Complementary Mechanochemical and Biphasic Approach for the Synthesis of Organic Thiocyanates using Hexacyanoferrates as Non-Toxic Cyanide Sources

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Supporting Information

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Experimental Section

General Experimental Information

Unless stated otherwise, all commercially available solvents and reagents were used as provided without further purification. Two of the eluents that were used for column chromatography (ethyl acetate (EtOAc) and cyclohexane (^{c}Hex)) were purchased in technical grade and distilled prior to use. Deuterated solvents were purchased from *Deutero GmbH* (Kastellaun). Solvents were evaporated under reduced pressure at 40 °C (water bath temperature).

Flash column chromatography was performed on 35–70 µm silica gel. For automatic flash column chromatography, an automatic flash chromatography system (*Isolera One*™) with UV-diode array detector was used together with silica gel filled cartridges (10 g or 25 g) as solid phases. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F_{245}, visualized by irradiation with UV light (λ = 254 nm and λ = 365 nm) or TLC staining reagents. R_f values are referred to the corresponding eluents.

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a *Bruker* Avance III HD 300, Avance II 400 or Avance III 600 spectrometer. Chemical shifts were referred to the corresponding deuterated solvents (for ^{1}H-NMR: δ($CDCl_3$) = 7.26 ppm, δ(MeOH-d_4) = 3.31 ppm and δ(DMSO-d_6) = 2.50 ppm; for ^{13}C-NMR: δ($CDCl_3$) = 77.16 ppm, δ(MeOH-d_4) = 49.00 and δ(DMSO-d_6) = 39.52 ppm) and reported in parts per million (ppm, δ) relative to tetramethylsilane (δ(TMS) = 0.00 ppm).[1] Coupling constants (J) were reported in Hz and the following abbreviations for NMR signal multiplicities were used: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and combinations of these. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

Electrospray Ionization (ESI) masses were recorded by LC-MS on a 1260- series Infinity II HPLC-system using a binary pump system, a C18 column (2.7 μm, 30x2.1 mm) at 40 °C and an integrated diode array detector coupled to a LC/MSD Infinitylab LC/MSD (G6125B LC/MSD). High resolution mass spectrometry was performed on a G6545AQ-ToF with electrospray ionization (ESI). Sample inlet was performed via a 1260 Infinity II HPLC system with a G7111B 1260 quaternary pump, a G7129A 1260 vial sampler, and a G7116A 1260 multicolumn thermostat. Mass calibration was performed on the day of measurement using a suitable external calibrant. The mass accuracy of the measurement results is better than 5 ppm. Preparative HPLC separations were performed on an Infinity II 1260 system using a high-pressure gradient mixture together with a DAD and a fraction collector. As eluents, acetonitrile and water were used at a flowrate of 42.5 mL/min. An Macherey-Nagel Nucleodur C18 HTec (150 mm x 40 mm, 5 µm) column was used for sample separation with an MeCN content of the solvent mixture at either 15%, 29%, 40%, 50% or 80%. Chiral HPLC analysis (normal phase, isocratic mode with ethanol:*n*-hexane = 10:90) was performed using a CHIRALPAK IF-3 column (Daicel Corporation) on a 1260-series Infinity II HPLC system (Agilent Technologies).

Gas chromatographic measurements were performed on an 8890 GC system coupled to a 5977 GC/MS detector. As solid phase a HP 5MS UI GC column (30 m x 0.25 mm x 0.25 µm) was used and helium was applied as carrier gas with a flowrate of 1.2 mL/min. The injection temperature was 250 °C, the transfer line temperature was 250 °C, the MS-source temperature was 230 °C and the MS-quadrupole temperature was 150 °C. The column stove temperature was adjusted to 40 °C for 2 minutes followed by a temperature gradient of 50 °C/min over 5.6 minutes to 320 °C. This temperature was kept for 7.4 minutes.

All mechanochemical reactions were carried out in a "Pulverisette 7 Premium Line" planetary micro mill from FRITSCH GmbH (Idar-Oberstein, Germany). The grinding bowls and balls were made of inert

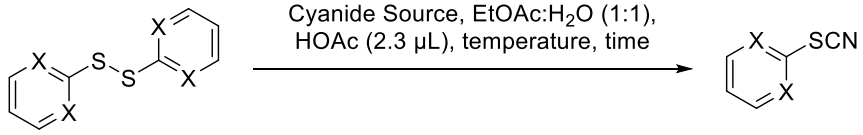
ZrO_2. The grinding was carried out with 18 balls each (diameter 10 mm). The ball mill with the respective charged milling jars can be seen in Figure F1.
Melting points are uncorrected and were measured on a *KRÜSS Optronic KPS I N* melting point meter or on a Mettler Toledo MP30 melting point system in open capillary tubes.
Infrared spectra were recorded as FT-IR spectra on a *Tensor 27* spectrometer (*Bruker Corporation*) using a diamond ATR unit and are reported in terms of frequency of absorption ($\tilde{\nu}$, cm^{-1}).
The optical rotation was measured on a Perkin-Elmer 241 polarimeter at 589 nm and extrapolated using Drude's equation.[2]

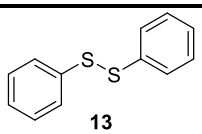
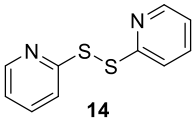
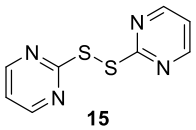
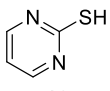
Figure F1: *Pulverisette 7 Premium Line* with the respective milling jars.

Optimization in Batch

Based on a previously published biphasic reaction system for the synthesis of α-aminonitriles with hexacyanoferrates as non-toxic cyanide source developed by the Opatz group,[3] the same reaction conditions (EtOAc:H_2O as the solvent system and a mixture of $K_3[Fe(CN)_6]$ and $K_4[Fe(CN)_6]$ as the cyanide source) were initially applied for the synthesis of thiocyanates using diphenyl disulfide **13** as the substrate (see Table T1, entry 1).

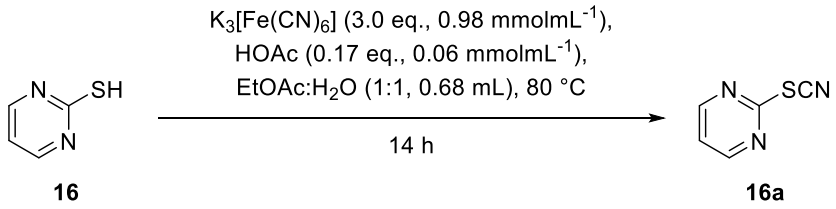
Table T1: Initial experiments and successive linear optimization for the synthesis of thiocyanates.



Substrate	Entry	Cyanide Source	Eq.	Time [h]	T [°C]	Yield* [%]
 **13**	1	$K_3[Fe(CN)_6]$:$K_4[Fe(CN)_6]$ (3:4)	1.0	70	80	—[a]
 **14**	2	$K_3[Fe(CN)_6]$:$K_4[Fe(CN)_6]$ (3:4)	1.0	70	80	31[a]
 **15**	3	$K_3[Fe(CN)_6]$:$K_4[Fe(CN)_6]$ (3:4)	1.0	25	80	22[a]
	4	$K_3[Fe(CN)_6]$:$K_4[Fe(CN)_6]$ (3:4)	1.0	14	80	53
	5	$K_3[Fe(CN)_6]$	1.0	14	80	57
	6	$K_4[Fe(CN)_6]$	1.0	14	80	25
	7	$K_3[Fe(CN)_6]$	1.5	14	80	62
	8	$K_3[Fe(CN)_6]$	2.0	14	80	71
	9	$K_3[Fe(CN)_6]$	2.5	14	80	65
	10	$K_3[Fe(CN)_6]$	3.0	14	80	59
 **16**	11	$K_3[Fe(CN)_6]$	0.16	14	80	5
	12	$K_3[Fe(CN)_6]$	1.0	14	80	72
	13	$K_3[Fe(CN)_6]$	1.5	14	80	83
	14	**$K_3[Fe(CN)_6]$**	**2.0**	**14**	**80**	**95**
	15	$K_3[Fe(CN)_6]$	2.5	14	80	77
	16	**$K_3[Fe(CN)_6]$**	**3.0**	**14**	**80**	**100**
	17	$K_3[Fe(CN)_6]$	3.5	14	80	85
	18	$K_3[Fe(CN)_6]$	4.0	14	80	78
	19	$K_3[Fe(CN)_6]$+I_2 (1 mol%)	1.0	14	80	72
	20	$K_3[Fe(CN)_6]$	2.0	2	80	28
	21	$K_3[Fe(CN)_6]$	2.0	4	80	48
	22	$K_3[Fe(CN)_6]$	2.0	8	80	86
	23	$K_3[Fe(CN)_6]$	2.0	12	80	90
	24	$K_3[Fe(CN)_6]$	2.0	14	r.t.	27[b]
	25	$K_3[Fe(CN)_6]$	2.0	14	40	44[b]
	26	$K_3[Fe(CN)_6]$	2.0	14	60	31; 27[b]
	27	$K_3[Fe(CN)_6]$+H_2O (without EtOAc)	3.0	14	80	81
	28	$K_3[Fe(CN)_6]$+MeCN:H_2O (1:1)	3.0	14	80	61
	29	$K_3[Fe(CN)_6]$+MeOH	3.0	14	80	14
	30	$K_3[Fe(CN)_6]$	3.0	16	80	49[c]

*Isolated Yields. [a] Vial was opened during reaction for monitoring via TLC. [b] Disulfide as product. [c] Reaction was performed in gram scale.

As described in entry 1, no product formation could be observed after 70 h of heating the reaction mixture to 80 °C. The substrate was changed to 1,2-di(pyridin-2-yl)disulfide **14**, as the S–S bond should be more reactive towards oxidation due to the electron withdrawing effect of the ring nitrogen (entry 2). Product formation could be observed in 31% yield, but the reaction vial was opened for TLC and LCMS monitoring, so gaseous HCN might have been released and the reaction and the conversion of substrate **14** was therefore limited. To increase the electron withdrawing effects, 1,2-di(pyrimidin-2-yl)disulfide **15** was applied as another benchmark substrate which furnished the desired pyrimidine thiocyanate **16a** in 22% yield after opening the reaction vial for reaction monitoring. This yield could be increased to 53% by leaving the reaction vessel closed during the reaction (entries 3+4). Next, the cyanide source was investigated. When applying exclusively $K_3[Fe(CN)_6]$ in the protocol, the desired product could be obtained in 57% yield, whereas the application of only $K_4[Fe(CN)_6]$ decreases the yield to 25%. As can be seen in entries 5–10, no $K_4[Fe(CN)_6]$ is needed in the reaction mixture for increasing yields, and therefore, all further optimization was performed with only $K_3[Fe(CN)_6]$ as the cyanide source. Afterwards, the cyanide equivalents were investigated and it was found that increasing the equivalents from 1.0 to 3.0 equiv. does not lead to significant increases in yield, but 2.0 equiv. showed the highest yield (71%) when applying the respective disulfide **15** as starting material. As $K_3[Fe(CN)_6]$ itself is a known oxidizing agent, it was investigated if a direct application of thiols instead of disulfides can also be successful in this reaction setup. When applying pyrimidine-2-thiol **16** to the reaction conditions, 72% of the desired product **16a** could be obtained, which could be increased to 95% and even quantitative yield by increasing the cyanide equivalents (entries 12-18). By decreasing the cyanide amount to 0.16 eq., corresponding to the minimum possible amount of cyanide release to convert one equivalent of thiol, yield significantly decreased to only 5% (entry 11). The addition of 1 mol% of iodine as a catalyst for faster *in-situ* formation of the corresponding disulfide did not lead to higher yields (entry 19). In the next step, the reaction time was investigated (entries 20-23), and as can be seen, shorter reaction times of less than 12–14 h lead to significantly decreasing product yields, so 14 h were chosen as the optimum. In the last step, the reaction temperature was investigated (entries 24-26). At lower reaction temperatures, only disulfide formation or significantly lower product formation could be observed, so heating the reaction mixture up to 80 °C in presence of an acid (2.3 µL) as confirmed by various literature reports is assumed to be crucial for the reaction to proceed.[4-6] To investigate solvent effects on the reaction outcome, a 1:1 mixture of acetonitrile and water was applied yielding the respective product in a decreased yield of 61% (entry 28) compared to the initial solvent mixture. Using solely methanol led to a significant yield decline down to 14%, while application of exclusively water as the solvent for the reaction furnished the corresponding thiocyanate **16a** in 81% yield (entry 27). The developed procedure might be adapted to solvents with different polarity, but as solubility issues could be a problem for less polar substrates in such reaction settings the biphasic system ethyl acetate and water in a 1:1 mixture was chosen to be the most suitable solvent system for the formation of thiocyanates in general. To conclude, the optimized reaction conditions can be found in Scheme S1.



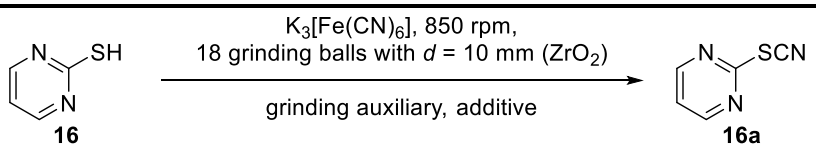
16 **16a**

Scheme S1: Optimized reaction conditions for the formation of thiocyanates.

Optimization in Ball Mill

As an initial experiment (Table T2, entry 1), the developed batch protocol was successfully transferred to the ball mill with the addition of silica as grinding auxiliary[7] affording the desired product **16a** in 12% ^{1}H-NMR yield after 10 min of milling. Initial work-up of the slurry reaction mixture included neutralization of acetic acid with an aqueous sodium bicarbonate solution, followed by extraction with ethyl acetate. As can be seen in entry 2, no additional acetic acid was needed for the cyanide release from ferricyanide, as pure silica also furnished the desired product **16a** (47%), while no disulfide **15** was detected. Based on this result, the optimized work-up emerged as transfer of the solid reaction mixture and the milling balls to an Erlenmeyer flask with the addition of acetone (50 mL) followed by ultrasonication for 10 min and filtration of the solid residues. Next, the equivalents of ferricyanide were kept on a constant level and the milling time was investigated (entries 3–7). With shorter reaction times (entry 7), **15** was still detected as a byproduct, whereas longer milling (entry 2) led to a decrease in product yield. The highest yield was obtained after 6 min of reaction time and the equivalents of the cyanide source were investigated subsequently (entries 8–12). With the optimized conditions (6 min, 1.0 eq.), an isolated yield of 72% of the desired product **16a** was obtained. Furthermore, additional grinding auxiliaries as quartz or the acidic $KHSO_4$ were tested as well as dividing the milling time into smaller fractions (entries 13–15).

Table T2: Optimization of mechanochemical parameters.

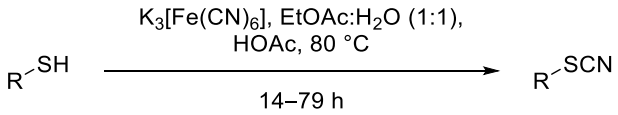


16 **16a**

Entry	Grinding Auxiliary	Time [min]	Eq.	Analysis of Byproducts via ESI-LCMS (DAD)/^{1}H-NMR	SCN Yield [%]
1	SiO_2[b)]	10	1.5	**15** as a byproduct	12
2	SiO_2	10	1.5	–	47
3	**SiO_2**	**6**	**1.5**	–	**63**
4	SiO_2	5	1.5	–	54
5	SiO_2	4	1.5	**15** as a byproduct	51
6	SiO_2	3	1.5	**15** as a byproduct	38
7	SiO_2	2	1.5	**15** as the major product	16
8	SiO_2	6	1.3	–	50
9	**SiO_2**	**6**	**1.0**	**–**	**72**[a)]
10	SiO_2	6	0.8	–	53
11	SiO_2	6	0.5	**15** as a byproduct	37
12	SiO_2	6	0.3	**15** as the major product	27
13	$KHSO_4$[c)]	10	1.5	Exclusive formation of **15**	–
14	Quartz[c)]	10	1.5	Traces of **15** and **16**	51
15	SiO_2[b)]	6 x 1 min	1.5	Exclusive formation of **15**	–
16	SiO_2	90 min overall	1.0	**15** as a byproduct	15[a,d)]

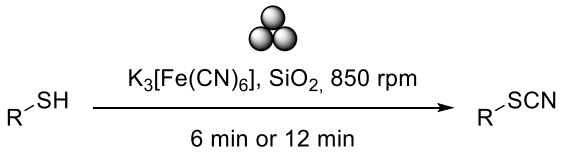
Unless stated otherwise, all optimization reactions were performed on a 75 mg scale of 2-thiopyrimidine **16** with 1.5 g of grinding auxiliary and full conversion of **16** was observed via ESI-LCMS (DAD) or ^{1}H-NMR. Furthermore, all yields are based on ^{1}H-NMR analysis using dimethylsulfoxide as the internal standard. [a)] Isolated yield. [b)] 0.7 g of grinding auxiliary was applied together with 0.9 mL of acetic acid as additive. [c)] 1.0 g of grinding auxiliary was applied. [d)] Reaction was performed in gram scale.

General Batch Procedure A



To a 10 mL reaction vial sealed with a rubber septum were added the corresponding thiol (0.23 mmol, 1.0 eq.) and $K_3[Fe(CN)_6]$ (222.2 mg, 0.67 mmol, 3.0 eq.). Both were dissolved in a biphasic solvent mixture of ethyl acetate and water (1:1, 0.68 mL). Acetic acid (2.3 µL) was added and the tightly sealed reaction vessel was heated to 80 °C. After the reaction was completed (14-79 h, followed via TLC and GC/LCMS), the reaction mixture was poured into a saturated $NaHCO_3$ solution (10 mL) and extracted with ethyl acetate (3x15 mL). The combined organic layers were washed with a saturated NaCl solution (10 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using SiO_2 as the stationary phase. Considering the sustainability of the developed procedure, distillation, continuous extraction of the aqueous phase using a Kutscher-Steudel apparatus or crystallization could also be applied as alternative purifications of the crude products instead of column chromatography. This was exemplarily demonstrated on selected compounds, but for comparison reasons, column chromatography was used as the standard purification method.

General Ball Mill Procedure B

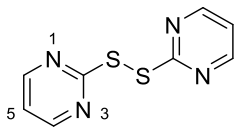


Each grinding bowl was placed in the heating oven at 80 °C for several hours prior to use and, after cooling to ambient temperature, was subsequently charged with 18 grinding balls, $K_3[Fe(CN)_6]$ (0.669 mmol, 1.0 eq.), the respective thiol (0.669 mmol, 1.0 eq.) as well as silica gel (to act as acidic grinding auxiliary, 1.5 g). The grinding bowl was accelerated for 6 min to 850 rpm. After cooling down to ambient temperature, the respective powder and the balls were sinked in acetone, sonicated in an ultrasonic bath for 10 min* and then filtered over silica. The solvent was removed under reduced pressure and the crude product was subjected to further suitable purification. Column chromatography using SiO_2 as the stationary phase was applied as standard method for comparison reasons.

* Sonification for 30 min of the starting materials without milling did not lead to any product formation.

Substrate Scope in Batch and Ball Mill

1,2-Di(pyrimidin-2-yl)disulfide (15)



According to a modified procedure of *B. Zeynizadeh*.[8]
A 50 mL round bottom flask was charged with 2-mercaptopyrimidine **16** (500 mg, 4.46 mmol, 1.0 eq.) and suspended in a mixture of acetonitrile and water (5:1, 14 mL). Iodine (567 mg, 2.23 mmol, 0.5 eq.) was added and after 30 min (reaction followed by TLC), the reaction mixture was quenched by a 1% solution of thiosulfate (10 mL). After extraction with ethyl acetate (3x20 mL), the combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, *Isolera One*™ 0%-100% EtOAc), furnishing the product as a slightly yellow solid.

Yield: 433.8 mg (1.95 mmol, 44%).

R_f = 0.12 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 223.0 ($[M+H]^+$).

GC-MS: *m* = 222.0 [M].

Mp: 136.2–138.7 °C (Lit.:[9] 132–135 °C)

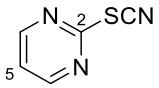
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3070, 1549, 1372, 1195, 1166, 821, 767, 744, 628, 448.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.57 (d, *J* = 4.8 Hz, 4H, 4-H, 6-H), 7.08 (t, *J* = 4.8 Hz, 2H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 169.7 (2-C), 157.9 (4-C, 6-C), 118.2 (5-C).

The obtained data are in accordance with the literature.[9]

Pyrimidine-2-ylthiocyanate (16a)



Following the general procedure A using 2-mercaptopyrimidine **16** (25.2 mg, 0.23 mmol, 1.0 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 20%–80% EtOAc) afforded the title compound as a colorless solid. General procedure B was alternatively applied. Alternatively, purification could be achieved via crystallization from DMSO.

Yield: 31.7 mg (0.23 mmol, 100%, procedure A), 65.6 mg (0.48 mmol, 72%, procedure B).

R_f = 0.51 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 138.1 $[M+H]^+$.

Mp: 110.2–110.6 °C (Lit.:[10] 112.6–113.0 °C)

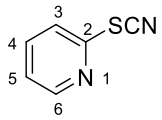
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2174, 1561, 1378, 1278, 1180, 814, 767, 742, 627.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.69 (d, *J* = 4.9 Hz, 2H, 4-H, 6-H), 7.28 (t, *J* = 4.9 Hz, 1H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 164.4 (2-C), 159.1 (4-C, 6-C), 119.9 (5-C), 107.5 (S*C*N).

The obtained data are in accordance with the literature.[10]

Pyridine-2-ylthiocyanate (17a)



Following the general batch procedure using 2-mercaptopyridine **17** (25.0 mg, 0.23 mmol, 1.0 eq.). After 14 h, purification by column chromatography (SiO_2, *Isolera One*™ 20%–80% EtOAc) afforded the product as a colorless oil.

Yield: 21.9 mg (0.16 mmol, 72%).

R_f = 0.54 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 137.0 $[M+H]^+$.

GC-MS: *m* = 136.1 [M], 78.1[M−SCN].

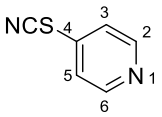
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2162, 1573, 1563, 1450, 1420, 1119, 989, 760, 716, 615.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.51 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H, 6-H), 7.76 (td, *J* = 7.8, 1.9 Hz, 1H, 4-H), 7.59 (dt, *J* = 8.1, 1.0 Hz, 1H, 3-H), 7.27 (ddd, *J* = 7.5, 4.8, 1.0 Hz, 1H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 150.6 (6-C), 150.0 (2-C), 138.6 (4-C), 122.9 (5-C), 122.1 (3-C), 109.1 (S*C*N).

The obtained data are in accordance with the literature.[11]

Pyridine-4-ylthiocyanate (18a)



Following the general batch procedure using 4-mercaptopyridine **18** (55.6 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 0.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 16 h, purification by column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the product as a colorless solid.

Yield: 36.1 mg (0.27 mmol, 53%).

R_f = 0.19 (^{c}Hex:EtOAc = 2:1).

Mp: 54.7–55.7 °C (Lit.:[12] 54–56 °C).

ESI-LCMS: *m/z* = 137.0 $[M+H]^+$.

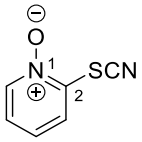
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3033, 2164, 1571, 1544, 1482, 1407, 1222, 1067, 811, 802, 696.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.69–8.52 (m, 2H, 2-H, 6-H), 7.44–7.31 (m, 2H, 3-H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 150.8 (2-C, 6-C), 136.8 (4-C), 121.6 (3-C, 5-C), 107.4 (S*C*N).

The obtained data are in accordance with the literature.[13]

2-Thiocyanatopyridine-*N*-oxide (19a)



Following the general procedure A using 2-mercaptopyridine-*N*-oxide **19** (28.6 mg, 0.23 mmol, 1.0 eq.). After 14 h, purification by column chromatography (SiO_2, *Isolera One*™ 20%–80% EtOAc) afforded the title compound as a colorless solid.

Yield: 17.1 mg (0.13 mmol, 50%).

R_f = 0.35 (EtOAc).

ESI-LCMS: *m/z* = 153.0 $[M+H]^+$.

ESI-HRMS ($C_6H_4N_2OS$ $[M]^+$): calculated: *m/z* = 152.0044

found: *m/z* = 152.0045.

Mp: 154.2–155.1 °C (Lit.:[14] 158–160 °C).

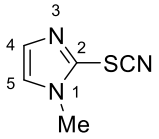
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3097, 2168, 1468, 1421, 1253, 1225, 1140, 841, 760, 705, 529.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.28 (dd, *J* = 6.3, 1.2 Hz, 1H, 6-H), 7.80 (dd, *J* = 8.3, 1.7 Hz, 1H, 3-H), 7.46 (t, 1H, 4-H), 7.34 (m, 1H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 143.9 (2-C), 138.1 (6-C), 127.3 (4-C), 124.2 (5-C), 123.2 (3-C), 109.5 (S*C*N).

No spectroscopic data available in the literature.

1-Methyl-1*H*-imidazole-2-yl thiocyanate (20a)



Following the general batch procedure using 2-mercapto-1-methylimidazole **20** (25.7 mg, 0.23 mmol, 1.0 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of either 6 min or 12 min.

Yield: 25.0 mg (0.18 mmol, 80%, procedure A), no conversion of **20** with procedure B.

***R*$_f$** = 0.93 (^{c}Hex:EtOAc = 2:1).

GC-MS: *m* = 138.9 [M].

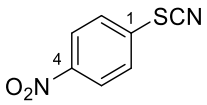
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3115, 2162, 1506, 1462, 1413, 1279, 1124, 915, 766, 684, 515.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.19 (d, *J* = 1.3 Hz, 1H, 4-H), 7.17 (d, *J* = 1.3 Hz, 1H, 5-H), 3.86 (s, 3H, C*H*$_3$).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 131.8 (4-C), 126.6 (2-C), 126.2 (5-C), 107.5 (S*C*N), 34.59 (*C*H_3).

The obtained data are in accordance with the literature.[15]

4-Nitrophenylthiocyanate (21a)



Following the general procedure A using 4-nitrothiophenol **21** (34.8 mg, 0.23 mmol, 1.0 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 10%–80% EtOAc) yielded the title compound as a colorless solid. General procedure B was alternatively applied with a reaction time of 12 min.

Yield: 24.5 mg (0.14 mmol, 61%, procedure A), 80.7 mg (0.45 mmol, 67%, procedure B).

***R*$_f$** = 0.51 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 181.0 $[M+H]^+$.

Mp: 129.9–130.8 °C. (Lit.:[16] 127–129 °C).

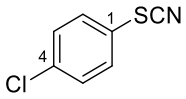
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2164, 1603, 1578, 1517, 1318, 1342, 1121, 855, 843, 737.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.37–8.26 (m, 2H, 3-H, 5-H), 7.73–7.63 (m, 2H, 2-H, 6-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 148.0 (4-C), 133.4 (1-C), 128.7 (2-C, 6-C), 125.1 (3-C, 5-C), 108.1 (S*C*N).

The obtained data are in accordance with the literature.[16]

1-Chloro-4-thiocyanatobenzene (22a)



Following the general procedure A using 4-chlorothiophenol **22** (72.0 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of 12 min.

Yield: 17.0 mg (0.10 mmol, 20%, procedure A), 58.2 mg (0.34 mmol, 51%, procedure B).

R_f = 0.62 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 169.0 [M].

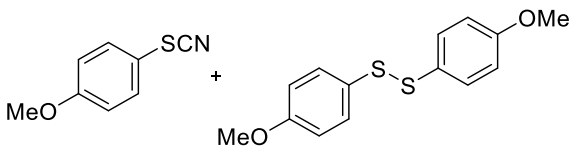
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3085, 2925, 2853, 2159, 1582, 1476, 1391, 1090, 1011, 817, 742, 701, 548, 501.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 7.50–7.45 (m, 2H, 2-H, 6-H), 7.44–7.40 (m, 2H, 3-H, 5-H).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 136.3(4-C), 131.6 (2-C, 6-C), 130.6 (3-C, 5-C), 122.9 (1-C), 110.1 (S*C*N).

The obtained data match to those reported in the literature.[16]

1-Methoxy-4-thiocyanatobenzene (23a) and 1,2-Bis(4-methoxyphenyl)disulfide (23b)



Following the general procedure B using 4-methoxythiophenol **23** (93.8 mg, 0.67 mmol, 1.0 eq.) as reagent with a milling time of 12 min. Separation of the desired product **23a** from the respective disulfide **23b** was not feasible by column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc). Therefore, the yield was determined by ^{1}H-NMR using dimethylsulfone as the internal standard. Following the general procedure A using **23** (70.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded exclusively **23b** as a yellow oil, after 16 h of reaction time.

Procedure B:

^{1}H-NMR yield of 23a: 0.21 mmol, 32%.

^{1}H-NMR yield of 23b: 0.21 mmol, 58%.

NMR data of 23a:

^{1}H-NMR, COSY (400 MHz, DMSO-d_6): δ [ppm] = 7.63–7.59 (m, 2H, 2-H, 6-H), 7.09–7.05 (m, 2H, 3-H, 5-H), 3.79 (s, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (101 MHz, DMSO-d_6): δ [ppm] =160.8 (4-C), 133.8 (2-C, 6-C), 116.0 (3-C, 5-C), 113.7 (1-C), 112.3 (S*C*N), 55.5 (*C*H_3).

The obtained data match to those reported in the literature.[17]

NMR data of 23b:

^{1}H-NMR, COSY (400 MHz, DMSO-d_6): δ [ppm] = 7.43–7.38 (m, 4H, 2-H, 6-H), 6.96–6.92 (m, 4H, 3-H, 5-H), 3.75 (s, 6H, CH_3).

^{13}C-NMR, HSQC, HMBC (101 MHz, DMSO-d_6): δ [ppm] =159.6 (4-C), 132.0 (2-C, 6-C), 126.9 (1-C), 114.9 (3-C, 5-C), 55.2 (*C*H_3).

The obtained data match to those reported in the literature.[18]

Procedure A:

Yield: 45.8 mg (0.17 mmol, 66%).

R_f = 0.26 (^{c}Hex:EtOAc = 50:1).

ESI-LCMS: *m/z* = 279.0 $[M+H]^+$.

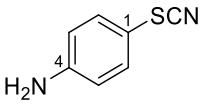
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3003, 2938, 2835, 1589, 1489, 1461, 1288, 1243, 1171, 1029, 824.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.45–7.36 (m, 4H, 2 H, 6-H), 6.89–6.77 (m, 4H, 3-H, 5-H), 3.80 (s, 6H, OCH_3).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 160.0 (4-C), 132.8 (2-C, 6-C), 128.5 (1-C), 114.7 (3-C, 5-C), 55.5 (O*C*H_3).

The obtained data are in accordance with the literature.[19]

4-Aminophenylthiocyanate (25a)



Following the general procedure A using 4-mercaptoaniline **25** (56.3 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 30 h, an additional

equivalent of $K_3[FeCN_6]$ and acetic acid was added, and the reaction was heated for another 24 h. After work-up of the reaction mixture according to the general procedure, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) furnished the title compound as a brown oil. General procedure B was alternatively applied.

Yield: 9.30 mg (0.06 mmol, 14%, procedure A), 37.0 mg (0.25 mmol, 37%, procedure B).

R_f = 0.63 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 151.1 $[M+H]^+$.

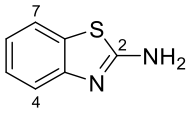
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3474, 3375, 2152, 1625, 1595, 1496, 1302, 824, 522.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.42–7.30 (m, 2H, 2-H, 6-H), 6.73–6.62 (m, 2H, 3-H, 5-H), 3.96 (bs, 2H, NH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 148.7 (4-C), 134.5 (2-C, 6-C), 116.1 (3-C, 5-C), 112.3 (S*C*N), 109.7 (1-C).

The obtained data are in accordance with the literature.[20]

Benzo[*d*]thiazol-2-amine (26a)



Following the general procedure A using 2-aminothiophenol **26** (56.3 mg, 0.45 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 15 h, column chromatography (SiO_2, *Isolera One*™ 20%–80% EtOAc) furnished the product as a colorless solid.

Yield: 27.2 mg (0.18 mmol, 40%).

R_f = 0.13 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 151.1 $[M+H]^+$.

Mp: 107.9–108.7 °C (Lit.:[21] 112–113 °C).

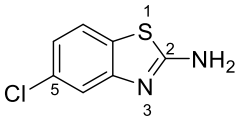
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3397, 3056, 1642, 1527, 1446, 1285, 1067, 845, 741, 720.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.61–7.53 (m, 1H, 7-H), 7.58–7.51 (m, 1H, 4-H), 7.30 (td, *J* = 7.7, 1.3 Hz, 1H, 5-H), 7.12 (td, *J* = 7.7, 1.3 Hz, 1H, 6-H), 5.82 (bs, 2H, NH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 166.4 (2-C), 152.1 (3a-C), 131.5 (7a-C), 126.1 (5-C), 122.3 (6-C), 121.0 (7-C), 119.1 (4-C).

The obtained data are in accordance with the literature.[22]

5-Chlorobenzo[*d*]thiazol-2-amine (27a)



Following the general procedure A using 2-amino-4-chlorothiophenol **27** (71.6 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 15 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid.

Yield: 34.5 mg (0.19 mmol, 42%).

R_f = 0.29 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 185.0 $[M+H]^+$.

ESI-HRMS ($C_7H_6ClN_2S$ $[M+H]^+$): calculated: *m/z* = 184.9935;

found: *m/z* = 184.9928.

Mp: 198.1–200.4 °C (Lit.:[23] 201–202 °C).

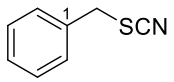
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2498, 2282, 1598, 1551, 1449, 1417,1073, 855, 790, 739.

^{1}H-NMR, COSY (300 MHz, MeOH-*d*$_4$): δ [ppm] = 7.51 (d, *J* = 8.4 Hz, 1H, 7-H), 7.34 (d, *J* = 2.1 Hz, 1H, 4-H), 7.03 (dd, *J* = 8.4, 2.1 Hz, 1H, 6-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, MeOH-*d*$_4$): δ [ppm] = 169.1 (2-C), 152.2 (3a-C), 130.6 (5-C), 128.4 (7a-C), 120.6 (7-C), 120.5 (6-C), 116.4 (4-C).

The spectroscopic data match to those reported in the literature.[24]

Benzylthiocyanate (28a)



Following the general batch procedure using benzylmercaptane **28** (62.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of 12 min.

Yield: 28.5 mg (0.19 mmol, 38%, procedure A), 10.4 mg (0.07 mmol, 10%, procedure B).

R_f = 0.37 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 149.0 [M].

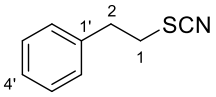
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3064, 3032, 2153, 1495, 1455, 1245, 1203, 1074, 766, 698, 646.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 7.42–7.34 (m, 5H, Ar-H), 4.17 (s, 2H, CH_2).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 134.3 (1-C), 129.2 (2-C, 6-C), 129.0 (3-C), 128.9 (4-C), 112.0 (S*C*N), 38.4 (*C*H_2).

The obtained data are in accordance with the literature.[25]

2-Phenylethylthiocyanate (29a)



Following the general batch procedure using 2-phenylethan-1-thiol **29** (200.0 µL, 1.50 mmol, 1.0 eq.), $K_3[Fe(CN)_6]$ (1.48 g, 4.50 mmol, 3.0 eq.), H_2O (2 mL), EtOAc (2.0 mL) and HOAc (15.0 µL). After 79 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of 12 min.

Yield: 165.0 mg (1.01 mmol, 67%, procedure A), 38.2 mg (0.23 mmol, 35%, procedure B).

R_f = 0.39 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 163.1 [M].

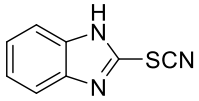
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3029, 2153, 1603, 1497, 1454, 1283, 1232, 752, 701, 565, 491.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 7.41–7.34 (m, 2H, 2'-H, 6'-H), 7.33–7.28 (m, 1H, 4'-H), 7.27–7.22 (m, 2H, 3'-H, 5'-H), 3.24–3.18 (m, 2H, 1-CH_2), 3.17–3.12 (m, 2H, 2-CH_2).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 137.7 (1'-C), 128.9 (2'-C, 6'-C), 128.7 (3'-C, 5'-C), 127.3 (4'-C), 112.1 (S*C*N), 36.1 (2-C), 35.2 (1-C).

The obtained data are in accordance with the literature.[16]

1*H*-Benzimidazol-2-ylthiocyanat (32a)



Following the general procedure A using 2-mercaptobenzimidazole **32** (67.5 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, purification by column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid. General procedure B was alternatively applied with a reaction time of 12 min but no product formation could be observed.

Yield: 24.6 mg (0.14 mmol, 31%, procedure A).

R_f = 0.75 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 176.0 $[M+H]^+$.

Mp: 149.9–150.6 °C (EtOAc). (Lit.:[26] 163 °C).

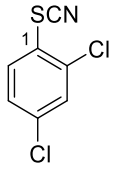
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3069, 2962, 2167, 1689, 1424, 1270, 1222, 1008, 979, 744.

^{1}H-NMR, COSY (400 MHz, MeOH-*d*$_4$): δ [ppm] = 7.63–7.57 (m, 2H, 5-H,6-H), 7.35–7.30 (m, 2H, 4-H,7-H).

^{13}C-NMR, HSQC, HMBC (101 MHz, MeOH-*d*$_4$): δ [ppm] = 135.4 (3a-C, 7a-C), 122.9 (4,5,6,7-C), 114.2 (br, 2-C), 106.1 (S*C*N).

The obtained data are in accordance with the literature.[27]

2,4-Dichlorthiocyanatobenzene (33a)



Following the general procedure B using 2,4-dichlorthiophenol **33** (119.8 mg, 0.67 mmol, 1.0 eq.) as the reagent with a milling time of 10 min. Column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid.

Yield: 67.5 mg (0.33 mmol, 49%).

***R*$_f$** = 0.48 (^{c}Hex:EtOAc = 20:1).

ESI-LCMS: *m/z* = 205.1 $[M+H]^+$.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3088, 2165, 1569, 1452, 1375, 1136, 1101, 858, 814.

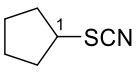
Mp: 70.1–71.1 °C, H_2O. (Lit.:[28] 72°C, H_2O).

^{1}H-NMR, COSY (300 MHz, CDCl$_3$): δ [ppm] = 7.64 (d, *J* = 8.6 Hz, 1H, 6-H), 7.49 (d, *J* = 2.2 Hz, 1H, 3-H), 7.38 (dd, *J* = 8.6, 2.2 Hz, 1H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, CDCl$_3$): δ [ppm] = 136.0 (2-C), 133.6 (4-C), 130.7 (6-C), 130.3 (3-C), 128.8 (5-C), 123.3 (1-C), 108.8 (S*C*N).

The analytical data match those reported in the literature.[16]

Cyclopentylthiocyanate (34a)



Following the general procedure A using cyclopentanethiol **34** (51.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, ^{c}Hex:EtOAc 10:1) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of either 6 or 12 min but no product formation could be observed.

Yield: 23.4 mg (0.18 mmol, 37%, procedure A).

R_f = 0.41 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 127.0 [M], 69.10 [M−SCN].

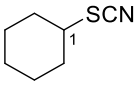
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957, 2924, 2853, 2153, 1725, 1452, 1377, 1321, 1243.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 3.66 (qd, *J* = 7.4, 5.2 Hz, 1H, 1-H), 2.13 (ddt, *J* = 11.0, 7.5, 5.2 Hz, 2H, 2-H$_a$, 5-H$_a$), 1.90–1.60 (m, 6H, 2-H$_b$, 3-H, 4-H, 5-H$_b$).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 112.5 (S*C*N), 47.7 (1-C), 33.9 (2-C, 5-C), 24.4 (3-C, 4-C).

The obtained data are in accordance with the literature.[29]

Cyclohexylthiocyanate (35a)



Following the general procedure A using cyclohexanethiol **35** (58.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, Cy:EtOAc 10:1) afforded the title compound as a colorless oil. Alternatively, distillation of the crude reaction mixture was performed, furnishing the title compound in comparable 5% product yield. General procedure B was alternatively applied with a reaction time of either 6 or 12 min but no product formation could be observed.

Yield: 5.0 mg (0.04 mmol, 7%, procedure A).

R_f = 0.53 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 141.0 [M], 83.08 [M−SCN].

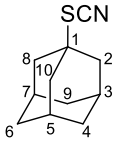
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2935, 2857, 2152, 1450, 1343, 1264, 1206, 1183, 995, 889, 716.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 3.24 (tt, *J*= 10.9, 3.8 Hz, 1H, 1-H), 2.33–2.02 (m, 2H, 2-H$_a$', 6-H$_a$'), 1.84 (m, 2H, 3-H$_a$, 5-H$_a$), 1.70–1.60 (m, 2H, 4-H$_a$), 1.60–1.52 (m, 2H, 2-H$_b$, 6-H$_b$), 1.48–1.32 (m, 2H, 3-H$_b$, 5-H$_b$), 1.31–1.19 (m, 1H, 4-H$_b$).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 111.8 (S*C*N), 48.1 (1-C), 33.8 (2-C, 6-C), 26.0 (3-C, 5-C), 25.0 (4-C).

The obtained data are in accordance with the literature.[30]

1-Thiocyanatoadamantane (36a)



Following the general procedure A using adamantane-1-thiol **36** (75.6 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 15 h, column chromatography (SiO_2, ^{c}Hex:EtOAc = 20:1) afforded the title compound as a colorless oil. General procedure B was applied with a reaction time of 12 min but no product formation could be observed.

Yield: 14.5 mg (0.08 mmol, 17%, procedure A).

$\boldsymbol{R_f}$ = 0.44 (^{c}Hex:EtOAc = 20:1).

GCMS: m = 193.1 [M]; 135.1 [M-SCN].

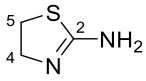
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2913, 2854, 2144, 1453, 1343, 1301, 1035, 684.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 2.22–2.12 (m, 3H, 3-H, 5-H, 7-H), 2.07 (d, *J* = 2.9 Hz, 6H, 2-H, 8-H, 10-H), 1.72 (t, *J* = 2.3 Hz, 6H, 4-H, 6-H, 9-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 111.0 (S*C*N), 54.1 (1-C), 43.7 (2-C, 8-C, 10-C), 35.5 (4-C, 6-C, 9-C), 30.4 (3-C, 5-C, 7-C).

The obtained data are in accordance with the literature.[10]

4,5-Dihydrothiazol-2-amine (37a)



Following the general batch procedure using cysteamine **37** (34.7 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 26 h, continuous extraction of the aqueous phase with ethyl acetate (4 days) afforded the title compound as a light-brown oil. For proper yield determination, the product yield was determined via ^{1}H-NMR using phenanthrene as the internal standard. General procedure B was alternatively applied with a reaction time of 12 min.

^{1}H-NMR yield: 0.42 mmol, 92%, procedure A; 0.07 mmol, 11%, procedure B.

$\boldsymbol{R_f}$ = 0.86 (acetone:^{i}PrOH = 4:1).

ESI-LCMS: *m/z* = 103.1 $[M+H]^+$.

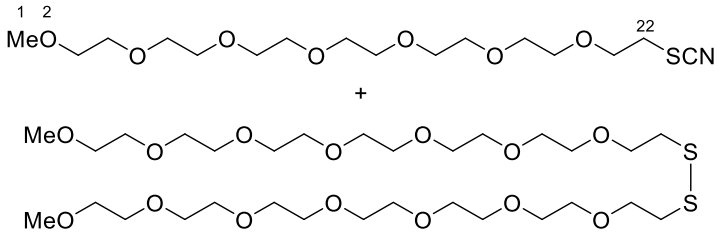
ESI-HRMS ($C_3H_7N_2S$ $[M+H]^+$): calculated: *m/z* = 103.0325;

found: *m/z* = 103.0326.

Characteristic ^{1}H-NMR signal (300 MHz, $CDCl_3$): δ [ppm] = 3.89 (t, 2H, 4-H).

The obtained data are in accordance with the literature.[31]

22-Thiocyanato-2,5,8,11,14,17,20-heptaoxadocosane (38a) and
2,5,8,11,14,17,20,27,30,33,36,39,42,45-tetradecaoxa-23,24-dithiahexatetracontane (38b)



Following the general procedure A using 2,5,8,11,14,17,20-heptaoxadocosane-22-thiol **38** (160.3 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 24 h, work up according to the general procedure afforded the title compound together with **62** as an inseparable mixture as a colorless oil. General procedure B was alternatively applied with a reaction time of 12 min yielding exclusively **38a** using 2,5,8,11,14,17,20-heptaoxadocosane-22-thiol **38** (22.6 mg, 0.07 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (20.9 mg, 0.07 mmol, 1.0 eq.).

Yield: overall 102.1 mg, **38a**: 55.05 mg (0.14 mmol, 29%); **38b**: 47.05 mg (0.07 mmol, 7%) based on ^{1}H-NMR ratio of 22-H (**38a**): 22-H (**38b**), procedure A.

^{1}H-NMR yield 38a: 0.02 mmol, 29%, procedure B.

R_f = 0.71 (on AlO_x, EtOAc:MeOH = 20:1).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2868, 2153, 1455, 1350, 1295, 1248, 1199, 1099, 1038, 947, 850.

NMR data of 38a:

ESI-LCMS: *m/z* = 404.2 $[M+Na]^+$.

ESI-HRMS ($C_{16}H_{31}NO_7S$ $[M+Na]^+$): calculated: *m/z* = 404.1713;

found: *m/z* = 404.1711.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 3.81 (t, *J* = 5.9 Hz, 2H, 21-H), 3.67–3.59 (m, 22H, 4,6,7,9,10,12,13,15,16,18,19-H), 3.53–3.51 (m, 2H, 3-H), 3.35 (s, 3H, 1-H), 3.14 (t, *J* = 5.9 Hz, 2H, 22-H).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 112.2 (S*C*N), 71.9 (3-C), 70.8–70.4 (11C, 4,6,7,9,10,12,13,15,16,18,19-C), 68.9 (21-C), 59.0 (1-C), 33.9 (22-C).

NMR data of 38b:

ESI-LCMS: *m/z* = 733.3 $[M+Na]^+$.

ESI-HRMS ($C_{30}H_{62}O_{14}S_2$ $[M+Na]^+$): calculated: *m/z* = 733.3454;

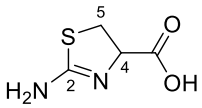
found: *m/z* = 733.3460.

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ [ppm] = 3.70 (t, *J* = 6.7 Hz, 2H, 21-H), 3.67–3.59 (m, 22H, 4,6,7,9,10,12,13,15,16,18,19-H), 3.53–3.51 (m, 2H, 3-H), 3.35 (s, 3H, 1-H), 2.86 (t, *J* = 6.7 Hz, 2H, 22-H).

^{13}C-NMR, HSQC, HMBC (101 MHz, $CDCl_3$): δ [ppm] = 71.9 (3-C), 69.6 (21-C), 70.8–70.4 (11C, 4,6,7,9,10,12,13,15,16,18,19-C), 59.0 (1-C), 38.3 (22-C).

No spectroscopic data available in the literature.

2-Amino-4,5-dihydrothiazol-4-carboxylic acid (39a)



Following the general procedure A using L-cystine **39** (108.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 22.5 h, continuous extraction of the aqueous phase with ethyl acetate (2 days) afforded the title compound as a colorless solid. For proper yield determination, the product yield was determined via ^{1}H-NMR using phenanthrene as the internal standard as signals of acetic acid were still present after extraction. General procedure B was applied with a reaction time of 12 min but no product formation could be observed.

^{1}H-NMR yield: 0.09 mmol, 21%.

***R*$_f$** = 0.91 (EtOAc).

ESI-LCMS: *m/z* = 146.9 $[M+H]^+$.

ESI-HRMS ($C_4H_7N_2O_2S$ $[M+H]^+$): calculated: *m/z* = 147.0223;

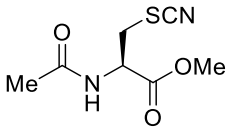
found: *m/z* = 147.0228.

^{1}H-NMR, COSY (300 MHz, MeOH-*d*$_4$): δ [ppm] = 4.66 (t, *J* = 7.9 Hz, 1H, 4-H), 3.81–3.62 (m, 2H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, MeOH-*d*$_4$): δ [ppm] = 173.1 (*C*OO^-), 171.9 (2-C), 64.3 (4-C), 33.3 (5-C).

The obtained data are in accordance with the literature.[32]

Methyl-*N*-acetyl-S-cyano-L-cysteinate (40a)



Following the general procedure B using *N*-acetyl-L-cysteine methyl ester **40** (118.5 mg, 0.67 mmol, 1.0 eq.) as the reagent with a milling time of 6 min. Column chromatography (SiO_2, ^{c}Hex:EtOAc = 1:1) afforded the title compound as yellow oil.*

Yield: 18.9 mg (0.09 mmol, 13%).

***R*$_f$** = 0.29 (^{c}Hex:EtOAc = 1:1).

IR = 3297, 2956, 2160, 1744, 1662, 1537, 1438, 1374.

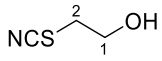
Optical rotation: $[\alpha]_D^{21}$ = +50.3 (0.1, $CHCl_3$).

ESI-LCMS: *m/z* = 203.0 $[M+H]^+$.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 6.55 (d, *J* = 6.4 Hz, 1H, N*H*), 4.96 (dt, *J* = 6.4, 4.2 Hz, 1H, C*H*), 3.86 (s, 3H, OCH_3), 3.62 (dd, *J* = 14.2, 4.2 Hz, 1H, CH_{2a}), 3.43 (dd, *J* = 14.2, 3.8 Hz, 1H, CH_{2b}), 2.09 (s, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 170.4 (*C*OCH_3), 169.2 (*C*O_2CH_3), 111.4 (S*C*N), 53.4 (O*C*H_3), 52.4 (*C*H), 35.5 (*C*H_2), 23.0 (*C*H_3).

2-Thiocyanatoethan-1-ol (41a)



Following the general procedure A using 2-mercaptoethan-1-ol **41** (35.1 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 14 h of heating, work-up of the crude reaction mixture was performed according to the general procedure and the yield was determined via ^{1}H-NMR using phenanthrene as the internal standard. General procedure B was alternatively applied with a reaction time of either 6 or 12 min but no product formation was observed.

^{1}H-NMR yield: 0.16 mmol, 35%, procedure A.

***R*$_f$** = 0.48 (EtOAc).

GC-MS: *m* = 102.9 [M].

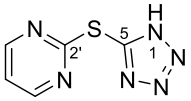
ESI-HRMS (C_3H_6NOS $[M+H]^+$): calculated: *m/z* = 104.0165;

found: *m/z* = 104.0164.

Characteristic ^{1}H-NMR Signal (300 MHz, $CDCl_3$): δ [ppm] = 2.87 (t, *J* = 5.8 Hz, 2H, CH_2SCN).

No spectroscopic data available in the literature.

2-((1*H*-Tetrazol-5-yl)thio)pyrimidine (60)



According to a modified procedure of *L. Myznikov et al*.[33]
In a 10 mL reaction vial pyrimidine-2-ylthiocyanate **16a** (61.7 mg, 0.45 mmol, 1.0 eq.), sodium azide (35.1 mg, 0.54 mmol, 1.2 eq.) and zinc(II)chloride (61.3 mg, 0.45 mmol, 1.0 eq.) were dissolved in isopropanol (1.5 mL) and the reaction mixture was heated to 50 °C. After the reaction was finished (3 h, reaction followed by TLC and LCMS), the solvent was evaporated under reduced pressure, 5% NaOH solution (3 mL) was added to the residue and the mixture was stirred for further 20 min until a suspension had formed. This mixture was filtrated and the remaining solid was washed with 5% NaOH solution (3 mL). The filtrate was adjusted to pH = 1 using concentrated HCl, which was accompanied by a color change from colorless to yellow. After extraction with ethyl acetate (3x15 mL), the combined

organic layers were washed with saturated NaCl solution, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The title compound was obtained as a colorless solid.

Yield: 67.8 mg (0.38 mmol, 84%).

R_f = 0.81 (H_2O:MeCN = 90:10).

ESI-LCMS: *m/z* = 181.0 $[M+H]^+$.

ESI-HRMS ($C_5H_4N_6S$ $[M+H]^+$): calculated: *m/z* = 181.0291;

found: *m/z* = 181.0288.

Mp: 143.5–146.3 °C. There is no melting point reported in the literature.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3075, 2155, 1558, 1445, 1384, 1208, 1012, 827, 767, 635.

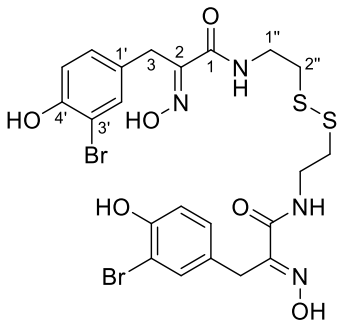
^{1}H-NMR, COSY (300 MHz, DMSO-d_6): δ [ppm] = 8.68 (d, *J* = 4.9 Hz, 2H, 4'-H, 6'-H), 7.40 (t, *J* = 4.9 Hz, 1H, 5'-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, DMSO-d_6): δ [ppm] = 192.6 (5-C), 167.1 (2'-C), 158.8 (4'C, 6'-C), 119.2 (5'-C).

No spectroscopic data available in the literature.

Synthesis of Psammaplins A and B

Psammaplin A (55)



According to a modified procedure of *J. R. Sufrin et al*.[34]
To a stirred solution of **57** (135 mg, 0.49 mmol, 1.0 eq.), *N*-hydroxysuccinimide (85 mg, 0.74 mmol, 1.5 eq.) and DCC (152 mg, 0.74 mmol, 1.5 eq.) in dry DMF (10 mL), cysteamine (**37**, 55 mg, 0.25 mmol, 0.5 eq.) and TEA (136 µL, 0.98 mmol, 2.0 eq.) were added and the reaction was stirred for 16 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified via preparative HPLC (40% MeCN, Machery Nagel Nucleodur C18 HTec column). The title compound was obtained as a colorless oil.

Yield: 78.1 g (0.12 mmol, 24%).

R_f = 0.37 (H_2O:MeCN = 50:50).

ESI-LCMS: *m/z* = 662.9 $[M+H]^+$.

ESI-LCMS: *m/z* = 661.0 $[M-H]^-$.

ESI-HRMS ($C_{22}H_{24}Br_2N_4O_6S_2Na$ $[M+Na]^+$): calculated: *m/z* = 684.9396;

found: *m/z* = 684.9396.

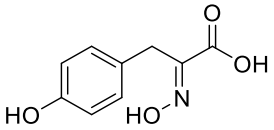
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3357, 2930, 2853, 1659, 1625, 1534, 1494, 1255, 1211, 1015.

^{1}H NMR (300 MHz, MeOH-d_4) δ [ppm] = 7.37 (d, *J* = 2.1 Hz, 2H, H-2'), 7.07 (dd, *J* = 8.3, 2.1 Hz, 2H, H-6'), 6.76 (d, *J* = 8.3 Hz, 2H, H-5'), 3.79 (s, 4H, H-3), 3.51 (t, *J* = 6.7 Hz, 4H, H-1''), 2.79 (t, *J* = 6.7 Hz, 4H, H-2'').

^{13}C NMR (75 MHz, MeOH-d_4) δ [ppm] = 165.8 (C-1), 153.6 (C-4'), 153.0 (C-2), 134.4 (C-2), 130.5 (C-1'), 130.3 (C-6'), 117.0 (C-5'), 110.4 (C-3'), 39.5 (C-1''), 38.4 (C-2''), 28.6 (C-3).

The analytical data are in accordance with the literature.[34]

(*E*/*Z*)-2-(Hydroxyimino)-3-(4-hydroxyphenyl)propanoic acid (56)



According to a modified procedure of *J. R. Sufrin et al*.[34]

A solution of hydroxyphenylpyruvic acid **54** (1.10 g, 6.12 mmol, 1.0 eq.) and hydroxylamine hydrochloride (638 mg, 9.18 mmol, 1.5 eq.) in dry pyridine (20 mL) was stirred for 5 h at room temperature. The solvent was removed under reduced pressure yielding the pyridinium salt. The salt was dissolved in 2 M HCl (50 mL) and the aqueous phase was extracted with ethyl acetate (3x50 mL). The combined organic layers were dried over $MgSO_4$ and the solvents were removed under reduced pressure to yield the title compound as a beige oil.

Yield: 750 mg (3.84 mmol, 63%).

R_f = 0.59 (H_2O:MeCN = 50:50).

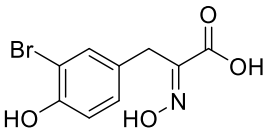
ESI-LCMS: *m/z* = 196.0 $[M+H]^+$.

ESI-LCMS: *m/z* = 194.1 $[M-H]^-$.

^{1}H-NMR, COSY (300 MHz, MeOH-d_4): δ [ppm] = 7.09 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 2H).

The obtained data are in accordance with the literature.[34]

(*E*/*Z*)-3-(3-Bromo-4-hydroxyphenyl)-2-(hydroxyimino)propanoic acid (57)



According to a modified procedure of *J. R. Sufrin et al*.[34]
A solution of **56** (248 mg, 1.27 mmol, 1.0 eq.) and *N*-bromosuccinimide (180 mg, 1.02 mmol, 0.8 eq.) in methanol (5 mL) was stirred for 16 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (C_{18}, H_2O:MeCN = 90:10 to MeCN) yielding the title compound **57** in the first fraction as a brown solid. As a side product, (*E*/*Z*)-3-(3,5-dibromo-4-hydroxyphenyl)-2-(hydroxy-imino)propanoic acid **58** was obtained in a second fraction as a lyophilisate.

(*E*/*Z*)-3-(3-bromo-4-hydroxyphenyl)-2-(hydroxyimino)propanoic acid (**57**):
Yield: 135 mg (0.49 mmol, 39%).

R_f = 0.69 (H_2O:MeCN = 50:50).

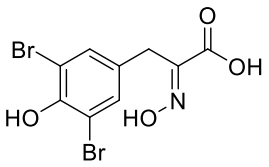
ESI-LCMS: *m/z* = 274.0 $[M+H]^+$.

ESI-LCMS: *m/z* = 271.9 $[M-H]^-$.

^{1}H-NMR, COSY (300 MHz, MeOH-d_4): δ [ppm] = 7.37 (d, *J* = 2.2 Hz, 1H), 7.08 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.78 (d, *J* = 8.3 Hz, 1H), 3.80 (s, 2H).

The analytical data are in accordance with the literature.[34]

(*E*/*Z*)-3-(3,5-dibromo-4-hydroxyphenyl)-2-(hydroxy-imino)propanoic acid (**58**):



Yield: 45 mg (0.13 mmol, 10%).

R_f = 0.76 (H_2O:MeCN = 50:50).

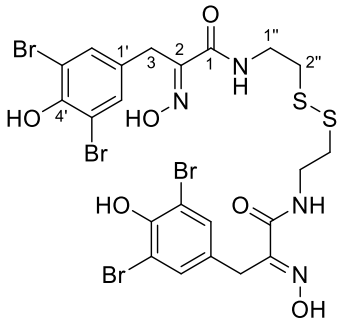
ESI-LCMS: *m/z* = 349.9 $[M+H]^+$.

ESI-LCMS: *m/z* = 351.9 $[M-H]^-$.

^{1}H-NMR, COSY (300 MHz, MeOH-d_4): δ [ppm] =7.40 (s, 2H), 3.80 (s, 2H).

The analytical data match to those reported in the literature.[34]

5,5'-Dibromopsammaplin A (59)



According to a modified procedure of *J. R. Sufrin et al*.[34]
To a stirred solution of **58** (48 mg, 0.14 mmol, 1.0 eq.), *N*-hydroxysuccinimide (24 mg, 0.20 mmol, 1.5 eq.) and DCC (42 mg, 0.20 mmol, 1.5 eq.) in dry DMF (5 mL), cysteamine (15 mg, 0.07 mmol, 0.5 eq.) and TEA (38 µL, 0.27 mmol, 2.0 eq.) were added and the reaction was stirred for 16 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified via preparative HPLC (50% MeCN, Machery Nagel Nucleodur C18 HTec column). The title compound was obtained as a colorless oil.

Yield: 21.1 mg (0.026 mmol, 13%).

R_f = 0.19 (H_2O:MeCN = 50:50).

ESI-LCMS: *m/z* = 818.8 $[M+H]^+$.

ESI-LCMS: *m/z* = 816.8 $[M-H^+]^-$.

ESI-HRMS ($C_{22}H_{22}Br_4N_4O_6S_2Na$ $[M+Na]^+$): calculated: *m/z* = 840.7606;

found: *m/z* = 840.7597.

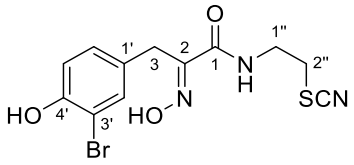
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3222, 2872, 1656, 1556, 1474, 1408, 1317, 1258, 997.

^{1}H NMR (300 MHz, MeOH-d_4) δ [ppm] = 7.39 (s, 4H, H-2', H-6'), 3.79 (s, 4H, H-3), 3.53 (t, *J* = 6.7 Hz, 4H, H-1''), 2.82 (t, *J* = 6.7 Hz, 4H, H-2'').

^{13}C NMR (75 MHz, MeOH-d_4) δ [ppm] = 165.6 (C-1), 152.5 (C-2), 150.7 (C-4'), 133.9 (C-2', C-6'), 132.2 (C-1'), 111.9 (C-3', C-5'), 39.6 (C-1''), 38.6 (C-2''), 28.4 (C-3).

The analytical data are in accordance with the literature.[34]

Psammaplin B (1)



Following the general procedure, Psammaplin A **55** (24.0 mg, 0.04 mmol, 1.0 eq.) was used together with $K_3[FeCN_6]$ (35.7 mg, 0.11 mmol, 3.0 eq.) in 108 µL solvent mixture. The reaction was monitored via LCMS, and after 7 h, additional $K_3[FeCN_6]$ (3 eq.) was added to the reaction mixture. After 23 h, another 1.5 eq. of $K_3[FeCN_6]$ were added, so that in total 7.5 eq. of $K_3[FeCN_6]$ were applied. The reaction was quenched with saturated $NaHCO_3$ solution after 72 h, and the following work-up was performed according to the general procedure. The title compound **1** was obtained as colorless lyophilisate after purification of the crude product via preparative HPLC (29% MeCN, Machery Nagel Nucleodur C18 HTec column).

Yield: 3.405 mg (9.51 nmol, 26%).

R_f = 0.50 (H_2O:MeCN = 50:50).

ESI-LCMS: *m/z* = 358.0 $[M+H]^+$.

ESI-HRMS ($C_{12}H_{12}BrN_3O_3SNa$ $[M+Na]^+$):	calculated:	*m/z* = 379.9675;
	found:	*m/z* = 379.9668.
ESI-HRMS ($C_{12}H_{12}BrN_3O_3SK$ $[M+K]^+$):	calculated:	*m/z* = 395.9415;
	found:	*m/z* = 395.9404.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3325, 2928, 2514, 2158, 1657, 1493, 1466, 1421, 1206, 996.

^{1}H NMR (600 MHz, MeOH-d_4) δ [ppm] = 7.37 (d, *J* = 2.2 Hz, 1H, H-2'), 7.07 (dd, *J* = 8.3, 2.2 Hz, 1H, H-6'), 6.76 (d, *J* = 8.3 Hz, 1H, H5'), 3.79 (s, 2H, H-3), 3.62 (t, *J* = 6.4 Hz, 2H, H-1''), 3.14 (t, *J* = 6.4 Hz, 2H, H-2'').

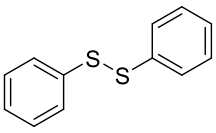
^{13}C NMR (151 MHz, MeOH-d_4) δ [ppm] = 166.2 (C-1), 153.7 (C-4'), 152.8 (C-2), 134.5 (C-2'), 130.5 (C-1'), 130.4 (C-6'), 116.9 (C-5'), 113.3 (S*C*N), 110.4 (C-3'), 40.1 (C-1''), 34.1 (C-2''), 28.6 (C-3).

No spectroscopic data available.

Isolated Side Products

Disulfides

Diphenyl disulfide (13)



Following the general procedure A using thiophenol **46** (55.1 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 36 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid.

Yield: 47.1 mg (0.22 mmol, 86%).

R_f = 0.24 (^{c}Hex).

GC-MS: *m* = 218.1 [M].

Mp: 57.6–58.7 °C. (Lit.:[35] 58–60 °C).

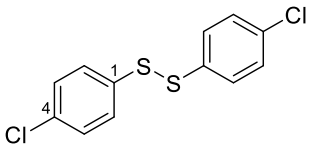
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3071, 1576, 1475, 1437, 1072, 1022, 739, 688, 473, 464.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.62–7.47 (m, 4H, 2-H, 6-H), 7.43–7.30 (m, 4H, 3-H, 5-H), 7.29–7.20 (m, 2H, 4-H, 4'-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 137.2 (1-C), 129.2 (3-C, 5-C), 127.6 (2-C, 6-C), 127.3 (4-C).

The obtained data are in accordance with the literature.[35]

1,2-Bis(4-chlorophenyl)disulfide (22b)



Following the general procedure A using 4-chlorothiophenol **22** (32.4 mg, 0.23 mmol, 1 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid.

Yield: 14.3 mg (0.05 mmol, 22%).

R_f = 0.20 (^{c}Hex).

GC-MS: *m* = 285.9 [M].

Mp: 66.5–69.6 °C (Lit.:[36] 68–70 °C).

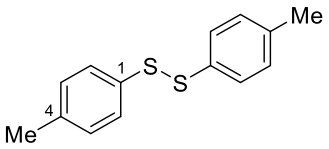
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3078, 1473, 1387, 1090, 1010, 812, 741, 536, 483, 1633.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.43–7.37 (m, 4H, 2-H, 6-H), 7.31–7.25 (m, 4H, 3-H, 5-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 135.1 (1-C), 133.6 (4-C), 129.3 (2-C, 3-C, 5-C, 6-C).

The obtained data are in accordance with the literature.[36]

Bis(4-tolyl)disulfide (24b)



Following the general procedure A using 4-mercaptotoluene **24** (62.1 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 15 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of 6 min.

Yield: 18.0 mg (0.07 mmol, 29%, procedure A), 40.1 mg (0.16 mmol, 49%, procedure B).

R_f = 0.24 (^{c}Hex).

GC-MS: *m* = 246.1 [M].

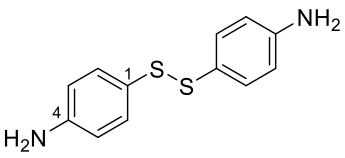
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3919, 2920, 2863, 1489, 1338, 1397, 1210, 1116, 1016, 803, 486.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.41–7.38 (m, 4H, 2-H, 6-H), 7.13–7.10 (m, 4H, 3-H, 5-H), 2.33 (s, 6H, CH_3).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 137.6 (4-C), 134.0 (1-C), 129.9 (3-C, 5-C), 128.7 (2-C, 6-C), 21.2 (CH$_3$).

The obtained data are in accordance with the literature.[37]

Bis(4-aminophenyl)disulfide (25b)



Following the general procedure A using 4-aminothiophenol **25** (62.6 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 59 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a brown oil.

Yield: 4.4 mg (0.02 mmol, 7%).

R_f = 0.52 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 249.0 $[M+H]^+$.

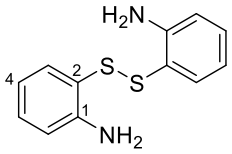
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3473, 3376, 3035, 2922, 2852, 2152, 1625, 1595, 1496, 1304, 825.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.44–7.30 (m, 4H, 2-H, 6-H), 6.82–6.56 (m, 4H, 3-H, 5-H), 3.96 (s, 4H, NH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 148.9 (4-C), 134.7 (3-C, 5-C), 116.2 (2-C, 6-C), 109.8 (1-C).

The obtained data are in accordance with the literature.[38]

2,2'-Disulfidediyldianiline (26b)



Following the general batch procedure using 2-aminothiophenol **26** (28.1 mg, 0.23 mmol, 1 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a yellow oil.

Yield: 22.1 mg (0.09 mmol, 40%).

R_f = 0.49 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 249.0 $[M+H]^+$.

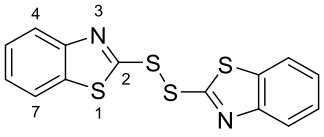
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3464, 3364, 1605, 1562, 1475, 1445, 1308, 1250, 1158, 747.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.22–7.10 (m, 4H, 3-H, 3'-H, 5-H, 5'-H), 6.77–6.68 (m, 2H, 6-H, 6'-H), 6.59 (td, *J* = 7.5, 1.3 Hz, 2H, 4-H, 4'-H), 4.33 (bs, 4H, NH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 148.7 (1-C, 1'-C), 136.9 (3-C, 3'-C), 131.7 (5-C, 5'-C), 118.8 (2-C, 2'-C), 118.3 (4-C, 4'-C), 115.31 (6-C, 6'-C).

The obtained data are in accordance with the literature.[39]

Di(benzothiazole-2yl)disulfide (30b)



Following the general procedure A using 2-mercaptobenzothiazole **30** (37.6 mg, 0.23 mmol, 1.0 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a slightly yellow solid.

Yield: 31.4 mg (0.01 mmol, 42%).

***R*f** = 0.78 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 332.9 $[M+H]^+$.

Mp: 101.3–102.1 °C. (Lit.:[40] 102–106 °C).

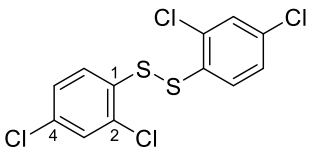
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3060, 1455, 1417, 1312, 1237, 1079, 1008, 991, 755, 726.

^{1}H-NMR, COSY (300 MHz, DMSO-*d*$_6$): δ [ppm] = 8.14 (ddd, *J* = 7.9, 1.5, 0.7 Hz, 2H, 7-H), 8.05 (ddd, *J* = 8.1, 1.4, 0.7 Hz, 2H, 4-H), 7.61–7.54 (m, 2H, 5-H), 7.50 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 2H, 6-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, DMSO-*d*$_6$): δ [ppm] = 159.7 (2-C), 152.2 (3a-C), 136.0 (7a-C), 126.9 (5-C), 125.9 (6-C), 122.4 (4-C), 122.2 (7-C).

The obtained data are in accordance with the literature.[41, 42]

1,2-Bis(2,4-dichlorophenyl)disulfide (33b)



Following the general procedure A using 2,4-dichlorobenzenethiol **33** (42.5 mg, 0.23 mmol, 1 eq.). After 22 h, the title compound could be obtained as a colorless solid.

Yield: 46.8 mg (0.13 mmol, 55%).

***R*f** = 0.85 (^{c}Hex:EtOAc = 9:1).

ESI-LCMS: *m/z* = 354.8 ($[M+H]^+$).

Mp: 78.7–80.5 ° (Lit.:[43] 82–84 °C).

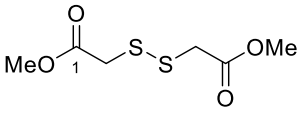
IR (ATR): $\tilde{\nu}$ [cm^{-1}] =2923, 1568, 1551, 1448, 1371, 1095, 1028, 865, 807, 550.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.46 (d, *J* = 8.6 Hz, 2H, 6-H, 6'-H), 7.39 (d, *J* = 2.2 Hz, 2H, 3-H, 3'-H), 7.20 (dd, *J* = 8.6, 2.2 Hz, 2H, 5-H 5'-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 133.5 (2-C, 2'-C), 132.8 (4-C, 4'-C), 132.7 (1-C, 1'-C), 129.6 (3-C, 3'-C), 128.5 (6-C, 6'-C), 128.0 (5-C, 5'-C).

The obtained data are in accordance with the literature.[44]

Dimethyl 2,2'-disulfidediyldiacetate (43b)



Following the general procedure A using thioglycolic acid methyl ester **43** (47.7 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 16 h, column chromatography (SiO_2, ^{c}Hex:EtOAc = 2:1) afforded the title compound as a colorless oil.

Yield: 11.1 mg (0.05 mmol, 12%).

$\boldsymbol{R_f}$ = 0.46 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 210.9 ($[M+H]^+$); *m/z* = 232.9 $[M+Na]^+$.

ESI-HRMS ($C_6H_{11}O_4S_2$ $[M+H]^+$): calculated: *m/z* = 211.0094;

found: *m/z* = 211.0095.

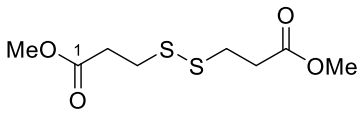
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2954, 1732, 1435, 1273, 1155, 1126, 1007.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 3.76 (s, 6H, OCH_3), 3.59 (s, 4H, CH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 169.9 (*C*O), 52.8 (O*C*H_3), 41.3 (*C*H_2).

The obtained data are in accordance with the literature.[45]

Dimethyl-3,3'-disulfidediyldipropionate (44b)



Following the general procedure A using 3-mercaptopropioic acid methyl ester **44** (54.0 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, ^{c}Hex:EtOAc = 2:1) afforded the title compound as a colorless oil.

Yield: 38.2 mg (0.16 mmol, 36%).

$\boldsymbol{R_f}$ = 0.52 (^{c}Hex:EtOAc = 2:1).

ESI-LCMS: *m/z* = 239.0 $[M+H]^+$; 261.0 $[M+Na]^+$.

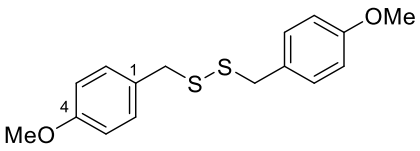
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2953, 1731, 1564, 1436, 1356, 1239, 1171, 1141, 1048, 1016, 824.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 3.69 (s, 6H, OCH_3), 2.91 (td, *J* = 7.1, 0.9 Hz, 4H, 3-H, 3'-H), 2.72 (td, *J* = 7.1, 0.9 Hz, 4H, 2-H, 2'-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 172.2 (*C*OCH_3), 52.0 (CO*C*H_3), 33.9 (2-C, 2'-C), 33.1 (3-C, 3'-C).

The obtained data are in accordance with the literature.[46]

1,2-Bis(4-methoxybenzyl)disulfide (45b)



Following the general procedure A using (4-methoxyphenyl)methanethiol **45** (69.3 mg, 0.50 mmol, 1 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 42 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil. General procedure B was alternatively applied with a reaction time of 6 min.

Yield: 8.1 mg (0.03 mmol, 6%, Procedure A), 15.9 mg (0.05 mmol, 16%, procedure B).

R_f = 0.47 (^{c}Hex:EtOAc = 10:1).

ESI-LCMS (pos. found for $C_8H_9O^+$)**:** *m/z* = 121.1 [M-$C_8H_9OS_2$].

ESI-HRMS ($C_{16}H_{18}O_2S_2Na$ $[M+Na]^+$): calculated: *m/z* = 329.0640;

found: *m/z* = 329.0609.

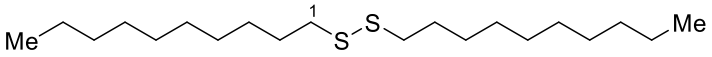
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2834, 1609, 1510, 1463, 1301, 1248, 1175, 1033, 832.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.21–7.15 (m, 4H, 2-H, 6-H), 6.89–6.82 (m, 4H, 3-H, 5-H), 3.80 (s, 6H, OCH_3), 3.59 (s, 4H, CH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 159.1 (4-C), 130.6 (2-C, 6-C), 129.5 (1-C), 114.0 (3-C, 5-C), 55.4 (OCH_3), 42.9 (CH_2).

The obtained data are in accordance with the literature.[35]

Didecyldisulfide (53b)



Following the general procedure B using decanthiol **53** (116.6 mg, 0.669 mmol, 1.0 eq.) with a milling time of either 6 or 12 min. Column chromatography (SiO_2, *Isolera One*™ 10%–80% EtOAc) afforded the title compound as a colorless oil.

Yield: 66.9 mg (0.19 mmol, 58%, Procedure B).

R_f = 0.60 (^{c}Hex).

ESI-LCMS: *m/z* = 369.0 $[M+Na]^+$.

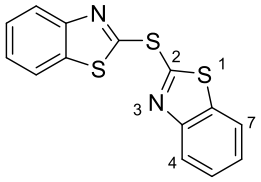
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2922, 2852, 1463, 1377, 721.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 2.69–2.66 (m, 4H, CH_2S), 1.69–1.64 (m, 4H, 2-H), 1.42–1.35 (m, 4H), 1.32–1.24 (m, 24H), 0.88 (t, J = 7.0 Hz, 6H, 10-H)

^{13}C-NMR, HSQC, HMBC (151 MHz, $CDCl_3$): δ [ppm] = 39.3 (CH$_2$S), 32.0, 29.7, 29.7, 29.5, 29.4, 29.4, 28.7, 22.8, 14.3 (CH$_3$).

Further Side Products

Bis(benzothiazol-2-yl)sulfide (30c)



Following the general procedure A using 2-mercaptobenzothiazole **30** (37.6 mg, 0.23 mmol, 1.0 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a slightly yellow solid.

Yield: 40.2 mg (0.01 mmol, 54%).

R_f = 0.60 (^{c}Hex:EtOAc= 3:1).

ESI-LCMS: *m/z*= 301.0 $[M+H]^+$.

Mp: 99.0–99.8 °C (Lit.:[42]101–102 °C).

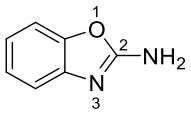
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3061, 1471, 1450, 1427, 1410, 1238, 1026, 1010, 990, 754, 727.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 8.08–8.02 (m, 2H, 4-H), 7.88–7.81 (m, 2H, 7-H), 7.52 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 2H, 5-H), 7.42 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 2H, 6-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 160.0 (2-C), 152.9 (3a-C), 136.6 (7a-C), 126.6 (5-C), 125.7 (6-C), 123.0 (4-C), 121.2 (7-C).

The obtained data are in accordance with the literature.[41, 42]

Benzo[d]oxazol-2-amine (31b)



Following the general procedure A using 2-mercaptobenzoxazol **31** (34.0 mg, 0.23 mmol, 1 eq.). After 14 h, column chromatography (SiO_2, *Isolera One*™ 10%–80% EtOAc) afforded the title compound as a colorless oil.

Yield: 5.2 mg (0.04 mmol, 17%).

R_f = 0.10 (^{c}Hex:EtOAc = 2:1).

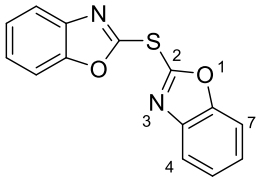
ESI-LCMS: *m/z* = 135.1 $[M+H]^+$.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.39–7.33 (m, 1H, 7-H), 7.31–7.27 (m, 1H, 4-H), 7.20 (td, *J* = 7.7, 1.2 Hz, 1H, 6-H), 7.10 (td, *J* = 7.7, 1.3 Hz, 1H, 5-H), 4.87 (bs, 2H, NH_2).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 161.2 (*C*NH_2), 148.0 (3a-C), 139.8 (7a-C), 124.7 (6-C), 122.2 (5-C), 116.0 (7-C), 109.5 (4-C).

The obtained data are in accordance with the literature.[47]

Bis(benzoxazol-2-yl)sulfide (31c)



Following the general procedure A using 2-mercaptobenzoxazole **31** (67.9 mg, 0.5 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (444.5 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 18 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless solid. General procedure B was alternatively applied with a reaction time of 6 min.

Yield: 18.2 mg (0.07 mmol,15%, procedure A), 29.7 mg (0.11 mmol, 33%, procedure B).

R_f = 0.70 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 269.0 $[M+H]^+$.

Mp: 121.3–124.6 °C (Lit.:[48] 132–133 °C).

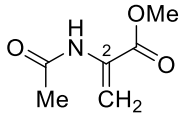
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 1815, 1496, 1447, 1321, 1239, 1119, 1089, 929, 803, 742.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.81–7.69 (m, 2H, 4-H), 7.59–7.49 (m, 2H, 7-H), 7.45–7.33 (m, 4H, 5-H, 6-H).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 155.4 (2-C), 152.5 (7a-C), 141.8 (3a-C), 126.0 (6-C), 125.1 (5-C), 120.3 (4-C), 110.9 (7-C).

The obtained data are in accordance with the literature.[48]

Methyl-2-acetamidoacrylate (40b)



Following the general procedure A using *N*-acetyl-L-cysteine methyl ester **40** (40.7 mg, 0.23 mmol, 1.0 eq.). After 20 h, column chromatography (SiO_2, ^{c}Hex:EtOAc = 1:1) afforded the title compound as a colorless solid.

Yield: 3.1 mg (0.02 mmol, 10%).

R_f = 0.48 (^{c}Hex:EtOAc = 1:1).

ESI-LCMS: *m/z* = 144.1 $[M+H]^+$.

ESI-HRMS ($C_6H_{10}NO_3$ $[M+H]^+$): calculated: *m/z* = 144.0659;

found: *m/z* = 144.0655.

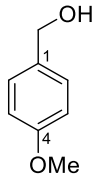
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3364, 1728, 1676, 1635, 1515, 1440, 1371, 1324, 1202, 1171, 995, 902.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.72 (bs, 1H, N*H*), 6.60 (s_{app}, 1H, C$H_{2,a}$), 5.88 (d, *J* = 1.5 Hz, 1H, C$H_{2,b}$), 3.85 (s, 3H, OCH_3), 2.13 (s, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 168.8 (CH_3*C*ONH), 164.6 (*C*OOCH_3), 130.8 (2-C), 108.7 (*C*H_2), 53.0 (COO*C*H_3), 24.7 (*C*H_3CONH).

The obtained data are in accordance with the literature.[49]

***p*-Anisyl alcohol (45c)**



Following the general procedure A using (4-methoxyphenyl)methanethiol **45** (69.3 mg, 0.50 mmol, 1.0 eq.) and $K_3[FeCN_6]$ (494 mg, 1.50 mmol, 3.0 eq.) in 1.36 mL solvent mixture. After 42 h, column chromatography (SiO_2, *Isolera One*™ 0%–80% EtOAc) afforded the title compound as a colorless oil.

Yield: 16.9 mg (0.12 mmol, 27%).

R_f = 0.08 (^{c}Hex:EtOAc = 10:1).

GC-MS: *m* = 138.0 [M].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3343, 1612, 1512, 1463, 1302, 1245, 1174, 1032, 816, 572.

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ [ppm] = 7.32–7.26 (m, 2H, 2-H, 6-H), 6.92–6.85 (m, 2H, 3-H, 5-H), 4.60 (s, 2H, CH_2), 3.81 (s, 3H, OCH_3).

^{13}C-NMR, HSQC, HMBC (75 MHz, $CDCl_3$): δ [ppm] = 159.2 (4-C), 133.1 (1-C), 128.7 (2-C, 6-C), 113.9 (3-C, 5-C), 65.0 (*C*H_2), 55.3 (O*C*H_3).

The obtained data are in accordance with the literature.[50]

Crystallographic Data

For psammaplin B (**1**), an X-ray molecular structure was obtained. Supplementary crystallographic data for this publication is contained in CCDC 2206744. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

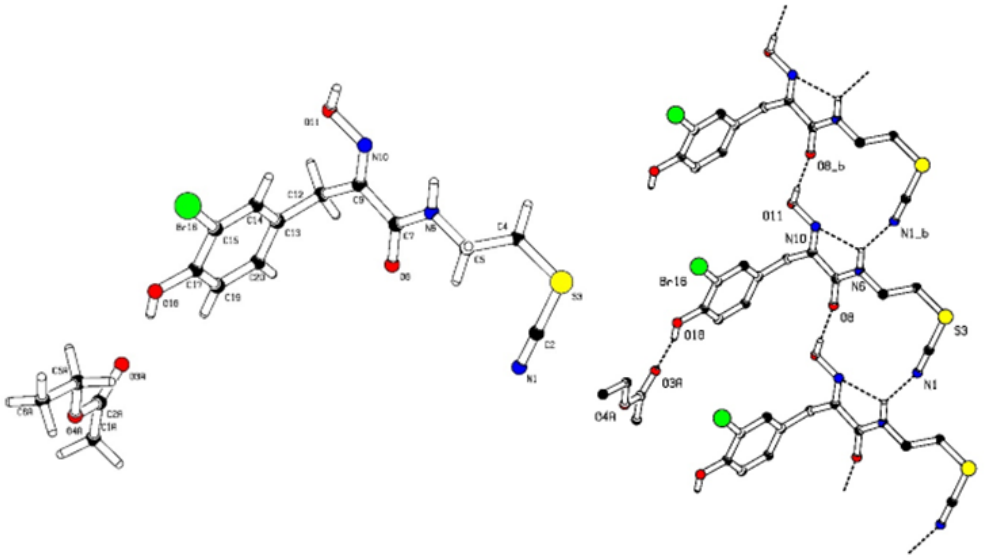


Figure F2: Molecular crystallographic structure of compound **1** at 120 K (C: black, O: red, N: blue, S: yellow, Br: green).

Table 3: Crystal structure determination of compound **1**.

Crystal data:

Sum formular	$C_{16}H_{20}BrN_3O_5S$
Molecular formular	$C_{12}H_{12}BrN_3O_3S$, $C_4H_8O_2$
Molar mass	446.32 g mol^{-1}
Temperature	120 K
Wavelength	0.71073Å, MoKα
Diffractometer	STOE IPDS 2T
Crystal system	Monoclinic
Space group	P $2_1/c$
Habitus	Colorless plate
Crystal size	0.030 x 0.230 x 0.570 mm^3
Lattice constants (from 13589 reflections with 2.70° <=Θ<= 28.31°)	*a* = 19.9760(12), α = 90° *b* = 6.7233(3) Å, β = 100.337(5)° *c* = 14.7489(10) Å, γ = 90° *V* = 1948.7(2) $Å^3$ *F*(000) = 912
Density (calculated)	1.521 Mg/m^3
Absorption coefficient	2.248 mm^{-1}

Data collection:

Wavelength, radiation	0.71073Å, MoKα
Diffractometer	STOE IPDS 2T
Scan width	2.813–28.017°.
Scan range	−19<=*h*<=26,
	−8<=*k*<=8,
	−19<=*l*<=19
Measured reflections	9405
Independent reflections	4610 [R_{int} = 0.0253]
Observed reflections	3789 [I>2σ(I)]
Integrity at Θ_{max}= 25.2°	99.2%

Data correction, structure solution and refinement:

Absorption correction	Integration
Refinement	Full-matrix least-squares on F^2
Reflexes/Restraints/Parameters	4610/0/286
Goodness on fit for F^2	1.134
Final R values [I>2σ(I)]	R1 = 0.0437, wR_2 = 0.0869
R value (all data)	R_1 = 0.0619, wR_2 = 0.0966
Fourier synthesis	0.646 and -0.439 eÅ^{-3}
Annotation	H-Atoms partly isotropically refined

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^{1}H– and ^{13}C–NMR Spectra of Compounds

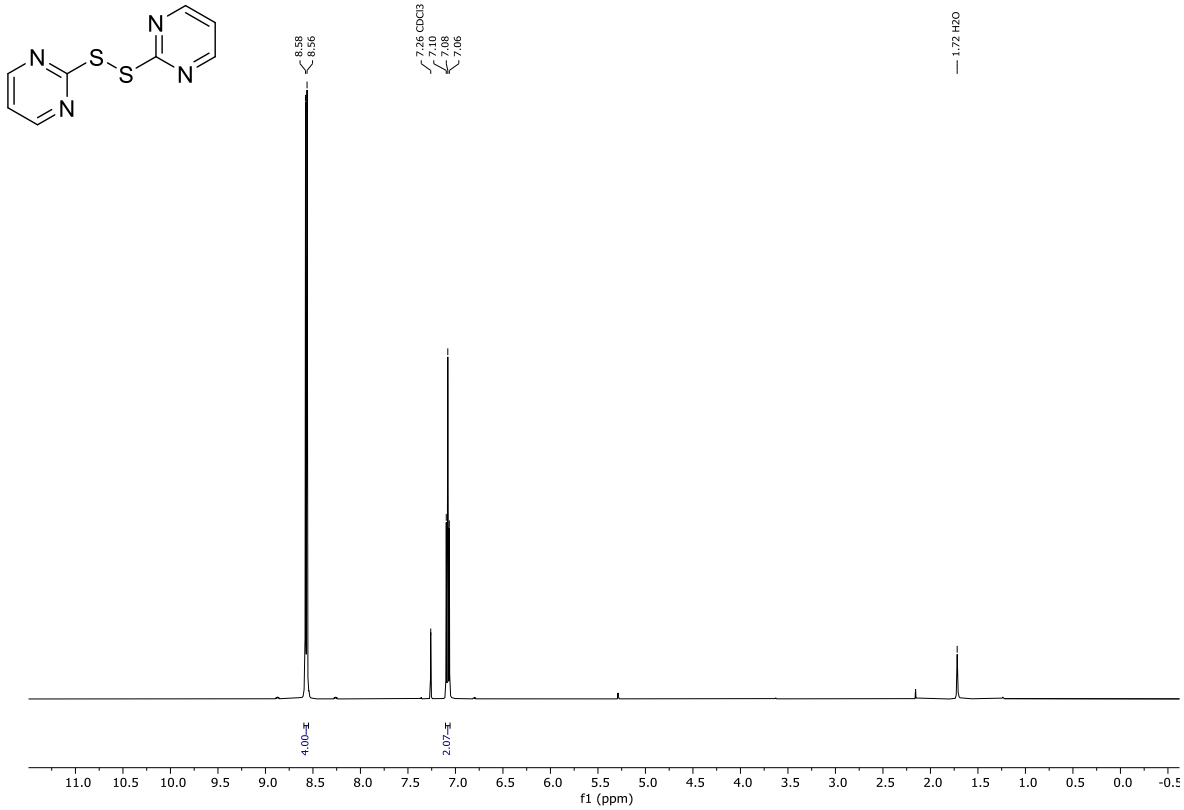

Figure F3: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **15**.

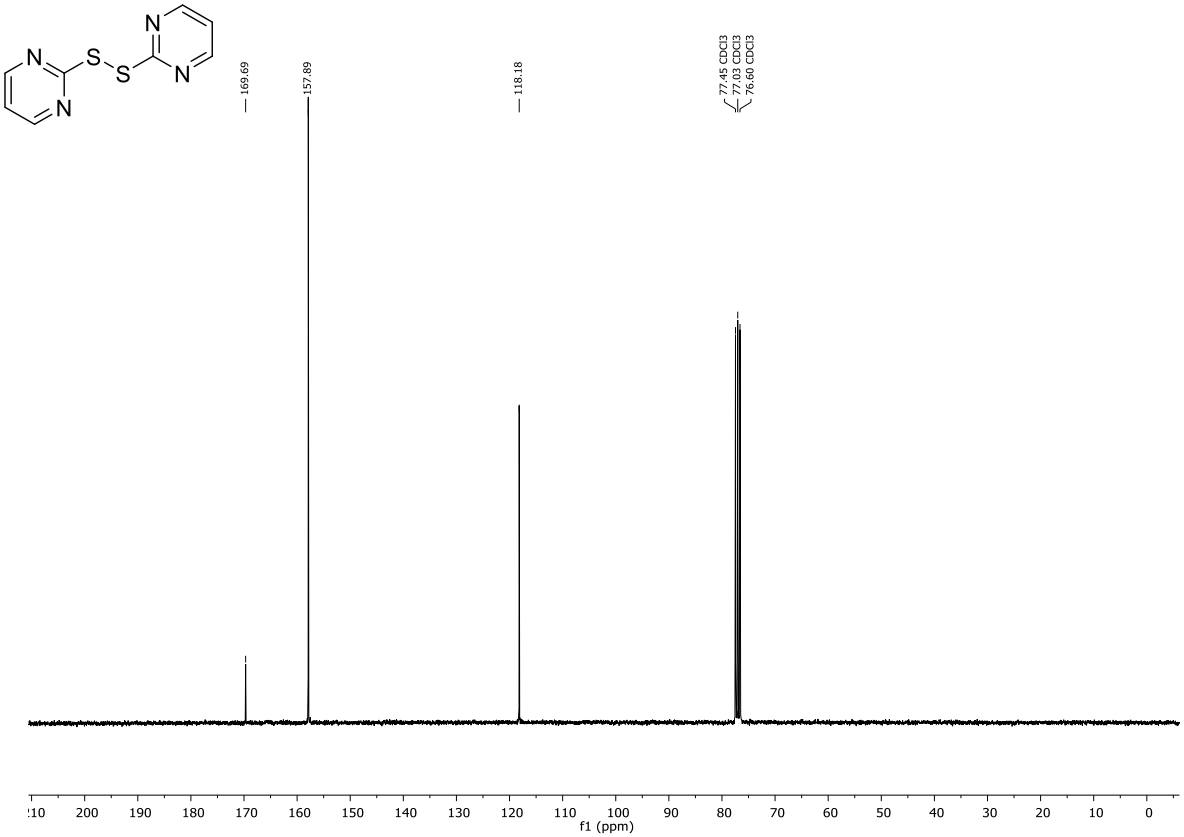

Figure F4: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **15**.

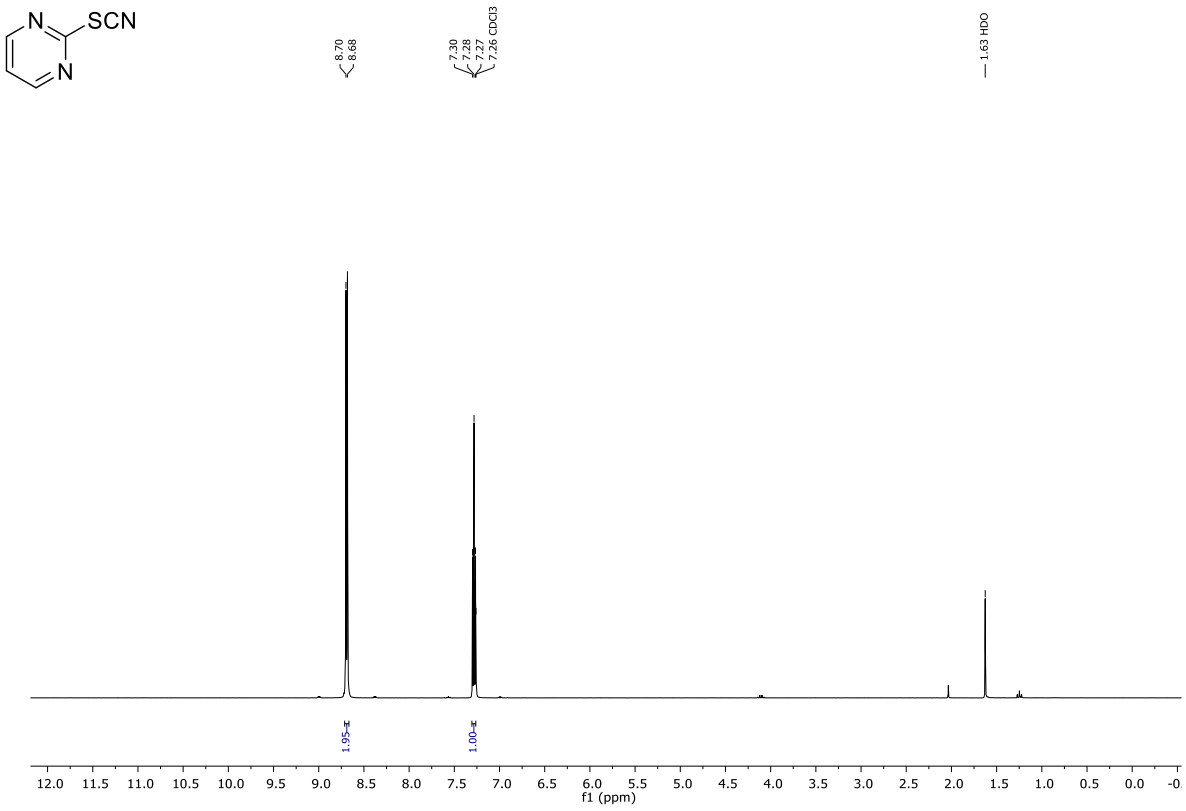

Figure F5: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **16a**.

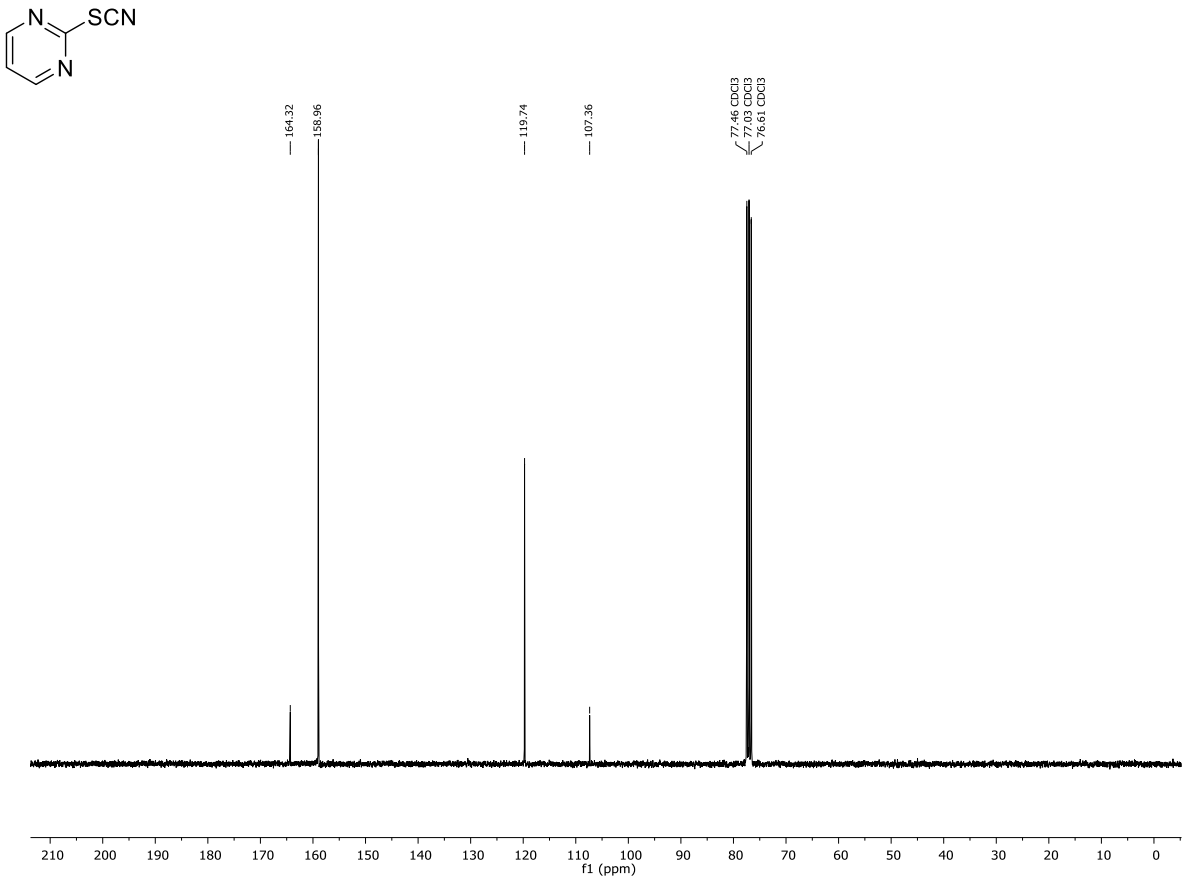

Figure F6: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **16a**.

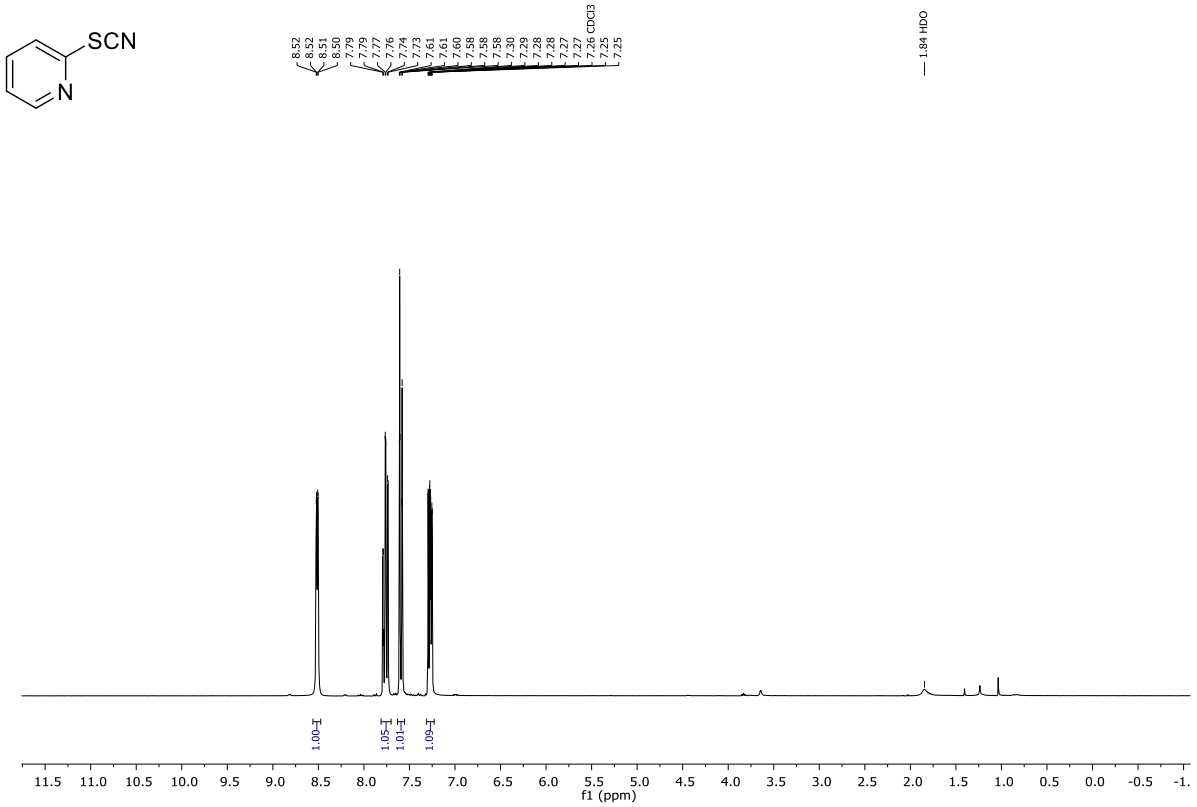

Figure F7: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **17a**.

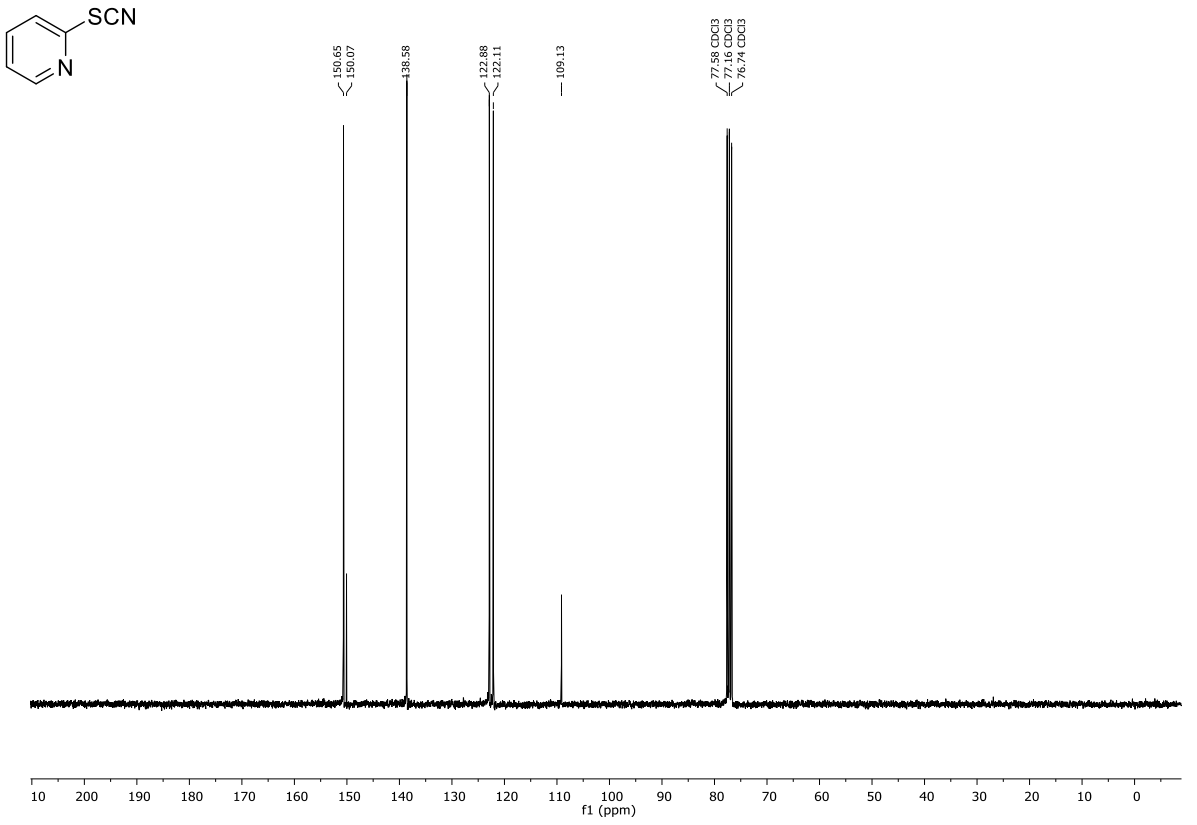

Figure F8: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **17a**.

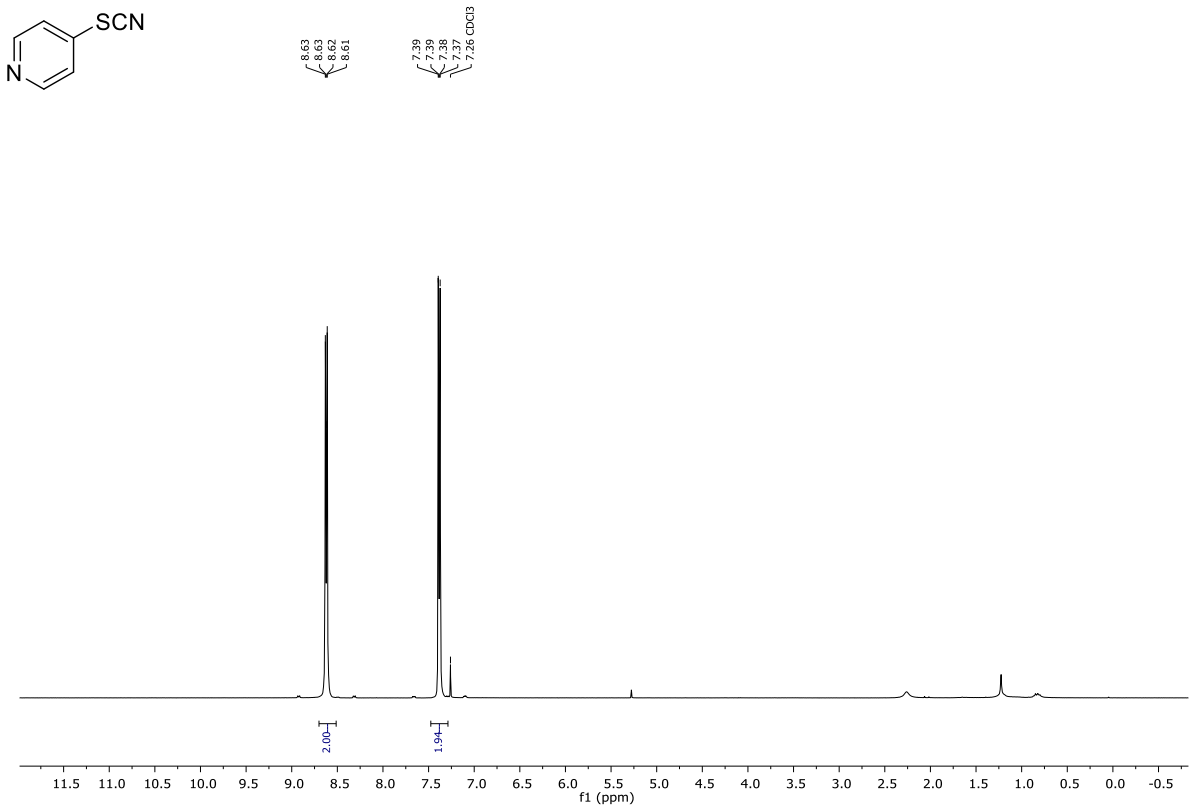

Figure F9: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **18a**.

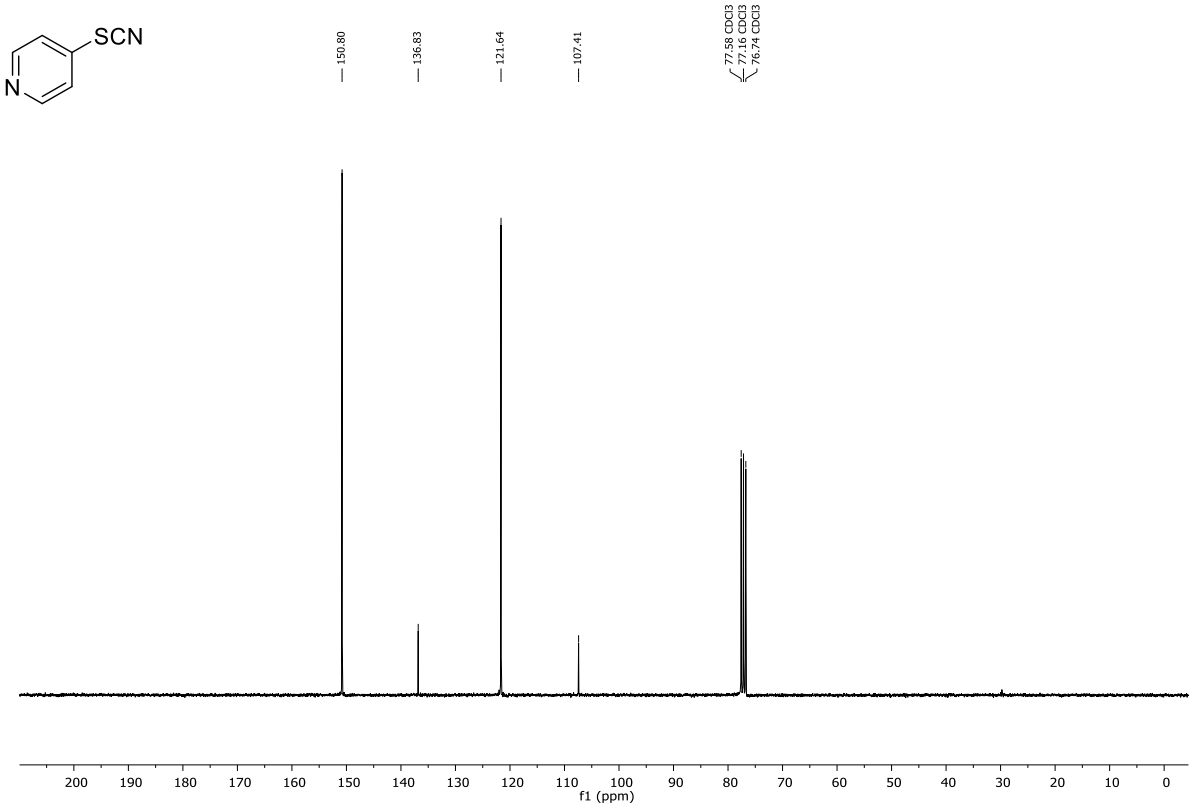

Figure F10: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **18a**.

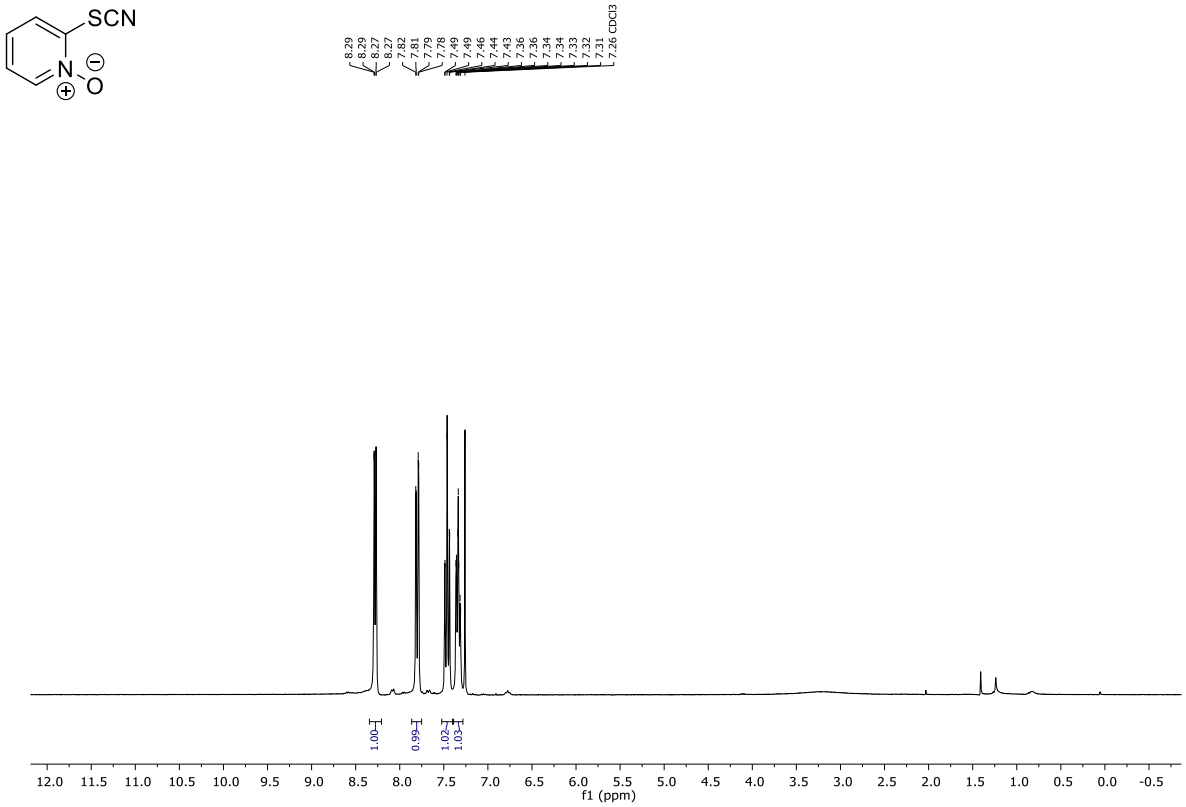

Figure F11: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **19a**.

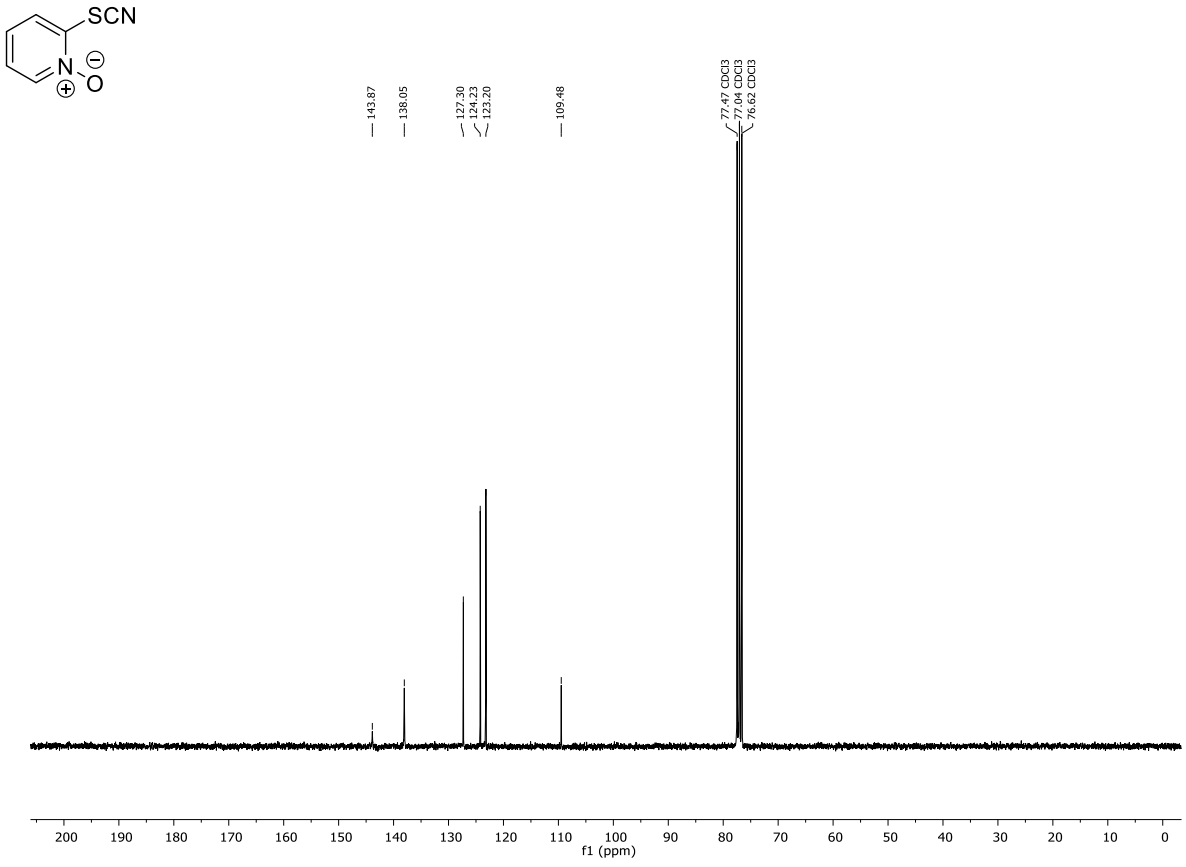

Figure F12: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **19a**.

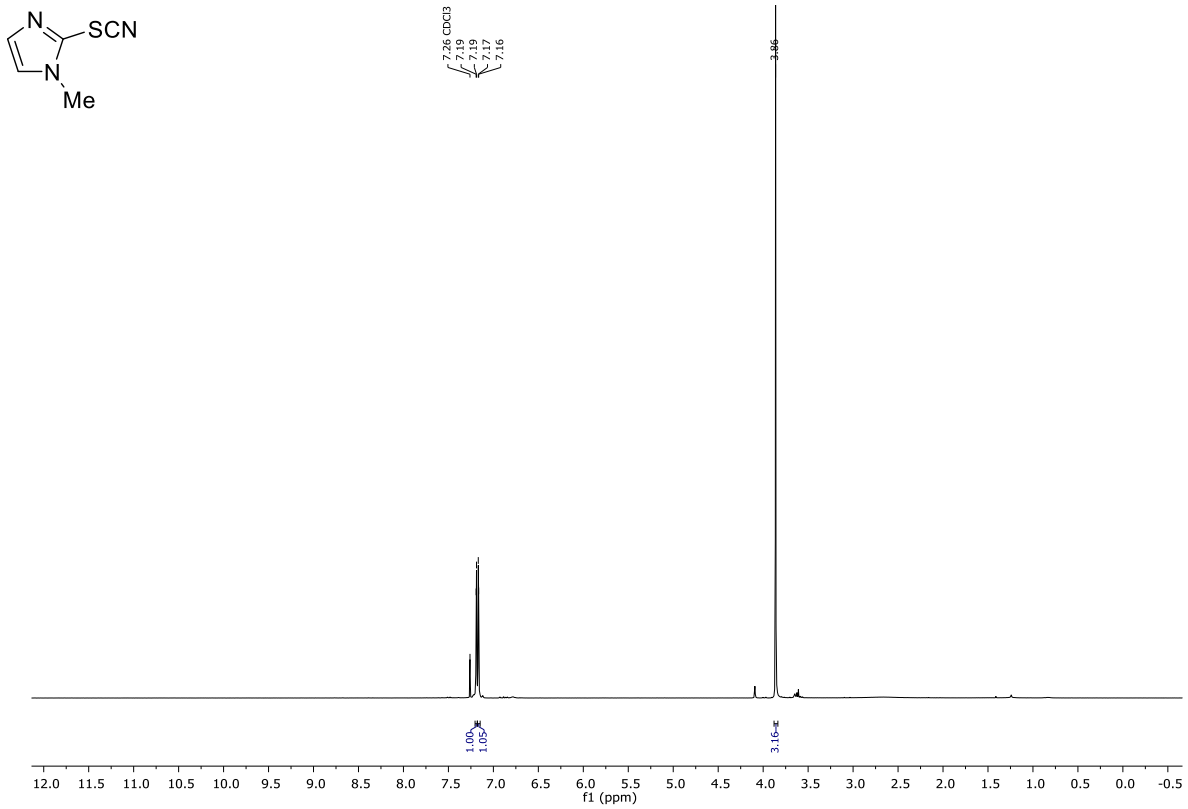

Figure F13: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **20a**.

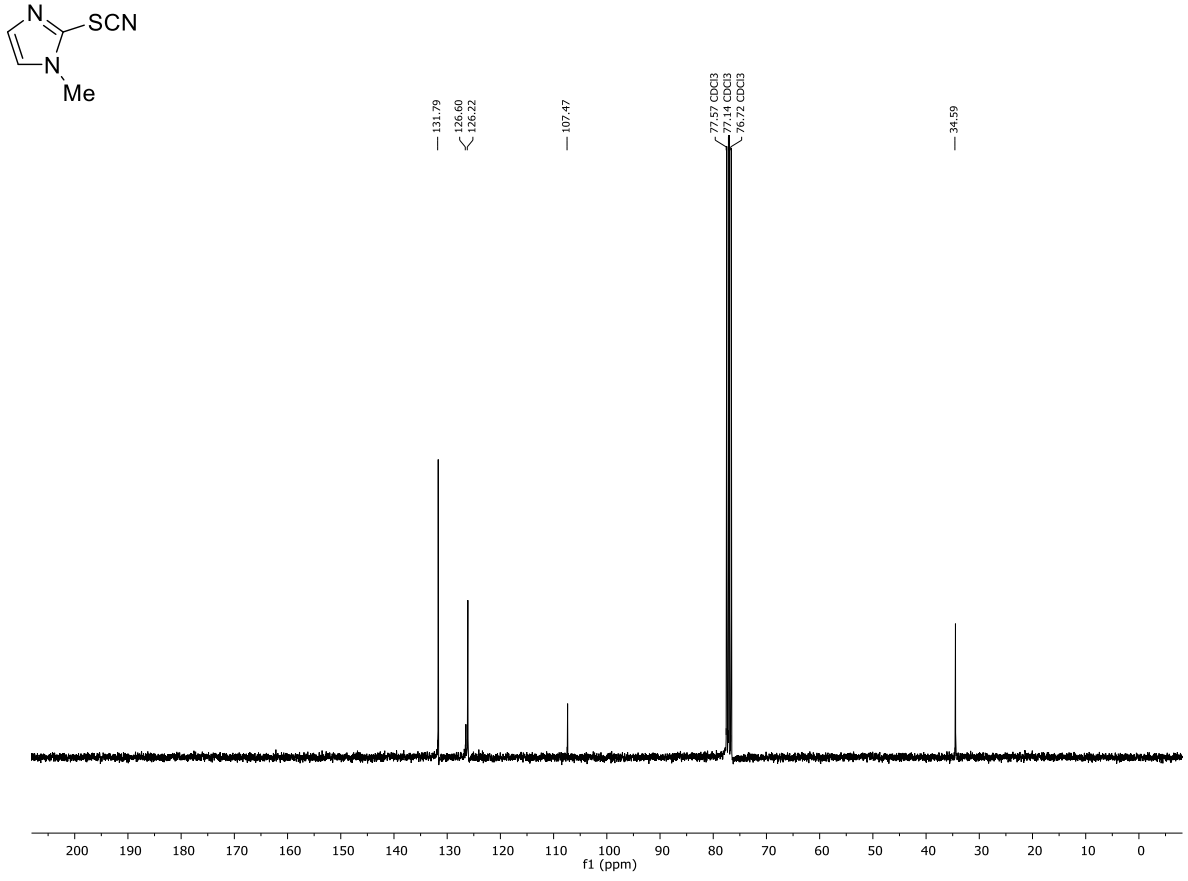

Figure F14: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **20a**.

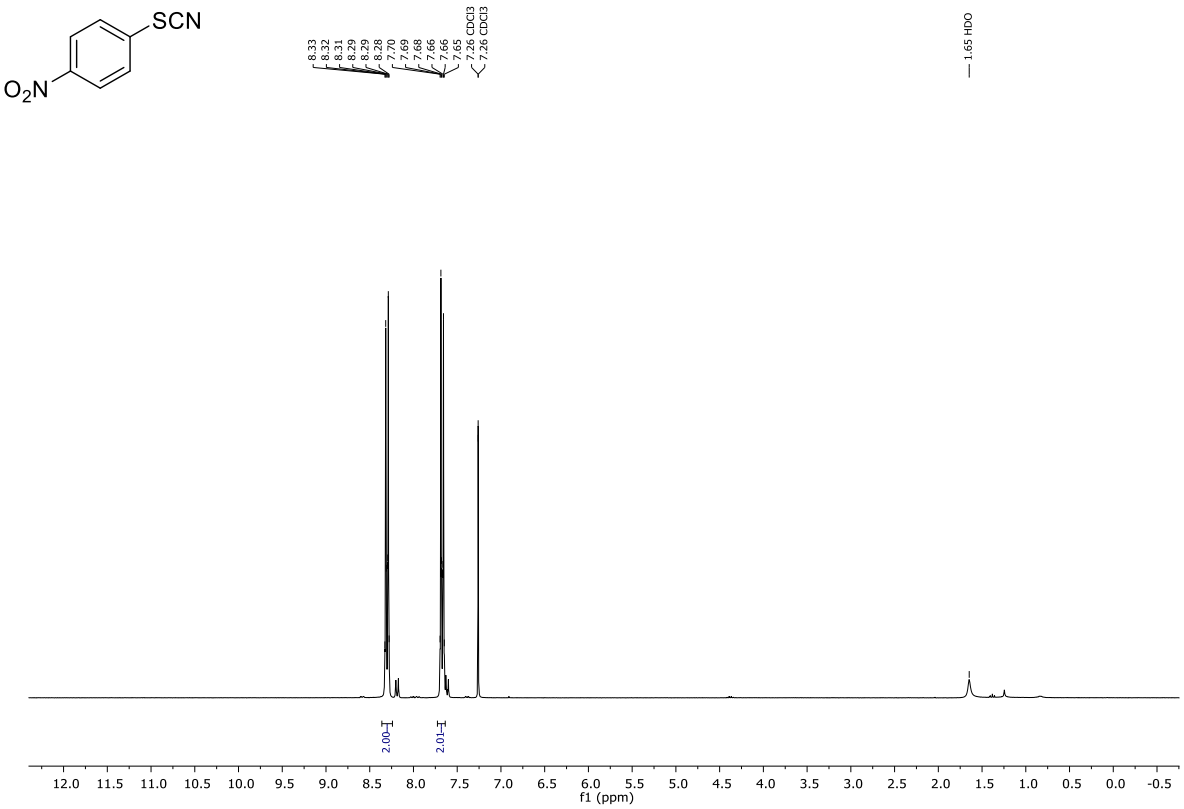

Figure F15: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **21a**.

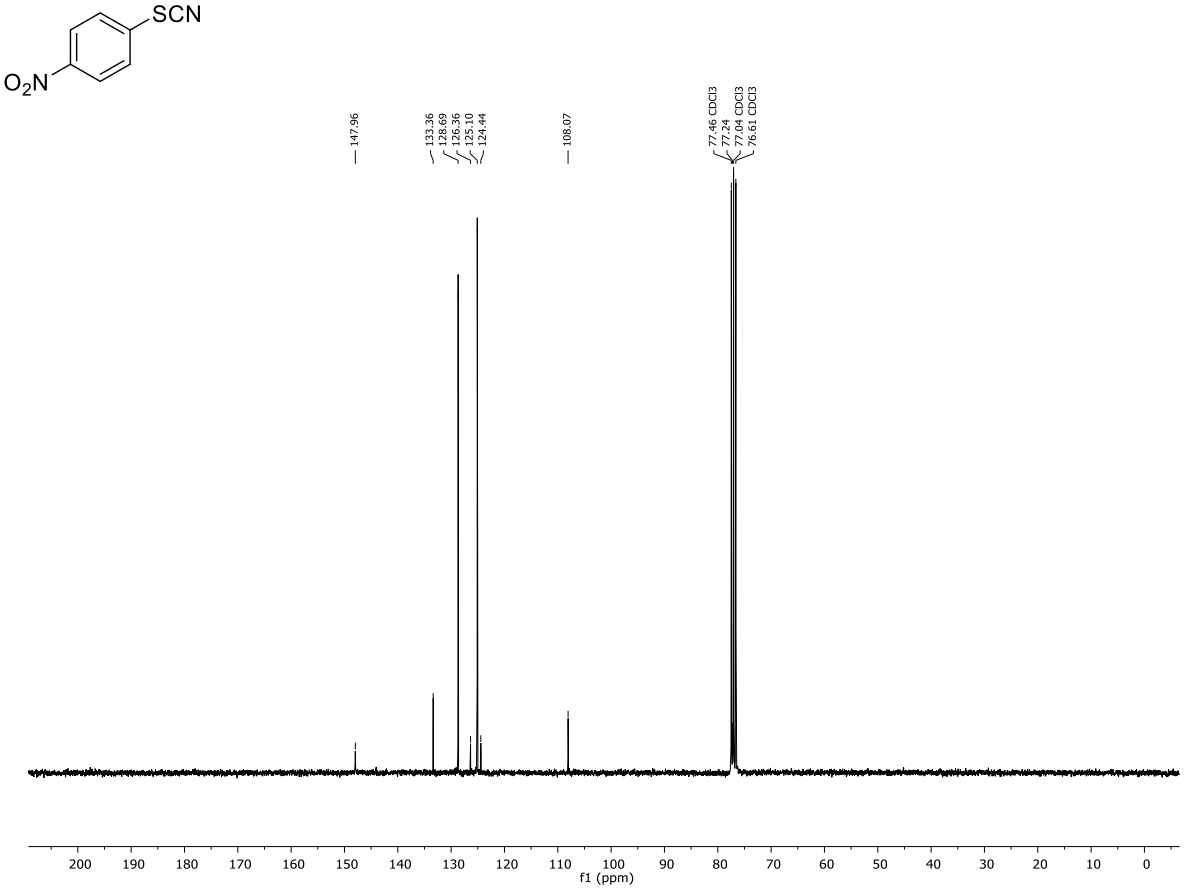

Figure F16: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **21a**.

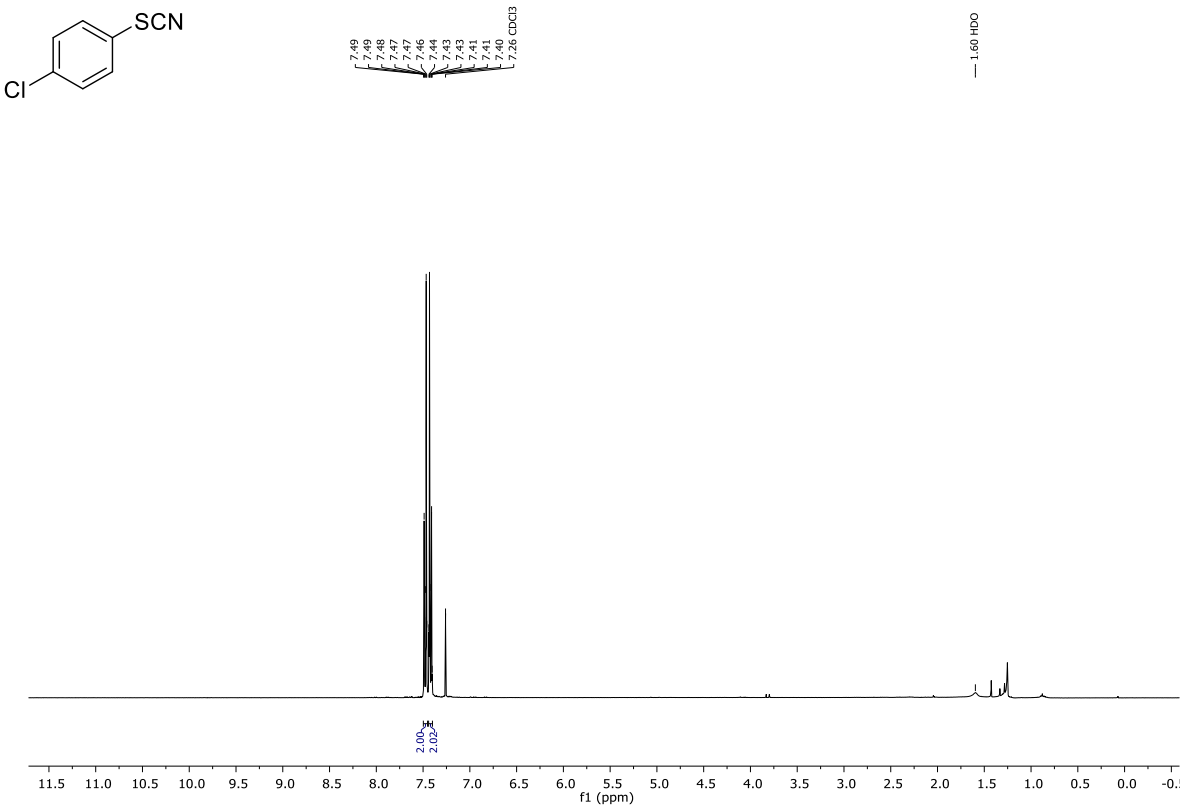

Figure F17: ^{1}H-NMR ($CDCl_3$, 400 MHz) of compound **22a**.

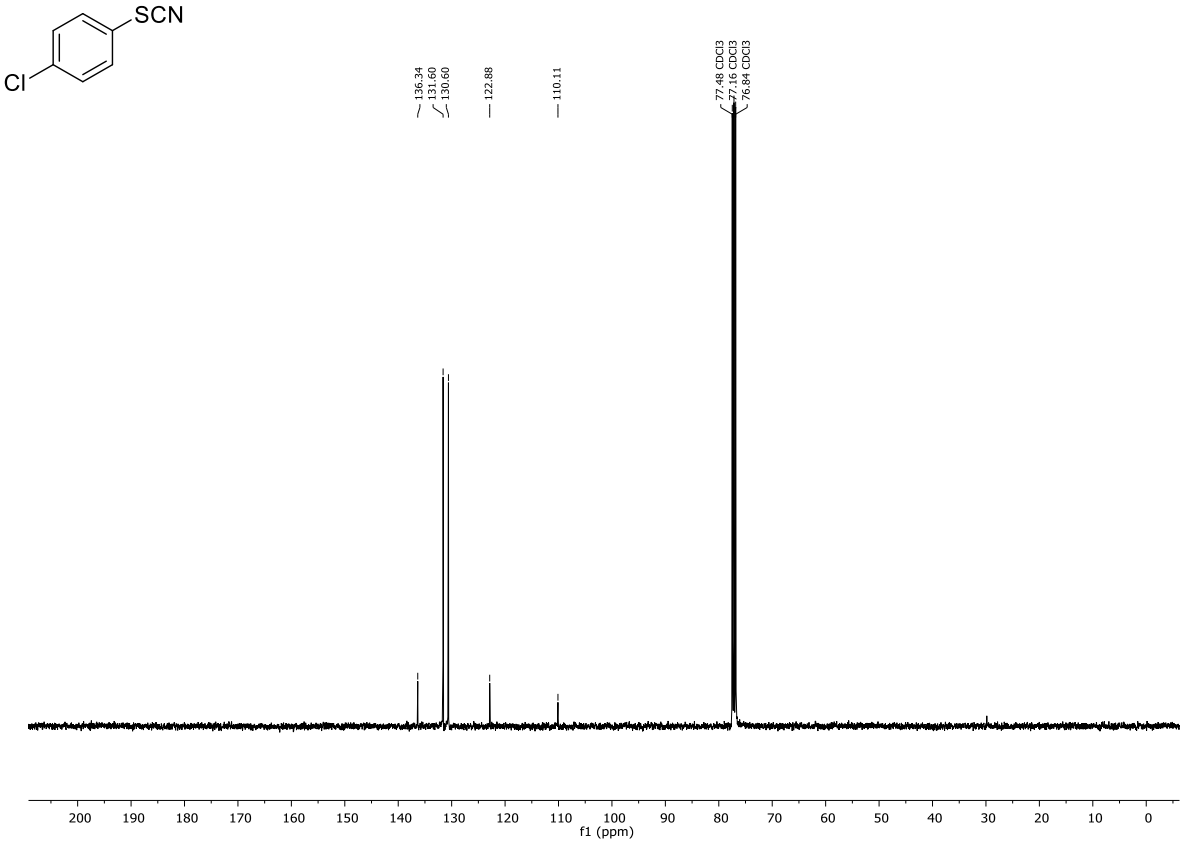

Figure F18: ^{13}C-NMR ($CDCl_3$, 101 MHz) of compound **22a**.

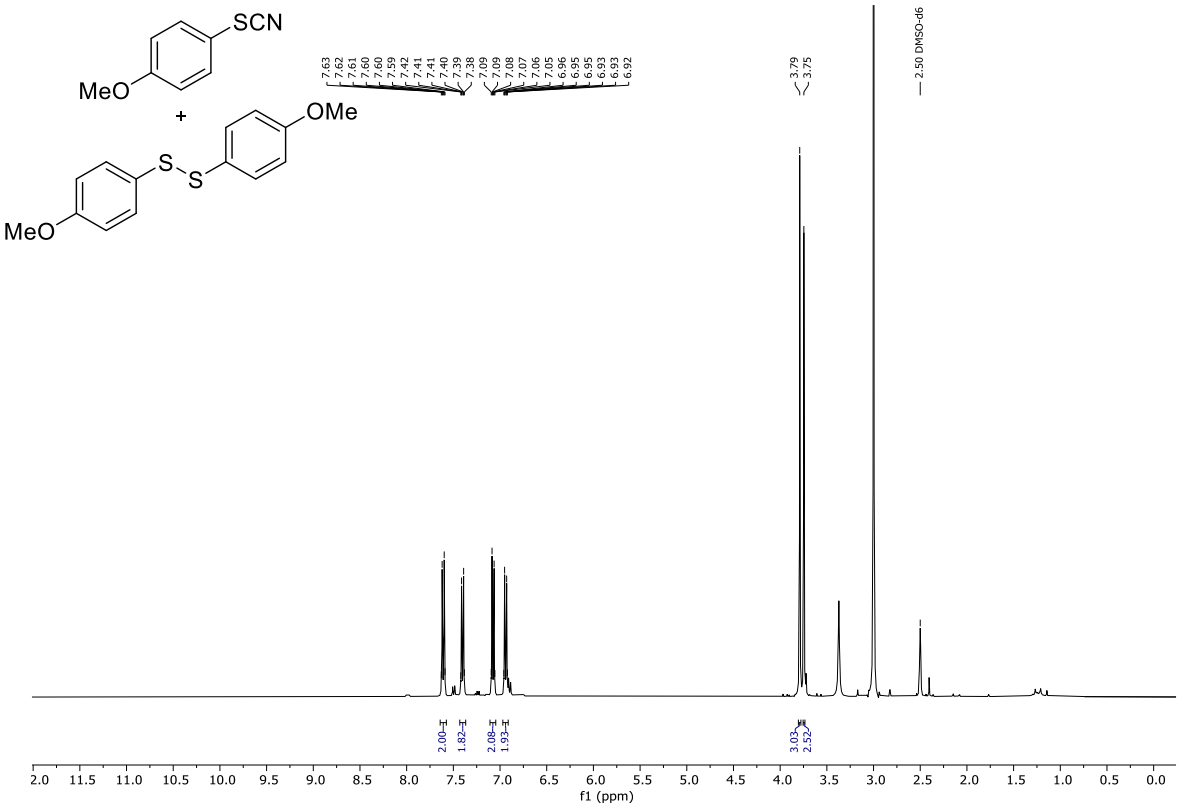

Figure F19: ^{1}H-NMR (DMSO-d_6, 300 MHz) of compound **23a**+**23b** with dimethylsulfone as internal standard.

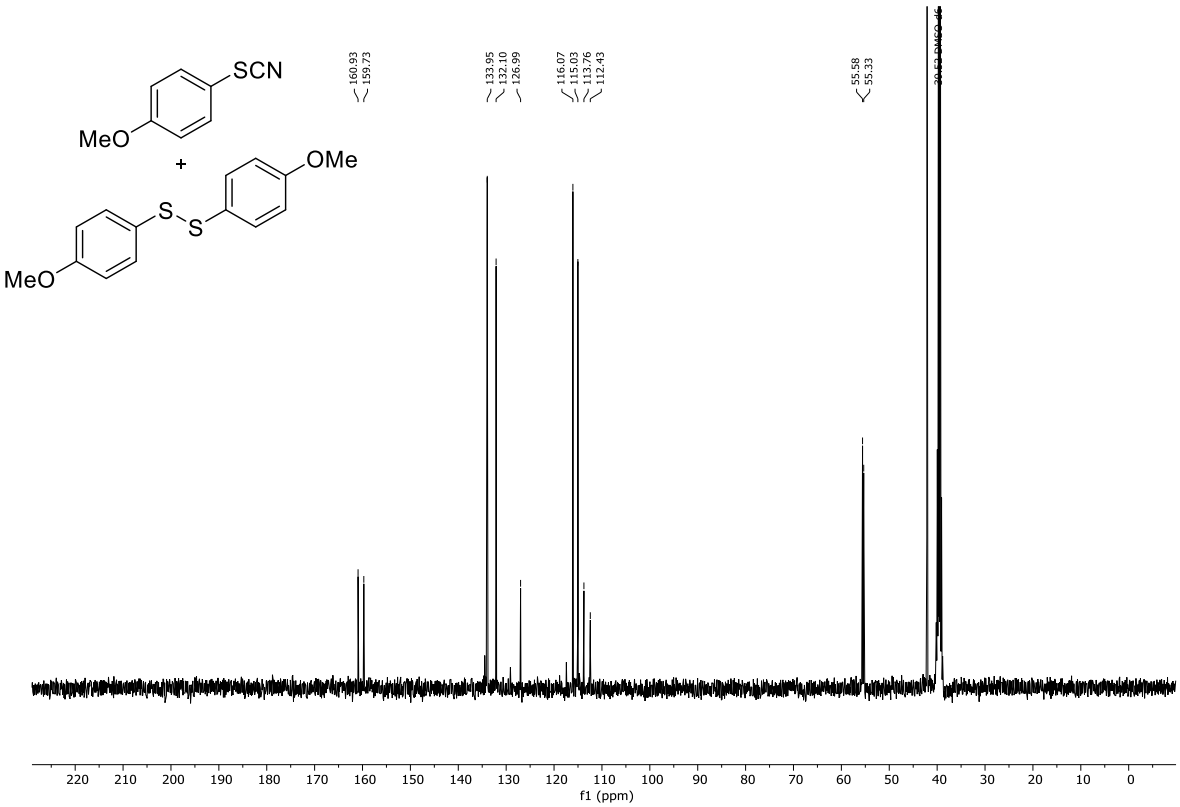

Figure F20: ^{13}C-NMR (DMSO-d_6, 75 MHz) of compound **23a**+**23b** with dimethylsulfone as internal standard.

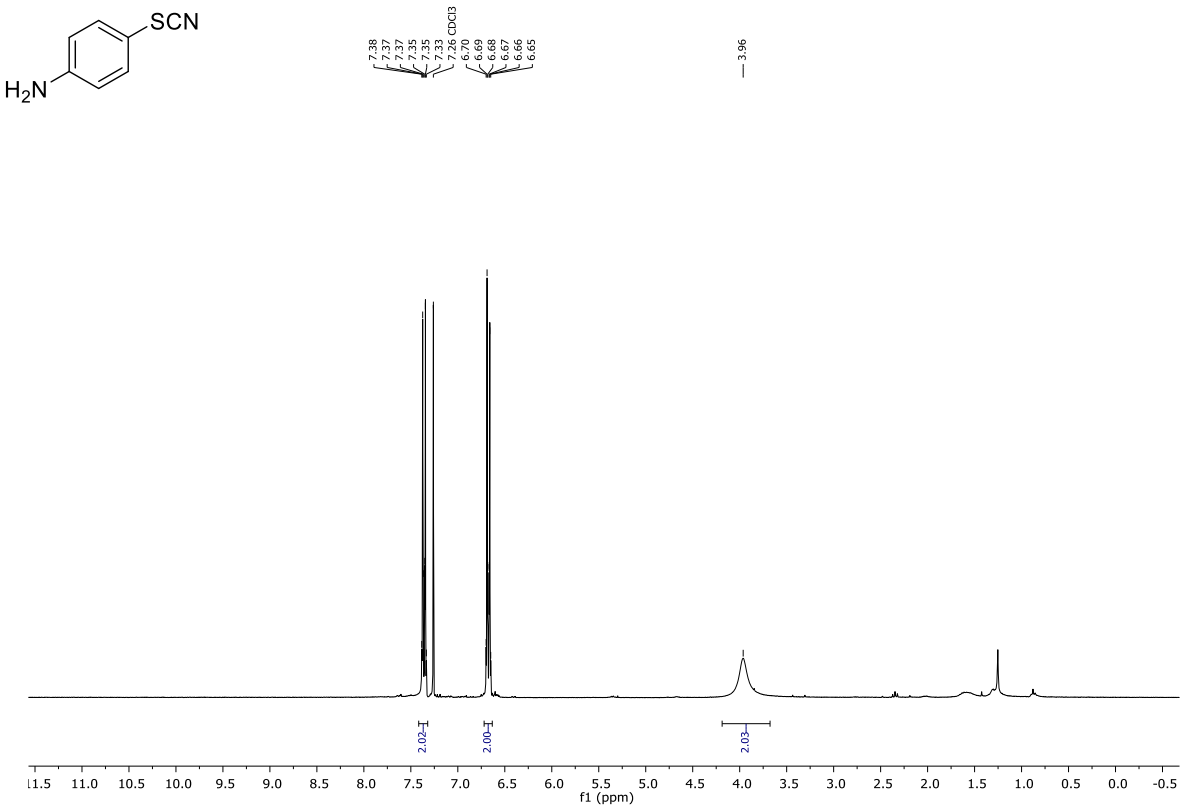

Figure F21: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **25a**.

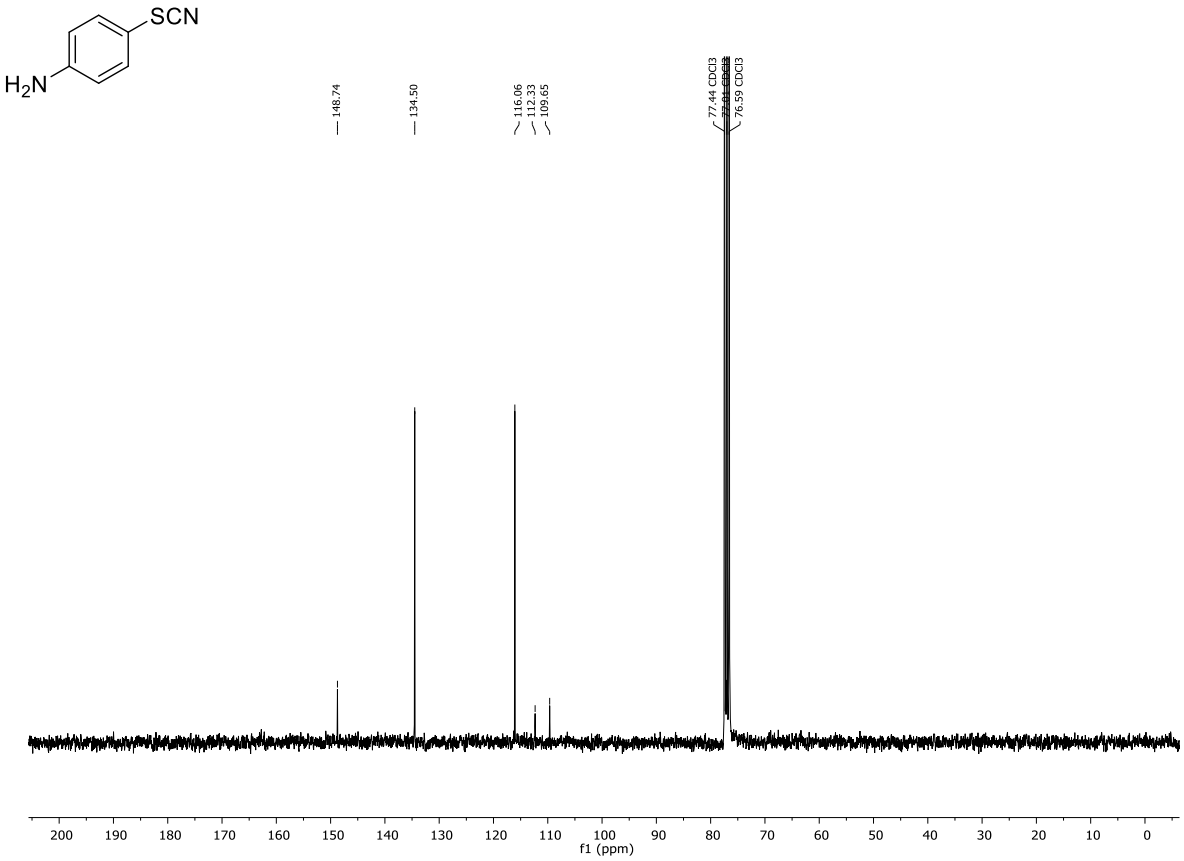

Figure F22: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **25a**.

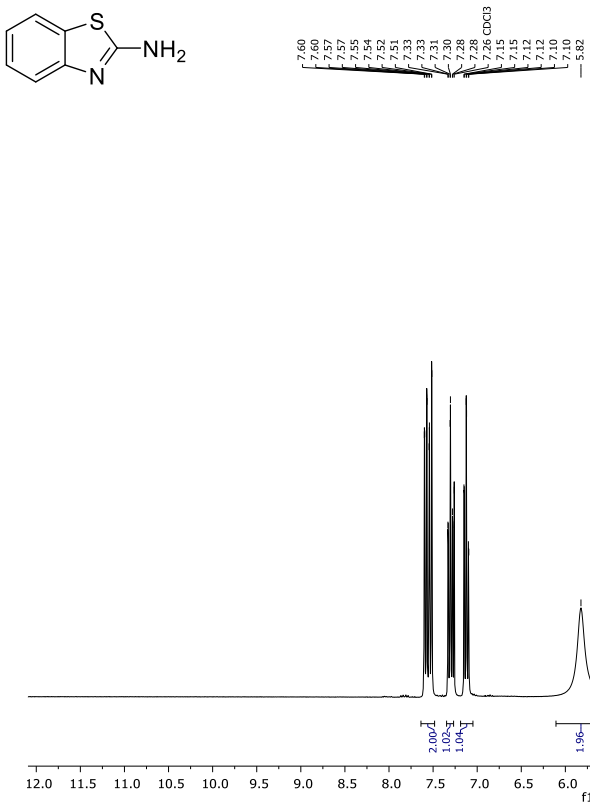

Figure F23: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **26a**.

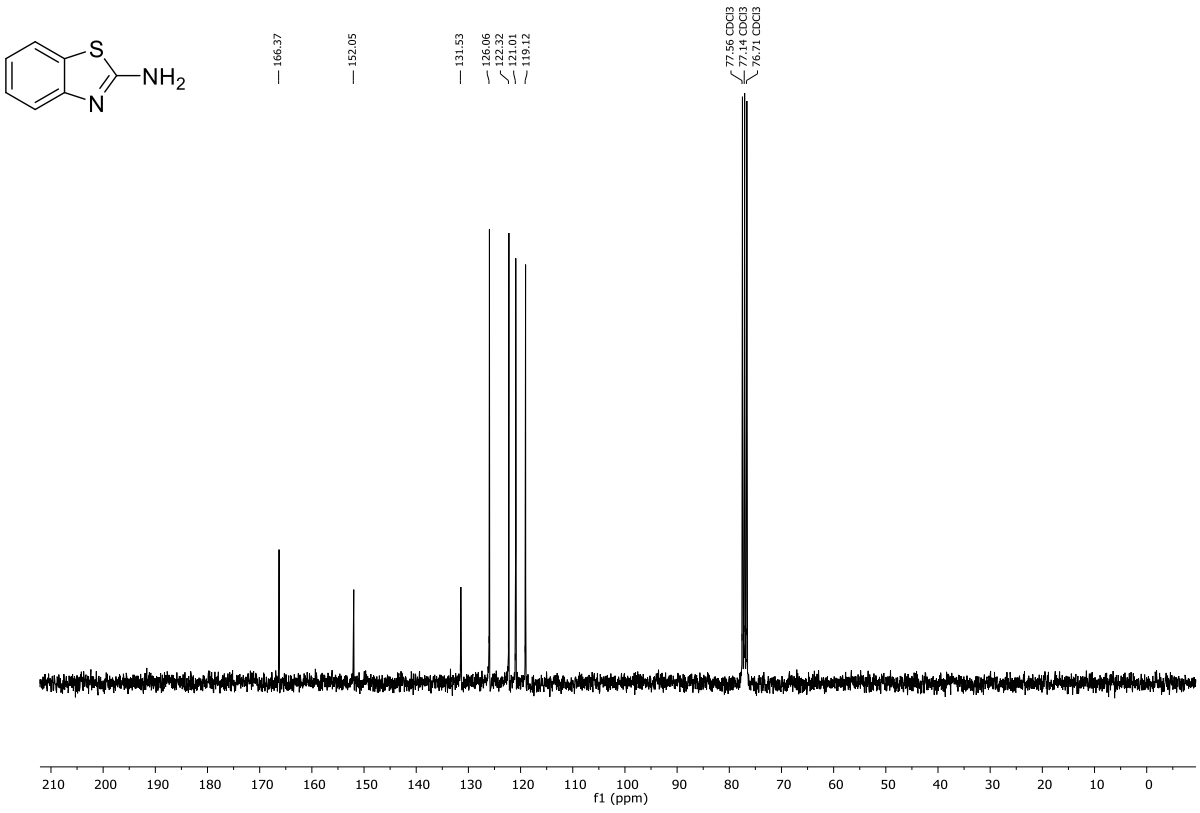

Figure F24: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **26a**.

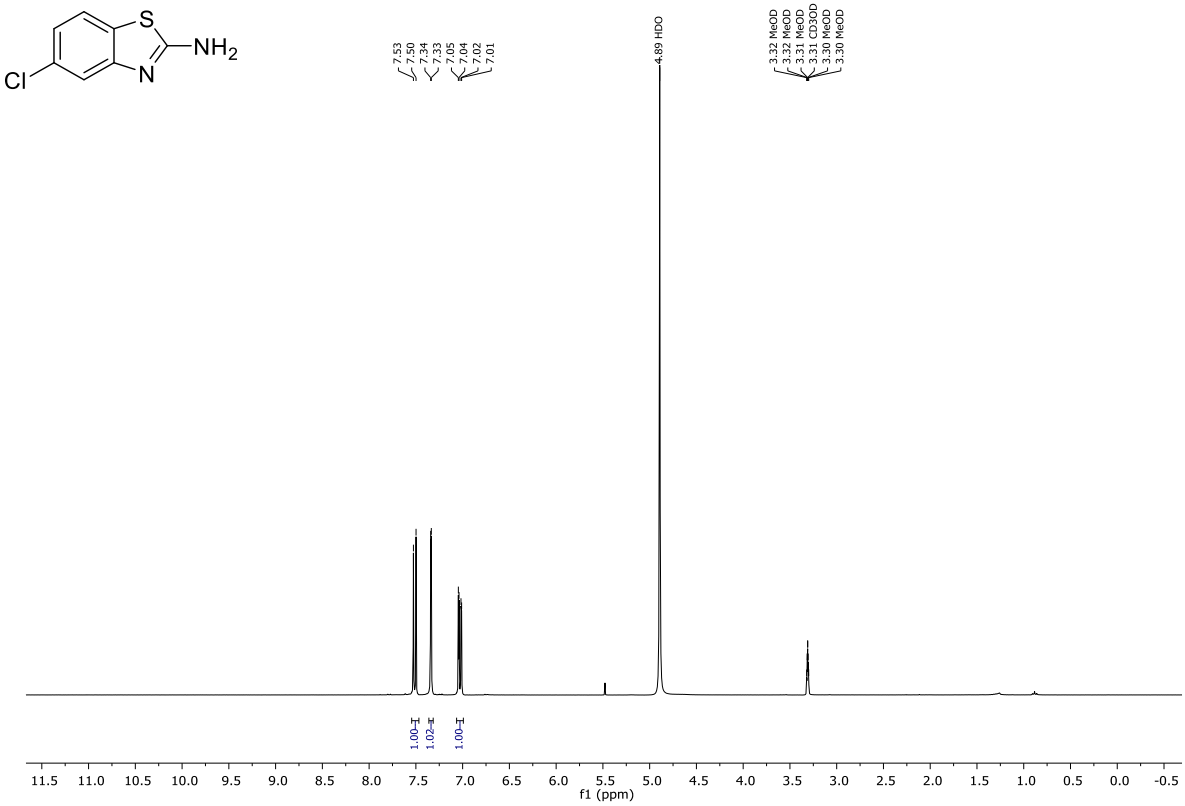

Figure F25: ^{1}H-NMR (MeOH-d_4, 300 MHz) of compound **27a**.

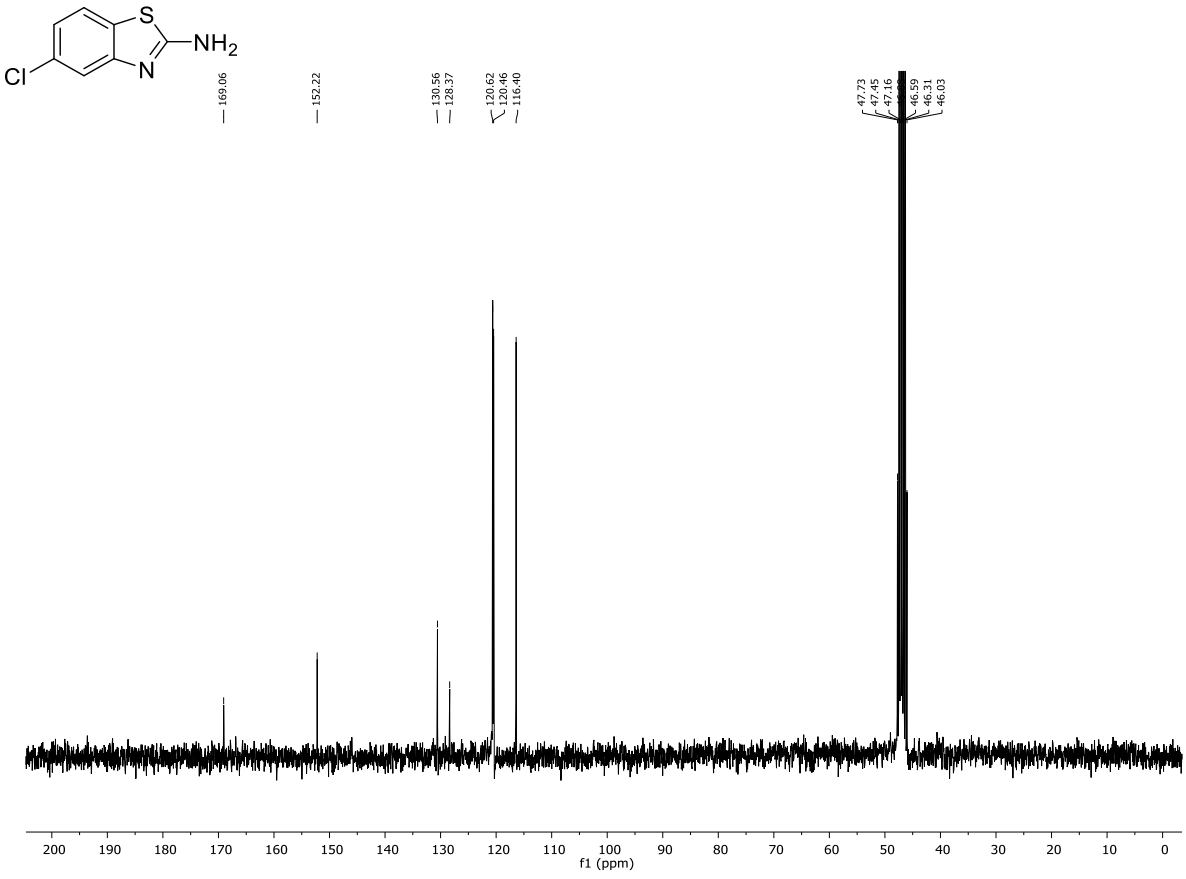

Figure F26: ^{13}C-NMR (MeOH-d_4, 75 MHz) of compound **27a**.

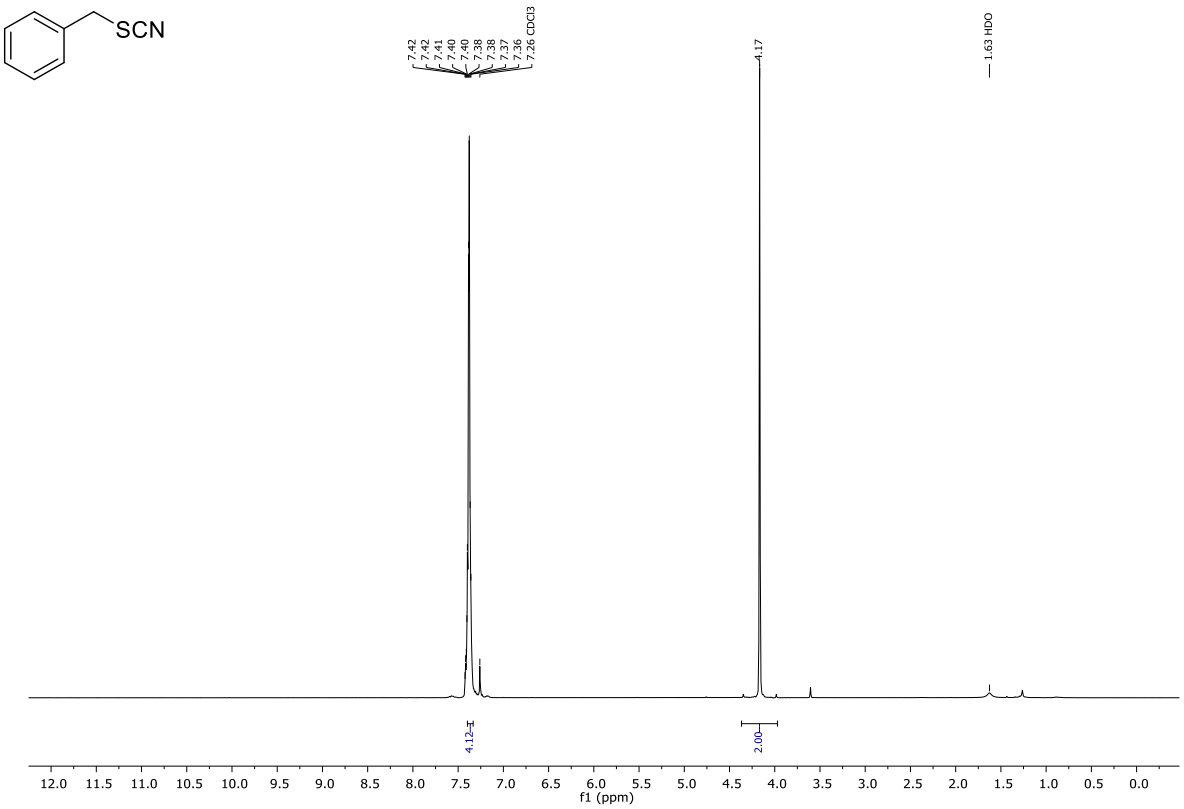

Figure F27: ^{1}H-NMR ($CDCl_3$, 400 MHz) of compound **28a**.

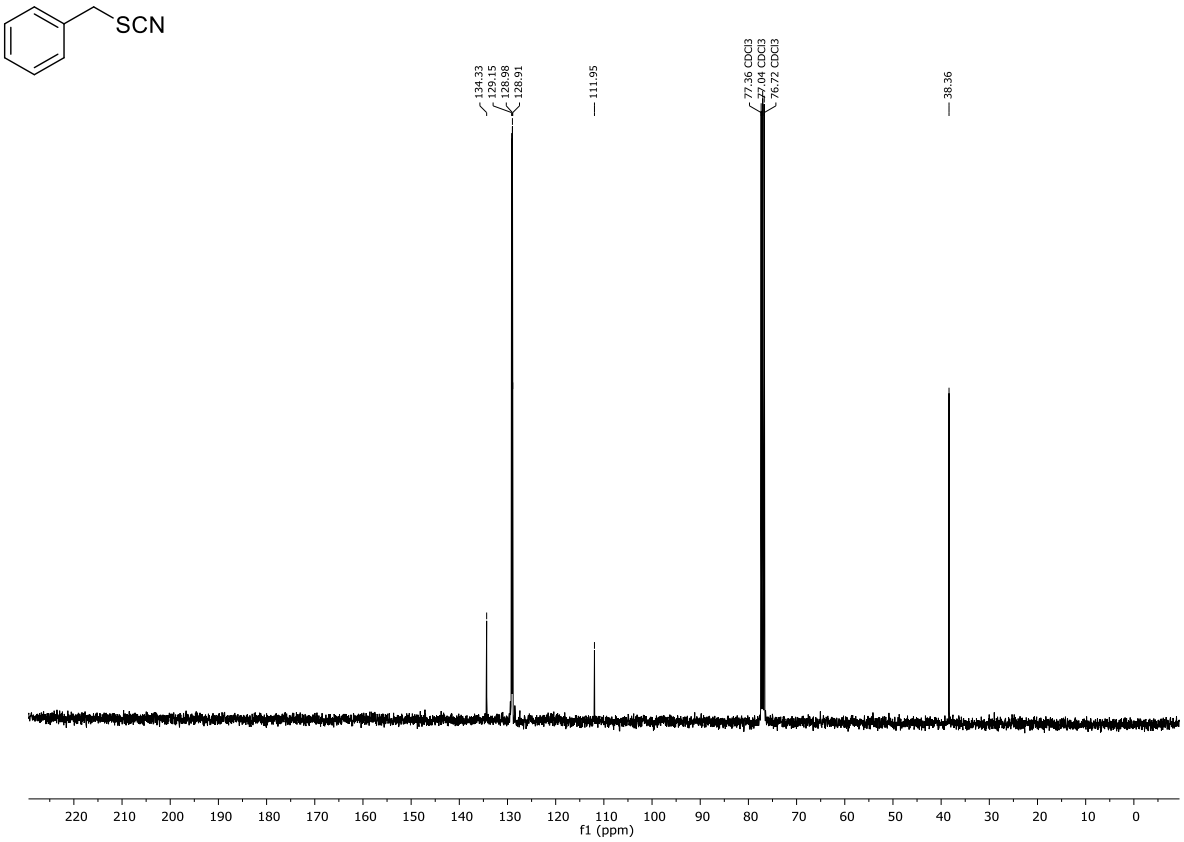

Figure F28: ^{13}C-NMR ($CDCl_3$, 101 MHz) of compound **28a**.

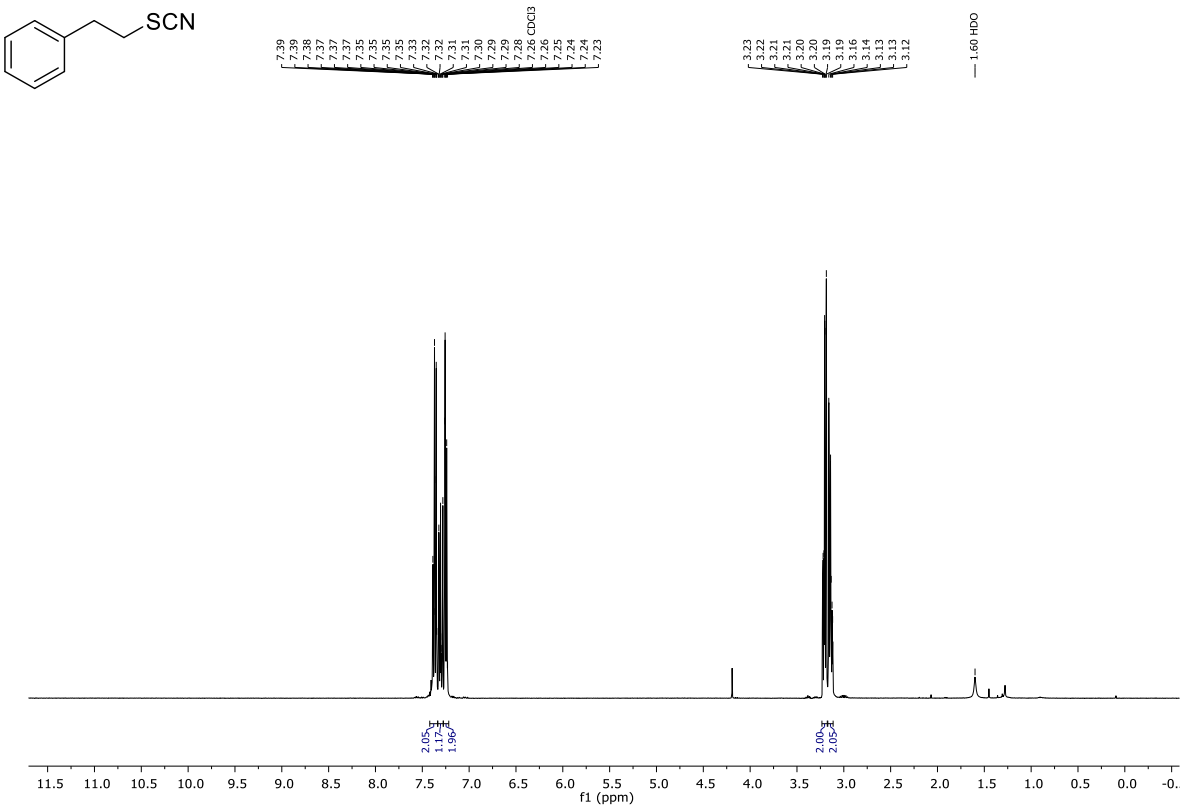

Figure F29: ^{1}H-NMR ($CDCl_3$, 400 MHz) of compound **29a**.

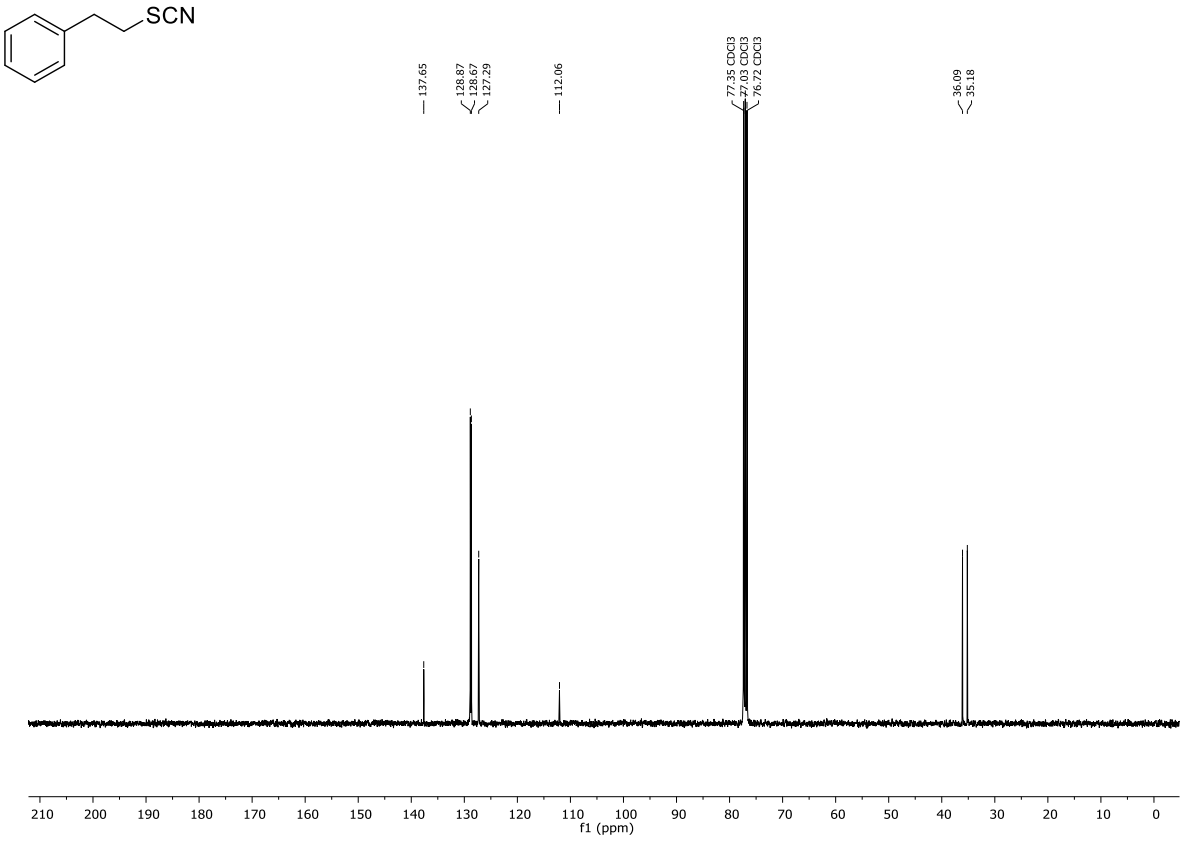

Figure F30: ^{13}C-NMR ($CDCl_3$, 101 MHz) of compound **29a**.

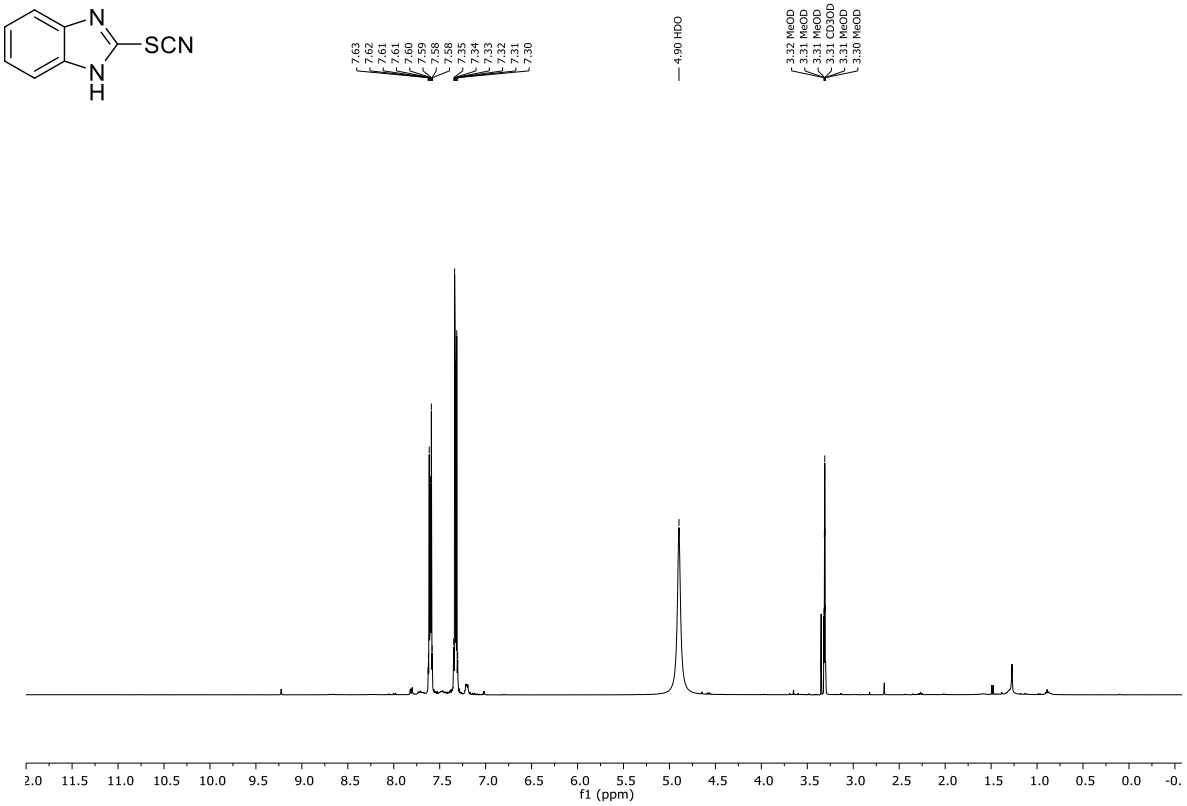

Figure F31: ^{1}H-NMR (MeOH-d_4, 400 MHz) of compound **32a**.

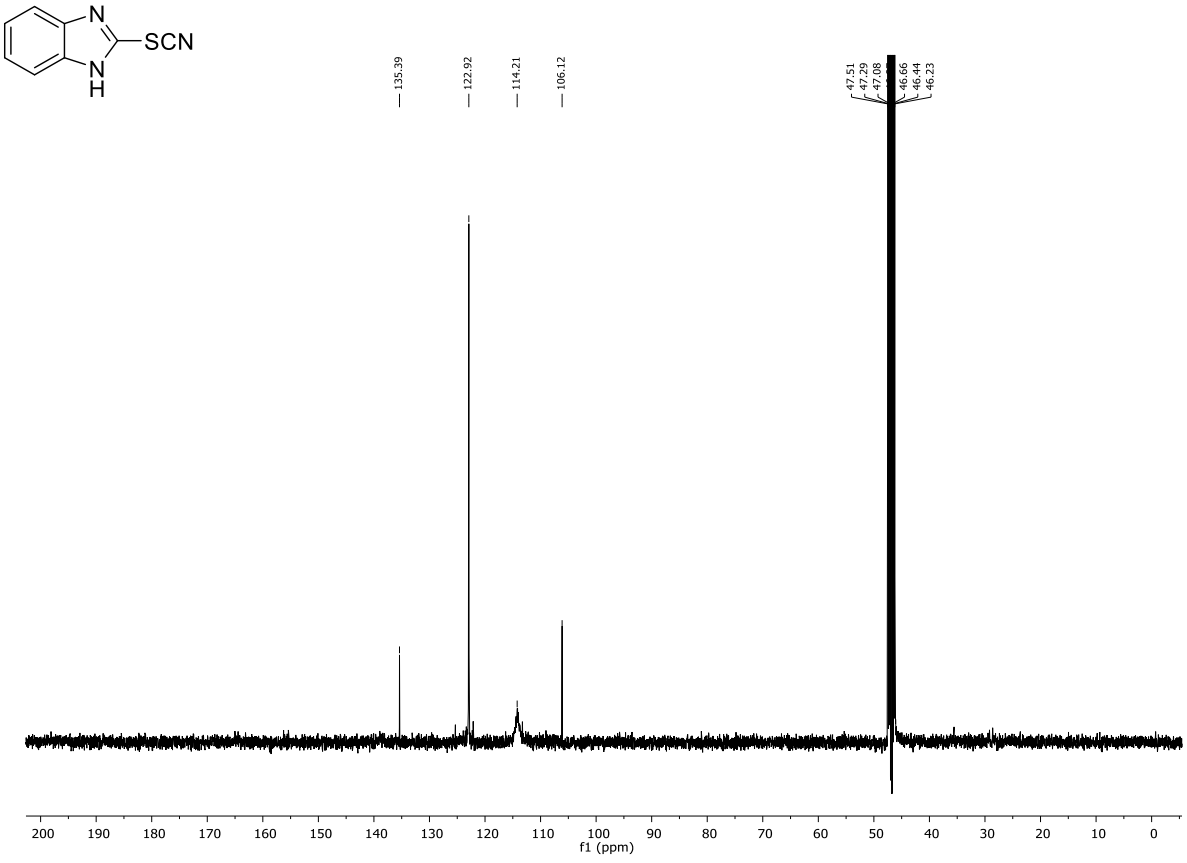

Figure F32: ^{13}C-NMR (MeOH-d_4, 101 MHz) of compound **32a**.

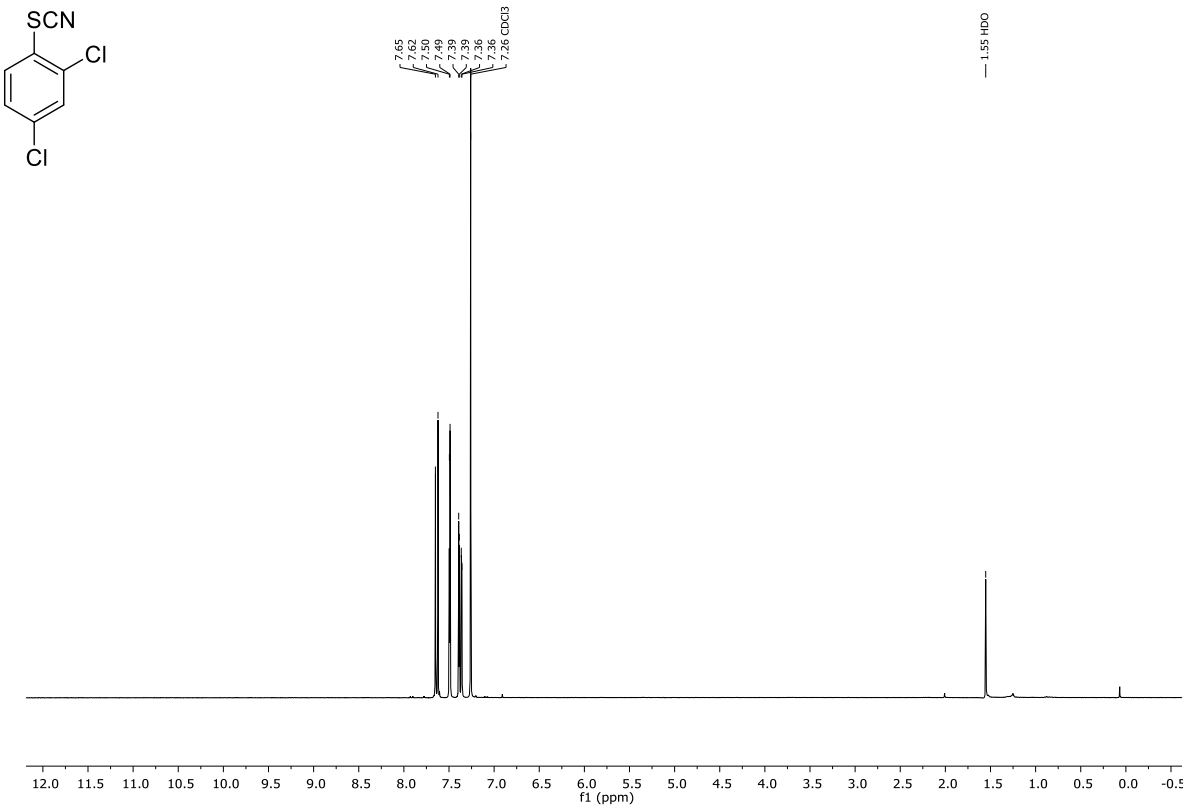

Figure F33: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **33a**.

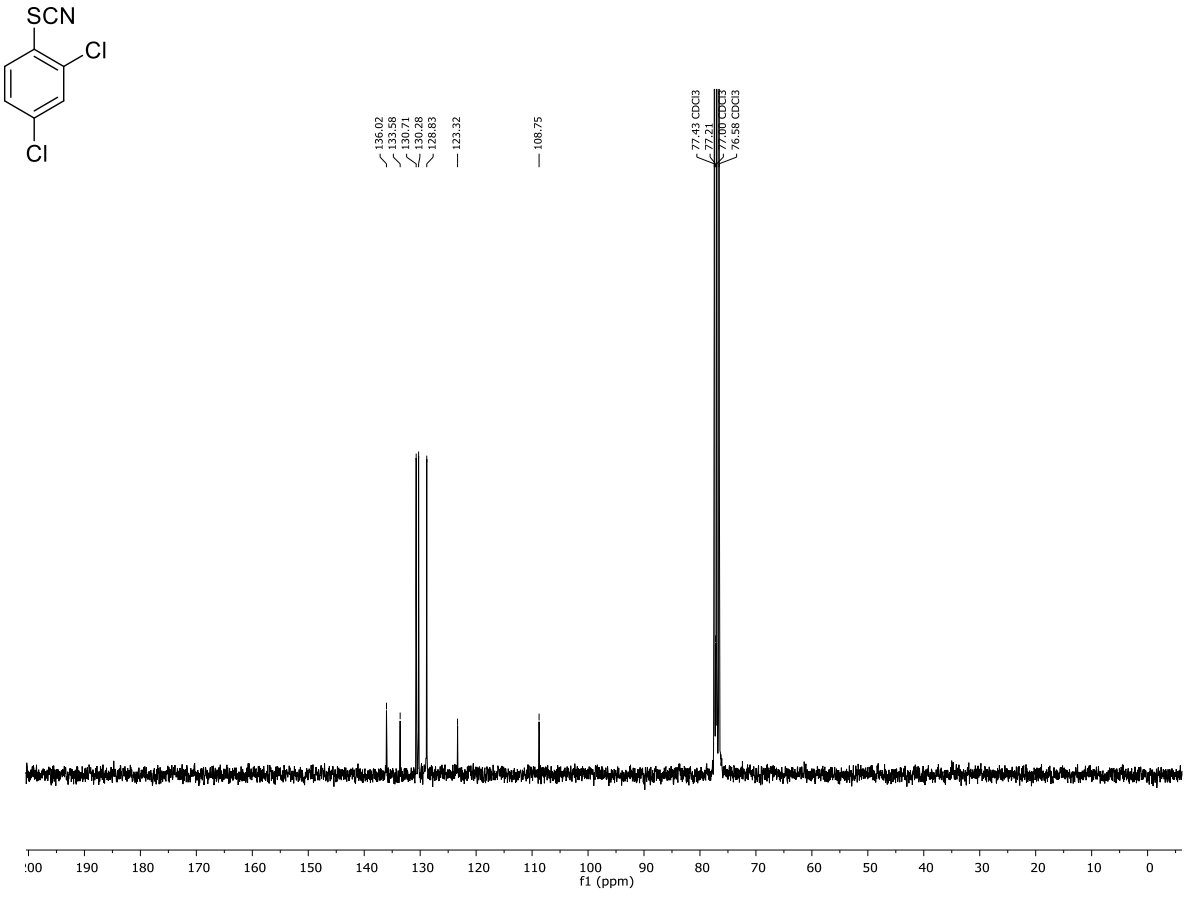

Figure F34: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **33a**.

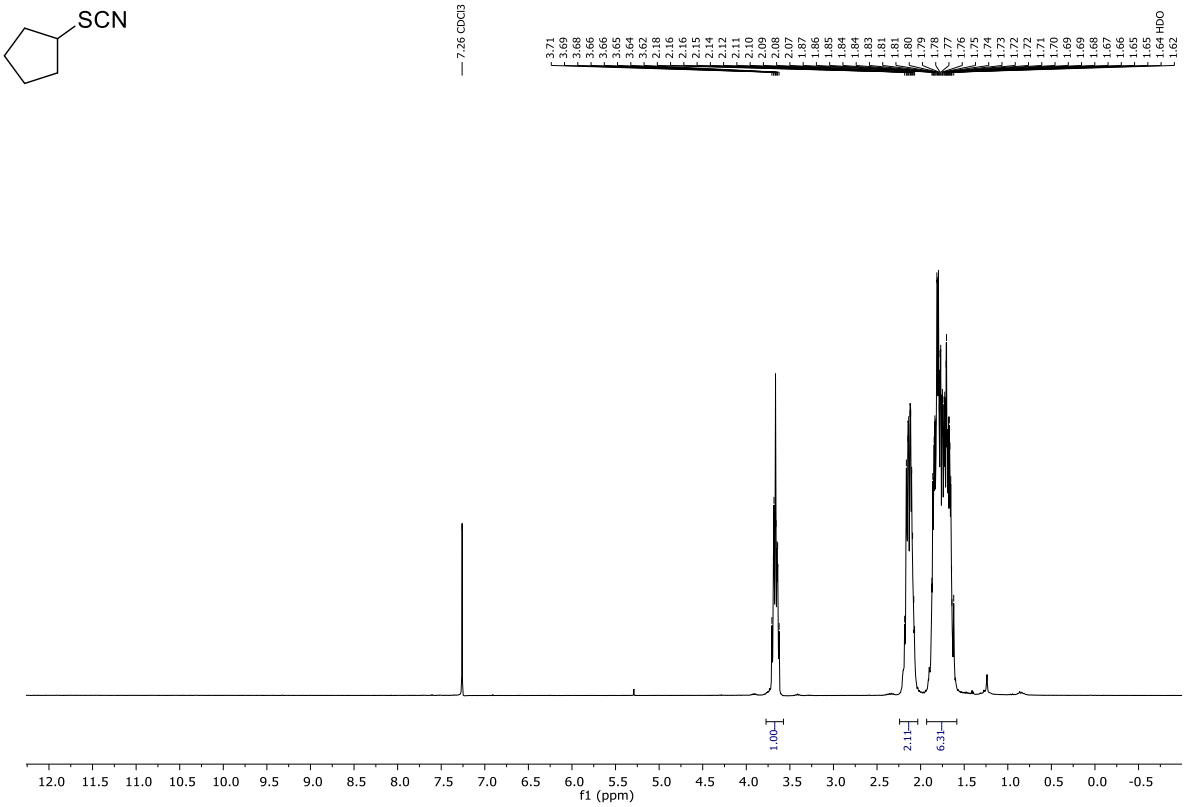

Figure F35: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **34a**.

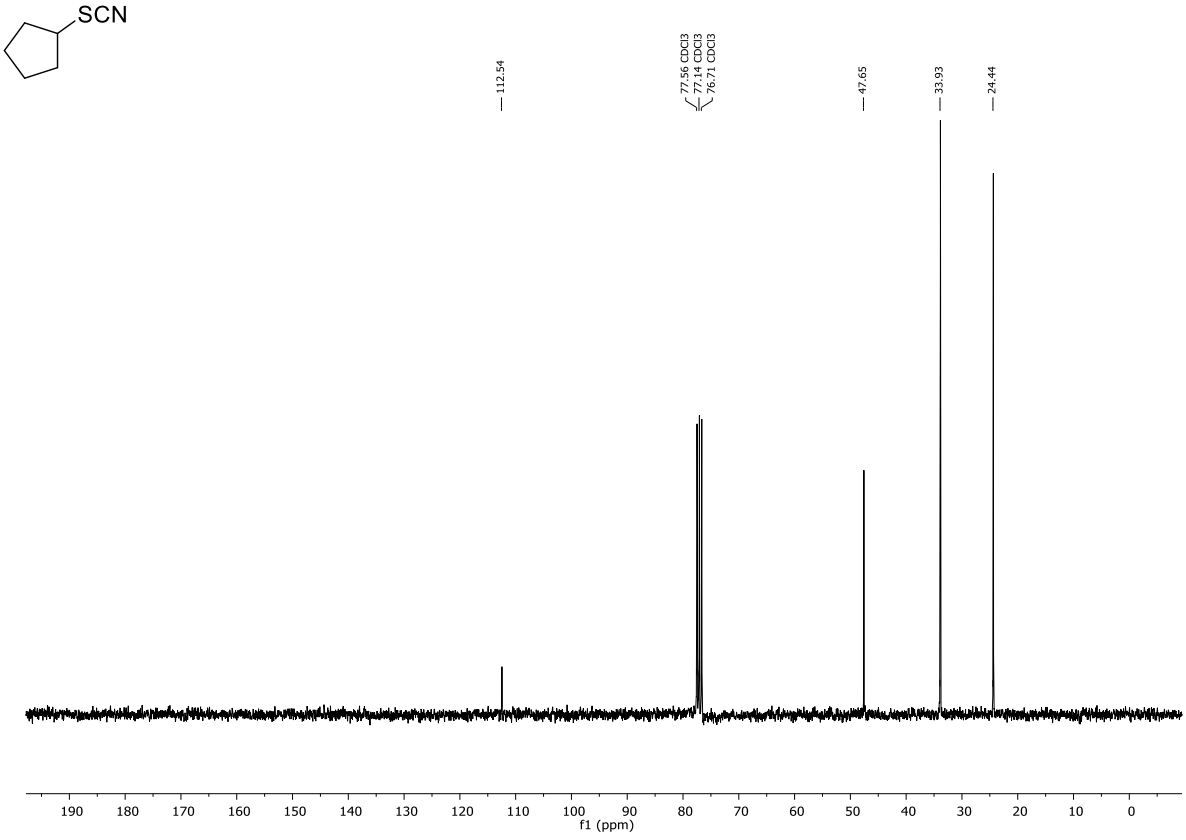

Figure F36: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **34a**.

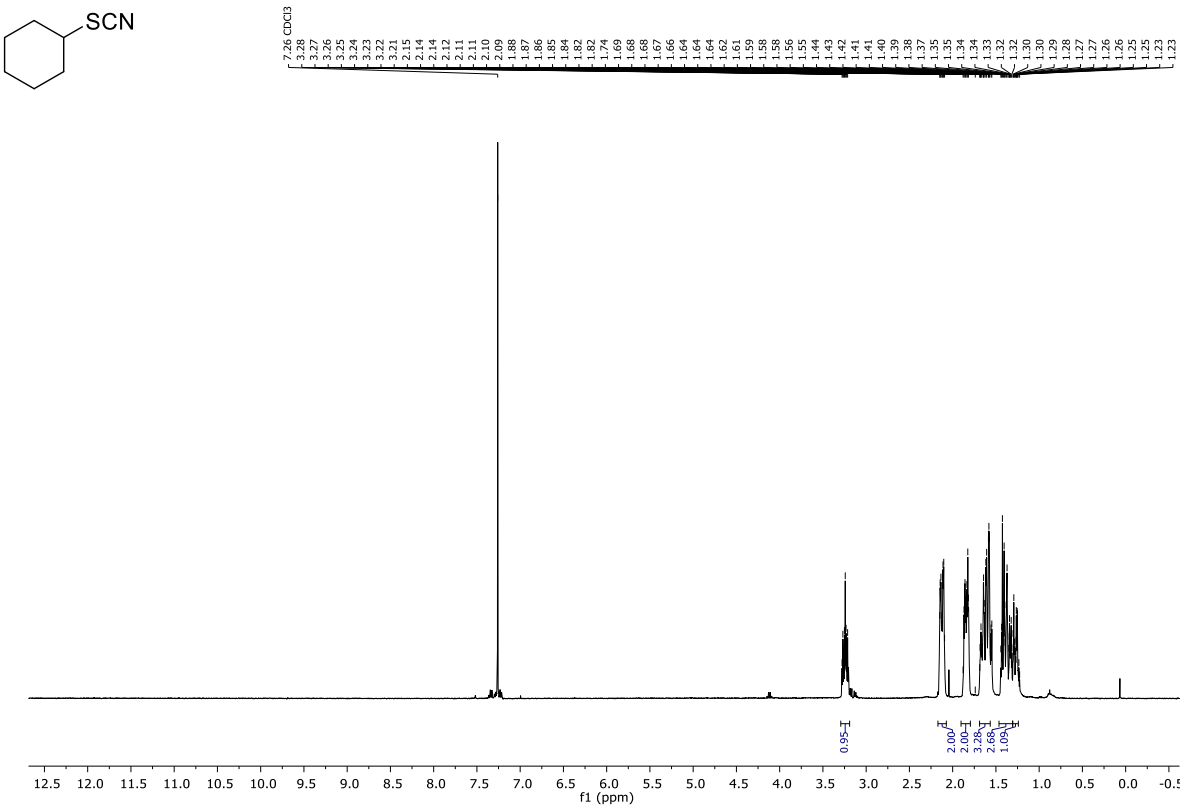

Figure F37: ^{1}H-NMR ($CDCl_3$, 400 MHz) of compound **35a**.

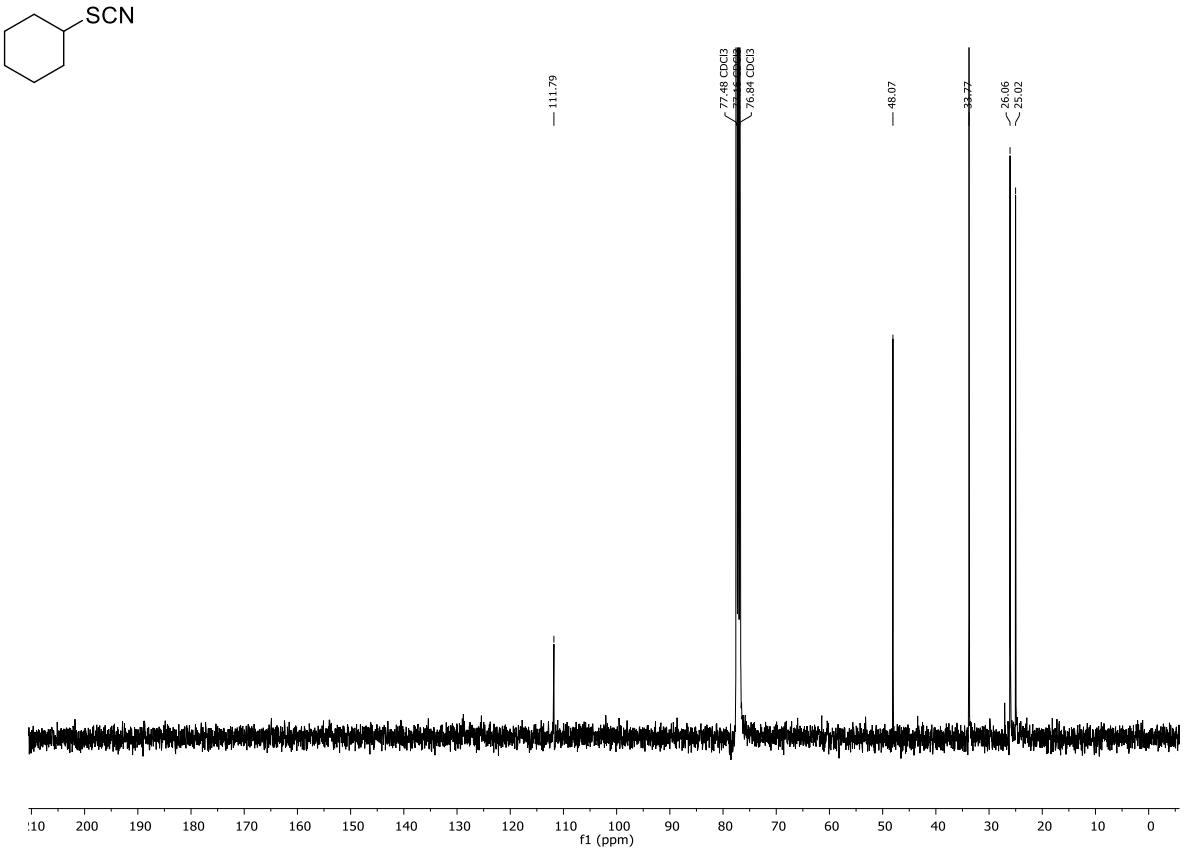

Figure F38: ^{13}C-NMR ($CDCl_3$, 101 MHz) of compound **35a**.

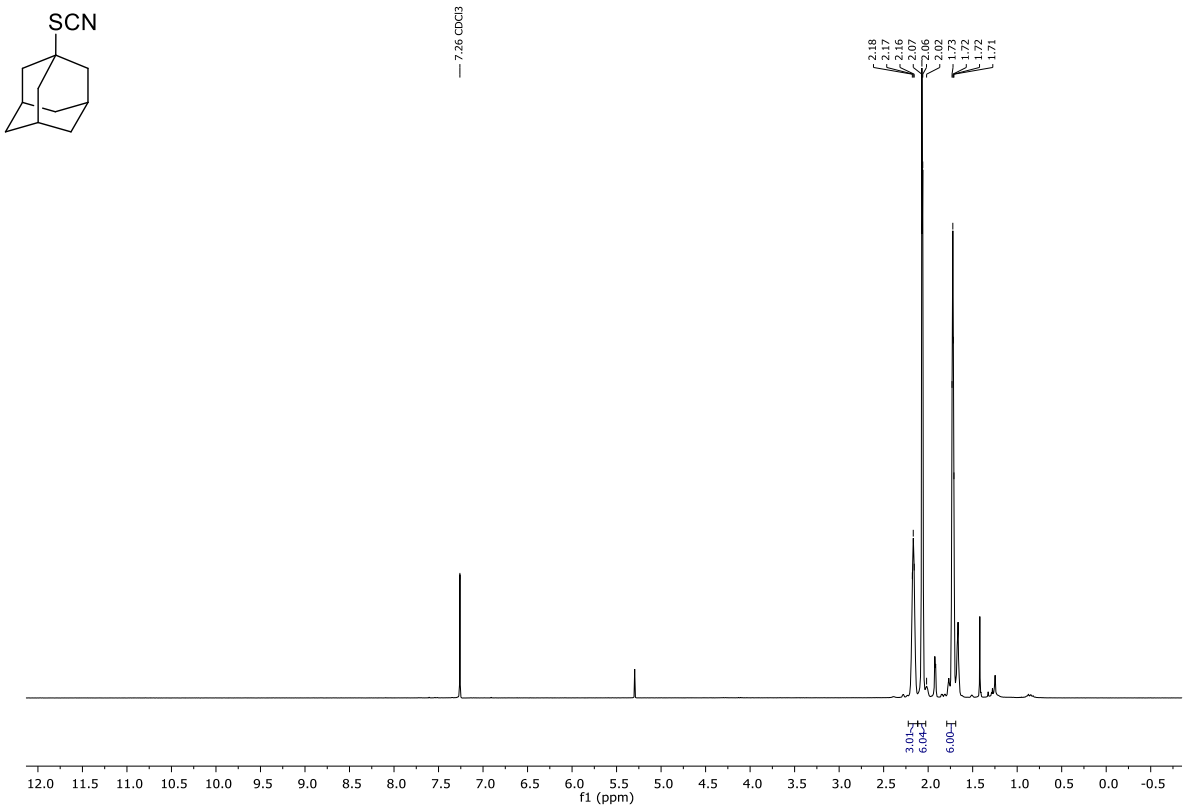

Figure F39: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **36a**.

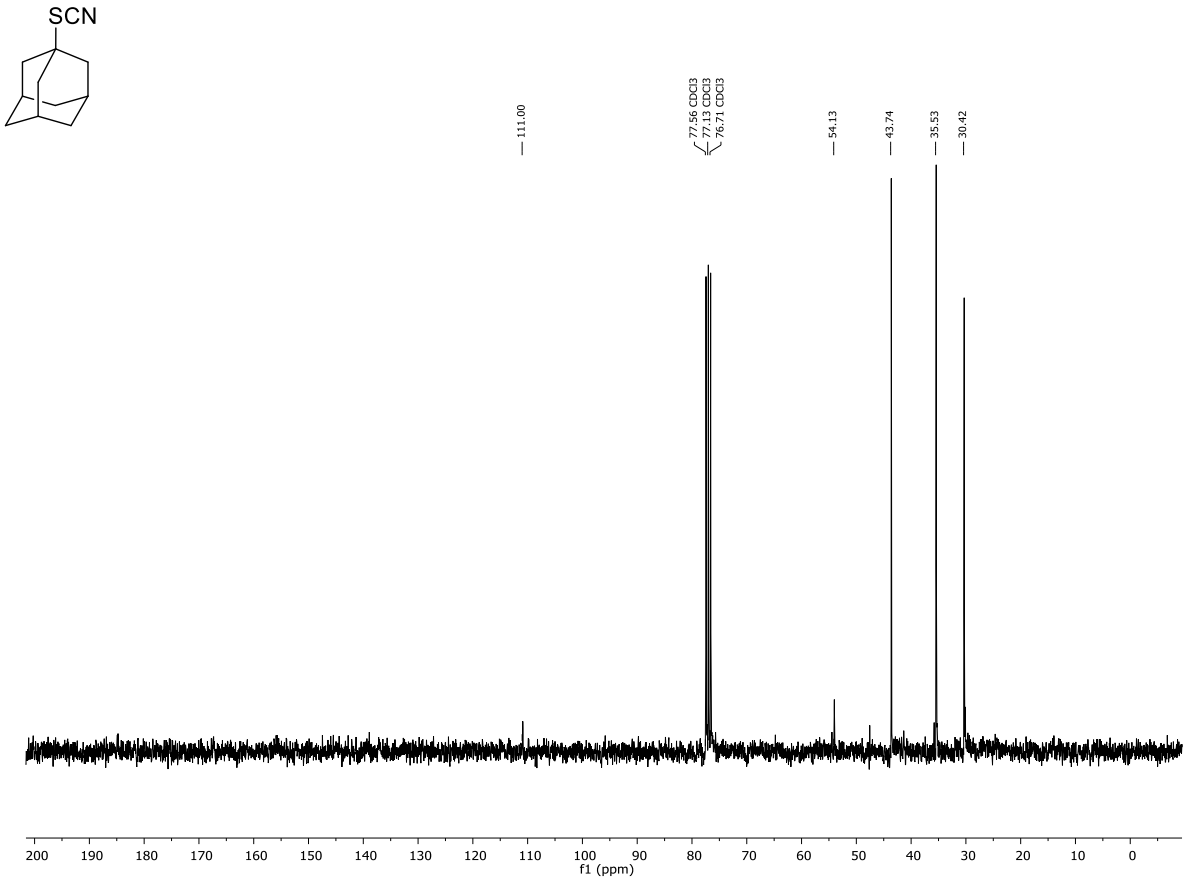

Figure F40: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **36a**.

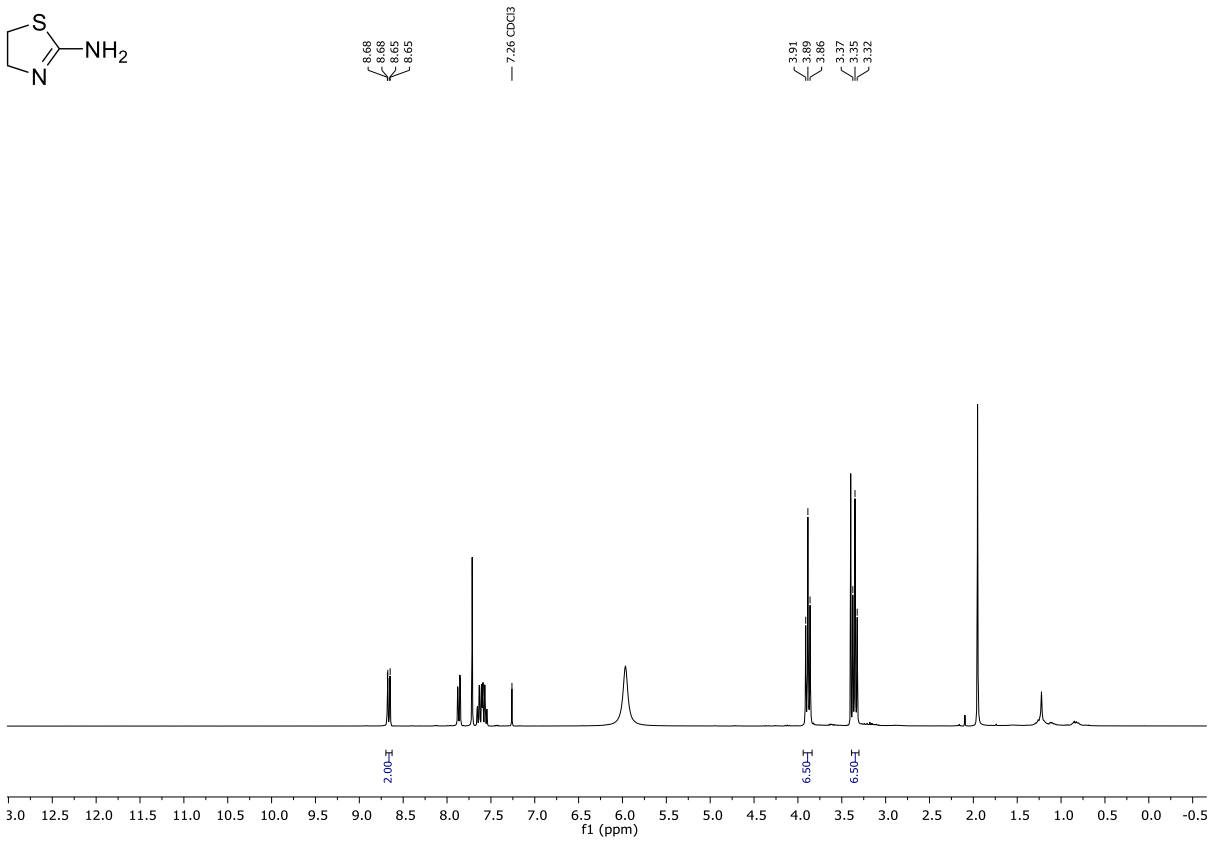

Figure F41*:* ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **37a** with internal standard phenanthrene.

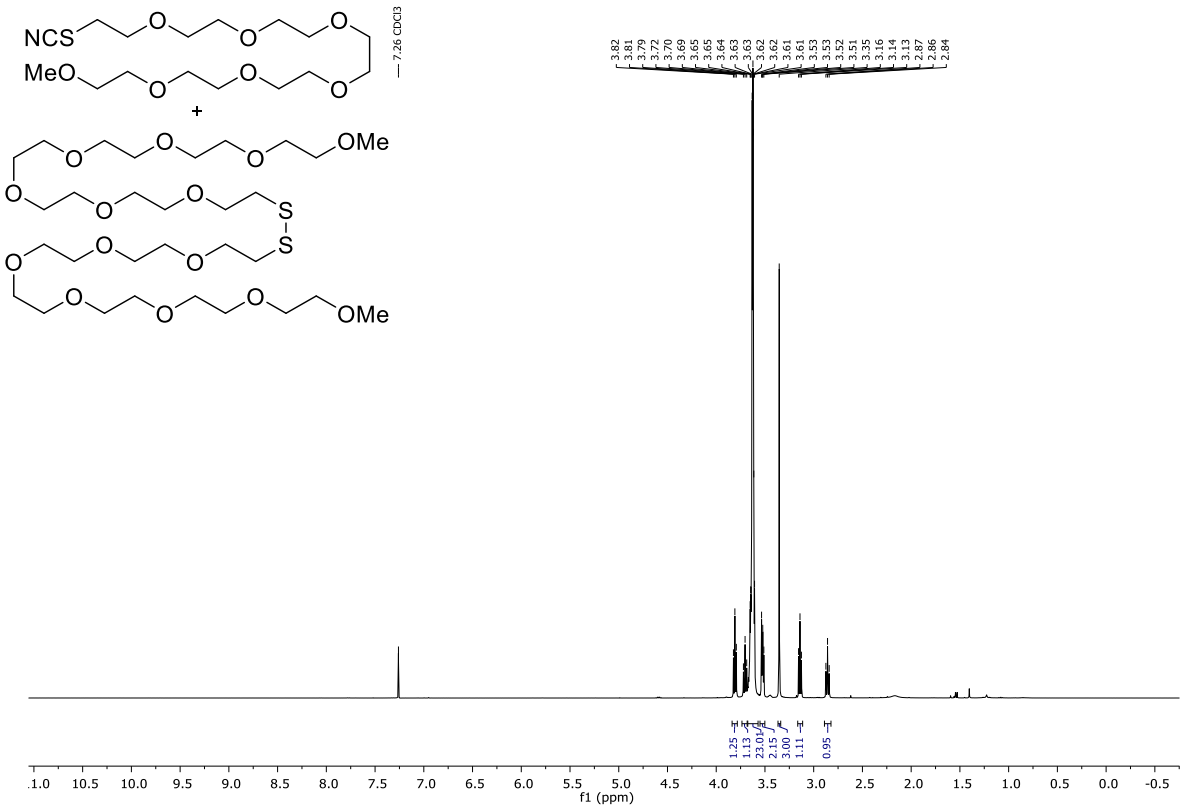

Figure F42*:* ^{1}H-NMR ($CDCl_3$, 400 MHz) of compound **38a**+**38b**.

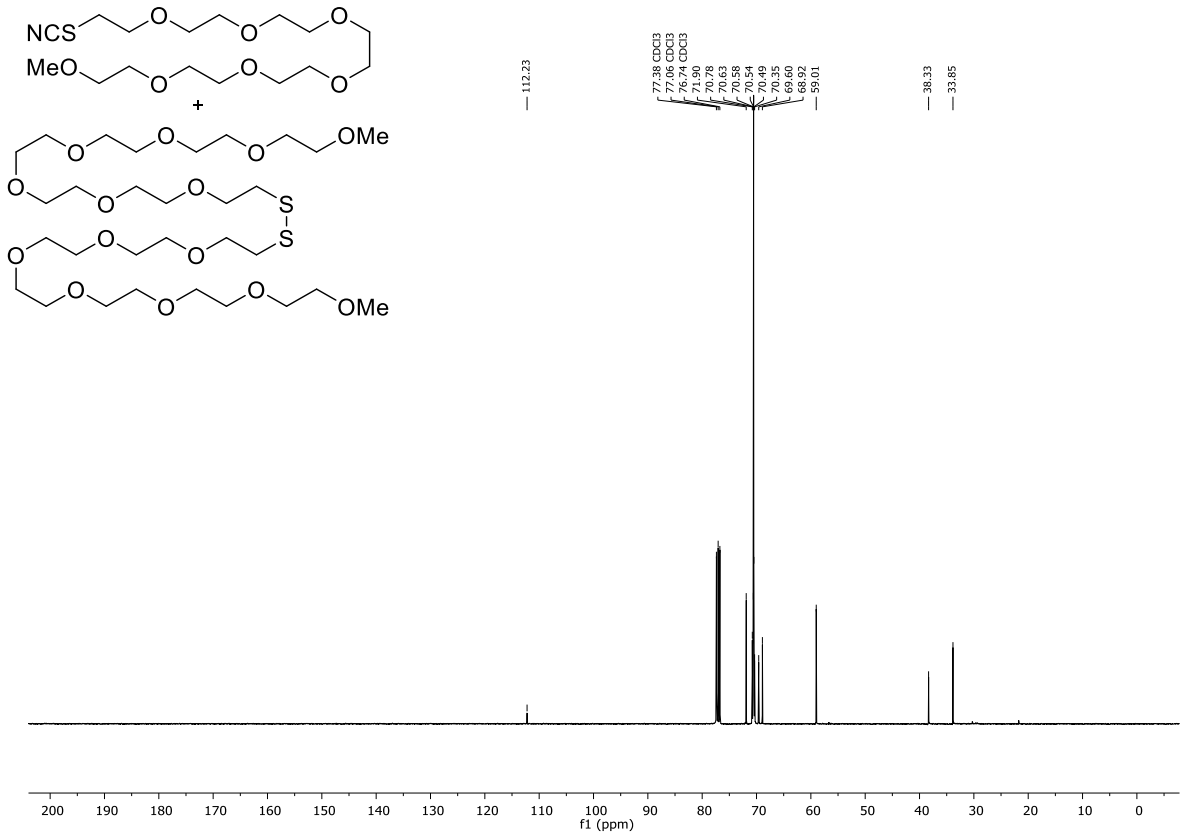

Figure F43: ^{13}C-NMR ($CDCl_3$, 101 MHz) of compound **38a**+**38b**.

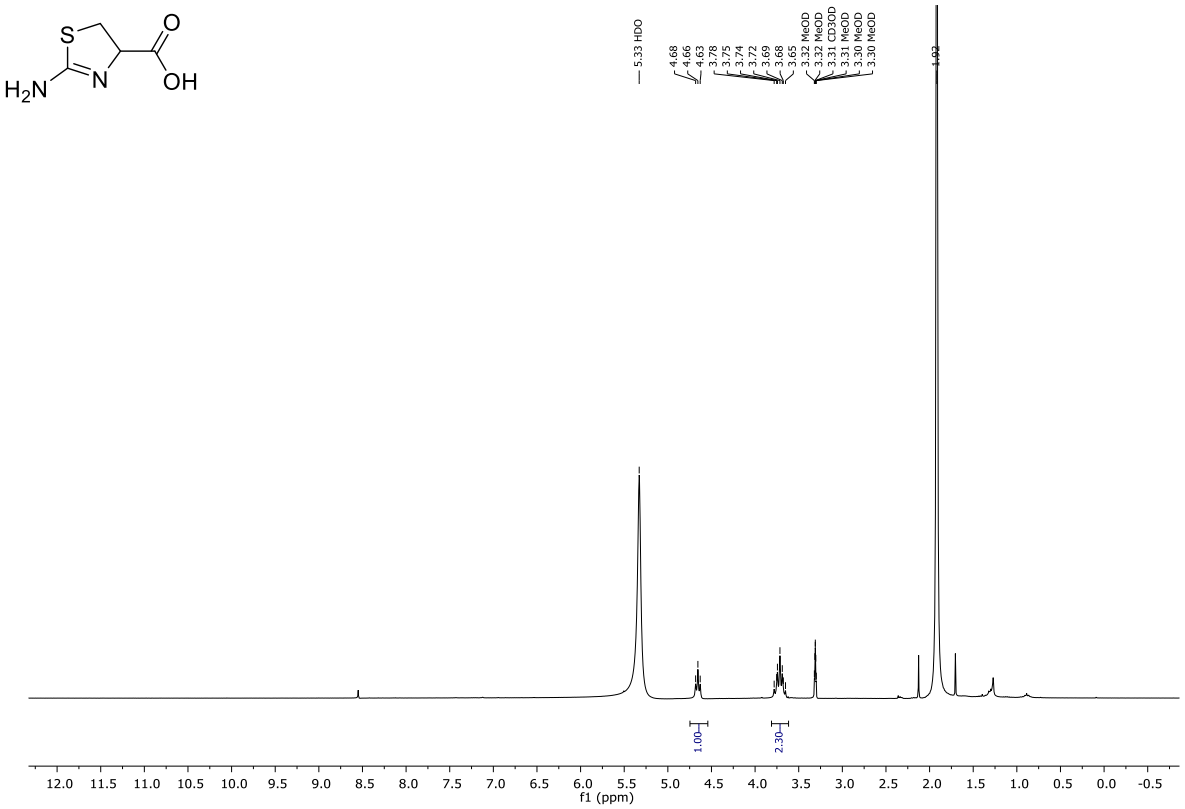

Figure F44: ^{1}H-NMR (MeOH-d_4, 300 MHz) of compound **39a** with HOAc as impurity after continuous extraction with EtOAc.

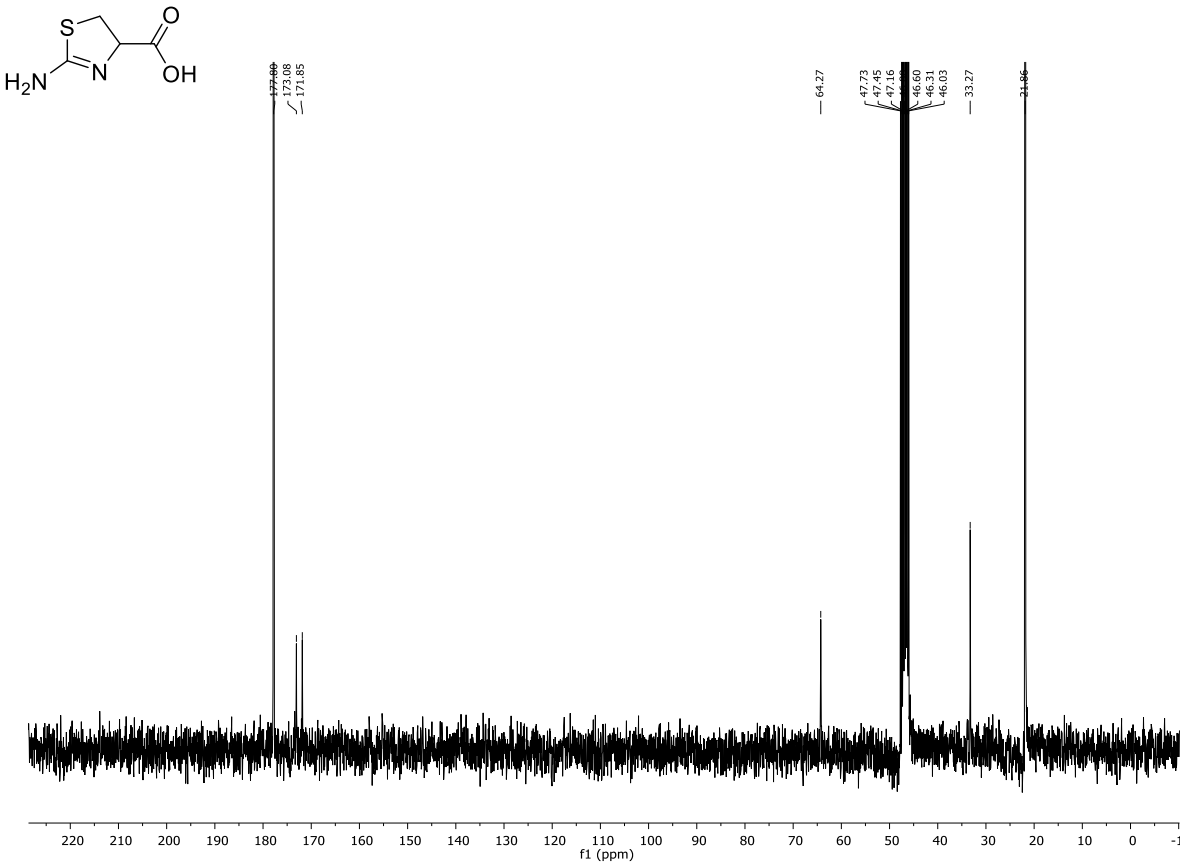

Figure F45: ^{13}C-NMR (MeOH-d_4, 75 MHz) of compound **39a** with HOAc as impurity after continuous extraction with EtOAc.

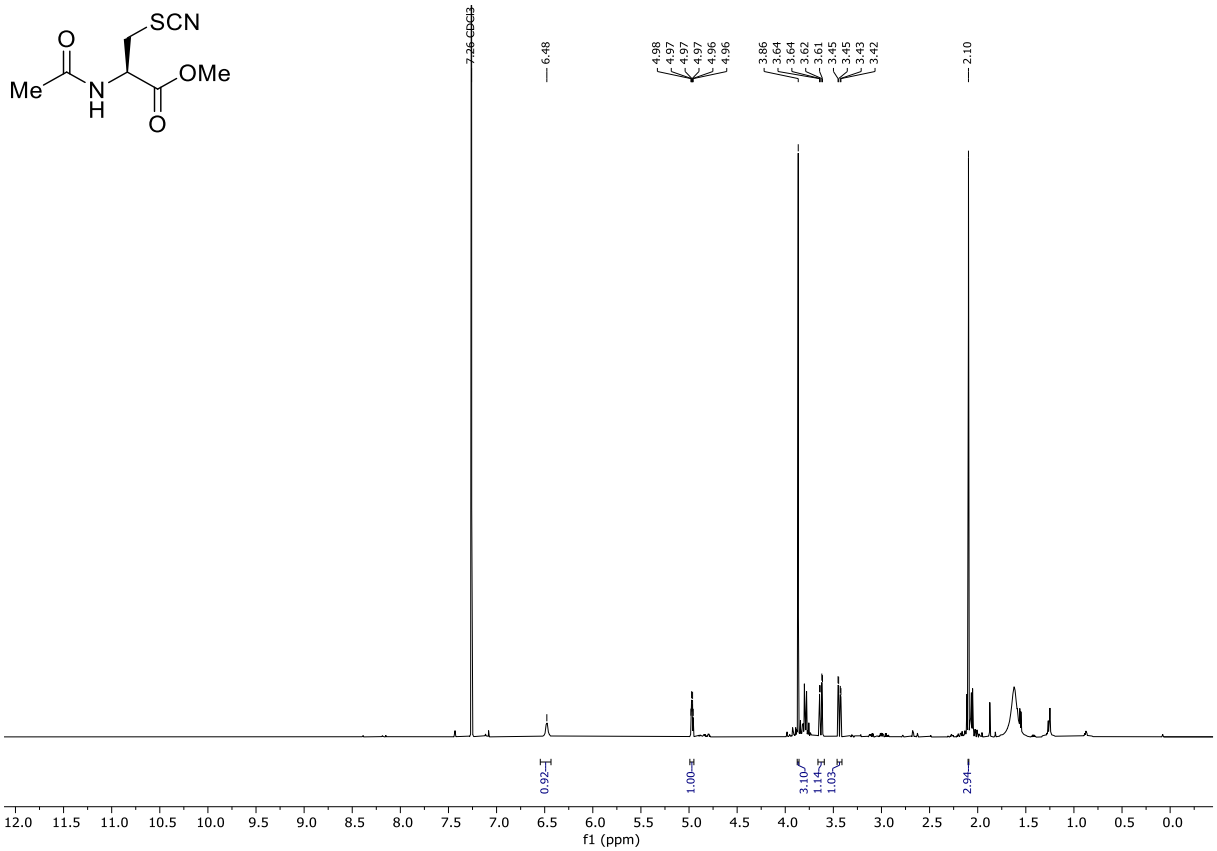

Figure F46: ^{1}H-NMR ($CDCl_3$, 600 MHz) of compound **40a.**

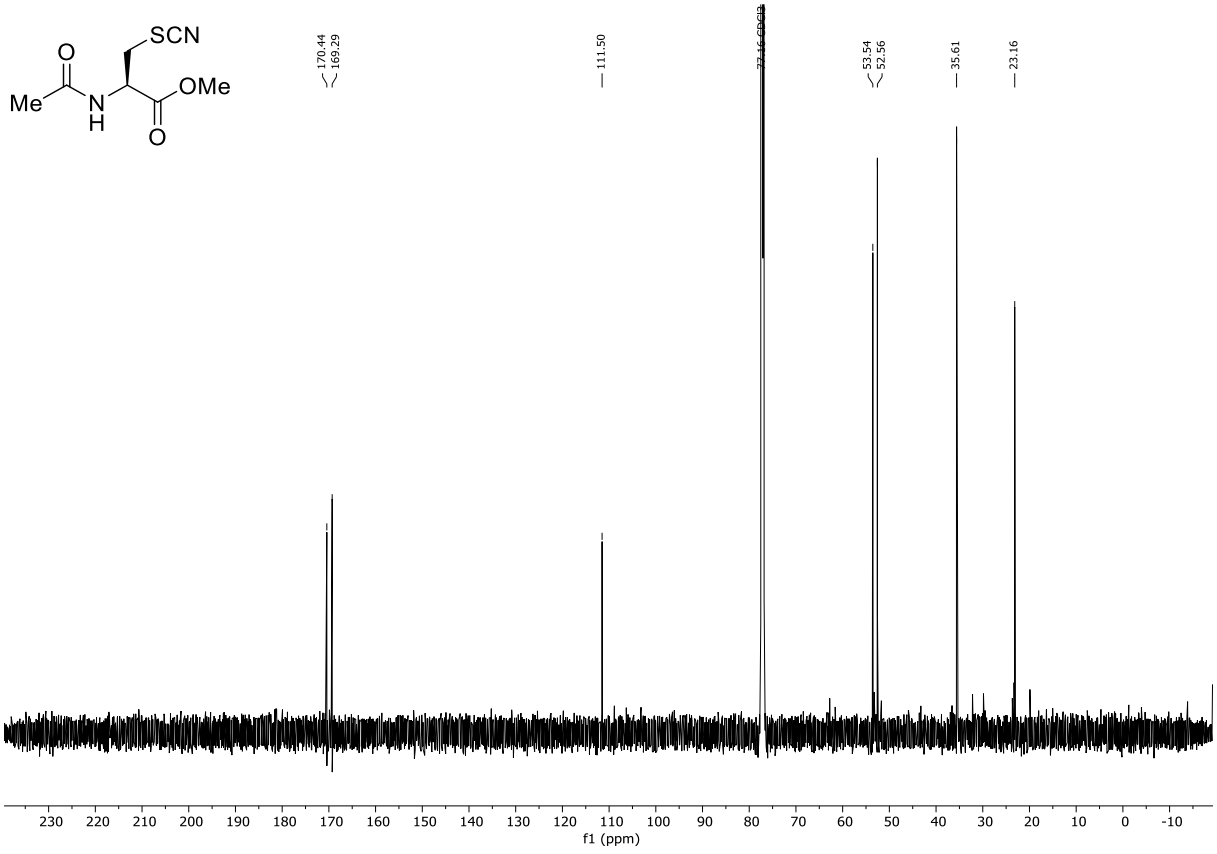

Figure F47: ^{13}C-NMR ($CDCl_3$, 151 MHz) of compound **40a**.

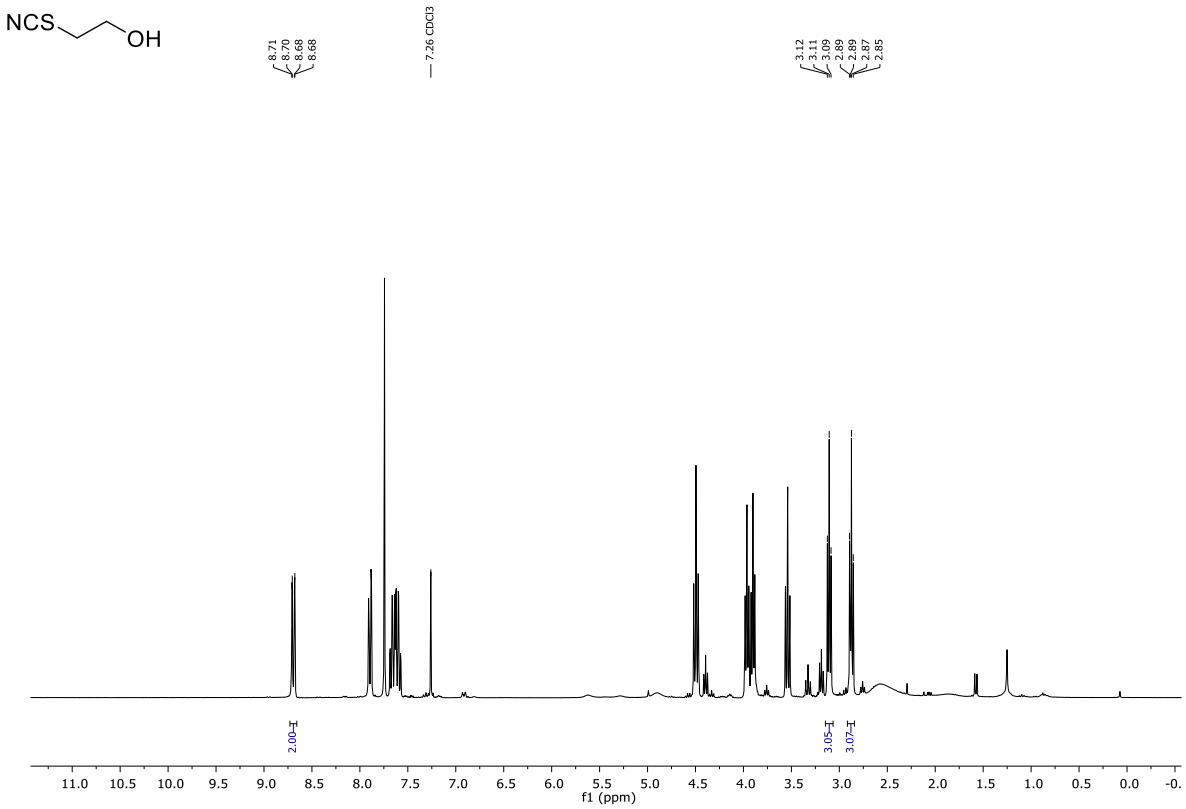

Figure F48: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **41a** with internal standard phenanthrene.

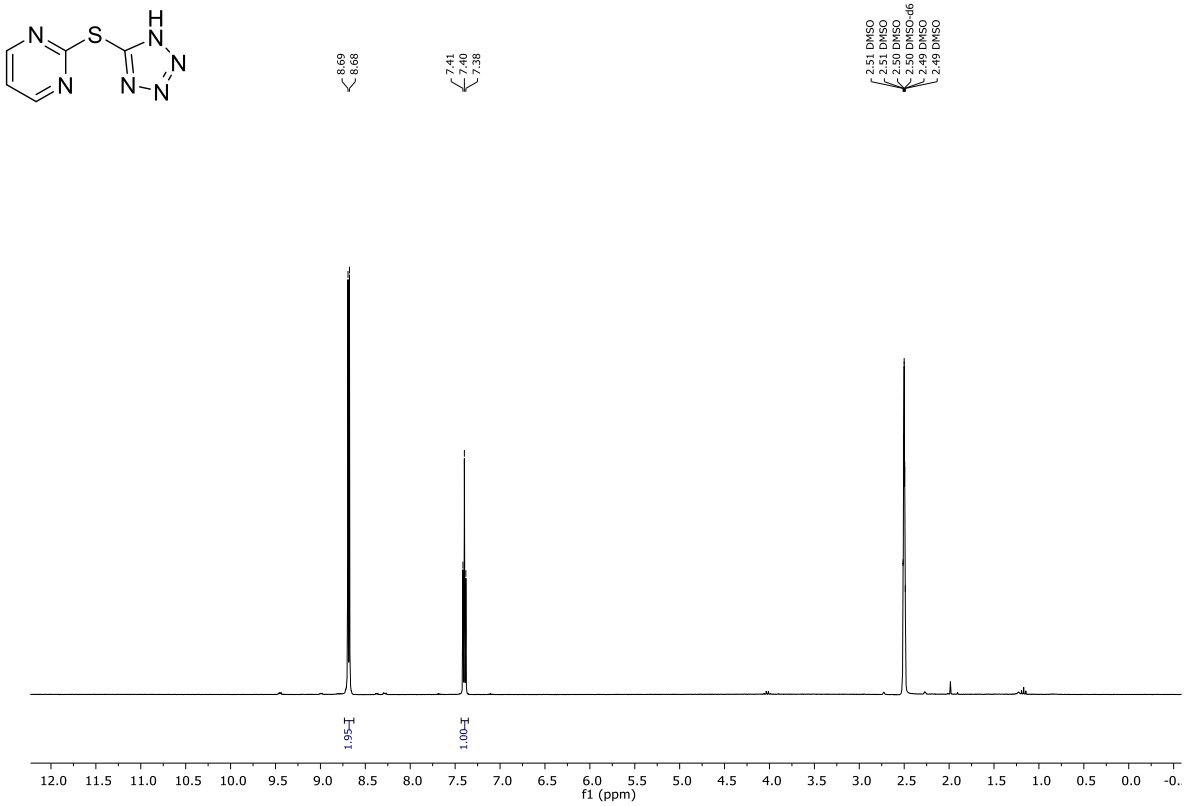

Figure F49: ^{1}H-NMR (DMSO-d_6, 300 MHz) of compound **60**.

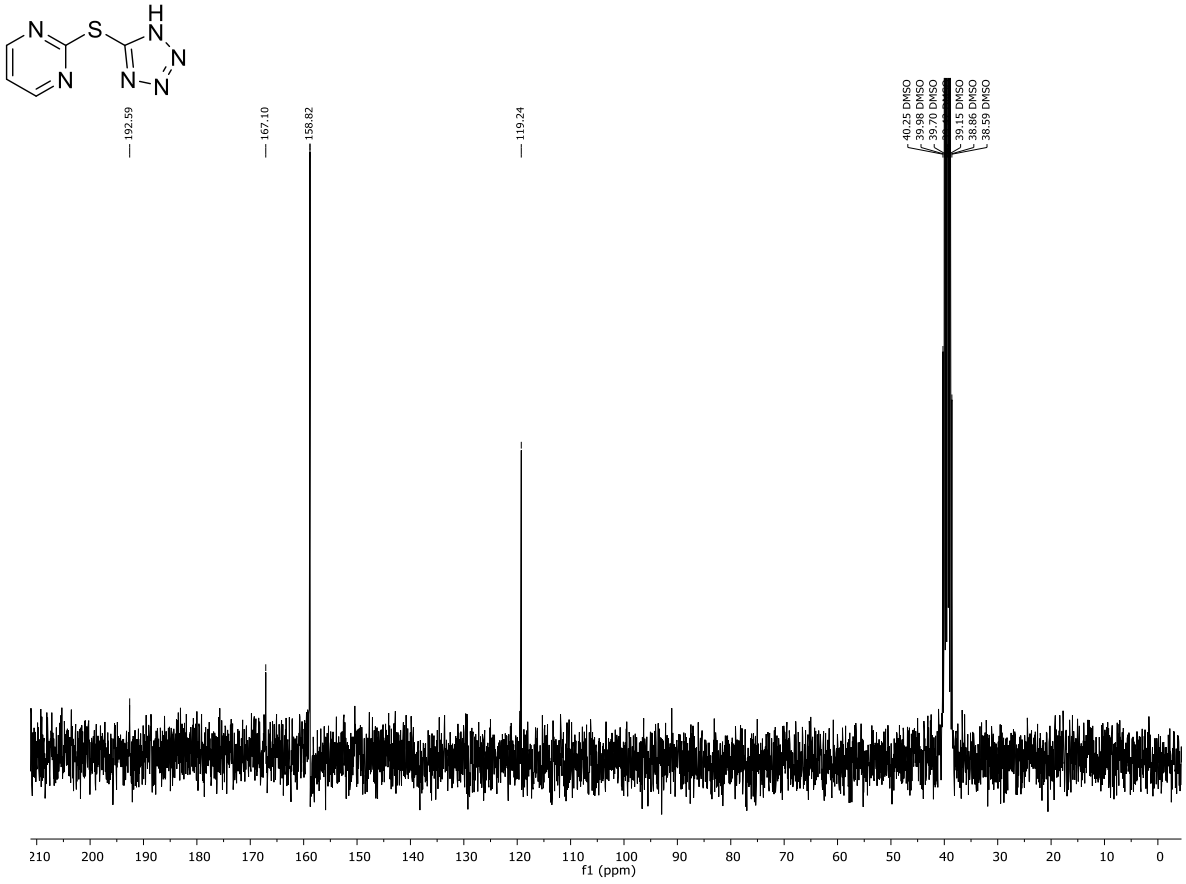

Figure F50: ^{13}C-NMR (DMSO-d_6, 75 MHz) of compound **60**.

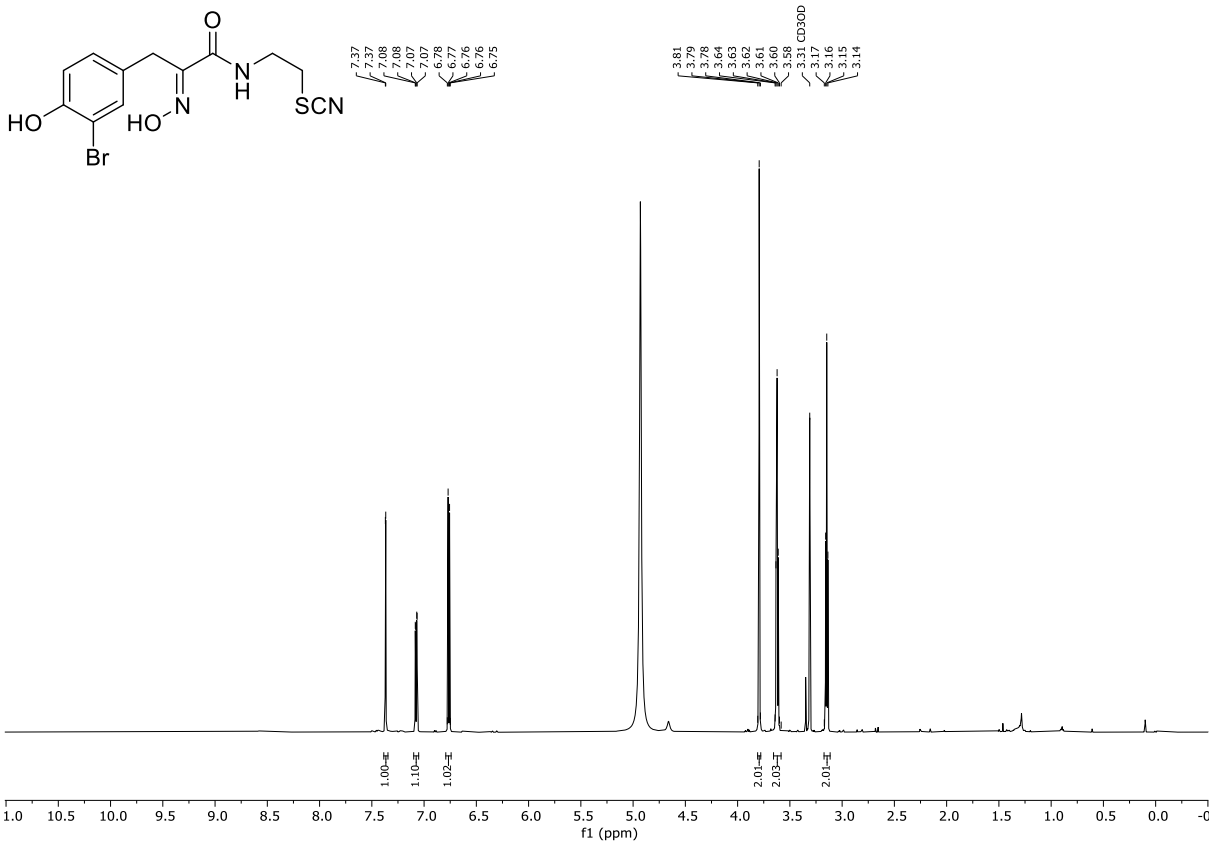

Figure F51: ^{1}H-NMR (MeOH-d_4, 600 MHz) of Psammaplin B (**1**).

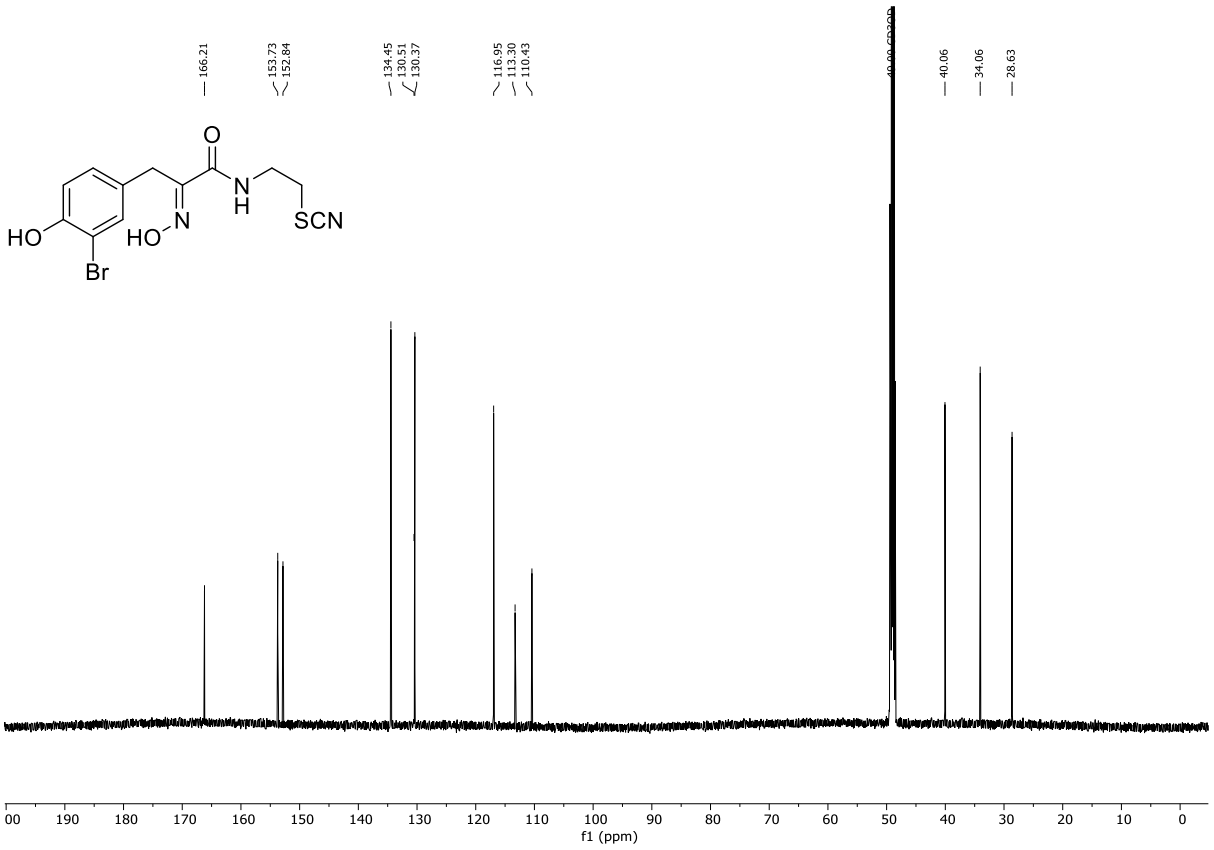

Figure F52: ^{13}C-NMR (MeOH-d_4, 151 MHz) of Psammaplin B (**1**).

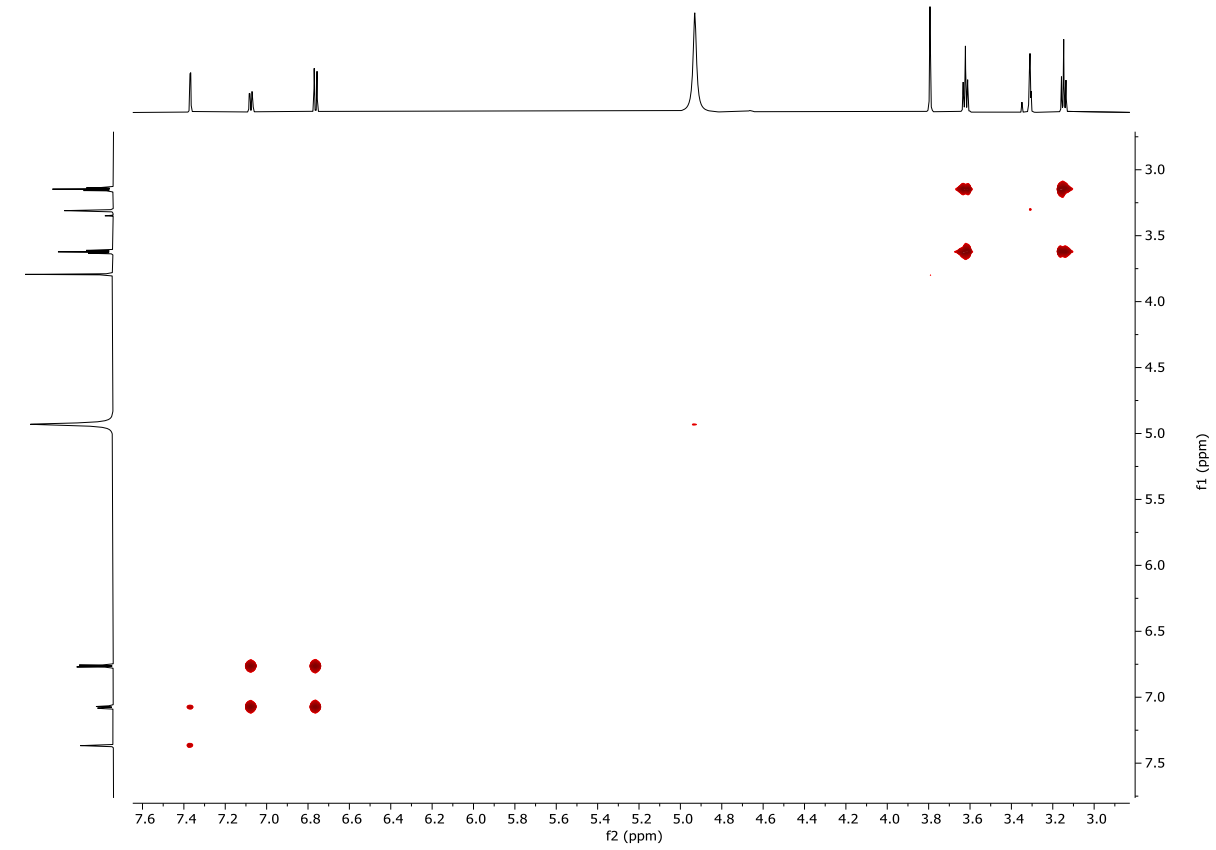

Figure F53: ^{1}H–^{1}H-COSY (MeOH-d_4) of Psammaplin B (**1**).

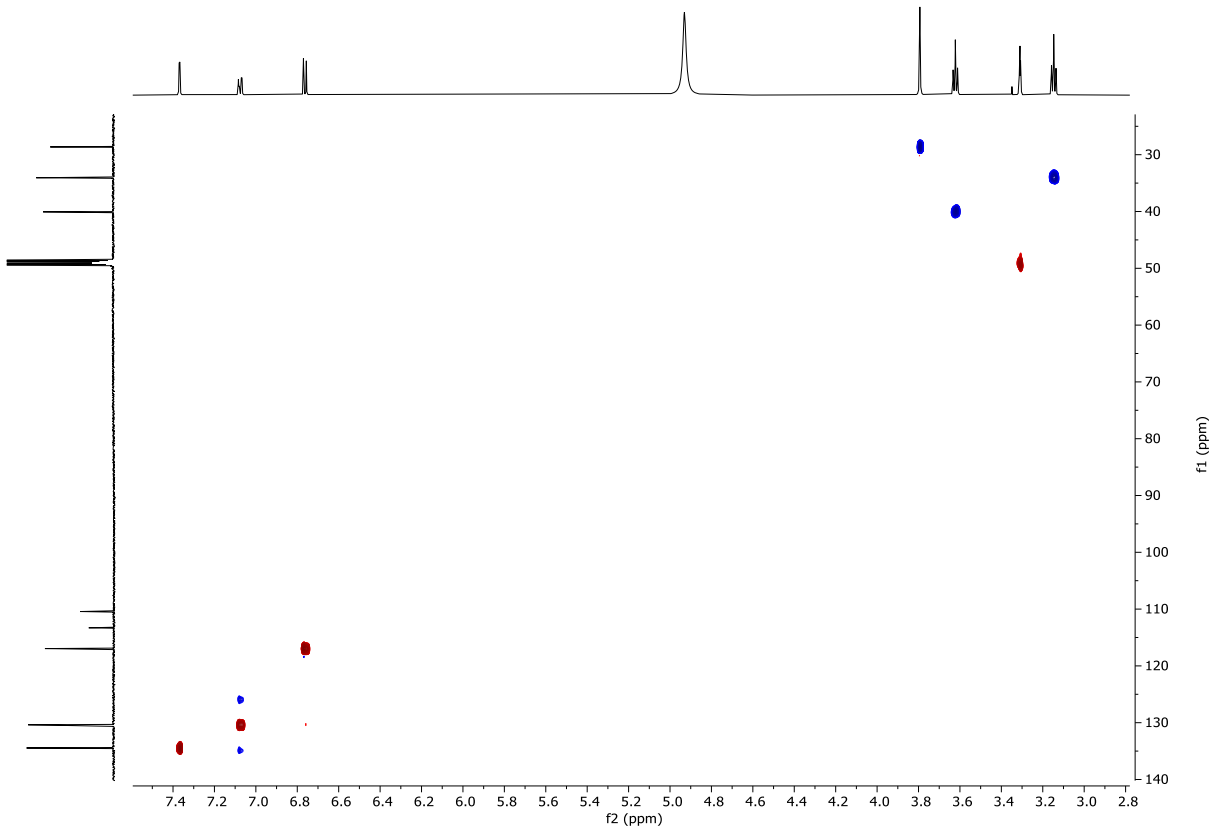

Figure F54: ^{1}H–^{13}C-HSQC (MeOH-d_4) of Psammaplin B (**1**).

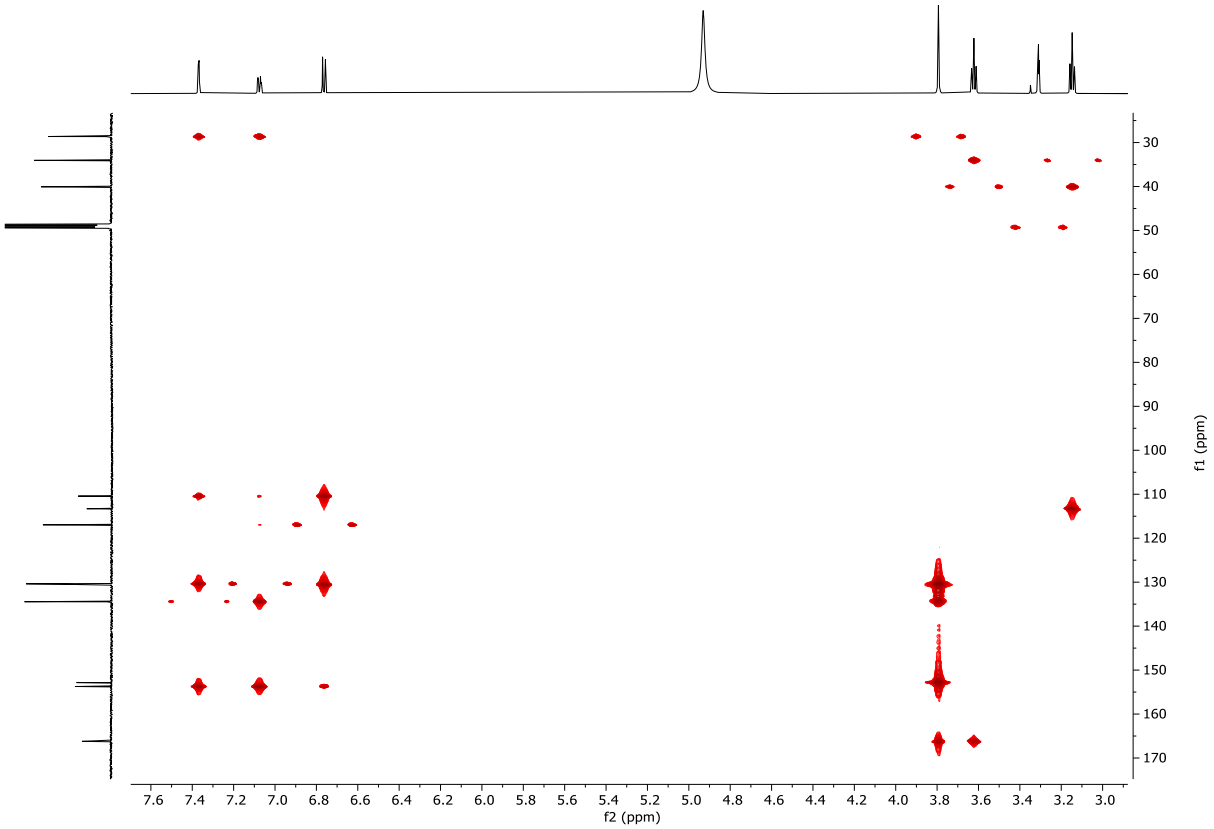

Figure F55: ^{1}H–^{13}C-HMBC (MeOH-d_4) of Psammaplin B (**1**).

Spectra of Isolated Side Products

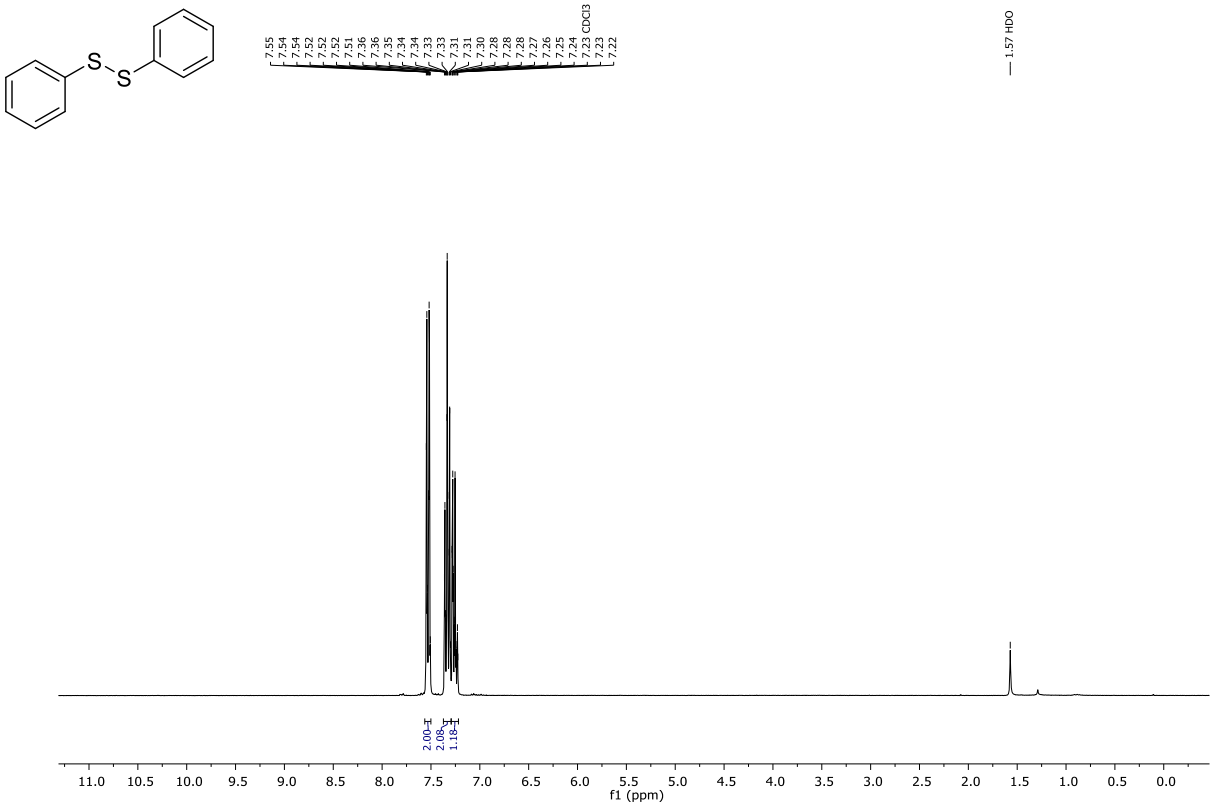

Figure F56: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **13**.

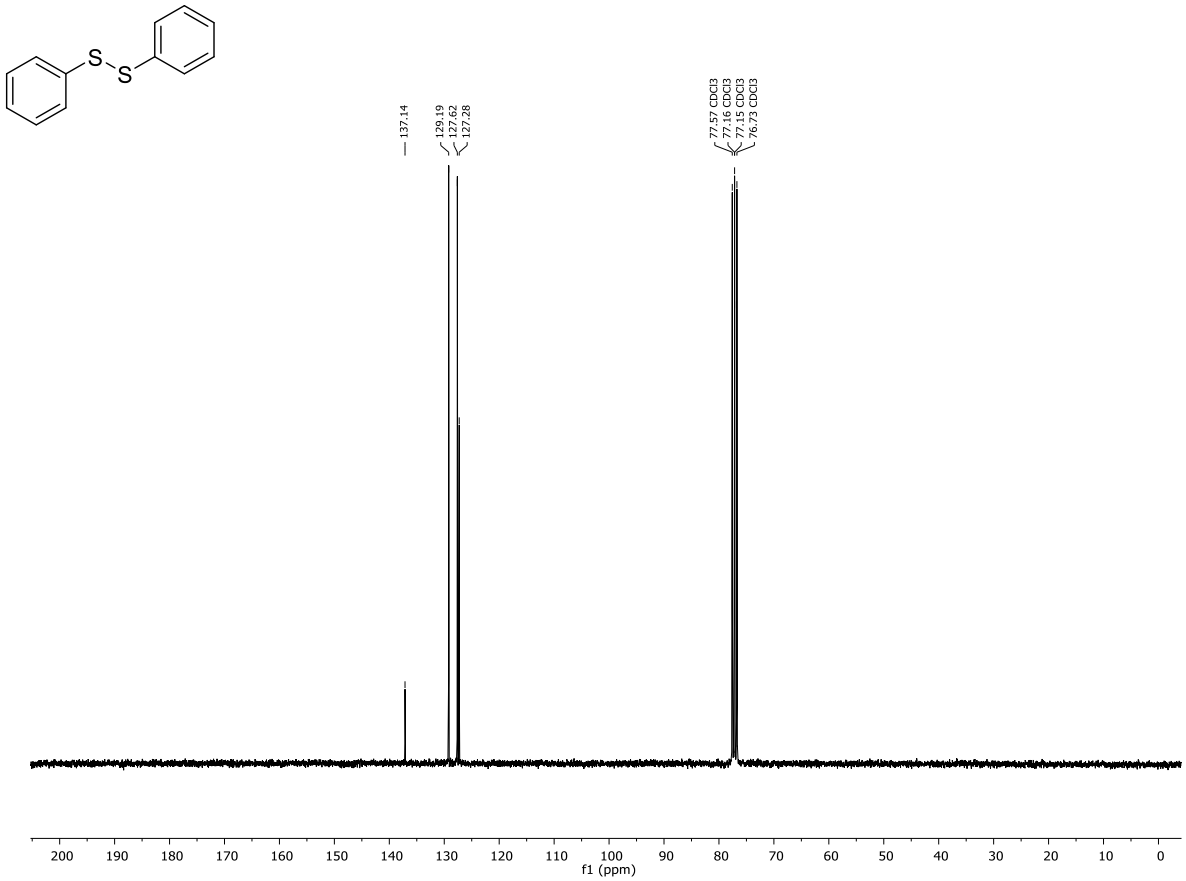

Figure F57*:* ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **13**.

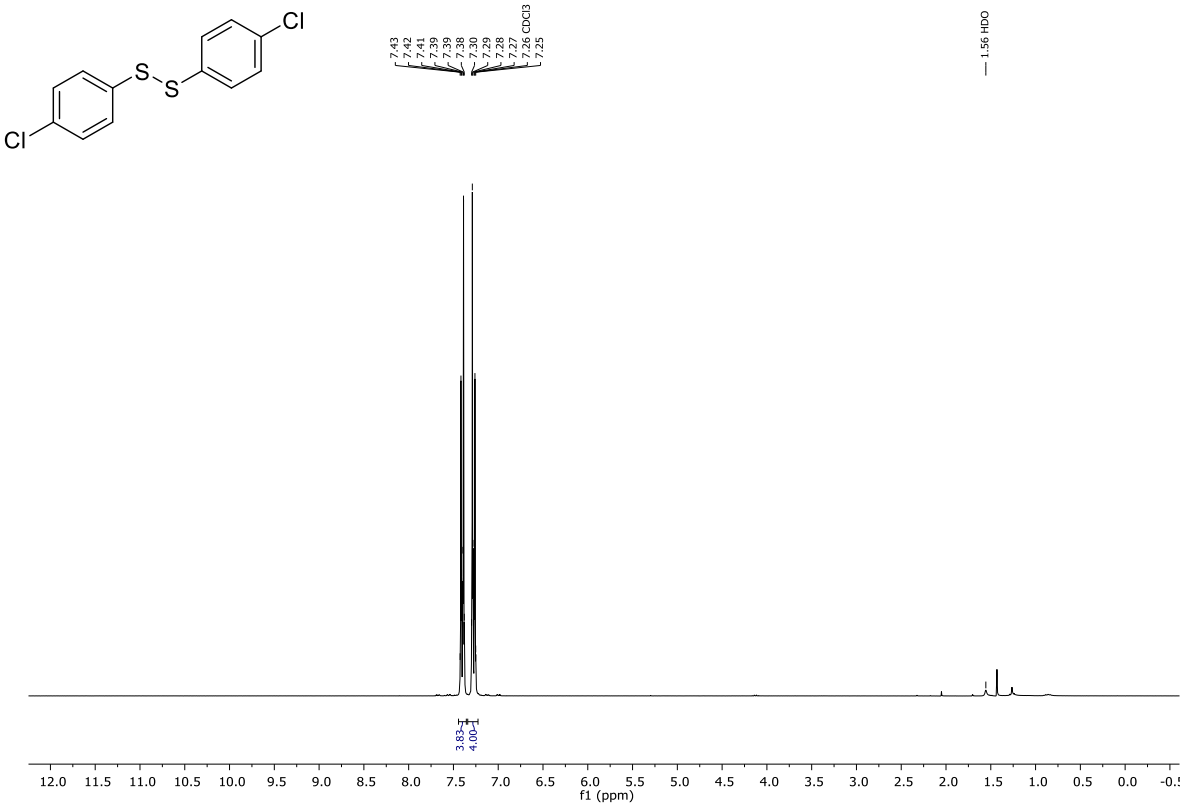

Figure F58: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **22b**.

Figure F59*:* ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **22b**.

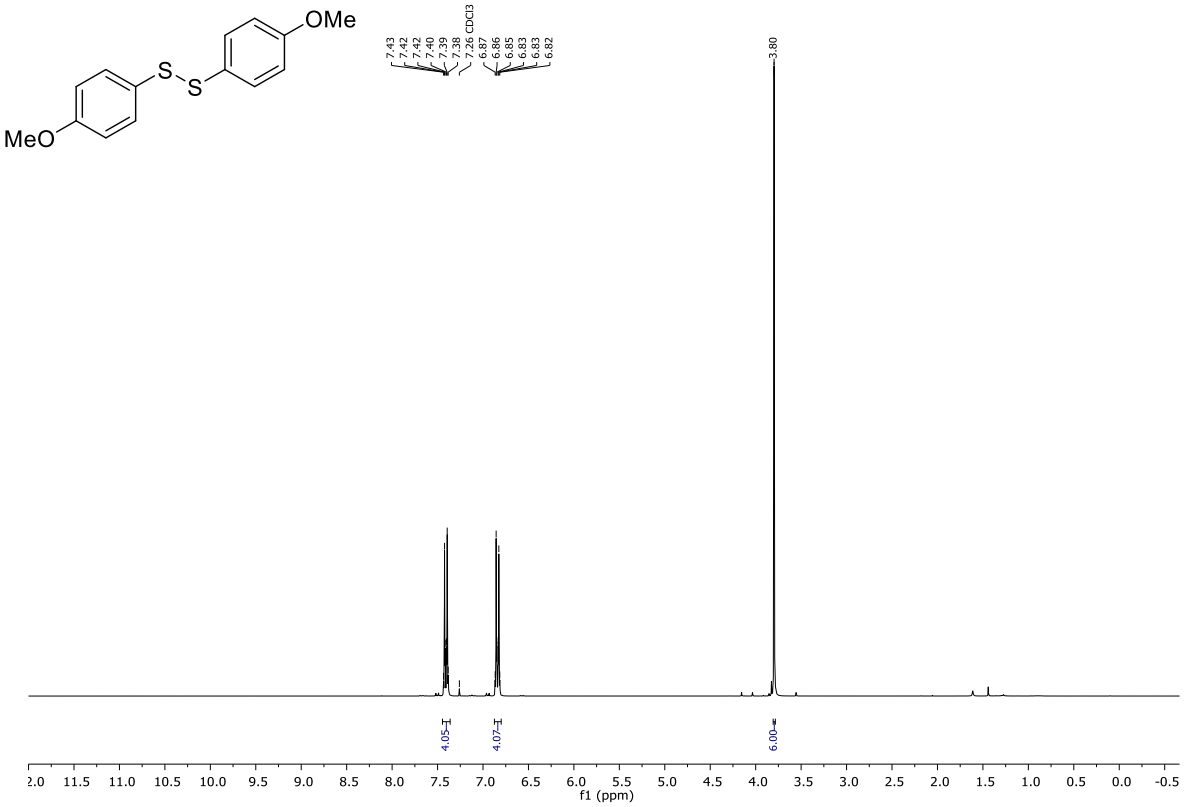

Figure F60: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **23b**.

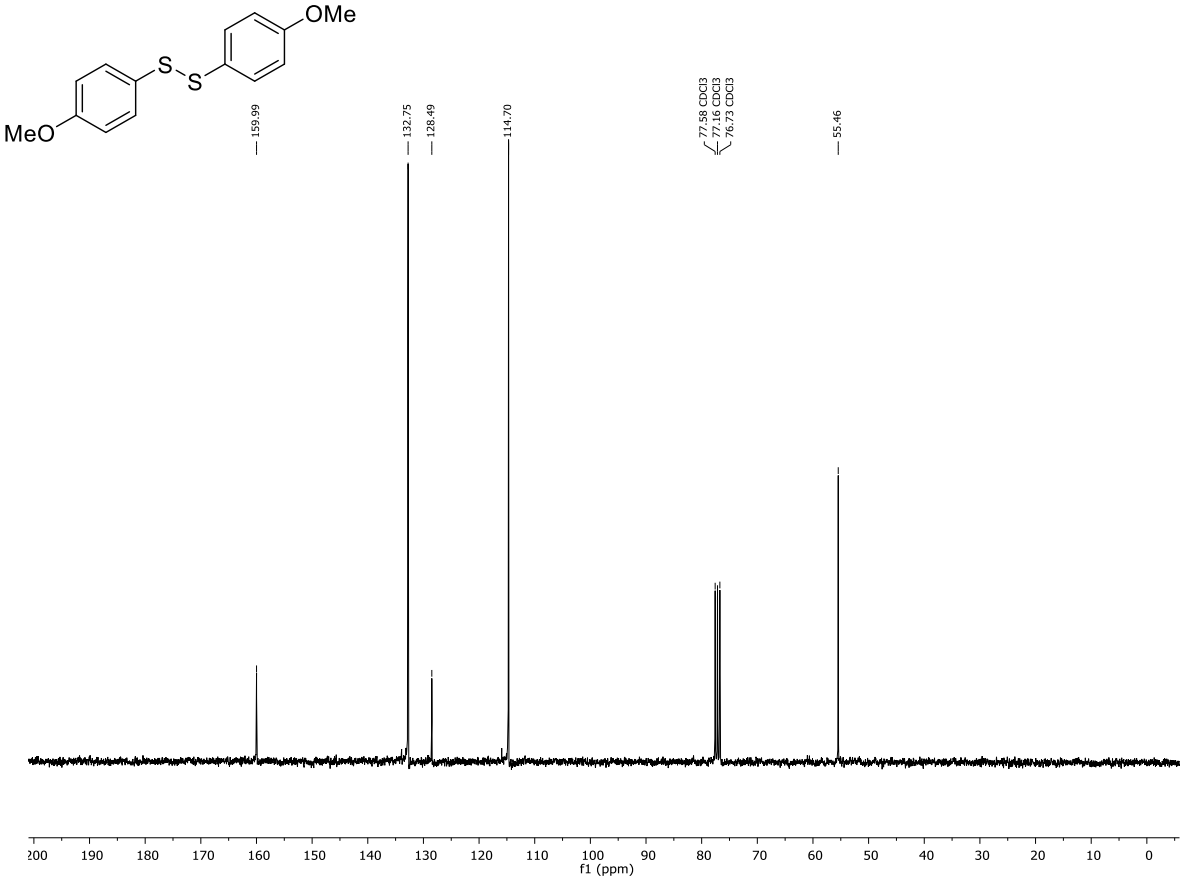

Figure F61: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **23b**.

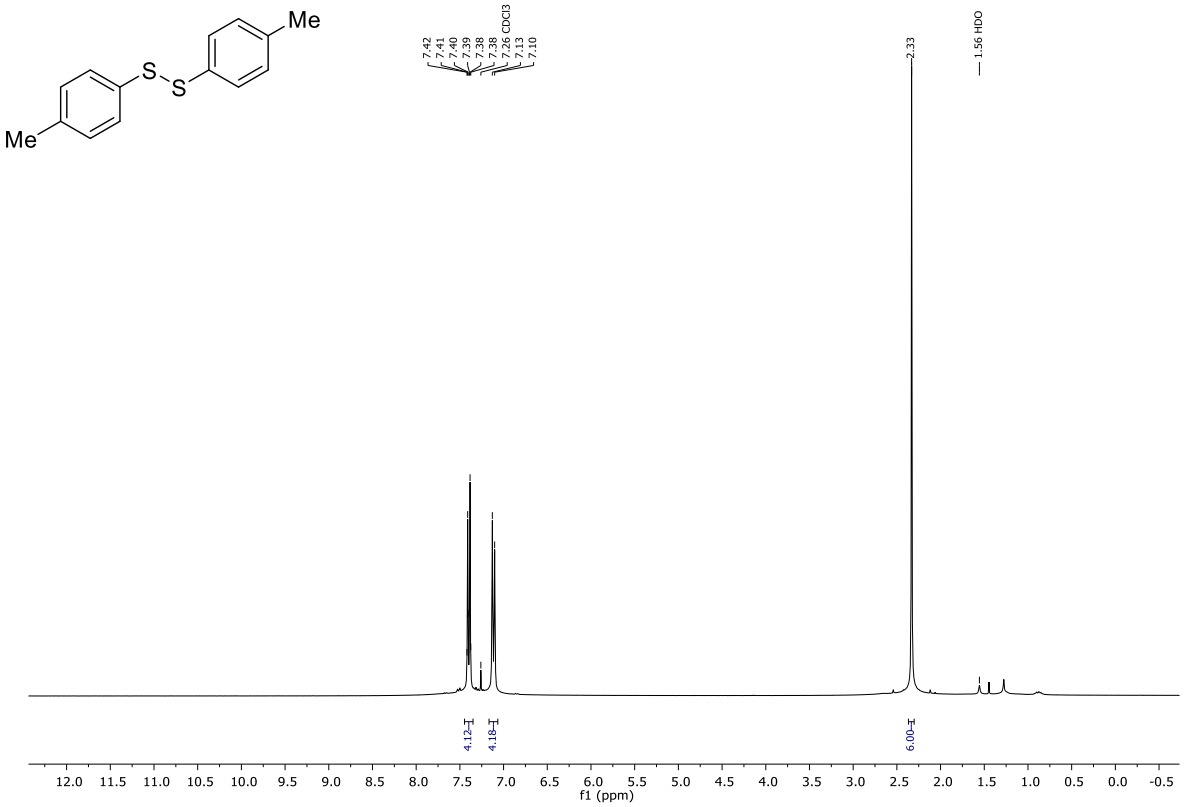

Figure F62: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **24b**.

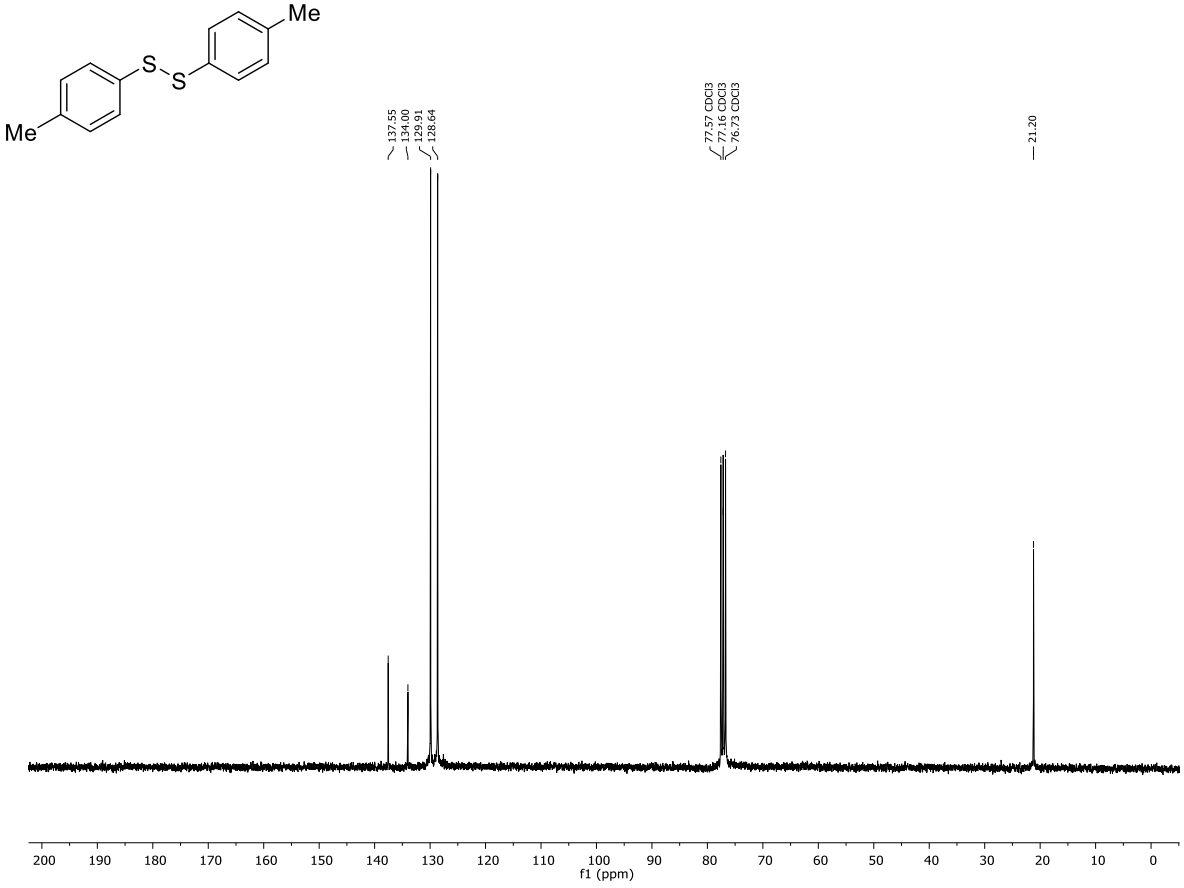

Figure F63: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **24b**.

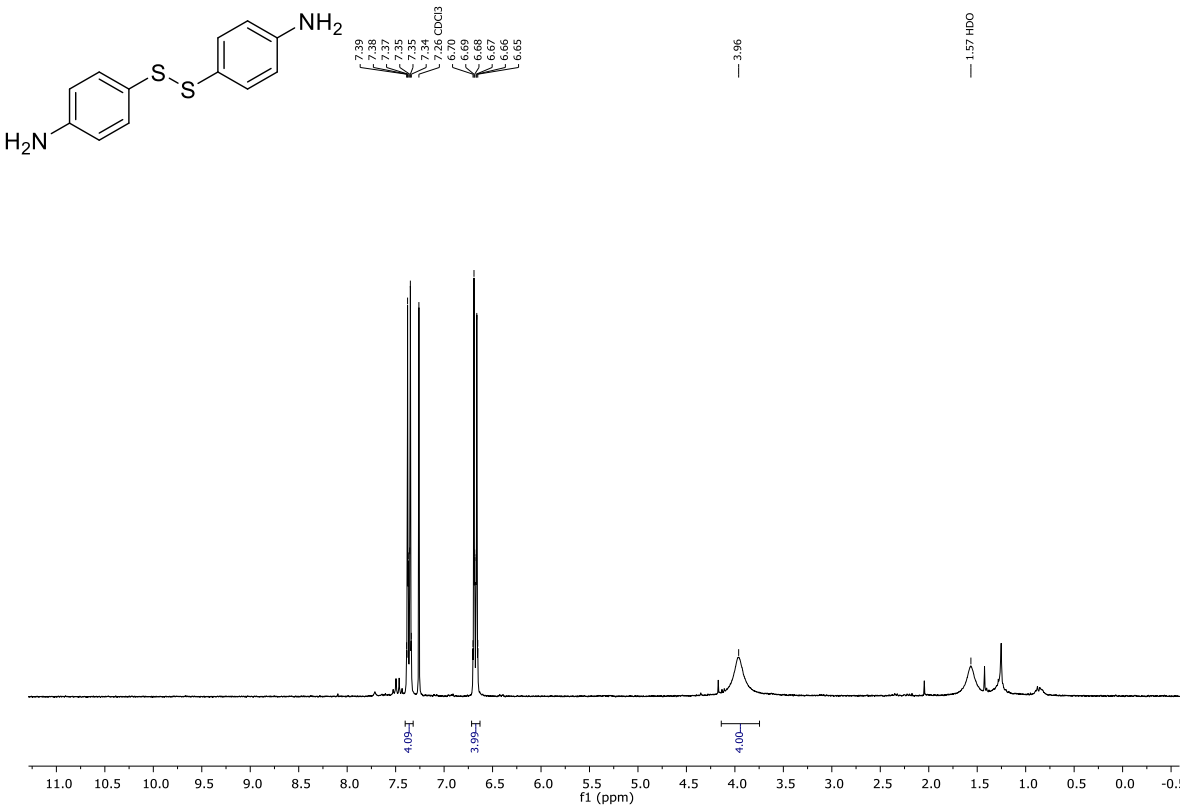

Figure F64: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **25b**.

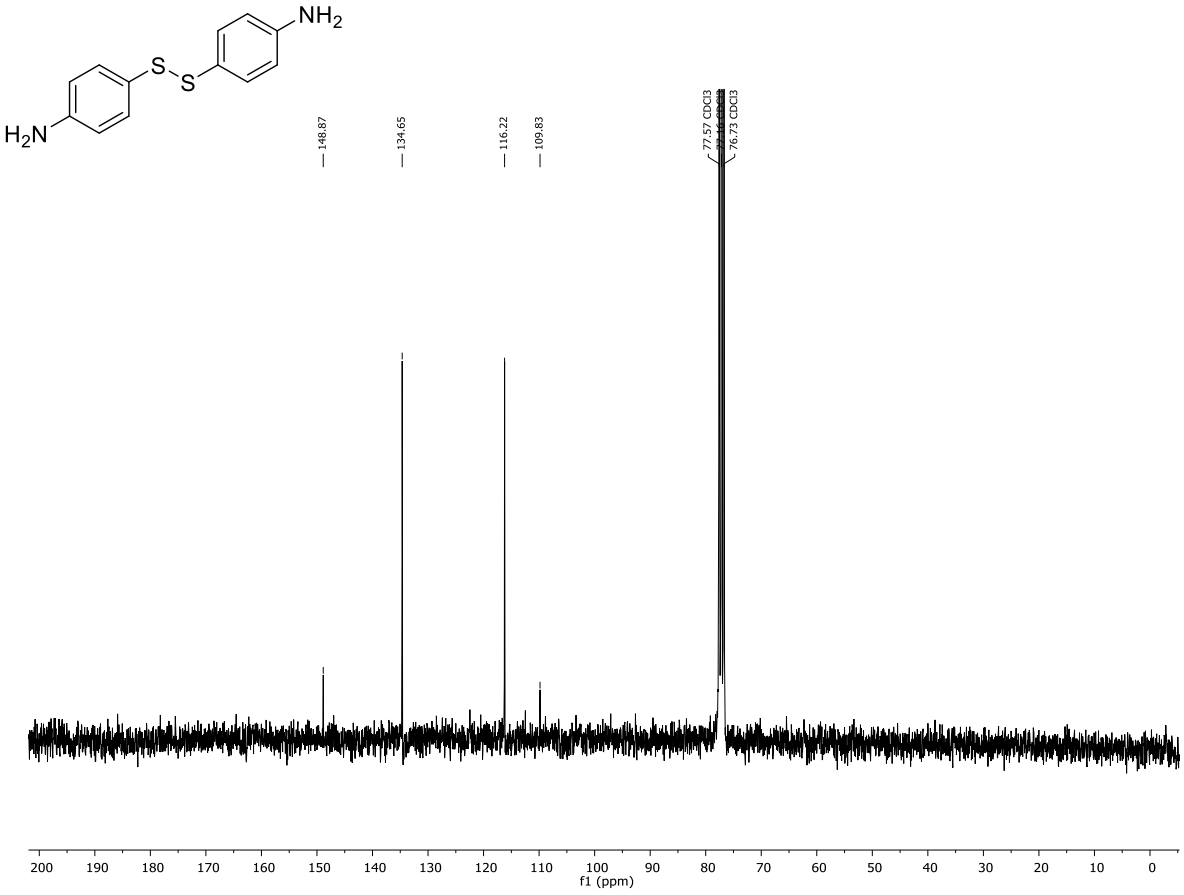

Figure F65*:* ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **25b**.

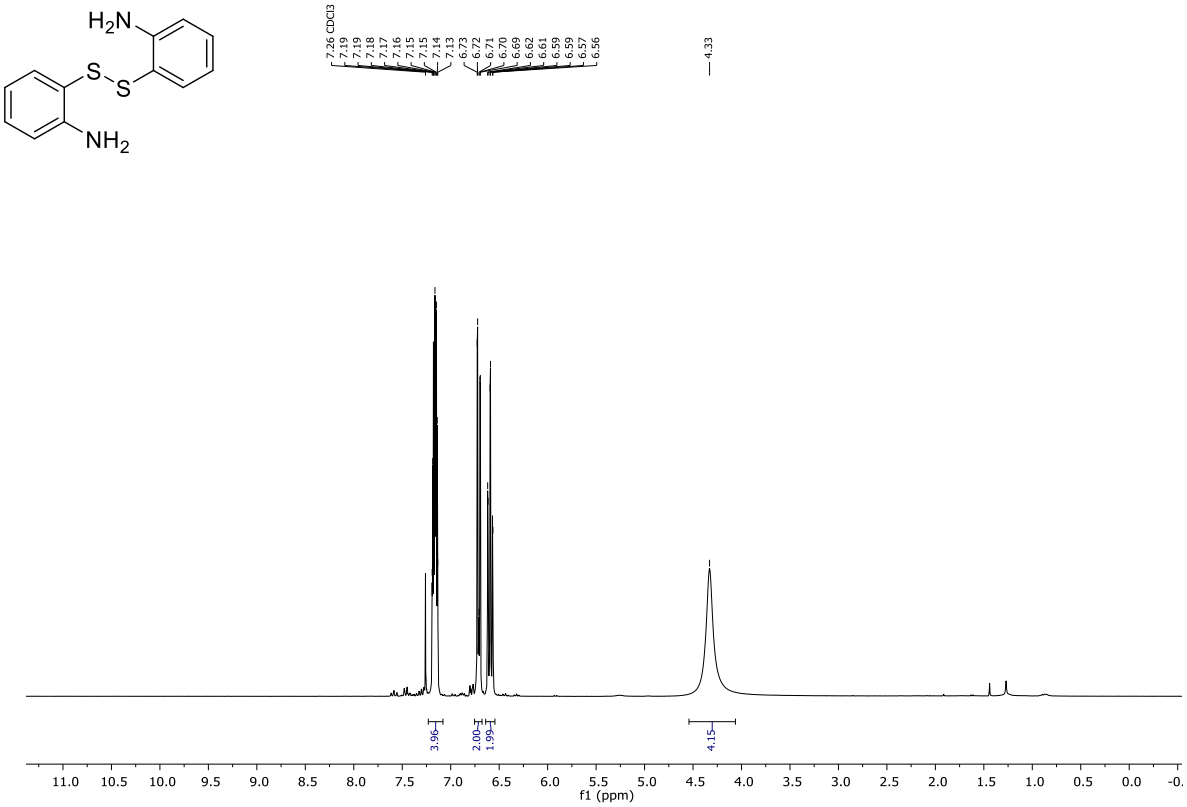

Figure F66: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **26b**.

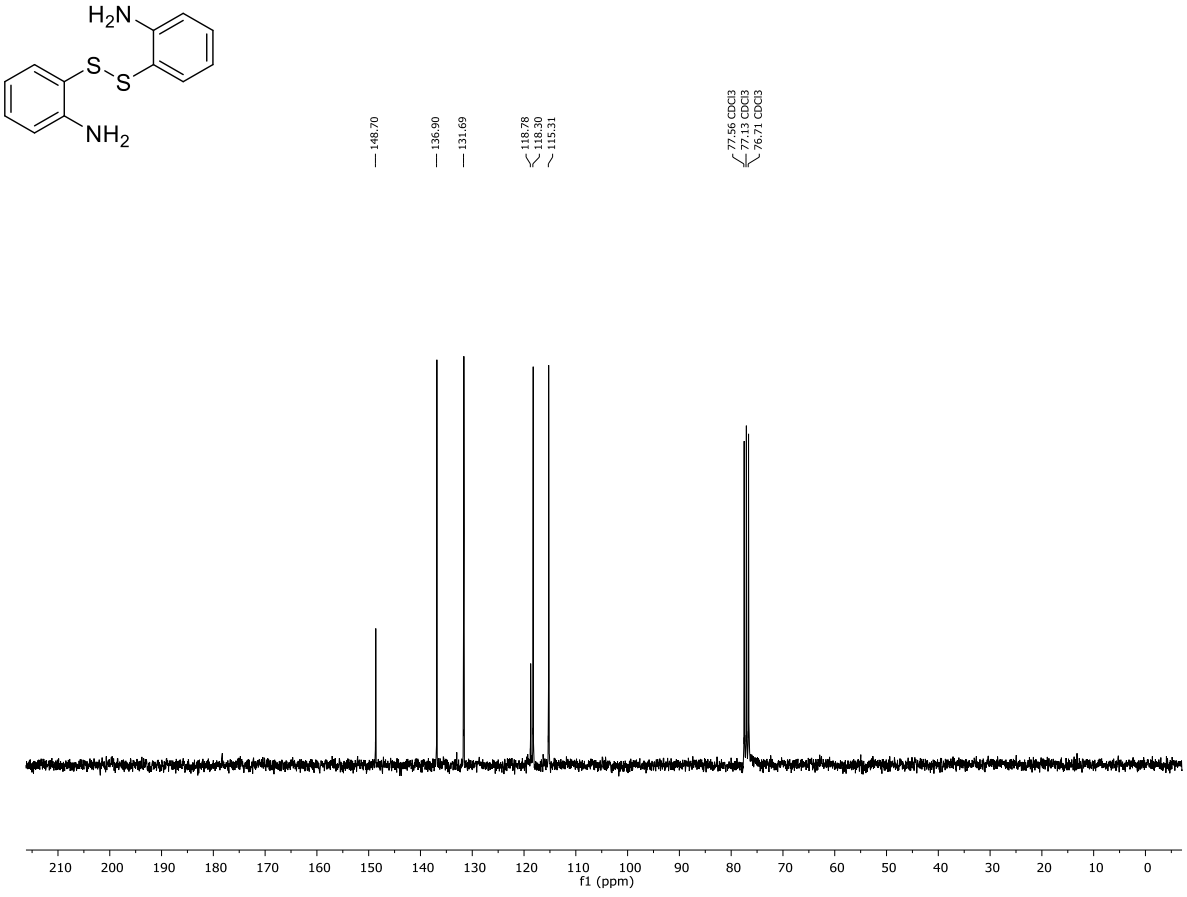

Figure F67: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **26b**.

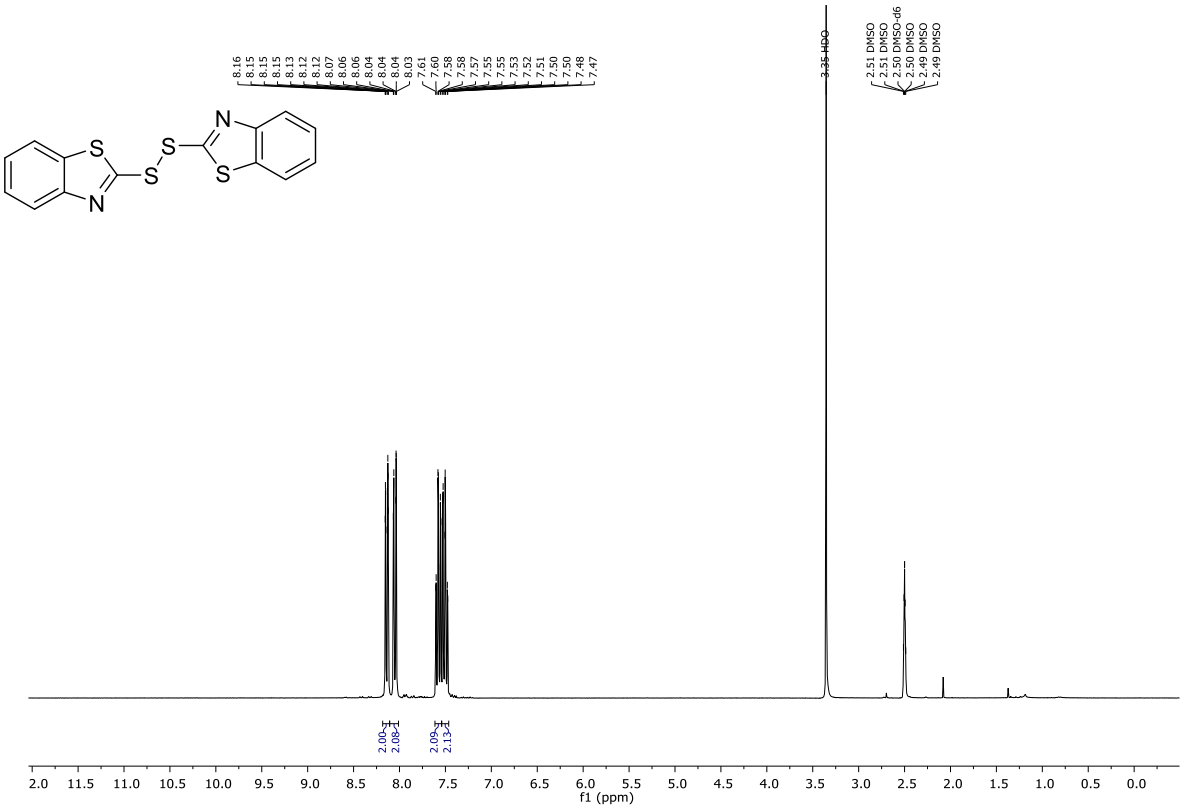

Figure F68: ^{1}H-NMR (DMSO-d_6, 300 MHz) of compound **30b**.

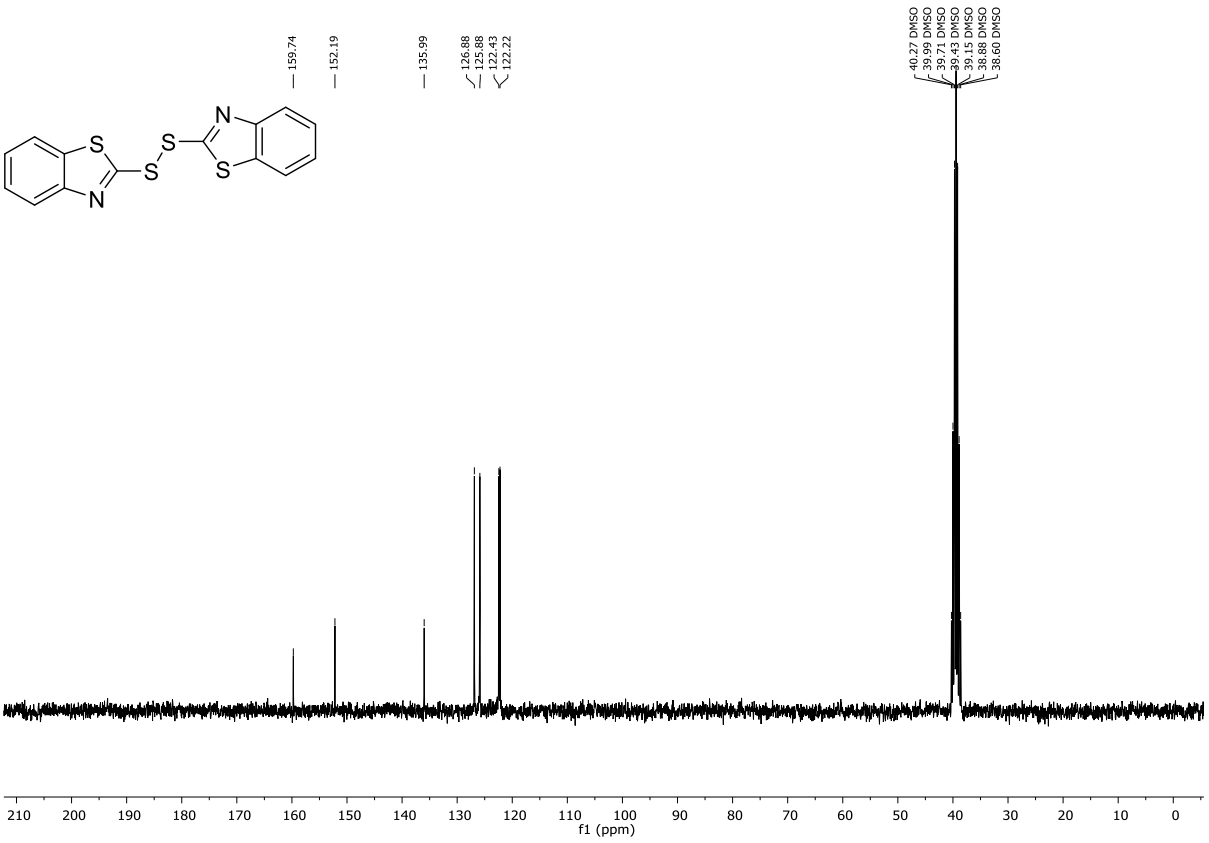

Figure F69: ^{13}C-NMR (DMSO-d_6, 75 MHz) of compound **30b**.

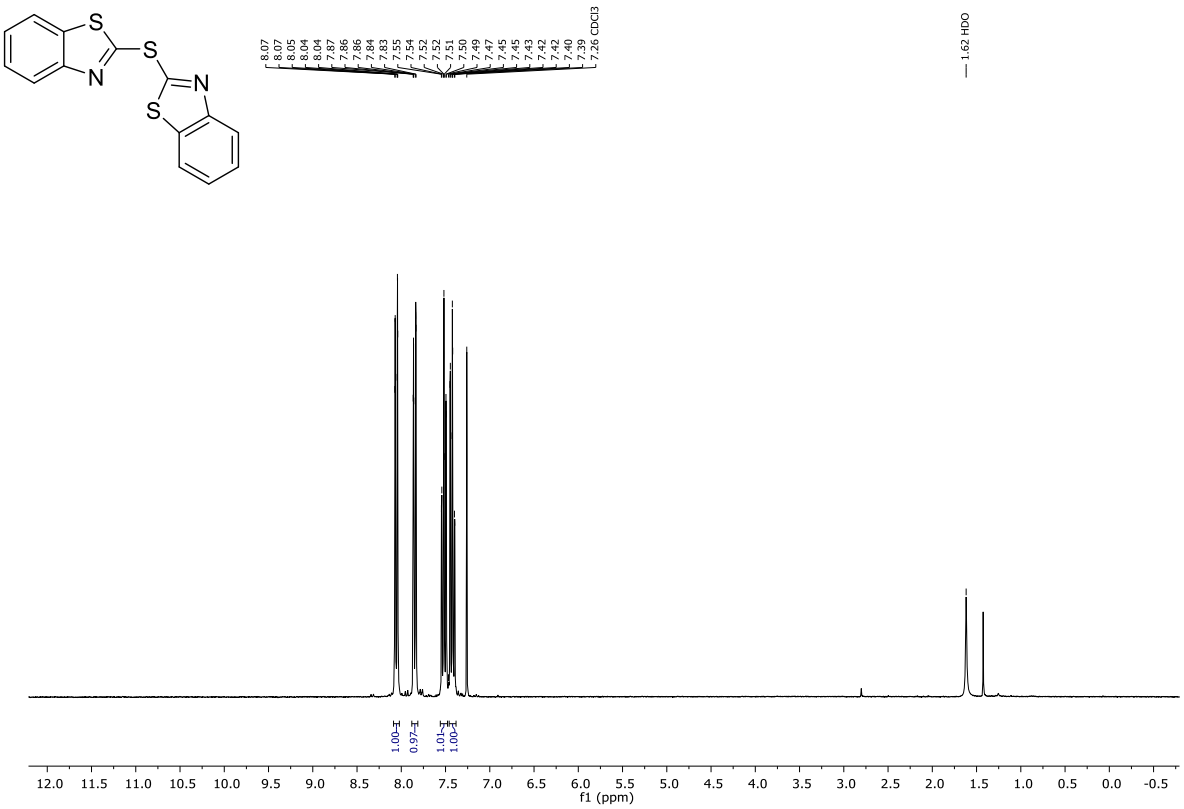

Figure F70: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **30c**.

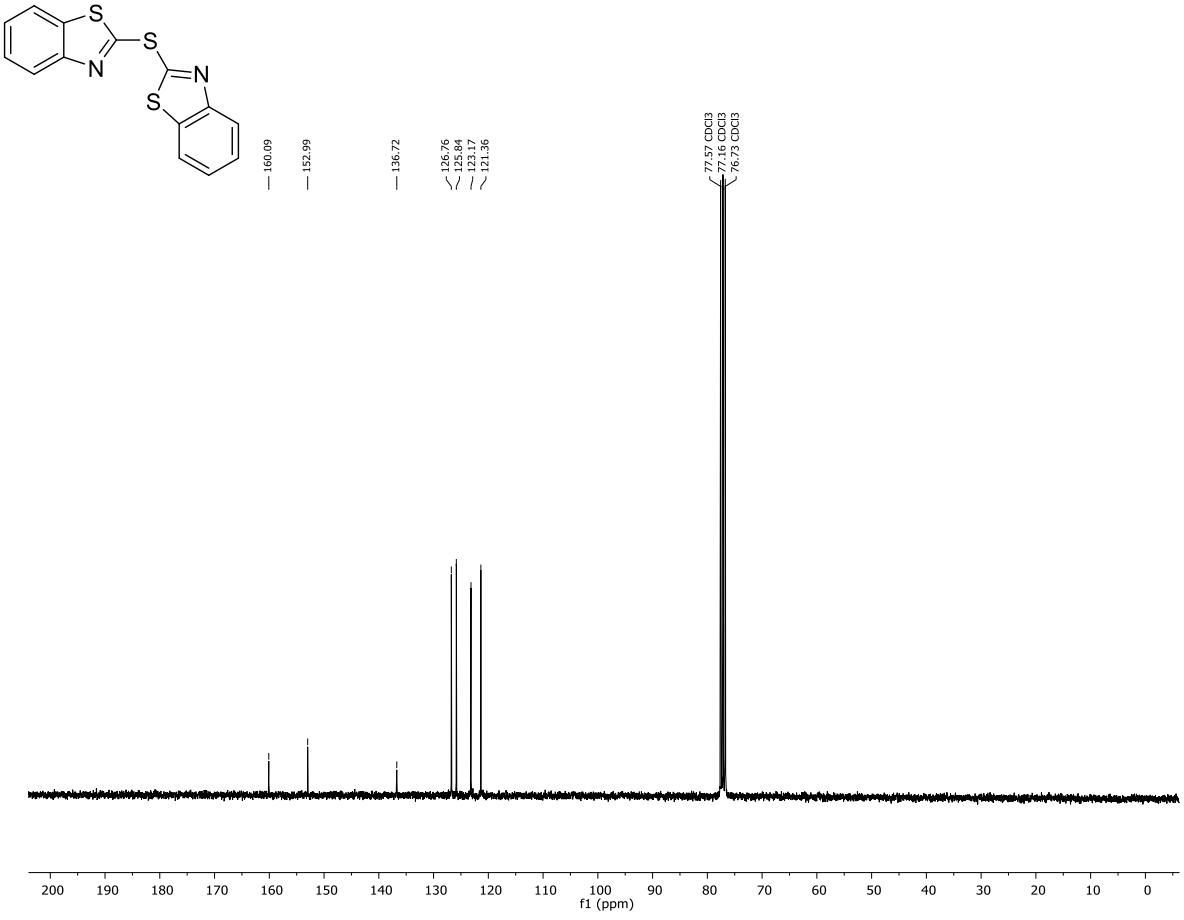

Figure F71: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **30c**.

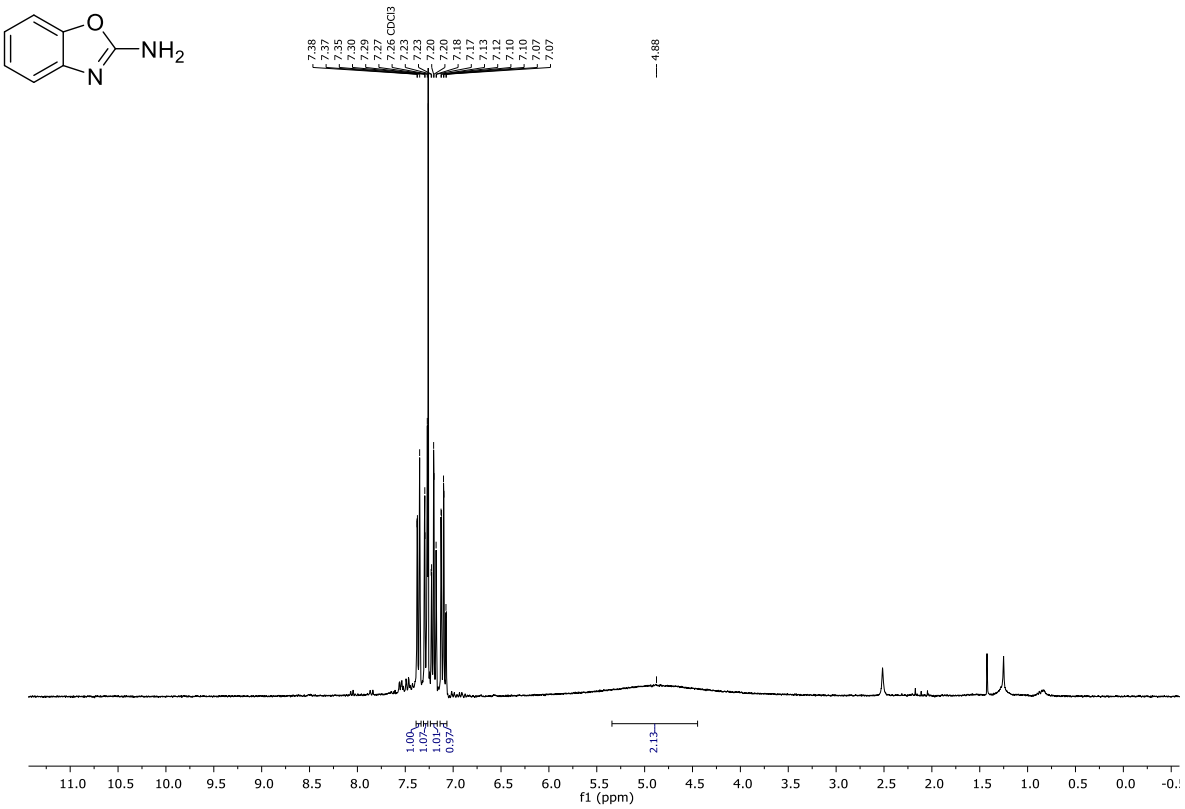

Figure F72: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **31b**.

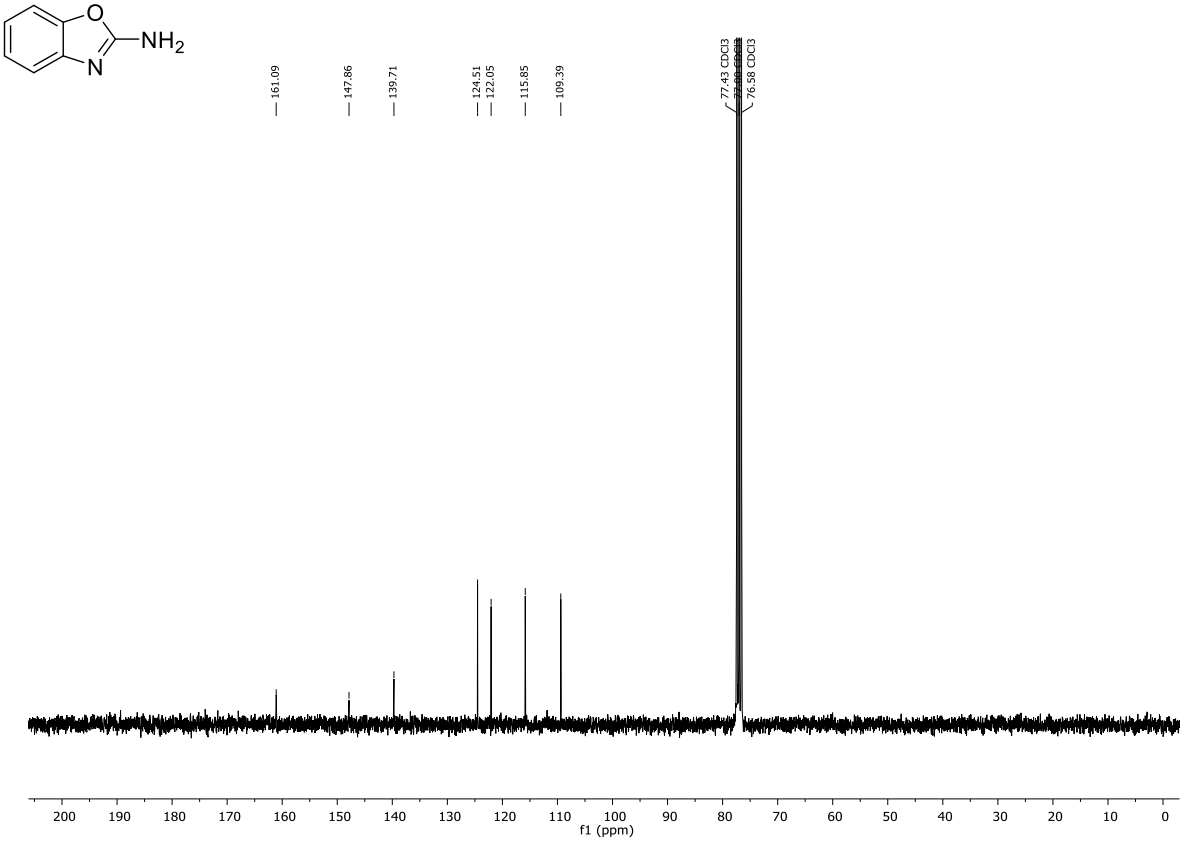

Figure F73: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **31b**.

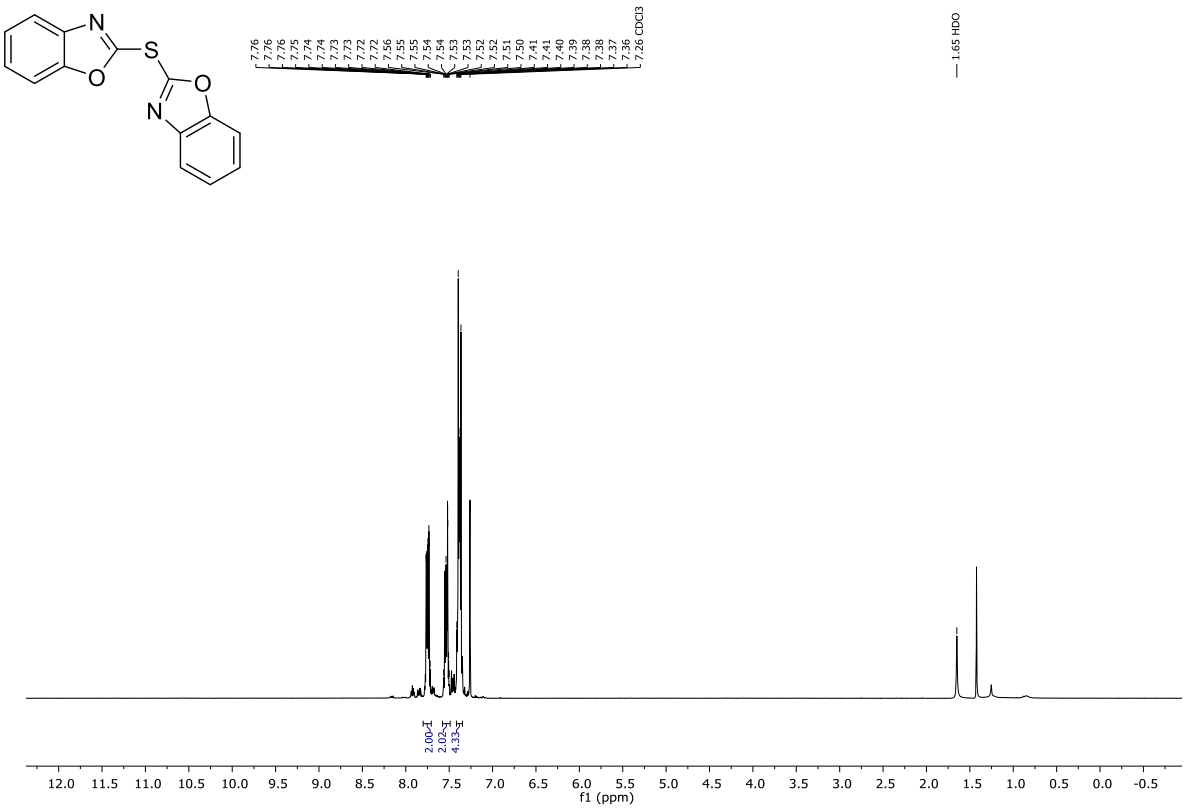

Figure F74: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **31c**.

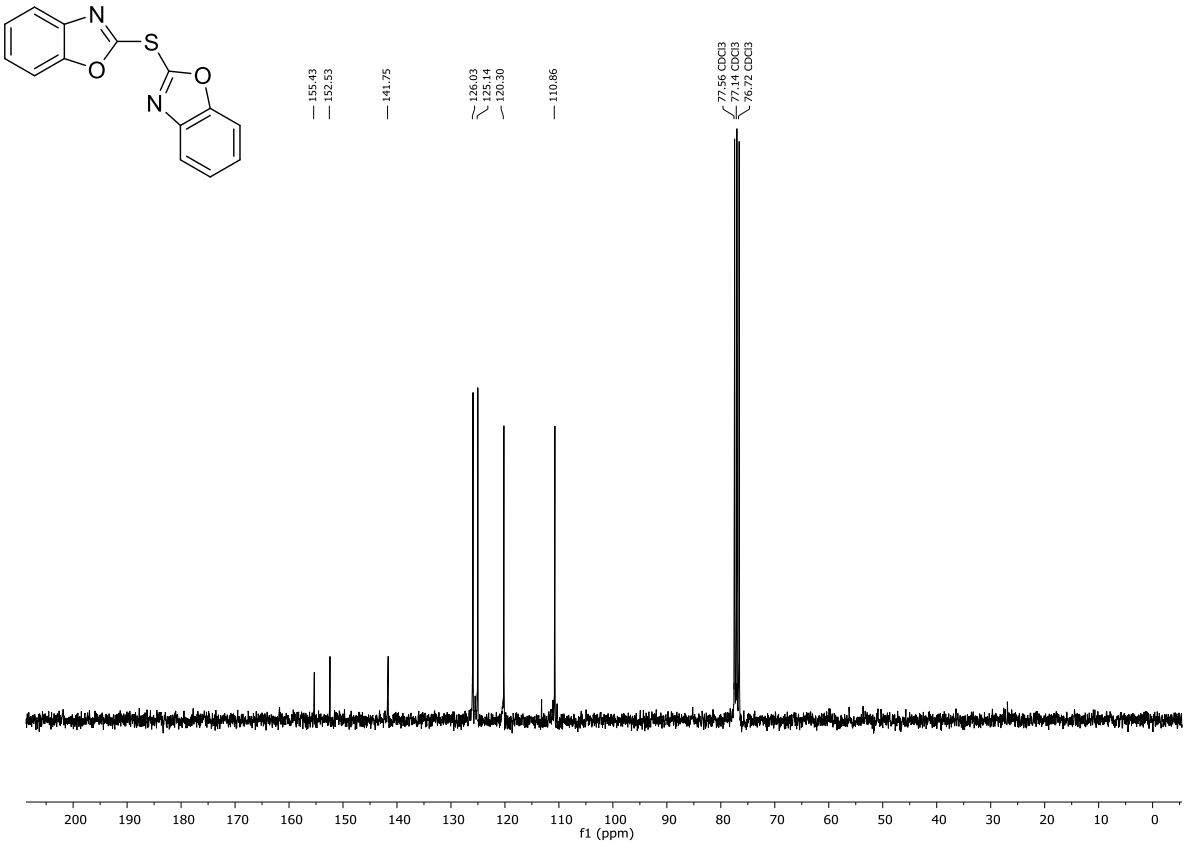

Figure F75: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **31c**.

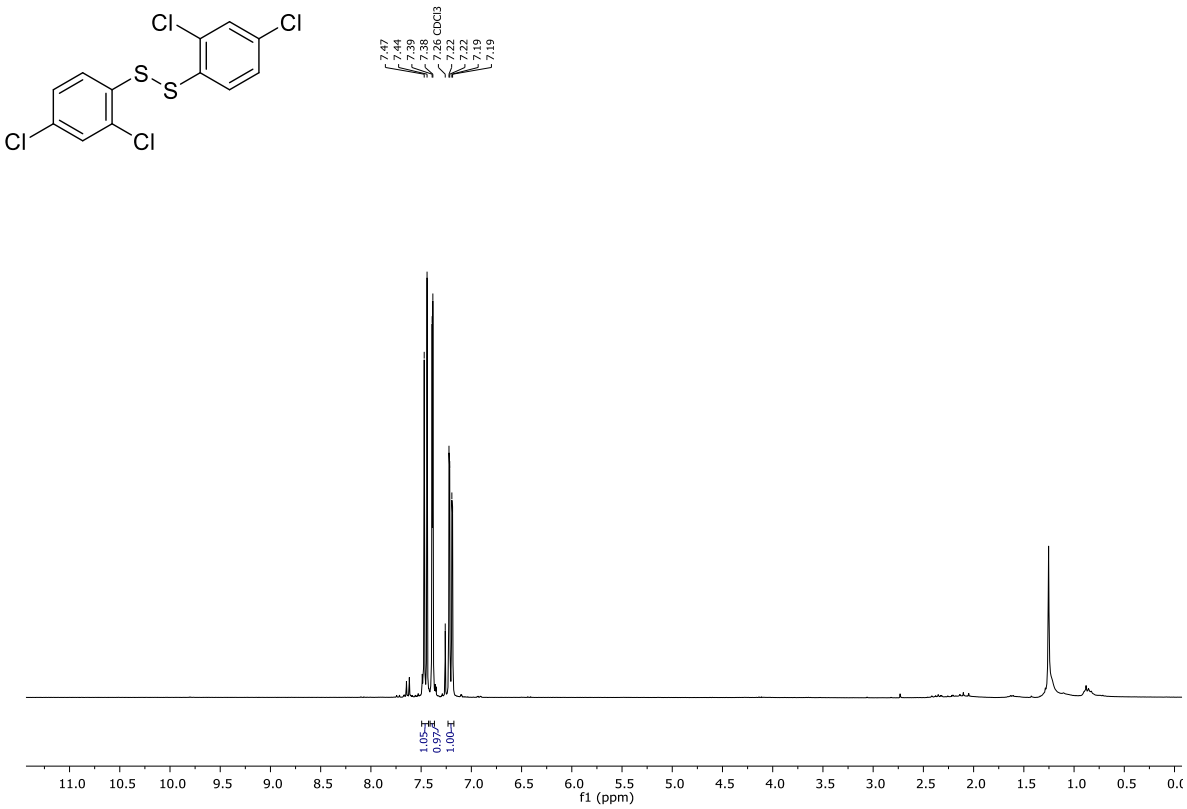

Figure F76: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **33b**.

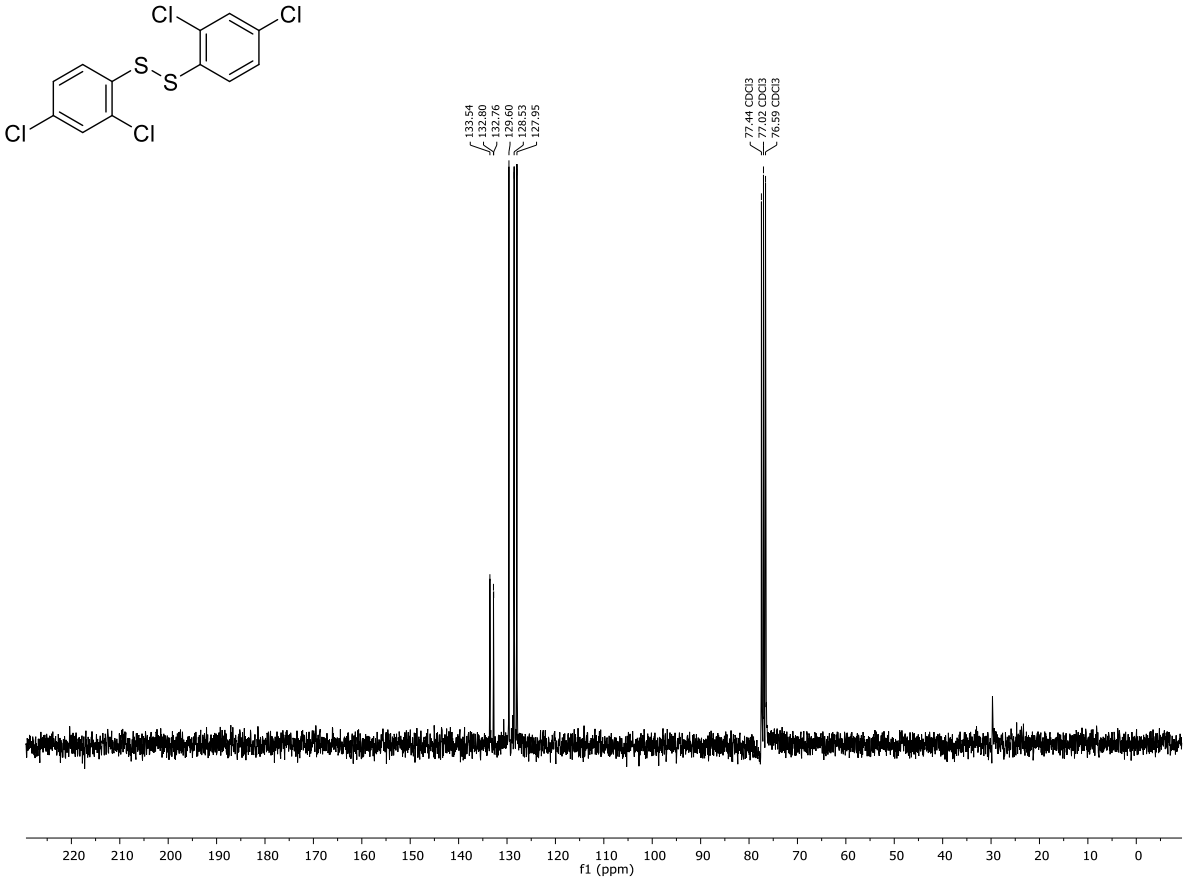

Figure F77: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **33b**.

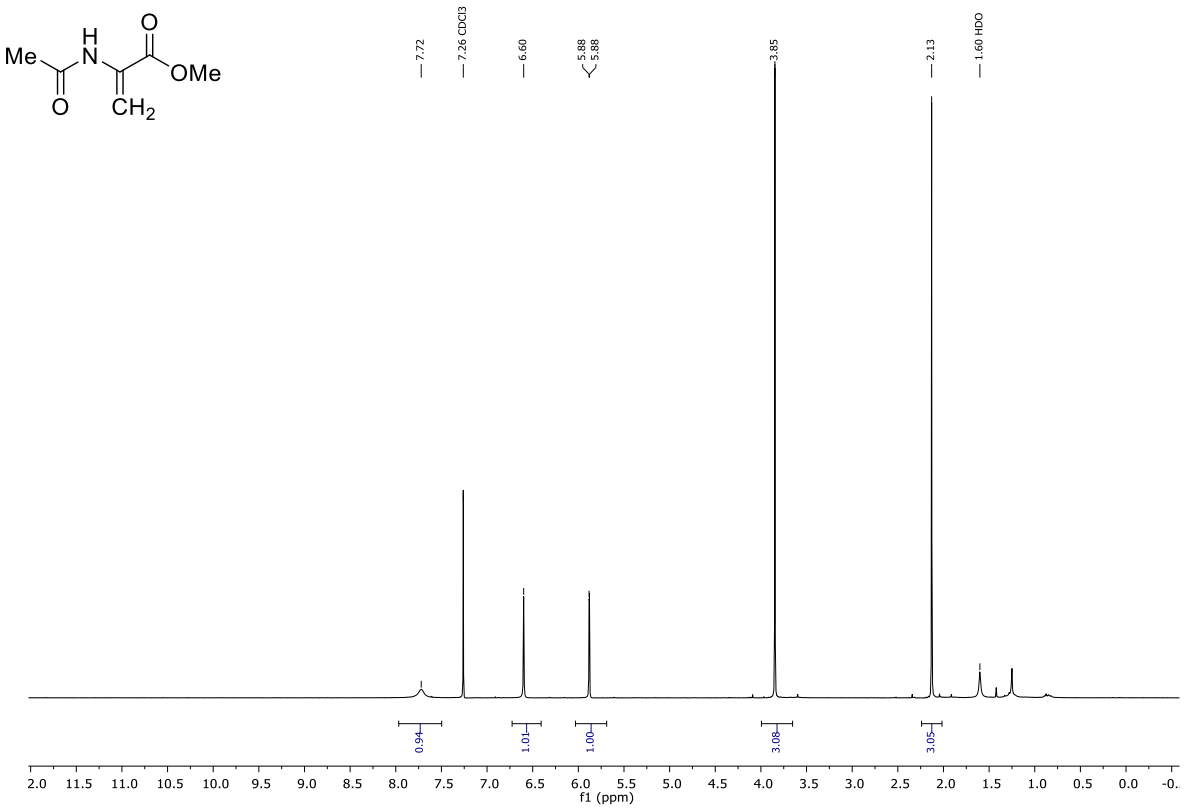

Figure F78: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **40b**.

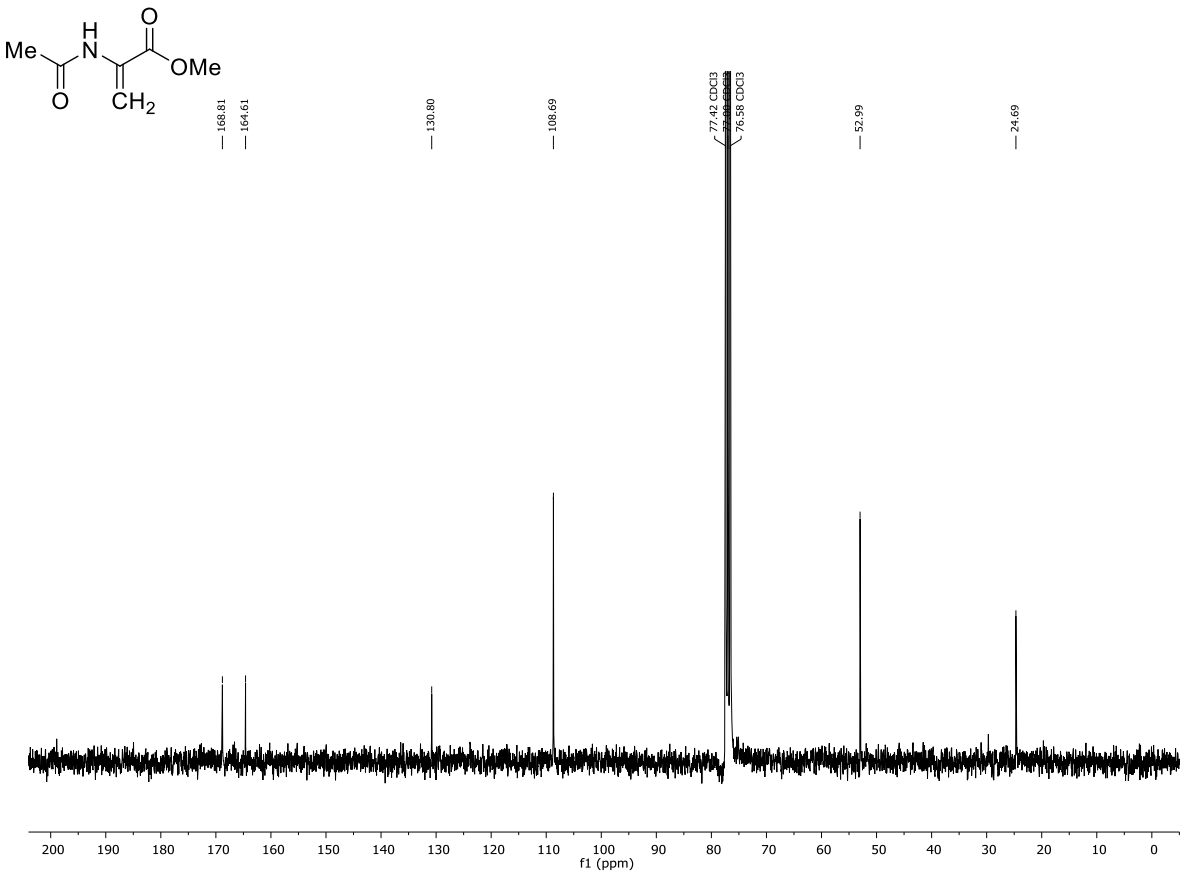

Figure F79: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **40b**.

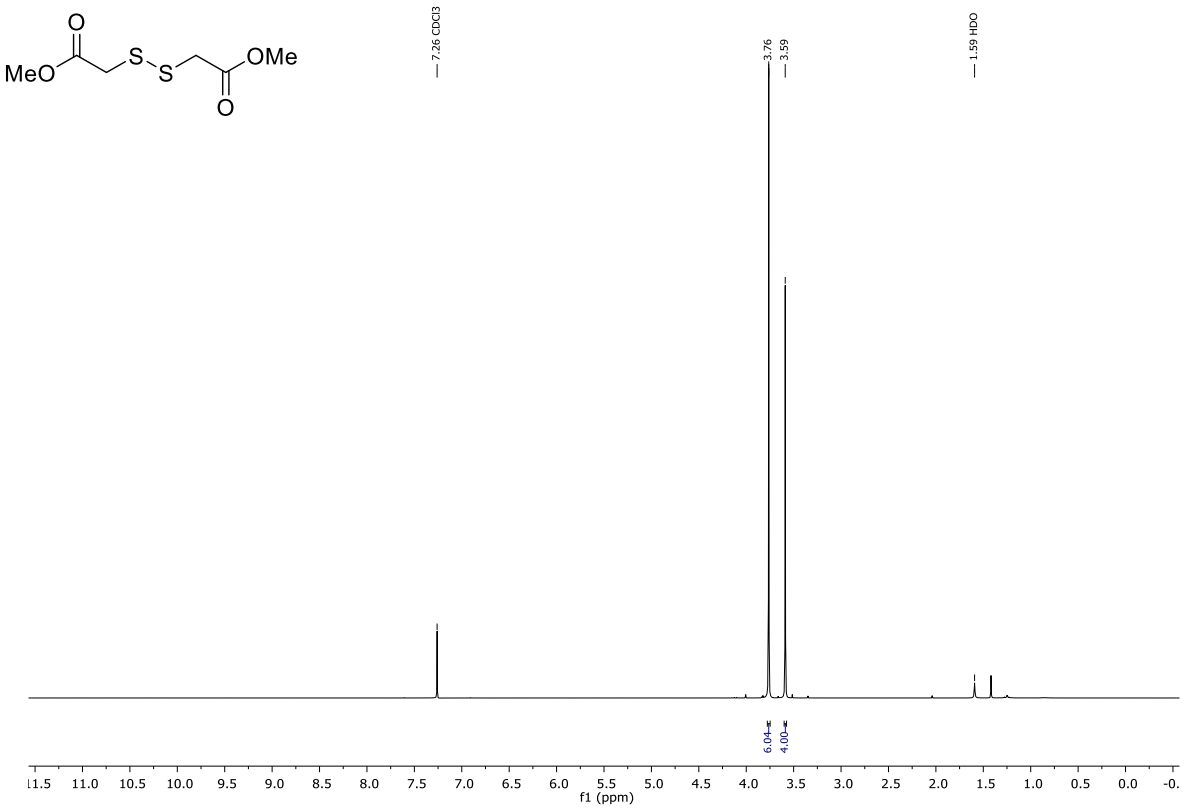

Figure F80: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **43b**.

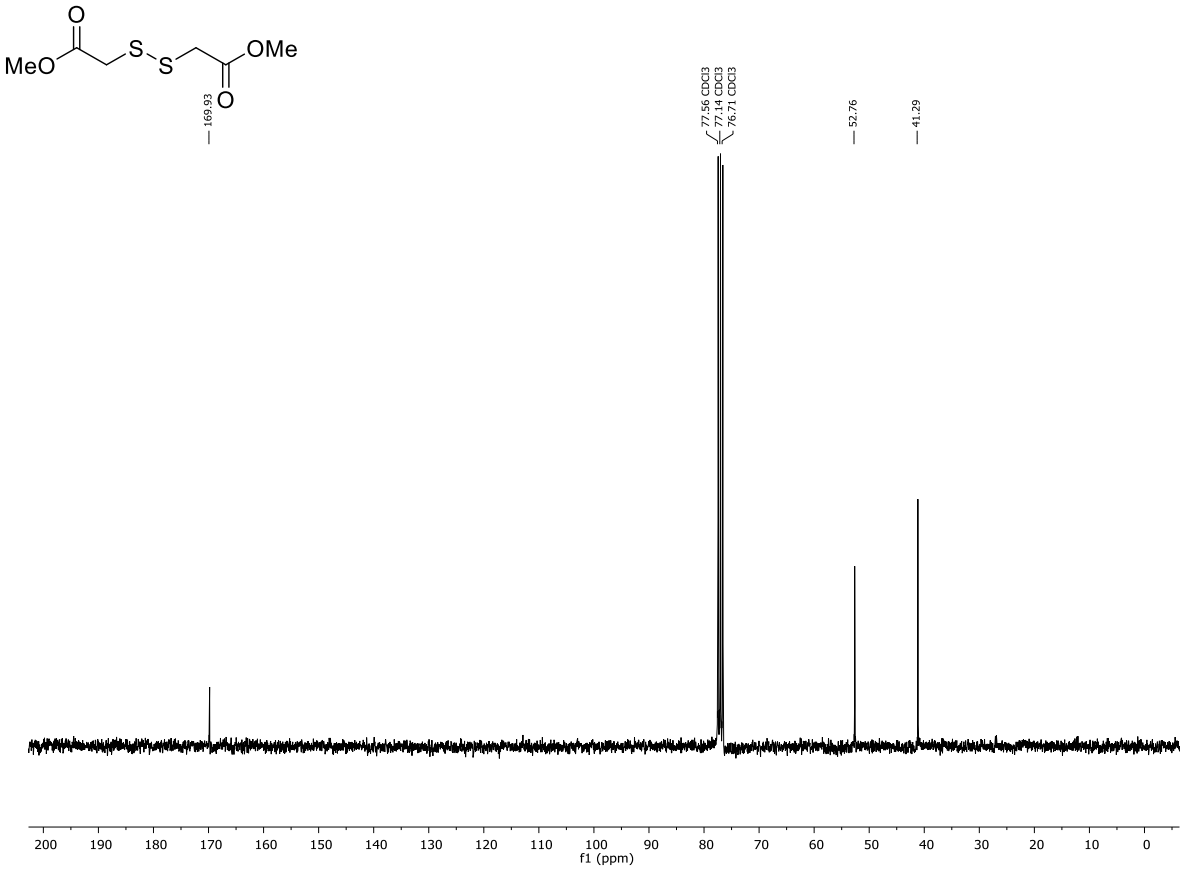

Figure F81: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **43b**.

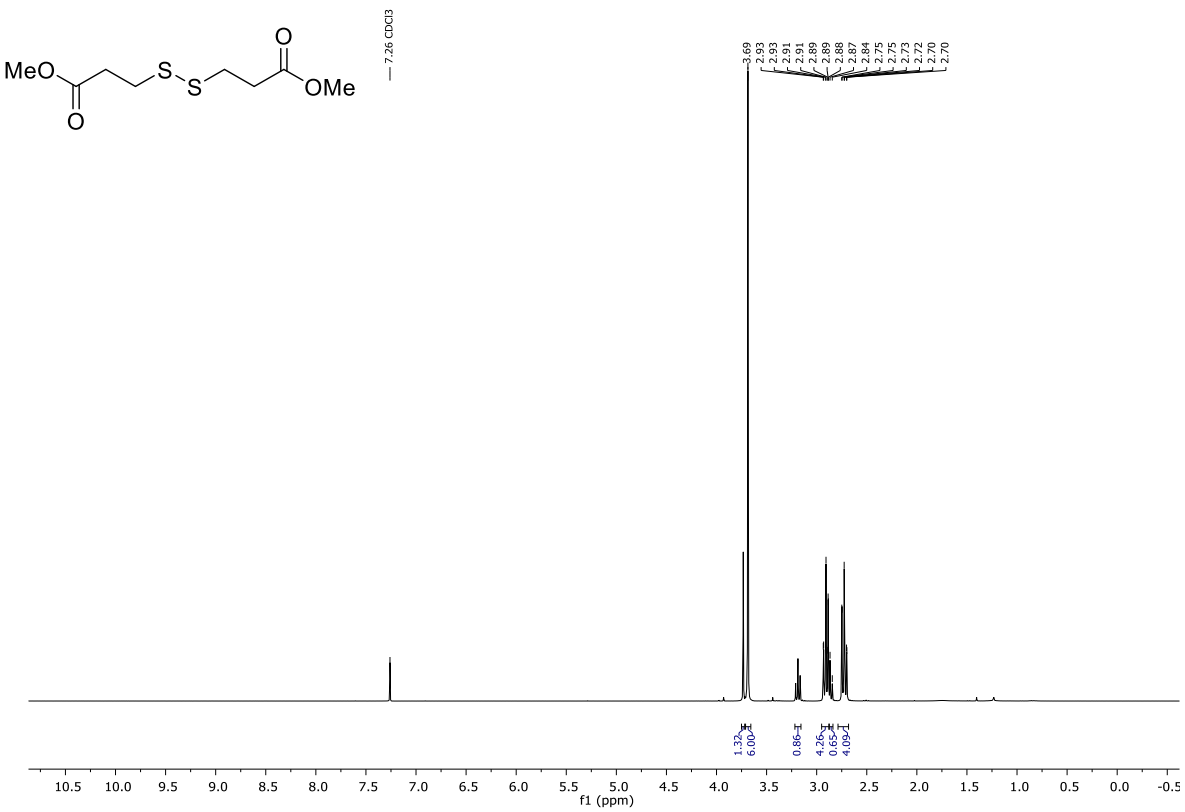

Figure F82: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **44b**.

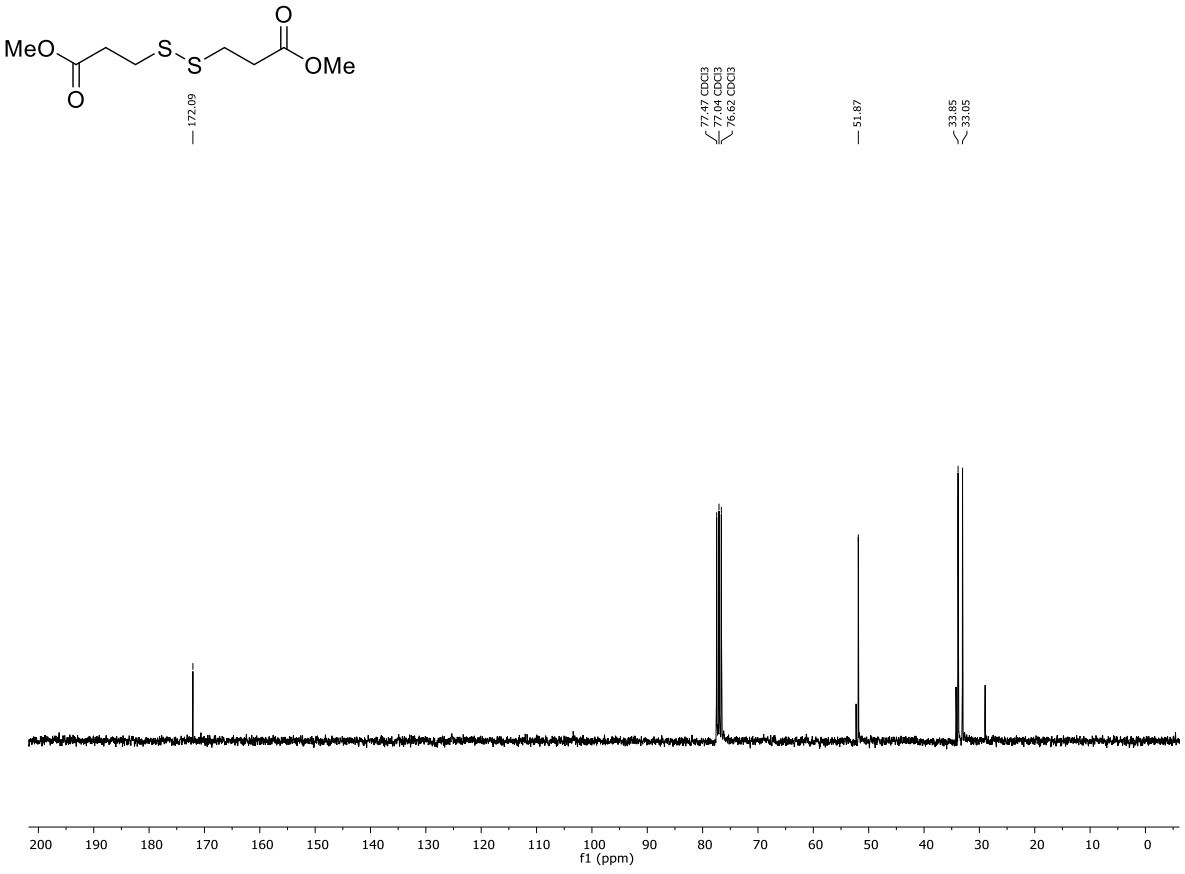

Figure F83: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **44b**.

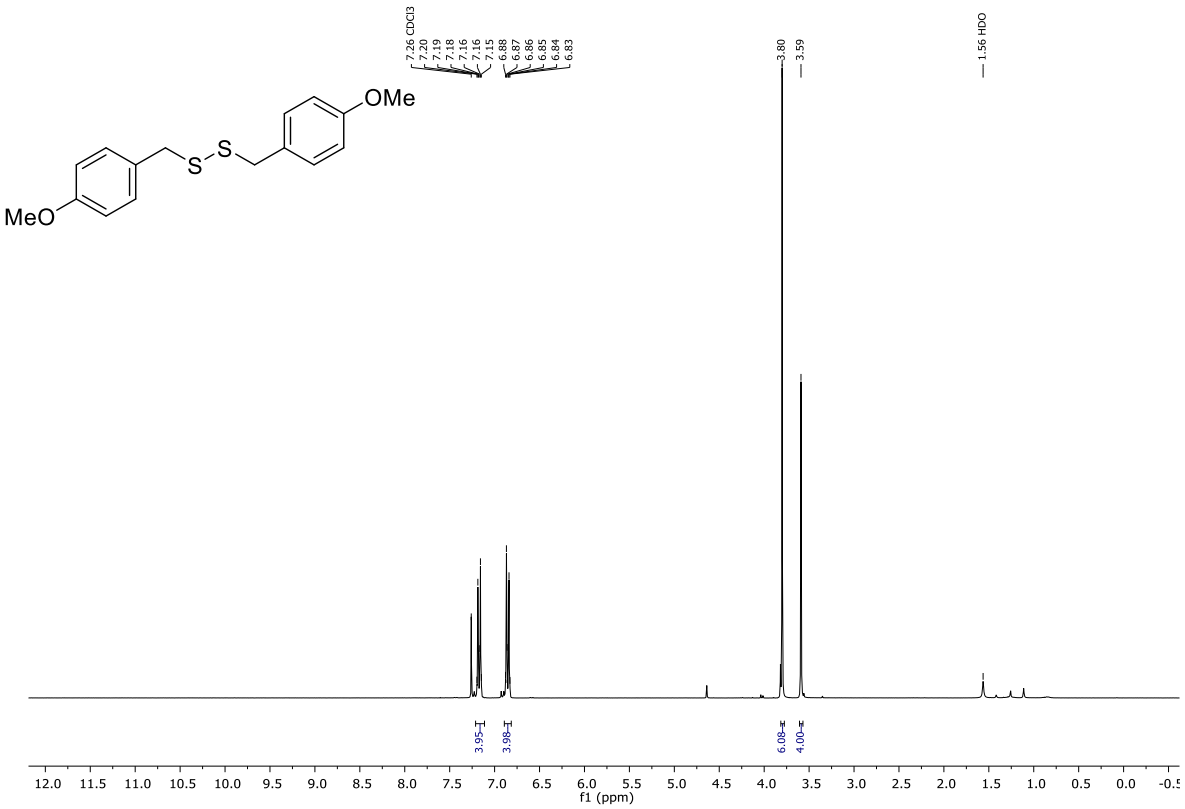

Figure F84: ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **45b**.

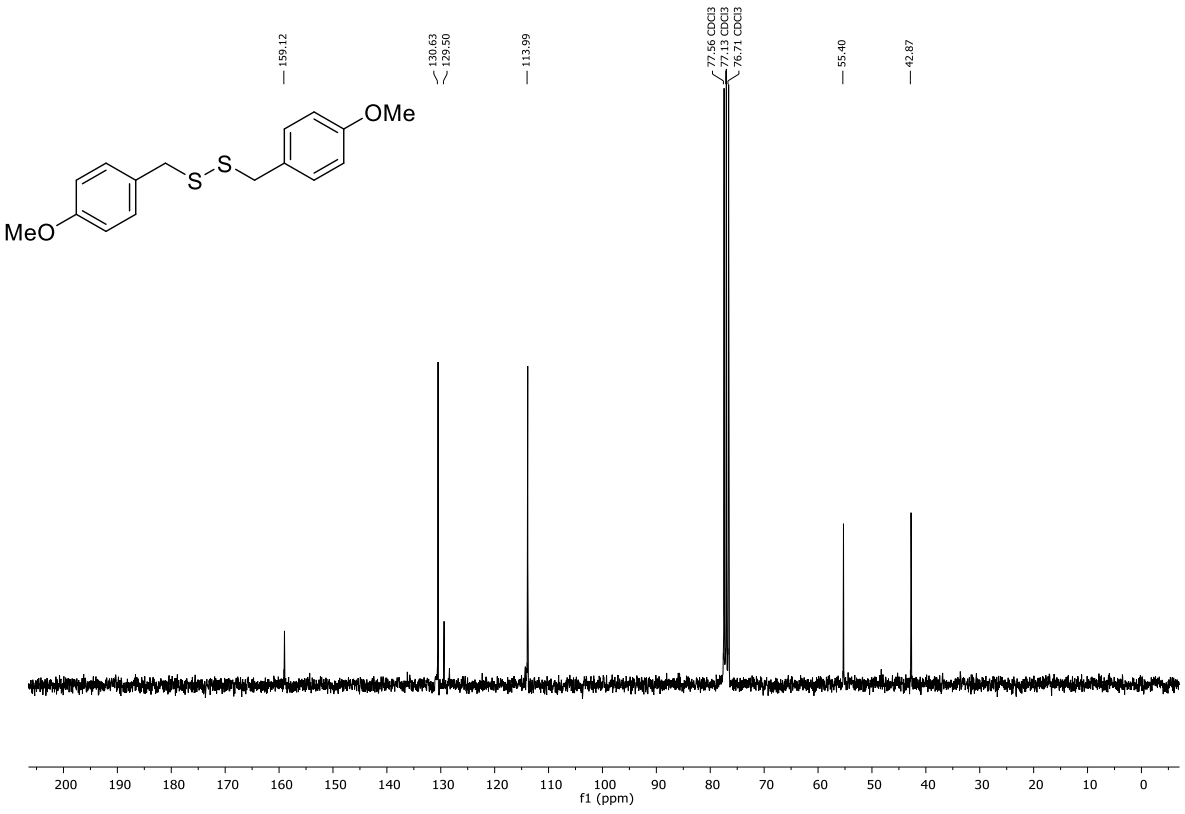

Figure F85*:* ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **45b**.

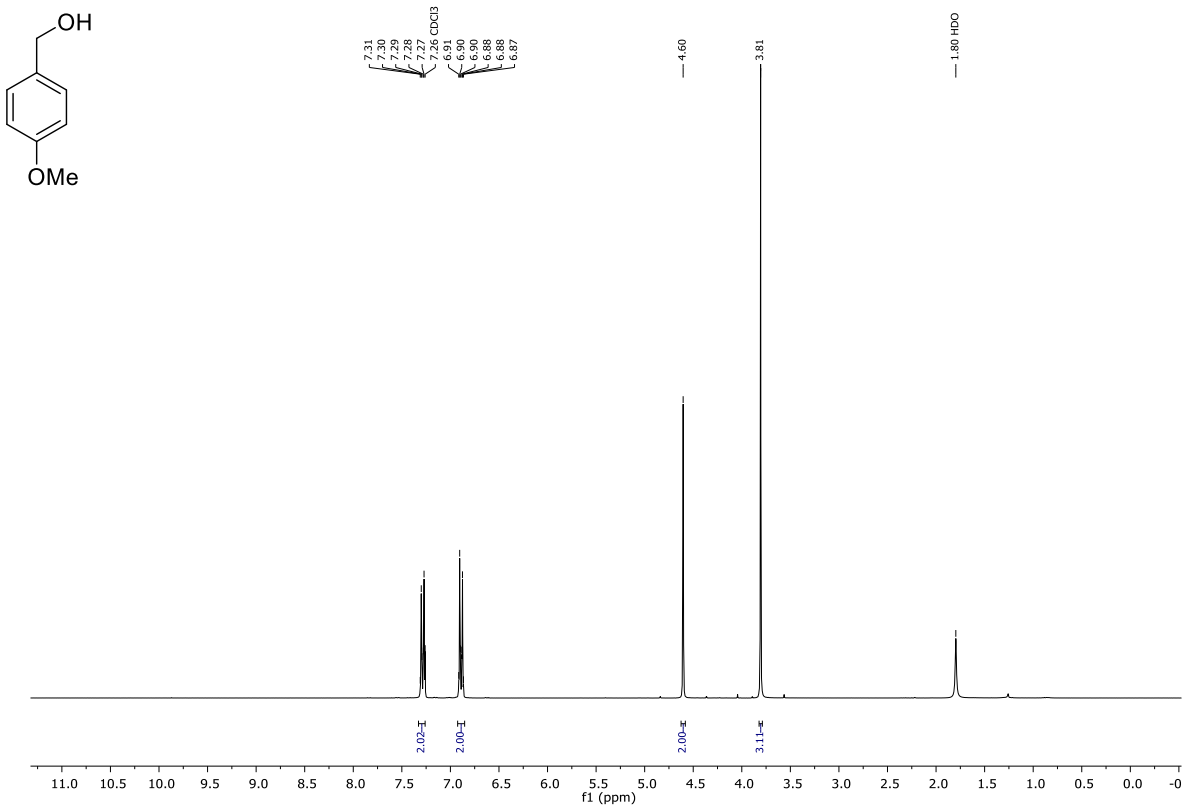

Figure F86*:* ^{1}H-NMR ($CDCl_3$, 300 MHz) of compound **45c**.

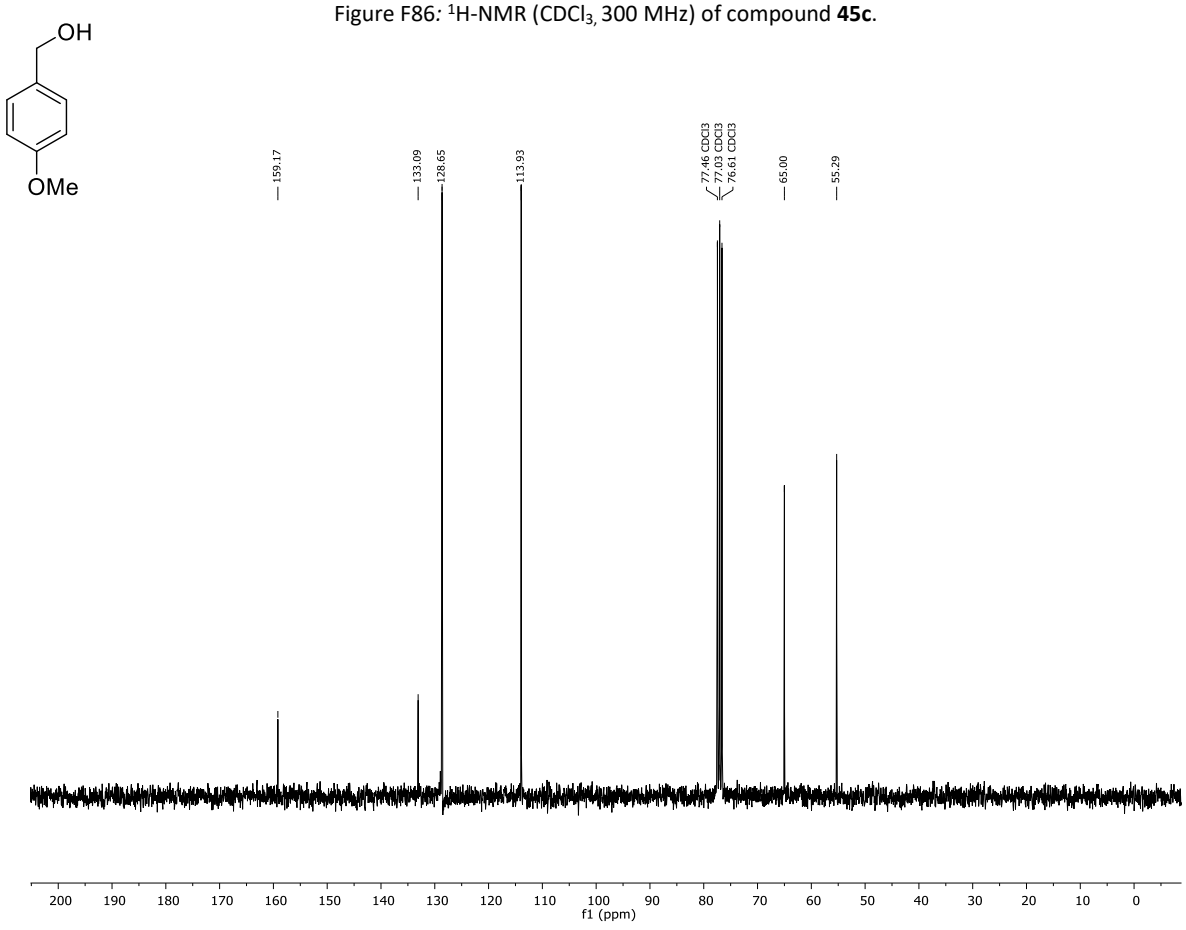

Figure F87: ^{13}C-NMR ($CDCl_3$, 75 MHz) of compound **45c**.

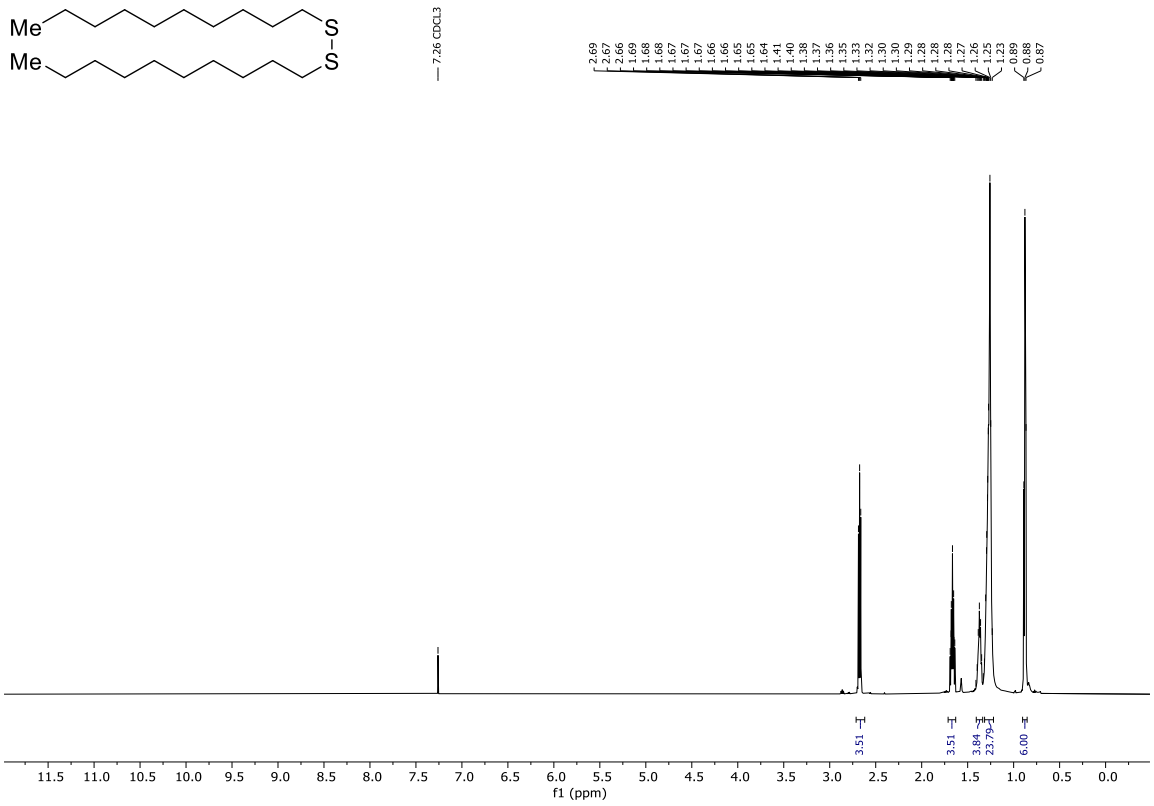

Figure F88: ^{1}H-NMR ($CDCl_3$, 600 MHz) of compound **53b**.

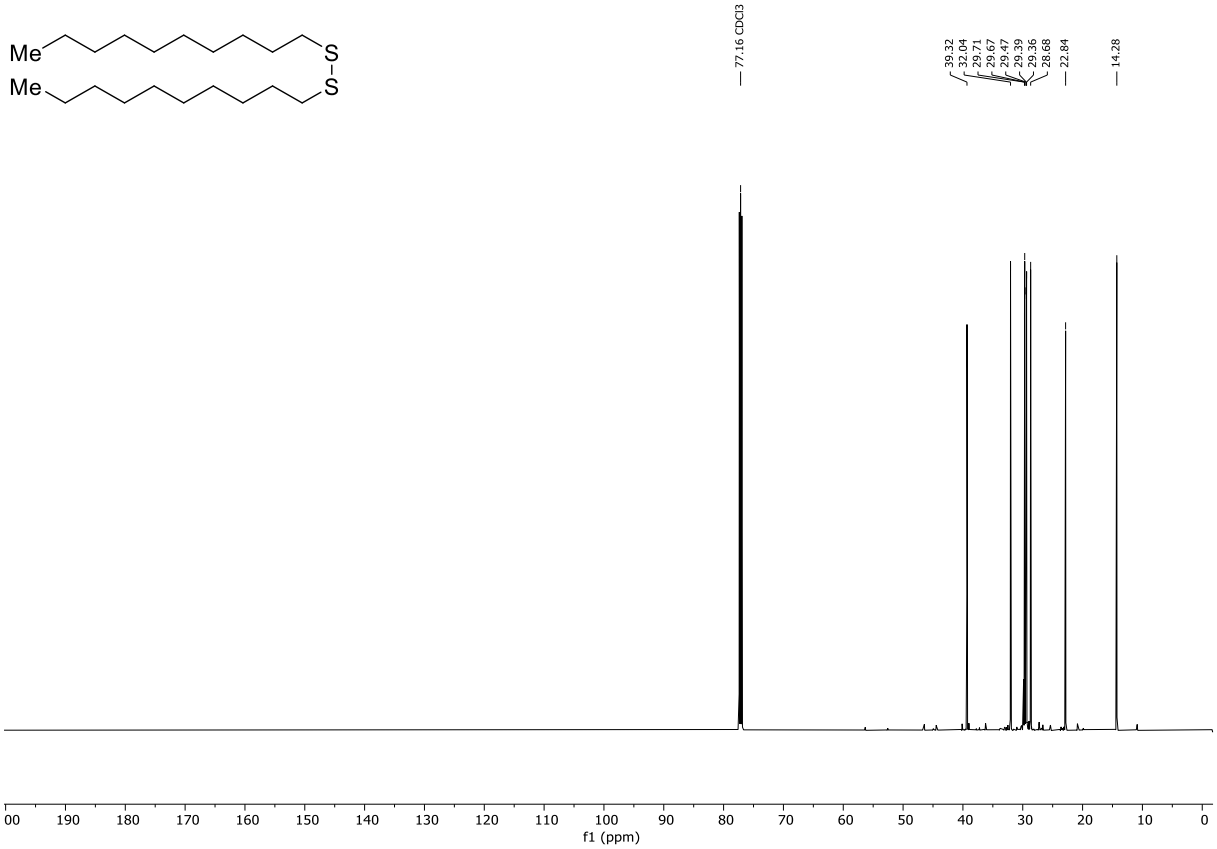

Figure F89: ^{13}C-NMR ($CDCl_3$, 151 MHz) of compound **53b.**