Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Unprecedented thiocarbamidation of nitroarenes: A facile one-pot route to unsymmetrical thioureas

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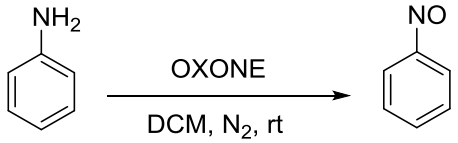
A. General Information

IR spectra were recorded on JASCO FT/IR-4600 in neat condition. NMR spectra were recorded using Bruker Spectrometer at 300, 400, 500, 600 MHz for 1H spectra and at 75, 100, 125, 150 MHz for 13C spectra in $CDCl_3$ and DMSO-d_6 solution. High-resolution mass spectra (HRMS) were performed in methanol solvent on a Waters Micromass Q-tofMicromass spectrometer using electrospray ionization method. Melting points were determined by a LabX India digital melting point apparatus.

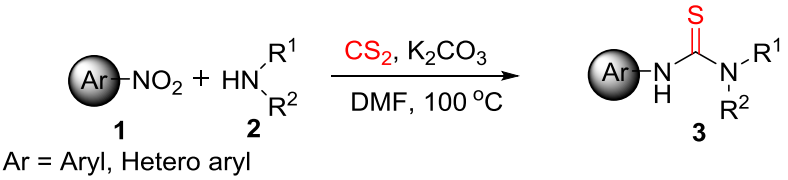
B. Experimental Procedure for the Synthesis of Nitrosobenzene.[1]



Aniline (2 mmol, 0.186 g) was added into dichloromethane (5 ml) and stirred at room temperature for 5 min. Potassium peroxomonosulfate (oxone, 2.2 mmol, 1.35 g) was dissolved in water (5 ml) and added drop wise into the reaction mixture. After stirring for 30 min, the reaction mixture was extracted with dichloromethane (3×10 ml). The organic layer was dried with anhydrous sodium sulfate, filtered and concentrated under reduced pressure to give nitrosobenzene as a black-green oil (0.165 g, yield 77%).

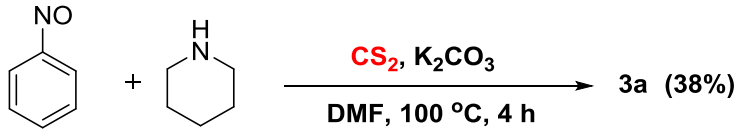
[1] Tian, X.; Zhang, C.; Xu, Q.; Li, Z.; Shao, X.; *Org. Biomol. Chem*. **2017**, *15*, 3320.

C. General Experimental Procedure



2 mmol of CS_2 was added dropwise to a cooled solution of amine (1.2 mmol) in DMF (3 ml) at 0 – 5 ^oC. K_2CO_3 (1.5 mmol) was added to the resulting mixture and it was stirred for 5 min at 0 - 5^oC. Nitroarene (1 mmol) was added to the reaction mixture followed by heating at 100 ^oC for the required time period (monitored by TLC) as mentioned in **Table 2**. After completion of the reaction, the crude product was obtained by usual work-up procedure using EtOAc and the crude was purified by column chromatography using EtOAc-hexane solvent mixture.

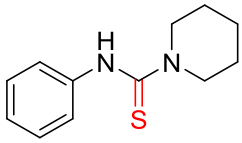
D. Experimental Procedure of the Control Experiment with Nitrosobenzene



Nitrosobenzene (1mmol, 107 mg) was added to a cooled mixture of piperidine (1.2 mmol, 102 mg), CS_2 (2 mmol, 152 mg), K_2CO_3 (1.5 mmol, 207 mg) in DMF (2 ml) followed by stirring at 100 ^oC for 4 h (checked by TLC). After completion of the reaction, the crude product was obtained by usual work up procedure using EtOAc-water mixture. The crude product was purified by column chromatography using EtOAc-hexane solvents mixture to afford **3a** (83 mg, 38%).

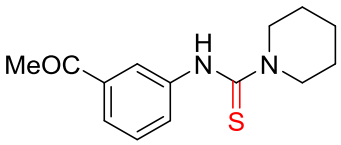
E. Characterization Data of Synthesized Compounds

N-phenylpiperidine-1-carbothioamide (Table 2, 3a)



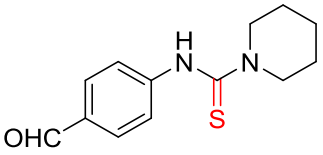
White solid (198 mg, 90% yield); R_f - 0.18 (EtOAc/ Hexane = 10/90, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 96°C; IR (neat) υ 3750, 3704, 3502, 2939, 1697, 1592, 1319, 1131, 854, 739 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.38 (s, 1*H*), 7.33-7.29 (m, 2*H*), 7.14-7.10 (m, 3*H*), 3.77-3.76 (m, 4*H*), 1.65 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 182.53, 140.38, 128.95, 124.77, 122.90, 50.80, 25.47, 24.08 ppm.

N-(3-acetylphenyl)piperidine-1-carbothioamide (Table 2, 3b)



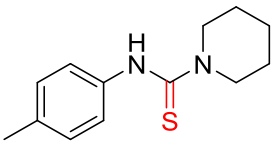
White solid (241 mg, 92% yield); R_f - 0.2 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 20/80, v/v); melting point: 140-142°C; IR (neat) υ 3553, 3462, 2687, 1669, 1482, 1397, 1266, 895, 727 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.74 (s, 1*H*), 7.69 (s, 1*H*), 7.62 (d, *J* = 10 Hz, 1*H*), 7.43 (d, *J* = 5 Hz, 1*H*), 7.32 (m, 1*H*), 3.80-3.79 (m, 4*H*), 2.5 (s, 3*H*), 1.62 (s, 6*H*) ppm.^{13}C NMR ($CDCl_3$, 125 MHz) δ197.86, 181.69, 140.85, 137.44, 128.79, 128.65, 124.59, 123.22, 50.23, 26.61, 25.48, 24.02 ppm. HRMS: calcd for $C_{14}H_{18}N_2OS$ $[M]^+$ 262.1140; found 262.7686.

N-(4-formylphenyl)piperidine-1-carbothioamide (Table 2, 3c)



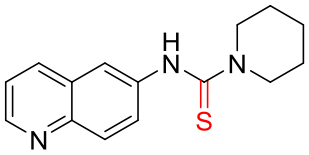
Yellow oil (198 mg, 80% yield); R_f - 0.16 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 20/80, v/v); IR (neat) υ 3845, 3628, 2884, 1694, 1471, 1262, 985, 763cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ9.88 (s, 1*H*), 7.80 (d, *J* = 10 Hz, 2*H*), 7.55 (s, 1*H*), 7.19 (d,*J* = 5 Hz, 2*H*), 3.80-3.79 (m, 4*H*), 1.68 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ190.92, 181.21, 145.89, 131.49, 130.72, 120.80, 50.96, 25.46, 23.89 ppm. HRMS: calcd for $C_{13}H_{16}N_2OS$ $[M+H]^+$249.0983; found 249.1951.

N-(p-tolyl)piperidine-1-carbothioamide (Table 2, 3d)



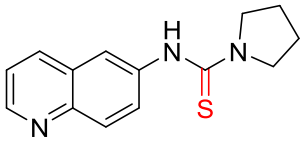
White solid (217 mg, 93% yield); R_f - 0.18 (EtOAc/ Hexane = 10/90, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 126-127°C; IR (neat) υ 3605, 3448, 2930, 1526, 1426, 1302, 1120, 1009, 812, 723 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.26 (s, 1*H*), 7.15-7.10 (m, 2*H*), 7.00 (d, *J* = 10Hz, 2*H*), 3.76-3.75 (m, 4*H*), 2.31 (s, 3*H*)1.64 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ182.97, 137.92, 134.88, 129.71, 123.40, 50.79, 25.57, 24.22, 21.00 ppm.

N-(quinolin-6-yl)piperidine-1-carbothioamide (Table 2, 3e)



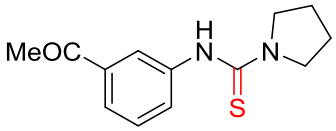
White solid (224 mg, 83% yield); R_f - 0.45 (EtOAc/ Hexane = 40/60, v/v); purified by column chromatography using EtOAc/hexane = 20/80, v/v); melting point: 155-156°C; IR (neat) υ 3740, 3543, 2943, 1547, 1495, 1252, 1005, 835, 718 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ8.82-8.80 (m, 1*H*), 8.03-8.00 (m, 2*H*), 7.55-7.48 (m, 2*H*), 7.44 (s, 1*H*), 7.36-7.33 (m, 1*H*), 3.83-3.82 (m, 4*H*), 1.66 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ169.74, 151.02, 147.67, 144.67, 131.58, 127.92, 124.18, 123.32, 122.88, 121.03, 49.72, 25.22, 24.13 ppm. HRMS: calcd for $C_{15}H_{17}N_3S$ $[M]^+$271.1143; found 271.0937.

N-(quinolin-6-yl)pyrrolidine-1-carbothioamide (Table 2, 3f)



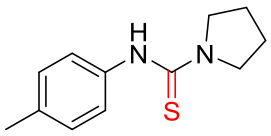
White solid (215 mg, 84% yield); R_f - 0.18 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 20/80, v/v); melting point: 156°C; IR (neat) υ3697, 3457, 3170, 2884, 1549, 1263, 987, 894, 718 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ8.88-8.87 (m, 1*H*), 8.09 (t, *J* = 3 Hz, 2*H*), 7.89 (d, *J* = 3 Hz, 1*H*), 7.79 – 7.76 (m, 1*H*), 7.41-7.37 (m, 1*H*), 7.29 (s, 1*H*), 3.74 (brs, 4*H*),2.05 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ178.30, 150.03, 146.38, 137.57, 135.88, 129.74, 128.51, 128.45, 121.73, 121.53, 43.59, 25.94 ppm. HRMS: calcd for $C_{14}H_{15}N_3S$ $[M+H]^+$258.0987; found 258.1922.

N-(3-acetylphenyl)pyrrolidine-1-carbothioamide (Table 2, 3g)



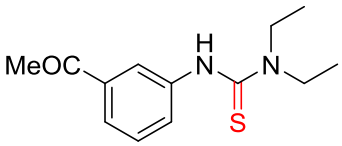
White solid (203 mg, 82% yield); R_f - 0.32 (EtOAc/ Hexane = 40/60, v/v); purified by column chromatography using EtOAc/hexane = 25/75, v/v); melting point: 118°C; IR (neat) υ 3733, 3434, 2982, 1696, 1546, 1267, 896, 745 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz) δ7.92-7.91 (m, 1*H*), 7.77-7.71 (m, 2*H*), 7.46-7.41 (m, 1*H*), 7.11 (s, 1*H*), 3.73 (brs, 4*H*), 2.59 (s, 3*H*), 2.05 (s, 4*H*) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz) δ197.81, 177.97, 139.75, 137.47, 130.30, 128.69, 125.46, 124.76, 52.52, 48.11, 26.76, 26.26, 24.76 ppm. HRMS: calcd for $C_{13}H_{16}N_2OS$ $[M+H]^+$249.0983; found 249.1790.

N-(p-tolyl)pyrrolidine-1-carbothioamide (Table 2, 3h)



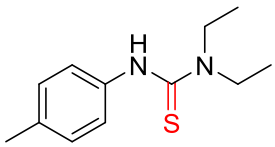
White solid (187 mg, 85% yield); R_f - 0.4 (EtOAc/ Hexane = 50/50, v/v); purified by column chromatography using EtOAc/hexane = 25/75, v/v); melting point: 166-168°C; IR (neat) υ3731, 3334, 2883, 1520, 1394, 1285, 811, 726 cm^{-1}. ^{1}H NMR (DMSO-d_6, 500 MHz) δ8.78 (s, 1*H*), 7.24 (d, *J* = 10 Hz, 2*H*), 7.10 (d, *J* = 10 Hz, 2*H*), 3.62 (s, 4*H*), 2.29 (s, 3*H*), 2.00-1.93 (m, 4*H*) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz),δ177.68, 137.98, 133.32, 128.14, 125.71, 49.94, 24.85, 20.38 ppm.

3-(3-acetylphenyl)-1,1-diethylthiourea (Table 2, 3i)



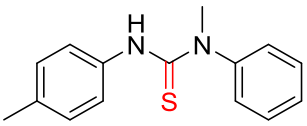
Brown solid (192 mg, 77% yield); R_f - 0.42 (EtOAc/ Hexane= 50/50, v/v); purified by column chromatography using EtOAc/hexane = 25/75, v/v); melting point: 110°C; IR (neat) υ 3667, 3497, 2976, 1685, 1428, 1263, 898, 736 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz) δ7.83 (s, 1*H*), 7.71 (d, *J* = 4Hz, 1*H*), 7.63 (d, *J* = 8Hz, 1*H*), 7.39 (d, *J* = 4Hz, 1*H*), 7.28(s, 1*H*), 3.77-3.75 (m, 4*H*), 2.54 (s, 3*H*), 1.28 (t, *J* = 8Hz, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 100MHz),δ198.03, 180.45, 140.41, 137.53, 131.10, 128.76, 125.69, 125.35, 45.86, 26.91, 12.83ppm. HRMS: calcd for $C_{13}H_{18}N_2OS$ $[M+H]^+$251.1140; found 251.0291.

1,1-diethyl-3-(p-tolyl)thiourea (Table 2, 3j)



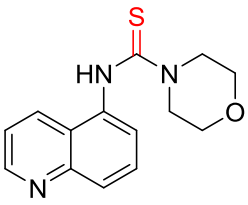
Yellow oil (177 mg, 80% yield); R_f - 0.32 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); IR (neat) υ 3780, 3253, 2885, 1528, 1350, 1280, 828, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ7.26-7.07 (m, 4*H*), 7.02 (s, 1*H*), 3.75-3.73 (m, 4*H*), 2.32 (s, 3*H*), 1.28 (m, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ180.52, 136.84, 135.33, 128.96, 125.92, 45.34, 20.75, 12.40 ppm.

1-methyl-1-phenyl-3-(p-tolyl)thiourea (Table 2, 3k)



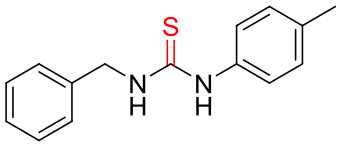
Yellow solid (212 mg, 83% yield); R_f - 0.44 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 10/90, v/v); melting point: 116-118°C; IR (neat) υ 3630, 3370, 2982, 2684, 1514, 1263, 1099, 816, 733 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ7.52 (t, J = 10 Hz, 2*H*), 7.42 (t, J = 10 Hz, 1*H*), 7.38 (d, J = 5 Hz, 2*H*), 7.16 (d, J = 10 Hz, 2*H*), 7.12 (d, J = 10 Hz, 2*H*), 6.91 (s, 1*H*), 3.74 (s, 3*H*), 2.59 (s, 3*H*), 2.30(s, 3*H*) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ182.08, 143.39, 136.95, 135.97, 130.84, 129.33, 128.79, 127.14, 125.92, 43.66, 21.07 ppm.

N-(quinolin-5-yl)morpholine-4-carbothioamide (Table 2, 3l)



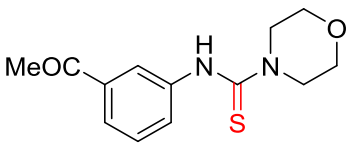
Yellow solid (237 mg, 87% yield); R_f - 0.34 (EtOAc/ Hexane = 50/50, v/v); purified by column chromatography using EtOAc/hexane = 25/75, v/v); melting point: 114°C; IR (neat) υ 3854, 3668, 2870, 1510, 1258, 875, 720 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.95 (s, 1*H*), 8.29 (d, J = 8 Hz, 1*H*), 8.02 (d, J = 12 Hz, 1*H*), 7.69 (t, J = 8 Hz, 1*H*), 7.46 (t, J = 8Hz, 1*H*), 7.33 (d, J = 4 Hz, 1*H*), 3.84-3.83 (m, 4*H*), 3.74-3.71 (m, 4*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ185.37, 151.07, 149.11, 136.18, 131.08, 129.16, 128.58, 124.42, 122.73, 121.63, 66.23, 49.82 ppm. HRMS: calcd for $C_{14}H_{15}N_3OS$ $[M+H]^+$274.0936; found 274.1769.

1-benzyl-3-(p-tolyl)thiourea (Table 2, 3m)



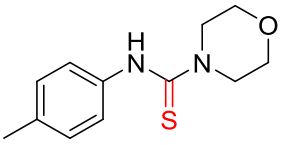
White solid (230 mg, 90% yield); R_f - 0.40 (EtOAc/ Hexane= 20/80, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 118°C; IR (neat) υ 3845, 3682, 3128, 2981, 1690, 1509, 1247, 814, 726 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ7.72 (s, 1*H*), 7.30-7.24 (m, 5*H*), 7.17 (d, J = 8 Hz, 2*H*), 7.07 (d, J = 8 Hz, 2*H*), 6.16 (s, 1*H*), 4.84 (d, J = 4 Hz, 2*H*), 2.31(s, 3*H*) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz) δ180.31, 130.86, 130.18, 128.80, 127.74, 127.65, 125.63, 125.55, 49.46, 21.11 ppm.

N-(3-acetylphenyl)morpholine-4-carbothioamide (Table 2, 3n)



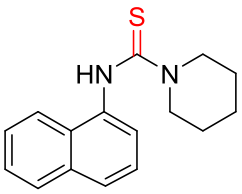
White solid (234 mg, 89% yield); R_f - 0.48 (EtOAc/ Hexane= 30/70, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 150-152°C; IR (neat) υ3618, 3327, 2985, 1683, 1556, 1391, 1263, 895, 728 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz) δ7.76-7.72 (m, 2*H*), 7.68 (s, 1*H*), 7.53-7.49 (m, 1*H*), 7.43 (t, J = 12 Hz, 1*H*), 3.90-3.89 (m, 4*H*), 3.77-3.76 (m, 4*H*), 2.58 (s, 3*H*) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz) δ197.87, 183.05, 140.36, 137.75, 129.10, 128.88, 125.39, 123.06, 66.16, 49.15, 26.79 ppm. HRMS: calcd for $C_{13}H_{16}N_2O_2S$ $[M]^+$264.0932; found 264.0849.

N-(p-tolyl)morpholine-4-carbothioamide (Table 2, 3o)



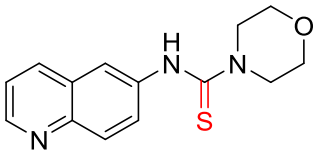
White solid (205 mg, 87% yield); R_f - 0.4 (EtOAc/ Hexane = 30/70, v/v); purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 146-148°C; IR (neat) υ 3637, 3114, 2681, 1560, 1328, 1263, 890, 743 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz) δ7.46 (s, 1*H*), 7.12 (d, *J* = 6 Hz, 2*H*), 7.02 (d, *J* = 6 Hz, 2*H*), 3.78-3.77 (m, 4*H*), 3.70-3.68 (m, 4*H*), 2.32 (s, 3*H*) ppm.^{13}C NMR ($CDCl_3$, 150 MHz) δ183.39, 137.20, 135.40, 129.69, 123.90, 66.11, 49.33, 20.98 ppm.

N-(naphthalen-1-yl)piperidine-1-carbothioamide (Table 2, 3p)



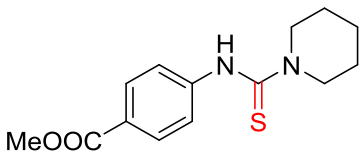
Yellow oil (218 mg, 81% yield); R_f - 0.36 (EtOAc/ Hexane = 10/90, v/v); purified by column chromatography using EtOAc/hexane = 10/90, v/v); IR (neat) υ 3650, 3399, 2835, 1502, 1331, 1028, 749 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.90 (s, 1*H*), 7.84-7.79 (m, 1*H*), 7.66-7.58 (m, 2*H*), 7.46-7.36 (m, 3*H*), 7.16 (d, *J* = 5 Hz, 1*H*), 3.66 (s, 1*H*), 1.54-1.42 (m, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ184.05, 136.52, 134.38, 128.44, 127.41, 126.61, 125.54, 123.50, 122.69, 122.11, 121.36, 51.07, 25.43, 24.05 ppm. HRMS: calcd for $C_{16}H_{18}N_2S$ $[M]^+$270.1191; found 270.1987.

N-(quinolin-6-yl)morpholine-4-carbothioamide (Table 2, 3q)



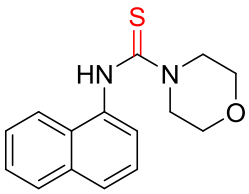
White solid (232 mg, 85% yield); R_f - 0.2 (EtOAc/ Hexane = 50/50, v/v); purified by column chromatography using EtOAc/hexane = 30/70, v/v); melting point: 110°C; IR (neat) υ 3845, 3554, 2984, 1508, 1265, 897, 745 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ9.63 (s, 1*H*), 8.89 (s, 1*H*), 8.24 (d, *J* = 8Hz, 1*H*), 7.94 (d, *J* = 8 Hz, 1*H*), 7.74 (t, *J* = 8Hz, 1*H*), 7.52-7.40 (m, 2*H*) 3.99 (s, 4*H*), 3.73 (s, 4*H*)ppm. ^{13}C NMR (DMSO-d_6, 100 MHz) δ183.03, 150.32, 148.21, 137.53, 132.53, 132.48, 128.84, 127.44, 125.90, 125.88, 121.03, 65.78, 48.41 ppm. HRMS: calcd for $C_{14}H_{15}N_3OS$ $[M+H]^+$274.0936; found 274.1769.

methyl 4-(piperidine-1-carbothioamido)benzoate (Table 2, 3r)



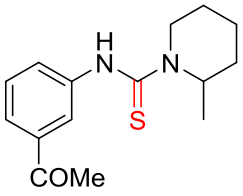
Brown solid (233 mg, 84% yield); R_f - 0.34 (EtOAc/ Hexane= 50/50, v/v); purified by column chromatography using EtOAc/hexane = 25/75, v/v); melting point: 148°C; IR (neat) υ 3520, 3421, 3181, 2889, 1937, 1713, 1606, 1248, 1108, 848, 765 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ7.94 (d, *J* = 10Hz, 2*H*), 7.55(s, 1*H*), 7.10 (d, *J* = 10 Hz, 2*H*), 3.87 (s, 3*H*), 3.75 (s, 4*H*), 1.65 (s, 6*H*) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ182.40, 166.50, 144.57, 130.74, 125.52, 120.60, 51.93, 51.18, 25.54, 24.07 ppm. HRMS: calcd for $C_{14}H_{18}N_2O_2S$ $[M+H]^+$ 279.1089; found 279.1947.

N-(naphthalen-1-yl)morpholine-4-carbothioamide (Table 2, 3s)



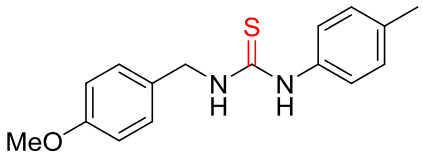
Yellow oil (212 mg, 78% yield); R_f - 0.24 (EtOAc/ Hexane = 30/70, v/v); purified by column chromatography using EtOAc/hexane = 20/80, v/v); IR (neat) υ 3550, 3280, 2848, 1524, 1420, 1320, 887, 750 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ7.97 (d, J = 5Hz, 1*H*), 7.90-7.87 (m, 1*H*), 7.76 (d, J = 5 Hz, 1*H*), 7.60-7.43 (m, 4*H*), 7.28 (s, 1*H*), 3.84 (m, 4*H*),3.67 (m, 4*H*) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ185.45, 136.16, 134.58, 128.70, 128.40, 126.97, 126.83, 126.78, 125.66, 122.03, 121.64, 66.17, 50.09 ppm.

N-(3-acetylphenyl)-2-methylpiperidine-1-carbothioamide (Table 2, 3t)



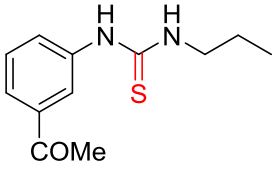
Yellow solid (248 mg, 90% yield); R_f - 0.42 (EtOAc/ Hexane = 30/70, v/v), purified by column chromatography using EtOAc/hexane = 15/85, v/v); melting point: 122°C; IR (neat) υ 3751, 3617, 3177, 1685, 1567, 1310, 1262, 890, 743 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ7.69-7.61 (m, 3*H*), 7.42 (d, J = 5Hz, 1*H*), 7.32 (t, J = 5 Hz, 1*H*), 5.15 (s, 1*H*), 4.37 (d, J = 10Hz, 1*H*), 3.07 (t, J = 10 Hz, 1*H*), 2.50 (s, 3*H*), 1.75-1.48 (m, 6*H*), 1.23 (d, J = 5Hz, 3*H*)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ197.88, 182.02, 140.97, 137.44, 128.91, 128.69, 124.66, 123.31, 52.00, 44.13, 29.94, 26.65, 25.42, 18.32, 15.46 ppm.HRMS: calcd for $C_{15}H_{20}N_2OS$ $[M+Na]^+$299.1296; found 299.2150.

1-(4-methoxybenzyl)-3-(p-tolyl)thiourea (Table 2, 3u)



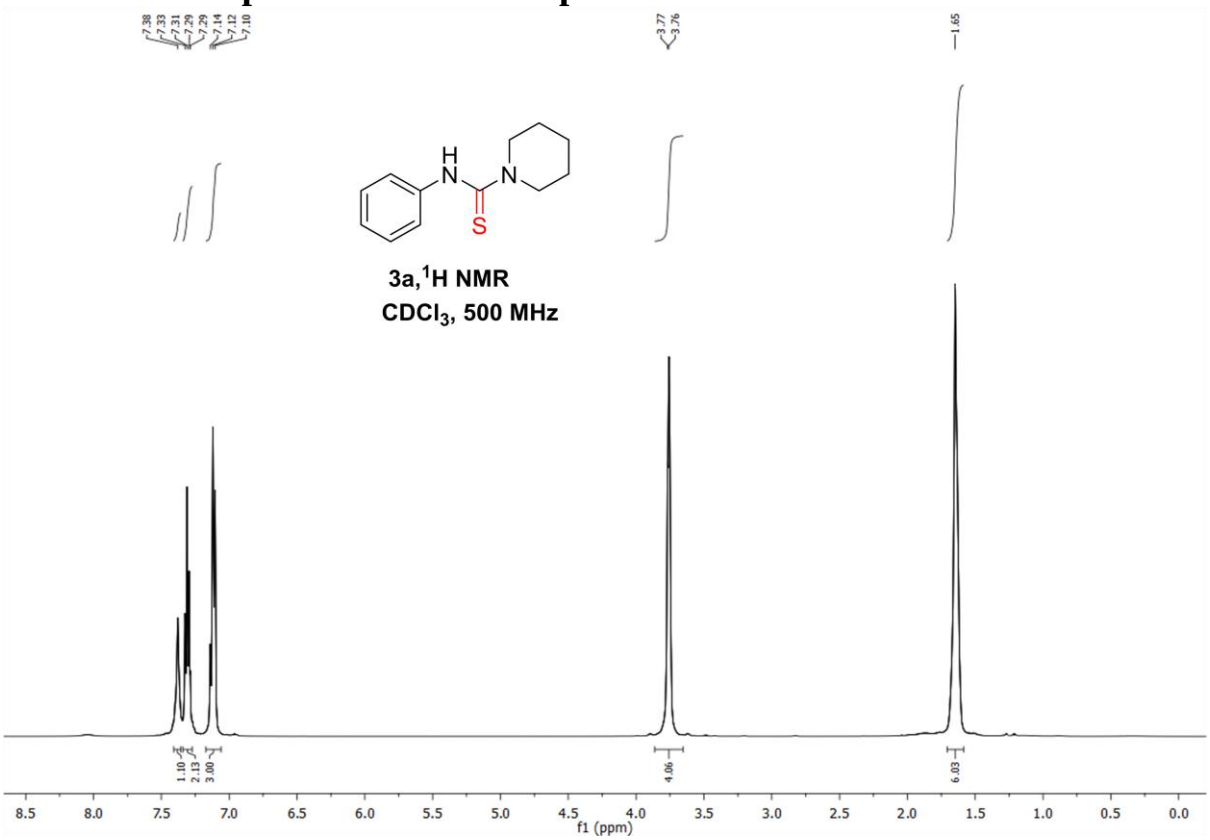
Yellow oil (243 mg, 85% yield); R_f - 0.46 (EtOAc/ Hexane = 20/80, v/v); purified by column chromatography using EtOAc/hexane = 15/75, v/v); IR (neat) υ 3851, 3217, 3067, 2945, 1592, 1566, 1462, 1132, 1022, 924, 812 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ7.74 (s, 1*H*), 7.27 (d, J = 8 Hz, 2*H*), 7.17 (d, J = 8 Hz, 2*H*), 7.07 (d, J = 8 Hz, 2*H*), 6.83 (d, J = 8 Hz, 2*H*), 6.18 (s, 1*H*), 4.83 (d, J = 4 Hz, 2*H*), 3.75 (s, 3*H*), 2.33 (s, 3*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ179.31, 159.11, 137.23, 134.45, 133.32, 130.12, 128.70, 125.55, 113.95, 64.68, 55.34, 21.18 ppm. HRMS: calcd for $C_{16}H_{18}N_2OS$ $[M]^+$286.1140; found 286.1274.

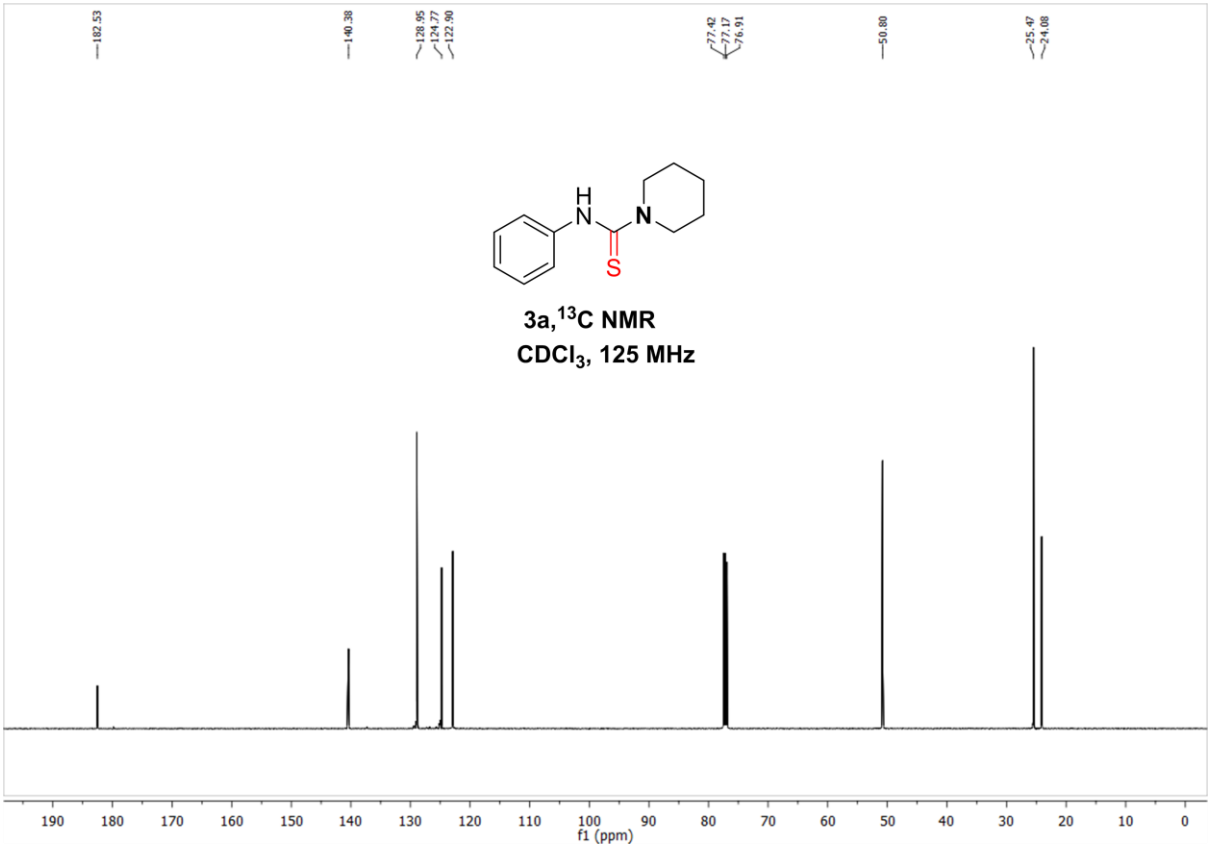
1-(3-acetylphenyl)-3-propylthiourea (Table 2, 3v)

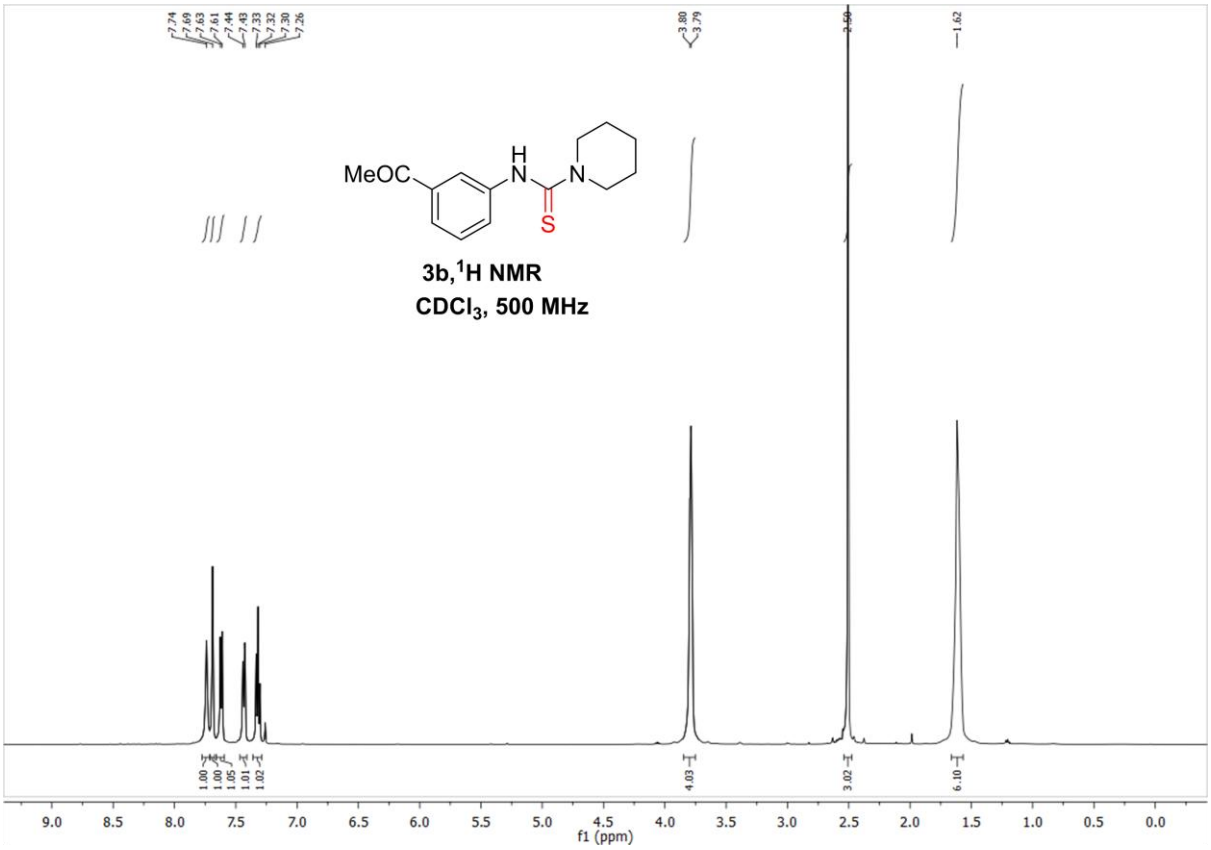


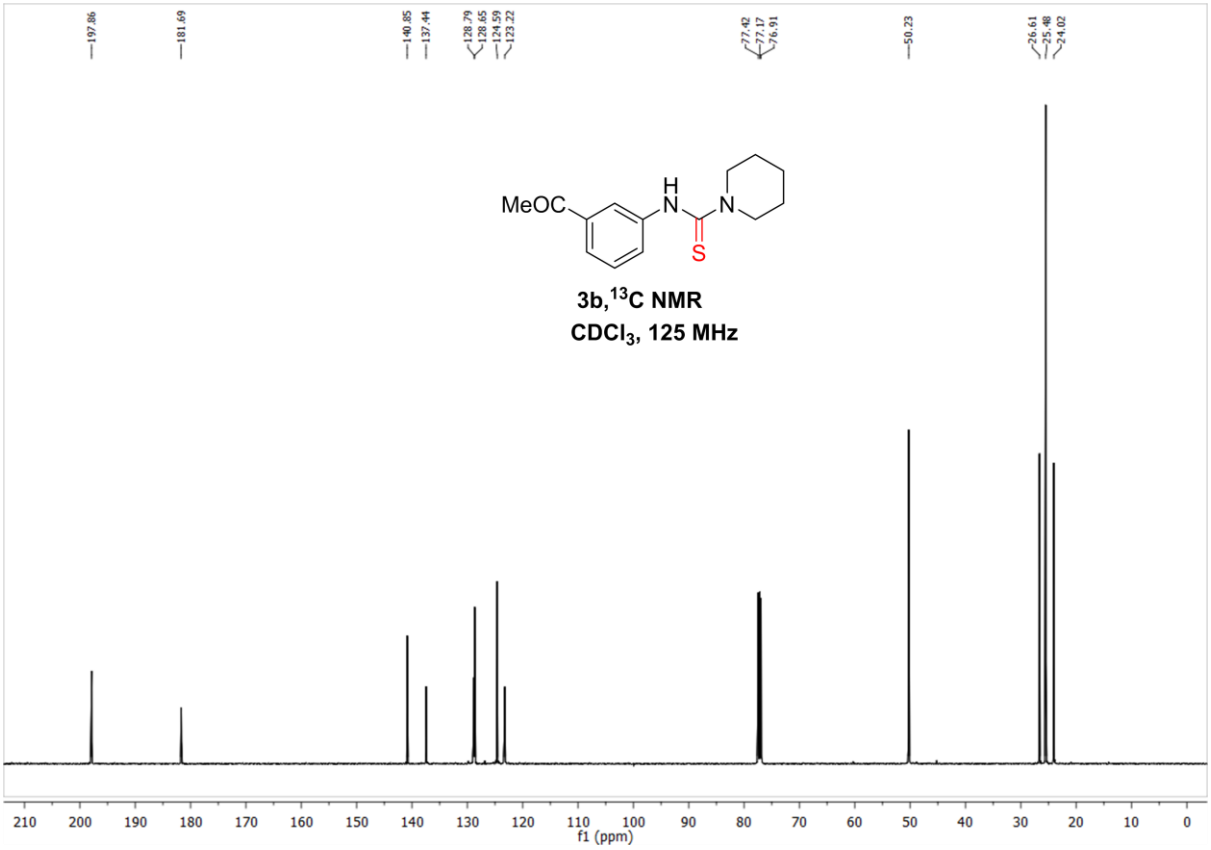
Yellow oil (207 mg, 88% yield); R_f - 0.62 (EtOAc/ Hexane = 30/70, v/v); purified by column chromatography using EtOAc/hexane = 10/90, v/v); IR (neat) υ 3782, 3644, 1572, 1340, 1254, 875, 812 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ7.94 (s, 1*H*), 7.82 (s, 1*H*), 7.71 (d, J = 8 Hz, 1*H*), 7.52 (d, J = 8 Hz, 1*H*), 7.41 (t, J = 8 Hz, 1*H*), 6.53 (s, 1*H*), 3.51 (m, 2*H*), 2.52 (s, 3*H*), 1.62-1.53 (m, 2*H*), 0.88 (t, J = 4 Hz, 3*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ197.46, 180.87, 138.33, 138.05, 129.83, 129.18, 125.93, 124.08, 46.93, 26.66, 22.20, 11.36 ppm. HRMS: calcd for $C_{12}H_{16}N_2OS$ $[M+H]^+$ 237.0983; found 237.9657.

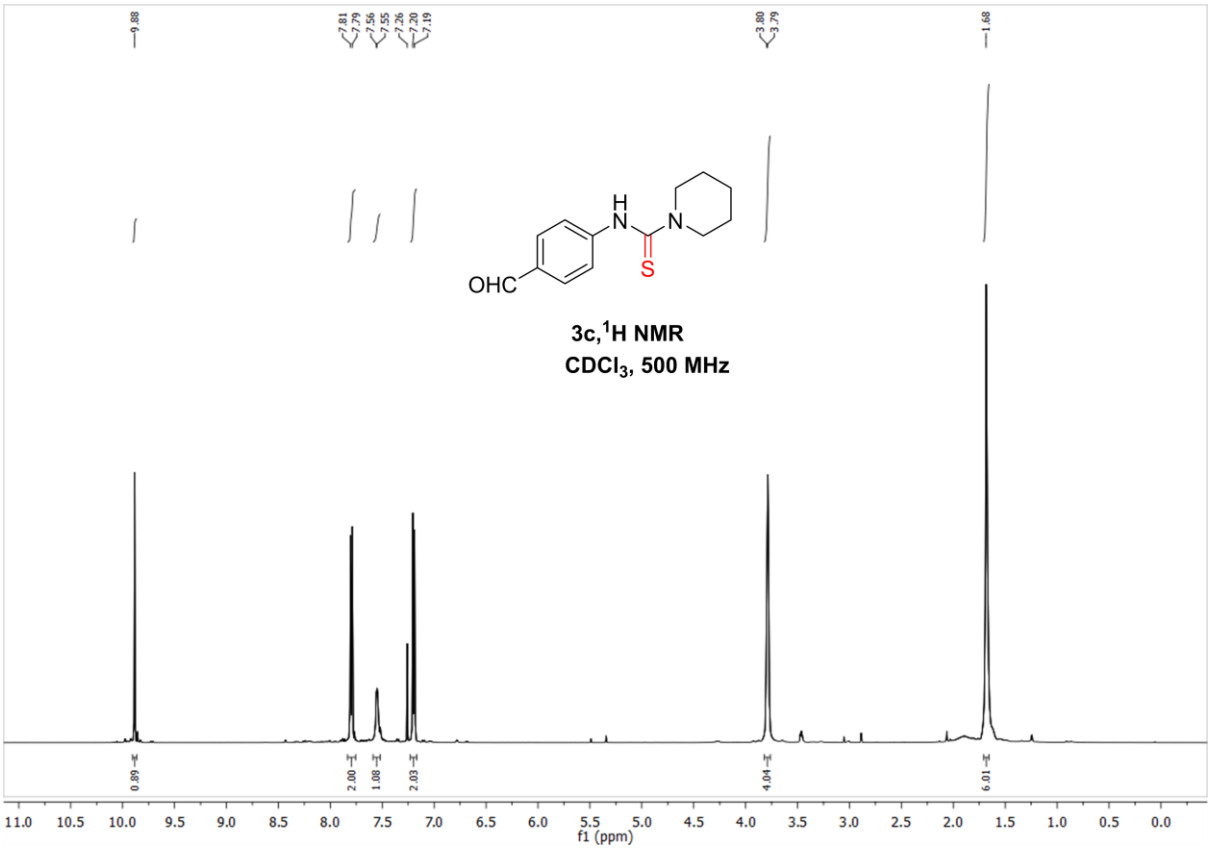
F. ^{1}H and ^{13}C Spectrum of All Compounds



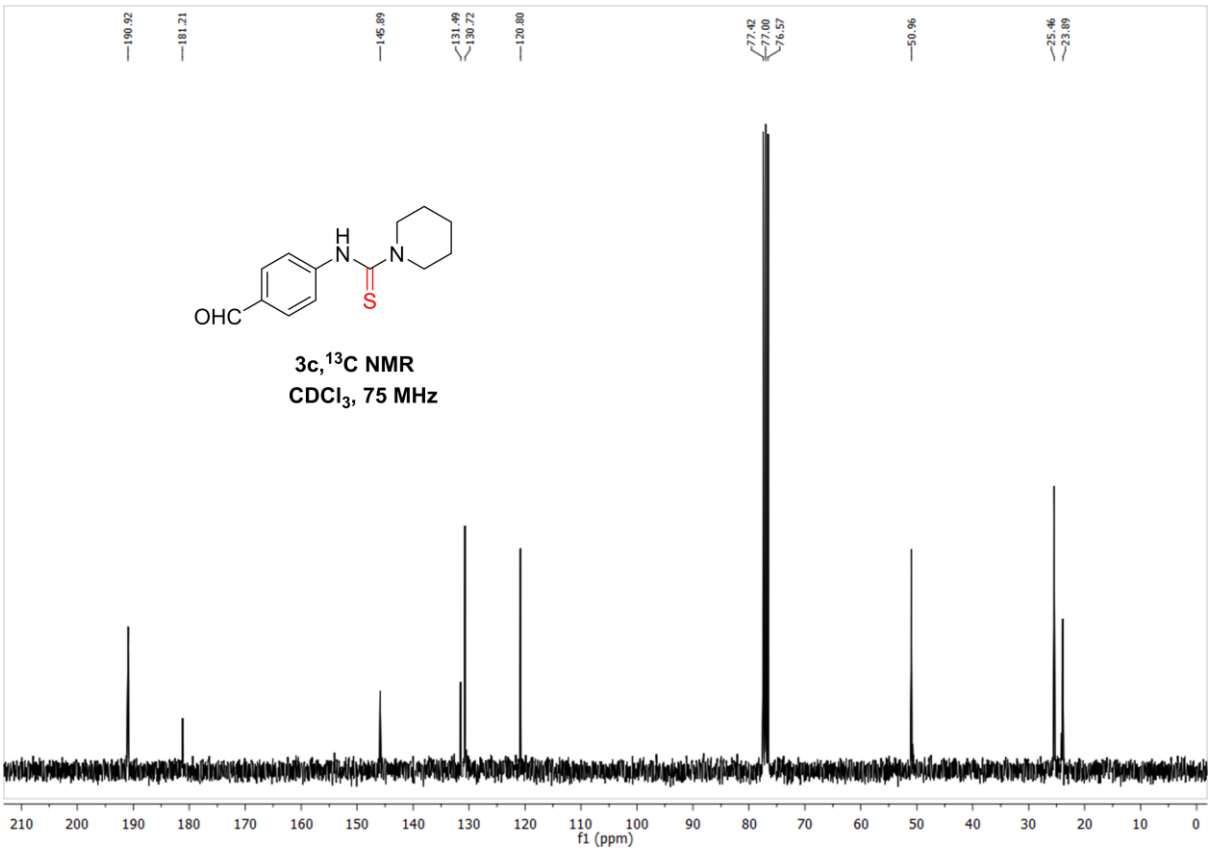



MeOC
H
N
N
S
3b,^{1}H NMR
CDCl$_3$, 500 MHz
f1 (ppm)

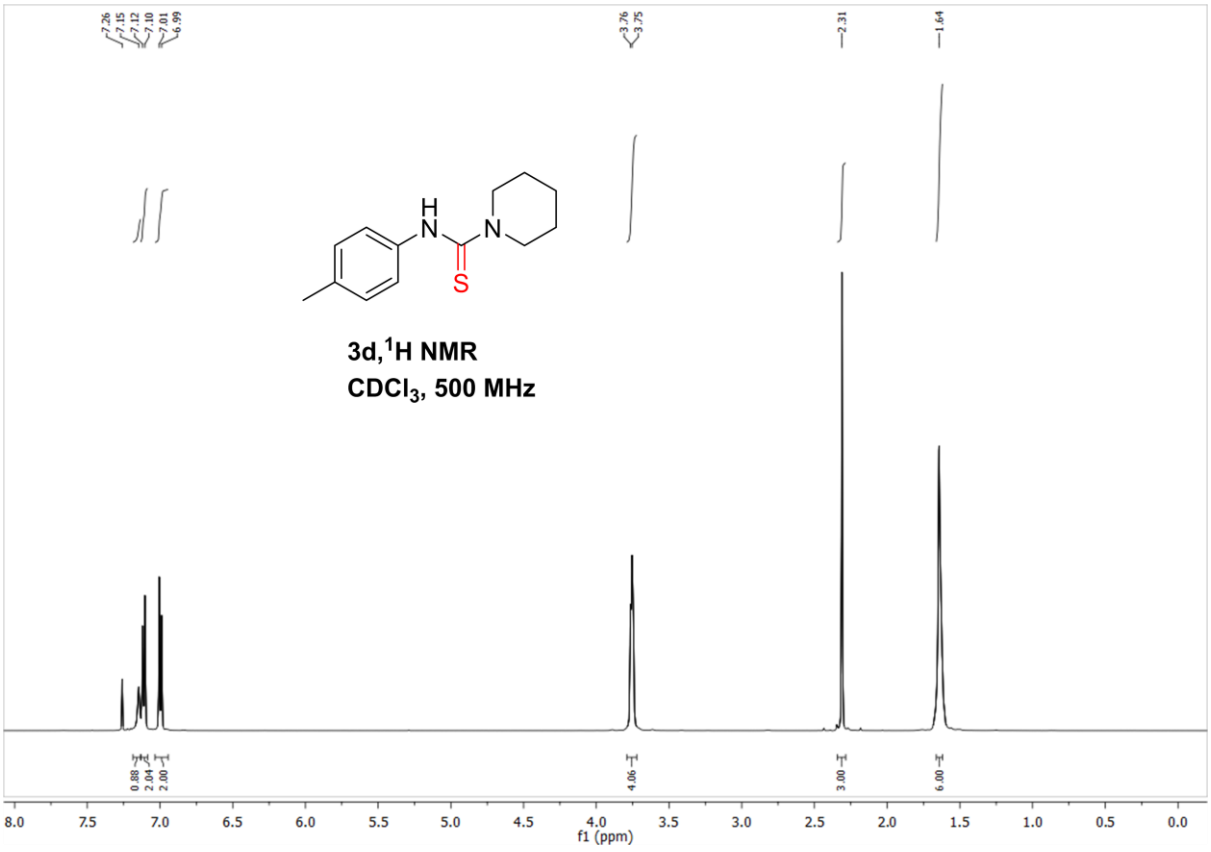

MeOC
H
N
N
S
3b,^{13}C NMR
CDCl$_3$, 125 MHz
f1 (ppm)



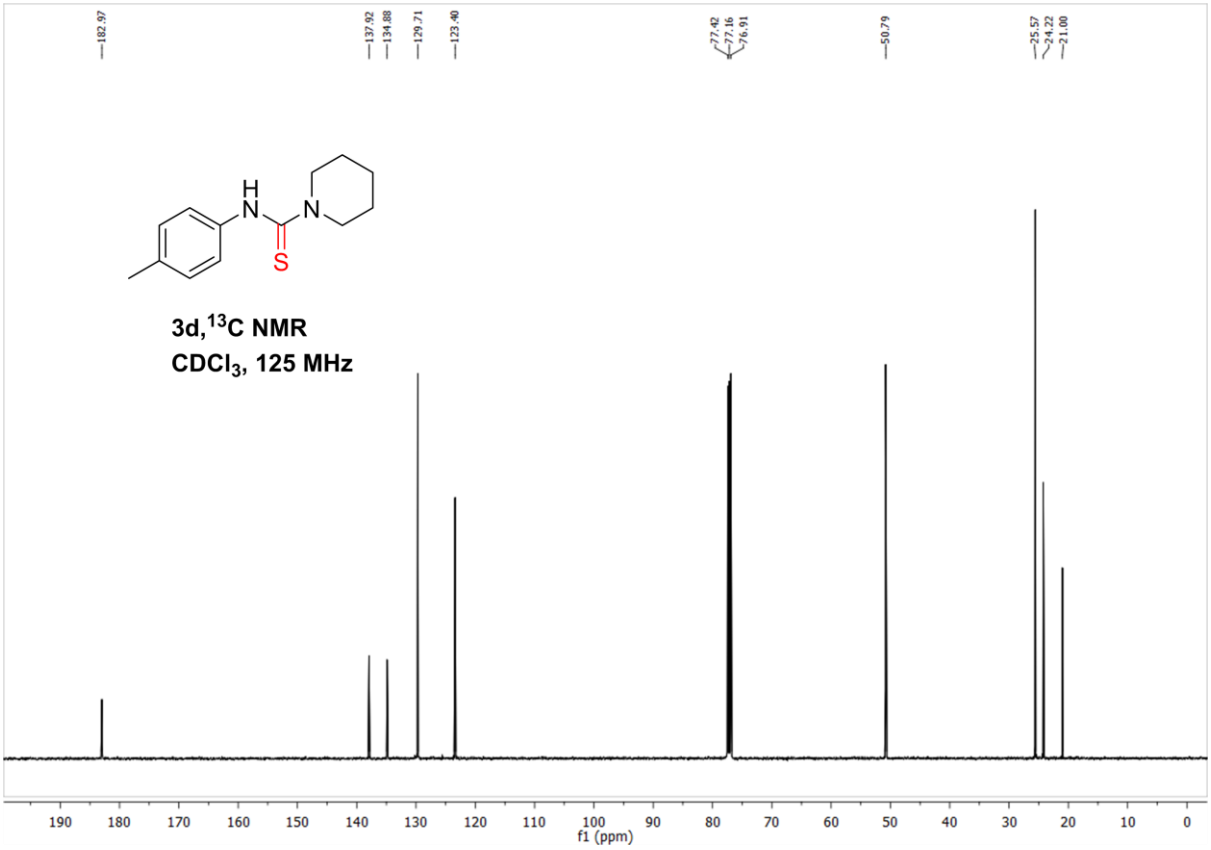
3c, ^{1}H NMR
$CDCl_3$, 500 MHz



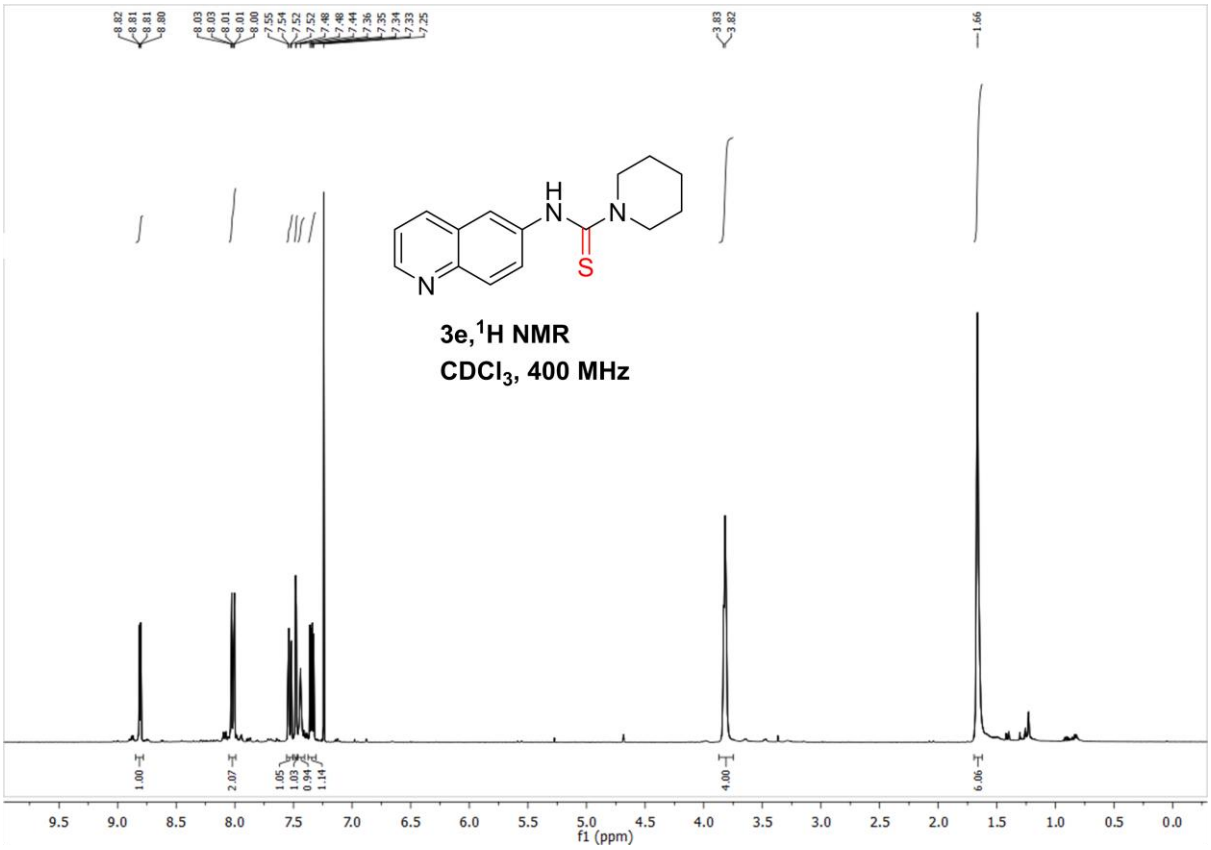
3c, ^{13}C NMR
$CDCl_3$, 75 MHz

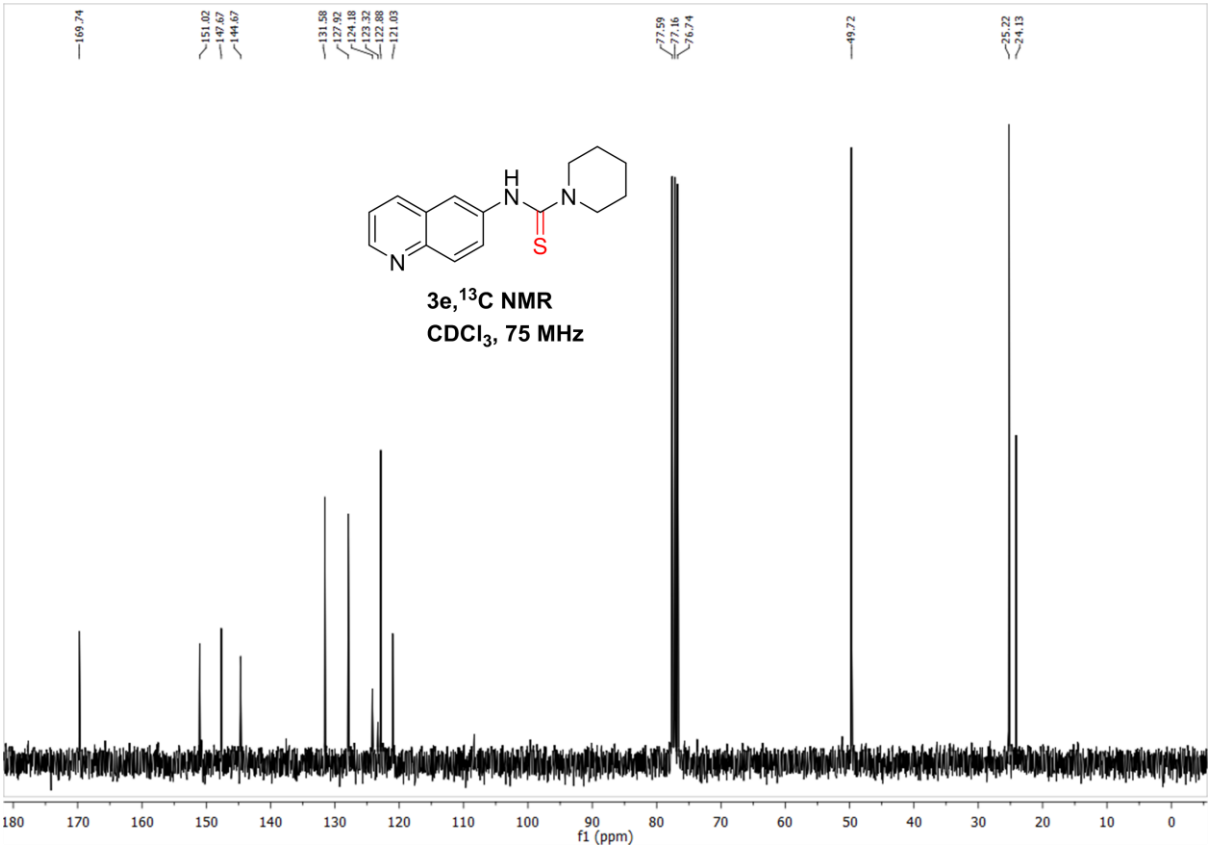


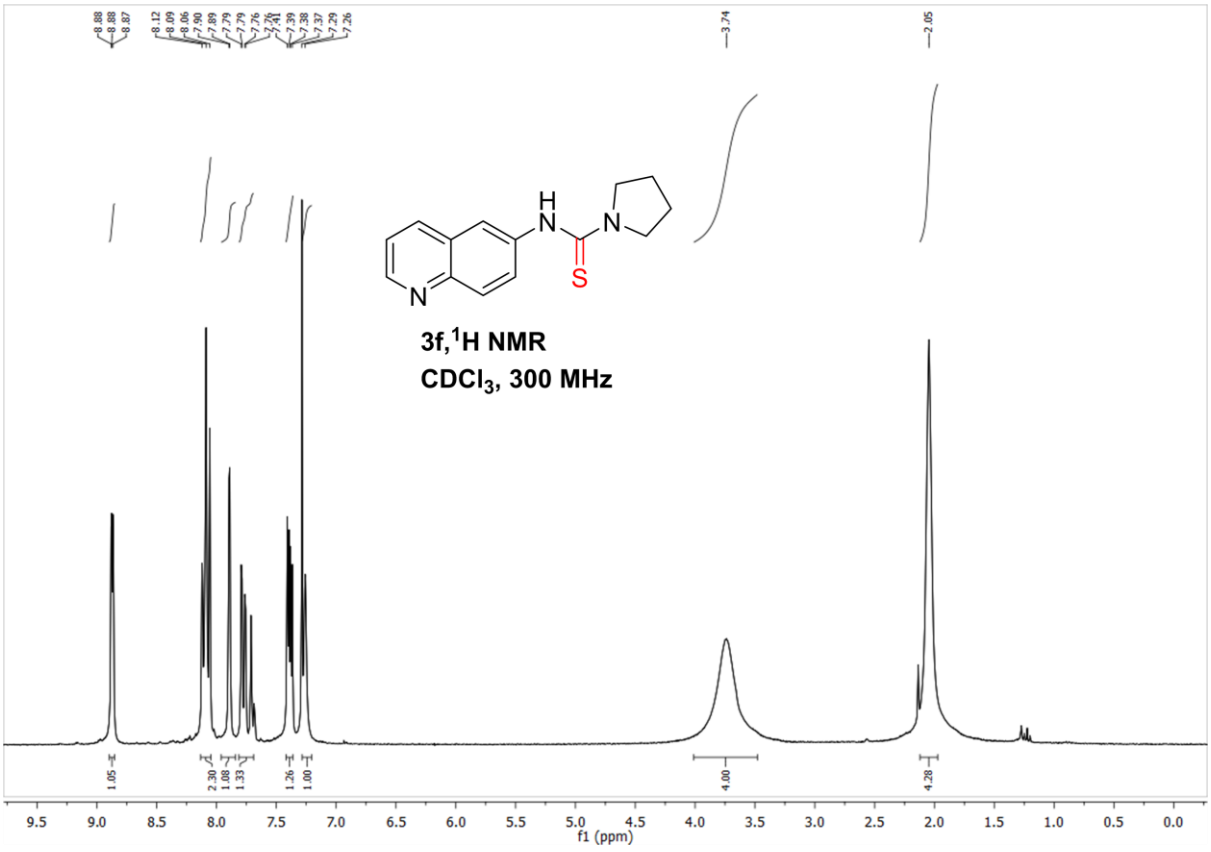
3d,^{1}H NMR
$CDCl_3$, 500 MHz

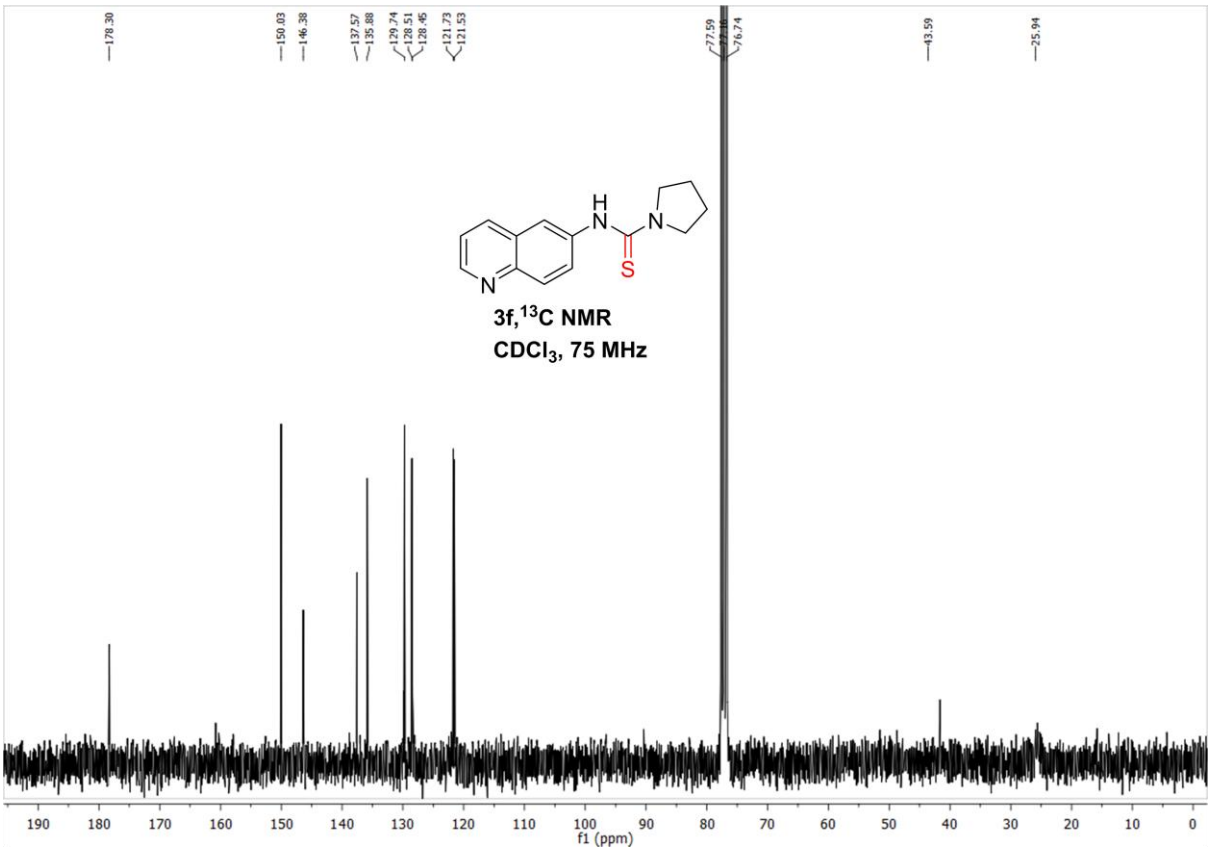


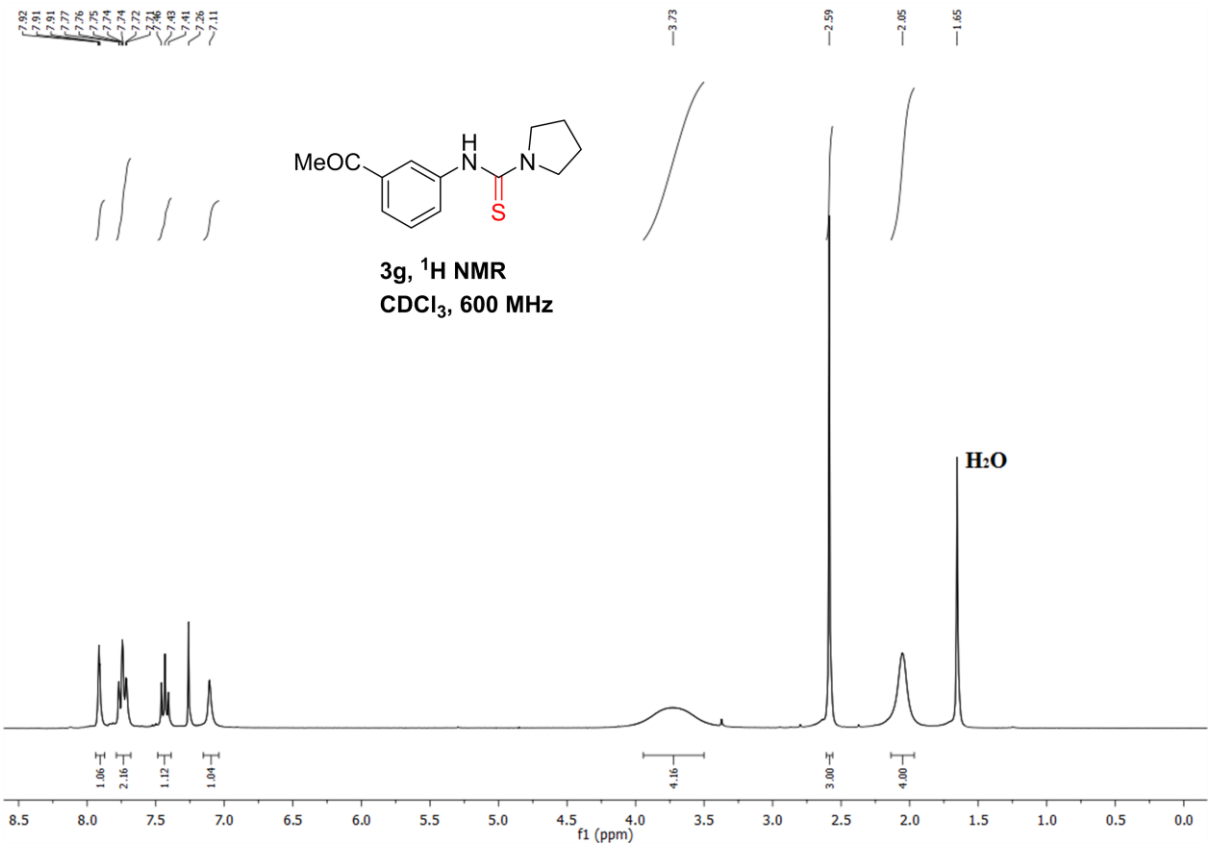
3d,^{13}C NMR
$CDCl_3$, 125 MHz

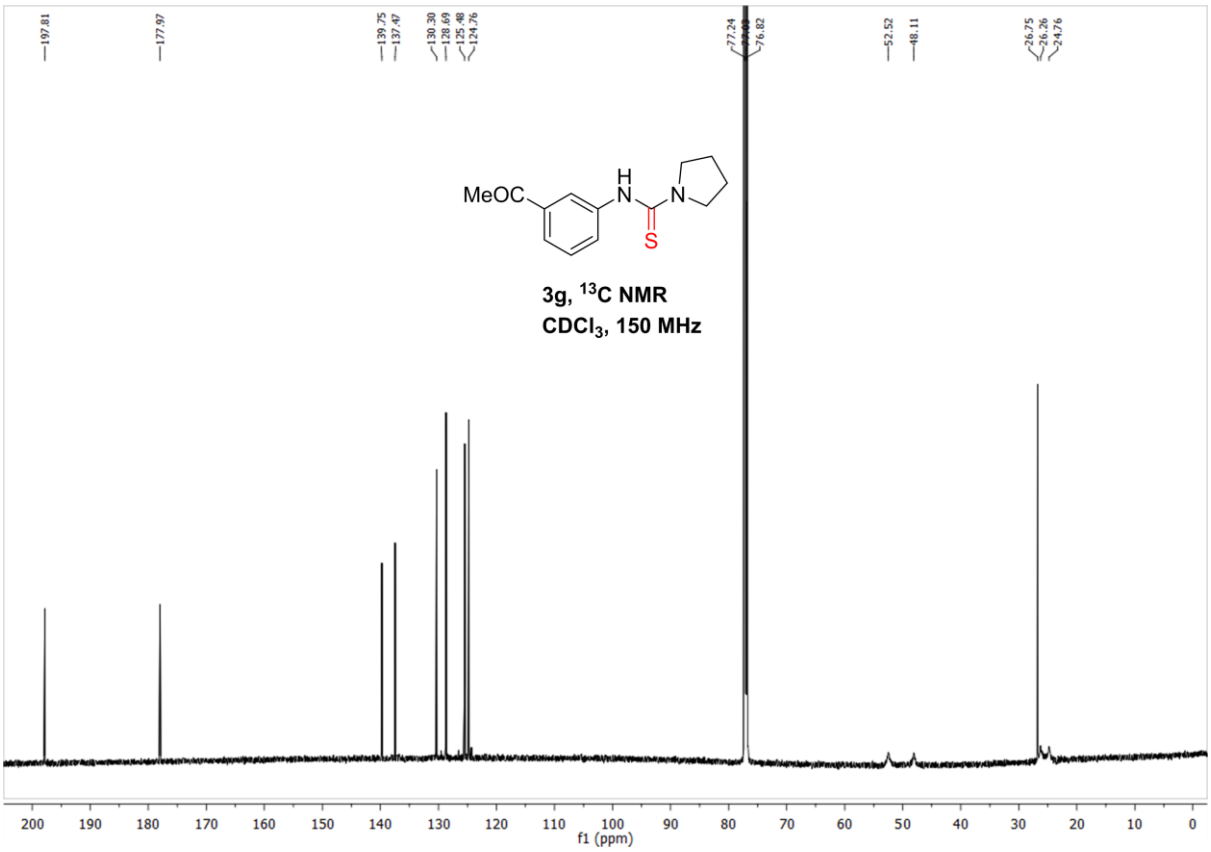

8.82
8.81
8.81
8.80
8.03
8.03
8.01
8.01
8.00
7.55
7.54
7.52
7.52
7.48
7.48
7.44
7.36
7.35
7.34
7.33
7.25
3.83
3.82
1.66
H
N
N
S
N
3e, 1H NMR
CDCl3, 400 MHz
1.00
2.07
1.05
1.03
0.94
1.14
4.00
6.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

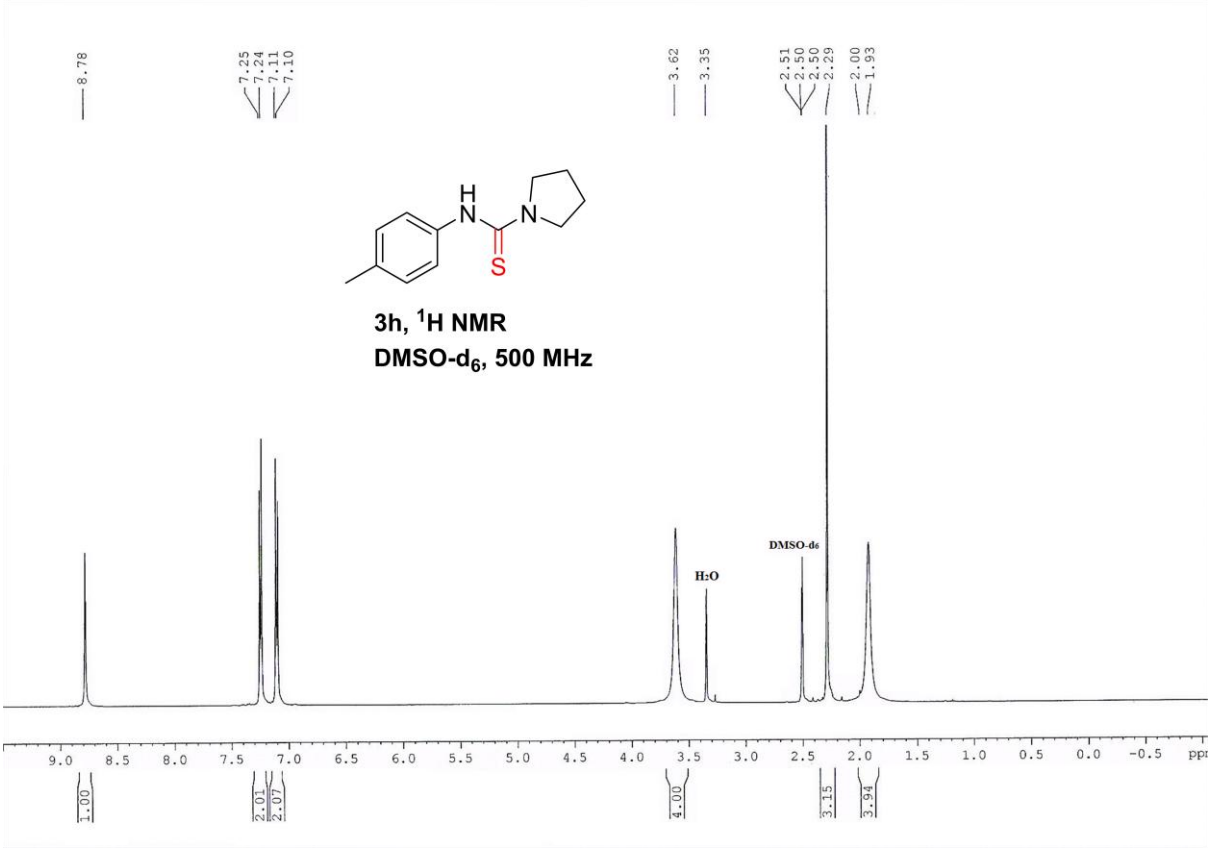

169.74
151.02
147.67
144.67
131.58
127.92
124.18
123.32
122.88
121.03
77.59
77.16
76.74
49.72
25.22
24.13
H
N
N
S
N
3e, 13C NMR
CDCl3, 75 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

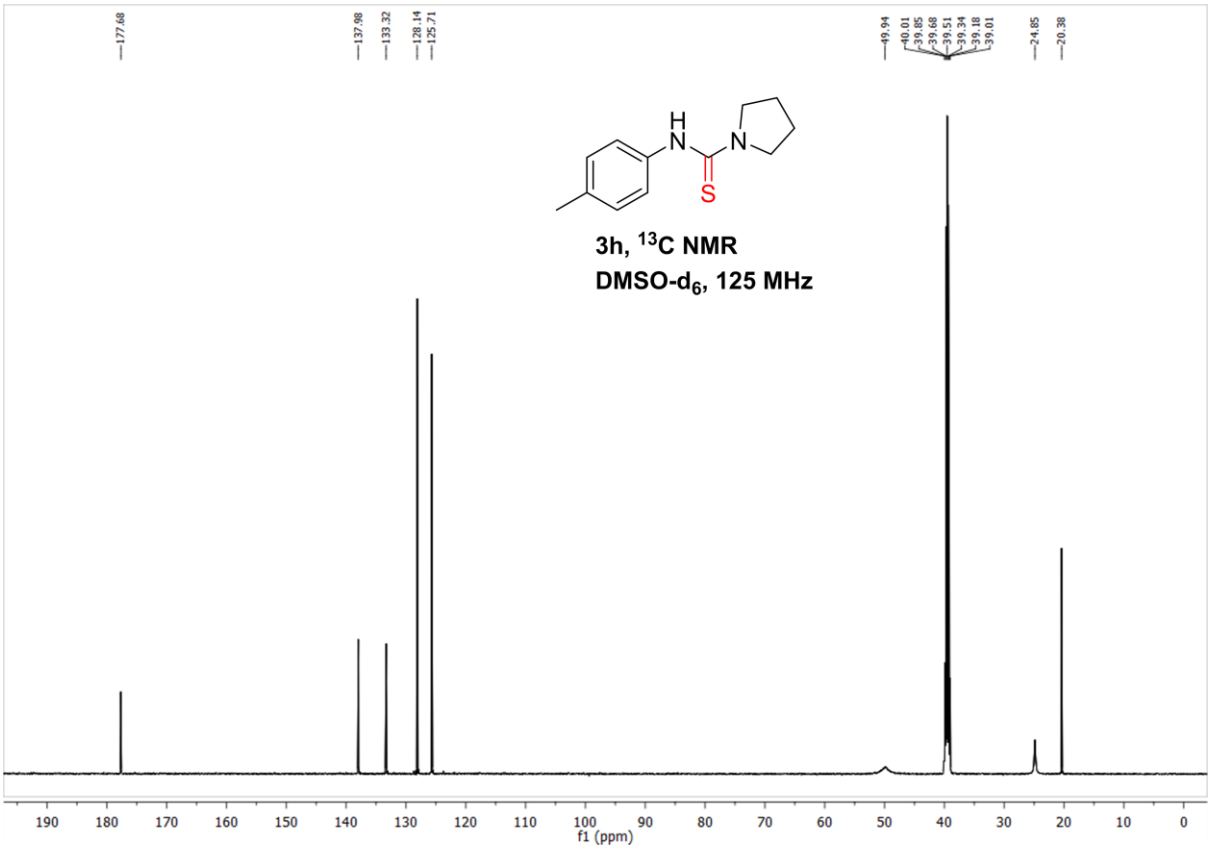

3f,^{1}H NMR
$CDCl_3$, 300 MHz
f1 (ppm)

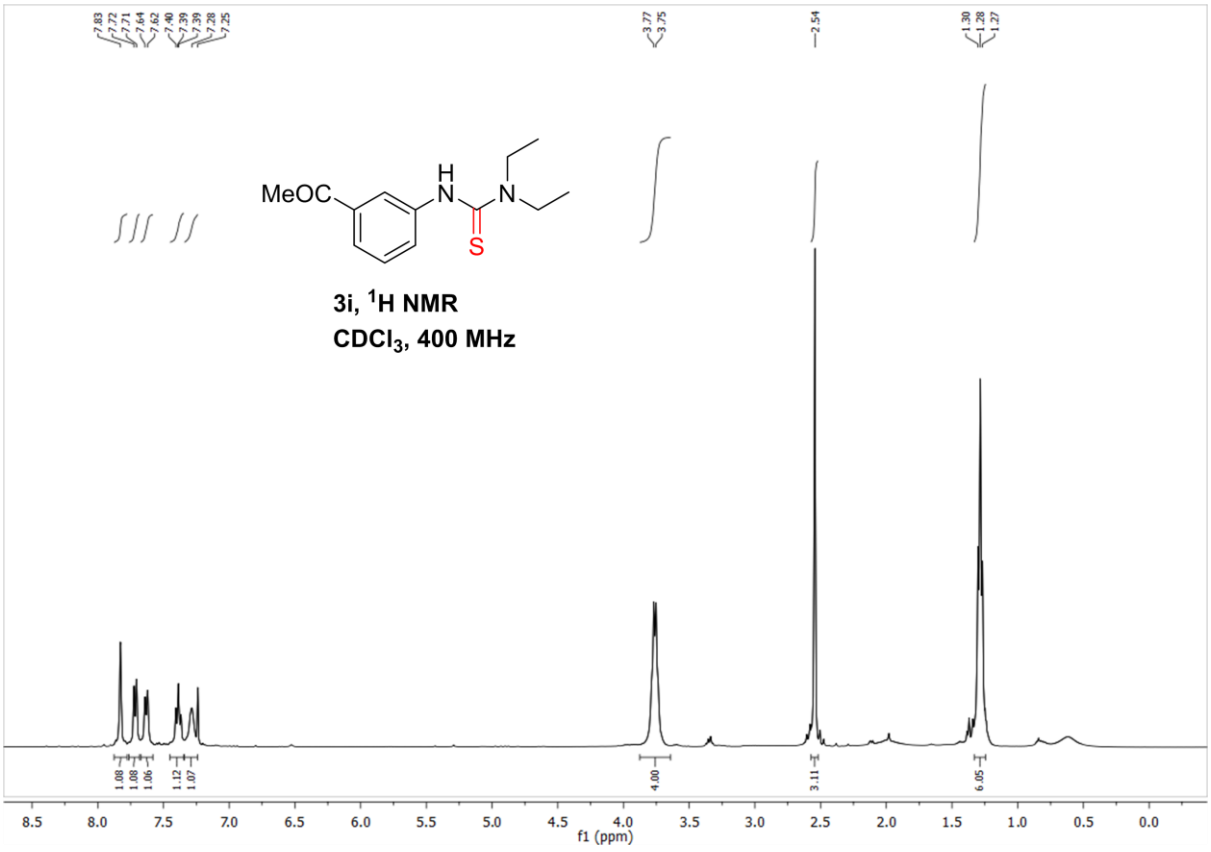

3f,^{13}C NMR
$CDCl_3$, 75 MHz
f1 (ppm)

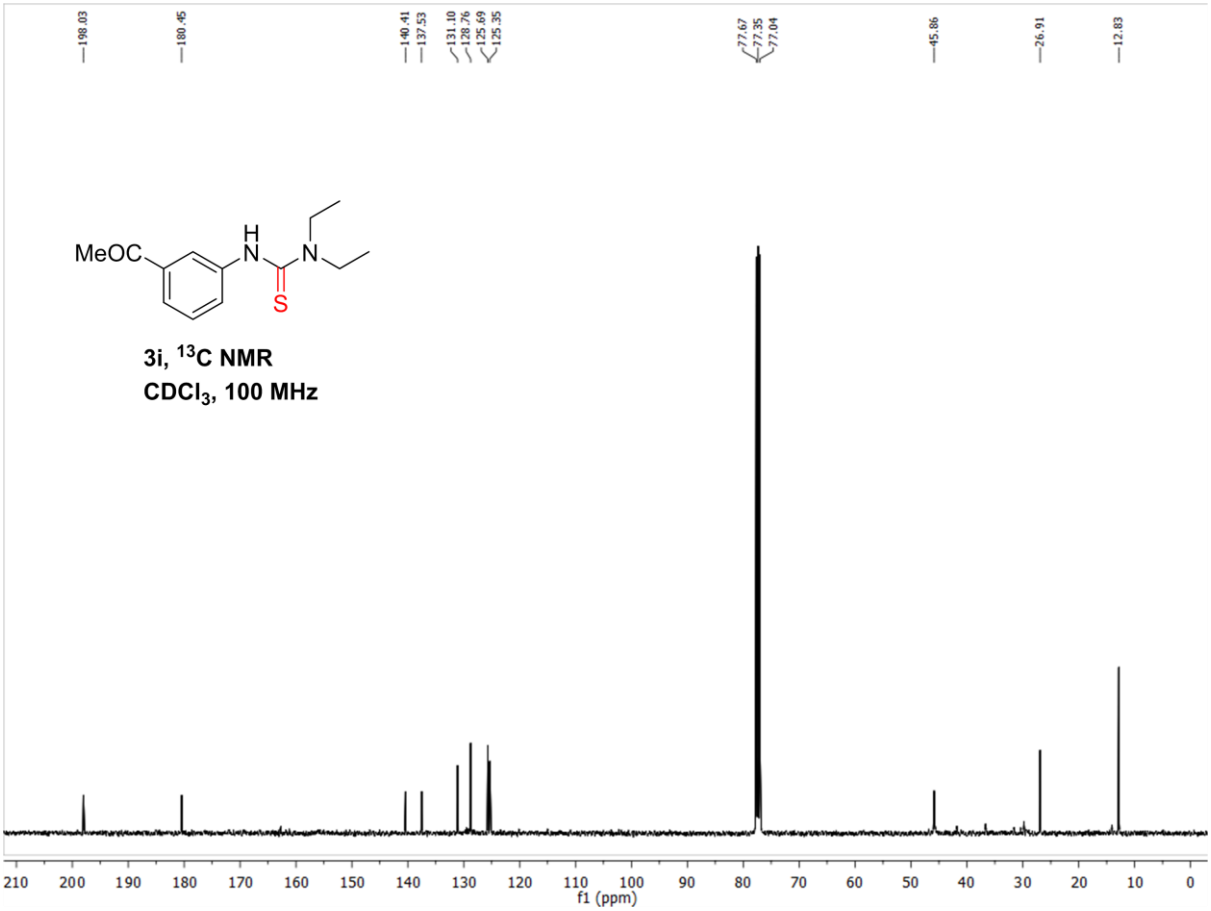

MeOC
H
N
N
S
3g, ^{1}H NMR
$CDCl_3$, 600 MHz
H₂O
f1 (ppm)

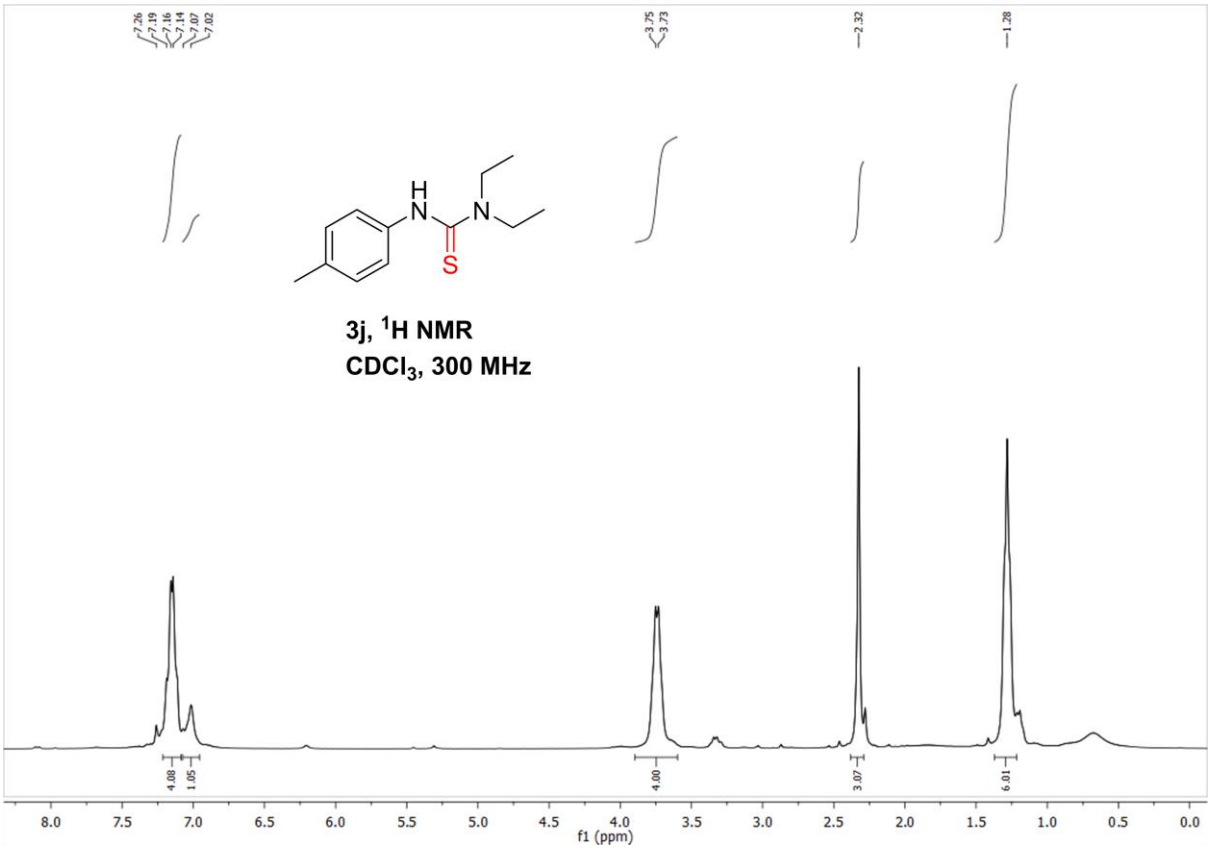

MeOC
H
N
N
S
3g, ^{13}C NMR
$CDCl_3$, 150 MHz
f1 (ppm)


8.78
7.25
7.24
7.11
7.10
3.62
3.35
2.51
2.50
2.50
2.29
2.00
1.93
H
N
N
S
3h, 1H NMR
DMSO-d6, 500 MHz
DMSO-d6
H2O
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 ppm
1.00
2.01
2.07
4.00
3.15
3.94

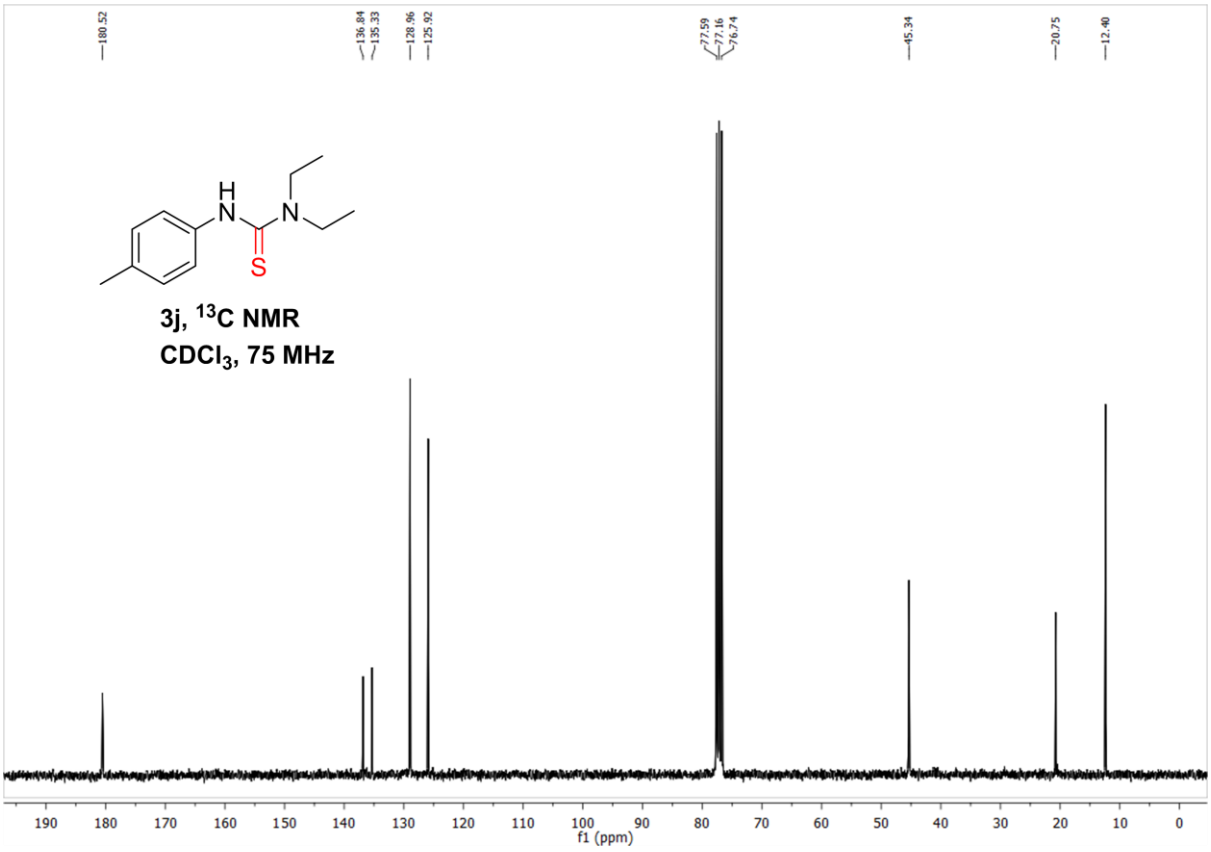

177.68
137.98
133.32
128.14
125.71
49.94
40.01
39.85
39.68
39.51
39.34
39.18
39.01
24.85
20.38
H
N
N
S
3h, 13C NMR
DMSO-d6, 125 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeOC
H
N
N
S
3i, ^{1}H NMR
CDCl$_3$, 400 MHz
f1 (ppm)

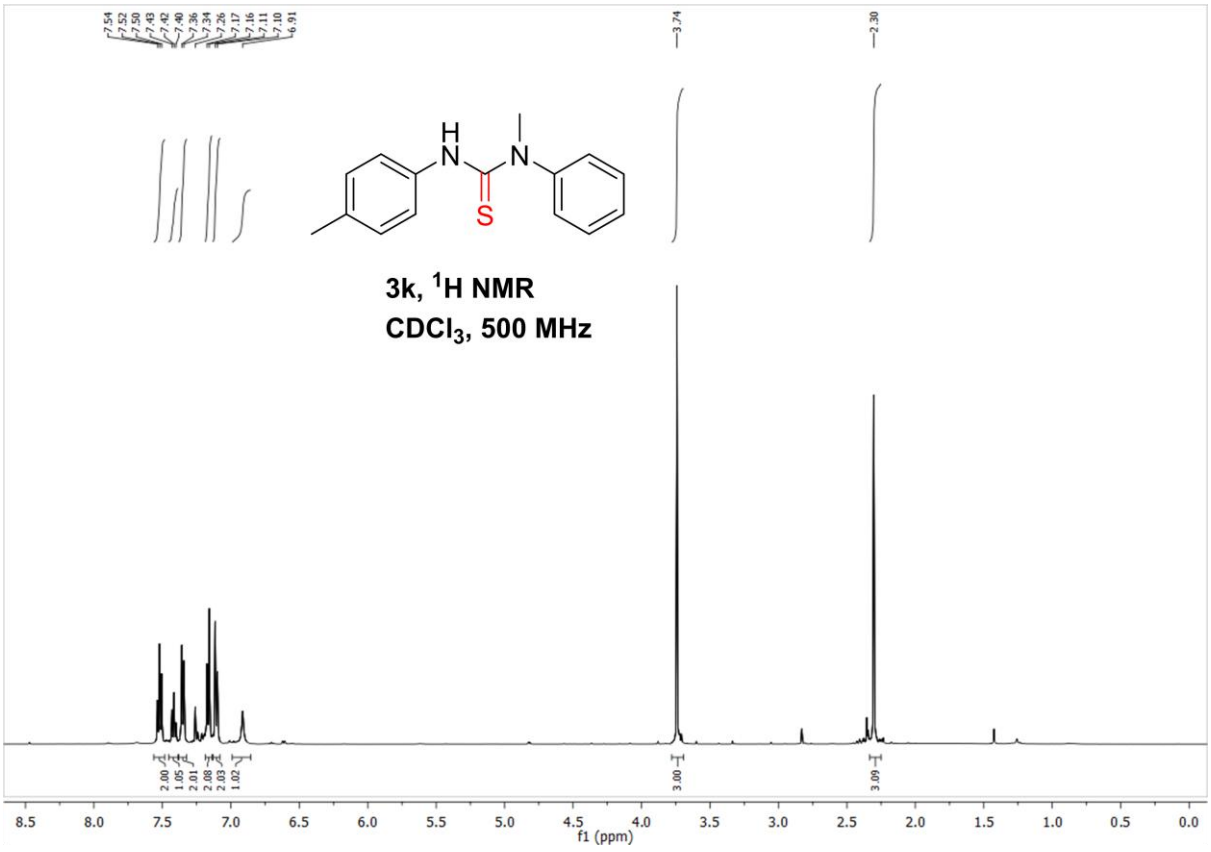

MeOC
H
N
N
S
3i, ^{13}C NMR
CDCl$_3$, 100 MHz
f1 (ppm)

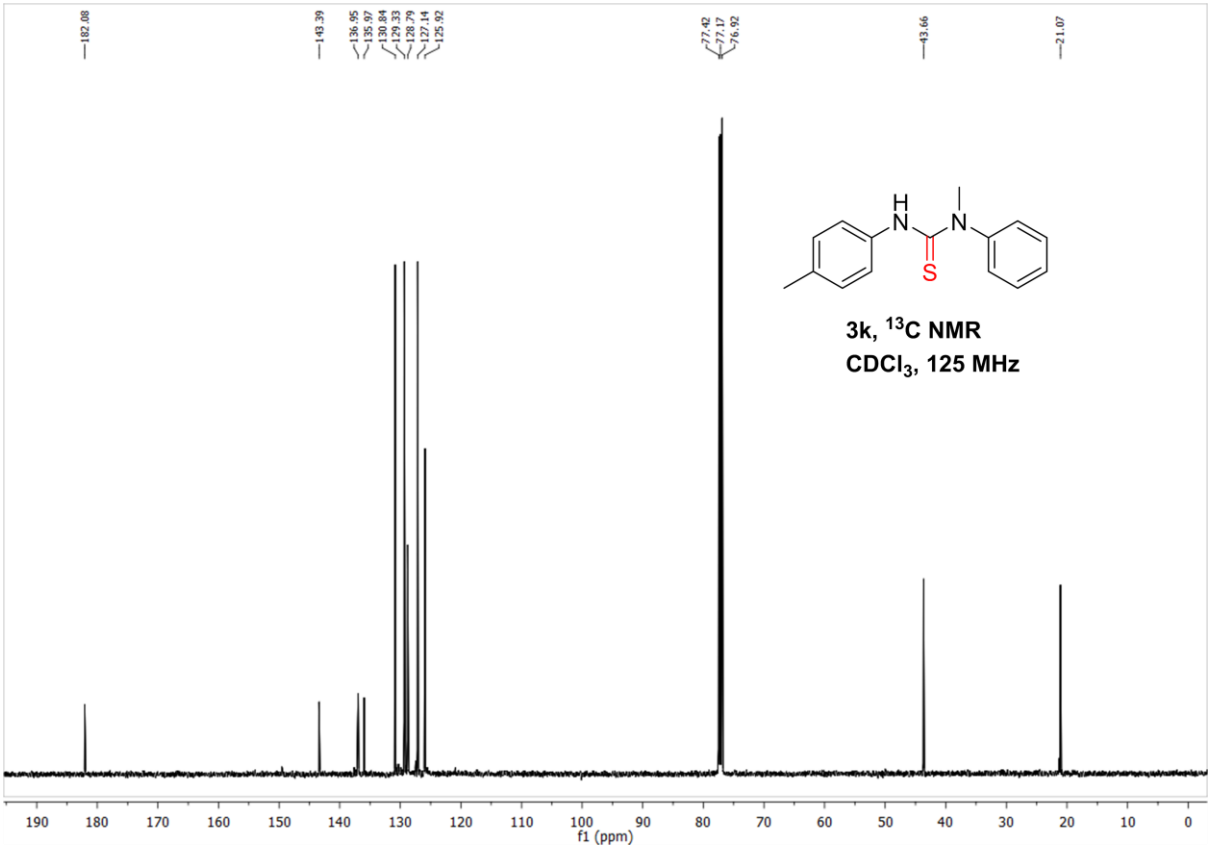


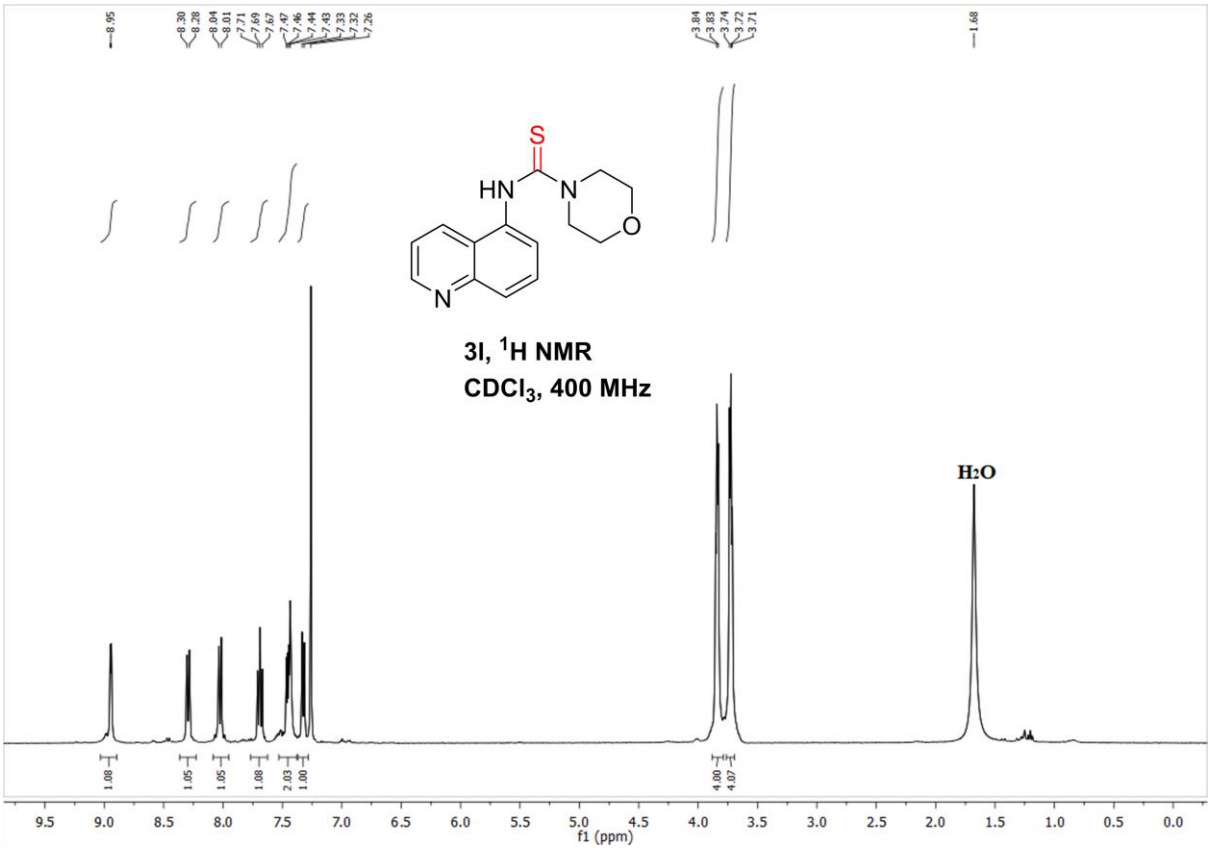
3j, ^{1}H NMR
$CDCl_3$, 300 MHz

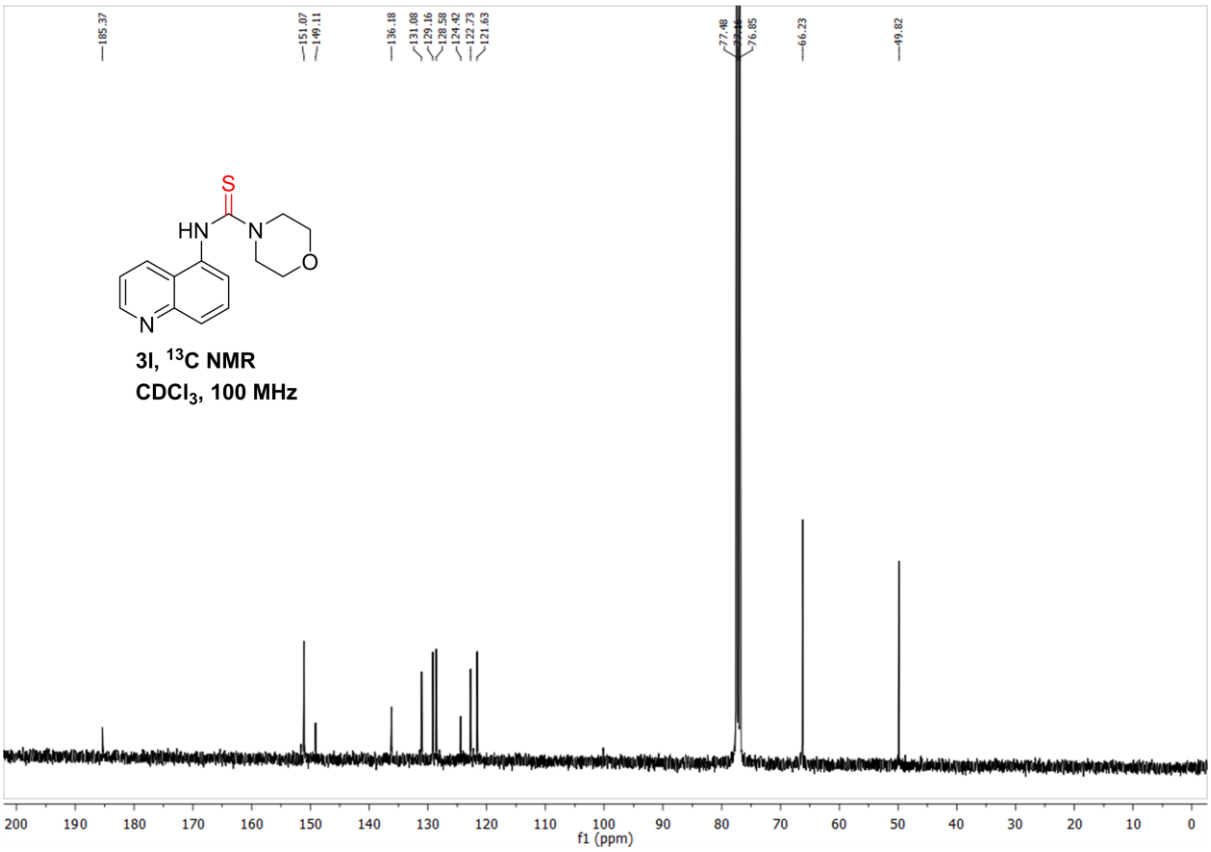


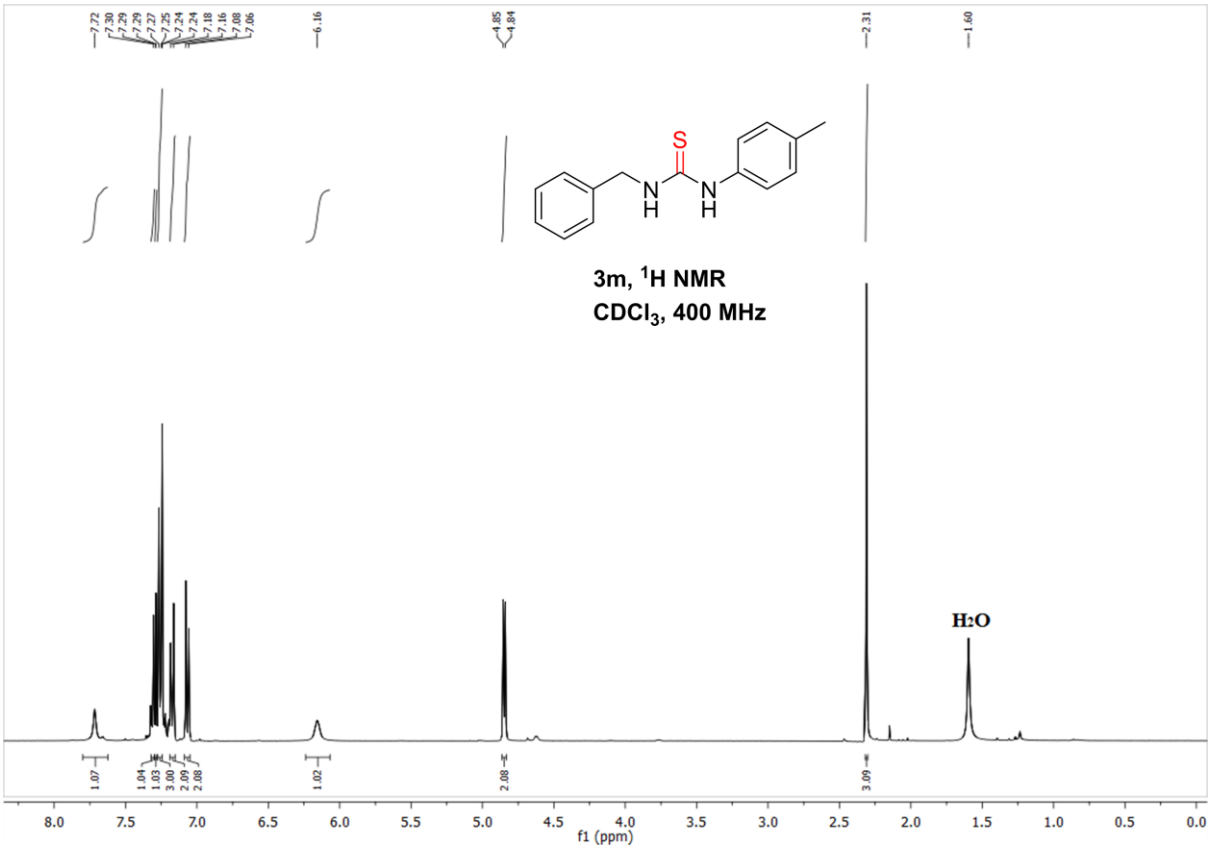
3j, ^{13}C NMR
$CDCl_3$, 75 MHz

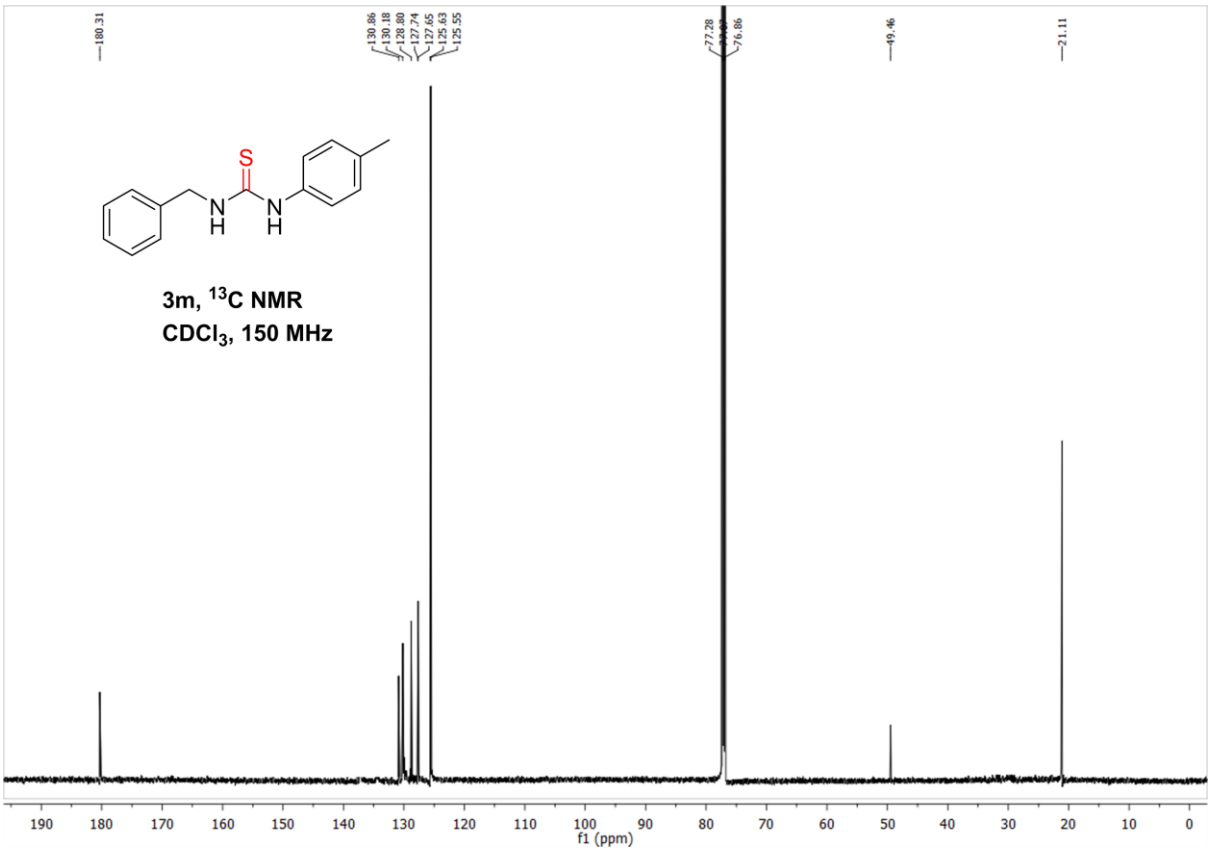

7.54
7.52
7.50
7.43
7.42
7.40
7.36
7.34
7.26
7.17
7.16
7.11
7.10
6.91
3.74
2.30
H
N
N
S
3k, ^{1}H NMR
$CDCl_3$, 500 MHz
2.00
1.05
2.01
2.08
2.03
1.02
3.00
3.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

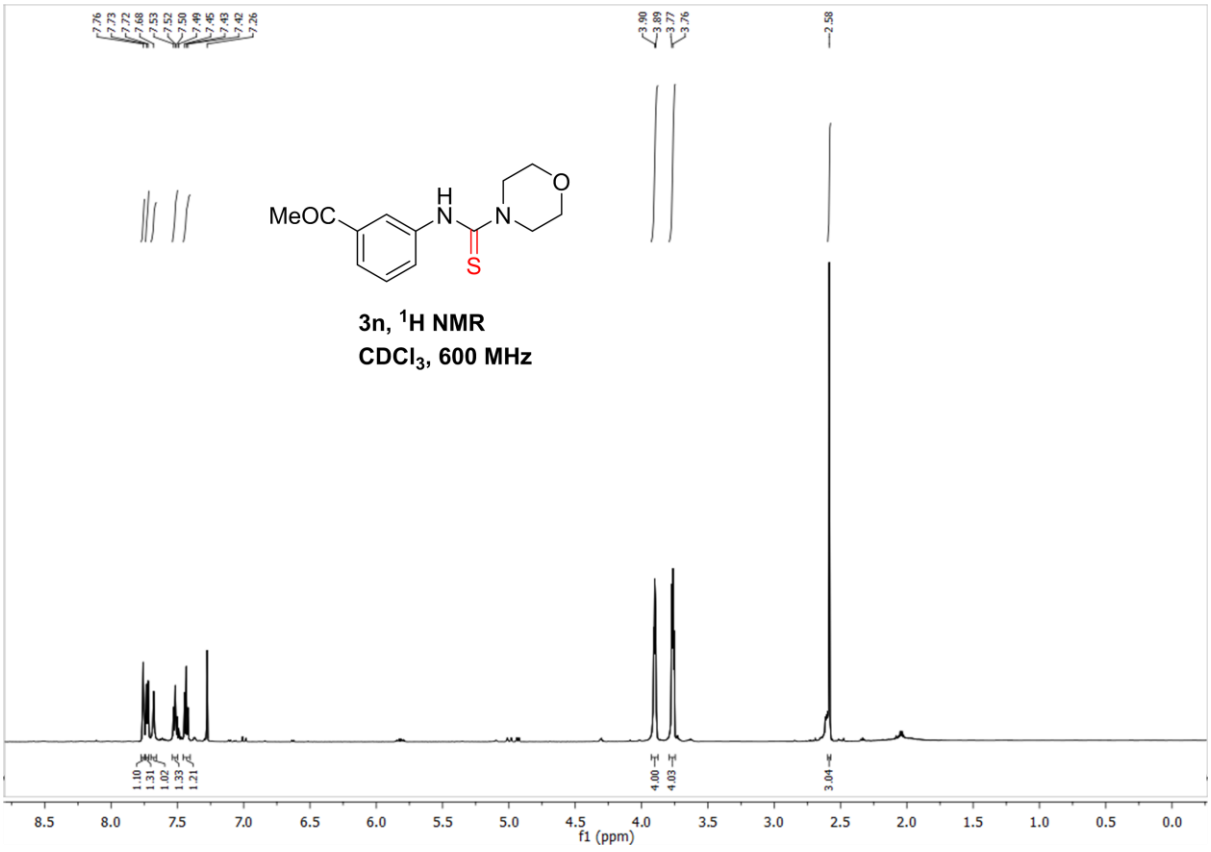

182.08
143.39
136.95
135.97
130.84
129.33
128.79
127.14
125.92
77.42
77.17
76.92
43.66
21.07
H
N
N
S
3k, ^{13}C NMR
$CDCl_3$, 125 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

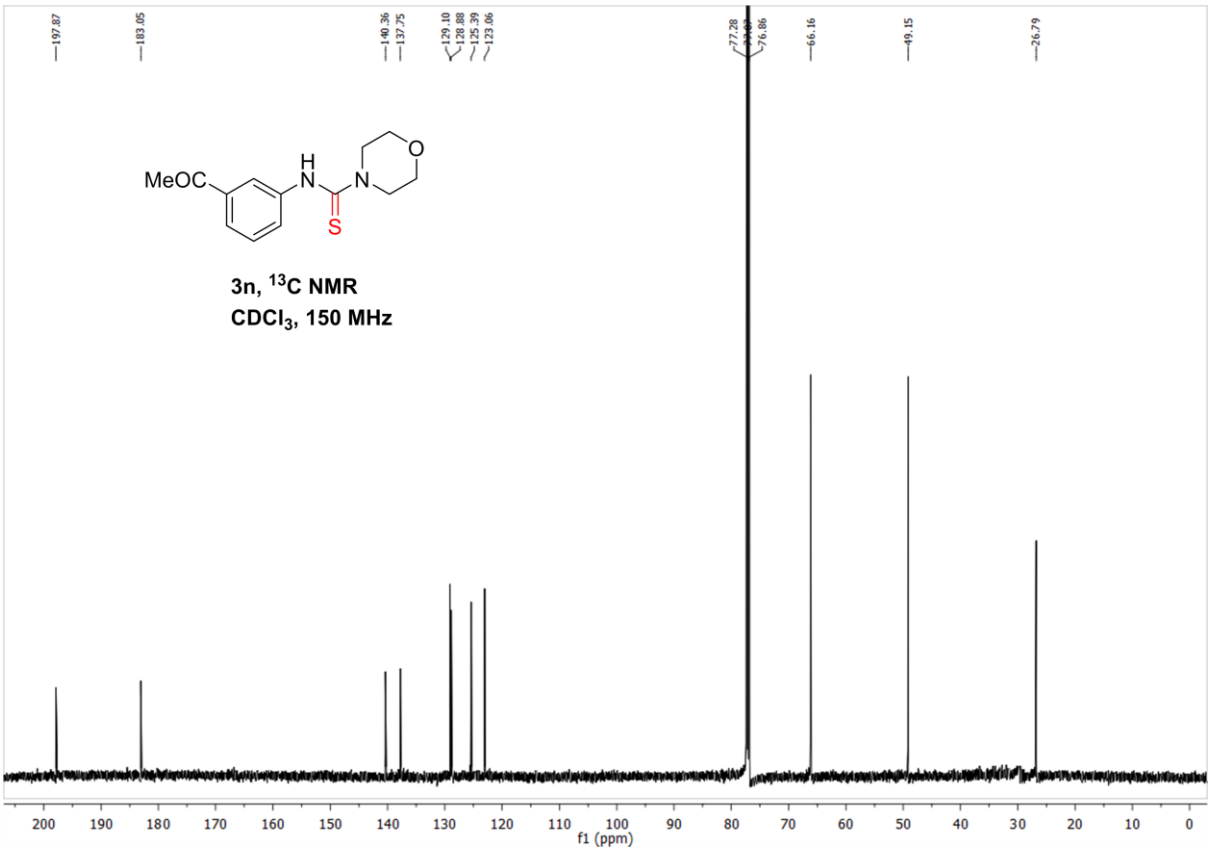

8.95
8.30
8.28
8.04
8.01
7.71
7.69
7.67
7.47
7.46
7.44
7.43
7.33
7.32
7.26
3.84
3.83
3.74
3.72
3.71
1.68
S
HN
N
O
N
3l, ^{1}H NMR
CDCl$_3$, 400 MHz
H2O
1.08
1.05
1.05
1.08
2.03
1.00
4.00
4.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

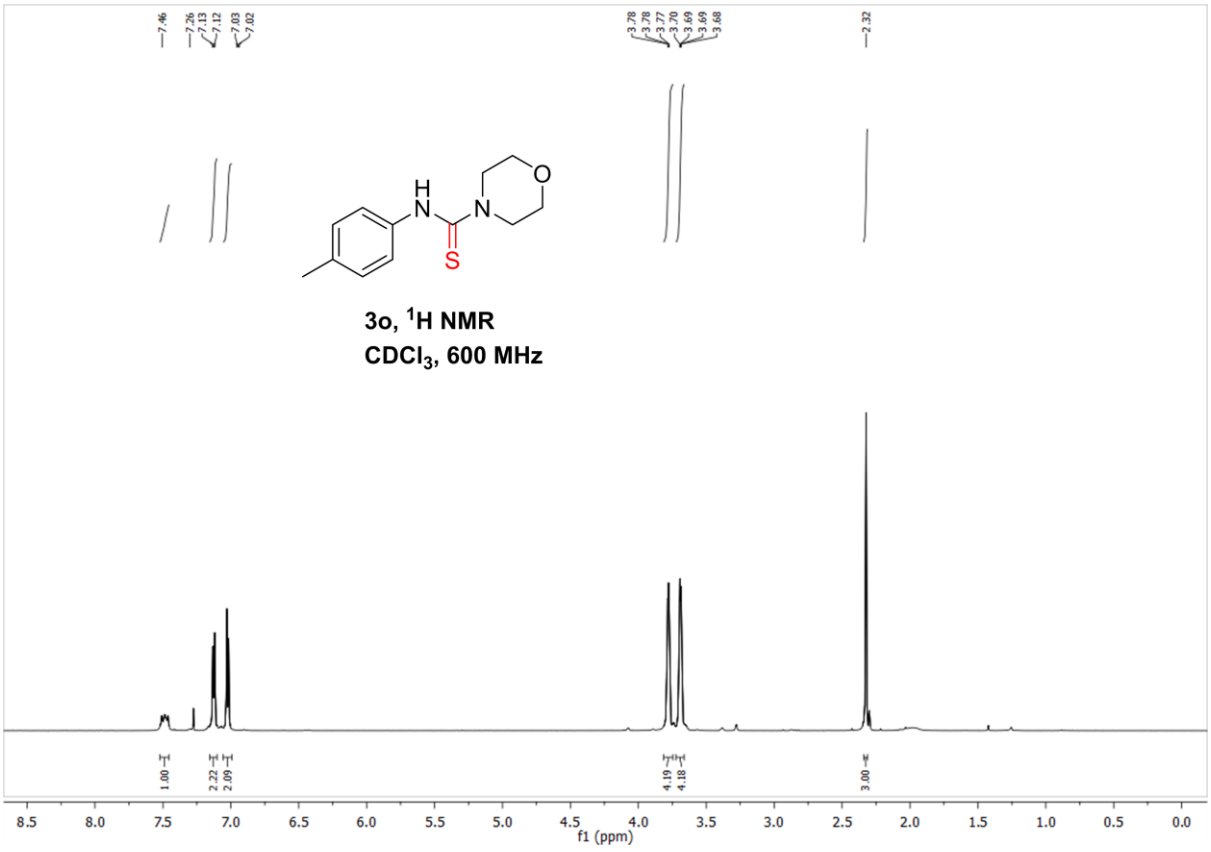

185.37
151.07
149.11
136.18
131.08
129.16
128.58
124.42
122.73
121.63
77.48
77.16
76.85
66.23
49.82
S
HN
N
O
N
3l, ^{13}C NMR
CDCl$_3$, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.72
7.30
7.29
7.29
7.27
7.25
7.24
7.24
7.18
7.16
7.08
7.06
6.16
4.85
4.84
2.31
1.60
S
N
H
N
H
3m, ^{1}H NMR
$CDCl_3$, 400 MHz
H2O
1.07
1.04
1.03
3.00
2.09
2.08
1.02
2.08
3.09
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
f1 (ppm)

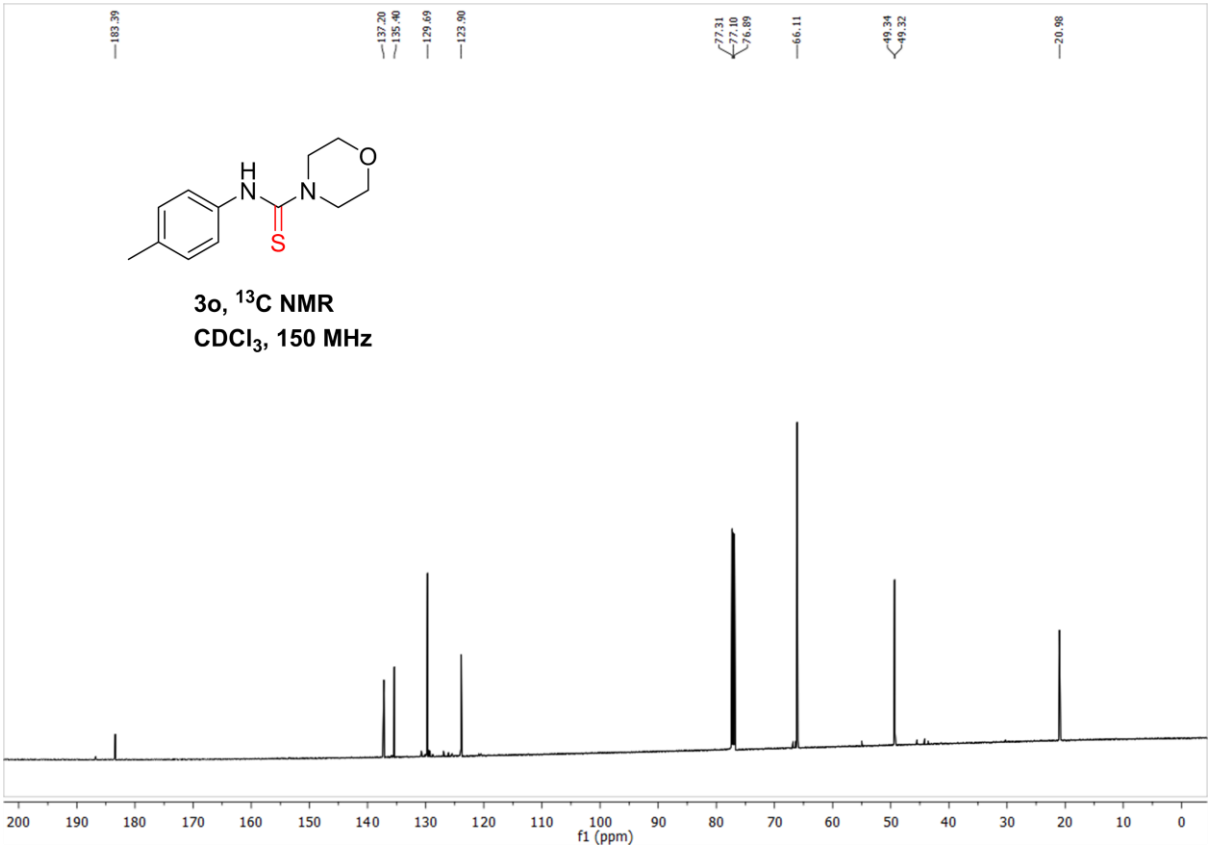

180.31
130.86
130.18
128.80
127.74
127.65
125.63
125.55
77.28
76.86
49.46
21.11
S
N
H
N
H
3m, ^{13}C NMR
$CDCl_3$, 150 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeOC
H
N
N
O
S
3n, ^{1}H NMR
$CDCl_3$, 600 MHz
f1 (ppm)

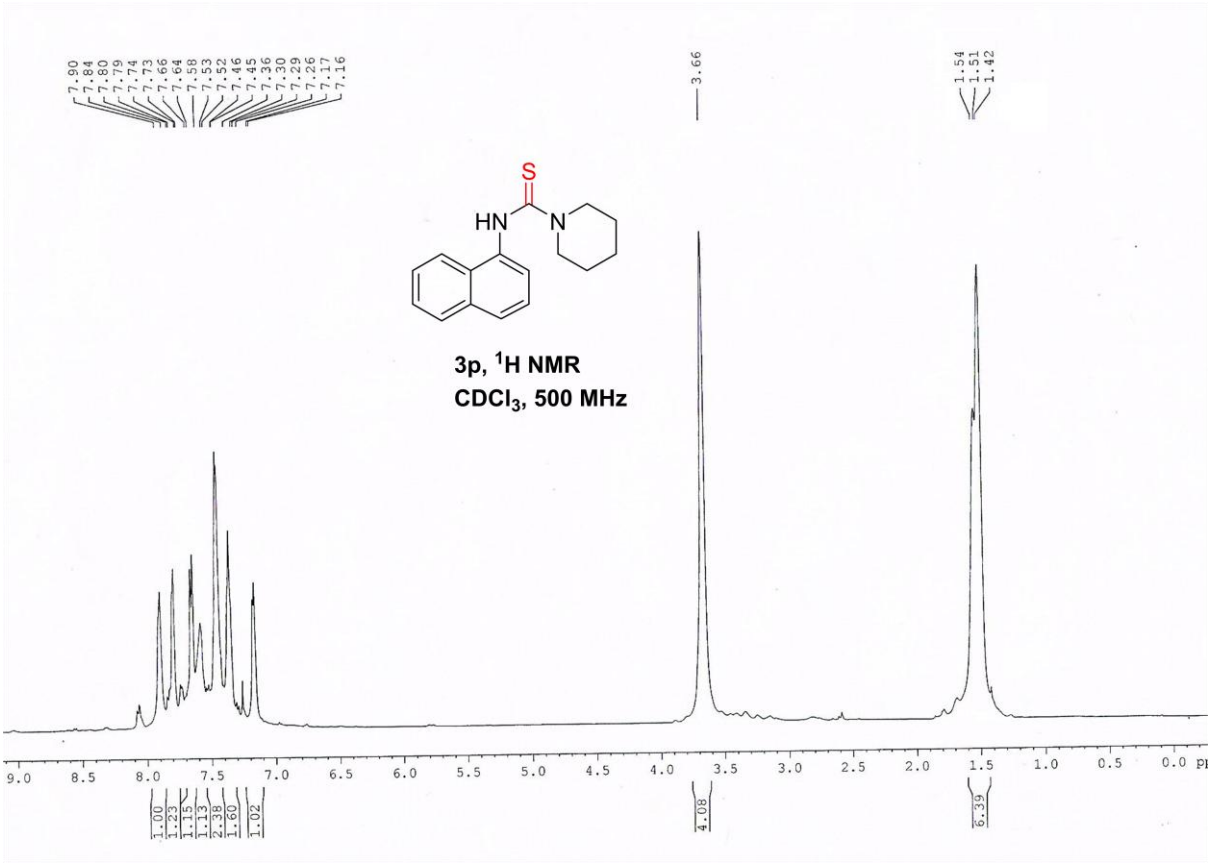

MeOC
H
N
N
O
S
3n, ^{13}C NMR
$CDCl_3$, 150 MHz
f1 (ppm)

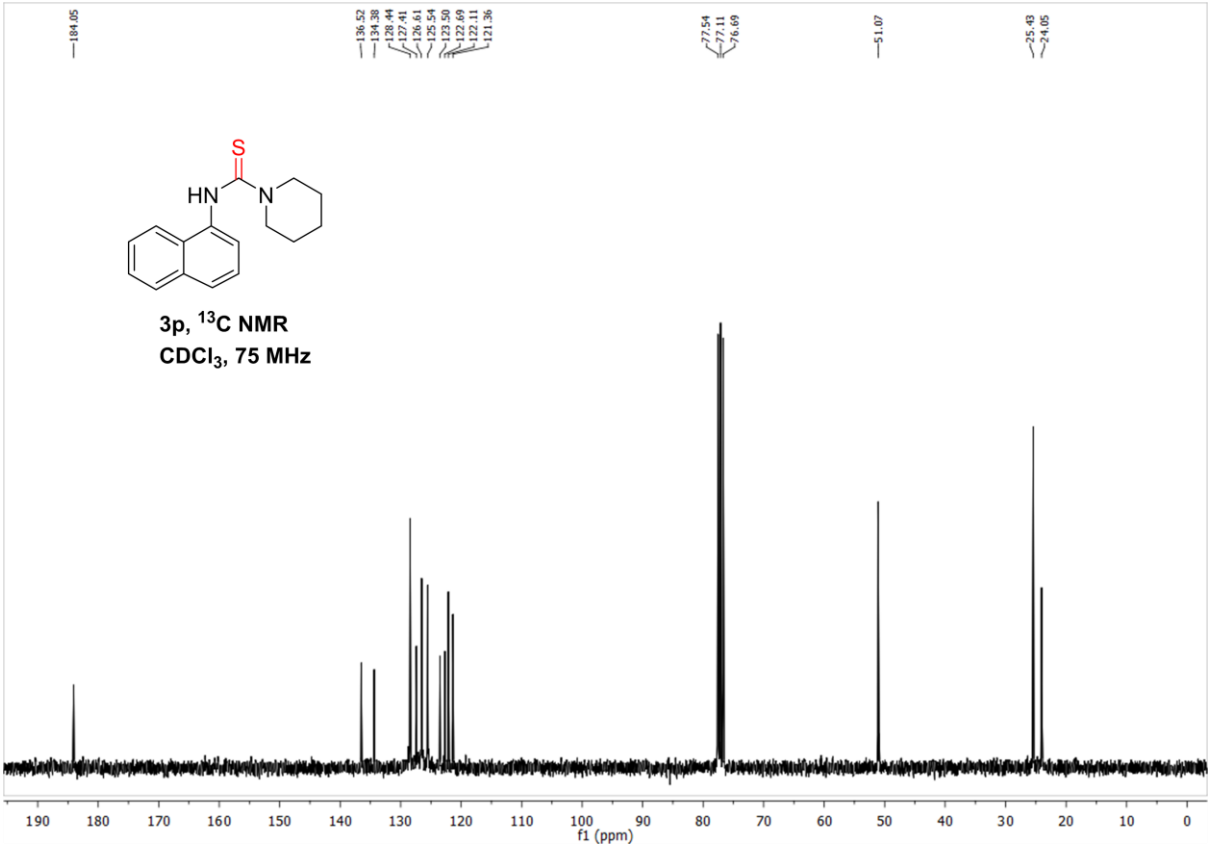


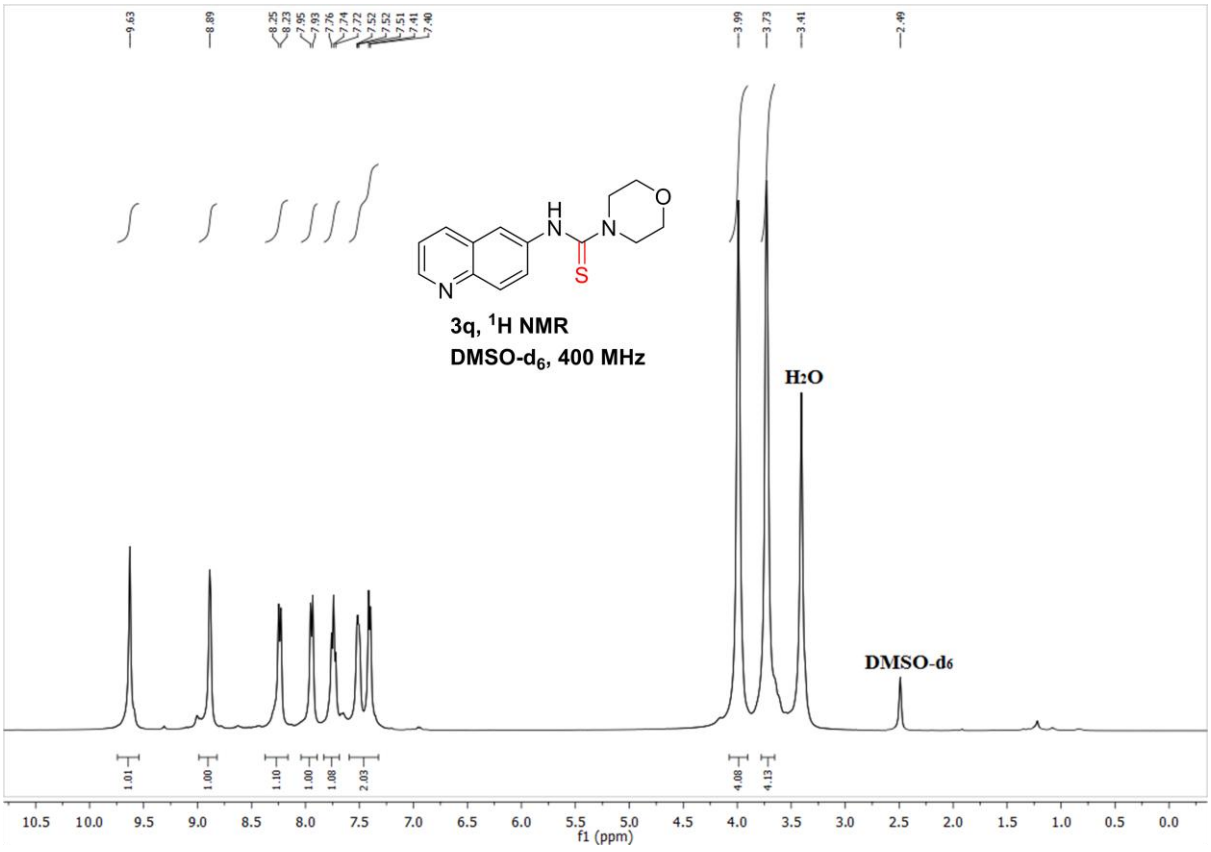
3o, ^{1}H NMR
$CDCl_3$, 600 MHz

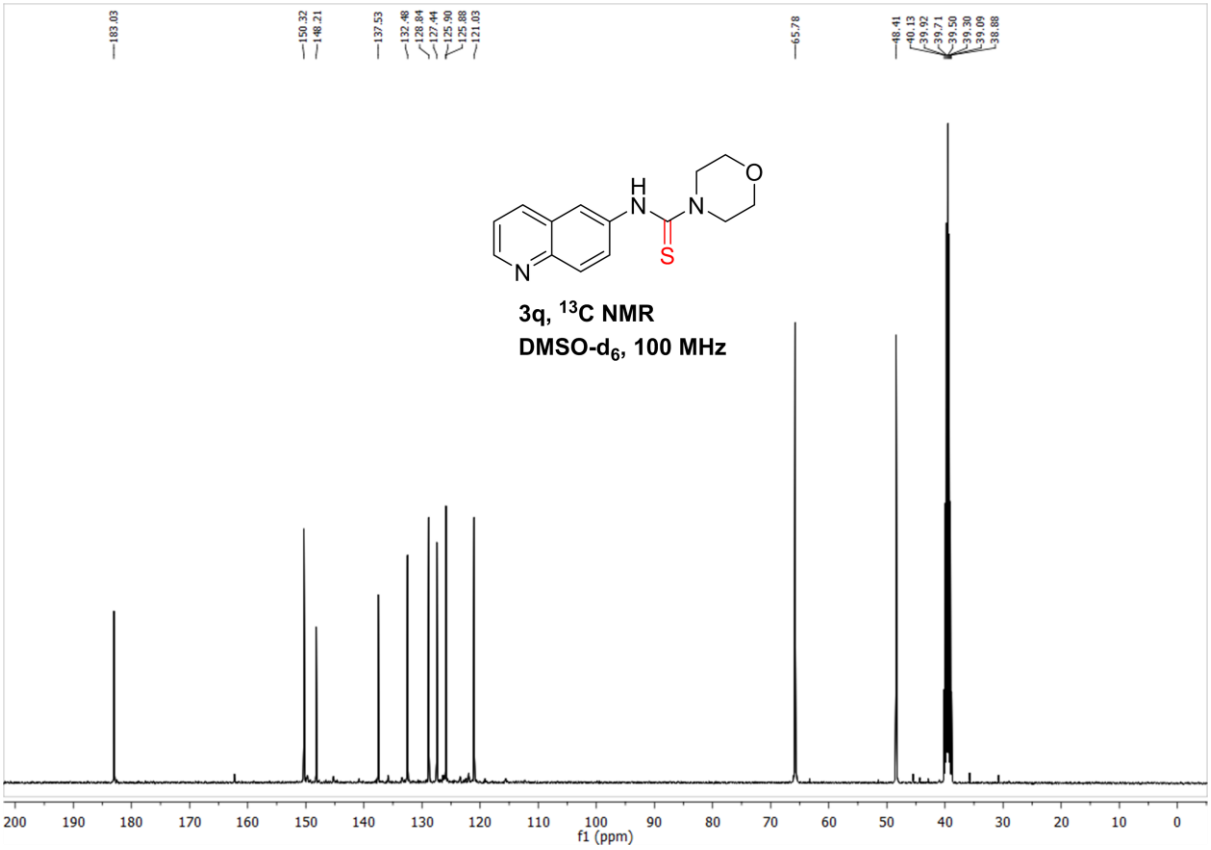


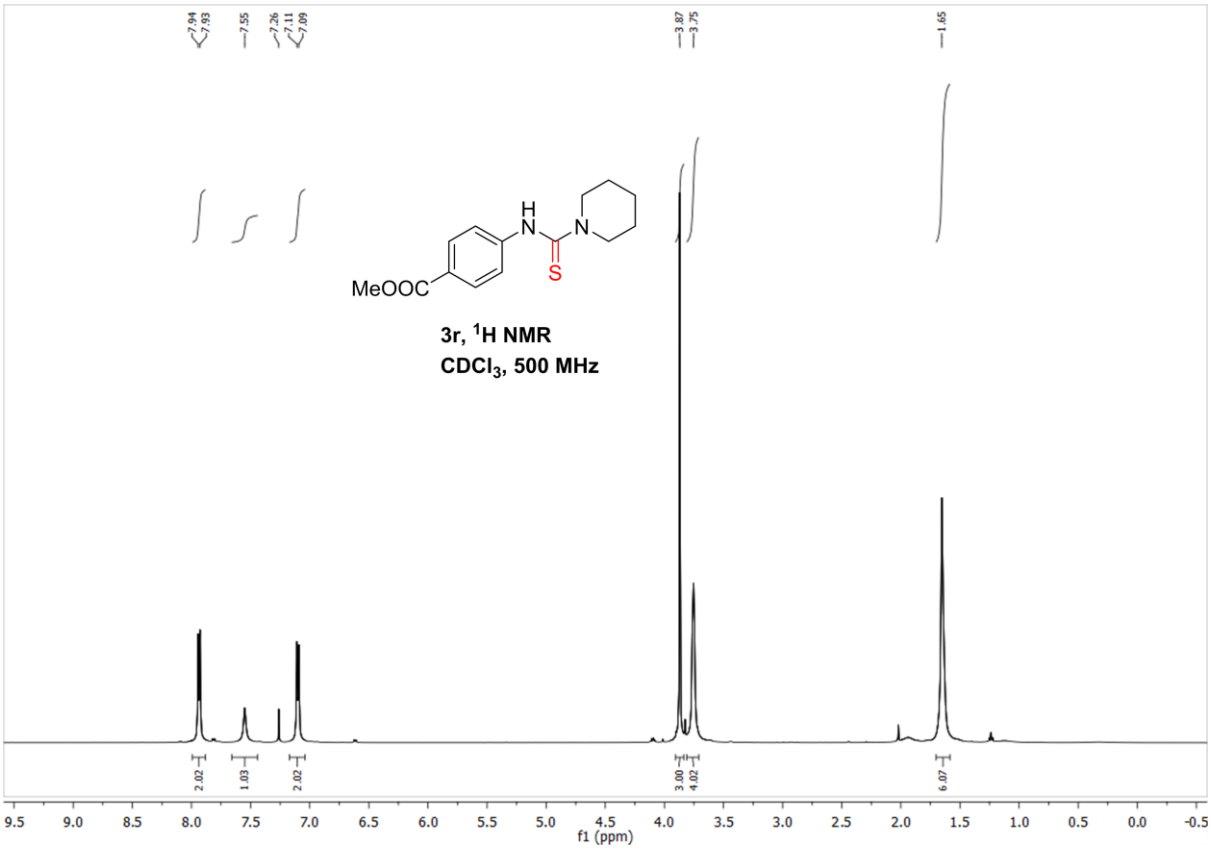
3o, ^{13}C NMR
$CDCl_3$, 150 MHz


7.90
7.84
7.80
7.79
7.74
7.73
7.66
7.64
7.58
7.53
7.52
7.46
7.45
7.36
7.30
7.29
7.26
7.17
7.16
3.66
1.54
1.51
1.42
S
HN
N
3p, ^{1}H NMR
CDCl$_3$, 500 MHz
1.00
1.23
1.15
1.13
2.38
1.60
1.02
4.08
6.39

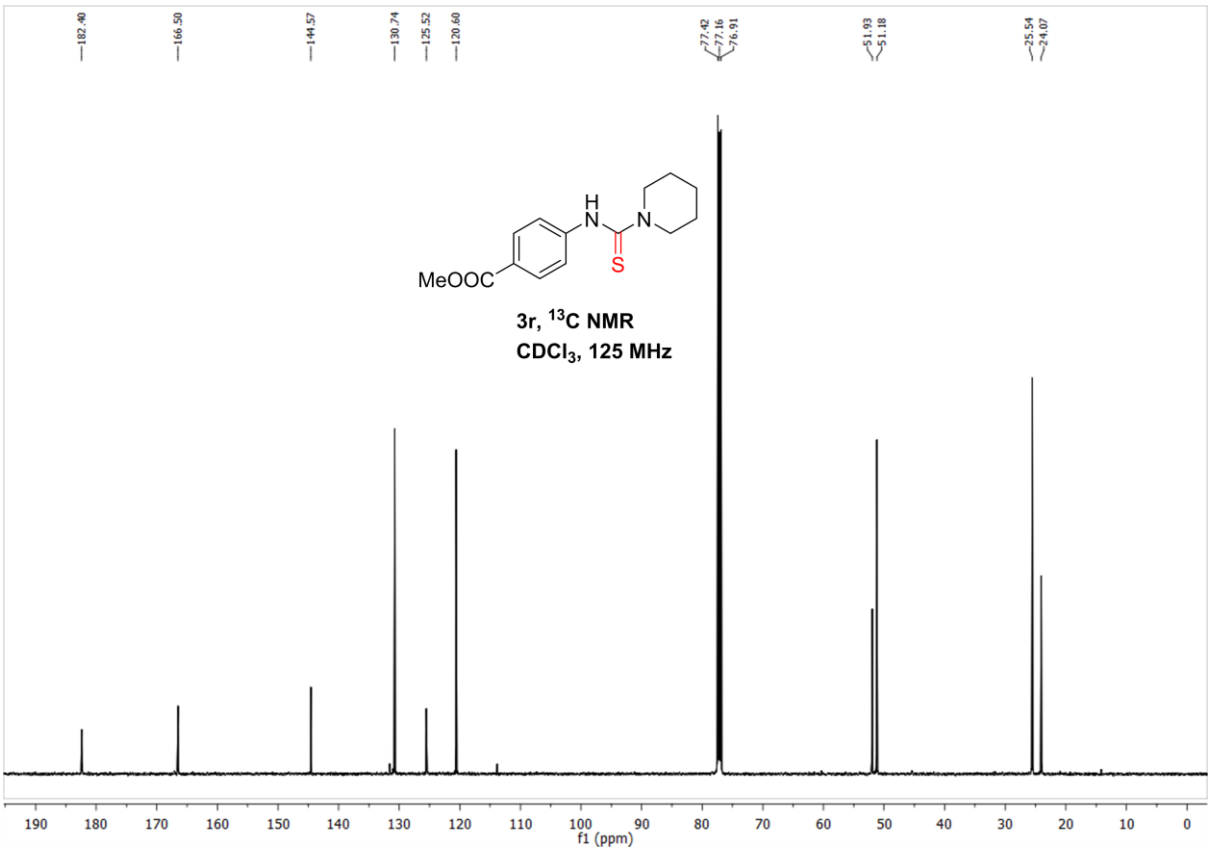

184.05
136.52
134.38
128.44
127.41
126.61
125.54
123.50
122.69
122.11
121.36
77.54
77.11
76.69
51.07
25.43
24.05
S
HN
N
3p, ^{13}C NMR
CDCl$_3$, 75 MHz
f1 (ppm)


9.63
8.89
8.25
8.23
7.95
7.93
7.76
7.74
7.72
7.52
7.52
7.51
7.41
7.40
3.99
3.73
3.41
2.49
3q, ^{1}H NMR
DMSO-d$_6$, 400 MHz
H2O
DMSO-d6
1.01
1.00
1.10
1.00
1.08
2.03
4.08
4.13
f1 (ppm)

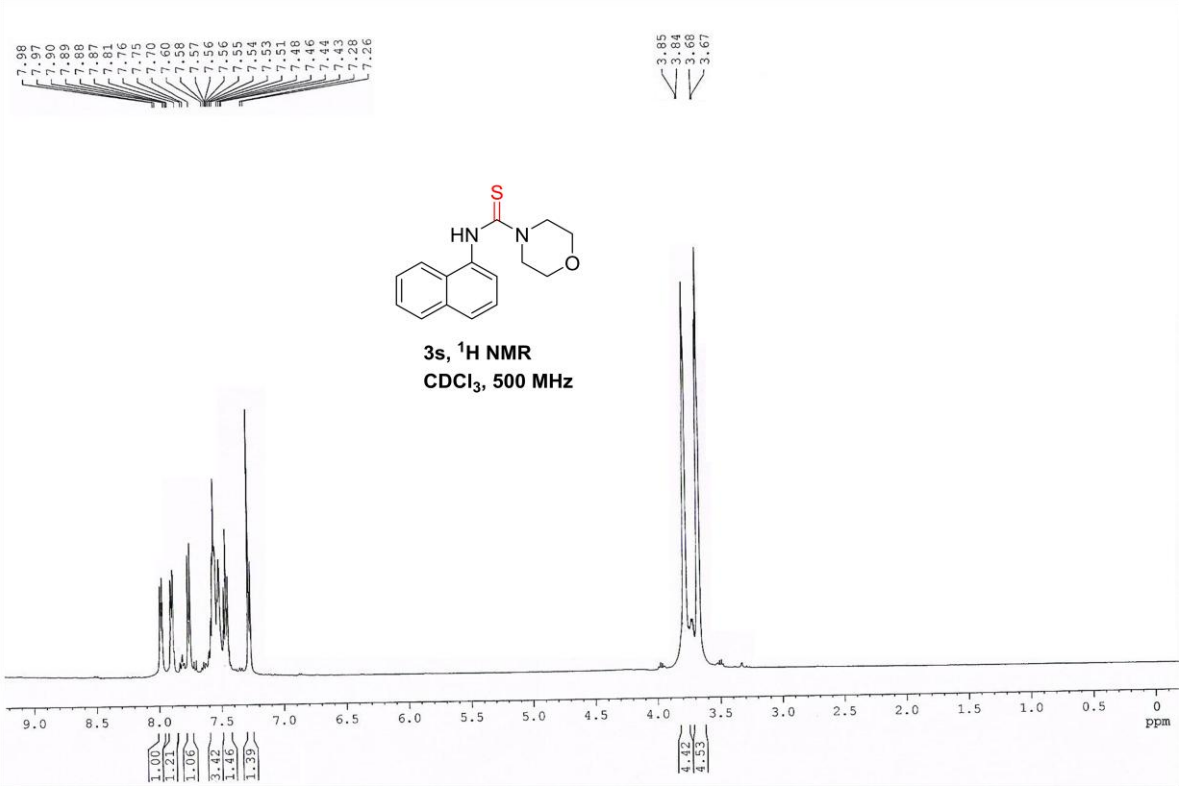

183.03
150.32
148.21
137.53
132.48
128.84
127.44
125.90
125.88
121.03
65.78
48.41
40.13
39.92
39.71
39.50
39.30
39.09
38.88
3q, ^{13}C NMR
DMSO-d$_6$, 100 MHz
f1 (ppm)

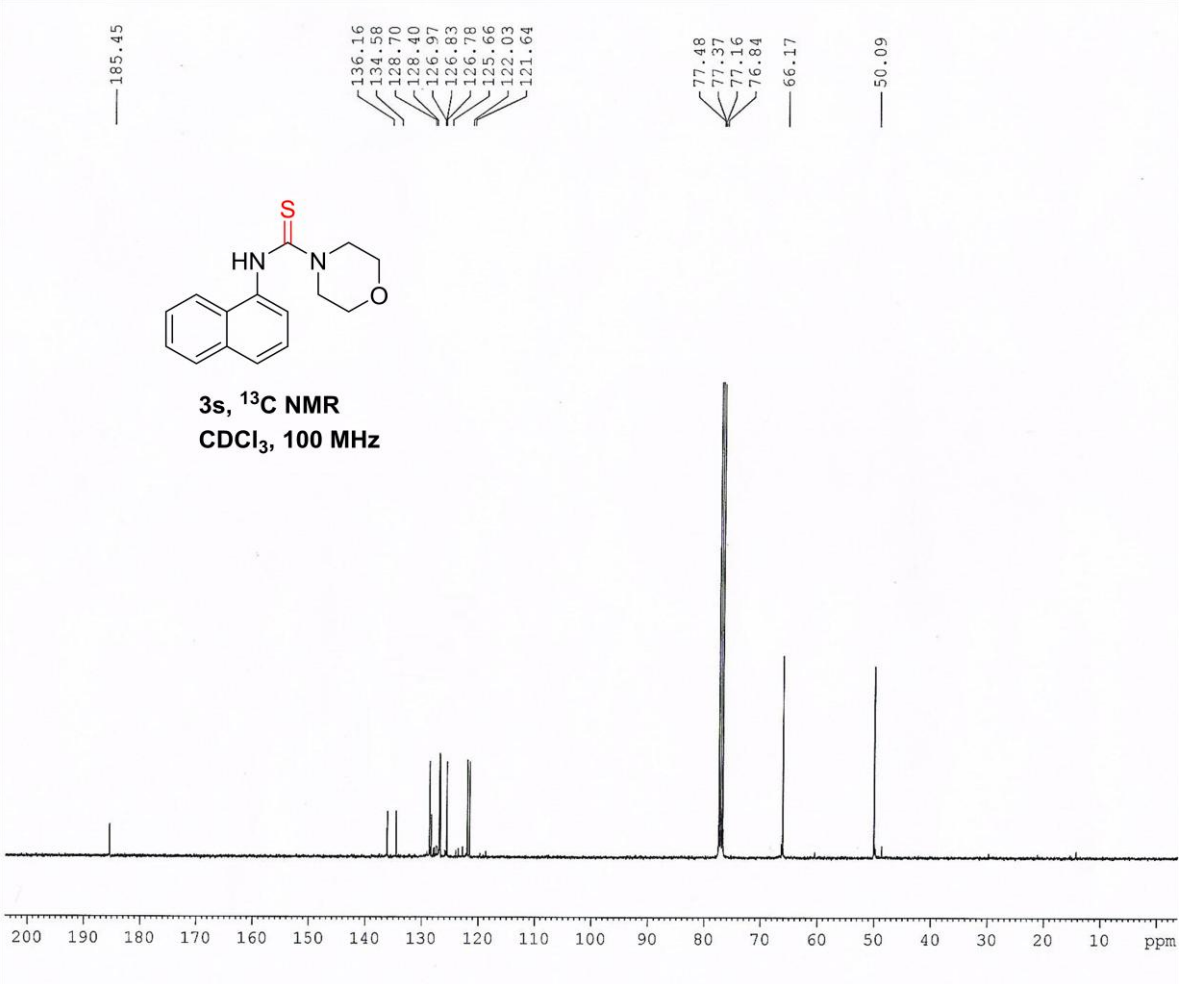


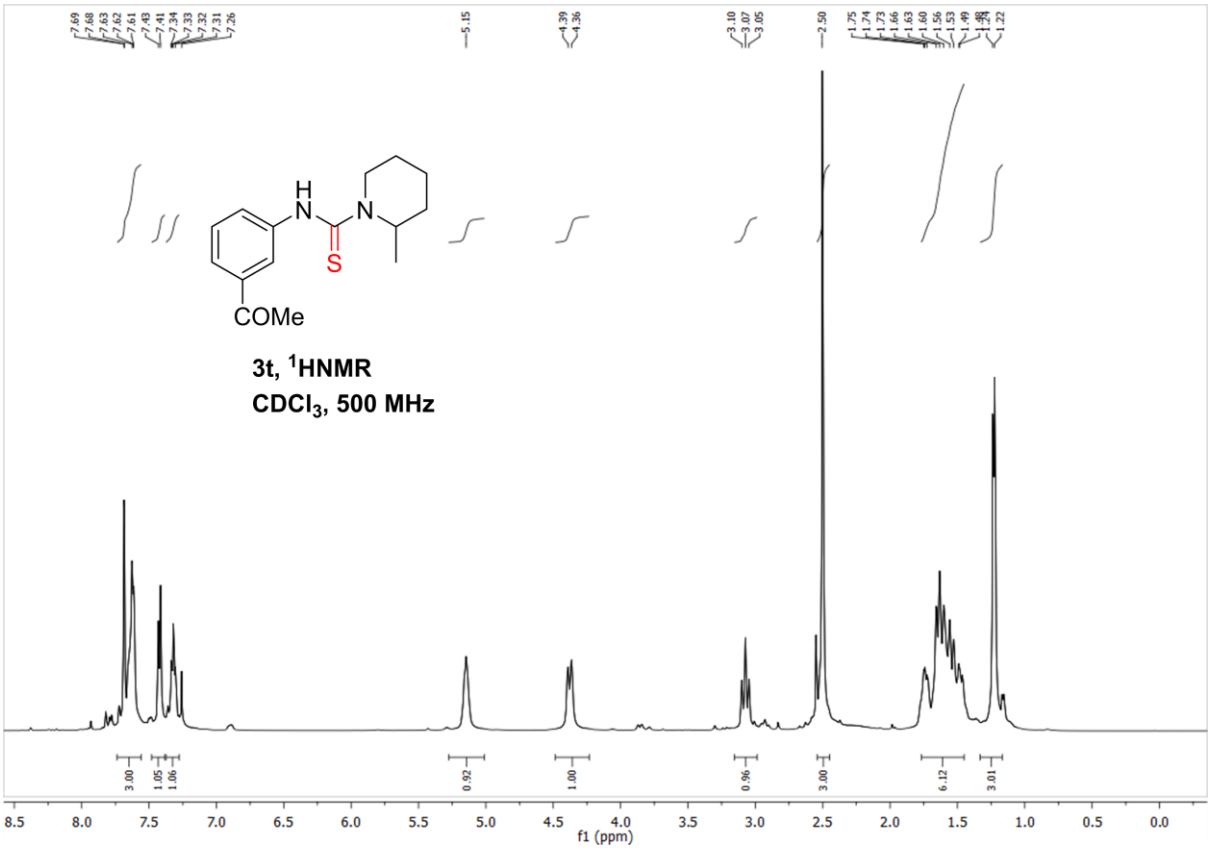
3r, ^{1}H NMR
$CDCl_3$, 500 MHz

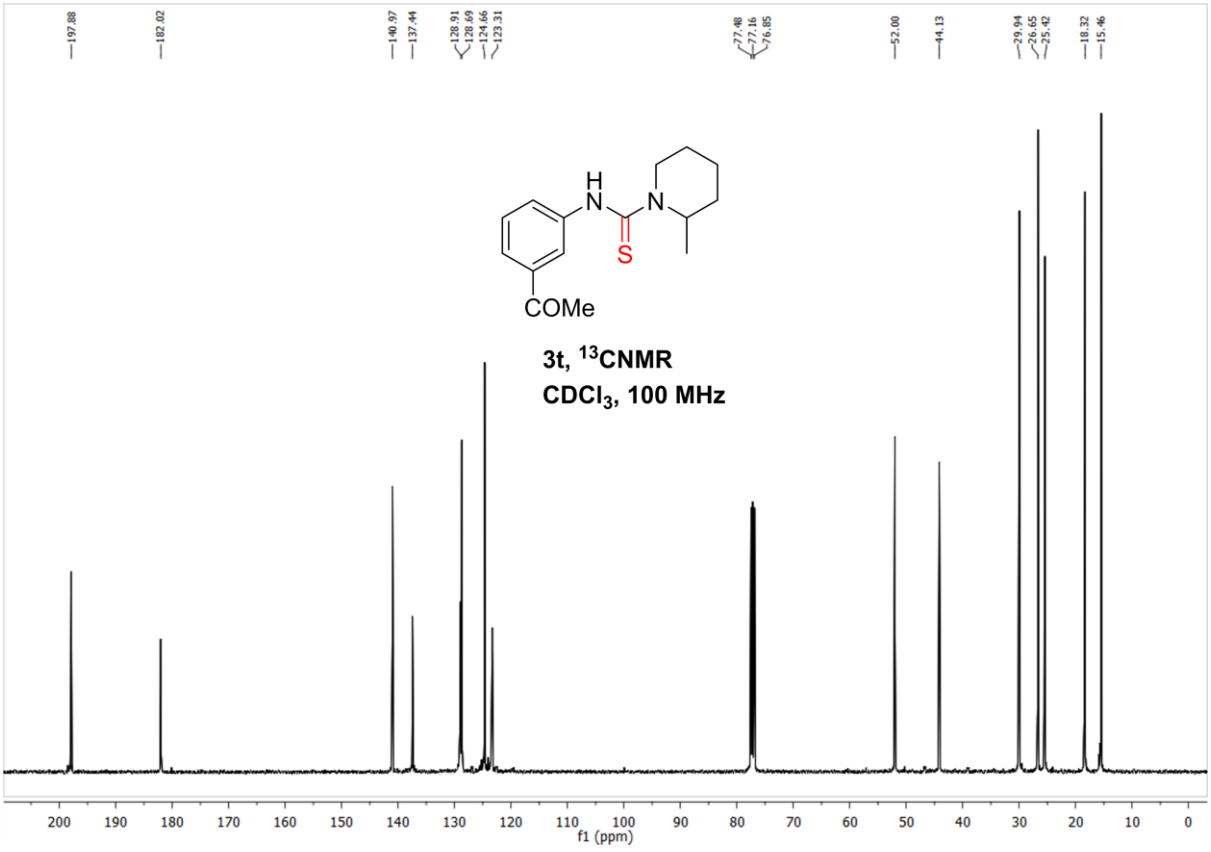


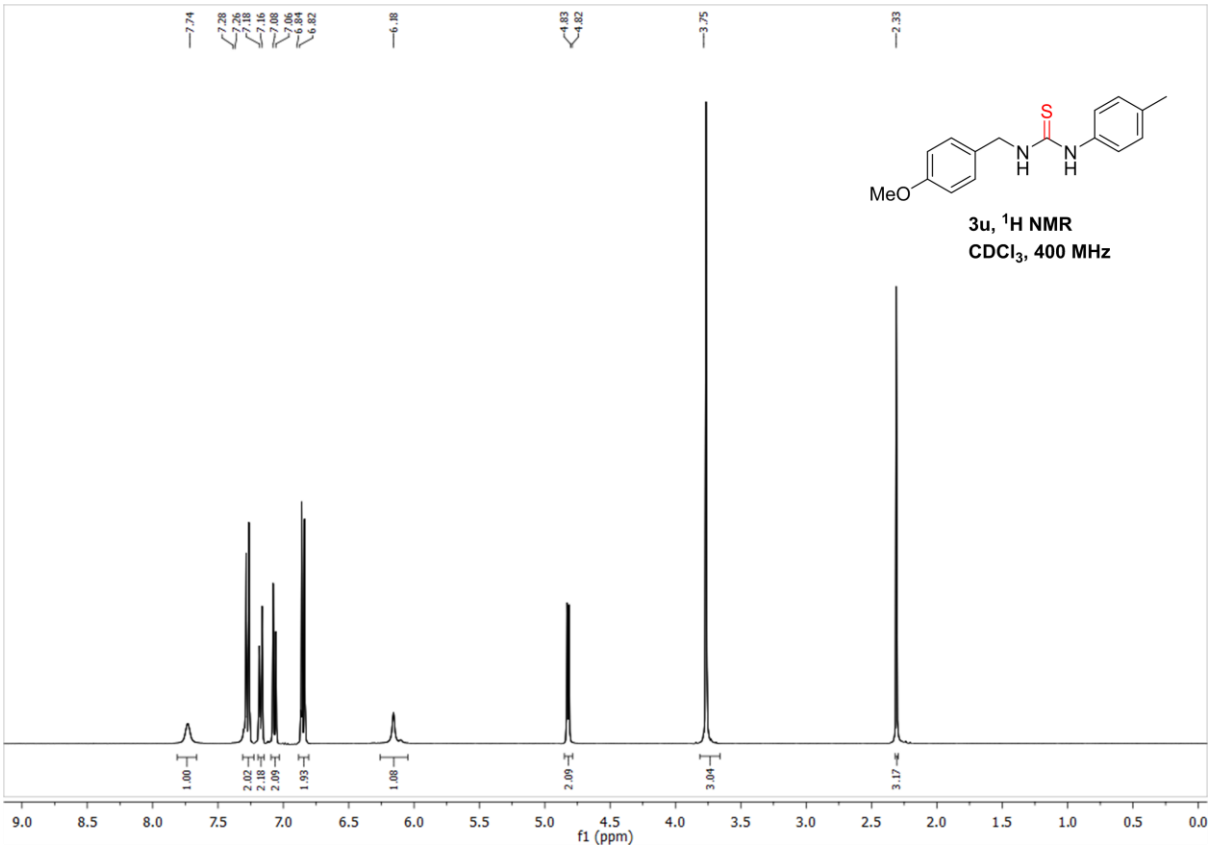
3r, ^{13}C NMR
$CDCl_3$, 125 MHz

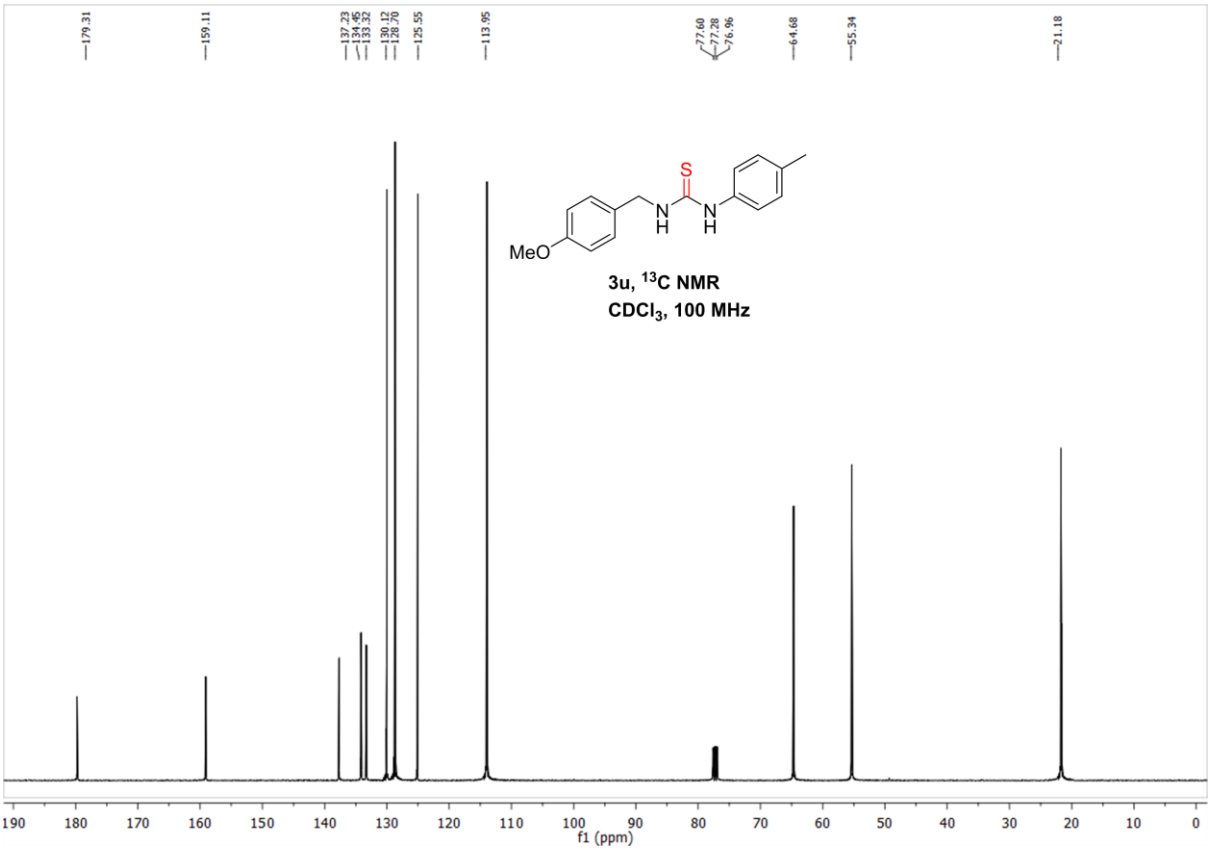

7.98
7.97
7.90
7.89
7.88
7.87
7.81
7.76
7.75
7.70
7.60
7.58
7.57
7.56
7.56
7.55
7.54
7.53
7.51
7.48
7.46
7.44
7.43
7.28
7.26
3.85
3.84
3.68
3.67
S
HN
N
O
3s, 1H NMR
CDCl3, 500 MHz
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm
1.00
1.21
1.06
3.42
1.46
1.39
4.42
4.53

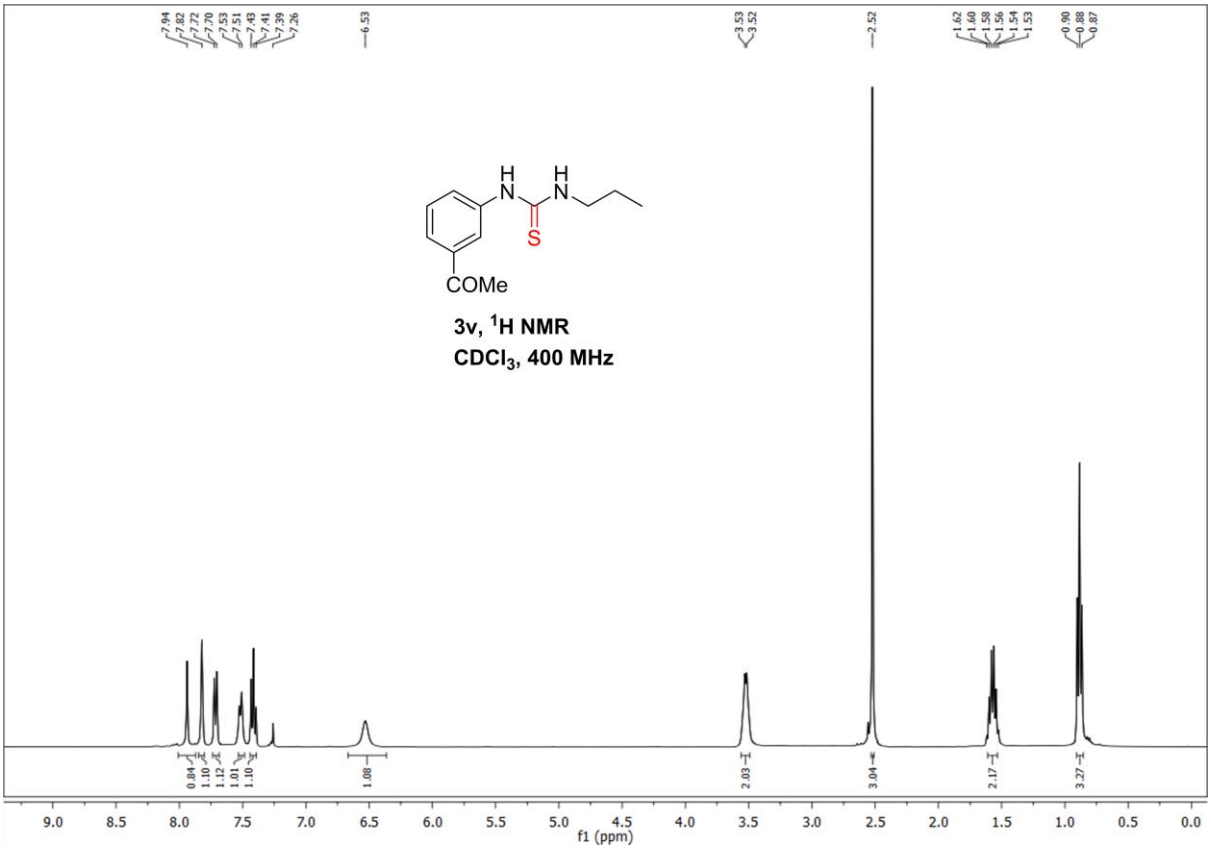

185.45
136.16
134.58
128.70
128.40
126.97
126.83
126.78
125.66
122.03
121.64
77.48
77.37
77.16
76.84
66.17
50.09
S
HN
N
O
3s, 13C NMR
CDCl3, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

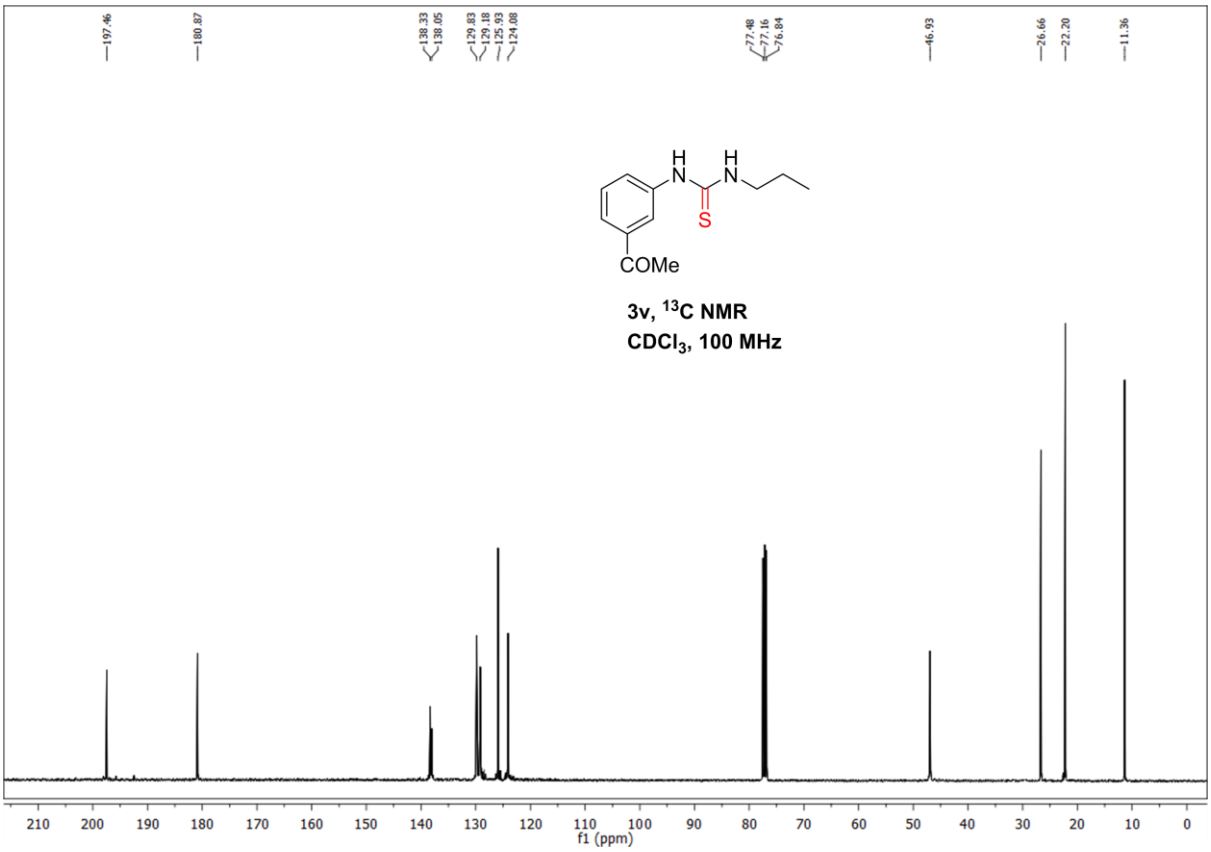

COMe
3t, ^{1}HNMR
$CDCl_3$, 500 MHz
f1 (ppm)


COMe
3t, ^{13}CNMR
$CDCl_3$, 100 MHz
f1 (ppm)


7.74
7.28
7.26
7.18
7.16
7.08
7.06
6.84
6.82
6.18
4.83
4.82
3.75
2.33
S
N
H
N
H
MeO
3u, ^{1}H NMR
$CDCl_3$, 400 MHz
1.00
2.02
2.18
2.09
1.93
1.08
2.09
3.04
3.17
f1 (ppm)

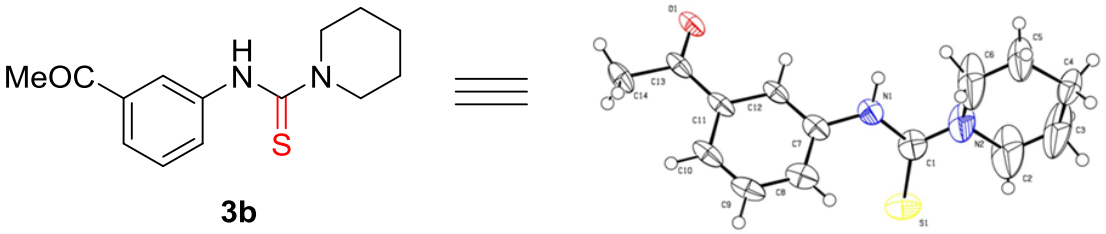

179.31
159.11
137.23
134.45
133.32
130.12
128.70
125.55
113.95
77.60
77.28
76.96
64.68
55.34
21.18
S
N
H
N
H
MeO
3u, ^{13}C NMR
$CDCl_3$, 100 MHz
f1 (ppm)


7.94
7.82
7.72
7.70
7.53
7.51
7.43
7.41
7.39
7.26
6.53
3.53
3.52
2.52
1.62
1.60
1.58
1.56
1.54
1.53
0.90
0.88
0.87
0.84
1.10
1.12
1.01
1.10
1.08
2.03
3.04
2.17
3.27
H
N
H
N
S
COMe
3v, ^{1}H NMR
$CDCl_3$, 400 MHz
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
f1 (ppm)


197.46
180.87
138.33
138.05
129.83
129.18
125.93
124.08
77.48
77.16
76.84
46.93
26.66
22.20
11.36
H
N
H
N
S
COMe
3v, ^{13}C NMR
$CDCl_3$, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G. X-ray Crystallography Data

Figure 1. ORTEP diagram of the crystal structure of 3b at 50% probability level



Details of the crystal structure investigation can be obtained from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (**3b**:CCDC deposition no.1856683)

Crystallographic data and structural refinement parameters for 3b

Bond precision:	C-C = 0.0093 A	Wavelength = 0.71073	
Cell:	A = 5.5091(7)	B = 7.2665(8)	C = 16.992(2)
	alpha = 80.823(5)	beta = 83.934(4)	gamma = 78.863(4)
Temperature:	99 K		

	Calculated	Reported
Volume	656.90(14)	656.90(14)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C_{14} $H_{18}N_2OS$	
Sum formula	C_{14} $H_{18}N_2OS$	C_{14} $H_{18}N_2OS$
Mr	262.36	262.36
Dx,g cm-3	1.326	1.326
Z	2	2
Mu (mm-1)	0.236	0.236
F000	280.0	280.0
F000'	280.34	
h,k,l max	6,8,20	6,8,20
Nref	2321	2310
T min,T max		
Tmin'		

Correction method = Not given

Data completeness = 0.995	Theta(max) = 24.999
R(reflections) = 0.1014(1873)	wR2(reflections) = 0.2926(2310)
S = 1.091	Npar = 164