

# An Efficient Method to Convert Lactams and Amides into 2,2-Dialkylated Amines

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## Supporting Information

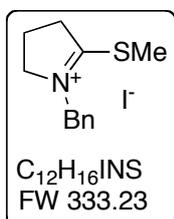
### General:

All reactions were performed under a nitrogen atmosphere in oven-dried flasks (120 °C) unless otherwise stated. Dry solvents for reactions were filtered through a column of dry alumina under a positive pressure of argon. Solvents for flash chromatography were of technical grade and used without purification. Other chemicals were obtained from commercial sources and used without further purifications. The reaction were monitored by TLC (analytical plates, Merck silica gel 60 F<sub>254</sub>) and visualized under UV light and/or stained with a solution of KMnO<sub>4</sub> or phosphomolibdic acid followed by heating. Flash chromatography (FC) was performed using *Baker* silica gel (0.065-0.200 mm). Melting points (M.p.) are not corrected. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on *Bruker Avance-300* (<sup>1</sup>H: 300 MHz, <sup>13</sup>C: 75.5 MHz) or *Bruker DRX-400* (<sup>1</sup>H: 400 MHz, <sup>13</sup>C: 75.5 MHz) spectrometers. The <sup>1</sup>H spectra were referred to an internal standard (TMS, 0 ppm) or to the residual <sup>1</sup>H of CDCl<sub>3</sub> (7.26 ppm). The <sup>13</sup>C spectra were referred to residual signal of CDCl<sub>3</sub> (77.0 ppm). IR spectra were recorded on *Jasco FT-IR 460 plus*. Mass spectroscopy (MS) and high resolution mass spectroscopy (HRMS) analysis were performed on *Waters Micromass Autospec Q* or *Qstar Pulsar*.

### General procedure A: synthesis of thioiminium ions

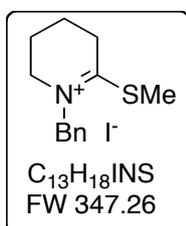
Lawesson's reagent (2.02 g, 5.0 mmol) was added to a solution of the lactam (10 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The mixture was stirred at room temperature for 1-4 h until the starting material was consumed (TLC monitoring). The solvent was evaporated and the crude mixture was filtered on short column of silica gel (cyclohexane/EtOAc). The thiolactam (10 mmol) was suspended in dry THF (100 ml) and MeI (1.0 mL, 16 mmol) was added. The mixture was stirred at room

temperature overnight. The thioiminium ion was isolated by filtration and washed with cold THF to obtain a yellowish solid.



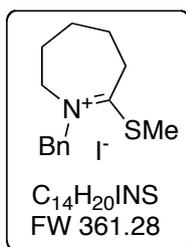
### 1-Benzyl-5-methylsulfanyl-3,4-dihydro-2H-pyrrolidinium iodide (3a)

According to general procedure A. *N*-Benzylpyrrolidin-2-one (1.75 g, 10 mmol) afforded **3a** (2.73g, 82%). White solid. M.p. = 94-95 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.42 (m, 5H), 4.94 (s, 2H), 4.19 (t,  $J = 7.9$  Hz, 2H), 3.78 (t,  $J = 7.5$ Hz, 2H), 2.98 (s, 3H), 2.44 (q,  $J = 7.9$  Hz).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 193.54, 129.83, 129.24, 129.15, 128.87, 59.87, 40.90, 18.98, 17.39. IR (diamond ATR): 1599, 1451, 1444, 1299  $cm^{-1}$ . MS (ESI<sup>+</sup>): 206 (100,  $M-I^+$ ), 176.4 (14), 102.2 (15). HRMS calcd for  $C_{12}H_{16}NS^+$  206.1003; found 206.1009



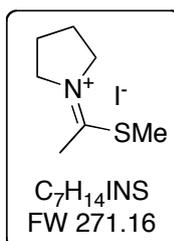
### 1-Benzyl-6-methylsulfanyl-2,3,4,5-tetrahydropyridinium iodide (3b)

According to the general procedure A. *N*-Benzylpiperidin-2-one (1.89 g, 10 mmol) afforded **3b** (2.15g, 62%). White solid. M.p. = 103-106 °C.  $^1H$  NMR ( $CDCl_3$ , 400 MHz): 7.40 (m, 5H), 5.13 (s, 2H), 3.83 (t,  $J = 5.5$  Hz, 2H), 3.33 (t,  $J = 5.9$  Hz, 2H), 2.92 (s, 3H), 2.14-2.04 (m, 4H).  $^{13}C$  NMR ( $CDCl_3$ , 133,3 MHz, ): 192.58, 130.13, 129.40, 129.12, 128.24, 60.92, 54.33, 33.32, 20.66, 18.06, 16.82 . IR (diamond ATR): 1597, 1448, 1159  $cm^{-1}$ . MS (ESI<sup>+</sup>): 220.4 (100,  $M-I^+$ ), 190.4 (16). HRMS calcd for  $C_{13}H_{18}NS^+$  220.1159; found 220.1167.



### 1-Benzyl-7-methylsulfanyl-3,4,5,6-tetrahydro-2H-azepinium iodide (3c)

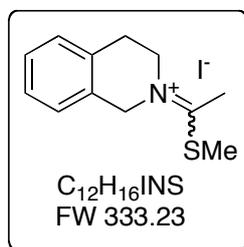
According to general procedure starting A. *N*-Benzylazepan-2-one (2.033g, 10 mmol) afforded **3c** (2.71 g, 75%). Yellow solid. Decomposition 124 °C .  $^1H$  NMR ( $CDCl_3$ , 400 MHz): 7.36 (m, 5H) 5.17 (s, 2H) 4.17 (m, 2H) 3.44 (m, 2H) 2.94 (s, 3H) 1.84 (m, 4H) 1.58 (m, 2H) .  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz, ): 197.95, 130.37, 129.50, 128.81, 6.09, 58.56, 34.94, 28.10, 24.95, 24.95, 22.24, 18.92 . IR (diamond ATR): 2922, 1569, 1431  $cm^{-1}$ . MS (ESI<sup>+</sup>): 234 (100). HRMS calcd for  $C_{14}H_{20}NS^+$  234.1316; found 234.1324.



### 1-(1-(Methylthio)ethylidene)pyrrolidinium iodide (7)

Prepared according general procedure A. *N*-acetylpyrrolidine (1,13 g, 10.0 mmol) afforded **7** (2.62 g, 76%). Pale yellow solid. Decomposition 115°C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 4.14 (m, 2H) 3.72 (m, 2H) 2.83 (s, 3H) 2.80 (s, 3H) 2.22 (m, 4H).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 187.52, 57.15, 55.00, 25.17, 25.10, 25.02,

17.81. IR (diamond ATR): 2964, 1598, 1432, 696  $\text{cm}^{-1}$ . MS ( $\text{EI}^+$ ) 144. HRMS: calcd for  $\text{C}_7\text{H}_{14}\text{NS}^+$  144.0847; found 144.0850.



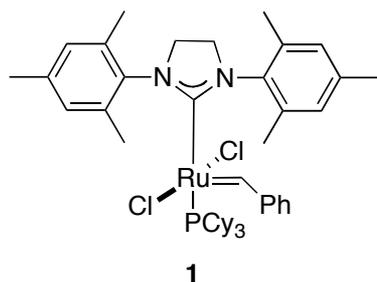
### 2-(1-(Methylthio)ethylidene)-1,2,3,4-tetrahydroisoquinolinium iodide (**13**)

Prepared according general procedure A. *N*-acetyl-1,2,3,4-tetrahydroisoquinoline (1.36 g, 7.9 mmol) afforded **13** (1.17 g, 45%). Orange solid. M.p. = 115-119  $^{\circ}\text{C}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz): 7.37-7.19 (m, 8H) 5.27 (s, 2H) 4.94 (s, 2H) 4.27-4.23 (t,  $J = 3\text{Hz}$ , 2H) 3.97-3.93 (t,  $J = 6\text{Hz}$ , 2H)

3.20-3.18 (t,  $J = 6\text{Hz}$ , 2H) 3.01 (s, 3H) 2.99 (s, 3H) 2.98 (s, 3H) 2.88 (s, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75.5 MHz, ): 191.44, 191.12, 134.06, 133.74, 129.48, 128.86, 128.72, 128.32, 127.94, 127.71, 127.62, 127.39, 127.12, 126.58, 56.05, 54.52, 53.02, 51.96, 28.34, 27.84, 24.49, 18.46, 18.39. IR (diamond ATR): 2967, 1980, 1496, 1243, 608  $\text{cm}^{-1}$ . MS ( $\text{EI}^+$ ): 206 (22.6), 132 (22.6). HRMS: calcd. for  $\text{C}_{12}\text{H}_{16}\text{NS}^+$  206.1003; found 206.1000.

### General procedure B: bisallylation of thioiminium ions

Allylmagnesium bromide (15 mL, 15 mmol) was added to a suspension of thioiminium ion (5 mmol) in dry THF (50 mL) at  $0^{\circ}\text{C}$ , the cooling bath was removed and stirring was continued for 5 h. The mixture was treated with saturated ammonium chloride solution and the aqueous phase extracted with  $\text{CH}_2\text{Cl}_2$ . The collected organic phases were washed with brine and dried over  $\text{MgSO}_4$ . The solvent was evaporated under reduced pressure to afford the crude product, which was purified by FC (cyclohexane/ $\text{EtOAc}$ ) affording the pure bisallylated amine.

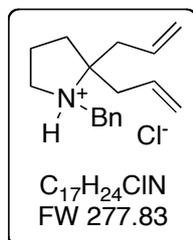


Second generation Grubbs' catalyst

### General procedure C: ring closing metathesis of *gem*-diallylated amines

Acetyl chloride (290  $\mu\text{L}$ , 4.07 mmol) was added at  $0^{\circ}\text{C}$  to MeOH (4 mL). The mixture was stirred for 5 min and the free amine (3.7 mmol) was added. Stirring was continued for 20 min at room temperature, the solvent was evaporated. The crude oily product was triturated with  $\text{Et}_2\text{O}$  to afford the amine hydrochloride as pale white solid. The catalyst **1** (157 mg, 0.185 mmol) was added to a solution of the amine hydrochloride (3.7 mmol) in  $\text{CH}_2\text{Cl}_2$  (37 mL). The mixture was heated at

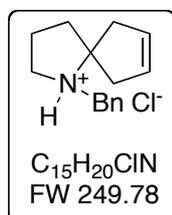
reflux for 1.5 h and was treated with NaOH 1M (10 mL). The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> and the collected organic phases were dried over MgSO<sub>4</sub>. Evaporation of the solvent under reduced pressure followed by FC of the residue (cyclohexane/EtOAc) afforded the spirocyclic amine.



### 2,2-Diallyl-1-benzylpyrrolidine hydrochloride (**4a**)

According general procedure **B**. Thioiminium ion **3a** (1.6 g, 4.8 mmol) afforded the free amine (975 mg) after FC (cyclohexane/EtOAc 9:1) as yellowish oil. The free amine was treated with HCl (generated from acetyl chloride and MeOH) affording **4a** (1.1g, 83%). Greyish solid. Decomposition 140°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>,

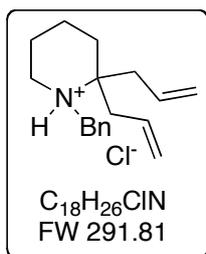
300 MHz): 11.98 (bs, 1H) 7.72 (m, 2H) 7.41 (m, 3H) 5.90 (m, 2H) 5.37 (m, 4H) 4.53 (B part of ABX,  $J_{AB} = 12.6$ ,  $J_{BX} = 4$  Hz, 1H) 3.92 (A part of ABX,  $J_{AB} = 12.6$  Hz  $J_{AX} = 8.5$  Hz, 1H) 3.55-3.34 (m, 1H) 3.06 (B part of ABX,  $J_{AB} = 14.2$ ,  $J_{BX} = 6$  Hz, 1H) 3.01-2.85 (m, 2H) 2.66 (B part of ABX,  $J_{AB} = 14.2$ ,  $J_{BX} = 6.4$  Hz, 1H) 2.55-2.38 (m, 2H) 2.27-2.08 (m, 2H) 1.91 (m, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz): 131.62, 131.15, 131.01, 129.69, 129.52, 129.00, 121.04, 120.80, 73.38, 52.69, 51.93, 40.19, 36.47, 33.70, 19.37. IR (diamond ATR) 2480, 1440, 1427, 1007, 925 cm<sup>-1</sup>. MS (ESI<sup>+</sup>): 242.4 (100, M-Cl<sup>+</sup>), 200.4 (63). HRMS: calcd for C<sub>17</sub>H<sub>24</sub>N<sup>+</sup> 242.1908 found 242.1898.



### 1-Benzyl-1-azaspiro[4.4]non-7-ene hydrochloride (**9a**)

According to general procedure **C**. The amine hydrochloride **4a** (1.03 g, 3.7mmol) afforded the spirocyclic free amine (777mg) after FC (cyclohexane/EtOAc 9:1) as brown oil. The spirocyclic free amine was converted into its hydrochloride by treatment with HCl (generated from acetyl chloride in MeOH) affording **9a** (880 mg, 97% yield).

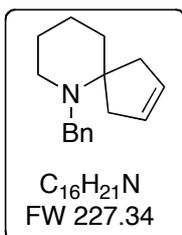
Brown solid. M.p.= 167-168 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): 12.25 (bs, 1H) 7.74 (m, 2H) 7.37 (m, 3H) 5.83 (m, 1H) 5.77 (m, 1H) 4.35 (B part of ABX  $J_{AB} = 13.0$  Hz  $J_{BX} = 3.6$  Hz), 3.58 (A part of ABX  $J_{AB} = 13.0$  Hz,  $J_{AX} = 9.0$  Hz, 1H) 3.51 (B part of AB,  $J = 19$  Hz, 1H) 3.20 (m, 1H) 2.88 (m, 4H) 2.44 (A part of AB,  $J = 19$  Hz, 1H) 2.09 (m, 2H) 1.94 (m, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 133.3 MHz): 130.97, 130.27, 129.59, 129.43, 128.86, 127.17, 76.81, 51.81, 48.82, 39.76, 39.25, 36.46, 19.22. IR (diamond ATR) 2444, 1444, 696 cm<sup>-1</sup>. MS (ESI<sup>+</sup>): 214.4 (100, M-Cl<sup>+</sup>). HRMS: calcd for C<sub>15</sub>H<sub>20</sub>N<sup>+</sup> 214.1595; found 214.1594. Elemental analysis (C<sub>15</sub>H<sub>20</sub>NCl<sup>+</sup>): calcd C 72.18% H 8.01% N 5.61%; found C 71.83% H 8.16% N 5.54%.



### 2,2-diallyl-1-benzylpiperidine hydrochloride (**4b**)

According to general procedure **B**. Thiominium ion **3b** (1.74 g, 5mmol) afforded free amine (1.24 g) after FC (cyclohexane/EtOAc 95:5) as colourless oil. The free amine was then treated with HCl (generated from acetyl chloride and MeOH) affording **4b** (1.41 g, 97%). White solid. M.p.= 152-154°C.  $^1H$  NMR ( $CDCl_3$ ,

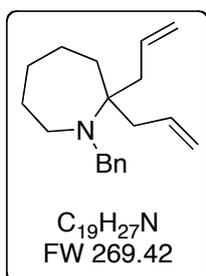
400.13 MHz): 12.79 (bs, 1H) 7.72 (m, 2H) 7.40 (m, 3H) 5.97 (m, 2H) 5.35-5.25 (m, 4H) 4.78 (B part of ABX,  $J_{AB} = 13.0$  Hz,  $J_{BX} = 4$ Hz, 1H) 3.84 (A part of ABX,  $J_{AB} = 13.0$  Hz,  $J_{AX} = 9$ Hz, 1H) 3.23 (B part of ABX,  $J_{AB} = 14.0$  Hz,  $J_{BX} = 7.2$  Hz, 1H) 3.16-3.03 (m, 2H) 2.85-2.71 (m, 3H) 2.46-2.38 (m, 1H) 2.32-2.10 (m, 1H) 1.85-1.60 (m, 1H) 1.74-1.54 (m, 3H).  $^{13}C$  NMR ( $CDCl_3$ , 133 MHz): 131.82, 131.51, 130.71, 129.67, 128.97, 128.82, 66.84, 53.20, 46.33, 40.67, 34.42, 31.20, 21.38, 17.83. IR (diamond ATR) 2525, 1462, 1428  $cm^{-1}$ . MS (ESI<sup>+</sup>): 256.4 (100, M-Cl<sup>+</sup>), 242.4 (19). HRMS: calcd for  $C_{18}H_{26}N^+$  256.2056; found 256.2056.



### 6-Benzyl-6-azaspiro[4.5]dec-2-ene (**9b**)

According to general procedure **C** The amine hydrochloride **4b** (50 mg, 0.17 mmol) afforded amine **8b** (32 mg, 82% yield). Brownish oil. FC (cyclohexane/EtOAc 95:5).  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.27-7.07 (m, 5H) 5.58 (s, 2H) 3.23 (s, 2H) 2.52 (m, 2H) 2.27 (m, 2H) 2.11 (m, 2H) 1.61 (m, 2H) 1.40 (m,

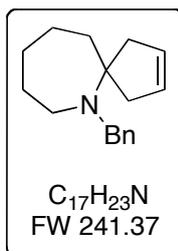
2H).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 141.32, 129.44, 128.47, 128.16, 126.46, 65.25, 54.70, 48.37, 40.66, 26.42, 22.17. IR (diamond ATR): 2924, 2848, 2789, 1451, 1430  $cm^{-1}$ . MS (ESI<sup>+</sup>): 228 (M<sup>+</sup>, 100%), 215 (40%). HRMS: calcd for  $C_{16}H_{22}N^+$  228.1752; found 228.1746.



### 2,2-Diallyl-1-benzylazepane (**4c**)

According to general procedure **B**. Thioiminium ion **3c** (180 mg, 0.5 mmol) afforded **4c** (113 mg, 85%). Viscous oil. FC (cyclohexane/EtOAc 9:1).  $^1H$  NMR ( $CDCl_3$ , 400 MHz): 7.39 (m, 2H) 7.30 (m, 2H) 7.23-7.18 (m, 1H) 6.02-5.92 (m, 2H) 5.08-5.03 (m, 4H) 3.81 (s, 2H) 2.64 (m, 2H) 2.43 (B part of ABX,  $J_{AB} = 14.0$  Hz,  $J_{BX} = 7.2$  Hz, 2H) 2.30 (A part of ABX,  $J_{AB} = 14.0$  Hz,  $J_{AX} = 7.2$  Hz, 2H)

1.68 (m, 4H) 1.43 (m, 2H) 1.30 (m, 2H).  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz): 142.28, 136.09, 128.45, 127.94, 126.40, 116.88, 61.19, 54.81, 48.73, 42.84, 37.19, 31.87, 29.98, 22.74. IR (diamond ATR): 3072, 2925, 1636, 1440  $cm^{-1}$ . MS (ESI<sup>+</sup>): 270.4 (100, M+H<sup>+</sup>), 230.4 (14), 180.2 (83). HRMS: calcd for  $C_{19}H_{28}N^+$  270.2221; found: 270.2221.



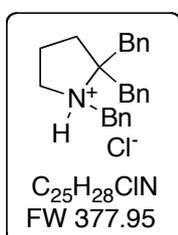
### 6-Benzyl-6-azaspiro[4.6]undec-2-ene (9c)

According to general procedure C. Bisallylated amine **4c** (113 mg, 0.47 mmol) afforded **8c** (28 mg, 83%). Greenish oil. FC (cyclohexane/EtOAc 95:5). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): 7.42 (d, J = 7.2 Hz, 2H) 7.29 (m, 3H) 7.20 (m, 1H) 5.58 (s, 2H) 3.42 (s, 2H) 2.58 (m, 4H) 2.23 (dm, J = 14.5 Hz, 2H) 1.80 (m, 2H) 1.69 (m, 2H)

1.52 (m, 2H) 1.41 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz): 142.3, 129.6, 128.6, 128.1, 126.5, 68.4, 55.6, 48.5, 44.1, 43.9, 31.4, 29.8, 23.1. IR (diamond ATR): 3046, 2923, 2848, 1450, 1439 cm<sup>-1</sup>. MS (EI<sup>+</sup>): 241 (26, M<sup>+</sup>), 212 (48), 136 (36), 96 (47), 91 (100). HRMS: calcd for C<sub>17</sub>H<sub>24</sub>N<sup>+</sup> 242.1908; found: 242.1905.

### General procedure D: synthesis of *gem*-dibenzylated amines

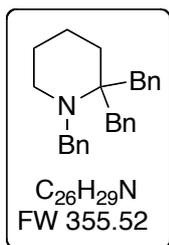
Benzyl magnesium chloride (2 mL, 2.0 mmol) was added to a suspension of thioiminium ion (1.0 mmol) in dry THF (10 ml) at room temperature. After 10 min a solid was formed and the mixture was stirred for 10 h at room temperature, treated with saturated solution of ammonium chloride. The aqueous phase was extracted with EtOAc, the collected organic phase were washed with brine and dried over MgSO<sub>4</sub>. Evaporation of the solvent at reduced pressure afforded a crude product which was purified by FC (cyclohexane/EtOAc).



### 2,2-Dibenzyl-N-benzylpyrrolidine hydrochloride (5a)

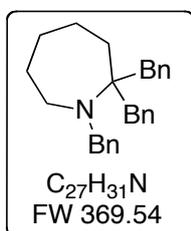
According to general procedure starting D. Thioiminium ion **3a** (333 mg, 1 mmol) afforded free amine (280 mg) after FC (cyclohexane/EtOAc 9:1) as brown oil. The free amine was converted into its hydrochloride by treatment with HCl (generated from AcCl in MeOH) affording **5a** (314 mg, 92%). Pink solid. Decomposition 170

°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): 12.35 (s, 1H) 7.71 (dd, J<sub>1</sub> = 8.0 Hz, J<sub>2</sub> = 2.0 Hz, 2H) 7.61 (d, J = 8.0 Hz, 2H) 7.35 (m, 11H) 4.29 (B part of AB, J = 12.4, 3.4 Hz, 1H) 3.97 (A part of AB, J = 12.6, 8.7 Hz, 1H) 3.84 (B part of ABX, J<sub>AB</sub> = 13.7 Hz, 1H) 3.43 (A part of ABX, J<sub>AB</sub> = 13.7 Hz, 1H) 3.38 (m, 1H) 3.28 (B part of AB, J = 14.6 Hz, 1H) 3.07 (A part of AB, J = 14.5 Hz, 1H) 2.80-2.62 (m, 1 H) 2.68-2.51 (m, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 133.33 MHz): 135.80, 135.35, 131.29, 130.48, 130.01, 129.90, 129.35, 129.30, 129.05, 128.20, 127.92, 75.69, 52.78, 52.34, 42.44, 37.56, 34.46, 19.73. IR (diamond ATR): 3469, 3387, 1633, 1602, 1495, 1462 cm<sup>-1</sup>. Elemental analysis (C<sub>25</sub>H<sub>28</sub>NCl·0.6 H<sub>2</sub>O): calcd C 77.28% H 7.52% N 3.60%; found C 77.27% H 7.53% N 3.65%.



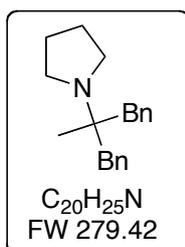
### 2,2-Dibenzyl-N-benzylpiperidine (5b)

According to general procedure D. Thioiminium ion **3b** (100 mg, 0.29 mmol) afforded **5b** (89 mg, 86%) Orange glue. FC (cyclohexane/EtOAc 9:1).  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.28-7.15 (m, 5H) 4.02 (s, 2H) 3.30 (d,  $J = 13.6$  Hz, 2H) 2.58 (d,  $J = 13.6$  Hz, 2H) 2.52 (t,  $J = 5.8$  Hz, 2H) 1.67 (m, 2H) 1.48 (m, 2H) 1.38 (m, 2H).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 139.39, 137.90, 130.32, 127.33, 127.16, 126.78, 125.47, 124.93, 59.92, 52.50, 45.84, 37.78, 29.87, 25.14, 20.41. IR (diamond ATR): 2914, 1492, 1454  $cm^{-1}$ . MS ( $ESI^+$ ): 356.23 (100,  $M+H^+$ ), 273.17 (33), 215.13 (83). HRMS: calcd for  $C_{26}H_{30}N^+$  356.2374; found: 356.2376.



### 2,2-dibenzyl-N-benzylazepine (5c)

According to general procedure D. Thioiminium ion **3c** (100 mg, 0.28 mmol) afforded **5c** (78 mg, 79 %). White oil. FC (cyclohexane/EtOAc 9:1).  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.57 (d,  $J = 7.2$  Hz, 2H) 7.42-7.25 (m, 13H) 4.31 (s, 2H) 3.17 (d,  $J = 13.6$  Hz, 2H) 2.80 (d,  $J = 13.6$  Hz, 2H) 2.41 (m, 2H) 1.69 (m, 4H) 1.32 (m, 2H) 1.22 (m, 2H).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 142.74, 139.39, 131.43, 128.47, 128.16, 127.88, 126.60, 126.01, 63.61, 56.05, 50.42, 43.89, 35.00, 32.49, 30.24, 23.27. IR (diamond ATR): 2947, 2926, 1493, 1453  $cm^{-1}$ . MS ( $ESI^+$ ): 350.25 (100,  $M+H^+$ ), 353.27 (31), 273.17 (18), 215.13 (59). HRMS: calcd for  $C_{27}H_{32}N$  370.2539; found: 370.2534.



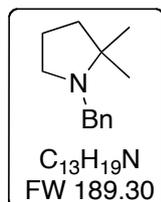
### 1-(1-Benzyl-1-methyl-2-phenyl-ethyl)-pyrrolidine (8)

According general procedure **D**. Thioiminium ion **7** (0.277g, 1.02 mmol) afforded **8** (0.253g, 87%). Transparent oil. FC (cyclohexane/EtOAc 9:1).  $^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.27-7.20 (m, 10H) 2.94 (B part of AB,  $J = 13.5$  Hz, 2H) 2.85 (m, 4H) 2.70 (A part of AB,  $J = 13.5$  Hz, 2H) 1.78 (m, 4H) 0.91 (s, 3H).  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 139.52, 130.93, 127.79, 125.81, 58.67, 45.37, 41.71, 24.36, 23.06. IR (diamond ATR): 3060, 3025, 2968, 1738  $cm^{-1}$ . MS ( $EI^+$ ): 188 (100,  $[M-C_7H_7]^+$ ), 91 (28). HRMS: calcd for  $C_{20}H_{26}N^+$  280.2065; found: 280.2072.

### General procedure E: synthesis of *gem*-dialkylated amines

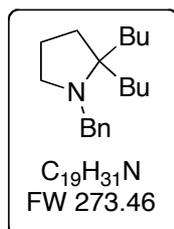
A suspension of  $CeCl_3$  (0.296 g, 1.2 mmol) in dry THF (4 ml) was sonicated at room temperature for 30 min. The suspension was cooled down to  $-78$  °C and the alkyllithium reagent solution (1.2 mmol) was added dropwise. The solution became pale yellow and stirring was continued for 30

min. The thioiminium salt was added as a solid (0.3 mmol), the cooling bath was removed and the mixture was stirred for 6 h. The dark brown suspension was treated with saturated  $\text{NH}_4\text{Cl}$  and the aqueous phases were extracted with dichloromethane (3 x). The collected organic phases were dried over  $\text{MgSO}_4$ , filtrated and the solvent evaporated under reduced pressure. The crude product was purified by FC (cyclohexane/*tert*-BuOMe) to afford the gem-dialkylated amine.



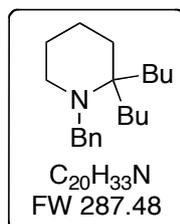
### 1-Benzyl-2,2-dimethylpyrrolidine (10a)<sup>1</sup>

According general procedure E. Thioiminium ion **3a** (0.200 g, 0.74 mmol) afforded **9a** (0.088 g, 77%). Transparent oil. FC (cyclohexane/*tert*-BuOMe 85:15).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz): 7.22-7.18 (m, 5H) 3.43 (s, 2H) 2.56-2.53 (m, 2H) 1.62-1.60 (m, 4H) 1.01 (s, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75.5 MHz): 141.09, 128.57, 128.133, 126.50, 76.60, 67.99, 60.05, 53.21, 50.94, 39.98, 29.72, 25.64, 23.07, 20.50. IR (diamond ATR): 3025, 2958, 2866, 1453  $\text{cm}^{-1}$ . MS ( $\text{EI}^+$ ): 189(9), 185(14), 174 (59). HRMS: calcd for  $\text{C}_{13}\text{H}_{20}\text{N}^+$  190.1599; found 190.1595.



### 1-Benzyl-2,2-dibutylpyrrolidine (11a)

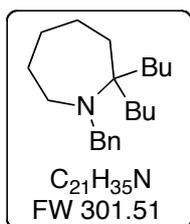
According general procedure E. Thioiminium ion **3a** (0.200 g, 0.74 mmol) afforded **11a** (0.144 g, 88%). Pale yellow oil. FC (cyclohexane/*tert*-BuOMe 9:1).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz): 7.27-7.24 (m, 5H) 3.52 (s, 2H) 2.53-2.51 (t,  $J = 6$  Hz, 2H) 1.59-1.56 (m, 4H) 1.35-1.12 (m, 14H) 0.85 (t,  $J = 6$  Hz, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75.5 MHz): 141.50, 128.30, 128.09, 126.35, 76.59, 67.98, 64.52, 52.22, 50.76, 35.18, 32.98, 26.81, 25.63, 23.78, 21.82, 14.27. IR (diamond ATR): 3026, 2954, 2858, 1454  $\text{cm}^{-1}$ . MS ( $\text{EI}^+$ ): 274(65), 215(28). HRMS: calcd for  $\text{C}_{19}\text{H}_{32}\text{N}^+$  274.2534; found 274.2541.



### 1-Benzyl-2,2-dibutylpiperidine (11b)

According general procedure E. Thioiminium ion **3b** (0.078 g, 0.29 mmol) afforded **11b** (0.057g, 69%). Colourless oil. FC (cyclohexane/*tert*-BuOMe 9:1).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz): 7.31-7.14 (m, 5H) 3.45 (s, 2H) 2.33-2.29 (m, 2H) 1.66-1.65 (m, 2H) 1.43-1.22 (m, 20H) 0.83-0.81 (m, 8H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75.5 MHz): 128.48, 128.08, 127.90, 126.21, 126.18, 67.98, 60.11, 57.50, 54.29, 52.77, 48.28, 45.82, 38.13, 37.09, 33.30, 31.58, 30.06, 27.07, 26.36, 25.70, 25.63, 23.95, 23.80, 23.11, 20.81, 14.26, 14.23. IR (diamond ATR): 2930, 2858, 2793, 1452  $\text{cm}^{-1}$ . MS ( $\text{EI}^+$ ): 288, 273, 215. HRMS: calcd for  $\text{C}_{20}\text{H}_{34}\text{N}^+$  288.2691; found 288.2687.

<sup>1</sup> Denton, M. S.; Wood, A. *Synlett* **1999**, 55-56

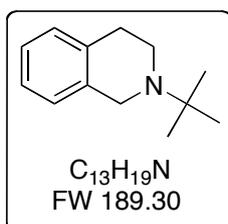


### 1-Benzyl-2,2-dibutylazepane (11c)

According general procedure **E**. Thioiminium ion **3c** (0.100 g, 0.28 mmol) afforded **11c** (0.062 g, 71 %). Colourless oil. FC (cyclohexane/*tert*-BuOMe 95:5).

$^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.36-7.12 (m, 5H) 3.65 (s, 2H) 2.56 (t,  $J = 3$  Hz, 2H) 1.58-1.22 (m, 21H) 0.84 (t,  $J = 9$ Hz, 6H) .  $^{13}C$  NMR ( $CDCl_3$ , 100 Hz): 142.94,

128.48, 127.90, 126.21, 60.12, 54.29, 48.28, 38.13, 37.09, 31.60, 30.06, 29.72, 27.07, 23.96, 23.11, 14.27 . IR (diamond ATR): 2923, 2853, 1493, 1455  $cm^{-1}$ . MS ( $EI^+$ ): 302, 273, 215, 212. HRMS: calcd for  $C_{21}H_{36}N^+$  302.2847; found 302.2848.

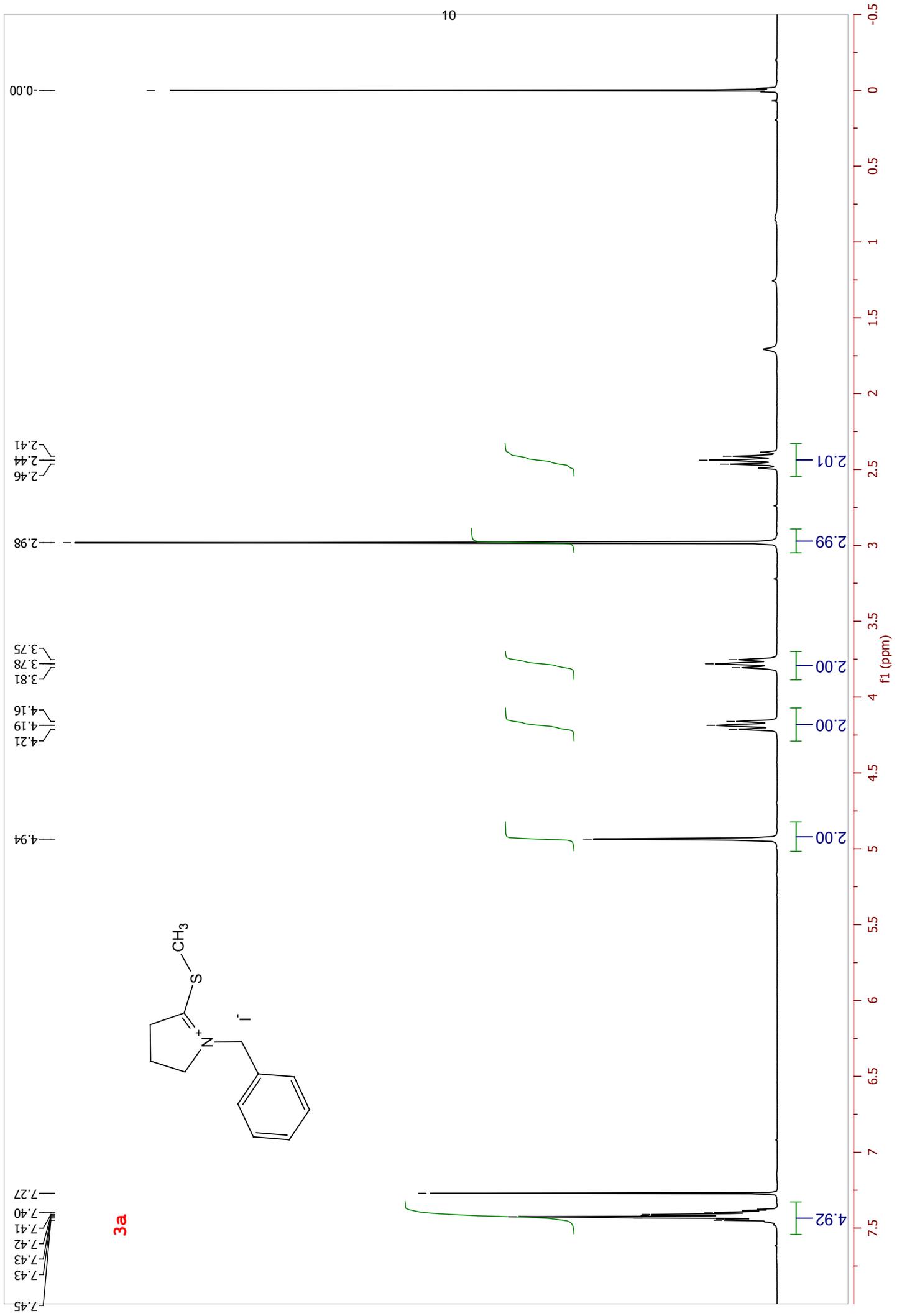


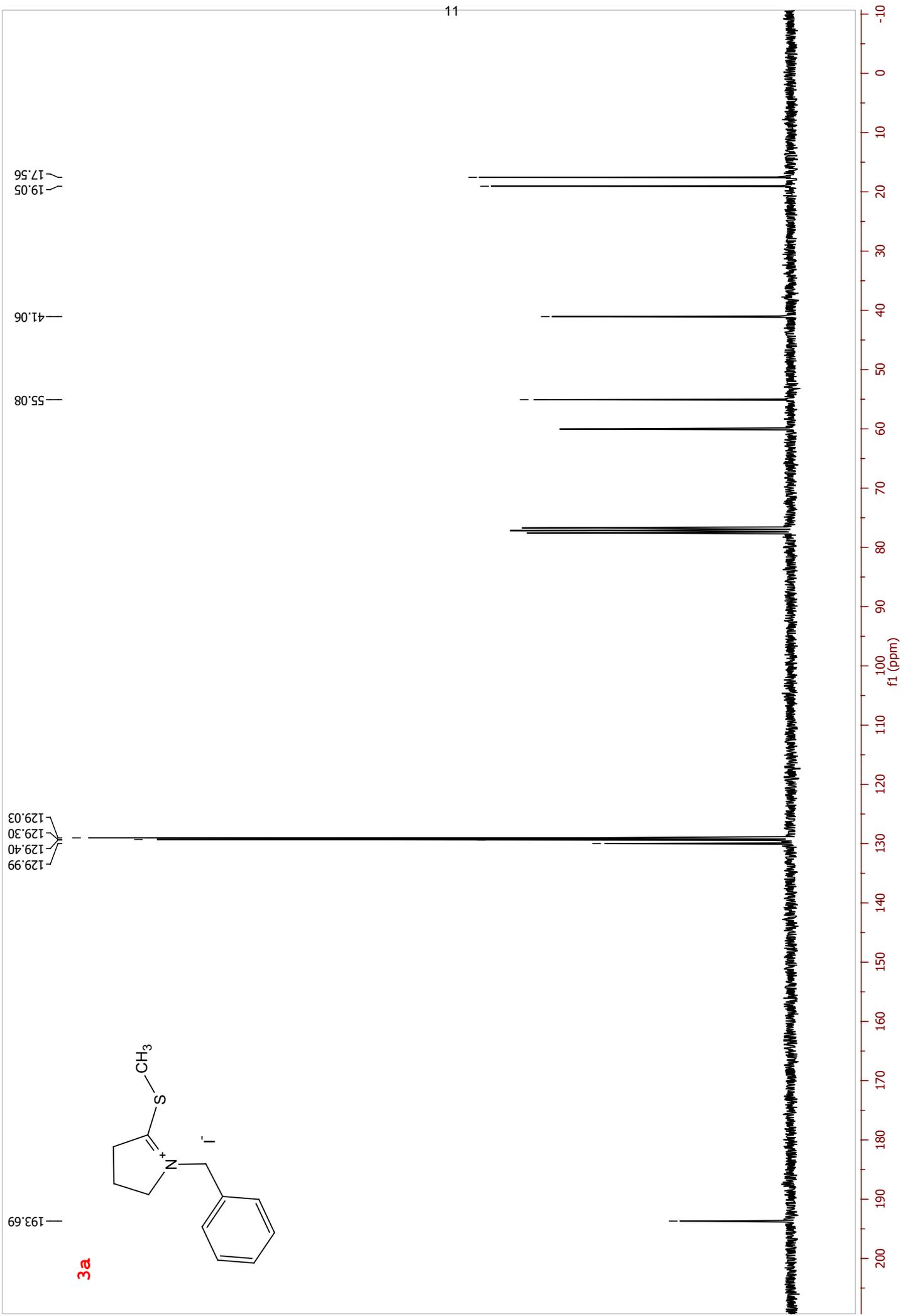
### 2-*tert*-Butyl-1,2,3,4-tetrahydroisoquinoline (14)

According general procedure **E**. Thioiminium ion **13** (0.100 g, 0.3 mmol) afforded **14** (0.047g, 83%). Yellow liquid. . FC (cyclohexane/*tert*-BuOMe 8:2).

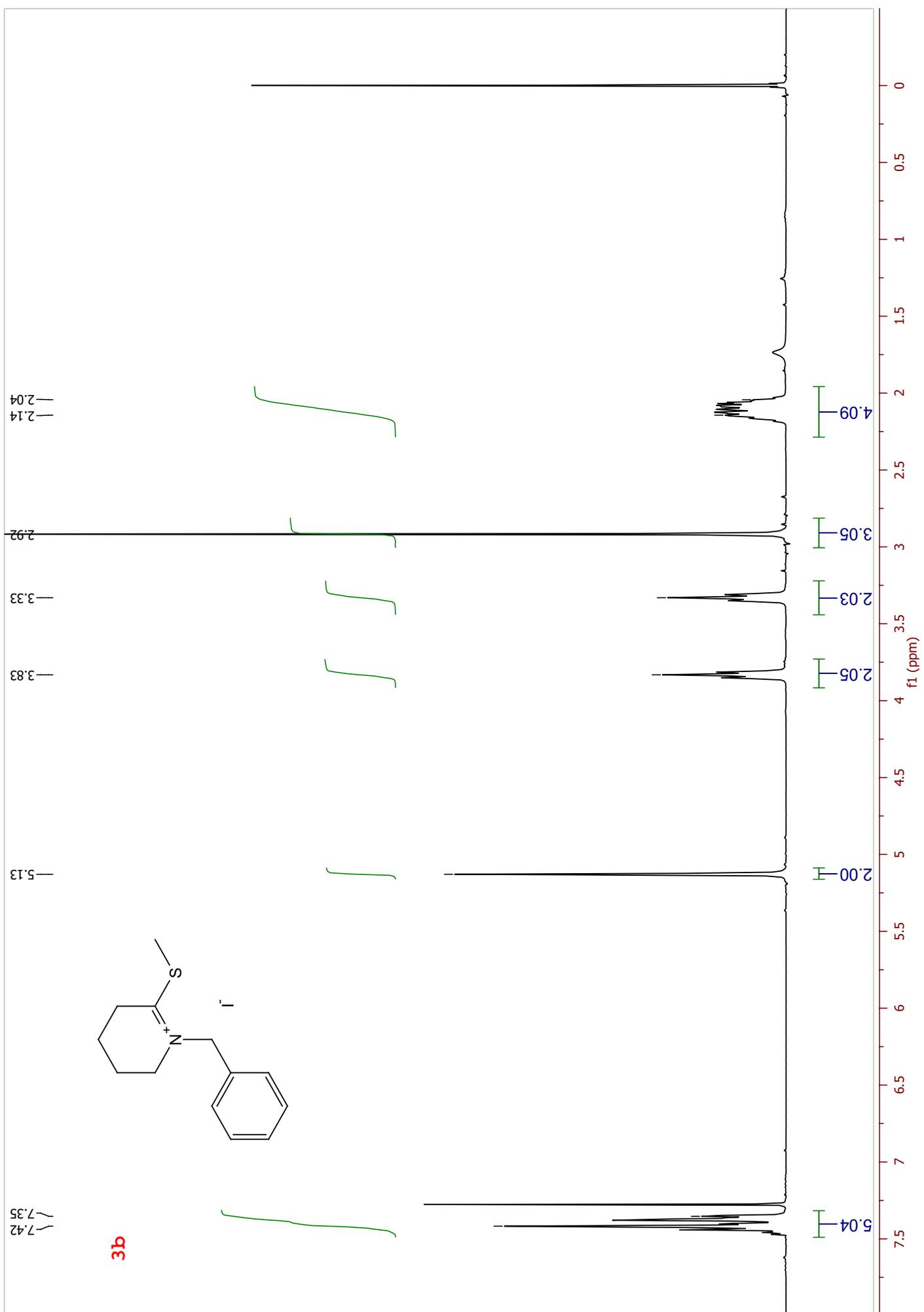
$^1H$  NMR ( $CDCl_3$ , 300 MHz): 7.02 (m, 4H) 3.72 (s, 2H) 2.79-2.73 (m, 4H) 1.11 (s, 9H) .  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz): 134.93, 128.77, 127.07, 125.92, 125.57,

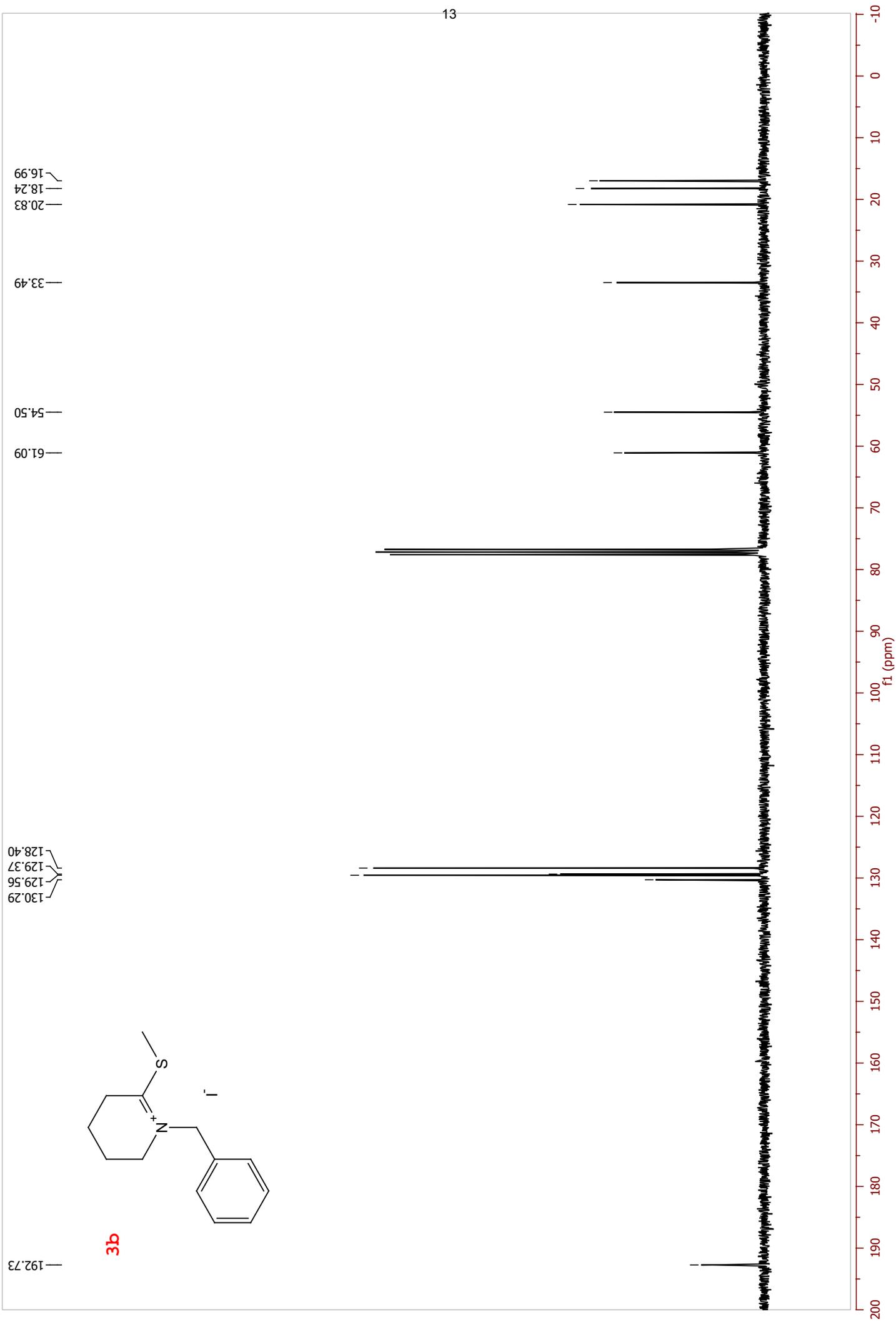
54.06, 49.19, 44.26, 30.71, 26.05. IR (diamond ATR): 2968, 2916, 1585, 1454  $cm^{-1}$ . MS ( $EI^+$ ): 190, 188, 134, 132. HRMS: calcd for  $C_{13}H_{20}N^+$  190.1596; found 190.1593.

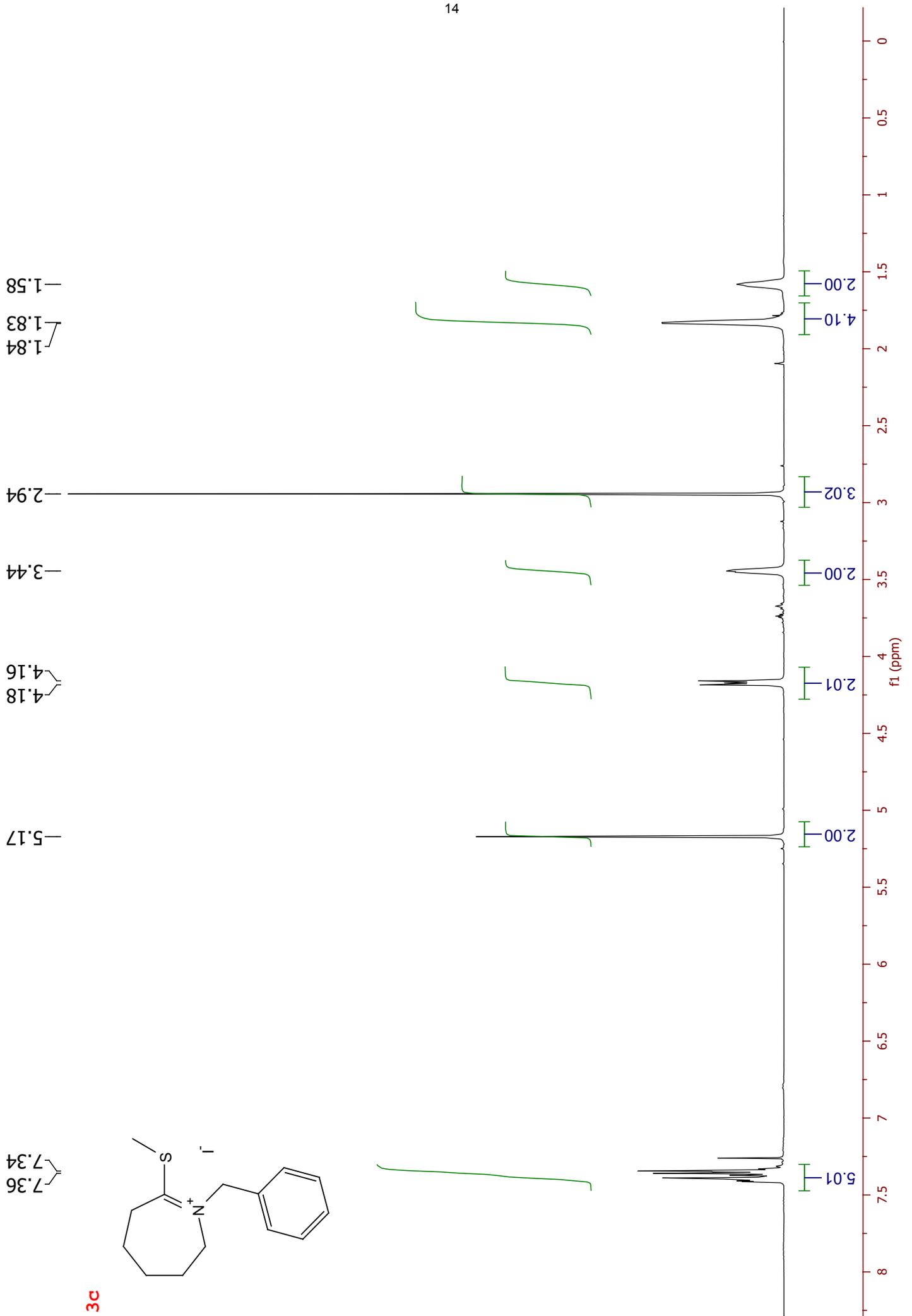


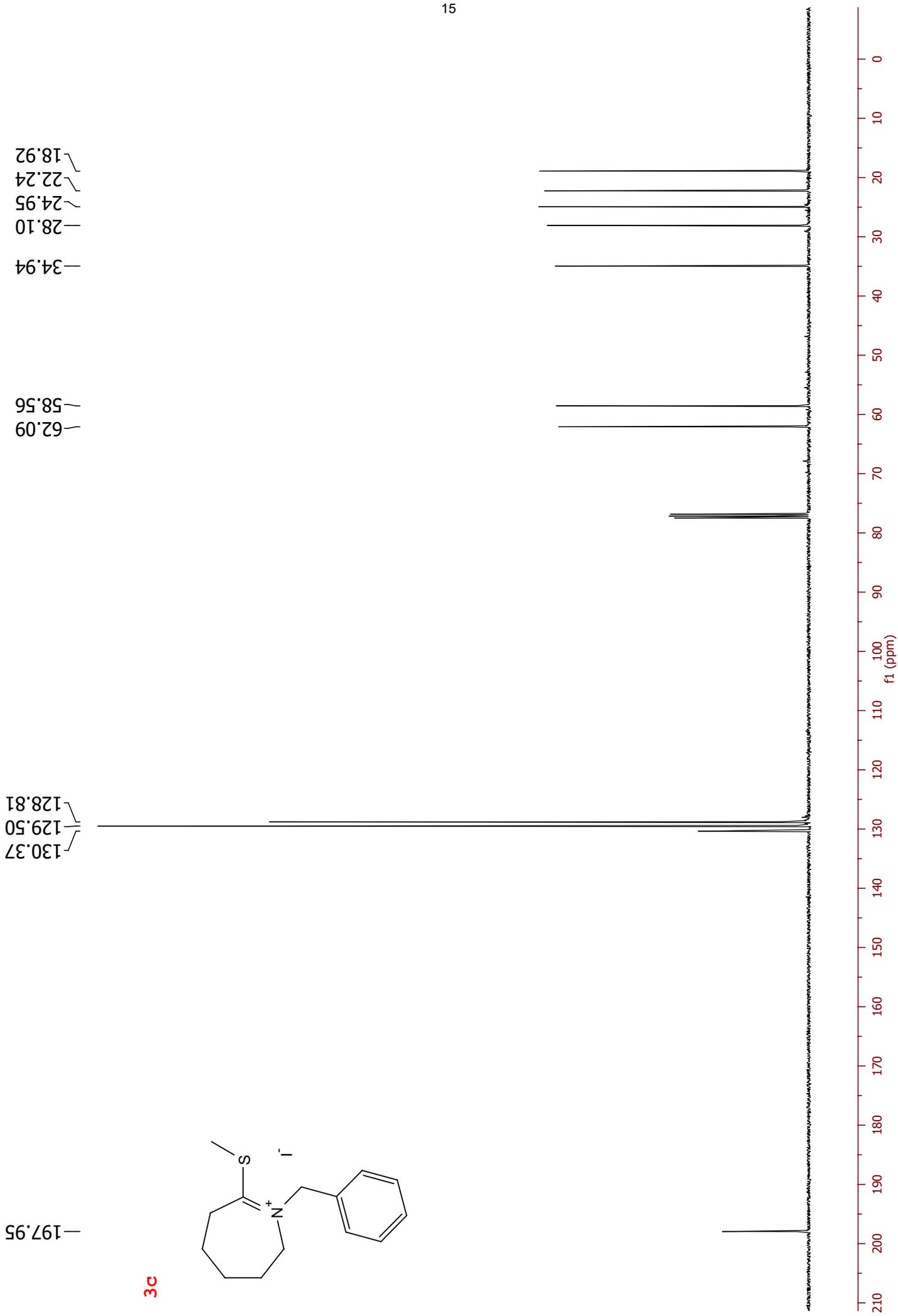


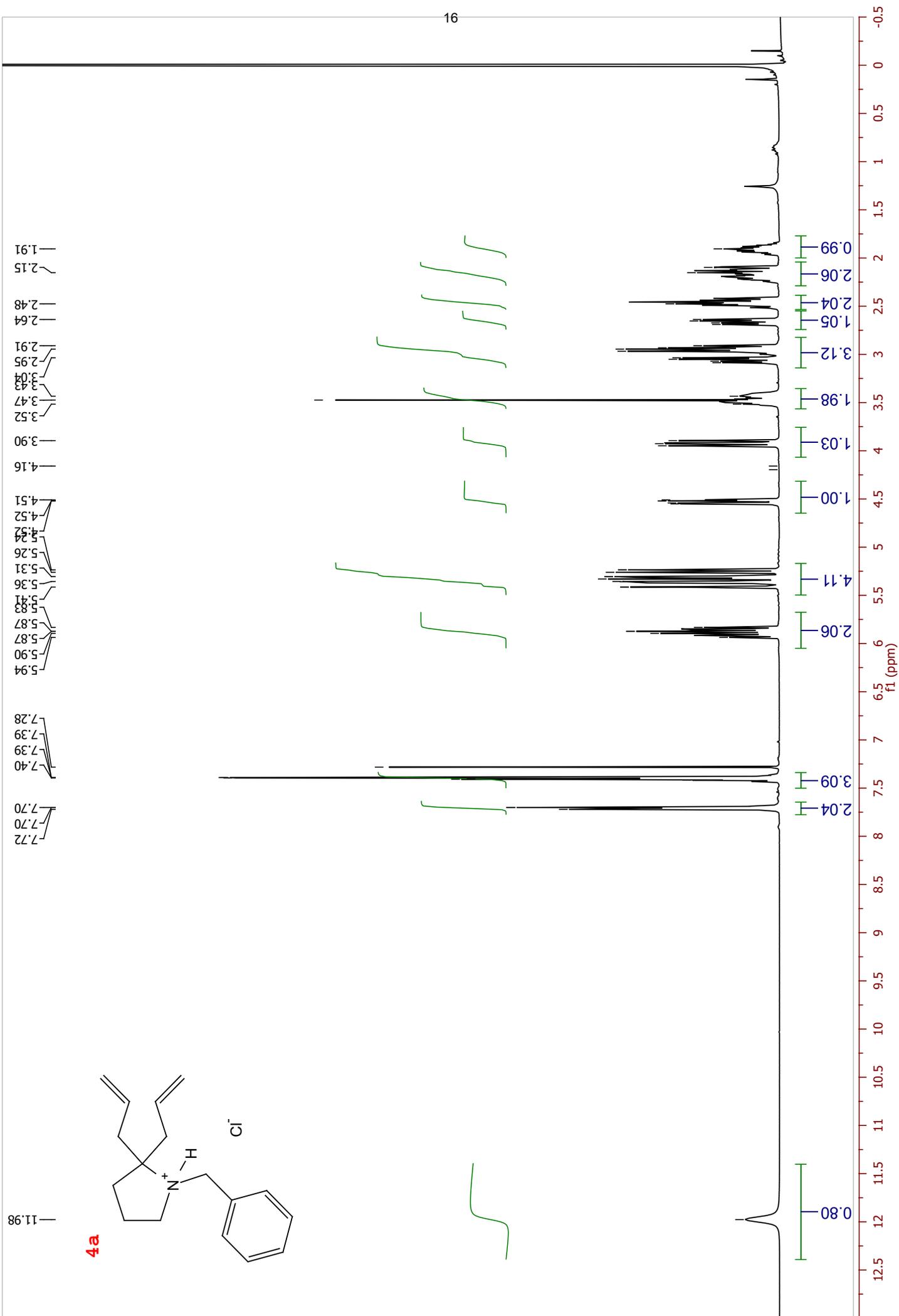
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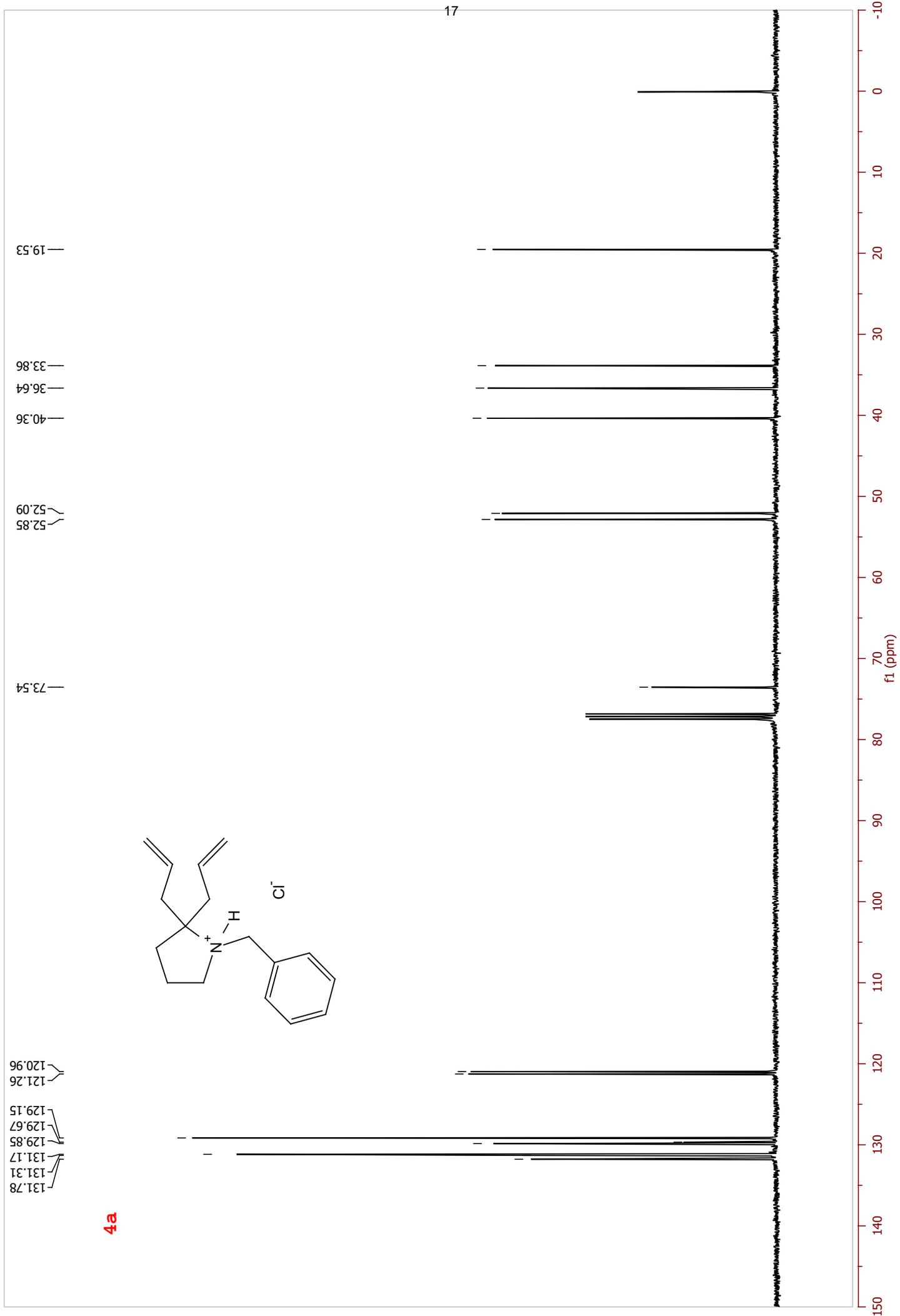


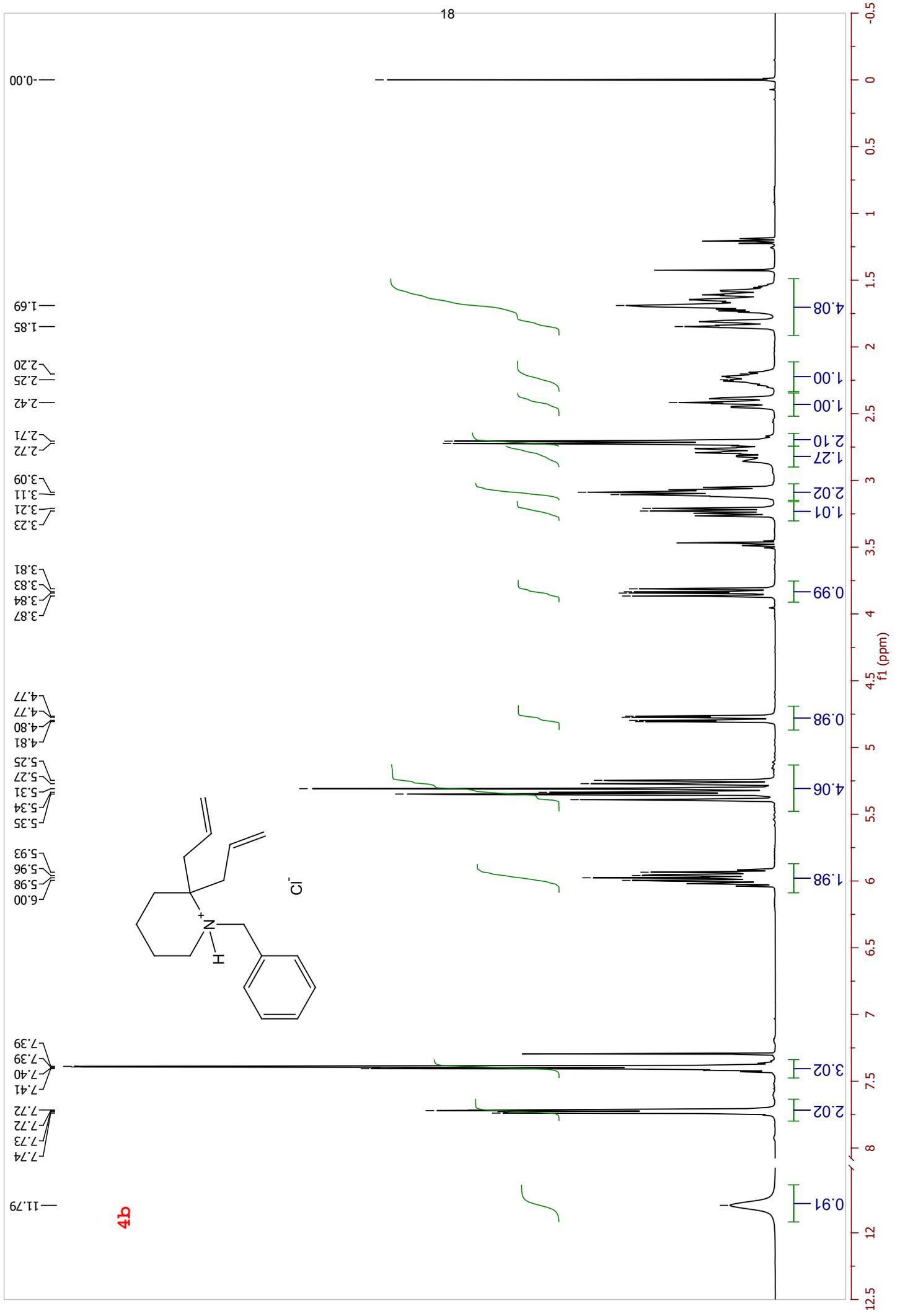


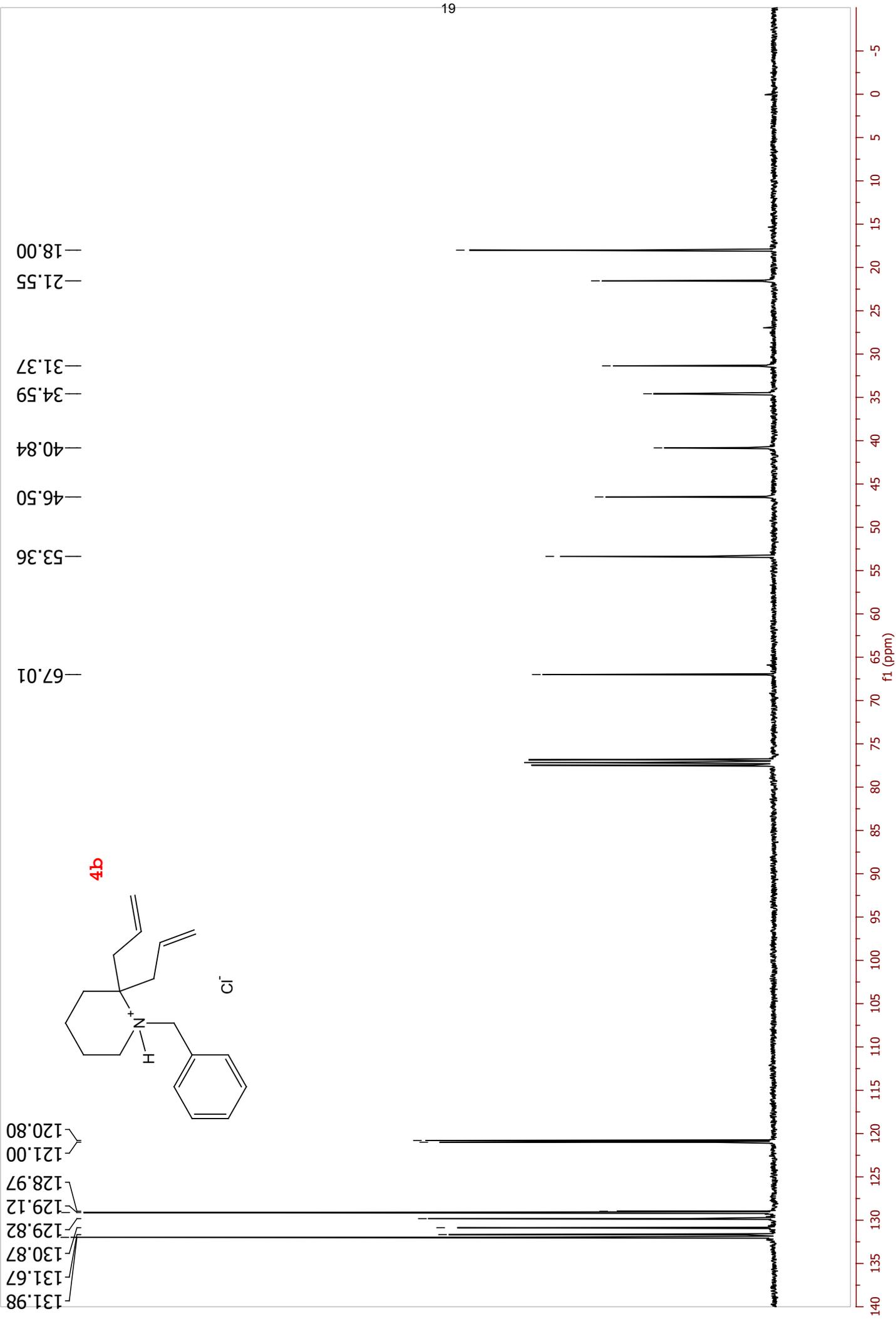


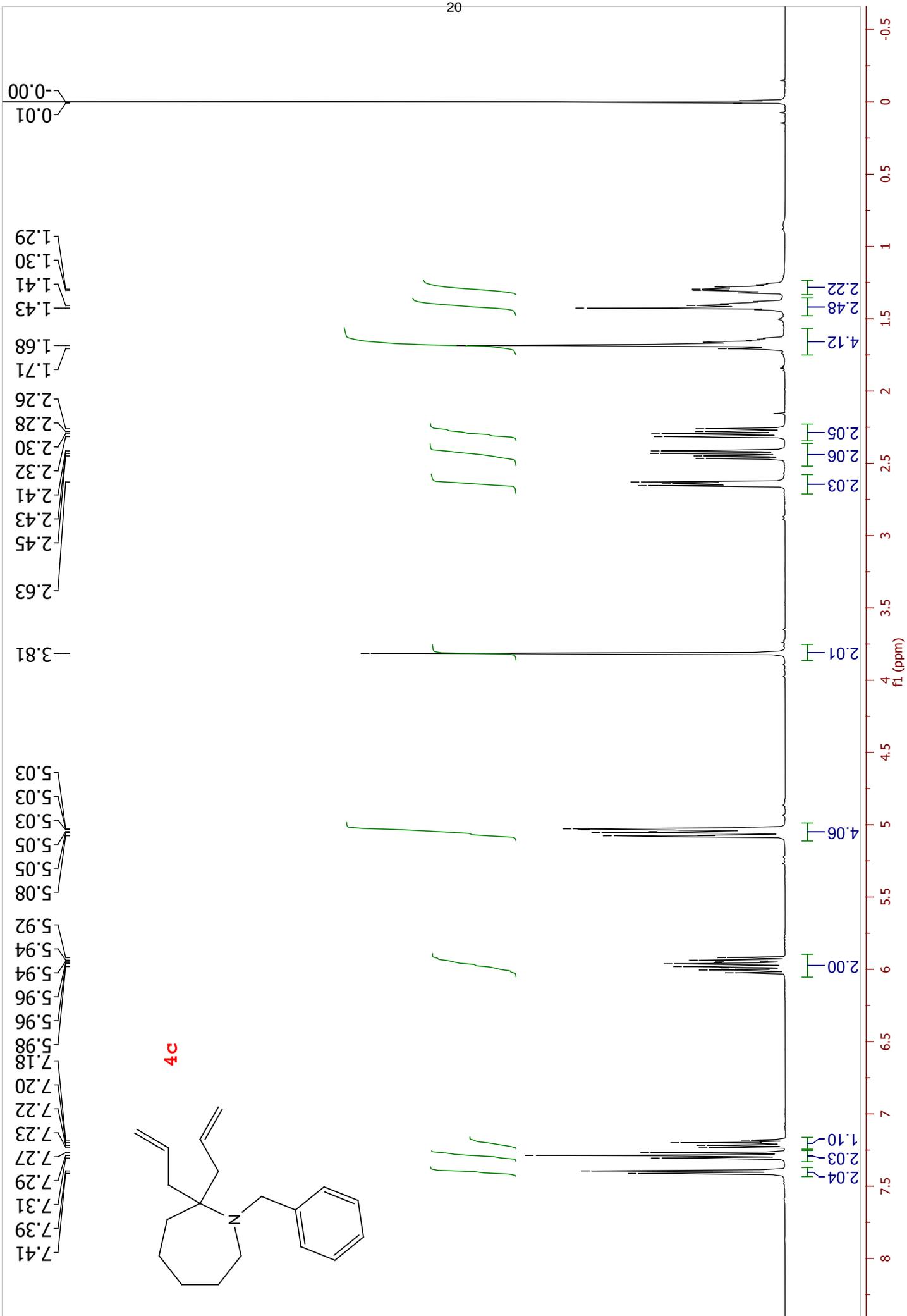


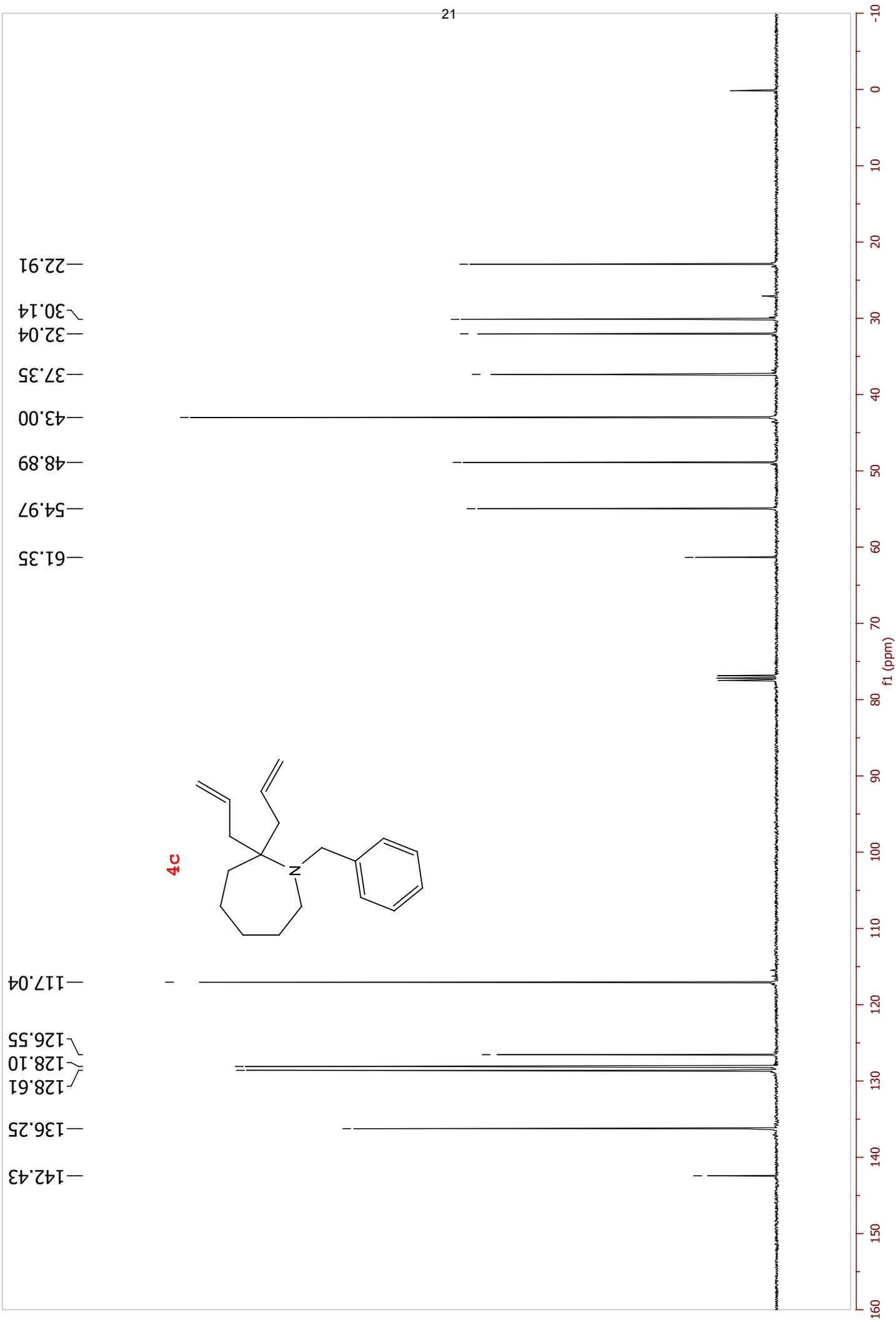


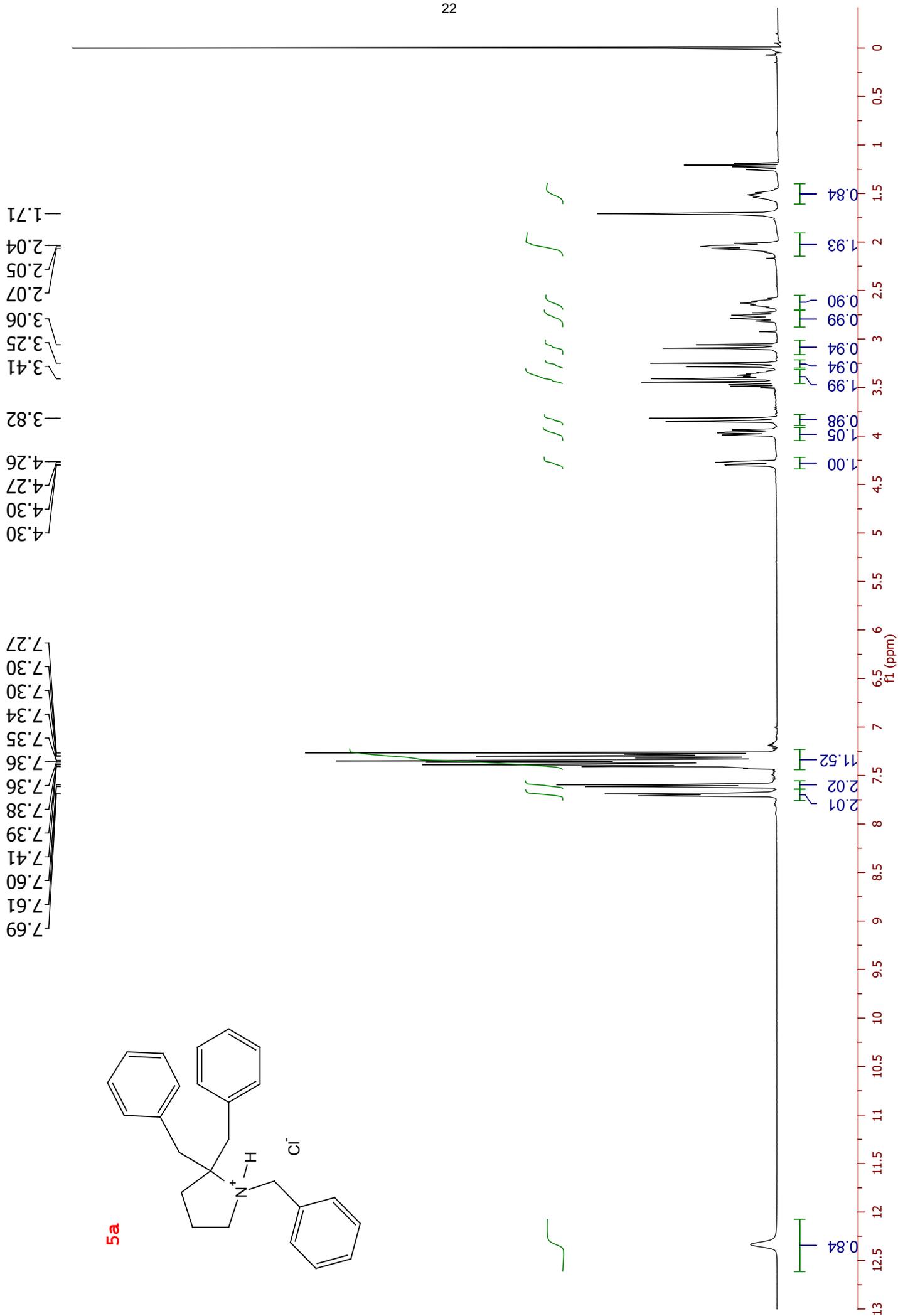


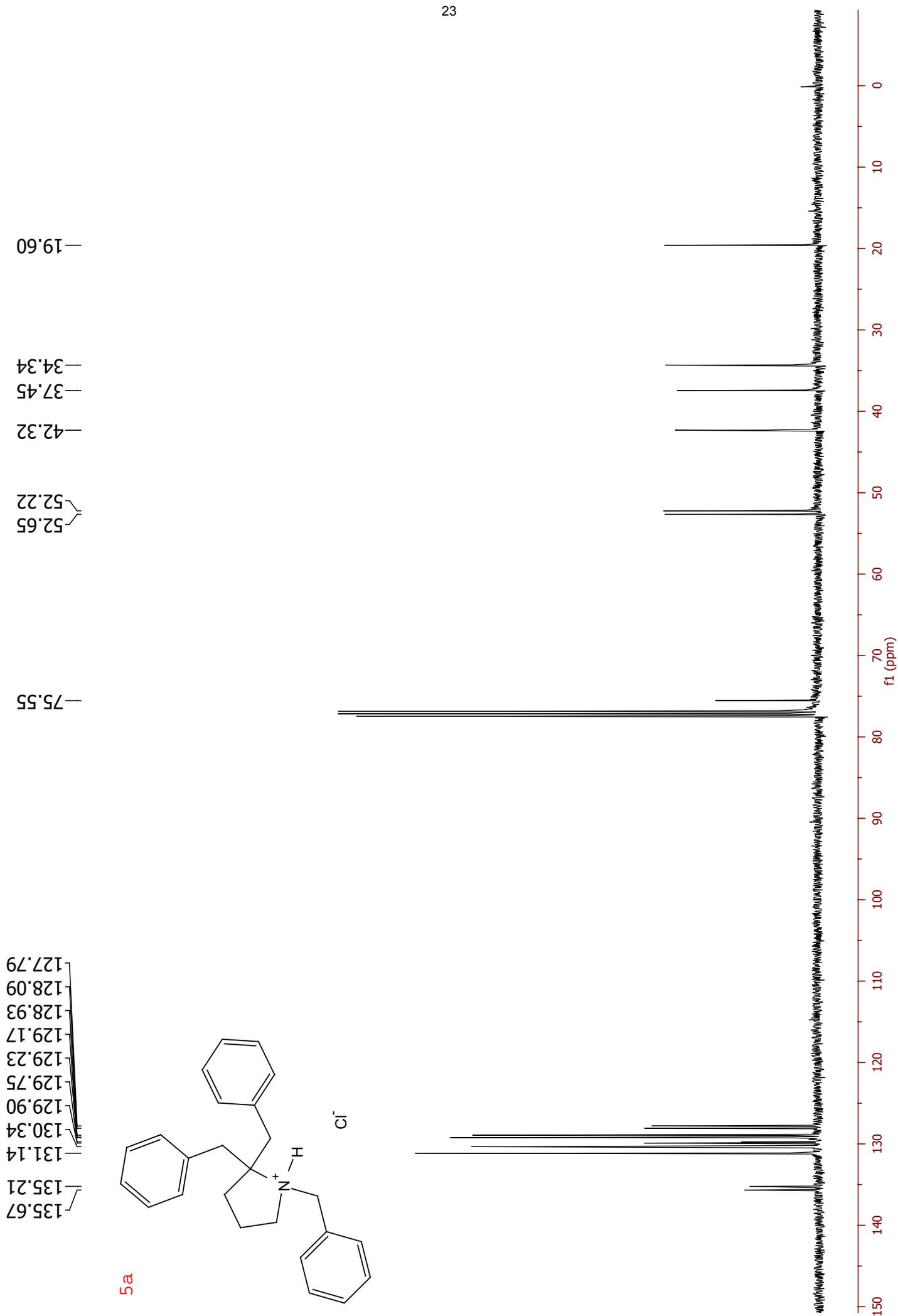






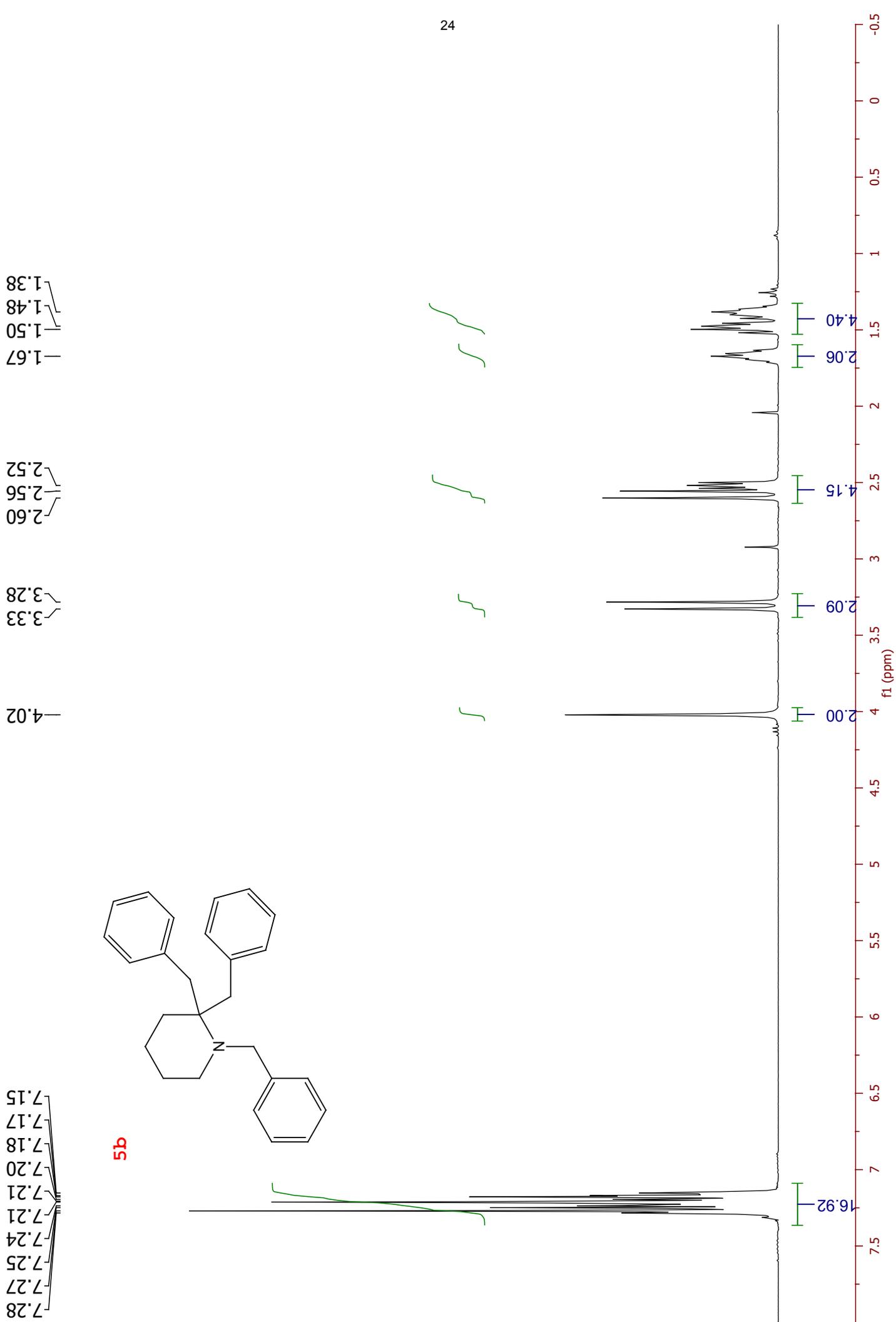
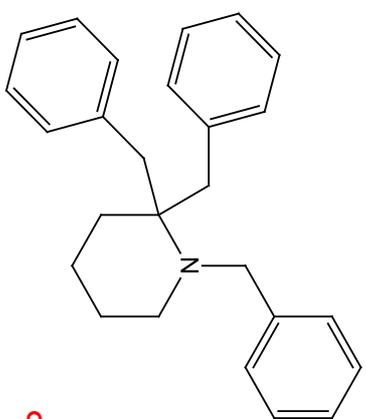


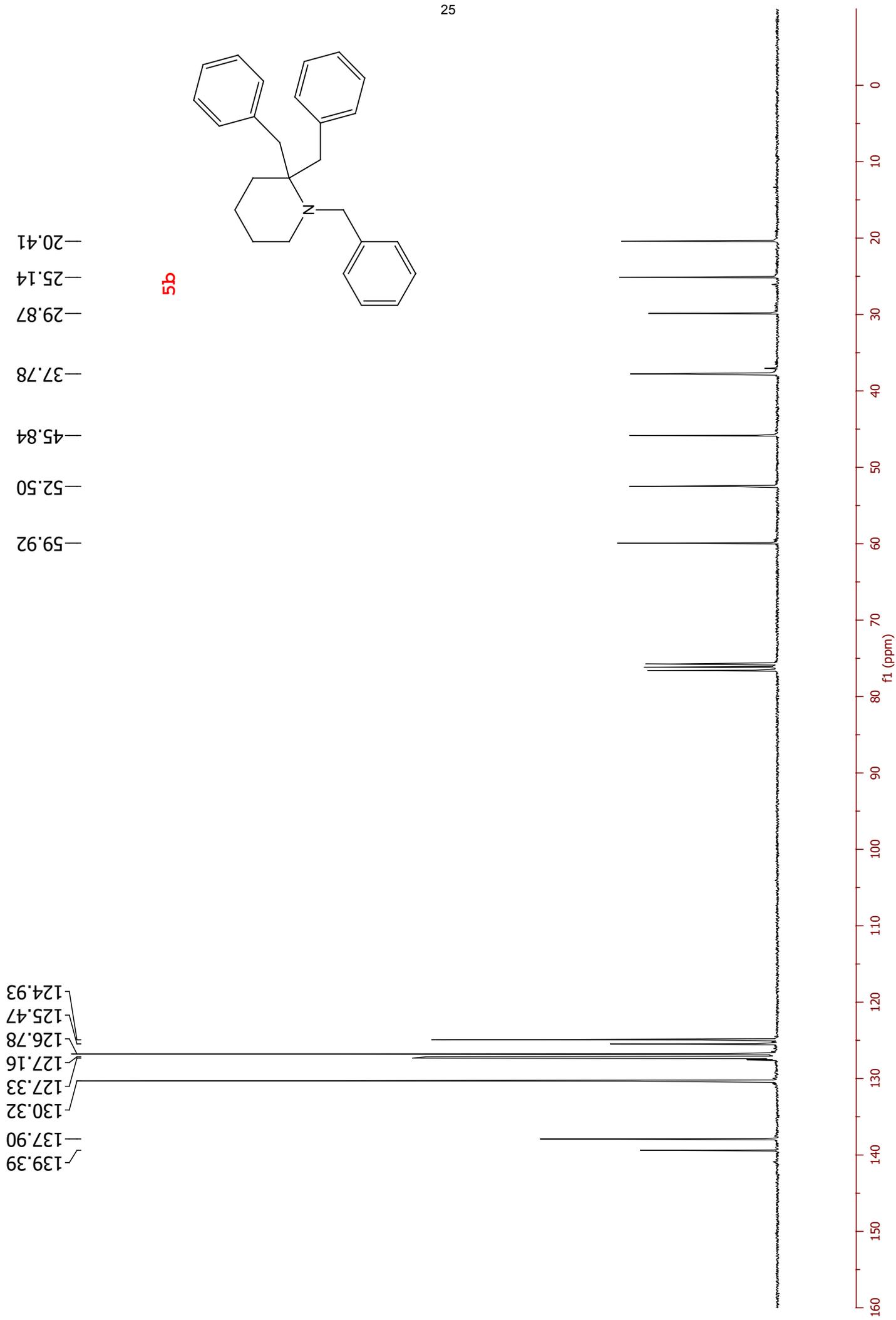


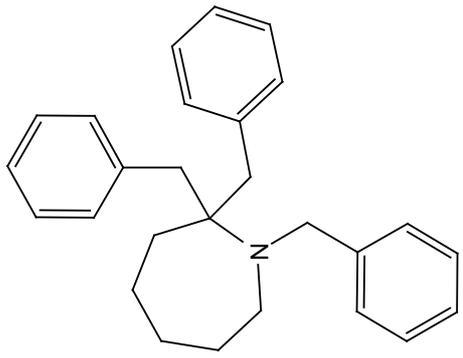


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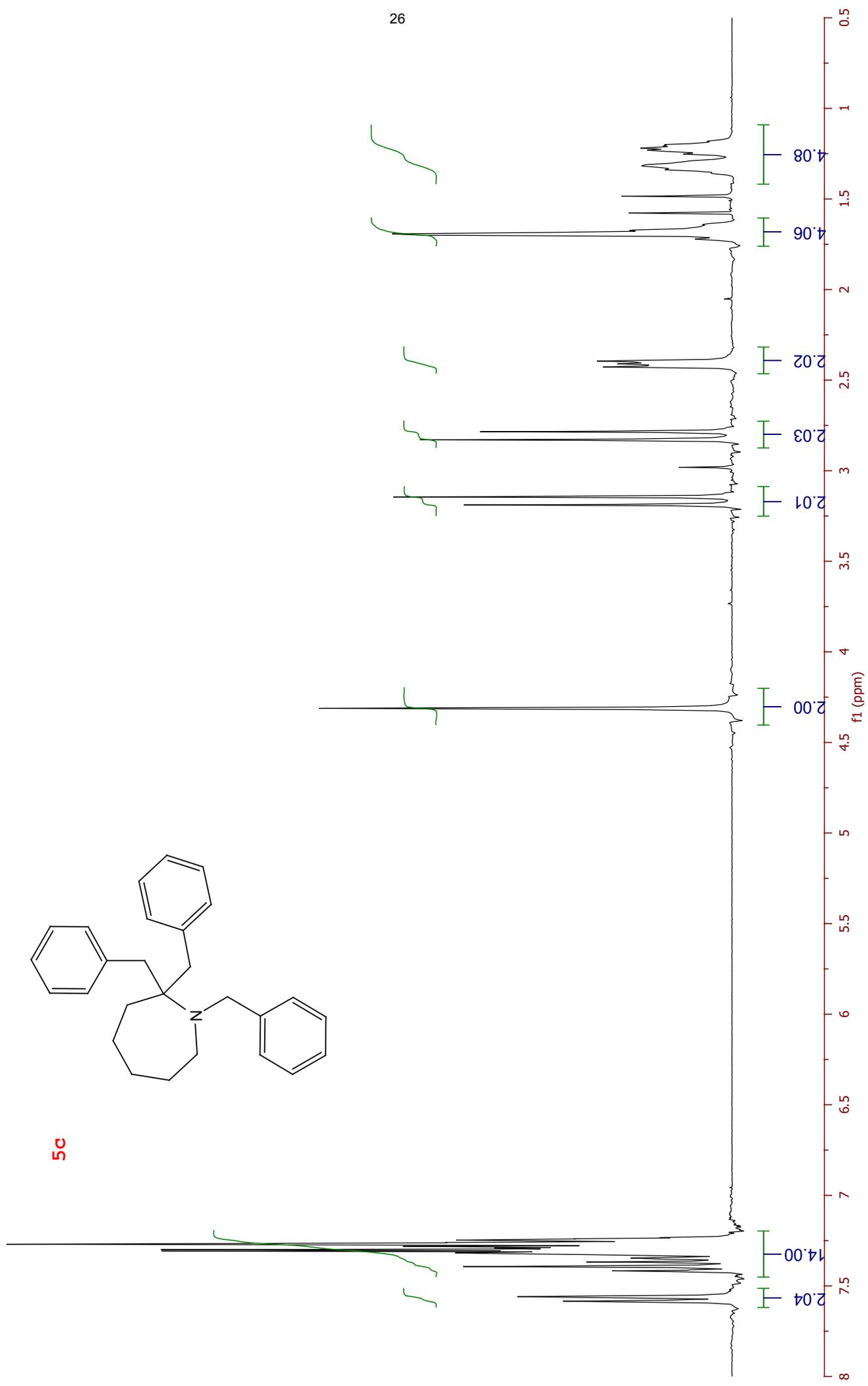


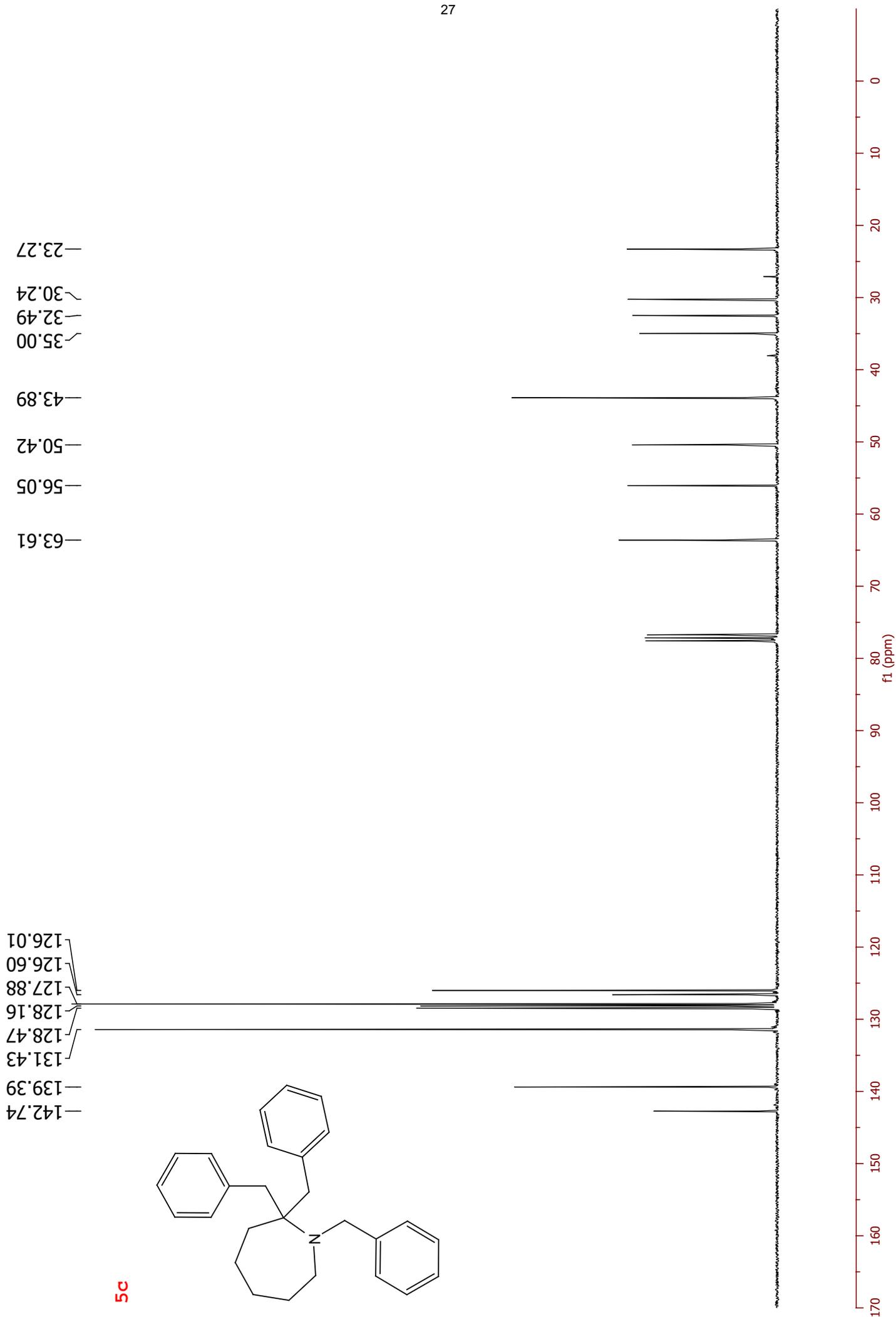


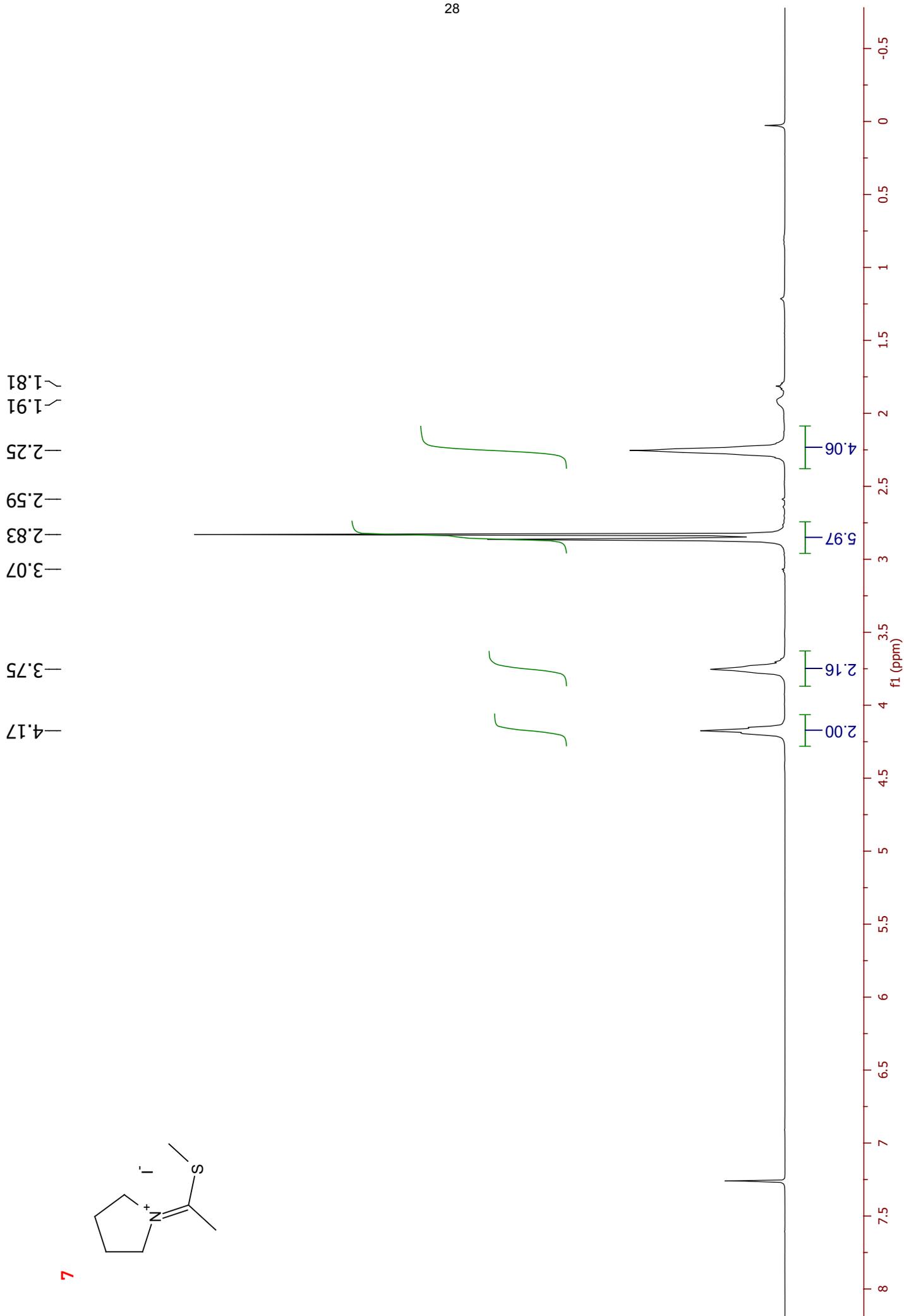
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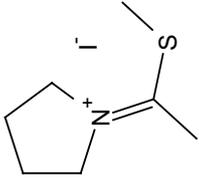
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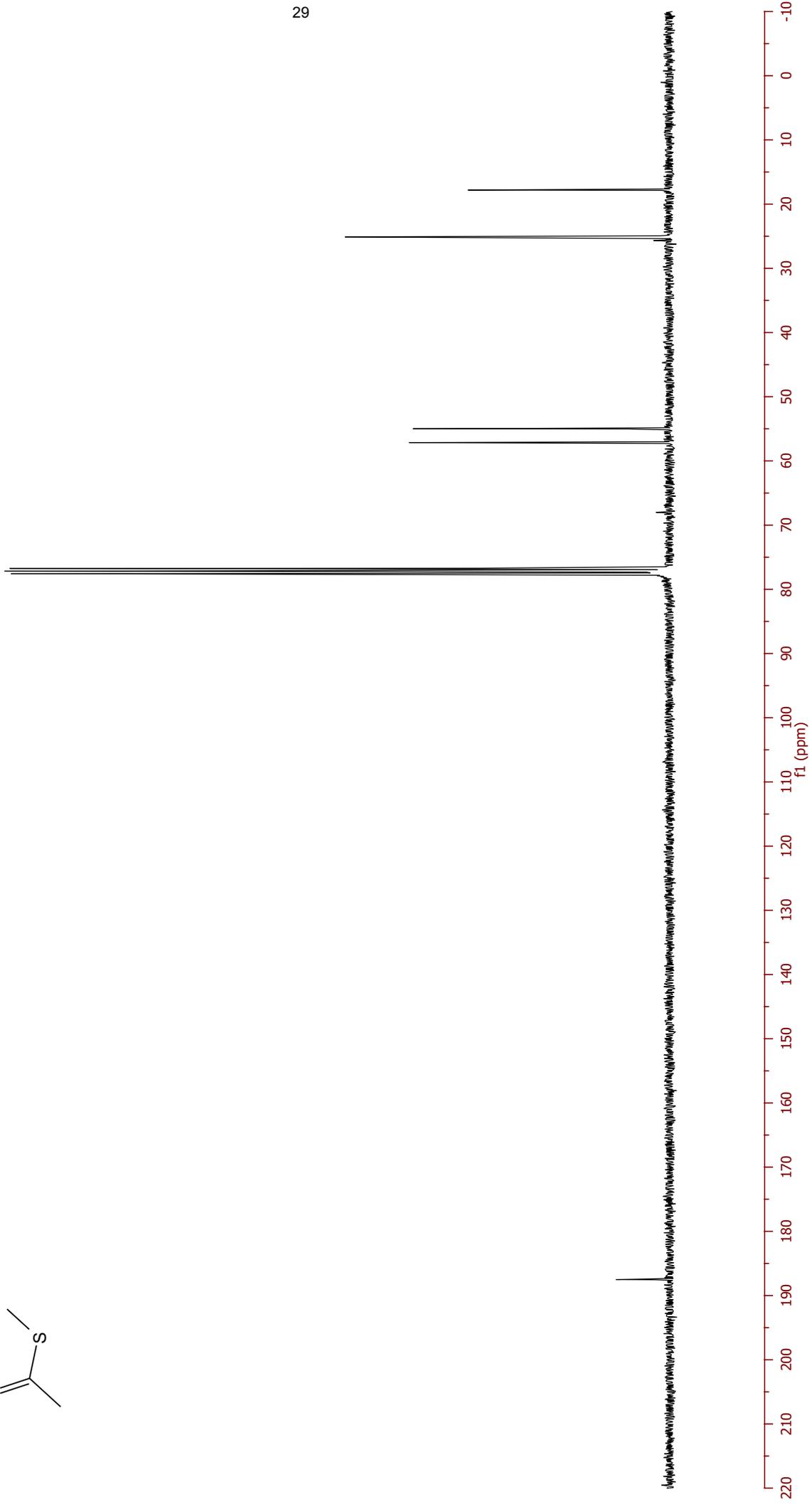


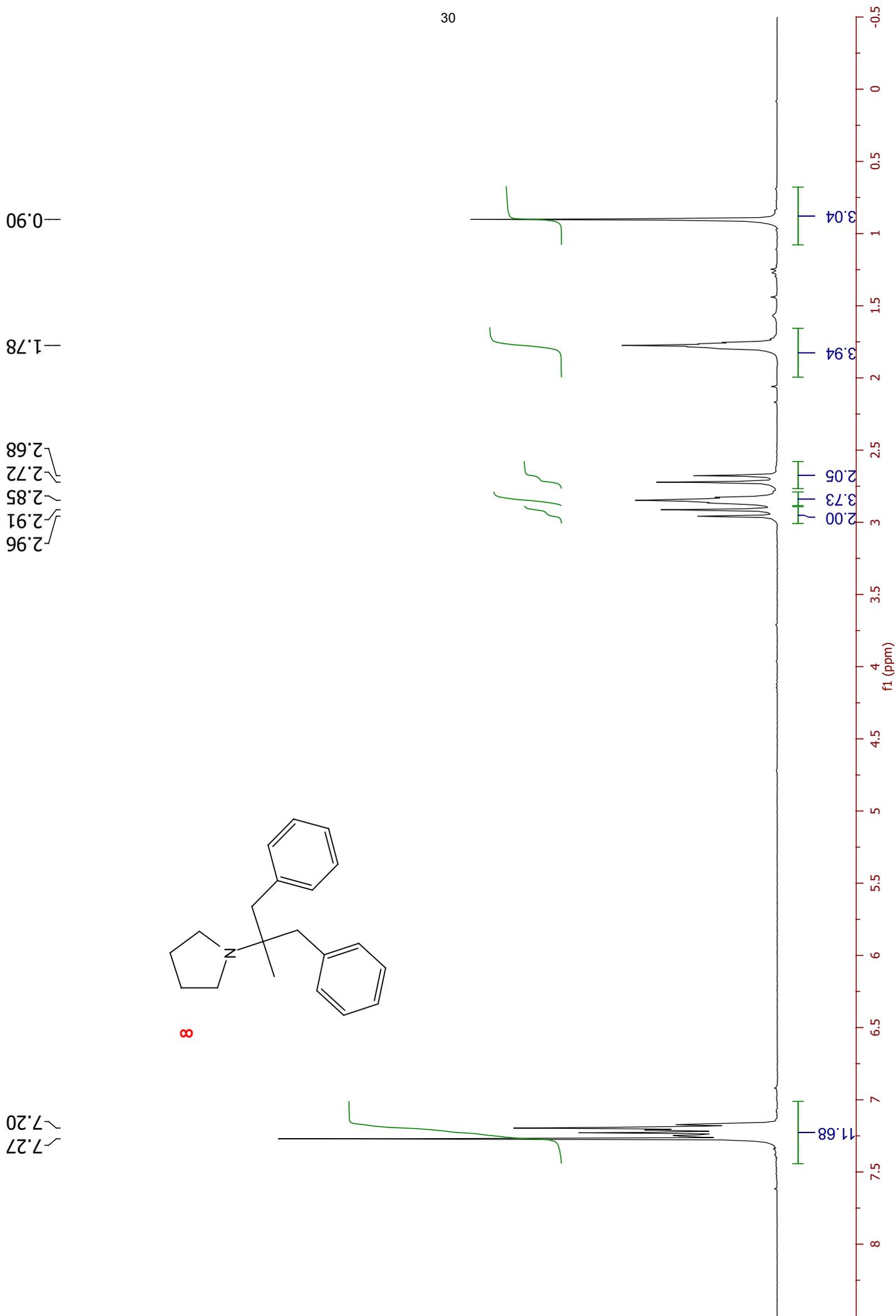
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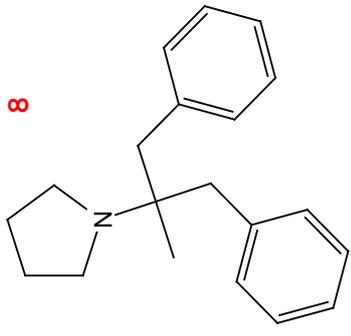


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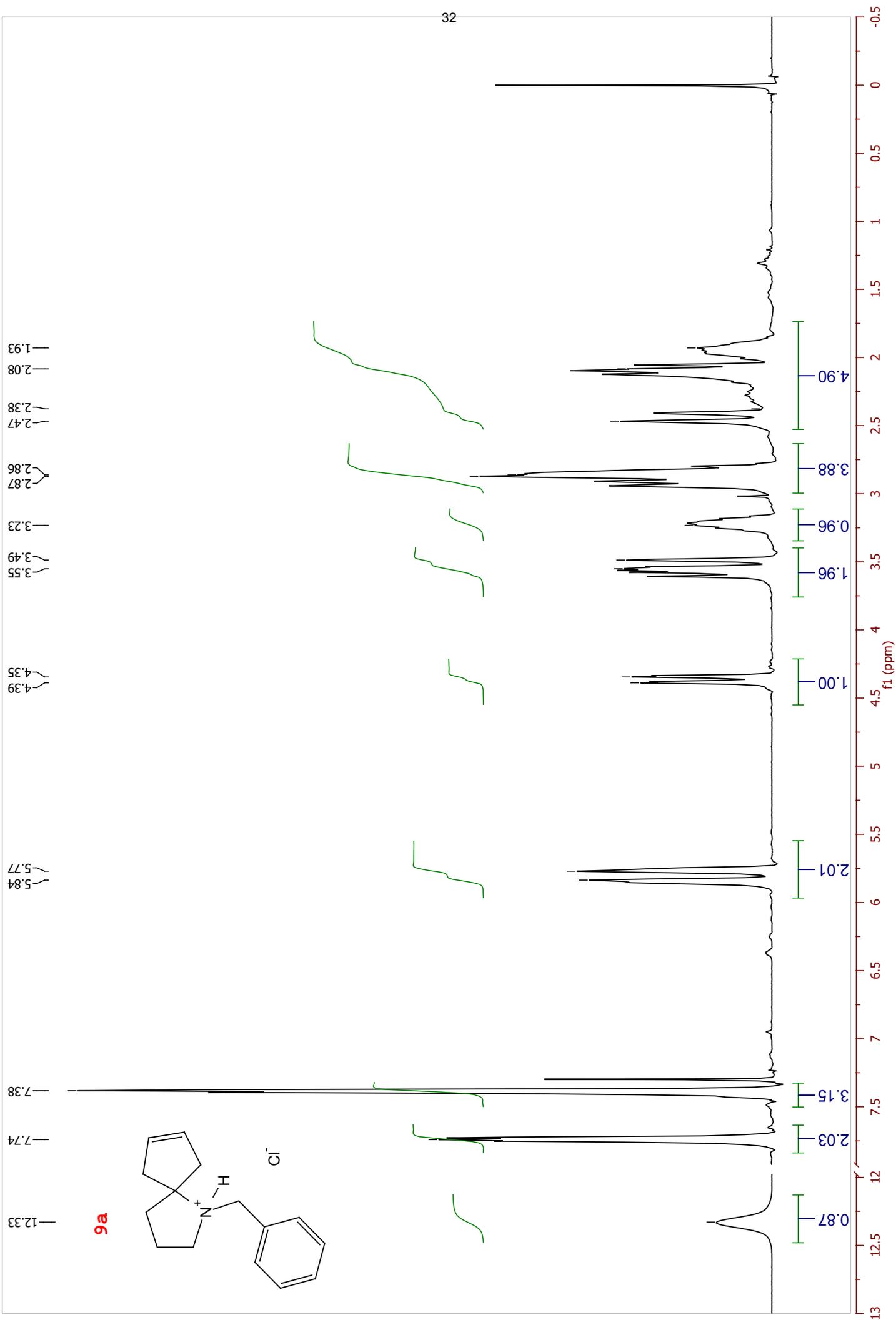


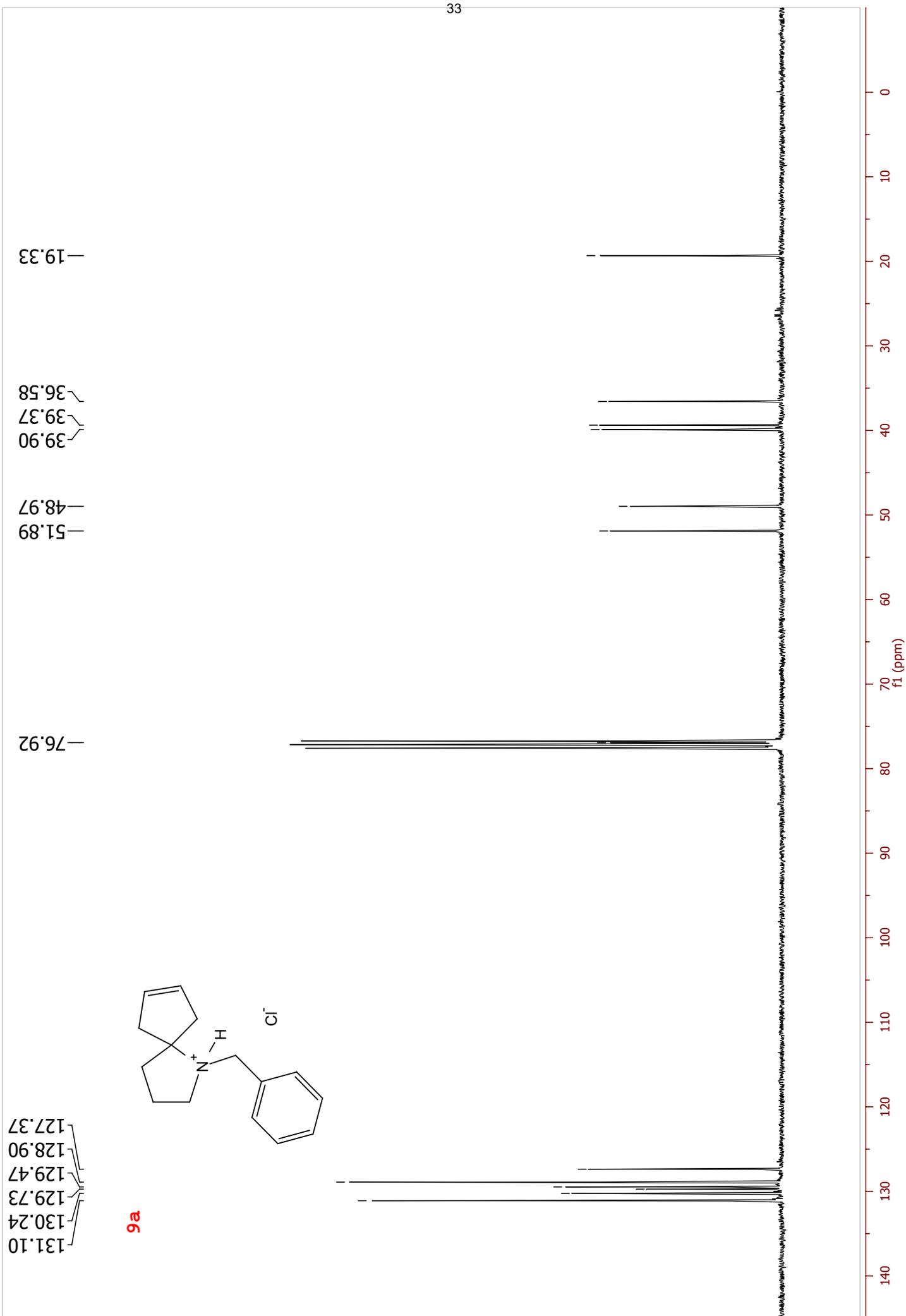


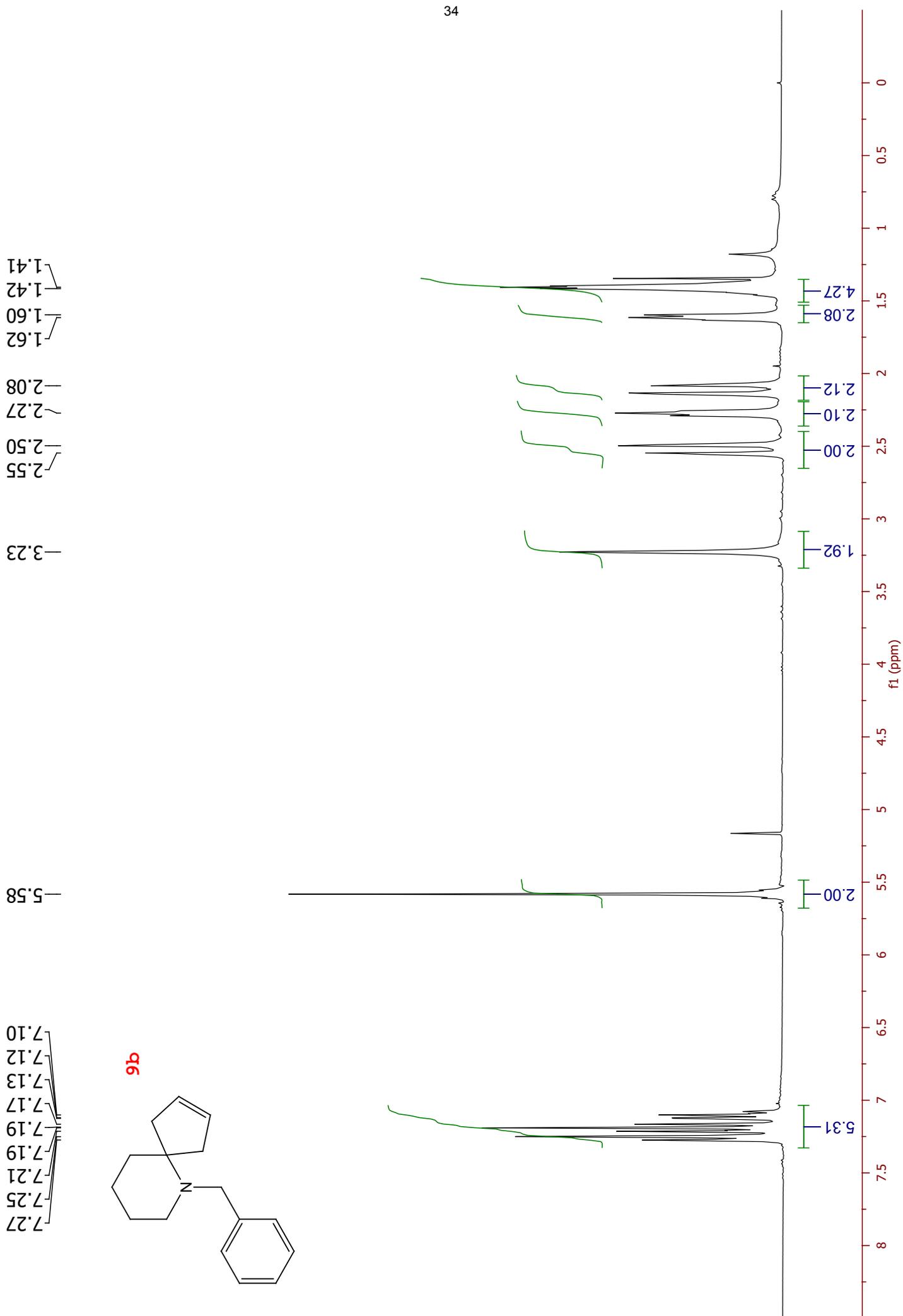


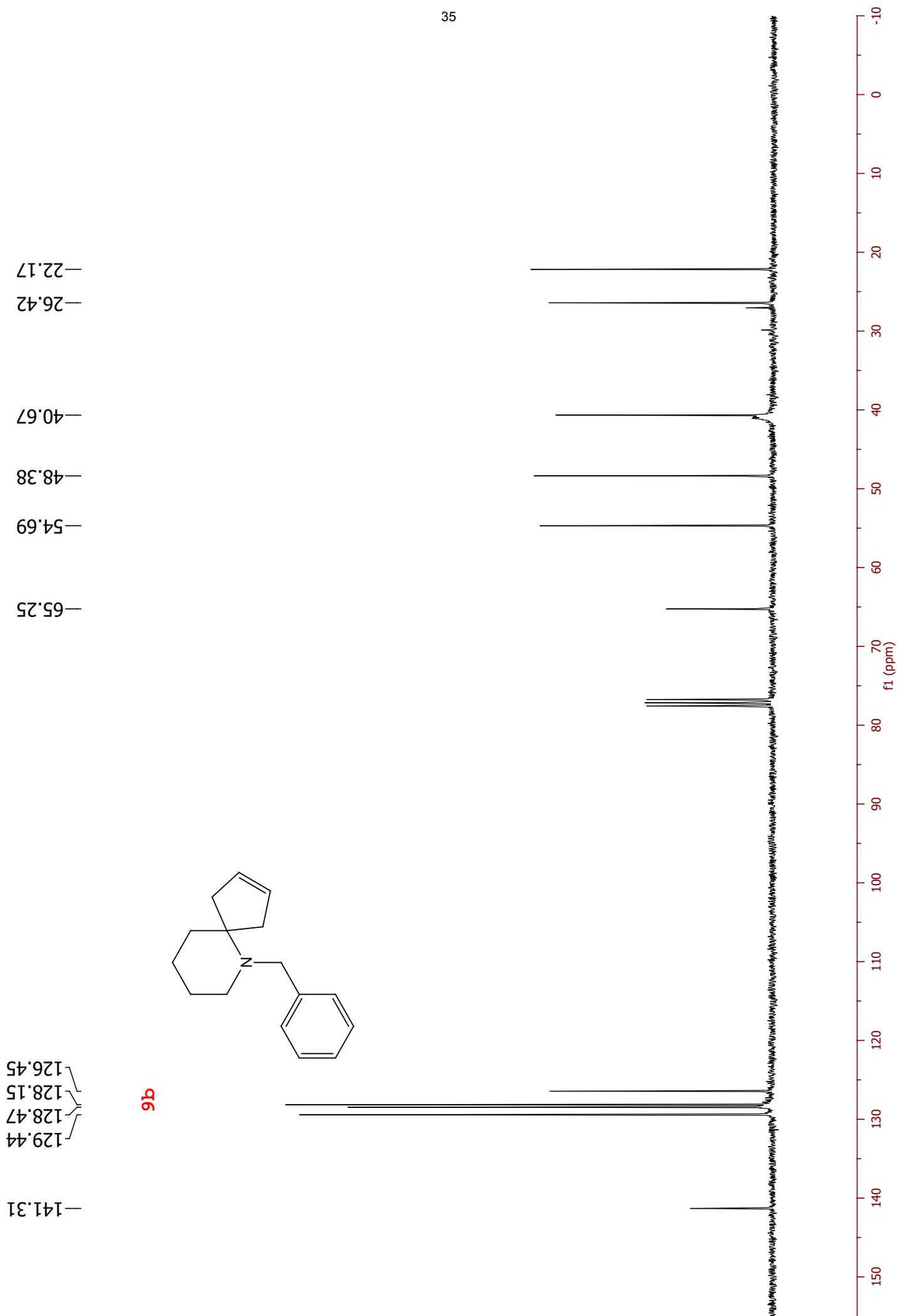
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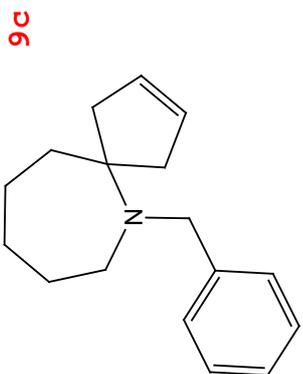
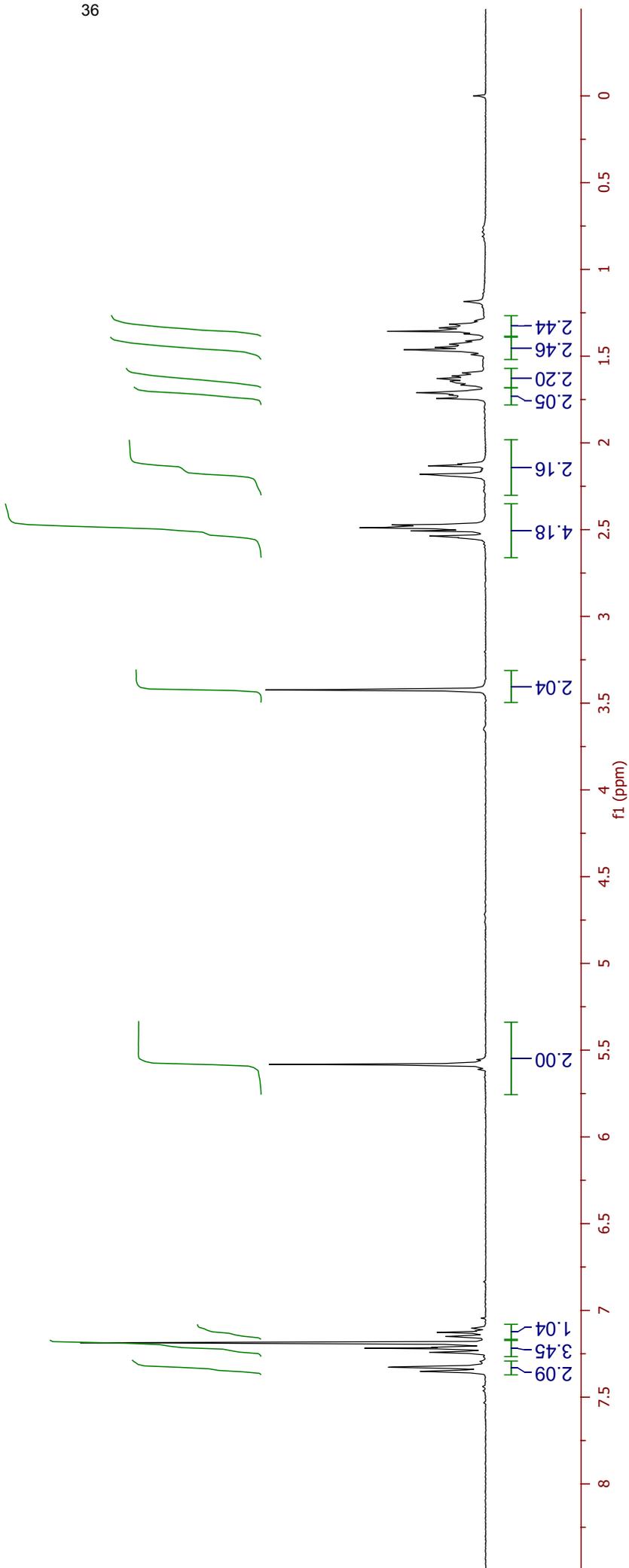




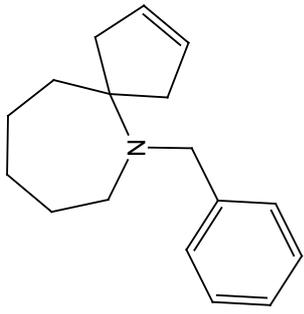








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- 7.24
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- 7.15
- 7.13
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6c

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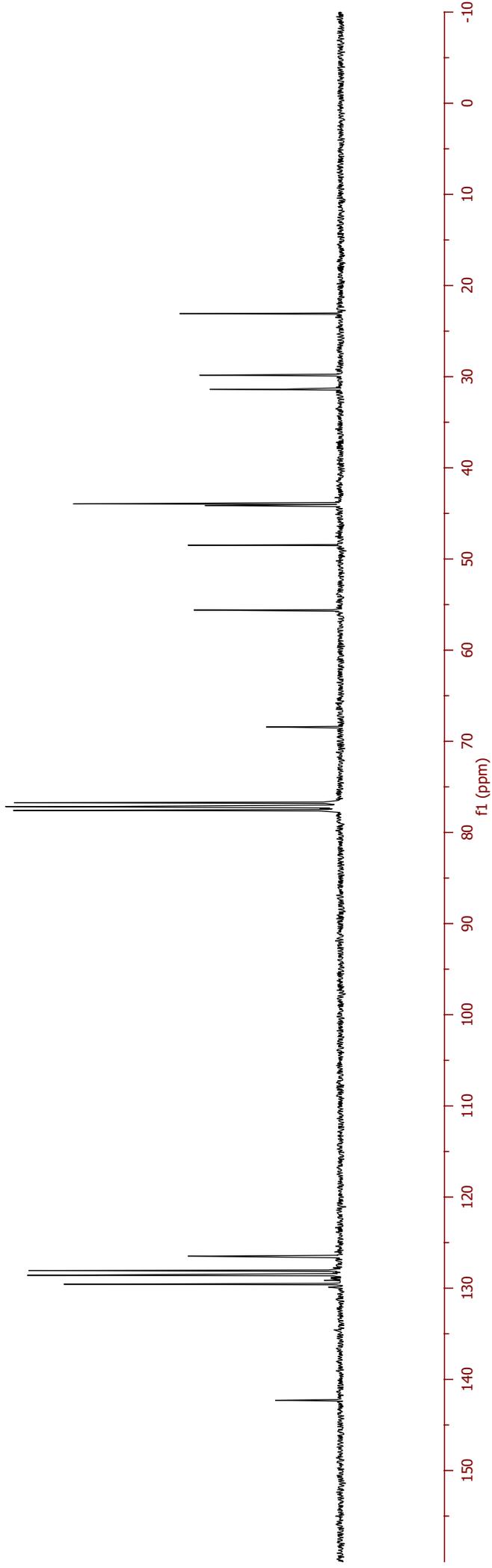
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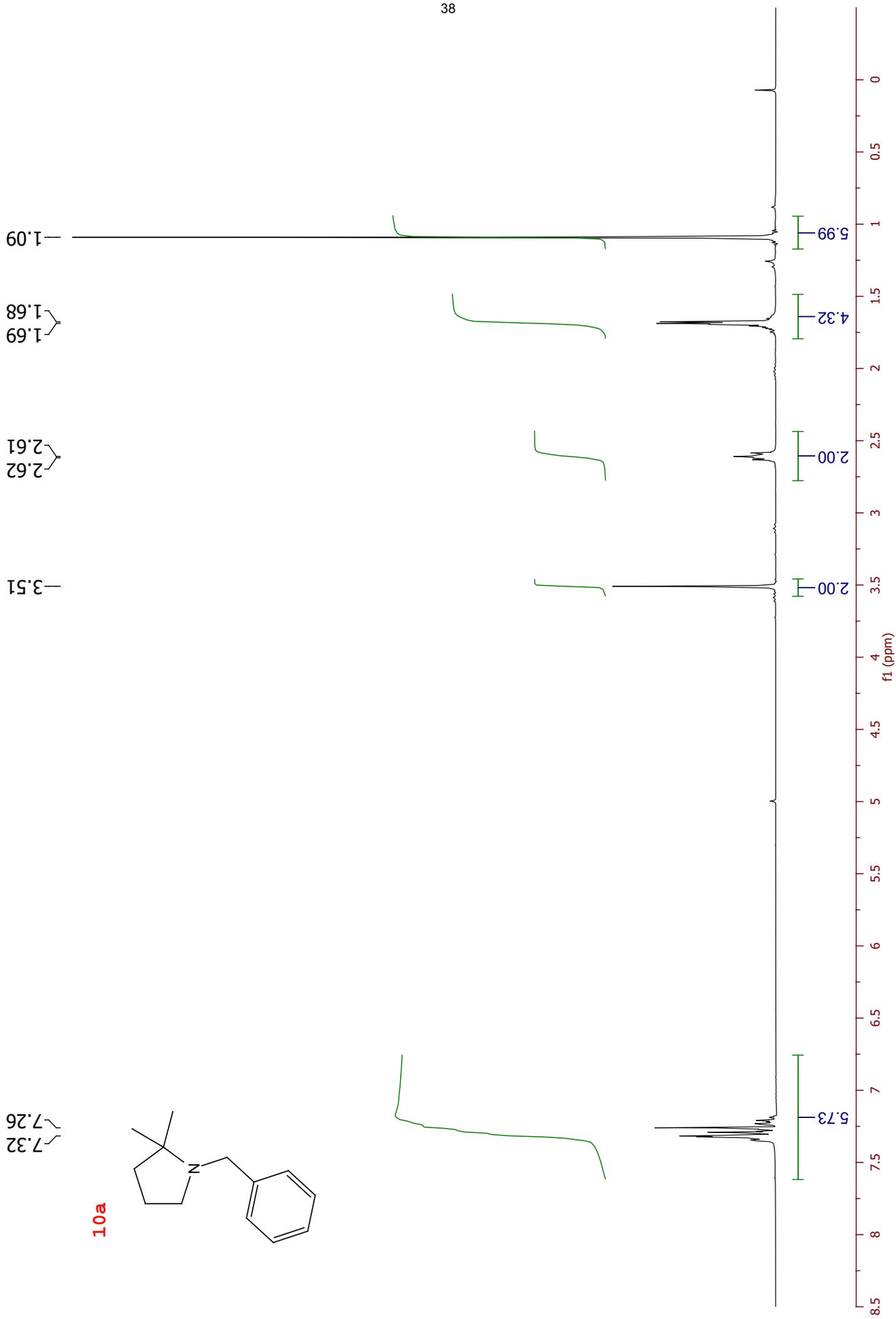
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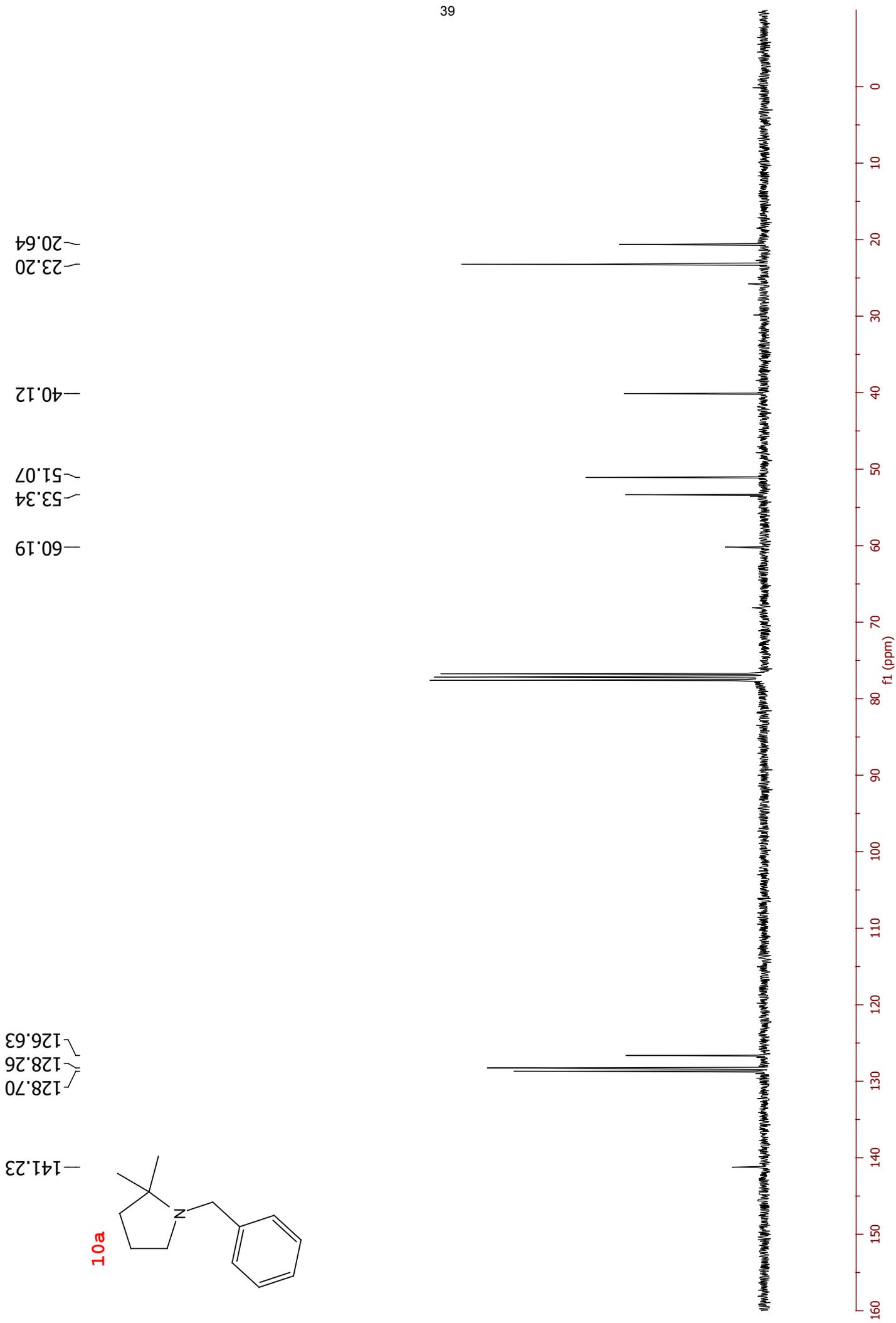
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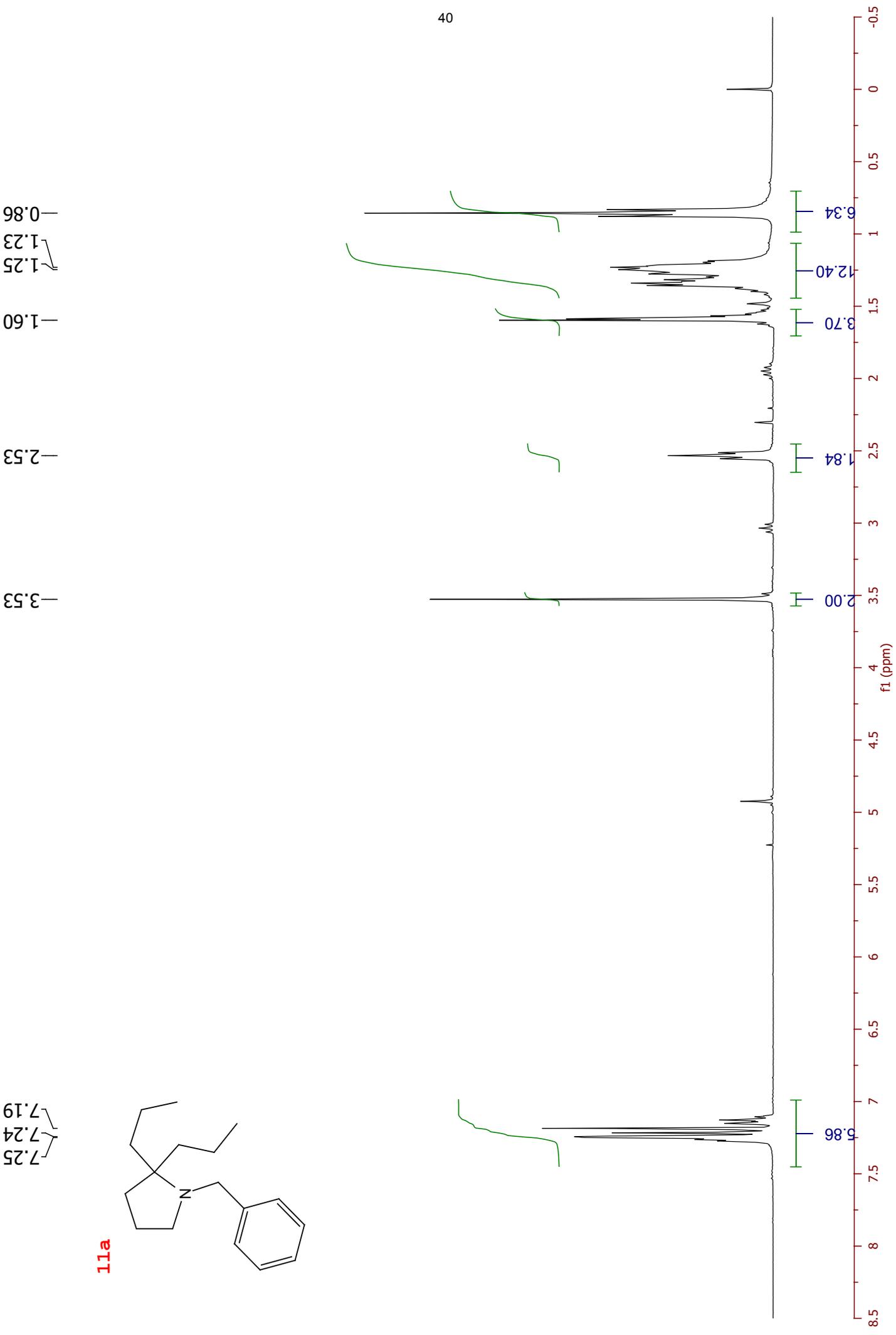
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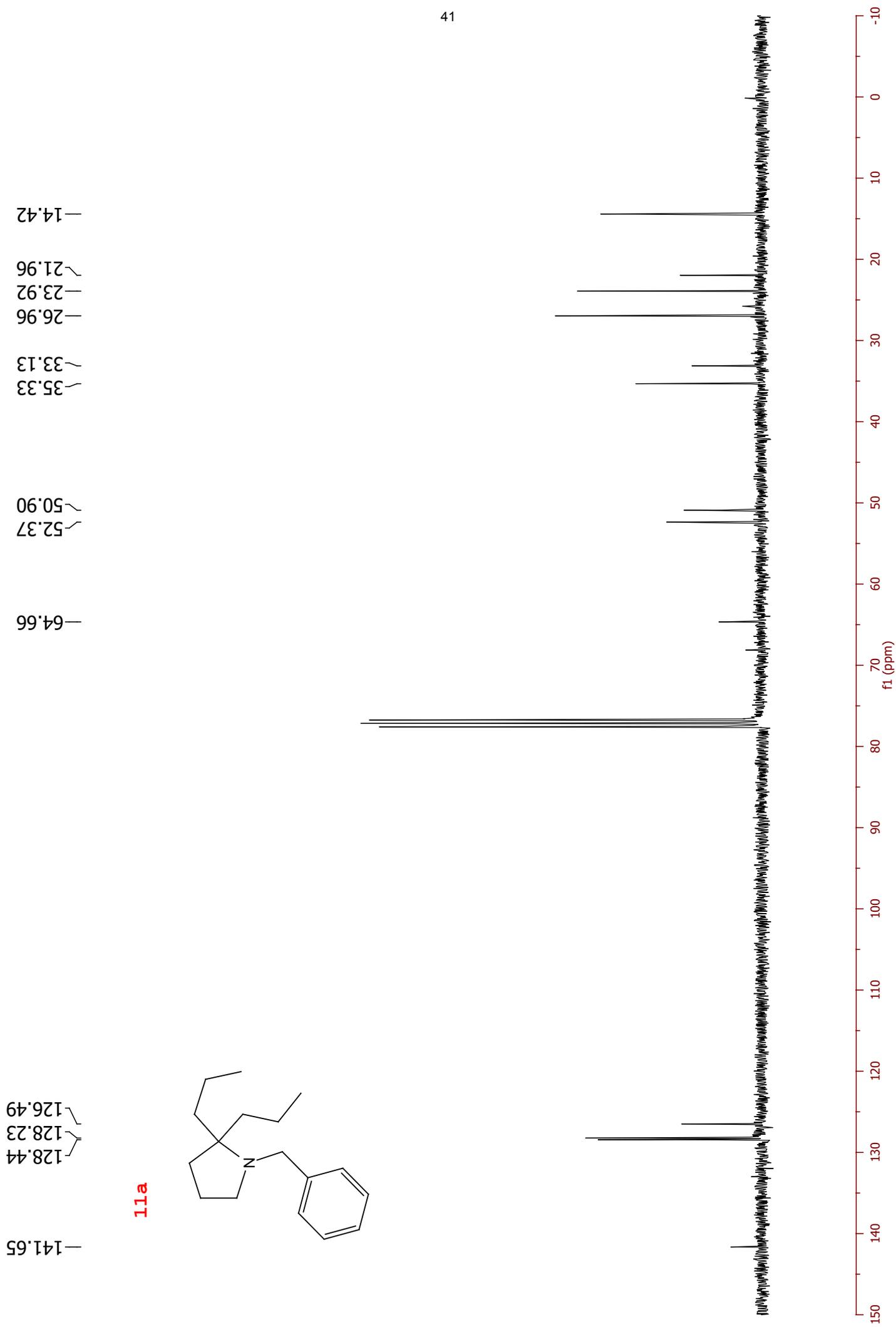


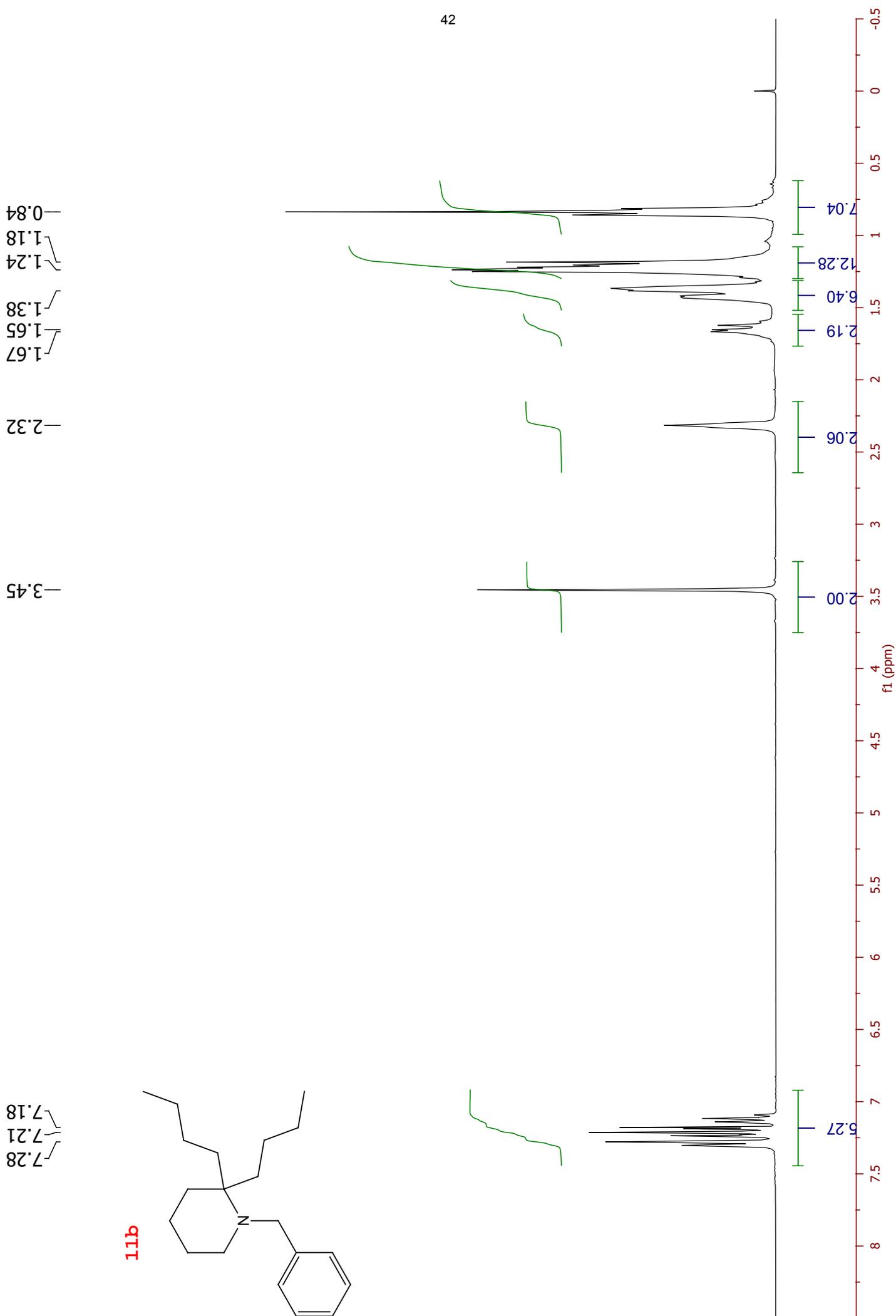






11a

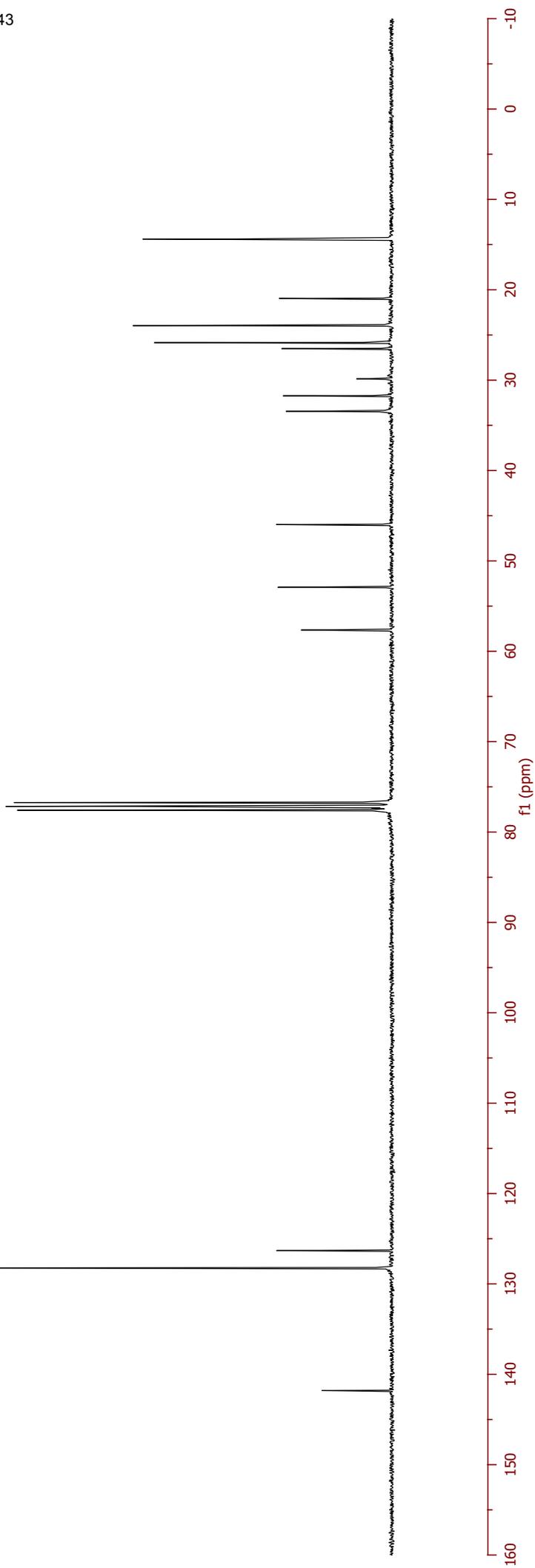
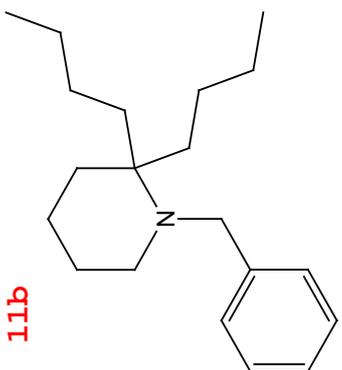


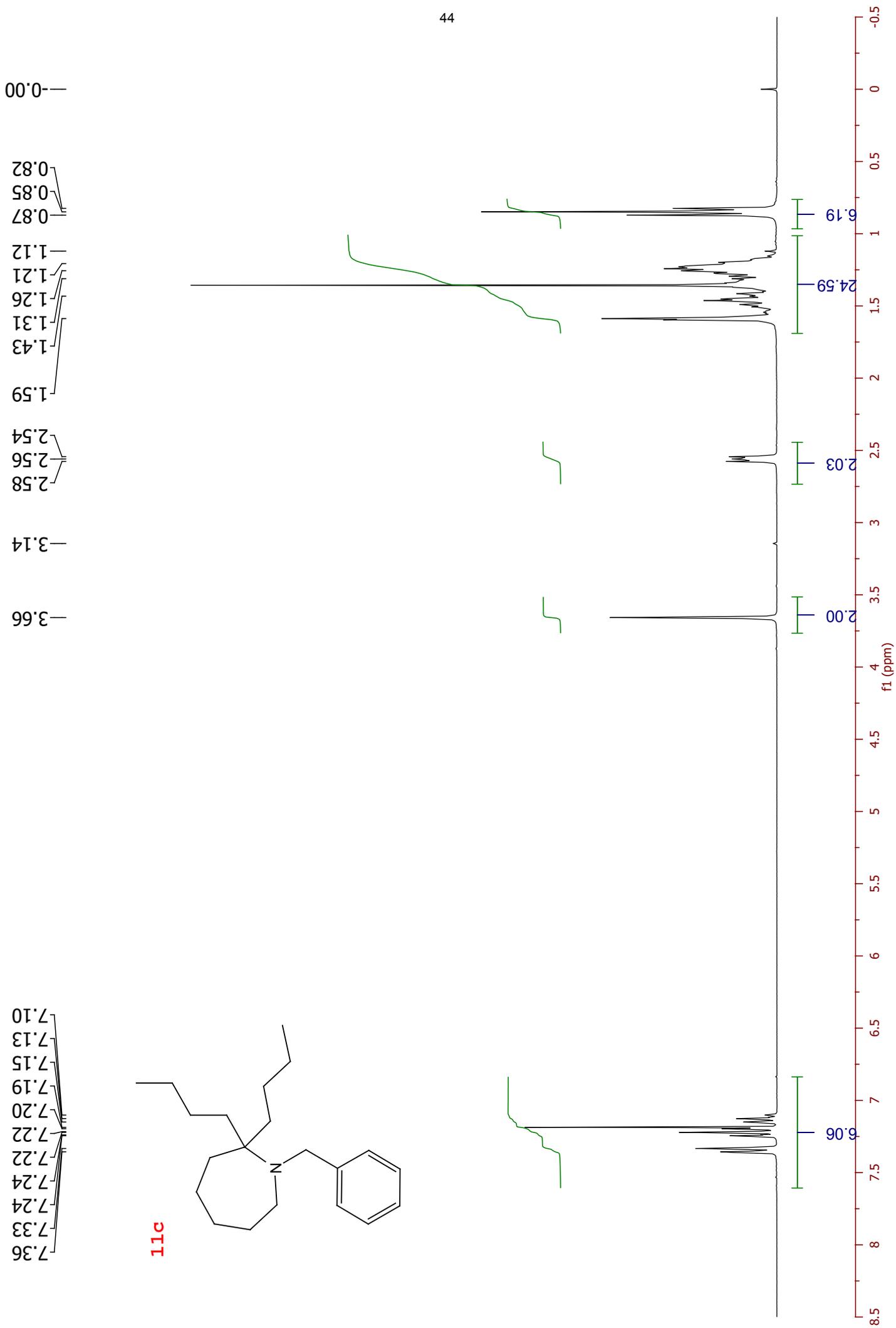


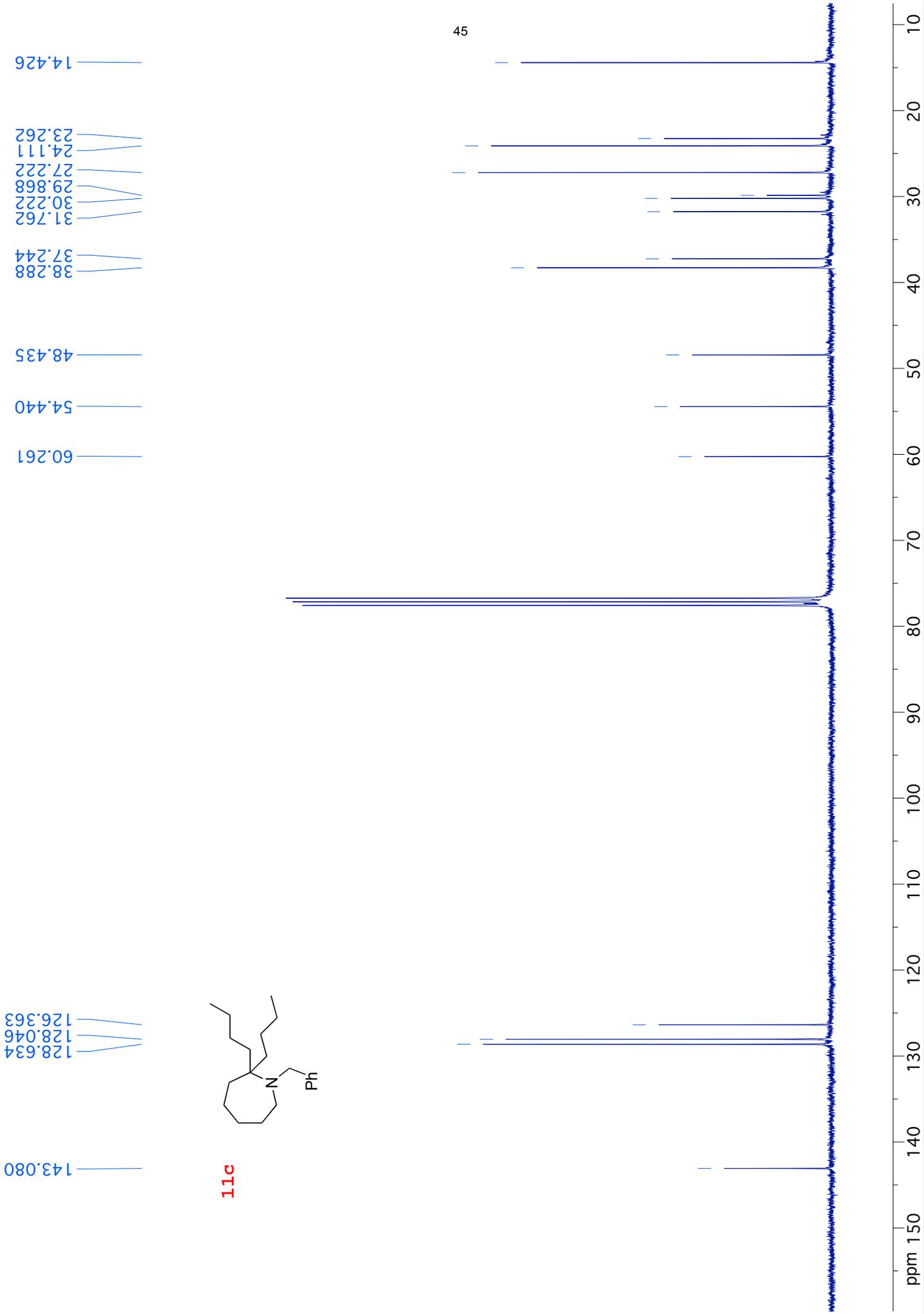
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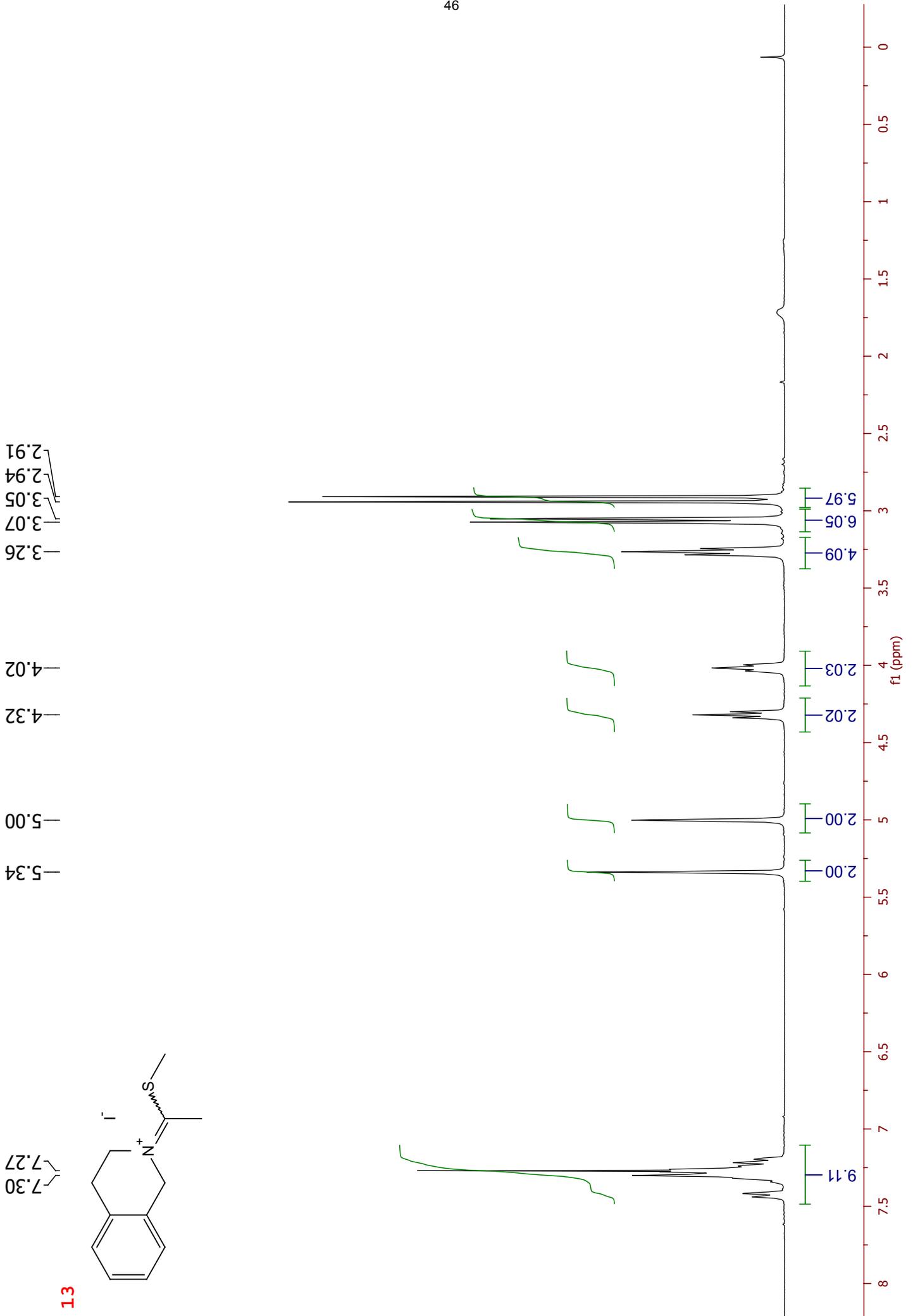
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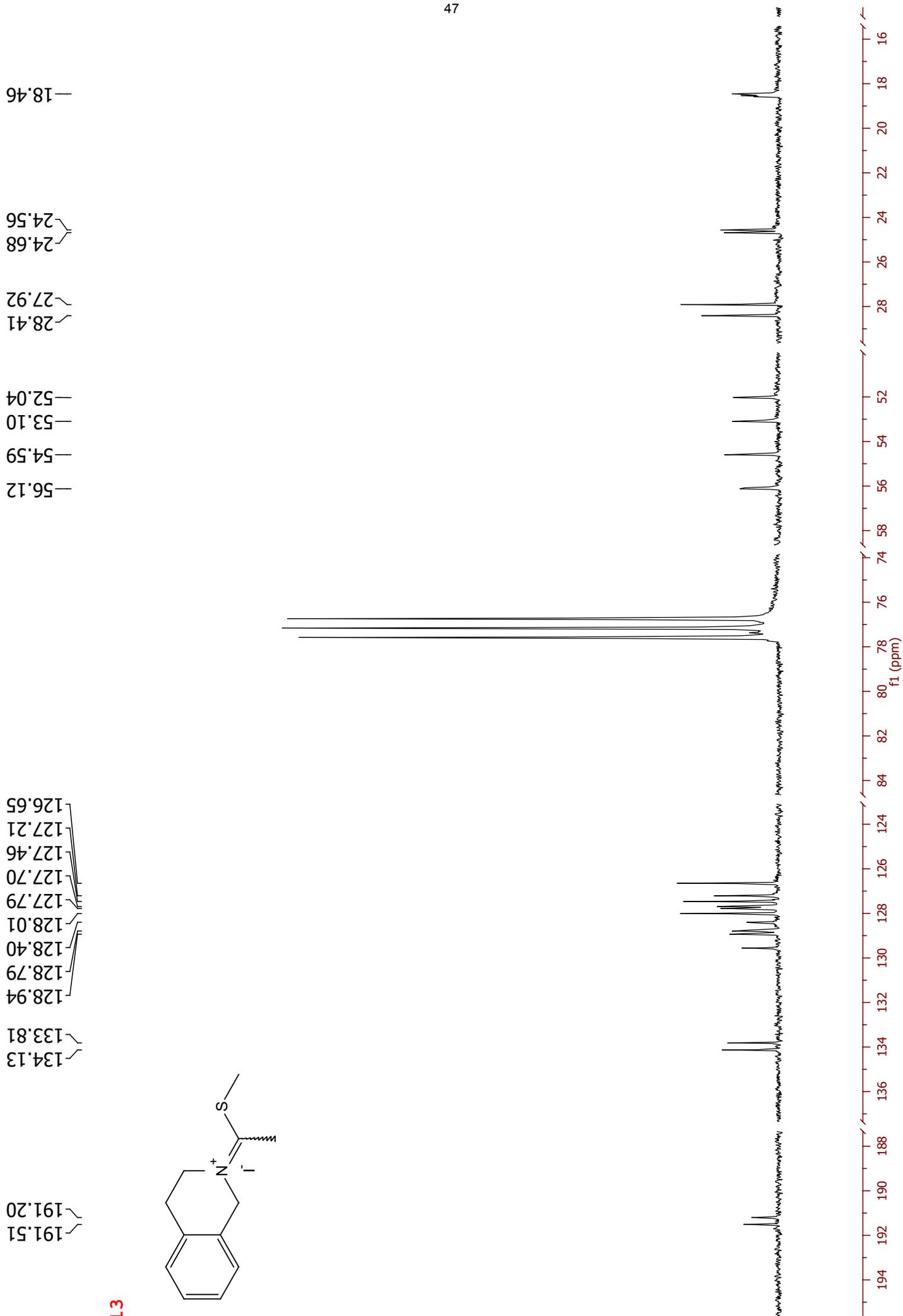
**11b**











13

