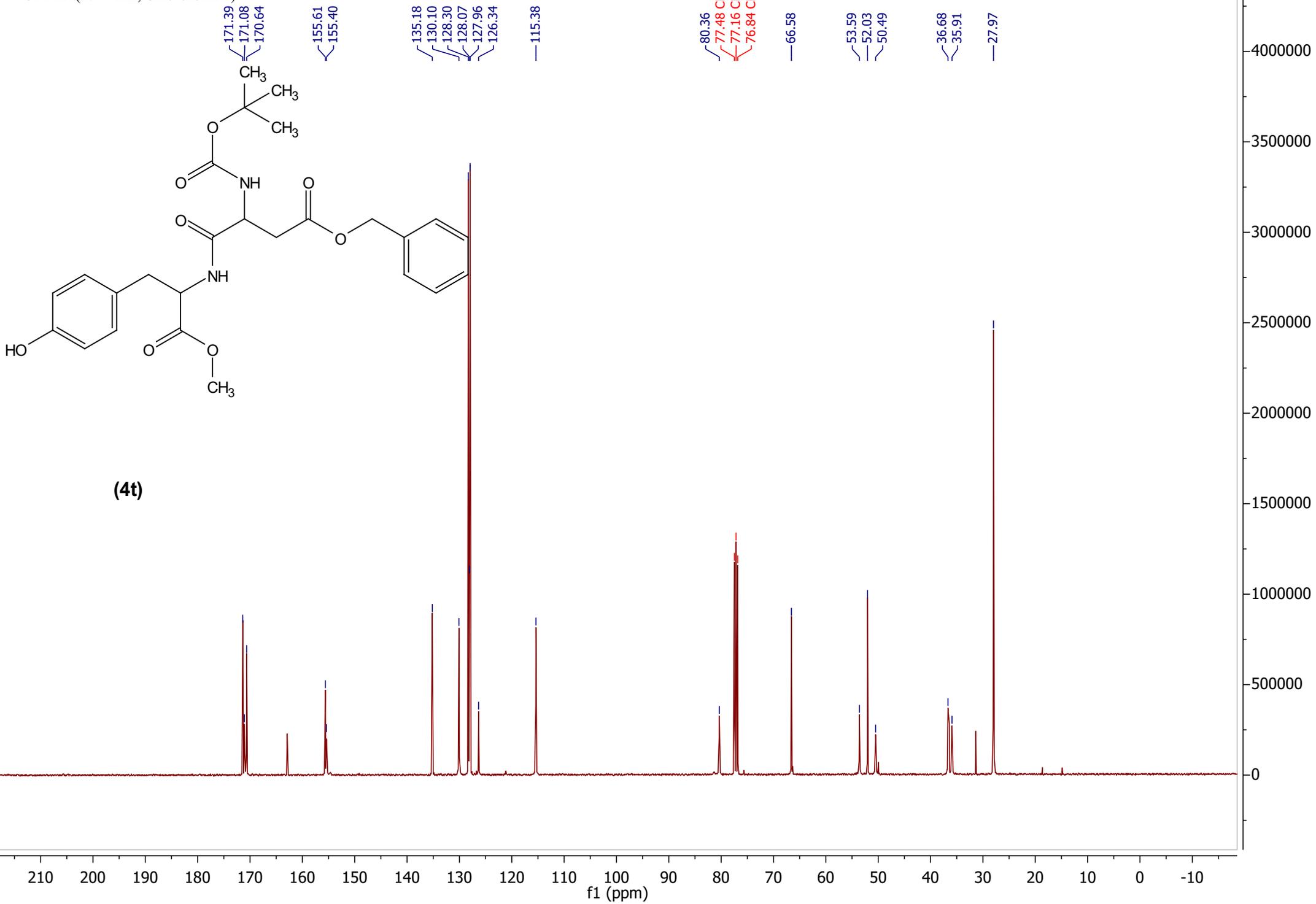
¹H NMR (400 MHz, Chloroform-*d*)



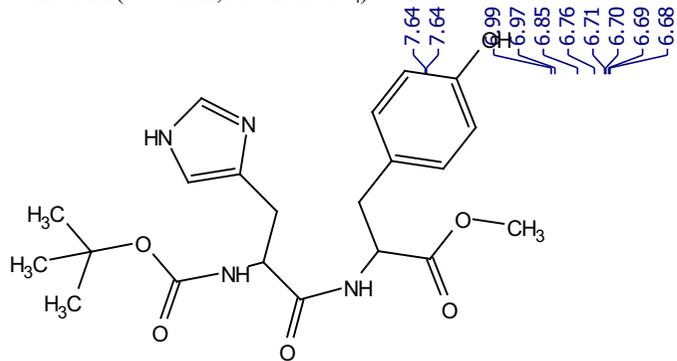
(4t)



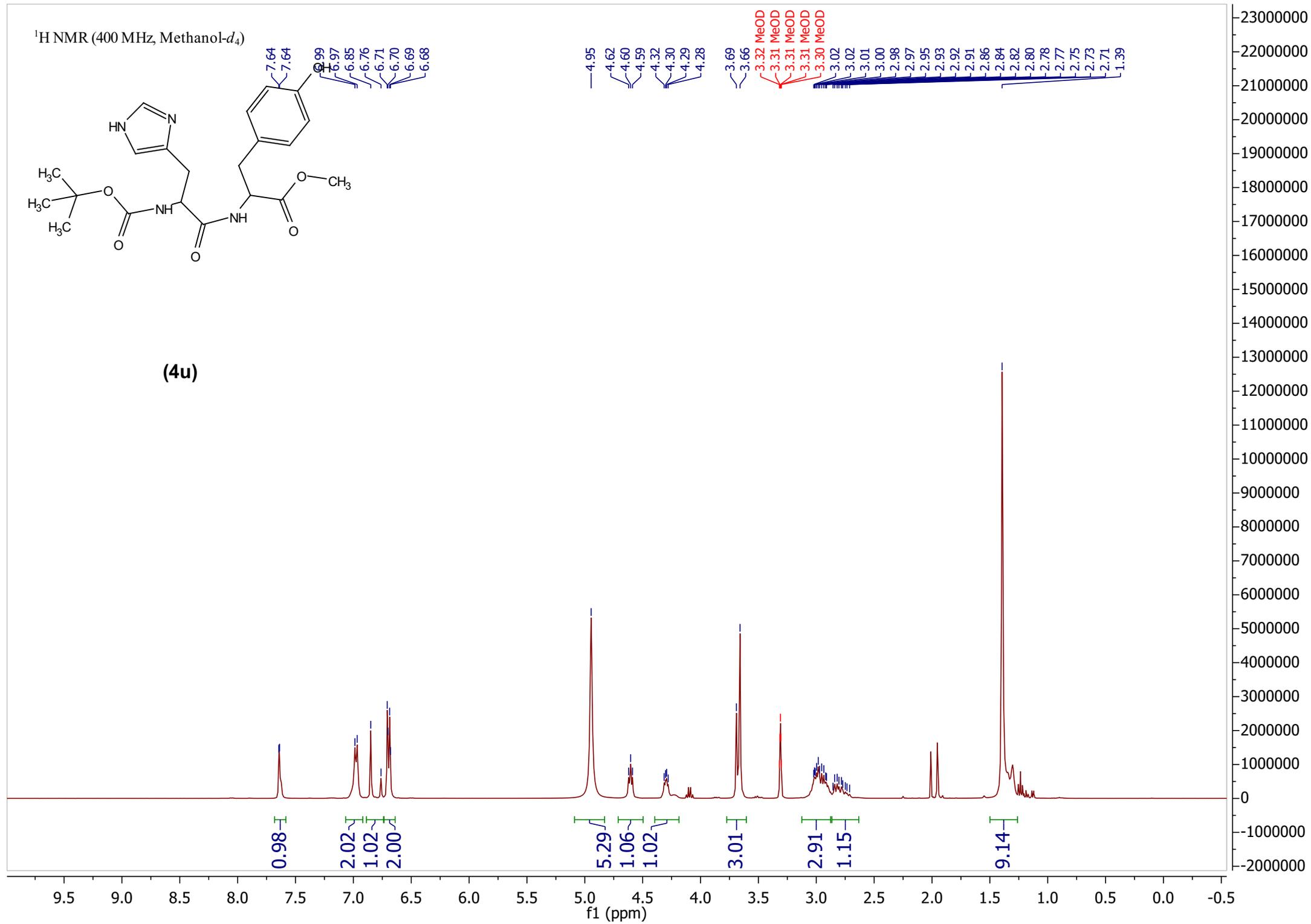
¹³C NMR (101 MHz, Chloroform-*d*)



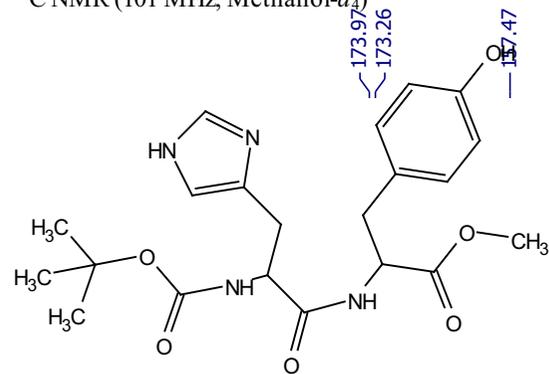
¹H NMR (400 MHz, Methanol-d₄)



(4u)



¹³C NMR (101 MHz, Methanol-*d*₄)



(4u)

136.09
134.34
131.31
131.28
128.34
118.52
116.34
116.30

80.72

55.94
55.31
52.65
49.64 MeOD
49.43 MeOD
49.21 MeOD
49.00 MeOD
48.79 MeOD
48.57 MeOD
48.36 MeOD
37.64

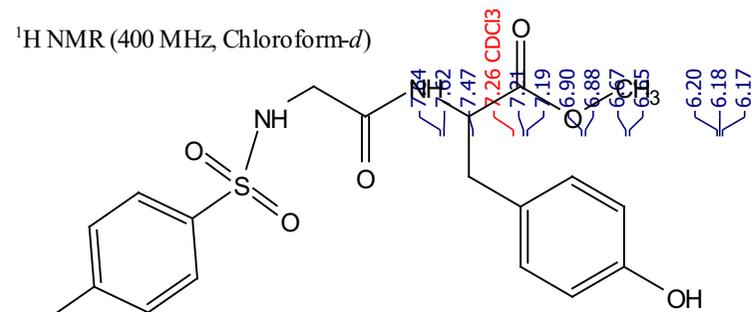
30.53
28.65

14.46

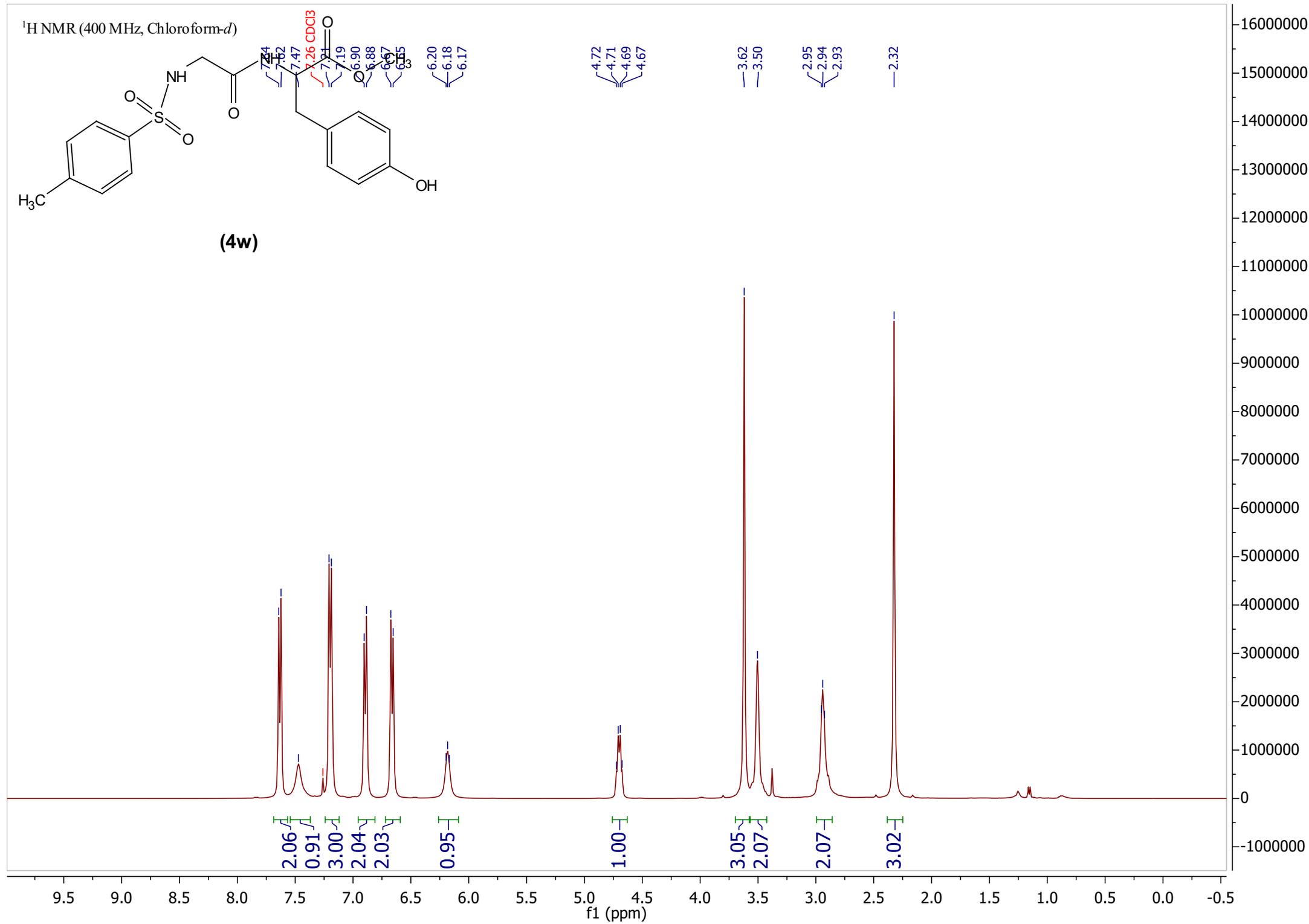
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2800000
2600000
2400000
2200000
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
-200000

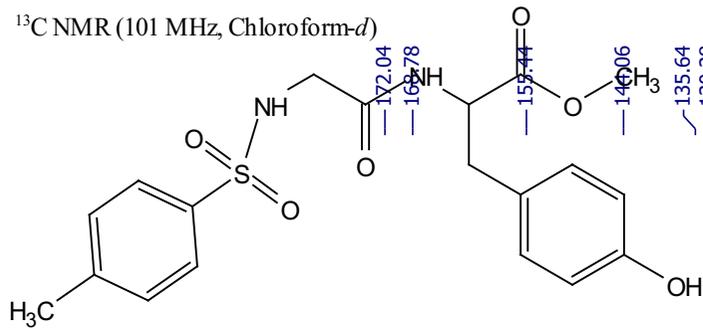
¹H NMR (400 MHz, Chloroform-*d*)



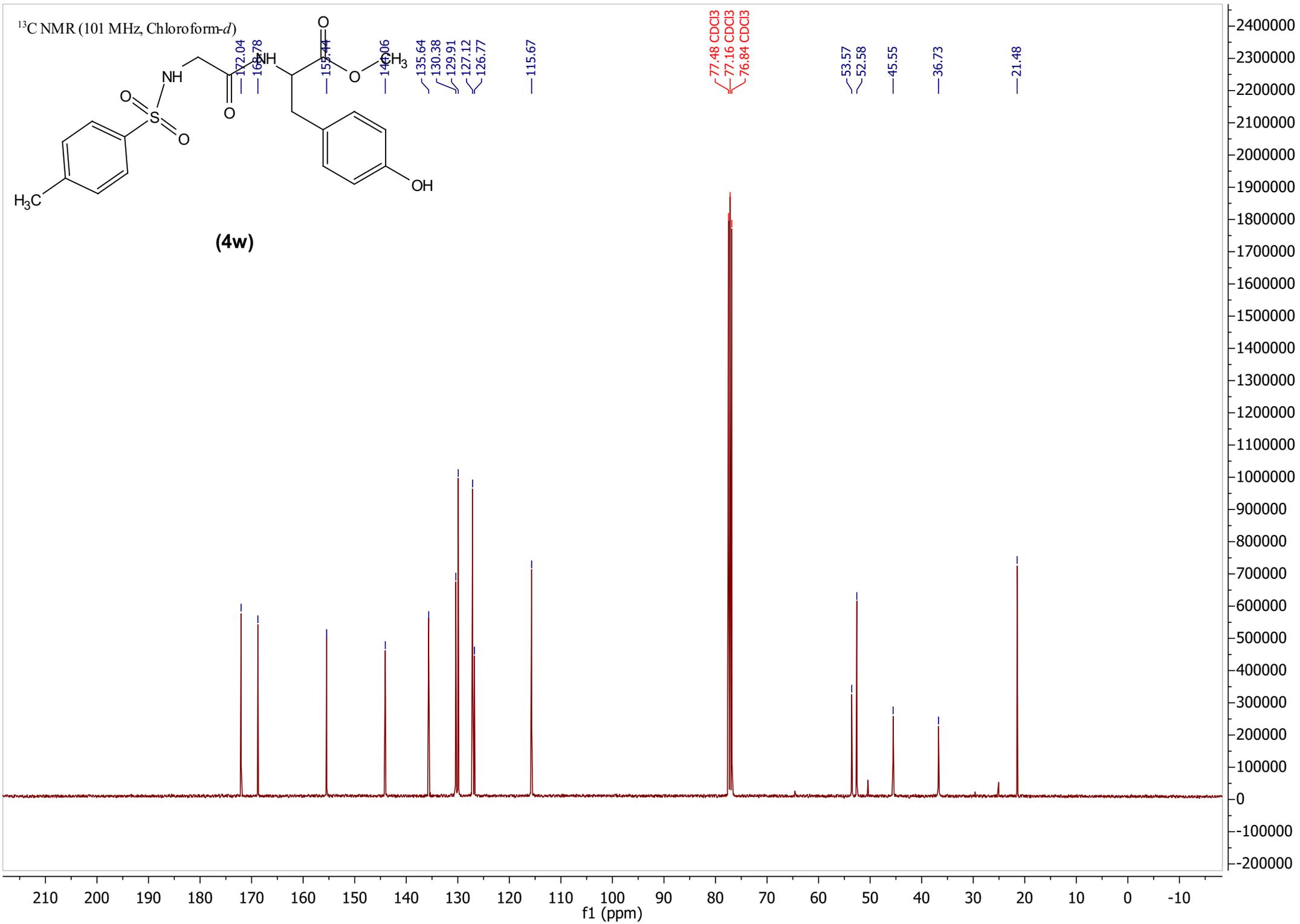
(4w)



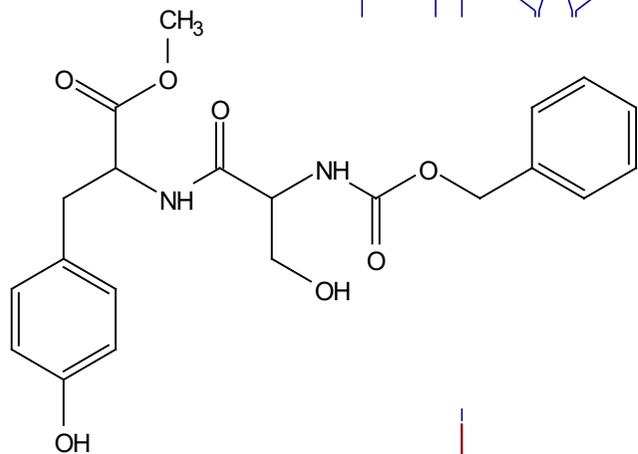
¹³C NMR (101 MHz, Chloroform-*d*)



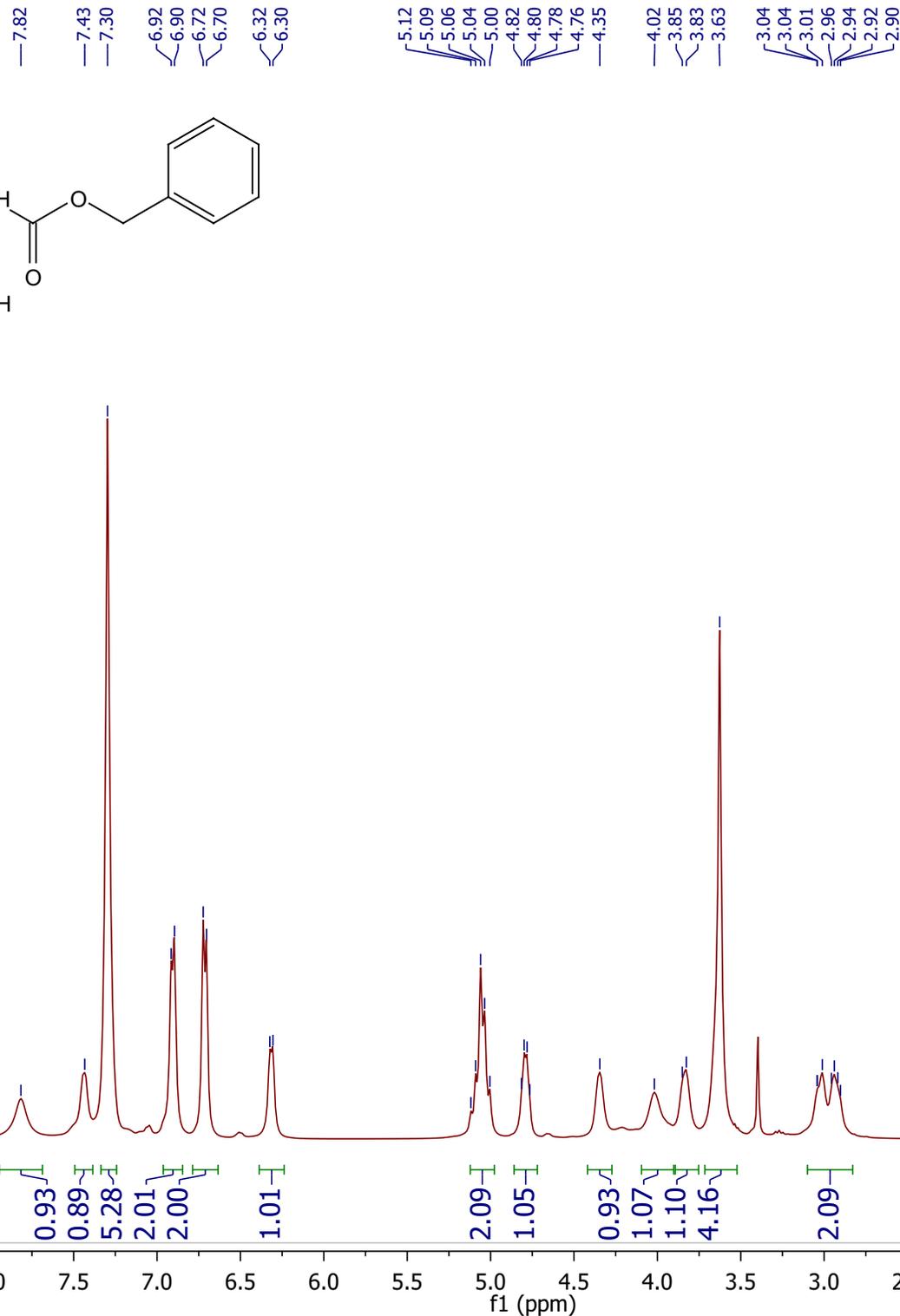
(4w)



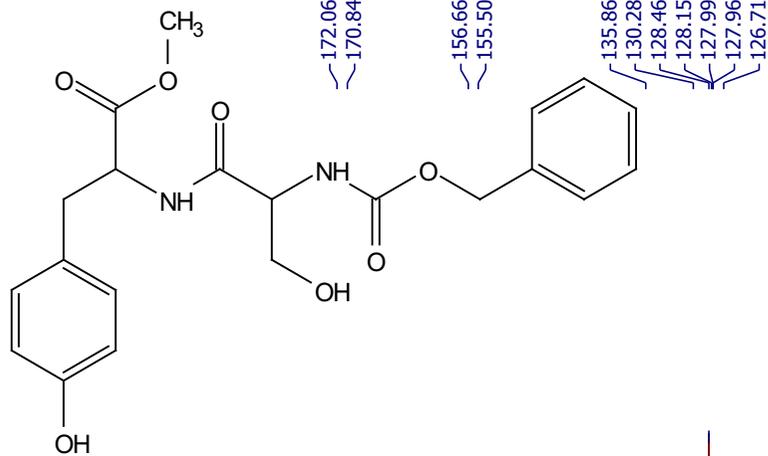
¹H NMR (400 MHz, Chloroform-*d*)



(4x)



¹³C NMR (101 MHz, Chloroform-*d*)



(4x)

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

67.26

62.53

55.98

53.75

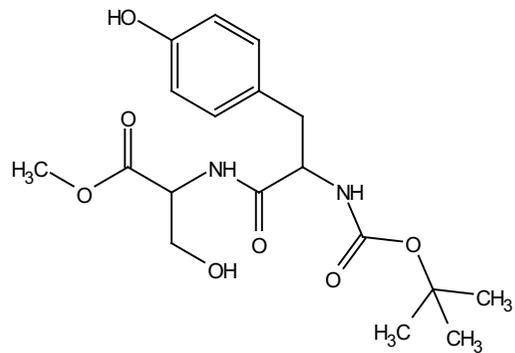
52.45

36.58

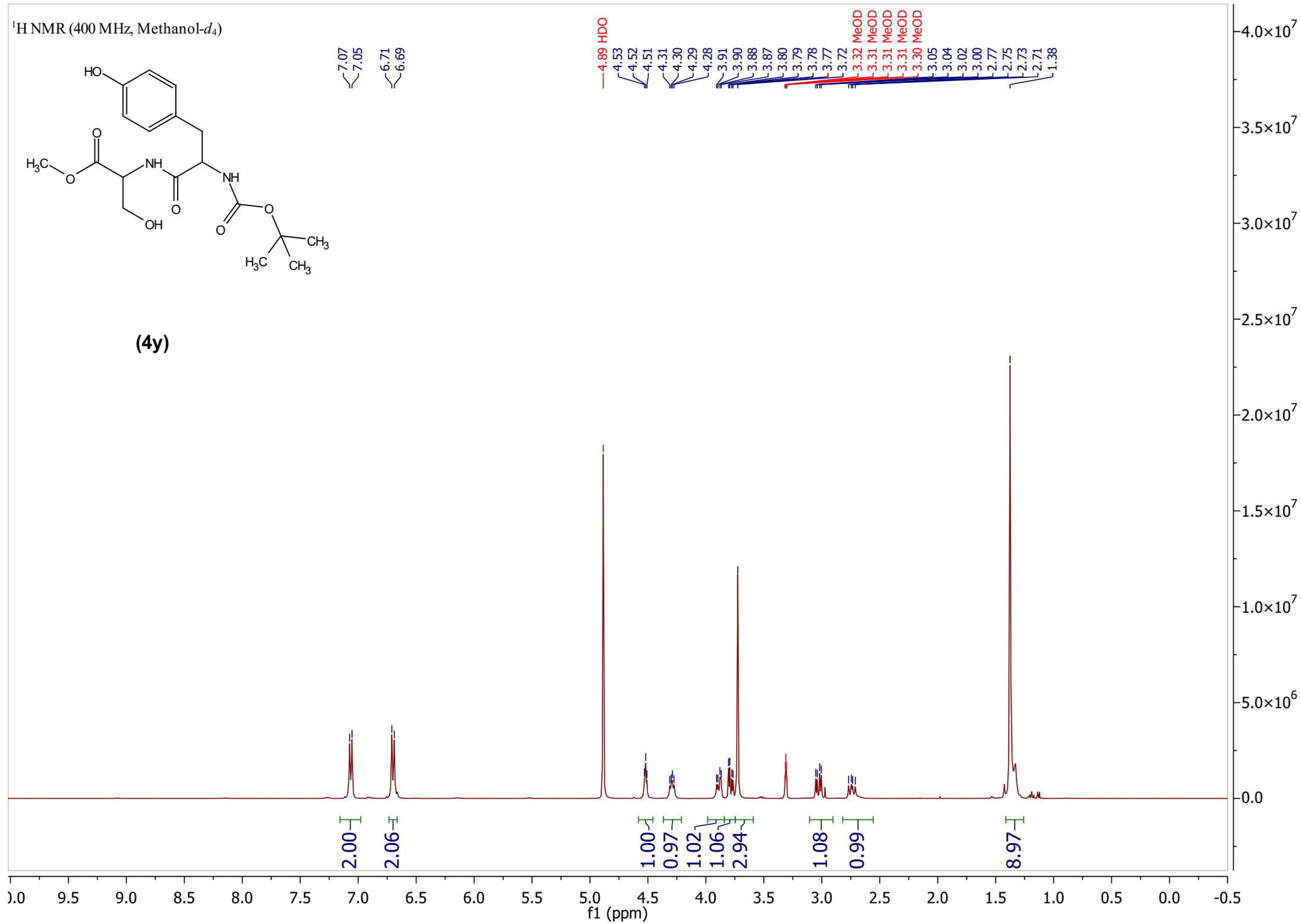
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3000000
2500000
2000000
1500000
1000000
500000
0

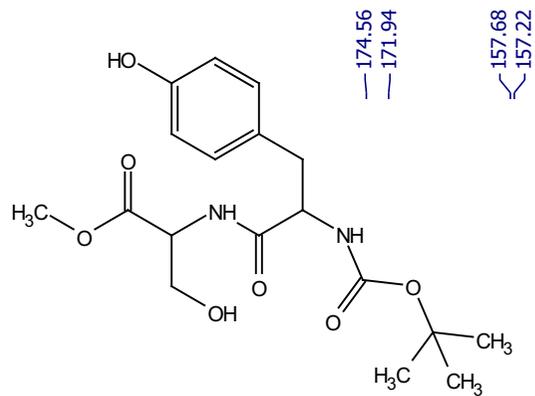
¹H NMR (400 MHz, Methanol-*d*₄)



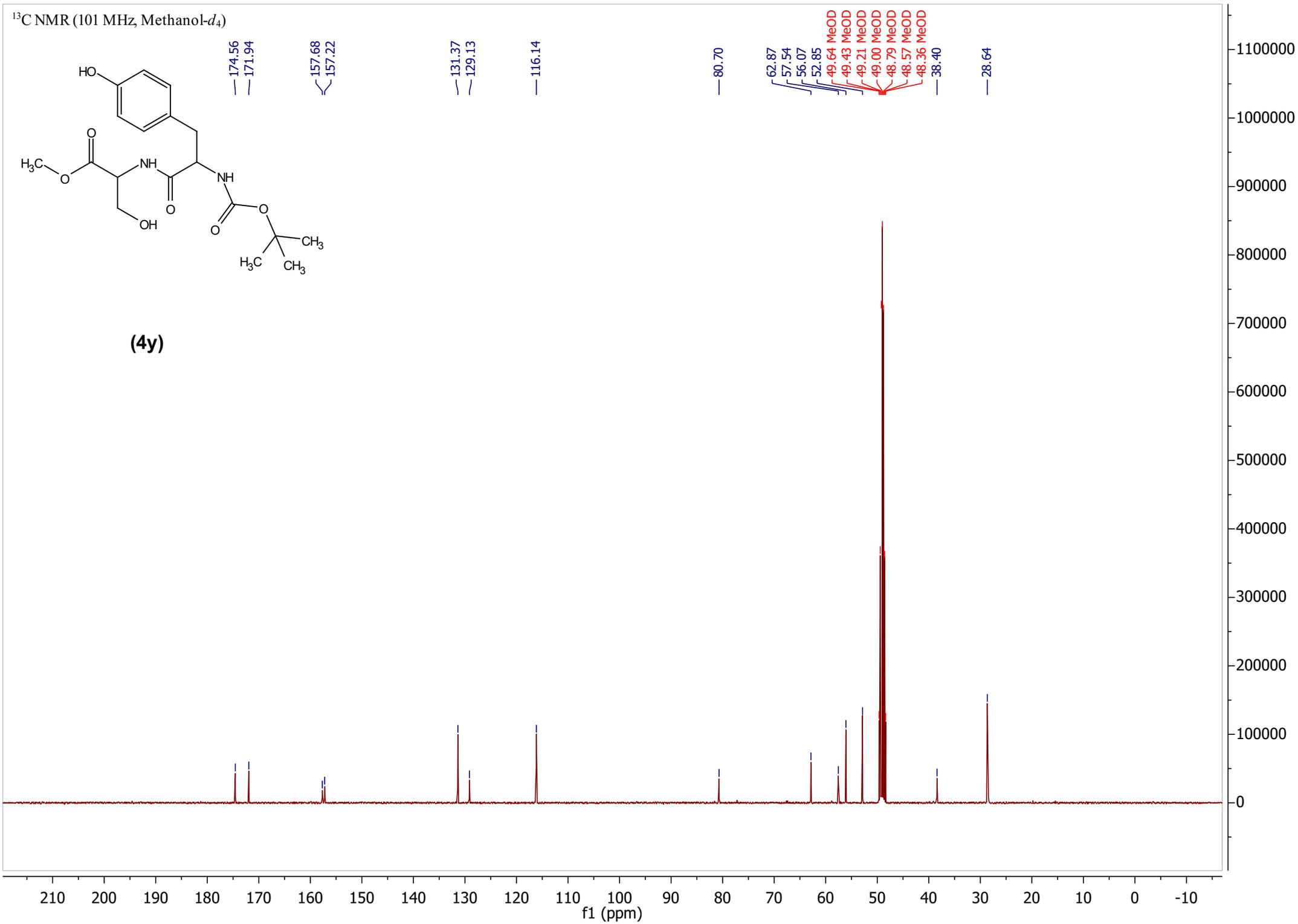
(4y)



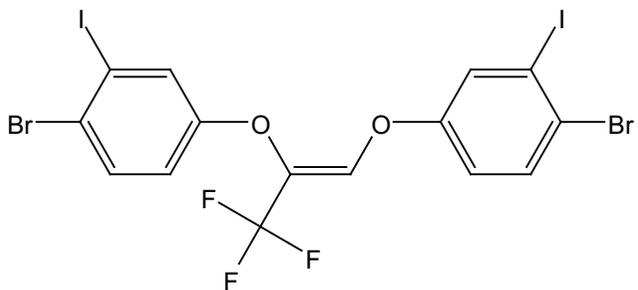
¹³C NMR (101 MHz, Methanol-*d*₄)



(4y)



¹H NMR (400 MHz, Chloroform-*d*)



(3a)

7.55
7.55
7.54
7.53
7.50
7.47
7.46
7.26 CDCl₃
7.11
6.94
6.93
6.91
6.87
6.86
6.85
6.84

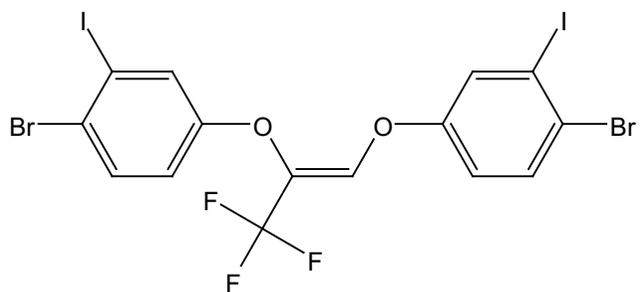
2.98
0.99
1.00
1.04
1.01

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 0.5 0.0

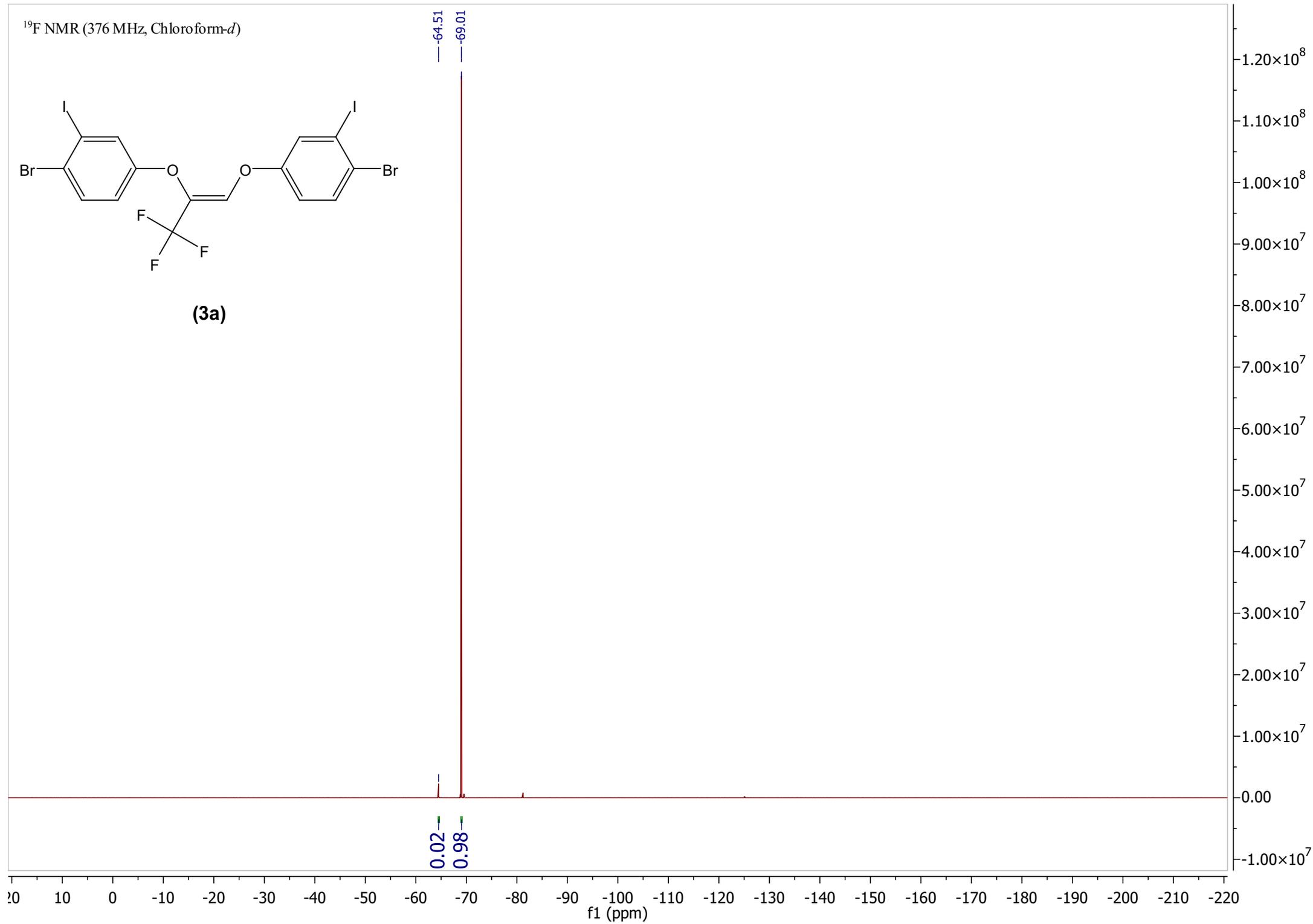
f1 (ppm)

1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

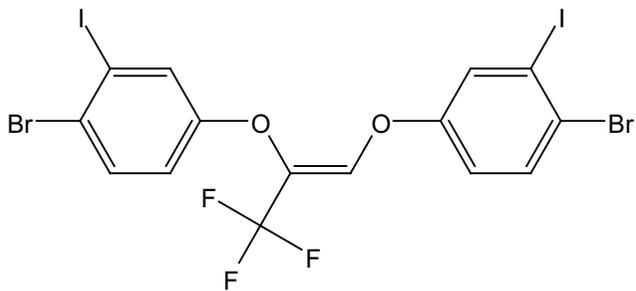
¹⁹F NMR (376 MHz, Chloroform-*d*)



(3a)



¹³C NMR (101 MHz, Chloroform-*d*)



(3a)

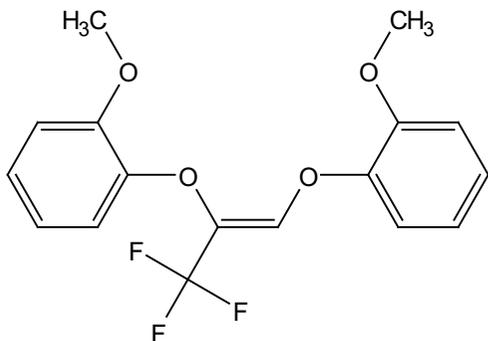
155.27
154.59
137.02
136.97
136.92
136.87
133.34
132.94
128.62
127.76
127.40
127.28
127.05
126.69
125.57
125.05
123.40
122.34
119.63
118.33
116.92
116.89
101.77
101.23

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

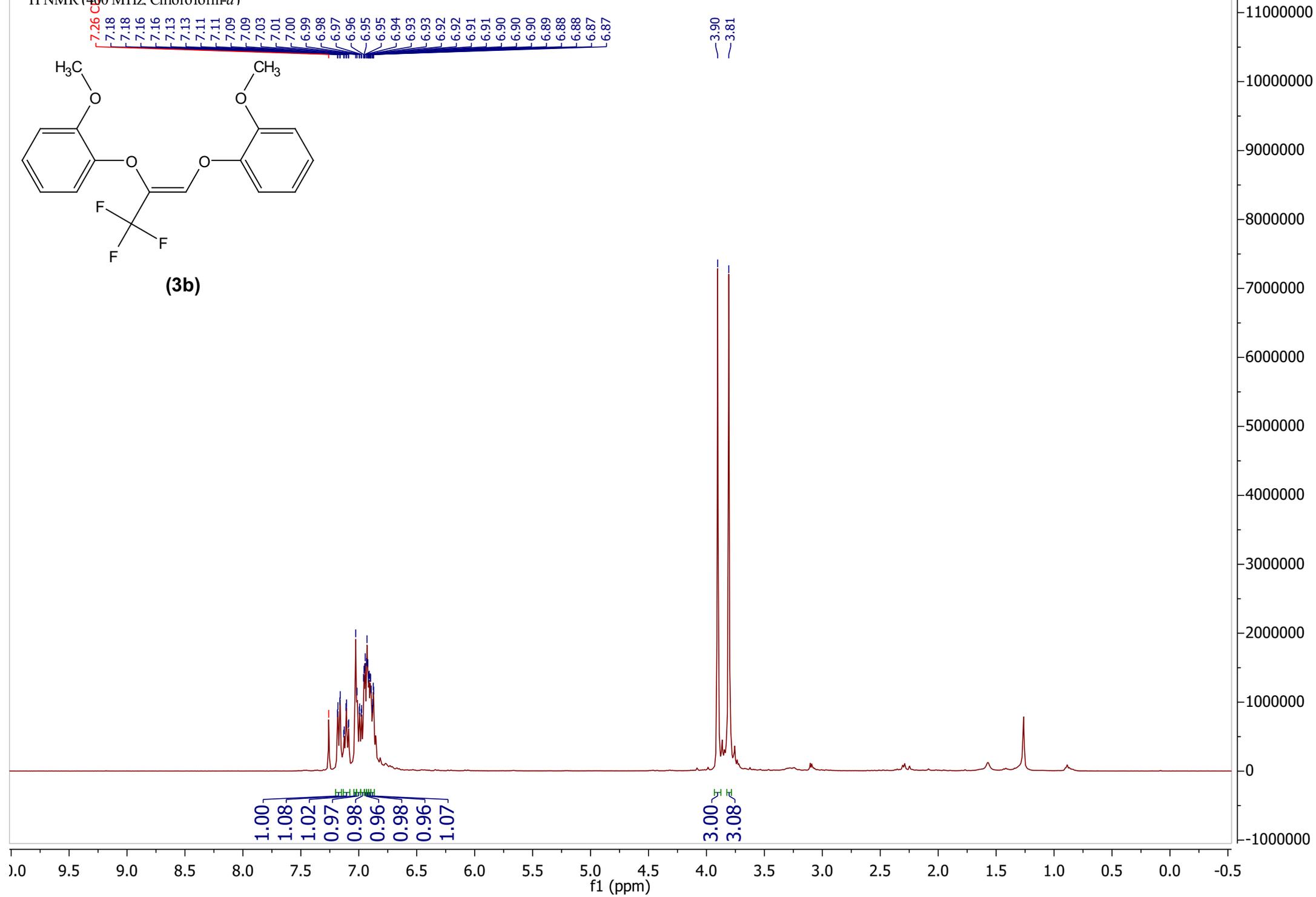
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

450000
400000
350000
300000
250000
200000
150000
100000
50000
0

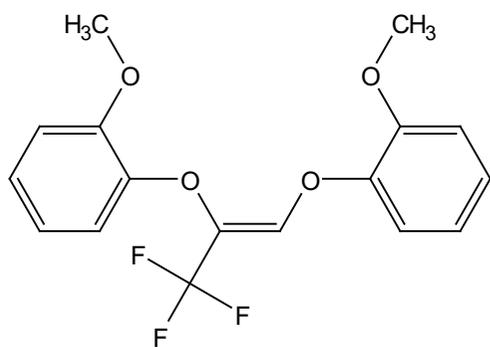
¹H NMR (400 MHz, Chloroform-*d*)



(3b)



^{19}F NMR (376 MHz, Chloroform-*d*)



(3b)

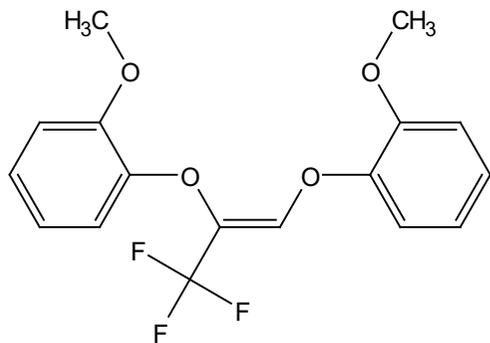
— 64.70
— 68.60

0.03
0.97

f1 (ppm)

2.4×10^7
 2.2×10^7
 2.0×10^7
 1.8×10^7
 1.6×10^7
 1.4×10^7
 1.2×10^7
 1.0×10^7
 8.0×10^6
 6.0×10^6
 4.0×10^6
 2.0×10^6
0.0
 -2.0×10^6

¹³C NMR (101 MHz, Chloroform-*d*)



(3b)

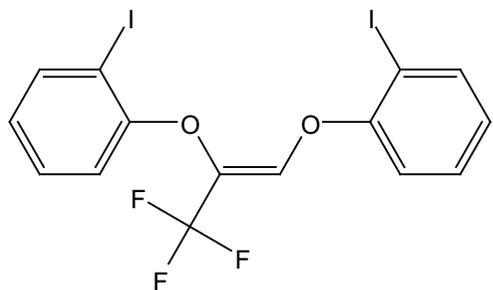
150.53
149.35
146.22
145.93
140.42
140.37
140.32
140.27
126.05
125.91
125.49
125.14
124.78
124.43
123.40
123.21
121.10
120.67
120.51
120.16
117.80
115.10
113.31
112.88

77.48 CDCl3
77.16 CDCl3
76.84 CDCl3

56.32
56.16

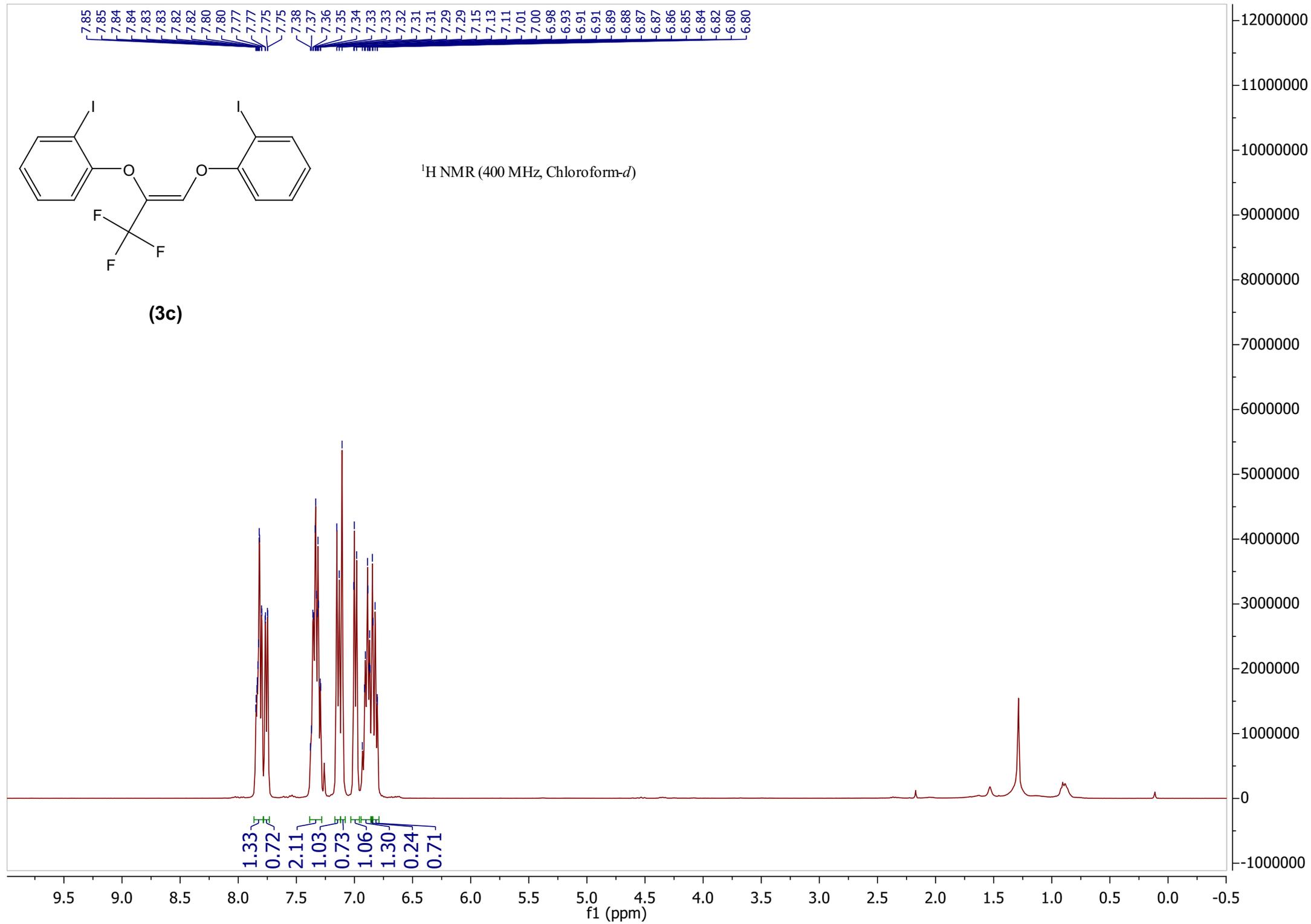
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

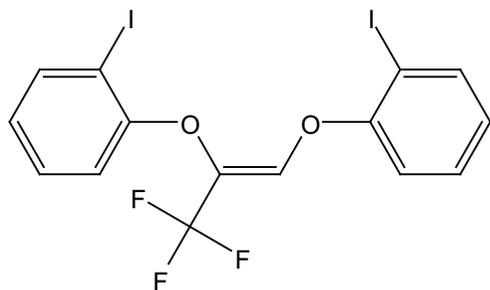


(3c)

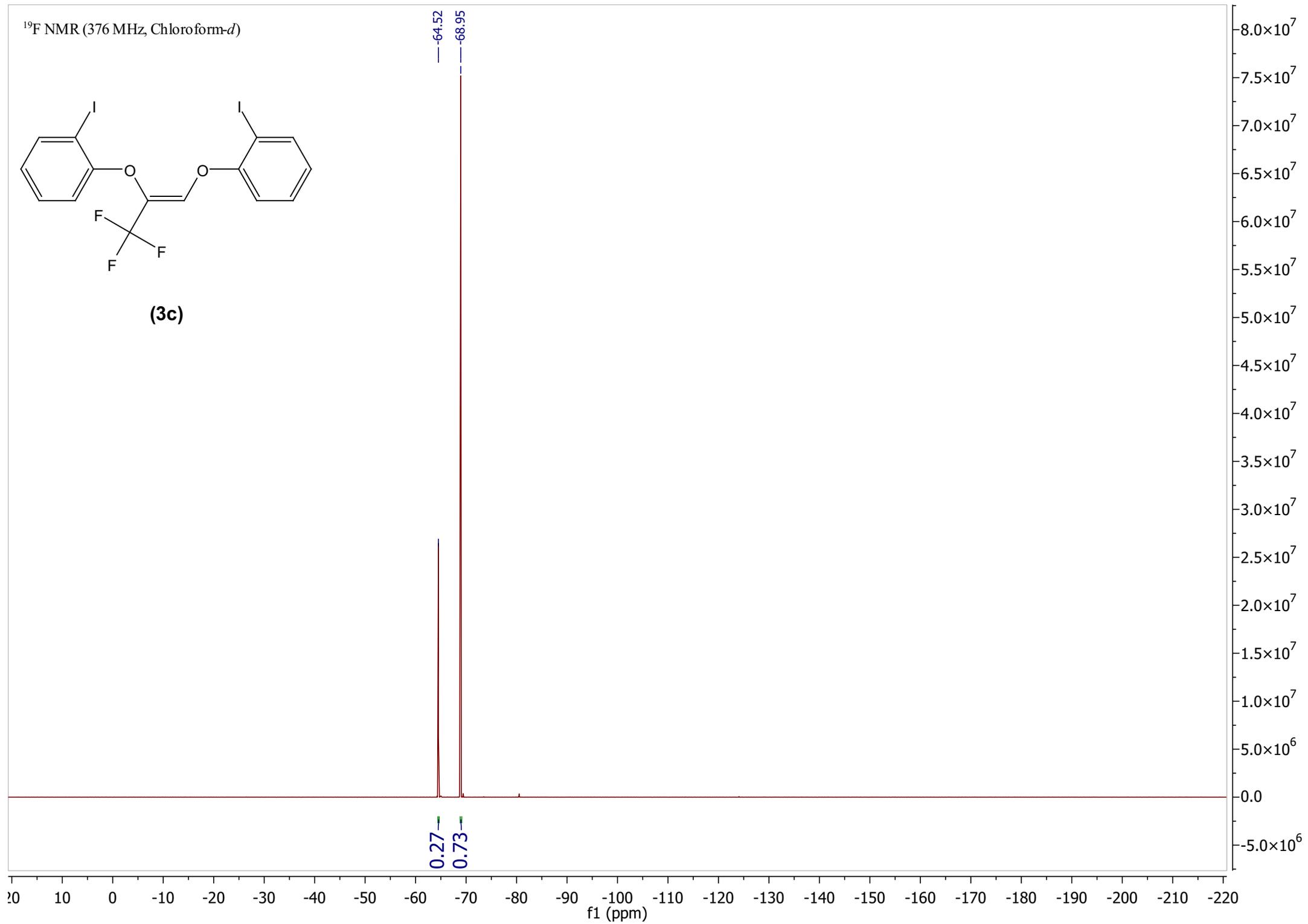
¹H NMR (400 MHz, Chloroform-*d*)



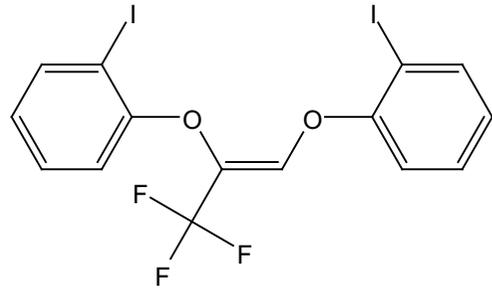
^{19}F NMR (376 MHz, Chloroform-*d*)



(3c)



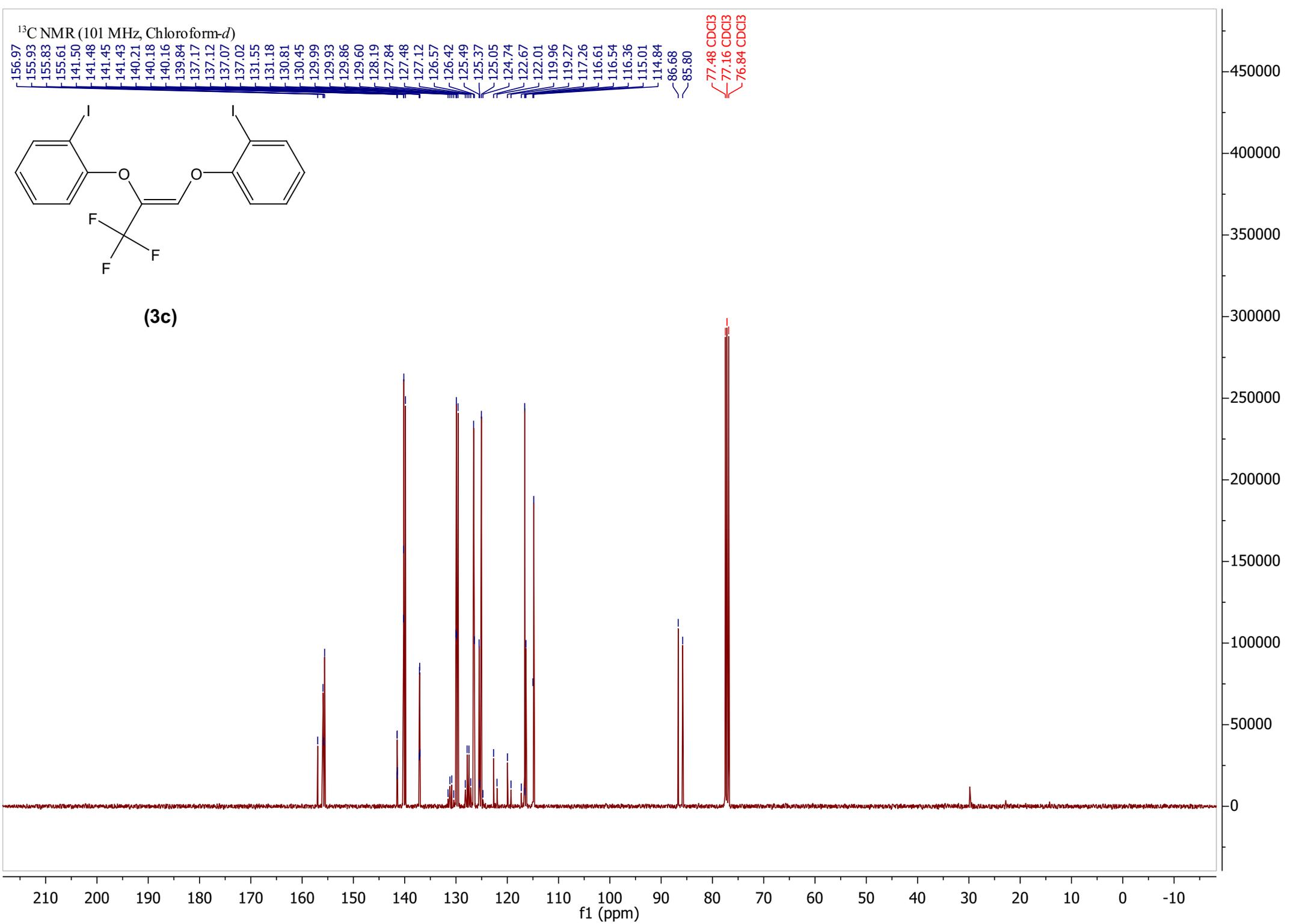
¹³C NMR (101 MHz, Chloroform-*d*)

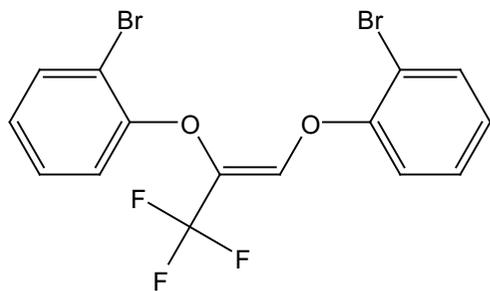


(3c)

156.97
155.93
155.83
155.61
141.50
141.48
141.45
141.43
140.21
140.18
140.16
139.84
137.17
137.12
137.07
137.02
131.55
131.18
130.81
130.45
129.99
129.93
129.86
129.60
128.19
127.84
127.48
127.12
126.57
126.42
125.49
125.37
125.05
124.74
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116.61
116.54
116.36
115.01
114.84
86.68
85.80

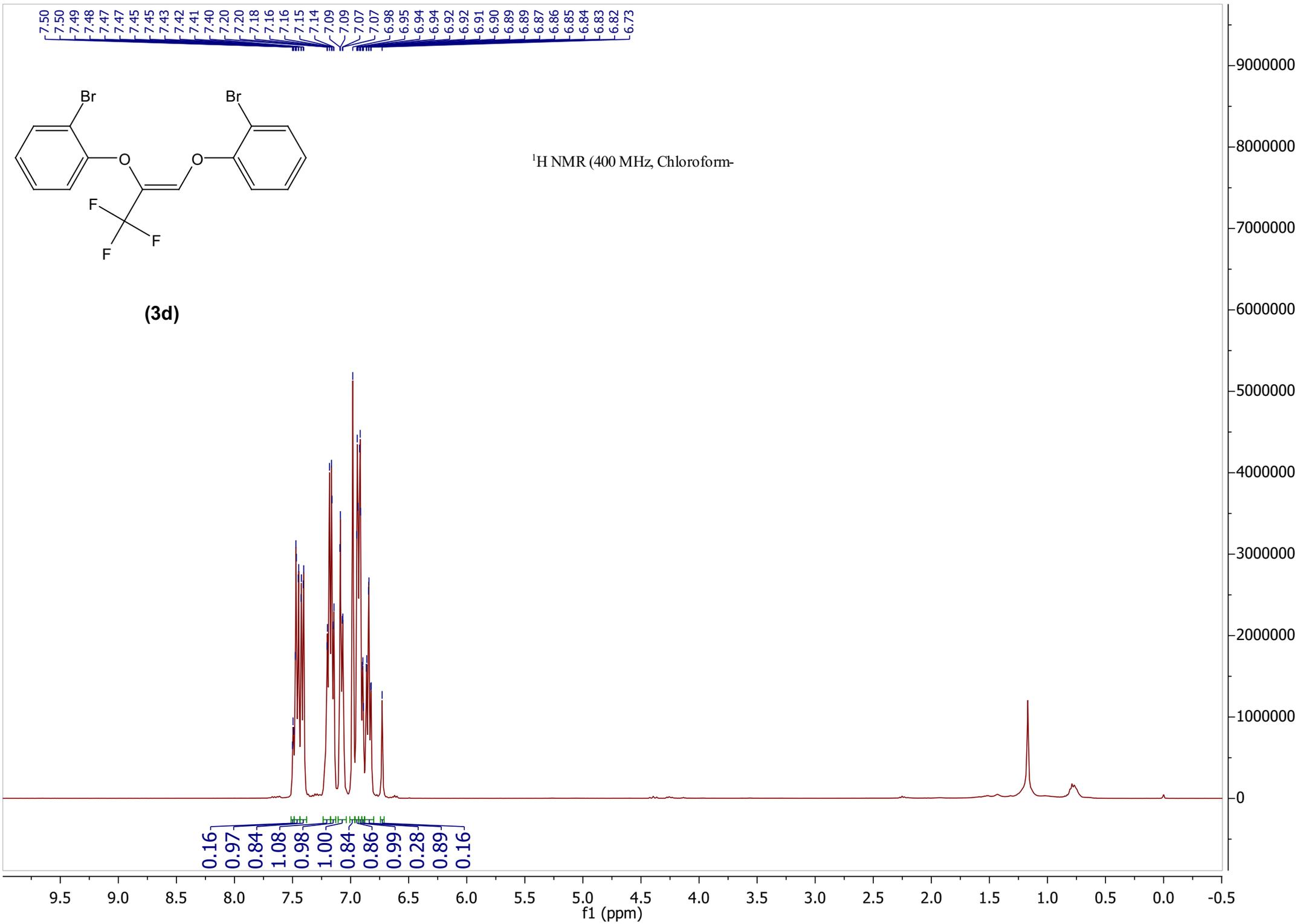
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃



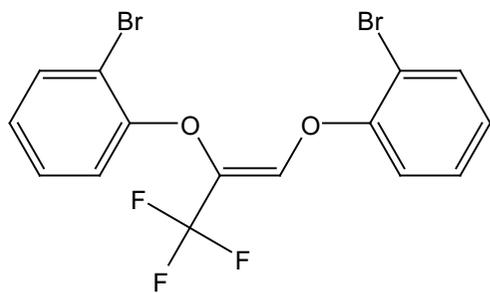


(3d)

¹H NMR (400 MHz, Chloroform-



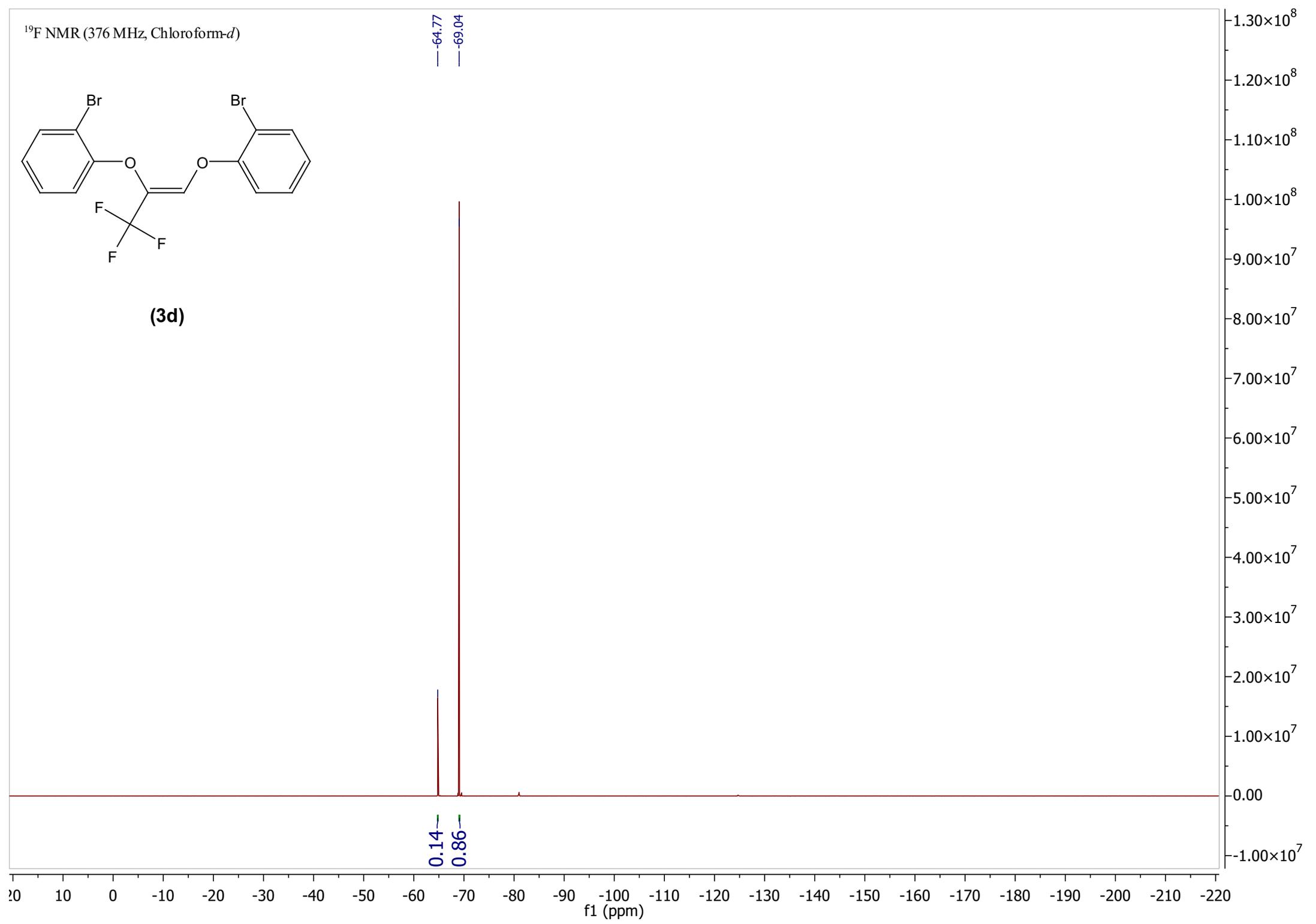
^{19}F NMR (376 MHz, Chloroform-*d*)



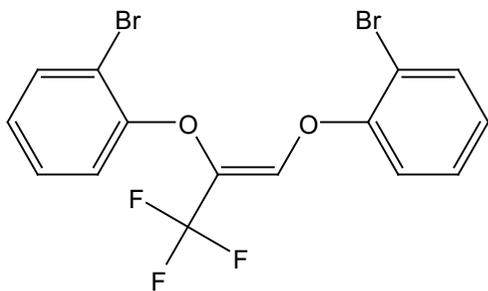
(3d)

—64.77
—69.04

0.14
0.86



¹³C NMR (101 MHz, Chloroform-*d*)

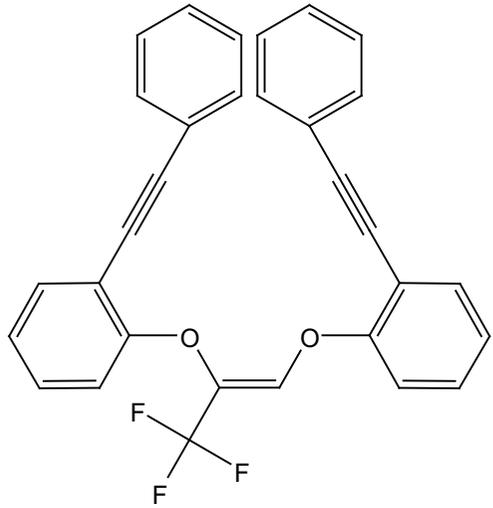


(3d)

154.43
153.42
153.35
153.17
141.46
141.44
141.42
141.40
137.56
137.51
137.46
137.41
134.15
134.11
134.07
133.77
131.56
131.19
130.83
130.46
128.99
128.96
128.86
128.51
127.86
127.50
127.15
126.79
126.33
126.06
125.39
125.07
124.80
124.55
122.68
122.04
119.98
119.31
118.21
117.64
117.28
116.58
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113.39
113.31
112.36
112.17
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3

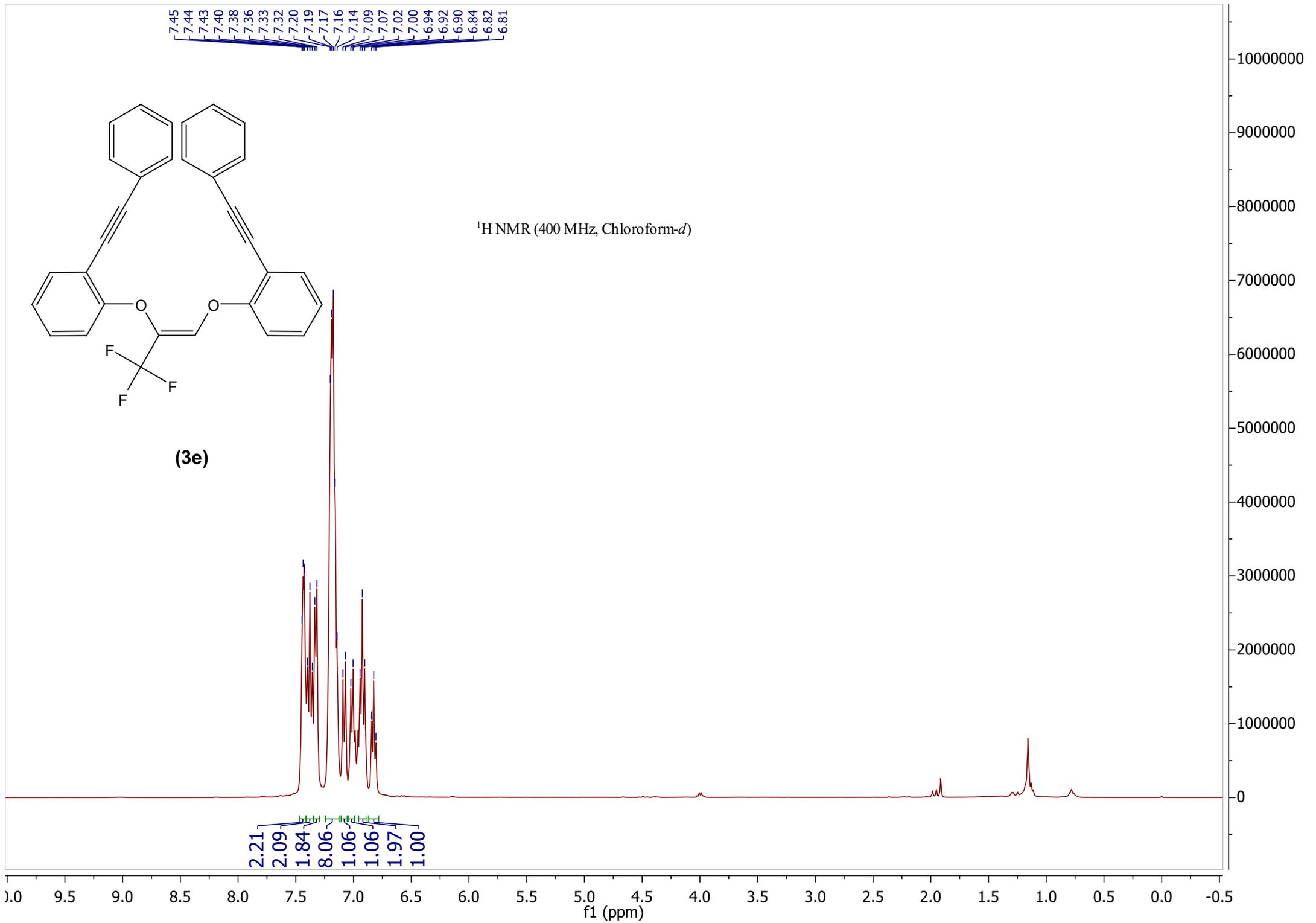
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

380000
360000
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
-40000

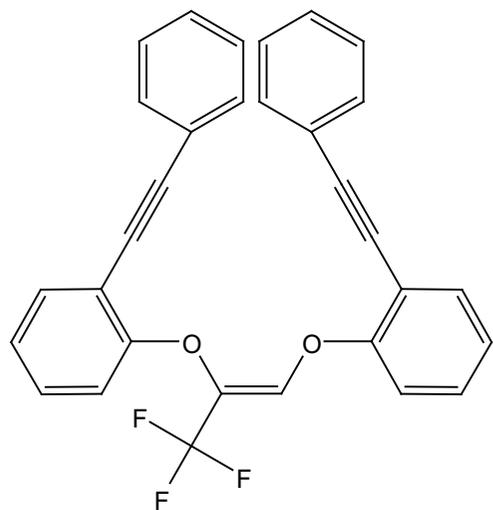


(3e)

¹H NMR (400 MHz, Chloroform-*d*)

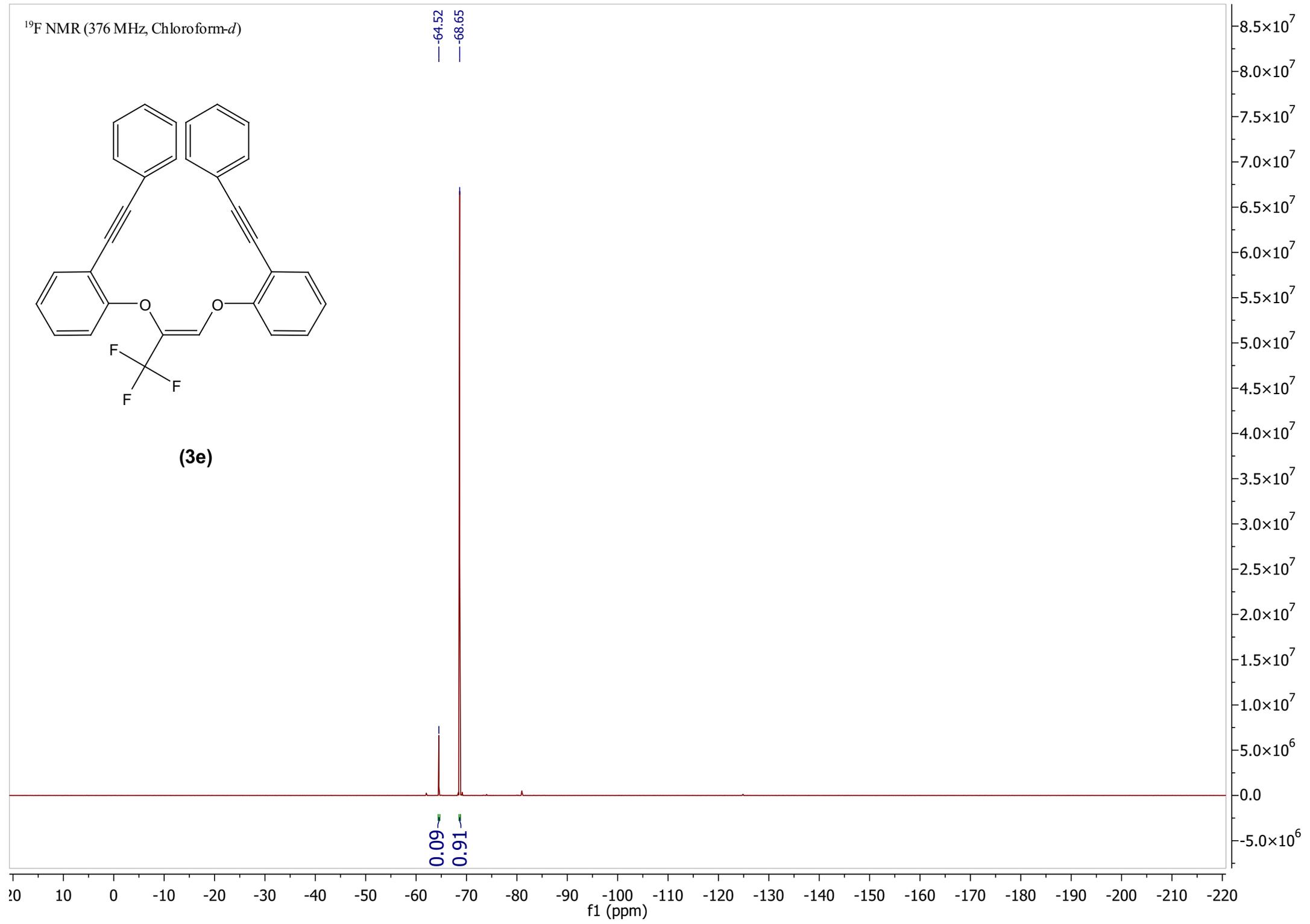


^{19}F NMR (376 MHz, Chloroform-*d*)

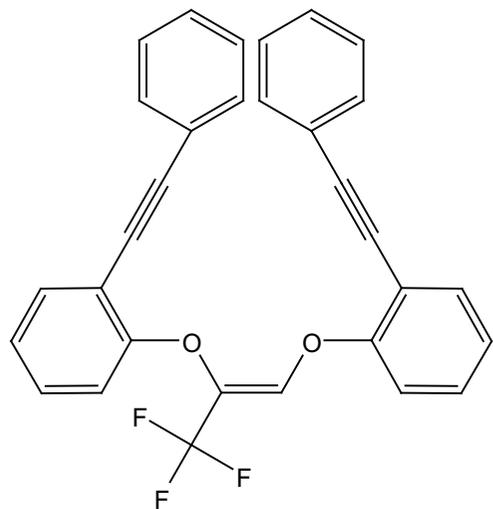


(3e)

— 64.52
— 68.65
0.09
0.91



¹³C NMR (101 MHz, Chloroform-*d*)



(3e)

157.03
156.68
138.89
138.84
138.79
138.74
133.89
133.49
131.80
131.72
129.87
129.49
128.76
128.46
128.38
128.32
126.57
126.21
125.86
125.74
125.51
125.03
123.64
123.04
122.94
122.78
120.33
117.91
117.62
114.84
114.31
113.51
95.46
94.34

84.94

83.92

77.48 CDCl₃

77.16 CDCl₃

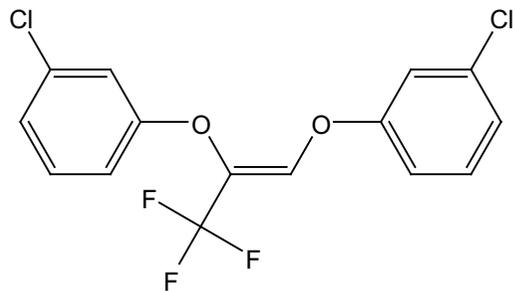
76.84 CDCl₃

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

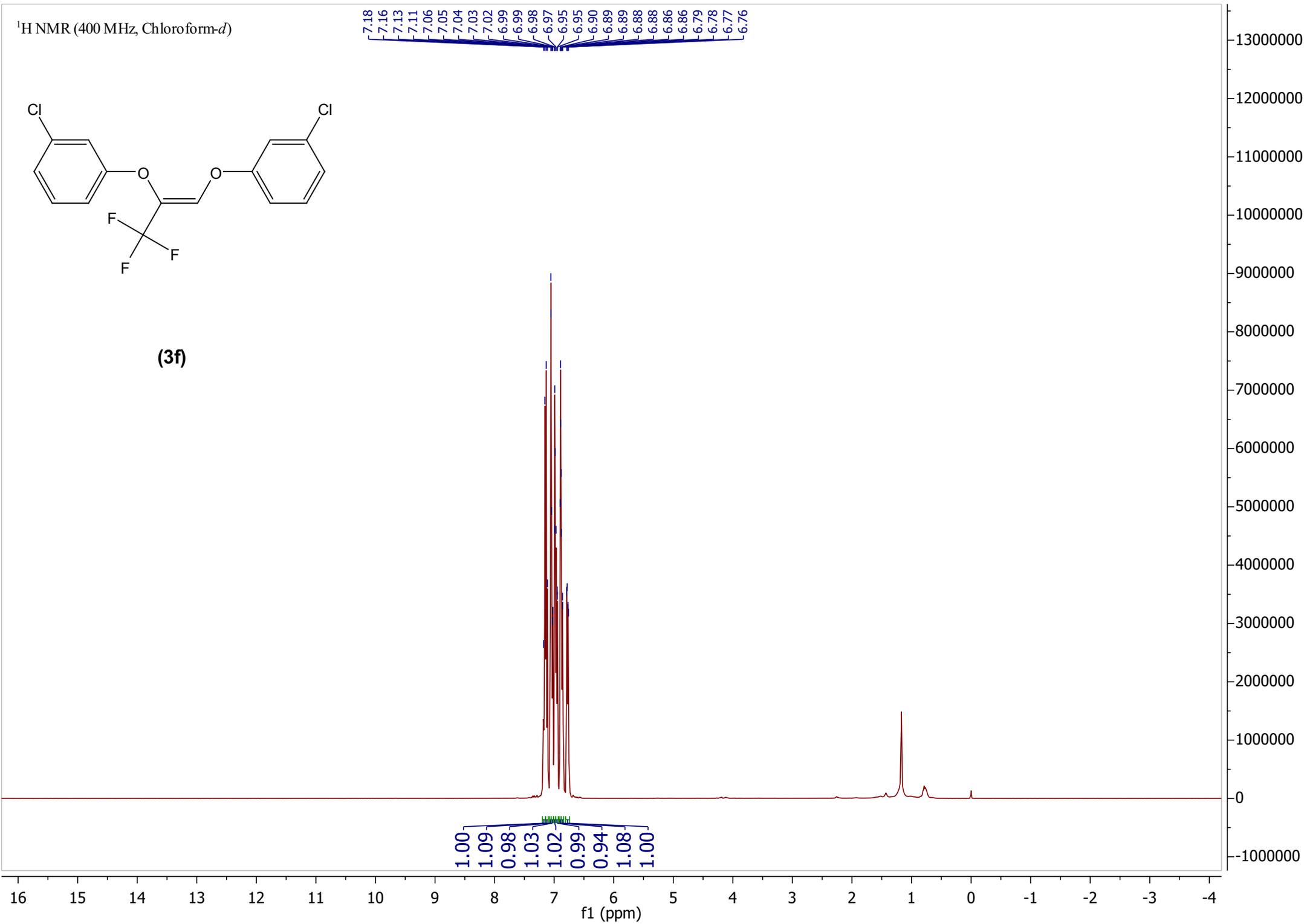
f1 (ppm)

1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

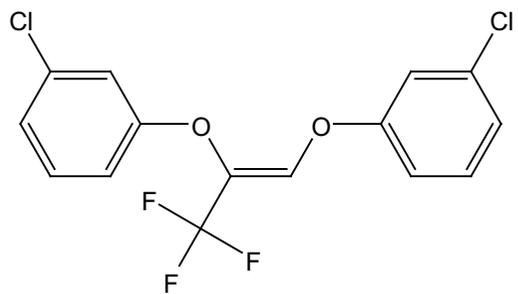
¹H NMR (400 MHz, Chloroform-*d*)



(3f)

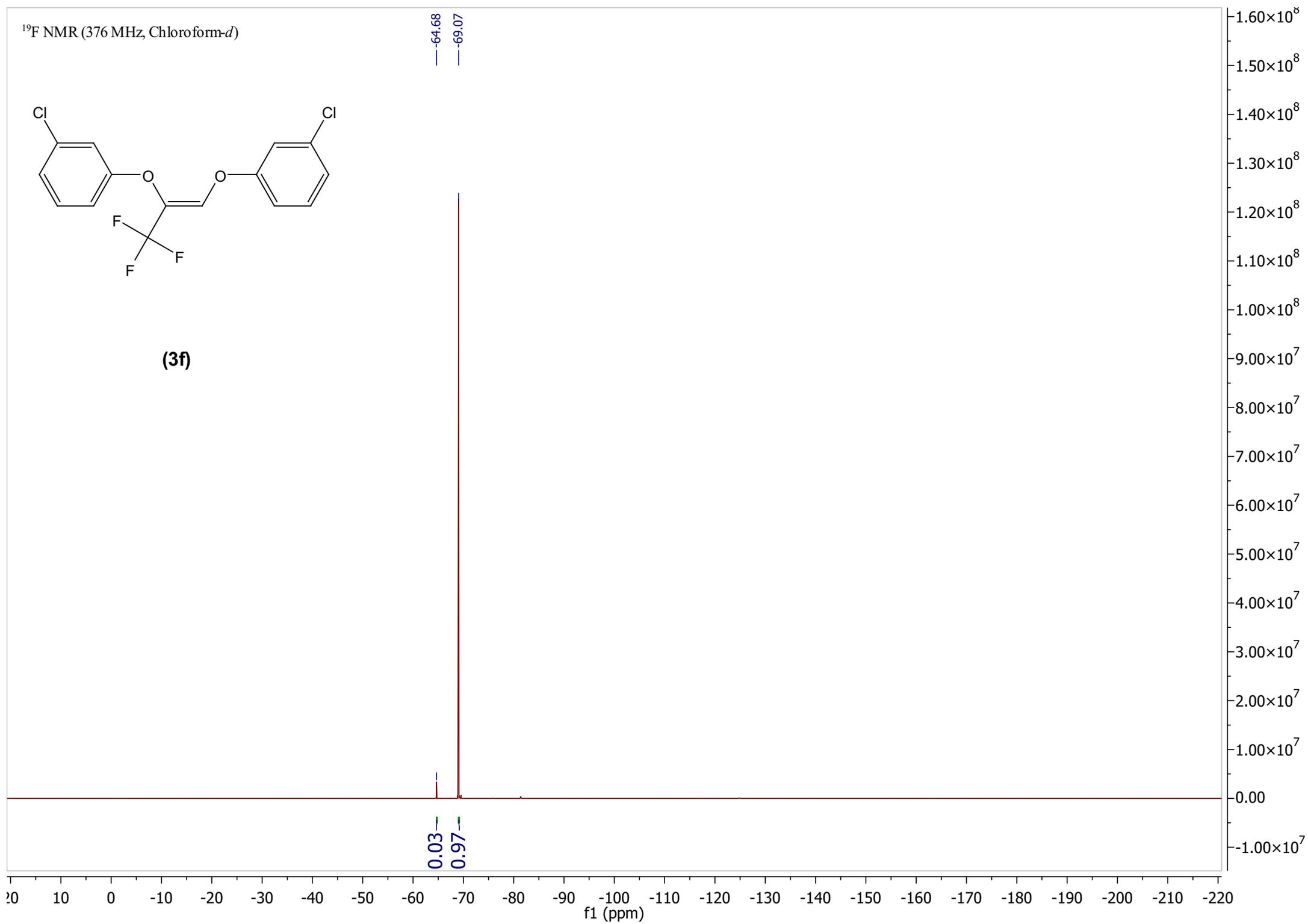


¹⁹F NMR (376 MHz, Chloroform-*d*)

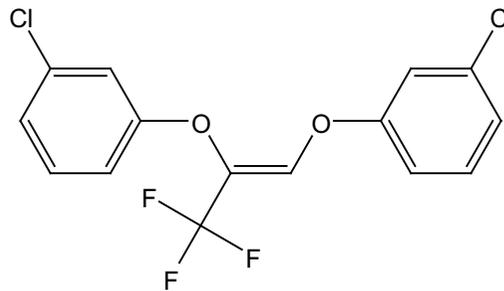


(3f)

64.68
69.07
0.03
0.97



¹³C NMR (101 MHz, Chloroform-*d*)



(3f)

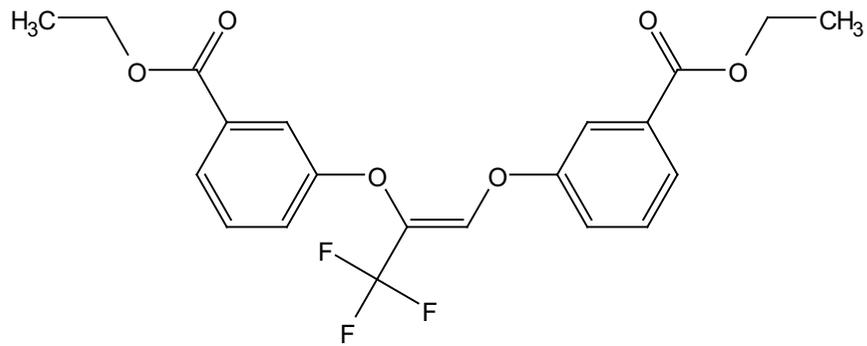
157.26
156.60
137.32
137.28
137.23
137.18
135.57
135.14
130.92
130.48
127.68
127.32
126.96
126.61
125.38
125.22
123.58
122.68
119.97
117.76
117.27
116.27
115.23
113.85

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

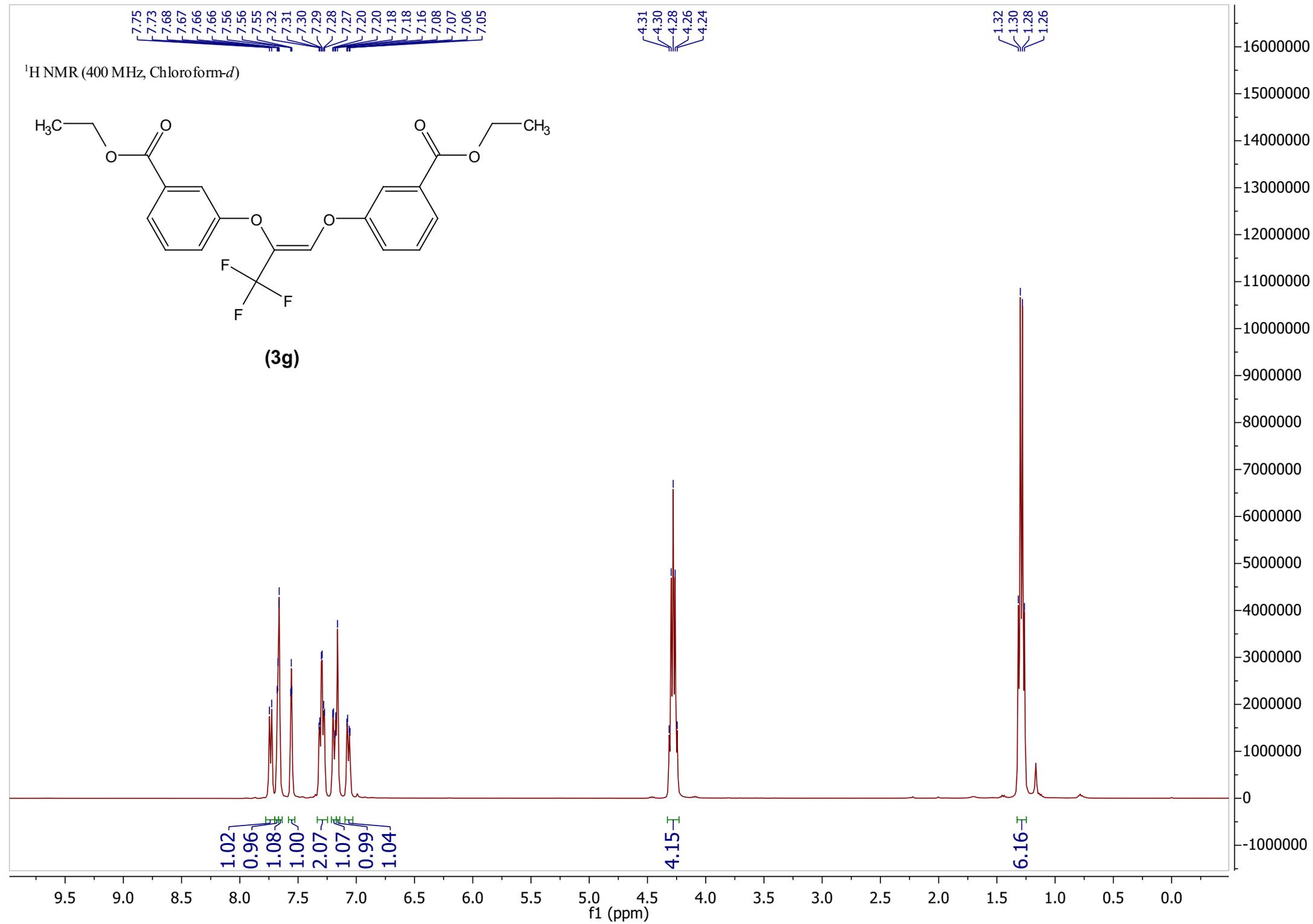
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

380000
360000
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

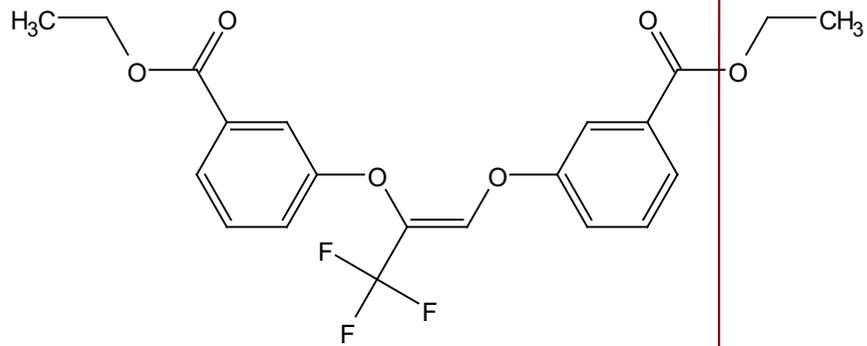
¹H NMR (400 MHz, Chloroform-*d*)



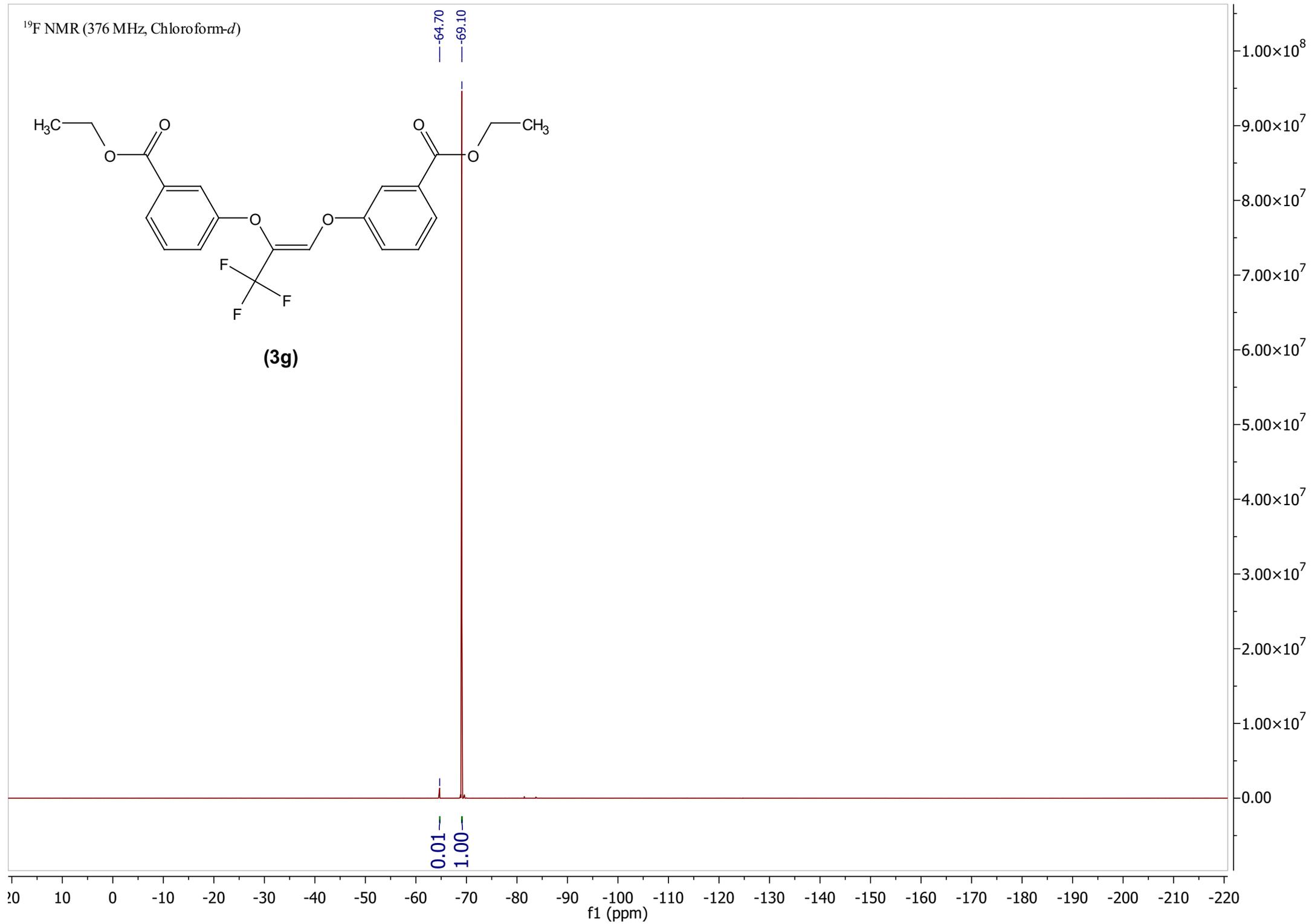
(3g)



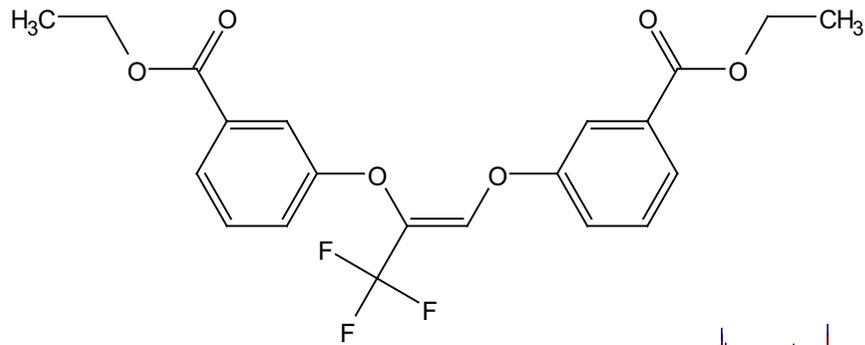
¹⁹F NMR (376 MHz, Chloroform-*d*)



(3g)



¹³C NMR (101 MHz, Chloroform-*d*)



(3g)

165.95
165.53
156.62
156.10
137.53
137.48
137.43
137.38
132.66
132.25
130.09
129.63
127.51
127.15
126.80
126.44
126.44
125.94
125.47
124.40
122.76
121.67
120.07
120.06
117.68
117.35
116.43

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

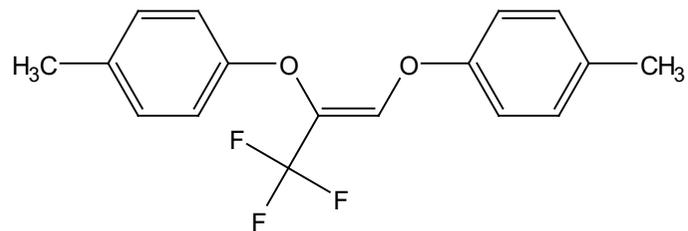
61.53
61.26

14.34

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

¹H NMR (400 MHz, Chloroform-*d*)



(3h)

7.26 CDCl₃
7.15
7.15
7.13
7.13
7.11
7.11
7.02
7.00
6.92
6.91
6.89

2.33
2.32

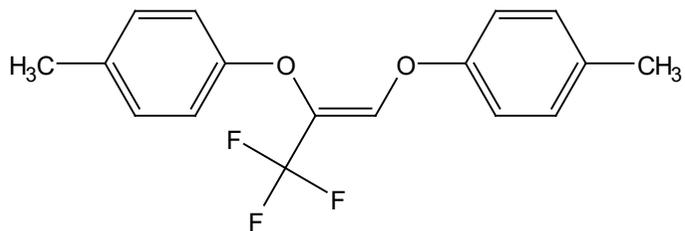
5.00
2.08
1.98

6.02

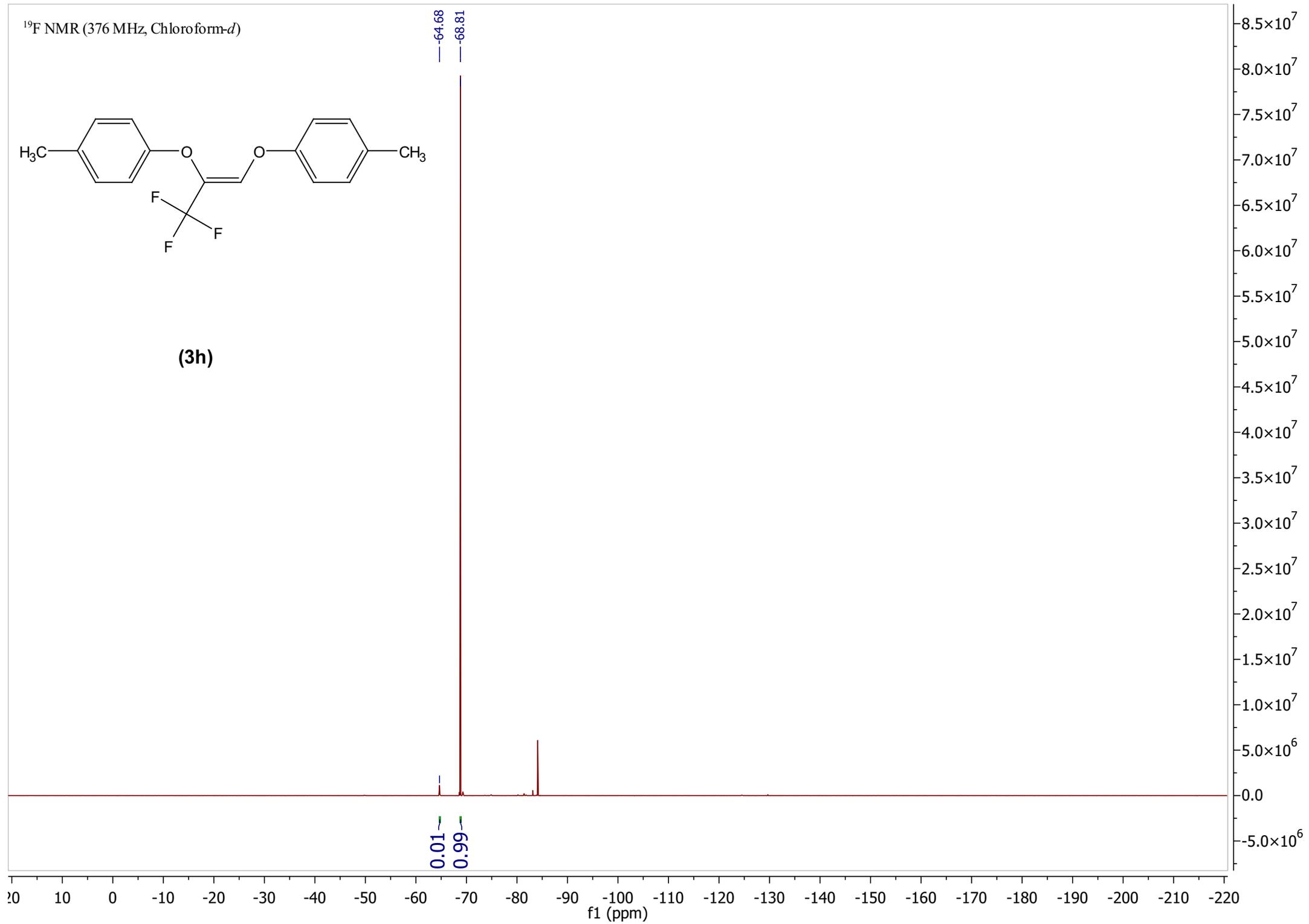
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

3.0 × 10⁷
3.4 × 10⁷
3.2 × 10⁷
3.0 × 10⁷
2.8 × 10⁷
2.6 × 10⁷
2.4 × 10⁷
2.2 × 10⁷
2.0 × 10⁷
1.8 × 10⁷
1.6 × 10⁷
1.4 × 10⁷
1.2 × 10⁷
1.0 × 10⁷
8.0 × 10⁶
6.0 × 10⁶
4.0 × 10⁶
2.0 × 10⁶
0.0
-2.0 × 10⁶

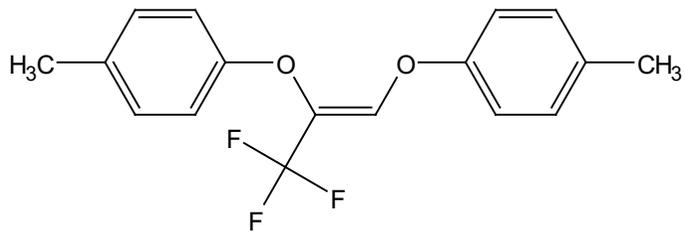
^{19}F NMR (376 MHz, Chloroform-*d*)



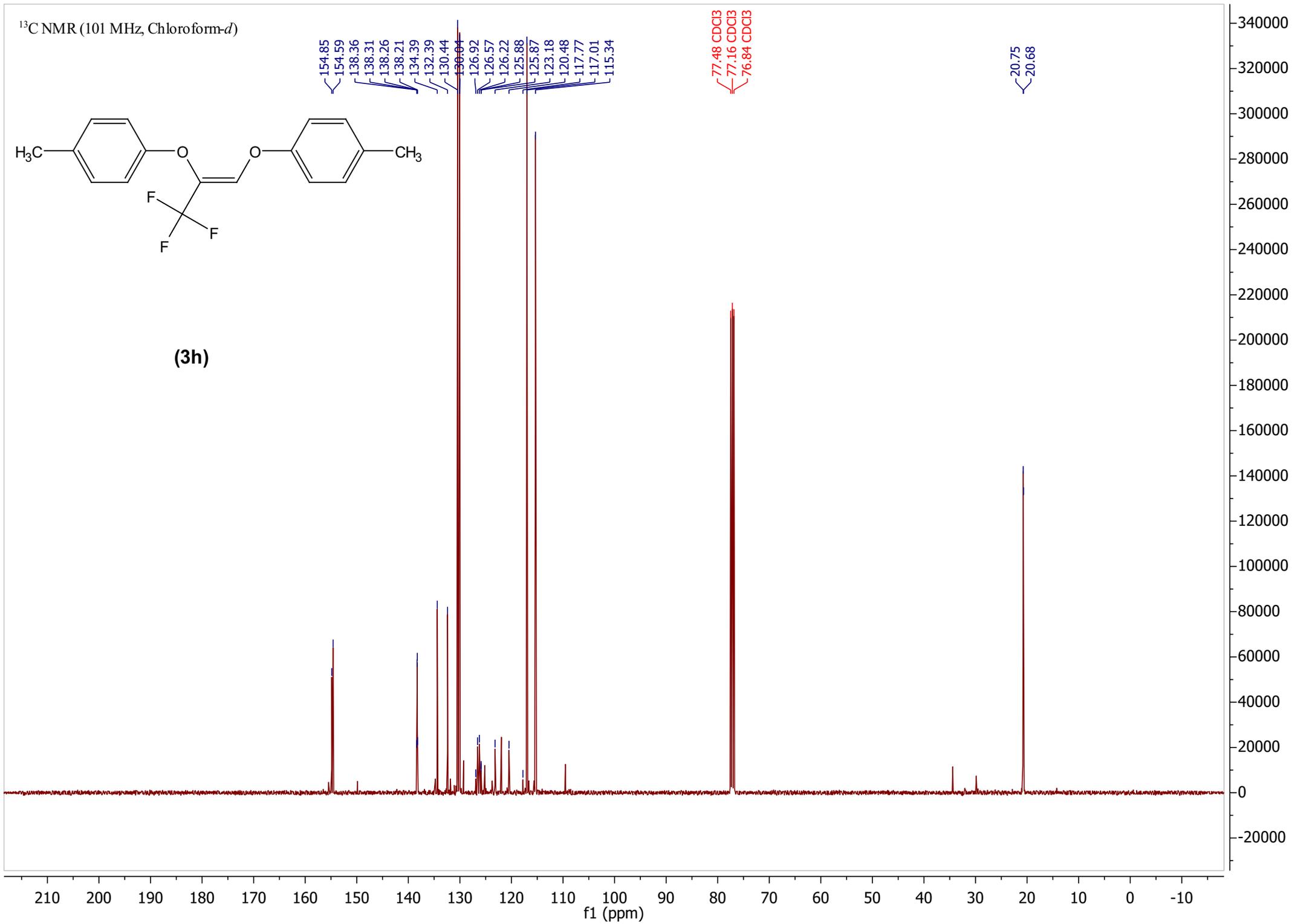
(3h)



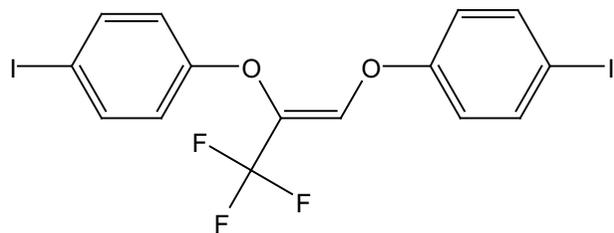
¹³C NMR (101 MHz, Chloroform-*d*)



(3h)



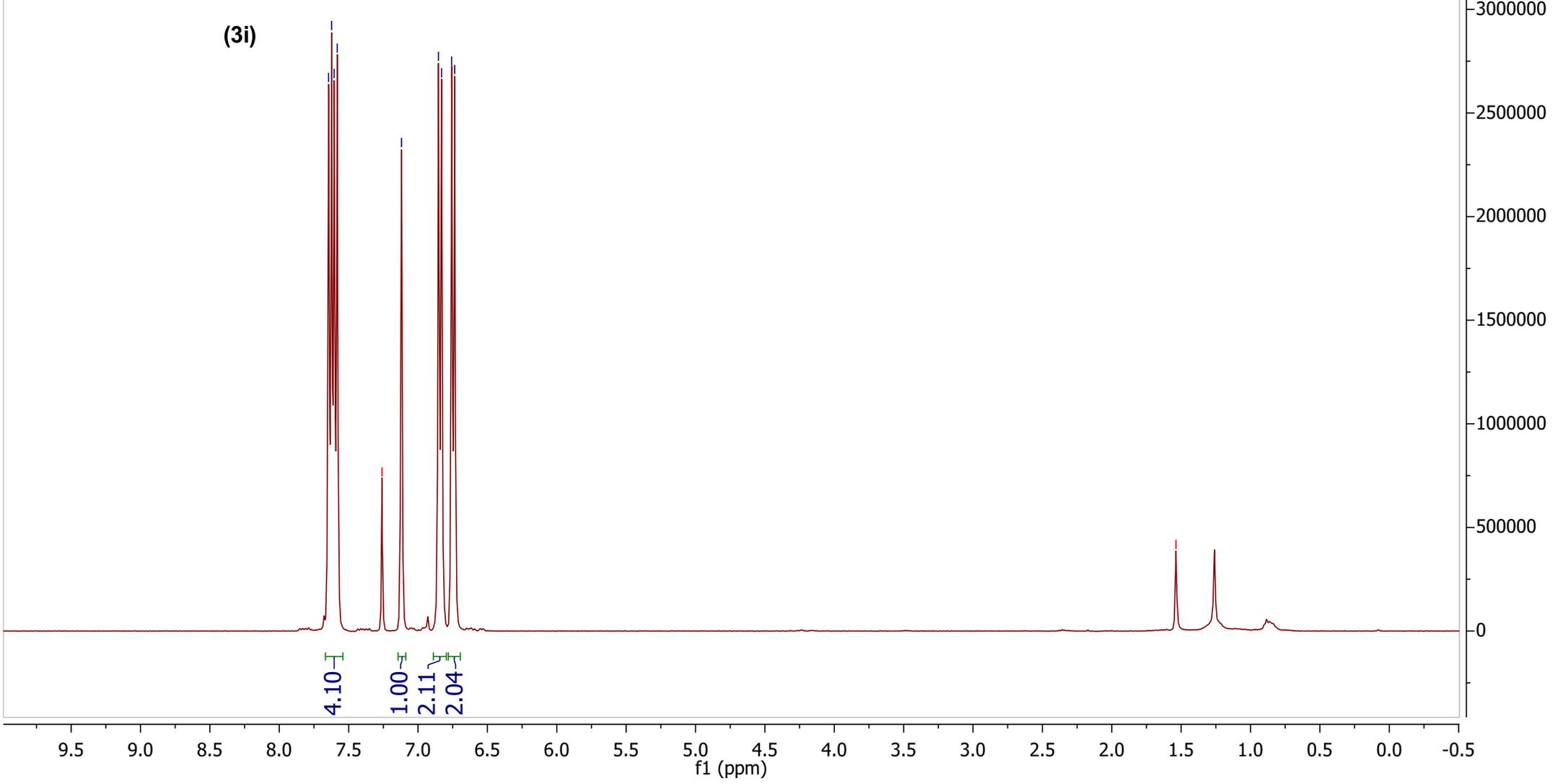
¹H NMR (400 MHz, Chloroform-*d*)



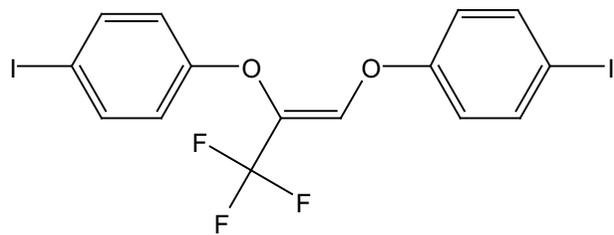
(3i)

7.65
7.62
7.60
7.58
— 7.26 CDCl₃
— 7.12
6.85
6.83
6.76
6.74

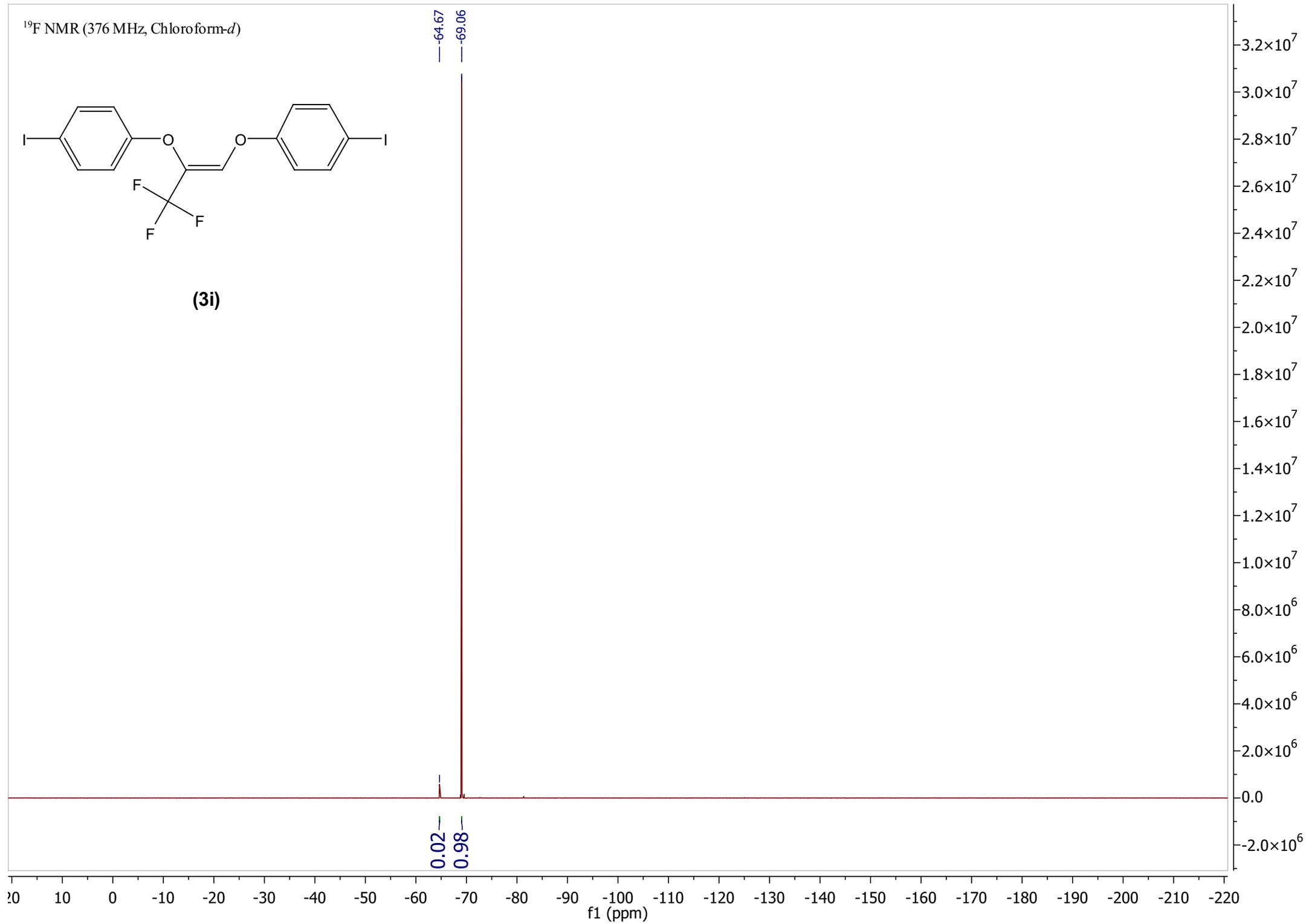
— 1.54 H₂O



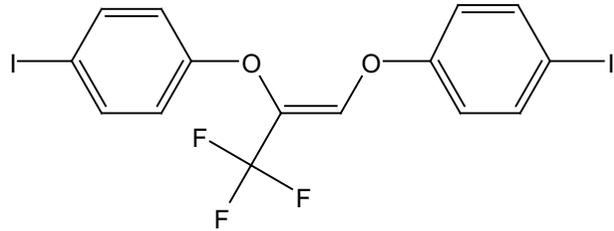
¹⁹F NMR (376 MHz, Chloroform-*d*)



(3i)



¹³C NMR (101 MHz, Chloroform-*d*)



(3i)

156.69
156.05
139.08
138.56
137.29
137.24
137.19
137.14
127.57
127.21
126.86
126.51
125.39
122.69
119.98
119.15
117.82
117.27

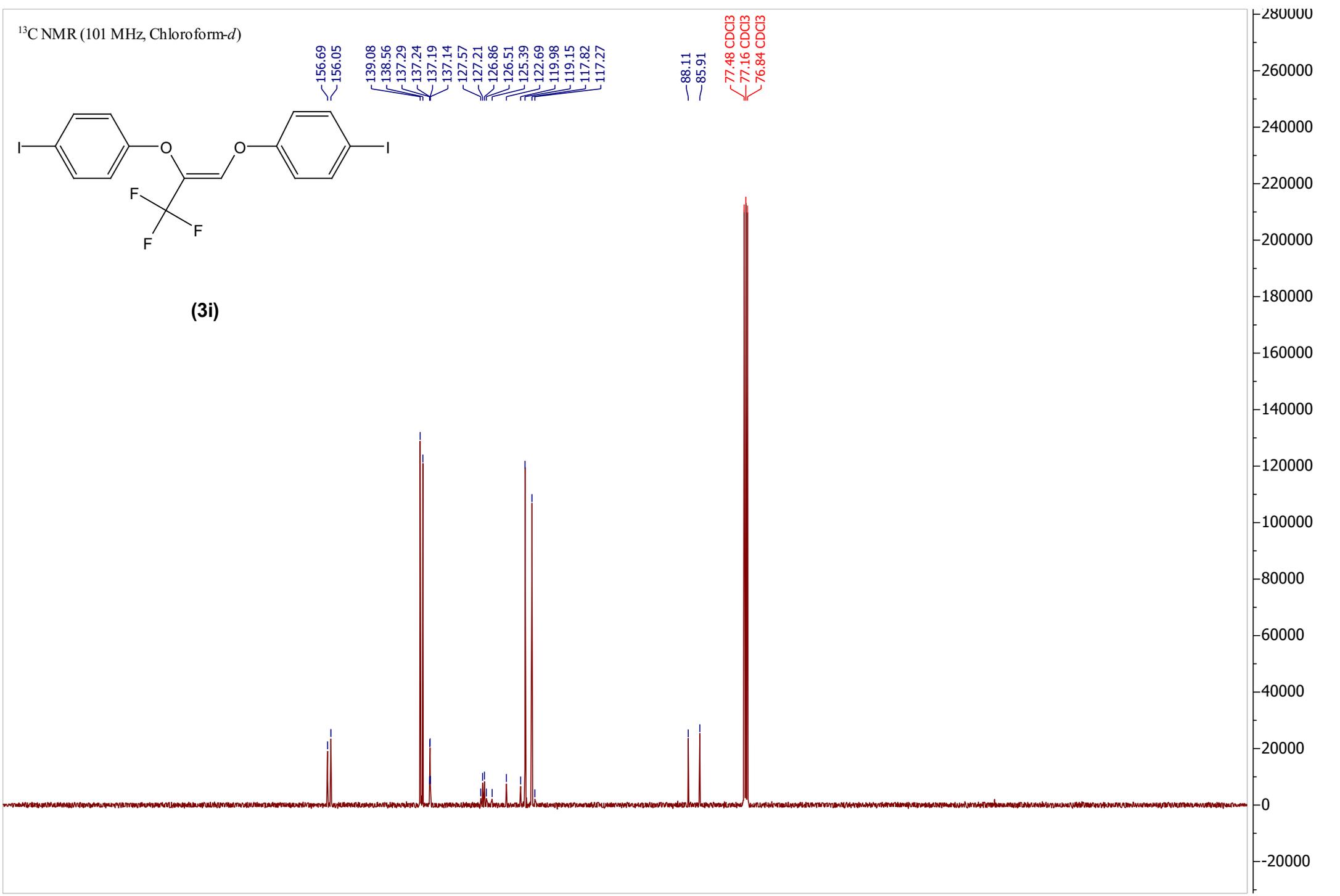
88.11
85.91

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

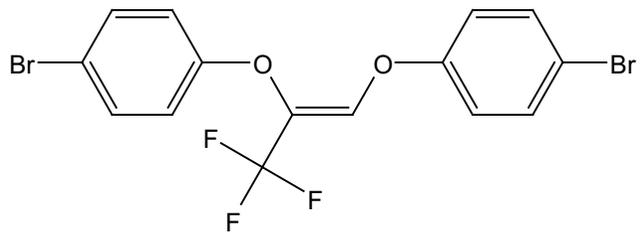
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000



¹H NMR (400 MHz, Chloroform-*d*)



(3j)

7.34
7.32
7.32
7.29
7.02
6.87
6.85
6.76
6.74

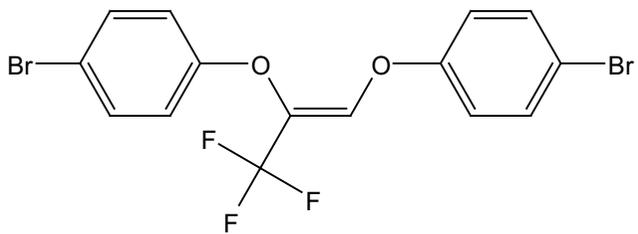
4.09
1.00
2.09
2.01

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 0.5 0.0

f1 (ppm)

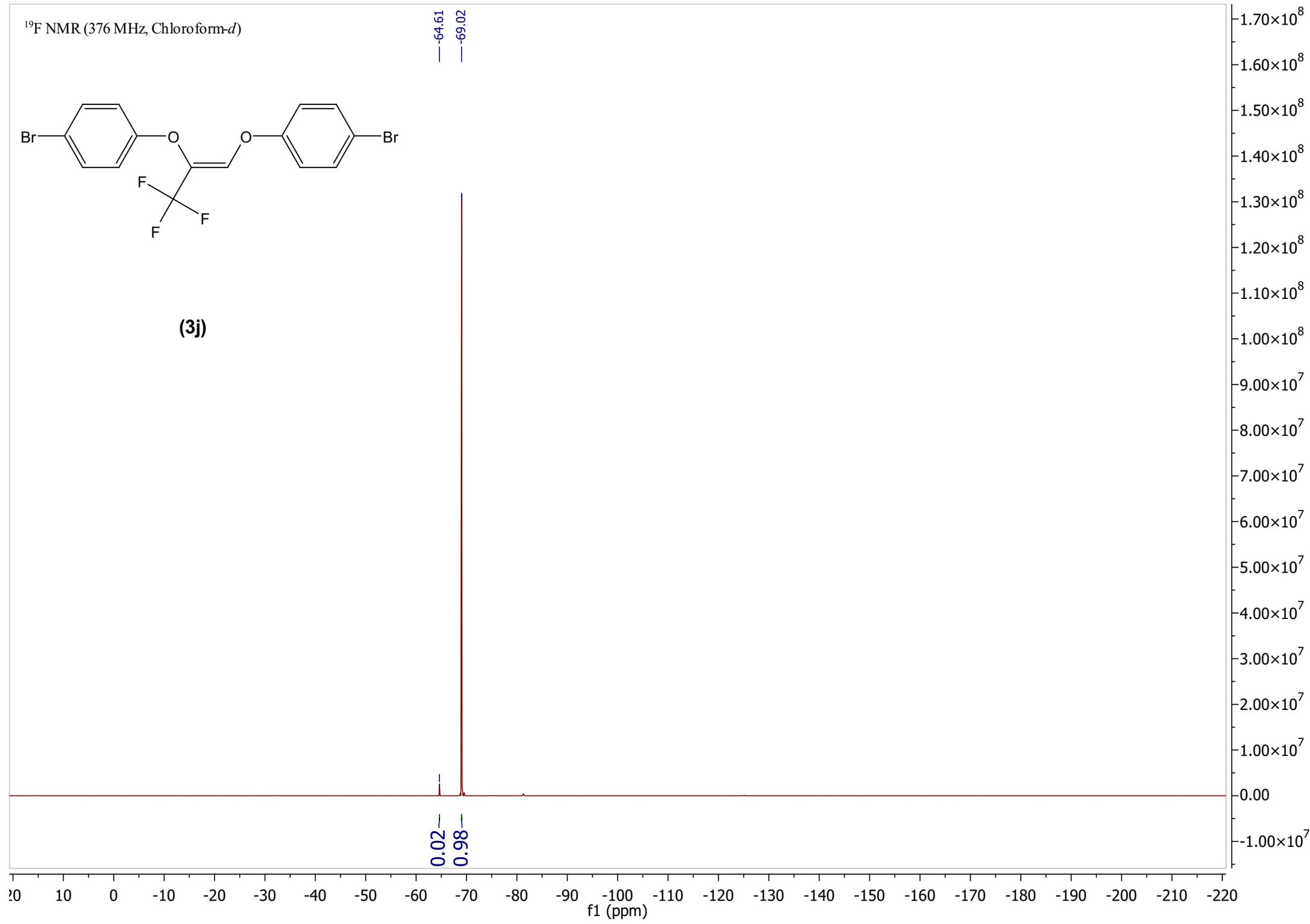
16000000
15000000
14000000
13000000
12000000
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000

¹⁹F NMR (376 MHz, Chloroform-*d*)

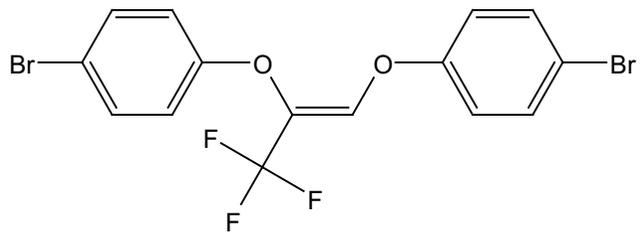


(3j)

64.61
69.02
0.02
0.98



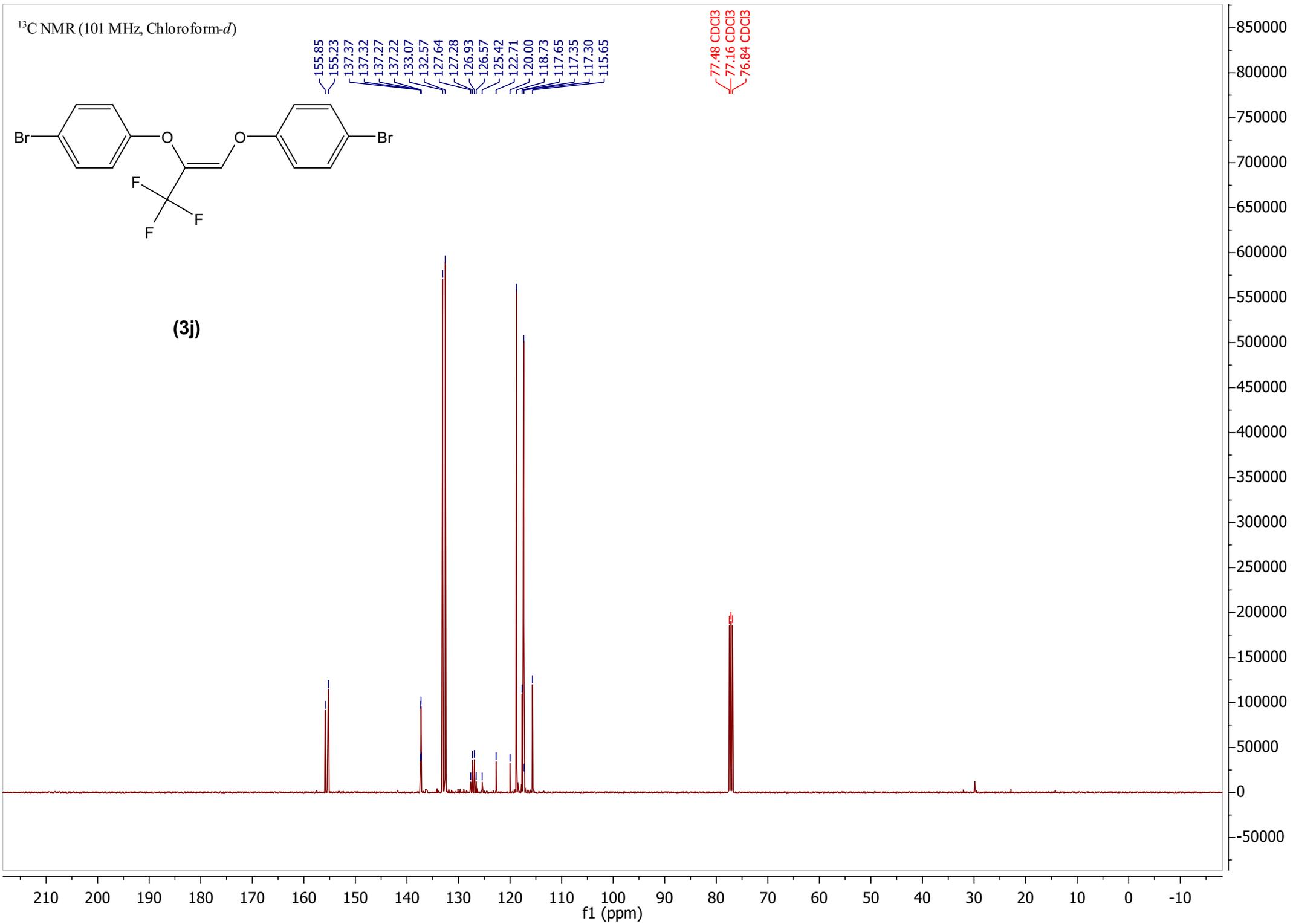
¹³C NMR (101 MHz, Chloroform-*d*)



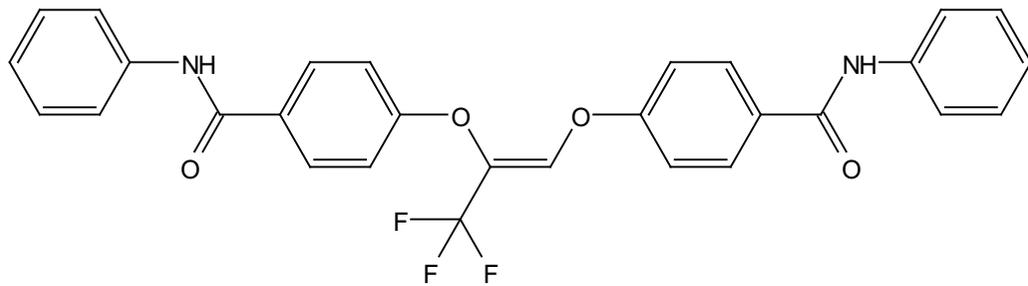
(3j)

155.85
155.23
137.37
137.32
137.27
137.22
133.07
132.57
127.64
127.28
126.93
126.57
125.42
122.71
120.00
118.73
117.65
117.35
117.30
115.65

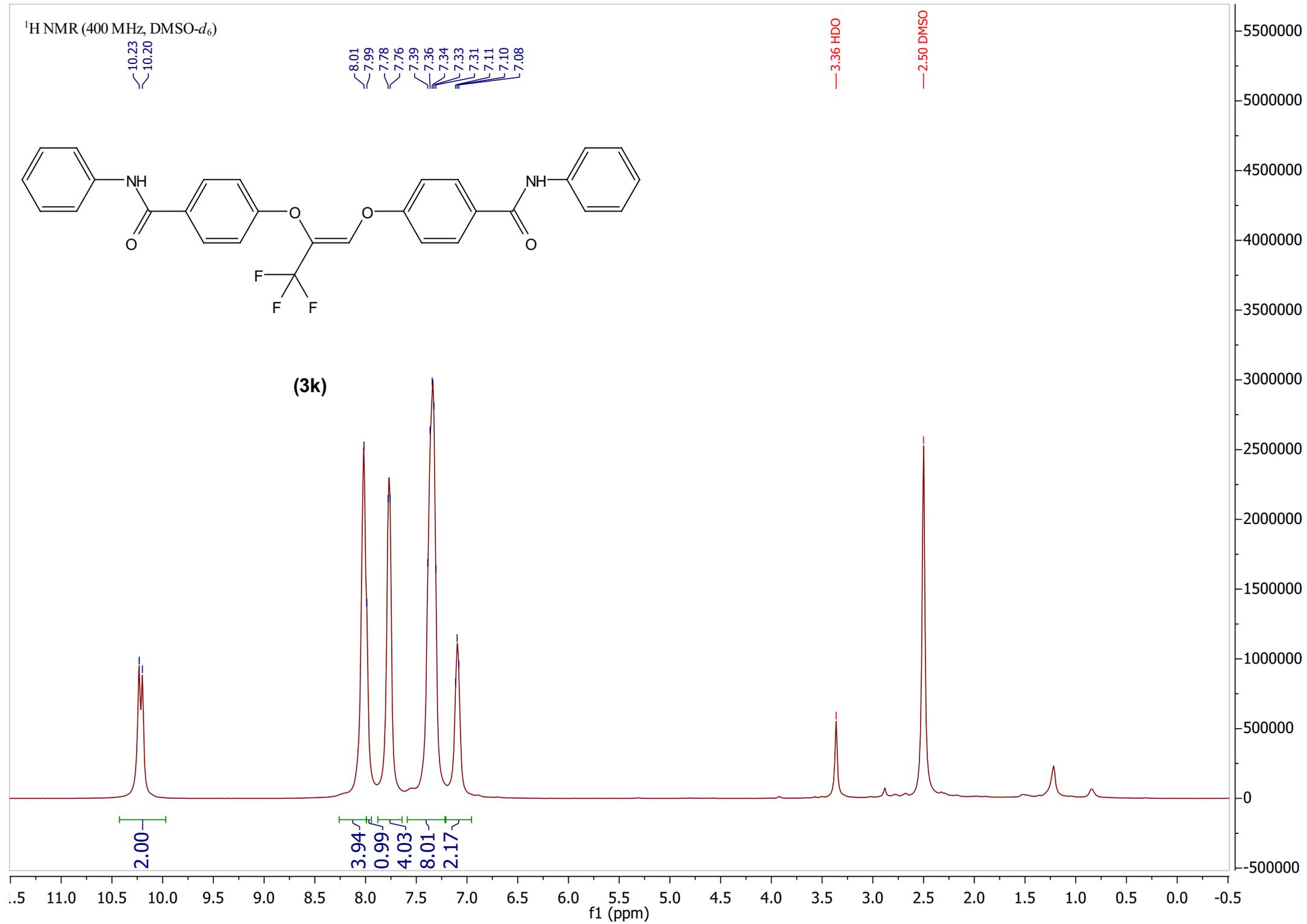
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃



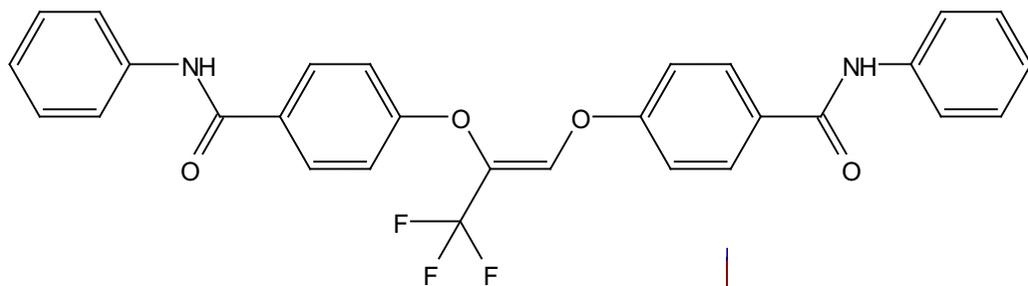
¹H NMR (400 MHz, DMSO-*d*₆)



(3k)



^{19}F NMR (376 MHz, $\text{DMSO-}d_6$)



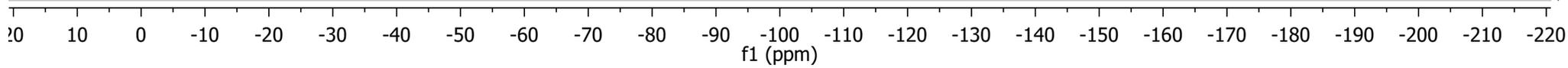
(3k)

— -63.26

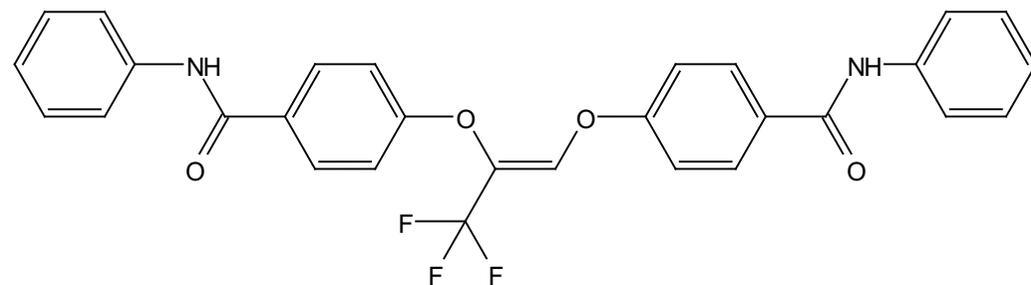
— -67.65

0.02

0.98



¹³C NMR (101 MHz, DMSO-*d*₆)



(3k)

164.68
164.36
158.48
157.51
139.38
139.35
139.30
139.25
139.20
139.08
130.98
129.87
129.84
128.58
125.52
125.07
124.72
124.37
124.01
123.69
123.57
122.82
120.44
120.33
120.12
120.12
116.61
116.17
114.58

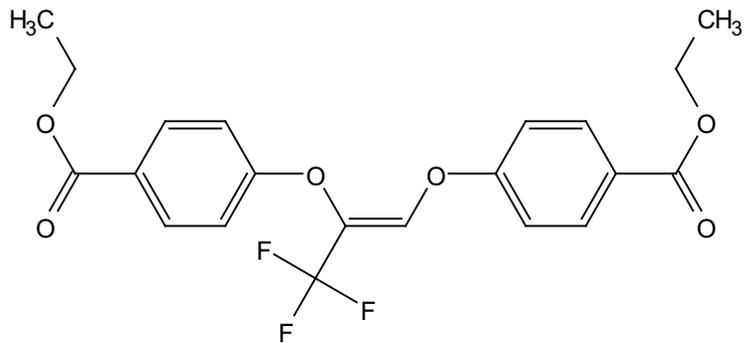
40.15 DMSO
39.99 DMSO
39.94 DMSO
39.78 DMSO
39.73 DMSO
39.57 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
38.89 DMSO

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

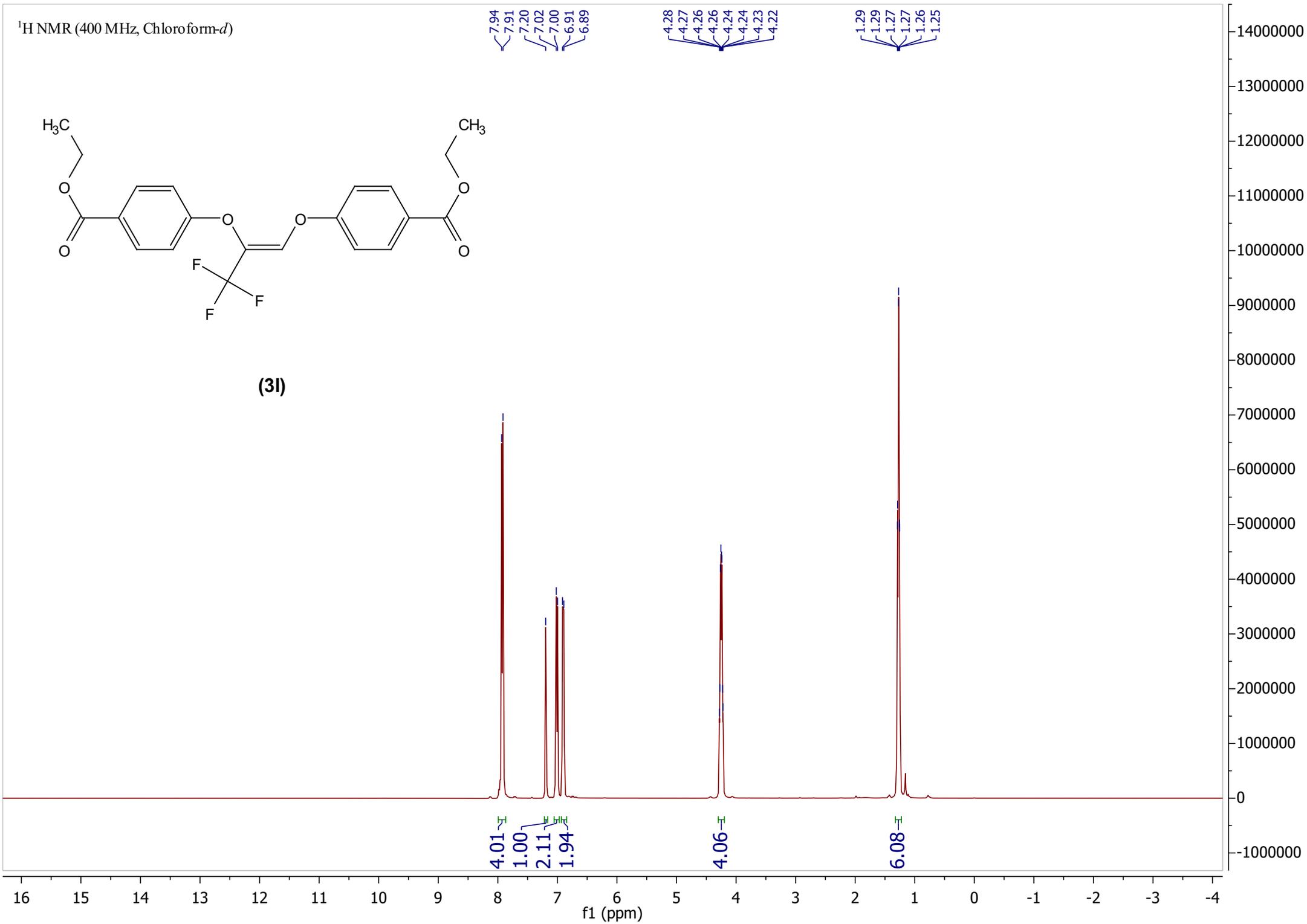
f1 (ppm)

100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000

¹H NMR (400 MHz, Chloroform-*d*)

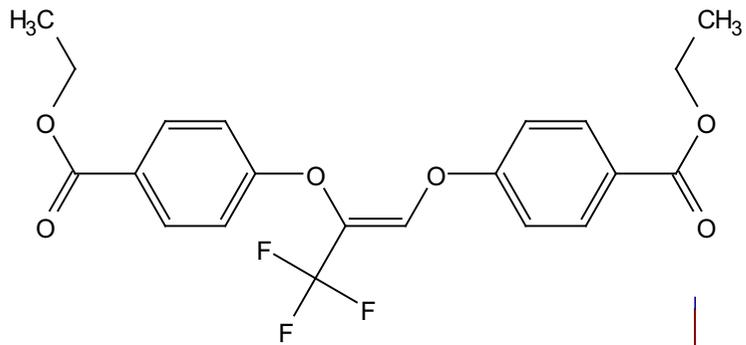


(3I)



^{19}F NMR (376 MHz, Chloroform-*d*)

64.71
69.20



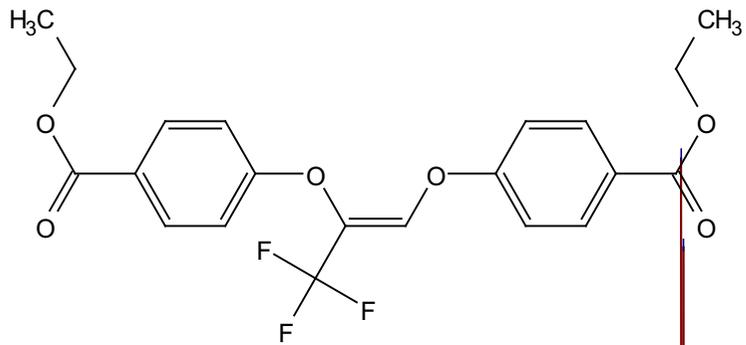
(3I)

20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

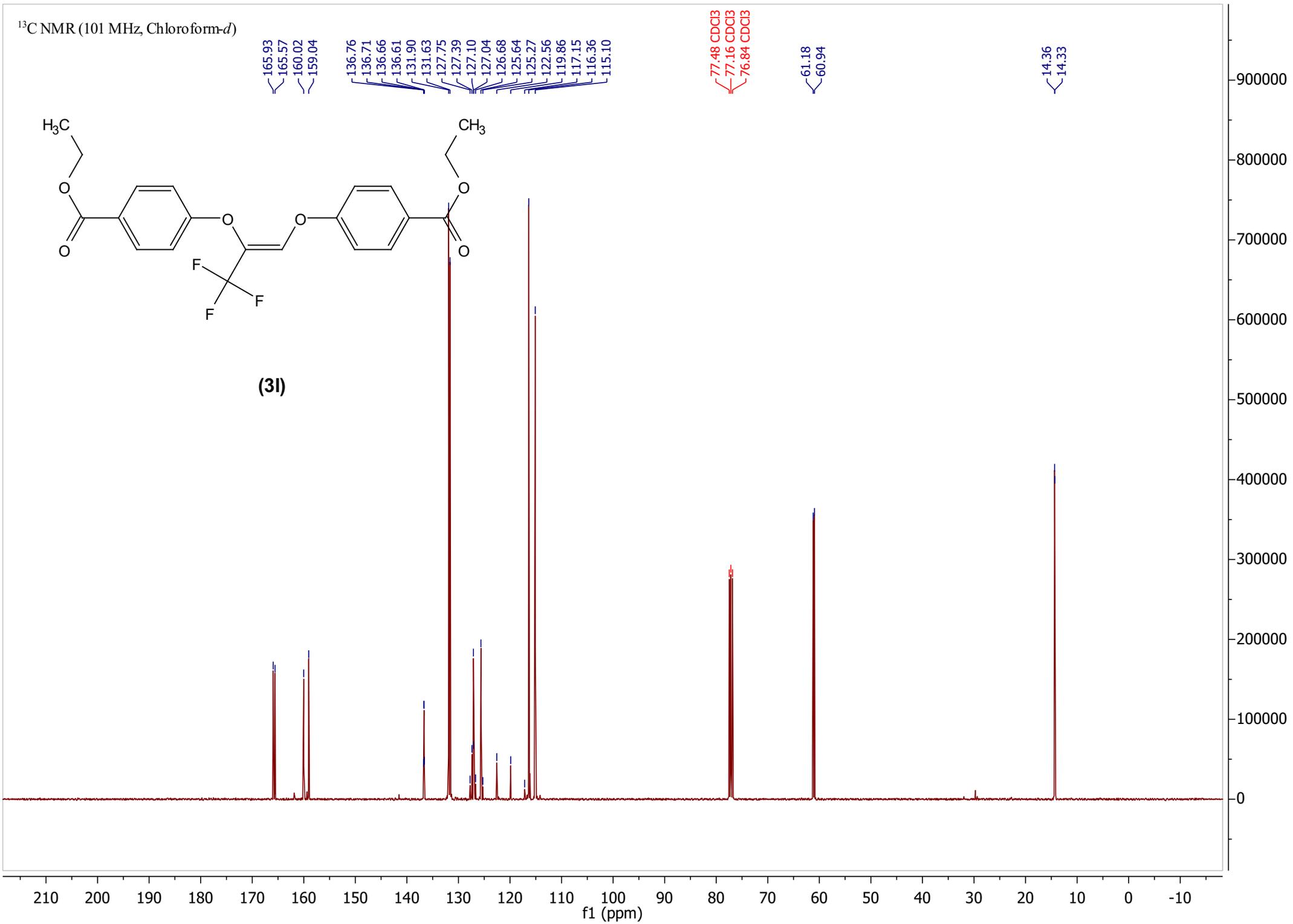
0.03
0.97

1.90×10^{-1}
 1.80×10^8
 1.70×10^8
 1.60×10^8
 1.50×10^8
 1.40×10^8
 1.30×10^8
 1.20×10^8
 1.10×10^8
 1.00×10^8
 9.00×10^7
 8.00×10^7
 7.00×10^7
 6.00×10^7
 5.00×10^7
 4.00×10^7
 3.00×10^7
 2.00×10^7
 1.00×10^7
0.00
 -1.00×10^7

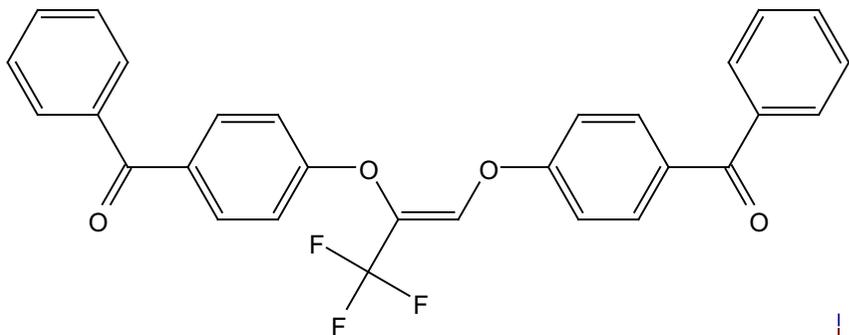
¹³C NMR (101 MHz, Chloroform-*d*)



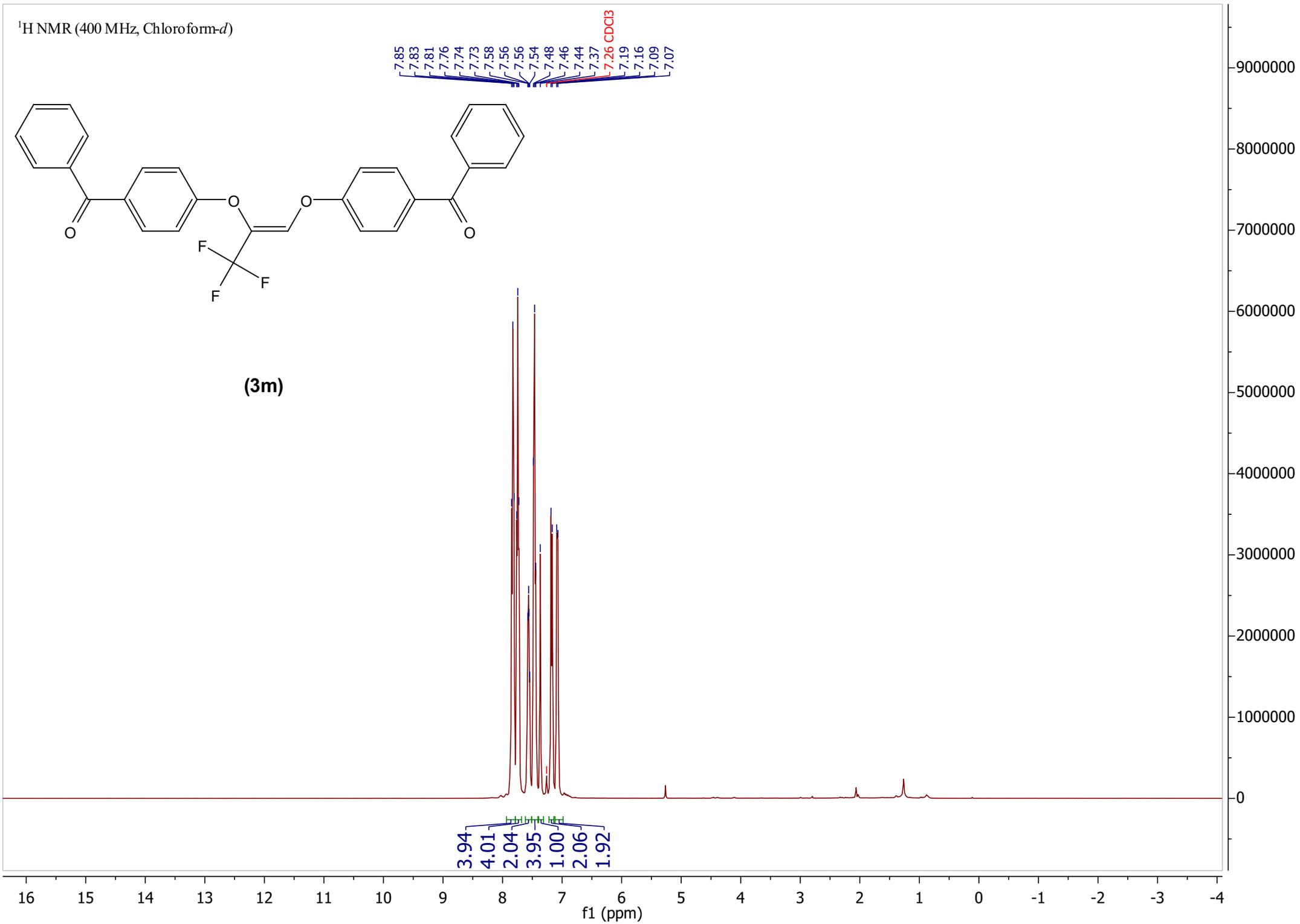
(31)



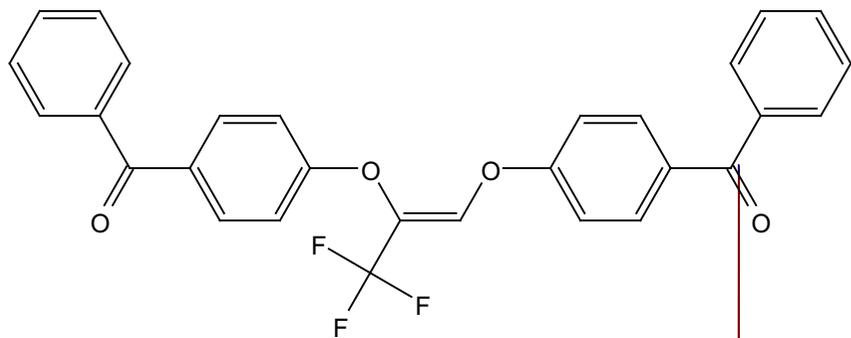
¹H NMR (400 MHz, Chloroform-*d*)



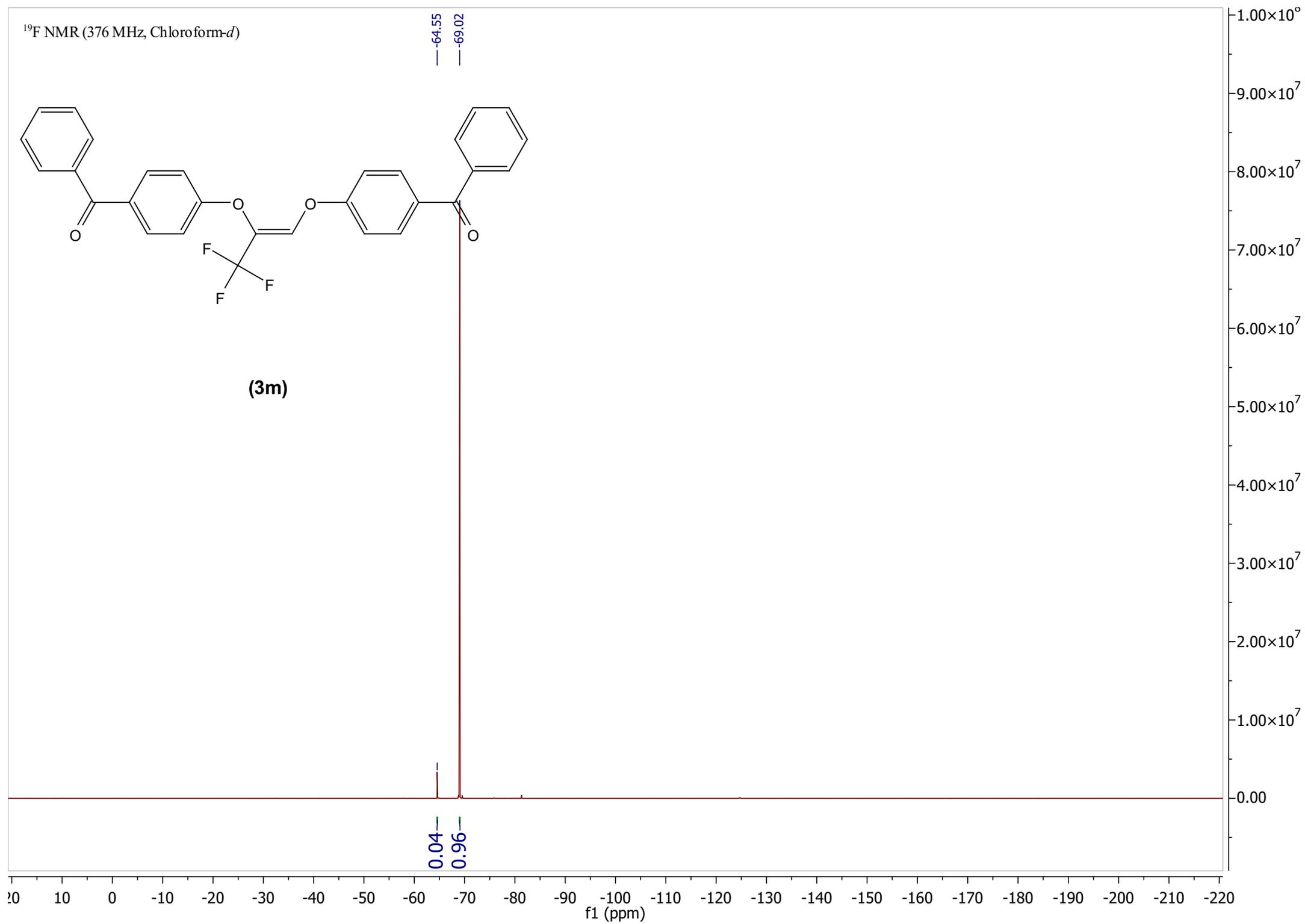
(3m)



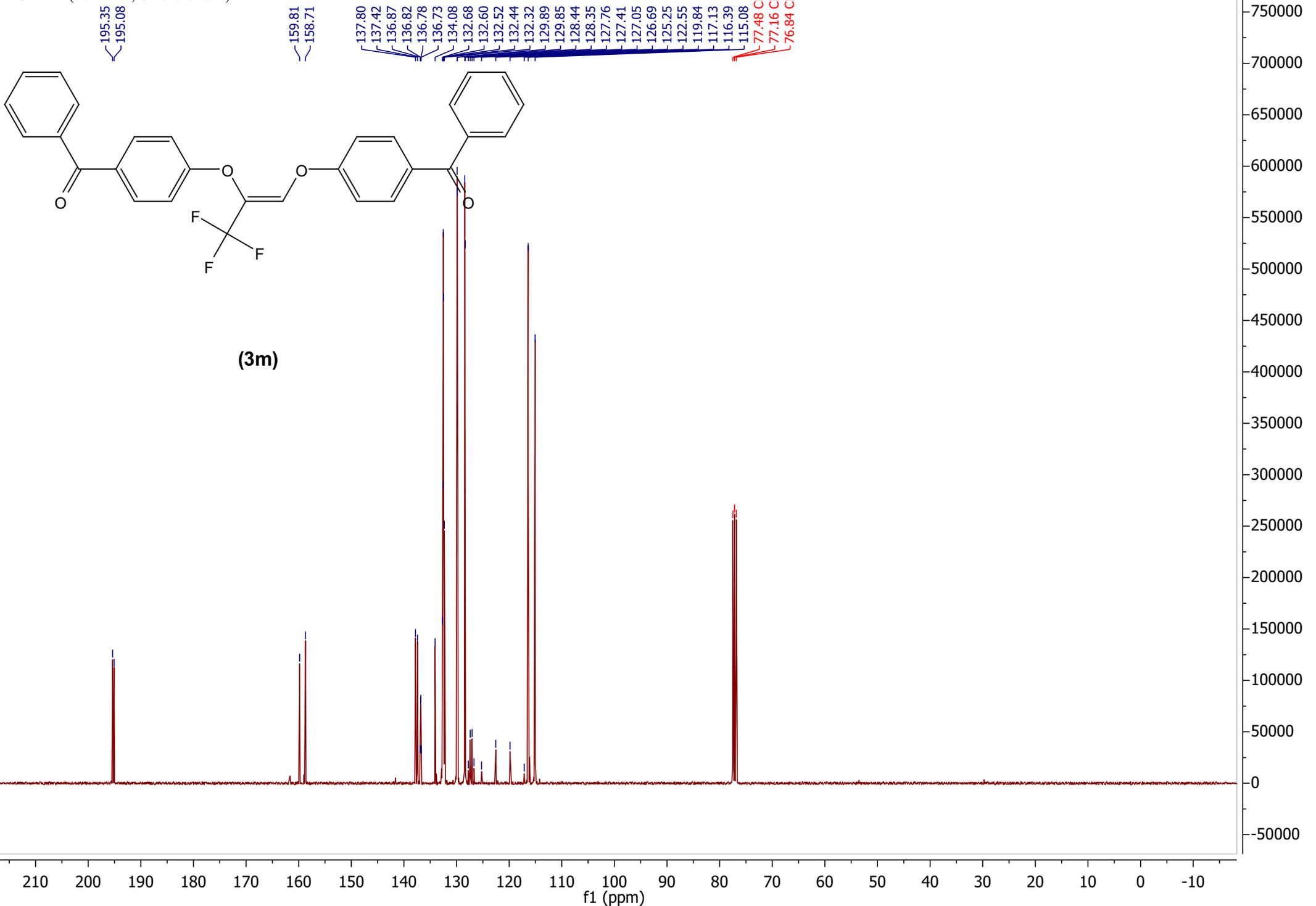
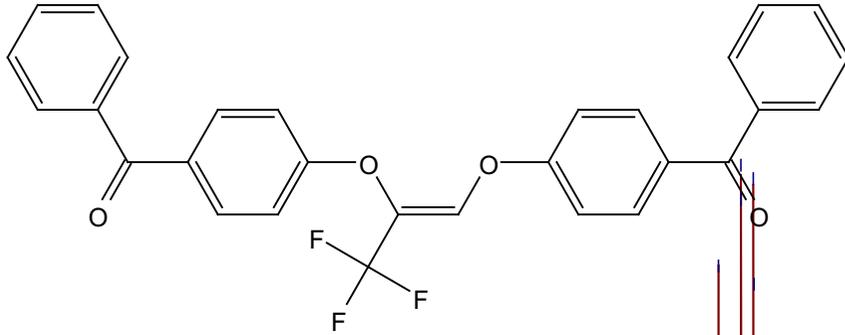
^{19}F NMR (376 MHz, Chloroform-*d*)



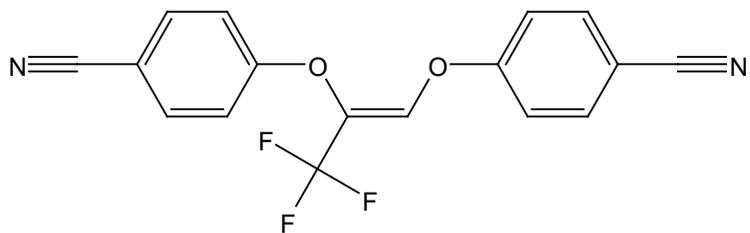
(3m)



¹³C NMR (101 MHz, Chloroform-*d*)



¹H NMR (400 MHz, Chloroform-*d*)

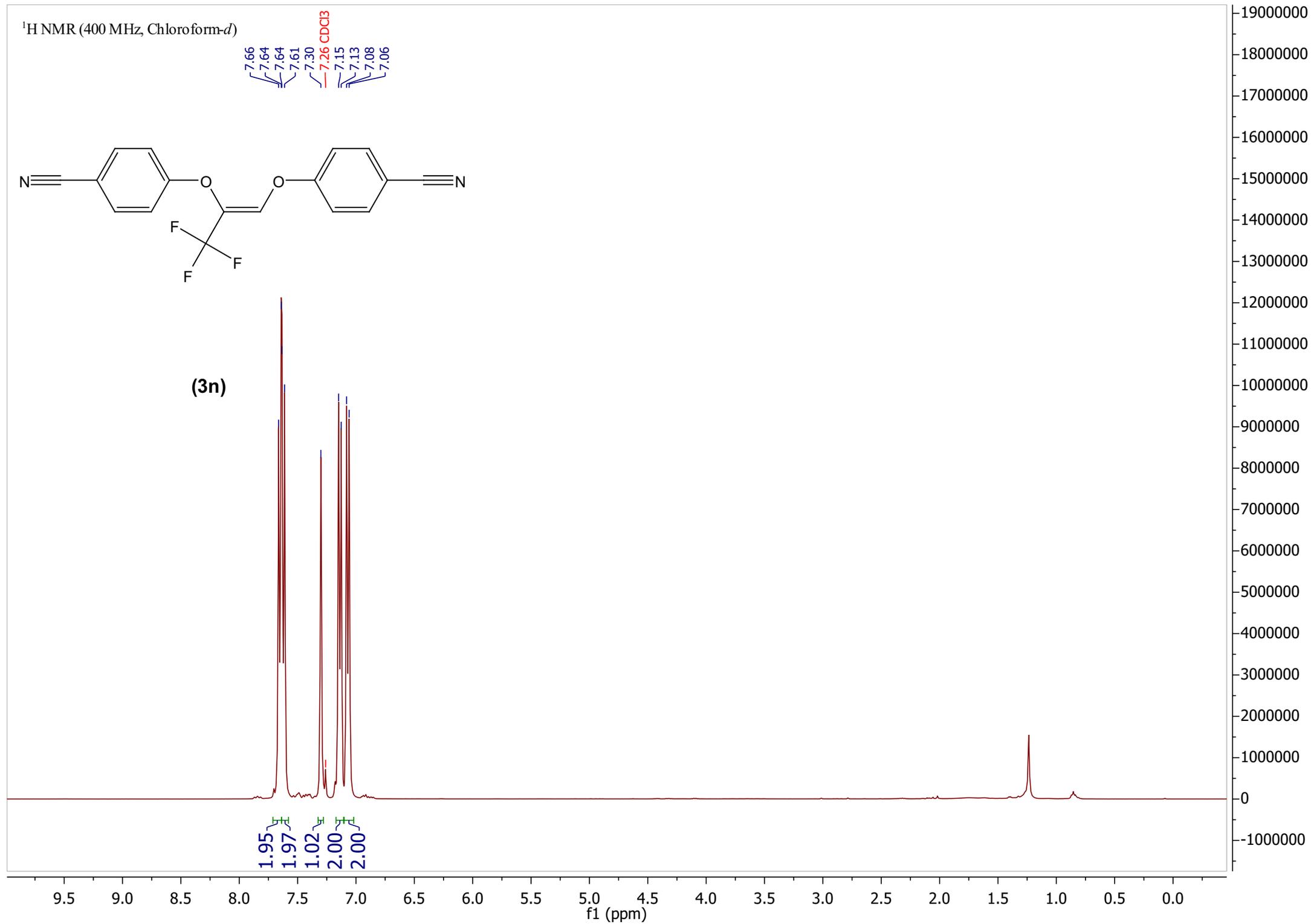


(3n)

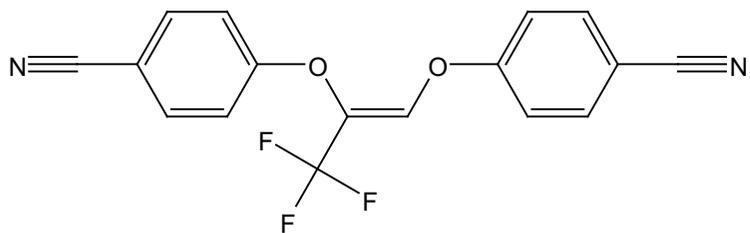
7.66
7.64
7.64
7.61
7.30
7.26 CDCl₃
7.15
7.13
7.08
7.06

1.95
1.97
1.02
2.00
2.00

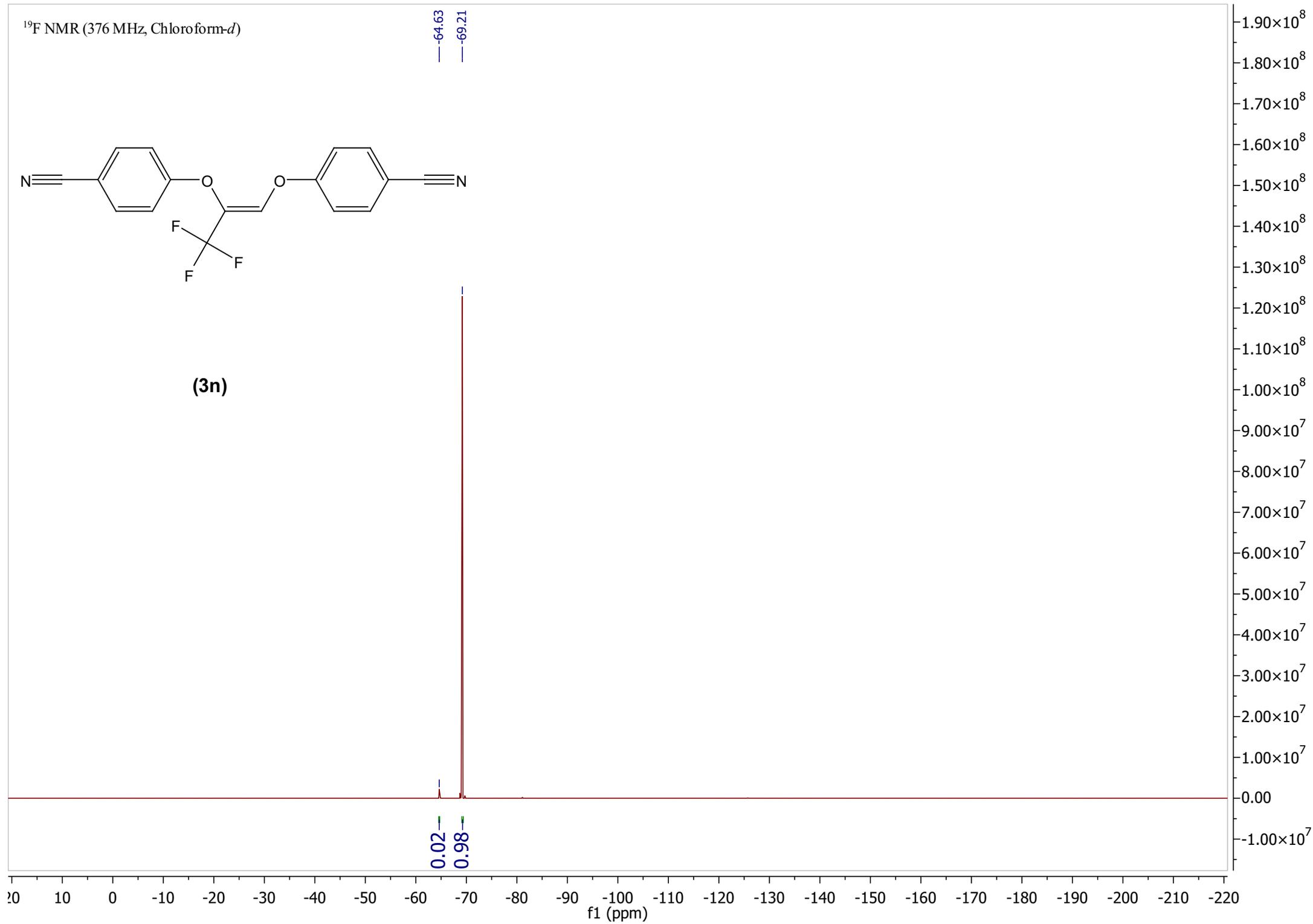
f1 (ppm)



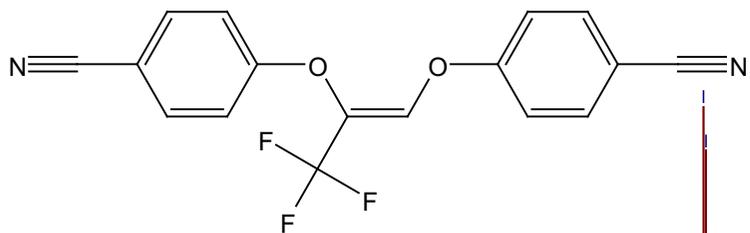
^{19}F NMR (376 MHz, Chloroform-*d*)



(3n)



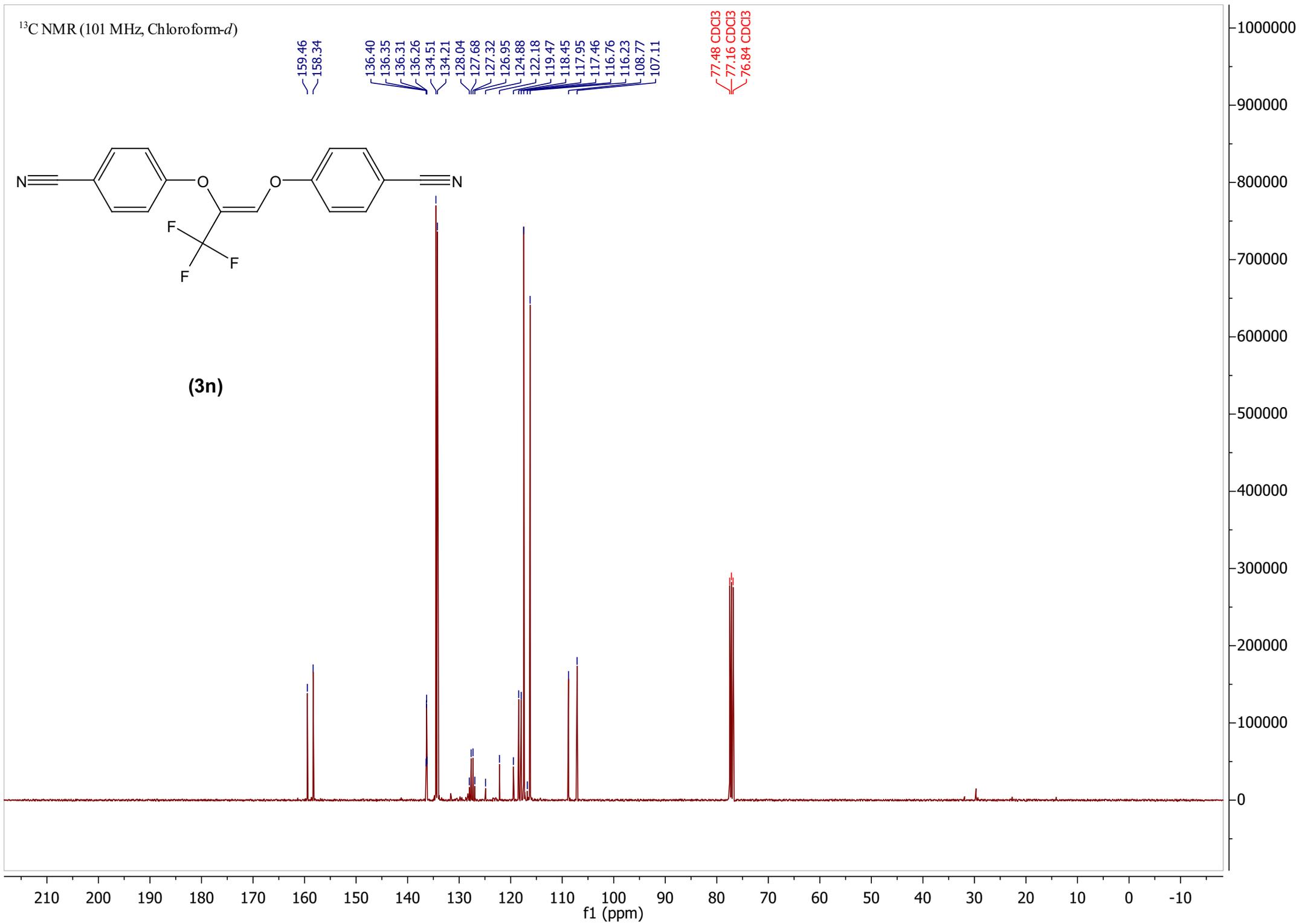
¹³C NMR (101 MHz, Chloroform-*d*)



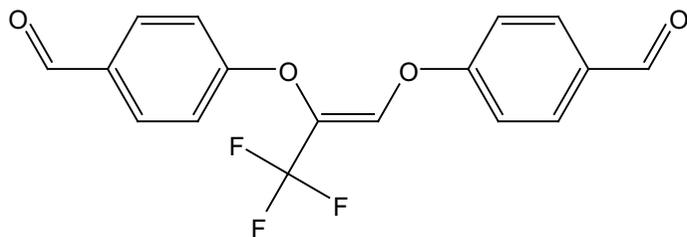
(3n)

159.46
158.34
136.40
136.35
136.31
136.26
134.51
134.21
128.04
127.68
127.32
126.95
124.88
122.18
119.47
118.45
117.95
117.46
116.76
116.23
108.77
107.11

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃



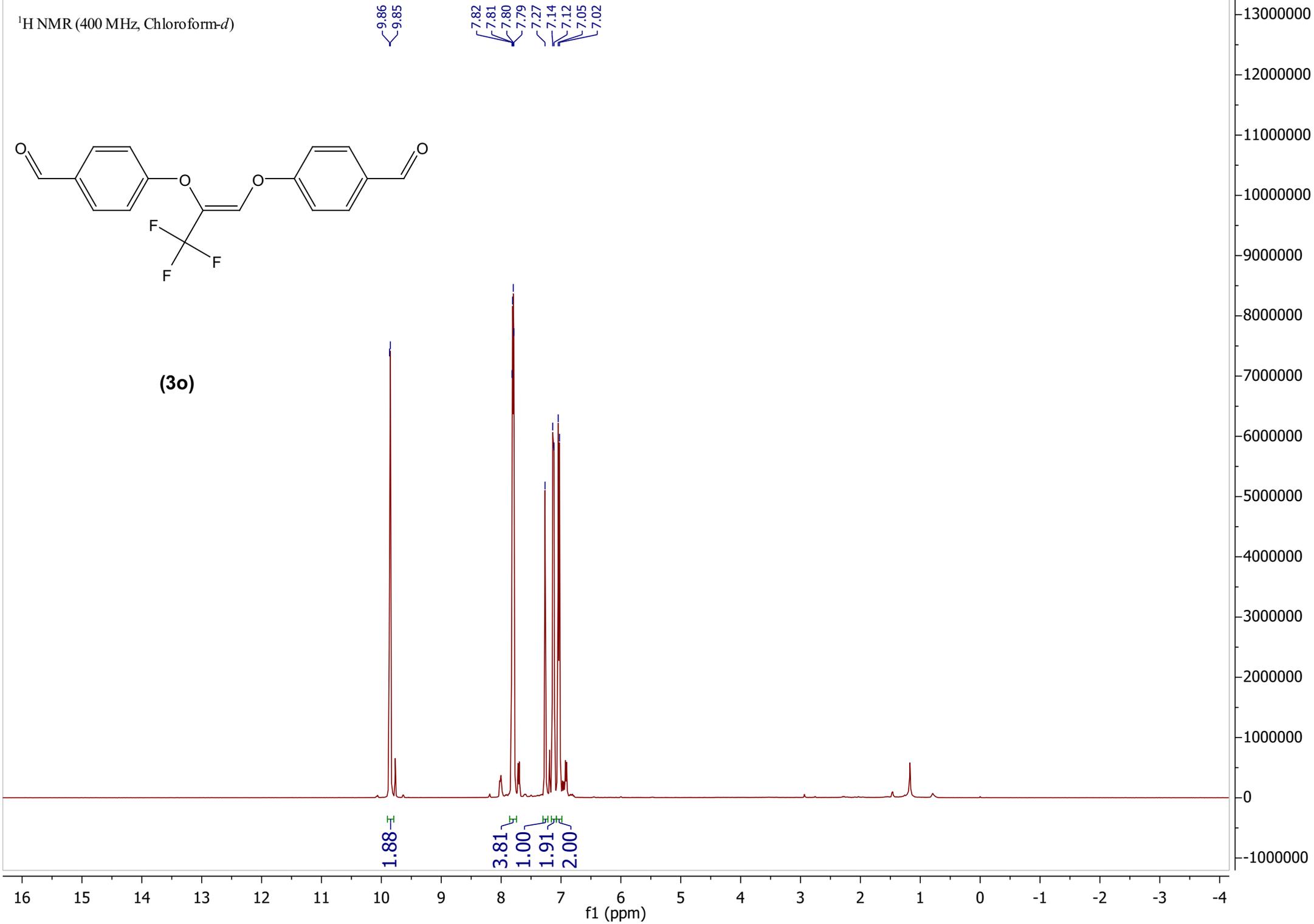
¹H NMR (400 MHz, Chloroform-*d*)



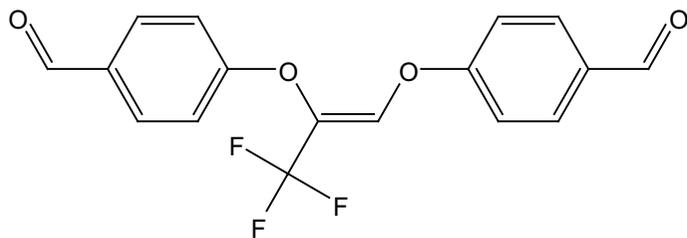
(3o)

9.86
9.85
7.82
7.81
7.80
7.79
7.27
7.14
7.12
7.05
7.02

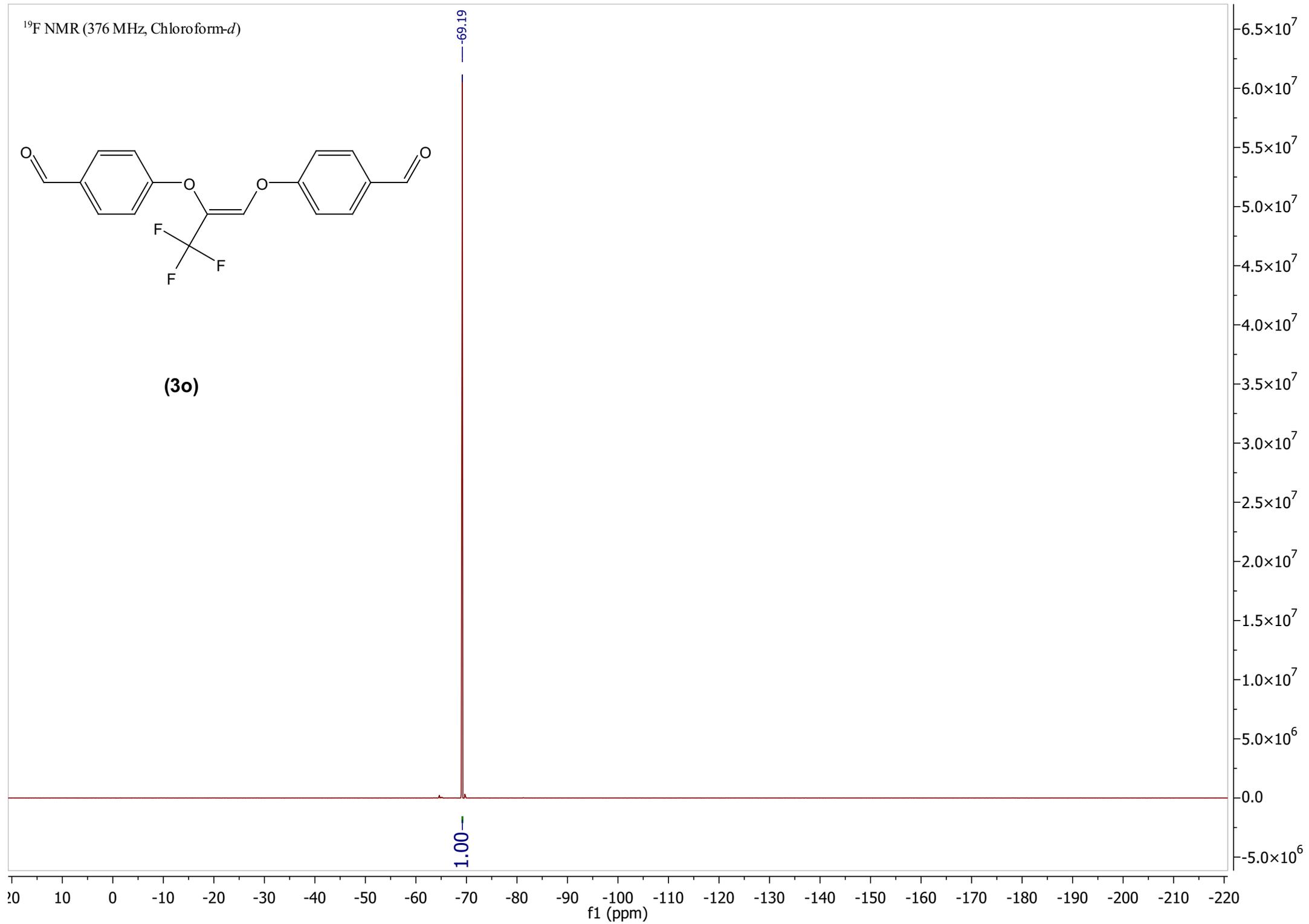
1.88
3.81
1.00
1.91
2.00



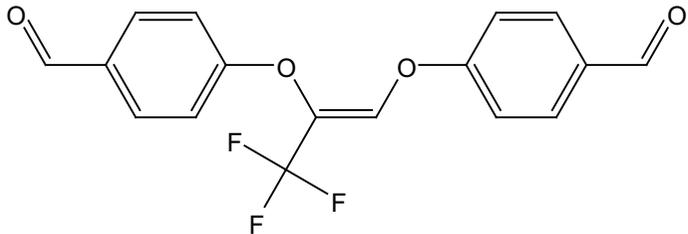
^{19}F NMR (376 MHz, Chloroform-*d*)



(3o)



¹³C NMR (101 MHz, Chloroform-*d*)



(3o)

190.79
190.53

161.14
159.95

136.48

136.44

136.39

136.34

133.21

132.16

132.02

128.10

127.74

127.38

127.02

125.10

122.39

119.68

117.09

116.98

115.89

77.48 CDCl₃

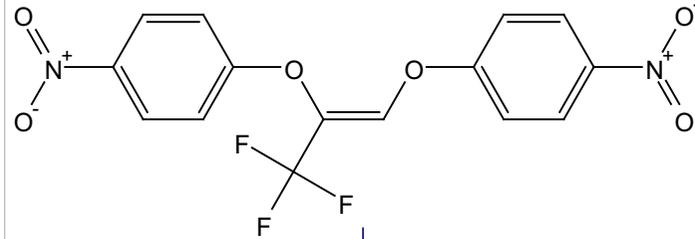
77.16 CDCl₃

76.84 CDCl₃

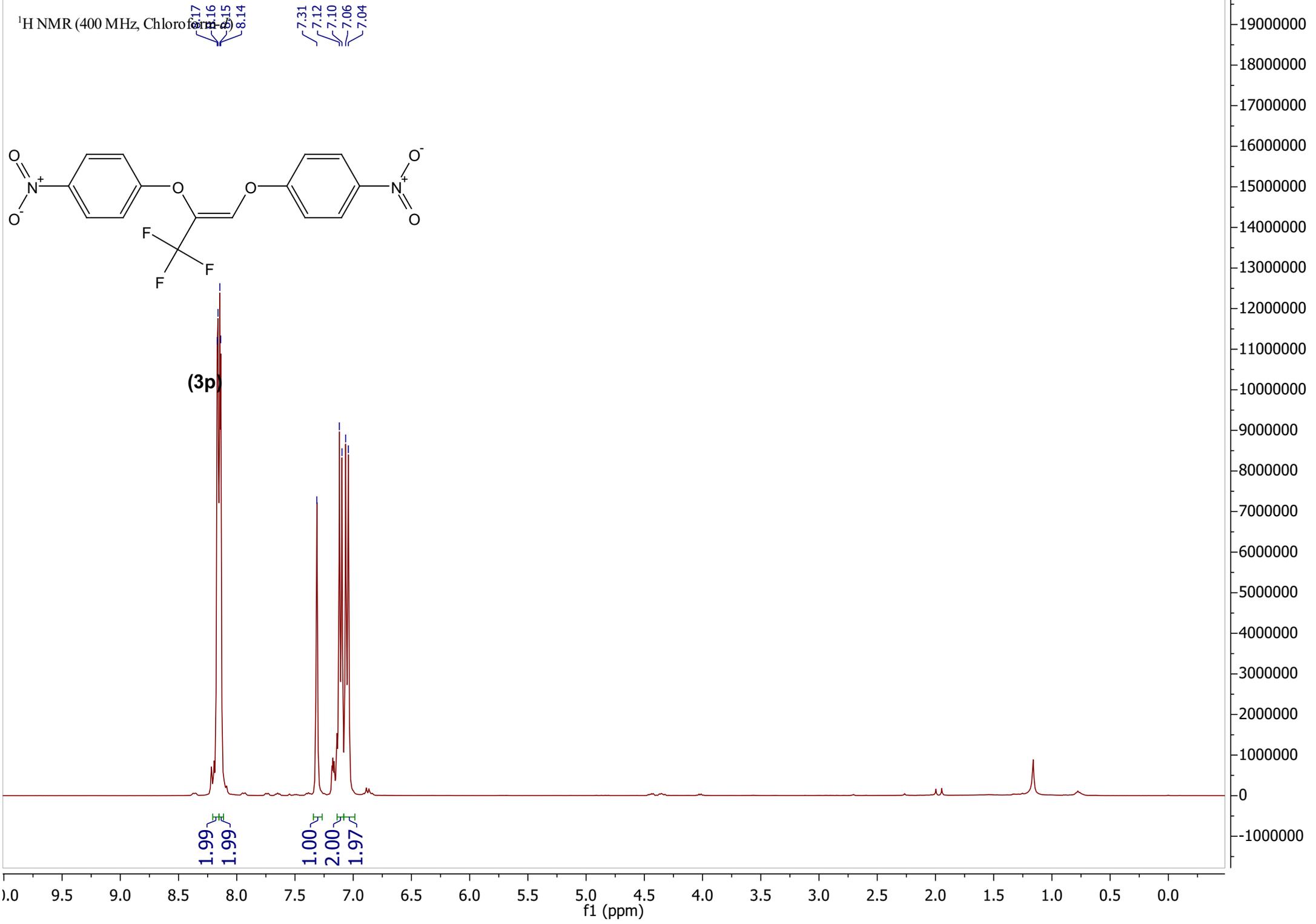
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

380000
360000
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

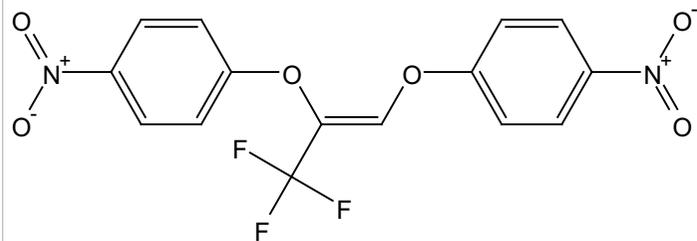
¹H NMR (400 MHz, Chloroform-d)



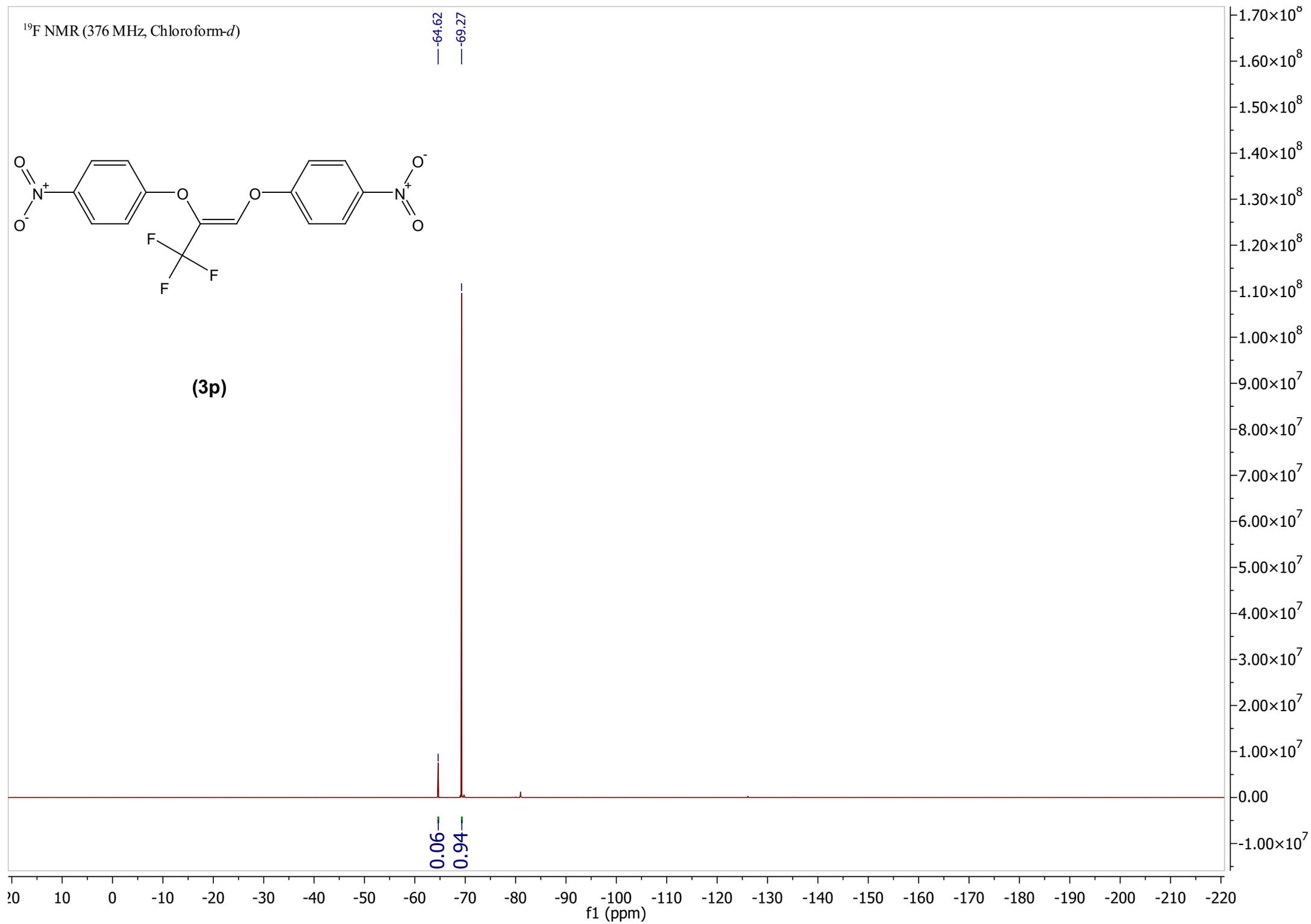
(3p)



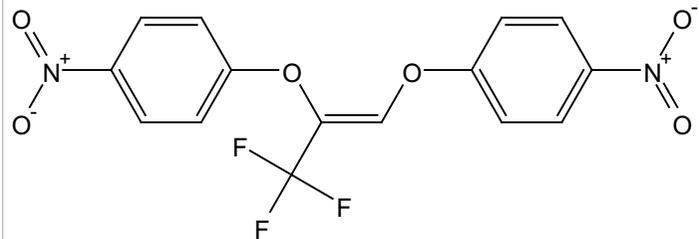
^{19}F NMR (376 MHz, Chloroform-*d*)



(3p)



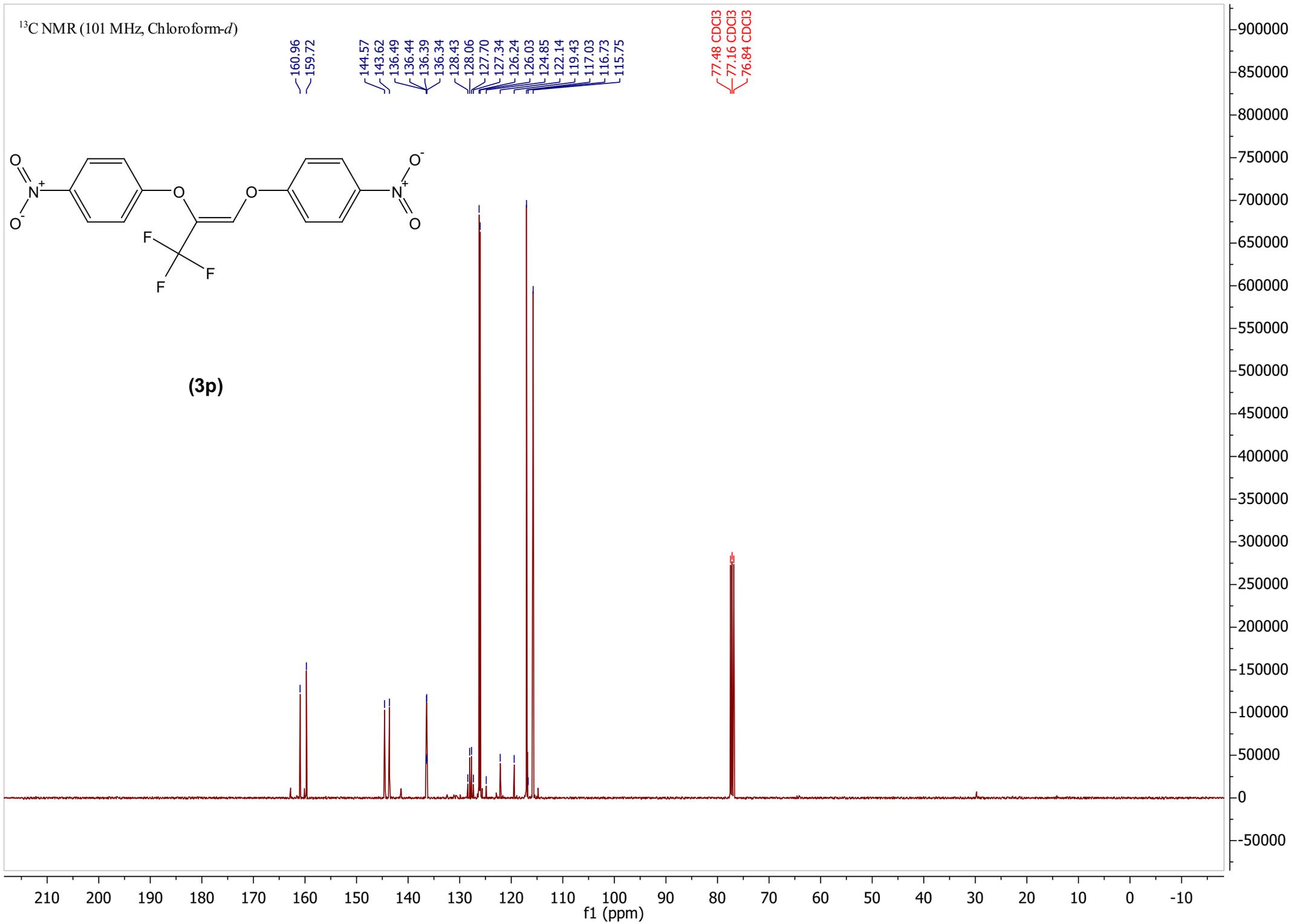
¹³C NMR (101 MHz, Chloroform-*d*)



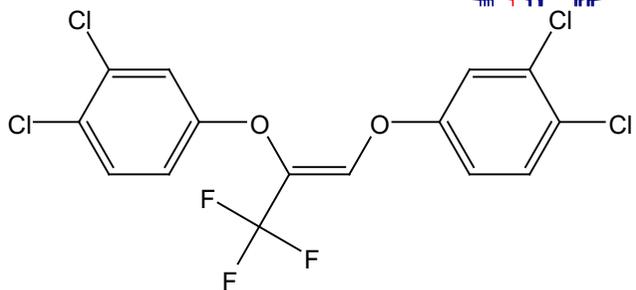
(3p)

160.96
159.72
144.57
143.62
136.49
136.44
136.39
136.34
128.43
128.06
127.70
127.34
126.24
126.03
124.85
122.14
119.43
117.03
116.73
115.75

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃



¹H NMR (400 MHz, Chloroform-*d*)



7.43
7.41
7.39
7.36
7.26 CDCl₃
7.18
7.17
7.12
7.12
7.11
7.11
6.94
6.93
6.92
6.91
6.87
6.87
6.85
6.84

(3q)

— 1.54 H₂O

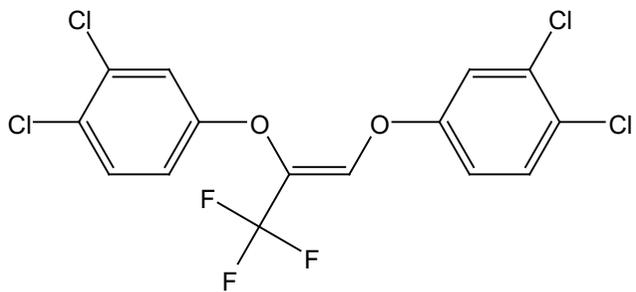
1.04
1.00
1.02
1.95
1.02
1.00

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 0.5 0.0

f1 (ppm)

3500000
3000000
2500000
2000000
1500000
1000000
500000
0

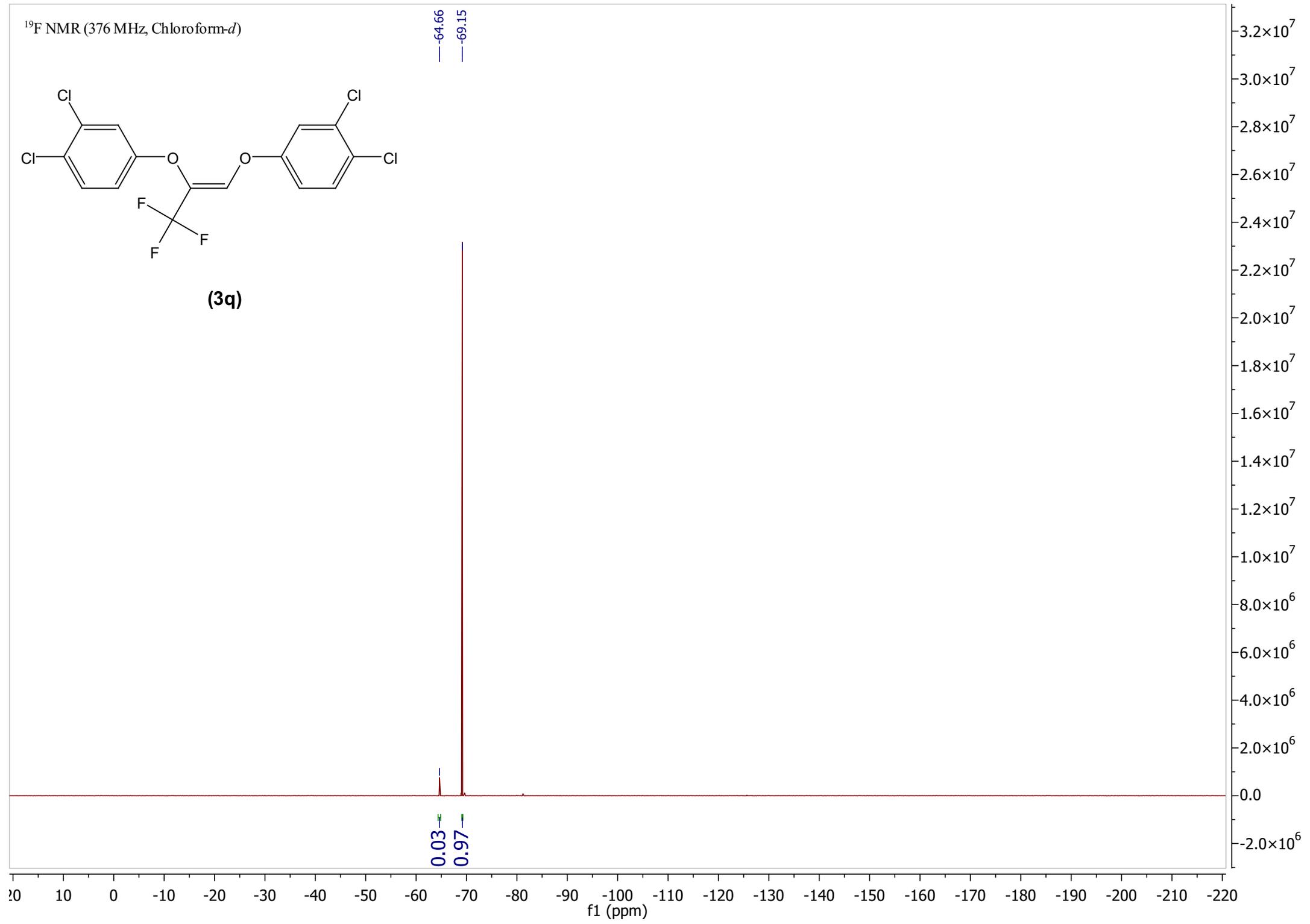
^{19}F NMR (376 MHz, Chloroform-*d*)



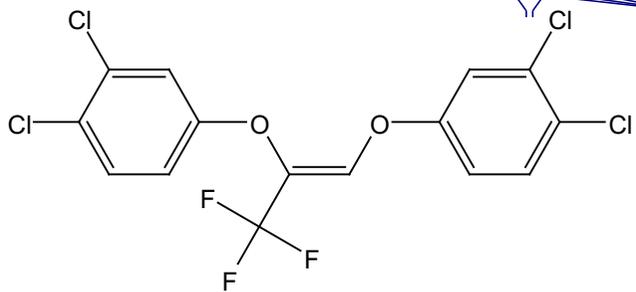
(3q)

—64.66
—69.15

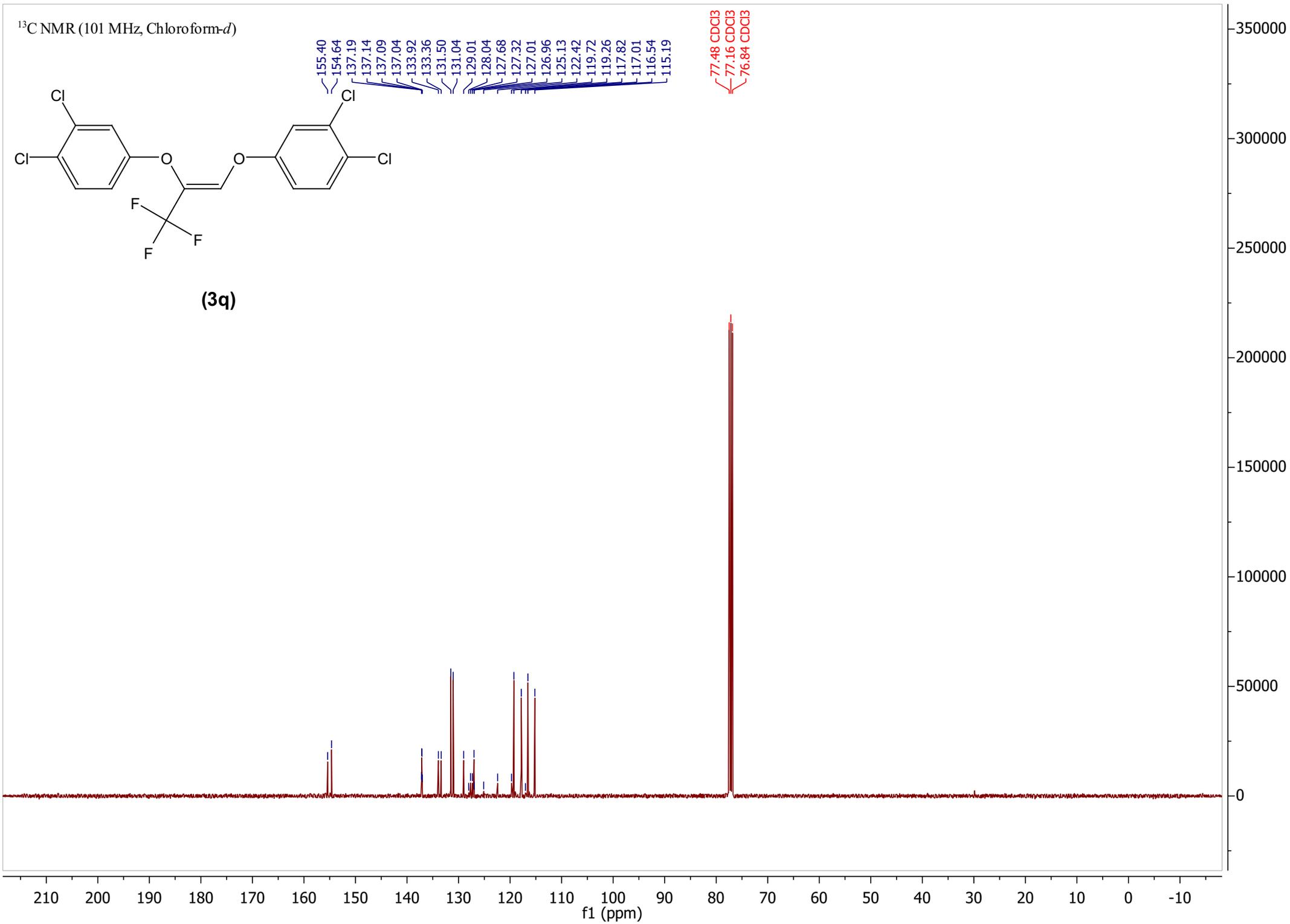
0.03
0.97



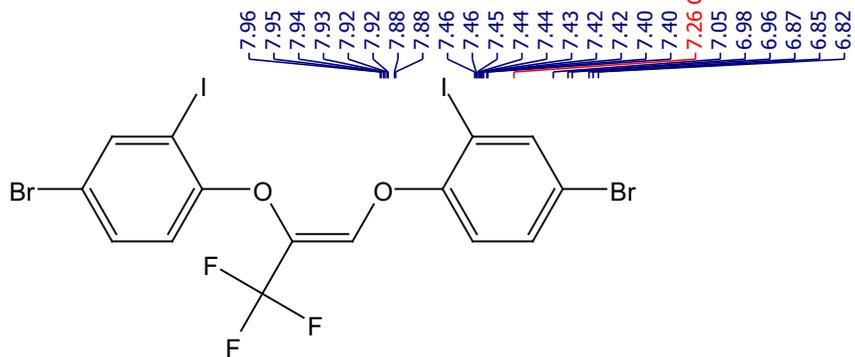
¹³C NMR (101 MHz, Chloroform-*d*)



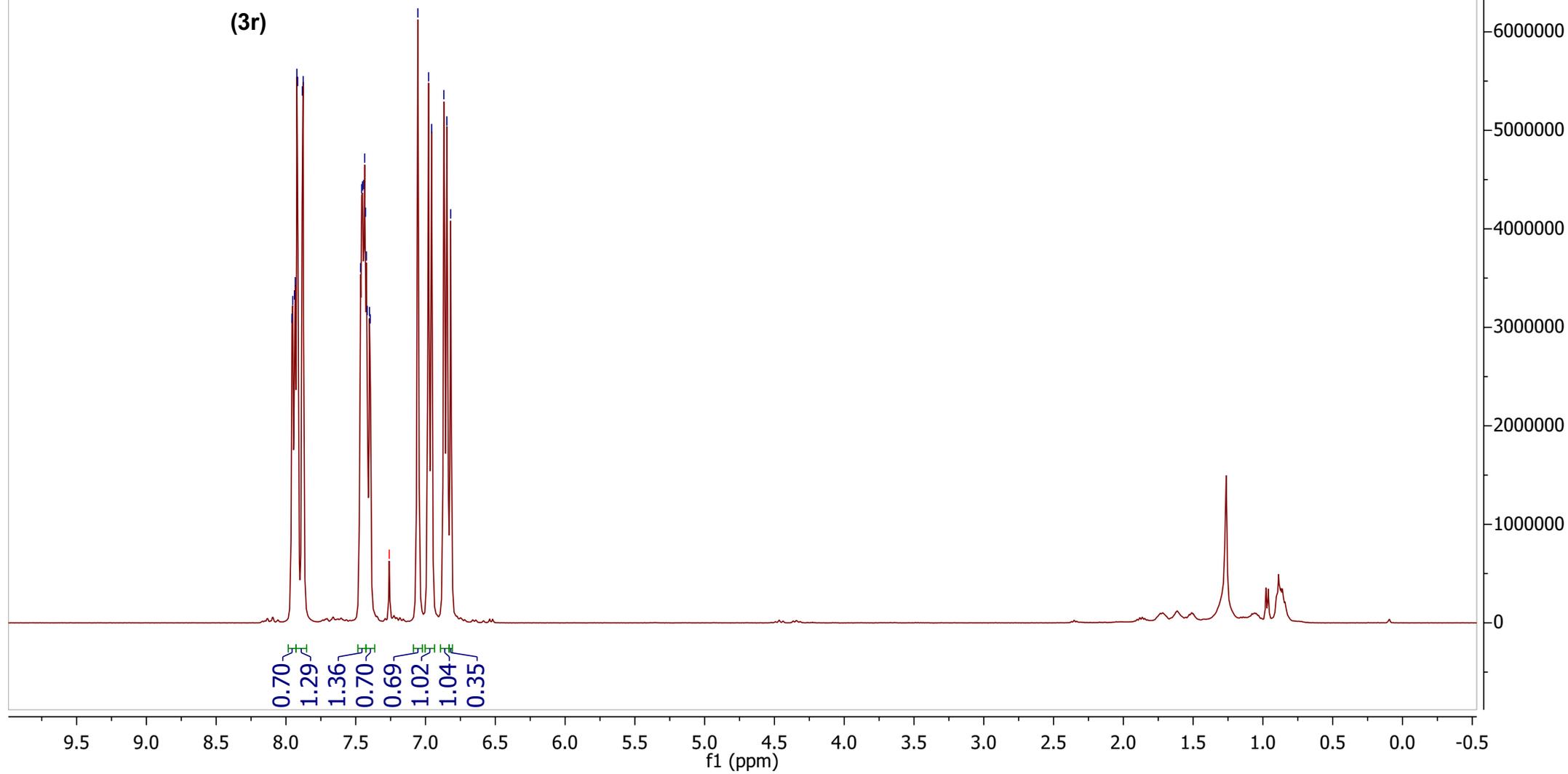
(3q)



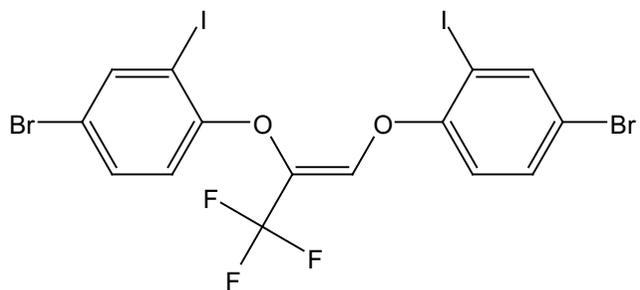
¹H NMR (400 MHz, Chloroform-*d*)



(3r)



¹⁹F NMR (376 MHz, Chloroform-*d*)



(3r)

—64.41

—69.07

0.31

0.69

9.0×10^7

8.0×10^7

7.0×10^7

6.0×10^7

5.0×10^7

4.0×10^7

3.0×10^7

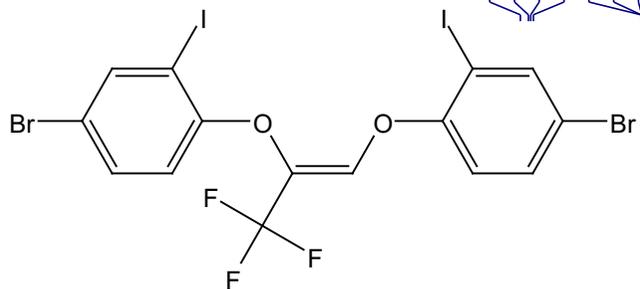
2.0×10^7

1.0×10^7

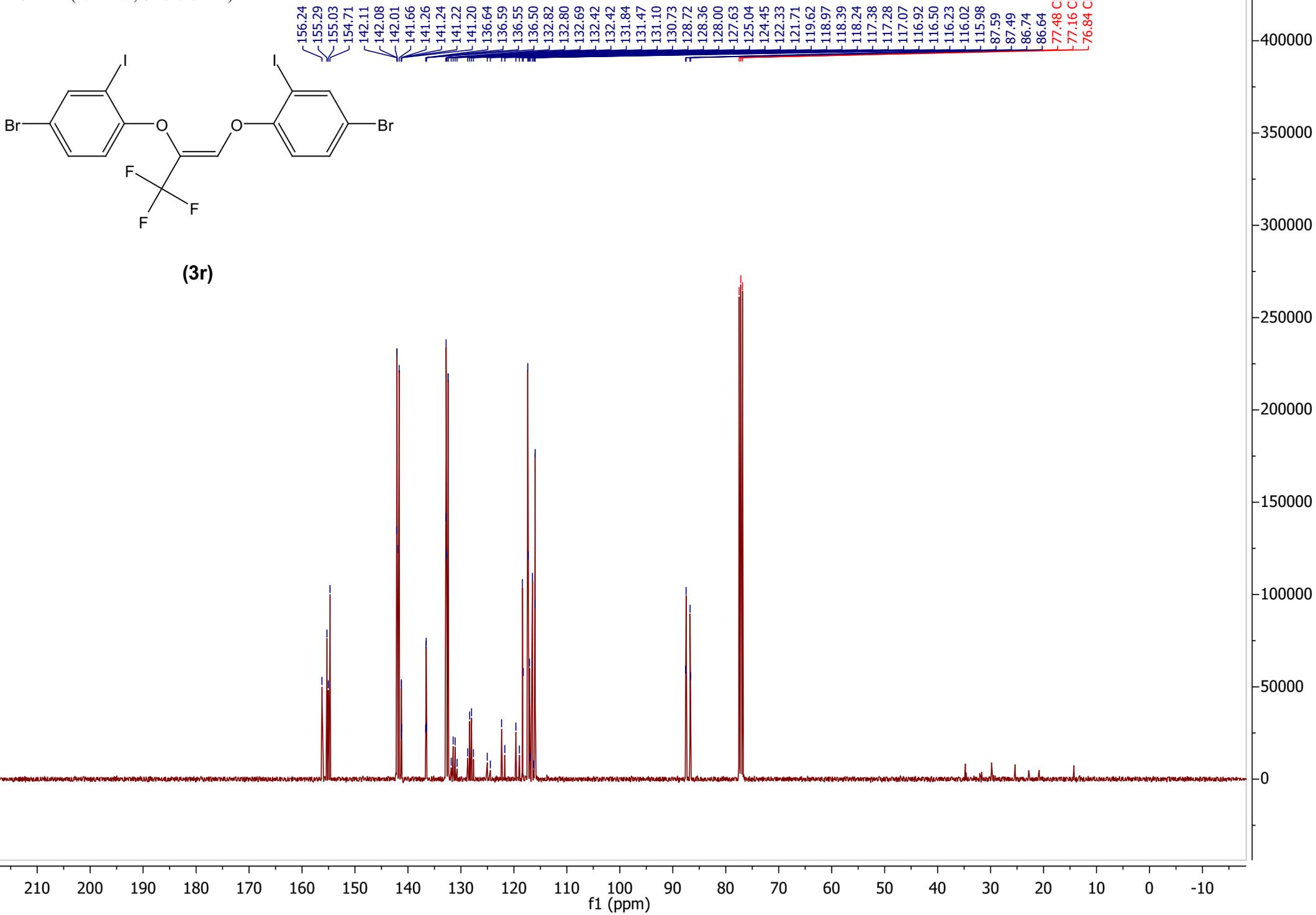
0.0

20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

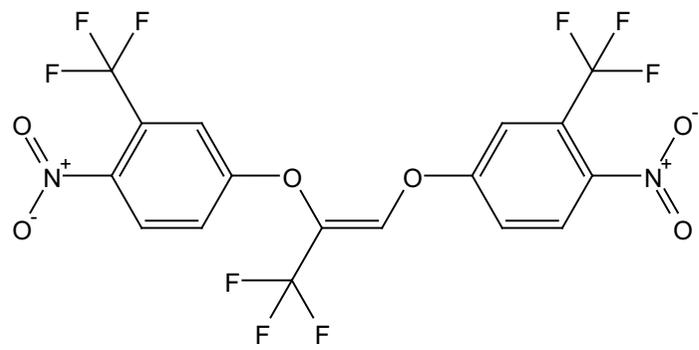
¹³C NMR (101 MHz, Chloroform-*d*)



(3r)



¹H NMR (400 MHz, Chloroform-*d*)



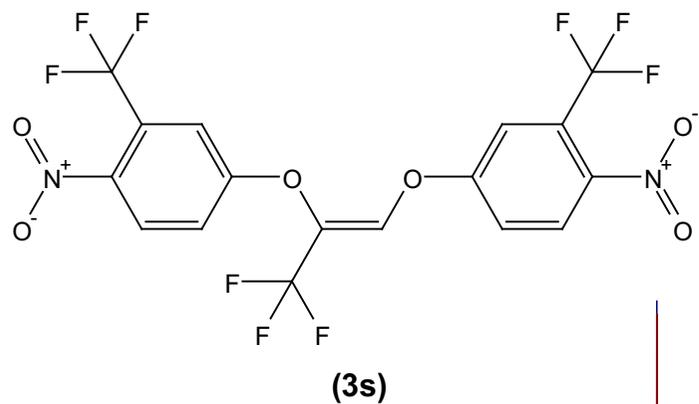
8.03
8.03
8.01
8.01
7.50
7.43
7.42
7.40
7.40
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.26 CDCl₃

1.00
1.03
0.98
1.07
1.06
1.04
0.97

10.0 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 0.5 0.0 -0.5
f1 (ppm)

8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000

¹⁹F NMR (376 MHz, Chloroform-*d*)



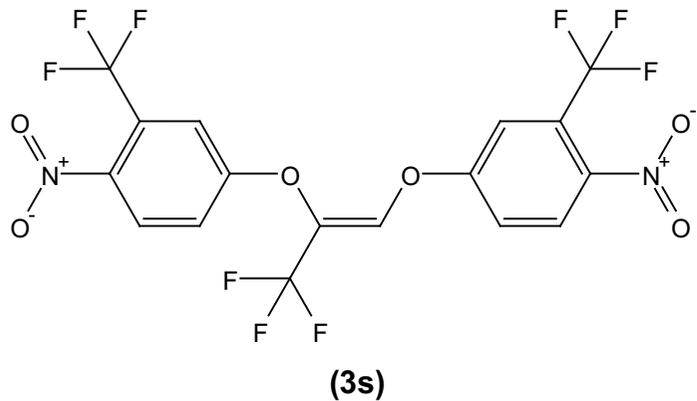
-60.28
-60.31
-64.52
-69.23

20 10 0 -10 -20 -30 -40 -50 -60 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

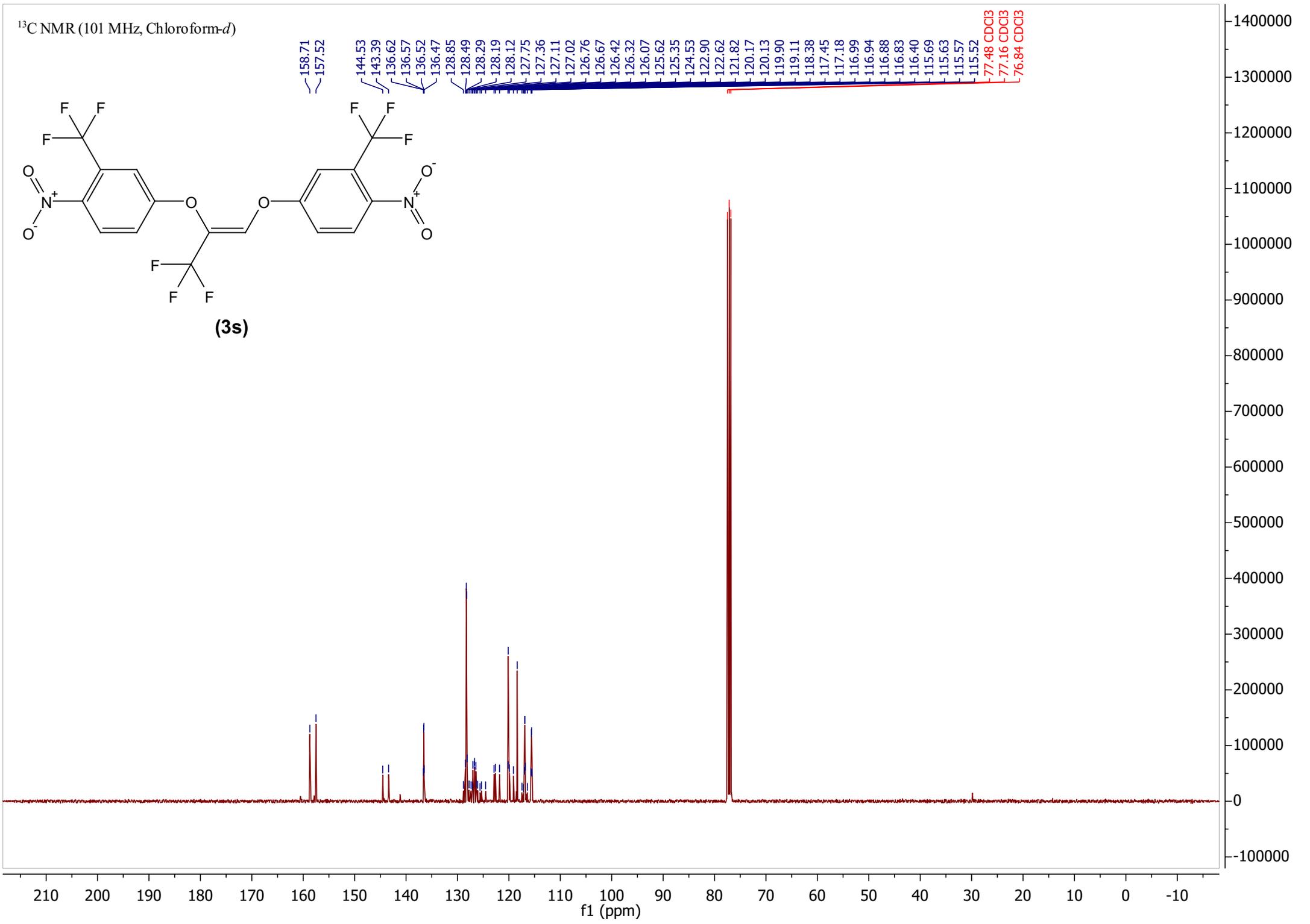
1.10×10⁸
1.00×10⁸
9.00×10⁷
8.00×10⁷
7.00×10⁷
6.00×10⁷
5.00×10⁷
4.00×10⁷
3.00×10⁷
2.00×10⁷
1.00×10⁷
0.00
-1.00×10⁷

0.99
1.04
0.08
1.00

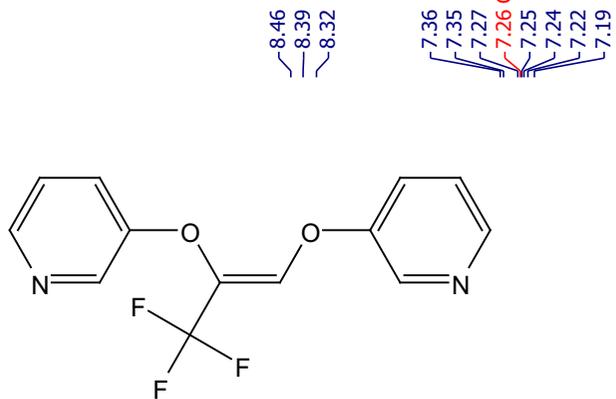
¹³C NMR (101 MHz, Chloroform-*d*)



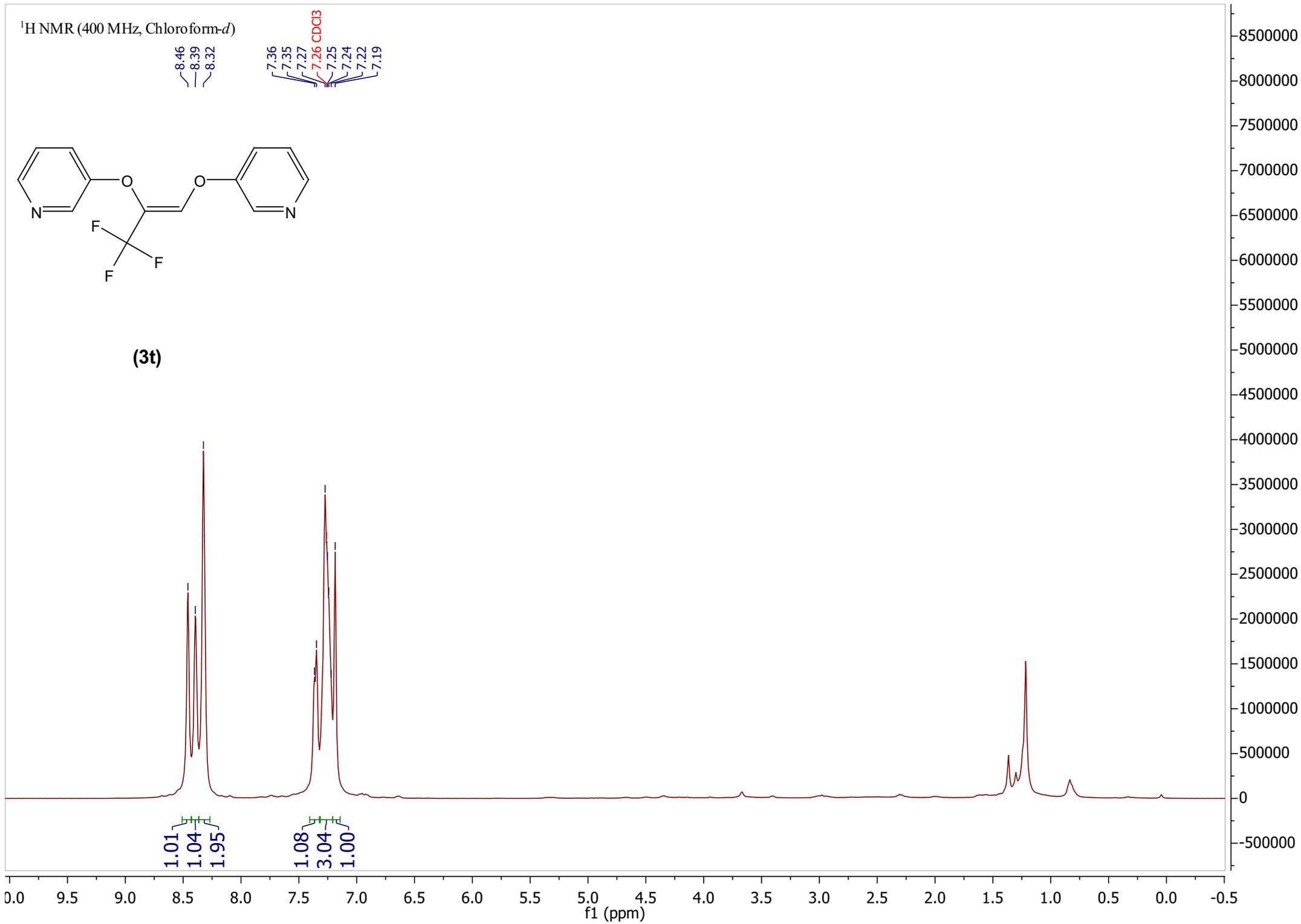
158.71
157.52
144.53
143.39
136.62
136.57
136.52
136.47
128.85
128.49
128.29
128.19
128.12
127.75
127.36
127.11
127.02
126.76
126.67
126.42
126.32
126.07
125.62
125.35
124.53
122.90
122.62
121.82
120.17
120.13
119.90
119.11
118.38
117.45
117.18
116.99
116.94
116.88
116.83
116.40
115.69
115.63
115.57
115.52
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3



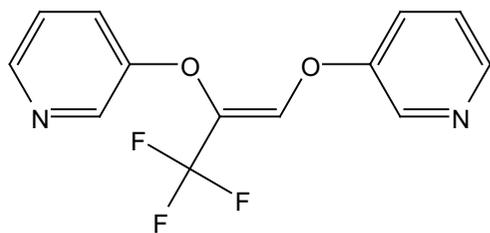
¹H NMR (400 MHz, Chloroform-*d*)



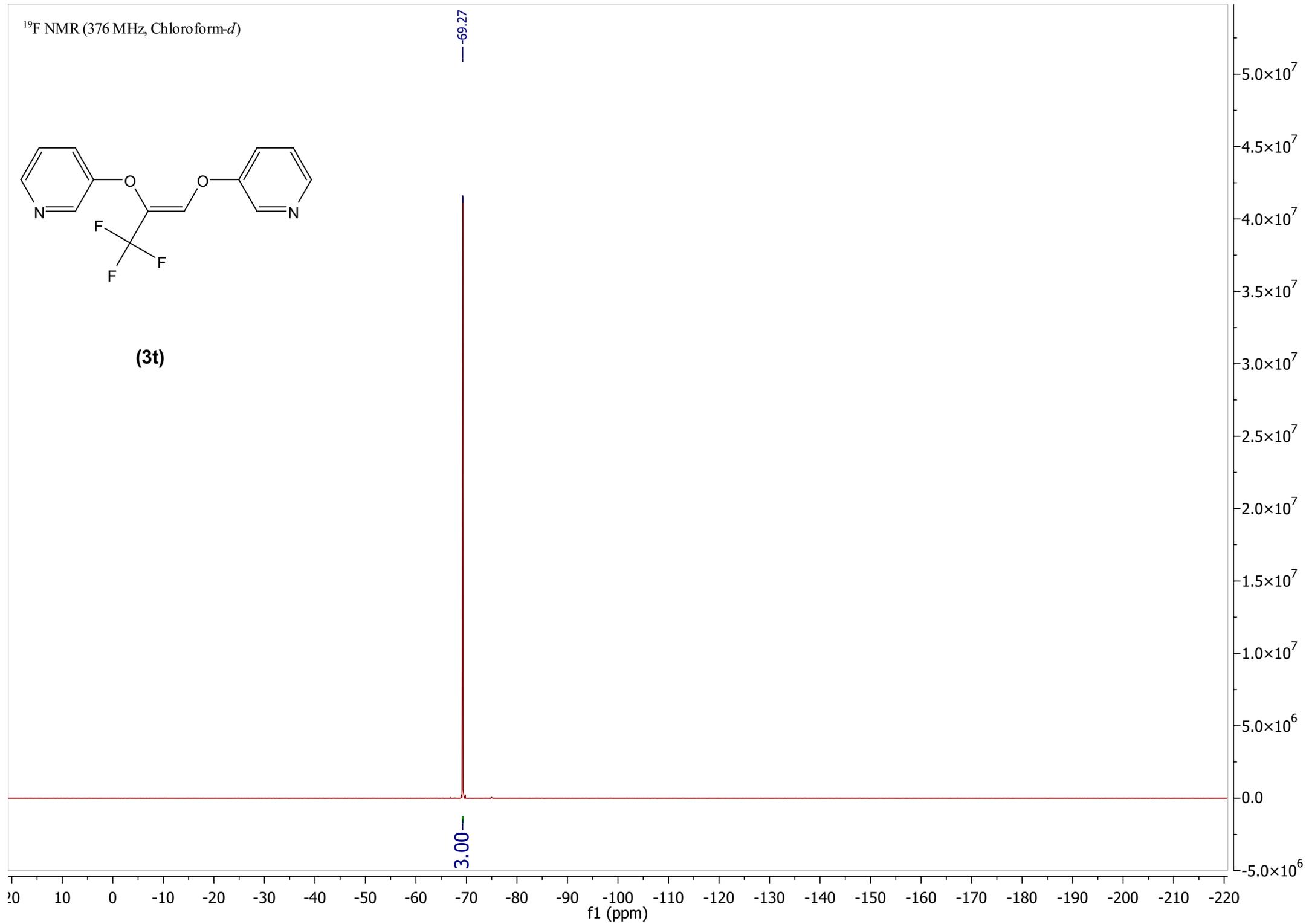
(3t)



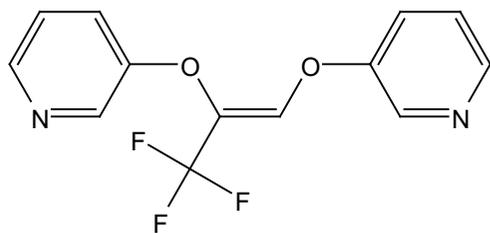
¹⁹F NMR (376 MHz, Chloroform-*d*)



(3t)



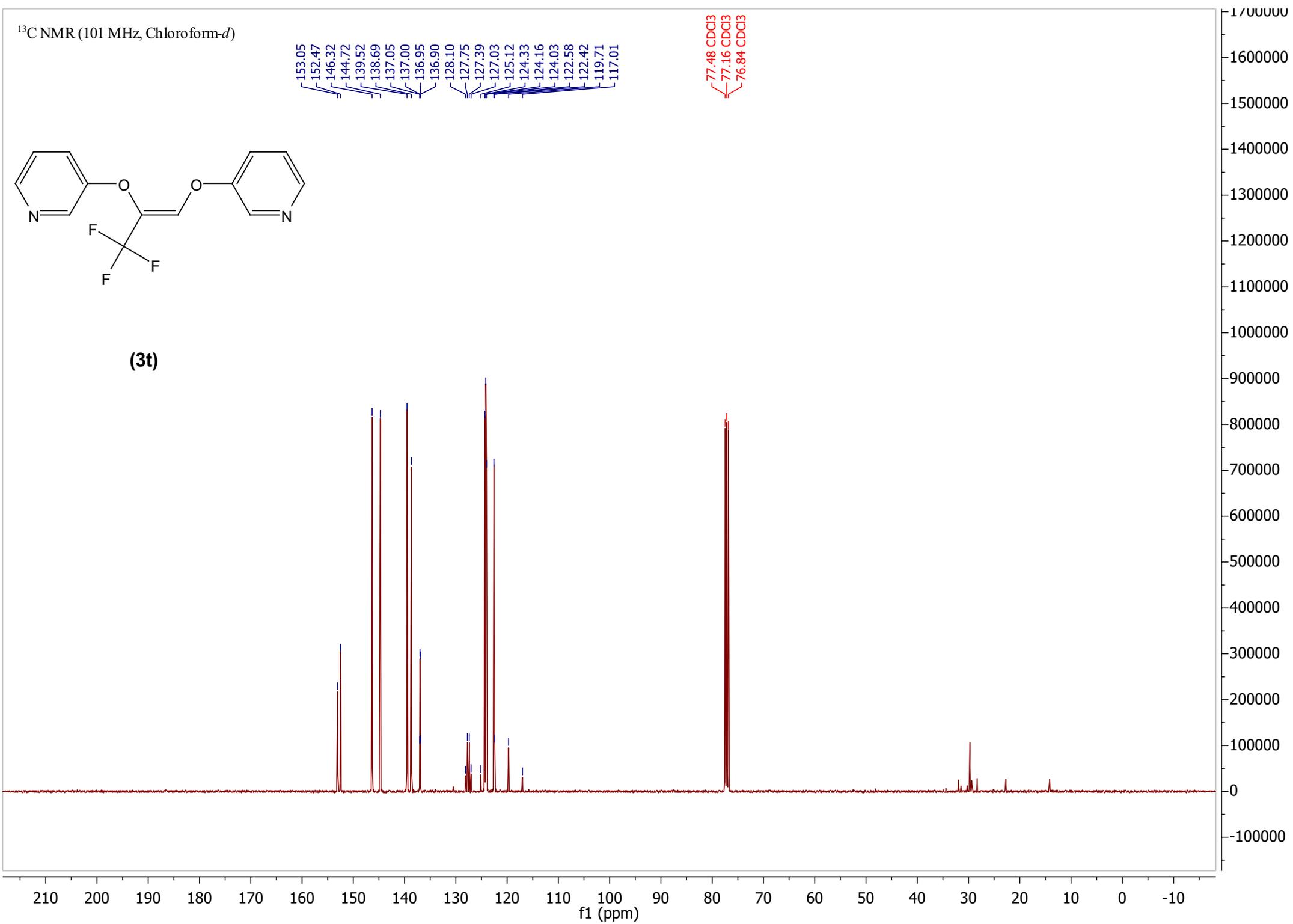
¹³C NMR (101 MHz, Chloroform-*d*)



(3t)

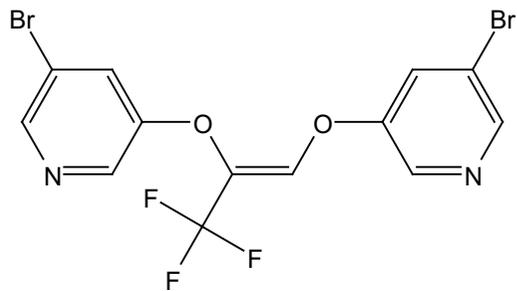
153.05
152.47
146.32
144.72
139.52
138.69
137.05
137.00
136.95
136.90
128.10
127.75
127.39
127.03
125.12
124.33
124.16
124.03
122.58
122.42
119.71
117.01

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃



¹H NMR (400 MHz, Chloroform-*d*)

8.48
8.48
8.40
8.40
8.37
8.37
8.29
8.28
7.53
7.52
7.51
7.51
7.50
7.49
7.26 CDCl₃
7.21
7.21
7.20
7.20



(3u)

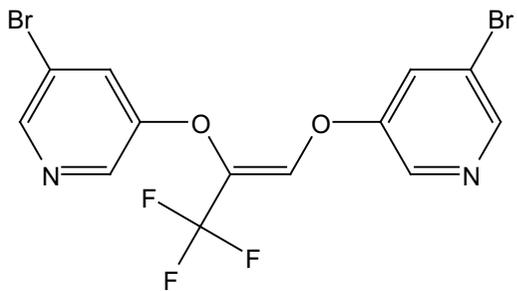
1.00
1.02
1.00
0.98
1.01
0.95
1.00

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 0.5 0.0

f1 (ppm)

2.0 × 10⁷
2.4 × 10⁷
2.2 × 10⁷
2.0 × 10⁷
1.8 × 10⁷
1.6 × 10⁷
1.4 × 10⁷
1.2 × 10⁷
1.0 × 10⁷
8.0 × 10⁶
6.0 × 10⁶
4.0 × 10⁶
2.0 × 10⁶
0.0
-2.0 × 10⁶

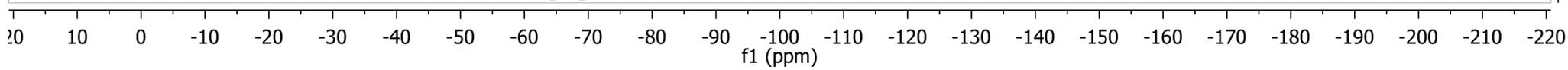
¹⁹F NMR (376 MHz, Chloroform-*d*)



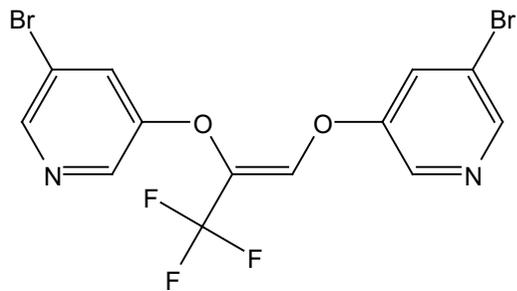
(3u)

— 64.67
— 69.23

0.03
0.97



¹³C NMR (101 MHz, Chloroform-*d*)



(3u)

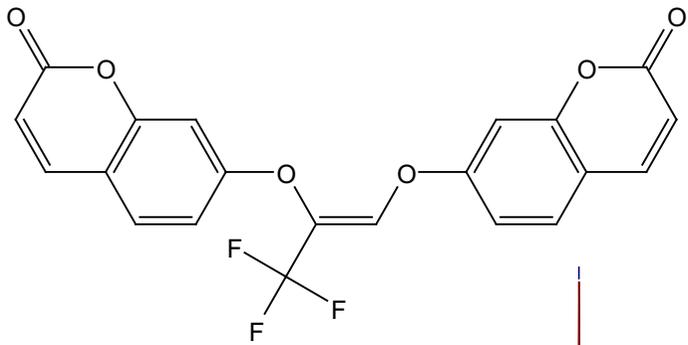
152.88
152.13
147.56
145.93
137.55
136.77
136.72
136.72
136.67
136.63
128.40
128.04
127.67
127.31
127.17
125.63
124.75
122.04
120.65
120.41
119.33
116.63

77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

¹H NMR (400 MHz, Chloroform-*d*₃)



(3v)

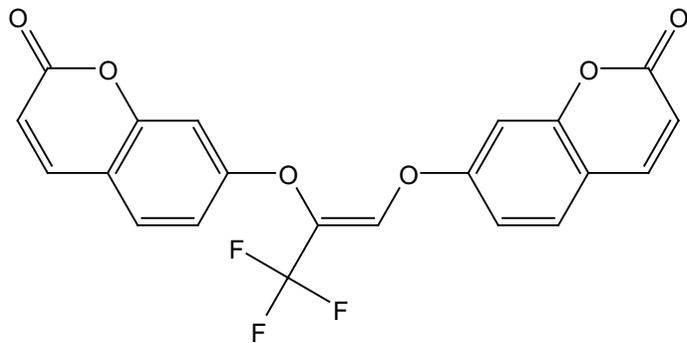
7.67
7.67
7.65
7.64
7.47
7.45
7.45
7.44
7.31
7.26
7.04
7.04
7.02
7.01
7.00
6.94
6.93
6.91
6.90
6.36
6.34
6.32
6.30

2.03
2.05
1.00
1.97
1.98
1.97

10.0 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 0.5 0.0
f1 (ppm)

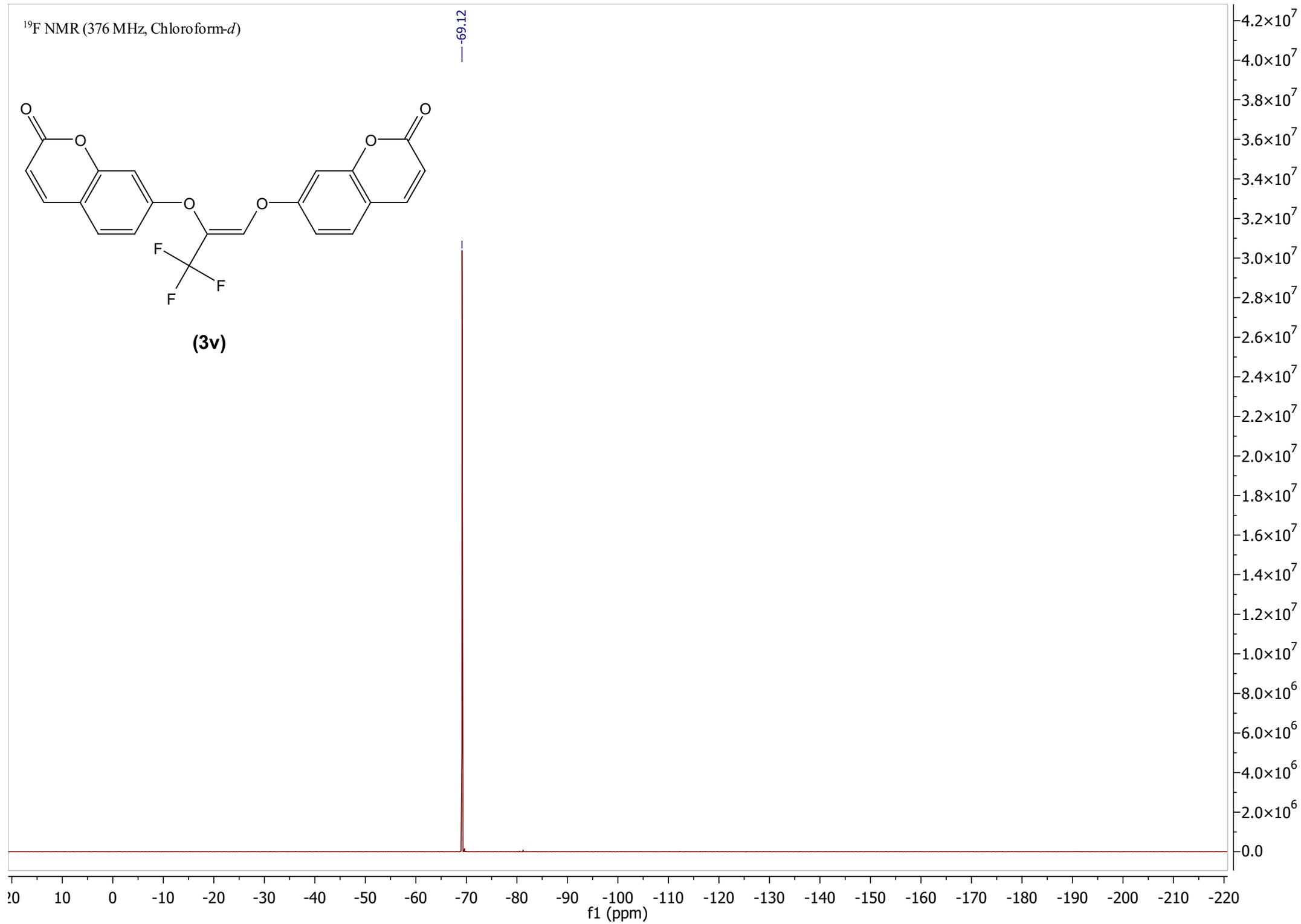
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000

^{19}F NMR (376 MHz, Chloroform-*d*)

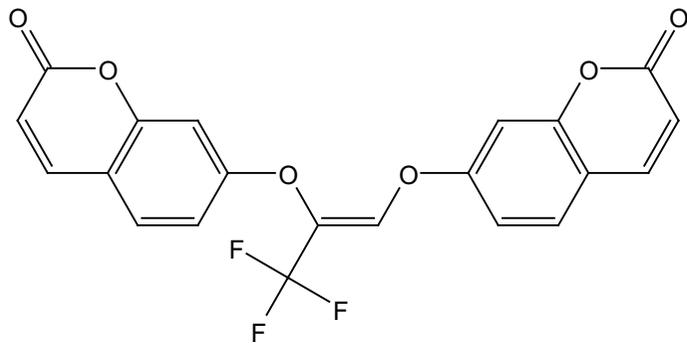


(3v)

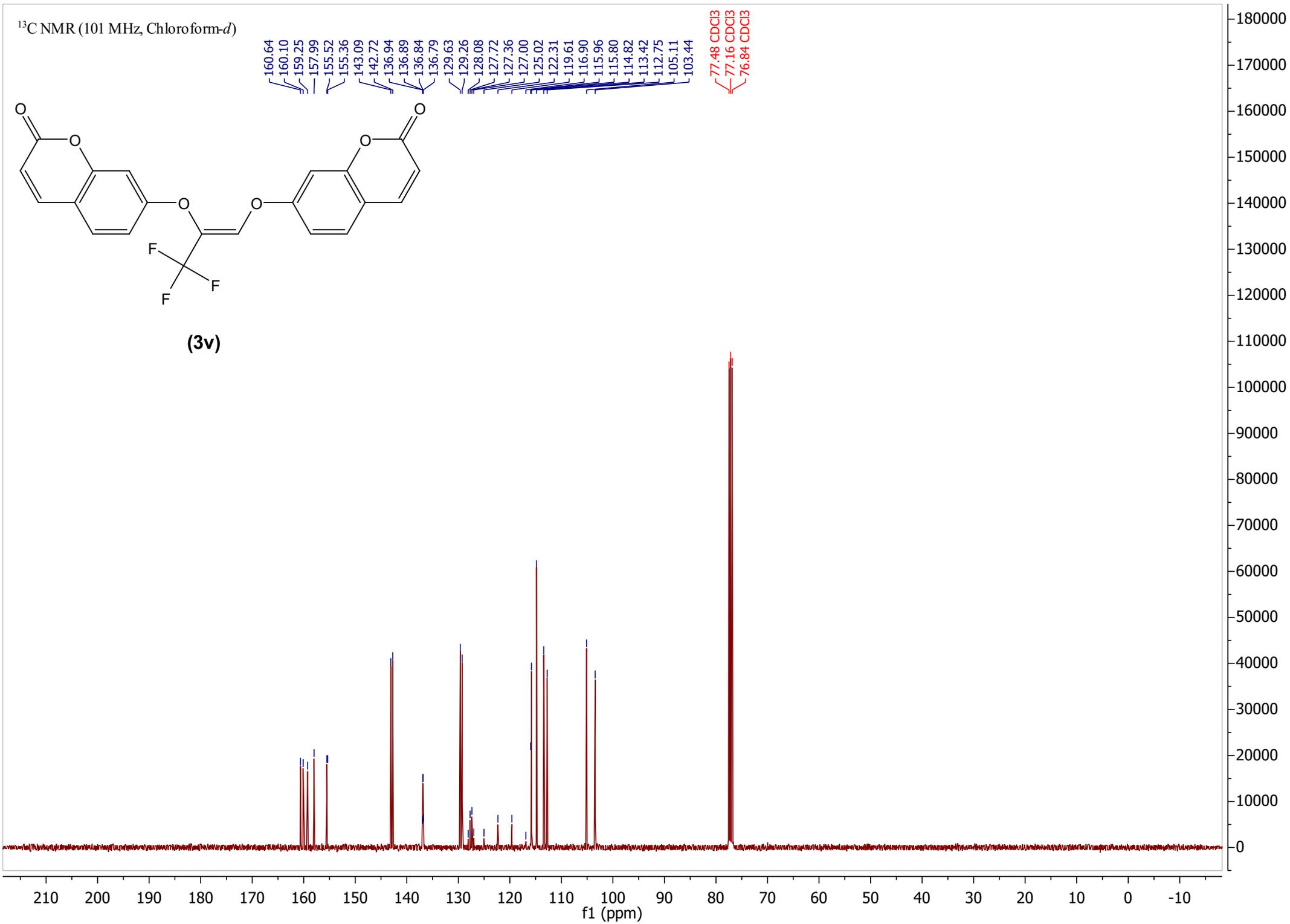
— -69.12



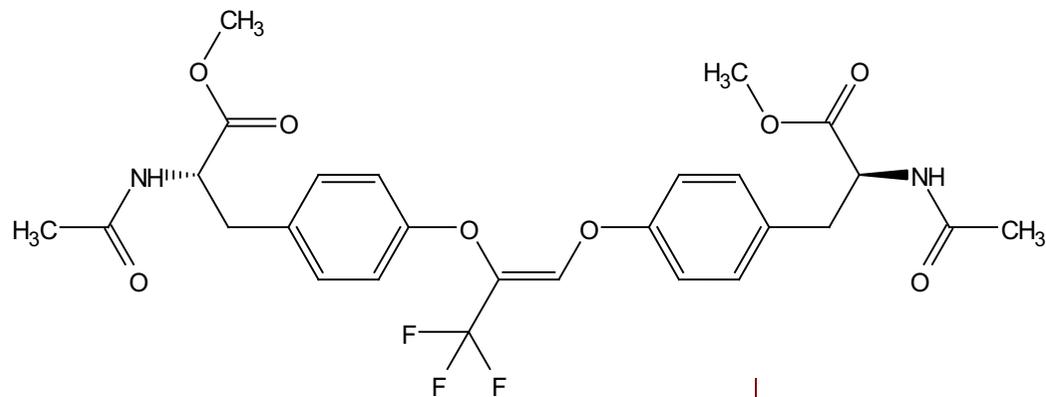
¹³C NMR (101 MHz, Chloroform-*d*)



(3v)

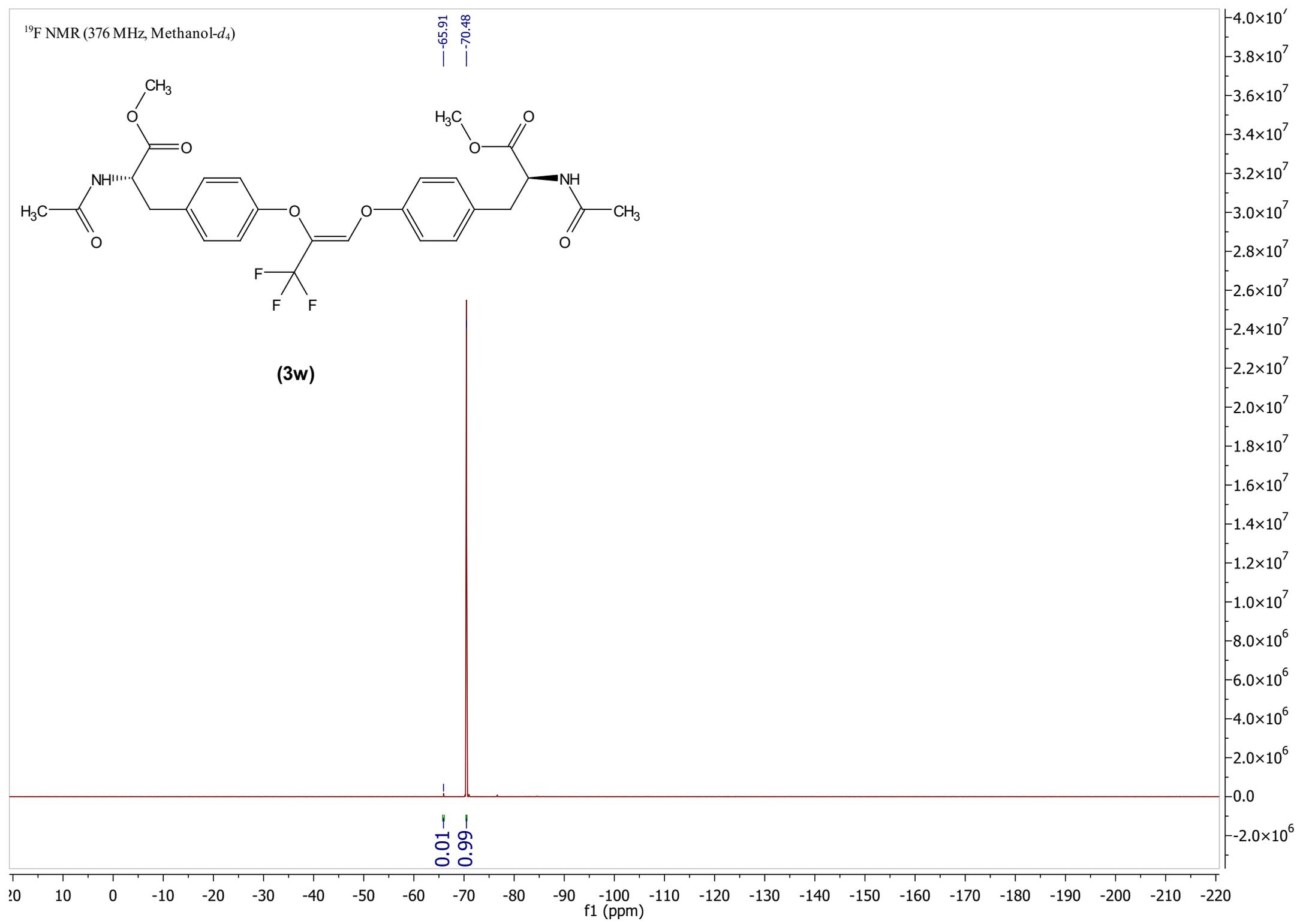


^{19}F NMR (376 MHz, Methanol- d_4)



(3w)

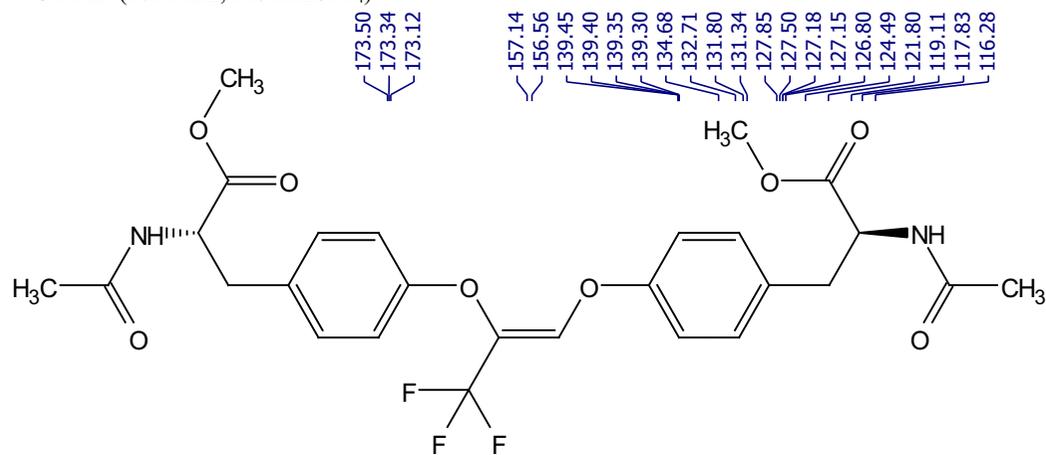
-65.91
-70.48



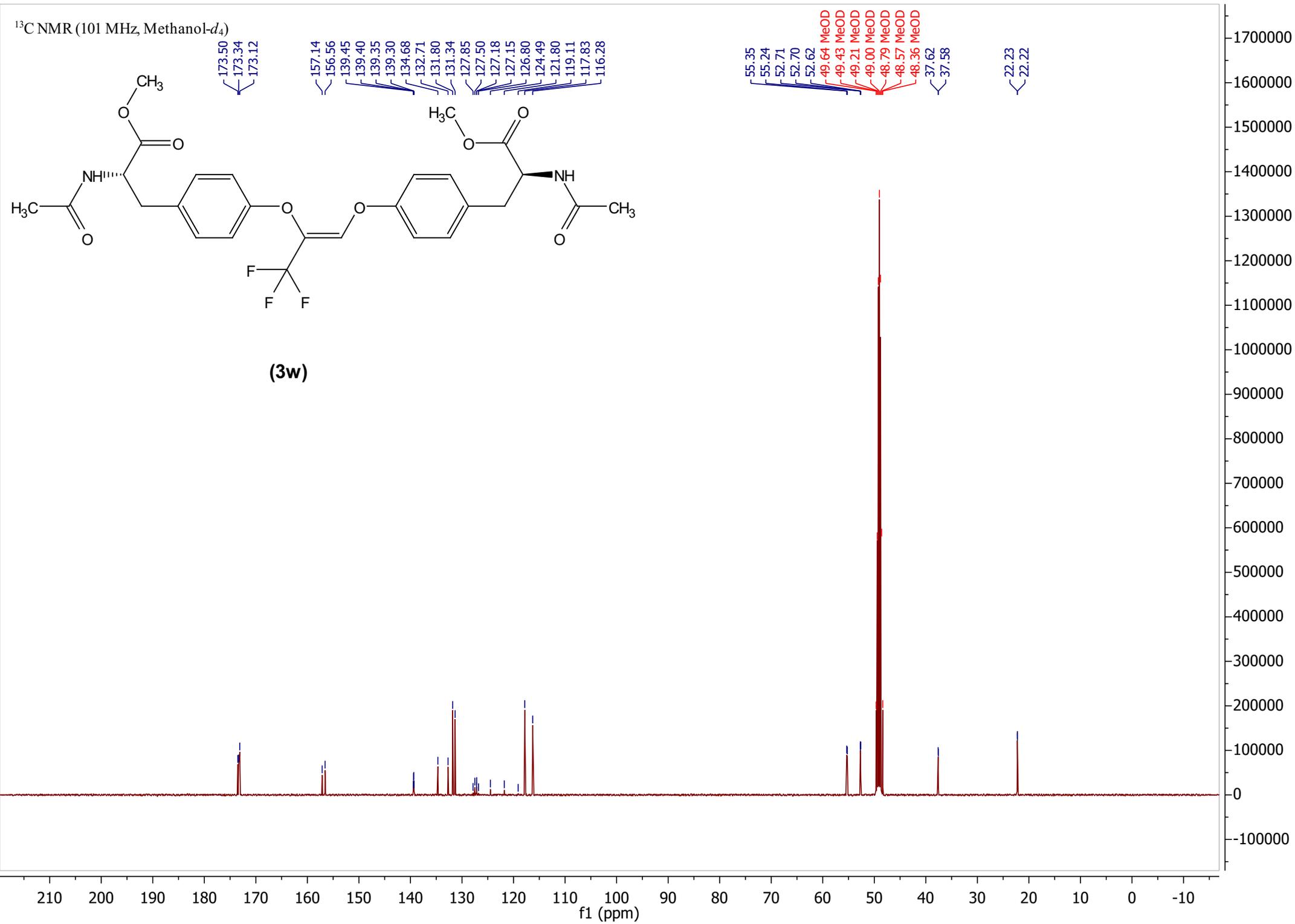
0.01
0.99

f1 (ppm)

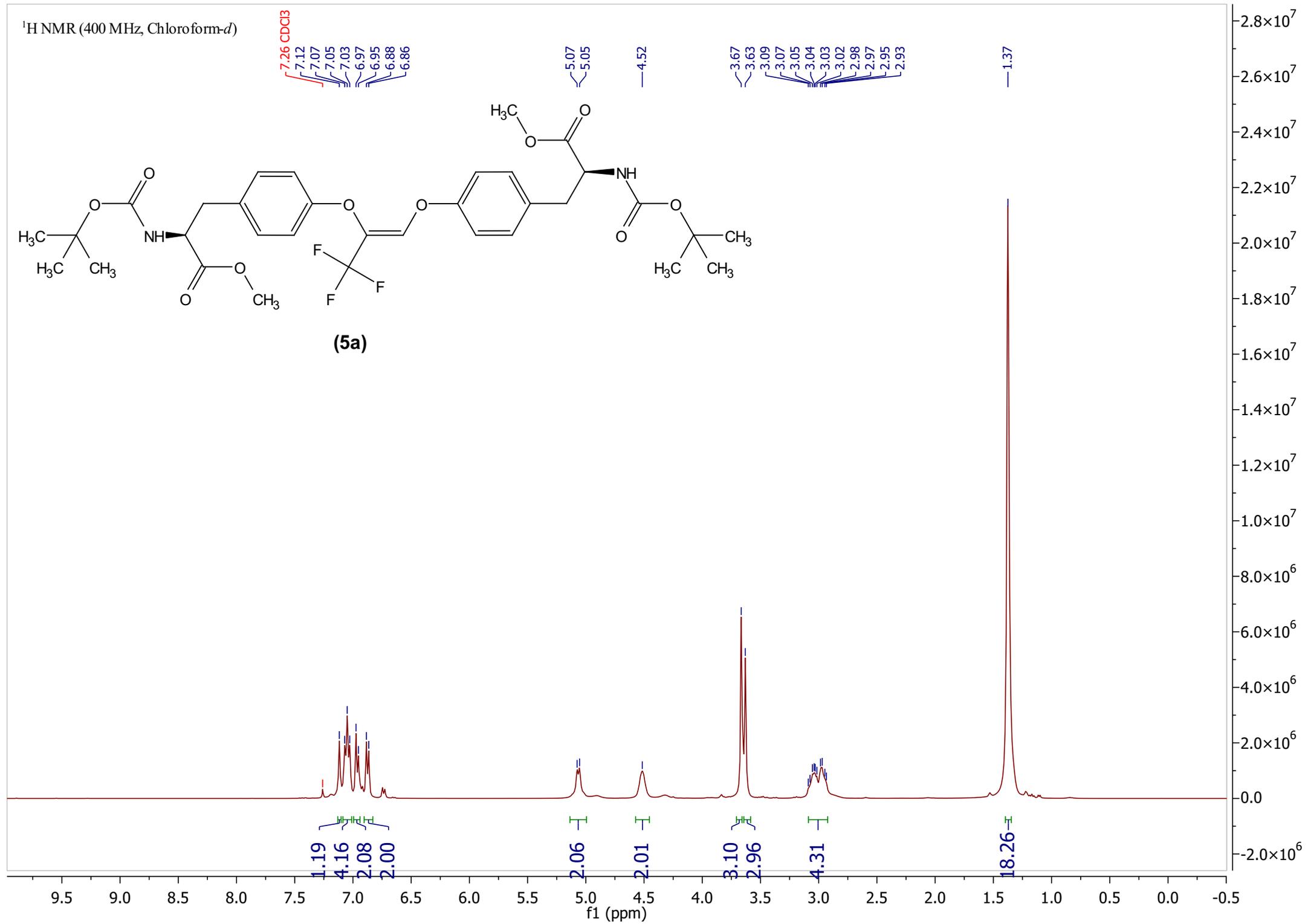
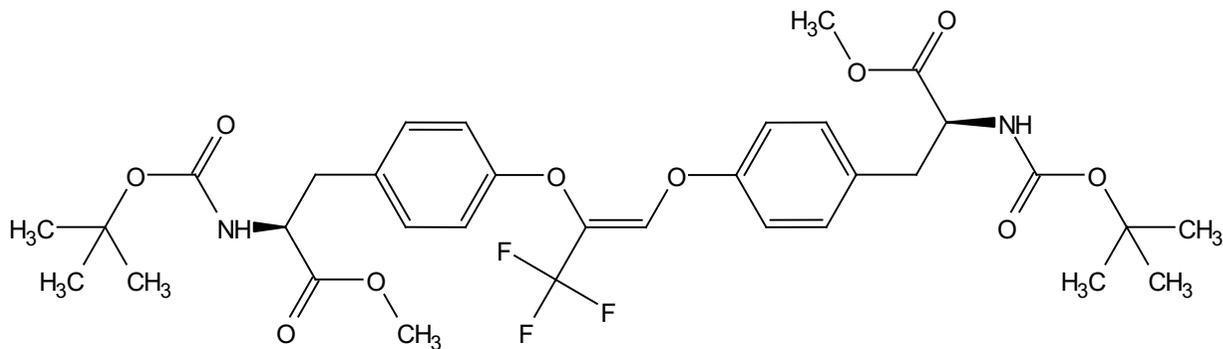
¹³C NMR (101 MHz, Methanol-d₄)



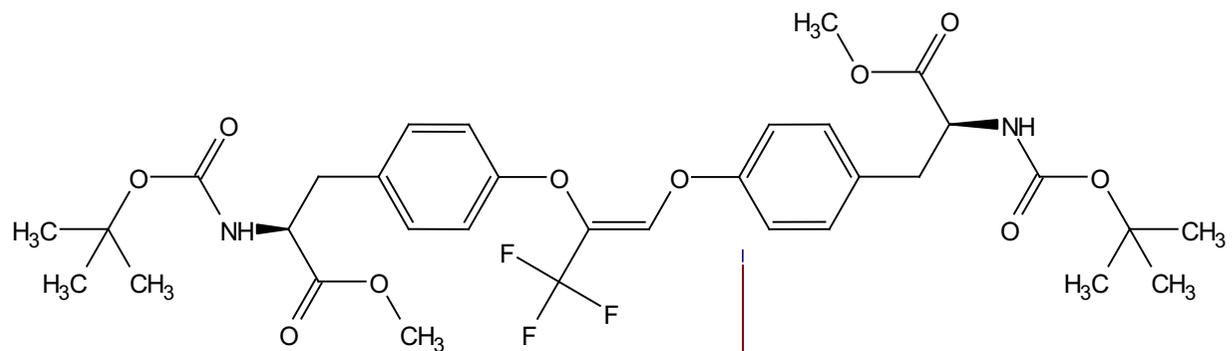
(3w)



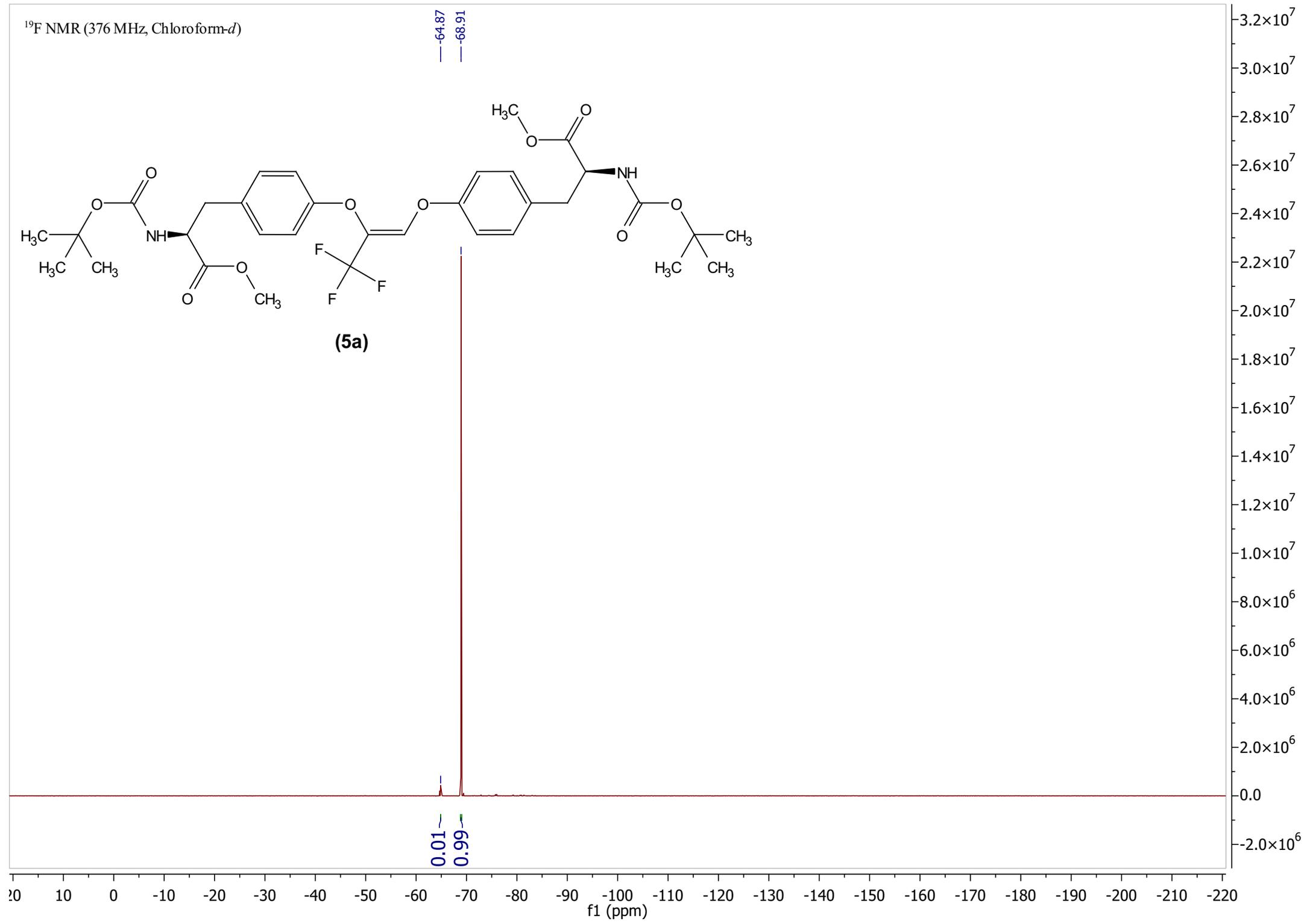
¹H NMR (400 MHz, Chloroform-*d*)



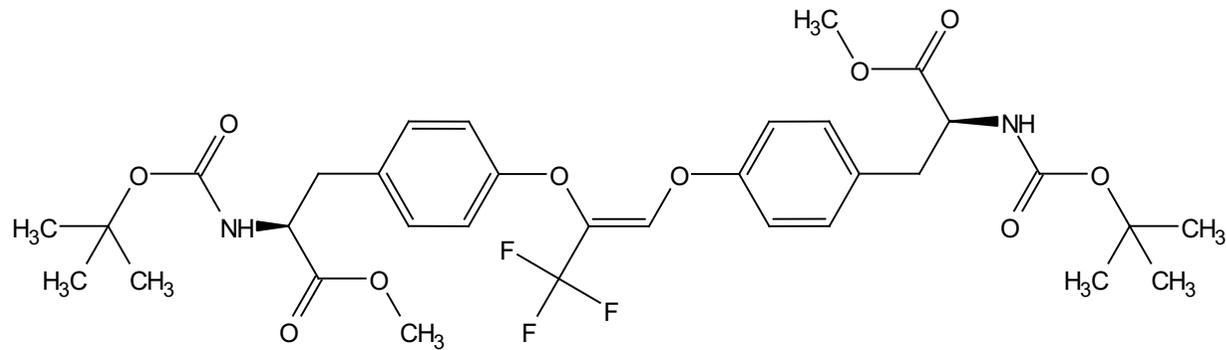
^{19}F NMR (376 MHz, Chloroform-*d*)



64.87
68.91



¹³C NMR (101 MHz, Chloroform-*d*)



(5a)

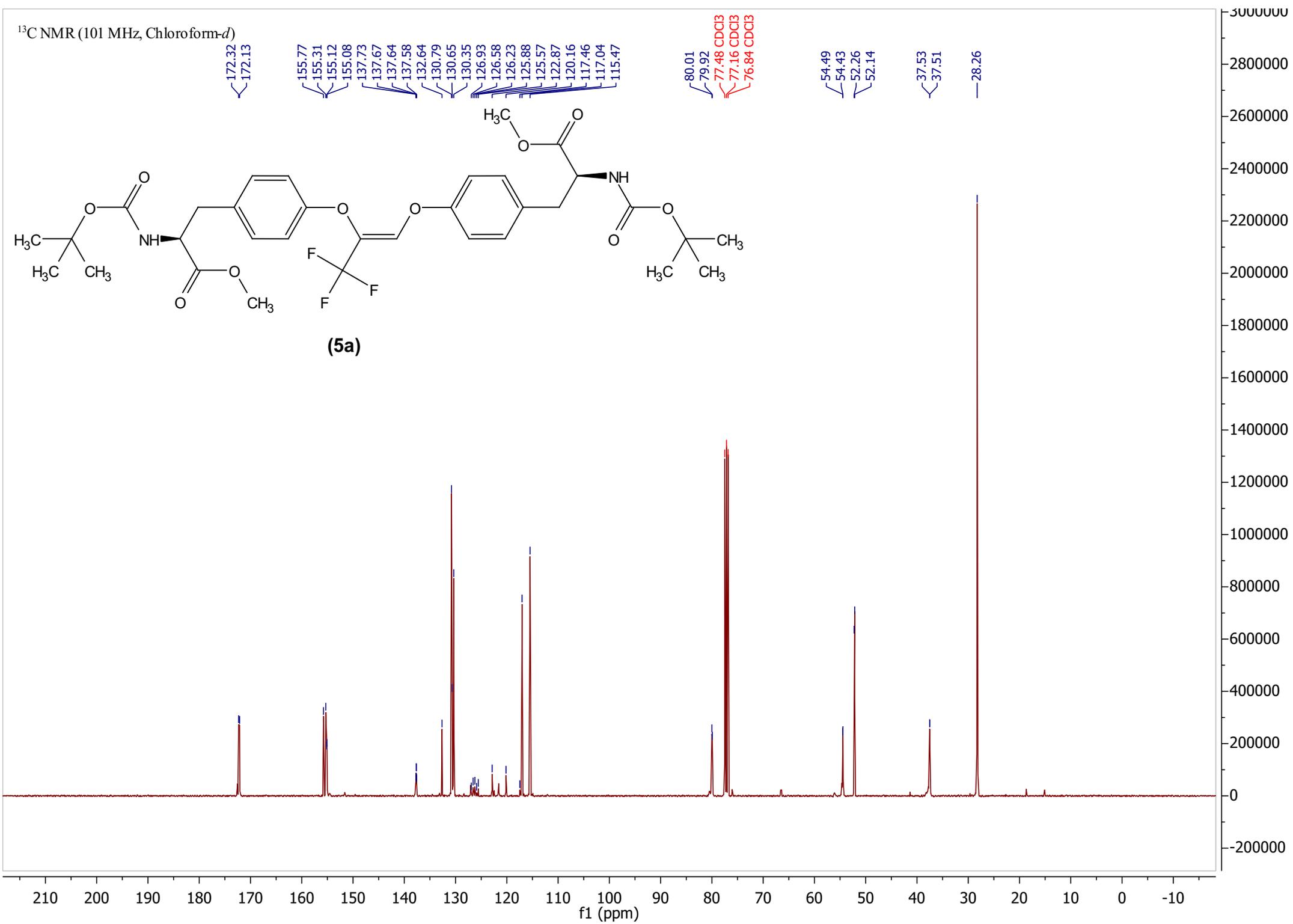
172.32
172.13
155.77
155.31
155.12
155.08
137.73
137.67
137.64
137.58
132.64
130.79
130.65
130.35
126.93
126.58
126.23
125.88
125.57
122.87
120.16
117.46
117.04
115.47

80.01
79.92
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

54.49
54.43
52.26
52.14

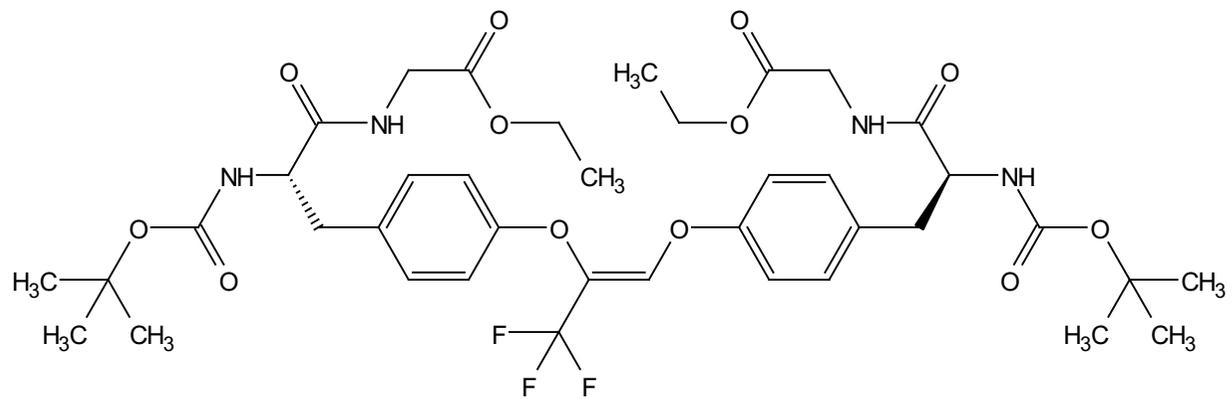
37.53
37.51

28.26

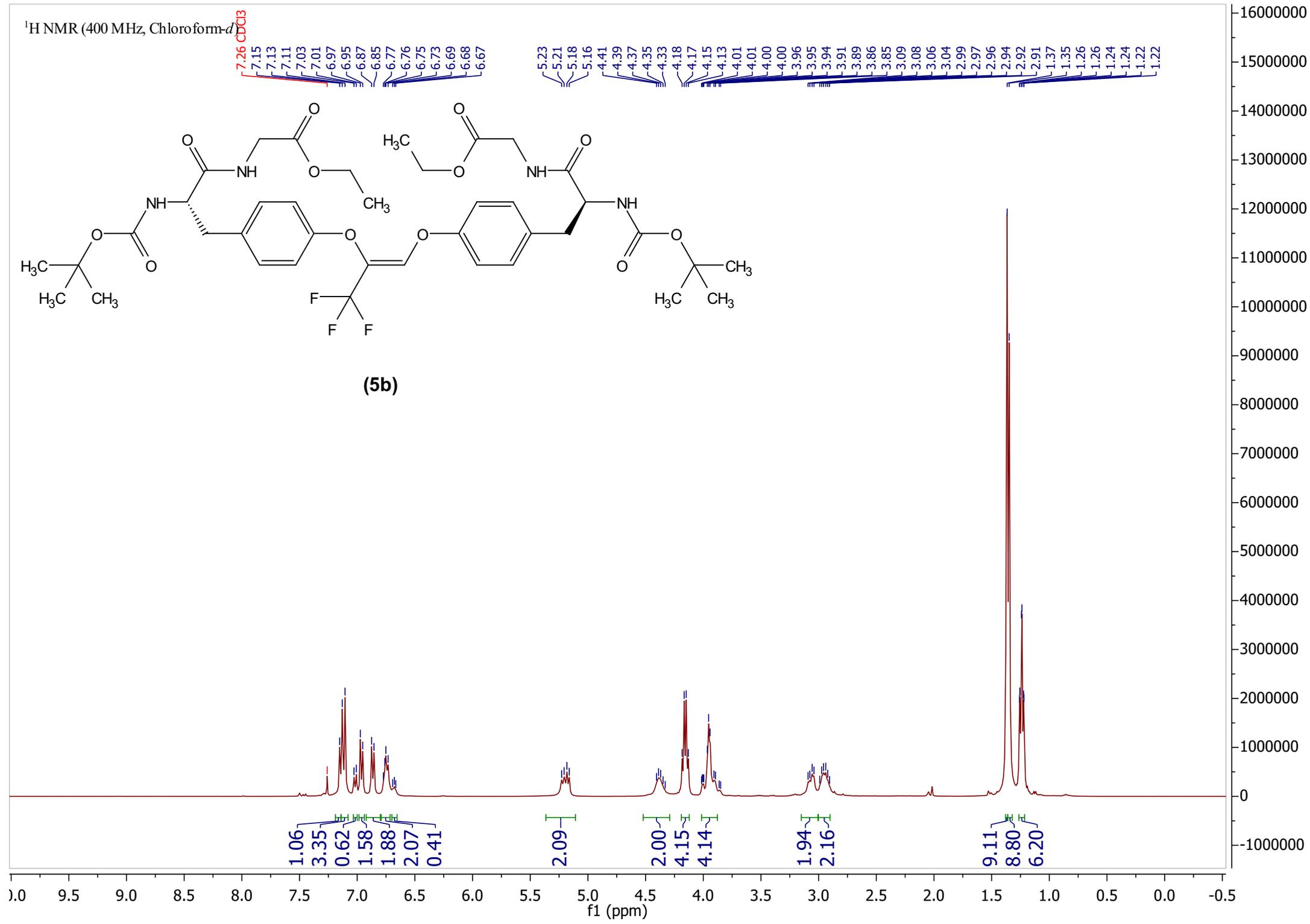


¹H NMR (400 MHz, Chloroform-*d*)

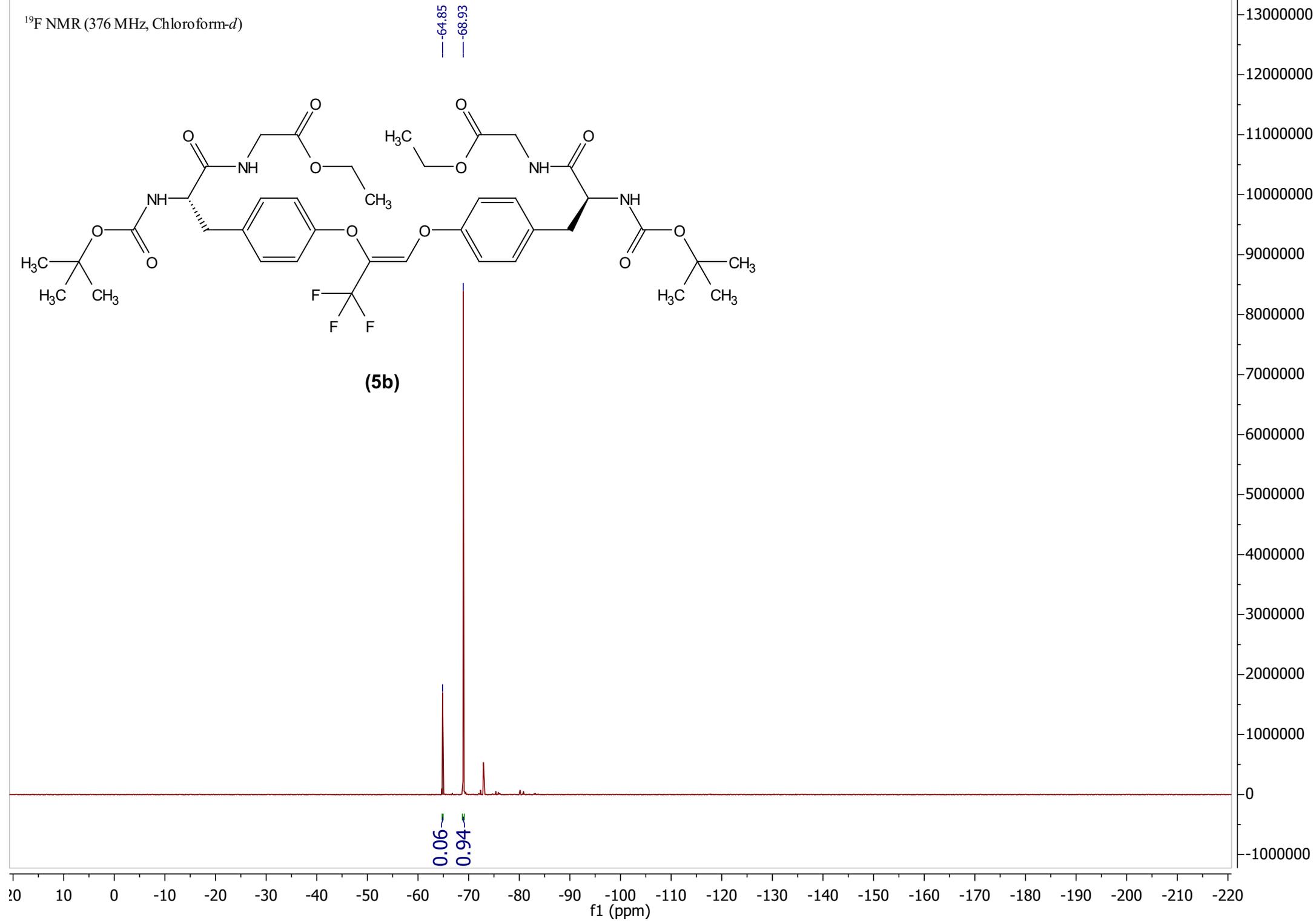
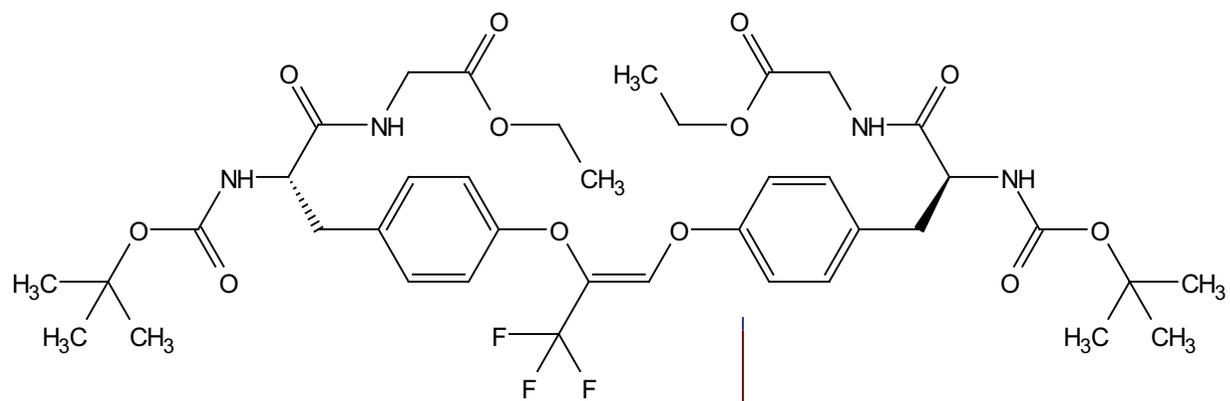
7.26 CDCl₃



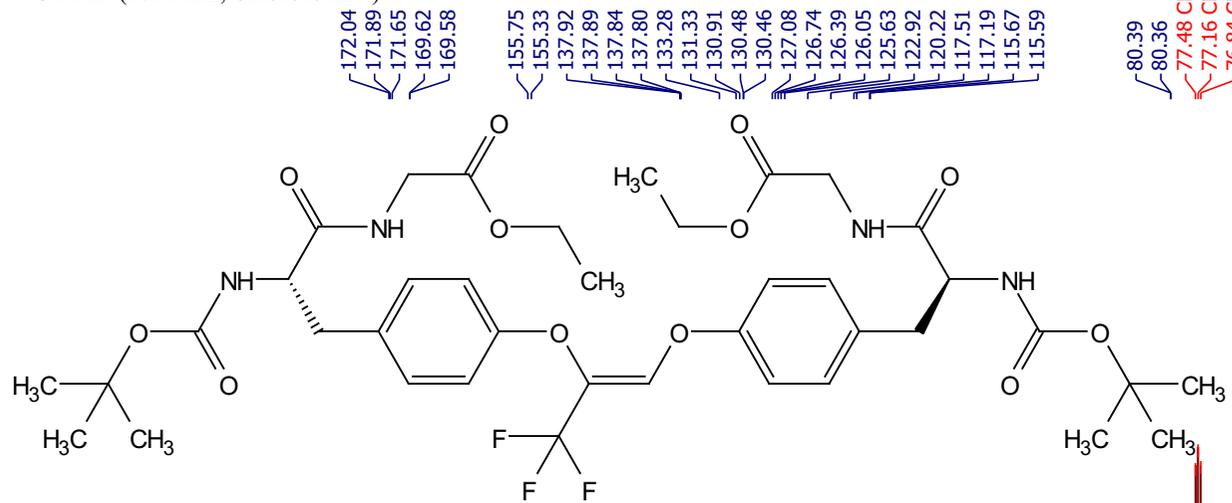
(5b)



¹⁹F NMR (376 MHz, Chloroform-*d*)



¹³C NMR (101 MHz, Chloroform-*d*)



(5b)

172.04
171.89
171.65
169.62
169.58
155.75
155.33
137.92
137.89
137.84
137.80
133.28
131.33
130.91
130.48
130.46
127.08
126.74
126.39
126.05
125.63
122.92
120.22
117.51
117.19
115.67
115.59

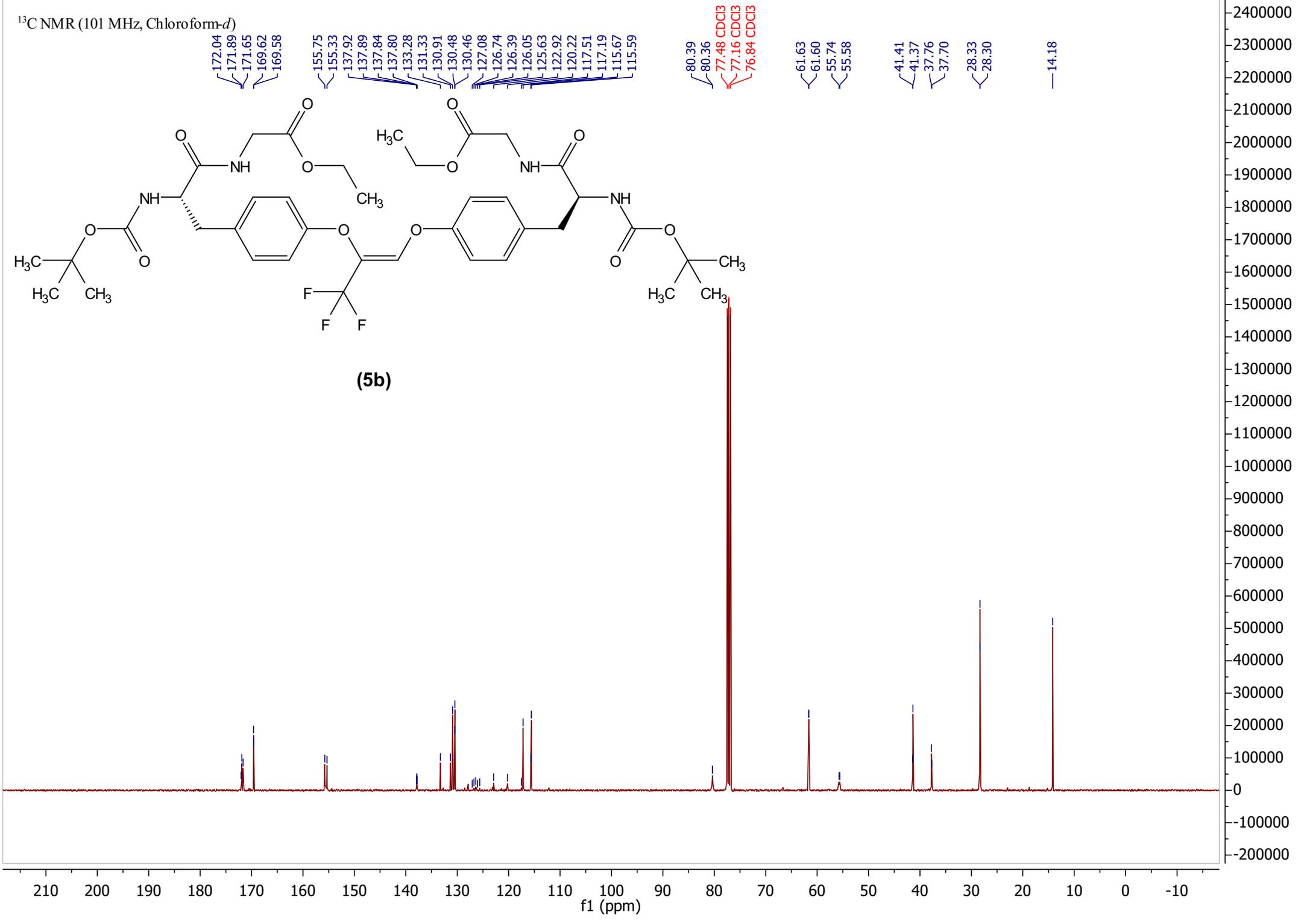
80.39
80.36
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

61.63
61.60
55.74
55.58

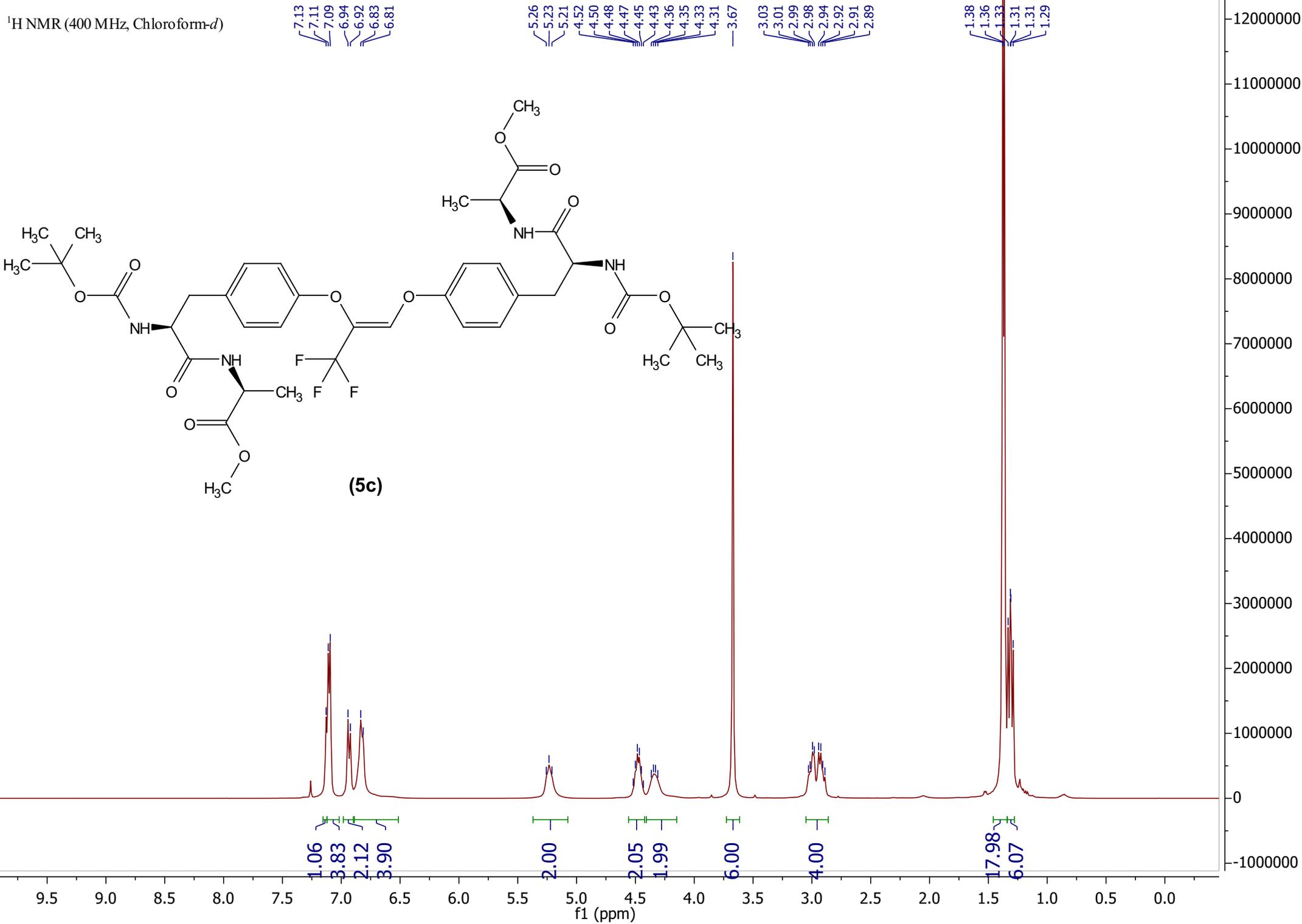
41.41
41.37
37.76
37.70

28.33
28.30

14.18

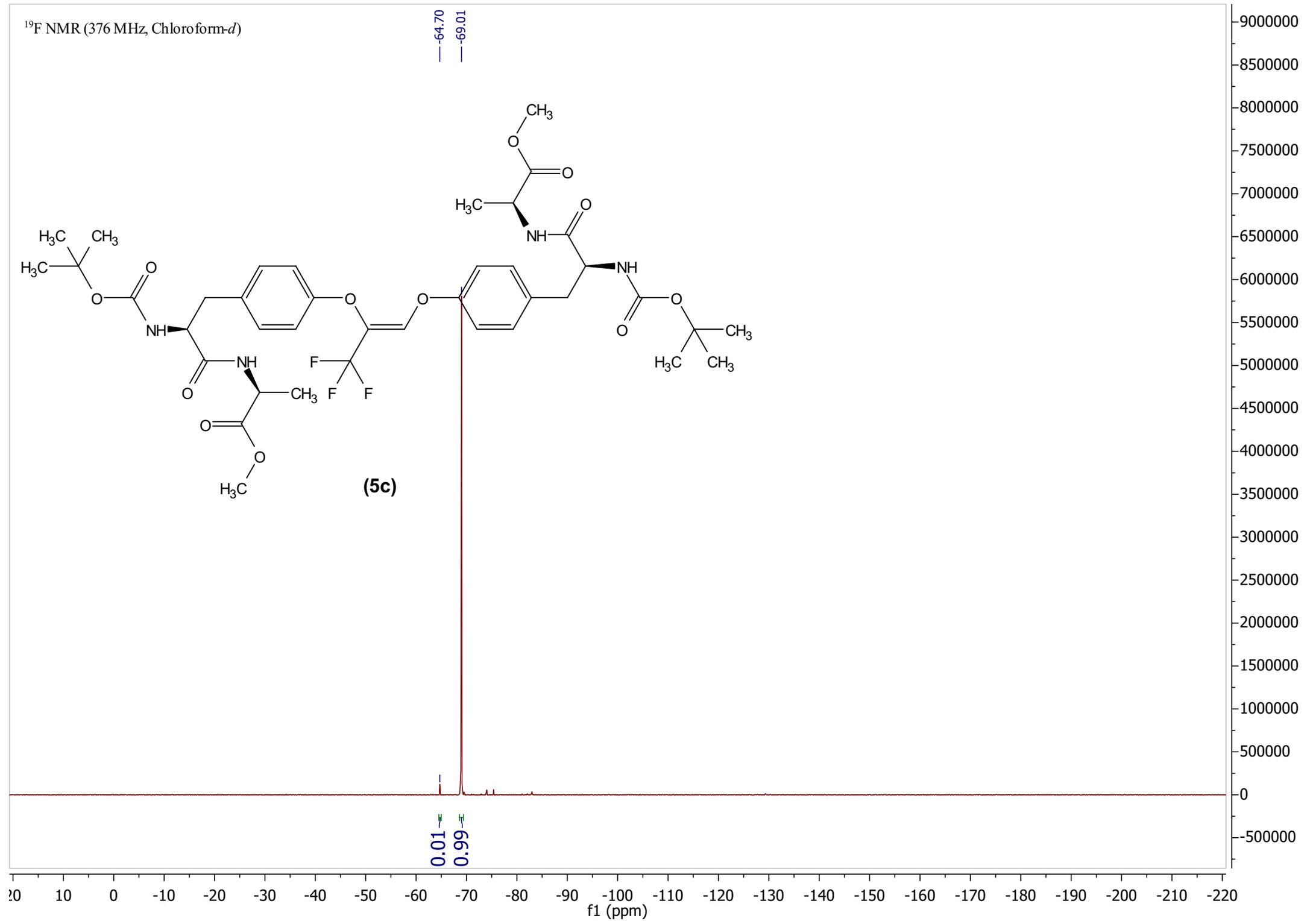
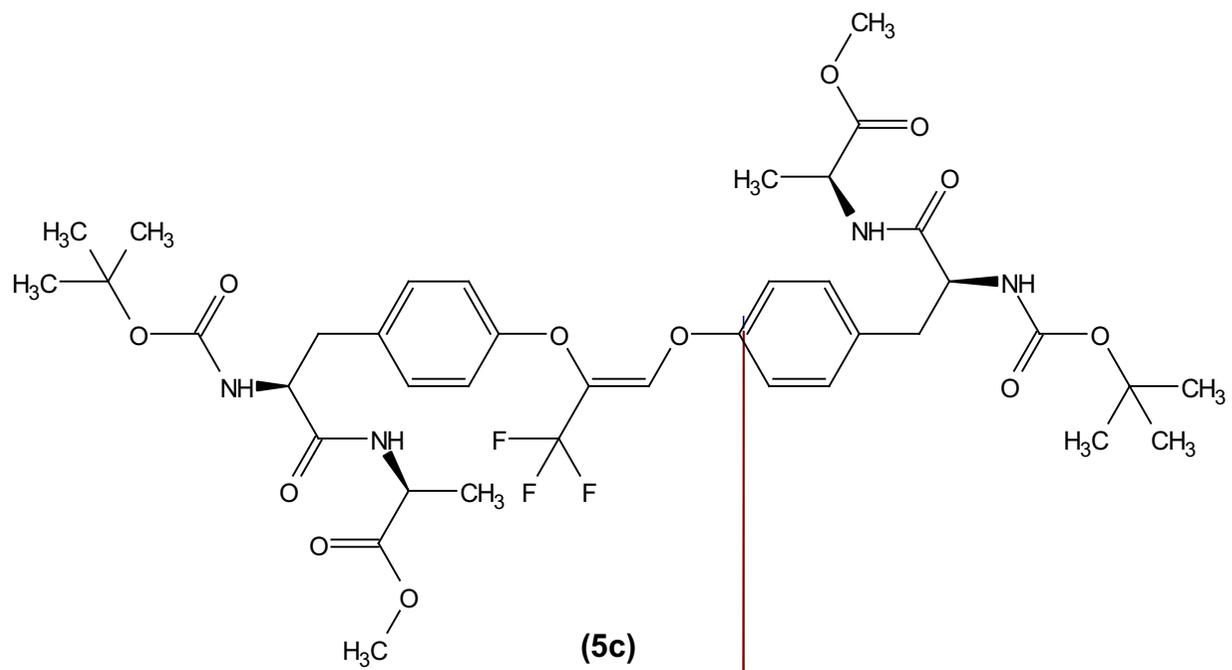


¹H NMR (400 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)

-64.70
-69.01



¹H NMR (400 MHz, Chloroform-*d*)

7.26 CDCl₃

7.11
7.08
7.05
7.03
6.97
6.95
6.88
6.86
6.51
6.50
6.49
6.48

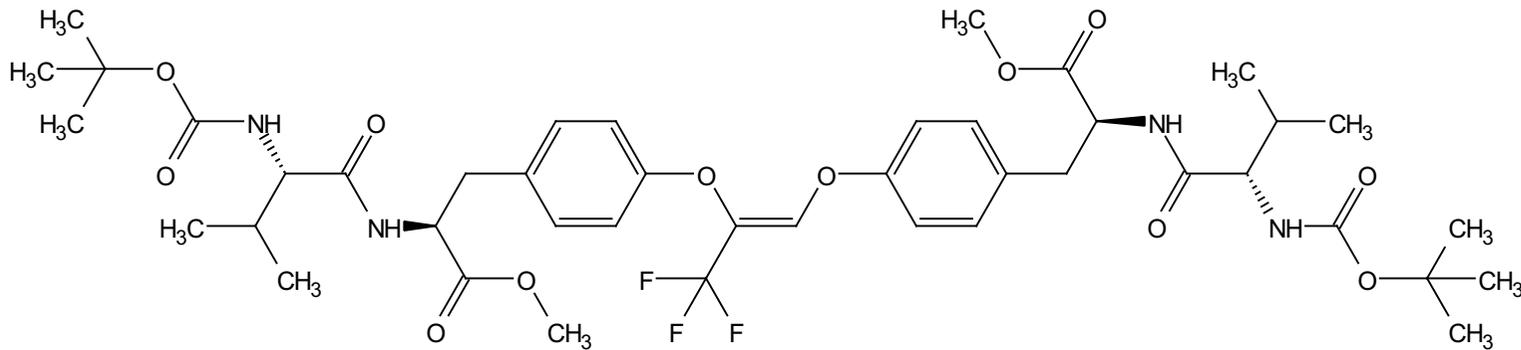
5.10
5.08
4.84
4.82
4.82
4.80
4.80
4.79
4.78

3.93
3.90
3.88
3.86
3.68
3.64

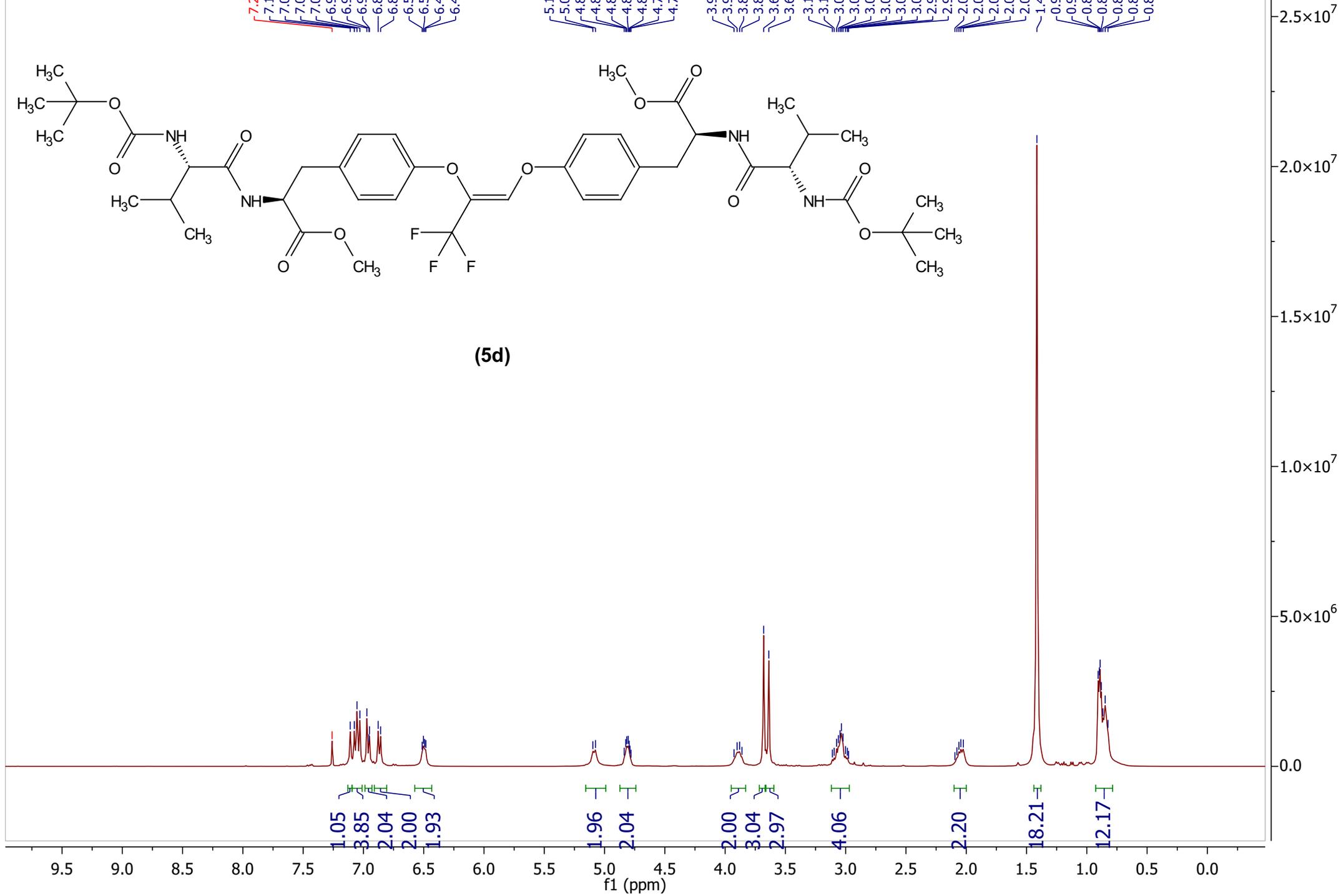
3.11
3.10
3.08
3.06
3.05
3.04
3.02
3.00
2.99
2.98

2.09
2.08
2.06
2.04
2.02

1.41
0.91
0.90
0.89
0.88
0.87
0.85
0.82



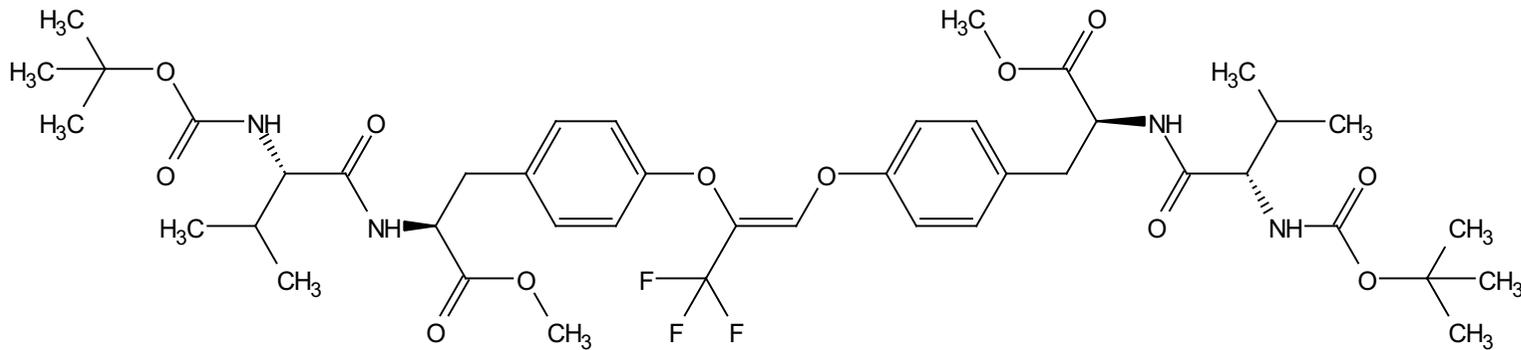
(5d)



¹⁹F NMR (376 MHz, Chloroform-*d*)

64.89

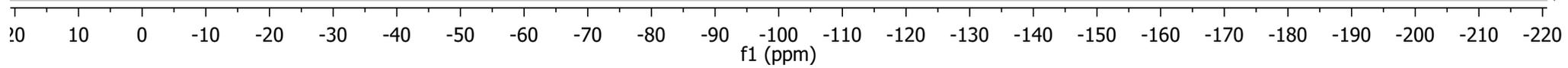
68.89



(5d)

0.05

0.95



¹³C NMR (101 MHz, Chloroform-*d*)

171.70
171.53
171.45
171.38

155.84
155.78
155.35

137.61
137.57
137.53
137.49

132.28
130.80
130.34
130.30

127.03
126.68
126.34

125.96
125.52
122.82
120.11

117.41
117.07
115.59

79.88
77.39 CDCl₃
77.07 CDCl₃
76.76 CDCl₃

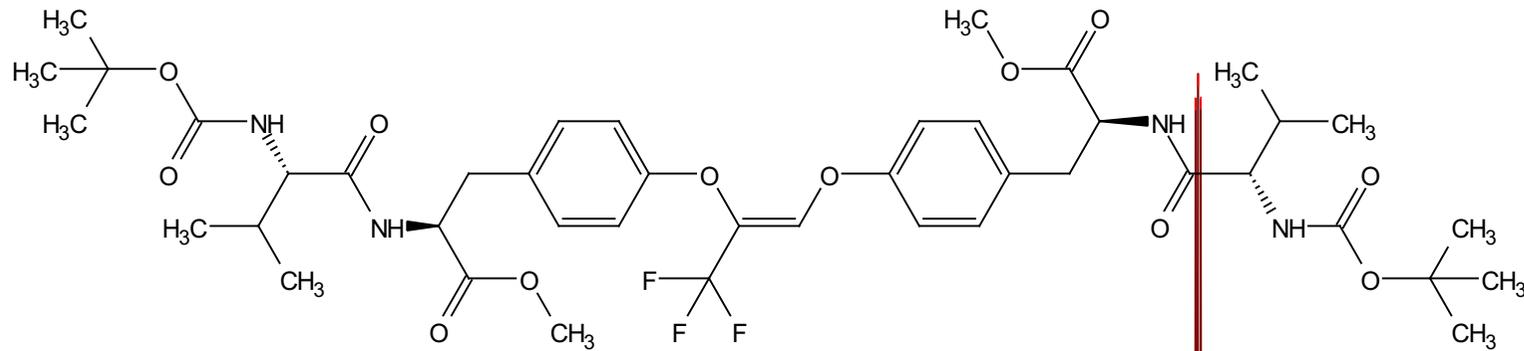
59.98
59.95
53.22

53.13
52.38
52.25

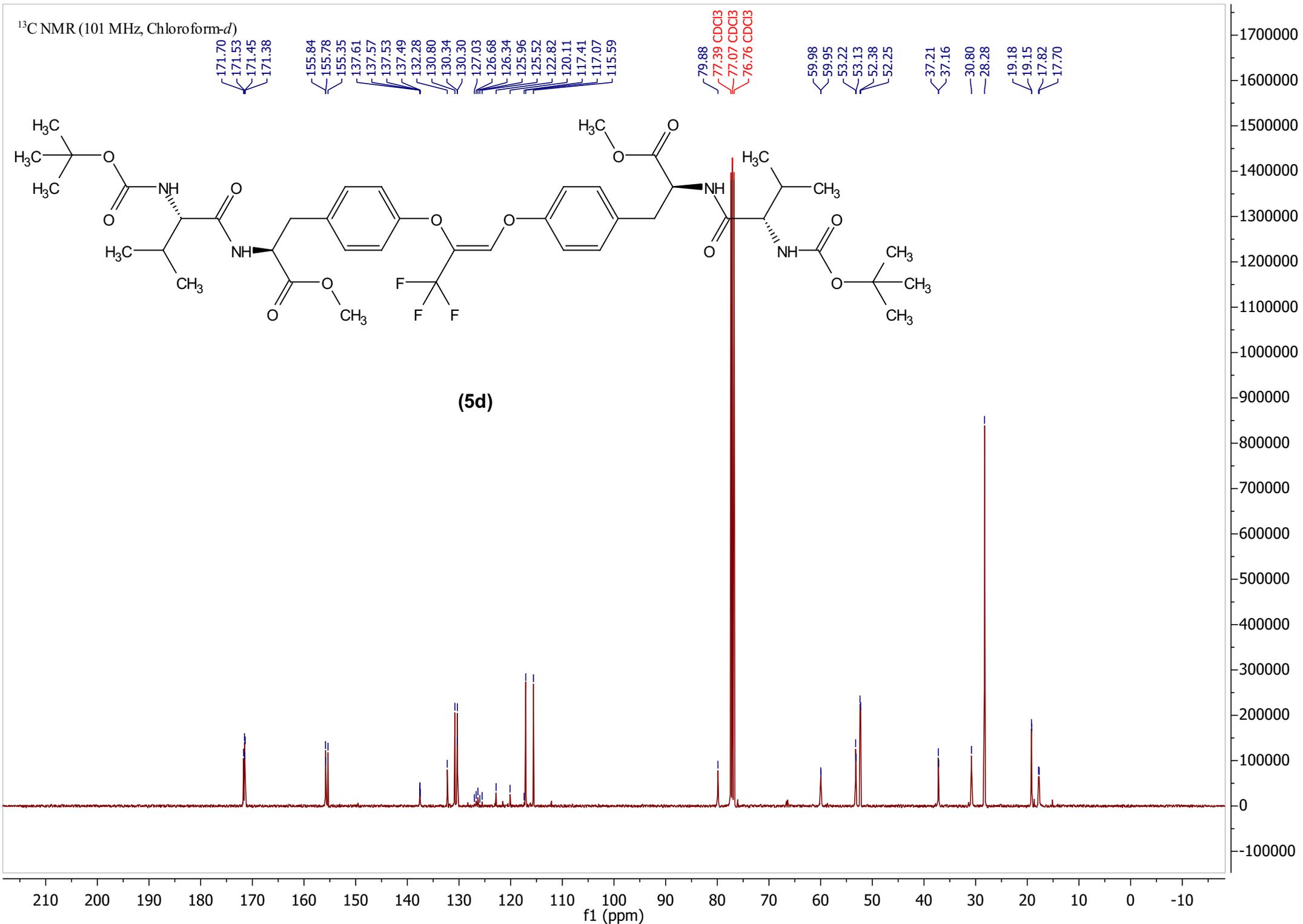
37.21
37.16

30.80
28.28

19.18
19.15
17.82
17.70



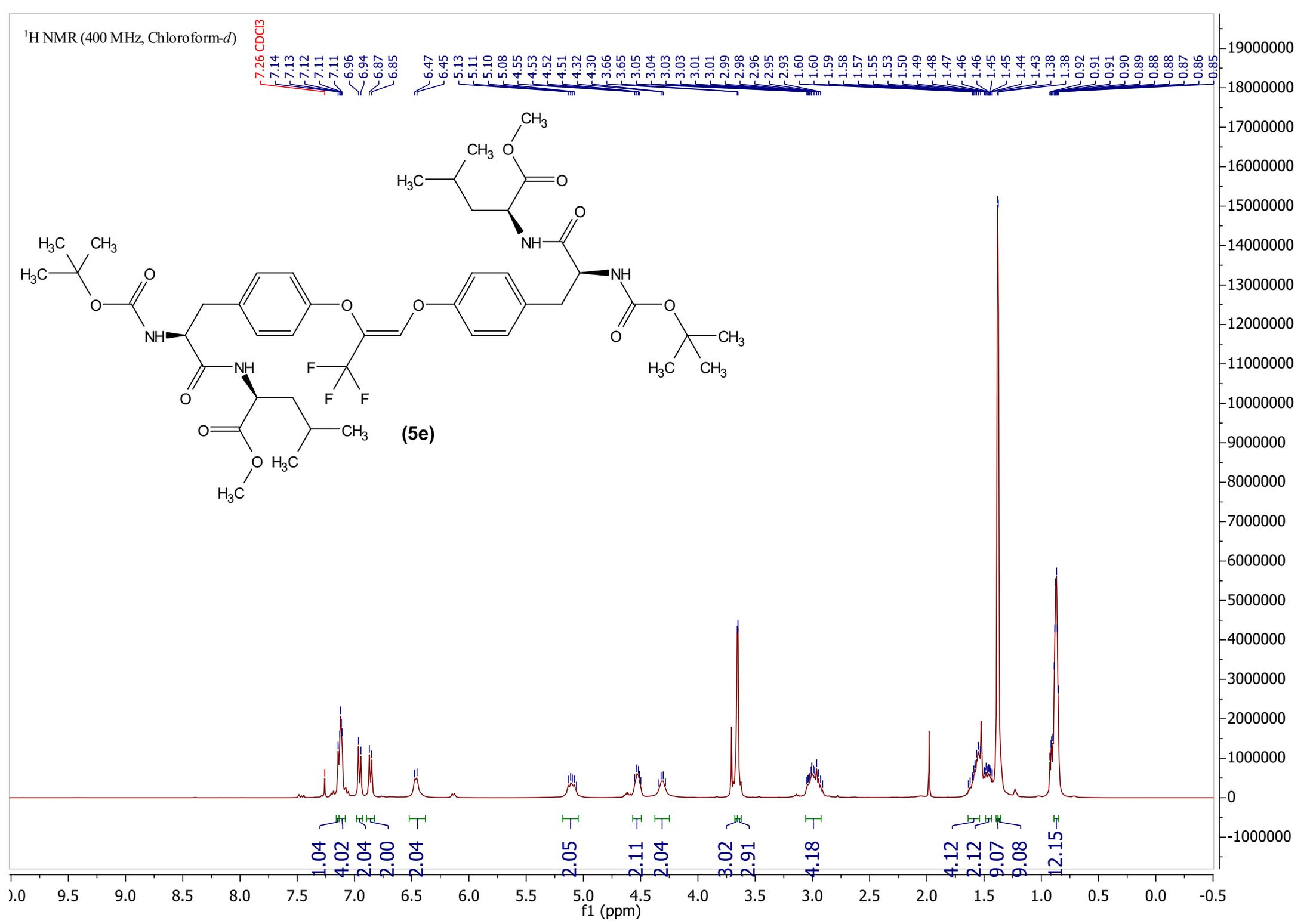
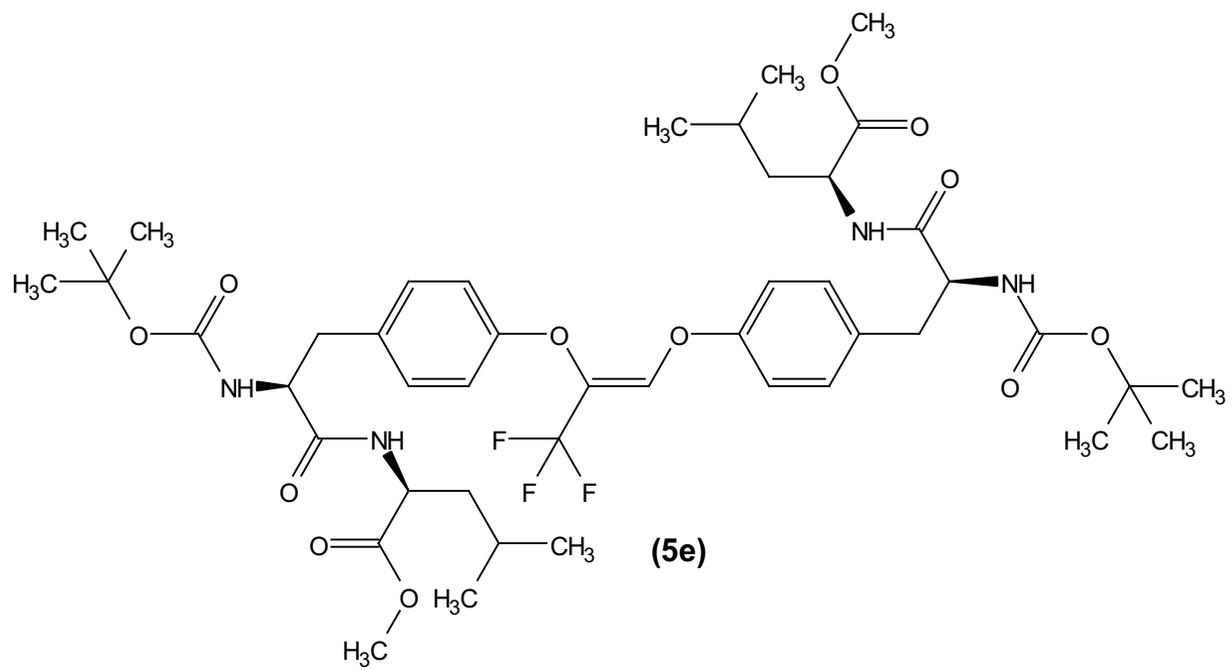
(5d)



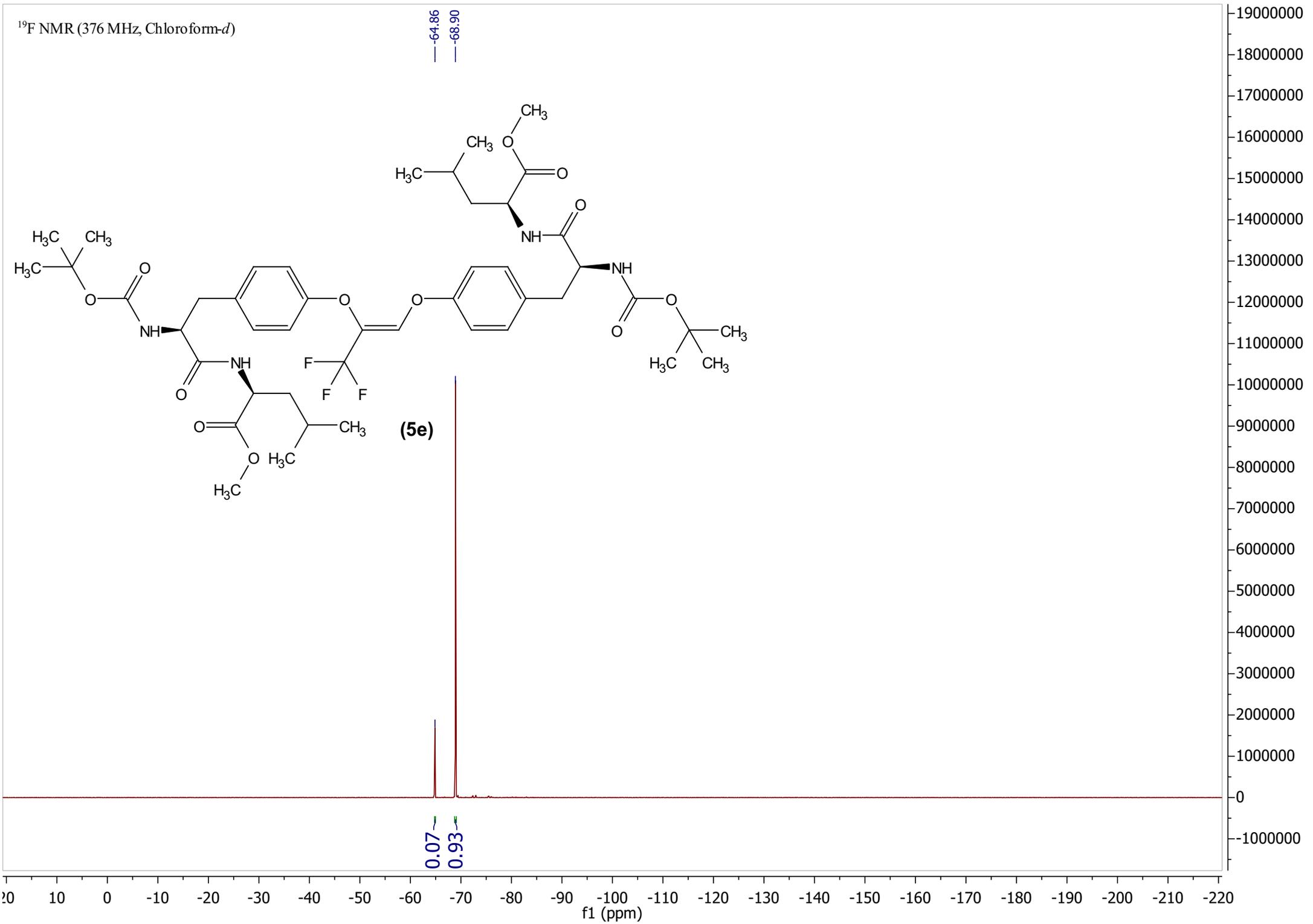
¹H NMR (400 MHz, Chloroform-*d*)

7.26 CDCl₃

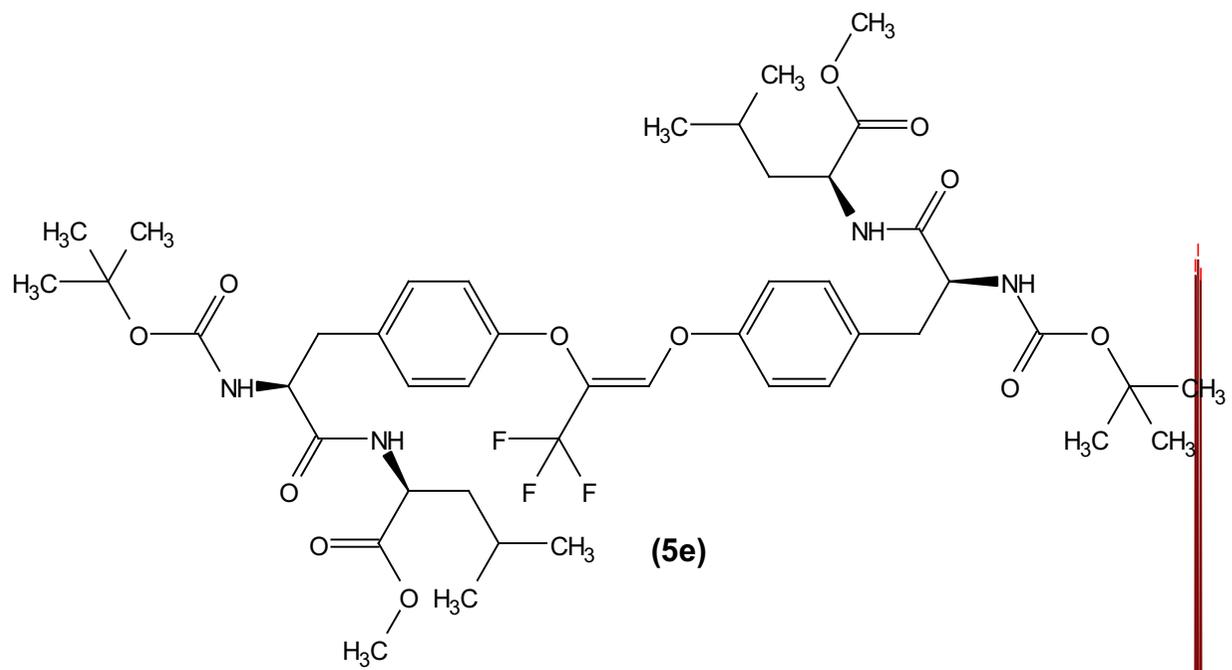
7.14
7.13
7.12
7.11
7.11
6.96
6.94
6.87
6.85
6.47
6.45
5.13
5.11
5.10
5.08
4.55
4.53
4.52
4.51
4.32
4.30
3.66
3.65
3.05
3.04
3.03
3.03
3.01
3.01
2.99
2.98
2.96
2.95
2.93
1.60
1.60
1.59
1.58
1.57
1.55
1.53
1.50
1.49
1.48
1.47
1.46
1.46
1.45
1.45
1.44
1.43
1.38
1.38
0.92
0.91
0.91
0.90
0.89
0.88
0.88
0.87
0.86
0.85



^{19}F NMR (376 MHz, Chloroform-*d*)



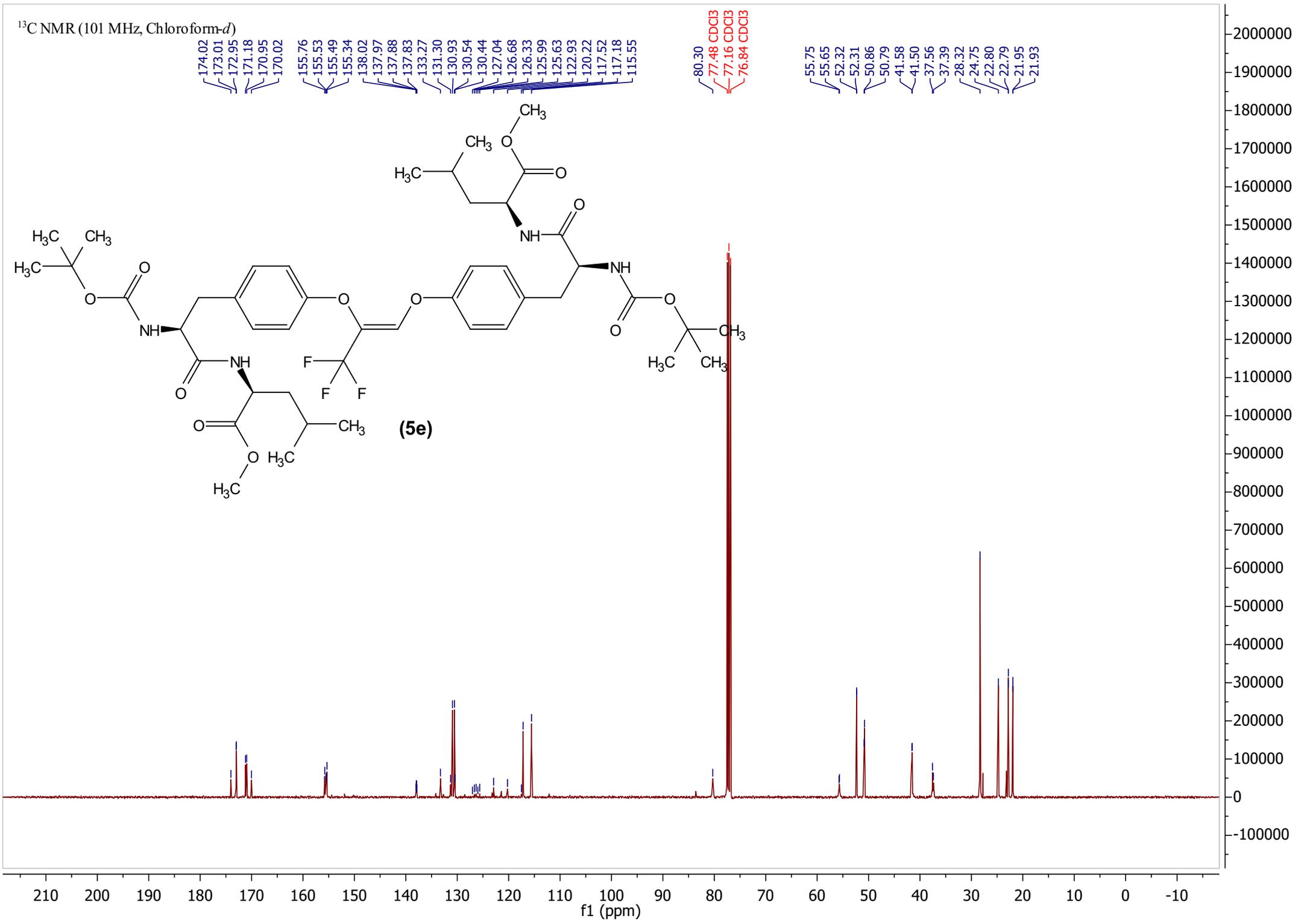
¹³C NMR (101 MHz, Chloroform-d)



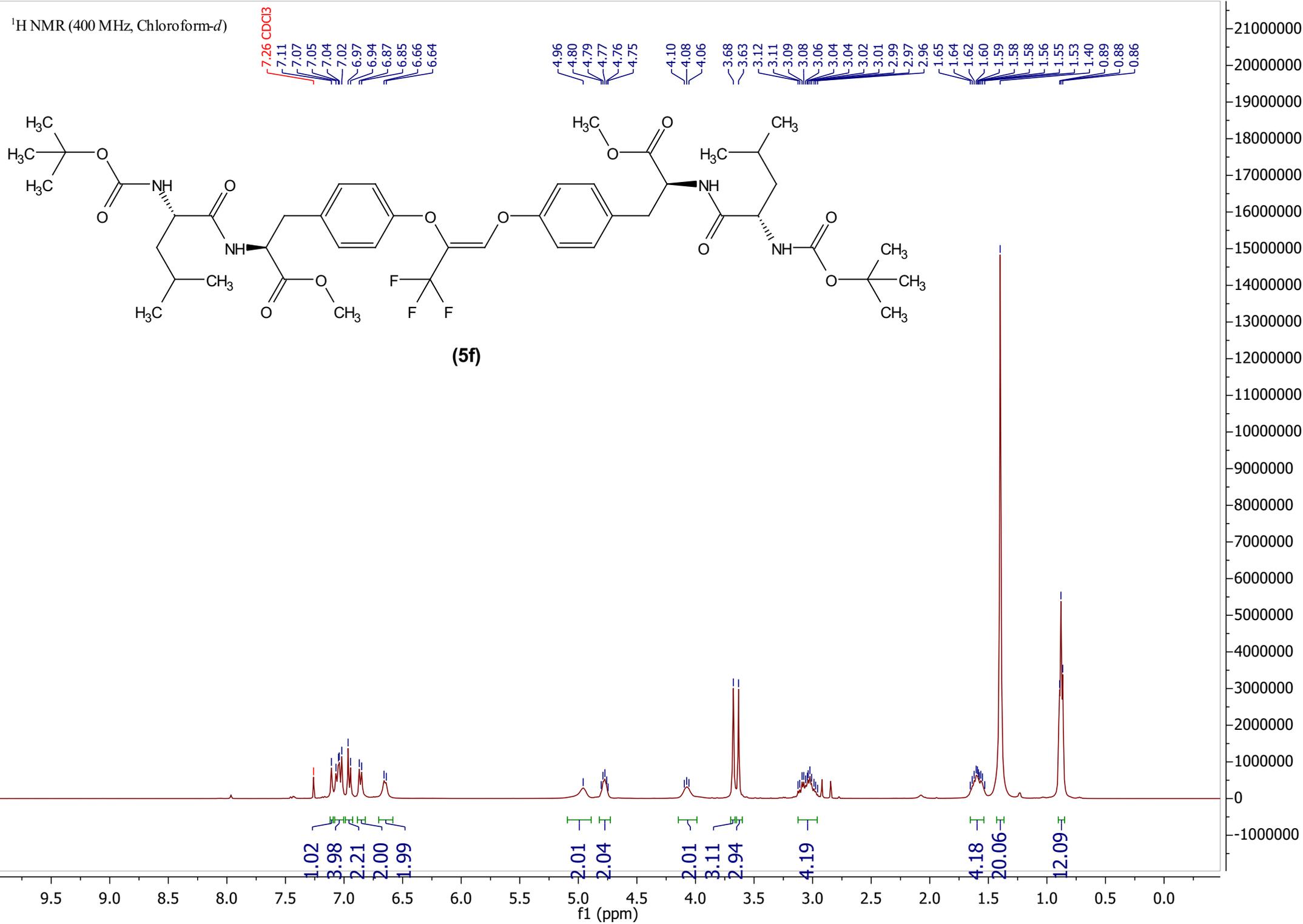
174.02
173.01
172.95
171.18
170.95
170.02
155.76
155.53
155.49
155.34
138.02
137.97
137.88
137.83
133.27
131.30
130.93
130.54
130.44
127.04
126.68
126.33
125.99
125.63
122.93
120.22
117.52
117.18
115.55

80.30
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3

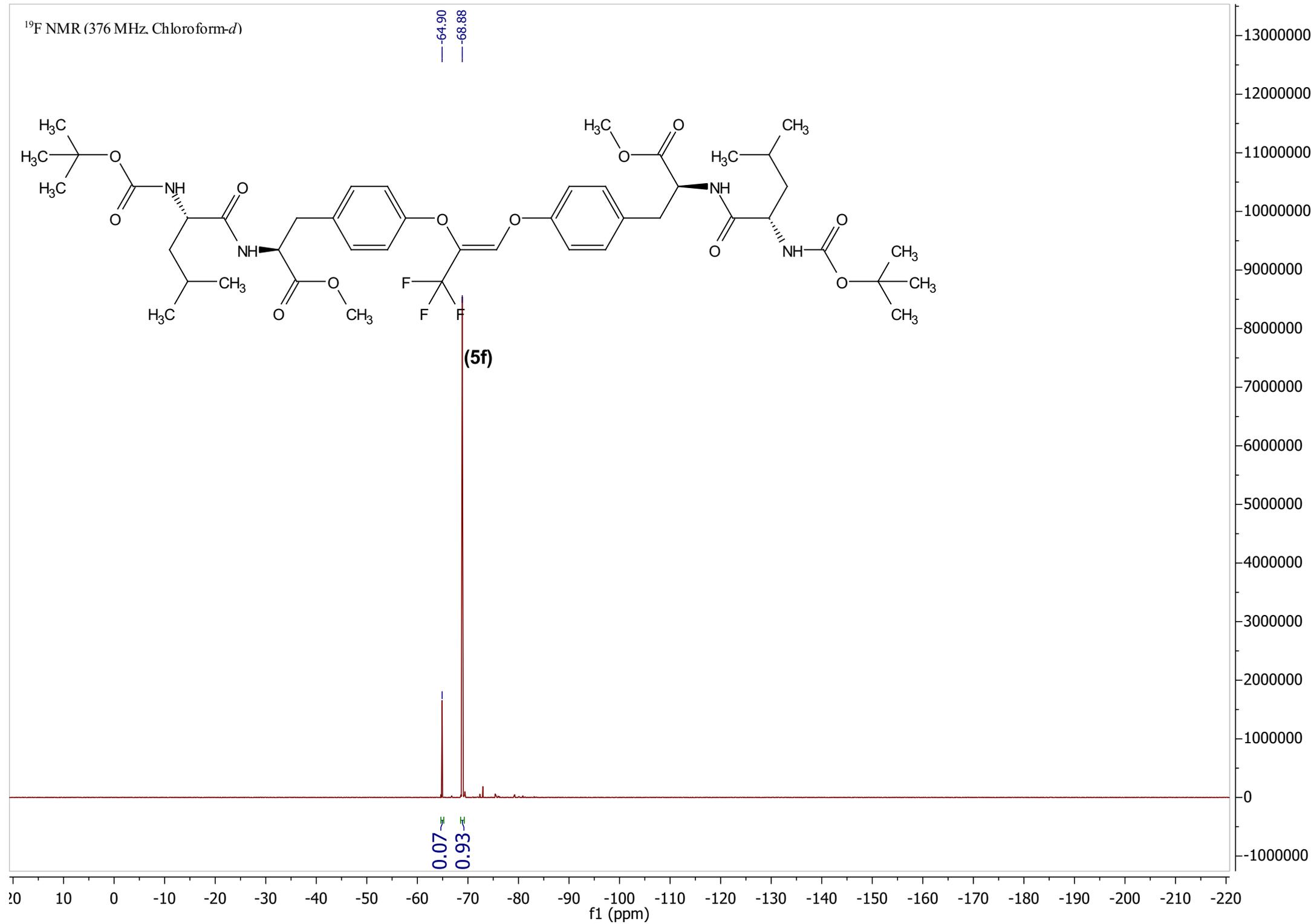
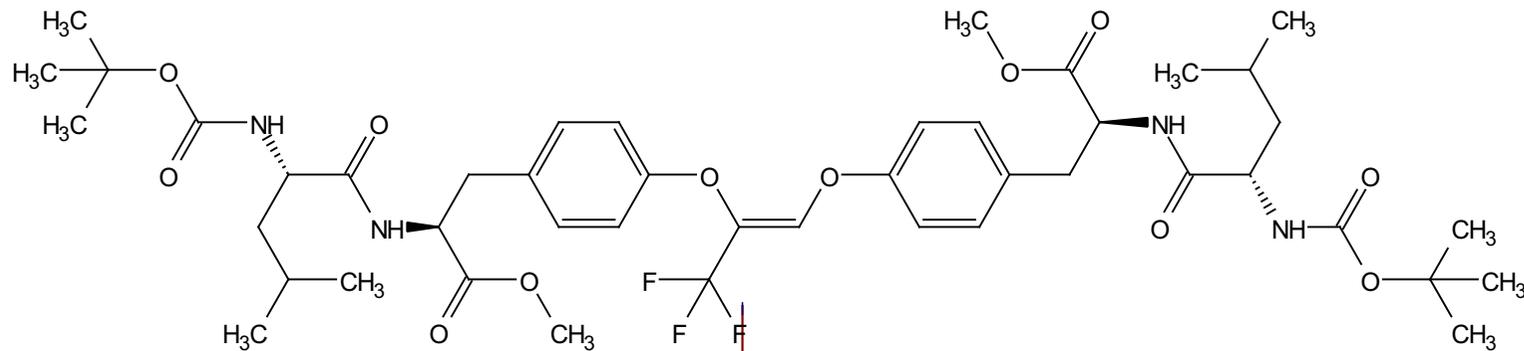
55.75
55.65
52.32
52.31
50.86
50.79
41.58
41.50
37.56
37.39
28.32
24.75
22.80
22.79
21.95
21.93



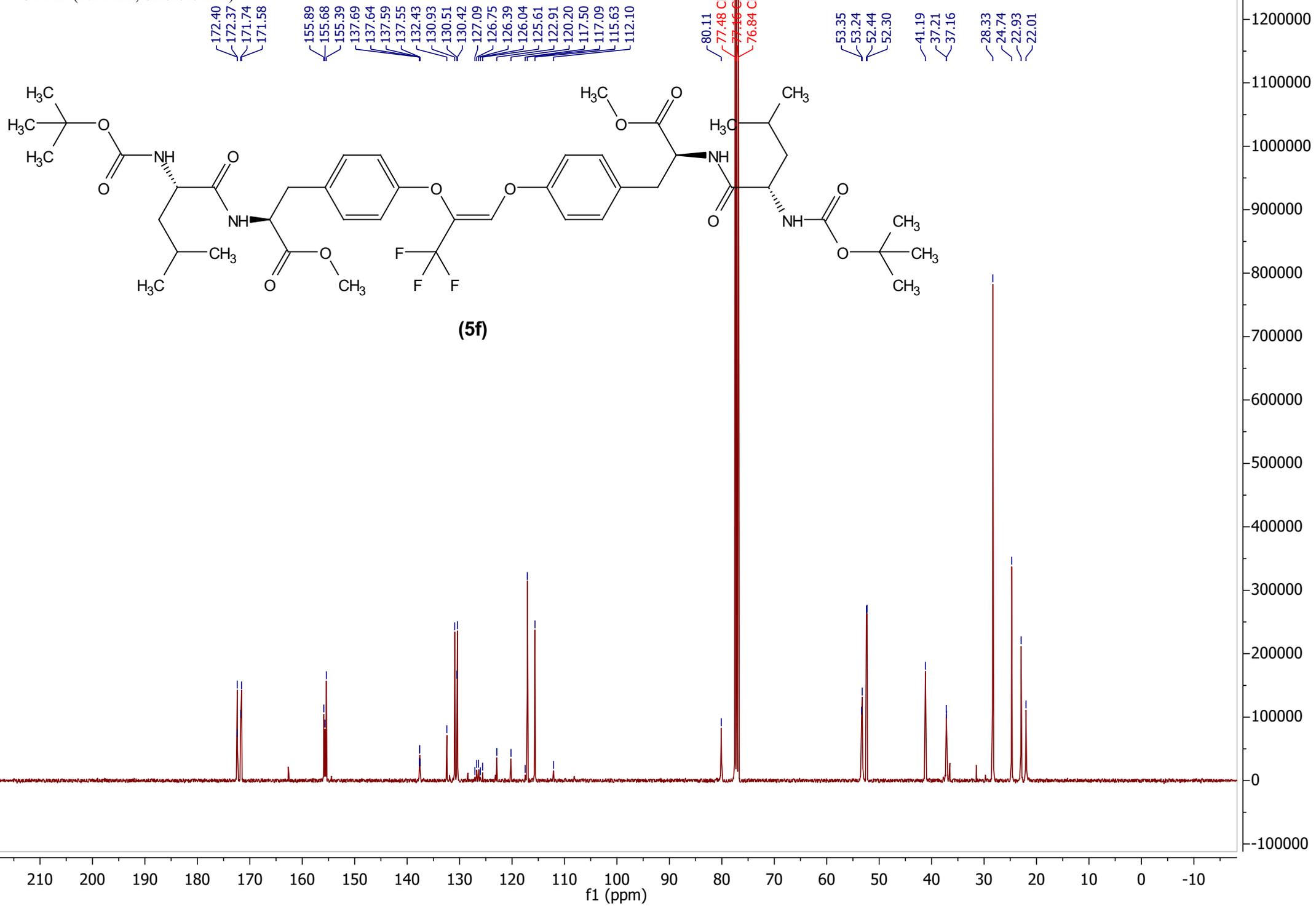
¹H NMR (400 MHz, Chloroform-*d*)



¹⁹F NMR (376 MHz, Chloroform-*d*)

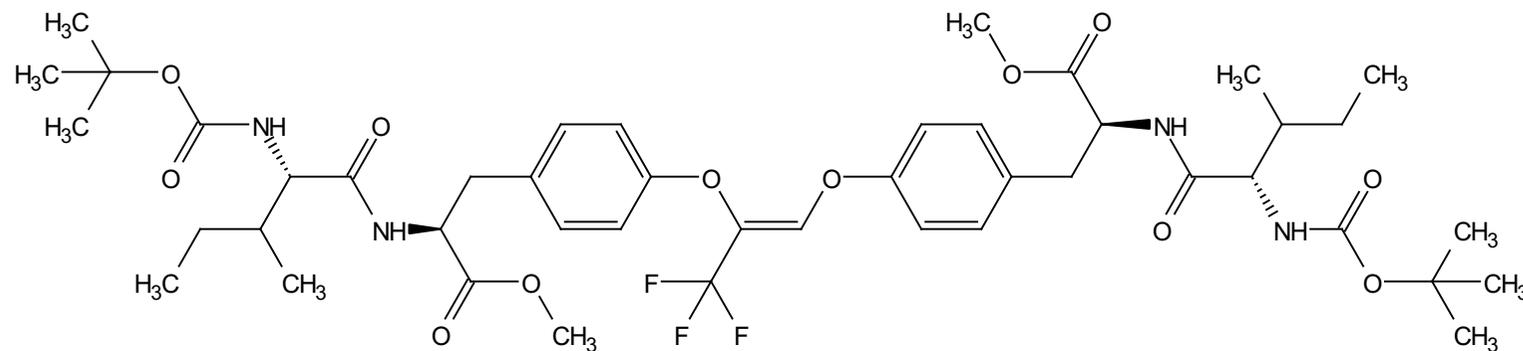


¹³C NMR (101 MHz, Chloroform-*d*)

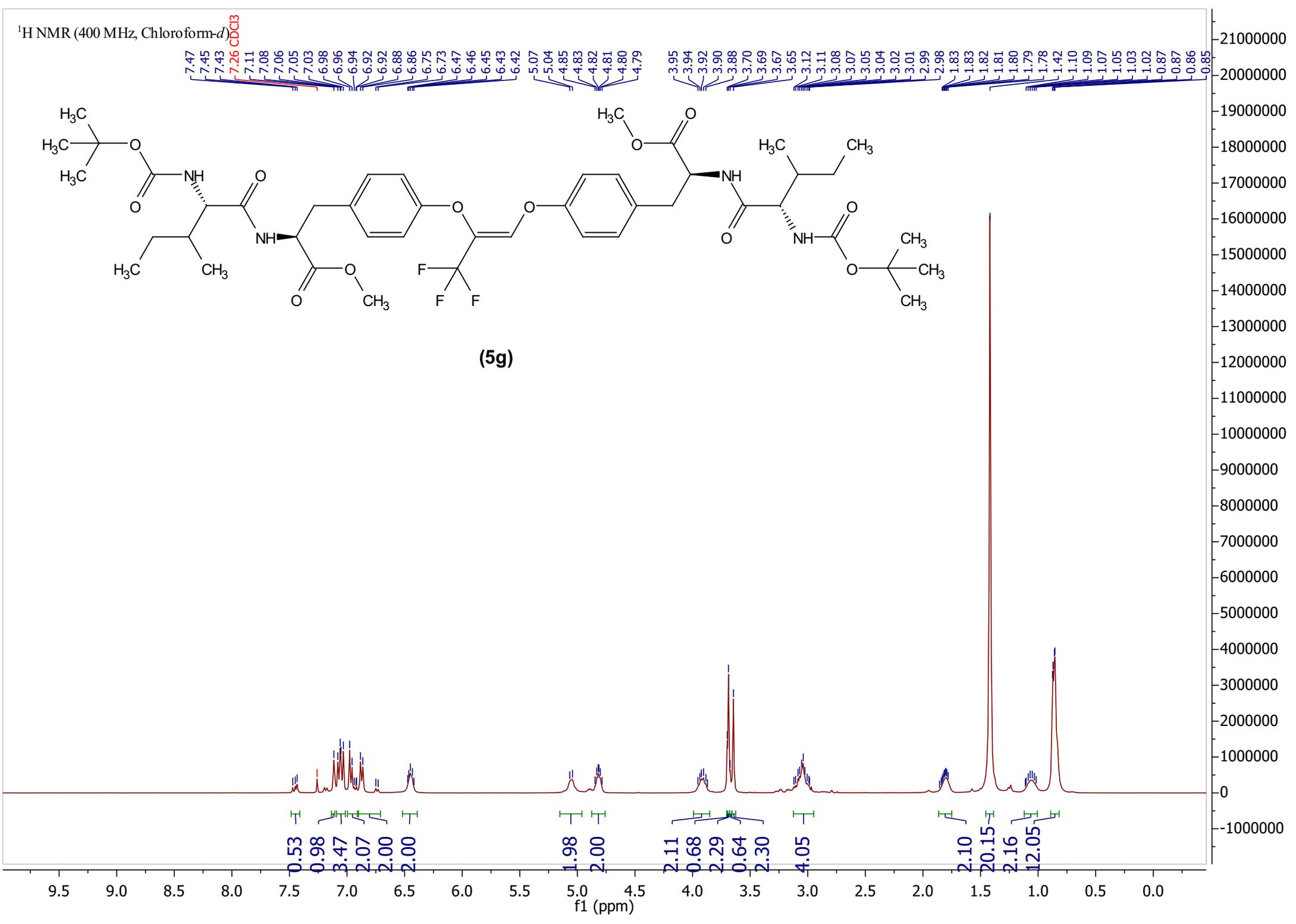


¹H NMR (400 MHz, Chloroform-*d*)

7.26 CDCl₃



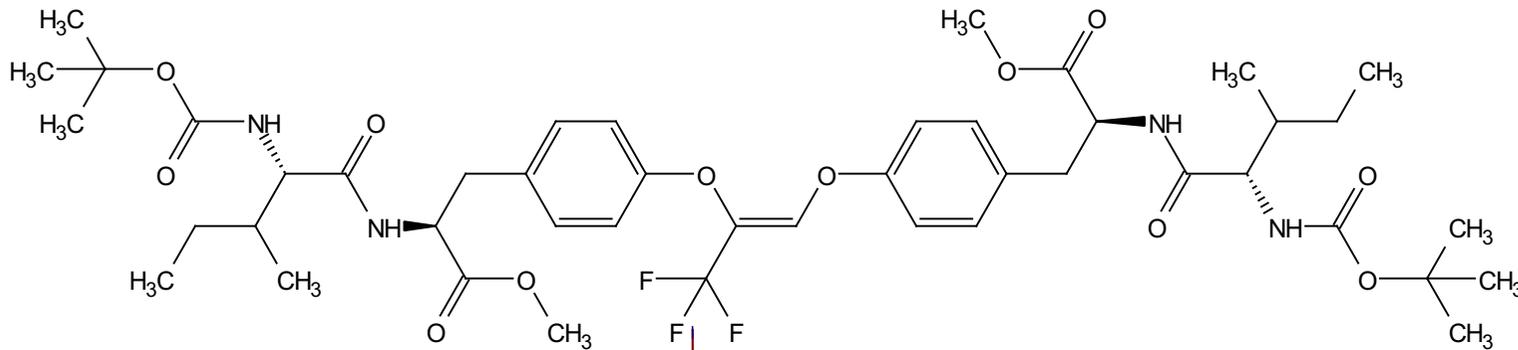
7.47
7.45
7.43
7.11
7.08
7.06
7.05
7.03
6.98
6.96
6.94
6.92
6.92
6.88
6.86
6.75
6.73
6.47
6.46
6.45
6.43
6.42
5.07
5.04
4.85
4.83
4.82
4.81
4.80
4.79
3.95
3.94
3.92
3.90
3.88
3.70
3.69
3.67
3.65
3.12
3.11
3.08
3.07
3.05
3.04
3.02
3.01
2.99
2.98
1.83
1.83
1.82
1.81
1.80
1.79
1.78
1.42
1.10
1.09
1.07
1.05
1.03
1.02
0.87
0.87
0.86
0.85



¹⁹F NMR (376 MHz, Chloroform-*d*)

64.90

68.89



(5g)

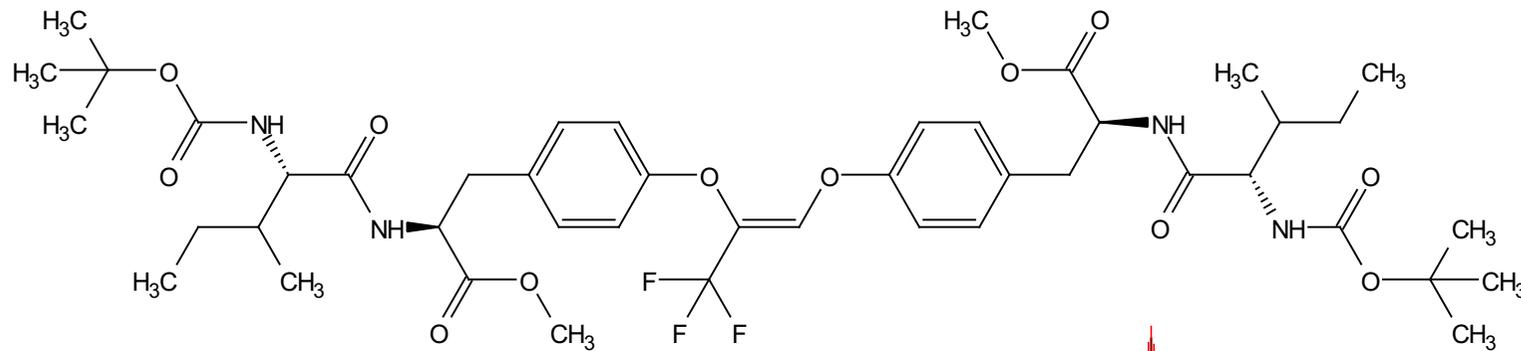
0.22

0.78

f1 (ppm)

1700000
1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

¹³C NMR (101 MHz, Chloroform-*d*)



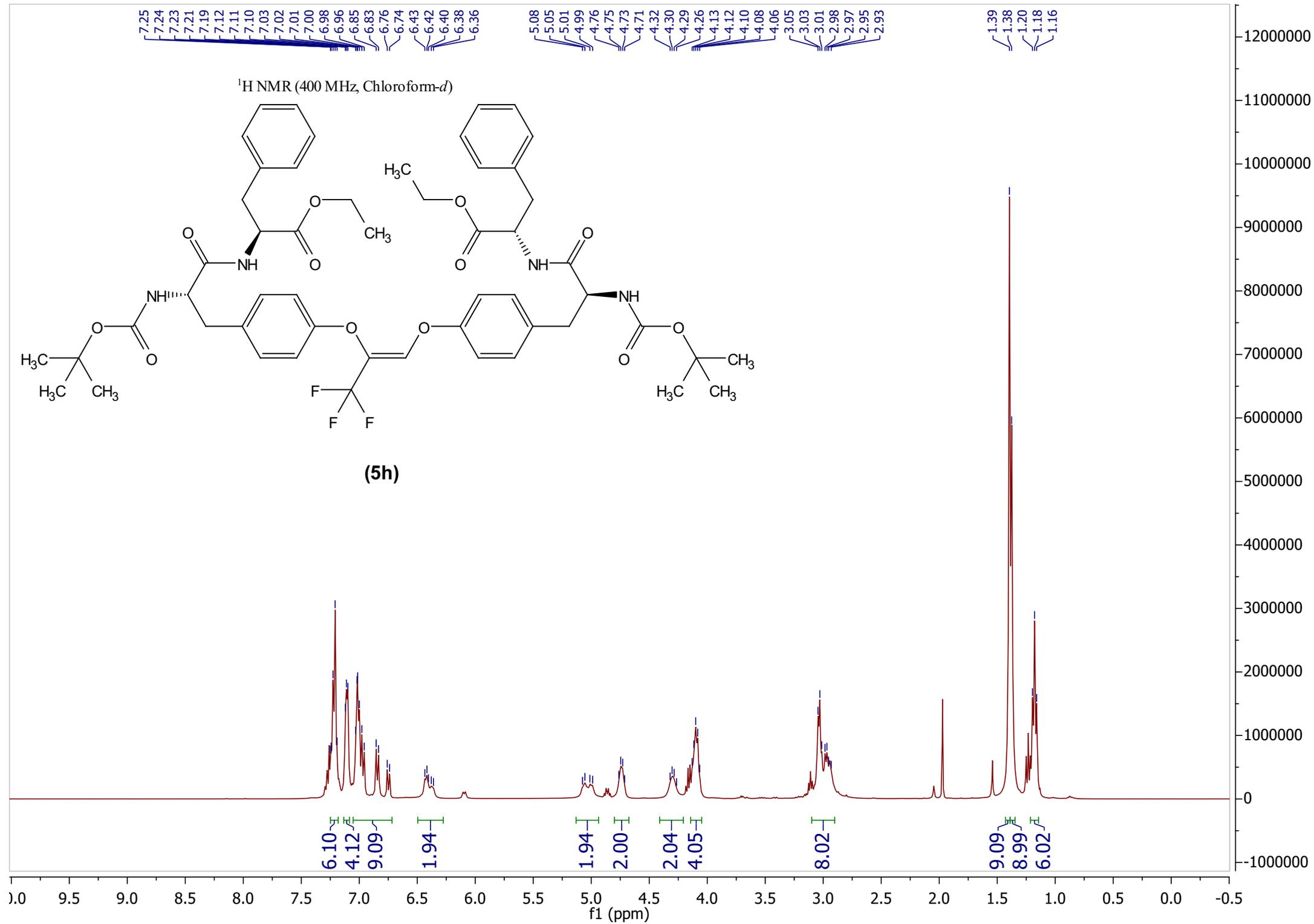
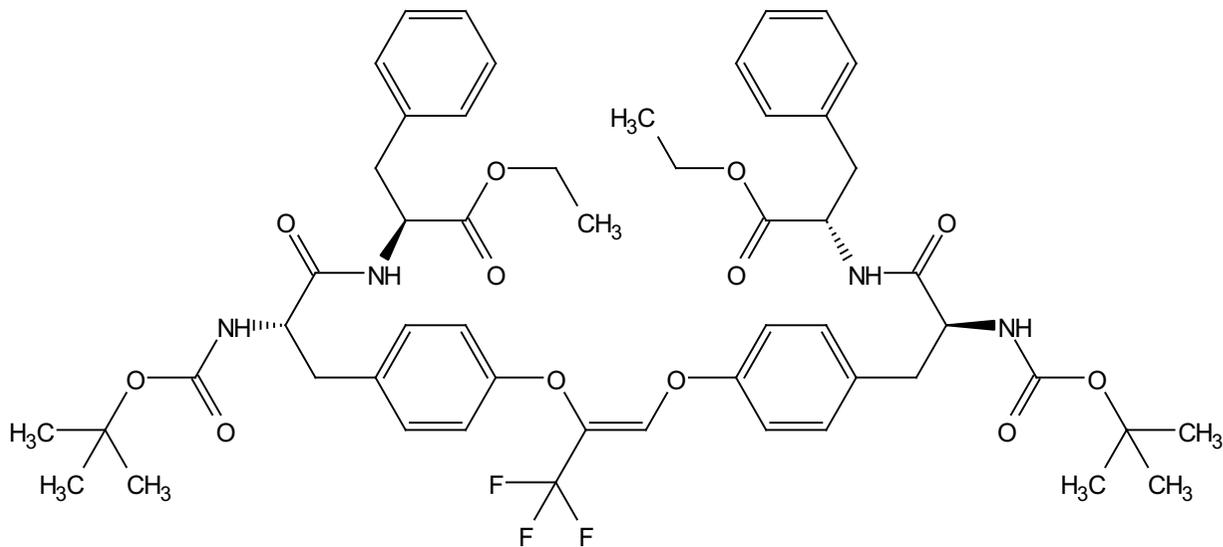
(5g)

- 171.74
- 171.67
- 171.58
- 171.51
- 171.44
- 171.37
- 155.95
- 155.80
- 155.46
- 137.72
- 137.67
- 137.63
- 137.57
- 132.35
- 131.84
- 130.91
- 130.41
- 128.41
- 127.19
- 126.98
- 126.77
- 126.56
- 126.43
- 126.08
- 125.62
- 123.15
- 122.92
- 120.63
- 120.21
- 117.99
- 117.51
- 117.16
- 115.70
- 112.20
- 108.17
- 108.14
- 80.02
- 77.48 CDCl₃
- 77.16 CDCl₃
- 76.84 CDCl₃
- 59.39
- 53.42
- 53.30
- 53.19
- 52.52
- 52.49
- 52.35
- 52.32
- 37.31
- 37.24
- 37.19
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- 15.54
- 15.53
- 11.49
- 11.46
- 11.42
- 11.39

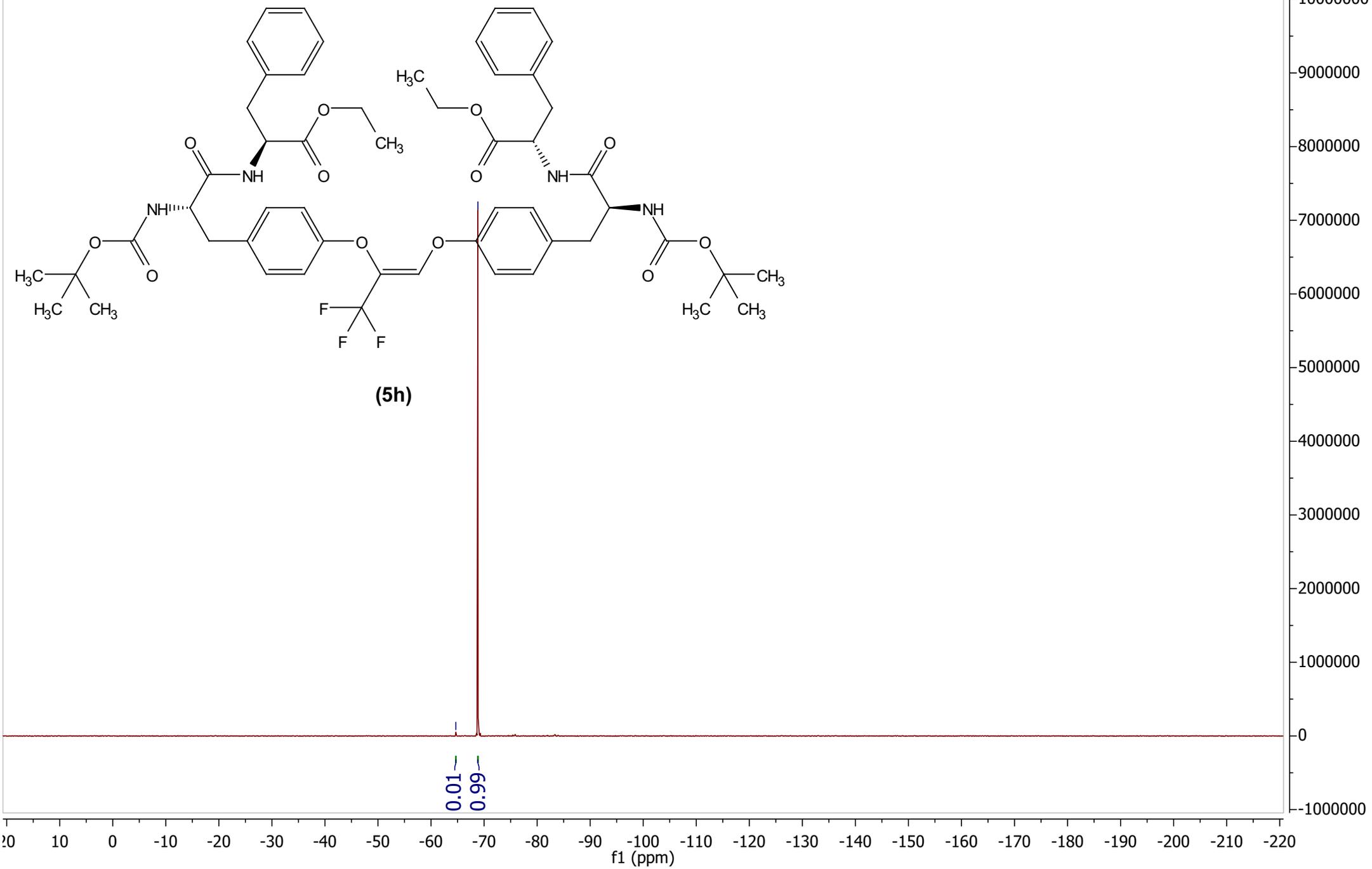
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

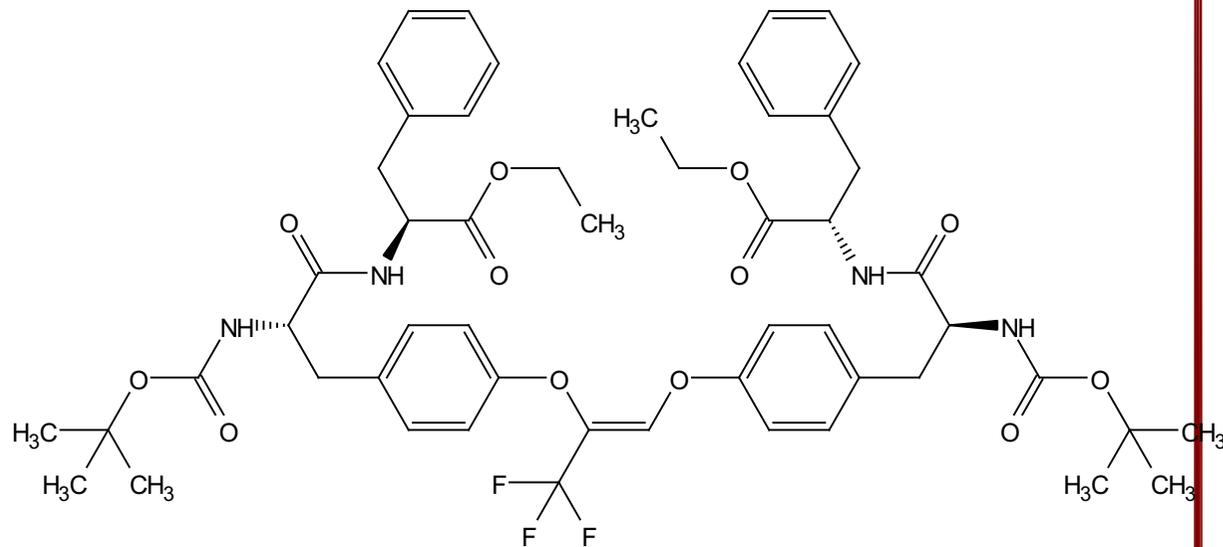
¹H NMR (400 MHz, Chloroform-*d*)



¹⁹F NMR (376 MHz, Chloroform-*d*)



¹³C NMR (101 MHz, Chloroform-*d*)

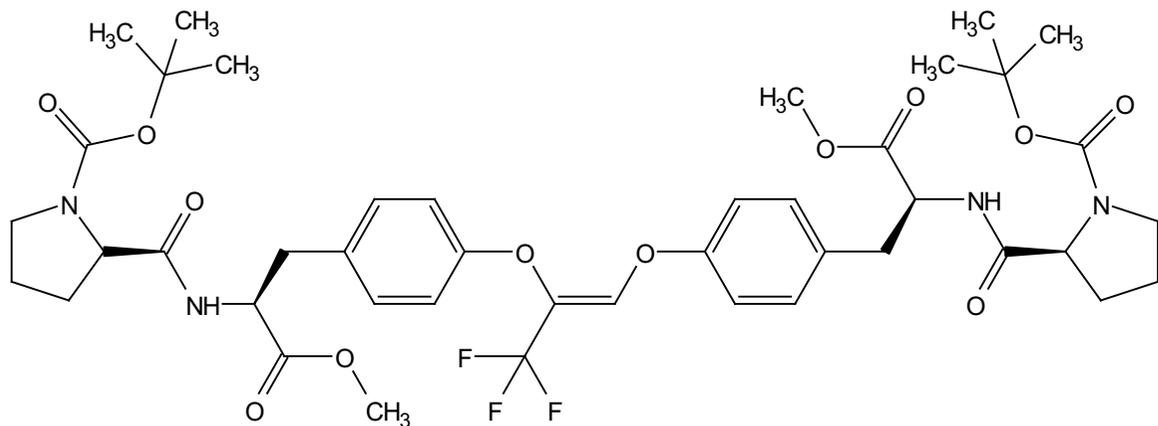


(5h)

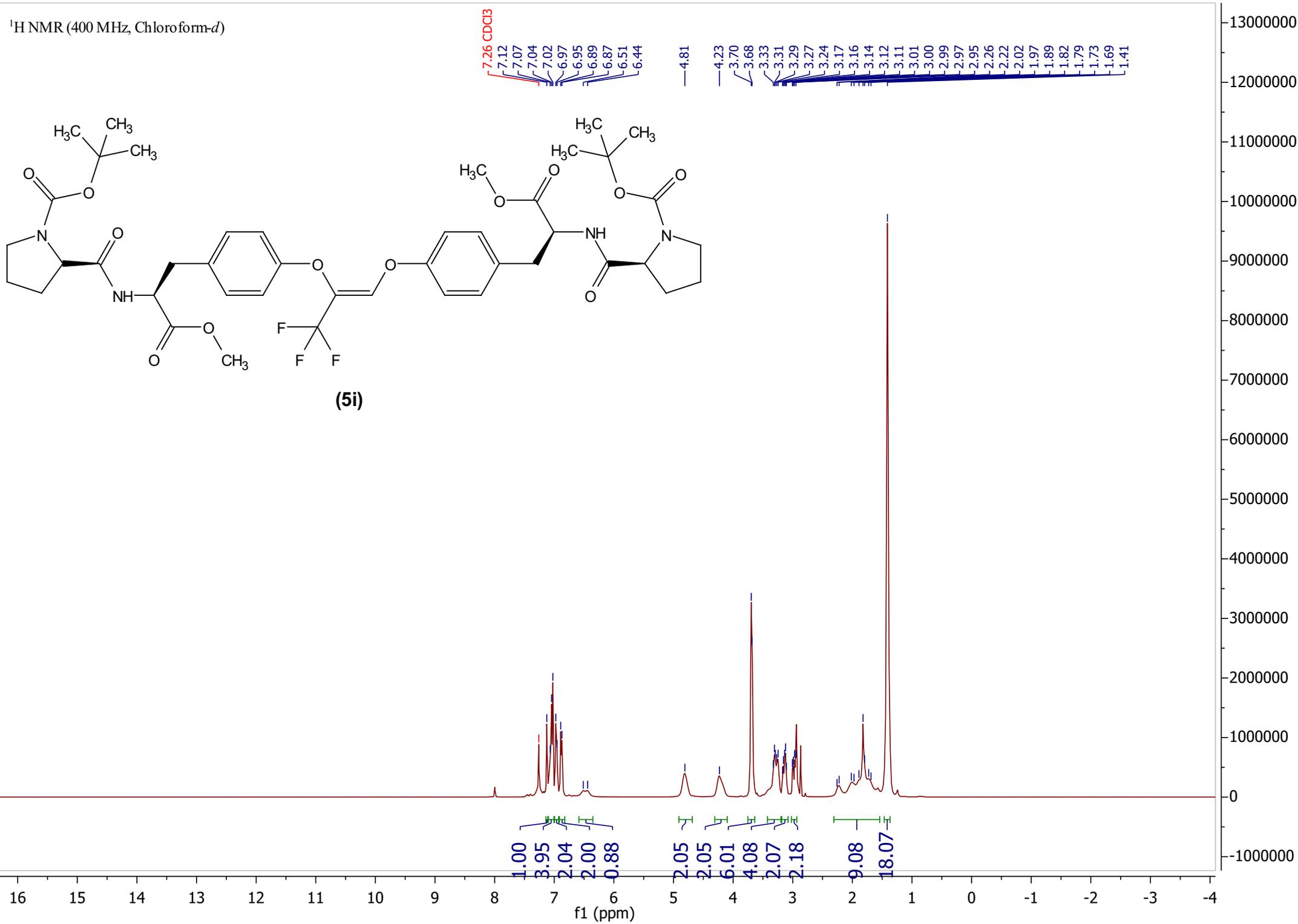
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0

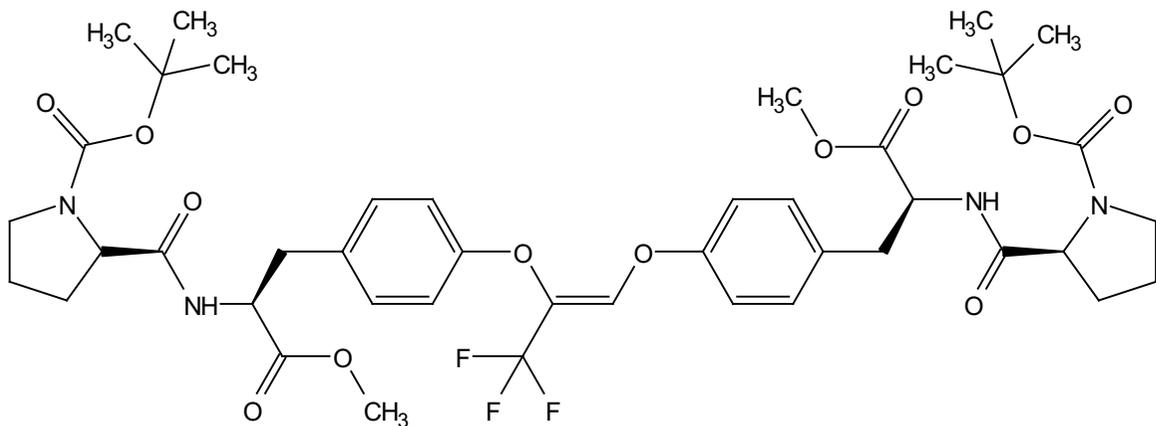
¹H NMR (400 MHz, Chloroform-*d*)



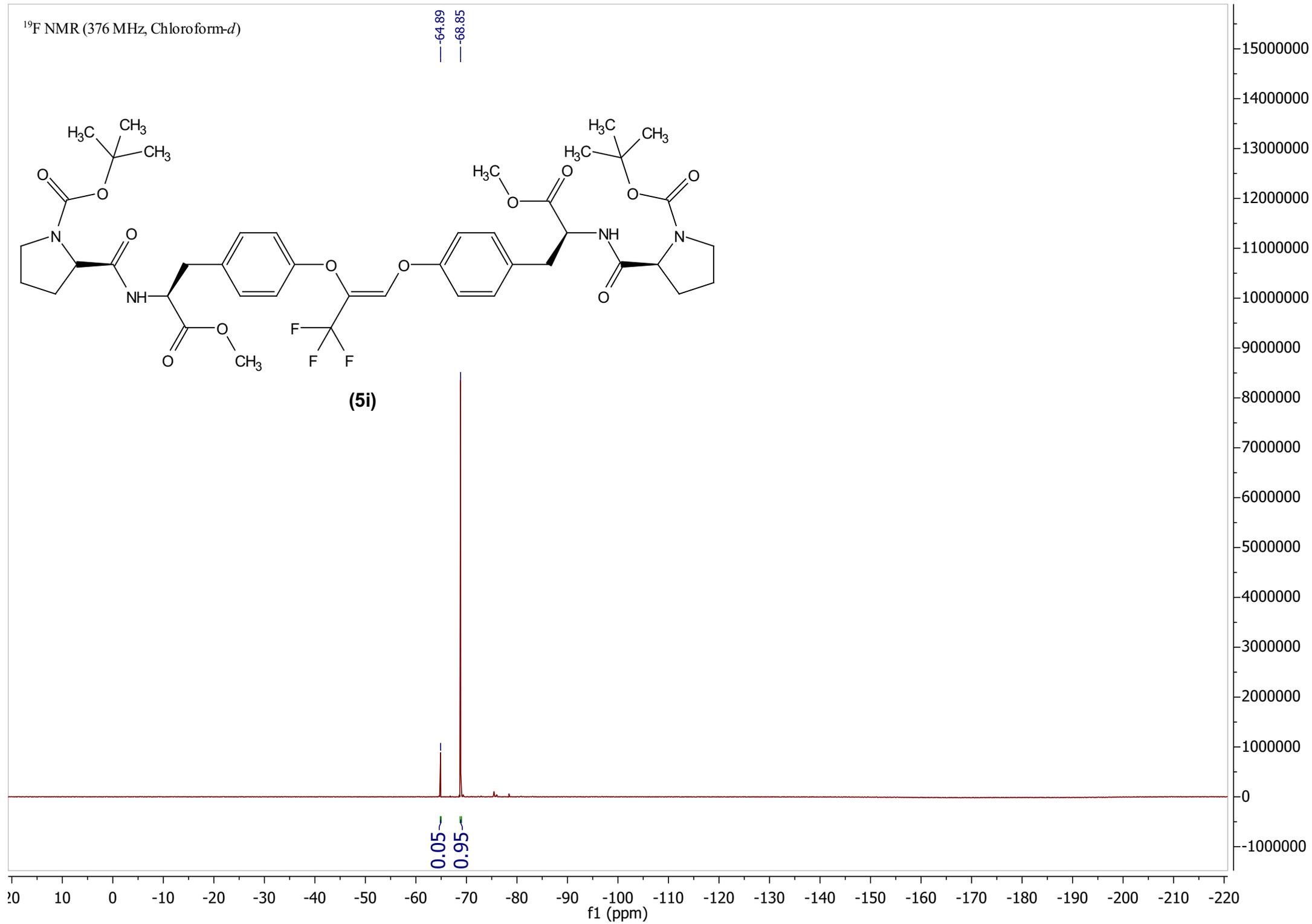
(5i)



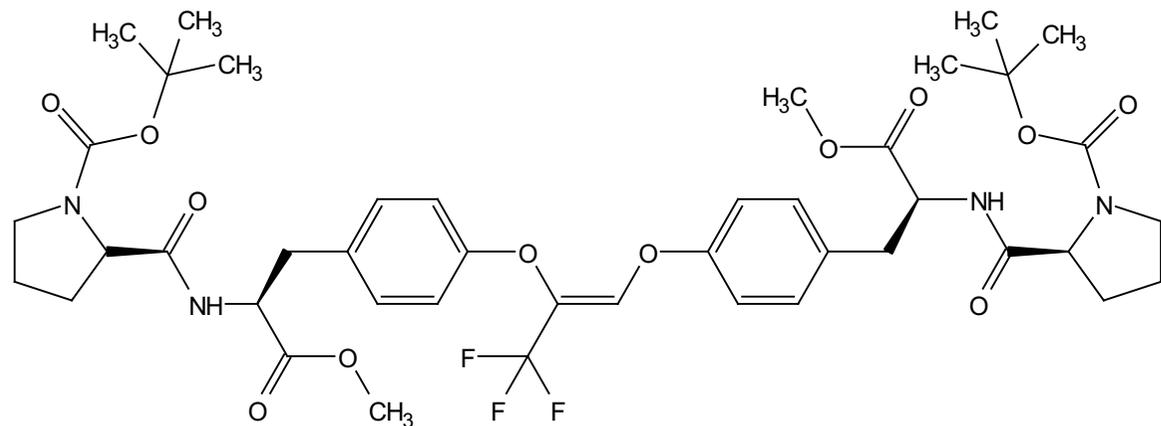
^{19}F NMR (376 MHz, Chloroform-*d*)



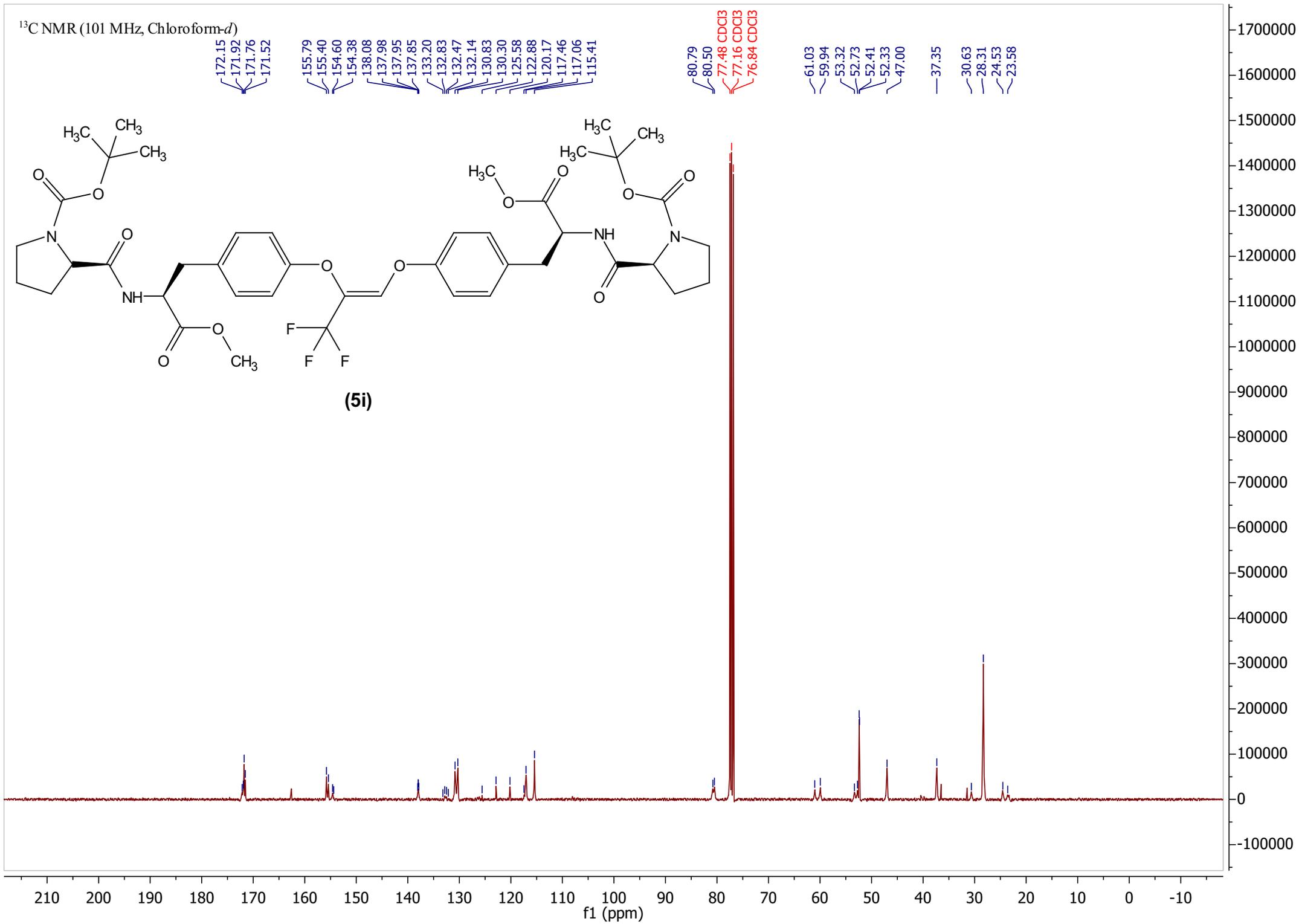
(5i)



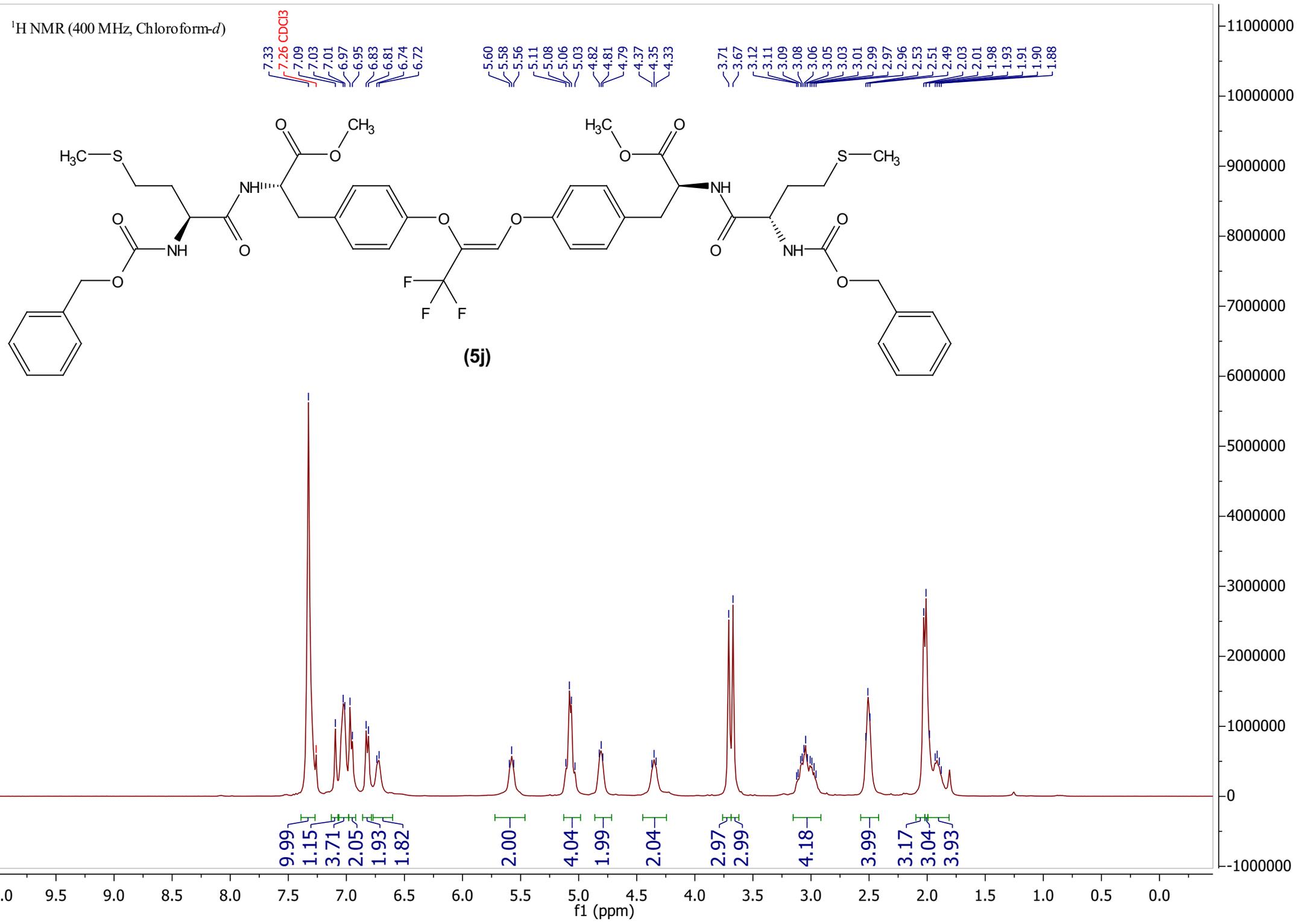
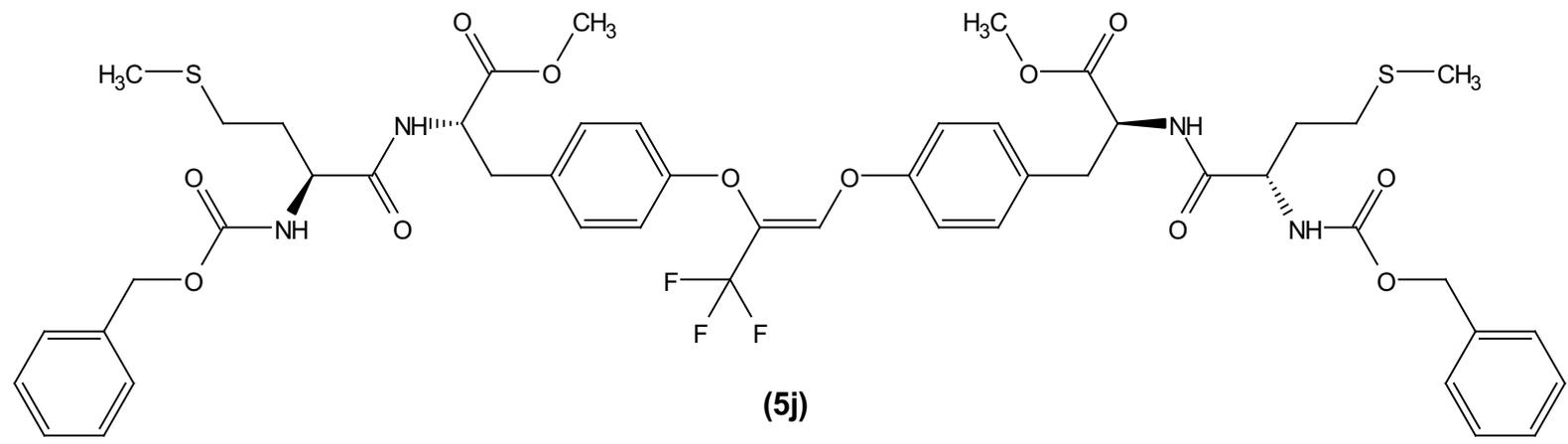
¹³C NMR (101 MHz, Chloroform-*d*)



(5i)

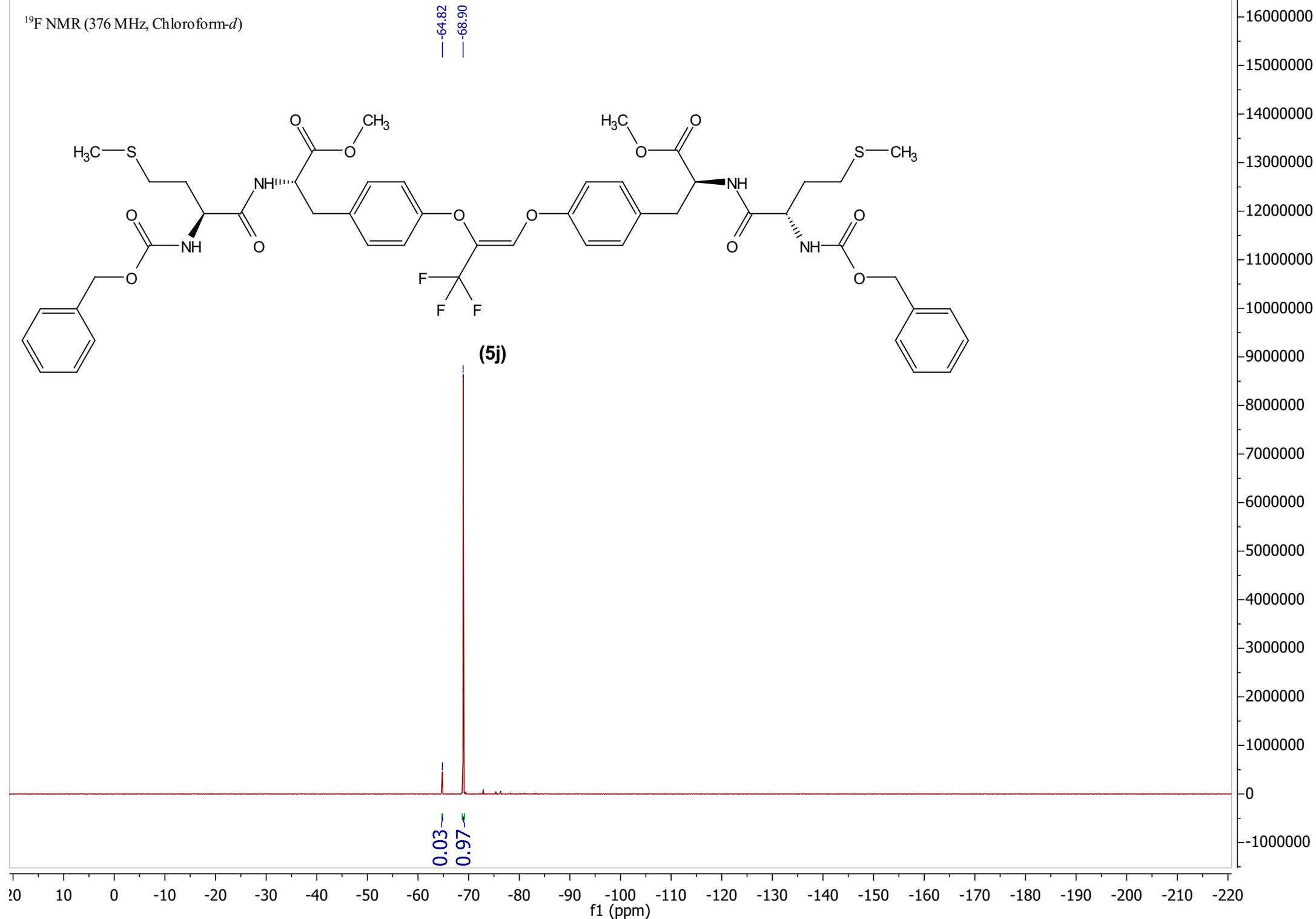
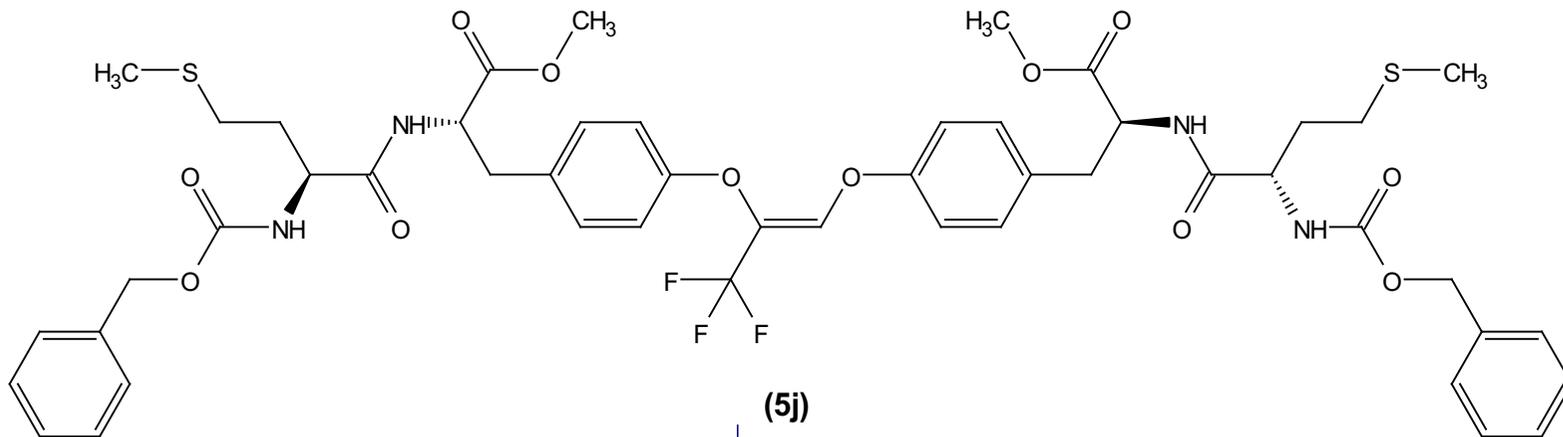


¹H NMR (400 MHz, Chloroform-*d*)

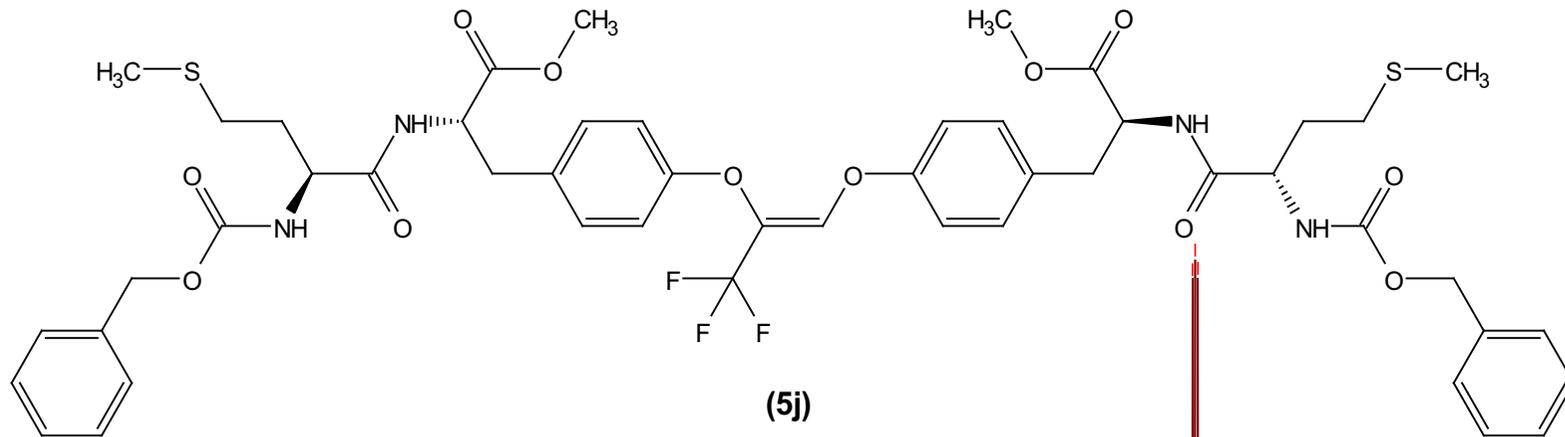


^{19}F NMR (376 MHz, Chloroform-*d*)

64.82
68.90



¹³C NMR (101 MHz, Chloroform-*d*)



171.66
171.50
170.97
170.94

156.10
155.99
155.41

137.59
137.54
137.50
137.45
136.24

132.22
130.87
130.39
130.28

128.69
128.66
128.38
128.33
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127.18
126.83
126.47
126.12

125.62
122.92
120.22
117.52
117.21
115.78

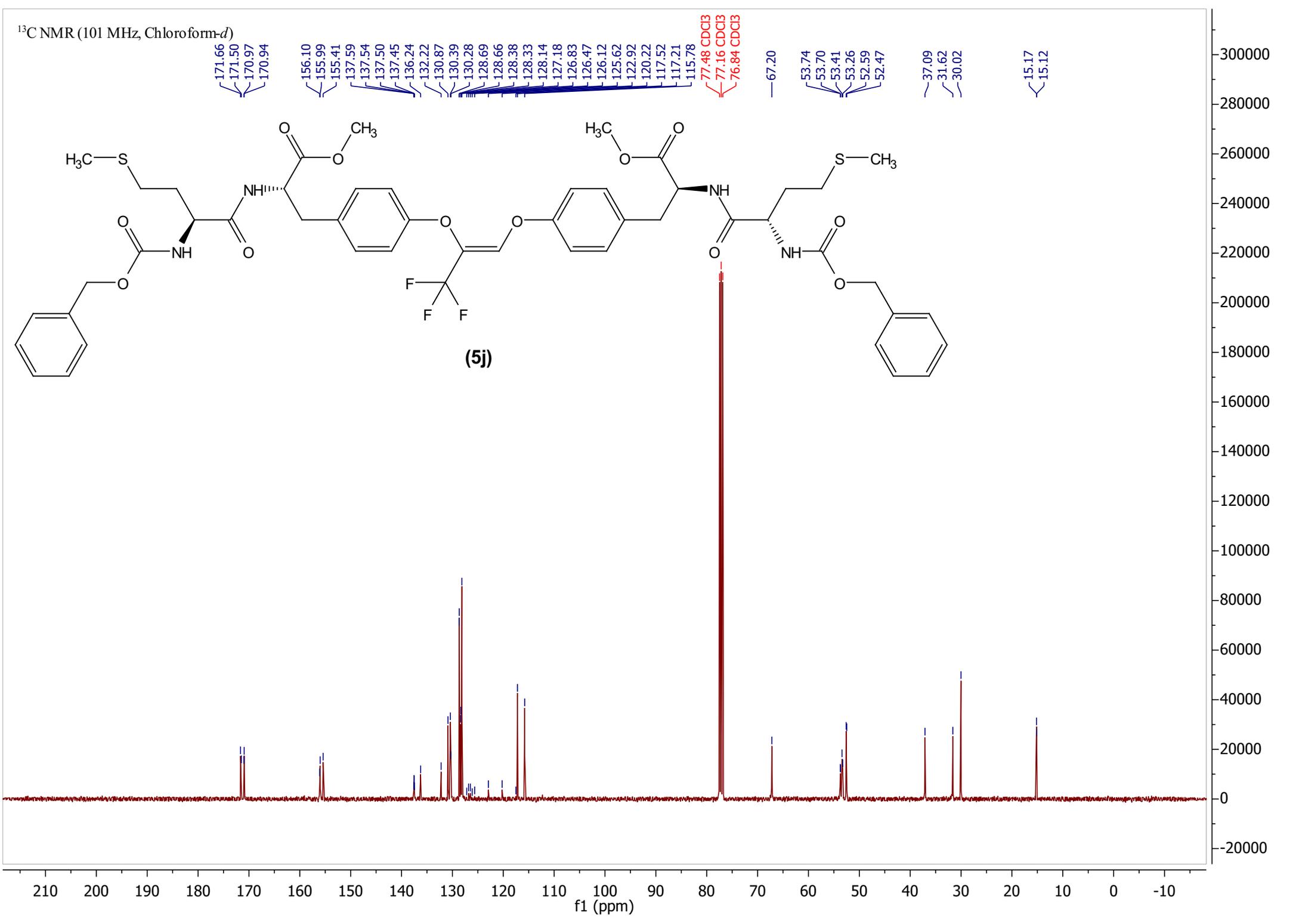
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

67.20

53.74
53.70
53.41
53.26
52.59
52.47

37.09
31.62
30.02

15.17
15.12

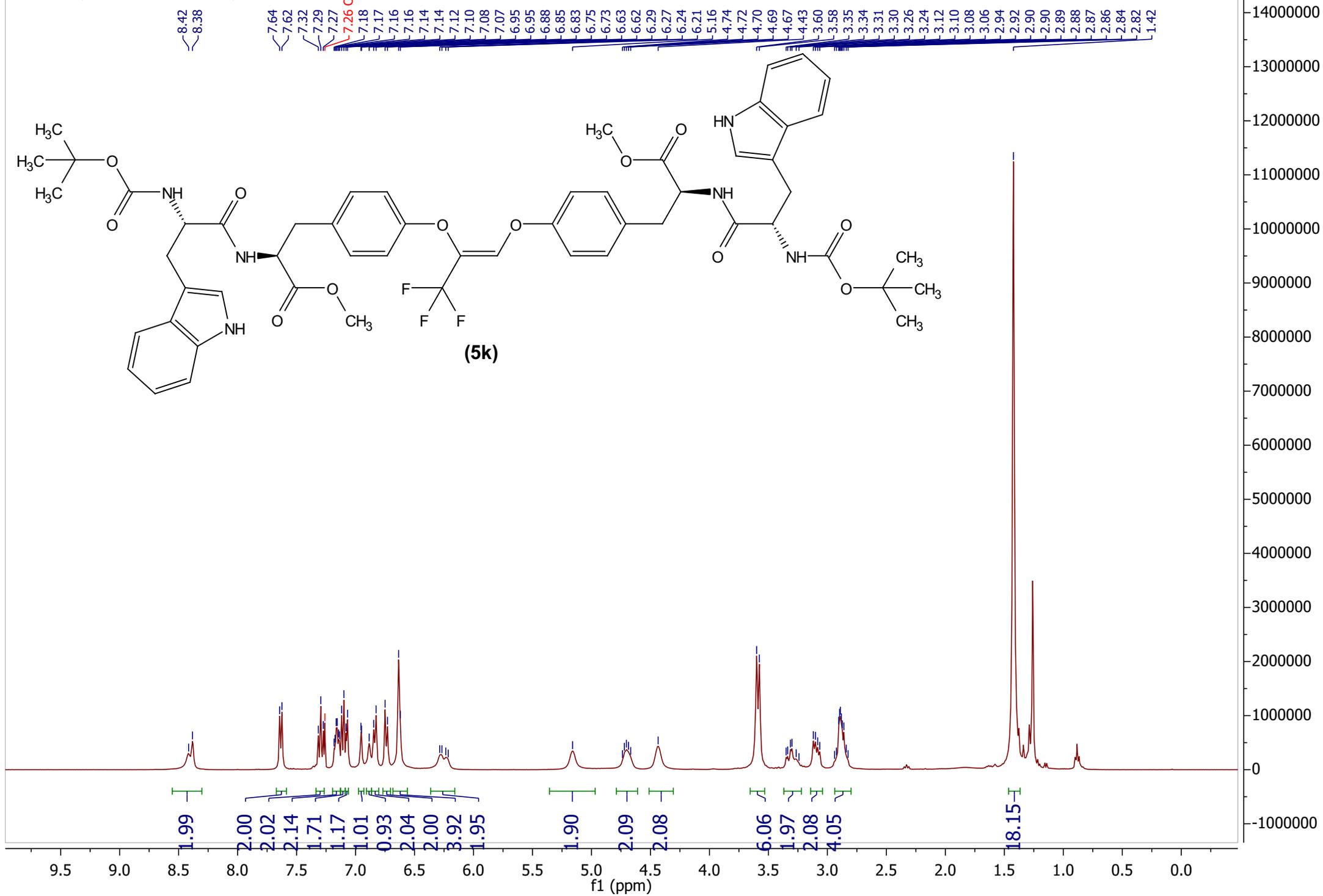
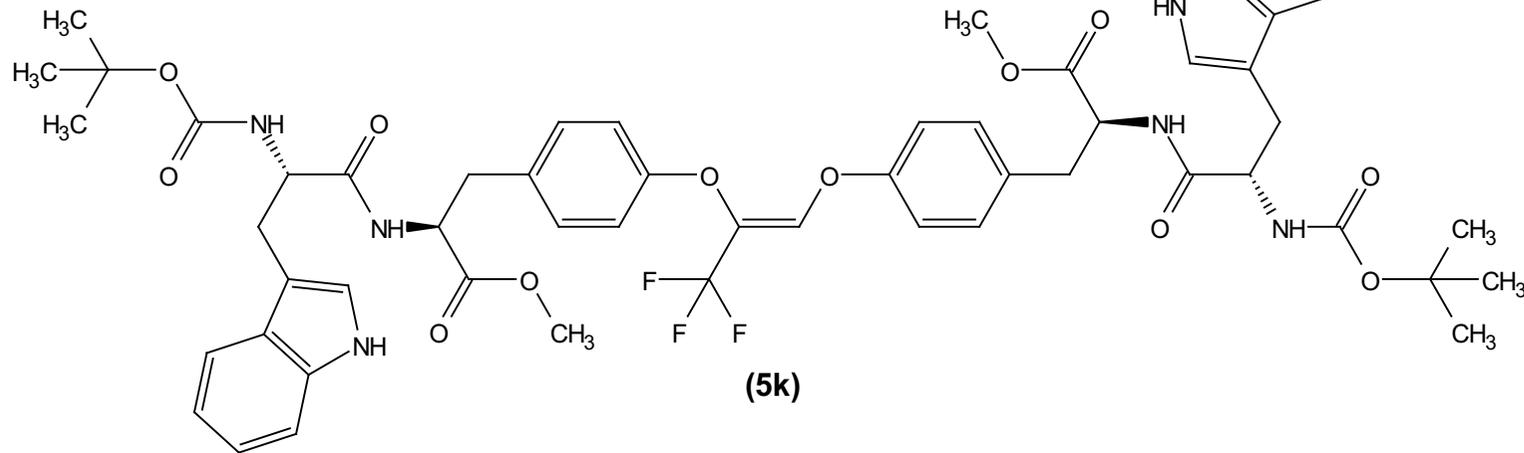


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

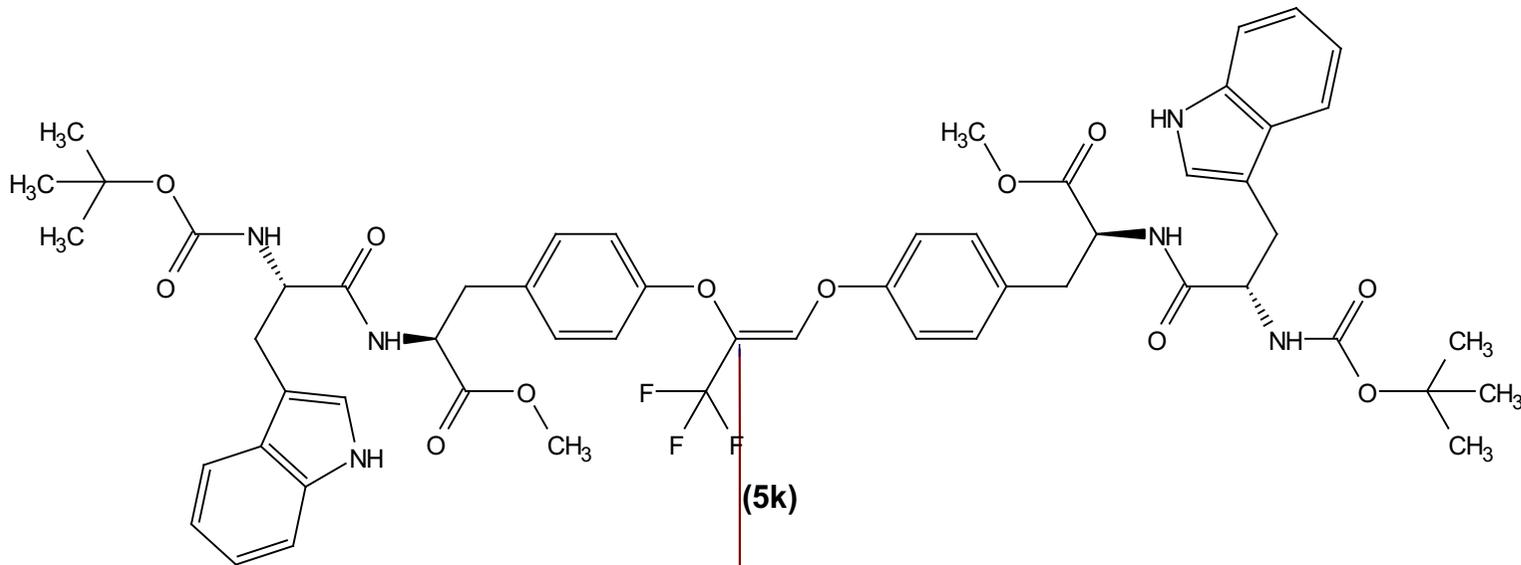
¹H NMR (400 MHz, Chloroform-*d*)



¹⁹F NMR (376 MHz, Chloroform-*d*)

64.85

68.88



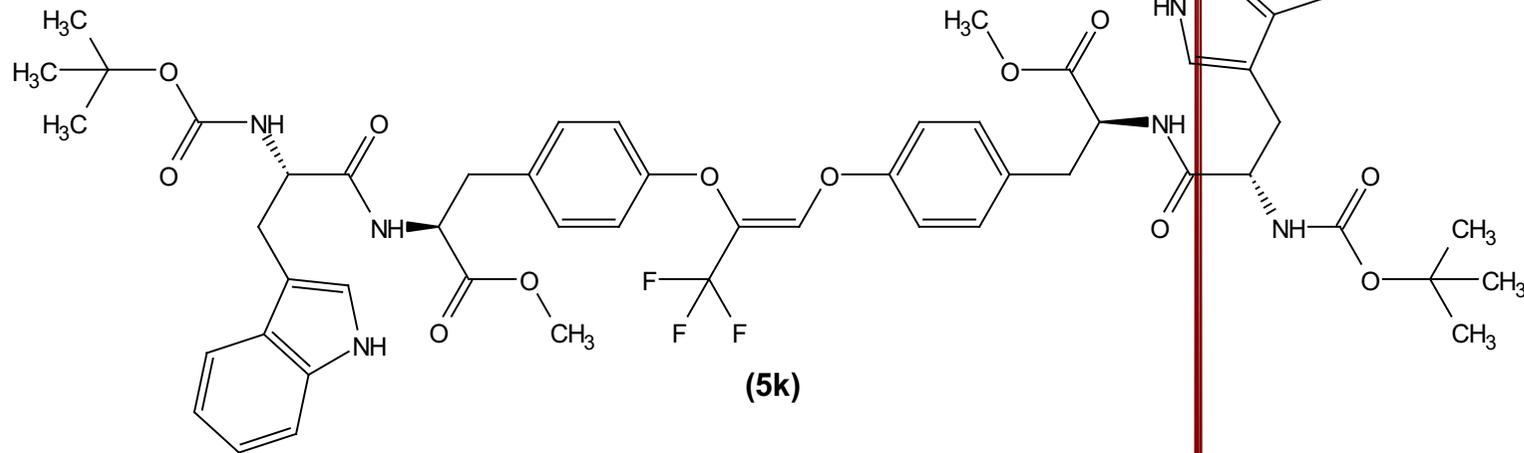
f1 (ppm)

0.01

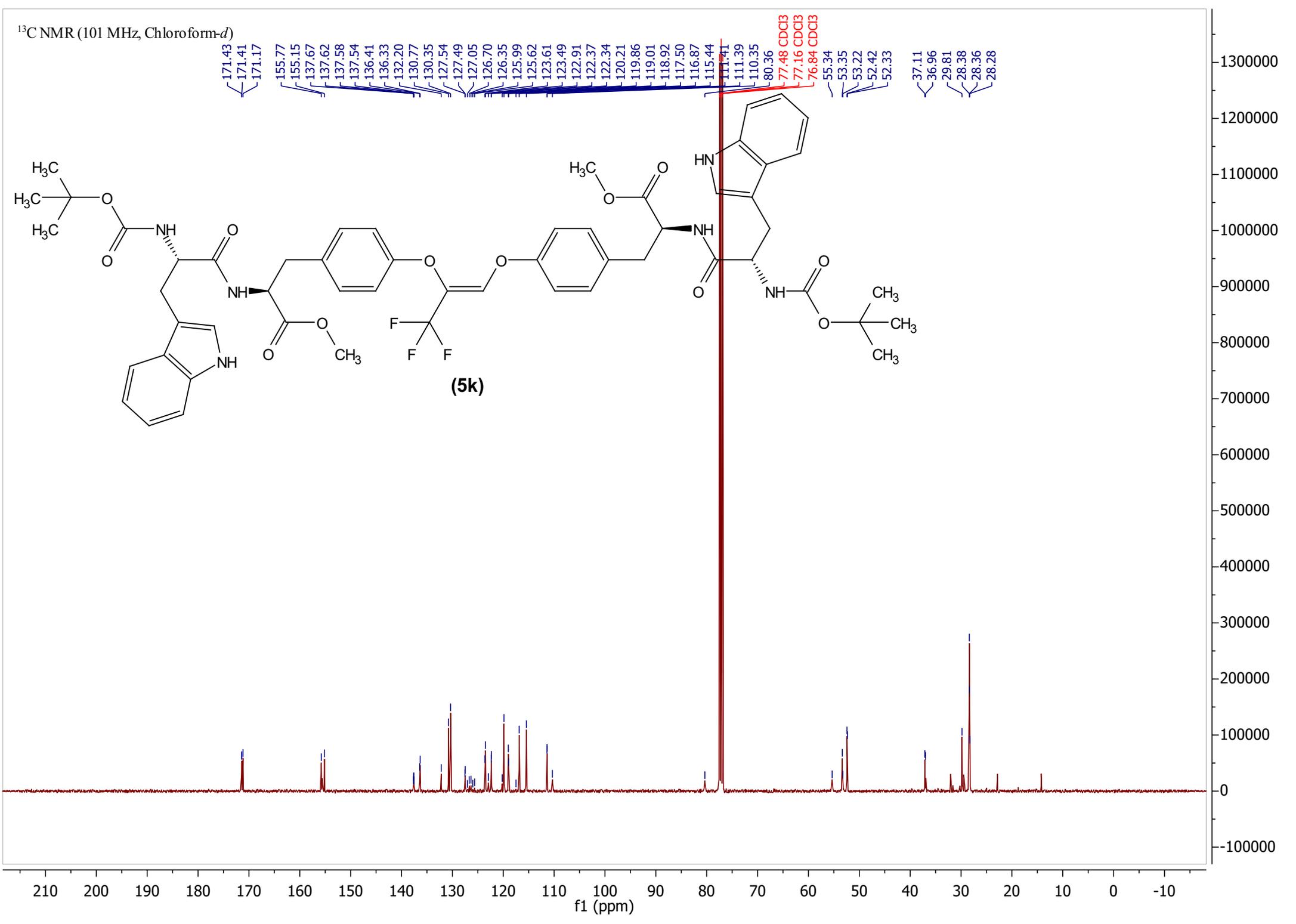
0.99

1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000

¹³C NMR (101 MHz, Chloroform-*d*)

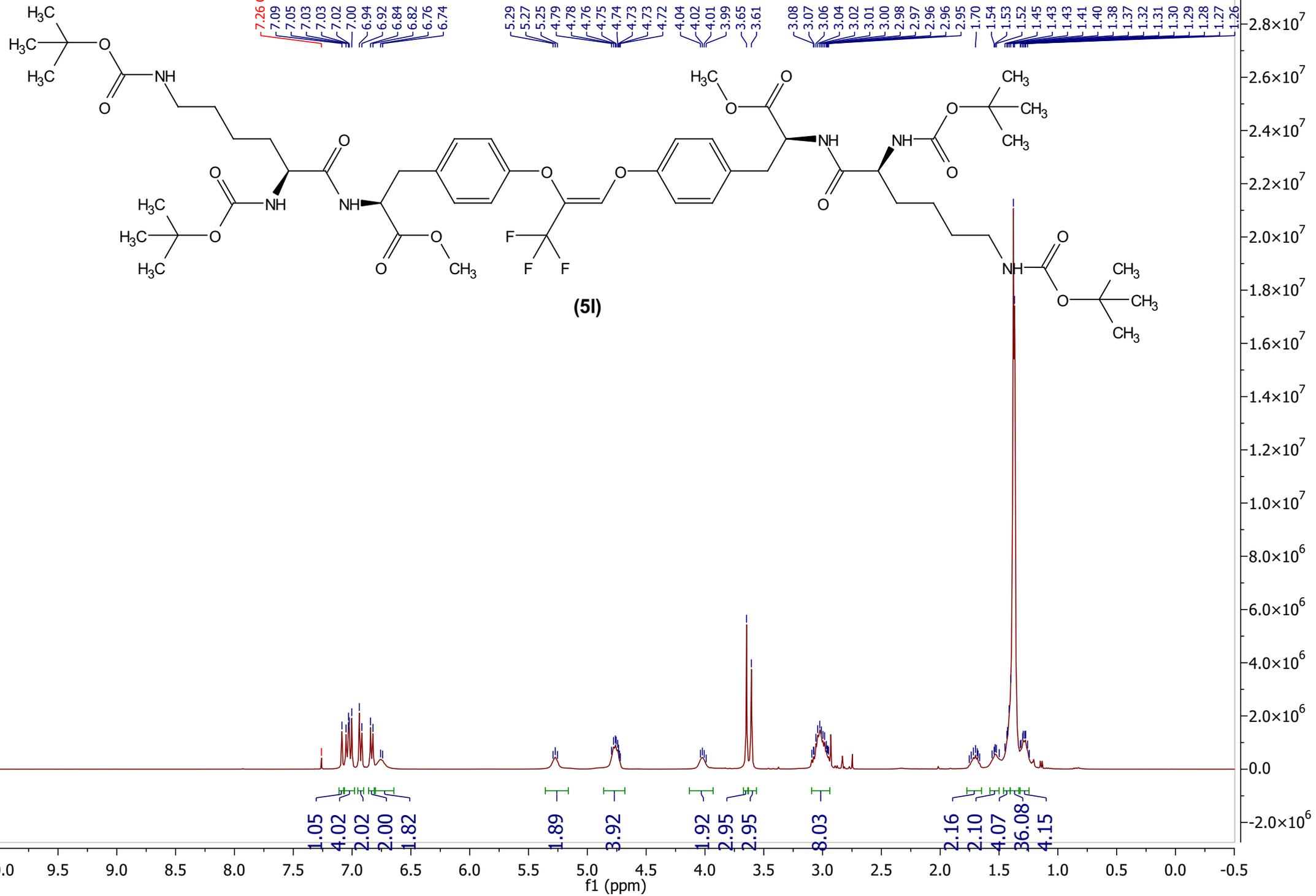


171.43
171.41
171.17
155.77
155.15
137.67
137.62
137.58
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136.41
136.33
132.20
130.77
130.35
127.54
127.49
127.05
126.70
126.35
126.35
125.99
125.62
123.61
123.49
122.91
122.37
122.34
120.21
119.86
119.01
118.92
117.50
116.87
115.44
111.71
111.39
110.35
80.36
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃
55.34
53.35
53.22
52.42
52.33
37.11
36.96
29.81
28.38
28.36
28.28

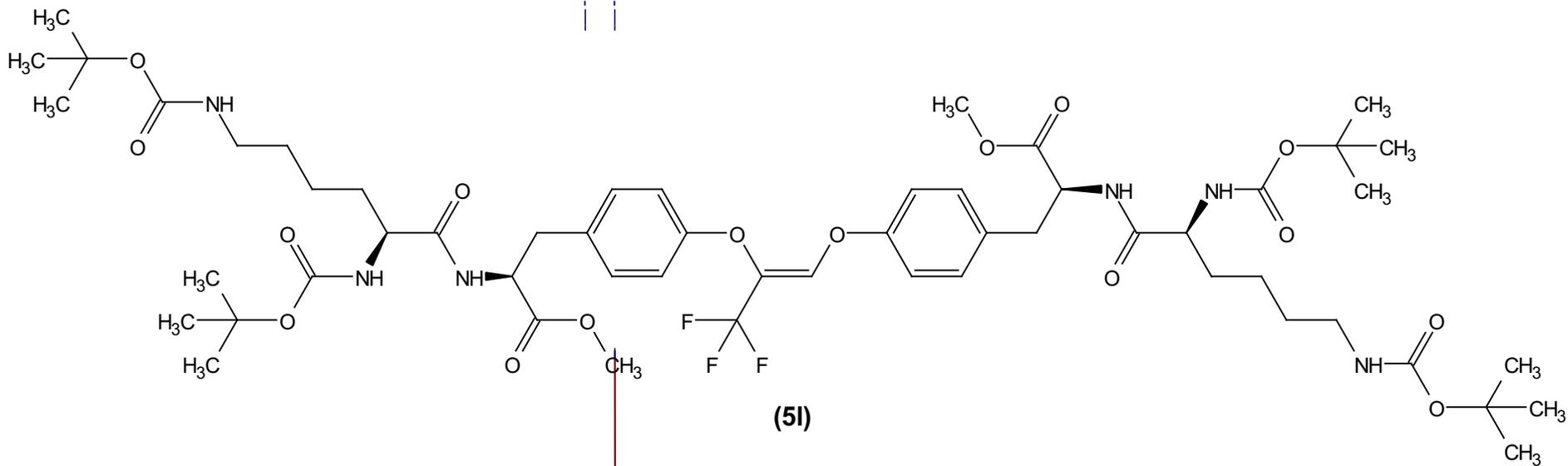


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

¹H NMR (400 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)



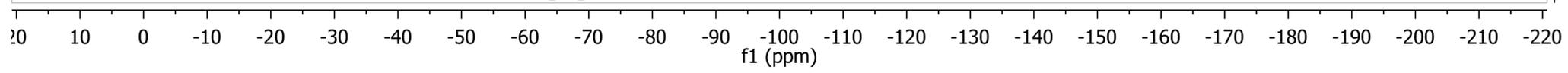
64.64

68.88

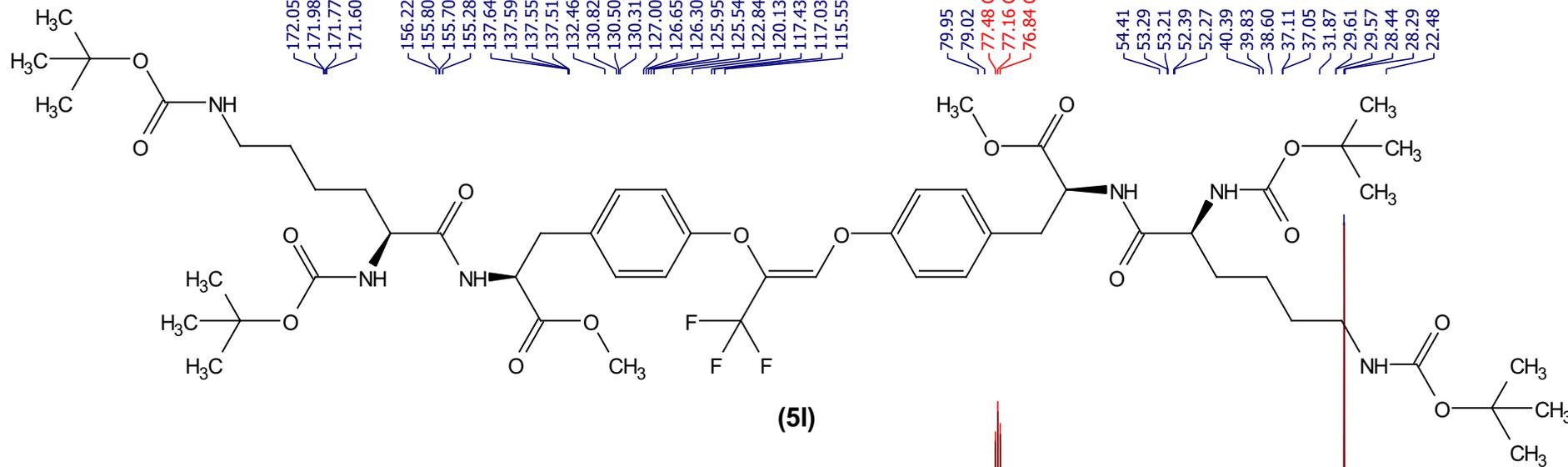
(5I)

0.01

0.99



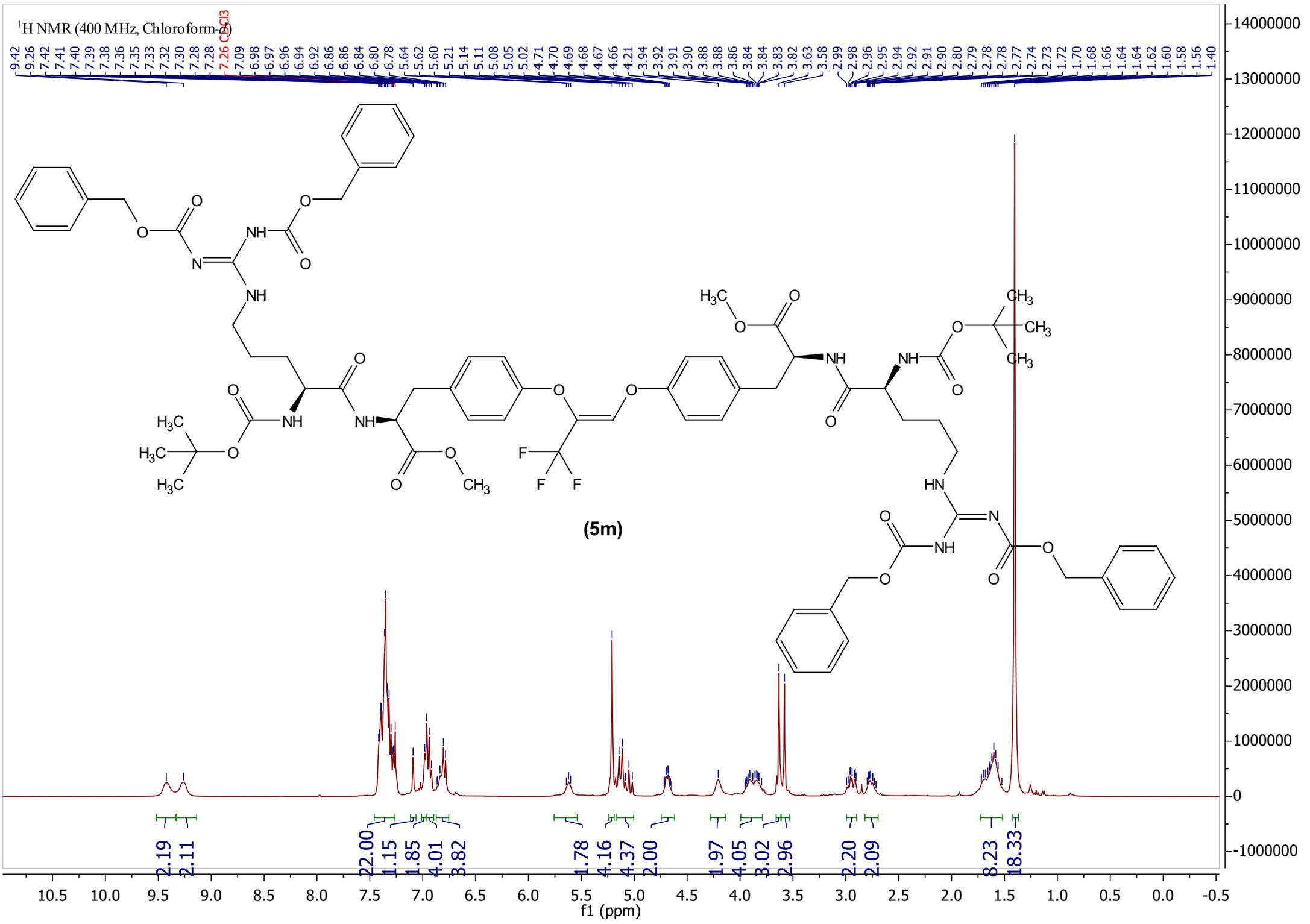
¹³C NMR (101 MHz, Chloroform-*d*)



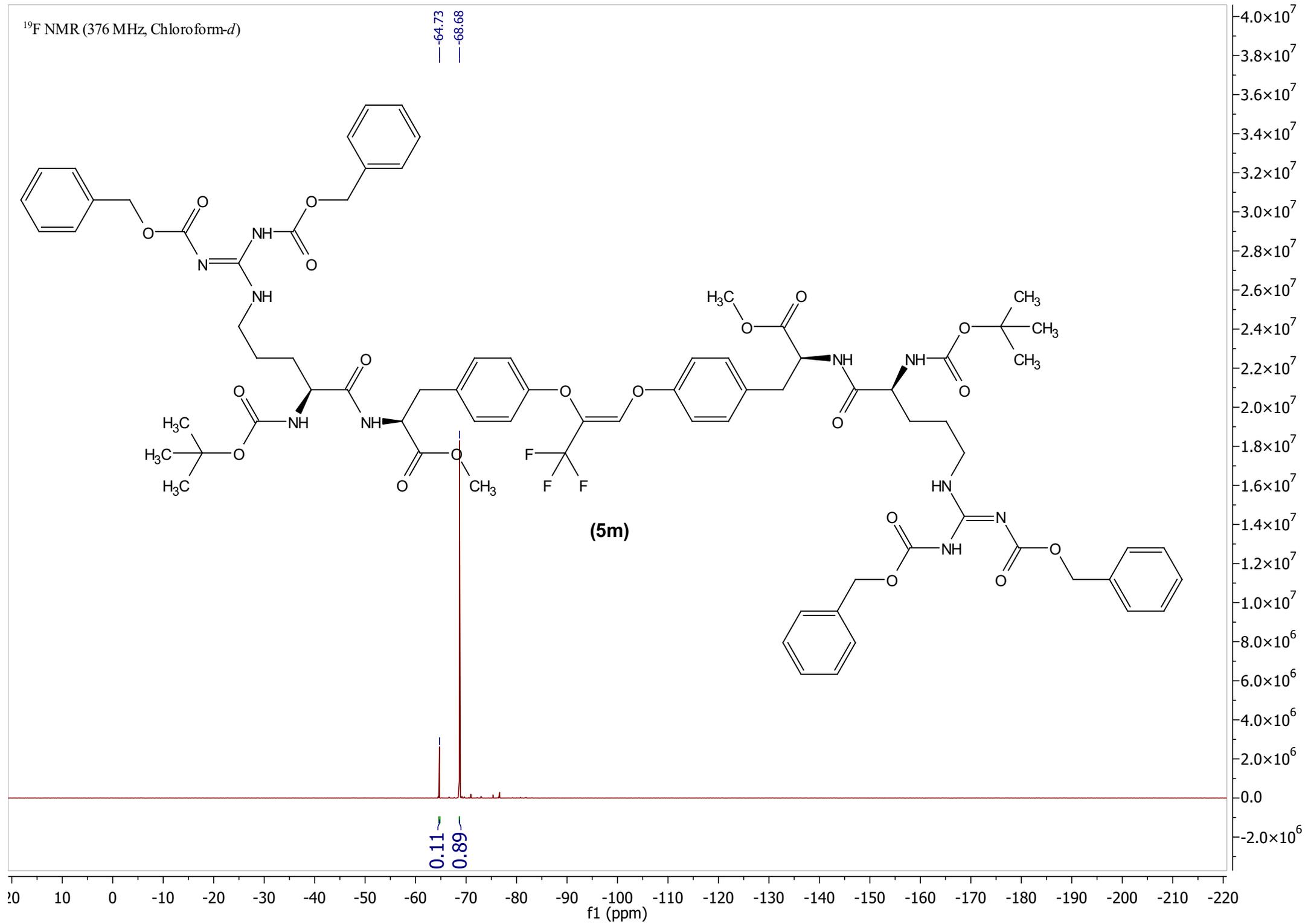
(5I)

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

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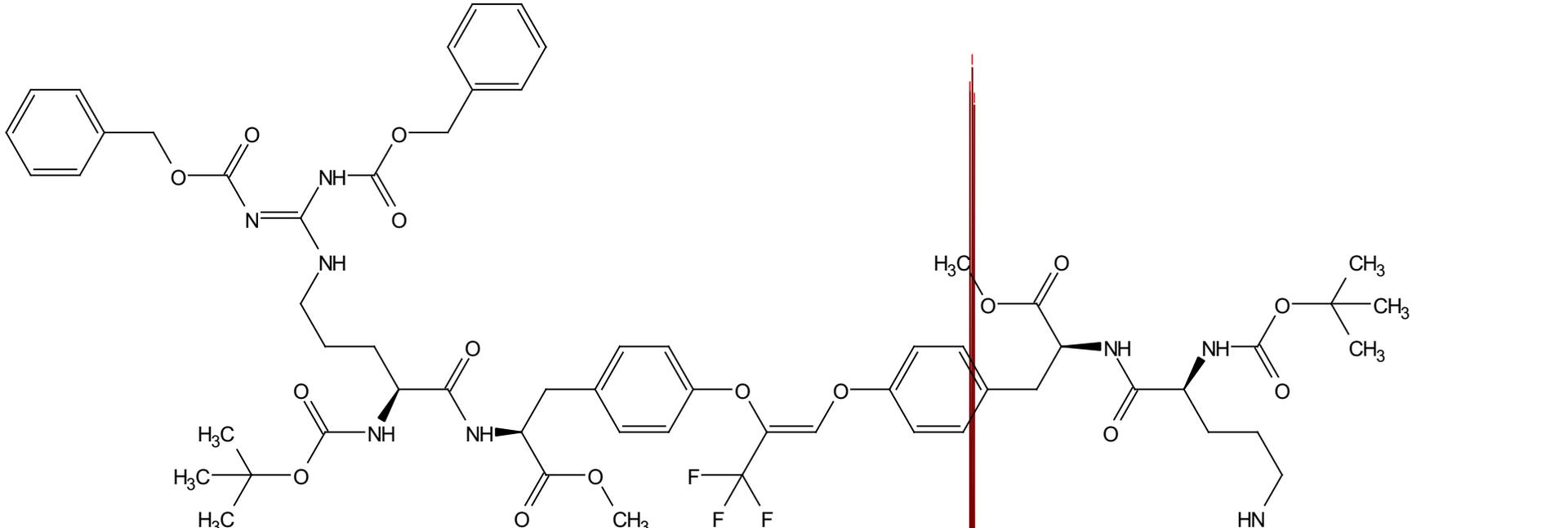


^{19}F NMR (376 MHz, Chloroform-*d*)

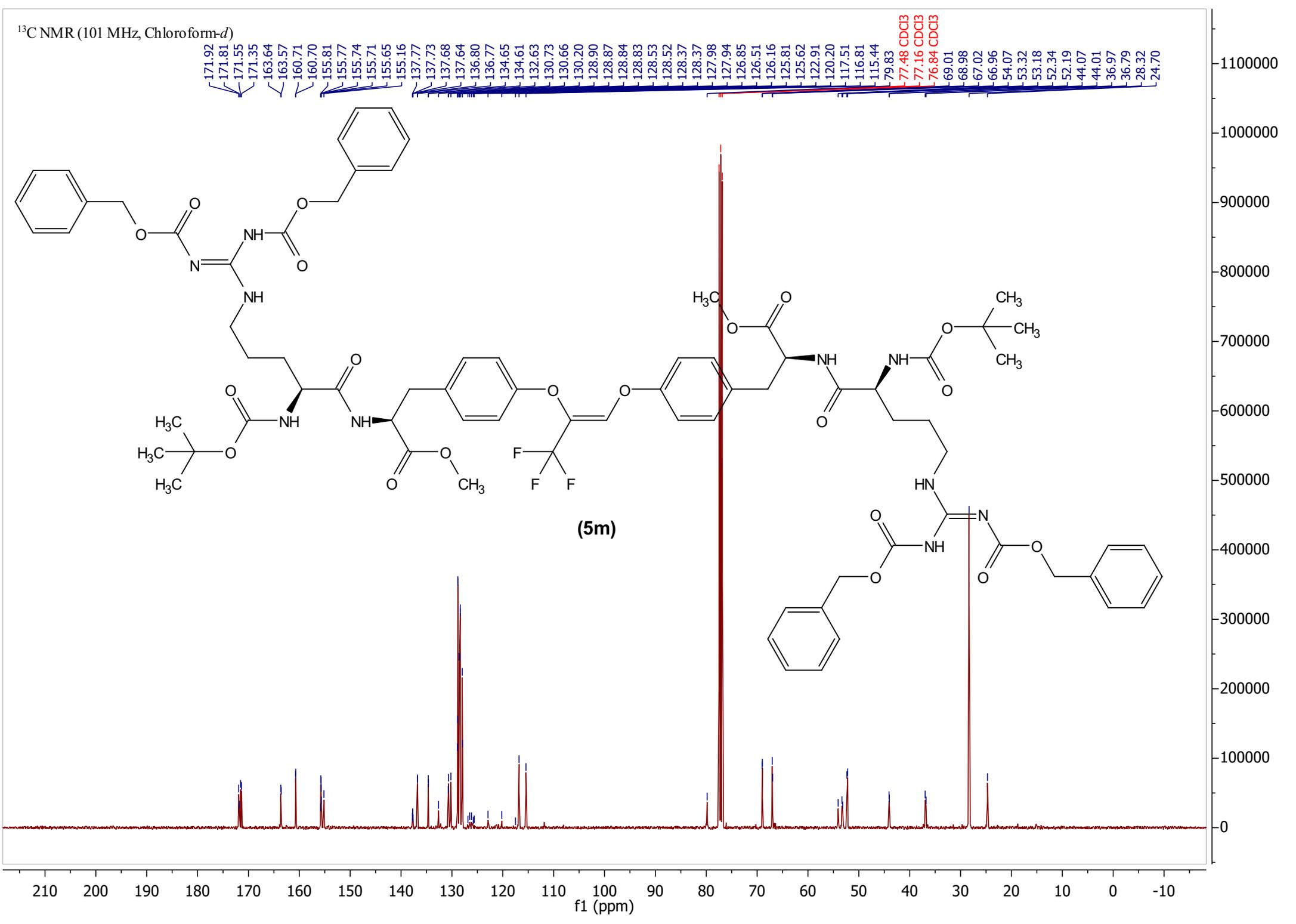


¹³C NMR (101 MHz, Chloroform-*d*)

171.92, 171.81, 171.55, 171.35, 163.64, 163.57, 160.71, 160.70, 155.81, 155.77, 155.74, 155.71, 155.65, 155.16, 137.77, 137.73, 137.68, 137.64, 136.80, 136.77, 134.65, 134.61, 132.63, 130.73, 130.66, 130.20, 128.90, 128.87, 128.84, 128.83, 128.53, 128.52, 128.37, 128.37, 127.98, 127.94, 126.85, 126.51, 126.16, 125.81, 125.62, 122.91, 120.20, 117.51, 116.81, 115.44, 79.83, 77.48 CDCl₃, 77.16 CDCl₃, 76.84 CDCl₃, 69.01, 68.98, 67.02, 66.96, 54.07, 53.32, 53.18, 52.34, 52.19, 44.07, 44.01, 36.97, 36.79, 28.32, 24.70

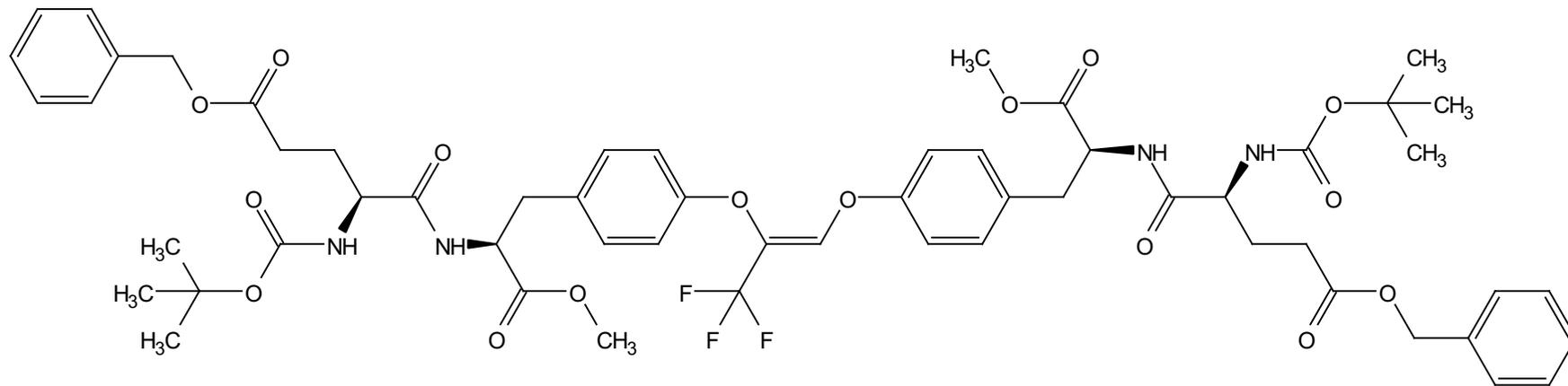


(5m)

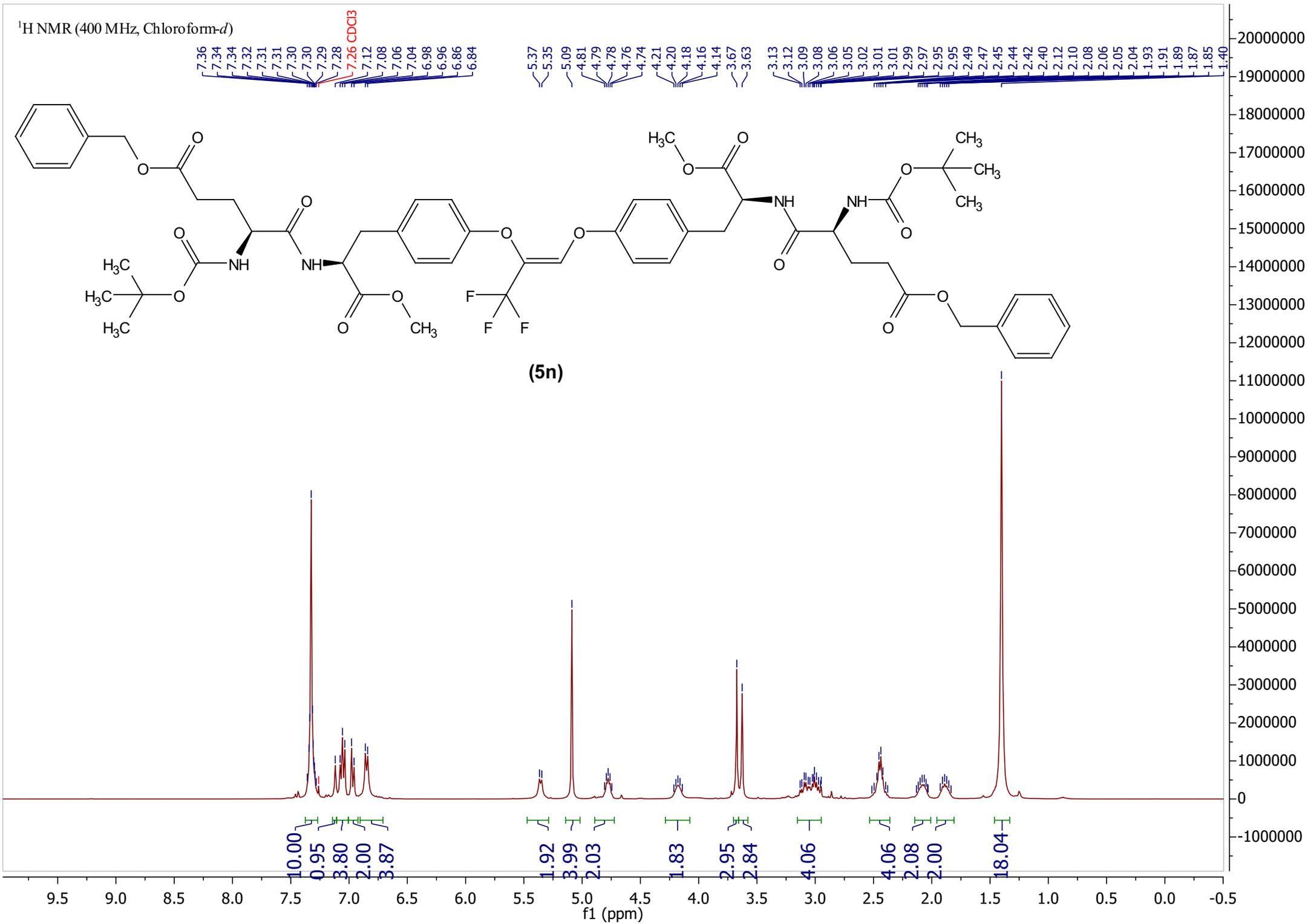


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

¹H NMR (400 MHz, Chloroform-*d*)

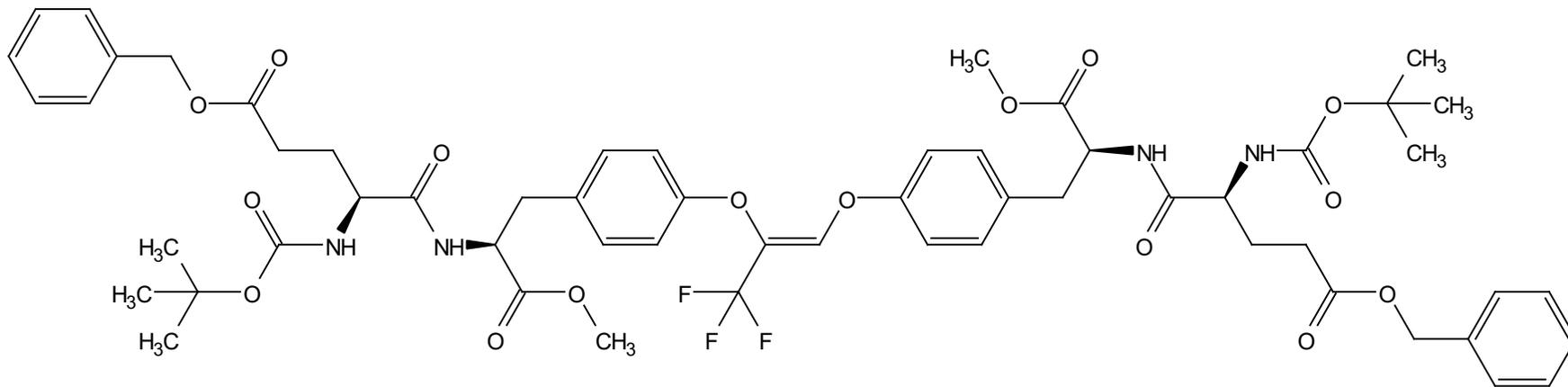


(5n)



^{19}F NMR (376 MHz, Chloroform-*d*)

64.81
68.84



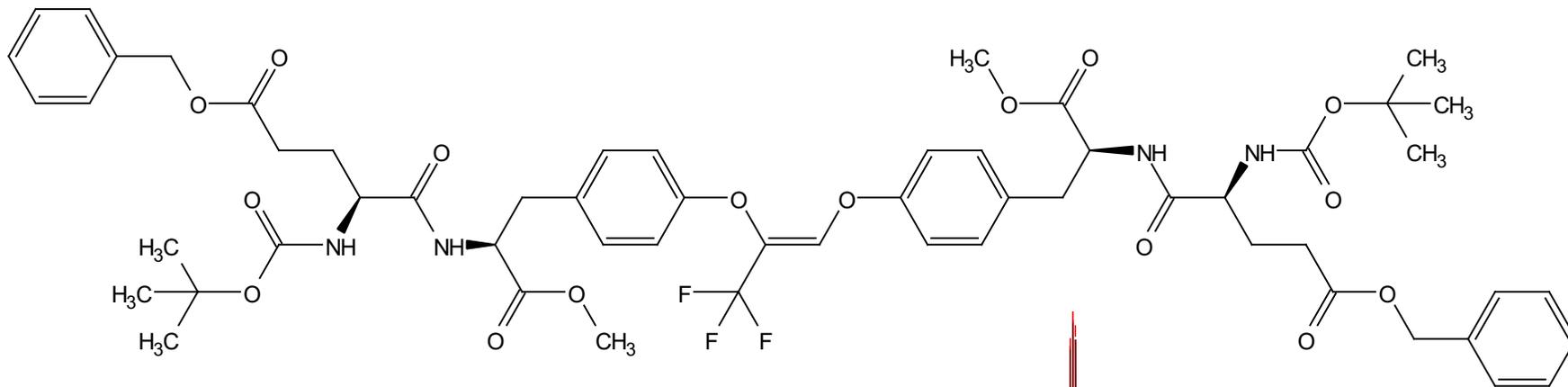
(5n)

20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

0.12
0.88

3.2×10^7
 3.0×10^7
 2.8×10^7
 2.6×10^7
 2.4×10^7
 2.2×10^7
 2.0×10^7
 1.8×10^7
 1.6×10^7
 1.4×10^7
 1.2×10^7
 1.0×10^7
 8.0×10^6
 6.0×10^6
 4.0×10^6
 2.0×10^6
0.0
 -2.0×10^6

¹³C NMR (101 MHz, Chloroform-*d*)

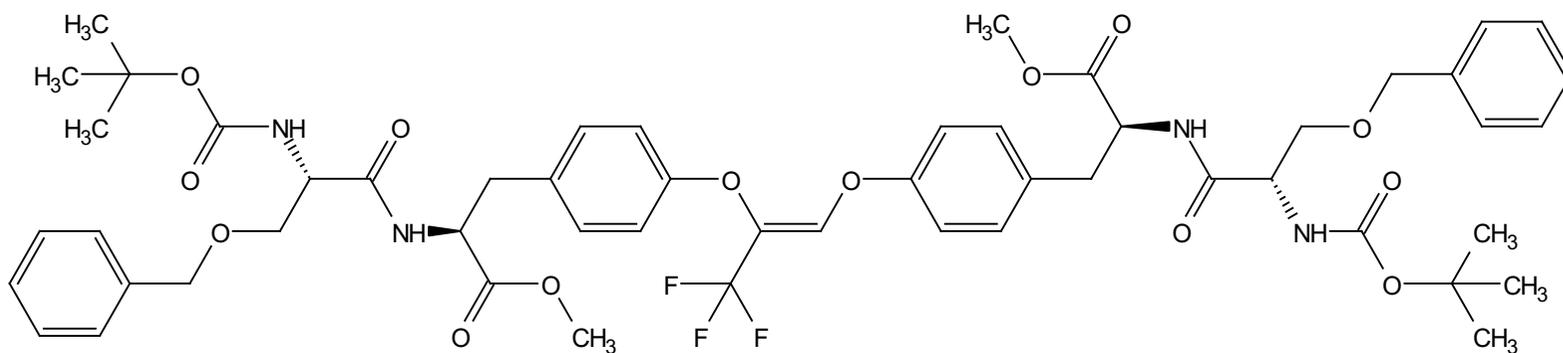


(5n)

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2200000
2100000
2000000
1900000
1800000
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1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000
-200000

^{19}F NMR (376 MHz, Chloroform-*d*)



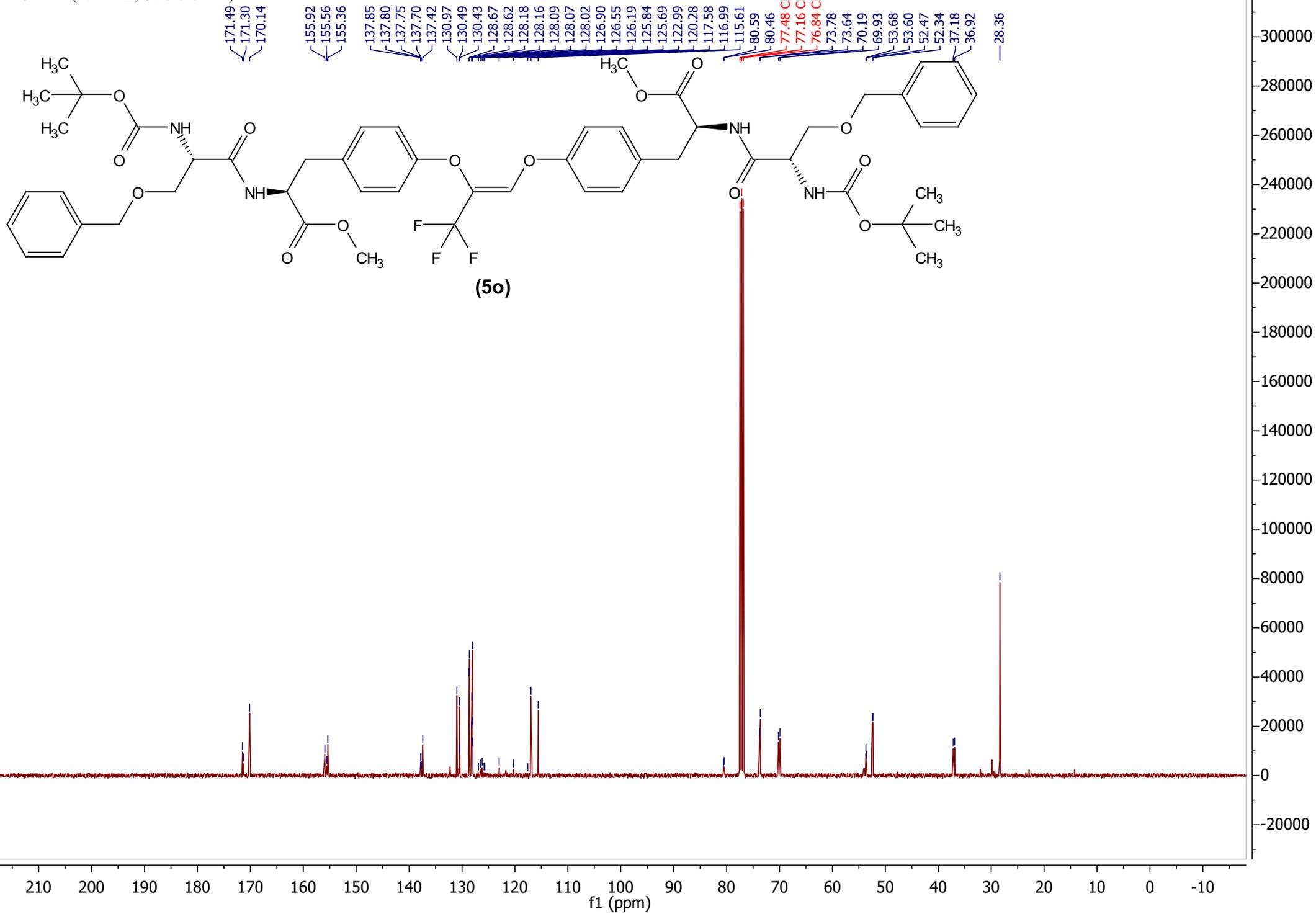
64.60
68.75

f1 (ppm)

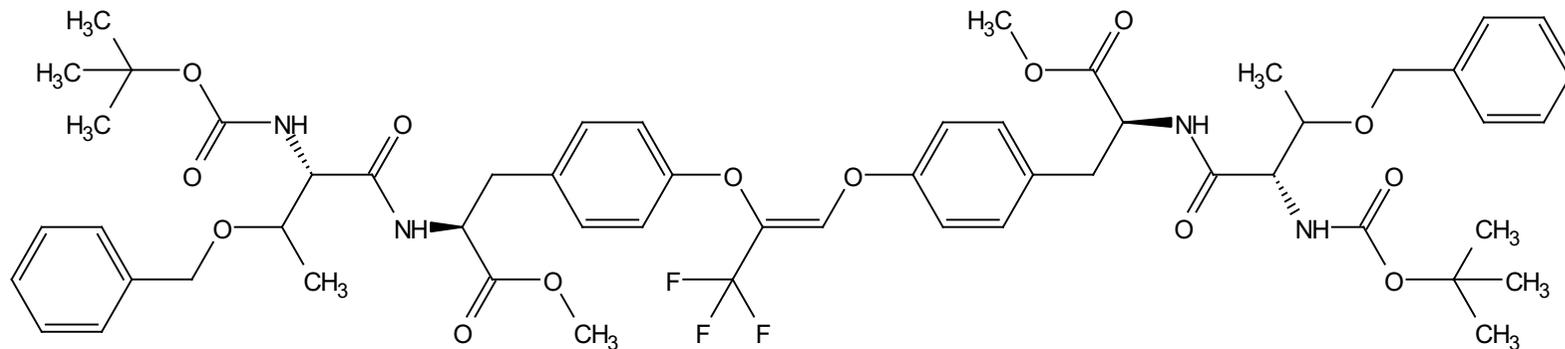
0.01
0.99

2.5×10^7
 2.0×10^7
 1.5×10^7
 1.0×10^7
 5.0×10^6
0.0

^{13}C NMR (101 MHz, Chloroform-*d*)



¹H NMR (400 MHz, Chloroform-*d*)



7.20, 7.08, 7.07, 7.06, 7.04, 6.94, 6.85, 6.83, 6.81, 6.79, 6.77, 6.57, 6.55, 5.39, 5.38, 5.36, 5.34, 4.72, 4.70, 4.68, 4.67, 4.65, 4.55, 4.52, 4.50, 4.44, 4.41, 4.21, 4.20, 4.19, 4.11, 4.10, 4.08, 4.06, 4.06, 3.58, 3.52, 3.01, 3.00, 2.97, 2.96, 2.95, 2.93, 2.92, 2.90, 2.88, 2.87, 2.85, 2.83, 1.35, 1.14, 1.12, 1.10

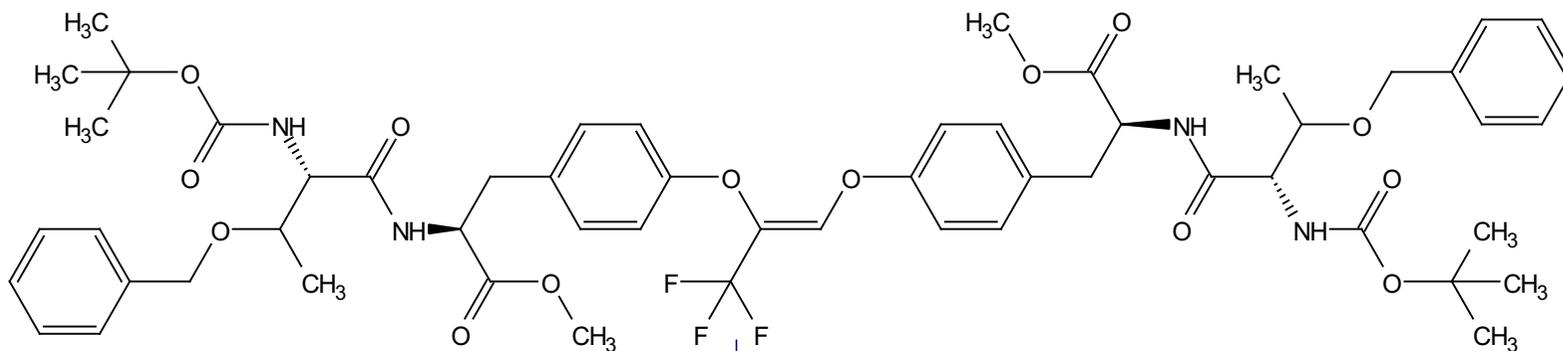
10.00, 1.81, 1.06, 5.86, 1.93, 1.89, 2.01, 1.98, 2.00, 1.82, 2.16, 3.00, 2.75, 4.04, 18.07, 6.07

1.0, 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, 0.5, 0.0

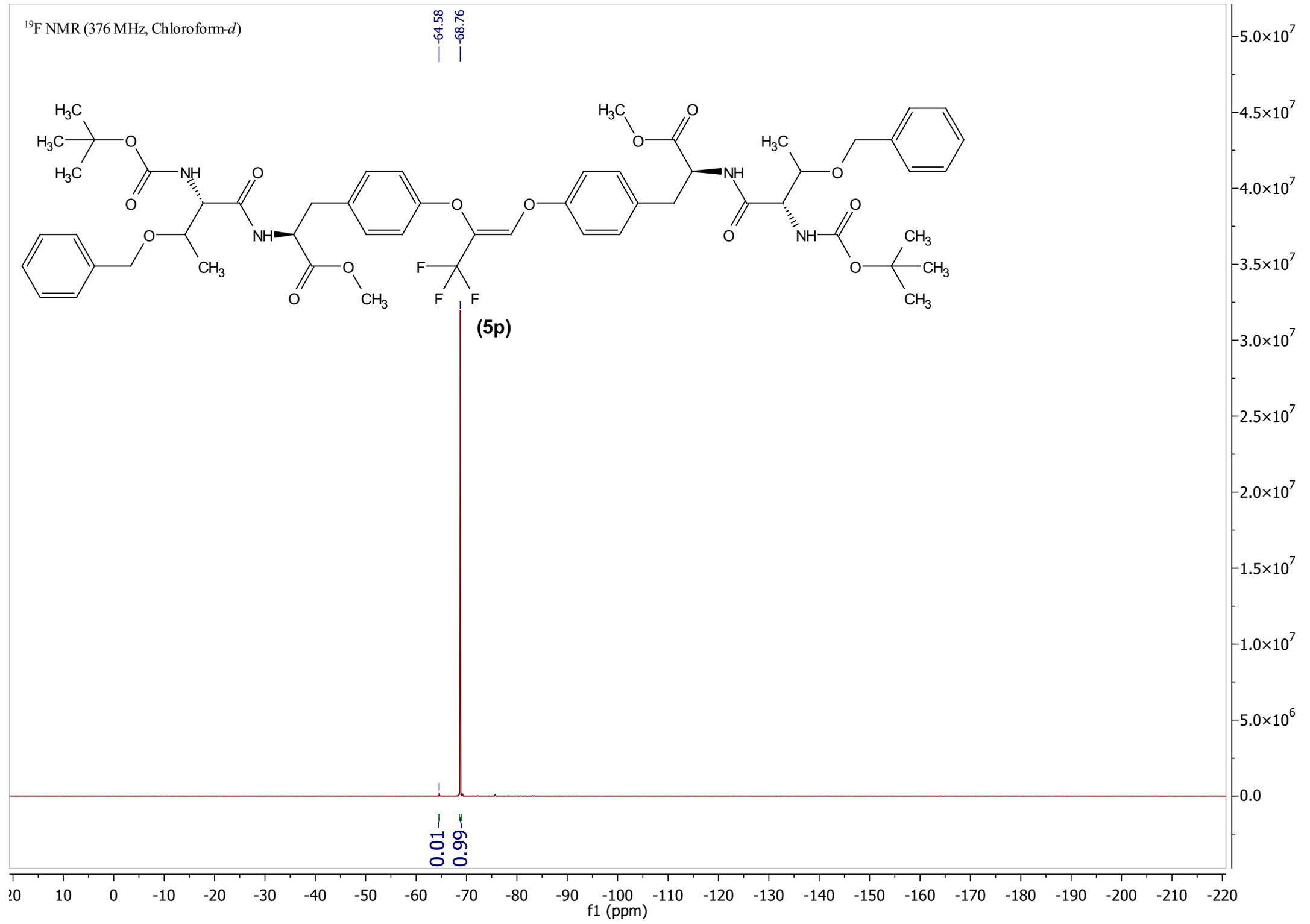
f1 (ppm)

2000000, 1900000, 1800000, 1700000, 1600000, 1500000, 1400000, 1300000, 1200000, 1100000, 1000000, 900000, 800000, 700000, 600000, 500000, 400000, 300000, 200000, 100000, 0, -100000

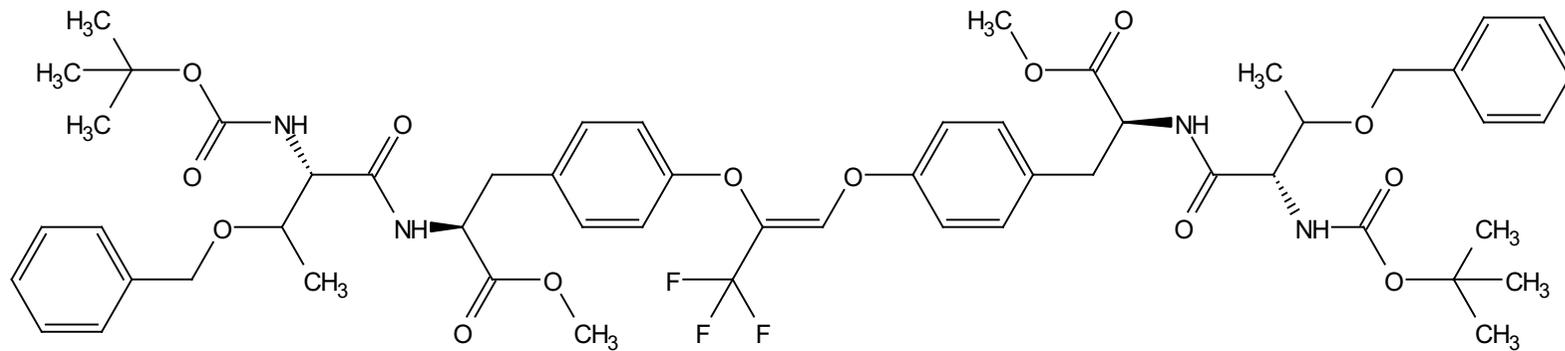
^{19}F NMR (376 MHz, Chloroform-*d*)



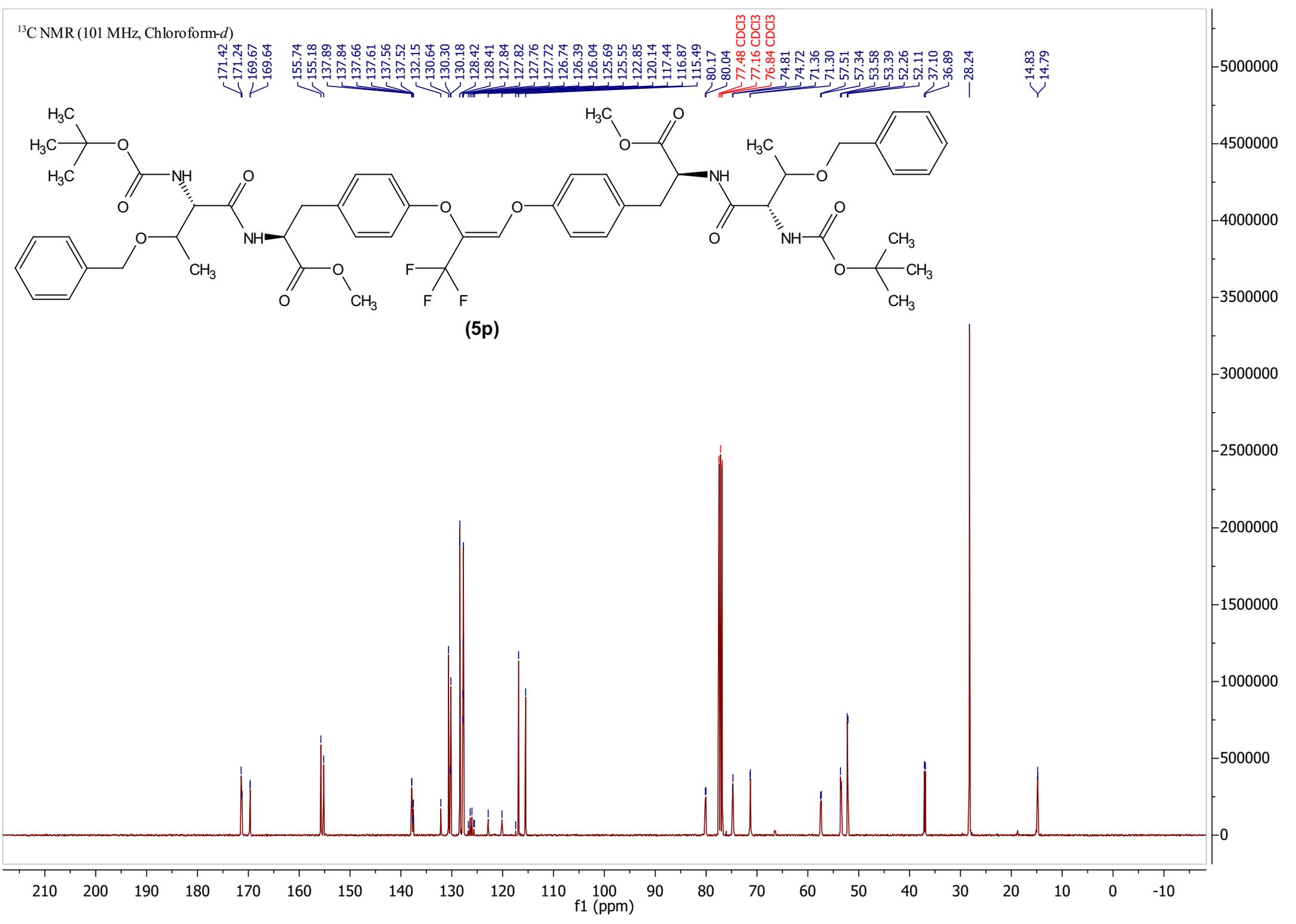
(5p)



¹³C NMR (101 MHz, Chloroform-*d*)

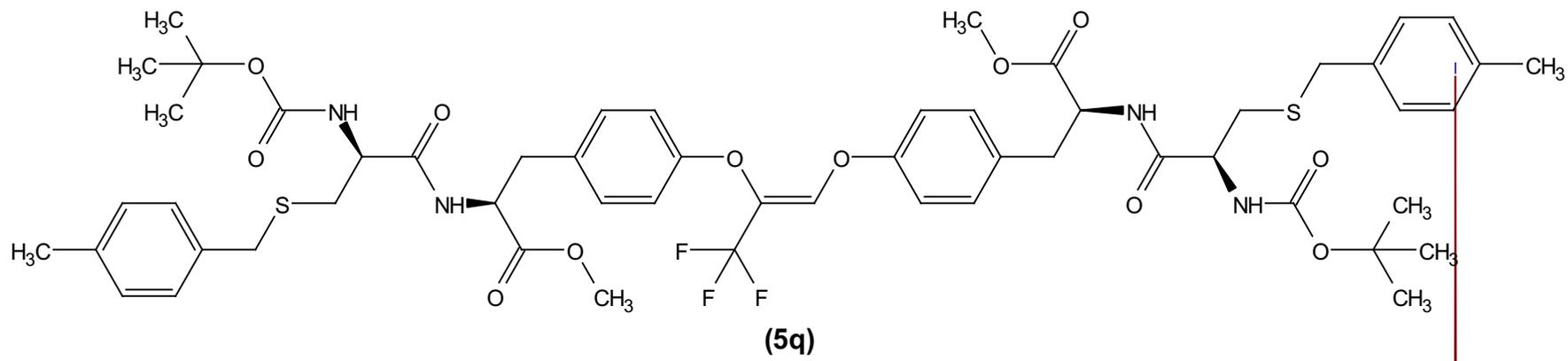


171.42, 171.24, 169.67, 169.64, 155.74, 155.18, 137.89, 137.84, 137.66, 137.61, 137.56, 137.52, 132.15, 130.64, 130.30, 130.18, 128.42, 128.41, 127.84, 127.82, 127.76, 127.72, 126.74, 126.39, 126.04, 125.69, 125.55, 122.85, 120.14, 117.44, 116.87, 115.49, 80.17, 80.04, 77.48 CDCl₃, 77.16 CDCl₃, 76.84 CDCl₃, 74.81, 74.72, 71.36, 71.30, 57.51, 57.34, 53.58, 53.39, 52.26, 52.11, 37.10, 36.89, 28.24, 14.83, 14.79



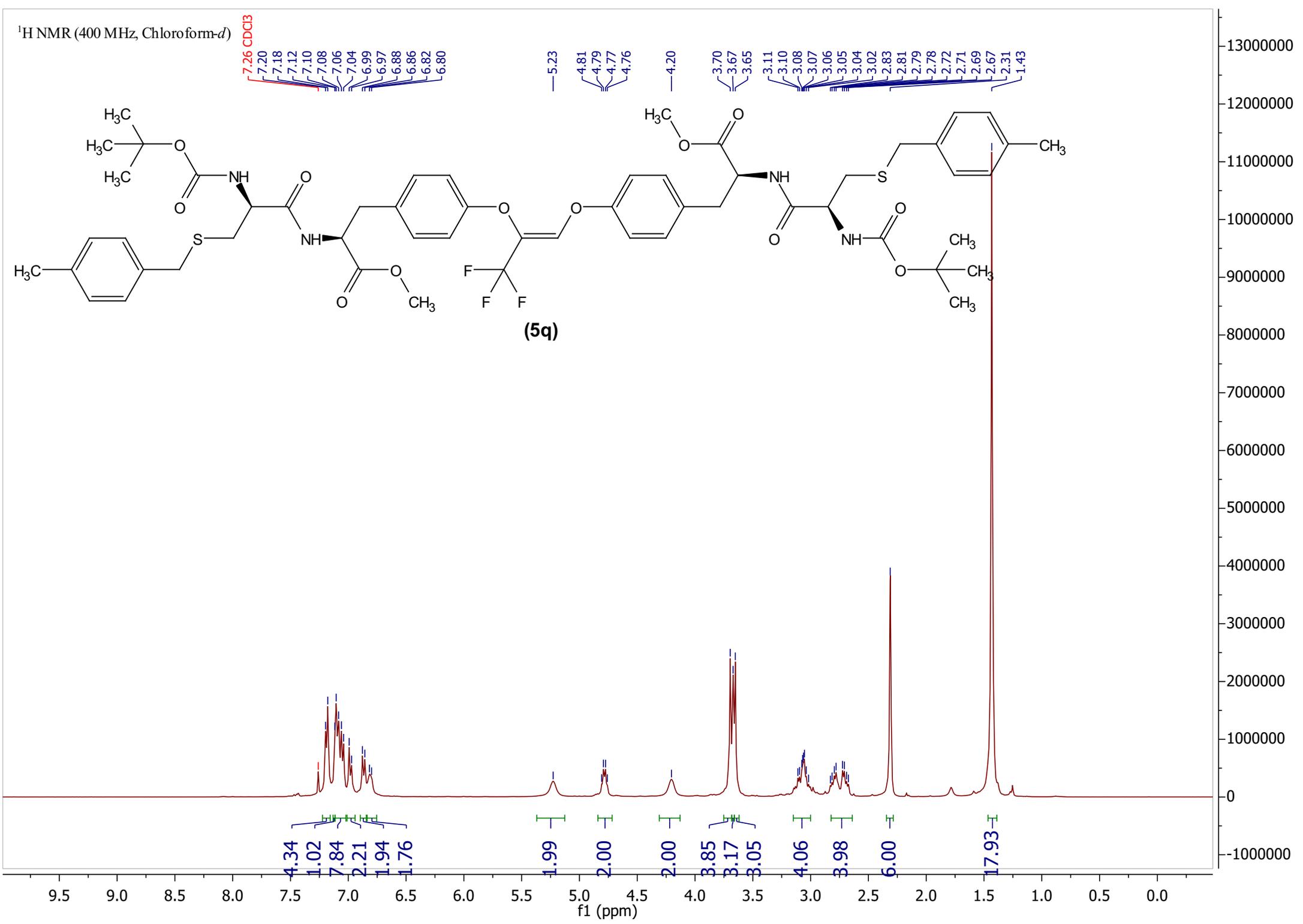
¹H NMR (400 MHz, Chloroform-*d*)

7.26 CDCl₃



7.20 7.18 7.12 7.10 7.08 7.06 7.04 6.99 6.97 6.88 6.86 6.82 6.80

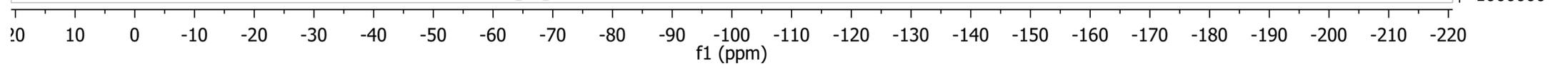
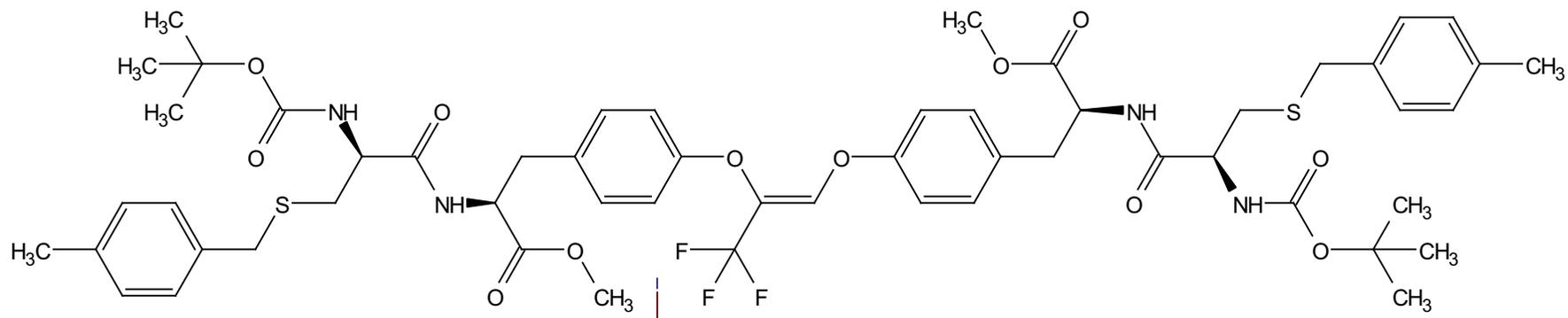
5.23 4.81 4.79 4.77 4.76 4.20 3.70 3.67 3.65 3.11 3.10 3.08 3.07 3.06 3.05 3.04 3.02 2.83 2.81 2.79 2.78 2.72 2.71 2.69 2.67 2.31 1.43



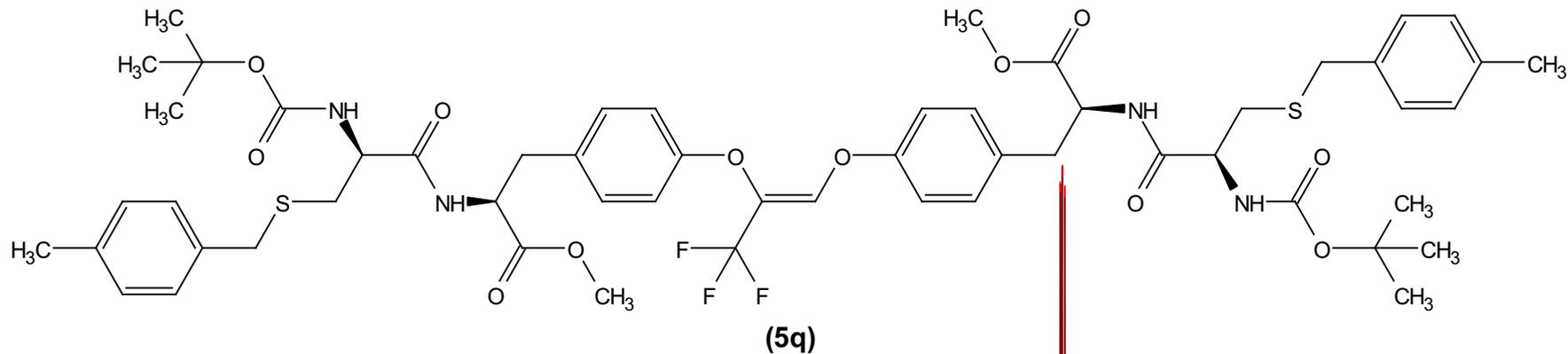
¹⁹F NMR (376 MHz, Chloroform-*d*)

64.85

68.81



¹³C NMR (101 MHz, Chloroform-*d*)



171.47
171.33
170.49
170.46

155.96
155.45

137.76
137.71
137.66
137.62
137.04
136.97

134.78
134.69
132.36
130.93
130.46
130.41

129.41
129.40
128.99
127.09
126.75
126.40
126.05
125.63
122.93
120.23

117.52
117.17
115.69

80.51
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3

53.83
53.78
53.61
53.53
52.53
52.39

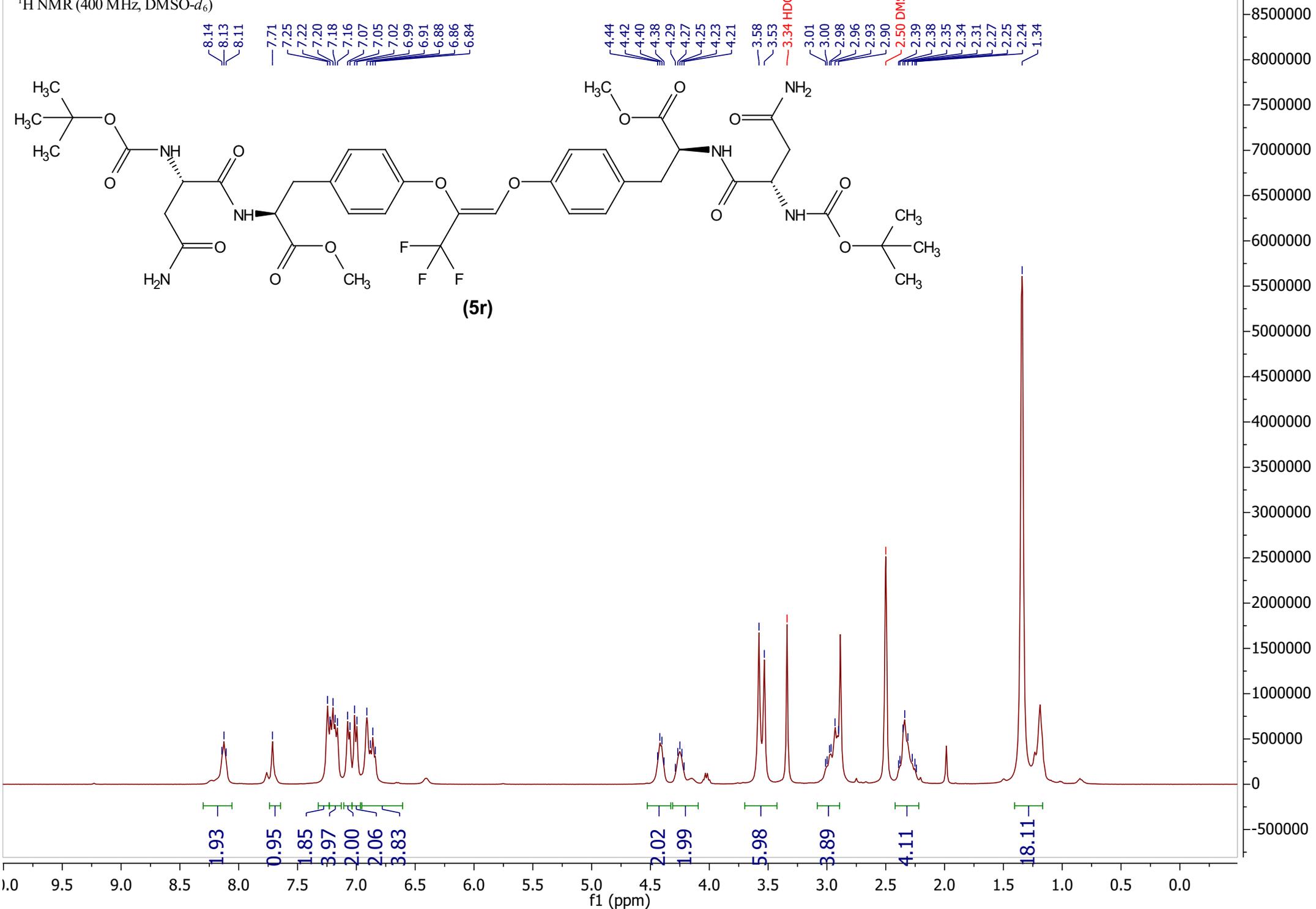
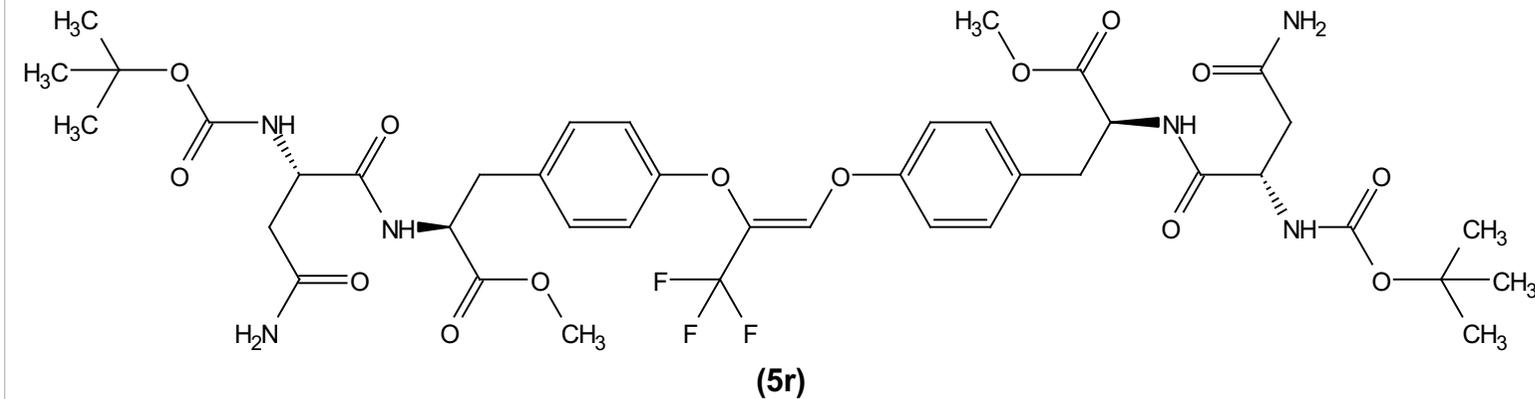
37.22
37.16
36.27
36.23
33.54
28.34

21.19

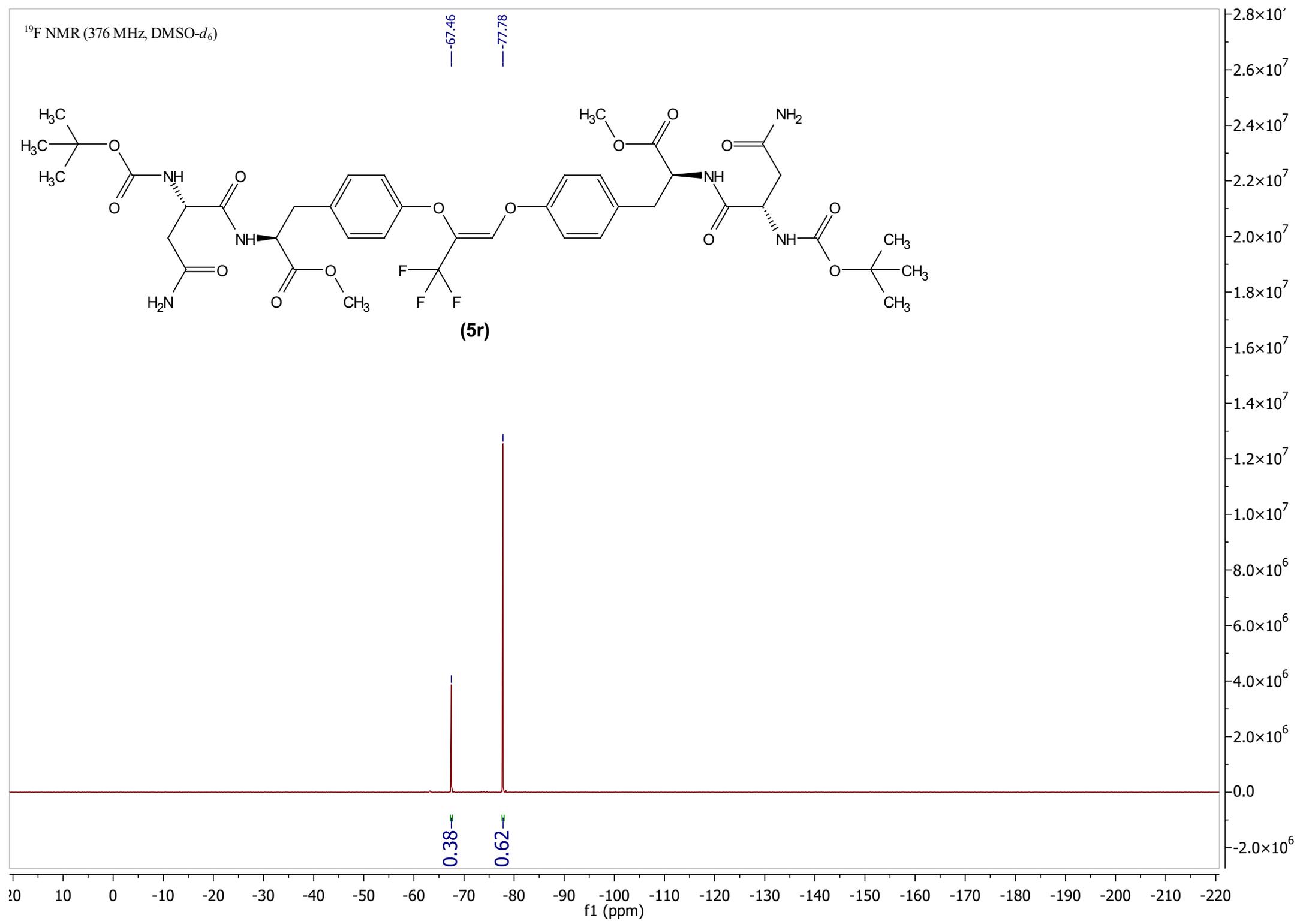
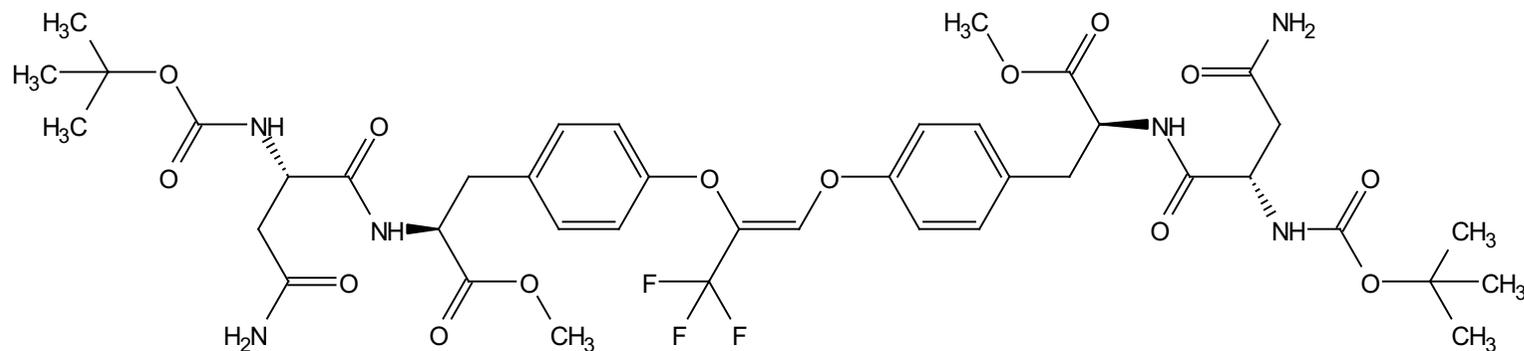
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2000000
1900000
1800000
1700000
1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
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0
-100000

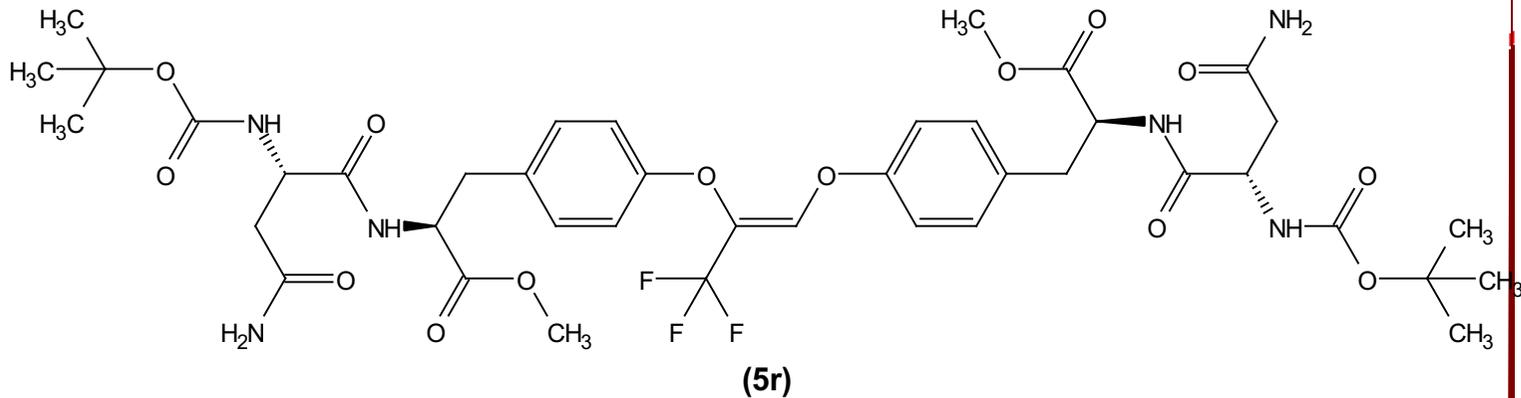
¹H NMR (400 MHz, DMSO-d₆)



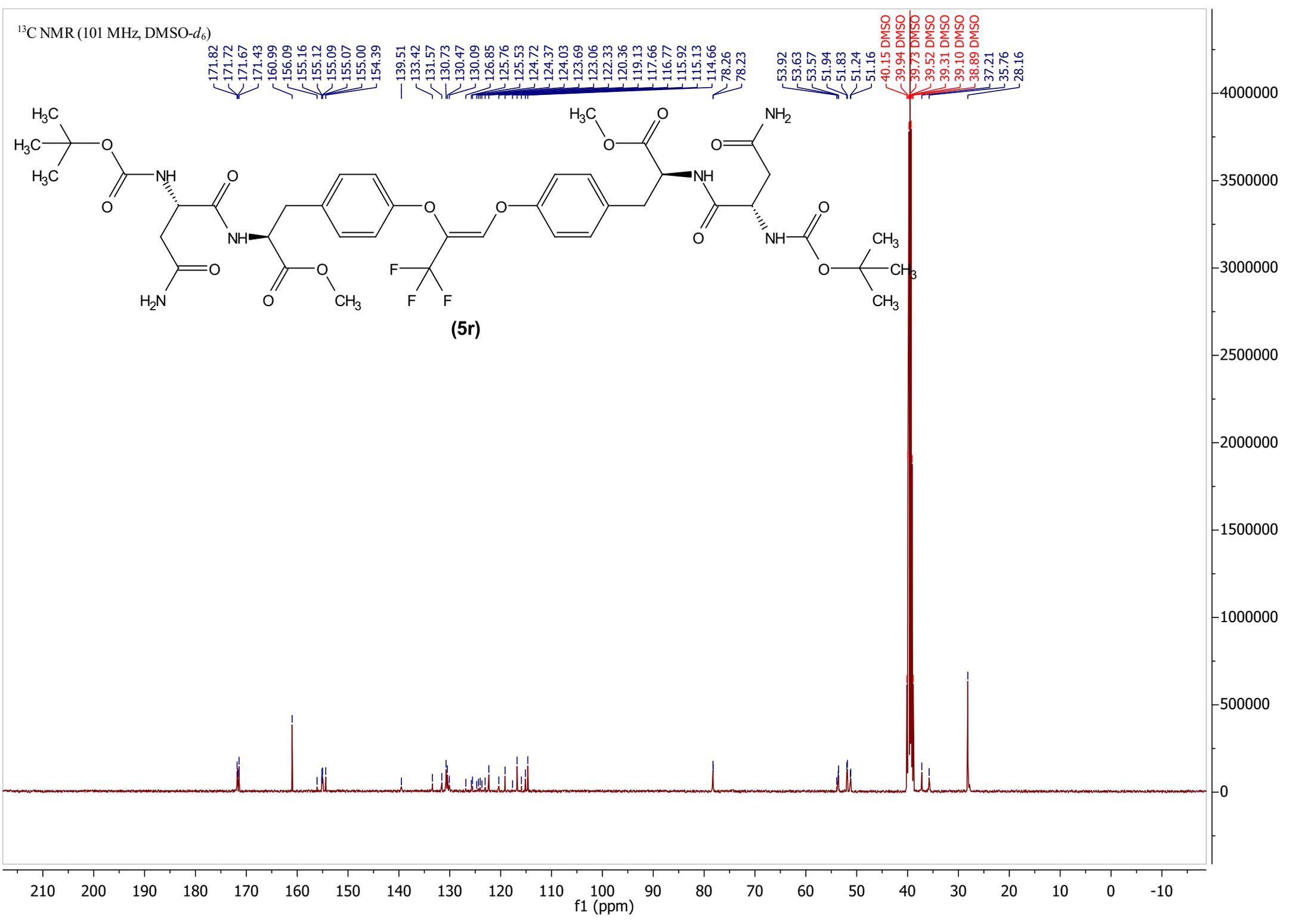
^{19}F NMR (376 MHz, $\text{DMSO-}d_6$)



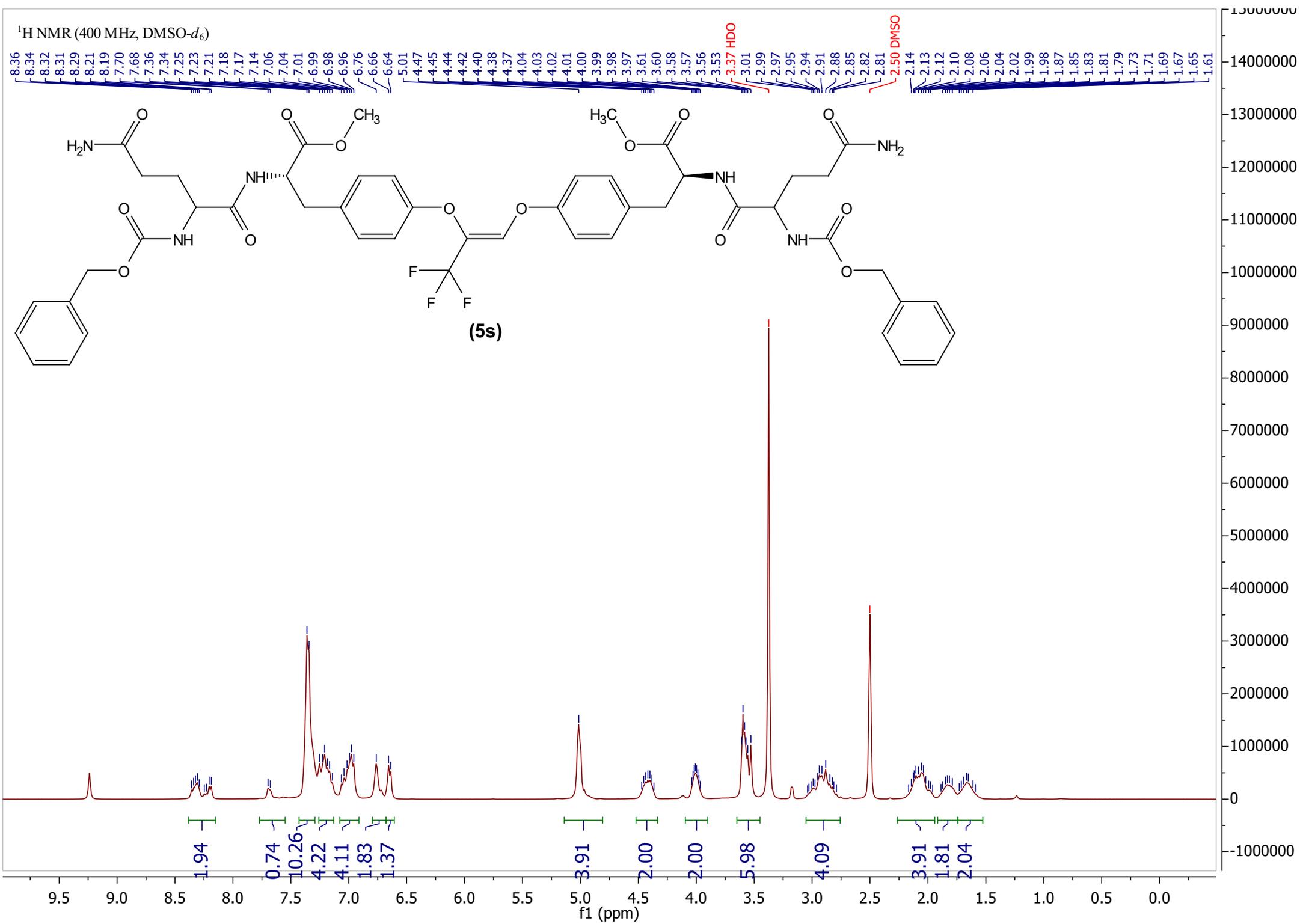
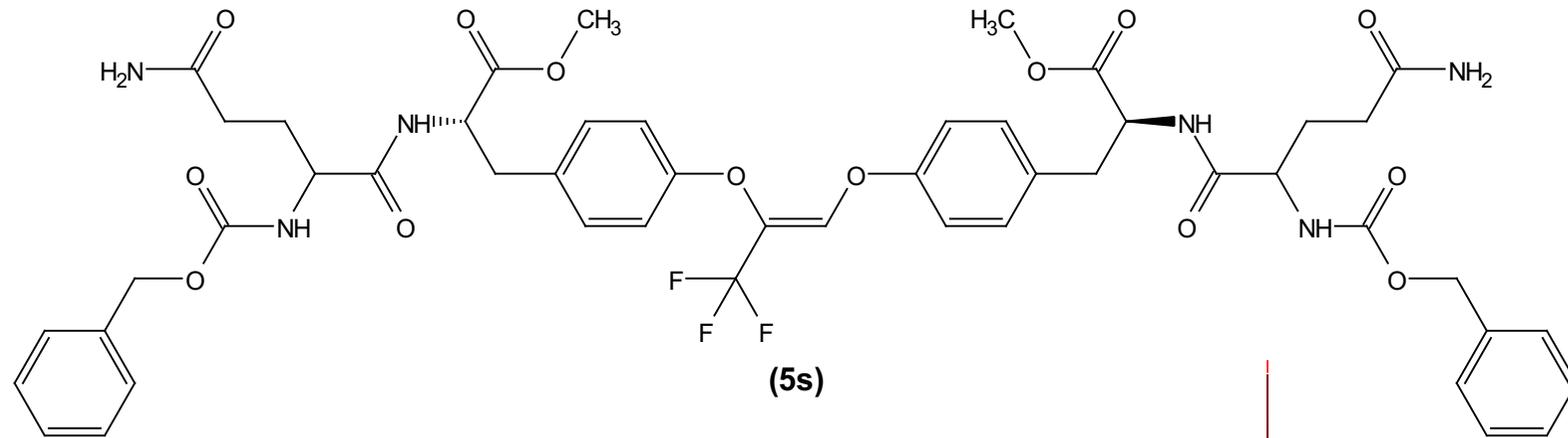
¹³C NMR (101 MHz, DMSO-*d*₆)



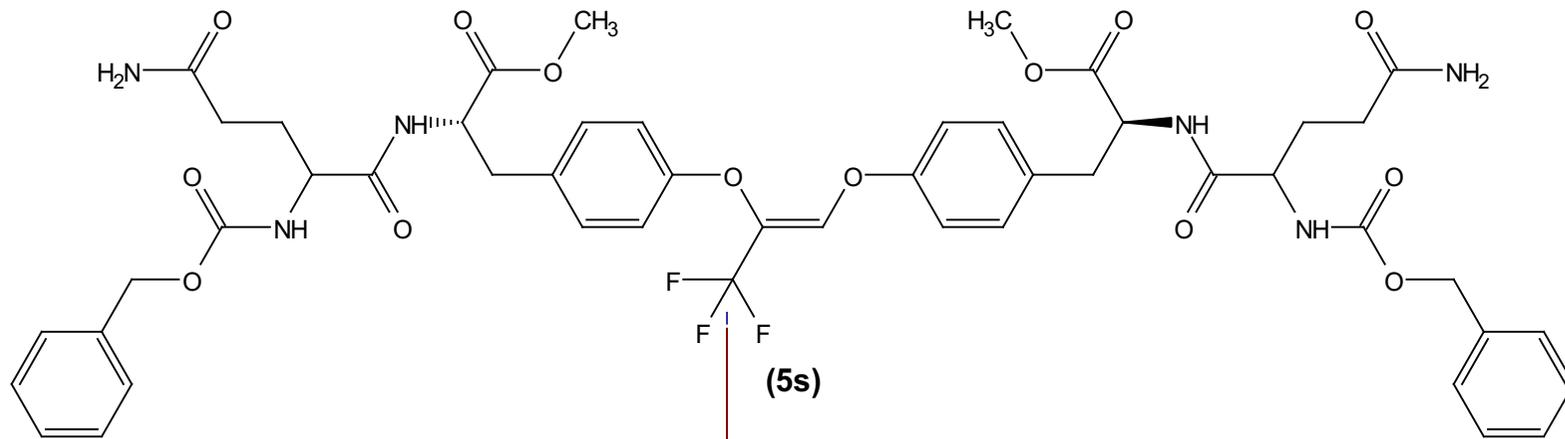
171.82, 171.72, 171.67, 171.43, 160.99, 156.09, 155.16, 155.12, 155.09, 155.07, 155.00, 154.39, 139.51, 133.42, 131.57, 130.73, 130.47, 130.09, 126.85, 125.76, 125.53, 124.72, 124.37, 124.03, 123.69, 123.06, 122.33, 120.36, 119.13, 117.66, 116.77, 115.92, 115.13, 114.66, 78.26, 78.23, 53.92, 53.63, 53.57, 51.94, 51.83, 51.24, 51.16, 40.15 DMSO, 39.94 DMSO, 39.73 DMSO, 39.52 DMSO, 39.31 DMSO, 39.10 DMSO, 38.89 DMSO, 37.21, 35.76, 28.16



¹H NMR (400 MHz, DMSO-*d*₆)

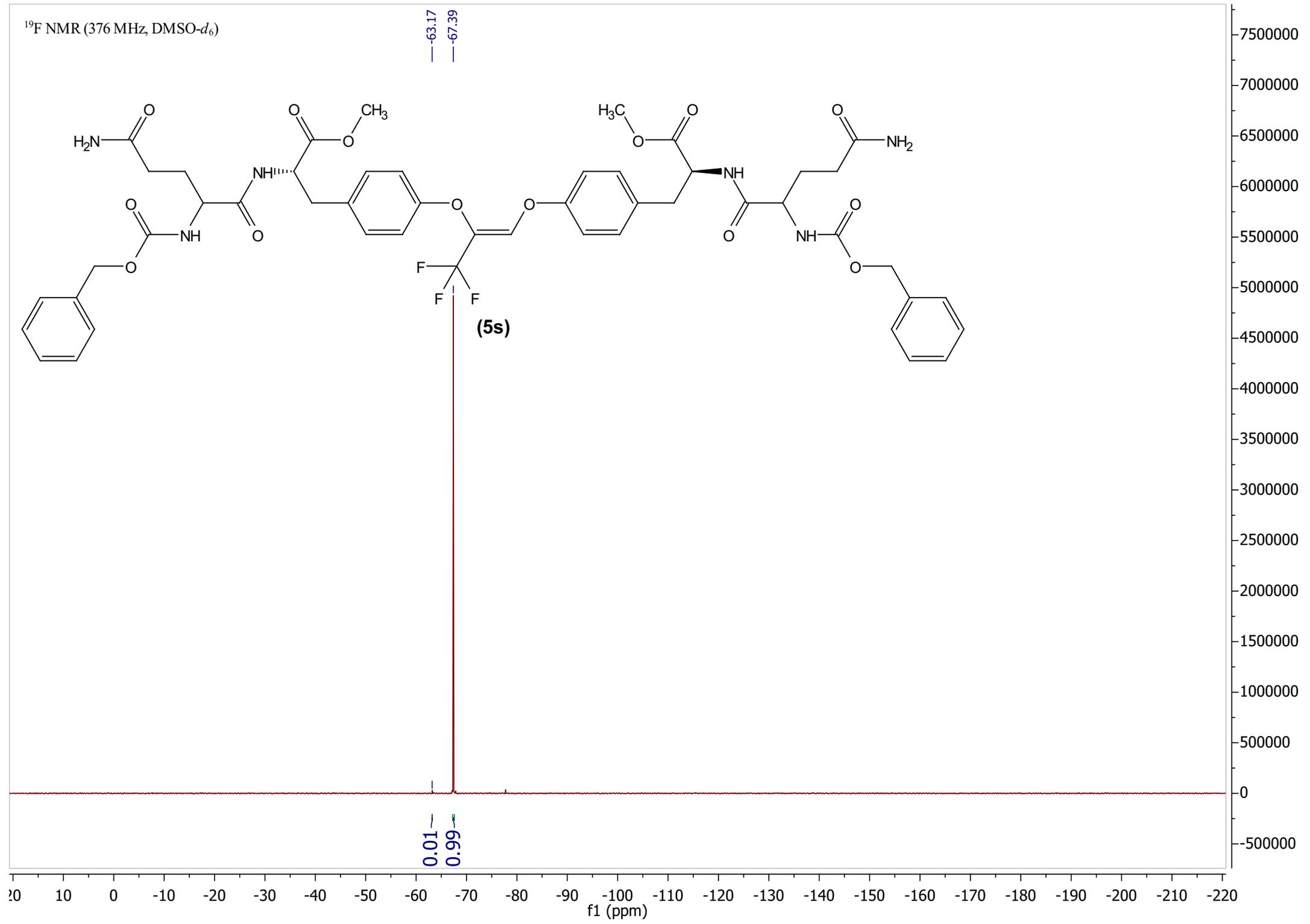


¹⁹F NMR (376 MHz, DMSO-*d*₆)

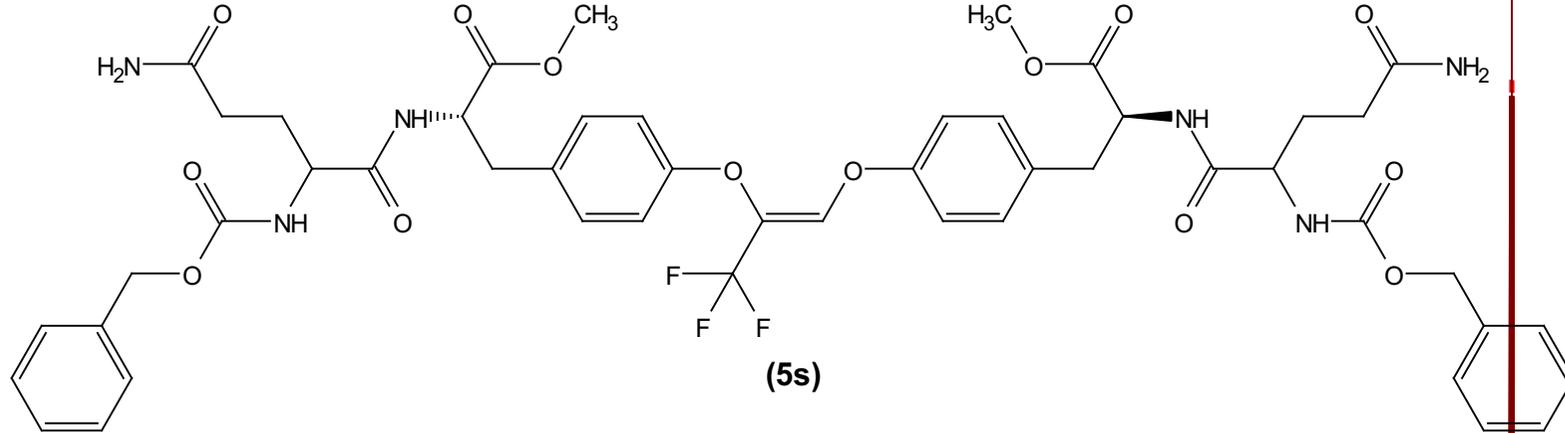


— -63.17
— -67.39

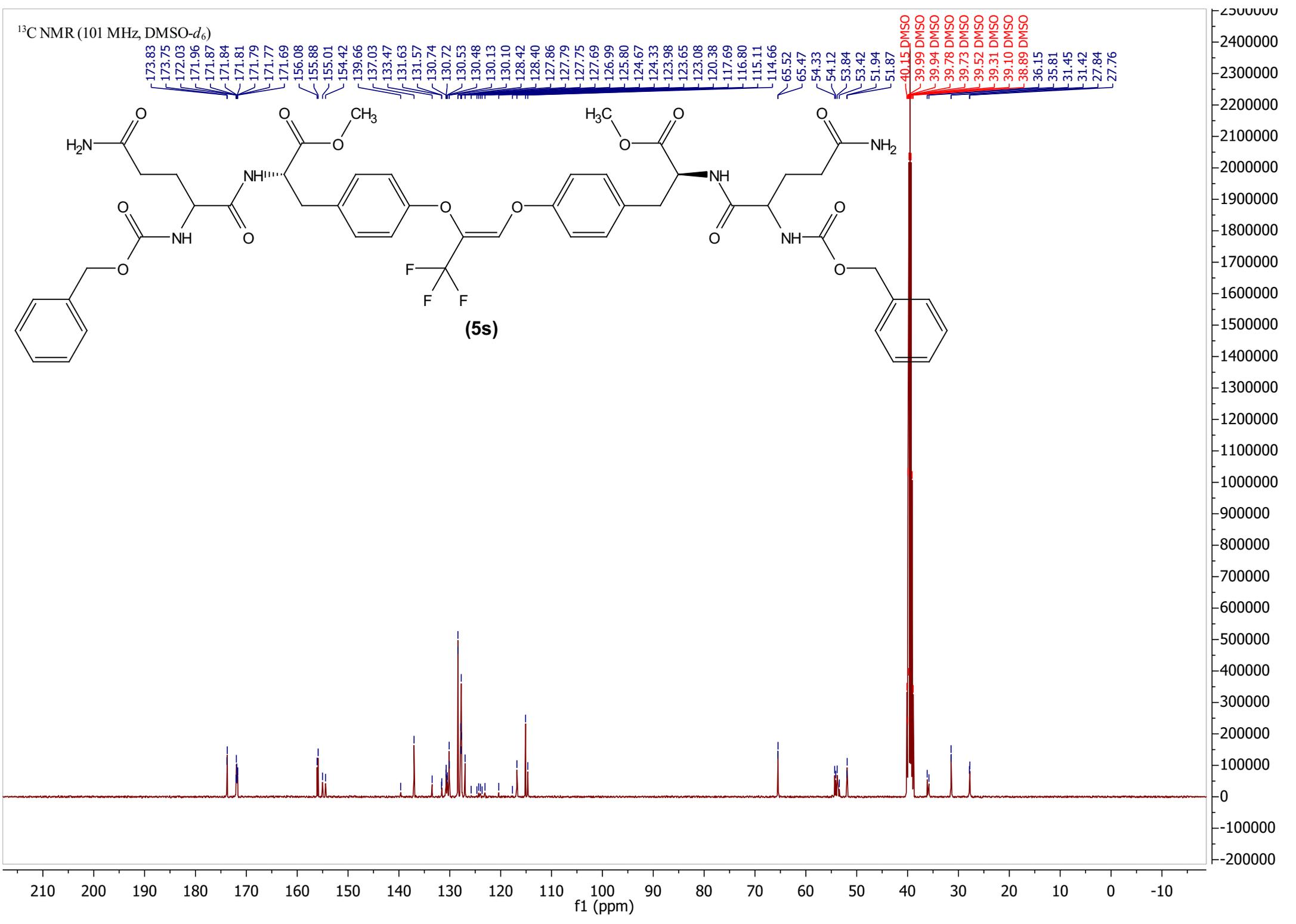
0.01
0.99



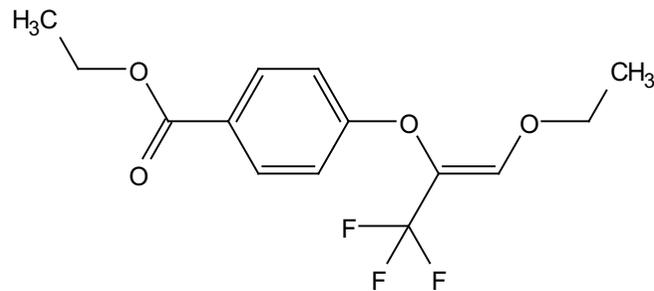
^{13}C NMR (101 MHz, $\text{DMSO-}d_6$)



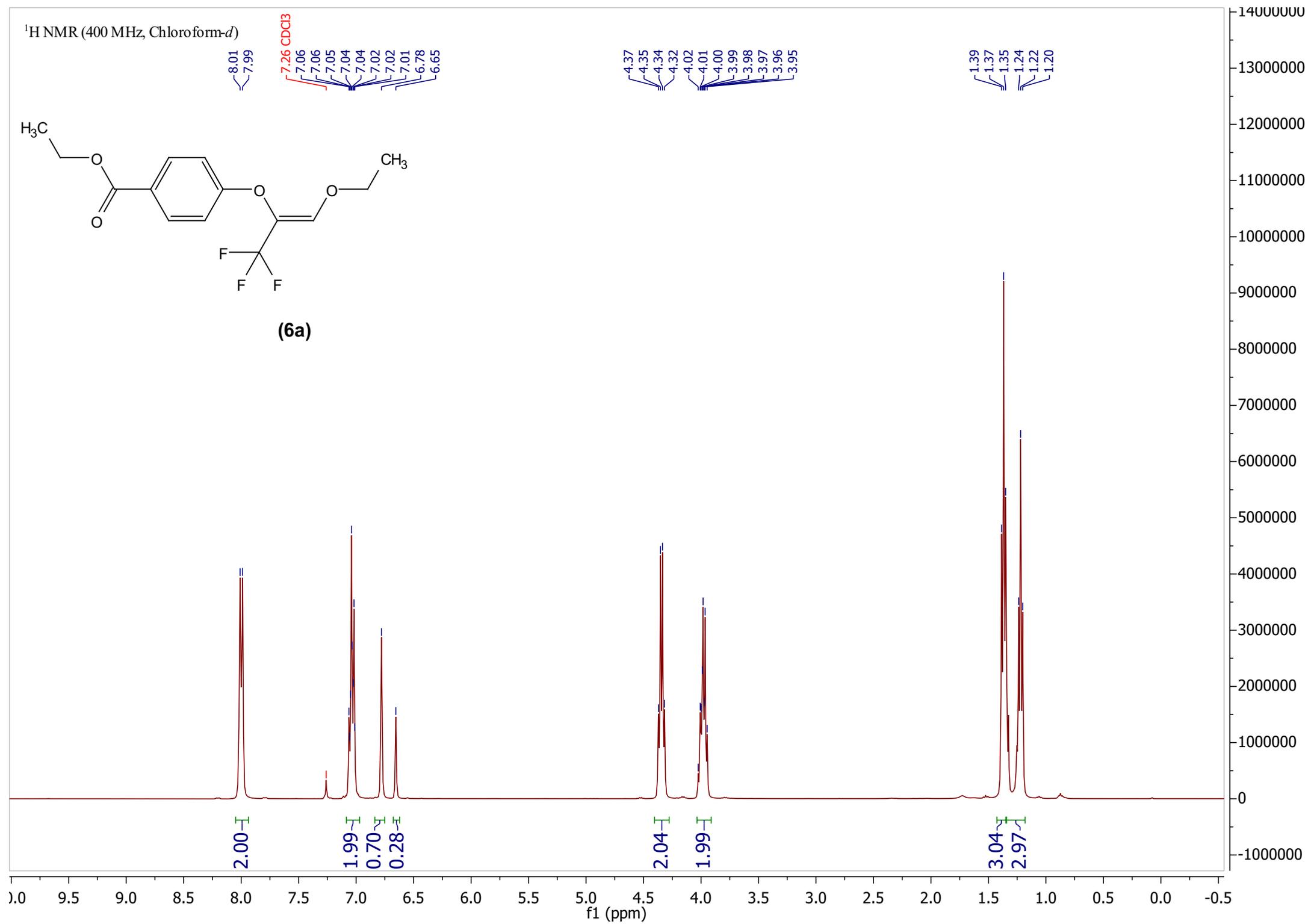
173.83, 173.75, 172.03, 171.96, 171.87, 171.84, 171.81, 171.79, 171.77, 171.69, 156.08, 155.88, 155.01, 154.42, 139.66, 137.03, 133.47, 131.63, 131.57, 130.74, 130.72, 130.53, 130.48, 130.13, 130.10, 128.42, 128.40, 127.86, 127.79, 127.75, 127.69, 126.99, 125.80, 124.67, 124.33, 123.98, 123.65, 123.08, 120.38, 117.69, 116.80, 115.11, 114.66, 65.52, 65.47, 54.33, 54.12, 53.84, 53.42, 51.94, 51.87, 40.15 DMSO, 39.99 DMSO, 39.94 DMSO, 39.78 DMSO, 39.73 DMSO, 39.52 DMSO, 39.31 DMSO, 39.10 DMSO, 38.89 DMSO, 36.15, 35.81, 31.45, 31.42, 27.84, 27.76



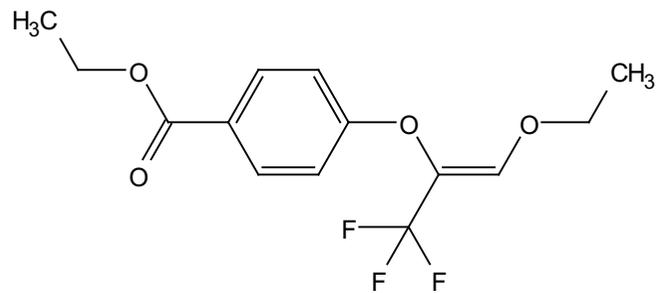
¹H NMR (400 MHz, Chloroform-*d*)



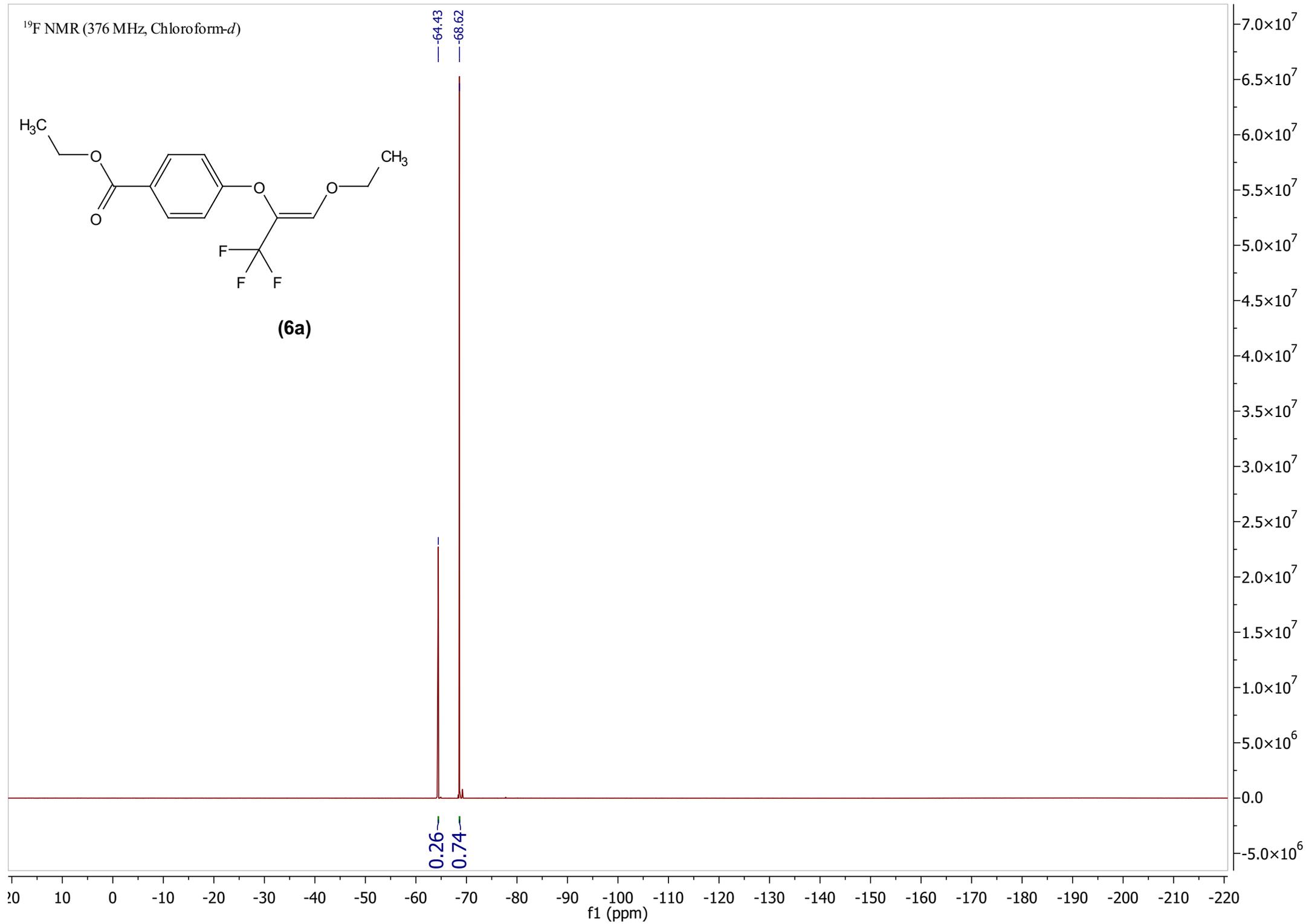
(6a)



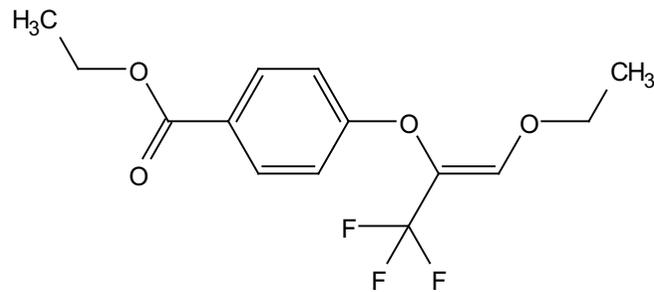
¹⁹F NMR (376 MHz, Chloroform-*d*)



(6a)



¹³C NMR (101 MHz, Chloroform-*d*)



(6a)

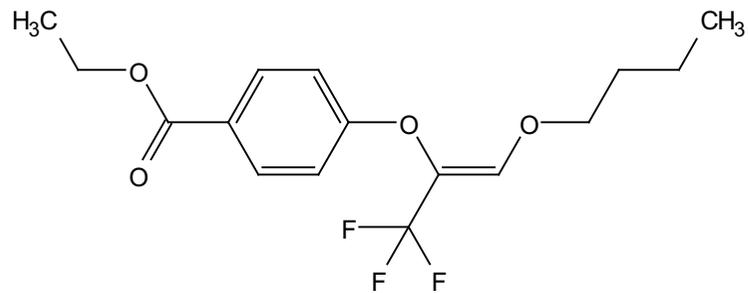
166.20
166.10
162.83
160.45
147.58
147.56
147.53
147.51
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141.85
141.81
131.73
131.51
125.95
125.41
125.17
125.05
125.01
124.64
124.28
123.91
123.26
122.70
122.68
122.35
122.00
121.64
120.57
119.96
117.88
117.23
114.96
114.90
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃
70.97
70.78
60.94
60.89

15.29
15.20
14.43

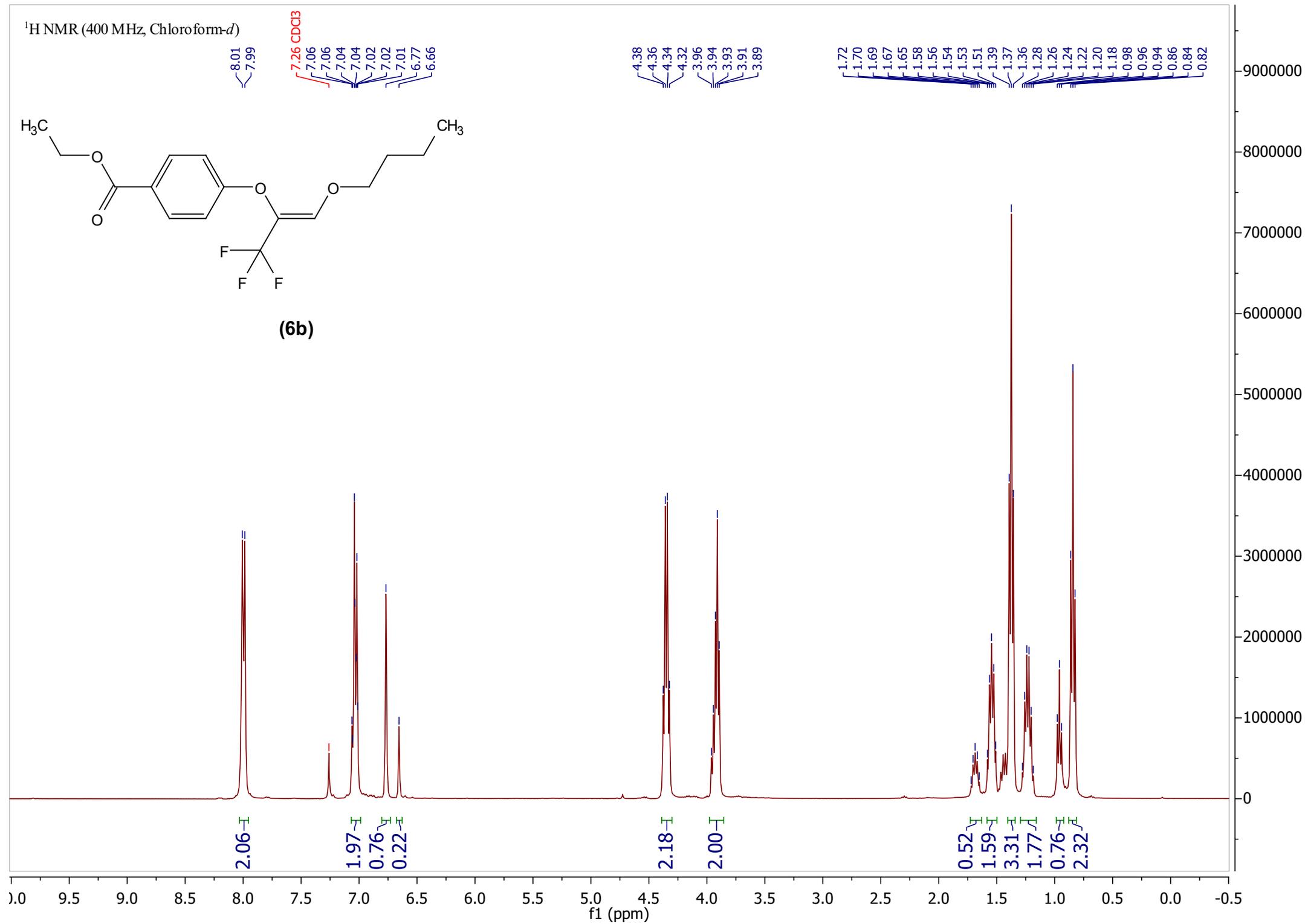
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f1 (ppm)

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400000
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300000
250000
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50000
0

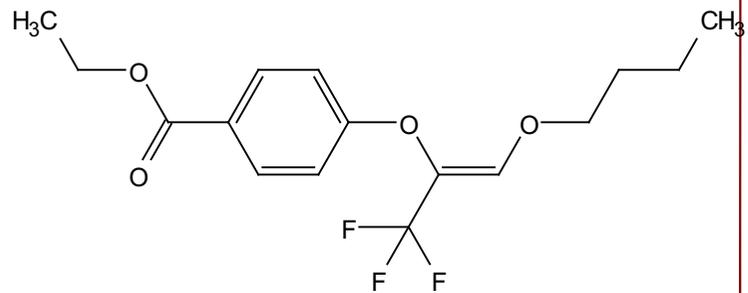
¹H NMR (400 MHz, Chloroform-*d*)



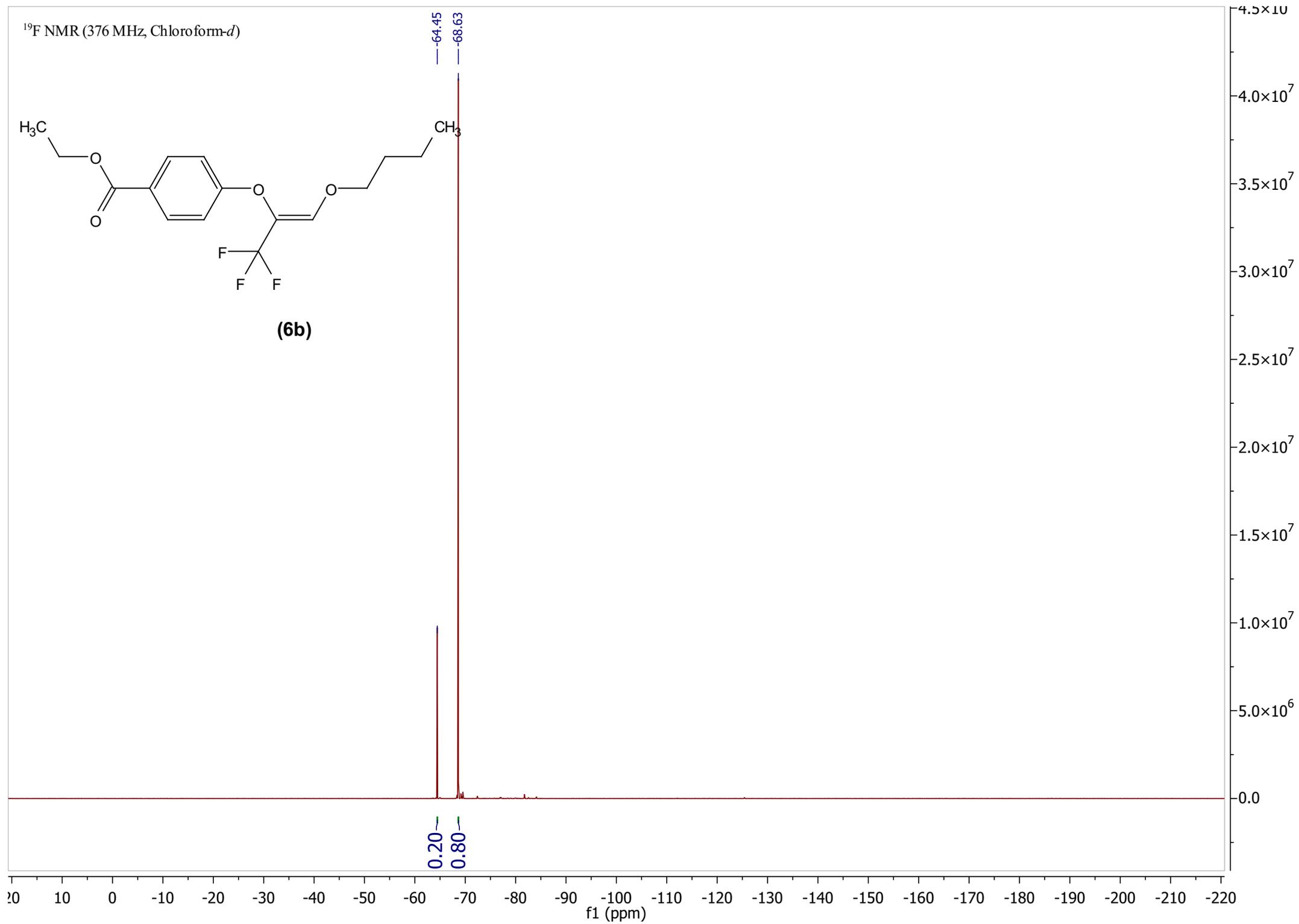
(6b)



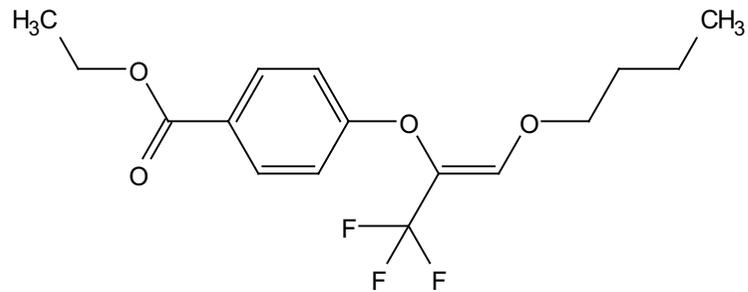
¹⁹F NMR (376 MHz, Chloroform-*d*)



(6b)

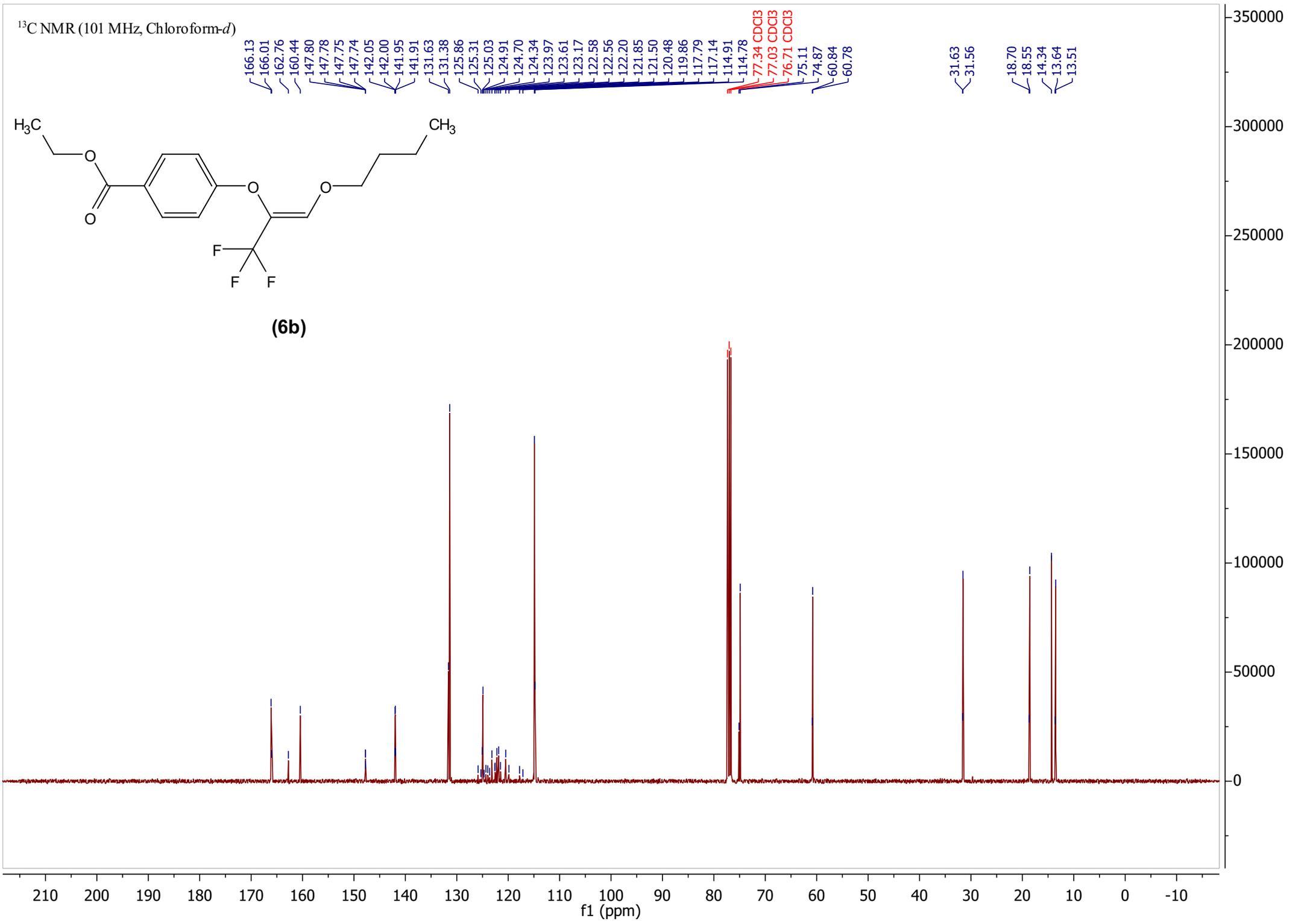


¹³C NMR (101 MHz, Chloroform-*d*)

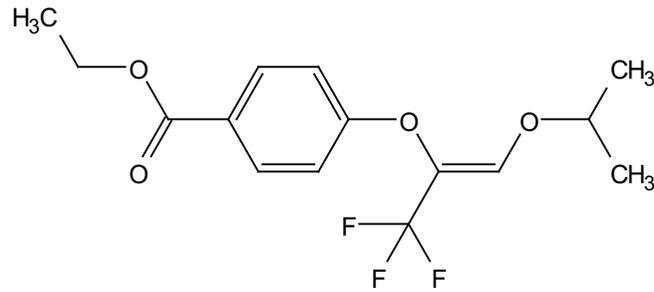


(6b)

- 166.13
- 166.01
- 162.76
- 160.44
- 147.80
- 147.78
- 147.75
- 147.74
- 142.05
- 142.00
- 141.95
- 141.91
- 131.63
- 131.38
- 125.86
- 125.31
- 125.03
- 124.91
- 124.70
- 124.34
- 123.97
- 123.61
- 123.17
- 122.58
- 122.56
- 122.20
- 121.85
- 121.50
- 120.48
- 119.86
- 117.79
- 117.14
- 114.91
- 114.78
- 77.34 CDCl₃
- 77.03 CDCl₃
- 76.71 CDCl₃
- 75.11
- 74.87
- 60.84
- 60.78
- 31.63
- 31.56
- 18.70
- 18.55
- 14.34
- 13.64
- 13.51



¹H NMR (400 MHz, Chloroform-*d*)



(6c)

8.01
7.98

7.26 CDCl₃

7.04

7.01

6.82

6.68

4.38

4.36

4.34

4.32

4.16

4.15

4.13

4.12

4.10

4.09

4.07

1.39

1.38

1.36

1.34

1.32

1.22

1.20

2.00

2.00

0.90

0.10

2.03

1.02

3.06

0.31

0.28

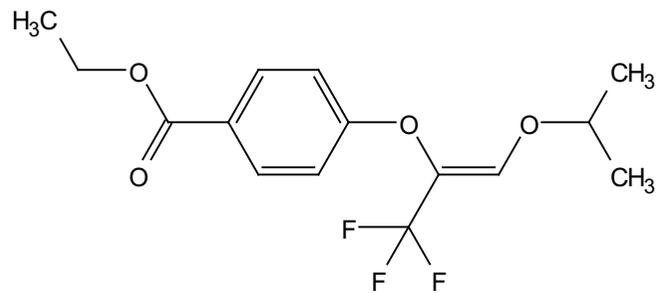
2.71

2.64

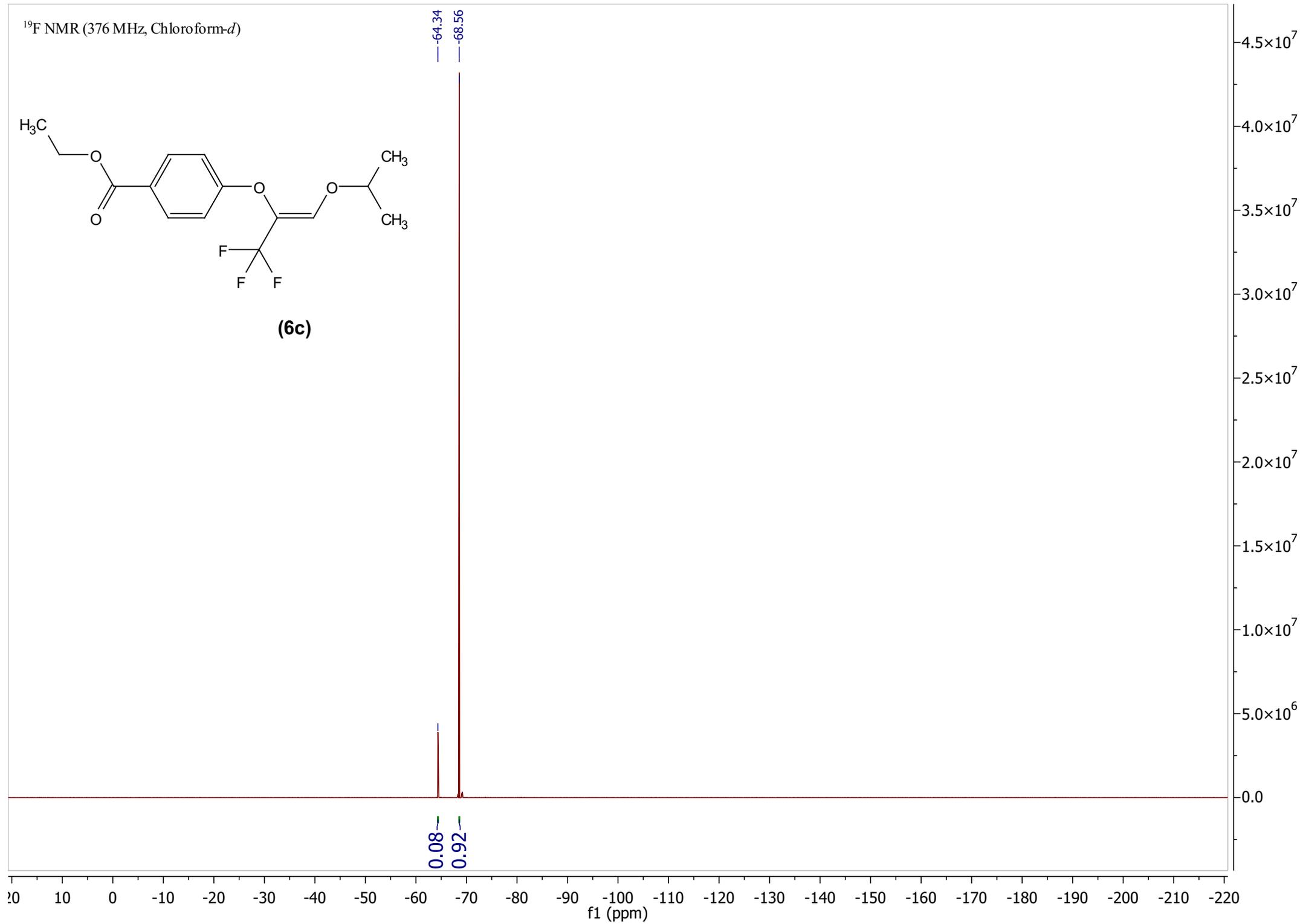
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

2500000
2400000
2300000
2200000
2100000
2000000
1900000
1800000
1700000
1600000
1500000
1400000
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1200000
1100000
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900000
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000
-200000

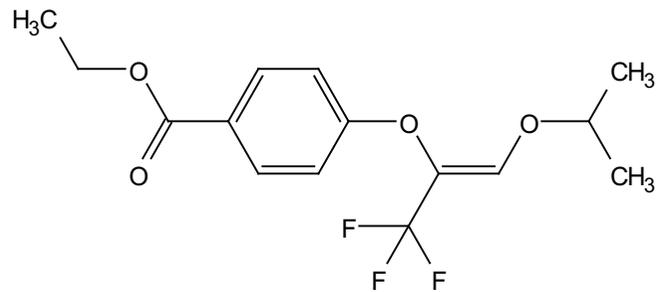
¹⁹F NMR (376 MHz, Chloroform-*d*)



(6c)



¹³C NMR (101 MHz, Chloroform-*d*)



(6c)

166.29
166.14
162.96
160.55
146.45
146.42
146.40
146.38
140.72
140.67
140.63
140.58
131.76
131.44
126.06
125.12
124.97
123.37
122.66
122.31
121.95
121.60
120.67
117.98
115.09
114.89

78.20
78.11
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃

60.96
60.91

22.42
22.35

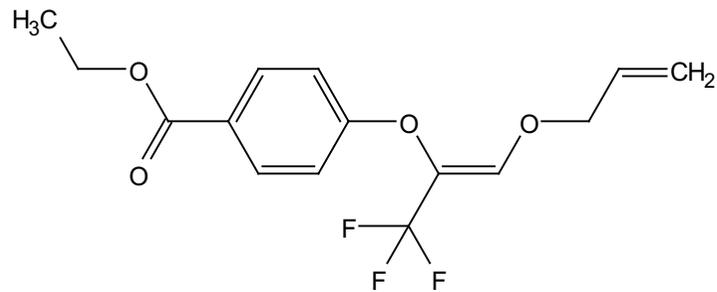
14.48

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

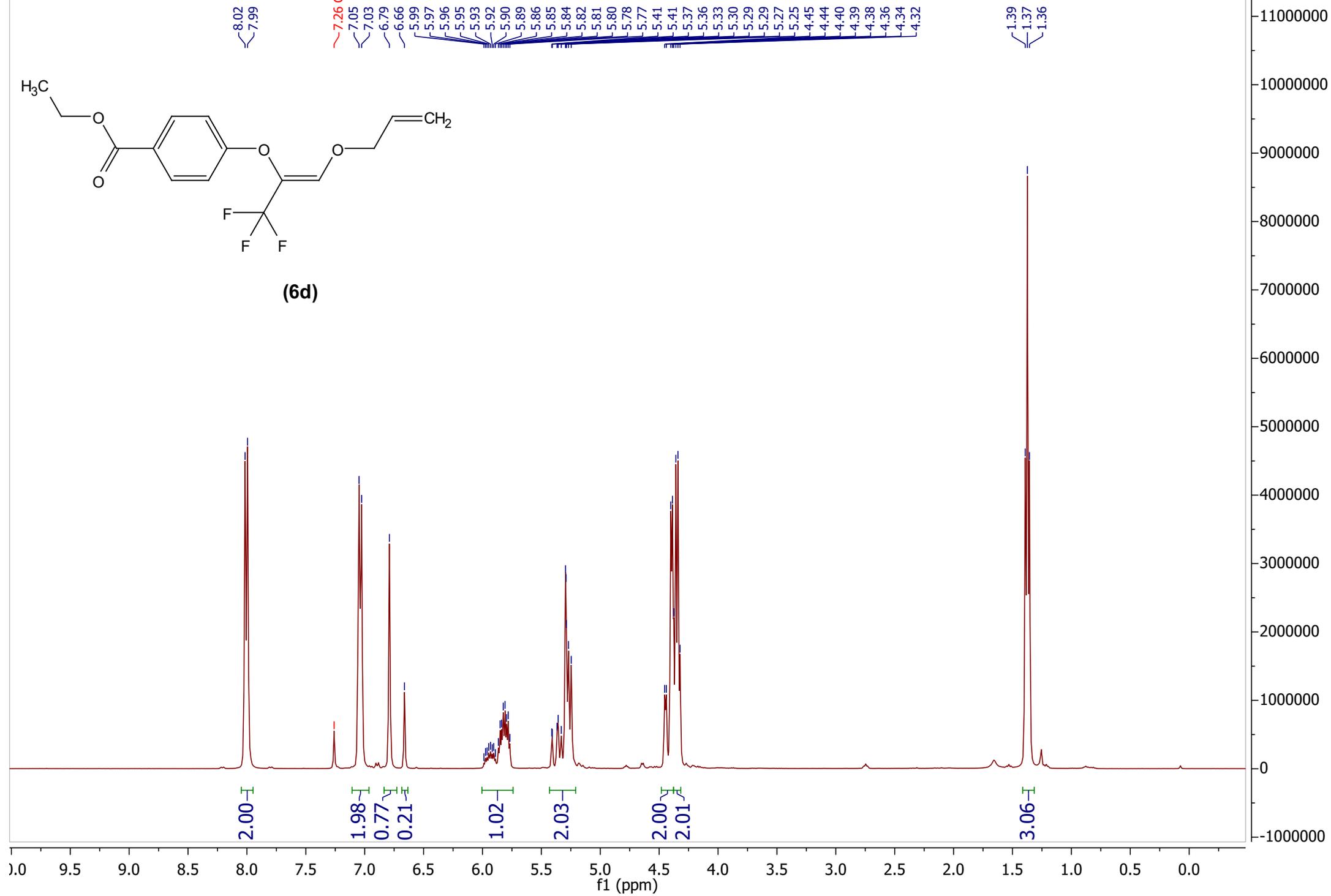
f1 (ppm)

280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000

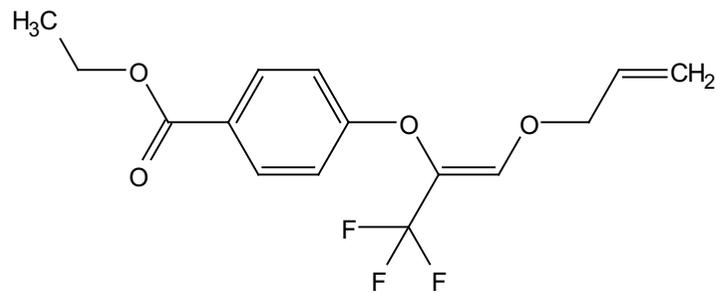
¹H NMR (400 MHz, Chloroform-*d*)



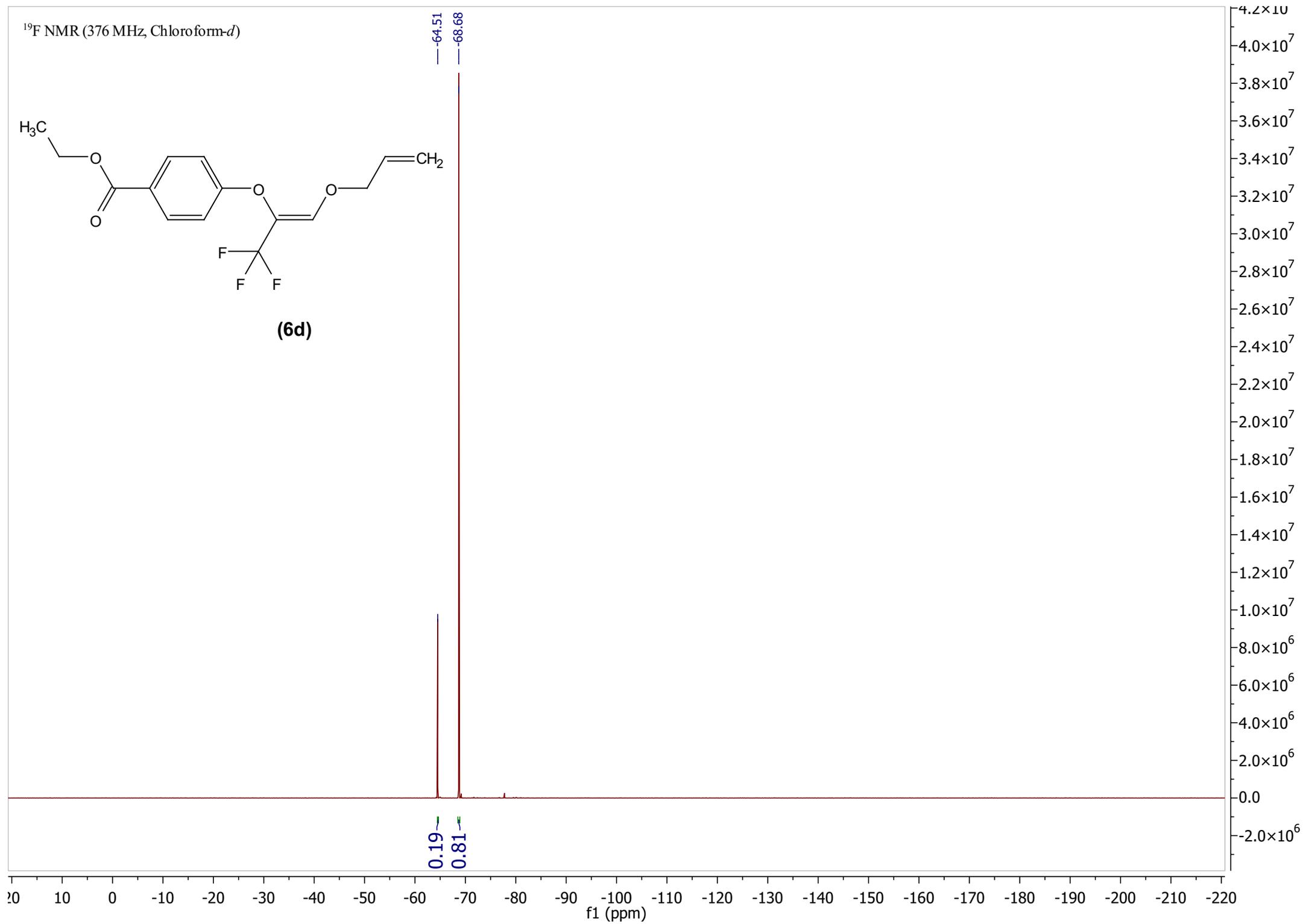
(6d)



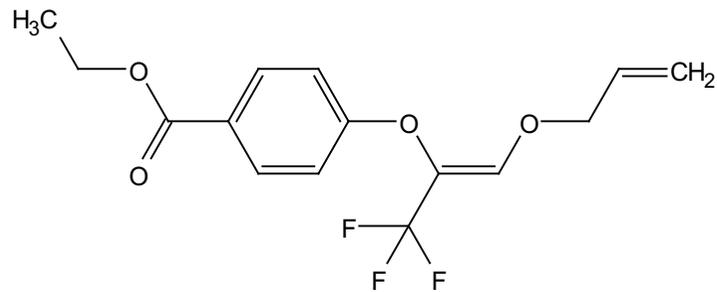
¹⁹F NMR (376 MHz, Chloroform-*d*)



(6d)



¹³C NMR (101 MHz, Chloroform-*d*)



(6d)

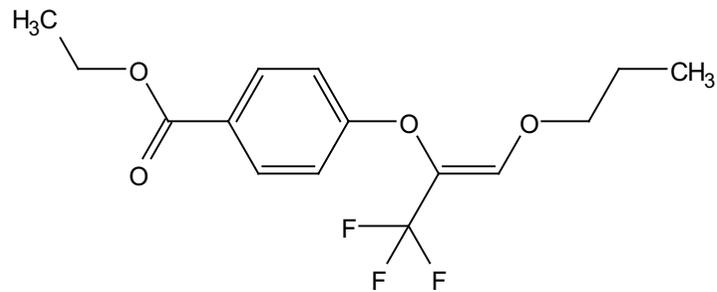
166.20
166.10
162.72
160.40
147.10
147.08
147.06
147.04
141.32
141.27
141.22
141.18
132.19
132.00
131.76
131.57
125.85
125.33
125.32
125.24
125.13
124.97
124.60
124.24
123.15
123.14
122.78
122.60
122.43
122.08
120.46
119.87
119.83
119.68
117.77
117.32
114.99
114.92
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃
75.19
74.98
60.97
60.92

14.47

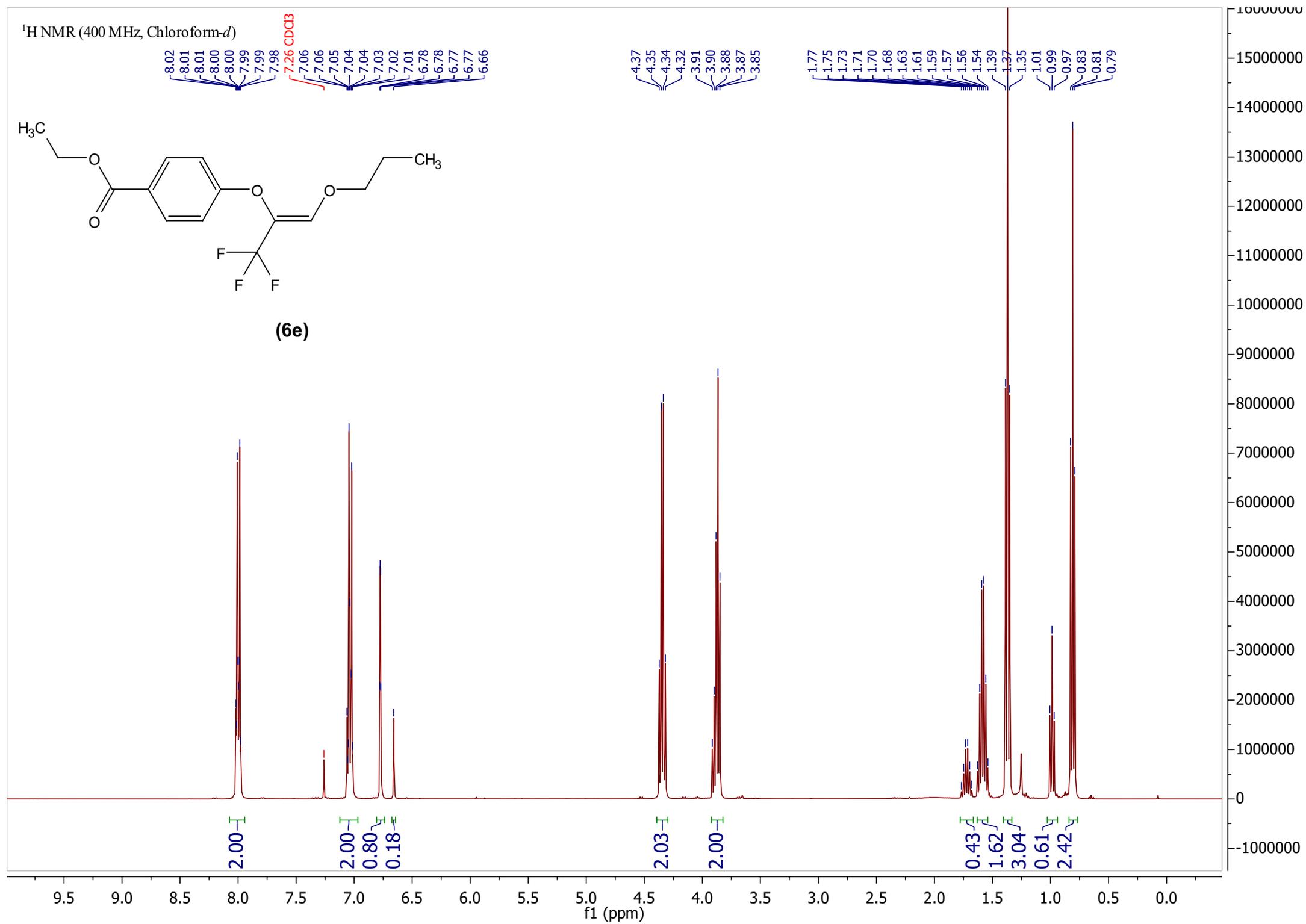
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

450000
400000
350000
300000
250000
200000
150000
100000
50000
0

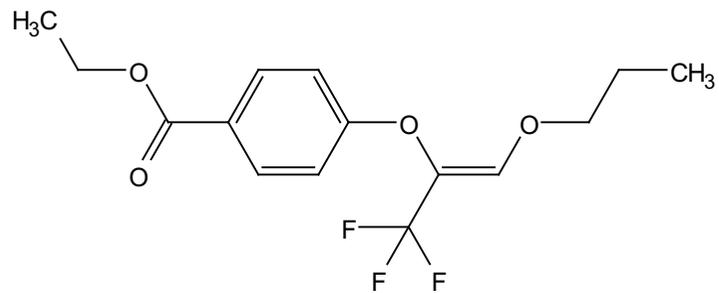
¹H NMR (400 MHz, Chloroform-*d*)



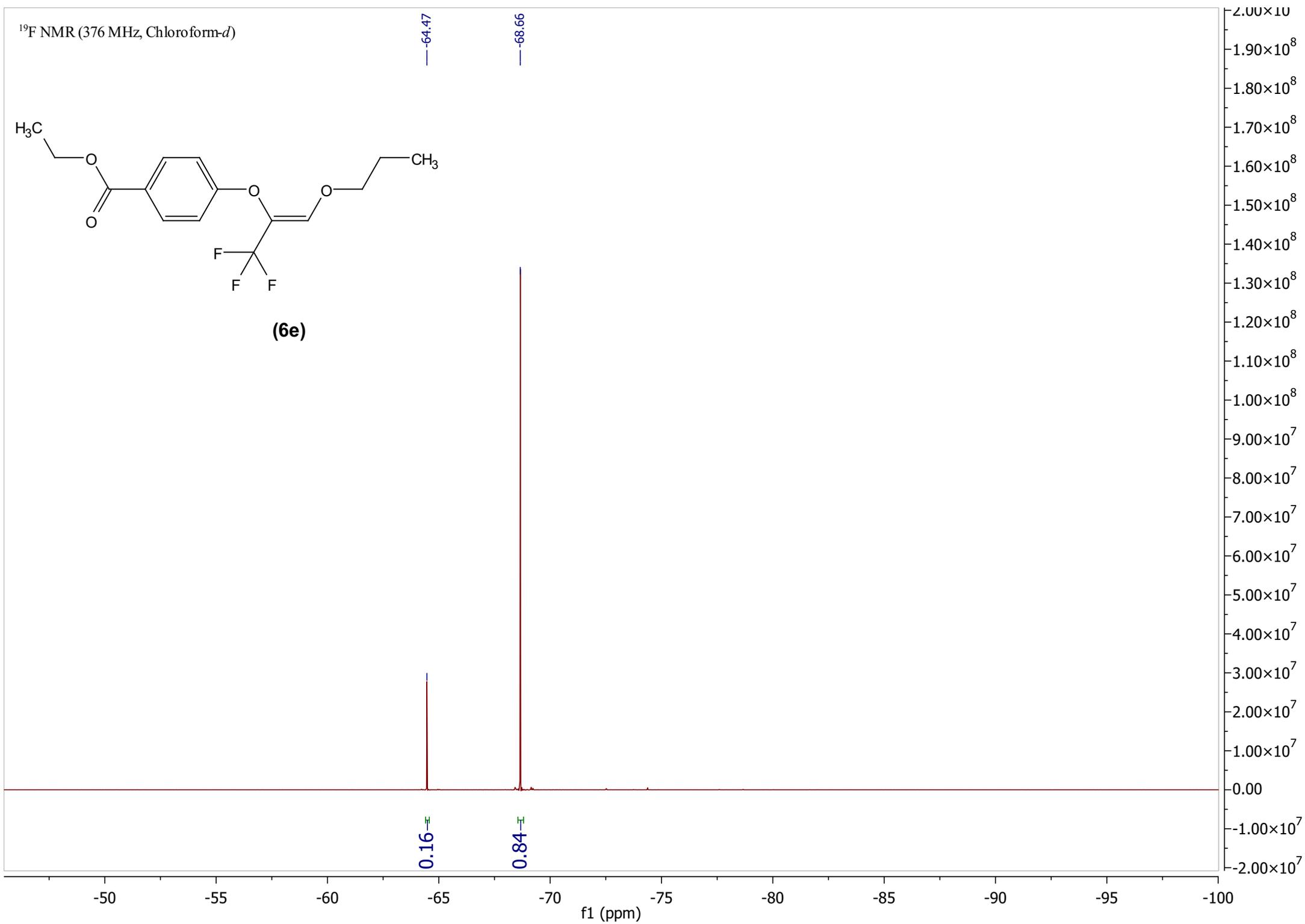
(6e)



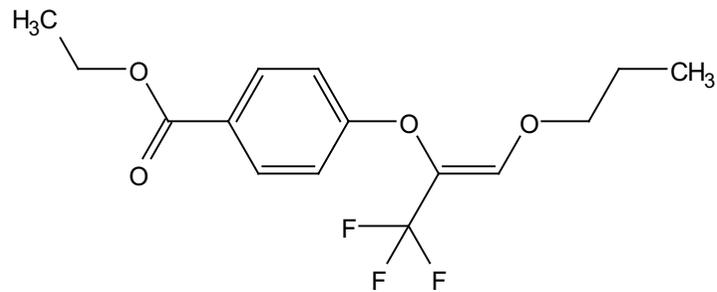
^{19}F NMR (376 MHz, Chloroform-*d*)



(6e)

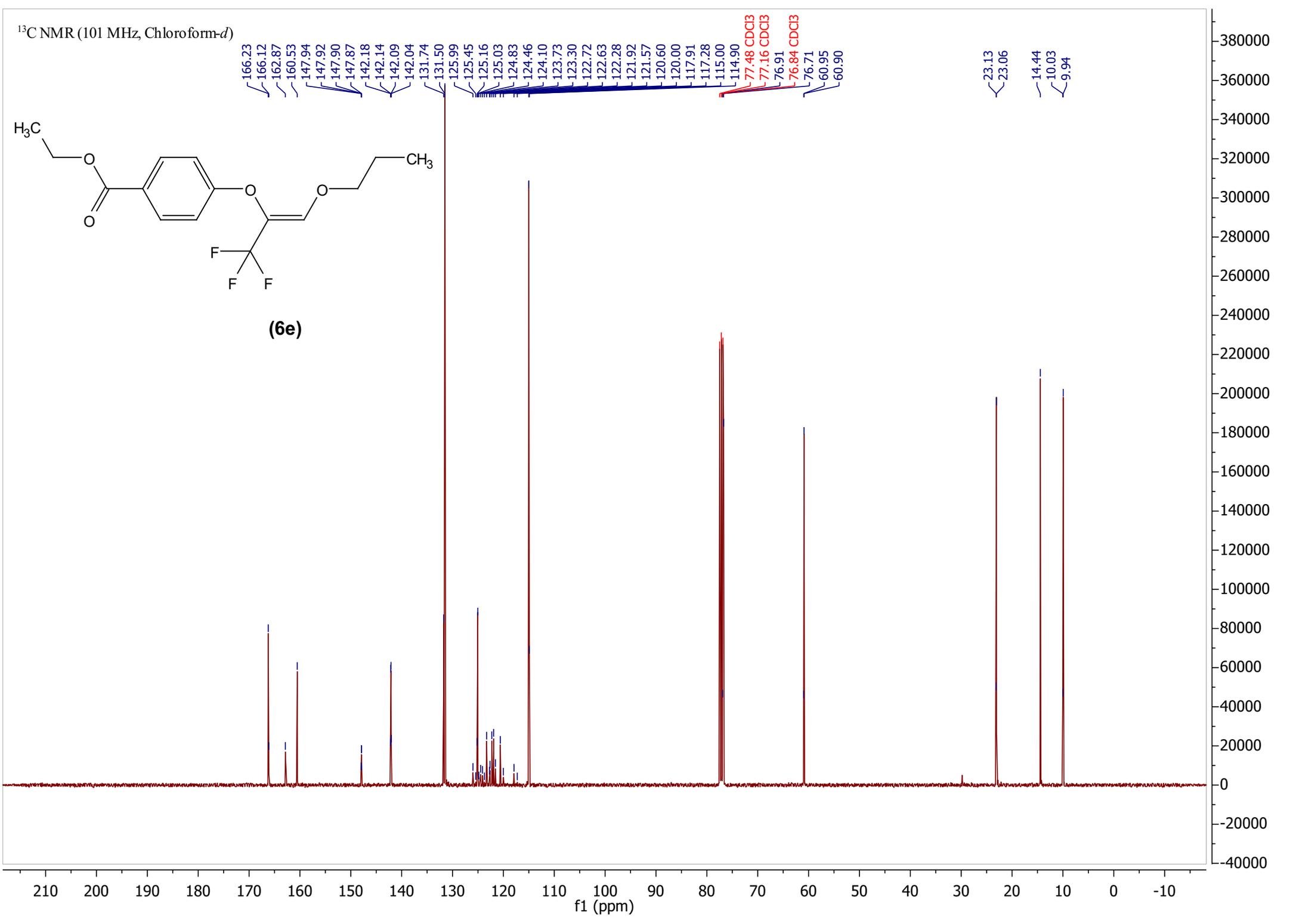


¹³C NMR (101 MHz, Chloroform-*d*)

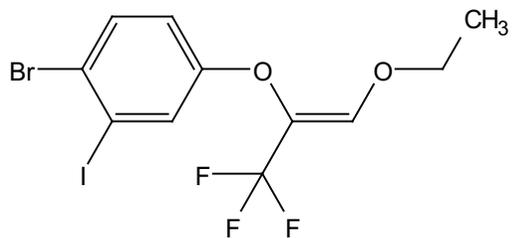


(6e)

- 166.23
- 166.12
- 162.87
- 160.53
- 147.94
- 147.92
- 147.90
- 147.87
- 142.18
- 142.14
- 142.09
- 142.04
- 131.74
- 131.50
- 125.99
- 125.45
- 125.16
- 125.03
- 124.83
- 124.46
- 124.10
- 123.73
- 123.30
- 122.72
- 122.63
- 122.28
- 121.92
- 121.57
- 120.60
- 120.00
- 117.91
- 117.28
- 115.00
- 114.90
- 77.48 CDCl₃
- 77.16 CDCl₃
- 76.91
- 76.84 CDCl₃
- 76.71
- 60.95
- 60.90
- 23.13
- 23.06
- 14.44
- 10.03
- 9.94



¹H NMR (400 MHz, Chloroform-*d*)



(6e)

7.52
7.51
7.51
7.50
7.49
7.49
7.48
7.48
7.26 CDCl₃
6.92
6.91
6.90
6.89
6.87
6.87
6.76
6.76
6.75
6.75
6.64

4.03
4.03
4.02
4.01
4.00
3.99
3.98
3.97

1.37
1.35
1.34
1.28
1.26
1.25

2.00

1.01

0.77

0.23

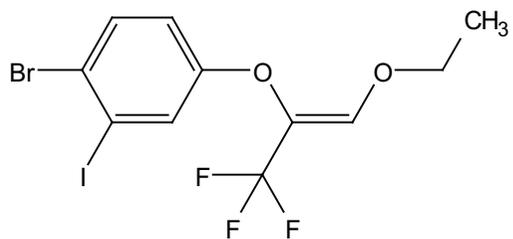
2.06

0.66

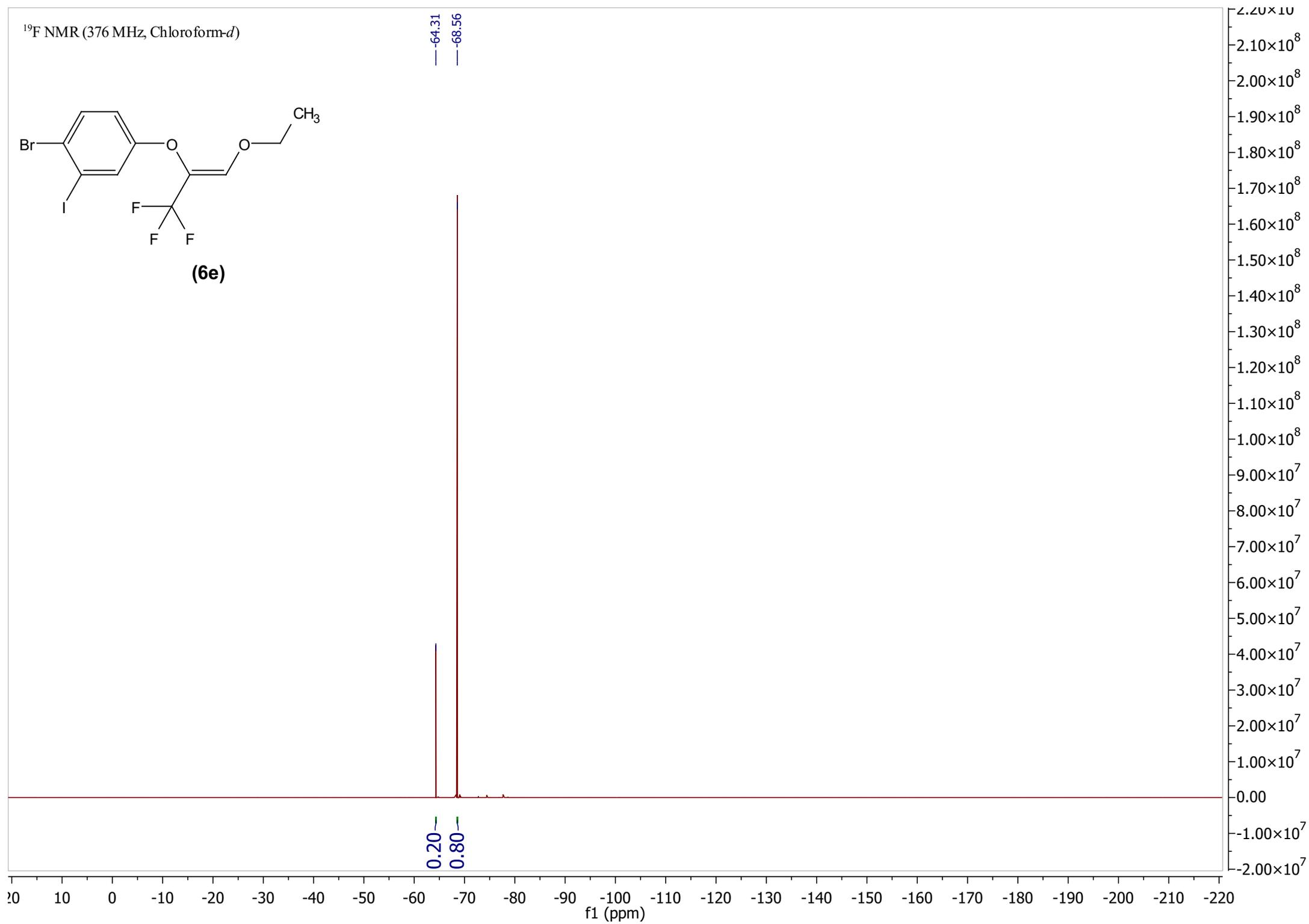
2.51

f1 (ppm)

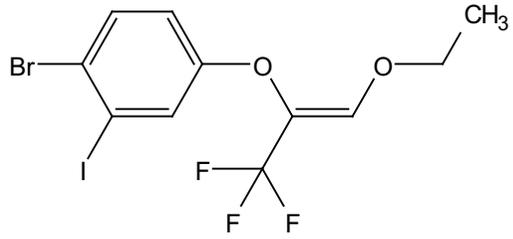
^{19}F NMR (376 MHz, Chloroform-*d*)



(6e)



¹³C NMR (101 MHz, Chloroform-*d*)



(6e)

158.19
155.76
147.68
147.65
147.63
147.61
141.99
141.94
141.89
141.85
132.99
132.75
127.13
125.84
125.31
125.04
124.67
124.31
123.94
123.14
122.81
122.80
122.58
122.52
122.45
122.10
121.75
120.45
119.86
117.76
117.14
116.98
116.82
101.26
100.88
77.48 CDCl₃
77.16 CDCl₃
76.84 CDCl₃
71.09
70.95
15.41
15.22

