



Supporting Information

for

A chromatography-free and aqueous waste-free process for thioamide preparation with Lawesson's reagent

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NMR data for compounds 2–6 and thiophosphonic acid

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1. Modified process for the synthesis of **2e**.

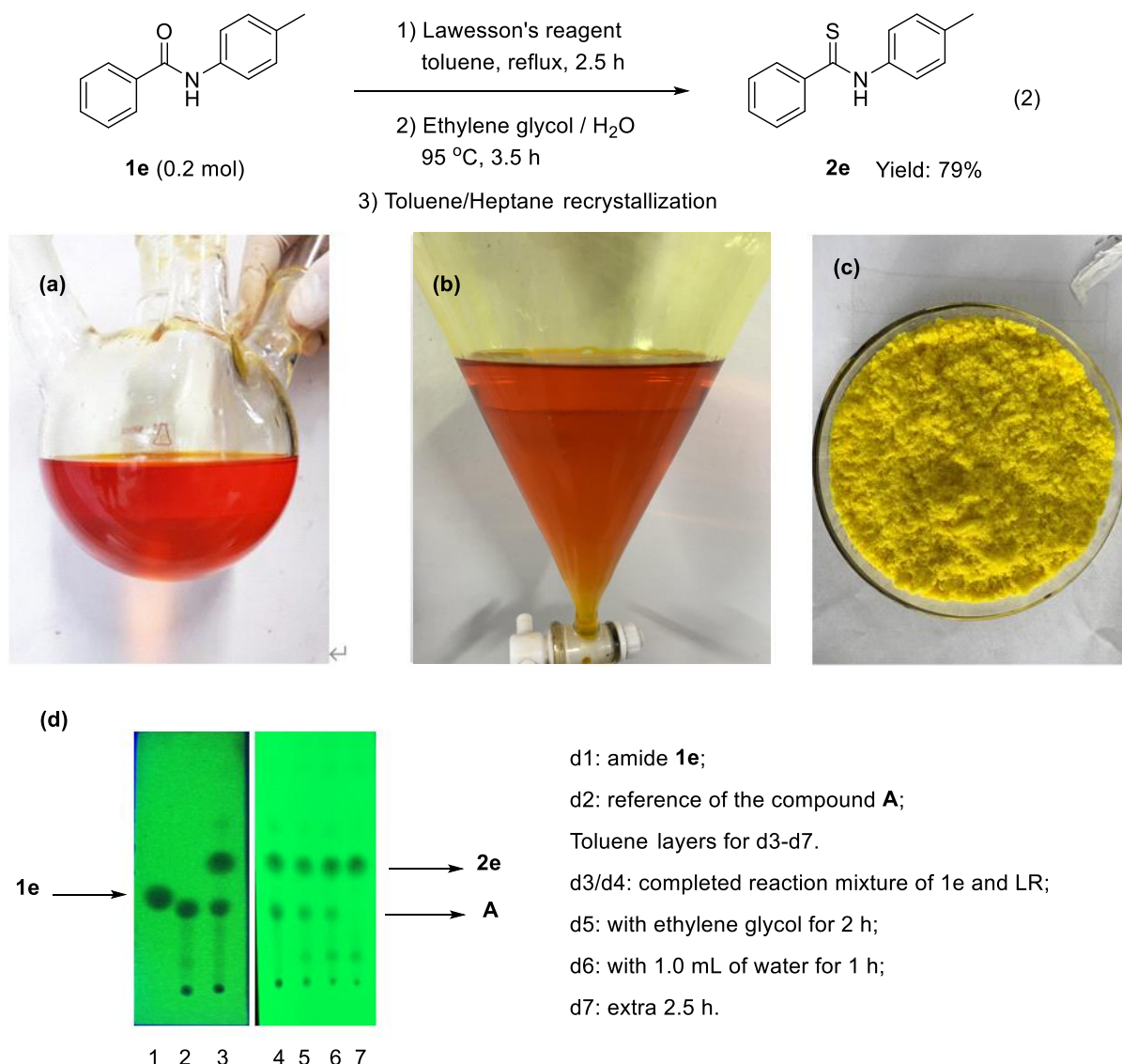


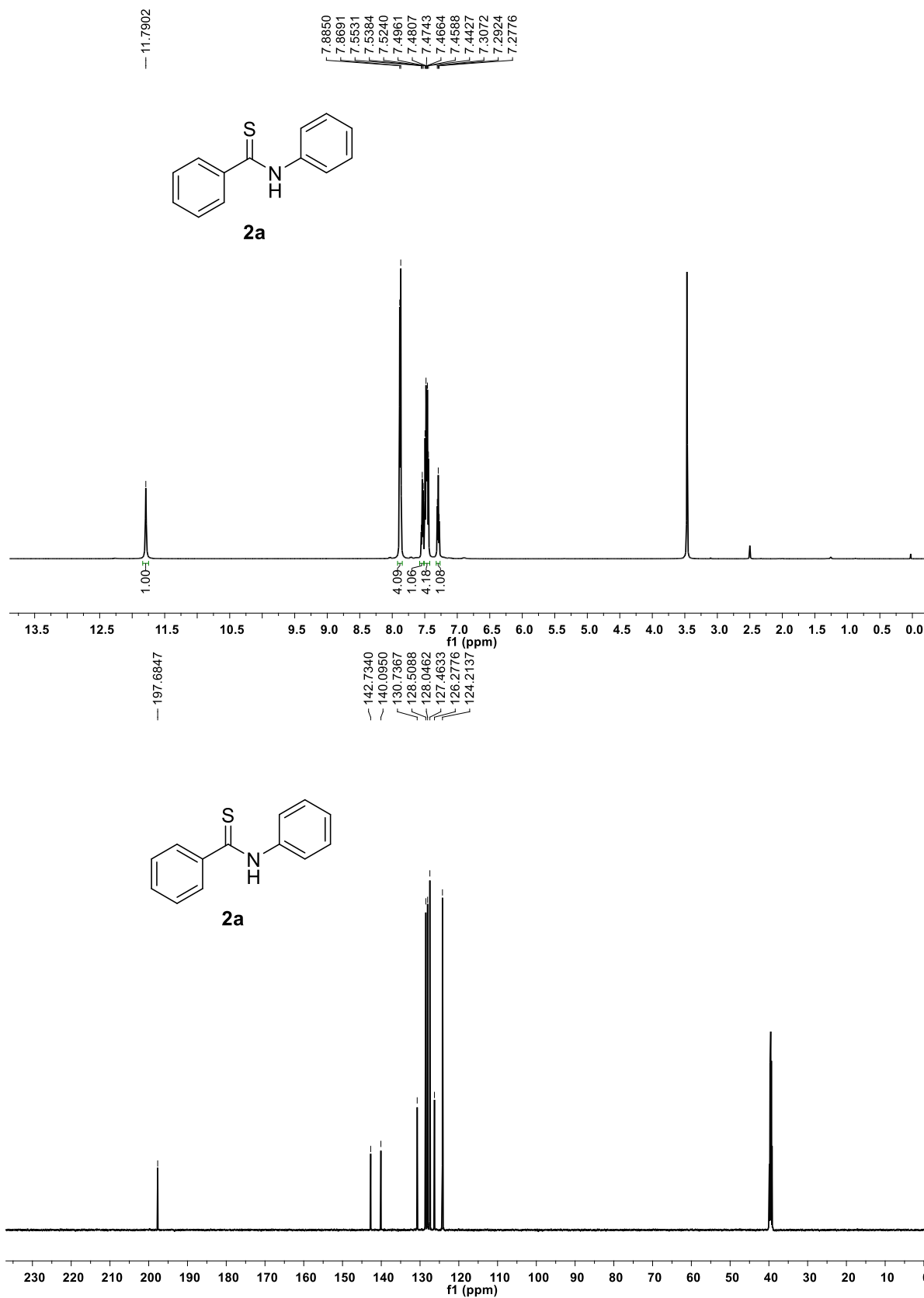
Figure S1: Phase-separation of the reaction mixture, recrystallization of the product, and TLC monitoring of the treatment with ethylene glycol. (a: Complete reaction mixture (upper layer is toluene); b: back extraction (upper layer is toluene); c: product **2e** after recrystallization; d: TLC monitoring of the reaction mixture and reaction workup between amide **1e** and LR).

After the completion of the thioamidation reaction of **1e** (0.20 mol) and LR (0.102 mol) (Figure S1, d3 and d4), excess ethylene glycol was added to decompose compound **A**, following the previous EtOH treatment procedure. To our astonishment, the decomposition was much slower as expected by TLC monitoring (Figure S1, d5). It was assumed that the ring-opening could be interfered by water or accelerated by the in-situ generated thiophosphonic acid. Thus, 1.0 mL of water was added into the mixture. We were pleased to find that the compound **A** smoothly decomposed by water-containing ethylene glycol at 95 °C

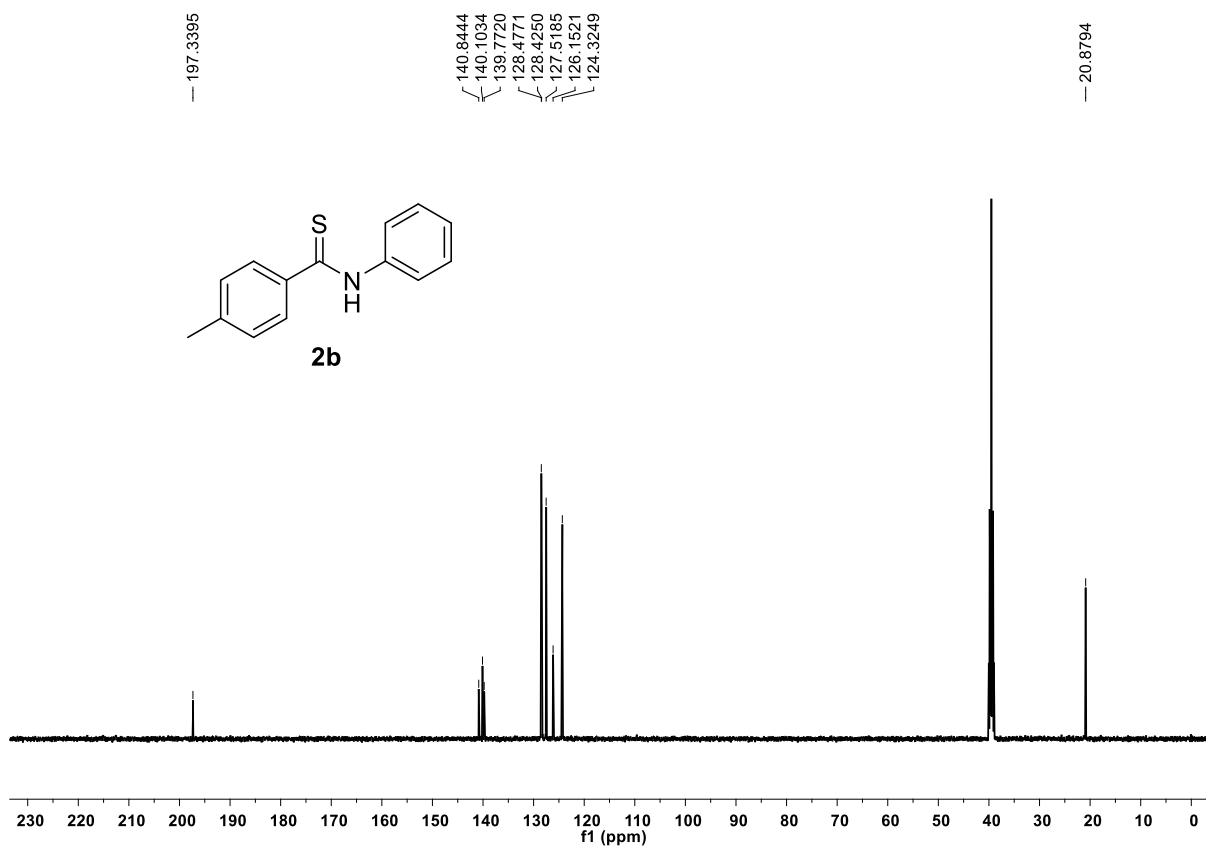
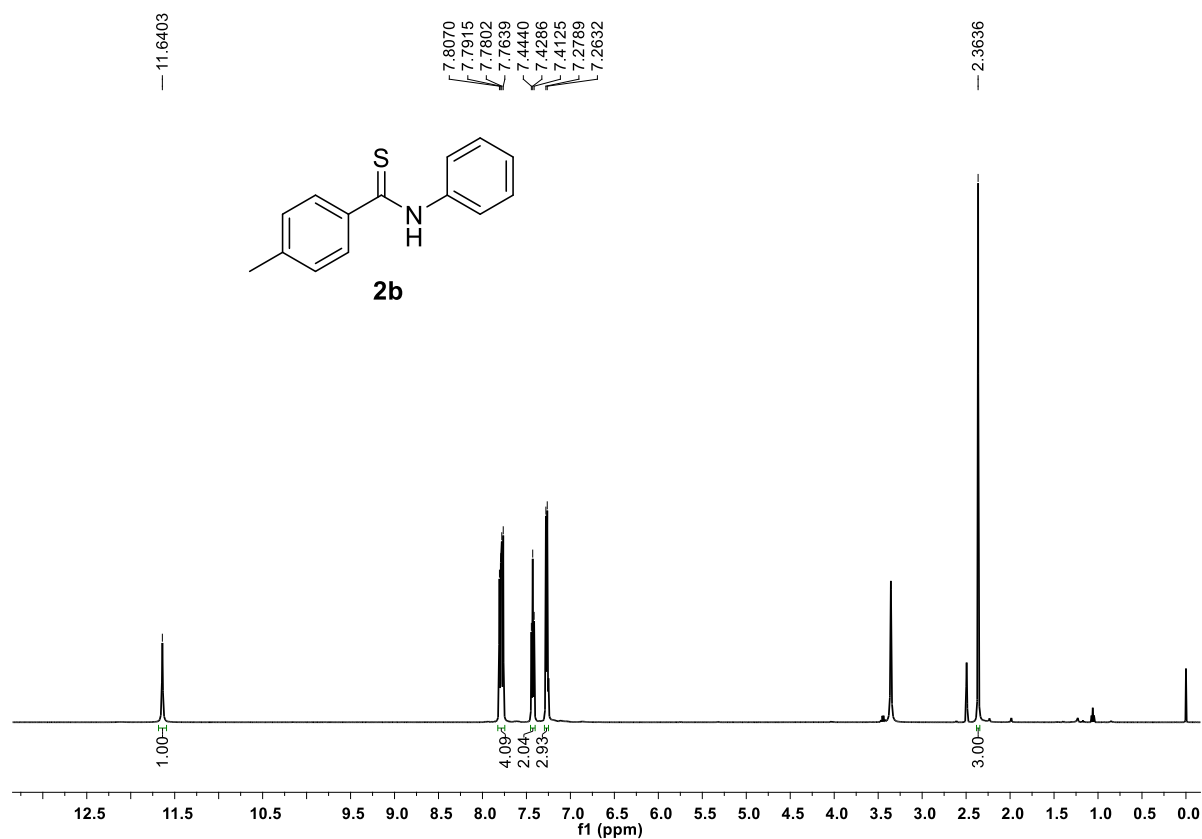
within 3.5 h. With the decline of compound **A** in the toluene layer, a new compound **C2** was observed (Figure S1, d7). It was also noticed that the pH of the ethylene glycol layer was about 2–3. Thus, we reckoned that the assumed byproduct **C2** was further decomposed to the thiophosphonic acid which is well soluble in ethylene glycol. After phase separation at around 50 °C (Figure S1, a), the ethylene glycol phase was back-extracted with toluene (Figure S1, b). The cooled toluene layers were treated with activated carbon and filtered. Toluene and the potential volatiles were removed, the residue recrystallized from a mixture of toluene and heptane to afford 36.0 g of the desired thioamide (**2e**) as yellow crystalline solid (Figure S1, c).

2. NMR data of amides 2–6

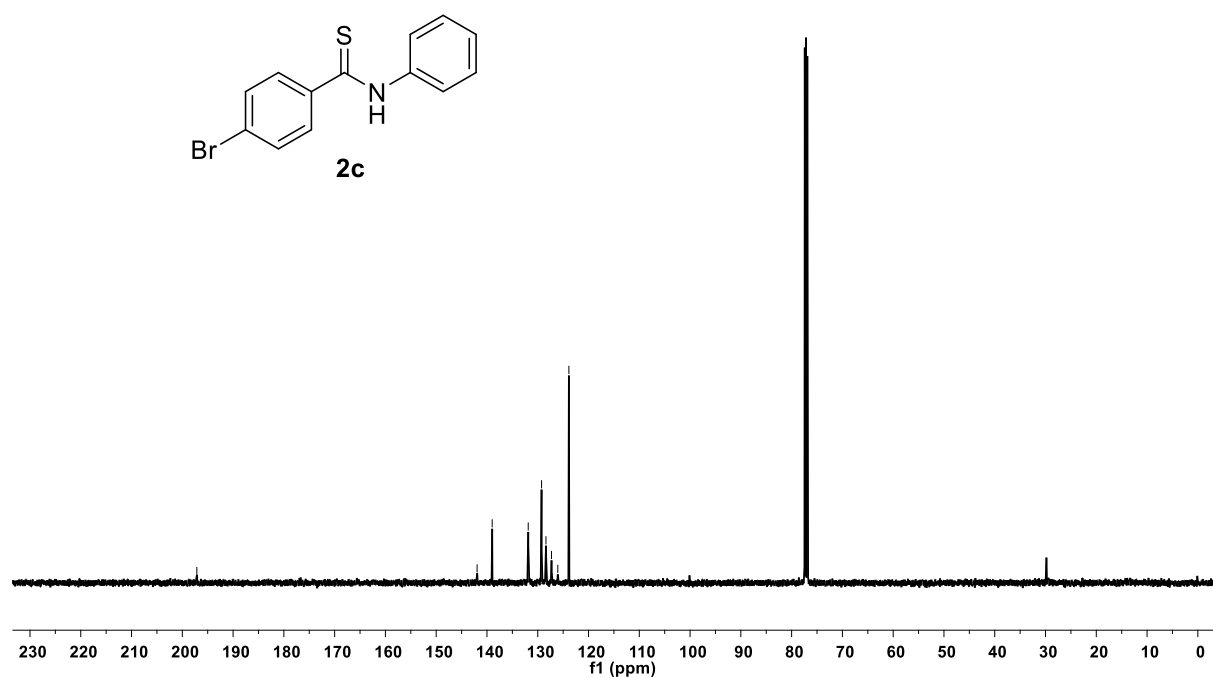
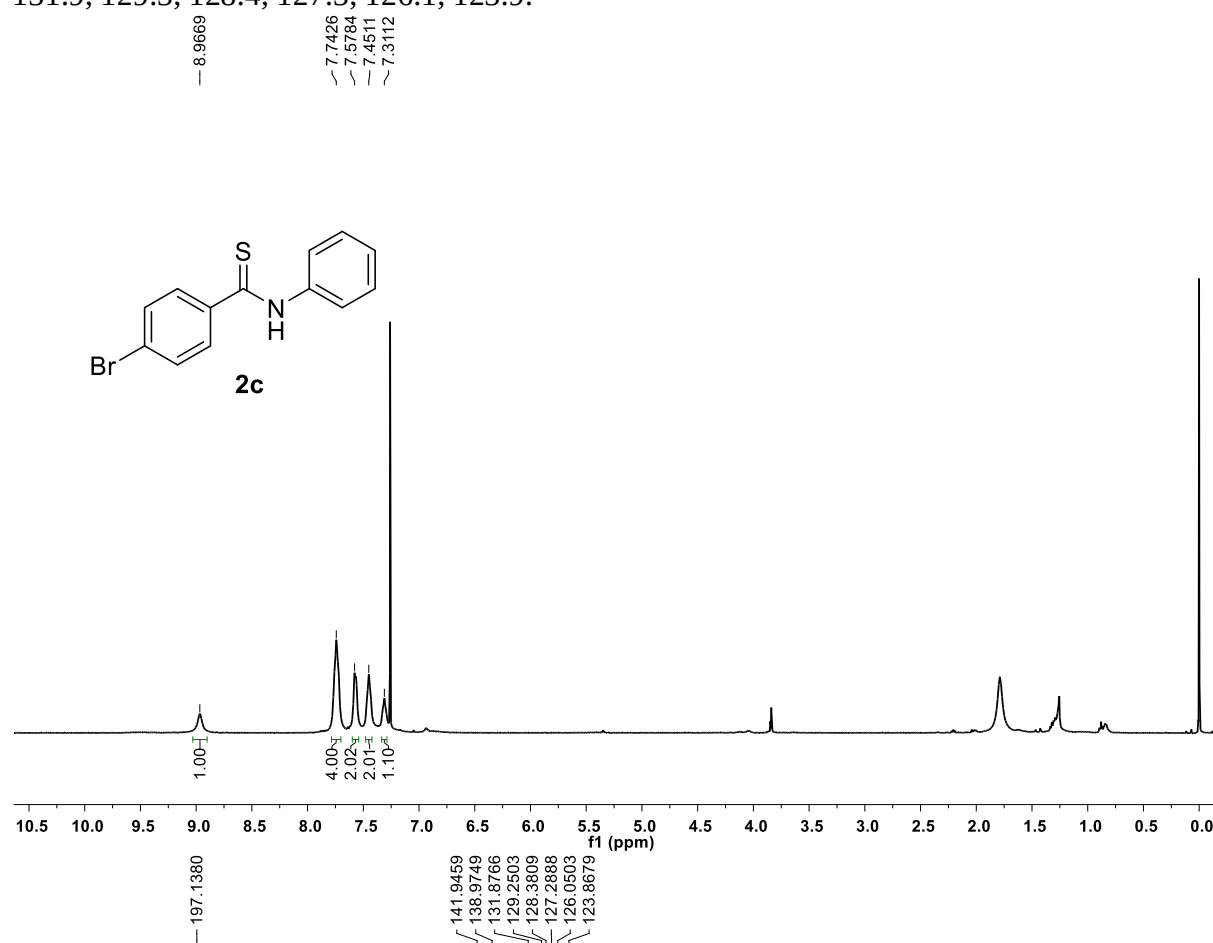
N-Phenyl benzothioamide (2a)^[1] Yield: 85%; Yellow solid, m.p.: 103.6-104.5 °C; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 11.79 (br, 1H), 7.88 (d, *J* = 7.5 Hz, 4H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.51-7.43 (m, 4H), 7.29 (t, *J* = 7.5 Hz, 1H). ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 197.7, 142.7, 140.1, 130.7, 128.5, 128.0, 127.5, 126.3, 124.2.



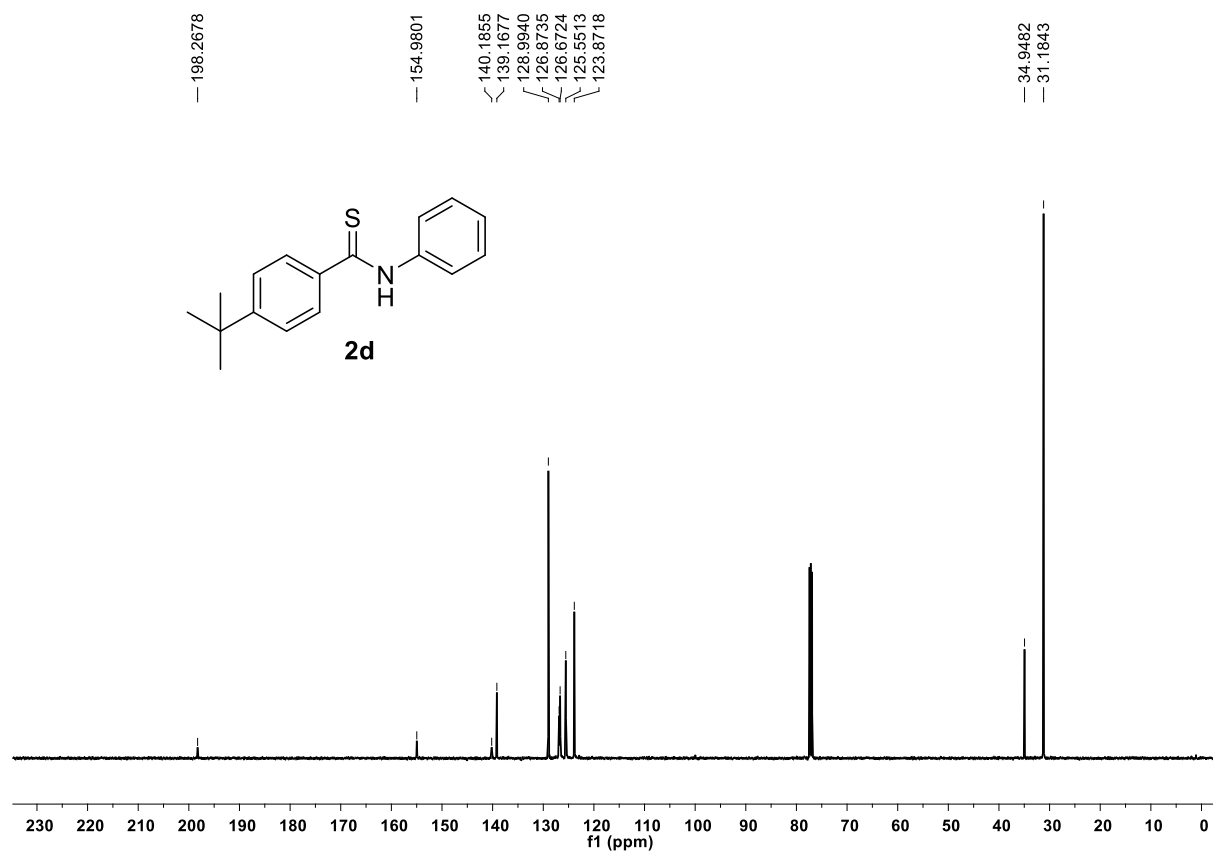
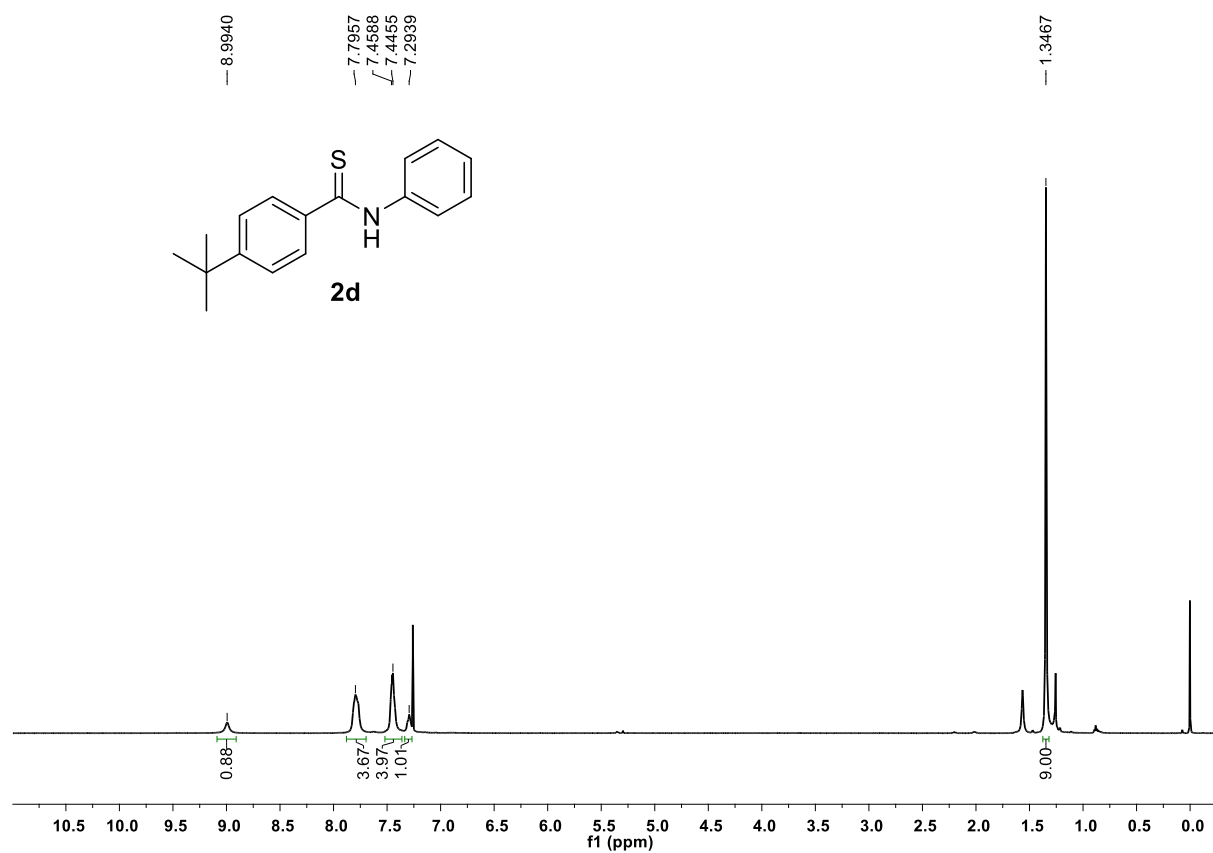
***N*-Phenyl 4-methylbenzothioamide (2b)**^[2] Yield: 79%; Yellow solid, m.p.: 128.5-130.2 °C; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 11.64 (br, 1H), 7.82-7.75 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.30-7.24 (m, 3H), 2.36 (s, 3H). ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 197.3, 140.8, 140.1, 139.8, 128.5, 128.4, 127.5, 126.2, 124.3, 20.9.



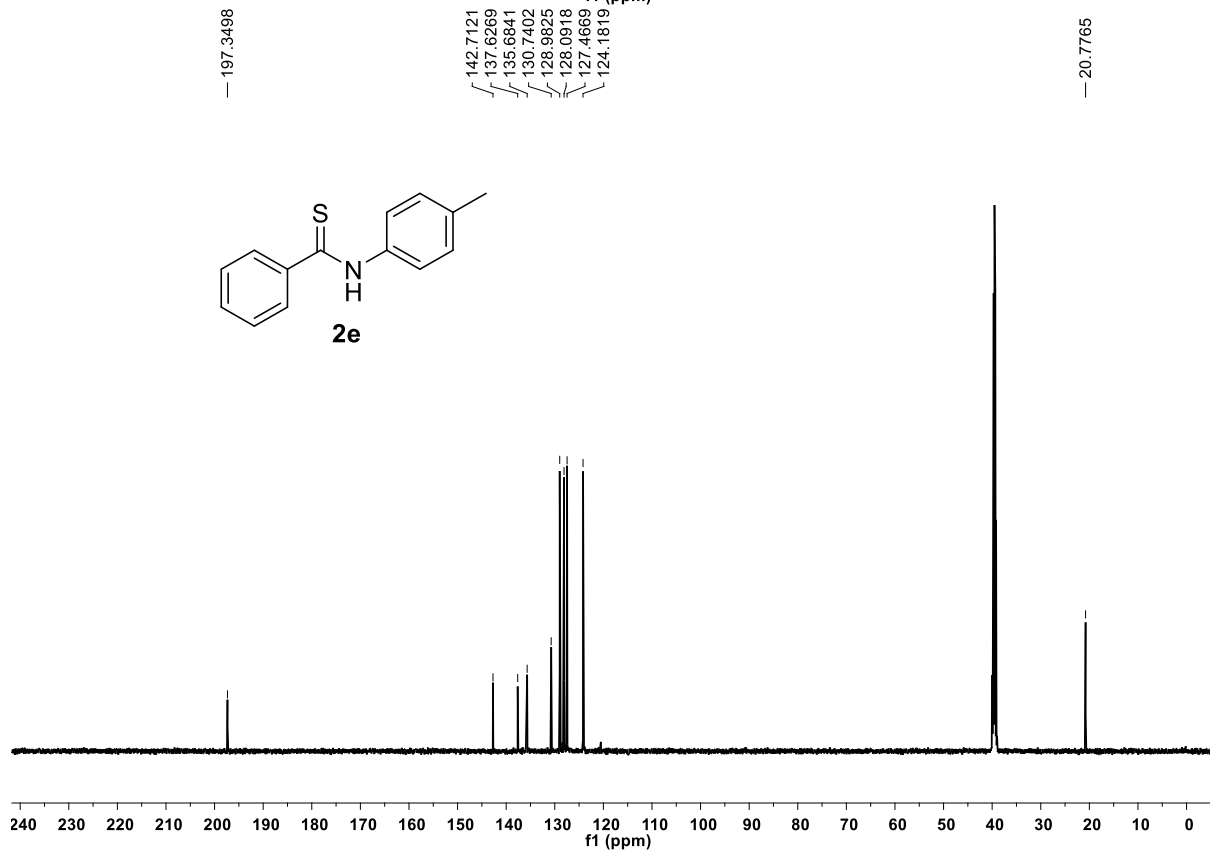
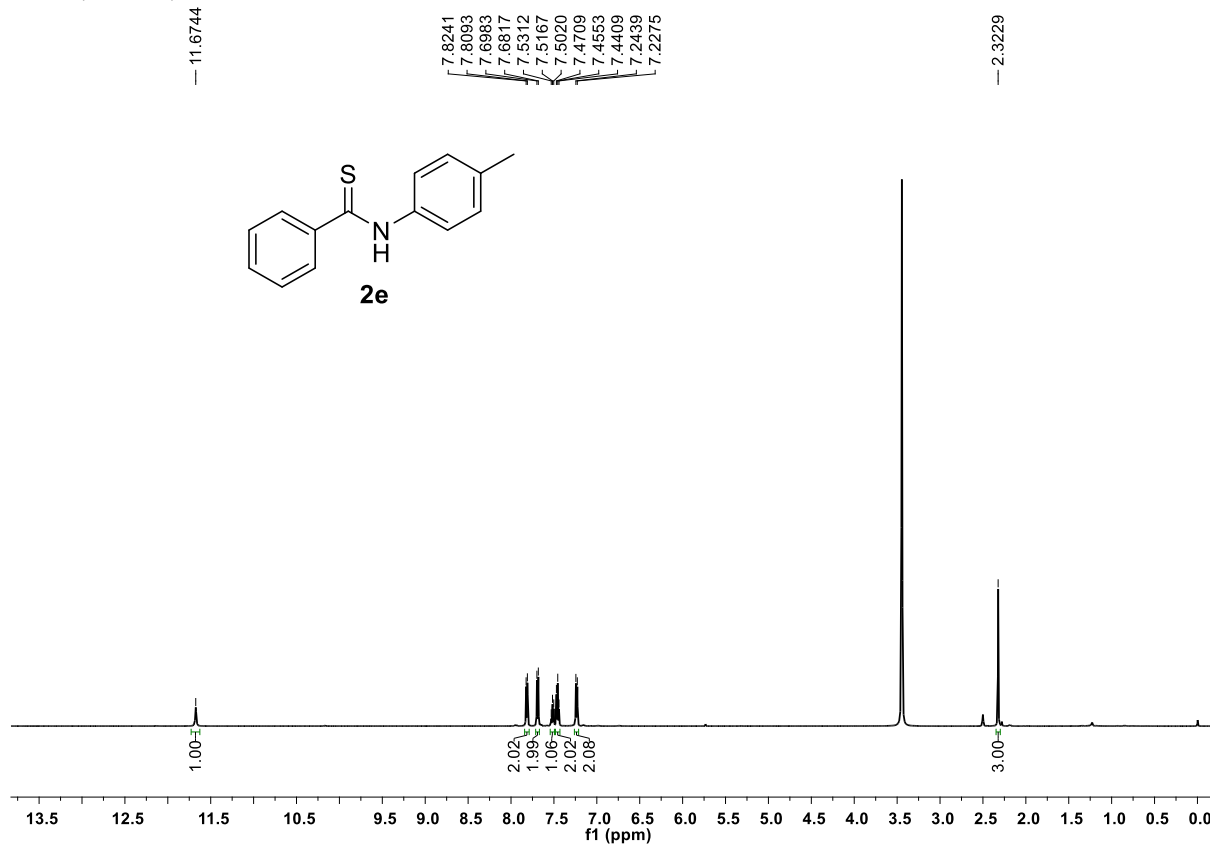
***N*-Phenyl 4-bromobenzothioamide (2c)**^[3] Yield: 79%; Yellow solid, m.p.: 128.5-130.3 °C; ¹H NMR (CDCl₃, 500 MHz): δ = 8.97 (br, 1H), 7.80-7.68 (m, 4H), 7.62-7.53 (m, 2H), 7.49-7.40 (m, 2H), 7.35-7.28 (m, 1H). ¹³C NMR (CDCl₃, 125 MHz): δ = 197.1, 141.9, 139.0, 131.9, 129.3, 128.4, 127.3, 126.1, 123.9.



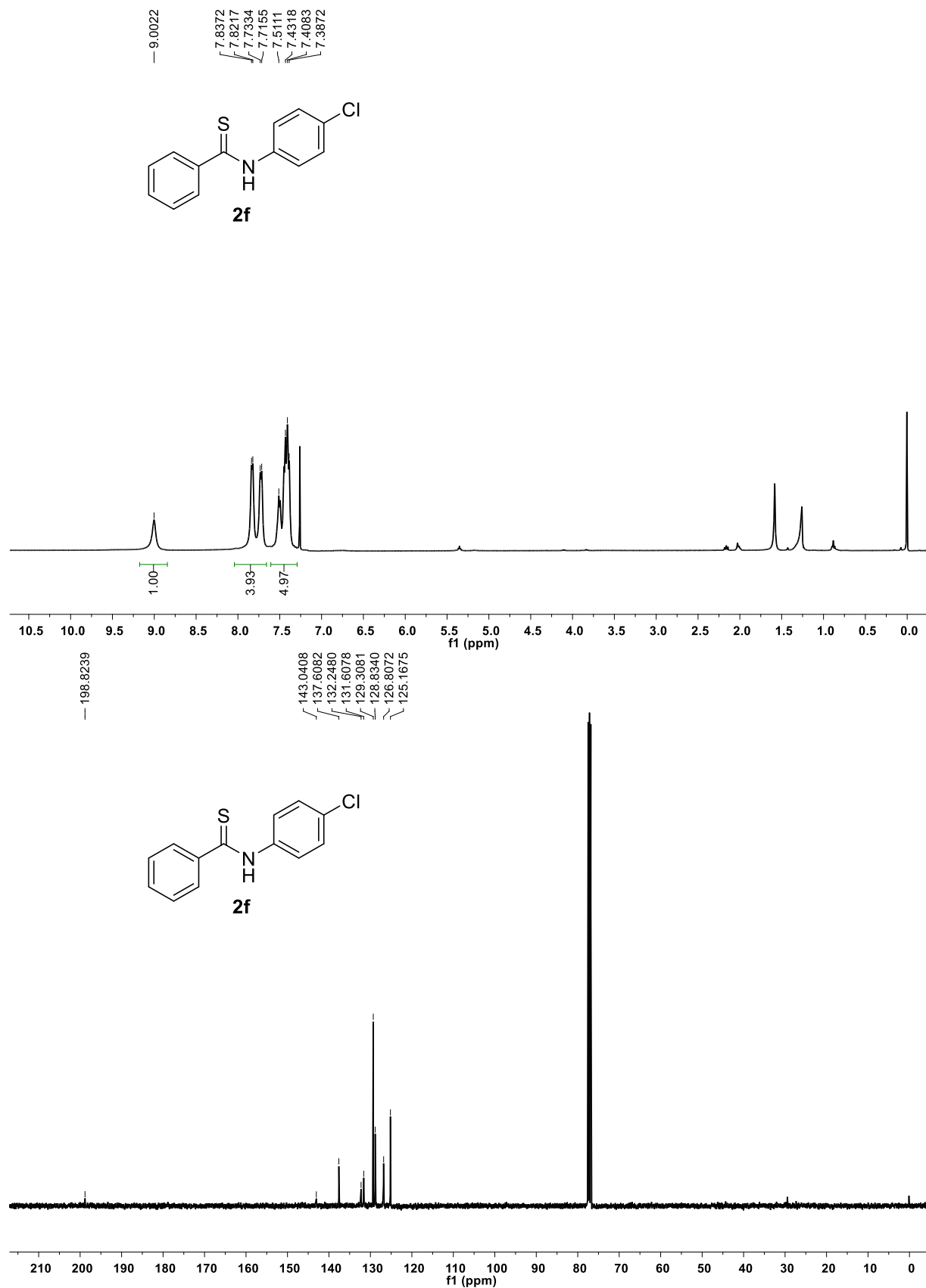
***N*-Phenyl 4-*tert*-butylbenzothioamide (2d)**^[4] Yield: 75%; Yellow solid, m.p.: 131.6-132.9 °C; ¹H NMR (CDCl₃, 500 MHz): δ = 8.99 (br, 1H), 7.87-7.70 (m, 4H), 7.51-7.39 (m, 4H), 7.33-7.27 (m, 1H), 1.35 (s, 9H). ¹³C NMR (CDCl₃, 125 MHz): δ = 198.3, 155.0, 140.2, 139.2, 129.0, 126.9, 126.7, 125.6, 123.9, 35.0, 31.2.



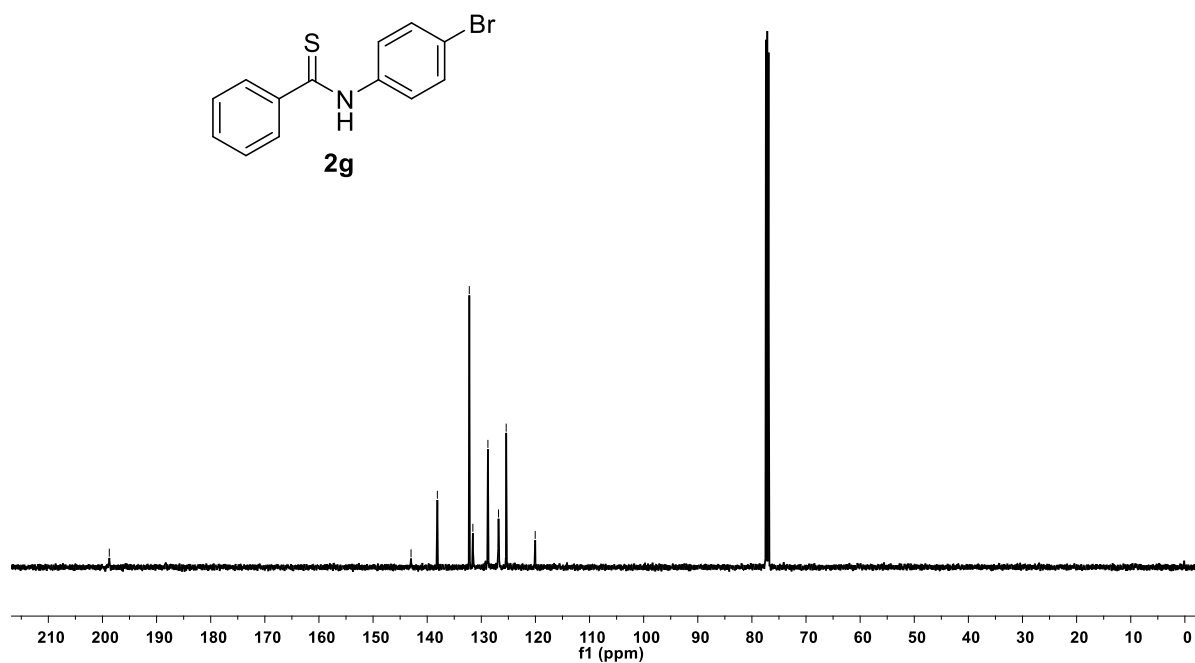
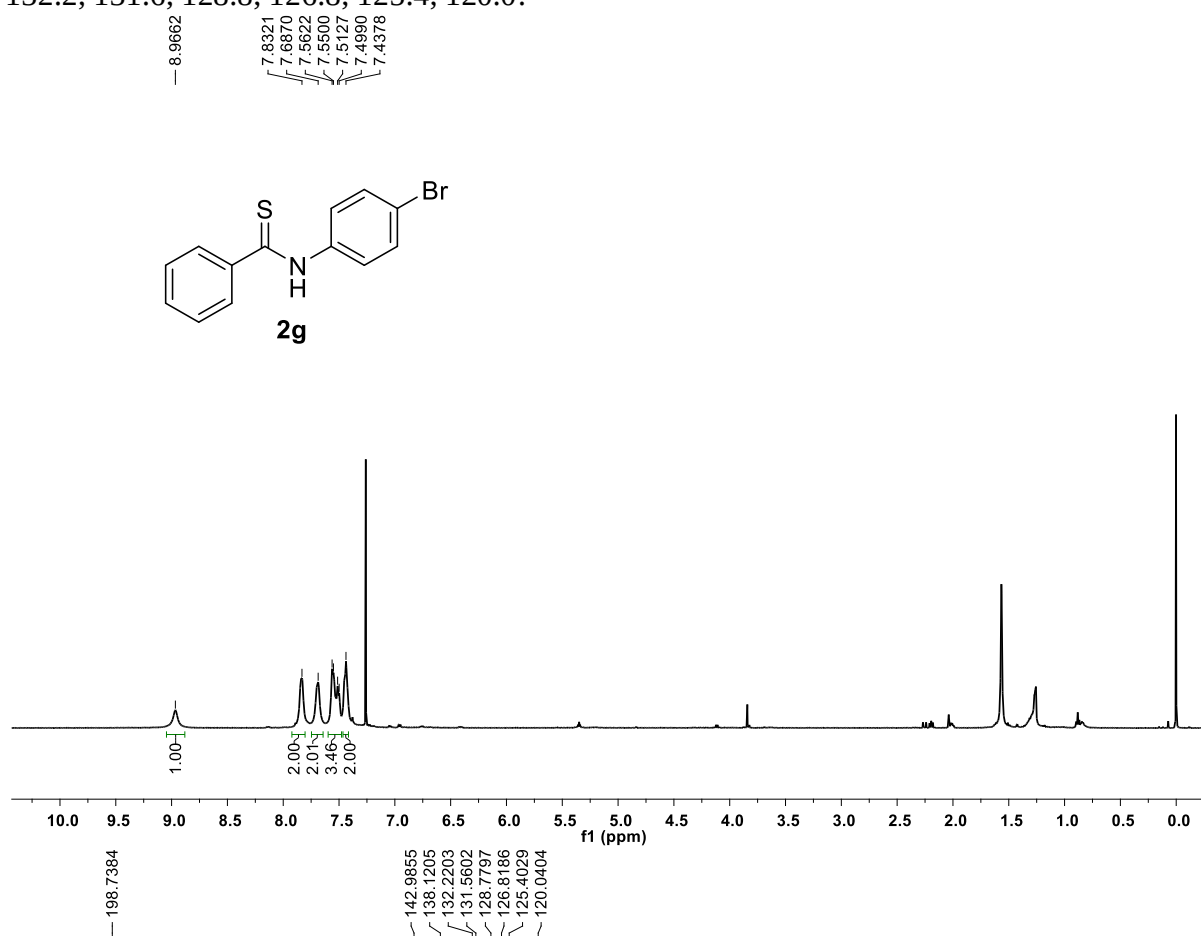
***N*-(4-Methylphenyl) benzothioamide (2e)**^[1] Yield: 82%; Yellow solid, m.p.: 128.5-130.1 °C; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 11.67 (br, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.52 (t, *J* = 7.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 7.6 Hz, 2H), 2.32 (s, 3H). ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 197.4, 142.7, 137.6, 135.7, 130.7, 129.0, 128.1, 127.5, 124.2, 20.8.



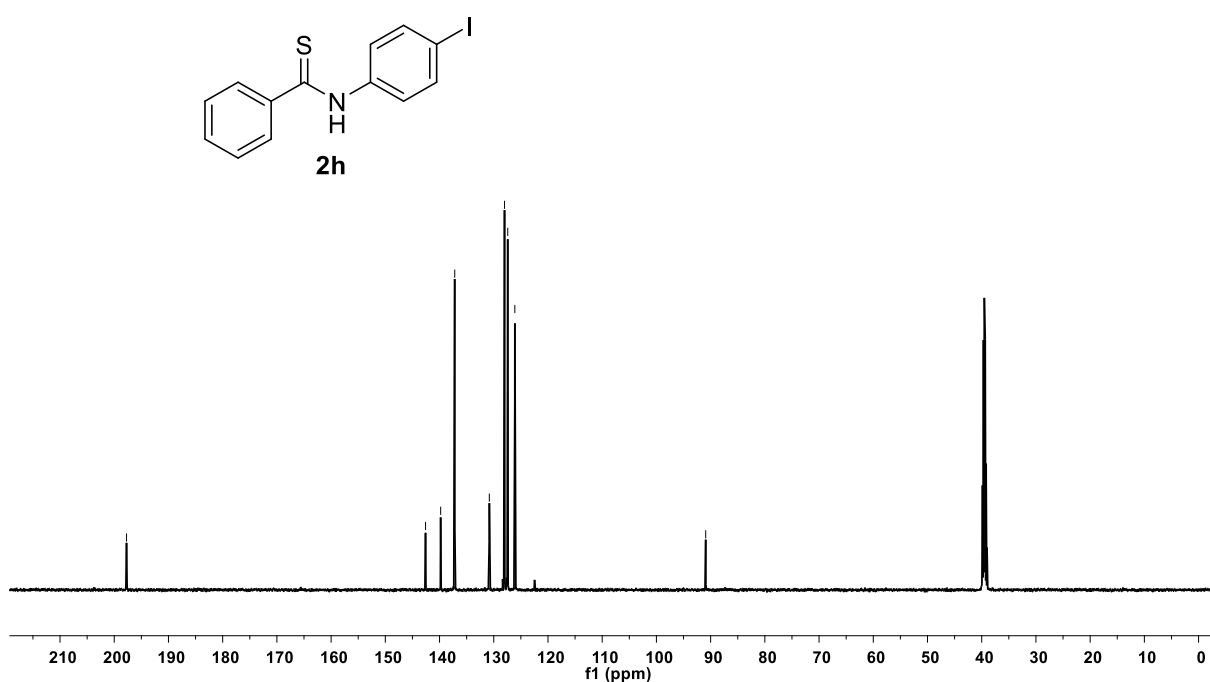
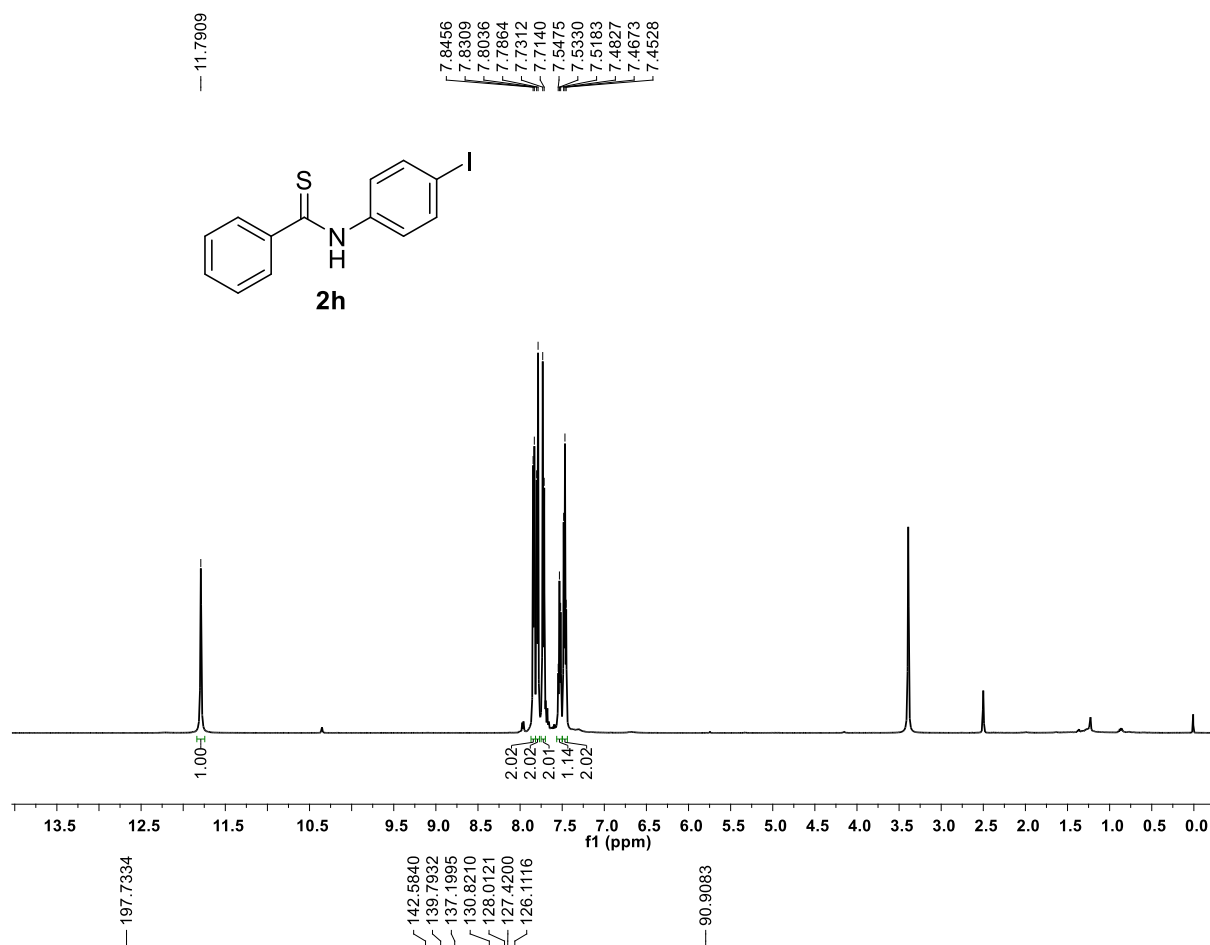
***N*-(4-Chlorophenyl) benzothioamide (2f)**^[3] Yield: 92%; Yellow solid, m.p.: 151.5-153 °C;
¹H NMR (CDCl₃, 400 MHz): δ = 9.00 (br, 1H), 7.92-7.65 (m, 4H), 7.58-7.32 (m, 5H). ¹³C
 NMR (CDCl₃, 100 MHz): δ = 198.8, 143.0, 137.6, 132.3, 131.6, 129.3, 128.8, 126.8, 125.2.



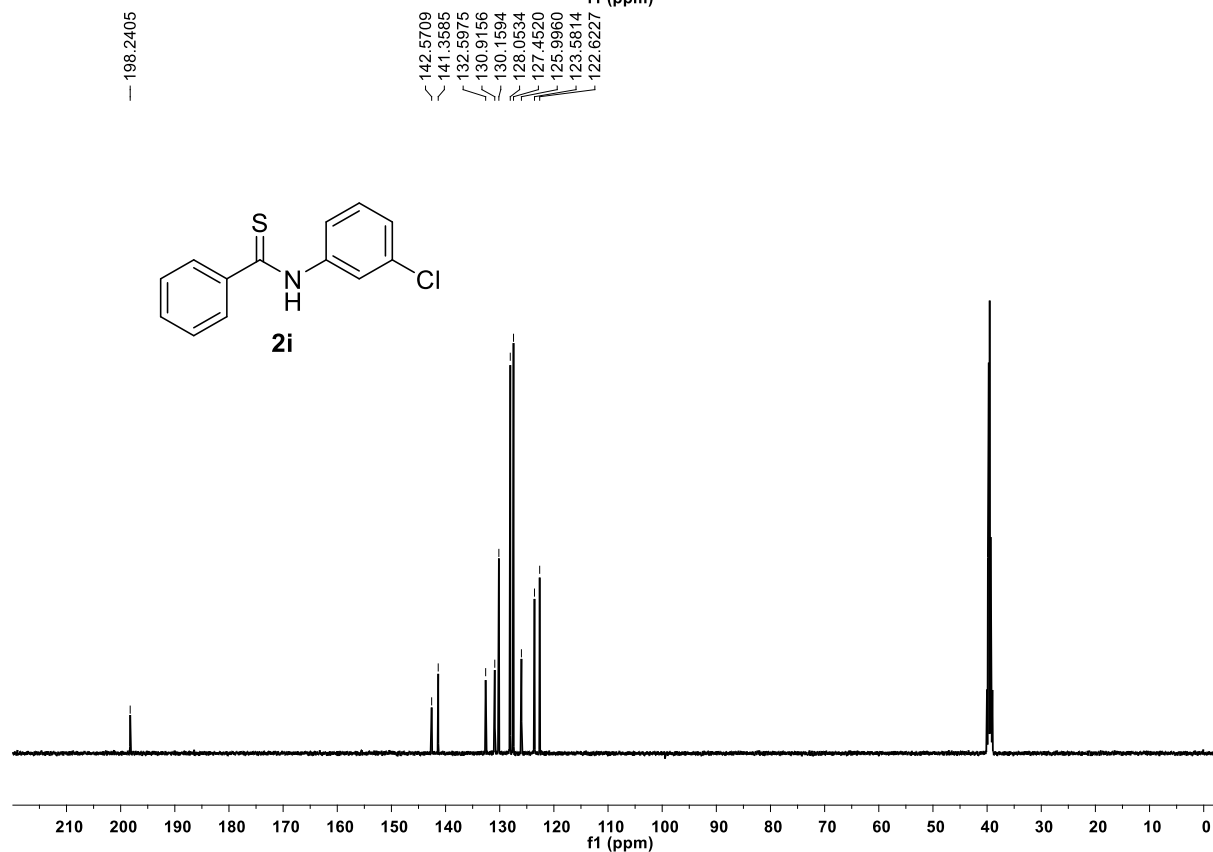
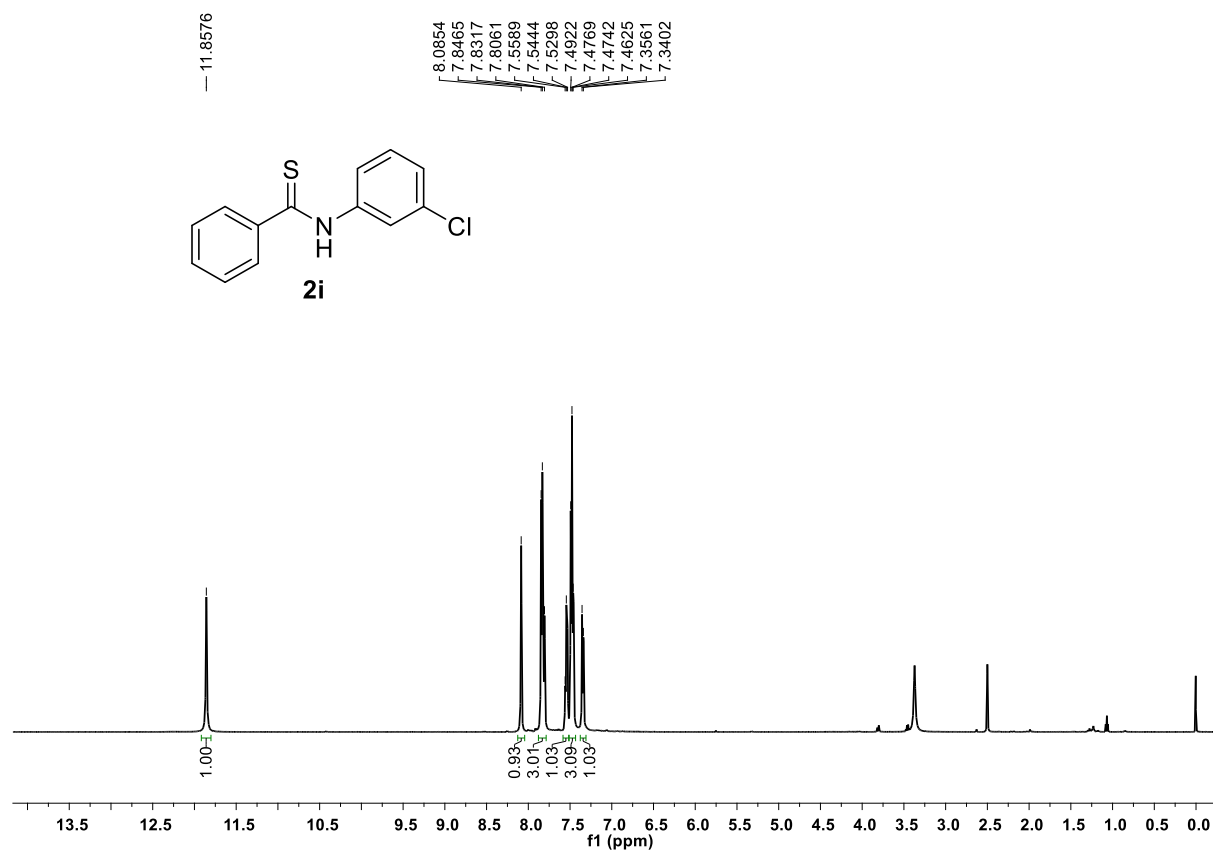
***N*-(4-Bromophenyl) benzothioamide (2g)**^[3] Yield: 84%; Yellow solid, m.p.: 148.5-150.3 °C; ¹H NMR (CDCl₃, 500 MHz): δ = 8.97 (br, 1H), 7.90-7.80 (m, 2H), 7.75-7.64 (m, 2H), 7.60-7.48 (m, 3H), 7.47-7.39 (m, 2H). ¹³C NMR (CDCl₃, 125 MHz): δ = 198.7, 143.0, 138.1, 132.2, 131.6, 128.8, 126.8, 125.4, 120.0.



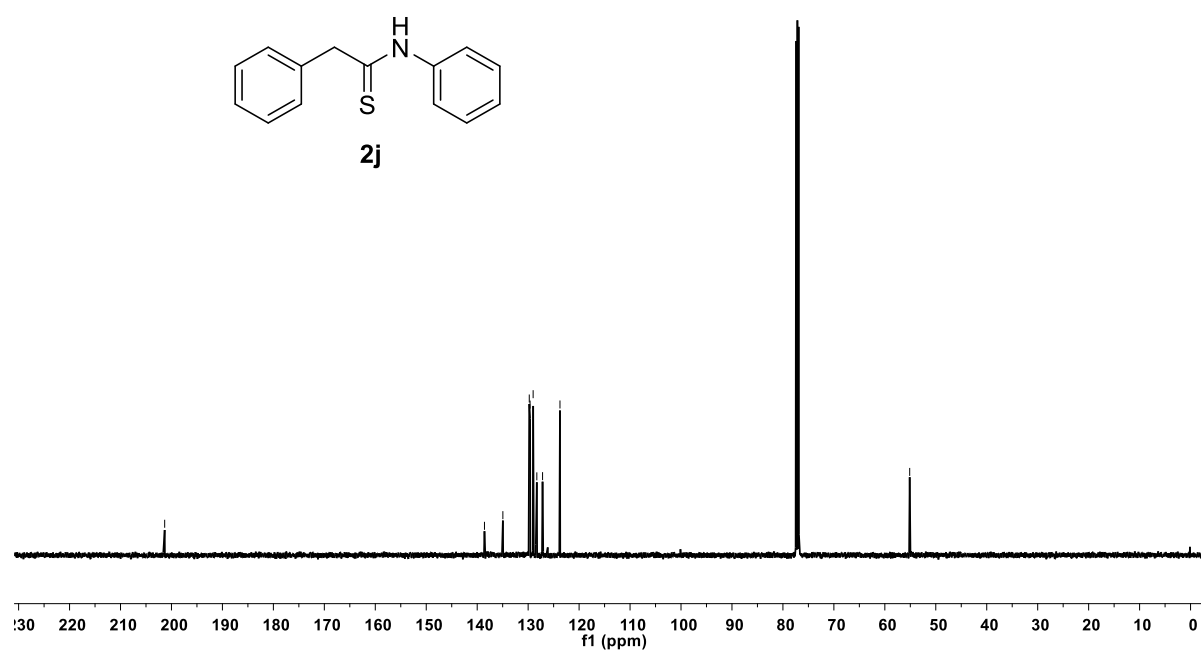
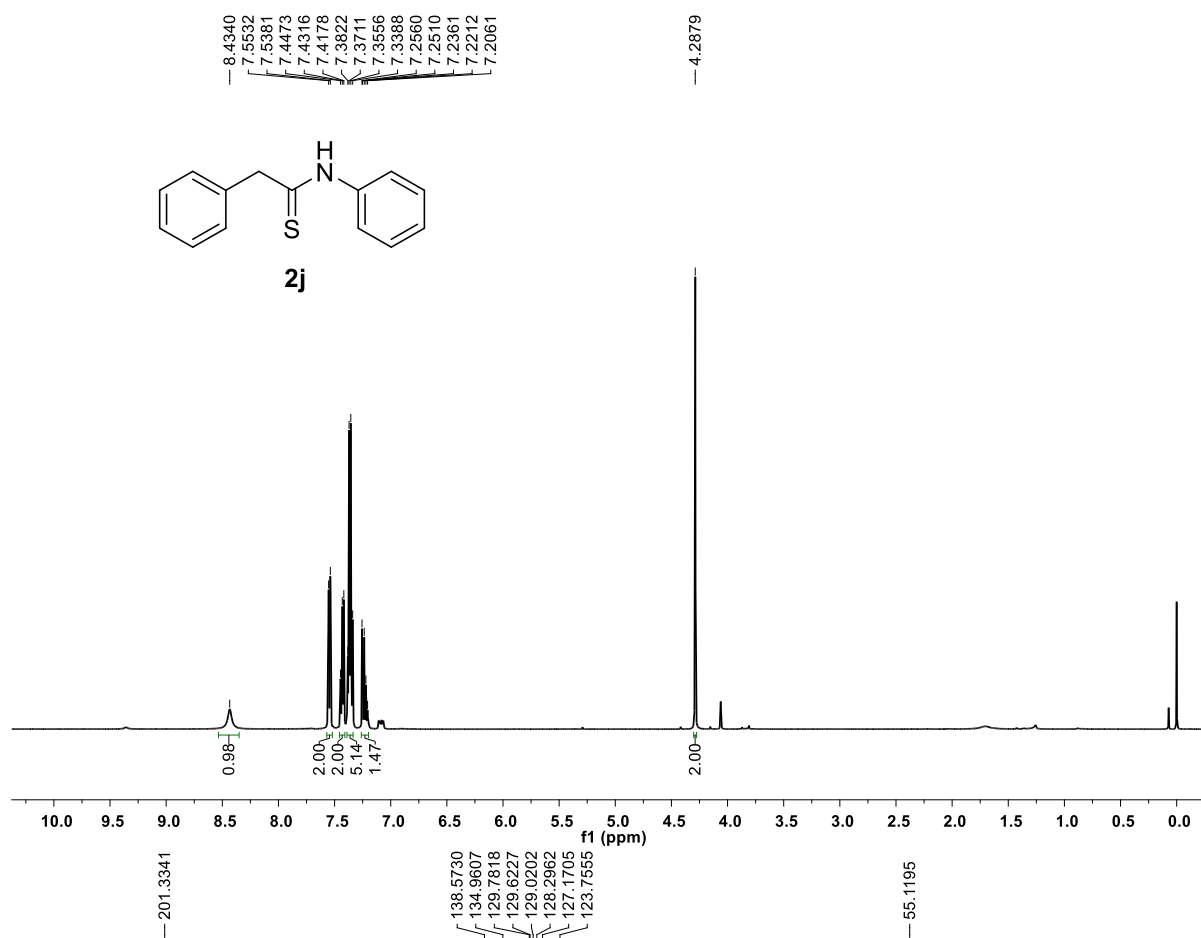
***N*-(4-Iodophenyl) benzothioamide (2h)**^[5] Yield: 78%; Yellow solid, m.p.: 143.6-145.9 °C; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 11.79 (br, 1H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.56-7.50 (m, 1H), 7.50-7.42 (m, 2H). ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 197.7, 142.6, 139.8, 137.2, 130.8, 128.0, 127.4, 126.1, 90.9.



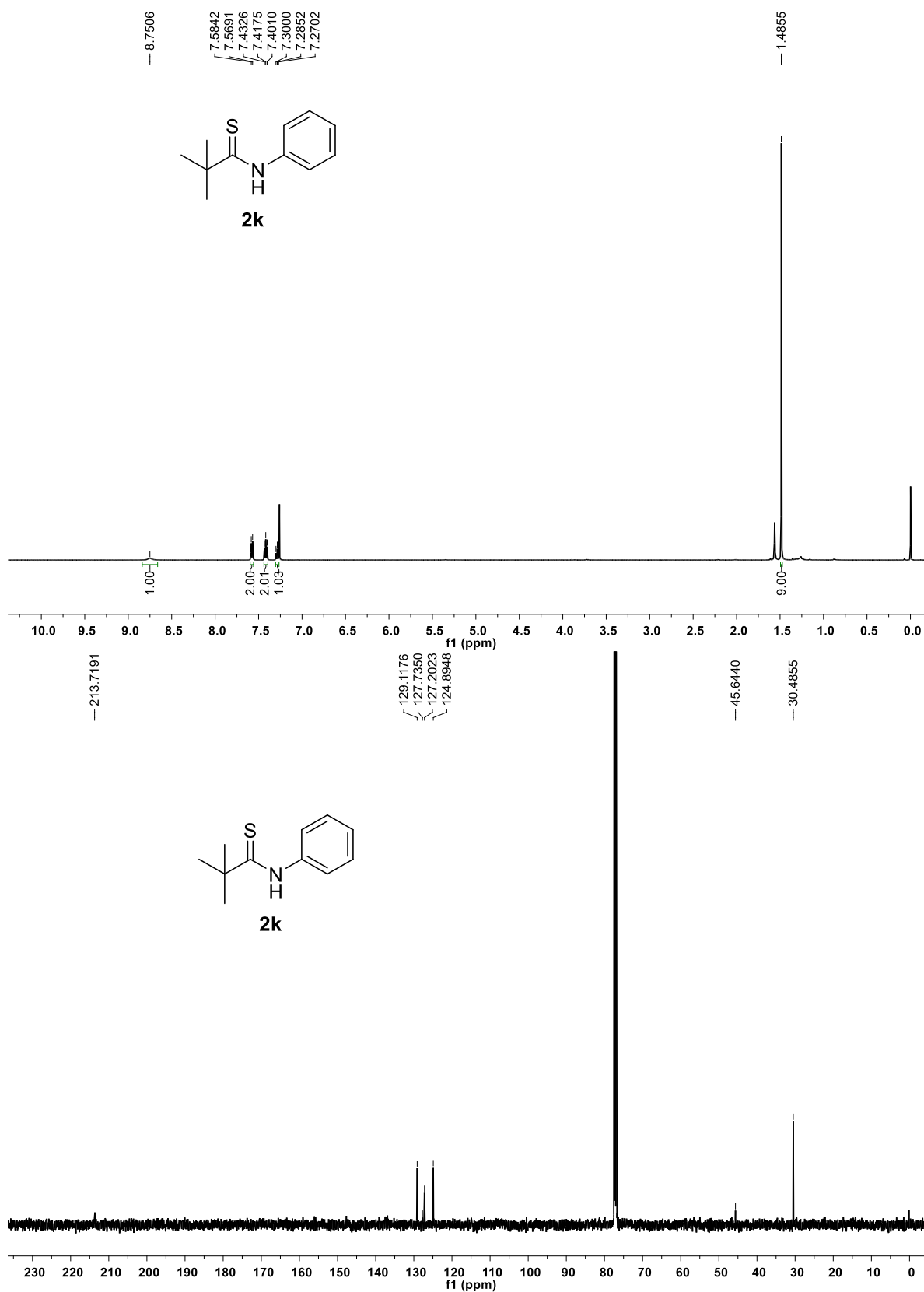
***N*-(3-Chlorophenyl) benzothioamide (2i)**^[3] Yield: 75%; Yellow solid, m.p.: 96.5-97.8 °C; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 11.86 (br, 1H), 8.08 (s, 1H), 7.88-7.78 (m, 3H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.51-7.45 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 198.2, 142.6, 141.4, 132.6, 130.9, 130.2, 128.1, 127.5, 126.0, 123.6, 122.6.



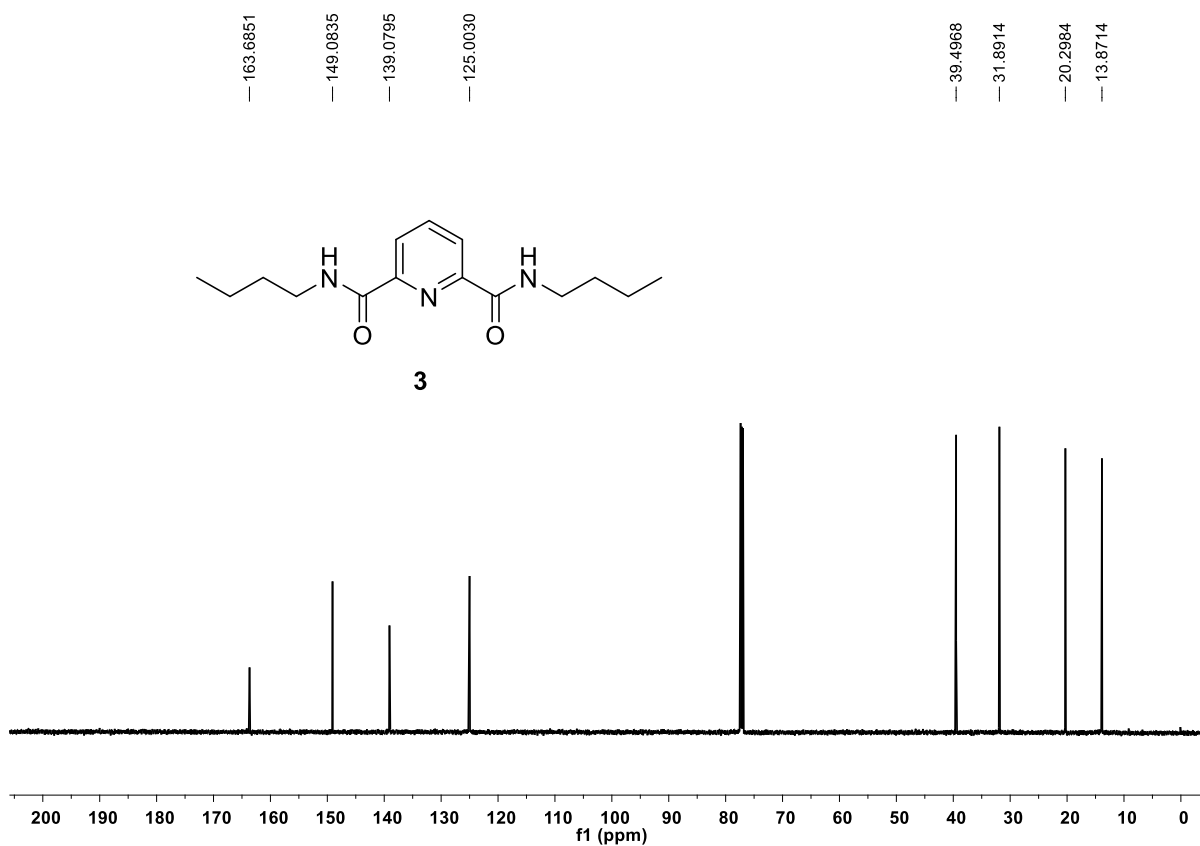
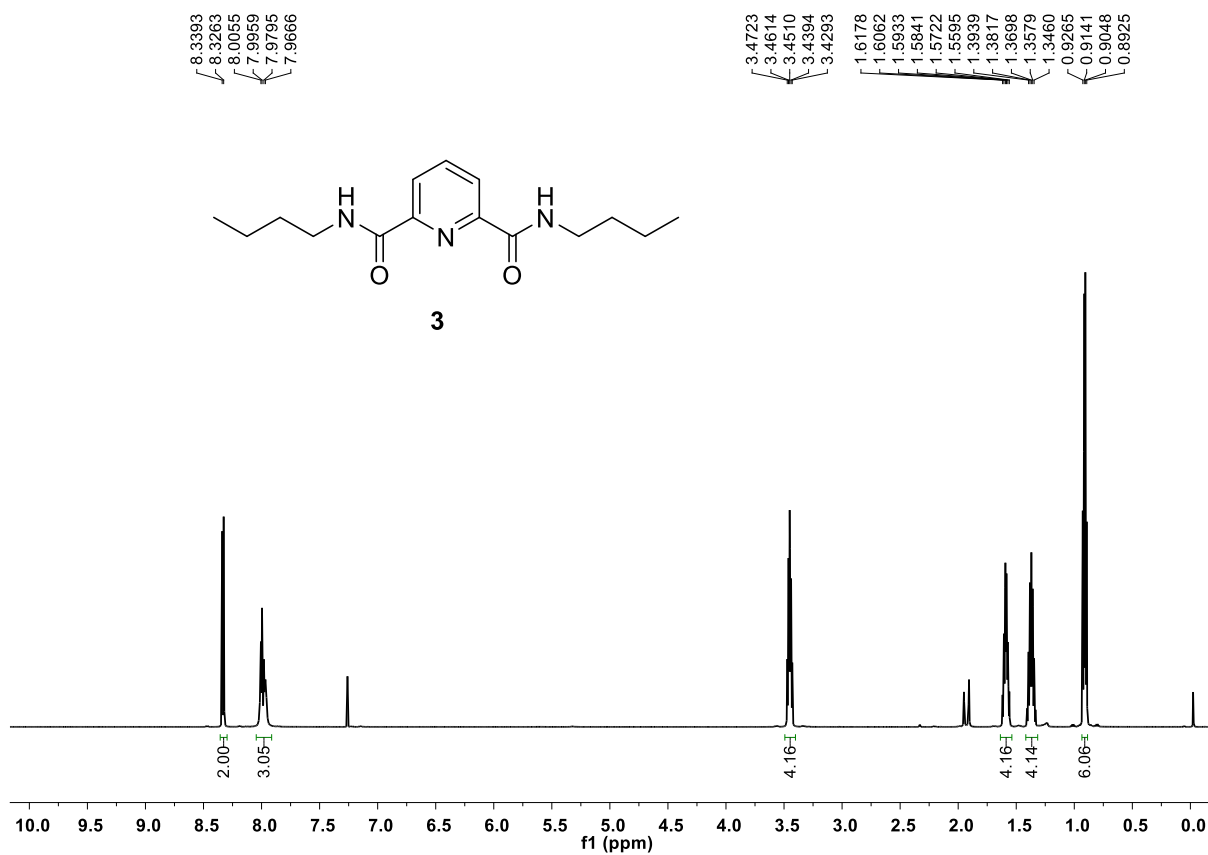
N-Phenyl phenylacetothioamide (2j)^[6] Yield: 70%; Yellow solid, m.p.: 88.5-89.1 °C; ¹H NMR (CDCl₃, 500 MHz): δ = 8.43 (br, 1H), 7.55 (d, *J* = 7.7 Hz, 2H), 7.46-7.41 (m, 2H), 7.39-7.33 (m, 5H), 7.26-7.20 (m, 1H), 4.29 (s, 2H). ¹³C NMR (CDCl₃, 125 MHz): δ = 201.3, 138.6, 135.0, 129.8, 129.6, 129.0, 128.3, 127.2, 123.8, 55.1.



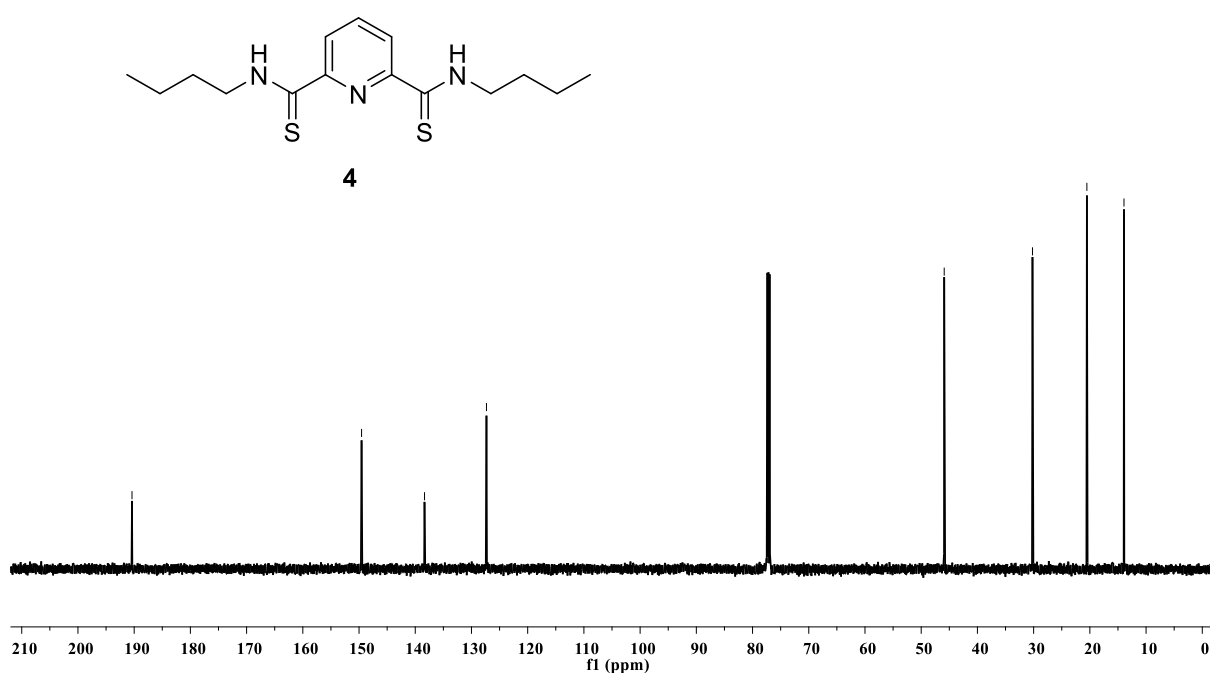
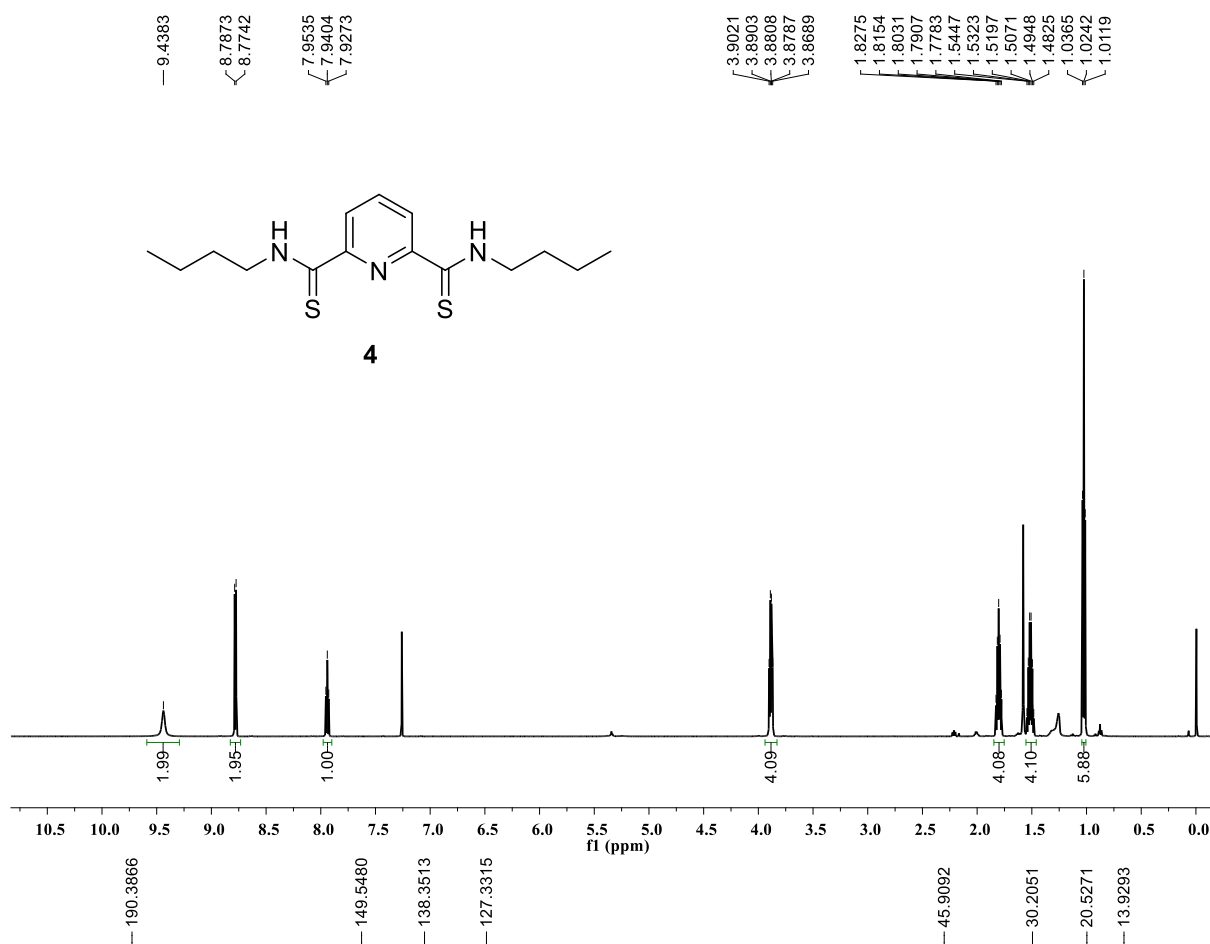
***N*-Phenyl pivalthioamide (2k)**^[7] Yield: 76%; Yellow solid, m.p.: 86.5-88.3 °C; ¹H NMR (CDCl₃, 500 MHz): δ = 8.75 (br, 1H), 7.58 (d, *J* = 7.7 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 1.49 (s, 9H). ¹³C NMR (CDCl₃, 125 MHz): δ = 213.7, 129.1, 127.7, 127.2, 124.9, 45.6, 30.5.



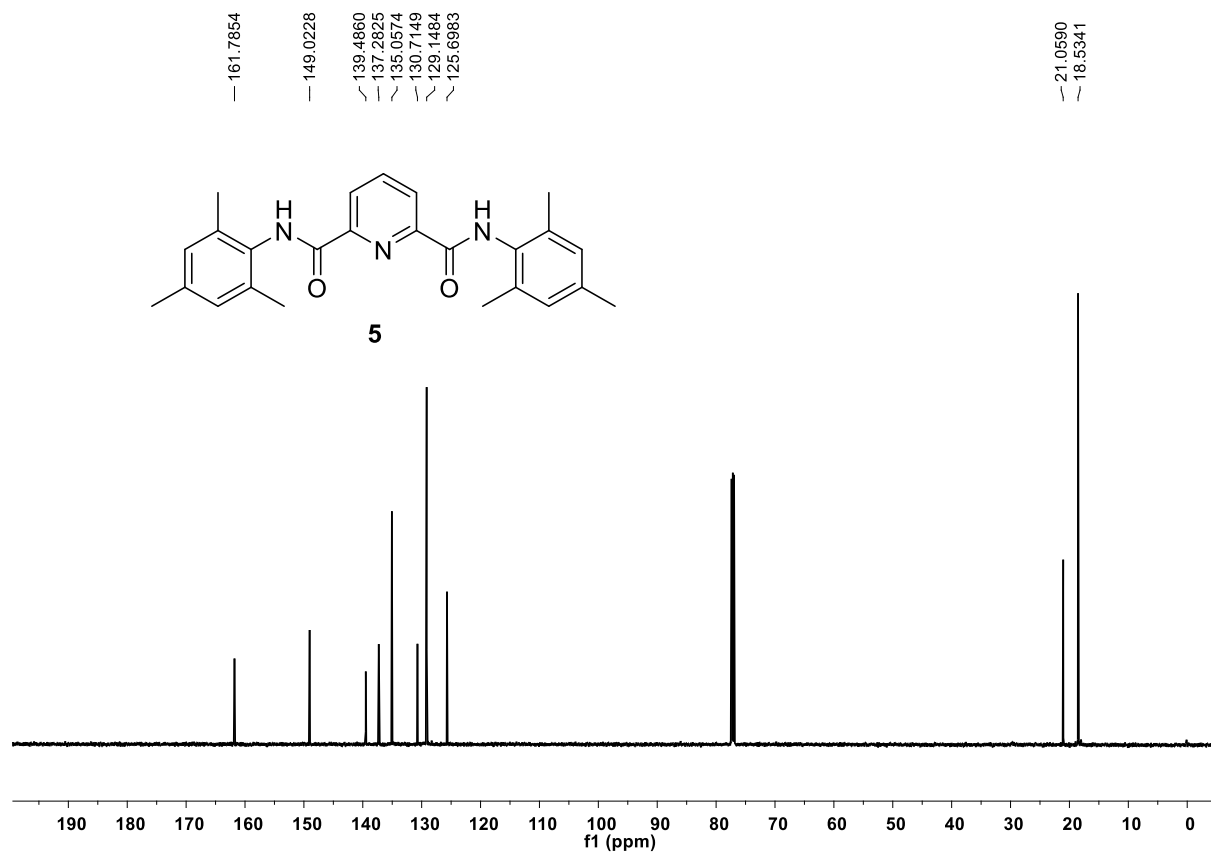
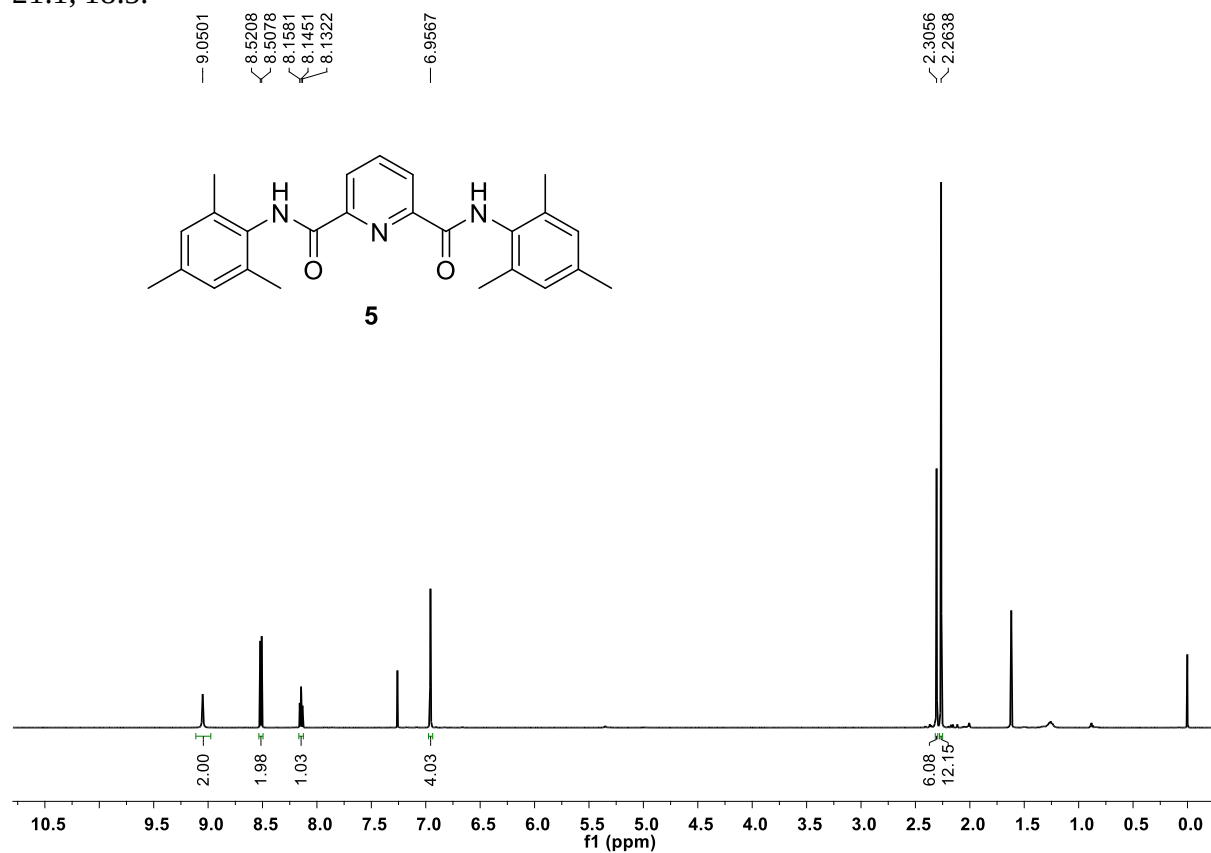
***N*²,*N*⁶-Di(*n*-butyl)pyridine-2,6-(carbothioamide) (3)**^[8] Yield: 70%; White solid. M.p.: 155.2-158.0 °C; ¹H NMR (CDCl₃, 600 MHz): δ = 8.33 (d, *J* = 7.8 Hz, 2H), 8.03-7.94 (m, 3H), 3.48-3.42 (m, 4H), 1.63-1.55 (m, 4H), 1.42-1.32 (m, 4H), 0.93-0.89 (m, 6H). ¹³C NMR (150 MHz, CDCl₃) δ = 163.7, 149.1, 139.1, 125.0, 39.5, 31.9, 20.3, 13.9.



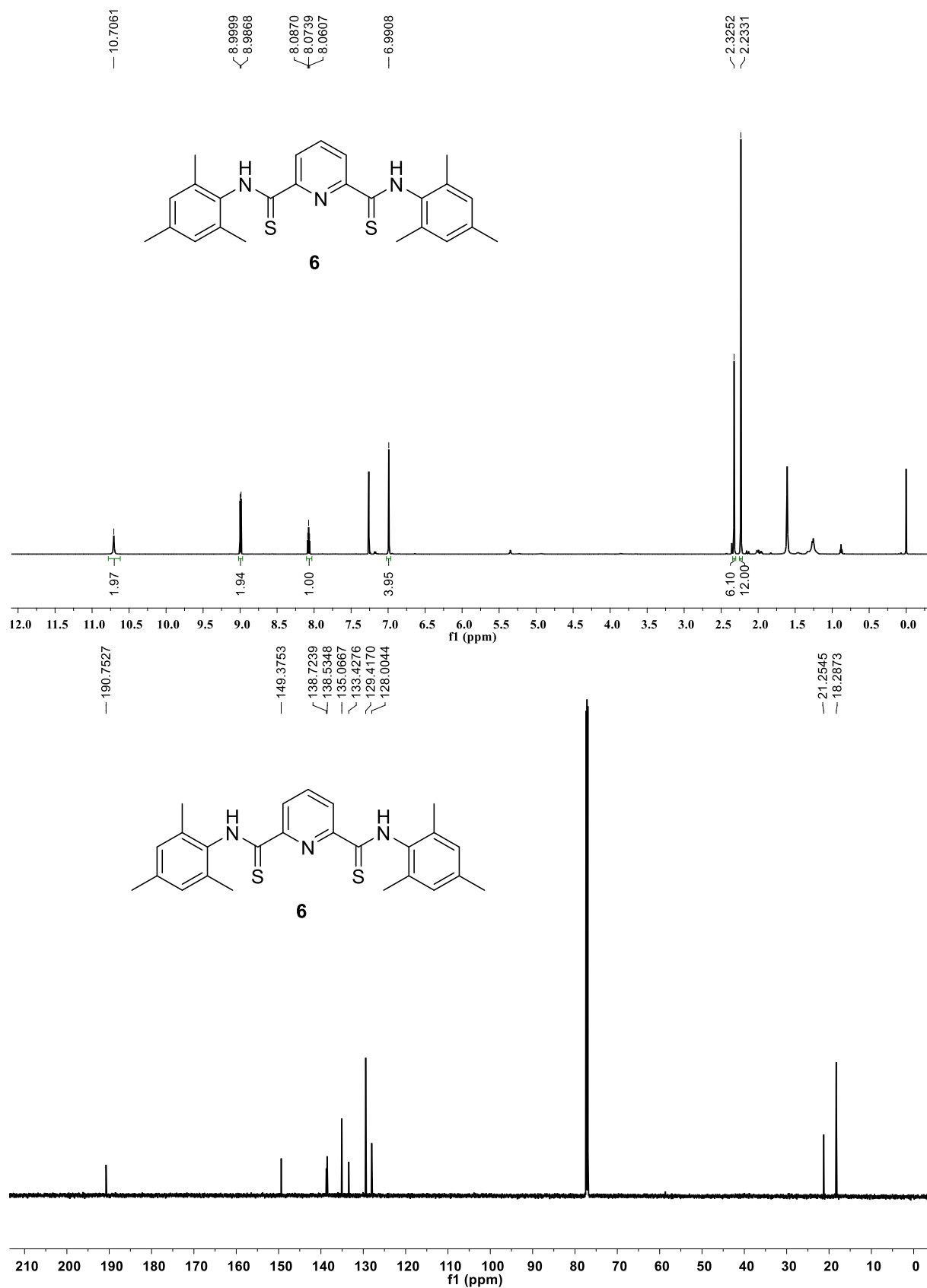
***N*²,*N*⁶-Di(*n*-butyl)pyridine-2,6-bis(carbothioamide) (4)**^[8] Yield: 84%; Yellow solid, m.p.: 72.2-74.5 °C; ¹H NMR (CDCl₃, 600 MHz): δ = 9.44 (br, 2H), 8.78 (d, *J* = 7.8 Hz, 2 H), 7.94 (t, *J* = 7.8 Hz, 1H), 3.91-3.86 (m, 4H), 1.84-1.77 (m, 4H), 1.55-1.48 (m, 4H), 1.02 (t, *J* = 7.4 Hz, 6H). ¹³C NMR (150 MHz, CDCl₃) δ = 190.4, 149.6, 138.4, 127.3, 45.9, 30.2, 20.5, 13.9.



***N*²,*N*⁶-Bis(2,4,6-trimethylphenyl)pyridine-2,6-(carbothioamide) (5)**^[8] Yield: 92%; White solid. M.p.: 191.5-193.3 °C; ¹H NMR (CDCl₃, 600 MHz): δ = 9.05 (s, 1H), 8.51 (d, *J* = 7.8 Hz, 2H), 8.15 (t, *J* = 7.8 Hz, 1H), 6.96 (s, 4H), 2.31 (s, 6H), 2.26 (s, 12 H). ¹³C NMR (150 MHz, CDCl₃) δ = 161.8, 149.0, 139.5, 137.3, 135.1, 130.7, 129.2, 125.7, 77.4, 77.2, 77.0, 21.1, 18.5.

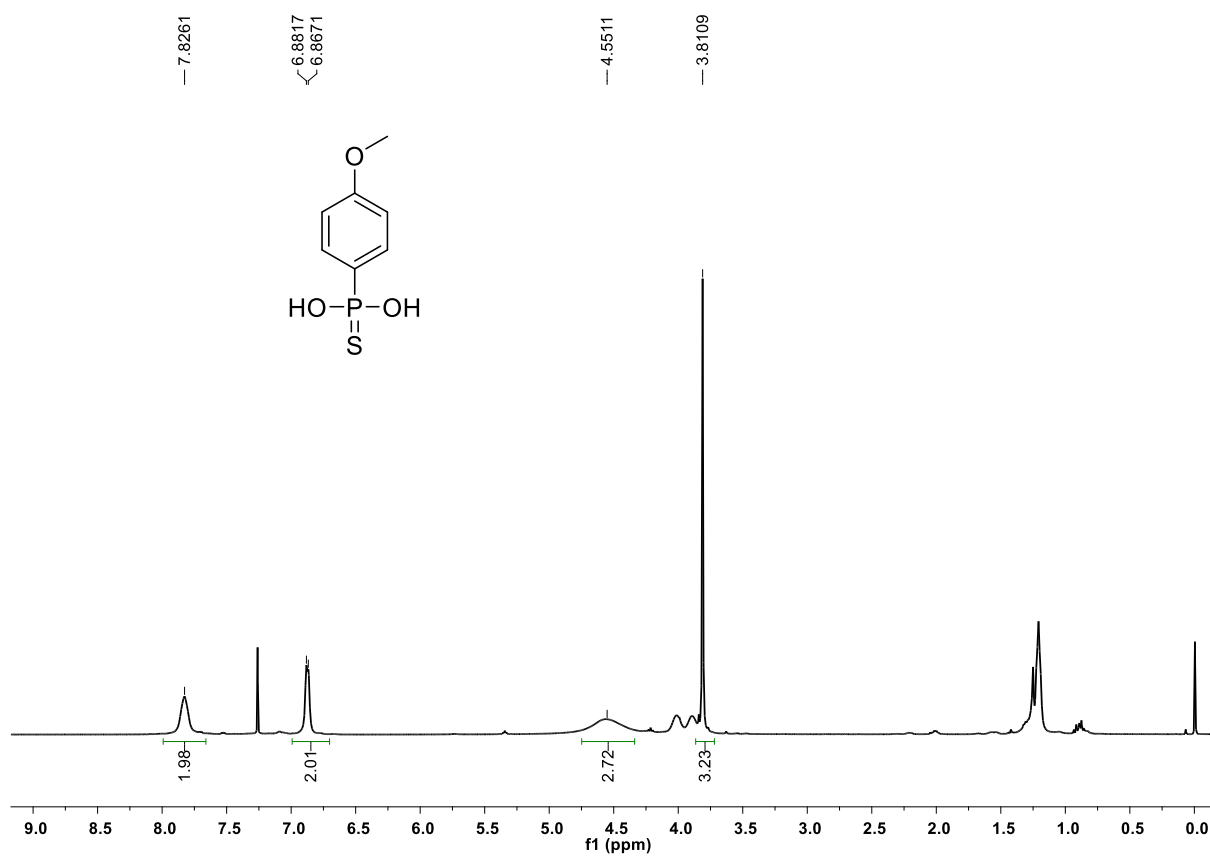


***N*²,*N*⁶-Bis(2,4,6-trimethylphenyl)pyridine-2,6-bis(carbothioamide) (6)^[8]** Yield: 91%; Yellow solid, m.p.: 190.5-193.6 °C; ¹H NMR (CDCl₃, 600 MHz): δ = 10.71 (br, 2H), 8.99 (d, *J* = 7.8 Hz, 2H), 8.07 (t, *J* = 7.8 Hz, 1H), 6.99 (s, 4H), 2.33 (s, 6H), 2.23 (s, 12 H). ¹³C NMR (150 MHz, CDCl₃) δ = 190.8, 149.4, 138.7, 138.5, 135.1, 133.4, 129.4, 128.0, 21.3, 18.3.



(4-Methoxyphenyl)phosphonothioic *O,O*-acid ^[9]

¹H NMR (CDCl₃, 400 MHz): δ = 7.83 (br, 2H), 6.95-6.81 (m, 2H), 4.55 (br, 2H), 3.81 (s, 3H).



3. References

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