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Supporting Information

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Supporting information for

Microwave-assisted Synthesis of 2-Substituted-2-thiazolines and 5,6-Dihydro-4*H*-1,3-thiazines

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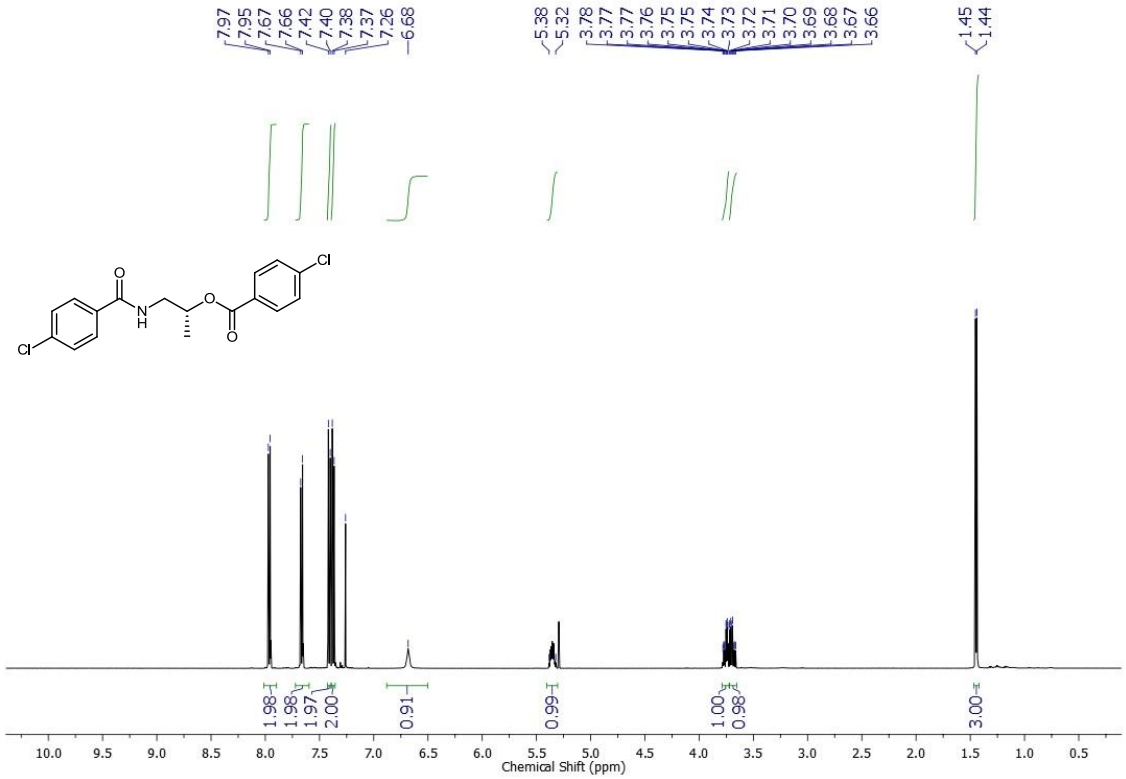
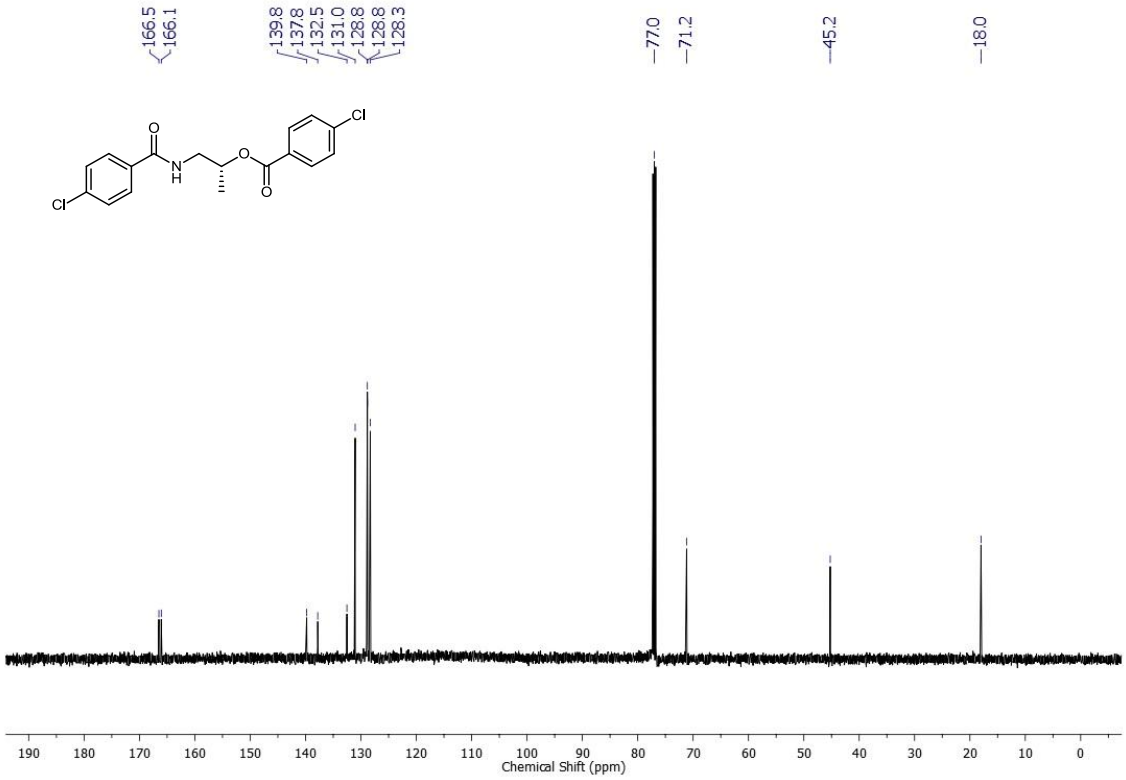
1. Copies of ^{1}H and ^{13}C NMR spectra of (*R*)-1-(4-chlorobenzamido)propan-2-yl 4-chlorobenzoate

^{1}H NMR (600 MHz, $CDCl_3$) spectrum of (*R*)-1-(4-chlorobenzamido)propan-2-yl 4-chlorobenzoate

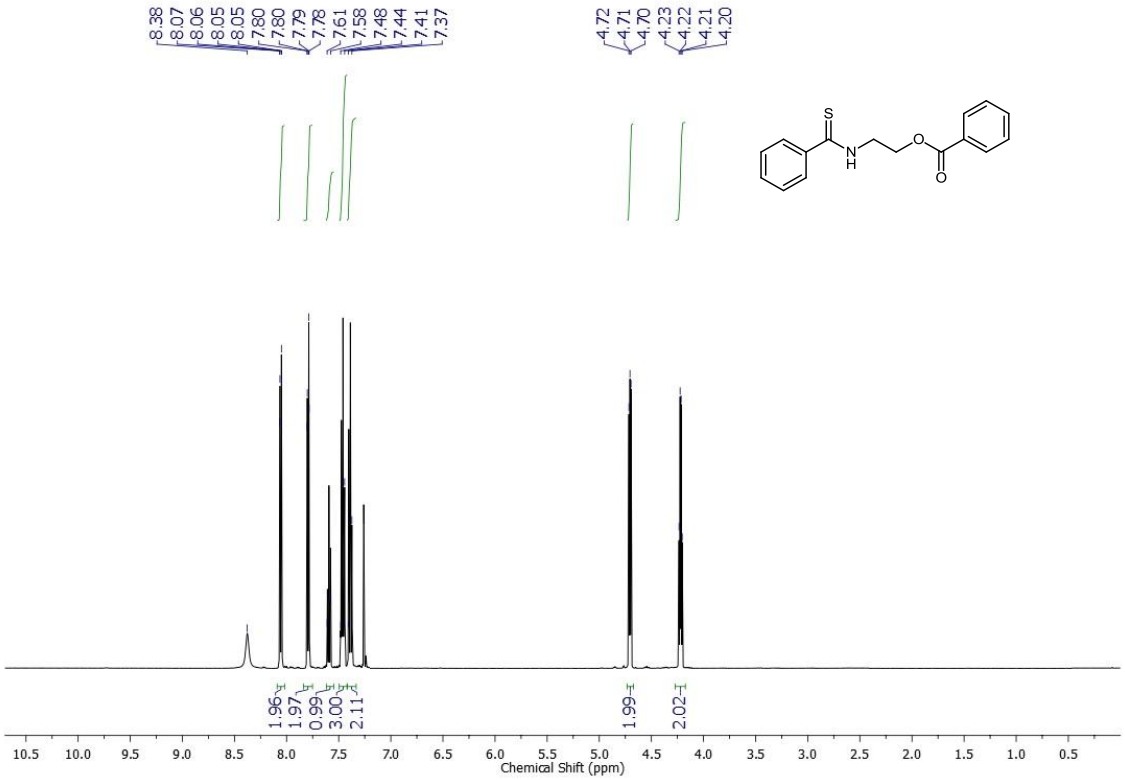


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of (*R*)-1-(4-chlorobenzamido)propan-2-yl 4-chlorobenzoate

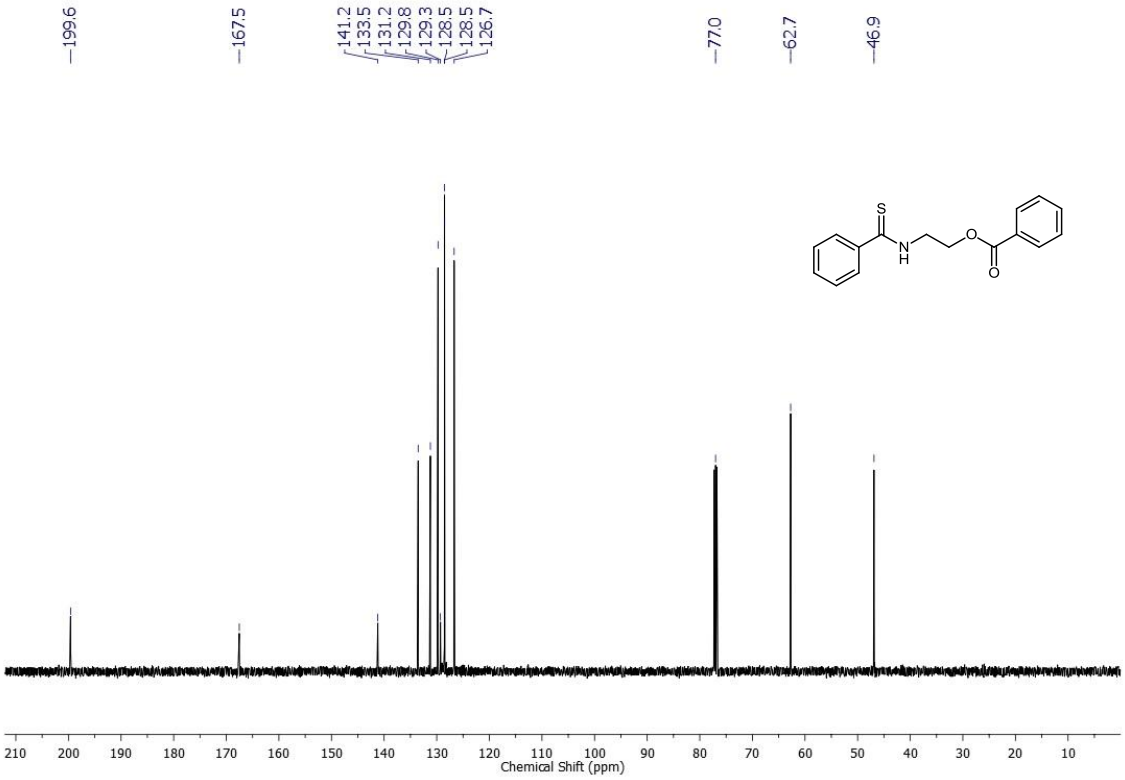


2. Copies of ^{1}H and ^{13}C NMR spectra of 2-phenylthioamidoethyl benzoate and (*R*)-1-(4-chlorophenylthioamido)propan-2-yl 4-chlorobenzoate

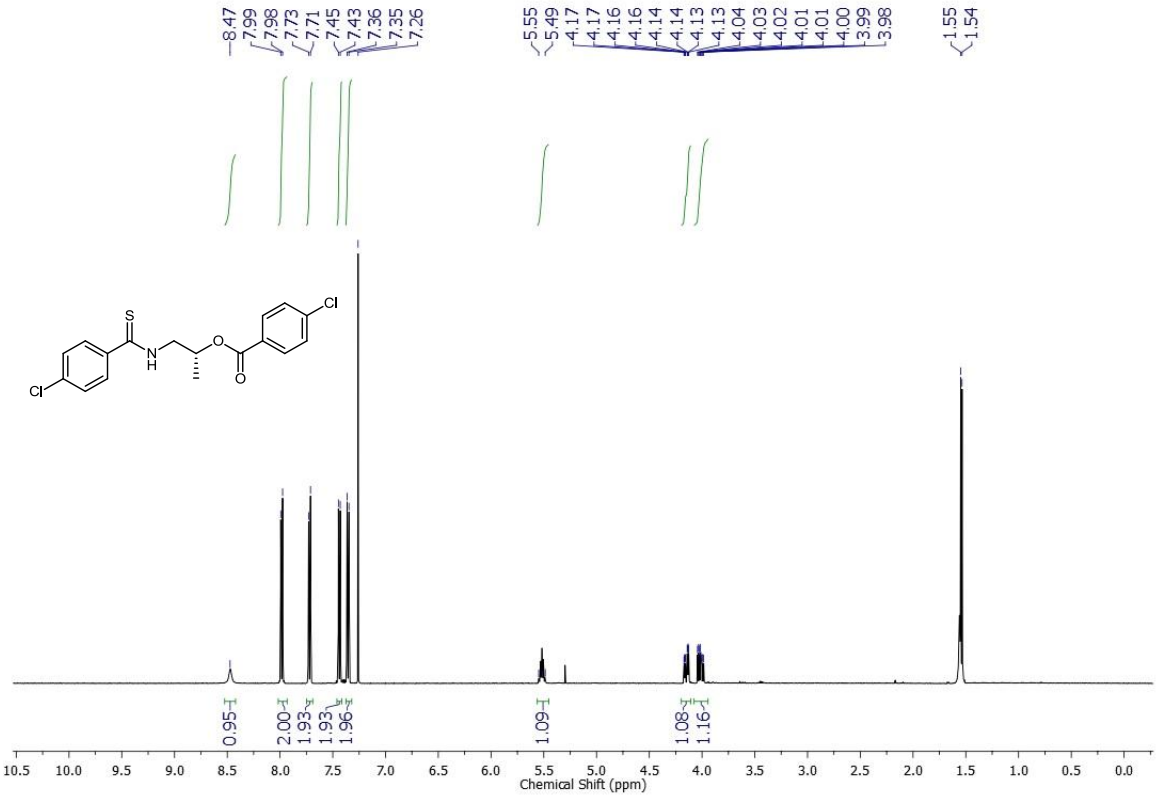
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 2-phenylthioamidoethyl benzoate



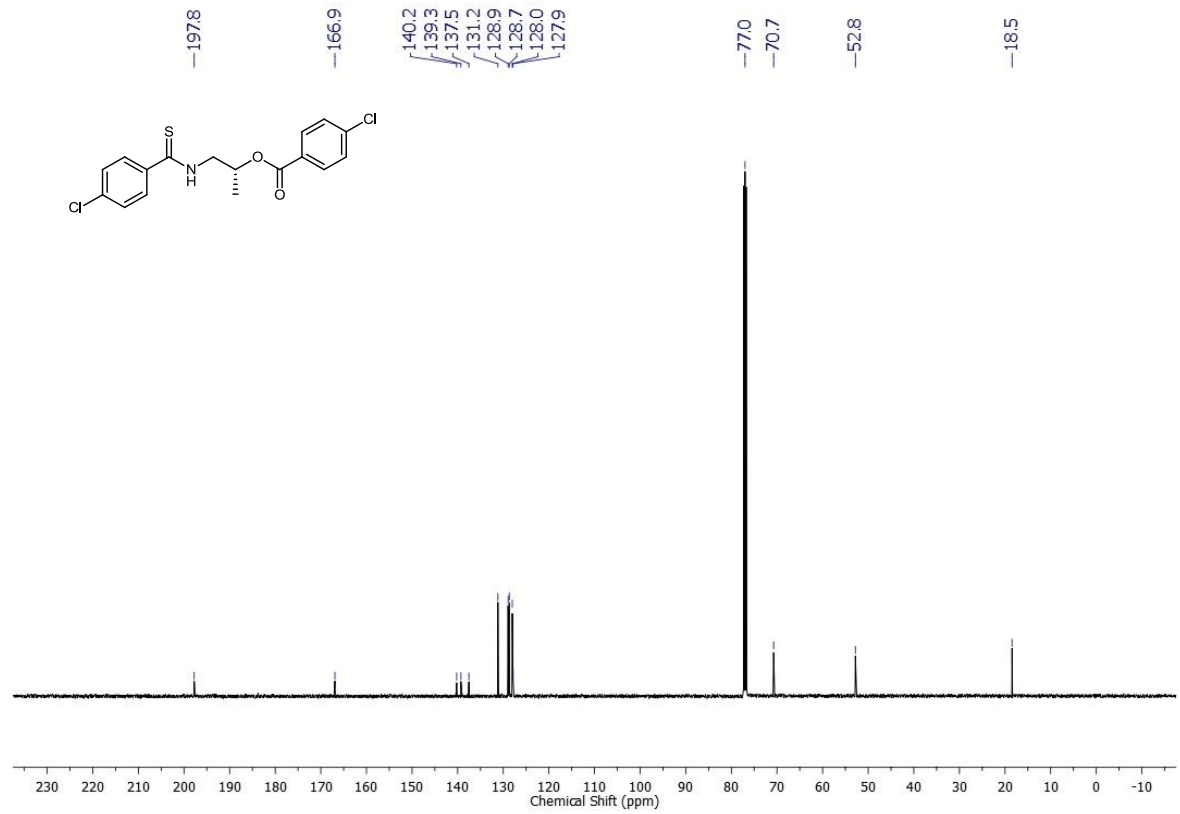
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of 2-phenylthioamidoethyl benzoate



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of (*R*)-1-(4-chlorophenylthioamido)propan-2-yl 4-chlorobenzoate

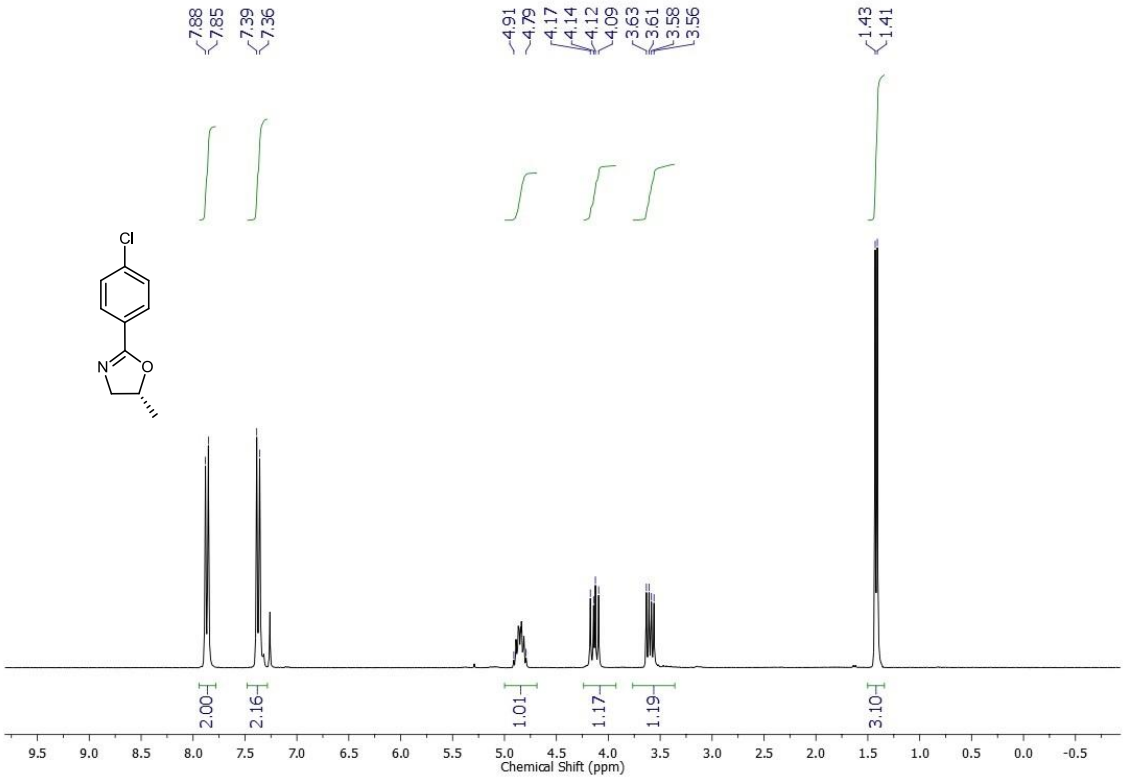


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of (*R*)-1-(4-chlorophenylthioamido)propan-2-yl 4-chlorobenzoate

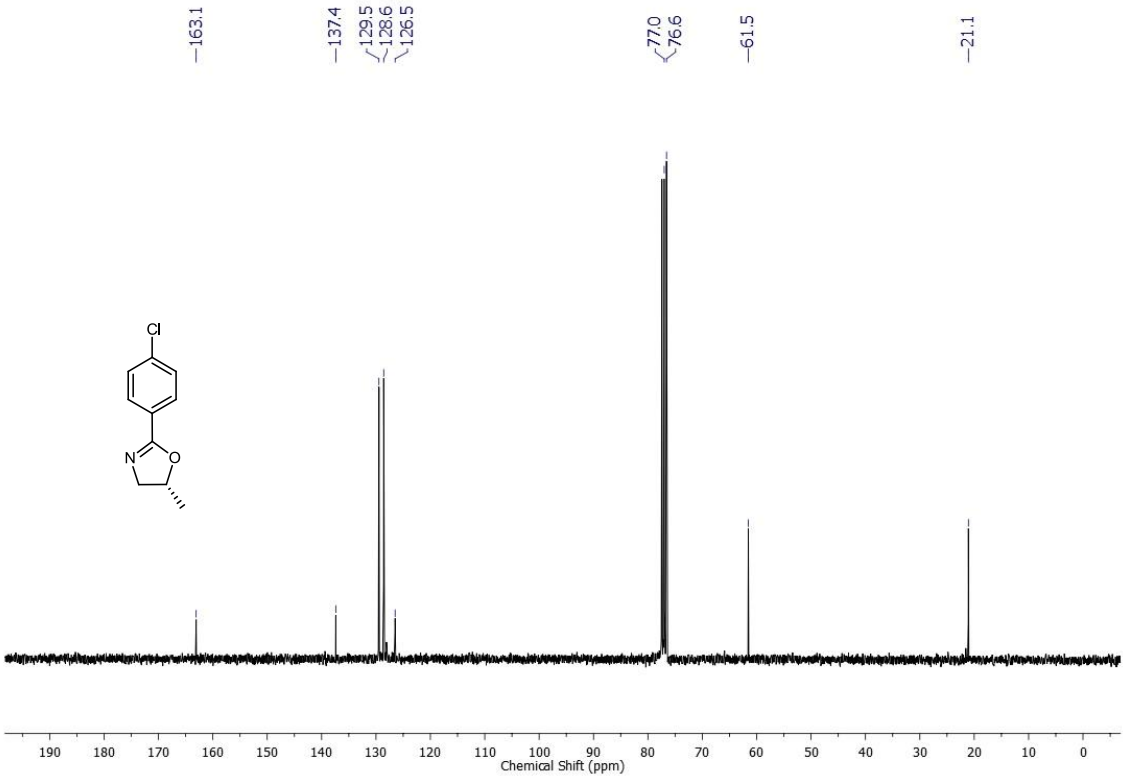


3. Copies of ^{1}H and ^{13}C NMR spectra of (*R*)-2-(4-chlorophenyl)-5-methyl-4,5-dihydrooxazole

^{1}H NMR (600 MHz, $CDCl_3$) spectrum of (*R*)-2-(4-chlorophenyl)-5-methyl-4,5-dihydrooxazole

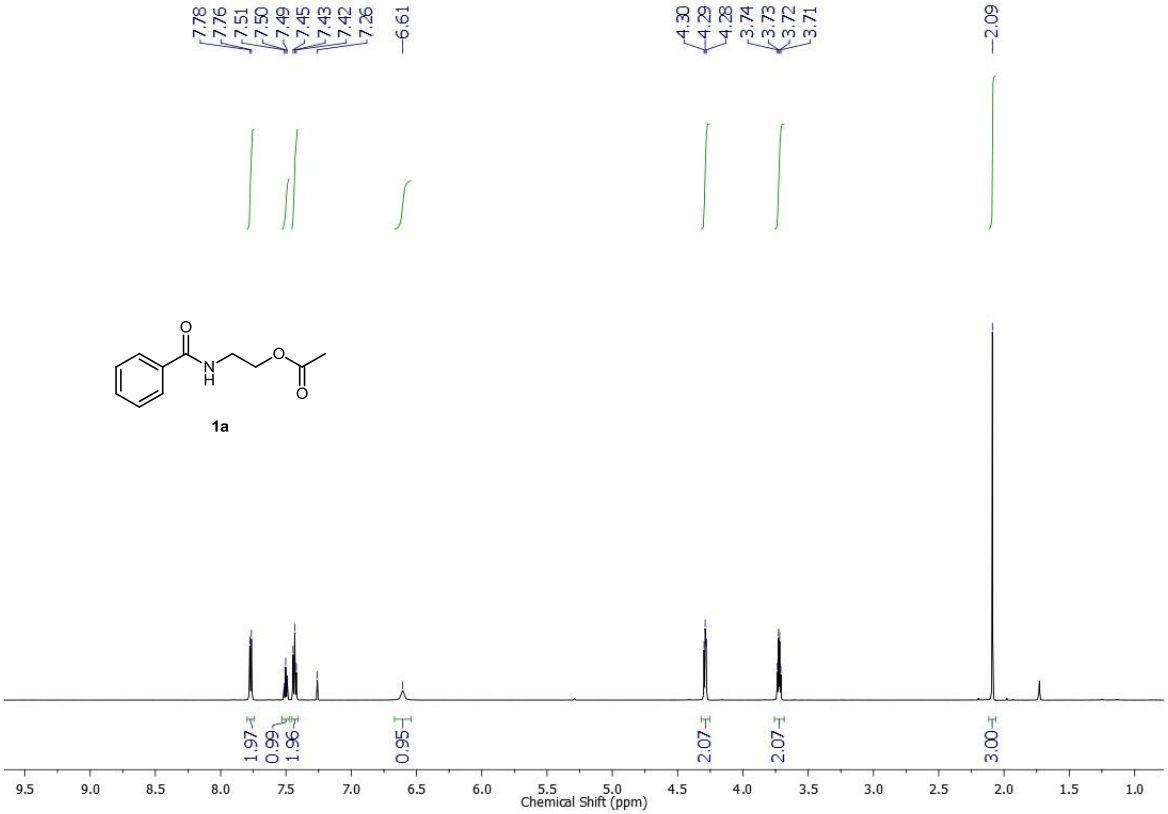


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of (*R*)-2-(4-chlorophenyl)-5-methyl-4,5-dihydrooxazole

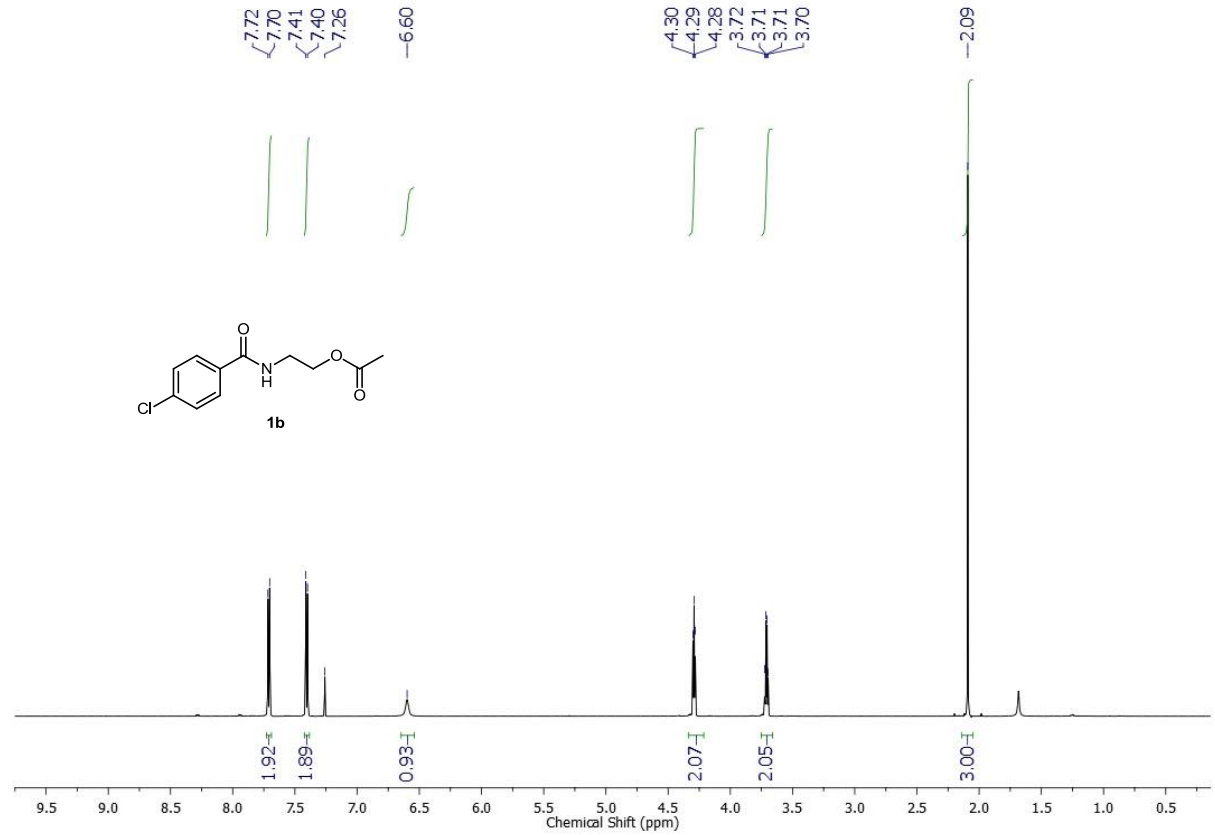


4. Copies of ^{1}H and ^{13}C NMR spectra of compounds 1-2

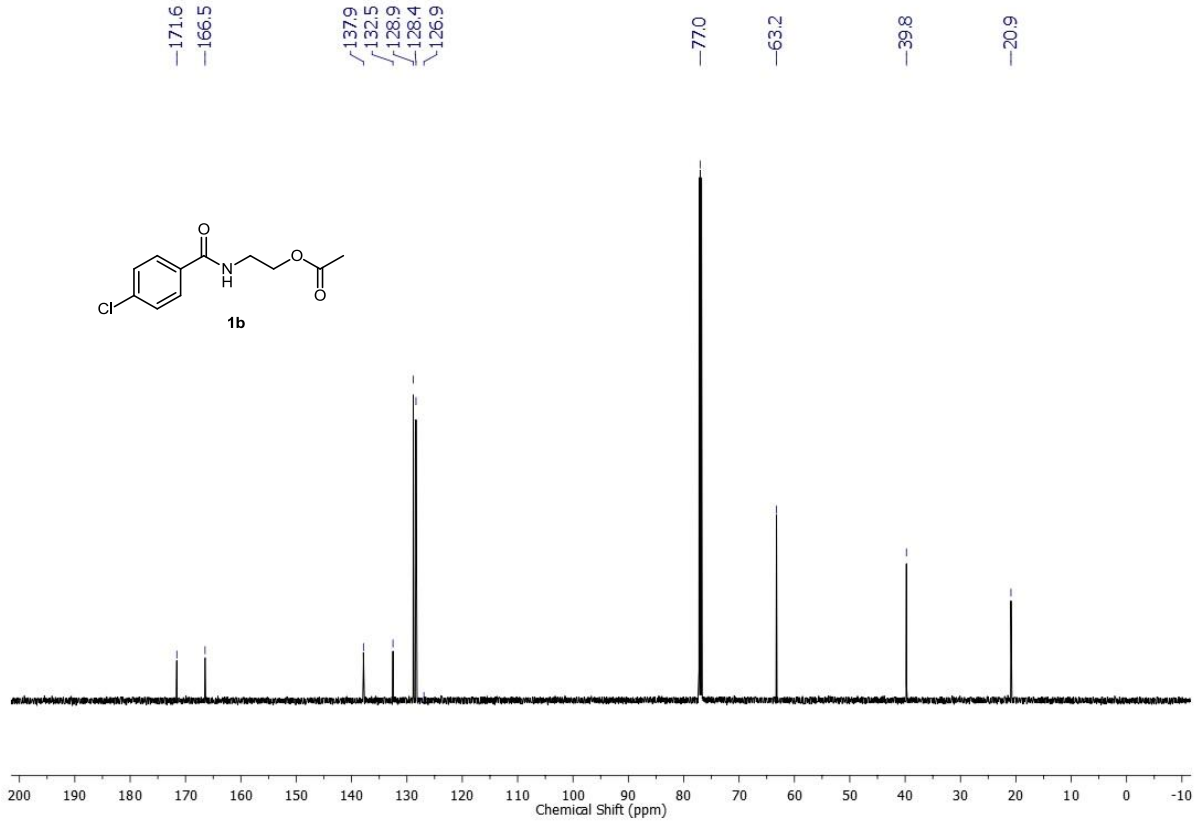
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1a**



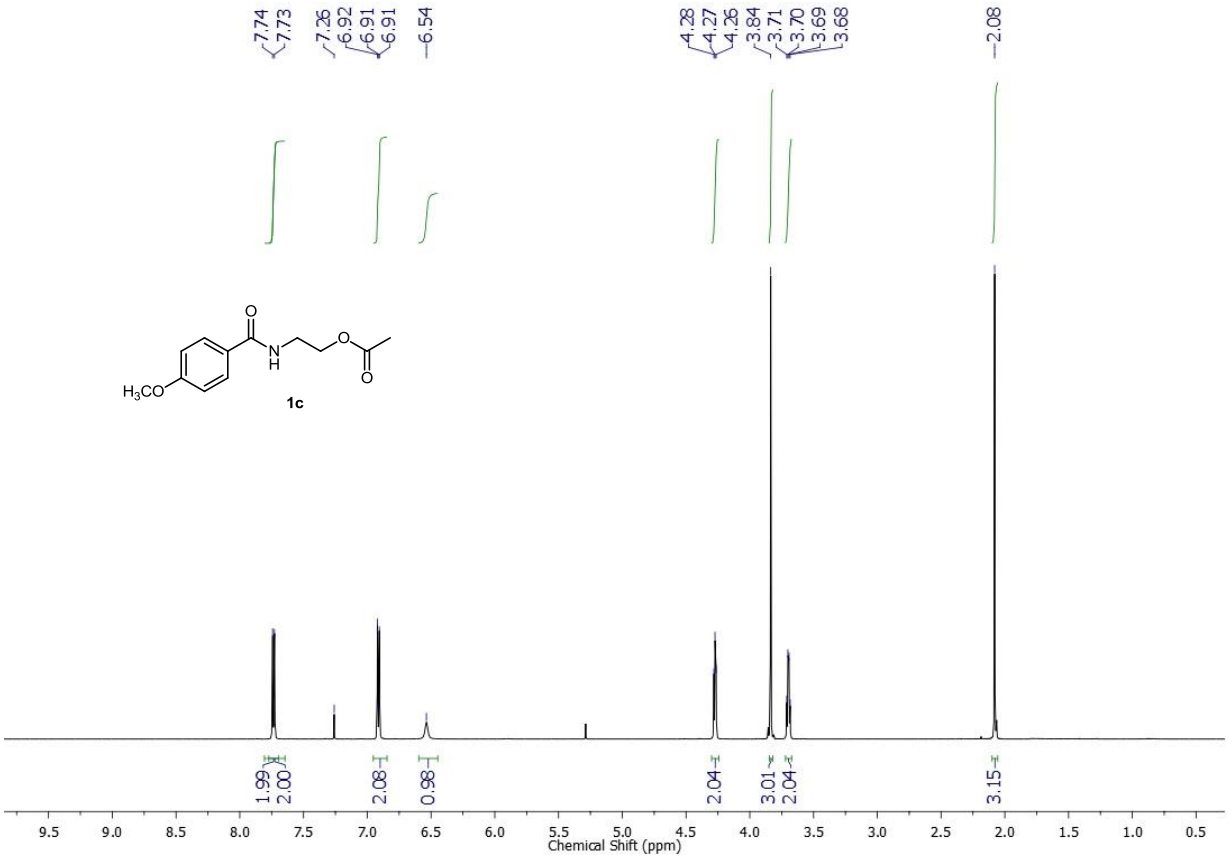
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1b**



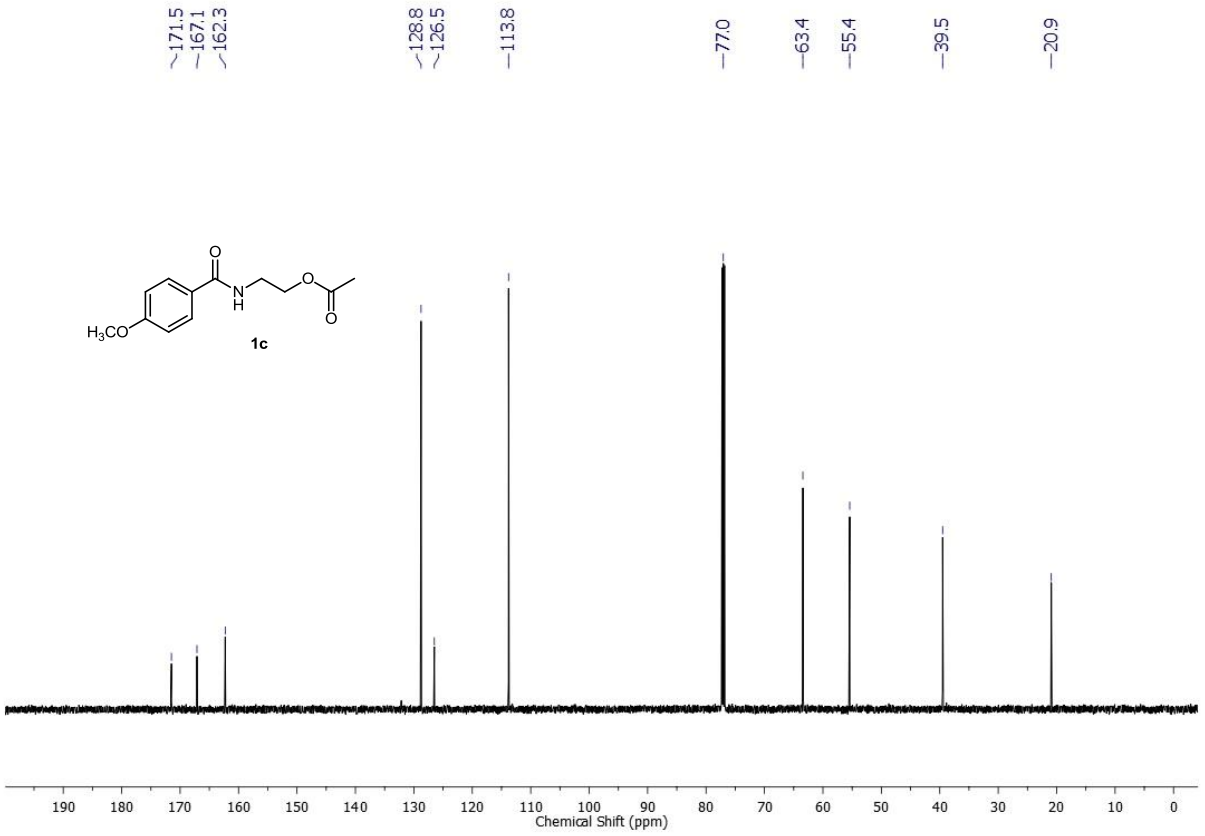
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1b**



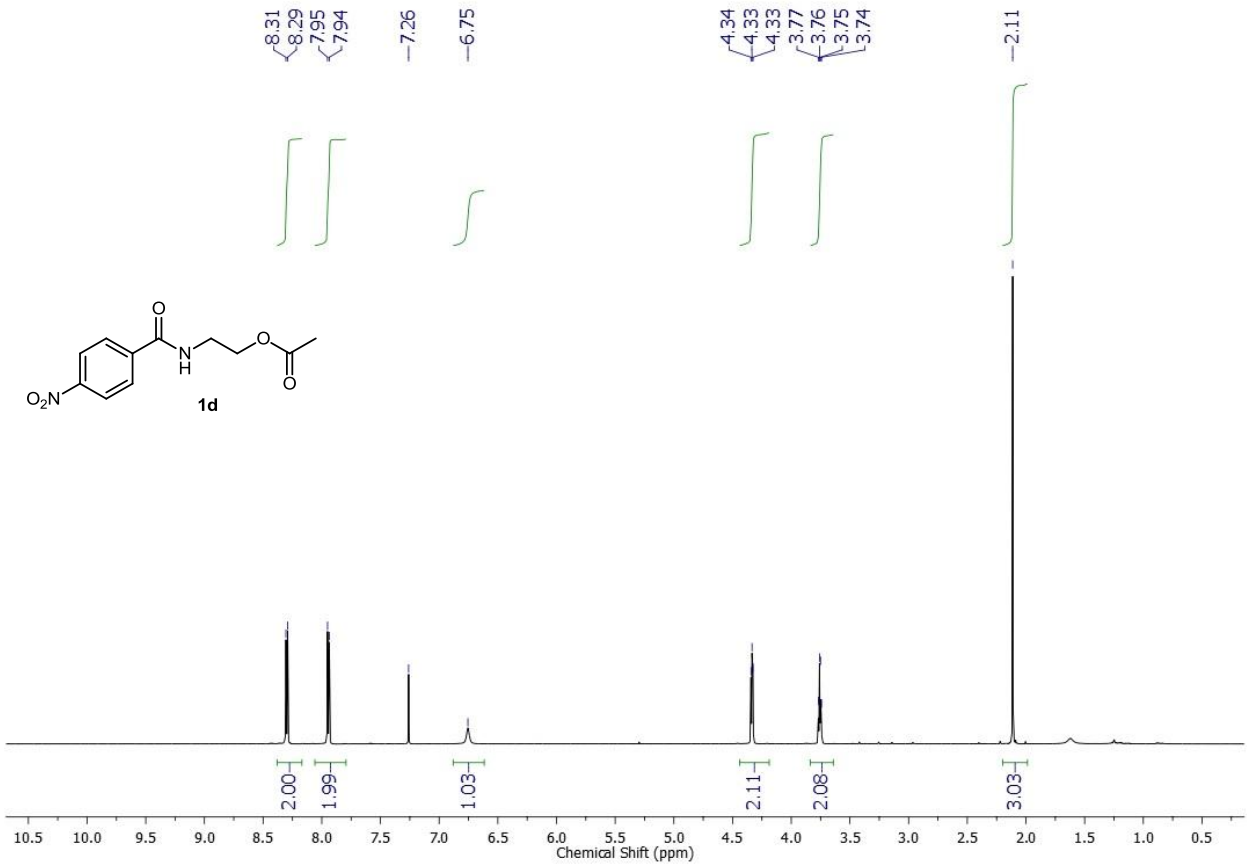
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1c**



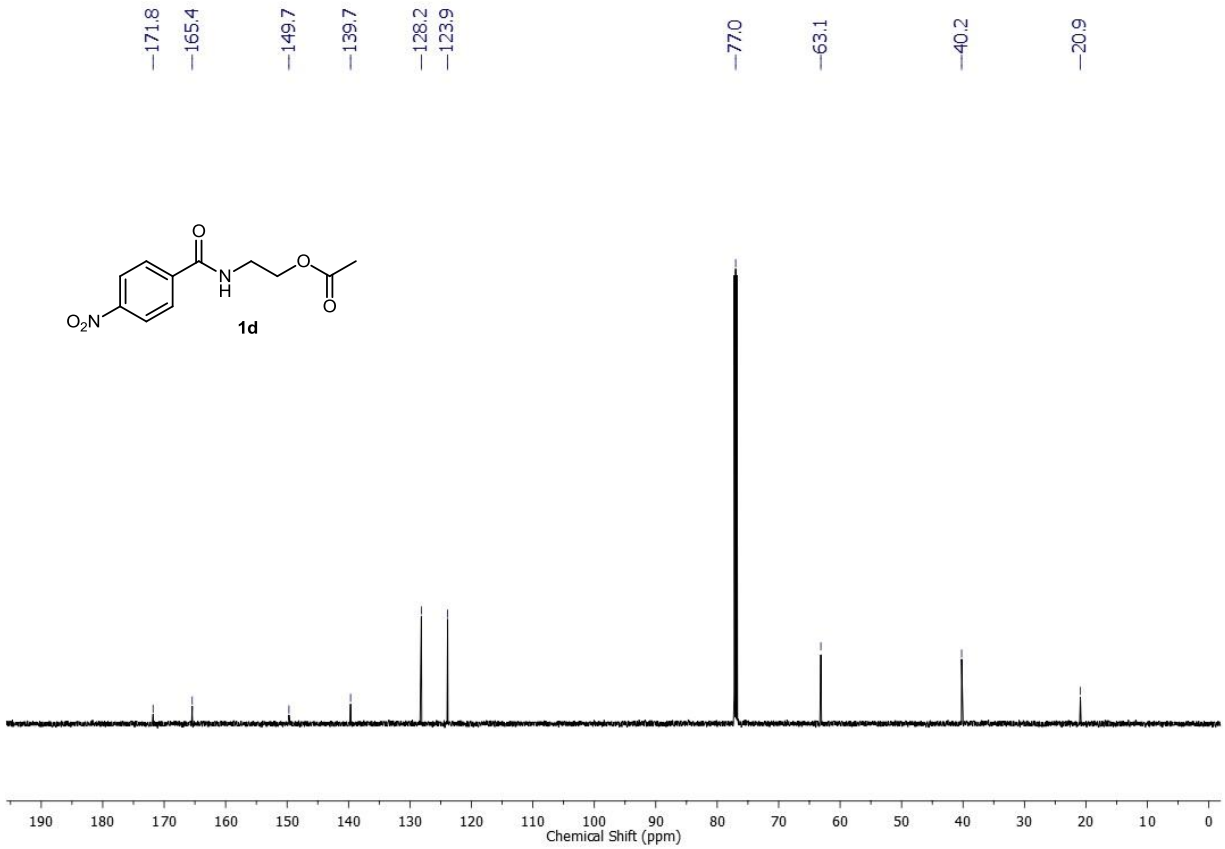
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1c**



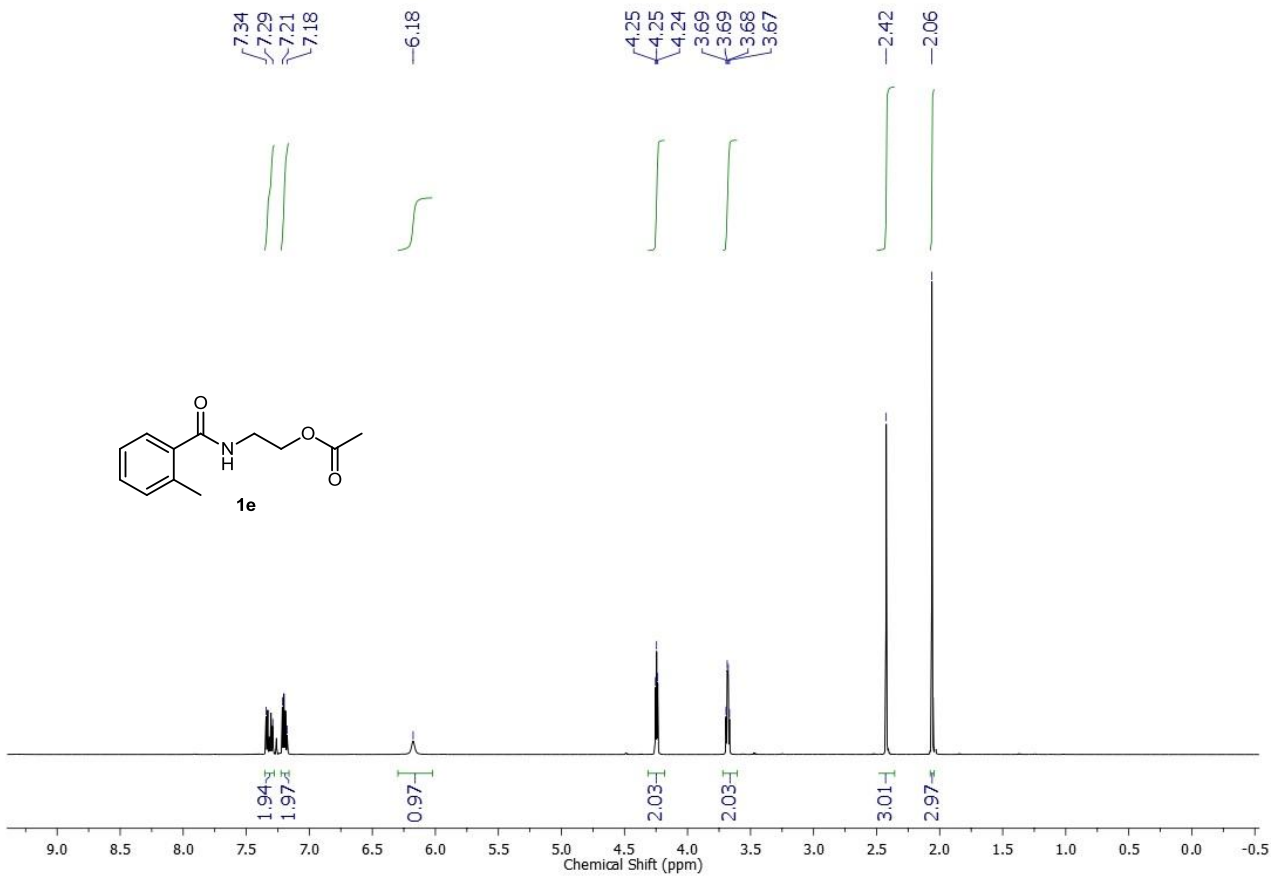
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1d**



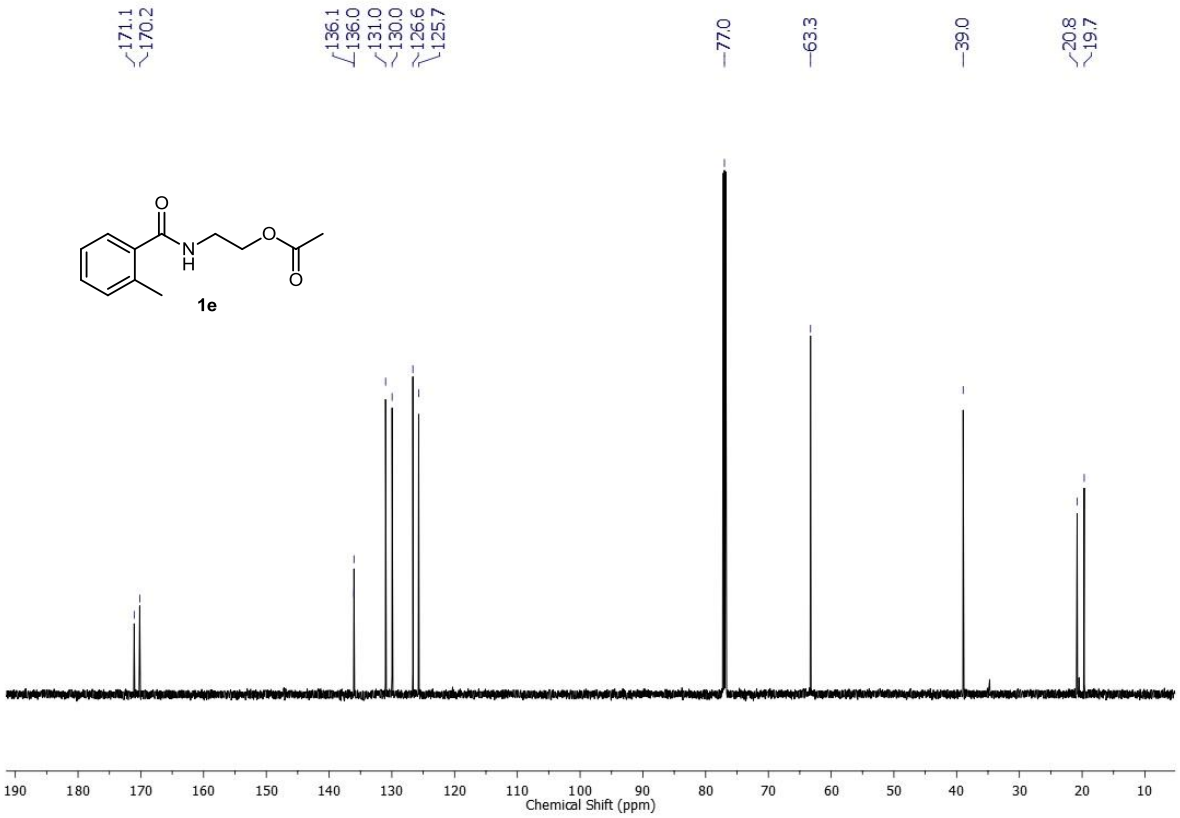
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1d**



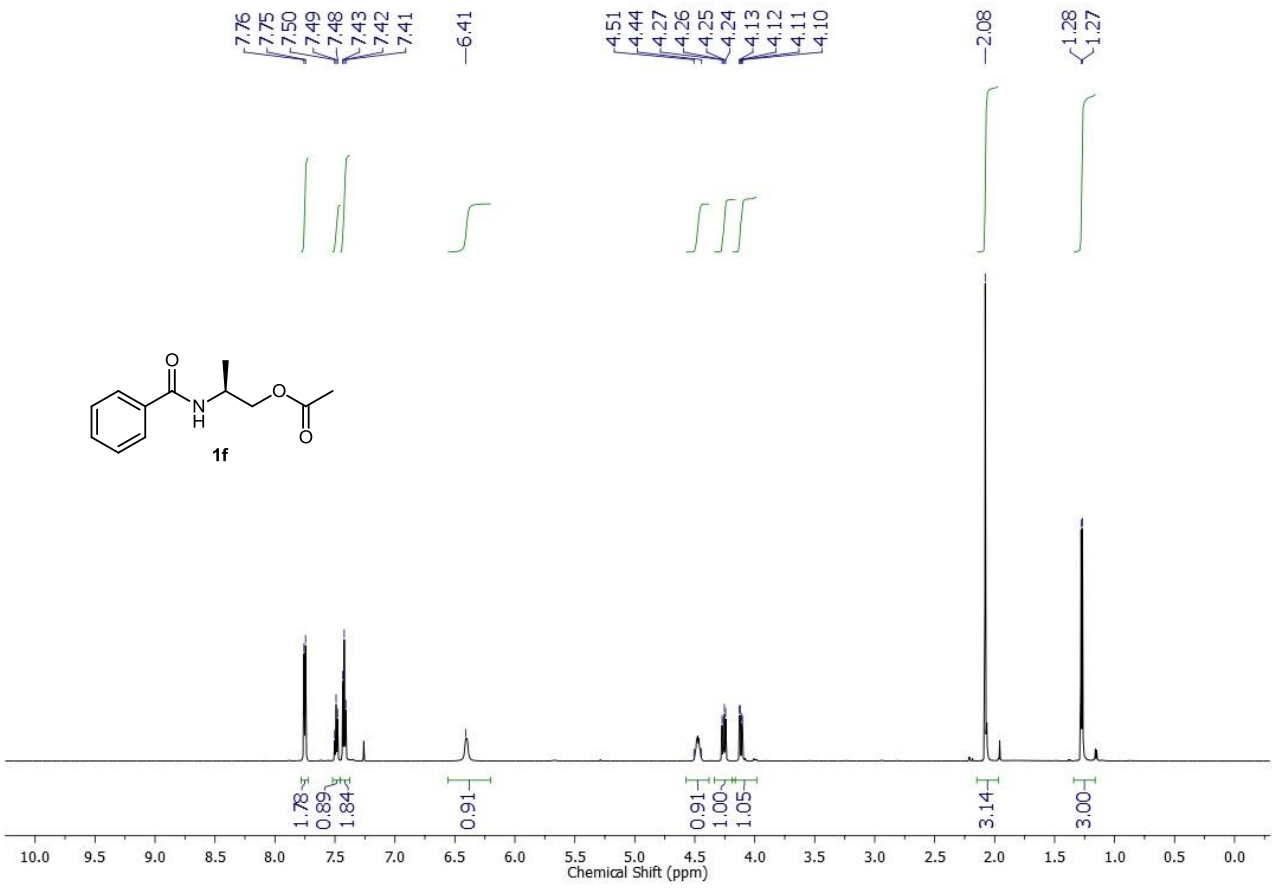
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1e**



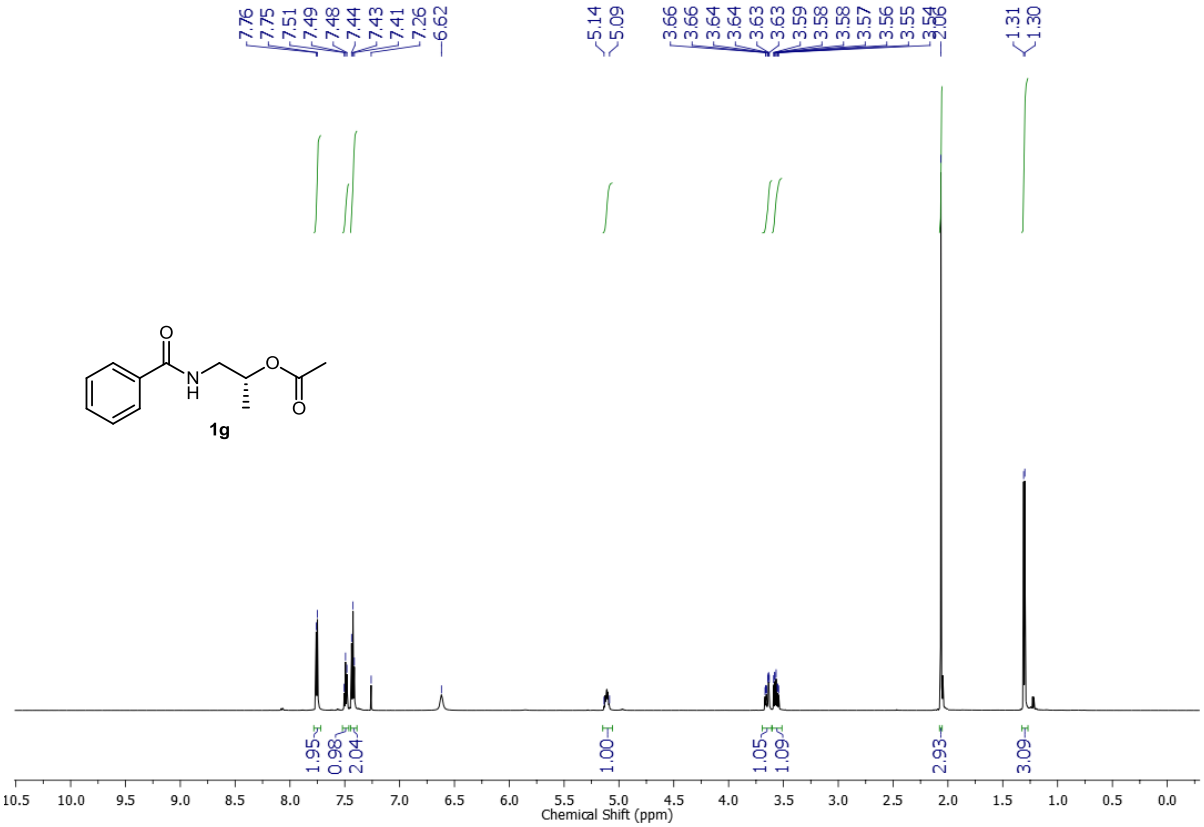
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1e**



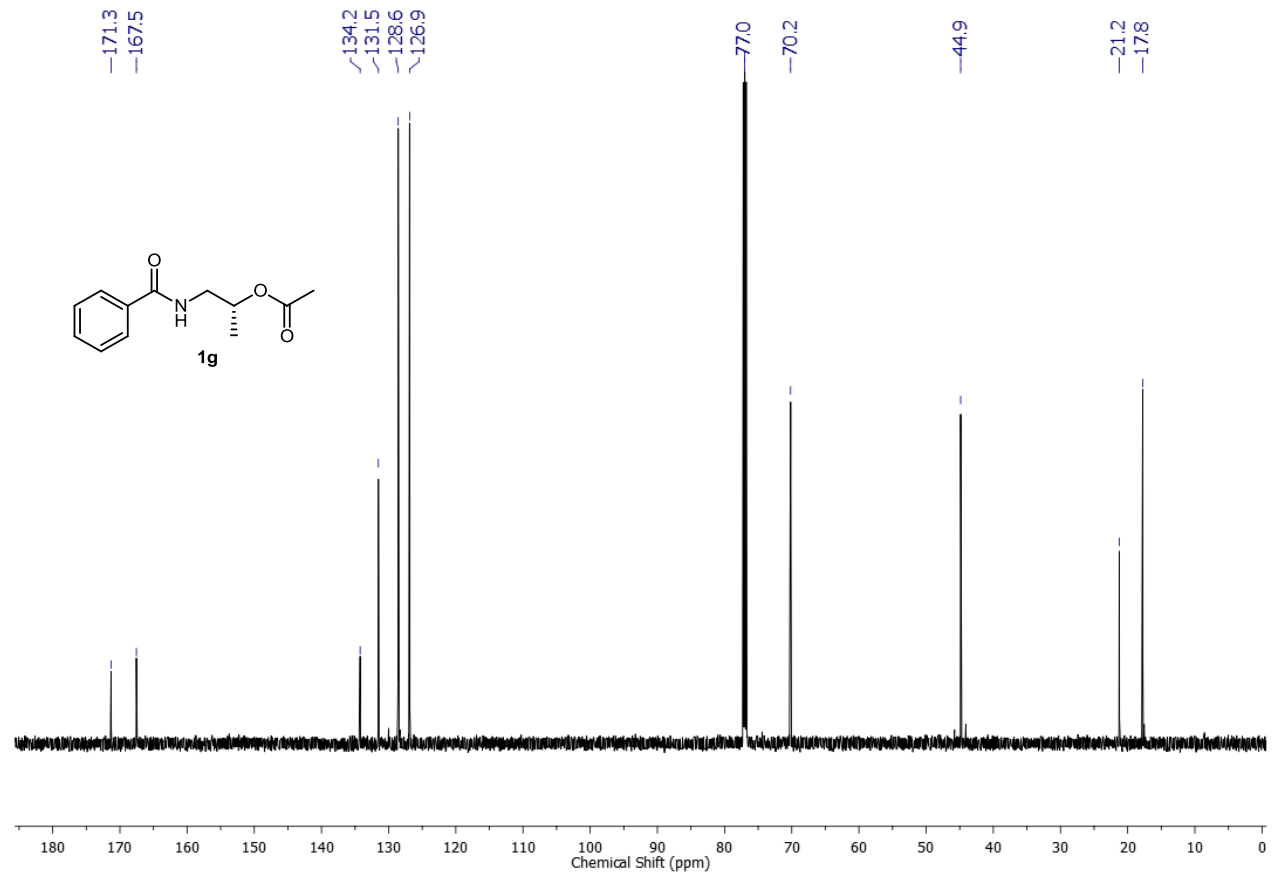
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1f**



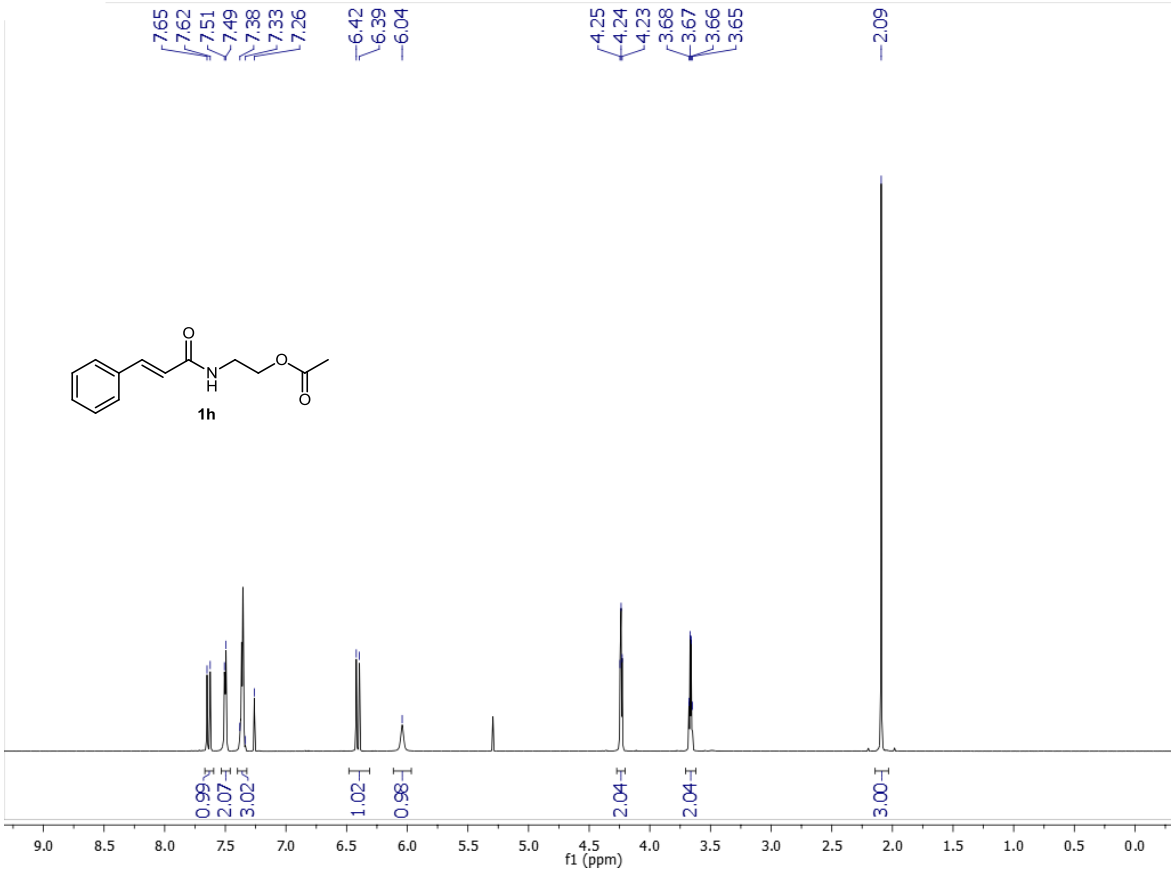
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1g**



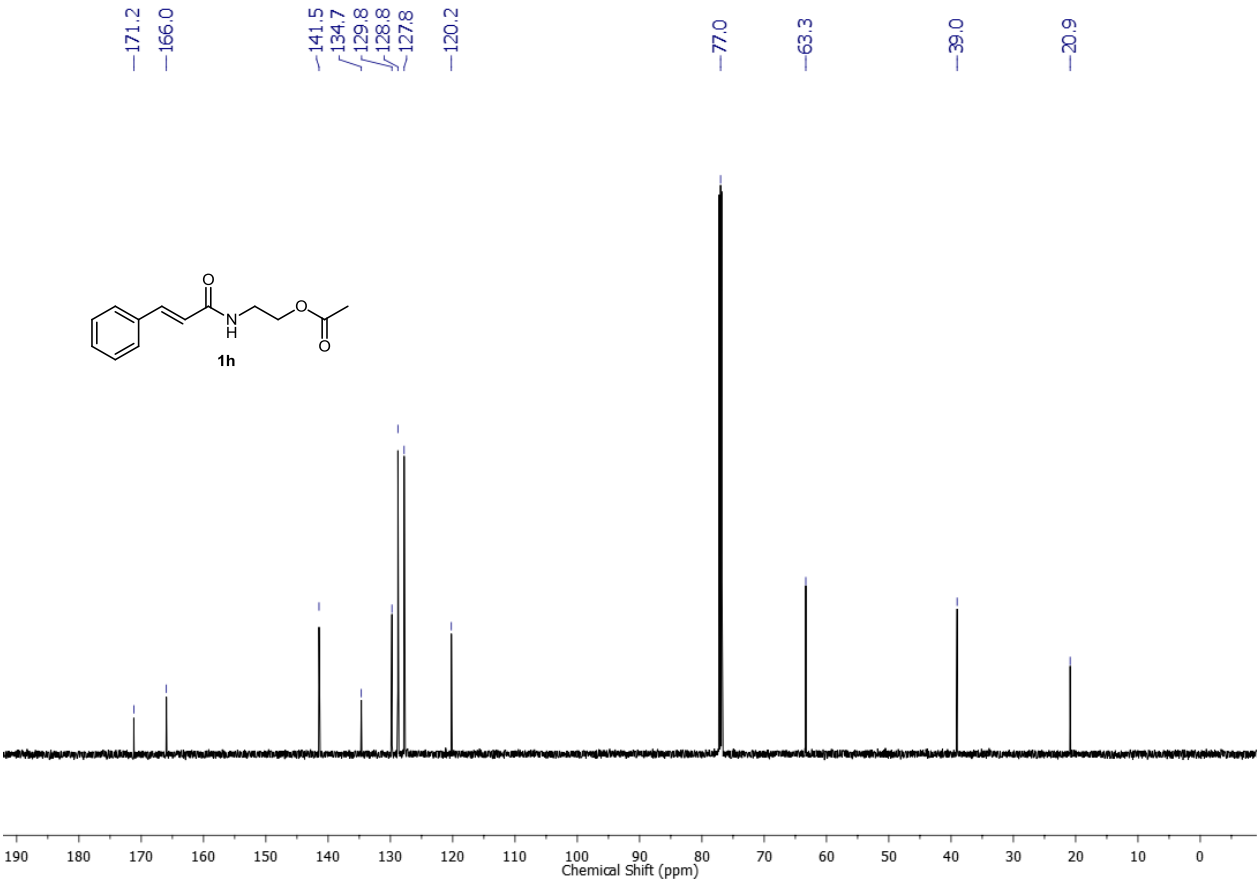
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1g**



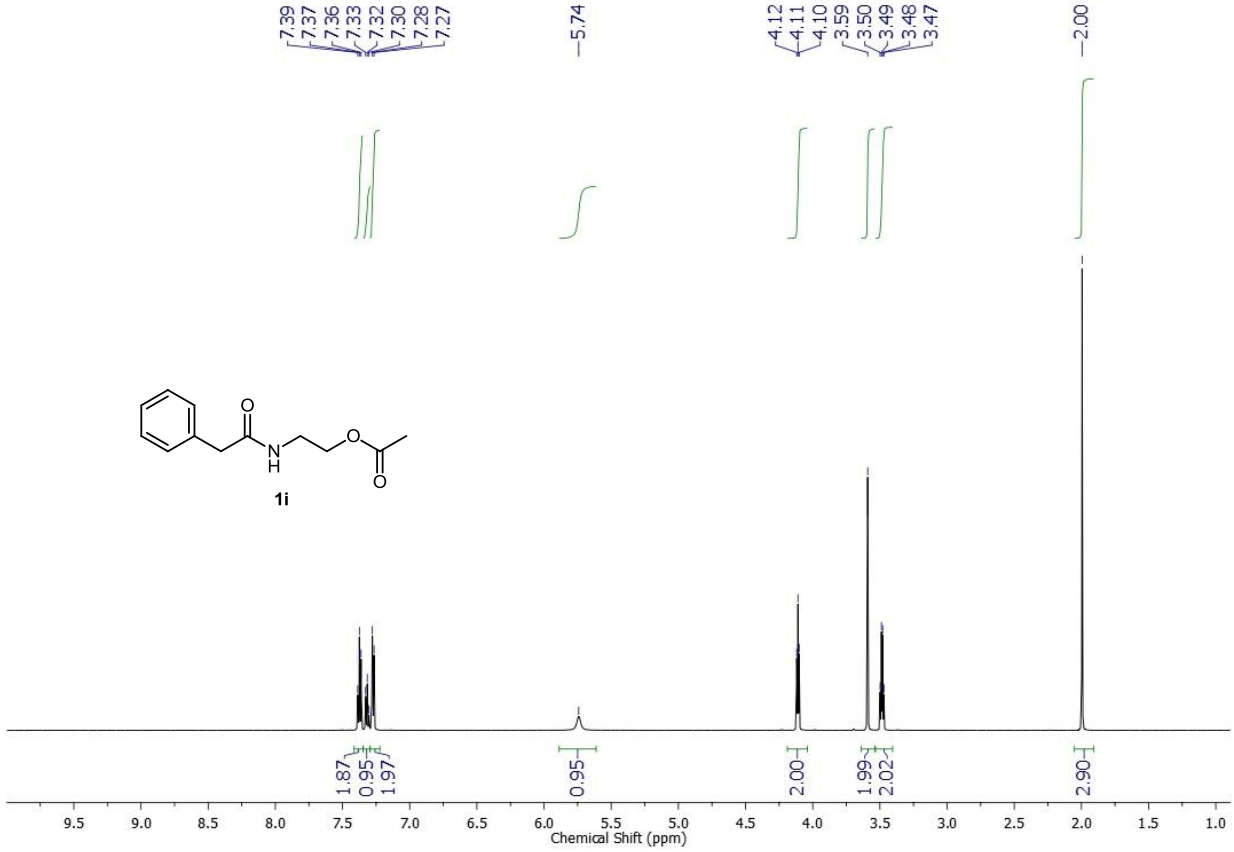
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1h**



^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **1h**

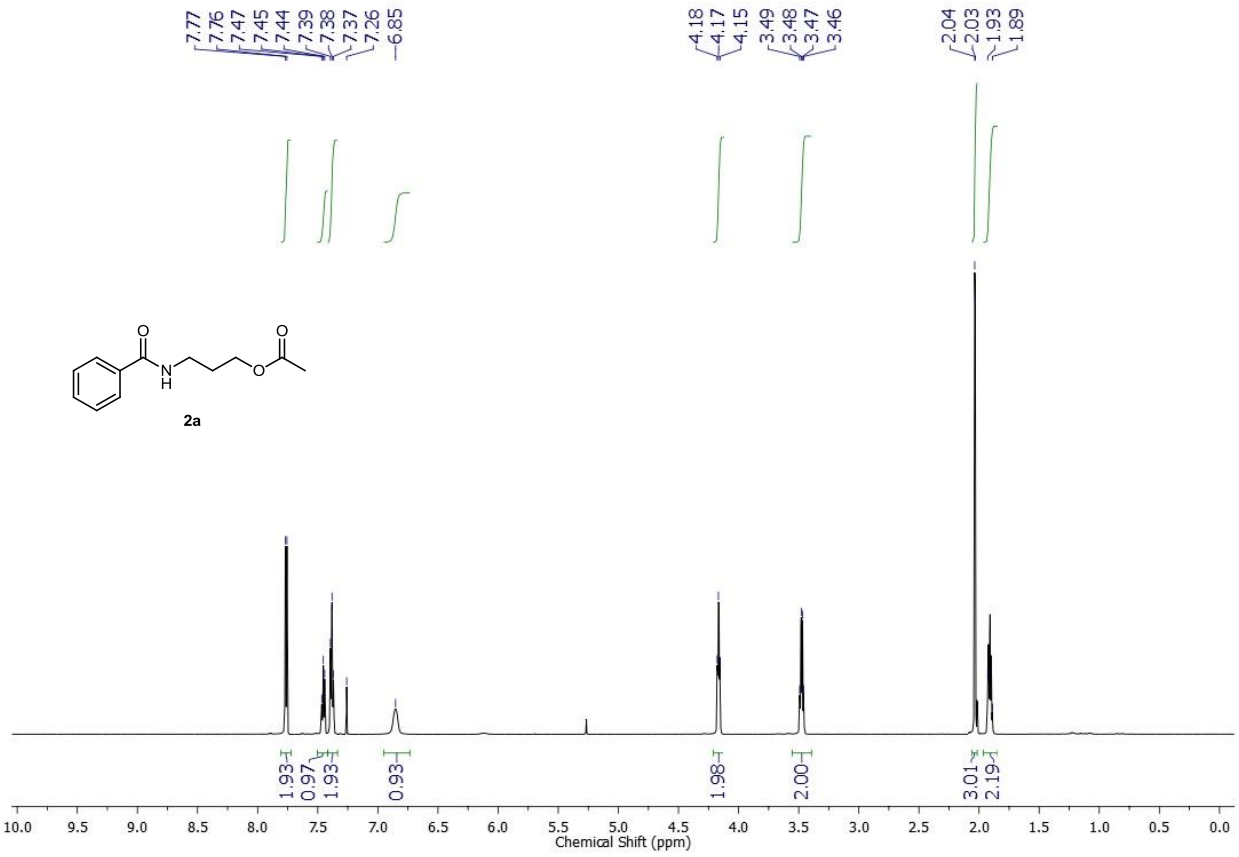


^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **1i**



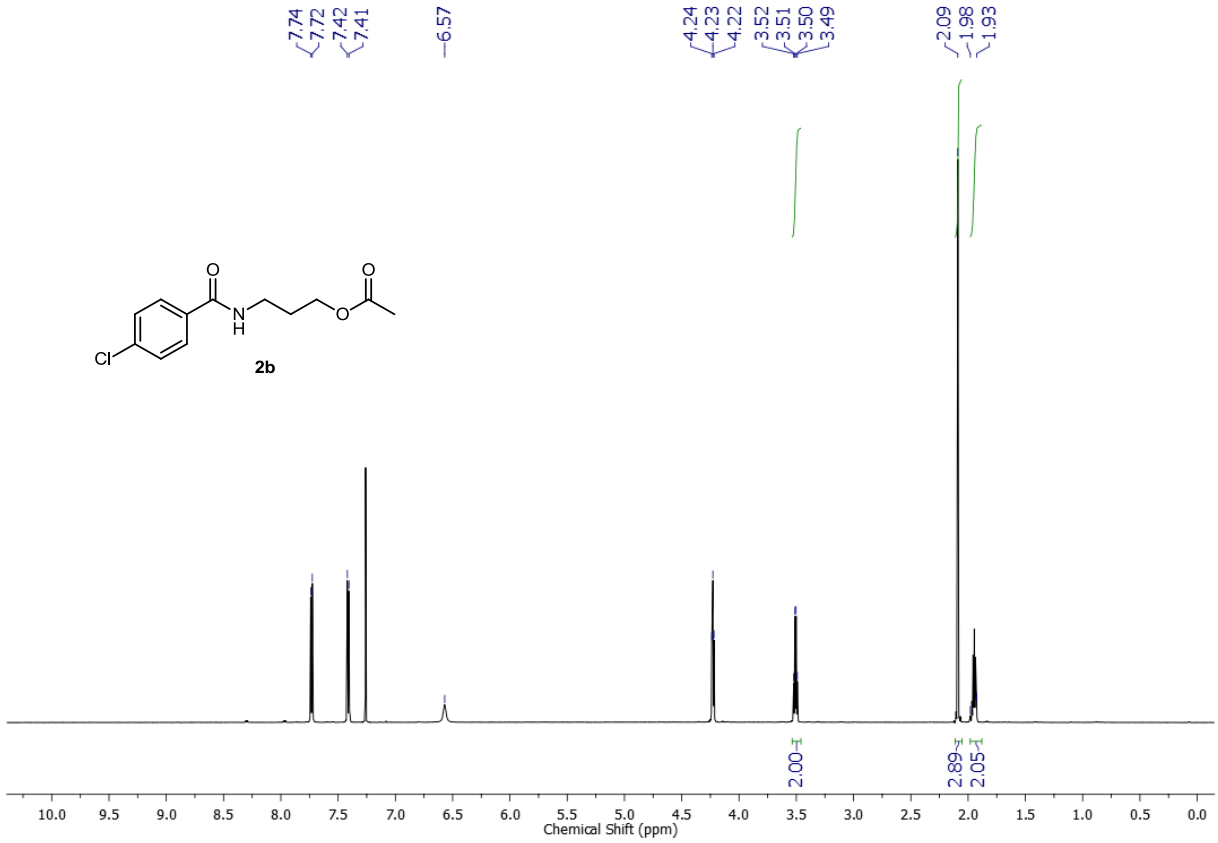
1i

^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2a**

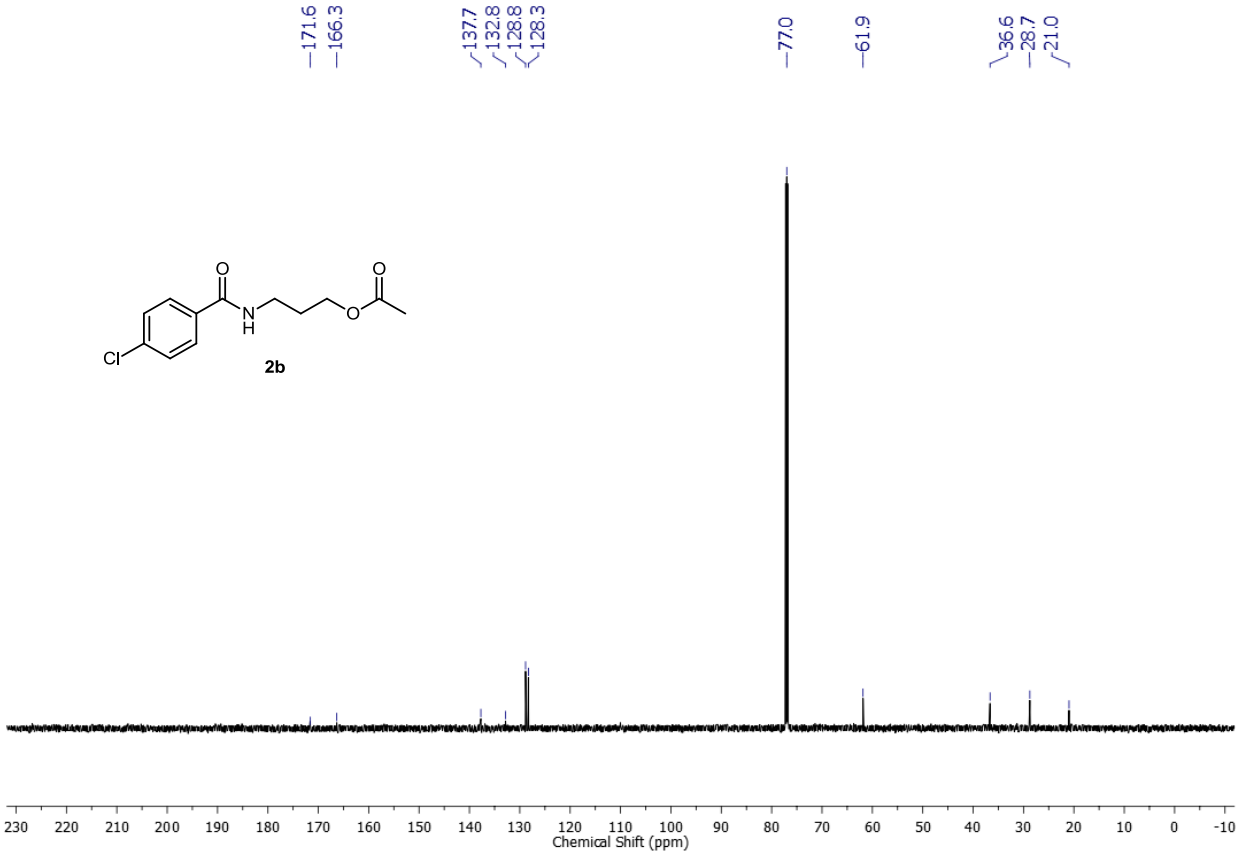


2a

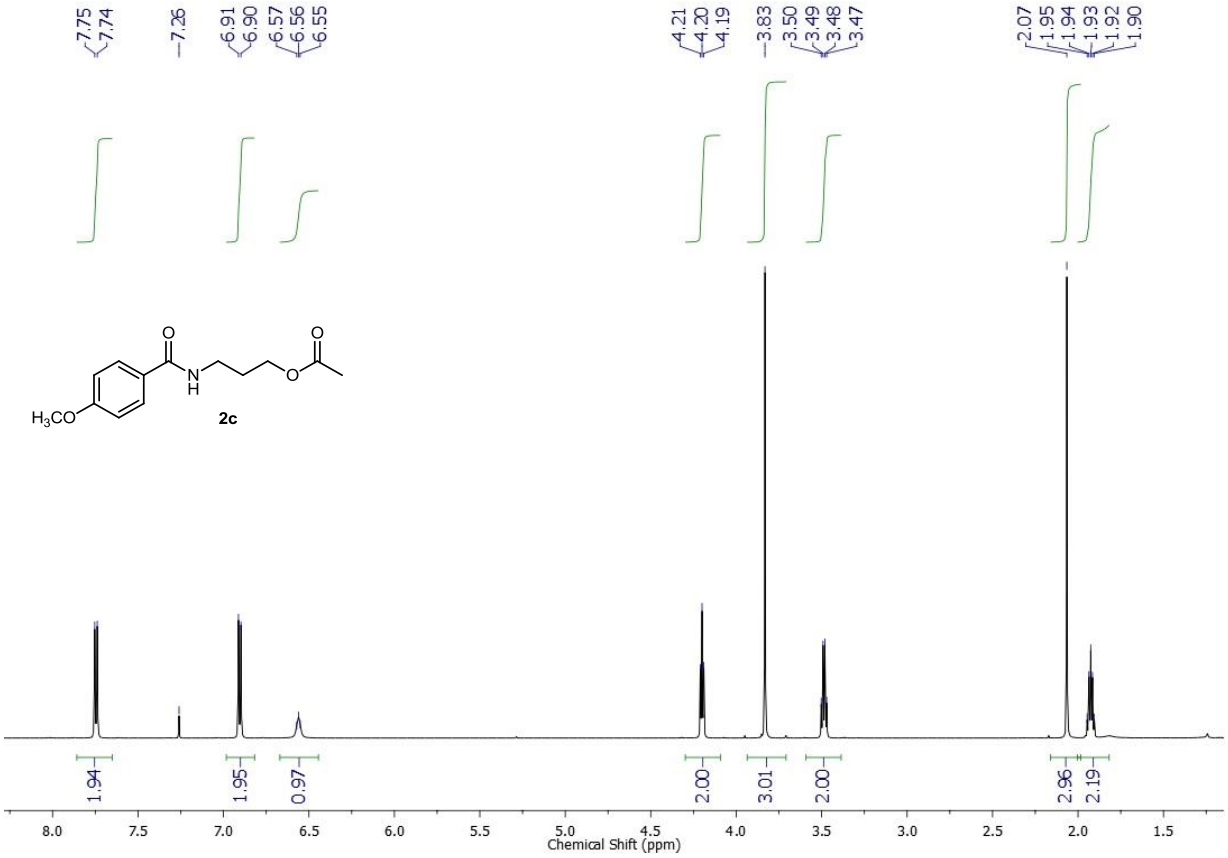
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2b**



^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2b**

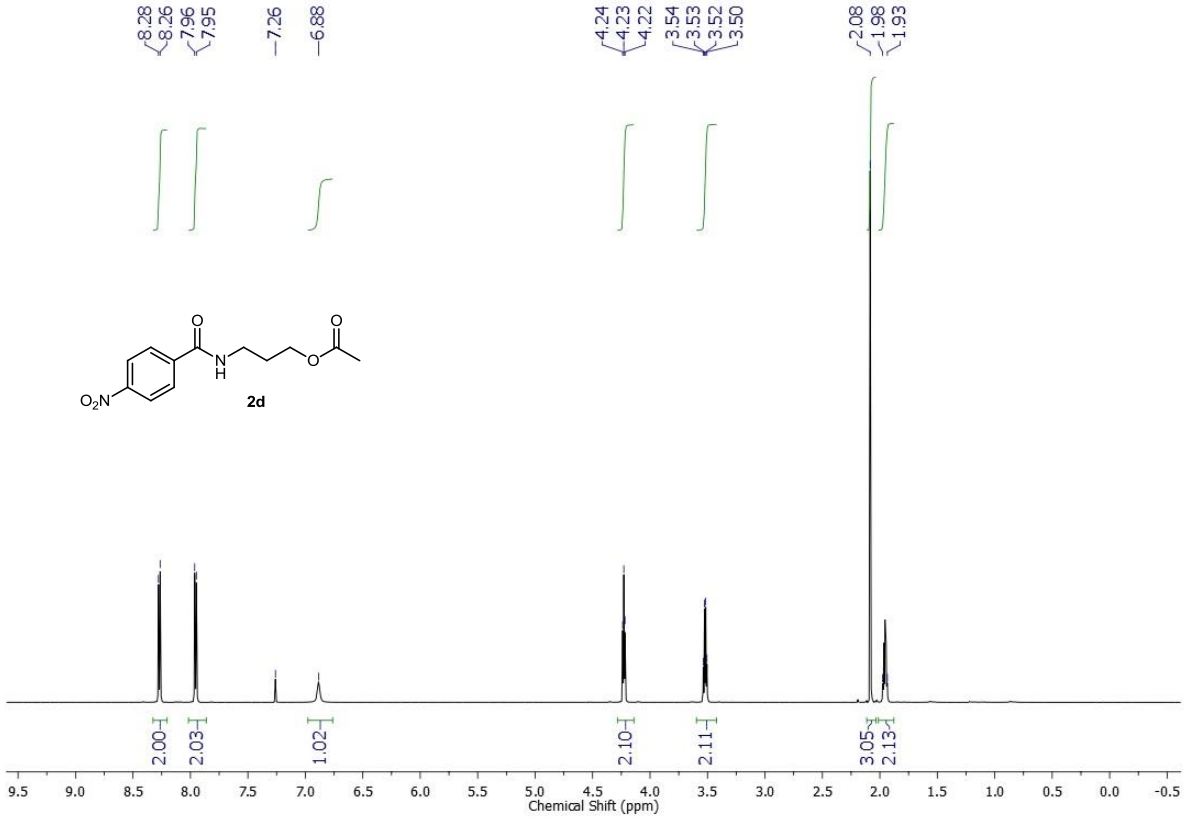


^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2c**



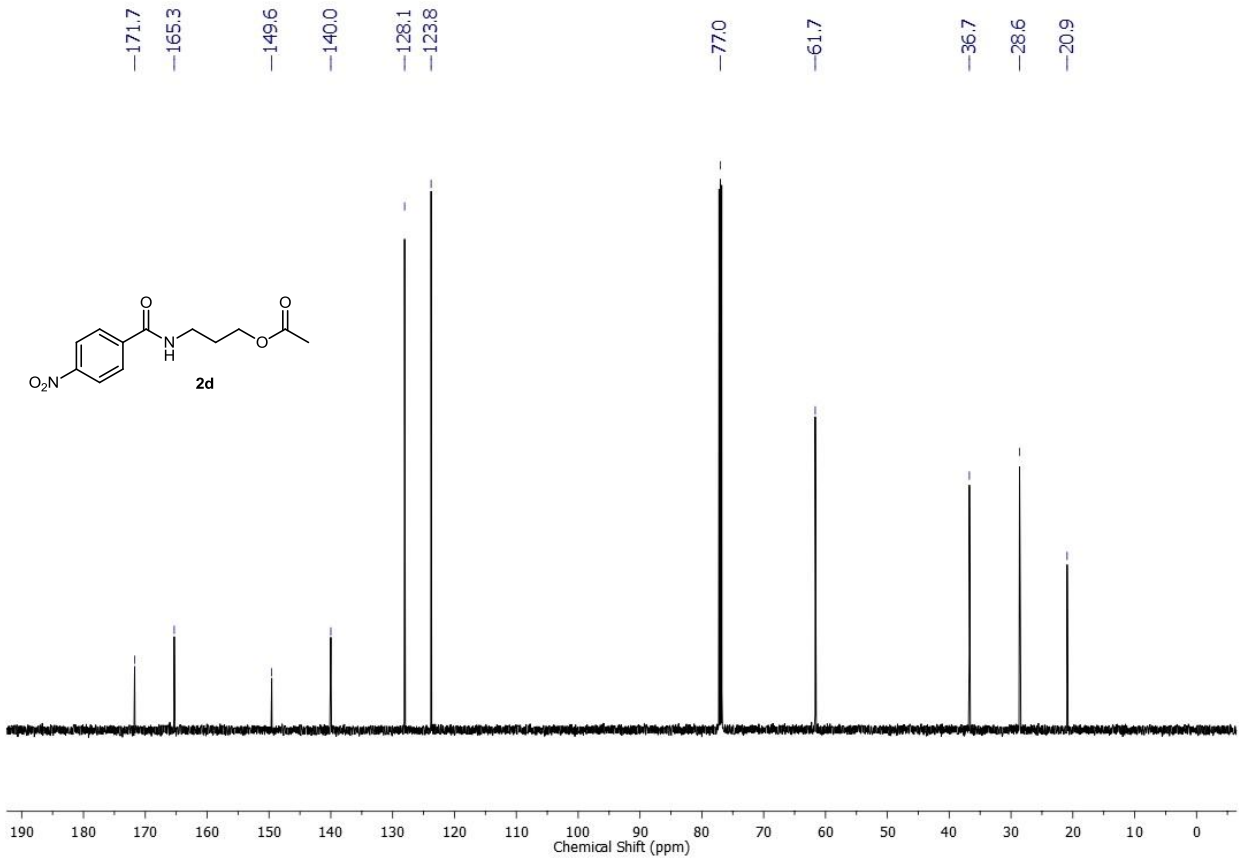
2c

^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2d**

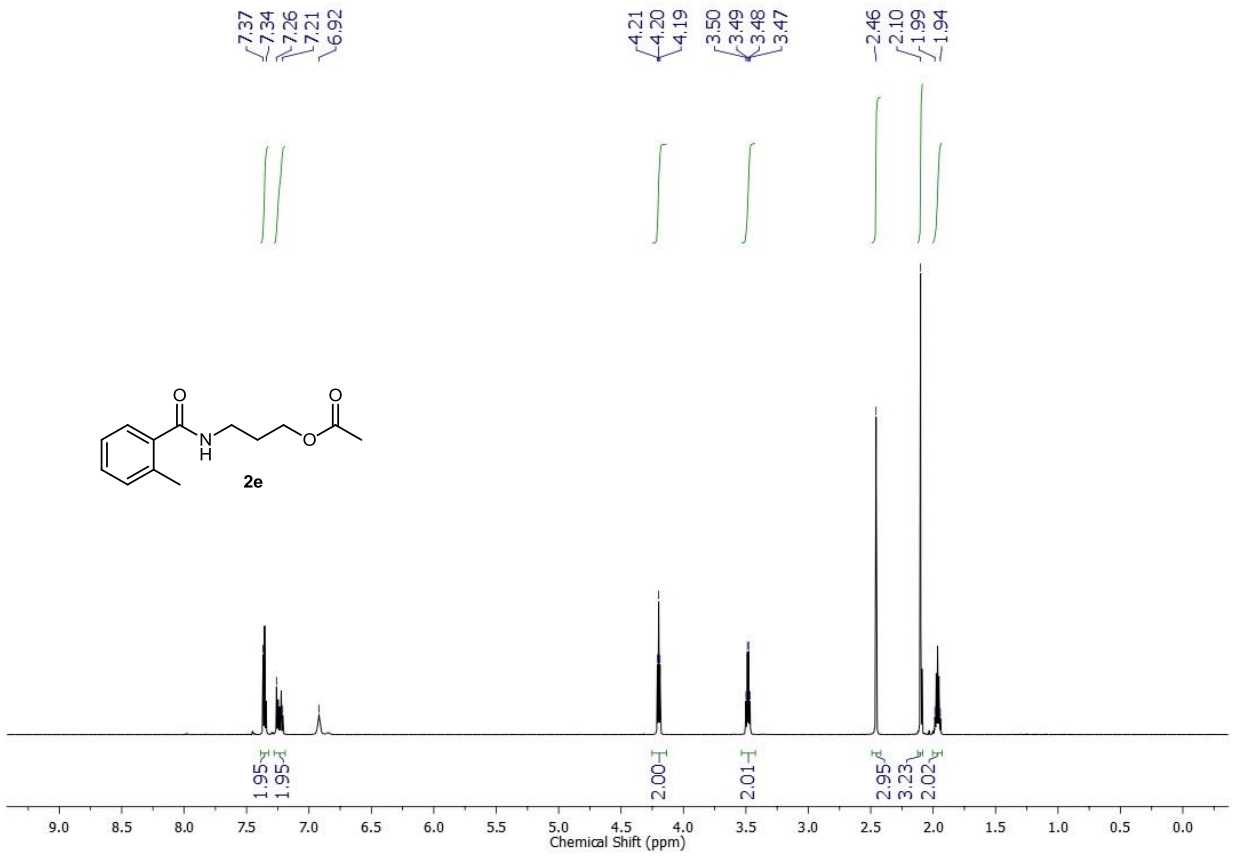


2d

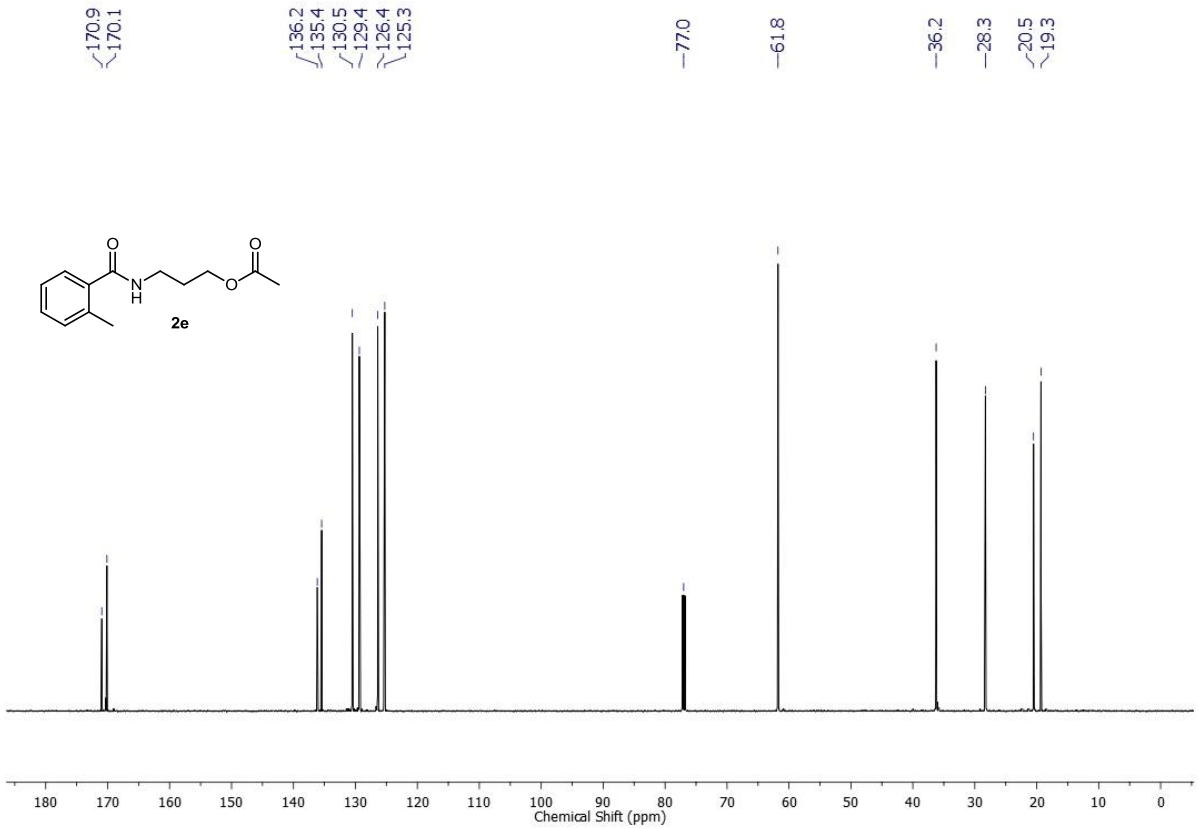
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2d**



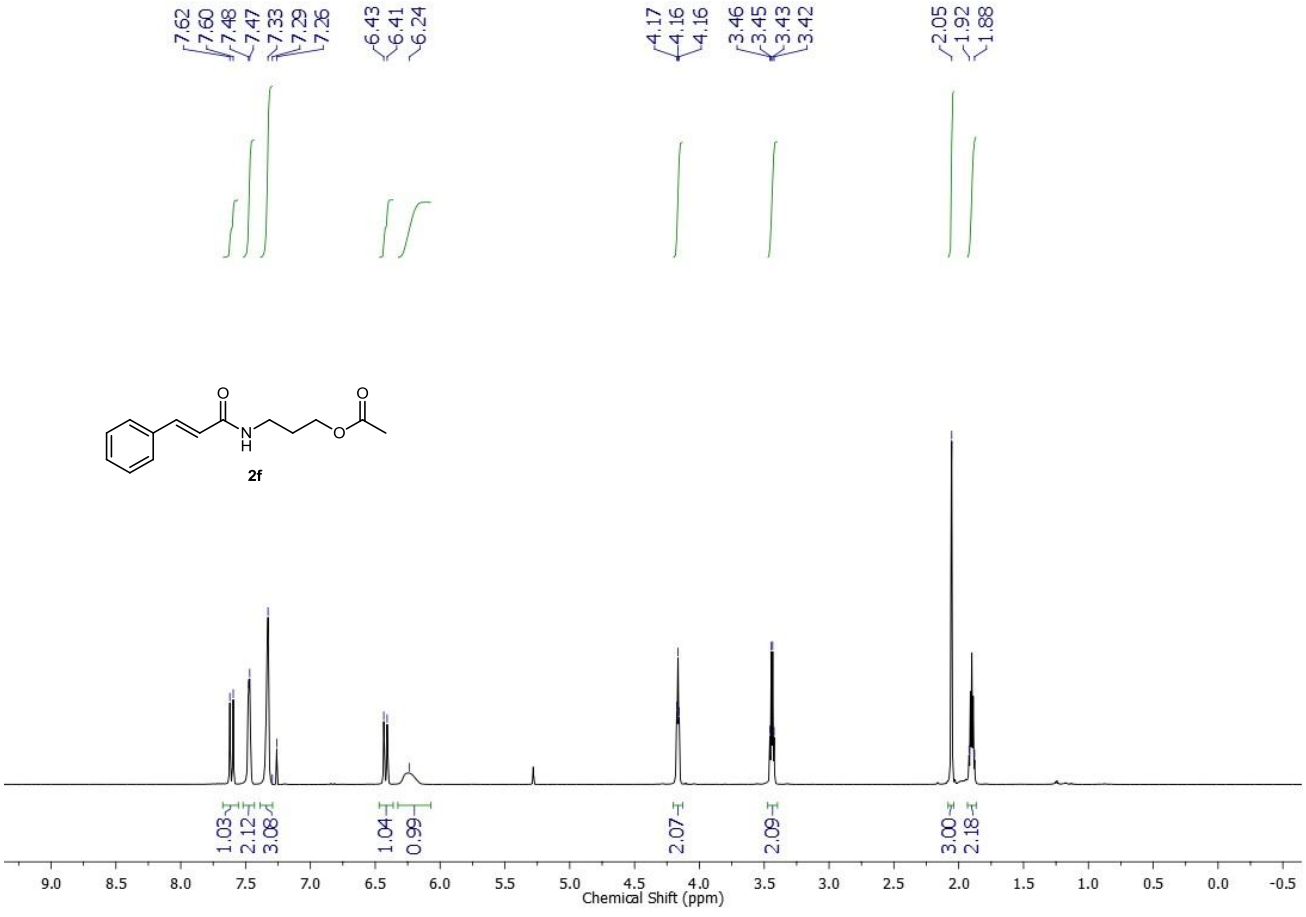
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2e**



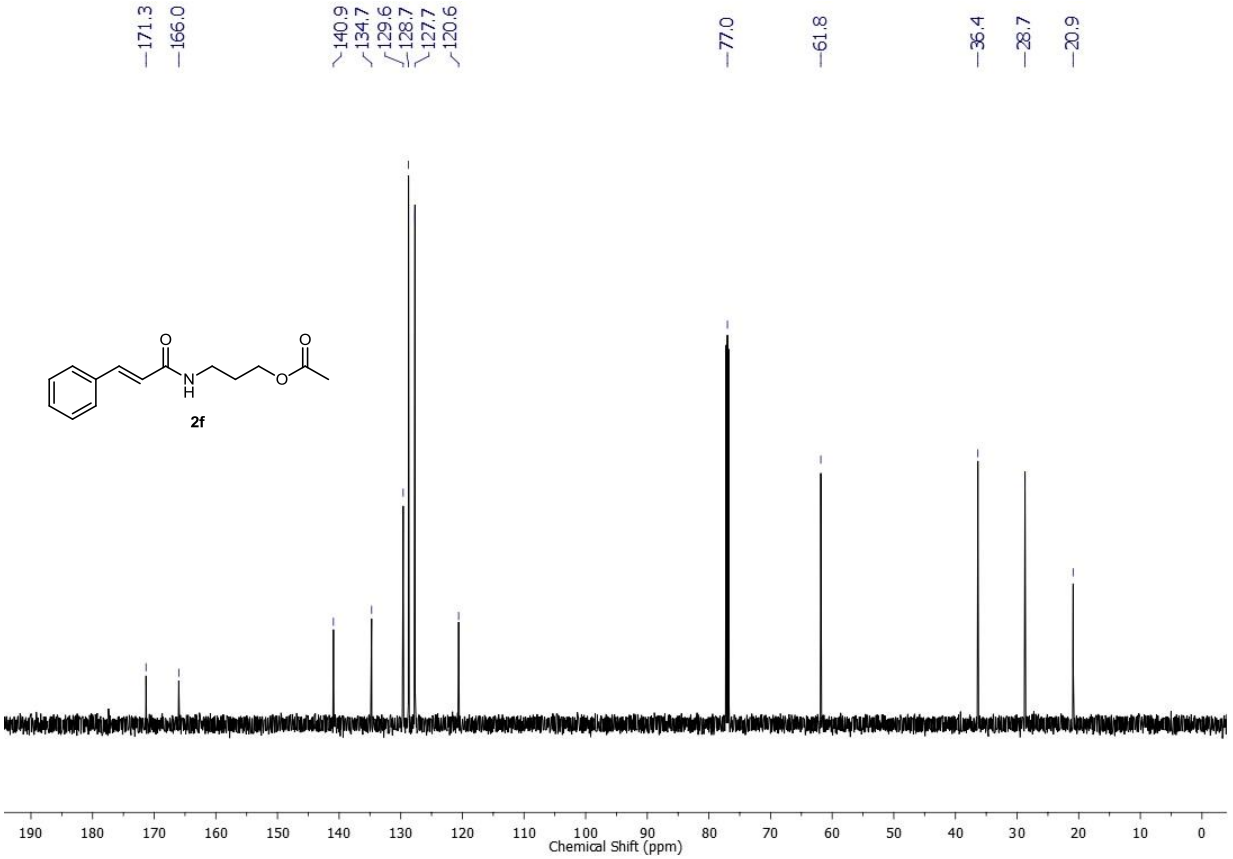
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2e**



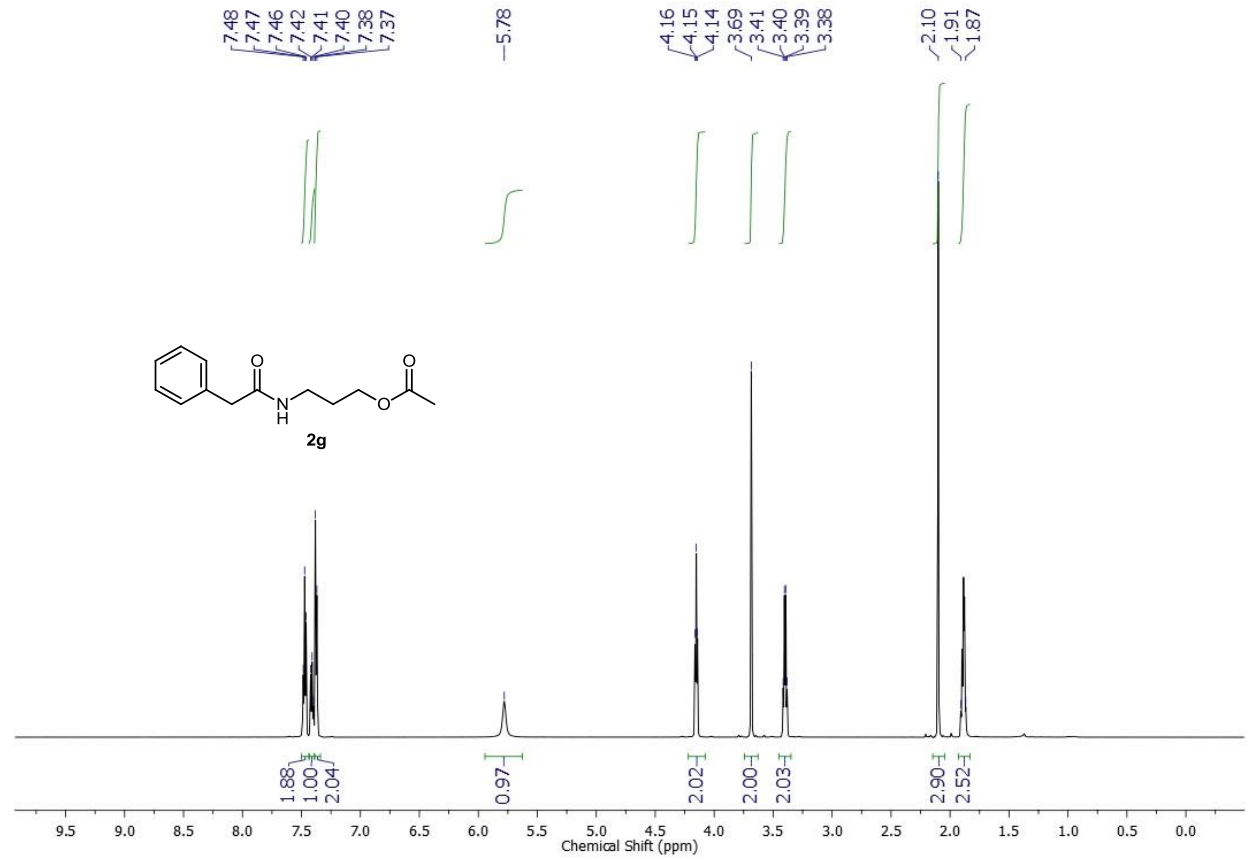
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2f**



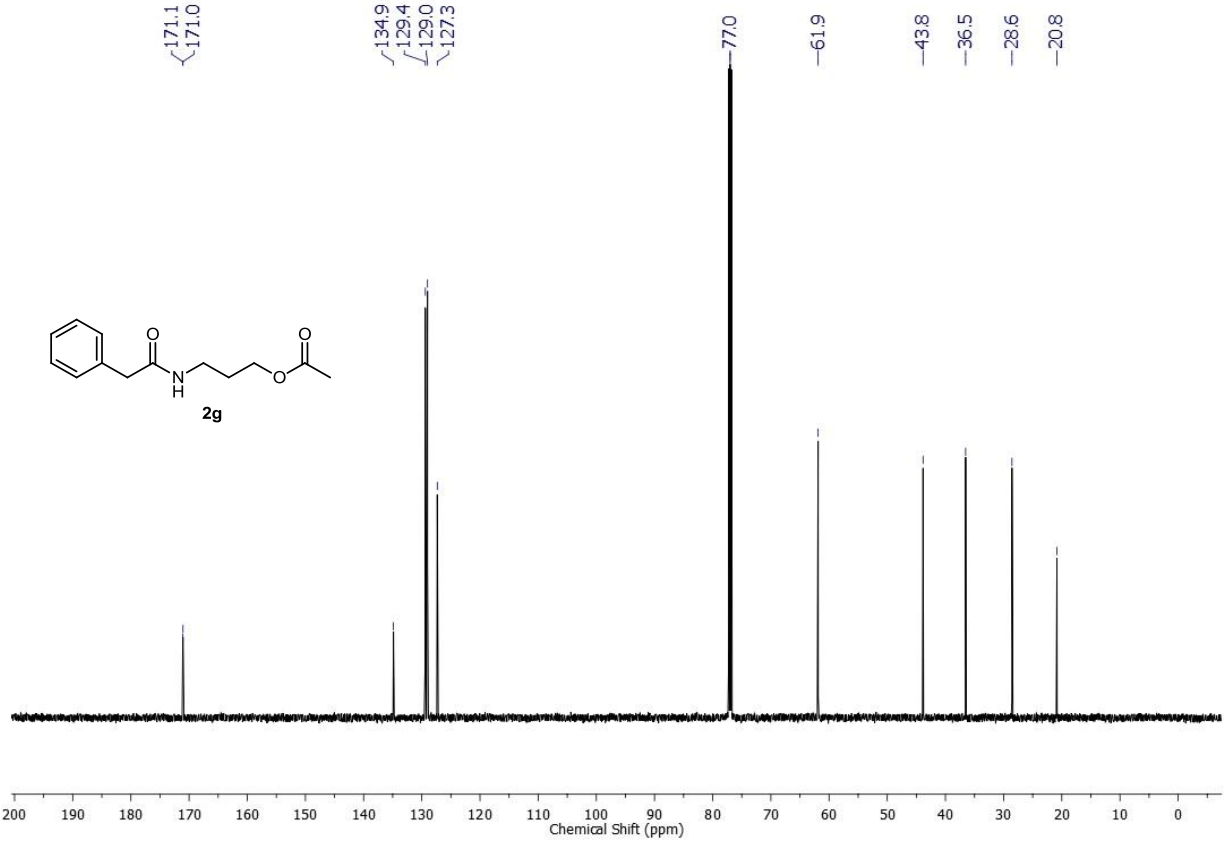
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2f**



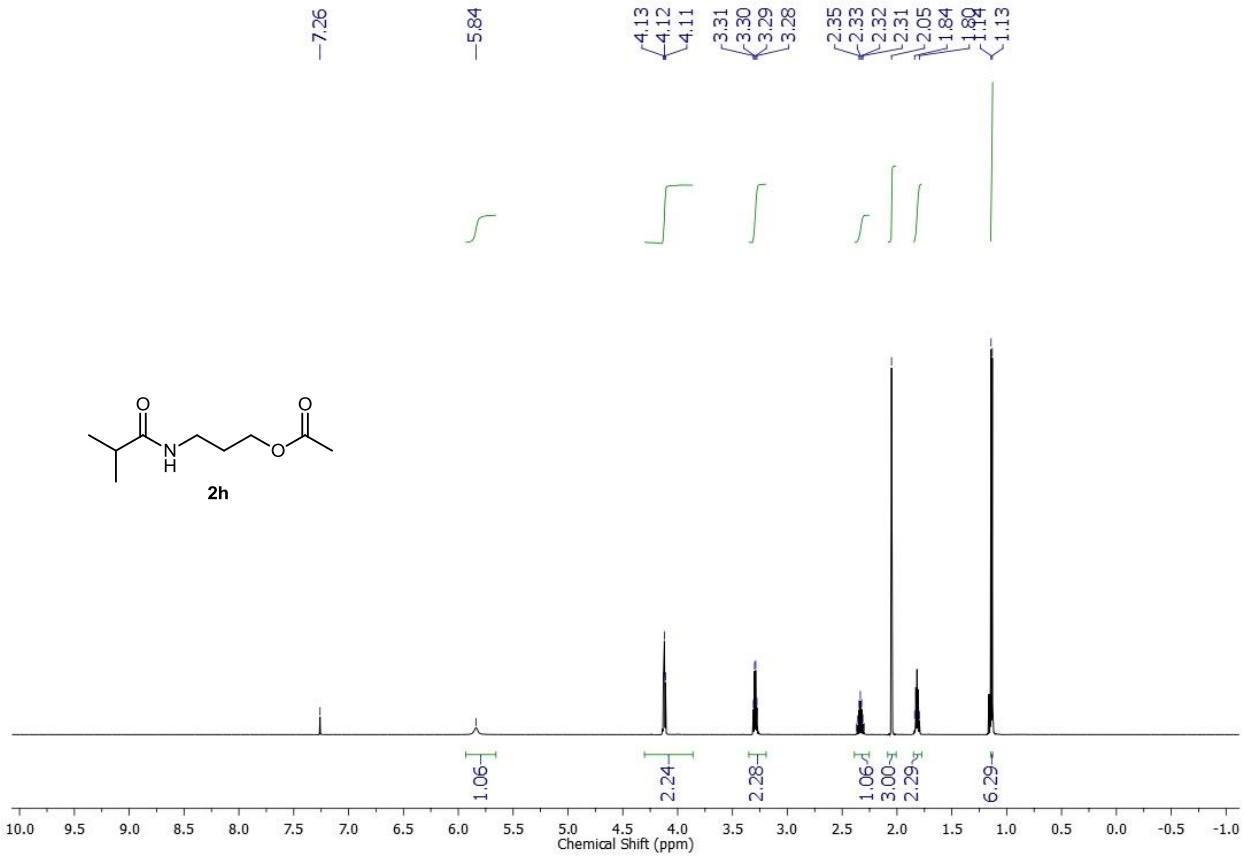
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2g**



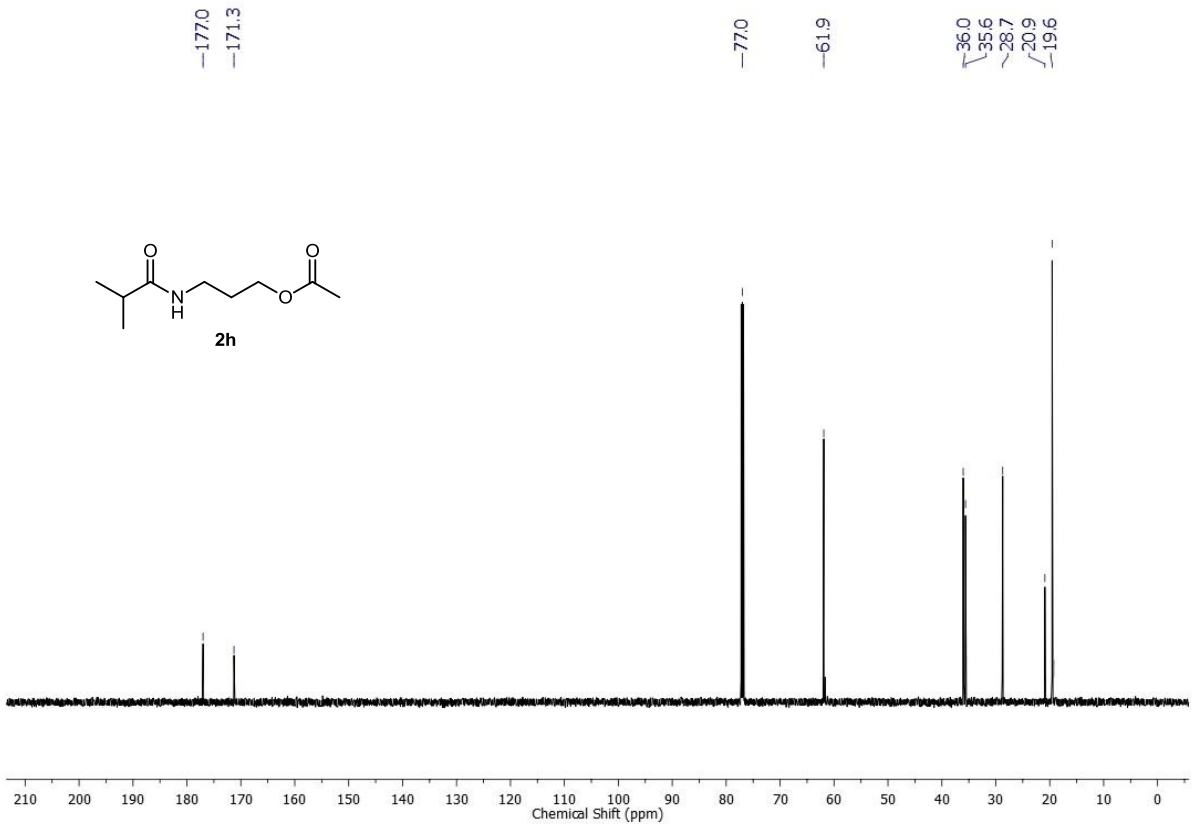
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2g**



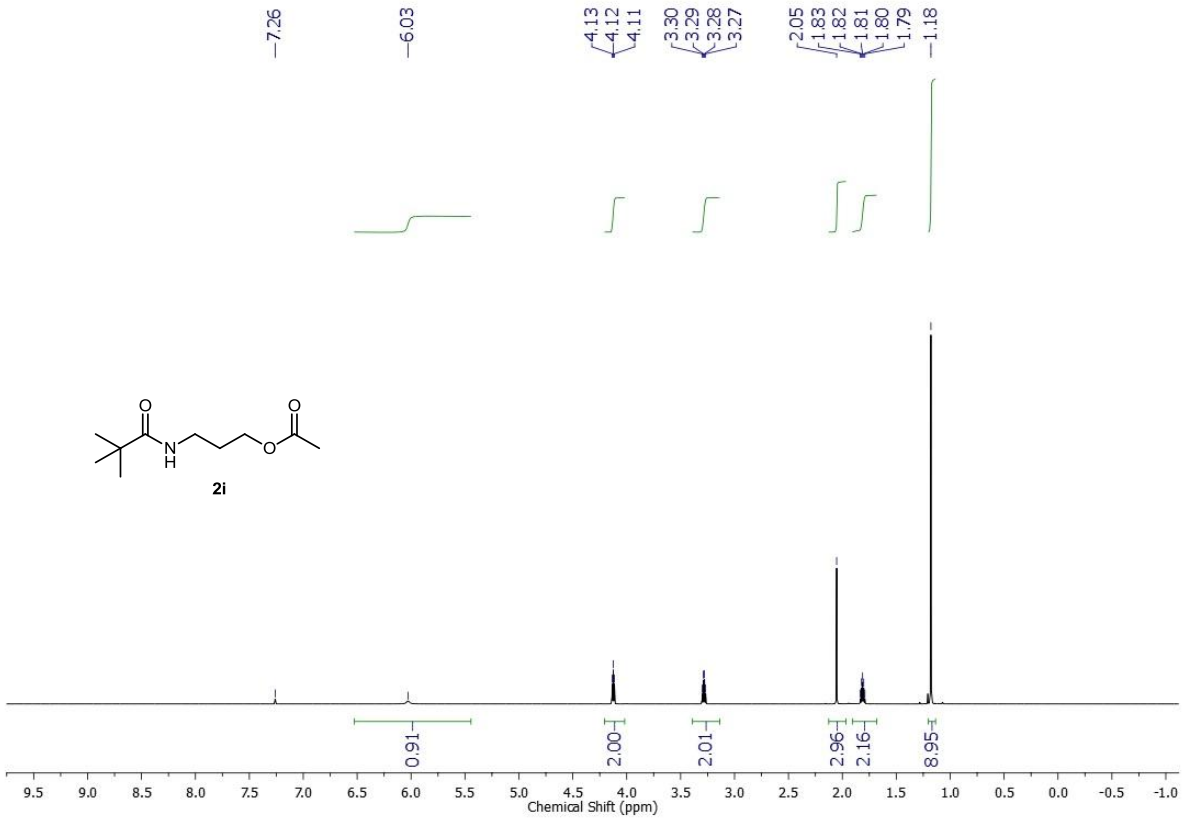
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2h**



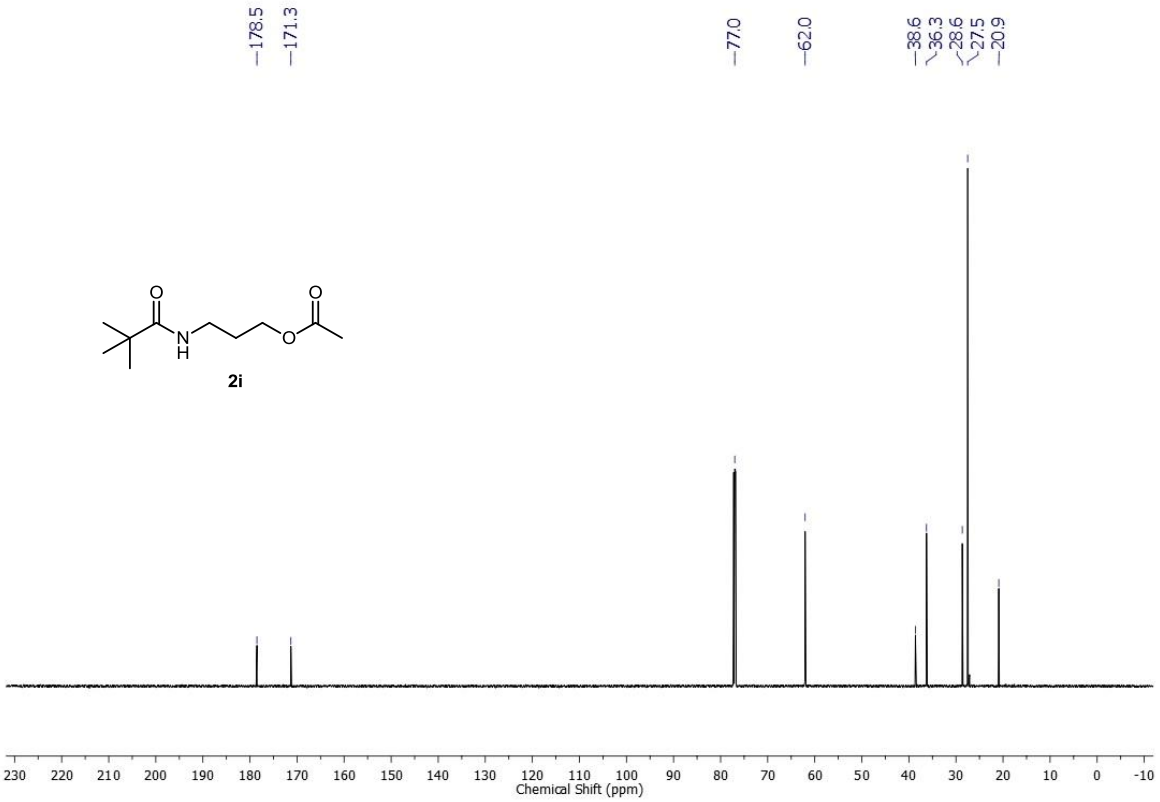
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2h**



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **2i**

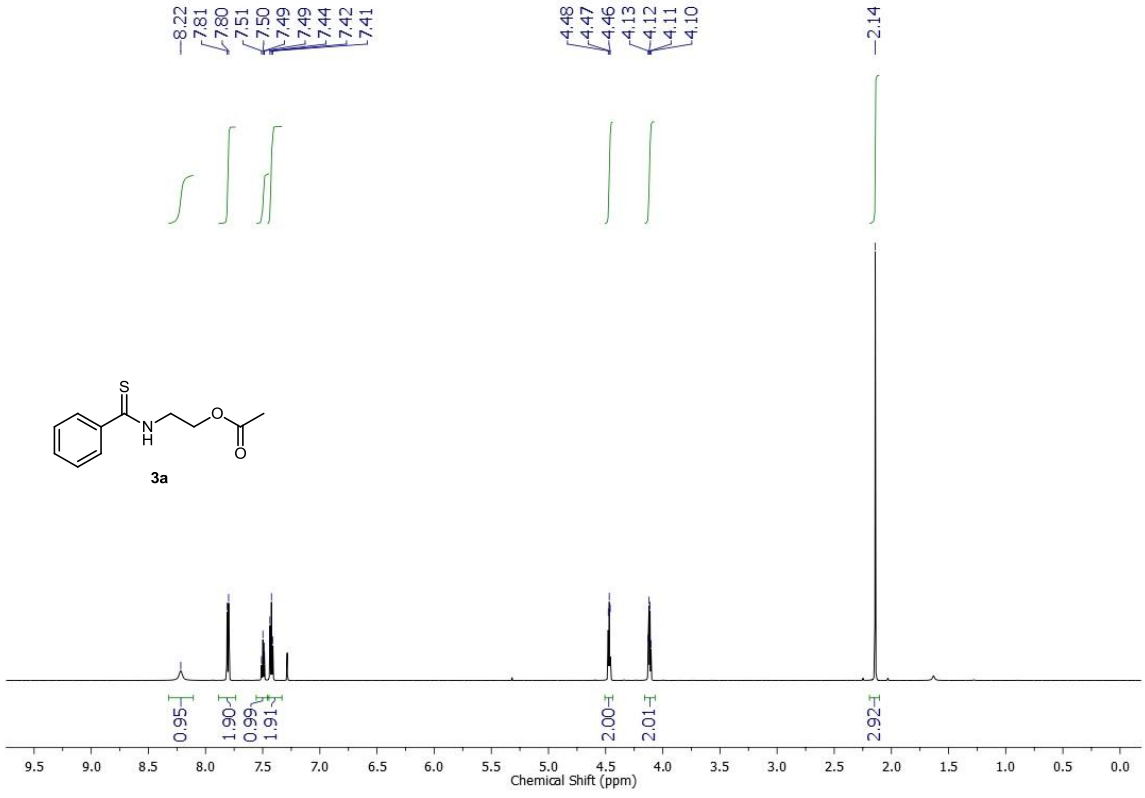


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **2i**

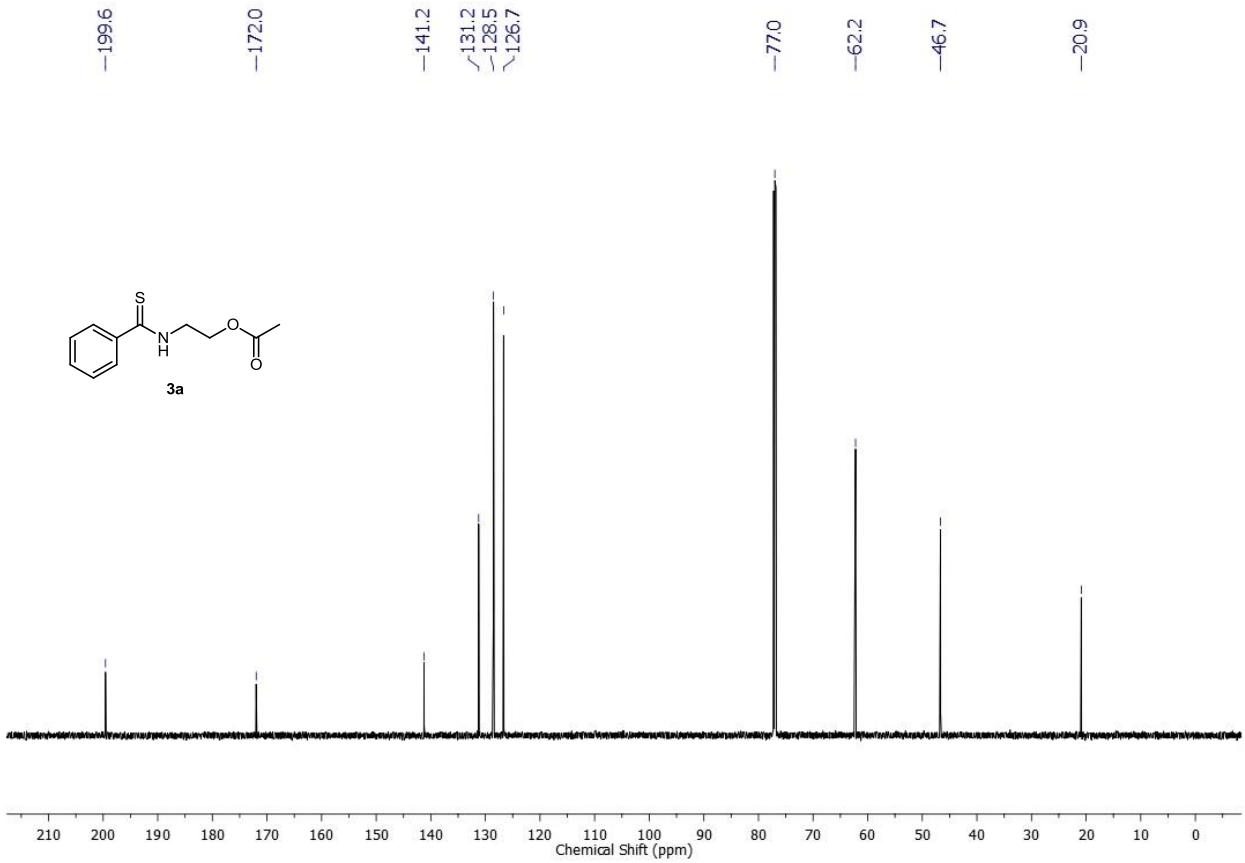


5. Copies of ^{1}H and ^{13}C NMR spectra of compounds 3-4

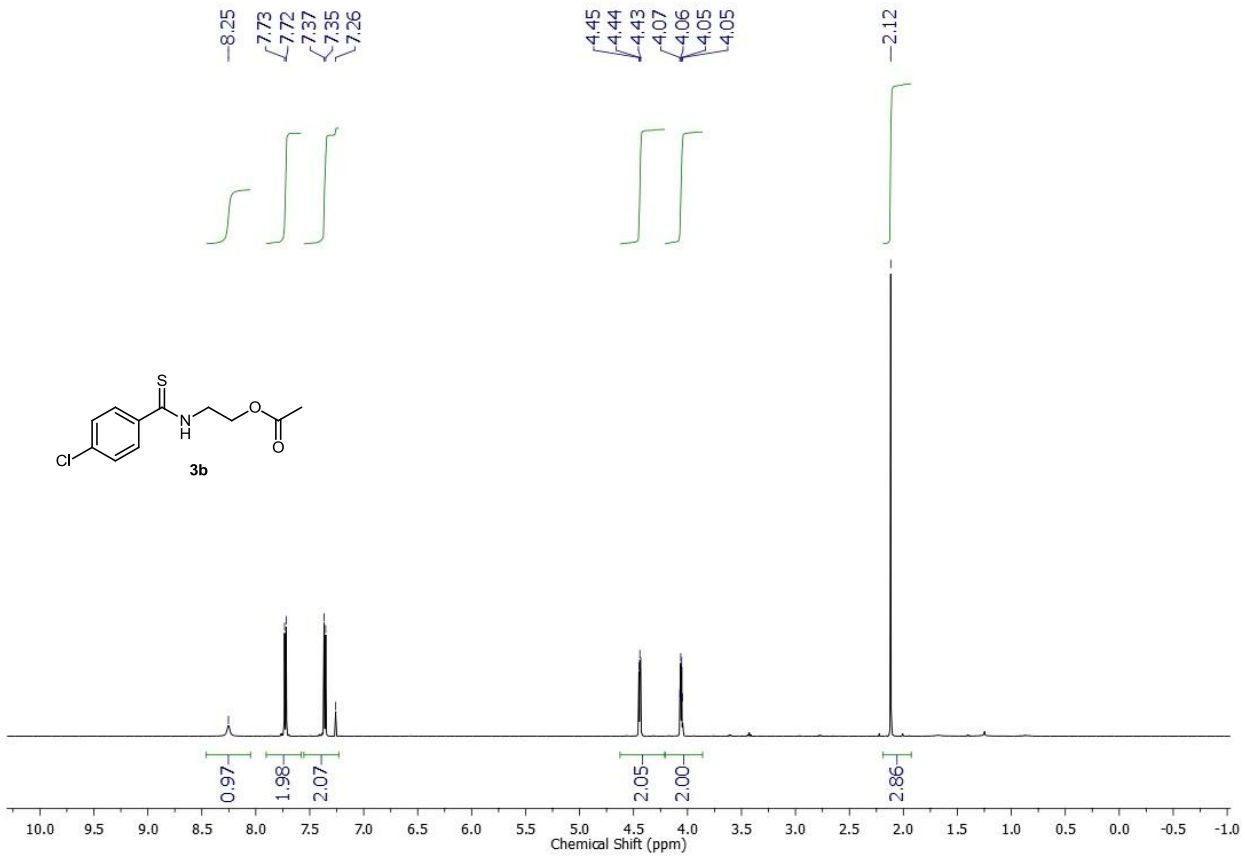
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3a**



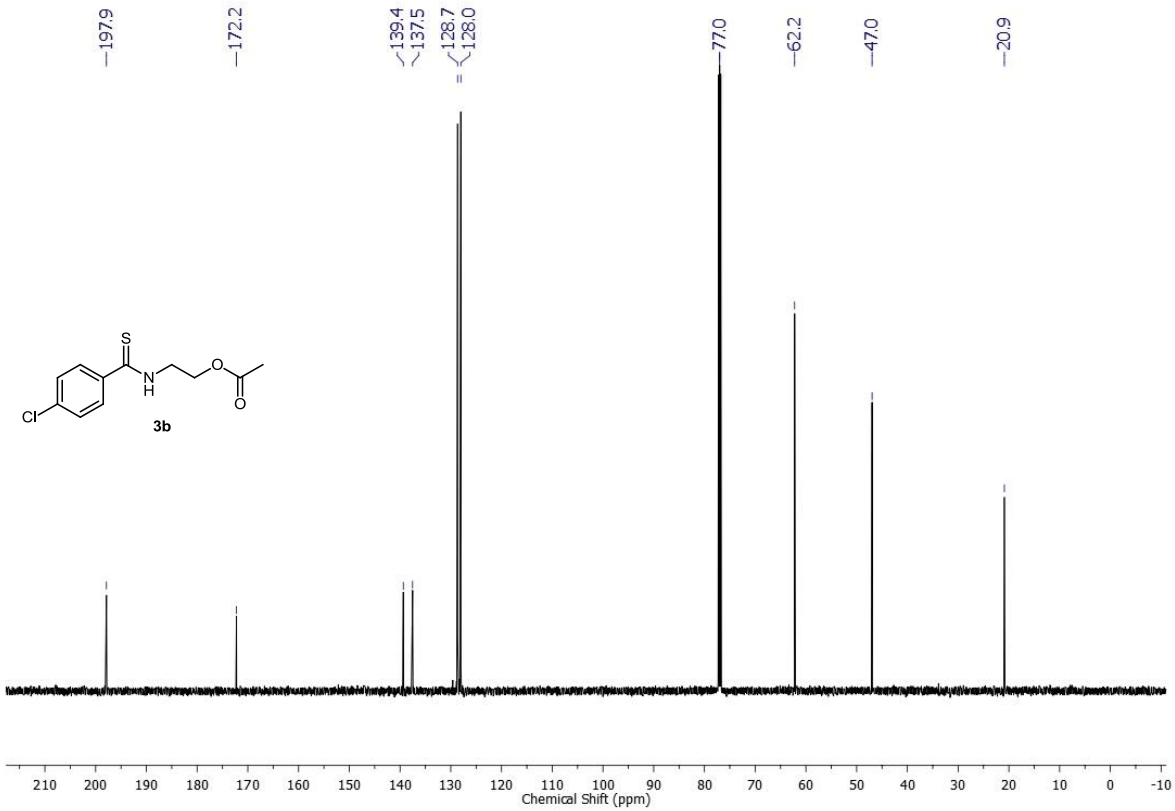
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3a**



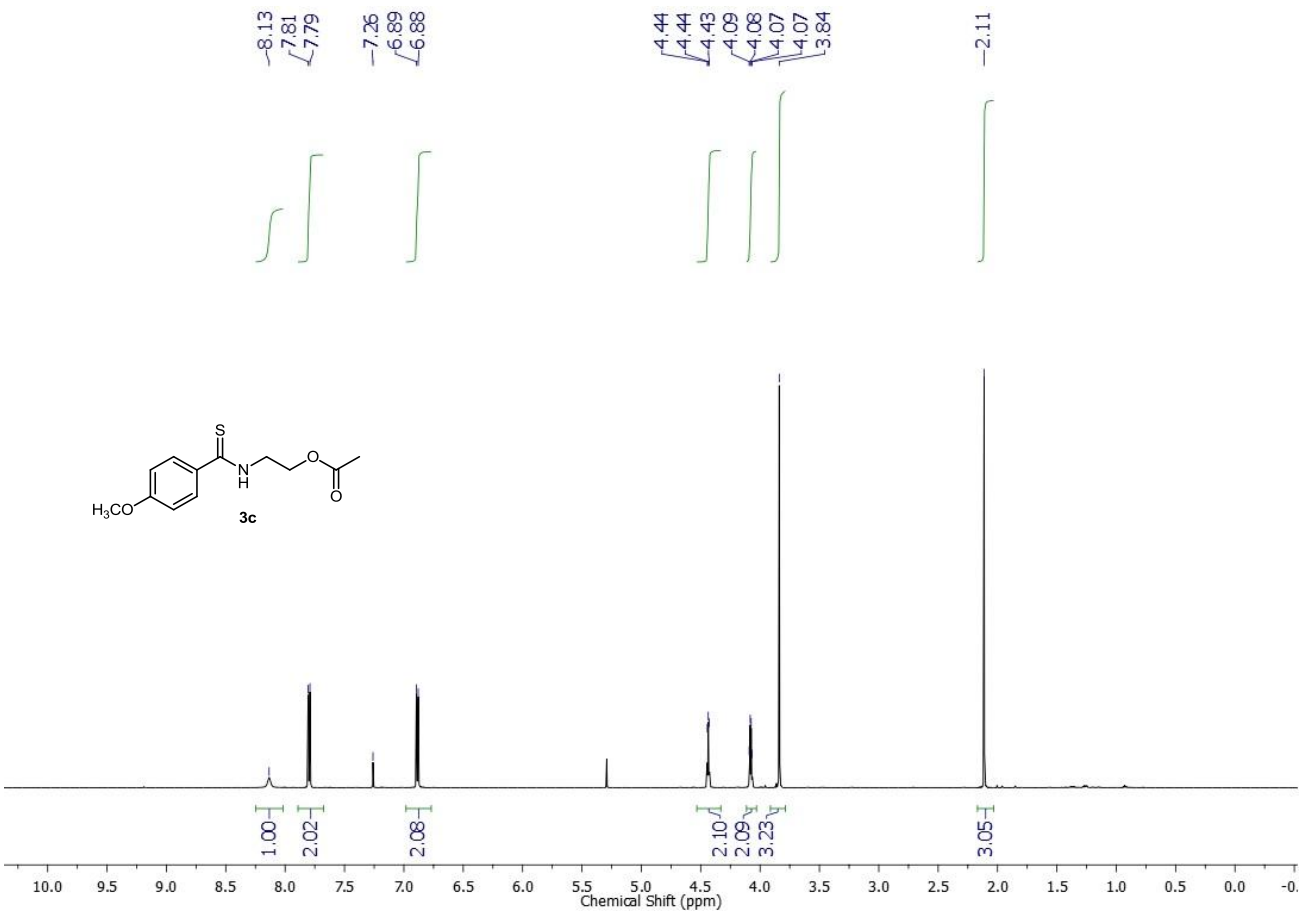
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3b**



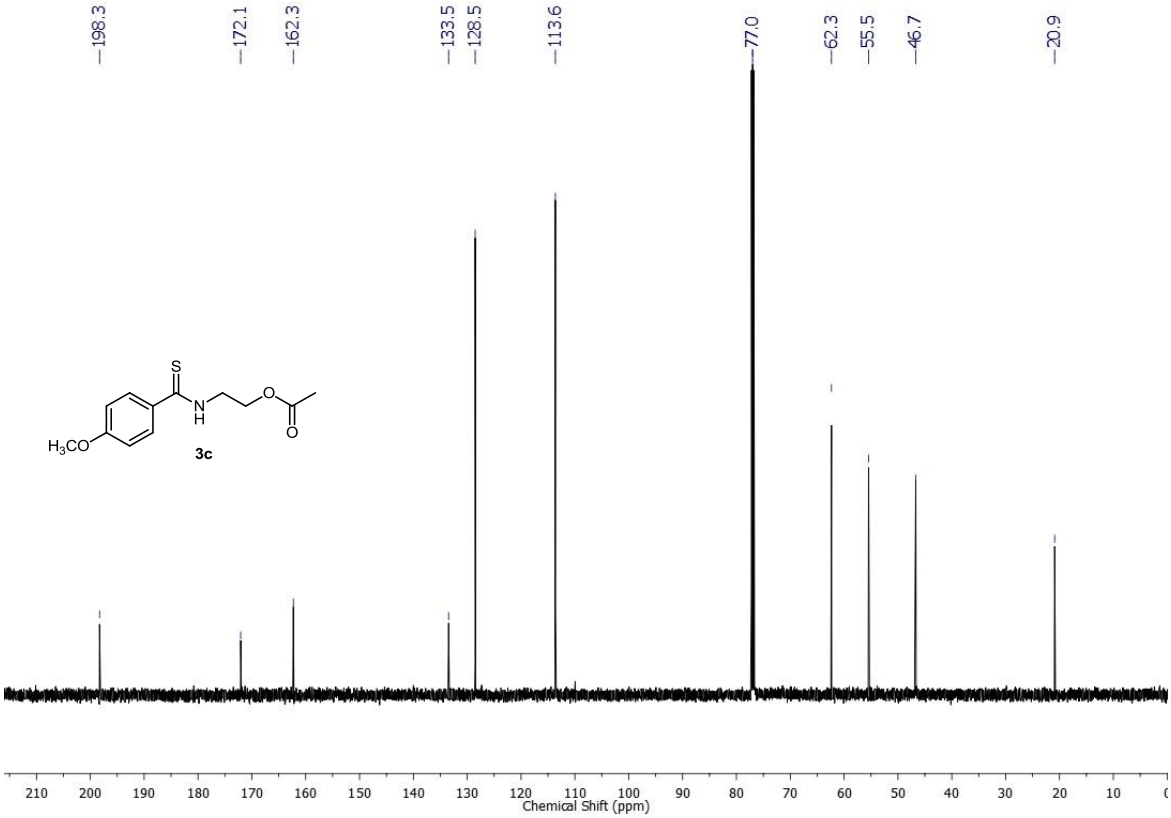
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3b**



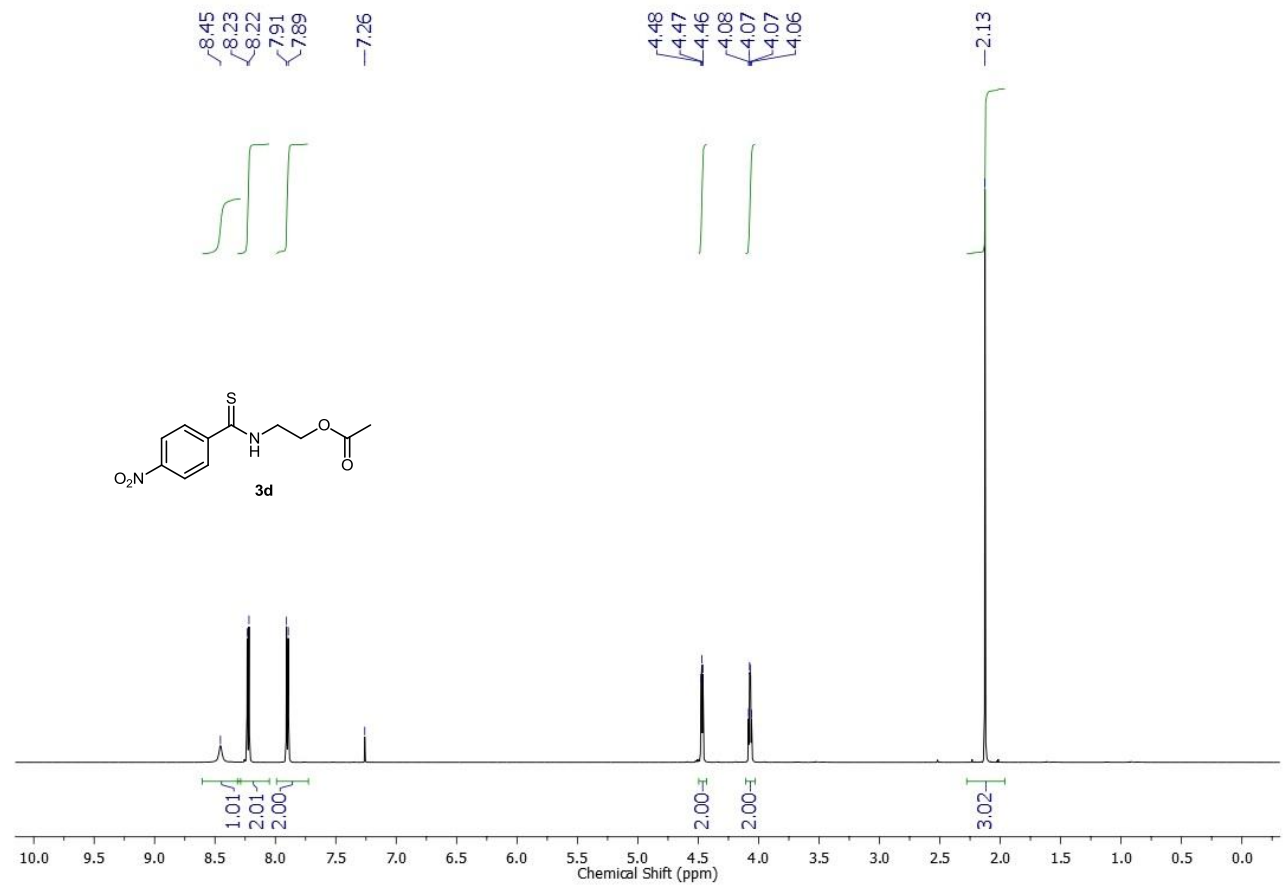
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3c**



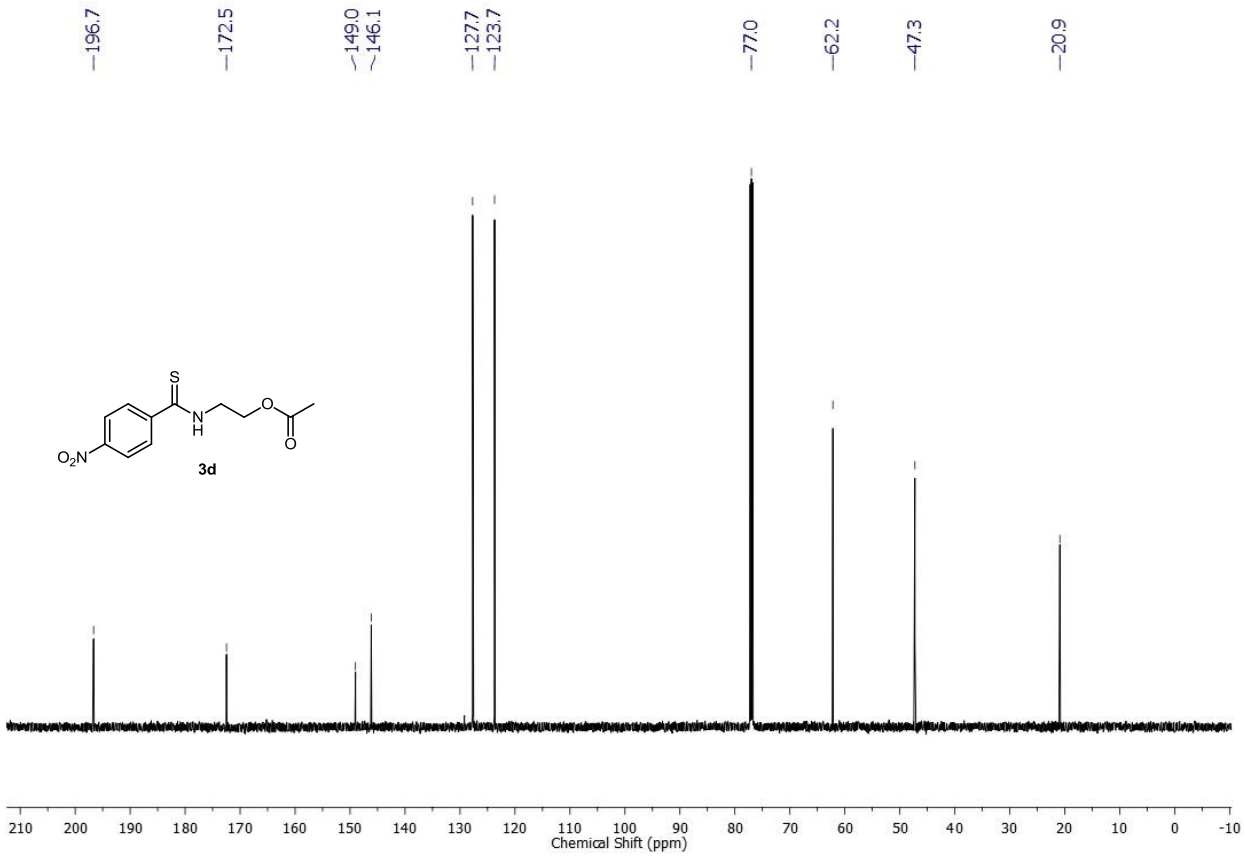
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3c**



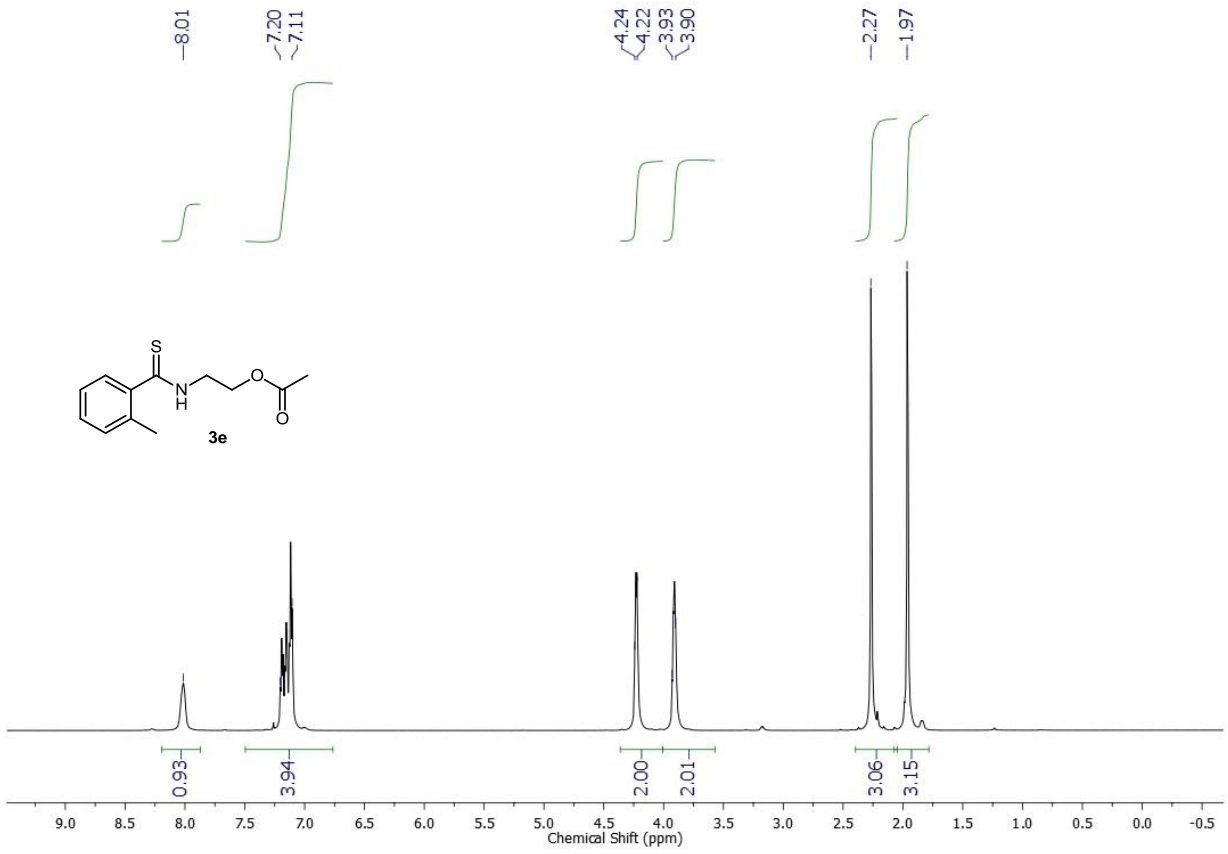
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3d**



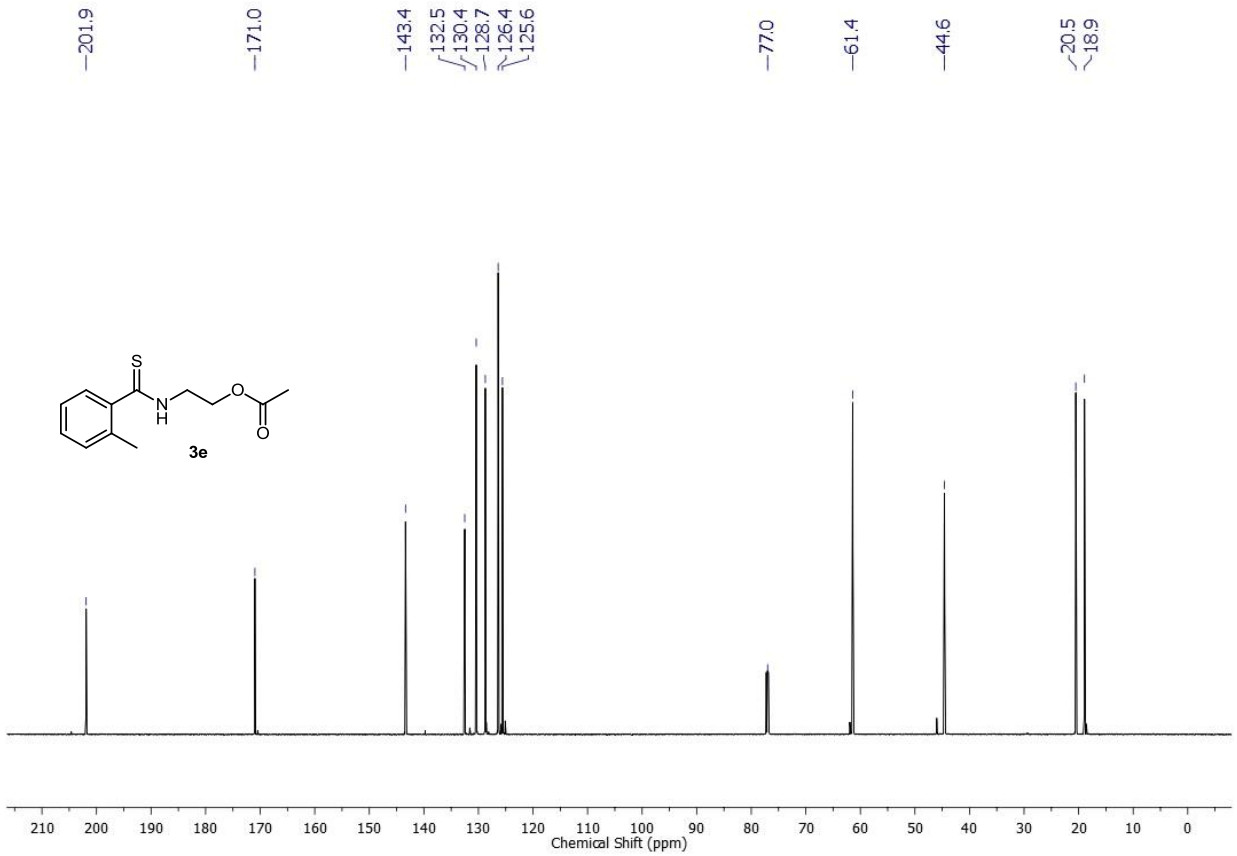
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3d**



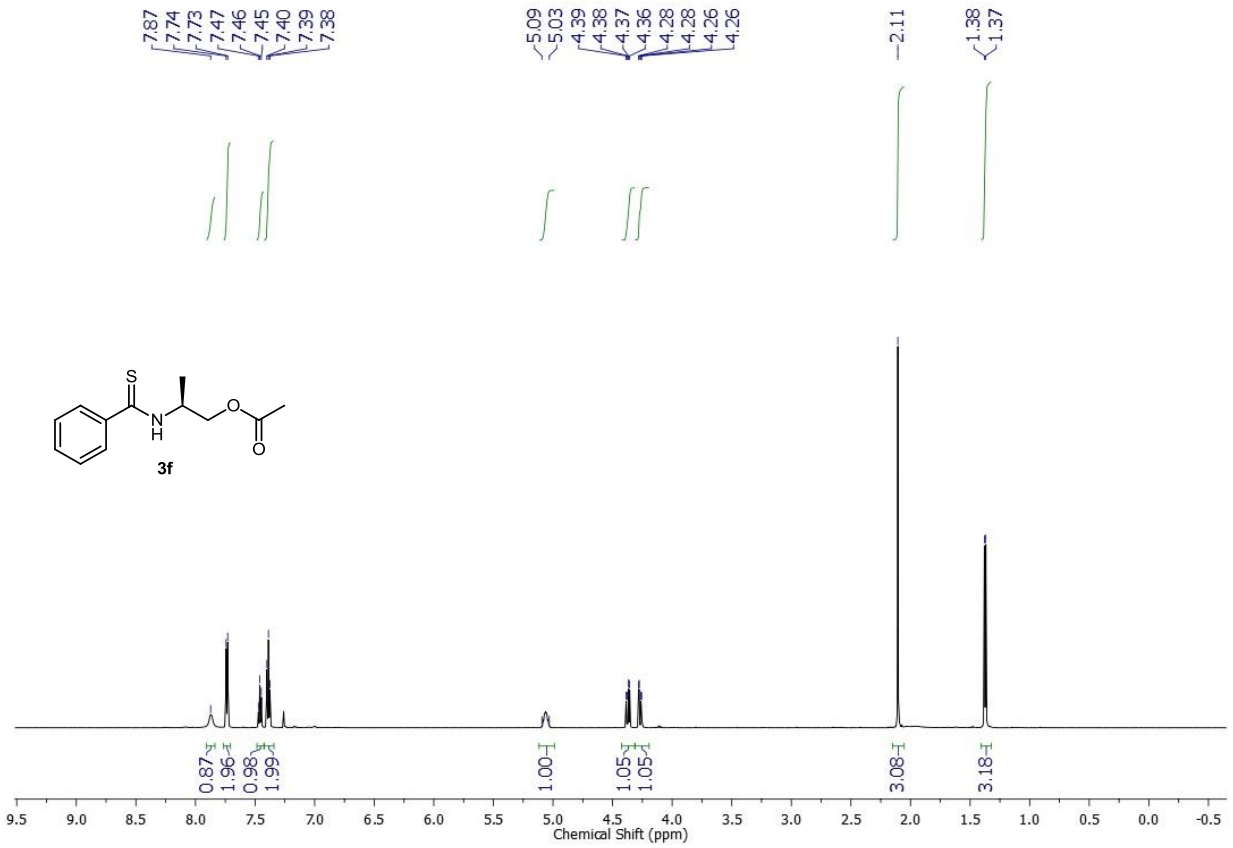
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3e**



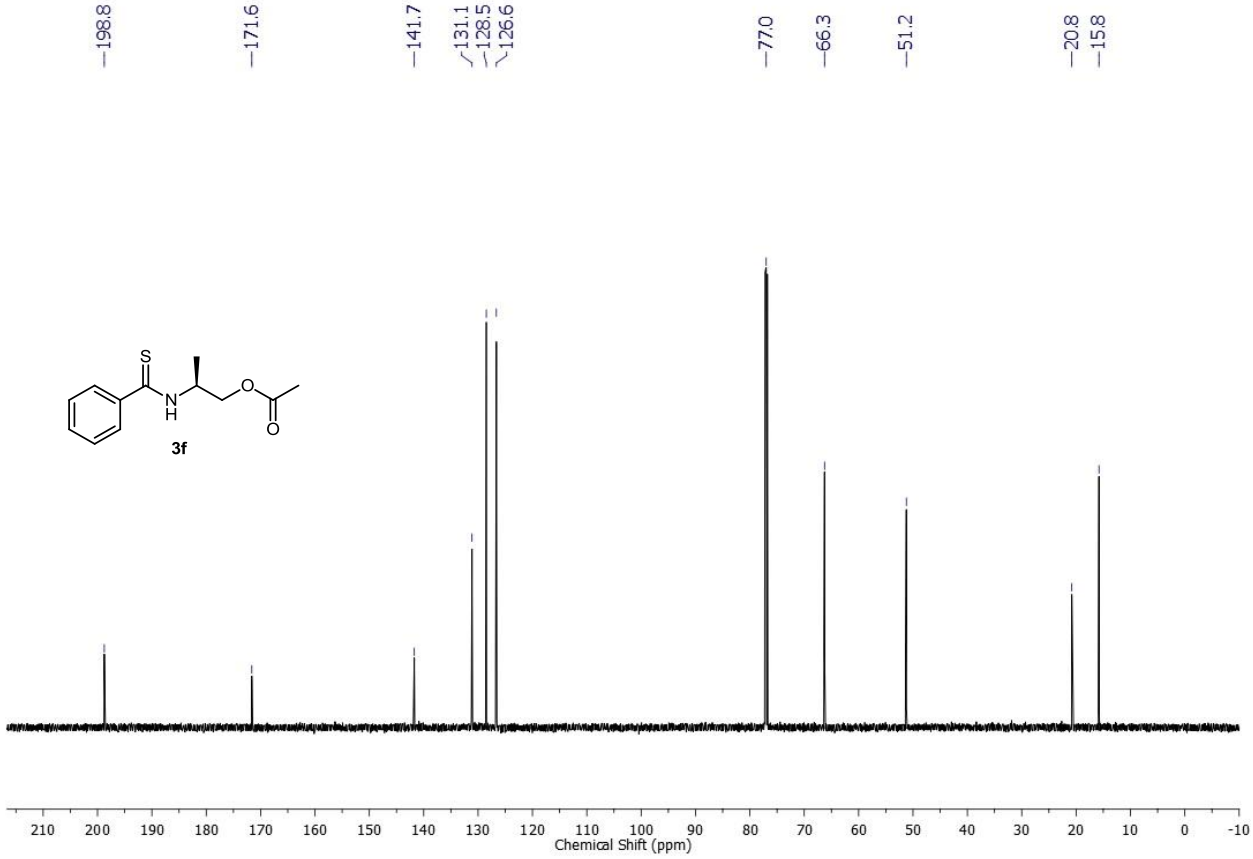
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3e**



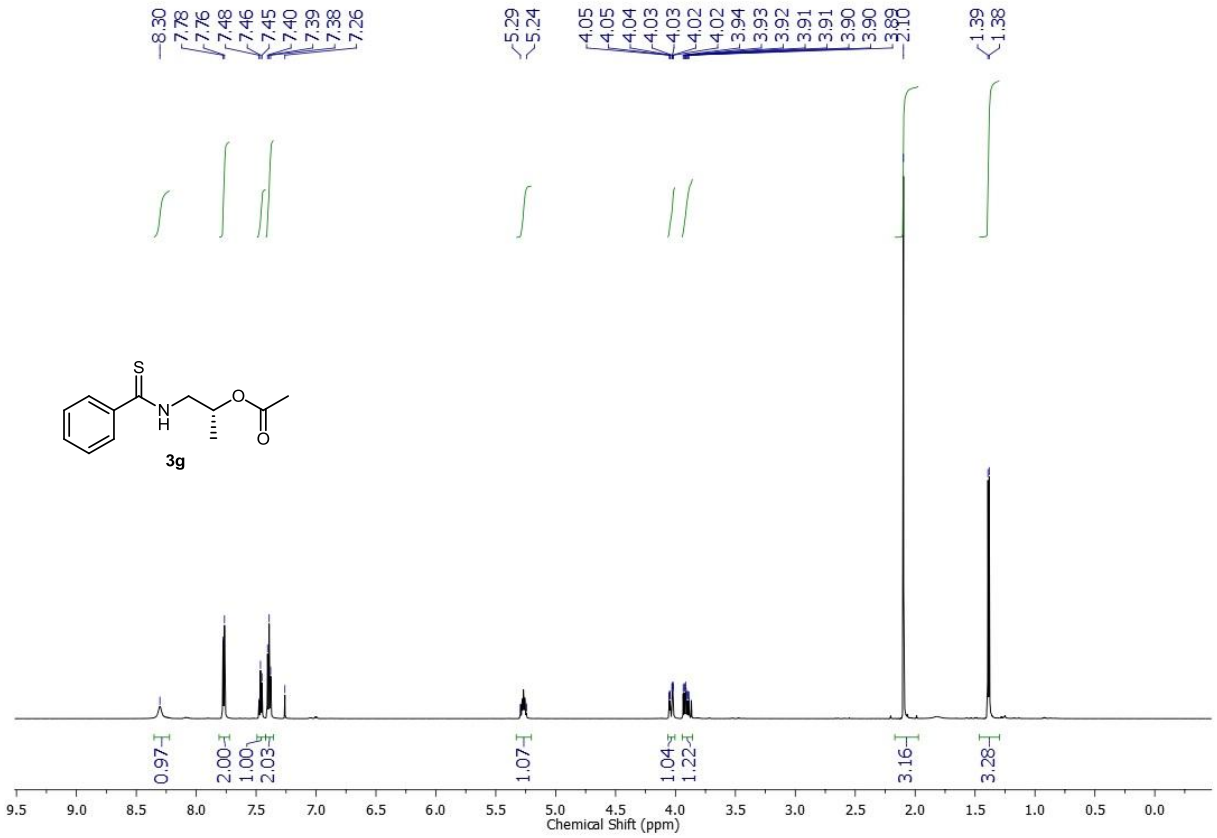
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3f**



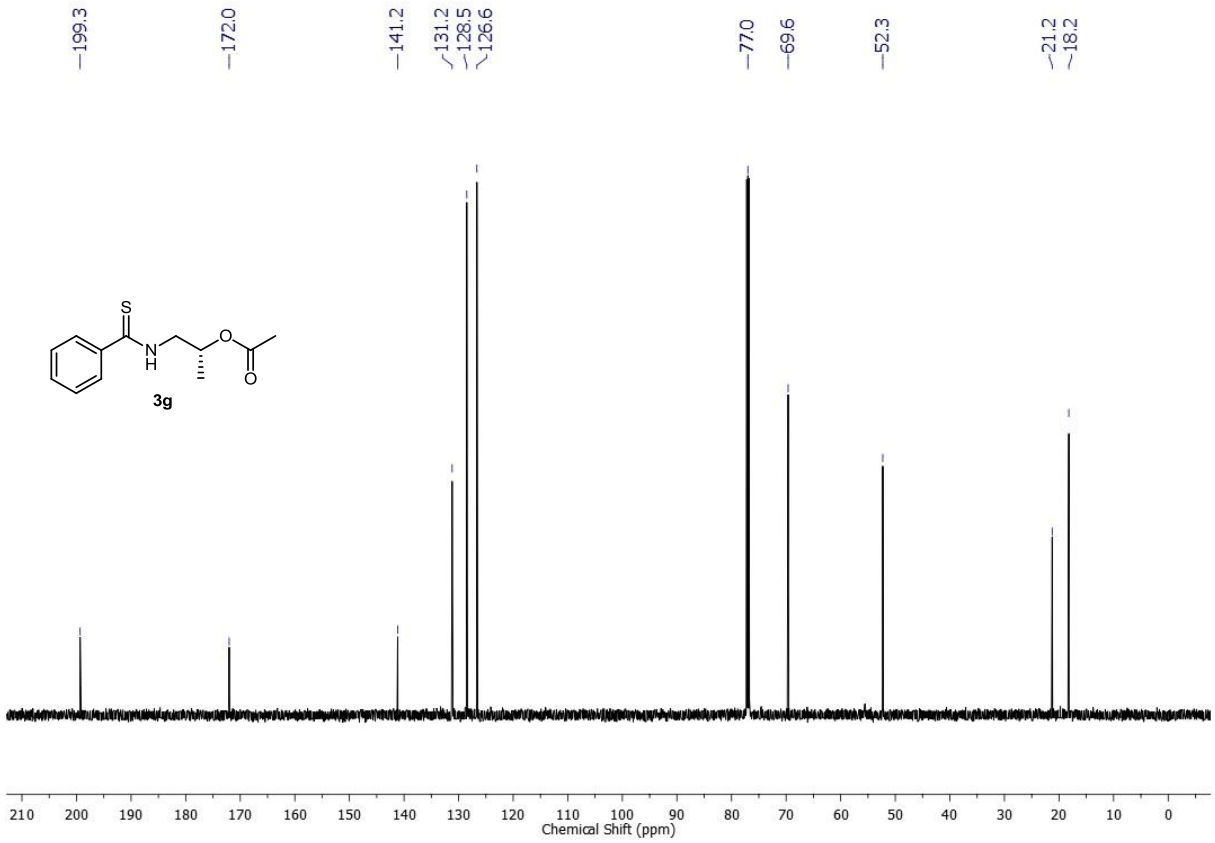
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3f**



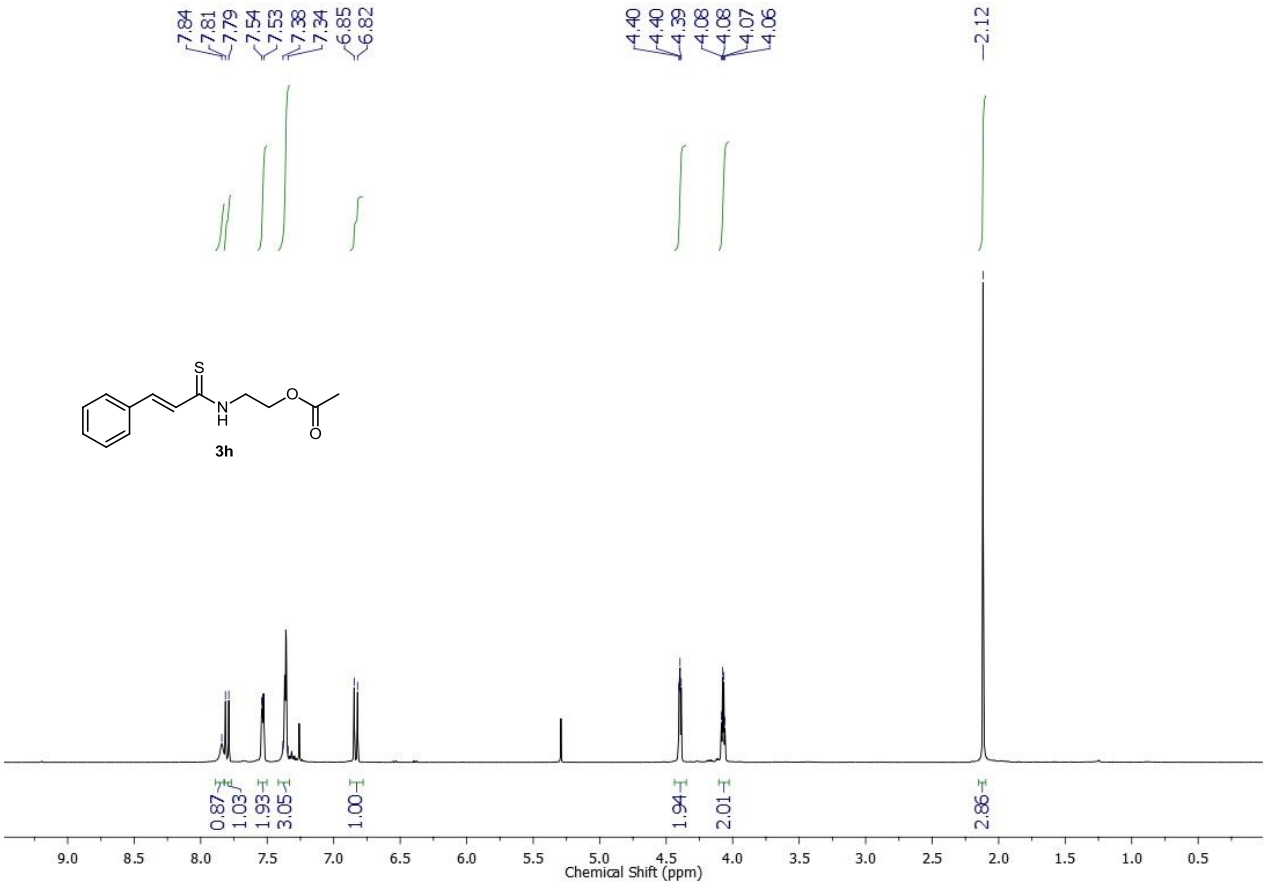
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3g**



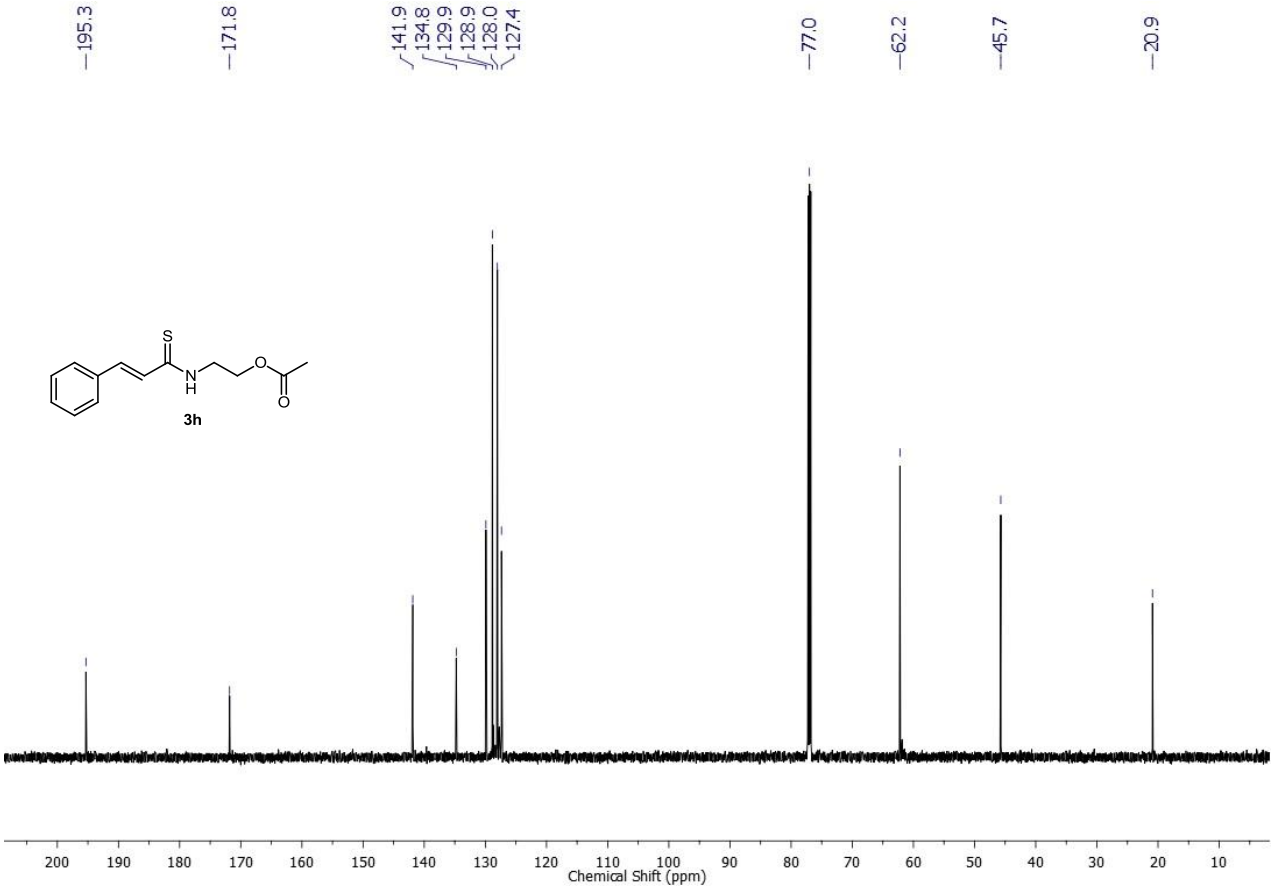
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3g**



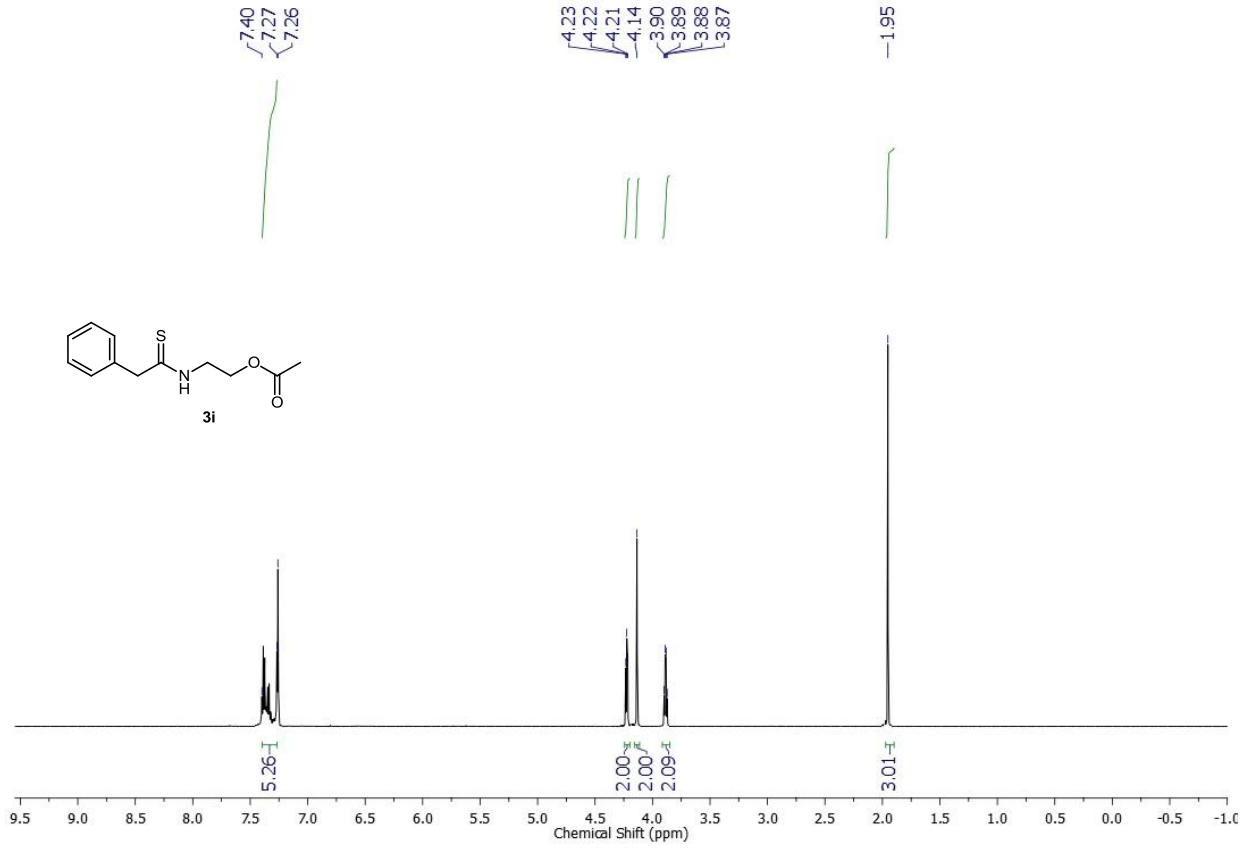
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3h**



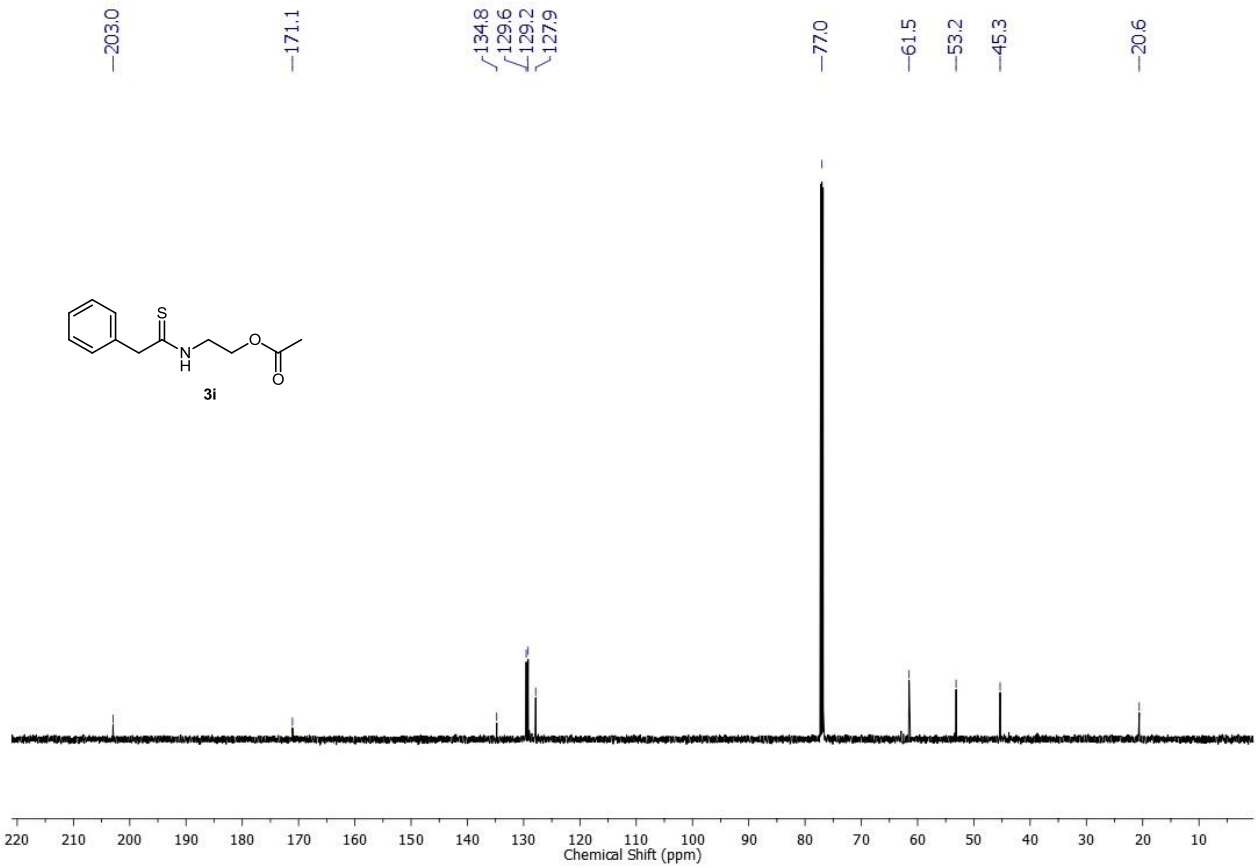
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3h**



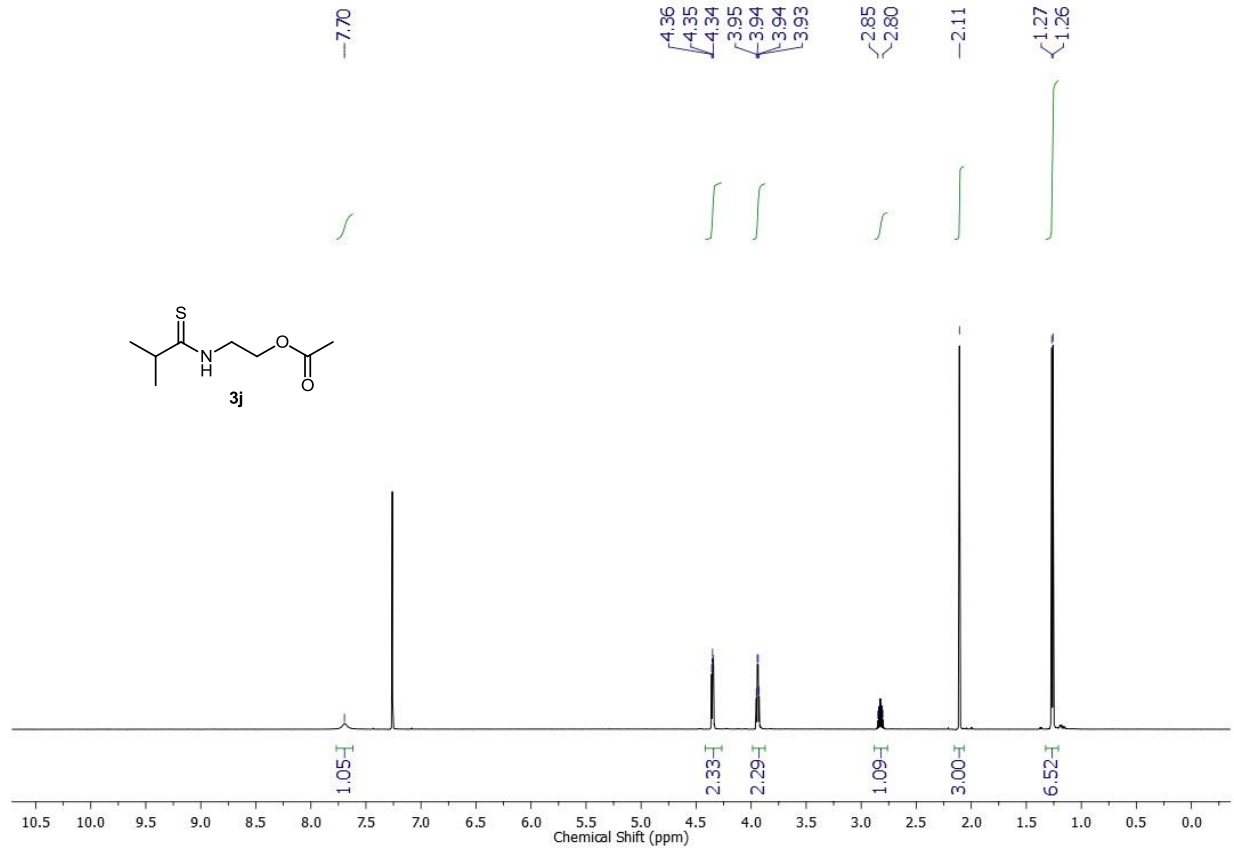
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3i**



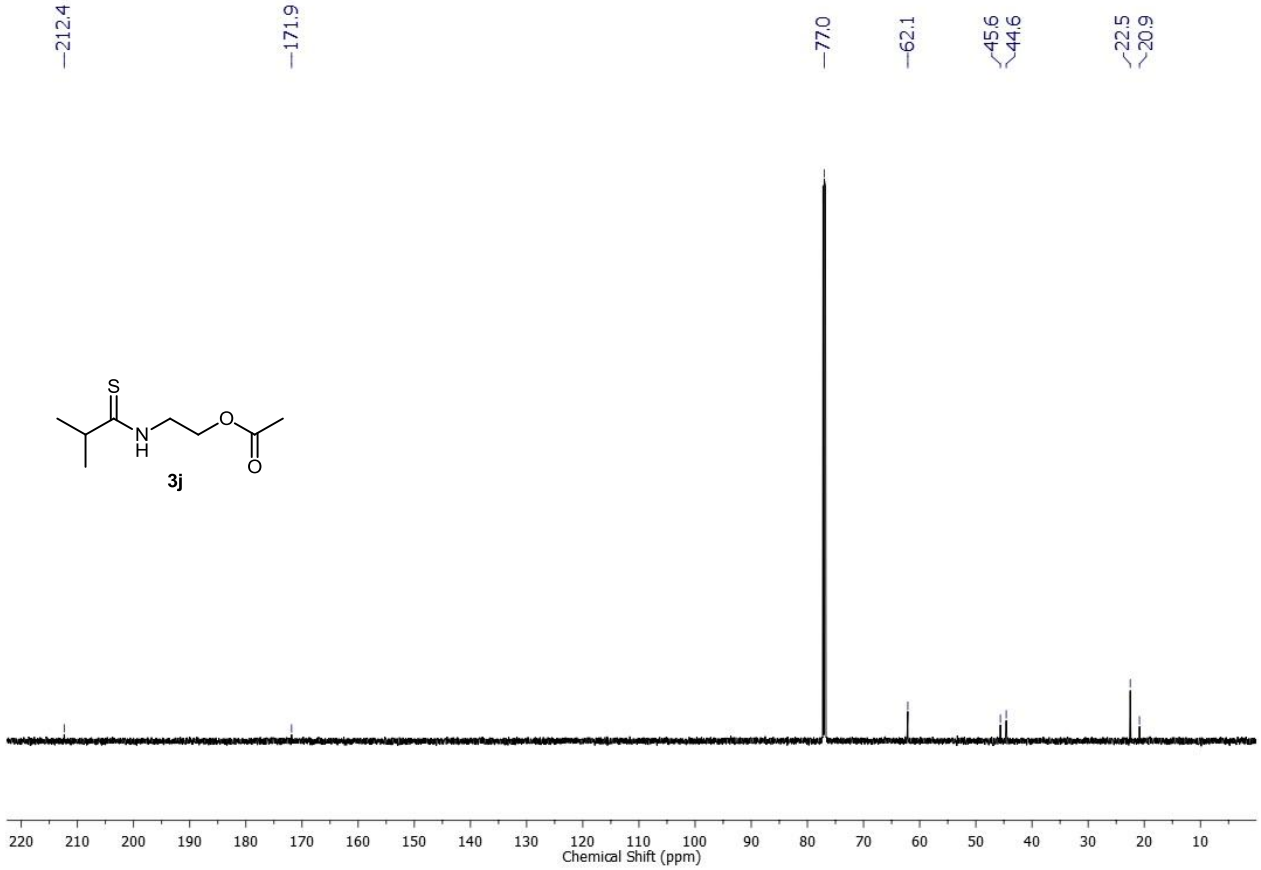
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3i**



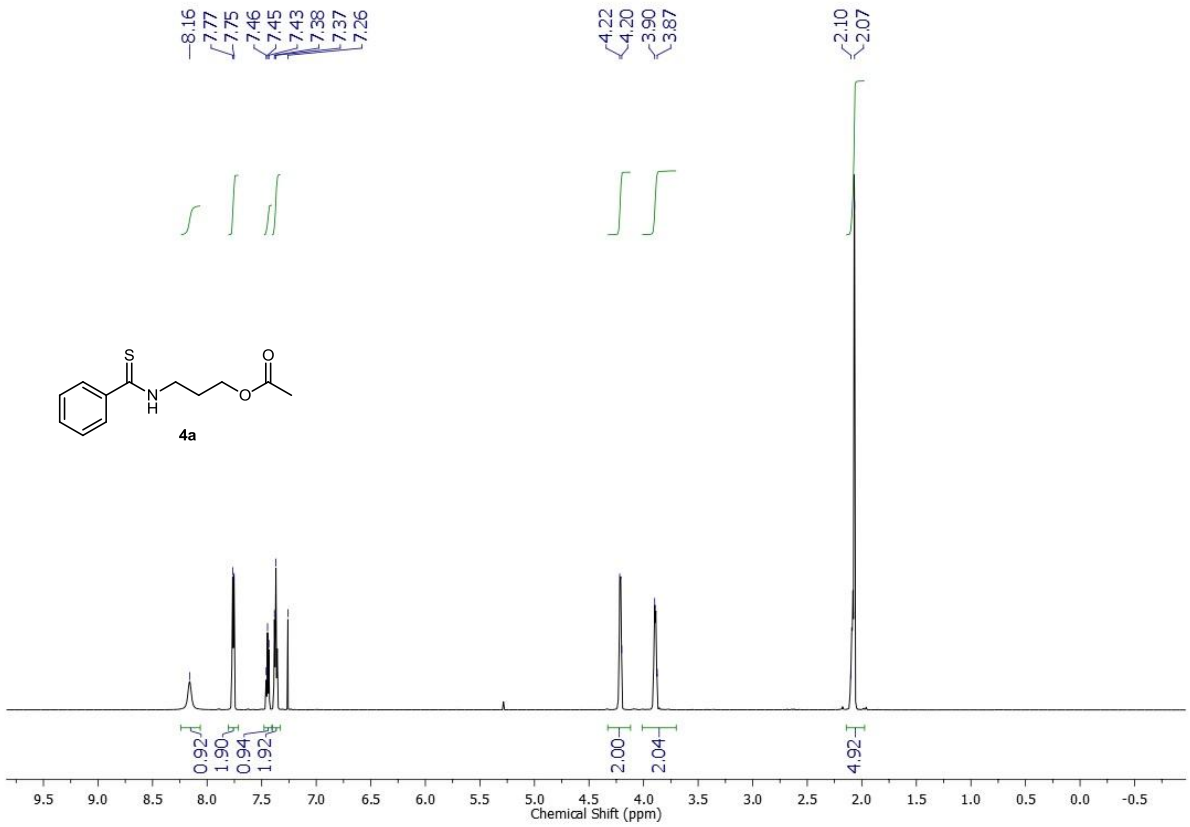
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3j**



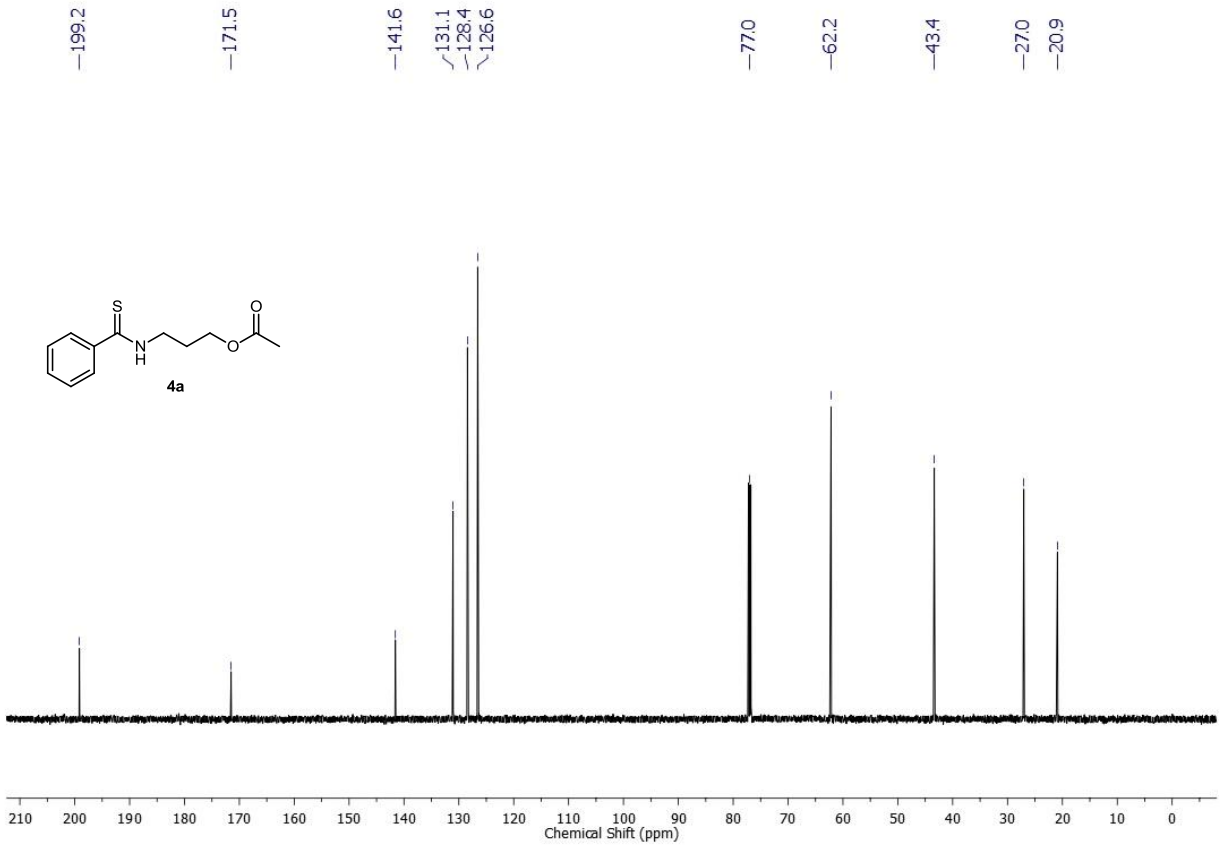
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **3j**



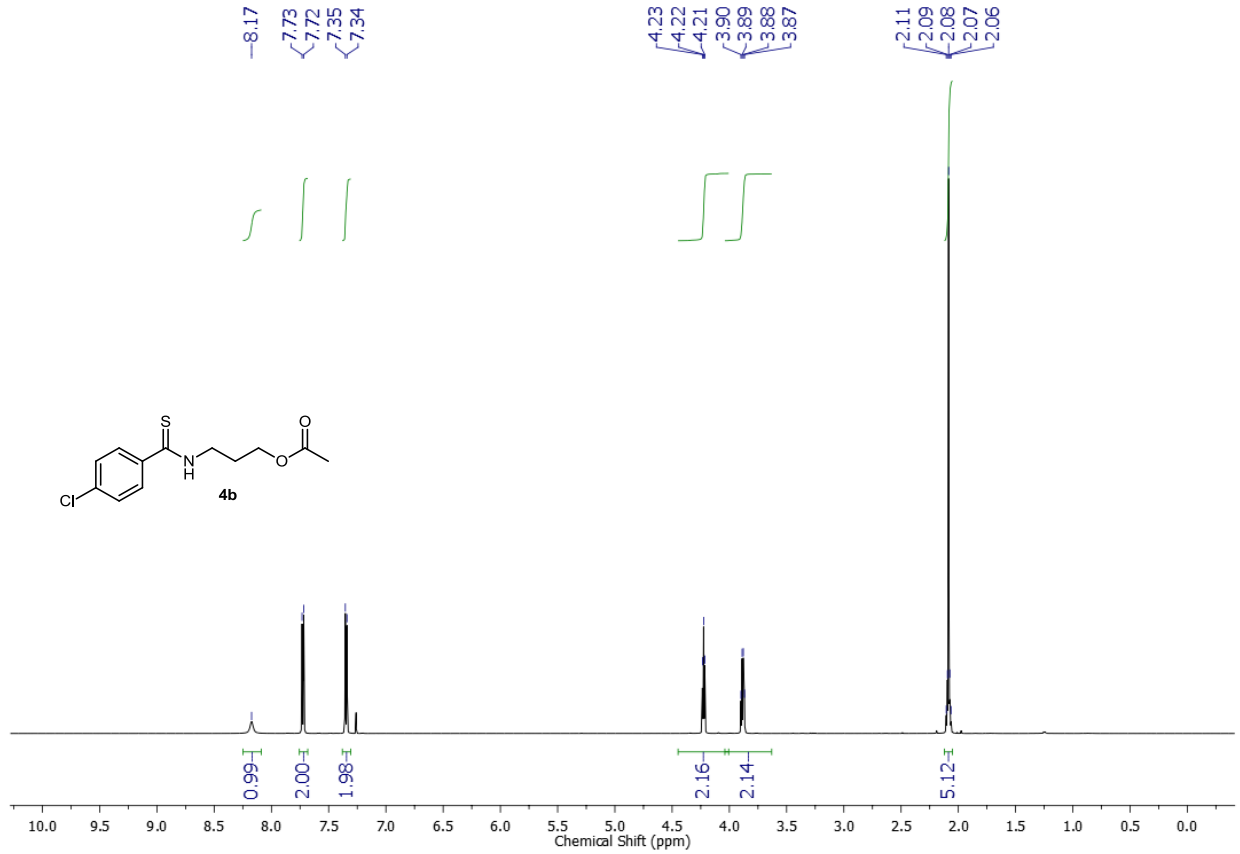
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4a**



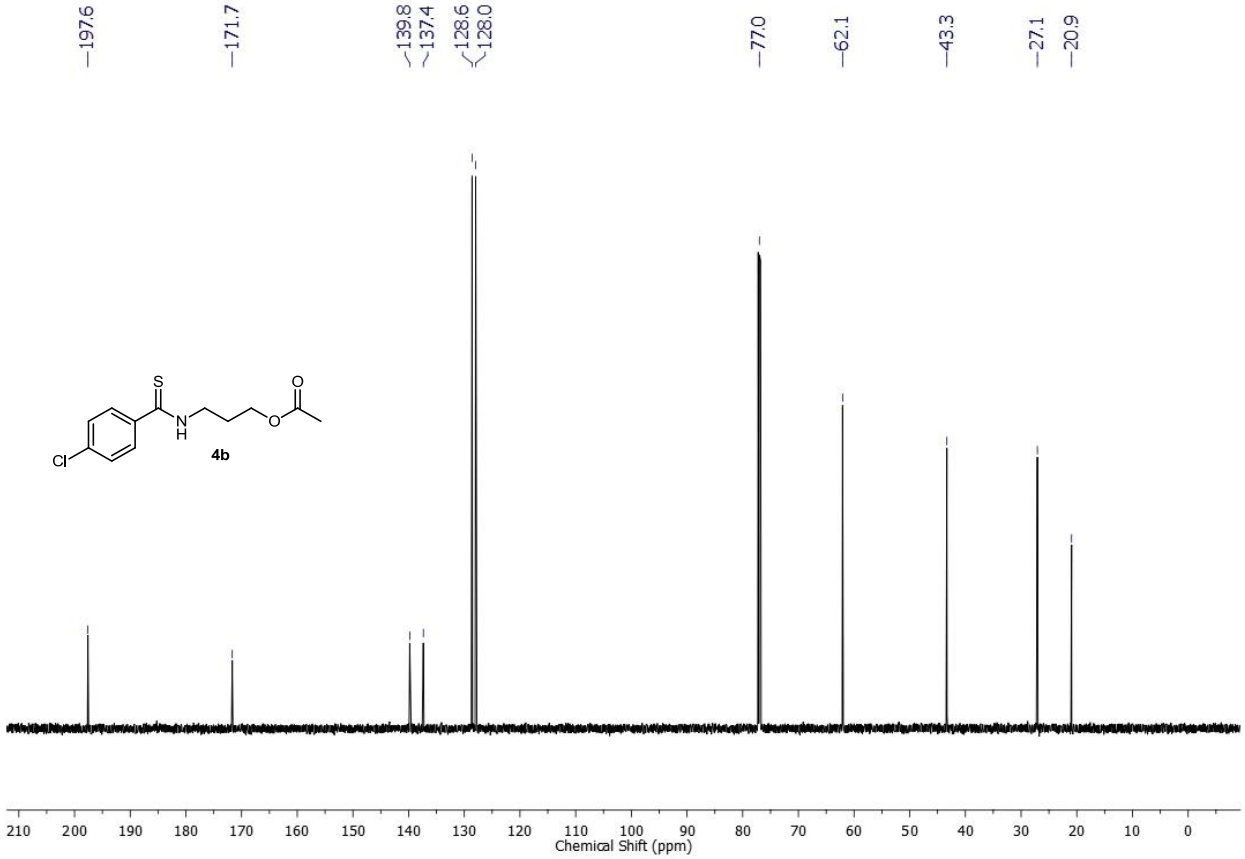
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4a**



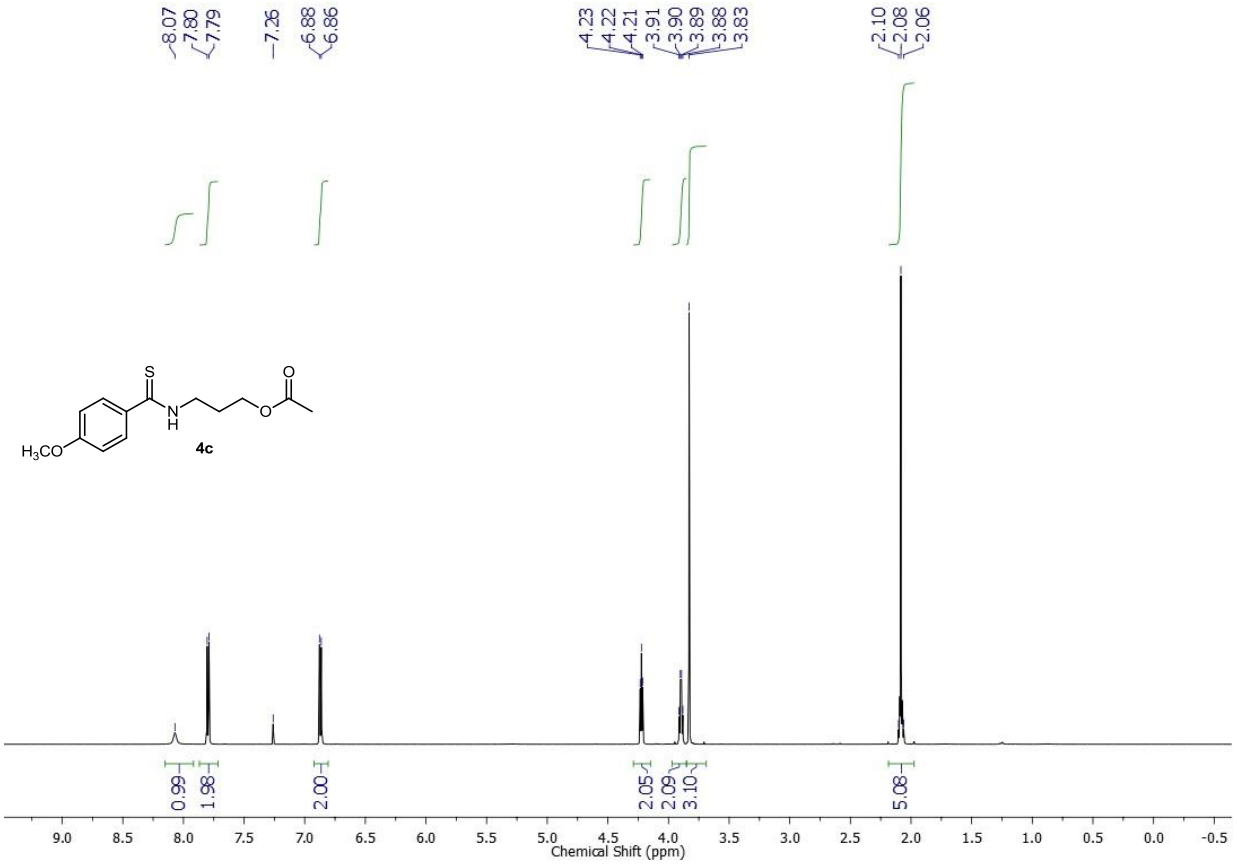
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4b**



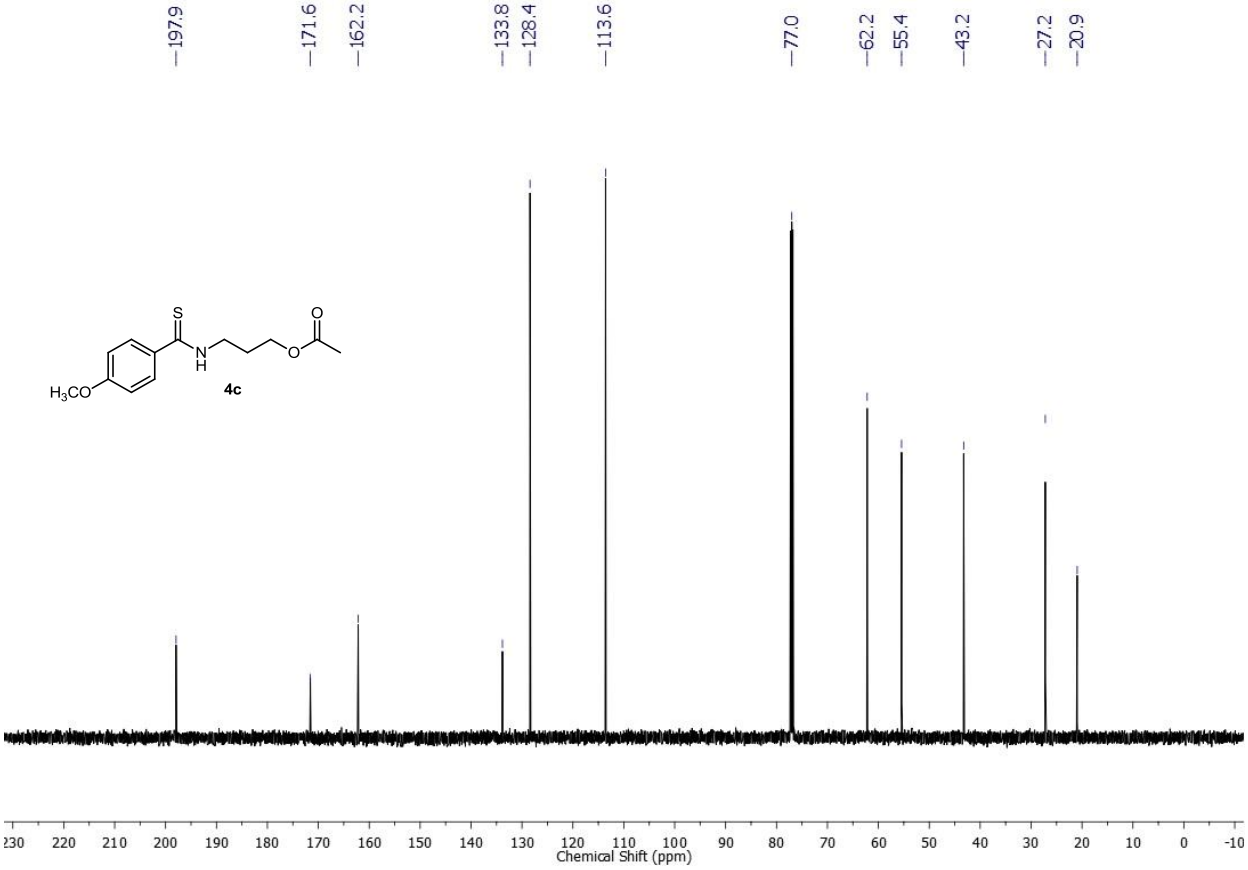
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4b**



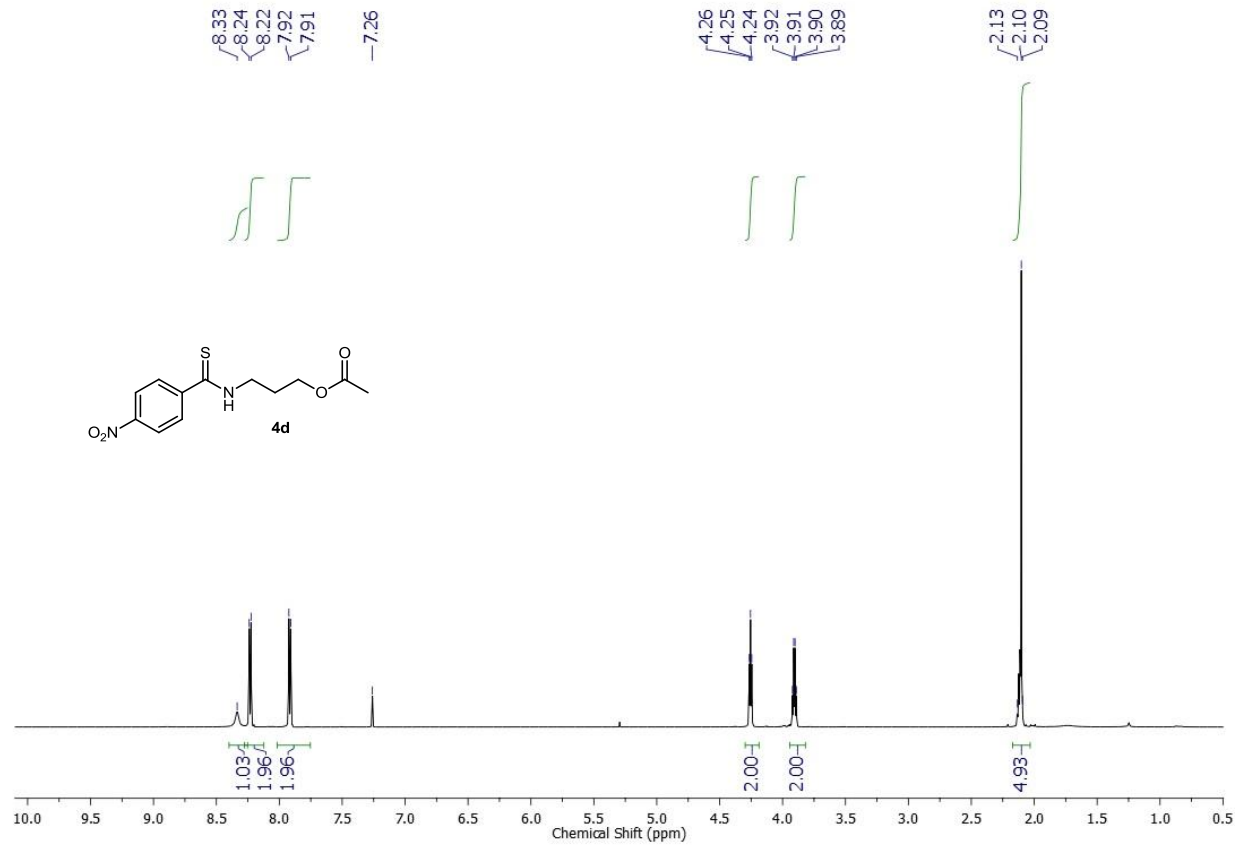
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4c**



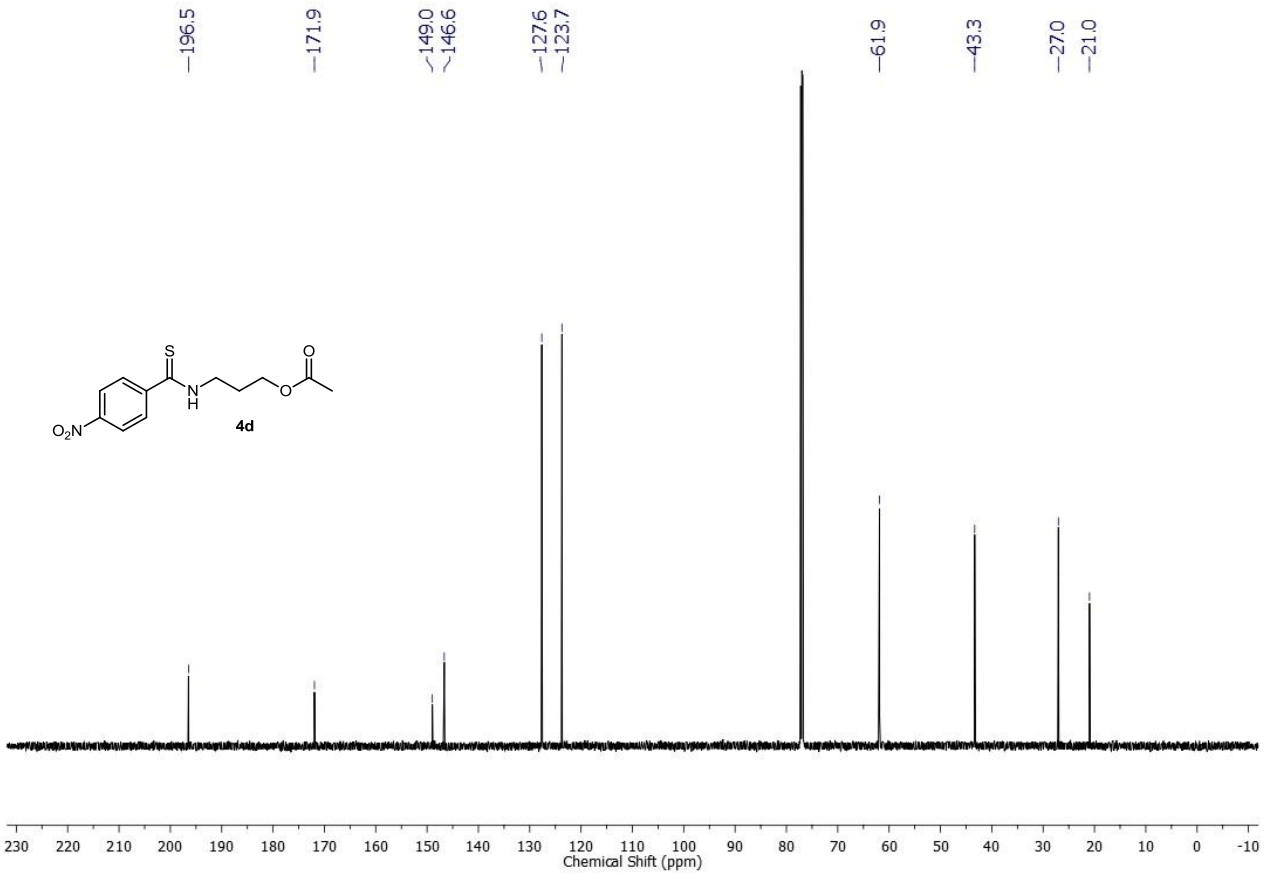
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4c**



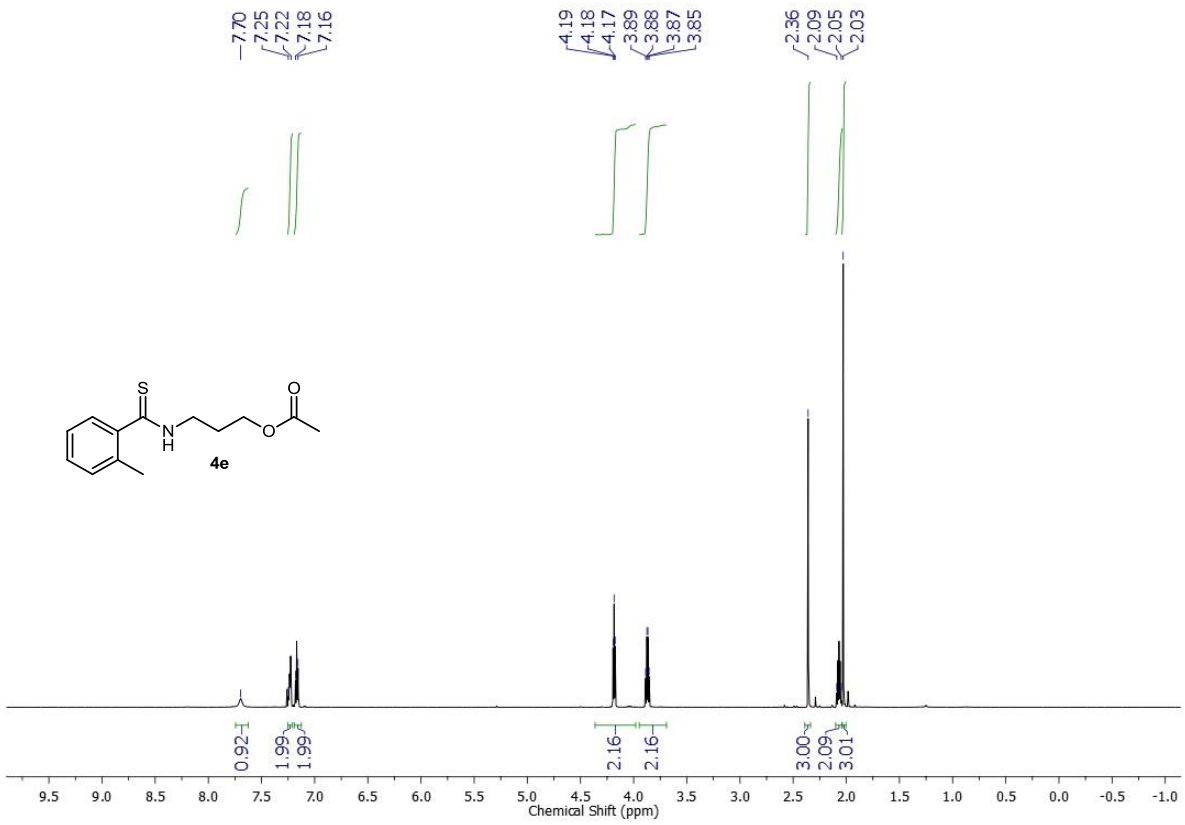
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4d**



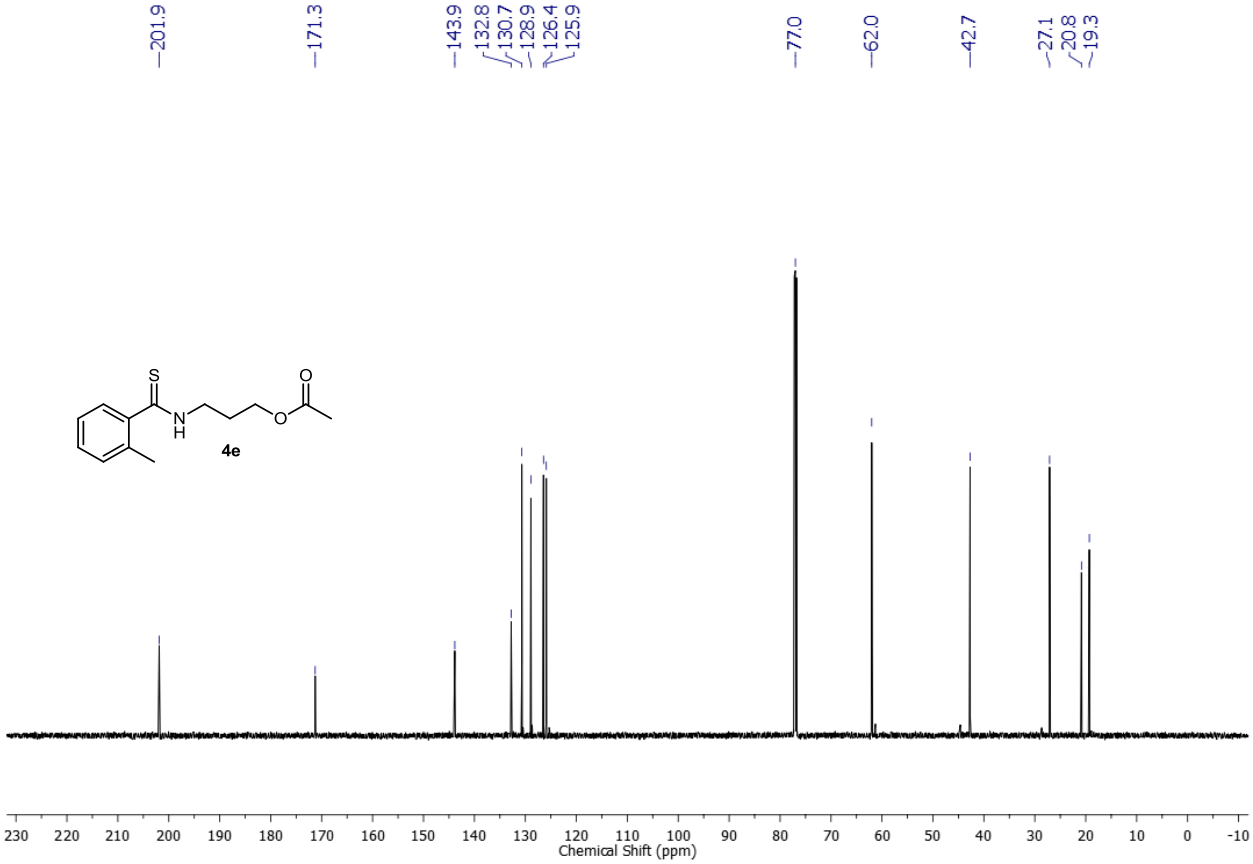
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4d**



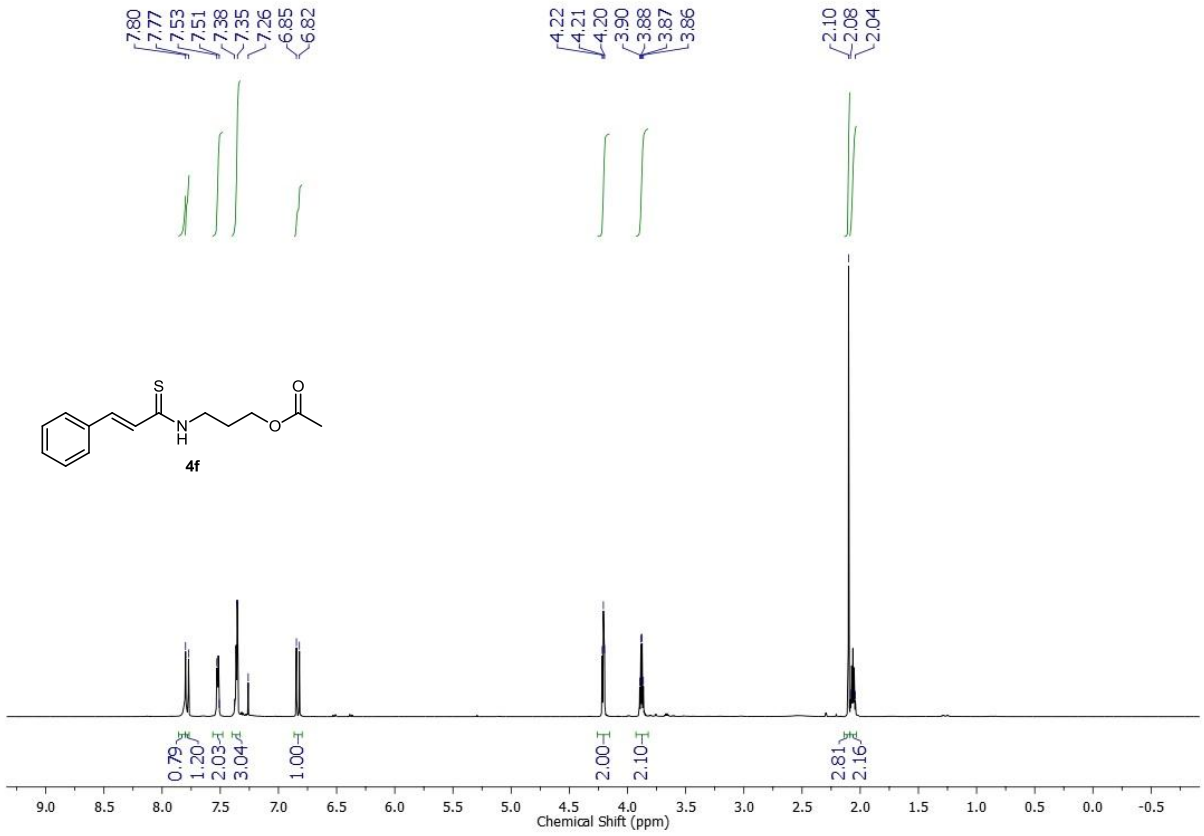
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4e**



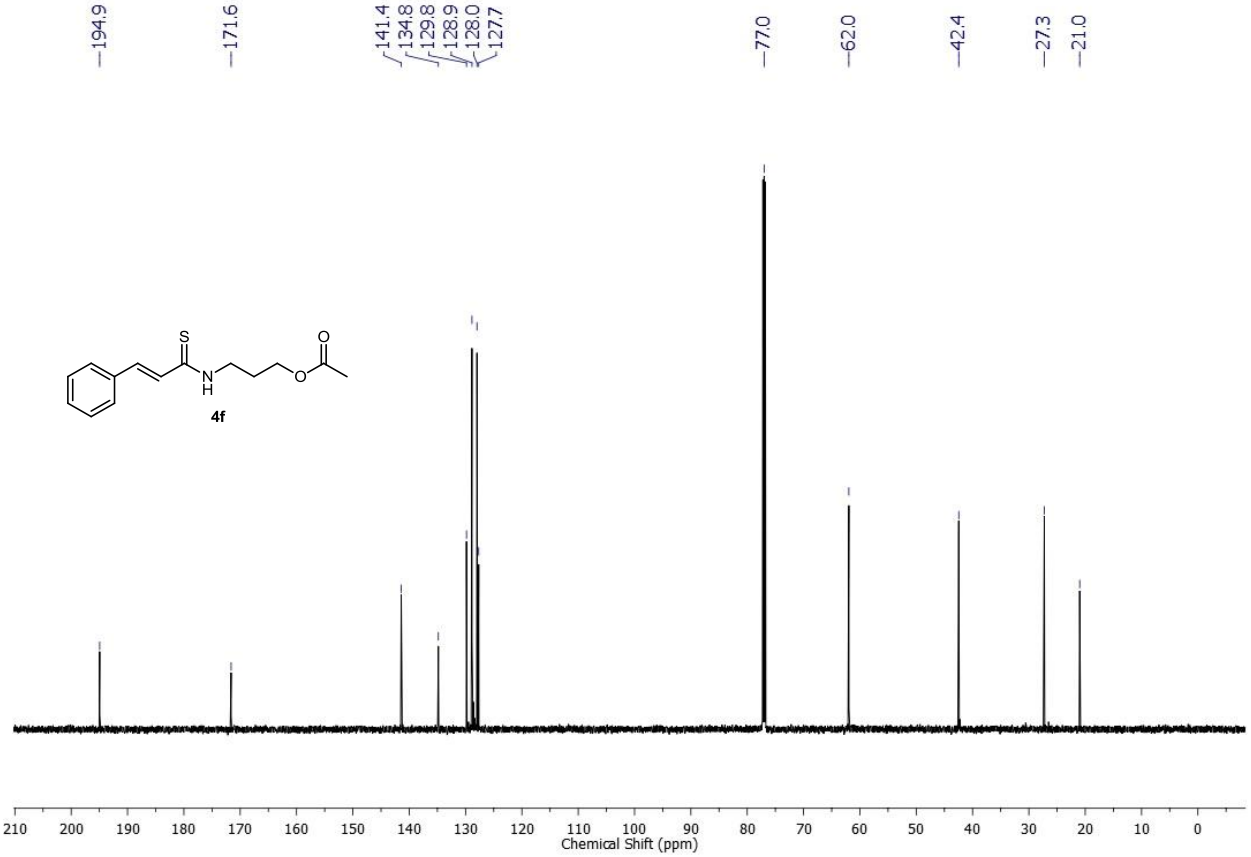
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4e**



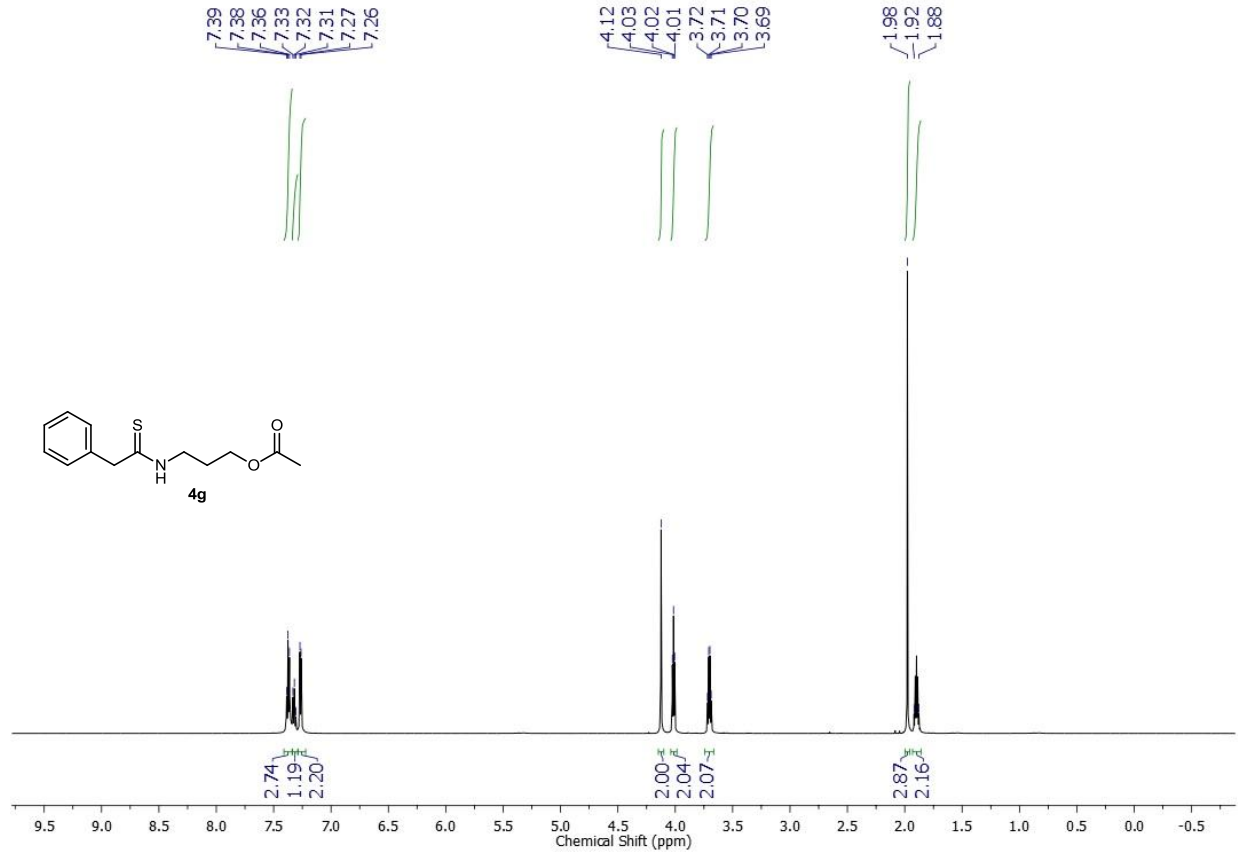
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4f**



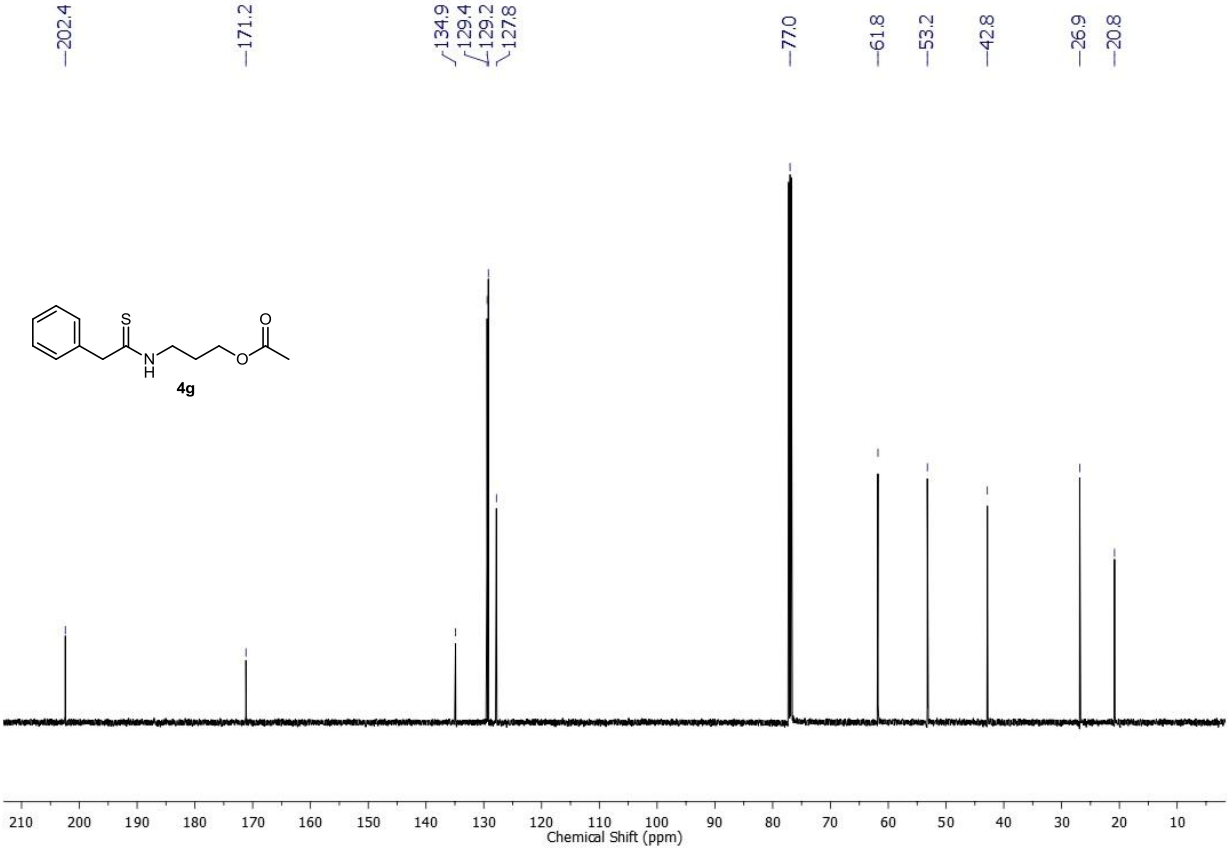
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4f**



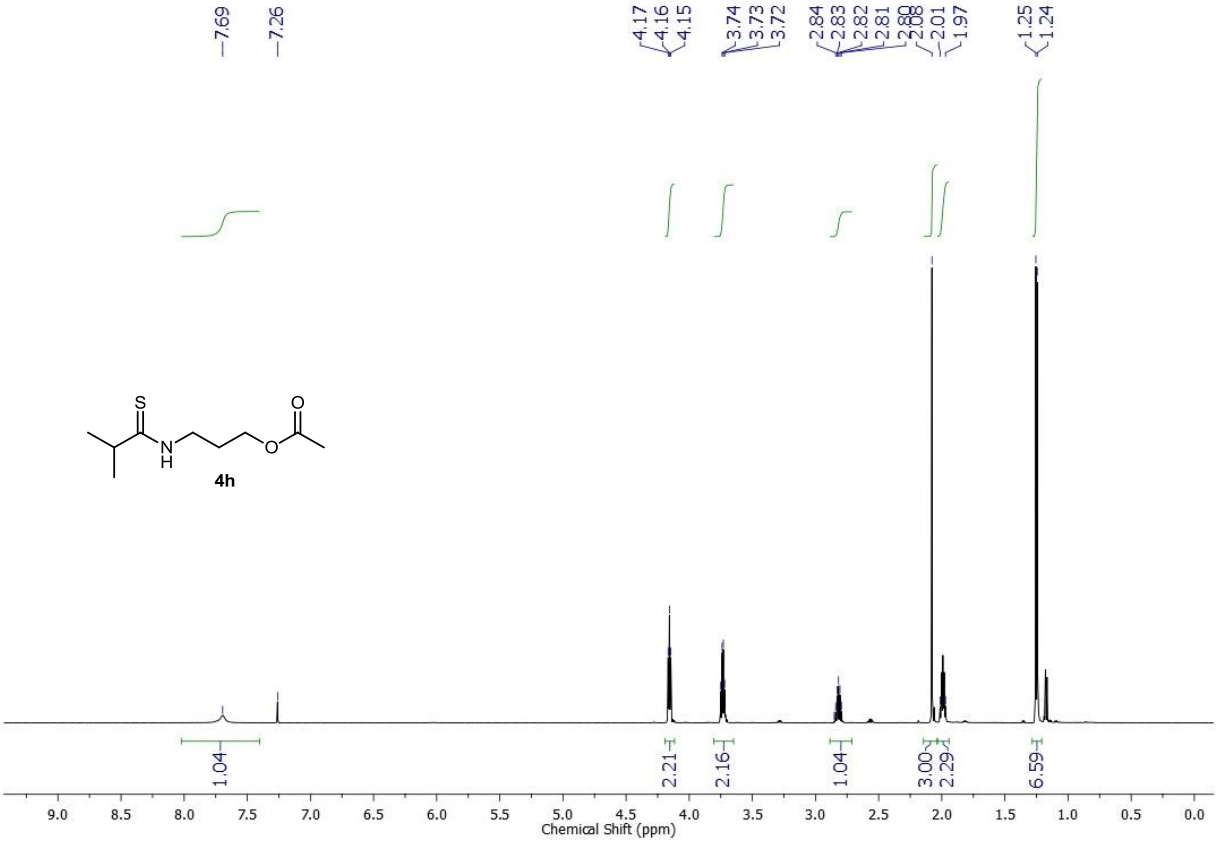
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4g**



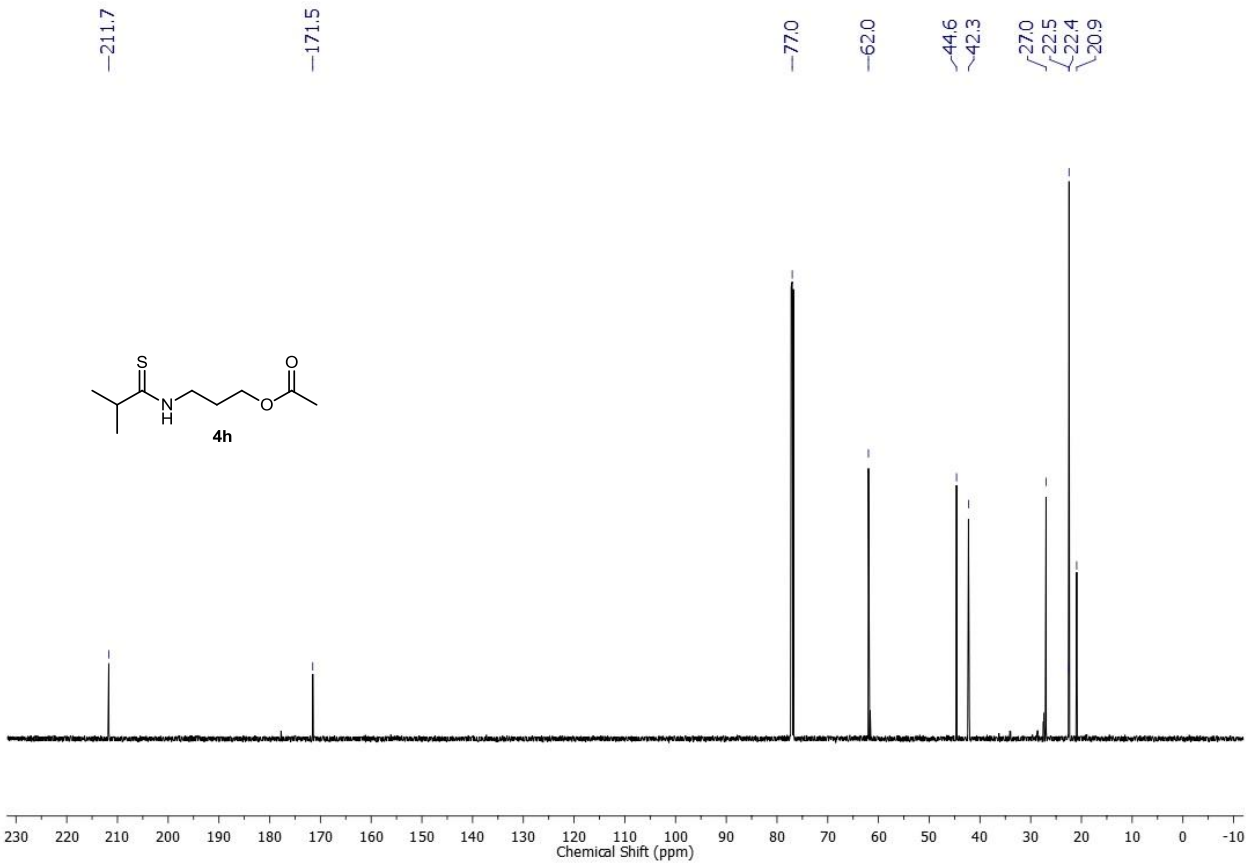
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4g**



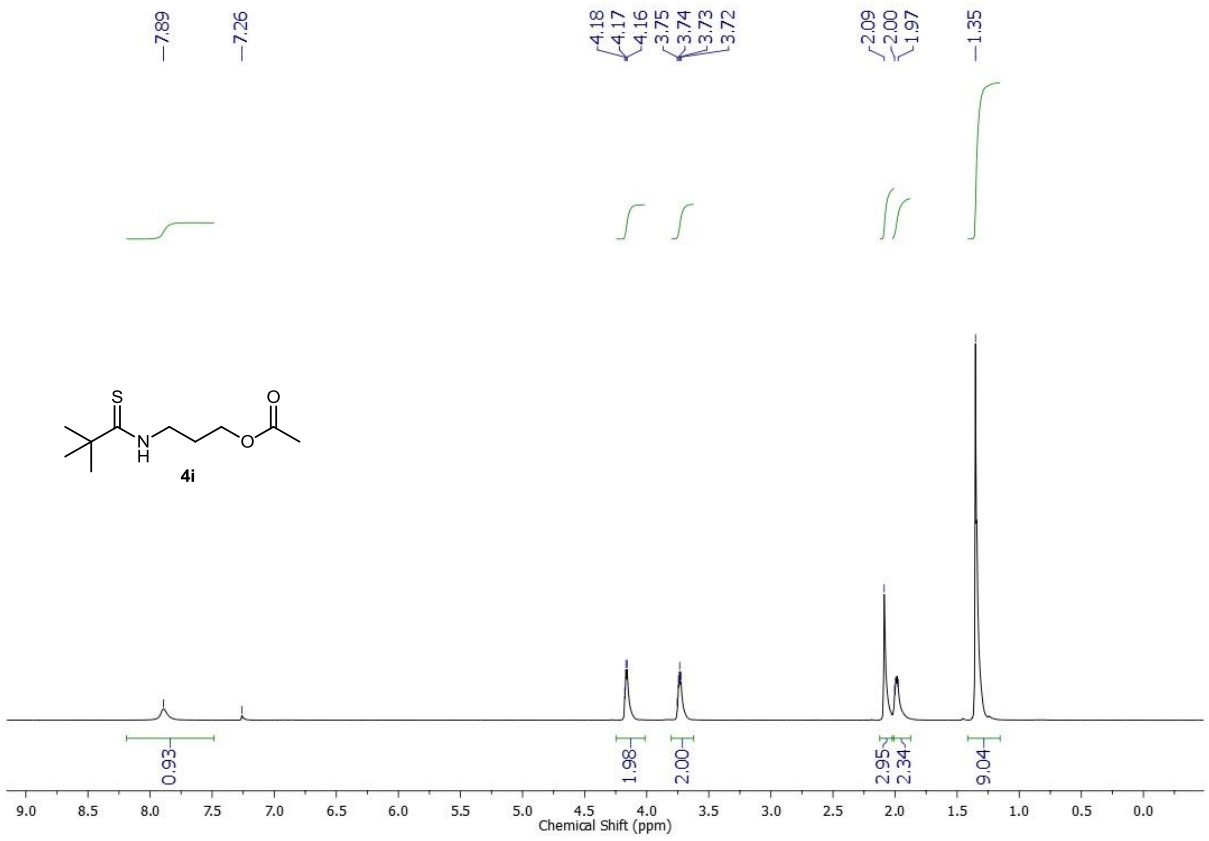
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4h**



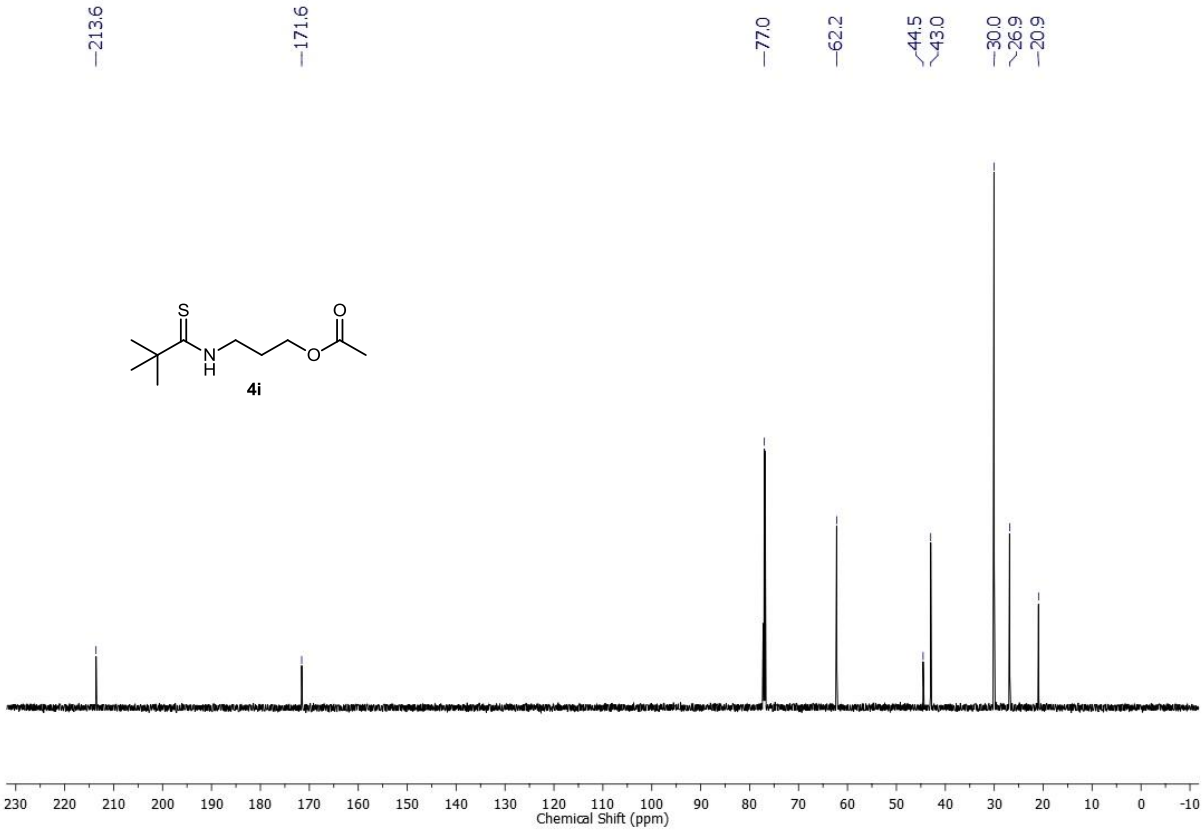
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4h**



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **4i**

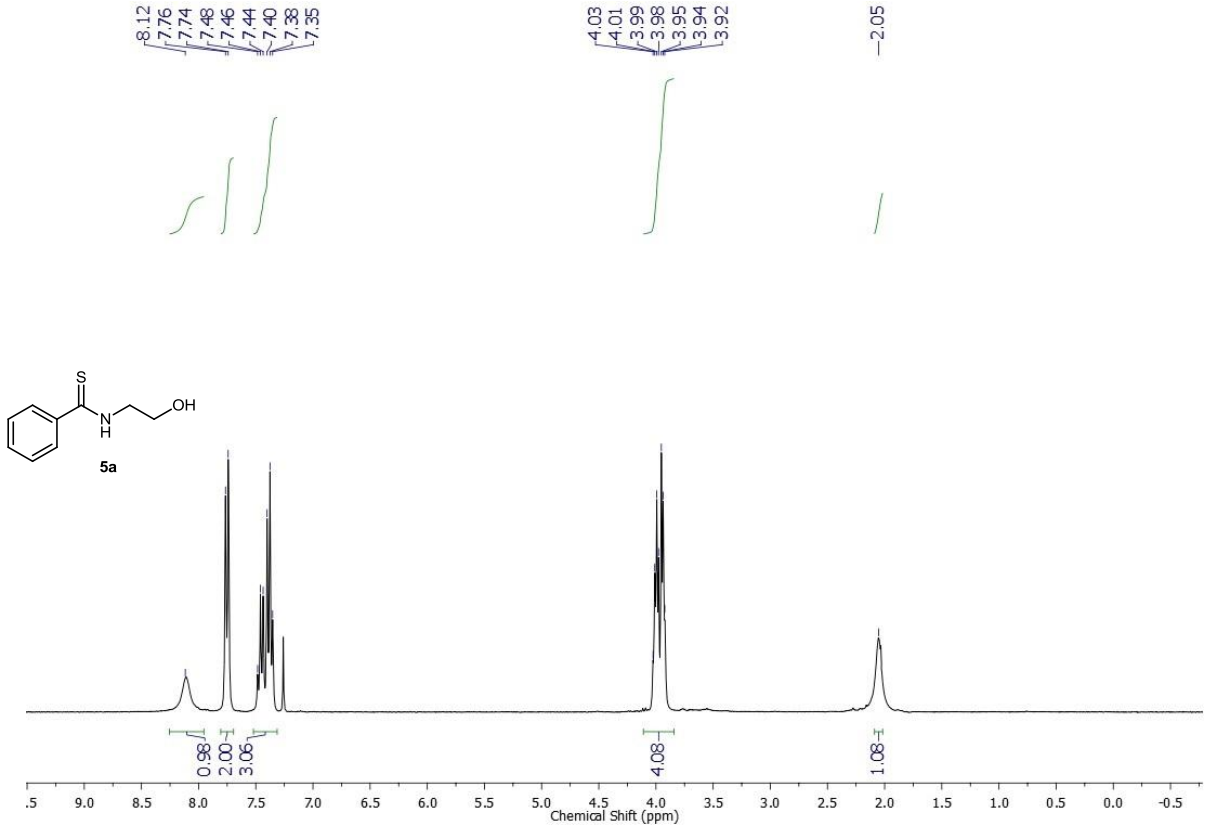


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **4i**

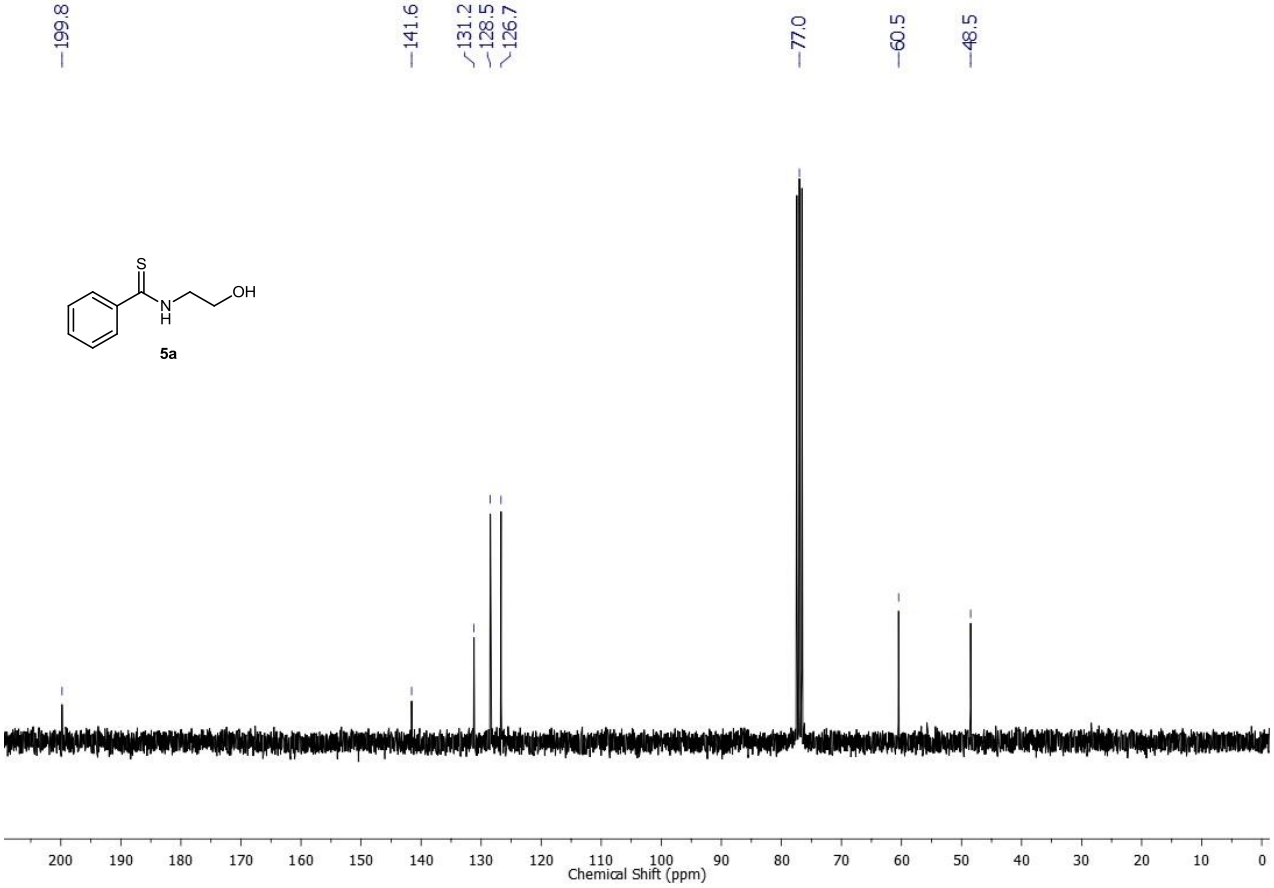


6. Copies of ^{1}H and ^{13}C NMR spectra of compounds 5-6

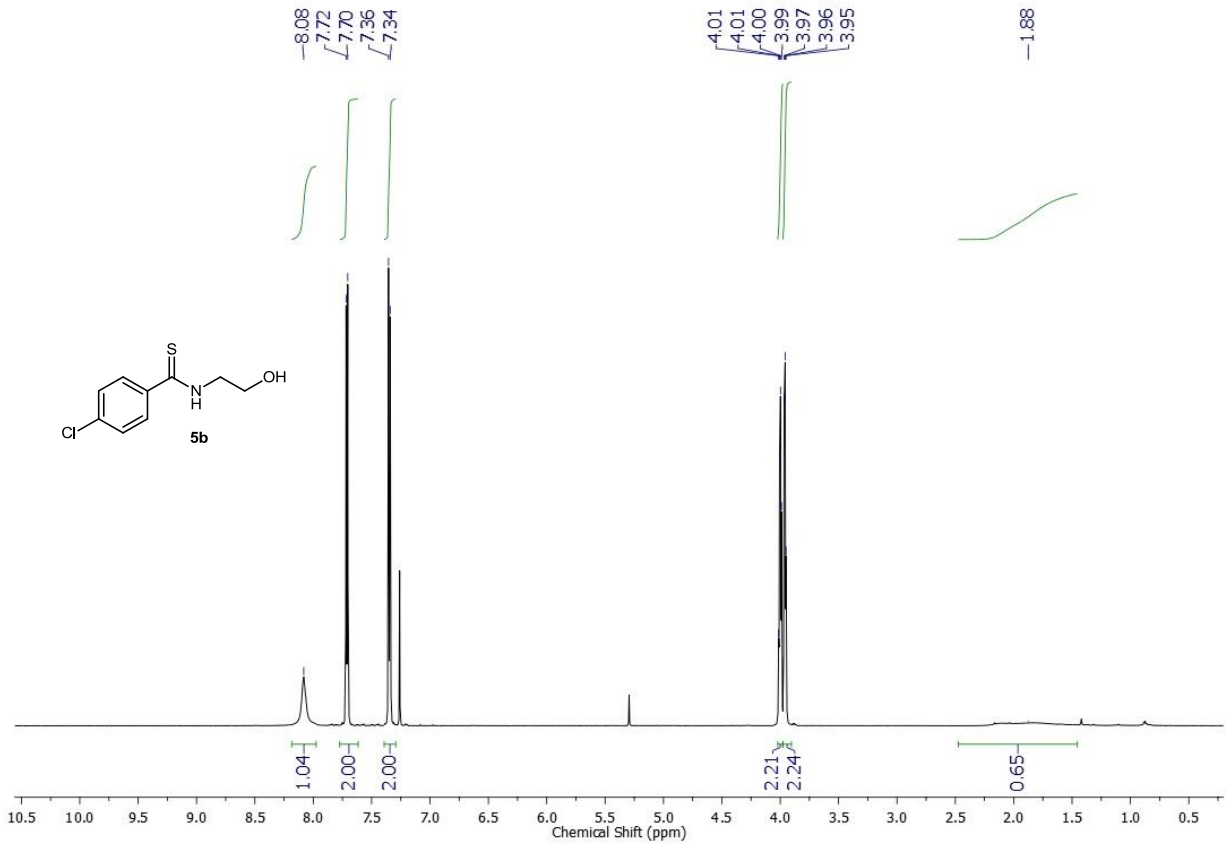
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5a**



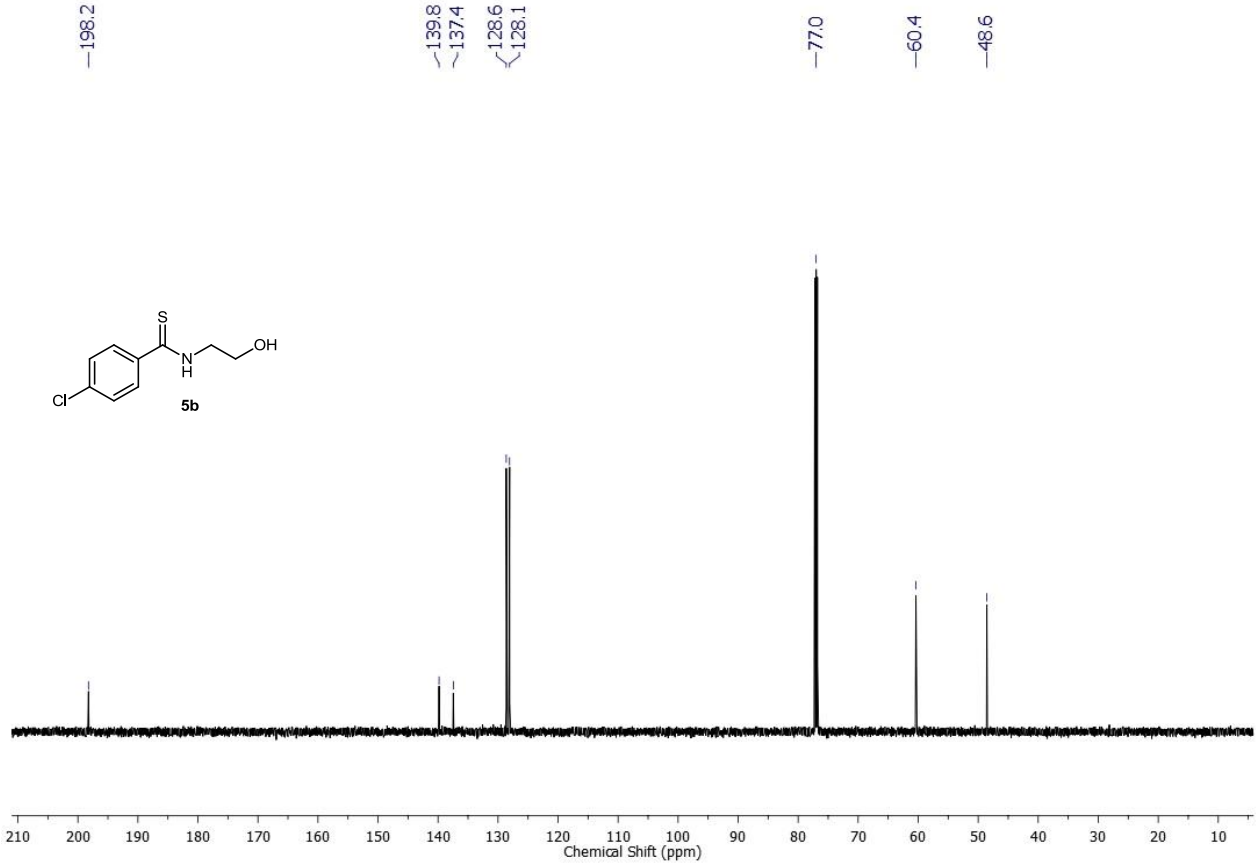
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5a**



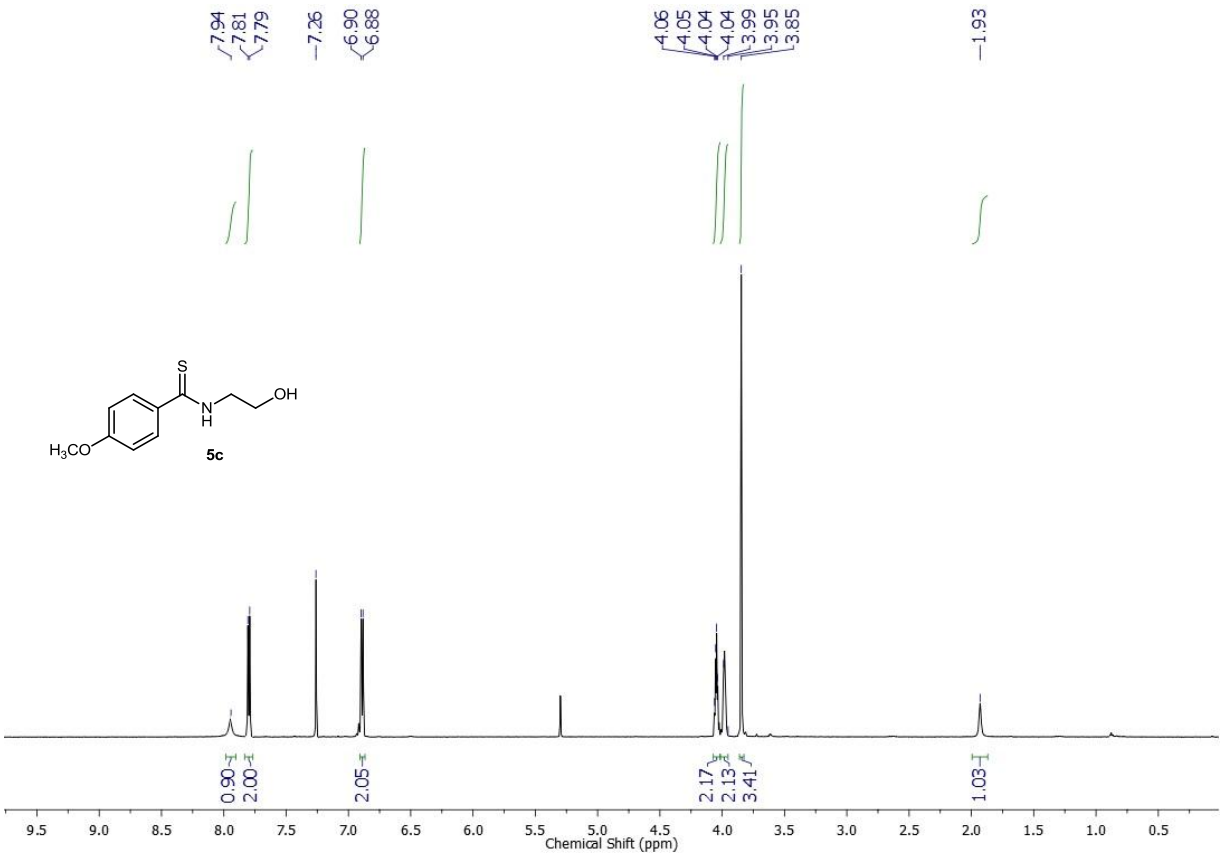
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5b**



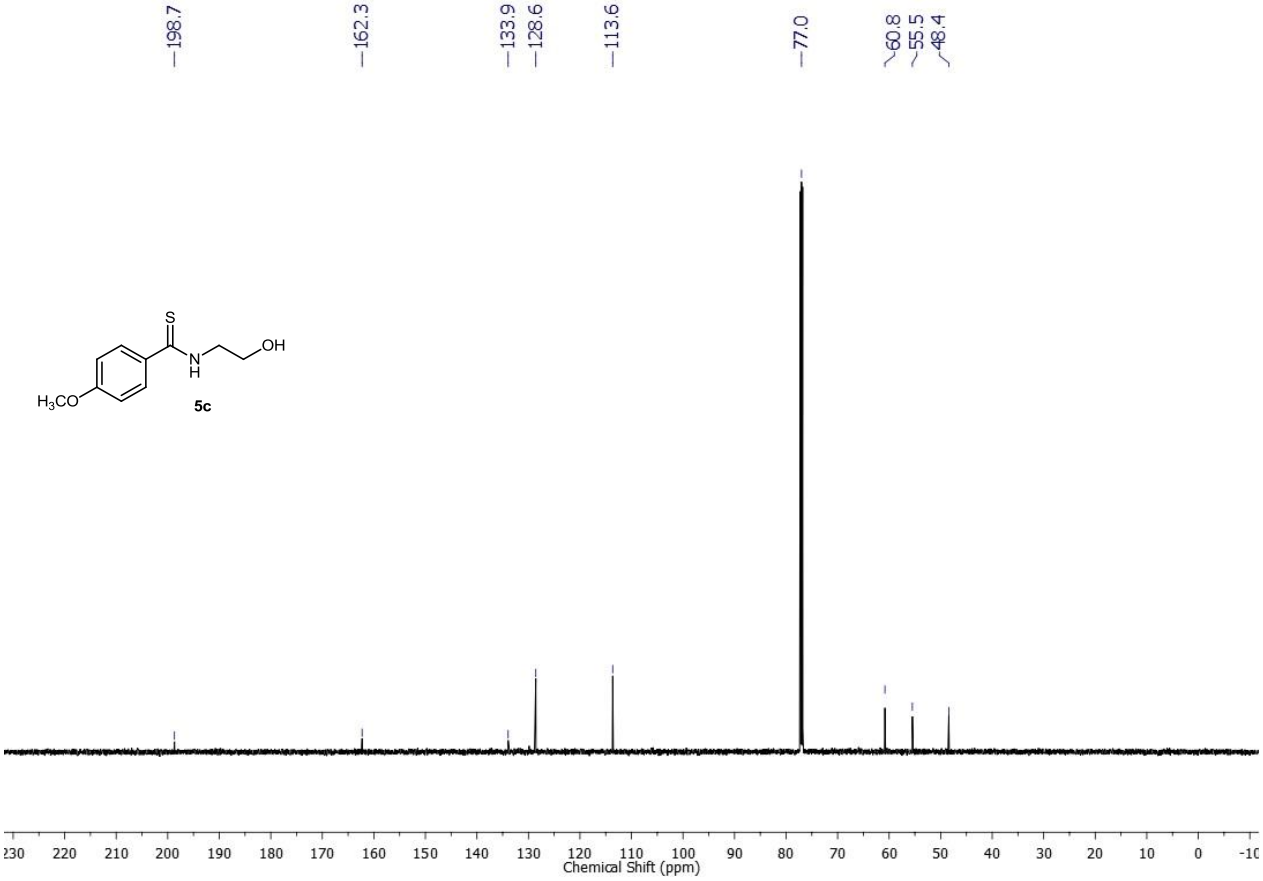
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5b**



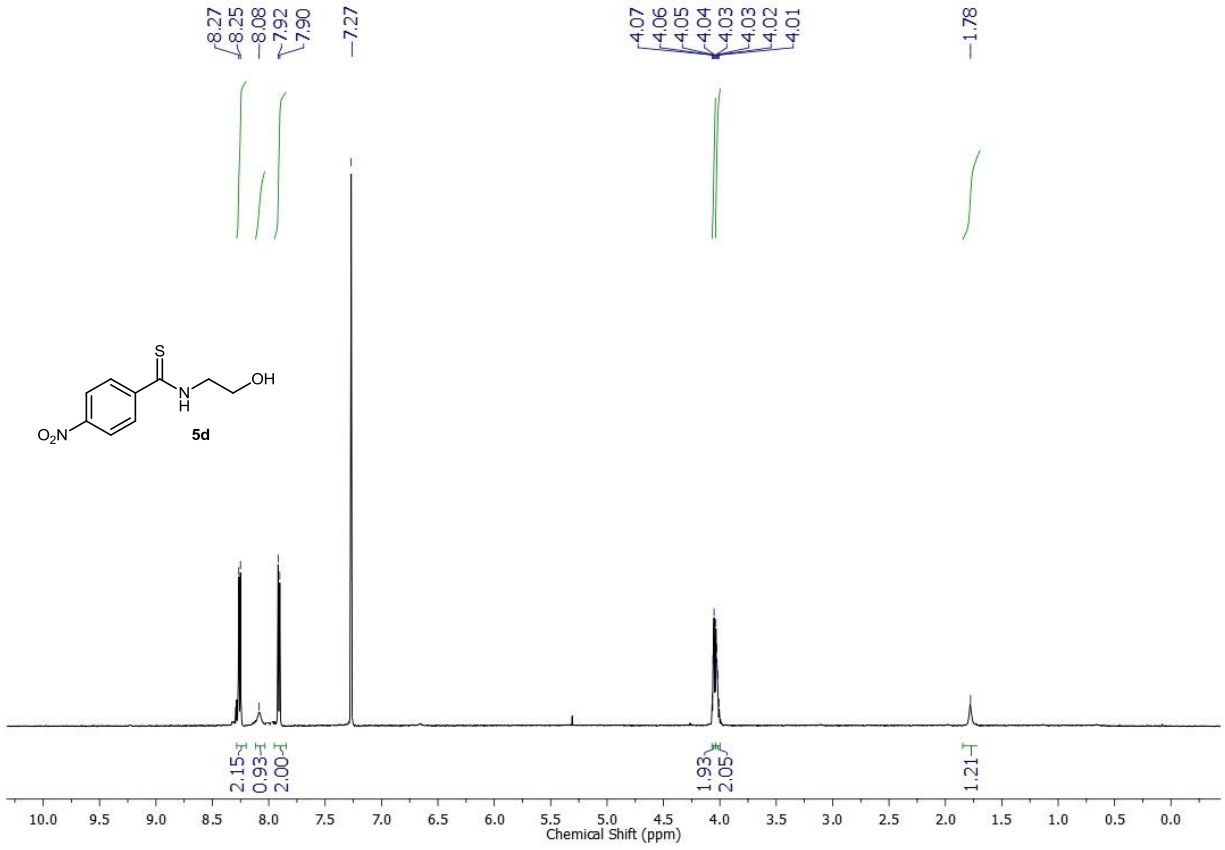
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5c**



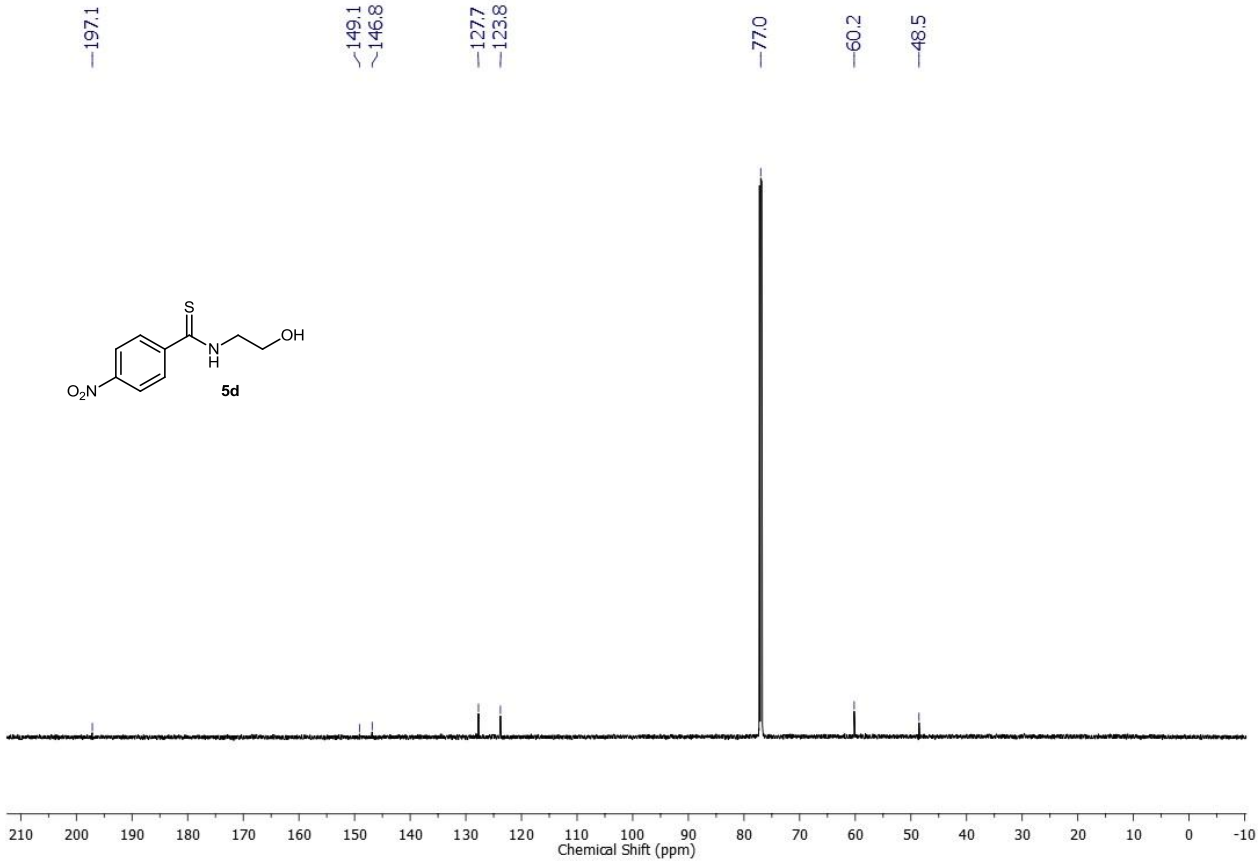
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5c**



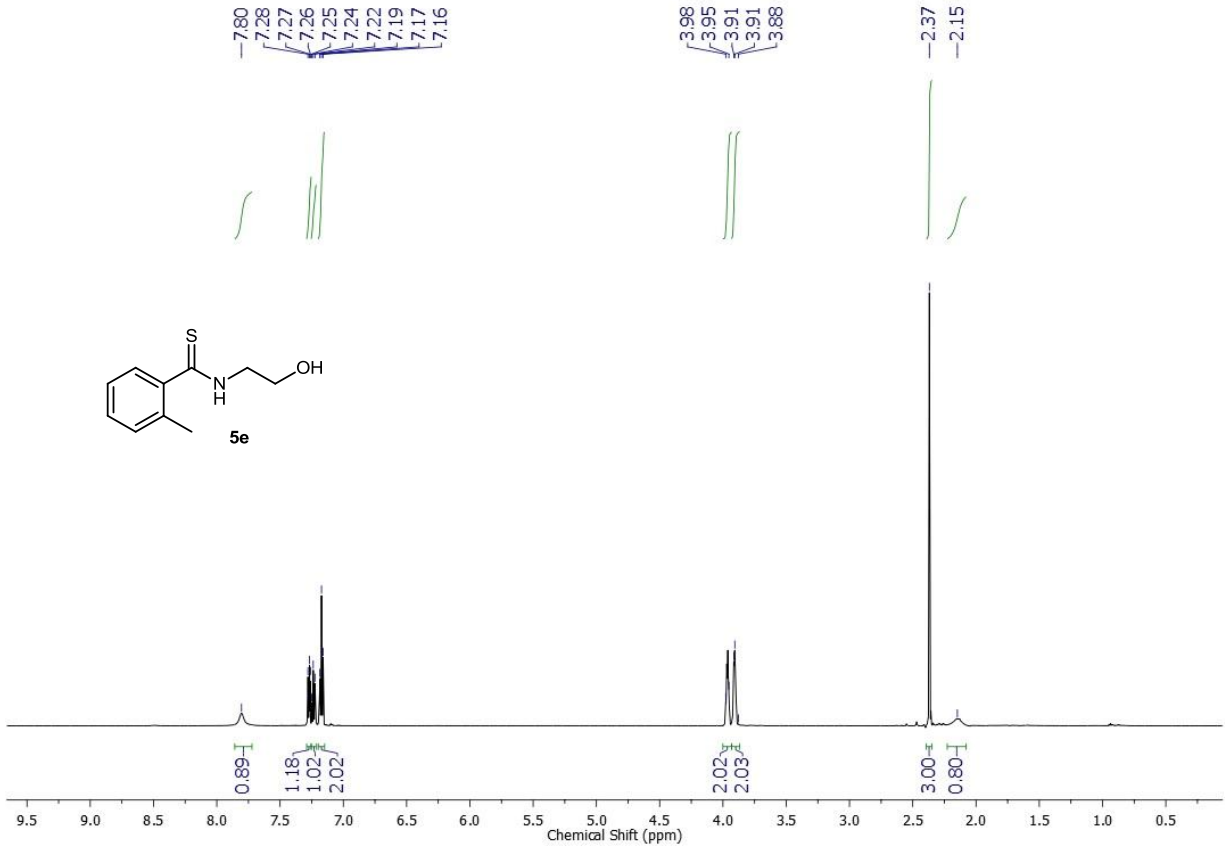
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5d**



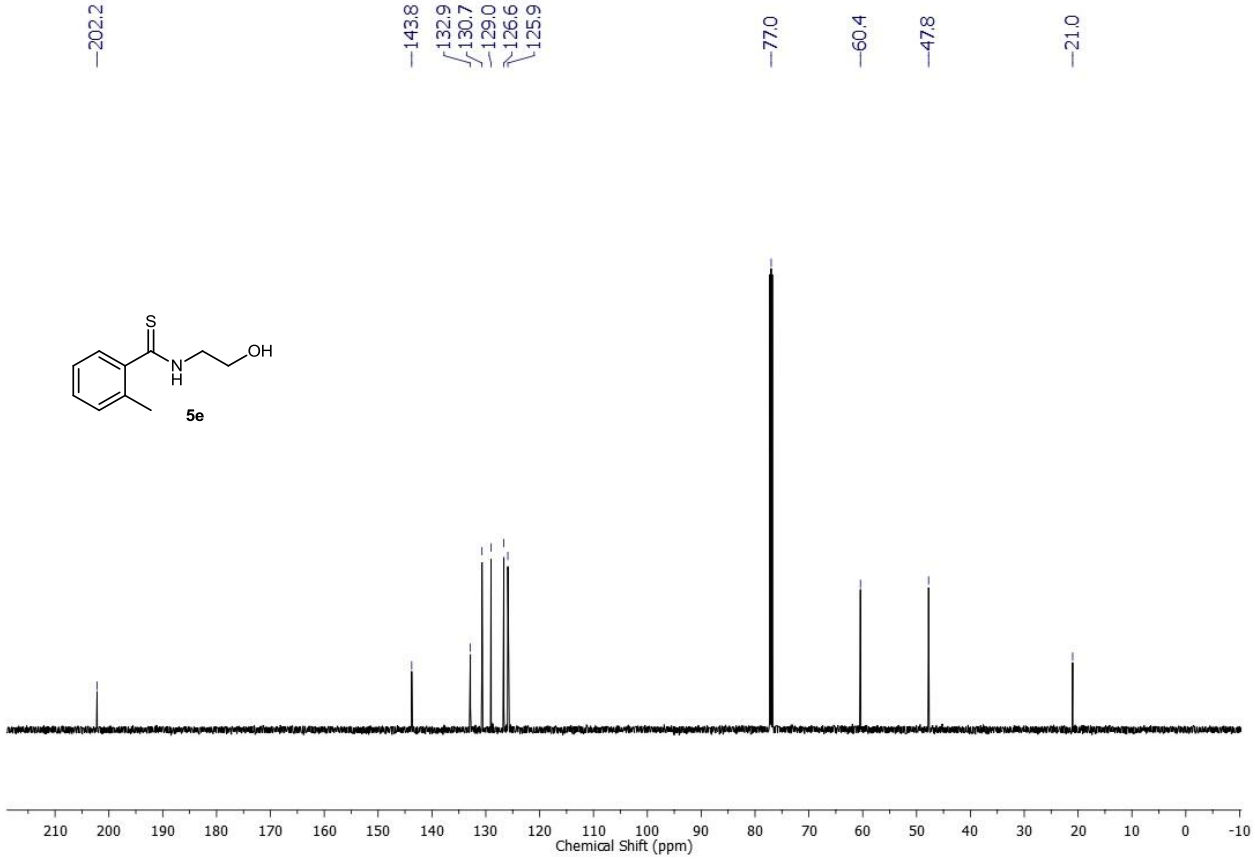
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5d**



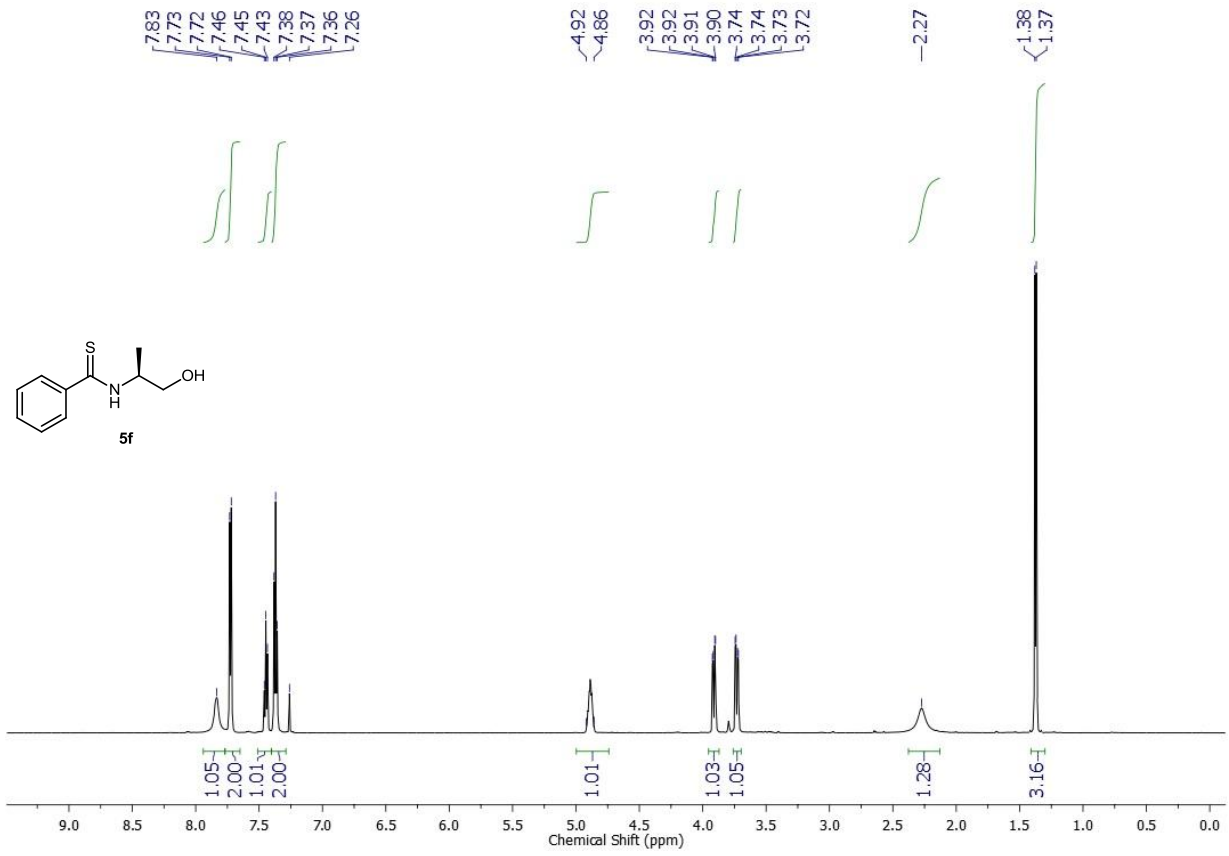
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5e**



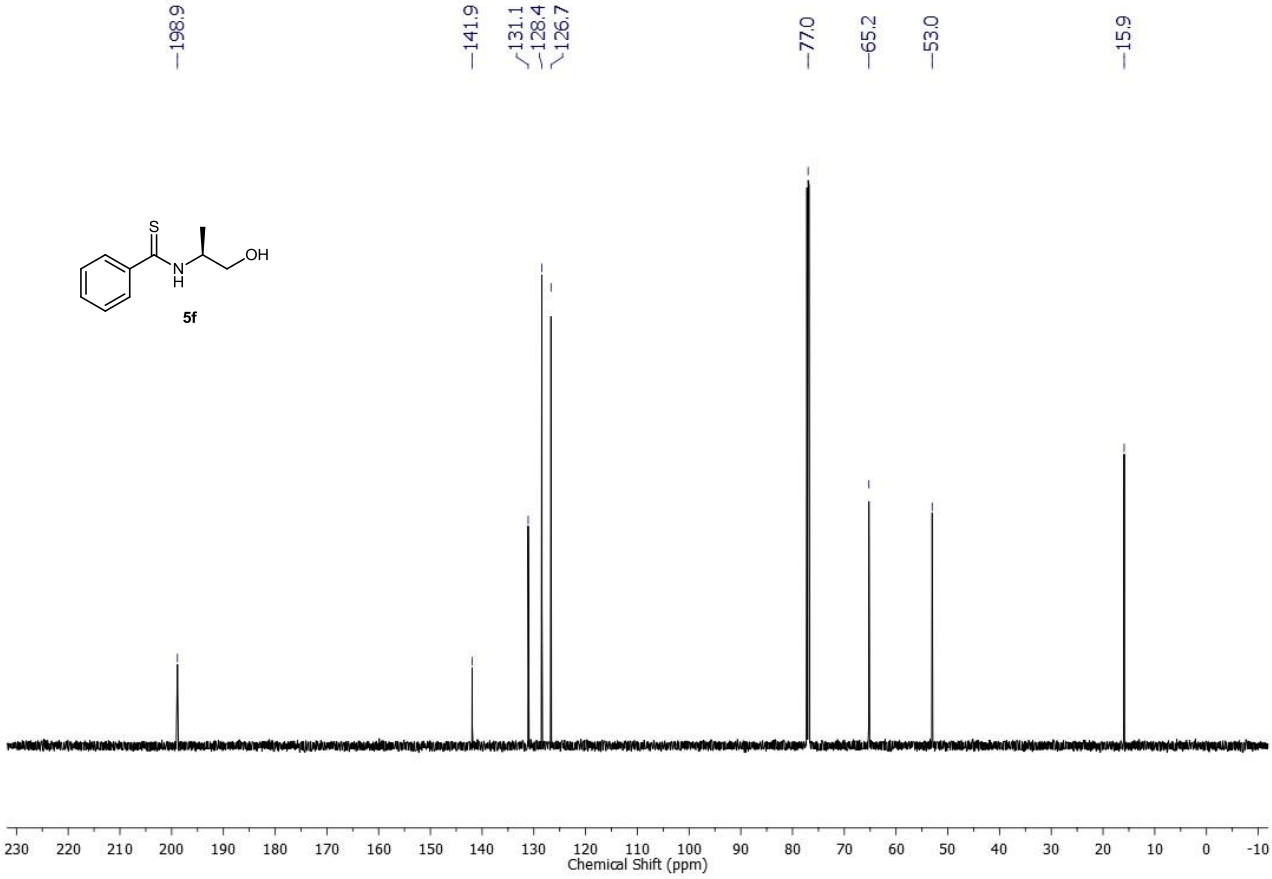
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5e**



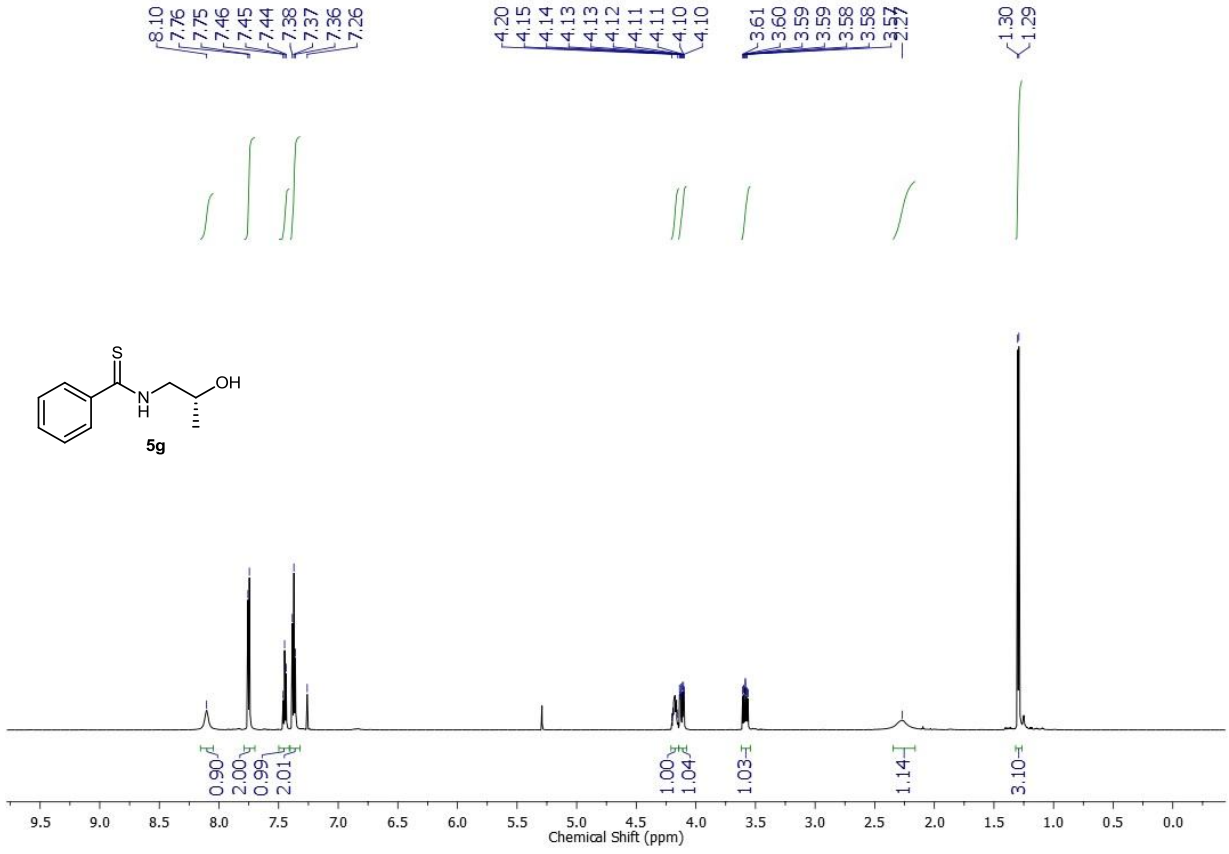
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5f**



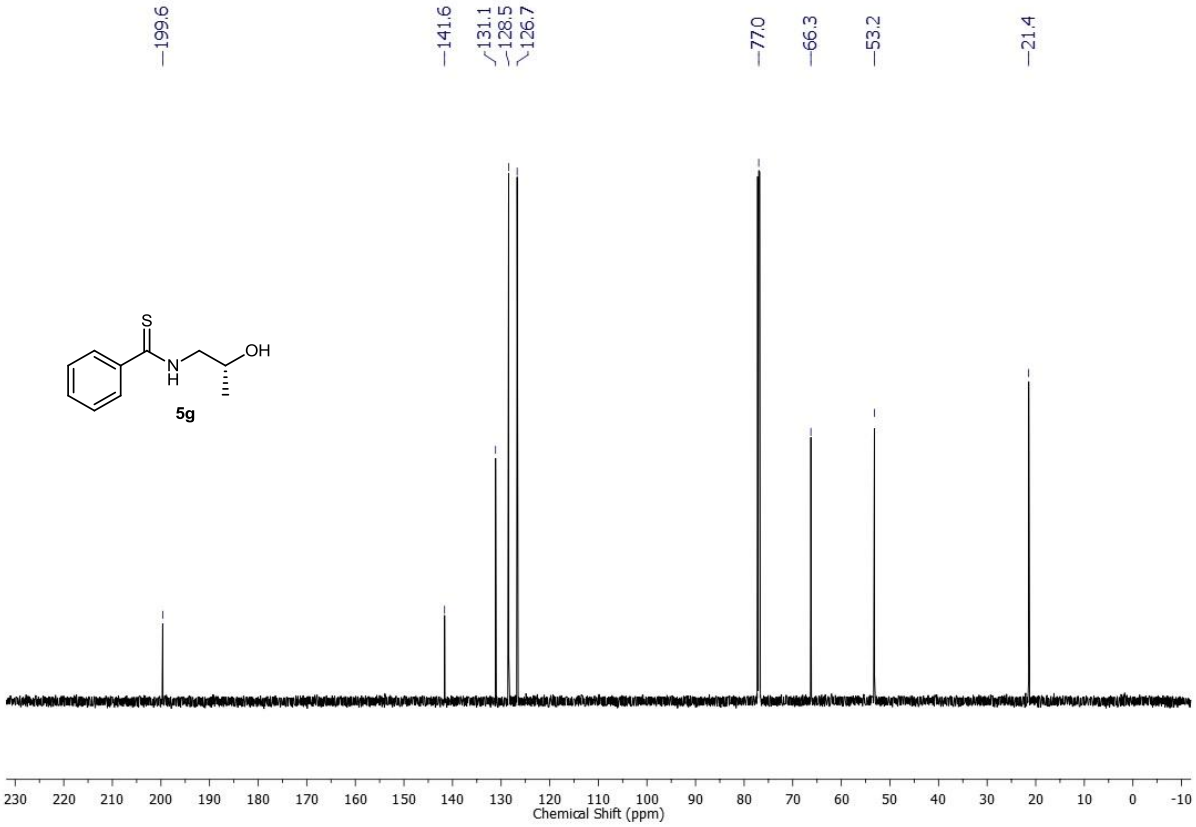
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5f**



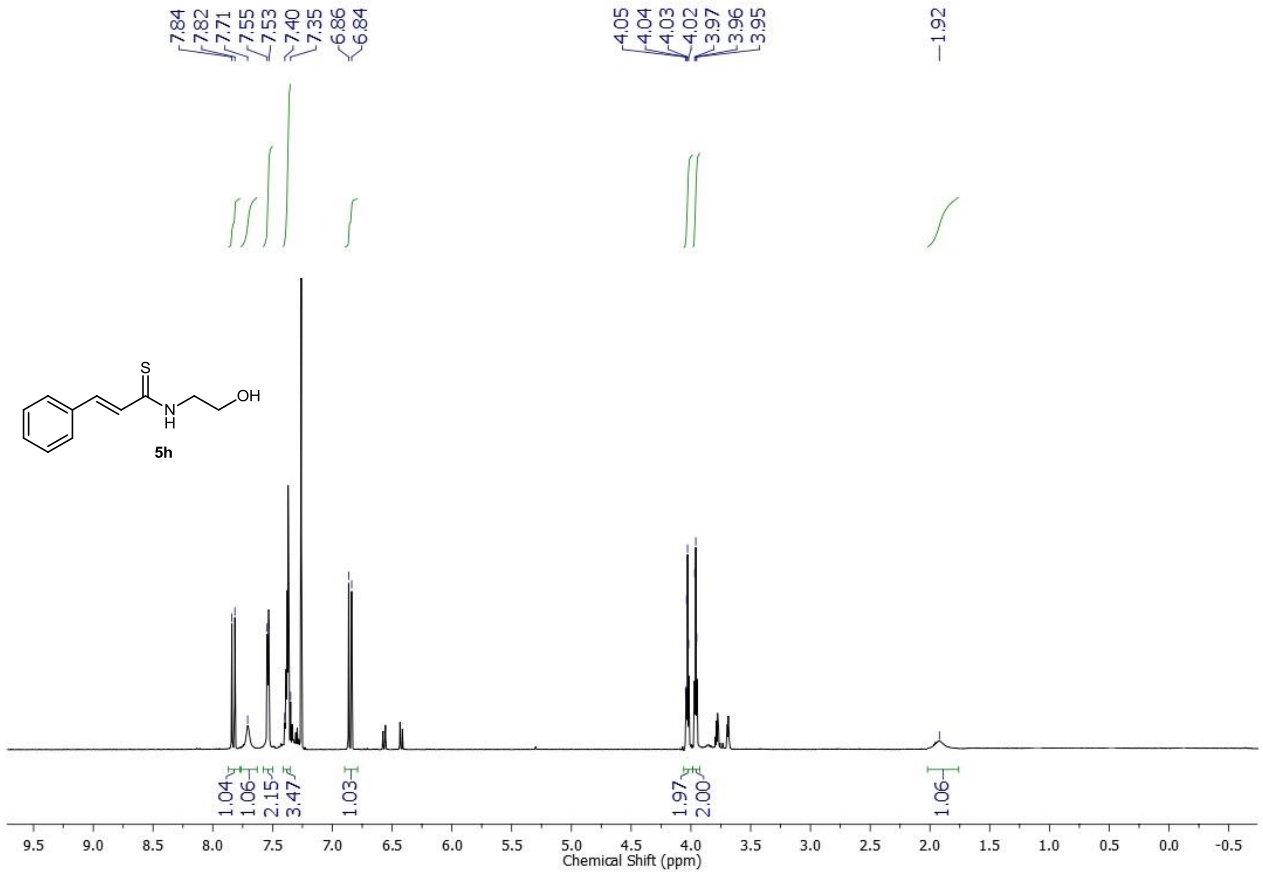
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5g**



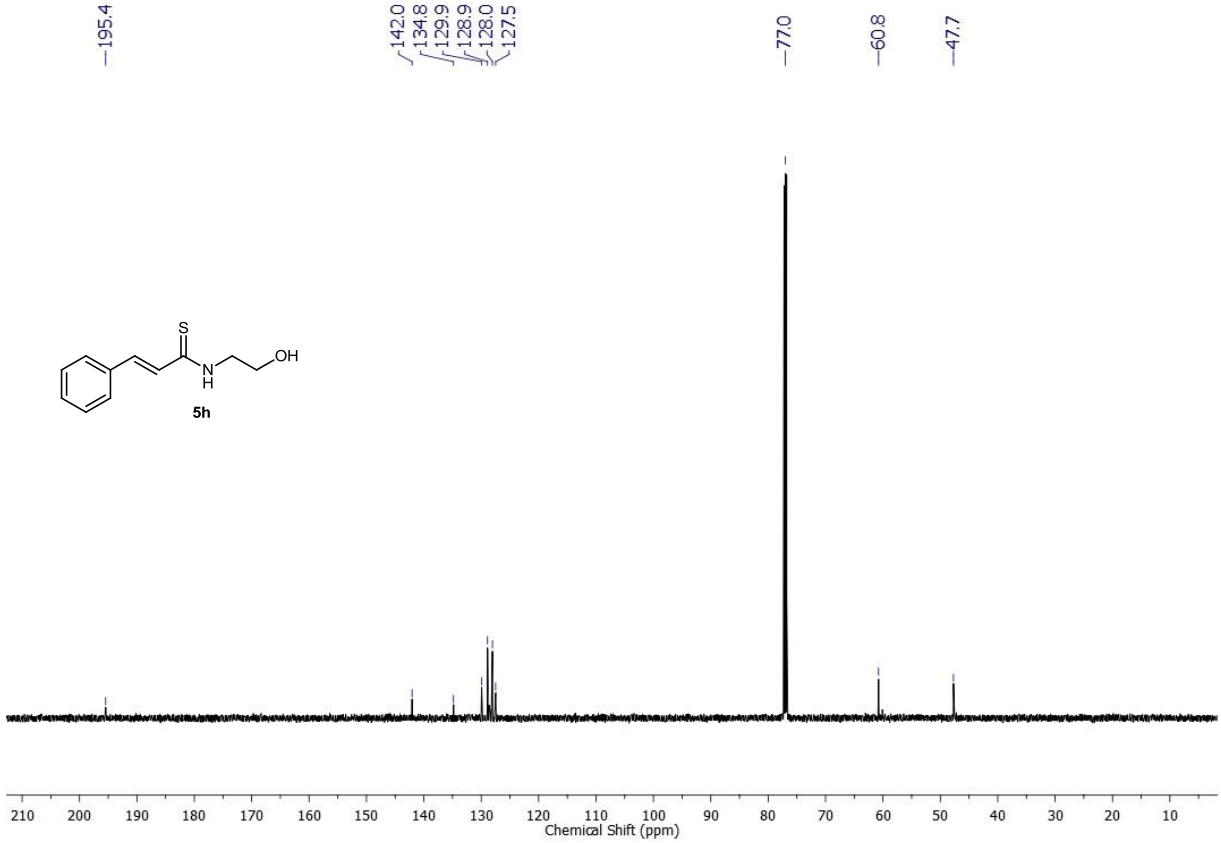
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5g**



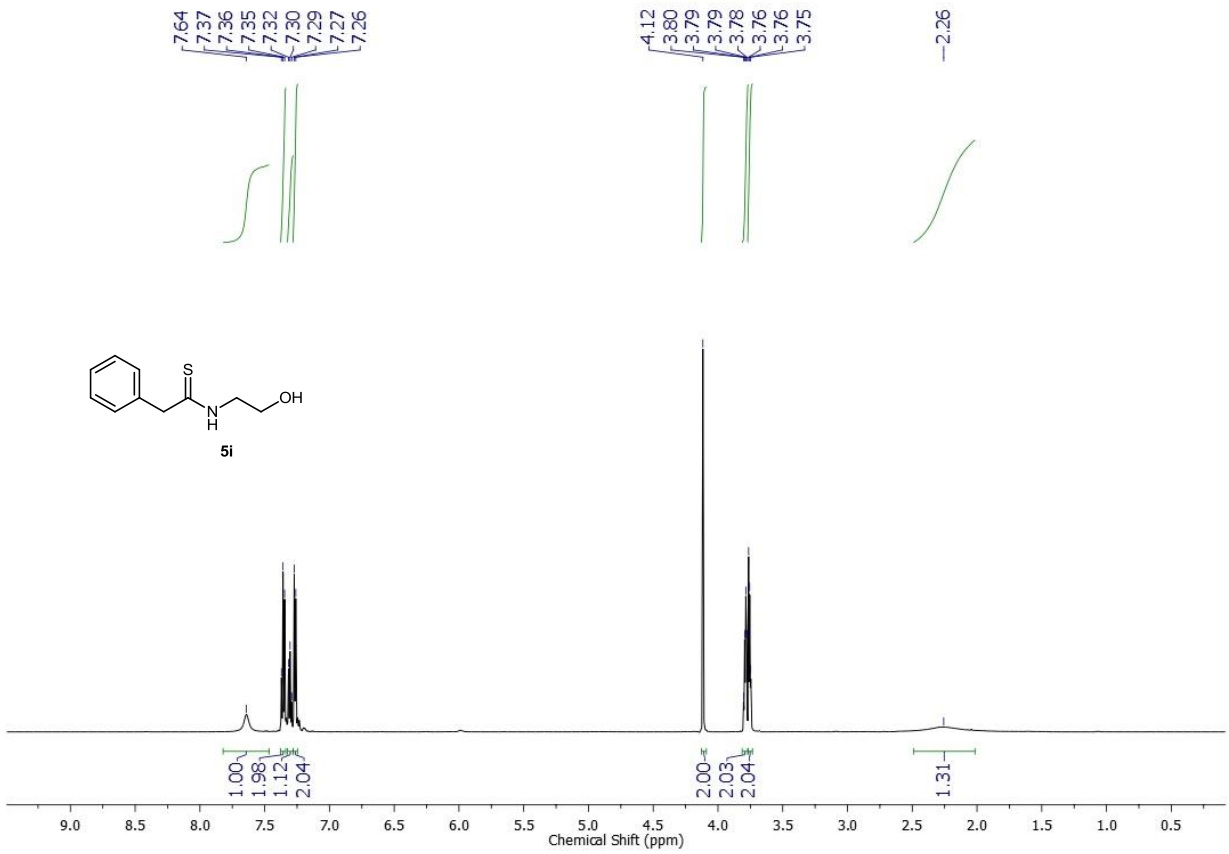
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5h**



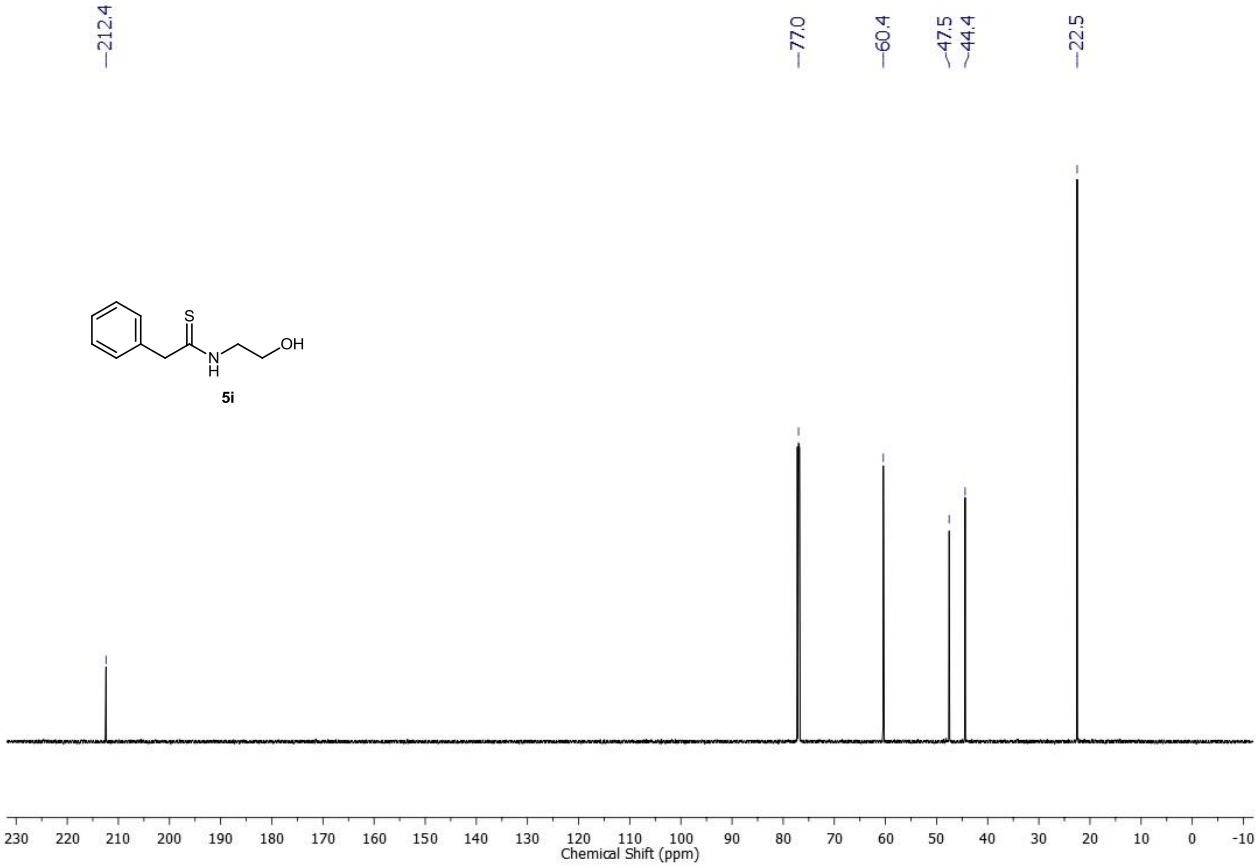
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5h**



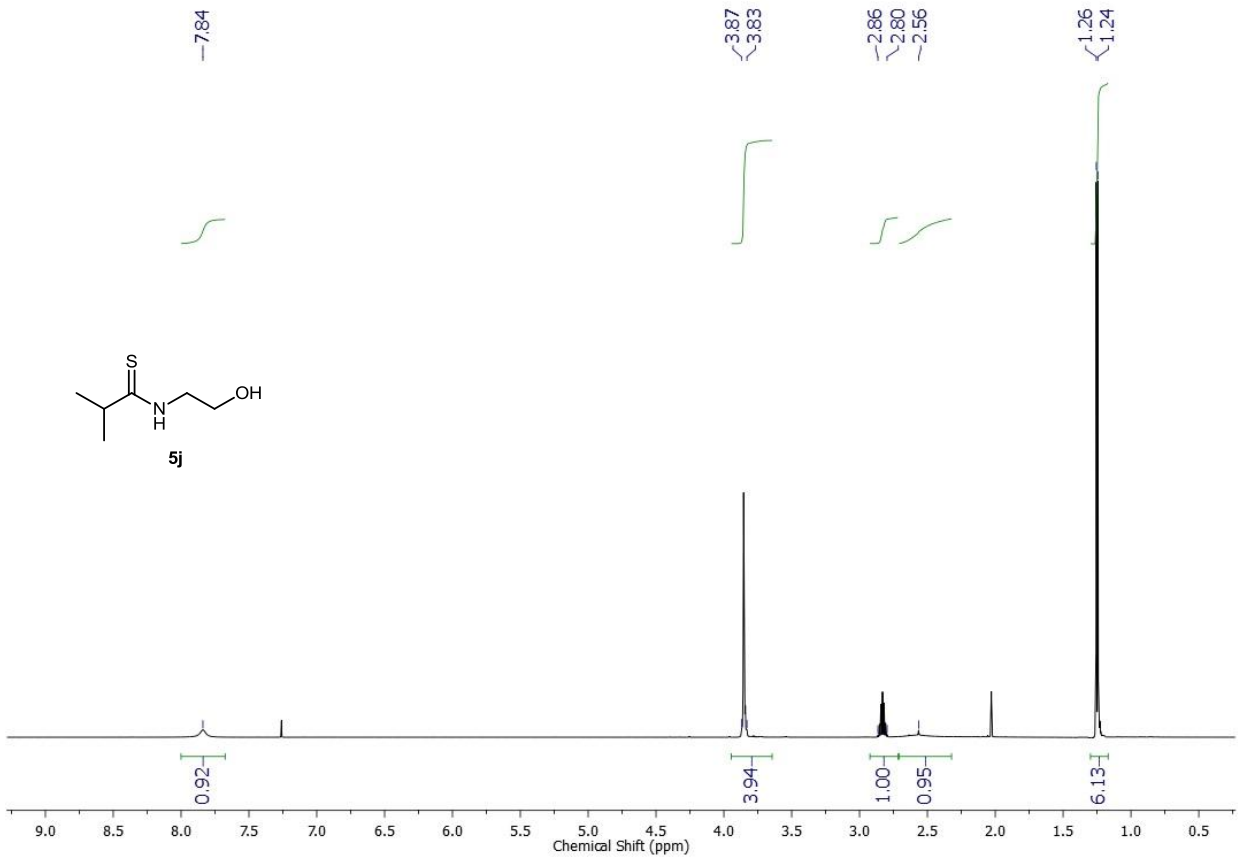
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5i**



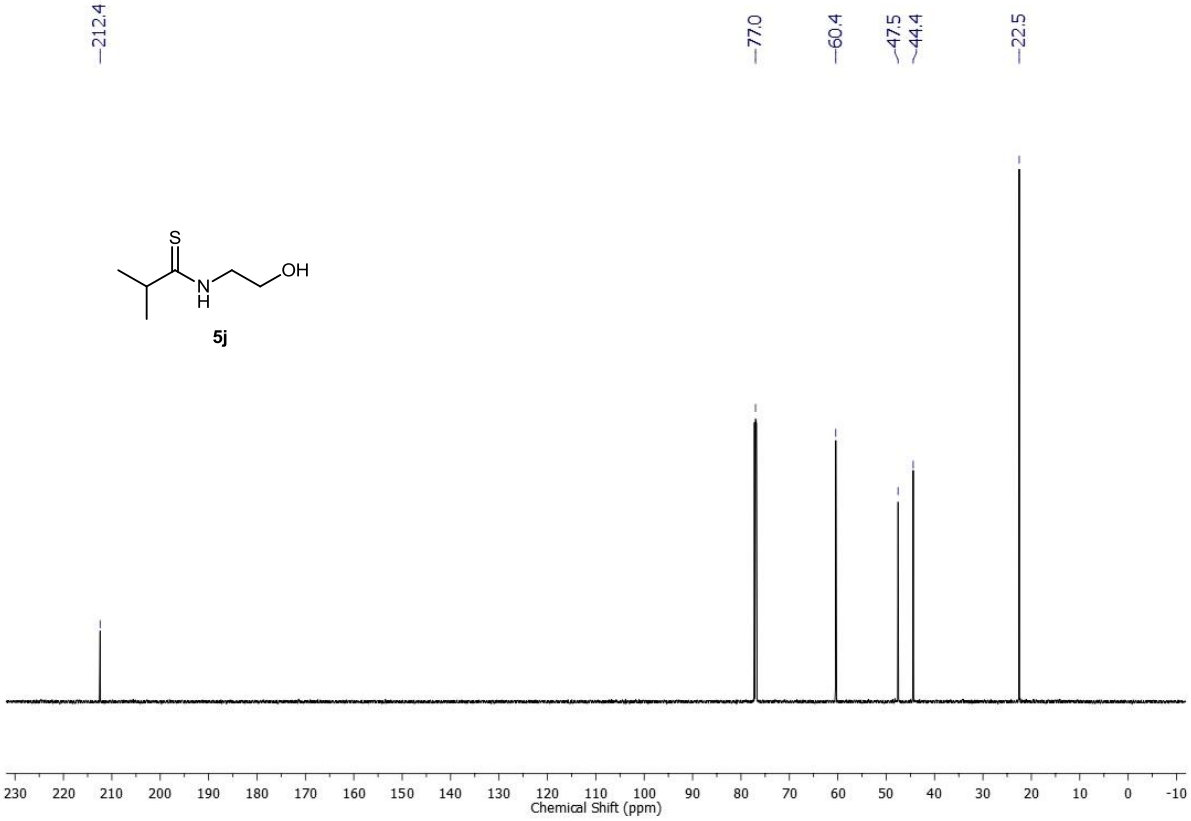
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5i**



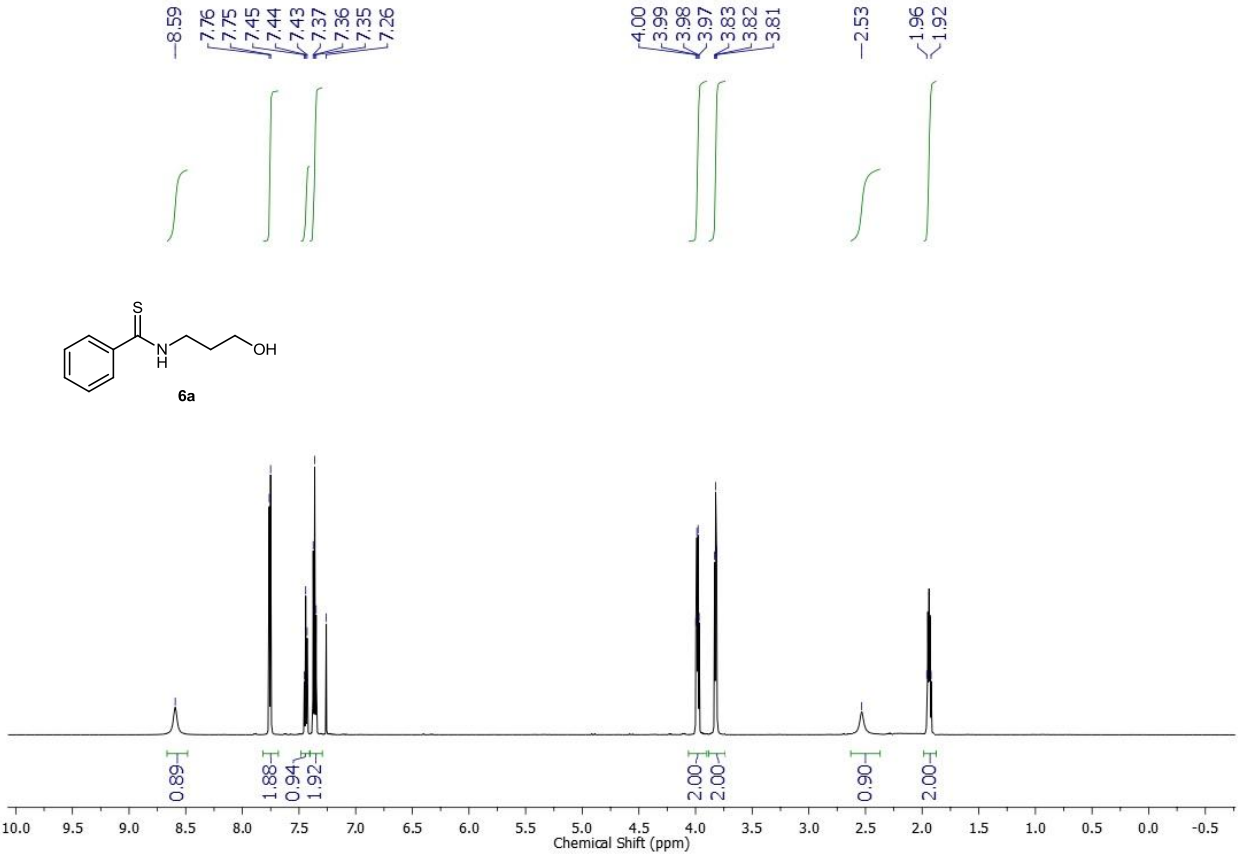
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **5j**



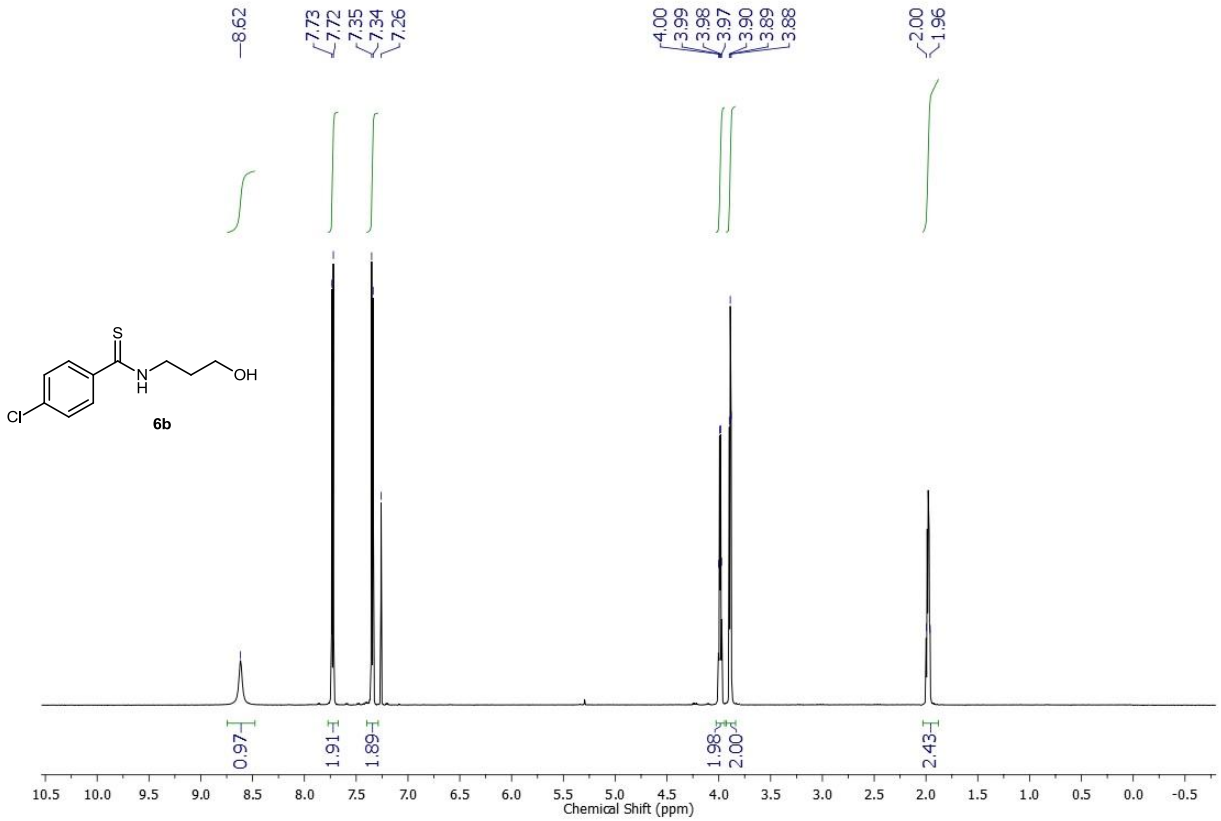
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **5j**



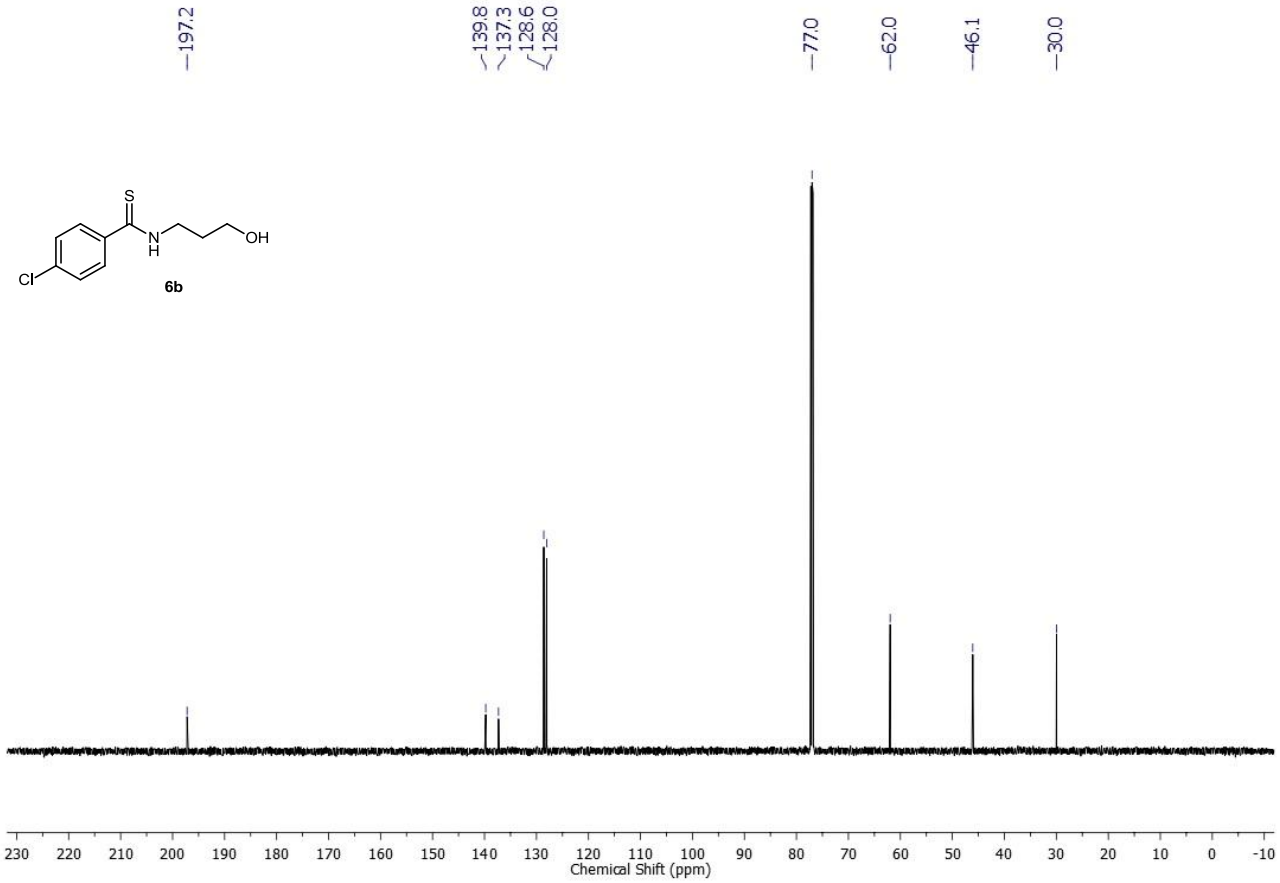
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6a**



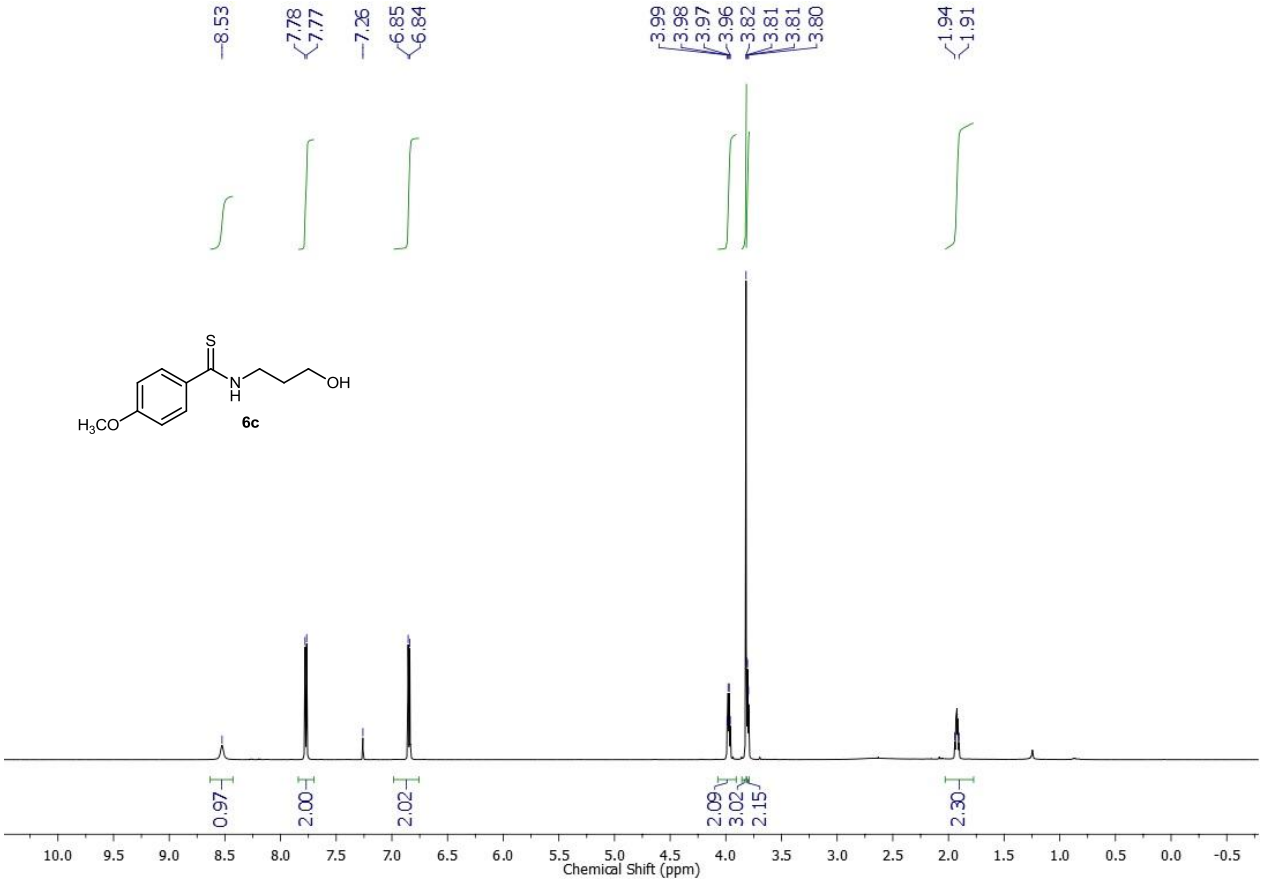
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6b**



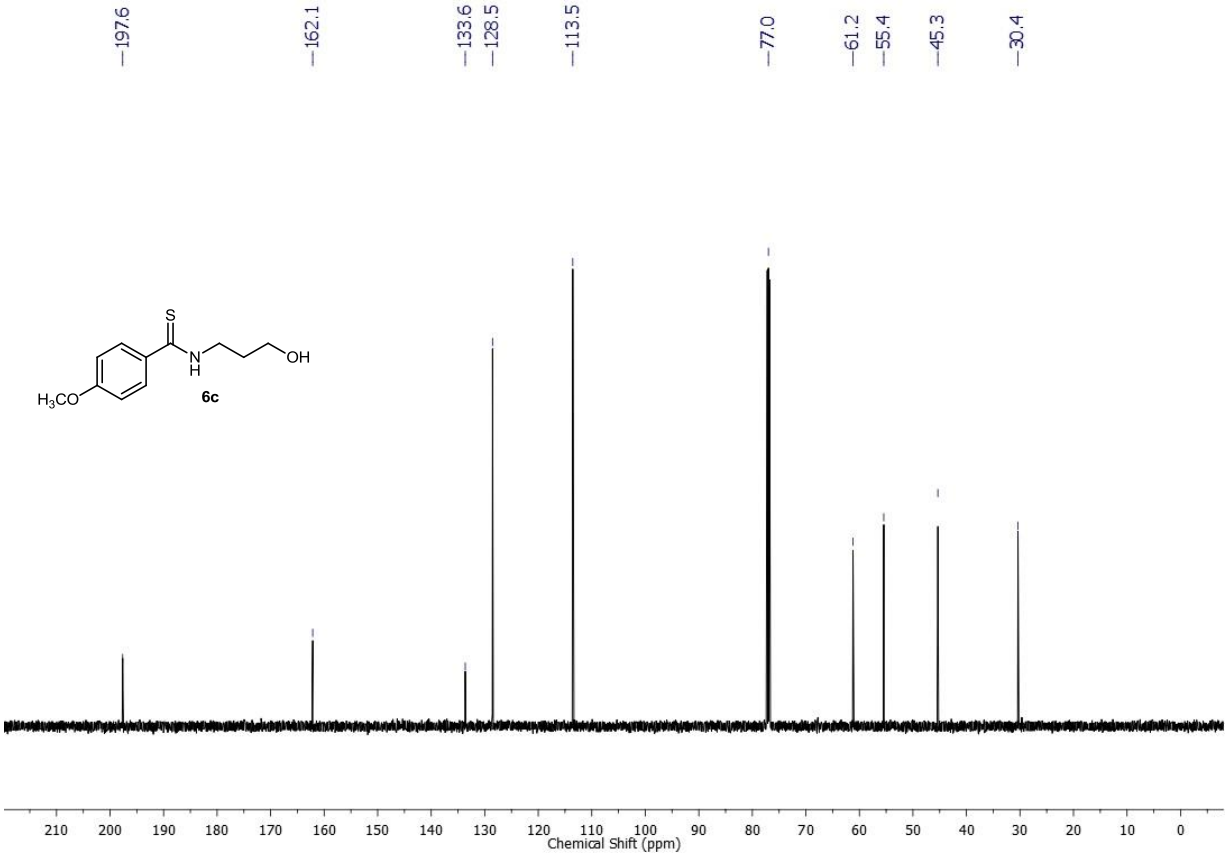
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6b**



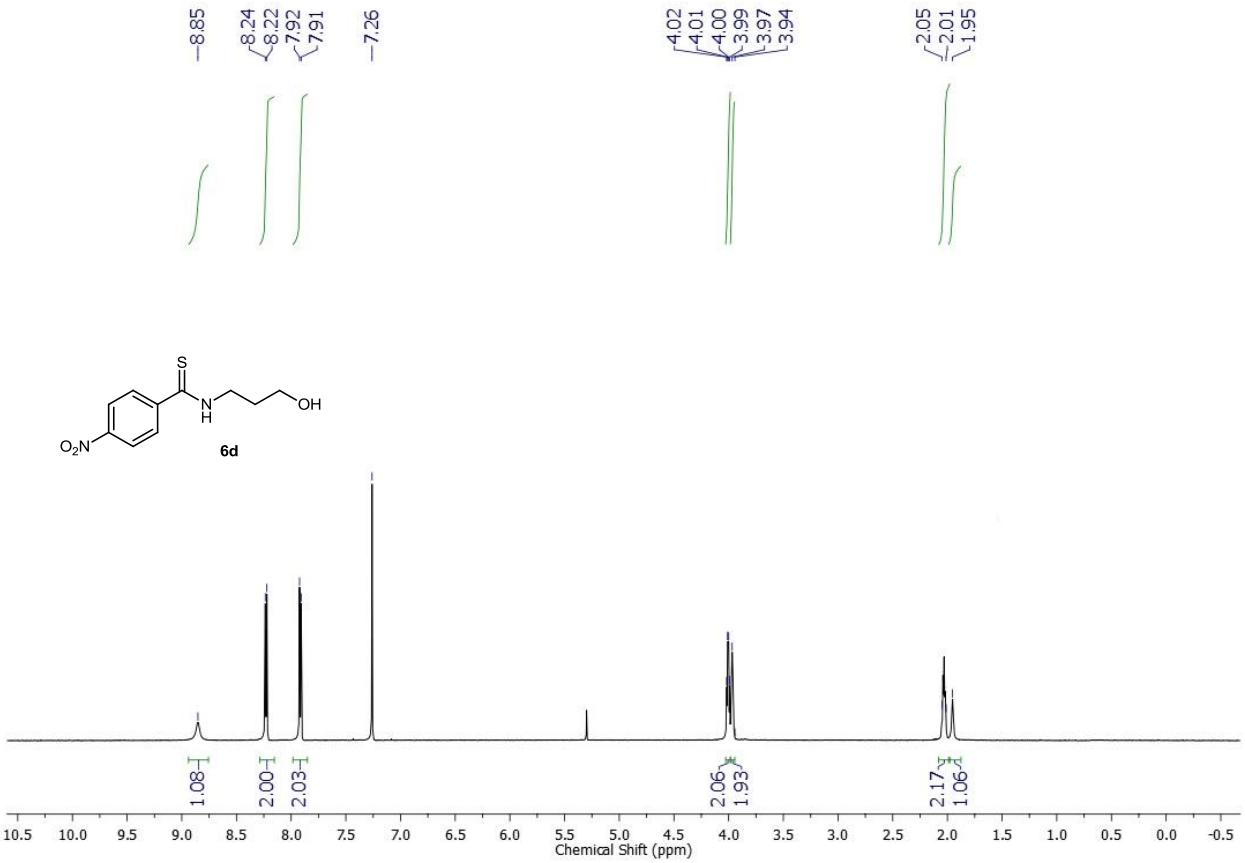
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6c**



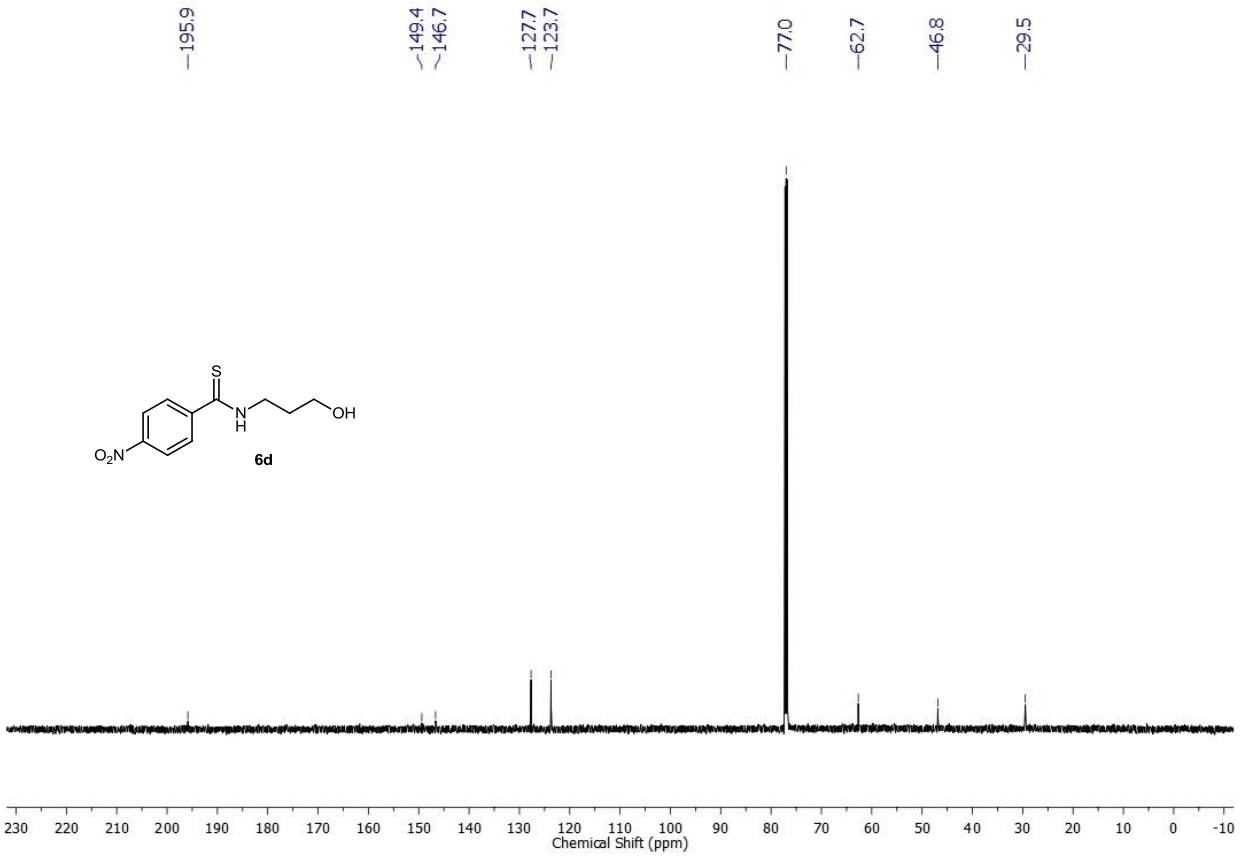
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6c**



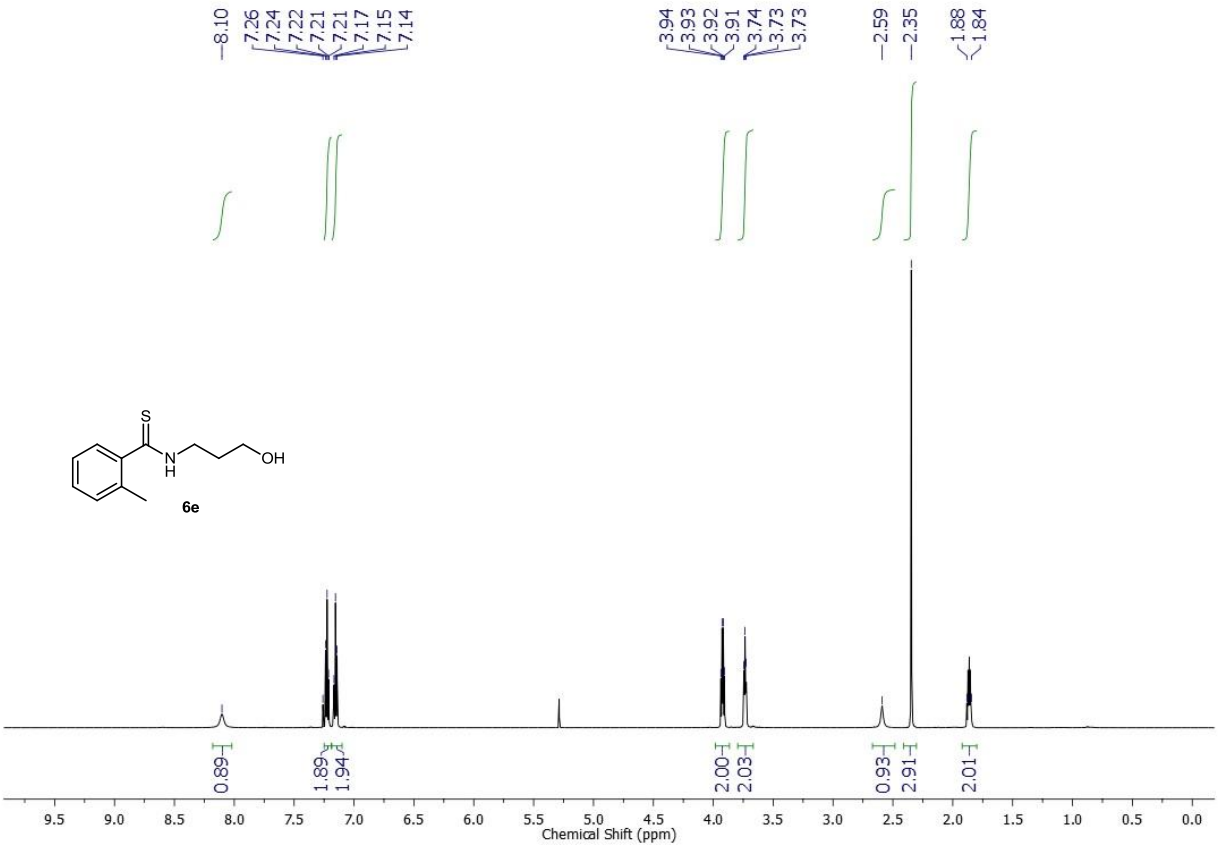
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6d**



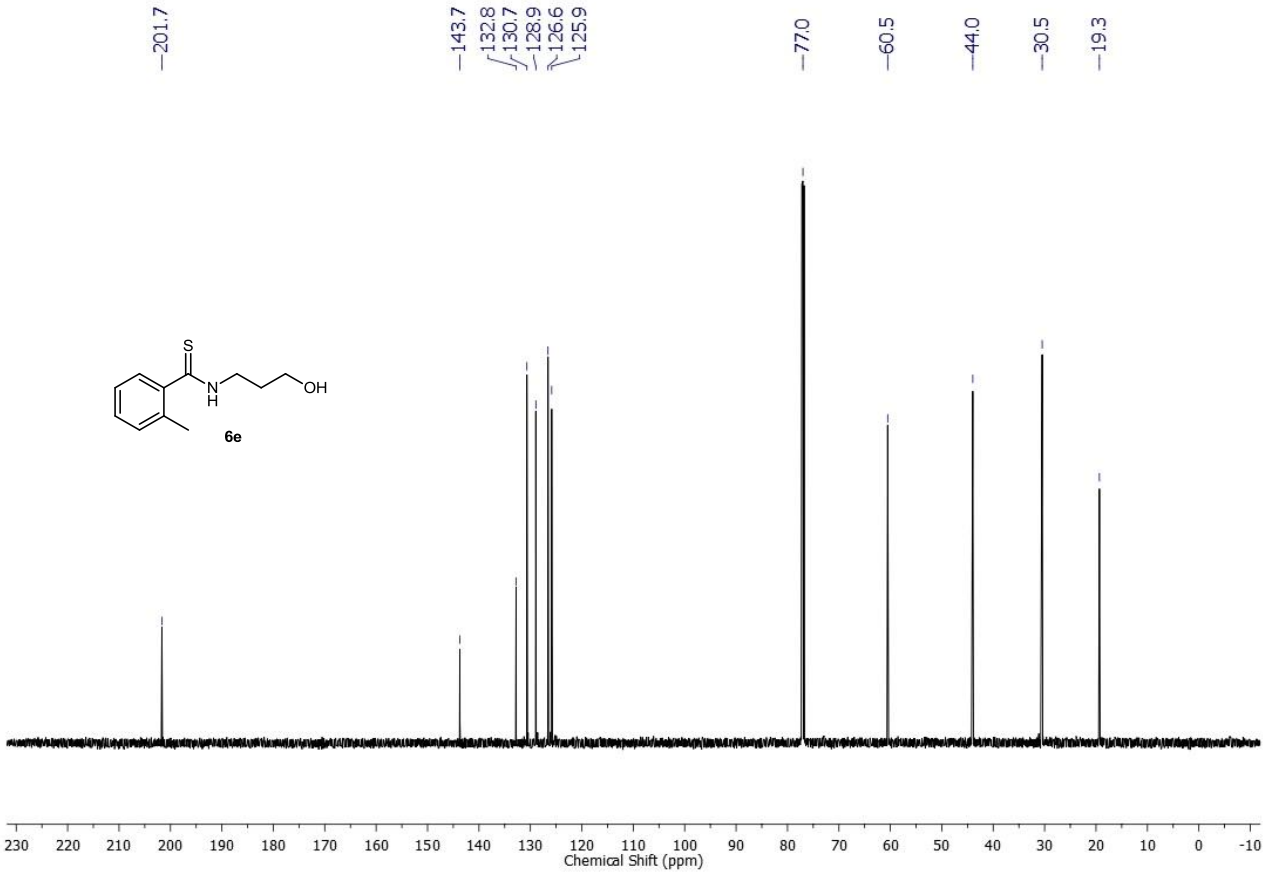
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6d**



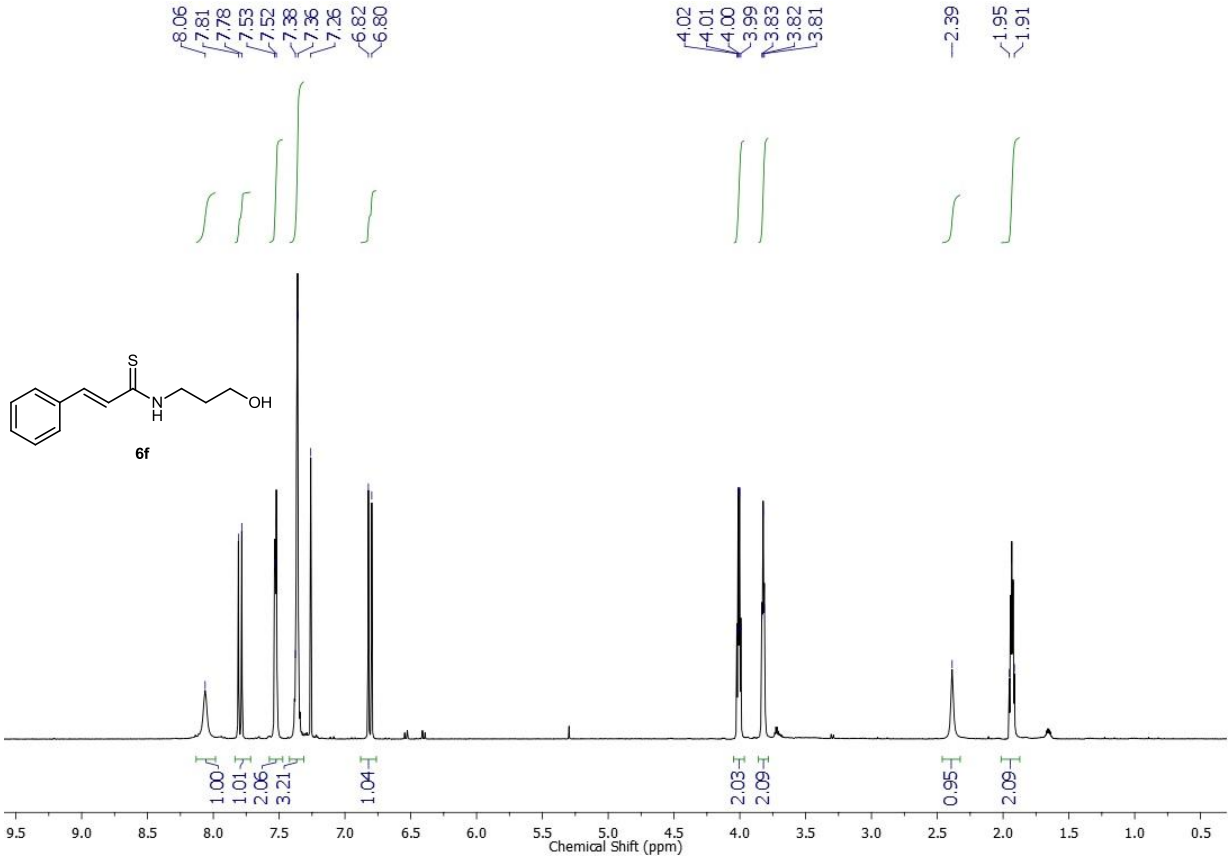
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6e**



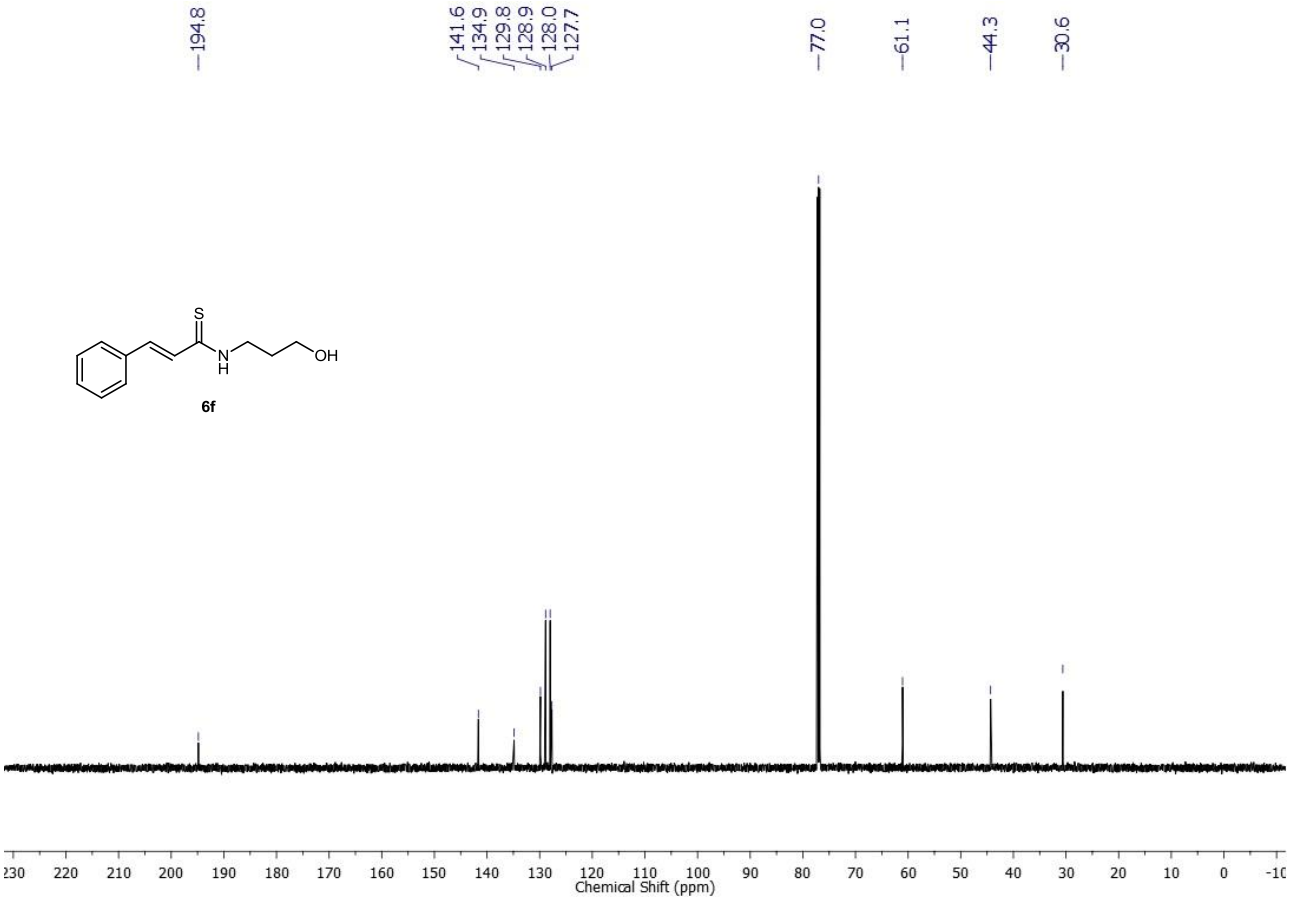
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6e**



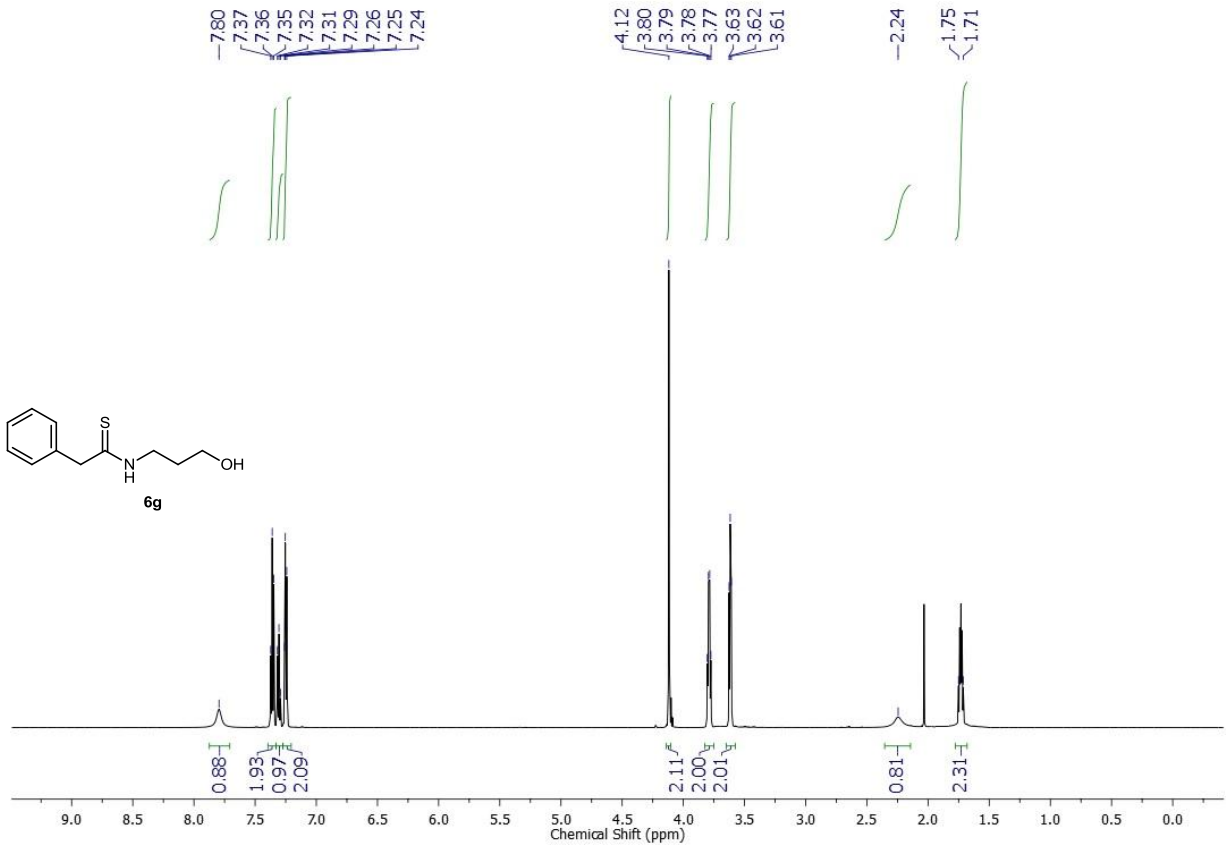
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6f**



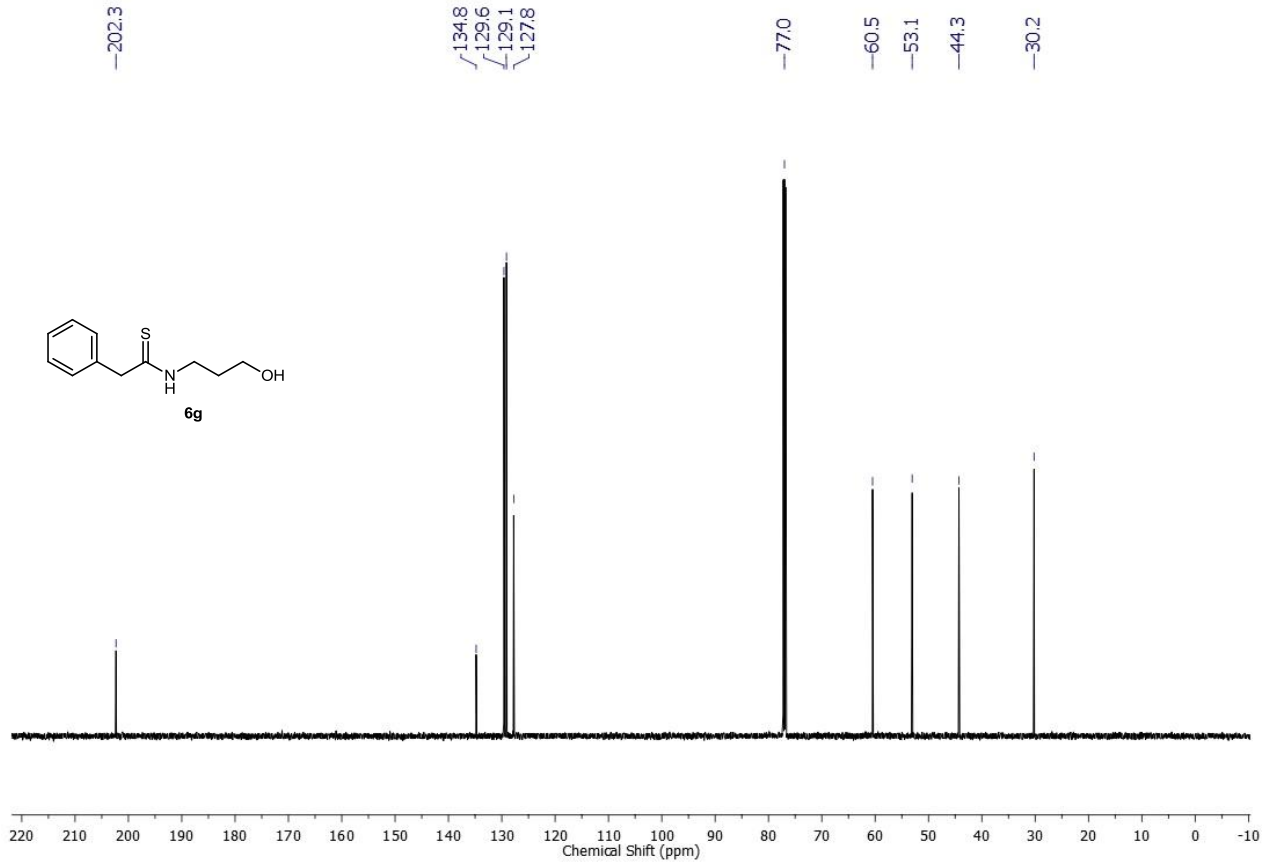
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6f**



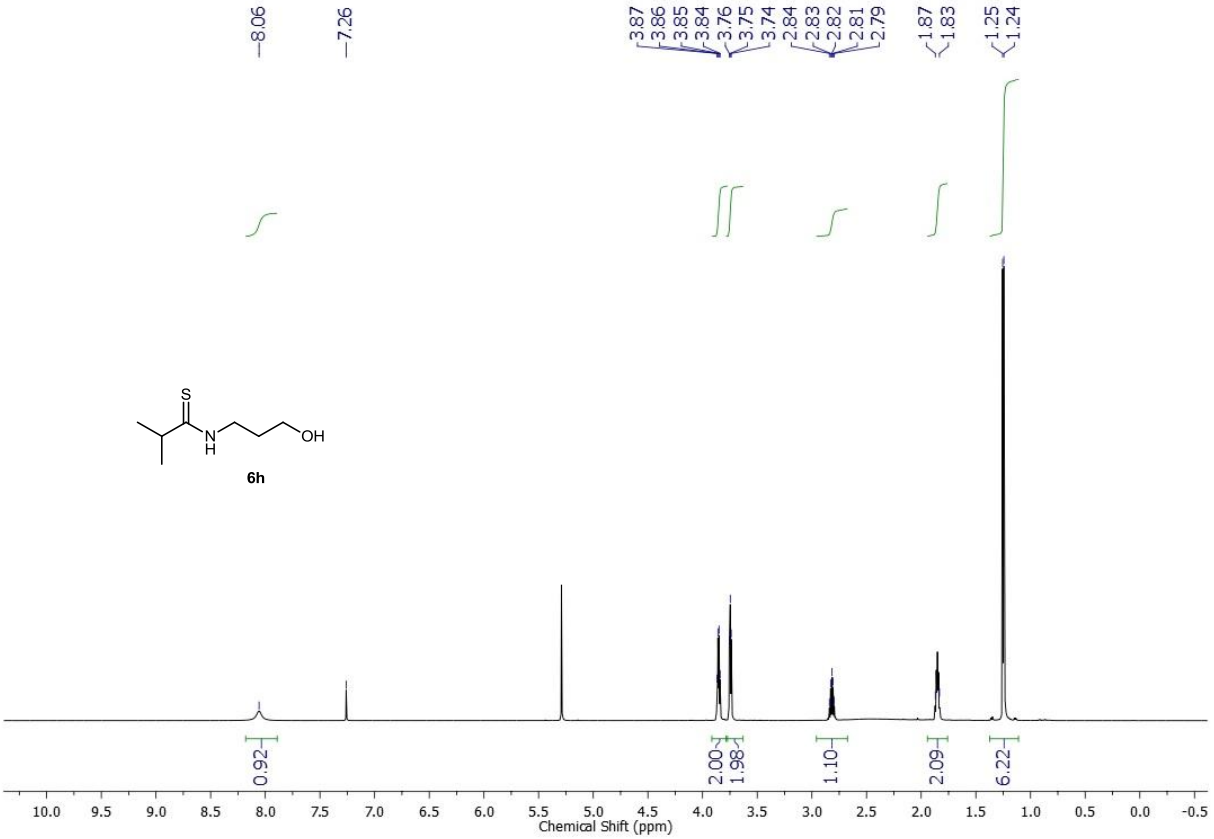
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6g**



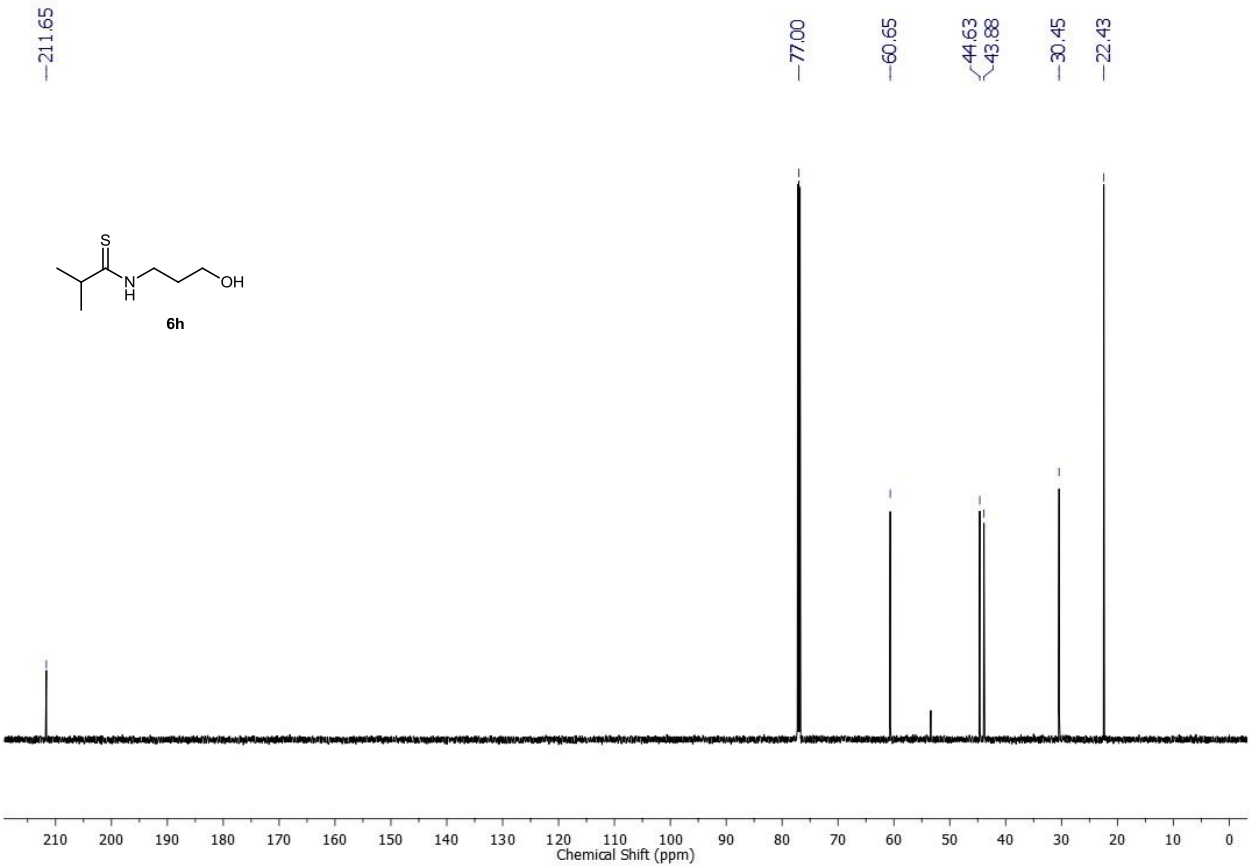
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6g**



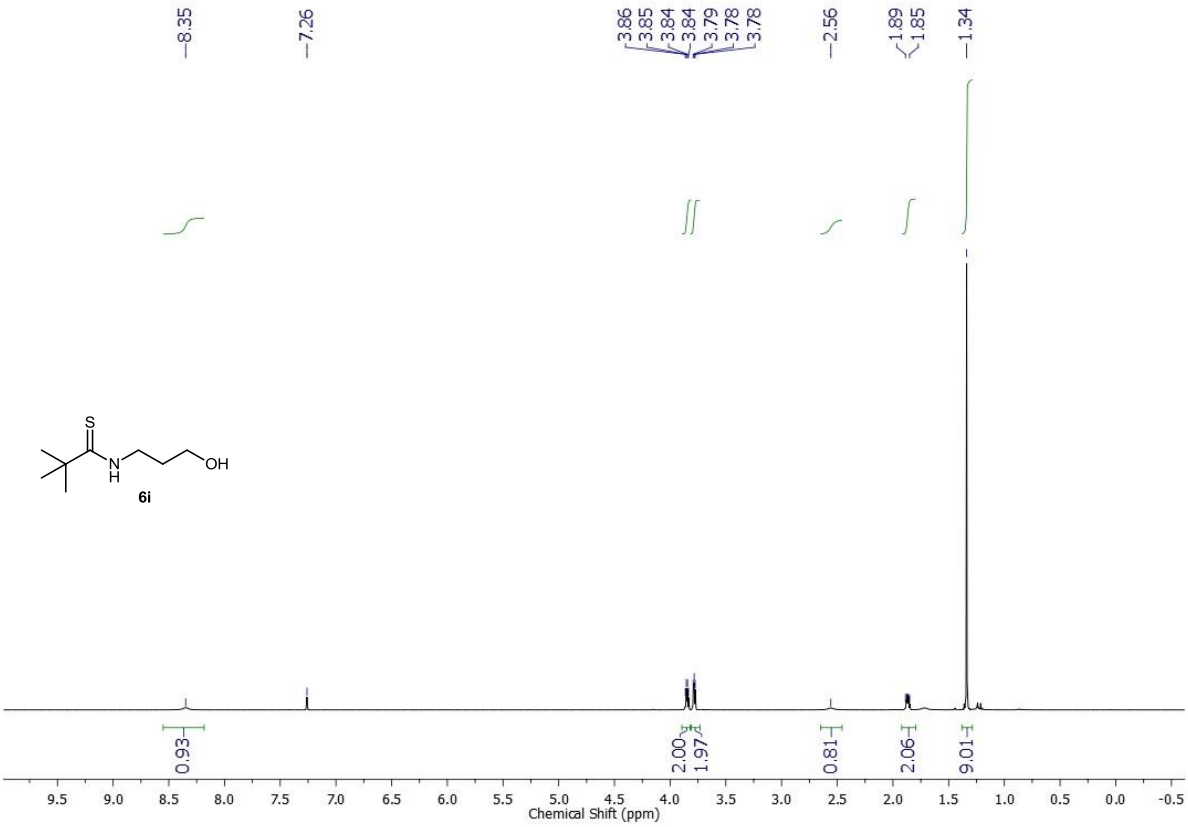
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6h**



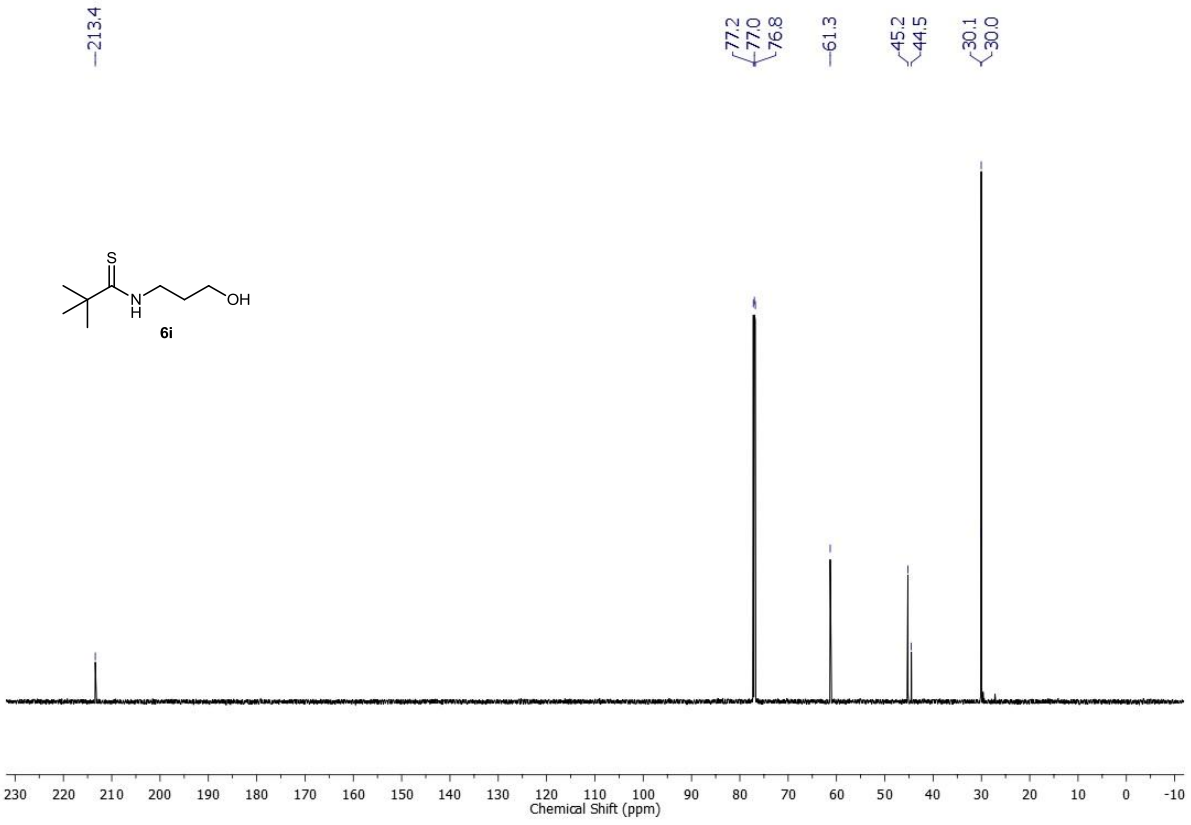
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6h**



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **6i**

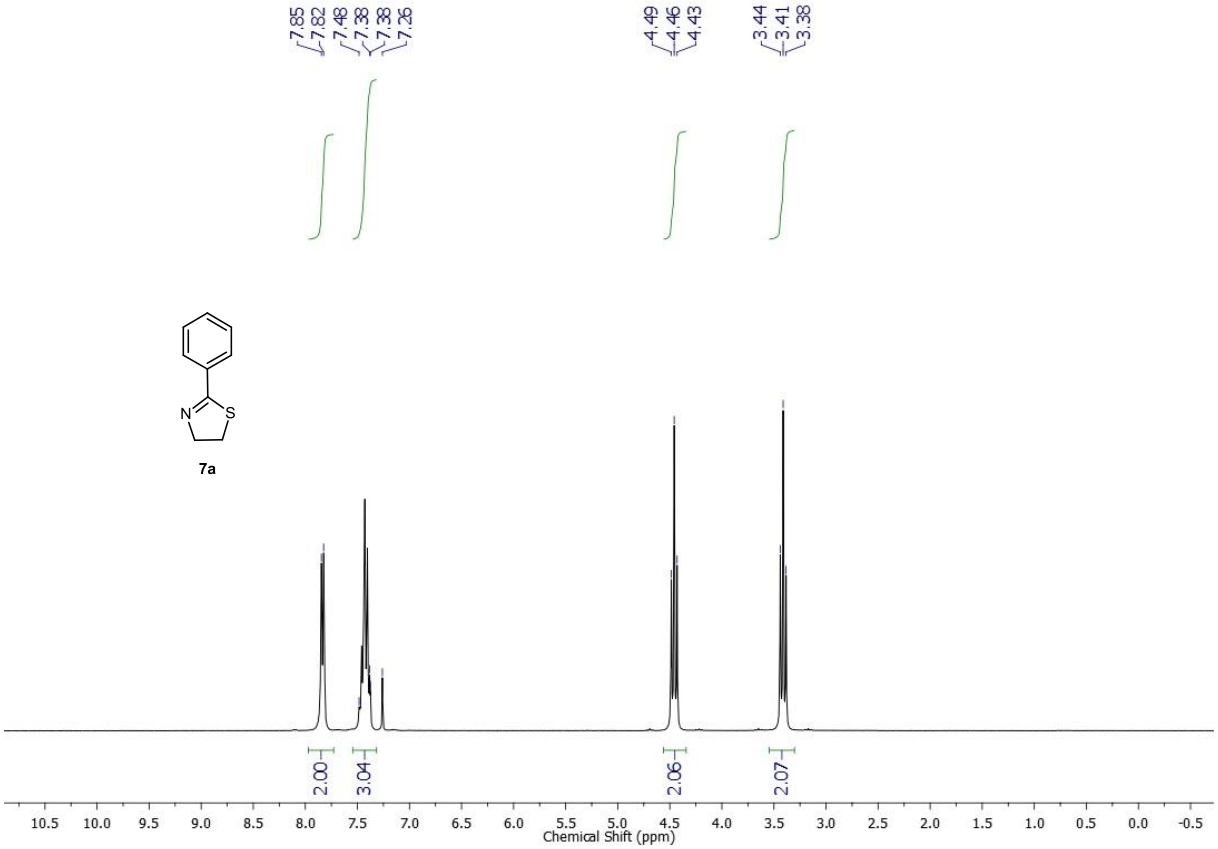


^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **6i**

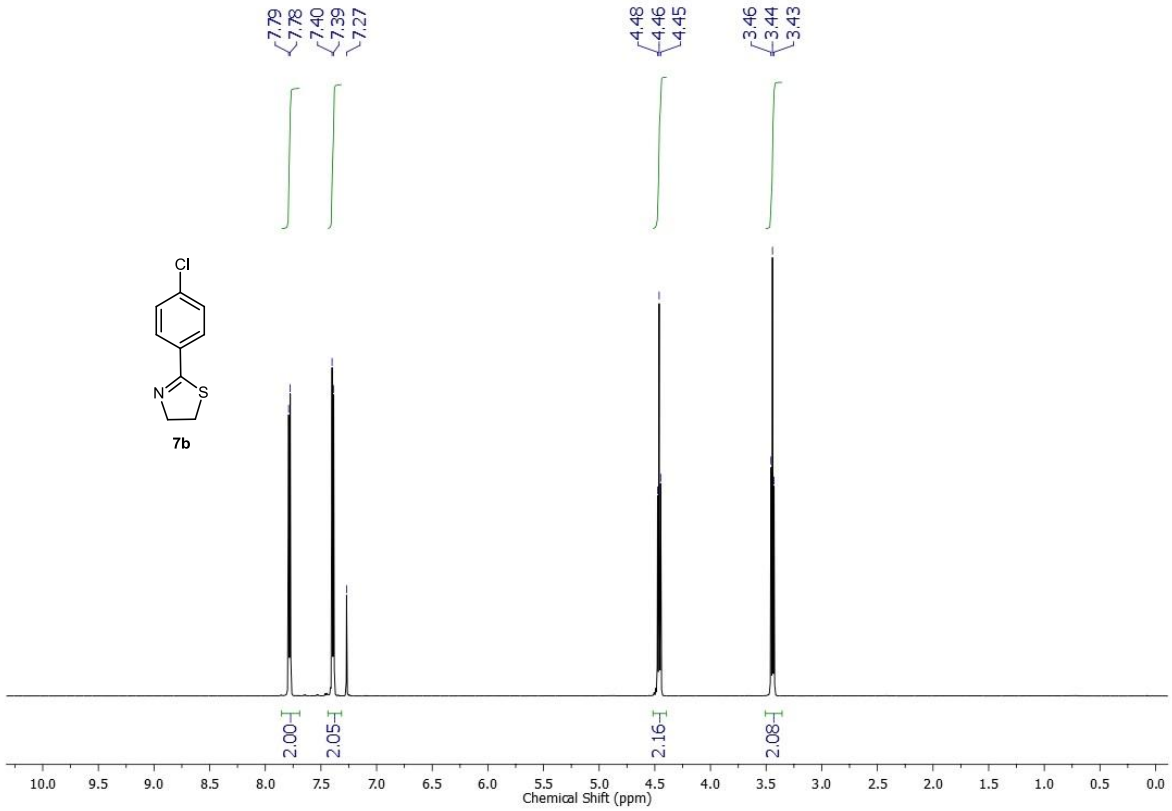


7. Copies of ^{1}H and ^{13}C NMR spectra of compounds 7-8

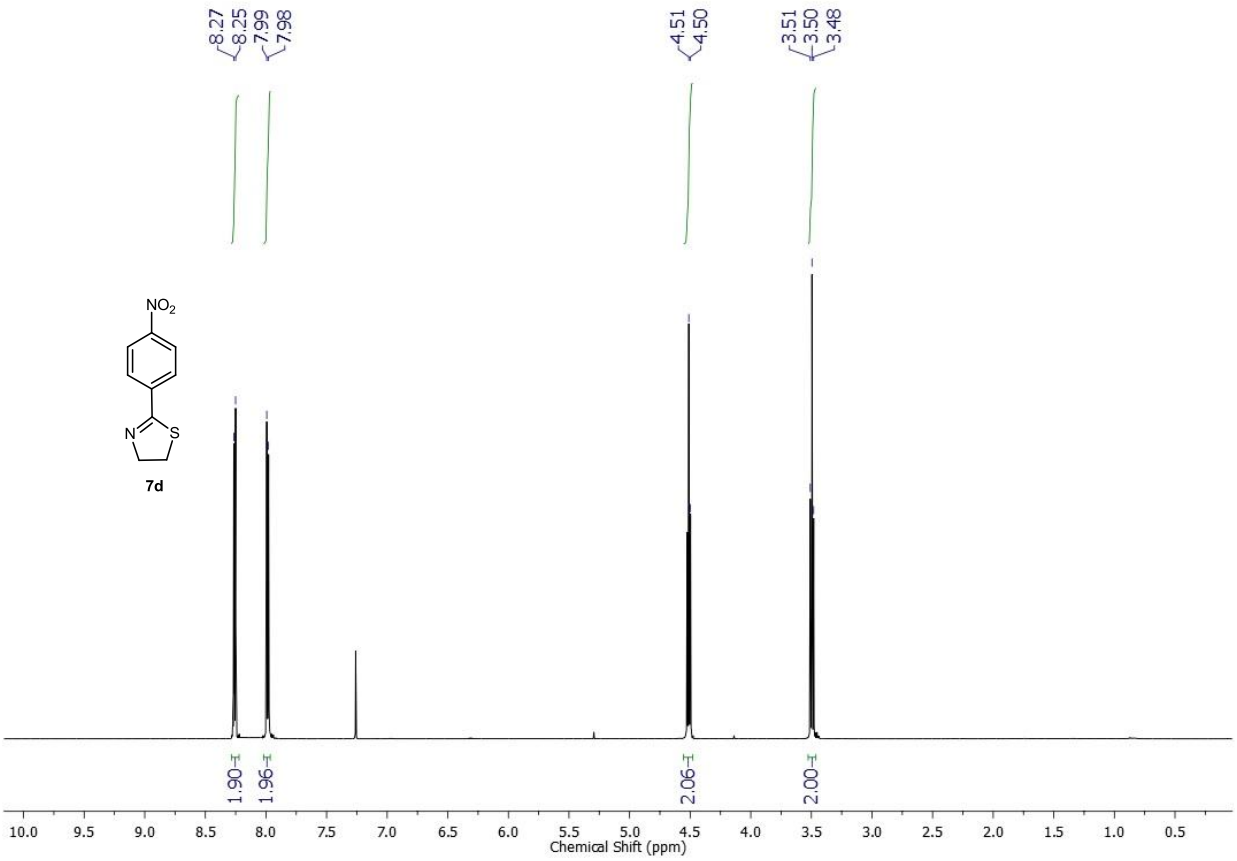
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7a**



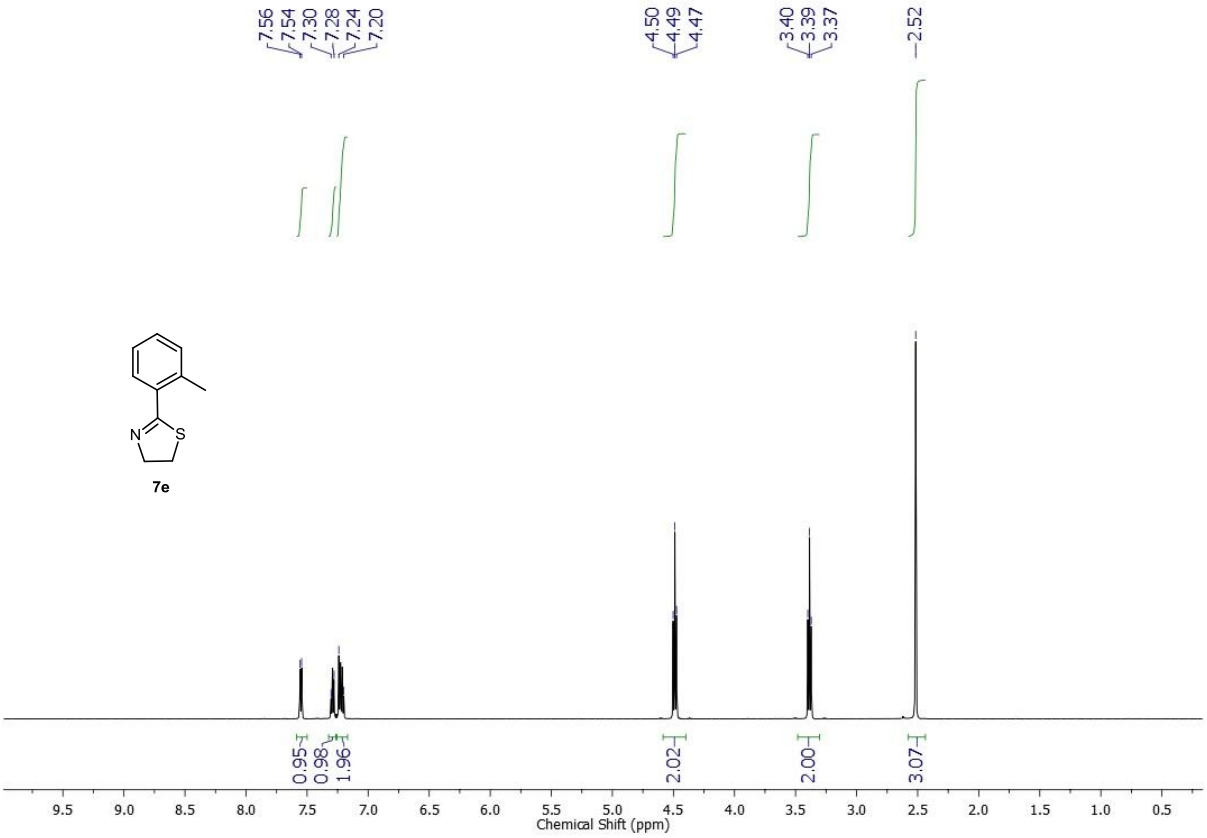
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7b**



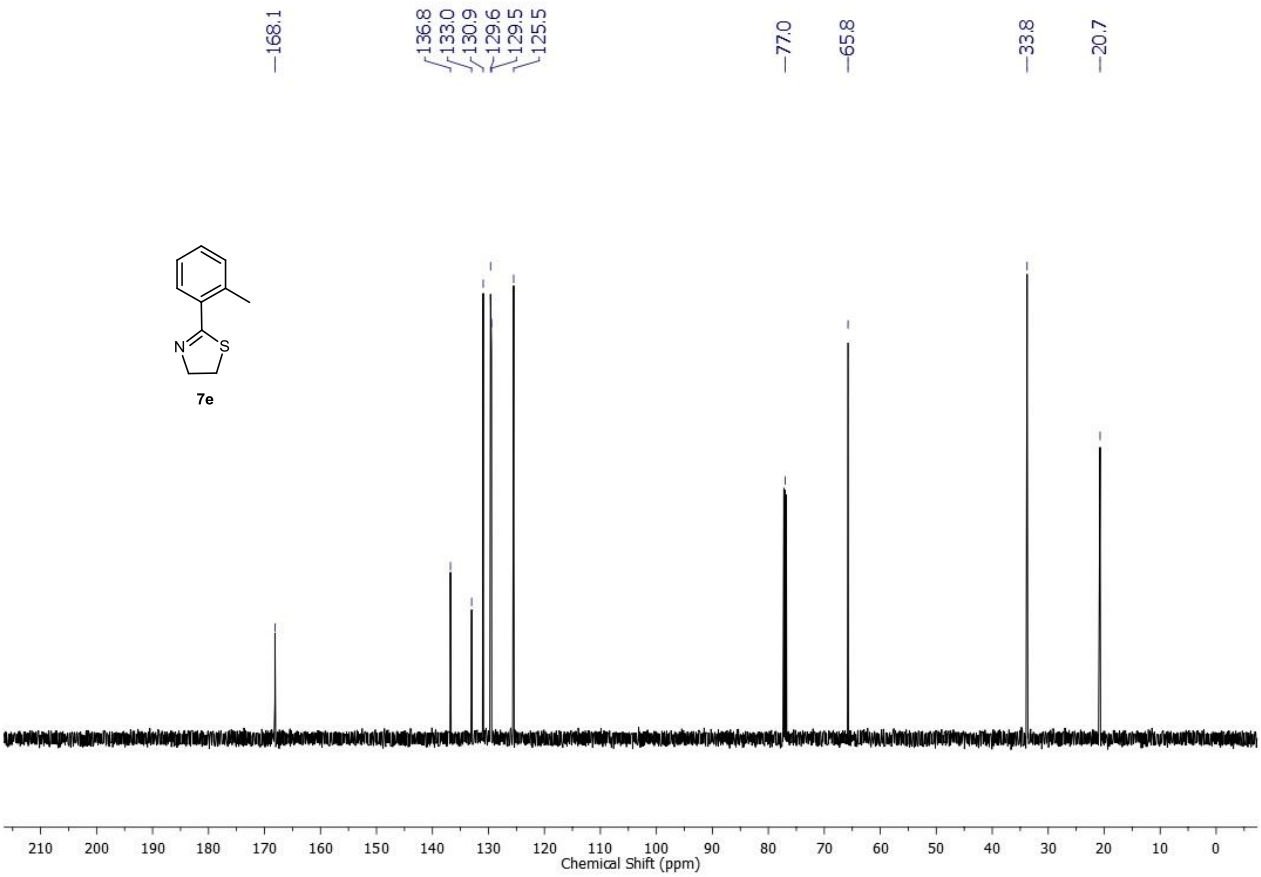
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7d**



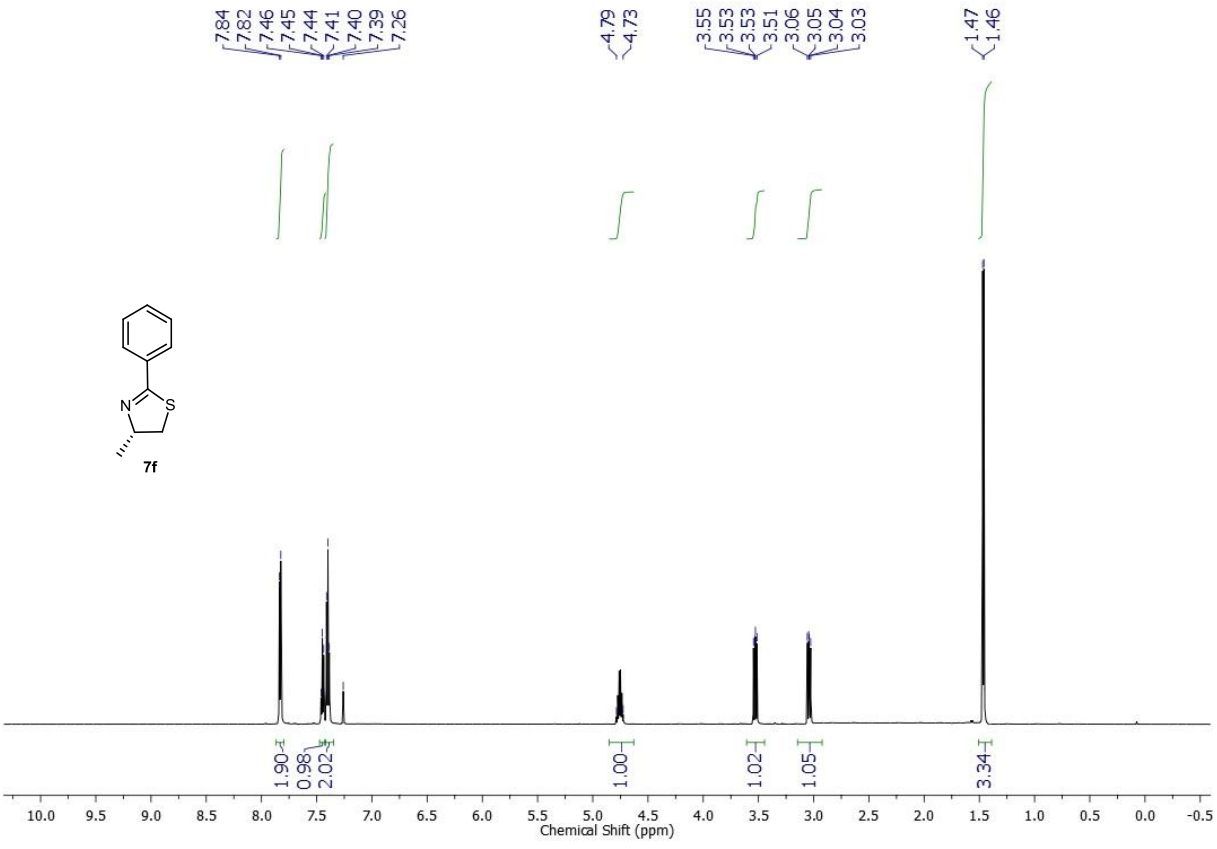
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7e**



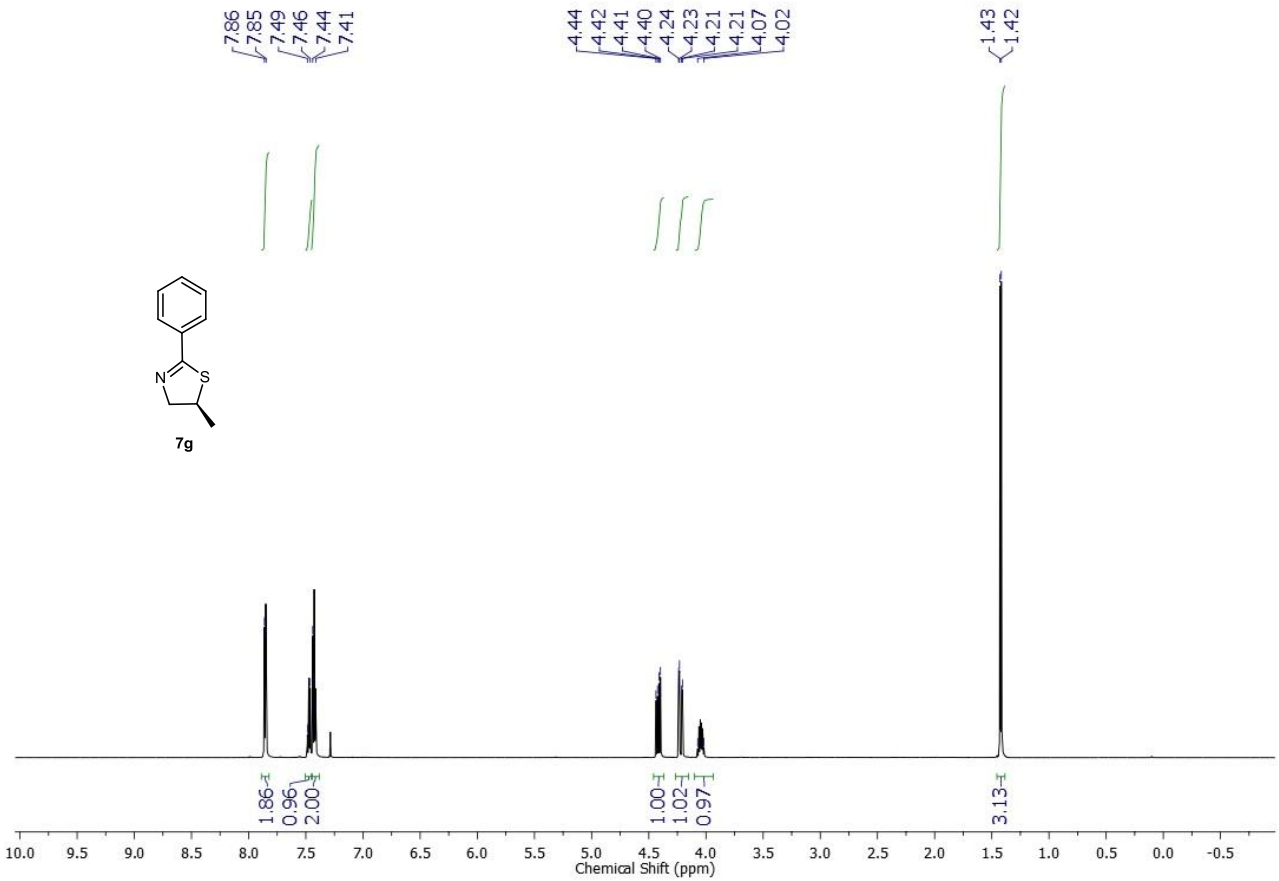
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **7e**



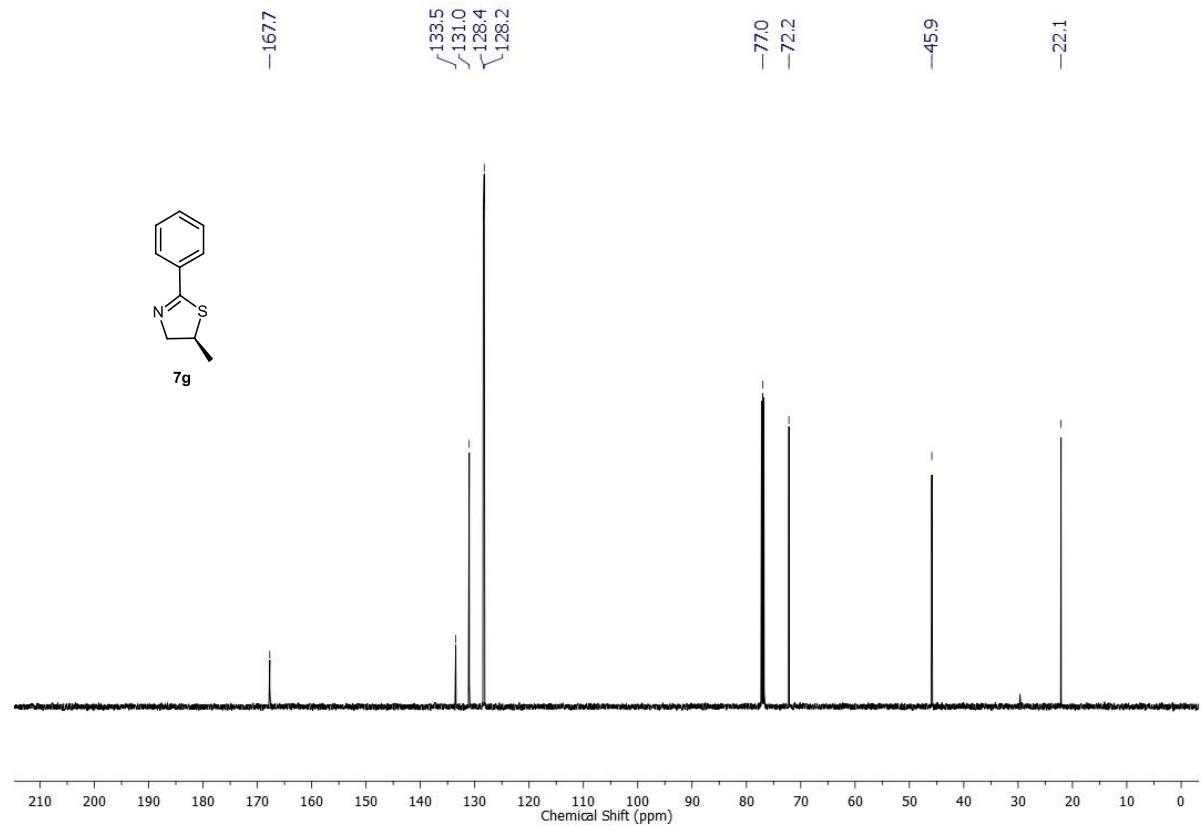
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7f**



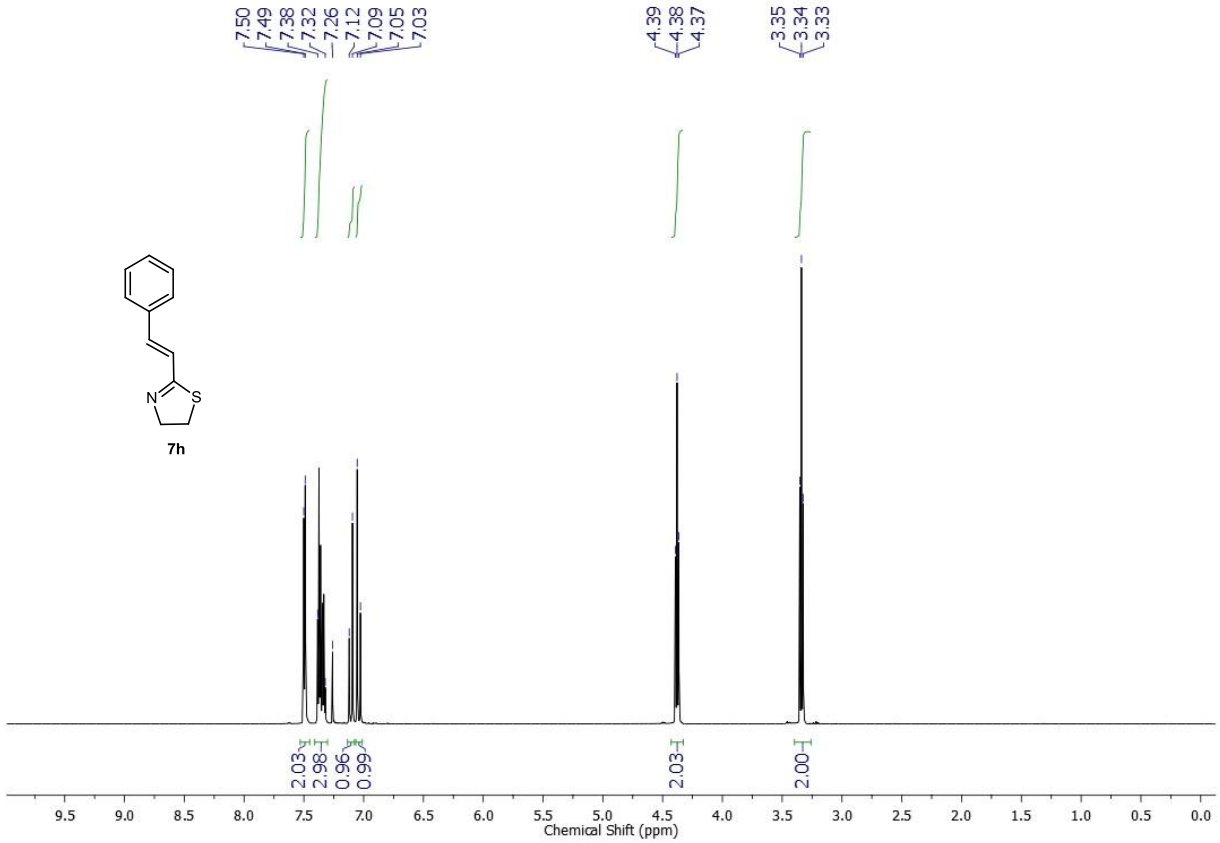
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7g**



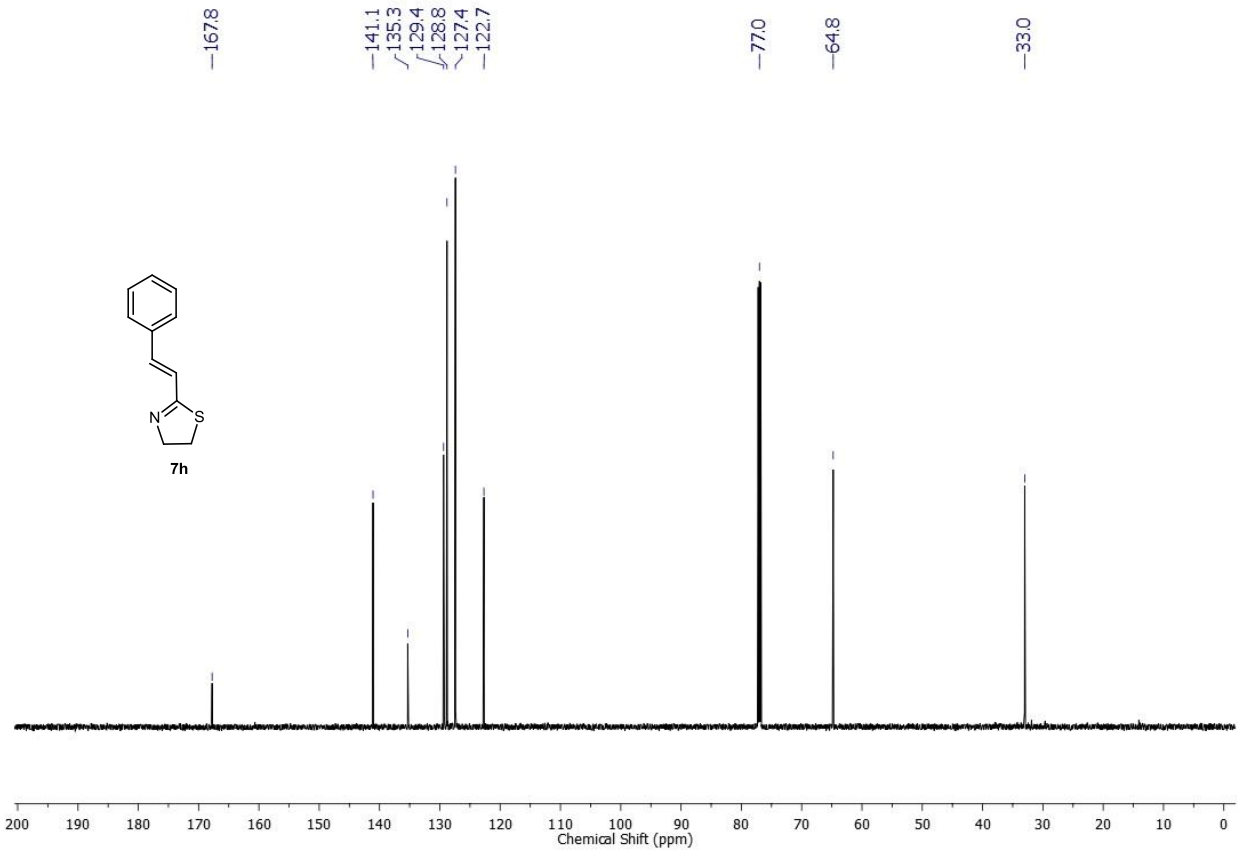
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **7g**



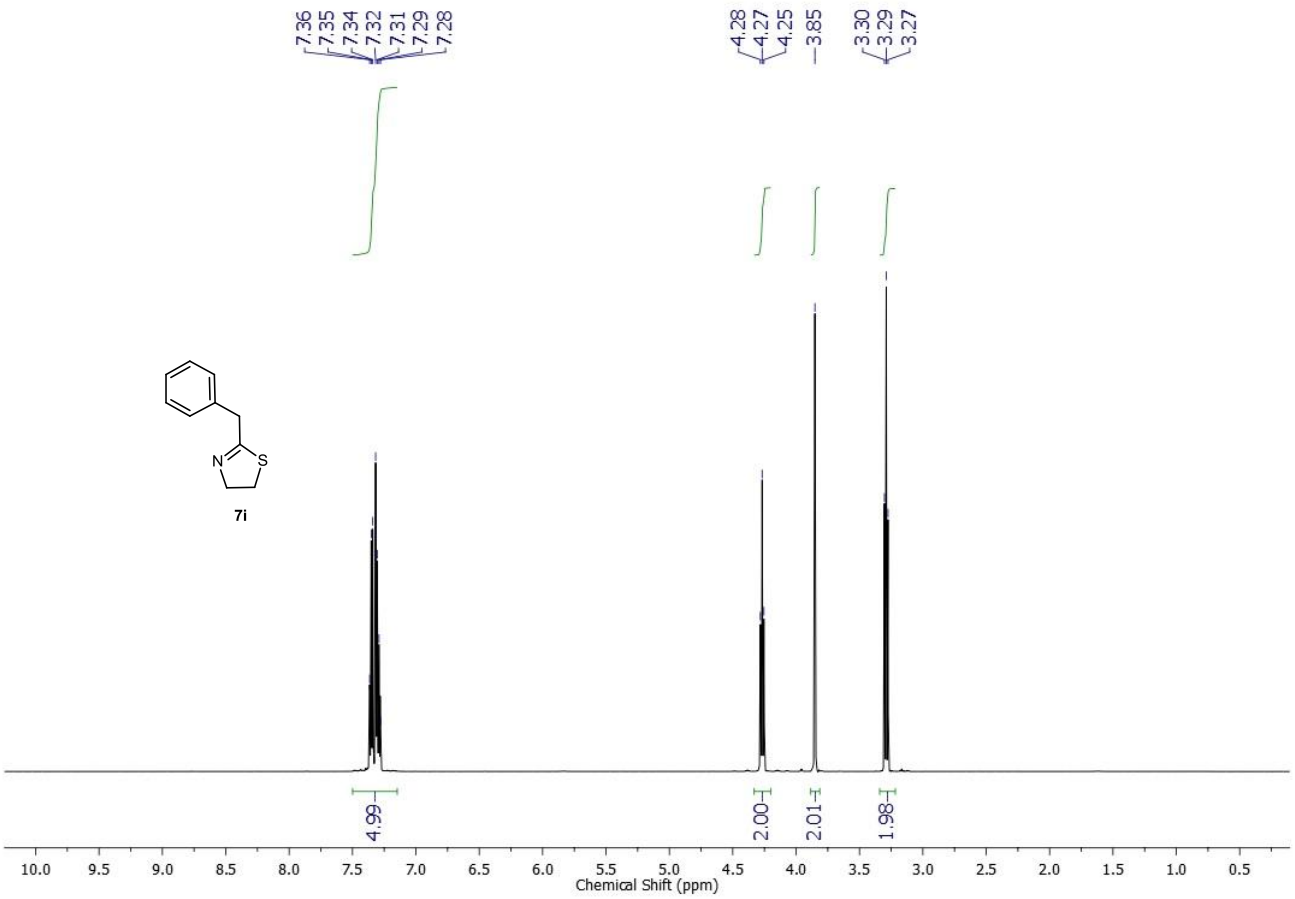
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7h**



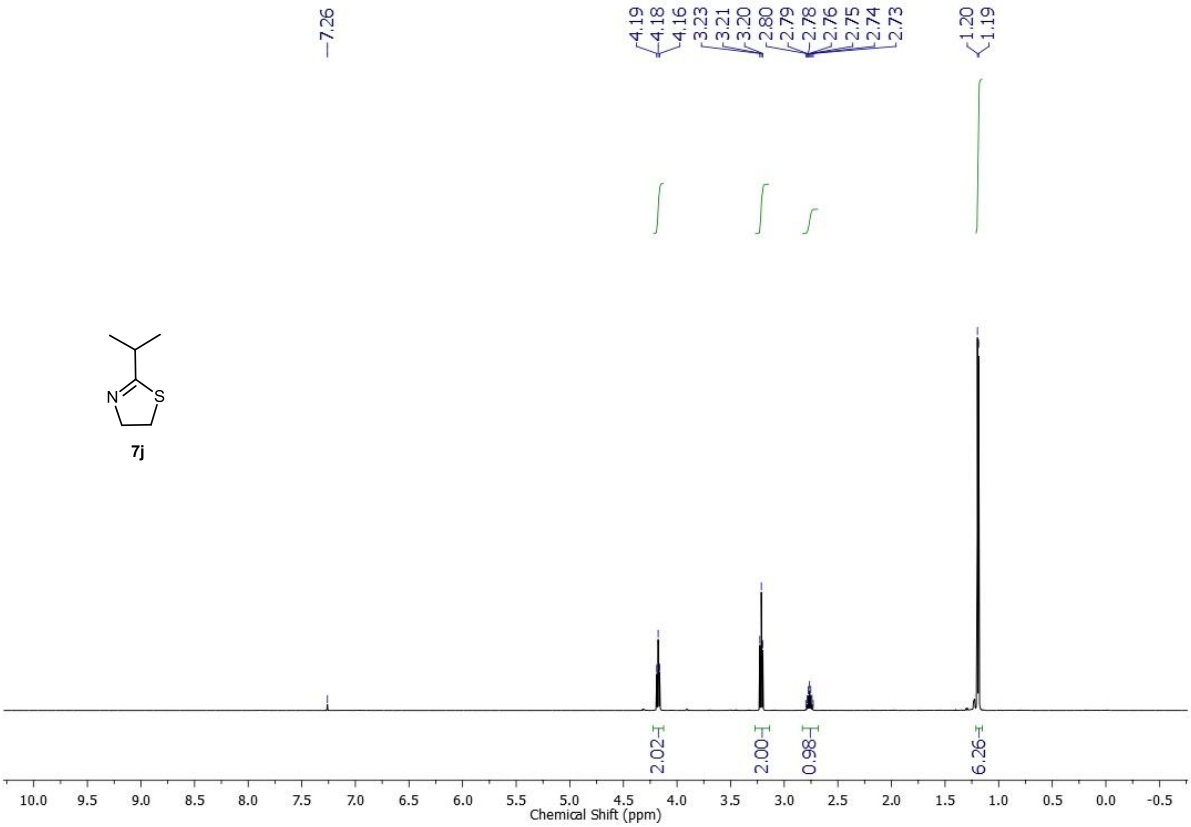
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **7h**



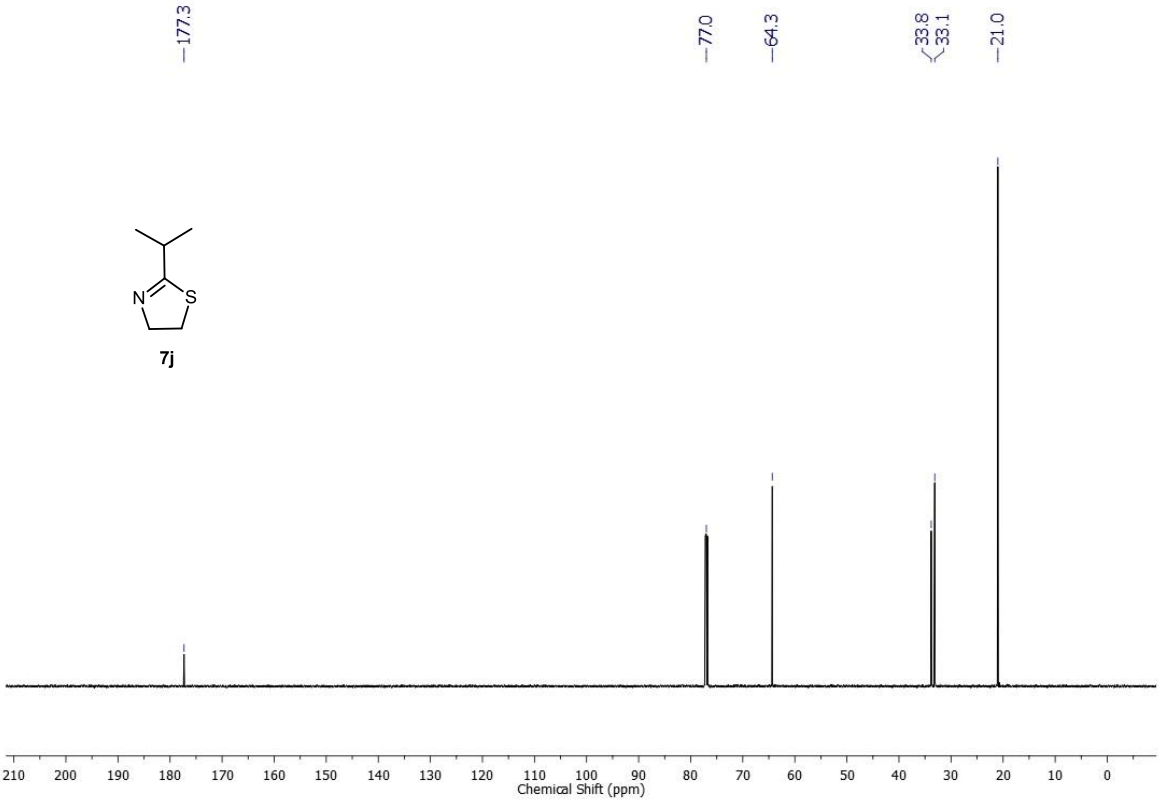
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7i**



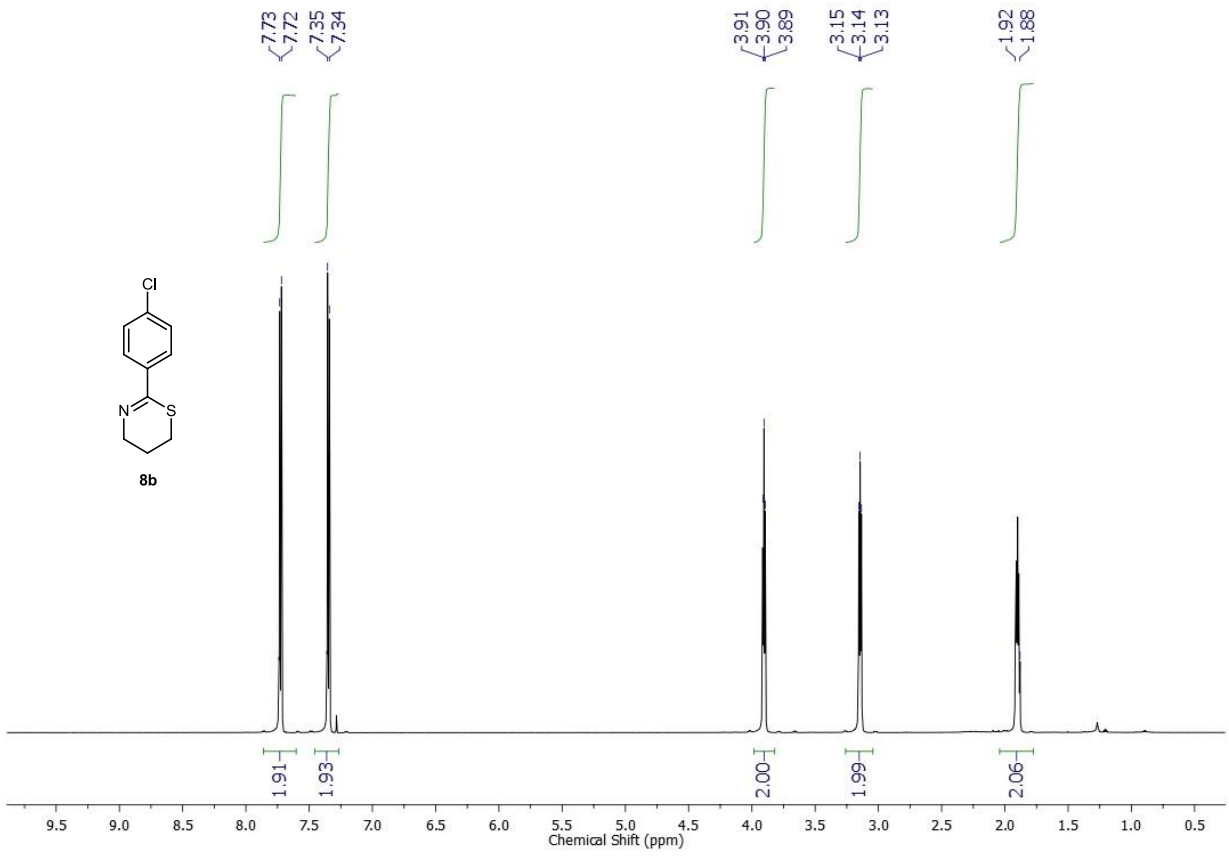
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **7j**



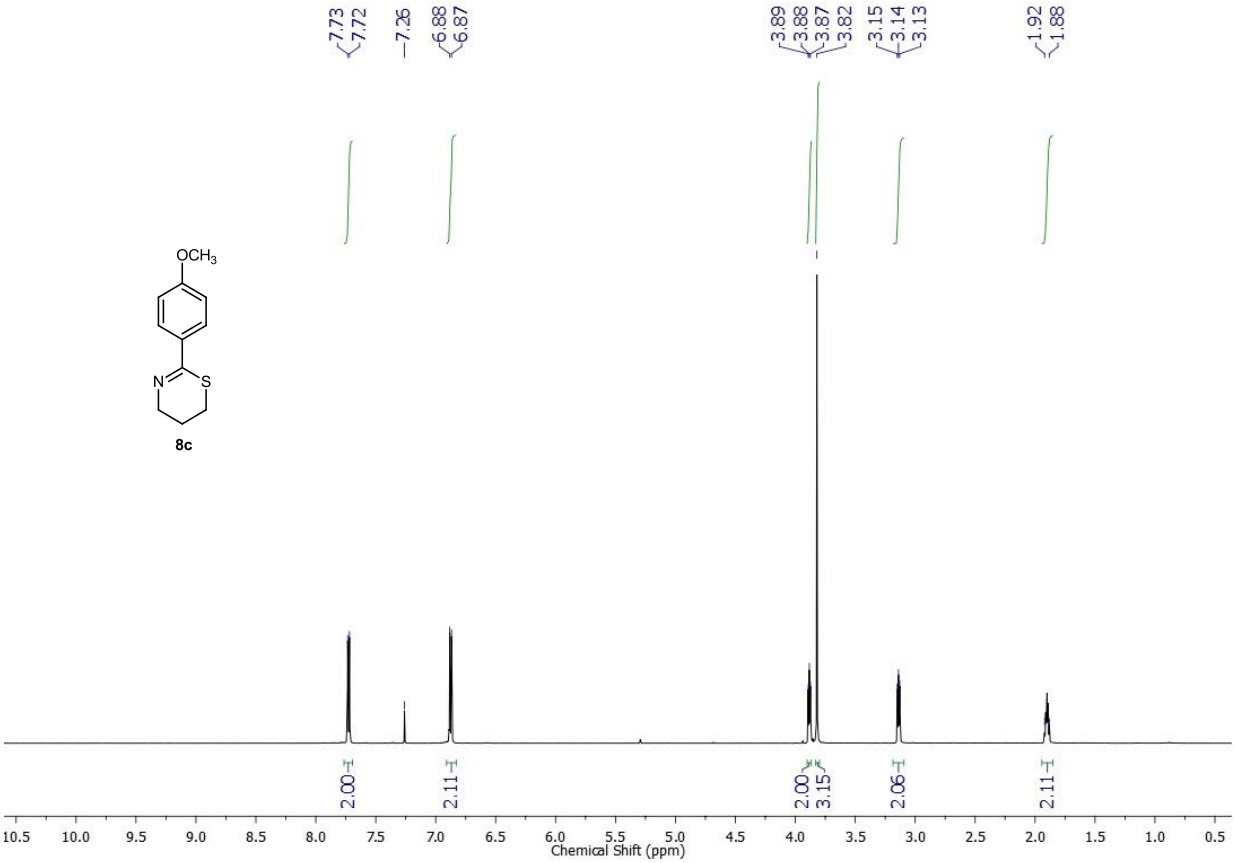
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **7j**



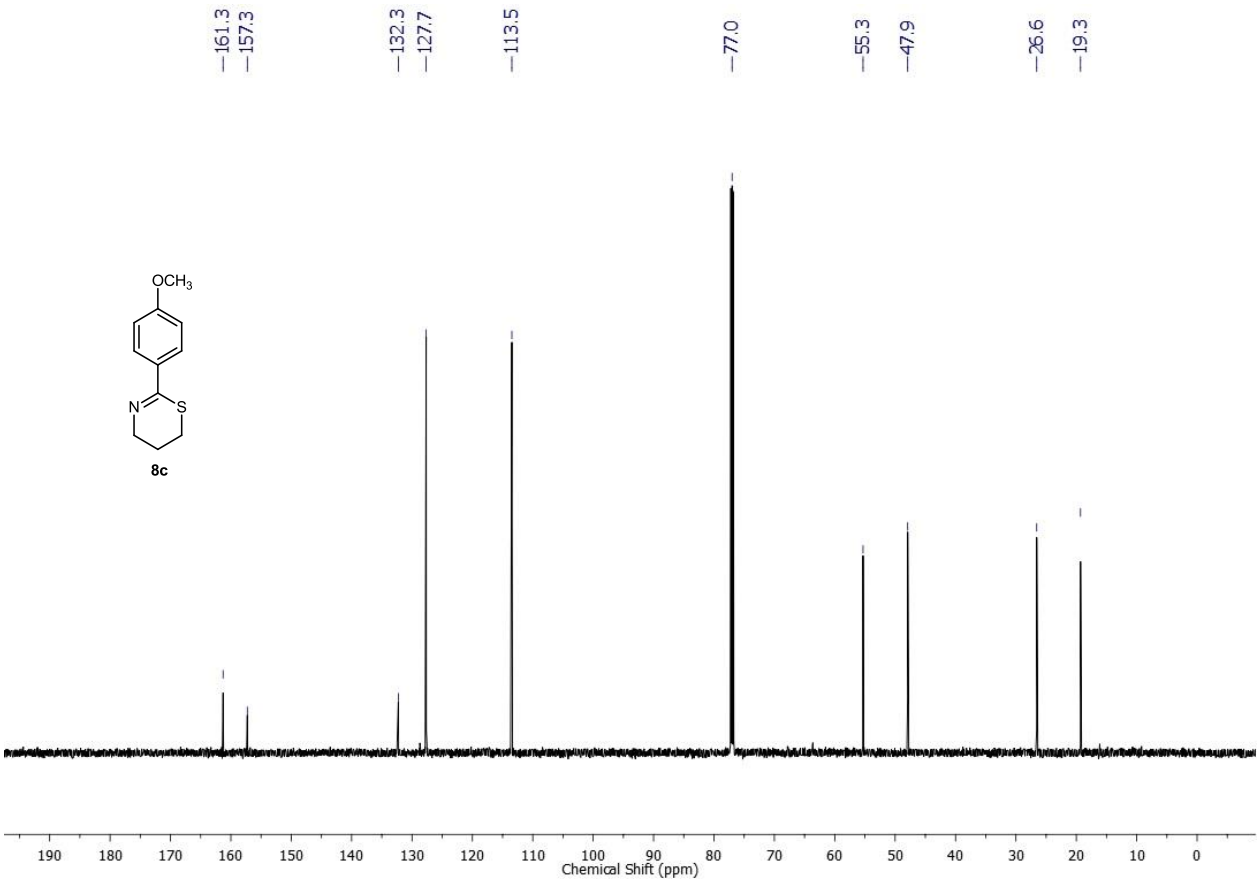
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8b**



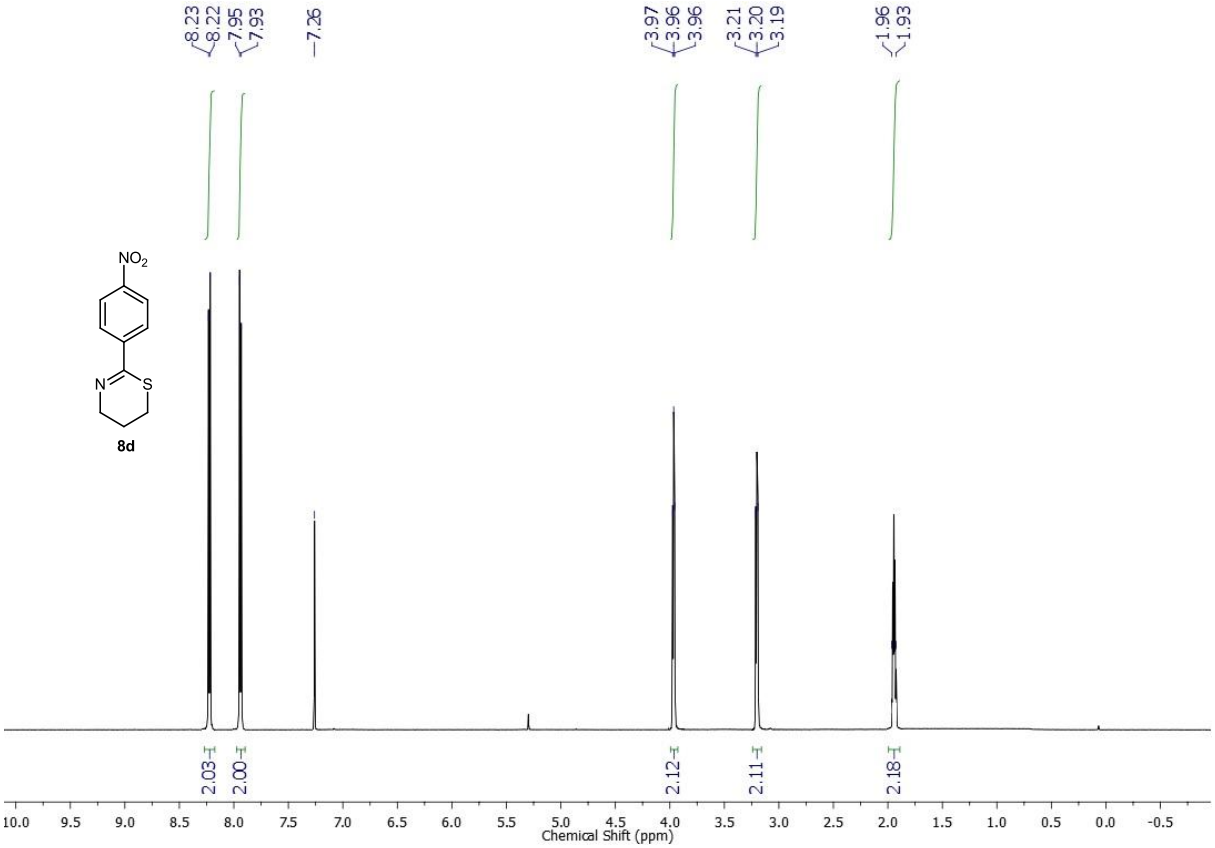
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8c**



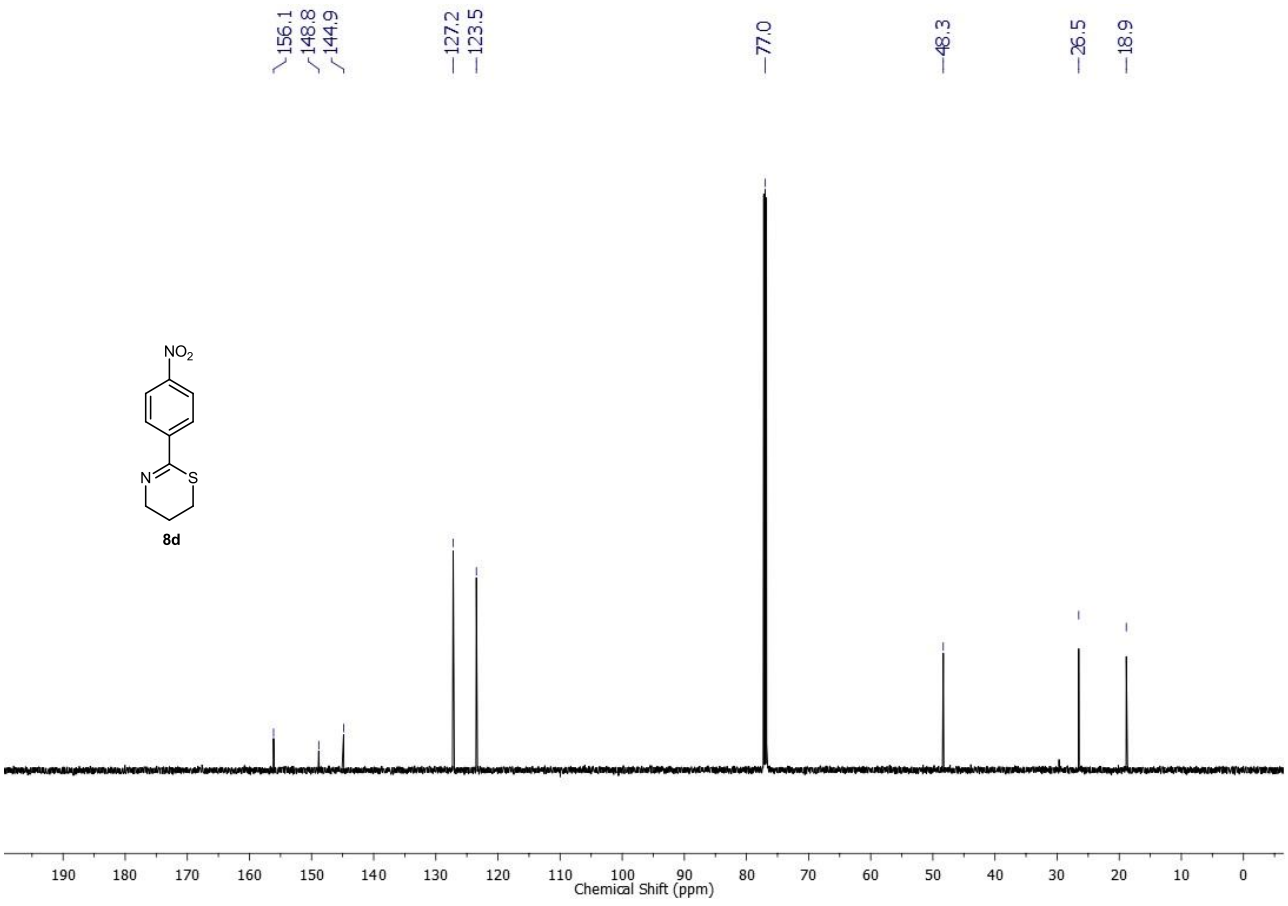
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8c**



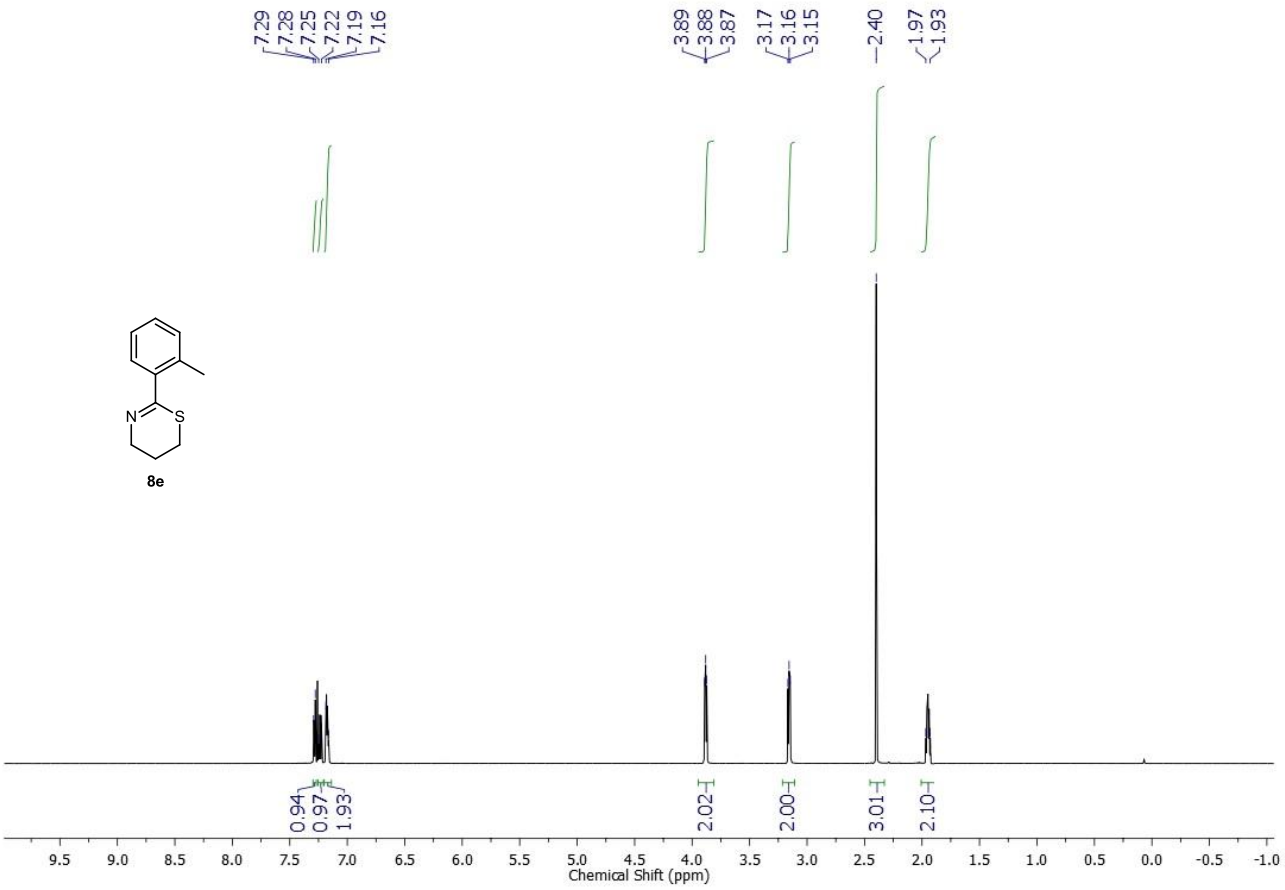
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8d**



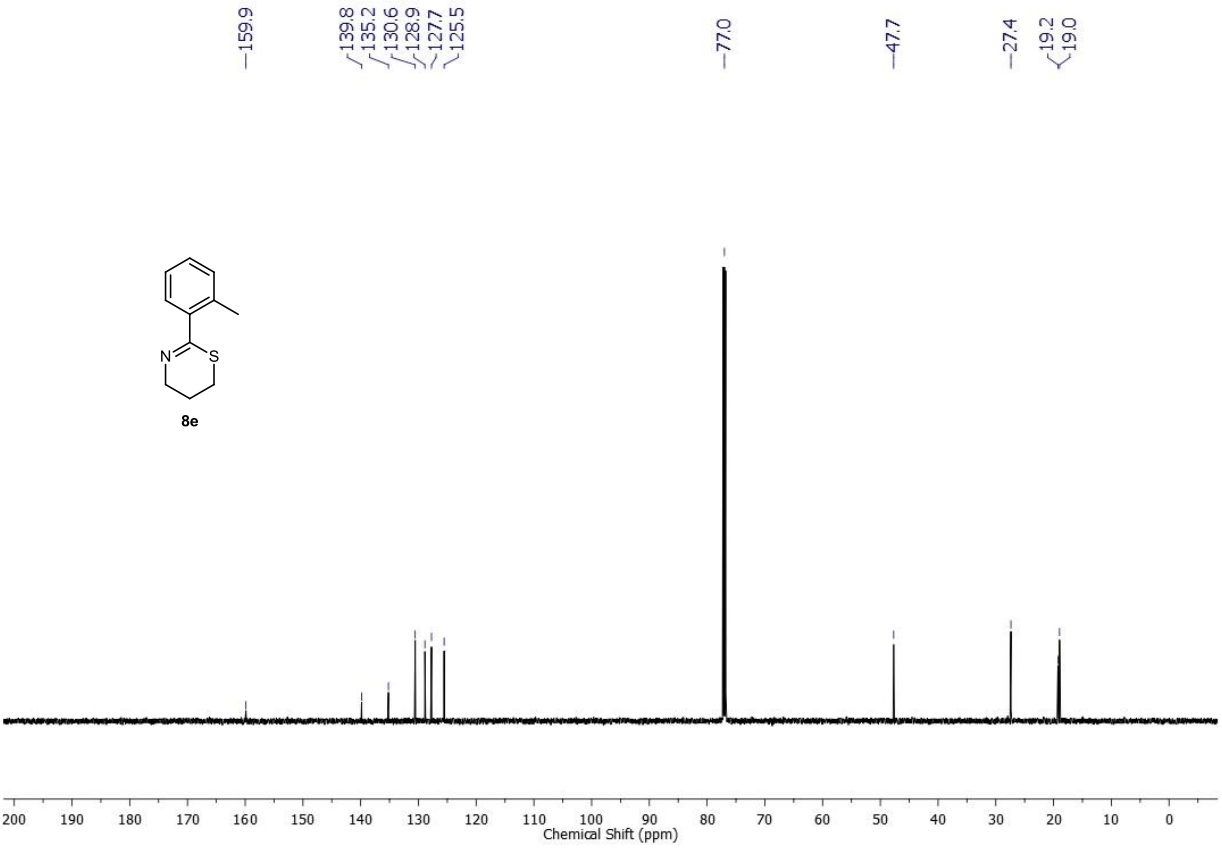
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8d**



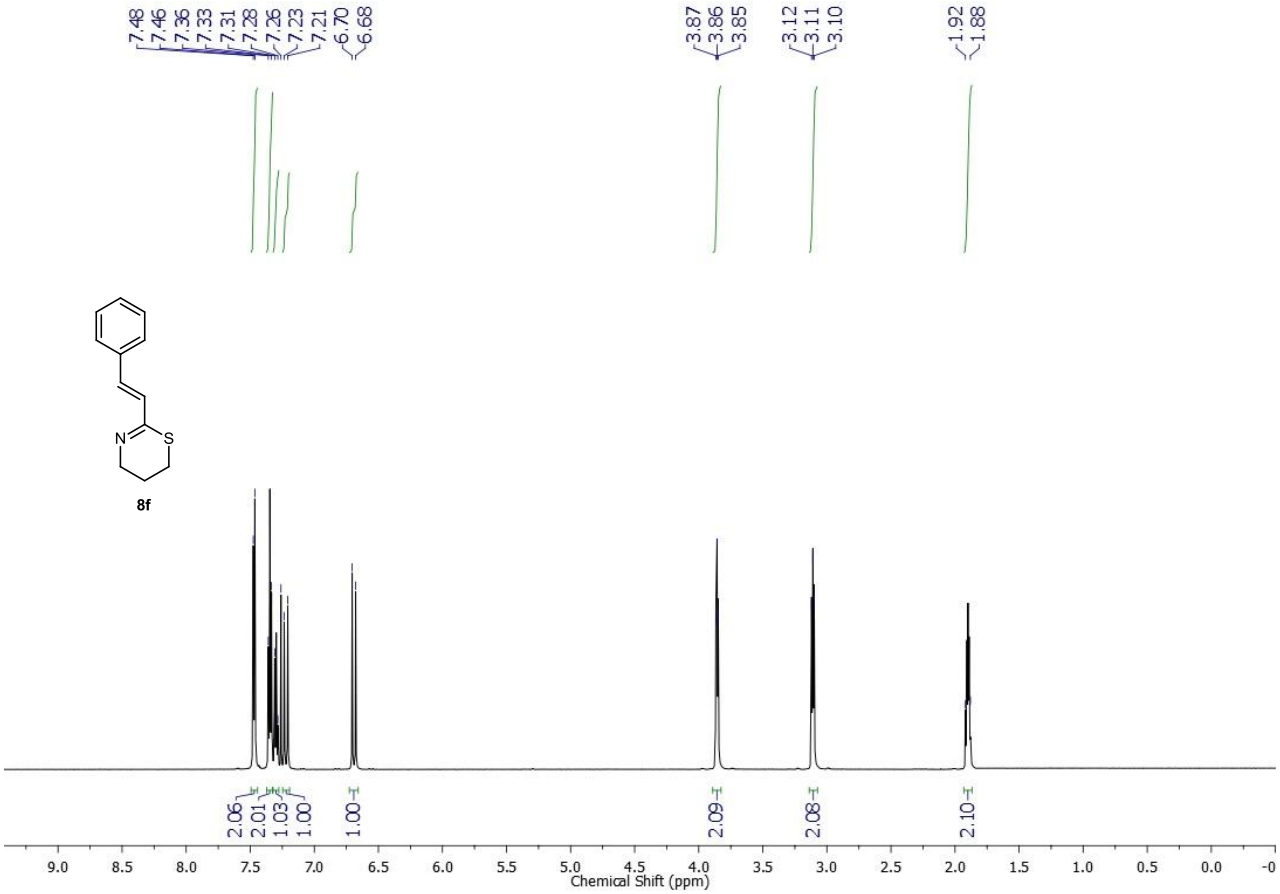
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8e**



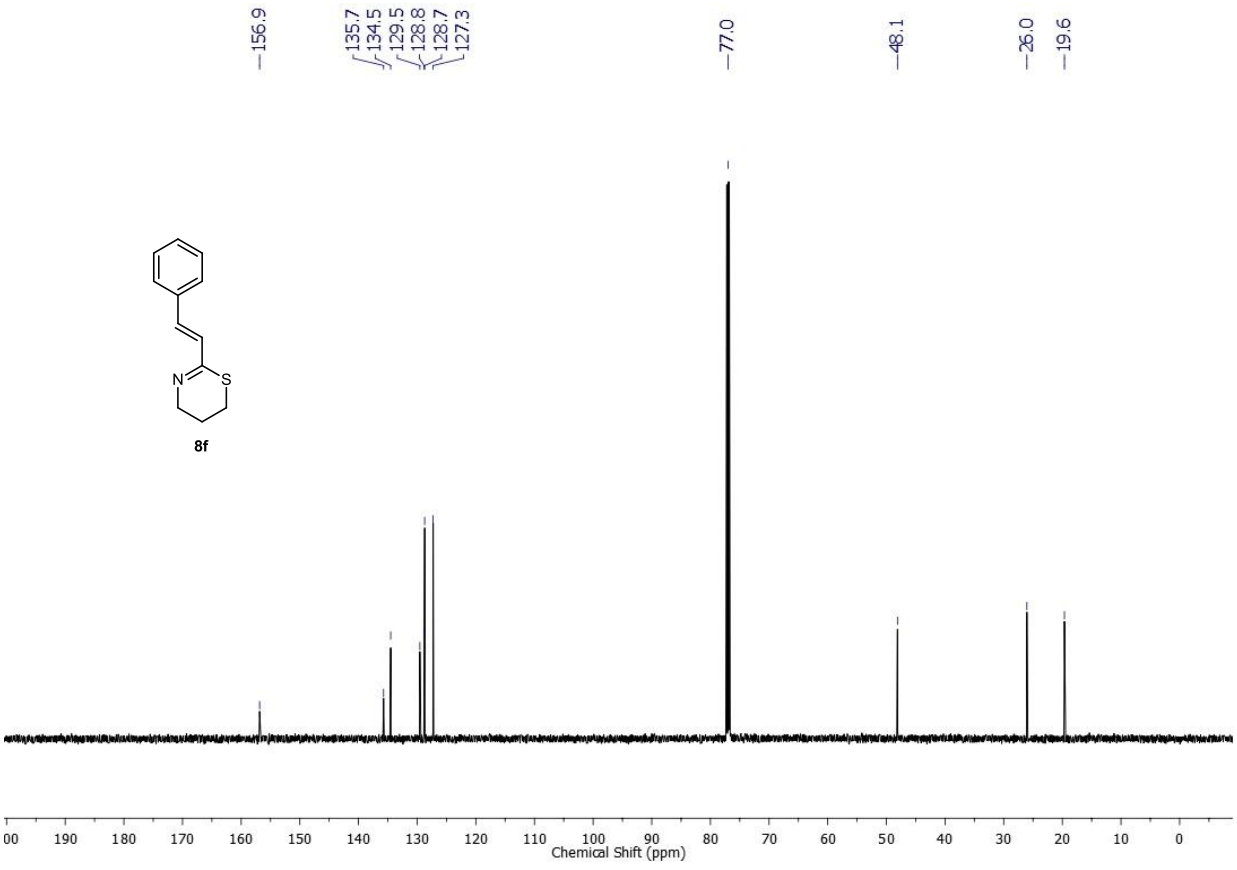
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8e**



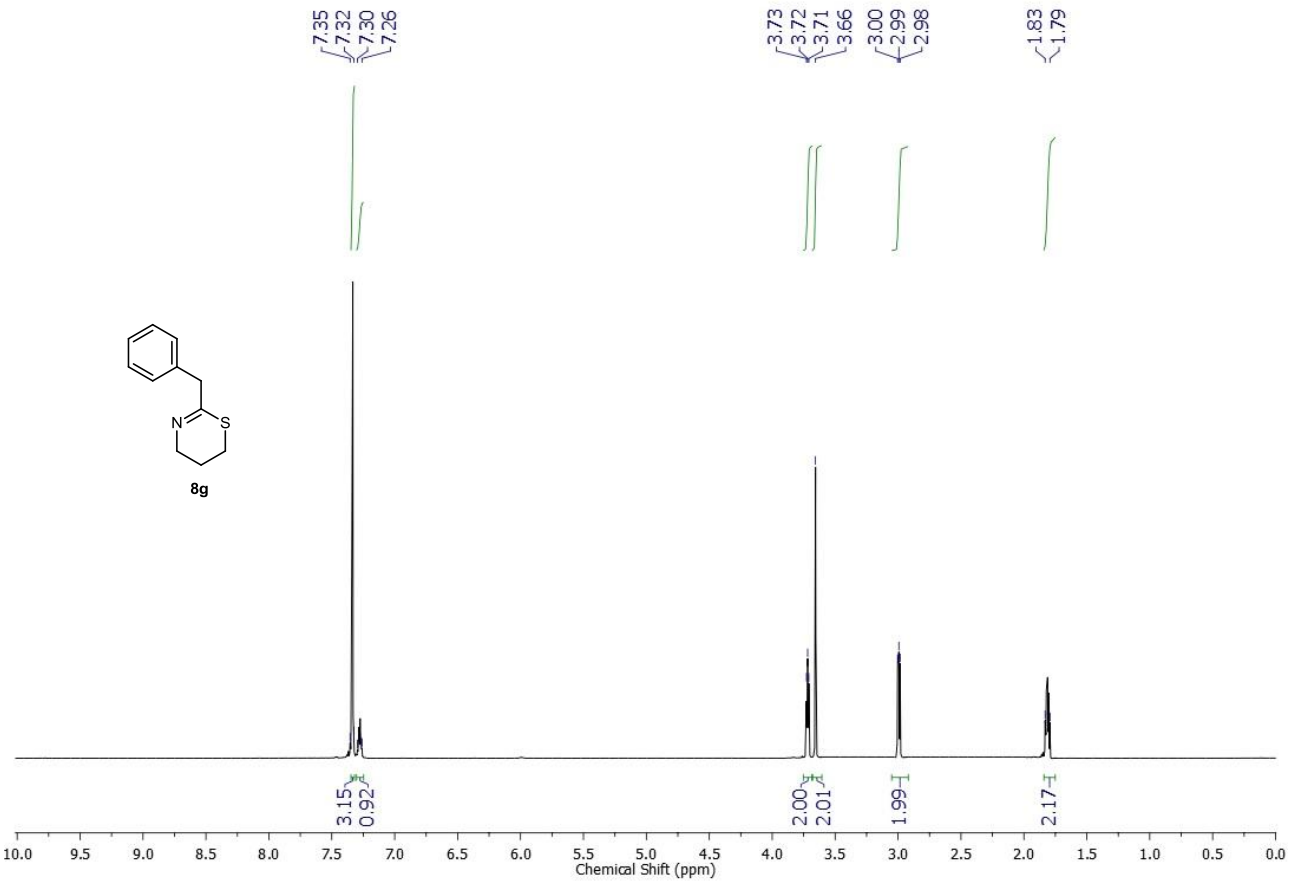
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8f**



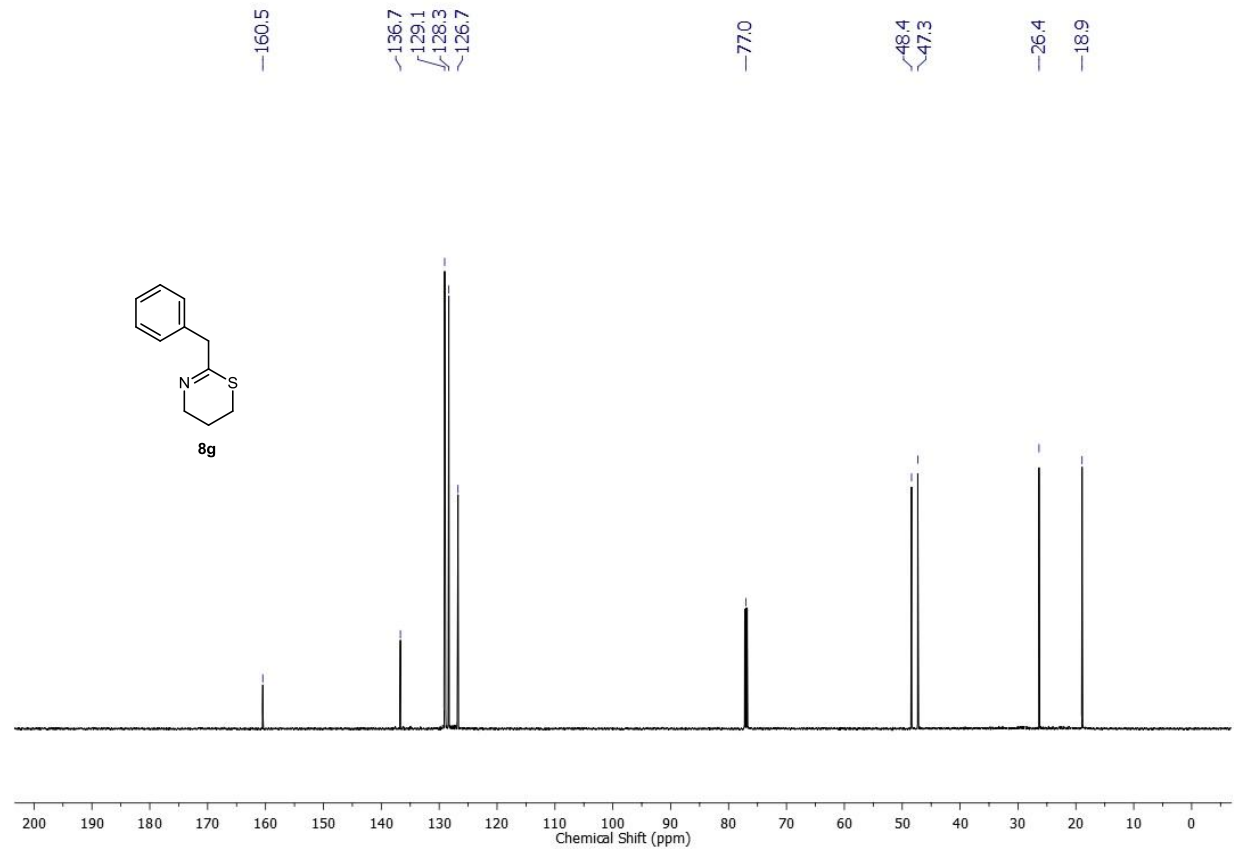
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8f**



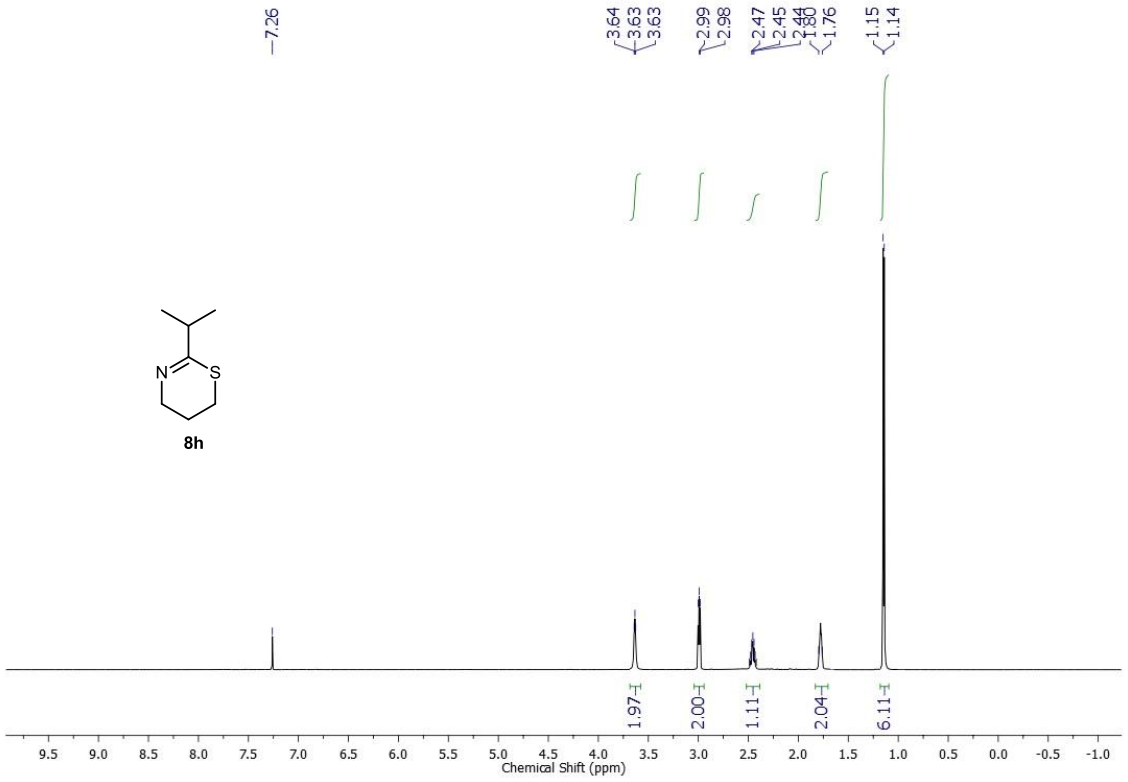
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8g**



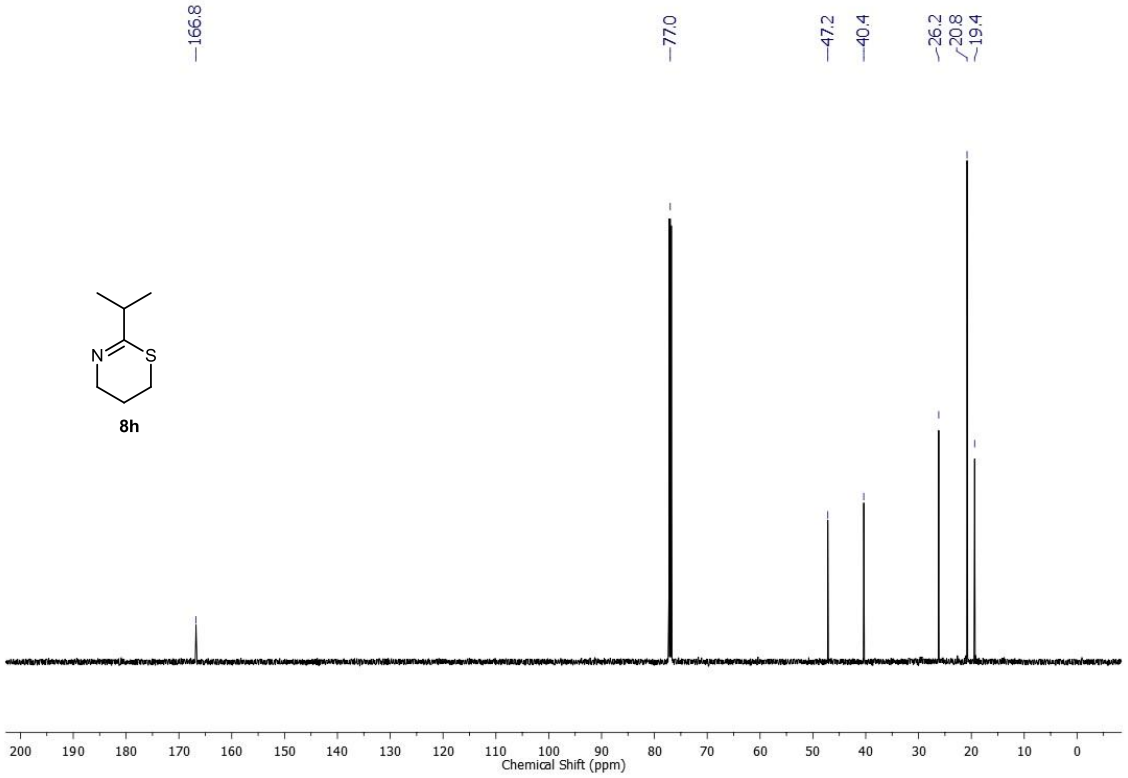
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8g**



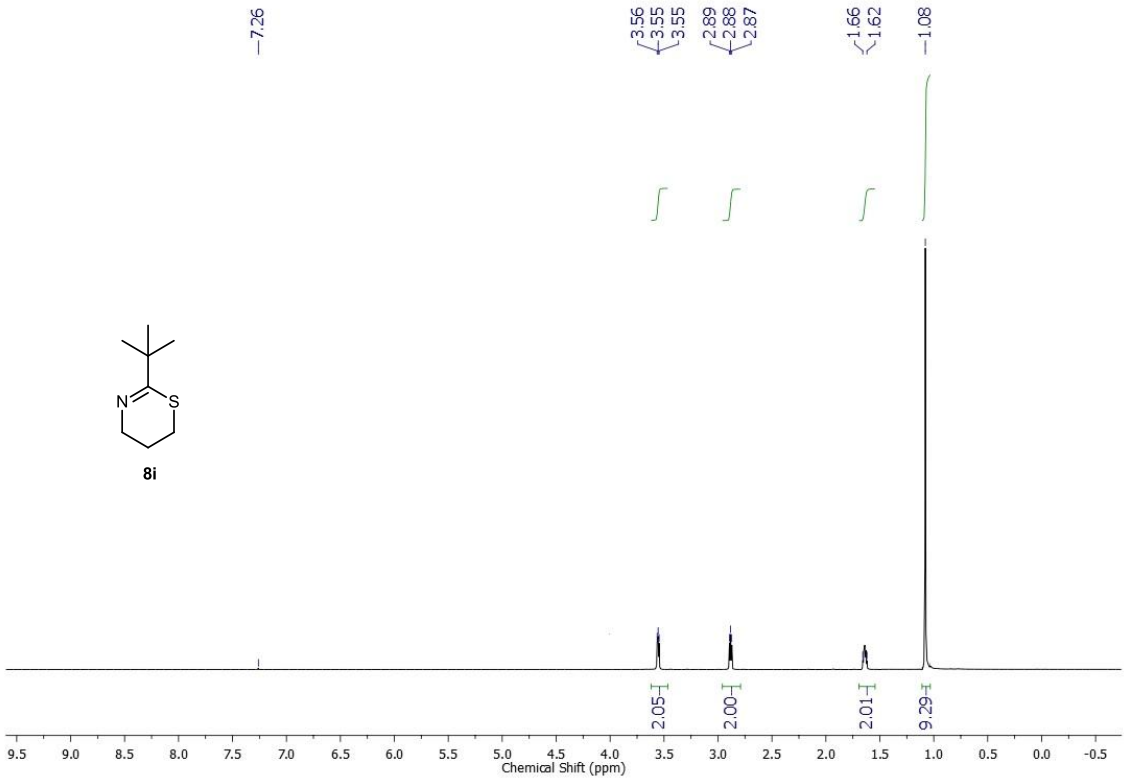
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8h**



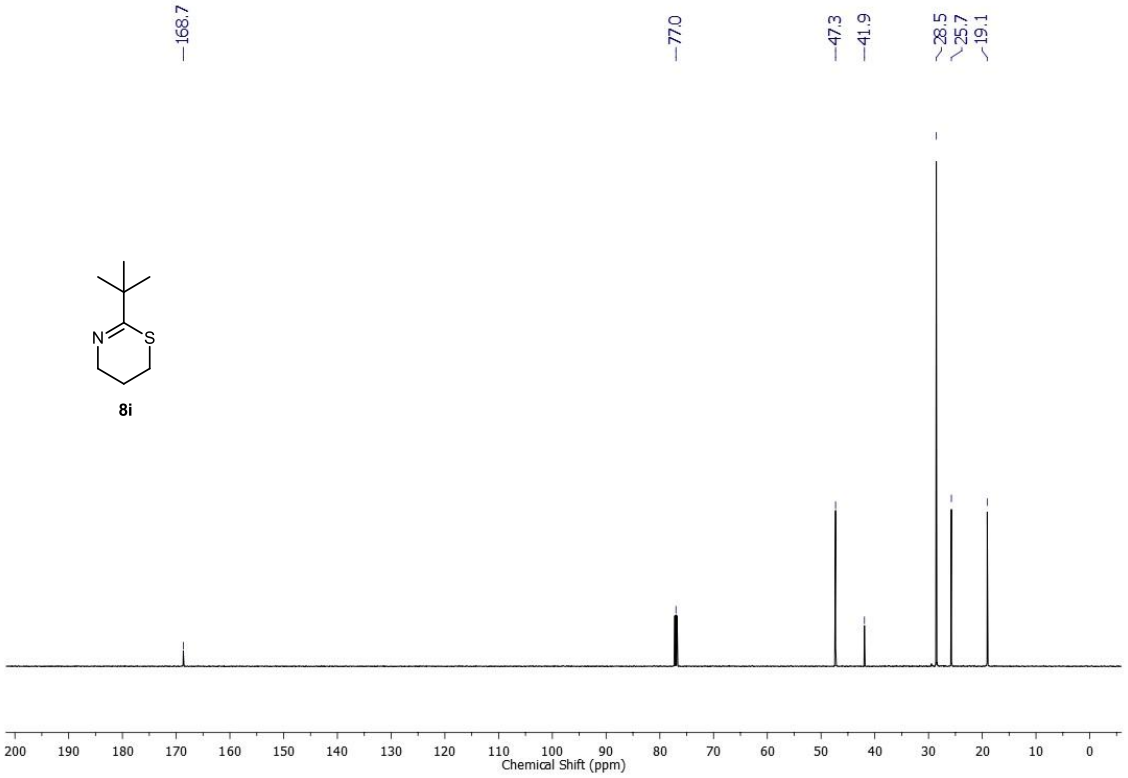
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8h**



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **8i**



^{13}C NMR (151 MHz, $CDCl_3$) spectrum of compound **8i**



8. Absolute configuration of compound 7g

Experimental UV and ECD spectra

ECD spectra were recorded on a Jasco 810 spectropolarimeter at +25 °C in far-UV HPLC grade acetonitrile solutions. The concentrations of the samples (about 10^{-4} M) were tuned by dilution of a mother solution ($1 \cdot 10^{-3}$ M) to obtain a maximum absorbance of about 1 in the UV spectrum when using a 0.2 cm path length. The acquisition was made recording a window between 400 and 190 nm by step of 1 nm for 32 seconds with high sensitivity mode.

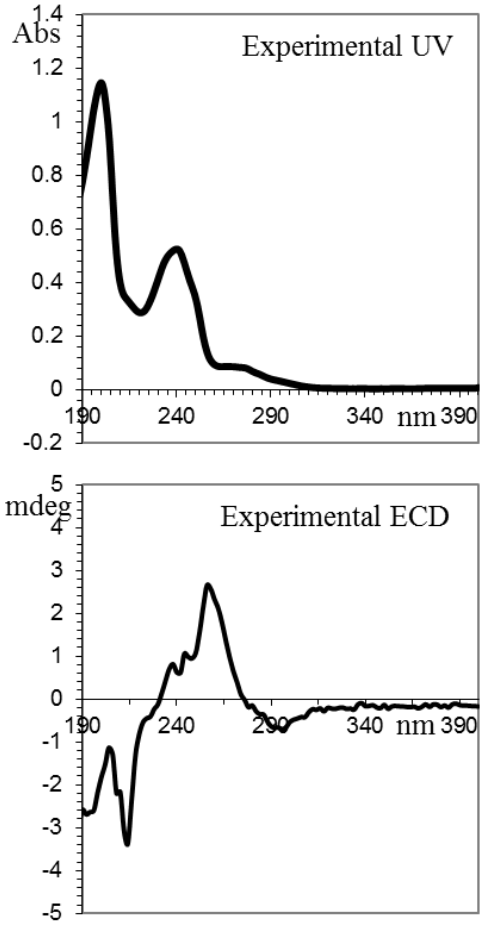


Figure S1. Experimental UV and ECD spectra of compound **7g**.

Experimental IR and VCD spectra

Compound **7g** was dissolved in CCl_4 to give an IR spectra with a maximum absorbance less than 1 Abs in a 0.1 mm path length cell with BaF_2 windows. The IR and VCD spectra were obtained by subtracting the CCl_4 IR spectrum. IR and VCD spectra were recorded in the 2000-800 cm^{-1} region on a ChiralIR-2X FT-VCD spectrometer (Biotools, Inc.) equipped with single PEM at 36kHz and 4 cm^{-1} resolution, with the parameters optimized for 1400 cm^{-1}. 12 blocks of 3120 scans were acquired with a total acquisition time of 12 hours.

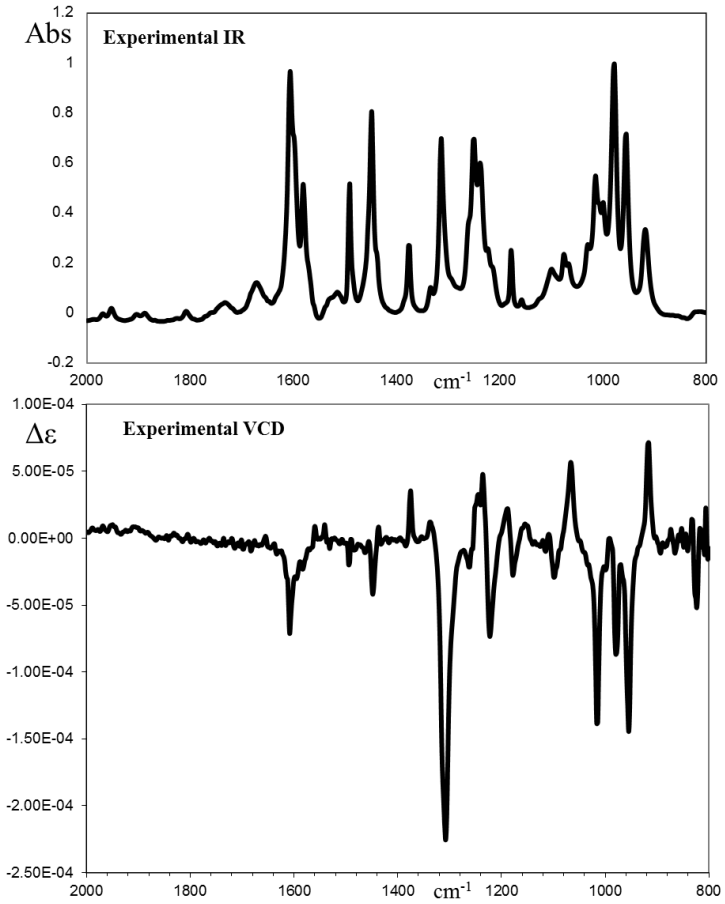


Figure S2. Experimental IR and VCD spectra of compound **7g**.

Absolute Configuration[1]

Conformational analysis of compound 7g

As the first step for AC assignment, we performed a conformational search on compound **7g**, assuming *S* absolute configuration. The PES was explored by means of ComputeVOA™ program[2] using the MMFF94 force field. The energy minima enclosed in a 5 kcal/mol window were then optimized using DFT calculations at the B3LYP/6-311+G(2d,p) and M06-2X/6-311+G(2d,p) levels. After DFT optimization two conformations (Figure S3) were found to be enclosed in a very narrow energy window (1 kcal/mol). Both conformations differed in the orientation of the methyl group that can be in a pseudo-axial or pseudo-equatorial disposition with a planar or distorted five member ring, respectively.

GS1	GS2
B3LYP E = 0.000 kcal/mol 68.4 %	B3LYP E = 0.456 kcal/mol 31.6 %
M06-2X E = 0.000 kcal/mol 80.4 %	M06-2X E = 0.836 kcal/mol 19.6 %

Figure S3. Calculated conformations of compound **7g** using 6-311+G(2d,p) as basis set with *S* absolute configuration.

Absolute configuration of compound 7g by ECD method

The ECD spectra have been calculated for the isolated molecule in the gas phase for the two conformations of **7g** using TD-DFT with four different functionals, to ascertain if different computational approaches provided different shapes of the simulated spectra (Figure S4).[3] Simulations were performed with the hybrid functionals BH&HLYP[4] and M06-2X,[5] with ωB97X-D that includes empirical dispersion,[6] and CAM-B3LYP that includes long range corrections using the Coulomb Attenuating Method.[7] The calculations employed the 6-311++G(2d,p) basis set that has proven many times to provide good accuracy at a moderate computational cost.[8]

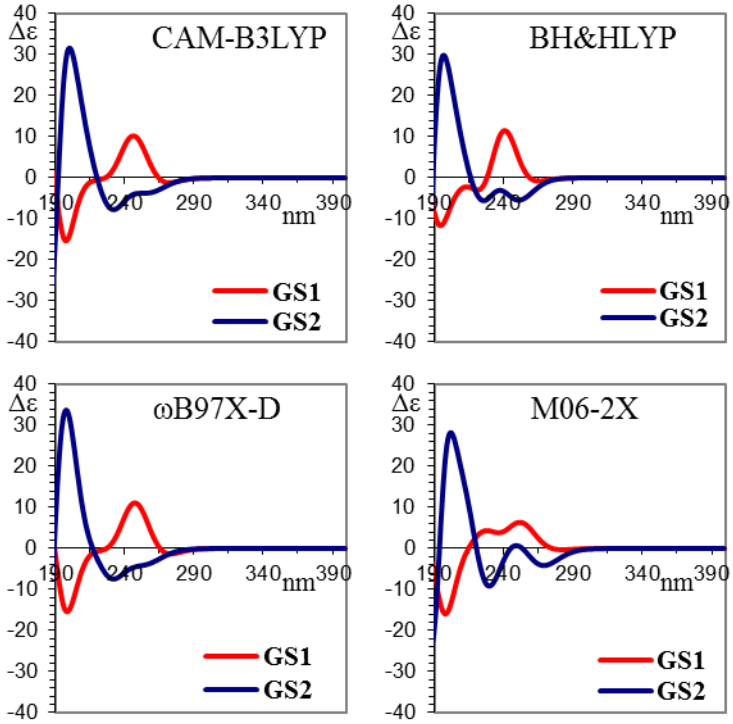


Figure S4. TD-DFT spectra calculated for the two conformations of (*S*)-**7g** using four different functionals (CAM-B3LYP, BH&HLYP, M06-2X, ωB97X-D) and the same 6-311++G(2d,p) basis set. For each conformation the first 70 excited states were calculated, and the spectrum was obtained using a 0.25 eV line width at half height.

The two calculated ECD spectra have opposite sign bands at about 245 nm and 195 nm, therefore the simulated spectra to be compared with the experimental were obtained using Boltzmann weighting with the total energies calculated using B3LYP and M06-2X (Figures S5-S6).

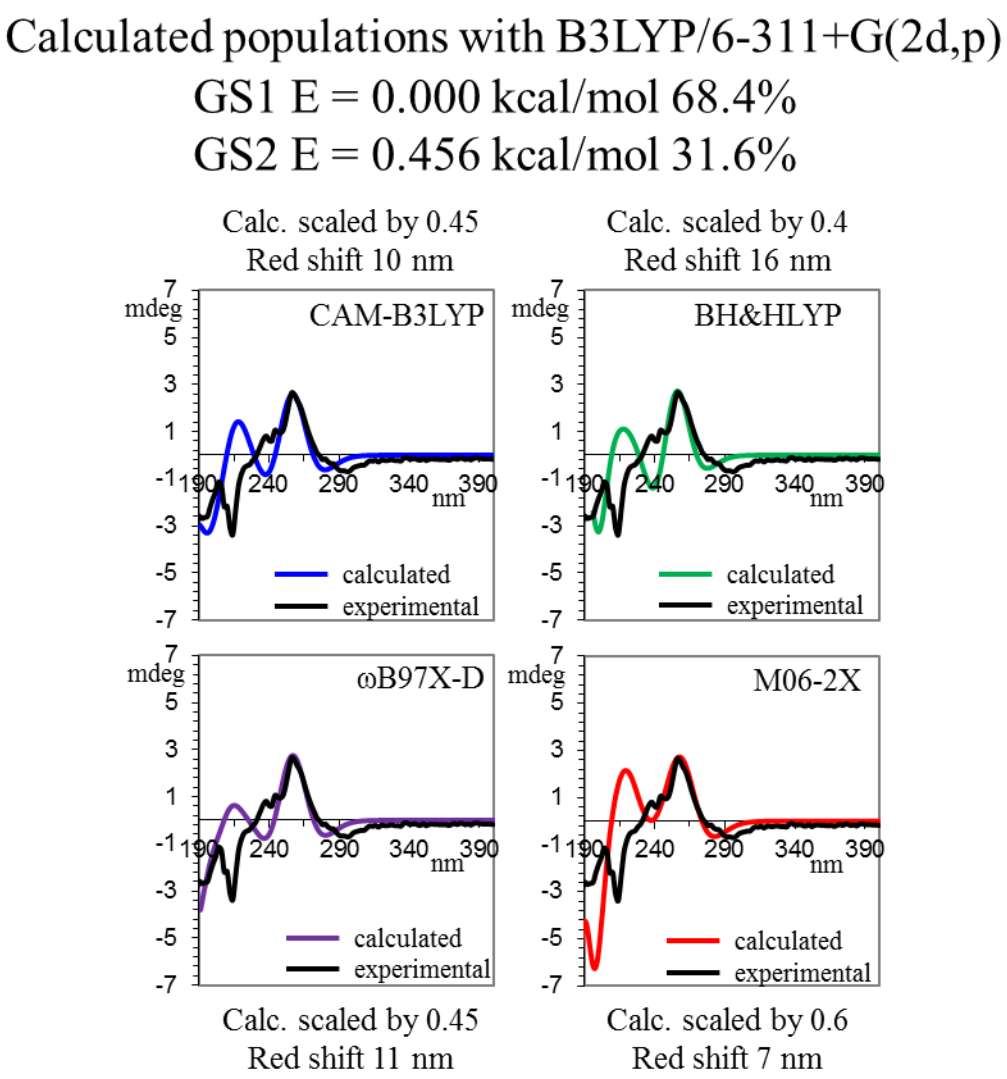


Figure S5. Simulations of the experimental ECD spectrum of **7g**. The calculated spectra for the two conformations have been mixed using the energies from B3LYP/6-311+G(2d,p) level. For each quarter, the black line corresponds to the experimental spectrum and the colored line to the TD-DFT simulations (6-311++G(2d,p) basis set). The simulated spectra were vertically scaled and red-shifted to get the best match with the experimental spectrum. All the simulations are for the *S* absolute configuration.

Calculated populations with M06-2X/6-311+G(2d,p)
GS1 E = 0.000 kcal/mol 80.4%
GS2 E = 0.836 kcal/mol 19.6%

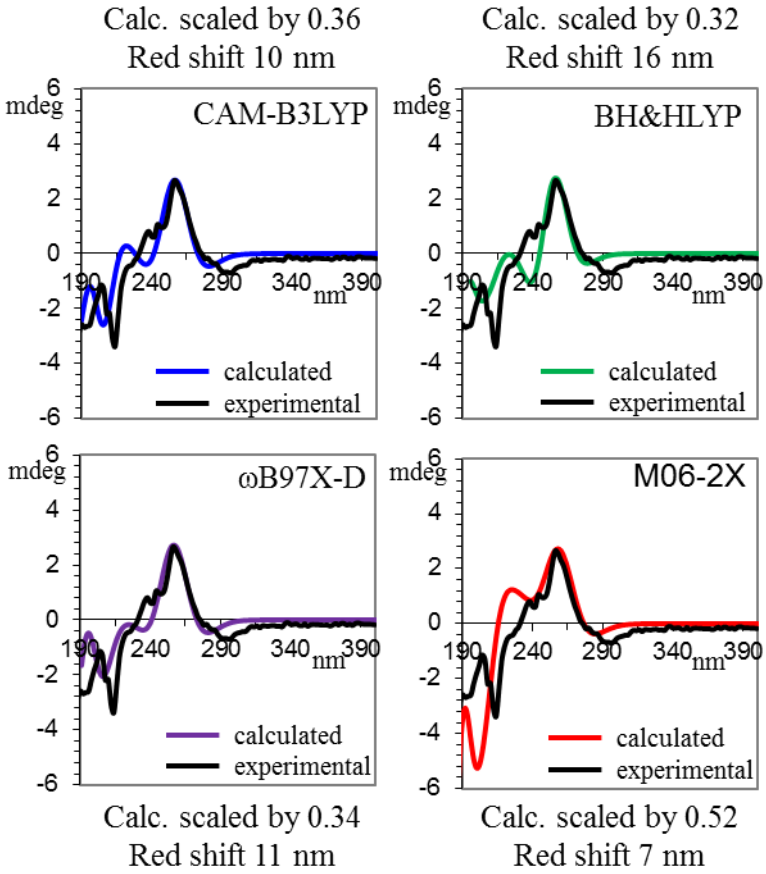


Figure S6. Simulations of the experimental ECD spectrum of **7g**. The calculated spectra for the two conformations have been mixed using the energies from M06-2X/6-311+G(2d,p) level. For each quarter, the black line corresponds to the experimental spectrum and the colored line to the TD-DFT simulations (6-311++G(2d,p) basis set). The simulated spectra were vertically scaled and red-shifted to get the best match with the experimental spectrum. All the simulations are for the *S* absolute configuration.

The best simulations of the experimental ECD spectrum are those obtained using the total energies calculated with M06-2X functional, and the *S* absolute configuration.

Absolute configuration of compound 7g by VCD method[9]

The IR and VCD spectra of the two conformations (GS1 and GS2 in Figure S2) were theoretically calculated assuming the *S* absolute configuration at the B3LYP/6-311+G(2d,p) level, providing the spectra shown in Figure S7.

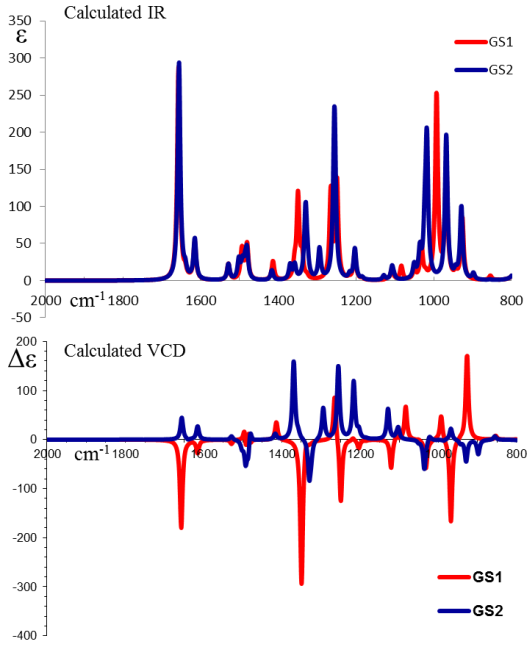


Figure S7. Calculated IR and VCD spectra of the two conformations (GS1 and GS2) of compound **7g**.

The calculated IR and VCD spectra to be compared with the experimental ones were calculated as the weighted sum of the two spectra using Boltzmann distribution, giving the spectra shown in Figure 1 of the main manuscript. The weighted spectrum was generated using the relative energies suggested by B3LYP calculations. The ECD and VCD spectra were recorded in different solvents, so the experimental conformational ratio can be different.

9. References

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