Supporting Information

Less-toxic Amphiphilic Molecules linked by Aromatic: Broad-spectrum Antibacterial Activity and Less Drug Resistance

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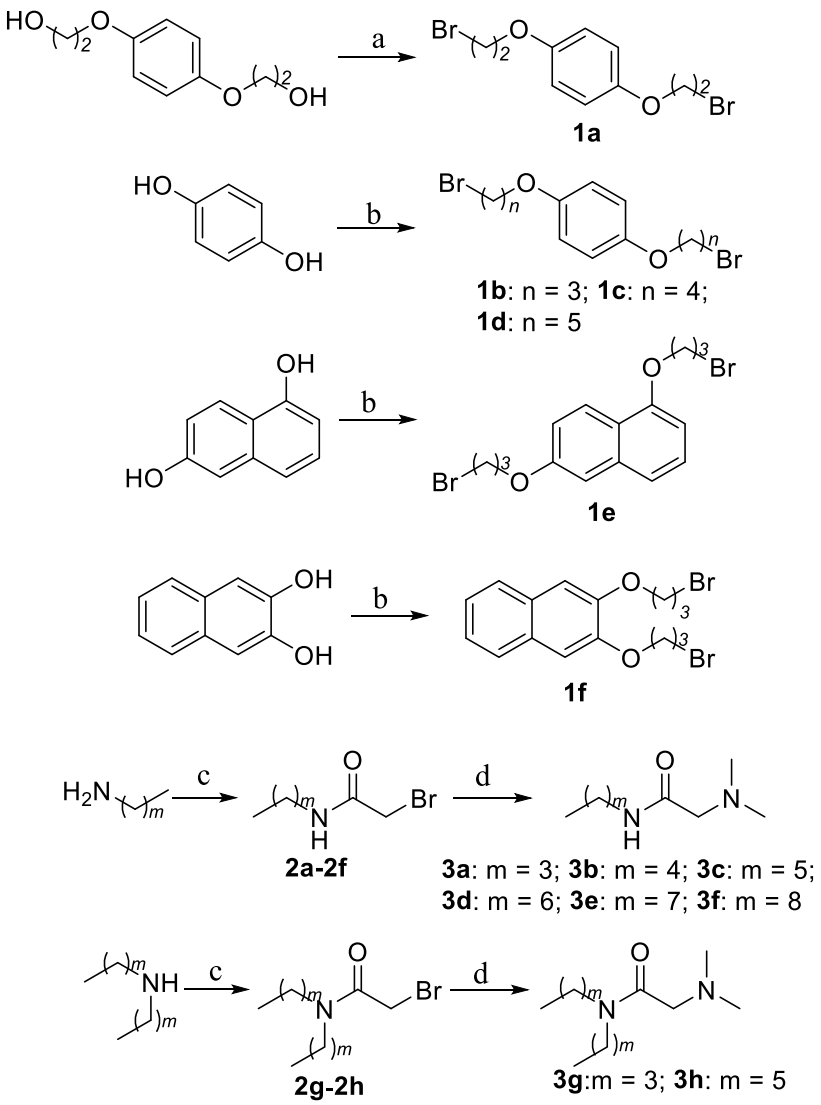
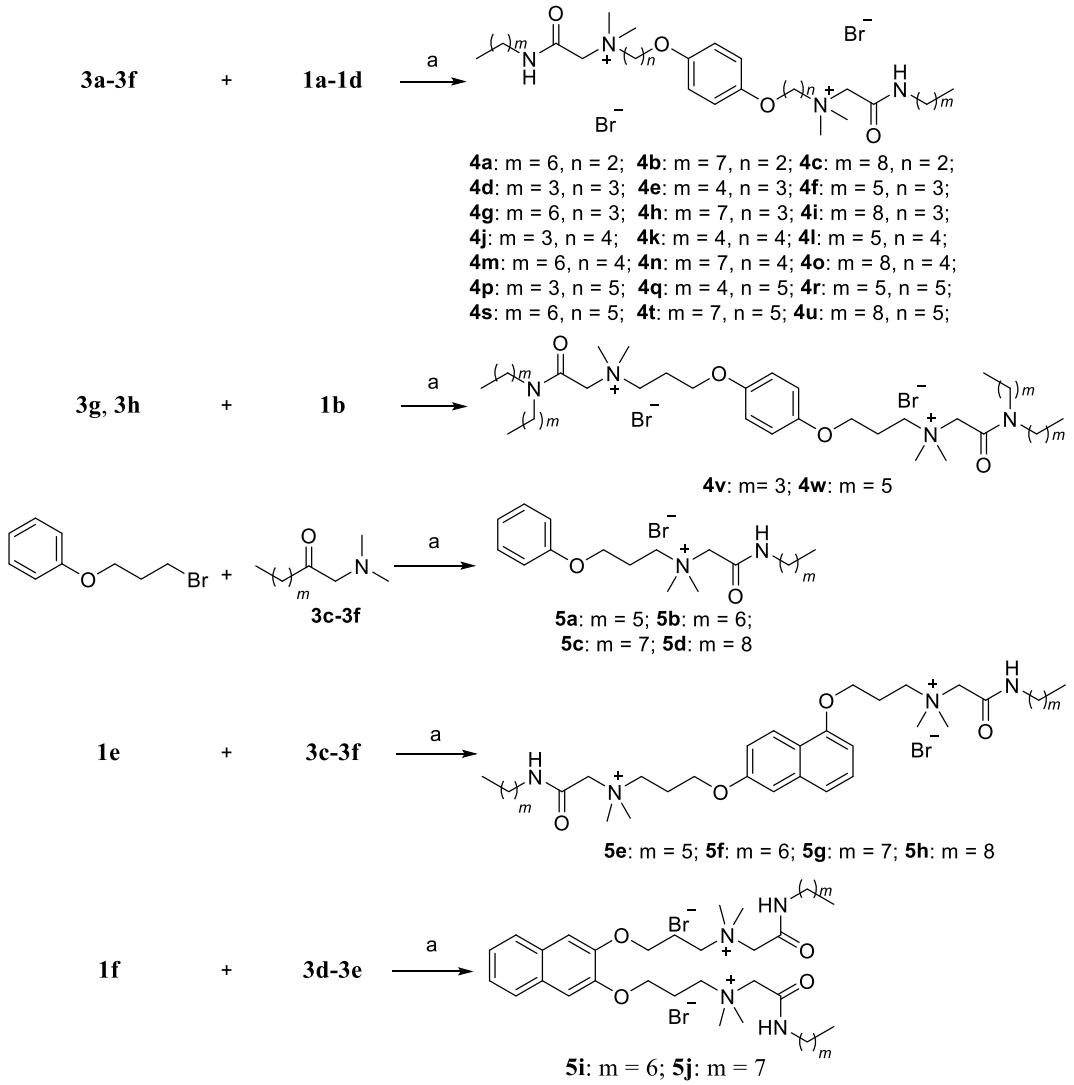


reaction conditions: a) CBr_4, PPh_3, CH_3CN, rt, 4h; b) $Br(CH_2)_nBr$, K_2CO_3, acetone, reflux, 24h; c) Bromoacetylbromide, K_2CO_3, DCM, H_2O; d) Aqueous dimethylamine, EtOH, reflux, 10h;

Scheme S1. Synthesis of intermediate **1a**-**1f** and **3a**-**3h.**



reaction conditions: a) EtOH, 85°C, pressure tube, 24h.

Scheme S2. Synthesis of amphiphilic molecules **4a**-**4w** and **5a**-**5j**

Table S1. MICs of selected compounds against clinical resistant bacterial isolates

Strains	MIC (μg/mL)							
	4a	**4b**	**4g**	**4m**	**4r**	**4s**	**5e**	**5f**
[a](G+) MRSA-1114044	1	0.5	0.5	1	1	1	0.5	0.5
(G+) MRSA-1115041	1	0.5	0.5	0.5	1	0.5	0.5	0.5
(G+) MRSA-1202610	1	1	0.5	0.5	0.5	0.5	0.5	0.5
(G+) MRSA-1202628	4	1	2	2	2	0.5	2	1
(G+) MRSA-20130910162	4	1	2	2	1	1	2	1
(G+) MRSA-20130911034 sall	1	0.5	0.5	0.5	0.5	0.5	0.5	0.5
(G+) MRSA-831164	1	1	0.5	0.5	0.5	0.5	0.5	0.5
(G+) MRSA-826084	4	1	2	1	1	0.5	4	1
(G+) MRSA-905132	4	1	2	1	1	0.5	1	0.5

(G+) MRSA-904142	1	0.5	0.5	0.5	0.5	0.5	0.5	0.5
[b](G-) *K. peneumoniae*-13-10 (*bla*$_{NDM-1}$)	4	1	4	2	2	1	1	2
(G-) *E. coli*-13-22 (*bla*$_{NDM-1}$)	2	4	4	8	8	2	8	4
(G-) *E. coli*-13-33 (*bla*$_{NDM-1}$)	2	1	2	2	2	2	2	1
(G-) *C. freundii*-13-61 (*bla*$_{NDM-1}$)	1	1	2	2	2	1	4	1
(G-) *E. cloacae*-14-56 (*bla*$_{NDM-1}$)	2	1	2	2	2	1	4	1
(G-) E. aerogenes-15-92 (*bla*$_{KPC}$)	2	1	2	2	2	2	2	2

[a](G+): Gram positive bacteria; [b](G-): Gram negative bacteria.

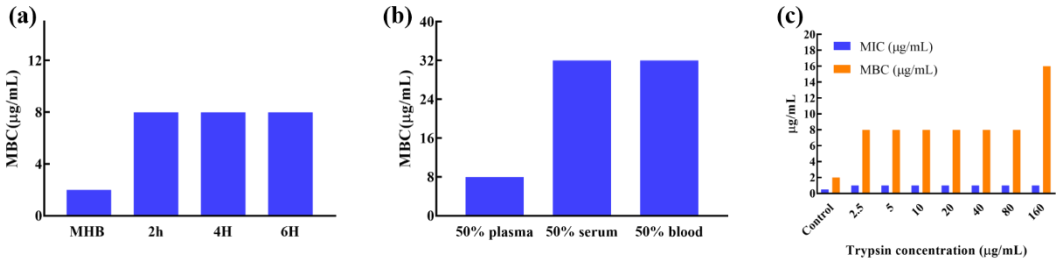


Fig S1. (a) Compound **4g** was incubated in 50% plasma for different times, then its bactericidal activity against *S. aureus* was evaluated; (b) Compound **4g** was evaluated against MRSA strain 1115041 in different culture media (50% plasma, 50% serum and 50% blood). (c) The MIC and MBC values of compound **4g** at different concentrations of trypsin.

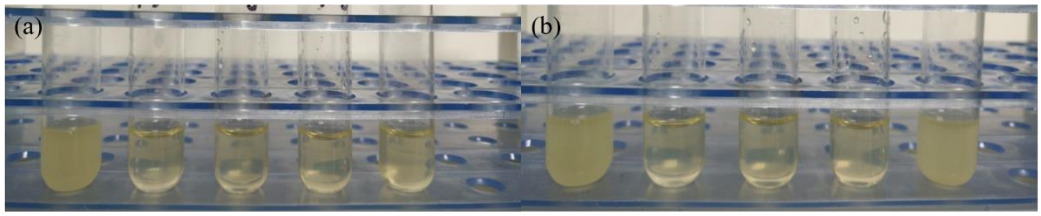


Fig S2. Photographs of *S. aureus* (a) exponential phase and (b) stationary phase after treatment with compound **4g** or commercial antibiotics.

Table S2. MBIC and MBEC of compound **4g** against *S. aureus* and *E. coli*.

Compd.	MBIC$_{50}$/MBIC$_{70}$/MBIC$_{80}$ (μg/mL)		MBEC (μg/mL)	
	S. aureus	*E. coli*	*S. aureus*	*E. coli*
4g	1.8 / 10.1 / 30.1	11.3 / 22.9 / 36	8	16

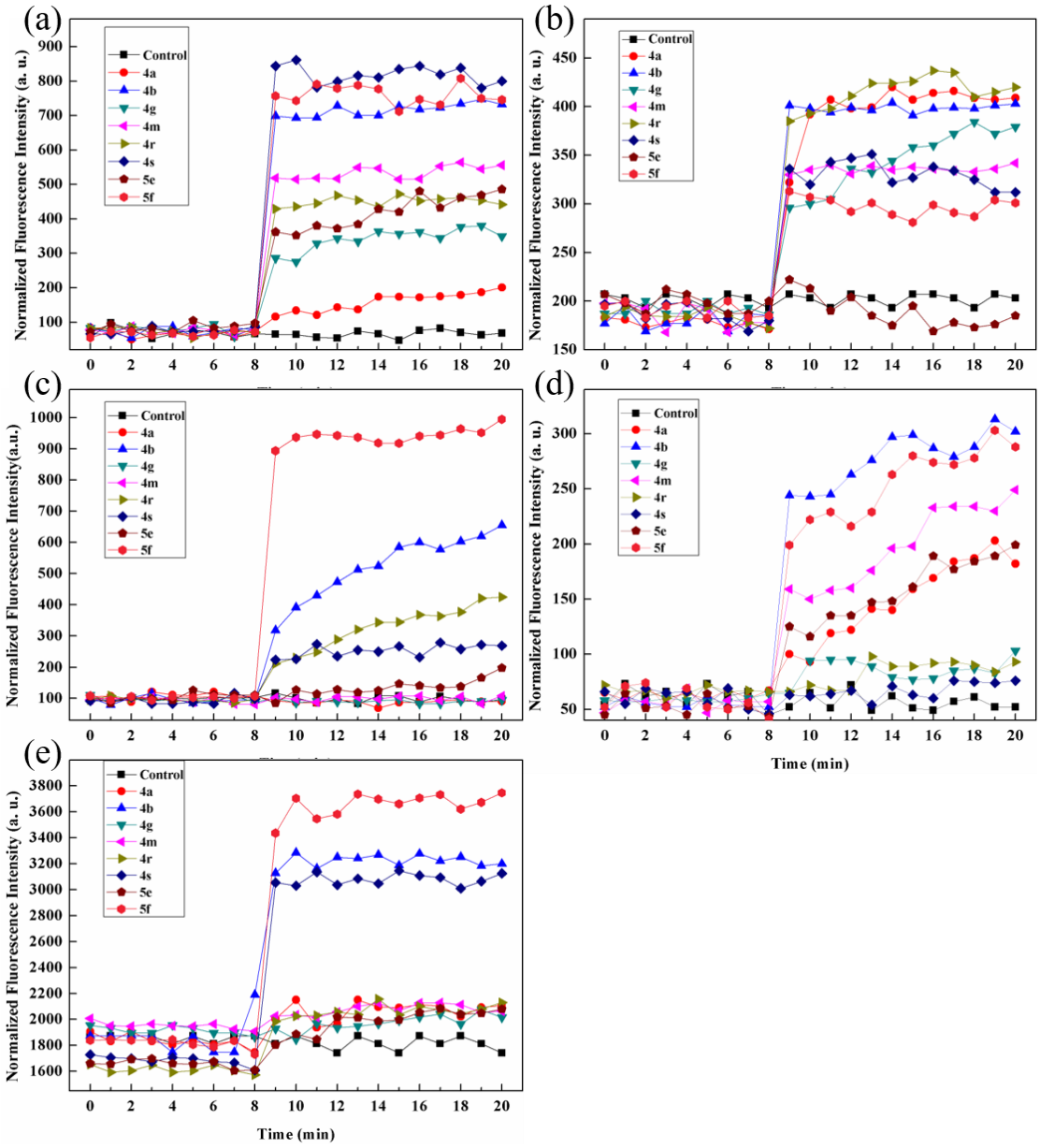


Fig S3. Mechanism of antibacterial action of molecules at 10 μg/mL. (a) and (b) Cytoplasmic membrane depolarization of *S. aureus* and *E. coli*, respectively. (c) and (d) Inner membrane permeabilization of *S. aureus* and *E. coli*, respectively. (e) Outner membrane permeabilization of *E. coli*. The control was treatment with sterile water.

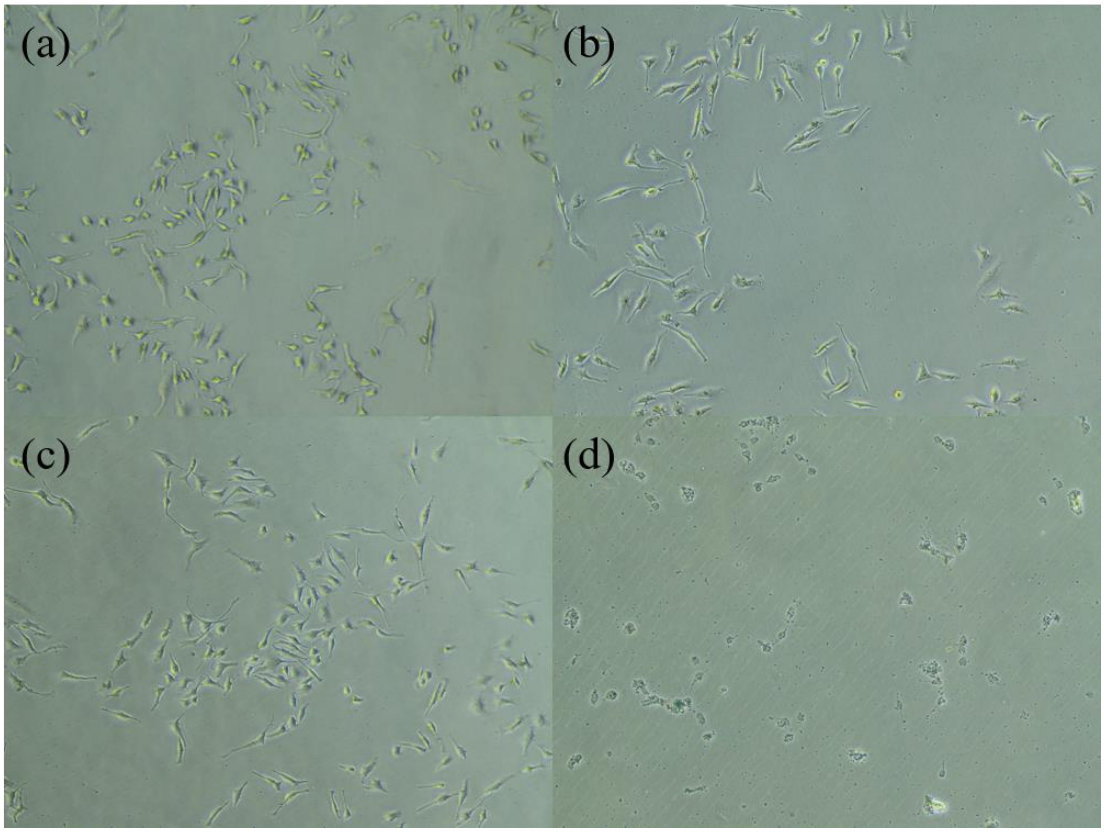


Fig S4. Electron scanning microscopy images of HeLa cells. (a) Non-treated cells (negative). Cells treated with **4g** at (b) 64 × MIC and (c) 8 × MIC of *S. aureus* for 24 h. (d) Cells treated with 0.1% Triton X (positive).

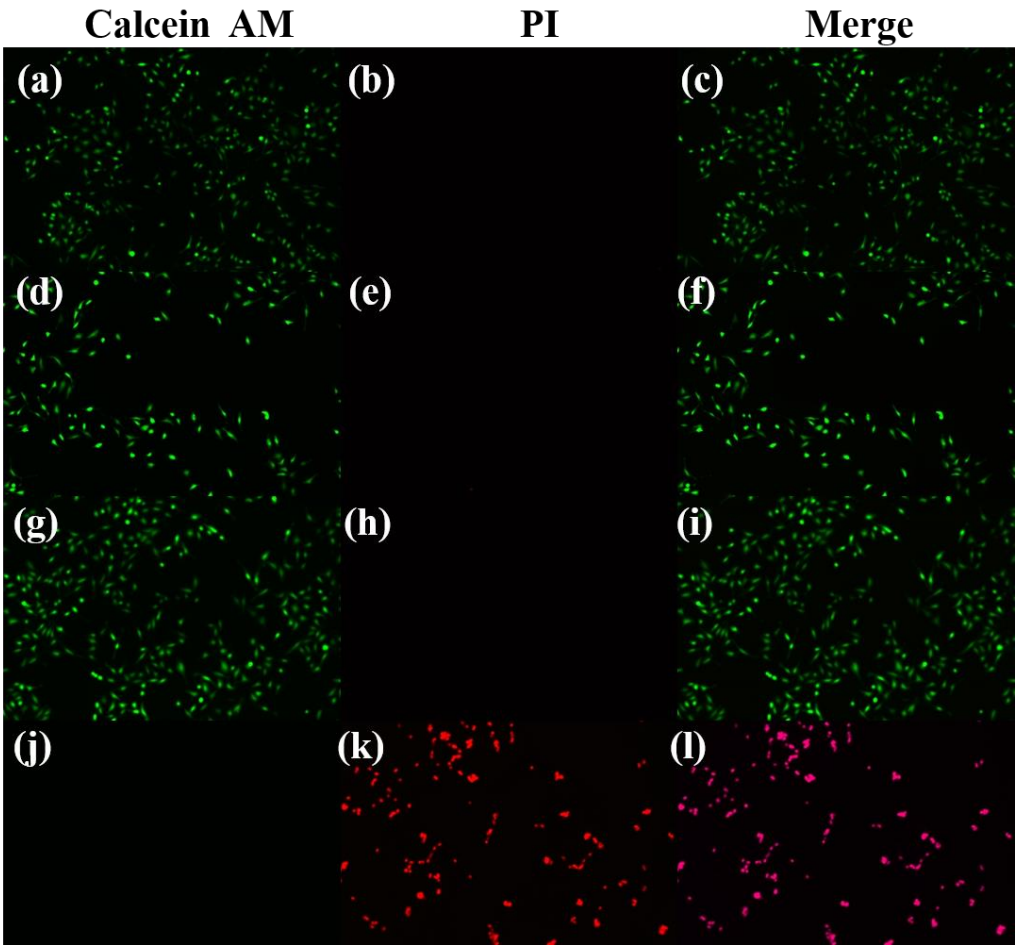


Fig S5. Fluorescence microscopy images of HeLa cells after treatment with **4g** for 24 h and staining with calcein AM and propidium iodide. (a-c) Non-treated cells (negative). (d-f) Cells treated with **4g** (64 × MIC of *S. aureus*). (g-i) Cells treated with **4g** (8 × MIC of *S. aureus*), and (j-l) Cells treated with 0.1% Triton-X (positive).

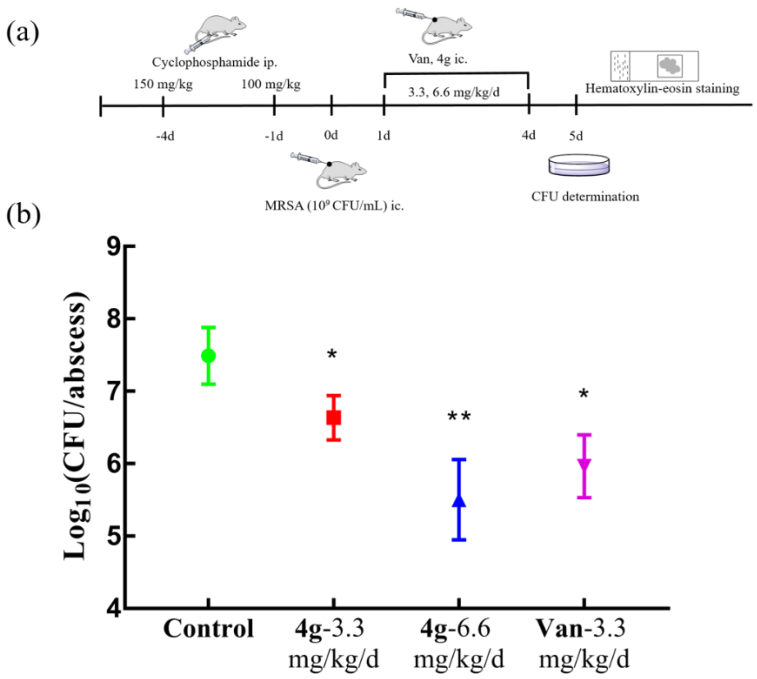


Fig S6. (a) The process of the In vivo experiment; (b) *In vivo* efficacy of compound **4g** in a mouse model of MRSA-1115041 skin infection. Bacterial counts of skin samples. P-values (*) were 0.041, 0.0072, and 0.0106 for samples treated with 3.3 mg/kg/d **4g**, 6.6 mg/kg/d **4g**, and 3.3 mg/kg/d vancomycin (Van), compared with the control.

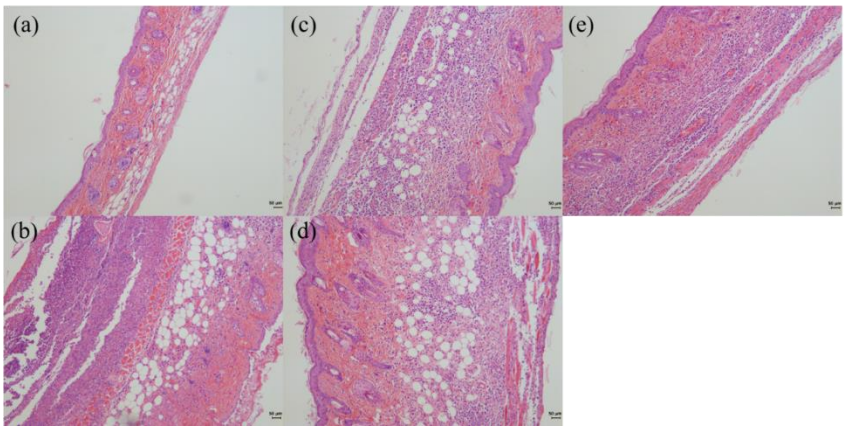


Fig S7. Pathological assay based on hematoxylin and eosin (H&E) staining. (a) Untreated skin; (b) Infected skin without any antibacterial treatment; (c), (d) Infected skin treated with 6.6 mg/kg/d and 3.3 mg/kg/d **4g**, respectively; (e): Infected skin treated with 3.3 mg/kg/d vancomycin. All the skin showing architecture of epidermis, dermis, and subcutaneous tissues. Scale bar 50 μm.

Experimental section

Materials and instrumentation

Reagents and solvents were purchased from commercial sources (shanghai darui finechemical, Energy Chemical, Aladdin, Macklin) and were used without further purification. All the solvents were of analytical grade. All the chemicals were used as supplied. Drug-sensitive bacterial strains, *E. coli, S. aureus, E. faecalis, S. maltophilia* obtained from American type culture collection. Drug-resistant bacteria, Methicillin-resistant *S. aureus* (MRSA), Carbapenemase-producing *E. aerogenes (bla$_{KPC}$)* and NDM-1-producing *Enterobacteriaceae* (*bla$_{NDM-1}$*) were collected from a teaching hospital located in Zhengzhou, Henan Province. All isolates were identified by VITEK2 compact (bioMerieux, France) and 16S rRNA gene sequencing. PCR and nucleotide sequencing were employed to screen for the presence of *bla*$_{NDM}$ gene, the primers and PCR program conditions were described previously[1]. Sheep RBCs were used for hemolytic assay.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz and 100 MHz spectrometer, respectively, and TMS as internal standard reference. Coupling constants (J) are given in hertz (Hz). High resolution mass spectra (HRMS) were recorded on a Waters Micromass Q-T of Micromass spectrometer. Analytical thin layer chromatography (TLC) was performed on glass plates pre-coated with silica gel (5–40um, Qingdao Marine Chemical Factory China) to monitor the reactions. Visualization was accomplished using UV light, ethanol solution of phospho molybdate and iodine powder. Column chromatography was performed on silica gel. For optical density and fluorescence measurements, Tecan Infinite Pro series M200 Microplate Reader was used. The biological experiments were performed with a 1300 series A2 Biological Safety Cabinet. TDL-5M Desktop Low-speed Refrigerated Centrifuge was used in antibacterial studies. SEM images were obtained on a Field Emission Scanning Electron Microscope TSM-7500F (JEOL Ltd. Japan) at 10.0kv. All the membrane-active agents were confirmed with ≥95% purity by using HPLC (Waters alliance acquity e2698HPLC C-18 4.6 × 250 mm, 5 μm) analysis in the eluate MeCN / H_2O containing 0.1% TFA.

General Procedure for the Synthesis compounds 1a-1f.

1. The Synthesis of 1,4-bis(2-bromoethoxy) benzene (1a).

Carbon tetrabromide (19.9 g, 60 mmol, 2.4 eq) was added in small portions to a solution of 1,4-bis(2-hydroxyethoxy)benzene (5.0 g, 25 mmol, 1 eq) and triphenylphosphine (15.7 g, 60 mmol, 2.4 eq) in anhydrous acetonitrile (0.12 L); the reaction mixture was kept at 0°C during the addition. The resulting mixture was then warmed to 25°C for 4 h under argon atmosphere. The product was precipitated by the addition of cold water (0.2 L), and the solid was filtered and washed with methanol/water (3:2, 3 × 100 mL). The product was recrystallized from methanol to obtain the title compound as white crystals [2]. Yield 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 4H), 4.24 (t, J = 6.3 Hz, 4H), 3.61 (t, J = 6.3 Hz, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 152.85, 116.12, 68.74, 29.25.

2. The Synthesis of 1,4-bis(n-bromoethoxy) benzene (1b-1f).

A mixture of hydroquinone / naphthalene-1,6-diol / naphthalene-2,3-diol (73 mmol, 1 eq), dibromoalkane (0.22 mol, 3 eq), and potassium carbonate (45 g, 0.33 mol, 4.5 eq) were refluxed in acetone (150 mL) for 24 h under argon atmosphere. After the reaction mixture was cooled to 25 °C and filtered through celite, and the solvent was evaporated under vacuum. The residue was dissolved in dichloromethane (100mL) and washed with water (2 × 50 mL), and brine (2 × 50 mL) and dried with sodium sulfate and concentrated in vacuo. The product was purified by column chromatography (silica gel; eluent: petroleum ether /EtOAc=300:1-60:1), afforded products as a white solid. All the intermediates were characterized by ^{1}H NMR, ^{13}C NMR.

1,4-bis(3-bromoethoxy) benzene (1b): Yield 64%. White solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 4H), 4.05 (t, J = 5.8 Hz, 4H), 3.60 (t, J = 6.5 Hz, 4H), 2.33 – 2.25 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.09, 115.60, 66.05, 32.49, 30.08.

1,4-bis(4-bromoethoxy) benzene (1c): Yield 59%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 4H), 3.93 (t, J = 6.1 Hz, 4H), 3.48 (t, J = 6.7 Hz, 4H), 2.11 – 2.00 (m, 4H), 1.96 – 1.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.11, 115.44, 67.49, 33.55, 29.54, 28.03.

1,4-bis(5-bromoethoxy) benzene (1d): Yield 70%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 4H), 3.94 (t, *J* = 6.3 Hz, 4H), 3.46 (t, *J* = 6.8 Hz, 4H), 2.01 – 1.91 (m, 4H), 1.86 – 1.77 (m, 4H), 1.68 – 1.59 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.13, 114.43, 67.21, 32.59, 31.50, 27.53, 23.84.

1,6-bis(3-bromopropoxy) naphthalene (1e): Yield 57%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 9.9 Hz, 1H), 8.32 – 8.24 (m, 2H), 8.11-8.00 (m, 2H), 7.65 (d, *J* = 6.4 Hz, 1H), 5.21 (t, *J* = 5.7 Hz, 2H), 5.16 (t, *J* = 5.8 Hz, 2H), 4.65 (t, *J* = 6.5 Hz, 2H), 4.60 (t, *J* = 6.4 Hz, 2H), 3.40 (dt, *J* = 12.1, 6.0 Hz, 2H), 3.33 (dt, *J* = 12.1, 6.1 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.96, 149.30, 130.67, 121.46, 118.42, 115.65, 114.27, 112.47, 101.52, 97.84, 60.26, 60.11, 27.28, 27.15, 24.86, 24.79.

2,3-bis(3-bromopropoxy) naphthalene (1f): Yield 48%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, J = 6.1, 3.3 Hz, 2H), 7.34 (dd, J = 6.2, 3.2 Hz, 2H), 7.17 (s, 2H), 4.26 (t, J = 5.9 Hz, 4H), 3.67 (t, J = 6.4 Hz, 4H), 2.43 (p, J = 6.1 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.88, 129.35, 126.35, 124.36, 124.15, 108.54, 66.29, 32.30, 30.08.

General Procedure for the Synthesis of compounds 2a-2h.

1-Aminoalkanes (60 mmol 1eq) were dissolved in CH_2Cl_2 (200 mL), K_2CO_3 (90 mmol 1.5eq) was dissolved in water (100 mL), and the aqueous solution was then added to the organic solution. The two-phase solution was cooled to 0 °C. Bromoacetyl bromide (90 mmol 1.5eq) was added through syringe dropwise to the solution while maintaining the temperature at 0 °C for about 30 min. The reaction mixture was then set at room temperature and stirred for about 6 h. After the reaction organic layer was collected, the aqueous solution was washed with CH_2Cl_2. The organic solution was then washed with water (3 × 100 mL) and dried over anhydrous Na_2SO_4. The organic layer was removed under reduced pressure to obtain colorless liquids or solids with 100% yield. The products were characterized by ^{1}H NMR, and ^{13}C NMR spectroscopy.

2-bromo-N-butylacetamide (2a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 3.75 (s, 2H), 3.13 (dd, *J* = 13.0, 7.1 Hz, 2H), 1.40 (dt, *J* = 14.9, 7.4 Hz, 2H), 1.23 (dq, *J* = 14.3,

7.3 Hz, 2H), 0.79 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.48, 39.84, 31.14, 29.08, 19.92, 13.63.

2-bromo-N-pentylacetamide (2b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (s, 1H), 3.90 (s, 2H), 3.29 (dd, *J* = 13.2, 7.0 Hz, 2H), 1.66 – 1.45 (m, 2H), 1.45 – 1.22 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.29, 40.25, 29.41, 28.95, 22.31, 13.97.

2-bromo-N-hexylacetamide (2c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 1H), 3.86 (s, 2H), 3.26 (dd, *J* = 13.1, 7.1 Hz, 2H), 1.62 – 1.42 (m, 2H), 1.39 – 1.18 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.93, 40.55, 31.38, 29.02, 28.97, 26.45, 26.21, 22.51, 13.98.

2-bromo-N-heptylacetamide (2d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 1H), 3.86 (s, 2H), 3.26 (dd, *J* = 13.2, 7.1 Hz, 2H), 1.59 – 1.47 (m, 2H), 1.37 – 1.22 (m, 8H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.26, 40.26, 31.67, 29.34, 29.25, 28.87, 26.76, 22.54, 14.02.

2-bromo-N-octylacetamide (2e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (s, 1H), 3.88 (s, 2H), 3.27 (dd, *J* = 13.1, 7.1 Hz, 2H), 1.59 – 1.48 (m, 2H), 1.36 – 1.22 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.20, 40.27, 31.75, 29.36, 29.25, 29.17, 29.13, 26.80, 22.61, 14.05.

2-bromo-N-nonylacetamide (2f): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 3.88 (s, 2H), 3.23 (dd, *J* = 13.2, 7.0 Hz, 2H), 1.59 – 1.40 (m, 2H), 1.34-1.11 (m, 12H), 0.83 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.29, 40.44, 31.81, 29.42, 29.19, 29.18, 29.10, 26.77, 26.14, 22.62, 14.06.

2-bromo-N,N-dibutylacetamide (2g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 2H), 3.41 – 3.14 (m, 4H), 1.65 – 1.54 (m, 2H), 1.54 – 1.45 (m, 2H), 1.30 (tq, *J* = 14.8, 7.4 Hz, 4H), 0.91 (dt, *J* = 16.5, 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.81, 48.62, 46.05, 31.15, 29.25, 26.48, 26.13, 20.03, 13.79, 13.71.

2-bromo-N,N-dihexylacetamide (2h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 2H),

3.37 – 3.16 (m, 4H), 1.65 – 1.54 (m, 2H), 1.54 – 1.45 (m, 2H), 1.33 – 1.22 (m, 12H), 0.86 (q, J = 6.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.24, 47.82, 45.16, 30.56, 30.47, 28.15, 26.19, 25.53, 25.51, 21.55, 12.99, 12.95.

General Procedure for the Synthesis of compounds 3a-3h.

4 mL aqueous dimethylamine (40%, m/m, excessive) reacted with 5 mmol N-alkyl-2-bromoe-thanamides in **30** mL ethanol under stirring and reflux for 10 h, then the organic phases of the mixture was removed by rotary evaporator. Water (30ml) then add to the mixture, the water phase was extracted by CH_2Cl_2. The organic phases were combined and dried by Na_2SO_4. After the solvent had been removed under reduced pressure, the crude product was chromatographed on a silica gel column (DCM/MEOH/TEA=22:1

:0.05 V/V/V) to give light yellow oil. The compounds were characterized by ^{1}H NMR, and ^{13}C NMR spectroscopy.

2-(dimethylamino)-N-butylacetamide (3a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 1H), 2.87 (dd, J = 13.4, 6.9 Hz, 2H), 2.52 (s, 2H), 1.89 (s, 6H), 1.12 (dt, J = 14.9, 7.2 Hz, 2H), 0.96 (dq, J = 14.2, 7.2 Hz, 2H), 0.54 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.33, 63.17, 45.97, 38.61, 31.77, 20.14, 13.76.

2-(dimethylamino)-N-pentylacetamide (3b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (s, 1H), 3.21 (dd, J = 13.5, 6.9 Hz, 2H), 2.88 (s, 2H), 2.23 (s, 6H), 1.53 – 1.41 (m, 2H), 1.37 – 1.18 (m, 4H), 0.85 (t, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.43, 62.21, 44.99, 37.87, 28.35, 28.11, 21.34, 12.96.

2-(dimethylamino)-N-hexylacetamide (3c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 3.25 (dd, J = 13.4, 7.0 Hz, 2H), 2.91 (s, 2H), 2.26 (s, 6H), 1.48 (dd, J = 14.6, 7.5 Hz, 2H), 1.35 – 1.21 (m, 6H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.27, 63.08, 45.84, 38.78, 31.35, 29.51, 26.49, 22.41, 13.86.

2-(dimethylamino)-N-heptylacetamide (3d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 1H), 3.15 (dd, J = 13.6, 6.7 Hz, 2H), 2.81 (s, 2H), 2.17 (s, 6H), 1.49 – 1.32 (m, 2H), 1.30 – 1.06 (m, 8H), 0.77 (t, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.38,

63.19, 45.96, 38.86, 31.69, 29.64, 28.91, 26.88, 22.53, 14.00.

2-(dimethylamino)-N-octylacetamide (3e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (s, 1H), 3.20 (dd, *J* = 13.6, 6.7 Hz, 2H), 2.86 (s, 2H), 2.22 (s, 6H), 1.55 – 1.38 (m, 2H), 1.34-1.12 (m, 10H), 0.81 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.36, 63.18, 45.96, 38.86, 31.74, 29.63, 29.19, 29.14, 26.91, 22.58, 14.02.

2-(dimethylamino)-N-nonylacetamide (3f): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (s, 1H), 3.27 (dd, *J* = 13.5, 6.8 Hz, 2H), 2.94 (s, 2H), 2.29 (s, 6H), 1.51 (dd, *J* = 14.0, 6.9 Hz, 2H), 1.37 – 1.22 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 170.28, 63.13, 45.91, 38.85, 31.79, 29.61, 29.42, 29.22, 29.16 , 26.90, 22.59, 14.02.

2-(dimethylamino)-N,N-dibutylacetamide (3g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27 – 3.12 (m, 4H), 2.98 (s, 2H), 2.18 (s, 6H), 1.48 – 1.36 (m, 4H), 1.19 (td, *J* = 15.2, 7.5 Hz, 4H), 0.87 – 0.75 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.06, 61.79, 47.02, 45.36, 45.22, 30.95, 29.60, 20.09, 20.98, 13.72, 13.66.

2-(dimethylamino)-N,N-dihexylacetamide (3h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 (s, 2H), 3.28 – 3.14 (m, 4H), 2.52 (s, 6H), 1.57 – 1.38 (m, 4H), 1.31 – 1.20 (m, 12H), 0.85 (q, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.67, 60.62, 47.41, 45.87, 45.31, 31.53, 31.46, 28.85, 27.54, 26.64, 26.50, 22.53, 22.51, 13.95, 13.93.

General Synthesis of aromatic derivatives 4a-4w, 5a-5j.

1,4-bis(n-bromoethoxy)benzene / (3-bromopropoxy)benzene (0.8 mmol, 1eq) were added to the organic solutions EtOH (10mL) of 2-(N, N-Dimethyl)-N- alkylethanamide (3eq) in a screw-top pressure tube at 85 °C for about 24 h. After the reaction, the solvent was evaporated, and the product was dissolved with a small volume of acetone, after precipitated using excess EtOAc or diethyl ether at low temperature for a few hours. Finally, the product was filtered and washed multiple times with EtOAc or diethyl ether. All the final products were characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

4a: Yield 45%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (t, *J* = 5.3 Hz, 2H), 6.97 (s, 4H), 4.46 – 4.34 (m, 4H), 4.20 (s, 4H), 4.04 – 3.93 (m, 4H), 3.31 (s, 12H), 3.11

(dd, J = 12.7, 6.7 Hz, 4H), 1.47 – 1.38 (m, 4H), 1.46-1.38 (m, 16H), 0.86 (t, J = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.03, 152.04, 115.75, 63.02, 62.72, 62.04, 52.08, 31.16, 28.63, 28.29, 26.28, 21.99, 13.90. HR-MS (ESI) Calculated for $C_{32}H_{60}Br_2N_4O_4$ [M-2Br]$^{2+}$: 282.2302, found: 282.2286.

4b: Yield 80%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (t, J = 5.4 Hz, 2H), 6.97 (s, 4H), 4.48 – 4.34 (m, 4H), 4.21 (s, 4H), 4.06 – 3.92 (m, 4H), 3.31 (s, 12H), 3.11 (dd, J = 12.6, 6.7 Hz, 4H), 1.42 (dd, J = 12.7, 6.1 Hz, 4H), 1.30-1.20 (m, 20H), 0.86 (t, J = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.01, 152.02, 115.74, 63.01, 62.73, 62.03, 52.11, 31.17, 28.60, 28.57, 26.31, 22.03, 13.90. HR-MS (ESI) Calculated for $C_{34}H_{64}Br_2N_4O_4$ [M-2Br]$^{2+}$: 296.2458, found: 296.2464.

4c: Yield 75%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (t, J = 5.5 Hz, 2H), 6.97 (s, 4H), 4.46 – 4.34 (m, 4H), 4.19 (s, 4H), 3.98 (s, 4H), 3.31 (s, 12H), 3.11 (dd, J = 12.6, 6.7 Hz, 4H), 1.47 – 1.37 (m, 4H), 1.31-1.18 (m, 24H), 0.86 (t, J = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.01, 152.02, 115.74, 63.00, 62.73, 62.02, 52.12, 31.23, 28.89, 28.63, 28.61, 28.59, 26.31, 22.03, 13.91. HR-MS (ESI) Calculated for $C_{36}H_{68}Br_2N_4O_4$ [M-2Br]$^{2+}$: 310.2615, found: 310.2621.

4d: Yield 45%. White oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.63 (s, 2H), 6.89 (s, 4H), 4.15 (s, 4H), 3.98 (t, J = 5.8 Hz, 4H), 3.82 – 3.57 (m, 4H), 3.25 (s, 12H), 3.12 (dd, J = 12.5, 6.8 Hz, 4H), 2.17 (dq, J = 11.7, 5.8 Hz, 4H), 1.46 – 1.37 (m, 4H), 1.35 – 1.24 (m, 4H), 0.86 (t, J = 7.3 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.37, 152.94, 116.01, 65.61, 62.62, 62.47, 51.74, 31.15, 22.99, 19.98, 14.04. HR-MS (ESI) Calculated for $C_{28}H_{52}Br_2N_4O_4$ [M-2Br]$^{2+}$: 254.1989, found: 254.1993.

4e: Yield 65%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (t, J = 5.4 Hz, 2H), 6.89 (s, 4H), 4.13 (s, 4H), 3.98 (t, J = 5.7 Hz, 4H), 3.76 – 3.60 (m, 4H), 3.24 (s, 12H), 3.11 (dd, J = 12.7, 6.7 Hz, 4H), 2.17 (dd, J = 9.5, 5.6 Hz, 4H), 1.48 – 1.39 (m, 4H), 1.31-1.21 (m, 8H), 0.86 (t, J = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.86, 152.46, 115.52, 65.13, 62.13, 62.01, 51.26, 28.48, 28.22, 22.49, 21.70, 13.83. HR-MS (ESI) Calculated for $C_{30}H_{56}Br_2N_4O_4$ [M-2Br]$^{2+}$: 268.2145, found: 268.2149.

4f: Yield 45%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (t, J = 5.4 Hz, 2H), 6.89 (s, 4H), 4.14 (s, 4H), 3.98 (t, J = 5.8 Hz, 4H), 3.72-3.60 (m, 4H), 3.24 (s, 12H), 3.12 (dd, J = 12.7, 6.7 Hz, 4H), 2.21-2.10 (m, 4H), 1.50-1.36 (m, 4H), 1.36-1.16 (m, 12H), 0.85 (t, J = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.87, 152.47, 115.55, 65.18, 62.16, 62.05, 51.23, 30.83, 28.50, 25.98, 22.53, 21.97, 13.85. HR-MS (ESI) Calculated for $C_{32}H_{60}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 282.2302, found: 282.2308.

4g: Yield 80%. White oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (t, J = 5.1 Hz, 2H), 6.89 (s, 4H), 4.16 (s, 4H), 3.98 (t, J = 5.6 Hz, 4H), 3.80 – 3.57 (m, 4H), 3.24 (s, 12H), 3.11 (dd, J = 12.4, 6.5 Hz, 4H), 2.27 – 2.06 (m, 4H), 1.54 – 1.35 (m, 4H), 1.34-1.13 (m, 16H), 0.85 (t, J = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.39, 152.95, 115.97, 65.61, 62.55, 51.72, 31.68, 29.08, 28.80, 26.78, 22.97, 22.51, 14.42. HR-MS (ESI) Calculated for $C_{34}H_{64}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 296.2458, found: 296.2462.

4h: Yield 41%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (t, J = 5.6 Hz, 2H), 6.80 (s, 4H), 4.58 (s, 4H), 3.99 (t, J = 5.3 Hz, 4H), 3.96 – 3.81 (m, 4H), 3.44 (s, 12H), 3.23 (dd, J = 14.0, 6.5 Hz, 4H), 240-2.20 (m, 4H), 1.65 – 1.43 (m, 4H), 1.40 – 1.12 (m, 20H), 0.85 (t, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.86, 152.48, 115.53, 65.17, 62.14, 62.04, 51.25, 31.18, 28.58, 28.55, 26.33, 22.52, 22.03, 13.90. HR-MS (ESI) Calculated for $C_{36}H_{68}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 310.2615, found: 310.2621.

4i: Yield 53%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (t, J = 5.4 Hz, 2H), 6.89 (s, 4H), 4.09 (s, 4H), 3.98 (t, J = 5.8 Hz, 4H), 3.73 – 3.59 (m, 4H), 3.23 (s, 12H), 3.12 (dd, J = 12.6, 6.7 Hz, 4H), 2.16 (td, J = 11.6, 5.8 Hz, 4H), 1.49 – 1.35 (m, 4H), 1.30-1.14 (m, 24H), 0.86 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.34, 152.95, 115.95, 65.58, 62.52, 62.45, 55.40, 51.80, 31.74, 29.42, 29.15, 29.13, 29.09, 26.82, 22.99, 22.56, 14.44. HR-MS (ESI) Calculated for $C_{38}H_{72}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 324.2771, found: 324.2778.

4j: Yield 45%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.54 (t, J = 5.4 Hz, 2H), 6.88 (s, 4H), 4.07 (s, 4H), 3.94 (t, J = 6.0 Hz, 4H), 3.60 – 3.51 (m, 4H), 3.21 (s, 12H), 3.11 (dd, J = 12.5, 6.8 Hz, 4H), 1.94 – 1.80 (m, 4H), 1.77 – 1.62 (m, 4H), 1.49 – 1.36

(m, 4H), 1.35 – 1.25 (m, 4H), 0.87 (t, J = 7.3 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.38, 153.01, 115.85, 67.63, 64.68, 62.22, 51.70, 38.74, 31.16, 26.14, 19.97, 19.65, 14.04. HR-MS (ESI) Calculated for $C_{30}H_{56}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 268.2145, found: 268.2148.

4k: Yield 78%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.64 (t, J = 5.2 Hz, 2H), 6.88 (s, 4H), 4.12 (s, 4H), 3.94 (t, J = 6.0 Hz, 4H), 3.64 – 3.47 (m, 4H), 3.22 (s, 12H), 3.10 (dd, J = 12.7, 6.8 Hz, 4H), 1.94 – 1.80 (m, 4H), 1.76 – 1.64 (m, 4H), 1.49 – 1.37 (m, 4H), 1.35 – 1.20 (m, 8H), 0.86 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.40, 153.01, 115.85, 67.63, 64.65, 62.23, 55.42, 51.66, 28.98, 28.73, 26.15, 22.21, 19.63, 14.36. HR-MS (ESI) Calculated for $C_{32}H_{60}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 282.2302, found: 282.2308.

4l: Yield 44%. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ8.62 (t, J = 5.2 Hz, 2H), 6.87 (s, 4H), 4.11 (s, 4H), 3.94 (t, J = 5.9 Hz, 4H), 3.64 – 3.50 (m, 4H), 3.22 (s, 12H), 3.10 (dd, J = 12.5, 6.6 Hz, 4H), 1.92-1.78 (m, 4H), 1.75 – 1.65 (m, 4H), 1.46-1.35 (m, 4H), 1.33-1.19 (m, 12H), 0.85 (t, J = 6.5 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.39, 153.00, 115.85, 67.63, 64.64, 62.23, 56.47, 55.44, 51.67, 31.34, 29.03, 26.48, 26.14, 22.50, 19.63, 14.39. HR-MS (ESI) Calculated for $C_{34}H_{64}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 296.2458, found: 296.2464.

4m: Yield 32%. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ8.50 (t, J = 5.5 Hz, 2H), 6.87 (s, 4H), 4.06 (s, 4H), 3.94 (t, J = 6.0 Hz, 4H), 3.64 – 3.44 (m, 4H), 3.21 (s, 12H), 3.10 (dd, J = 12.6, 6.8 Hz, 4H), 1.99 – 1.78 (m, 4H), 1.78 – 1.62 (m, 4H), 1.48 – 1.34 (m, 4H), 1.30-1.19 (m, 16H), 0.85 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.36, 153.02, 115.85, 67.65, 64.67, 62.25, 55.42, 51.74, 31.68, 29.09, 28.79, 26.77, 26.15, 22.51, 19.65, 14.41. HR-MS (ESI) Calculated for $C_{36}H_{68}Br_2N_4O_4$$[M\text{-}2Br]^{2+}$: 310.2615, found: 310.2622.

4n: Yield 47%. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (t, J = 5.5 Hz, 2H), 6.87 (s, 4H), 4.05 (s, 4H), 3.94 (t, J = 6.0 Hz, 4H), 3.62 – 3.50 (m, 4H), 3.21 (s, 12H), 3.10 (dd, J = 12.6, 6.8 Hz, 4H), 1.94 – 1.79 (m, 4H), 1.75 – 1.65 (m, 4H), 1.49 – 1.35

(m, 4H), 1.33-1.19 (m, 20H), 0.85 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.35, 153.01, 115.84, 67.64, 64.65, 62.24, 55.42, 51.74, 31.69, 31.19, 29.11, 29.09, 26.81, 26.14, 22.55, 19.65, 14.42. HR-MS (ESI) Calculated for $C_{38}H_{72}Br_2N_4O_4$ [M-2Br]$^{2+}$: 324.2771, found: 324.2774.

4o: Yield 66%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.62 (t, J = 5.1 Hz, 2H), 6.87 (s, 4H), 4.11 (s, 4H), 3.93 (t, J = 6.0 Hz, 4H), 3.63 – 3.50 (m, 4H), 3.21 (s, 12H), 3.10 (dd, J = 12.6, 6.6 Hz, 4H), 1.87 (dt, J = 15.7, 7.8 Hz, 4H), 1.78 – 1.63 (m, 4H), 1.46 – 1.38 (m, 4H), 1.31-1.14 (m, 24H), 0.85 (t, J = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.39, 153.00, 115.83, 67.62, 64.60, 62.22, 51.68, 31.75, 29.42, 29.14, 29.07, 26.82, 26.15, 22.56, 19.63, 14.44. HR-MS (ESI) Calculated for $C_{40}H_{76}Br_2N_4O_4$ [M-2Br]$^{2+}$: 338.2928, found: 338.2934.

4p: Yield 89%. Light yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (t, J = 5.5 Hz, 2H), 6.85 (s, 4H), 4.08 (s, 4H), 3.91 (t, J = 6.3 Hz, 4H), 3.55 – 3.42 (m, 4H), 3.20 (s, 12H), 3.12 (dd, J = 12.6, 6.8 Hz, 4H), 1.99 – 1.61 (m, 8H), 1.54 – 1.35 (m, 8H), 1.35 – 1.25 (m, 4H), 0.87 (t, J = 7.3 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.92, 152.57, 115.26, 67.40, 64.31, 61.73, 51.22, 30.66, 28.21, 22.40, 21.65, 19.47, 13.52. HR-MS (ESI) Calculated for $C_{32}H_{60}Br_2N_4O_4$ [M-2Br]$^{2+}$: 282.2302, found: 282.2312.

4q: Yield 77%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (t, J = 5.5 Hz, 2H), 6.85 (s, 4H), 4.08 (s, 4H), 3.91 (t, J = 6.3 Hz, 4H), 3.55 – 3.44 (m, 4H), 3.20 (s, 12H), 3.11 (dd, J = 12.7, 6.8 Hz, 4H), 1.85 – 1.67 (m, 8H), 1.47 – 1.37 (m, 8H), 1.31 – 1.22 (m, 8H), 0.86 (t, J = 6.9 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.91, 152.56, 115.25, 67.40, 64.28, 61.73, 51.24, 28.47, 28.23, 28.20, 22.40, 21.69, 21.64, 13.84. HR-MS (ESI) Calculated for $C_{34}H_{64}Br_2N_4O_4$ [M-2Br]$^{2+}$: 296.2458, found: 296.2463.

4r: Yield 89%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (s, 2H), 6.84 (s, 4H), 4.06 (s, 4H), 3.91 (t, J = 6.3 Hz, 4H), 3.54 – 3.42 (m, 4H), 3.19 (s, 12H), 3.11 (dd, J = 12.6, 6.6 Hz, 4H), 1.86 – 1.66 (m, 8H), 1.50-1.33 (m, 8H), 1.33-1.19(m, 12H), 0.86 (t, J = 6.6 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.90, 152.57, 115.24, 67.40, 64.25, 61.73, 51.26, 30.83, 28.55, 28.22, 25.96, 22.40, 21.99, 21.65, 13.86. HR-MS

(ESI) Calculated for $C_{36}H_{68}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 310.2615, found: 310.2618.

4s: Yield 85%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.58 (t, J = 5.4 Hz, 2H), 6.85 (s, 4H), 4.06 (s, 4H), 3.91 (t, J = 6.3 Hz, 4H), 3.55 – 3.43 (m, 4H), 3.19 (s, 12H), 3.11 (dd, J = 12.6, 6.7 Hz, 4H), 1.75 (tt, J = 14.6, 7.4 Hz, 8H), 1.49 – 1.35 (m, 8H), 1.31-1.19 (m, 16H), 0.85 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.90, 152.58, 115.25, 67.42, 64.26, 61.75, 51.26, 31.17, 28.58, 28.27, 28.21, 26.26, 22.41, 21.99, 21.65, 13.89. HR-MS (ESI) Calculated for $C_{38}H_{72}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 324.2771, found: 324.2778.

4t: Yield 80%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.58 (t, J = 5.0 Hz, 2H), 6.85 (s, 4H), 4.06 (s, 4H), 3.91 (t, J = 6.3 Hz, 4H), 3.54 – 3.43 (m, 4H), 3.19 (s, 12H), 3.11 (dd, J = 12.6, 6.7 Hz, 4H), 1.84 – 1.65 (m, 8H), 1.50 – 1.32 (m, 8H), 1.32-1.28 (m, 20H), 0.85 (t, J = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.90, 152.57, 115.23, 67.40, 64.22, 61.72, 54.89, 51.26, 31.19, 28.61, 28.59, 28.23, 26.32, 22.41, 22.04, 21.65, 13.91. HR-MS (ESI) Calculated for $C_{40}H_{76}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 338.2928, found: 338.2931.

4u: Yield 59%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.59 (t, J = 5.5 Hz, 2H), 6.84 (s, 4H), 4.06 (s, 4H), 3.90 (t, J = 6.3 Hz, 4H), 3.54 – 3.43 (m, 4H), 3.19 (s, 12H), 3.10 (dd, J = 12.6, 6.7 Hz, 4H), 1.85 – 1.63 (m, 8H), 1.49 – 1.34 (m, 8H), 1.31-1.14 (m, 24H), 0.85 (t, J = 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.90, 152.58, 115.24, 67.42, 64.23, 61.75, 51.28, 31.23, 28.92, 28.63, 28.61, 28.58, 28.22, 26.31, 22.41, 22.04, 21.66, 13.91. HR-MS (ESI) Calculated for $C_{42}H_{80}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 352.3084, found: 352.3090.

4v: Yield 45%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.88 (s, 4H), 4.54 (s, 4H), 3.98 (t, J = 5.7 Hz, 4H), 3.89 – 3.69 (m, 4H), 3.29 (s, 12H), 3.24 (dd, J = 15.1, 7.9 Hz, 8H), 2.12 (dd, J = 10.0, 5.5 Hz, 4H), 1.60 –1.48 (m, 4H), 1.48-1.37 (m, 4H), 1.27 (ddd, J = 19.0, 15.0, 7.4 Hz, 8H), 0.90 (dt, J = 18.9, 7.3 Hz, 12H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.95, 152.44, 115.55, 65.19, 61.58, 59.94, 54.91, 51.37, 46.46, 45.19, 30.12, 29.11, 22.54, 19.52, 19.44, 13.67, 13.62. HR-MS (ESI) Calculated for

$C_{36}H_{68}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 310.2615, found: 310.2621.

4w: Yield 40%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.88 (s, 4H), 4.52 (s, 4H), 3.97 (t, J = 5.7 Hz, 4H), 3.87 – 3.69 (m, 4H), 3.33-3.27(m, 12H), 3.27-3.10 (m, 8H), 2.23 – 2.03 (m, 4H), 1.58-1.49 (m, 4H), 1.49-1.39 (m, 4H), 1.35-1.18 (m, 24H), 0.86 (dt, J = 13.7, 6.7 Hz, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.93, 152.46, 115.51, 65.19, 61.54, 59.92, 54.89, 51.43, 46.69, 45.44, 30.92, 30.91, 28.04, 26.90, 25.90, 25.86, 22.55, 22.06, 21.99, 13.88, 13.83. HR-MS (ESI) Calculated for $C_{44}H_{84}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 366.3241, found: 366.3256.

5a: Yield 78%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 7.30 (t, J = 7.9 Hz, 2H), 7.00-6.88 (m, 3H), 4.19 (s, 2H), 4.05 (t, J = 5.9 Hz, 2H), 3.77 – 3.63 (m, 2H), 3.26 (s, 6H), 3.11 (dd, J = 12.7, 6.7 Hz, 2H), 2.21 (td, J = 11.6, 5.8 Hz, 2H), 1.48-1.37 (m, 2H), 1.29-1.19 (m, 6H), 0.85 (t, J = 6.6 Hz, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.87, 158.10, 129.50, 120.86, 114.46, 64.48, 62.10, 62.00, 51.23, 30.84, 28.51, 25.98, 22.44, 21.98, 13.86. HR-MS (ESI) Calculated for $C_{19}H_{33}BrN_2O_2$ $[M\text{-}Br]^+$: 321.2537, found: 321.2543.

5b: Yield 83%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.64 (t, J = 5.3 Hz, 1H), 7.30 (t, J = 8.0 Hz, 2H), 6.95 (t, J = 8.6 Hz, 3H), 4.16 (s, 2H), 4.05 (t, J = 5.9 Hz, 2H), 3.73 – 3.64 (m, 2H), 3.26 (s, 6H), 3.11 (dd, J = 12.6, 6.7 Hz, 2H), 2.21 (td, J = 11.6, 5.8 Hz, 2H), 1.47 – 1.39 (m, 2H), 1.33-1.15 (m, 8H), 0.85 (t, J = 6.7 Hz, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.86, 158.10, 129.50, 120.87, 114.45, 64.47, 62.09, 61.99, 51.25, 31.17, 28.57, 28.29, 26.28, 22.43, 22.00, 13.90. HR-MS (ESI) Calculated for $C_{20}H_{35}BrN_2O_2$ $[M\text{-}Br]^+$: 335.2693, found: 335.2710.

5c: Yield 75%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 (t, J = 5.4 Hz, 1H), 7.34 – 7.26 (m, 2H), 6.99-6.90 (m, 3H), 4.20 (s, 2H), 4.05 (t, J = 5.9 Hz, 2H), 3.81 – 3.61 (m, 2H), 3.27 (s, 6H), 3.11 (dd, J = 12.7, 6.7 Hz, 2H), 2.21 (td, J = 11.6, 5.9 Hz, 2H), 1.50-1.35 (m, 2H), 1.29-1.20 (m, 10H), 0.84 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.87, 158.10, 129.48, 120.84, 114.45, 64.48, 62.08, 61.99, 51.24, 31.19, 28.59, 28.55, 26.34, 22.46, 22.03, 13.90. HR-MS (ESI) Calculated for

$C_{21}H_{37}BrN_2O_2$ $[M\text{-}Br]^+$: 349.2850, found: 349.2858.

5d: Yield 33%. Yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (t, J = 5.2 Hz, 1H), 7.30 (dd, J = 8.4, 7.5 Hz, 2H), 6.98-6.92 (m, 3H), 4.19 (s, 2H), 4.05 (t, J = 5.9 Hz, 2H), 3.76 – 3.64 (m, 2H), 3.26 (s, 6H), 3.11 (dd, J = 12.6, 6.8 Hz, 2H), 2.21 (td, J = 11.7, 5.9 Hz, 2H), 1.47 – 1.38 (m, 2H), 1.28-1.21 (m, 12H), 0.85 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.86, 158.11, 129.48, 120.85, 114.47, 64.50, 62.11, 62.03, 51.26, 31.23, 28.90, 28.64, 28.61, 28.55, 26.33, 22.46, 22.04, 13.90. HR-MS (ESI) Calculated for $C_{22}H_{39}BrN_2O_2$ $[M\text{-}Br]^+$: 363.3006, found: 363.3013.

5e: Yield 65%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.78 – 8.63 (m, 2H), 8.17 (d, J = 9.1 Hz, 1H), 7.46-7.36 (m, 2H), 7.32 (s, 1H), 7.13 (d, J = 9.1 Hz, 1H), 6.84 (d, J = 4.7 Hz, 1H), 4.34-4.10 (m, 8H), 3.92 – 3.80 (m, 2H), 3.80 – 3.70 (m, 2H), 3.31 (d, J = 12.6 Hz, 12H), 3.20 – 3.03 (m, 4H), 2.41-2.32 (m, 2H), 2.32-2.21 (m, 2H), 1.50-1.36 (m, 4H), 1.32-1.12 (m, 12H), 0.91 – 0.77 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.94, 162.88, 156.49, 153.81, 135.48, 126.90, 123.50, 120.01, 119.40, 117.40, 106.89, 103.35, 64.70, 64.63, 62.13, 62.03, 61.96, 51.35, 51.29, 30.82, 28.52, 28.50, 25.99, 22.56, 22.41, 21.97, 21.96, 13.85. HR-MS (ESI) Calculated for $C_{36}H_{62}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 307.2380, found: 307.2383.

5f: Yield 69%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 – 8.65 (m, 2H), 8.17 (d, J = 9.2 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.32 (d, J = 2.3 Hz, 1H), 7.13 (dd, J = 9.2, 2.4 Hz, 1H), 6.84 (dd, J = 6.4, 2.0 Hz, 1H), 4.34 – 4.13 (m, 8H), 3.90 – 3.80 (m, 2H), 3.80 – 3.70 (m, 2H), 3.31 (d, J = 12.8 Hz, 12H), 3.20 – 3.04 (m, 4H), 2.42 – 2.33 (m, 2H), 2.32 – 2.22 (m, 2H), 1.52 – 1.35 (m, 4H), 1.30-1.13(m, 16H), 0.82 (q, J = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.94, 162.88, 156.49, 153.82, 135.49, 126.89, 123.51, 120.02, 119.40, 117.40, 106.90, 103.35, 64.71, 64.63, 62.13, 62.04, 61.96, 51.37, 51.29, 31.15, 31.14, 28.57, 28.55, 28.28, 26.29, 22.57, 22.43, 21.98, 13.87. HR-MS (ESI) Calculated for $C_{38}H_{66}Br_2N_4O_4$ $[M\text{-}2Br]^{2+}$: 321.2537, found: 321.2540.

5g: Yield 45%. Pink solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (dd, J = 13.6, 5.5 Hz, 2H), 8.16 (d, J = 9.2 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.32 (d, J = 2.2 Hz, 1H), 7.13 (dd,

J = 9.2, 2.3 Hz, 1H), 6.83 (dd, *J* = 6.2, 2.1 Hz, 1H), 4.36 – 4.08 (m, 8H), 3.90 – 3.79 (m, 2H), 3.79 – 3.66 (m, 2H), 3.28 (t, *J* = 14.2 Hz, 12H), 3.18 – 3.05 (m, 4H), 2.41-2.31 (m, 2H), 2.31-2.21 (m, 2H), 1.42 (d, *J* = 6.5 Hz, 4H), 1.28-1.14 (m, 20H), 0.83 (t, *J* = 6.6 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.94, 162.88, 156.49, 153.82, 135.49, 126.89, 123.49, 120.02, 119.40, 117.38, 106.89, 103.35, 64.72, 64.63, 62.12, 62.03, 61.95, 51.38, 51.31, 31.17, 28.58, 26.34, 22.56, 22.42, 22.02, 13.89. HR-MS (ESI) Calculated for $C_{40}H_{70}Br_2N_4O_4$ [M-2Br]$^{2+}$: 335.2693, found: 335.2697.

5h: Yield 66%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.62 (dd, *J* = 12.4, 5.7 Hz, 2H), 8.14 (d, *J* = 9.2 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.11 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.83 (dd, *J* = 5.2, 3.4 Hz, 1H), 4.26 – 4.10 (m, 8H), 3.86 – 3.77 (m, 2H), 3.77 – 3.68 (m, 2H), 3.28 (d, *J* = 12.3 Hz, 12H), 3.17 – 3.06 (m, 4H), 2.38-2.30 (m, 2H), 2.30-2.21 (m, 2H), 1.46 – 1.37 (m, 4H), 1.29-1.15 (m, 24H), 0.83 (dd, *J* = 6.9, 5.3 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.93, 162.87, 156.49, 153.81, 135.49, 126.91, 124.50, 123.46, 120.01, 119.40, 117.36, 106.88, 103.35, 64.62, 62.02, 51.41, 51.33, 31.22, 28.91, 28.89, 28.61, 26.34, 22.54, 22.41, 22.04, 13.91. HR-MS (ESI) Calculated for $C_{42}H_{74}Br_2N_4O_4$ [M-2Br]$^{2+}$: 349.2850, found: 349.2853.

5i: Yield 85%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (t, *J* = 5.4 Hz, 2H), 7.74 (dd, *J* = 6.1, 3.3 Hz, 2H), 7.38 (s, 2H), 7.34 (dd, *J* = 6.1, 3.2 Hz, 2H), 4.24 (s, 4H), 4.19 (t, *J* = 5.7 Hz, 4H), 3.83 – 3.71 (m, 4H), 3.31 (s, 12H), 3.10 (dd, *J* = 12.6, 6.7 Hz, 4H), 2.33 (dd, *J* = 9.8, 5.5 Hz, 4H), 1.48 – 1.34 (m, 4H), 1.27-1.67 (m, 16H), 0.82 (t, *J* = 6.7 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.93, 148.00, 128.96, 126.24, 124.14, 108.28, 65.42, 62.17, 51.39, 31.16, 28.53, 28.31, 26.32, 22.45, 21.99, 13.87. HR-MS (ESI) Calculated for $C_{38}H_{66}Br_2N_4O_4$ [M-2Br]$^{2+}$: 321.2537, found: 321.2544.

5j: Yield 31%. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.84 (t, *J* = 5.2 Hz, 2H), 7.75 (dd, *J* = 6.0, 3.3 Hz, 2H), 7.38 (s, 2H), 7.34 (dd, *J* = 6.1, 3.2 Hz, 2H), 4.28 (s, 4H), 4.18 (t, *J* = 5.5 Hz, 4H), 3.87 – 3.70 (m, 4H), 3.33 (s, 12H), 3.10 (dd, *J* = 12.4, 6.5 Hz, 4H), 2.38-2.30 (m, 4H), 1.47-1.35 (m, 4H), 1.30-1.15 (m, 20H), 0.82 (t, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.94, 148.02, 128.96, 126.23, 124.12, 108.26, 65.44, 62.23, 62.16, 51.36, 31.19, 28.61, 28.52, 26.39, 22.47, 22.02, 13.89. HR-MS

(ESI) Calculated for $C_{40}H_{70}Br_2N_4O_4$ $[M-2Br]^{2+}$: 335.2693, found: 335.2696.

Biological Section

Microorganisms and culture conditions: The antibacterial activity of all the molecules were evaluated against both Gram-positive bacteria (*S. aureus*, *E. faecalis*, MRSA) and Gram-negative bacteria (*E. coli*, *S. maltophilia*, bla_{NDM-1} -containing strains, bla_{KPC} -containing strains). All the bacteria were cultured in Muller-Hinton broth (5.0 g of beef extract, 17.5 g of casein hydrolysate, and 1.5 g of starch in 1000 mL of distilled water) while *E. coli* was grown in Luria-Bertani broth (10.0 g of tryptone, 5.0 g of yeast extract, and 10 .0 g of NaCl in 1000 mL of distilled water). Brain-heart infusion broth (5.0 g beef heart infusion form, 12.5 g of calf brains infusion form, 2.5 g Na_2HPO_4, 2.0 g D-glucose, 10 g of peptone and 5.0 g NaCl in 100 mL of sterile distilled water) was used for stock samples of bacteria, the freezed dried stock samples of bacteria in 33.3% glycerol were stored at -80 ºC. For solid media, Mueller-Hinton agar (5.0 g of beef extract, 17.5 g of casein hydrolysate, 1.5 g of starch and 12.5 g of agar in 1000 mL of distilled water) was used as growth medium.

Cell culture: Human cervical carcinoma cell line (HeLa cells), maintained in complete DMEM media (Bioind) supplemented with 10% FBS (Zeta Life), at 37 ºC in a humidified atmosphere of 5% CO_2 in air. All the cells were mycoplasma free. The cells were trypsinized, counted and seeded in 96-well plates for viability studies or in 12-well plates for other studies. The cells allowed to adhere overnight before they were used for experiments.

Antibacterial assay (minimum inhibitory concentration): Minimum inhibitory concentration (MIC) of all the molecules **(4a-4w, 5a-5j)** were determined by broth microdilution method according to CLSI guidelines. The test medium for most species was cation-adjusted Muller-Hinton broth (MHB). The 4-6 h grown culture as described in the microorganism and culture condition section gives about 10^8 CFU/mL of bacteria. The bacterial cultures were then diluted to give approximately 10^6 CFU/mL in different media (Muller-Hinton broth media for *S. aureus*, *E. faecalis*, *S. maltophilia*, MRSA,

bla$_{NDM-1}$ -containing strains, bla$_{KPC}$ -containing strains and Luria-Bertani media for *E. coli*) which were then used for determining antibacterial efficacy. All the final compounds were water soluble at room temperature. Stock solutions of the final compounds were prepared with sterile Milli-Q water. Then the stock solutions were serially diluted to different concentration (256 μg/mL, 128 μg/mL, 64 μg/mL, 32 μg/mL, 16 μg/mL, 8 μg/mL, 4 μg/mL, 2 μg/mL, 1 μg/mL, 0.5 μg/mL) by using different media (Muller-Hinton broth media for *S. aureus*, *E. faecalis*, *S. maltophilia*, MRSA, bla$_{NDM-1}$ -containing strains, bla$_{KPC}$ -containing strains and Luria-Bertani media for *E. coli*). These dilutions (100 μL) were added to the wells of 96 well plate followed by the addition of 100 μL of bacterial suspension (10^6 CFU/mL). Two controls were made: one containing 200 μL of media (negative contrast) and the other containing 200 μL of bacterial solution (10^6 CFU/mL, positive contrast). The plates were then incubated at 37 ºC for 16-20 h. After the incubation, read the results. Each concentration was determined in twice and the whole experiment was repeated at least twice. The antibacterial activity was thus expressed as minimum inhibitory concentration (MIC). A glycopeptides antibiotic vancomycin and a β-lactams antibiotic meropenem were used to compare the antibacterial efficacy in this study.

Antibacterial activity in plasma (Plasma stability): Bacteria (*S. aureus*) was grown in a similar way as mentioned in the microorganism and culture condition and finally diluted in the respective media to give 10^6 CFU/mL. The fresh sterile defiber sheep blood (from commercial resource) was centrifuged at 3500 rpm for 10 min. The plasma, separated from the blood cells after centrifugation, was carefully collected. The test compound **4g** was dissolved in 50% sterile Milli-Q water and 50% plasma at a concentration of 512 μg/mL. The test compound **4g** was dissolved in sterile Milli-Q water as the control. Three such test samples were preincubated at 37 °C in 50% plasma for 2 h, 4 h and 6 h respectively. Then the three samples were serially diluted to several concentration (256 μg/mL, 128 μg/mL, 64 μg/mL, 32 μg/mL, 16 μg/mL, 8 μg/mL, 4 μg/mL). After that, 50 μL of the above solutions was added to wells of a 96-well plate and 150 μL of the bacterial suspension (10^5 CFU/mL) was added to wells. The plate

was then incubated for 20-24 h at 37 °C. To determine the minimum bactericidal concentration (MBC), the bacterial suspension that appeared to have less/little turbidity was plated (20 μL) and the agar plates were incubated for 20-24 h at 37 °C. Concentration at which no bacterial growth (no bacterial colony) was observed was taken as the MBC of the respective compounds.

Bactericidal activity in complex mammalian fluids: The fresh sterile defiber sheep blood was bought from a biochemical reagent company (China). Plasma was obtained as mentioned above. Serum was used the Zeta Life fetal bovine serum. Methicillin-resistant *S. aureus* (MRSA-1115041) was grown in way as mentioned in the microorganism and culture conditions. Finally, MRSA was diluted with 50% Muller-Hinton broth (MHB) medium and 50% mammalian media (serum, plasma, blood), individually in a way to give 10^5 CFU/mL of MRSA in 50% serum, 50% plasma, and 50% blood (having 50% MHB medium). The tested molecule **4g** was dissolved in sterile water with the serial dilution method at the concentration of (512 μg/mL, 256 μg/mL, 128 μg/mL, 64 μg/mL, 32 μg/mL, 16 μg/mL, 8 μg/mL, 4 μg/mL). Then 50 μL of the dilutions was added to the wells of a 96-well plate and 150 μL of the bacterial suspension (10^5 CFU/mL) was added separately to the wells containing the dilutions of the compound **4g**. The plate was then incubated for 20-24 h at 37 °C and minimum bactericidal concentration of the test compounds was determined by plating the bacterial suspension (20 μL) directly from the wells onto Muller-Hinton agar (MHA) plate. The agar plates were incubated at 37 °C for 20-24 h and colonies were observed to determine the MBC.

Time-dependent killing: An overnight culture of bacteria *S. aureus* was diluted 1:10,000 in MHB medium and incubated at 37 °C with aeration at 225 rpm for 2 h (early exponential) or 5 h (late exponential). Bacteria at the early stage of growth were then challenged with compound **4g** at 2 μg/mL, 3 μg/mL, 4 μg/mL and antibiotics vancomycin (3 μg/mL) in culture tubes at 37 °C and 225 rpm; Bacteria at the last phase of growth were then challenged with compound **4g** at 6 μg/mL, 8 μg/mL, 12 μg/mL and antibiotics vancomycin (8 μg/mL) in culture tubes at 37 °C and 225 rpm. At different

intervals, 100 µL bacteria solution were removed to 96-well plate, centrifuged at 4,000 rpm for 3 min (TDL 5M centrifuge) and resuspended in 100 µL of sterile phosphate buffered saline (1×PBS). Ten-fold serially diluted suspensions were plated on MHA plates and incubated at 37 °C overnight. Colonies were counted and CFU per mL was calculated. Experiments were performed with biological replicates.

Biofilm disruption assay (determination of viable count and imaging): The bacteria *S. aureus* (4-6 h grown) were diluted to ~10^5 CFU/mL into suitable media. The 96-well plates containing 100 µL of these suspensions were incubated under stationary conditions (for about 24 h for *S. aureus*). After incubation, the bacteria suspensions were centrifuged at 3,500 rpm for 5 min, the medium was removed, and the wells were washed with 1×PBS once. Compound **4g** against *S. aureus* (100 µL at 2, 4, 8, 16, 32, 64, and 128 µg/mL) was then added to the wells containing preformed bacterial biofilms and allowed to incubate for 24 h at 37°C. A control was made where 100 µL of the above medium was added. After 24 h, medium was discarded, and the planktonic cells were removed by washing with 1×PBS. Then 100 µL of trypsin-EDTA solution was added to the treated biofilm to make the suspension of bacterial cells present within the biofilm. Cell suspension was then assessed by plating the 10-fold serial dilutions of the suspension on suitable agar plates. After 24 h of incubation, bacterial colonies were counted, and cell viability was expressed as $\log_{10}$ (CFU/well) along with the control. For visualizing the disruption of biofilm by the small molecules, 100 µL of 0.1% of crystal violet (CV) was added into the wells and incubated for 10 min. Then the crystal violet solution was discarded, and the plates were washed twice with 1×PBS. Finally, imaging of the stained wells was taken using a digital camera.

Minimum biofilm eradication concentration (MBEC) assay[3]: Biofilm eradication assays involve three phases separated by wash steps, including (i) initial biofilm establishment on well surfaces without test compound; (ii) biofilm treatment with test compound; and (iii) recovery of viable biofilms in fresh medium alone. This assay was used to demonstrate the biofilm eradication activities of compound **4g**. Biofilm eradication assays were performed in 96-well plates, and microtitre wells were

inoculated with 100 mL of a 1:1000-fold exponential phase *S. aureus* and *E. coli* (10^8 CFU/mL) and were incubated for 24 h at 37 °C. After 24h, medium and planktonic cells were removed and 100 mL of two-fold serial dilutions of test compound was added to the wells in fresh medium and was incubated for 24 h at 37 °C (phase 2). After this time, the contents were removed and 100 μL of fresh medium only was added to allow viable biofilms to recover and to disperse planktonic bacteria into the medium resulting in a turbid microtiter well (24 h incubation at 37 °C; phase 3). After this final phase, microtitre plates were examined for visible bacterial growth (turbidity) and the MBEC was recorded as the lowest concentration at which no turbidity could be observed (due to eradicated biofilms).

Minimum biofilm inhibitory concentration (MBIC) determination[3]: In 96-well plates, two-fold serial dilutions of test compounds **4g** was added in MHB medium. Then, 1:1000-fold exponential-phase *S. aureus* and *E. coli* (10^8 CFU/mL) in MHB was added to each well and allowed to incubate at 37 °C for 24 h. After this time, the contents from the 96-well plates were removed and the wells were rinsed with water, followed by the addition of 100 μL of 0.1% crystal violet to stain the biofilms (10 min incubation at room temperature). The plates were then rinsed, and 100 mL of ethanol was added to dissolve the crystal violet stained biofilms. Minimum concentrations required to inhibit 80% of biofilm formation ($MBIC_{80}$) were determined (OD_{540}) by comparing compound treated versus untreated wells and the resulting data were used to generate dose response curves using Spss 20.0. Note: these experiments were performed to determine whether the antibiofilm activities of compound **4g** were dependent on or independent of their antibacterial activities.

Scanning Electron Microscopy: Overnight culture of *S. aureus* was diluted in suitable media. Subsequently, cells were harvested by centrifugation at 4000 rpm for 3 min, then washed with 1×PBS Twice. Compound **4g** was added to *S. aureus* suspension respectively at a final concentration of 16 μg/mL, and samples were left at 37 ºC for 3h. A sample without antibacterial agents was used as a control. After the antibacterial agent treatment, cells were centrifuged and resuspended with 1×PBS Twice. The cells

were sequentially dehydrated with 50, 75, 95, and 100% ethanol. Finally, replacement of ethanol with tert-butanol. 5 μL of dehydrated cells was then dropped on a small piece of silicon wafer and dried at vacuum drying oven. Before being imaged, the silicon wafers containing bacteria were sputter coated with gold. The final results were examined in JEOL TSM-7500F Field Emission Scanning Electron Microscope at 10.0kv operating voltage.

Cytoplasmic membrane depolarization assay: The 4-6 h grown bacteria were harvested (3,500 rpm, 5 min), washed and resuspended with 1×PBS (*S. aureus*) and 5 mM HEPES buffer, 5 mM glucose and 100 mM KCl solution at 1:1:1 ratio (*E. coli*). Then the bacterial suspension (~10^8 CFU/mL, 150 μL) was added to the wells of a 96-well plate (Black plate, clear bottom with lid). Then 3,5-dipropyl-thiacarbocyanne ($diSC_3(5)$) (10 μM, 50 μL) was added to the wells containing bacterial suspension and pre-incubated for about 30 min for *S. aureus* and 40 min for *E. coli* (additional 50 μL of 200μM of EDTA was also added in case of *E. coli*). After the incubation, fluorescence was measured for the next 8 min at every 1 min interval at an excitation wavelength of 622 nm (slit width: 10 nm) and emission wavelength of 670 nm (slit width: 5 nm). Bacterial suspensions were then transferred to another well-plate containing 10 μL of 420 μg/mL of small molecules **4a**, **4b**, **4g**, **4m**, **4r**, **4s**, **5e**, **5f** and fluorescence intensity was monitored immediately for another 12 min at every 1 min interval, the final concentration of small molecules was 20 μg/mL. A control experiment was performed by treating the preincubated bacterial suspension and dye solution only with sterile Milli-Q water (50 μL).

Inner membrane permeabilization assay: The 4-6 h grown bacteria were harvested (3500 rpm, 5 min), washed and resuspended similarly as the previous method. Then the bacterial suspension (~10^8 CFU/mL, 150 μL) was added to the wells of a 96-well plate (Black plate, clear bottom with lid). Then propidium iodide (PI) (10 μM, 50 μL) was added to the wells containing bacterial suspension and pre-incubated for about 30 min for *S. aureus* and 40 min for *E. coli*. After the incubation, fluorescence was measured for the next 8 min at every 1 min interval at an excitation wavelength of 535 nm (slit

width: 10 nm) and emission wavelength of 617 nm (slit width: 5 nm). Bacterial suspensions were then transferred to another well-plate containing 10 μL of 420 μg/mL of small molecules and fluorescence intensity was monitored immediately for another 12 min at every 1 min interval, the final concentration of small molecules **4a**, **4b**, **4g**, **4m**, **4r**, **4s**, **5e**, **5f** was 20 μg/mL. A control experiment was performed by treating the preincubated bacterial suspension and dye solution only with sterile Milli-Q water (50 μL).

Outer membrane permeabilization assay: The outer membrane permeabilization activity of the small molecules**4a**, **4b**, **4g**, **4m**, **4r**, **4s**, **5e**, **5f** was determined by the N-phenylnapthylamine (NPN) assay. Mid-log phase bacteria (*E. coli*) were harvested similarly as mentioned in earlier experiments, washed and resuspended similarly as the previous method. Bacterial suspension (~10^8 CFU/mL, 150 mL) was transferred into the wells of a black 96-well plate. Then NPN dye (10 mM, 50 mL) was added to the wells containing bacterial suspension and pre-incubated for about 40 min for *E. coli*. After the incubation, fluorescence was monitored for next 8 min at every 1 min interval at an excitation wavelength of 350 nm (slit width: 10 nm) and emission wavelength of 420 nm (slit width: 5 nm). Then, the bacterial suspensions were transferred to another black well-plate containing 40 mL of 420 mg/mL of small molecules and fluorescence intensity was monitored immediately for another 12 min at every 1 min interval, the final concentration of small molecules was 40 mg/mL. A control experiment was performed by treating the preincubated bacterial suspension and dye solution only with sterile Milli-Q water (50 mL).

Propensity of bacterial resistance development: In order to evaluate the propensity of developing bacterial resistance towards the compounds, the potent compound **4g** was used in the study. First, MIC of compound **4g** was determined against *S. aureus* and *E. coli*, and subsequently the compound was challenged repeatedly at the 1/2 MIC level. Two control antibiotics norfloxacin and colistin were chosen for *S. aureus* and for *E. coli*, respectively. In case of norfloxacin and colistin, the initial MIC values were determined against respective bacteria. After the initial MIC experiment, serial

passaging was initiated by transferring bacterial suspension grown at the sub-MIC of the compound/antibiotics (at MIC/2) and was subjected to another MIC assay. After 24 h incubation period, cells grown at the sub-MIC of the test compound/antibiotics were once again transferred and assayed for MIC experiment. The process was repeated for16 passages for both *S. aureus* and *E. coli* respectively. The MIC for test compound to the control antibiotics was plotted against days to determine the propensity of bacterial resistance development.

Hemolytic activity: Red blood cells (RBCs) were isolated from sheep blood and resuspended in 1×PBS (5%). RBC suspension (150 μL) was then added to solutions of serially diluted small molecules **(4a-4w, 5a-5j)** at the concentration of (5120, 2560, 1280, 640, 320, 160, 80, 40, 20, 10 μg/mL) in a 96-well plate (50 μL). Two controls were prepared, one 50 μL RBC suspension (5%) and the other with 50 μL of 0.1% solution of Triton X-100. The plate was then incubated for 1 h at 37 °C. After the incubation, the plate was centrifuged at 3,500 rpm for 5 minutes. Supernatant (100 μL) from each well was then transferred to a fresh 96-well plate and absorbance at 540 nm was measured. Percentage of hemolysis was determined as $(A–A_0) / (A_{total}–A_0) \times 100$, where A is the absorbance of the test well, A_0 is the absorbance of the negative control (5% RBC suspensions), and A_{total} the absorbance of wells with 0.1% Triton X-100.

Cytotoxicity study: Cytotoxicity of the small molecules were evaluated by the Cell Counting Kit-8 (CCK-8). Briefly, 5×10^3cells in 100 μL medium were seeded to each of 96-well plates. After 24 h incubation at 37 °C, the culture medium was removed and replaced with fresh medium (100 μL) containing the candidate compound **4g** in different concentration. And only media was used as negative control. At the end of the treatment (24 h), the medium was discarded and washed twice with the new culture medium, then added 100 μL new medium (with 5% CCK-8) to each well. Cells were incubated at 37 °C for a further 4 h and then the absorbance at 450 nm was measured using a Microplate Reader. Results were expressed as percent viability = $[A\text{-}A_0 / A_{nc}\text{-}A_0] \times 100\%$, where A is the absorbance of the treated cells, A_{nc} is the absorbance of the negative control and A_0 is absorbance of the background (new medium containing

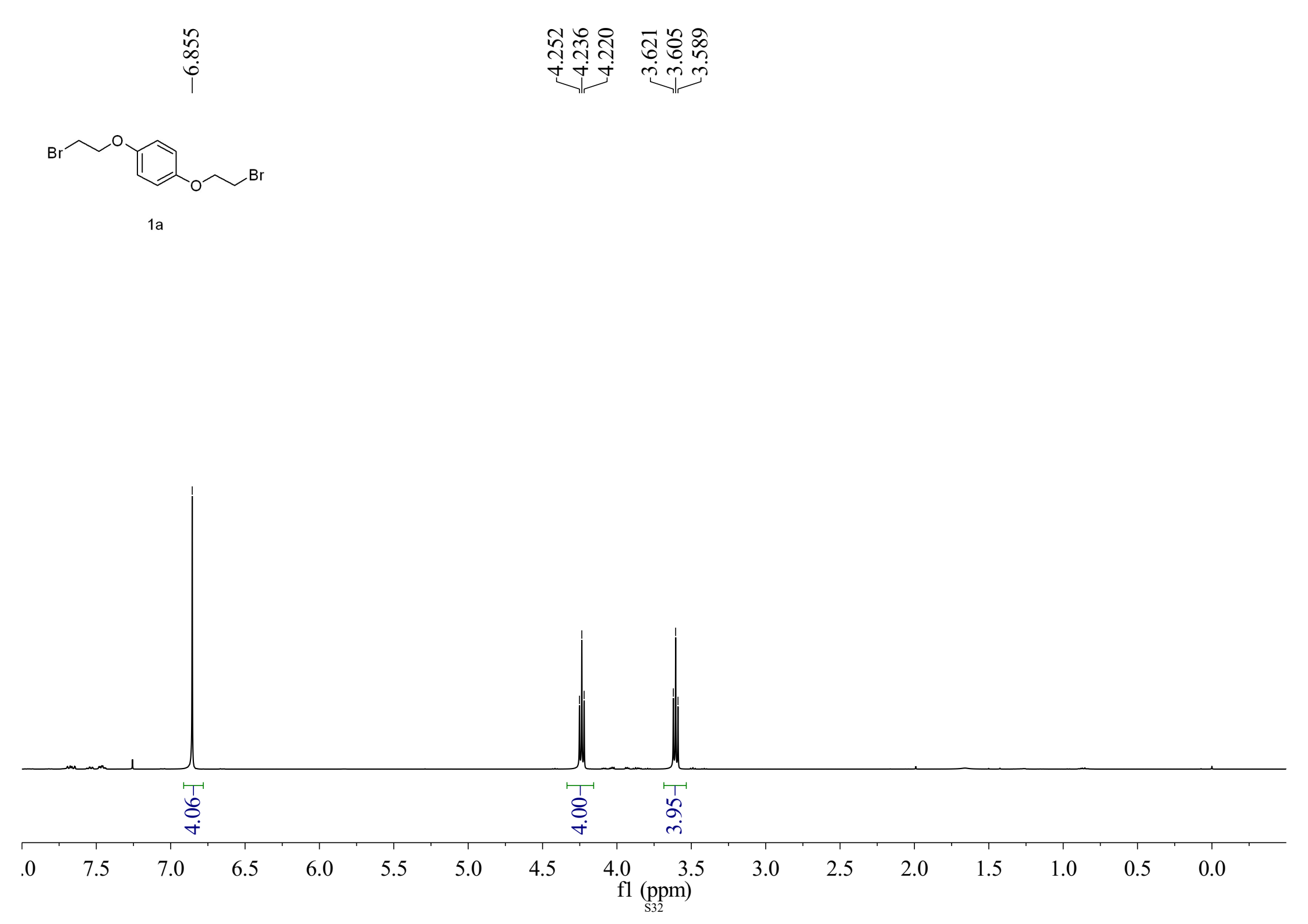
5% CCK-8). The average 50% inhibitory concentration (IC_{50}) was determined from the dose-response curves according to the inhibition ratio for each concentration. Each concentration was analyzed in triplicate and the experiment was repeated three times.

Fluorescence and electron scanning microscopy: As mentioned above for the cytotoxicity study, cells were seeded into the wells of a 12-well plate and then treated with compounds at various concentrations **4g**. For positive control 0.1% Triton X-100 was used. All the treated and untreated cells (as negative control) were washed once with 1×PBS (the images were captured with a 10× objective in electron microscope) and stained with 2μM calcein AM (Fluka) and 4.5μM propidium iodide (PI) (Sigma-Aldrich) (50 μL of 1:1 calcein AM: PI) for 15 min at 37 °C under 5% CO_2-95% air atmosphere. Finally, the images were captured with a 10× objective in fluorescence microscope using a band-pass filter for calcein AM at 500-550 nm and a long-pass filter for PI at 590-800 nm.

Acute dermal toxicity: All animal experiments were approved by the Institutional Animal Care and Use Committee and carried out in accordance to the policy of the National Ministry of Health of China. The mice were housed in individually ventilated cages (IVC) maintained with controlled environment. They were housed in pathogen free conventional caging systems, bedding material used were corncob. The husbandry conditions: Light: dark cycle—12:12 hours, Animal Room Temp: 22 ± 2°C, Relative humidity: 30–40%. Animals were randomly selected, marked to permit individual identification and kept in their cages for at least 5 days before the experiment to allow for acclimatization to the experimental conditions. The acute dermal toxicity was performed on female KM mice (~30g). The mice were anesthetized by intraperitoneal injection of chloral hydrate. The fur on the back of the mice were shaved using a sterile razor, then cover the shaved area with depilatory paste, after treated for 3 min remove depilatory paste thoroughly using gauze sponges and water. Compound **4g** was dissolved in saline at concentrations of 300 μg/mL, 900 μg/mL, 1500 μg/mL, 2100 μg/mL, 30000 μg/mL, respectively. Group (1, 2, 3, 4, 5) of mice (n = 3) were treated with 100 μL of **4g** (concentration of 300 μg/mL, 900 μg/mL, 1500 μg/mL, 2100 μg/mL,

30000 μg/mL) at the skin of back; The antibacterial agents were hypodermic injection once with 12 h intervals. The dosage for each group were continued for four days. The animals were observed carefully and then observed carefully every day. Particular attention was paid to the changes in fur, eyes and mucous membranes, and observations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. Acute dermal toxicity showed no sign of irritation or unnatural behave when the concentration is less than 1500 μg/mL.

In Vivo Study: female KM mice (~30g) were used for the experiments. The fur on the back of the mice were shaved using a sterile razor, then cover the shaved area with depilatory paste, after treated for 3 min remove depilatory paste thoroughly using gauze sponges and water. The 60μL ~10^9CFU/mL live MRSA was inoculated subcutaneously on the fur was shaved. The abscess can be seen after the bacteria inoculated for 24h. In the experiment one group of mice (n = 5) were left untreated and served as a control; Group (1) of mice (n = 5) were treated with 100 μL of vancomycin (concentration of 500/mL) at the site of infection; Group (2,3) of mice (n = 5) were treated with 100 μL of **4g** (concentration of 500 μg/mL, 1000 μg/mL) at the site of infection. The antibacterial agents were hypodermic injection once with 12 h intervals. The dosage for each group were continued for four days. 24h after the last dose the mice were sacrificed, and the infected skin was severed aseptically. The infected skin placed into 1 mL of sterile saline and homogenized. The dilutions of the homogenate were plated onto agar plates, which were incubated overnight at about 37°C. The bacterial titer was expressed as $\log_{10}$ (CFU/ abscess). The statistical significance of differences between control and experimental groups was calculated by using of the GraphPad Prism 7 statistical software. $P < 0.05$ was considered significant. The infected skin was also stained with hematoxylin and eosin (H&E), and their morphology was investigated under a light microscope at 10 ×magnification.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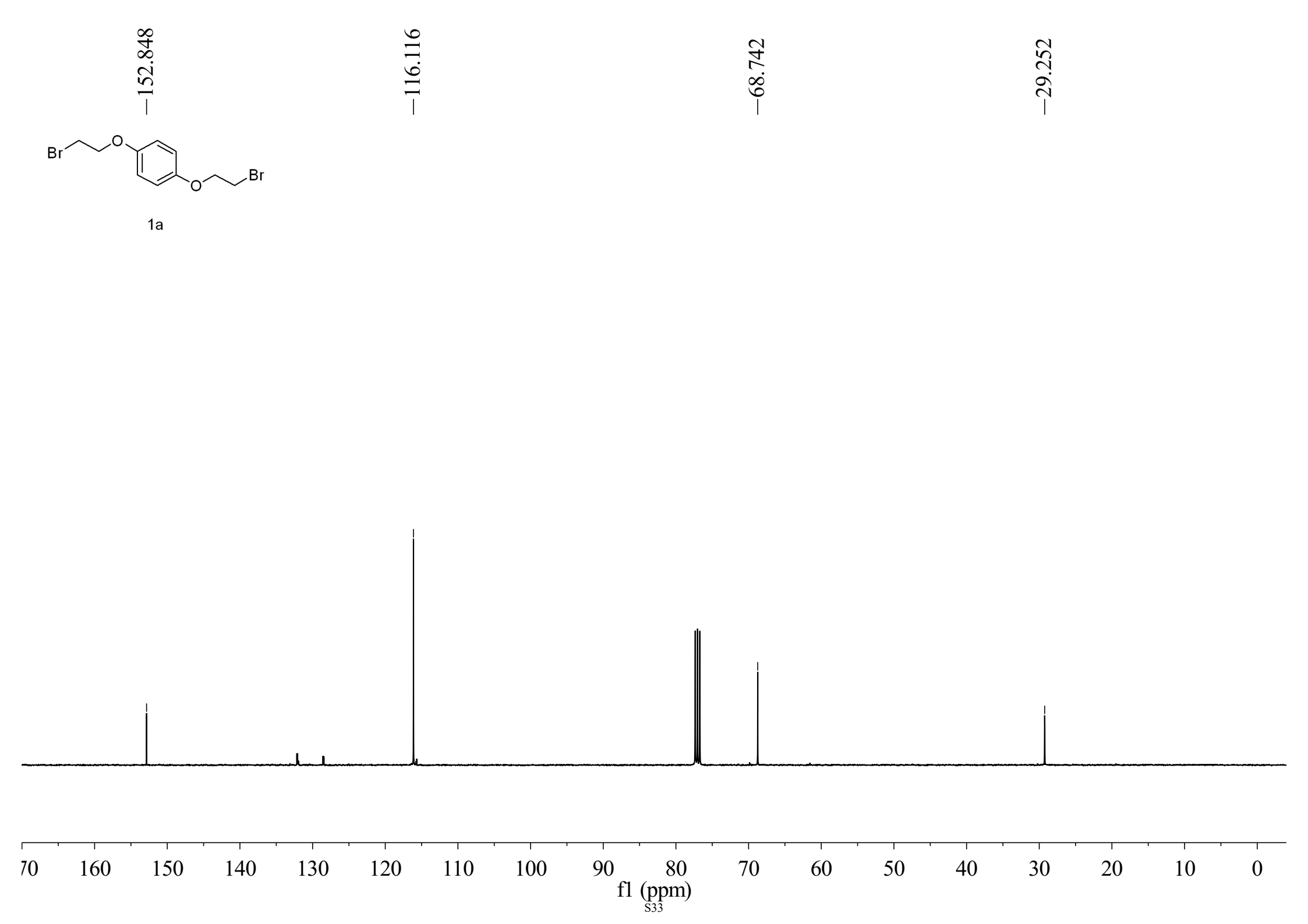
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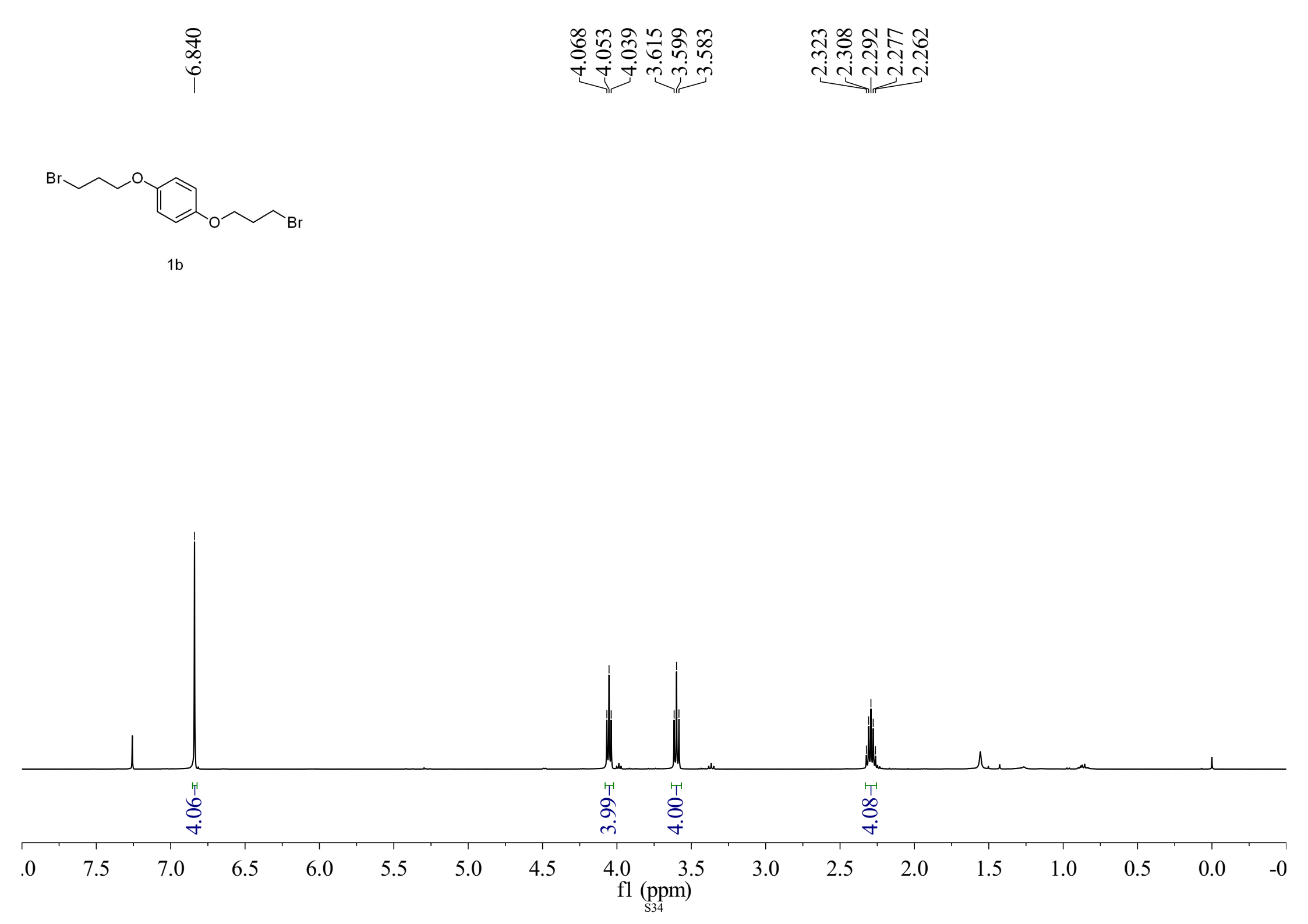
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Br
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4.00
4.08
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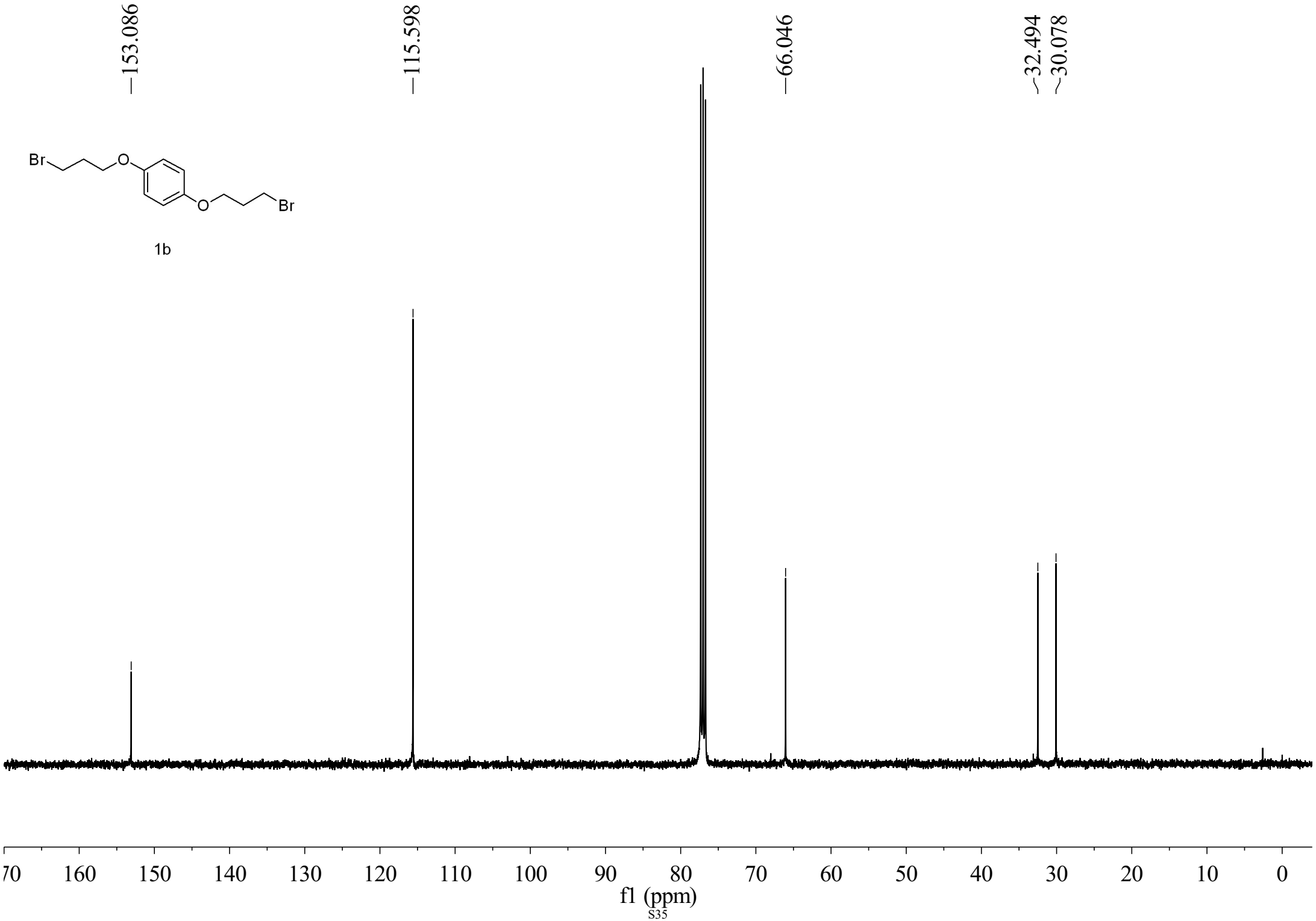
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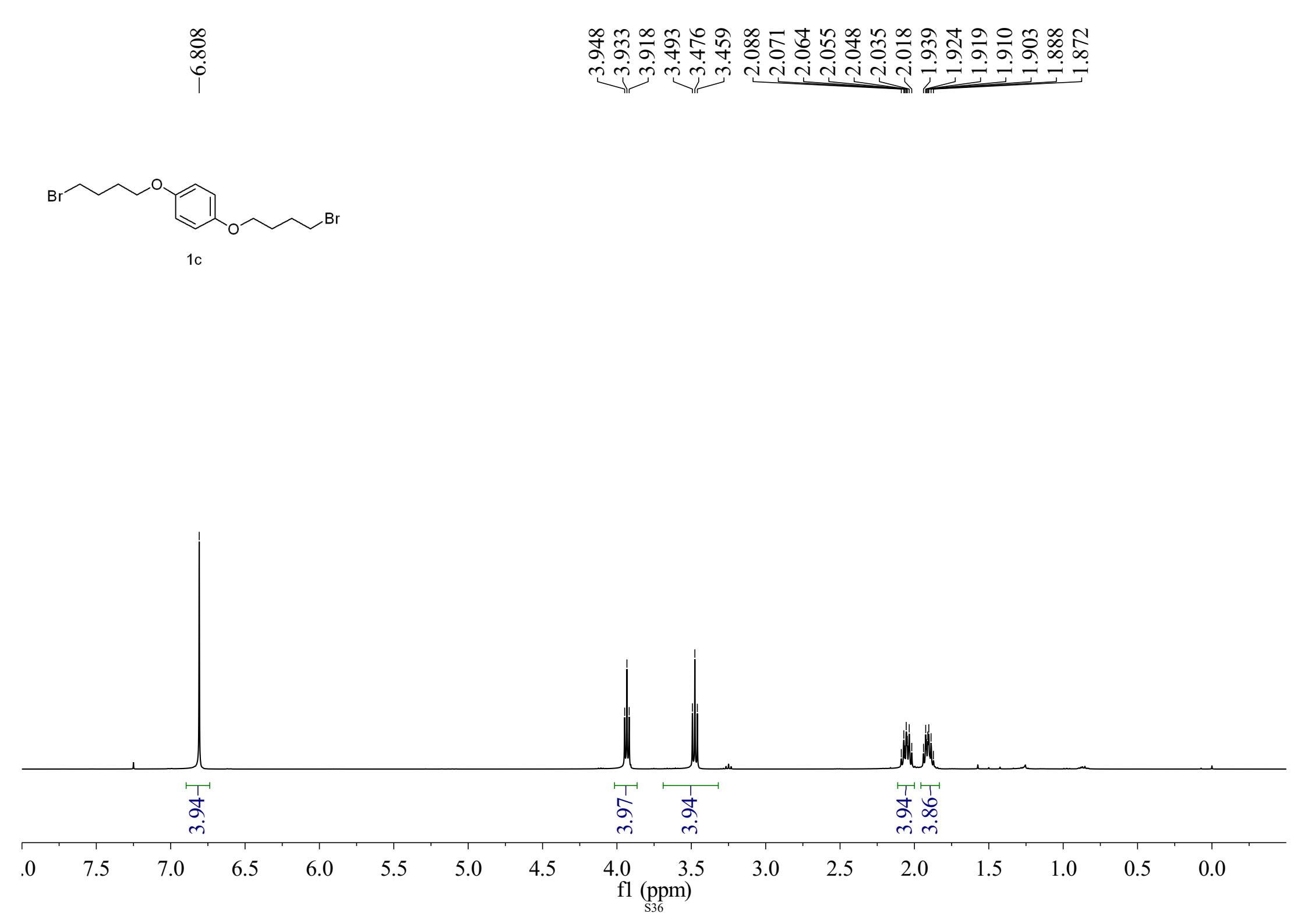
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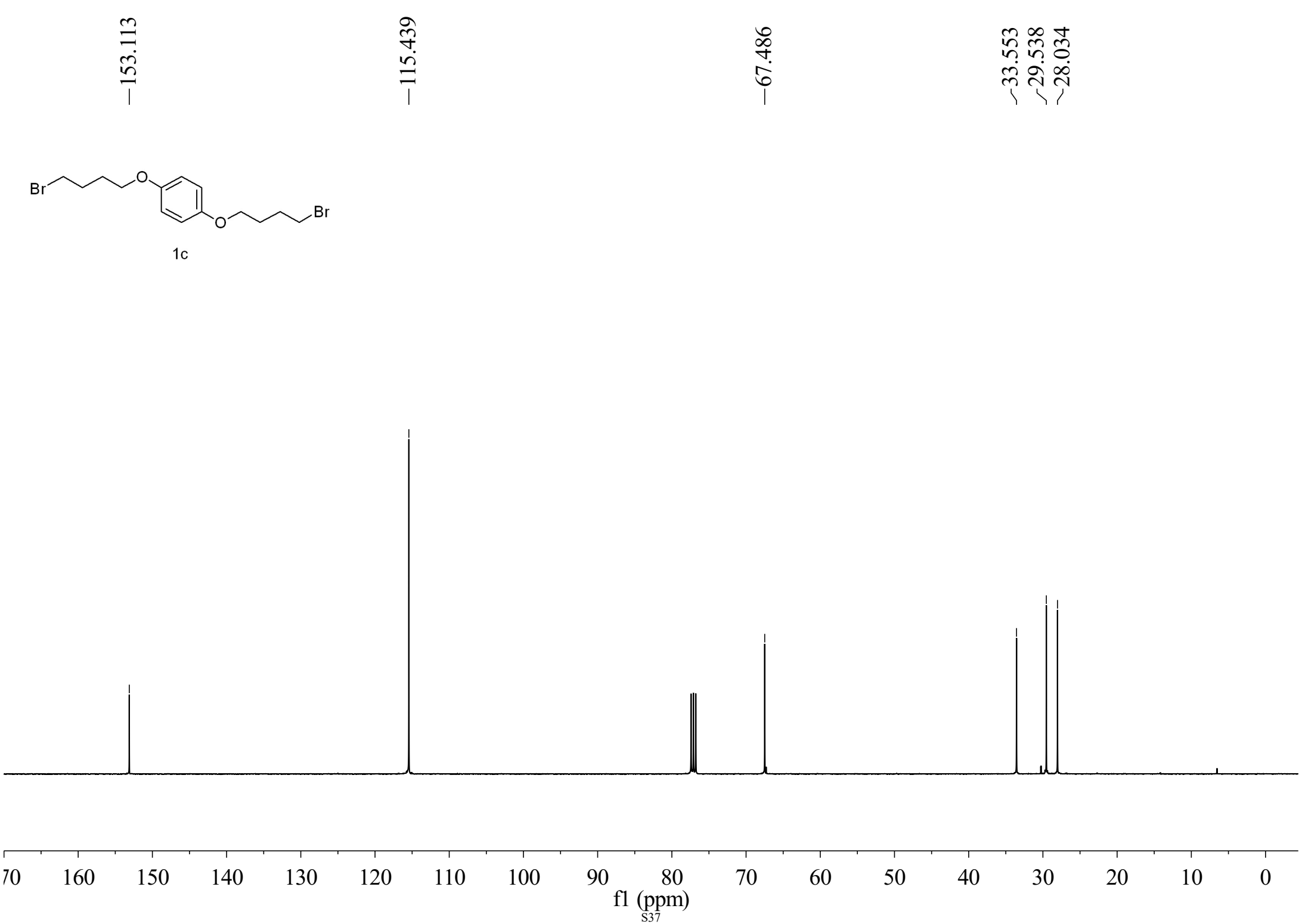
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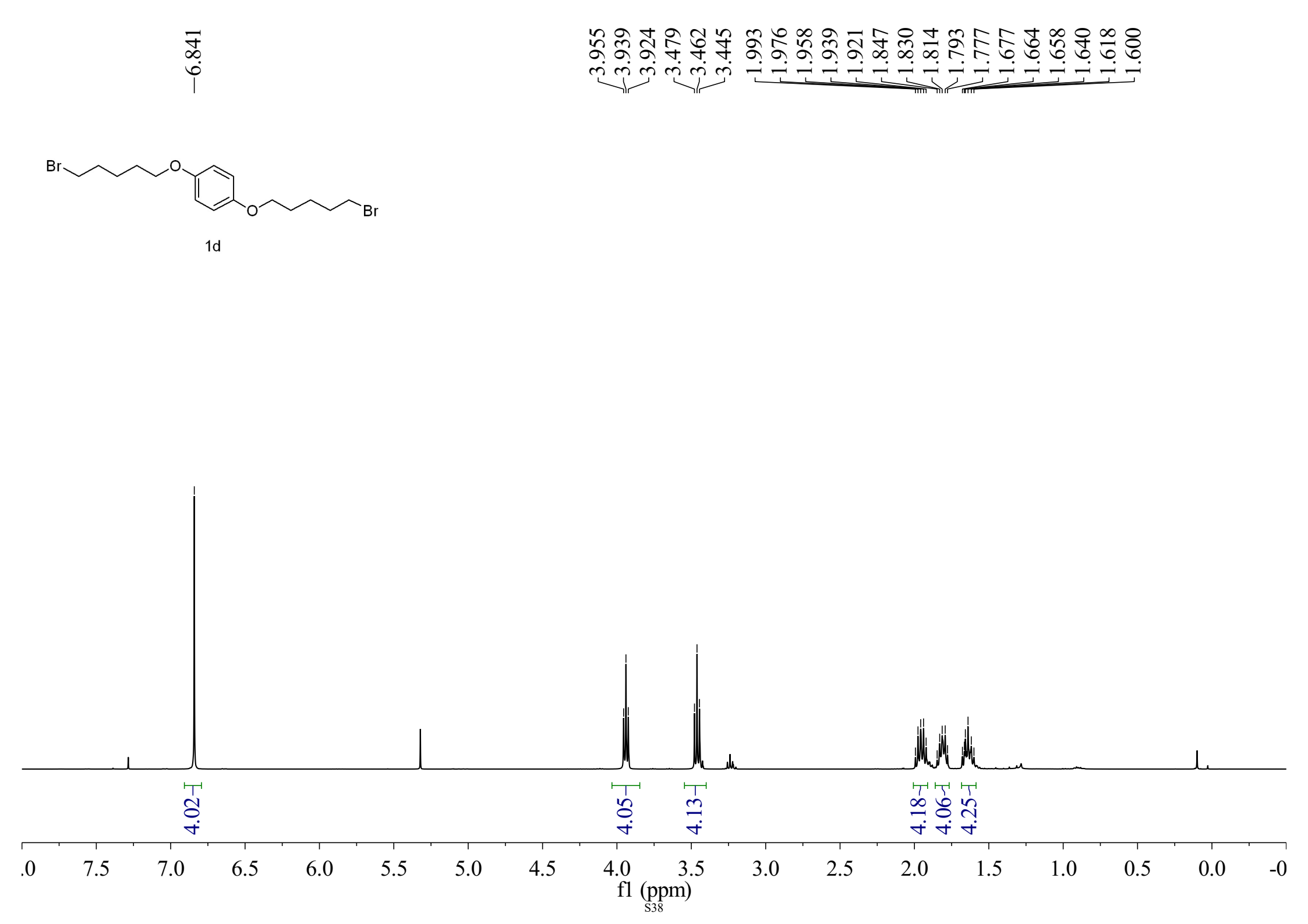
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1.814
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Br
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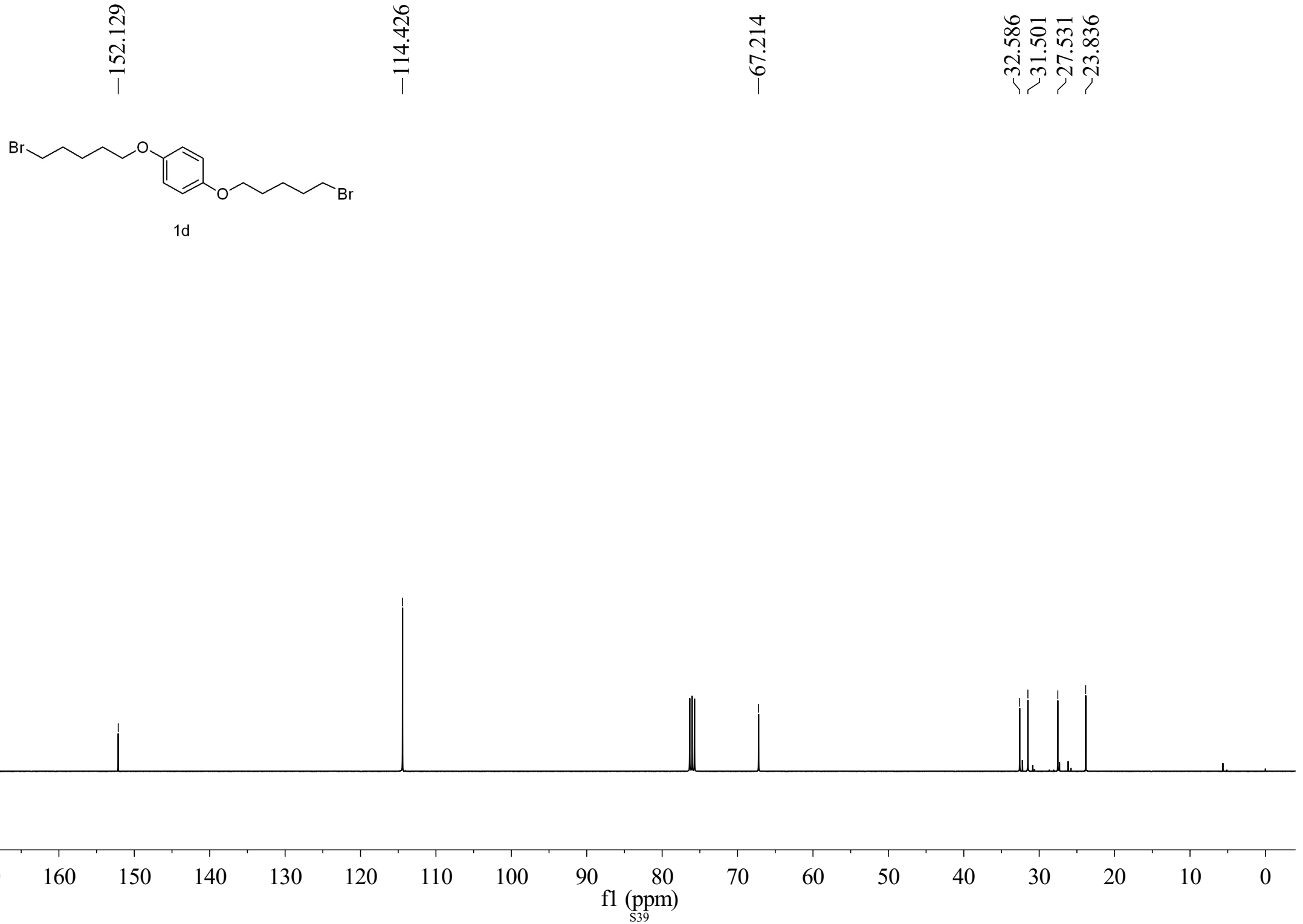
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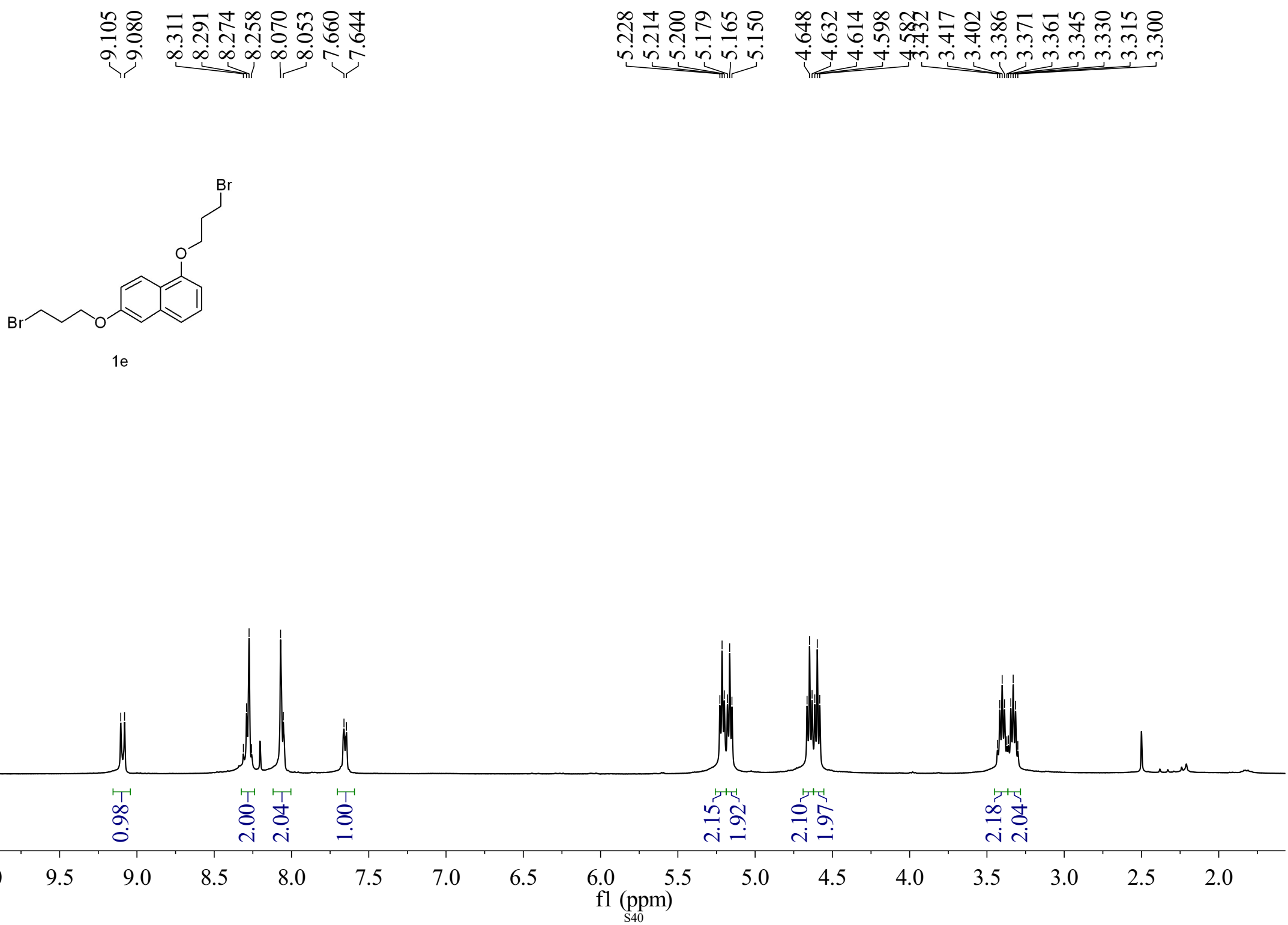
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3.345
3.330
3.315
3.300
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Br
O
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2.18
2.04
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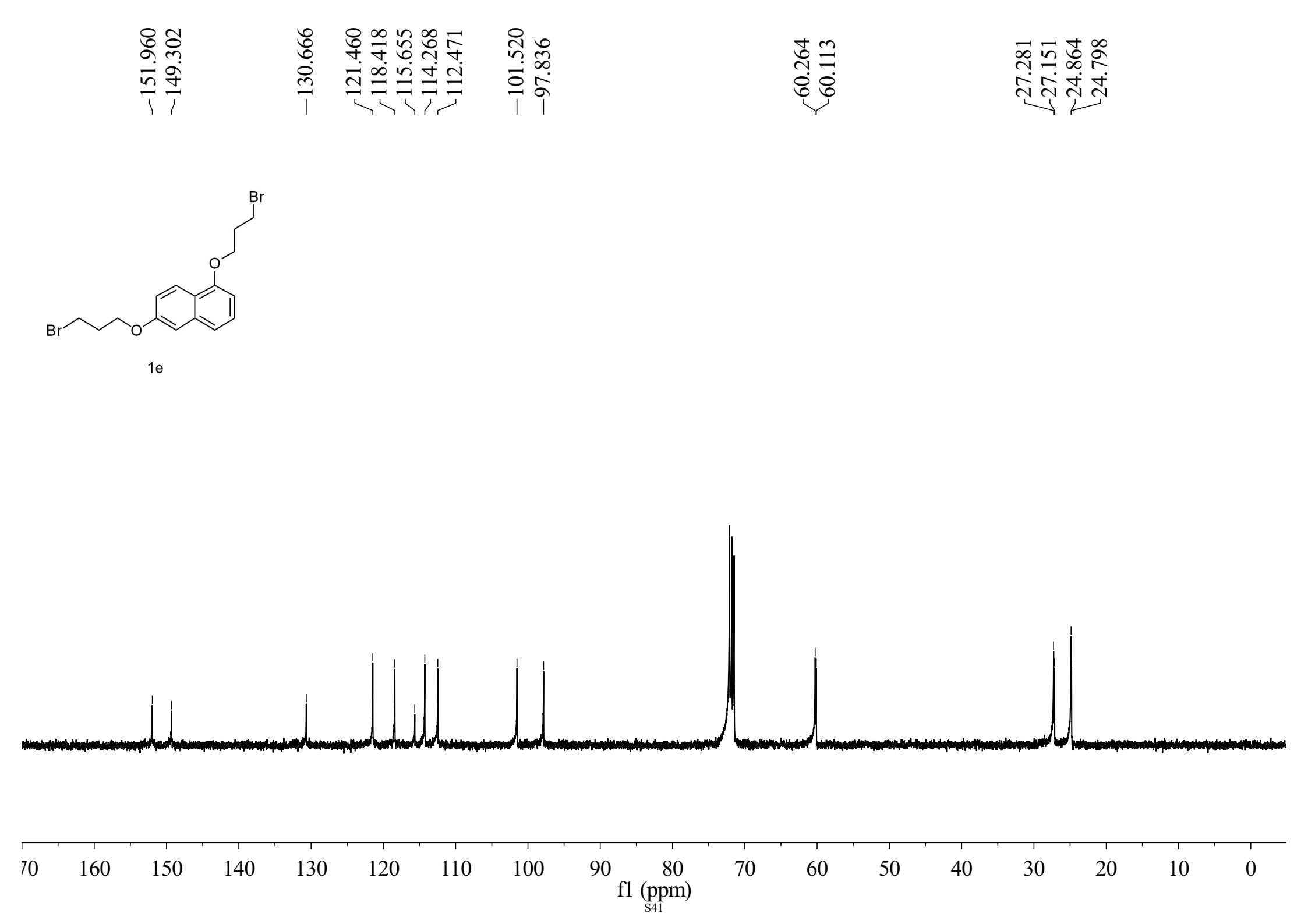
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27.151
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Br
O
1e
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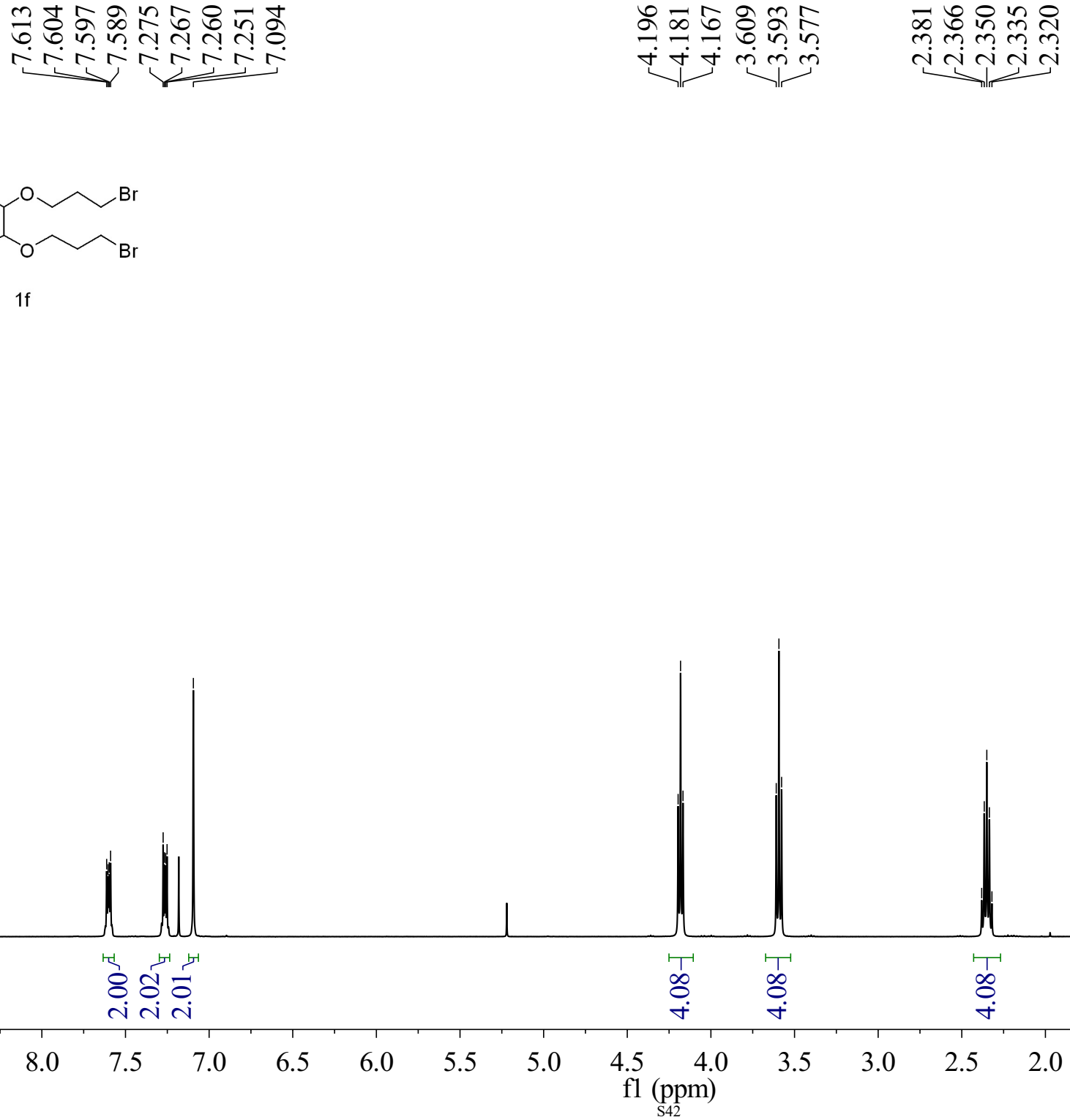
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O
Br
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2.01
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4.08
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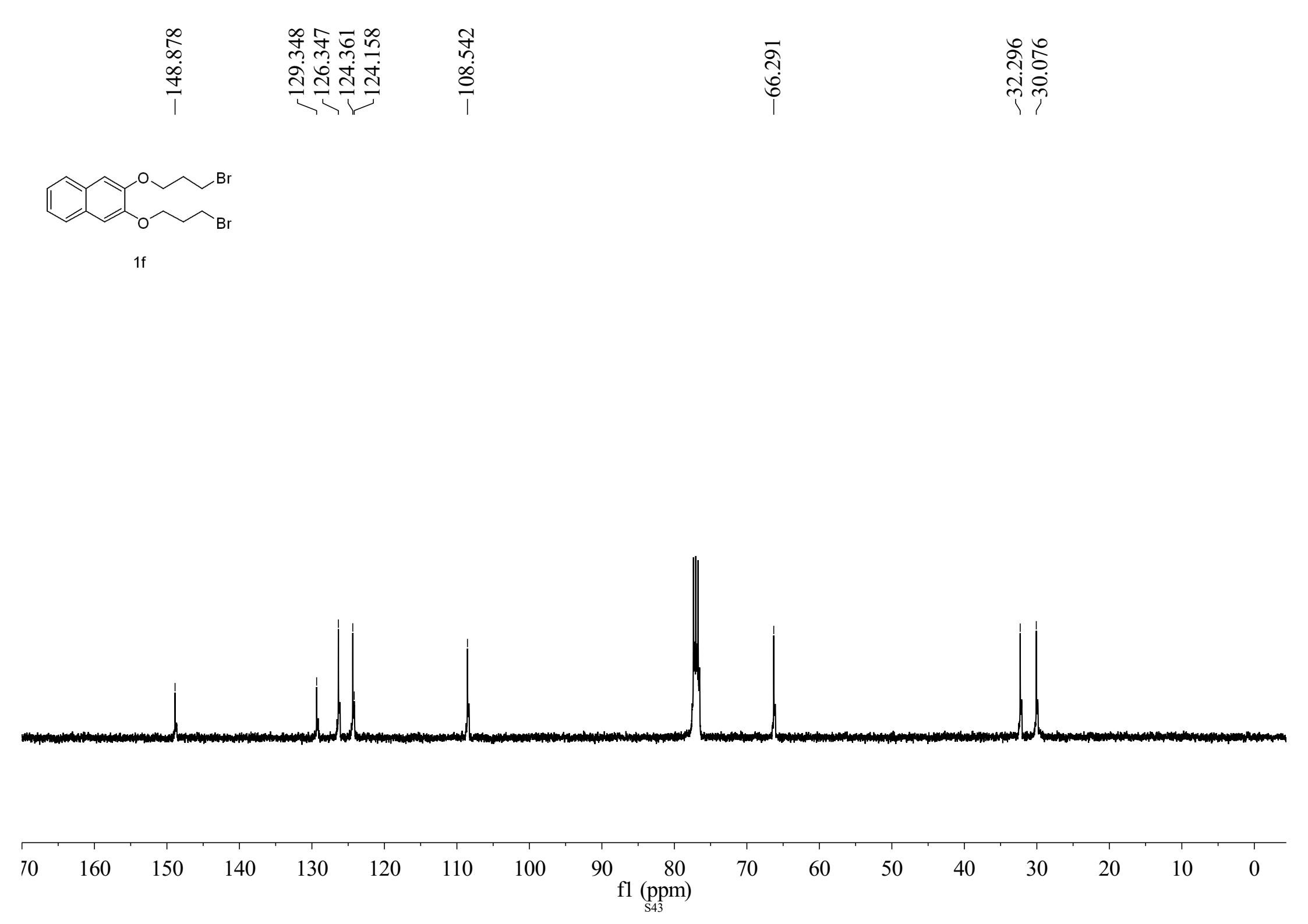
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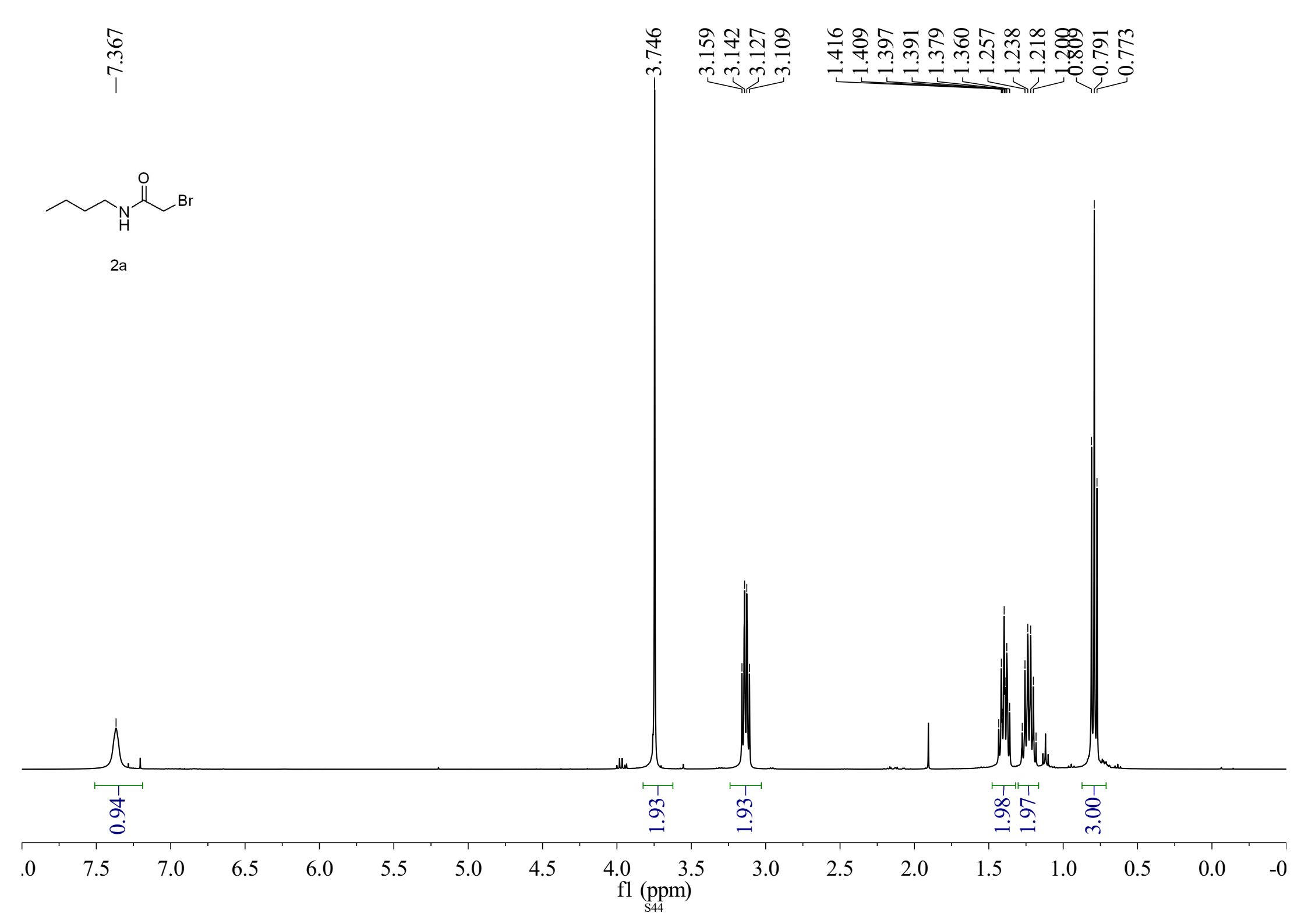
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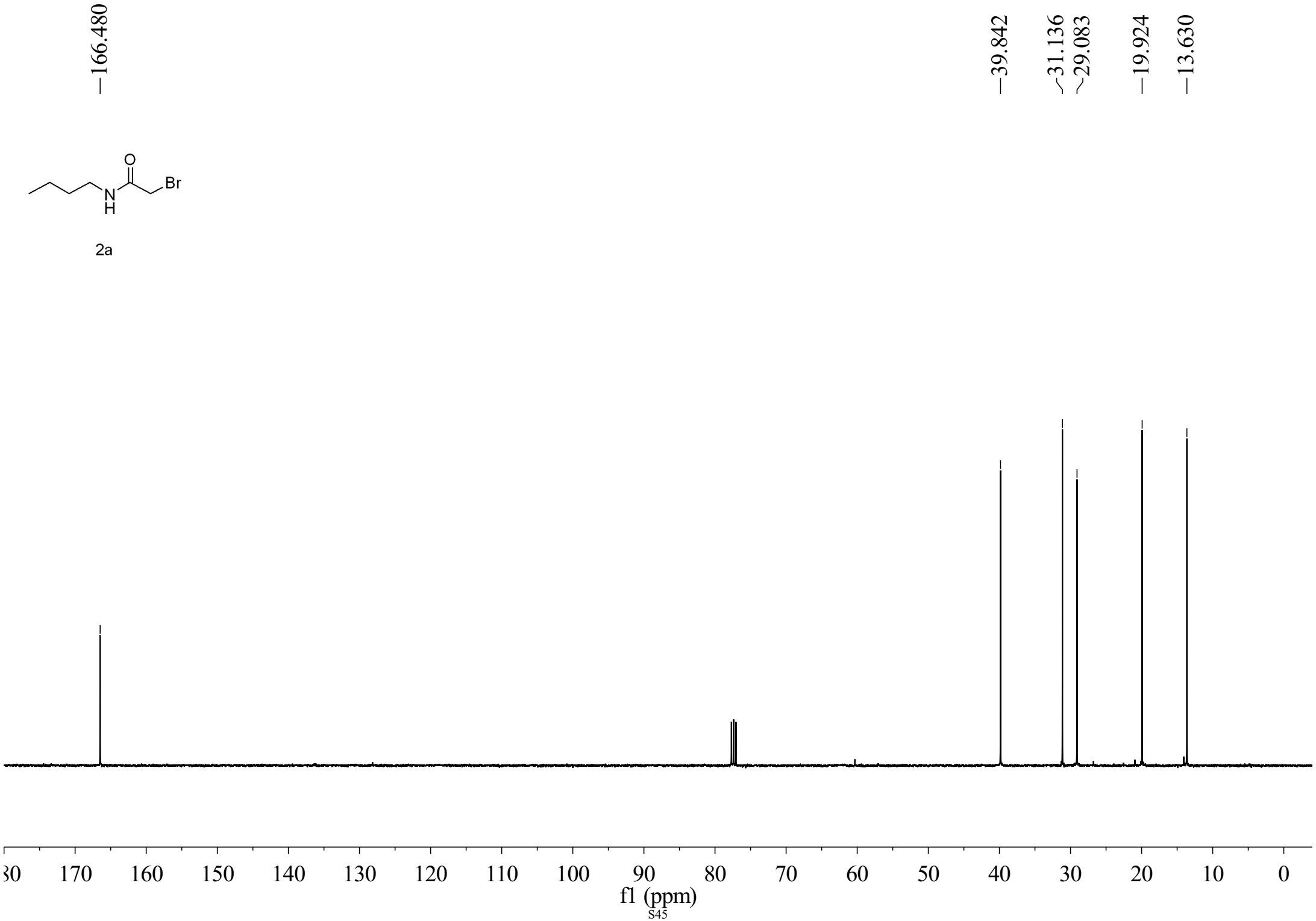
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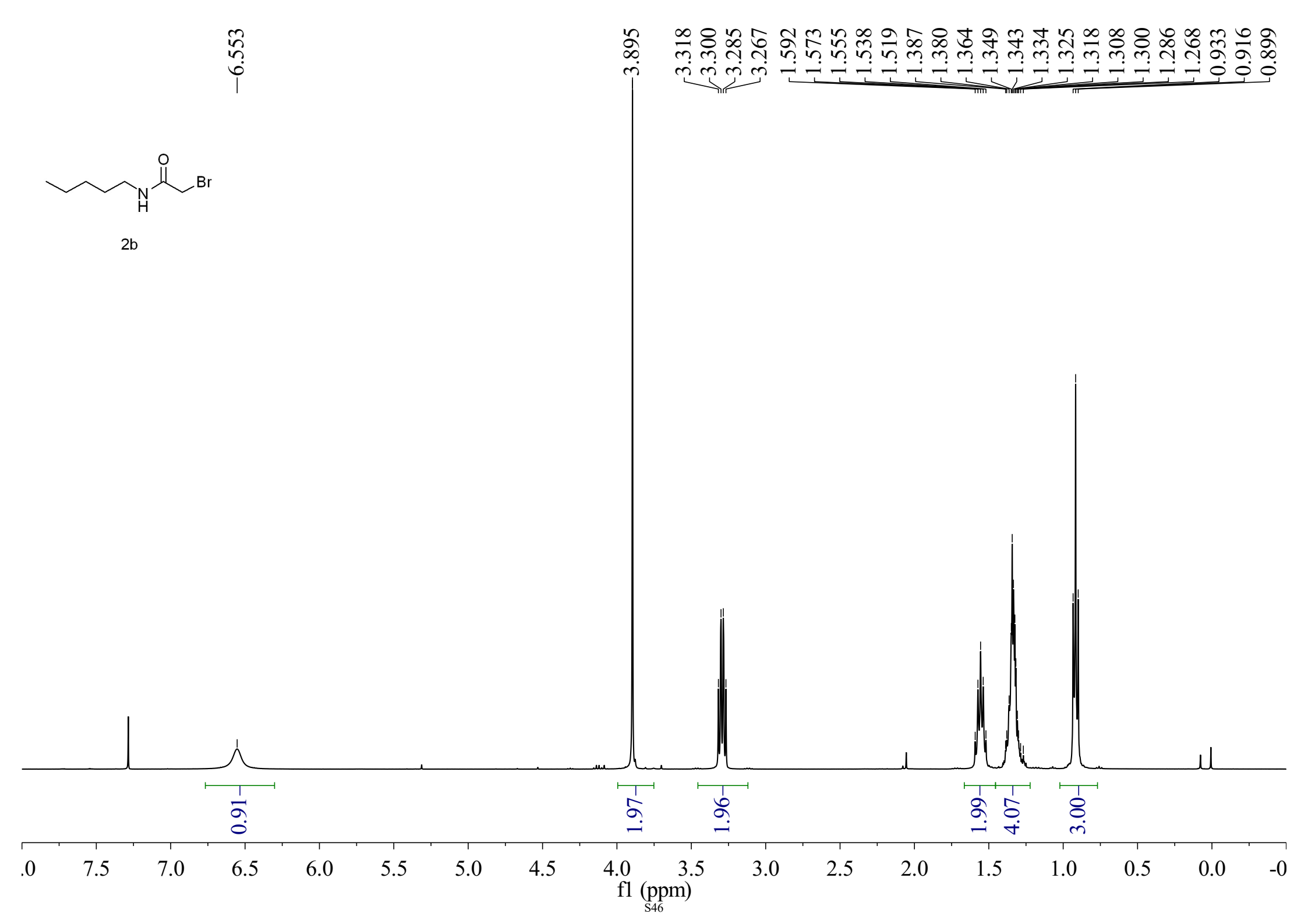
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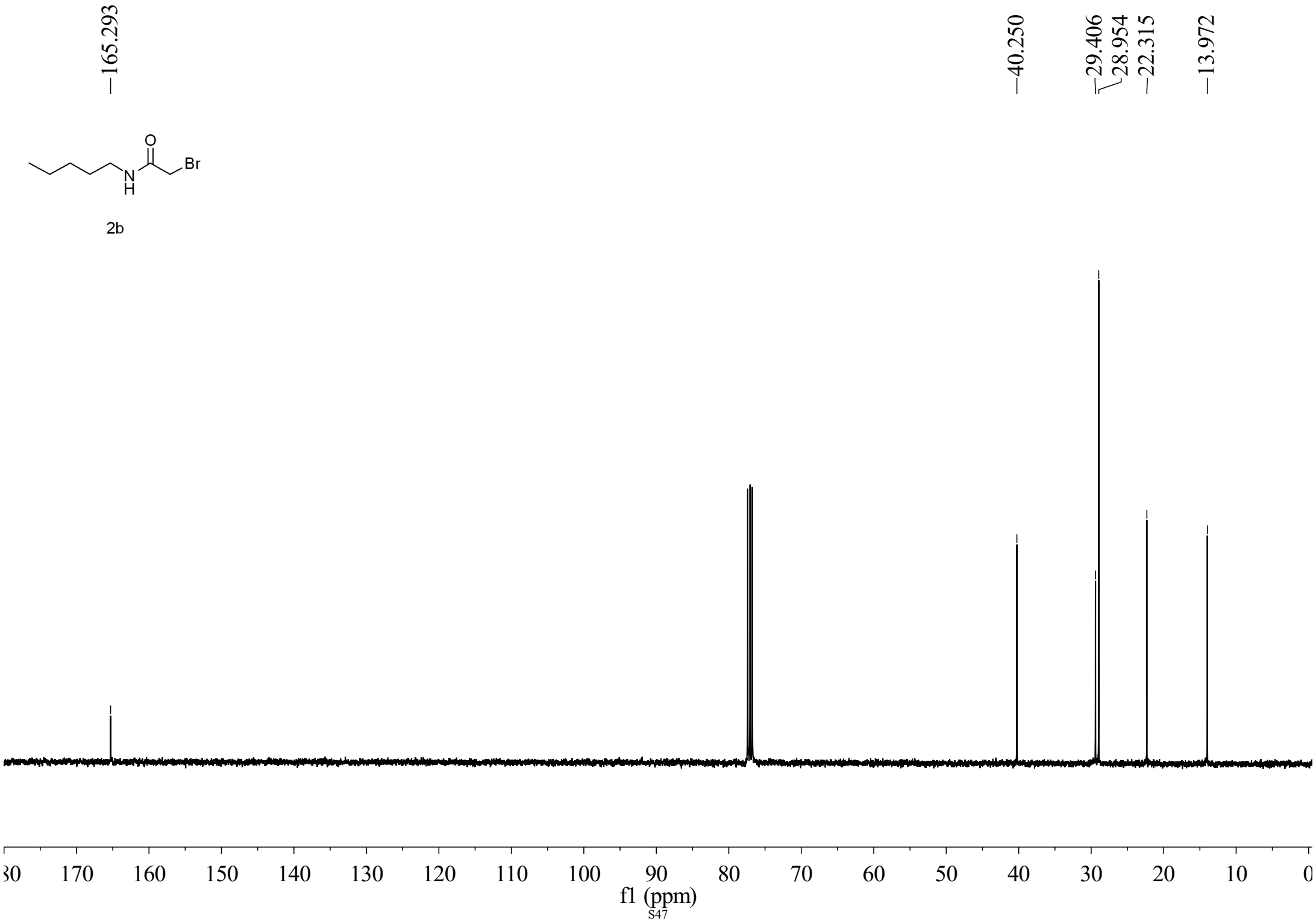
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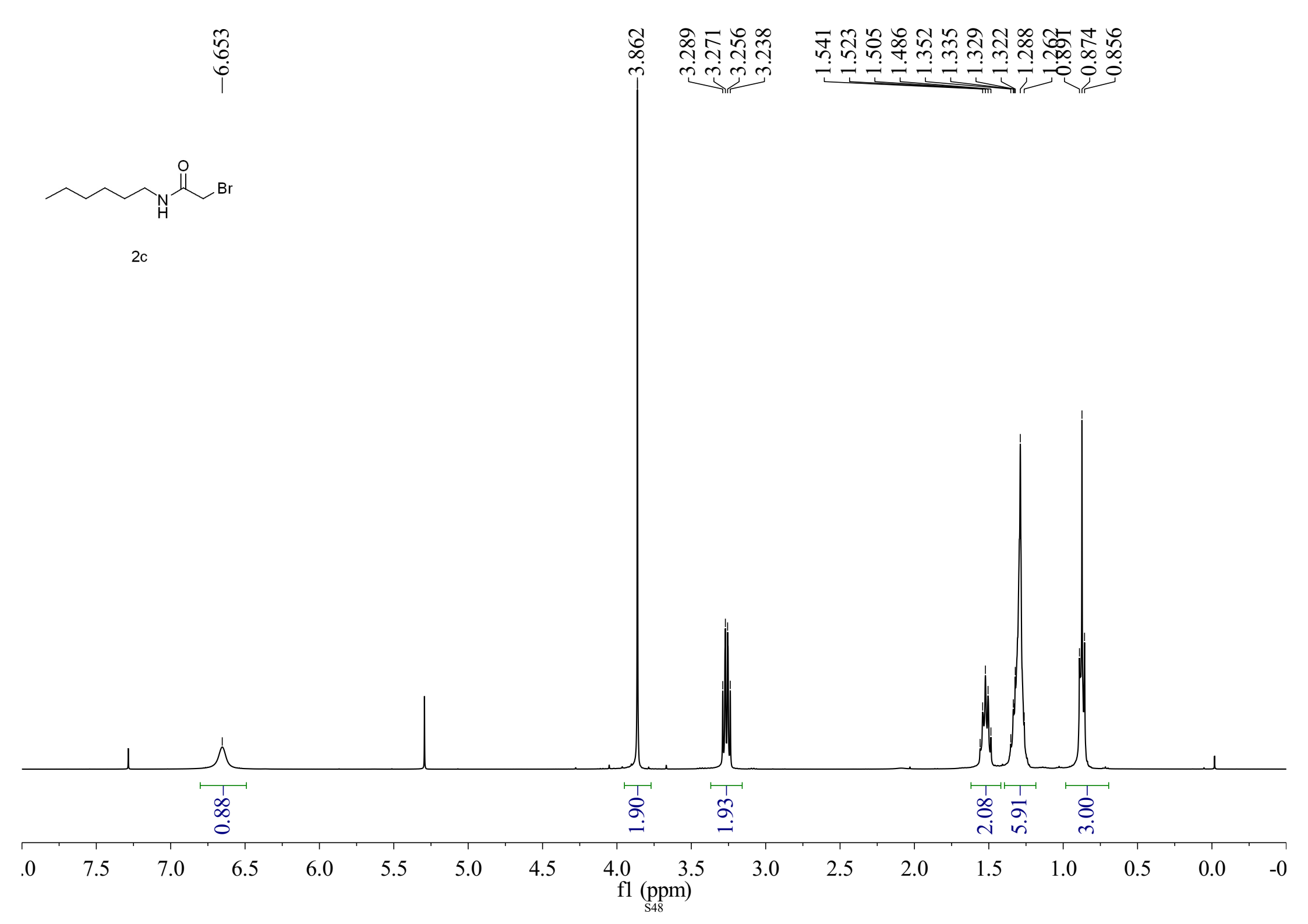
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H
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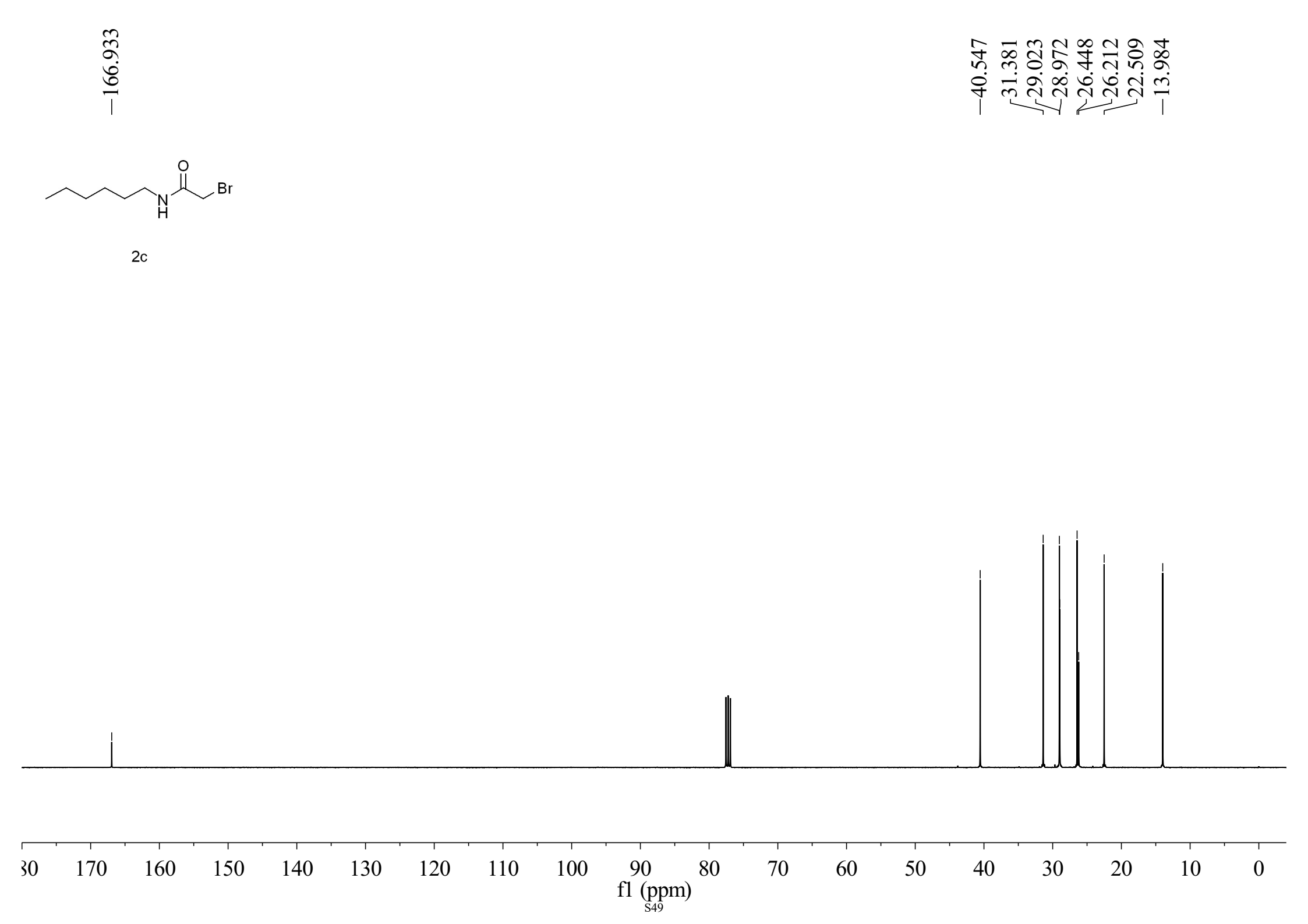
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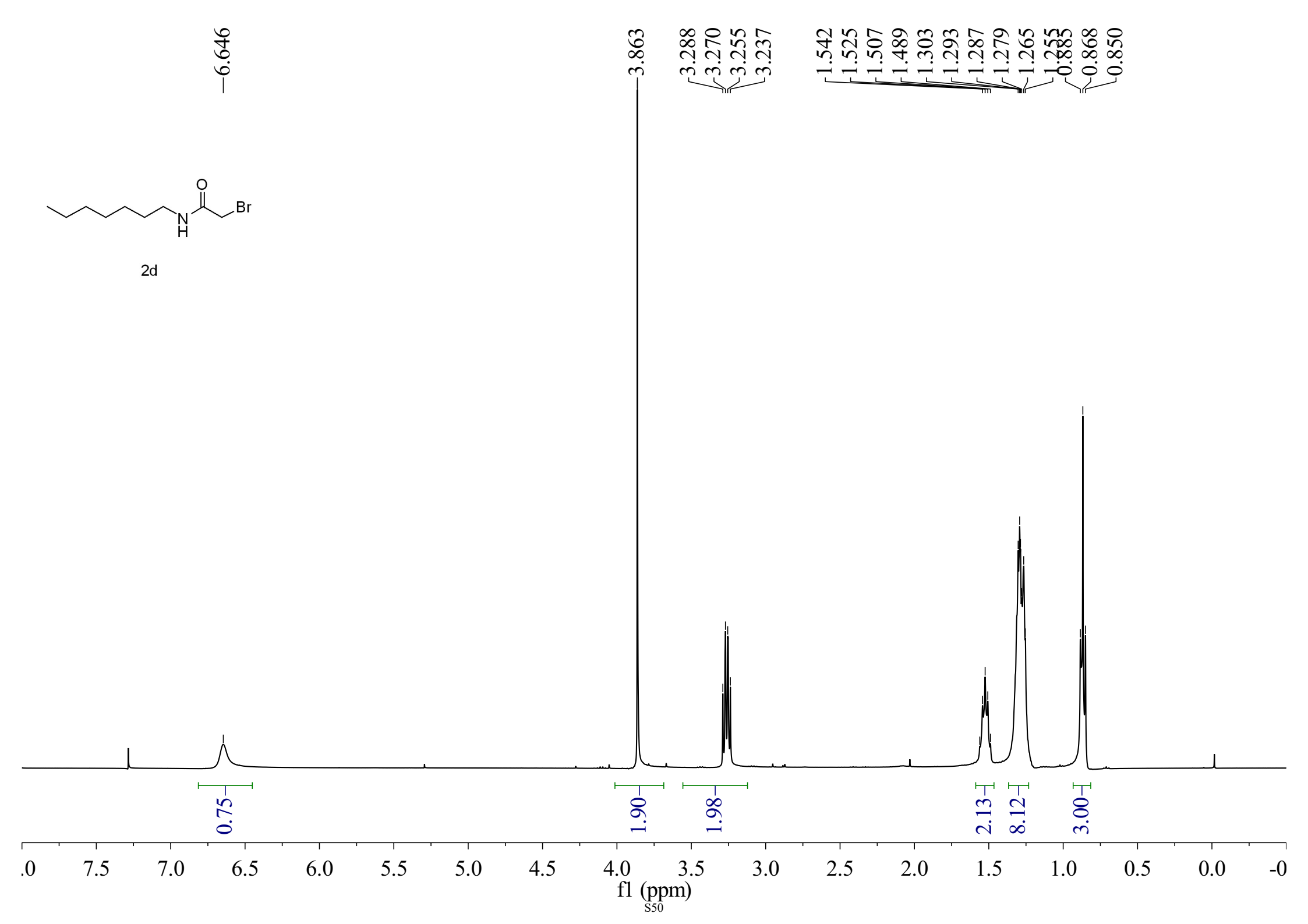
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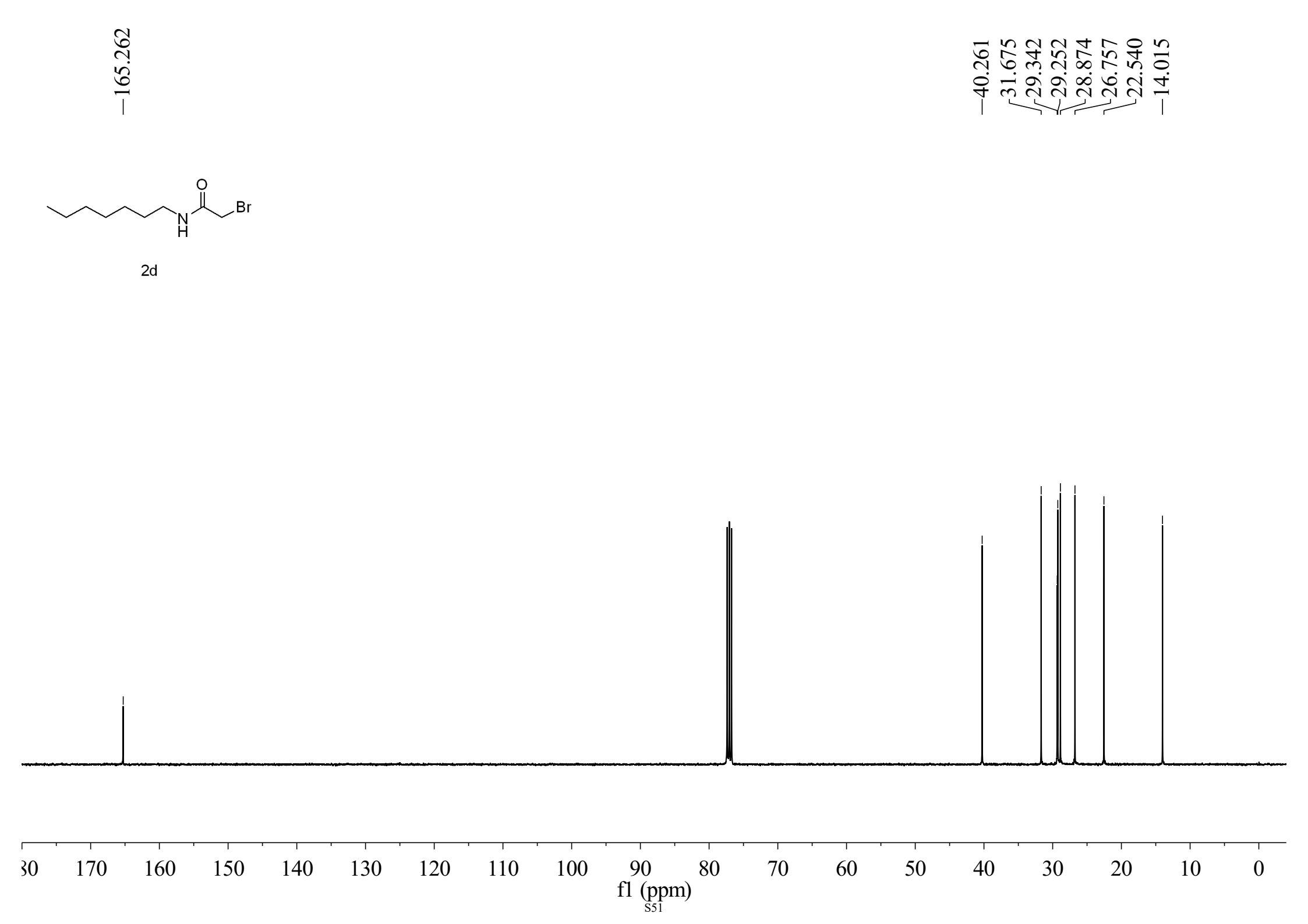
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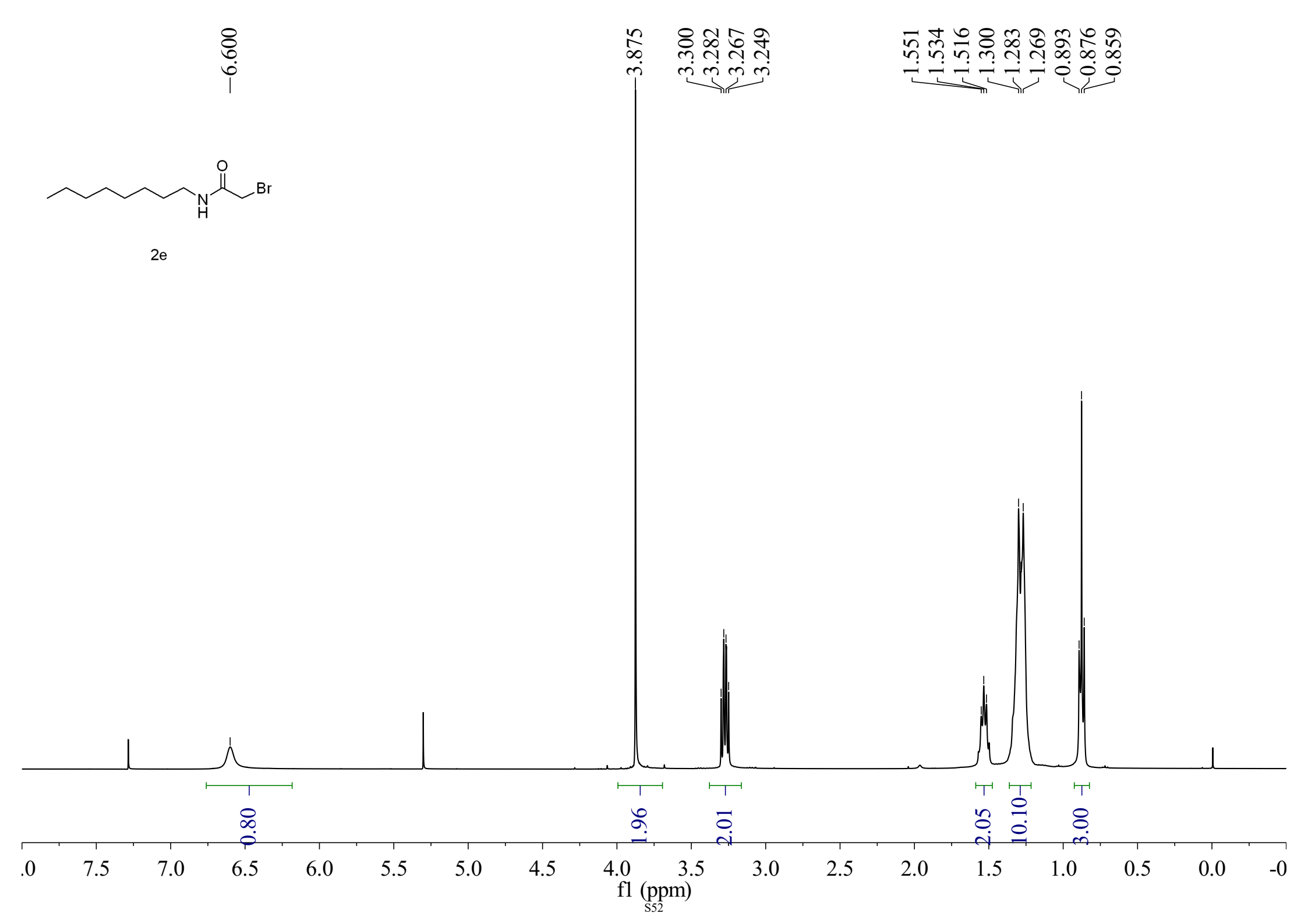
60
50
40
30
20
10
0
f1 (ppm)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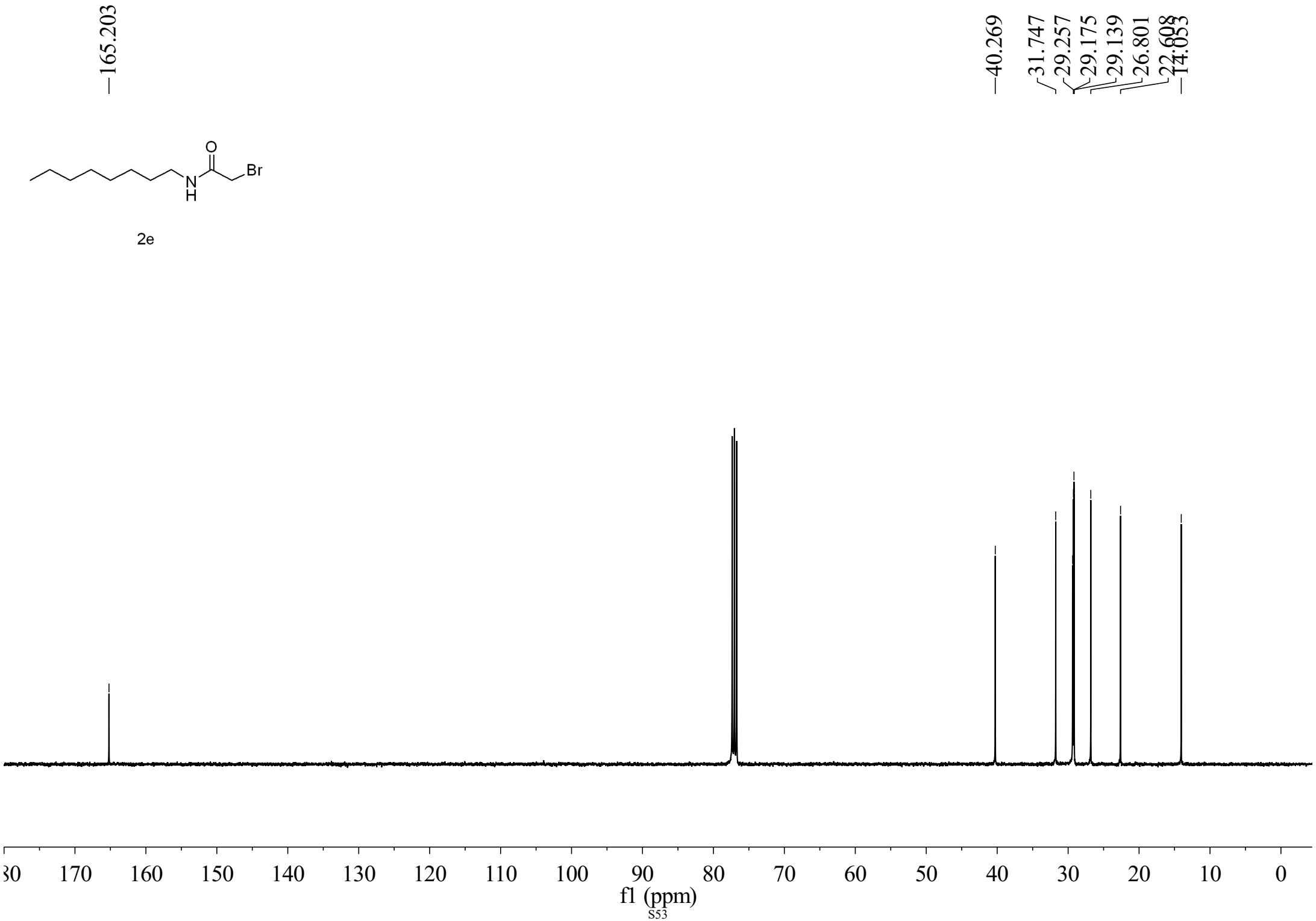
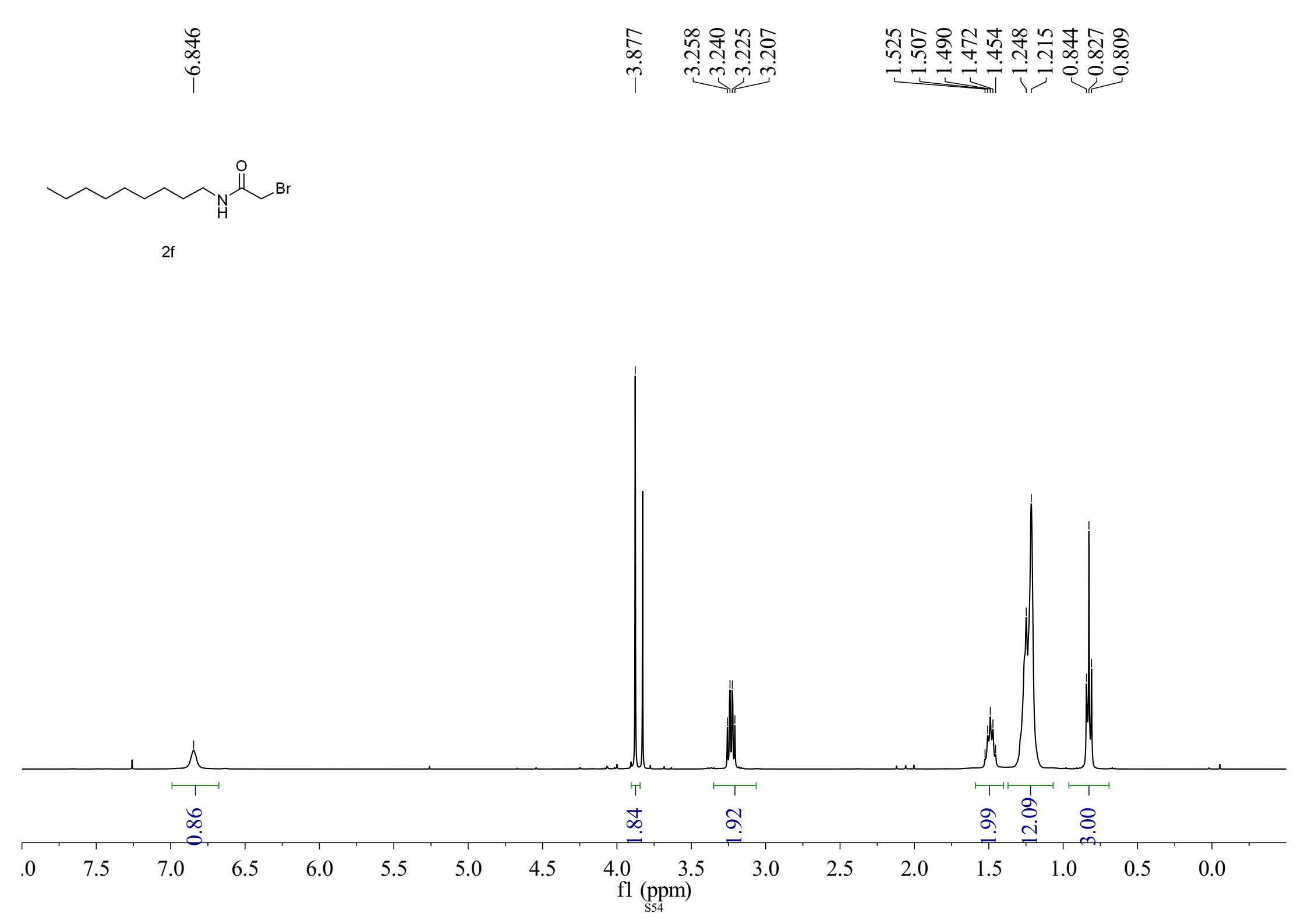
3.300
3.282
3.267
3.249
1.551
1.534
1.516
1.300
1.283
1.269
0.893
0.876
0.859
O
Br
N
H
2e
0.80
1.96
2.01
2.05
10.10
3.00
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


165.203
40.269
31.747
29.257
29.175
29.139
26.801
22.608
14.053
O
Br
N
H
2e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


6.846
3.877
3.258
3.240
3.225
3.207
1.525
1.507
1.490
1.472
1.454
1.248
1.215
0.844
0.827
0.809
O
Br
N
H
2f
0.86
1.84
1.92
1.99
12.09
3.00
.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
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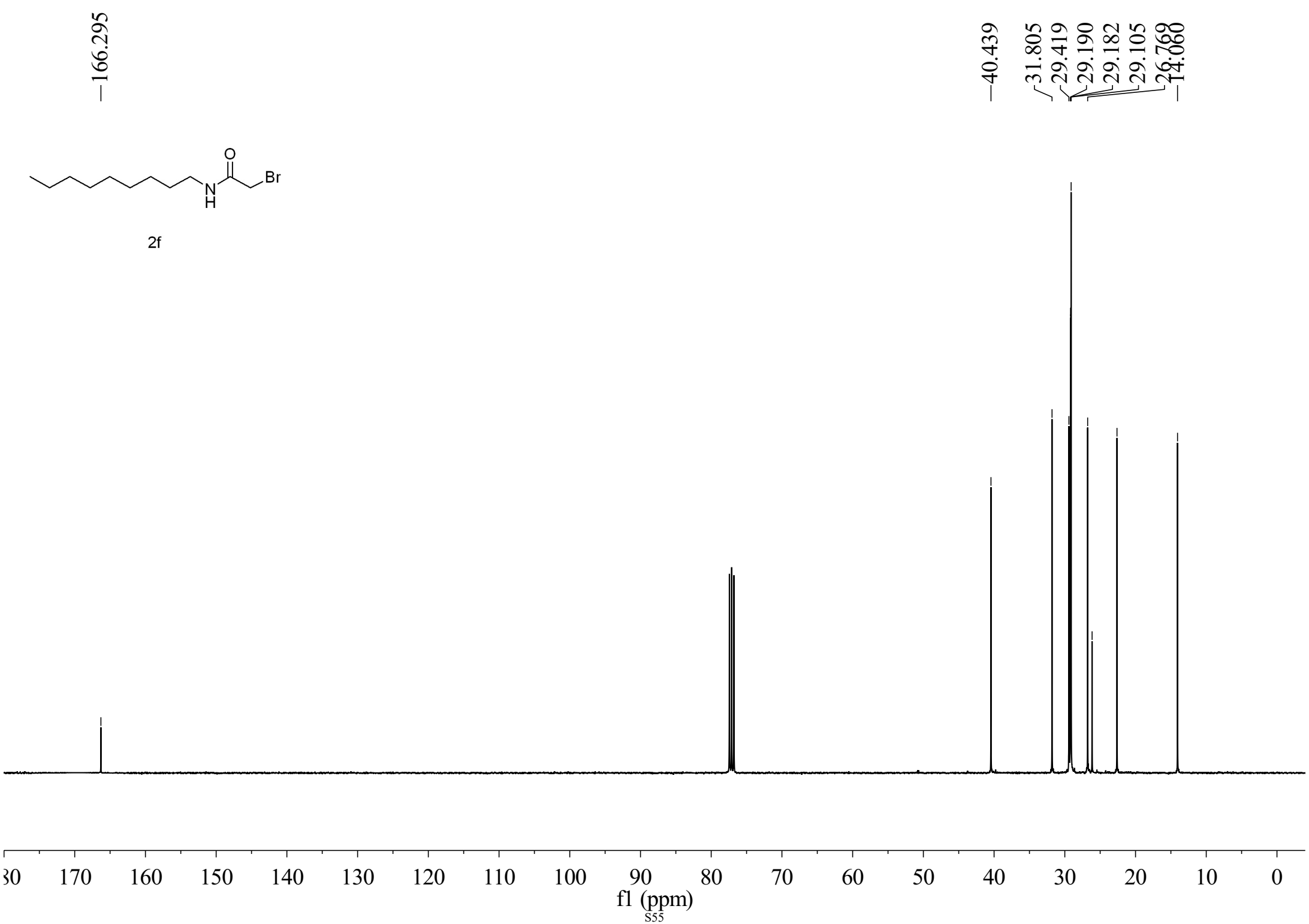
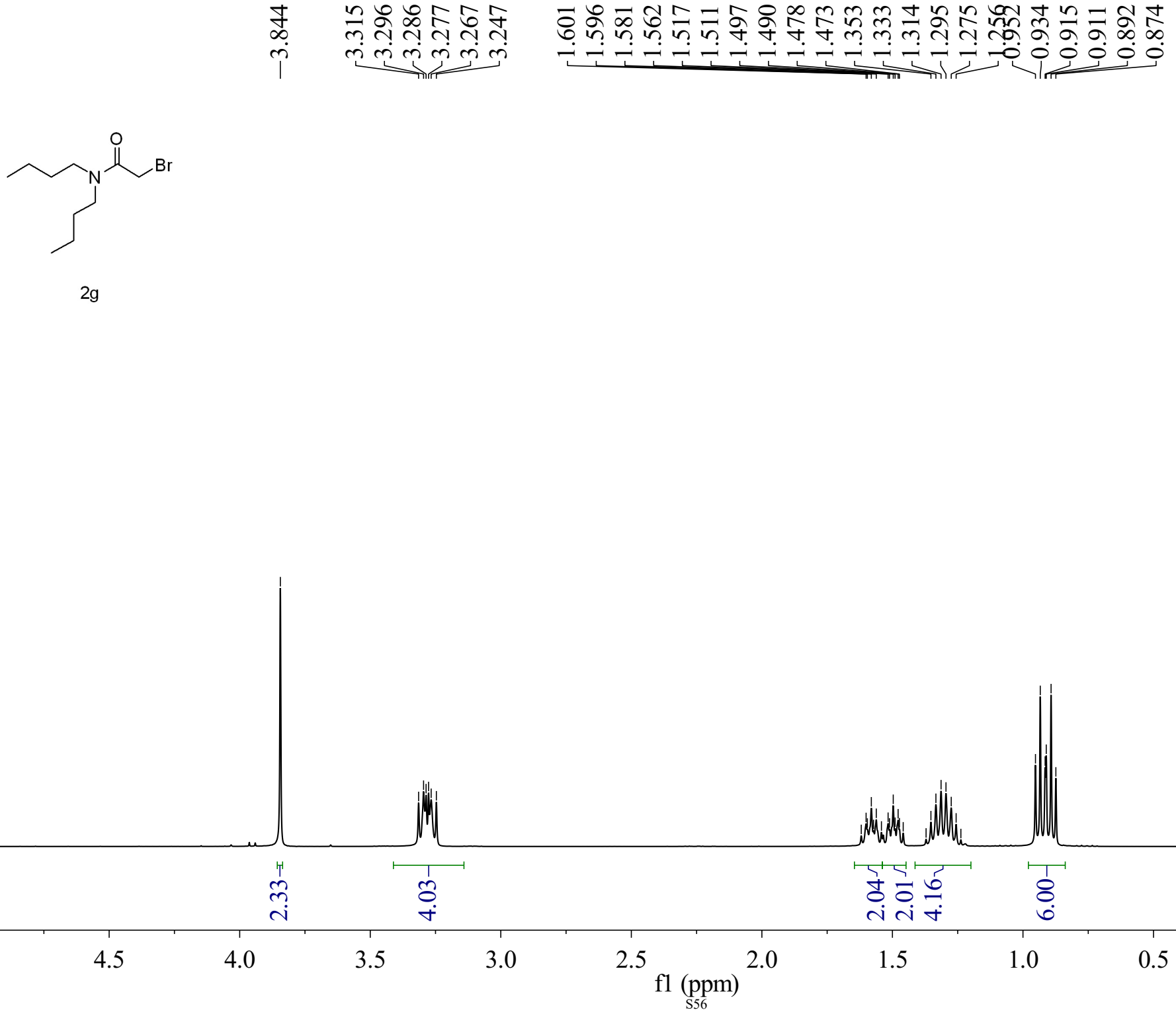
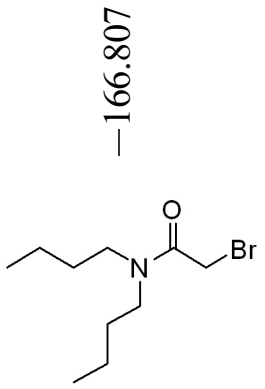
0.0
f1 (ppm)


166.295
40.439
31.805
29.419
29.190
29.182
29.105
26.769
14.080
O
N
H
Br
2f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3.844
3.315
3.296
3.286
3.277
3.267
3.247
1.601
1.596
1.581
1.562
1.517
1.511
1.497
1.490
1.478
1.473
1.353
1.333
1.314
1.295
1.275
0.952
0.934
0.915
0.911
0.892
0.874
O
N
Br
2g
2.33
4.03
2.04
2.01
4.16
6.00
.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

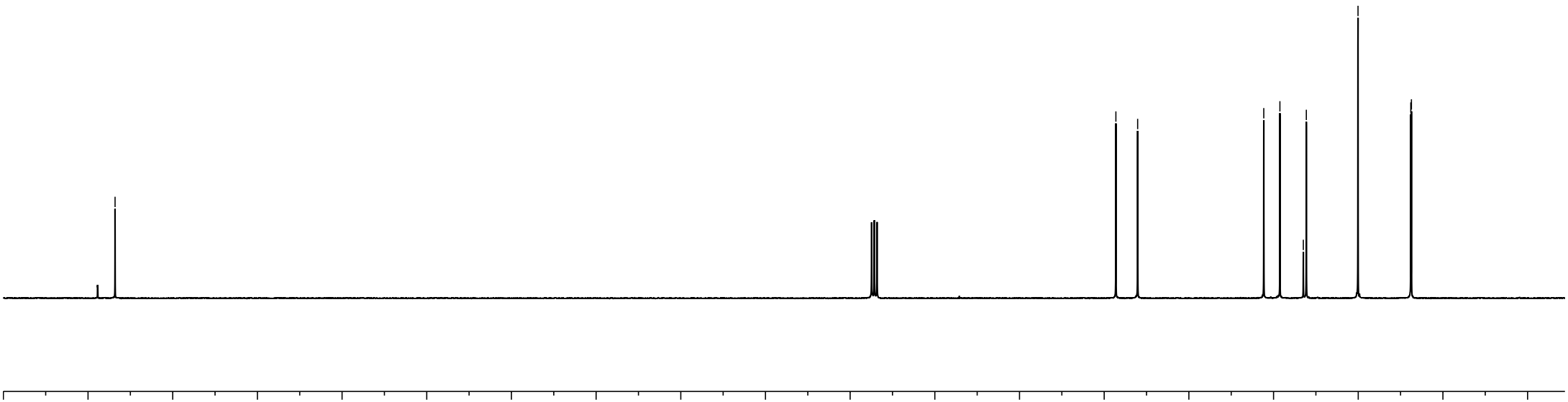


2g

166.807

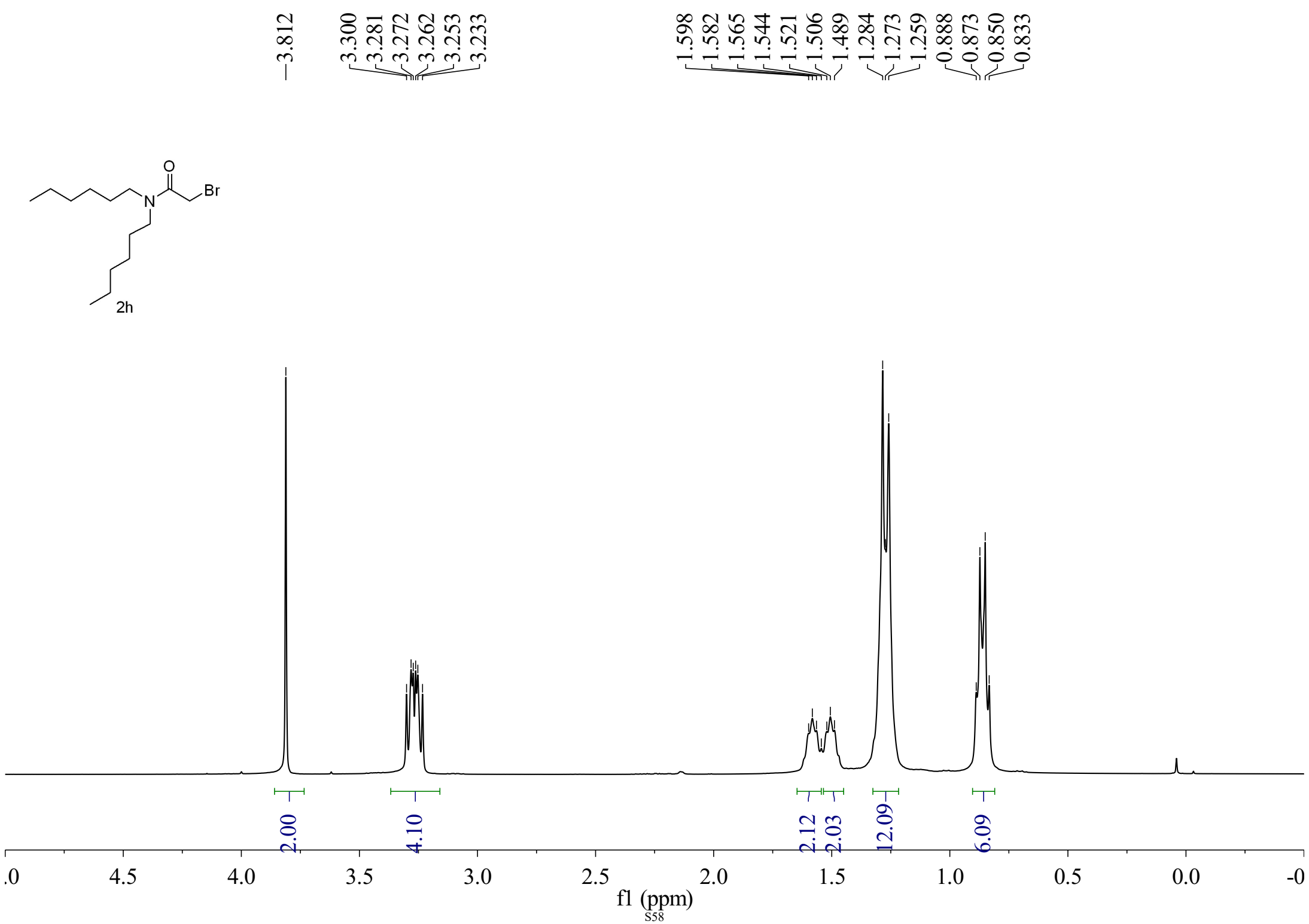
48.618
46.049

31.153
29.249
26.483
26.128
20.026
13.794
13.718



30 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)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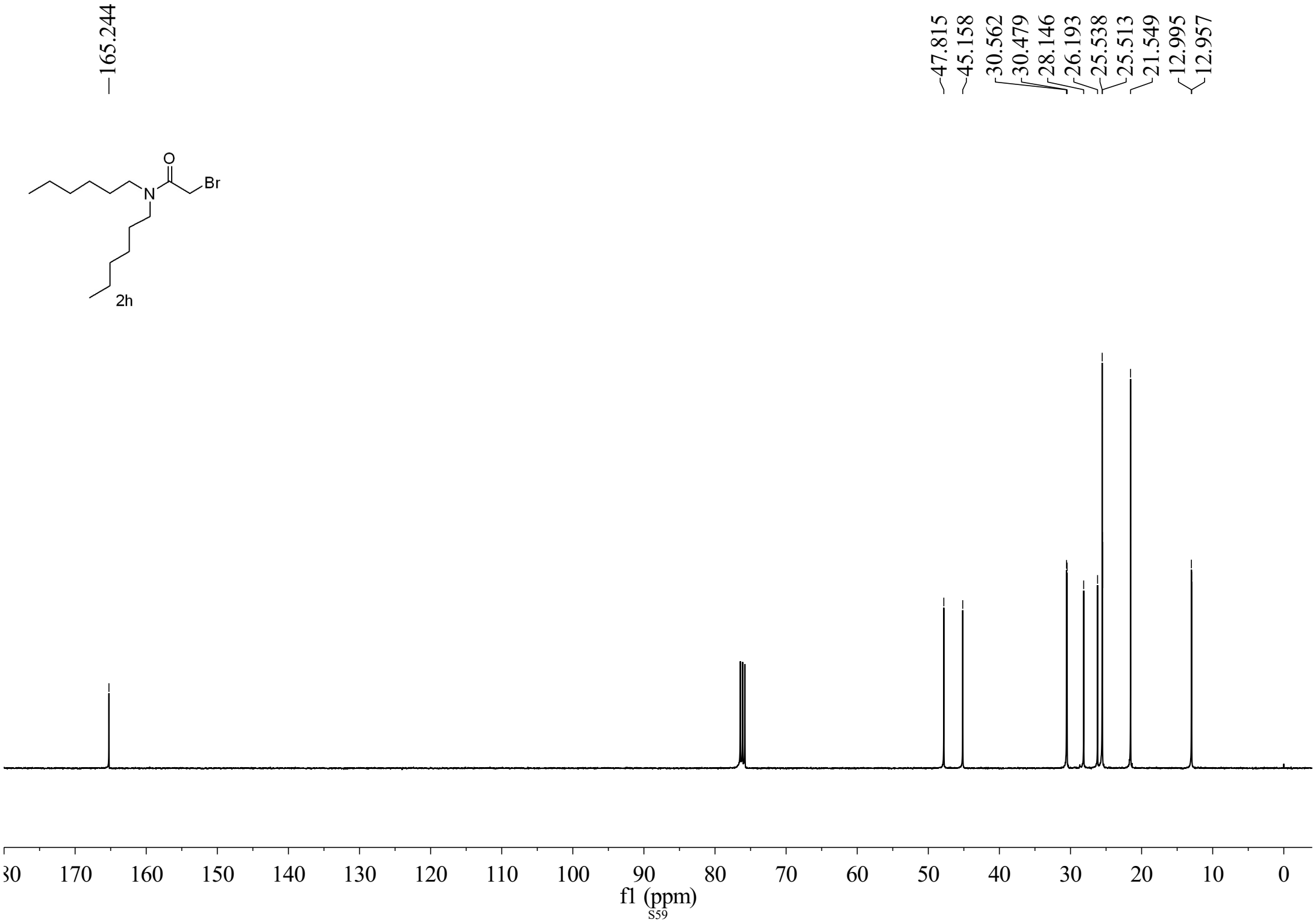
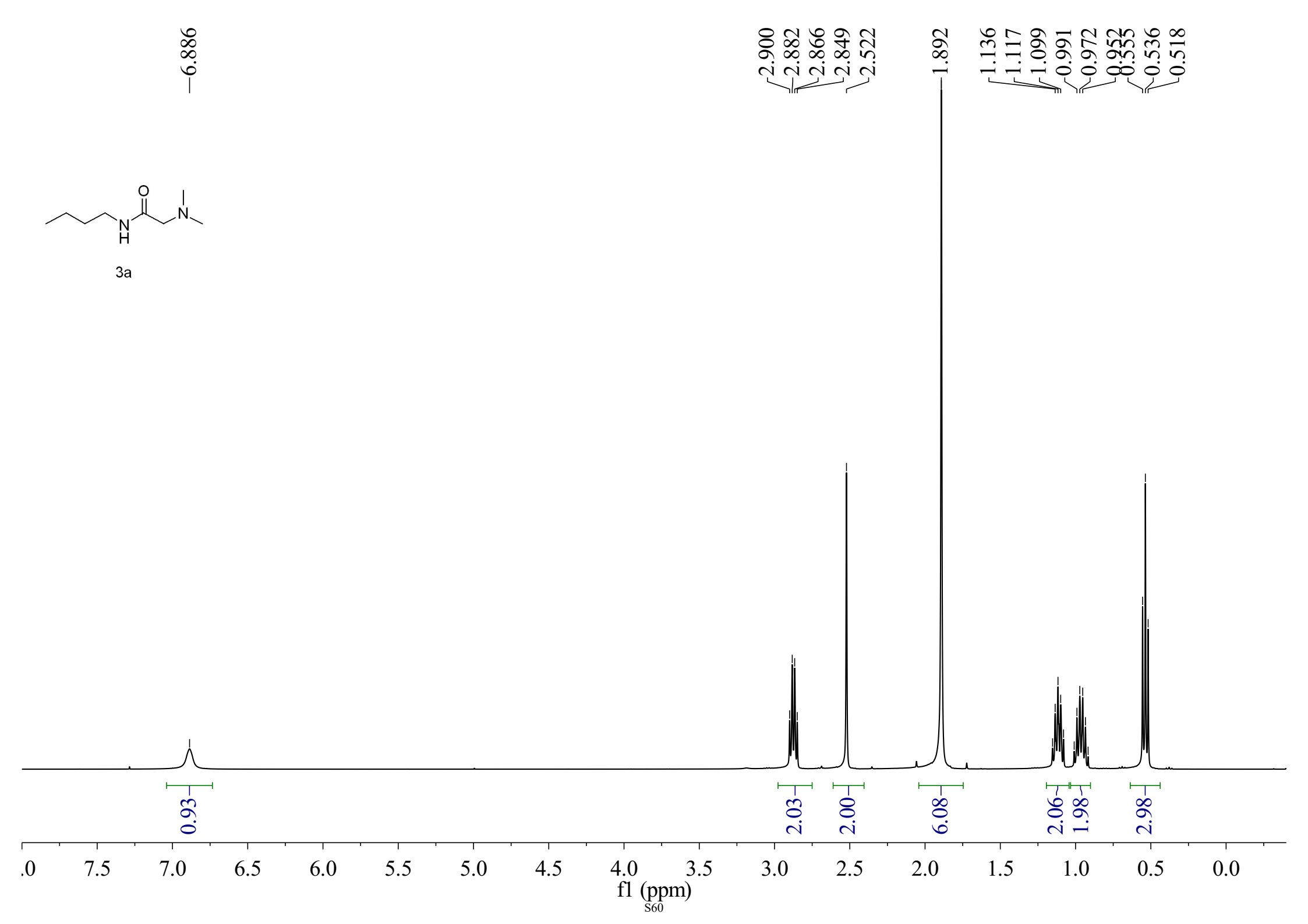
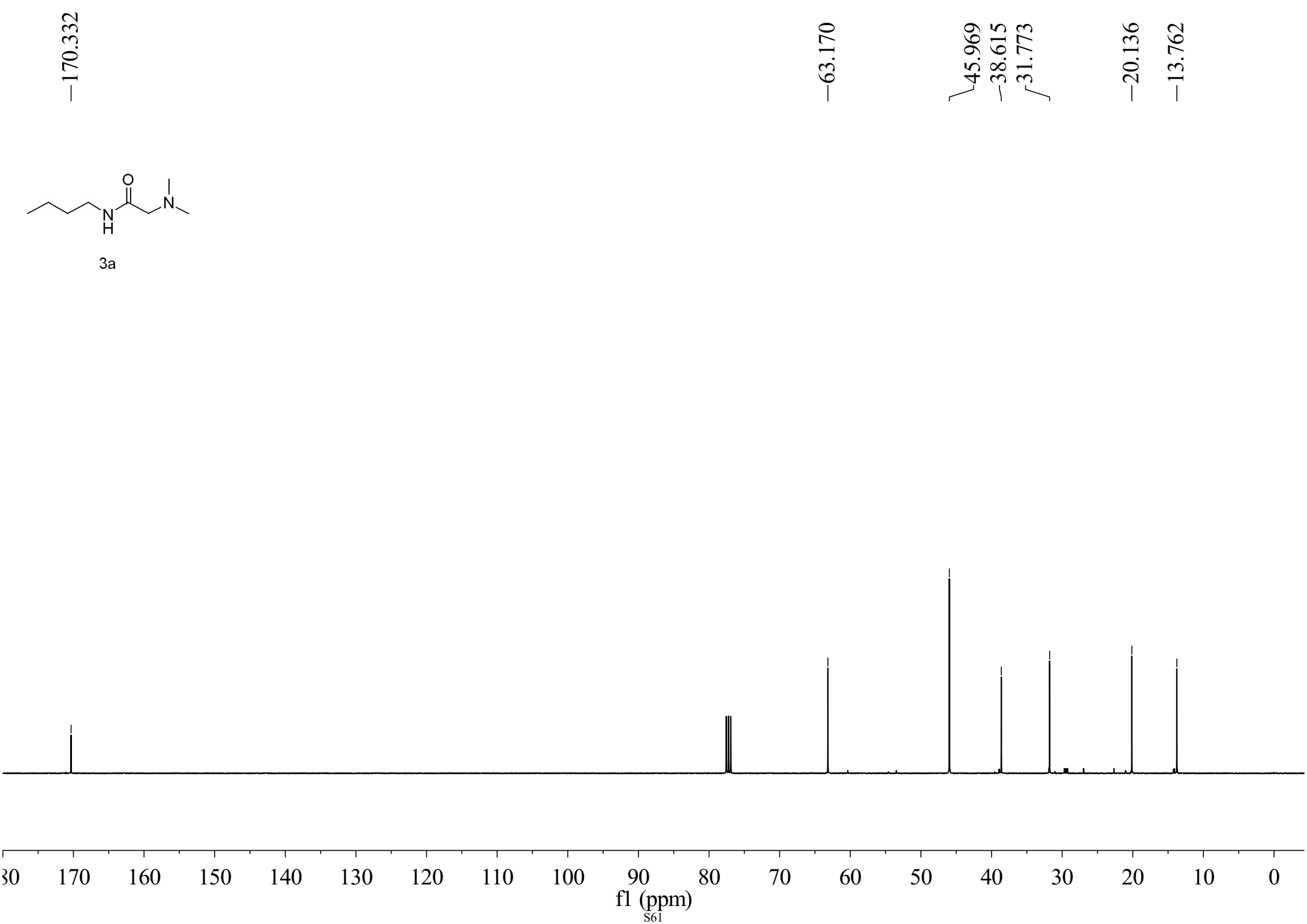
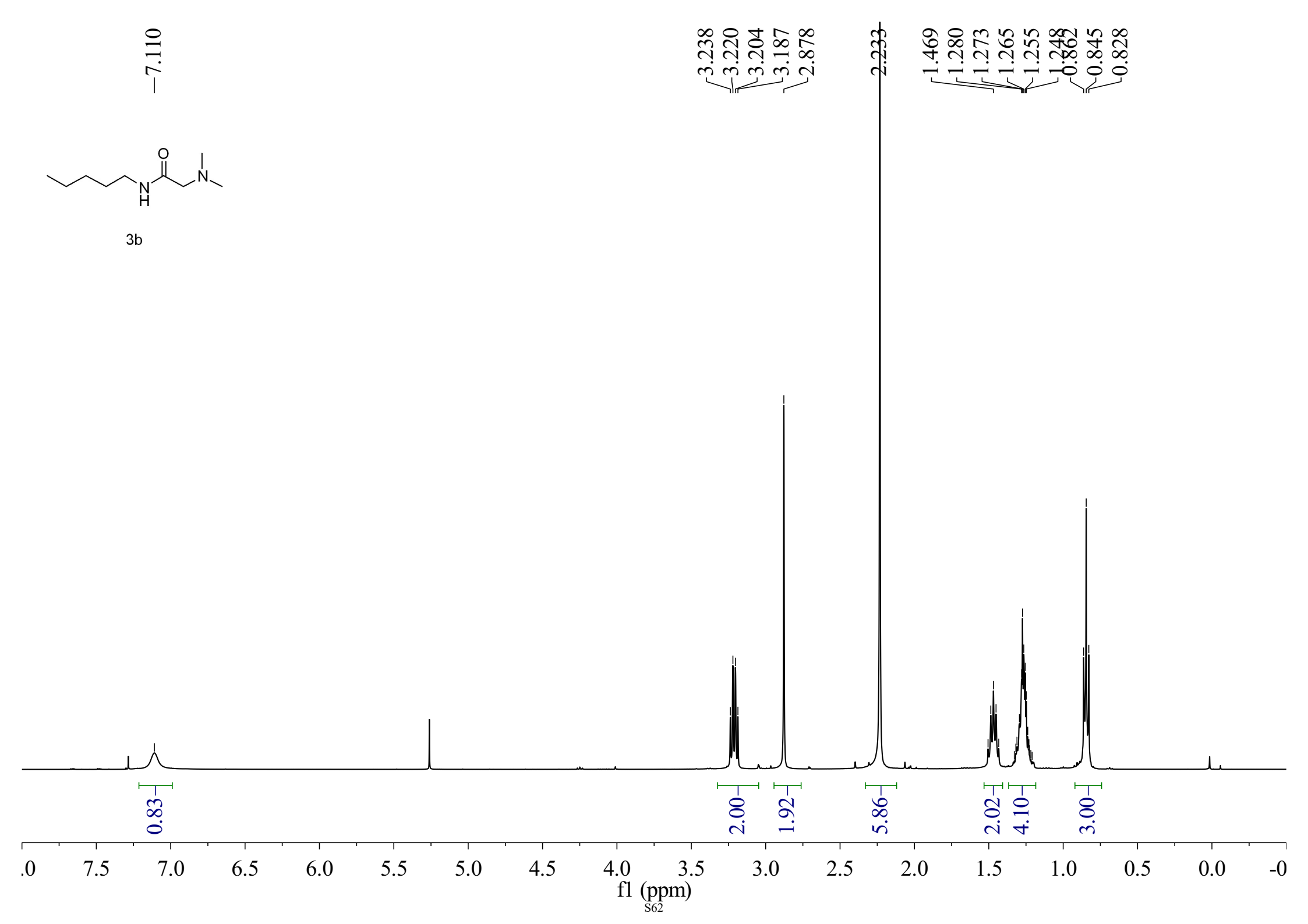
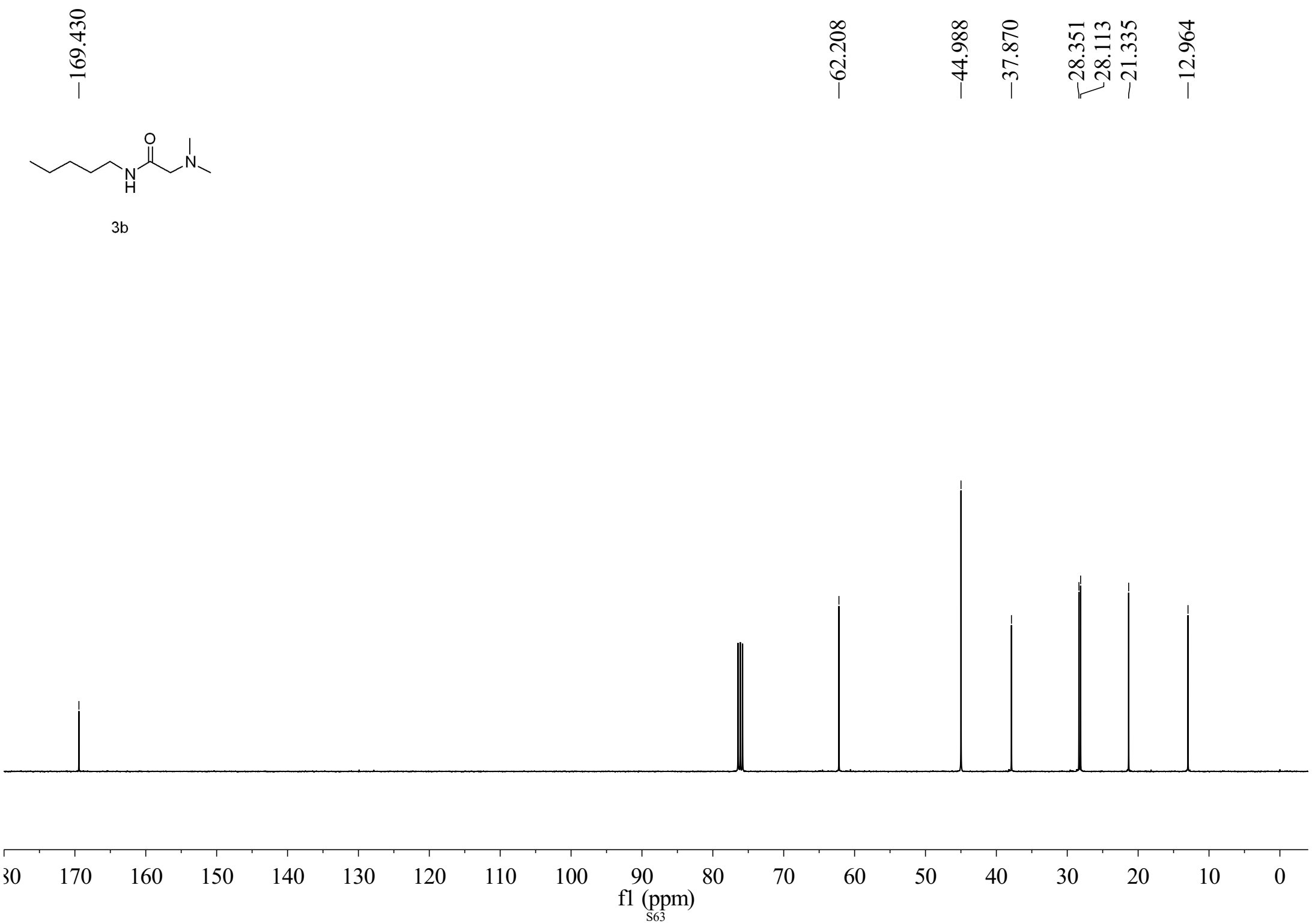
3.281
3.272
3.262
3.253
3.233
1.598
1.582
1.565
1.544
1.521
1.506
1.489
1.284
1.273
1.259
0.888
0.873
0.850
0.833
O
N
Br
2h
2.00
4.10
2.12
2.03
12.09
6.09
.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

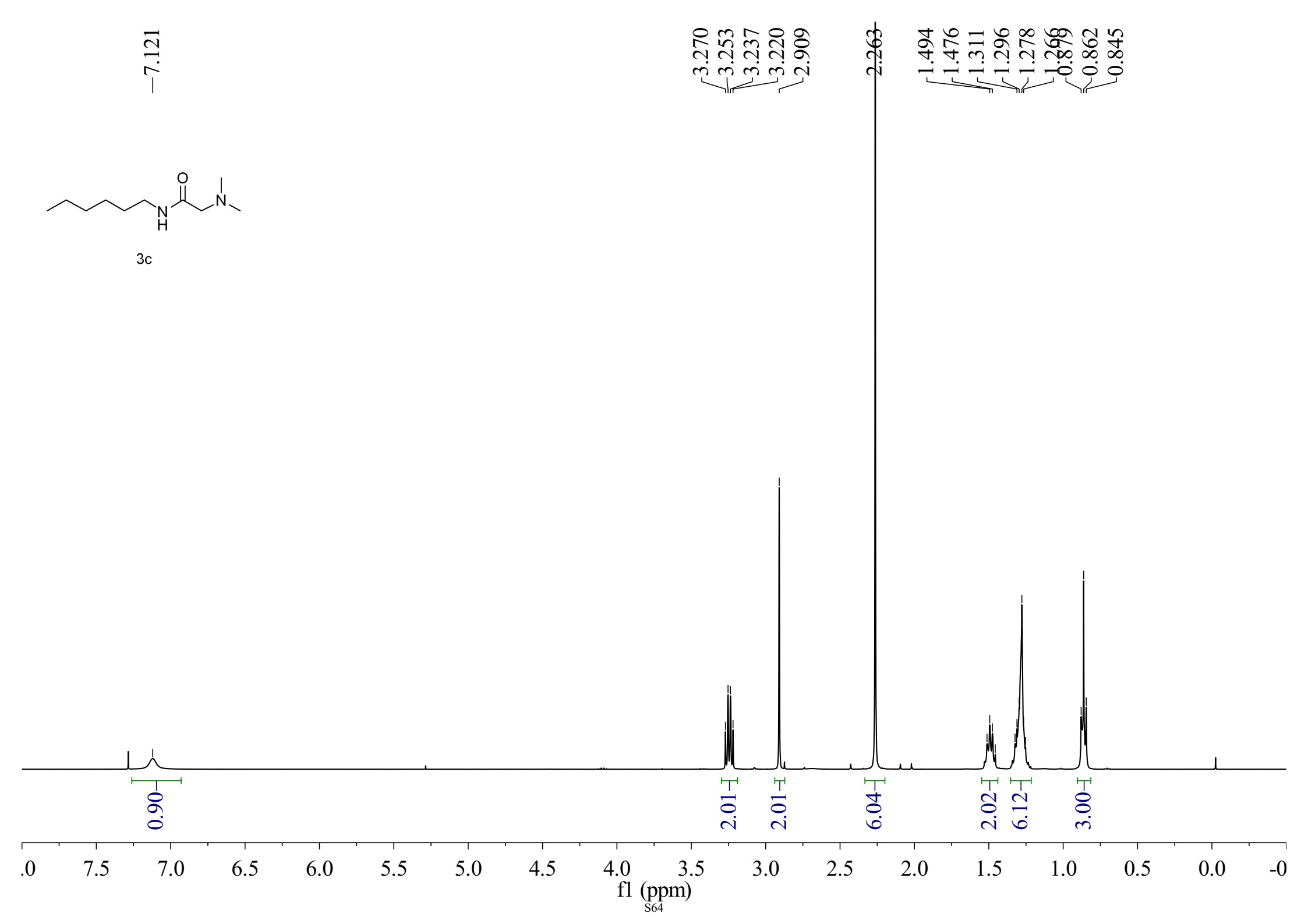

165.244
47.815
45.158
30.562
30.479
28.146
26.193
25.538
25.513
21.549
12.995
12.957
O
N
Br
2h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

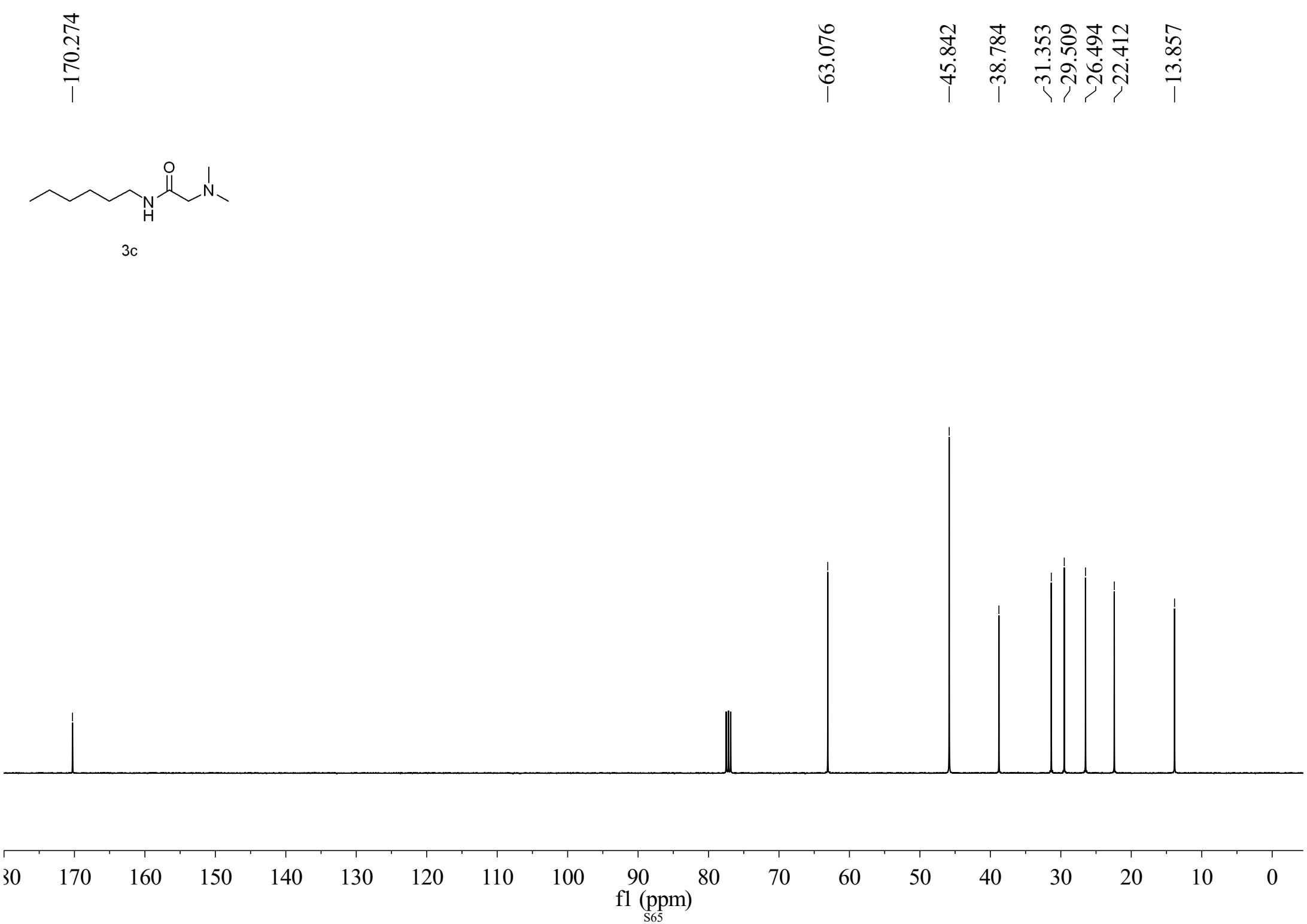

6.886
2.900
2.882
2.866
2.849
2.522
1.892
1.136
1.117
1.099
0.991
0.972
0.952
0.555
0.536
0.518
O
N
H
N
3a
0.93
2.03
2.00
6.08
2.06
1.98
2.98
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

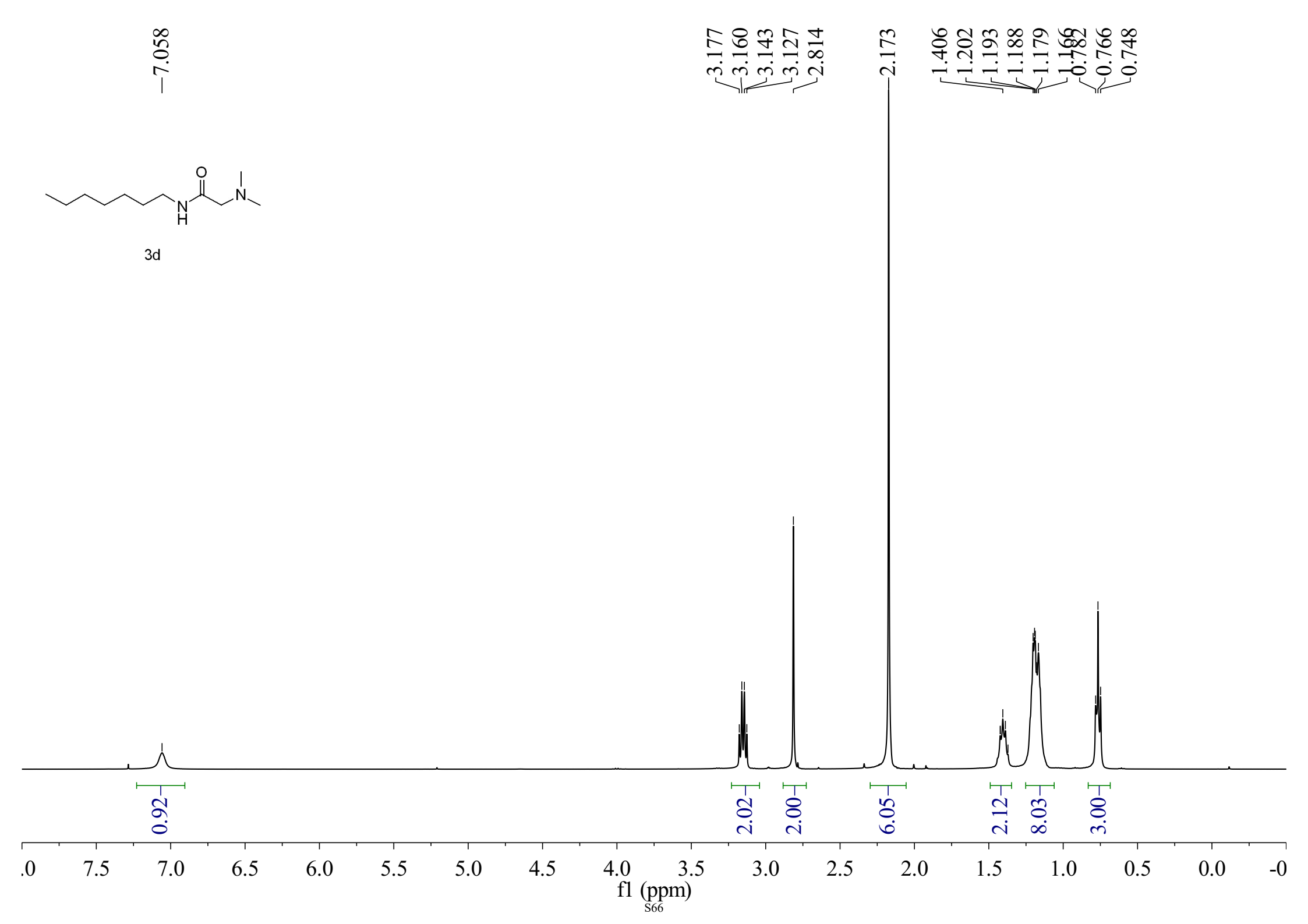

170.332
63.170
45.969
38.615
31.773
20.136
13.762
O
N
H
N
3a
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

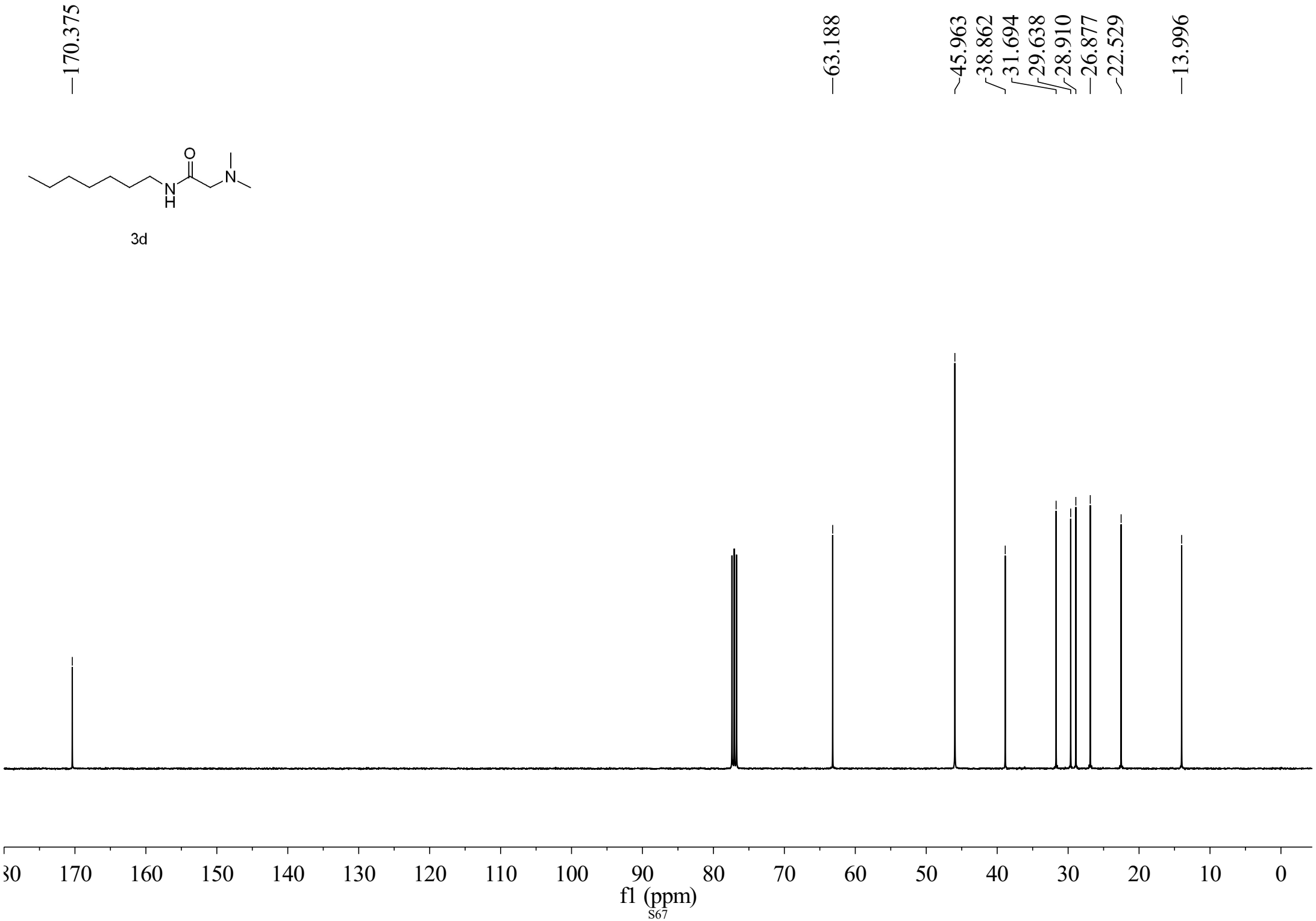

7.110
3.238
3.220
3.204
3.187
2.878
2.233
1.469
1.280
1.273
1.265
1.255
1.248
0.862
0.845
0.828
O
N
H
N
3b
0.83
2.00
1.92
5.86
2.02
4.10
3.00
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


169.430
62.208
44.988
37.870
28.351
28.113
21.335
12.964
O
N
H
N
3b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.121
3.270
3.253
3.237
3.220
2.909
2.263
1.494
1.476
1.311
1.296
1.278
1.266
0.879
0.862
0.845
O
N
H
N
3c
0.90
2.01
2.01
6.04
2.02
6.12
3.00
.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
f1 (ppm)


170.274
63.076
45.842
38.784
31.353
29.509
26.494
22.412
13.857
O
N
H
N
3c
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.058
3.177
3.160
3.143
3.127
2.814
2.173
1.406
1.202
1.193
1.188
1.179
1.166
0.782
0.766
0.748
O
N
H
N
3d
0.92
2.02
2.00
6.05
2.12
8.03
3.00
.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
f1 (ppm)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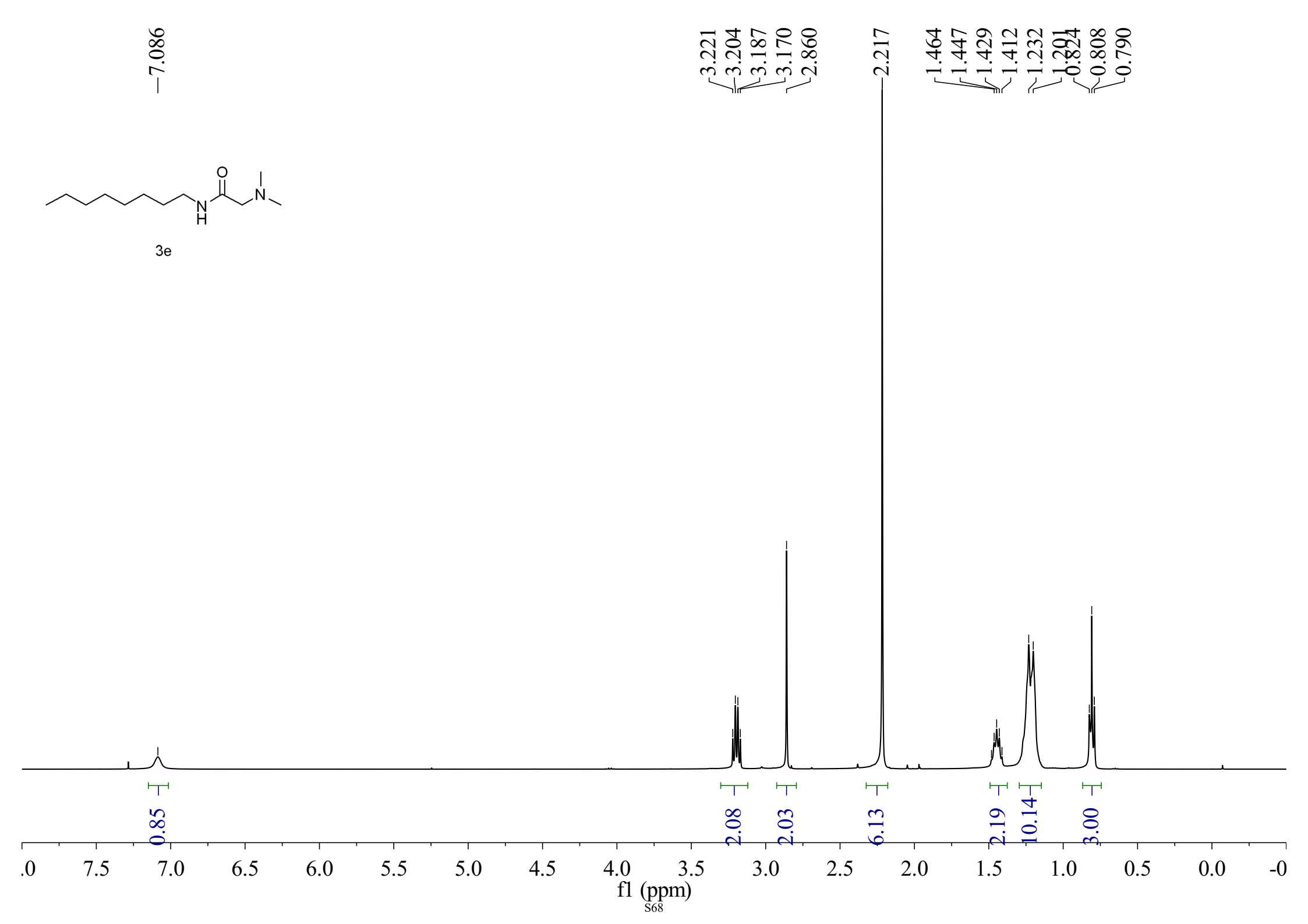
63.188
45.963
38.862
31.694
29.638
28.910
26.877
22.529
13.996
O
N
H
N
3d
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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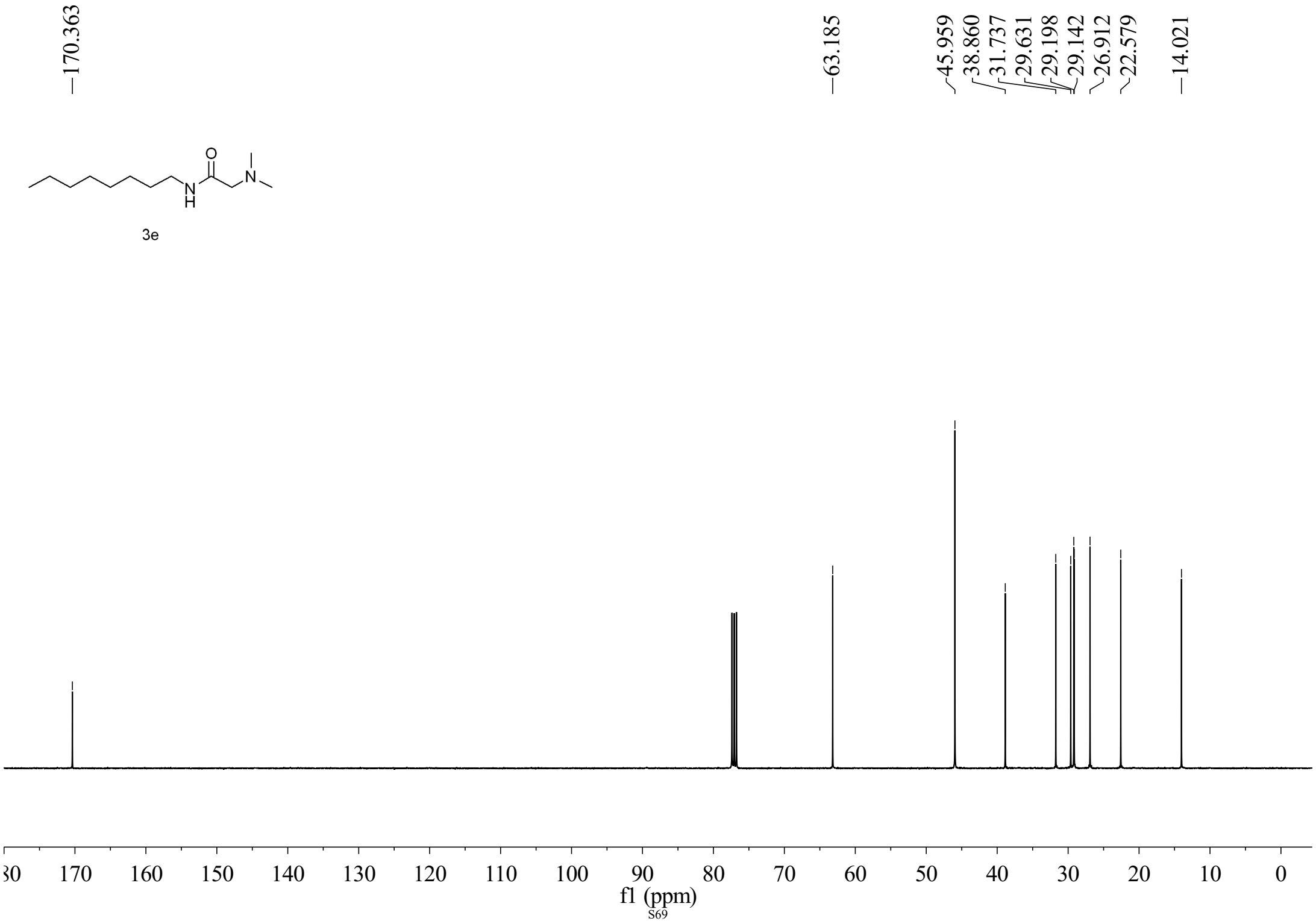
3.204
3.187
3.170
2.860
2.217
1.464
1.447
1.429
1.412
1.232
1.201
0.824
0.808
0.790
O
N
H
N
3e
0.85
2.08
2.03
6.13
2.19
10.14
3.00
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)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31.737
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29.142
26.912
22.579
14.021
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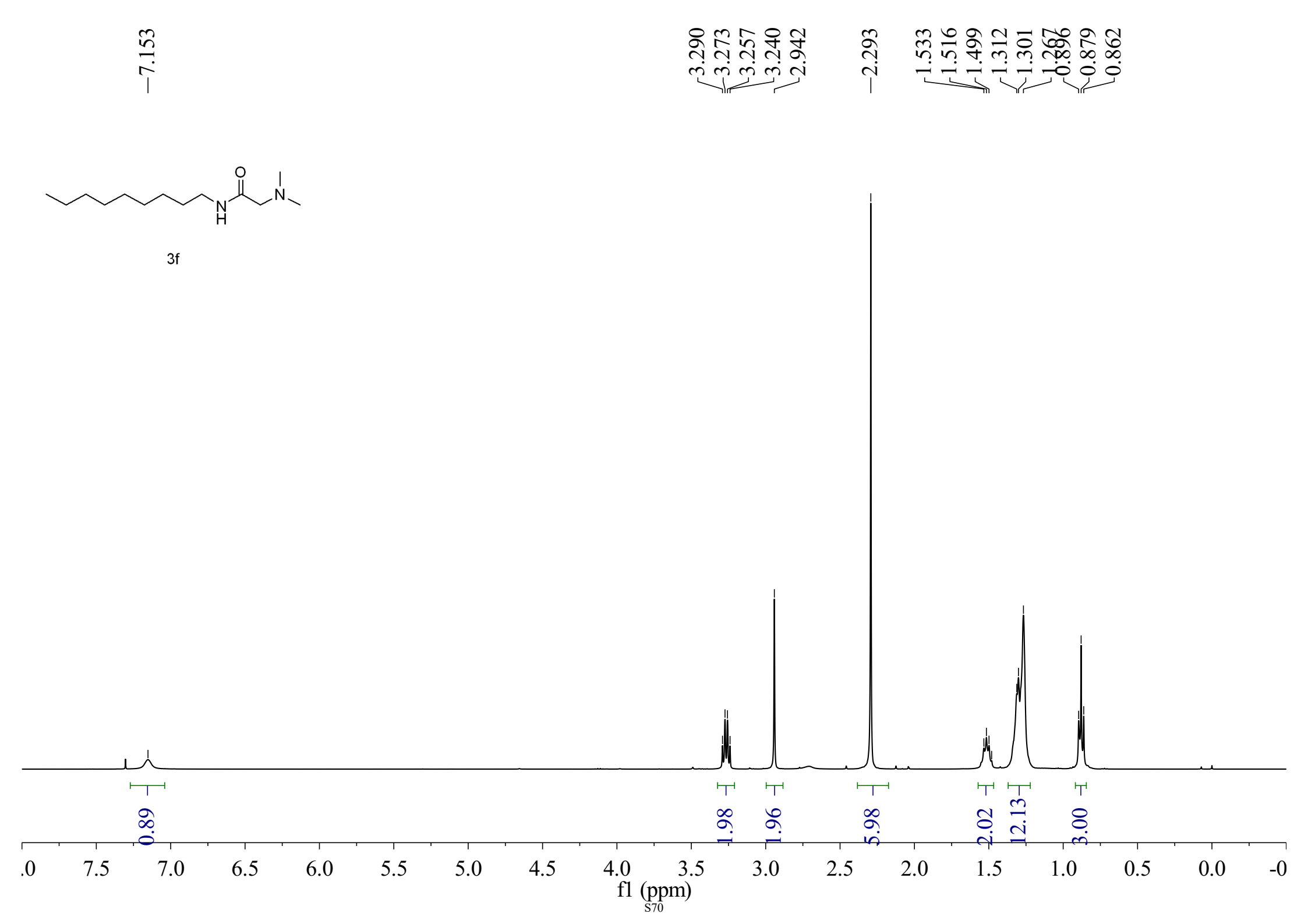
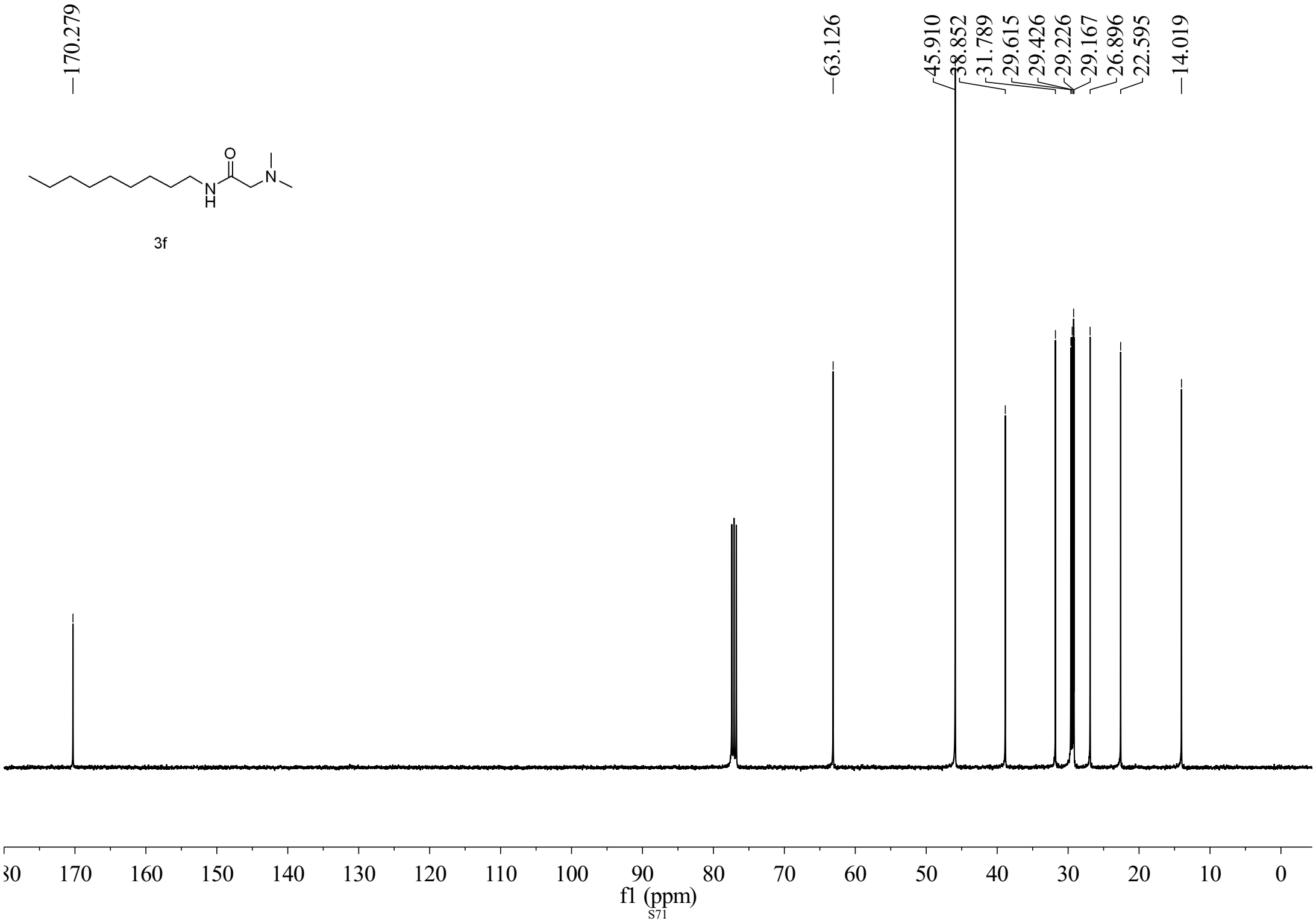
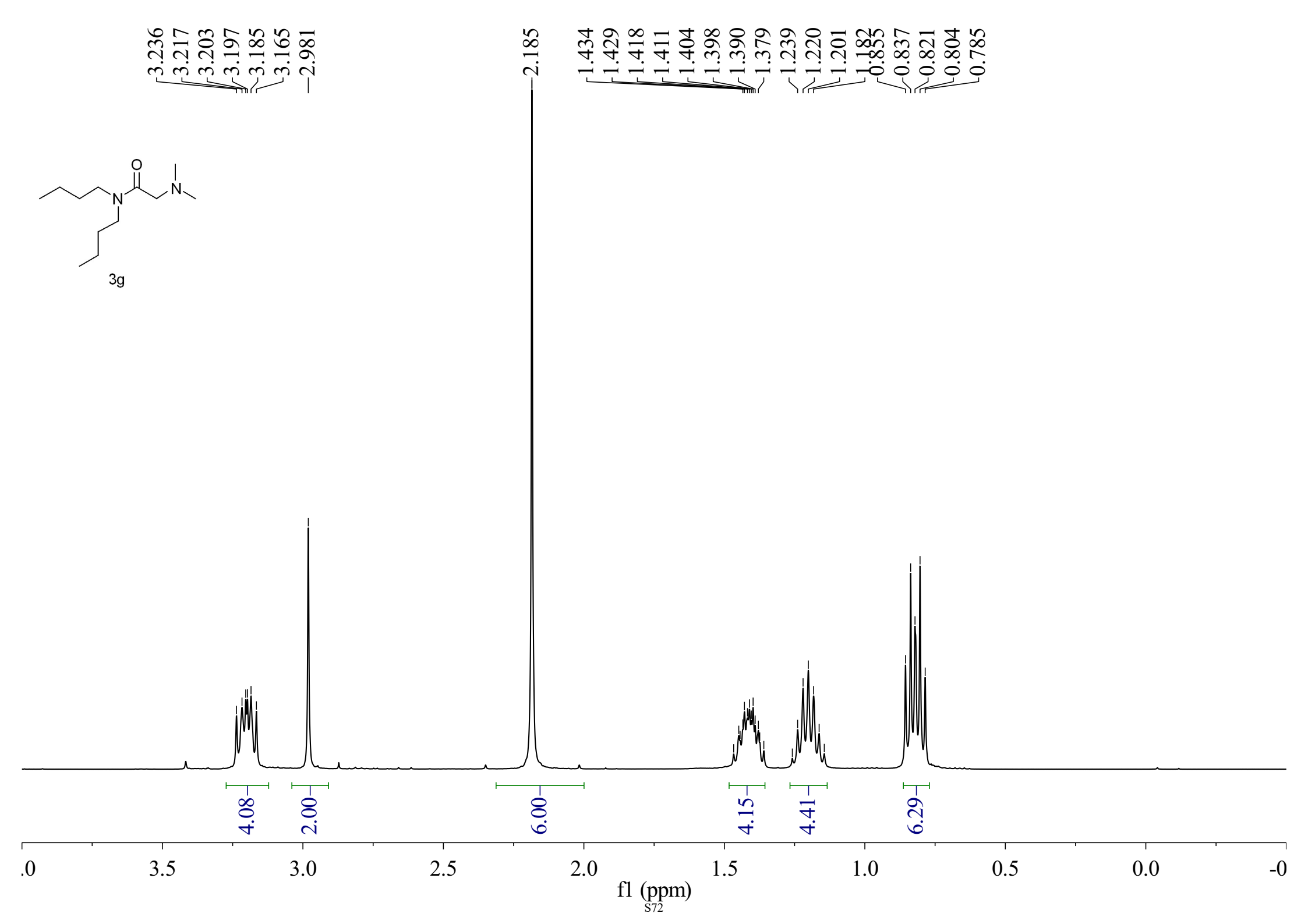
N
H
N
3e
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.153
3.290
3.273
3.257
3.240
2.942
2.293
1.533
1.516
1.499
1.312
1.301
1.267
0.896
0.879
0.862
O
N
H
N
3f
0.89
1.98
1.96
5.98
2.02
12.13
3.00
.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
f1 (ppm)


170.279
63.126
45.910
38.852
31.789
29.615
29.426
29.226
29.167
26.896
22.595
14.019
O
N
H
N
3f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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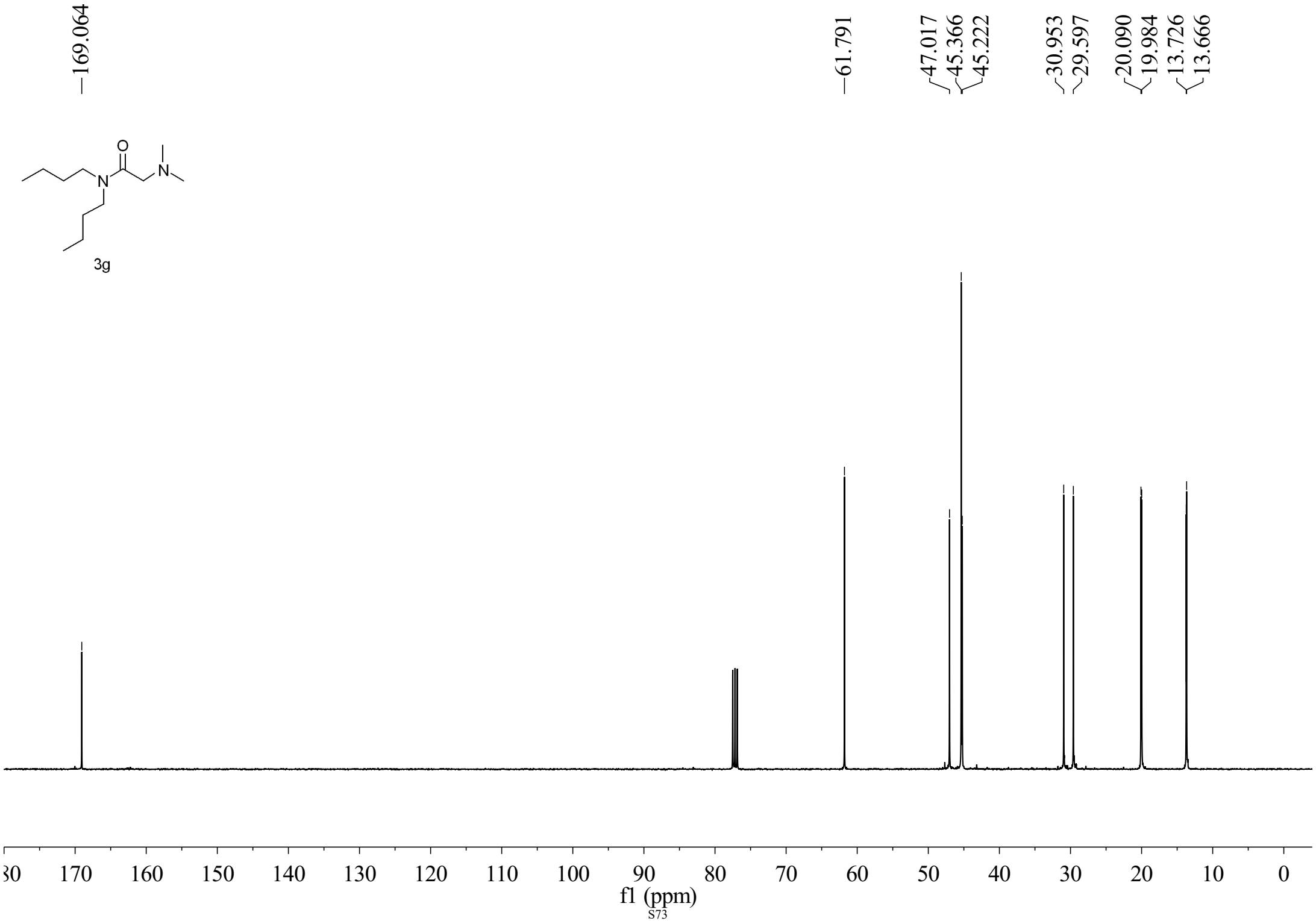
3.217
3.203
3.197
3.185
3.165
2.981
2.185
1.434
1.429
1.418
1.411
1.404
1.398
1.390
1.379
1.239
1.220
1.201
1.182
0.855
0.837
0.821
0.804
0.785
O
N
N
3g
4.08
2.00
6.00
4.15
4.41
6.29
.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)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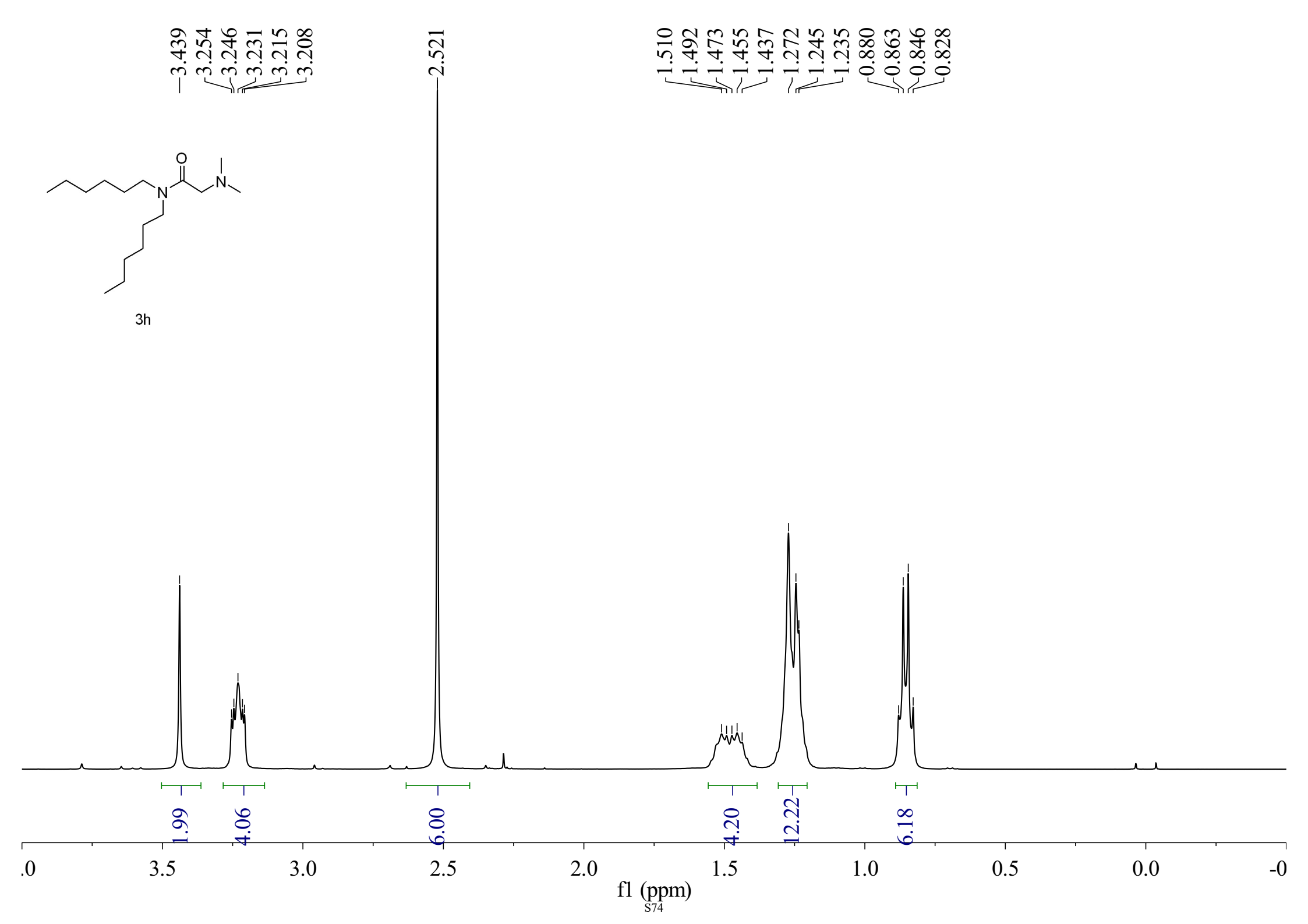
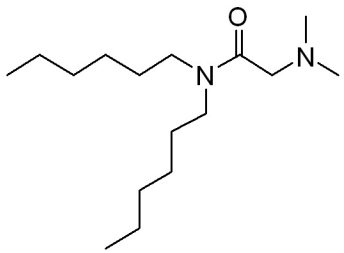
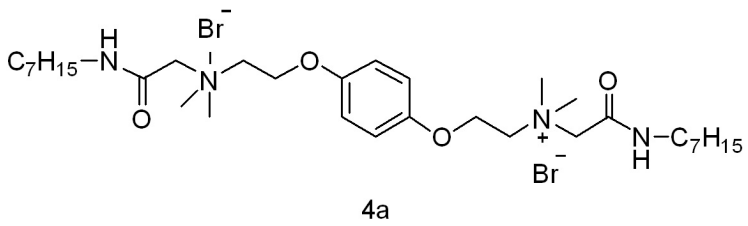
61.791
47.017
45.366
45.222
30.953
29.597
20.090
19.984
13.726
13.666
O
N
N
3g
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3.439
3.254
3.246
3.231
3.215
3.208
2.521
1.510
1.492
1.473
1.455
1.437
1.272
1.245
1.235
0.880
0.863
0.846
0.828
O
N
N
3h
1.99
4.06
6.00
4.20
12.22
6.18
.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


O
N
N

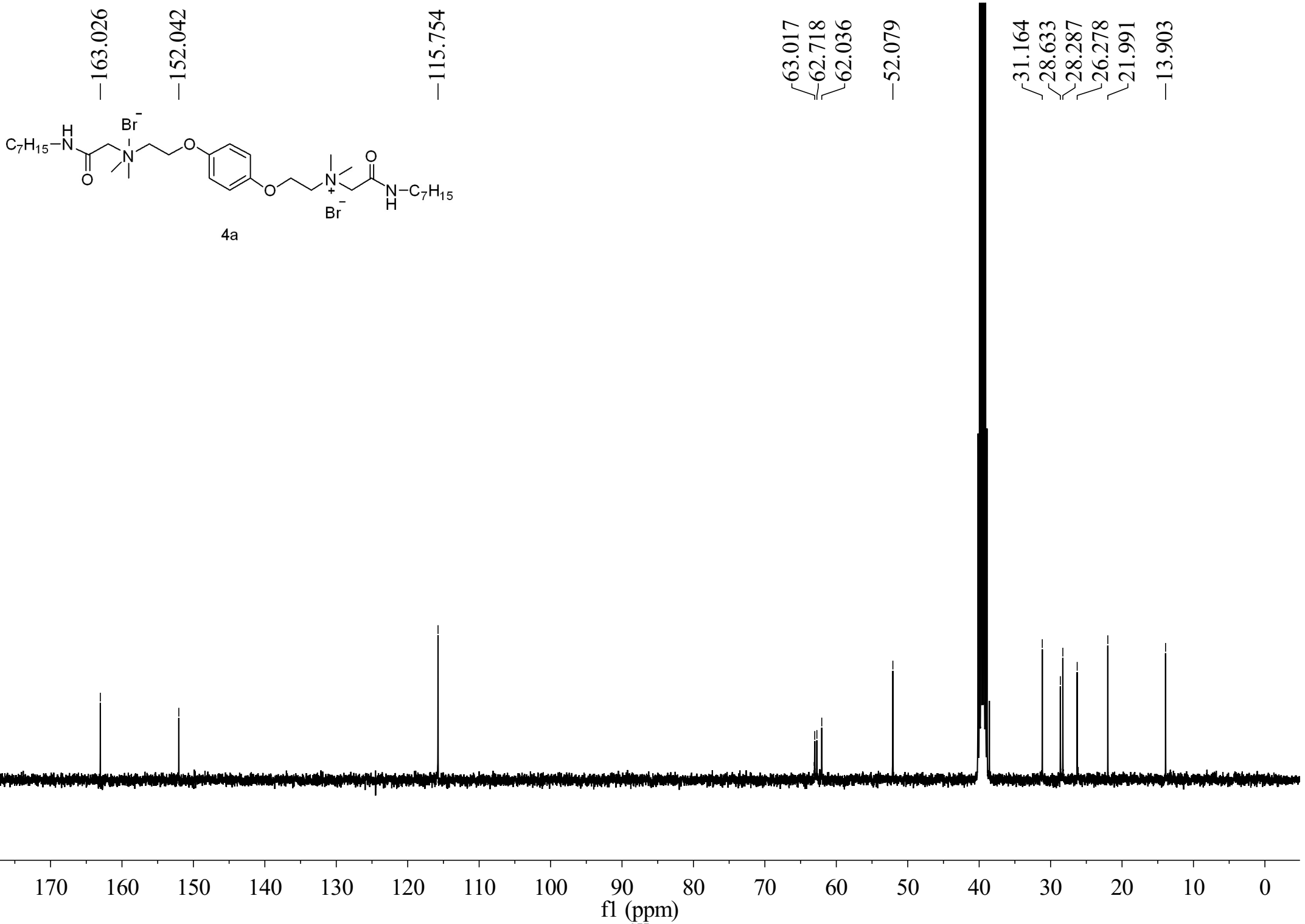
3h

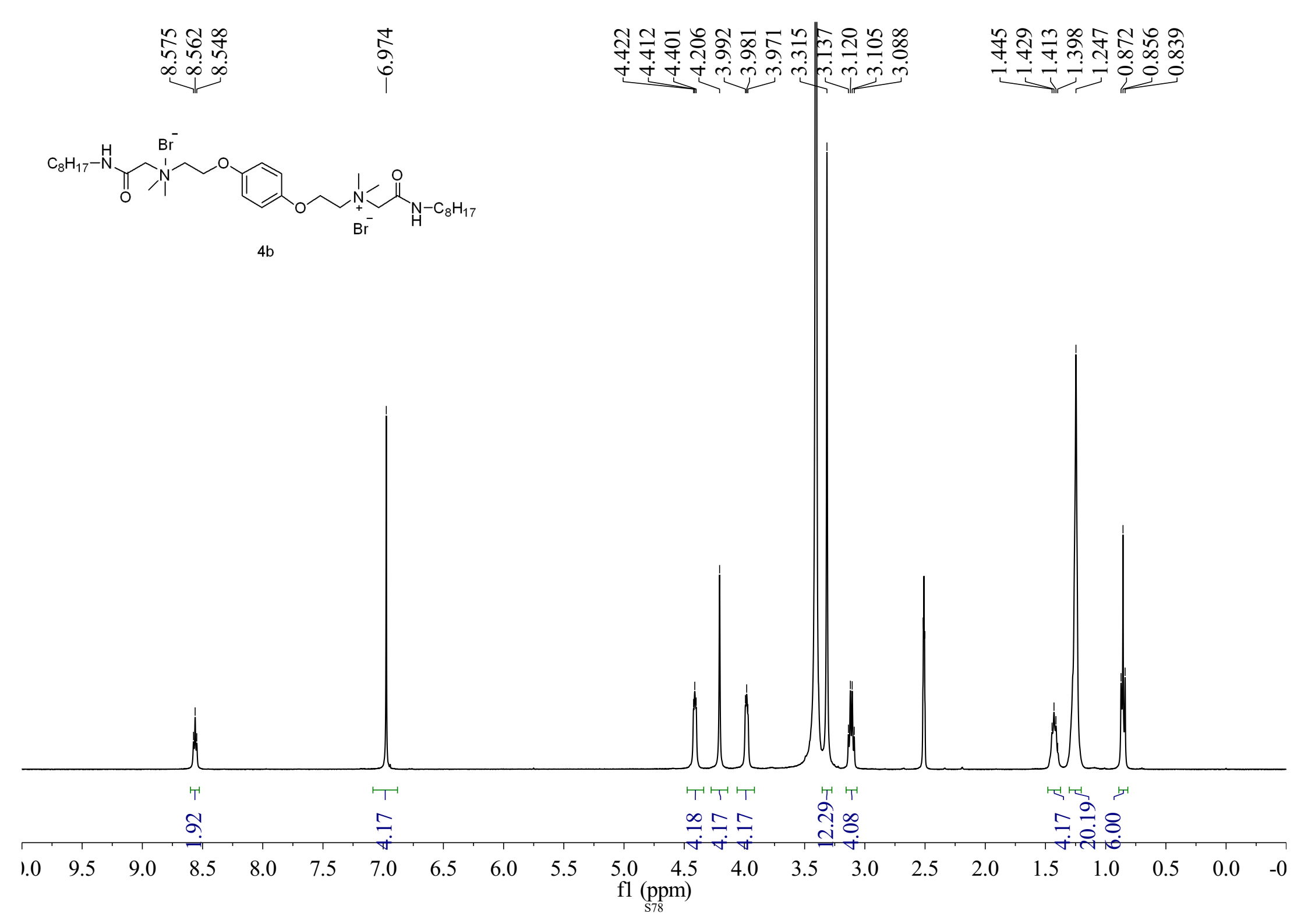
167.674
60.616
47.414
45.866
45.305
31.532
31.460
26.646
26.506
22.535
22.516
13.954
13.939
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

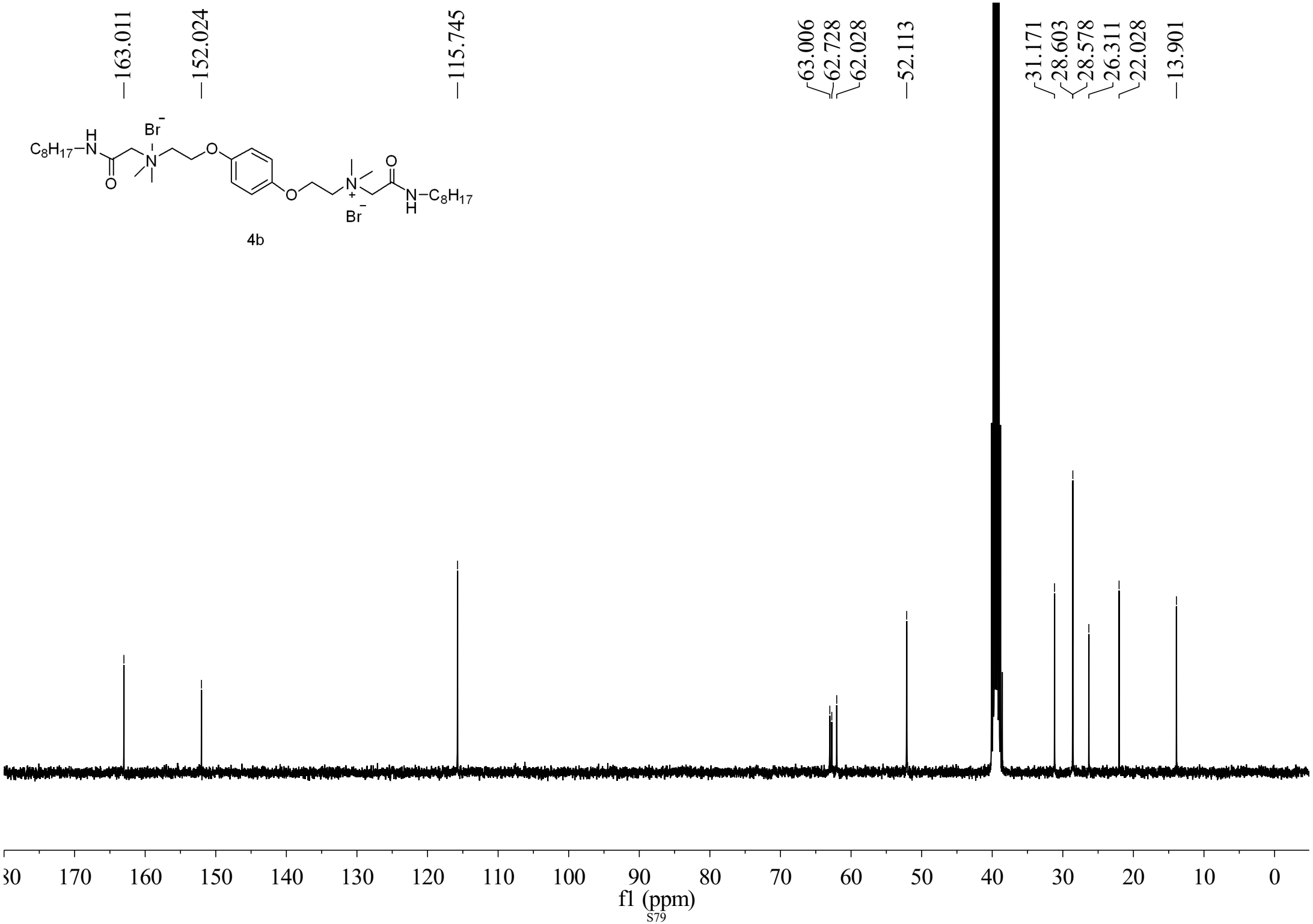

Br
C7H15
H
N
O
N
O
O
N
+
O
N
H
C7H15
Br

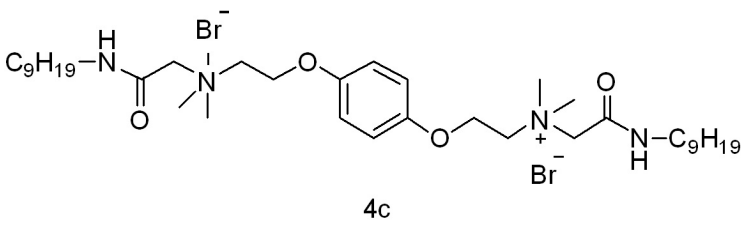
4a

8.565
8.552
8.539
6.971
4.419
4.409
4.398
4.199
3.988
3.978
3.968
3.308
3.135
3.118
3.103
3.086
1.442
1.426
1.410
1.249
0.874
0.858
0.840
2.07
4.24
4.16
4.21
4.06
11.78
4.24
4.08
16.02
6.00
f1 (ppm)


163.026
152.042
115.754
63.017
62.718
62.036
52.079
31.164
28.633
28.287
26.278
21.991
13.903
Br⁻
C7H15–N
H
O
N
O
O
N
+
O
N–C7H15
H
Br⁻
4a
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

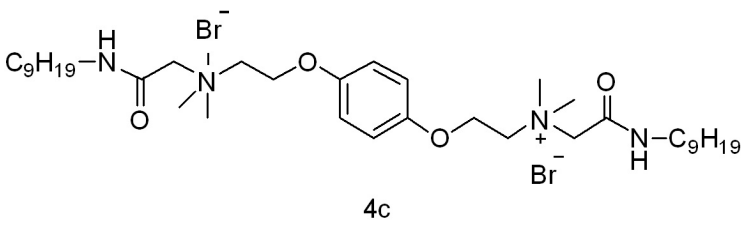

8.575
8.562
8.548
6.974
4.422
4.412
4.401
4.206
3.992
3.981
3.971
3.315
3.137
3.120
3.105
3.088
1.445
1.429
1.413
1.398
1.247
0.872
0.856
0.839
4b
1.92
4.17
4.18
4.17
4.17
12.29
4.08
4.17
20.19
6.00
fl (ppm)


163.011
152.024
115.745
63.006
62.728
62.028
52.113
31.171
28.603
28.578
26.311
22.028
13.901
4b
f1 (ppm)


Br
C9H19–N
H
O
N
O
O
O
N
+
O
N–C9H19
H
Br

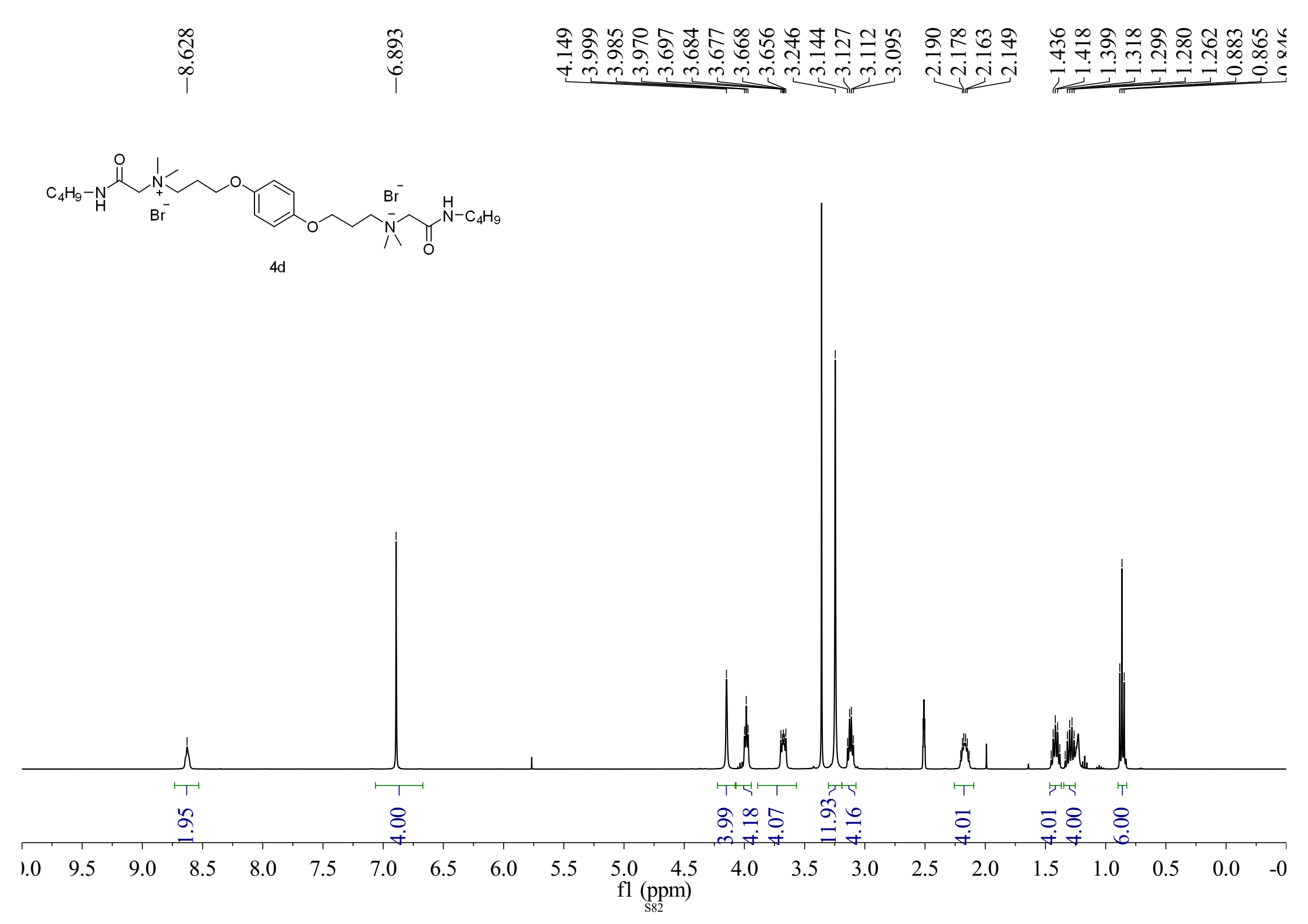
4c

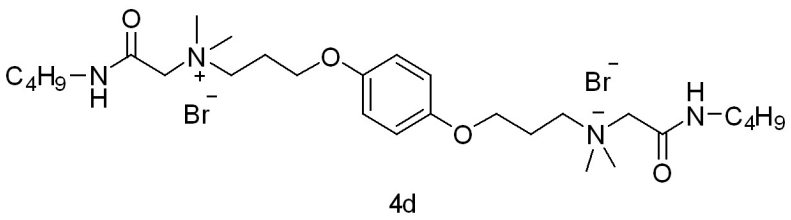
8.567
8.554
8.540
6.970
4.417
4.408
4.396
4.191
3.976
3.308
3.135
3.118
3.103
3.086
1.443
1.426
1.410
1.243
0.872
0.855
0.838
1.87
4.01
3.97
3.95
3.91
12.14
4.21
4.08
24.11
6.00
f1 (ppm)


Br
C9H19
N
H
O
O
N
O
O
N
+
O
N
H
C9H19
Br

4c

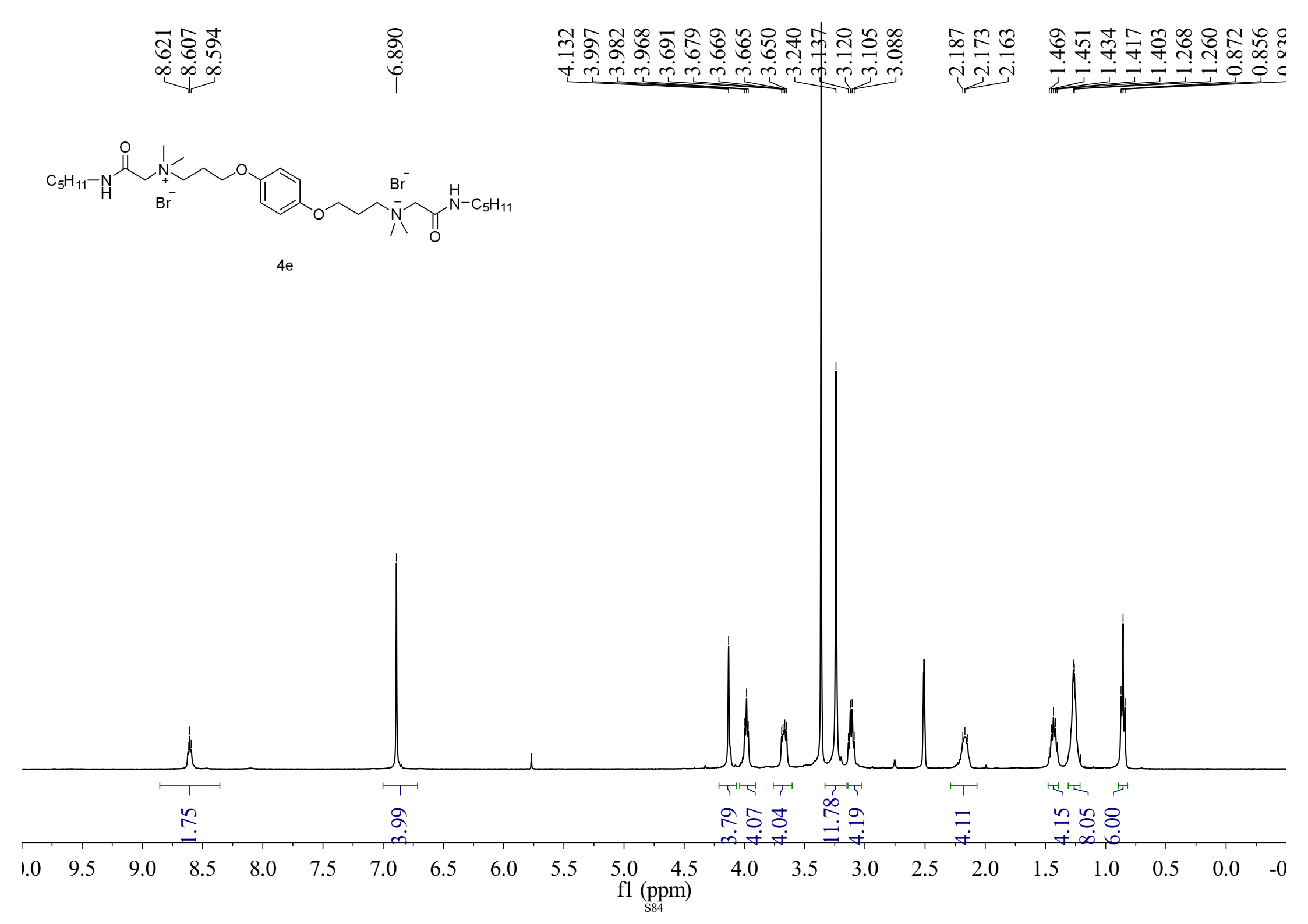
163.008
152.024
115.735
63.001
62.734
62.017
52.115
31.227
28.888
28.631
28.615
28.595
26.308
22.034
13.910
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.628
6.893
4.149
3.999
3.985
3.970
3.697
3.684
3.677
3.668
3.656
3.246
3.144
3.127
3.112
3.095
2.190
2.178
2.163
2.149
1.436
1.418
1.399
1.318
1.299
1.280
1.262
0.883
0.865
4d
1.95
4.00
3.99
4.18
4.07
11.93
4.16
4.01
4.01
4.00
6.00
f1 (ppm)

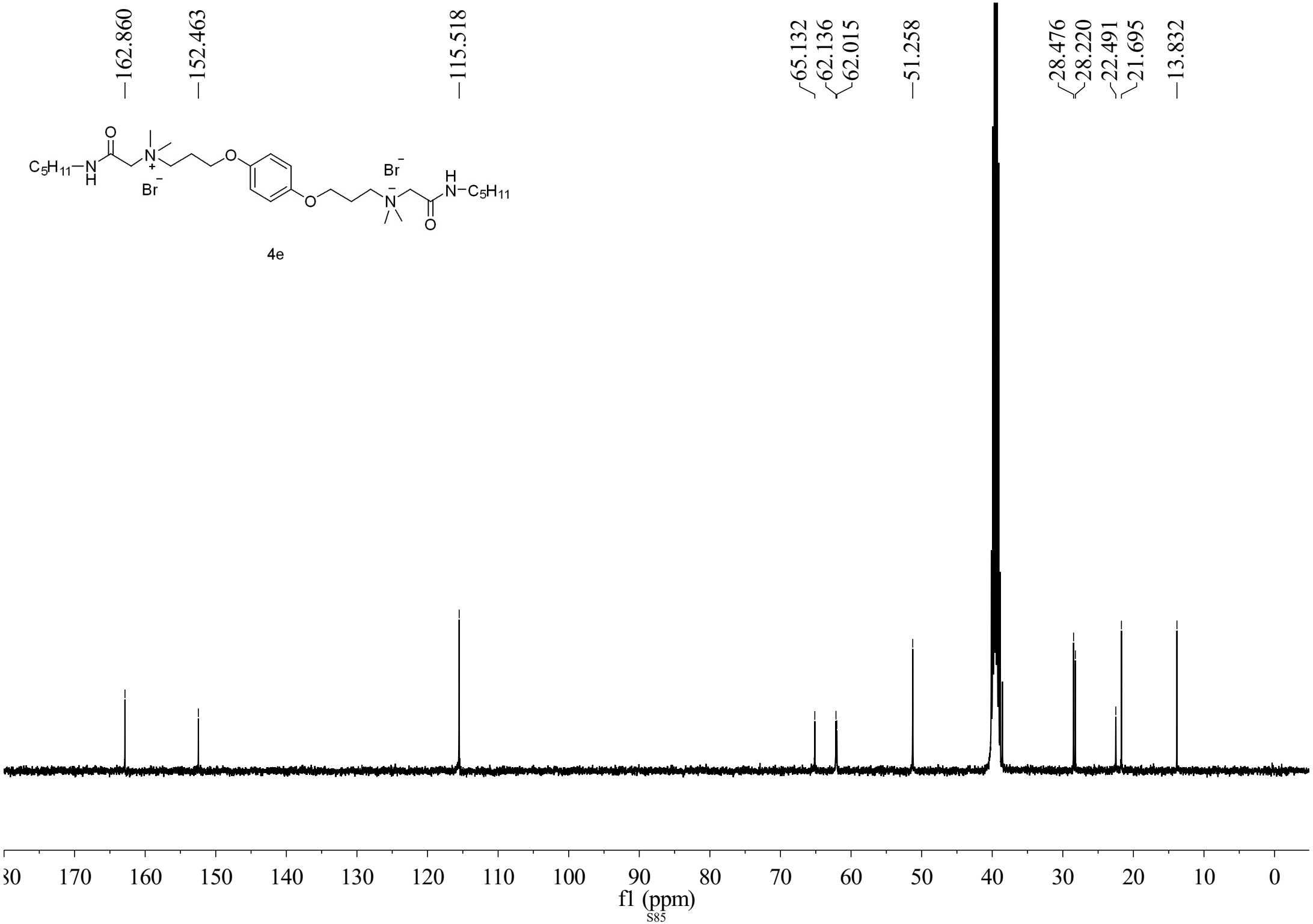

O
C4H9–N
H
N+
Br−
O
O
Br−
N
H
N–C4H9
O

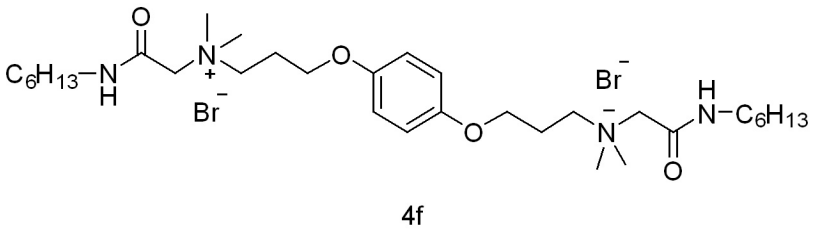
4d

163.371
152.938
116.008
65.609
62.626
62.478
51.736
31.147
22.985
19.981
14.044
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

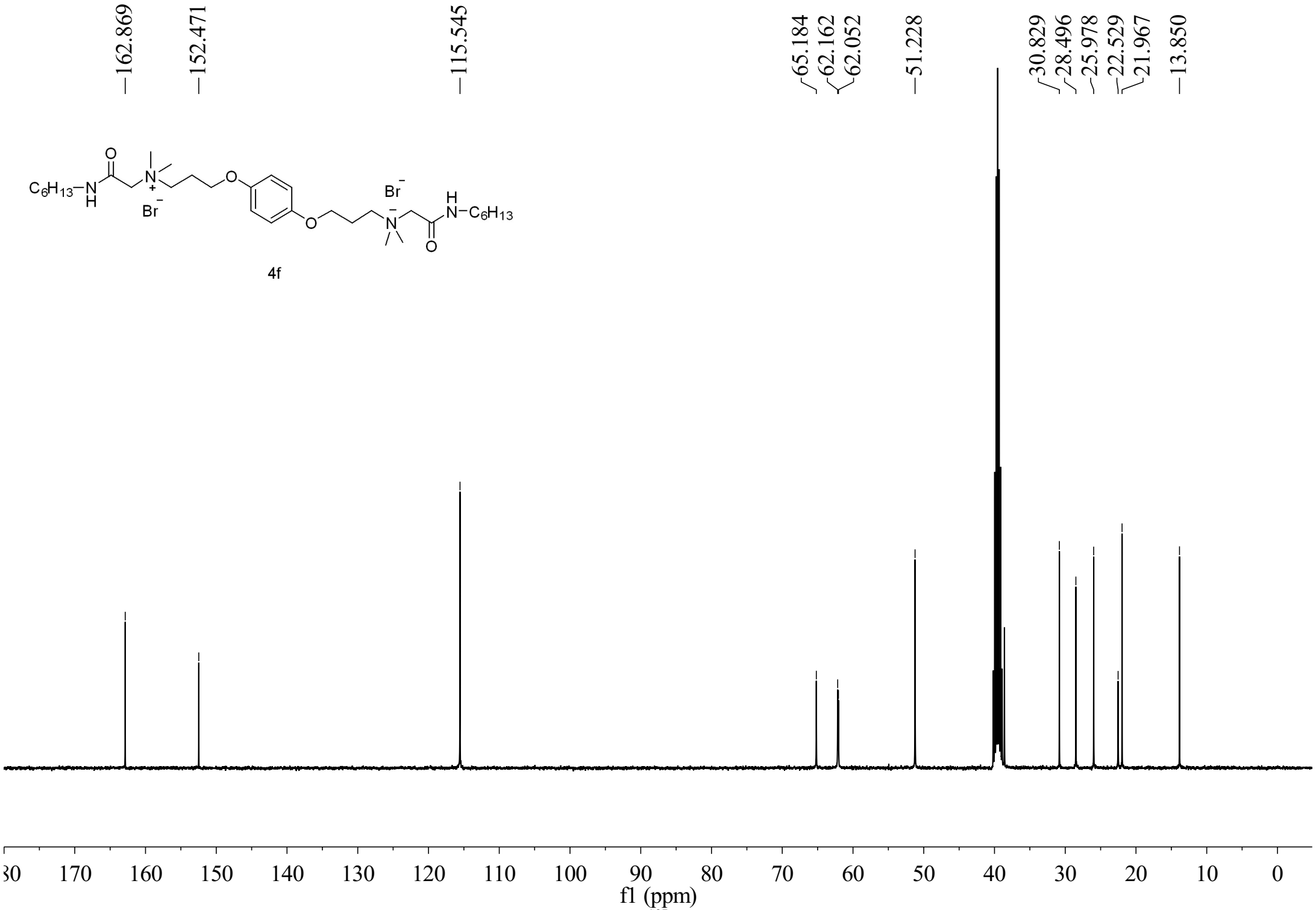

8.621
8.607
8.594
6.890
4.132
3.997
3.982
3.968
3.691
3.679
3.669
3.665
3.650
3.240
3.137
3.120
3.105
3.088
2.187
2.173
2.163
1.469
1.451
1.434
1.417
1.403
1.268
1.260
0.872
0.856
1.75
3.99
3.79
4.07
4.04
11.78
4.19
4.11
4.15
8.05
6.00
fl (ppm)

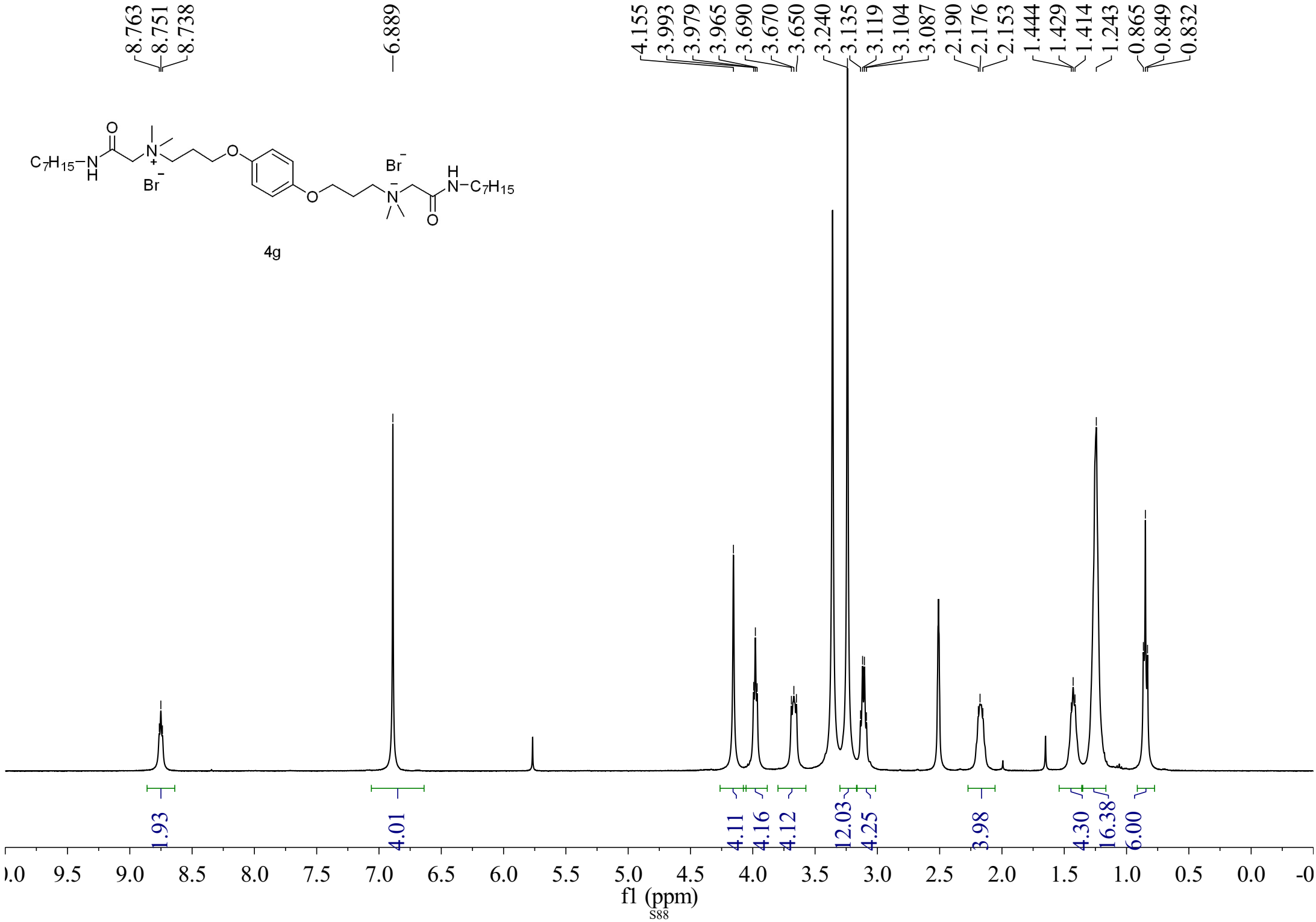
4e

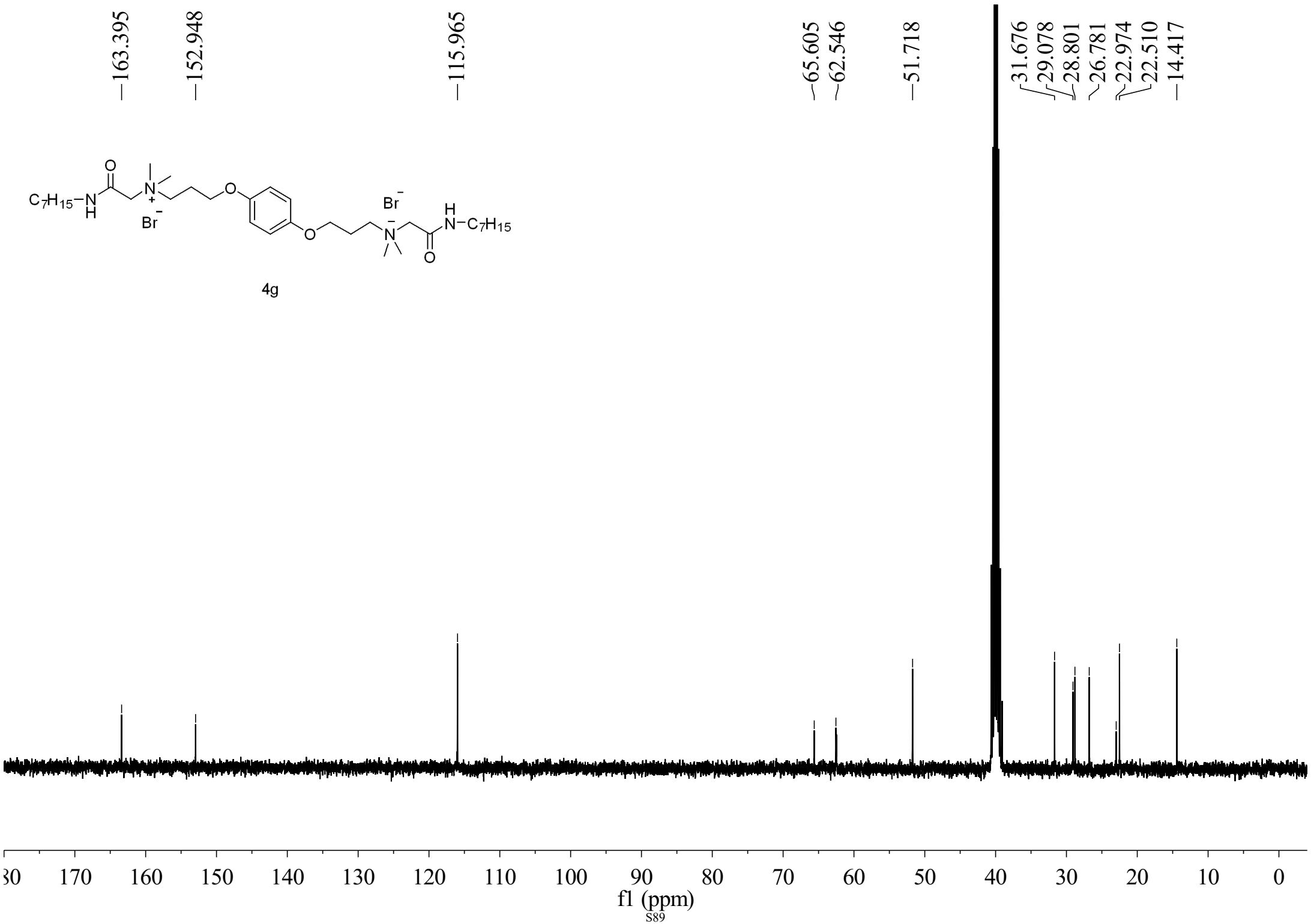

162.860
152.463
115.518
65.132
62.136
62.015
51.258
28.476
28.220
22.491
21.695
13.832
4e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

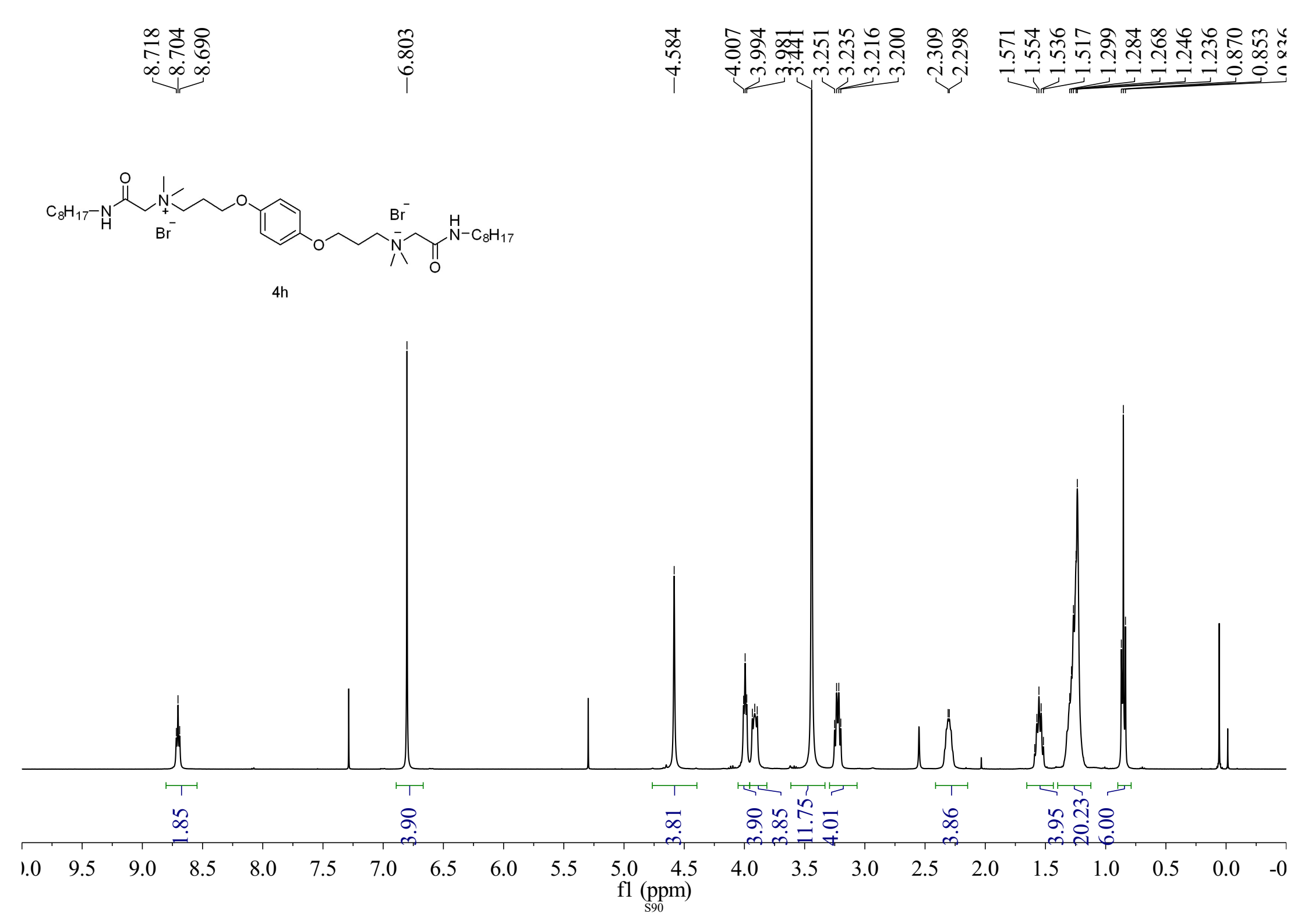


4f

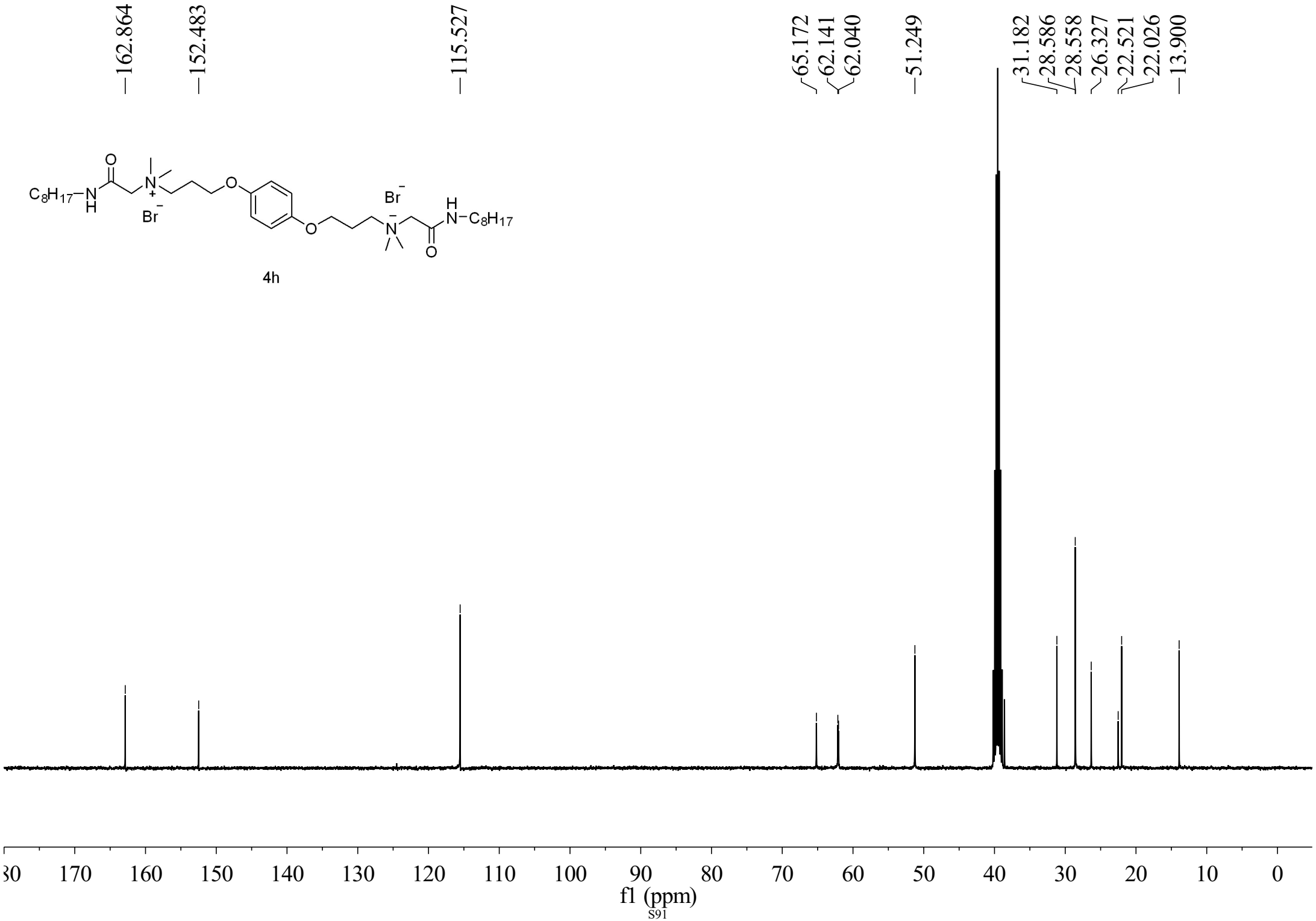

162.869
152.471
115.545
65.184
62.162
62.052
51.228
30.829
28.496
25.978
22.529
21.967
13.850
4f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

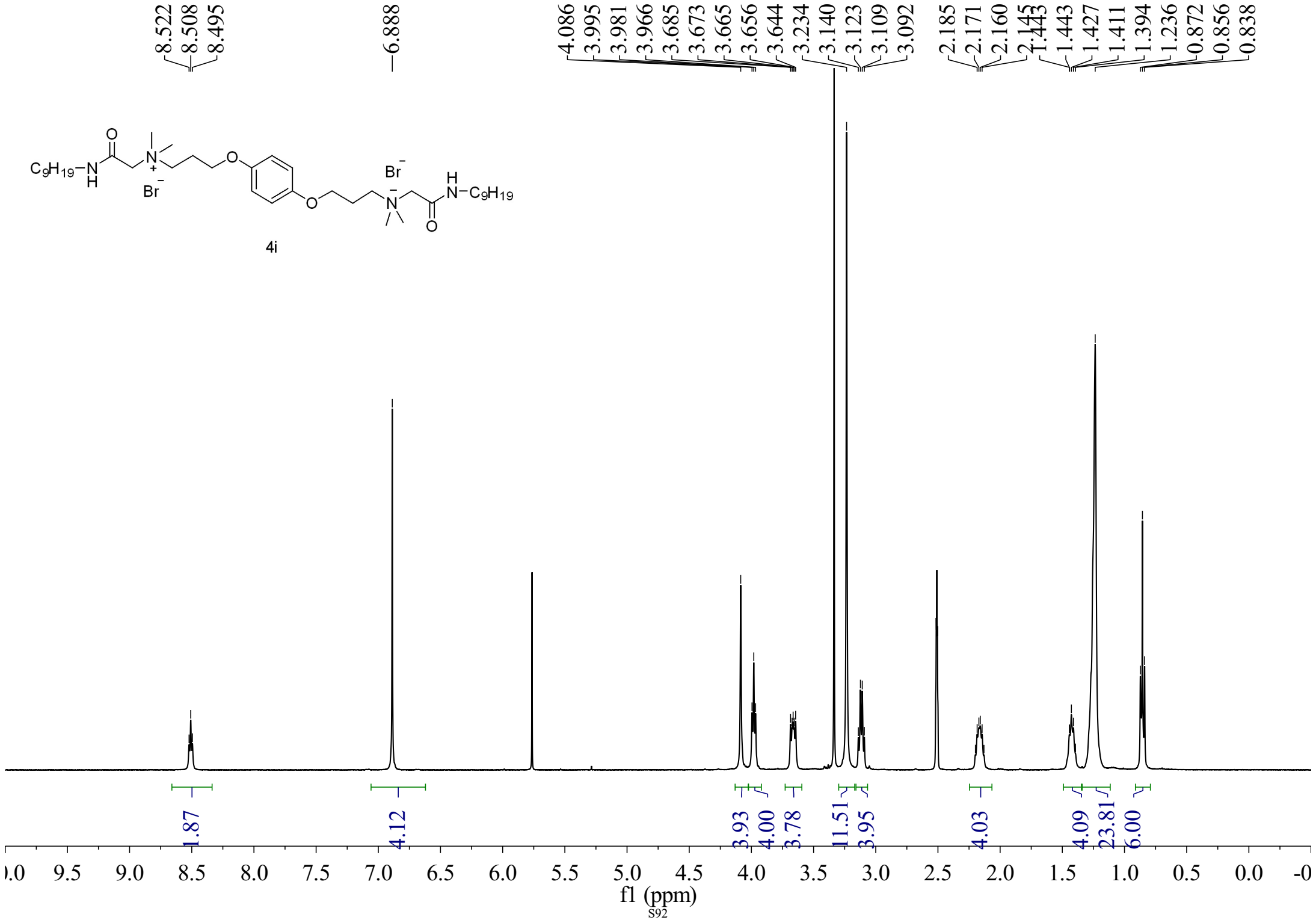

8.763
8.751
8.738
6.889
4.155
3.993
3.979
3.965
3.690
3.670
3.650
3.240
3.135
3.119
3.104
3.087
2.190
2.176
2.153
1.444
1.429
1.414
1.243
0.865
0.849
0.832
4g
1.93
4.01
4.11
4.16
4.12
12.03
4.25
3.98
4.30
16.38
6.00
f1 (ppm)


163.395
152.948
115.965
65.605
62.546
51.718
31.676
29.078
28.801
26.781
22.974
22.510
14.417
Br⁻
Br⁻
4g
f1 (ppm)

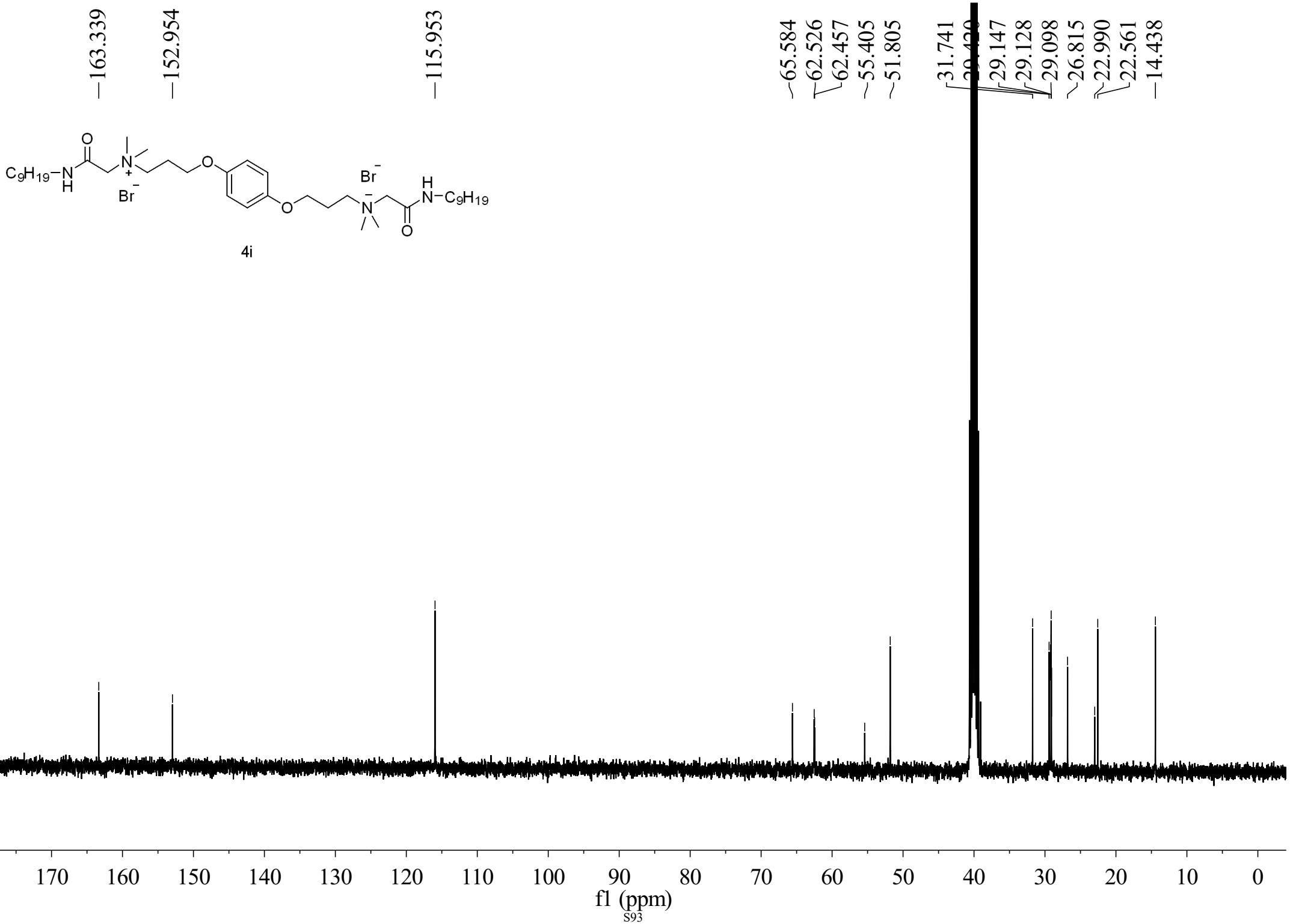

8.718
8.704
8.690
6.803
4.584
4.007
3.994
3.981
3.441
3.251
3.235
3.216
3.200
2.309
2.298
1.571
1.554
1.536
1.517
1.299
1.284
1.268
1.246
1.236
0.870
0.853
1.85
3.90
3.81
3.90
3.85
11.75
4.01
3.86
3.95
20.23
6.00
fl (ppm)

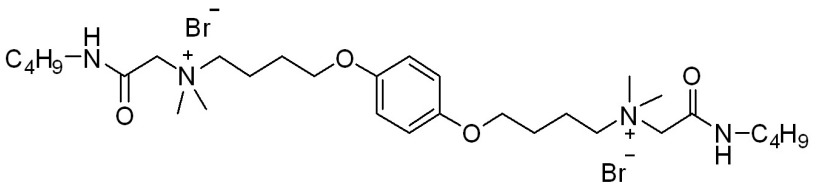
4h


162.864
152.483
115.527
65.172
62.141
62.040
51.249
31.182
28.586
28.558
26.327
22.521
22.026
13.900
4h
f1 (ppm)

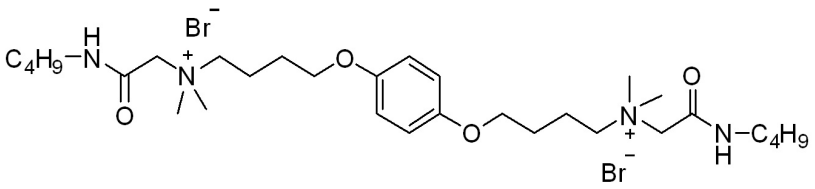

8.522
8.508
8.495
6.888
4.086
3.995
3.981
3.966
3.685
3.673
3.665
3.656
3.644
3.234
3.140
3.123
3.109
3.092
2.185
2.171
2.160
2.145
1.443
1.443
1.427
1.411
1.394
1.236
0.872
0.856
0.838
1.87
4.12
3.93
4.00
3.78
11.51
3.95
4.03
4.09
23.81
6.00
f1 (ppm)

4i


163.339
152.954
115.953
65.584
62.526
62.457
55.405
51.805
31.741
29.147
29.128
29.098
26.815
22.990
22.561
14.438
4i
f1 (ppm)

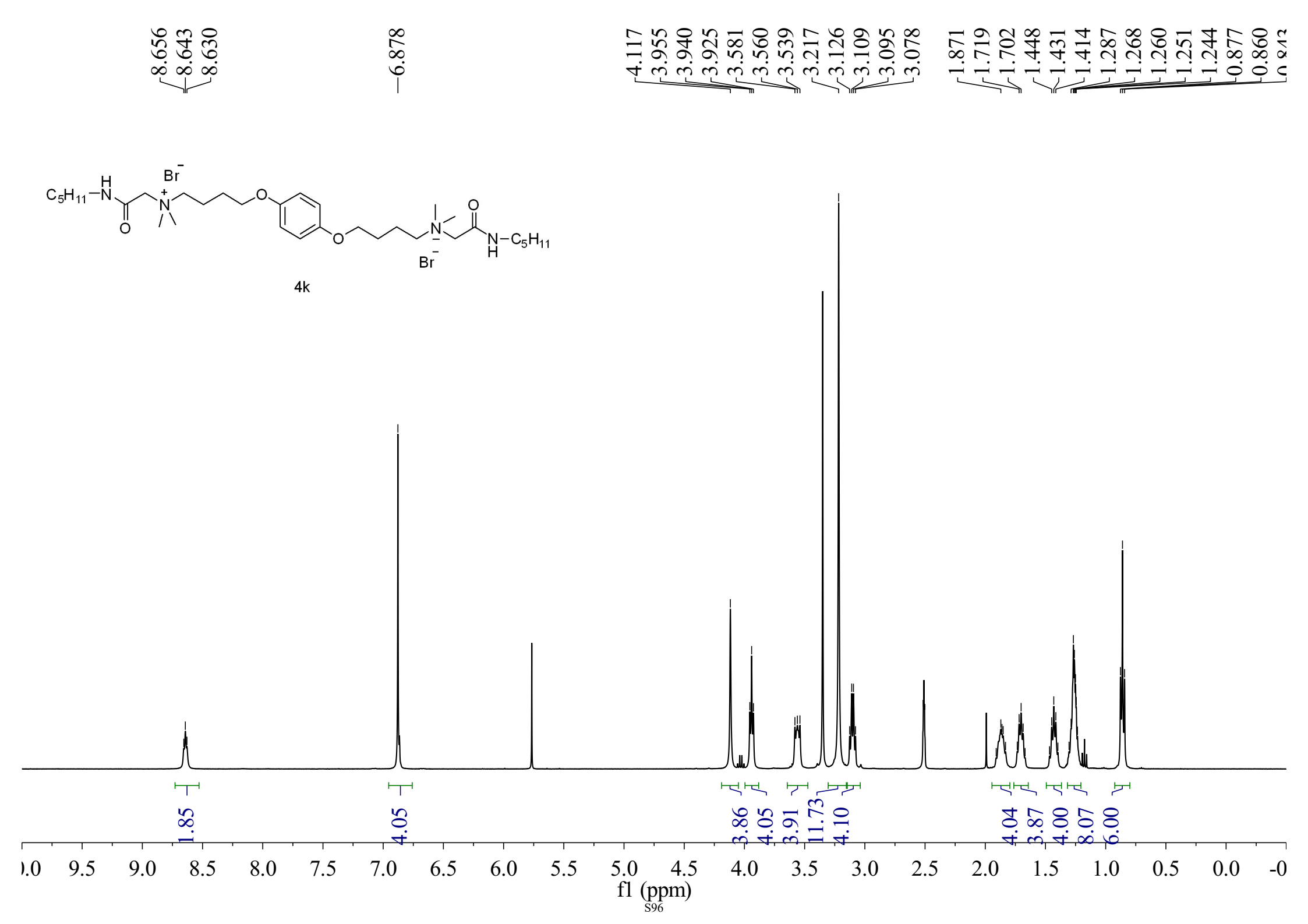


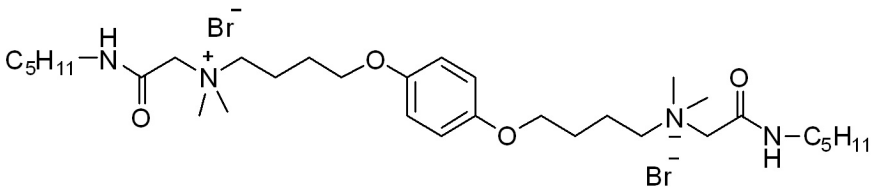
4j



4j

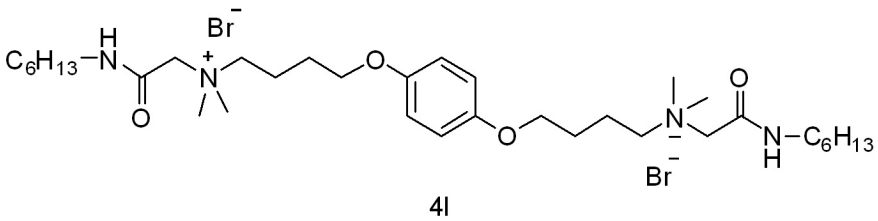
163.383
153.006
115.853
67.630
64.683
62.217
51.704
38.744
31.160
26.137
19.971
19.649
14.041
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.656
8.643
8.630
6.878
4.117
3.955
3.940
3.925
3.581
3.560
3.539
3.217
3.126
3.109
3.095
3.078
1.871
1.719
1.702
1.448
1.431
1.414
1.287
1.268
1.260
1.251
1.244
0.877
0.860
Br
C5H11
N
H
O
N
Br
O
N
C5H11
H
4k
1.85
4.05
3.86
4.05
3.91
11.73
4.10
4.04
3.87
4.00
8.07
6.00
f1 (ppm)



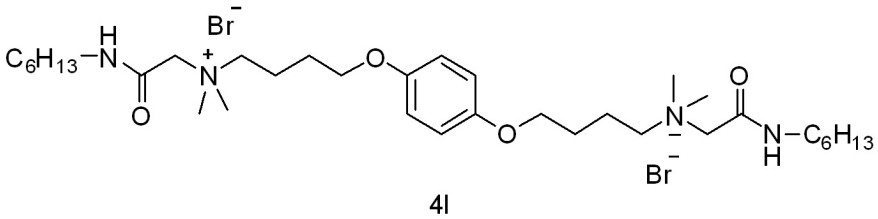
4k

163.400
153.006
115.850
67.626
64.651
62.231
55.420
51.656
28.983
28.734
26.149
22.211
19.631
14.356
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Br
C6H13
H
N
O
N
O
O
N
O
N
H
C6H13
Br

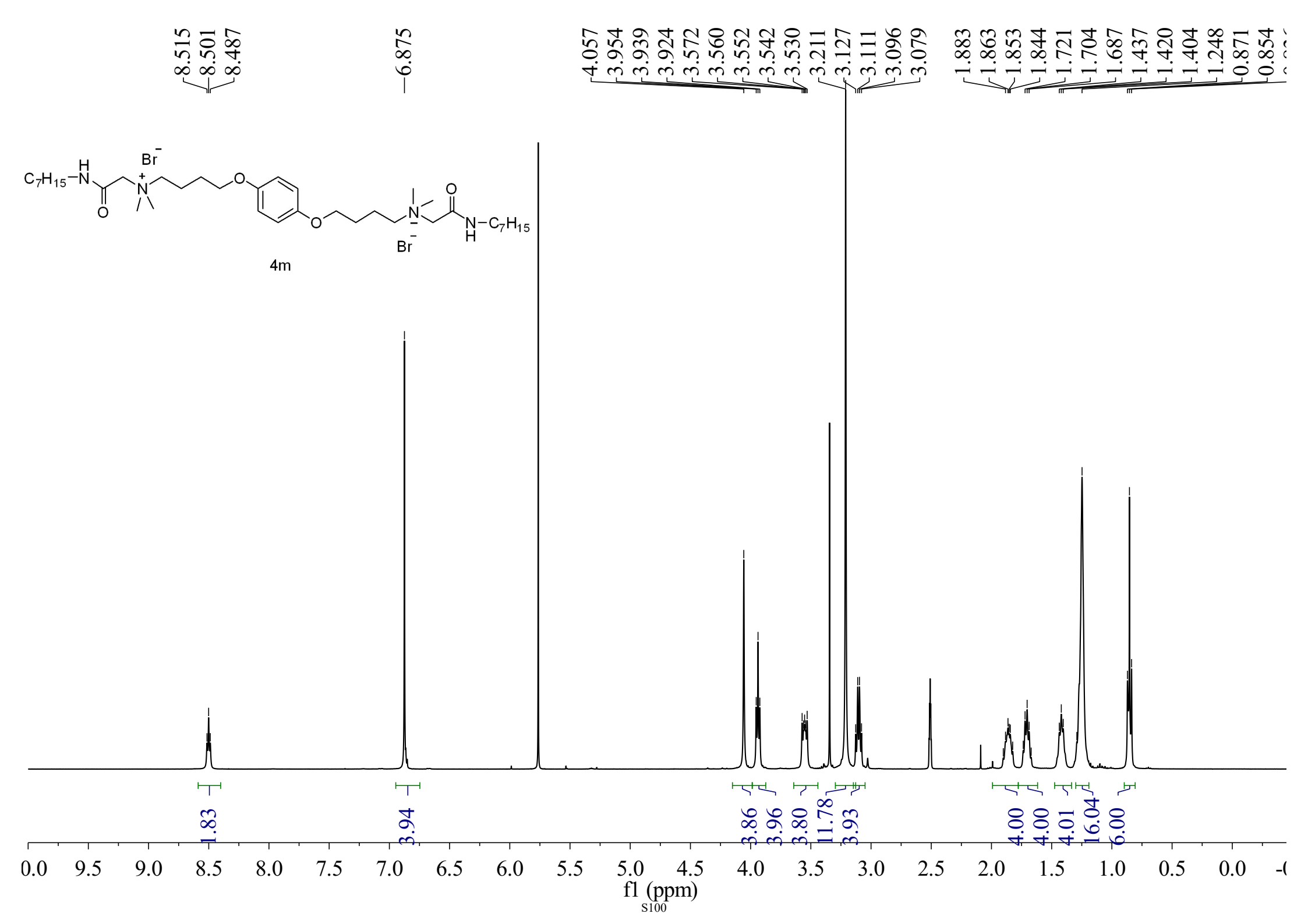
4l

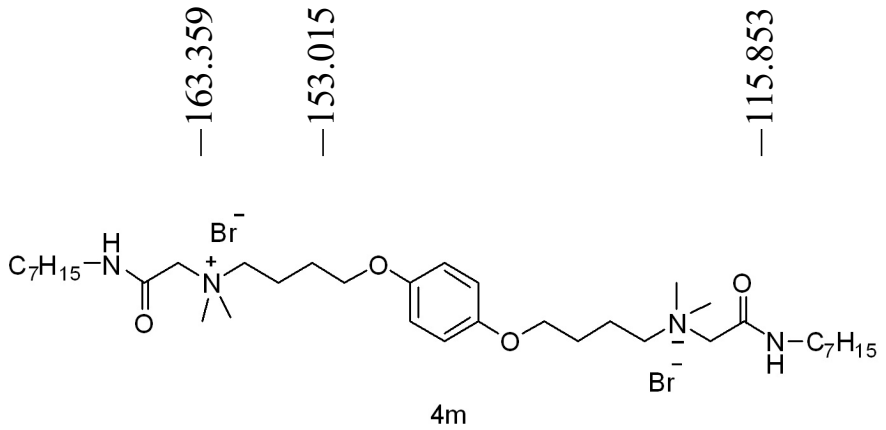
8.635
8.622
8.609
6.873
4.108
3.950
3.935
3.921
3.579
3.559
3.538
3.216
3.122
3.105
3.090
3.074
1.865
1.713
1.697
1.681
1.417
1.400
1.244
1.054
0.868
0.853
0.835
1.82
4.00
4.01
4.00
4.01
11.98
4.10
4.04
4.00
4.07
12.12
6.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Br
C6H13
H
N
O
N
O
O
N
O
N
H
C6H13
Br

4l

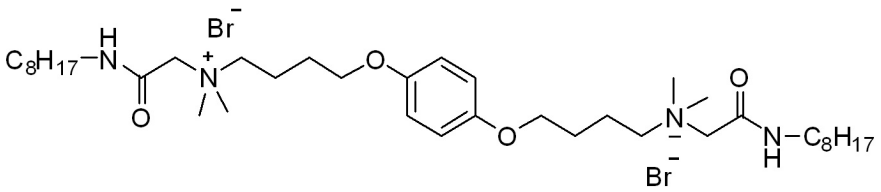
163.390
152.998
115.850
67.630
64.638
62.230
56.473
55.442
51.673
31.341
29.026
26.475
26.141
22.501
19.631
14.388
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.515
8.501
8.487
6.875
4.057
3.954
3.939
3.924
3.572
3.560
3.552
3.542
3.530
3.211
3.127
3.111
3.096
3.079
1.883
1.863
1.853
1.844
1.721
1.704
1.687
1.437
1.420
1.404
1.248
0.871
0.854
4m
1.83
3.94
3.86
3.96
3.80
11.78
3.93
4.00
4.00
4.01
16.04
6.00
fl (ppm)


Br
C7H15
H
N
O
N
O
O
N
O
N
H
C7H15
Br

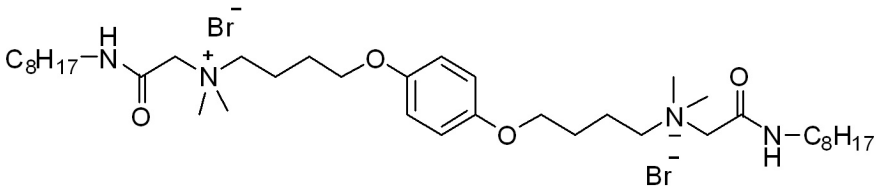
4m

163.359
153.015
115.853
67.649
64.669
62.248
55.421
51.736
31.683
29.091
28.788
26.766
26.148
22.507
19.652
14.415
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Br
C_8H_{17}
H
N
O
N
O
O
O
N
Br
O
N
H
C_8H_{17}

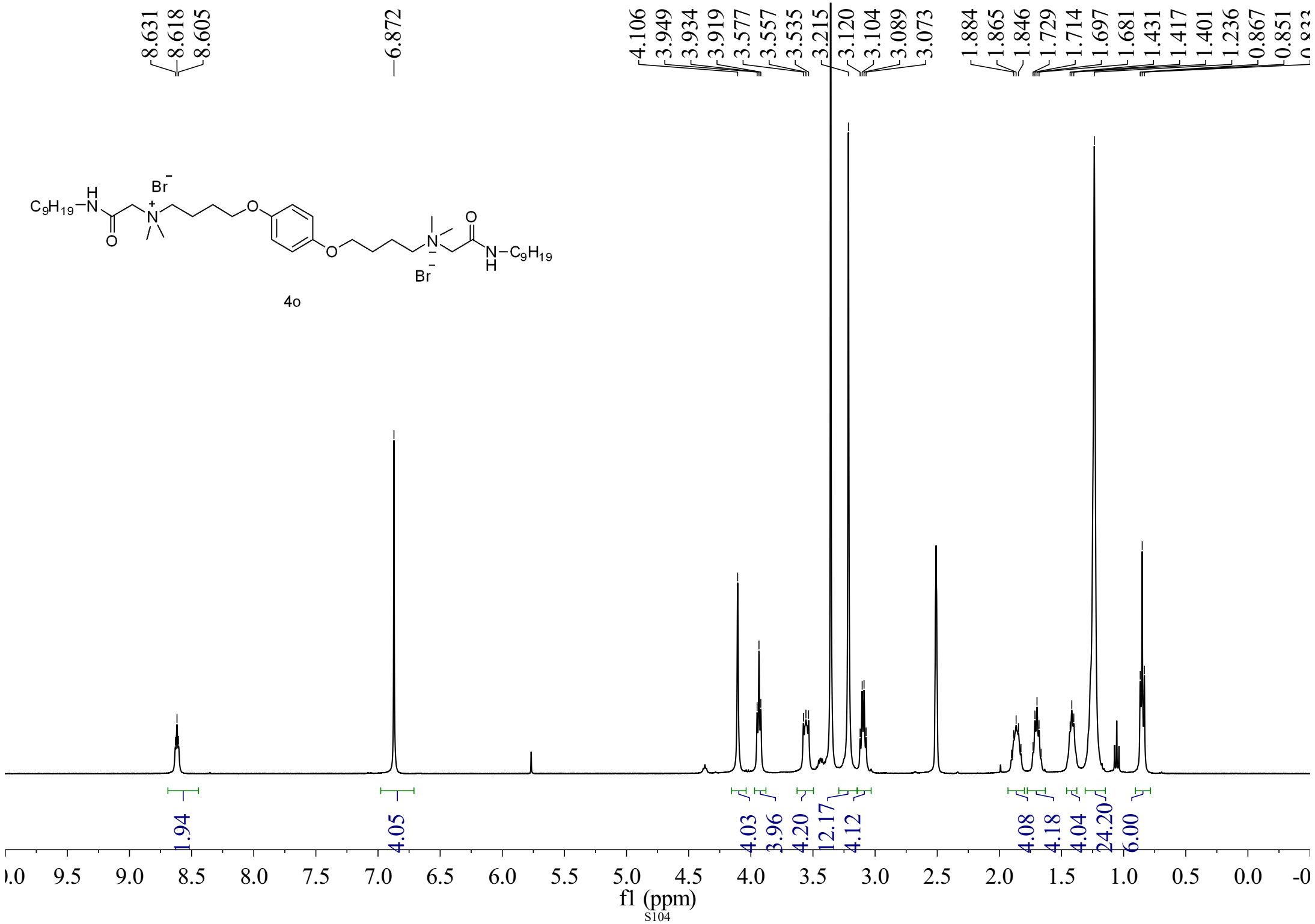
4n

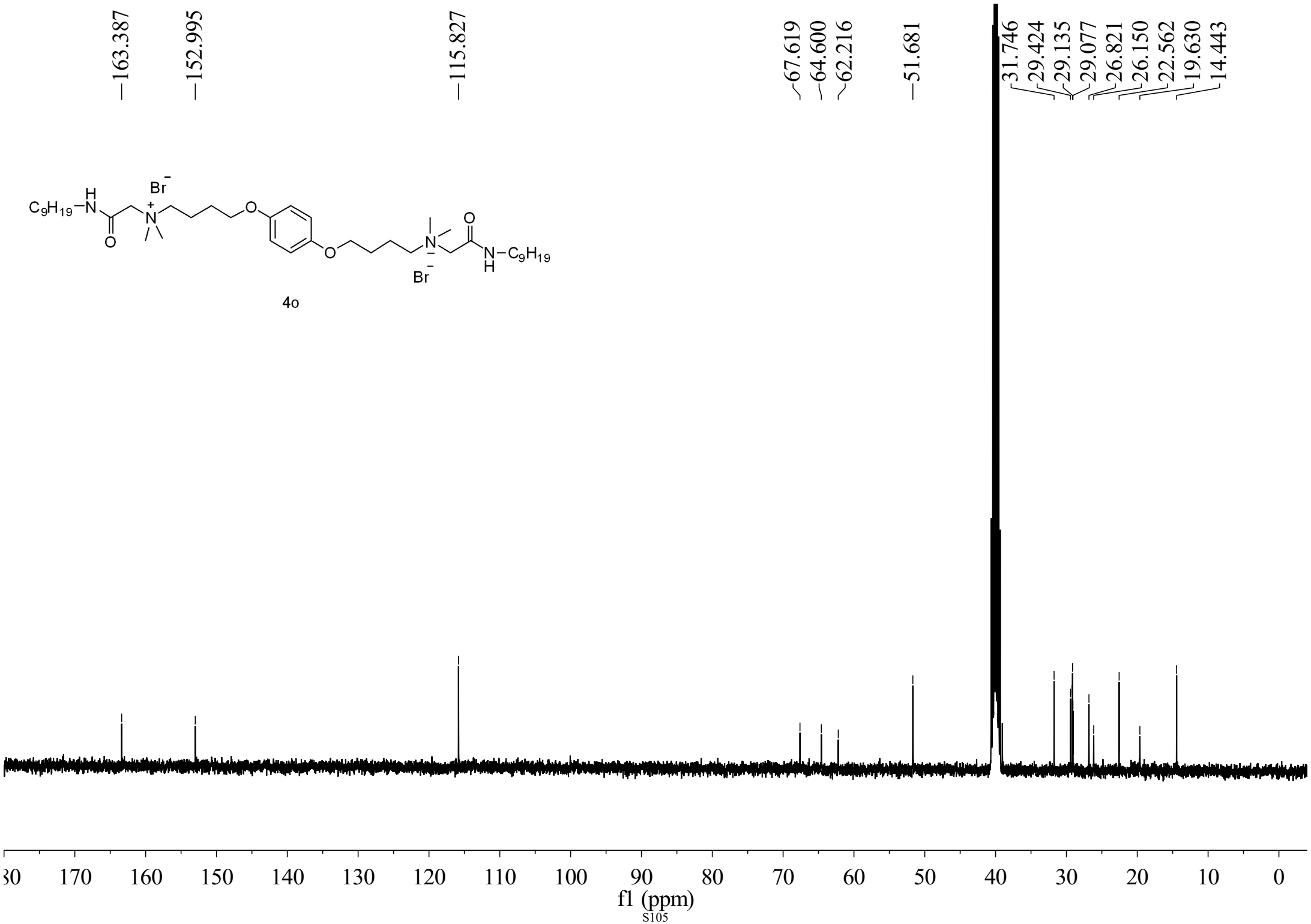
8.498
8.484
8.470
6.874
4.053
3.953
3.938
3.923
3.573
3.560
3.552
3.543
3.531
3.211
3.126
3.109
3.095
3.078
1.863
1.853
1.844
1.736
1.721
1.704
1.687
1.434
1.418
1.402
1.241
0.869
0.853
1.87
4.13
3.88
4.23
3.83
11.94
4.11
4.23
4.01
4.16
20.04
6.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

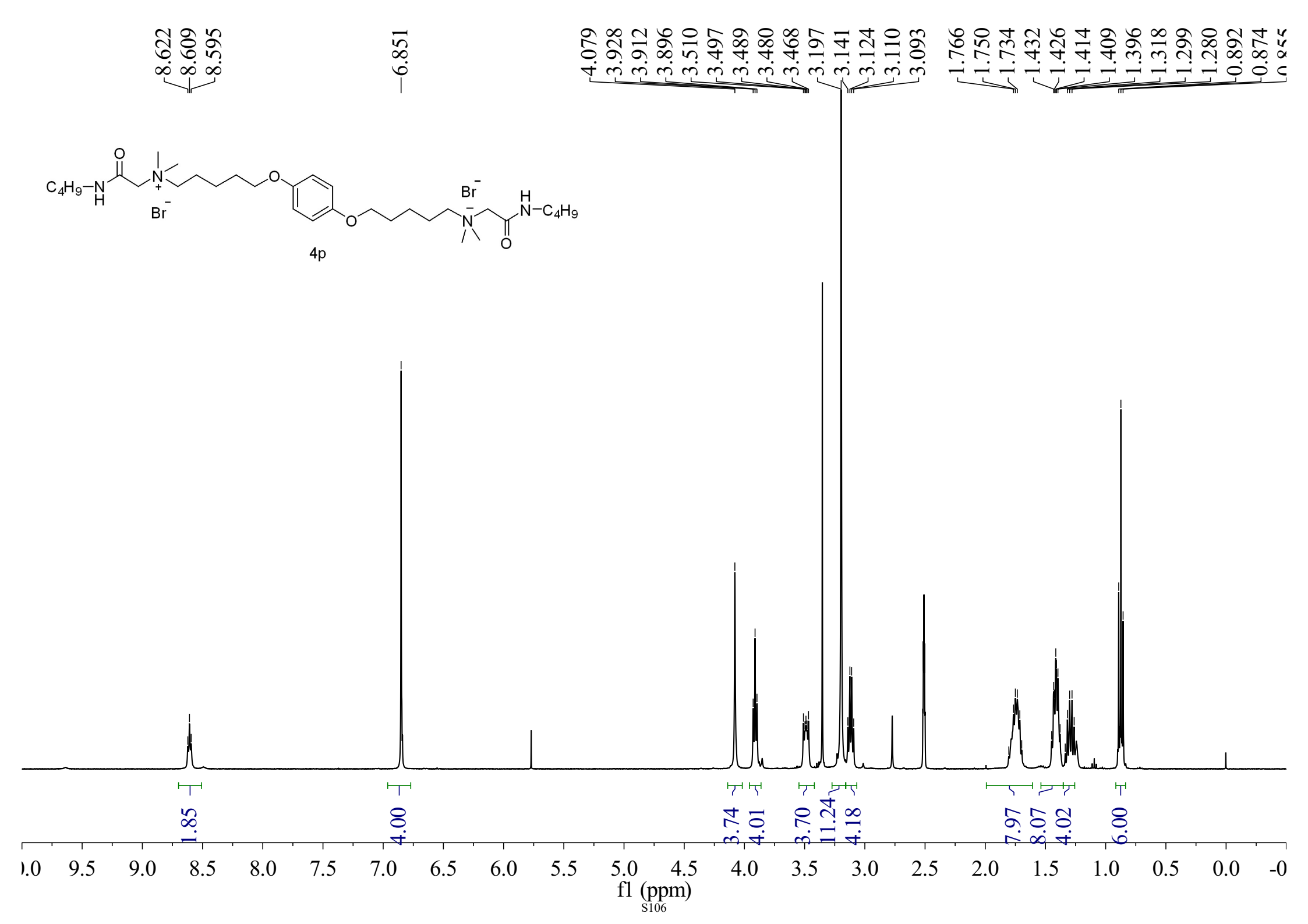


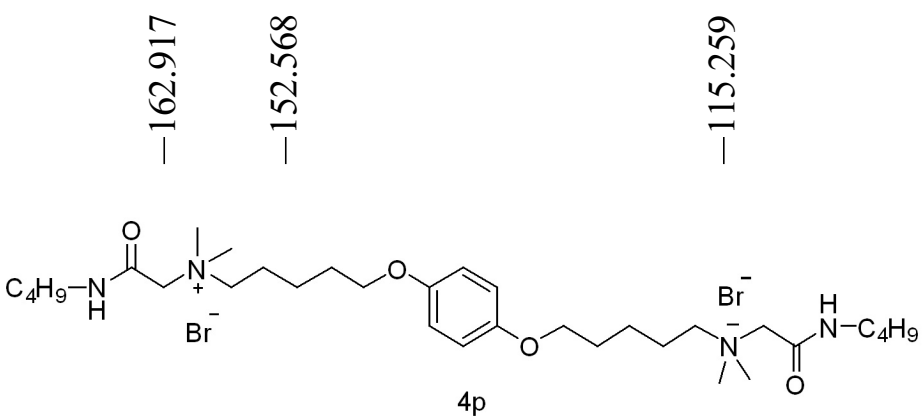
4n

163.350
157.411
153.008
115.842
67.641
64.654
62.236
55.420
51.744
31.692
31.188
29.114
29.092
26.812
26.145
22.548
19.652
14.420
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.631
8.618
8.605
6.872
4.106
3.949
3.934
3.919
3.577
3.557
3.535
3.215
3.120
3.104
3.089
3.073
1.884
1.865
1.846
1.729
1.714
1.697
1.681
1.431
1.417
1.401
1.236
0.867
0.851
Br
C9H19
N
H
O
Br
N
C9H19
H
4o
1.94
4.05
4.03
3.96
4.20
12.17
4.12
4.08
4.18
4.04
24.20
6.00
f1 (ppm)

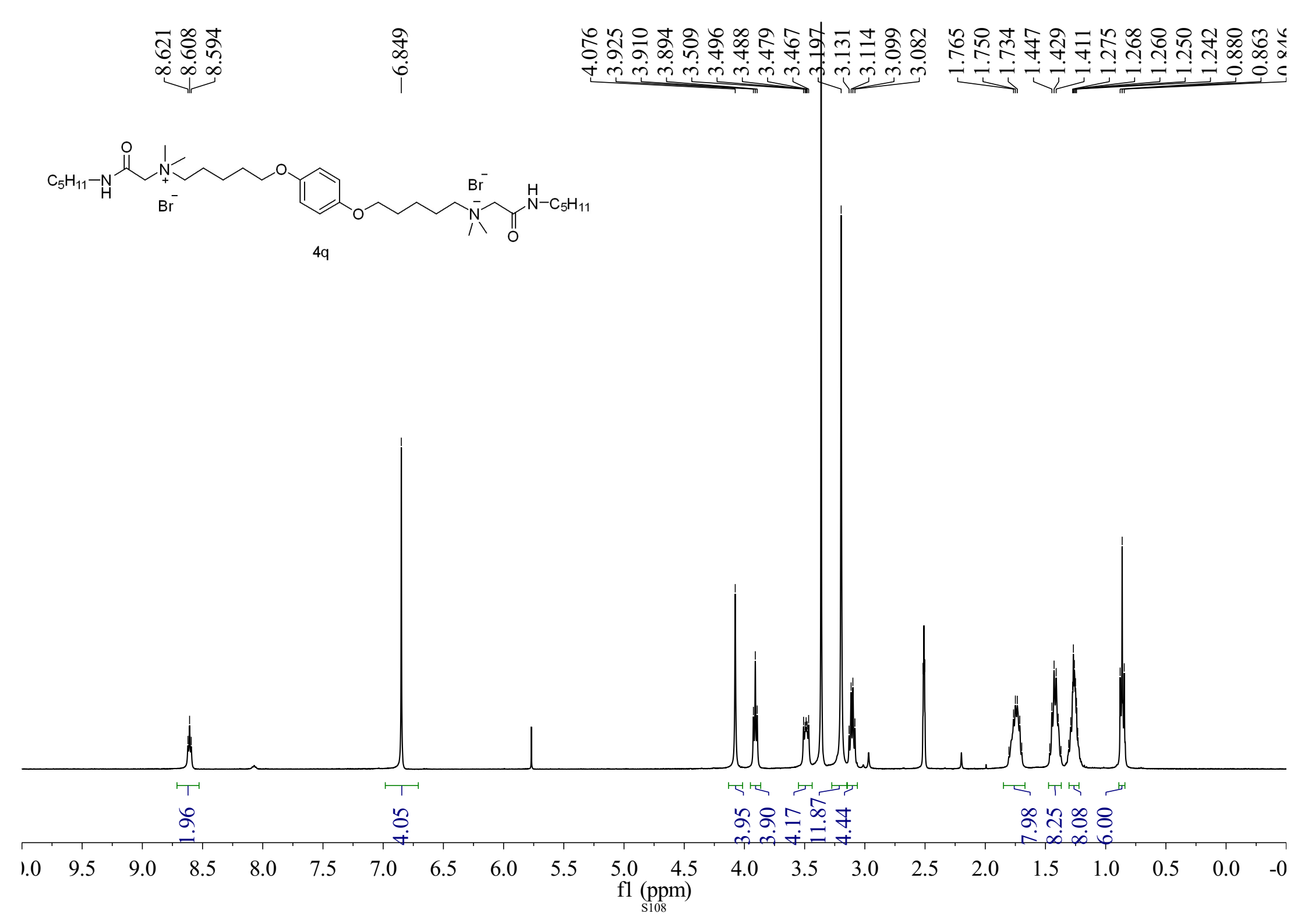

163.387
152.995
115.827
67.619
64.600
62.216
51.681
31.746
29.424
29.135
29.077
26.821
26.150
22.562
19.630
14.443
Br
Br
4o
f1 (ppm)

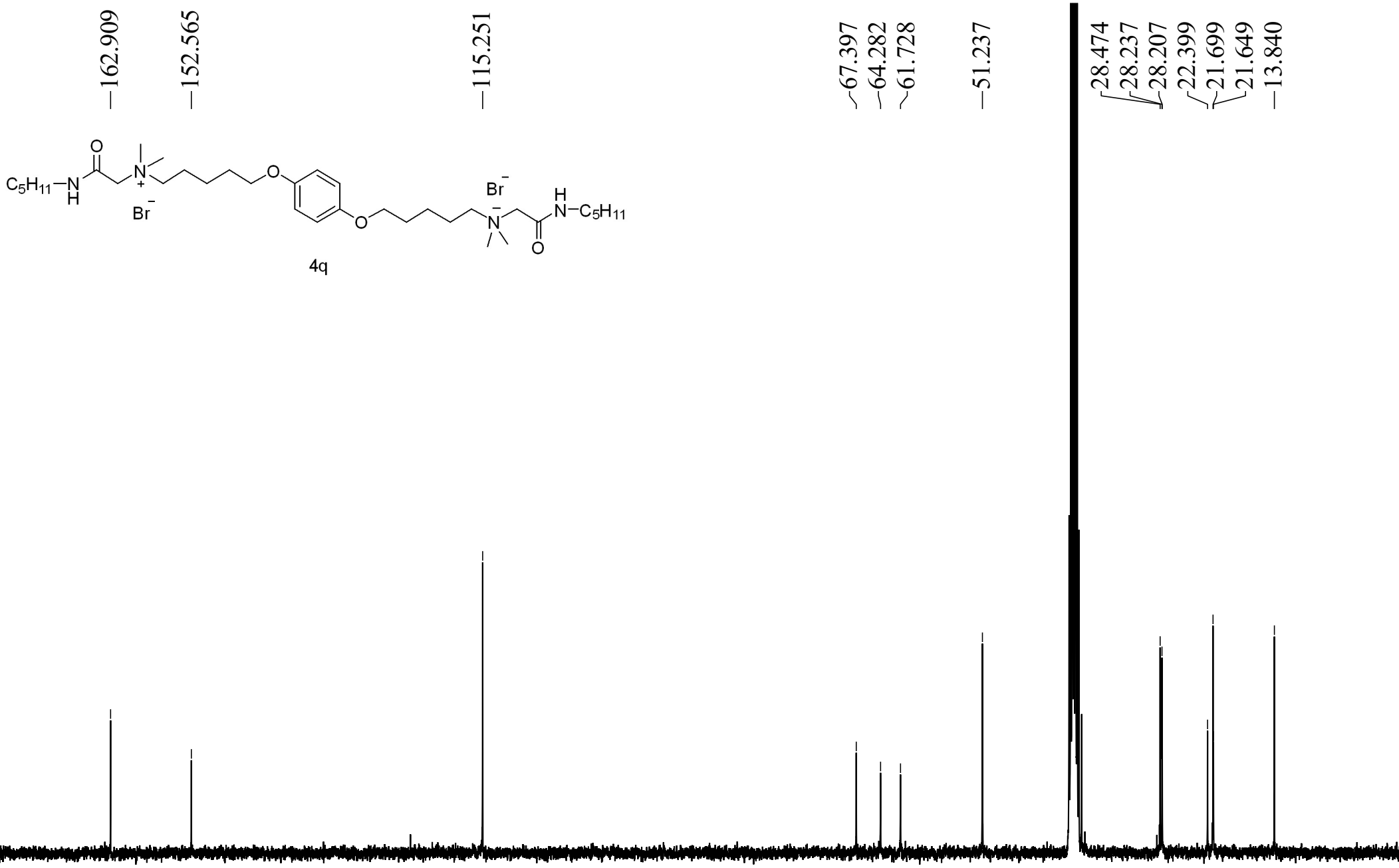

8.622
8.609
8.595
6.851
4.079
3.928
3.912
3.896
3.510
3.497
3.489
3.480
3.468
3.197
3.141
3.124
3.110
3.093
1.766
1.750
1.734
1.432
1.426
1.414
1.409
1.396
1.318
1.299
1.280
0.892
0.874
4p
1.85
4.00
3.74
4.01
3.70
11.24
4.18
7.97
8.07
4.02
6.00
f1 (ppm)

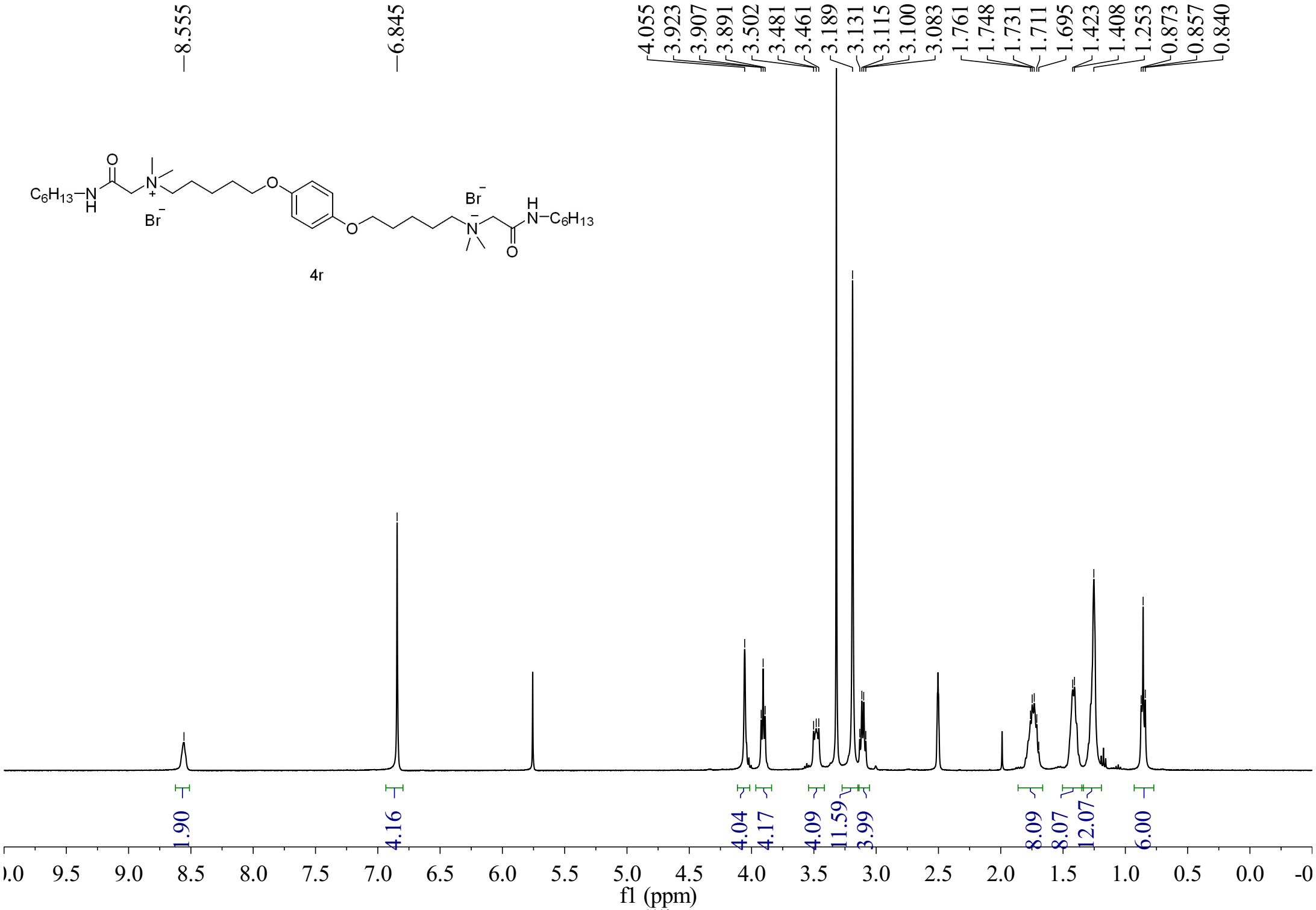

C4H9–N
H
O
N+
Br-
O
O
Br-
N
H
N–C4H9
O

4p

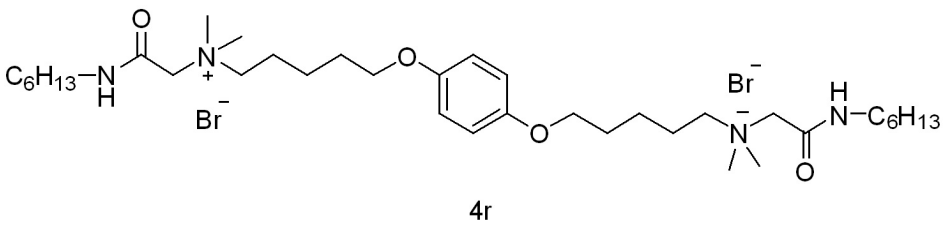
162.917
152.568
115.259
67.397
64.306
61.725
51.224
30.656
28.207
22.399
21.651
19.466
13.521
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.621
8.608
8.594
6.849
4.076
3.925
3.910
3.894
3.509
3.496
3.488
3.479
3.467
3.197
3.131
3.114
3.099
3.082
1.765
1.750
1.734
1.447
1.429
1.411
1.275
1.268
1.260
1.250
1.242
0.880
0.863
4q
1.96
4.05
3.95
3.90
4.17
11.87
4.44
7.98
8.25
8.08
6.00
f1 (ppm)


162.909
152.565
115.251
67.397
64.282
61.728
51.237
28.474
28.237
28.207
22.399
21.699
21.649
13.840
4q
f1 (ppm)

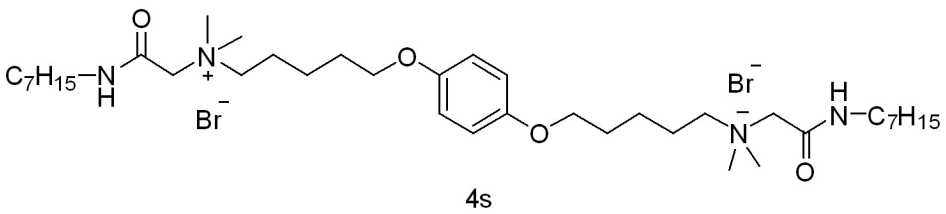

8.555
6.845
4.055
3.923
3.907
3.891
3.502
3.481
3.461
3.189
3.131
3.115
3.100
3.083
1.761
1.748
1.731
1.711
1.695
1.423
1.408
1.253
0.873
0.857
0.840
1.90
4.16
4.04
4.17
4.09
11.59
3.99
8.09
8.07
12.07
6.00
f1 (ppm)

4r


C6H13
H
N
O
N+
Br−
O
O
Br−
N−
H
N
C6H13
O

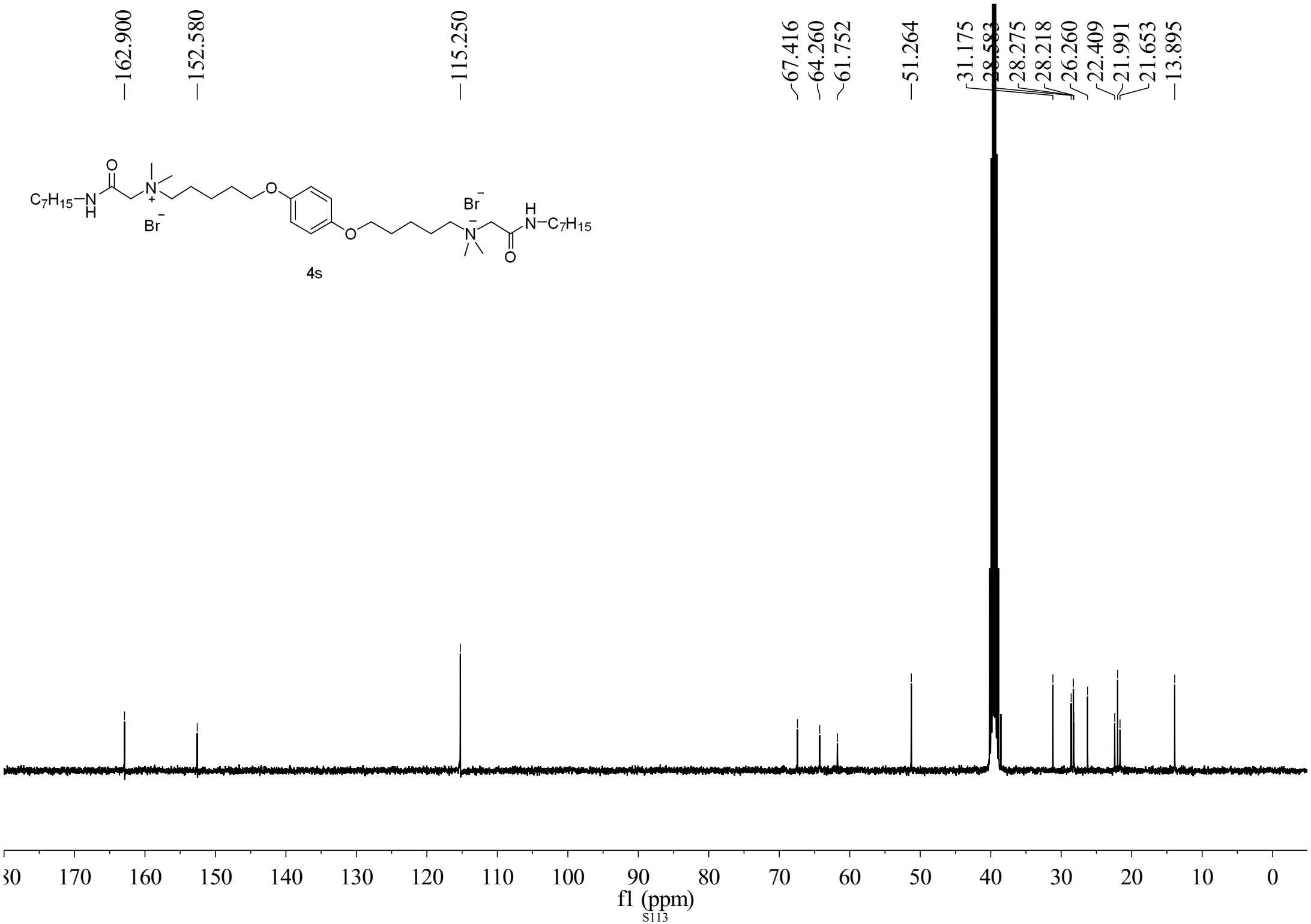
4r

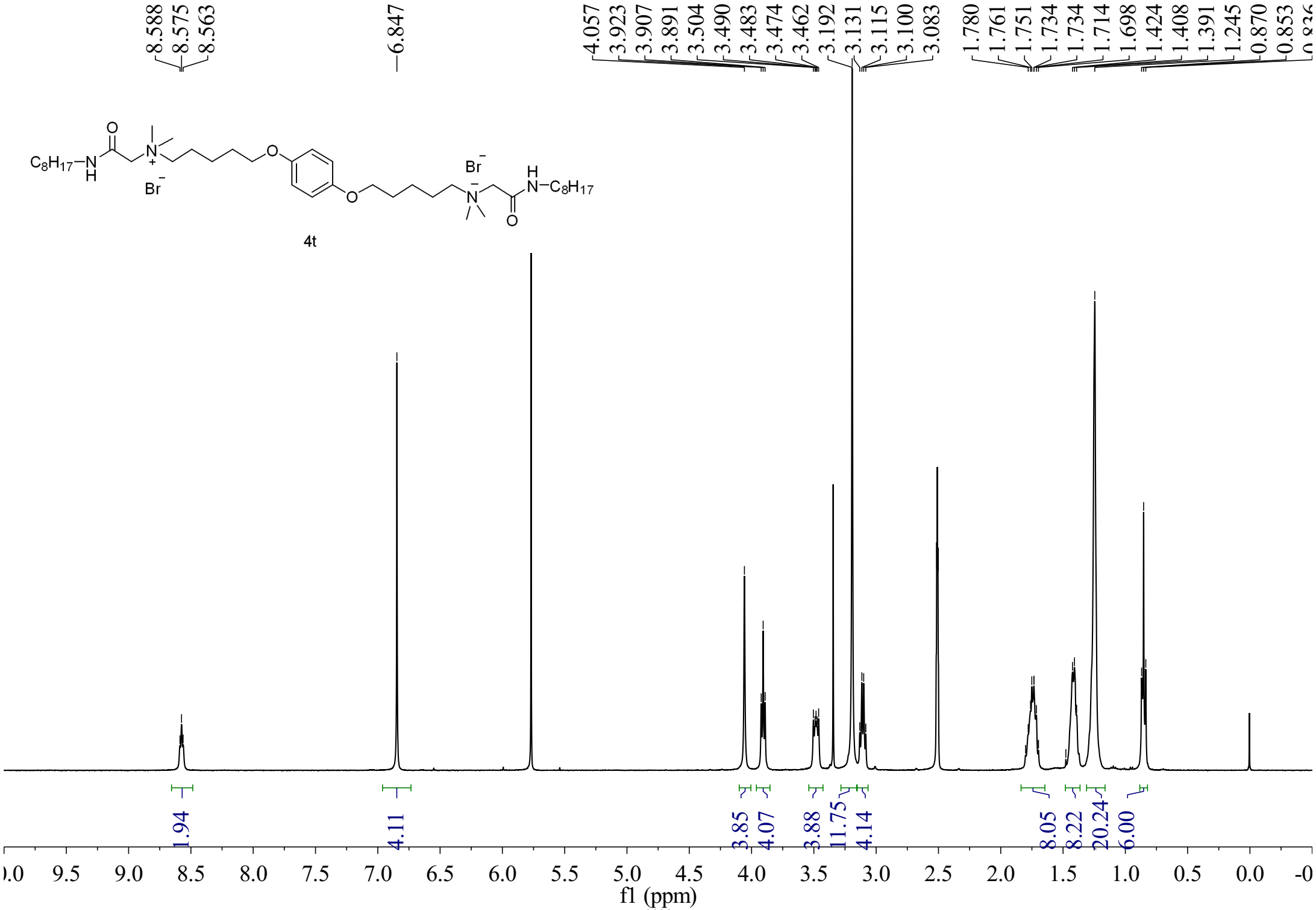
162.898
152.573
115.240
67.402
64.252
61.729
51.259
39.824
28.546
28.220
25.961
22.405
21.994
21.648
13.862
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


C7H15
N
H
O
N+
Br−
O
O
Br−
N
H
N−C7H15
O

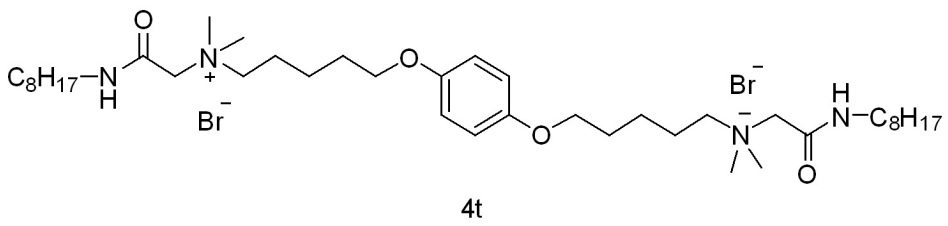
4s

8.598
8.585
8.571
6.847
4.060
3.923
3.907
3.891
3.503
3.491
3.483
3.474
3.461
3.192
3.131
3.114
3.100
3.083
1.780
1.760
1.750
1.733
1.713
1.697
1.423
1.407
1.390
1.292
1.250
0.871
0.855
2.01
4.04
4.11
4.07
4.40
11.87
4.14
8.04
8.26
16.03
6.00
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)


162.900
152.580
115.250
67.416
64.260
61.752
51.264
31.175
28.583
28.275
28.218
26.260
22.409
21.991
21.653
13.895
4s
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

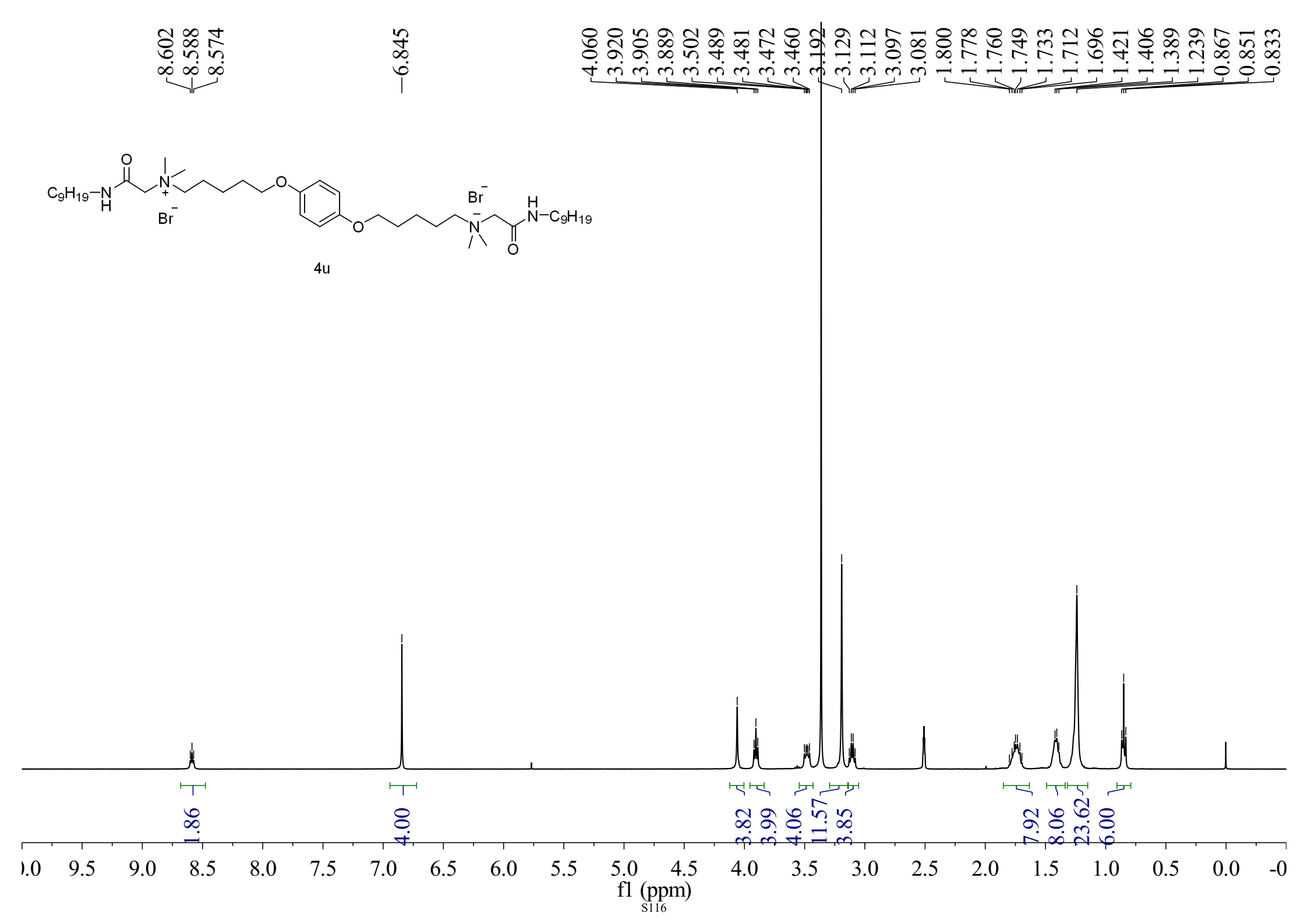

8.588
8.575
8.563
6.847
4.057
3.923
3.907
3.891
3.504
3.490
3.483
3.474
3.462
3.192
3.131
3.115
3.100
3.083
1.780
1.761
1.751
1.734
1.734
1.714
1.698
1.424
1.408
1.391
1.245
0.870
0.853
1.94
4.11
3.85
4.07
3.88
11.75
4.14
8.05
8.22
20.24
6.00
f1 (ppm)

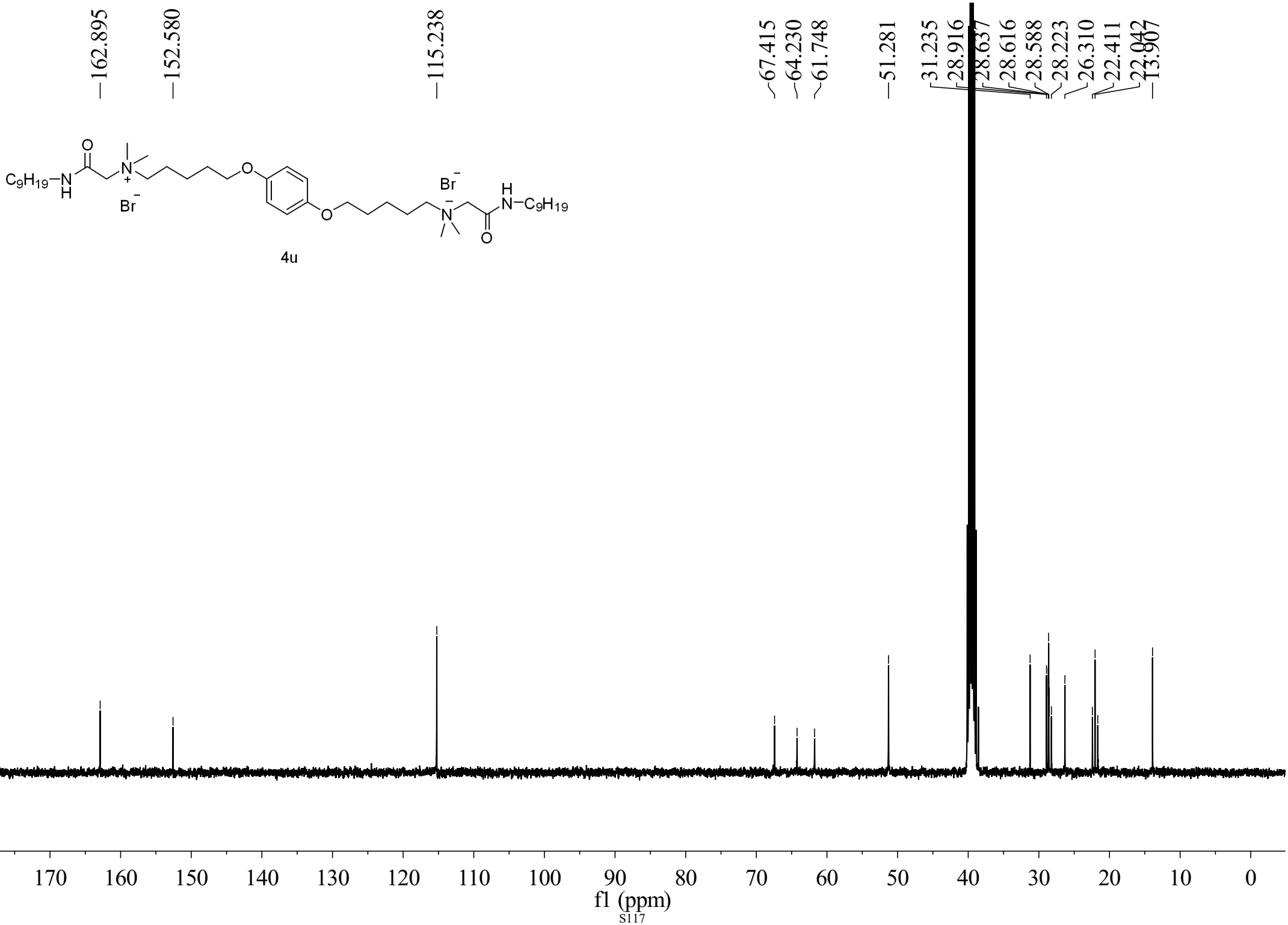
4t

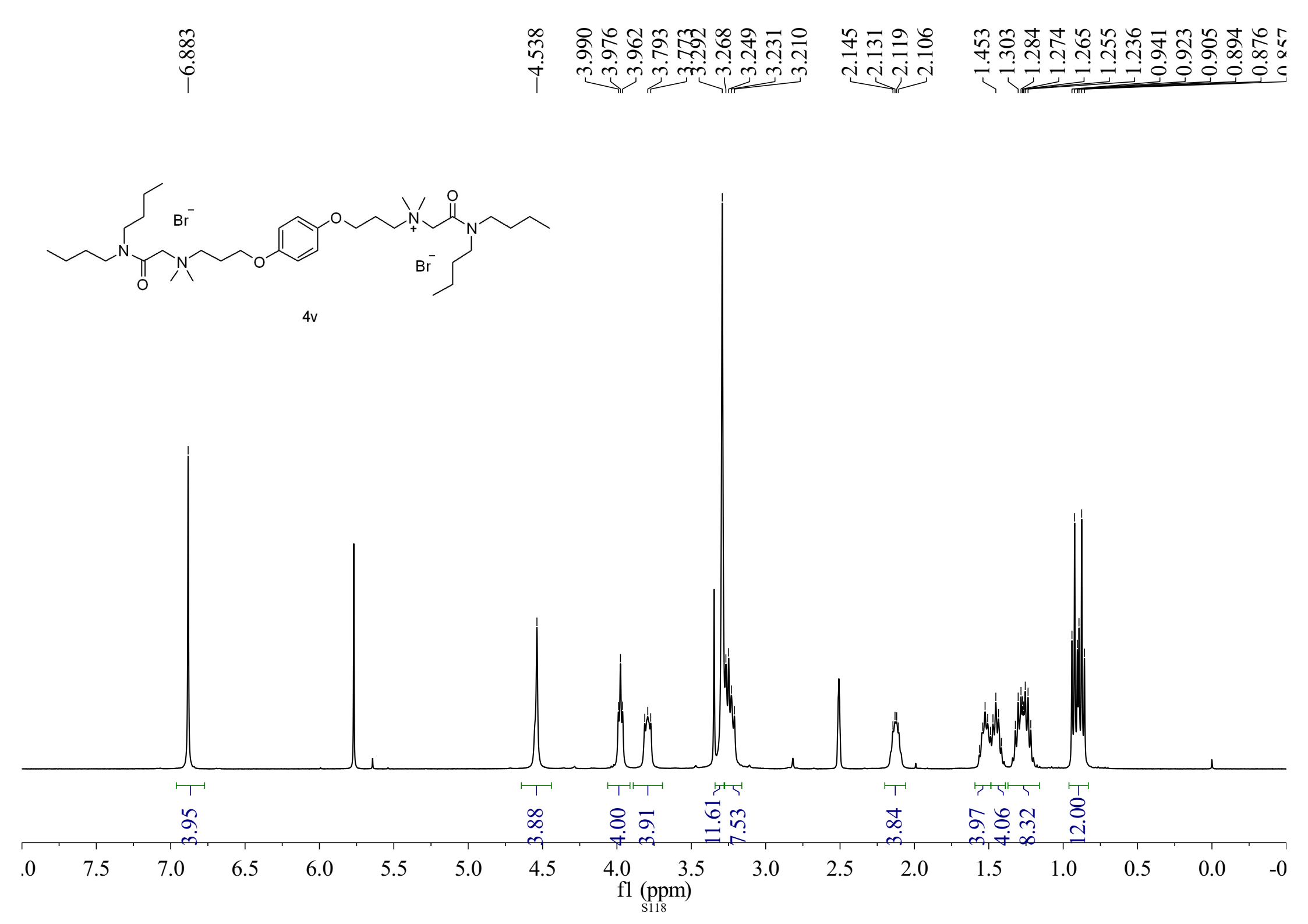

O
C8H17–N
H
N
+
Br
−
O
O
Br
−
N
−
H
N–C8H17
O

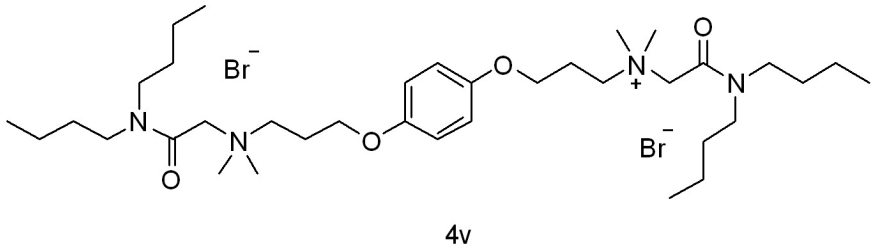
4t

162.901
152.574
115.228
67.399
64.224
61.723
54.891
51.264
31.188
28.592
28.227
26.315
22.412
22.040
21.655
13.907
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.602
8.588
8.574
6.845
4.060
3.920
3.905
3.889
3.502
3.489
3.481
3.472
3.460
3.192
3.129
3.112
3.097
3.081
1.800
1.778
1.760
1.749
1.733
1.712
1.696
1.421
1.406
1.389
1.239
0.867
0.851
0.833
4u
1.86
4.00
3.82
3.99
4.06
11.57
3.85
7.92
8.06
23.62
6.00
f1 (ppm)

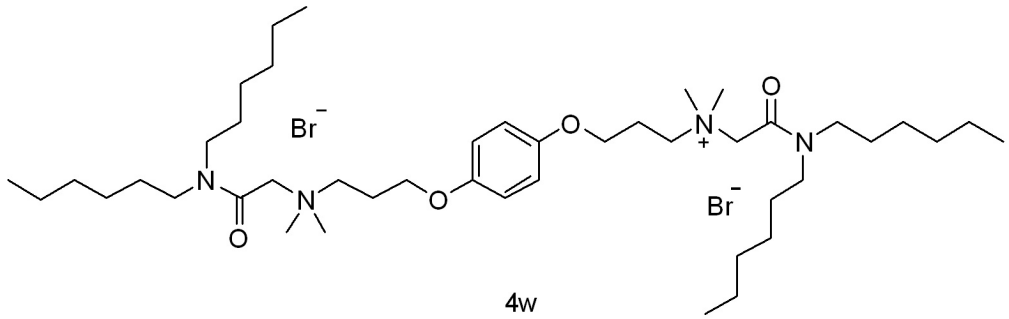

162.895
152.580
115.238
67.415
64.230
61.748
51.281
31.235
28.916
28.637
28.616
28.588
28.223
26.310
22.411
22.042
13.907
4u
f1 (ppm)


6.883
4.538
3.990
3.976
3.962
3.793
3.773
3.292
3.268
3.249
3.231
3.210
2.145
2.131
2.119
2.106
1.453
1.303
1.284
1.274
1.265
1.255
1.236
0.941
0.923
0.905
0.894
0.876
Br⁻
Br⁻
4v
3.95
3.88
4.00
3.91
11.61
7.53
3.84
3.97
4.06
8.32
12.00
f1 (ppm)


Br
Br
O
O
O
O
N
N
N
N
O

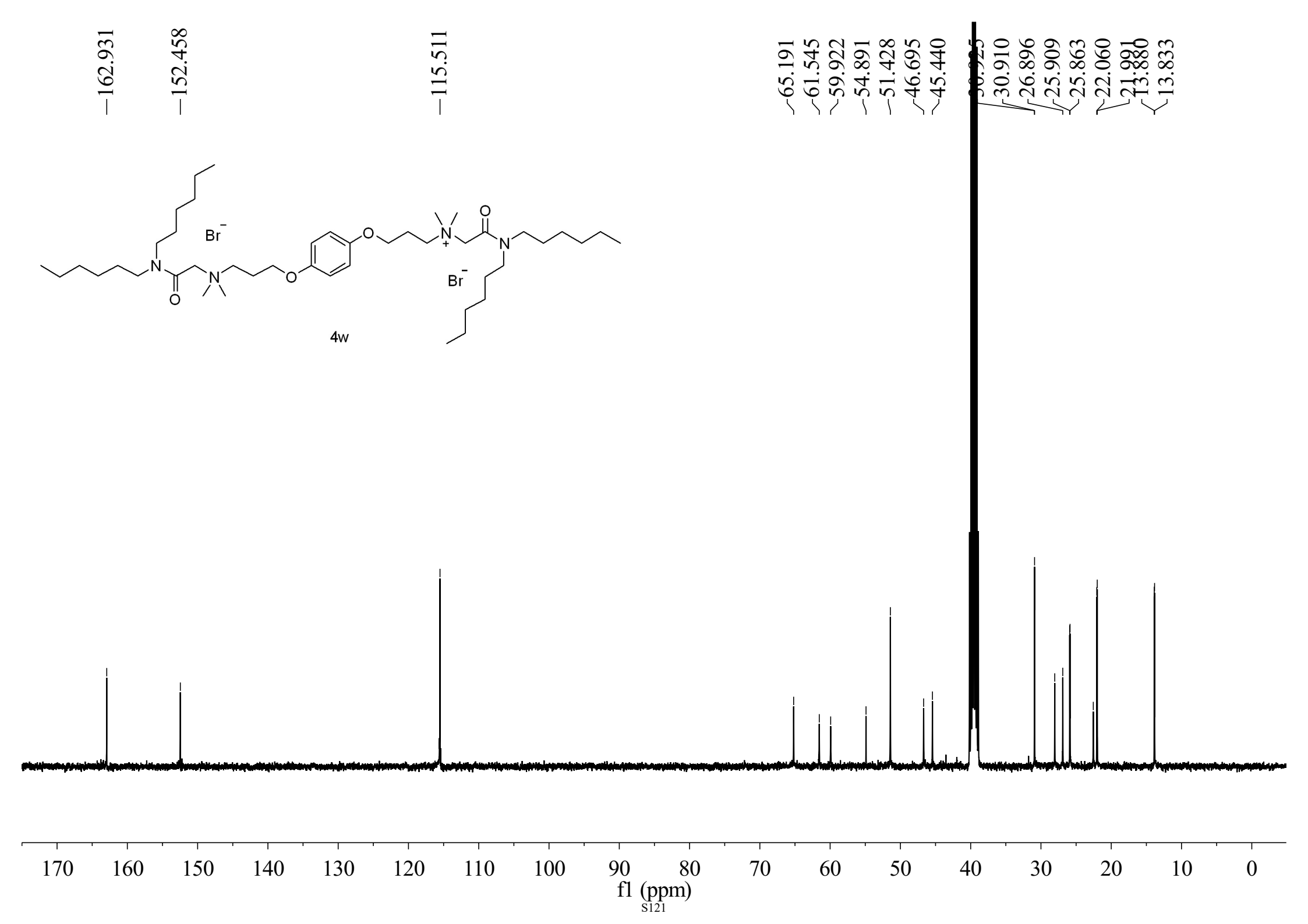
4v

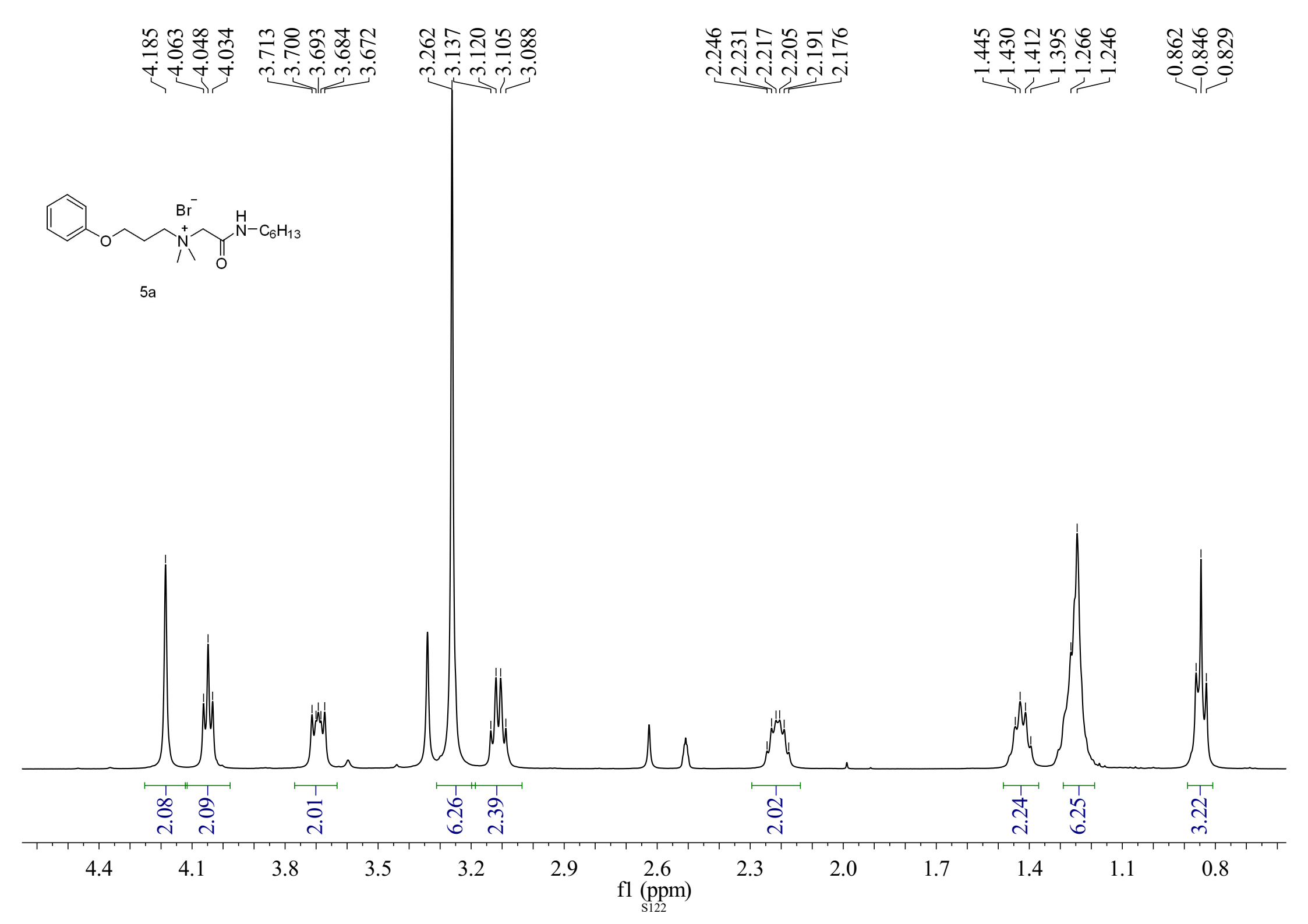
162.954
152.442
115.549
65.185
61.580
59.939
54.907
51.372
46.455
45.192
30.121
29.109
22.535
19.528
19.445
13.670
13.622
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

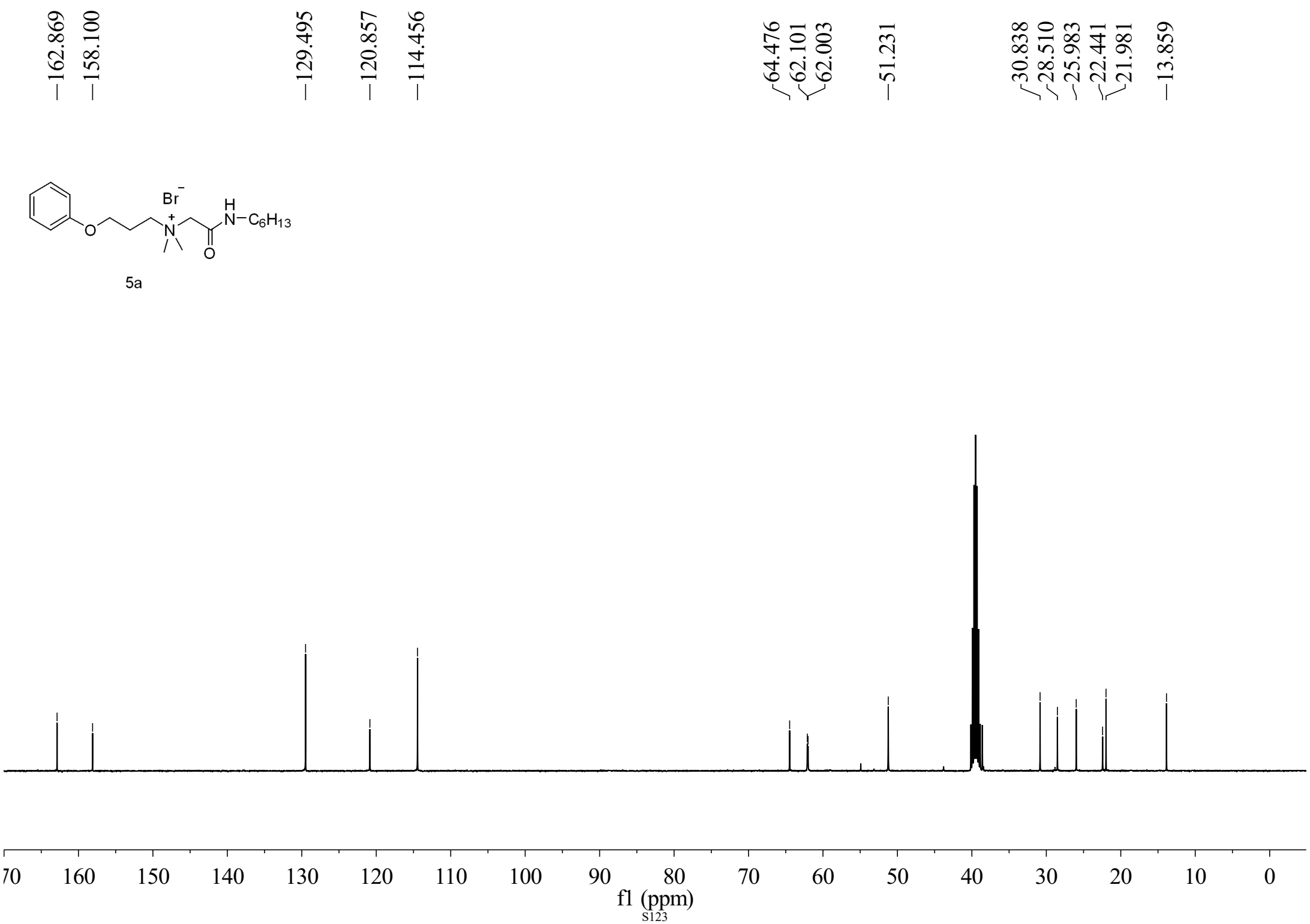

Br
Br
O
O
O
O
N
N
N
N
O
O

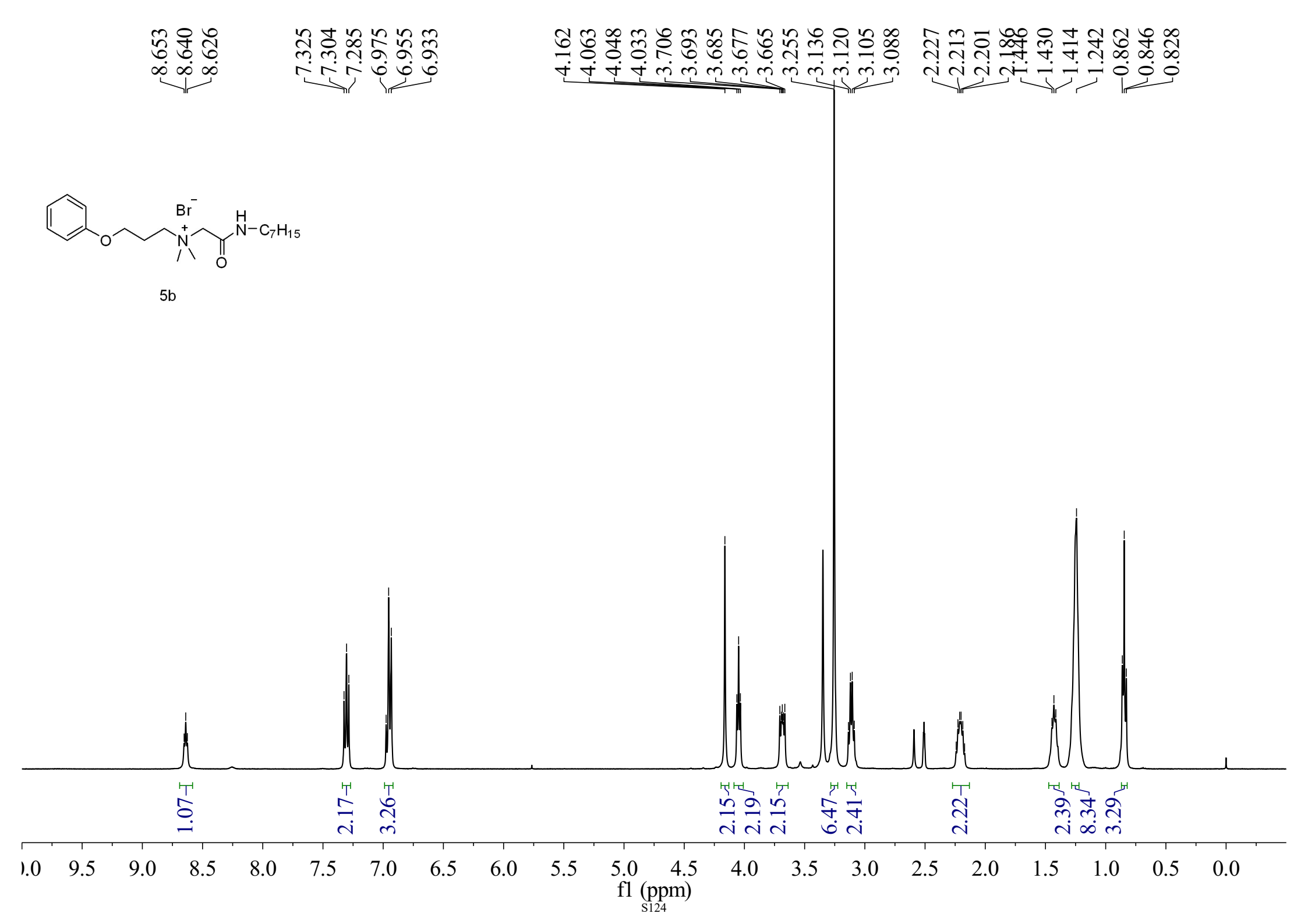
4w

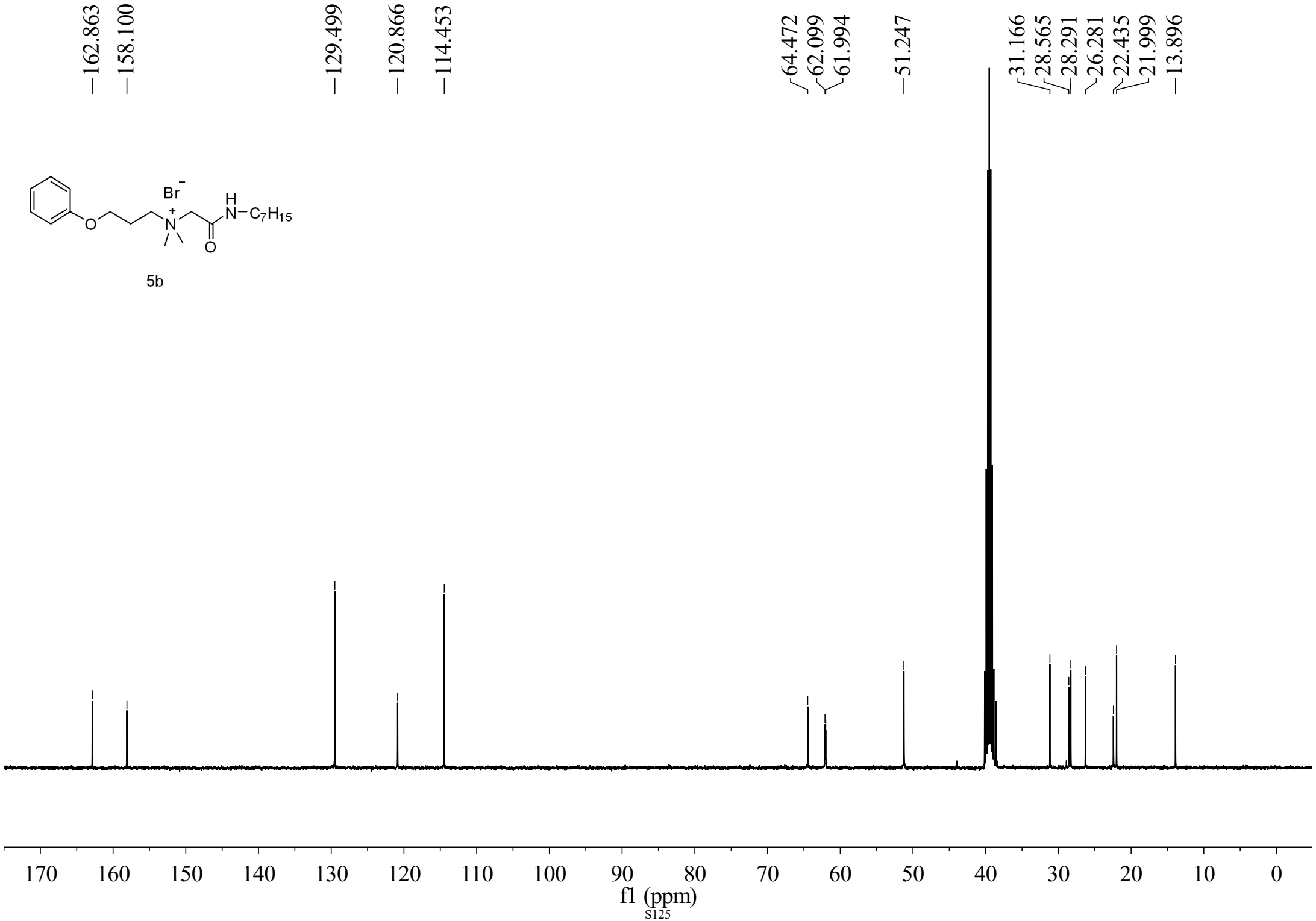
6.876
4.517
3.984
3.970
3.956
3.781
3.766
3.288
3.261
3.243
3.225
3.205
2.147
2.133
2.118
2.106
2.088
1.464
1.288
1.267
1.243
0.895
0.878
0.861
0.844
0.827
4.02
3.65
3.77
3.88
11.84
7.77
3.93
3.89
4.28
24.24
12.00
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

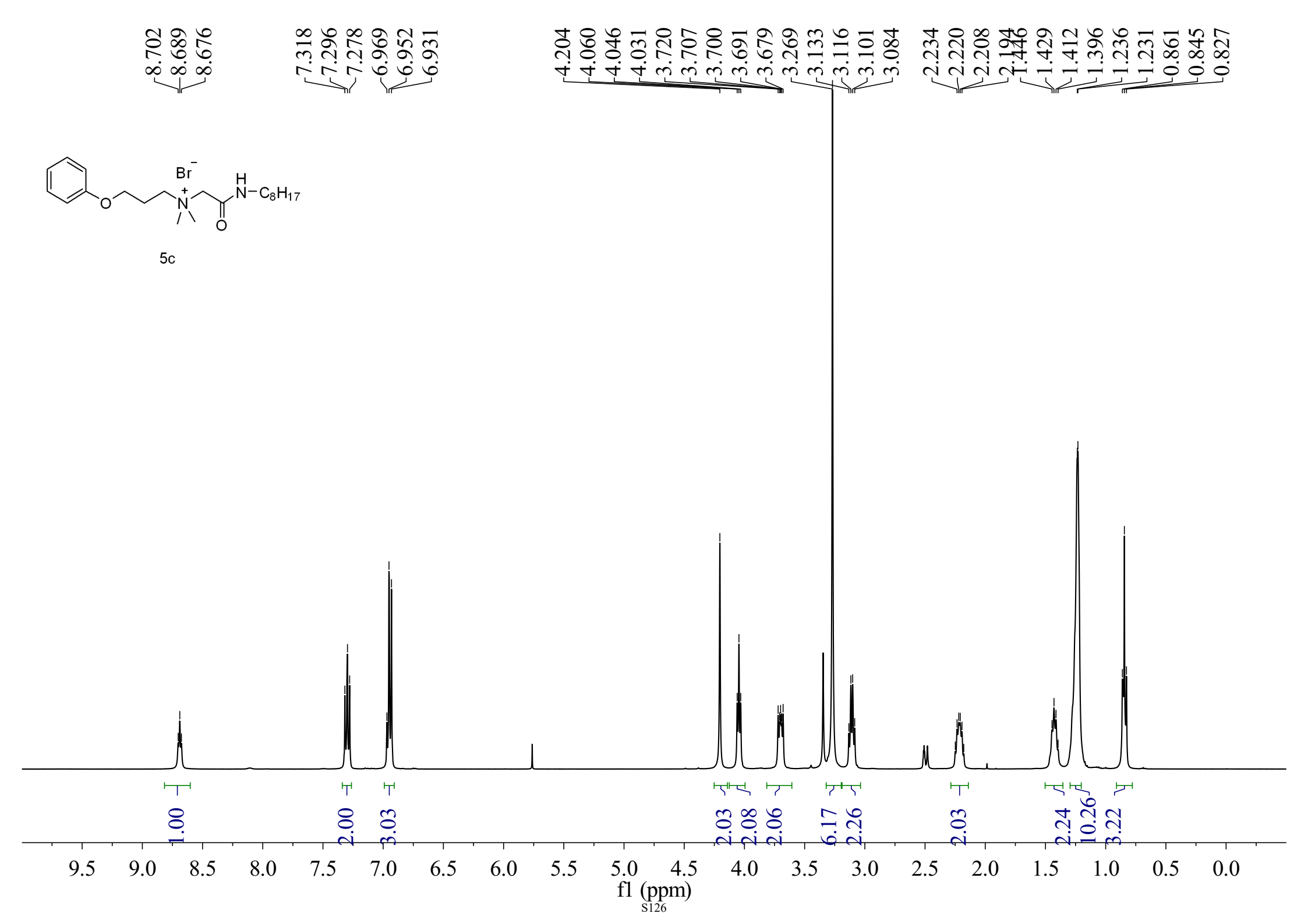

162.931
152.458
115.511
65.191
61.545
59.922
54.891
51.428
46.695
45.440
30.910
26.896
25.909
25.863
22.060
21.991
13.880
13.833
Br⁻
Br⁻
4w
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

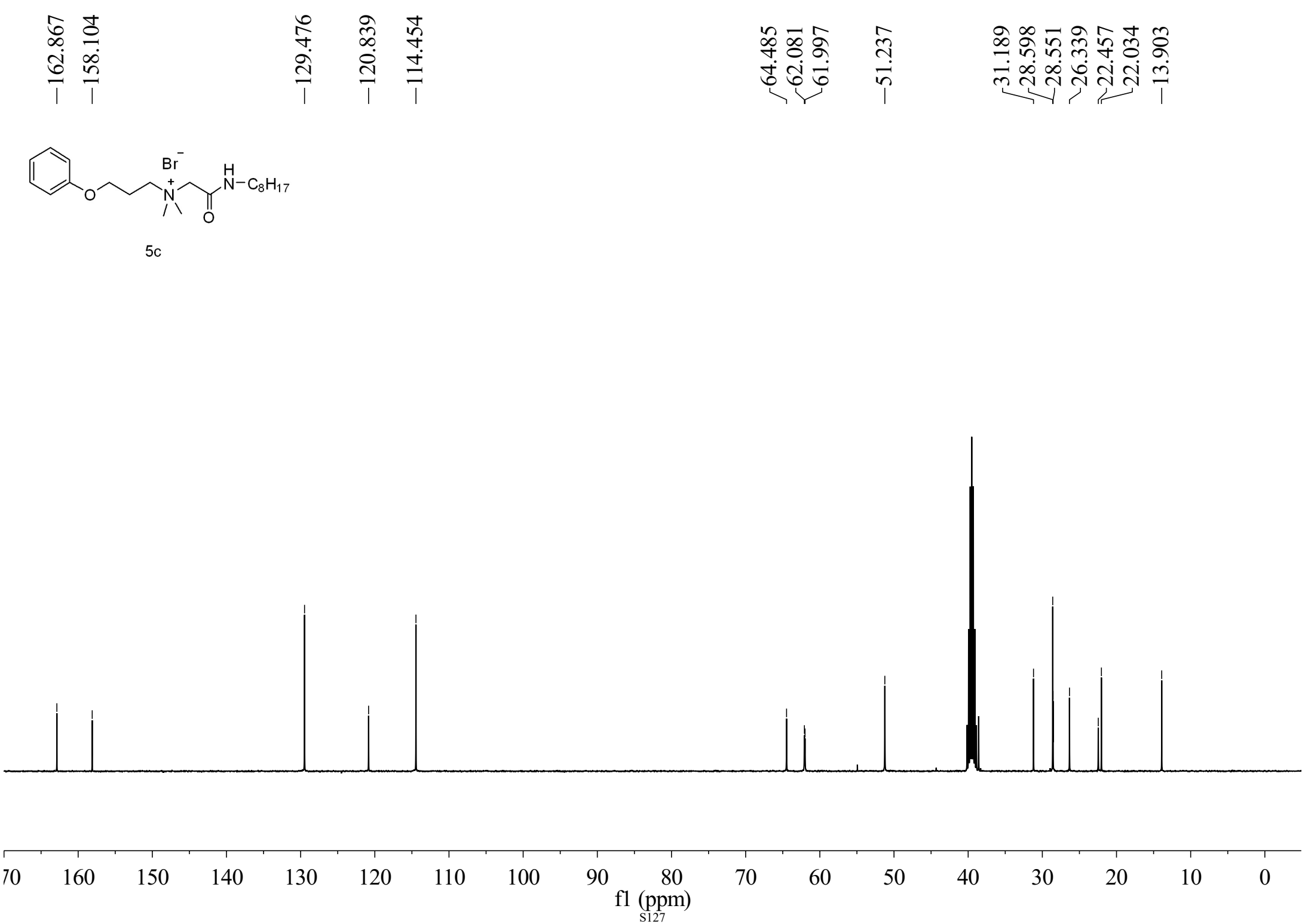

4.185
4.063
4.048
4.034
3.713
3.700
3.693
3.684
3.672
3.262
3.137
3.120
3.105
3.088
2.246
2.231
2.217
2.205
2.191
2.176
1.445
1.430
1.412
1.395
1.266
1.246
0.862
0.846
0.829
Br⁻
H
N−C6H13
O
N+
O
5a
2.08
2.09
2.01
6.26
2.39
2.02
2.24
6.25
3.22
4.4
4.1
3.8
3.5
3.2
2.9
2.6
2.3
2.0
1.7
1.4
1.1
0.8
f1 (ppm)

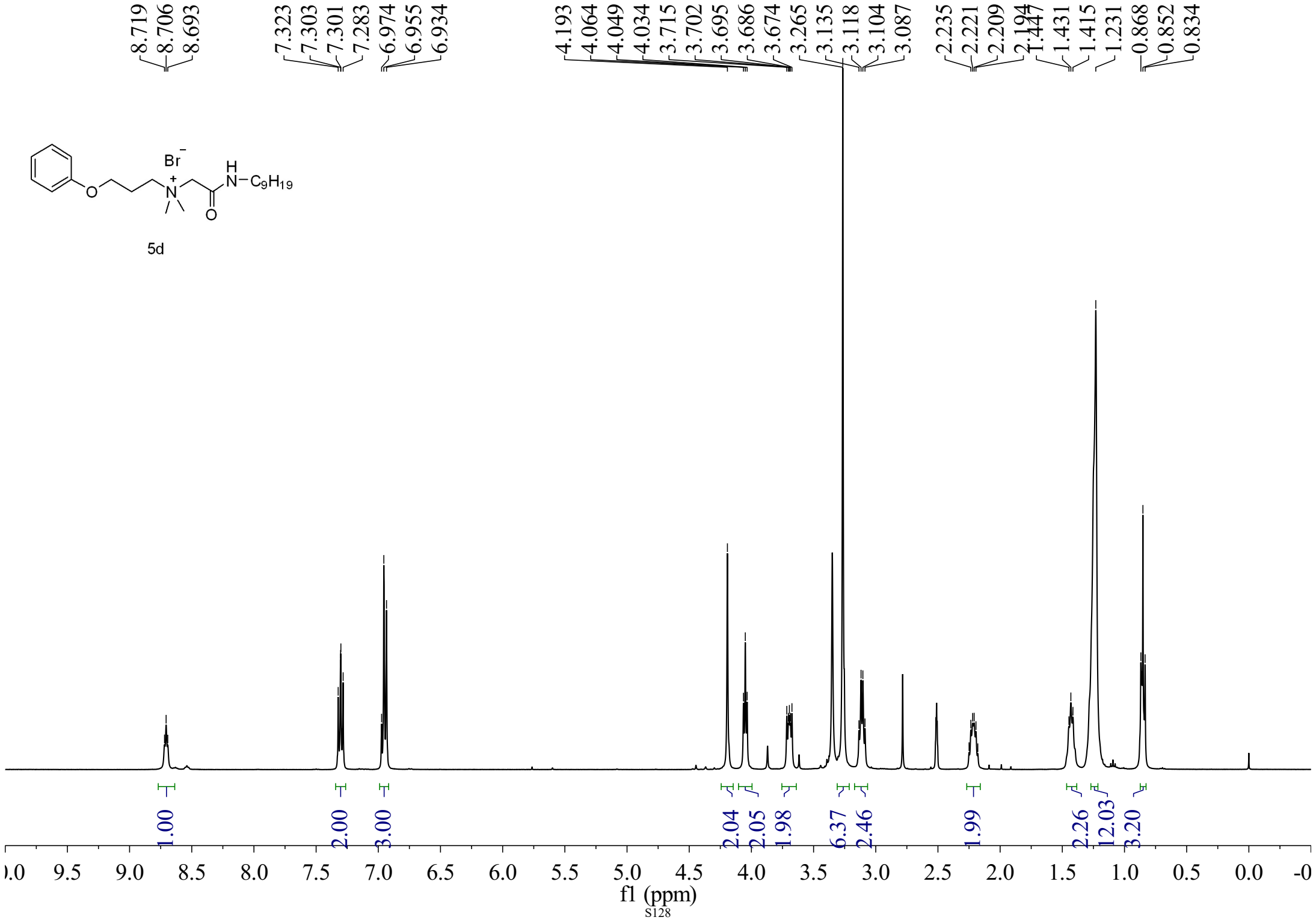

162.869
158.100
129.495
120.857
114.456
64.476
62.101
62.003
51.231
30.838
28.510
25.983
22.441
21.981
13.859
Br⁻
H
N−C6H13
O
N+
O
5a
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.653
8.640
8.626
7.325
7.304
7.285
6.975
6.955
6.933
4.162
4.063
4.048
4.033
3.706
3.693
3.685
3.677
3.665
3.255
3.136
3.120
3.105
3.088
2.227
2.213
2.201
2.186
1.446
1.430
1.414
1.242
0.862
0.846
0.828
Br⁻
H
N−C7H15
O
N+
O
5b
1.07
2.17
3.26
2.15
2.19
2.15
6.47
2.41
2.22
2.39
8.34
3.29
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)


162.863
158.100
129.499
120.866
114.453
64.472
62.099
61.994
51.247
31.166
28.565
28.291
26.281
22.435
21.999
13.896
Br⁻
H
N−C7H15
O
N+
O
5b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.702
8.689
8.676
7.318
7.296
7.278
6.969
6.952
6.931
4.204
4.060
4.046
4.031
3.720
3.707
3.700
3.691
3.679
3.269
3.133
3.116
3.101
3.084
2.234
2.220
2.208
2.194
1.446
1.429
1.412
1.396
1.236
1.231
0.861
0.845
0.827
Br⁻
H
N−C8H17
O
5c
1.00
2.00
3.03
2.03
2.08
2.06
6.17
2.26
2.03
2.24
10.26
3.22
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)


162.867
158.104
129.476
120.839
114.454
64.485
62.081
61.997
51.237
31.189
28.598
28.551
26.339
22.457
22.034
13.903
Br⁻
N⁺
H
N
C8H17
O
O
O
5c
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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6.934
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4.034
3.715
3.702
3.695
3.686
3.674
3.265
3.135
3.118
3.104
3.087
2.235
2.221
2.209
2.194
1.447
1.431
1.415
1.231
0.868
0.852
0.834
Br⁻
H
N
N−C9H19
O
O
5d
1.00
2.00
3.00
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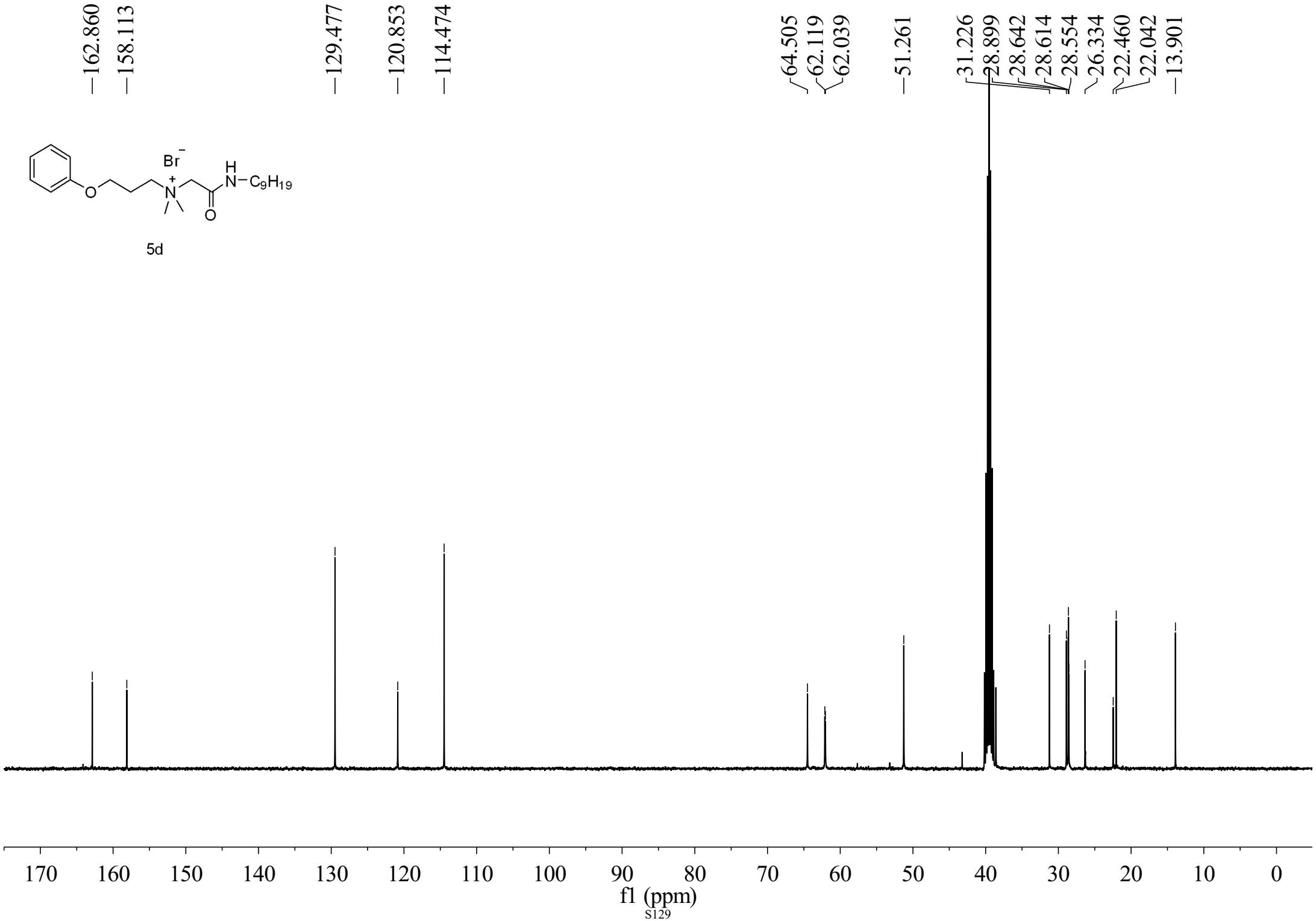
2.05
1.98
6.37
2.46
1.99
2.26
12.03
3.20
f1 (ppm)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28.614
28.554
26.334
22.460
22.042
13.901
Br⁻
O
N⁺
H
N
C9H19
O
5d
170
160
150
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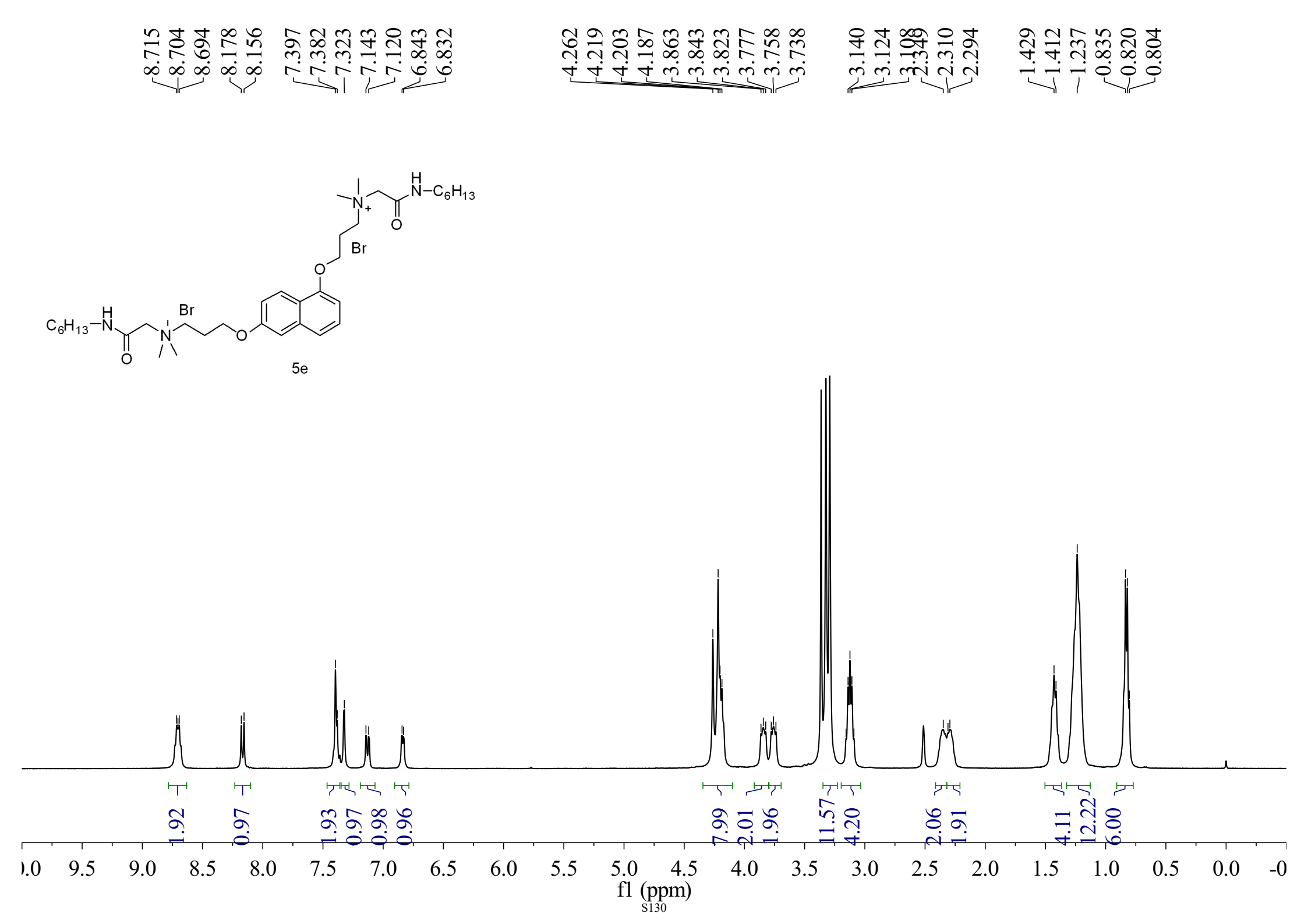
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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4.219
4.203
4.187
3.863
3.843
3.823
3.777
3.758
3.738
3.140
3.124
3.108
2.349
2.310
2.294
1.429
1.412
1.237
0.835
0.820
0.804
Br
Br
5e
1.92
0.97
1.93
0.97
0.98
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1.96
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1.91
4.11
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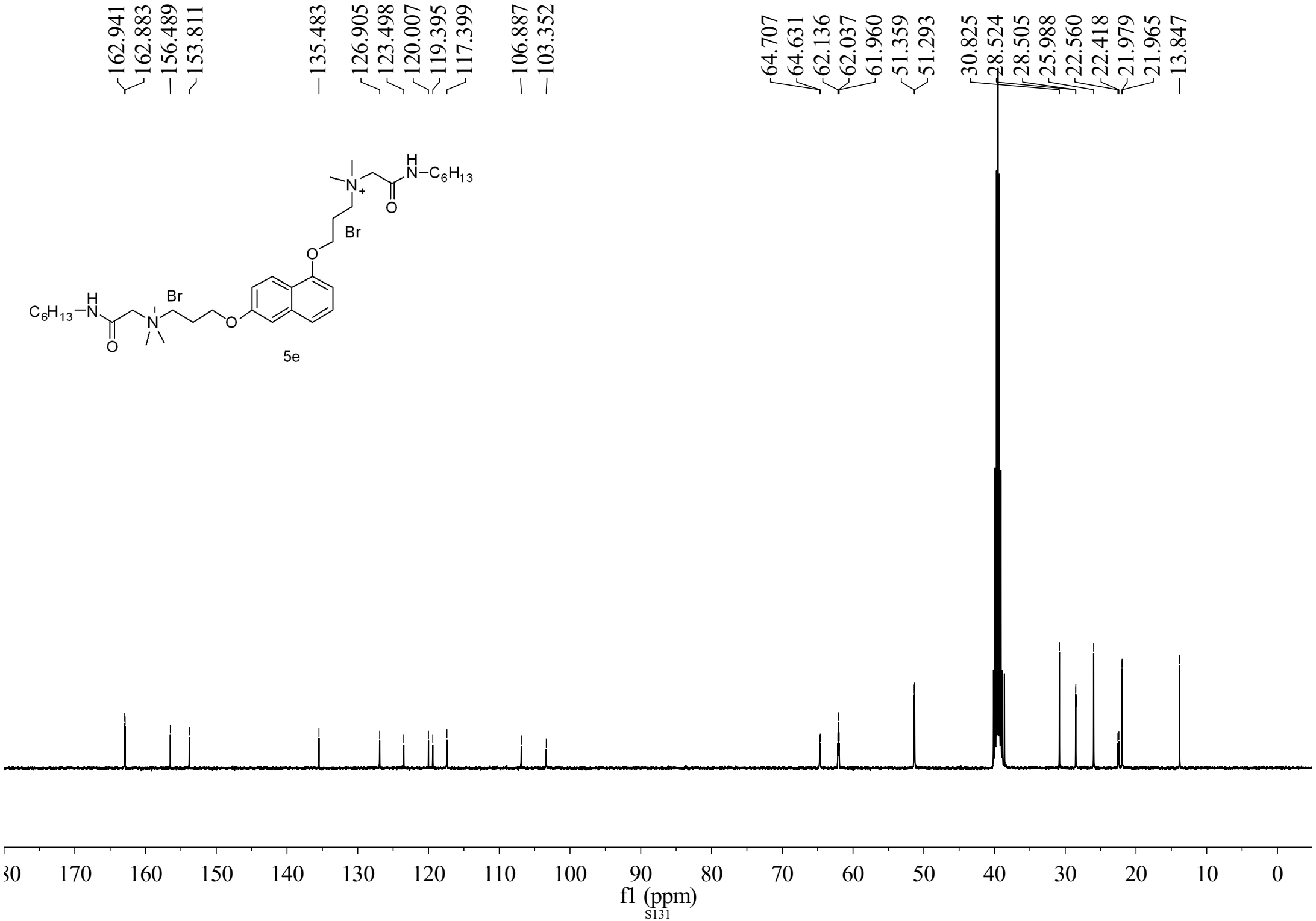
6.00
f1 (ppm)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117.399
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103.352
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64.631
62.136
62.037
61.960
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51.293
30.825
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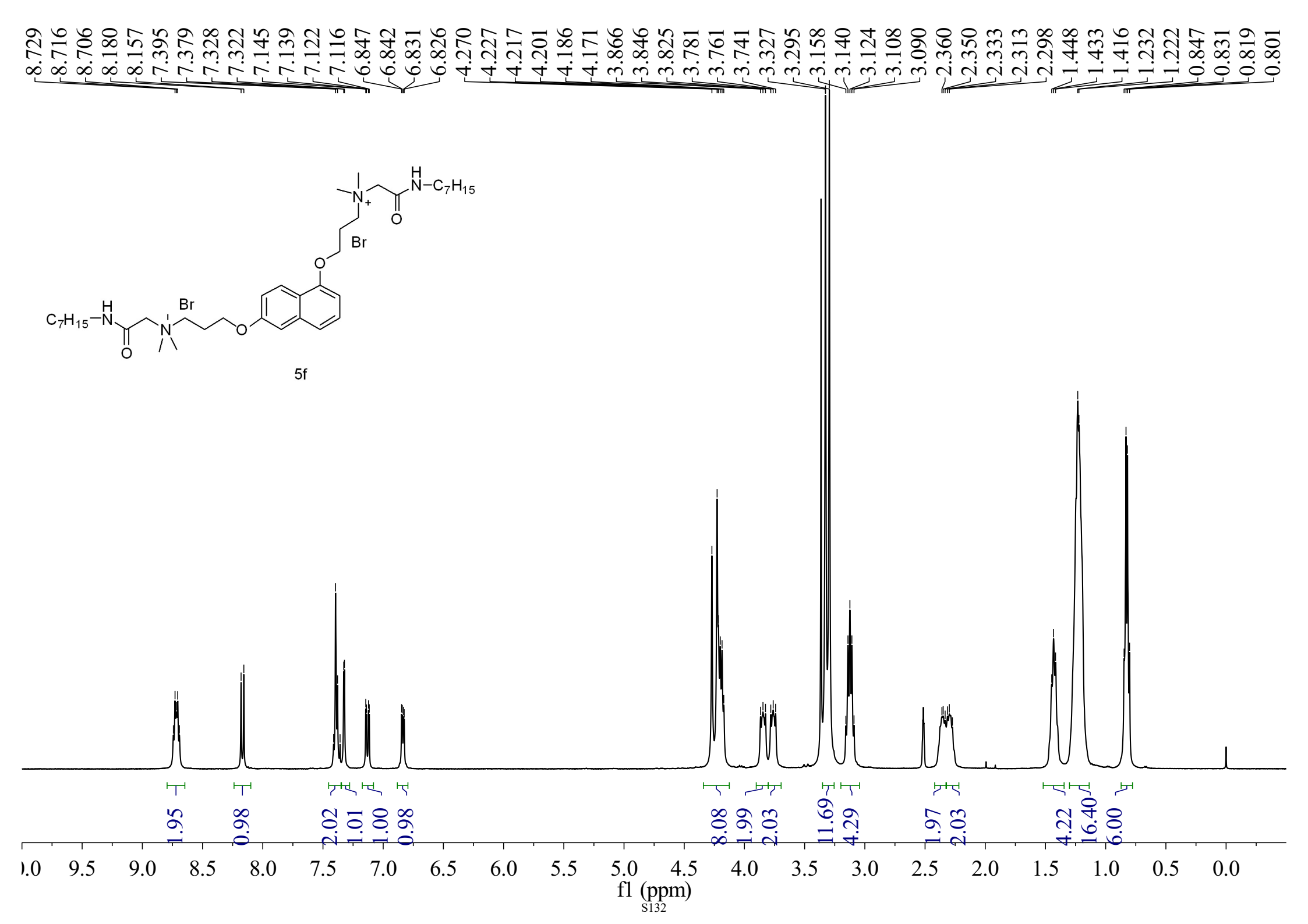
25.988
22.560
22.418
21.979
21.965
13.847
Br
Br
5e
f1 (ppm)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6.831
6.826
4.270
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4.217
4.201
4.186
4.171
3.866
3.846
3.825
3.781
3.761
3.741
3.327
3.295
3.158
3.140
3.124
3.108
3.090
2.360
2.350
2.333
2.313
2.298
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1.433
1.416
1.232
1.222
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0.831
0.819
0.801
Br
Br
5f
1.95
0.98
2.02
1.01
1.00
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4.29
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2.03
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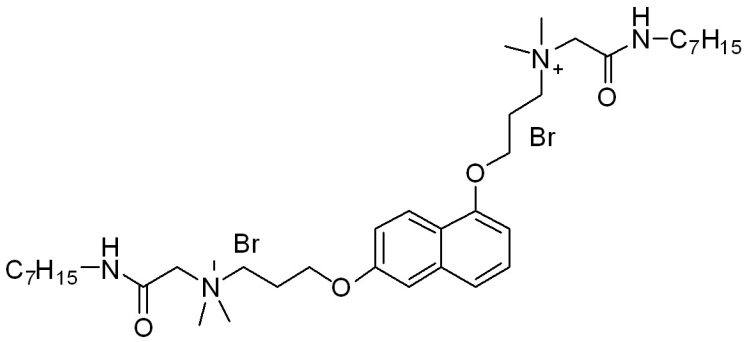
6.00
f1 (ppm)


Br
Br

5f

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103.348
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26.290
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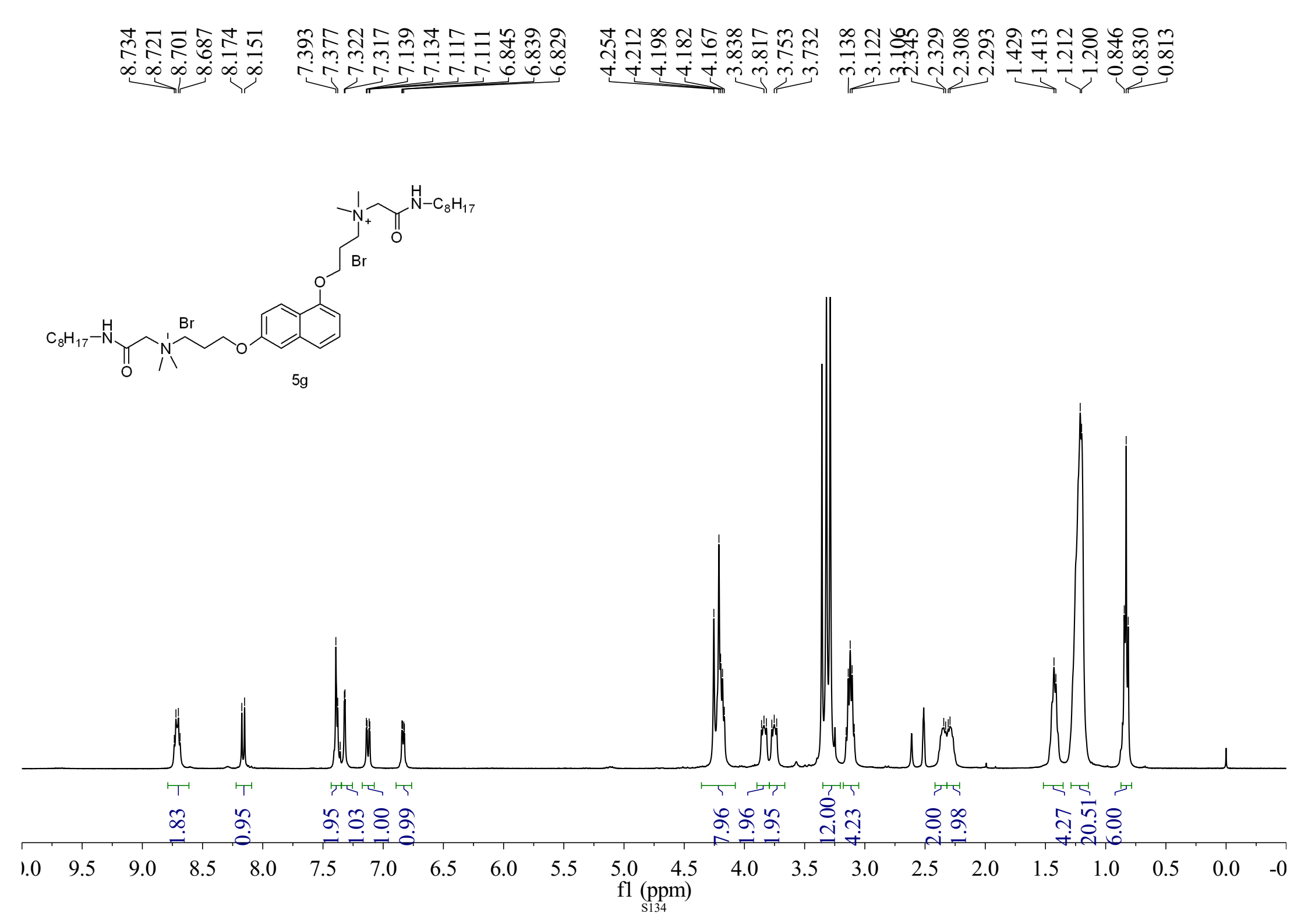
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7.134
7.117
7.111
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6.829
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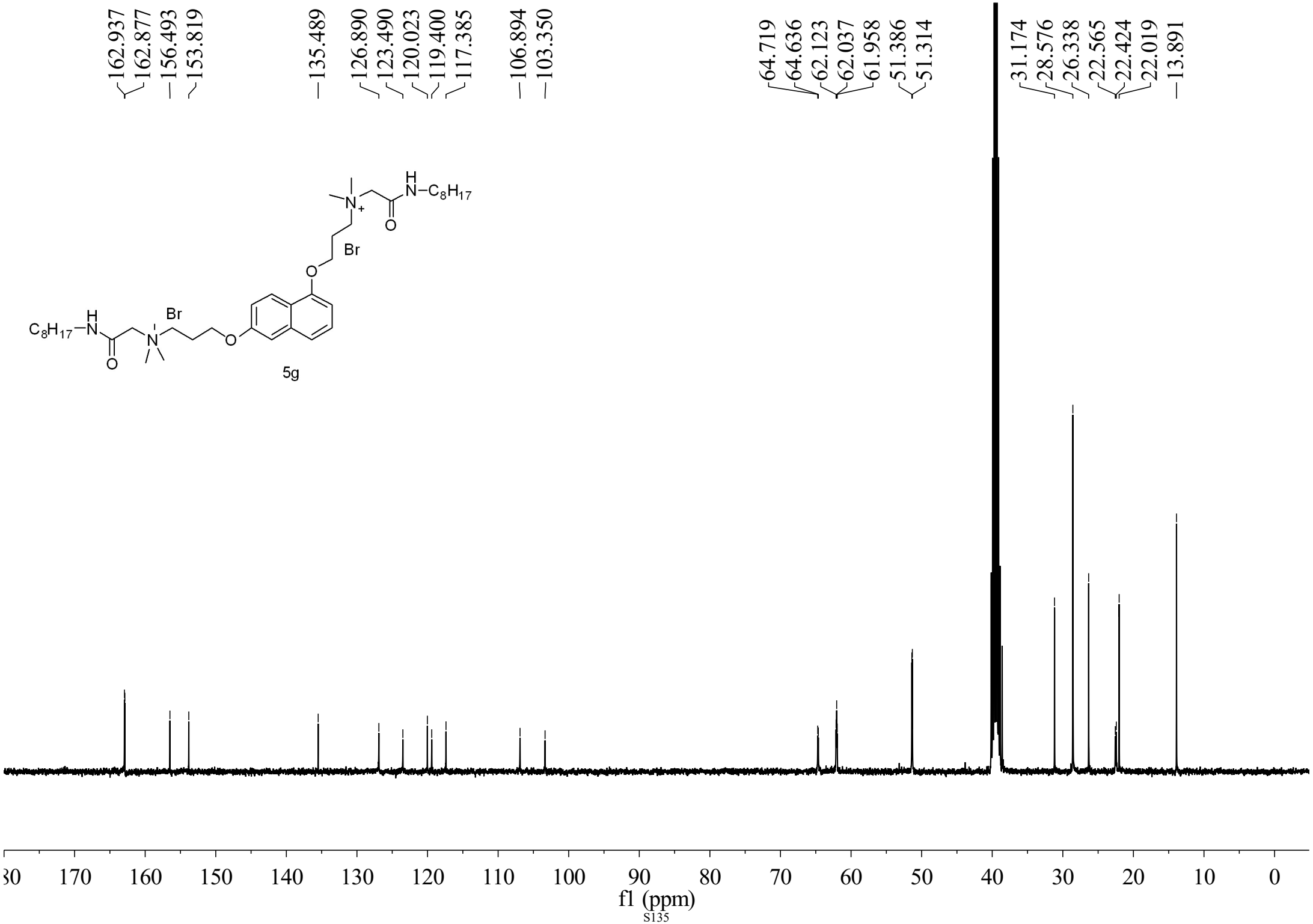
4.212
4.198
4.182
4.167
3.838
3.817
3.753
3.732
3.138
3.122
3.106
3.345
2.329
2.308
2.293
1.429
1.413
1.212
1.200
0.846
0.830
0.813
Br
Br
5g
1.83
0.95
1.95
1.03
1.00
0.99
7.96
1.96
1.95
12.00
4.23
2.00
1.98
4.27
20.51
6.00
f1 (ppm)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62.123
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61.958
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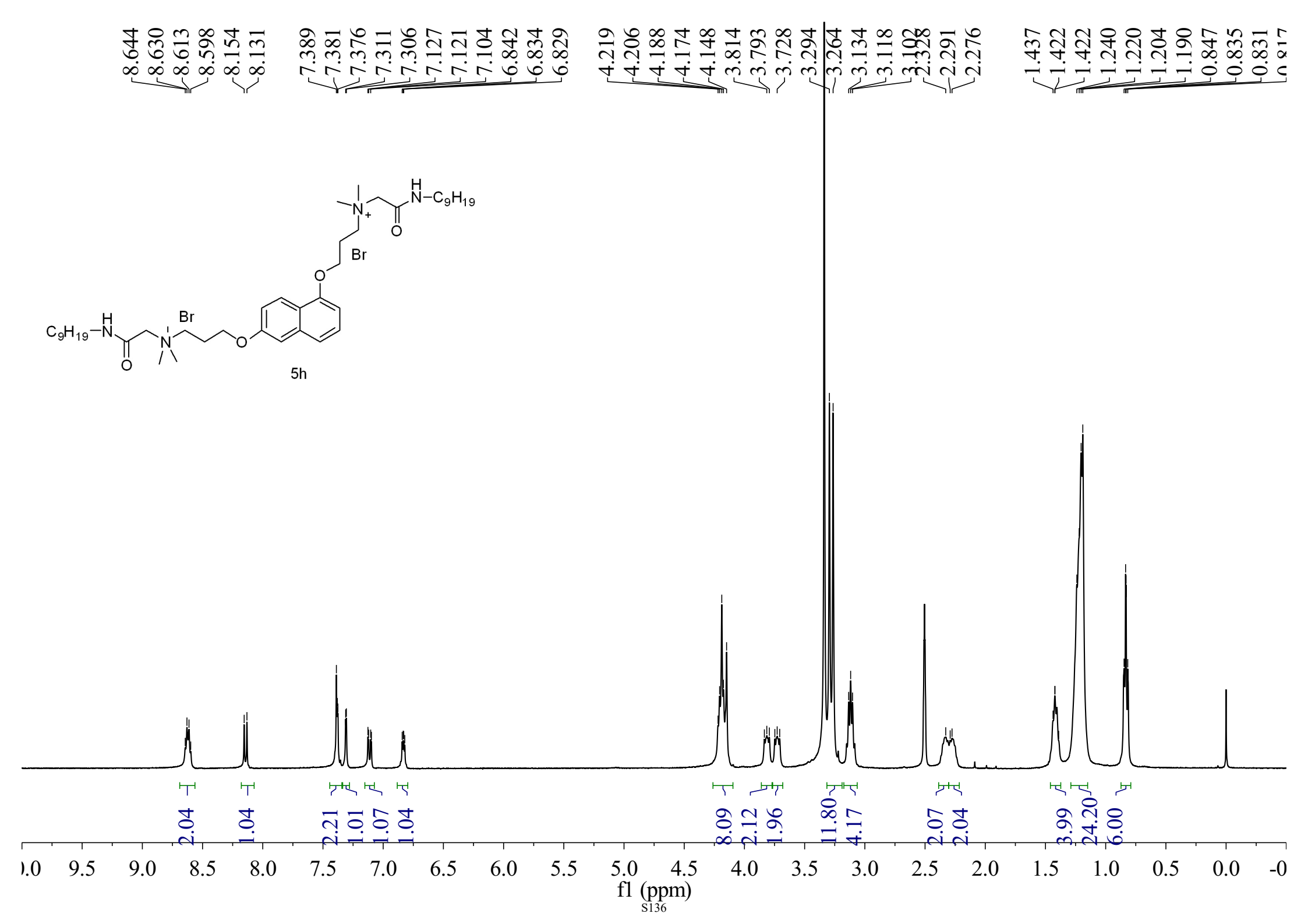
22.565
22.424
22.019
13.891
Br
Br
5g
f1 (ppm)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7.127
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6.842
6.834
6.829
4.219
4.206
4.188
4.174
4.148
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3.793
3.728
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1.422
1.422
1.240
1.220
1.204
1.190
0.847
0.835
0.831
Br
Br
5h
2.04
1.04
2.21
1.01
1.07
1.04
8.09
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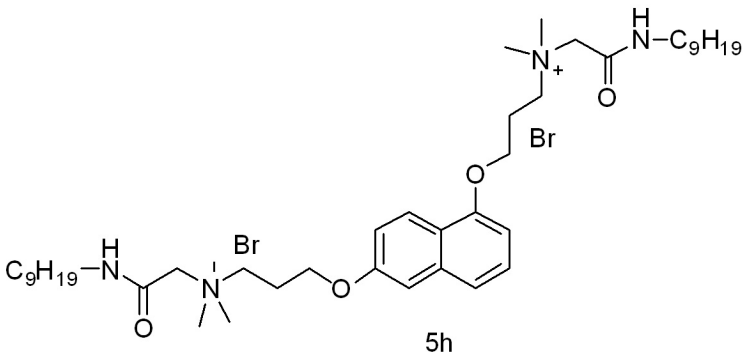
11.80
4.17
2.07
2.04
3.99
24.20
6.00
f1 (ppm)


Br
Br
5h

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123.461
120.007
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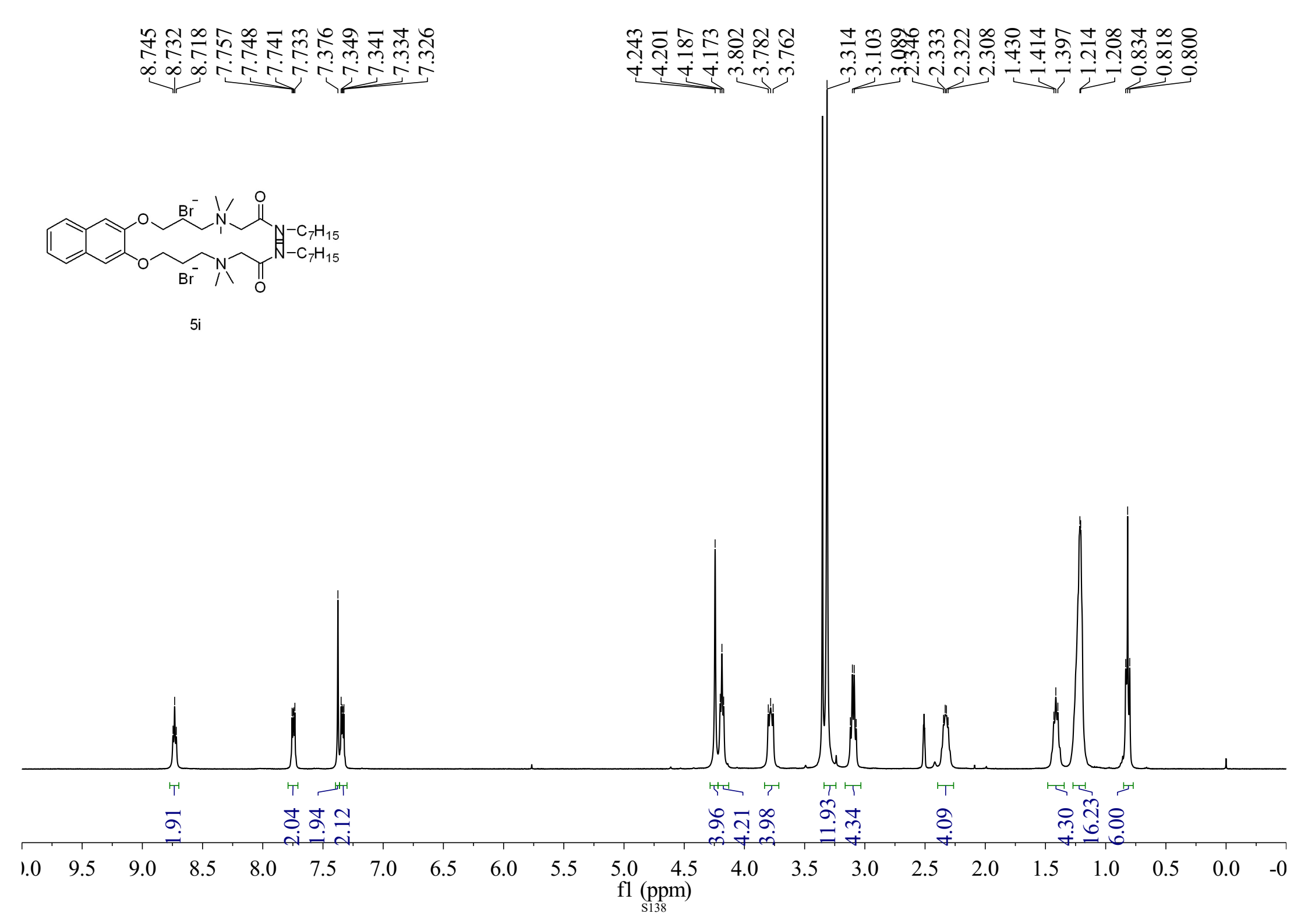
117.363
106.876
103.349
64.619
62.019
51.410
51.339
31.216
28.892
28.607
26.336
22.547
22.411
22.042
13.910
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.341
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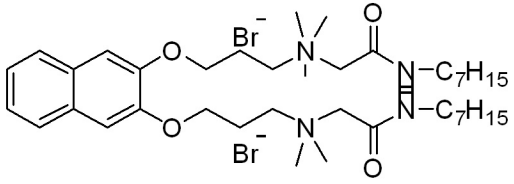
7.326
4.243
4.201
4.187
4.173
3.802
3.782
3.762
3.314
3.103
3.089
3.046
2.333
2.322
2.308
1.430
1.414
1.397
1.214
1.208
0.834
0.818
0.800
Br⁻
N
O
N–C7H15
N–C7H15
Br⁻
1.91
2.04
1.94
2.12
3.96
4.21
3.98
11.93
4.34
4.09
4.30
16.23
6.00
f1 (ppm)

5i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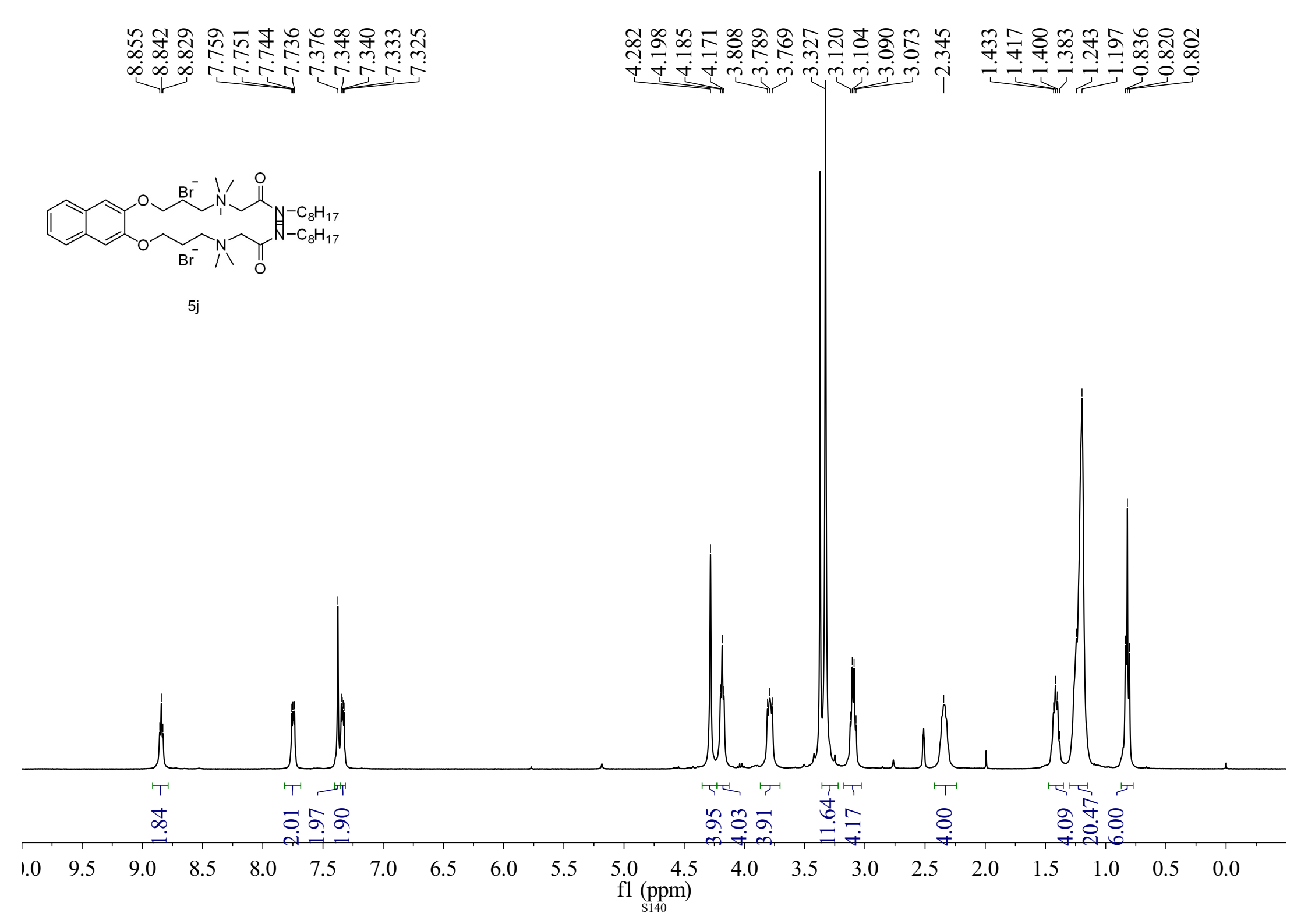
O
N
O
N–C7H15
N–C7H15
O
Br
O
N
O

5i

162.929
148.005
128.958
126.236
124.145
108.282
65.420
62.174
51.389
31.162
28.526
28.308
26.318
22.450
21.987
13.875
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.325
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4.198
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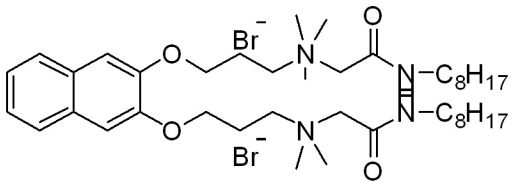
4.171
3.808
3.789
3.769
3.327
3.120
3.104
3.090
3.073
2.345
1.433
1.417
1.400
1.383
1.243
1.197
0.836
0.820
0.802
Br⁻
O
N
N–C8H17
N–C8H17
Br⁻
O
1.84
2.01
1.97
1.90
3.95
4.03
3.91
11.64
4.17
4.00
4.09
20.47
6.00
f1 (ppm)

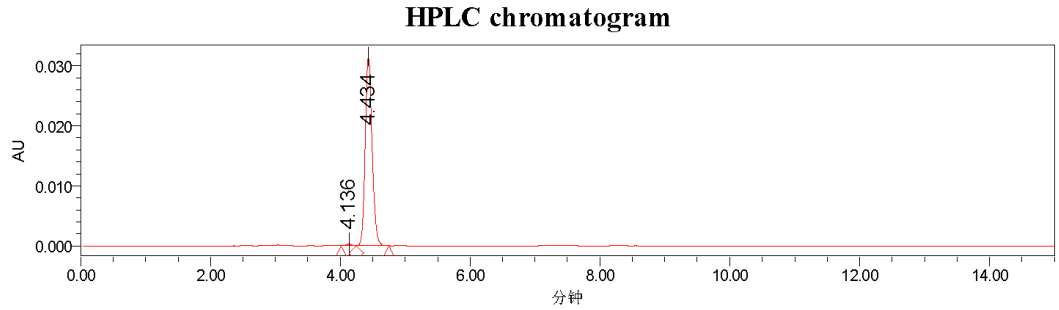
5j


Br
O
N
O
N–C8H17
N–C8H17
Br
O
N
O

5j

162.938
148.015
128.964
126.235
124.117
108.262
65.437
62.232
62.169
51.359
31.190
28.613
28.524
26.387
22.470
22.023
13.886
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

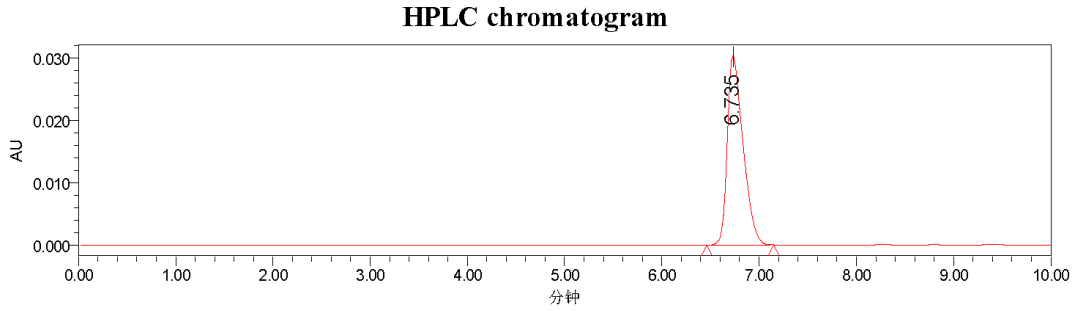
4a



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	4.14	1800	0.77
2	4.43	232988	99.23

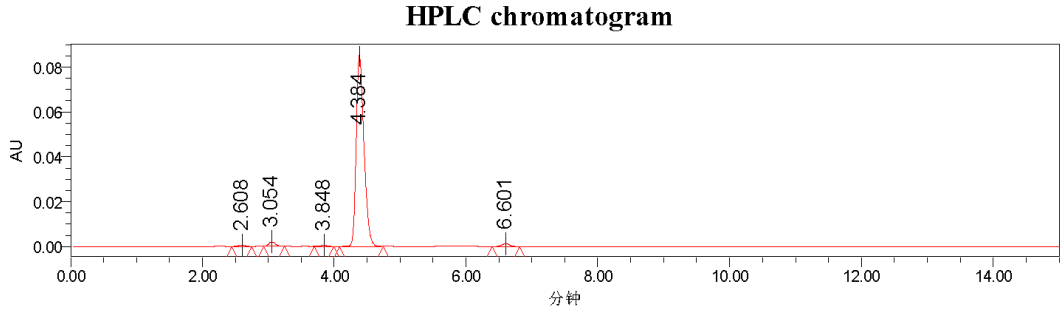
4b



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	6.74	340439	100.00

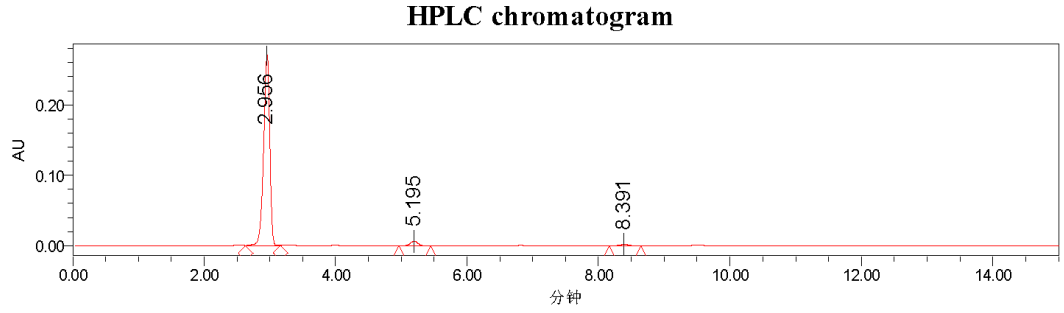
4c



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.61	4400	0.61
2	3.05	12737	1.77
3	3.85	4208	0.59
4	4.38	686325	95.56
5	6.60	10557	1.47

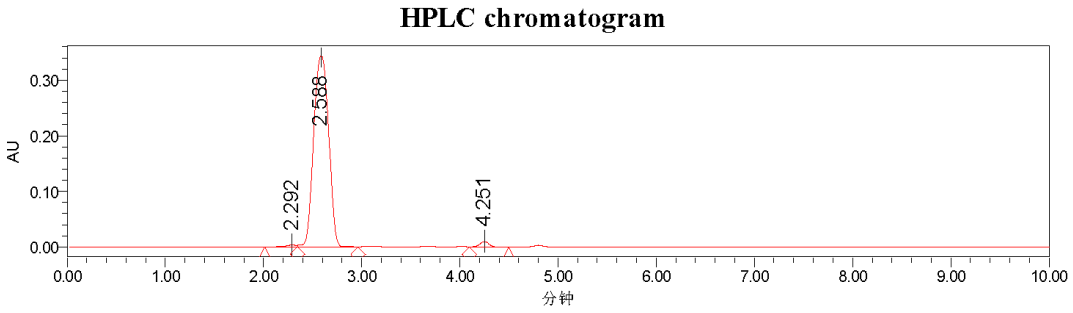
4d



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.96	1761931	96.06
2	5.19	52420	2.86
3	8.39	19903	1.09

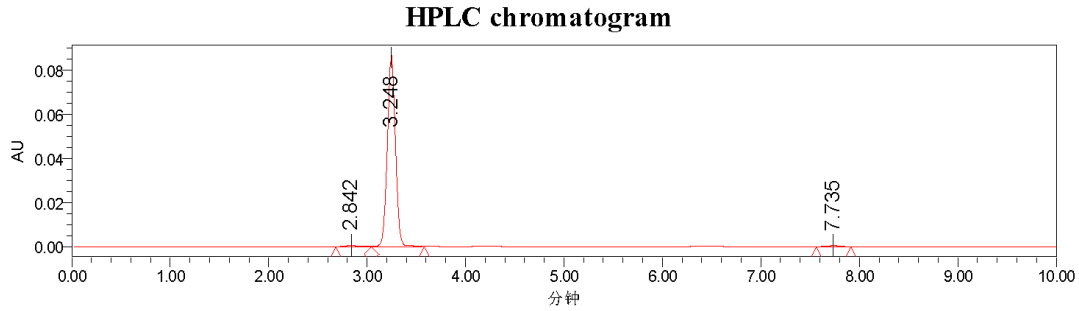
4e



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.29	31421	0.84
2	2.59	3627141	97.46
3	4.25	63198	1.70

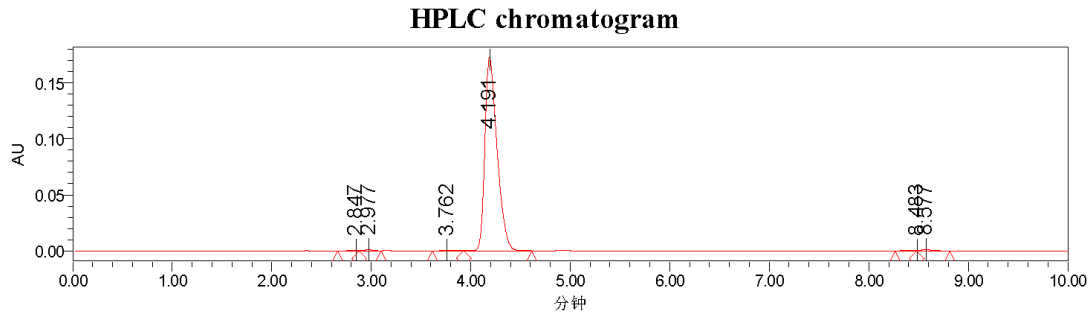
4f



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.84	7253	1.43
2	3.25	495888	97.76
3	7.74	4087	0.81

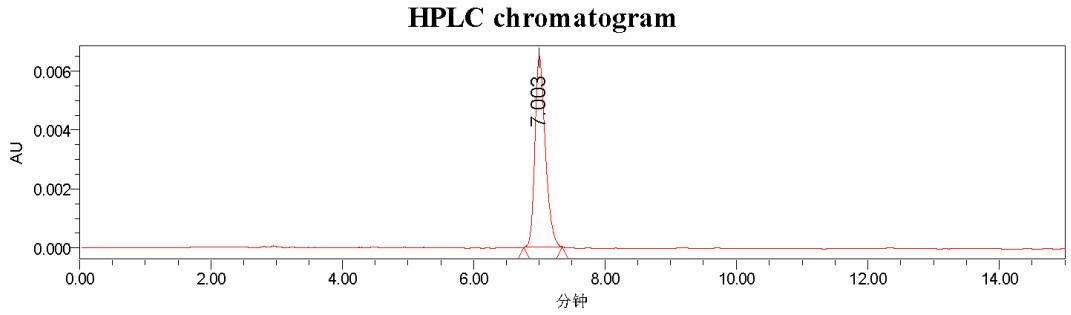
4g



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.85	3249	0.22
2	2.98	6386	0.43
3	3.76	4747	0.32
4	4.19	1459446	98.19
5	8.48	3308	0.22
6	8.58	9256	0.62

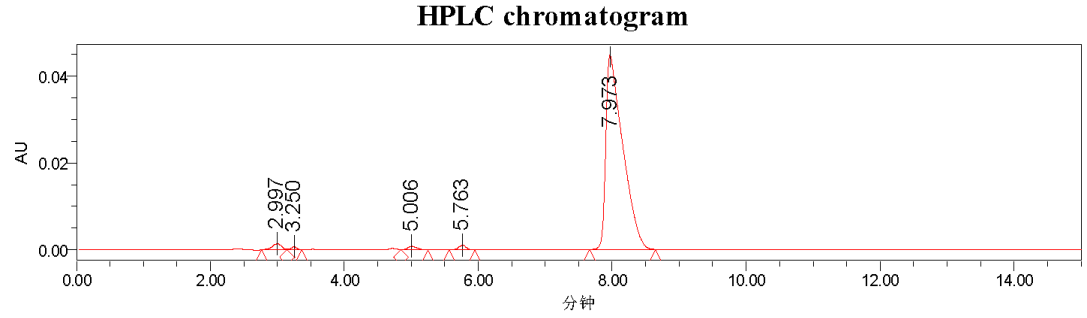
4h



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	7.00	71039	100.00

4i

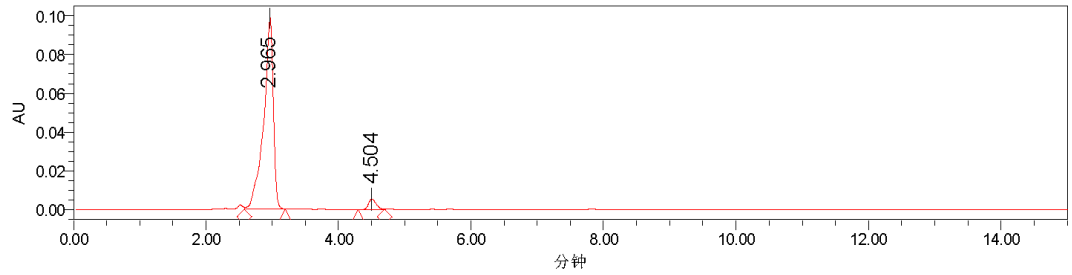


HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.00	13081	1.60
2	3.25	3768	0.46
3	5.01	7924	0.97
4	5.76	8145	1.00
5	7.97	782299	95.96

4j

HPLC chromatogram

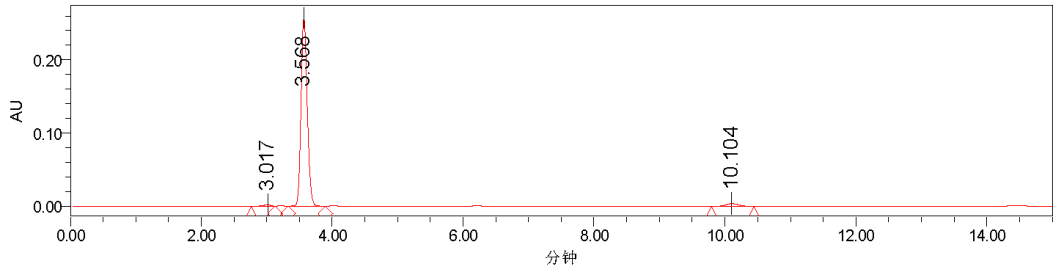


HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.96	1001424	95.91
2	4.50	42658	4.09

4k

HPLC chromatogram

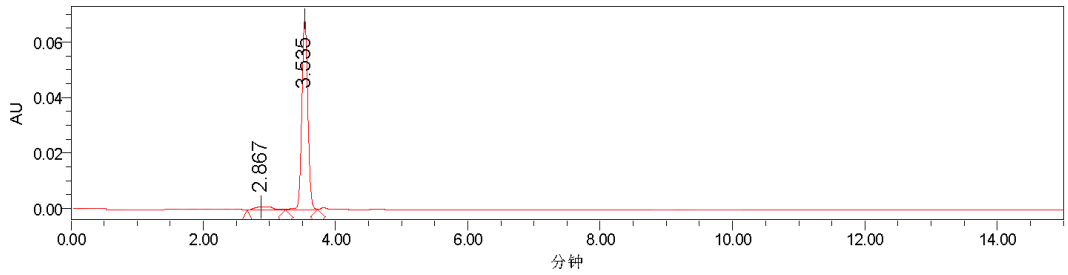


HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.02	17795	1.02
2	3.57	1675193	96.16
3	10.10	49054	2.82

4l

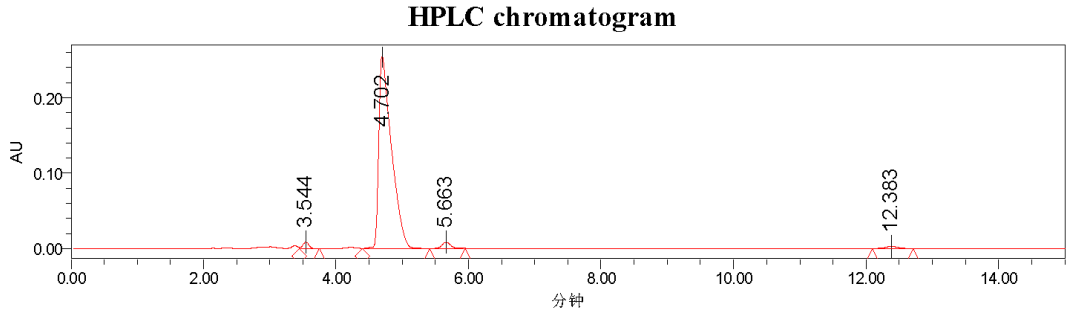
HPLC chromatogram



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.87	20308	4.59
2	3.53	421854	95.41

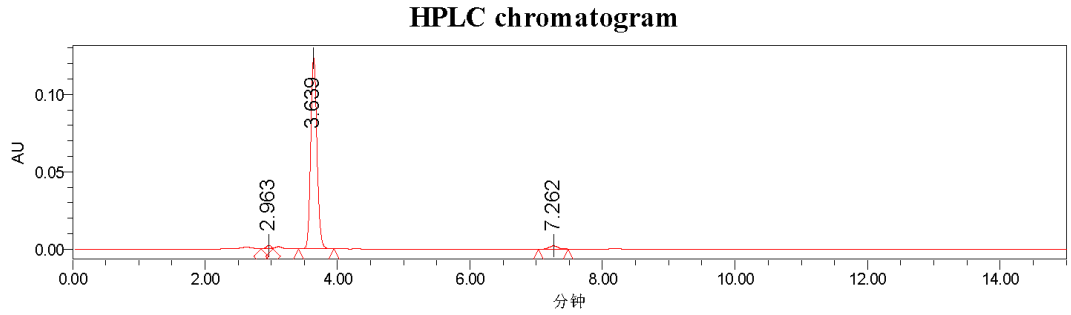
4m



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.54	52169	1.47
2	4.70	3386317	95.36
3	5.66	72764	2.05
4	12.38	39863	1.12

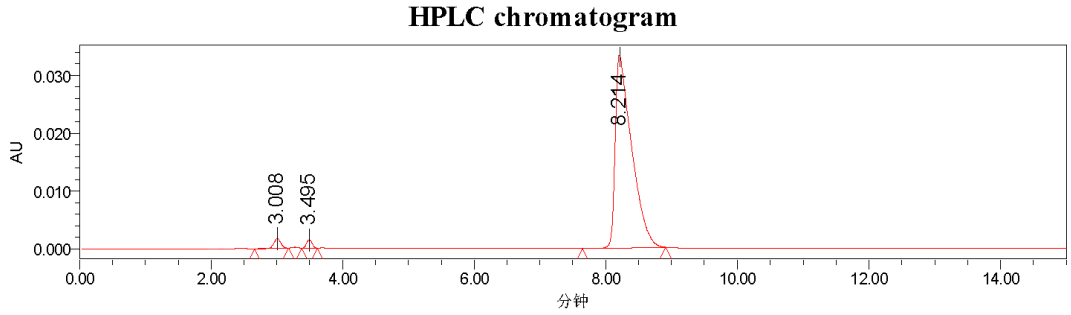
4n



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.96	12450	1.48
2	3.64	807236	96.19
3	7.26	19532	2.33

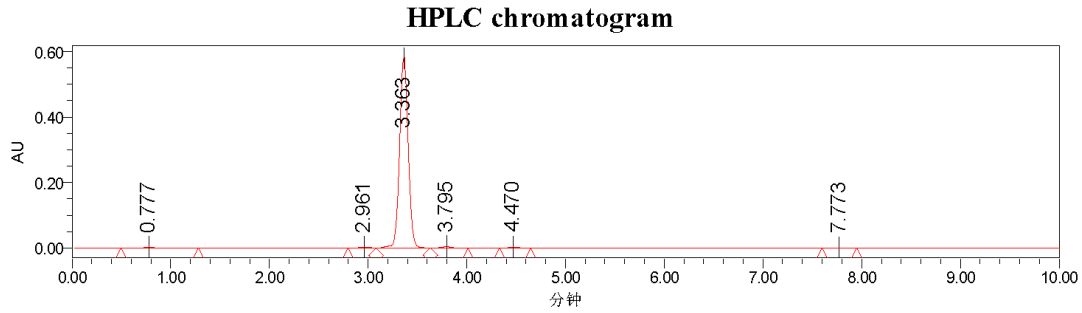
4o



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.01	12688	2.13
2	3.49	8345	1.40
3	8.21	575727	96.48

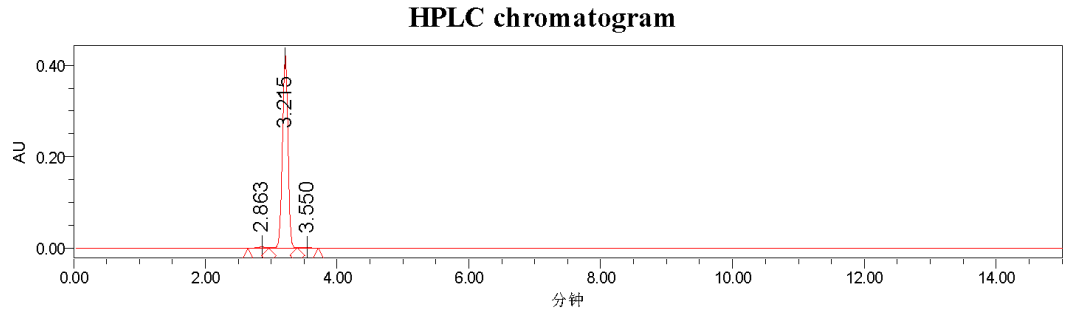
4p



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	0.78	16273	0.46
2	2.96	15317	0.43
3	3.36	3497118	97.80
4	3.80	26576	0.74
5	4.47	15952	0.45
6	7.77	4616	0.13

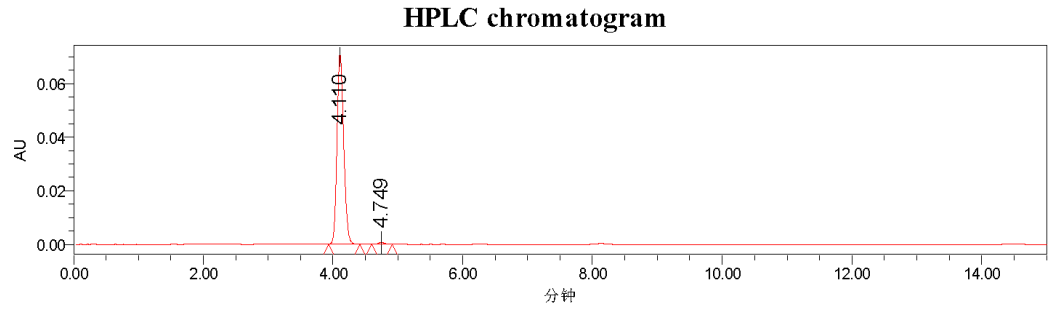
4q



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.86	21171	0.85
2	3.21	2454603	98.51
3	3.55	15992	0.64

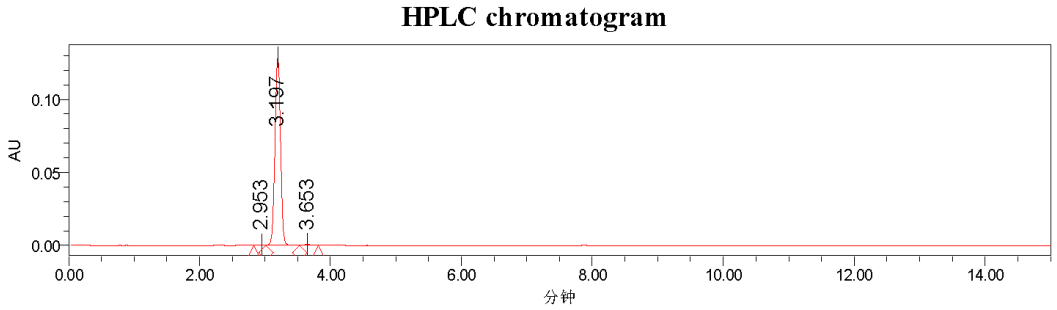
4r



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	4.11	501435	99.09
2	4.75	4606	0.91

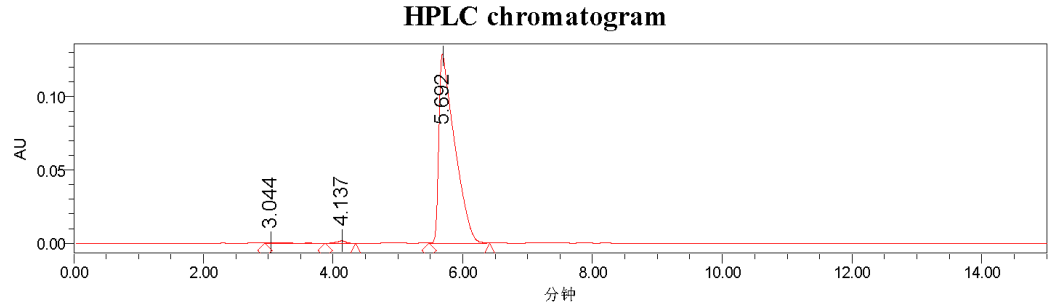
4s



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.95	2096	0.27
2	3.20	754788	99.02
3	3.65	5366	0.70

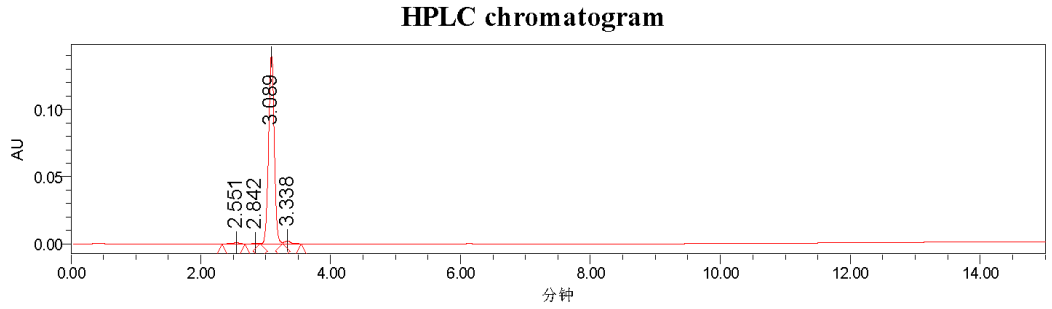
4t



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.04	9223	0.42
2	4.14	15916	0.73
3	5.69	2157979	98.85

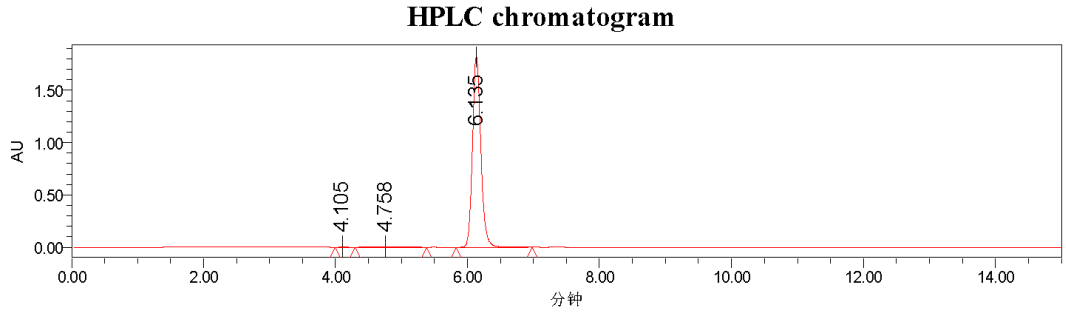
4u



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.55	7236	0.82
2	2.84	3795	0.43
3	3.09	854058	97.06
4	3.34	14833	1.69

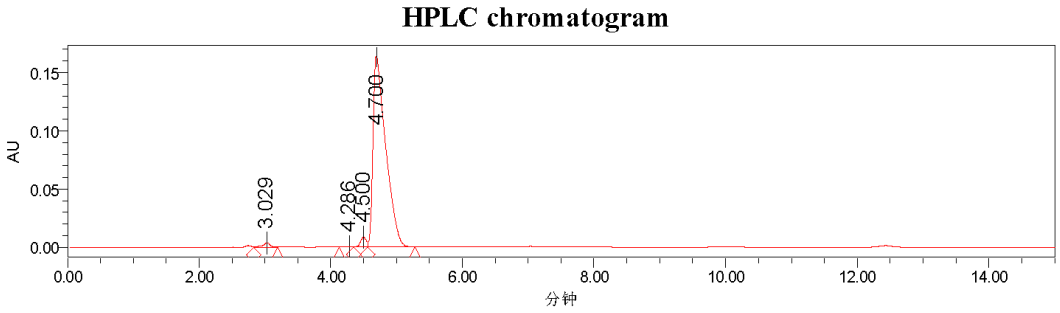
4v



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	4.10	6346	0.04
2	4.76	74447	0.46
3	6.14	16148035	99.50

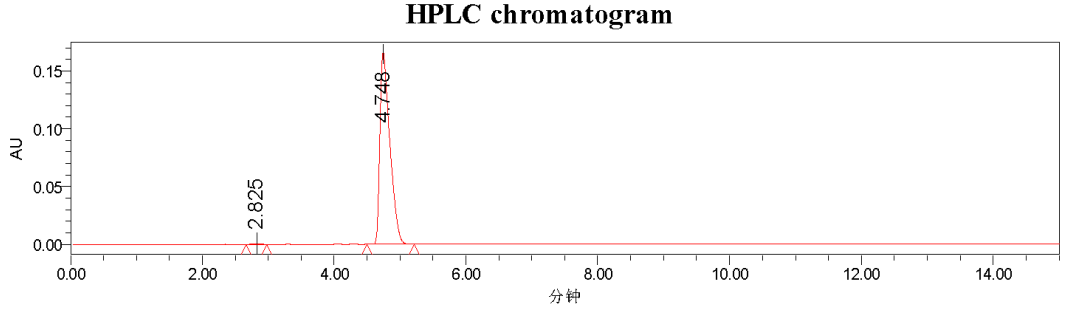
4w



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.03	27627	1.22
2	4.29	2179	0.10
3	4.50	52206	2.30
4	4.70	2190683	96.39

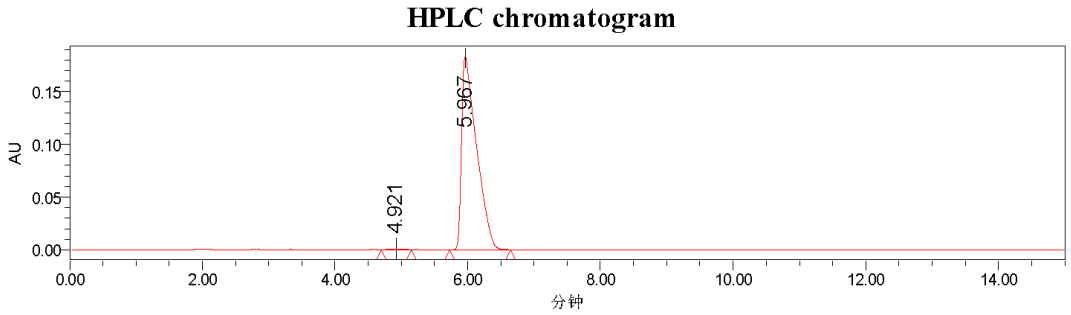
5a



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.83	4070	0.23
2	4.75	1730392	99.77

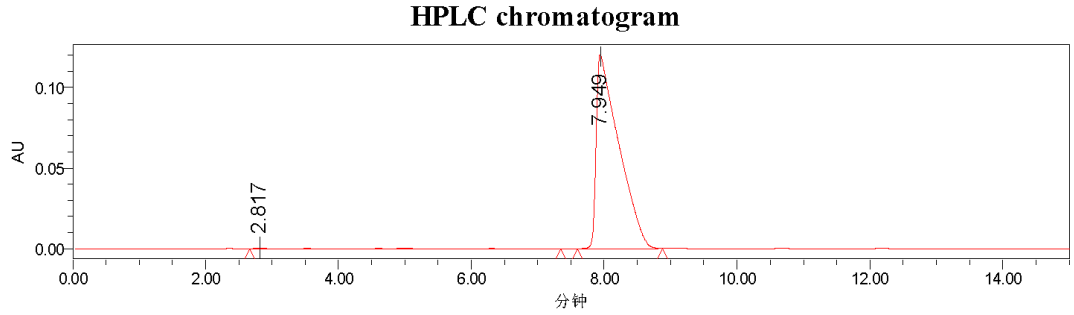
5b



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	4.92	8346	0.29
2	5.97	2847445	99.71

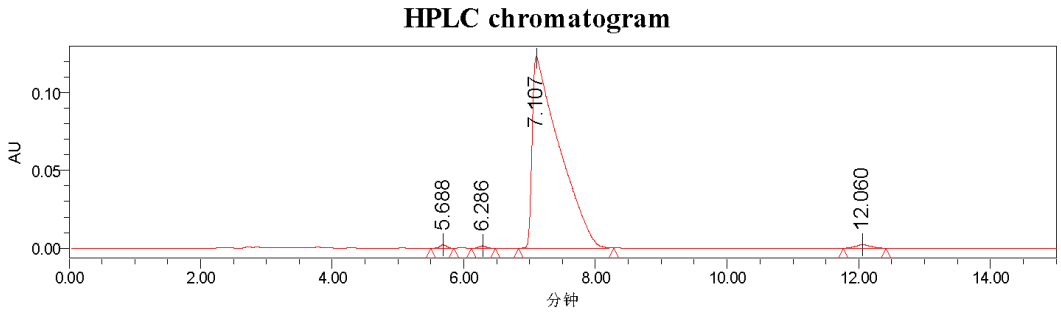
5c



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.82	26369	0.92
2	7.95	2826257	99.08

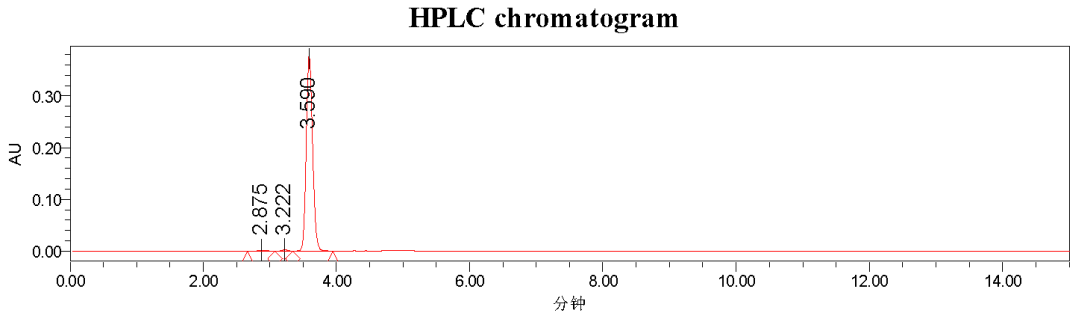
5d



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	5.69	15308	0.43
2	6.29	11493	0.32
3	7.11	3515800	98.24
4	12.06	36256	1.01

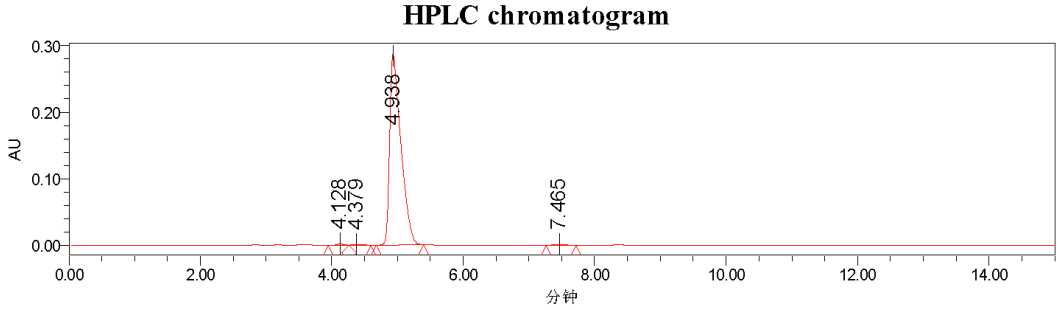
5e



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.88	14563	0.58
2	3.22	15740	0.63
3	3.59	2474294	98.79

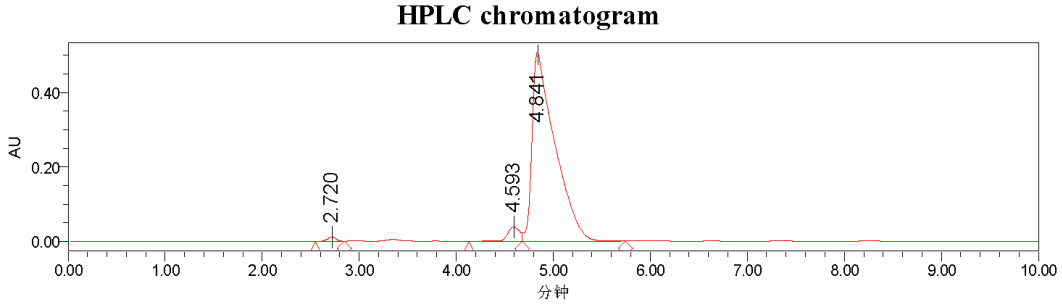
5f



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	4.13	14219	0.42
2	4.38	9378	0.28
3	4.94	3357792	98.94
4	7.46	12397	0.37

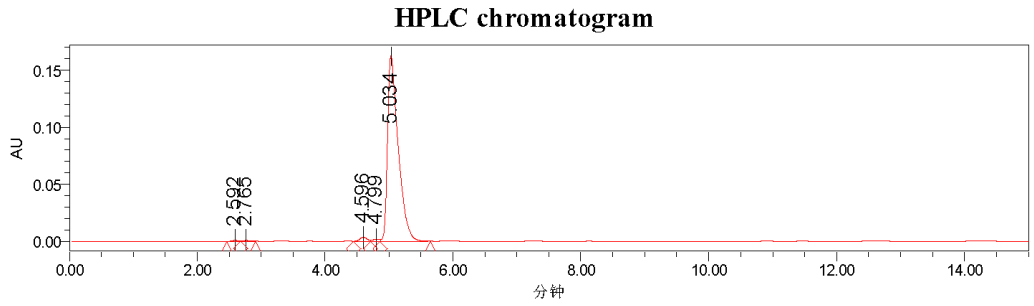
5g



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.72	75952	0.88
2	4.59	331545	3.82
3	4.84	8266033	95.30

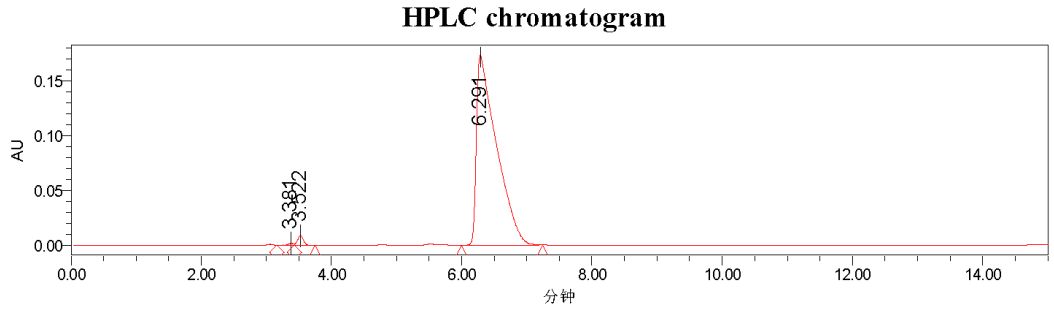
5h



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	2.59	5972	0.31
2	2.77	4836	0.25
3	4.60	29388	1.54
4	4.80	13419	0.70
5	5.03	1860468	97.20

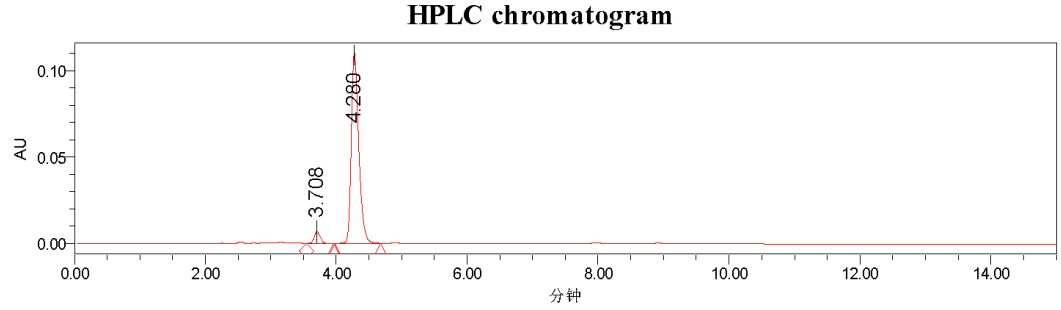
5i



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.38	10965	0.29
2	3.52	51975	1.39
3	6.29	3683914	98.32

5j



HPLC chromatogram

	Retention Time(min) (分钟)	Area (微伏*秒)	% Area
1	3.71	42625	4.67
2	4.28	869739	95.33

References

1. D. Doyle, G. Peirano, C. Lascols, T. Lloyd, D. L. Church and J. D. Pitout, *J. Clin. Microbiol.*, 2012, **50**, 3877-3880.
2. R. Joseph, A. Naugolny, M. Feldman, I. M. Herzog, M. Fridman and Y. Cohen, *J. Am. Chem. Soc.*, 2016, **138**, 754-757.
3. Y. Abouelhassan, Q. Yang, H. Yousaf, M. T. Nguyen, M. Rolfe, G. S. Schultz and R. W. Huigens, 3rd, *Int. J. Antimicrob. Agents*, 2017, **49**, 247-251.