Sodium sulfate-Hydrogen peroxide-Sodium chloride adduct: Regioselective Oxidation Protocol for, Oxidative bromination, iodination and temperature dependent selective oxidation of sulfide to sulfoxide and sulfones

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Supporting Information

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Experimental

General

All the reagent grade chemicals were purchased from sigma Aldrich, Sd fine, Alfa Aesar, and were used as received. Progress of the reactions were monitored using commercially available Thin-Layer Chromatography (TLC) plates of silica gel 60 F-254. The synthesized products were characterized using ^{1}HNMR. ^{1}H spectra were recorded on Agilent spectrometer at 500 MHz using $CDCl_3$-d and DMSO-d^6 as solvents. The chemical shifts are expressed in parts per million (ppm) and tetramethylsilane (TMS) was used as an internal reference.

Procedure for oxidative bromination and iodination of Aniline:

In 50 ml Round bottom flask, aniline **1a** (1.07 mmol) was added to acetic acid (3mL) at room temperature. Then potassium bromide/ potassium iodide (1.07 mmol) was added followed by the step wise addition of

adduct (1.07 mmol) at room temperature and stirred the reaction mass at 50-52°C for an appropriate time. Progress of the reaction was monitored by thin layer chromatography. After completion of reaction, the resulting reaction mixture was diluted with water, quenched with sodium bicarbonate and then extracted with ethyl acetate. The organic layers were washed with water and dried over Na_2SO_4 and the solvent was concentrated under vacuum. The residue was purified by column chromatography using hexane: ethyl acetate as eluent.

General procedure for the synthesis of sulfoxide and sulfone:

In 50 ml round bottom flask, methyl phenyl sulfide **4a** (0.833 mmol) was added to acetic acid (3mL) then $4Na_2SO_4.2H_2O_2.NaCl$ (3 equiv.) adduct was added slowly at room temperature, then reaction mass was heated at 50°C for sulfoxide synthesis and at 75°C for sulfone synthesis. The reaction was monitored by thin layer chromatography.After completion of reaction, the resulting reaction mixture was diluted with water, quenched with sodium bicarbonate and then extracted with ethyl acetate. The organic layer was washed with water and dried over Na_2SO_4, and the solvent was concentrated under vacuum. The residue was purified by column chromatography using hexane: ethyl acetate as eluent.

Spectroscopic data

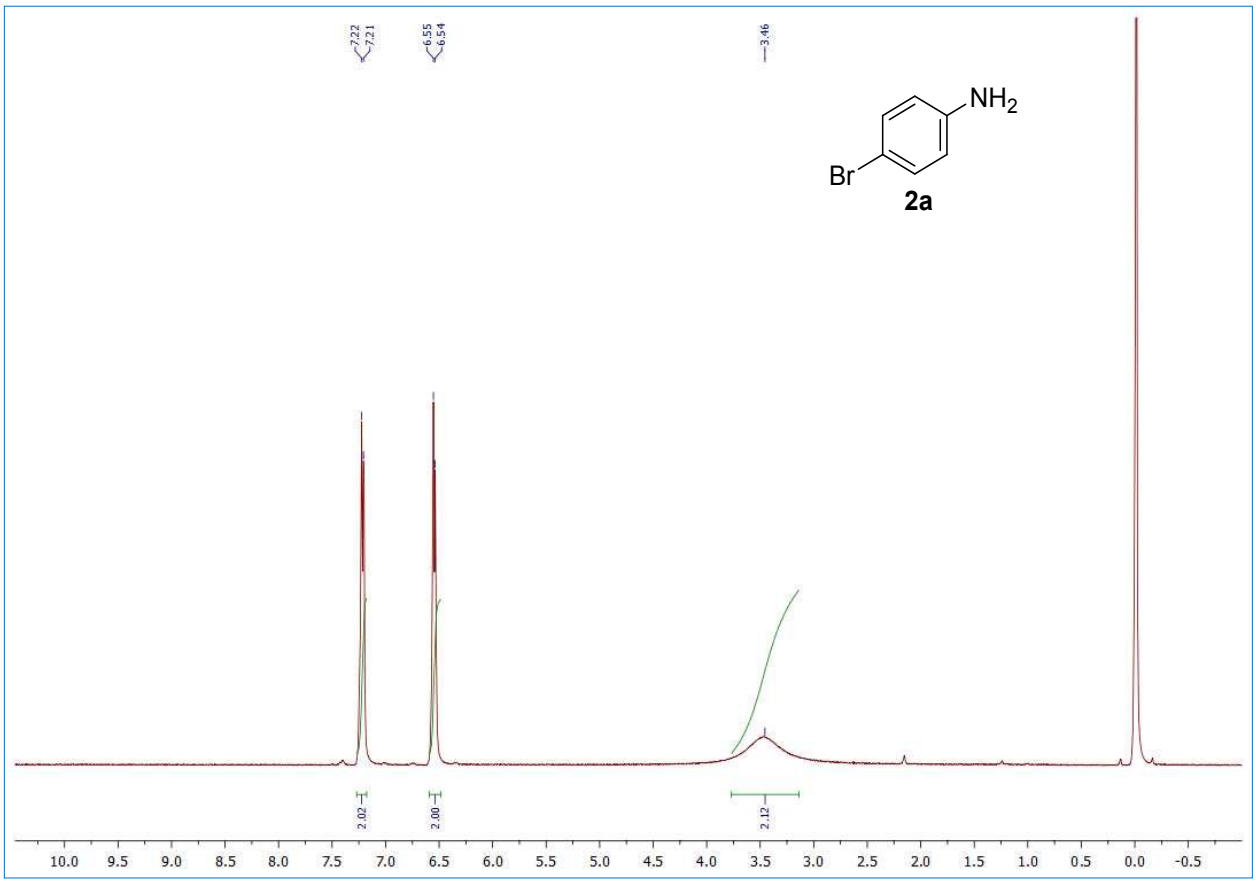
1. **4-bromoaniline**[1] **(2a):** White to light yellow solid; yield: 90%; mp 62-64°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 6.7 Hz, 2H), 6.55 (d, *J* = 6.7 Hz, 2H), 3.46 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.40, 131.99, 116.71, 110.17.
2. **4-bromo-2-methylaniline**[2] **(2b):** off white solid; yield: 88%; mp 56-58°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (s, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 3.01 (s, 2H), 2.12 (s, 4H).
3. **4-bromo-2-chloroaniline**[3] **(2e):** off white solid; yield: 86%; mp 70-72°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 4.04 (s, 2H).
4. **2, 4-dibromoaniline**[4] **(2g):** white solid; yield: 91%; mp 78-80°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.18 (d, *J* = 8.3 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 4.08 (s, 2H).
5. **2, 4, 6-tribromoaniline**[5] **(4)**: Brown to whitish solid; yield: 87%; mp 122-124°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 2H), 4.55 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.62, 141.13, 133.70, 108.61.

6. **4-bromo-2-nitroaniline**[2] **(2i):** orange solid; yield: 94%; mp 110-112°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 1.9 Hz, 1H), 7.40 (dd, *J* = 8.8, 1.9 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 6.11 (s, 2H).
7. **2-bromo-4-nitroaniline**[6] **(2k):** yellow solid; yield: 87%; mp 98-100°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 6.73 (d, *J* = 8.8 Hz, 1H), 4.82 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.60, 129.07, 124.84, 113.16, 106.97.
8. **4-iodoaniline**[7] **(3a) :** off white solid; yield: 90%; mp 60-62°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.0 Hz, 2H), 6.46 (d, *J* = 6.9 Hz, 2H), 3.79 – 3.44 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.03, 137.89, 117.28, 79.38.
9. **4-iodo-2-methylaniline**[8] **(3b) :** off white solid; yield: 88%; mp 88-90°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.27 (d, *J* = 8.5 Hz, 1H), 6.43 (d, *J* = 8.0 Hz, 1H), 3.59 (s, 2H), 2.09 (s, 3H).
10. **2-iodo-4-methylaniline**[9] **(3d):** Orange crystalline solid; yield: 83%; mp 45-47°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.92, 143.48, 140.15, 129.89, 117.76, 103.60, 20.78.
11. **2-chloro-4-iodoaniline**[10] **(3e):** off white solid; yield: 89 %; mp 68-70°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.49 (m, 1H), 7.30 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 4.04 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.69, 137.13, 136.29, 120.20, 117.41, 77.95.
12. **4-iodo-2-nitroaniline**[11] **(3i):** orange solid; yield: 95%; mp 118-120°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.7 Hz, 1H), 6.09 (s, 2H). ^{13}C NMR (126 MHz, cdcl3) δ 143.98, 143.72, 134.30, 133.08, 120.57, 75.90.
13. **2-iodo-4-nitroaniline**[12] **(3j):** yellow solid; yield: 86%; mp 102-104°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.04 (d, *J* = 8.9 Hz, 1H), 6.68 (d, *J* = 8.9 Hz, 1H), 4.84 (s, 2H).
14. **(Methylsulfinyl) benzene**[13] **(5a):** Yellow liquid; yield: 91%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 2H), 7.44 – 7.37 (m, 3H), 2.62 (s, 3H).

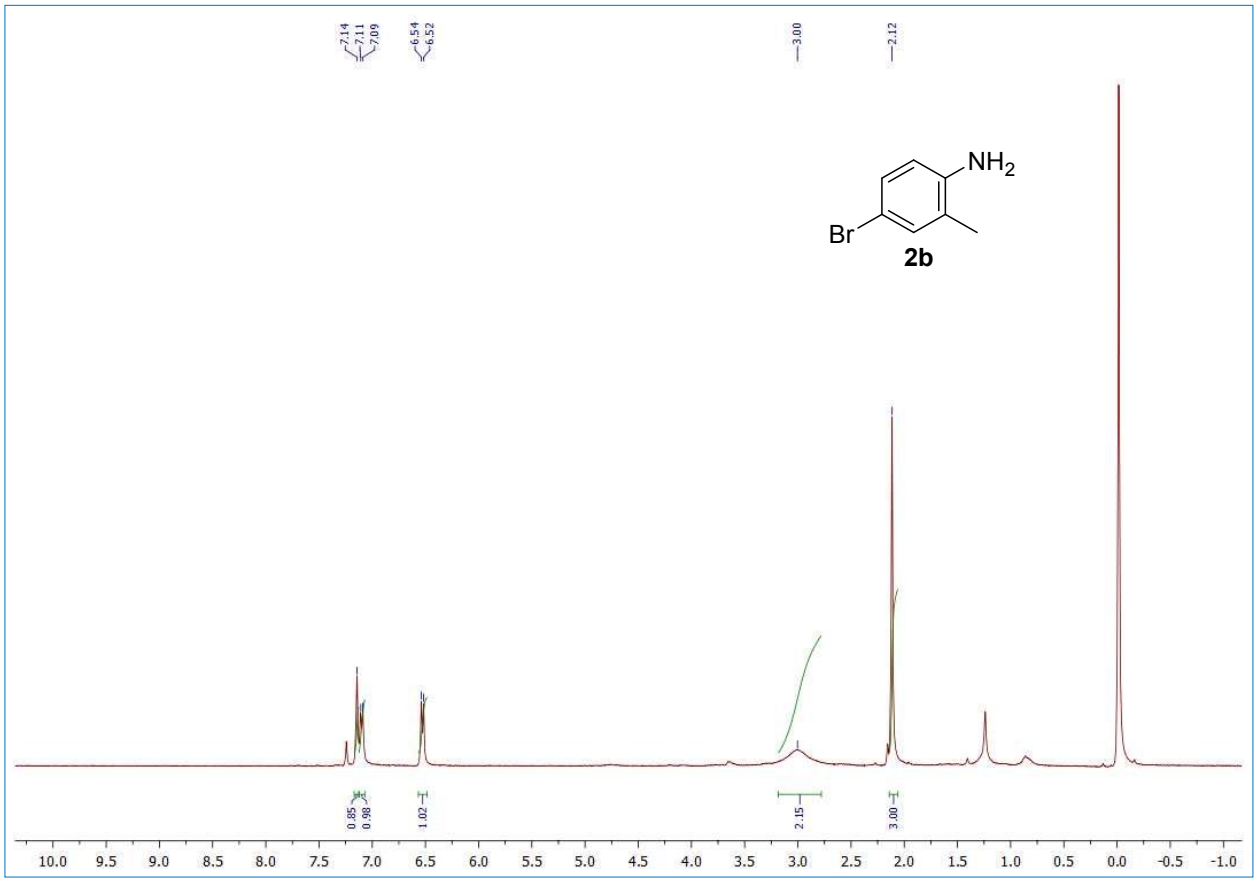
15. **(methylsulfonyl)benzene**[13] **(6a):** Colourless solid; yield: 93%; mp 88-90°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dt, *J* = 8.5, 1.7 Hz, 2H), 7.67 – 7.62 (m, 1H), 7.59 – 7.54 (m, 2H), 3.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.54, 133.69, 129.36, 127.31, 44.47.
16. **Sulfinyldibenzene**[14] **(5b):** white solid; yield: 87%; mp 68-70°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, *J* = 7.0, 1.2 Hz, 5H), 7.52 – 7.41 (m, 6H).
17. **2-(benzylsulfonyl) acetic acid**[15] **(6c):** white solid; yield: 87%; mp 138-140°C; ^{1}H NMR (500 MHz, DMSO) δ 7.45 – 7.36 (m, 5H), 4.62 (s, 2H), 4.15 (s, 2H).
18. **10-butyl-10*H*-phenothiazine 5,5-dioxide**[13] **(6f) :** white solid; yield: 88%; mp 148-150°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.9, 1.3 Hz, 2H), 7.62 (dd, *J* = 11.6, 4.2 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.27 (dd, *J* = 8.1, 7.0 Hz, 2H), 4.20 – 4.14 (m, 2H), 1.92 (dt, *J* = 15.5, 7.7 Hz, 2H), 1.56 – 1.46 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H).
19. **10-hexyl-10*H*-phenothiazine-3-carbaldehyde 5-oxide**[13] **(5g) :** white solid; yield: 85%; mp 138-140°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.44 (d, *J* = 2.0 Hz, 1H), 8.14 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.99 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.69 (ddd, *J* = 8.8, 7.3, 1.7 Hz, 1H), 7.49 (dd, *J* = 16.5, 7.9 Hz, 2H), 7.39 – 7.33 (m, 1H), 4.32 – 4.24 (m, 2H), 2.04 – 1.93 (m, 2H), 1.60 – 1.52 (m, 2H), 1.48 – 1.35 (m, 4H), 0.94 (t, *J* = 7.1 Hz, 3H).
20. **1-methoxy-4-(methylsulfinyl)benzene**[13] **(5h) :** Colourless oil; yield: 90%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 2H), 7.04 – 6.96 (m, 2H), 3.82 (s, 3H), 2.68 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.94, 136.39, 125.46, 114.83, 55.51, 43.90.
21. **methoxy-4-(methylsulfonyl)benzene**[16] **(6h) :** white solid; yield: 92%; mp 120-120°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.80 (m, 2H), 7.07 – 6.98 (m, 2H), 3.89 (s, *J* = 1.6 Hz, 3H), 3.03 (s, *J* = 1.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.67, 132.25, 129.53, 114.48, 55.70, 44.85.
22. **1-(methylsulfinyl)-4-nitrobenzene**[17] **(5i):** pale yellow solid; yield: 91%; mp 148-150°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 2.80 (s, 3H).
23. **1-(methylsulfonyl)-4-nitrobenzene**[18] **(6i):** pale yellow solid; yield: 93%; mp 138-140°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 1.7 Hz, 2H), 8.20 – 8.13 (m, 2H), 3.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.85, 145.92, 128.97, 124.63, 44.44.

4-bromoaniline (2a)

1.



4-bromo-2-methylaniline (2b)



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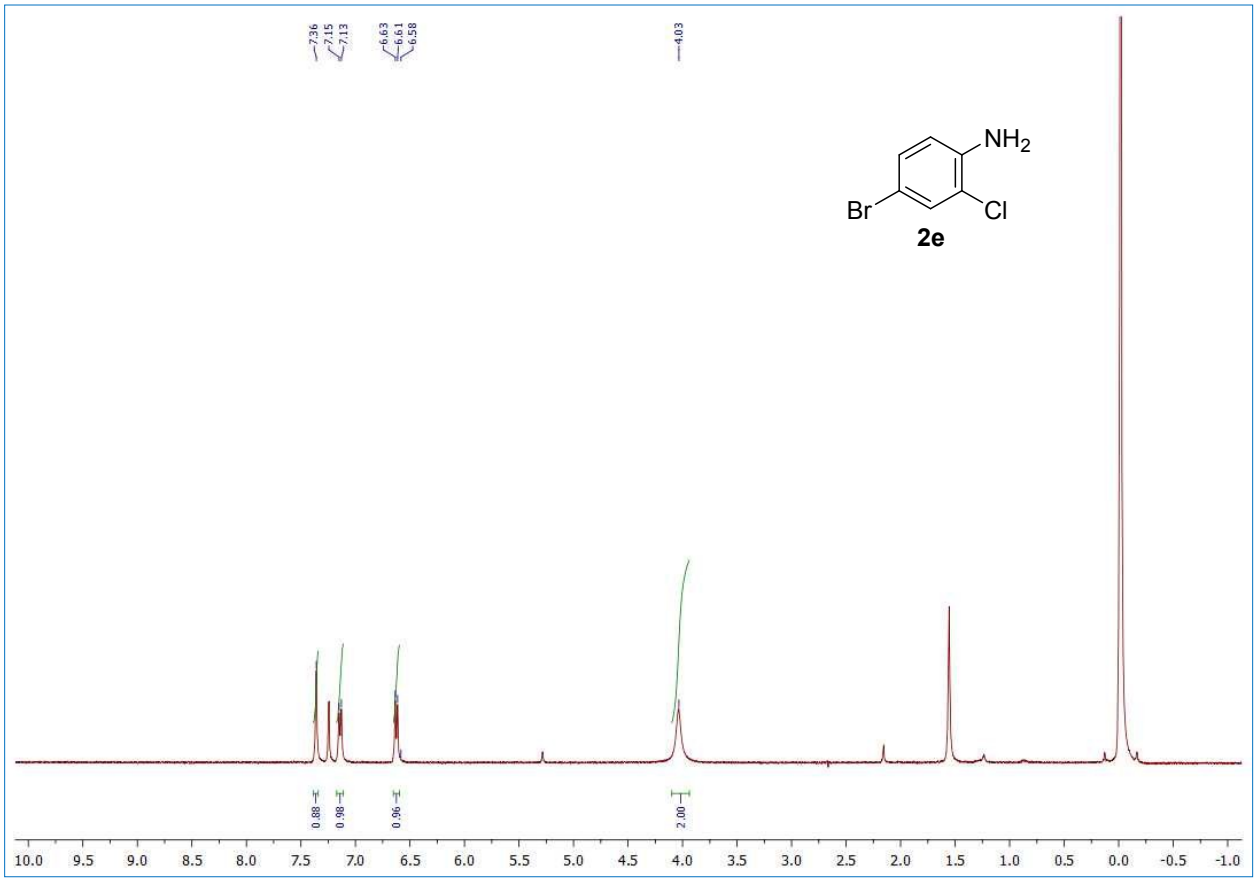
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6.63
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6.58
4.03
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Br
Cl
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0.96
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0

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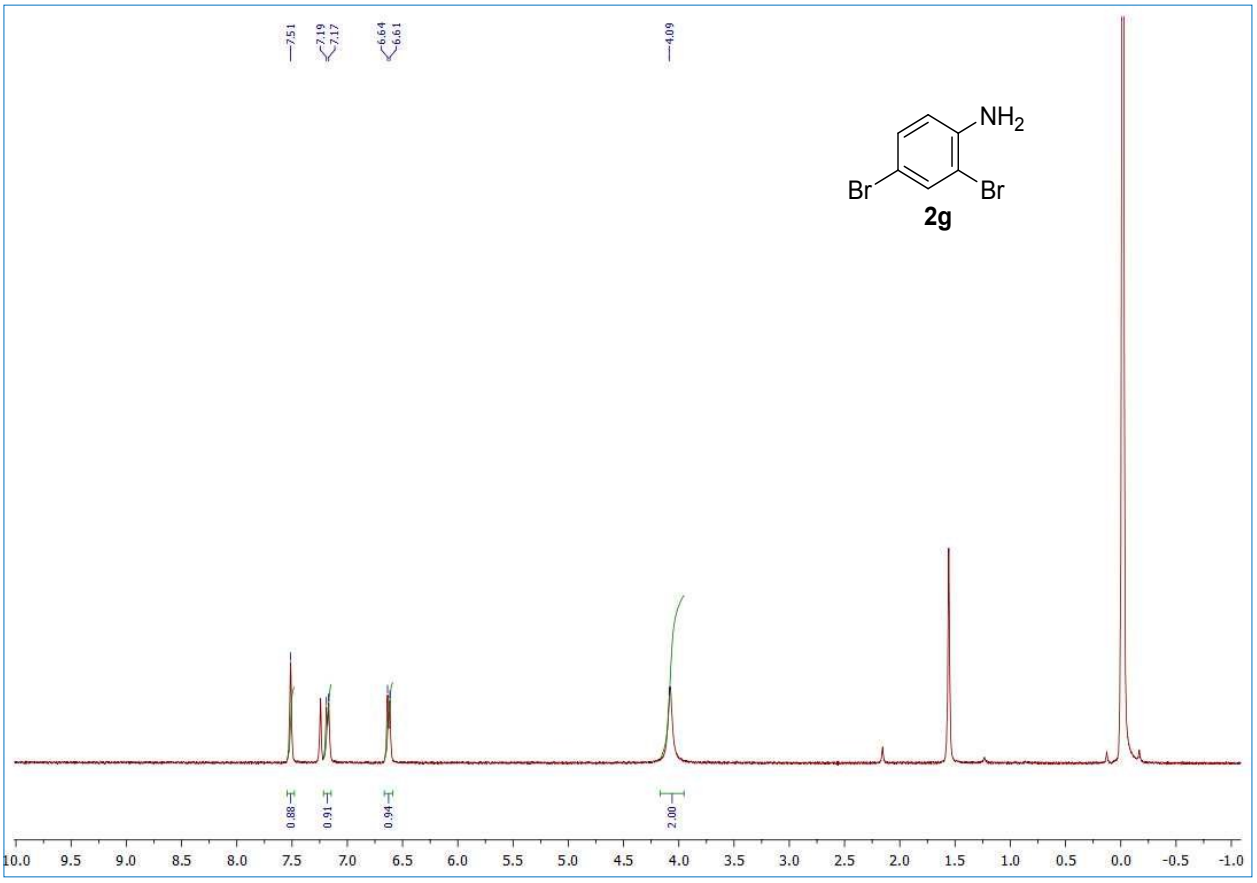

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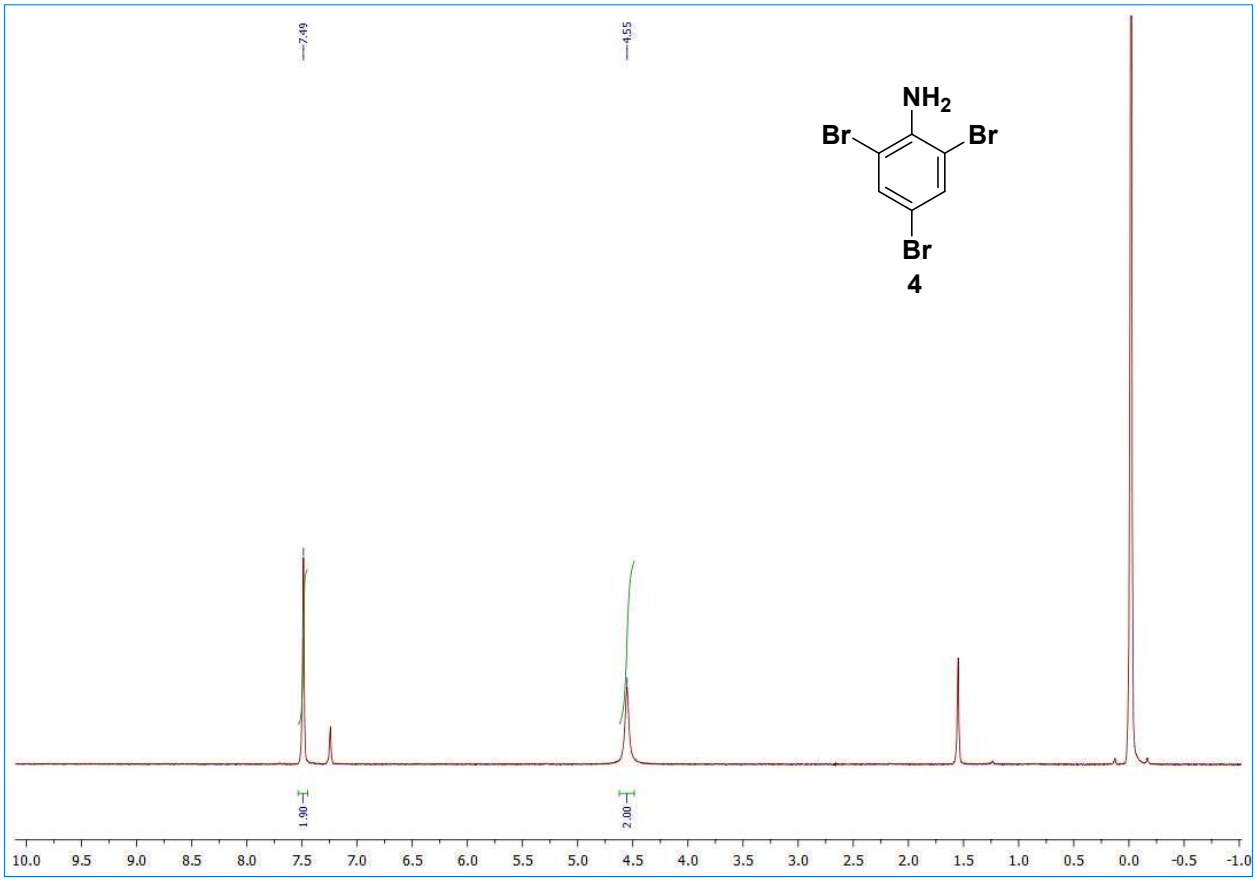

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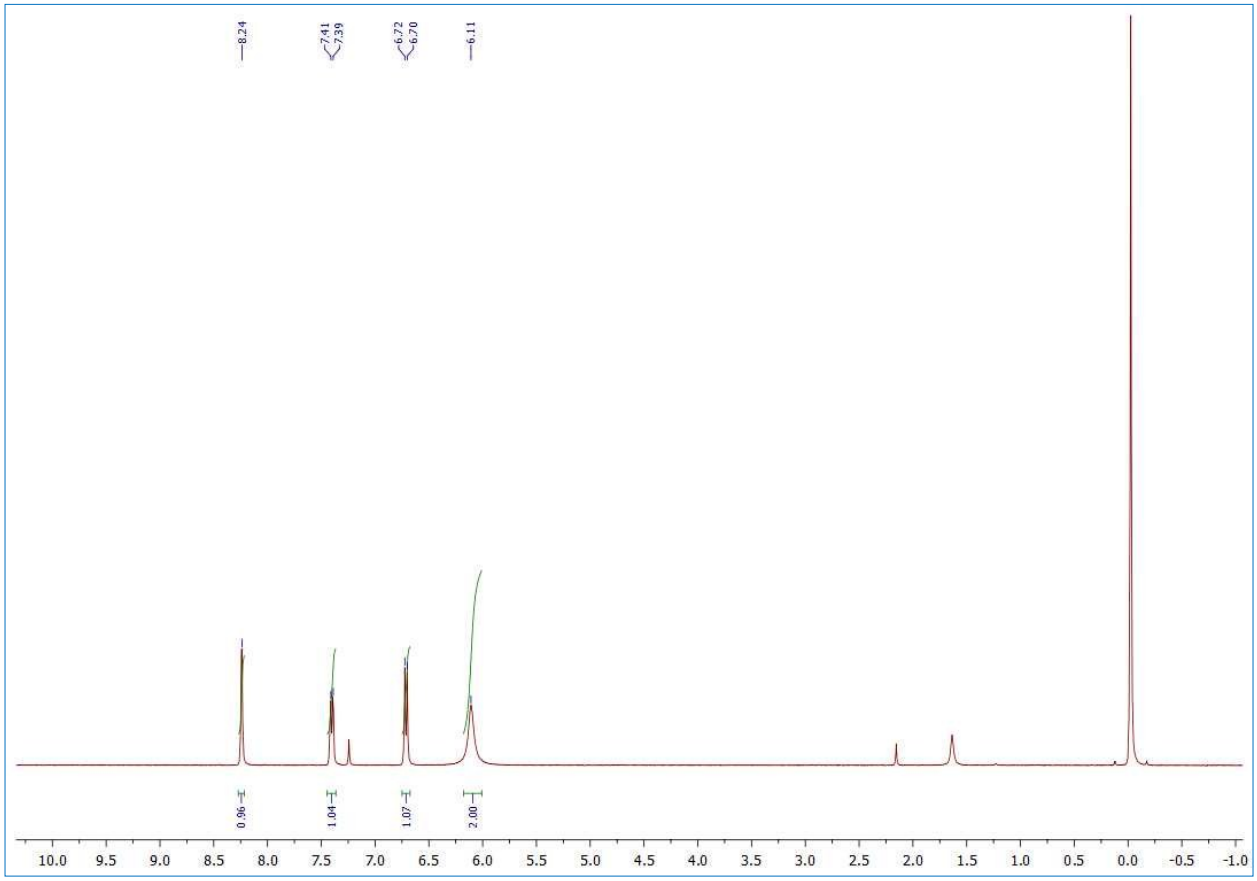

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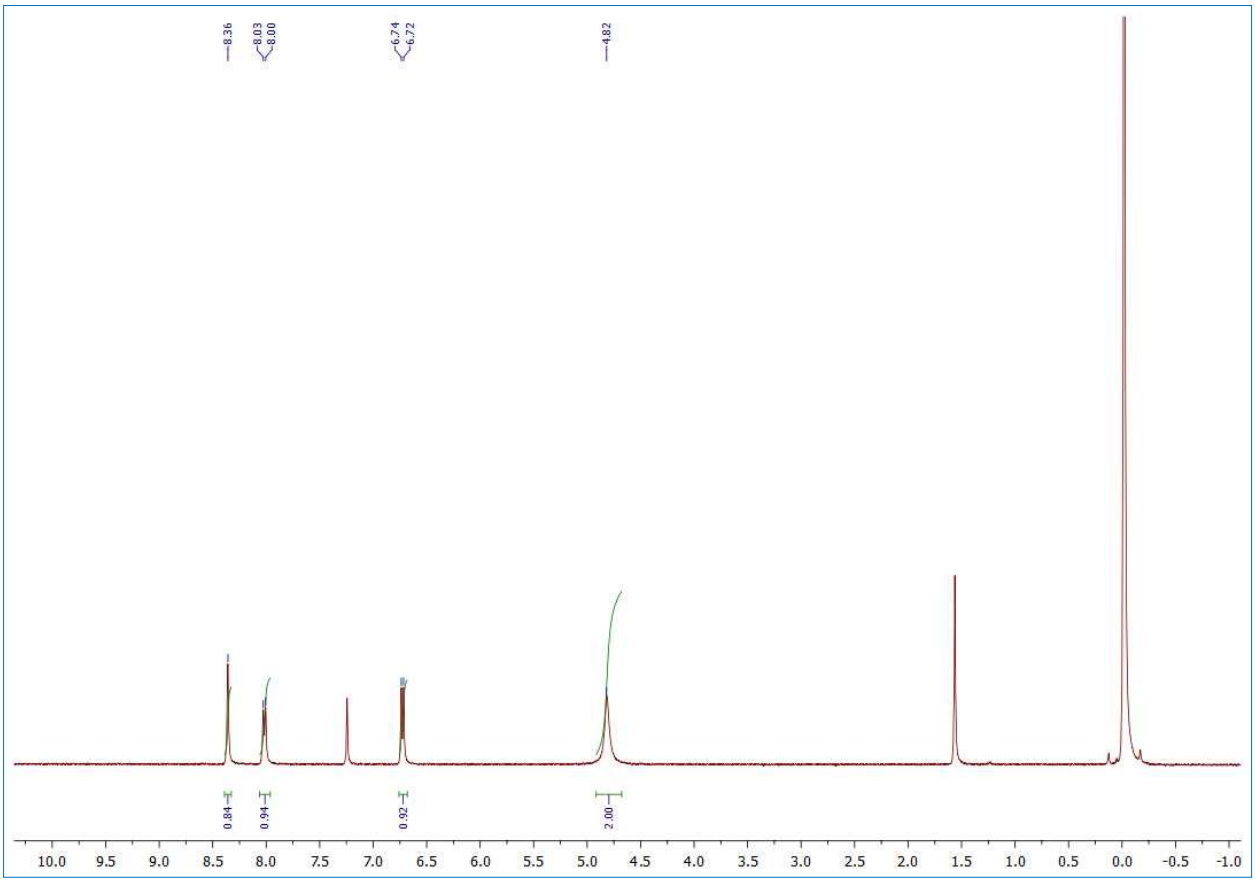

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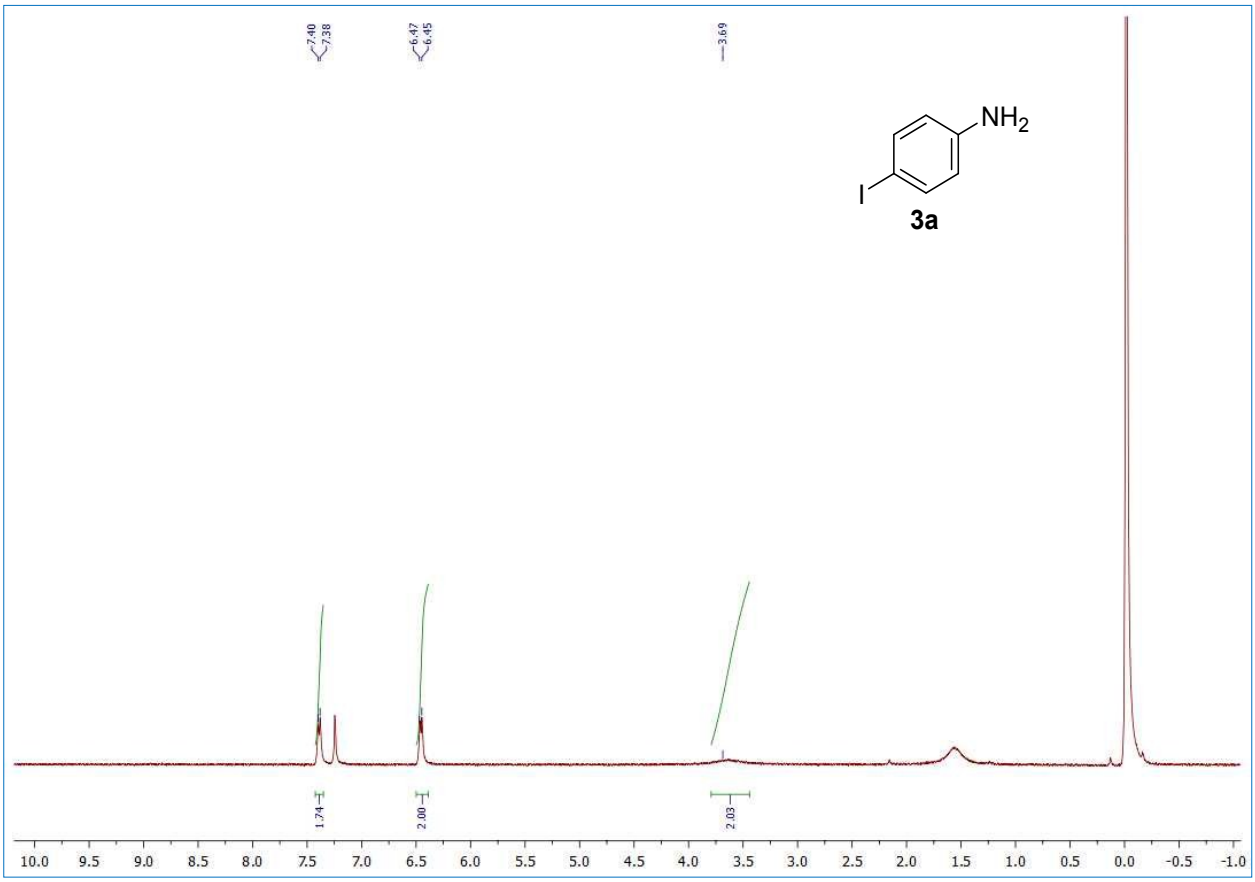

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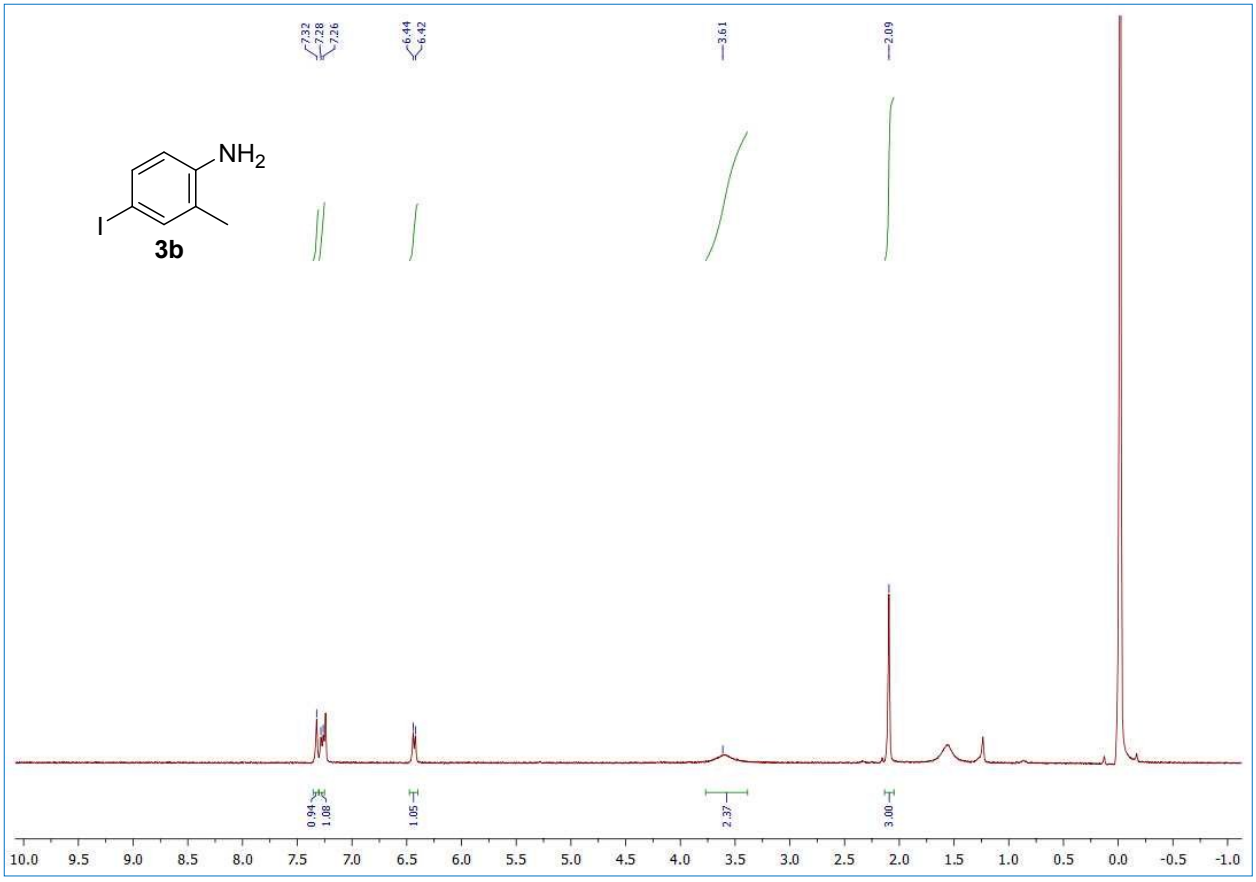

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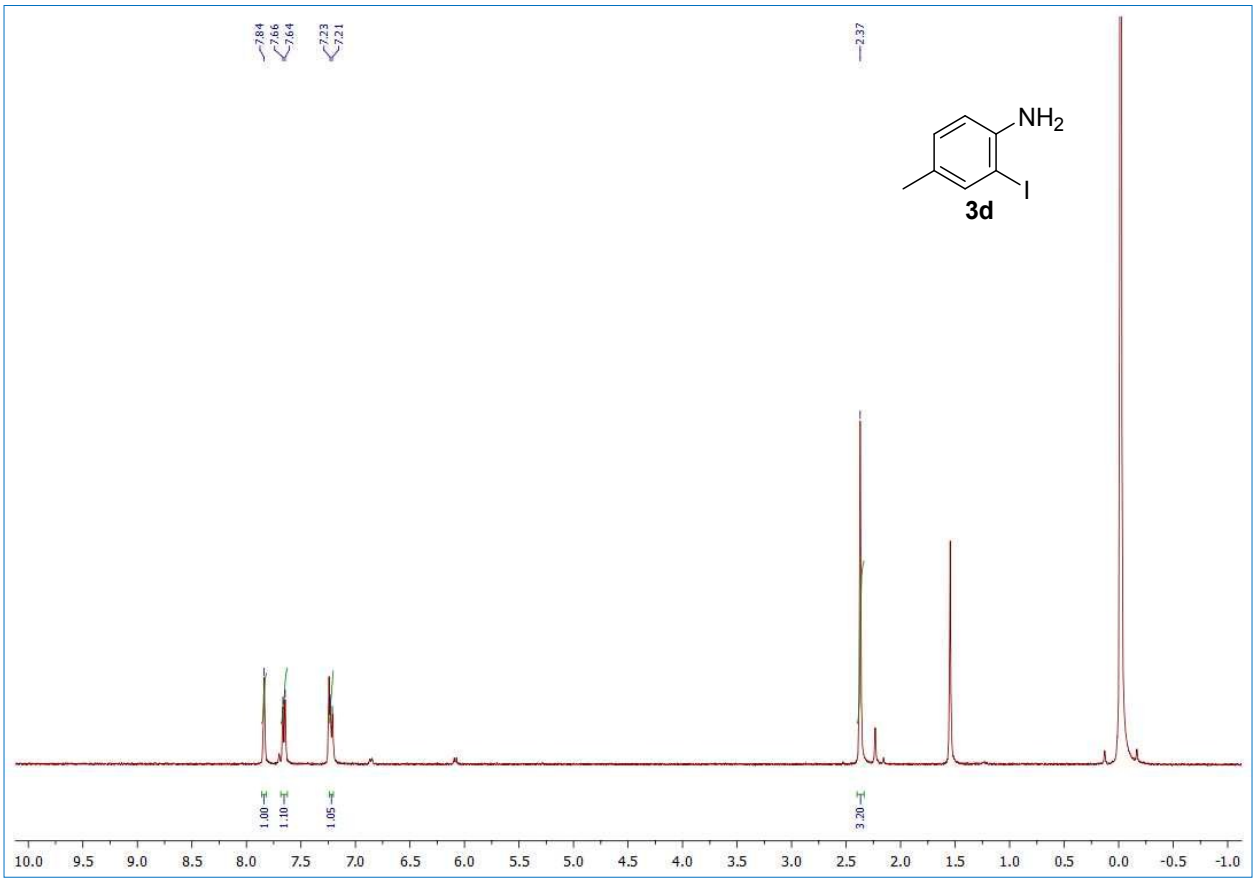

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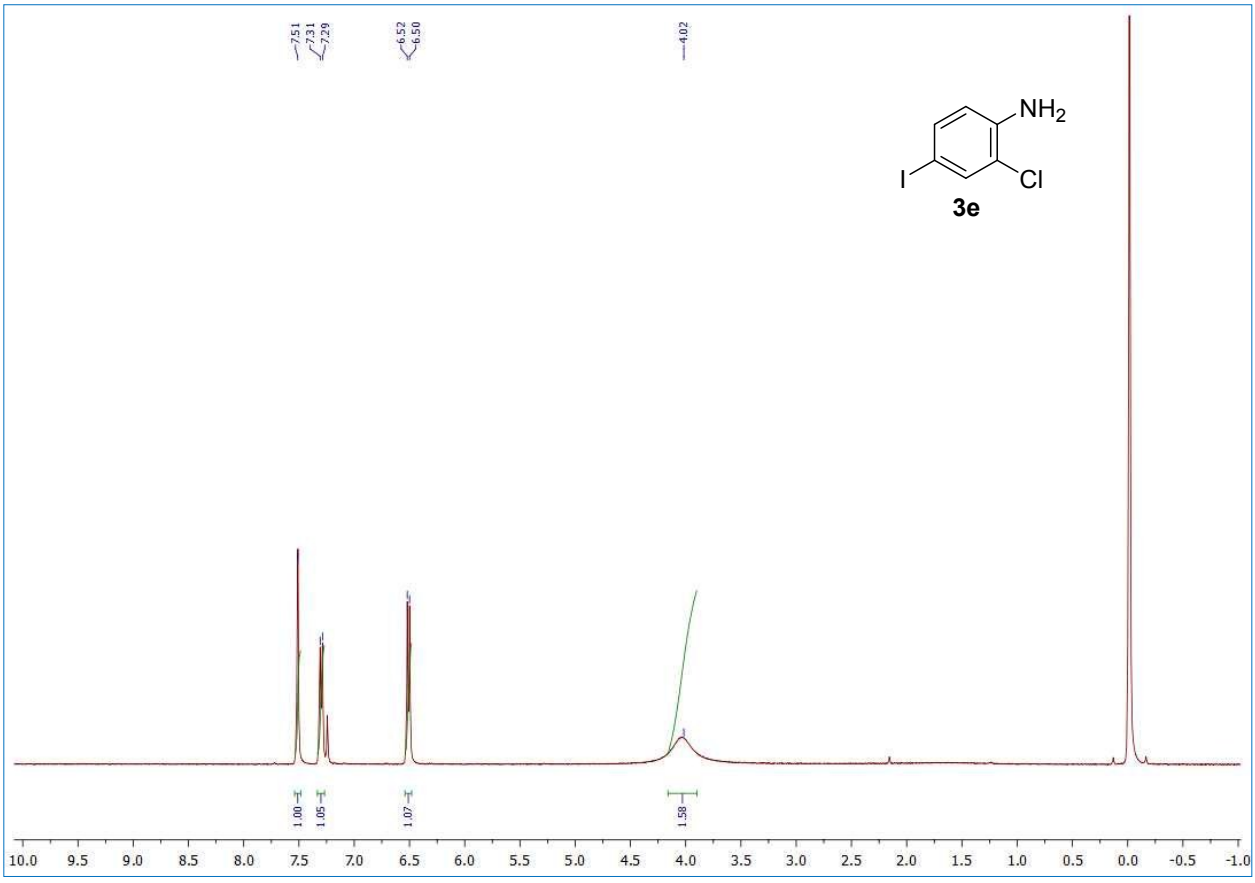

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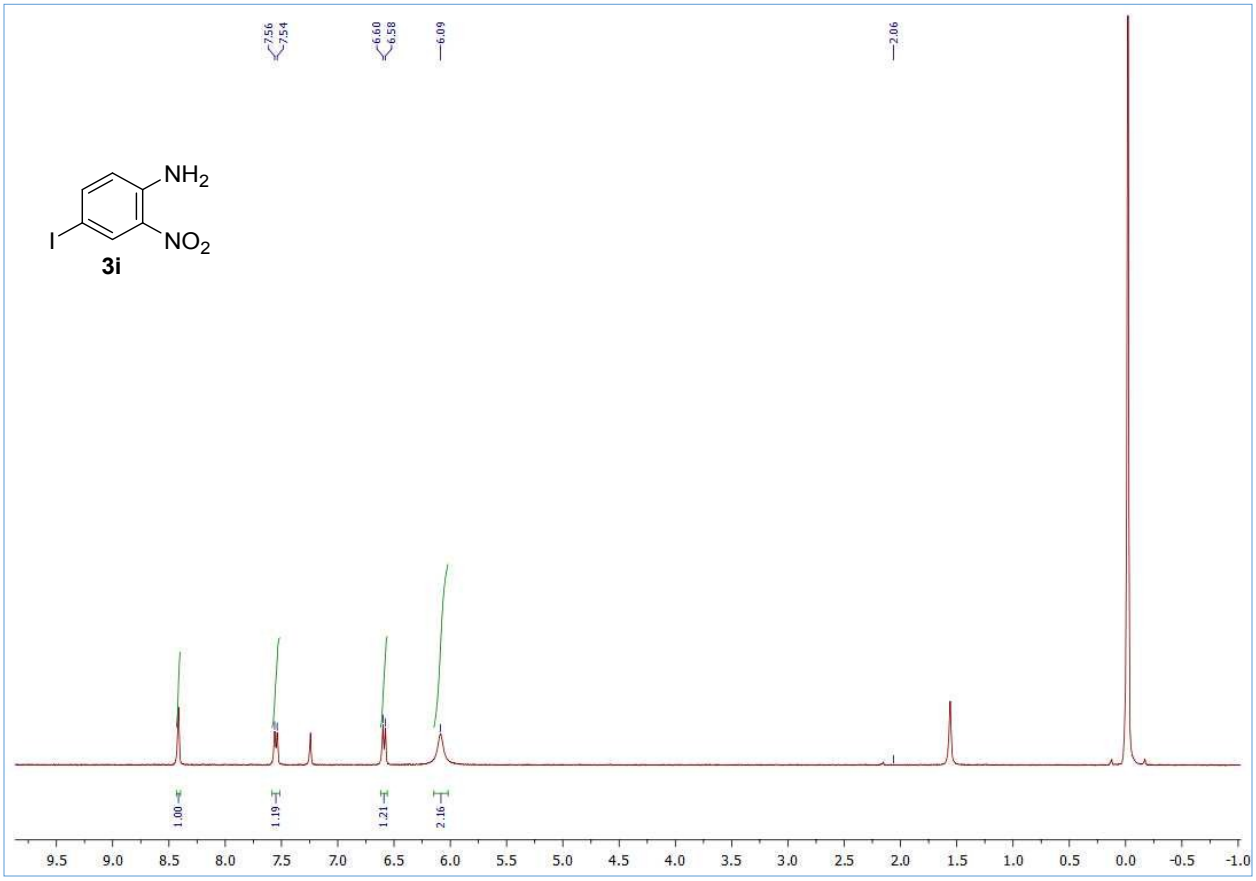

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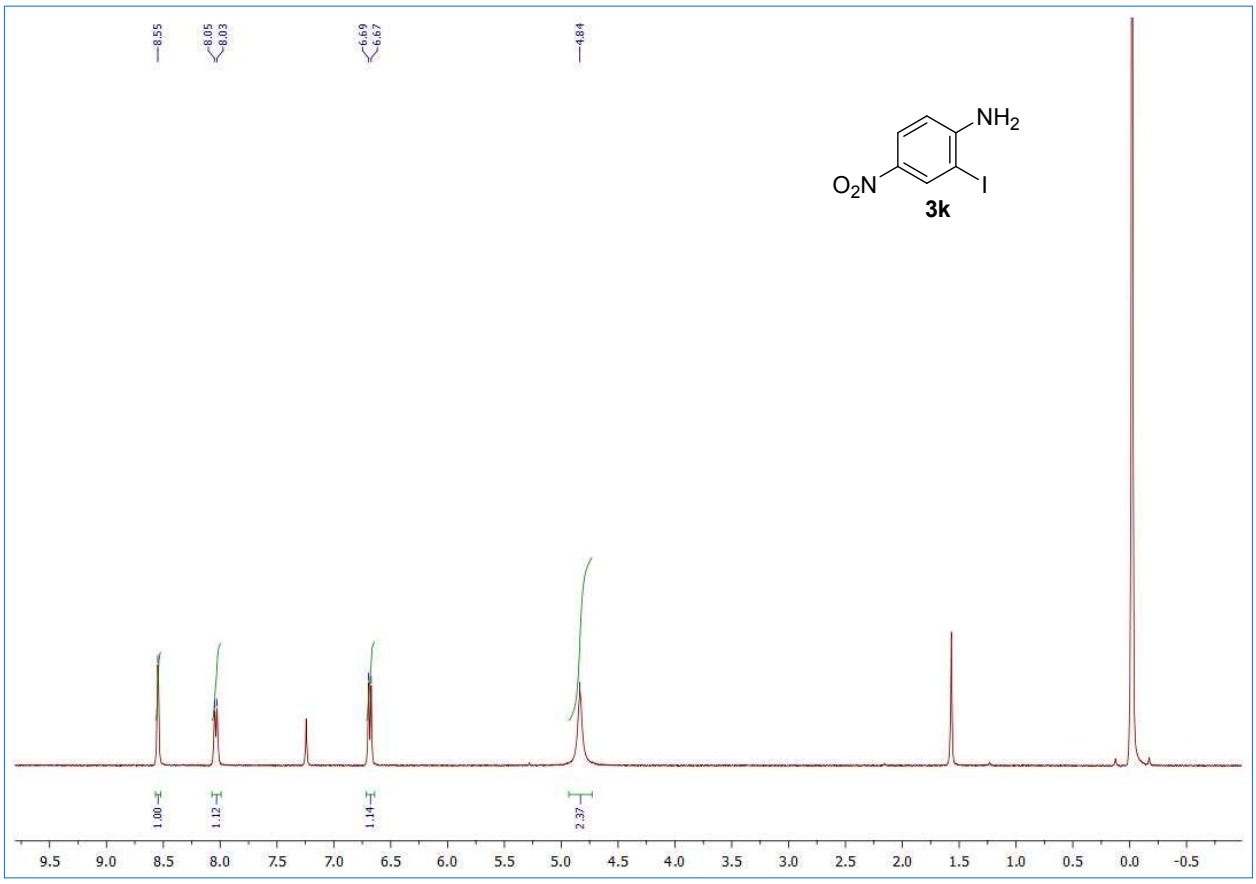
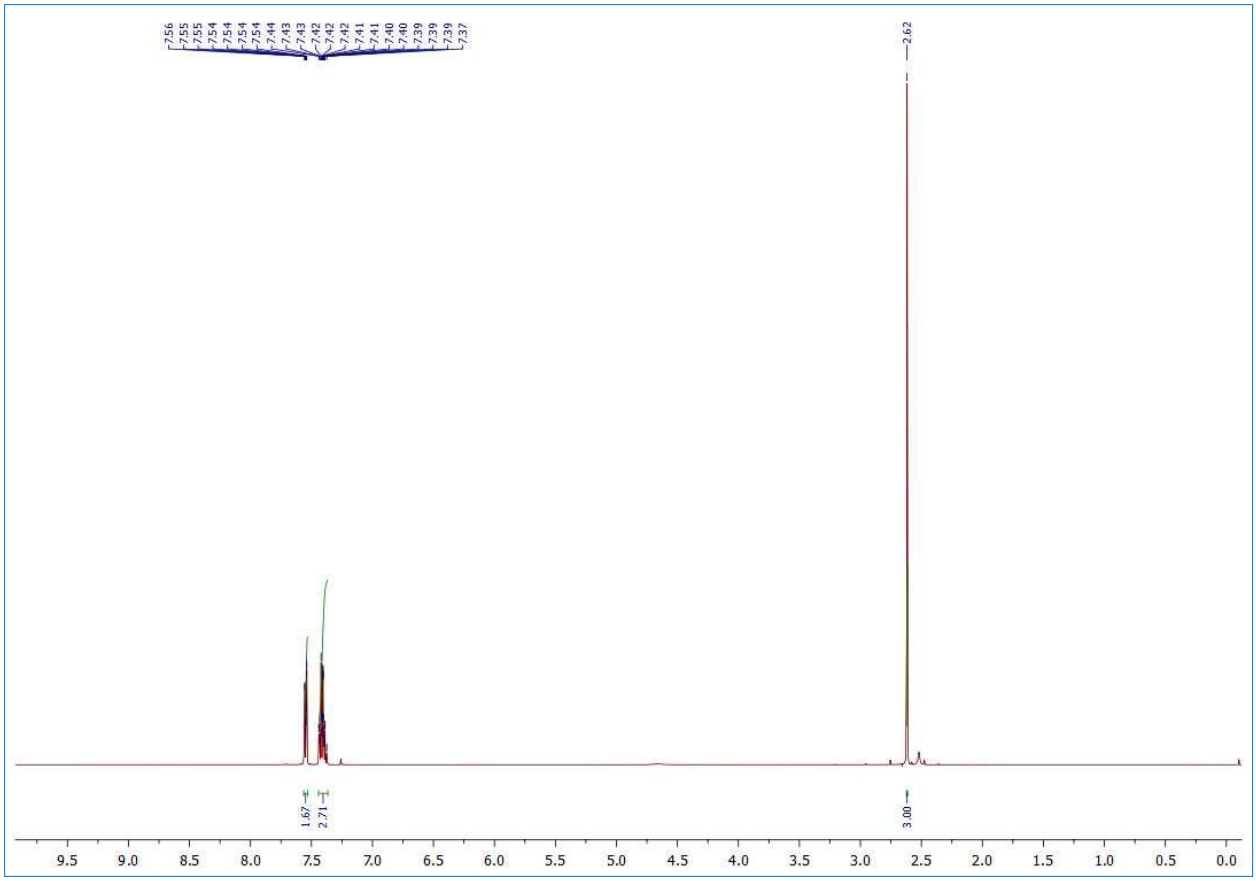


(Methylsulfinyl) benzene (5a):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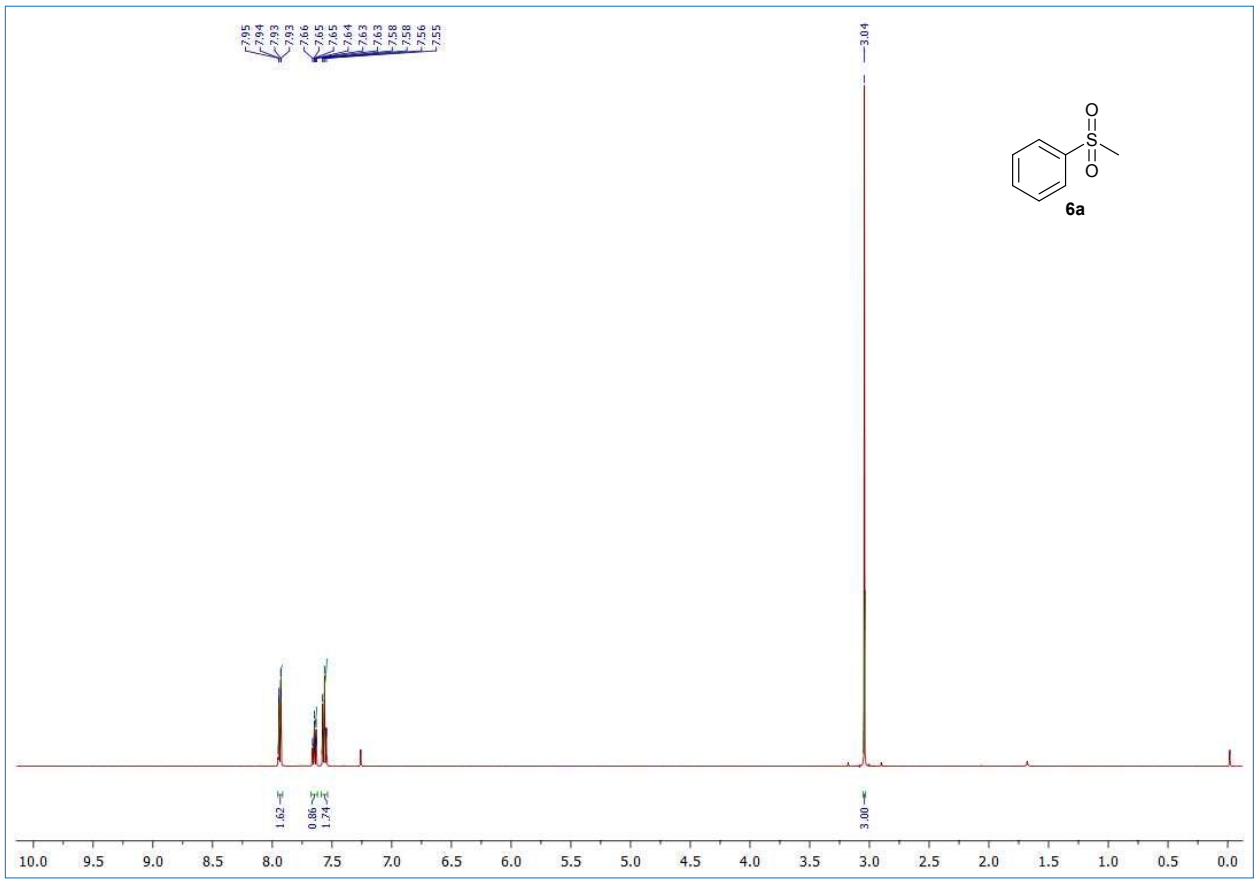
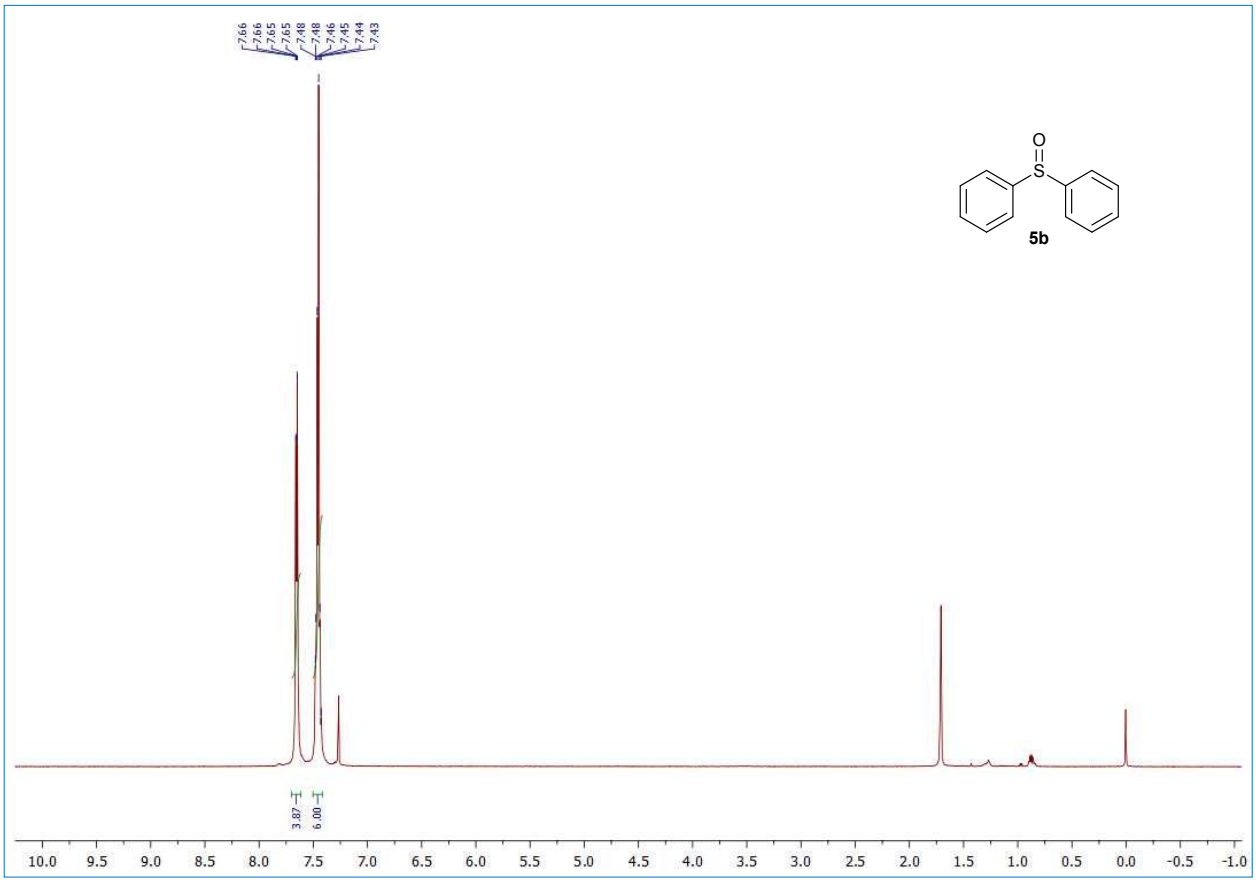
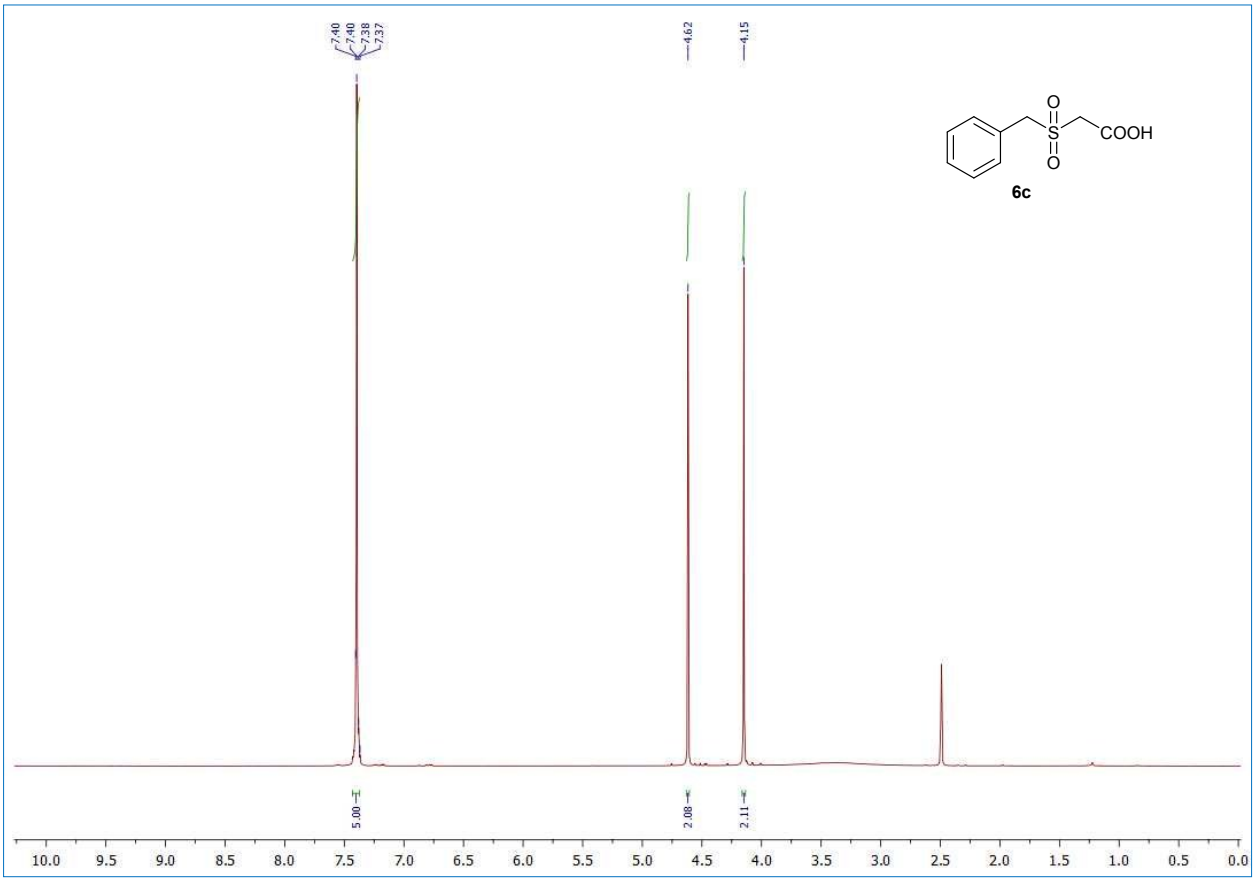
(methylsulfonyl)benzene (6a):



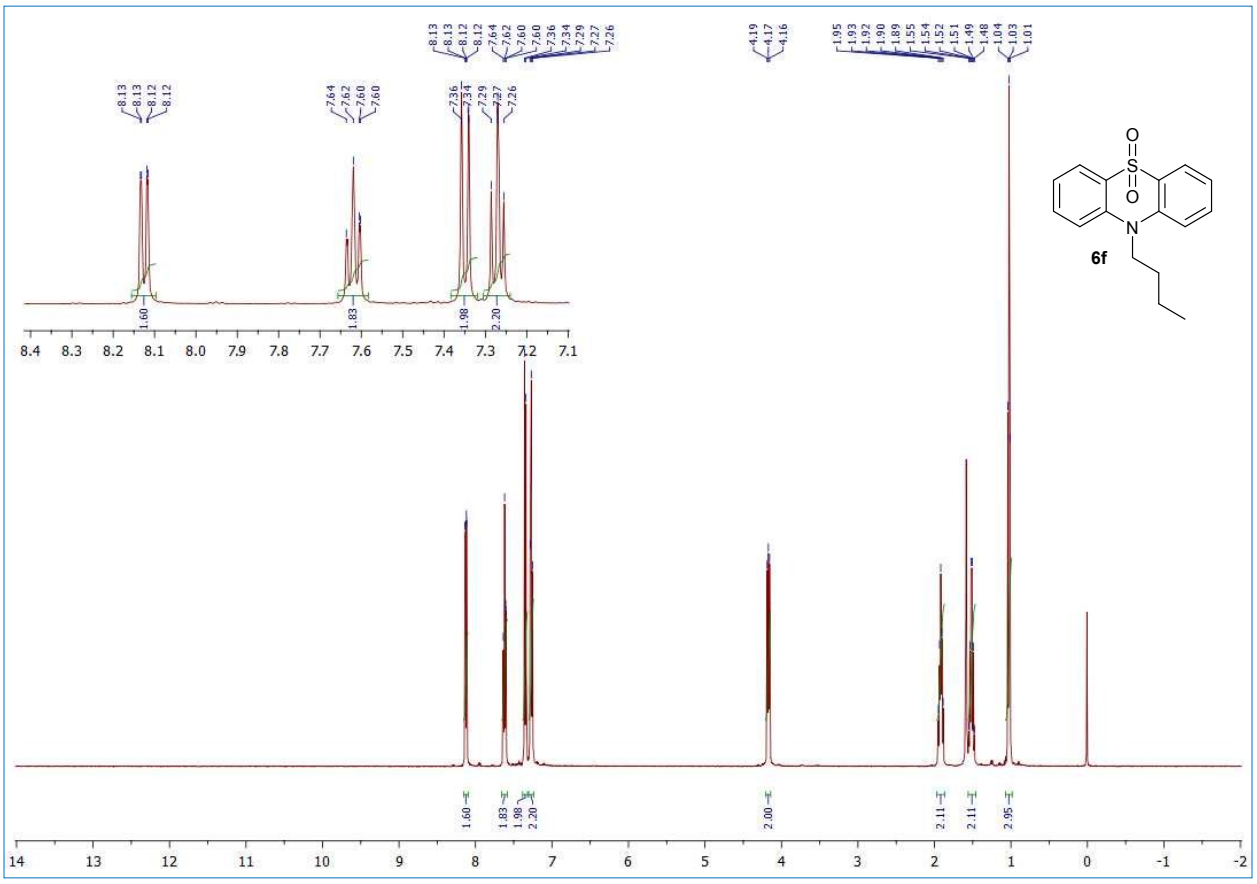
Sulfinyldibenzene (5b):



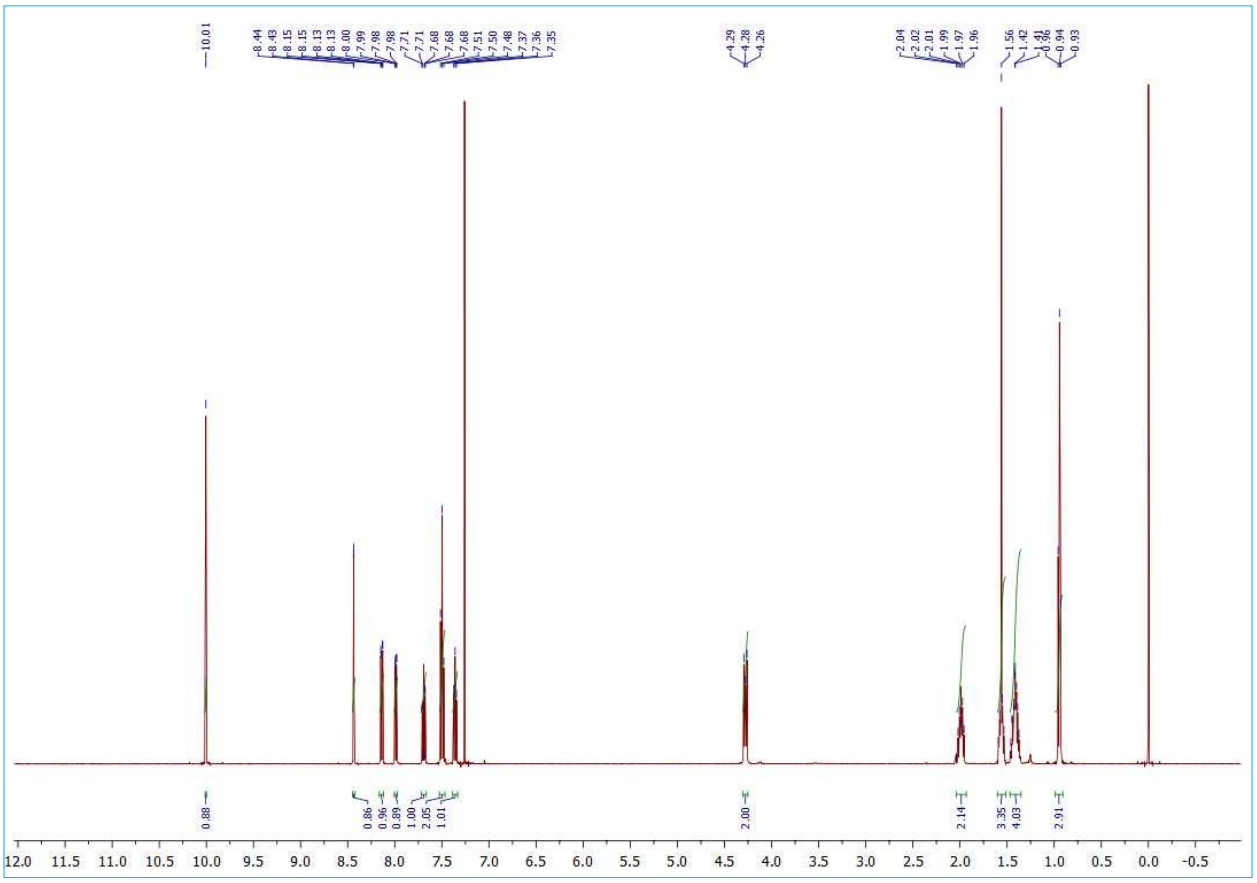
2-(benzylsulfonyl) acetic acid



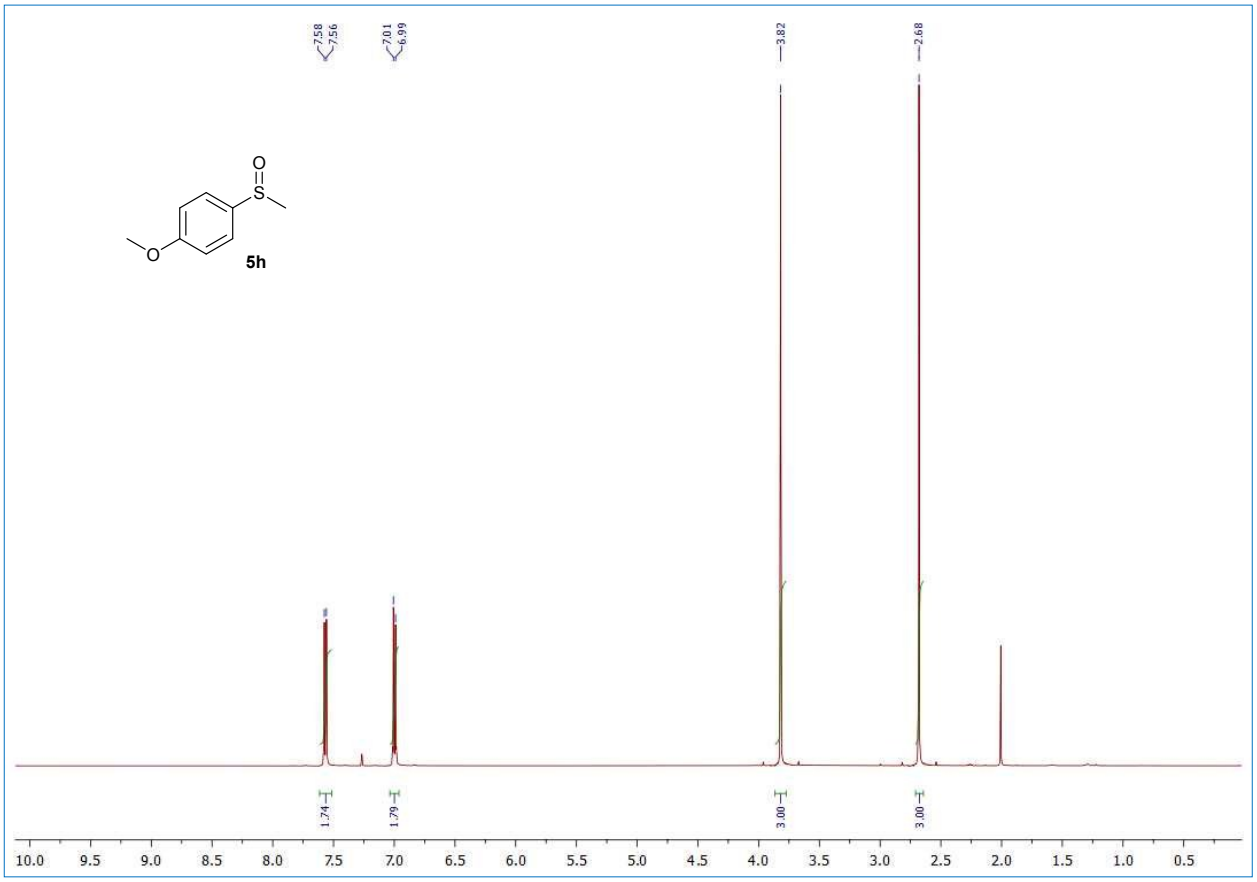
10-butyl-10*H*-phenothiazine 5,5-dioxide (6f) :



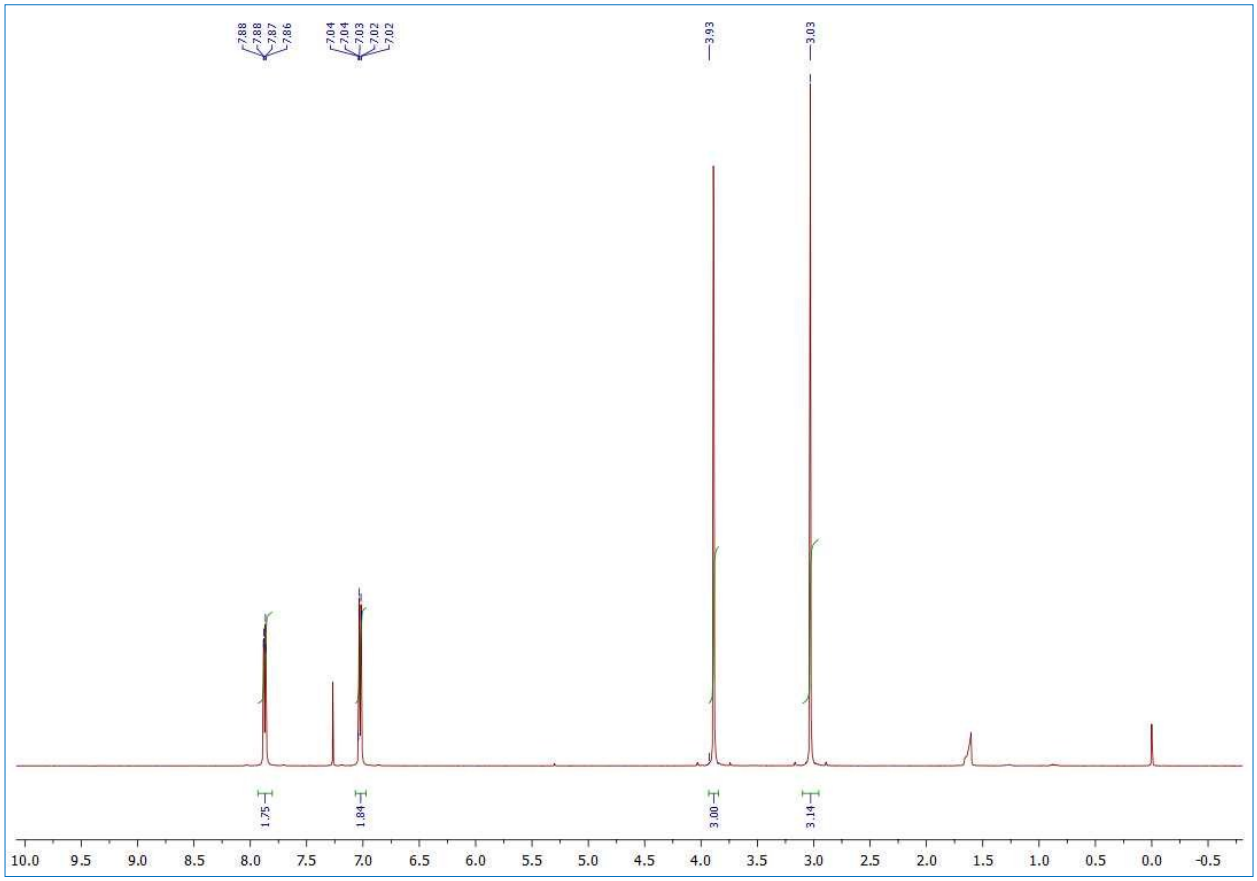
10-hexyl-10*H*-phenothiazine-3-carbaldehyde 5-oxide (5g) :



1-methoxy-4-(methylsulfinyl)benzene (5h) :



methoxy-4-(methylsulfonyl)benzene (6h) :



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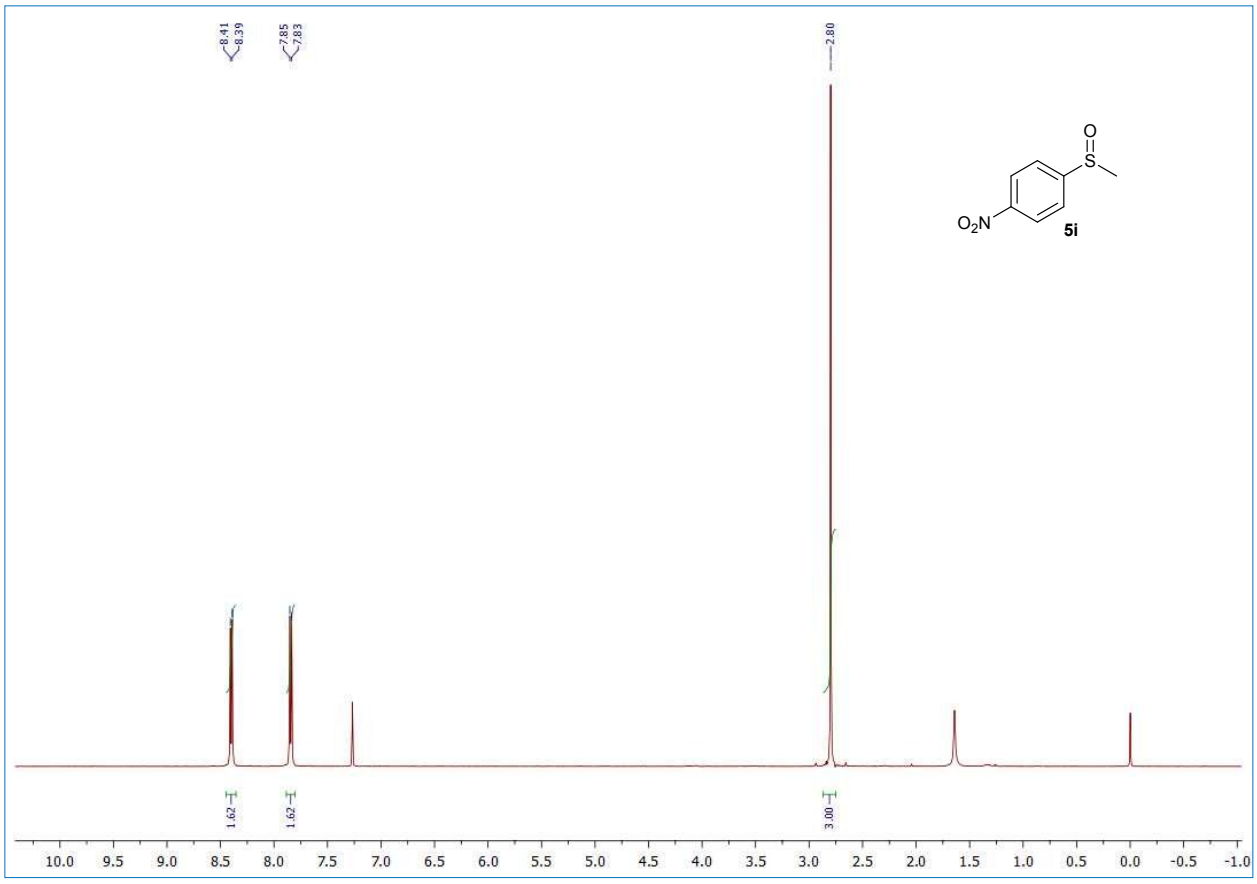

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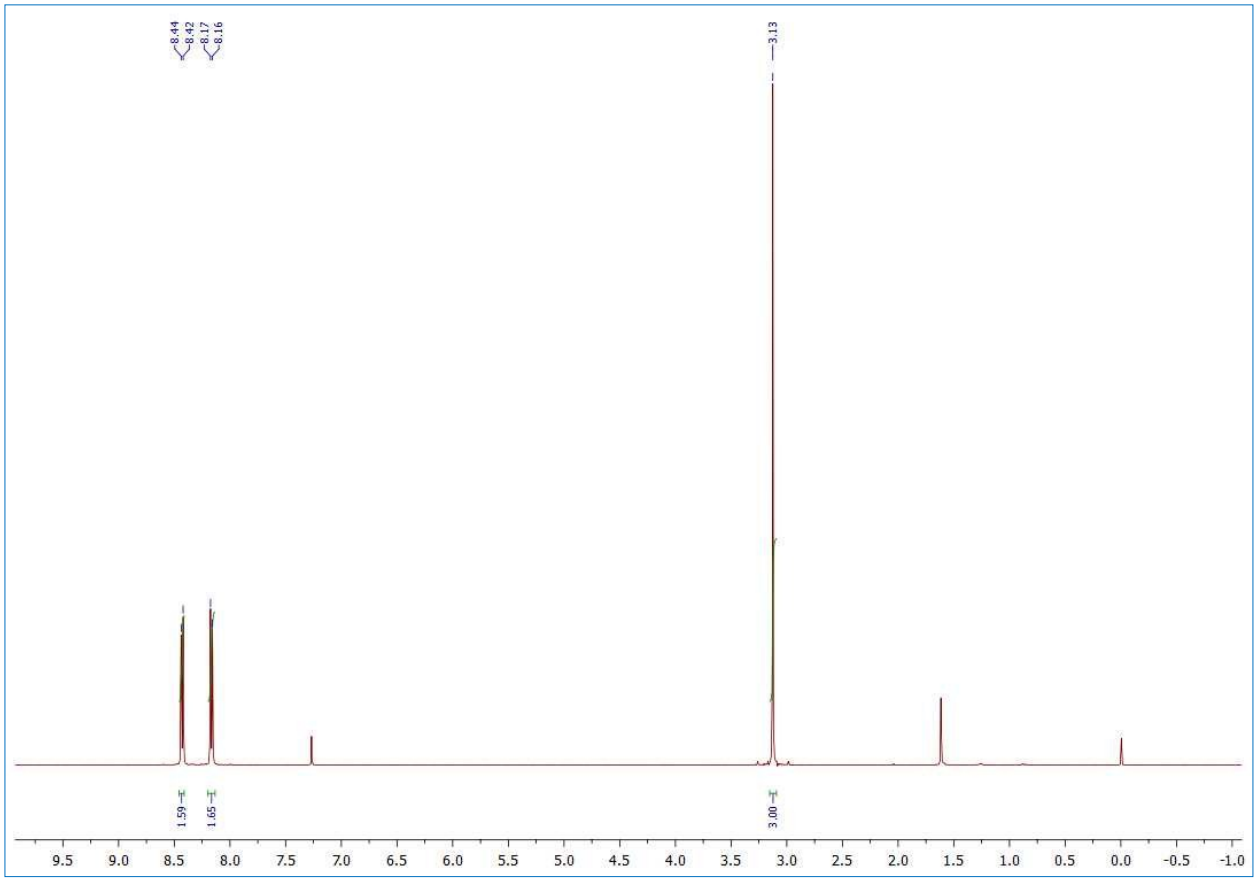
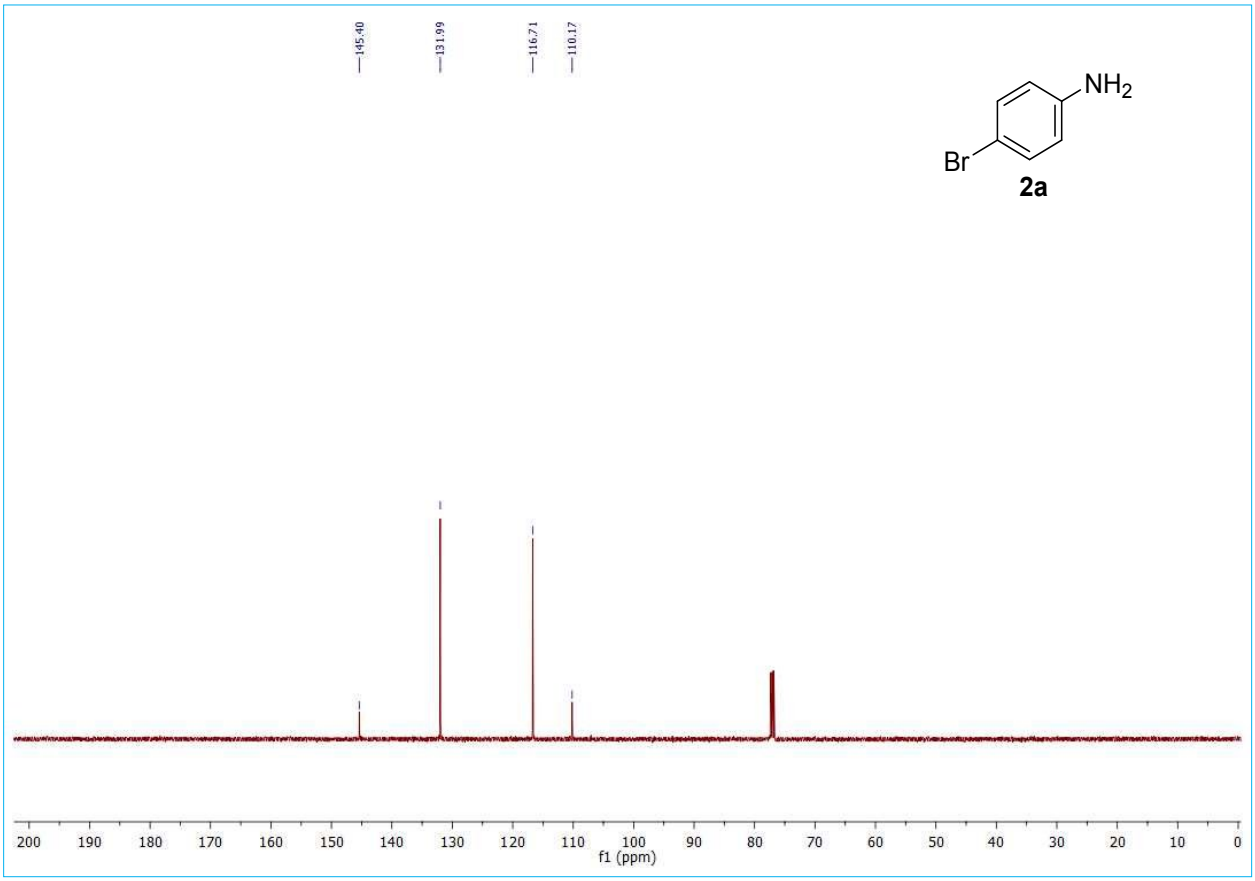
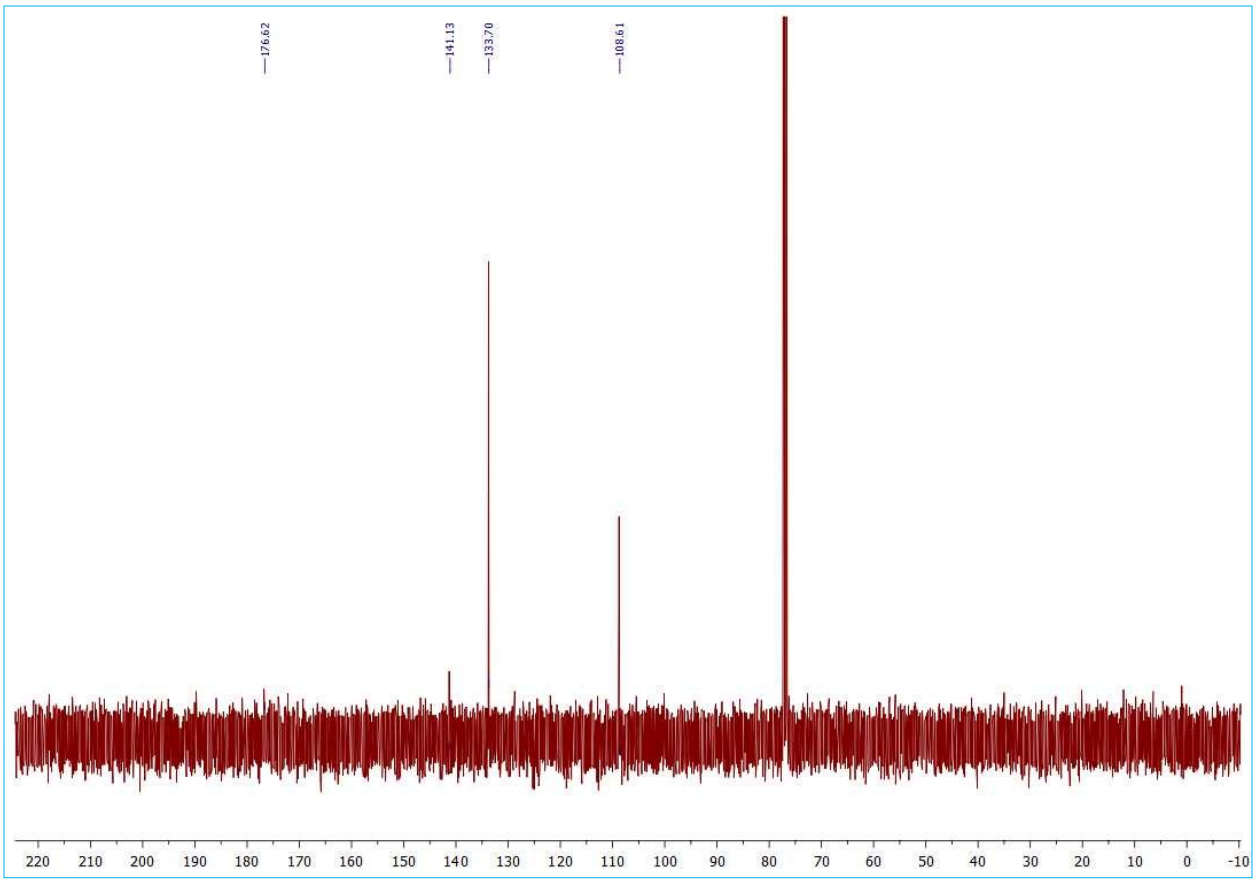


^{13}C NMR Spectra

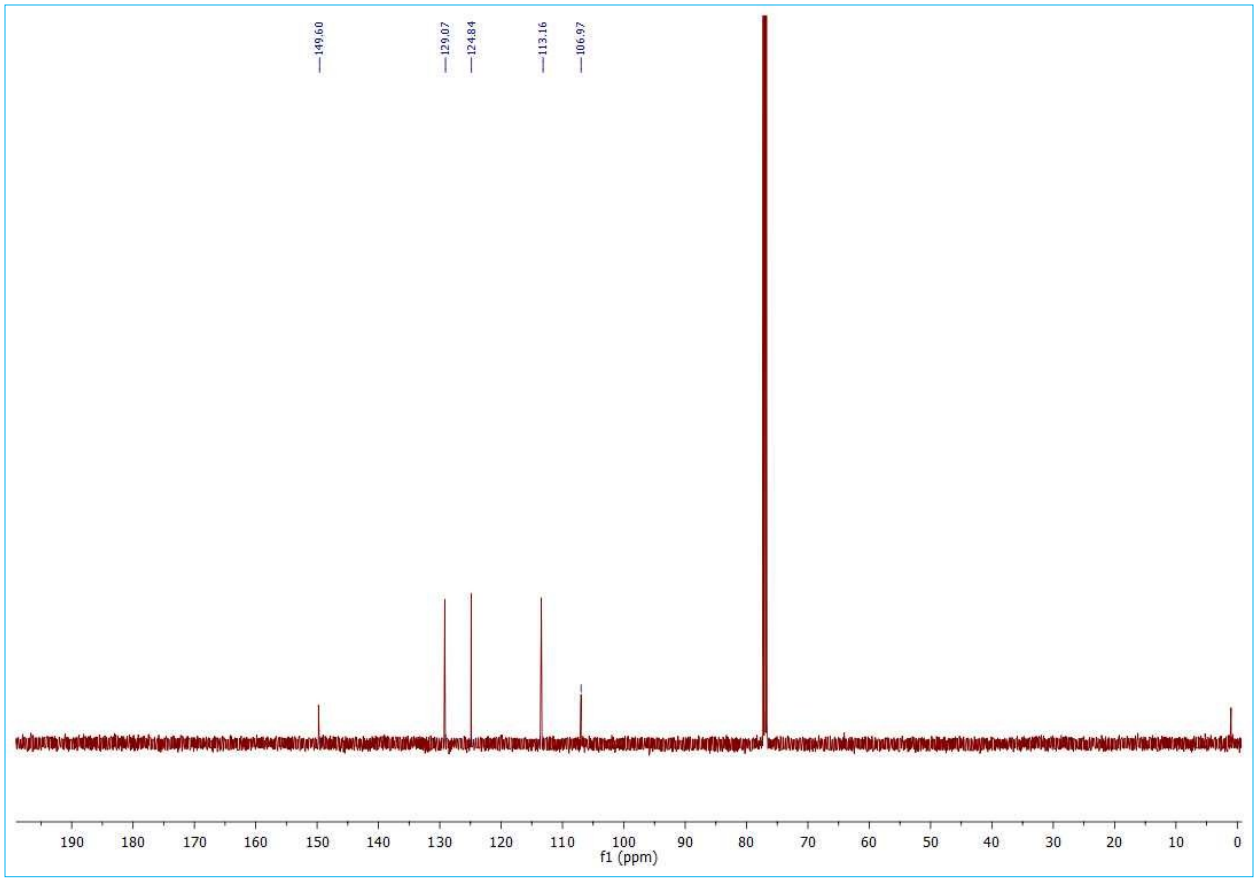
4-bromoaniline



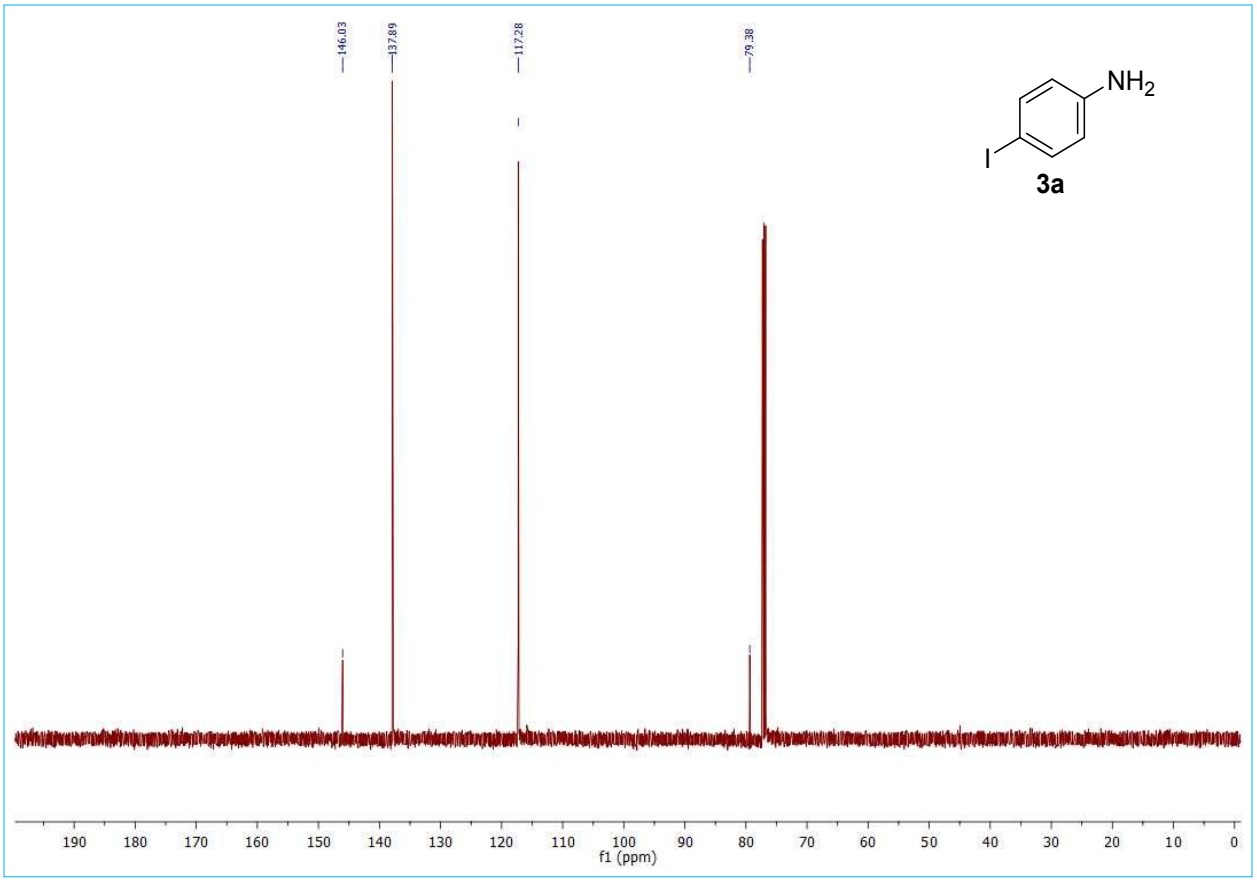
2, 4, 6-tribromoaniline



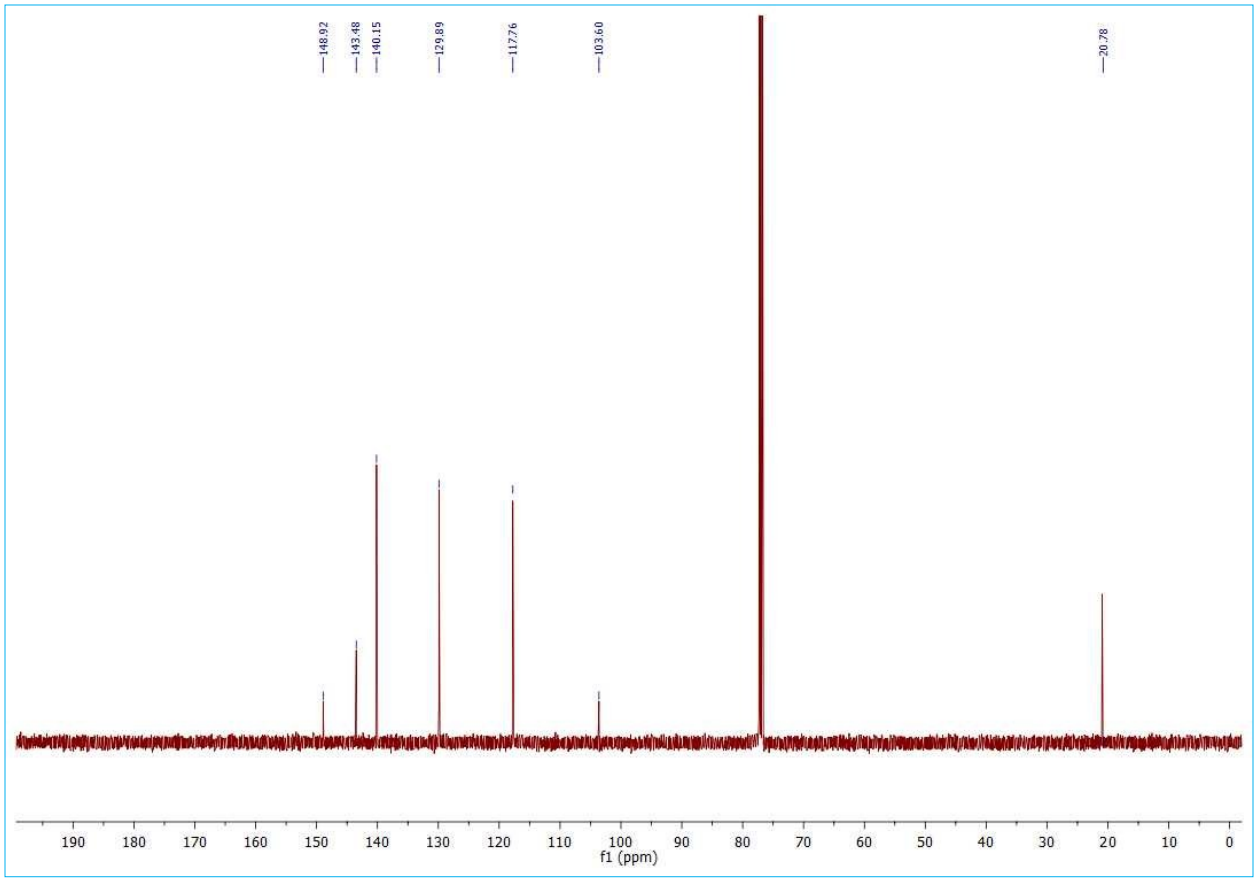
2-bromo-4-nitroaniline



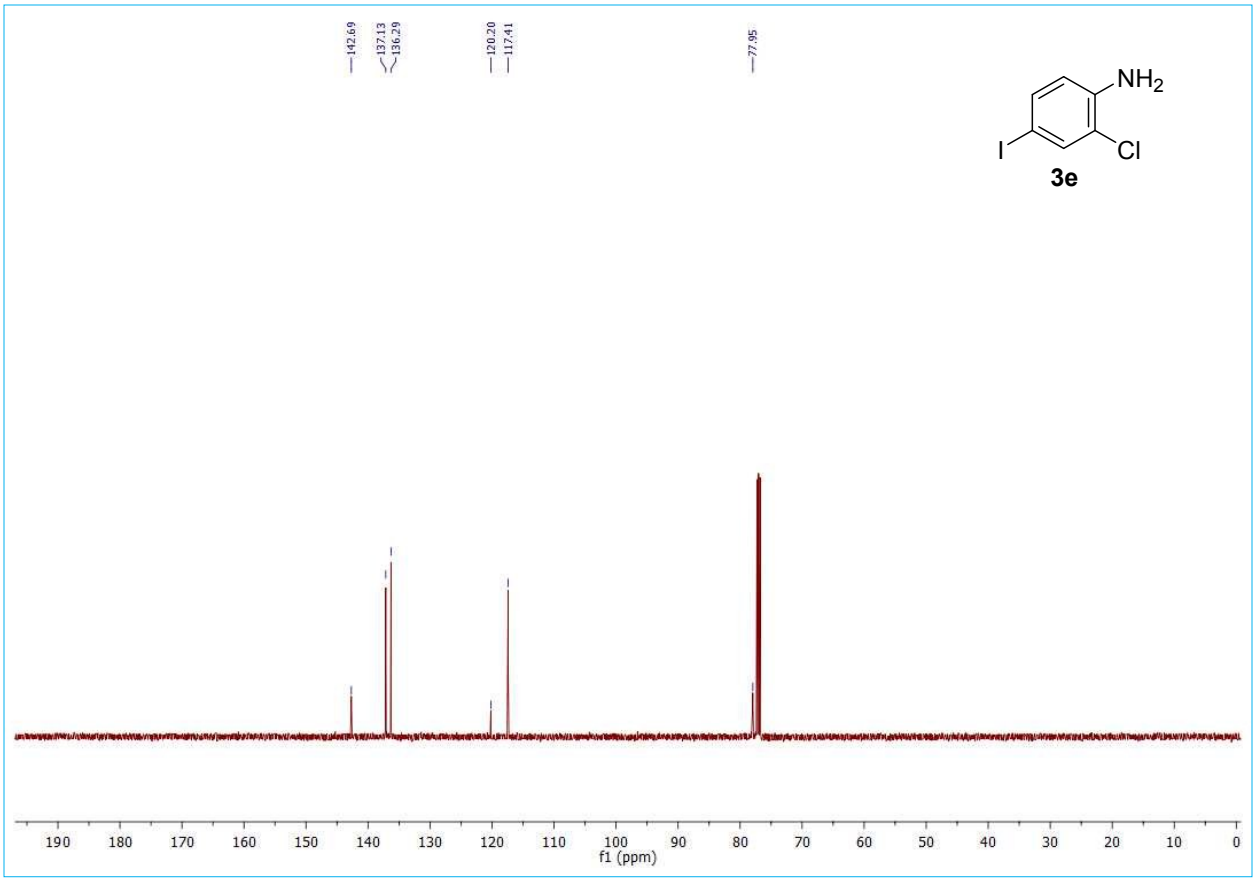
4-iodoaniline



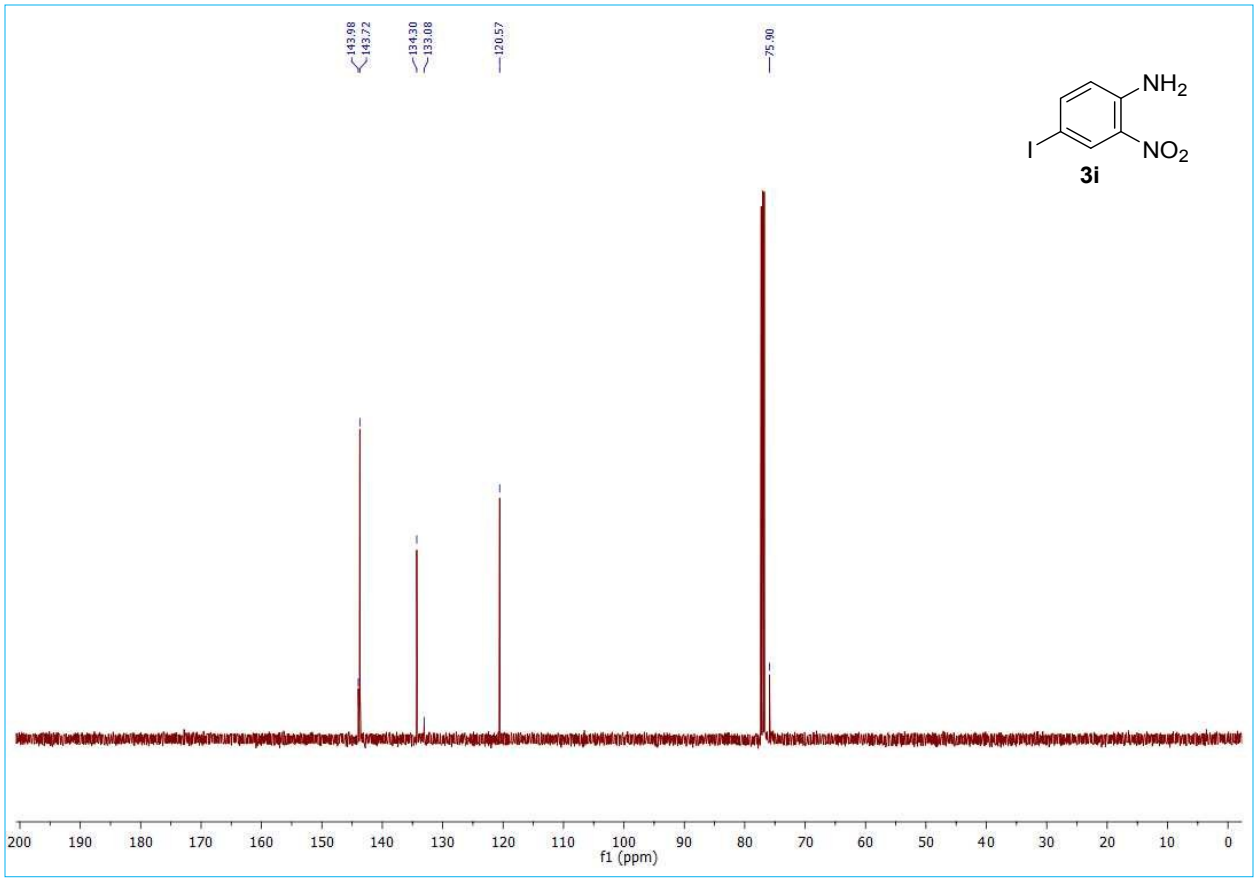
2-iodo-4-methylaniline



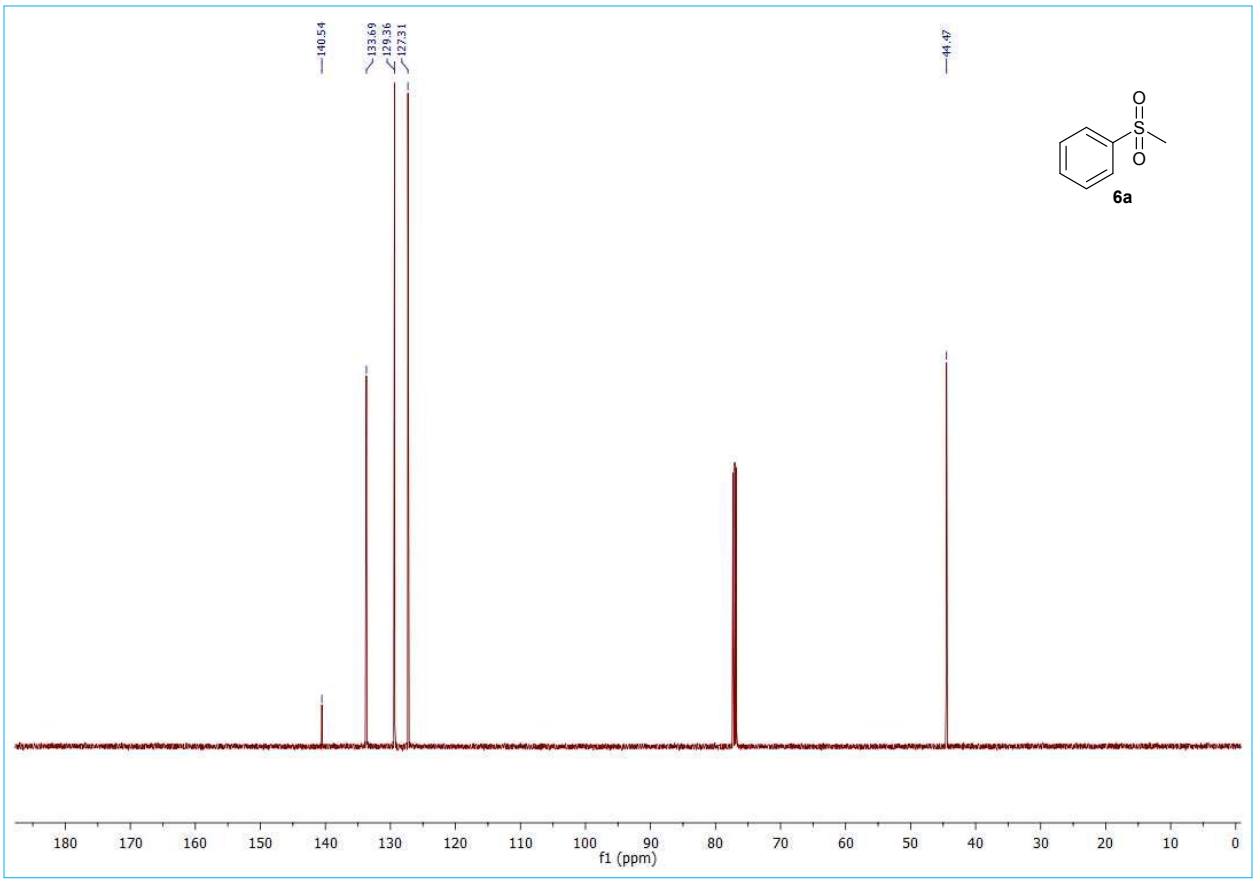
2-chloro-4-iodoaniline



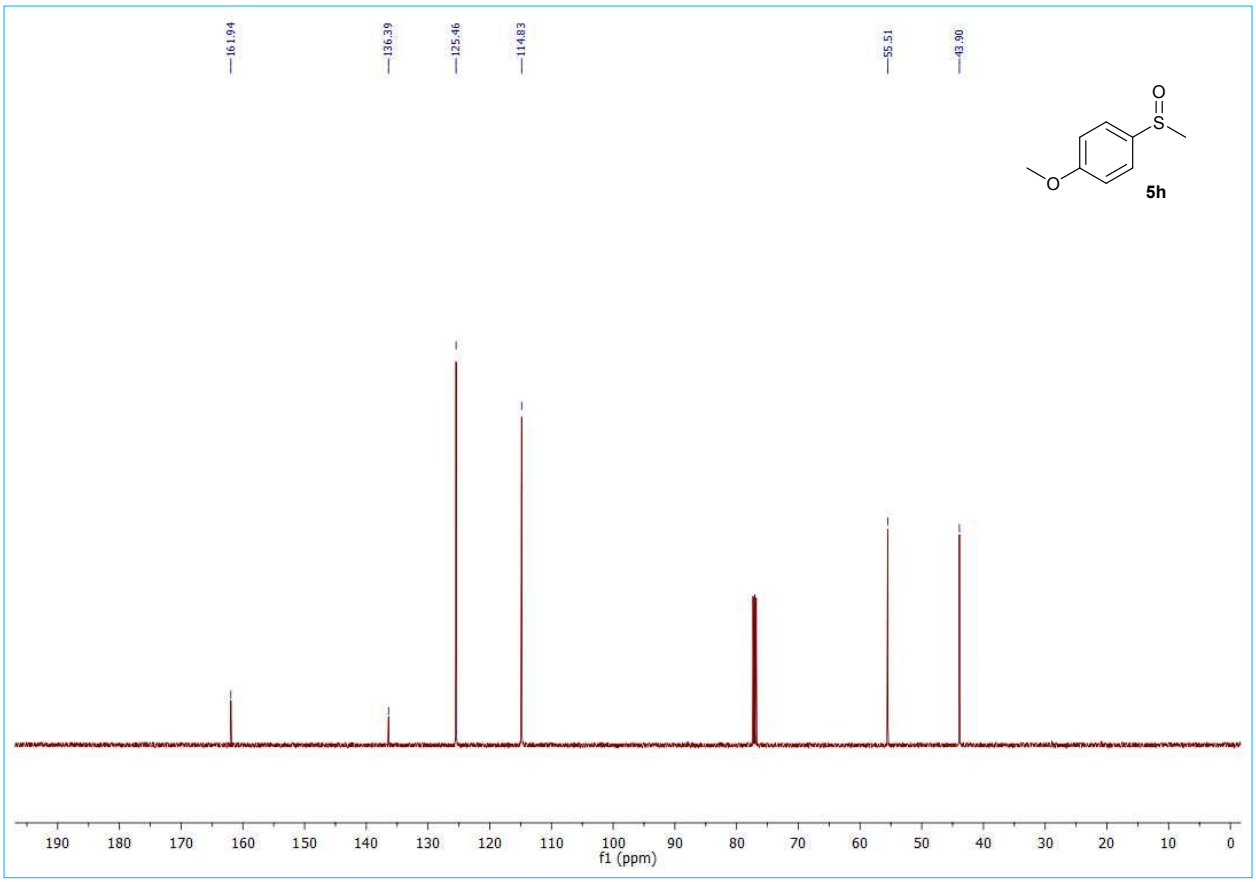
4-iodo-2-nitroaniline



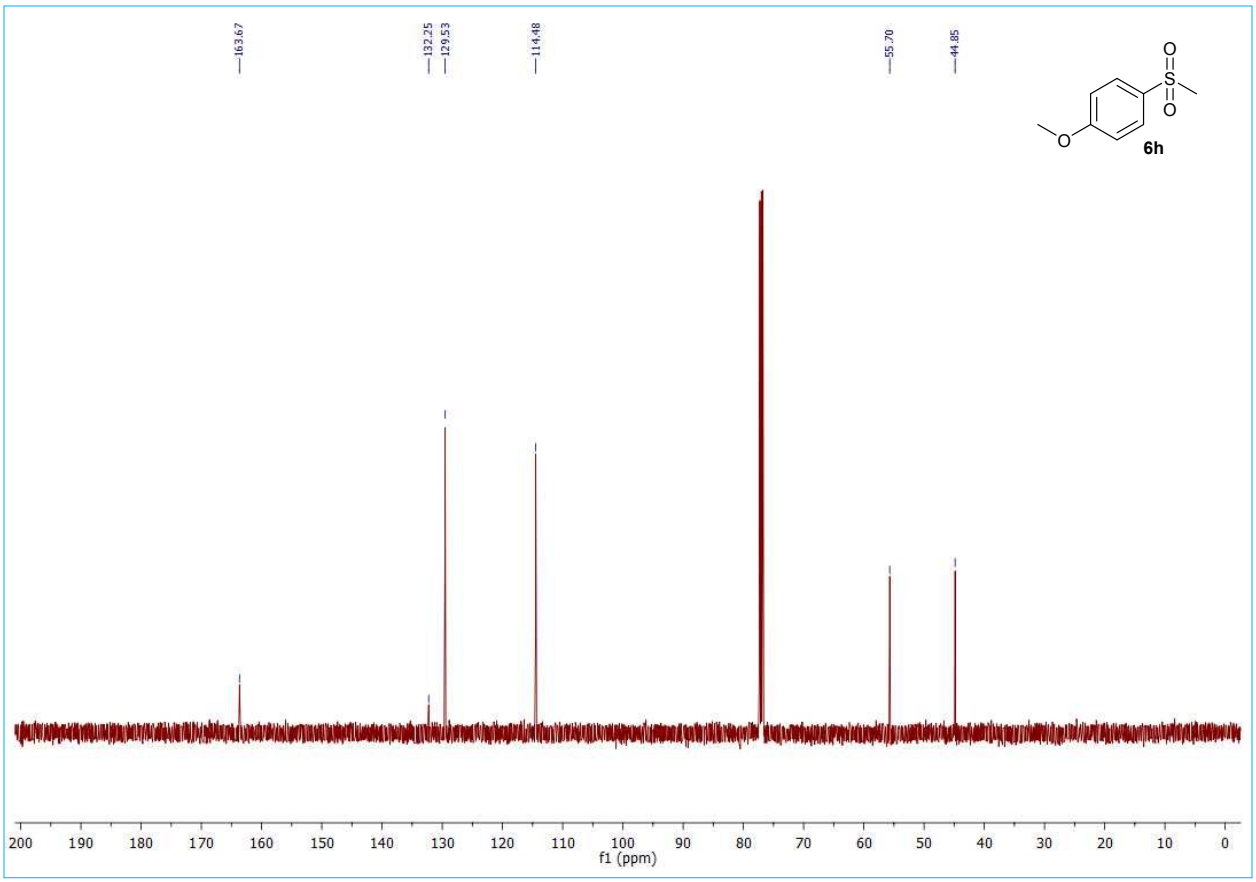
(methylsulfonyl)benzene



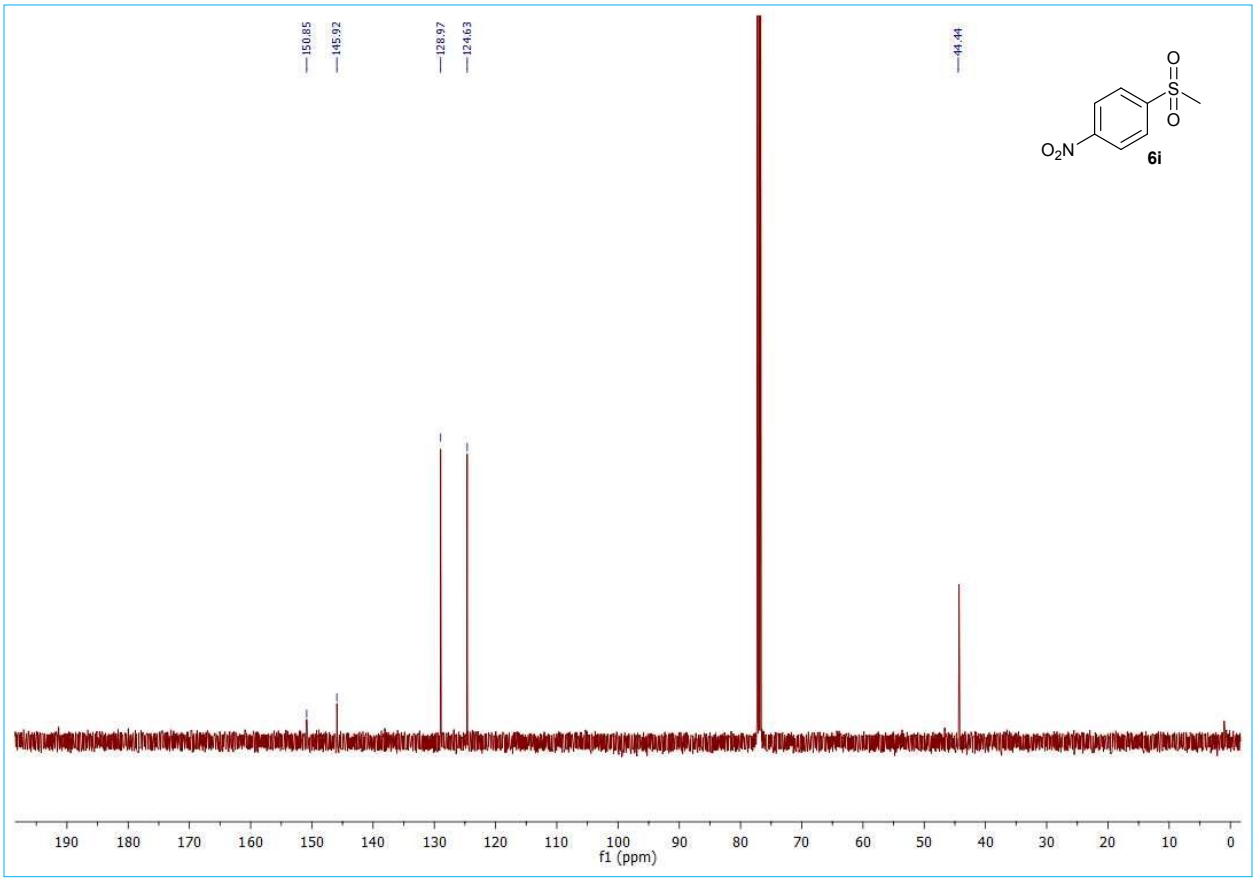
1-methoxy-4-(methylsulfinyl)benzene



1-methoxy-4-(methylsulfonyl)benzene



1-(methylsulfonyl)-4-nitrobenzene



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