Electronic Supplementary Material (ESI) for Green Chemistry

Towards a solvent-free organic synthesis laboratory: click-mechanosynthesis and direct structural characterization of thioureas without bulk solvents

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Supplementary Material

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1. Experimental

1.1 General comments

All chemicals were purchased from commercial sources (Sigma Aldrich or Alfa Aesar) and were used as received, except for 4-nitrophenyl isothiocyanate which was purified by column chromatography. The experiments were carried out in a Retsch MM200 mill at a frequency of 30 Hz using a 10 cm^3 stainless steel grinding jar and a single stainless steel ball of 12 mm diameter. Dry acetonitrile was used as a liquid phase throughout all liquid-assisted grinding (LAG) experiments.

Solution ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance (300 and 600 MHz) spectrometers with tetramethylsilane as an internal standard. Fourier transform infrared spectra were collected using a Perkin Elmer Fourier Transform-Infrared Attenuated Total Reflection spectrometer in the range 600 cm^{-1} to 3500 cm^{-1}.

Powder X-ray diffraction (PXRD) data were collected on a Philips X'Pert Pro diffractometer, equipped with an X'celerator RTMS detector, using Ni-filtered CuKα radiation and using a flat plate configuration. Powder diffraction data used for structural analysis of **1e** was collected by averaging 15 scans in the 2θ range 4^o-60^o, at a step size of 0.002^o and intensity integration time of 1.2 seconds per step. Data for the structural analysis of **1c** was obtained by averaging 20 scans collected in the angular 2θ region 5^o-50^o, at a step size of 0.017^o and intensity integration time of 10.3 seconds per step. Structural analysis of **2m** was performed using data obtained by averaging 20 scans in the 2θ region 5^o-50^o, at a step size of 0.017^o and intensity integration time of 10.3 seconds per step. Identical parameters were used to obtain PXRD data used for structural characterization of **4b**. PXRD data used in attempts to solve the structure of **3f** was obtained by averaging 30 scans collected in the data range 5^o-50^o, with a step size of 0.017^o and an integration time of 10.3 seconds per step.

1.2 Synthesis of thioureas

In a typical grinding experiment, 150-200 mg of the reactant mixture (in the case of liquid reactants, the appropriate volumes were measured) was ground manually in a mortar for 15-20 minutes (unless otherwise stated) or in a ball mill for 10 minutes (unless otherwise stated). In LAG experiments, 50 μL of acetonitrile was used (unless otherwise stated). Upon completion

of the reaction, the solid product was scraped off the walls of the grinding jar affording thiourea in quantitative (>99%) yield.

***N,N'*-di(4-methoxyphenyl)thiourea (1a)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 3.74 (6 H, s, OCH_3), 6.89 (4 H, d, *J* 8.8, Ar), 7.31 (4 H, d, *J* 8.8, Ar), 9.39 (2 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 55.2, 113.6, 126.1, 132.2, 156.5, 180.2.

***N*-(4-methoxyphenyl)-*N'*-(4-methylphenyl)thiourea (1b)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 2.28 (3 H, s, CH_3), 3.75 (3 H, s, OCH_3), 6.89 (2 H, d, *J* 8.9, Ar), 7.12 (2 H, d, *J* 8.1, Ar), 7.28-7.40 (4 H, m, overlapped Ar protons), 9.46 (1 H, s, NH), 9.49 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 20.4, 55.2, 113.6, 123.8, 125.9, 128.8, 132.2, 133.5, 136.8, 156.5, 179.9.

***N*-(4-methoxyphenyl)-*N'*-phenylthiourea (1c**; same as **2a)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.75 (3 H, s, OCH_3), 6.90 (2 H, d, *J* 8.9, Ar), 7.11 (1 H, t, *J* 7.3, Ph), 7.26-7.38 (4 H, m, overlapped Ar protons), 7.47 (2 H, d, *J* 7.6, Ph), 9.59 (1 H, s, NH), 9.61 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 55.2, 113.7, 123.6, 124.3, 126.0, 128.4, 132.1, 139.5, 156.5, 179.9.

***N*-(4-fluorophenyl)-*N'*-(4-methoxyphenyl)thiourea (1d**; same as **3a)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.74 (3 H, s, OCH_3), 6.90 (2 H, d, *J* 8.9, Ar), 7.15 (2 H, t, *J* 8.8, Ar), 7.31 (2 H, d, *J* 8.9, Ar), 7.40–7.50 (2 H, m, Ar), 9.55 (1 H, s, NH), 9.59 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 55.2, 113.7, 114.8;115.0 (d, *J* 22.4), 126.1, 126.2;126.3 (d, *J* 8.2), 132.0, 135.83;135.86 (d, *J* 2.6), 156.6, 157.5;160.7 (d, *J* 241.2), 180.2.

***N*-(4-chlorophenyl)-*N'*-(4-methoxyphenyl)thiourea (1e)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.74 (3 H, s, OCH_3), 6.91 (2 H, d, *J* 8.5, Ar), 7.26–7.42 (4 H, m, overlapped Ar protons), 7.50 (2 H, d, *J* 8.5, Ar), 9.62–9.74 (2 H, brs, overlapped NH protons). δ_C(75 MHz, d_6-DMSO; Me_4Si) 55.2, 113.7, 125.3, 126.0, 128.1, 128.2, 131.9, 138.6, 156.6, 179.9.

***N*-*i*-propyl-*N'*-(4-methoxyphenyl)thiourea (1f)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.13 (6 H, d, *J* 6.4, CH_3), 3.73 (3 H, s, OCH_3), 4.27–4.48 (1 H, m, CH), 6.88 (2 H, d, *J* 8.5, Ar), 7.24 (2 H, d, *J* 8.5, Ar), 7.32 (1 H, d, *J* 5.6, NH), 9.11 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 22.0, 45.4, 55.2, 113.7, 125.6, 132.0, 156.2, 179.6.

***N*-(3-dimethylaminopropyl)-*N'*-(4-methoxyphenyl)thiourea (1g)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.54-1.66 (2 H, m, CH_2), 1.99 (6 H, s, CH_3), 2.22 (2 H, t, *J* 6.2, CH_2), 3.40–3.52 (2 H, m, CH_2), 3.74 (3 H, s, OCH_3), 6.91 (2 H, d, *J* 8.8, Ar), 7.17 (2 H, d, *J* 8.8, Ar), 7.88 (1 H, t, *J* 4.8,

NH), 9.29 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 25.6, 43.8, 44.9, 55.2, 57.5, 114.0, 126.2, 131.3, 156.7, 180.5.

***N*-benzyl-*N'*-(4-methoxyphenyl)thiourea (1h)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 3.74 (3 H, s, OCH_3), 4.72 (2 H, d, *J* 4.6, CH_2), 6.90 (2 H, d, *J* 8.9, Ar), 7.25 (2 H, d, *J* 8.8, Ar), 7.30–7.35 (5 H, m, Ar), 7.92 (1 H, brs, NH), 9.38 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 47.2, 55.2, 113.9, 126.1, 126.7, 127.3, 128.2, 131.6, 139.2, 156.6, 181.1.

***N*-(4-methoxyphenyl)-*N'*-piperidinethiourea (1i)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.47-1.68 (6 H, m, CH_2), 3.73 (3 H, s, OCH_3), 3.85 (4 H, m, CH_2), 6.85 (2 H, d, *J* 8.9, Ar), 7.13 (2 H, d, *J* 8.9, Ar), 9.04 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 23.9, 25.4, 48.9, 55.1, 113.1, 127.3, 134.1, 156.3, 180.9.

***N*-(4-methoxyphenyl)-*N'*-morpholinethiourea (1j)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.60-3.68 (4 H, m, CH_2), 3.74 (3 H, s, OCH_3), 3.81-3.91 (4 H, m, CH_2), 6.86 (2 H, d, *J* 8.9, Ar), 7.16 (2 H, d, *J* 8.9, Ar), 9.21 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 48.2, 55.1, 65.7, 113.2, 127.4, 133.7, 156.5, 182.0.

***N*-(4-methoxyphenyl)-*N'*-thiomorpholinethiourea (1k)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.61-2.71 (4 H, m, CH_2), 3.74 (3 H, s, OCH_3), 4.12-4.24 (4 H, m, CH_2), 6.86 (2 H, d, *J* 8.9, Ar), 7.14 (2 H, d, *J* 8.9, Ar), 9.18 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 26.2, 50.8, 55.1, 113.2, 127.7, 133.7, 156.6, 181.3.

***N*-(2,4-dimethylphenyl)-*N'*-(4-methoxyphenyl)thiourea (1l)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.19 (3 H, s, CH_3), 2.26 (3 H, s, CH_3), 3.74 (3 H, s, OCH_3), 6.89 (2 H, d, *J* 8.8, Ar), 6.94-7.12 (3 H, m, Ar), 7.31 (2 H, d, *J* 8.9, Ar), 9.05 (1 H, s, NH), 9.31 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 17.7, 20.5, 55.2, 113.6, 126.1, 126.6, 127.9, 130.8, 132.2, 134.6, 135.1, 135.5, 156.5, 180.7.

***N*-(2,6-dimethylphenyl)-*N'*-(4-methoxyphenyl)thiourea (1m)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.20 (6 H, s, CH_3), 3.74 (3 H, s, OCH_3), 6.65-7.48 (7 H, m, overlapped Ar), 8.07-9.91 (2 H, brs, overlapped NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 18.0, 55.2, 113.9, 126.0, 126.9, 127.7, 136.4, 156.6, 180.5.

***N*-(4-methylphenyl)-*N'*-phenylthiourea (2b)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 2.28 (3 H, s, CH_3), 7.10-7.15 (3 H, m, overlapped Ar), 7.28-7.36 (4 H, m, overlapped Ar), 7.48 (2 H, d, *J* 7.5,

Ph), 9.65 (2 H, s, overlapped NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 20.5, 123.6, 123.9, 124.3, 128.4, 128.9, 133.7, 136.8, 139.5, 179.6.

***N,N'*-diphenylthiourea (2c)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 7.13 (2 H, t, *J* 7.4, Ph), 7.31-7.35 (4 H, m, Ph), 7.49 (4 H, d, *J* 7.5, Ph), 9.75 (2 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 123.6, 124.4, 128.4, 139.4, 179.6.

***N*-(4-fluorophenyl)-*N'*-phenylthiourea (2d**; same as **3c)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 7.09-7.20 (3 H, m, overlapped Ar), 7.30-7.38 (2 H, t, *J* 7.9, Ph), 7.43-7.52 (4 H, m, overlapped Ar), 9.70 (1 H, s, NH), 9.75 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 114.8;115.0 (d, *J* 22.2), 123.6, 124.4, 126.08 ;126.14 (d, *J* 8.4), 128.4, 135.69;135.71 (d, *J* 2.3), 139.3, 158.3;159.9 (d, *J* 241.5), 180.0.

***N*-(4-chlorophenyl)-*N'*-phenylthiourea (2e)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 7.13 (1 H, t, *J* 7.0, Ph), 7.27-7.60 (8 H, m, overlapped Ar), 9.85 (1 H, s, NH), 9.86 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 123.7, 124.6, 125.2, 128.2, 128.3, 128.5, 138.5, 139.3, 179.7.

***N*- *i*-propyl -*N'*-phenylthiourea (2f)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 1.16 (6 H, d, *J* 6.5, CH_3), 4.31-4.46 (1 H, m, CH), 7.07 (1 H, t, *J* 7.3, Ph), 7.30 (2 H, t, *J* 7.9, Ph), 7.43 (2 H, d, *J* 7.6, Ph), 7.55 (1 H, d, *J* 7.4, NH), 9.28 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 21.9, 45.3, 122.8, 123.8, 128.4, 139.5, 179.2.

***N*-(3-dimethylaminopropyl)-*N'*-phenylthiourea (2g)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.57-1.70 (2 H, m, CH_2), 2.02 (6 H, s, CH_3), 2.24 (2 H, t, *J* 6.5, CH_2), 3.41-3.56 (2 H, m, CH_2), 7.08-7.19 (1 H, m, Ph), 7.30-7.37 (4 H, m, Ph), 8.07 (1 H, t, *J* 4.8, NH), 9.51 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 25.7, 43.6, 44.9, 57.3, 123.5, 124.3, 128.6, 138.9, 180.1.

***N*-benzyl-*N'*-phenylthiourea (2h)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 4.74 (2 H, d, *J* 5.4, CH_2), 7.11 (1 H, t, *J* 7.4, Ph), 7.24-7.28 (1 H, m, Ar), 7.30-7.36 (6 H, m, Ar), 7.43 (2 H, d, *J* 7.6, Ar), 8.13 (1 H, s, NH), 9.57 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 47.2, 123.3, 124.25, 126.8, 127.4, 128.2, 128.6,139.0 139.1, 180.8.

***N*-phenyl-*N'*-piperidinethiourea (2i)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.45-1.74 (6H, m, overlapped CH_2 protons), 3.74-3.97 (4 H, m, CH_2), 7.00-7.14 (1 H, m, Ph), 7.17-7.35 (4 H, m, Ph), 9.18 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 23.9, 25.4, 49.2, 124.0, 125.0, 127.9, 141.2, 180.7.

***N*-phenyl-*N'*-morpholinethiourea (2j)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 3.65 (4 H, brs, CH_2), 3.88 (4 H, brs, CH_2), 7.11 (1 H, brs, Ph), 7.30 (4 H, brs, Ph), 9.32 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 48.4, 65.7, 124.3, 125.2, 127.9, 140.9, 181.8.

***N*-phenyl-*N'*-thiomorpholinethiourea (2k)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 2.66-2.73 (4 H, m, CH_2), 4.16-4.23 (4 H, m, CH_2), 7.12 (1 H, t, *J* 6.9, Ph), 7.25-7-33 (4 H, m, Ph), 9.29 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 26.3, 50.9, 124.4, 125.6, 127.9,140.9, 181.2.

***N*-(2,4-dimethylphenyl)-*N'*-phenylthiourea (2l)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.20 (3 H, s, CH_3), 2.27 (3 H, s, CH_3), 6.96-7.15 (4 H, m, Ar), 7.32 (2 H, t, *J* 7.9, Ar), 7.48 (2 H, d, *J* 7.5, Ar), 9.24 (1 H, s, NH), 9.55 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 17.8, 20.6, 123.7, 124.3, 126.7, 127.9, 128.3, 130.9, 134.6, 135.1, 135.6, 139.5, 180.4.

***N*-(2,6-dimethylphenyl)-*N'*-phenylthiourea (2m)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.22 (6 H, s, CH_3), 6.92-7.64 (8 H, m, overlapped Ar protons), 8.38-10.07 (2 H, brs, overlapped NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 18.0, 123.2, 124.4, 126.9, 127.7, 128.5, 136.3, 136.9 (low intensity signal), 139.5, 180.2.

***N*-(4-fluorophenyl)-*N'*-(4-methylphenyl)thiourea (3b)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 2.28 (3 H, s, CH_3), 7.11-7.18 (4 H, m, Ar), 7.32-7.35 (2 H, m, Ar), 7.45-7.49 (2 H, m, Ar), 9.62 (1 H, s, NH), 9.68 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 20.4, 114.8;114.9 (d, *J* 22.8), 123.9, 126.07;126.12 (d, *J* 8.4), 128.9, 133.7, 135.75;135.77 (d, *J* 2.9), 136.6, 158.2;159.8 (d, *J* 241.4), 180.0.

***N,N'*-di(4-fluorophenyl)thiourea (3d)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 7.16 (4 H, t, *J* 8.8, Ar), 7.43-7.50 (4 H, m, Ar), 9.72 (2 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 114.9;115.2 (d, *J* 22.5), 126.2;126.3 (d, *J* 8.3), 135.6;135.7 (d, *J* 2.7), 157.6;160.8 (d, *J* 241.5), 180.4.

***N*-(4-fluorophenyl)-*N'*-(4-chlorophenyl)thiourea (3e)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 7.00-7.65 (8 H, m, Ar), 9.82;9.85 (2 H, s, overlapped NH protons). δ_C(75 MHz, d_6-DMSO; Me_4Si) 114.9;115.2 (d, *J* 22.5), 125.3, 126.2;126.3 (d, *J* 8.2), 128.2, 128.3, 135.5;135.6 (d, *J* 2.4), 138.4, 157.6;160.8 (d, *J* 241.6), 180.0.

***N*-(4-fluorophenyl)-*N'*-*i*-propylthiourea (3f)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 1.16 (6 H, d, *J* 6.5, CH_3), 4.29-4.46 (1 H, m, CH), 7.10-7.16 (2 H, m, Ar), 7.38-7.44 (2 H, m, Ar), 7.55 (1 H, d,

J 5.4, NH), 9.25 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 21.9, 45.3, 114.8;115.0 (d, *J* 22.5), 125.3, 135.7, 157.9;159.5 (d, *J* 241.0), 179.6.

***N*-(3-dimethylaminopropyl)-*N'*-(4-fluorophenyl)thiourea (3g)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 1.60-1.67 (2 H, m, CH_2), 2.05 (6 H, s, CH_3), 2.25 (2 H, t, *J* 6.6, CH_2), 3.42-3.53 (2 H, m, CH_2), 7.13-7.18 (2 H, m, Ar), 7.31-7.38 (2 H, m, Ar), 7.97 (1 H, s, NH), 9.45 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 25.7, 43.5, 44.9, 57.2, 115.1;115.3 (d, *J* 22.7), 125.9, 135.2, 158.24;159.84 (d, *J* 241.5), 180.5.

***N*-benzyl-*N'*-(4-fluorophenyl)thiourea (3h)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 4.74 (2 H, d, *J* 5.5, CH_2), 7.13-7.18 (2 H, m, Ar), 7.23-7.28 (1 H, m, Ar), 7.31-7.36 (4 H, m, Ar), 7.40-7.46 (2 H, m, Ar), 8.13 (1 H, s, NH), 9.55 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 47.1, 115.02;115.17 (d, *J* 22.4), 125.8, 126.8, 127.3, 128.2, 135.4, 138.9, 158.2;159.8 (d, *J* 241.5), 181.2.

***N*-(4-fluorophenyl)-*N'*-piperidinethiourea (3i)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.47-1.69 (6 H, m, CH_2), 3.76-3.95 (4 H, m, CH_2), 7.10 (2 H, t, *J* 8.9, Ar), 7.20-7.30 (2 H, m, Ar), 9.16 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 23.9, 25.4, 49.0, 114.3;114.6 (d, *J* 22.4), 127.44;127.55 (d, *J* 8.2), 137.51;137.55 (d, *J* 2.5), 157.4;160.6 (d, *J* 240.8), 180.8.

***N*-(4-fluorophenyl)-*N'*-morpholinethiourea (3j)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.56-3.72 (4 H, m, CH_2), 3.78-3.95 (4 H, m, CH_2), 7.12 (2 H, t, *J* 8.9, Ar), 7.20-7.34 (2 H, m, Ar), 9.32 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 48.3, 65.7, 114.46;114.61 (d, *J* 22.9), 127.52;127.58 (d, *J* 8.3), 137.17;137.18 (d, *J* 2.4), 158.35;159.95 (d, *J* 241.2), 181.9.

***N*-(4-fluorophenyl)-*N'*-thiomorpholinethiourea (3k)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.62-2.74 (4 H, m, CH_2), 4.12-4.26 (4 H, m, CH_2), 7.13 (2 H, t, *J* 8.9, Ar), 7.21-7.31 (2 H, m, Ar), 9.29 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 26.3, 50.9, 114.41;114.71 (d, *J* 22.4), 127.99;128.10 (d, *J* 8.3), 137.21;137.24 (d, *J* 2.7), 157.7;160.9 (d, *J* 241.1), 181.2.

***N*-(2,4-dimethylphenyl)-*N'*-(4-fluorophenyl)thiourea (3l)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.19 (3 H, s, CH_3), 2.27 (3 H, s, CH_3), 6.94-7.20 (5 H, m, Ar), 7.37-7.50 (2 H, m, Ar), 9.28 (1 H, s, NH), 9.50 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 17.6, 20.5, 114.75;114.90 (d, *J* 22.2), 126.23;126.28 (d, *J* 8.1), 126.6, 127.8, 130.9, 134.6, 134.9, 135.6, 135.83;135.84 (d, *J* 2.0), 158.2;159.8(d, *J* 241.1), 180.8.

***N*-(2,6-dimethylphenyl)-*N'*-(4-fluorophenyl)thiourea (3m)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.20 (6 H, s, CH_3), 6.94-7.94 (7 H, m, overlapped Ar protons), 8.94 (1 H, s, NH), 9.85 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 17.9, 115.2, 125.7, 126.7, 127.6, 135.5, 136.3, 137.1, 158.32;159.91 (d, *J* 240.5), 180.6.

***N*-(4-methoxyphenyl)-*N'*-(4-nitrophenyl)thiourea (4a)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.75 (3 H, s, OCH_3), 6.94 (2 H, d, *J* 8.8, Ar), 7.36 (2 H, d, *J* 8.8, Ar), 7.84 (2 H, d, *J* 9.0, Ar), 8.19 (2 H, d, *J* 9.0, Ar), 10.06 (1 H, s, NH), 10.20 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 55.2, 113.8, 121.4, 124.3, 125.9, 131.6, 142.1, 146.4, 156.9, 179.5.

***N*-(4-methylphenyl)-*N'*-(4-nitrophenyl)thiourea (4b)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.29 (3 H, s, CH_3), 7.17 (2 H, d, *J* 8.3, Ar), 7.35 (2 H, d, *J* 8.3, Ar), 7.83 (2 H, d, *J* 9.2, Ar), 8.19 (2 H, d, *J* 9.2, Ar), 10.18 (1 H, s, NH), 10.29 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 20.5, 121.5, 123.8, 124.3, 129.1, 134.3, 136.3, 142.2, 146.4, 179.2.

***N* -(4-nitrophenyl)-*N'*-phenylthiourea (4c)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 7.17 (1 H, t, *J* 7.3, Ph), 7.37 (2 H, t, *J* 7.9, Ph), 7.49 (2 H, d, *J* 7.9, Ph), 7.84 (2 H, d, *J* 9.0, Ar), 8.20 (2 H, d, *J* 9.0, Ar), 10.26 (1 H, s, NH), 10.37 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 121.5, 123.7, 124.4, 125.0, 128.6, 138.9, 142.3, 146.3, 179.3.

***N*-(4-fluorophenyl)-*N'*-(4-nitrophenyl)thiourea (4d)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 7.20 (2 H, t, *J* 8.7, Ar), 7.39-7.56 (2 H, m, Ar), 7.83 (2 H, d, *J* 9.0, Ar), 8.20 (2 H, d, *J* 9.0, Ar), 10.21 (1 H, s, NH), 10.37 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 115.11;115.26 (d, *J* 22.4), 121.6, 124.3, 126.17;126.22 (d, *J* 8.5), 135.17;135.18 (d, *J* 2.2), 142.3, 146.1, 158.6;160.2 (d, *J* 242.5), 179.7.

***N*-(4-chlorophenyl)-*N'*-(4-nitrophenyl)thiourea (4e)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 7.42 (2 H, d, *J* 8.6, Ar), 7.54 (2 H, d, *J* 8.6, Ar), 7.82 (2 H, d, *J* 8.9, Ar), 8.20 (2 H, d, *J* 8.9, Ar), 10.31 (1 H, s, NH), 10.43 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 121.7, 124.4, 125.4, 128.5, 128.9, 137.9, 142.4, 146.1, 179.4.

***N*- *i*-propyl-*N'*-(4-nitrophenyl)thiourea (4f)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 1.19 (6 H, d, *J* 6.6, CH_3), 4.27-4.48 (1 H, m, CH), 7.83 (2 H, d, *J* 9.2, Ar), 8.16 (2 H, d, *J* 9.2, Ar), 8.22 (1 H, d, *J* 6.5, NH), 9.90 (1 H, brs, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 21.6, 45.5, 120.2, 124.4, 141.6, 146.6, 178.7.

***N*-(3-dimethylaminopropyl)-*N'*-(4-nitrophenyl)thiourea (4g)**: δ_H(600 MHz; d_6-DMSO; Me_4Si) 1.66-1.74 (2 H, m, CH_2), 2.13 (6 H, s, CH_3), 2.28 (2 H, t, *J* 6.8, CH_2), 3.52 (2 H, t, CH_2), 7.81 (2 H, d, *J* 9.1, Ar), 8.15-8.19 (2 H, m, Ar), 8.41 (1 H, brs, NH), 10.00 (1 H, brs, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 25.8, 42.7, 45.0, 56.8, 120.4, 124.4, 141.7, 146.3, 179.9.

***N*-benzyl-*N'*-(4-nitrophenyl)thiourea (4h)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 4.76 (2 H, s, CH_2), 7.22-7.31 (1 H, m, Ar), 7.36 (4 H, d, *J* 4.4, Ar), 7.87 (2 H, d, *J* 9.2, Ar), 8.18 (2 H, d, *J* 9.2, Ar), 8.69 (1 H, brs, NH), 10.10 (1 H, brs, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 47.2, 120.6, 124.5, 127.1, 127.6, 128.4, 138.2, 141.9, 146.3, 180.3.

***N*-(4-nitrophenyl) -*N'*-piperidinethiourea (4i)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 1.60 (6 H, m, CH_2), 3.88 (4 H, m, CH_2), 7.55 (2 H, brs, Ar), 8.14 (2 H, brs, Ar), 9.71 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 23.7, 25.5, 49.8, 122.0, 123.9, 141.7, 148.0, 180.0.

***N*-(4-nitrophenyl)-*N'*-morpholinethiourea (4j)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 3.60-3.74 (4 H, m, CH_2), 3.84-3.97 (4 H, m, CH_2), 7.61 (2 H, d, *J* 7.4, Ar), 8.16 (2 H, d, *J* 7.2, Ar), 9.83 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 49.0, 65.7, 122.5, 123.9, 142.1, 147.7, 180.9.

***N*-(4-nitrophenyl)-*N'*-thiomorpholinethiourea (4k)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.67-2.77 (4 H, m, CH_2), 4.13-4.26 (4 H, m, CH_2), 7.59 (2 H, d, *J* 8.6, Ar), 8.16 (2 H, d, *J* 8.6, Ar), 9.78 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 26.5, 51.4, 123.0, 123.8, 142.2, 147.7, 180.8.

***N*-(2,4-dimethylphenyl)-*N'*-(4-nitrophenyl)thiourea (4l)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.20 (3 H, s, CH_3), 2.28 (3 H, s, CH_3), 6.96-7.17 (3 H, m, overlapped Ar protons), 7.89 (2 H, d, *J* 9.1, Ar), 8.19 (2 H, d, *J* 9.1, Ar), 9.72 (1 H, s, NH), 10.19 (1 H, s, NH). δ_C(75 MHz, d_6-DMSO; Me_4Si) 17.7, 20.5, 121.5, 124.2, 126.8, 127.6, 131.0, 134.5, 134.6, 136.0, 142.2, 146.4, 180.3.

***N*-(2,6-dimethylphenyl)-*N'*-(4-nitrophenyl)thiourea (4m)**: δ_H(300 MHz; d_6-DMSO; Me_4Si) 2.21 (6 H, s, CH_3), 7.11 (3 H, s, Ar), 7.94 (2 H, d, *J* 7.8, Ar), 8.22 (2 H, d, *J* 7.9, Ar), 9.19;9.49 (1 H, s, NH), 9.98;10.54 (1 H, s, NH). δ_C(150 MHz, d_6-DMSO; Me_4Si) 17.9, 120.7, 124.4, 127.1, 127.7, 136.1, 136.4, 142.0, 146.3,180.0.

2. ^{1}H and ^{13}C NMR spectra

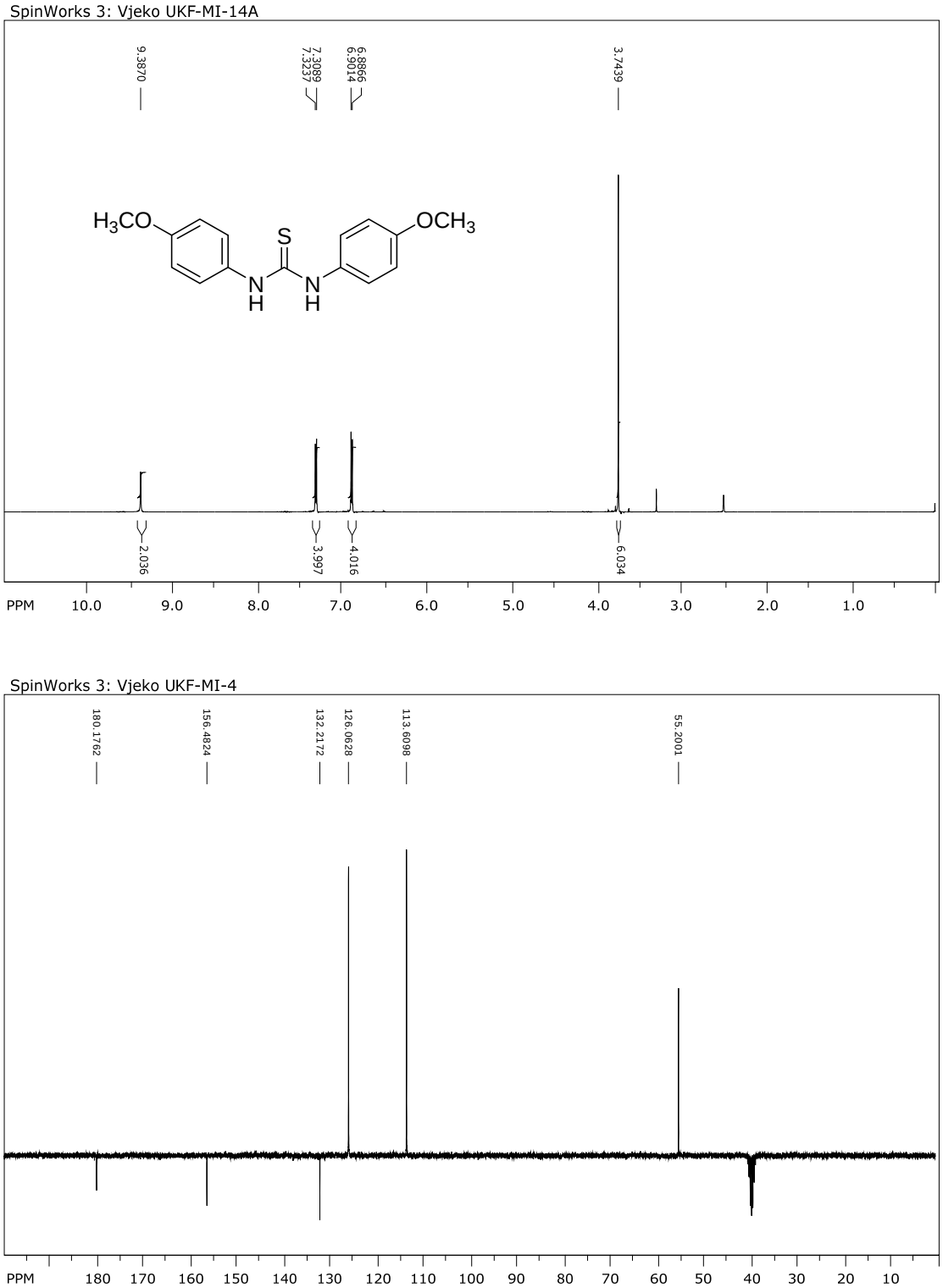


Figure S1. ^{1}H and ^{13}C NMR spectra of thiourea **1a**.

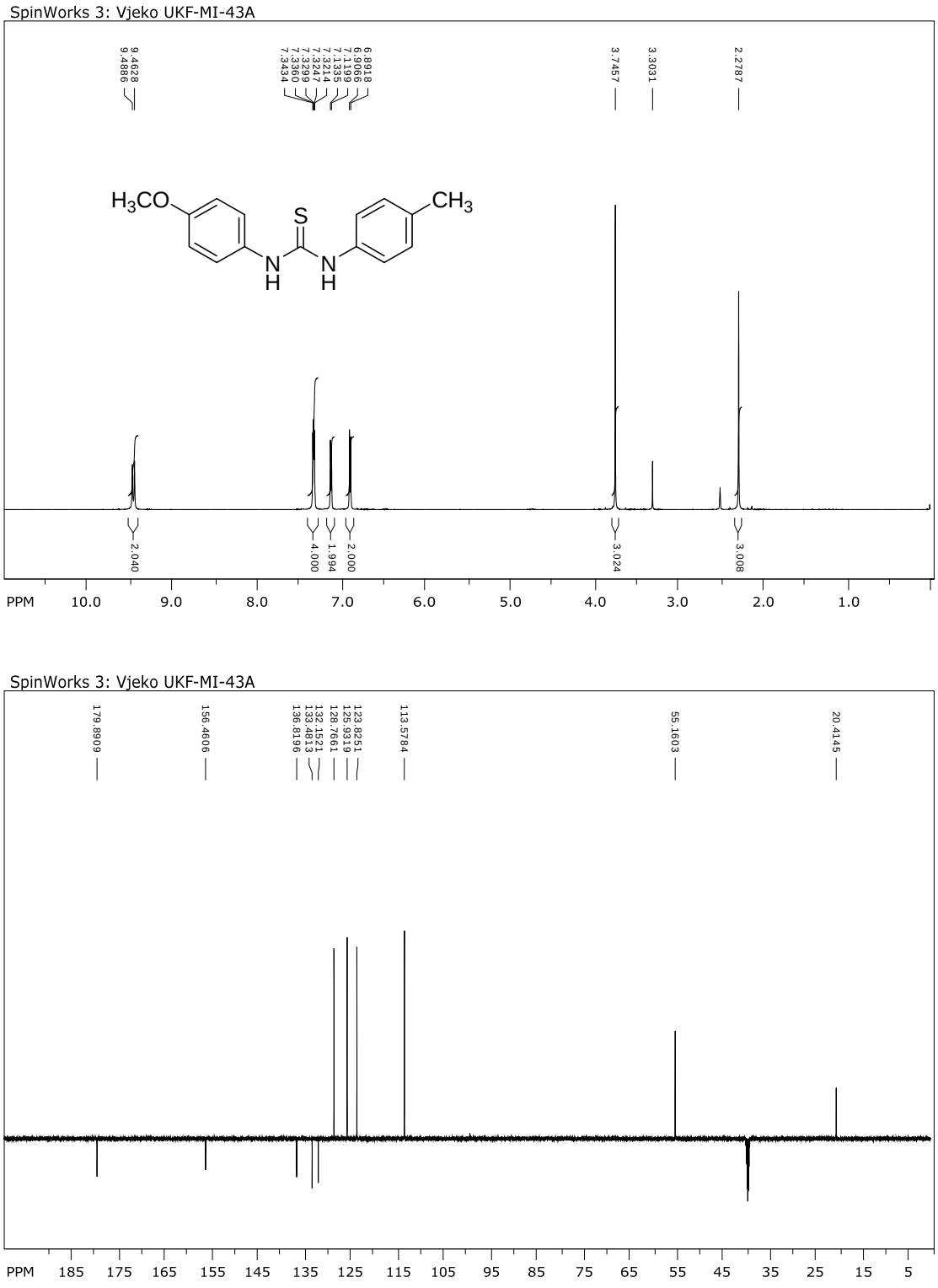


Figure S2. ^{1}H and ^{13}C NMR spectra of thiourea **1b**.

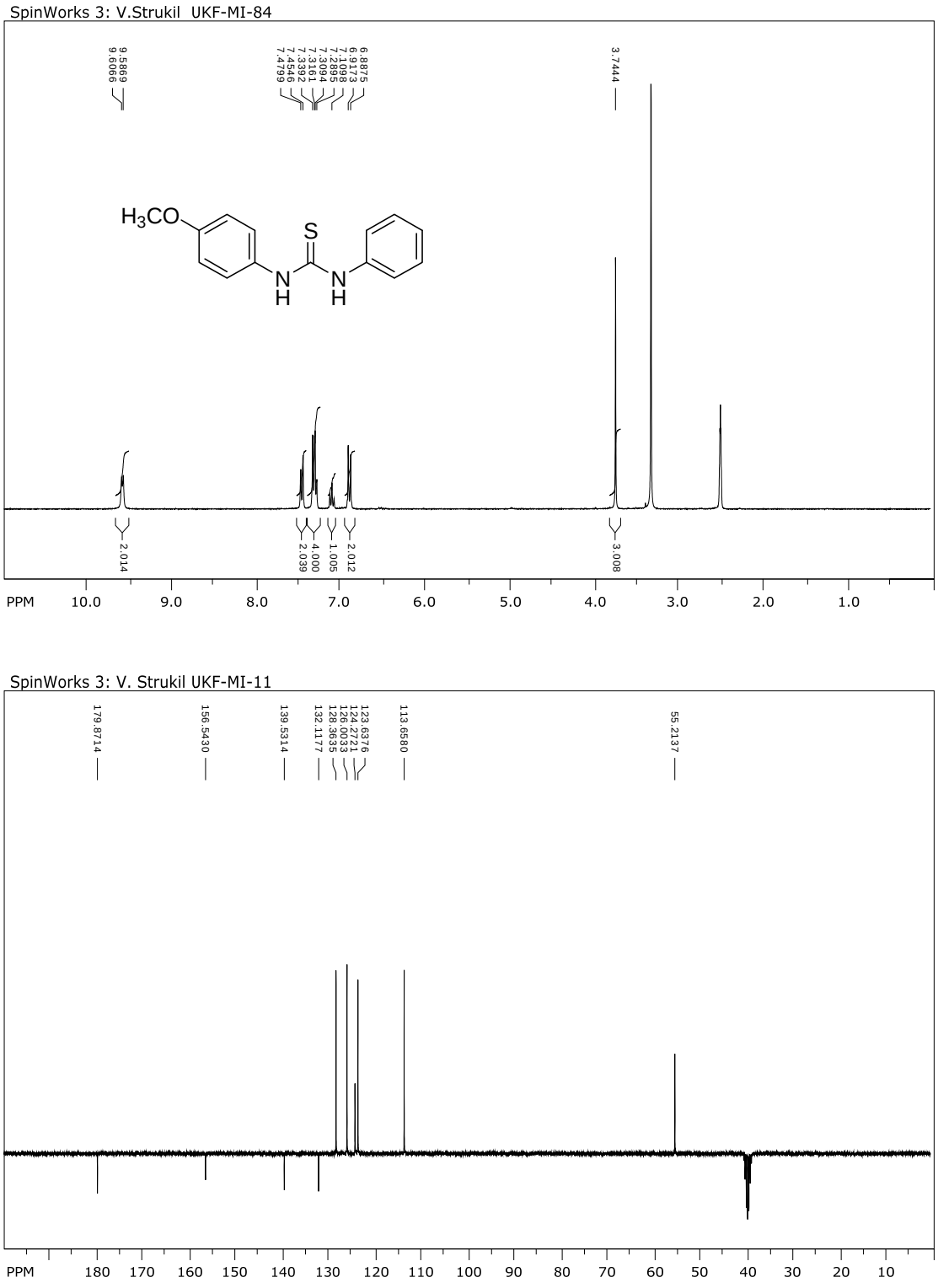


Figure S3. ^{1}H and ^{13}C NMR spectra of thiourea **1c** (same as **2a**).

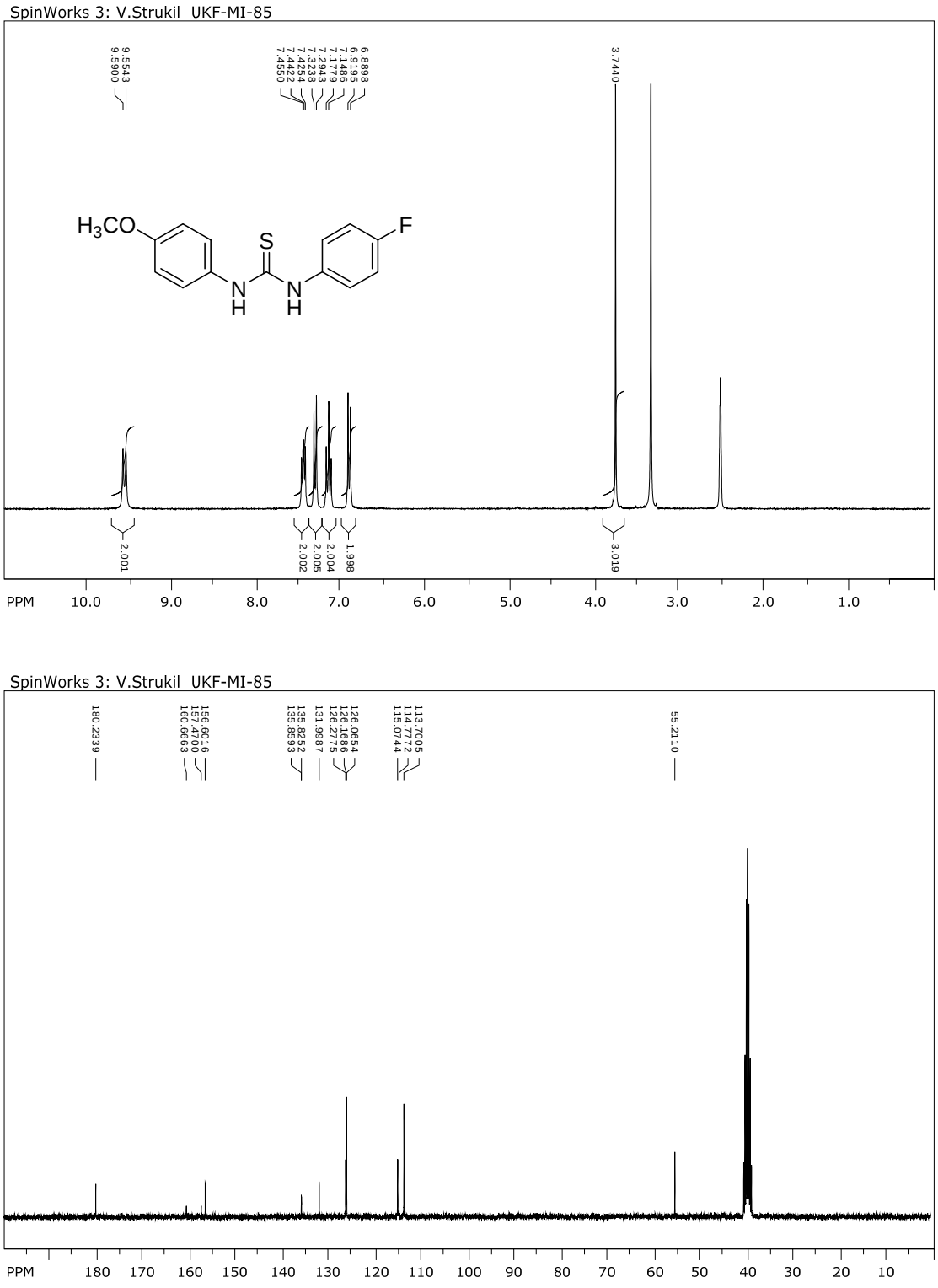


Figure S4. ^{1}H and ^{13}C NMR spectra of thiourea **1d** (same as **3a**).

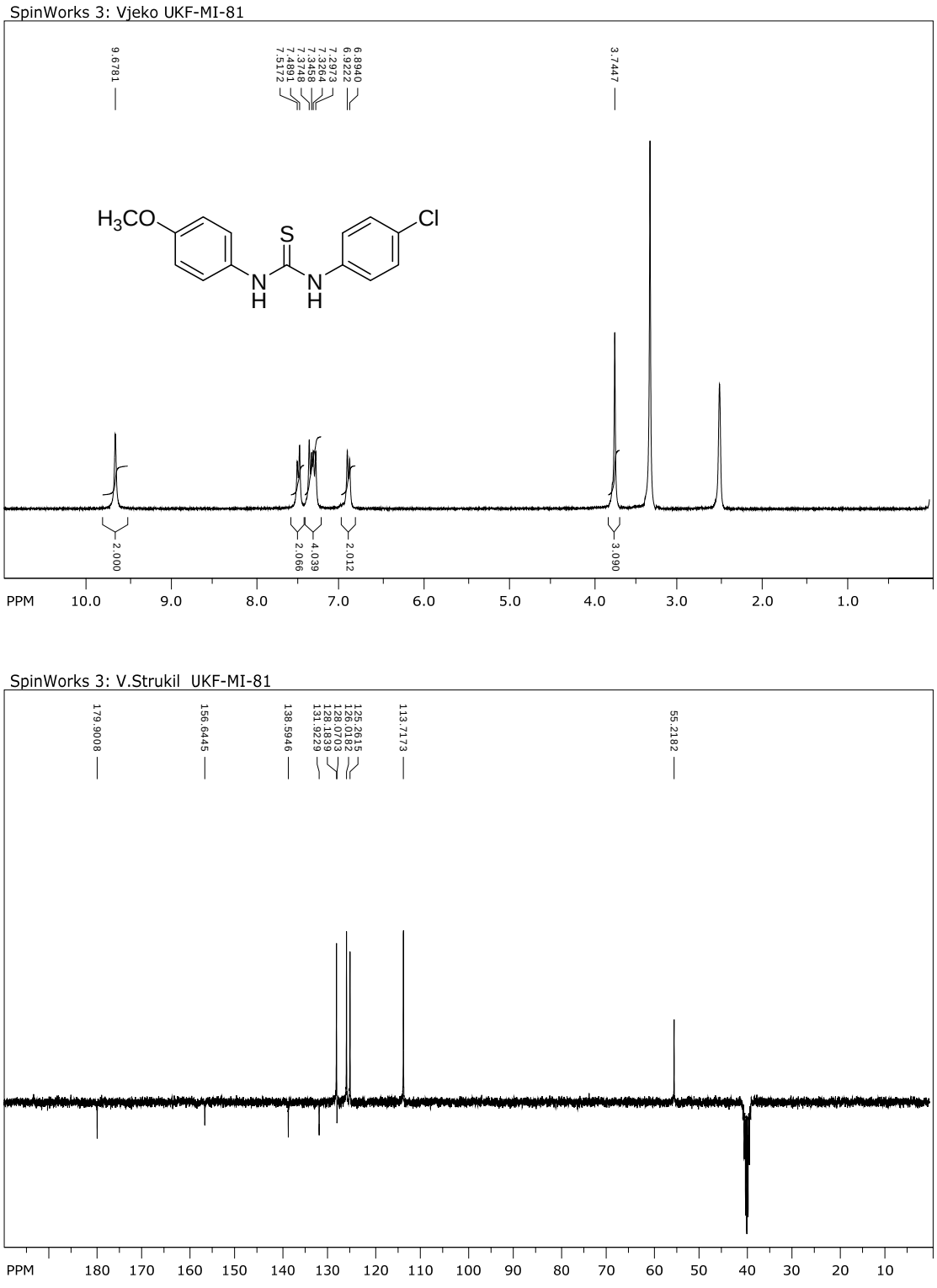


Figure S5. ^{1}H and ^{13}C NMR spectra of thiourea **1e**.

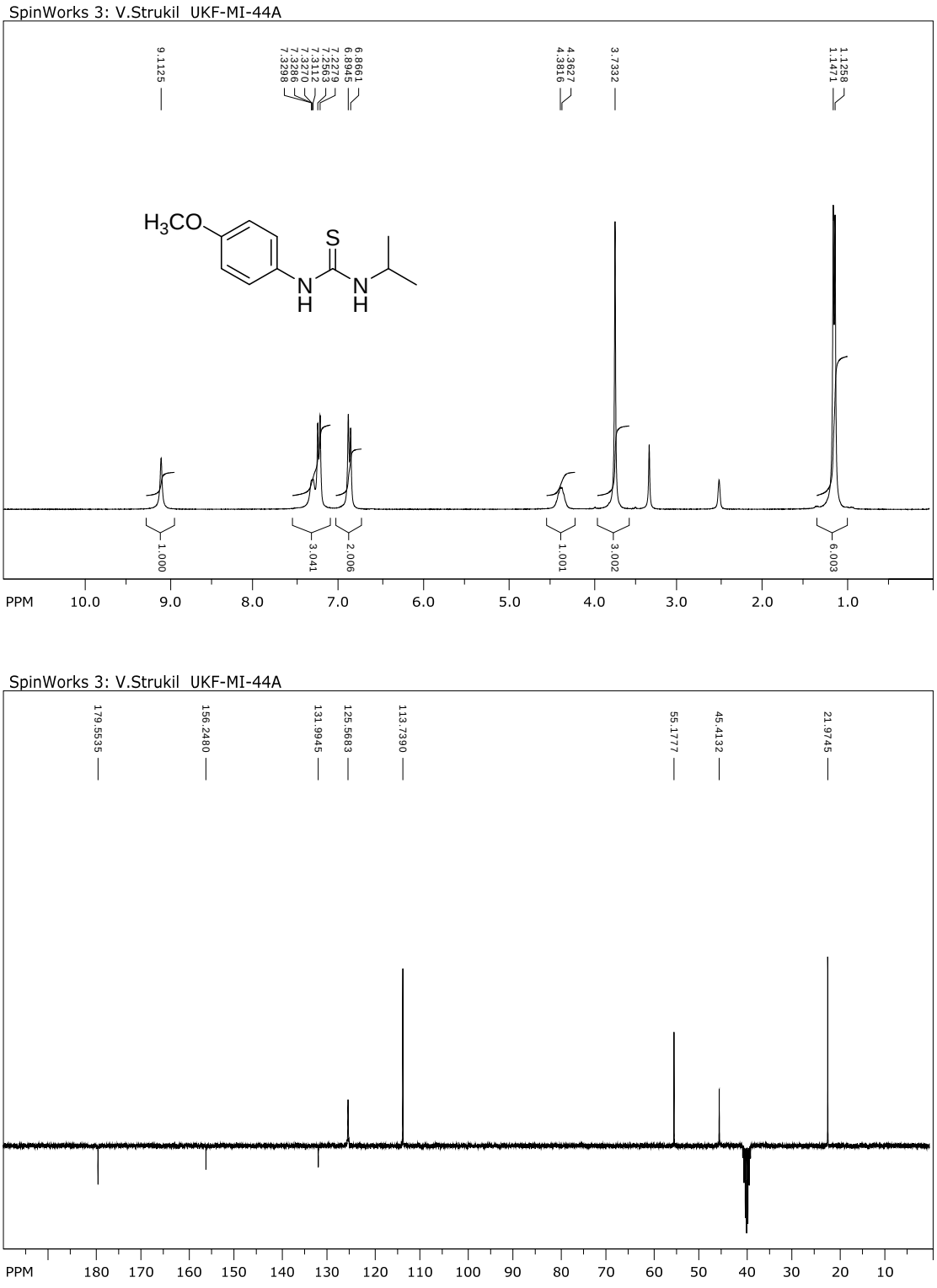


Figure S6. ^{1}H and ^{13}C NMR spectra of thiourea **1f**.

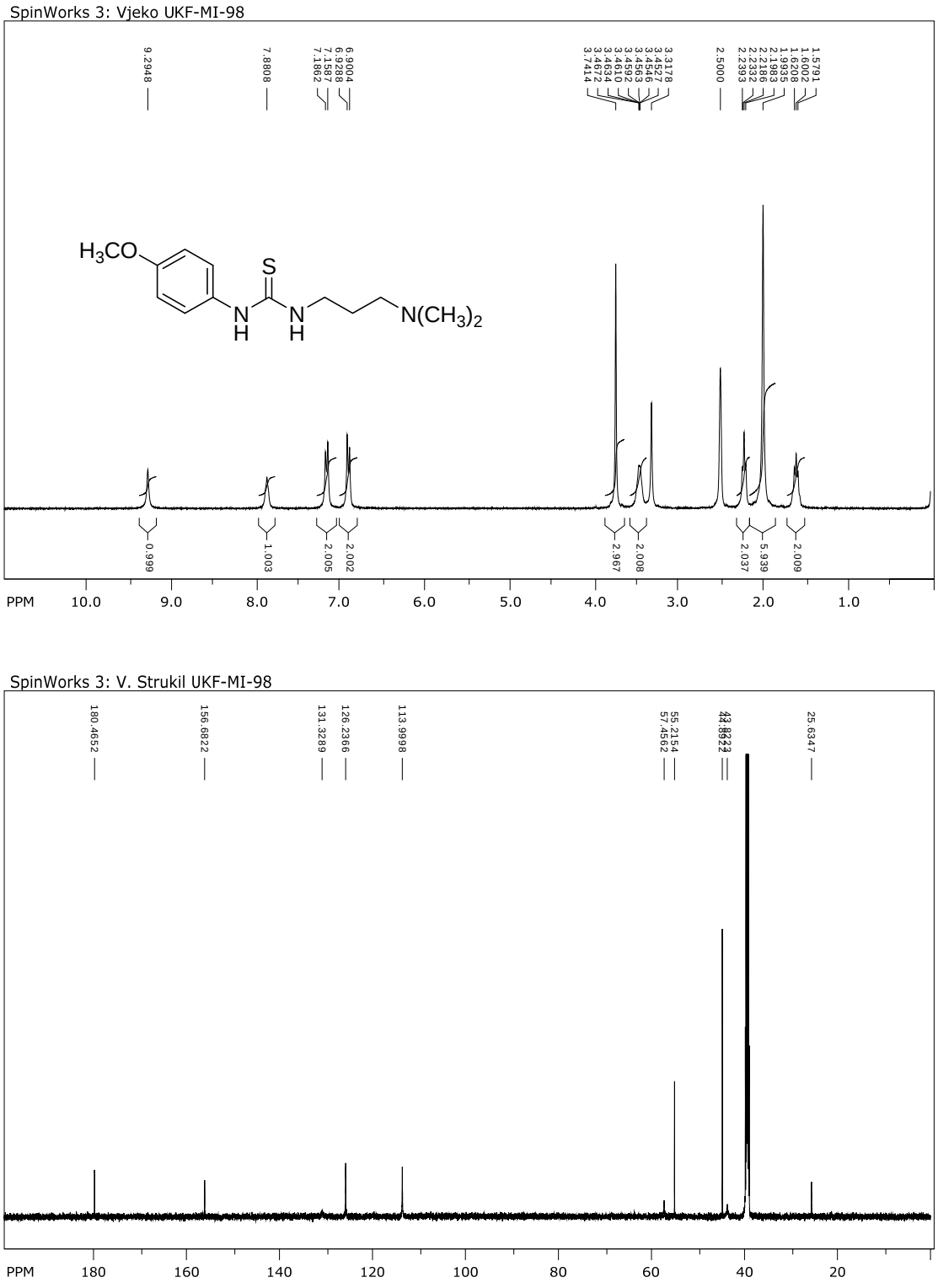


Figure S7. ^{1}H and ^{13}C NMR spectra of thiourea **1g**.

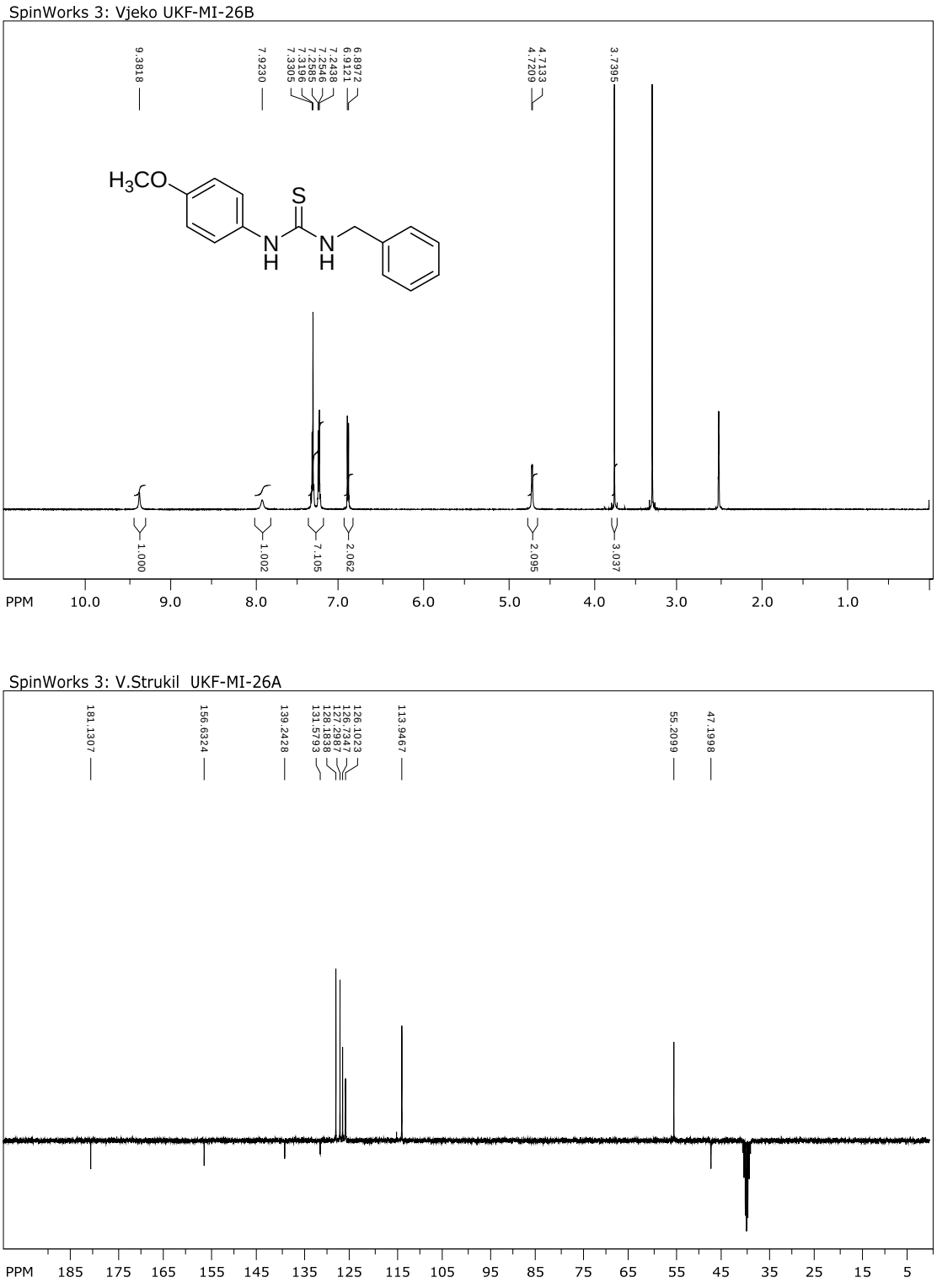


Figure S8. ^{1}H and ^{13}C NMR spectra of thiourea **1h**.

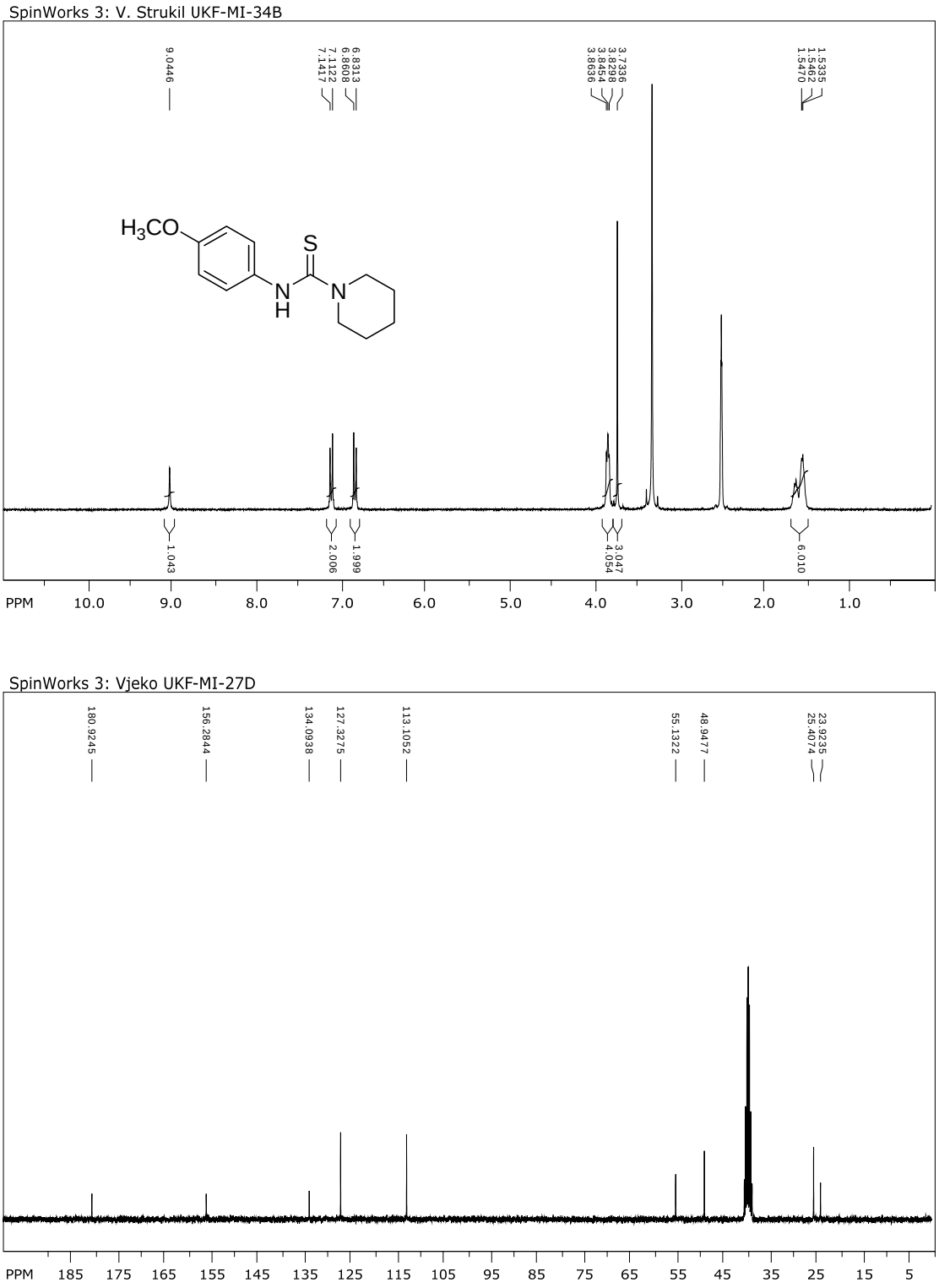


Figure S9. ^{1}H and ^{13}C NMR spectra of thiourea **1i**.

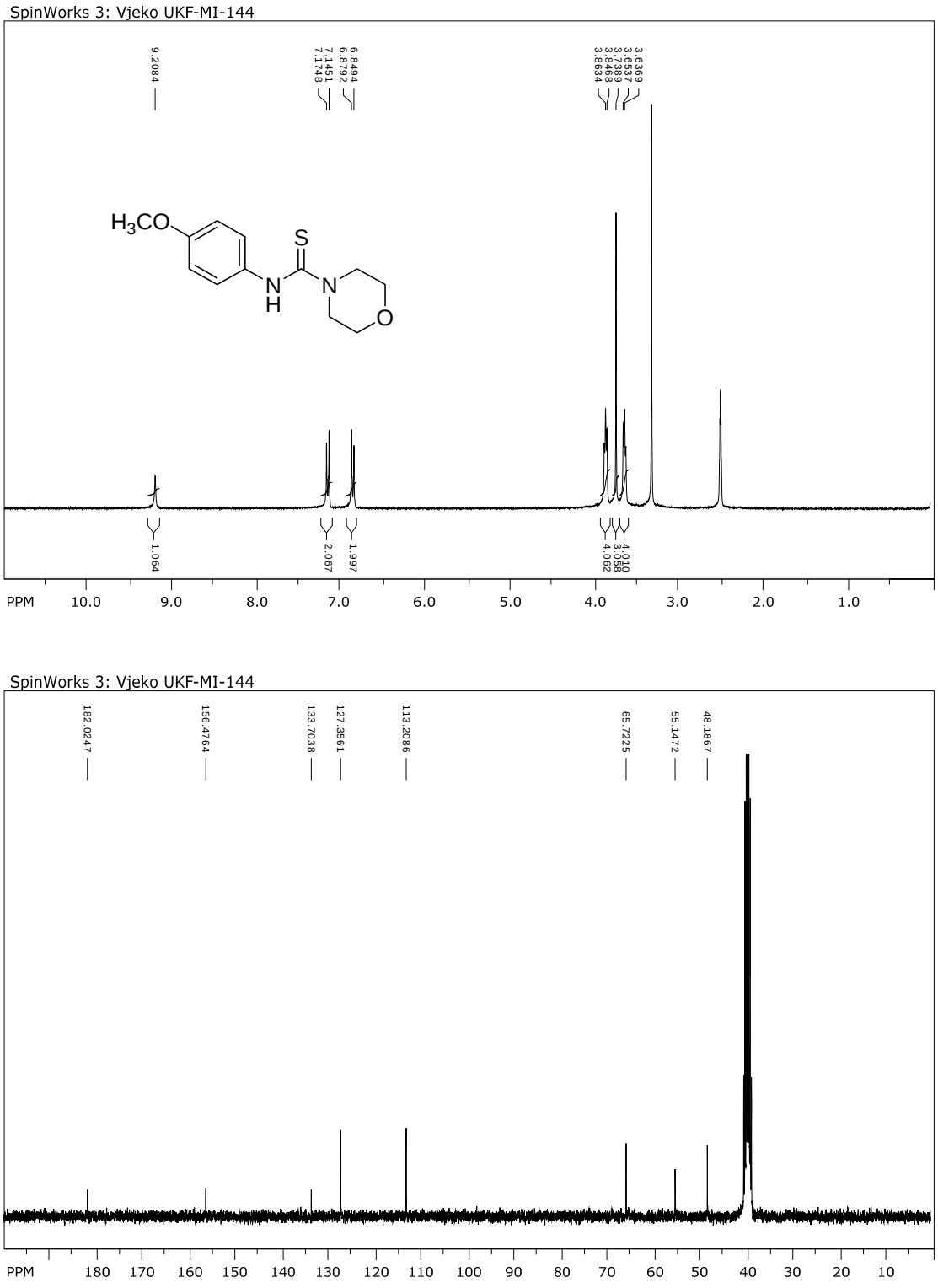


Figure S10. ^{1}H and ^{13}C NMR spectra of thiourea **1j**.

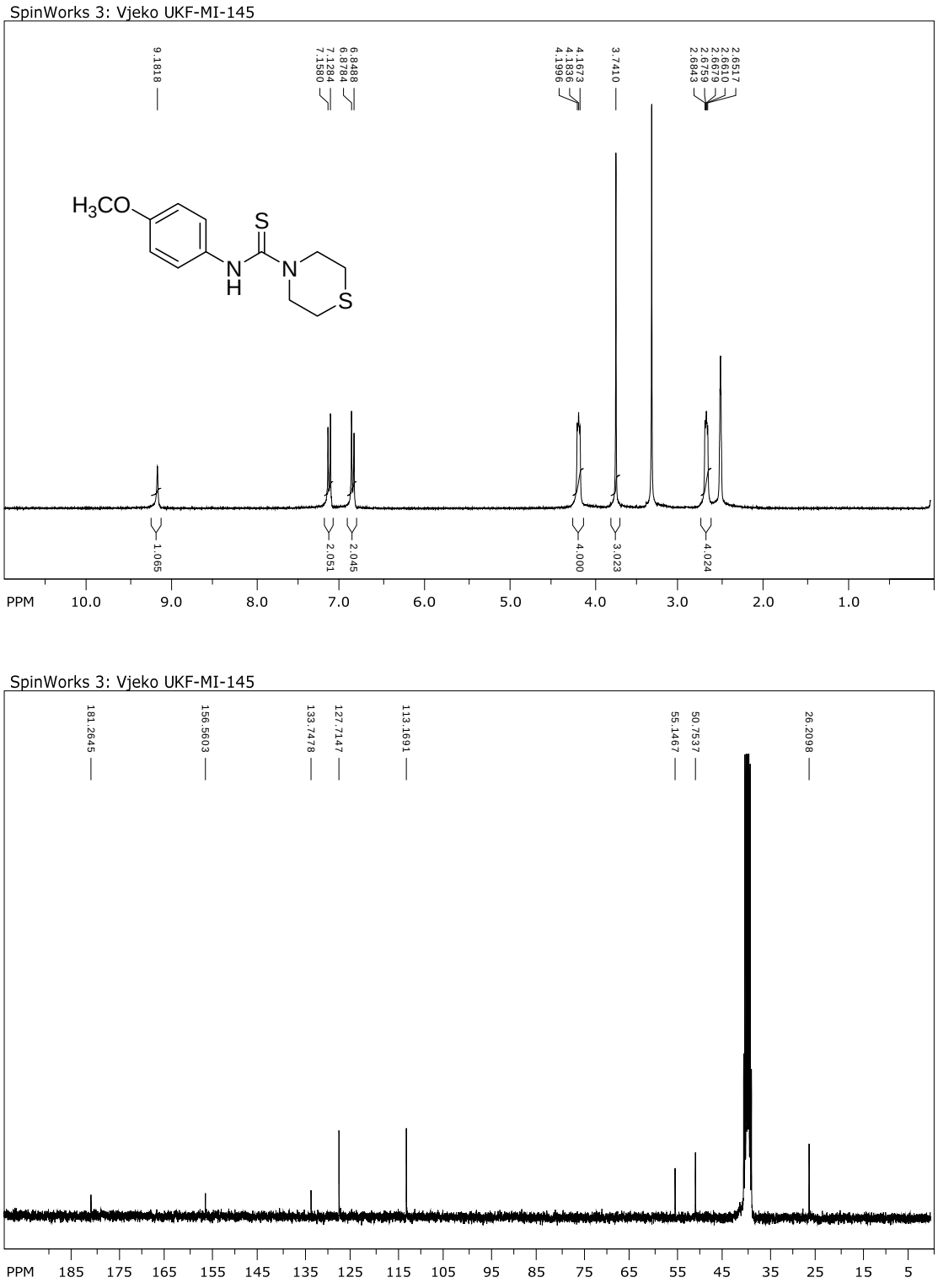


Figure S11. ^{1}H and ^{13}C NMR spectra of thiourea **1k**.

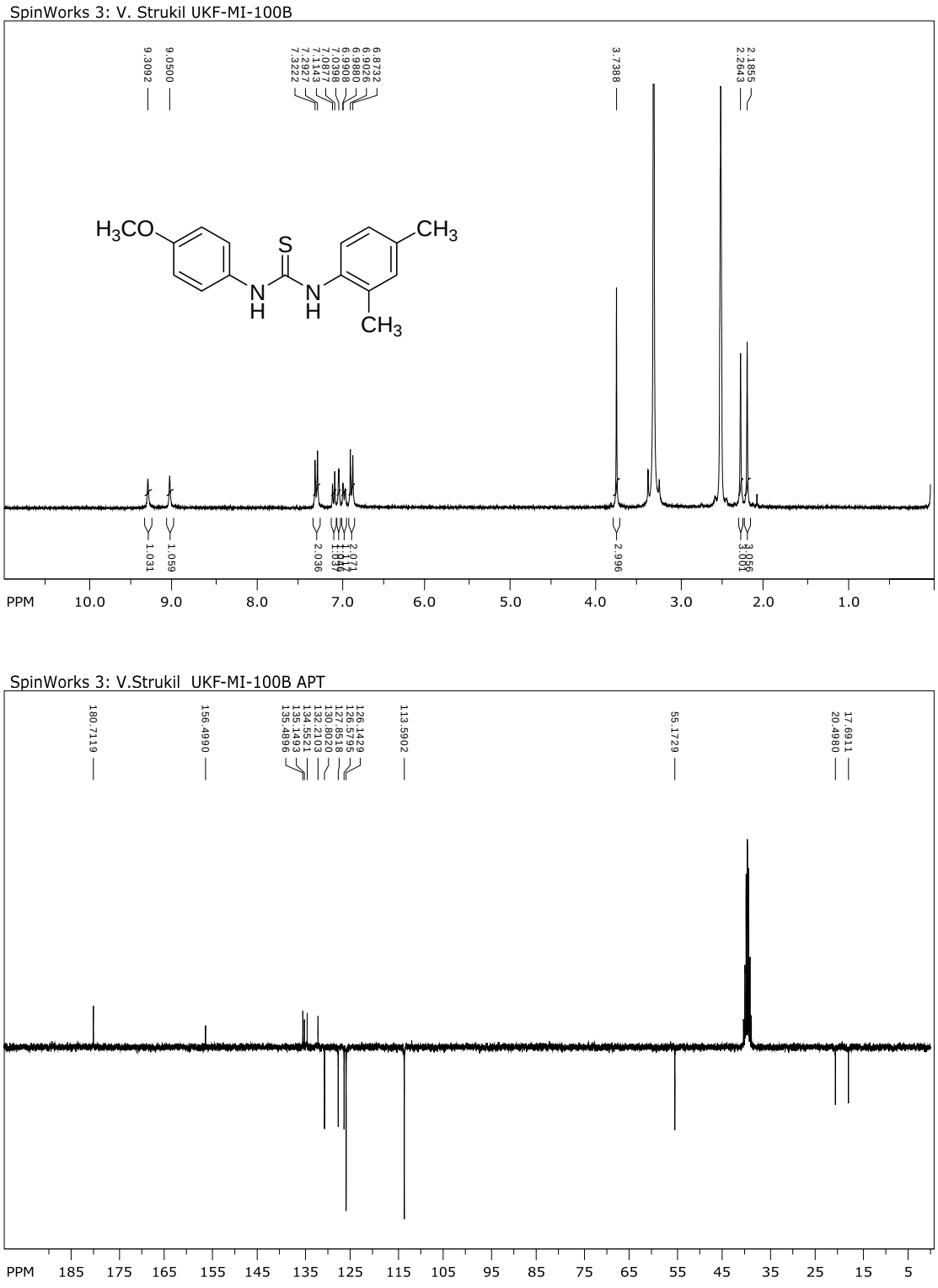


Figure S12. ^{1}H and ^{13}C NMR spectra of thiourea **1l**.

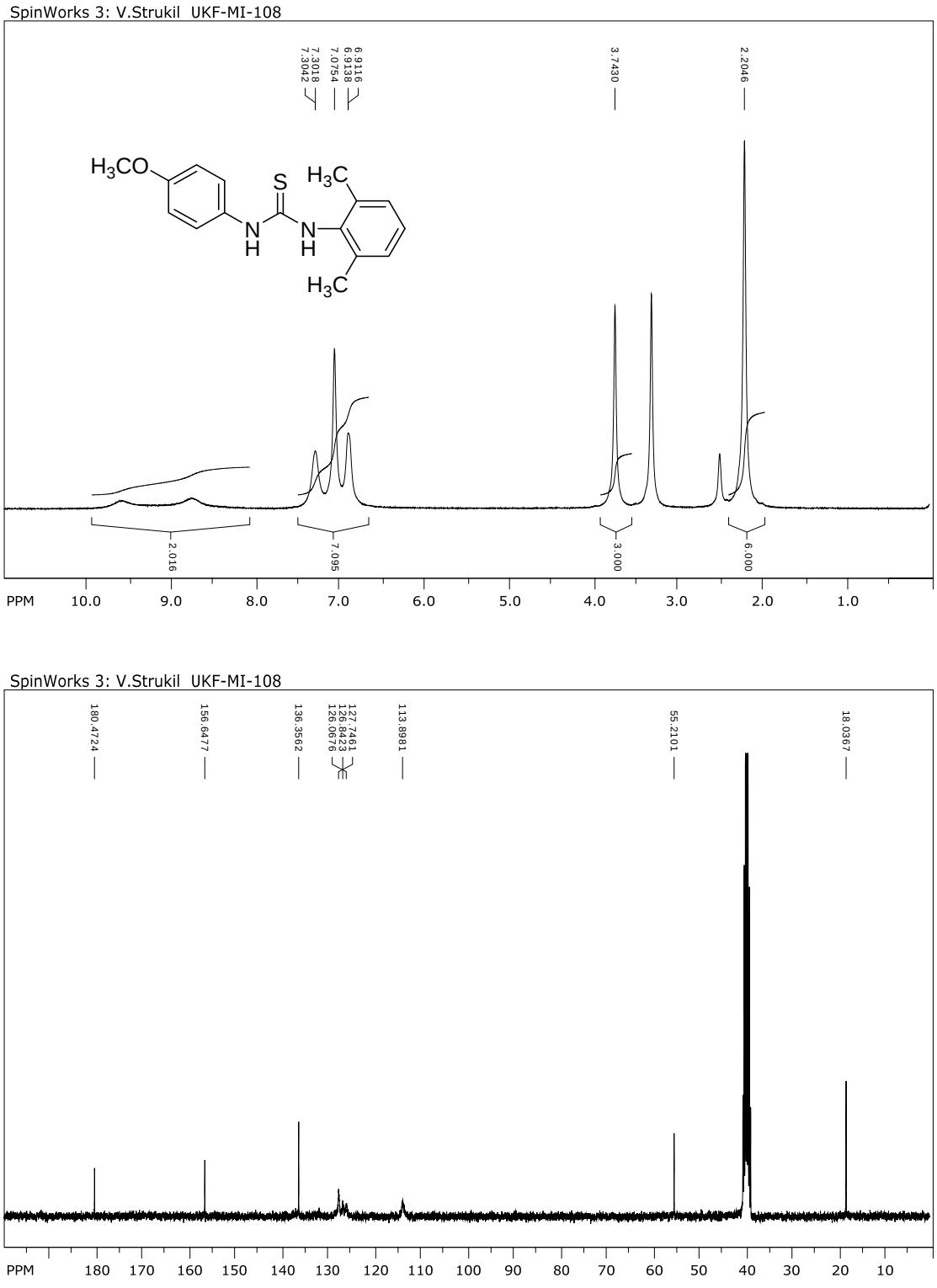


Figure S13. ^{1}H and ^{13}C NMR spectra of thiourea **1m**.

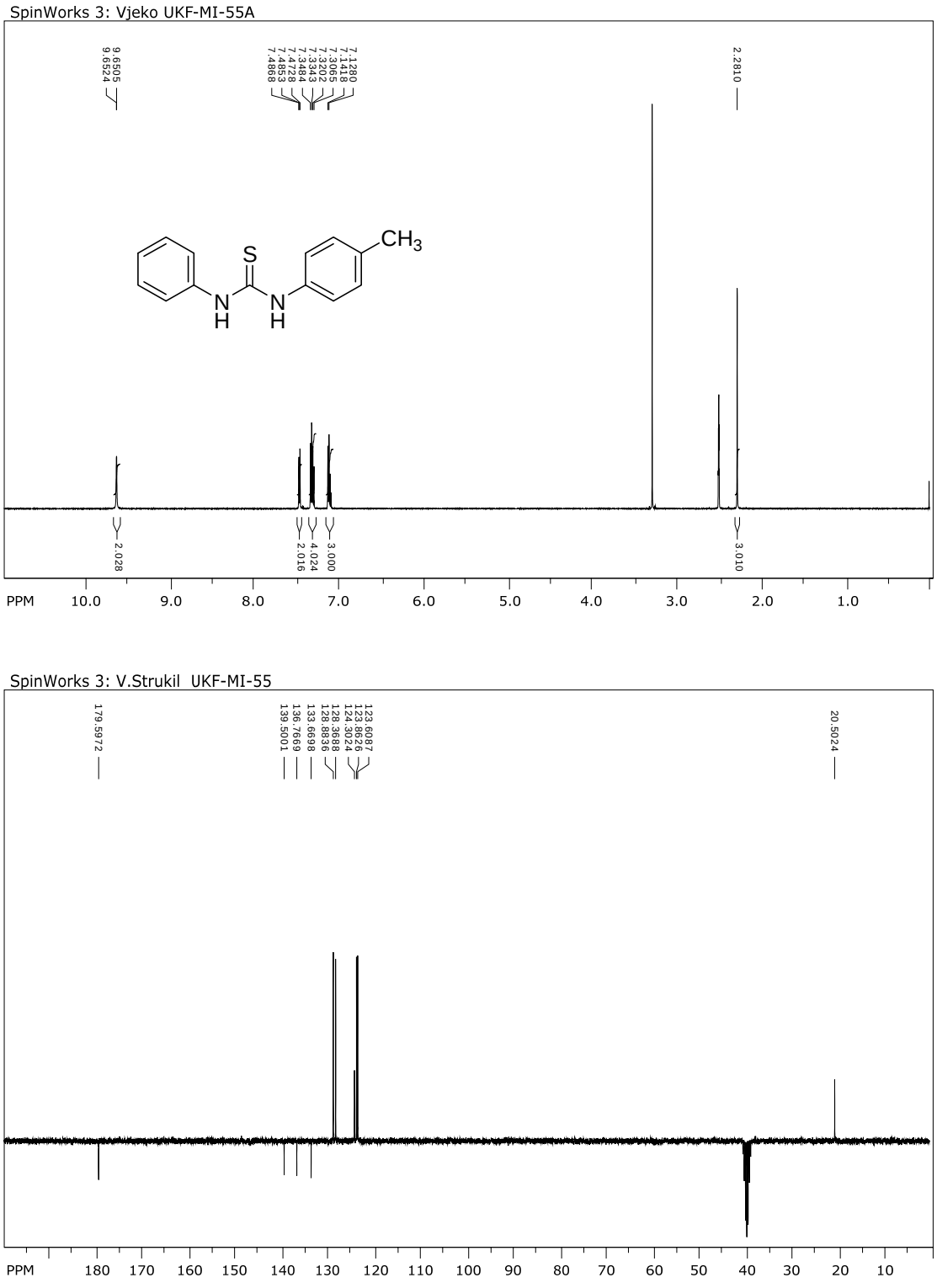


Figure S14. ^{1}H and ^{13}C NMR spectra of thiourea **2b**.

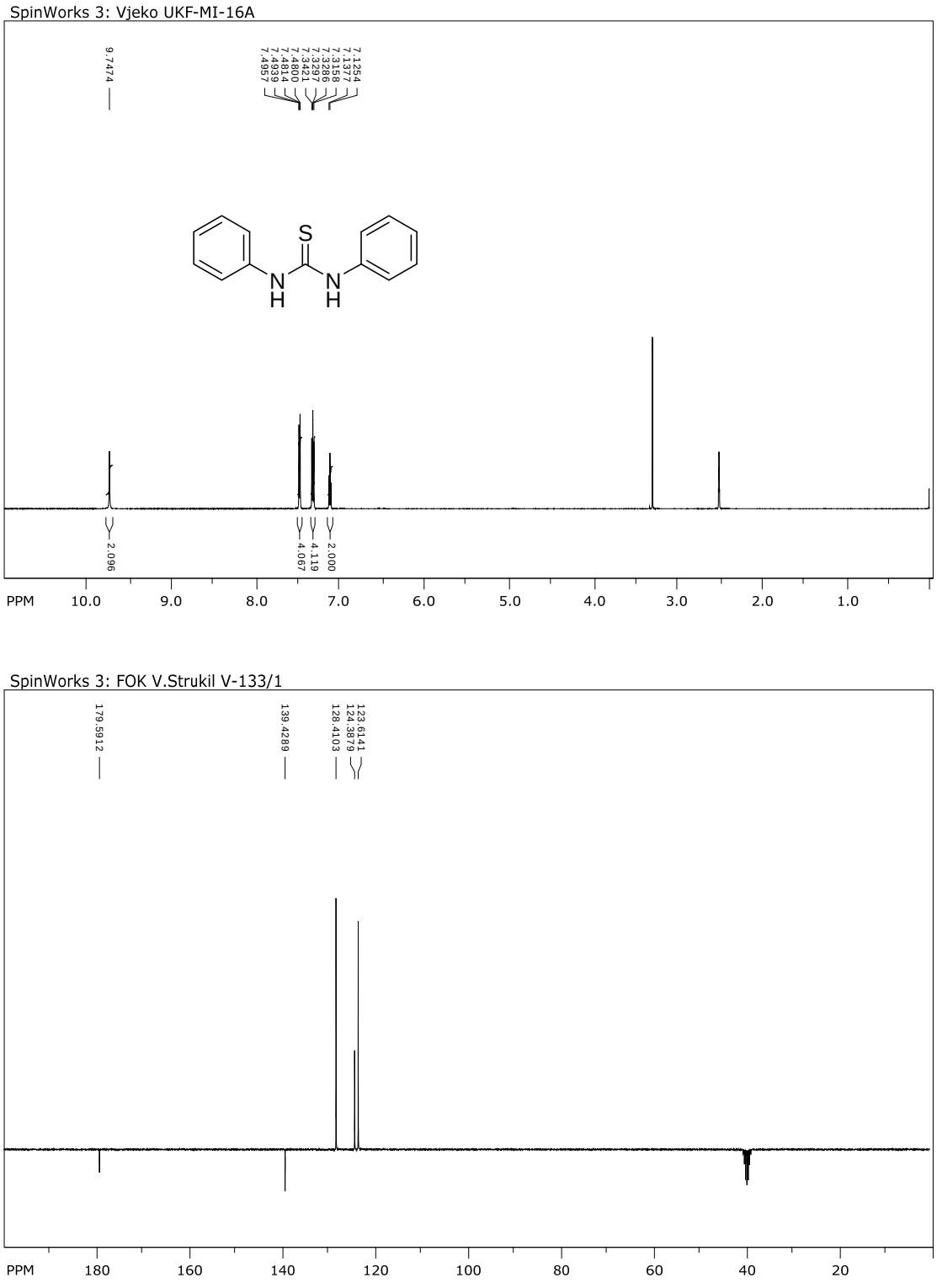
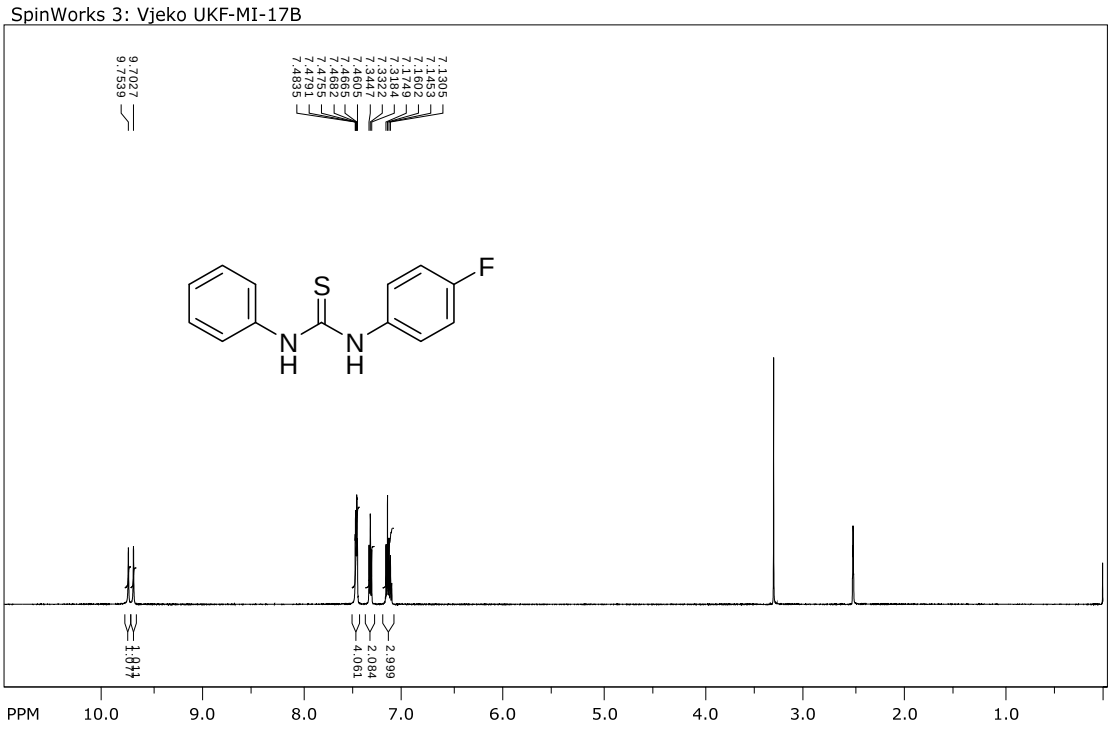


Figure S15. ^{1}H and ^{13}C NMR spectra of thiourea **2c**.



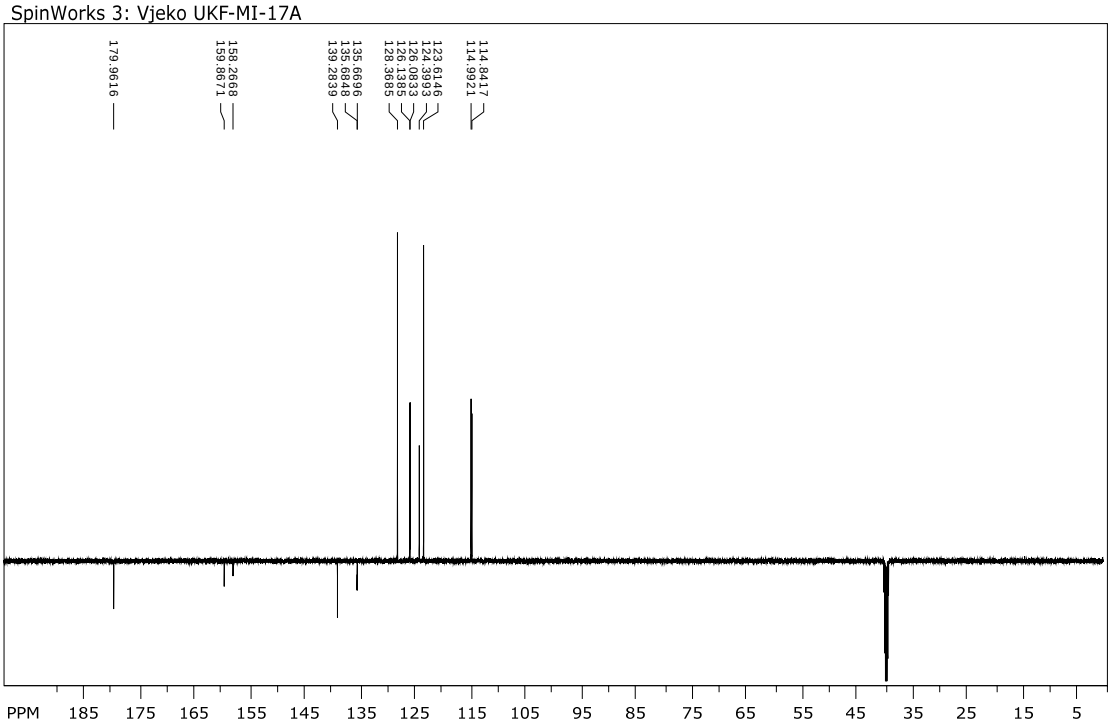


Figure S16. ^{1}H and ^{13}C NMR spectra of thiourea **2d** (same as **3c**).

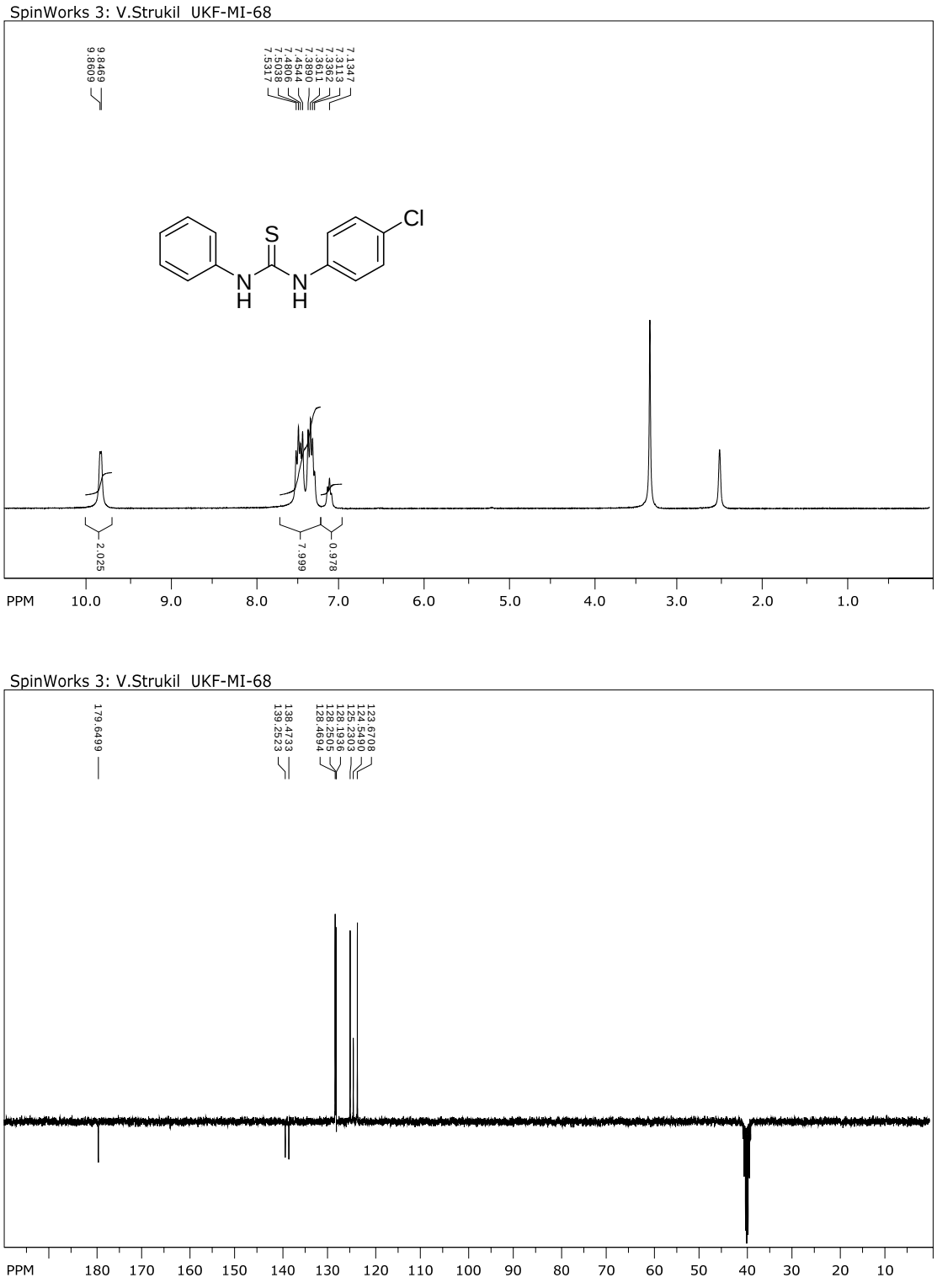


Figure S17. ^{1}H and ^{13}C NMR spectra of thiourea **2e**.

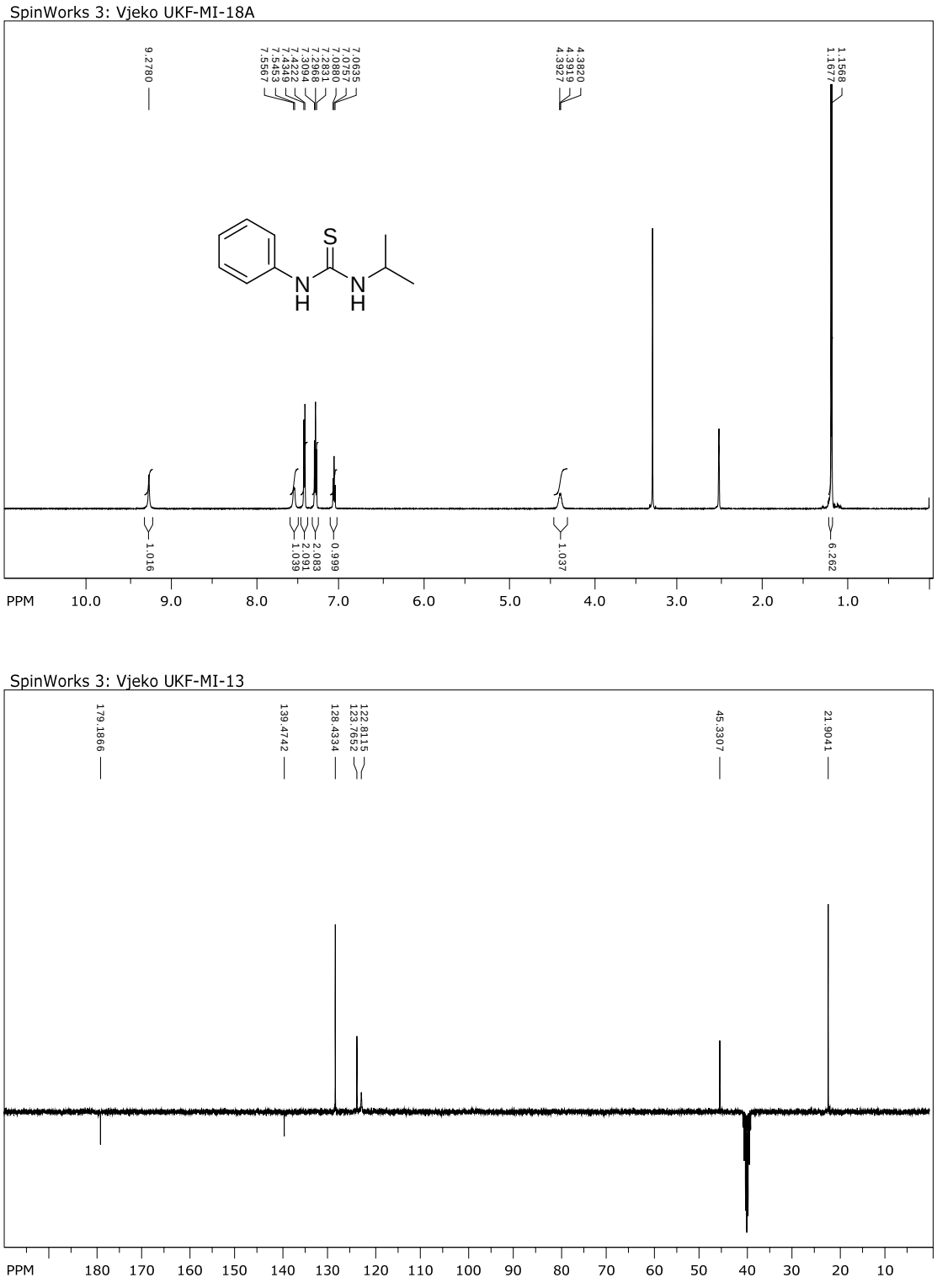


Figure S18. ^{1}H and ^{13}C NMR spectra of thiourea **2f**.

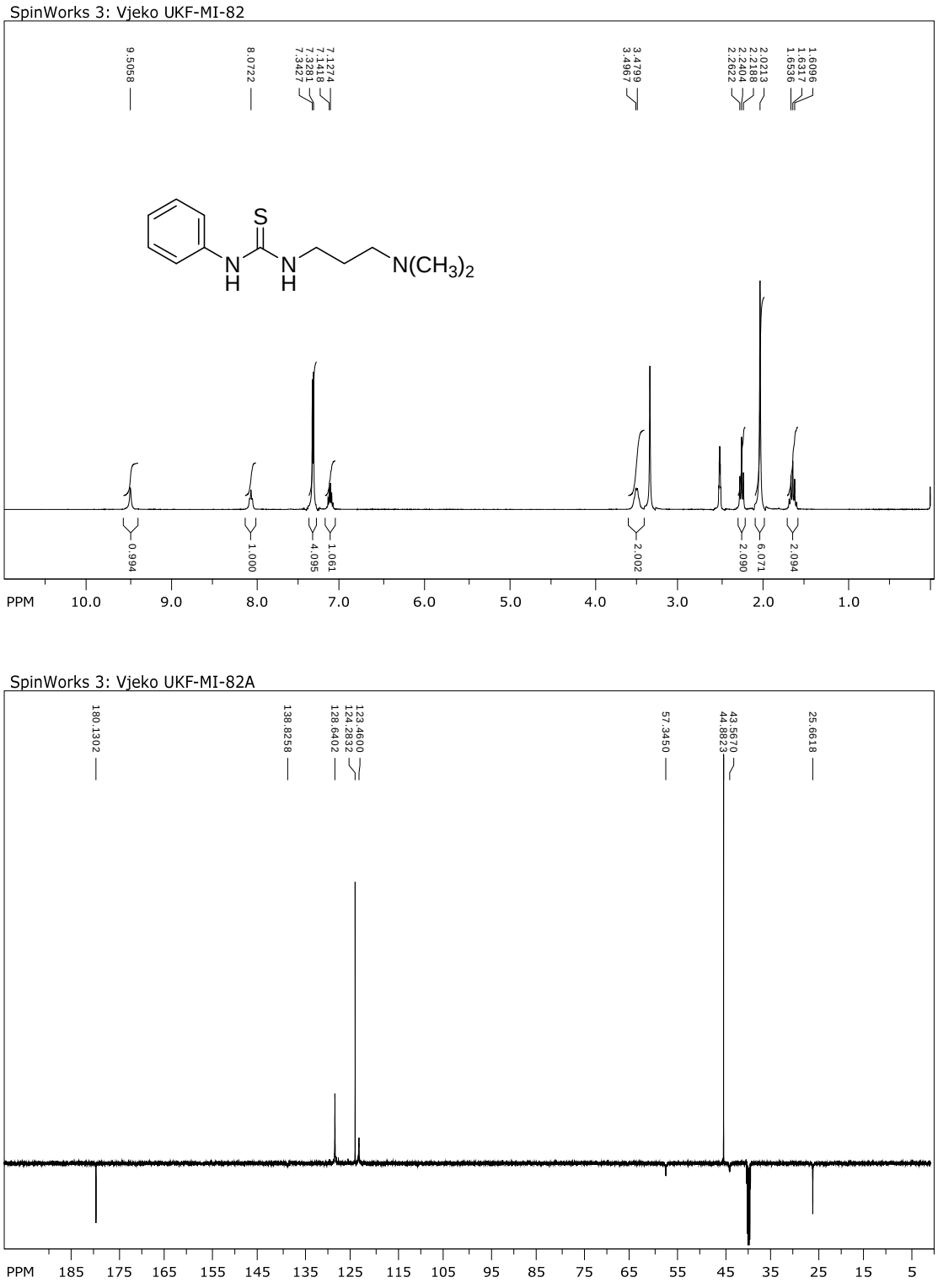


Figure S19. ^{1}H and ^{13}C NMR spectra of thiourea **2g**.

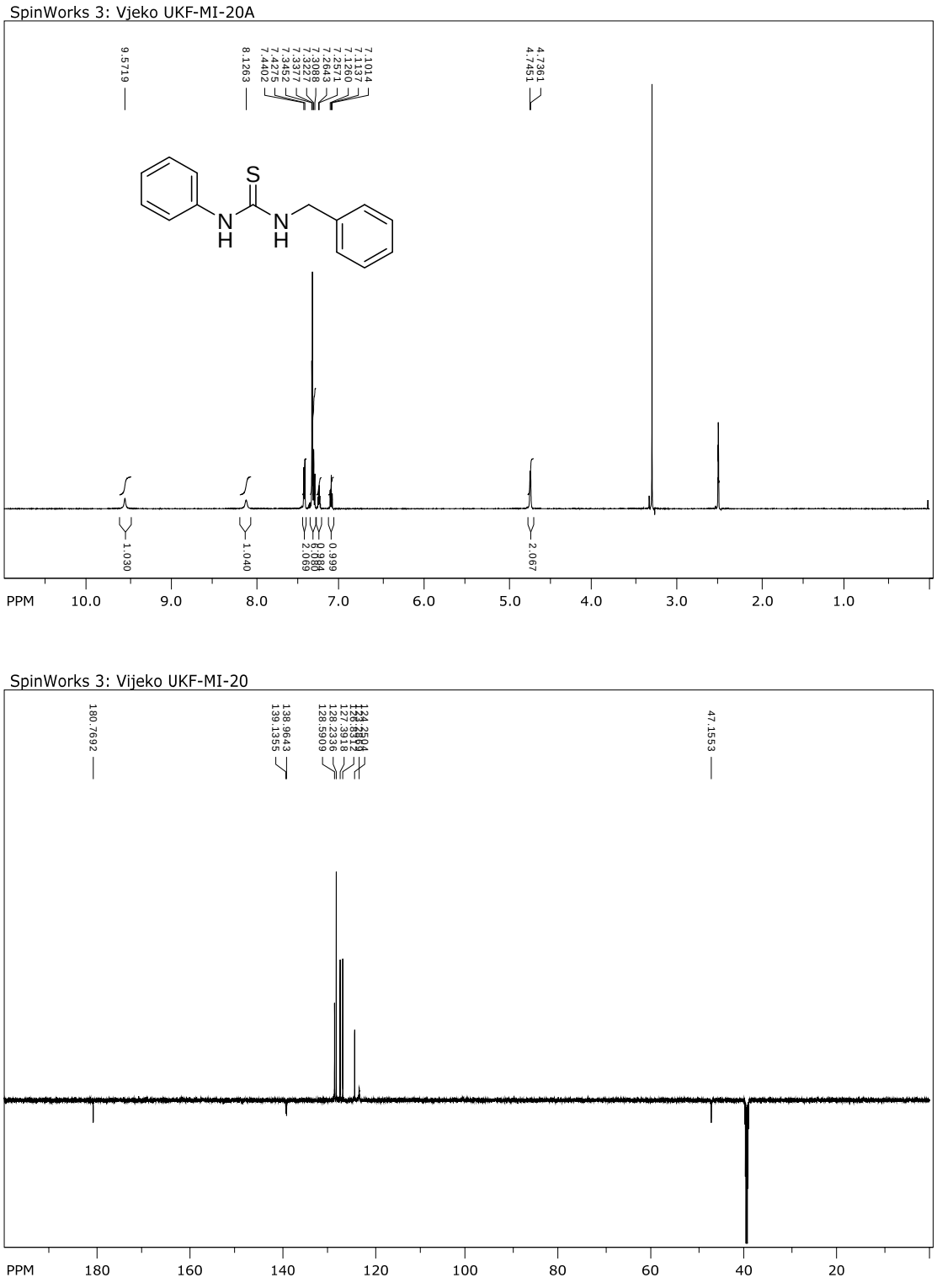


Figure S20. ^{1}H and ^{13}C NMR spectra of thiourea **2h**.

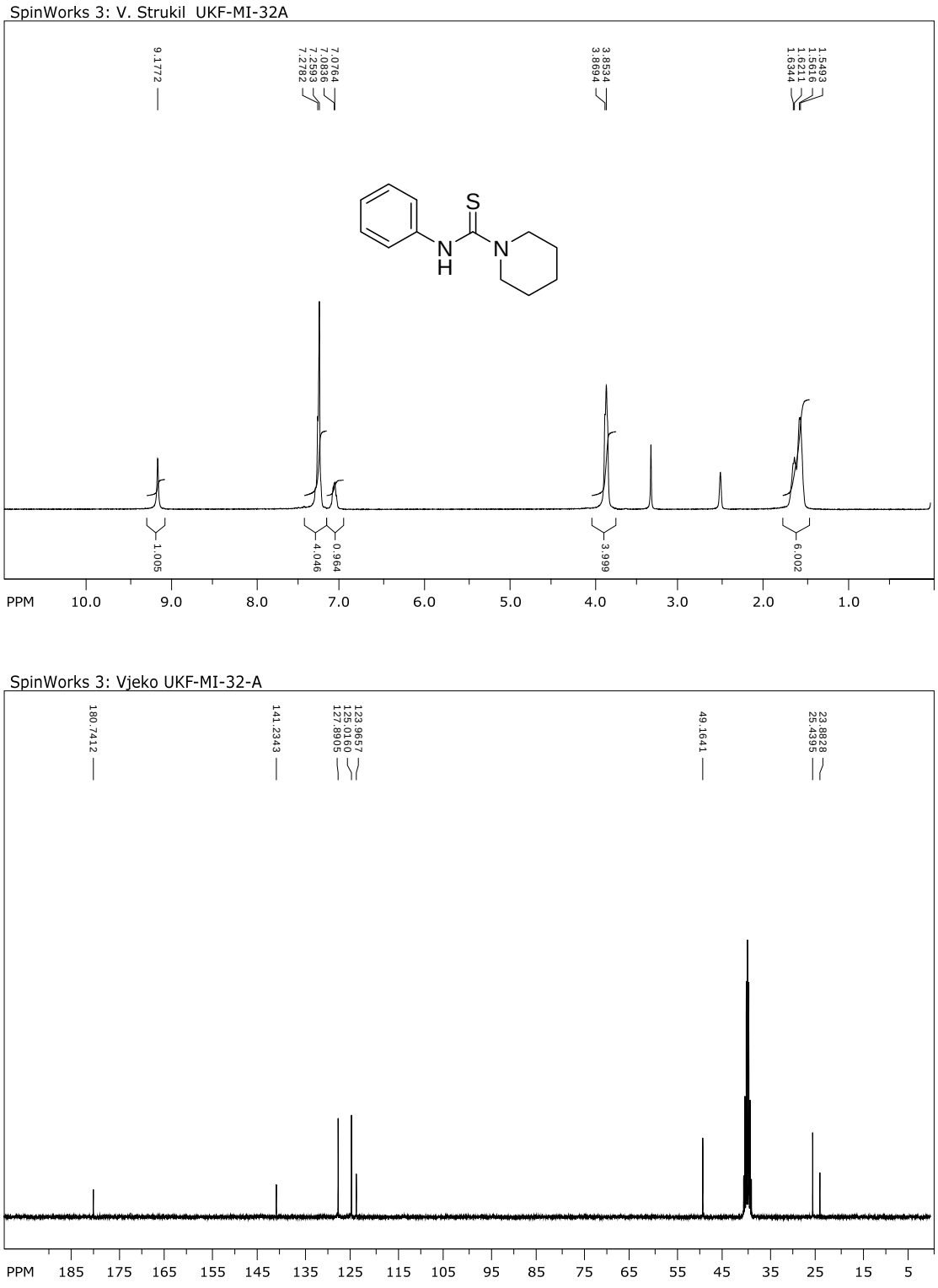


Figure S21. ^{1}H and ^{13}C NMR spectra of thiourea **2i**.

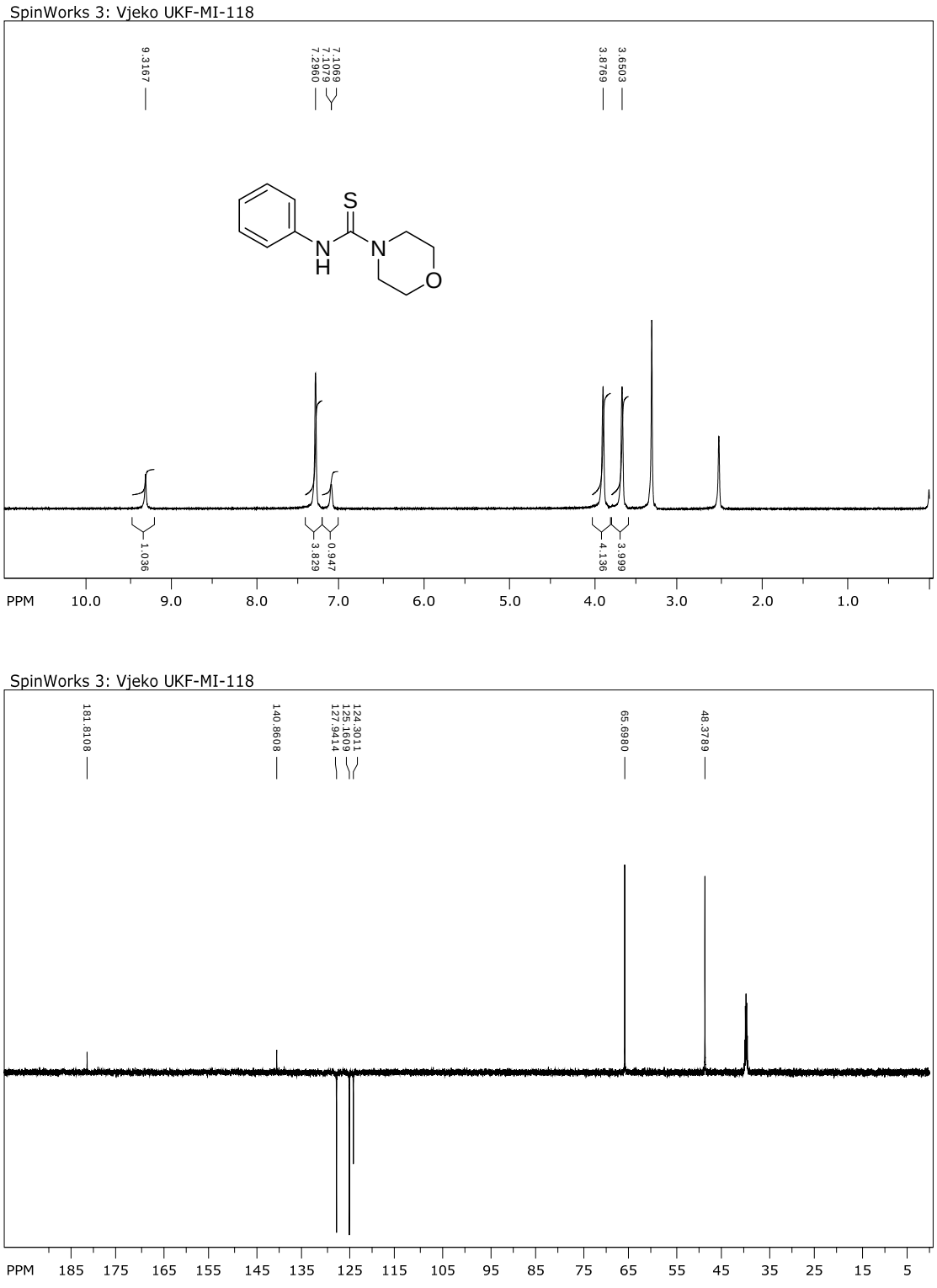


Figure S22. ^{1}H and ^{13}C NMR spectra of thiourea **2j**.

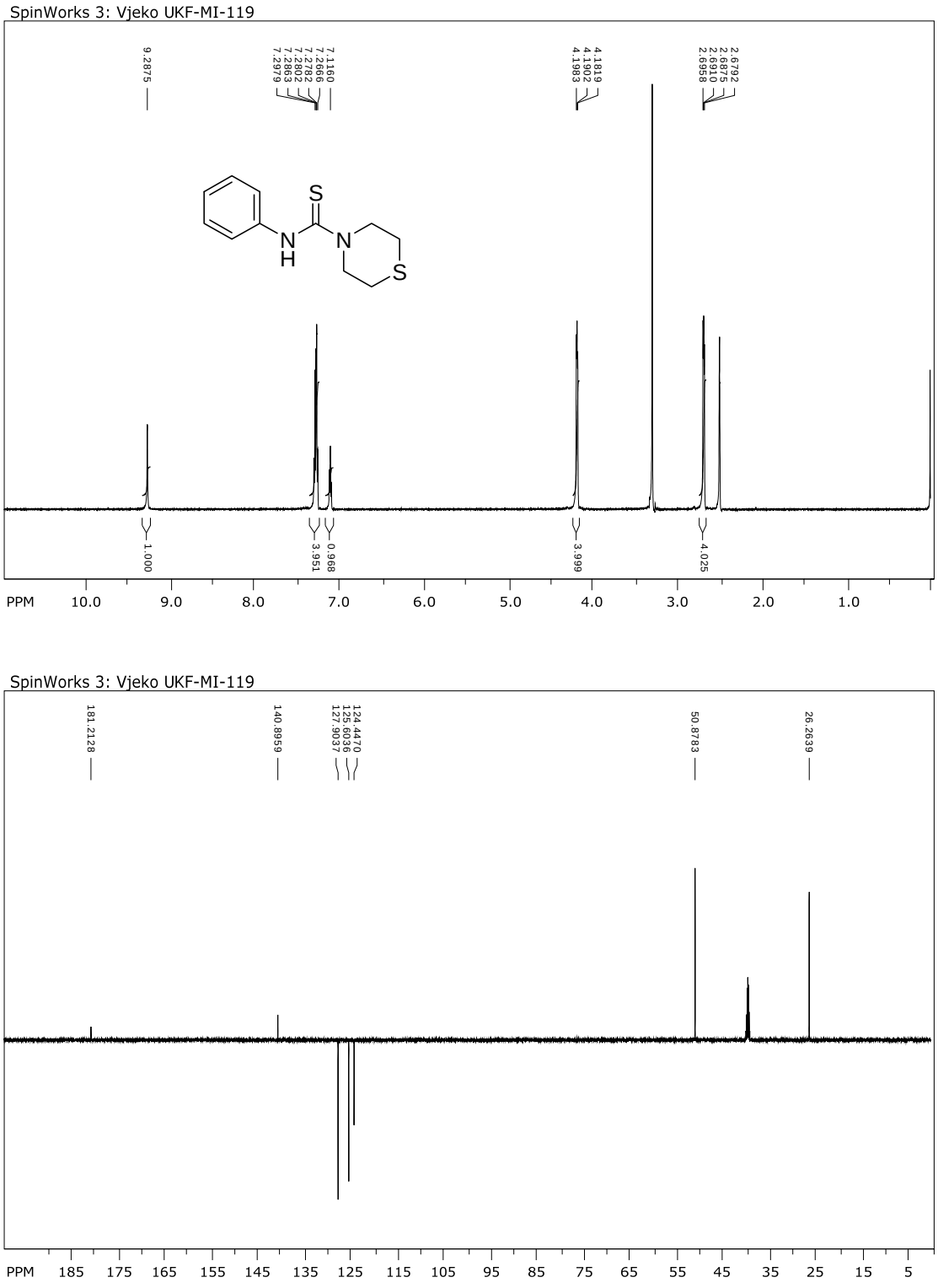


Figure S23. ^{1}H and ^{13}C NMR spectra of thiourea **2k**.

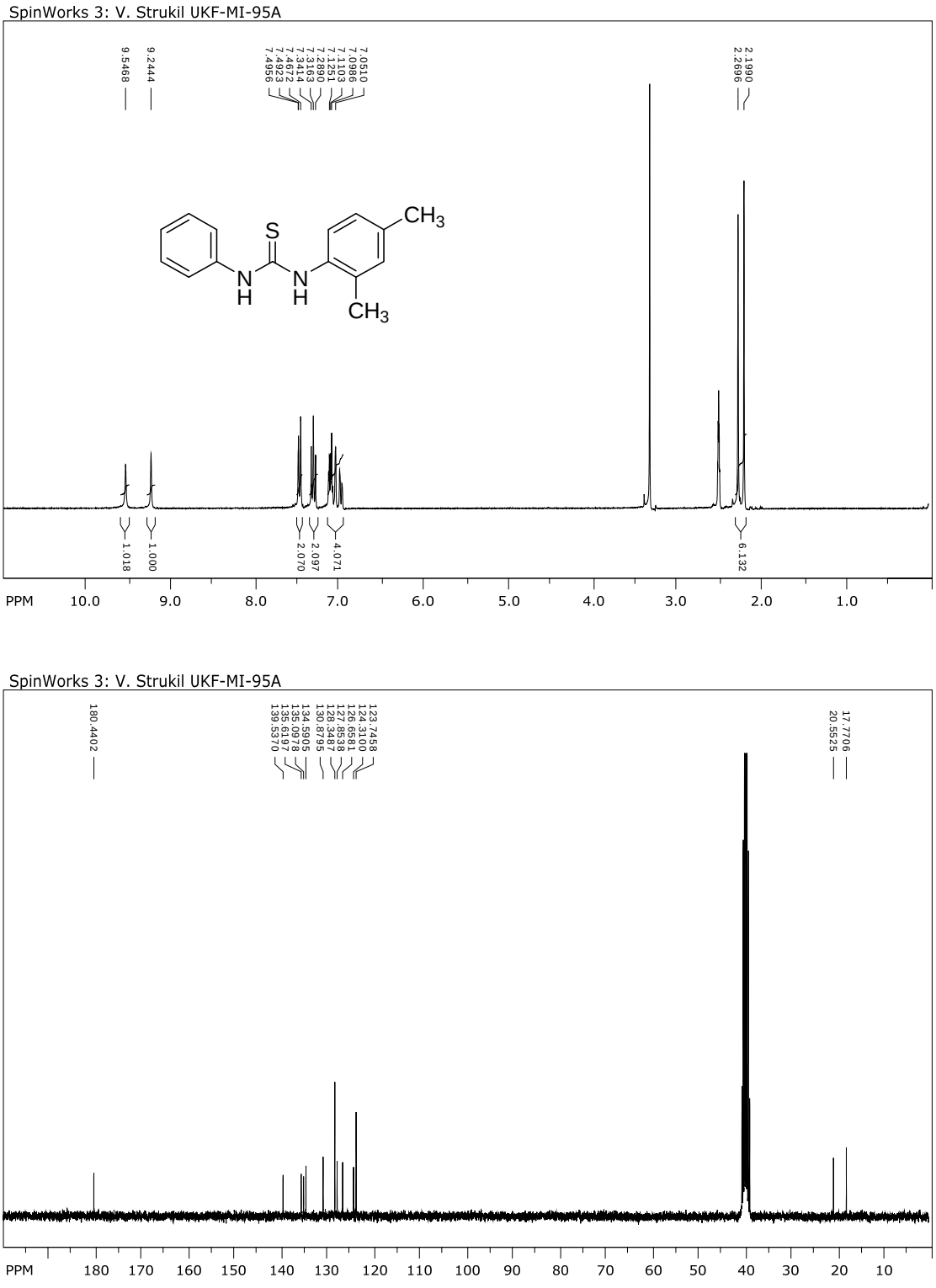


Figure S24. ^{1}H and ^{13}C NMR spectra of thiourea **2l**.

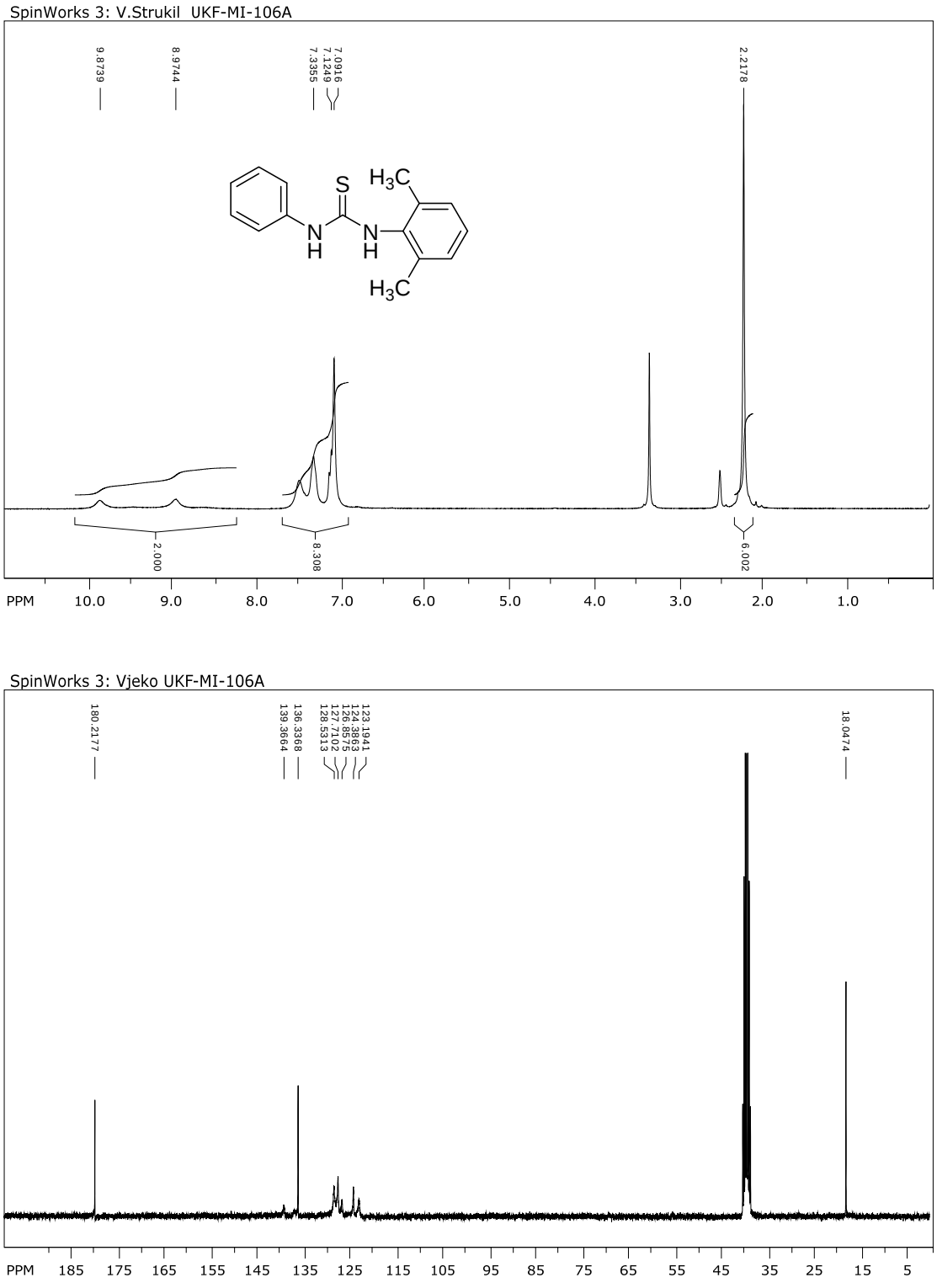


Figure S25. ^{1}H and ^{13}C NMR spectra of thiourea **2m**.

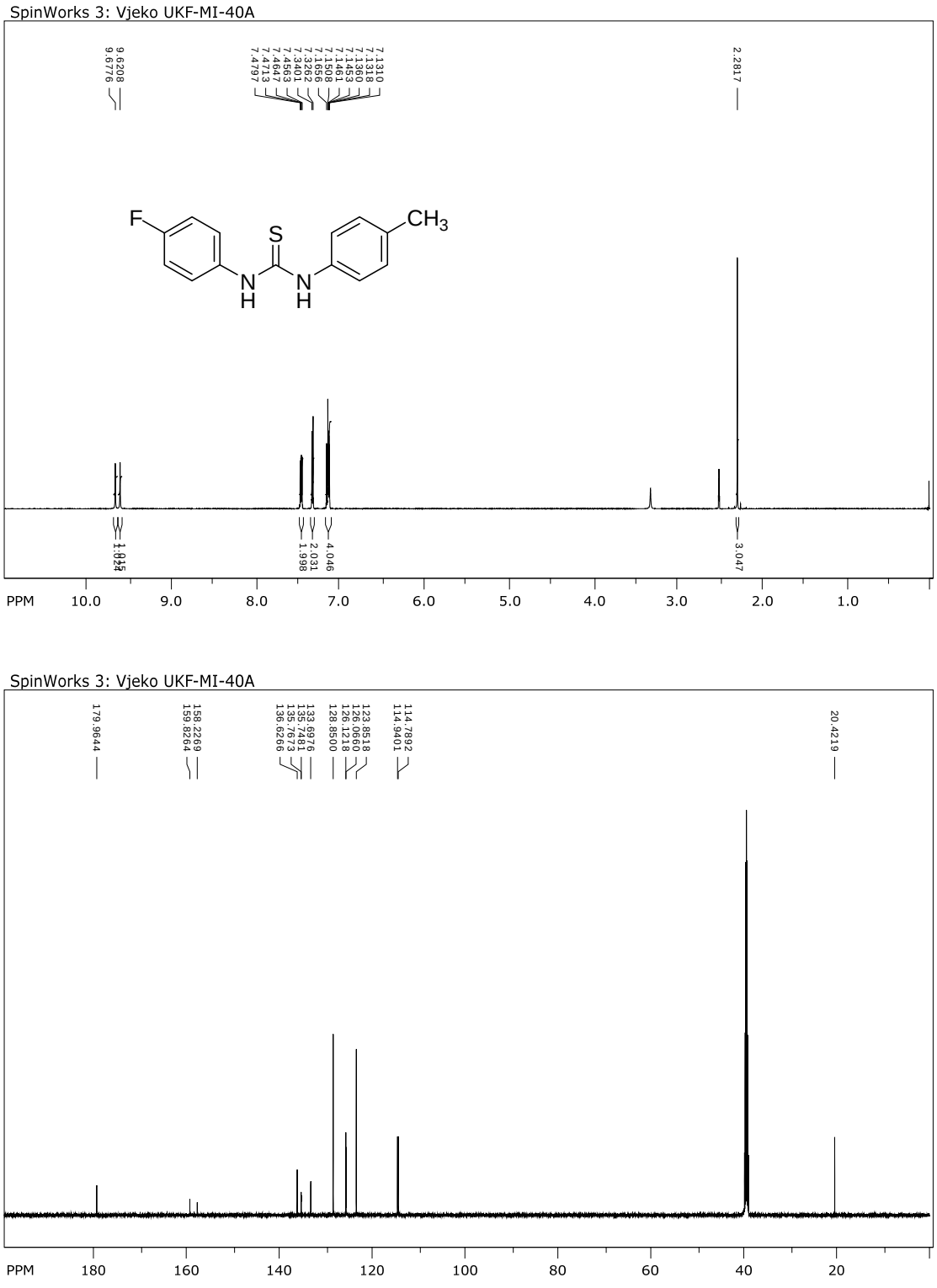


Figure S26. ^{1}H and ^{13}C NMR spectra of thiourea **3b**.

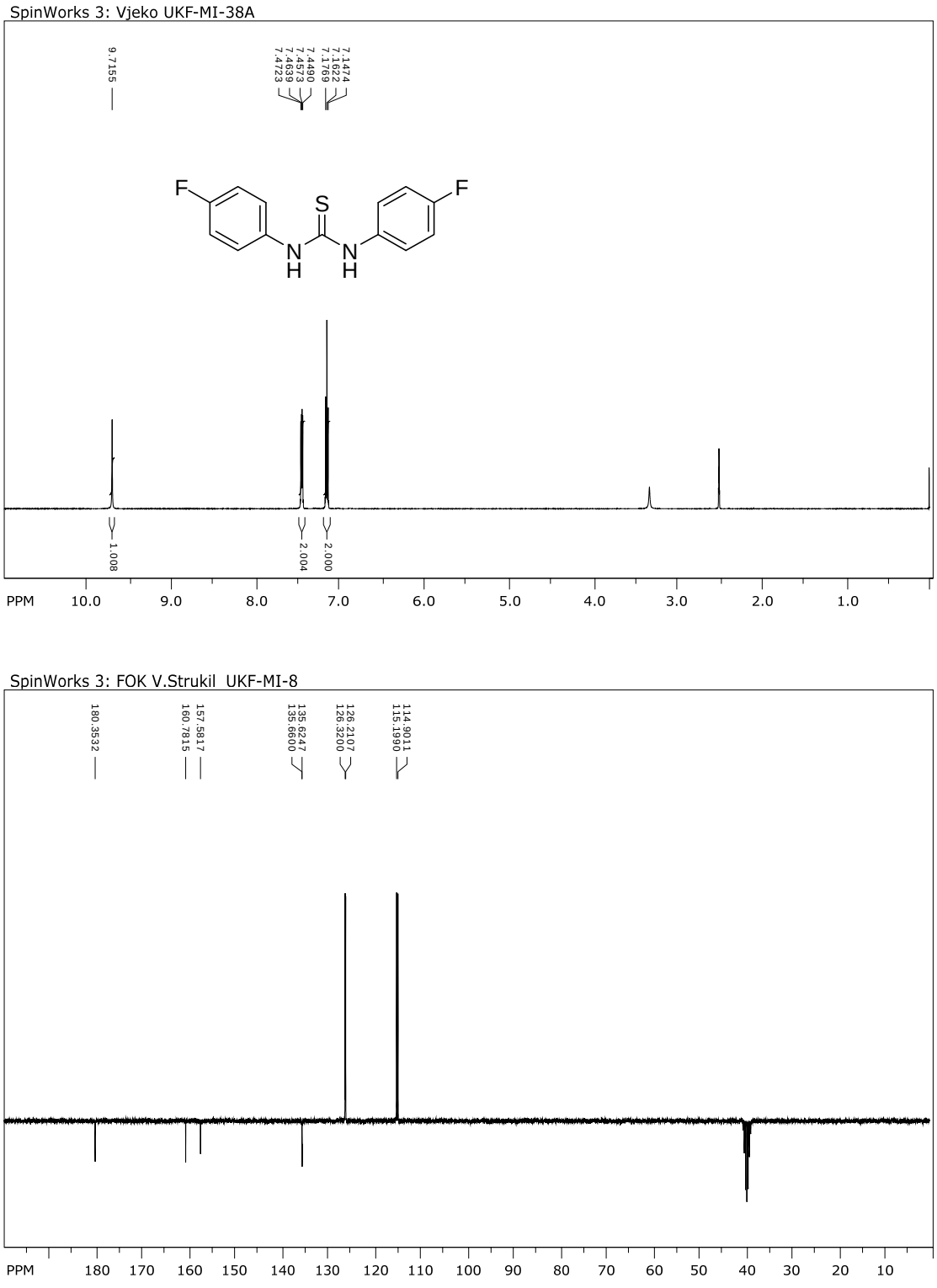


Figure S27. ^{1}H and ^{13}C NMR spectra of thiourea **3d**.

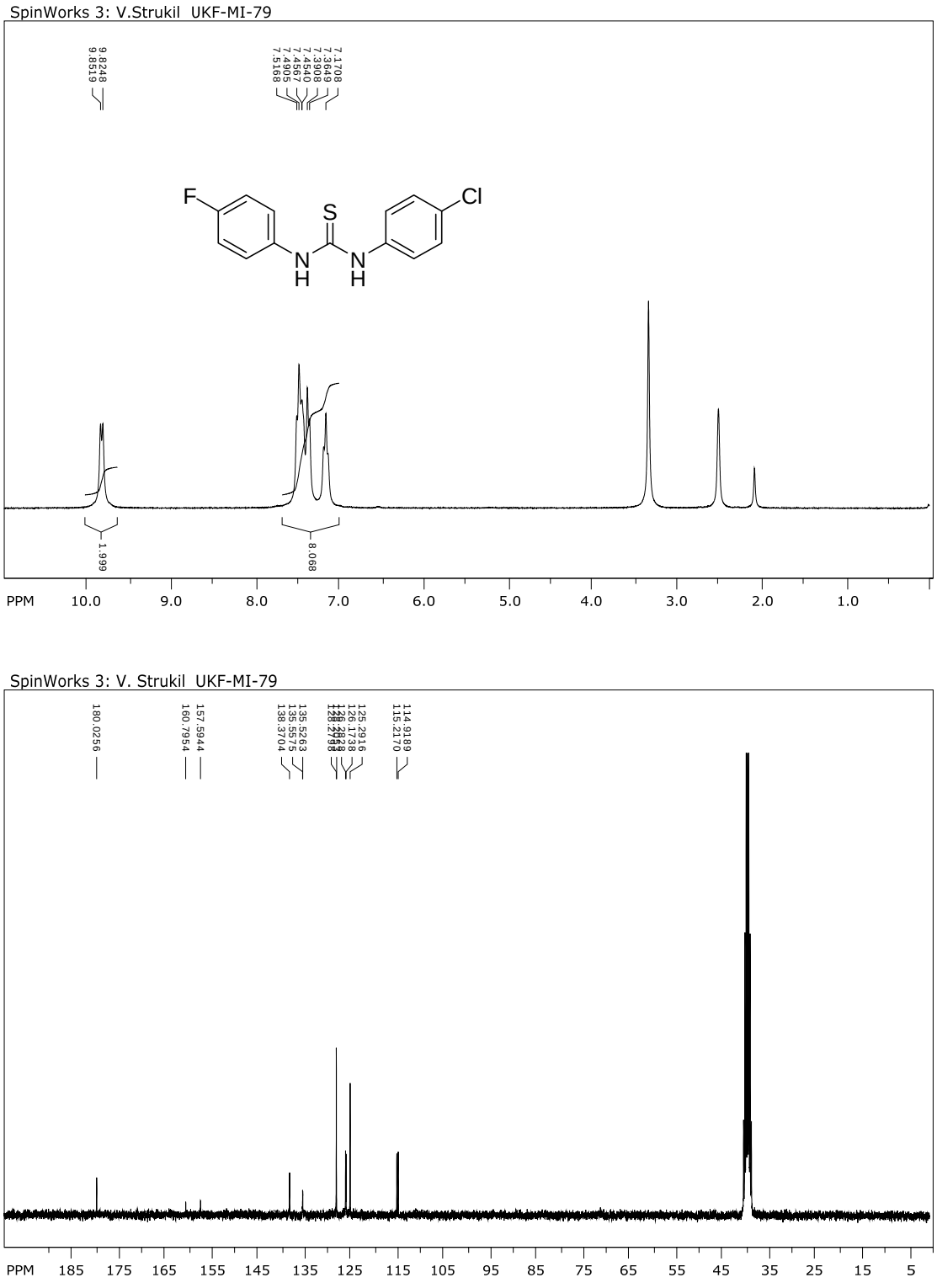


Figure S28. ^{1}H and ^{13}C NMR spectra of thiourea **3e**. (signal at 2.07 ppm corresponds to residual acetonitrile)

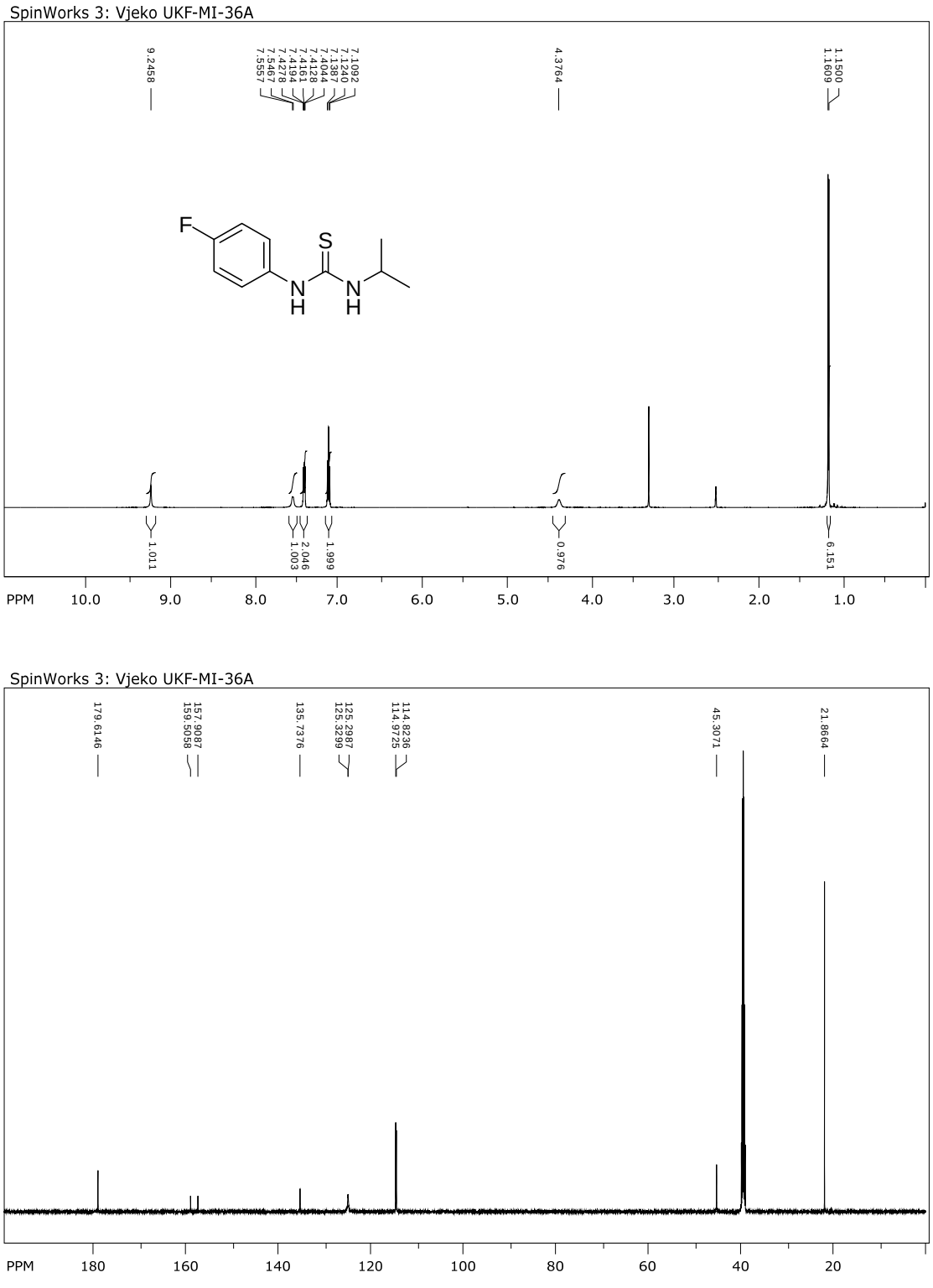


Figure S29. ^{1}H and ^{13}C NMR spectra of thiourea **3f**.

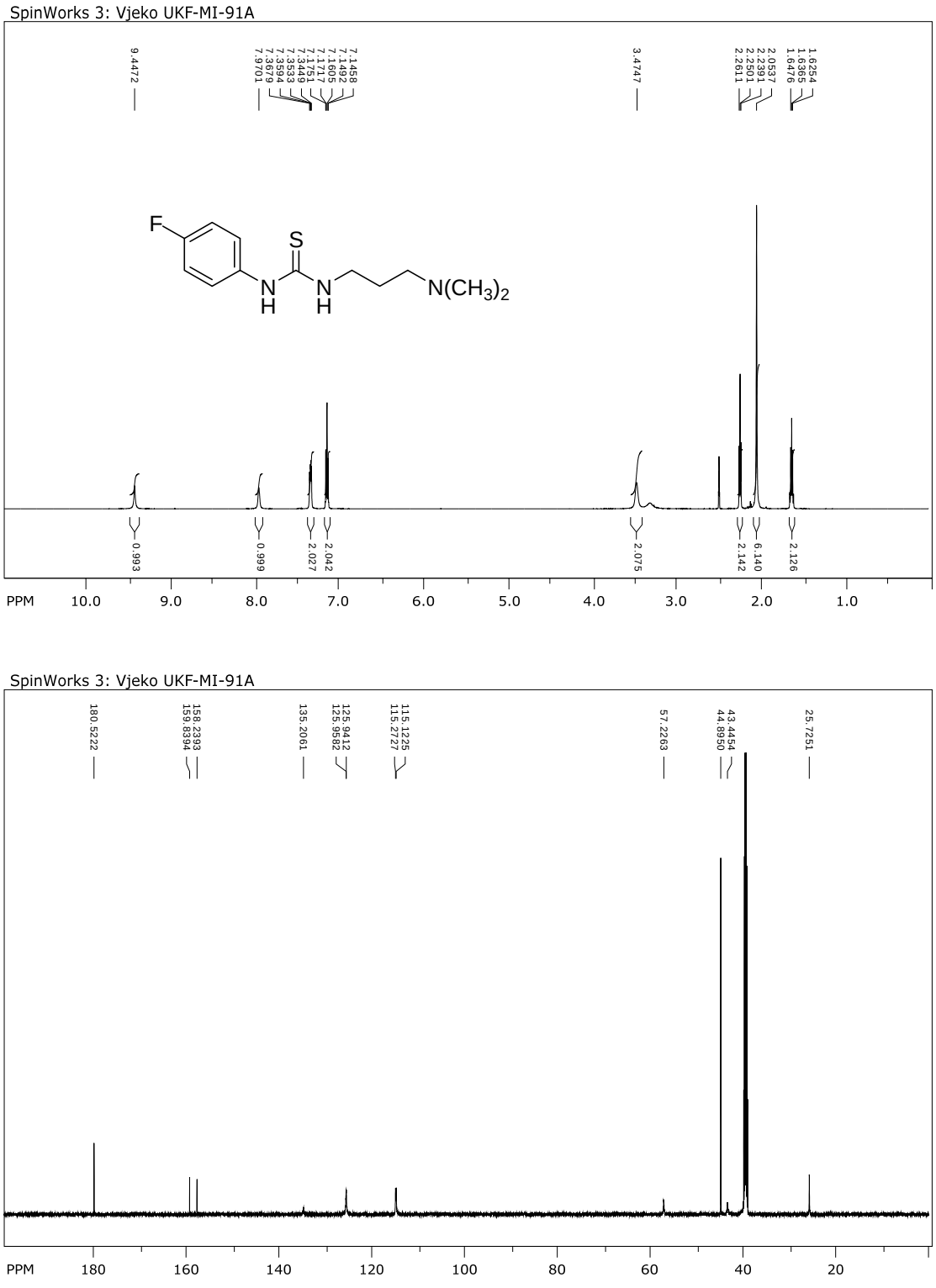


Figure S30. ^{1}H and ^{13}C NMR spectra of thiourea **3g**.

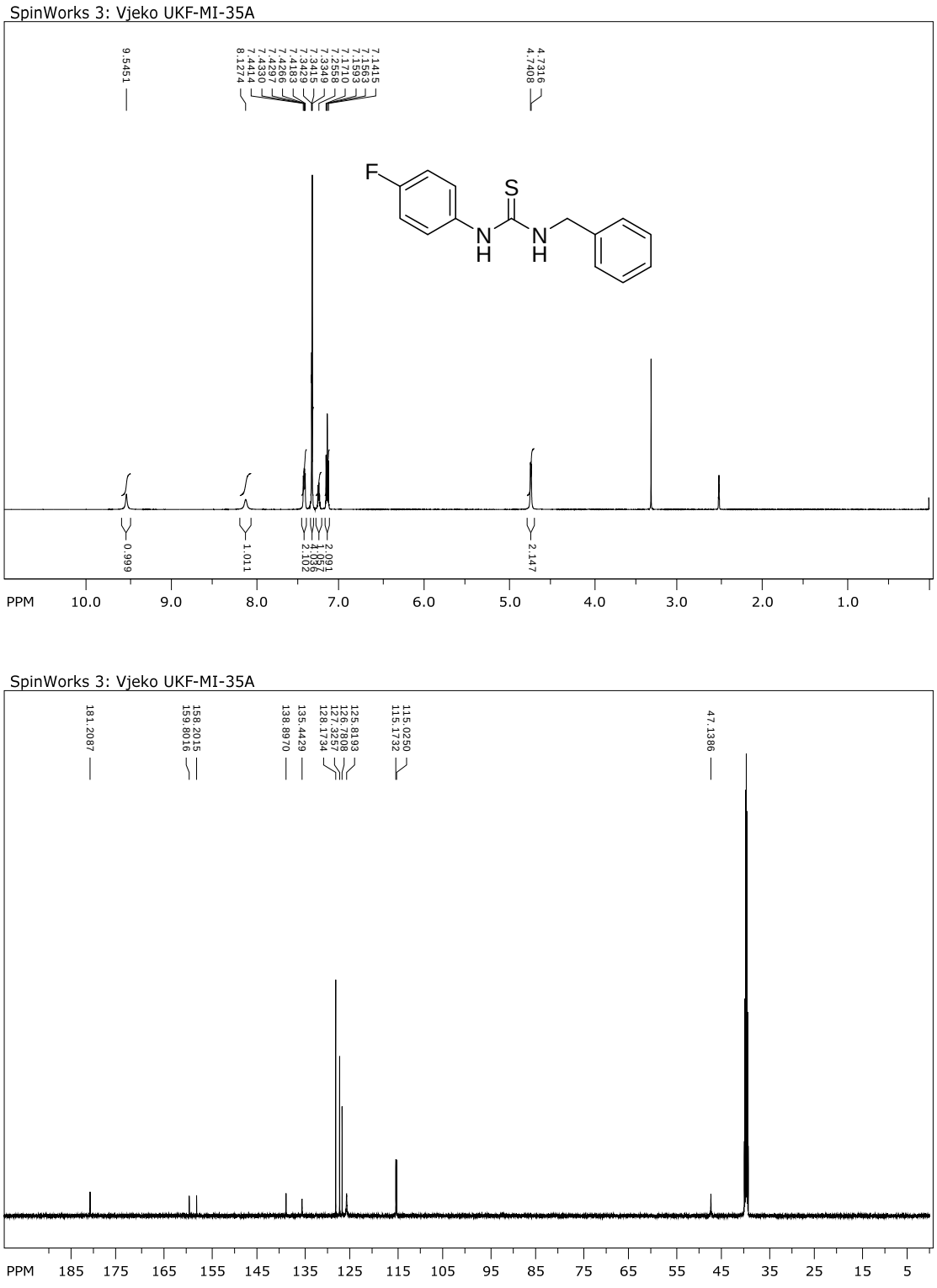


Figure S31. ^{1}H and ^{13}C NMR spectra of thiourea **3h**.

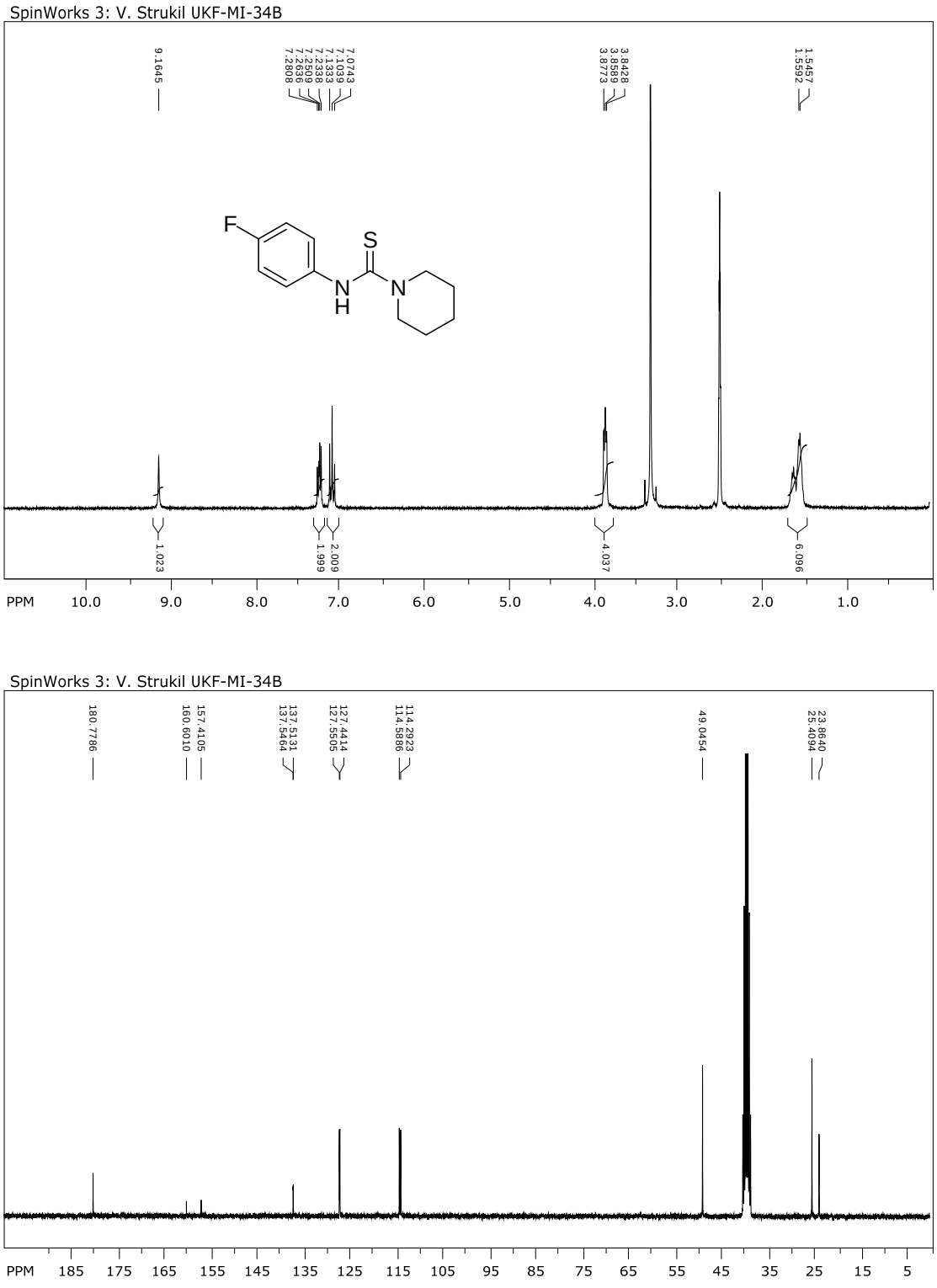


Figure S32. ^{1}H and ^{13}C NMR spectra of thiourea **3i**.

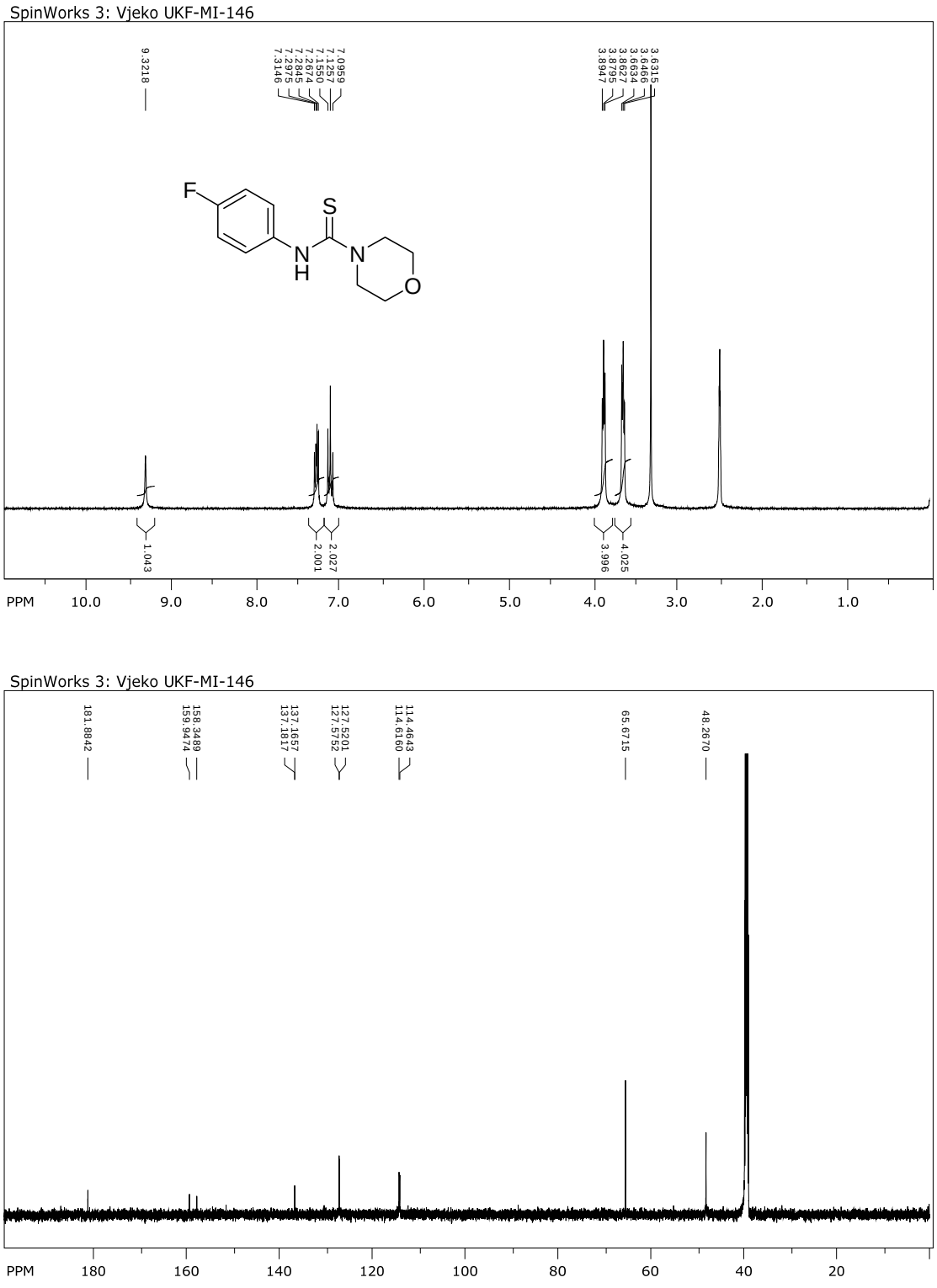


Figure S33. ^{1}H and ^{13}C NMR spectra of thiourea **3j**.

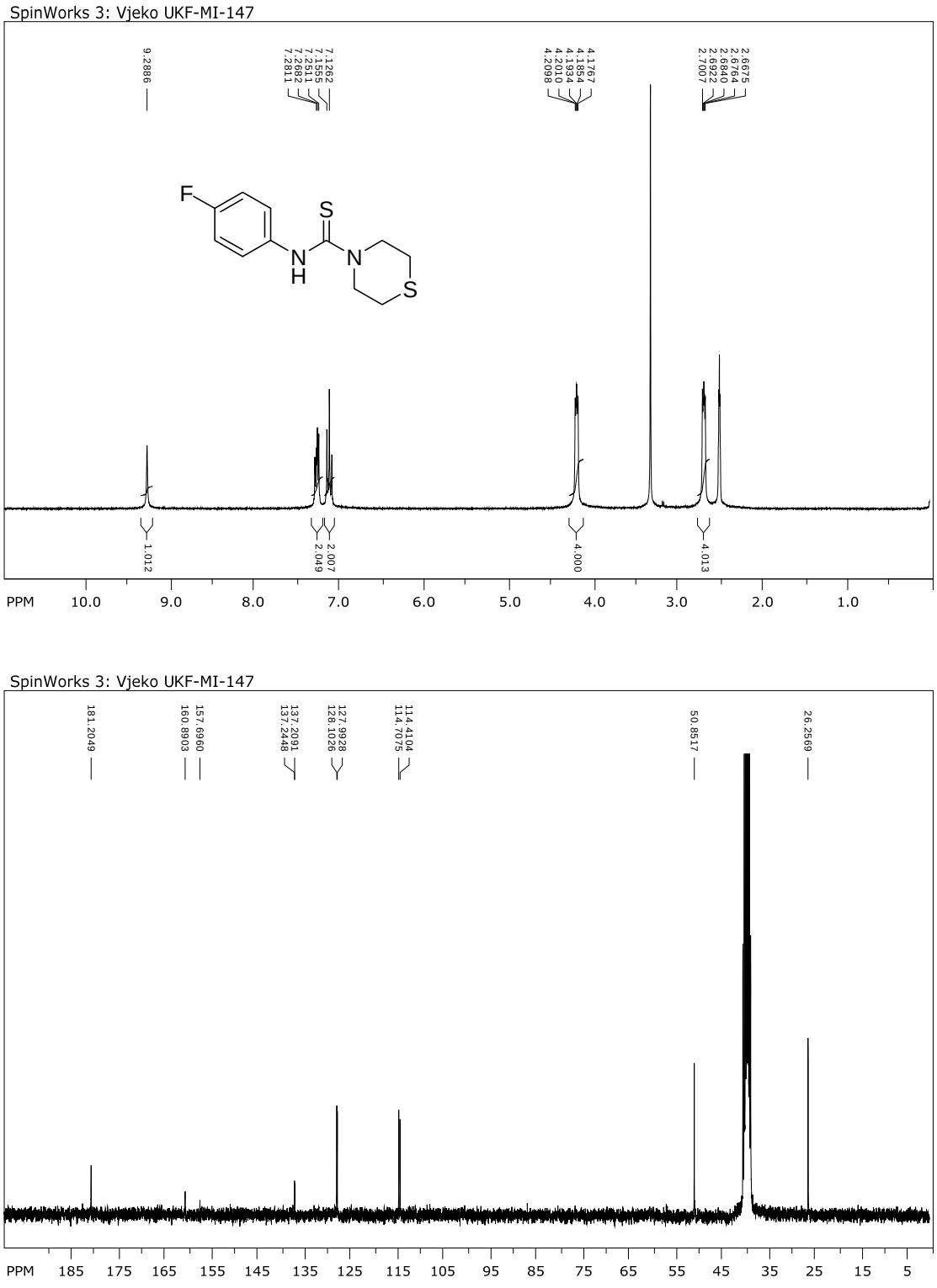


Figure S34. ^{1}H and ^{13}C NMR spectra of thiourea **3k**.

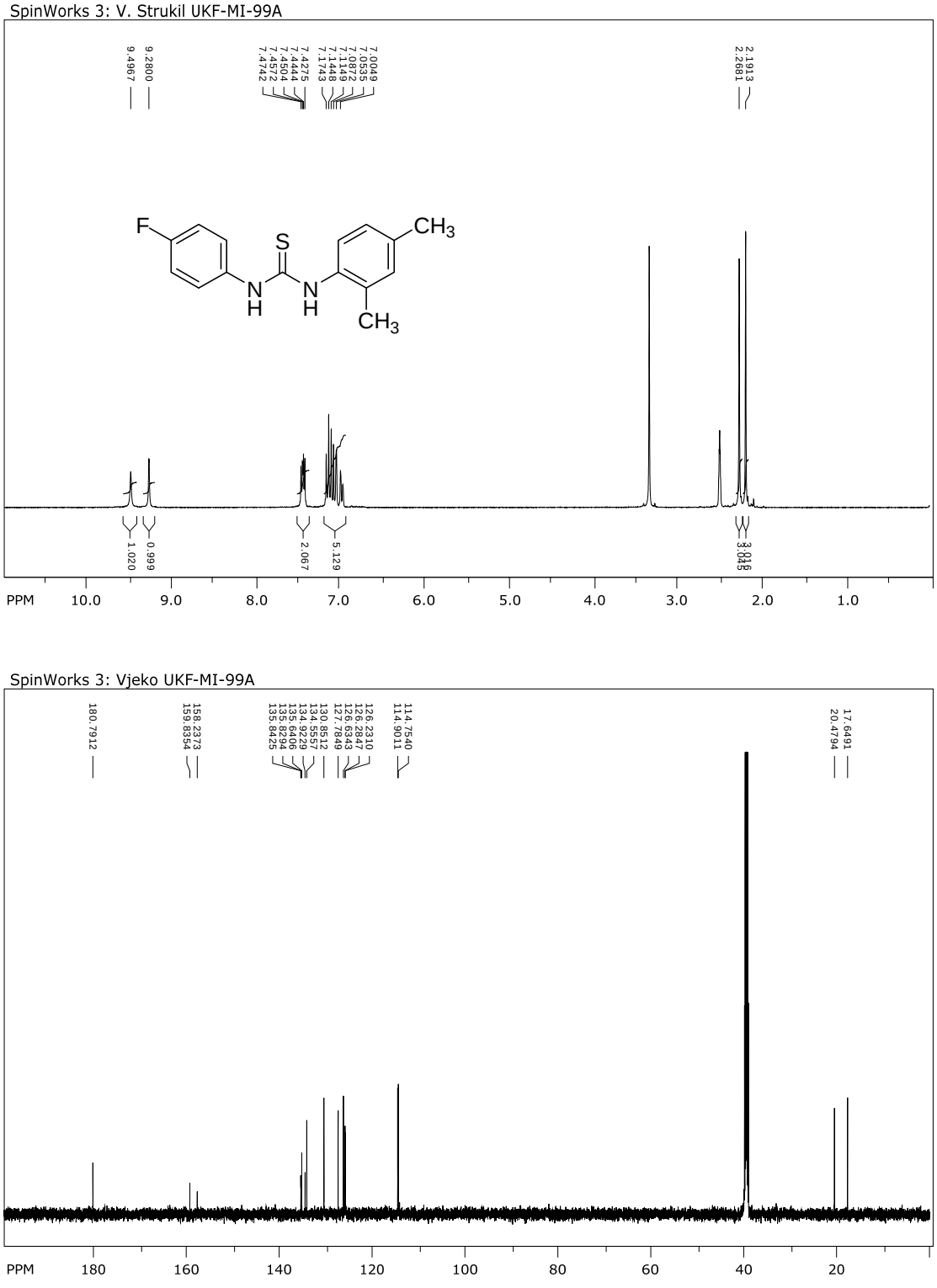


Figure S35. ^{1}H and ^{13}C NMR spectra of thiourea **3l**.

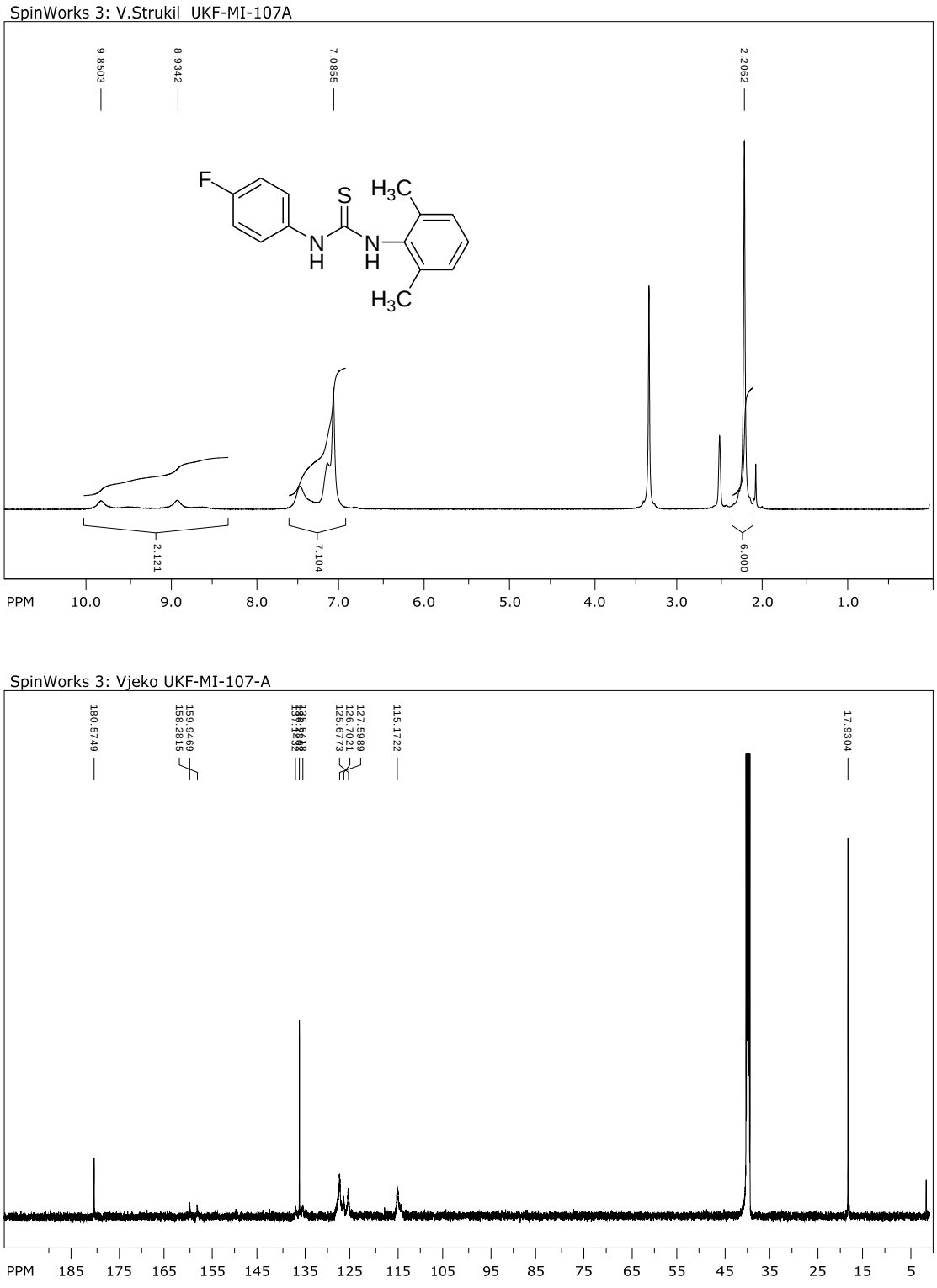


Figure S36. ^{1}H and ^{13}C NMR spectra of thiourea **3m**.

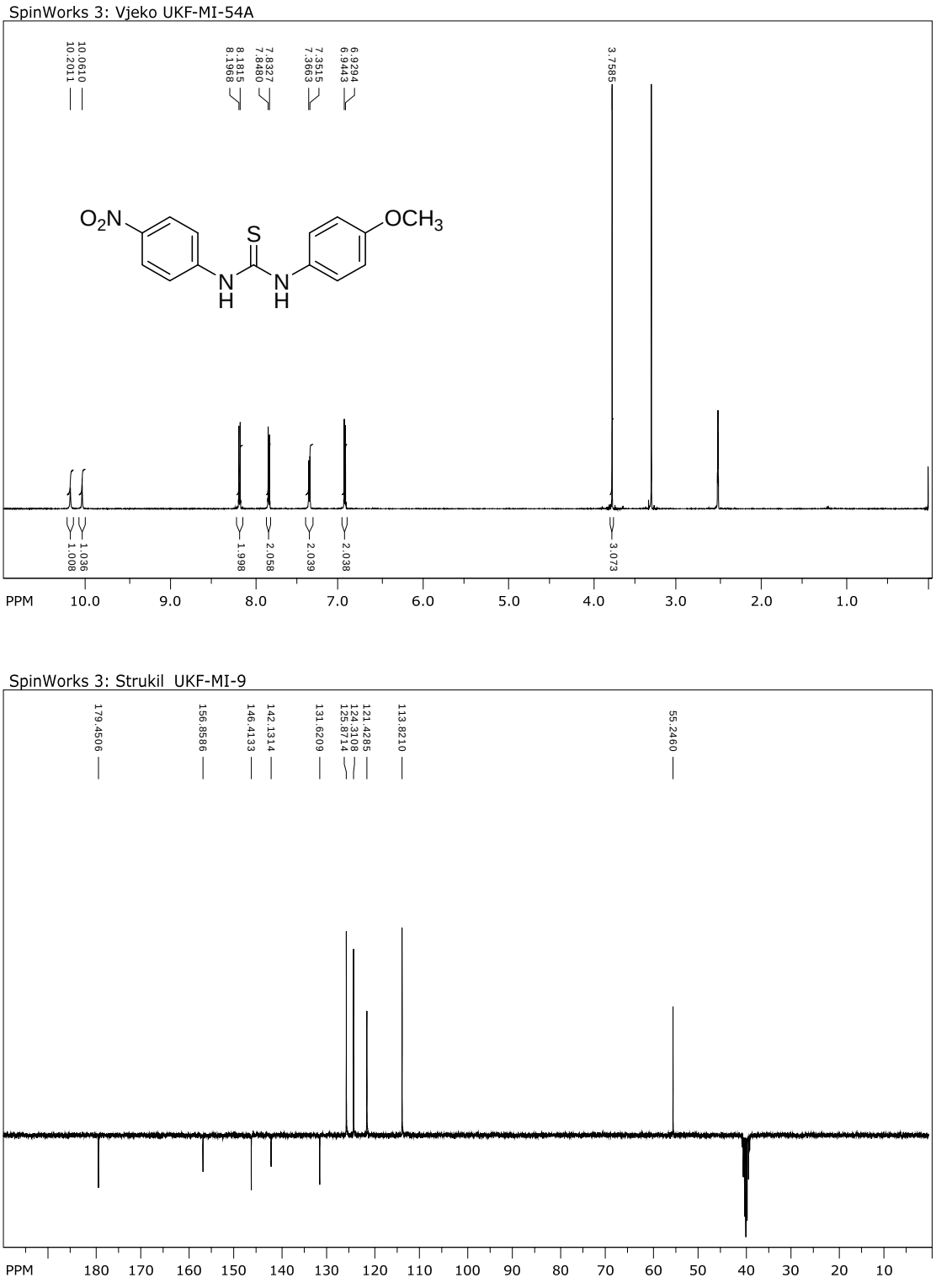


Figure S37. ^{1}H and ^{13}C NMR spectra of thiourea **4a**.

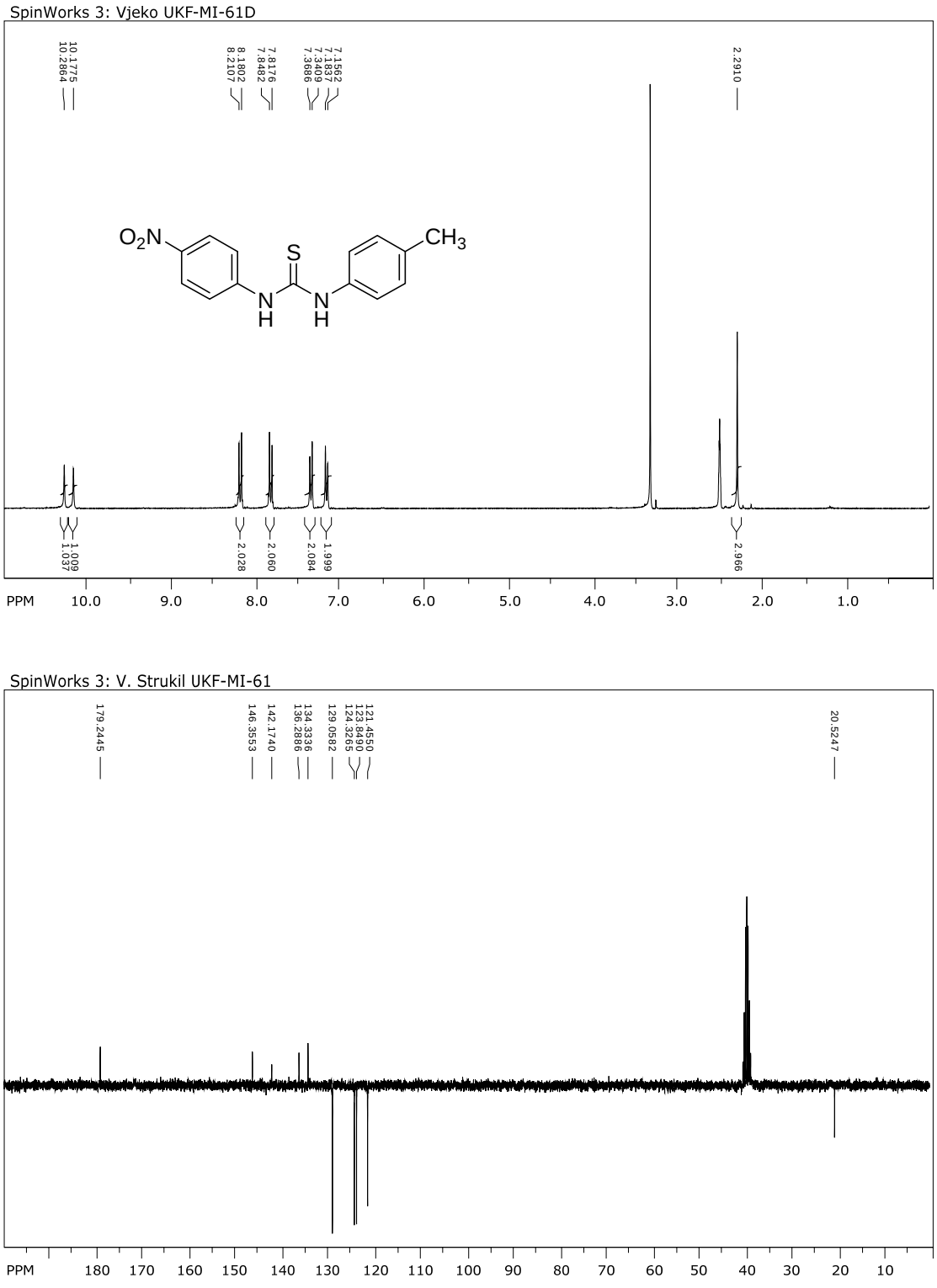


Figure S38. ^{1}H and ^{13}C NMR spectra of thiourea **4b**.

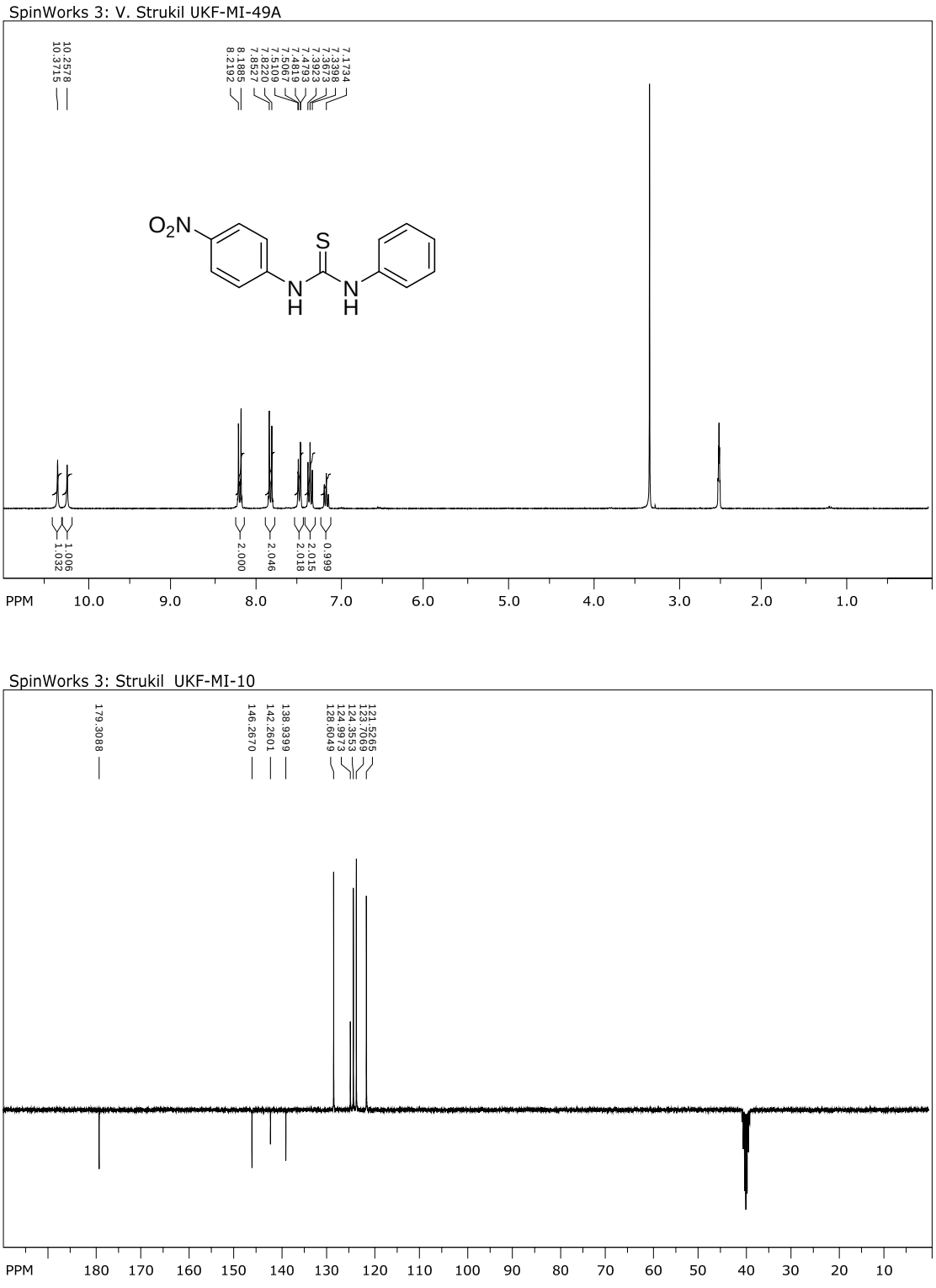


Figure S39. ^{1}H and ^{13}C NMR spectra of thiourea **4c**.

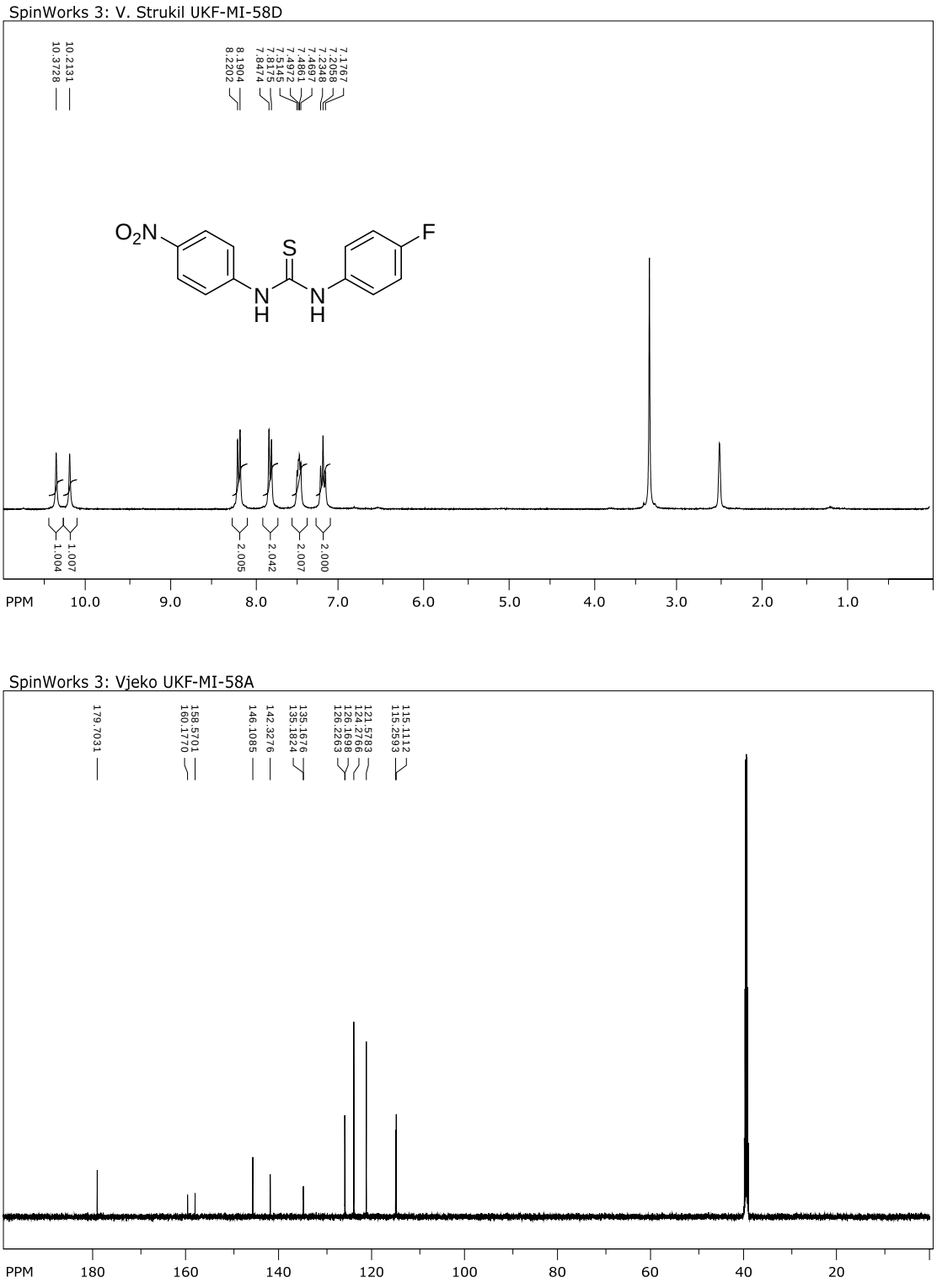


Figure S40. ^{1}H and ^{13}C NMR spectra of thiourea **4d**.

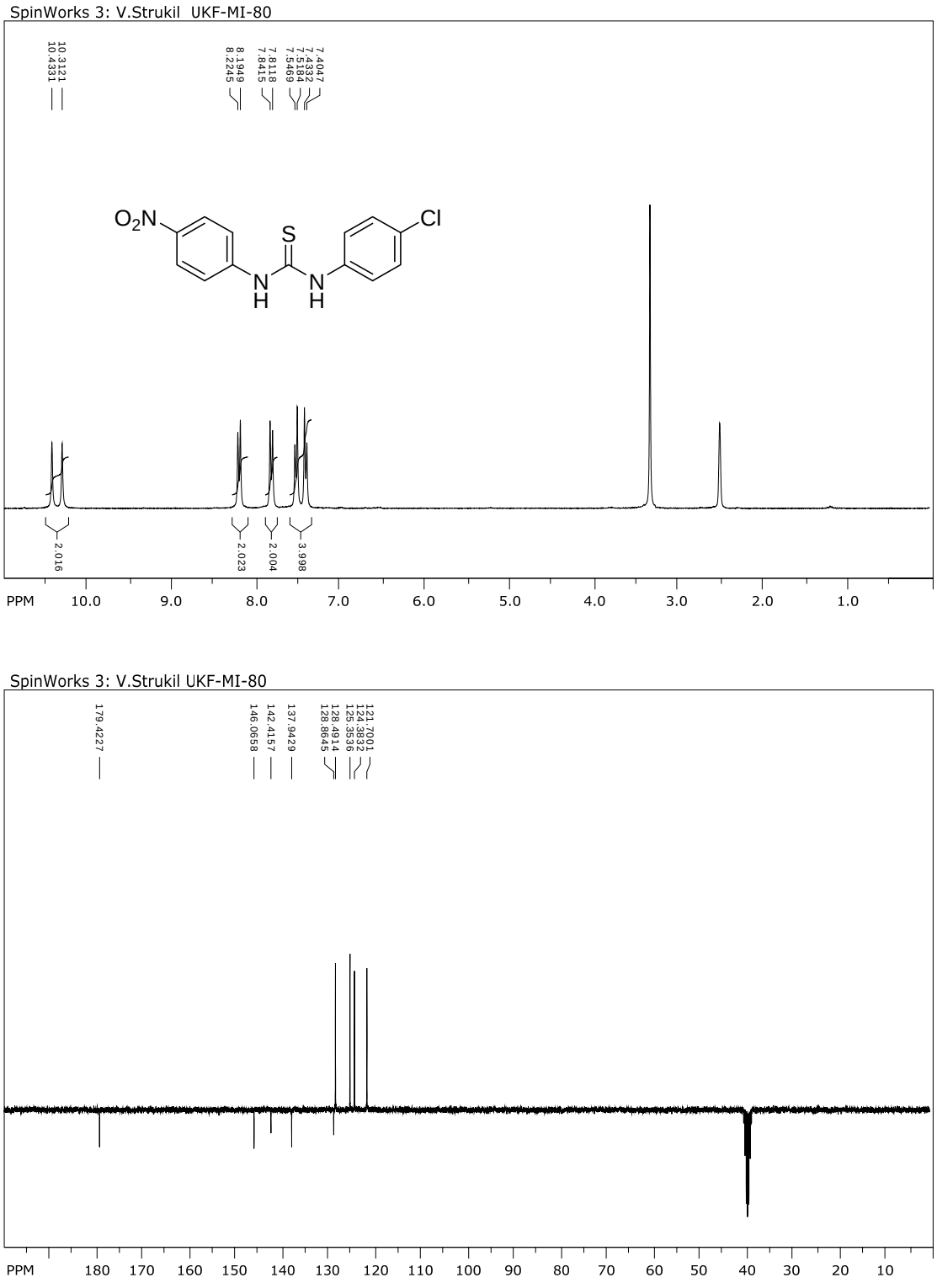


Figure S41. ^{1}H and ^{13}C NMR spectra of thiourea **4e**.

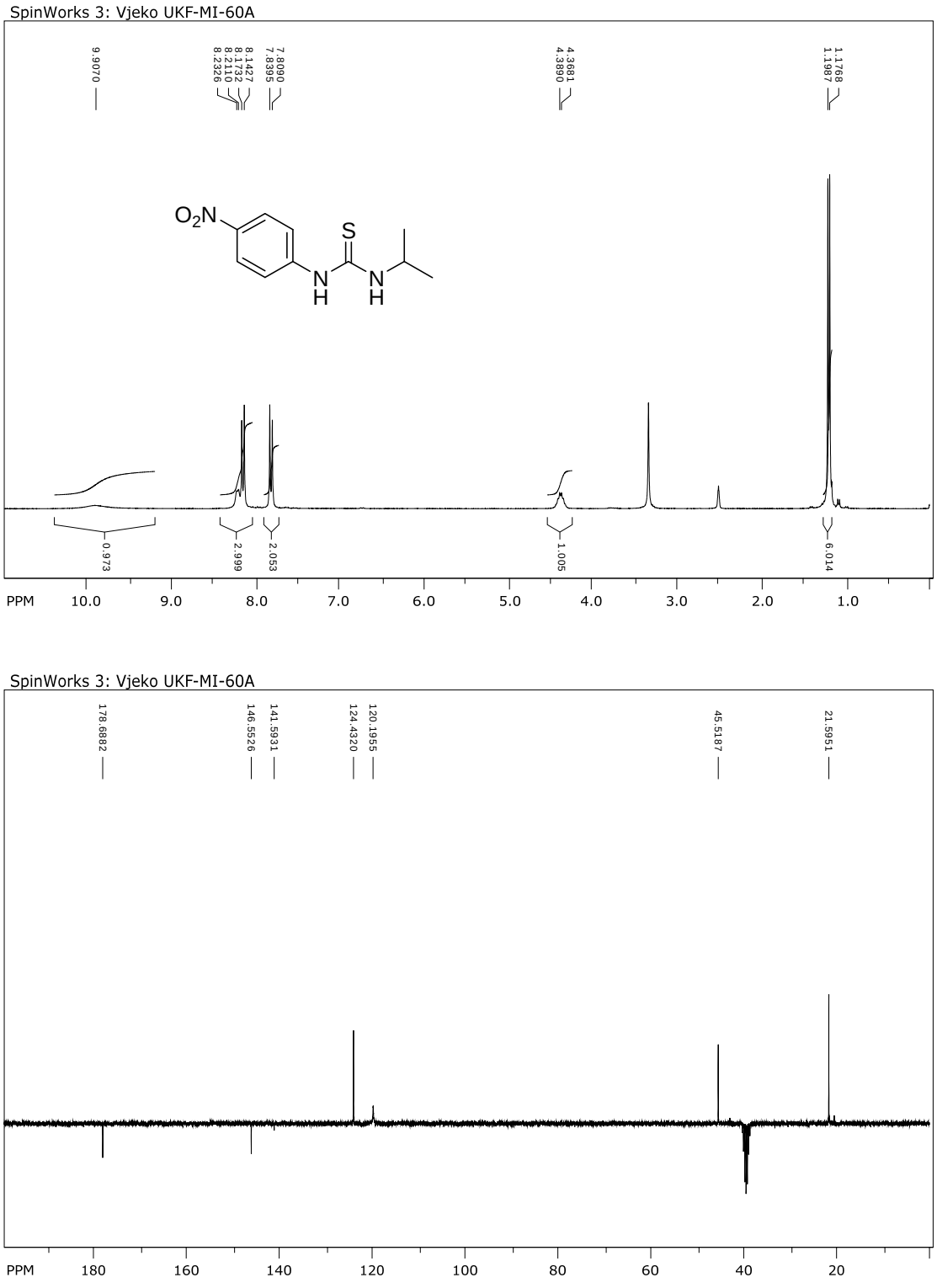


Figure S42. ^{1}H and ^{13}C NMR spectra of thiourea **4f**.

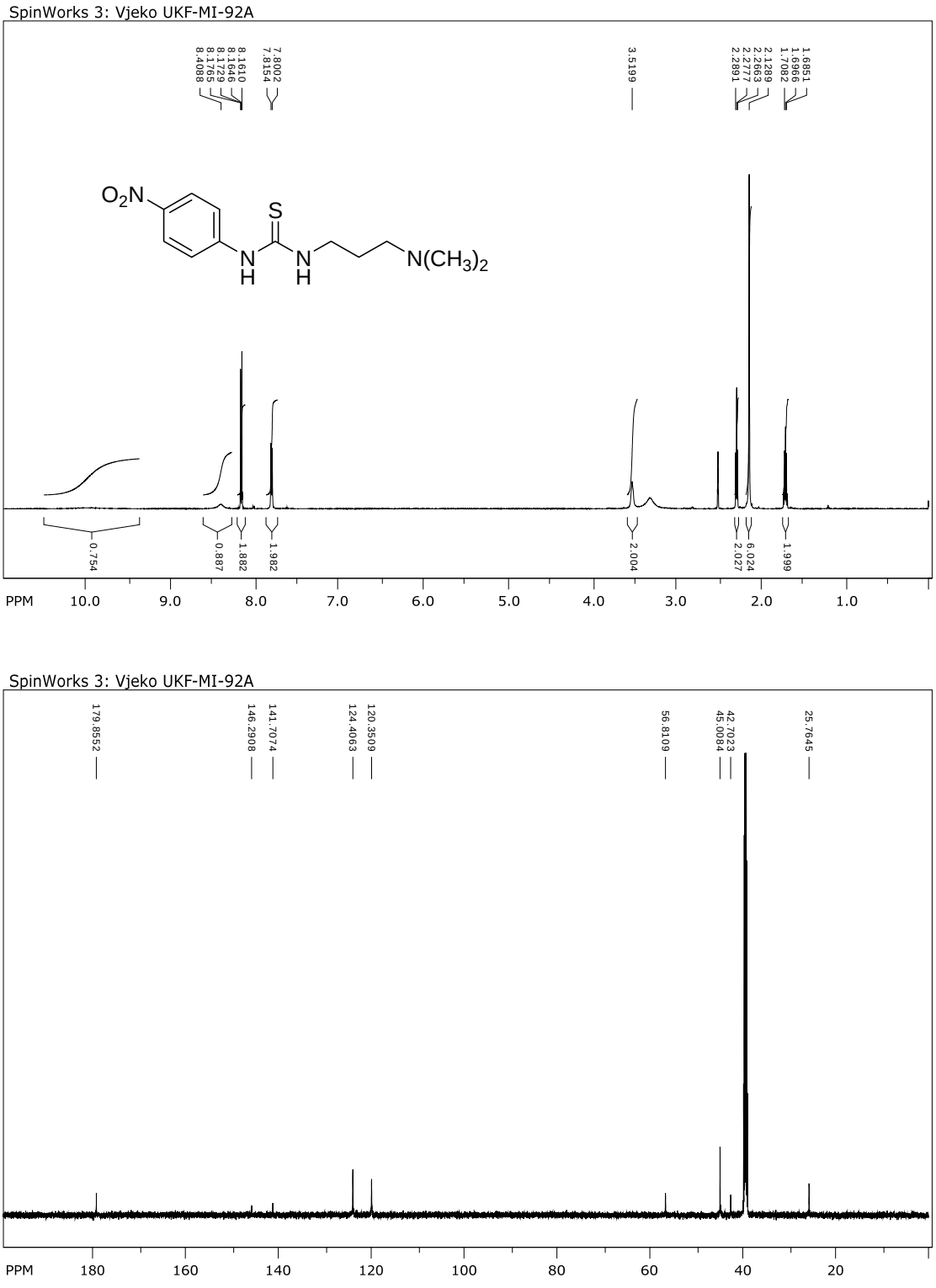


Figure S43. ^{1}H and ^{13}C NMR spectra of thiourea **4g**.

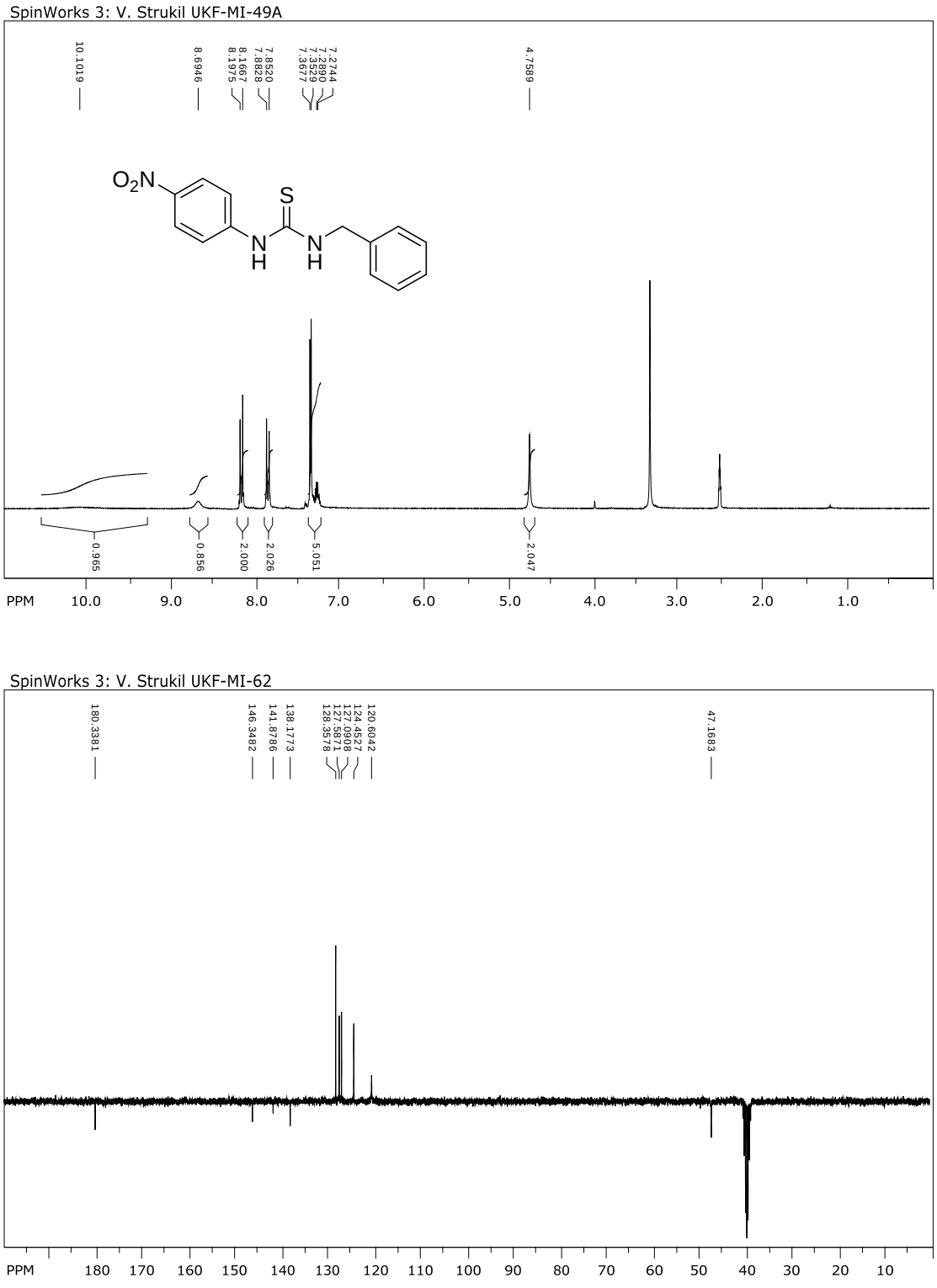


Figure S44. ^{1}H and ^{13}C NMR spectra of thiourea **4h**.

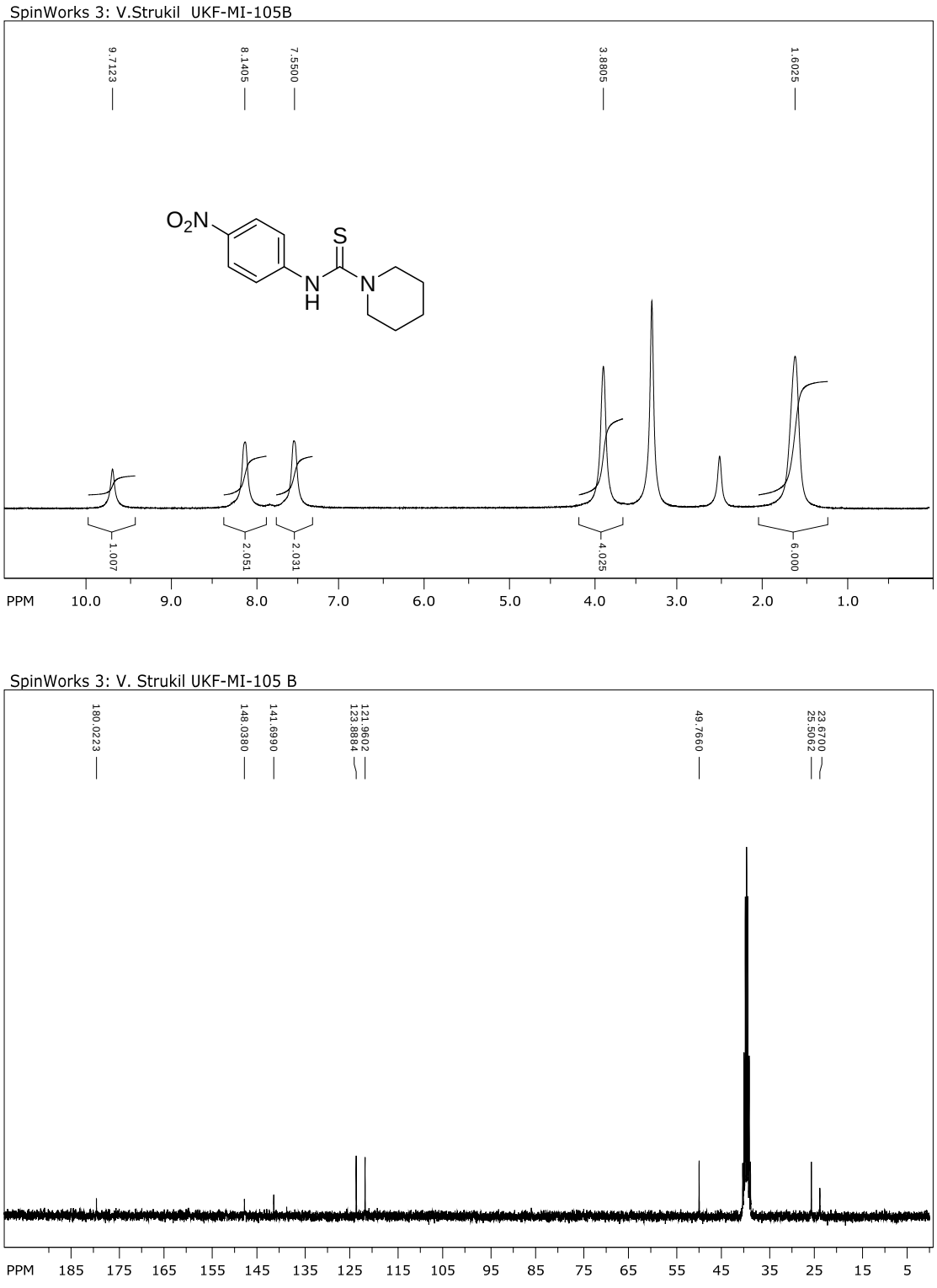


Figure S45. ^{1}H and ^{13}C NMR spectra of thiourea **4i**.

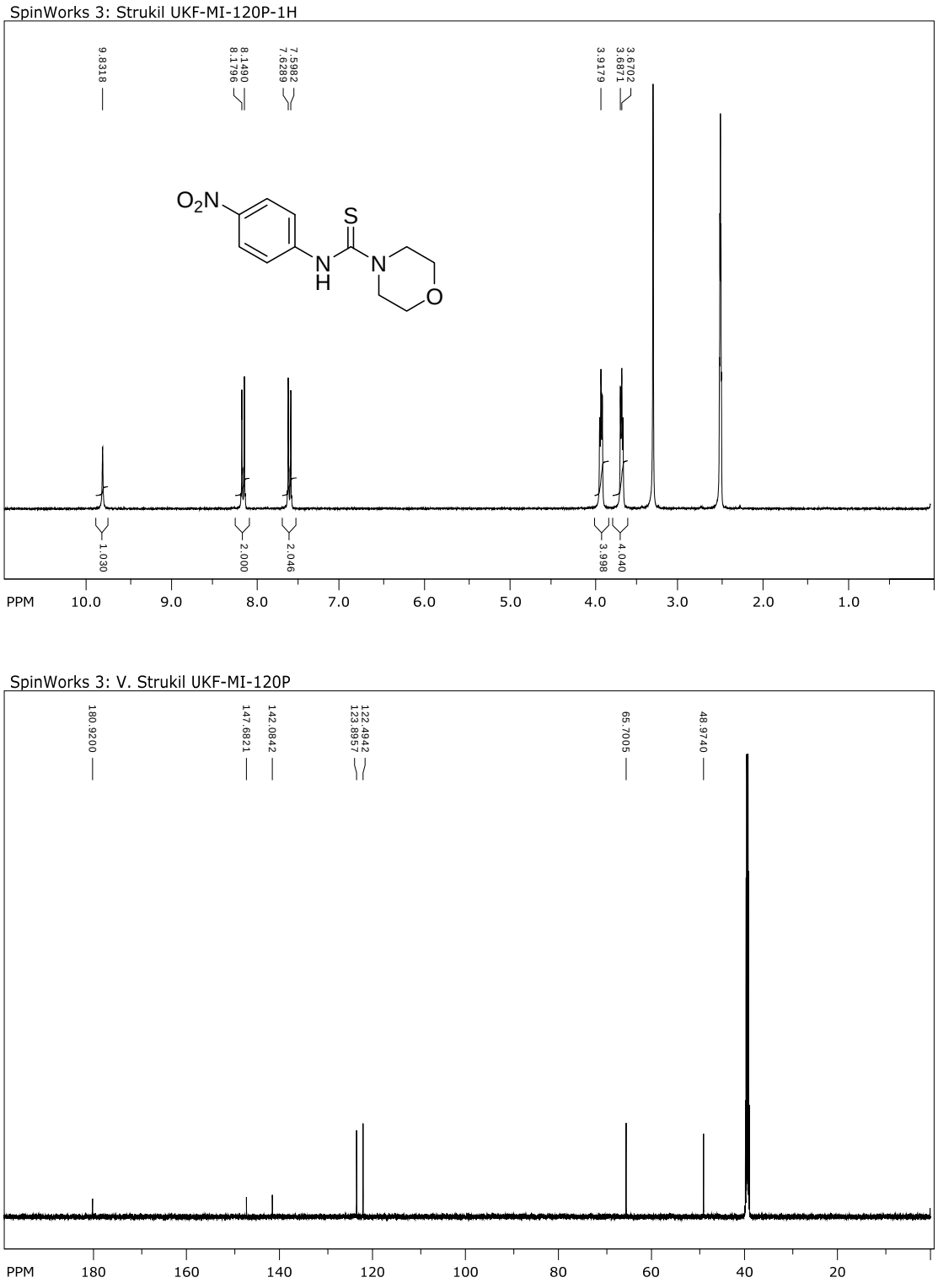


Figure S46. ^{1}H and ^{13}C NMR spectra of thiourea **4j**.

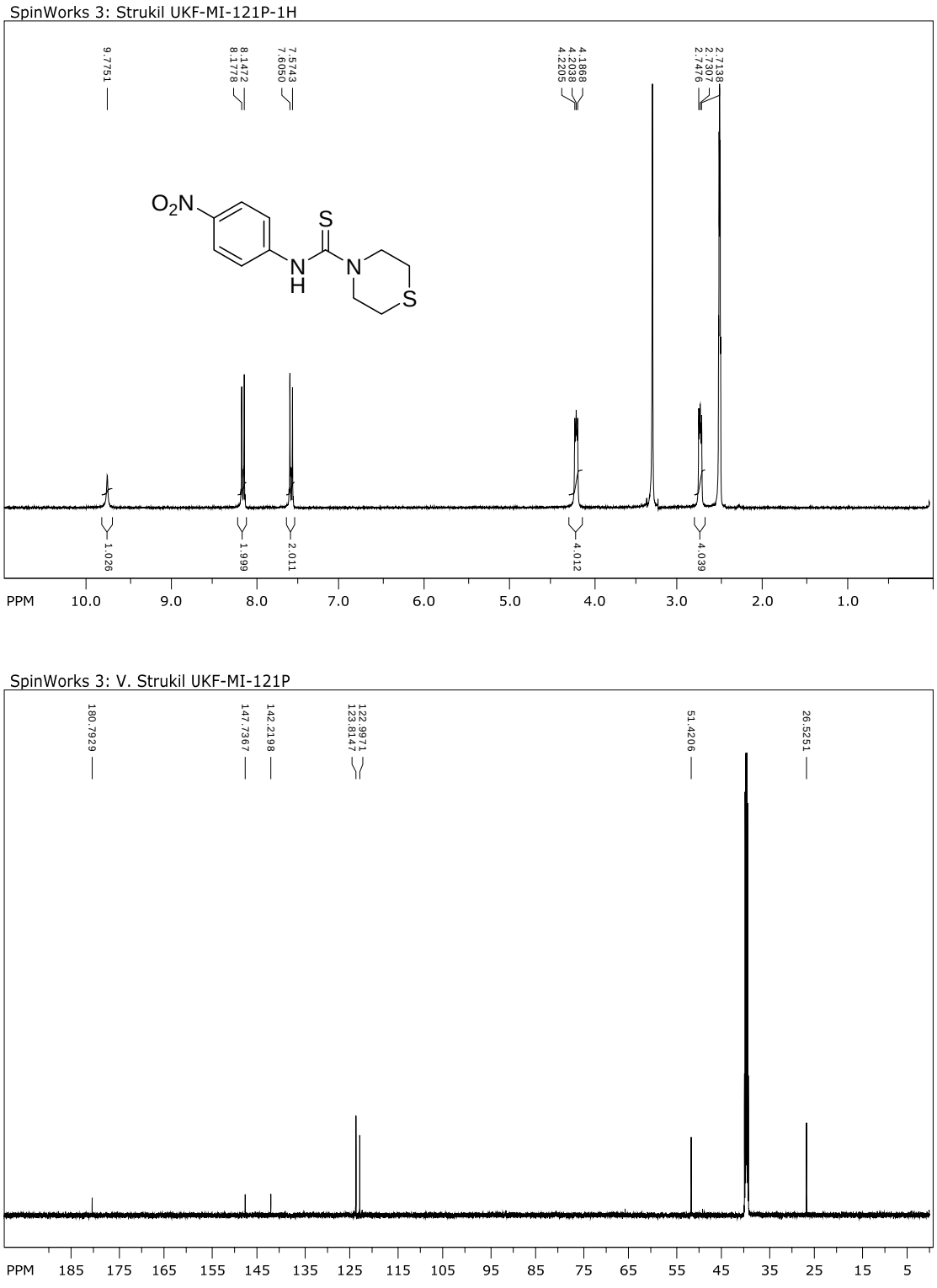


Figure S47. ^{1}H and ^{13}C NMR spectra of thiourea **4k**.

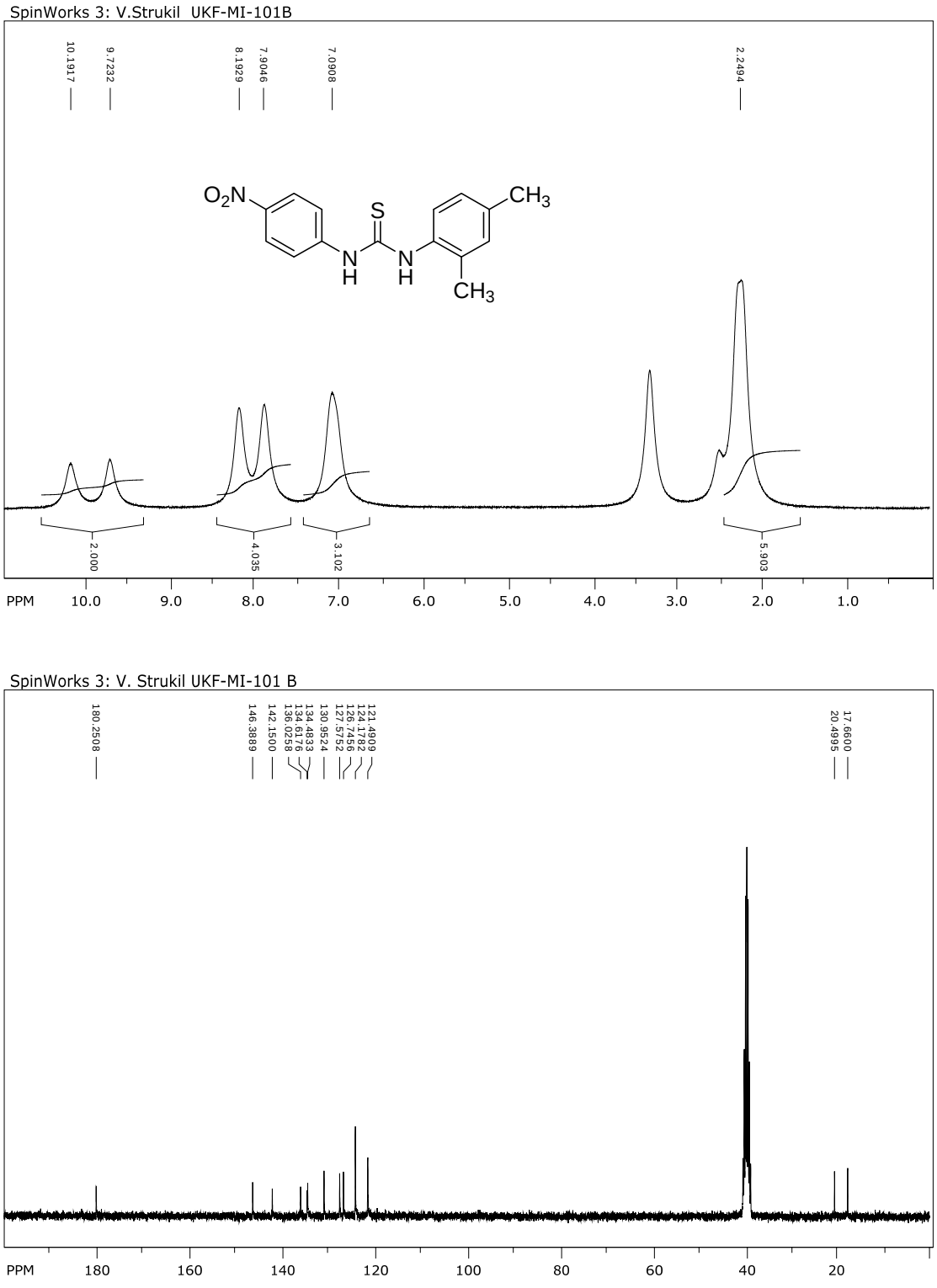


Figure S48. ^{1}H and ^{13}C NMR spectra of thiourea **4l**.

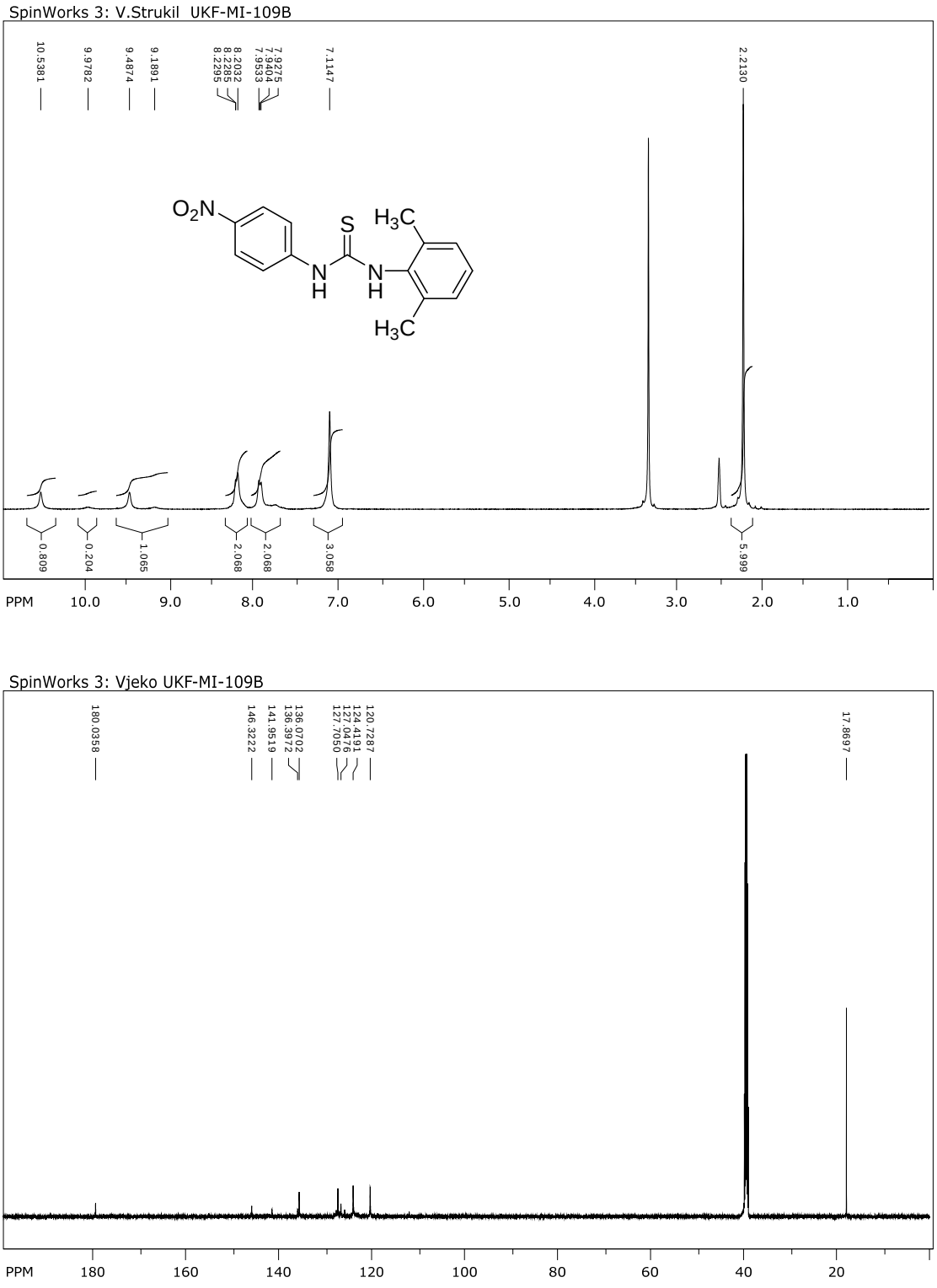


Figure S49. ^{1}H and ^{13}C NMR spectra of thiourea **4m**.

3. FTIR-ATR spectra

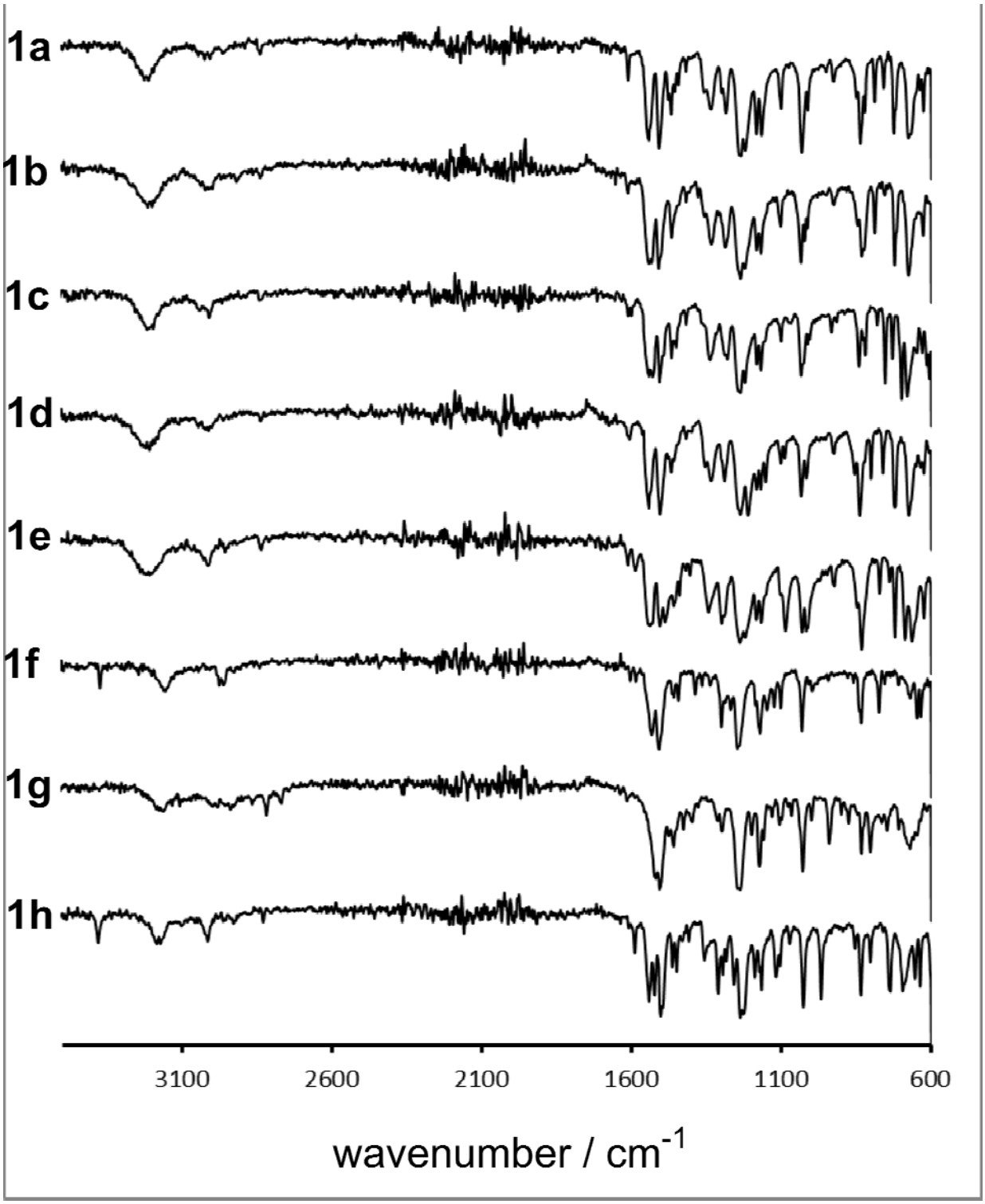


Figure S50. FTIR-ATR spectra of mechanochemically prepared thioureas **1a-h**.

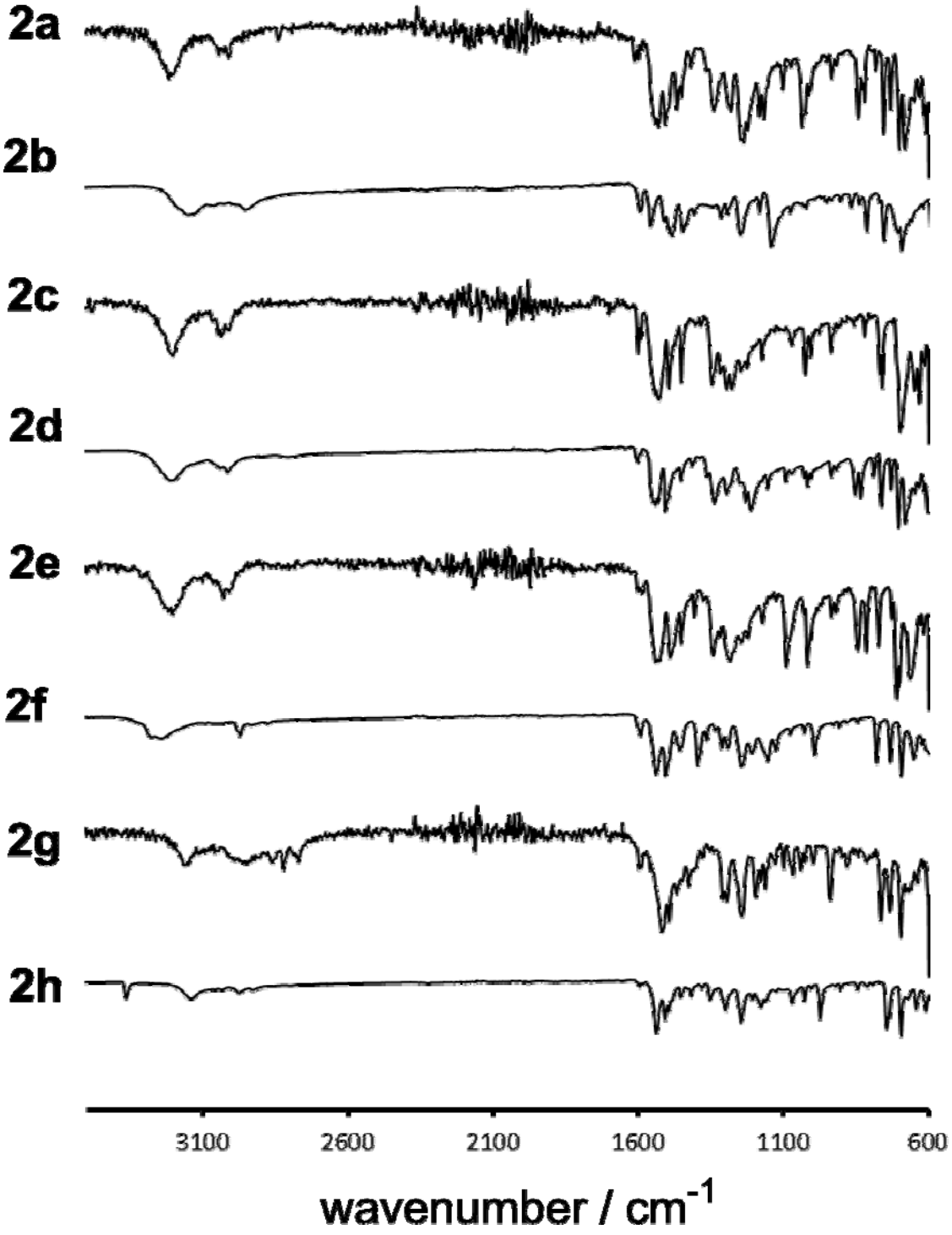


Figure S51. FTIR-ATR spectra of mechanochemically prepared thioureas **2a-h**.

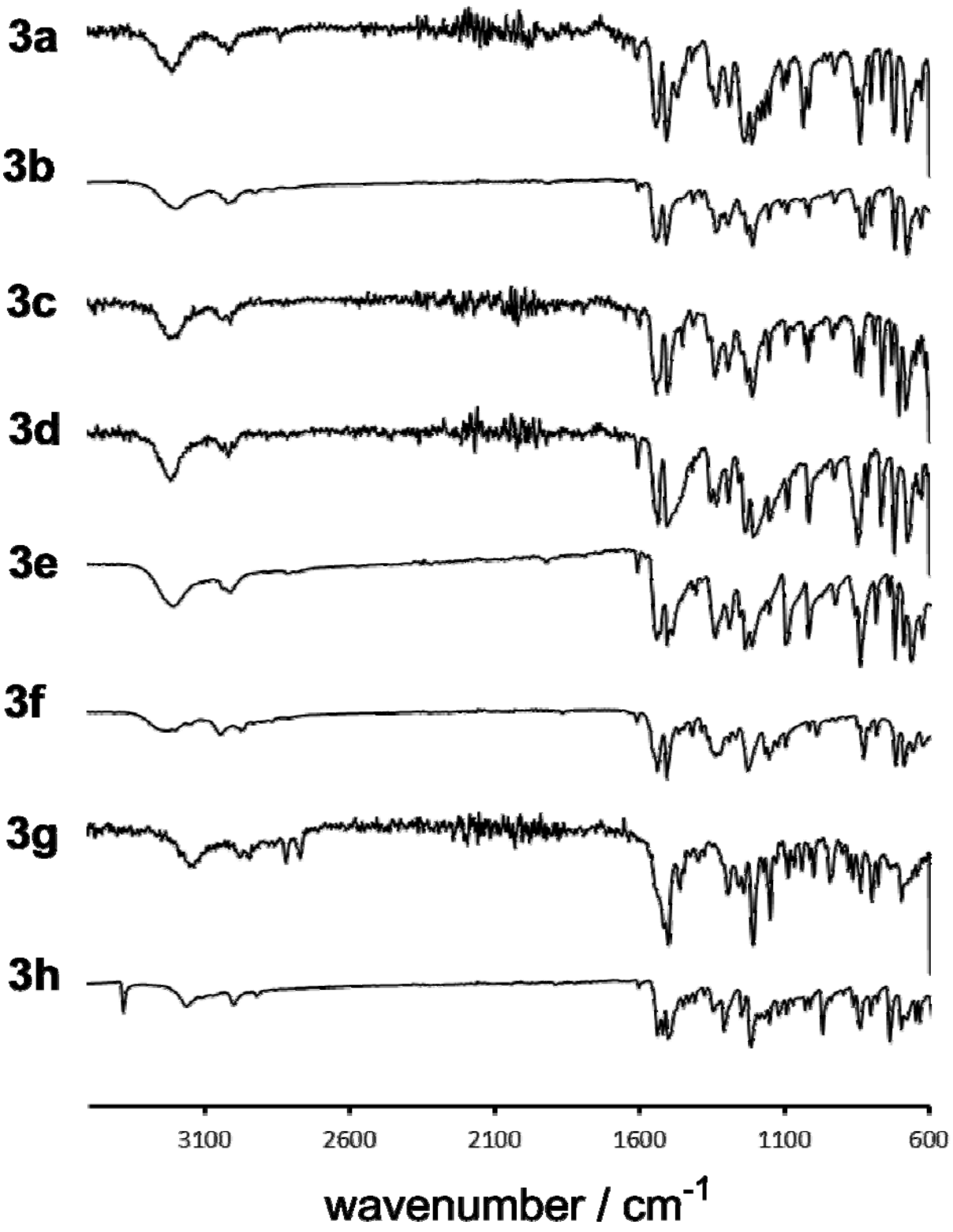


Figure S52. FTIR-ATR spectra of mechanochemically prepared thioureas **3a-h**.

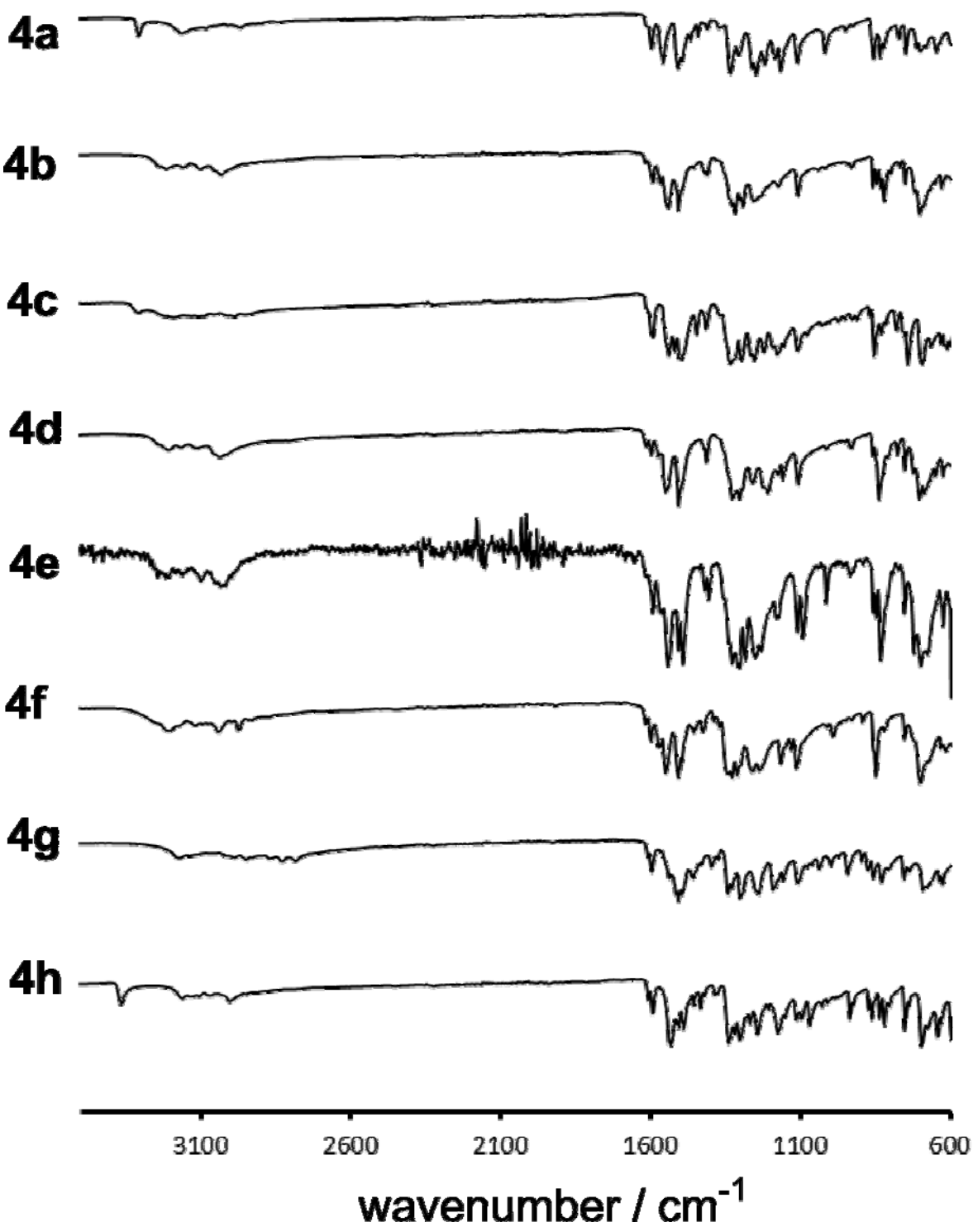


Figure S53. FTIR-ATR spectra of mechanochemically prepared thioureas **4a-h**.

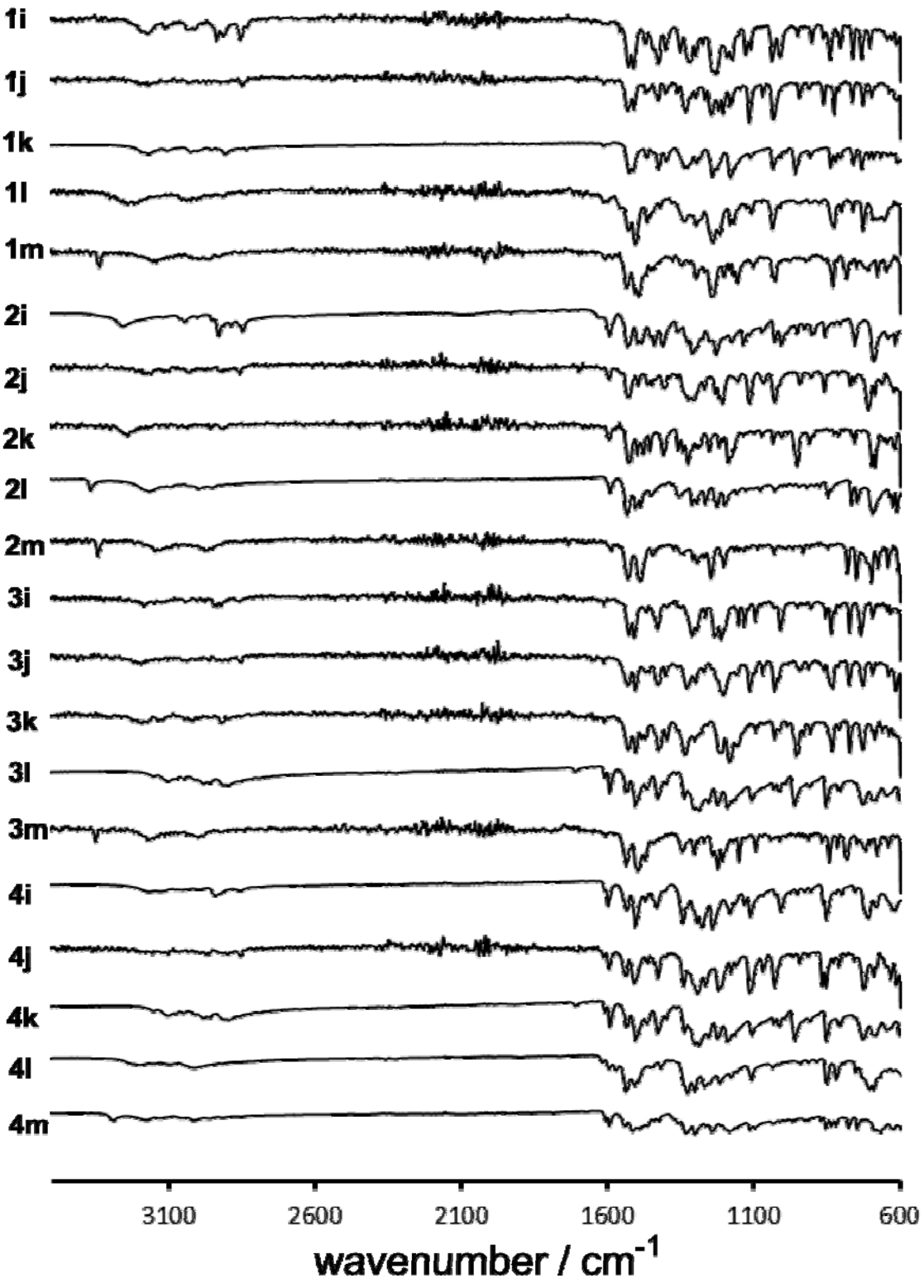


Figure S54. FTIR-ATR spectra of mechanochemically prepared thioureas involving secondary aliphatic amines or sterically hindered anilines **1i-m**, **2i-m**, **3i-m**, and **4i-m**.

4. Solid-state NMR

Solid state NMR was carried out using 4 mm outer diameter zirconia rotors and a Bruker AVANCE-400 9.4 Tesla wide bore spectrometer and dual channel broad band probe (Bruker, Karlsruhe, Germany), at a magic angle spinning (MAS) rate of 12.5 kHz, frequencies of 400.1 MHz (^{1}H) and 100.5 MHz (^{13}C), and standard cross polarization (CP) MAS techniques (^{1}H p/2 pulse length 2.5 ms, ^{1}H cross polarization field 70 kHz, ^{1}H-^{13}C cross-polarization contact time 2.5 ms, broadband TPPM15 decoupling during signal acquisition at a ^{1}H field strength of 100 kHz, recycle time 2 s, typical number of scans accumulated per spectrum ca. 3,000). Chemical shifts were referenced to the methylene signal from solid glycine at 43.1 p.p.m. relative to tetramethylsilane at 0 ppm.

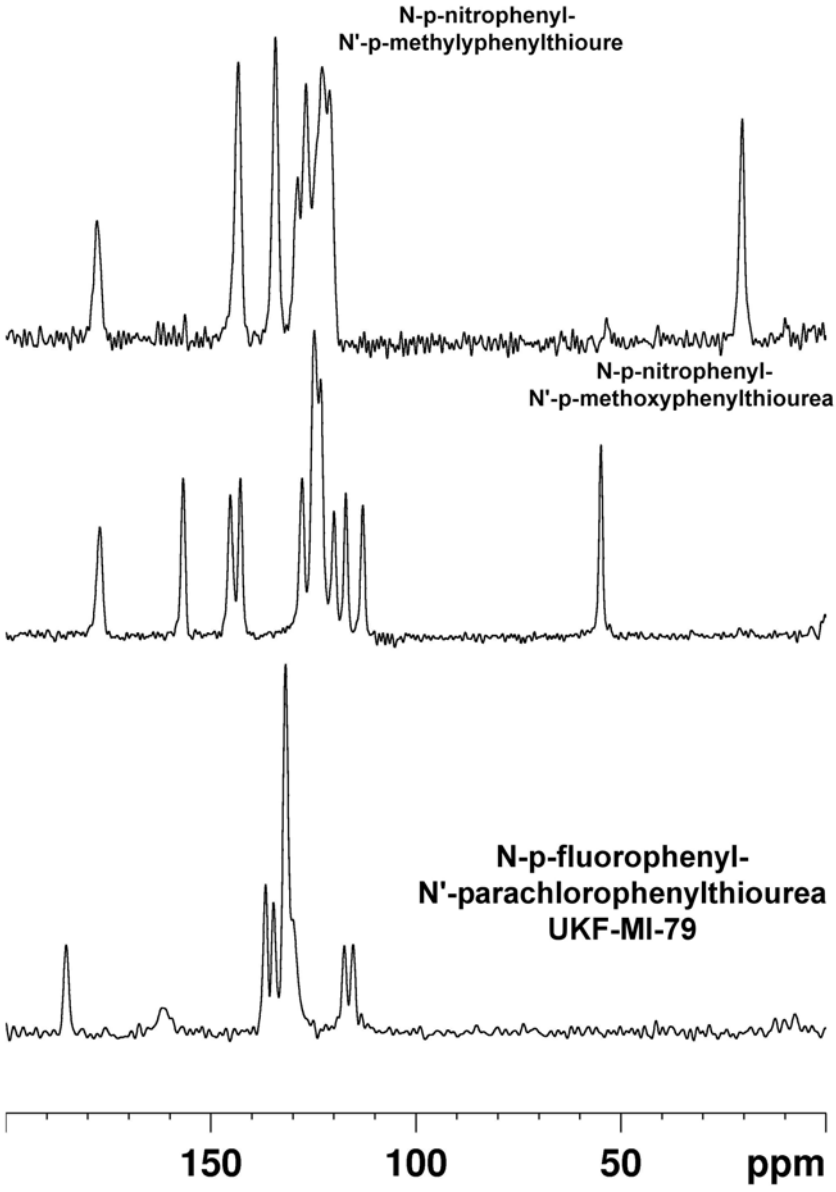


Figure S55. Selected solid-state CP-MAS ^{13}C NMR spectra of mechanochemically prepared thioureas: (top) **4b**; (middle) **4a** and (bottom) **3e**.

5. Powder X-ray diffraction (PXRD) patterns

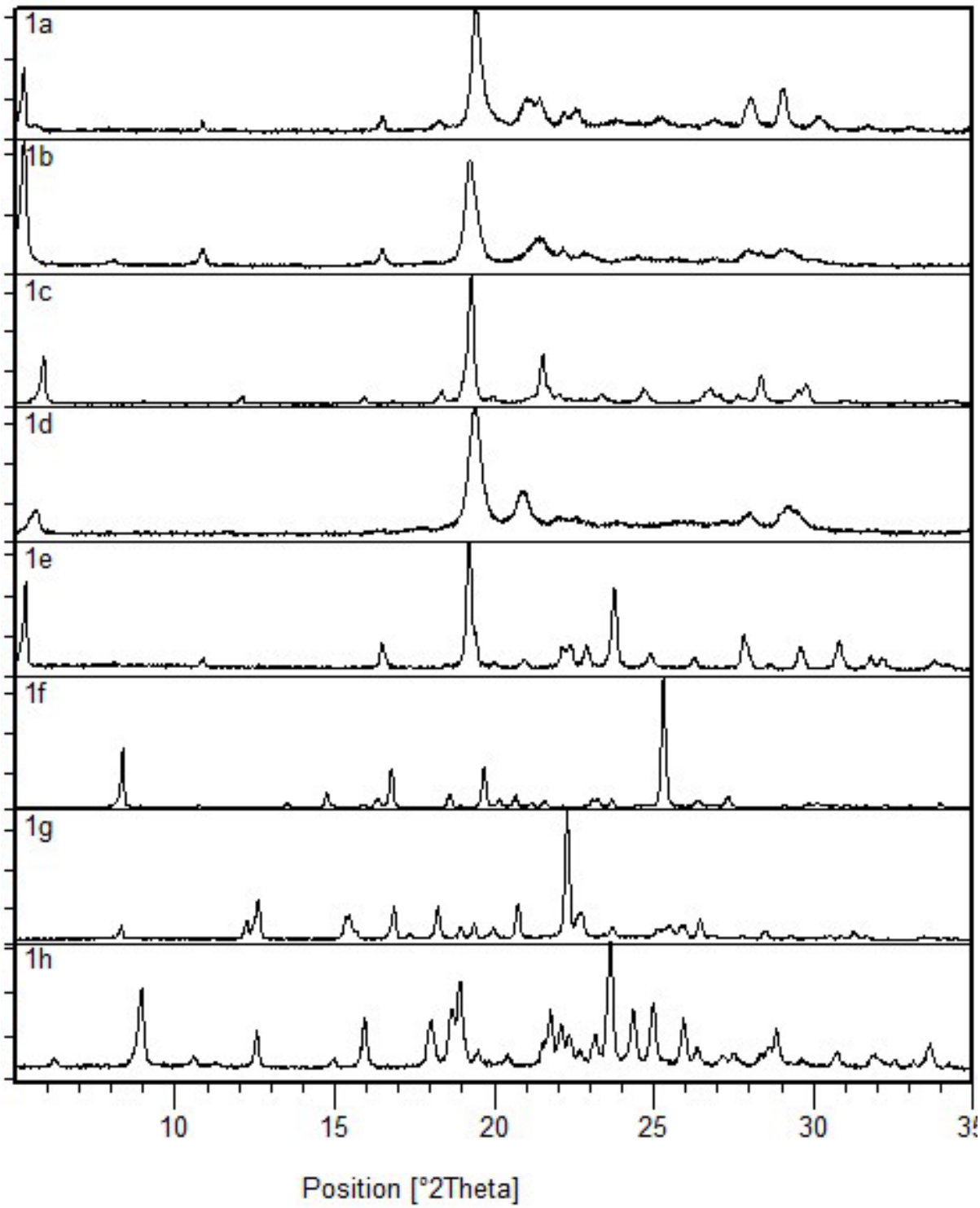


Figure S56. PXRD patterns for mechanochemically prepared thioureas **1a-h**.

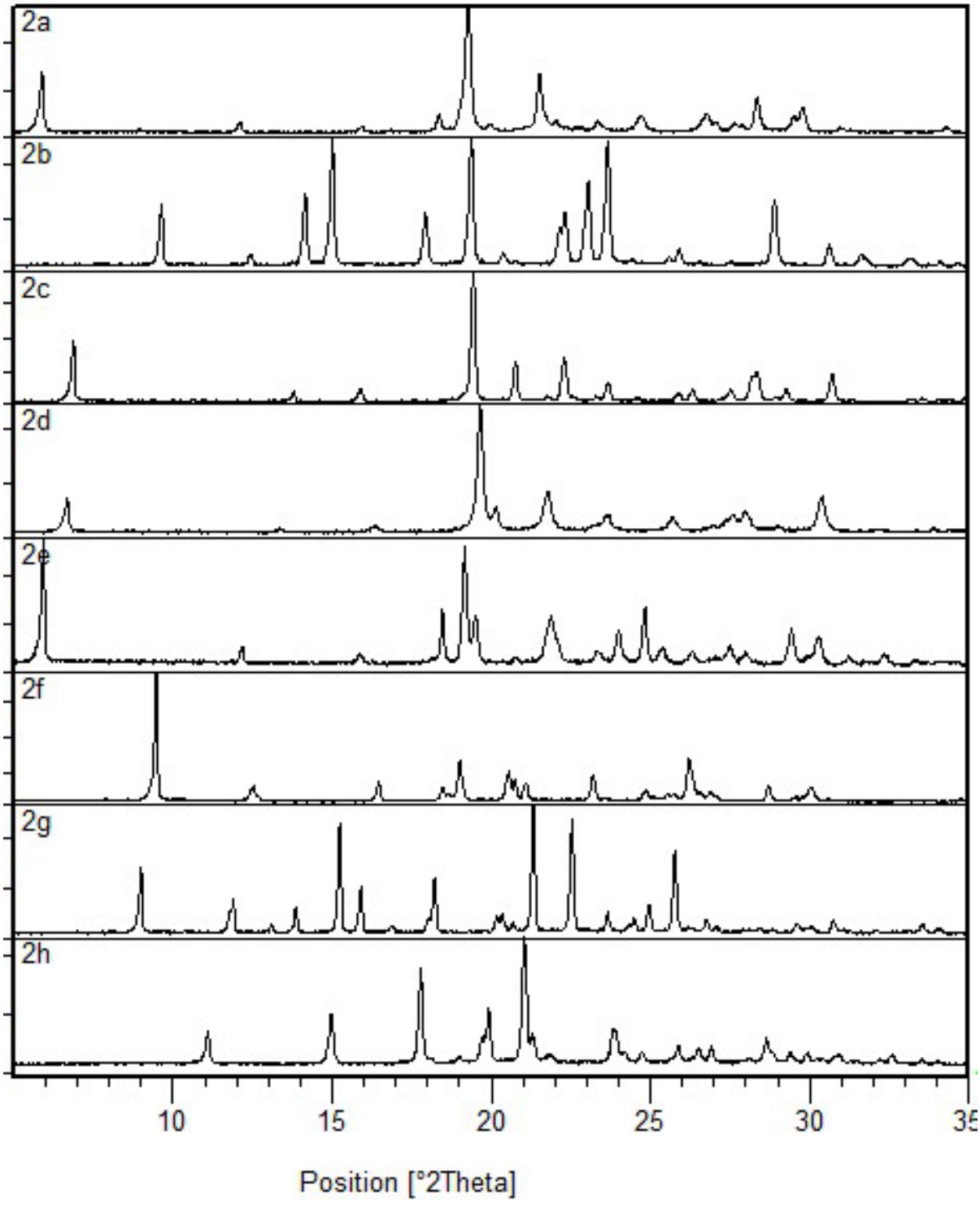


Figure S57. PXRD patterns for mechanochemically prepared thioureas **2a-h**.

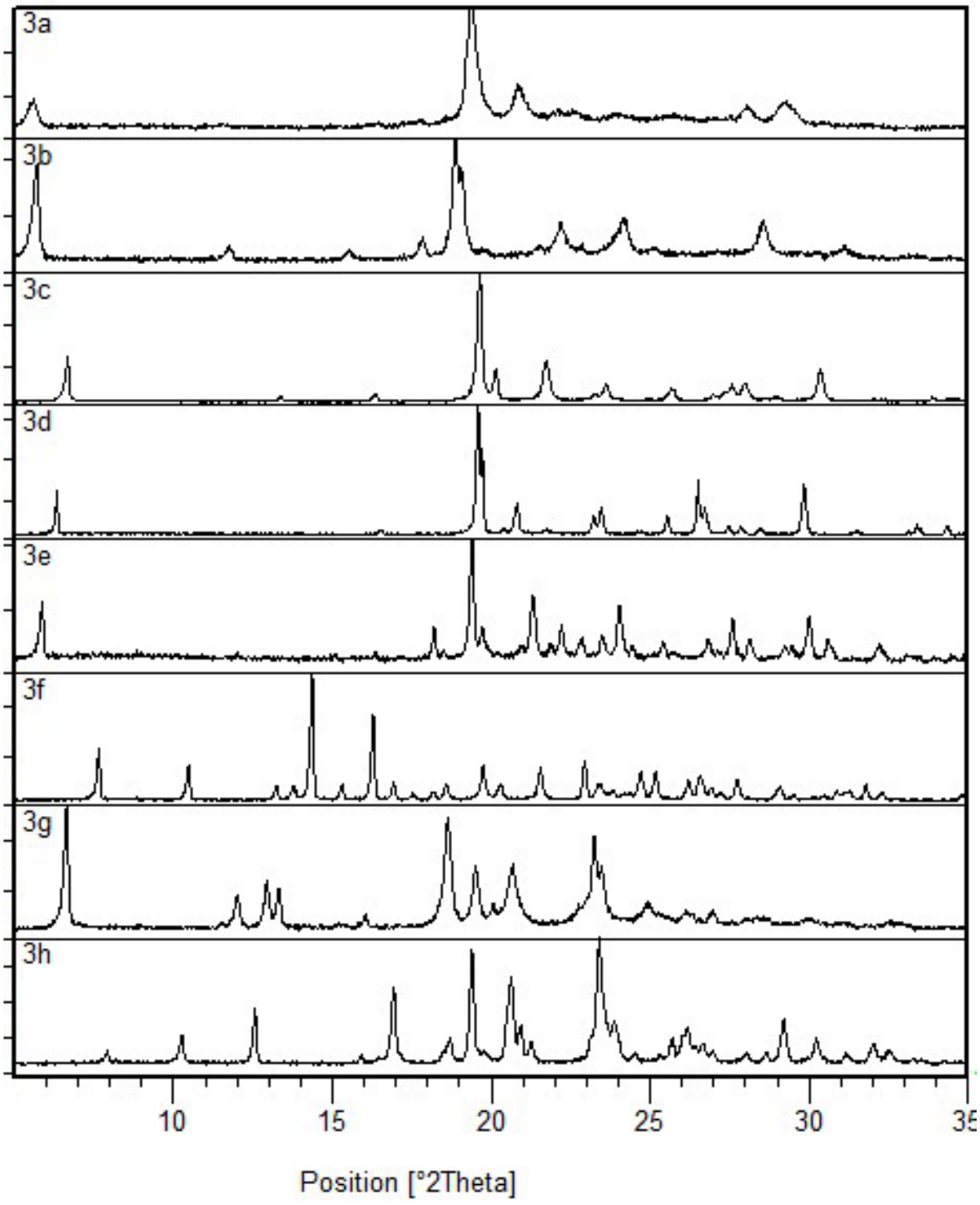


Figure S58. PXRD patterns for mechanochemically prepared thioureas **3a-h**.

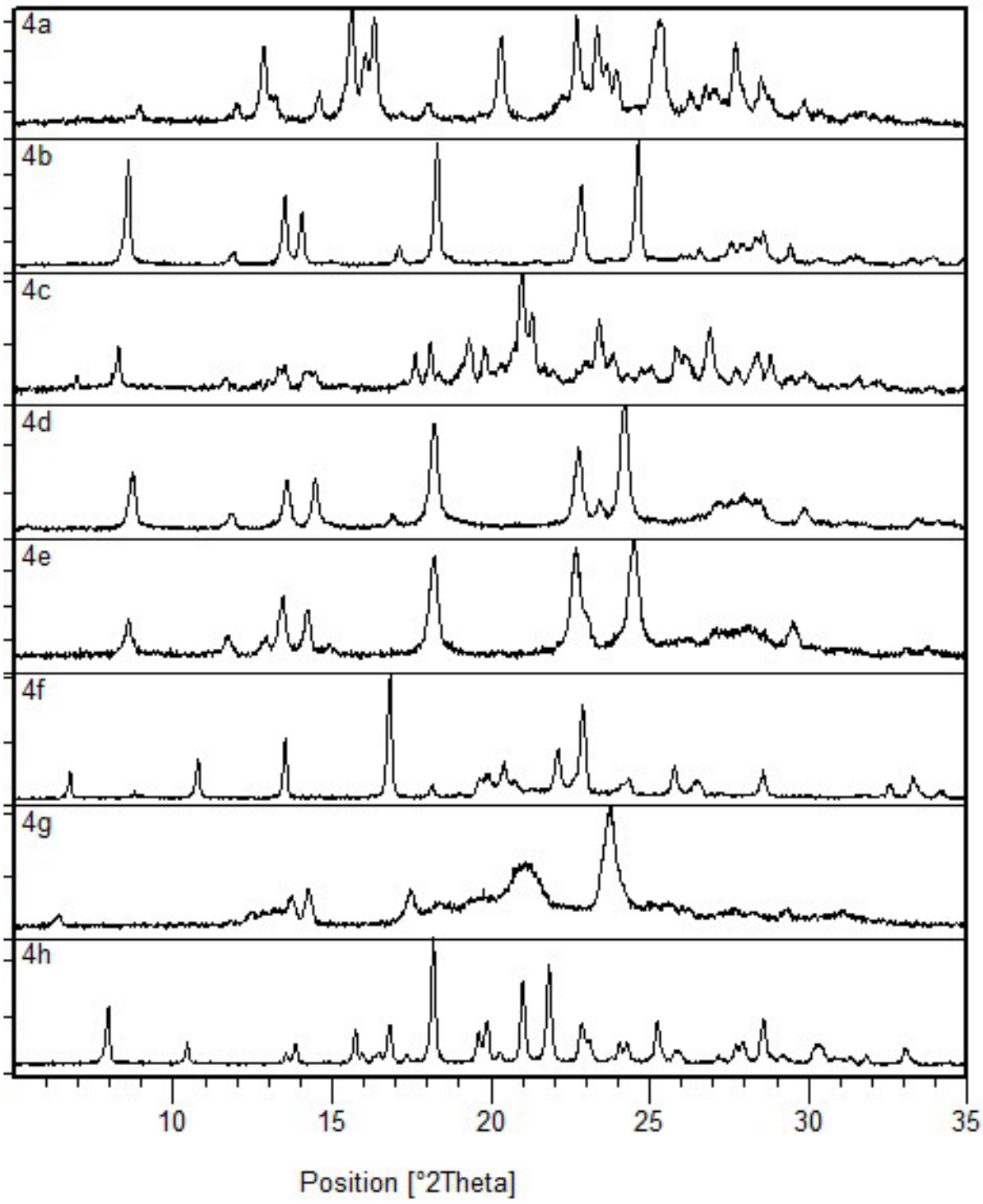


Figure S59. PXRD patterns for mechanochemically prepared thioureas **4a-h**.

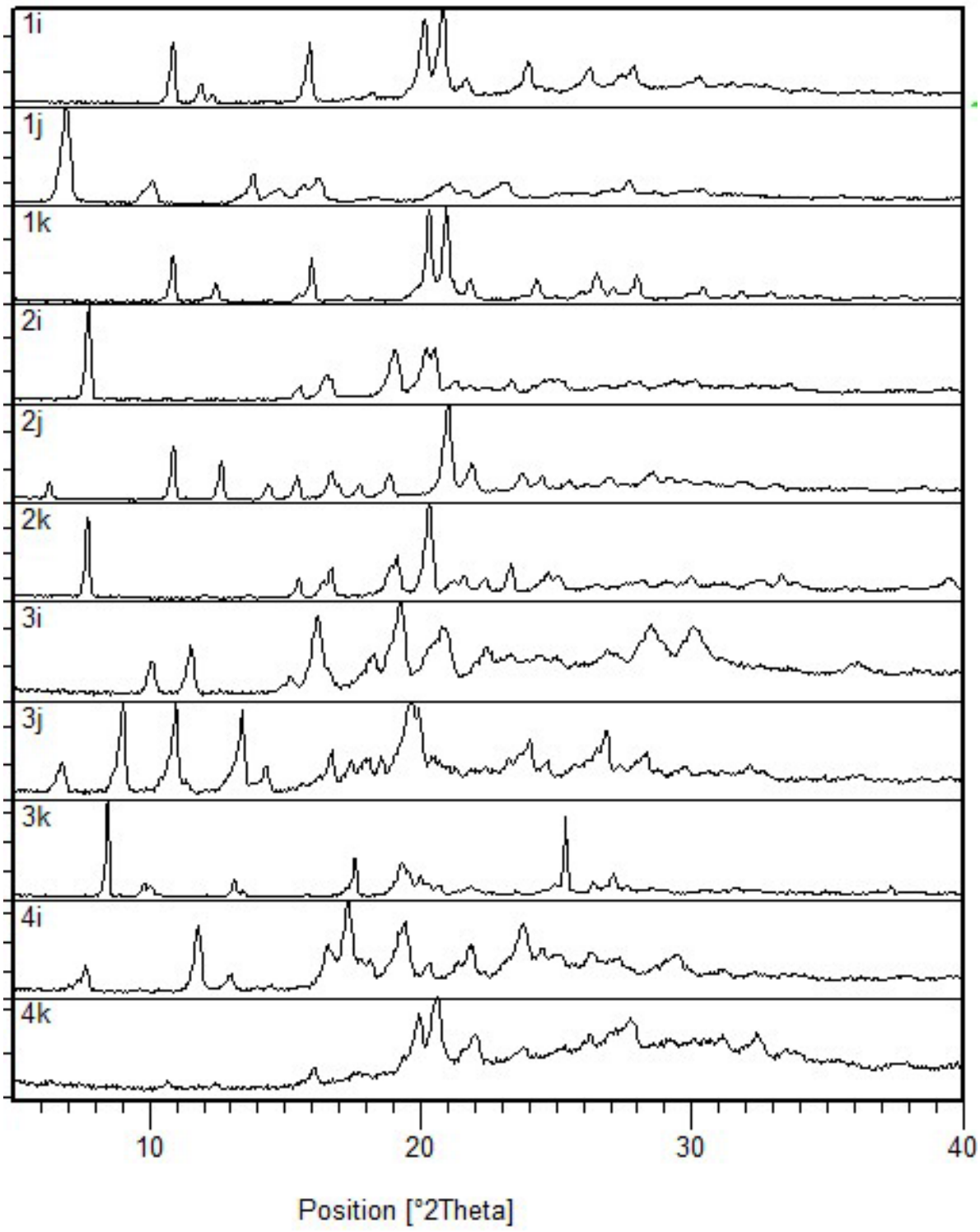


Figure S60. PXRD patterns for mechanochemically prepared thioureas based on cyclic secondary aliphatic amines piperidine, morpholine or thiomorpholine **1i-k**, **2i-k**, **3i-k** and **4i-k**.

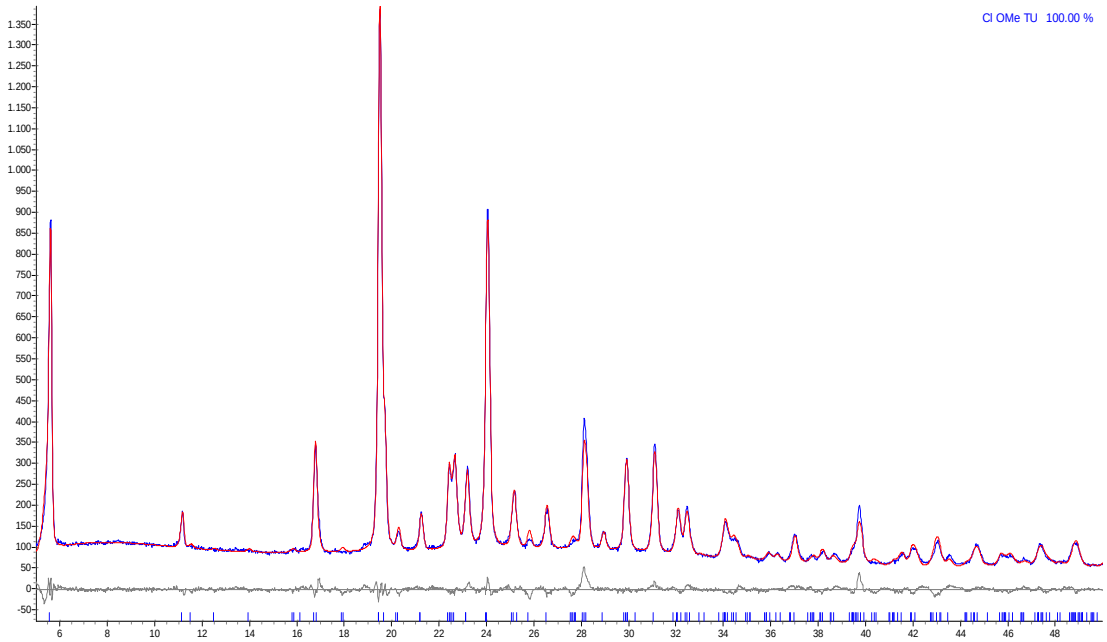


Figure S61. Rietveld fit for **1e-PXRD** in space group $P2_12_12$. Red – calculated, blue – measured, grey – difference, peak positions represented with tick marks.

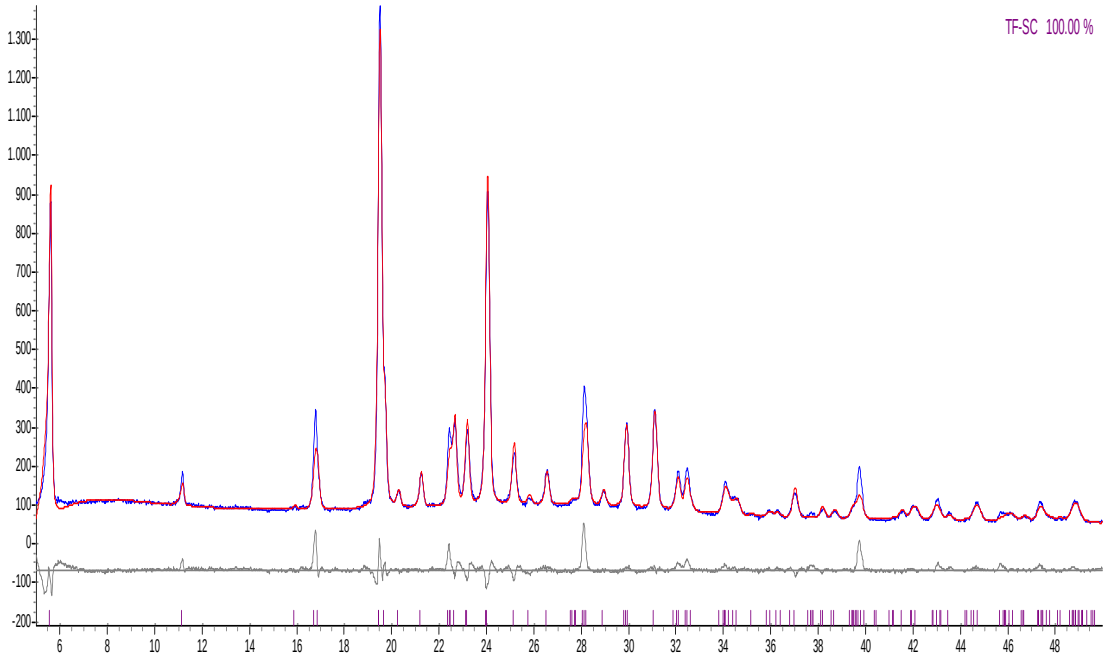


Figure S62. Rietveld fit for **1e-SC** using the disordered model in space group *Pbcm* obtained from single crystal diffraction. Slight preferred orientation is modelled using spherical harmonics of the 4th order. R_{wp} = 7.42 %.