

# **Synthesis of Thioethers *via* Metal-free Reductive Coupling of Tosylhydrazones with Thiols**

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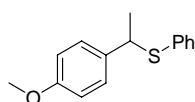
## **Supporting Information**

1. General materials and methods (S2).
2. Characterization data of compound **3** (S2-S8).
3. References (S8)
4. Copies of spectra of compound **3** (S9-S31).

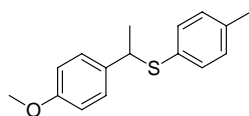
**General Materials and Methods:** All reactions were performed under nitrogen atmosphere. NMR samples were run in CDCl<sub>3</sub> or DMSO and <sup>1</sup>H NMR were referenced to TMS, <sup>13</sup>C NMR were referenced to CDCl<sub>3</sub> (δ = 77.0). All chemical shift values are quoted in ppm and coupling constants quoted in Hz.

**General procedure for metal-free reductive coupling reaction of tosylhydrazone 1 with thiol 2:**

A mixture of tosylhydrazone **1** (0.3 mmol), thiol **2** (0.6 mmol, 2.0 equiv), K<sub>2</sub>CO<sub>3</sub> (0.9 mmol, 3.0 equiv) in dioxane (3.0 mL) was stirred at 110 °C for 24h under N<sub>2</sub>. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature. After adding ethyl acetate (10 mL), the organic phase was washed with saturated brine, dried with MgSO<sub>4</sub>, and concentrated under reduced vacuum. The residue was then purified by flash chromatography on silica gel to afford product **3**.

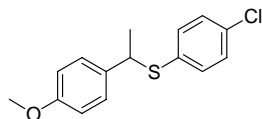


**(1-(4-methoxyphenyl)ethyl)(phenyl)sulfane<sup>1</sup> (3a)** Yield: 93%; Colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 1.60 (d, *J* = 7.2 Hz, 3H), 3.77 (s, 3H), 4.32 (q, *J* = 6.8 Hz, 1H), 6.80 (d, *J* = 7.2 Hz, 2H), 7.18-7.24 (m, 5H), 7.29 (d, *J* = 8.0 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 22.5, 47.4, 55.3, 113.8, 127.1, 128.4, 128.7, 132.5, 135.2, 135.3, 158.6.

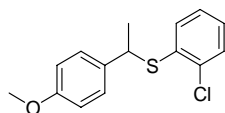


**(1-(4-methoxyphenyl)ethyl)(p-tolyl)sulfane (3b)** Yield: 77%; Colorless oil; <sup>1</sup>H NMR (400 MHz,

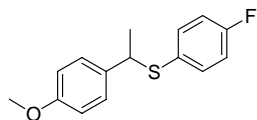
$\text{CDCl}_3$ )  $\delta$  1.61 (d,  $J = 6.8$  Hz, 3H), 2.33(s, 3H), 3.81 (s, 3H), 4.29 (q,  $J = 6.8$  Hz, 1H), 6.84 (d,  $J = 8.4$  Hz, 2H), 7.07 (d,  $J = 7.6$  Hz, 2H), 7.21-7.24 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  21.1, 22.3, 47.8, 55.3, 113.7, 128.4, 129.5, 131.5, 133.2, 135.4, 137.3, 158.6.



**(4-chlorophenyl)(1-(4-methoxyphenyl)ethyl)sulfane (3c)** Yield: 90%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.50 (d,  $J = 7.2$  Hz, 3H), 3.68 (s, 3H), 4.19 (q,  $J = 6.8$  Hz, 1H), 6.72 (d,  $J = 8.8$  Hz, 2H), 7.09 -7.11 (m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.3, 47.7, 55.3, 113.8, 128.4, 128.8, 133.3, 133.7, 133.9, 134.9, 158.7.

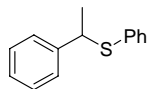


**(2-chlorophenyl)(1-(4-methoxyphenyl)ethyl)sulfane (3d)** Yield: 85%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.62 (d,  $J = 7.2$  Hz, 3H), 3.76 (s, 3H), 4.47 (q,  $J = 6.8$  Hz, 1H), 6.80 (d,  $J = 8.8$  Hz, 2H), 7.08 (d,  $J = 8.8$  Hz, 2H), 7.23-7.28 (m, 3H), 7.35 (t,  $J = 6.4$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) 22.4, 45.8, 55.3, 113.9, 126.9, 127.8, 128.3, 129.7, 132.7, 134.6, 134.8, 135.8, 158.8.

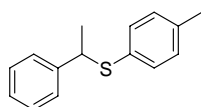


**(4-fluorophenyl)(1-(4-methoxyphenyl)ethyl)sulfane (3e)** Yield: 88%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.57 (d,  $J = 7.2$  Hz, 3H), 3.76 (s, 3H), 4.20 (q,  $J = 6.8$  Hz, 1H), 6.79 (d,  $J = 8.4$  Hz, 2H), 6.89 (t,  $J = 8.4$  Hz, 2H), 7.14 (d,  $J = 8.4$  Hz, 2H), 7.23 (dd,  $J = 5.2, 8.8$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.1, 48.3, 55.2, 113.7, 115.7 (d,  $^2J_{\text{CF}} = 22.0$  Hz), 128.4, 129.9, 135.0,

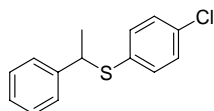
135.7 (d,  $^2J_{\text{CF}} = 8.0$  Hz), 158.7. 162.5 (d,  $^1J_{\text{CF}} = 246.0$  Hz).



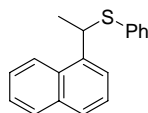
**phenyl(1-phenylethyl)sulfane<sup>1</sup> (3g)** Yield: 68%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.62 (d,  $J = 7.2$  Hz, 3H), 4.33 (q,  $J = 7.2$  Hz, 1H), 7.17-7.29 (m, 10H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.4, 48.0, 127.1, 127.2, 127.3, 128.4, 128.7, 132.5, 135.2, 143.2.



**(1-phenylethyl)(p-tolyl)sulfane (3h)** Yield: 61%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.60 (d,  $J = 7.2$  Hz, 3H), 2.29 (s, 3H), 4.26 (q,  $J = 7.2$  Hz, 1H), 7.02 (d,  $J = 8.0$  Hz, 2H), 7.18 (d,  $J = 8.0$  Hz, 2H), 7.21-7.27 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  21.4, 22.2, 48.4, 127.1, 127.3, 128.4, 129.5, 131.3, 133.2, 137.4, 143.4.

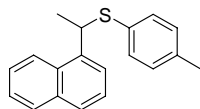


**(4-chlorophenyl)(1-phenylethyl)sulfane<sup>2</sup> (3i)** Yield: 60%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.61 (d,  $J = 7.2$  Hz, 3H), 4.29 (q,  $J = 7.2$  Hz, 1H), 7.17 (s, 4H), 7.18-7.23 (m, 1H), 7.25-7.27 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.2, 48.3, 127.2, 127.3, 128.5, 128.8, 133.4, 133.5, 134.0, 142.9.

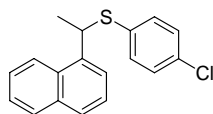


**(1-(naphthalen-1-yl)ethyl)(phenyl)sulfane (3j)** Yield: 50%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.77 (d,  $J = 6.8$  Hz, 3H), 5.16 (q,  $J = 6.8$  Hz, 1H), 7.18-7.24 (m, 3H), 7.29-7.31 (m, 2H), 7.40 (t,  $J = 8.0$  Hz, 1H), 7.48 (t,  $J = 8.0$  Hz, 1H), 7.52-7.58 (m, 2H), 7.74 (d,  $J$

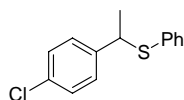
= 8.4 Hz, 1H), 7.86 (d,  $J = 8.0$  Hz, 1H), 8.22 (d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.1, 42.9, 123.1, 124.3, 125.4, 125.6, 126.1, 127.1, 127.9, 128.8, 129.0, 130.9, 132.2, 134.0, 135.3, 138.2.



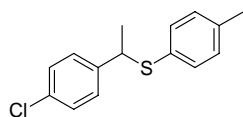
**(1-(naphthalen-1-yl)ethyl)(p-tolyl)sulfane (3k)** Yield: 45%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.75 (d,  $J = 6.8$  Hz, 3H), 2.29 (s, 3H), 5.08 (q,  $J = 6.8$  Hz, 1H), 7.03 (d,  $J = 8.0$  Hz, 2H), 7.21 (d,  $J = 8.0$  Hz, 2H), 7.40 (t,  $J = 7.6$  Hz, 1H), 7.48-7.55 (m, 3H), 7.74 (d,  $J = 8.0$  Hz, 1H), 7.86 (d,  $J = 8.0$  Hz, 1H), 8.23 (d,  $J = 8.8$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  21.1, 22.0, 43.3, 123.2, 124.3, 125.4, 125.6, 126.1, 127.8, 129.0, 129.5, 130.9, 131.4, 133.1, 134.0, 137.4, 138.4.



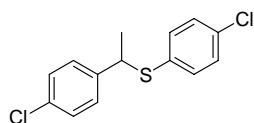
**(4-chlorophenyl)(1-(naphthalen-1-yl)ethyl)sulfane (3l)** Yield: 67%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.75 (d,  $J = 6.8$  Hz, 3H), 5.11 (q,  $J = 6.8$  Hz, 1H), 7.12-7.18 (m, 4H), 7.39 (t,  $J = 8.0$  Hz, 1H), 7.47-7.56 (m, 3H), 7.74 (d,  $J = 8.0$  Hz, 1H), 7.86 (d,  $J = 8.0$  Hz, 1H), 8.18 (d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  22.0, 43.1, 123.0, 124.4, 125.4, 125.7, 126.2, 128.1, 128.9, 129.1, 130.8, 133.4, 133.5, 133.7, 134.0, 137.8.



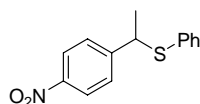
**(1-(4-chlorophenyl)ethyl)(phenyl)sulfane (3m)** Yield: 53%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.59 (d,  $J = 7.2$  Hz, 3H), 4.29 (q,  $J = 7.2$  Hz, 1H), 7.18-7.27 (m, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.2, 47.5, 127.4, 128.5, 128.6, 128.8, 132.7, 132.8, 134.6, 141.9.



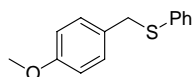
**(1-(4-chlorophenyl)ethyl)(p-tolyl)sulfane (3n)** Yield: 76%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.57 (d,  $J = 7.2$  Hz, 3H), 2.29 (s, 3H), 4.21 (q,  $J = 7.2$  Hz, 1H), 7.02 (d,  $J = 8.0$  Hz, 2H), 7.14-7.23(m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  21.1, 22.1, 47.8, 128.4, 128.7, 129.6, 130.7, 132.6, 133.4, 137.7, 142.0.



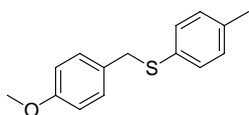
**(4-chlorophenyl)(1-(4-chlorophenyl)ethyl)sulfane (3o)** Yield: 70%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.58 (d,  $J = 6.8$  Hz, 3H), 4.24 (q,  $J = 6.8$  Hz, 1H), 7.15-7.18 (m, 6H), 7.21-7.24 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.1, 47.7, 128.6 (2C), 128.9, 132.9, 133.0, 133.7, 134.2, 141.5.



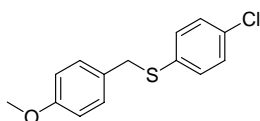
**(1-(4-nitrophenyl)ethyl)(phenyl)sulfane (3p)** Yield: 53%; Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.65 (d,  $J = 6.8$  Hz, 3H), 4.37 (q,  $J = 6.8$  Hz, 1H), 7.20-7.25 (m, 5H), 7.37 (d,  $J = 8.4$  Hz, 2H), 8.08 (d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 47.7, 123.6, 127.9, 128.1, 128.9, 133.2, 133.6, 136.5, 151.1.



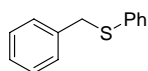
**(4-methoxybenzyl)(phenyl)sulfane<sup>3</sup> (3r)** Yield: 75%; mp: 89-90 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.77 (s, 3H), 4.07 (s, 2H), 6.81 ((d,  $J = 7.2$  Hz, 2H), 7.16-7.31 (m, 7H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  38.5, 55.3, 113.9, 126.3, 128.8, 129.4, 129.8, 130.0, 136.6, 158.8



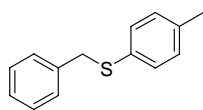
**(4-methoxybenzyl)(p-tolyl)sulfane<sup>4</sup> (3s)** Yield: 85%; mp: 66-68 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 2.30 (s, 3H), 3.78 (s, 3H), 4.02 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 21.1, 39.2, 55.3, 113.9, 129.6, 129.8, 130.0, 130.7, 132.7, 136.5, 158.7.



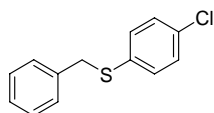
**(4-methoxybenzyl)(4-chlorophenyl)sulfane<sup>4</sup> (3t)** Yield: 72%; mp: 65-66 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.78 (s, 3H), 4.03 (s, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.20 (s, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 38.7, 55.3, 114.0, 128.9, 129.0, 129.9, 131.4, 132.4, 134.9, 158.9.



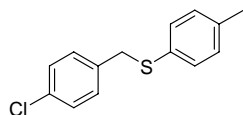
**benzyl(phenyl)sulfane<sup>5</sup> (3u)** Yield: 70%; Colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.11 (s, 2H), 7.15-7.29(m, 10H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 39.1, 126.4, 127.2, 128.5, 128.8, 129.9, 136.4, 137.5.



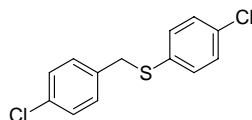
**benzyl(p-tolyl)sulfane<sup>5</sup> (3v)** Yield: 52%; Colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 2.30 (s, 3H), 4.06 (s, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.22-7.27(m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 21.1, 39.8, 127.1, 128.4, 128.9, 129.6, 130.7, 132.5, 136.6, 137.8.



**benzyl(4-chlorophenyl)sulfane**<sup>6</sup> (**3w**) Yield: 61%; mp: 43-44 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.07 (s, 2H), 7.20 (s, 4H), 7.21-7.26 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 39.3, 127.3, 128.6, 128.8, 129.0, 131.5, 132.5, 134.7, 137.1.



**(4-chlorobenzyl)(p-tolyl)sulfane**<sup>7</sup> (**3x**) Yield: 58%; mp: 64-65 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 2.30 (s, 3H), 4.00 (s, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.14 -7.23 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 21.0, 39.2, 128.5, 129.7, 130.1, 131.1, 131.7, 132.8, 136.5, 136.9.



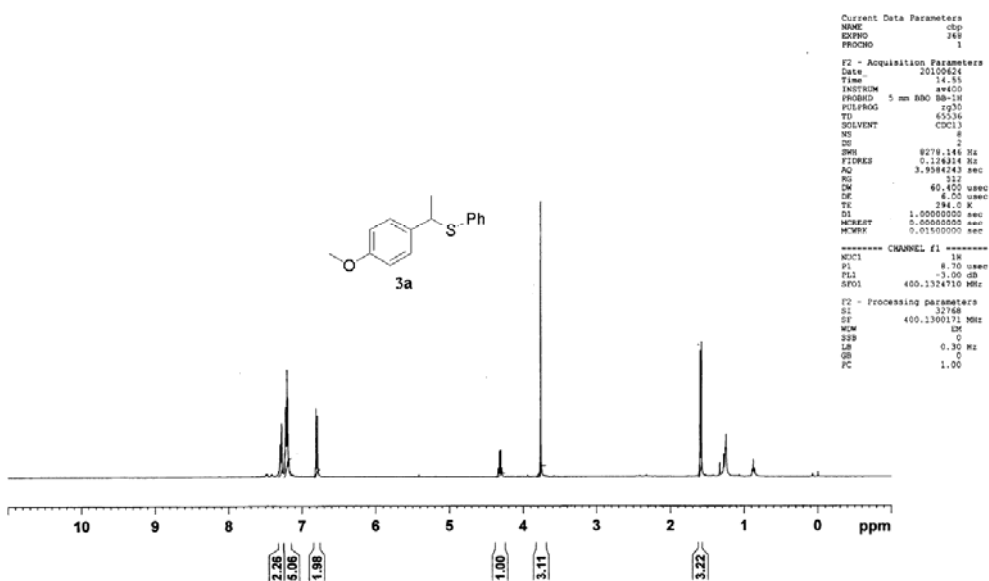
**(4-chlorobenzyl)(4-chlorophenyl)sulfane**<sup>8</sup> (**3y**) Yield: 48%; mp: 56-57 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.01 (s, 2H), 7.14 -7.25 (m, 8H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 38.8, 128.7, 129.0, 130.1, 131.8, 132.8, 133.1, 134.0, 135.8.

#### References:

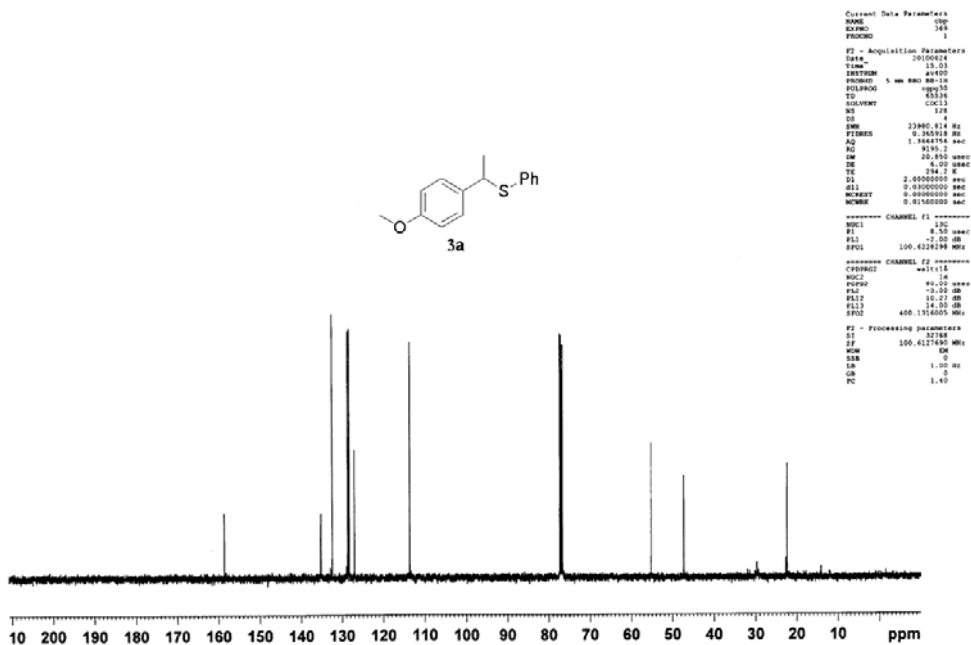
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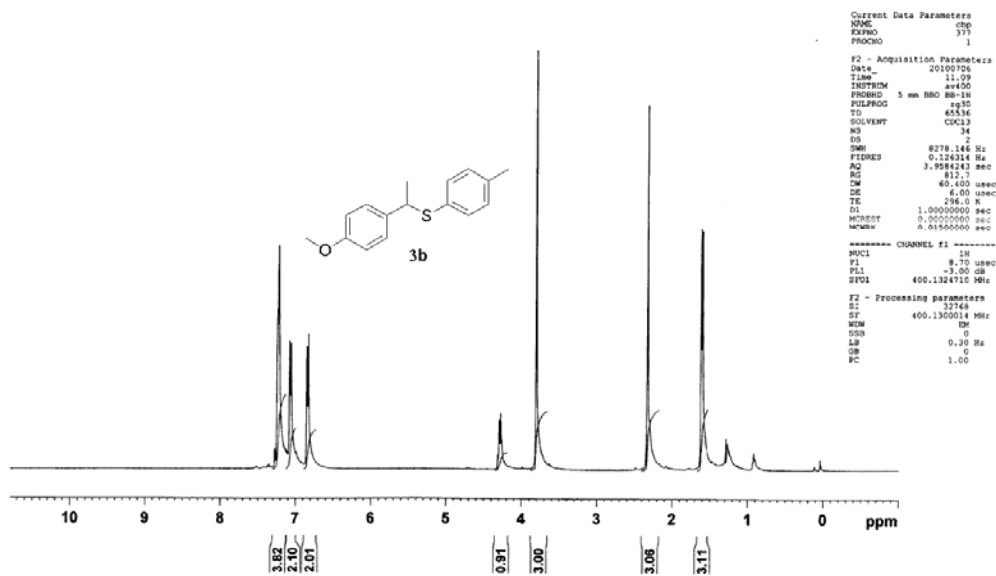
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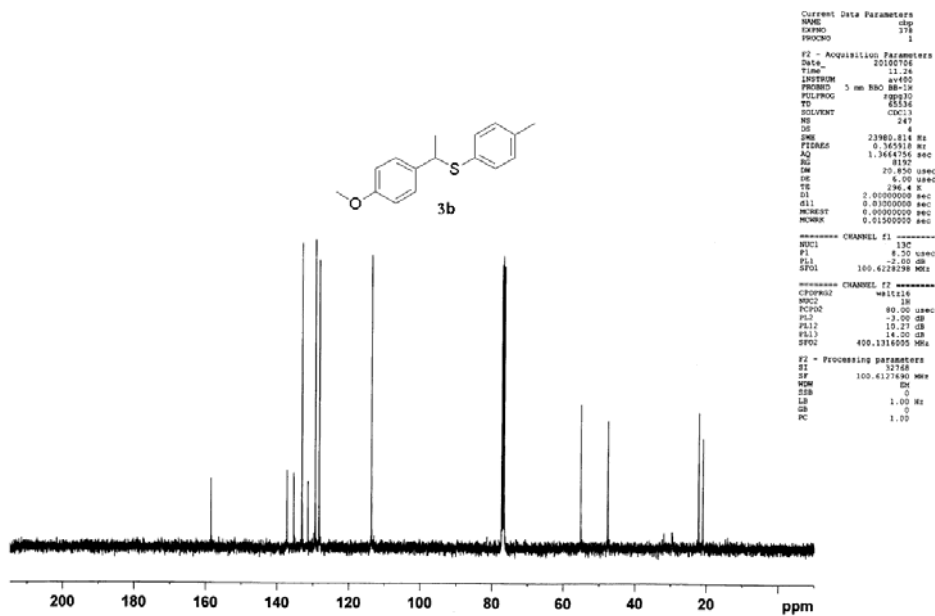
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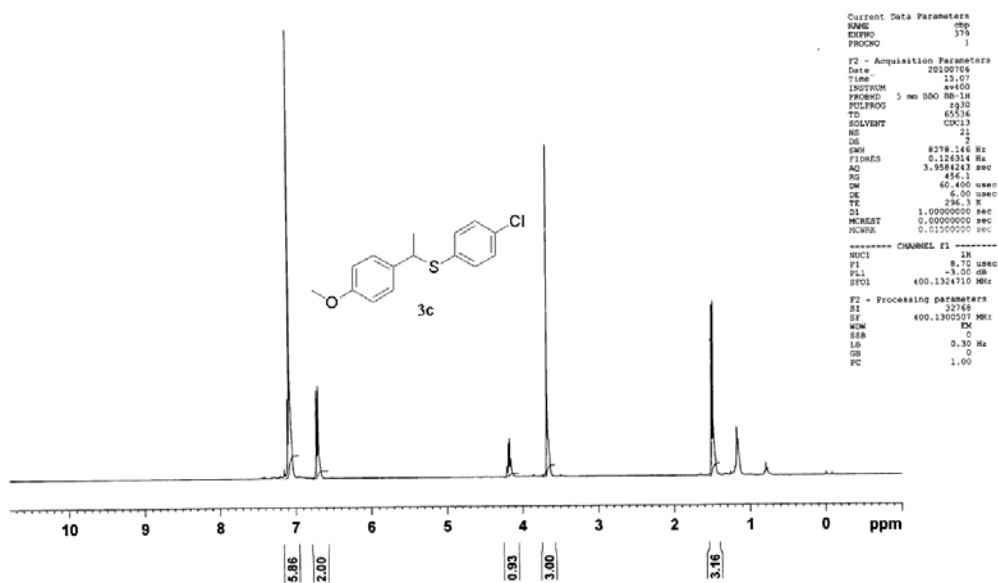
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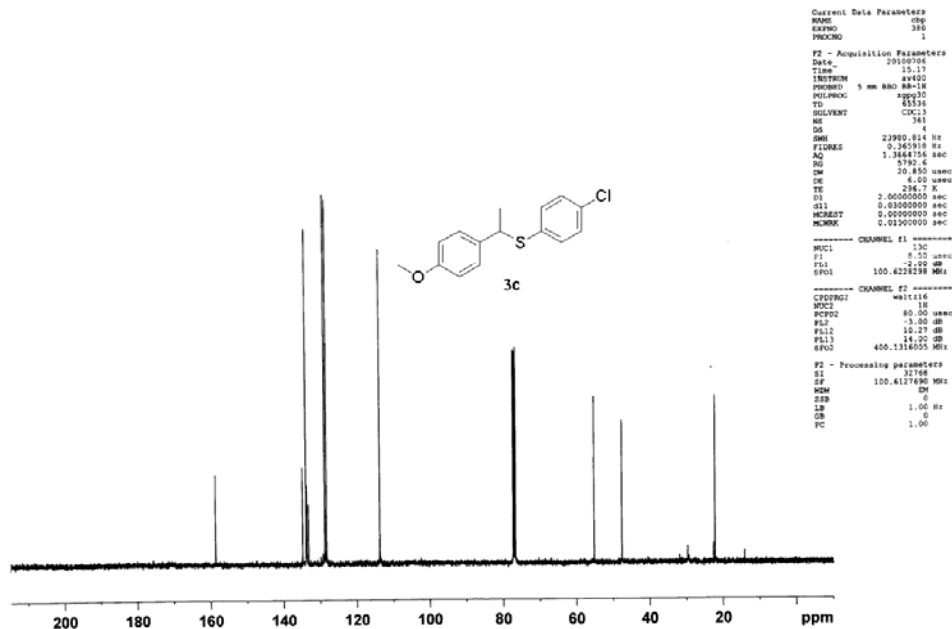
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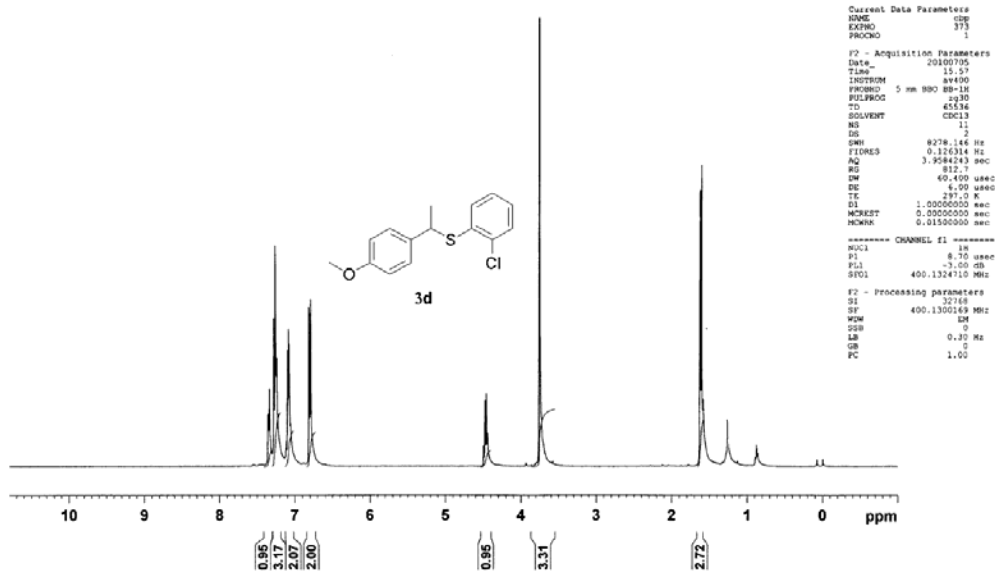
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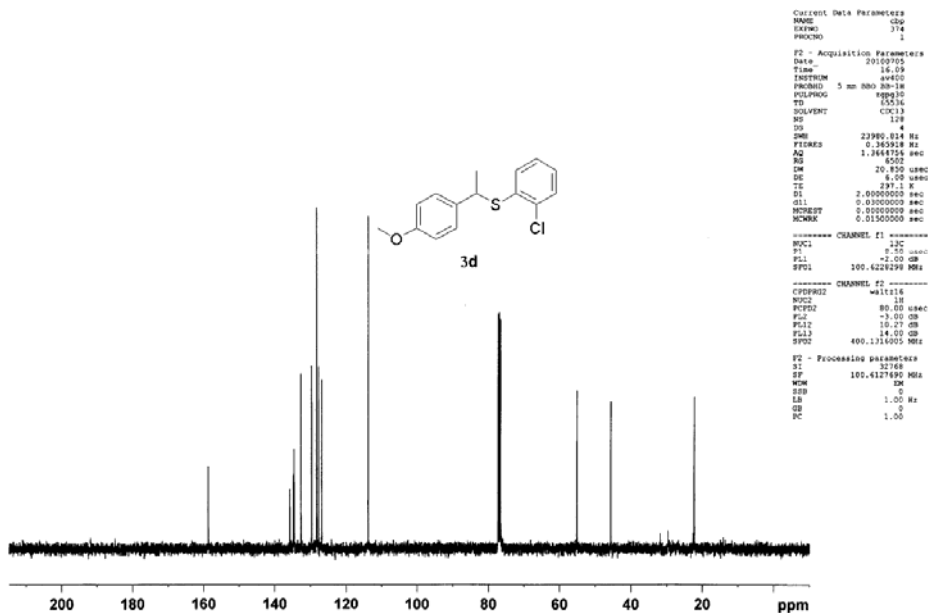
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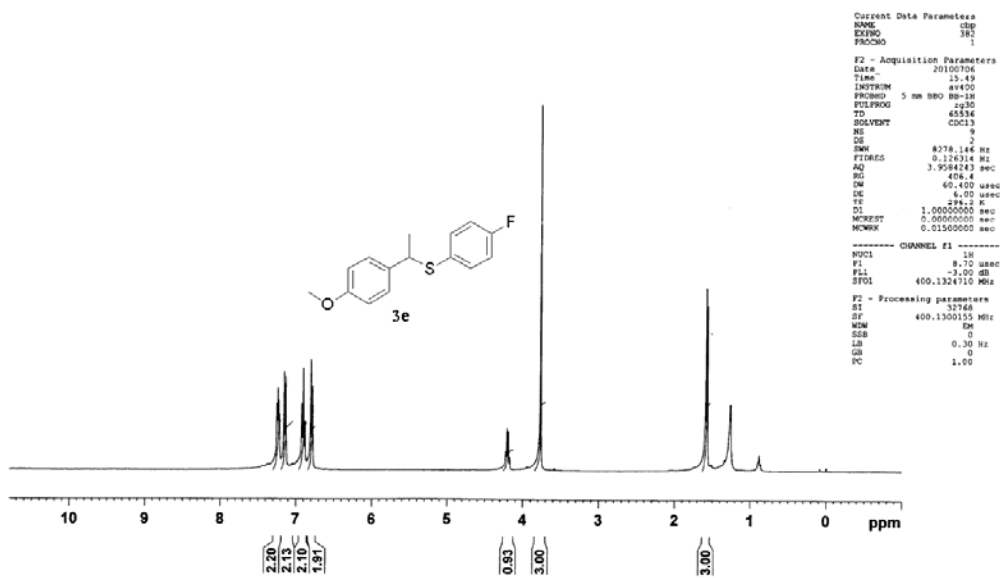
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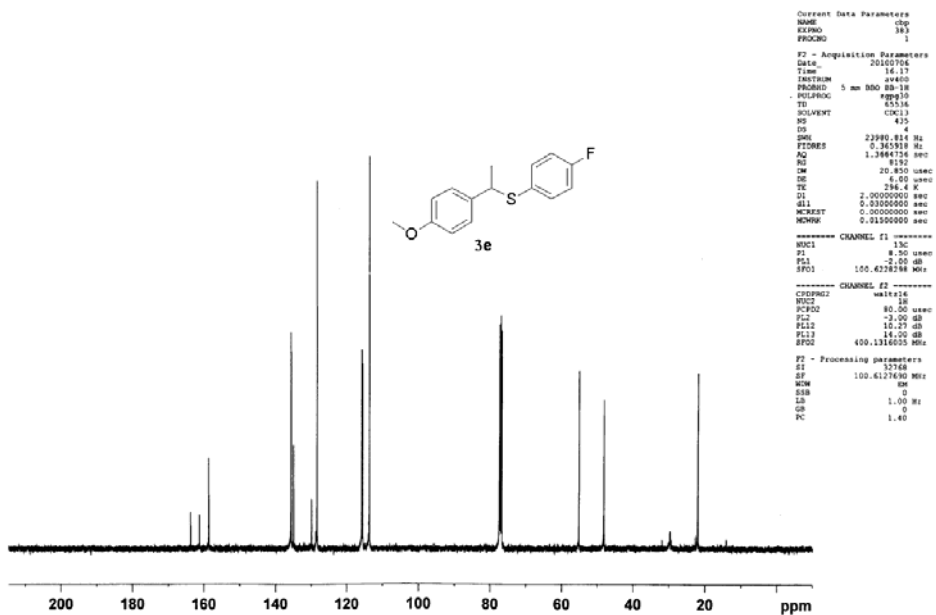
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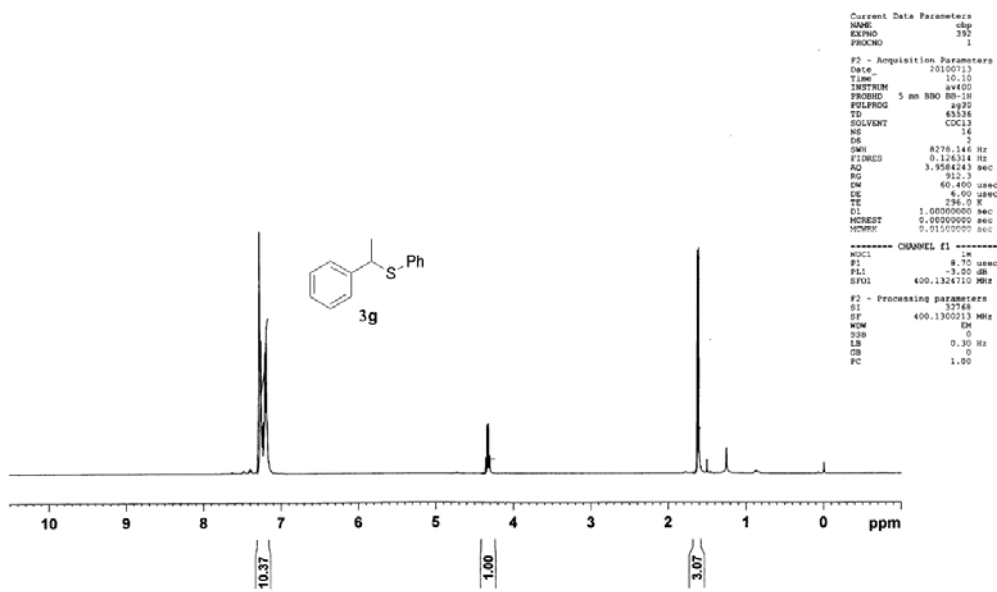
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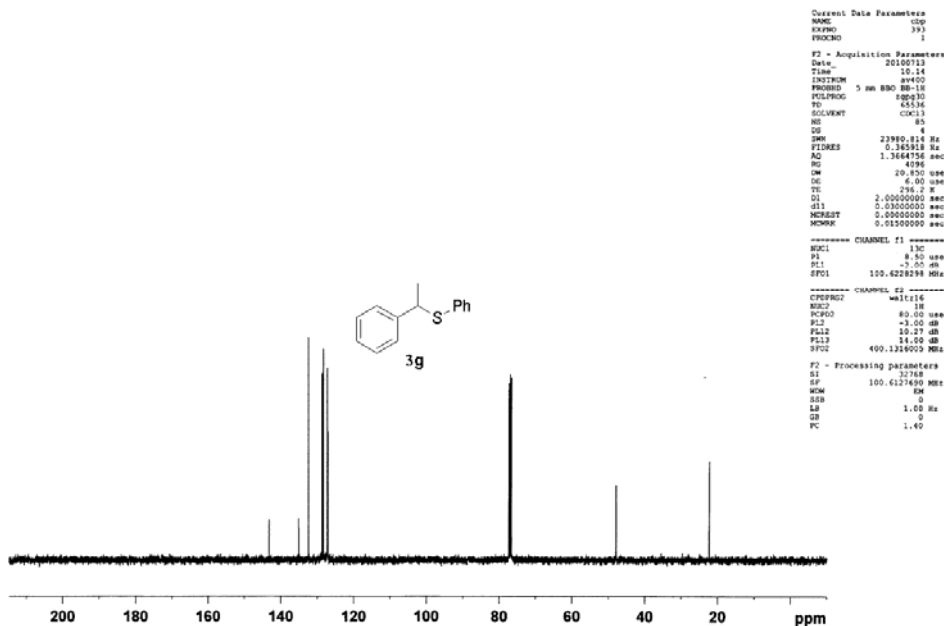
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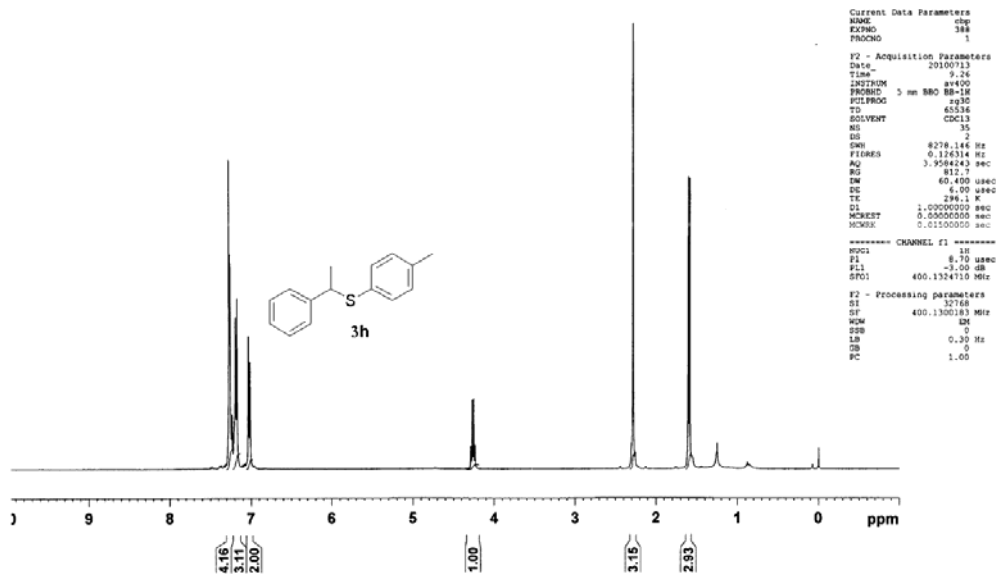
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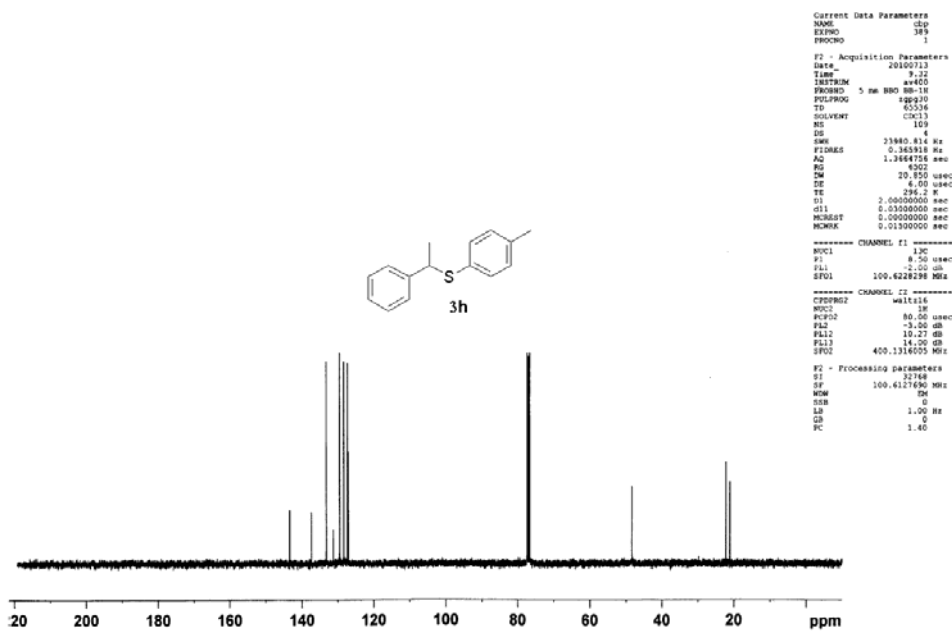
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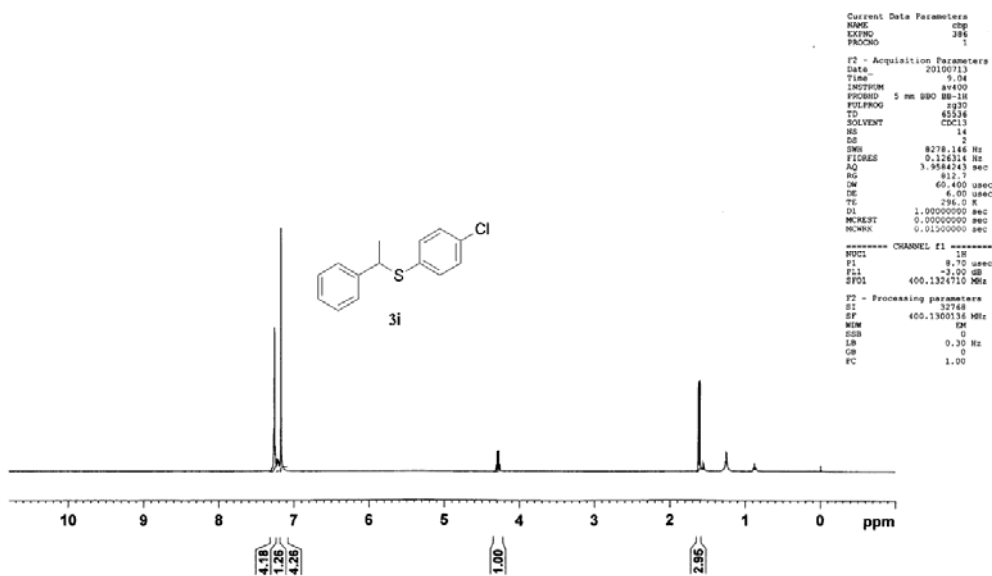
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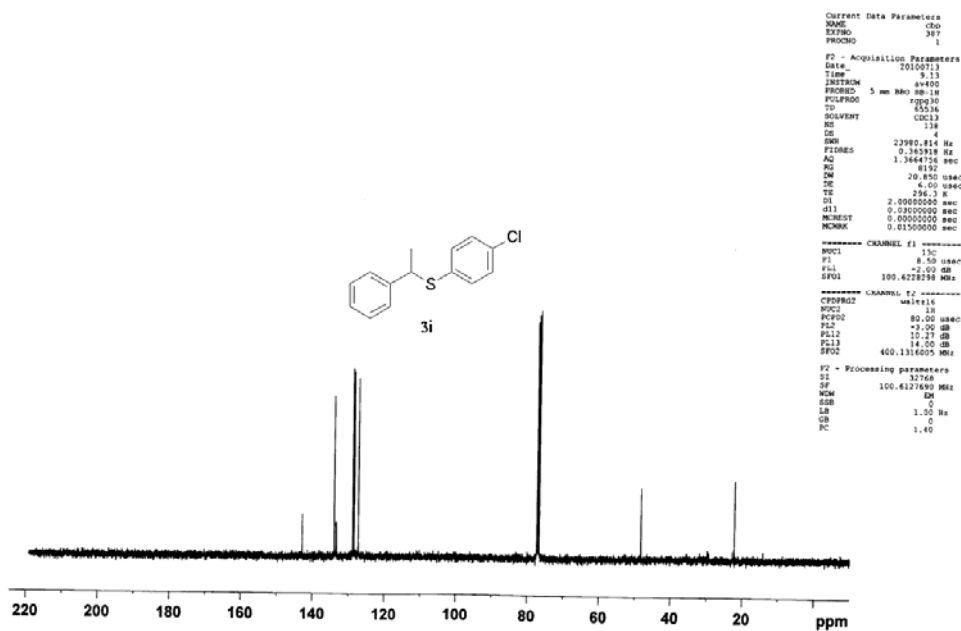
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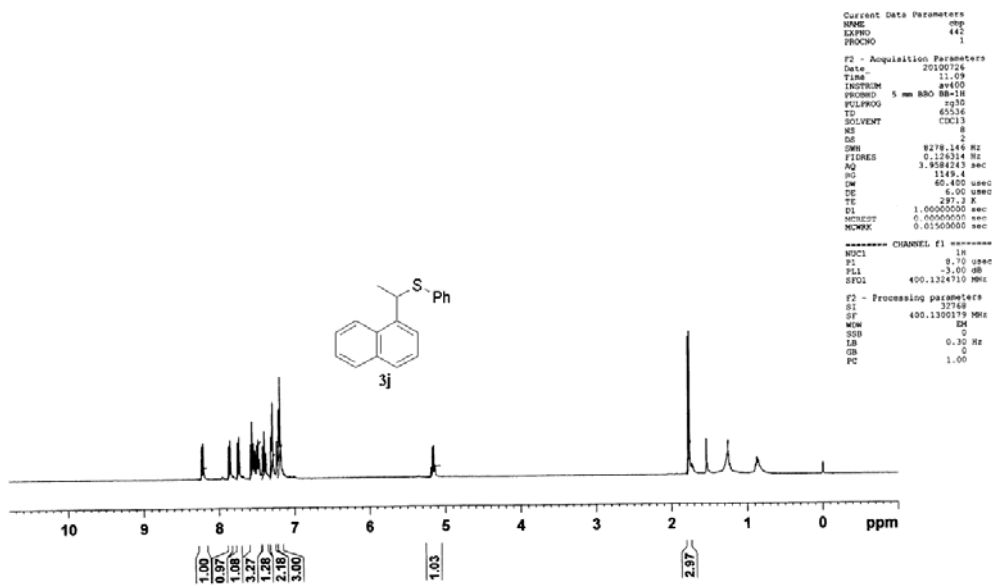


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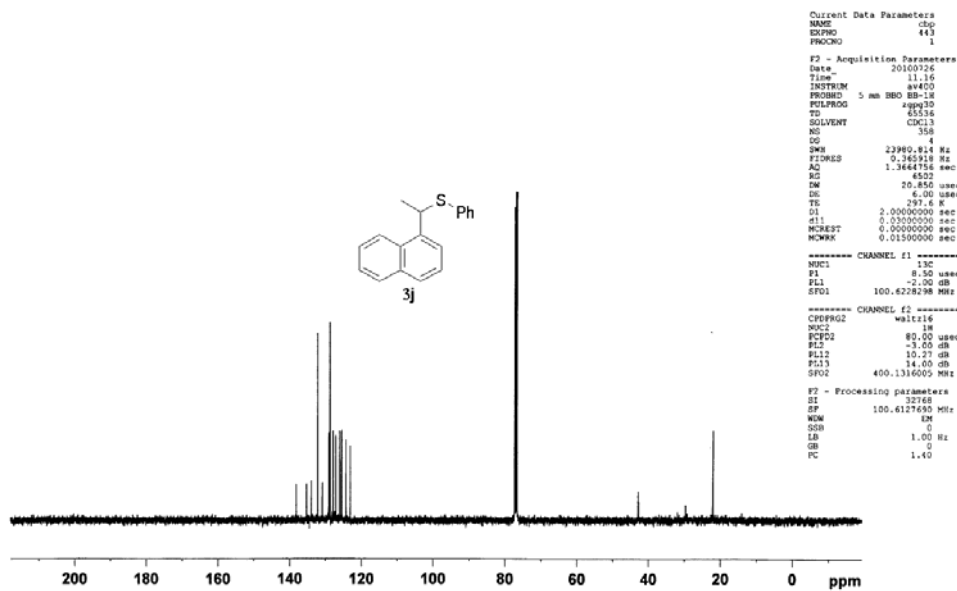




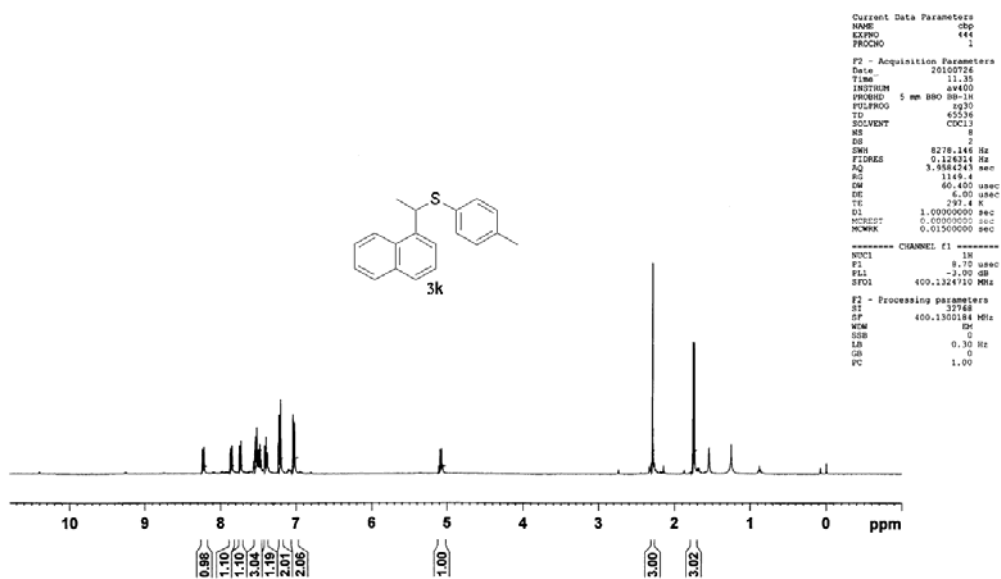
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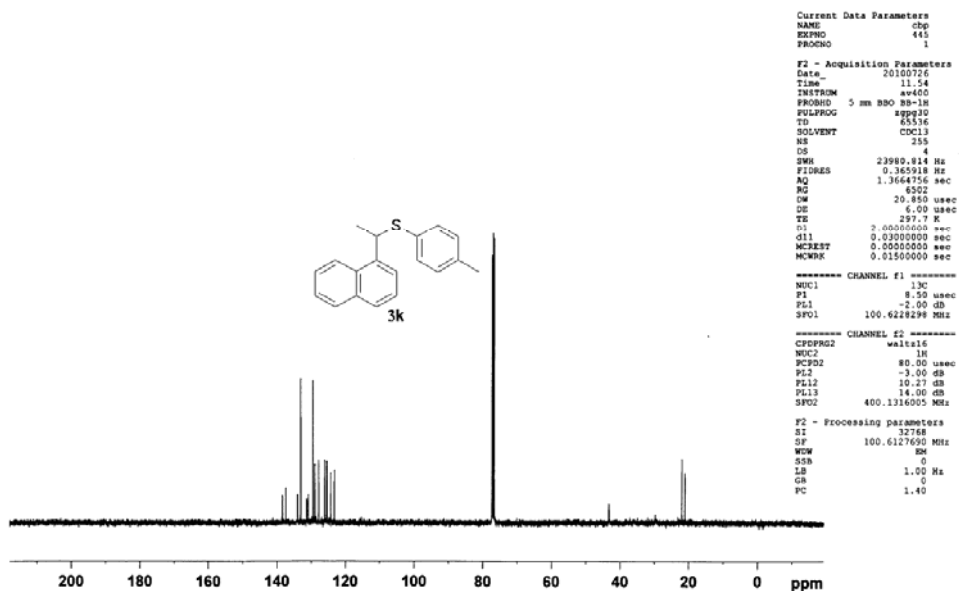
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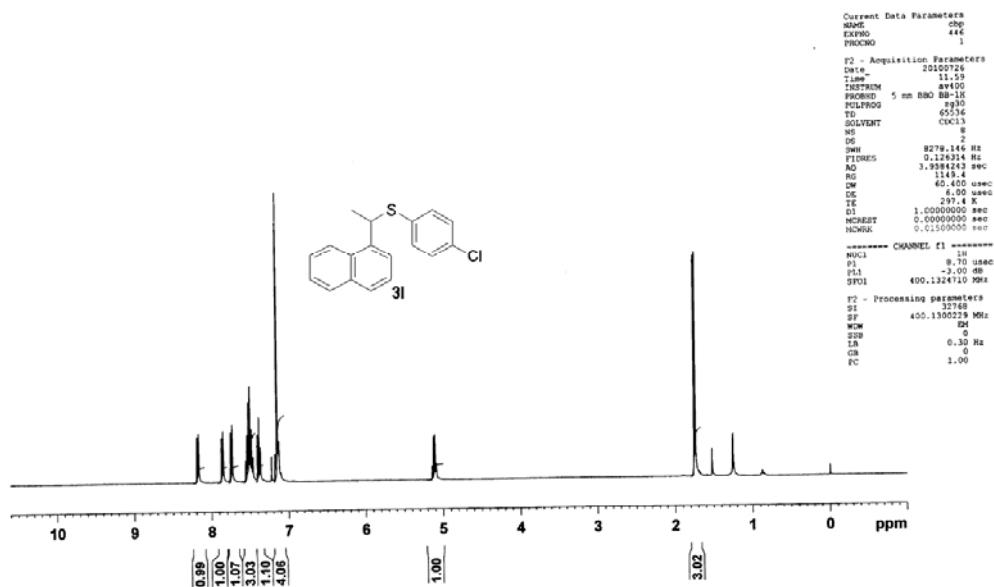
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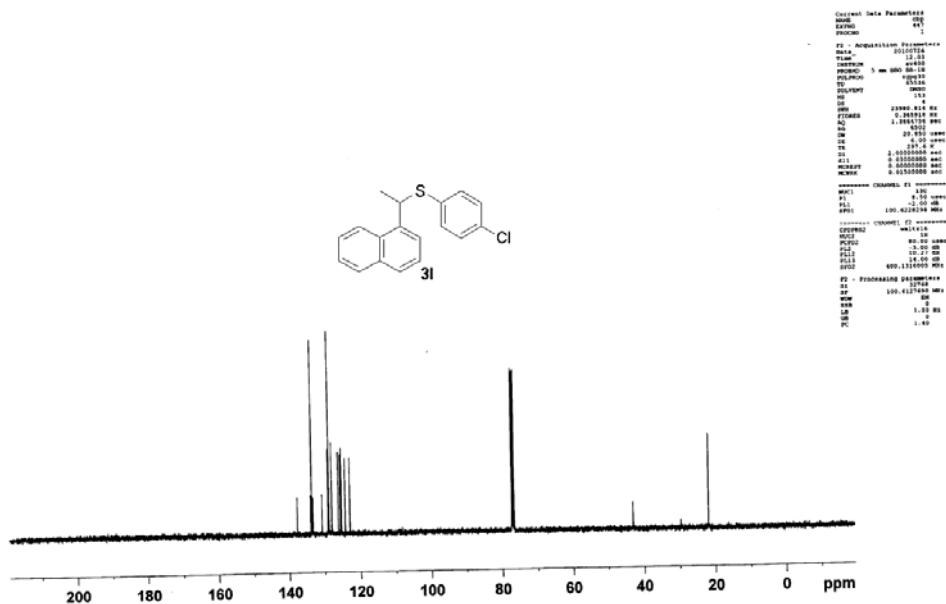
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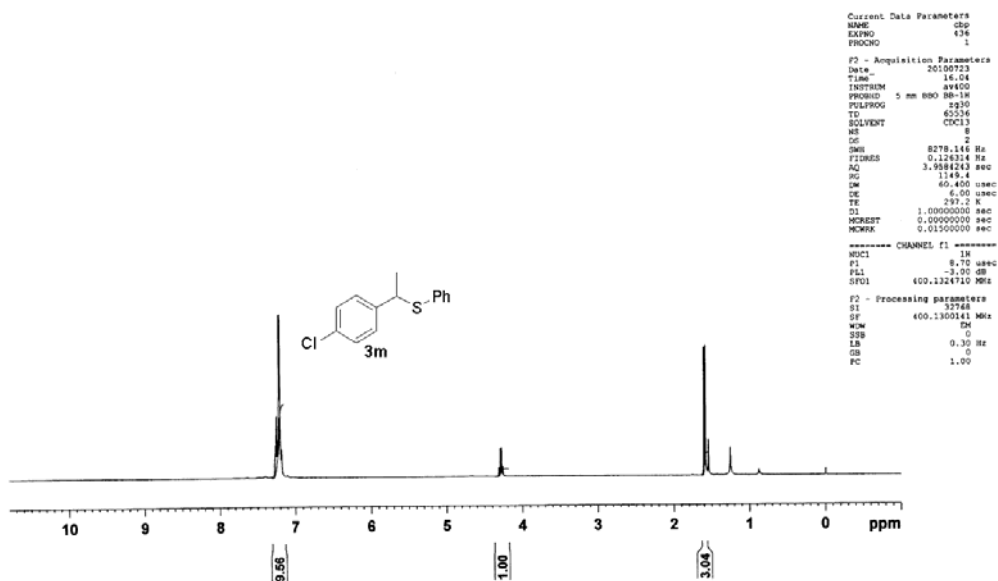
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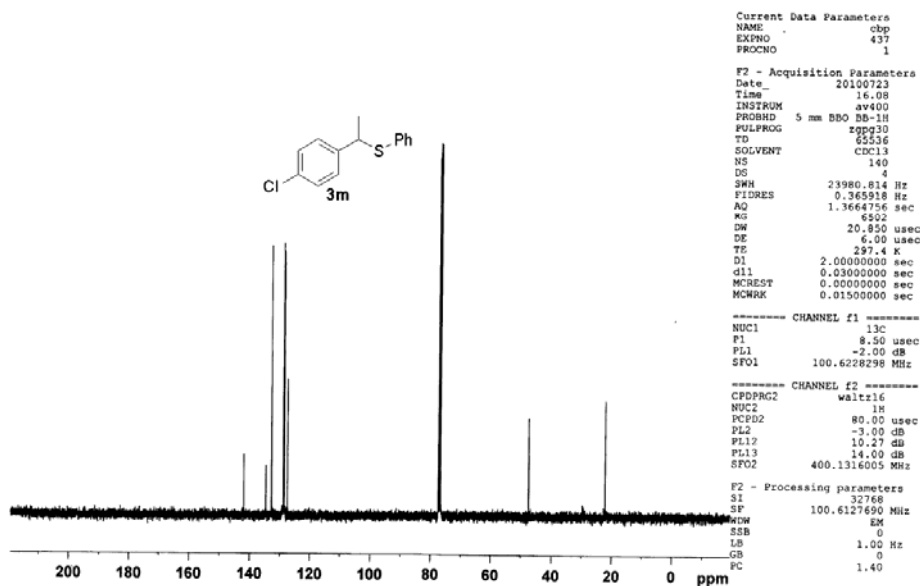
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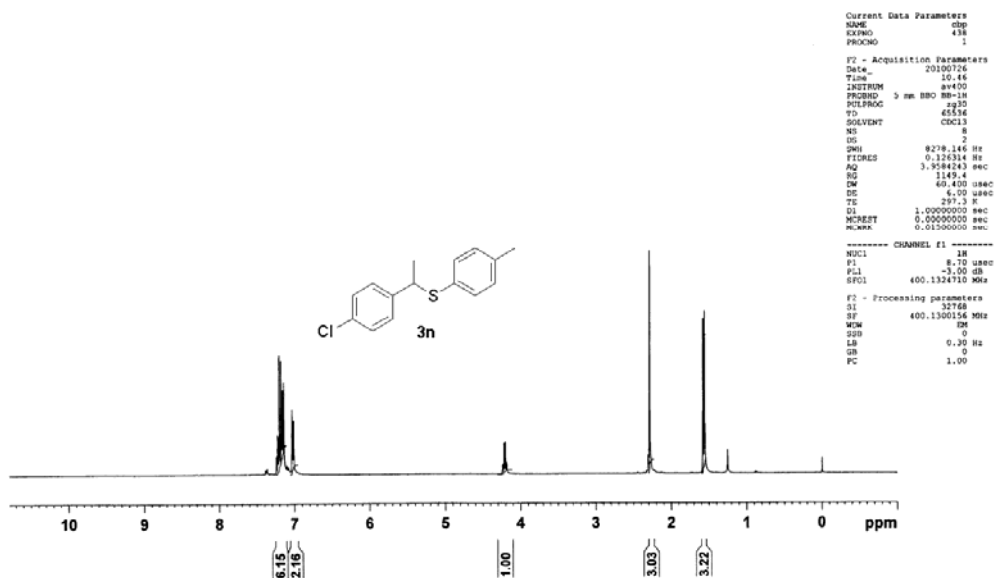
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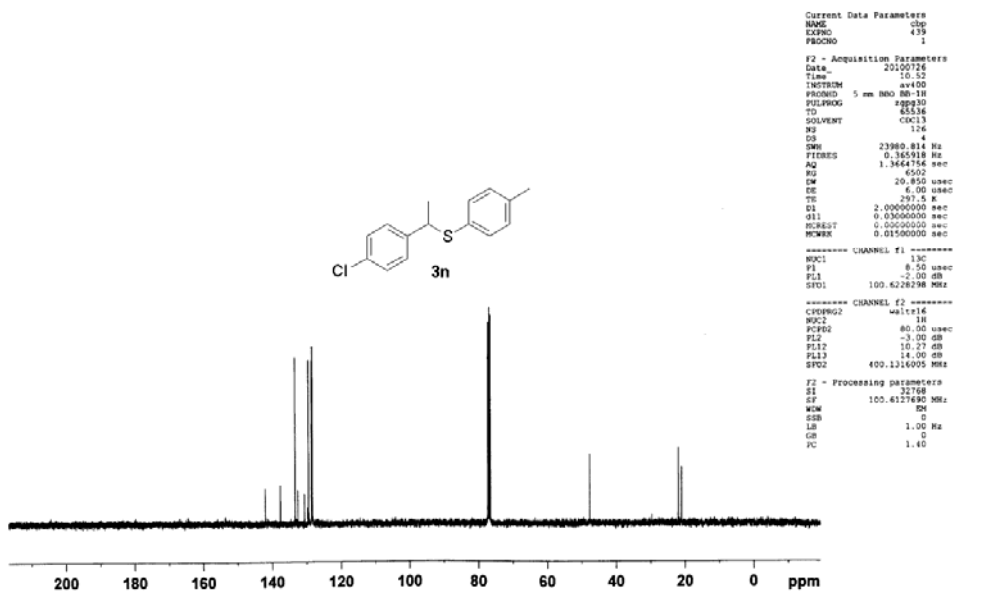
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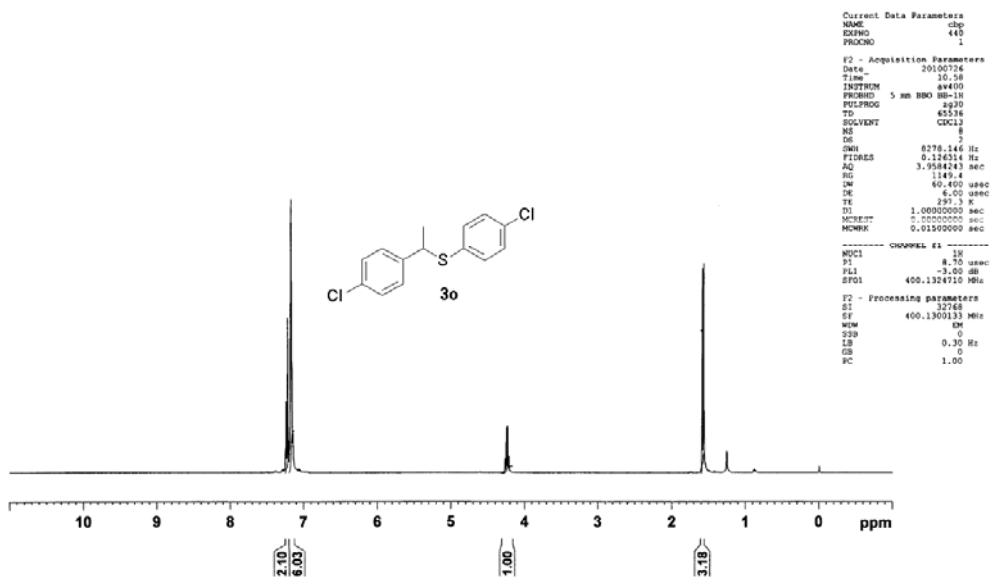
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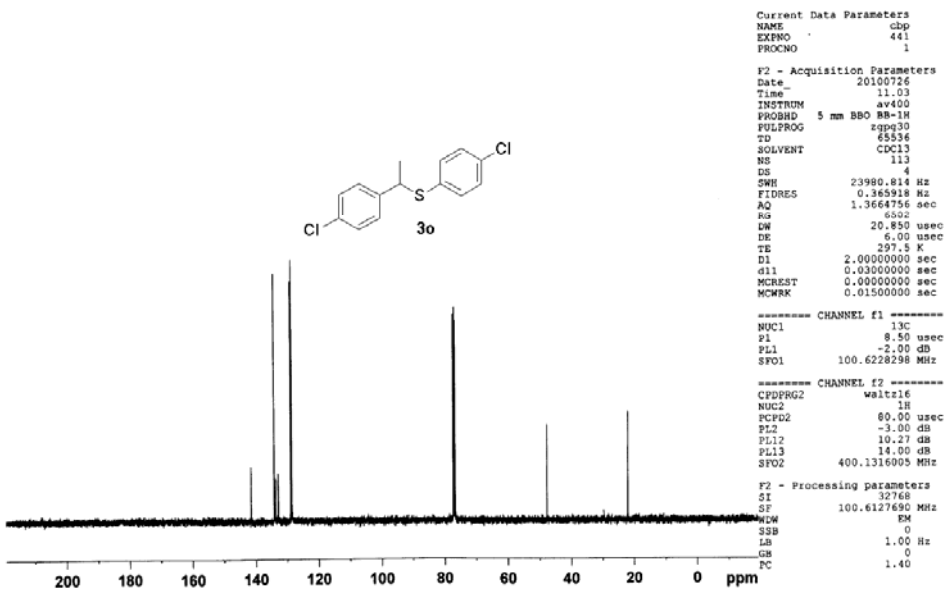
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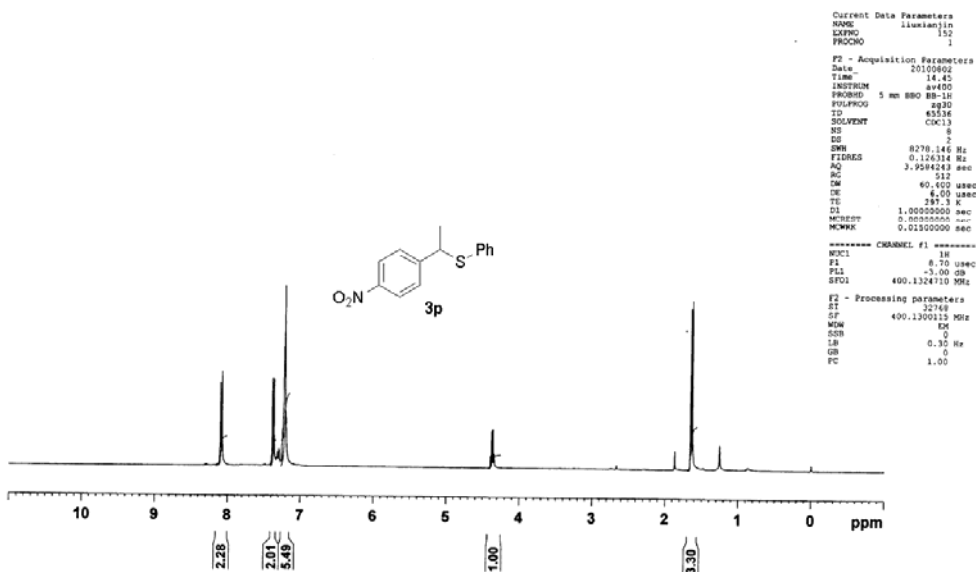
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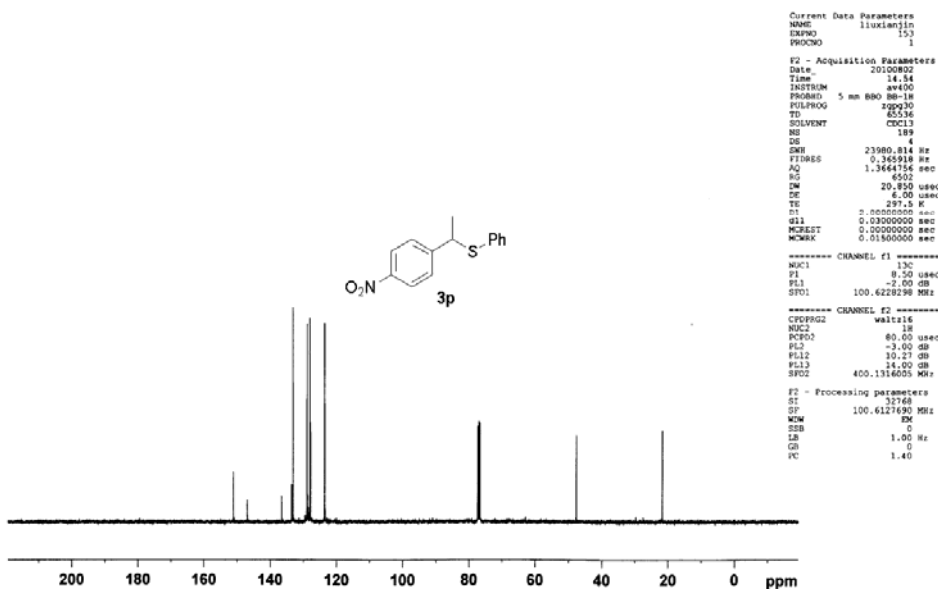
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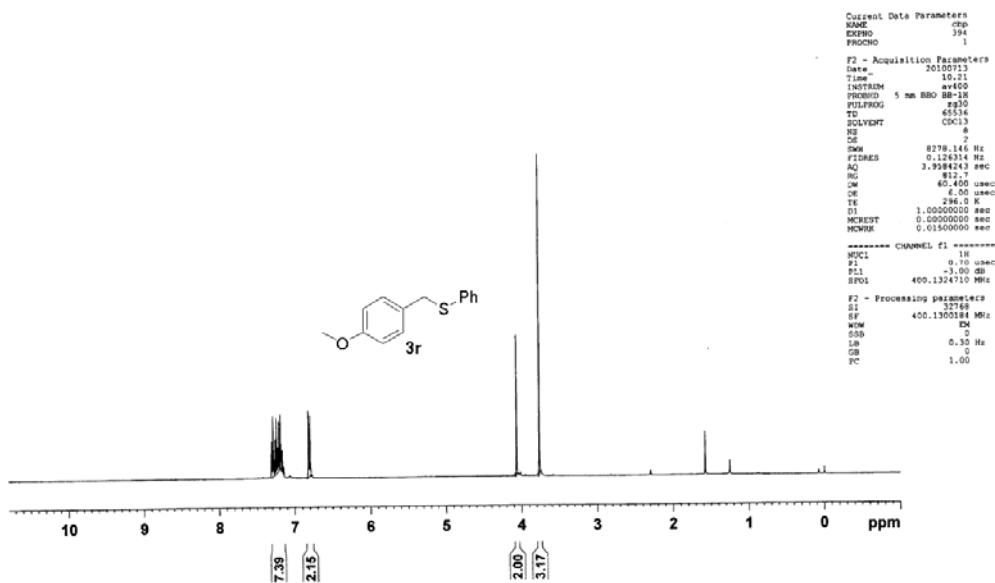
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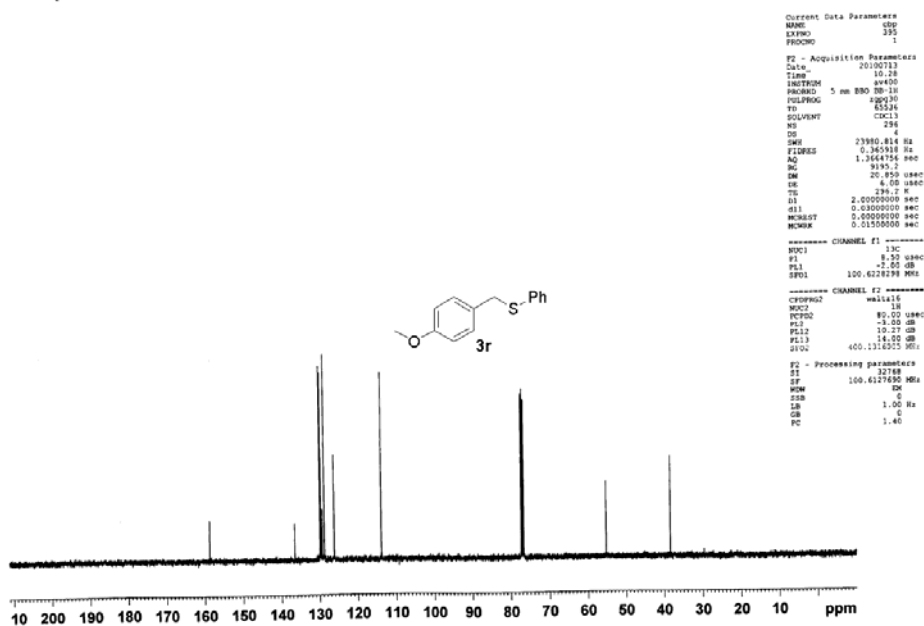
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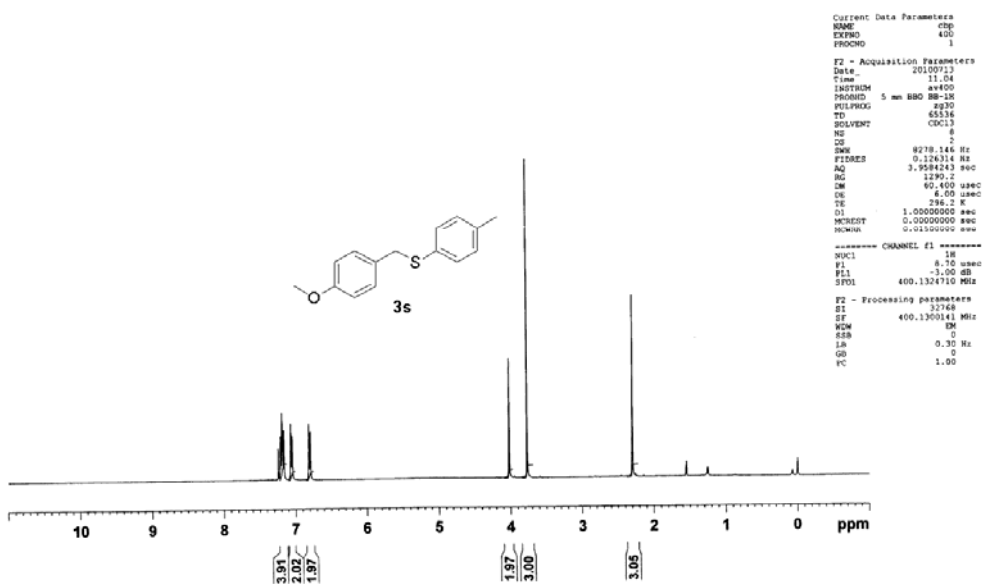


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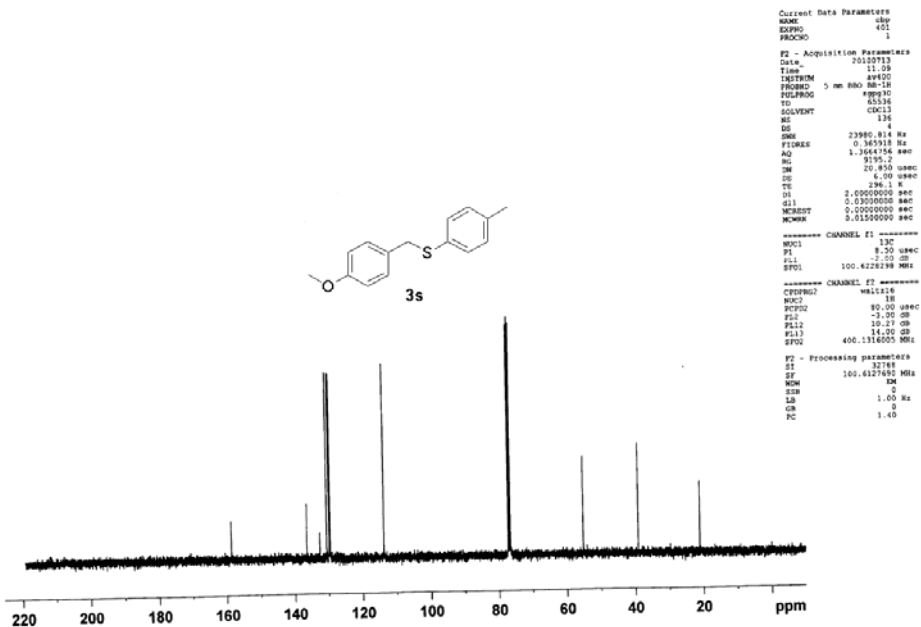




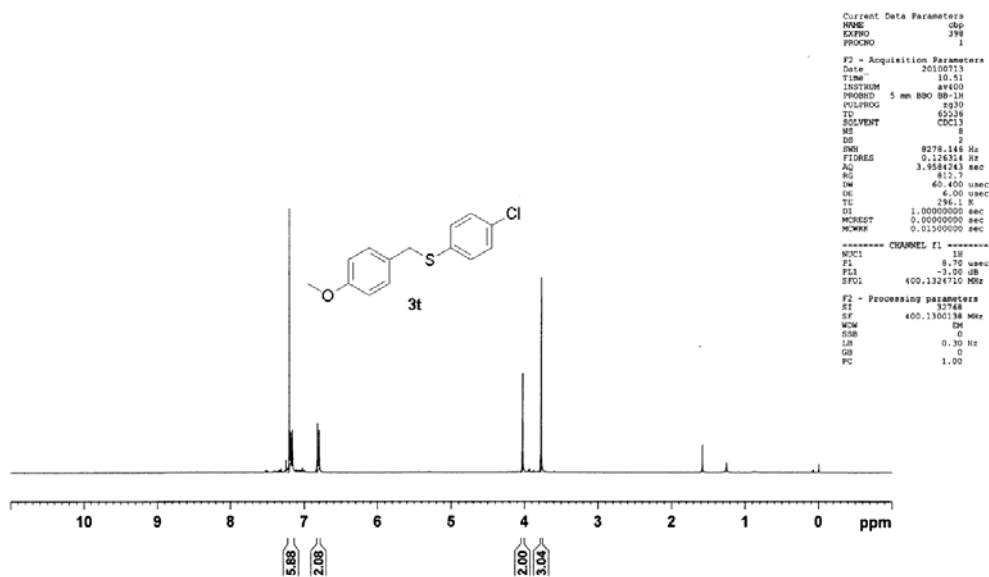
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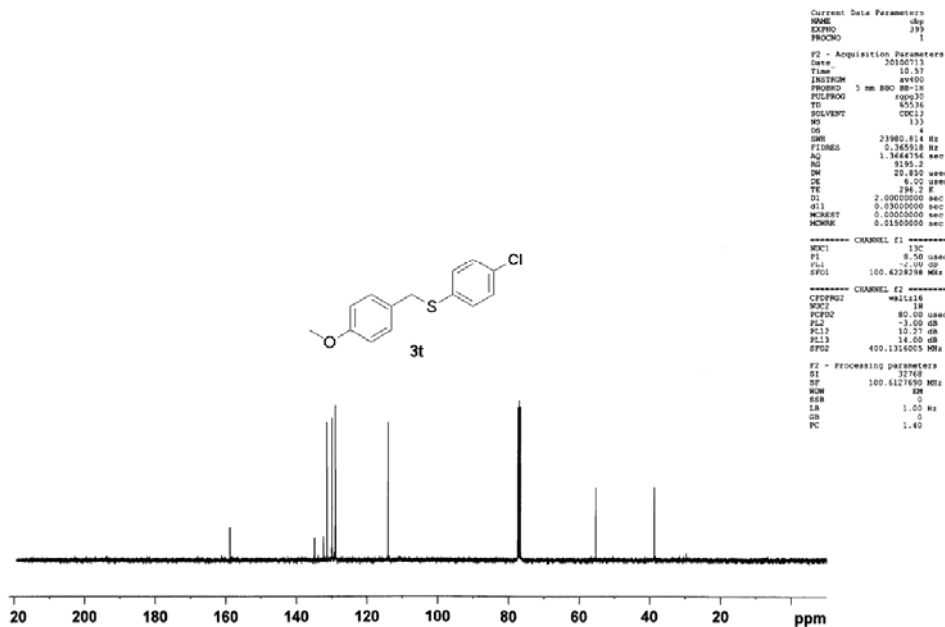
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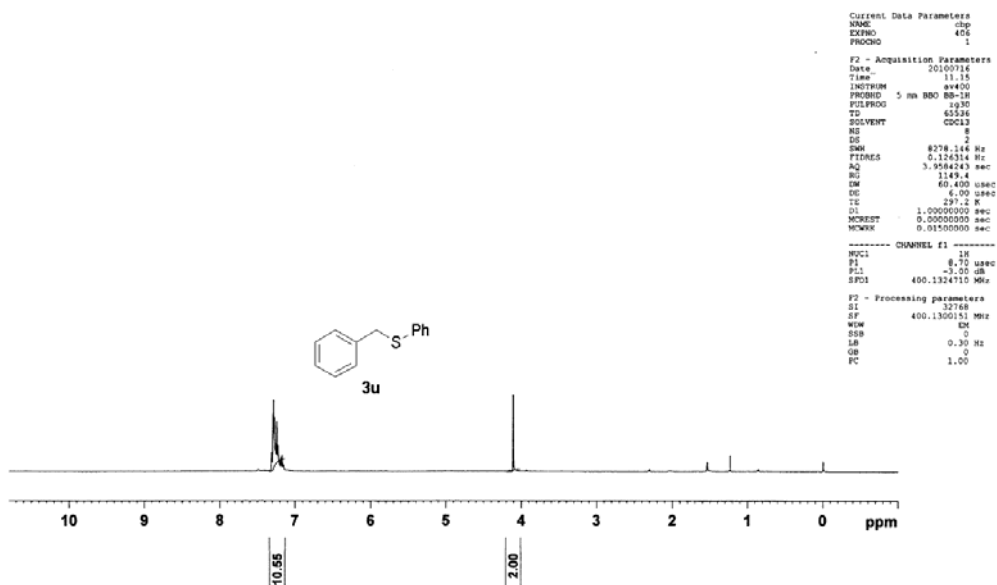
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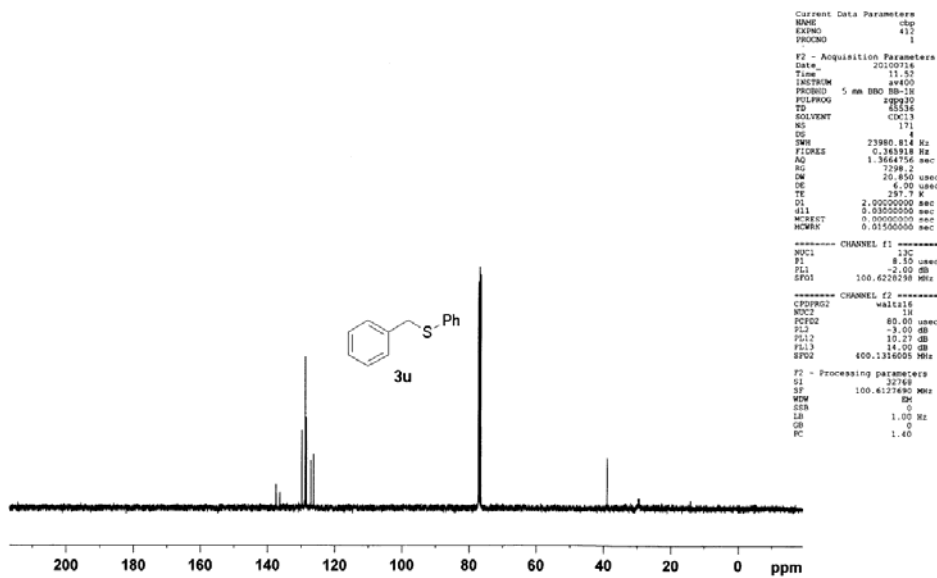
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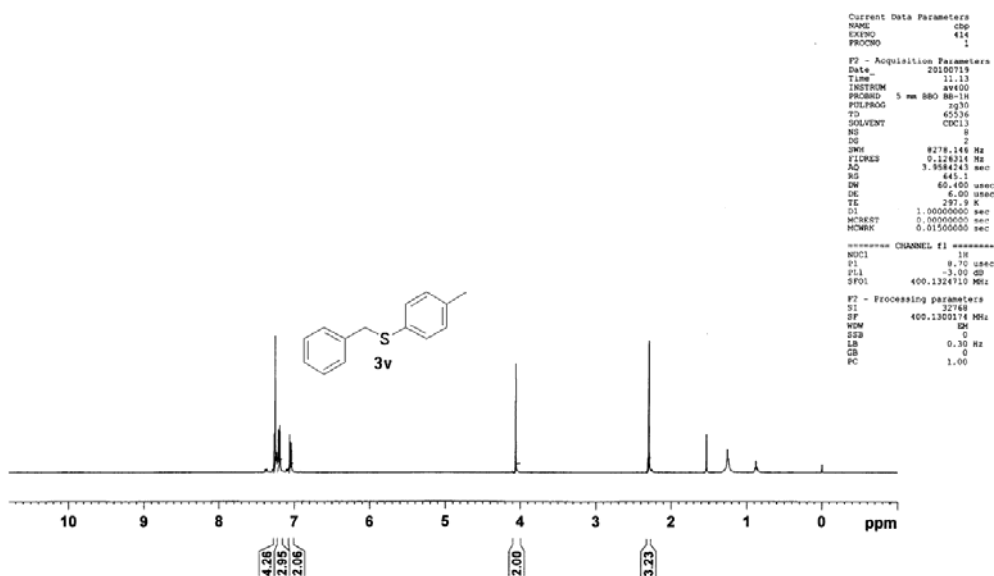
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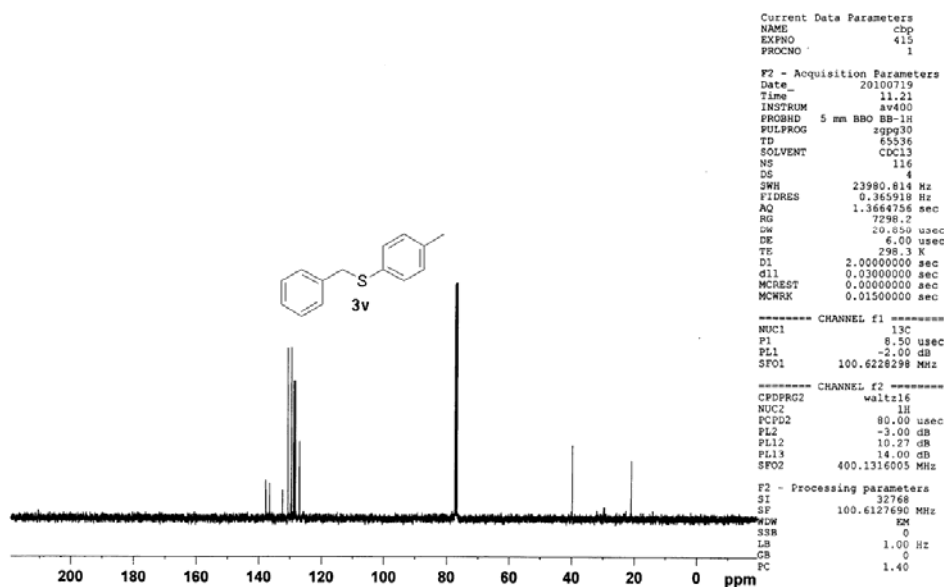
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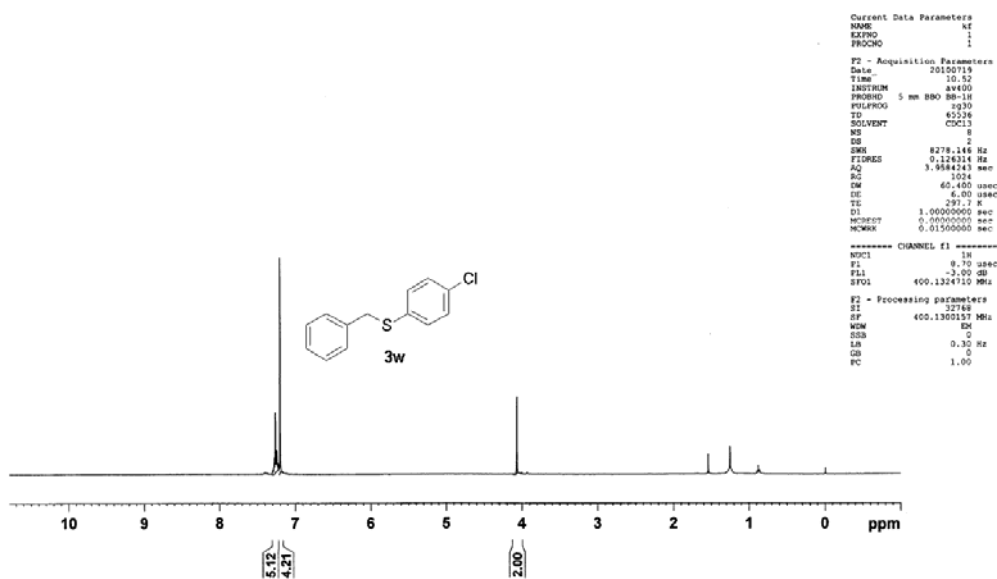
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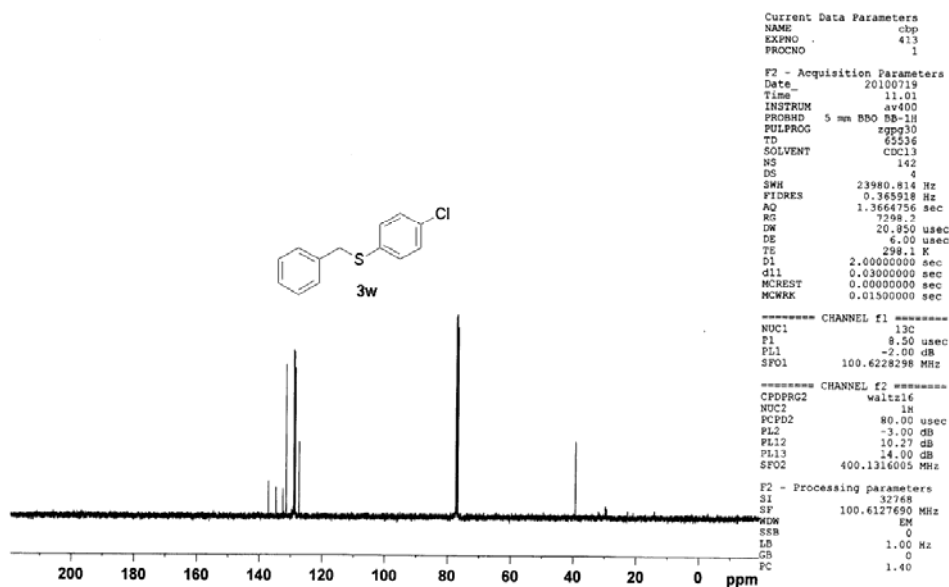
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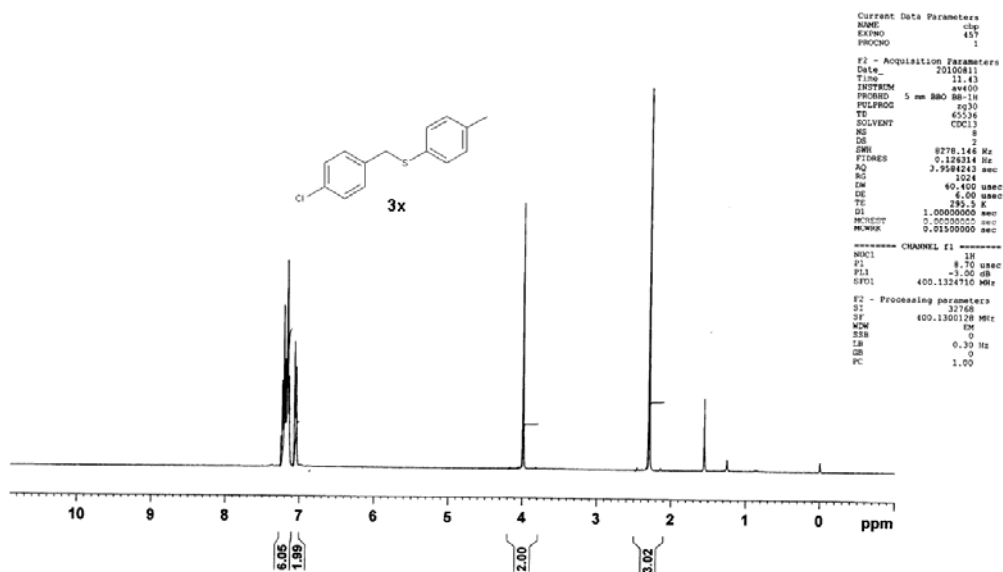
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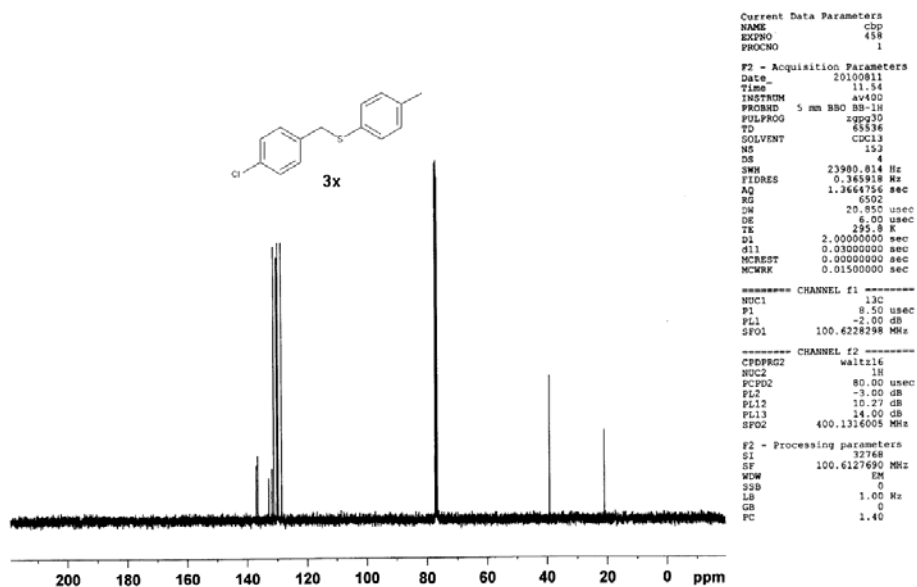
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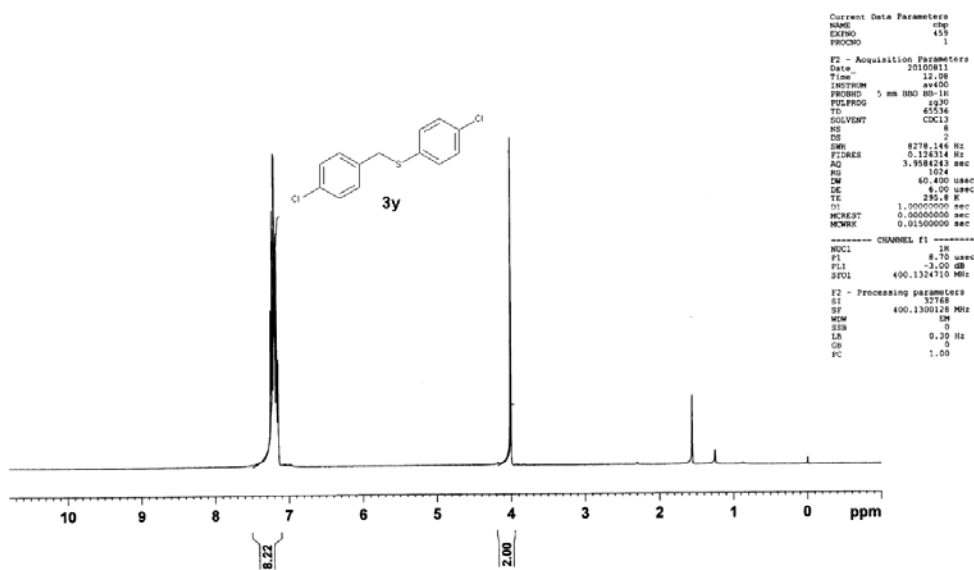
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1008-5-2



100805-3



100805-3

