

## Supporting Information

# Highly Selective Construction of Medium-Sized Lactams by Palladium-Catalyzed Intramolecular Hydroaminocarbonylation of Aminoalkynes

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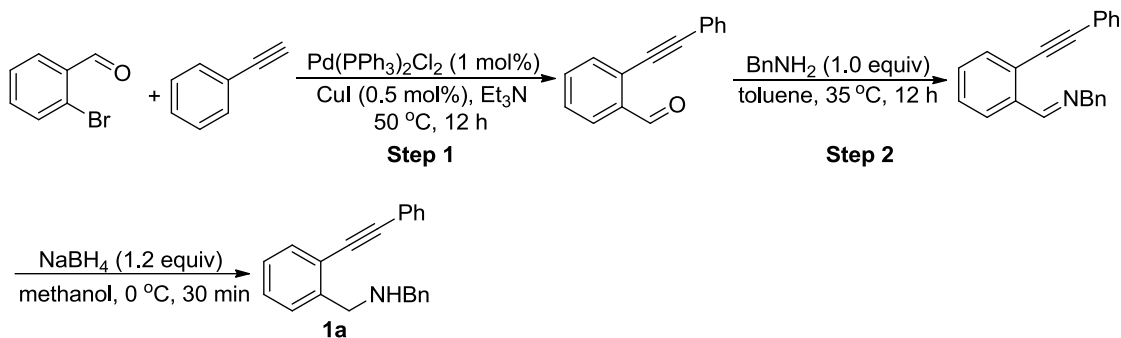
## 1. General experiment details and materials

**Experimental:** All non-aqueous reactions and manipulations were using standard Schlenk techniques. All solvents before use were dried and degassed by standard methods and stored under nitrogen atmosphere. All reactions were monitored by TLC with silica gel-coated plates. NMR spectra were recorded on BRUKER Avenice III 400 MHz spectrometers. Chemical shifts were reported in parts per million (ppm) down field from TMS with the solvent resonance as the internal standard. Coupling constants ( $J$ ) were reported in Hz and referred to apparent peak multiplications. High resolution mass spectra (HRMS) were recorded on Bruker MicroTOF-QII mass (ESI). GC analysis were performed on Agilent 7890 with OV-225 column or Hp-5 column. GC-MS analysis were performed with Agilent 7890A/5975C GC-MS system.

### General procedures for the synthesis of

#### *N*-benzyl-1-(2-(phenylethynyl)phenyl)methanamine derivatives:

##### Method A: Synthesis of substrate 1a.<sup>1</sup>



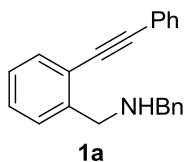
**Step 1.** To a solution of 2-bromobenzaldehyde (15.1 g, 81.7 mmol),  $\text{Pd(PPh}_3)_2\text{Cl}_2$  (1 mol%, 573.5 mg) in  $\text{Et}_3\text{N}$  (200 mL) was added phenylacetylene (10.0 g, 98.0 mmol) under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 20 minutes and then  $\text{CuI}$  (0.5 mol%, 77 mg) was added. The resulting mixture was stirred at  $50\text{ }^\circ\text{C}$  for 12 hours. After the reaction was completed, the crude mixture was cooled to room temperature and filtered through Celite. The filtrate was concentrated

under vacuum and diluted with water (50 mL). The resulting mixture was extracted by DCM (50 mL x 3) and the combined organic layer was washed with brine (50 mL x 2), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (50/1-20/1) to afford 2-(phenylethynyl)benzaldehyde (13.5 g, 80% yield).

**Step 2.** The mixture of 2-(phenylethynyl)benzaldehyde (8.0 g, 38.8 mmol), benzylamine (4.2 g, 38.8 mmol), toluene (50 mL) was added to a 250 mL Schlenk flask under nitrogen atmosphere and stirred at 35 °C for 12 hours. Then the solvent was removed under reduced pressure and the resulting residue was dissolved in methanol (50 mL) in a 250 mL flask. NaBH<sub>4</sub> (1.8 g, 46.6 mmol) was added to the reaction mixture in portions at 0 °C and the reaction mixture was stirred for 30 minutes at this temperature. Then the reaction was quenched by aqueous saturated ammonium chloride solution (20 mL). Methanol was removed under vacuum and the residue was extracted by ethyl acetate (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford *N*-benzyl-1-(2-(phenylethynyl)phenyl)methanamine **1a** (8.5 g, 74% yield).

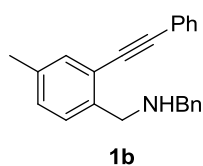
Other compounds including **1b-1j** and **1m-1x** were prepared by method **A**.

***N*-Benzyl-1-(2-(phenylethynyl)phenyl)methanamine (1a):** The title compound was



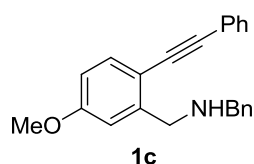
prepared according to the general procedure (Method **A**) and purified by column chromatography to give the yellow oil (8.5 g, 74% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.46-7.48 (m, 2H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.21-7.35 (m, 10H), 4.03 (s, 2H), 3.82 (s, 2H), 1.92 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 142.2, 140.4, 132.5, 131.7, 128.9, 128.6, 128.5, 128.3, 127.0, 127.0, 123.3, 122.5, 93.8, 87.6, 53.4, 52.0; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>20</sub>N [M+H]: 298.1590, found: 298.1591.

**N-Benzyl-1-(4-methyl-2-(phenylethynyl)phenyl)methanamine (1b):** The title



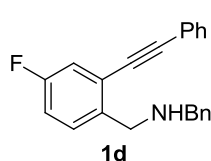
compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (9.0 g, 80% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.45 (dd, *J*<sub>1</sub> = 2.0 Hz, *J*<sub>2</sub> = 5.2 Hz, 2H), 7.20-7.36 (m, 10H), 7.11 (d, *J* = 7.6 Hz, 1H), 3.98 (s, 2H), 3.80 (s, 2H), 2.31 (s, 3H), 1.88 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 140.5, 139.2, 136.6, 132.9, 131.6, 129.4, 128.9, 128.4, 128.3, 128.3, 128.2, 126.9, 123.3, 122.3, 93.3, 87.8, 53.2, 51.6, 20.9; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>N [M+H]: 312.1747, found: 312.1749.

**N-Benzyl-1-(5-methoxy-2-(phenylethynyl)phenyl)methanamine (1c):** The title



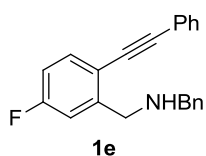
compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (5.5 g, 83% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.42-7.46 (m, 3H), 7.21-7.34 (m, 8H), 6.98 (d, *J* = 2.8 Hz, 1H), 6.76 (dd, *J*<sub>1</sub> = 2.8 Hz, *J*<sub>2</sub> = 8.4 Hz, 1H), 3.99 (s, 2H), 3.81 (s, 2H), 3.77 (s, 3H), 1.89 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.8, 144.1, 140.3, 133.7, 131.4, 128.4, 128.4, 128.3, 128.2, 128.0, 126.9, 123.5, 114.3, 112.6, 92.4, 87.6, 55.3, 53.3, 51.9; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>NO [M+H]: 328.1696, found: 328.1696.

**N-Benzyl-1-(4-fluoro-2-(phenylethynyl)phenyl)methanamine (1d):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (9.1 g, 81% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44-7.46 (m, 2H), 7.20-7.37 (m, 10H), 6.96-7.01 (m, 1H), 3.97 (s, 2H), 3.80 (s, 2H), 1.83 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 162.6 (d, *J*<sub>C-F</sub> = 244.1 Hz), 140.3, 138.2 (d, *J*<sub>C-F</sub> = 3.1 Hz), 131.7, 130.5 (d, *J*<sub>C-F</sub> = 8.4 Hz), 128.8, 128.5, 128.3, 127.0, 124.1 (d, *J*<sub>C-F</sub> = 9.6 Hz), 122.7, 118.9 (d, *J*<sub>C-F</sub> = 22.7 Hz), 115.8 (d, *J*<sub>C-F</sub> = 20.8 Hz), 94.5, 86.5 (d, *J*<sub>C-F</sub> = 3.2 Hz), 53.3, 51.1; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -115.6; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>FN [M+H]: 316.1496, found: 316.1501.

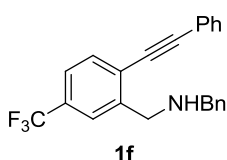
**N-Benzyl-1-(5-fluoro-2-(phenylethynyl)phenyl)methanamine (1e):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (5.2 g, 78% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

7.43-7.46 (m, 3H), 7.17-7.34 (m, 9H), 6.88-6.92 (m, 1H), 3.98 (s, 2H), 3.80 (s, 2H), 1.83 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 163.9 (d, *J*<sub>C-F</sub> = 248.4 Hz), 145.2 (d, *J*<sub>C-F</sub> = 7.3 Hz), 140.2, 134.1 (d, *J*<sub>C-F</sub> = 8.4 Hz), 131.5, 128.5 (d, *J*<sub>C-F</sub> = 3.1 Hz), 128.2, 127.1, 123.1, 118.3 (d, *J*<sub>C-F</sub> = 3.2 Hz), 115.7 (d, *J*<sub>C-F</sub> = 22.2 Hz), 114.2 (d, *J*<sub>C-F</sub> = 22.0 Hz), 93.5, 86.6, 53.3, 51.4; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -110.4; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>FN [M+H]: 316.1496, found: 316.1494.

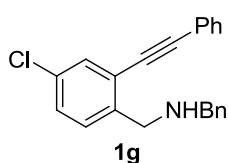
**N-Benzyl-1-(2-(phenylethynyl)-5-(trifluoromethyl)phenyl)methanamine (1f):** The



title compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (3.4 g, 77% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

7.74 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.48-7.51 (m, 3H), 7.25-7.38 (m, 8H), 4.08 (s, 2H), 3.86 (s, 2H), 1.88 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 143.1, 140.1, 132.7, 131.8, 130.4 (q, *J*<sub>C-F</sub> = 32.3 Hz), 129.1, 128.6, 128.4, 127.2, 126.2, 125.5 (q, *J*<sub>C-F</sub> = 3.7 Hz), 123.8 (q, *J*<sub>C-F</sub> = 3.8 Hz), 122.6, 96.1, 86.3, 53.6, 51.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -62.6; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>19</sub>F<sub>3</sub>N [M+H]: 366.1464, found: 366.1456.

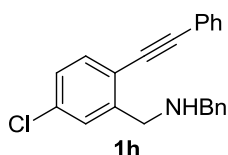
**N-Benzyl-1-(4-chloro-2-(phenylethynyl)phenyl)methanamine (1g):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (6.1 g, 80% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

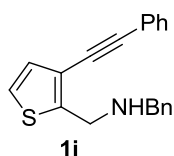
7.44-7.50 (m, 3H), 7.19-7.35 (m, 10H), 3.97 (s, 2H), 3.79 (s, 2H), 1.82 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 140.7, 140.2, 132.5, 131.9, 131.7, 130.1, 128.8, 128.6, 128.5, 128.3, 127.1, 124.1, 122.7, 94.8, 86.3, 53.3, 51.2; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>ClN [M+H]: 332.1201, found: 332.1190.

**N-Benzyl-1-(5-chloro-2-(phenylethynyl)phenyl)methanamine (1h):** The title compound was prepared according to the general procedure (Method A) and purified



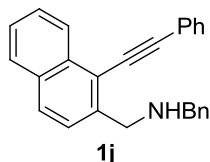
by column chromatography to give the yellow oil (5.5 g, 74% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.40-7.44 (m, 4H), 7.26-7.34 (m, 7H), 7.17-7.24 (m, 2H), 3.97 (s, 2H), 3.80 (s, 2H), 1.83 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 144.1, 140.1, 134.5, 133.4, 131.6, 128.8, 128.6, 128.5, 128.5, 128.3, 127.2, 127.1, 122.9, 120.9, 94.7, 86.6, 53.4, 51.4; **HRMS** (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>ClN [M+H]: 332.1201, found: 332.1204.

**N-Benzyl-1-(3-(phenylethynyl)thiophen-2-yl)methanamine (1i):** The title compound



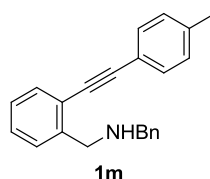
was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (7.0 g, 78% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.42-7.45 (m, 2H), 7.27-7.36 (m, 7H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 5.2 Hz, 1H), 7.07 (d, *J* = 4.8 Hz, 1H), 4.13 (s, 2H), 3.85 (s, 2H), 1.84 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 147.8, 140.1, 131.5, 129.7, 128.5, 128.4, 128.3, 128.3, 127.1, 123.6, 123.3, 119.7, 92.3, 83.8, 52.9, 46.6; **HRMS** (ESI) calcd. for C<sub>20</sub>H<sub>18</sub>NS [M+H]: 304.1154, found: 304.1158.

**N-benzyl-1-(1-(phenylethynyl)naphthalen-2-yl)methanamine (1j):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (4.0 g, 71% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.47 (d, *J* = 8.0 Hz, 1H), 7.81-7.85 (m, 2H), 7.57-7.60 (m, 4H), 7.48-7.52 (m, 1H), 7.35-7.39 (m, 5H), 7.27-7.32 (m, 2H), 7.21-7.24 (m, 1H), 4.25 (s, 2H), 3.86 (s, 2H), 1.91 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 141.3, 140.5, 133.7, 132.5, 131.7, 128.7, 128.6, 128.6, 128.5, 128.4, 128.3, 127.1, 127.0, 127.0, 126.4, 126.2, 123.5, 119.5, 99.2, 85.7, 53.4, 52.3; **HRMS** (ESI) calcd. for C<sub>26</sub>H<sub>22</sub>N [M+H]: 348.1747, found: 348.1746.

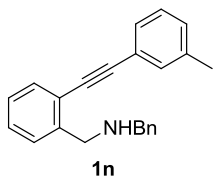
**N-Benzyl-1-(2-(p-tolylethynyl)phenyl)methanamine (1m):** The title compound was



prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (4.5 g, 74% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.21-7.40 (m, 10H), 7.15 (d, *J* = 7.6 Hz, 2H), 4.02 (s, 2H), 3.81 (s, 2H), 2.35 (s, 3H),

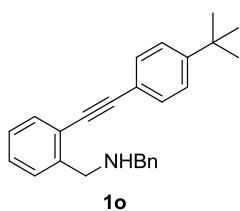
1.92 (br, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  142.1, 140.5, 138.6, 132.4, 131.5, 129.2, 129.0, 128.9, 128.5, 128.4, 128.3, 128.2, 127.0, 127.0, 122.7, 120.2, 94.0, 87.0, 53.3, 52.0, 21.6; **HRMS** (ESI) calcd. for  $\text{C}_{23}\text{H}_{22}\text{N}$   $[\text{M}+\text{H}]$ : 312.1747, found: 312.1741.

***N*-Benzyl-1-(2-(*m*-tolylethynyl)phenyl)methanamine (1n):** The title compound was



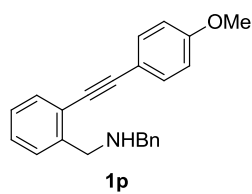
prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (4.8 g, 71% yield);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (dd,  $J_1 = 0.8$  Hz,  $J_2 = 7.6$  Hz, 1H), 7.41 (d,  $J = 7.2$  Hz, 1H), 7.21-7.36 (m, 10H), 7.15 (d,  $J = 7.6$  Hz, 1H), 4.03 (s, 2H), 3.82 (s, 2H), 2.34 (s, 3H), 1.98 (br, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  142.2, 140.4, 138.2, 132.5, 132.2, 129.4, 128.9, 128.8, 128.5, 128.4, 128.4, 127.1, 127.0, 123.1, 122.6, 94.0, 87.2, 53.3, 52.0, 21.4; **HRMS** (ESI) calcd. for  $\text{C}_{23}\text{H}_{22}\text{N}$   $[\text{M}+\text{H}]$ : 312.1747, found: 312.1743.

***N*-Benzyl-1-(2-((4-(*tert*-butyl)phenyl)ethynyl)phenyl)methanamine (1o):** The title



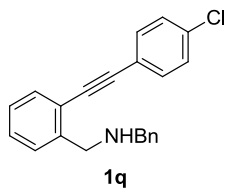
compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (4.5 g, 73% yield);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 (d,  $J = 7.6$  Hz, 1H), 7.20-7.43 (m, 12H), 4.02 (s, 2H), 3.81 (s, 2H), 1.94 (br, 1H), 1.31 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.7, 142.1, 140.4, 132.4, 131.4, 128.9, 128.5, 128.4, 128.3, 127.0, 125.5, 122.7, 120.2, 94.0, 87.0, 53.3, 52.0, 34.9, 31.3; **HRMS** (ESI) calcd. for  $\text{C}_{26}\text{H}_{28}\text{N}$   $[\text{M}+\text{H}]$ : 354.2216, found: 354.2218.

***N*-Benzyl-1-(2-((4-methoxyphenyl)ethynyl)phenyl)methanamine (1p):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (2.5 g, 60% yield);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (dd,  $J_1 = 0.8$  Hz,  $J_2 = 7.2$  Hz, 1H), 7.22-7.41 (m, 10H), 6.88 (d,  $J = 8.8$  Hz, 2H), 4.02 (s, 2H), 3.82 (s, 5H), 1.96 (br, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.8, 142.0, 140.5, 133.1, 132.3, 128.9, 128.5, 128.4, 128.3, 127.0, 127.0, 122.9, 115.4, 114.1, 93.8, 86.3, 55.4, 53.3, 52.1; **HRMS** (ESI) calcd. for  $\text{C}_{23}\text{H}_{22}\text{NO}$   $[\text{M}+\text{H}]$ : 328.1696, found: 328.1692.

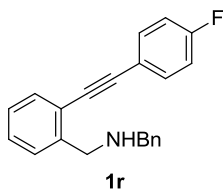
**N-Benzyl-1-(2-((4-chlorophenyl)ethynyl)phenyl)methanamine (1q):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (5.5 g, 81% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.53 (d, *J* = 7.2 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.22-7.36 (m, 11H),

4.00 (s, 2H), 3.82 (s, 2H), 1.86 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 142.3, 140.4, 134.5, 132.8, 132.5, 128.9, 128.8, 128.5, 128.3, 127.1, 127.1, 122.2, 121.8, 92.6, 88.6, 53.3, 51.8; **HRMS** (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>ClN [M+H]: 332.1201, found: 332.1192.

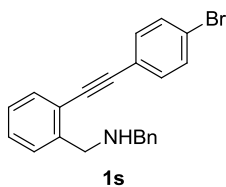
**N-Benzyl-1-(2-((4-fluorophenyl)ethynyl)phenyl)methanamine (1r):** The title



compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (2.9 g, 76% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.52 (d, *J* = 7.2 Hz, 1H), 7.39-7.43 (m, 3H), 7.22-7.35 (m, 7H), 7.01 (t,

*J* = 8.8 Hz, 2H), 4.01 (s, 2H), 3.81 (s, 2H), 1.88 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 163.9 (d, *J*<sub>C-F</sub> = 248.4 Hz), 142.2, 140.4, 133.6 (d, *J*<sub>C-F</sub> = 8.4 Hz), 132.4, 128.9 (d, *J*<sub>C-F</sub> = 26.0 Hz), 128.3 (d, *J*<sub>C-F</sub> = 17.7 Hz), 128.2, 127.0 (d, *J*<sub>C-F</sub> = 2.5 Hz), 122.3, 119.4 (d, *J*<sub>C-F</sub> = 3.4 Hz), 115.9 (d, *J*<sub>C-F</sub> = 21.9 Hz), 92.6, 87.3, 53.3, 51.9; **<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>) δ -110.6; **HRMS** (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>FN [M+H]: 316.1496, found: 316.1488.

**N-Benzyl-1-(2-((4-bromophenyl)ethynyl)phenyl)methanamine (1s):** The title

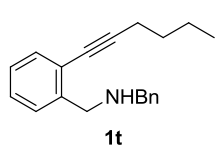


compound was prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (2.7 g, 66% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.41-7.47 (m, 3H), 7.23-7.35 (m, 9H), 4.01 (s,

2H), 3.82 (s, 2H), 1.87 (br, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 142.3, 140.4, 133.0, 132.5, 131.8, 131.7, 129.0, 128.9, 128.5, 128.3, 128.3, 127.1, 127.1, 122.7, 122.2, 122.2, 92.6, 88.8, 53.3, 51.8; **HRMS** (ESI) calcd. for C<sub>22</sub>H<sub>19</sub>BrN [M+H]: 378.0659, found: 378.0670.



**N-Benzyl-1-(2-(hex-1-yn-1-yl)phenyl)methanamine (1t):** The title compound was



prepared according to the general procedure (Method A) and purified by column chromatography to give the yellow oil (5.7 g,

80% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41 (dd, *J*<sub>1</sub> = 1.2 Hz,

*J*<sub>2</sub> = 7.6 Hz, 1H), 7.30-7.35 (m, 5H), 7.16-7.26 (m, 3H), 3.93 (s, 2H), 3.77 (s, 2H), 2.41

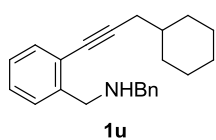
(t, *J* = 7.2 Hz, 2H), 1.93 (br, 1H), 1.53-1.60 (m, 2H), 1.41-1.50 (m, 2H), 0.93 (t, *J* = 7.2

Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 141.9, 140.6, 132.5, 128.9, 128.5, 128.3,

127.7, 127.0, 126.9, 123.4, 95.0, 78.8, 53.2, 52.1, 31.0, 22.2, 19.4, 13.8; HRMS (ESI)

calcd. for C<sub>20</sub>H<sub>24</sub>N [M+H]: 278.1903, found: 278.1900.

**N-Benzyl-1-(2-(3-cyclohexylprop-1-yn-1-yl)phenyl)methanamine (1u):** The title



compound was prepared according to the general procedure

(Method A) and purified by column chromatography to give the

yellow oil (6.0 g, 81% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

7.40-7.43 (m, 1H), 7.33 (t, *J* = 2.8 Hz, 5H), 7.18-7.24 (m, 3H), 3.95 (d, *J* = 4.4 Hz, 2H),

3.78 (d, *J* = 4.0 Hz, 2H), 2.31 (d, *J* = 2.0 Hz, 2H), 1.83-1.91 (m, 3H), 1.65-1.73 (m,

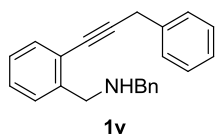
3H), 1.53 (t, *J* = 2.8 Hz, 1H), 1.04-1.27 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 142.0,

140.6, 132.6, 128.8, 128.4, 128.3, 127.7, 127.0, 126.9, 123.4, 93.9, 79.7, 53.2, 52.2,

37.6, 32.9, 27.5, 26.4, 26.3; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>28</sub>N [M+H]: 318.2216, found:

318.2207.

**N-Benzyl-1-(2-(3-phenylprop-1-yn-1-yl)phenyl)methanamine (1v):** The title



compound was prepared according to the general procedure

(Method A) and purified by column chromatography to give the

yellow oil (4.5 g, 69% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.46

(d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.2 Hz, 2H), 7.16-7.33 (m, 11H), 3.94 (s, 2H), 3.81 (s,

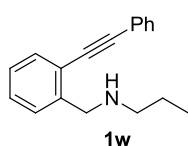
2H), 3.73 (s, 2H), 1.82 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 142.1, 140.4, 136.8,

132.6, 128.8, 128.7, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 127.0, 126.9, 126.9,

126.8, 122.9, 92.0, 80.8, 53.2, 53.2, 52.0, 26.0; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>N

[M+H]: 312.1747, found: 312.1749.

***N*-(2-(Phenylethynyl)benzyl)propan-1-amine (1w):** The title compound was

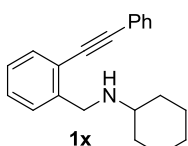


prepared according to the general procedure (Method A) and purified

by column chromatography to give the yellow oil (4.0 g, 83% yield);

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.54 (dd, *J*<sub>1</sub> = 2.4 Hz, *J*<sub>2</sub> = 8.0 Hz, 3H), 7.28-7.39 (m, 5H), 7.21-7.25 (m, 1H), 4.01 (s, 2H), 2.61 (t, *J* = 7.2 Hz, 2H), 1.49-1.58 (m, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 142.5, 132.4, 131.6, 128.8, 128.5, 128.5, 128.4, 128.2, 126.9, 123.3, 122.4, 93.6, 87.6, 52.6, 51.3, 23.4, 11.9; **HRMS** (ESI) calcd. for C<sub>18</sub>H<sub>20</sub>N [M+H]: 250.1590, found: 250.1598.

***N*-(2-(Phenylethynyl)benzyl)cyclohexanamine (1x):** The title compound was

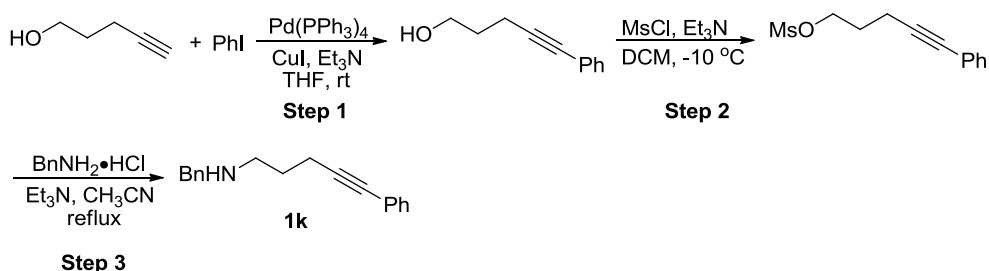


prepared according to the general procedure (Method A) and purified

by column chromatography to give the yellow oil (5.0 g, 89% yield);

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.51-7.54 (m, 3H), 7.27-7.39 (m, 5H), 7.21-7.25 (m, 1H), 4.02 (s, 2H), 2.46-2.52 (m, 1H), 1.94 (d, *J* = 11.6 Hz, 2H), 1.70-1.74 (m, 2H), 1.57-1.61 (m, 2H), 1.09-1.28 (m, 5H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 142.8, 132.5, 131.6, 128.9, 128.6, 128.5, 128.4, 126.9, 123.3, 122.4, 93.5, 87.7, 56.2, 49.8, 33.7, 26.3, 25.1; **HRMS** (ESI) calcd. for C<sub>21</sub>H<sub>24</sub>N [M+H]: 290.1903, found: 290.1898.

### Method B: Synthesis of substrate 1k.<sup>2</sup>



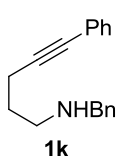
**Step 1.** The mixture of Pd(PPh<sub>3</sub>)<sub>4</sub> (398 mg, 0.8 mol%) and CuI (132 mg, 1.6 mol%) was added to the solution of pent-4-yn-1-ol (3.6 g, 43.0 mmol), iodobenzene (17.5 g, 86.0 mmol) and Et<sub>3</sub>N (124 mg, 890 mmol) in THF (20 mL) under nitrogen atmosphere. The reaction mixture was then allowed to stir at room temperature for 12 hours. The mixture was filtered and the filtrate was concentrated under reduced pressure. The

residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-3/1) to afford 5-phenylpent-4-yn-1-ol (6.5 g, 94% yield).

**Step 2.** Methanesulfonyl chloride (5.3 g, 46.6 mmol) was added successively to a solution of 5-phenylpent-4-yn-1-ol (6.5 g, 40.6 mmol) and Et<sub>3</sub>N (9.2 mL, 66.6 mmol) in DCM (100 mL) at -10 °C. The mixture was stirred for 30 minutes at this temperature and it was then poured into ice water. The organic layer was washed successively by 1 M HCl solution (30 mL x 2) and saturated aqueous sodium bicarbonate solution (30 mL x 2). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product of 5-phenylpent-4-yn-1-yl methanesulfonate (9.3 g) was obtained, which could be used directly in the next step without further purification.

**Step 3.** The crude 5-phenylpent-4-yn-1-yl methanesulfonate product (5.0 g) from the previous step was added to a solution of BnNH<sub>2</sub>·HCl (9.0 g, 63.0 mmol) and Et<sub>3</sub>N (4.3 mL, 31.5 mmol) in MeCN (50 mL) and heated to reflux for 5 hours. The reaction was allowed to cool to room temperature and concentrated under reduced pressure. Then the solution was made basic by addition of 1M NaOH and extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure. The excess BnNH<sub>2</sub> was removed by distillation and the residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-3/1) to afford *N*-benzyl-5-phenylpent-4-yn-1-amine **1k** (2.2 g, 42% yield over two steps).

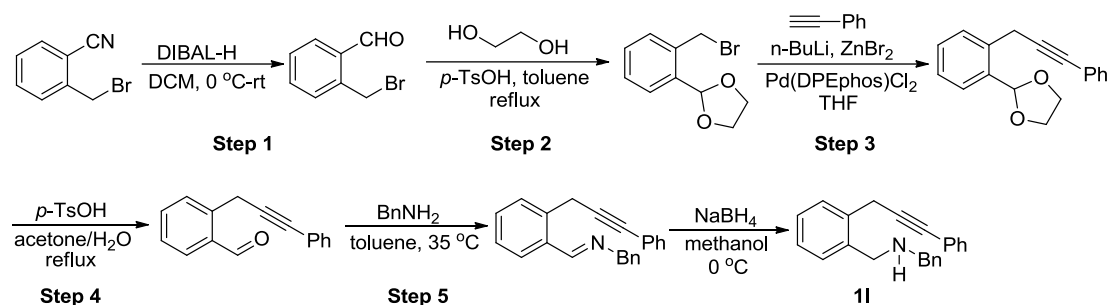
***N*-Benzyl-5-phenylpent-4-yn-1-amine (1k):** The title compound was prepared



according to the general procedure (Method **B**) and purified by column chromatography to give the yellow oil (2.2 g, 42% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34-7.36 (m, 2H), 7.27-7.31 (m, 4H), 7.24-7.25 (m, 4H), 3.79 (s, 2H), 2.78 (t, *J* = 6.8 Hz, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 1.75-1.82 (m, 2H), 1.31 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 140.6, 131.6, 128.4, 128.2, 128.2, 127.6, 126.9, 124.0, 89.9, 81.0, 54.0, 48.4, 29.0, 17.4; HRMS (ESI) calcd. for C<sub>18</sub>H<sub>20</sub>N

[M+H]: 250.1590, found: 250.1595.

**Method C: Synthesis of substrate 11.**<sup>3-5</sup>



**Step 1.** The mixture of 2-(bromomethyl)benzonitrile (10 g, 51.0 mmol) and DCM (150 mL) was added to a 500 mL Schlenk flask under nitrogen atmosphere. Then DIBAL-H (1.5 M in toluene, 34.7 mL) was added dropwise to the solution at 0 °C. The reaction mixture was then allowed to warm to room temperature within a period of 3 hours. Then the reaction mixture was cooled again with an ice-bath, and directly poured into a 1000 mL beaker containing ice (100 g) and a pre-cooled HBr aqueous solution (6.0 N, 100 mL). The resulting mixture was vigorously stirred for one hour and then extracted by CH<sub>2</sub>Cl<sub>2</sub> (100 mL x 3). The combined organic layer was washed by saturated NaHCO<sub>3</sub> solution, water and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-10/1) to afford 2-(bromomethyl)benzaldehyde (8.6 g, 85% yield).

**Step 2.** Ethylene glycol (2.7 g, 42.7 mmol) and *p*-toluenesulfonic acid (370 mg, 2.2 mmol) were added to a solution of 2-(bromomethyl)benzaldehyde (4.3 g, 21.4 mmol) in toluene (75 mL). The mixture was heated to reflux and stirred for 12 hours by using a Dean–Stark apparatus. The reaction mixture was then cooled to room temperature and diluted with water (20 mL). The resulting mixture was extracted by ethyl acetate (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product of 2-(2-(bromomethyl)phenyl)-1,3-dioxolane (5.0 g) was obtained which could be used in the next step without further purification.

**Step 3.** *n*-BuLi (9.9 mL, 24.7 mmol, 2.5 M in hexane) was added to a solution of

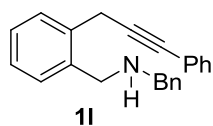
phenylacetylene (2.5 g, 24.7 mmol) in THF (50 mL) at -78 °C under nitrogen atmosphere. The resulting mixture was stirred for 30 minutes at -78 °C, followed by addition of a solution of dry ZnBr<sub>2</sub> (5.6 g, 24.7 mmol) in THF (30mL). The solution was stirred for 5 minutes at -78 °C and allowed to warm to room temperature slowly. Then Pd(DPEphos)Cl<sub>2</sub> (147.5 mg, 1.0 mol%) and the crude 2-(2-(bromomethyl)phenyl)-1,3-dioxolane (5.0 g) from the previous step were added at this temperature. After stirring for 12 hours, the reaction mixture was quenched with 1 M HCl and extracted by Et<sub>2</sub>O (50 mL x 3). The combined organic layer was washed with aqueous NaHCO<sub>3</sub>, dried over MgSO<sub>4</sub> and concentrated to afford the crude product of 2-(2-(3-phenylprop-2-yn-1-yl)phenyl)-1,3-dioxolane which could be used directly in the next step without further purification.

**Step 4.** The mixture of water (45 mL), *p*-toluenesulfonic acid (5 mol%, 177.2 mg), acetone (55 mL) and 2-(2-(3-phenylprop-2-yn-1-yl)phenyl)-1,3-dioxolane from previous step was added to a 250 mL Schlenk flask and the resulting mixture was heated to reflux and stirred for 3 hours. After the reaction completed, the mixture was concentrated and the residue was extracted by ethyl acetate (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (50/1-20/1) to afford 2-(3-phenylprop-2-yn-1-yl)benzaldehyde (2.0 g, 43% yield over three steps).

**Step 5.** Under nitrogen atmosphere, the mixture of 2-(3-phenylprop-2-yn-1-yl)benzaldehyde (1.6 g, 7.3 mmol), benzylamine (0.8 mL, 7.3 mmol), toluene (30 mL) was added to a 100 mL Schlenk flask and stirred at 35 °C for 12 hours. Then the solvent was removed under reduced pressure and the resulting residue was dissolved in methanol (50 mL) in a 100 mL three-neck flask. NaBH<sub>4</sub> (0.3 g, 8.8 mmol) was added to the reaction mixture in portions at 0 °C and stirred for 30 minutes at this temperature. The resulting mixture was quenched by aqueous saturated ammonium chloride solution (10 mL). Methanol was removed under reduced pressure and the residue was extracted by ethyl acetate (50 mL x 3). The combined organic

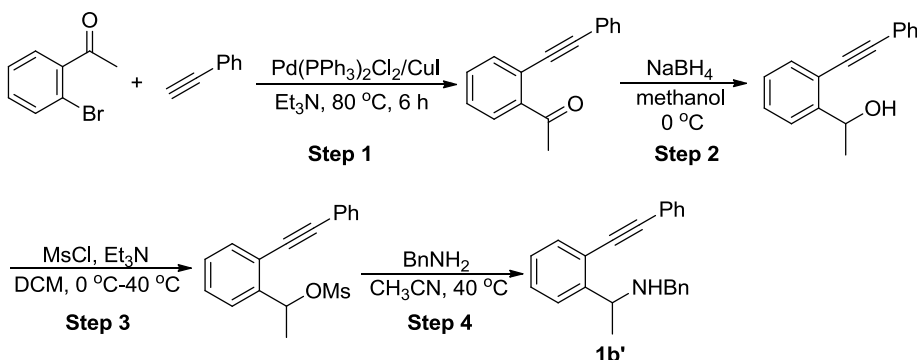
layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford *N*-benzyl-1-(2-(3-phenylprop-2-yn-1-yl)phenyl)methanamine **11** (1.8 g, 78% yield).

***N*-Benzyl-1-(2-(3-phenylprop-2-yn-1-yl)phenyl)methanamine (11):** The title



compound was prepared according to the general procedure (Method C) and purified by column chromatography to give the yellow oil (1.8 g, 78% yield); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.54 (d, *J* = 7.2 Hz, 1H), 7.21-7.39 (m, 13H), 3.91 (s, 2H), 3.87 (s, 2H), 3.84 (s, 2H), 1.56 (br, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>); δ 140.5, 137.9, 135.6, 131.7, 129.3, 129.2, 128.5, 128.3, 128.3, 127.9, 127.6, 127.1, 127.0, 123.8, 87.9, 82.9, 53.8, 51.2, 23.2; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>N [M+H]: 312.1747, found: 312.1740.

#### Method D: Synthesis of substrate 1y.



**Step 1.** To a solution of 1-(2-bromophenyl)ethanone (10.0 g, 50.3 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (353.1 mg, 1 mol%) in Et<sub>3</sub>N (200 mL) was added phenylacetylene (6.2 g, 60.3 mmol) under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 20 minutes and then CuI (48.0 mg, 0.5 mol%) was added. The resulting mixture was stirred at 80 °C for 6 hours. After the reaction was completed, the crude mixture was cooled to room temperature and filtered through Celite. The filtrate was concentrated under vacuum and diluted with water (50 mL). The resulting mixture was extracted by DCM (50 mL x 3) and the combined organic layer was washed with brine (50 mL x 2), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column

chromatography on silica gel and eluted with petroleum ether/ethyl acetate (50/1-10/1) to afford 1-(2-(phenylethynyl)phenyl)ethanone (7.8 g, 70% yield).

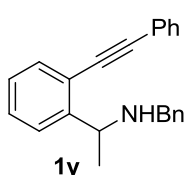
**Step 2.** The mixture of 1-(2-(phenylethynyl)phenyl)ethanone (5.5 g, 24.8 mmol) and methanol (50 mL) was added to a 250 mL Schlenk flask under nitrogen atmosphere. NaBH<sub>4</sub> (1.1 g, 29.8 mmol) was added to the reaction mixture in portions at 0 °C and stirred for 30 minutes at this temperature. The resulting mixture was quenched by aqueous saturated ammonium chloride solution (10 mL). Methanol was removed under reduced pressure and the residue was extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product of 1-(2-(phenylethynyl)phenyl)ethanol was obtained which could be used directly in the next step without further purification.

**Step 3.** Methanesulfonyl chloride (3.3 g, 28.5 mmol) was added successively to a solution of the crude 1-(2-(phenylethynyl)phenyl)ethanol from the previous step and Et<sub>3</sub>N (5.6 mL, 40.6 mmol) in DCM (100 mL) at 0 °C. The mixture was then heated to 40 °C and stirred for 48 hours at this temperature. After the reaction completed, it was poured into ice water. The organic layer was washed successively by 1 M HCl solution (50 mL x 2) and saturated aqueous sodium bicarbonate solution (50 mL x 2). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product of 1-(2-(phenylethynyl)phenyl)ethyl methanesulfonate was obtained, which could be used directly in the next step without further purification.

**Step 4.** BnNH<sub>2</sub> (15 mL) was added to a solution of the crude 1-(2-(phenylethynyl)phenyl)ethyl methanesulfonate from the previous step in CH<sub>3</sub>CN (15 mL) under nitrogen atmosphere and the resulting mixture was stirred at 40 °C for 72 hours. Then the reaction was allowed to cool to room temperature and diluted with water (10 mL). CH<sub>3</sub>CN was removed under reduced pressure and the resulting residue was extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure. Then the excess BnNH<sub>2</sub> was removed by distillation and the residue was purified by flash

column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford *N*-benzyl-1-(2-(phenylethynyl)phenyl)ethanamine **1y** (3.3 g, 43% yield over three steps).

***N*-benzyl-1-(2-(phenylethynyl)phenyl)ethanamine (1y):** The title compound was prepared according to the general procedure (Method **D**) and purified

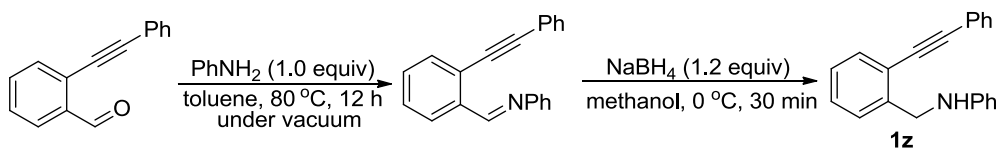


by column chromatography to give the yellow oil (3.3 g, 43% yield);

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 10.8 Hz, 2H), 7.43-7.46 (m, 2H), 7.18-7.37 (m, 10H), 4.46 (q, *J* = 6.8 Hz, 1H),

3.67 (dd, *J*<sub>1</sub> = 12.8 Hz, *J*<sub>2</sub> = 22.0 Hz, 2H), 1.80 (br, 1H), 1.44 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>); δ 147.4, 140.7, 132.6, 131.5, 129.0, 128.5, 128.4, 128.3, 126.9, 126.7, 126.1, 123.4, 121.9, 94.0, 87.7, 55.5, 51.9, 23.4; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>N [M+H]: 312.1747, found: 312.1749.

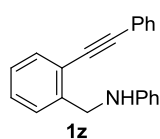
#### Method E: Synthesis of substrate **1z**.



The mixture of 2-(phenylethynyl)benzaldehyde (1.0 g, 4.9 mmol), aniline (0.5 g, 4.9 mmol), toluene (20 mL) was added to a 100 mL Schlenk flask under nitrogen atmosphere and stirred at 35 °C under vacuum for 12 hours. Then the solvent was removed under reduced pressure and the resulting residue was dissolved in methanol (20 mL) in a 100 mL flask. NaBH<sub>4</sub> (0.2 g, 5.9 mmol) was added to the reaction mixture in portions at 0 °C and the reaction mixture was stirred for 30 minutes at this temperature. Then the reaction was quenched by aqueous saturated ammonium chloride solution (10 mL). Methanol was removed under vacuum and the residue was extracted by ethyl acetate (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (50/1-20/1) to afford *N*-(2-(phenylethynyl)benzyl)aniline **1z** (1.1 g, 79% yield).

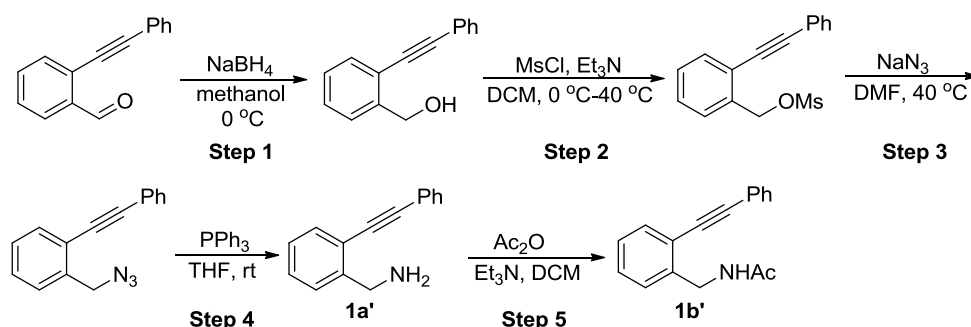
***N*-(2-(Phenylethynyl)benzyl)aniline (1z):** The title compound was prepared





according to the general procedure (Method E) and purified by column chromatography to give a yellow solid (1.1 g, 79% yield); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.53-7.55 (m, 1H), 7.39-7.46 (m, 3H), 7.22-7.31 (m, 5H), 7.13-7.18 (m, 2H), 6.68-6.72 (m, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 4.55 (s, 2H), 4.19 (s, 1H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 148.2, 141.3, 132.4, 131.7, 129.4, 128.7, 128.5, 128.5, 127.7, 127.1, 123.2, 122.1, 117.7, 113.1, 94.7, 87.2, 47.0; **HRMS** (ESI) calcd. for C<sub>21</sub>H<sub>18</sub>N [M+H]: 284.1434, found: 284.1440.

#### Method F: Synthesis of substrates 1a' and 1b'.<sup>6</sup>



**Step 1.** The mixture of 2-(phenylethynyl)benzaldehyde (5.7 g, 27.7 mmol) and methanol (50 mL) was added to a 250 mL Schlenk flask under nitrogen atmosphere. NaBH<sub>4</sub> (1.3 g, 33.2 mmol) was added to the reaction mixture in portions at 0 °C and stirred for 30 minutes at this temperature. The resulting mixture was quenched by aqueous saturated ammonium chloride solution (10 mL). Methanol was removed under reduced pressure and the residue was extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford (2-(phenylethynyl)phenyl)methanol (5.1 g, 88% yield).

**Step 2.** Methanesulfonyl chloride (3.2 g, 28.1 mmol) was added successively to a solution of (2-(phenylethynyl)phenyl)methanol (5.1 g, 24.5 mmol) and Et<sub>3</sub>N (5.6 mL, 40.2 mmol) in DCM (100 mL) at 0 °C. The mixture was then heated to 40 °C and stirred for 12 hours at this temperature. After the reaction completed, it was poured into ice water. The organic layer was washed successively by 1 M HCl solution (30

mL x 2) and saturated aqueous sodium bicarbonate solution (30 mL x 2). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product of 2-(phenylethynyl)benzyl methanesulfonate was obtained, which could be used directly in the next step without further purification.

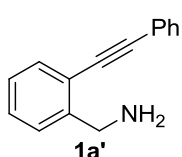
**Step 3.** Sodium azide (3.2 g, 49.0 mmol) was added to a solution of the crude 2-(phenylethynyl)benzyl methanesulfonate from the previous step in DMF (40 mL) under nitrogen atmosphere. The resulting mixture was stirred at 40 °C for 12 hours. Then the reaction was allowed to cool to room temperature and diluted with water (40 mL). The aqueous layer was extracted by Et<sub>2</sub>O (30 mL x 5) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (50/1-20/1) to afford 1-(azidomethyl)-2-(phenylethynyl)benzene (4.2 g, 74% yield).

**Step 4.** PPh<sub>3</sub> (9.4 g, 36.0 mmol) was added to a solution of 1-(azidomethyl)-2-(phenylethynyl)benzene (4.2 g, 18.0 mmol) in THF (40 mL) under nitrogen atmosphere and the resulting mixture was stirred at room temperature for 4 hours. Then water (40 mL) was added and the mixture was allowed to stir overnight. After the reaction completed, the mixture was concentrated and the residue was extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (10/1-2/1) with 10% Et<sub>3</sub>N to afford (2-(phenylethynyl)phenyl)methanamine **1a'** (3.0 g, 81% yield).

**Step 5.** Ac<sub>2</sub>O (0.5 mL, 4.8 mmol) was added to a solution of (2-(phenylethynyl)phenyl)methanamine **1a'** (1.0 g, 4.8 mmol) and Et<sub>3</sub>N (0.7 mL, 4.8 mmol) in DCM (20 mL) under nitrogen atmosphere and the resulting mixture was stirred at room temperature for 3 hours. After the reaction completed, water (5 mL) was added and the resulting residue was extracted by DCM (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was

removed under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (10/1-2/1) to afford *N*-(2-(phenylethynyl)benzyl)acetamide **1b'** (0.9 g, 75% yield).

**(2-(Phenylethynyl)phenyl)methanamine (1a')**: The title compound was prepared



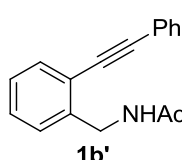
according to the general procedure (Method **F**) and purified by column chromatography to give the red oil (3.0 g, 81% yield); <sup>1</sup>H

NMR (400 MHz, CDCl<sub>3</sub>) δ 7.51-7.54 (m, 3H), 7.27-7.34 (m, 5H),

7.22 (t, *J* = 8.0 Hz, 1H), 4.03 (s, 2H), 1.58 (br, 2H); <sup>13</sup>C NMR (100

MHz, CDCl<sub>3</sub>); δ 145.5, 132.4, 131.5, 128.8, 128.4, 127.3, 126.8, 123.1, 121.8, 93.9, 87.3, 45.7; HRMS (ESI) calcd. for C<sub>15</sub>H<sub>14</sub>N [M+H]: 208.1121, found: 208.1125.

***N*-(2-(phenylethynyl)benzyl)acetamide (1b')**: The title compound was prepared



according to the general procedure (Method **F**) and purified by

column chromatography to give a white solid (0.9 g, 75% yield); <sup>1</sup>H

NMR (400 MHz, CDCl<sub>3</sub>) δ 7.52-7.54 (m, 3H), 7.27-7.35 (m, 6H),

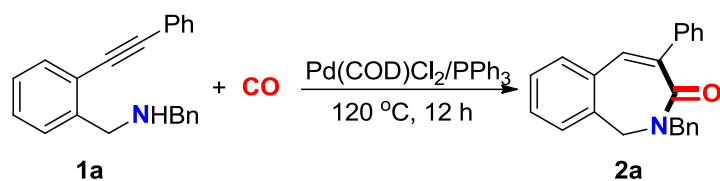
6.07 (br, 1H), 4.66 (d, *J* = 5.6 Hz, 2H), 1.99 (s, 3H); <sup>13</sup>C NMR (100

MHz, CDCl<sub>3</sub>); δ 170.0, 139.9, 132.5, 131.7, 128.9, 128.7, 128.6, 127.6, 123.0, 122.5, 94.3, 87.1, 42.6, 23.4; HRMS (ESI) calcd. for C<sub>17</sub>H<sub>15</sub>NNaO [M+Na]: 272.1046, found: 272.1051.

## 2. Optimization of the reaction conditions

A mixture of *N*-benzyl-1-(2-(phenylethynyl)phenyl)methanamine **1a** (118.8 mg, 0.4 mmol), [Pd] (0.02 mmol), ligand (0.022 mmol) and solvent (1 mL) was added into a glass tube which was placed in an autoclave. Then the autoclave was purged and charged with CO at designed pressure. The reaction mixture was stirred at designed temperature for designed hours. After the reaction finished, the autoclave was cooled to room temperature and the pressure was carefully released. Then the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford the desired product **2a**.

**Table S1. Screening of solvent<sup>a</sup>**



entry	solvent	yield(%) <sup>b</sup>
1	toluene	43
2	THF	36
3	CH <sub>3</sub> CN	53
4	DCE	59
5	PhCF <sub>3</sub>	54
6	anisole	62
7	DMA	47
8	Cl <sub>2</sub> CHCHCl <sub>2</sub>	40
9	NMP	trace

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (0.02 mmol), PPh<sub>3</sub> (0.044 mmol), solvent (1.0 mL), CO (30 atm), 120 °C, 12 h. <sup>b</sup>Isolated yield.

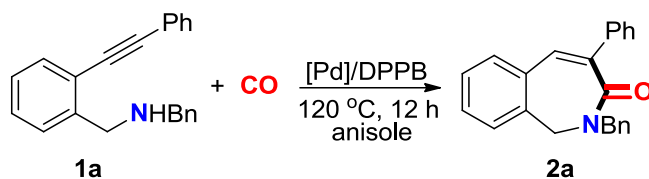
**Table S2. Screening of ligand<sup>a</sup>**



entry	ligand	yield(%) <sup>b</sup>
1	Xantphos	19
2	DPPM	30
3	DPPE	62
4	DPPP	84
5	DPPB	92
6	DPPPen	81
7	DPPHex	72
8	DPPOct	76
9	BINAP	37
10	DPPF	72
11	DPEphos	32

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (0.02 mmol), ligand (0.022 mmol), anisole (1.0 mL), CO (30 atm), 120 °C, 12 h. <sup>b</sup>Isolated yield.

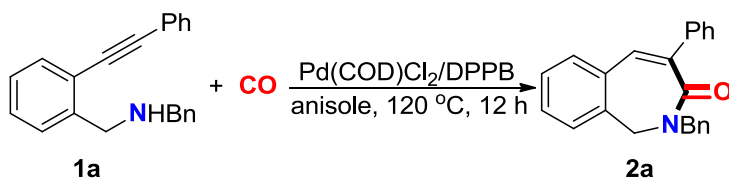
**Table S3. Screening of [Pd] precatalyst<sup>a</sup>**



entry	[Pd]/L	yield(%) <sup>b</sup>
1	Pd(COD)Cl <sub>2</sub> /DPPB	92
2	PdCl <sub>2</sub> /DPPB	82
3	Pd(OAc) <sub>2</sub> /DPPB	65
4	Pd(TFA) <sub>2</sub> /DPPB	61
5	Pd(Xantphos)Cl <sub>2</sub>	trace
6	Pd(CH <sub>3</sub> CN) <sub>2</sub> Cl <sub>2</sub> /DPPB	23
7	[Pd(allyl)Cl] <sub>2</sub> /DPPB	80
8	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>	48
9	Pd(Xantphos)(CH <sub>3</sub> CN) <sub>2</sub> (OTf) <sub>2</sub>	28

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), [Pd] (0.02 mmol), DPPB (0.022 mmol), anisole (1.0 mL), CO (30 atm), 120 °C, 12 h. <sup>b</sup>Isolated yield.

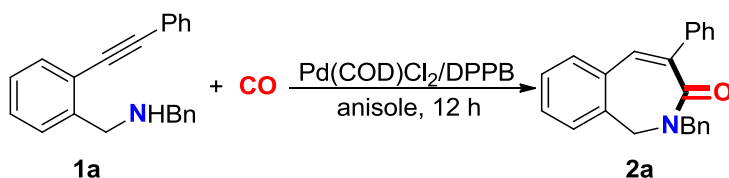
**Table S4. Screening of pressure of CO<sup>a</sup>**



entry	CO (atm)	yield (%) <sup>b</sup>
1	30	92
2	20	90
3	10	89
4	5	90
5	1	52

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (0.02 mmol), DPPB (0.022 mmol), anisole (1.0 mL), 120 °C, 12 h. <sup>b</sup>Isolated yield.

**Table S5. Screening of temperature<sup>a</sup>**

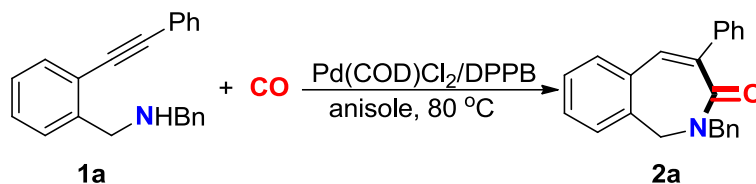


entry	T (°C)	yield(%) <sup>b</sup>
1	120	90
2	100	90

3	80	90
4	60	72

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (0.02 mmol), DPPB (0.022 mmol), anisole (1.0 mL), CO (5 atm), 12 h. <sup>b</sup>Isolated yield.

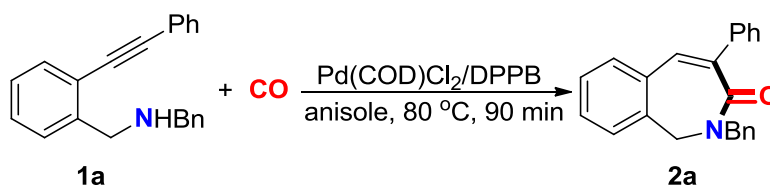
**Table S6. Screening of time<sup>a</sup>**



entry	time (h)	yield(%) <sup>b</sup>
1	12	90
2	6	88
3	3	89
4	1.5	90

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (0.02 mmol), DPPB (0.022 mmol), anisole (1.0 mL), CO (5 atm), 80 °C. <sup>b</sup>Isolated yields.

**Table S7. Screening of the loading of catalyst<sup>a</sup>**

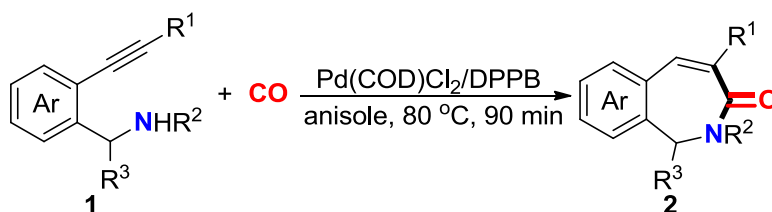


entry	Loading of [Pd]	yield(%) <sup>b</sup>
1	5.0 mol%	90
2	2.5 mol%	73

<sup>a</sup>Reaction conditions: **1a** (0.4 mmol), DPPB (0.022 mmol), anisole (1.0 mL), CO (5 atm), 80 °C, 90 min.

<sup>b</sup>Isolated yields.

### 3. General procedure for palladium-catalyzed hydroaminocarbonylation reaction

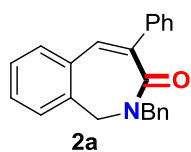


A mixture of **1** (0.4 mmol), Pd(COD)Cl<sub>2</sub> (5.7 mg, 0.02 mmol), DPPB (9.4 mg, 0.022 mmol) and anisole (1 mL) was added to a glass tube which was placed in an autoclave. Then the autoclave was purged and charged with CO at 5 atm. The reaction mixture was stirred at 80 °C for 90 minutes. After the reaction finished, the autoclave was cooled to room temperature and the pressure was carefully released. Then the

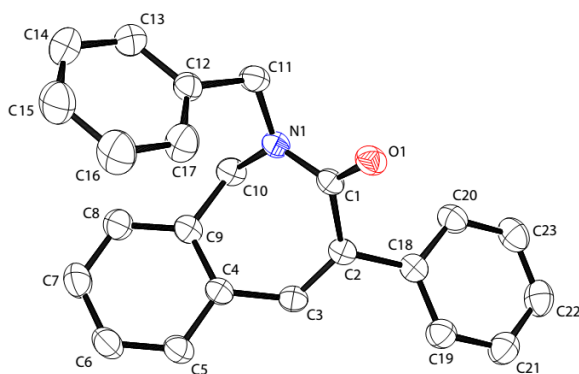
residue was purified directly by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford the desired products **2**.

#### 4. Experimental characterization data for products

**2-Benzyl-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2a):** The title compound was

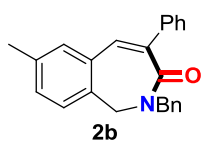


prepared according to the general procedure and purified by column chromatography to give a white solid, 116.5 mg, 90% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.69-7.71 (m, 2H), 7.40-7.43 (m, 3H), 7.27-7.36 (m, 8H), 7.20-7.24 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 4.74 (br, 2H), 4.22 (br, 2H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 166.8, 139.4, 139.3, 137.4, 136.3, 135.8, 132.2, 129.6, 128.7, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 127.6, 127.0, 50.3, 50.0; **HRMS** (ESI) calcd. for C<sub>23</sub>H<sub>20</sub>NO [M+H]: 326.1539, found: 326.1534.



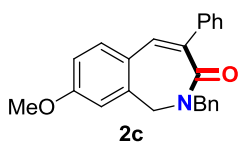
**Figure S1.** ORTEP drawing of product **2a**

**2-Benzyl-7-methyl-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2b):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 125 mg, 92% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.67-7.70 (m, 2H), 7.22-7.42 (m, 10H), 7.02-7.04 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 4.72 (br, 2H), 4.17 (br, 2H), 2.35 (s, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 166.9, 139.5, 139.3, 138.0, 137.4, 135.8, 133.6, 132.3, 130.1, 129.3, 128.7, 128.5, 128.4, 128.2, 128.0, 127.6, 126.9, 50.0, 49.9, 21.2; **HRMS** (ESI) calcd. for C<sub>24</sub>H<sub>21</sub>NONa [M+Na]: 362.1513, found: 362.1509.

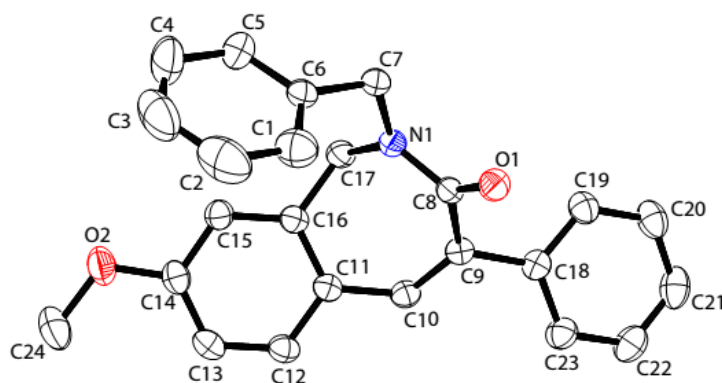
**2-Benzyl-8-methoxy-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2c):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 127.5 mg, 90% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.69 (d, *J* = 7.6

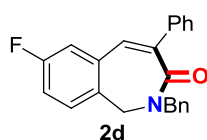


Hz, 2H), 7.27-7.42 (m, 10H), 6.87 (dd,  $J_1 = 2.8$  Hz,  $J_2 = 8.4$  Hz, 1H), 6.47 (d,  $J = 2.4$  Hz, 1H), 4.75 (br, 2H), 4.18 (br, 2H), 3.74 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.0, 159.9, 139.7, 137.9, 137.5, 137.3, 132.3, 131.2, 128.7, 128.6, 128.6, 128.4, 128.3, 127.8, 127.6, 113.8, 112.4, 55.5, 50.5, 50.1; **HRMS** (ESI) calcd. for  $\text{C}_{24}\text{H}_{21}\text{NO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ]: 378.1465, found: 378.1457.



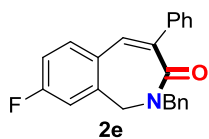
**Figure S2.** ORTEP drawing of product **2c**

**2-Benzyl-7-fluoro-4-phenyl-1H-benzo[*c*]azepin-3(2H)-one (2d):** The title compound



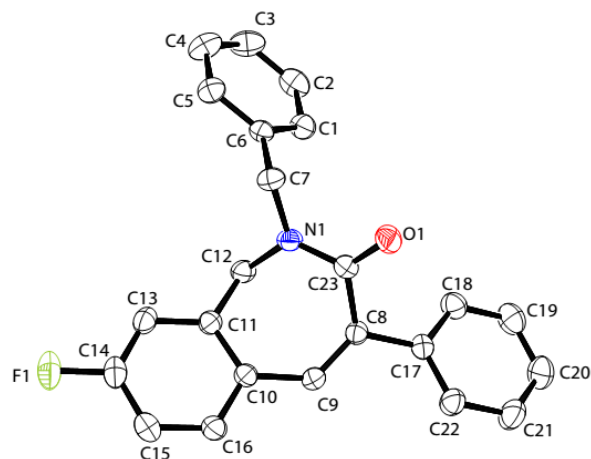
was prepared according to the general procedure and purified by column chromatography to give a white solid, 136.1 mg, 99% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (d,  $J = 7.2$  Hz, 2H), 7.22-7.42 (m, 9H), 7.09 (dd,  $J_1 = 2.0$  Hz,  $J_2 = 9.2$  Hz, 1H), 6.86-6.89 (m, 2H), 4.72 (br, 2H), 4.18 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 163.6 (d,  $J_{\text{C-F}} = 247.8$  Hz), 140.6, 138.9, 137.7 (d,  $J_{\text{C-F}} = 8.2$  Hz), 137.3, 132.5 (d,  $J_{\text{C-F}} = 2.8$  Hz), 130.8 (d,  $J_{\text{C-F}} = 2.1$  Hz), 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 127.7, 116.0 (d,  $J_{\text{C-F}} = 21.9$  Hz), 115.4 (d,  $J_{\text{C-F}} = 21.5$  Hz), 49.9, 49.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.7; **HRMS** (ESI) calcd. for  $\text{C}_{23}\text{H}_{19}\text{FNO}$  [ $\text{M}+\text{H}$ ]: 344.1445, found: 344.1450.

**2-Benzyl-8-fluoro-4-phenyl-1H-benzo[*c*]azepin-3(2H)-one (2e):** The title compound



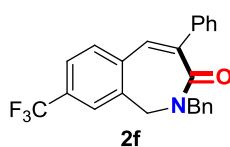
was prepared according to the general procedure and purified by column chromatography to give a white solid, 125.5 mg, 91% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 7.6$  Hz, 2H), 7.26-7.43 (m, 10H), 7.00-7.04 (m, 1H), 6.64 (dd,  $J_1 = 2.0$  Hz,  $J_2 = 8.4$  Hz, 1H), 4.75 (br, 2H), 4.18 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.7, 163.7 (d,  $J_{\text{C-F}} = 249.3$  Hz), 139.1

(d,  $J_{C-F} = 8.5$  Hz), 138.6 (d,  $J_{C-F} = 7.3$  Hz), 137.2, 132.0 (d,  $J_{C-F} = 3.3$  Hz), 131.5 (d,  $J_{C-F} = 8.4$  Hz), 131.1, 128.8, 128.5, 128.2, 128.2, 127.8, 115.4 (d,  $J_{C-F} = 21.5$  Hz), 114.2 (d,  $J_{C-F} = 22.0$  Hz), 50.1, 50.0;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -112.0; HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{18}\text{FNONa}$   $[\text{M}+\text{Na}]$ : 366.1260, found: 366.1263.



**Figure S3.** ORTEP drawing of product **2e**

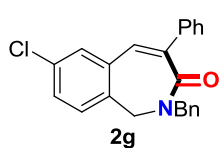
**2-Benzyl-4-phenyl-8-(trifluoromethyl)-1H-benzo[c]azepin-3(2H)-one (2f):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 146.9 mg, 93% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69-7.70 (m, 2H),

7.49-7.57 (m, 2H), 7.36-7.46 (m, 3H), 7.24-7.32 (m, 6H), 7.05 (s, 1H), 4.78 (s, 2H), 4.29 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4, 141.5, 139.0, 138.8, 137.2, 137.1, 130.4, 130.3 (q,  $J_{C-F} = 32.5$  Hz), 129.8, 128.8, 128.7, 128.6, 128.3, 128.1, 125.2 (q,  $J_{C-F} = 270.6$  Hz), 125.1 (q,  $J_{C-F} = 3.7$  Hz), 123.9 (q,  $J_{C-F} = 3.8$  Hz), 50.3, 50.0;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.5; HRMS (ESI) calcd. for  $\text{C}_{24}\text{H}_{19}\text{F}_3\text{NO}$   $[\text{M}+\text{H}]$ : 394.1413, found: 394.1412.

**2-Benzyl-7-chloro-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2g):** The title compound was prepared according to the general procedure and purified by column

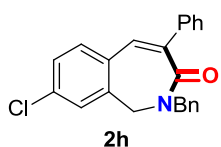


chromatography to give a white solid, 133.9 mg, 93% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66-7.68 (m, 2H), 7.21-7.43 (m, 10H), 7.16 (dd,  $J_1 = 2.0$  Hz,  $J_2 = 8.0$  Hz, 1H), 6.87 (d,  $J = 8.0$  Hz, 1H),

4.73 (br, 2H), 4.19 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 140.7, 138.9, 137.4,

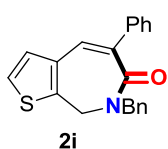
137.2, 134.8, 134.0, 130.6, 129.2, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 127.8, 50.0, 49.6; **HRMS** (ESI) calcd. for  $C_{23}H_{19}ClNO$   $[M+H]^+$ : 360.1150, found: 360.1148.

**2-Benzyl-8-chloro-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2h):** The title compound



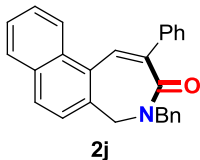
was prepared according to the general procedure and purified by column chromatography to give a white solid, 130.2 mg, 91% yield.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.68 (d,  $J$  = 7.6 Hz, 2H), 7.39-7.43 (m, 2H), 7.24-7.37 (m, 9H), 6.89 (d,  $J$  = 1.6 Hz, 1H), 4.75 (br, 2H), 4.18 (br, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  166.6, 139.9, 139.0, 137.9, 137.1, 134.3, 134.2, 130.9, 130.8, 128.8, 128.6, 128.6, 128.4, 128.3, 128.2, 127.9, 127.1, 50.0, 49.8; **HRMS** (ESI) calcd. for  $C_{23}H_{18}ClNONa$   $[M+Na]^+$ : 382.0969, found: 382.0963.

**7-Benzyl-5-phenyl-7,8-dihydro-6H-thieno[2,3-c]azepin-6-one (2i):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 93.5 mg, 75% yield.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.65-7.67 (m, 2H), 7.38-7.42 (m, 2H), 7.28-7.35 (m, 6H), 7.24 (s, 1H), 7.14 (d,  $J$  = 4.8 Hz, 1H), 7.07 (d,  $J$  = 4.8 Hz, 1H), 4.75 (br, 2H), 4.31 (br, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.8, 139.6, 139.1, 138.0, 137.2, 136.6, 128.8, 128.5, 128.4, 128.2, 128.0, 127.8, 127.6, 126.9, 124.1, 50.7, 43.9; **HRMS** (ESI) calcd. for  $C_{21}H_{18}NOS$   $[M+H]^+$ : 332.1104, found: 332.1099.

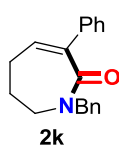
**4-Benzyl-2-phenyl-4,5-dihydro-3H-naphtho[2,1-c]azepin-3-one (2j):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 123.6 mg, 82% yield.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.19 (d,  $J$  = 8.4 Hz, 1H), 7.99 (s, 1H), 7.83-7.85 (m, 3H), 7.72 (d,  $J$  = 8.0 Hz, 1H), 7.39-7.61 (m, 5H), 7.29 (s, 5H), 7.09 (d,  $J$  = 8.4 Hz, 1H), 5.03 (d,  $J$  = 14.0 Hz, 1H), 4.57 (dd,  $J_1$  = 14.8 Hz,  $J_2$  = 21.2 Hz, 2H), 4.13 (d,  $J$  = 13.6 Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.2, 140.3, 139.3, 137.4, 135.6, 133.1, 131.9, 131.6, 129.2, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 127.7, 127.3, 126.3, 125.2, 123.9, 50.9, 49.9; **HRMS** (ESI) calcd. for

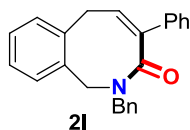
C<sub>27</sub>H<sub>21</sub>NNaO [M+Na]: 398.1515, found: 398.1527.

**1-Benzyl-3-phenyl-6,7-dihydro-1H-azepin-2(5H)-one (2k):** The title compound was



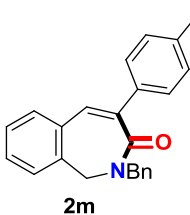
prepared according to the general procedure and purified by column chromatography to give a white solid, 56.1 mg, 51% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.50 (d, *J* = 7.2 Hz, 2H), 7.24-7.40 (m, 8H), 6.47 (t, *J* = 7.2 Hz, 1H), 4.78 (s, 2H), 3.37 (t, *J* = 6.4 Hz, 2H), 2.26 (q, *J* = 7.2 Hz, 2H), 1.70-1.76 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.4, 139.7, 138.4, 137.3, 129.2, 128.8, 128.5, 128.4, 127.8, 127.7, 127.0, 49.7, 45.6, 28.6, 23.6; HRMS (ESI) calcd. for C<sub>19</sub>H<sub>20</sub>NO [M+H]: 278.1539, found: 278.1548.

**(Z)-2-Benzyl-4-phenyl-1,2-dihydrobenzo[c]azocin-3(6H)-one (2l):** The title



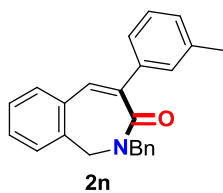
compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 55.3 mg, 41% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55-7.57 (m, 2H), 7.25-7.39 (m, 9H), 7.17-7.20 (m, 2H), 6.24 (t, *J* = 8.4 Hz, 1H), 5.41 (d, *J* = 14.4 Hz, 1H), 5.06 (d, *J* = 16.4 Hz, 1H), 3.86-4.01 (m, 3H), 3.41 (q, *J* = 7.2 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.9, 139.7, 137.1, 135.0, 134.7, 134.6, 131.2, 129.8, 128.9, 128.8, 128.7, 128.4, 127.8, 127.2, 126.2, 122.1, 51.6, 47.7, 35.1; HRMS (ESI) calcd. for C<sub>24</sub>H<sub>22</sub>NO [M+H]: 340.1696, found: 340.1702.

**2-Benzyl-4-(p-tolyl)-1H-benzo[c]azepin-3(2H)-one (2m):** The title compound was



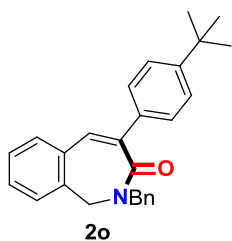
prepared according to the general procedure and purified by column chromatography to give a white solid, 120 mg, 88% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.28-7.36 (m, 7H), 7.20-7.24 (m, 3H), 7.02 (d, *J* = 7.2 Hz, 1H), 4.73 (br, 2H), 4.21 (br, 2H), 2.39 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.0, 139.4, 138.0, 137.5, 136.4, 136.3, 136.0, 131.4, 129.6, 129.2, 128.7, 128.5, 128.3, 128.1, 127.7, 127.0, 50.4, 49.9, 21.4; HRMS (ESI) calcd. for C<sub>24</sub>H<sub>22</sub>NO [M+H]: 340.1696, found: 340.1696.

**2-Benzyl-4-(m-tolyl)-1H-benzo[c]azepin-3(2H)-one (2n):** The title compound was prepared according to the general procedure and purified by column chromatography



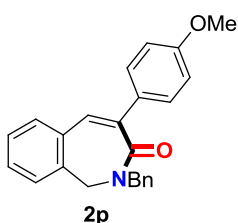
to give a white solid, 116.7 mg, 86% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.50 (t, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.28-7.36 (m, 8H), 7.16-7.25 (m, 2H), 7.01 (d, *J* = 7.6 Hz, 1H), 4.75 (br, 2H), 4.23 (br, 2H), 2.42 (s, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 166.9, 139.7, 139.4, 138.1, 137.5, 136.4, 135.9, 132.1, 129.6, 129.0, 128.9, 128.7, 128.6, 128.5, 128.5, 128.3, 127.7, 127.1, 125.4, 50.4, 50.0, 21.7; **HRMS** (ESI) calcd. for C<sub>24</sub>H<sub>21</sub>NONa [M+Na]: 362.1515, found: 362.1520.

**2-Benzyl-4-(4-(tert-butyl)phenyl)-1H-benzo[c]azepin-3(2H)-one (2o):** The title



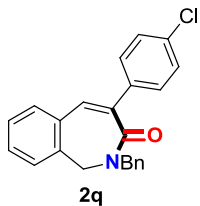
compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 136.6 mg, 90% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.41-7.46 (m, 3H), 7.28-7.36 (m, 7H), 7.21-7.24 (m, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 4.68-4.83 (m, 2H), 4.21 (br, 2H), 1.35 (s, 9H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 167.0, 151.2, 139.3, 137.5, 136.3, 136.1, 131.5, 129.6, 128.8, 128.5, 128.5, 128.3, 127.9, 127.7, 127.0, 125.5, 50.4, 49.9, 34.7, 31.4; **HRMS** (ESI) calcd. for C<sub>27</sub>H<sub>28</sub>NO [M+H]: 382.2165, found: 382.2171.

**2-Benzyl-4-(4-methoxyphenyl)-1H-benzo[c]azepin-3(2H)-one (2p):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 118.6 mg, 84% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.67 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.27-7.35 (m, 7H), 7.19-7.24 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.94-6.96 (m, 2H), 4.70 (br, 2H), 4.20 (br, 2H), 3.83 (s, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 166.9, 159.6, 138.8, 137.4, 136.2, 136.0, 131.7, 130.7, 129.5, 129.4, 128.7, 128.4, 128.4, 128.3, 127.6, 127.0, 113.9, 55.5, 50.3, 49.9; **HRMS** (ESI) calcd. for C<sub>24</sub>H<sub>21</sub>NO<sub>2</sub>Na [M+Na]: 378.1465, found: 378.1468.

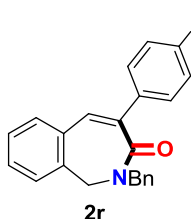
**2-Benzyl-4-(4-chlorophenyl)-1H-benzo[c]azepin-3(2H)-one (2q):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 121.9 mg, 85% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.66 (d, *J* = 8.8 Hz, 2H),

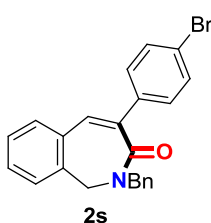
7.34-7.43 (m, 4H), 7.32 (s, 1H), 7.28-7.31 (m, 5H), 7.23-7.27 (m, 1H), 7.02 (d,  $J = 7.2$  Hz, 1H), 4.74 (br, 2H), 4.22 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 138.2, 137.8, 137.3, 136.4, 135.6, 134.1, 132.7, 129.8, 129.7, 128.9, 128.8, 128.7, 128.5, 128.4, 127.8, 127.1, 50.4, 50.1; HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{19}\text{NOCl}$   $[\text{M}+\text{H}]$ : 360.1150, found: 360.1143.

**2-Benzyl-4-(4-fluorophenyl)-1H-benzo[c]azepin-3(2H)-one (2r):** The title



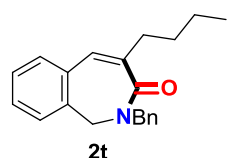
compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 120.9 mg, 88% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (dd,  $J_1 = 5.6$  Hz,  $J_2 = 8.8$  Hz, 2H), 7.22-7.43 (m, 9H), 7.08-7.12 (m, 2H), 7.02 (d,  $J = 7.6$  Hz, 1H), 4.75 (br, 2H), 4.23 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.7, 164.0 (d,  $J_{\text{C-F}} = 245.9$  Hz), 138.3, 137.3, 136.3, 135.7, 135.5 (d,  $J_{\text{C-F}} = 3.5$  Hz), 132.4, 130.2 (d,  $J_{\text{C-F}} = 8.0$  Hz), 129.7, 128.8, 128.5, 128.4, 127.7, 127.1, 115.5 (d,  $J_{\text{C-F}} = 21.3$  Hz), 50.4, 50.1;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.1; HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{18}\text{NOFNa}$   $[\text{M}+\text{Na}]$ : 366.1265, found: 366.1267.

**2-Benzyl-4-(4-bromophenyl)-1H-benzo[c]azepin-3(2H)-one (2s):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 95.3 mg, 59% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52-7.59 (m, 4H), 7.22-7.42 (m, 9H), 7.01 (d,  $J = 7.6$  Hz, 1H), 4.73 (br, 2H), 4.21 (br, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4, 138.3, 138.2, 137.3, 136.3, 135.6, 132.7, 131.6, 130.0, 129.7, 128.9, 128.8, 128.5, 128.4, 127.7, 127.1, 122.3, 50.4, 50.1; HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{18}\text{NOBrNa}$   $[\text{M}+\text{Na}]$ : 426.0464, found: 426.0461.

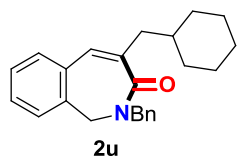
**2-Benzyl-4-butyl-1H-benzo[c]azepin-3(2H)-one (2t):** The title compound was



prepared according to the general procedure and purified by column chromatography to give the colorless oil, 58.6 mg, 48% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22-7.32 (m, 7H), 7.15-7.20 (m, 1H), 6.92-6.96 (m, 2H), 4.69 (br, 2H), 4.08 (br, 2H), 2.70 (br, 2H), 1.56-1.64 (m, 2H), 1.39-1.48 (m, 2H), 0.97 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,

CDCl<sub>3</sub>)  $\delta$  167.4, 140.8, 137.6, 136.2, 136.1, 131.6, 128.9, 128.7, 128.3, 128.1, 128.0, 127.5, 126.9, 50.3, 50.2, 35.6, 31.8, 22.6, 14.1; **HRMS** (ESI) calcd. for C<sub>21</sub>H<sub>24</sub>NO [M+H]: 306.1852, found: 306.1855.

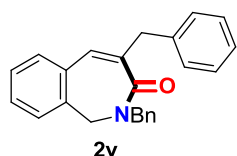
**2-Benzyl-4-(cyclohexylmethyl)-1H-benzo[c]azepin-3(2H)-one (2u):** The title



compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 68.8 mg, 50% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.26-7.32 (m, 5H),

7.22-7.24 (m, 2H), 7.16-7.20 (m, 1H), 6.98 (d,  $J$  = 7.2 Hz, 1H), 6.89 (s, 1H), 4.69 (br, 2H), 4.09 (br, 2H), 1.83 (d,  $J$  = 12.8 Hz, 2H), 1.56-1.75 (m, 5H), 1.14-1.32 (m, 4H), 1.01-1.04 (m, 2H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  167.5, 139.4, 137.7, 136.3, 136.2, 132.7, 129.0, 128.7, 128.3, 128.1, 128.1, 127.6, 126.9, 50.5, 50.2, 44.1, 37.7, 33.5, 26.7, 26.5; **HRMS** (ESI) calcd. for C<sub>24</sub>H<sub>27</sub>NONa [M+Na]: 368.1985, found: 368.1969.

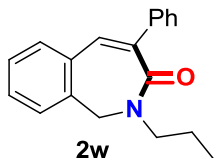
**2,4-Dibenzyl-1H-benzo[c]azepin-3(2H)-one (2v):** The title compound was prepared



according to the general procedure and purified by column chromatography to give the yellow oil, 73.1 mg, 54% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.18-7.37 (m, 11H), 6.94-7.01 (m,

4H), 4.65 (br, 2H), 3.99 (br, 4H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  166.9, 140.2, 140.0, 137.2, 136.3, 135.8, 132.2, 129.4, 129.1, 128.7, 128.6, 128.4, 128.2, 128.0, 127.4, 127.0, 126.5, 50.4, 50.2, 41.9; **HRMS** (ESI) calcd. for C<sub>24</sub>H<sub>21</sub>NONa [M+Na]: 362.1515, found: 362.1514.

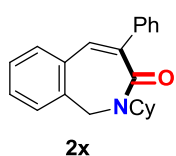
**4-Phenyl-2-propyl-1H-benzo[c]azepin-3(2H)-one (2w):** The title compound was



prepared according to the general procedure and purified by column chromatography to give a yellow solid, 106.5 mg, 96% yield. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.65-7.67 (m, 2H), 7.36-7.43

(m, 4H), 7.29-7.35 (m, 4H), 4.30 (br, 2H), 3.53 (br, 2H), 1.59-1.69 (m, 2H), 0.87 (t,  $J$  = 7.2 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  166.5, 139.9, 139.5, 137.0, 136.0, 131.8, 129.7, 128.7, 128.4, 128.4, 128.3, 128.0, 126.9, 51.6, 49.3, 21.8, 11.4; **HRMS** (ESI) calcd. for C<sub>19</sub>H<sub>20</sub>NO [M+H]: 278.1539, found: 278.1550.

**2-Cyclohexyl-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2x):** The title compound was



prepared according to the general procedure and purified by column

chromatography to give a white solid, 105.2 mg, 83% yield. <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>) δ 7.66 (d, *J* = 7.2 Hz, 2H), 7.36-7.41 (m, 2H),

7.30-7.35 (m, 5H), 7.26 (d, *J* = 3.6 Hz, 1H), 4.51-4.59 (m, 1H), 4.26 (s, 2H), 1.67-1.84

(m, 4H), 1.42-1.55 (m, 3H), 1.24-1.33 (m, 2H), 1.12-1.22 (m, 1H); <sup>13</sup>C NMR (100

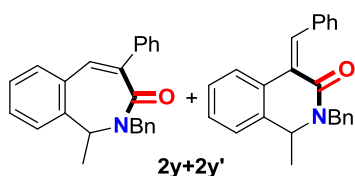
MHz, CDCl<sub>3</sub>) δ 166.2, 140.0, 139.9, 138.1, 136.2, 131.9, 129.6, 128.6, 128.4, 128.4,

128.1, 127.9, 127.0, 53.9, 45.8, 25.9, 25.8; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>24</sub>NO [M+H]:

318.1852, found: 318.1851.

**2-Benzyl-1-methyl-4-phenyl-1H-benzo[c]azepin-3(2H)-one (2y) and**

**(Z)-2-benzyl-4-benzylidene-1-methyl-1,2-dihydroisoquinolin-3(4H)-one (2y')**: The



title compounds were prepared according to the general

procedure and purified by column chromatography to

give the yellow oil, 130.9 mg, 97% yield (isomer ratio

1.4:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.77-7.79 (m,

0.76H), 7.61-7.63 (m, 1.13H), 7.12-7.44 (m, 12H), 7.08 (d, *J* = 8.0 Hz, 0.67H), 6.87 (d,

*J* = 7.2 Hz, 0.56H), 5.00 (d, *J* = 14.8 Hz, 0.54H), 4.87 (q, *J* = 7.2 Hz, 0.46H), 4.67-4.72

(m, 1.22H), 4.47 (q, *J* = 7.2 Hz, 0.57H), 1.68 (d, *J* = 7.2 Hz, 1.25H), 1.51 (d, *J* = 7.6

Hz, 1.75H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.9, 166.3, 140.4, 140.3, 140.2, 139.9,

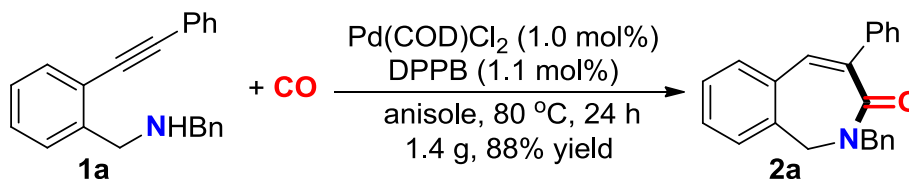
139.4, 139.1, 138.8, 137.6, 135.3, 133.6, 132.5, 131.1, 130.9, 129.6, 129.1, 128.6,

128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.6, 127.6, 127.4, 127.3,

126.8, 123.0, 59.2, 52.6, 52.5, 45.0, 27.0, 18.2, 15.1; HRMS (ESI) calcd. for

C<sub>24</sub>H<sub>21</sub>NNaO [M+Na]: 362.1515, found: 362.1518.

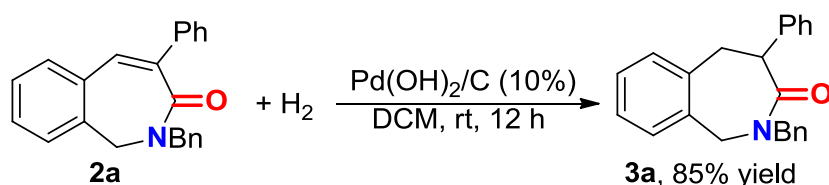
## 5. Gram-scale experiment and transformation of product



A mixture of **1** (1.5 g, 5.0 mmol), Pd(COD)Cl<sub>2</sub> (14.3 mg, 0.05 mol), DPPB (23.5 mg, 0.055 mmol) and anisole (5 mL) was added to a 50 mL flask which was placed in an

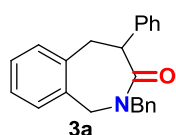


autoclave. Then the autoclave was purged and charged with CO at 5 atm. The reaction mixture was stirred at 80 °C for 24 h. After the reaction finished, the autoclave was cooled to room temperature and the pressure was carefully released. Then the residue was purified directly by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-5/1) to afford the desired products **2a** as a white solid (1.4 g, 88% yield).

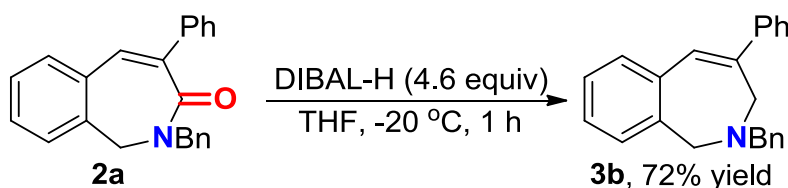


A mixture of **2a** (100 mg, 0.3 mmol), Pd(OH)<sub>2</sub>/C (10 mg) and DCM (2 mL) was added to a glass tube which was placed in an autoclave. Then the autoclave was purged and charged with H<sub>2</sub> at 40 atm. The reaction mixture was stirred at room temperature for 12 h. After the reaction finished, the pressure was carefully released. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (10/1-5/1) to afford the desired products **3a** as the colorless oil (83.5 mg, 85% yield).

**2-Benzyl-4-phenyl-4,5-dihydro-1H-benzo[c]azepin-3(2H)-one (3a):** The title

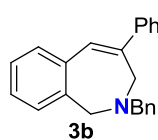


compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 83.5 mg, 85% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37 (d, *J* = 3.6 Hz, 4H), 7.18-7.28 (m, 7H), 7.14 (d, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 4.83-4.91 (m, 2H), 4.47-4.56 (m, 2H), 4.11 (d, *J* = 16.4 Hz, 1H), 3.56 (dd, *J*<sub>1</sub> = 12.0 Hz, *J*<sub>2</sub> = 16.8 Hz, 1H), 3.33 (dd, *J*<sub>1</sub> = 4.0 Hz, *J*<sub>2</sub> = 16.8 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 173.5, 140.3, 137.5, 137.3, 134.5, 130.5, 128.7, 128.6, 128.5, 128.5, 128.4, 128.1, 127.5, 127.2, 126.2, 51.3, 51.2, 48.0, 37.1; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>21</sub>NNaO [M+Na]: 350.1515, found: 350.1506.



The mixture of 2-benzyl-4-phenyl-1H-benzo[c]azepin-3(2H)-one (50 mg, 0.15 mmol) and THF (3 mL) was added to a 25 Schlenk tube under nitrogen atmosphere. Then DIBAL-H (460  $\mu$ L, 1.5 M in toluene) was added dropwise to the solution at -20 °C. The reaction mixture was continued to stir under this temperature for 1 hour. Then the reaction mixture was warmed to 0 °C and quenched by EtOAc (5 mL), followed by addition of 1M NaOH (5 mL). Solvent was removed under reduced pressure and the residue was extracted by ethyl acetate (10 mL x 3). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate (20/1-10/1) to afford 2-benzyl-4-phenyl-2,3-dihydro-1H-benzo[c]azepine **3b** as colorless oil (33.5 g, 72% yield).

**2-Benzyl-4-phenyl-2,3-dihydro-1H-benzo[c]azepine (3b):** The title compound was



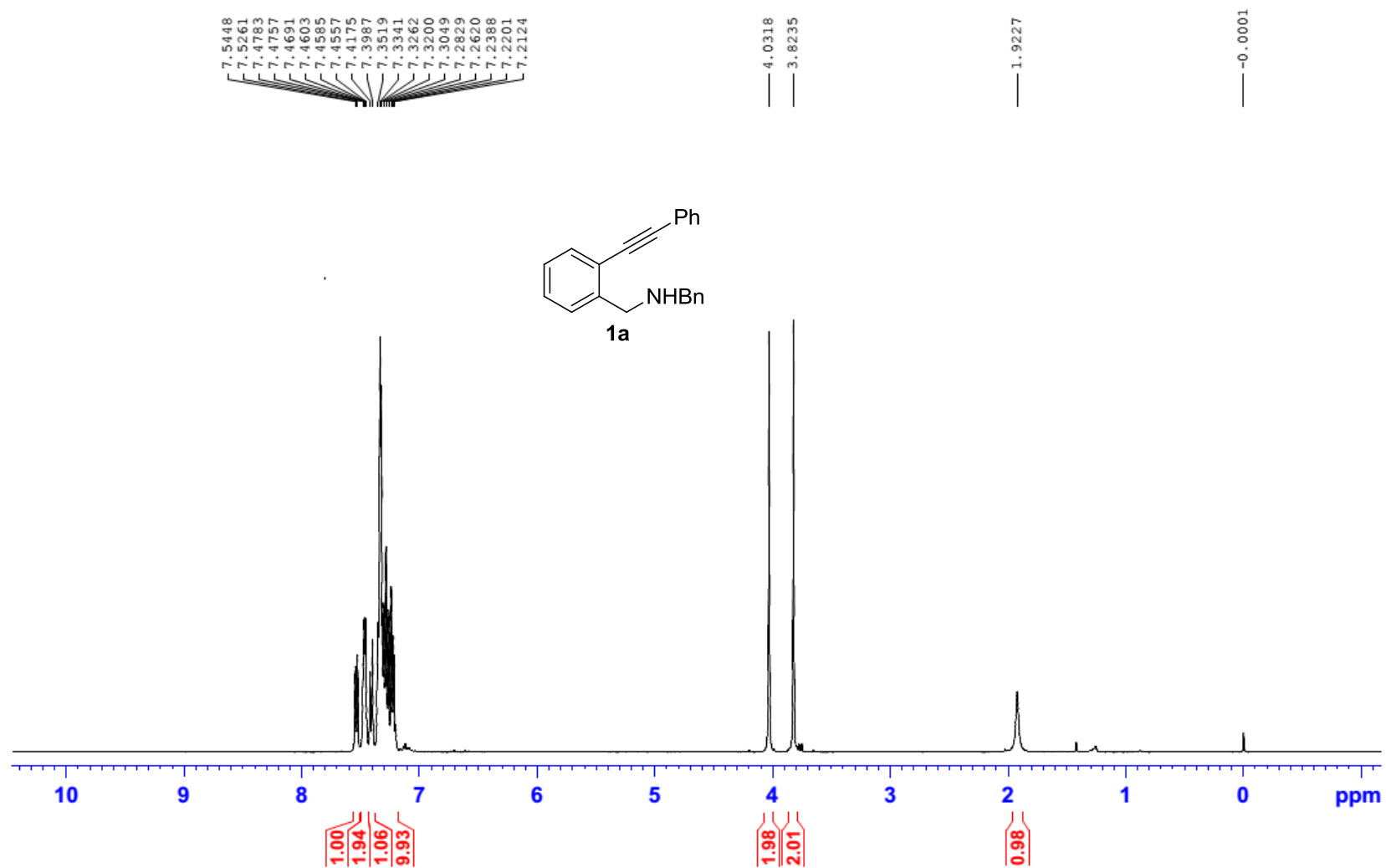
prepared according to the general procedure and purified by column chromatography to give the colorless oil, 33.5 mg, 72% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.31-7.33 (m, 2H), 7.15-7.28 (m, 10H), 7.07-7.11 (m, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.74 (s, 1H), 3.88 (s, 2H), 3.77 (s, 2H), 3.63 (s, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  143.0, 142.1, 139.3, 138.0, 137.1, 130.9, 129.8, 129.4, 129.2, 128.5, 128.4, 127.5, 127.3, 127.2, 127.1, 126.6, 58.6, 58.5, 58.1; HRMS (ESI) calcd. for C<sub>23</sub>H<sub>22</sub>N [M+H]<sup>+</sup>: 312.1747, found: 312.1733.

## 6. References:

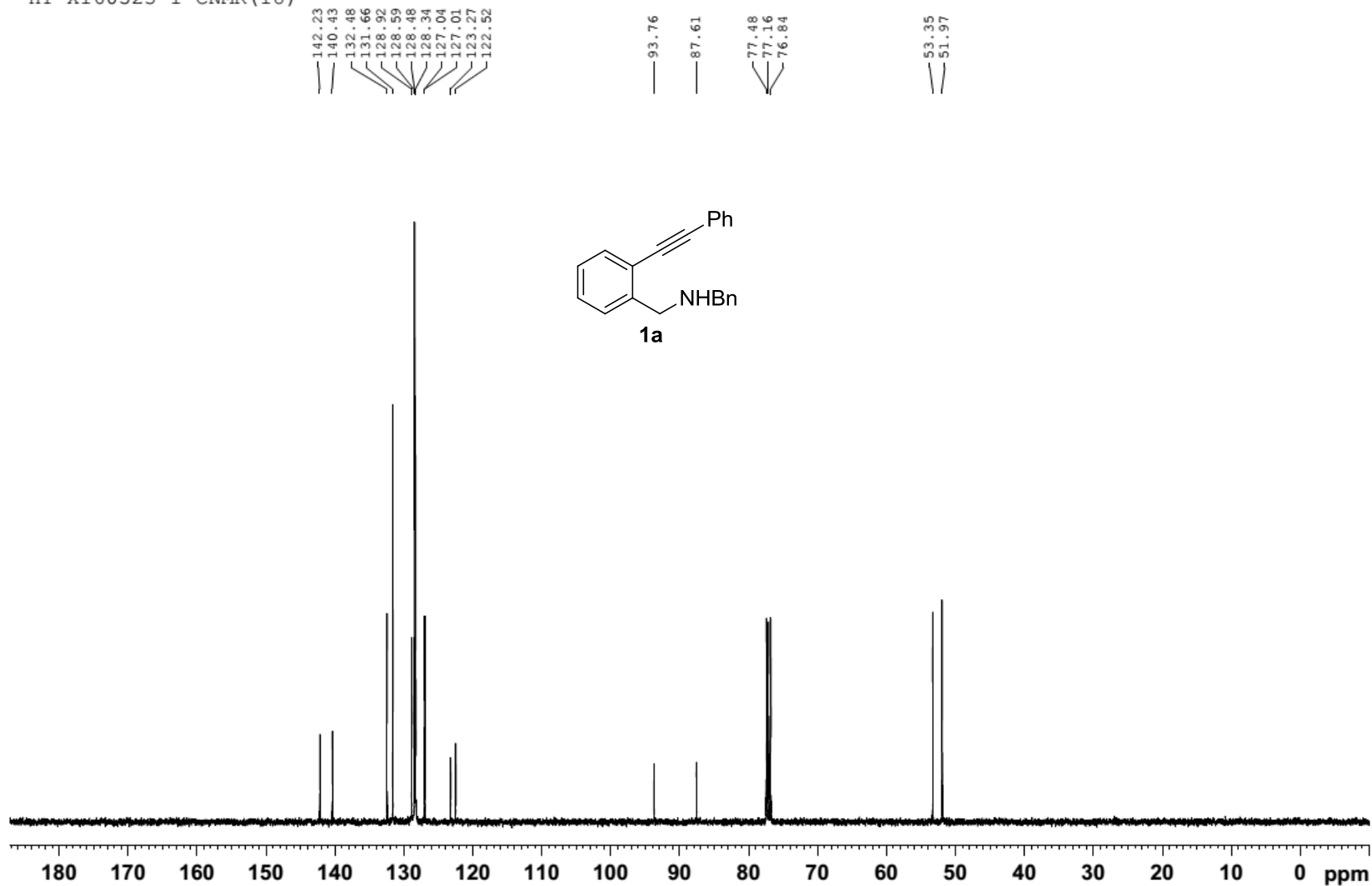
- (1) Park, J. H.; Bhilare, S. V.; Youn, S. W. *Org. Lett.* **2011**, *13*, 2228.
- (2) Lu, H.; Li, C.; Jiang, H.; Lizardi, C. L.; Zhang, X. P. *Angew. Chem. Int. Ed.* **2014**, *53*, 7028.
- (3) Shah, J. R.; Mosier, P. D.; Peddi, S.; Roth, B. L.; Westkaemper, R. B. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 935.
- (4) van der Linden, M.; Borsboom, J.; Kaspersen, F.; Kemperman, G. *Eur. J. Org. Chem.* **2008**, 2989.
- (5) Qian, M.; Negishi, E. *Tetrahedron Lett.* **2005**, *46*, 2927.
- (6) Lee, Y.; Klausen, R. S.; Jacobsen, E. N. *Org. Lett.* **2011**, *13*, 5564.

## **7. Copies for $^1\text{H}$ NMR and $^{13}\text{C}$ NMR**

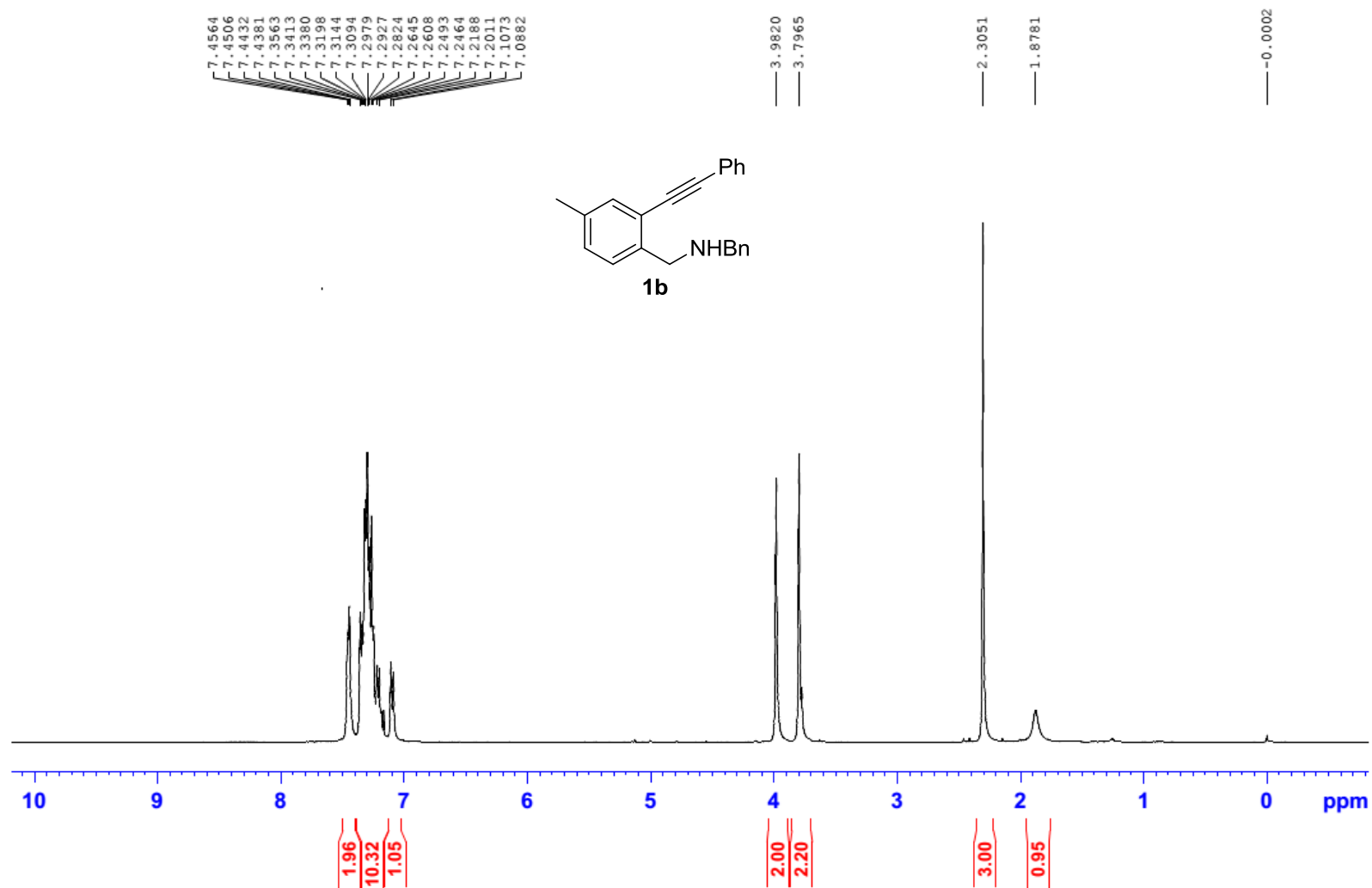
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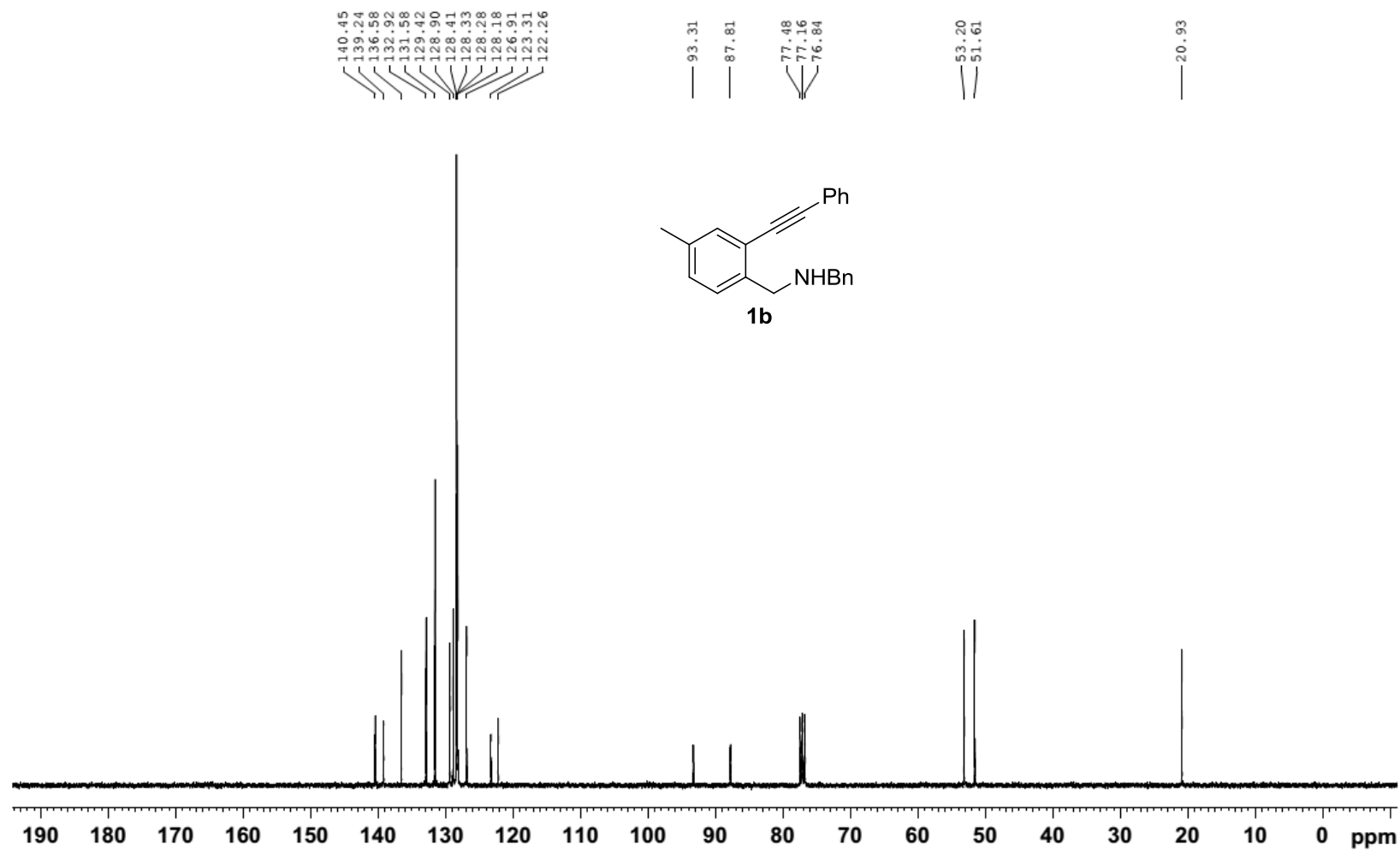
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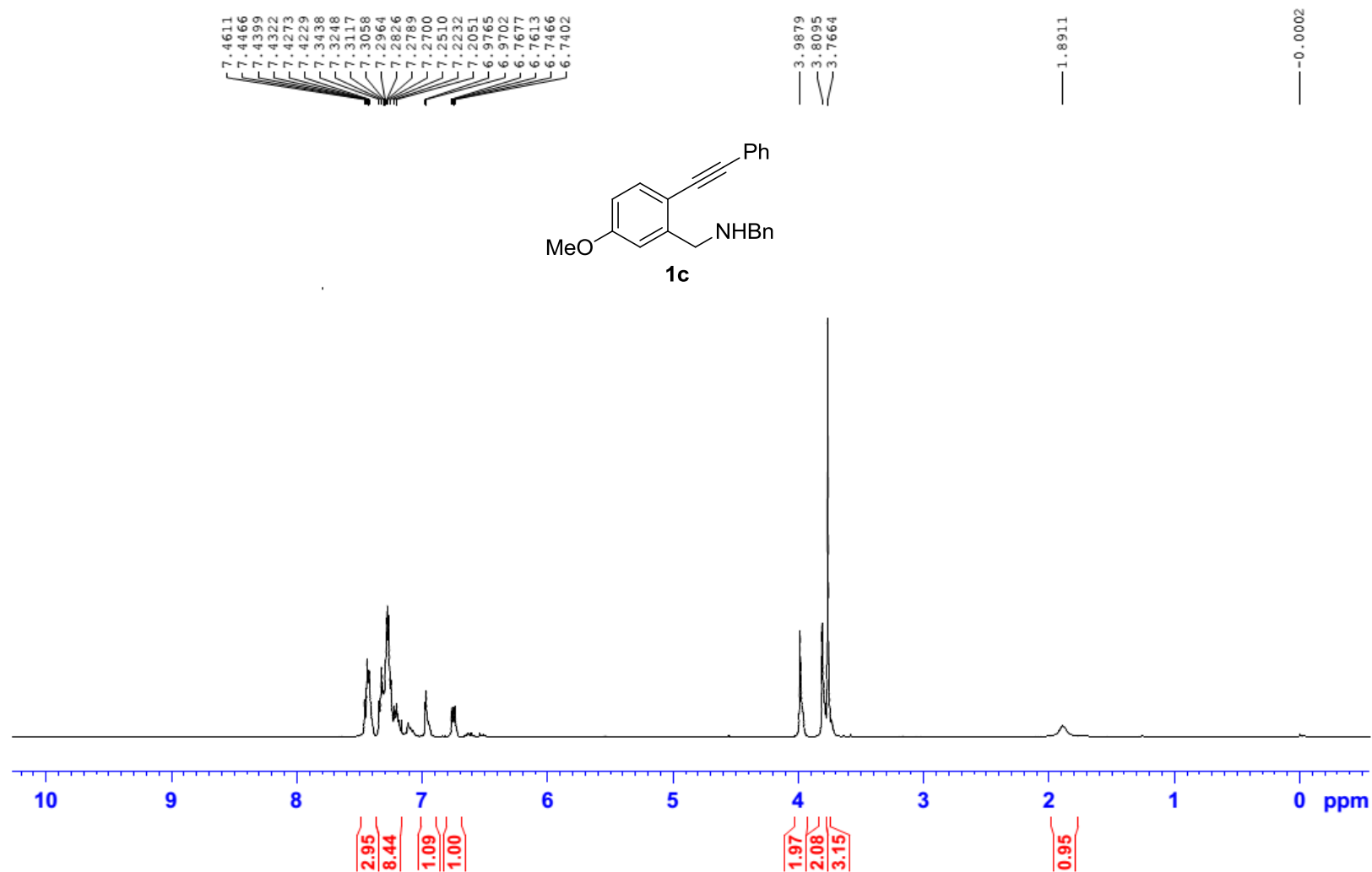
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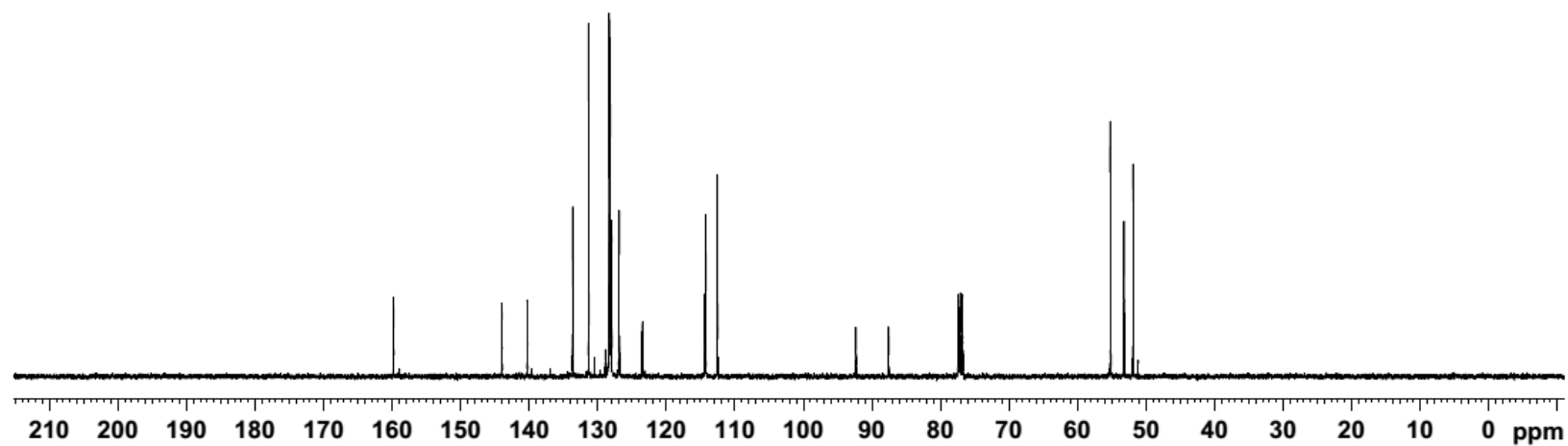
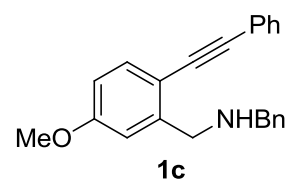


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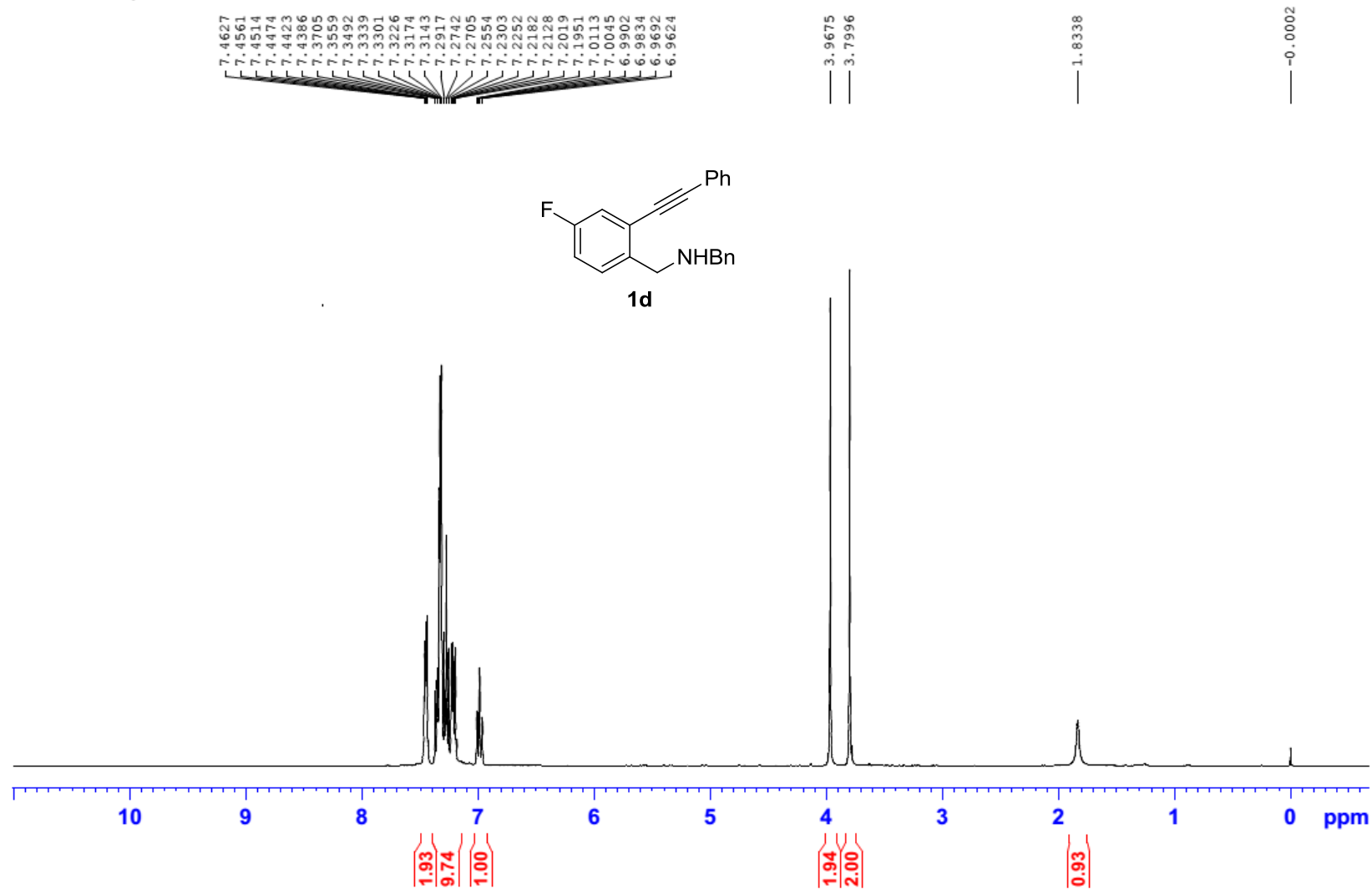




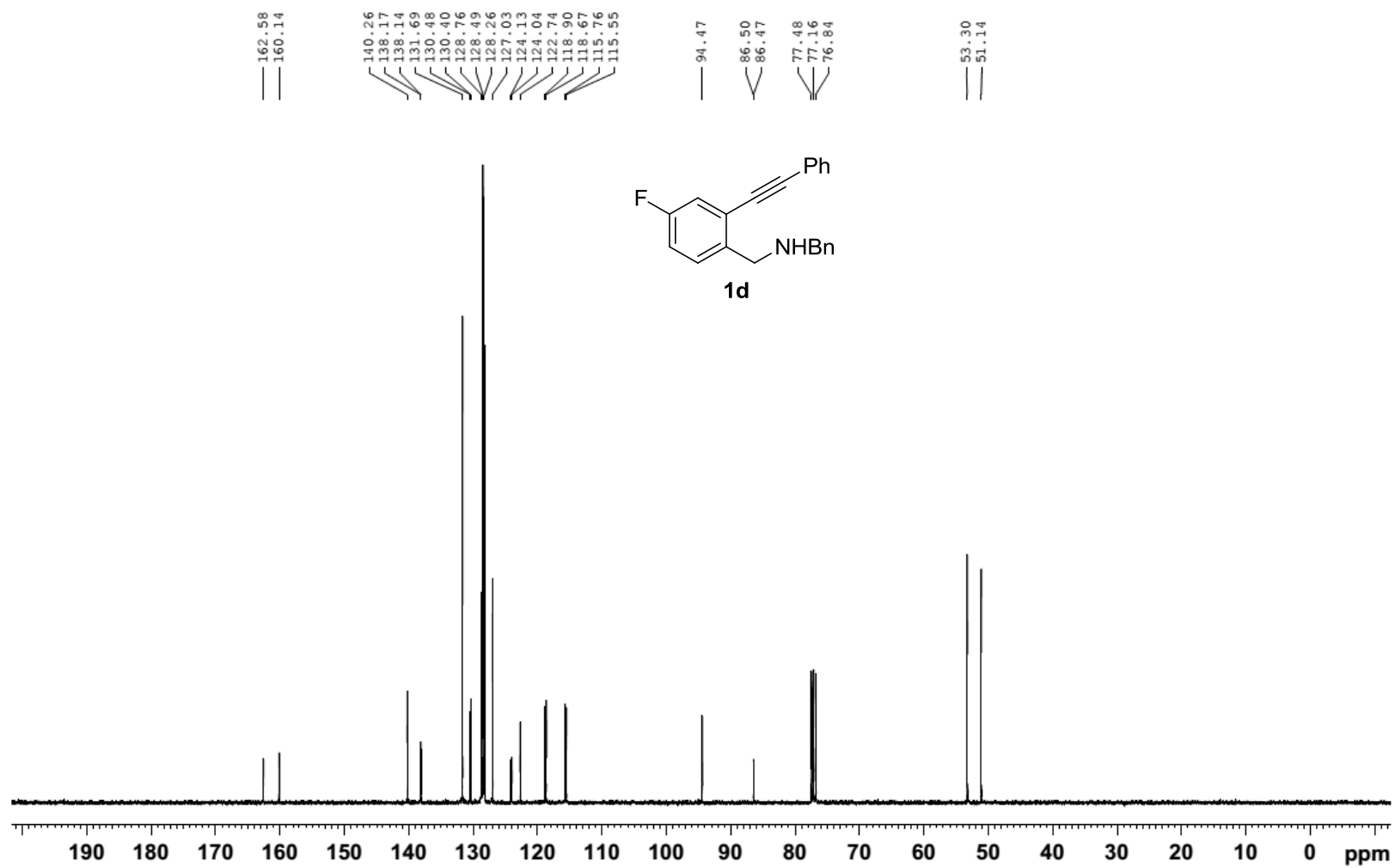
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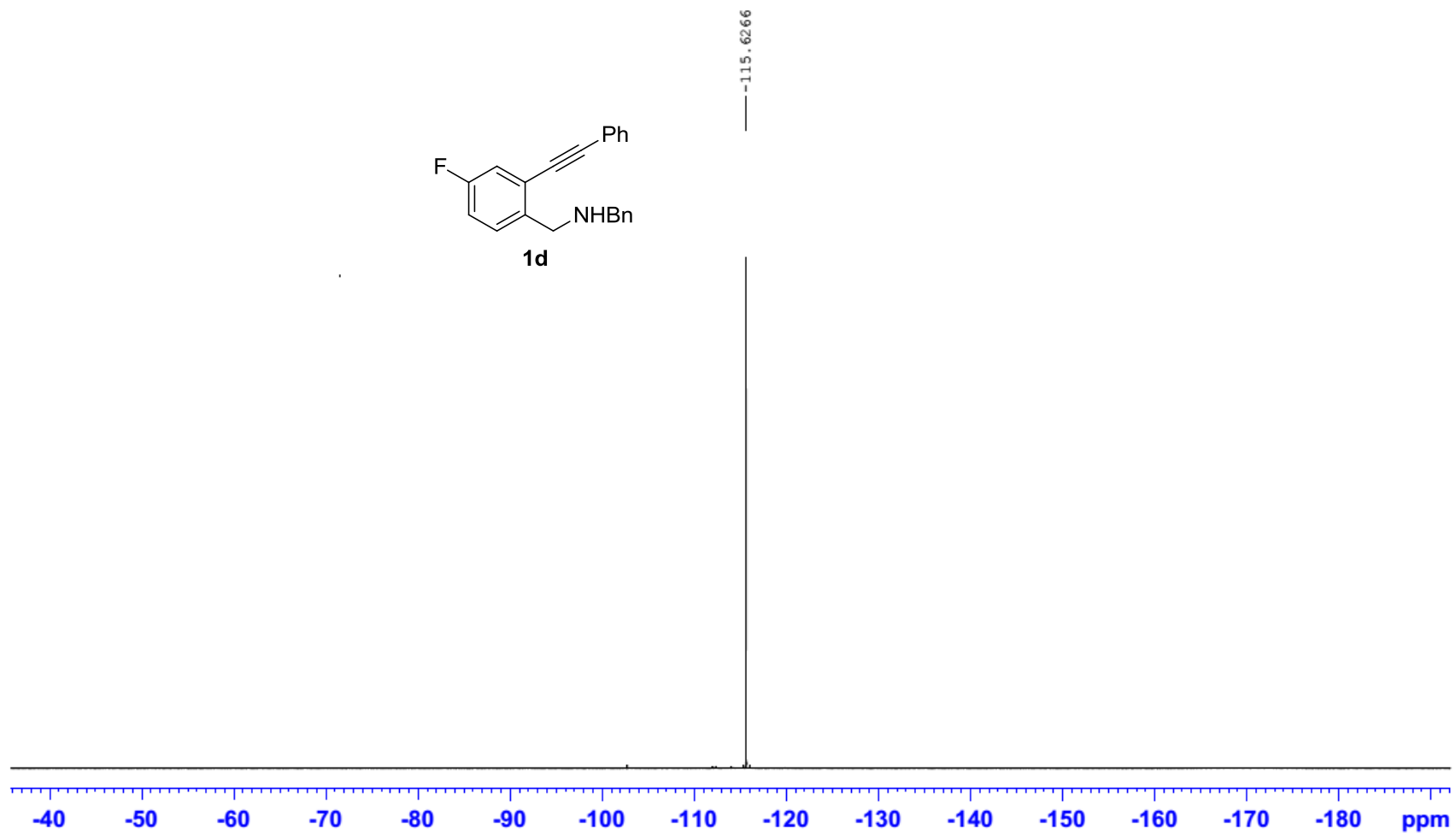
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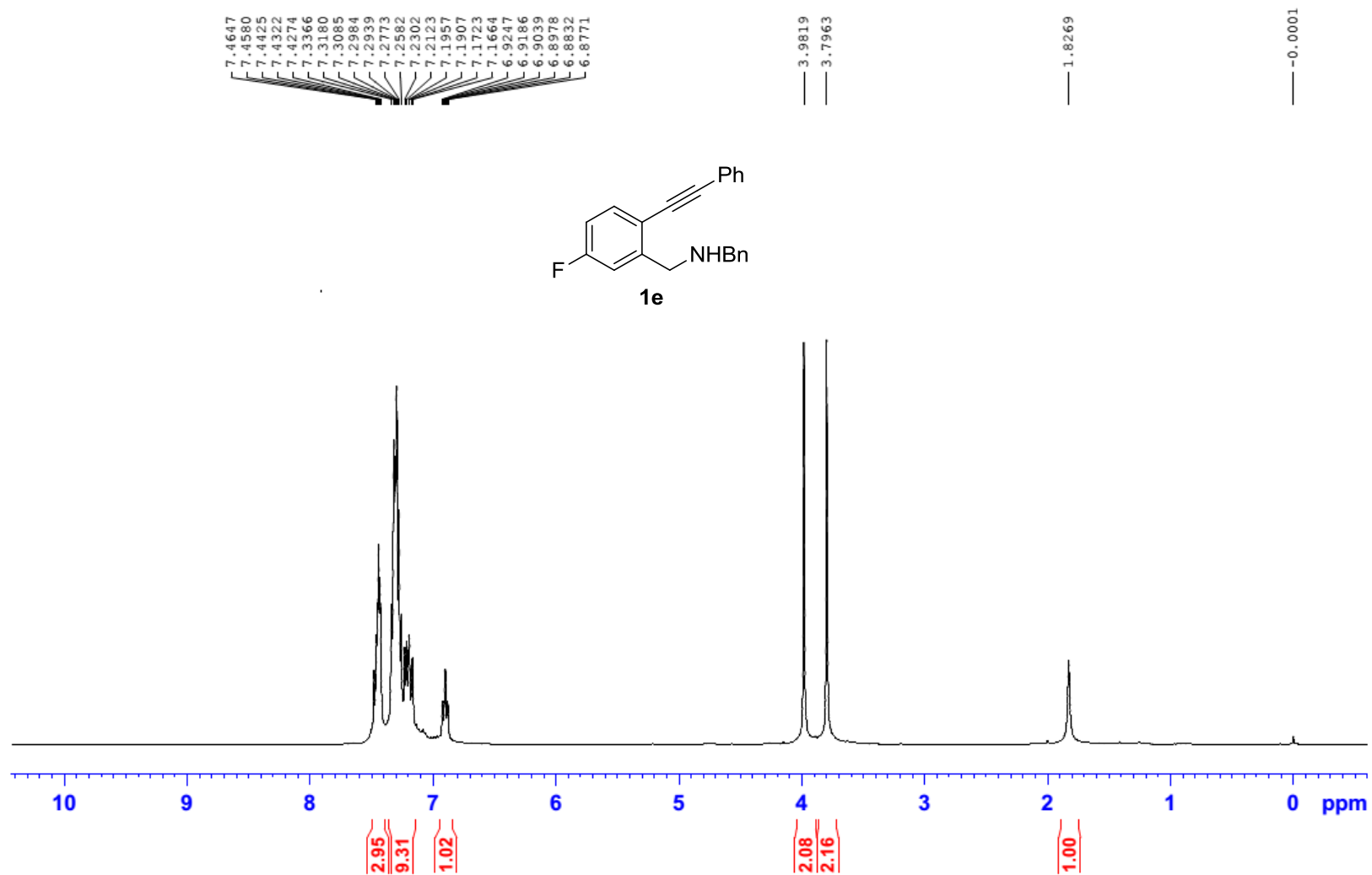
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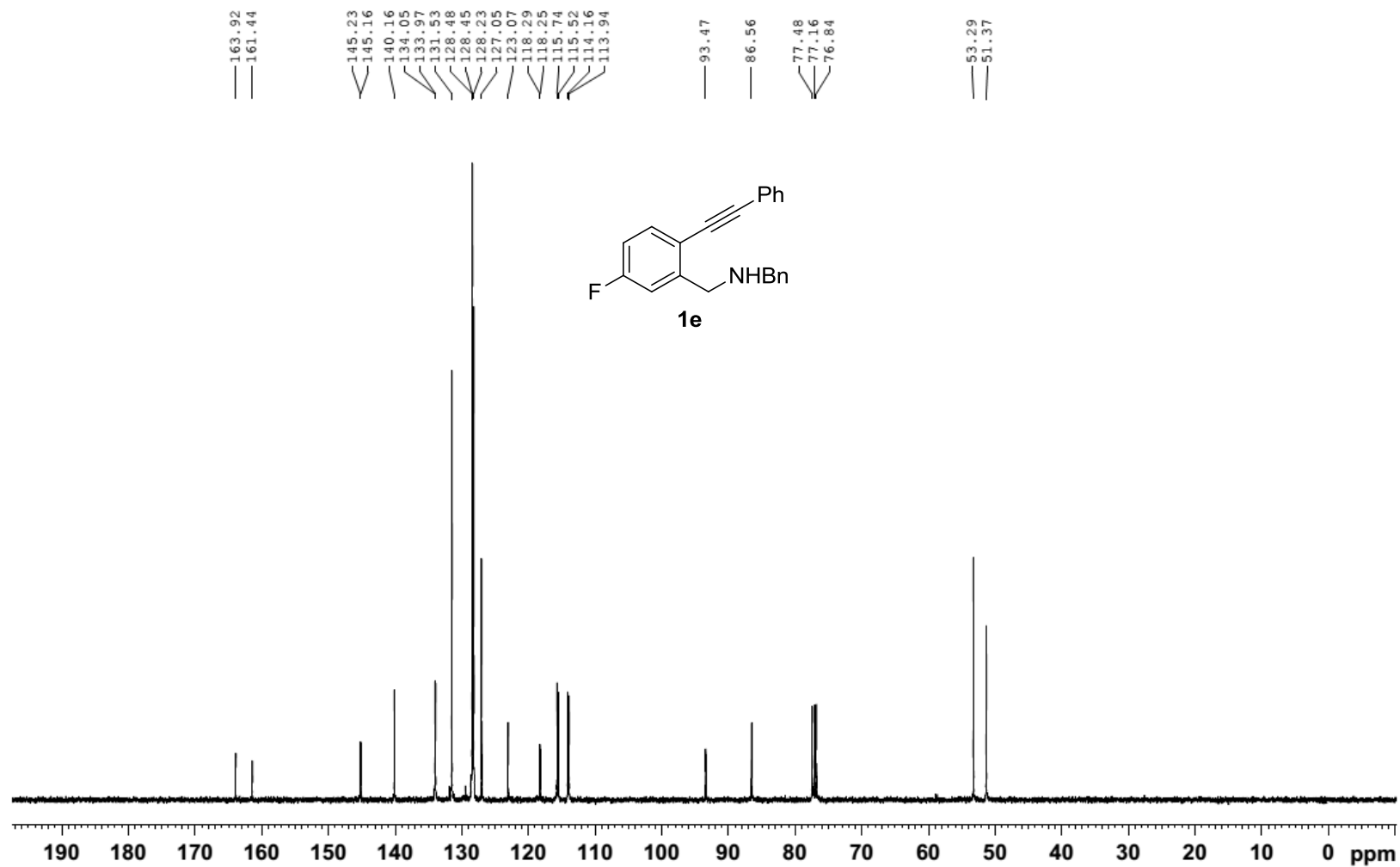
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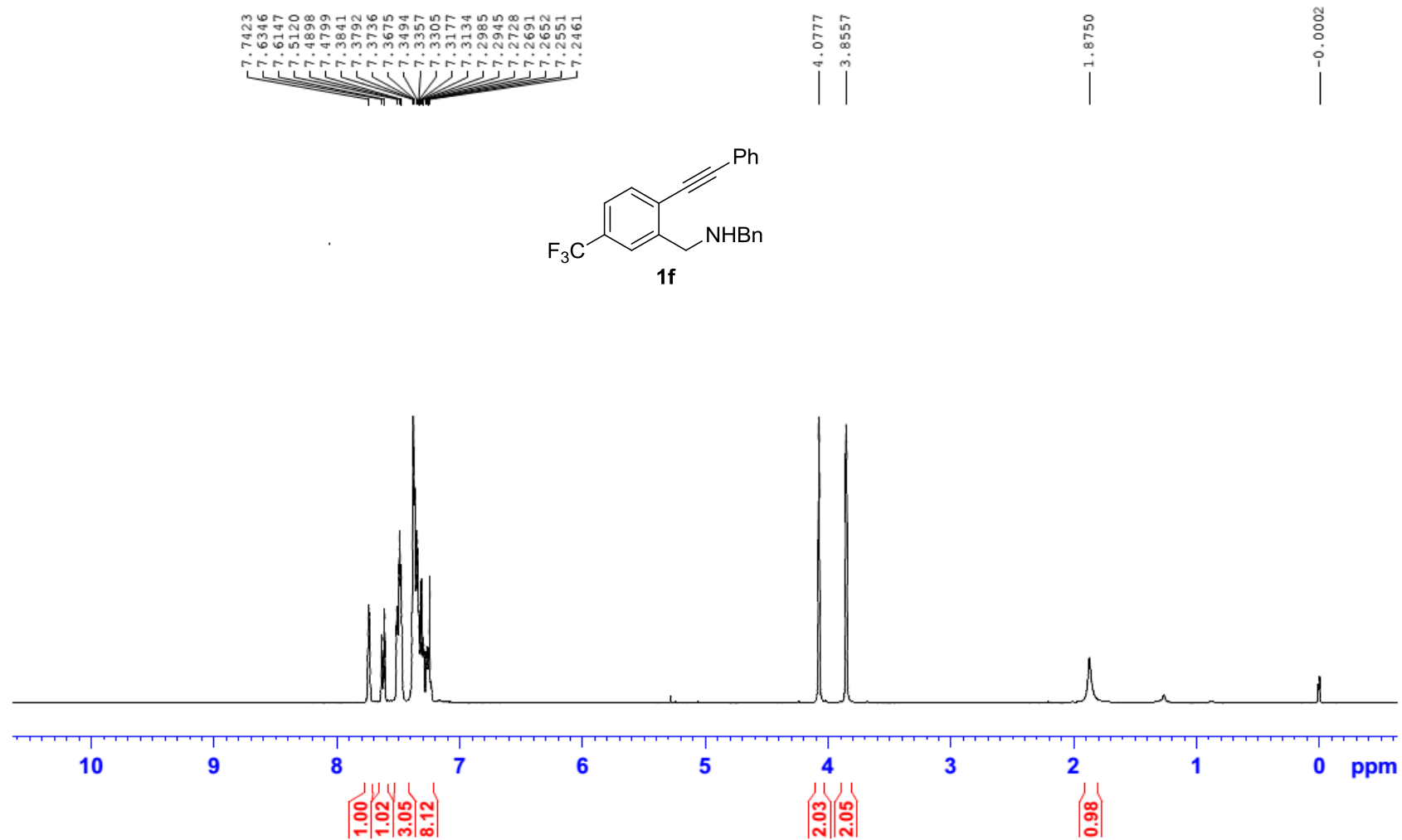
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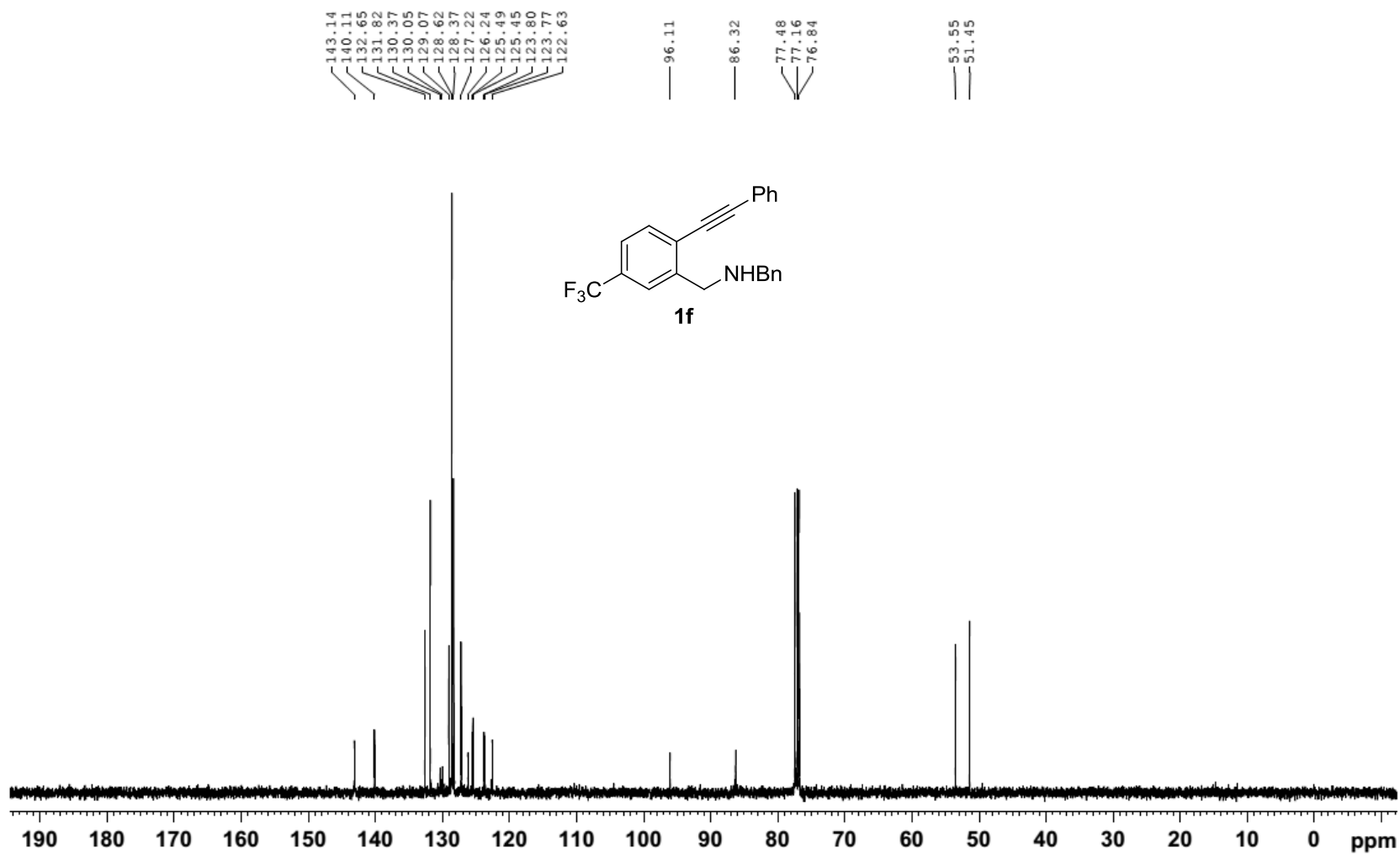


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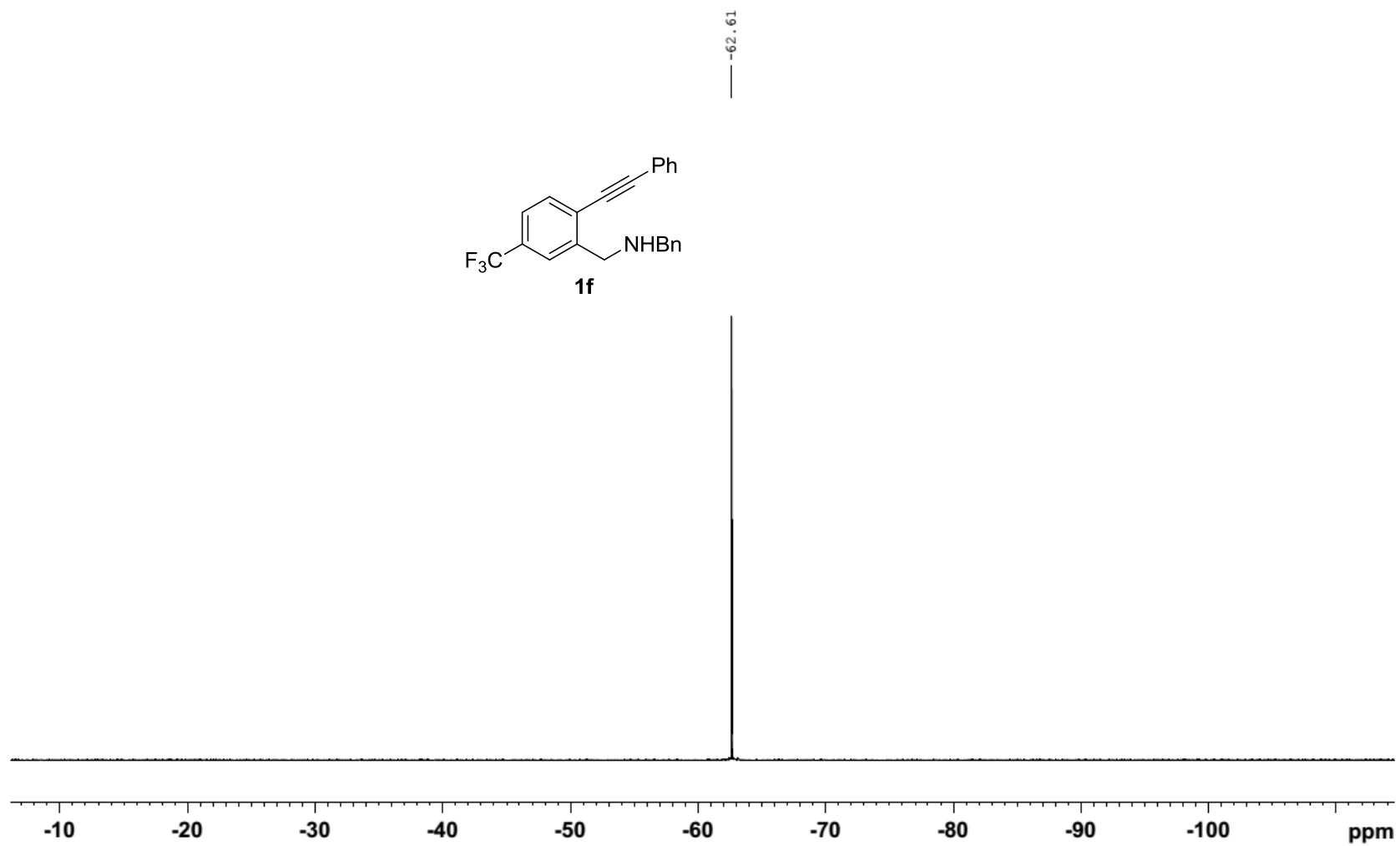




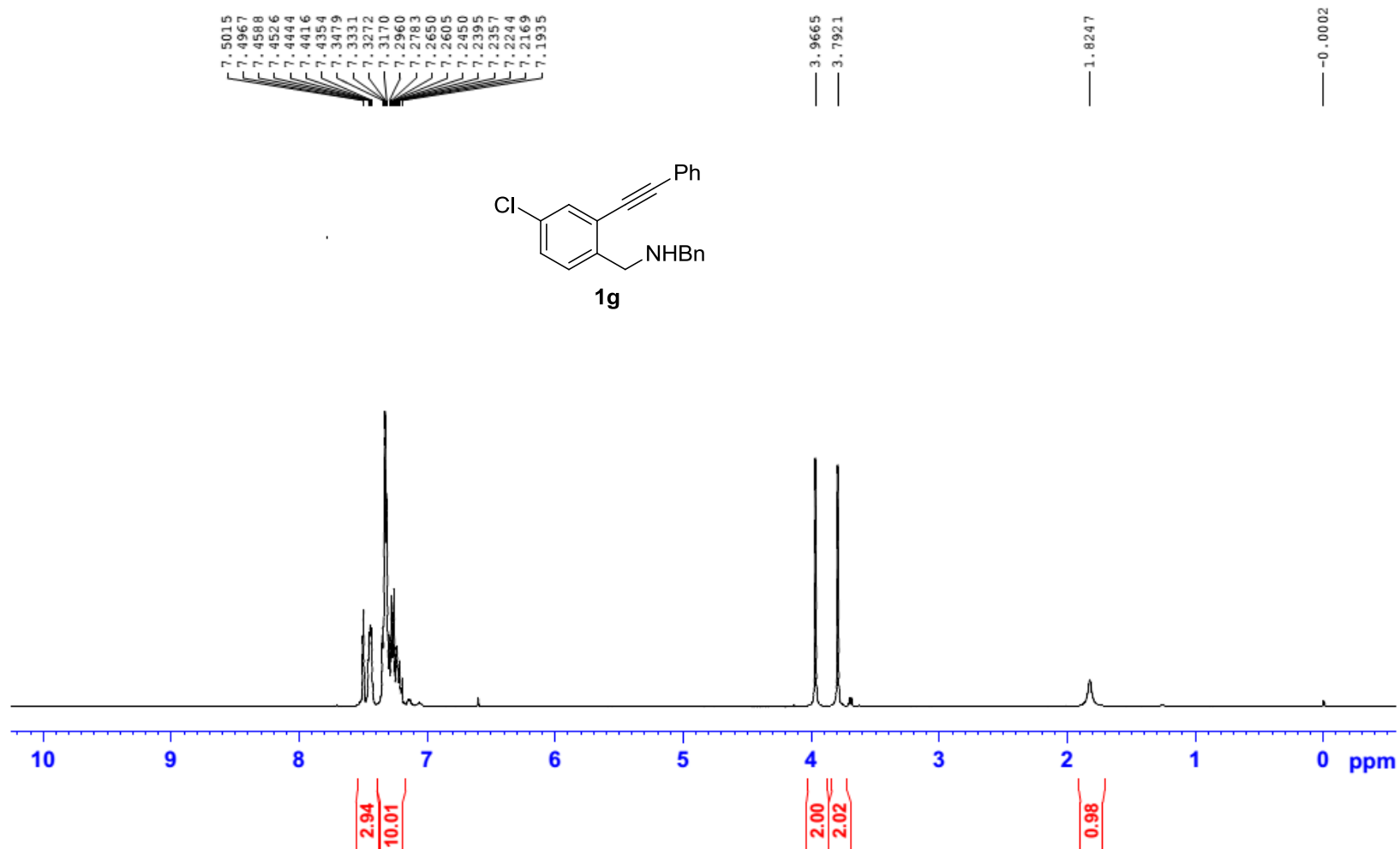
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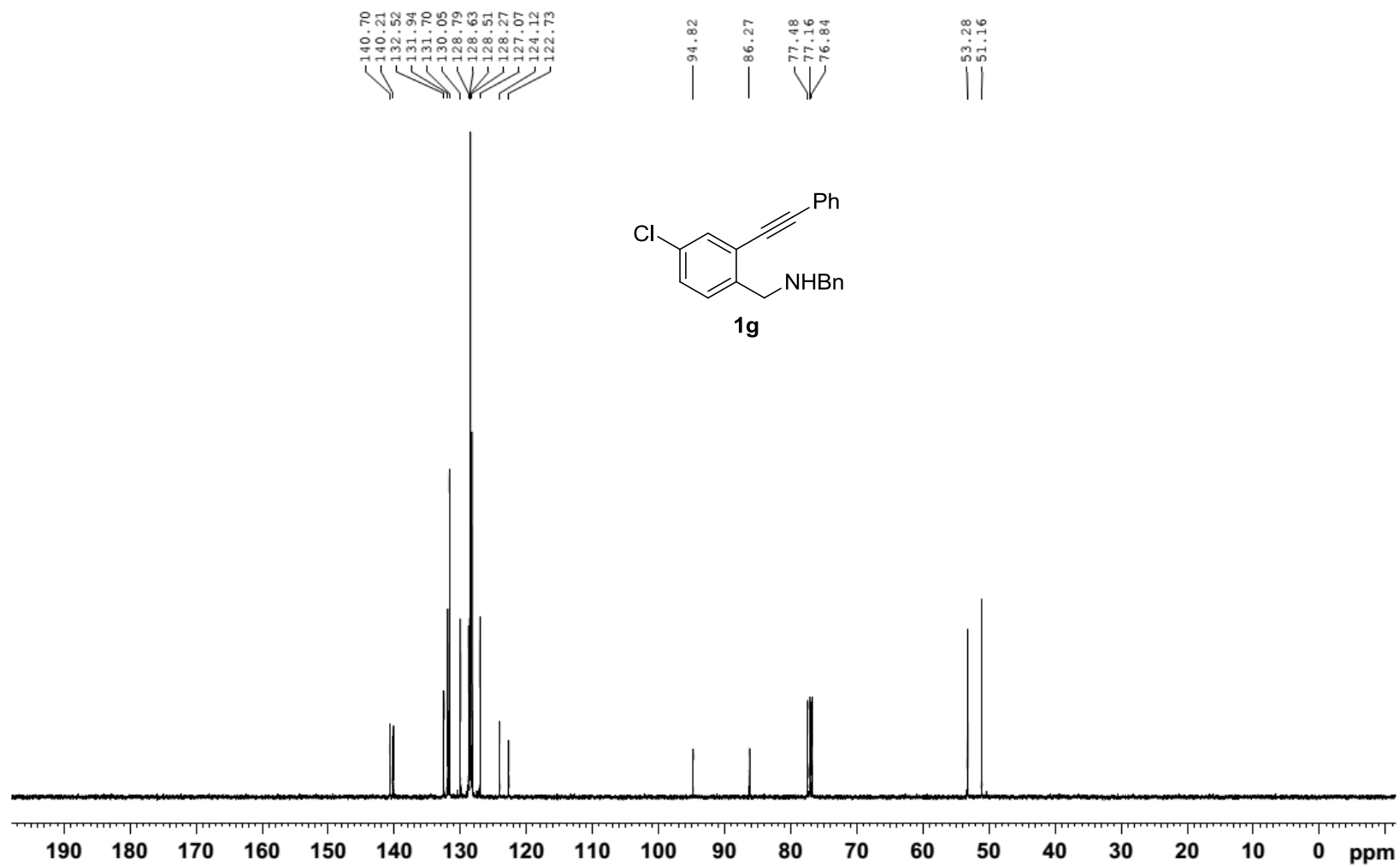
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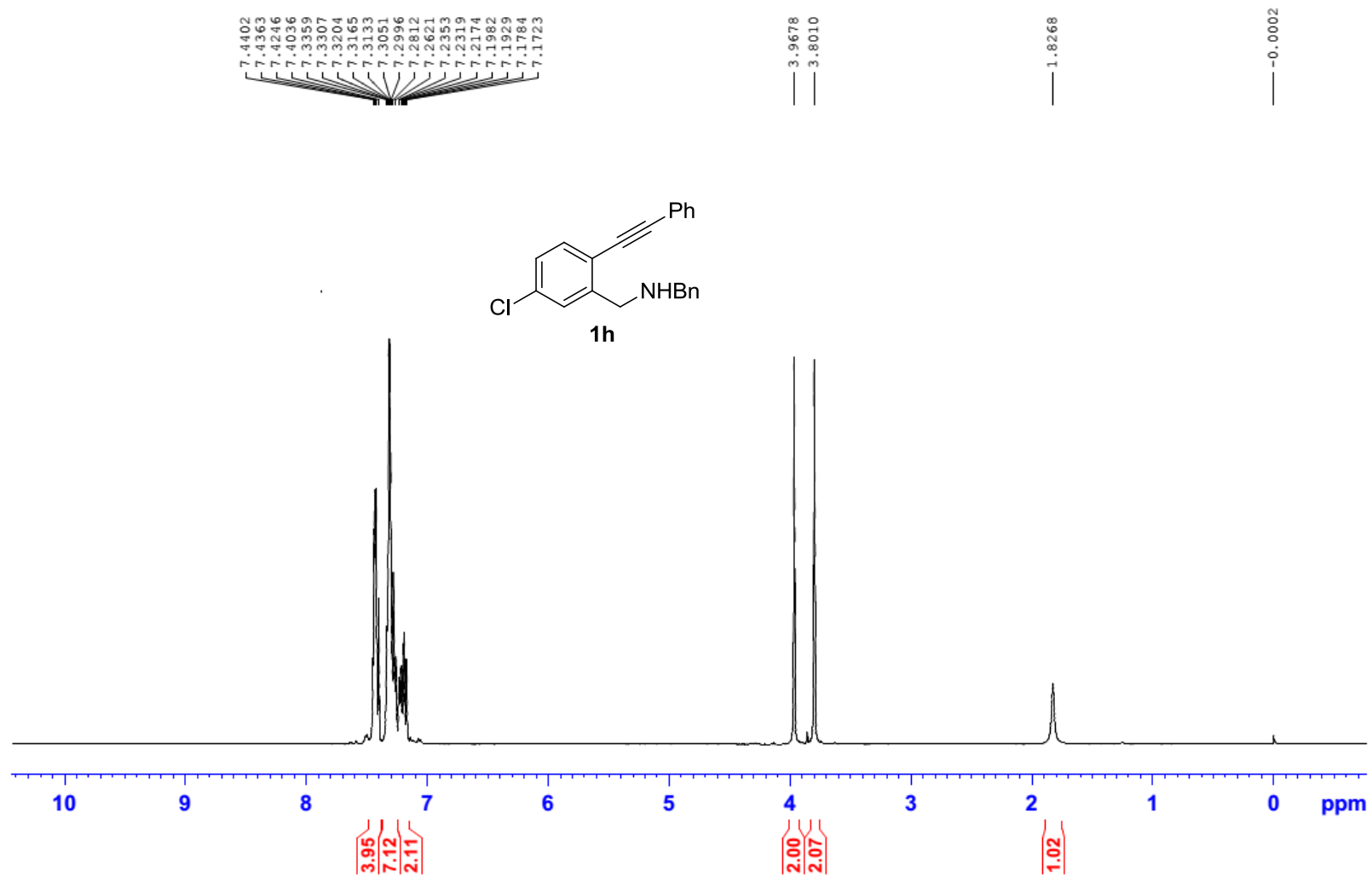
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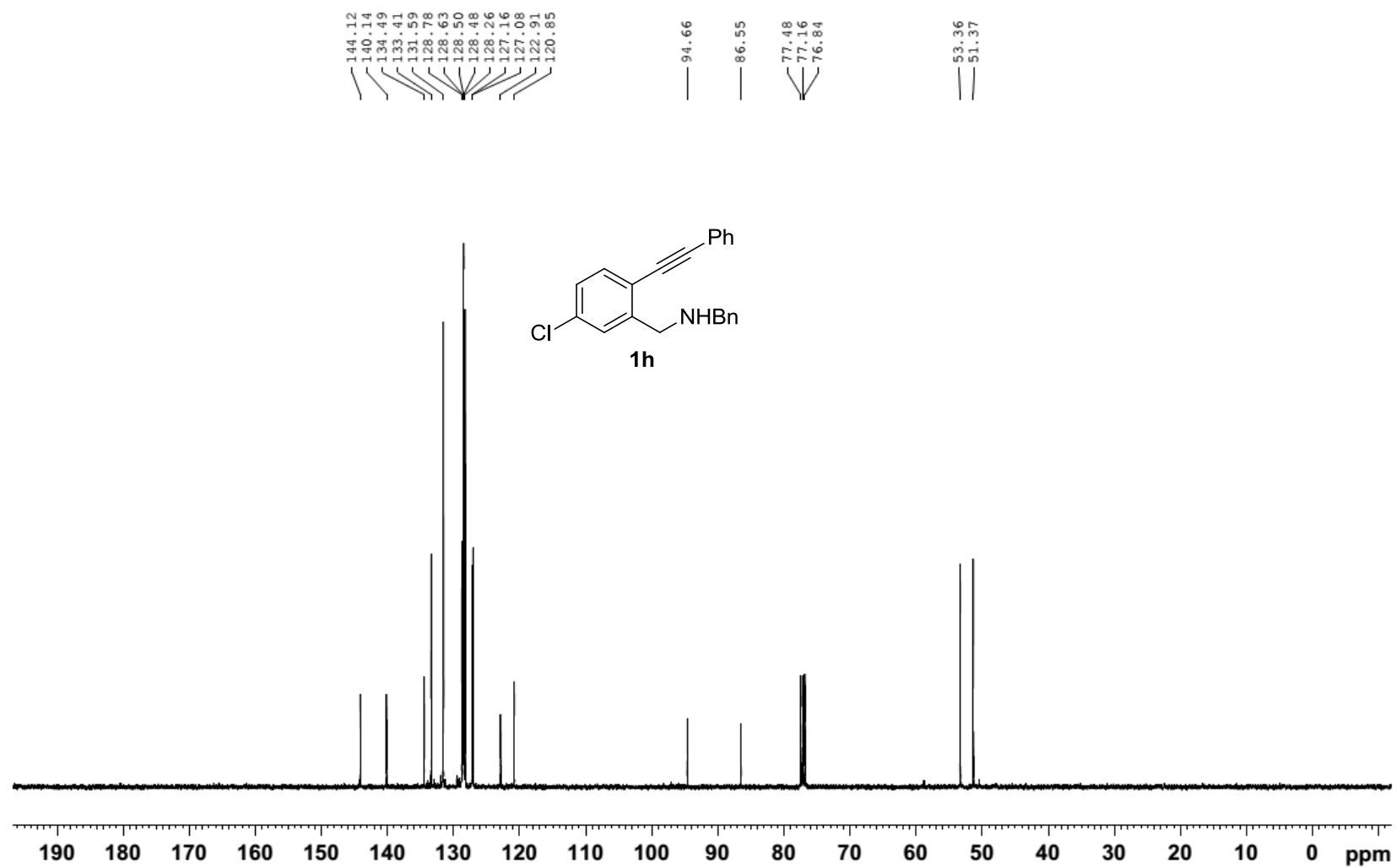
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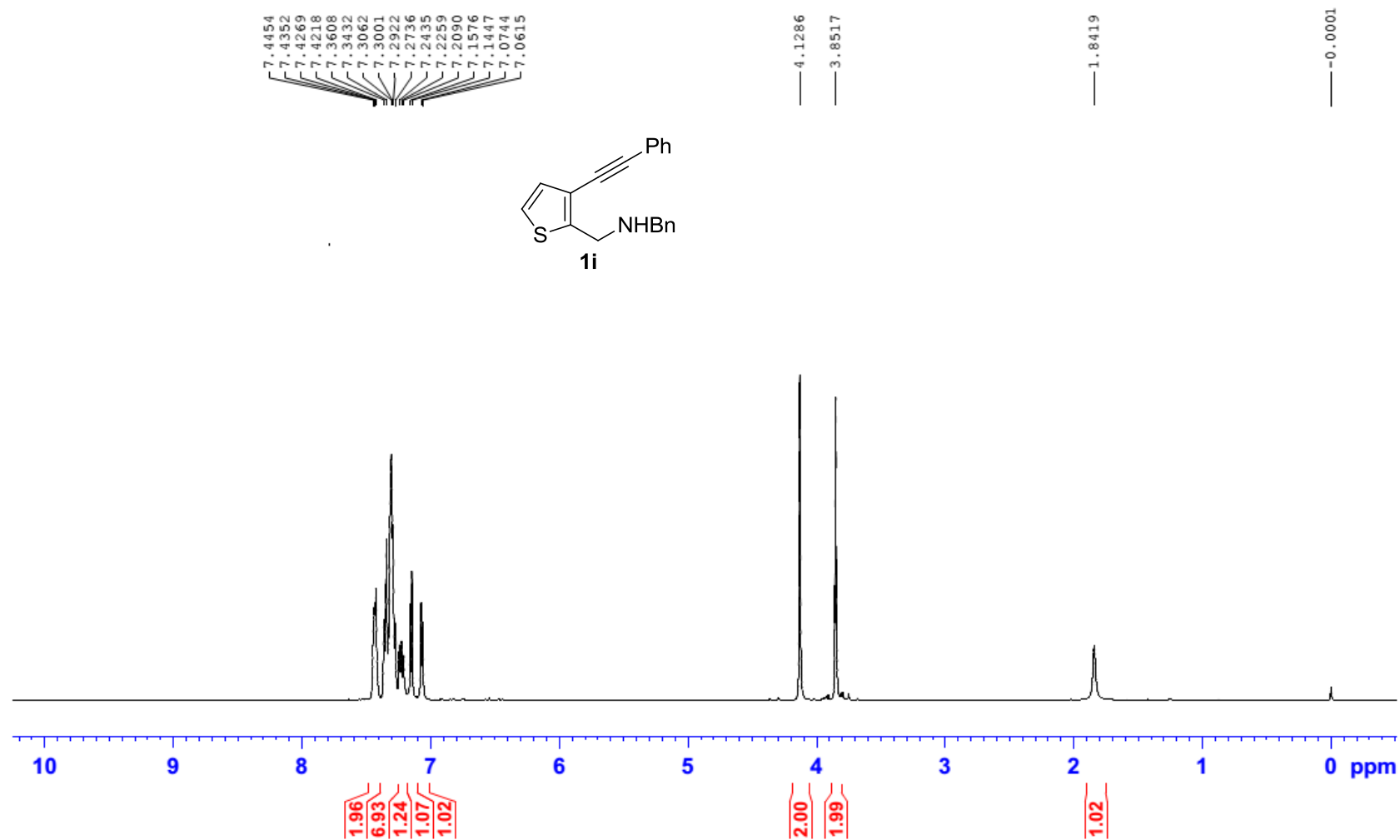
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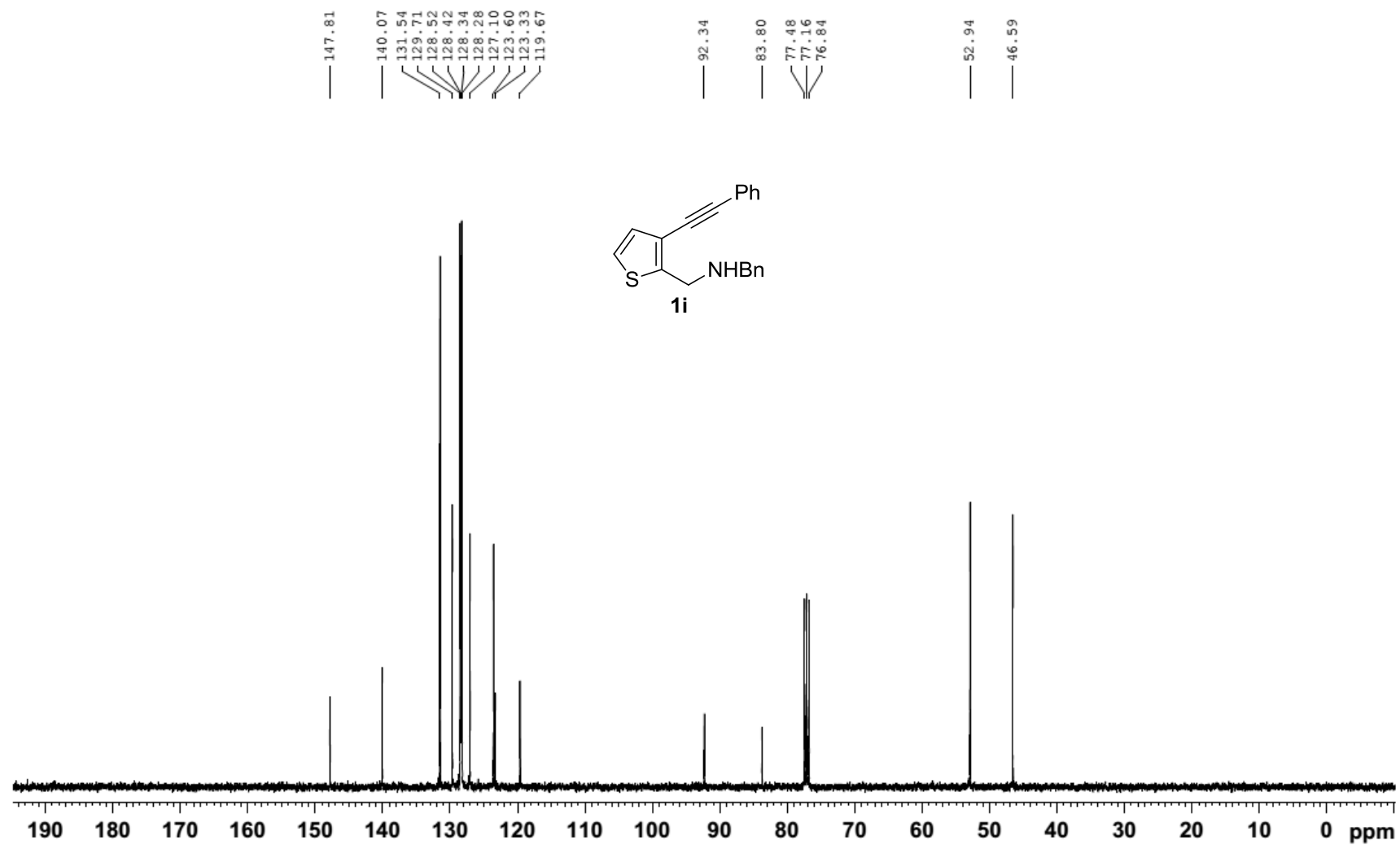
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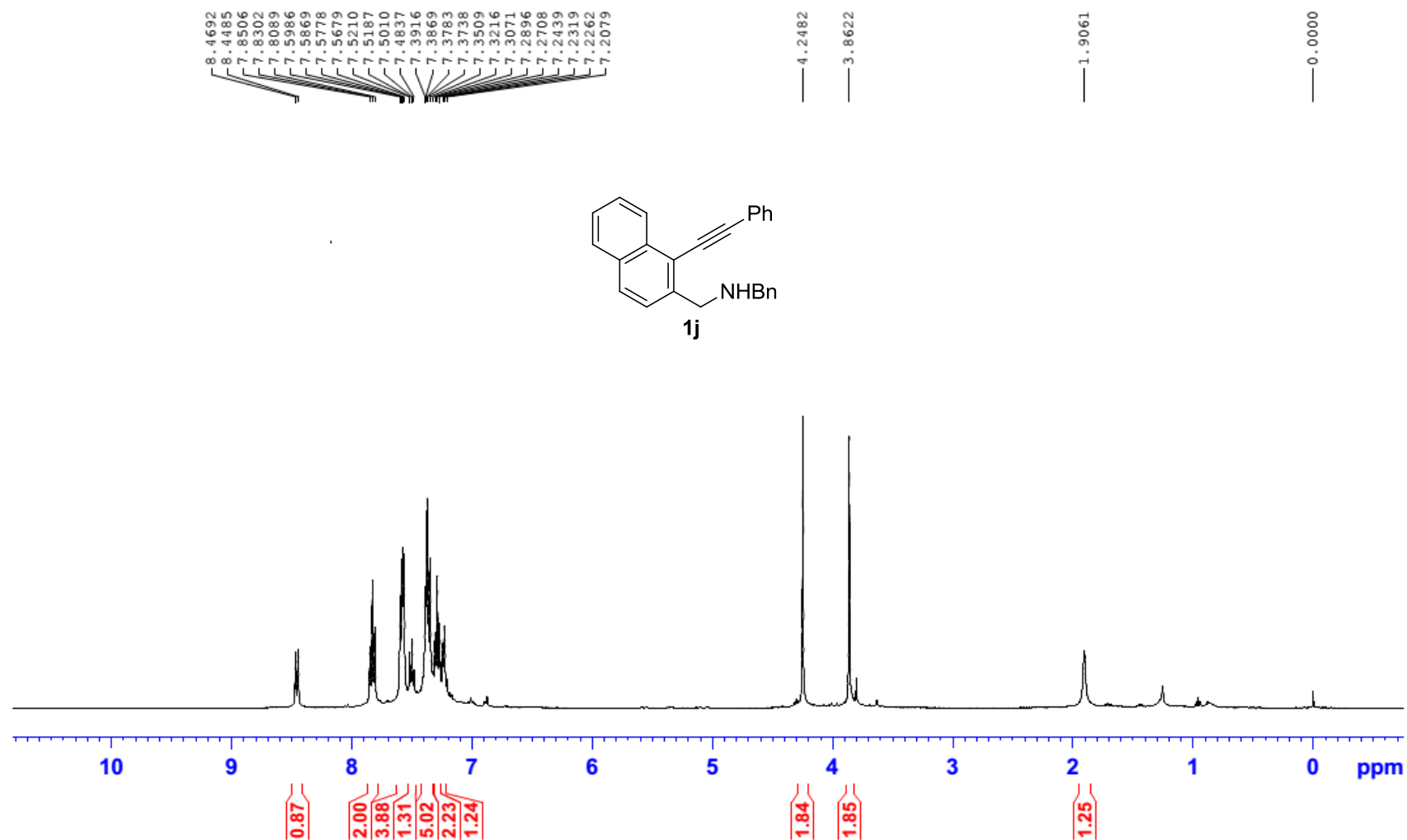


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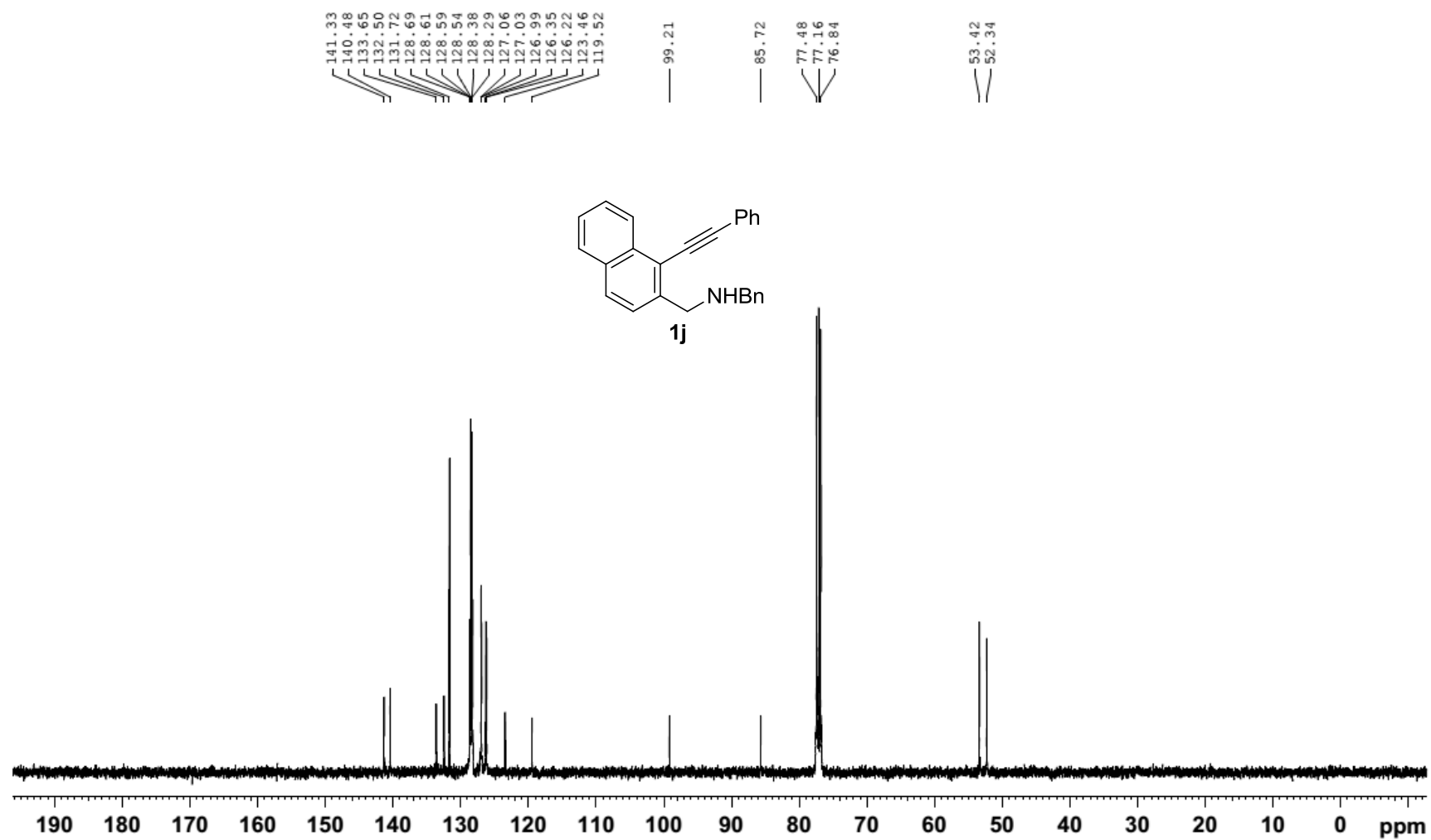




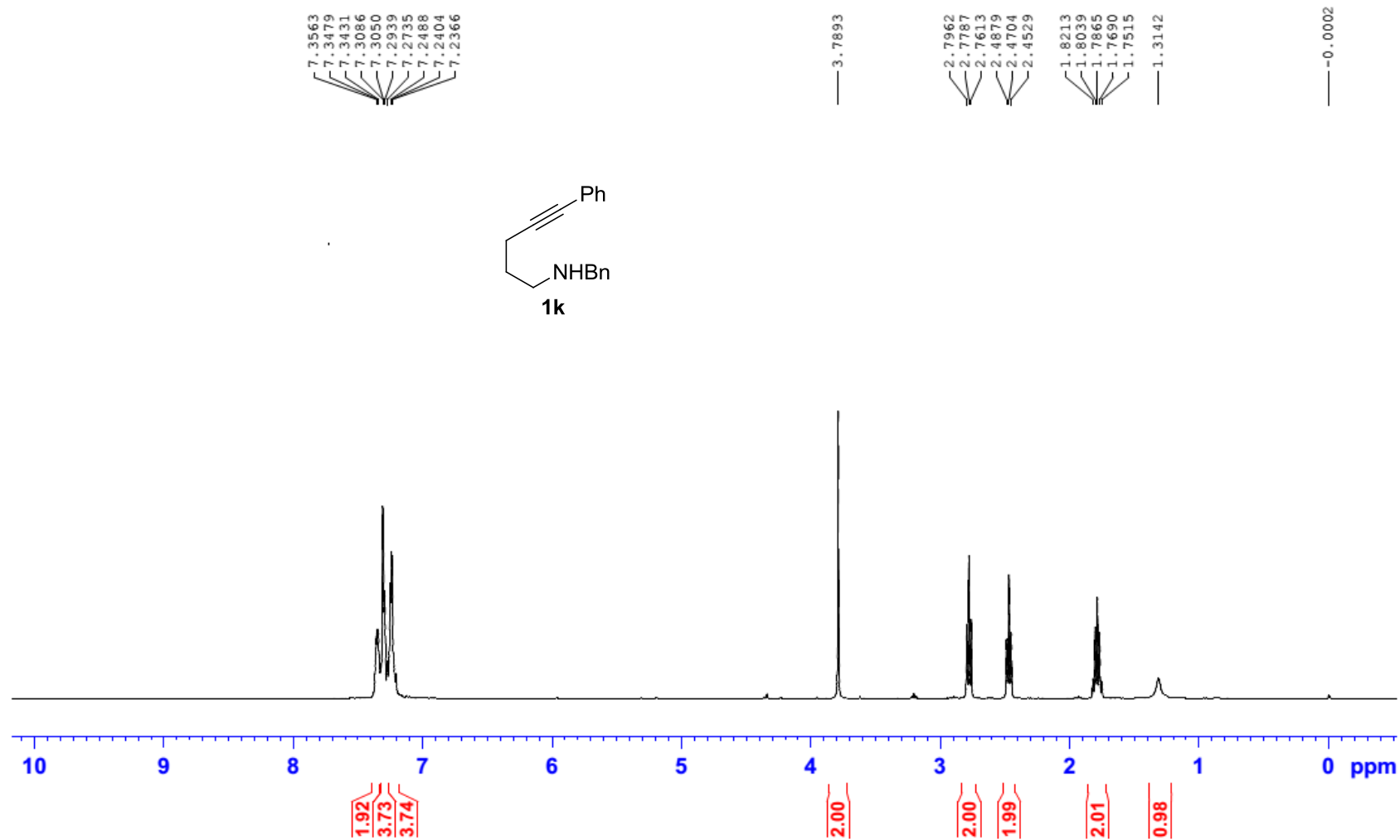
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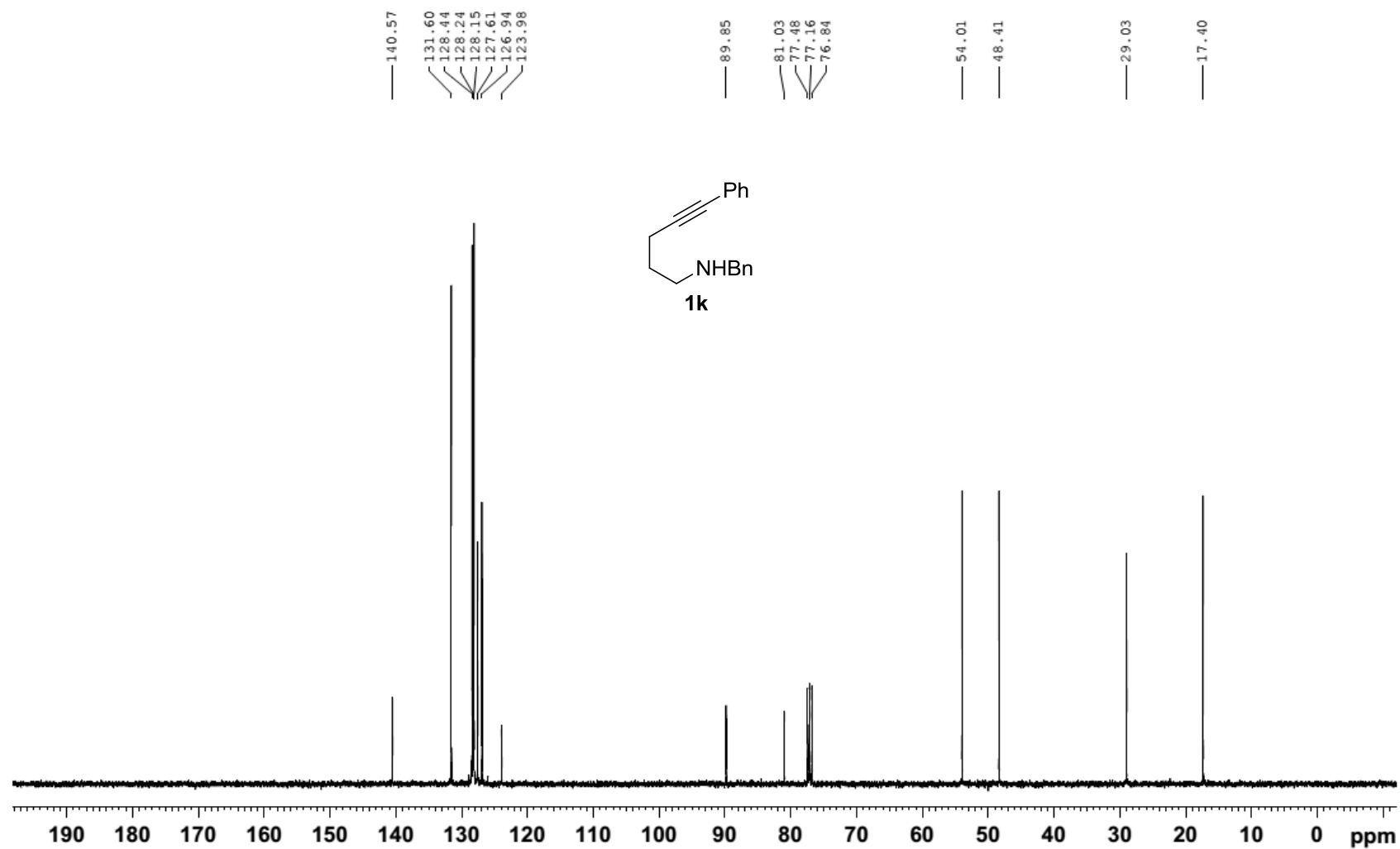
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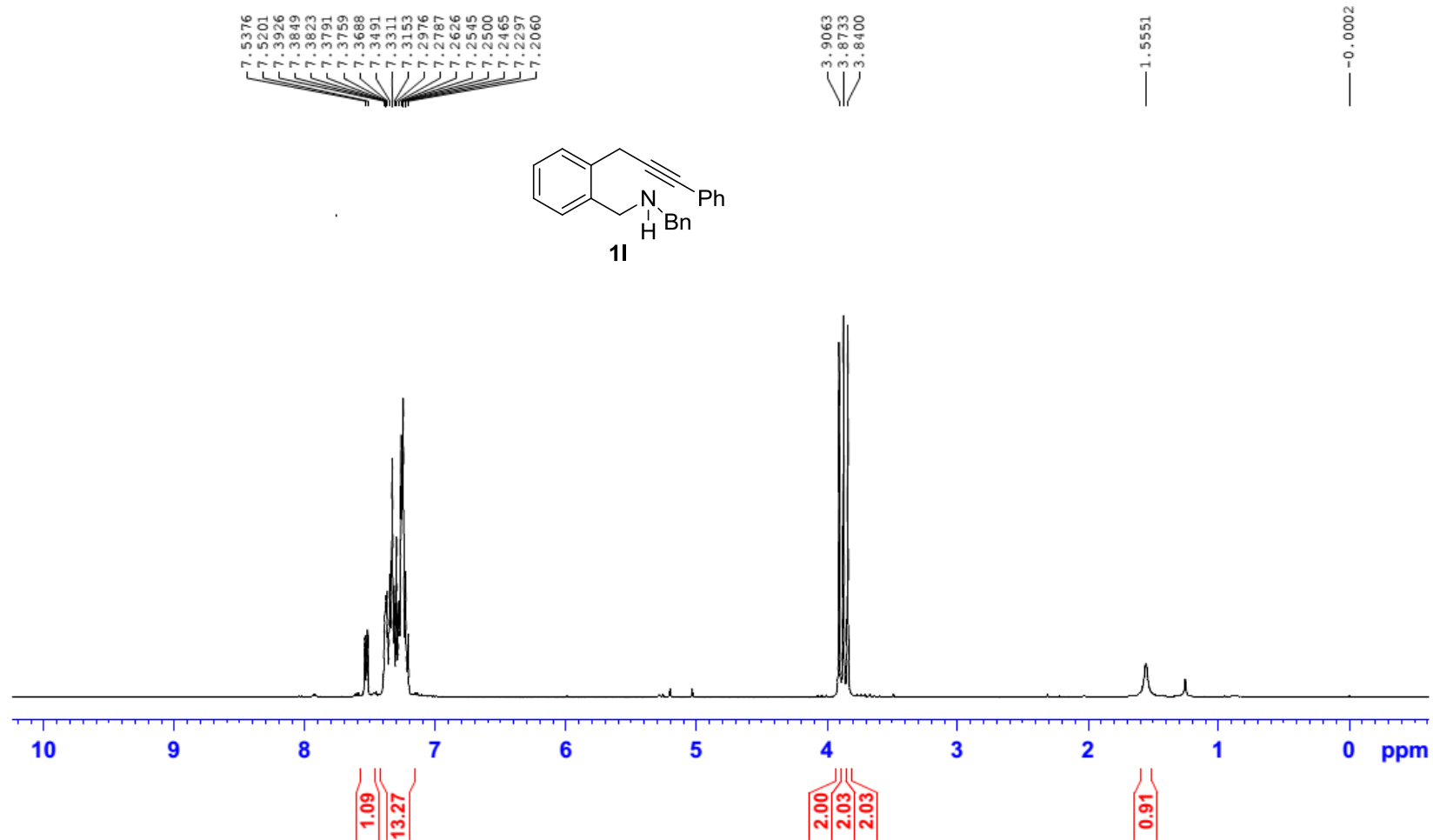
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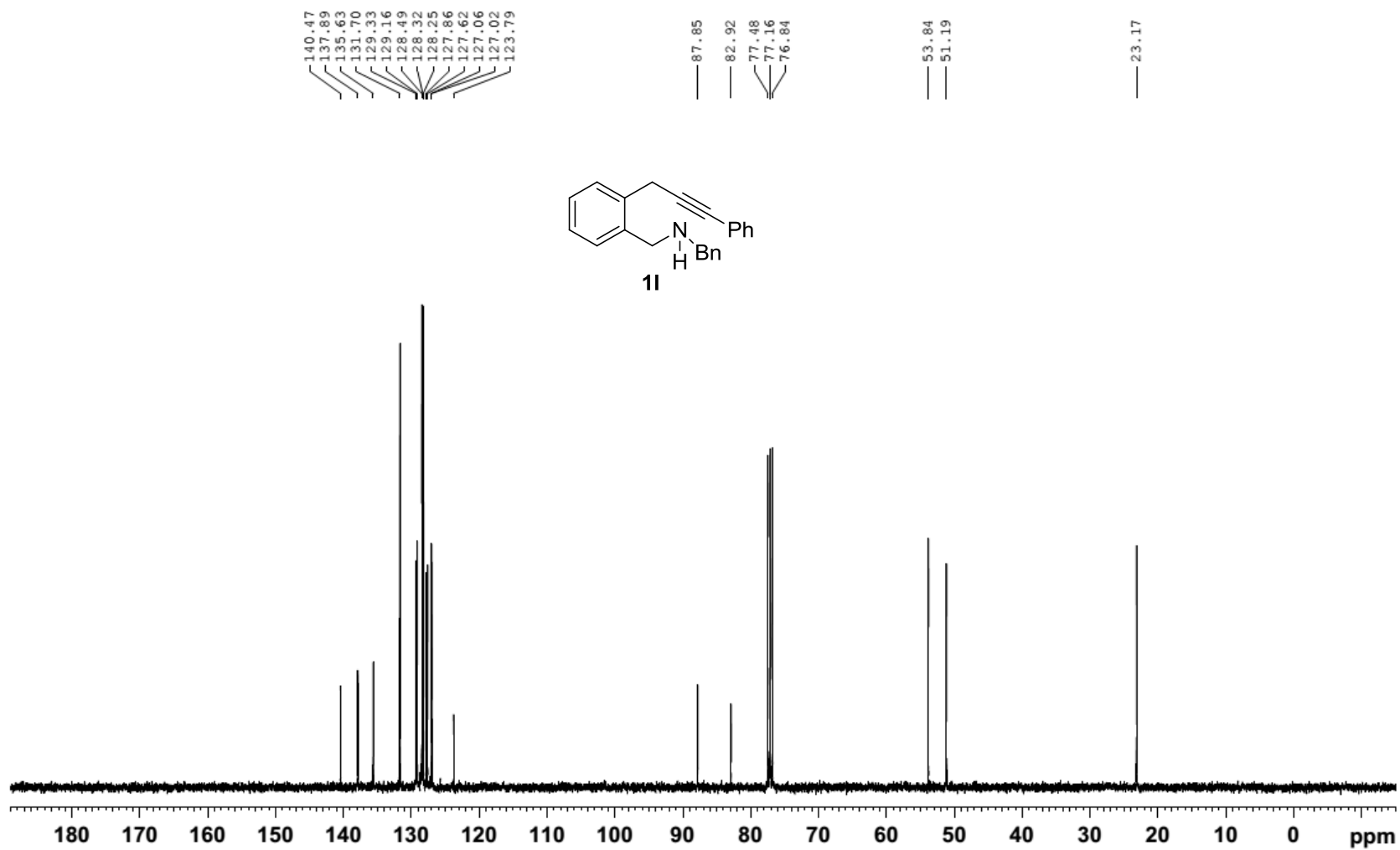
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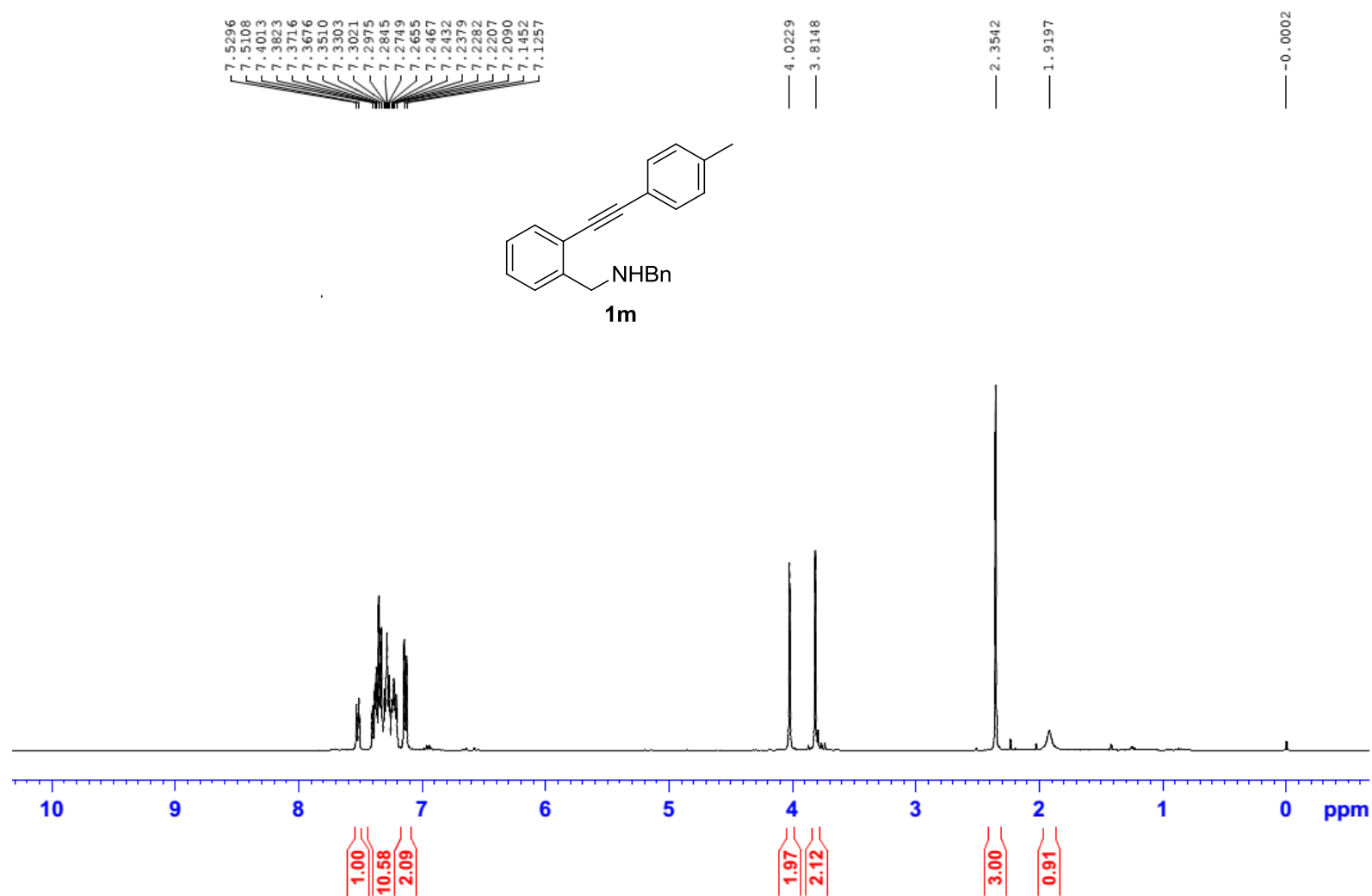
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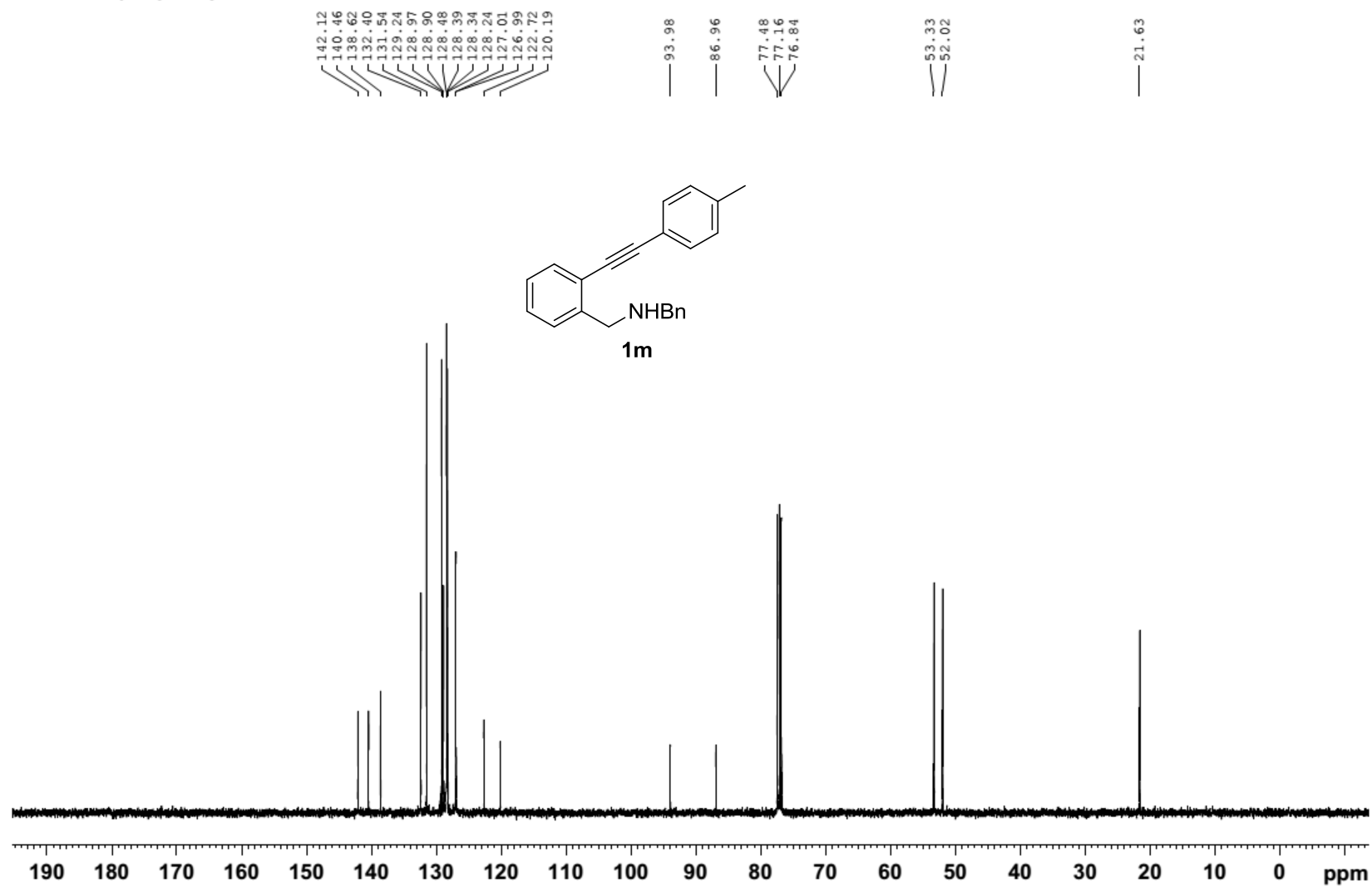
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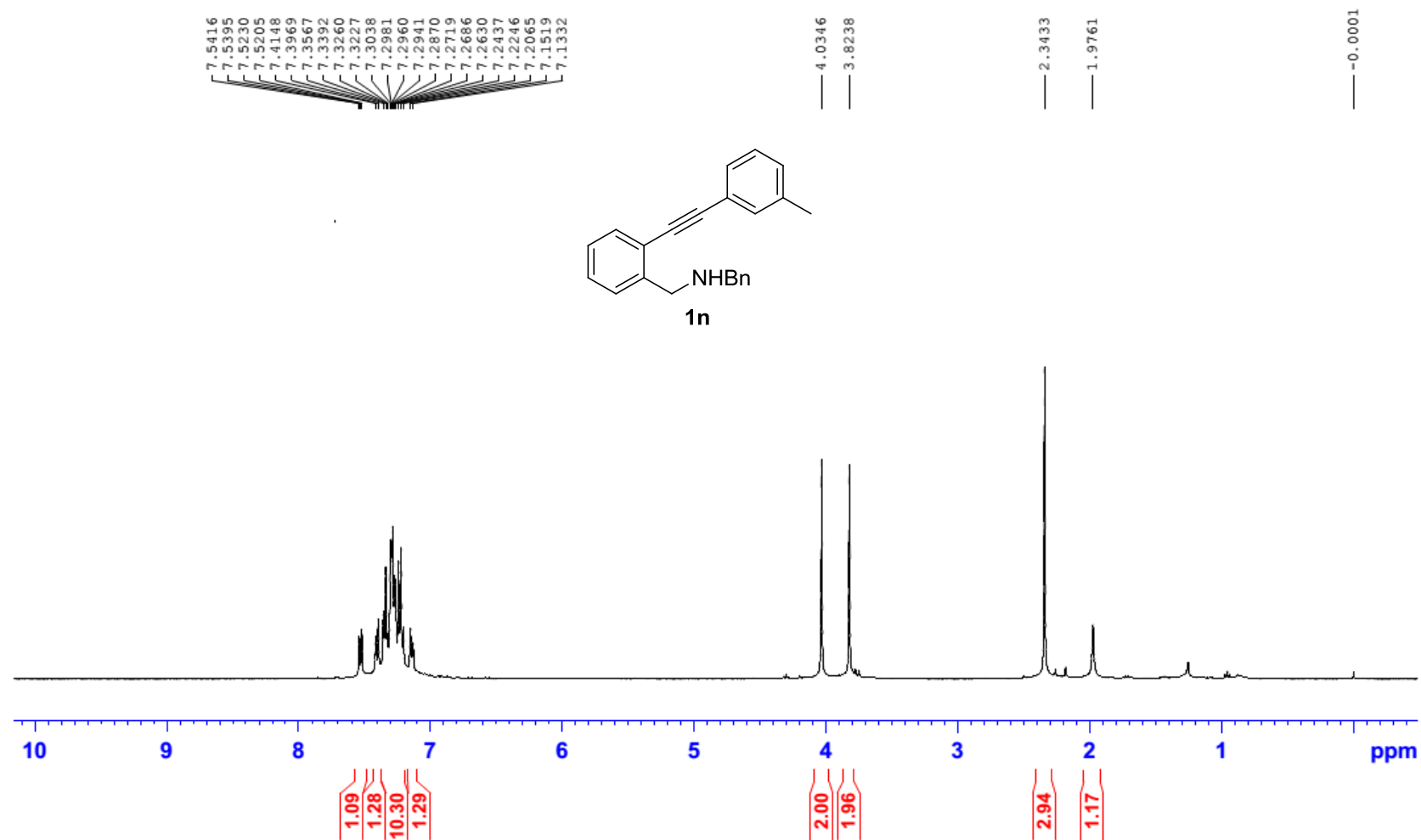


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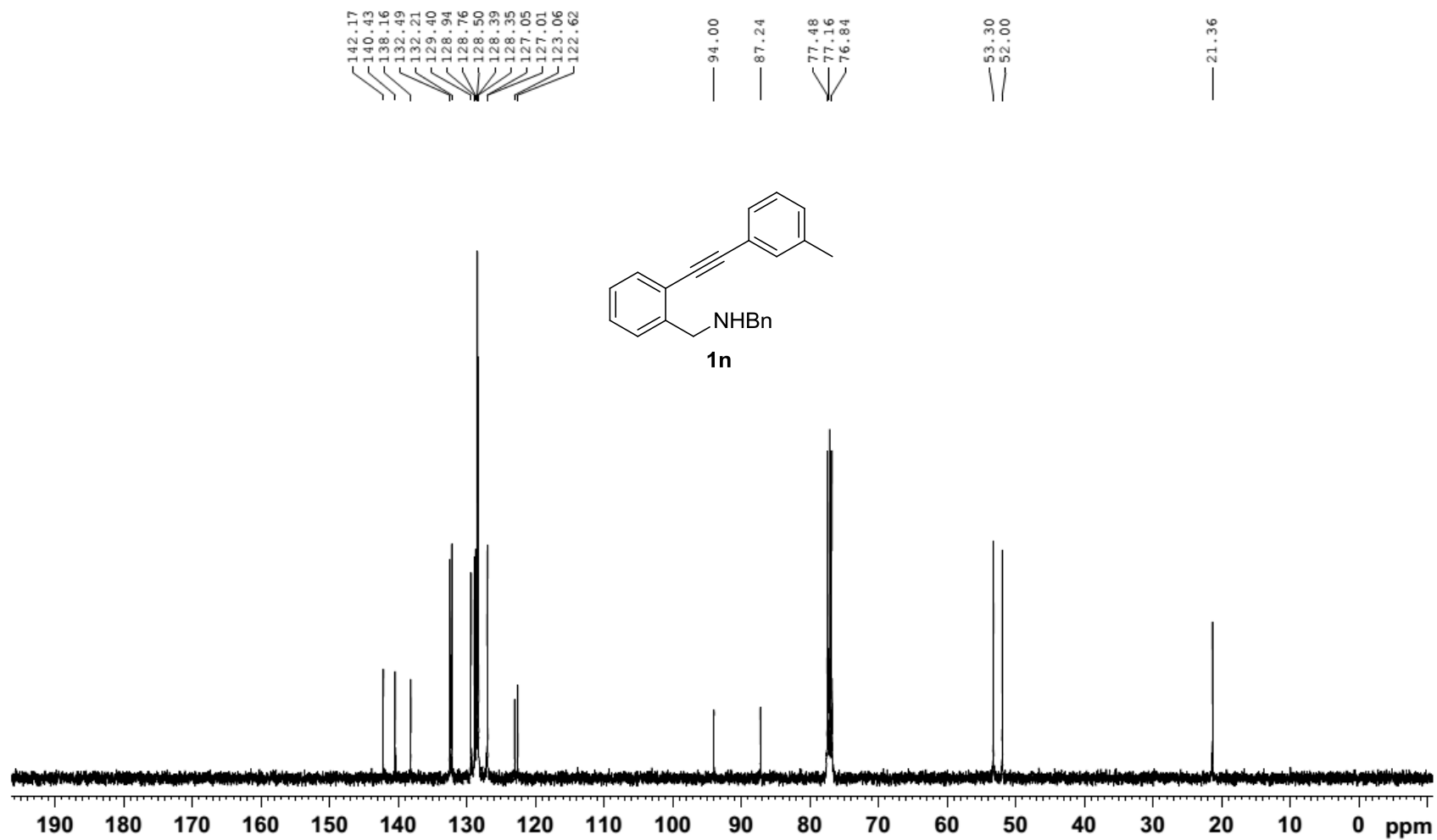




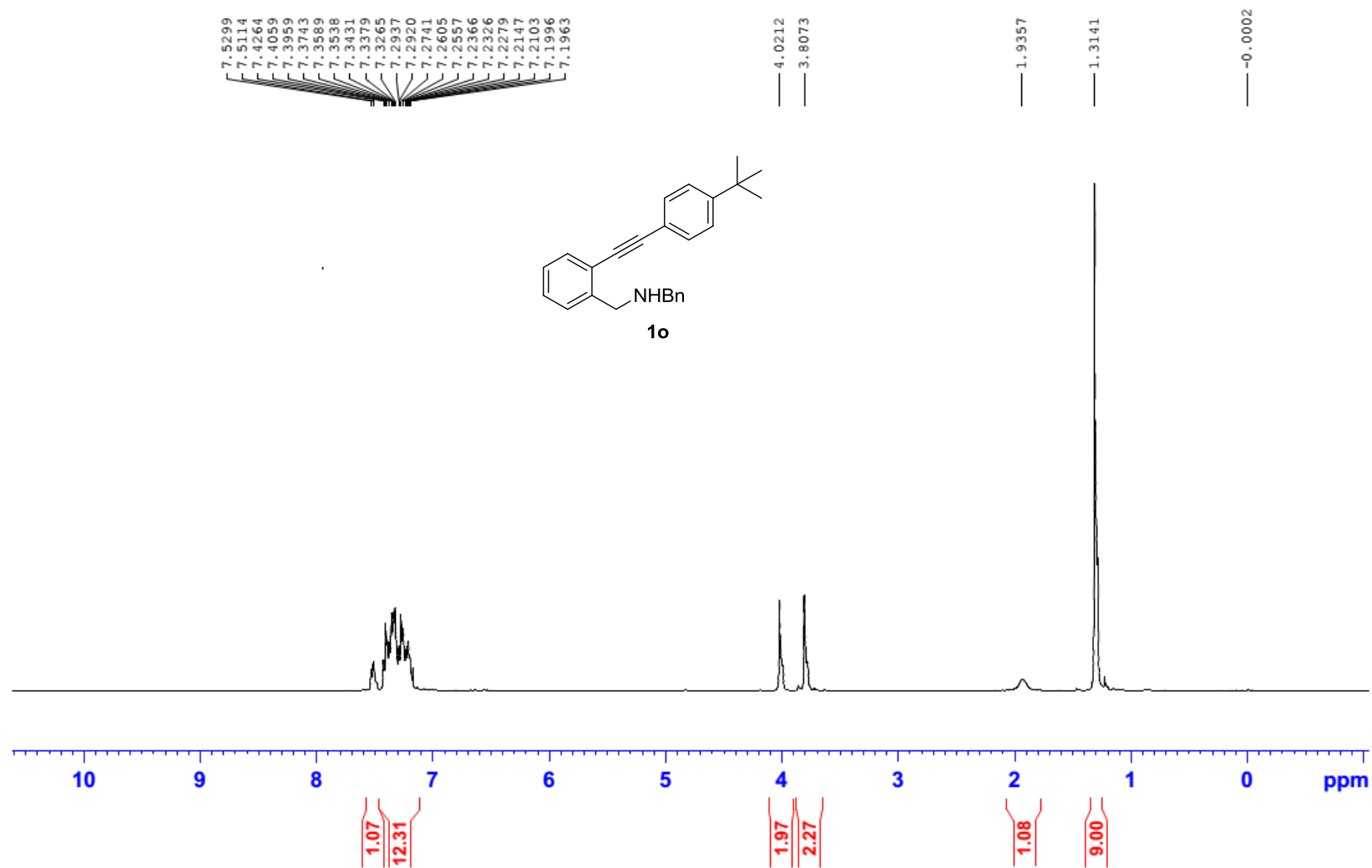
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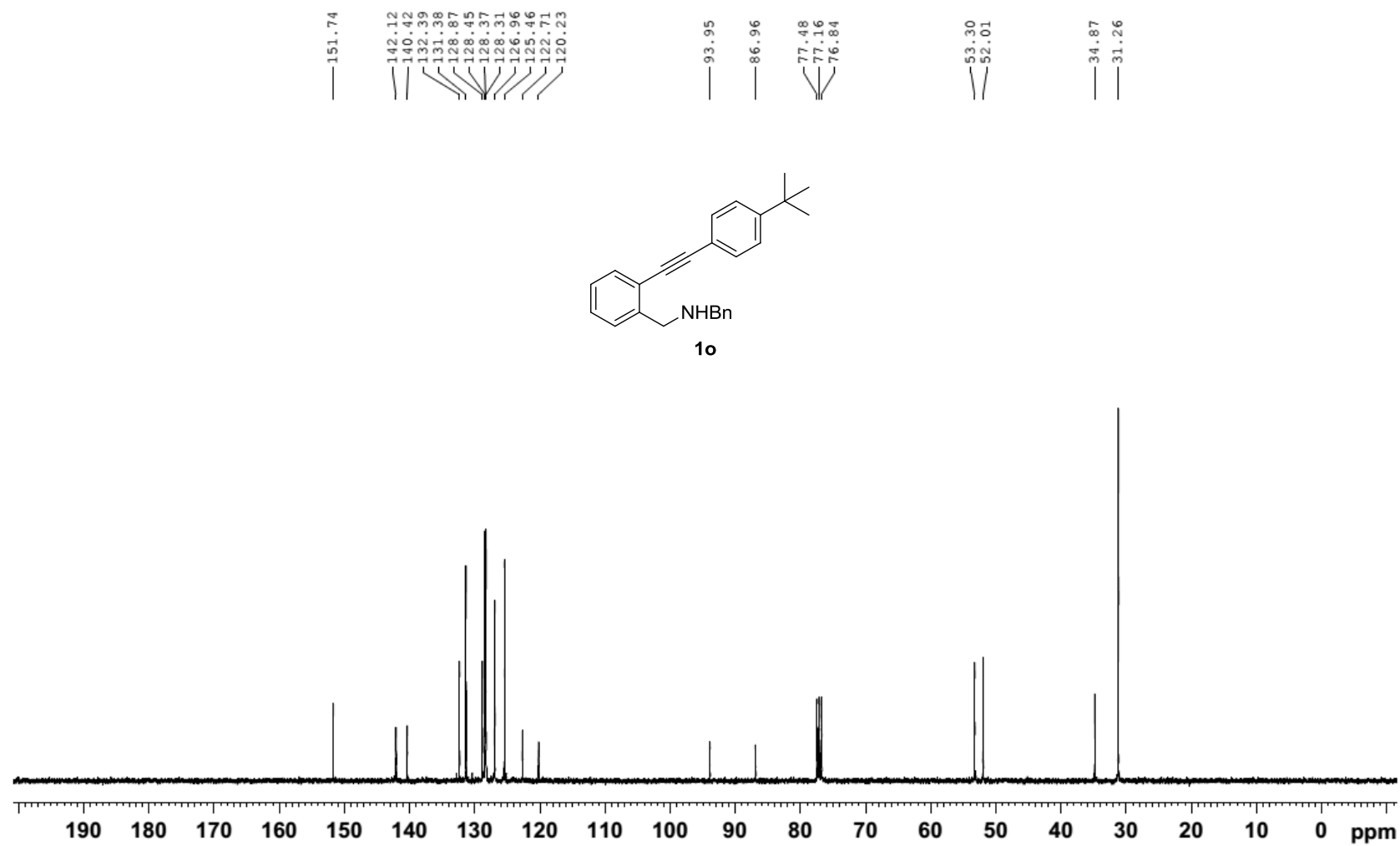
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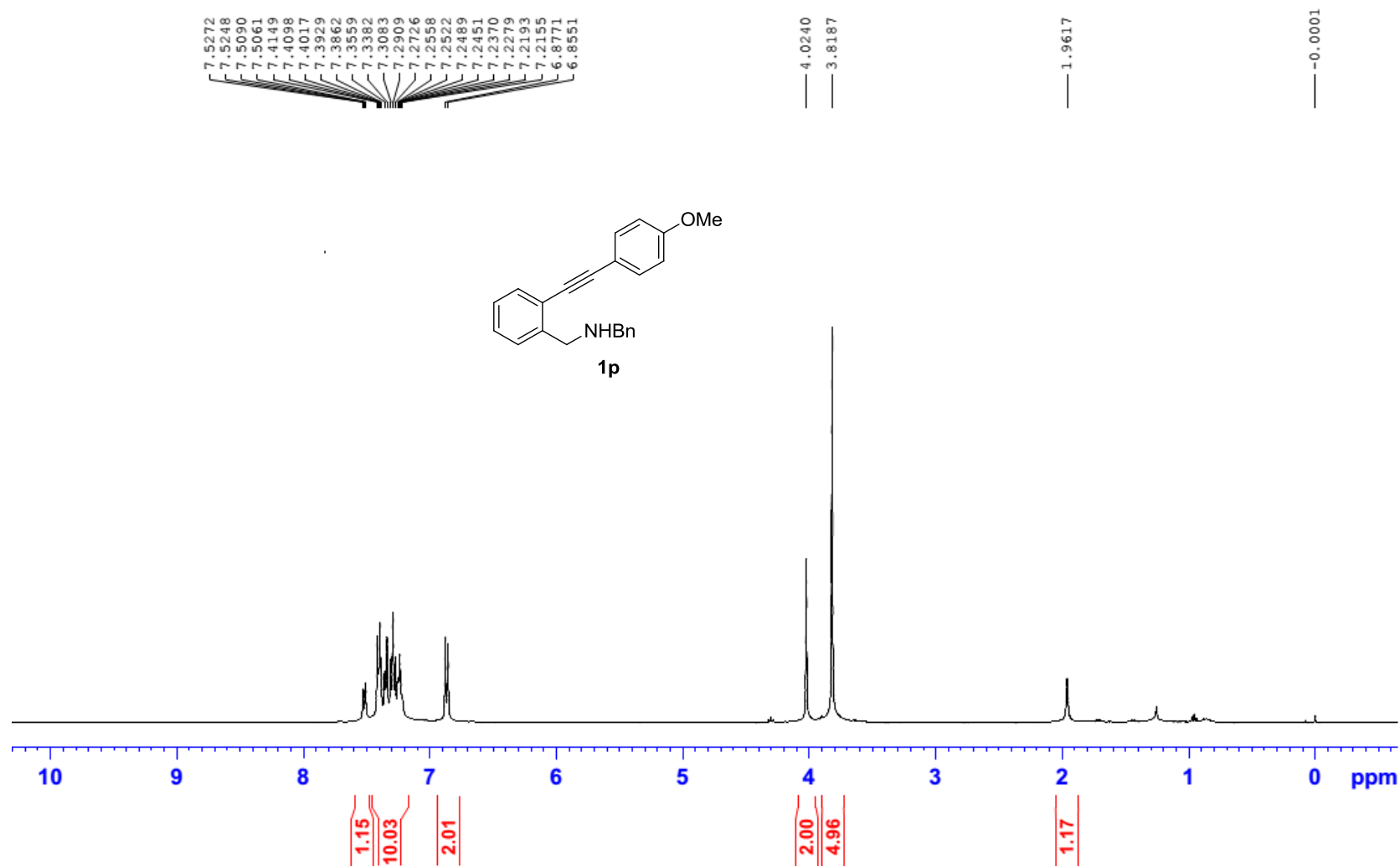
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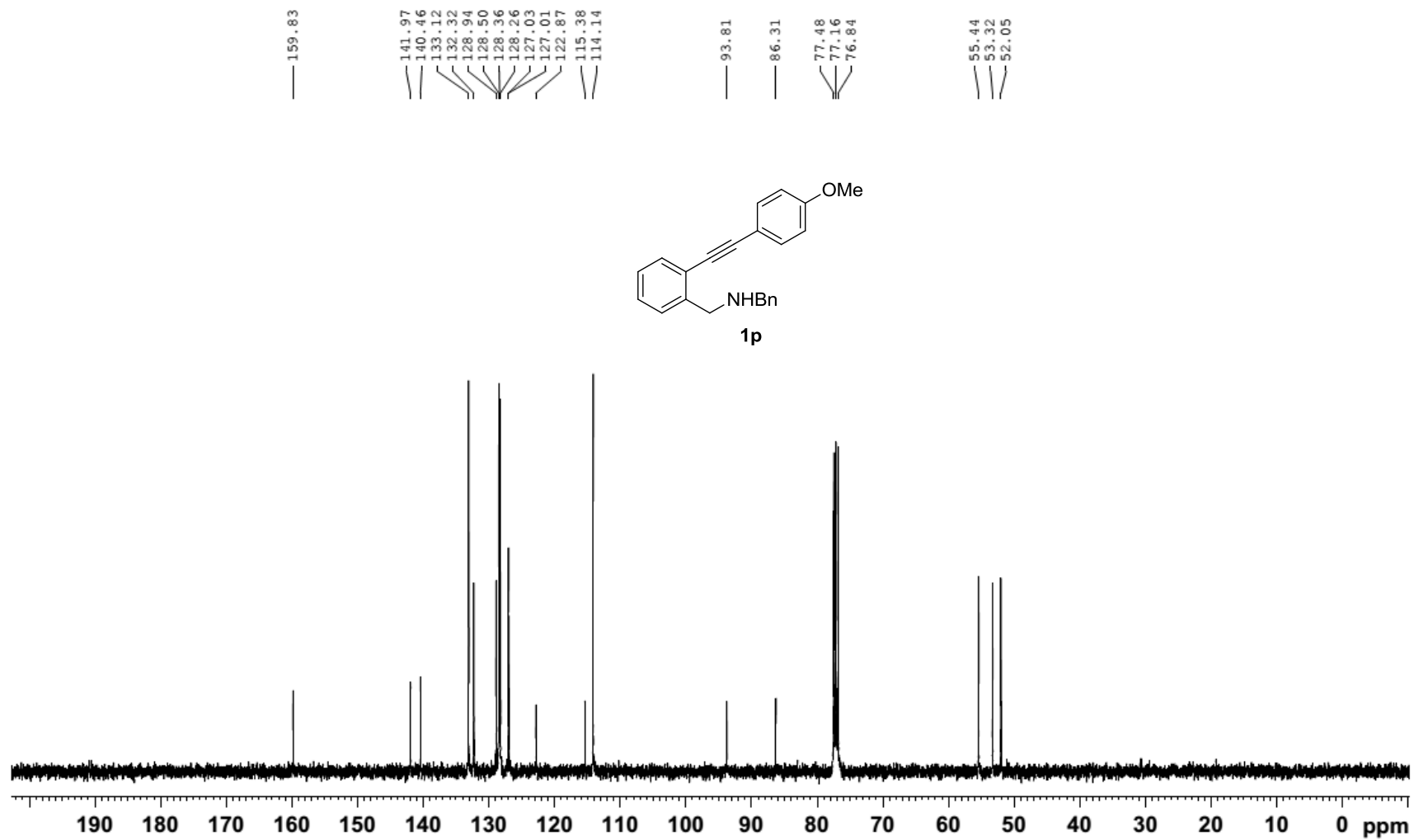
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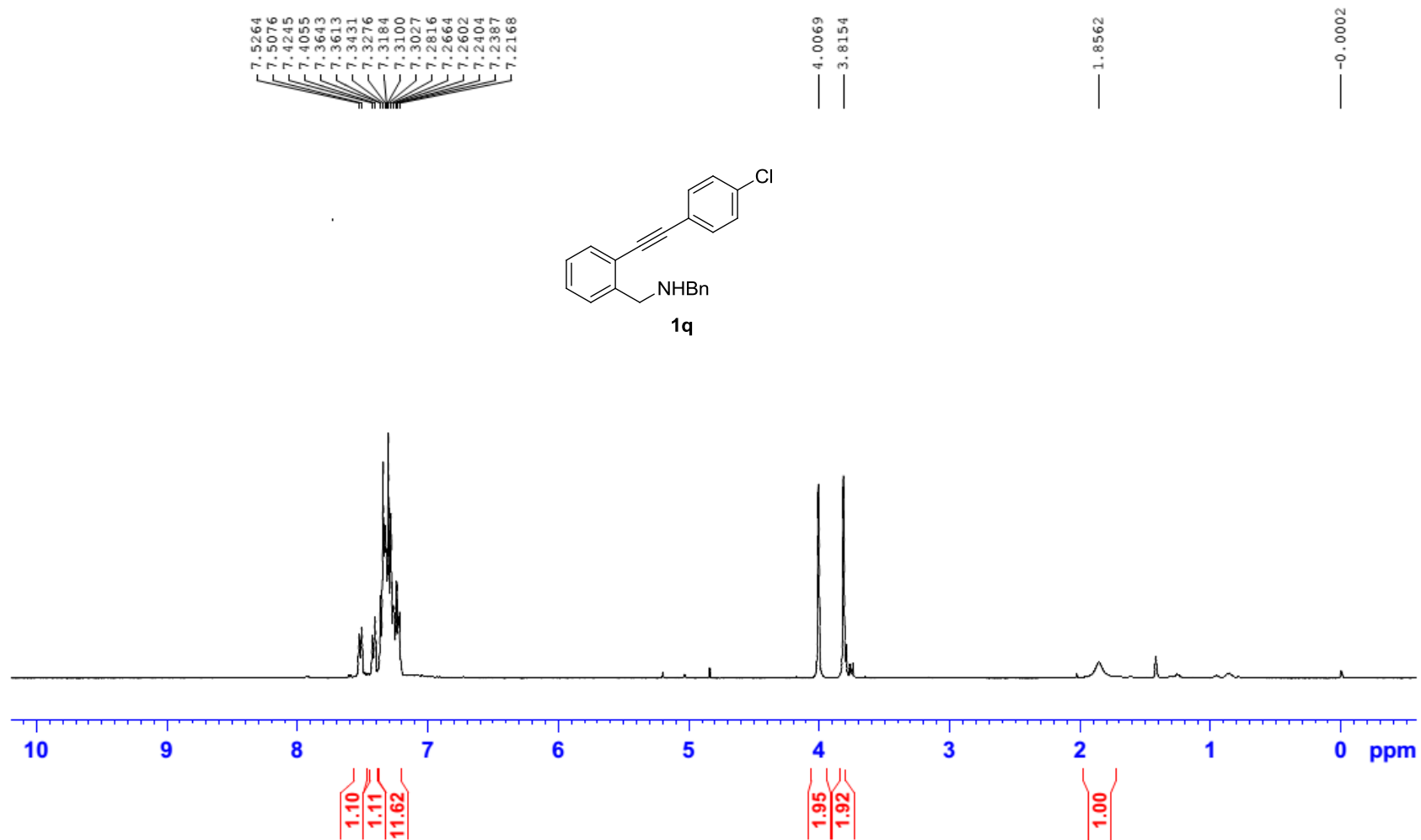
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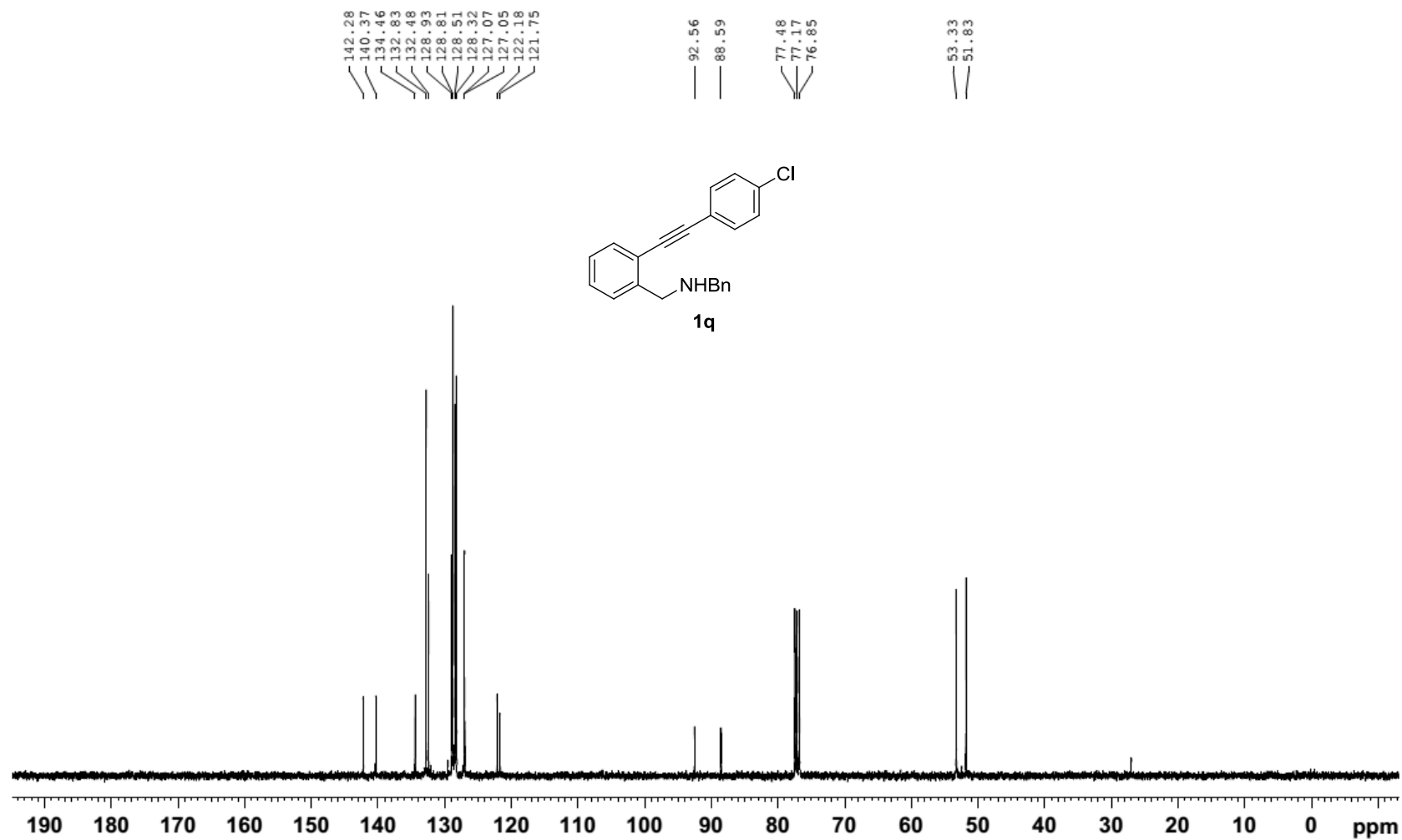
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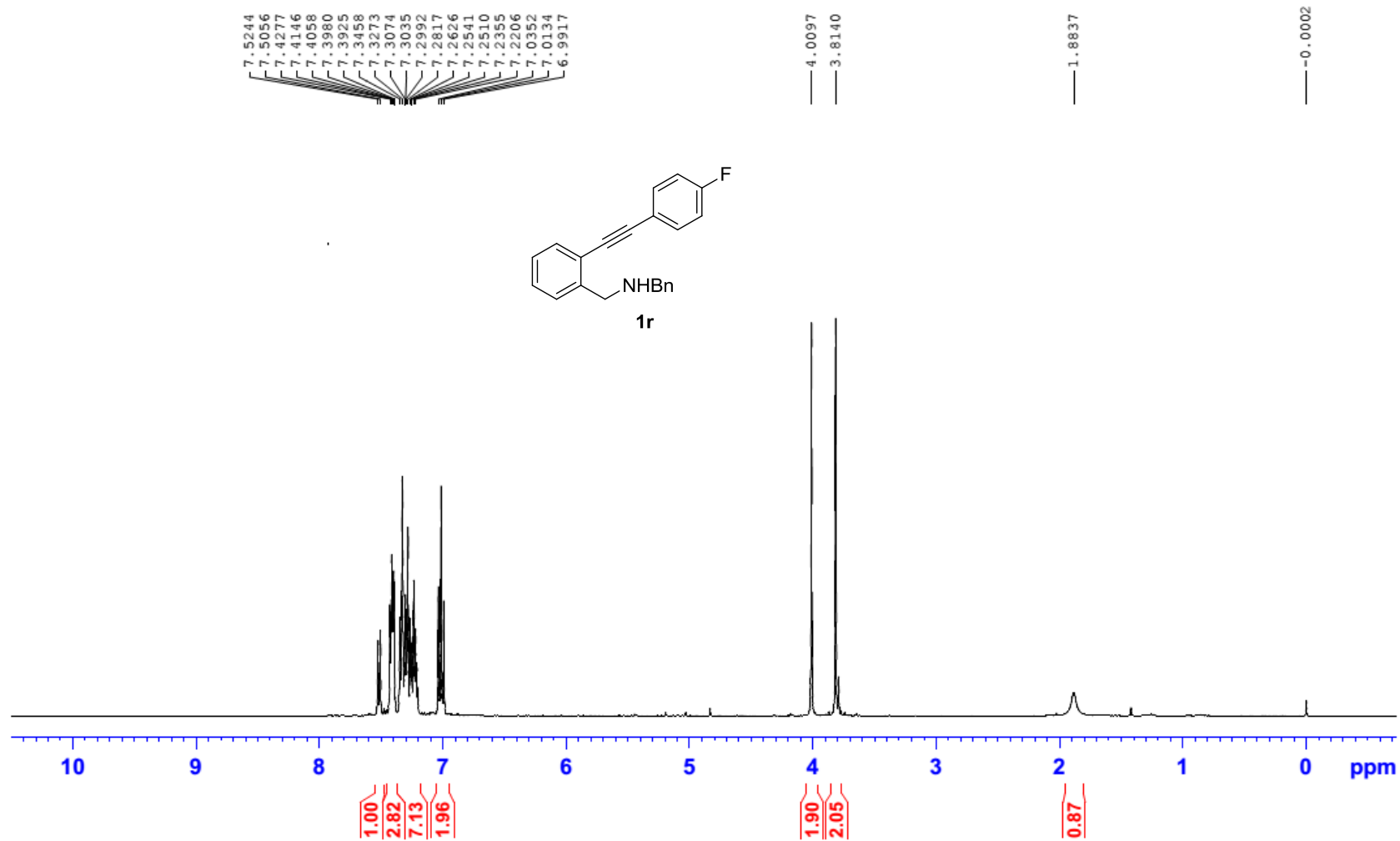


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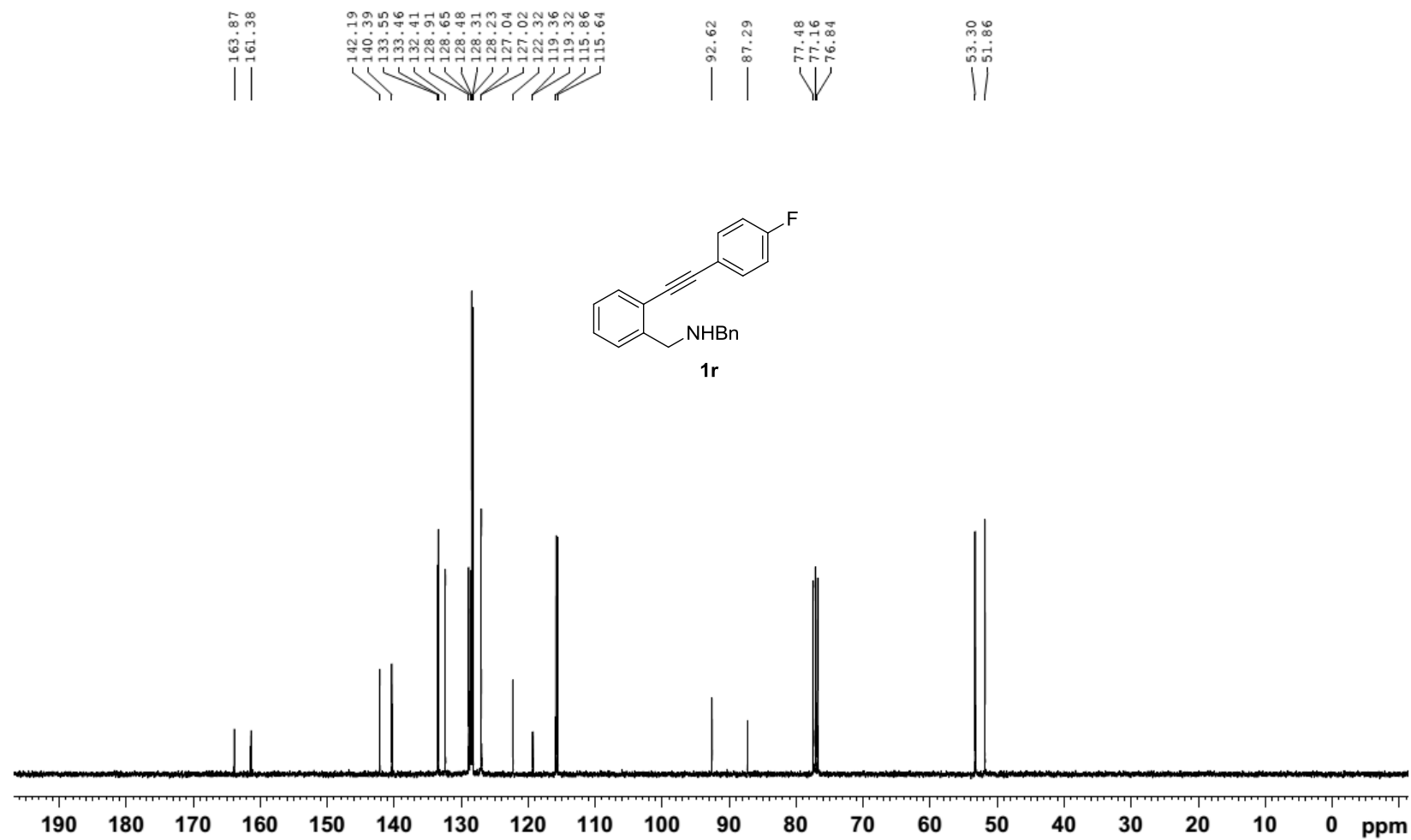




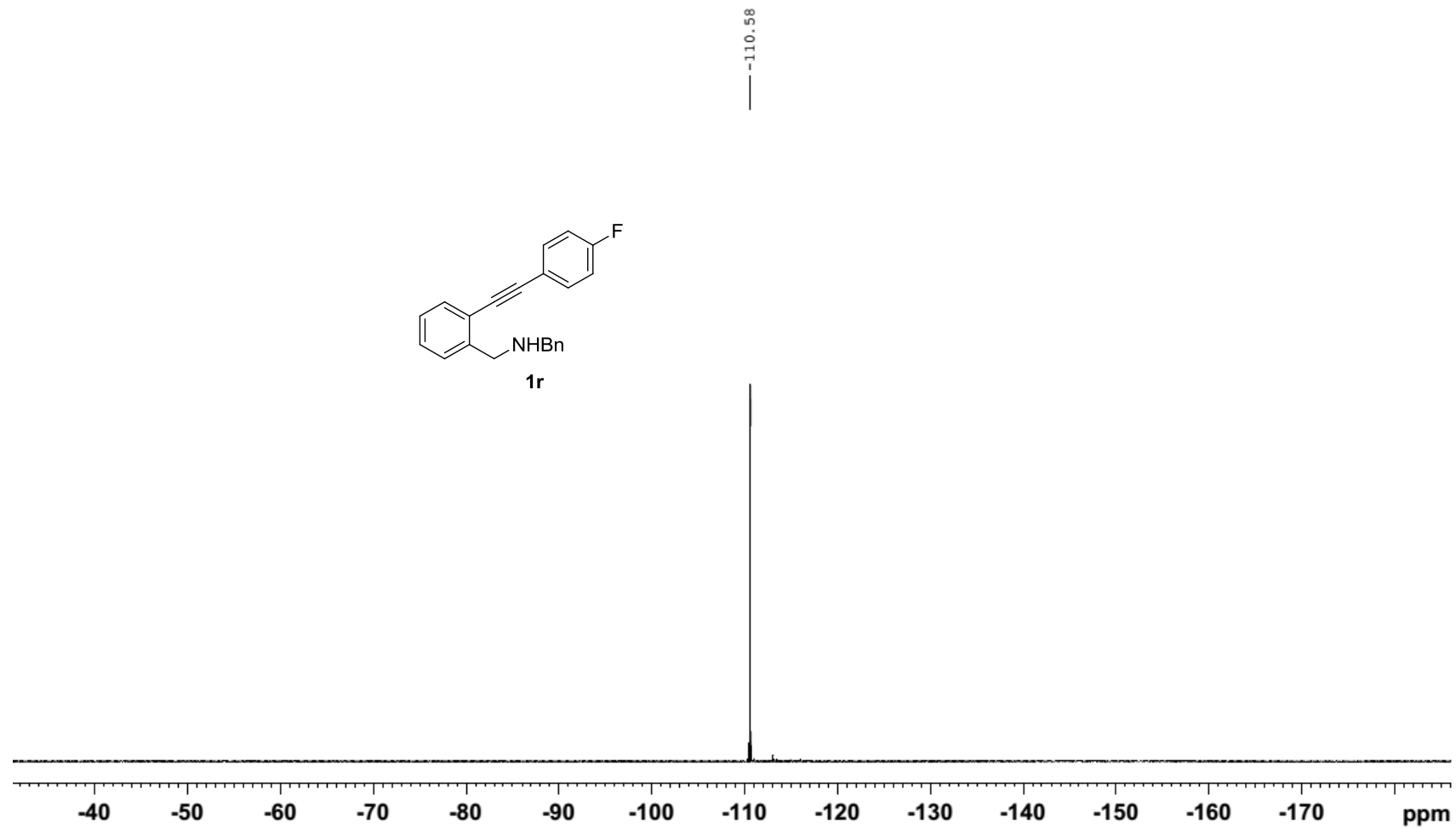
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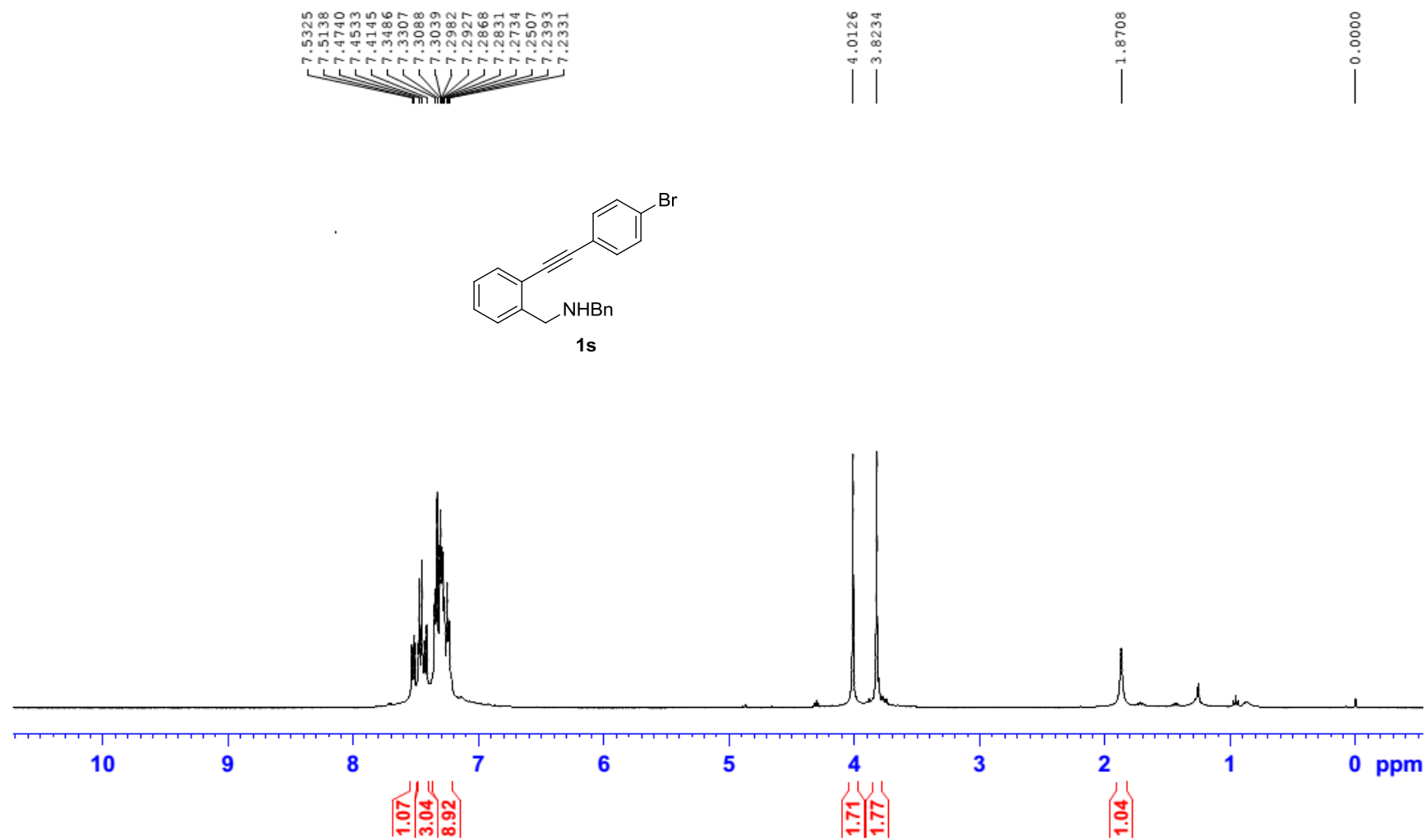
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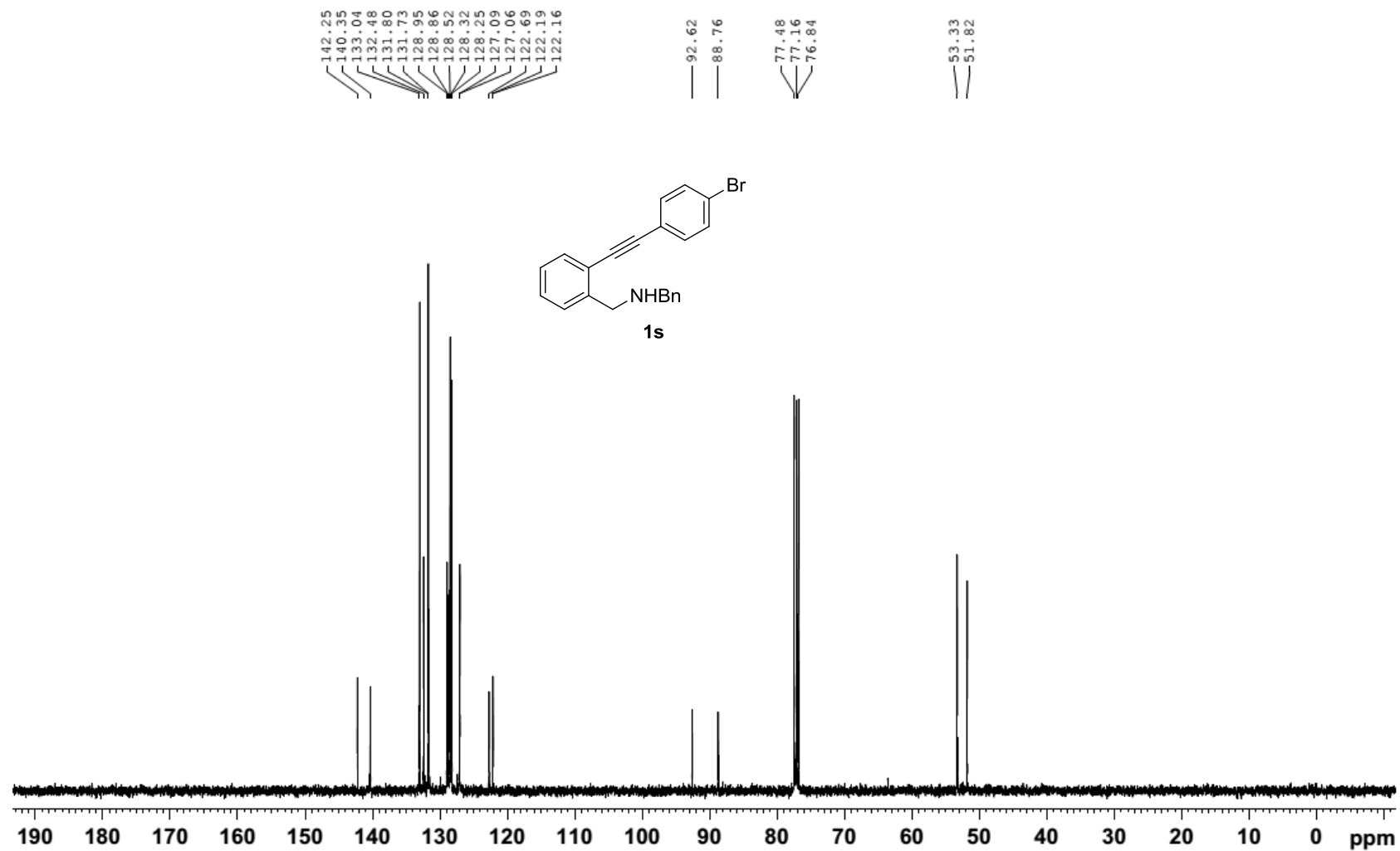
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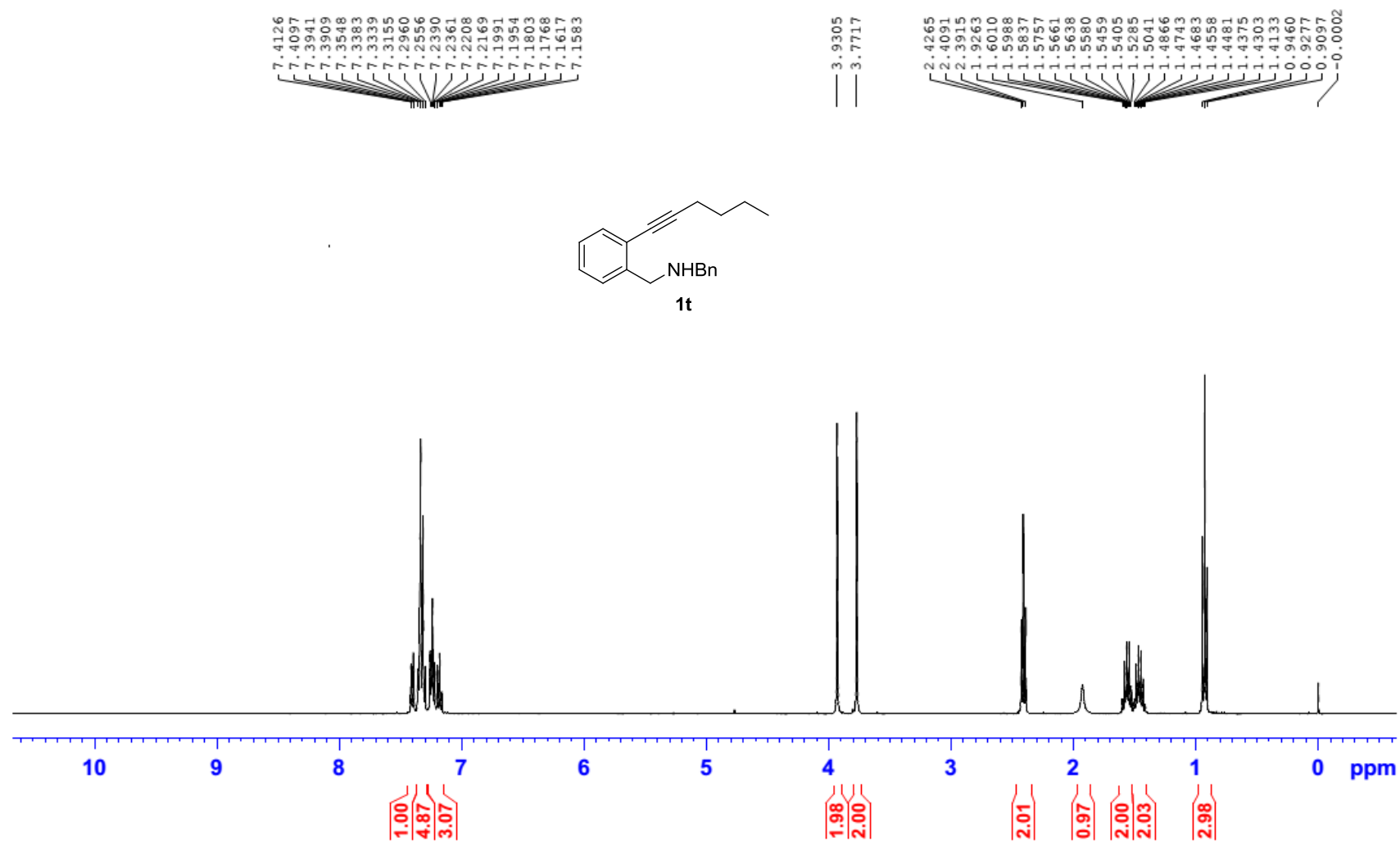
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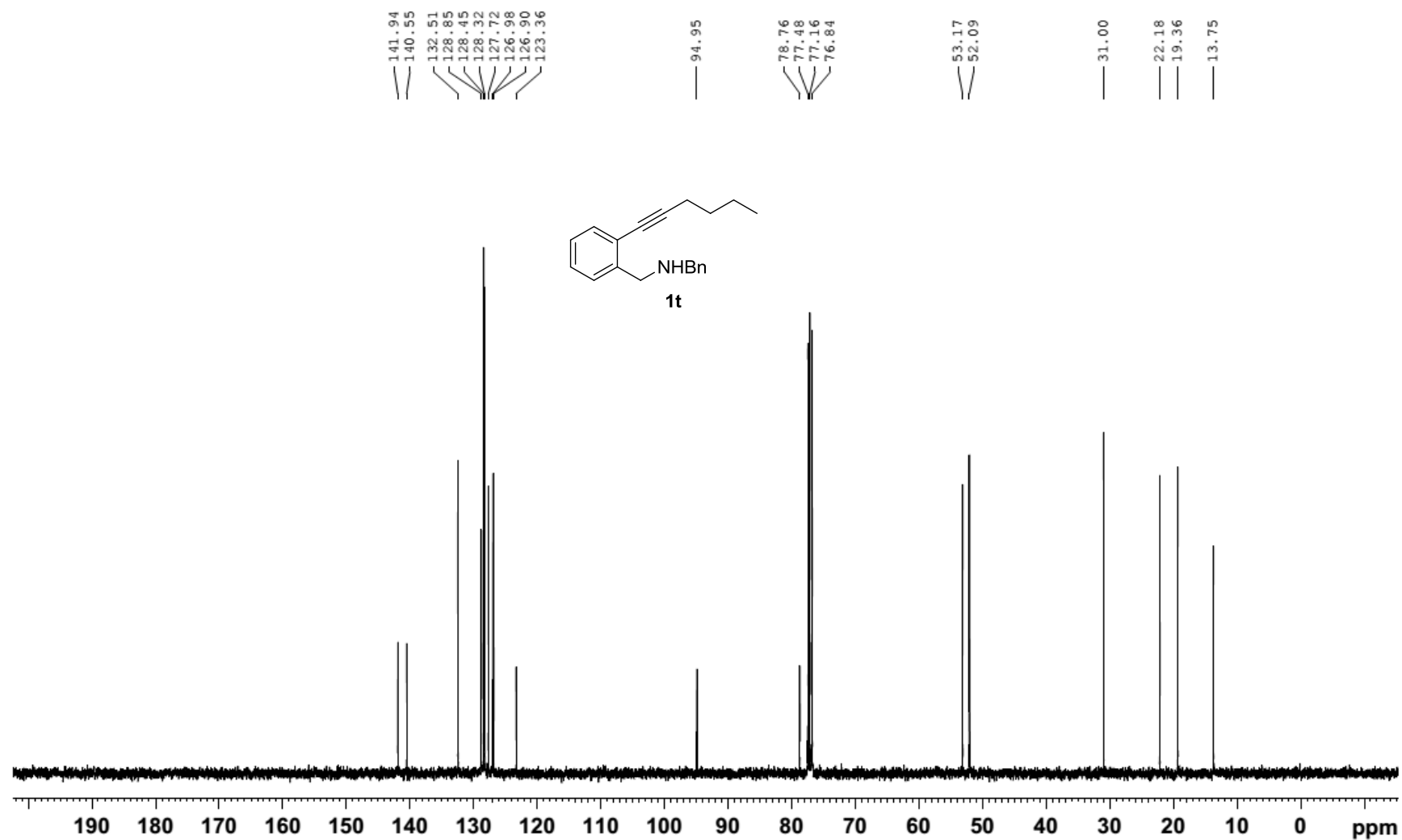
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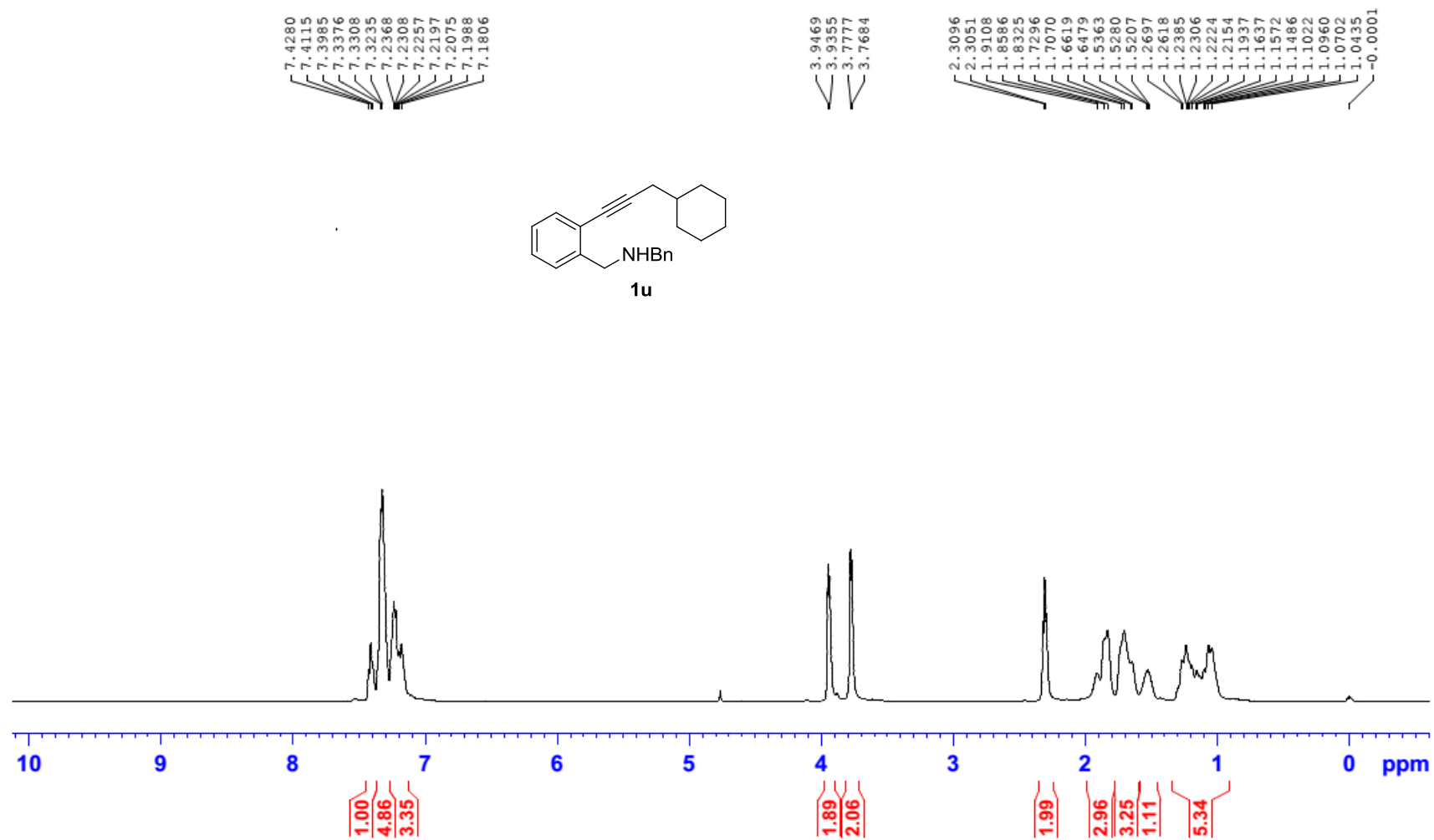
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HY-X170410-2-CNMR



HY-X170331-1HNMR





HY-X170331-1CNMR

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93.87

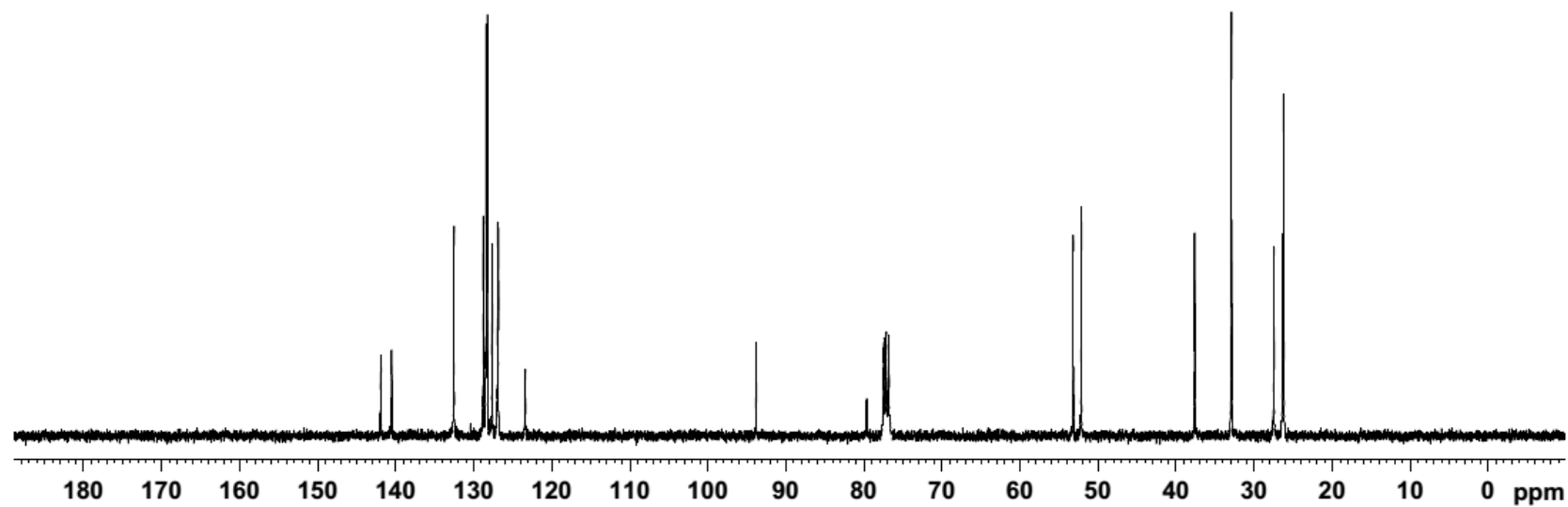
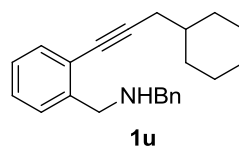
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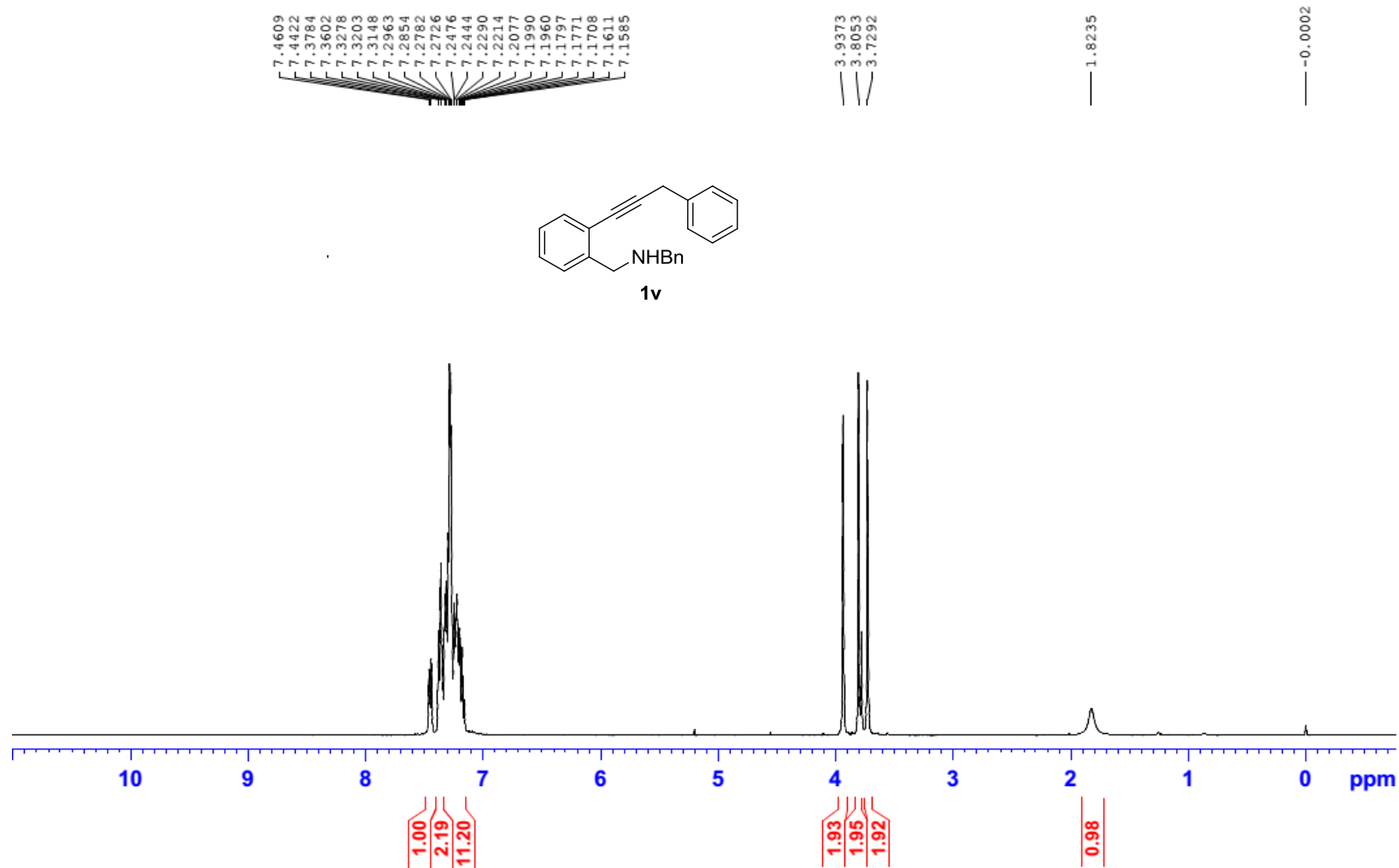
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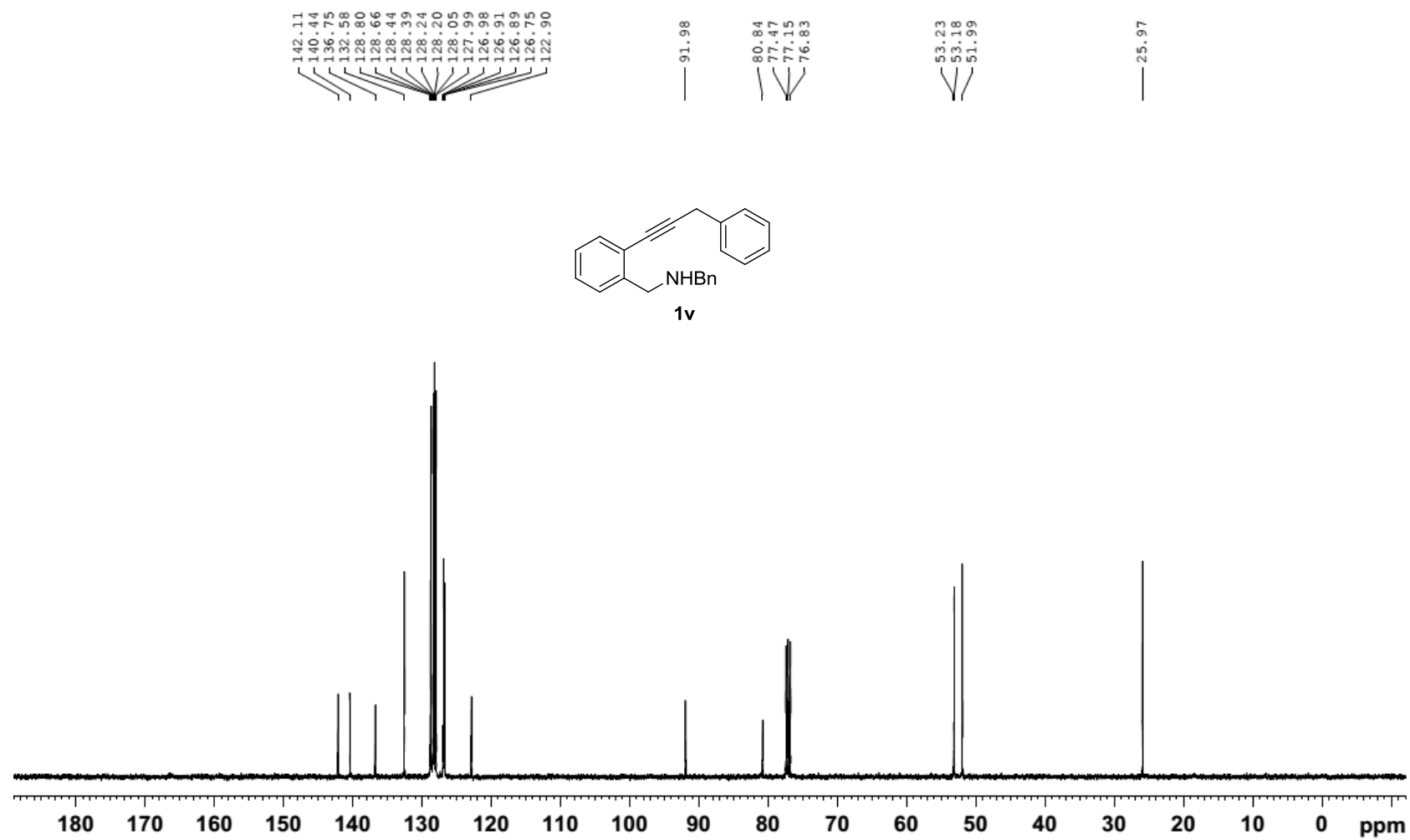
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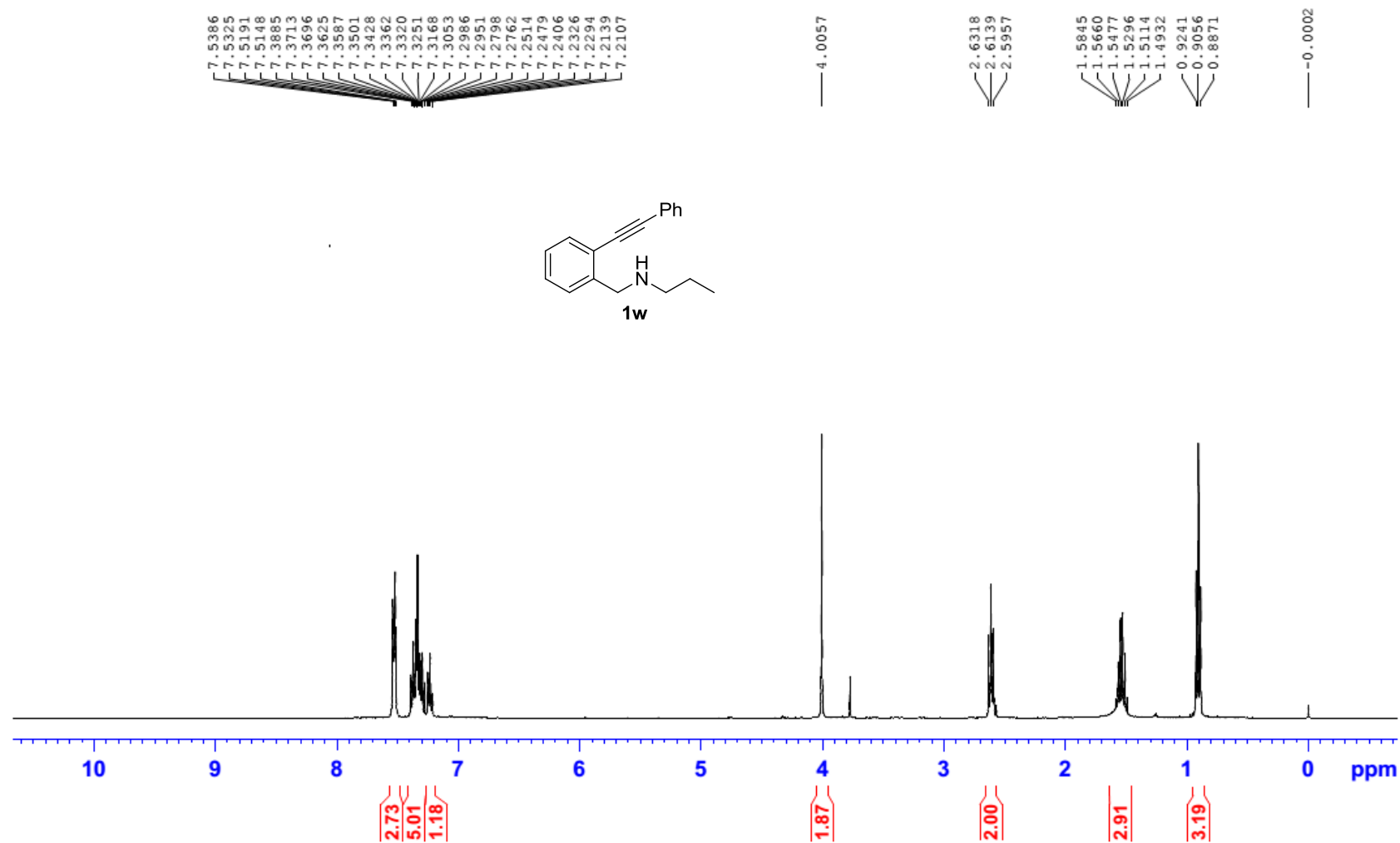
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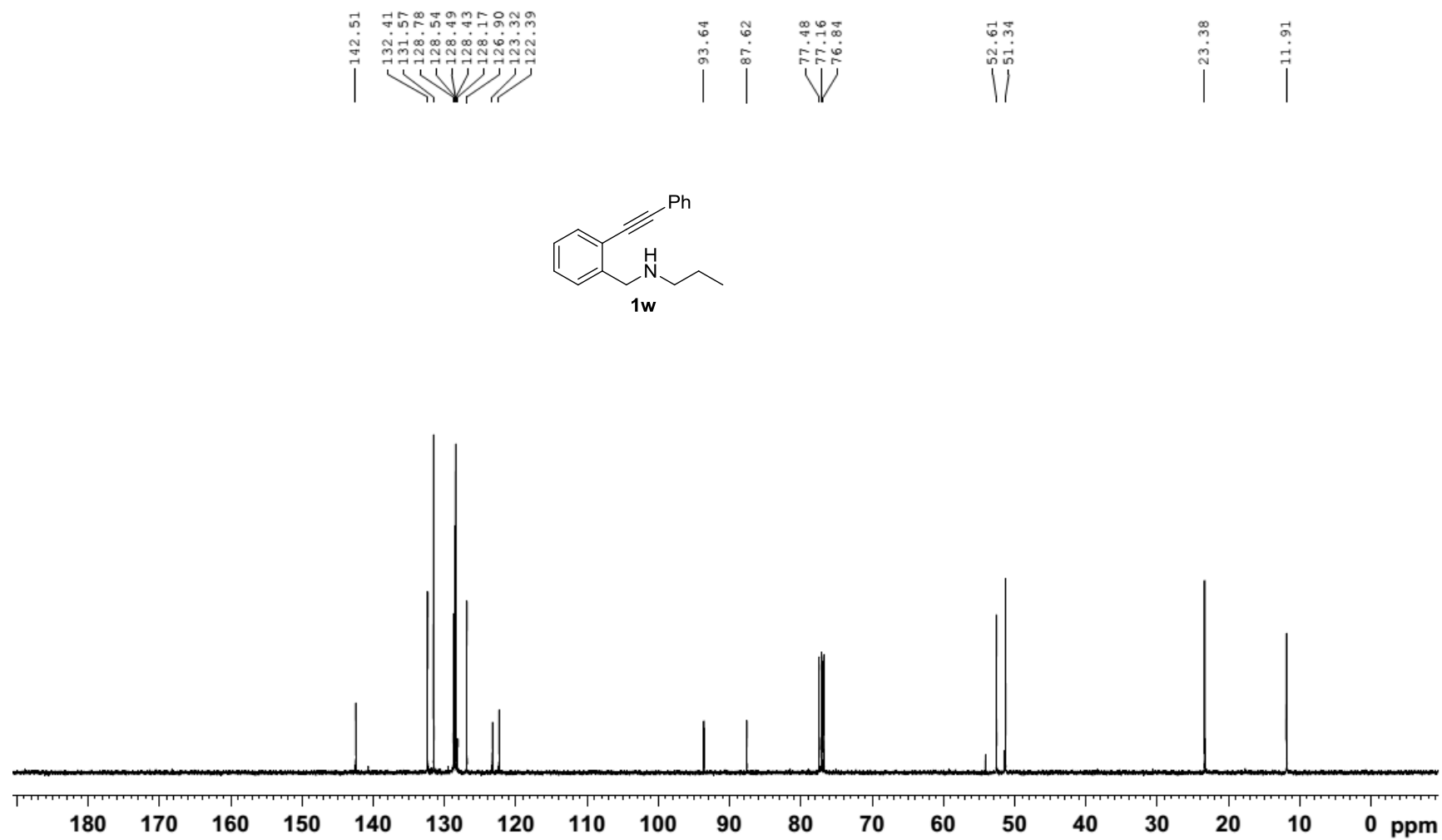
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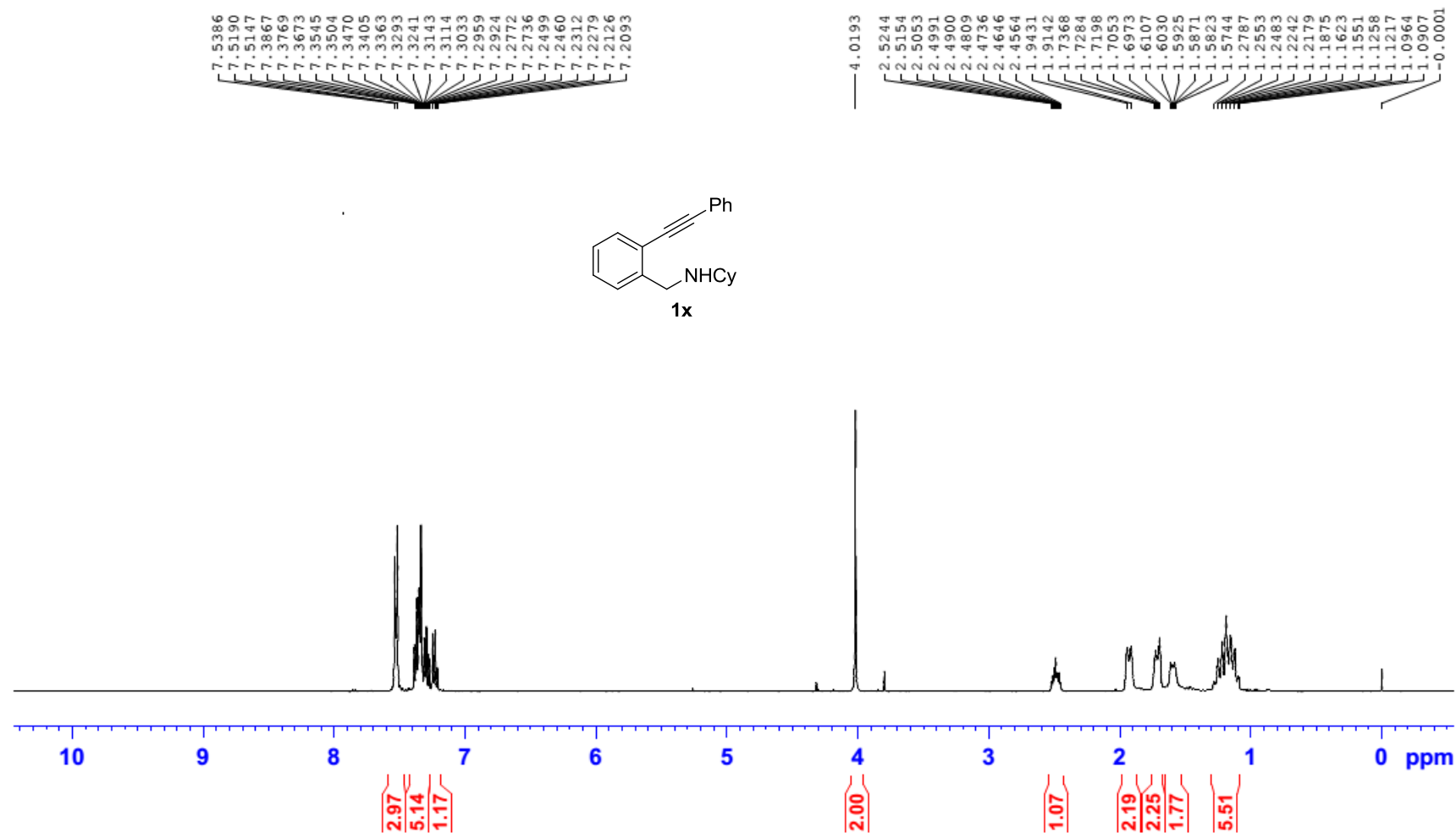
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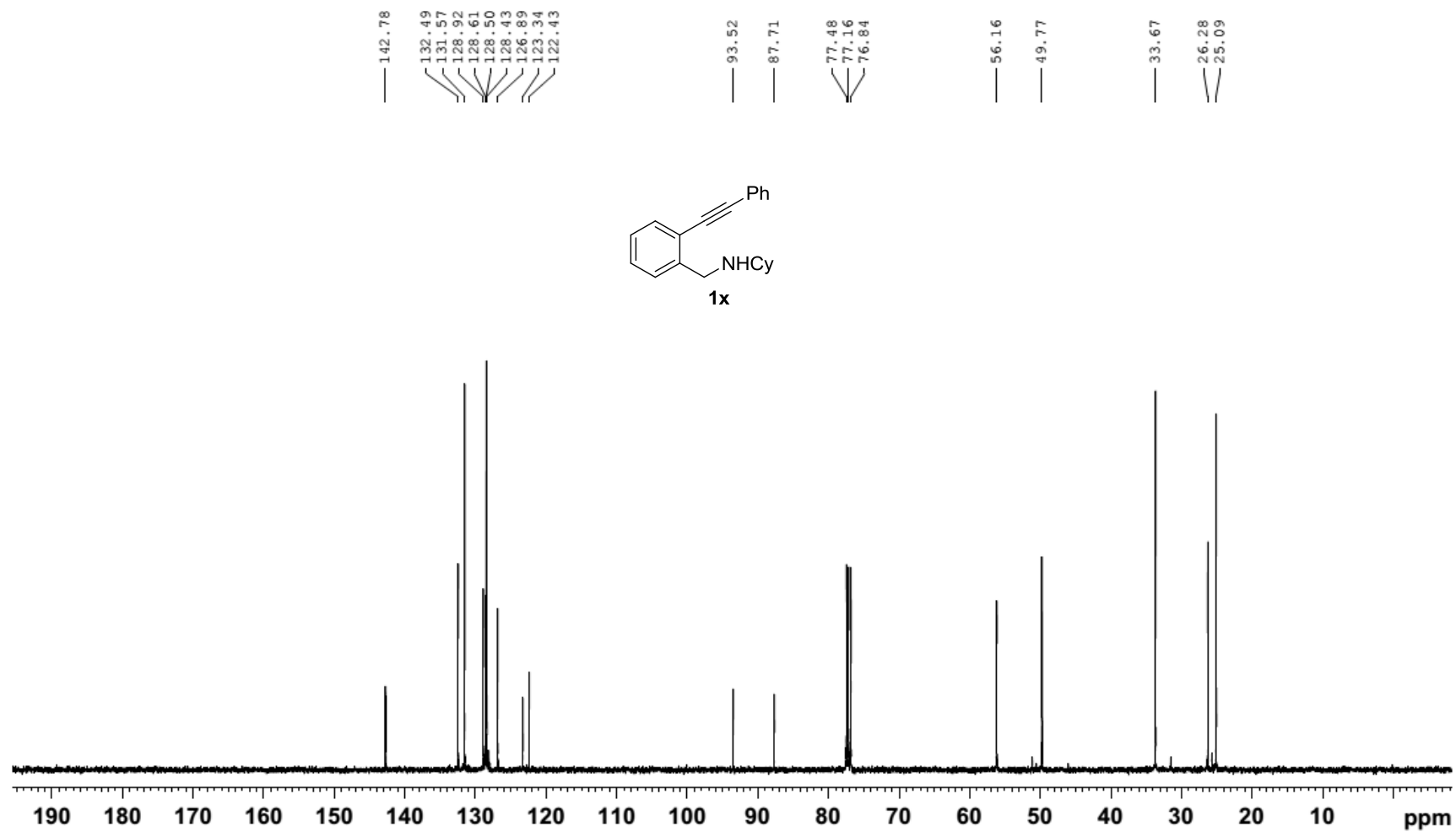
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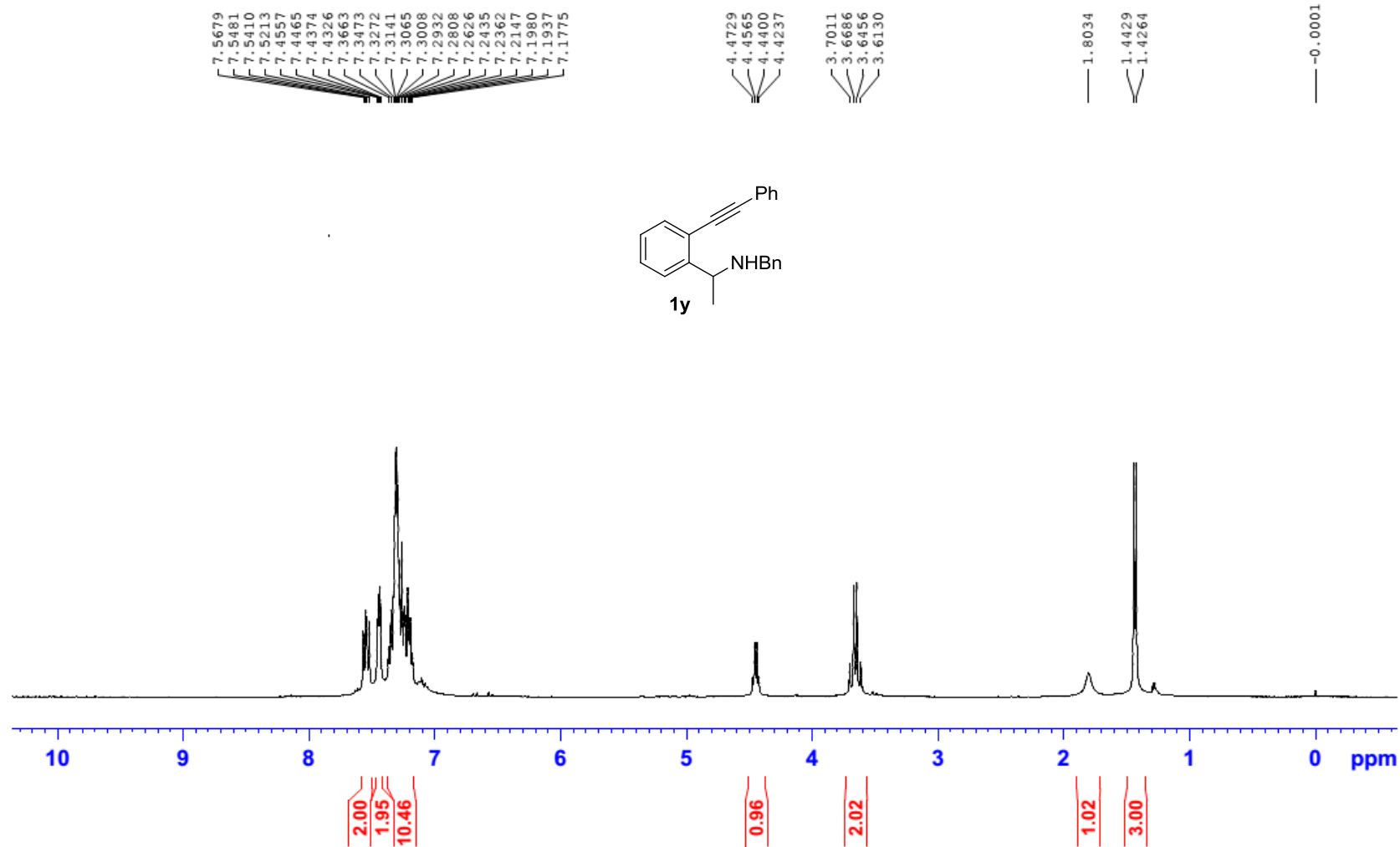
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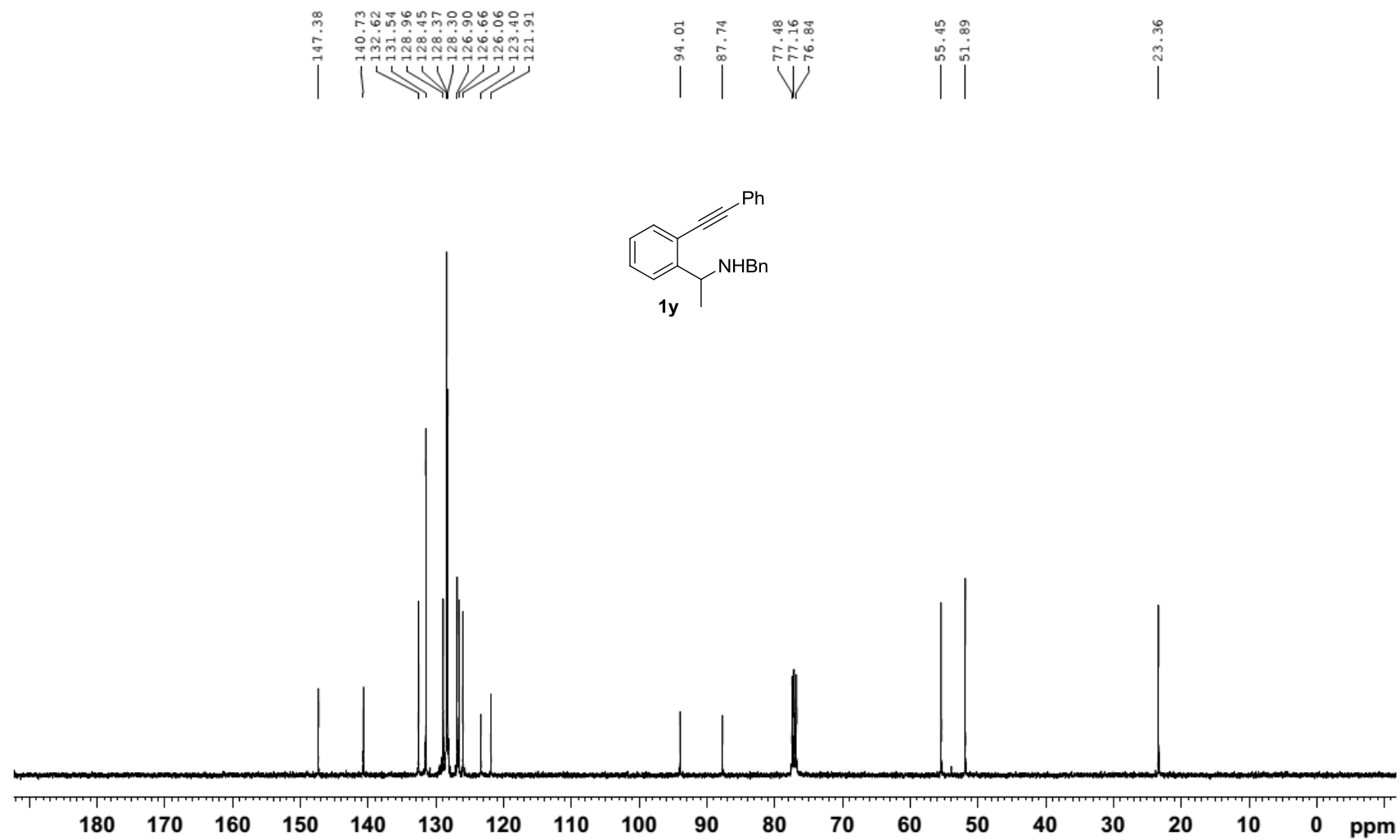


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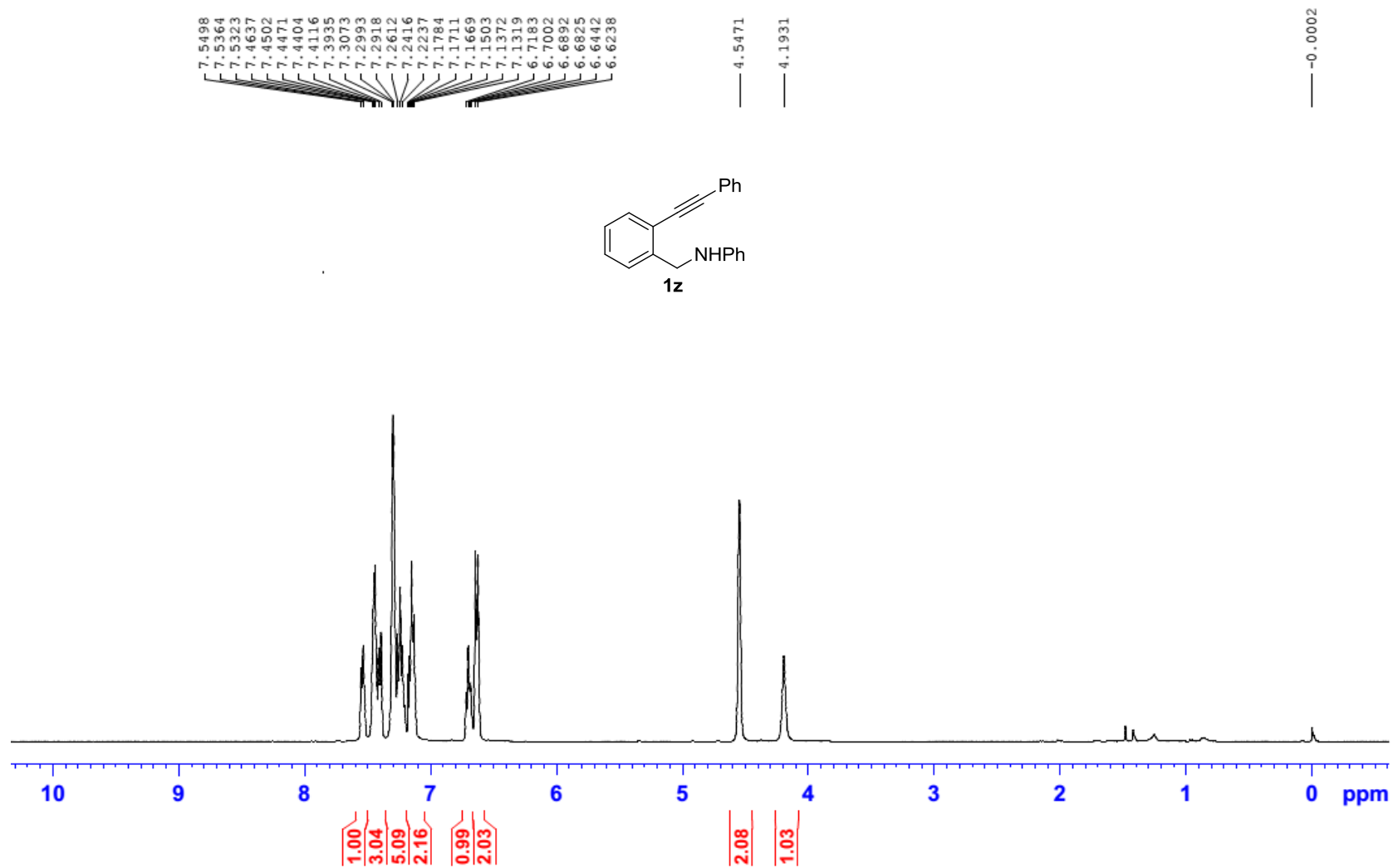




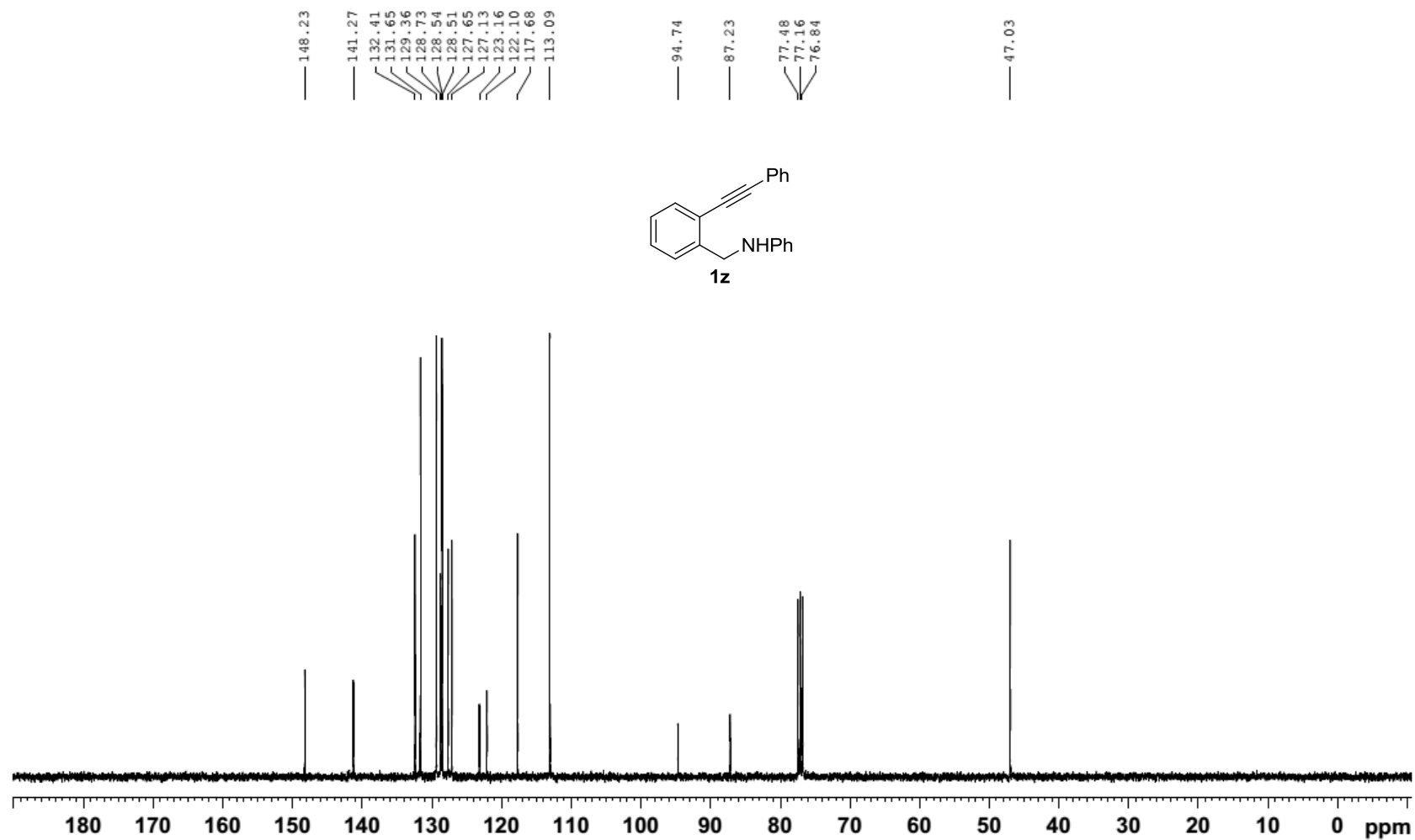
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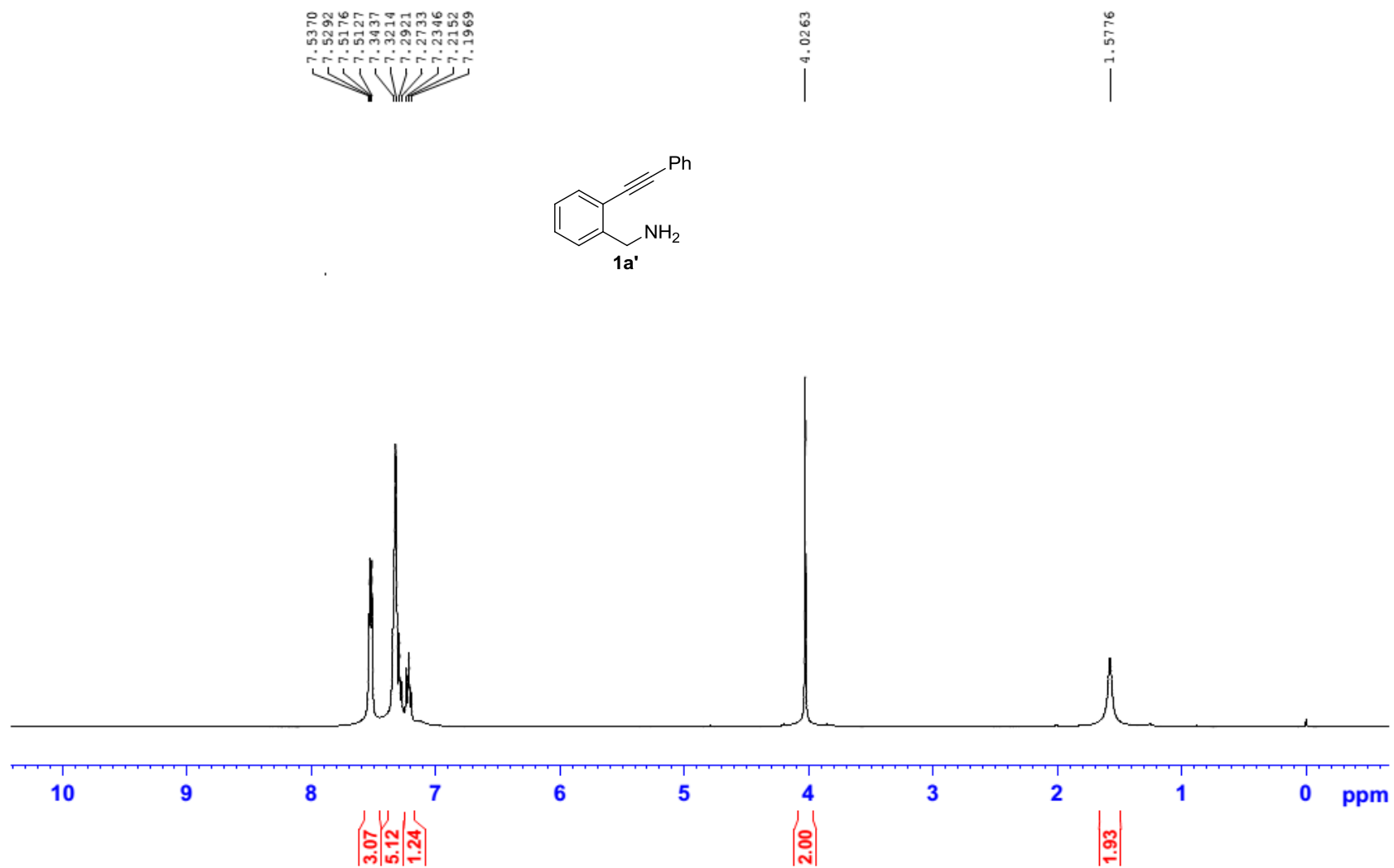
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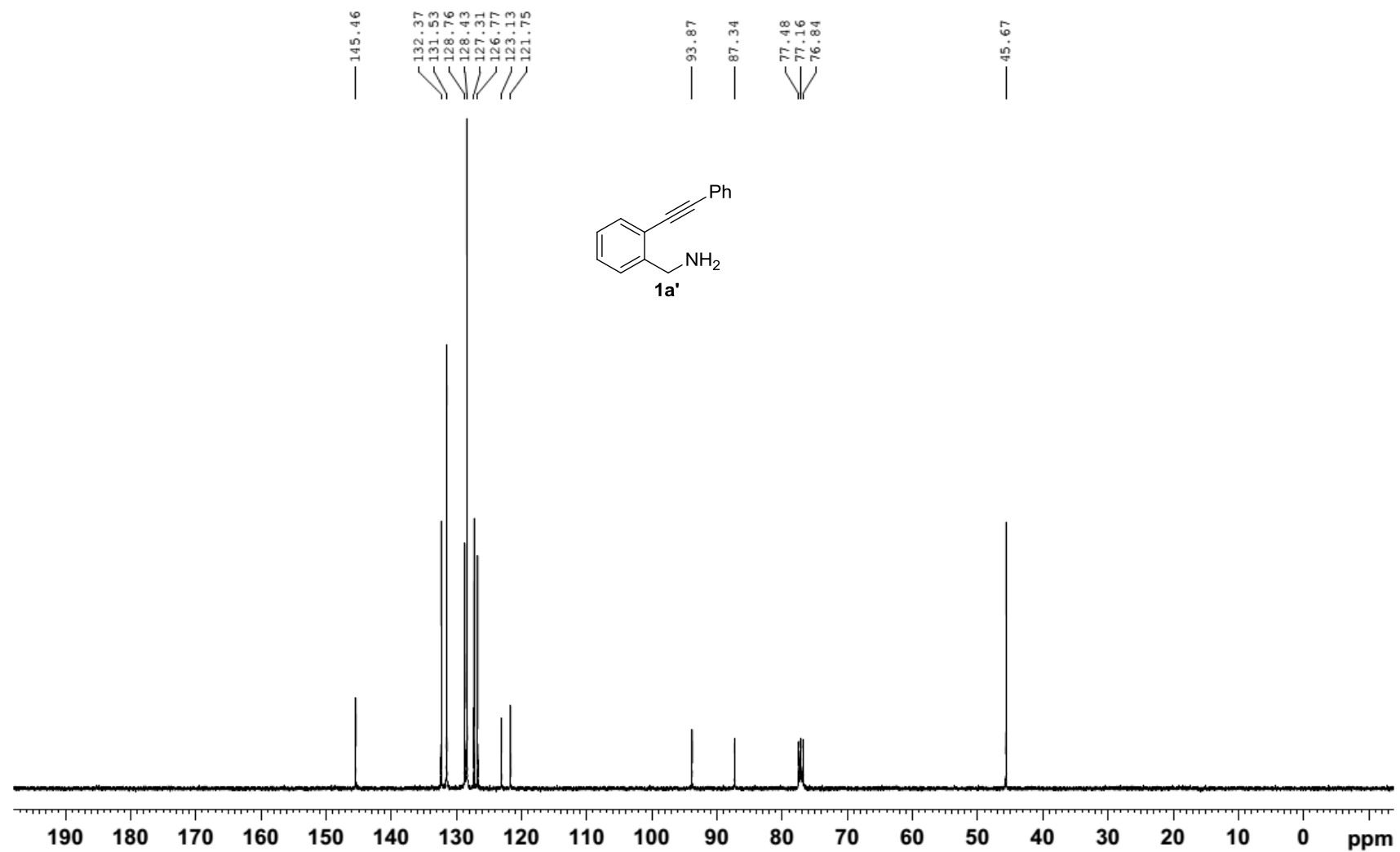
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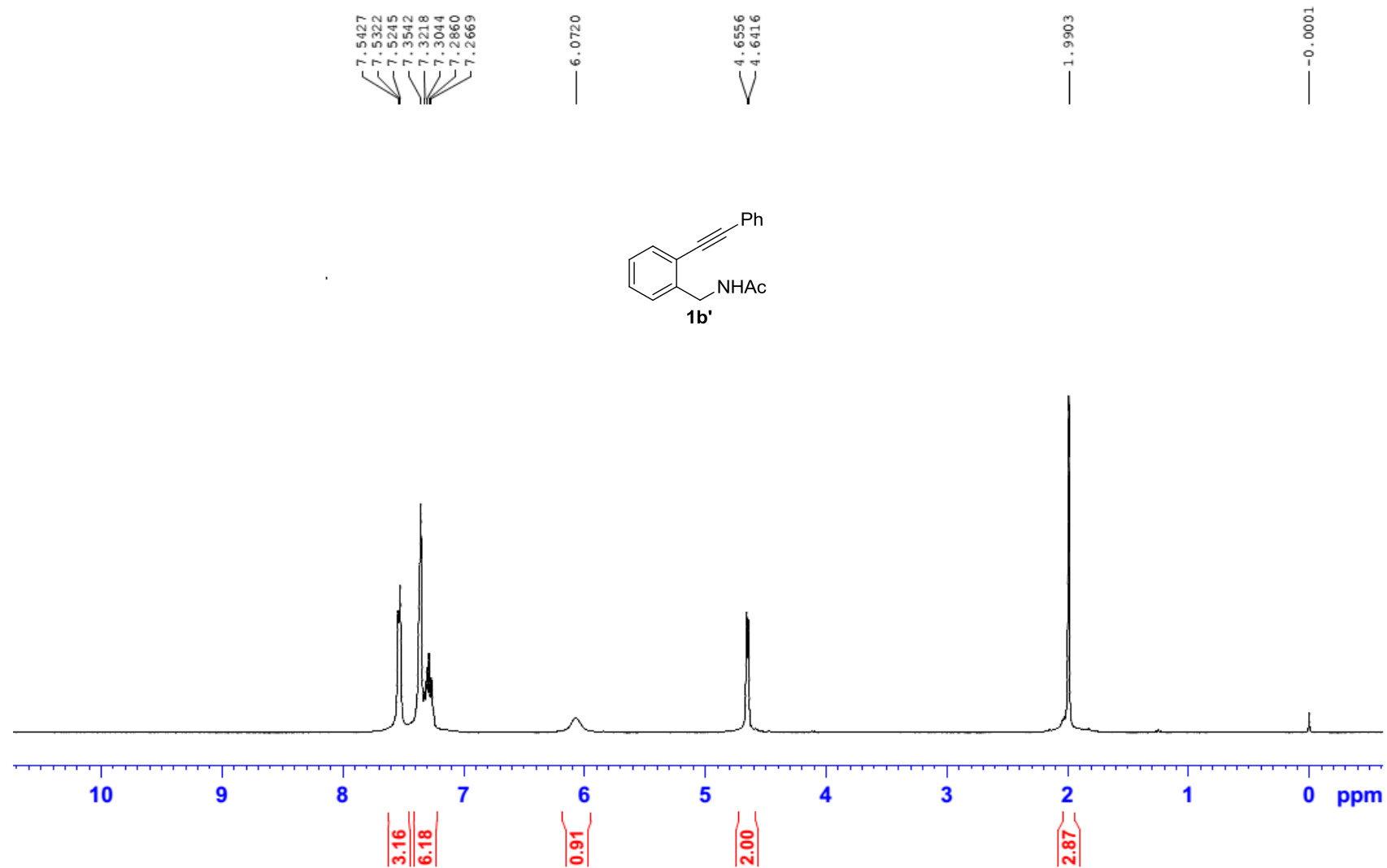
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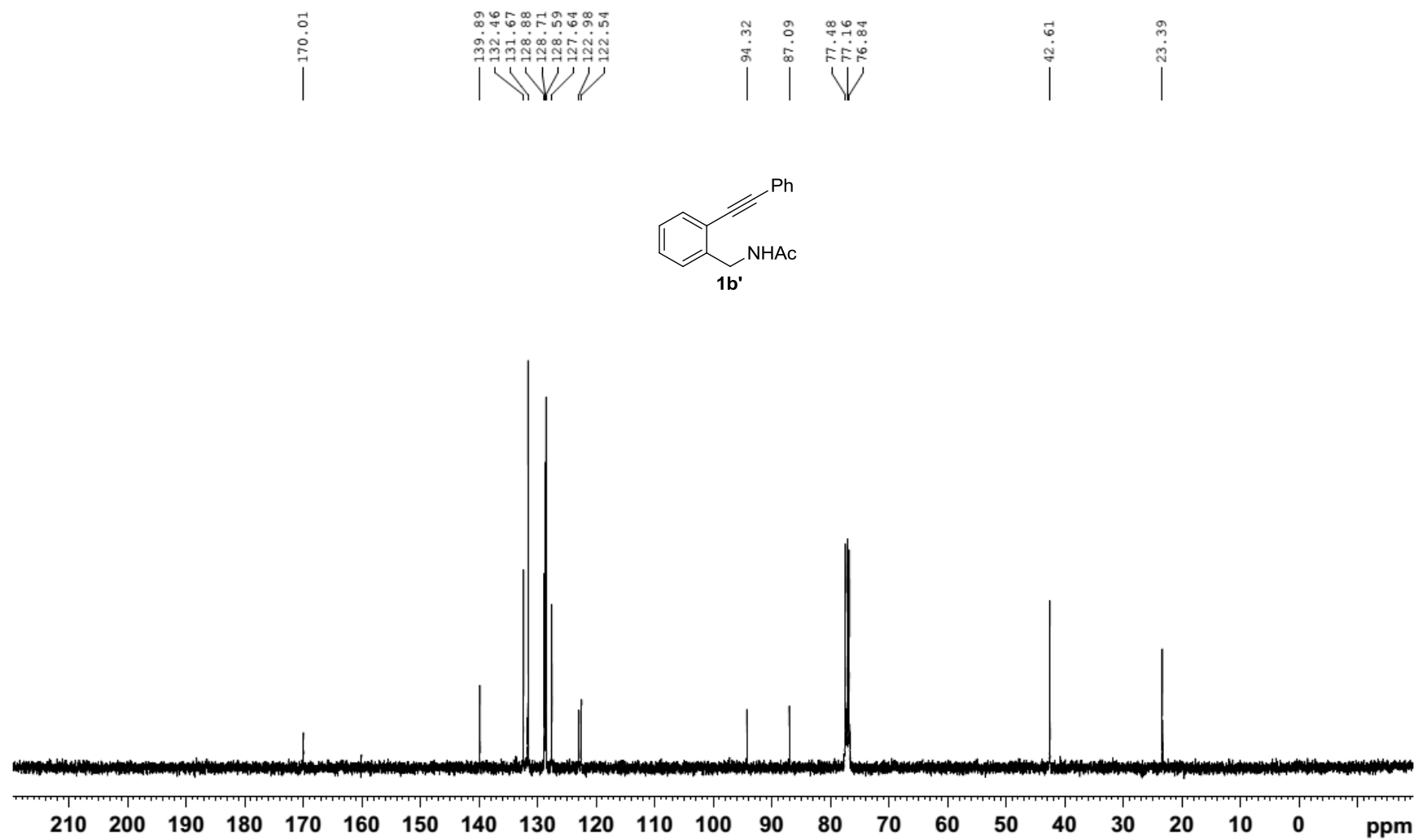
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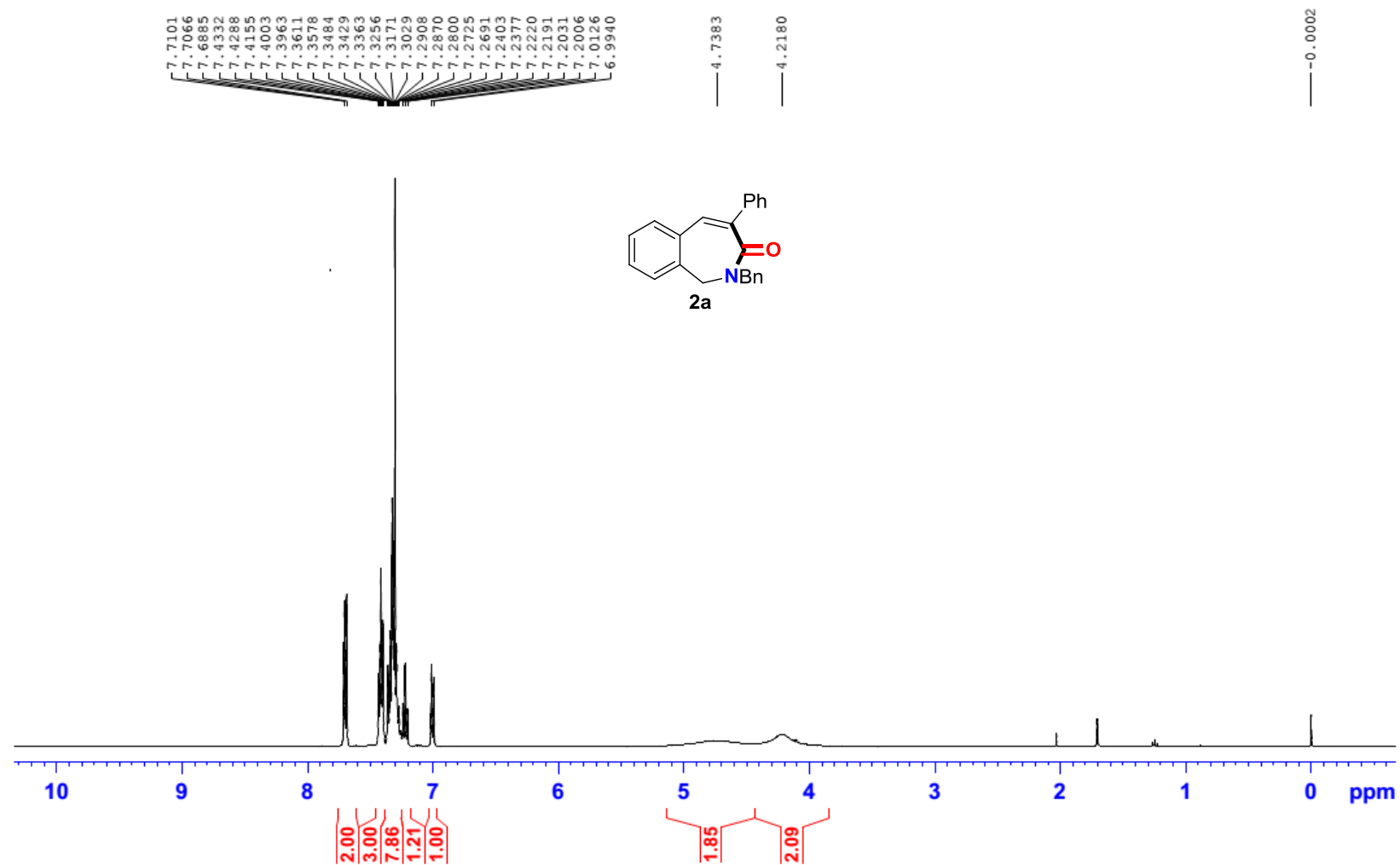
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HY-X170615-1CNMR

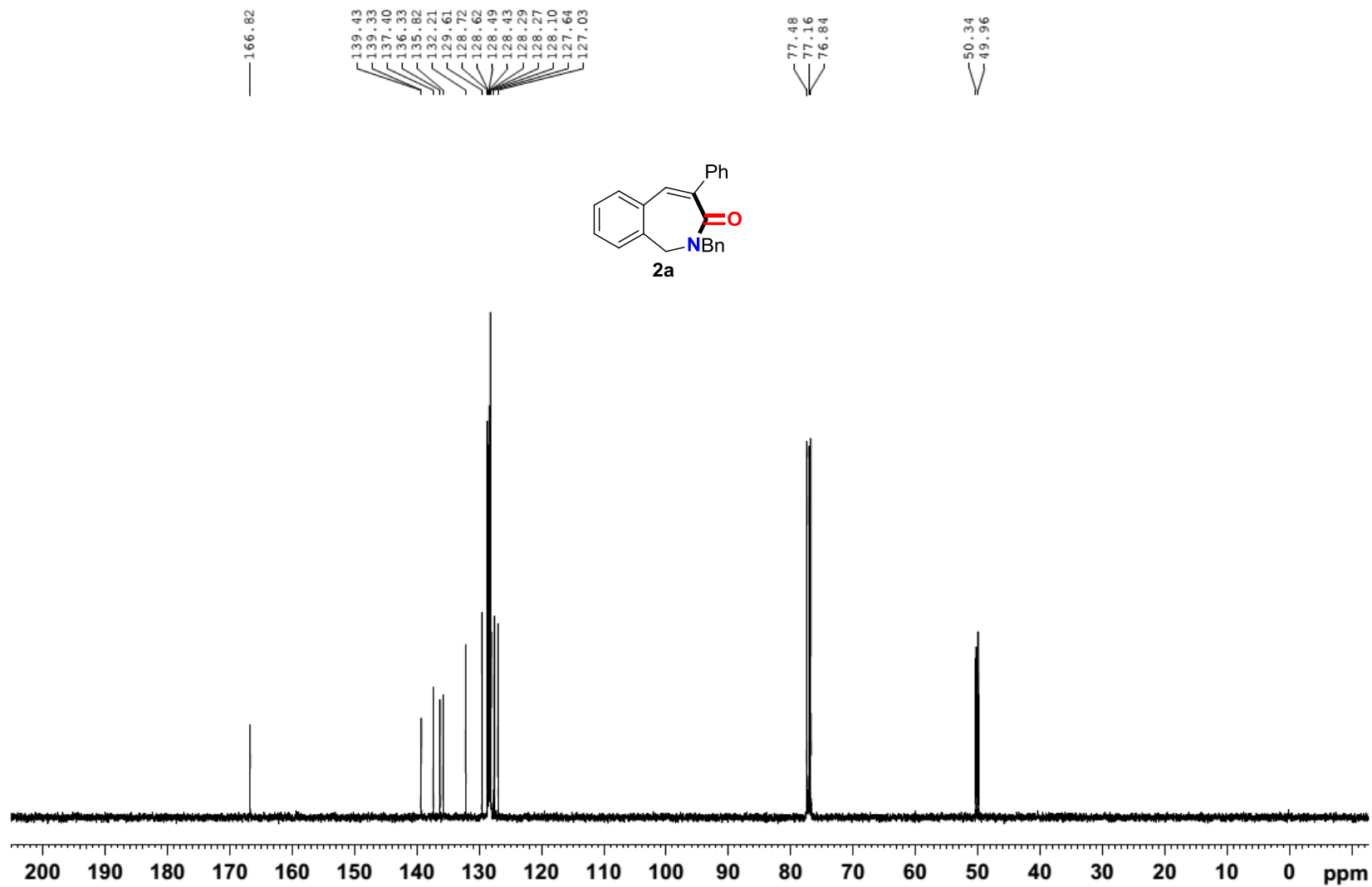


HY-X160831-1-HNMR

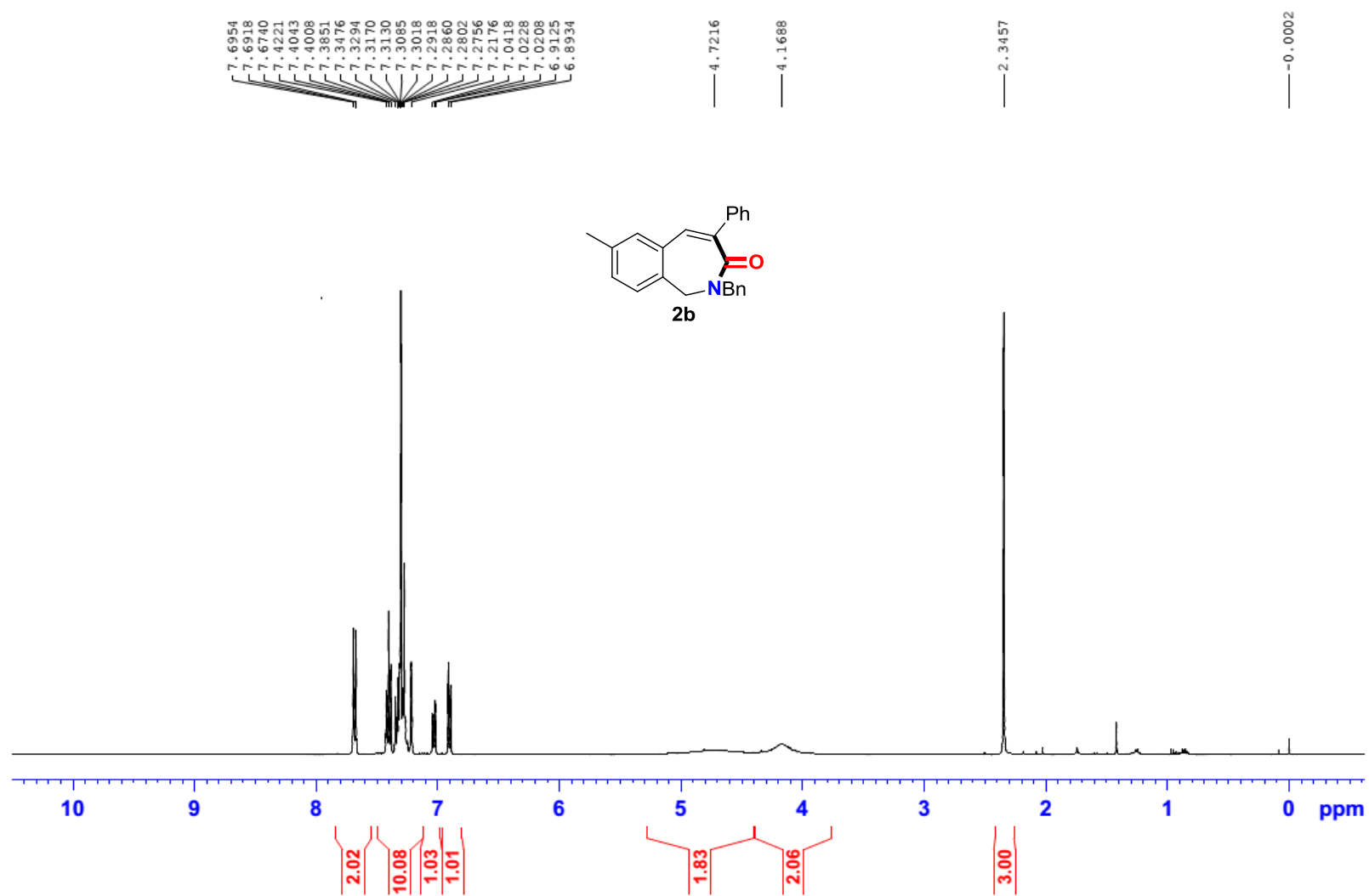




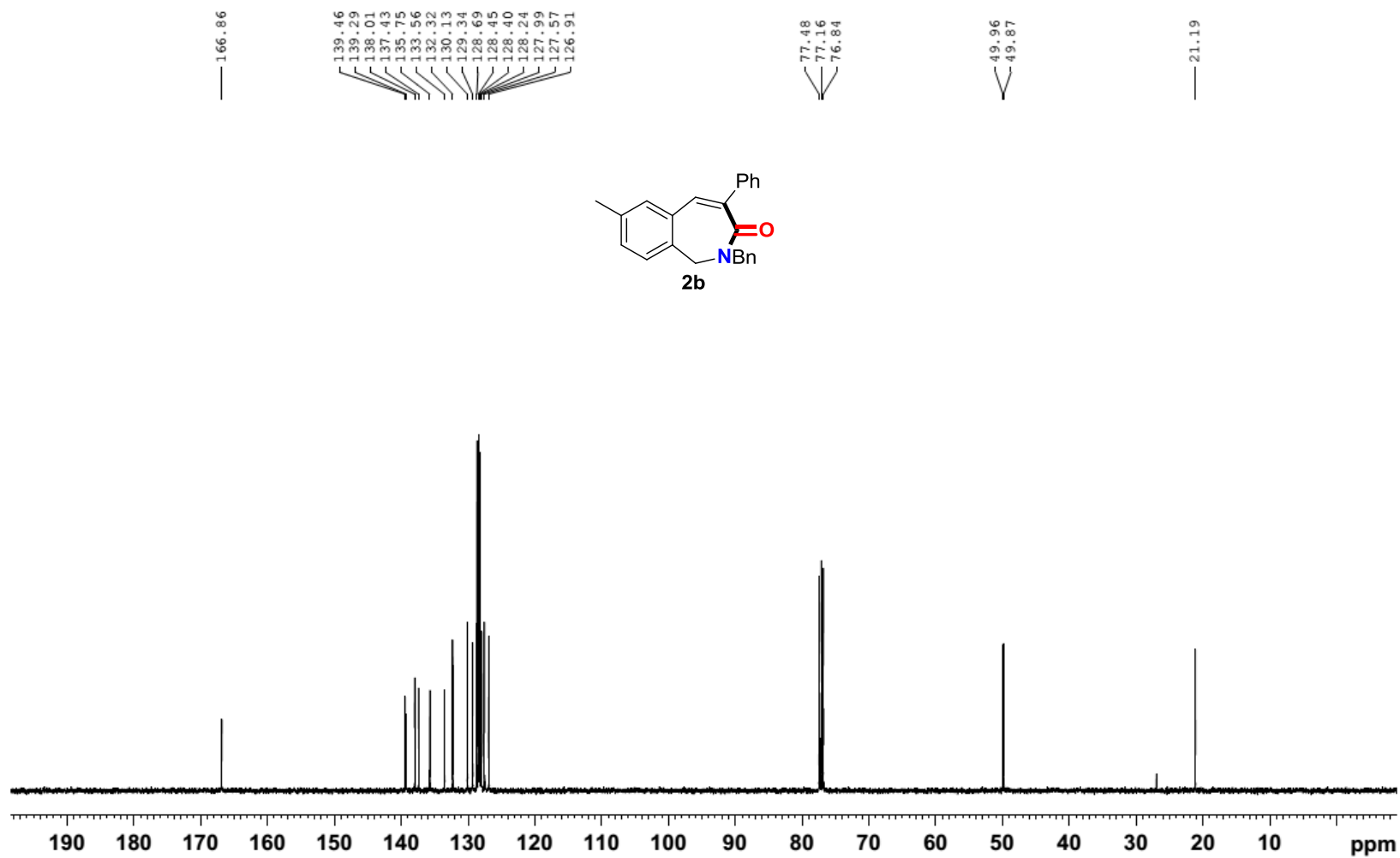
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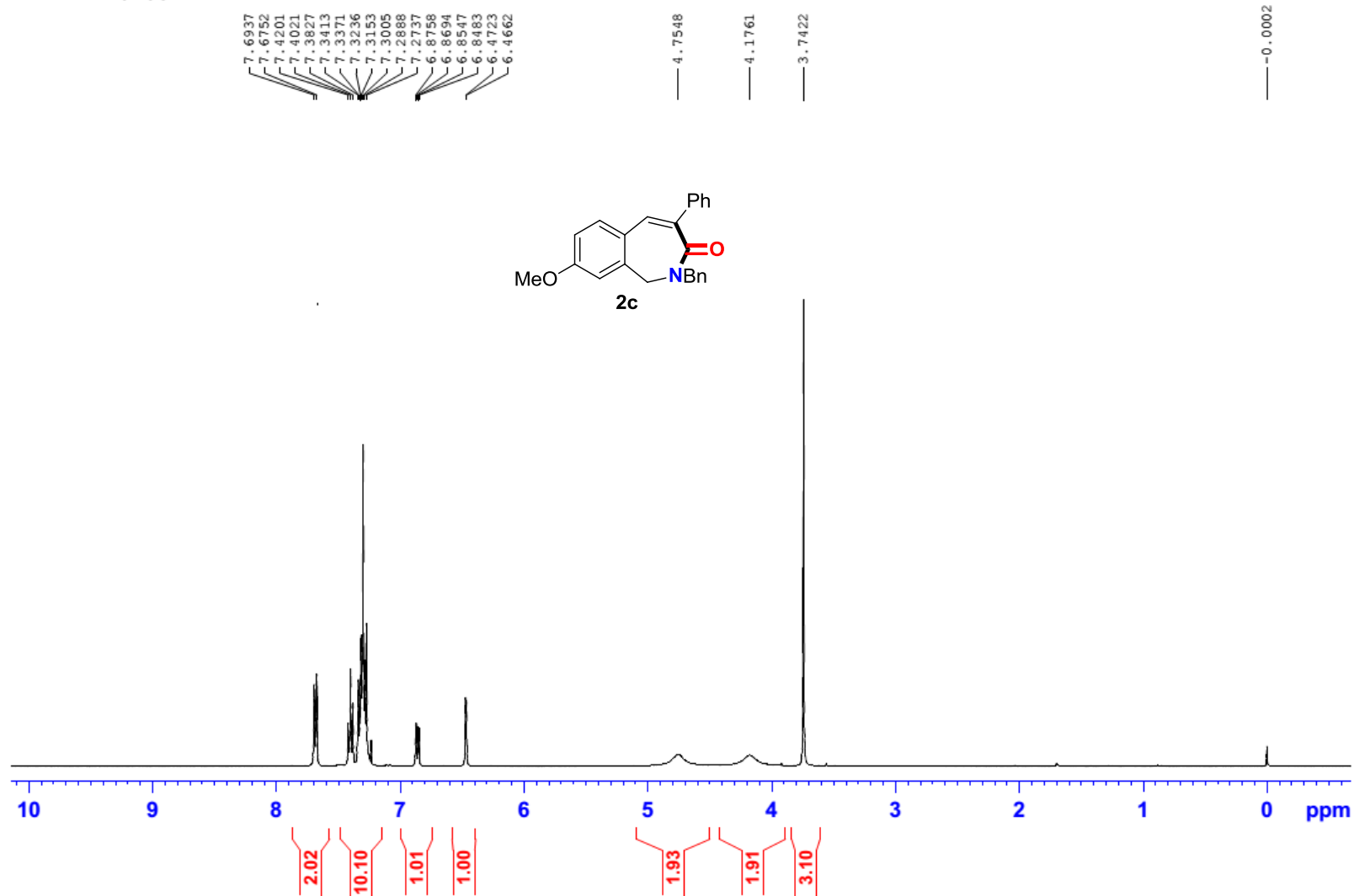
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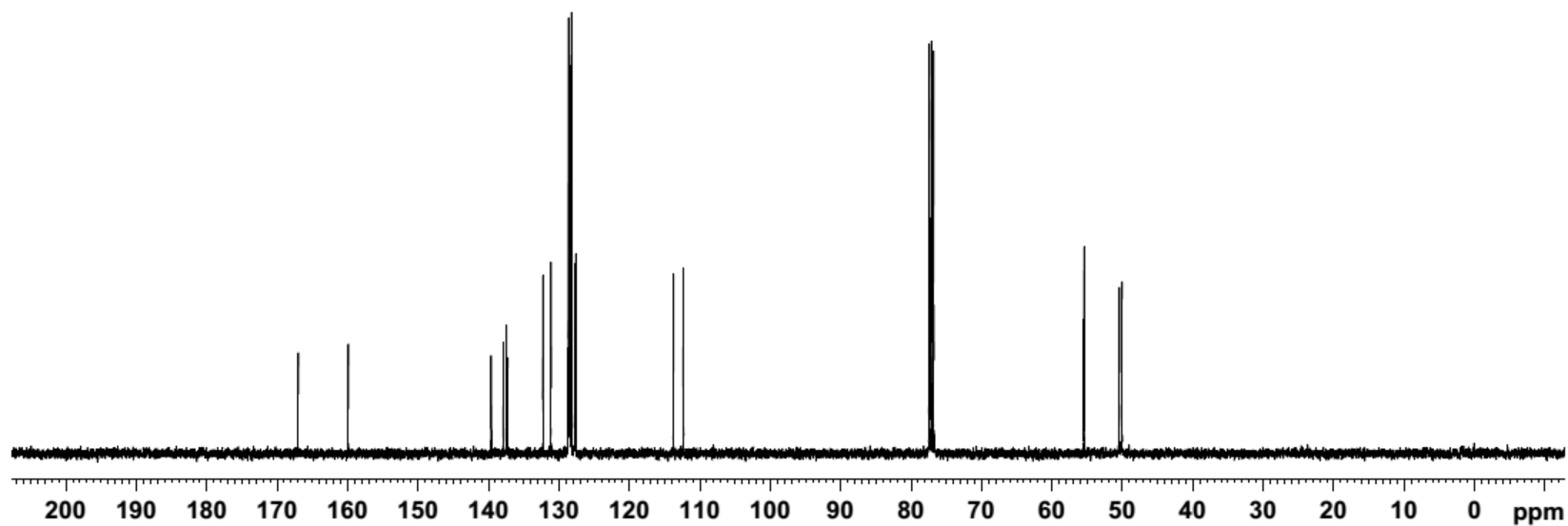
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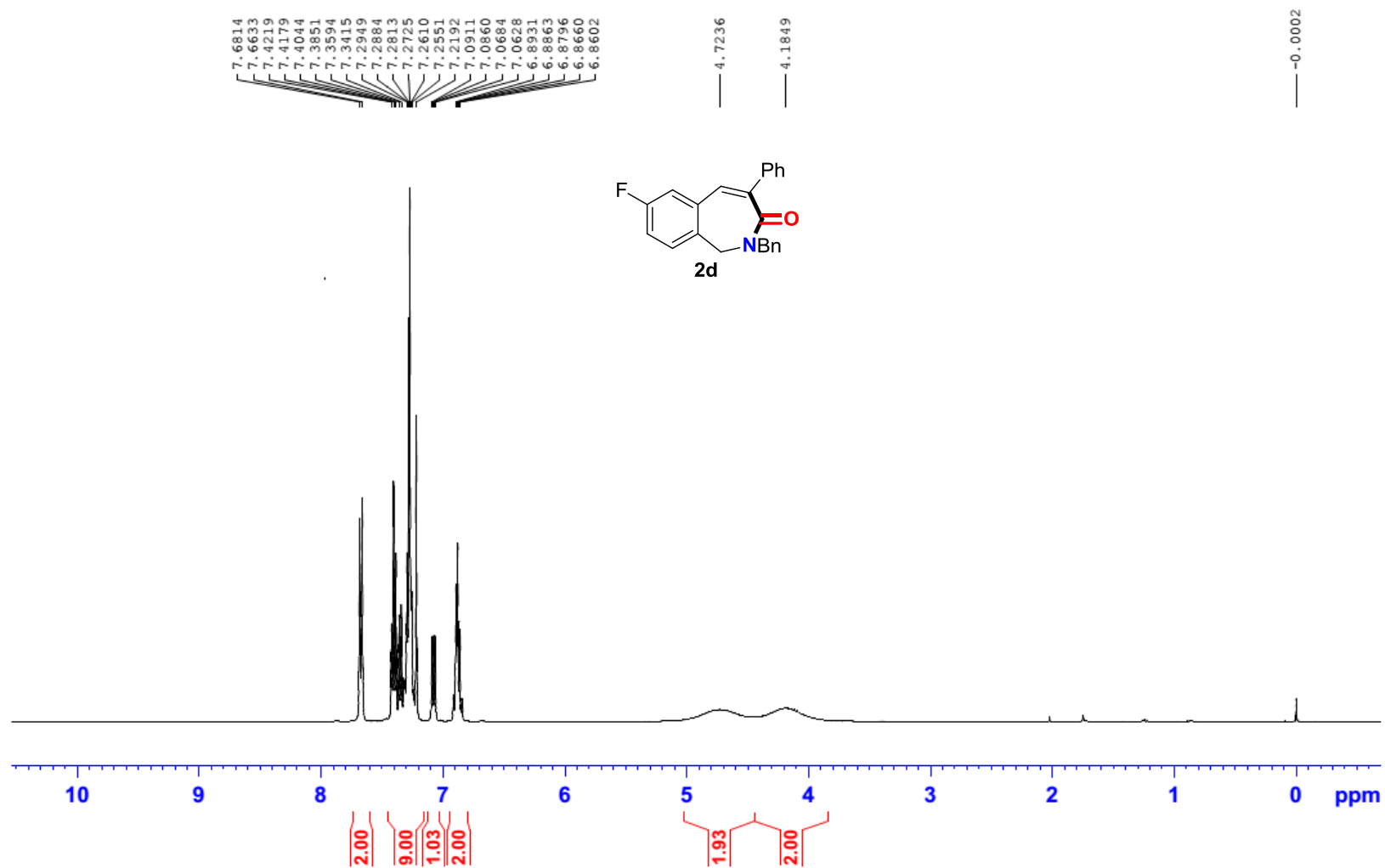
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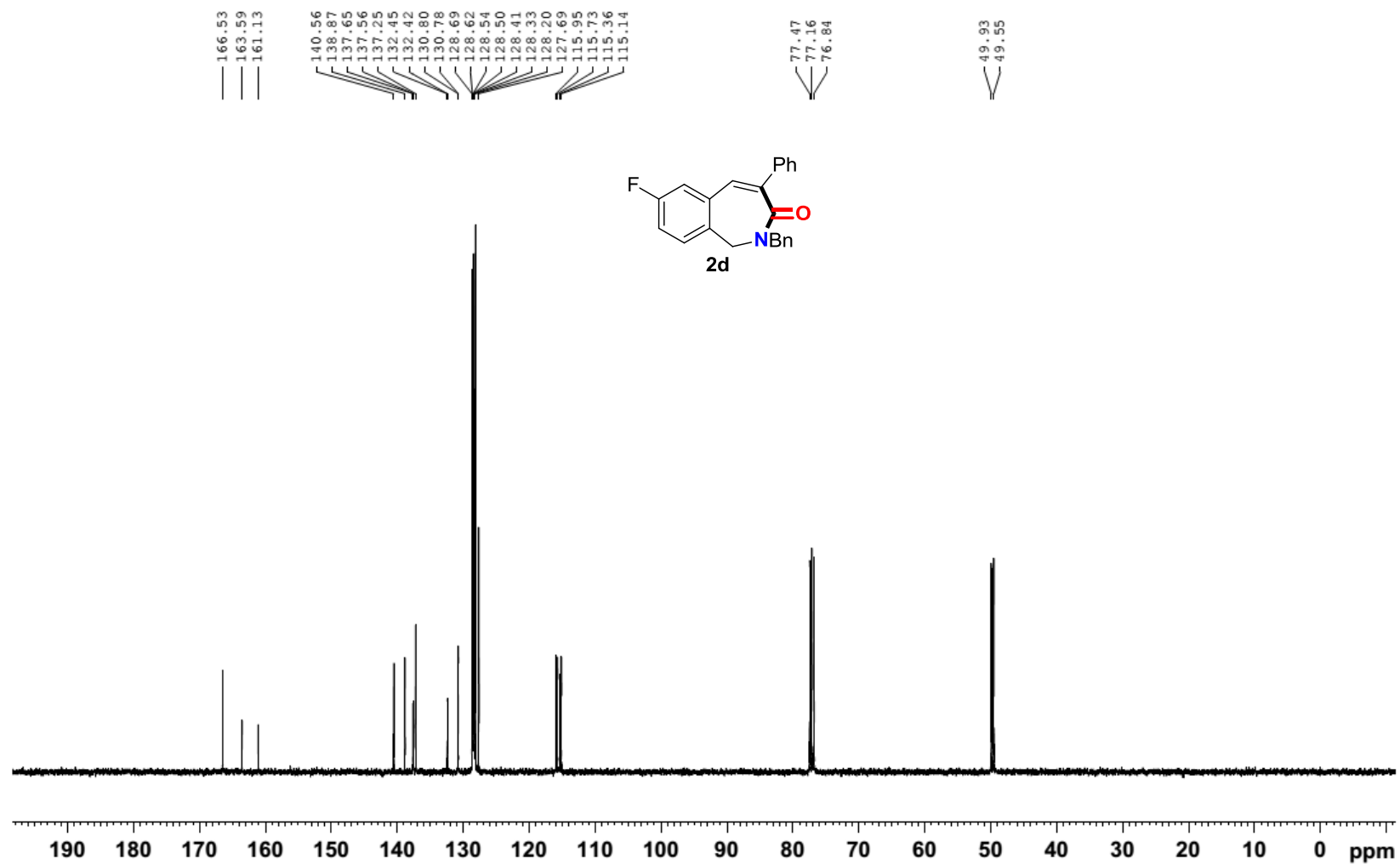
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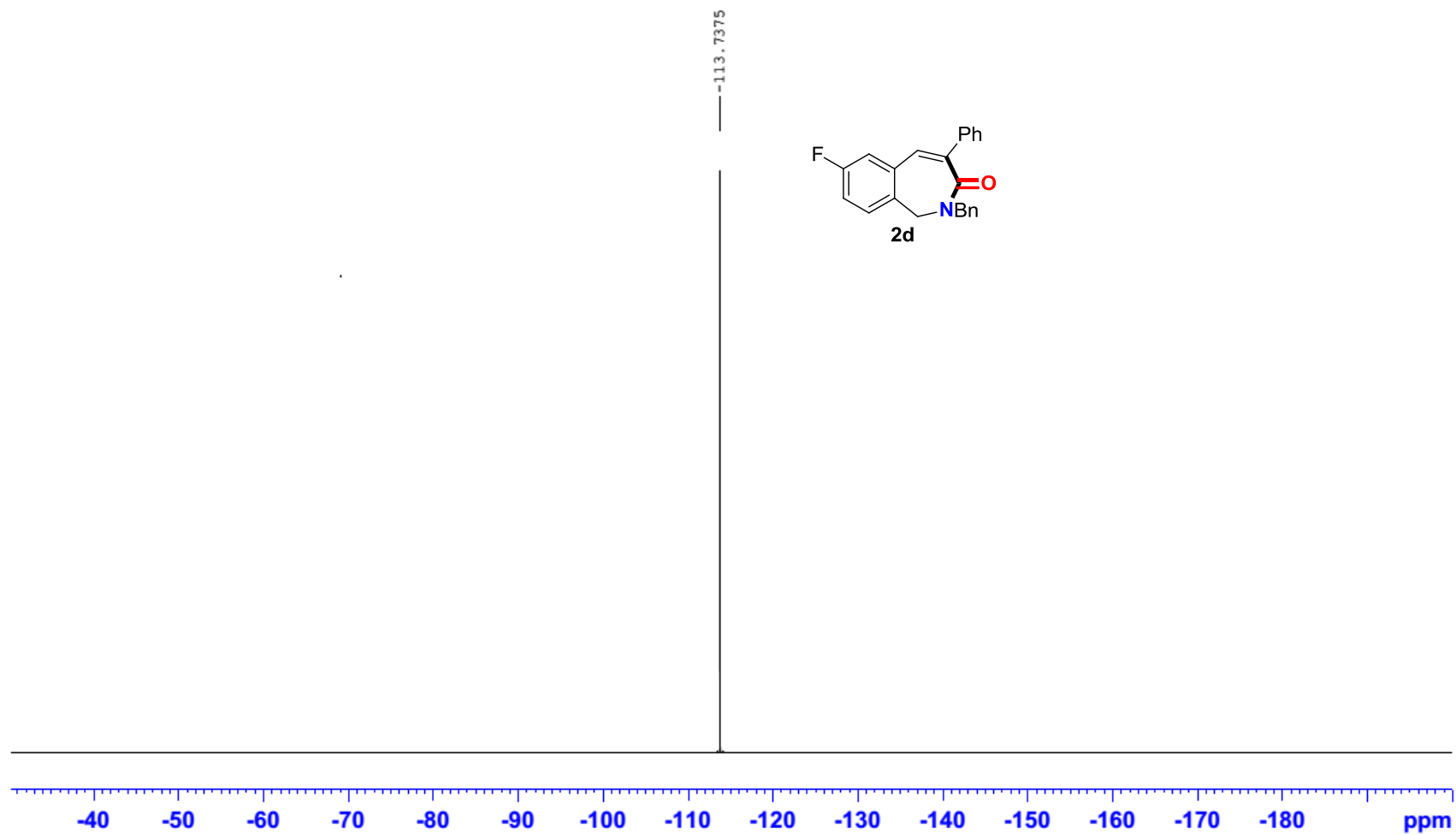
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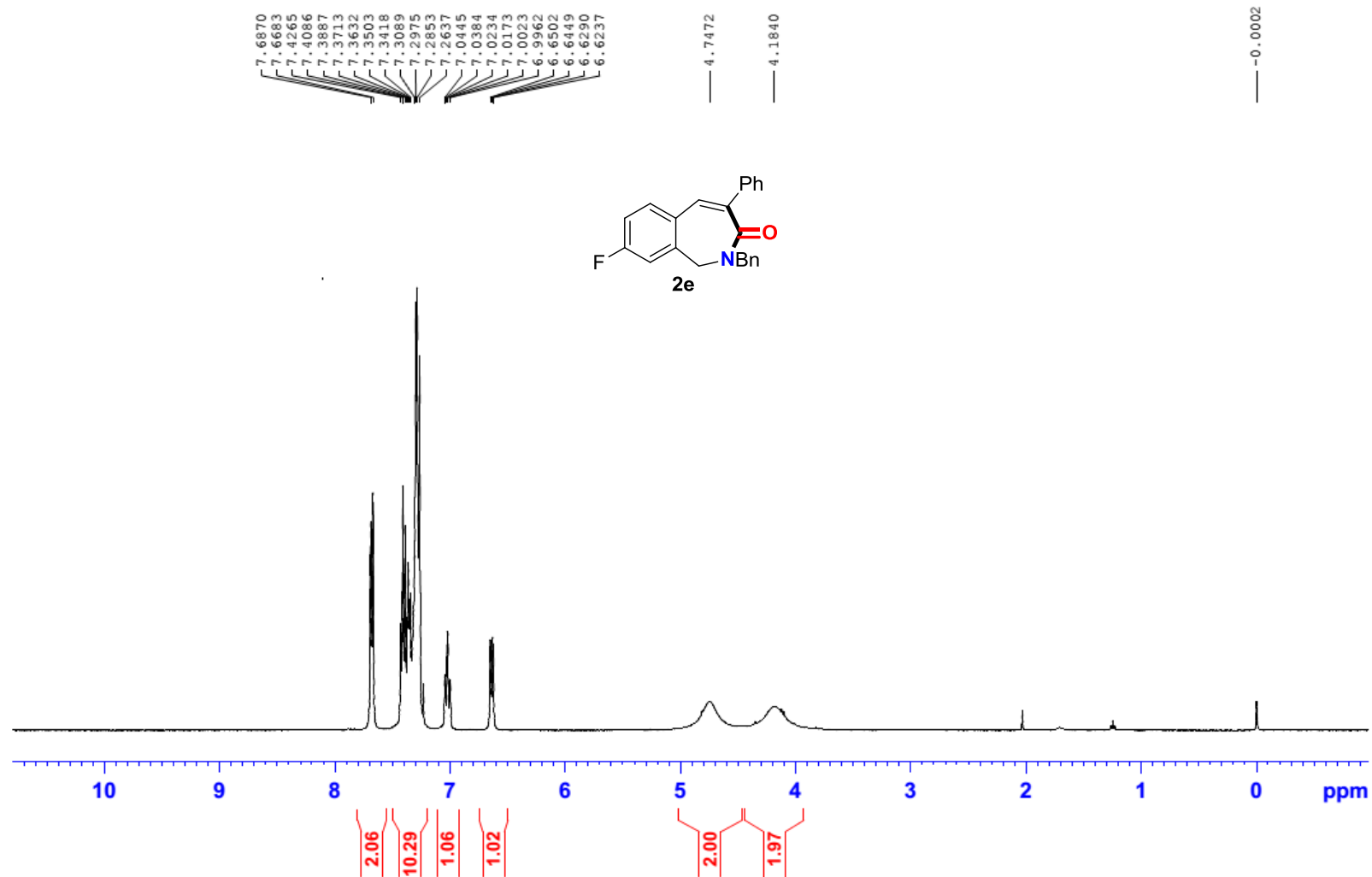


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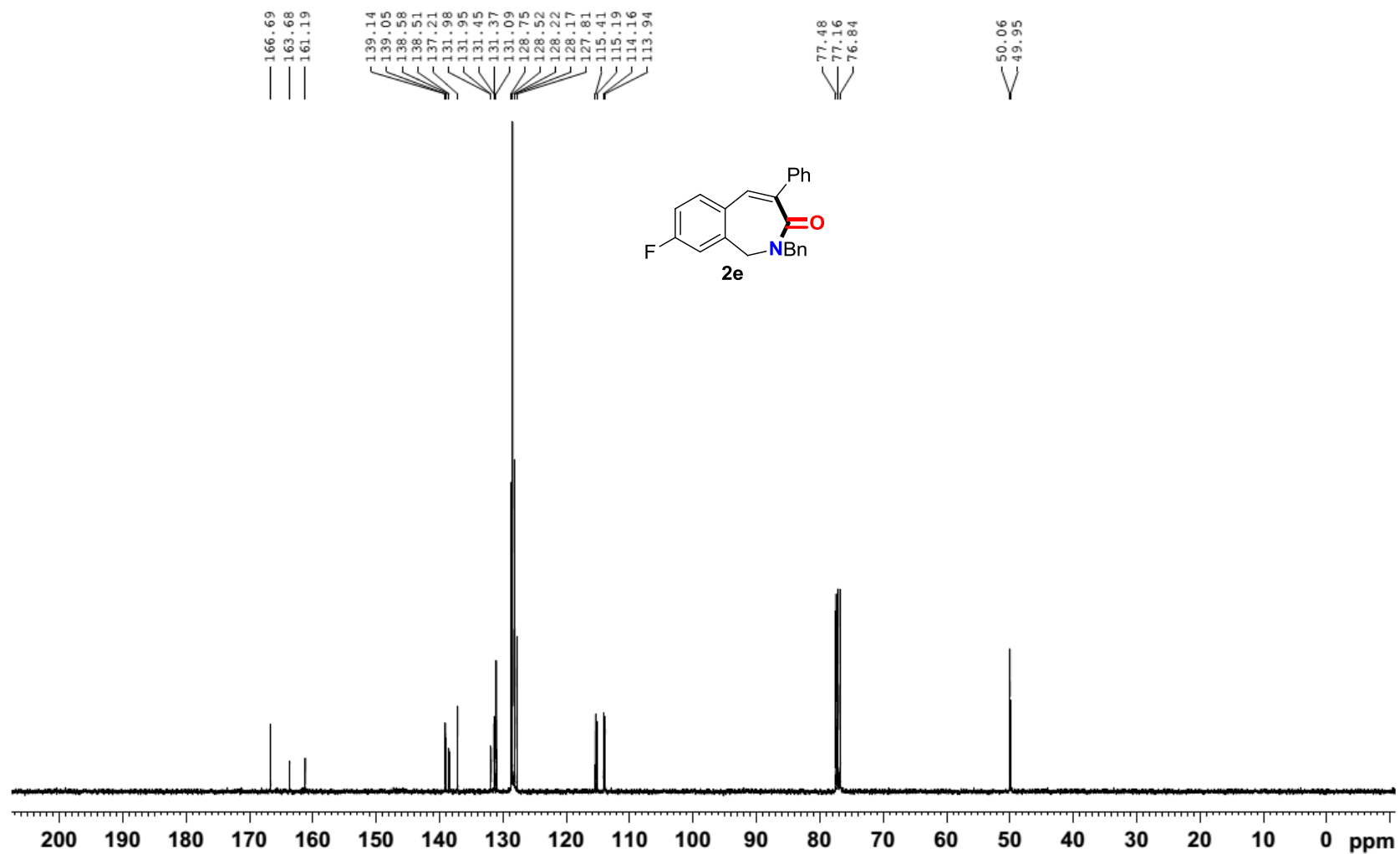




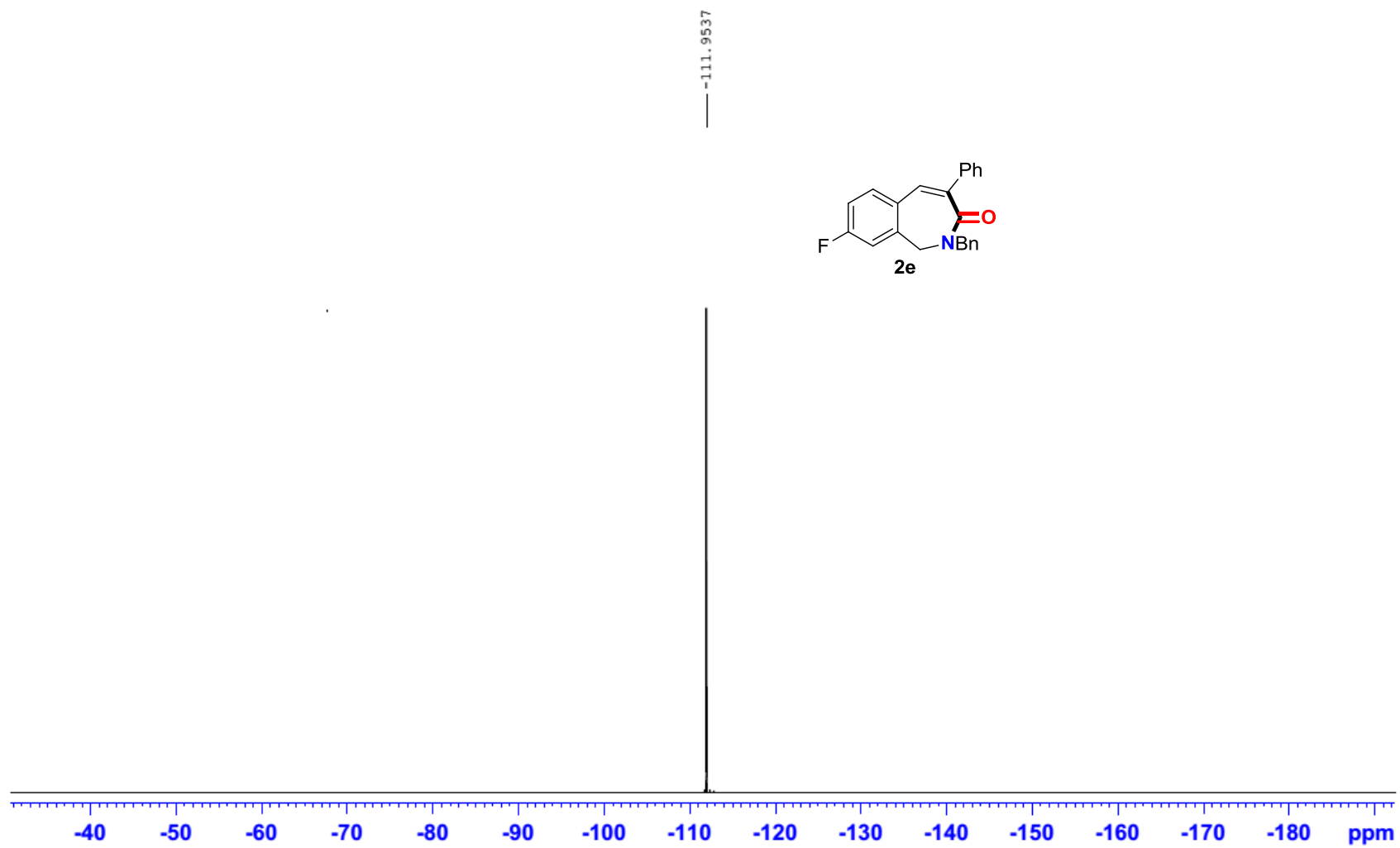
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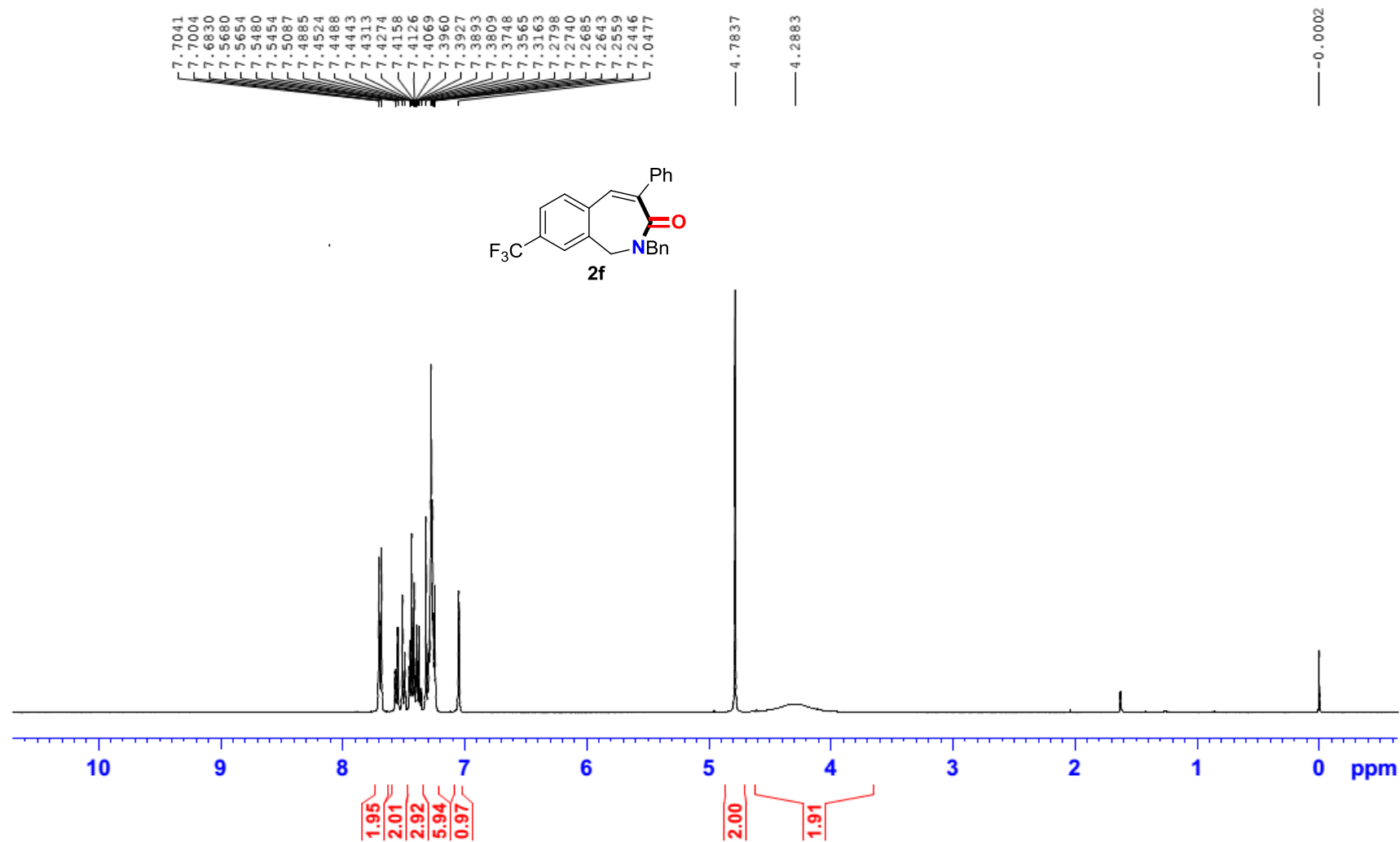
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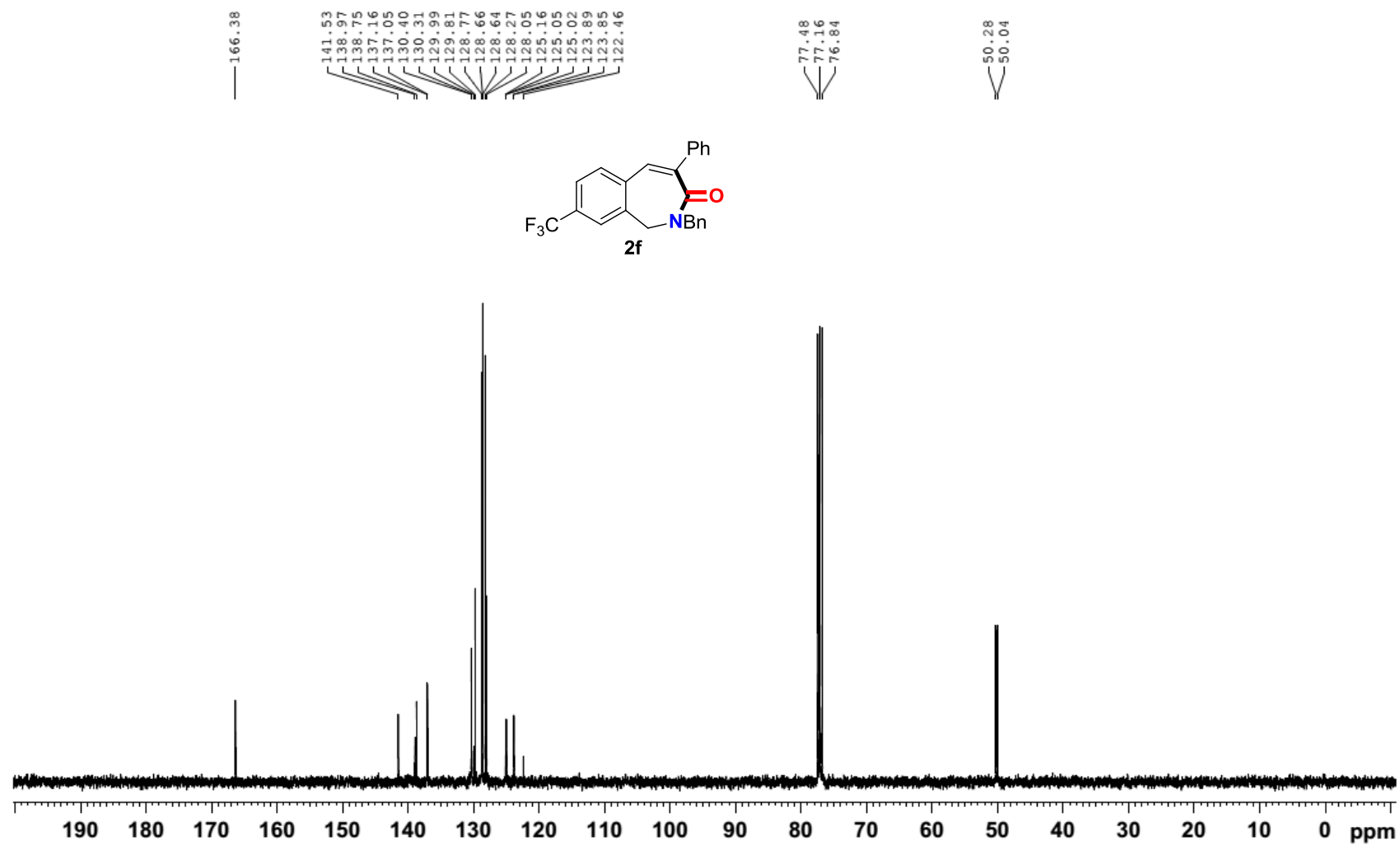
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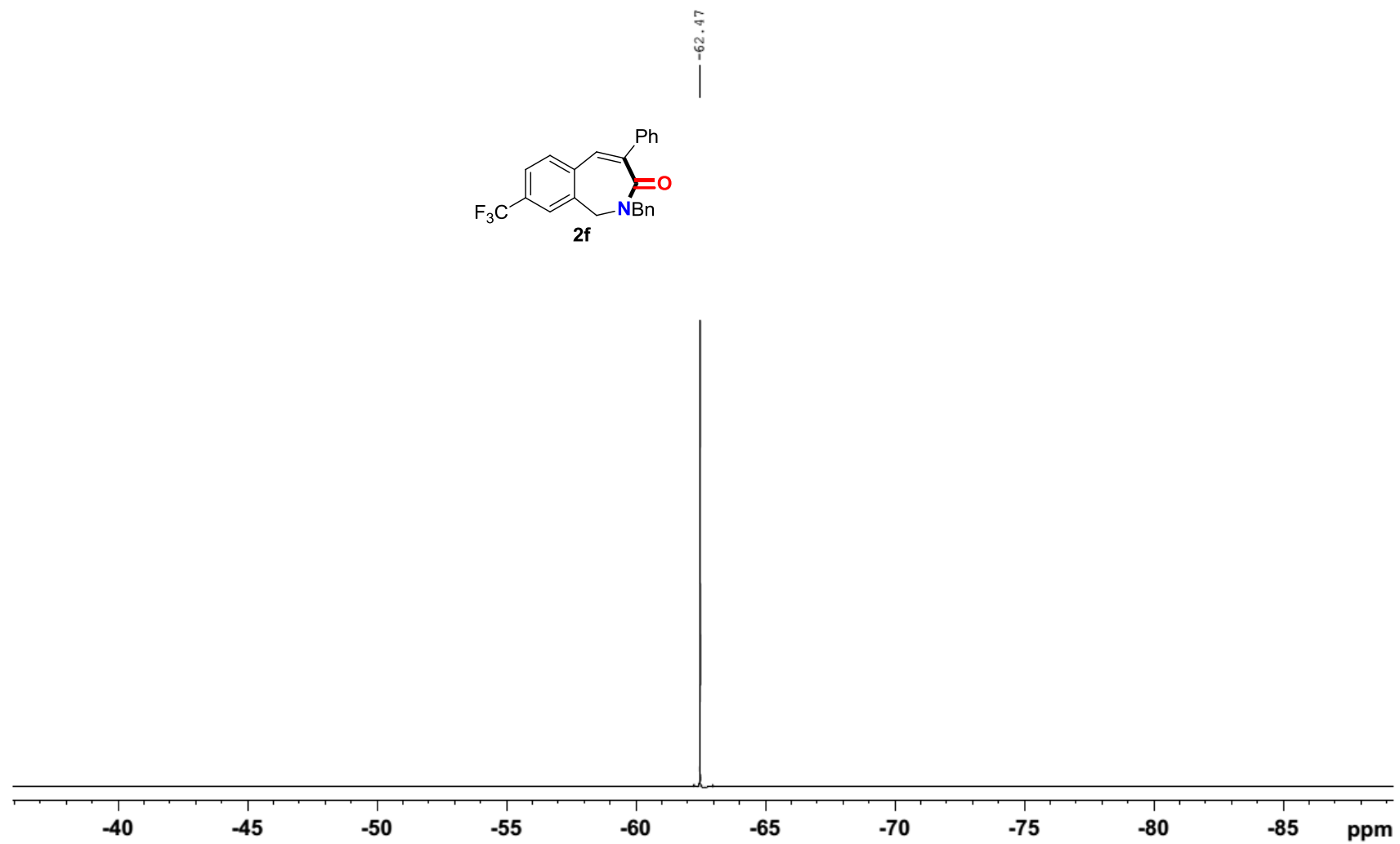
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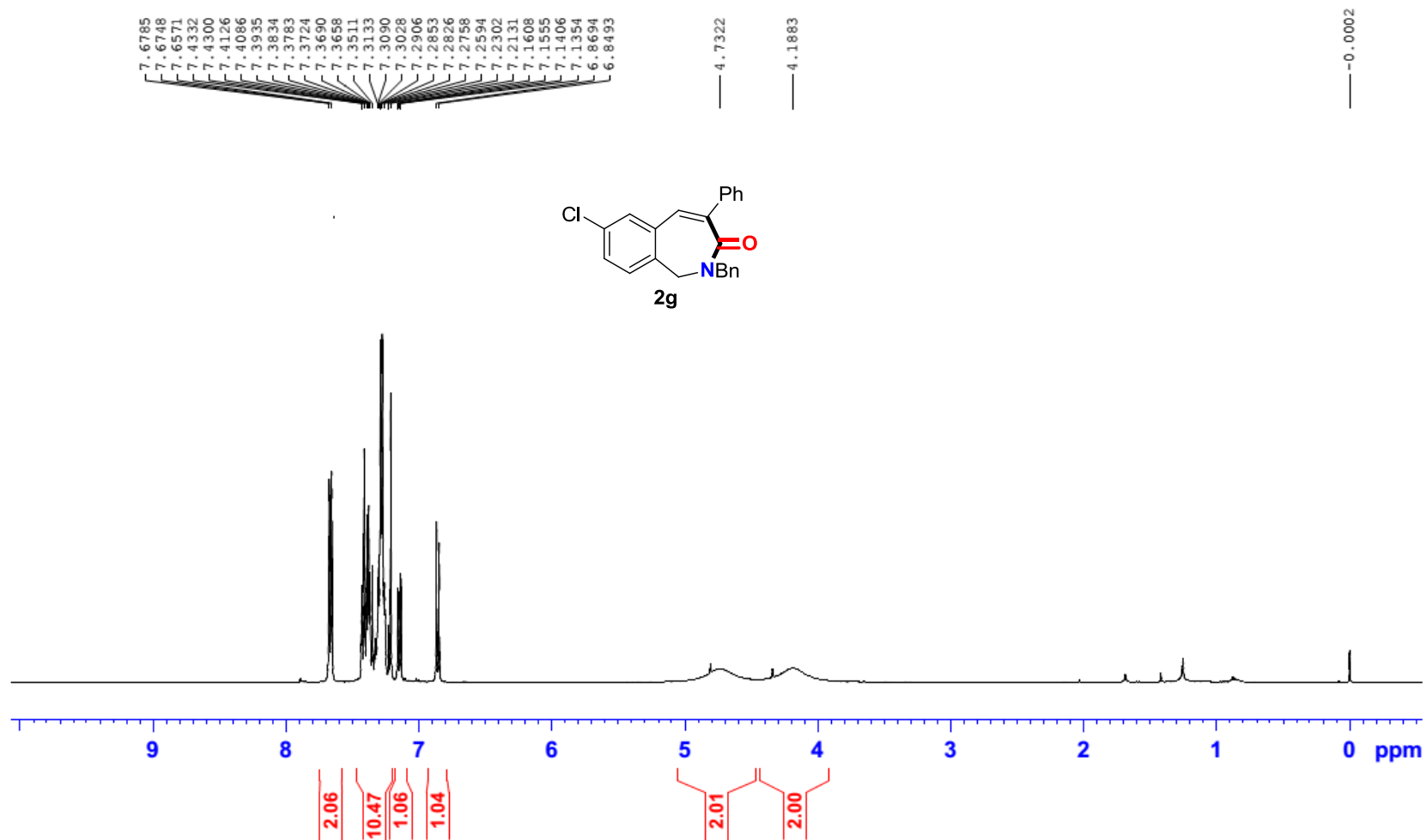
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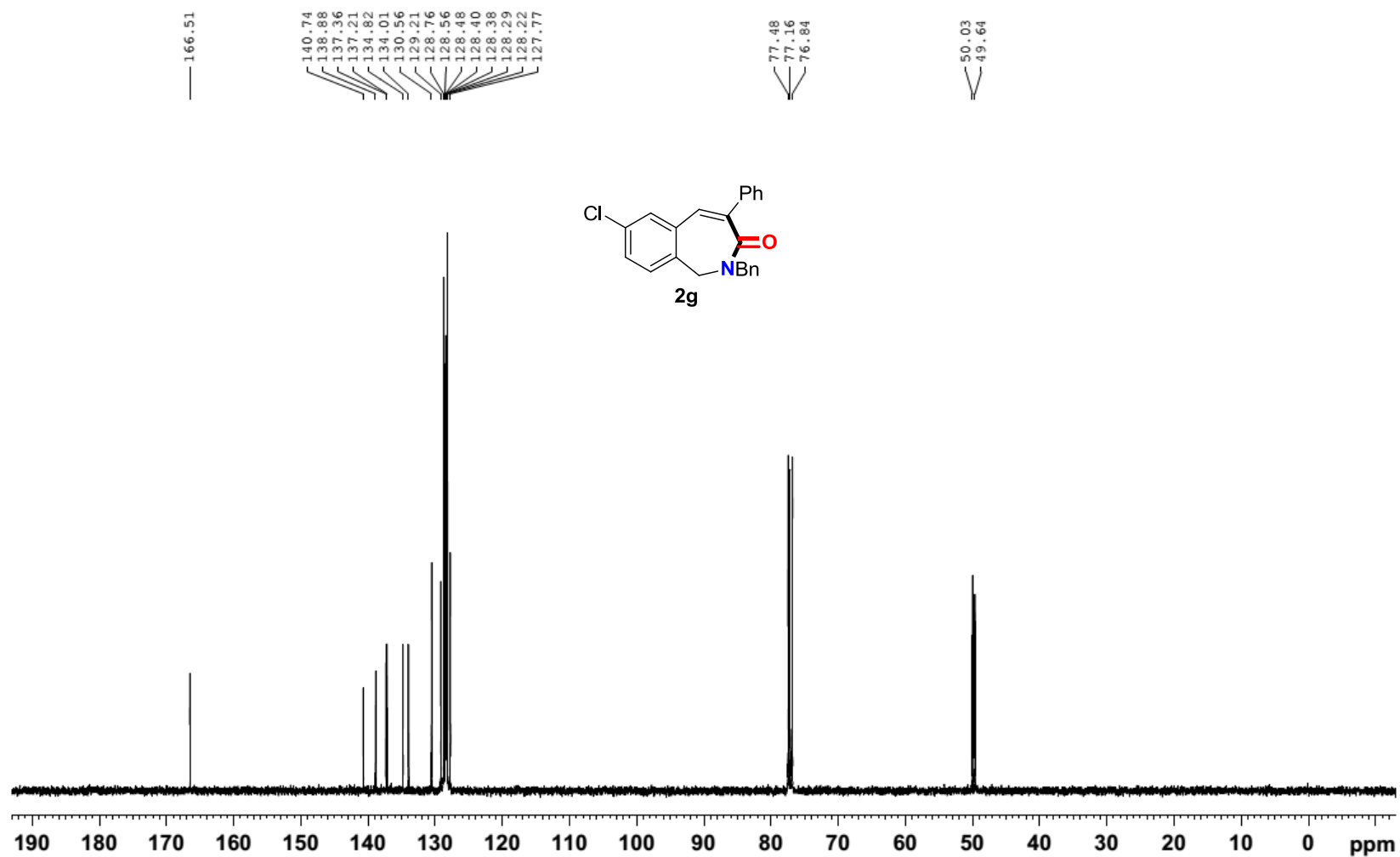
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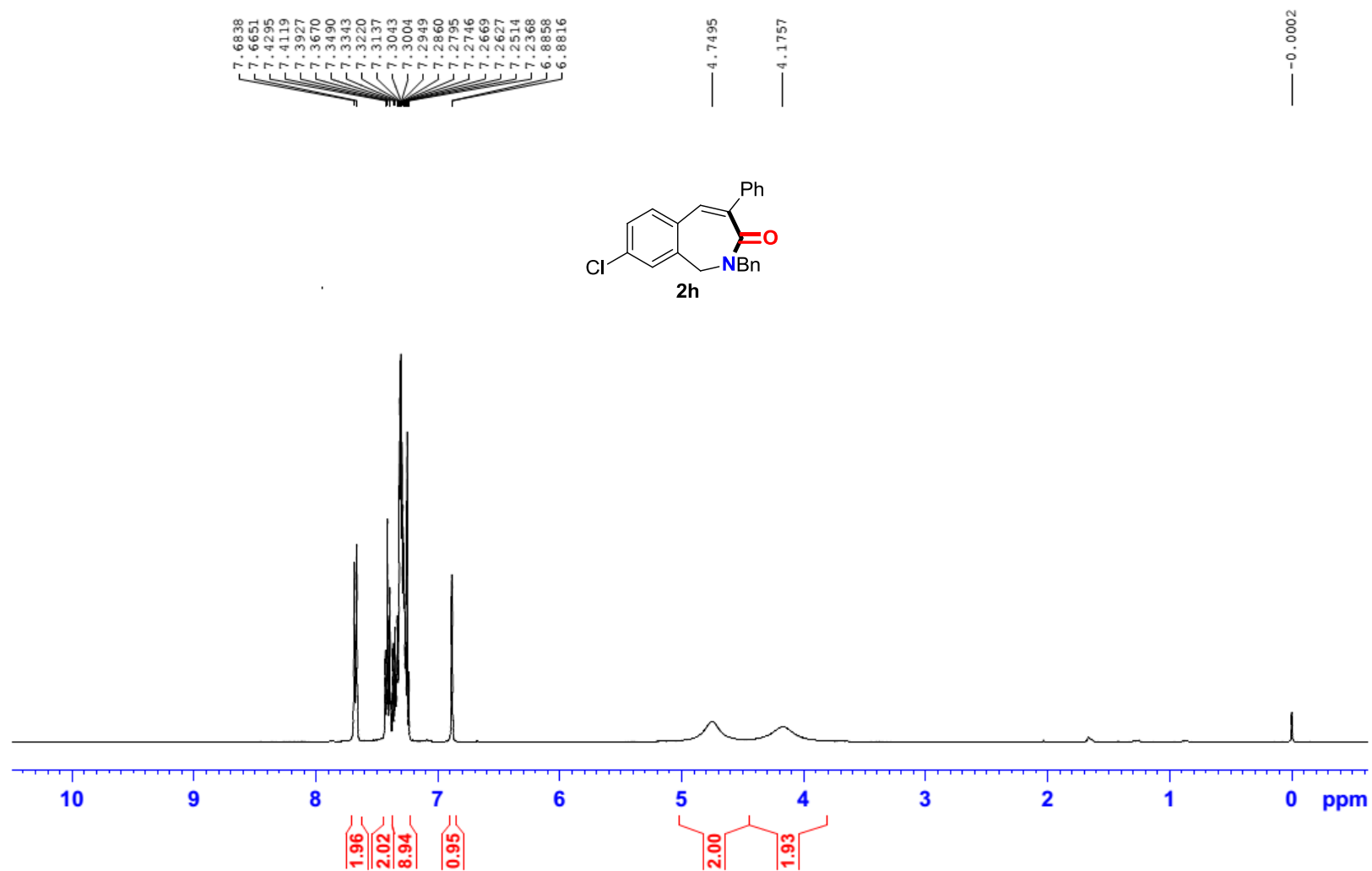


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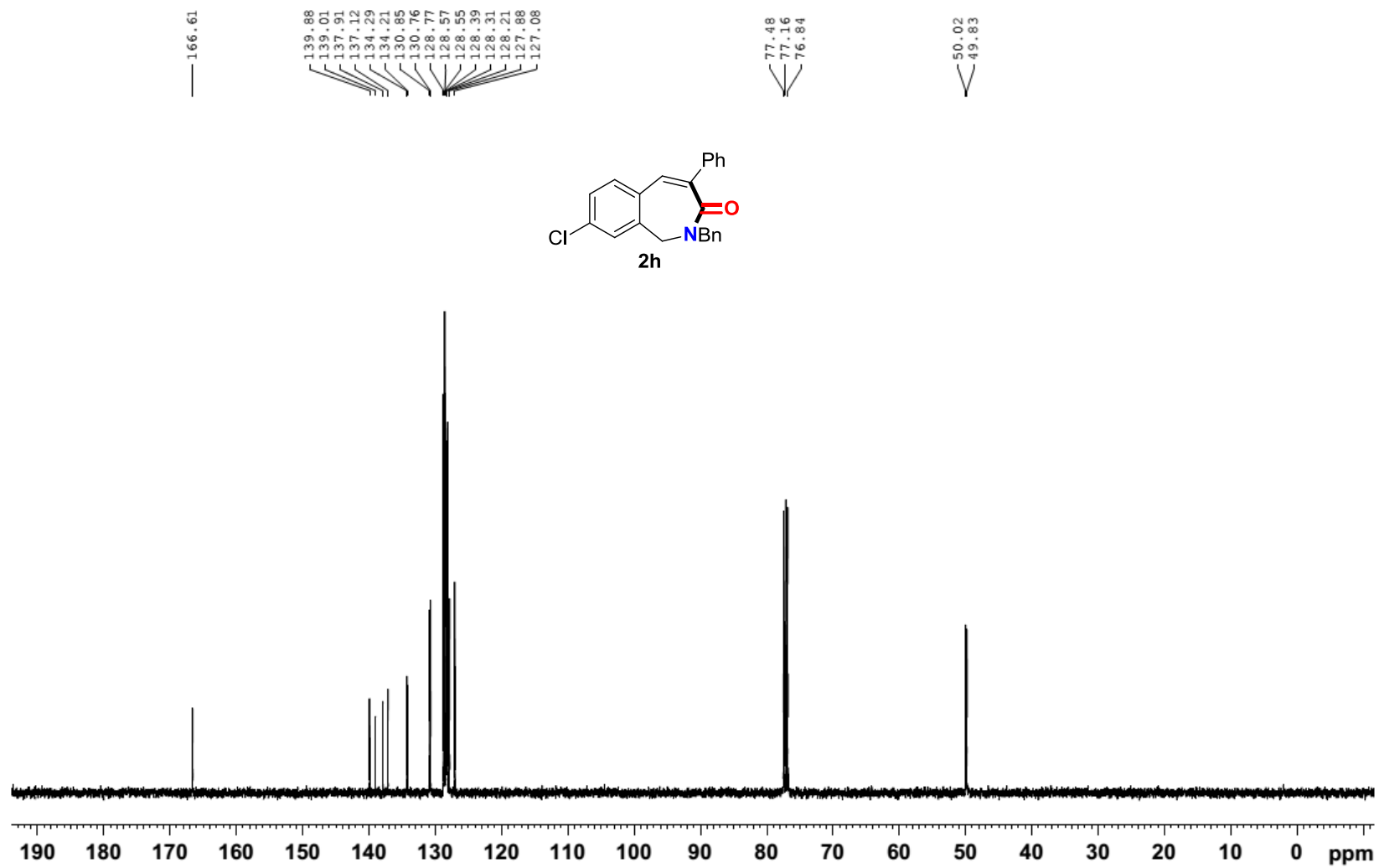




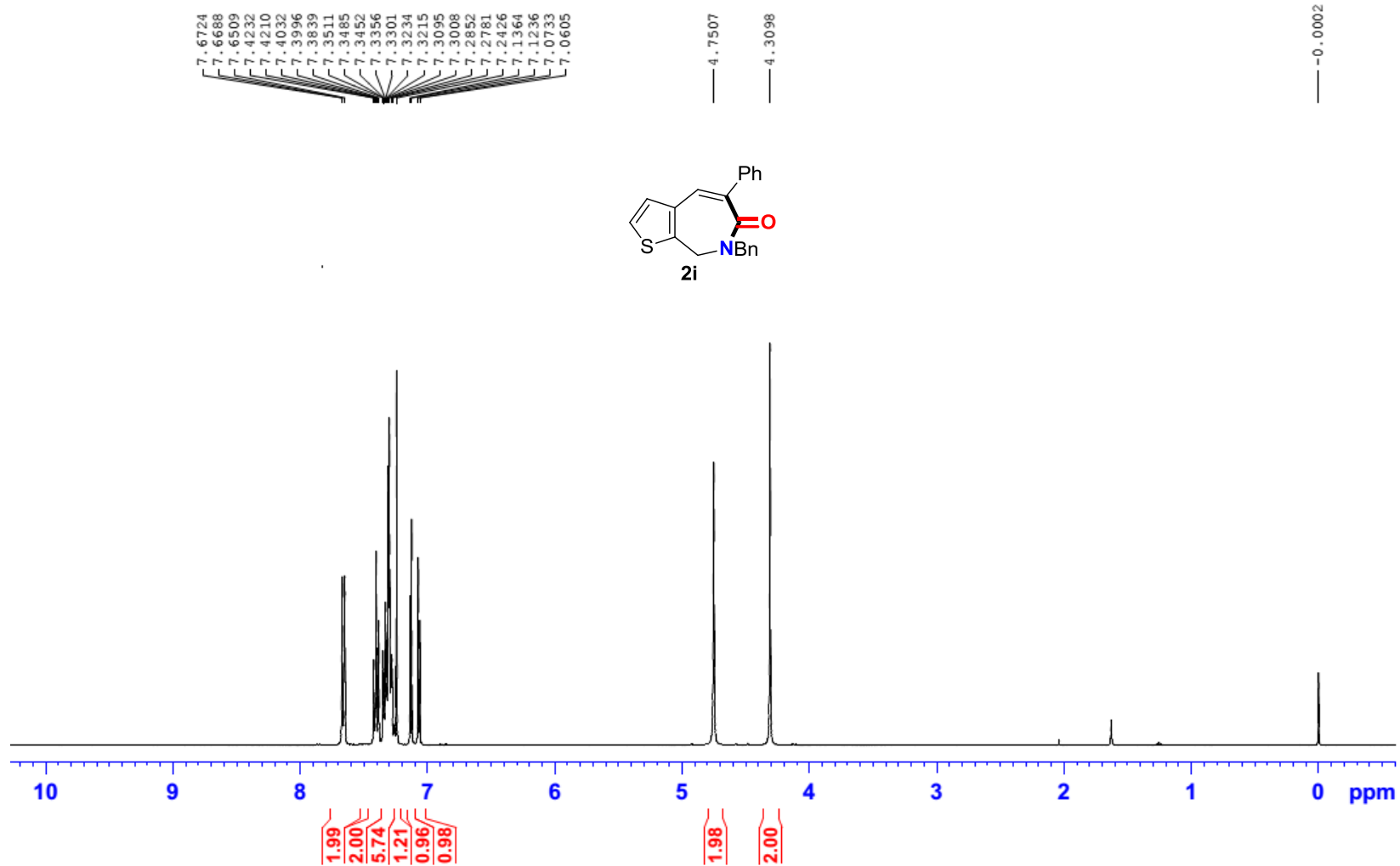
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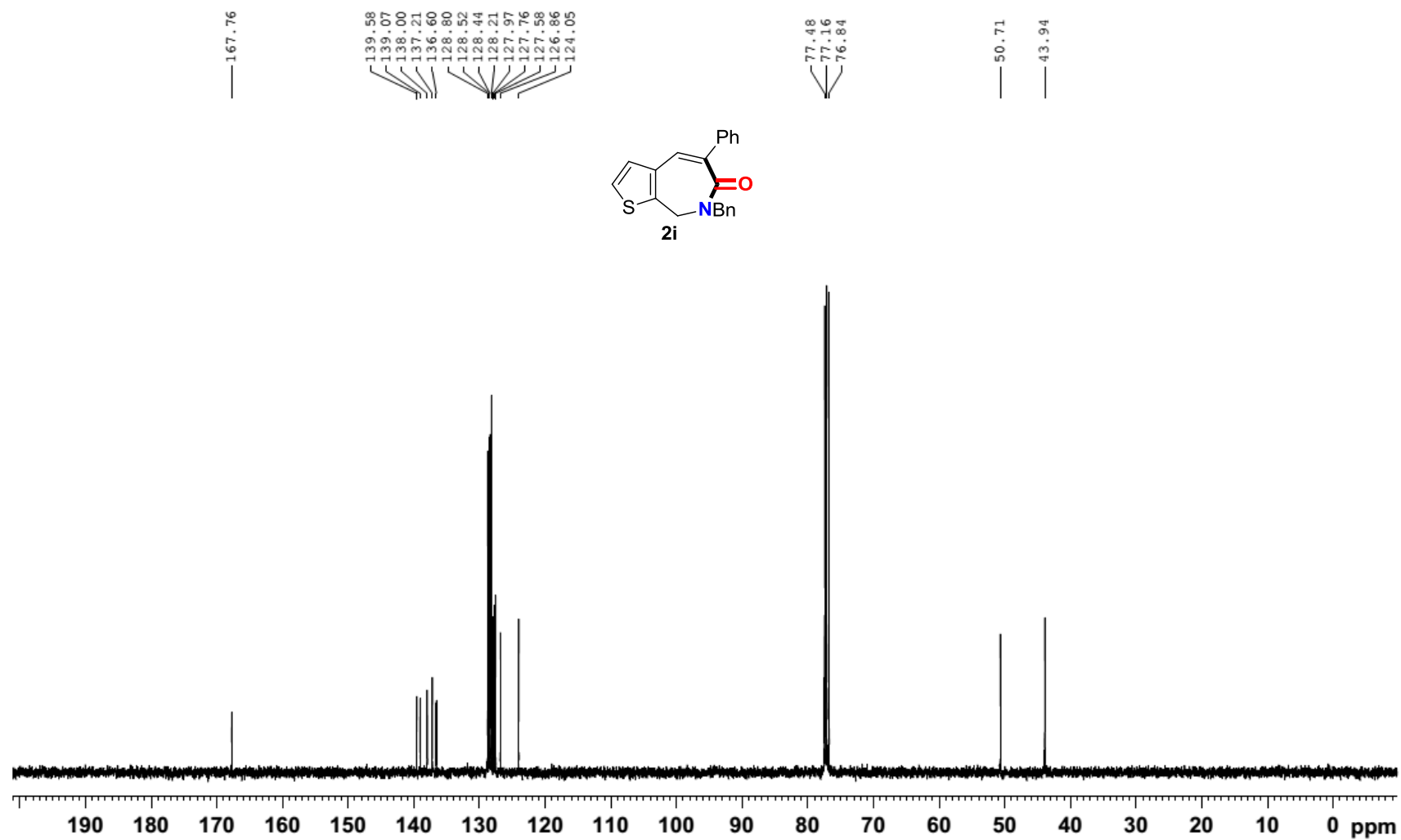
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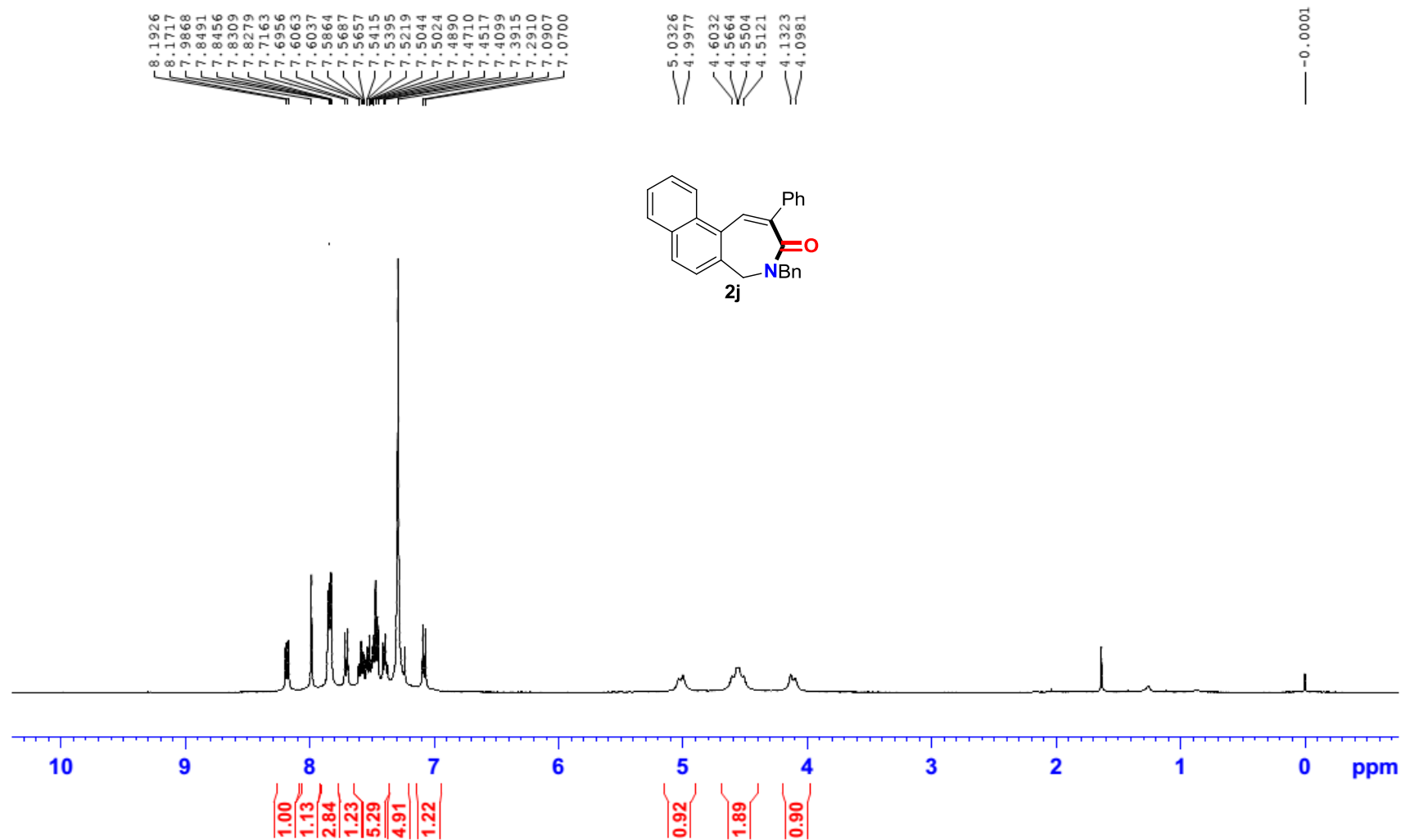
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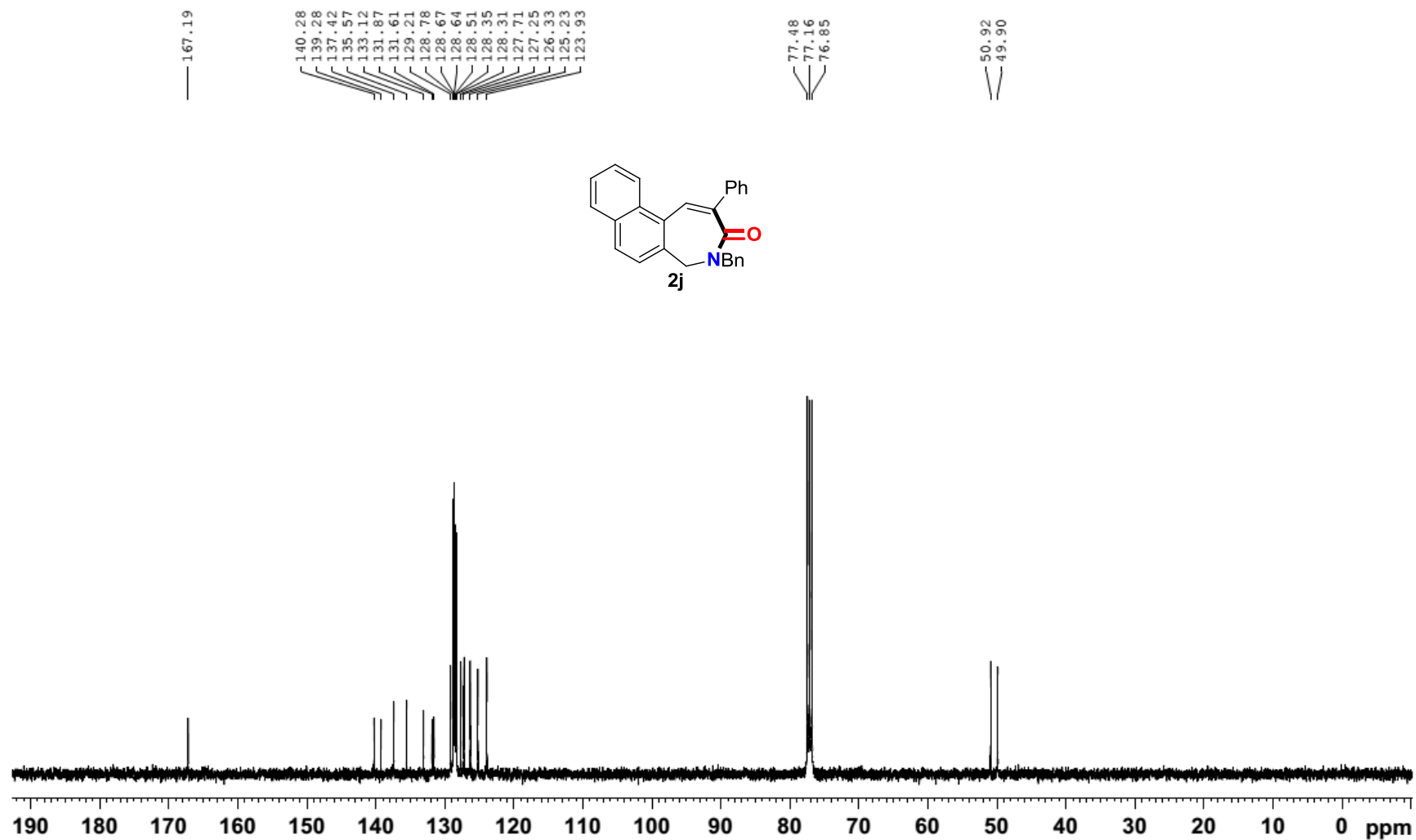
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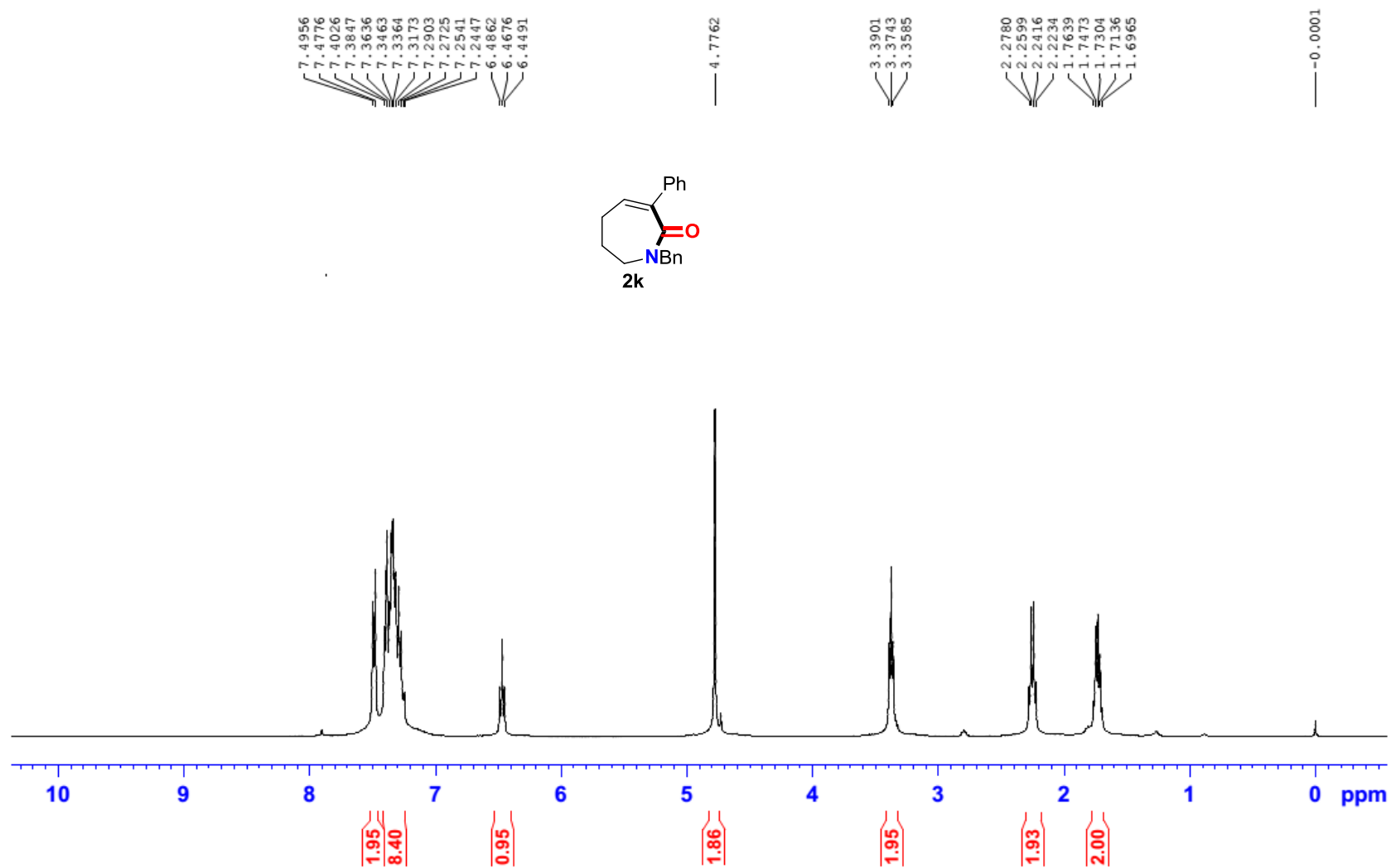
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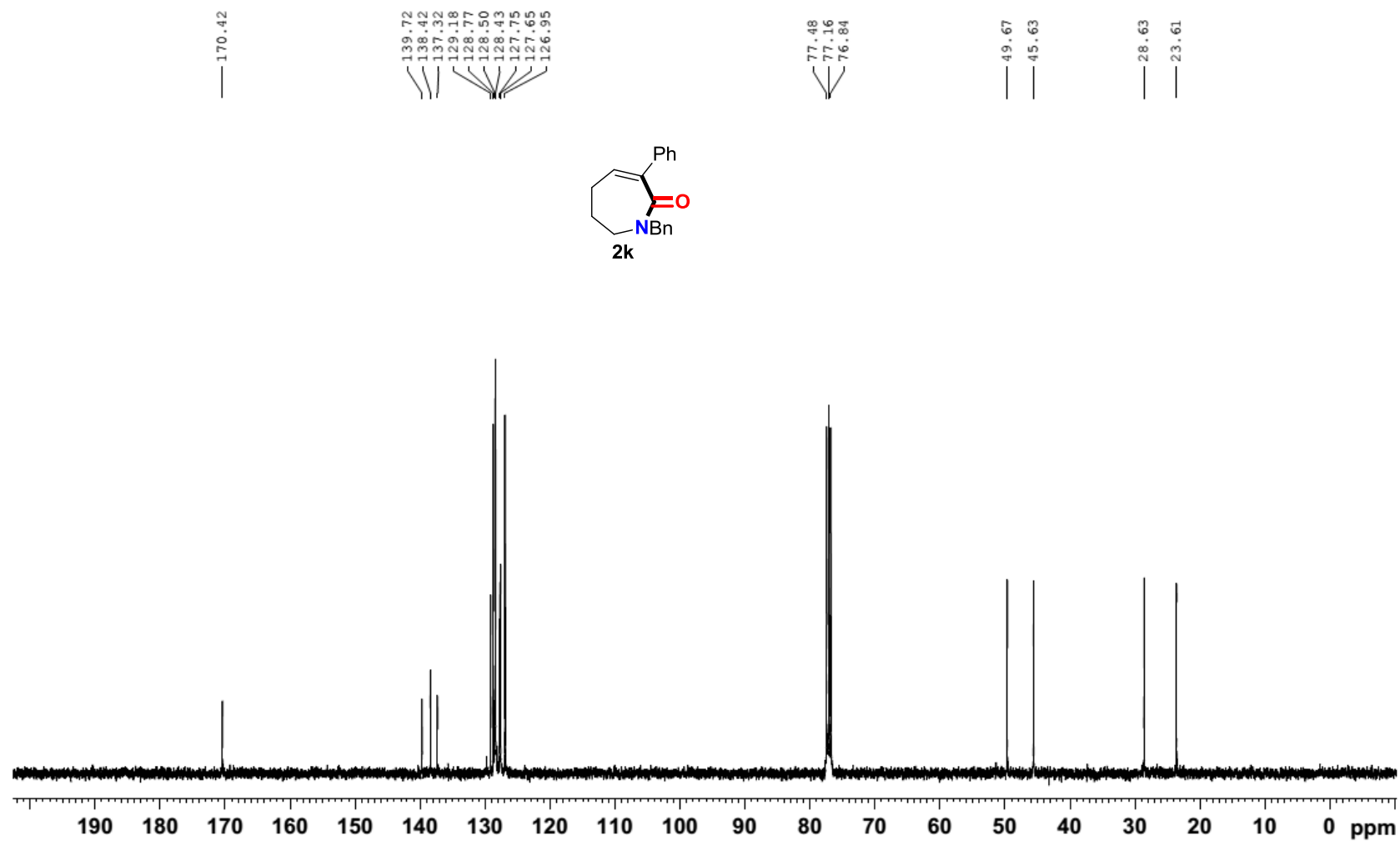
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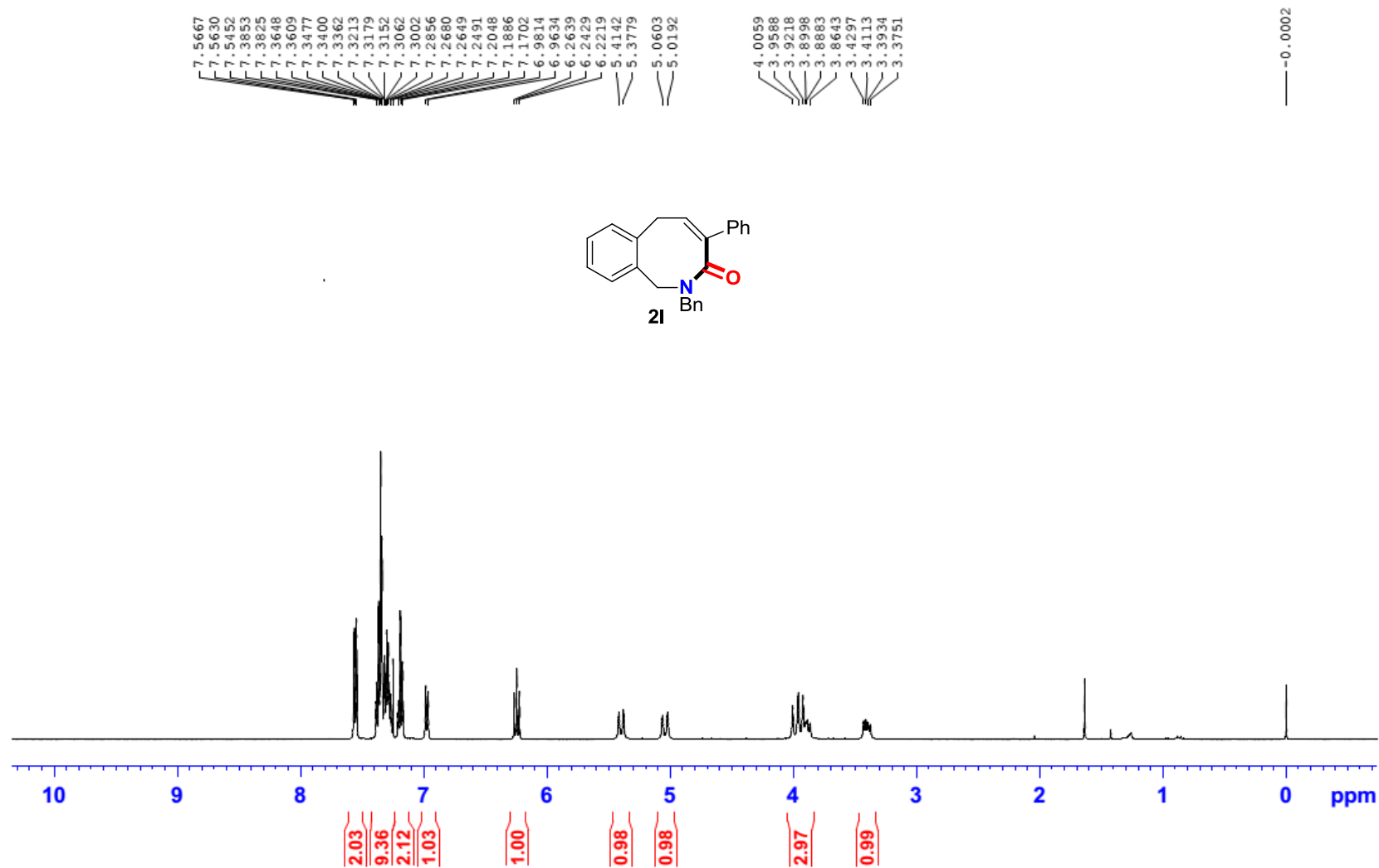


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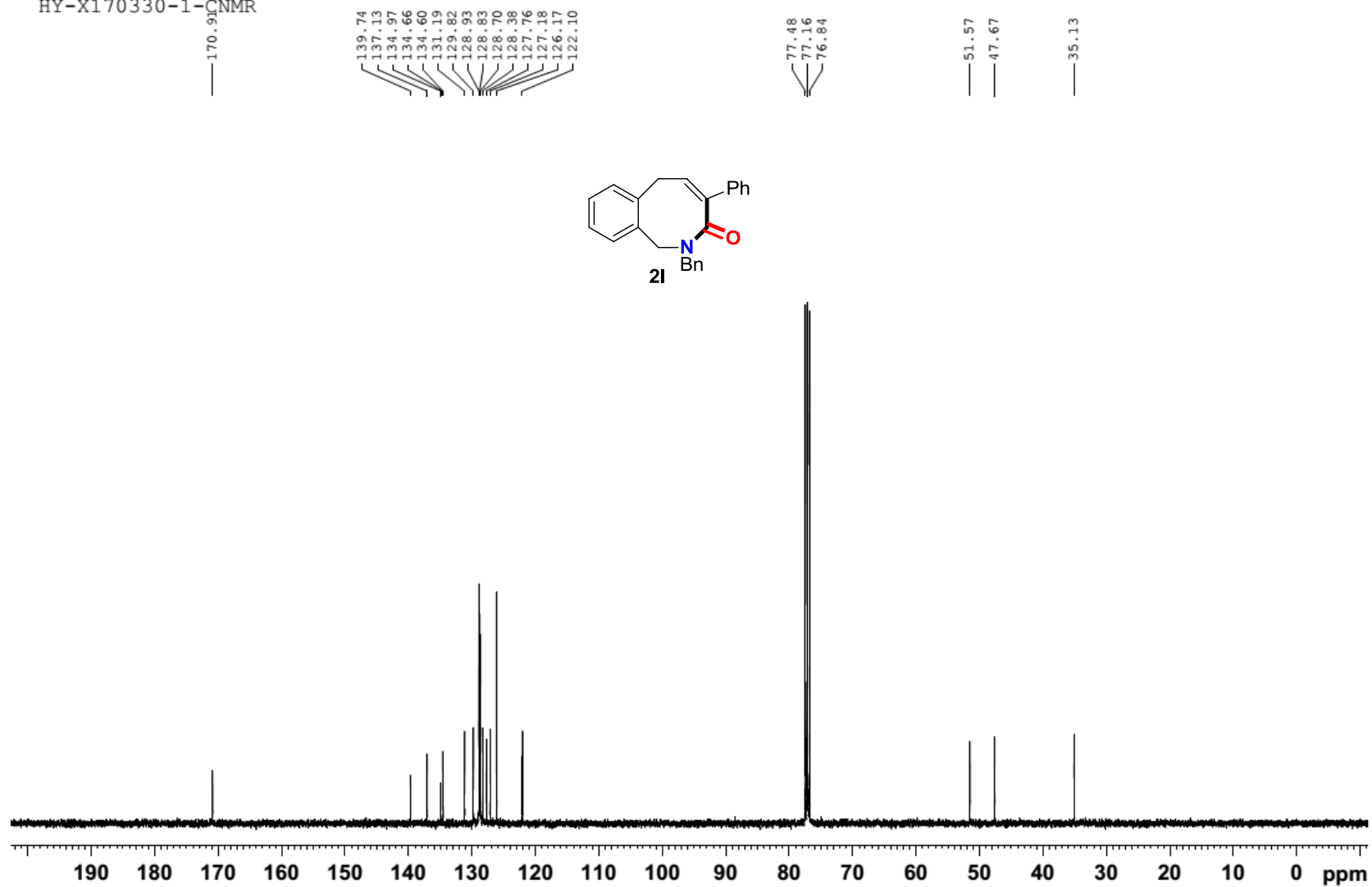




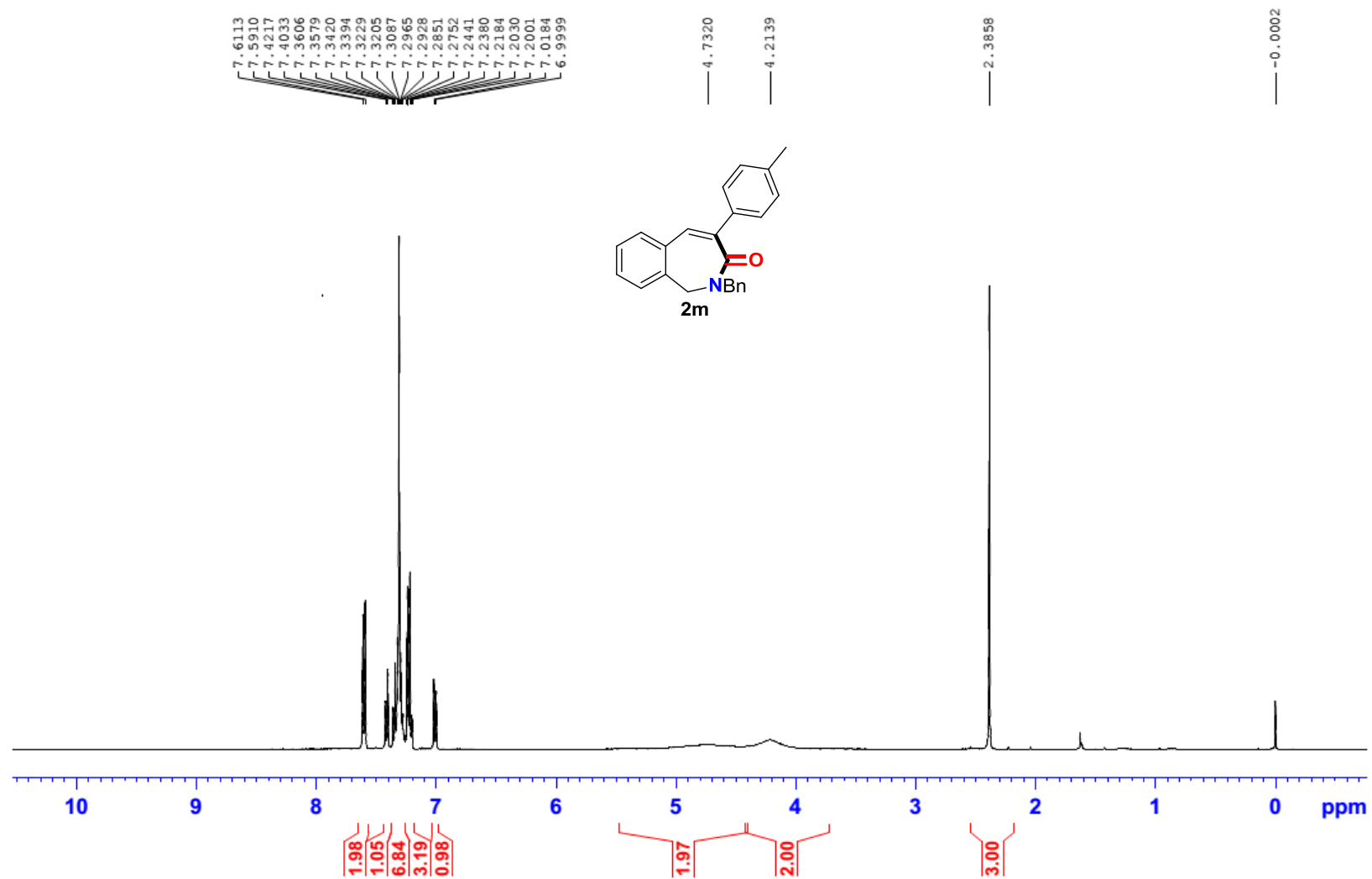
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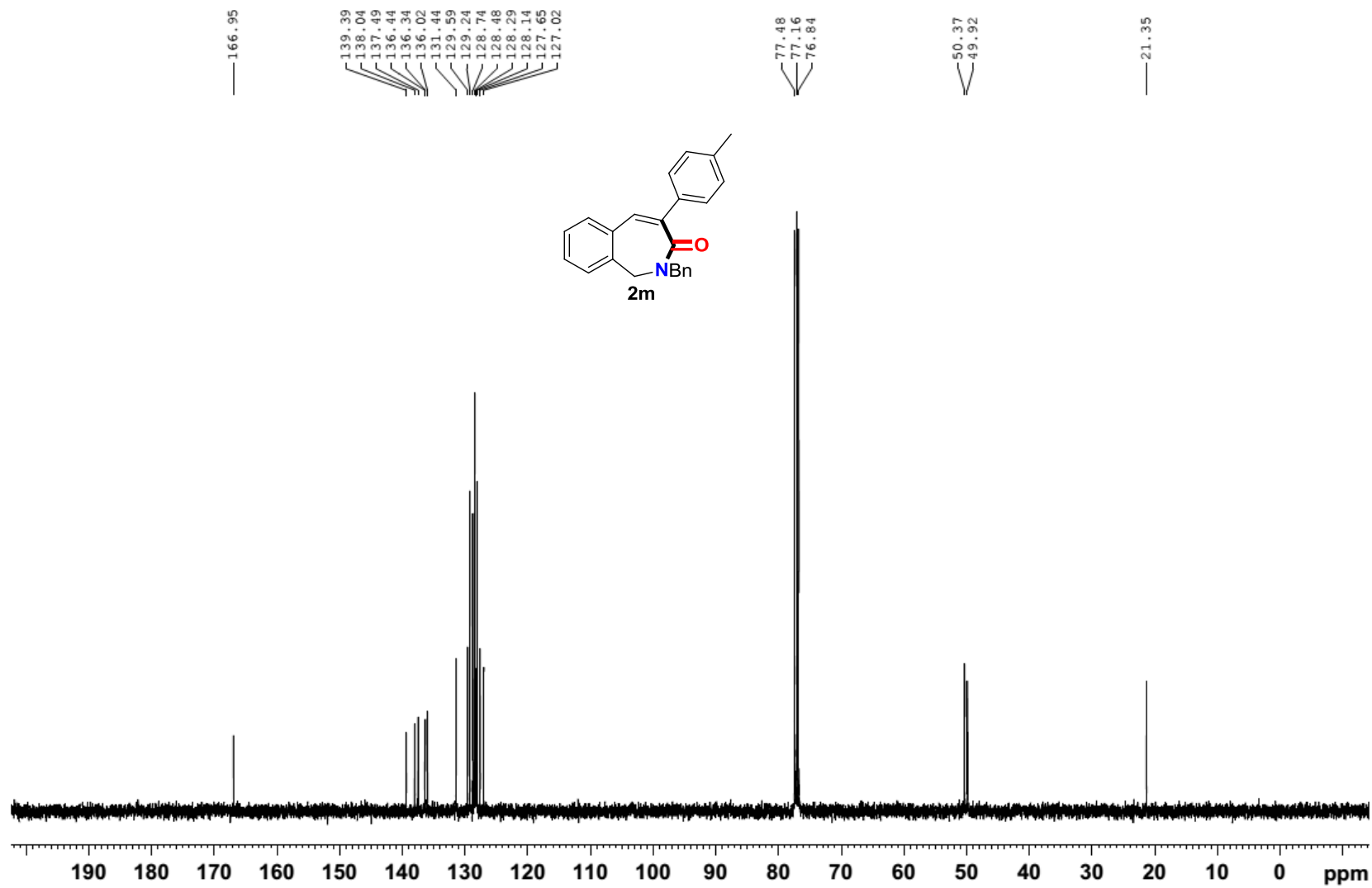
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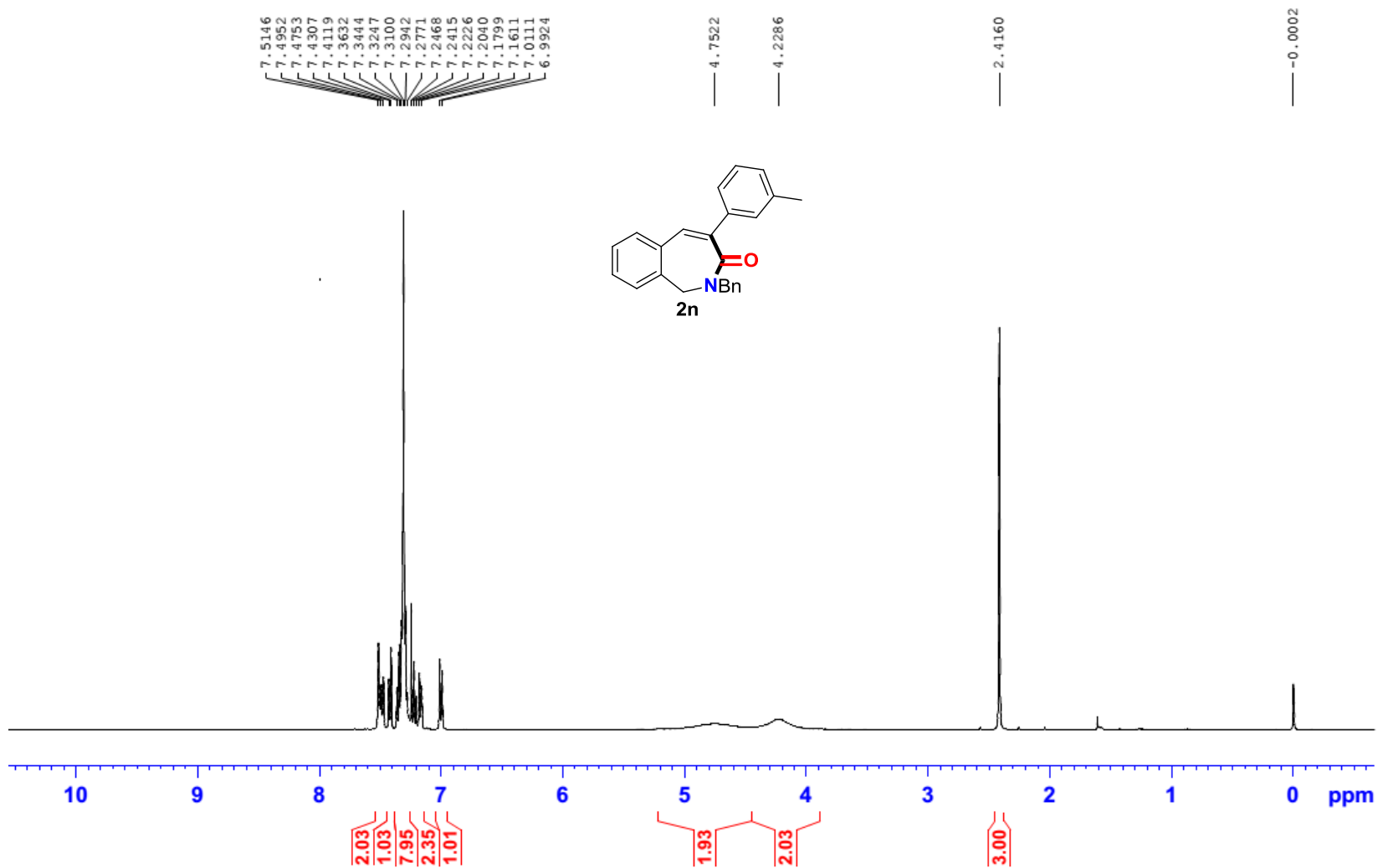
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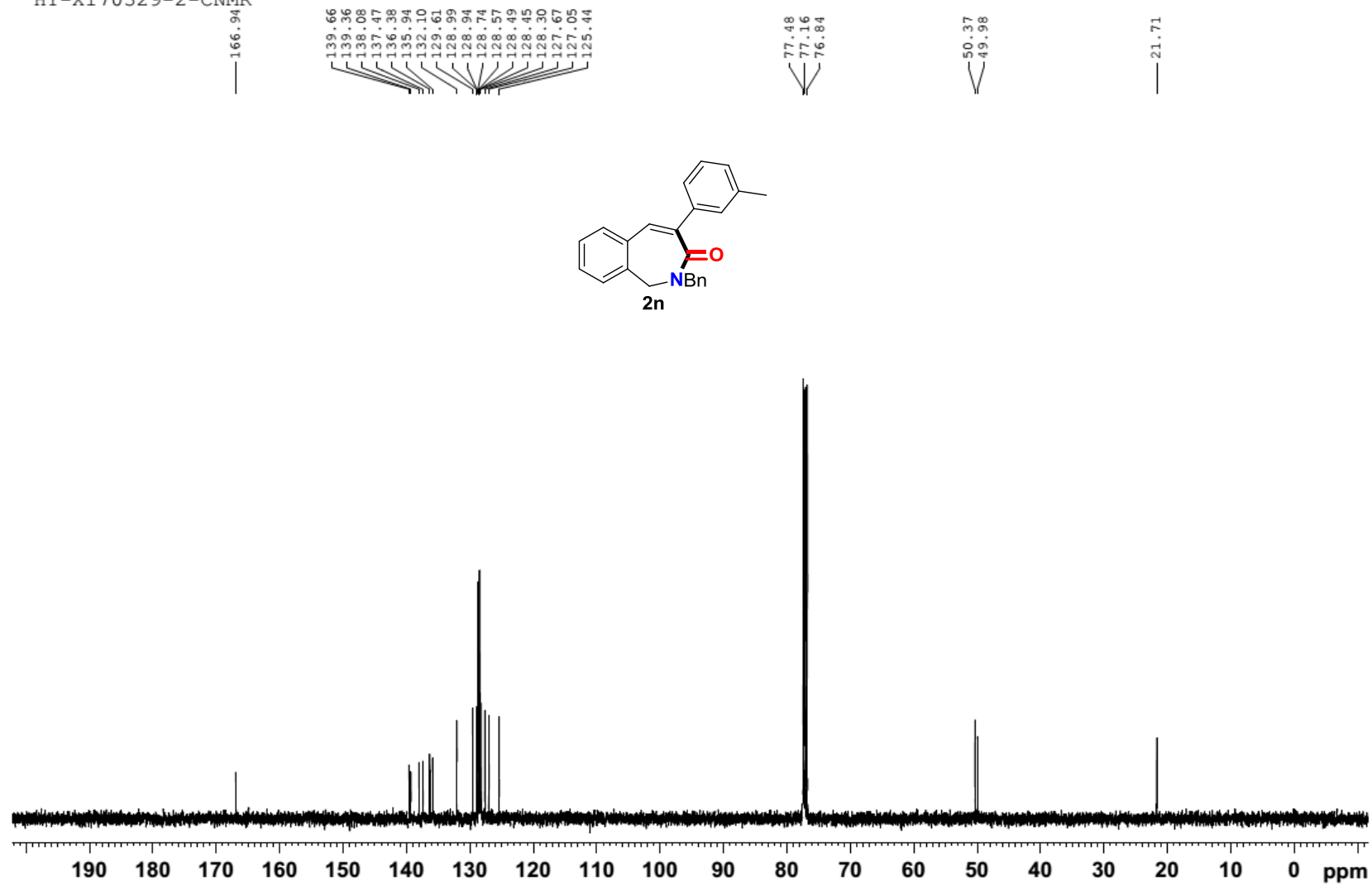
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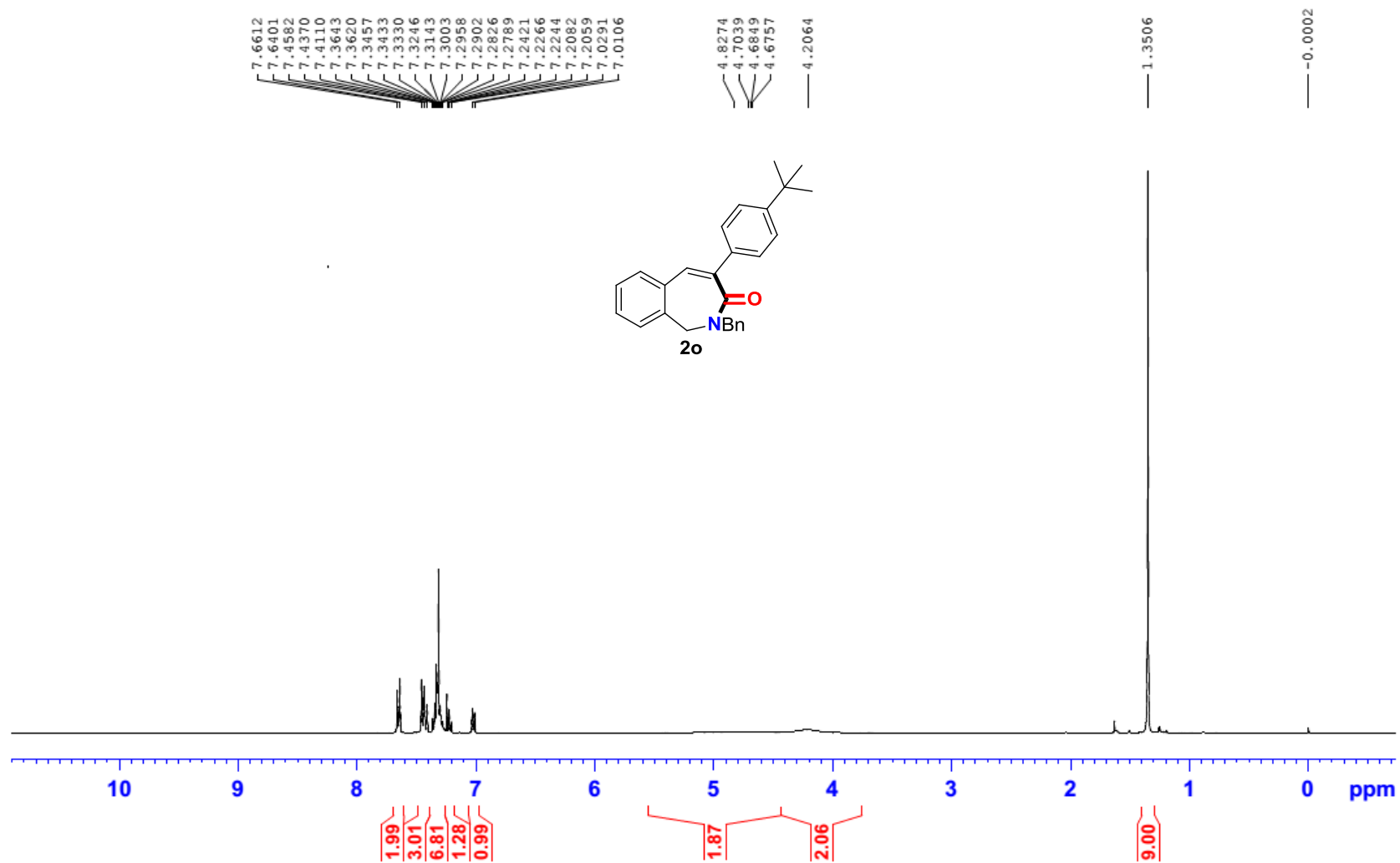
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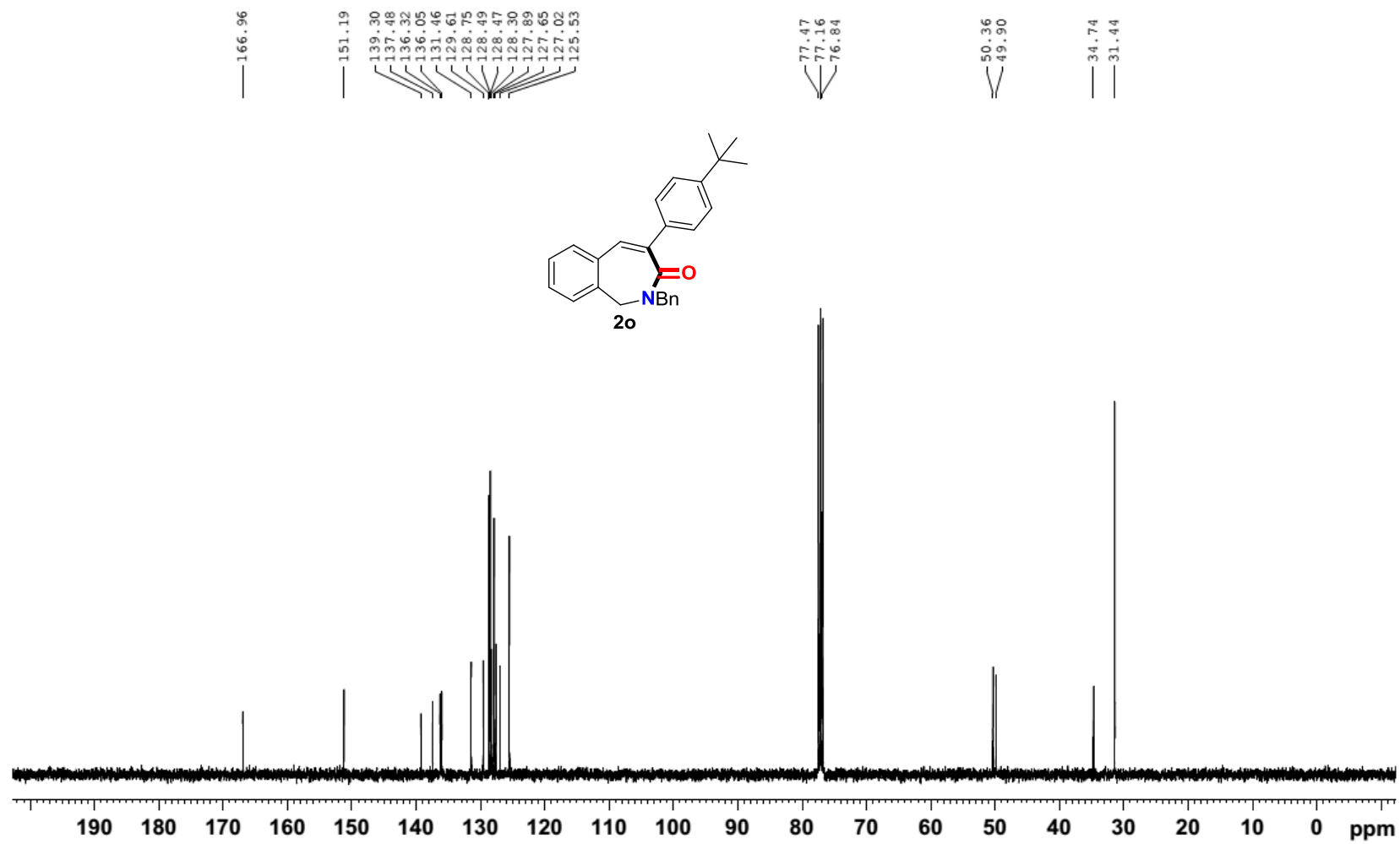
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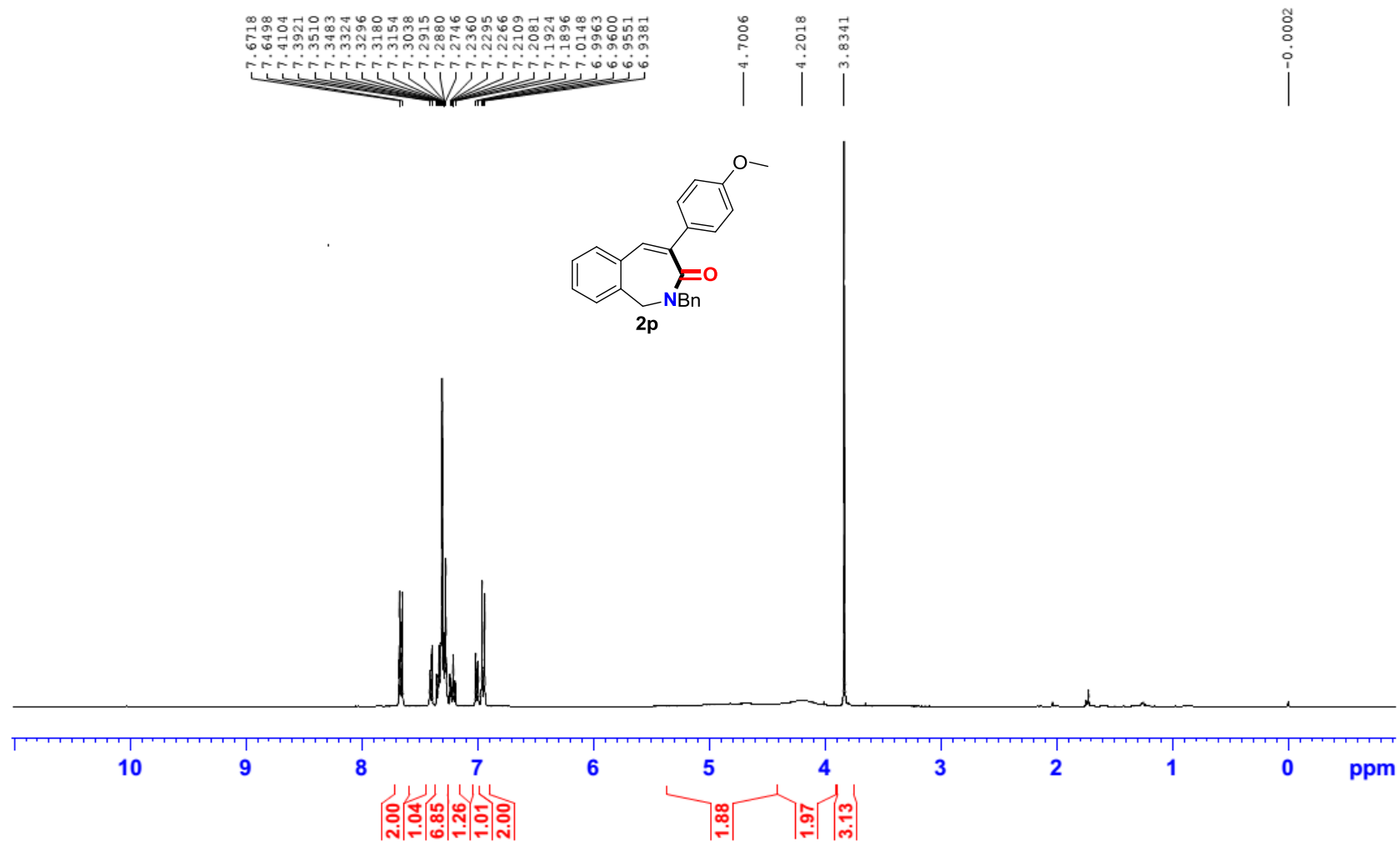


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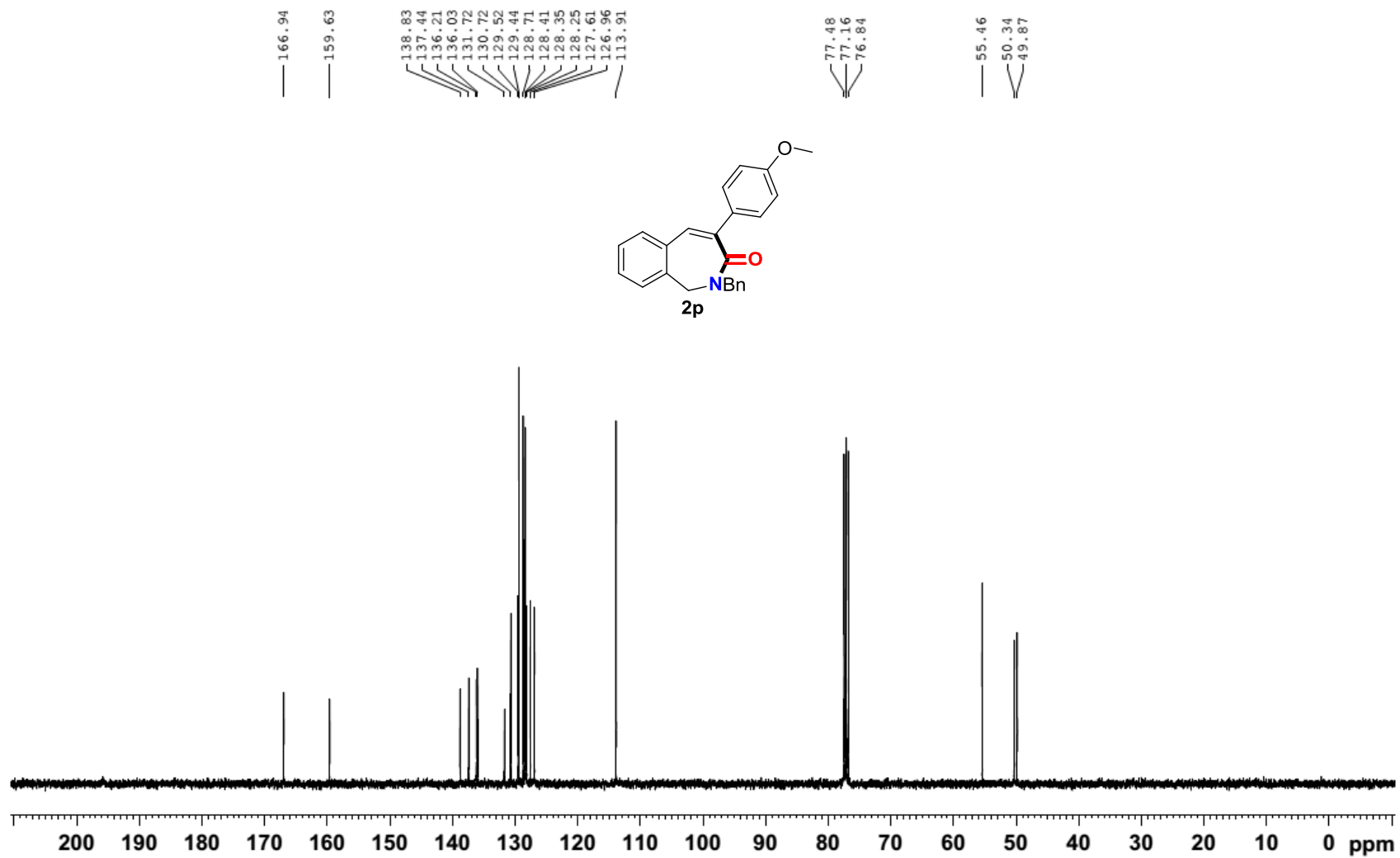




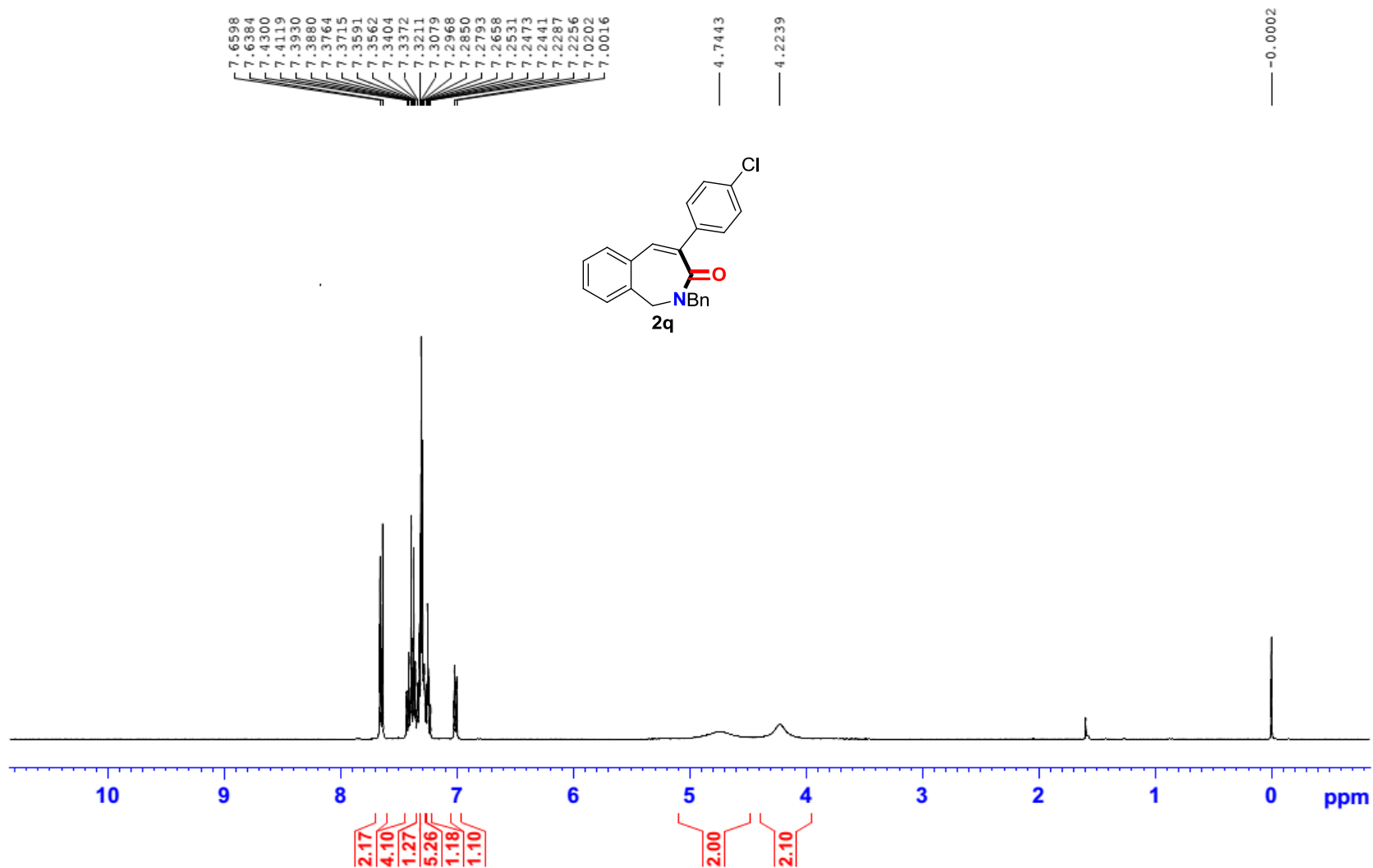
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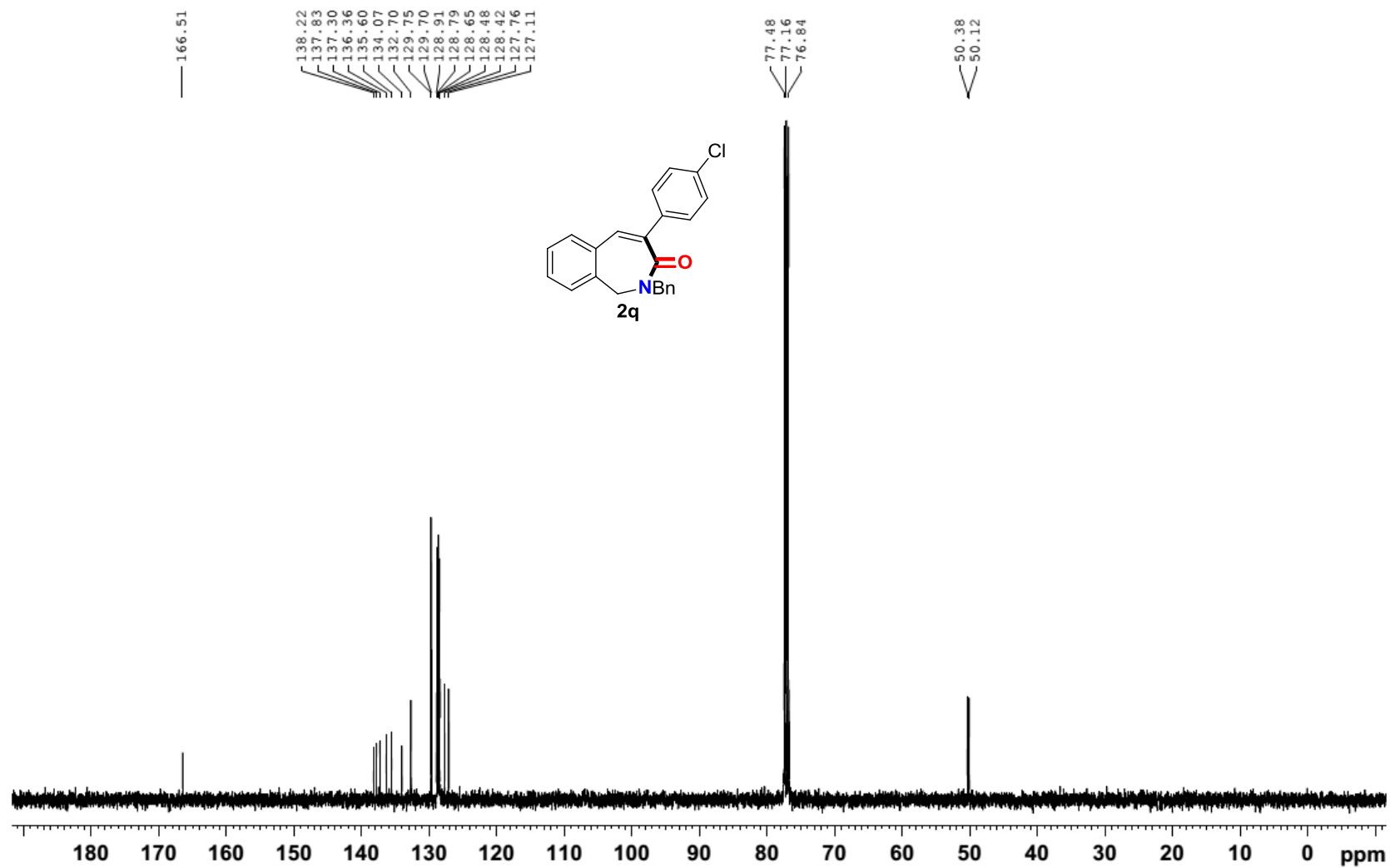
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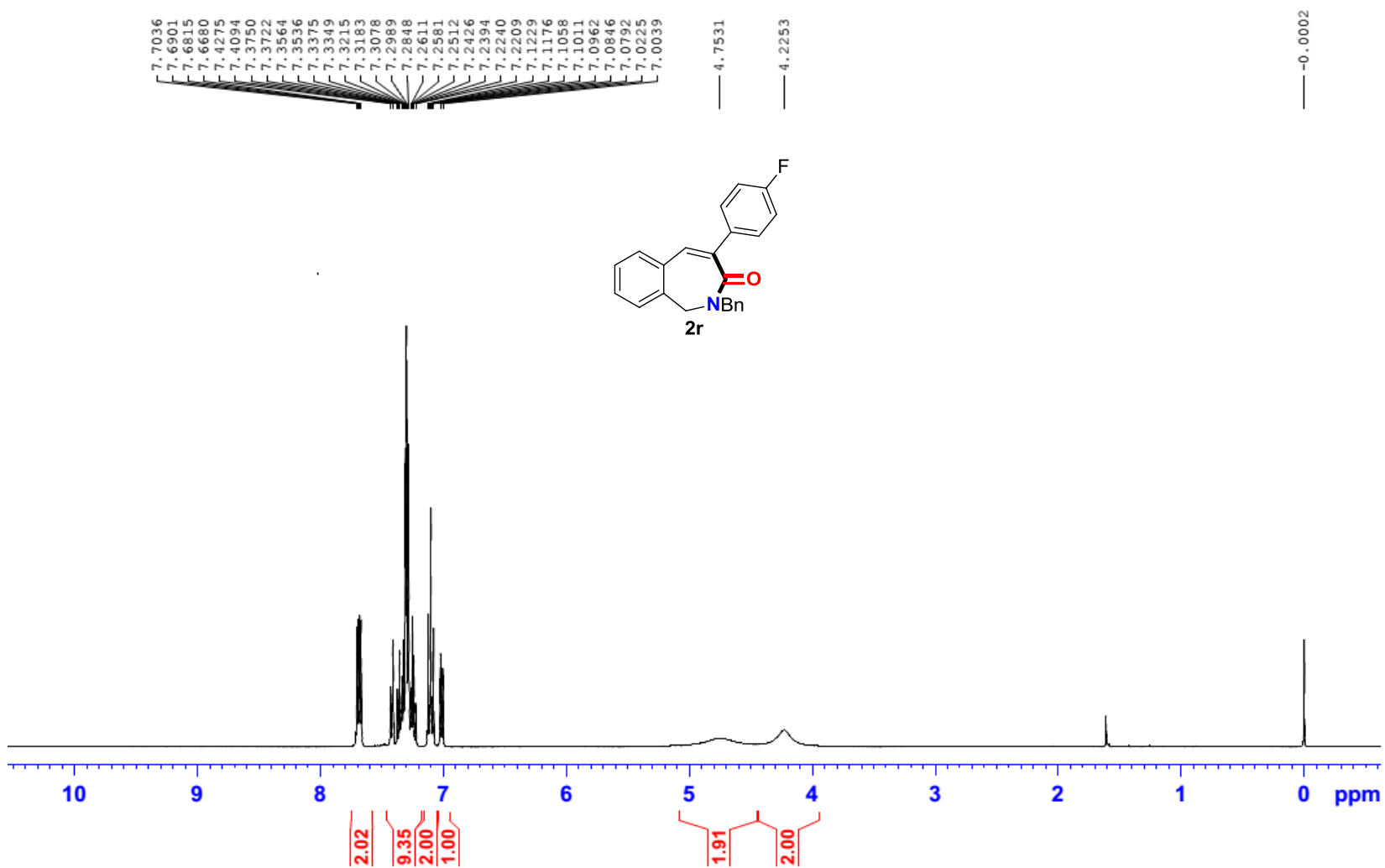
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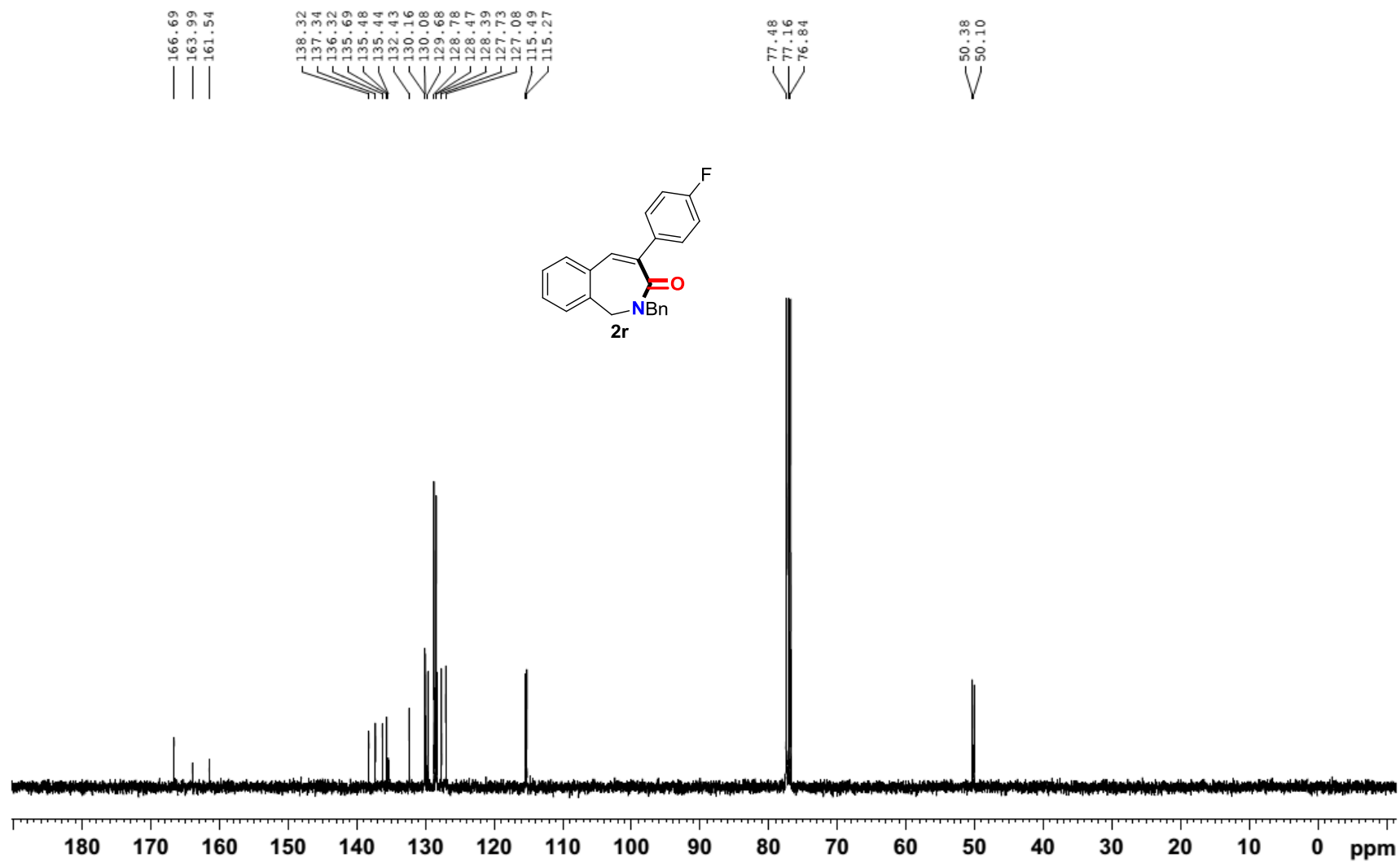
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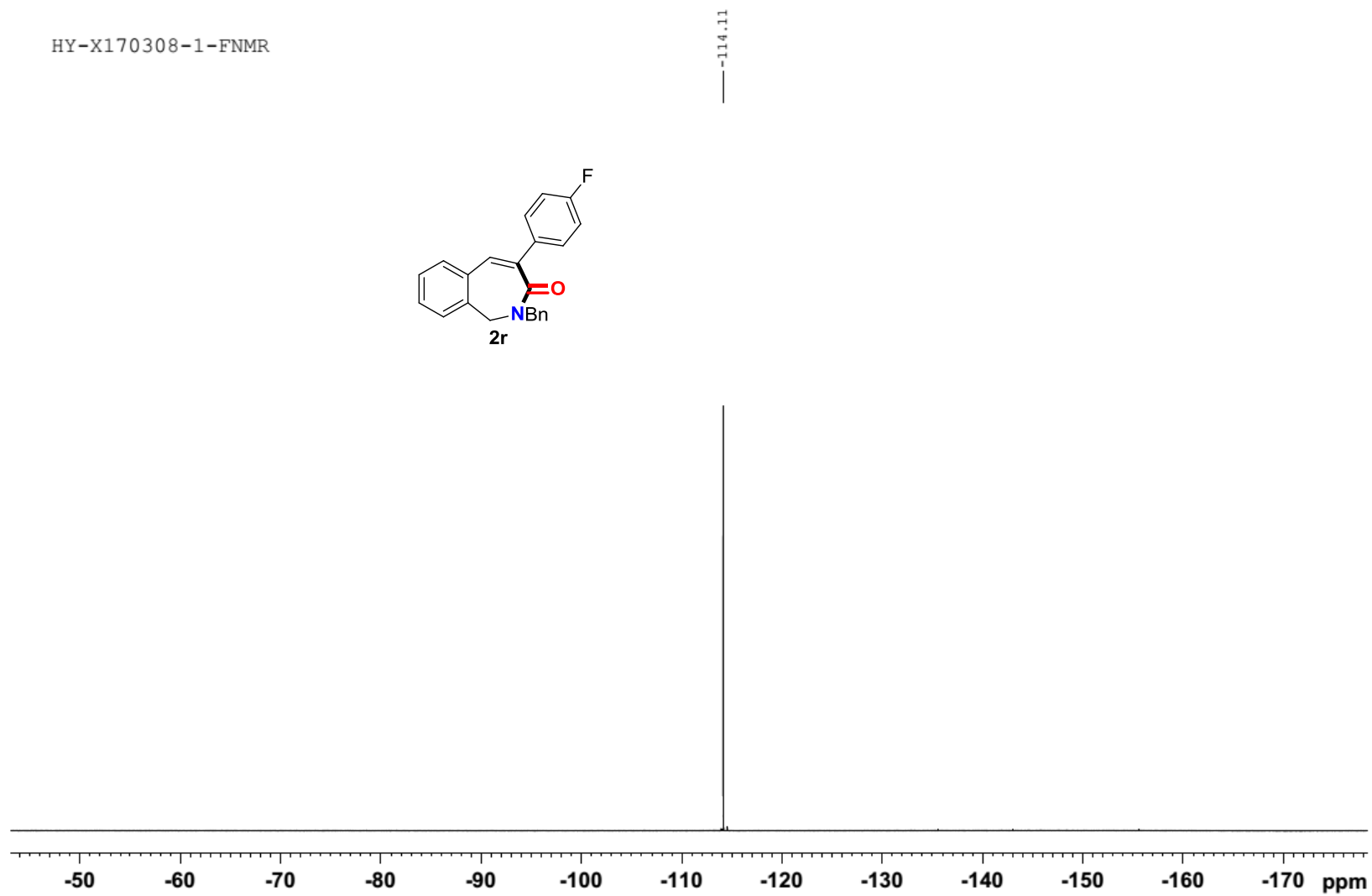
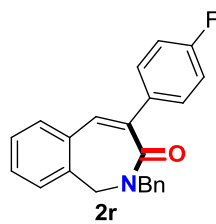
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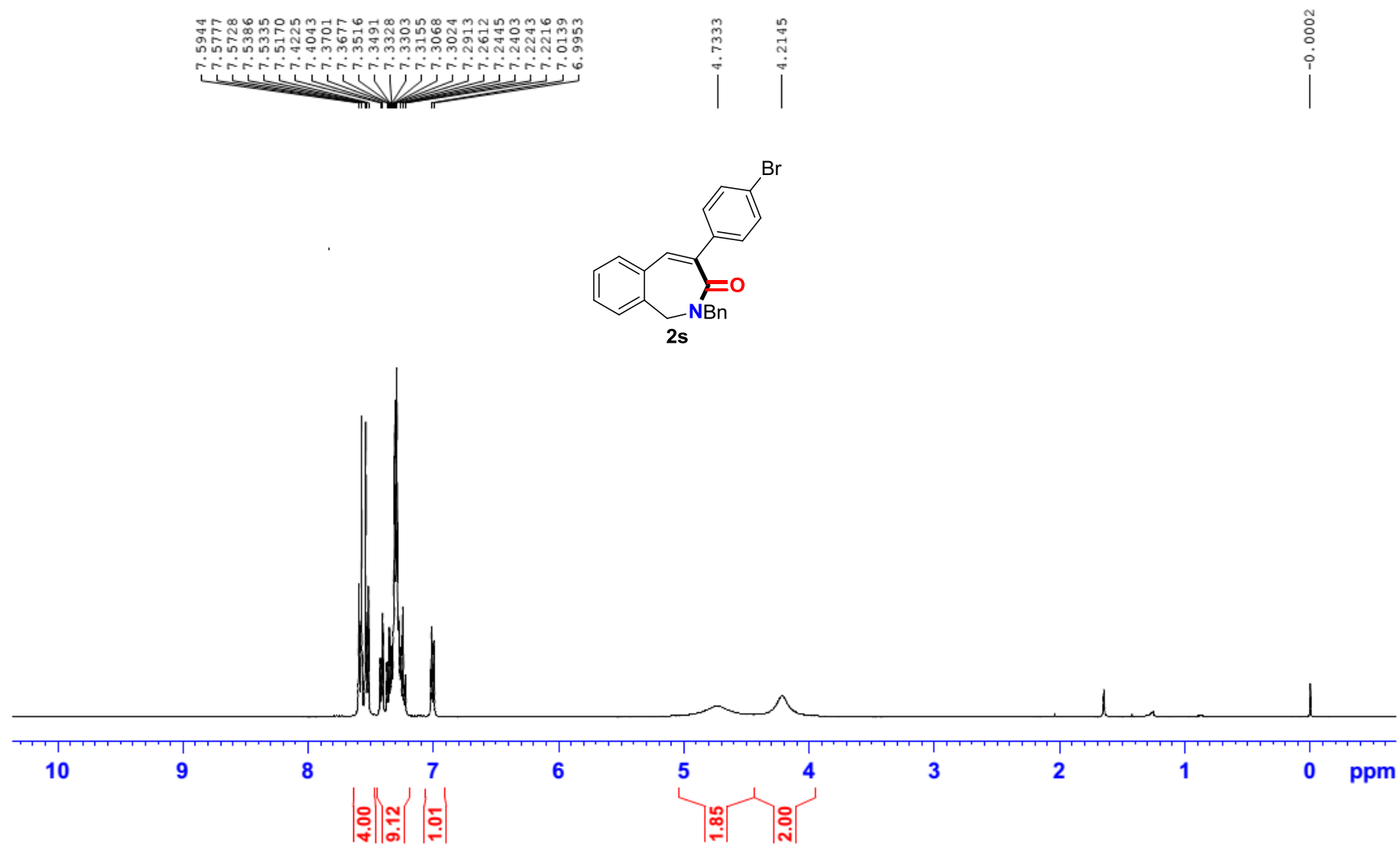
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HY-X170308-1-FNMR

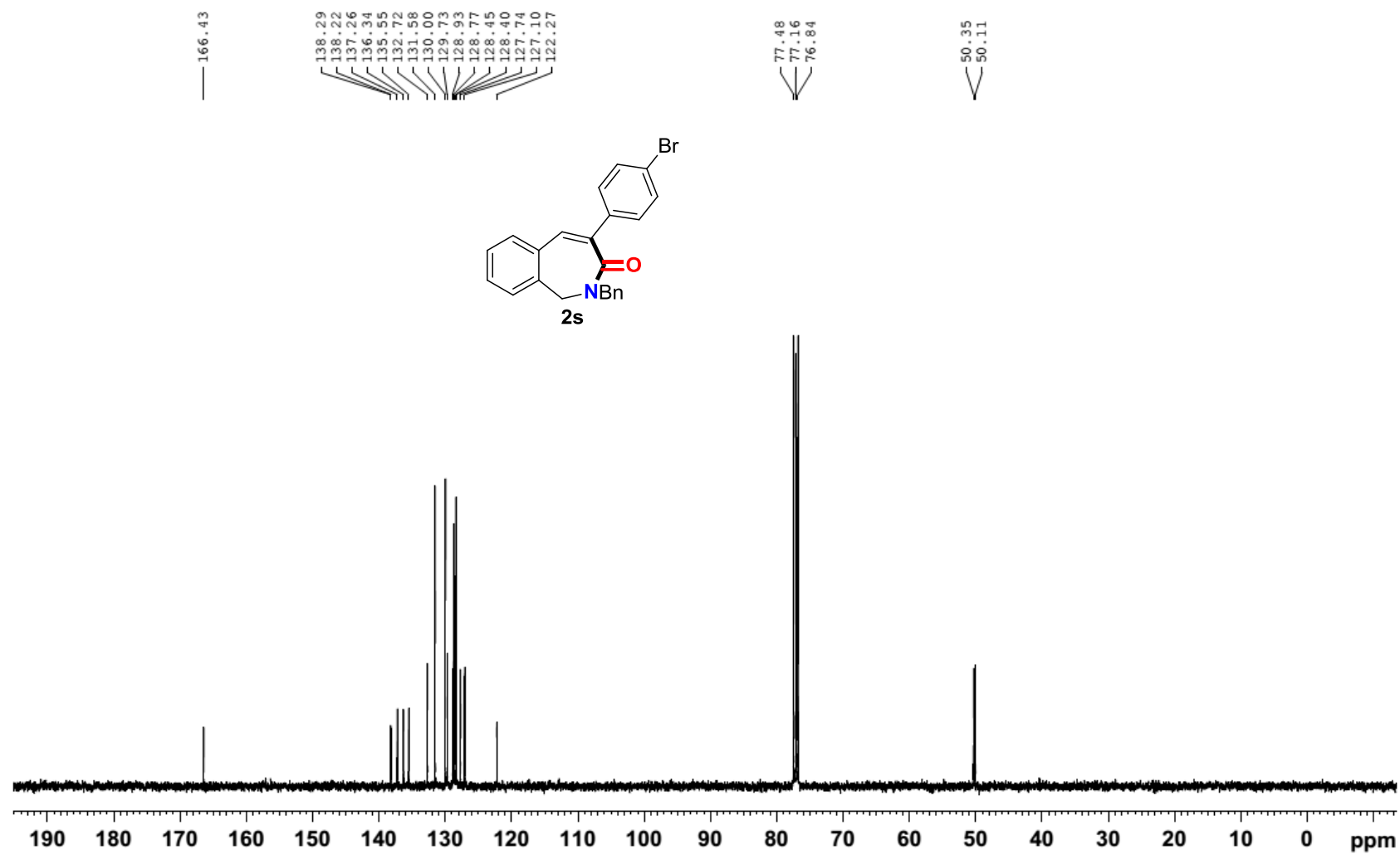


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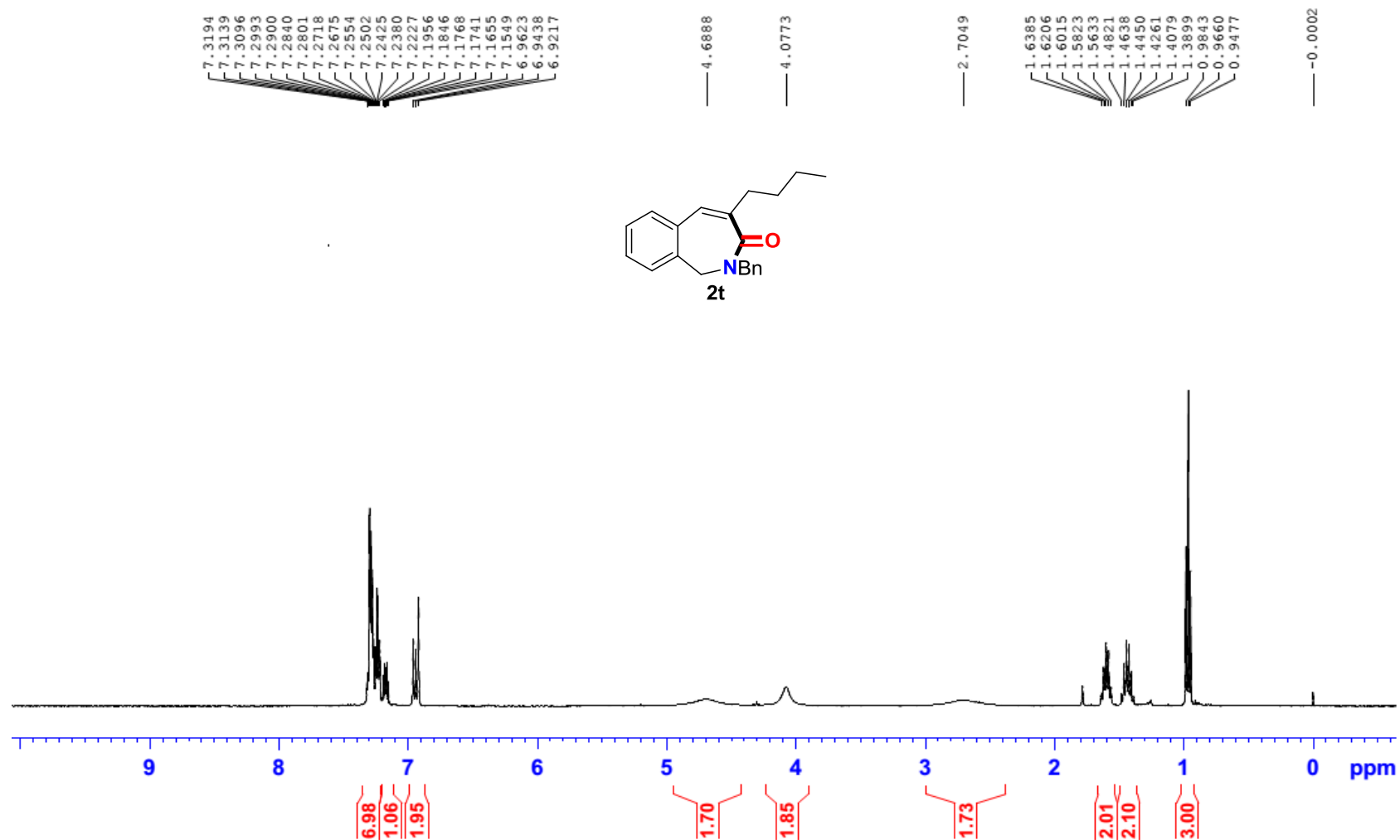




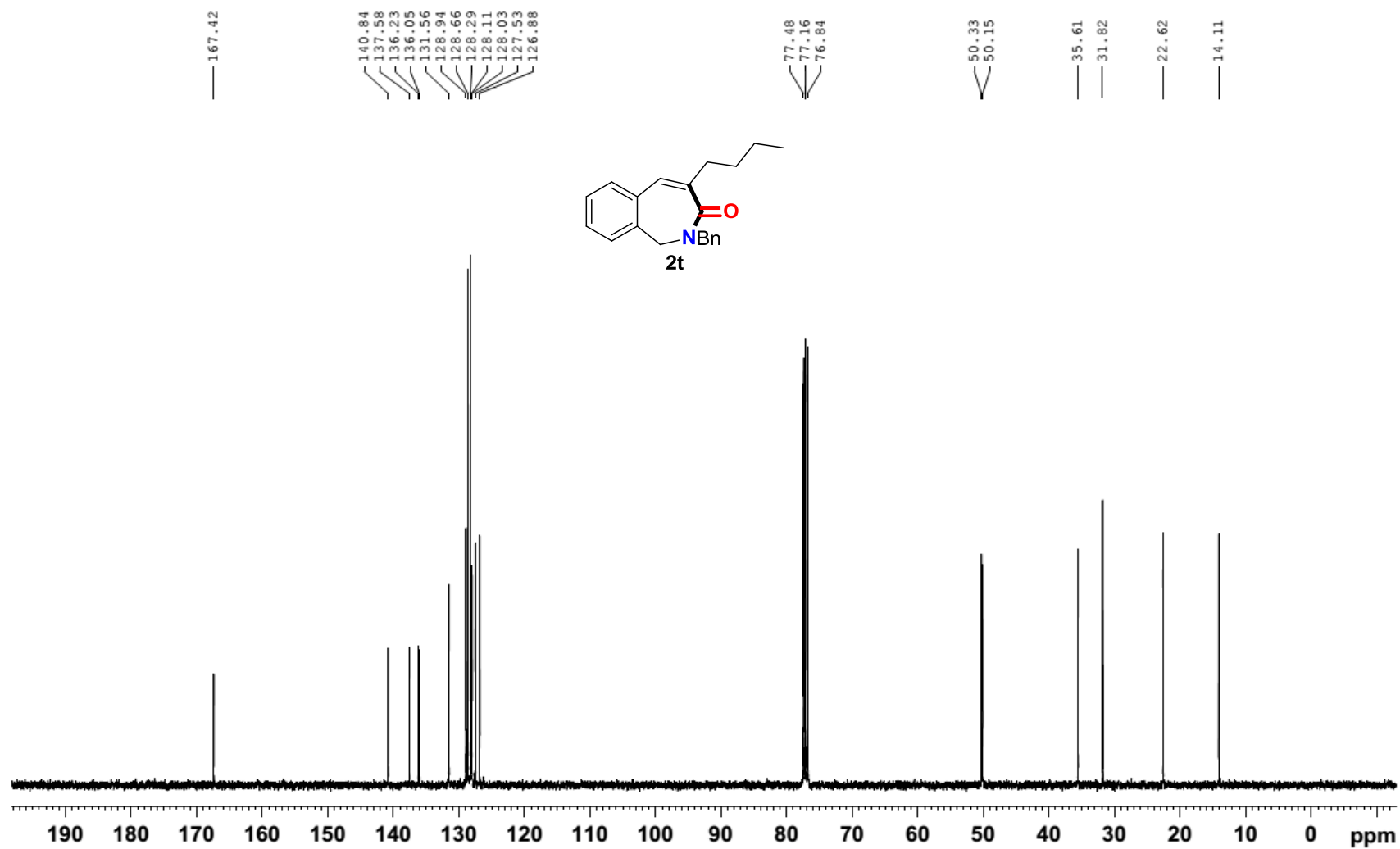
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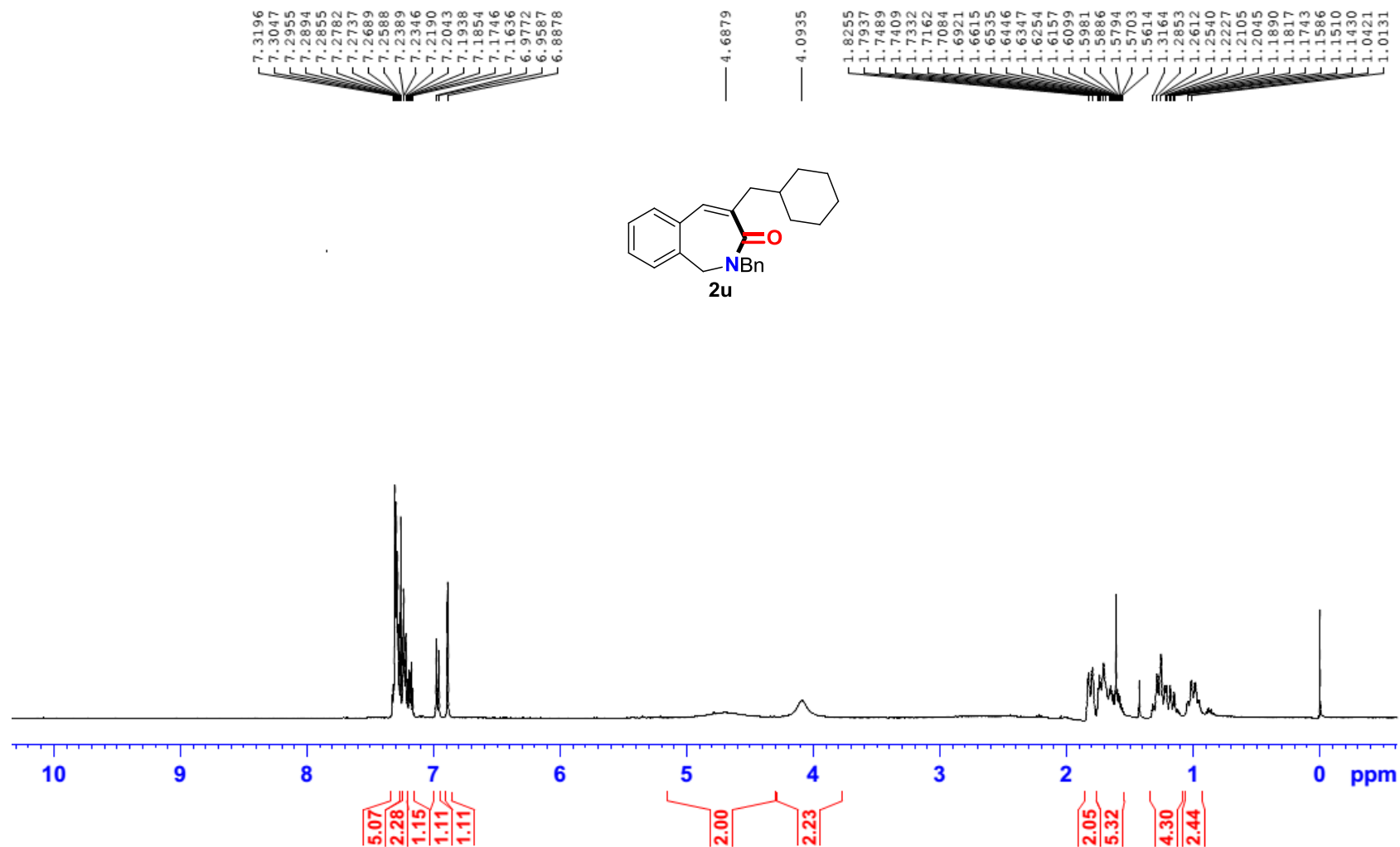
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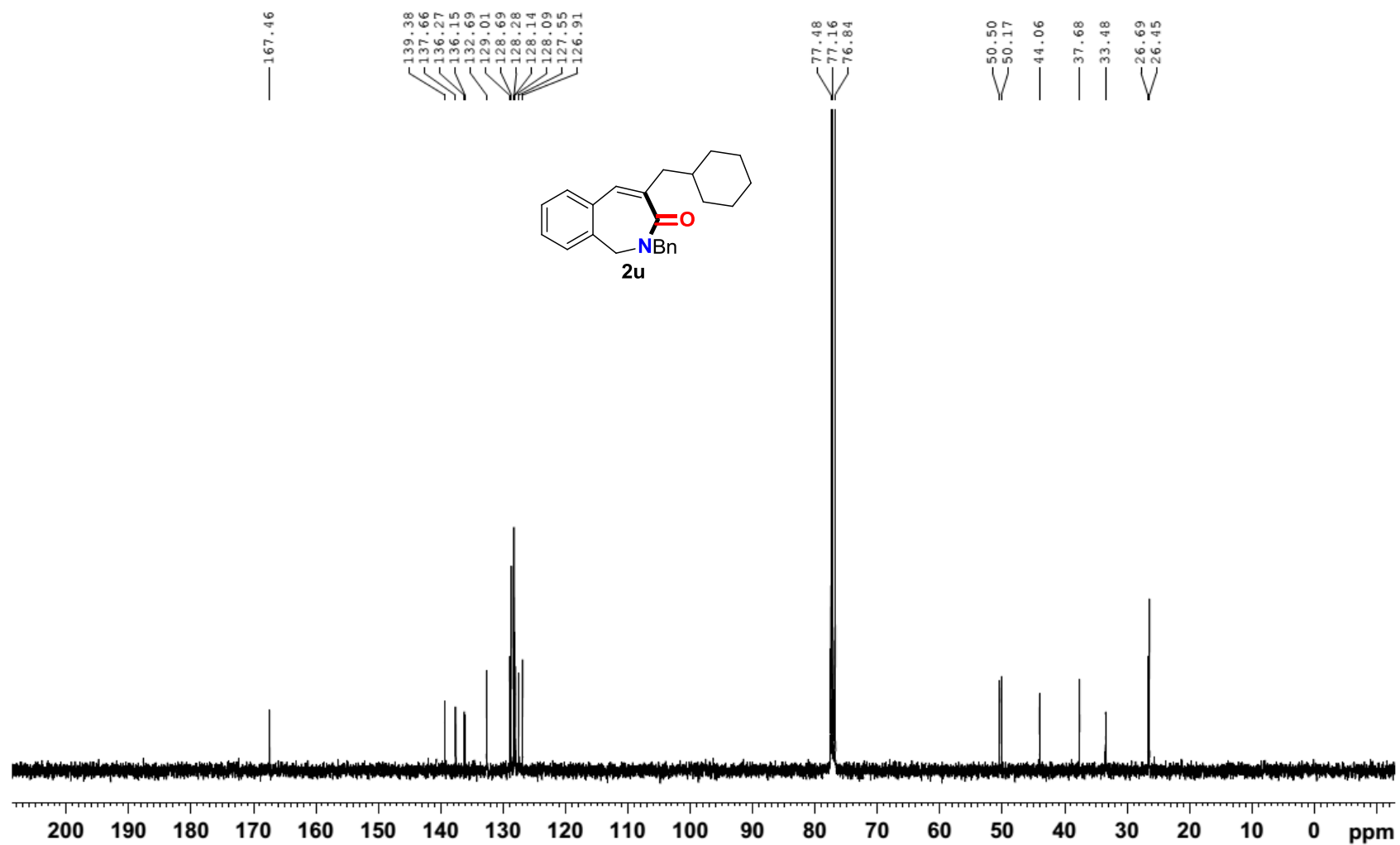
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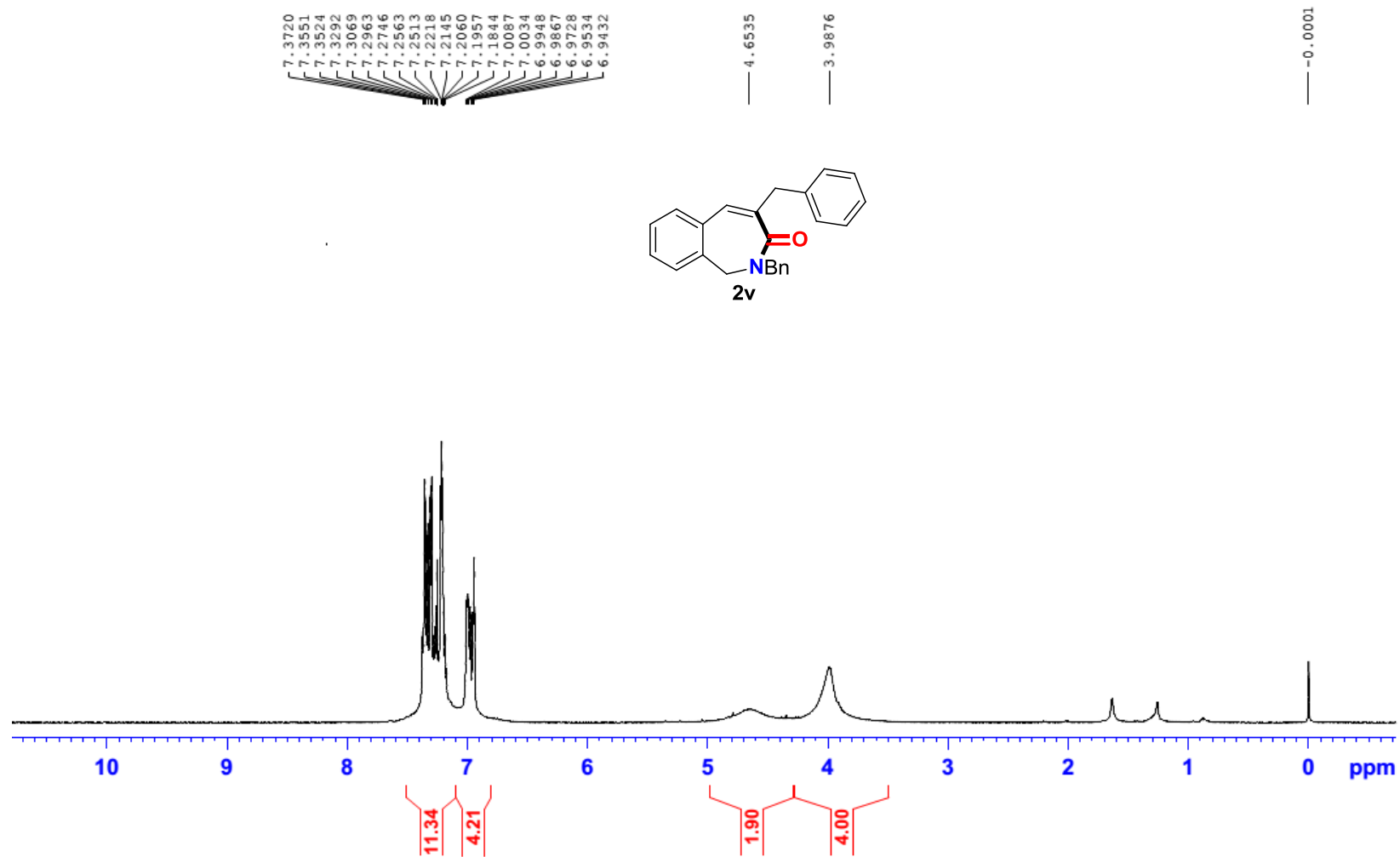
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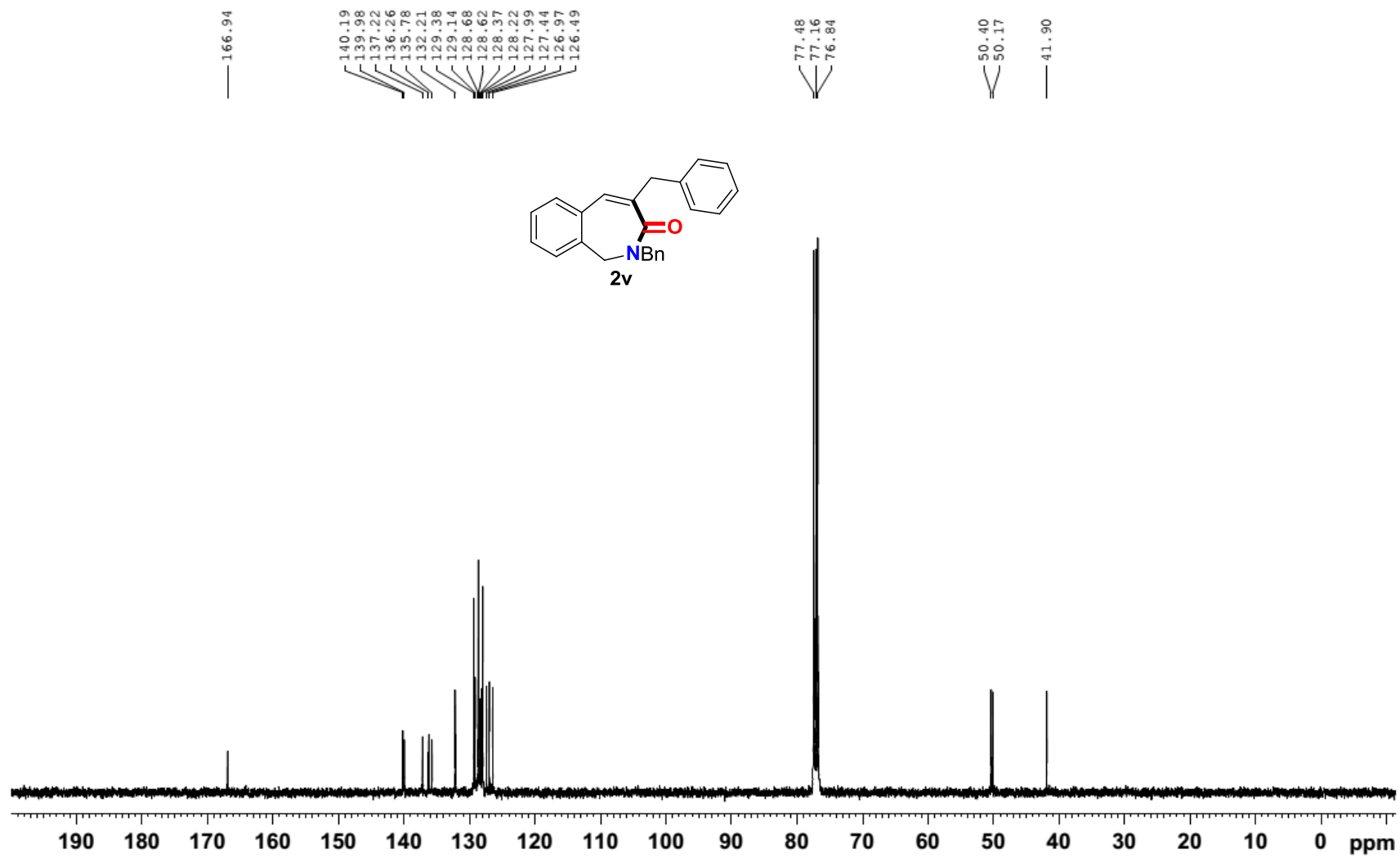
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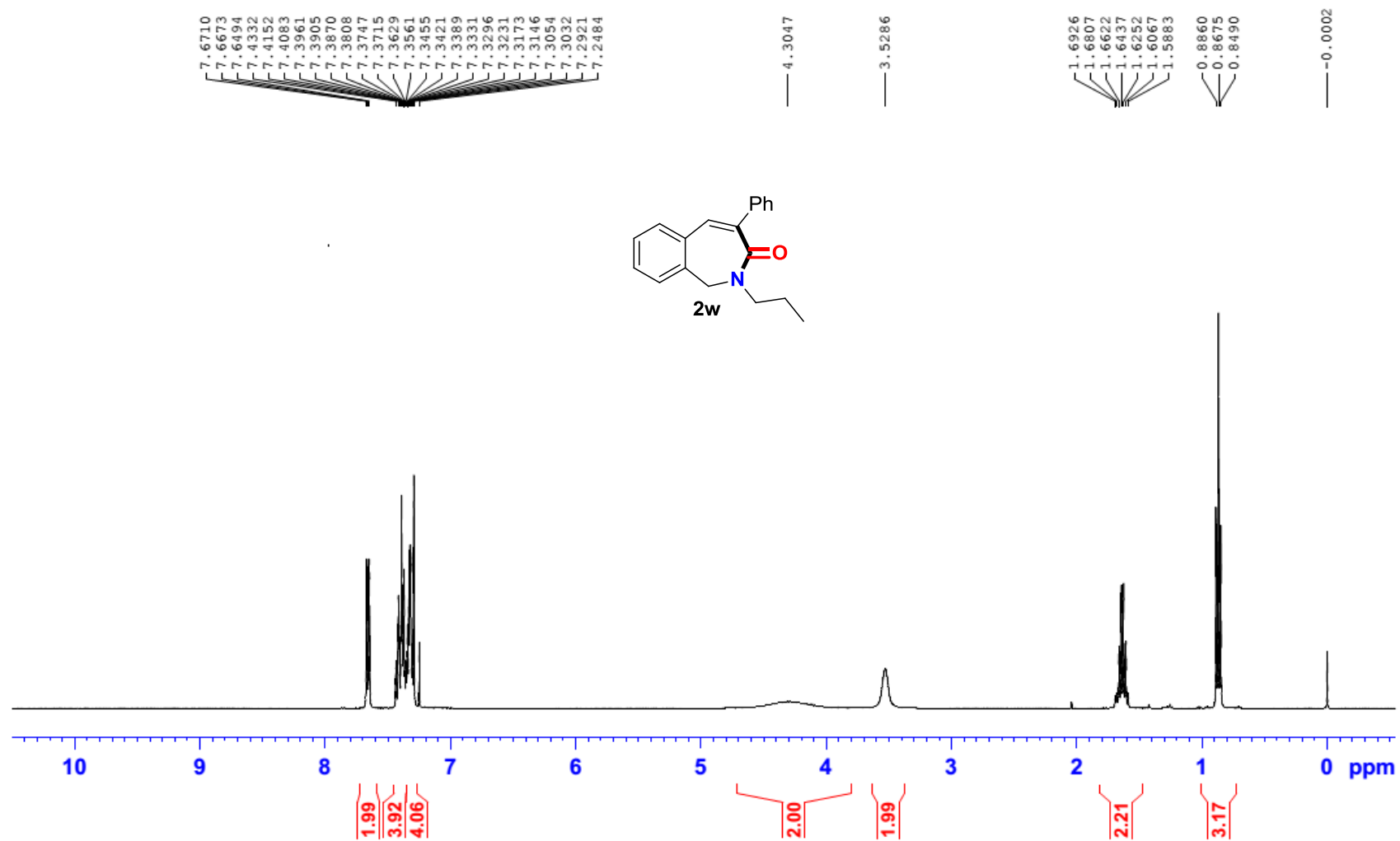
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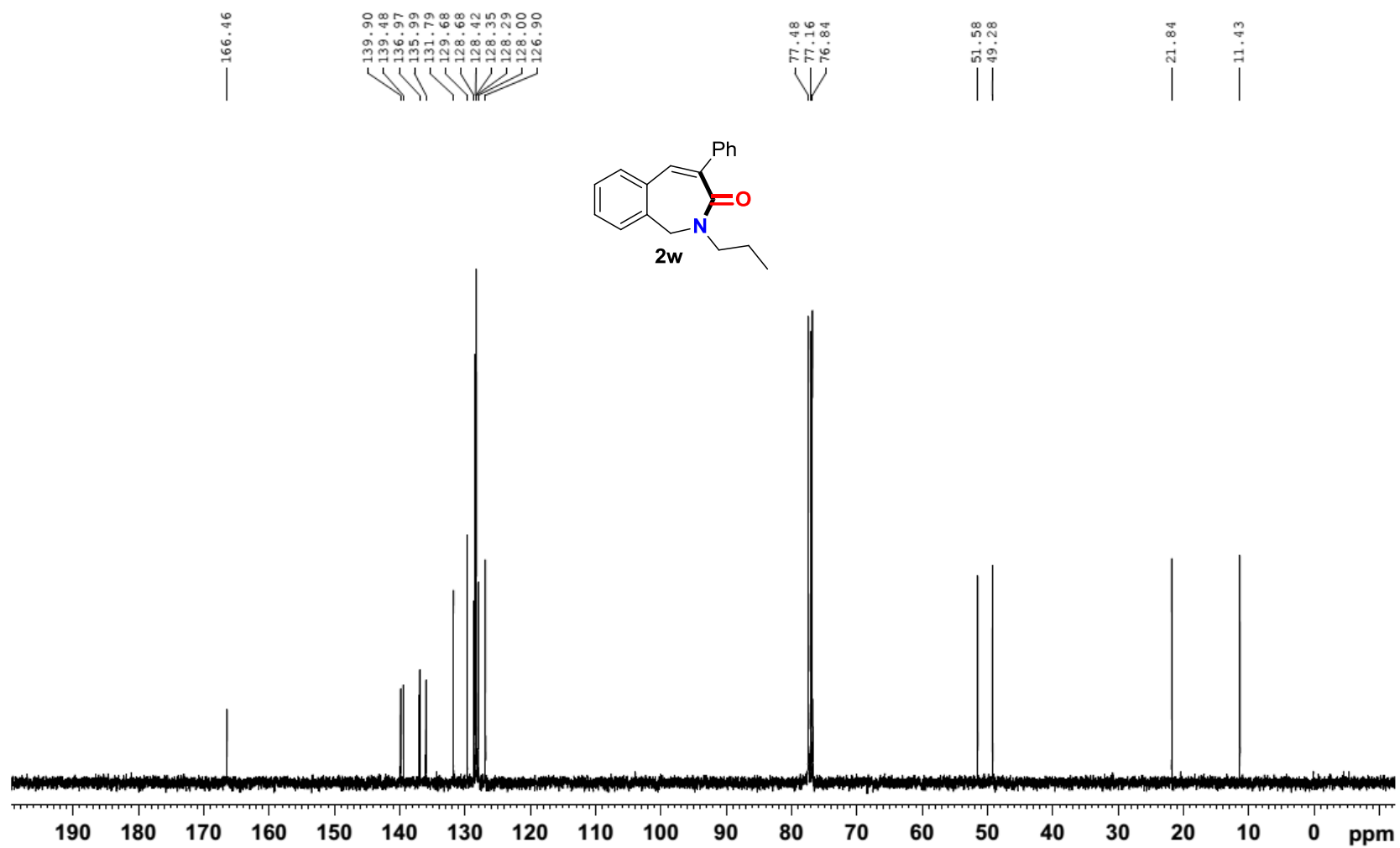


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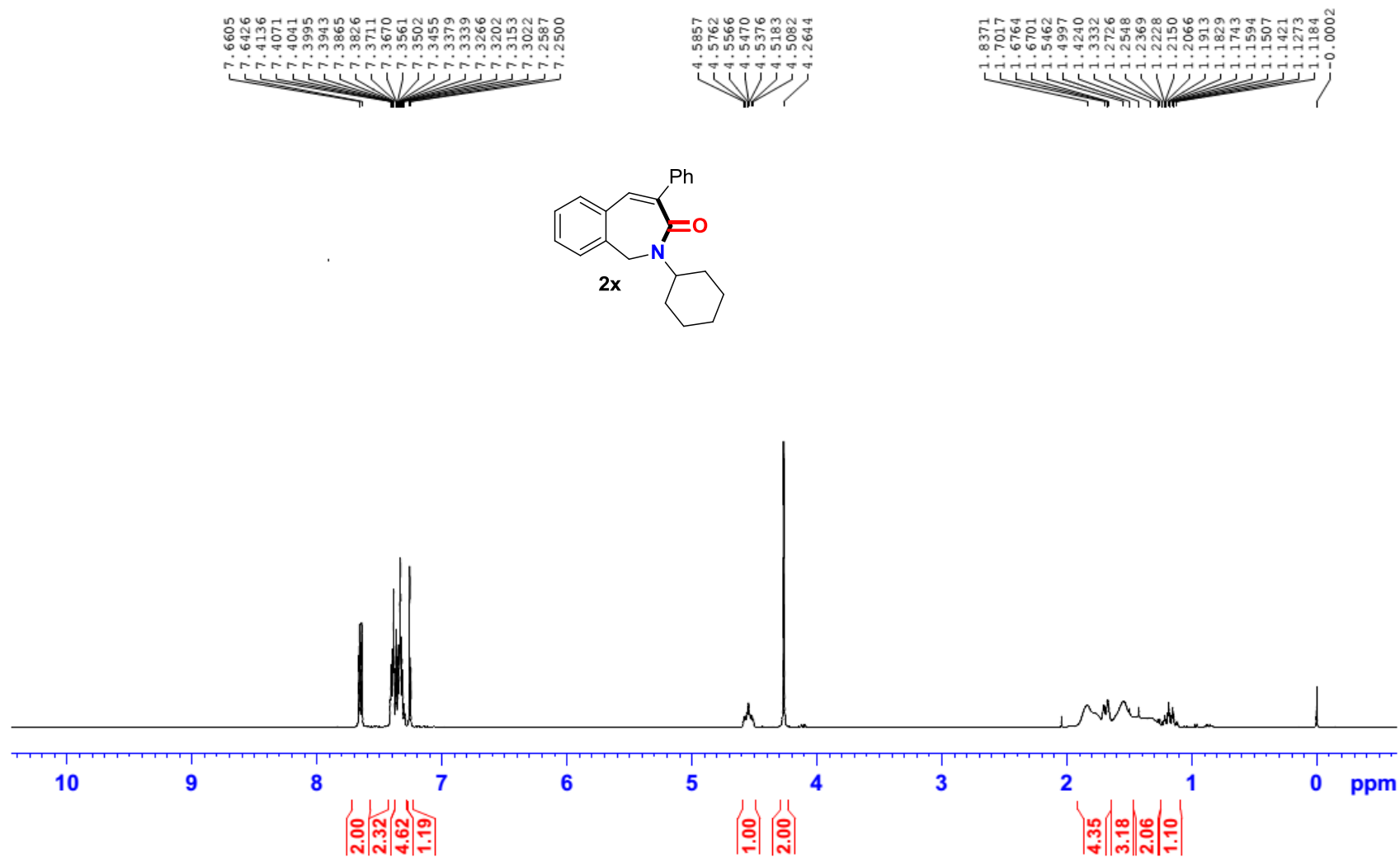




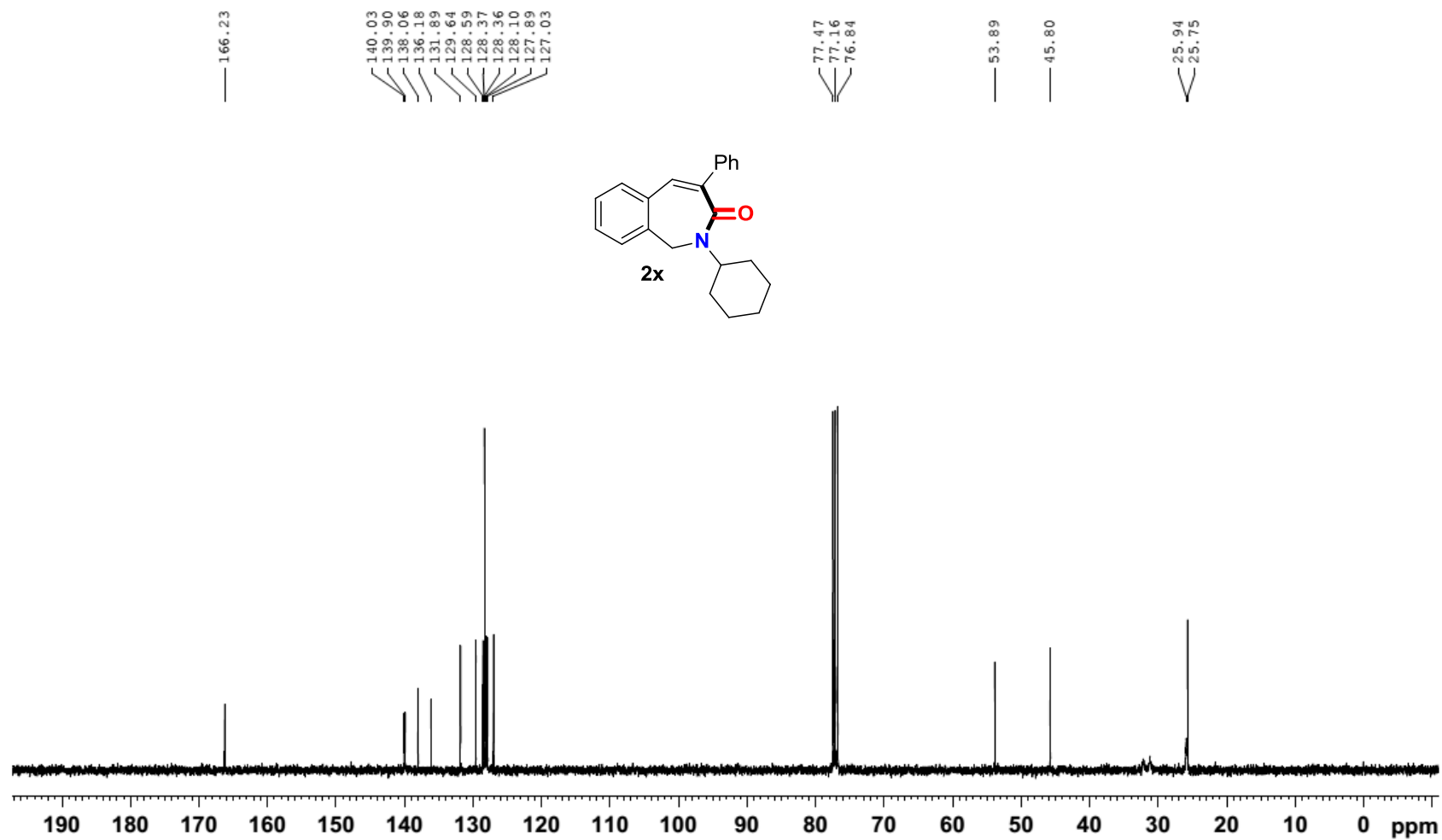
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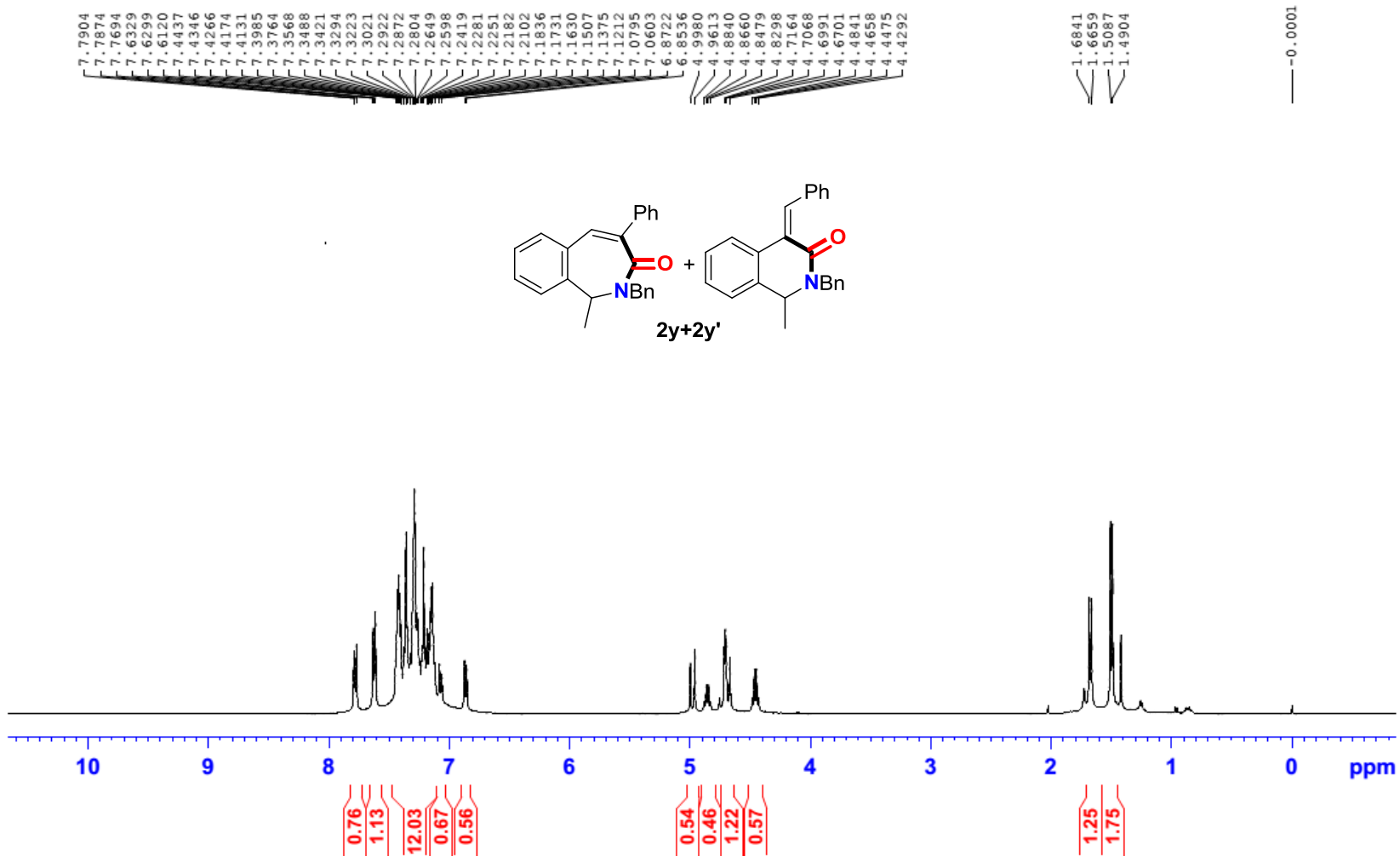
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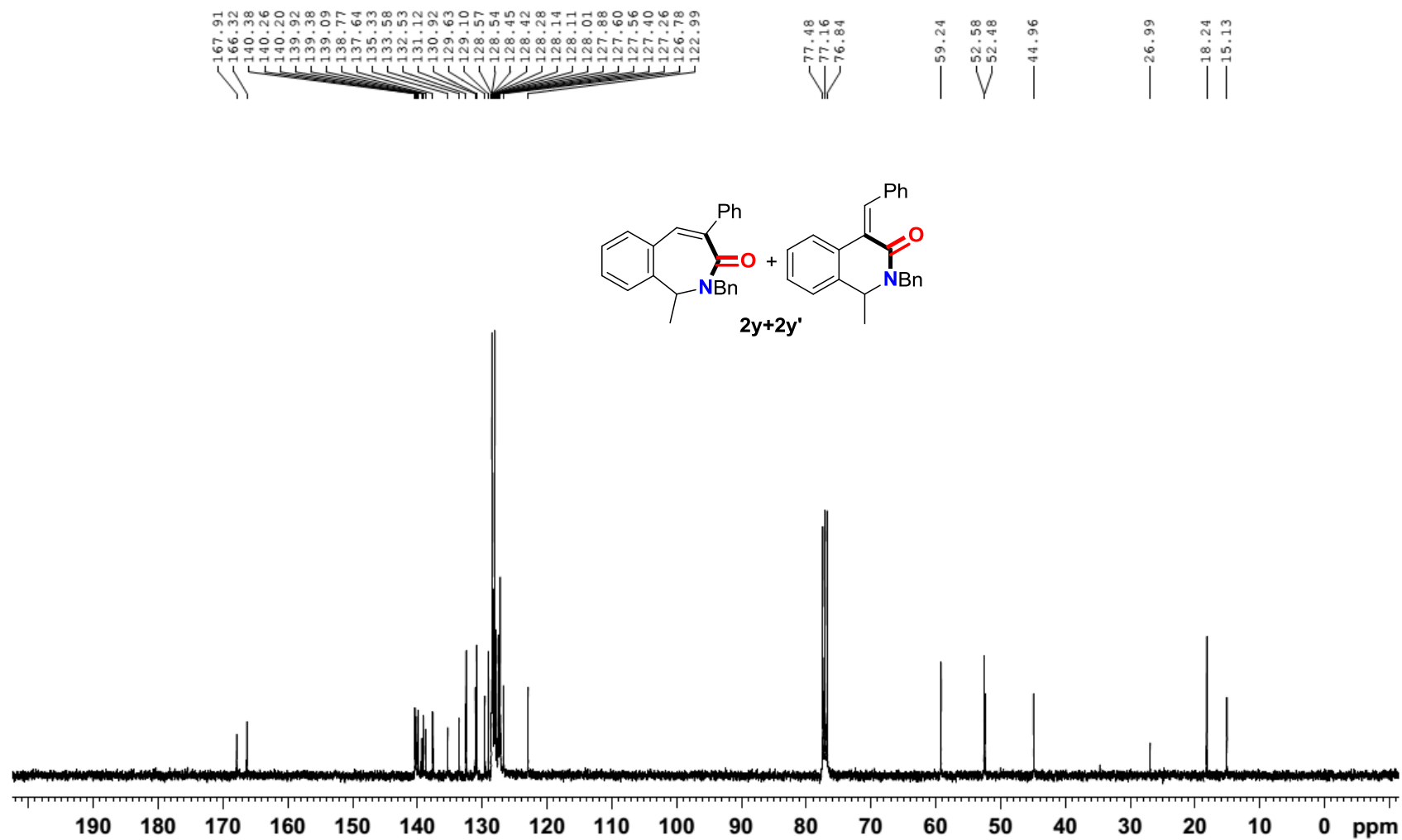
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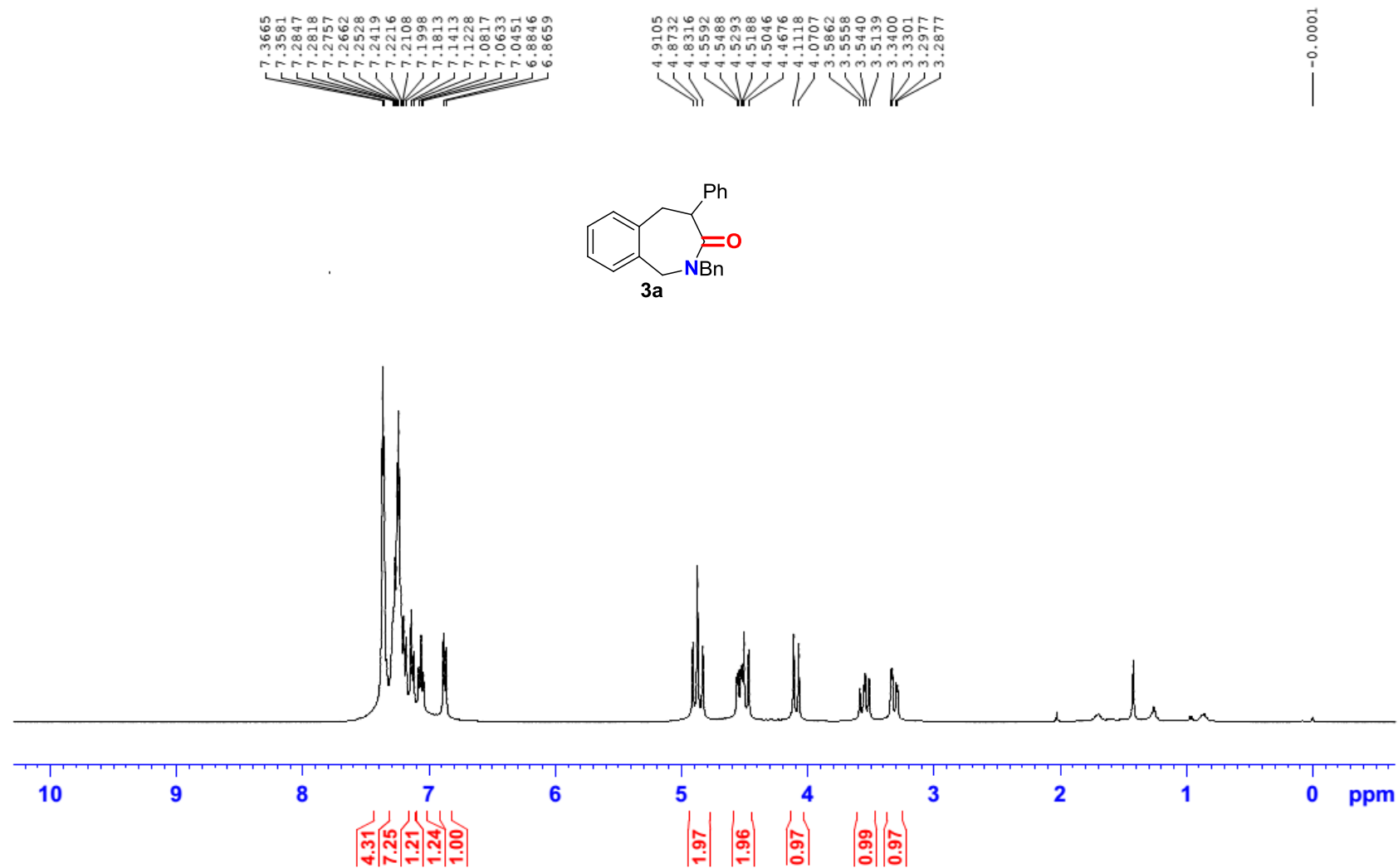
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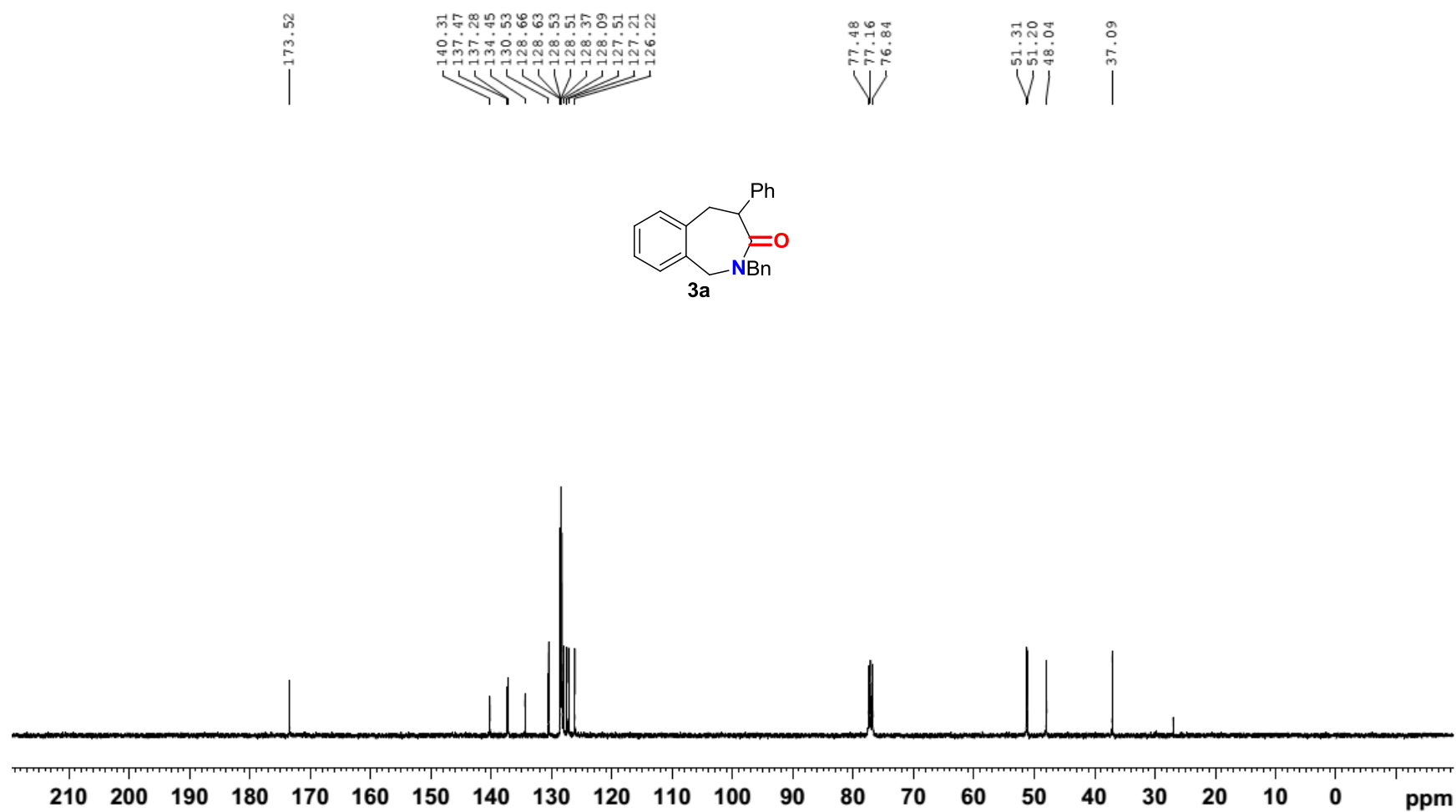
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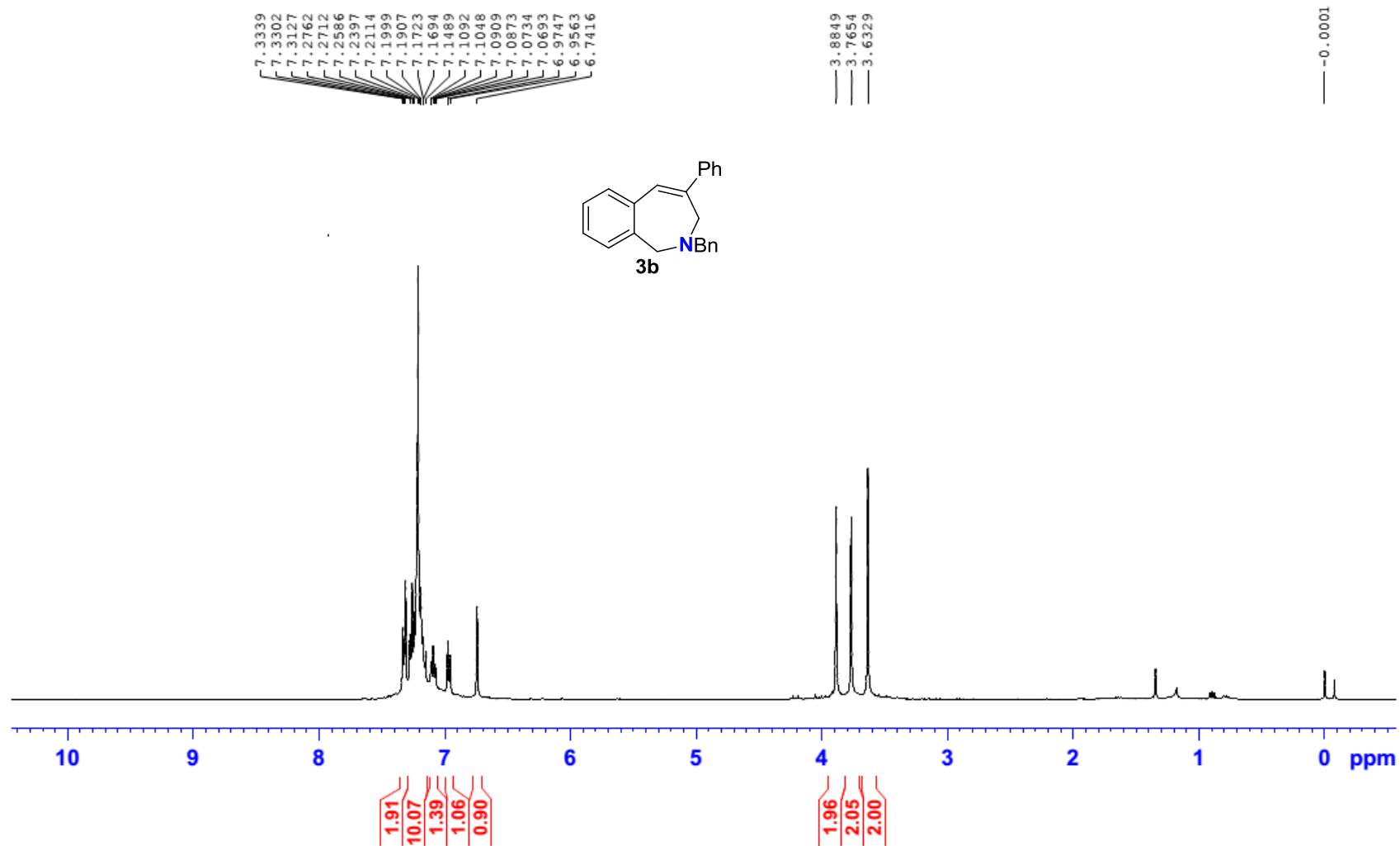
HY-X170620-2HNMR



HY-X170620-2CNMR



HY-X170622-1HNMR





HY-X170622-1CNMR

143.00  
142.11  
139.31  
138.03  
137.14  
130.92  
129.75  
129.42  
129.21  
128.53  
128.38  
127.51  
127.29  
127.18  
127.13  
126.63

77.48  
77.16  
76.84

58.55  
58.51  
58.14

