Synthesis of α-ketothioamides with elemental sulfur under solvent-free conditions in a mixer mill

*Chandan Chittapriya Sahu, Sourav Biswas, Renè Hommelsheim and Carsten Bolm **

Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, D-52074 Aachen, Germany.

*E-mail: Carsten.Bolm@oc.rwth-aachen.de

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1. General information

All chemicals used were purchased from commercial suppliers Merck, Sigma-Aldrich, Alfa Aesar, Chempur, ACROS ORGANICS or abcr and were used as received. Thin layer chromatography was performed using ALUGRAM Xtra SIL G/UV_{254} from MACHEREY-NAGEL. UV light (λ = 254 nm and 366 nm) was used for the detection of compounds. Flash column chromatography was performed using Silica gel 60 M (230-400 mesh). Ethyl acetate for column chromatography was distilled prior to use. NMR spectra of ^{1}H, ^{13}C nuclei were recorded in $CDCl_3$ on a Varian VNMRS 400 (400 MHz), Varian VNMRS 600 (600 MHz), Brucker Avance Neo 400 (400 MHz), or Bruker Avance Neo 600 (600 MHz) spectrometer at ambient temperature. The measured spectra were analysed using the software MestReNova and documented in the following order: chemical shifts (δ) are given in parts per million (ppm), multiplicities are stated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), ddd (doublet of doublets of doublets) and coupling constants (*J*) are given in Hz. The milling experiments were performed in a RETSCH Mixer Mill MM 400 using either a stainless-steel jar (SS) with a volume of 10 mL, a PTFE jar with a volume of 25 mL, a zirconium oxide yttria stabilized jar (ZrO_2) with a volume of 10 mL, or a tungsten carbide (WC) jar with a volume of 10 mL. In each case, a single ball of the same material (ø: 10 mm) were applied.

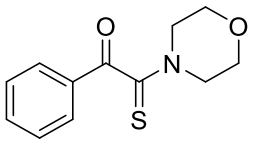
2. General procedure of synthesis of α-ketothioamide derivatives

A tungsten carbide (WC) milling jar (volume: 10 mL) equipped with one tungsten carbide milling ball (ø: 10 mm) was loaded with a methyl ketone (1 mmol), an amine (3 mmol), elemental sulfur (9 mmol), KOH (6 mmol, 6 equiv.), and silica (300 mg). After milling for 90 min at 25 Hz, the jar was opened, and the crude residue was extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, washed with water (2 × 20), dried over Na_2SO_4, and concentrated under reduced pressure. The resulting crude was subjected to flash chromatography. The product was purified by flash column chromatography using ethyl acetate and pentane as eluent on silica gel.

For the control experiment under inert gas (argon), the jar was filled with the reagents in a glove-box and tightly wrapped with a teflon tape.

3. Characterisation data

2-Morpholino-1-phenyl-2-thioxoethan-1-one (3aa)[S1]

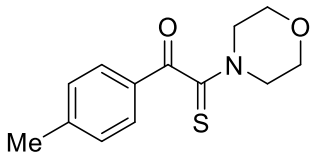


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a pale yellow solid (200.1 mg, 85% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.65 – 7.59 (m, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 4.33 (t, *J* = 4.8 Hz, 2H), 3.90 (t, *J* = 4.8 Hz, 2H), 3.70 – 3.68 (m, 2H), 3.61 – 3.58 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 195.8, 188.0, 134.6, 133.4, 123.0, 129.1, 66.6, 66.5, 52.0, 47.2 ppm.

2-Morpholino-2-thioxo-1-(*p*-tolyl)ethan-1-one (3ba)[S1]

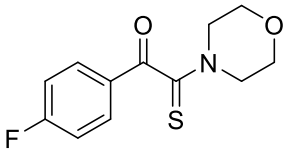


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a pale yellow solid (141.2 mg, 57% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 4.35 – 4.31 (m, 2H), 3.92 – 3.88 (m, 2H), 3.70 – 3.67 (m, 2H), 3.61 – 3.57 (m, 2H), 2.43 (s, 3H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 196.2, 188.0, 145.9, 130.9, 130.1, 129.8, 66.6, 66.5, 52.0, 47.2, 22.0 ppm.

1-(4-Fluorophenyl)-2-morpholino-2-thioxoethan-1-one (3ca)[S1]

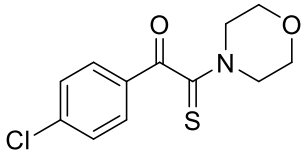


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a pale yellow solid (82.1 mg, 32% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.18 – 7.15 (m, 2H), 4.34 – 4.31 (m, 2H), 3.92 – 3.89 (m, 2H), 3.71 – 3.68 (m, 2H), 3.61 – 3.58 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 195.3, 186.5, 166.6 (d, *J* = 257.9 Hz), 132.8 (d, *J* = 9.9 Hz), 129.9 (d, *J* = 3.1 Hz), 116.4 (d, *J* = 22.1 Hz), 66.6, 66.5, 52.1, 47.3 ppm.

1-(4-Chlorophenyl)-2-morpholino-2-thioxoethan-1-one (3da)[S1]

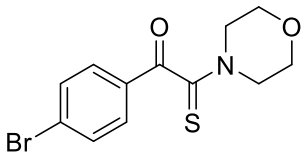


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a pale yellow solid (150 mg, 56% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 – 7.92 (m, 2H), 7.48 – 7.45 (m, 2H), 4.33 – 4.30 (m, 2H), 3.93 – 3.88 (m, 2H), 3.72 – 3.68 (m, 2H), 3.61 – 3.58 (m, 2H) ppm.

^{13}C {^{1}H} NMR 151 MHz, $CDCl_3$) δ 195.1, 186.6, 141.2, 131.9, 131.3, 129.5, 66.7, 66.5, 52.1, 47.3 ppm.

1-(4-Bromophenyl)-2-morpholino-2-thioxoethan-1-one (3ea)[S2]

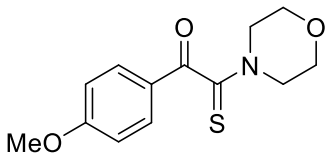


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a pale yellow solid (150.0 mg, 48% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 – 7.84 (m, 2H), 7.65 – 7.62 (m, 2H), 4.33 – 4.30 (m, 2H), 3.92 – 3.88 (m, 2H), 3.72 – 3.68 (m, 2H), 3.60 – 3.58 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 195.0, 186.7, 132.5, 132.3, 131.4, 130.0, 66.6, 66.5, 52.1, 47.3 ppm.

1-(4-Methoxyphenyl)-2-morpholino-2-thioxoethan-1-one (3fa)[S1]

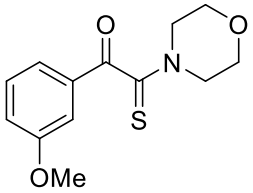


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:3). The product was obtained as a pale yellow solid (138.3 mg, 52% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 6.97 – 6.95 (m, 2H), 4.34 – 4.31 (m, 2H), 3.91 – 3.88 (m, 5H), 3.70 – 3.67 (m, 2H), 3.62 – 3.57 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 196.3, 187.4, 164.8, 132.5, 126.2, 114.4, 66.7, 66.5, 55.8, 52.0, 47.2 ppm.

1-(3-Methoxyphenyl)-2-morpholino-2-thioxoethan-1-one (3ga)[S1]

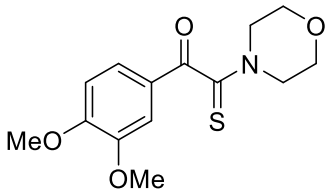


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a pale yellow solid (140.2 mg, 53% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.17 – 7.14 (m, 1H), 4.34 – 4.31 (m, 2H), 3.91 – 3.88 (m, 2H), 3.86-3.85(m, 3H), 3.71 – 3.68 (m, 2H), 3.61 – 3.58 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 195.8, 187.8, 160.1, 134.7, 130.1, 122.9, 121.3, 113.5, 66.6, 66.5, 55.7, 52.1, 47.2 ppm.

1-(3,4-Dimethoxyphenyl)-2-morpholino-2-thioxoethan-1-one (3ha)[S2]

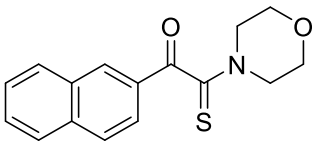


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a pale yellow solid (120.6 mg, 41% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.35 – 4.31 (m, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 3.90 (t, *J* = 4.8 Hz, 2H), 3.72 – 3.67 (m, 2H), 3.63 – 3.56 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 196.2, 187.5, 154.6, 149.6, 126.3, 125.8, 111.0, 110.4, 66.7, 66.5, 56.38, 56.2, 52.1, 47.3 ppm.

2-Morpholino-1-(naphthalen-2-yl)-2-thioxoethan-1-one (3ia)[S1]

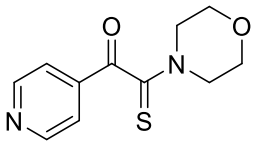


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a brown solid (150.7 mg, 53% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.06 – 8.02 (m, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.59 – 7.55 (m, 1H), 4.41 – 4.38 (m, 2H), 3.96 – 3.92 (m, 2H), 3.72 – 3.68 (m, 2H), 3.65 – 3.62 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 195.9, 188.2, 136.3, 132.6, 132.5, 130.7, 123.0, 129.5, 129.1, 128.1, 127.3, 124.4, 66.9, 66.6, 52.1, 47.3 ppm.

2-Morpholino-1-(pyridin-4-yl)-2-thioxoethan-1-one (3ja)[S3]

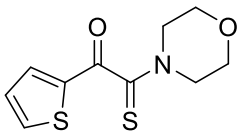


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 1:1). The product was obtained as a pale yellow solid (100.0 mg, 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 – 8.81 (m, 2H), 7.81 – 7.75 (m, 2H), 4.34 – 4.29 (m, 2H), 3.93 – 3.89 (m, 2H), 3.75 – 3.70 (m, 2H), 3.63 – 3.59 (m, 2H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 193.8, 185.5, 151.2, 140.0, 122.3, 66.7, 66.5, 52.1, 47.4 ppm.

2-Morpholino-1-(thiophen-2-yl)-2-thioxoethan-1-one (3ka)[S1]

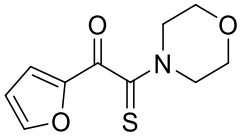


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a yellow solid (138.1 mg, 57% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.78 (m, 1H), 7.77 – 7.73 (m, 1H), 7.18 – 7.13 (m, 1H), 4.32 – 4.27 (m, 2H), 3.90 – 3.86 (m, 2H), 3.73 – 3.68 (m, 2H), 3.67 – 3.63 (m, 2H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 194.4, 181.1, 140.4, 136.3, 135.7, 128.8, 66.7, 66.4, 52.1, 47.4 ppm.

1-(Furan-2-yl)-2-morpholino-2-thioxoethan-1-one (3la)[S1]

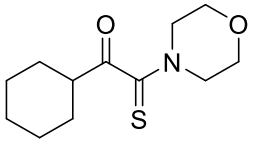


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a yellow solid (164.7 mg, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 4.0 Hz, 1H), 7.75 (d, J = 4.8 Hz, 1H), 7.15 (t, J = 4.4 Hz, 1H), 4.32 – 4.26 (m, 2H), 3.91 – 3.85 (m, 2H), 3.73 – 3.68 (m, 2H), 3.67 – 3.61 (m, 2H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 194.4, 181.1, 140.4, 136.3, 135.7, 128.8, 66.7, 66.4, 52.1, 47.4 ppm.

1-Cyclohexyl-2-morpholino-2-thioxoethan-1-one (3ma)[S3]

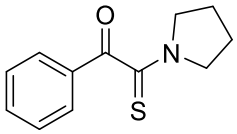


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:2). The product was obtained as a yellow oil (78.9 mg, 33% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.22 – 4.17 (m, 2H), 3.84 – 3.80 (m, 2H), 3.75 – 3.71 (m, 2H), 3.62 – 3.58 (m, 2H), 3.27 – 3.17 (m, 1H), 2.02 – 1.91 (m, 2H), 1.85 – 1.75 (m, 2H), 1.74 – 1.64 (m, 1H), 1.38 – 1.27 (m, 4H), 1.23 – 1.10 (m, 1H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 201.1, 198.0, 66.7, 66.4, 52.2, 47.6, 47.4, 28.2, 25.8, 25.6 ppm.

1-Phenyl-2-(pyrrolidin-1-yl)-2-thioxoethan-1-one (3ab)[S2]

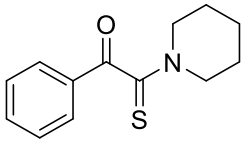


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a yellow oil (149.1 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.94 (m, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 3.92 (t, J = 6.4 Hz, 2H), 3.51 (t, J = 7.2 Hz, 2H), 2.10 – 1.98 (m, 4H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.7, 188.8, 134.2, 132.9, 130.1, 128.9, 51.3, 51.1, 26.1, 23.8 ppm.

1-Phenyl-2-(piperidin-1-yl)-2-thioxoethan-1-one (3ac)[S1]

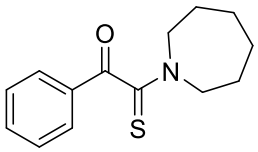


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a yellow solid (134.0 mg, 57% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.97 (m, 2H), 7.62 – 7.57 (m, 1H), 7.48 (t, J = 7.8 Hz, 2H), 4.25 (t, J = 5.4 Hz, 2H), 3.53 (t, J = 5.4 Hz, 2H), 1.85 – 1.80 (m, 2H), 1.79 – 1.74 (m, 2H), 1.64 – 1.59 (m, 2H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 194.6, 188.1, 134.3, 133.6, 129.9, 128.9, 53.1, 48.2, 26.5, 25.5, 24.2 ppm.

2-(Azepan-1-yl)-1-phenyl-2-thioxoethan-1-one (3ad)[S2]

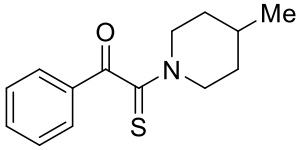


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a pale yellow solid (122.2 mg, 49% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.95 (m, 2H), 7.60 – 7.54 (m, 1H), 7.49 – 7.43 (m, 2H), 4.18 – 4.11 (m, 2H), 3.58 (t, *J* = 6.0 Hz, 2H), 1.97 (p, *J* = 6.0 Hz, 2H), 1.75 – 1.64 (m, 4H), 1.63 – 1.56 (m, 2H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 196.1, 187.8, 134.1, 133.6, 130.0, 128.8, 54.1, 51.4, 28.5, 27.5, 26.2, 25.5 ppm.

2-(4-Methylpiperidin-1-yl)-1-phenyl-2-thioxoethan-1-one (3ae)[S3]

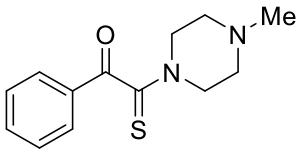


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a yellow solid (150.4 mg, 61% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.97 (m, 2H), 7.62 – 7.58 (m, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 5.42 – 5.38 (m, 1H), 3.79 – 3.75 (m, 1H), 3.29 (t, *J* = 12.6 Hz, 1H), 3.11 (td, *J* = 12.6, 3.0 Hz, 1H), 1.93 – 1.88 (m, 1H), 1.84 – 1.75 (m, 1H), 1.70 – 1.65 (m, 1H), 1.47 – 1.38 (m, 1H), 1.33 – 1.15 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H) ppm.

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 194.7, 188.1, 134.3, 133.5, 129.9, 129.0, 52.3, 47.5, 34.5, 33.4, 30.9, 21.3 ppm.

2-(4-Methylpiperazin-1-yl)-1-phenyl-2-thioxoethan-1-one (3af)[S1]

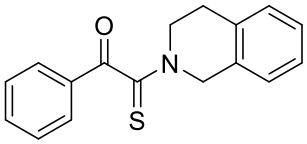


Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 1:9). The product was obtained as a yellow solid (124.2 mg, 50% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 4.35 – 4.29 (m, 2H), 3.61 – 3.56 (m, 2H), 2.65 – 2.59 (m, 2H), 2.44 – 2.40 (m, 2H), 2.33 (s, 3H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 195.5, 188.0, 134.4, 133.5, 129.9, 129.0, 54.8, 54.2, 51.5, 46.8, 45.7 ppm.

2-[3,4-Dihydroisoquinolin-2(1*H*)-yl]-1-phenyl-2-thioxoethan-1-one (3ag)[S4]



The ratio of two conformational isomers is about 2:1 as observed by ^{1}H NMR. Purification by silica gel chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a yellow oil (138.2 mg, 49% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 2H), 8.07 – 8.03 (m, 1H), 7.74 – 7.65 (m, 1.5H), 7.62 – 7.52 (m, 3H), 7.42 – 7.31 (m, 4.5H), 7.29 – 7.23 (m, 1H), 6.99 (d, *J* = 7.6 Hz, 0.5H), 5.43 (s, 2H), 4.80 (s, 1H), 4.51 (t, *J* = 6.0 Hz, 1H), 3.93 (t, *J* = 6.0 Hz, 2H), 3.23 (t, *J* = 6.0 Hz, 1H), 3.00 (t, *J* = 6.0 Hz, 2H) ppm.

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 195.8, 195.5, 188.1, 188.0, 134.5, 134.4, 134.4, 133.5, 133.4, 133.2, 131.2, 131.1, 130.0, 130.0, 129.0, 129.0, 128.6, 128.6, 128.0, 127.4, 127.3, 127.1, 126.9, 126.0, 52.7, 49.5, 49.4, 46.0, 29.4, 28.0 ppm.

4. References

S1. H.-Z. Li, W.-J. Xue and A.-X. Wu, *Tetrahedron,* 2014, **70**, 4645-4651.

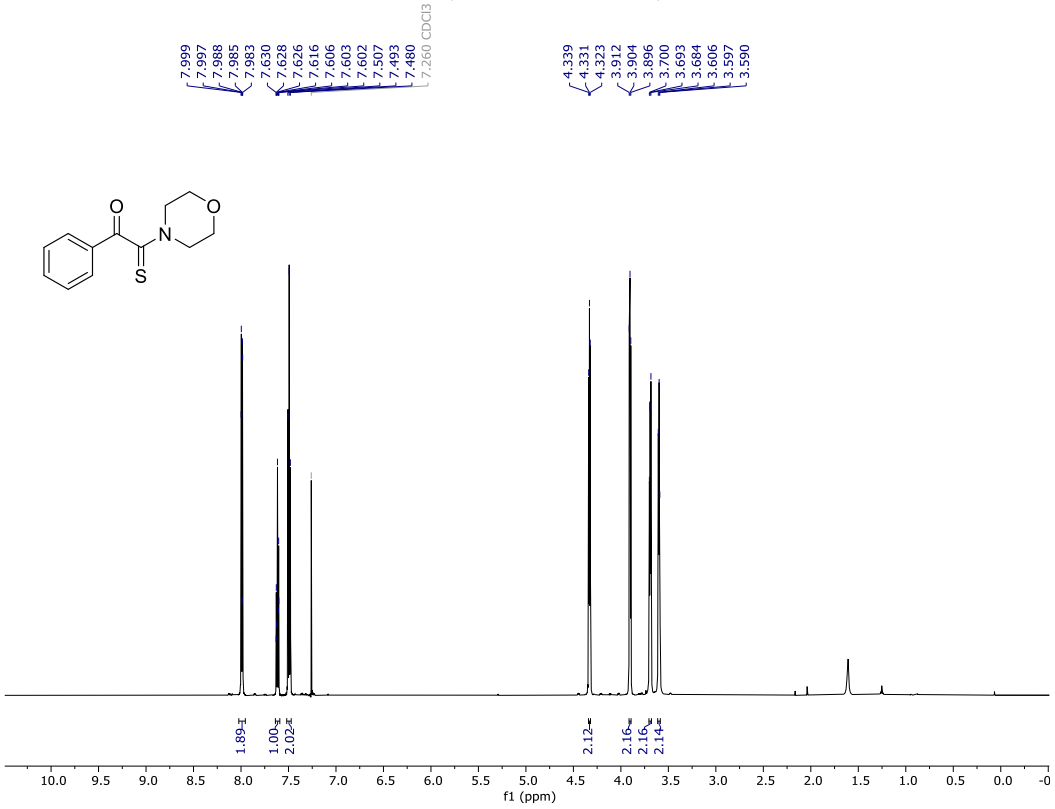
S2. T. B. Nguyen and P. Retailleau, *Green Chem.,* 2017, **19**, 5371-5374.

S3. Q. Spillier, S. Ravez, J. Unterlass, C. Corbet, C. Degavre, O. Feron and R. Frédérick, *Pharmaceuticals*, 2020, **13**, 20-41.

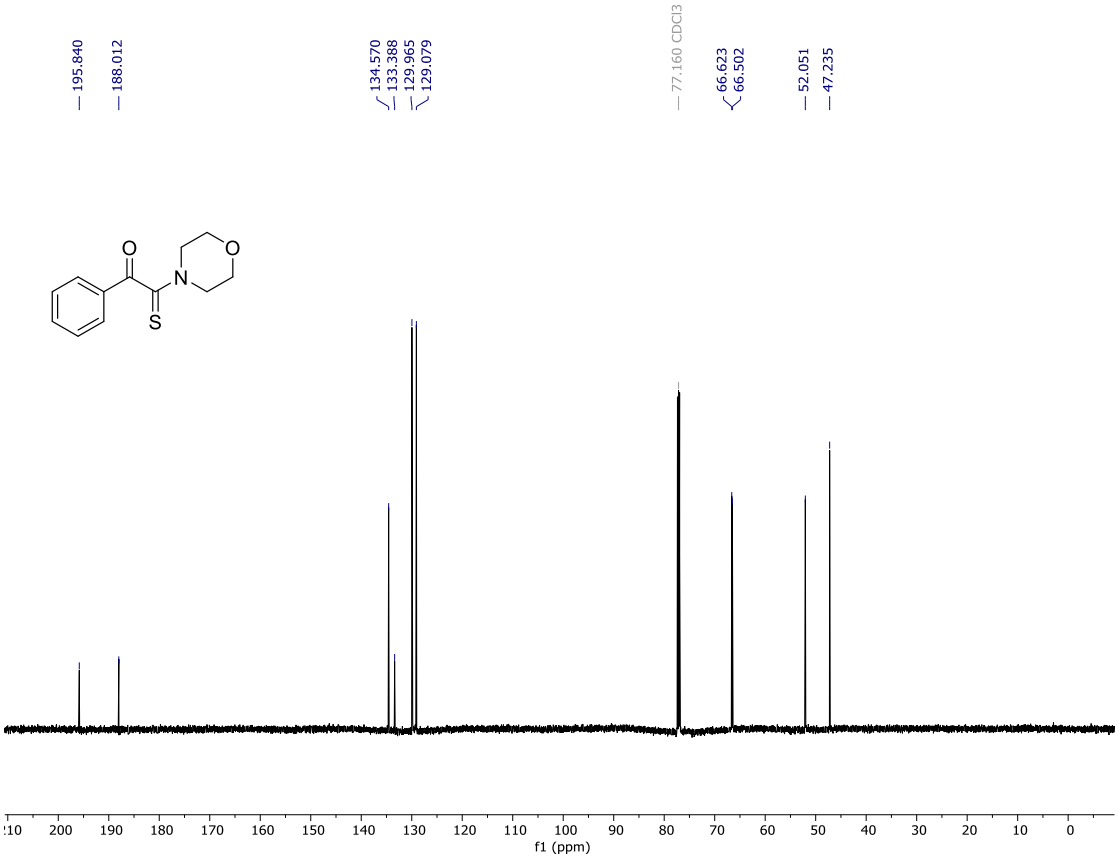
S4. J. Dong, C. Sheng, Y. Chen, C. Ni and Y. Wang, *Tetrahedron Lett.,* 2023, **115**, 154317.

5. NMR spectra

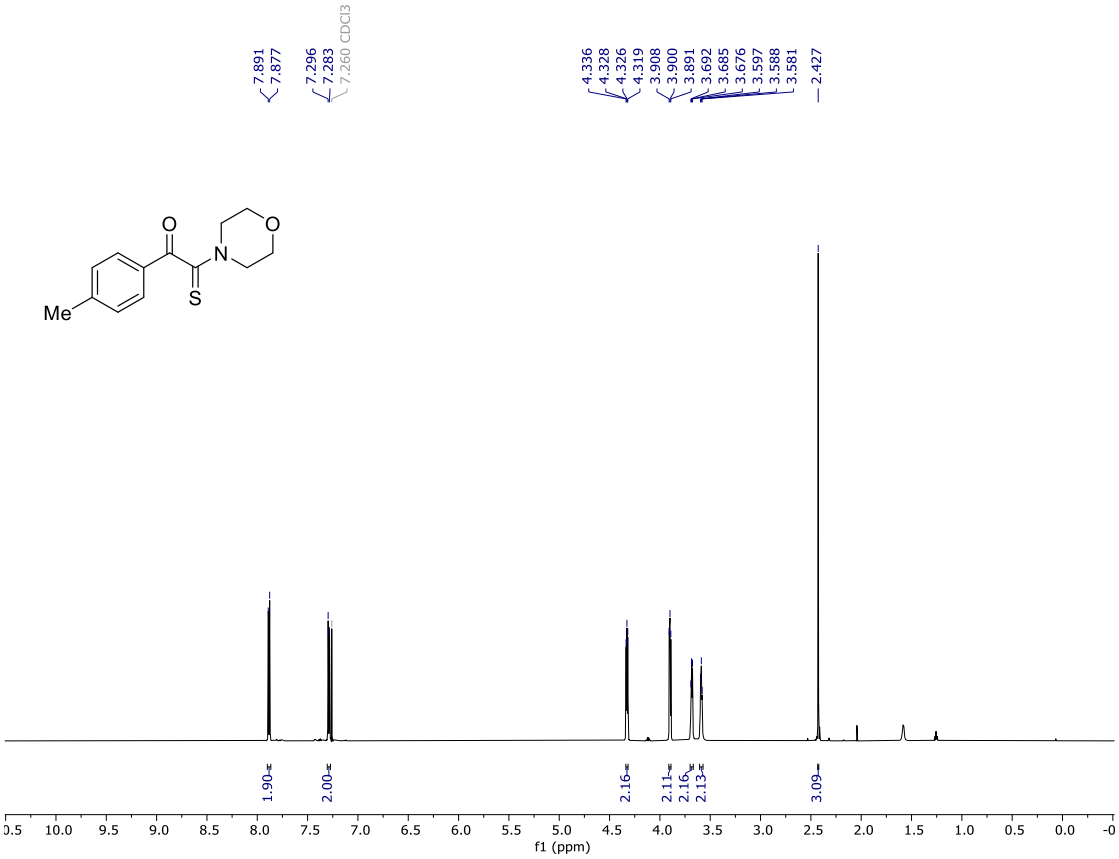
^{1}H NMR spectrum of compound **3aa** (600 MHz, $CDCl_3$)



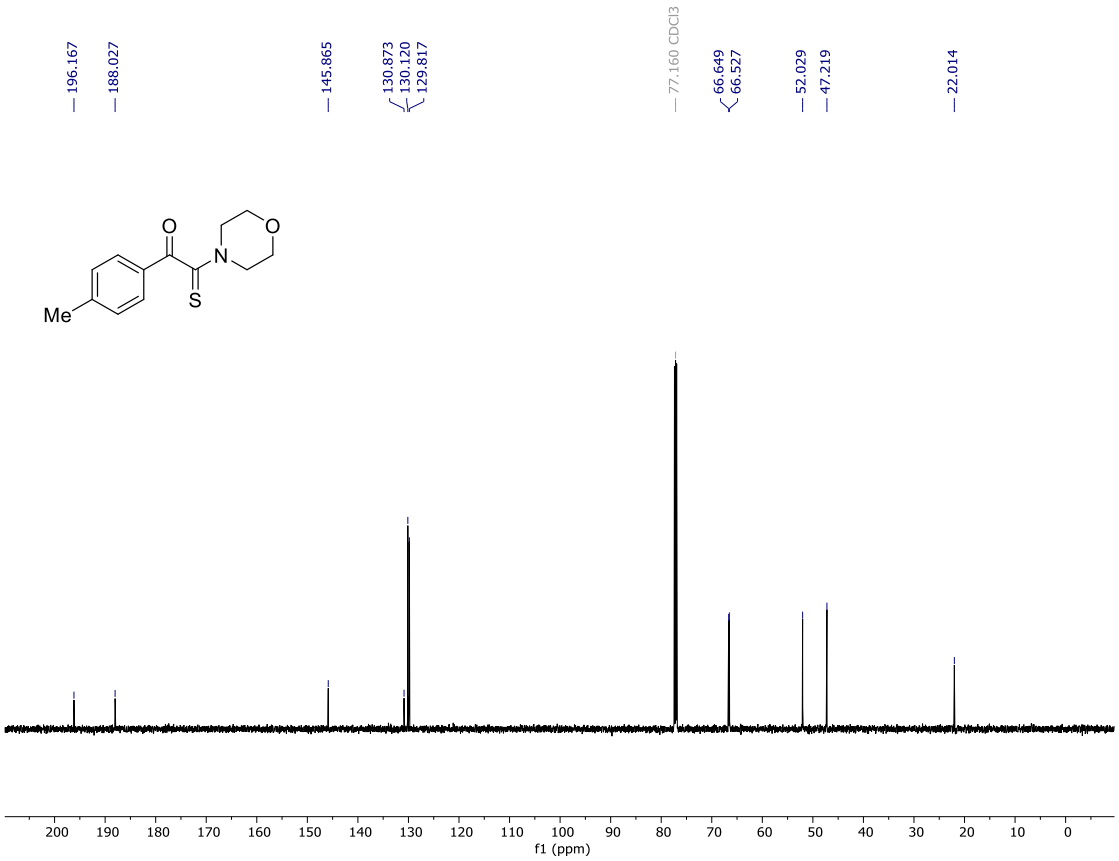
^{13}C {^{1}H} NMR spectrum of compound **3aa** (151 MHz, $CDCl_3$)



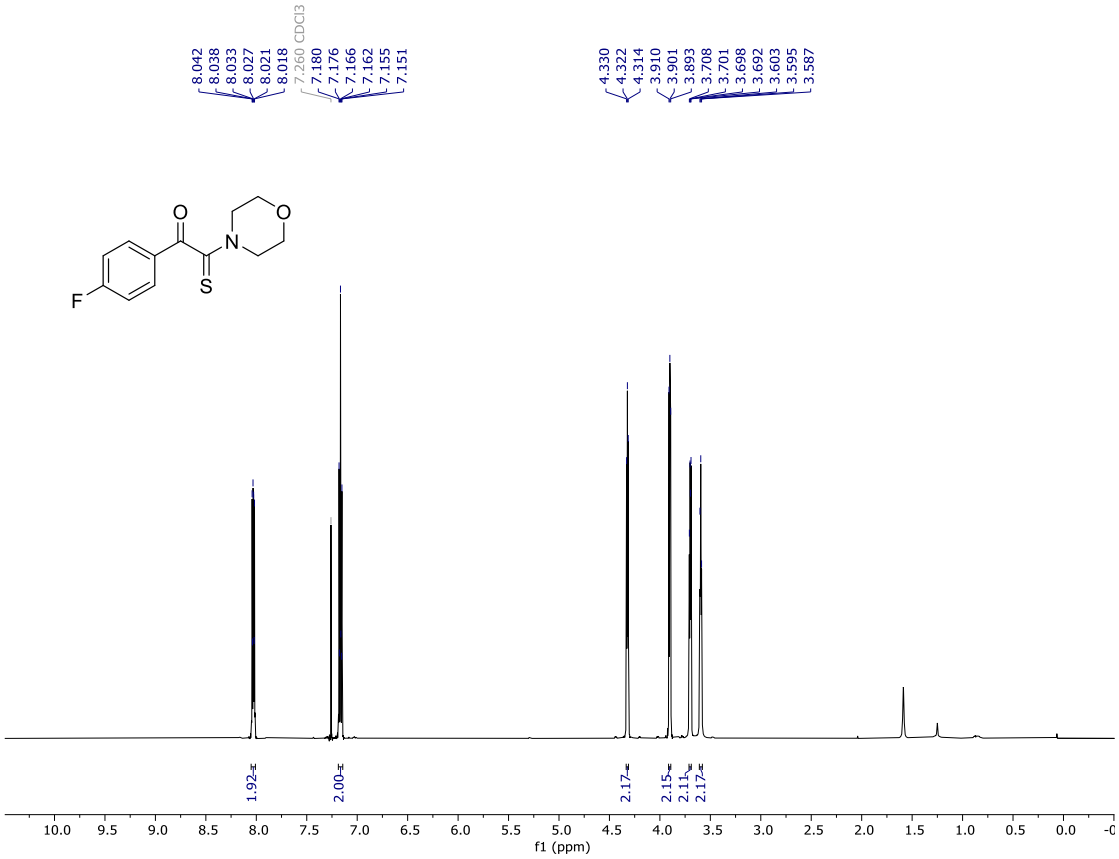
^{1}H NMR spectrum of compound **3ba** (600 MHz, $CDCl_3$)



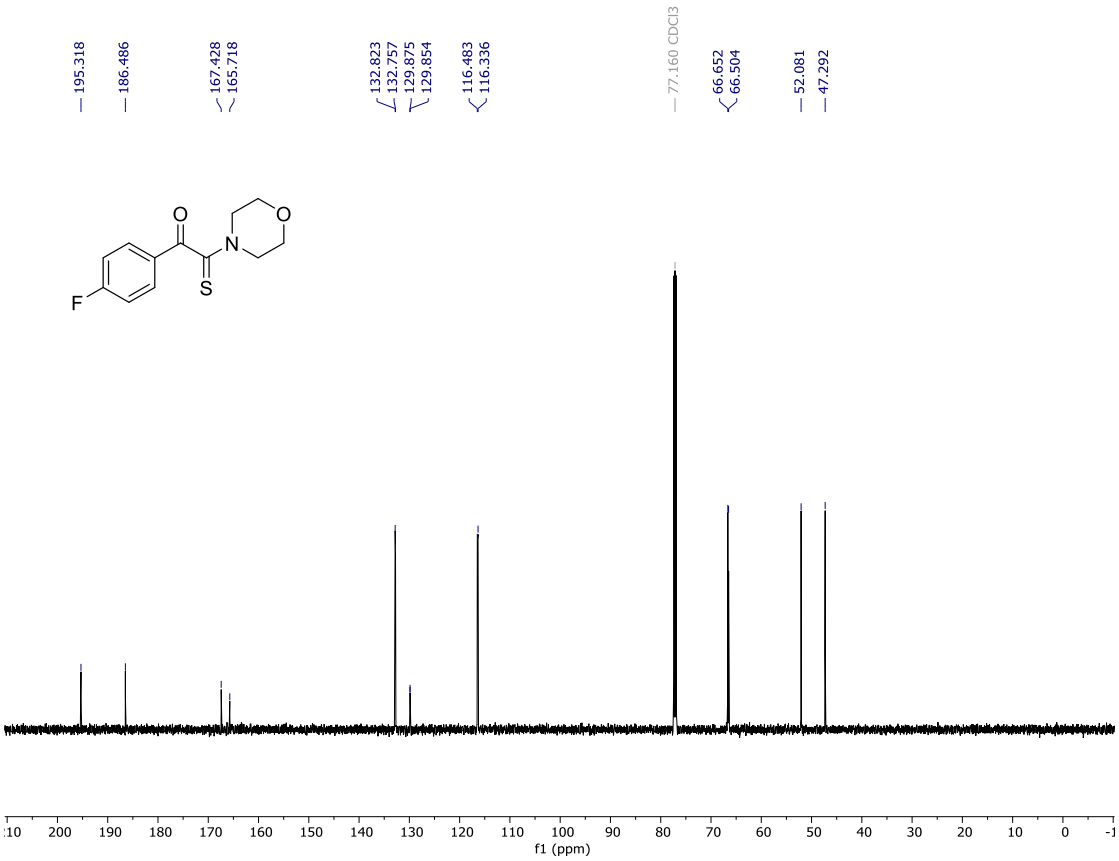
^{13}C {^{1}H} NMR spectrum of compound **3ba** (151 MHz, $CDCl_3$)



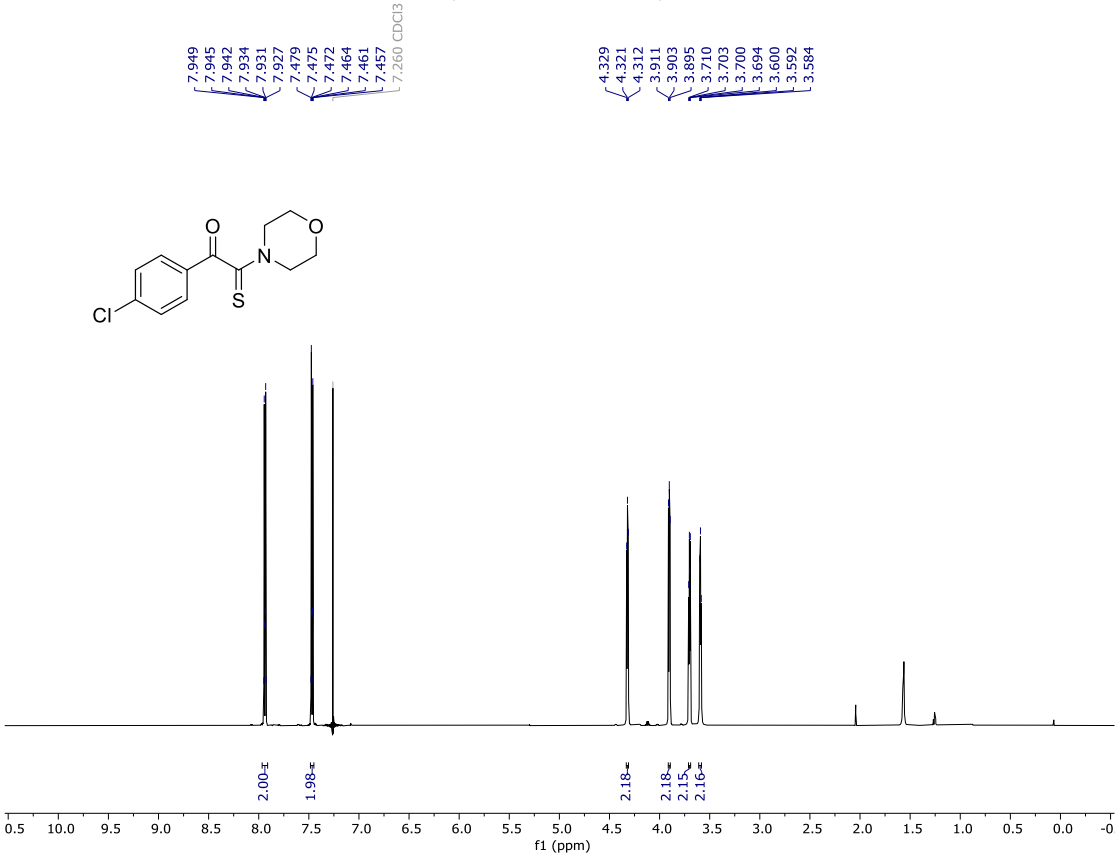
^{1}H NMR spectrum of compound **3ca** (600 MHz, $CDCl_3$)



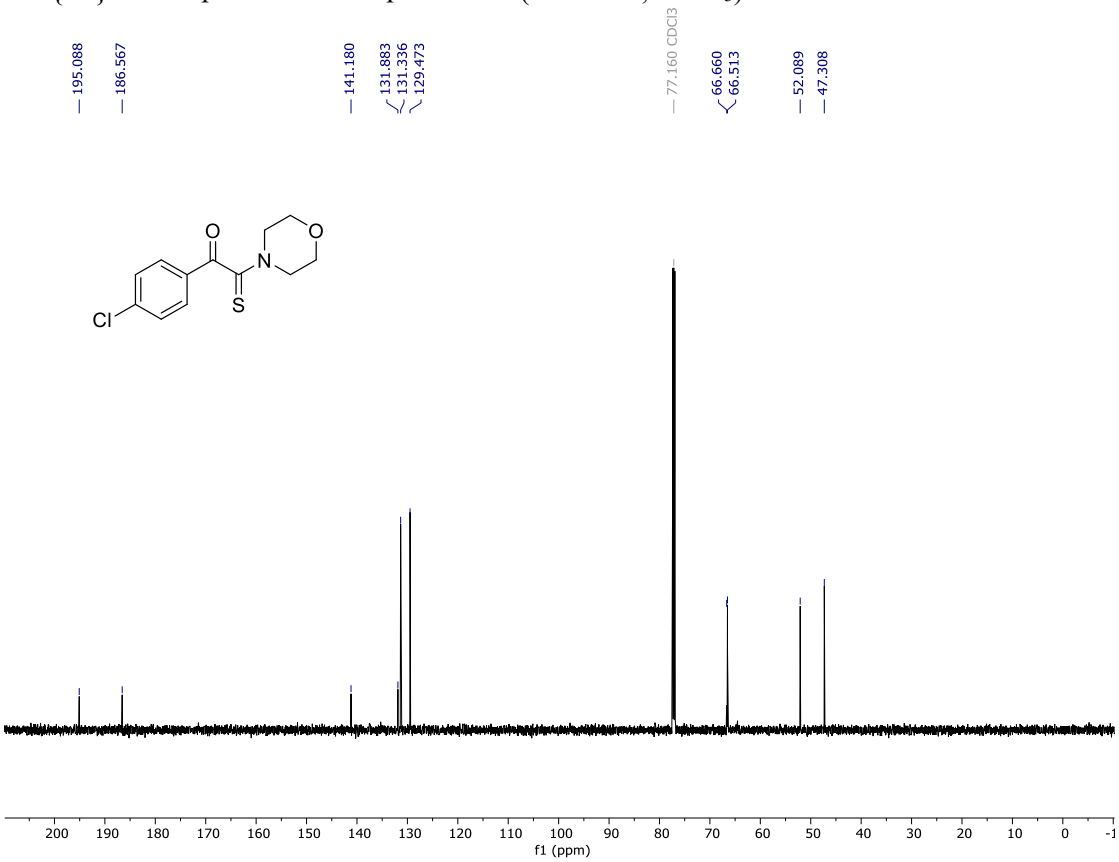
^{13}C {^{1}H} NMR spectrum of compound **3ca** (151 MHz, $CDCl_3$)



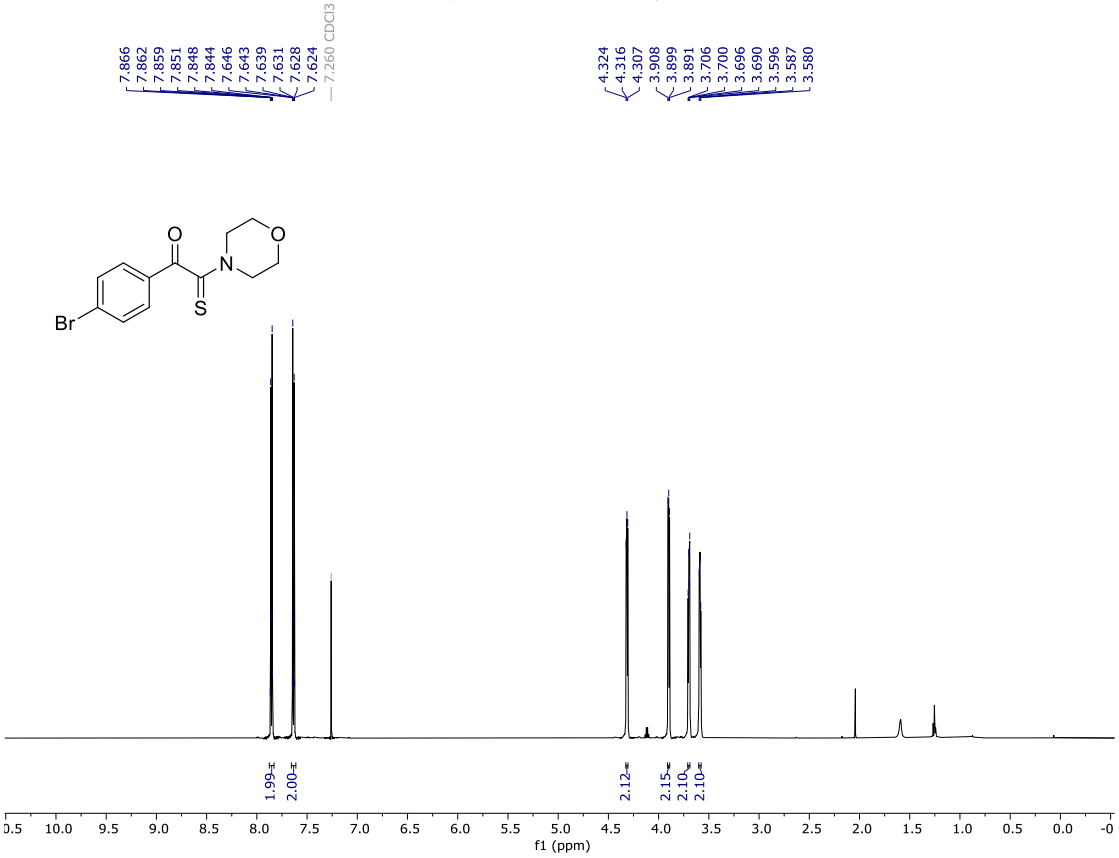
^{1}H NMR spectrum of compound **3da** (600 MHz, $CDCl_3$)



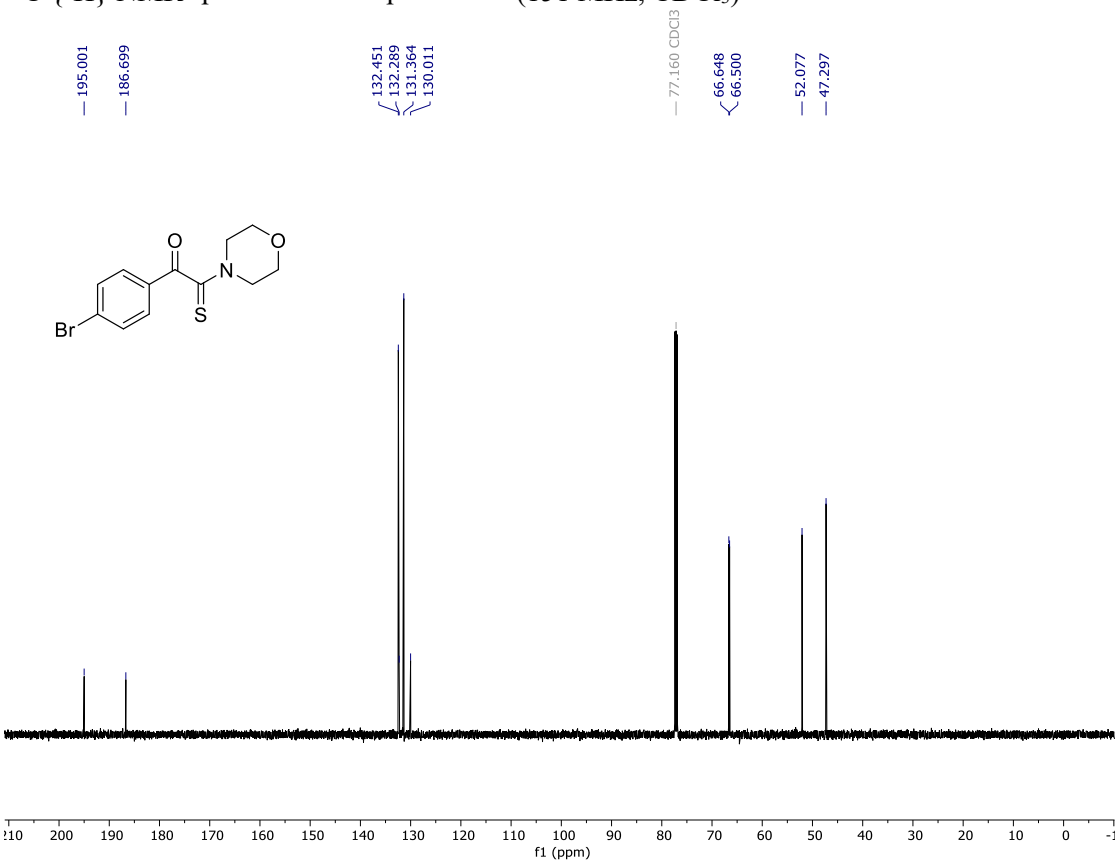
^{13}C {^{1}H} NMR spectrum of compound **3da** (151 MHz, $CDCl_3$)



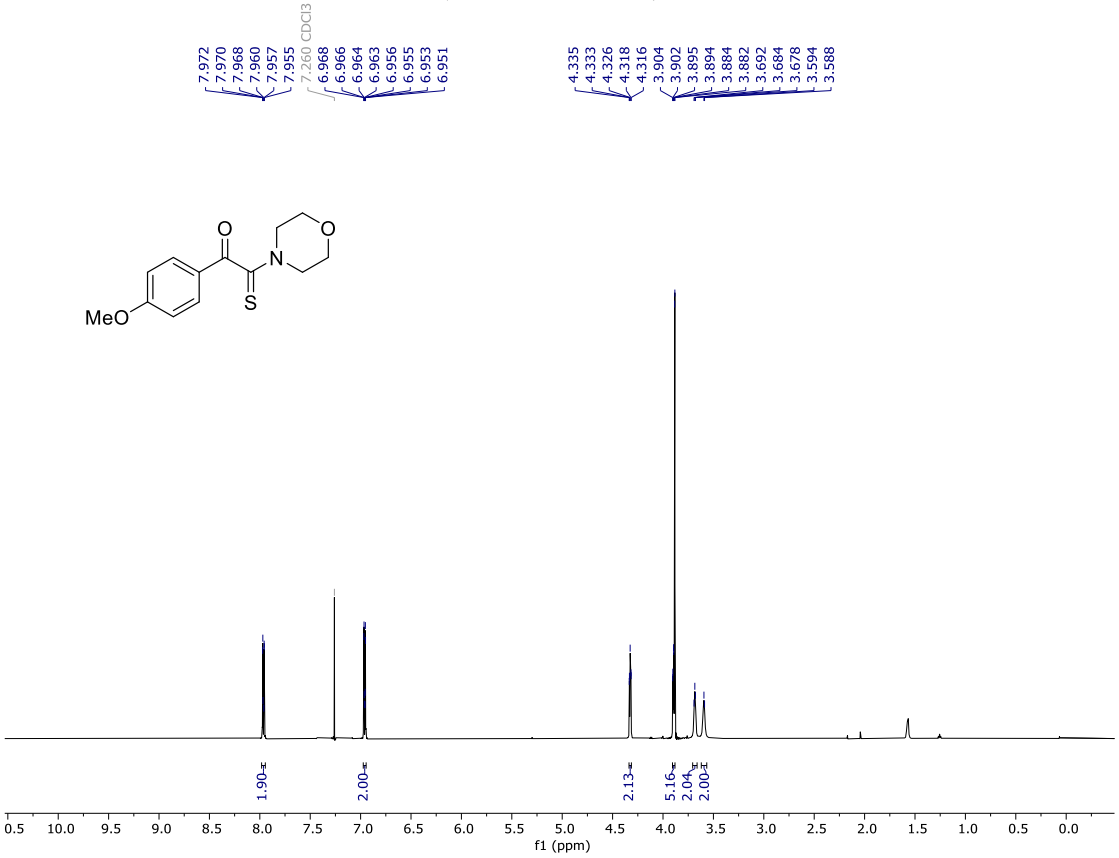
^{1}H NMR spectrum of compound **3ea** (600 MHz, $CDCl_3$)



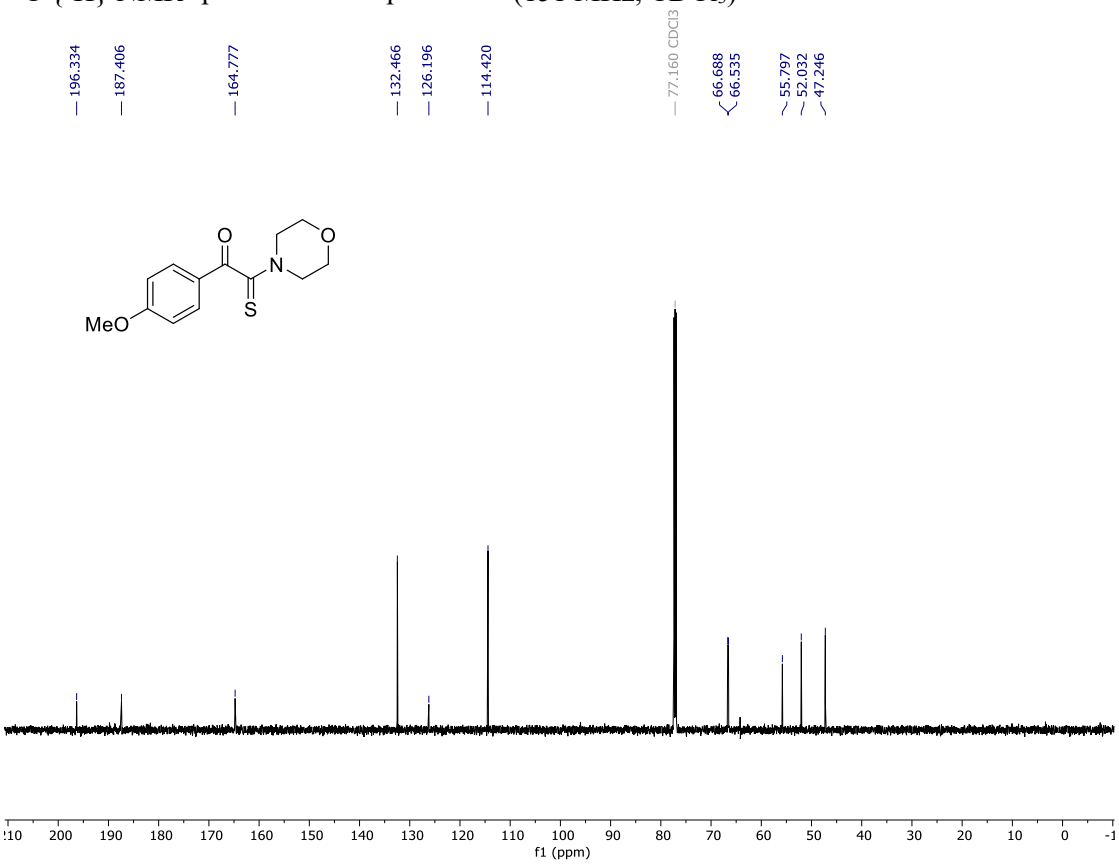
^{13}C {^{1}H} NMR spectrum of compound **3ea** (151 MHz, $CDCl_3$)



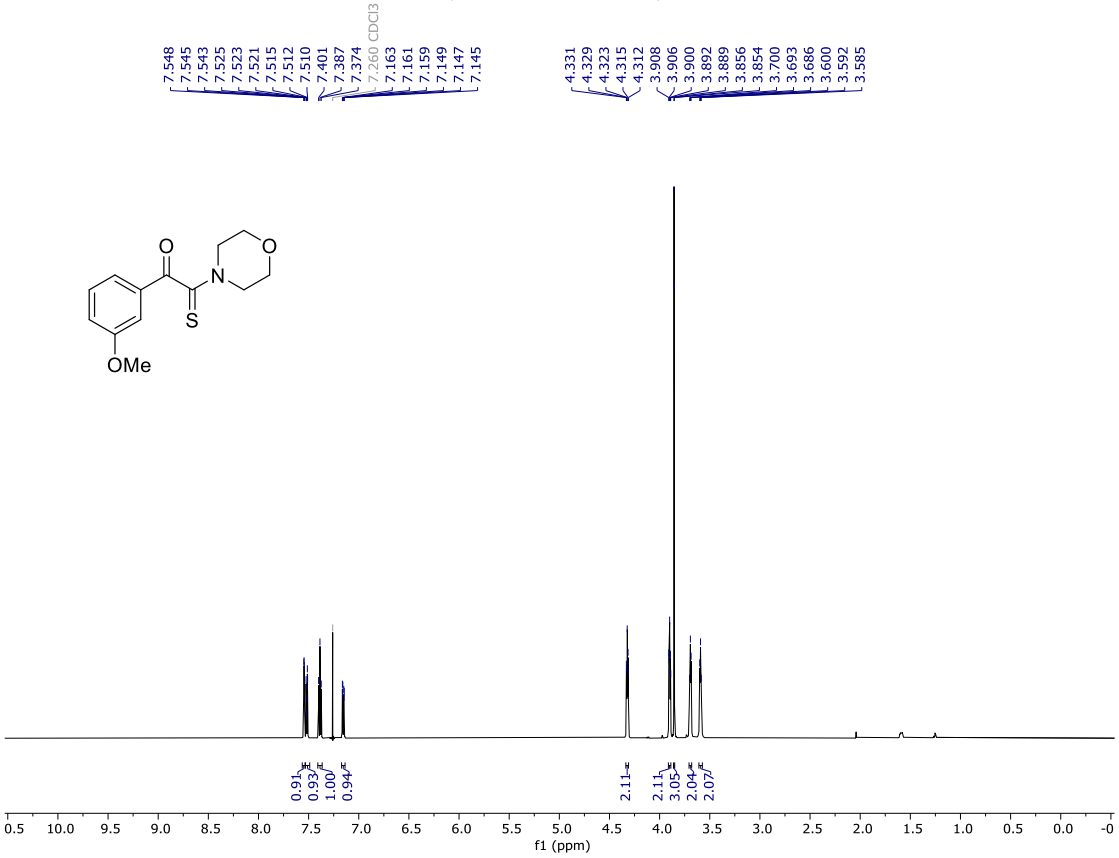
^{1}H NMR spectrum of compound **3fa** (600 MHz, $CDCl_3$)



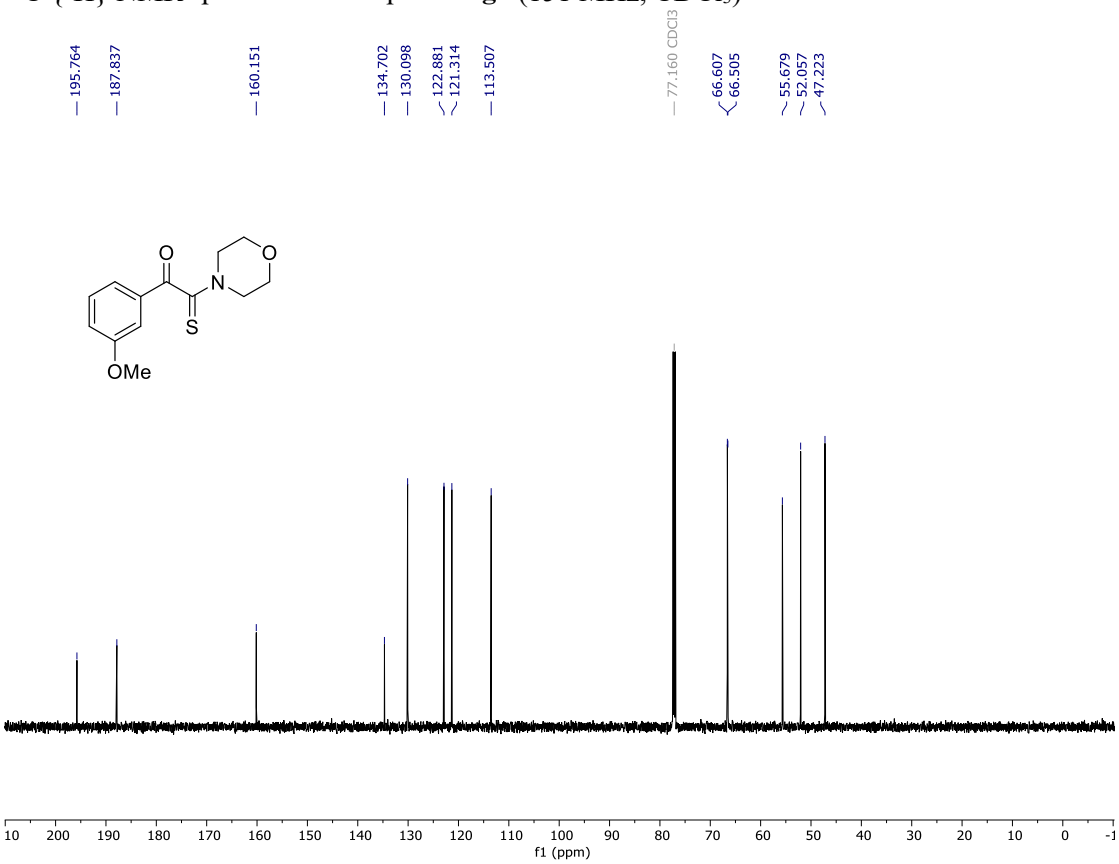
^{13}C {^{1}H} NMR spectrum of compound **3fa** (151 MHz, $CDCl_3$)



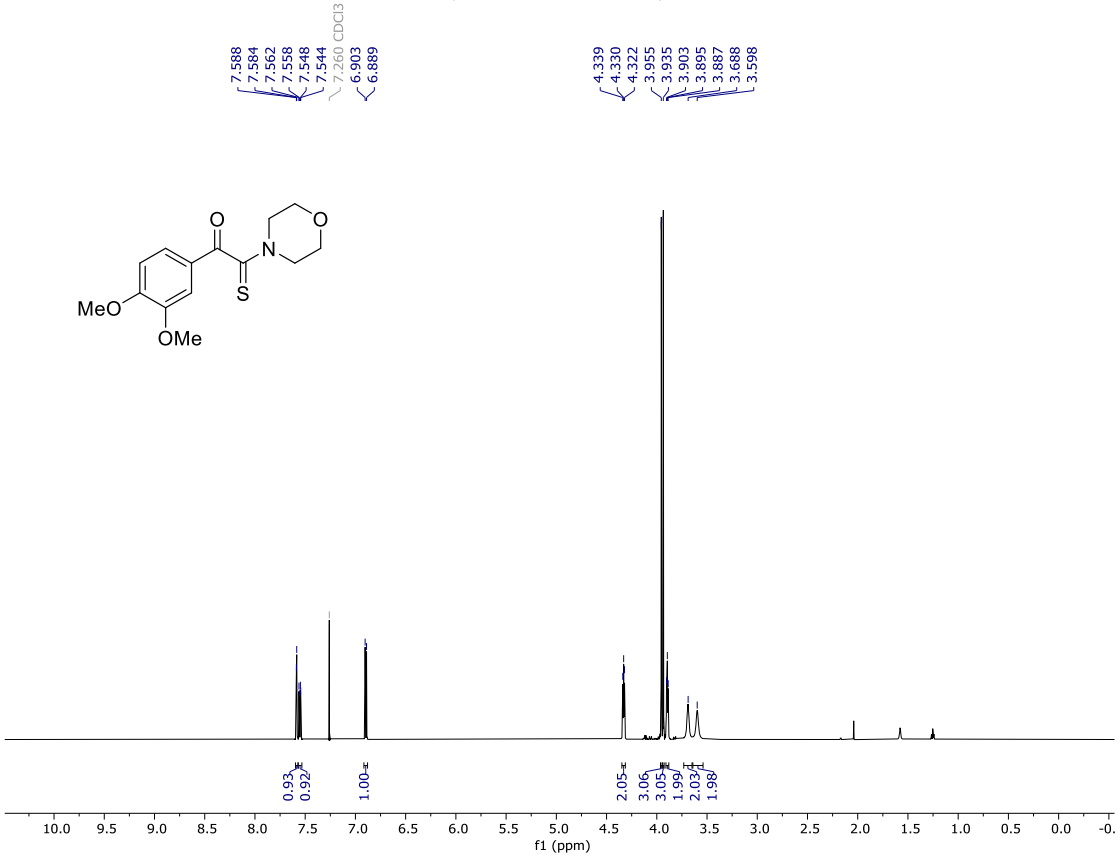
^{1}H NMR spectrum of compound **3ga** (600 MHz, $CDCl_3$)



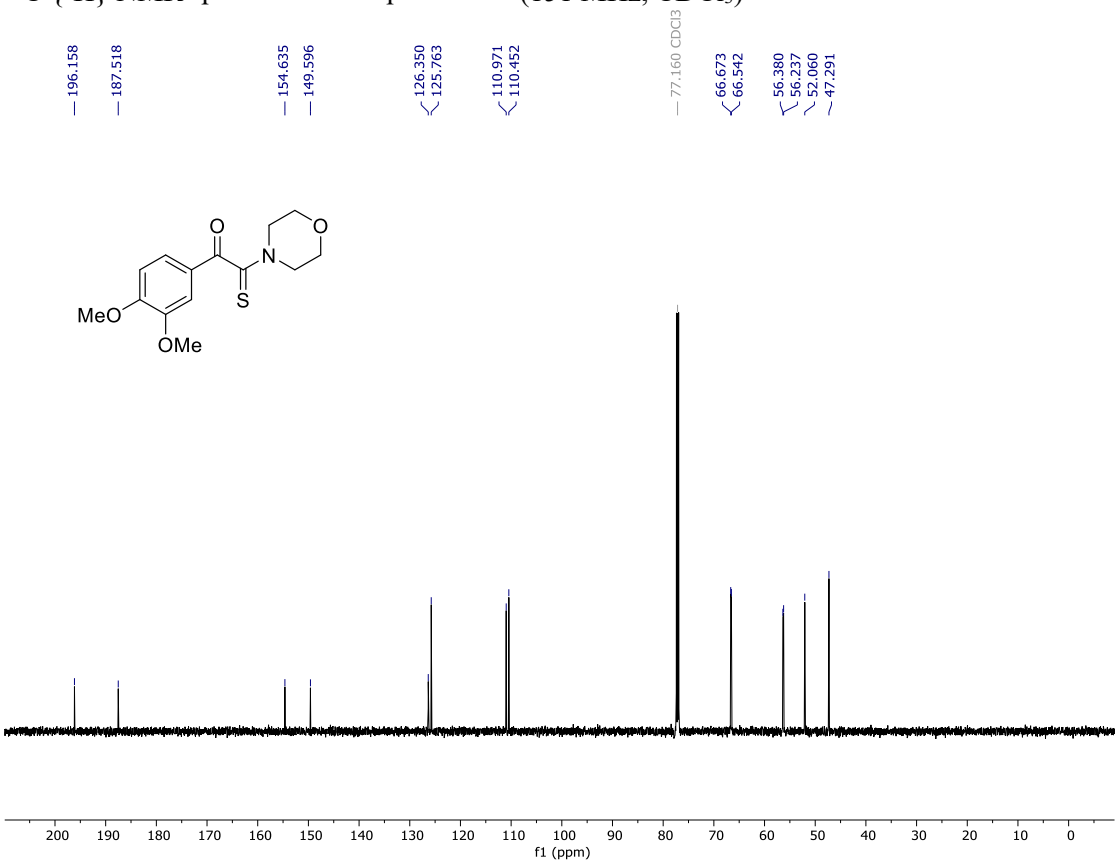
^{13}C {^{1}H} NMR spectrum of compound **3ga** (151 MHz, $CDCl_3$)



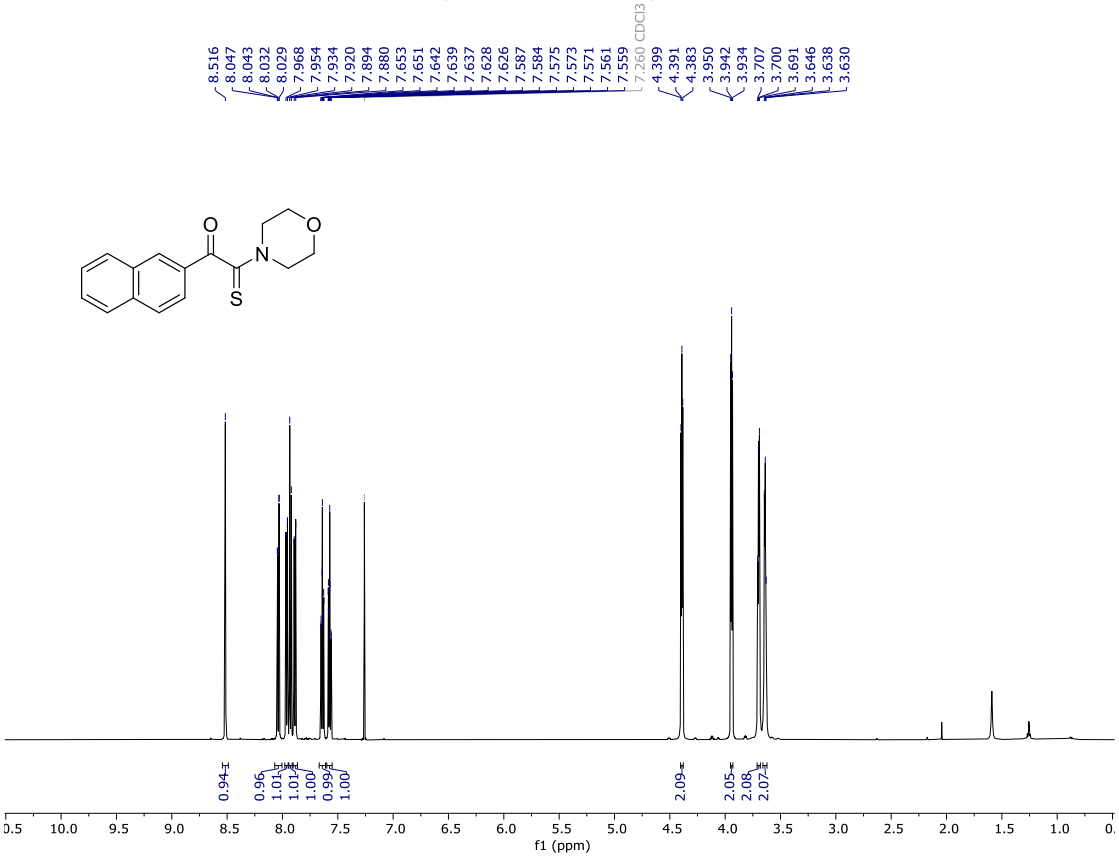
^{1}H NMR spectrum of compound **3ha** (600 MHz, $CDCl_3$)



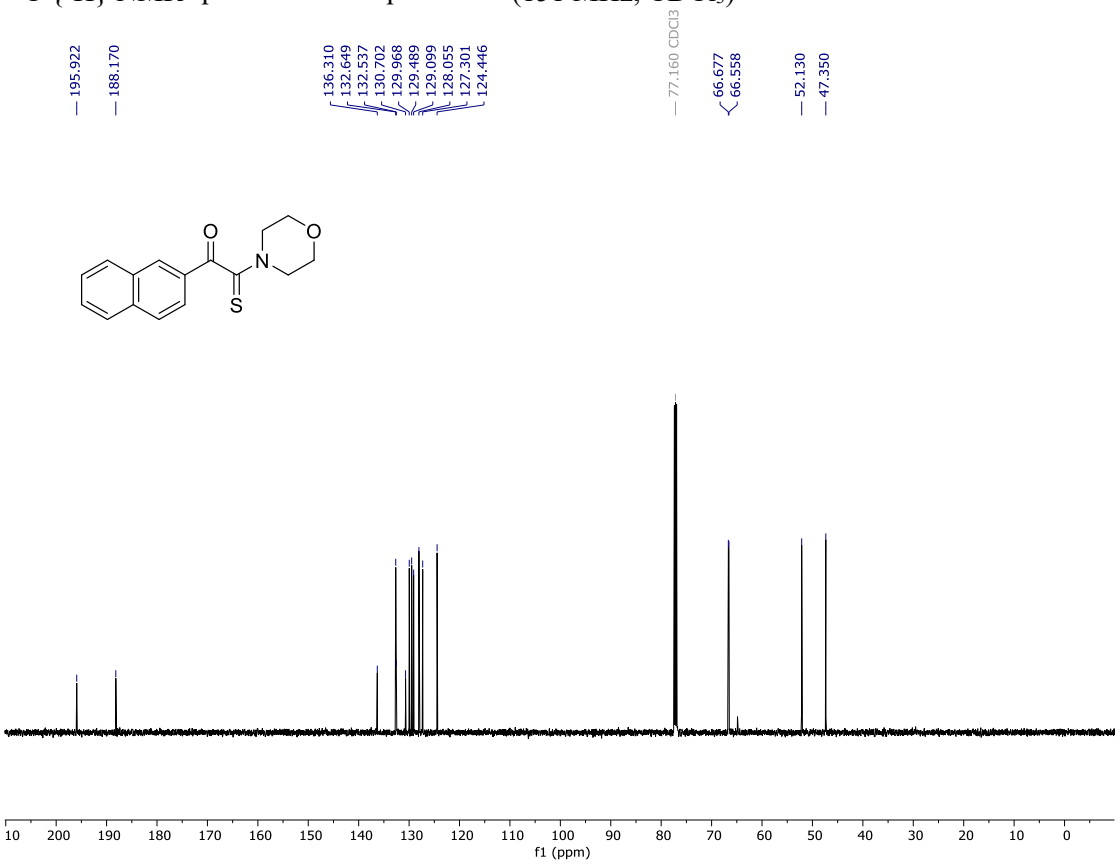
^{13}C {^{1}H} NMR spectrum of compound **3ha** (151 MHz, $CDCl_3$)



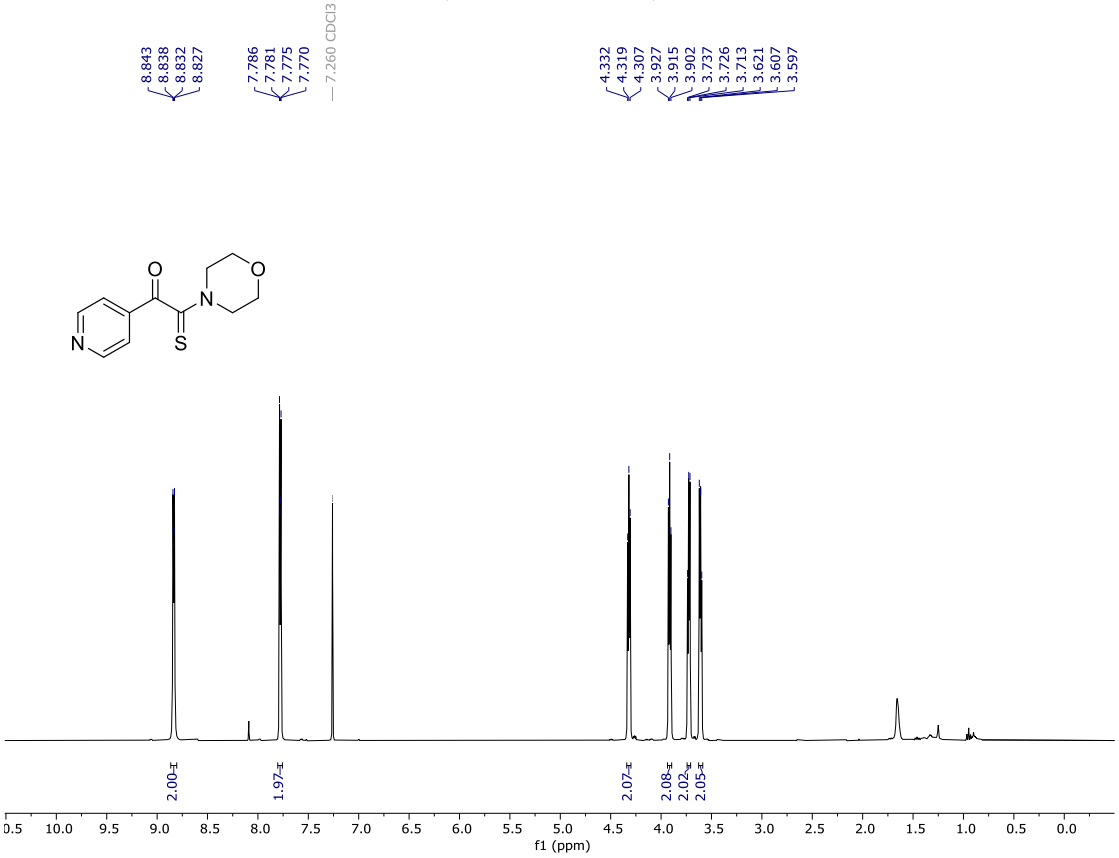
^{1}H NMR spectrum of compound **3ia** (600 MHz, $CDCl_3$)



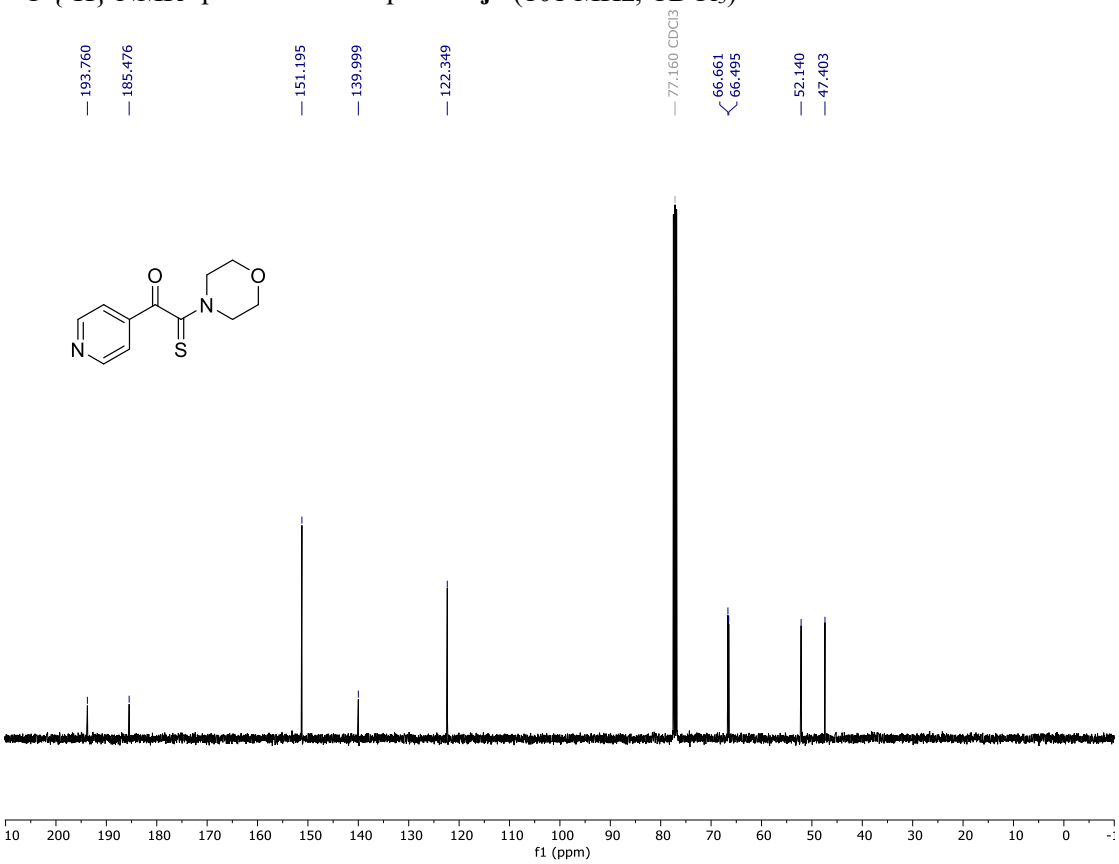
^{13}C {^{1}H} NMR spectrum of compound **3ia** (151 MHz, $CDCl_3$)



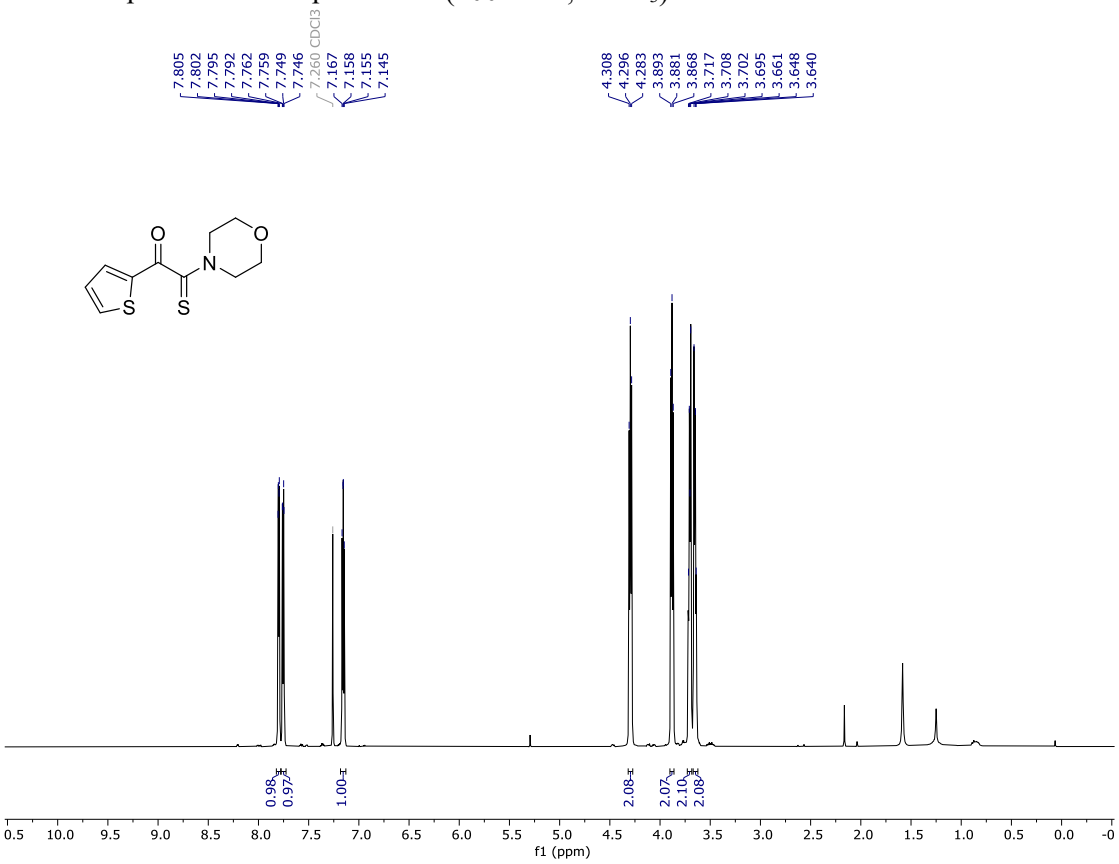
^{1}H NMR spectrum of compound **3ja** (400 MHz, $CDCl_3$)



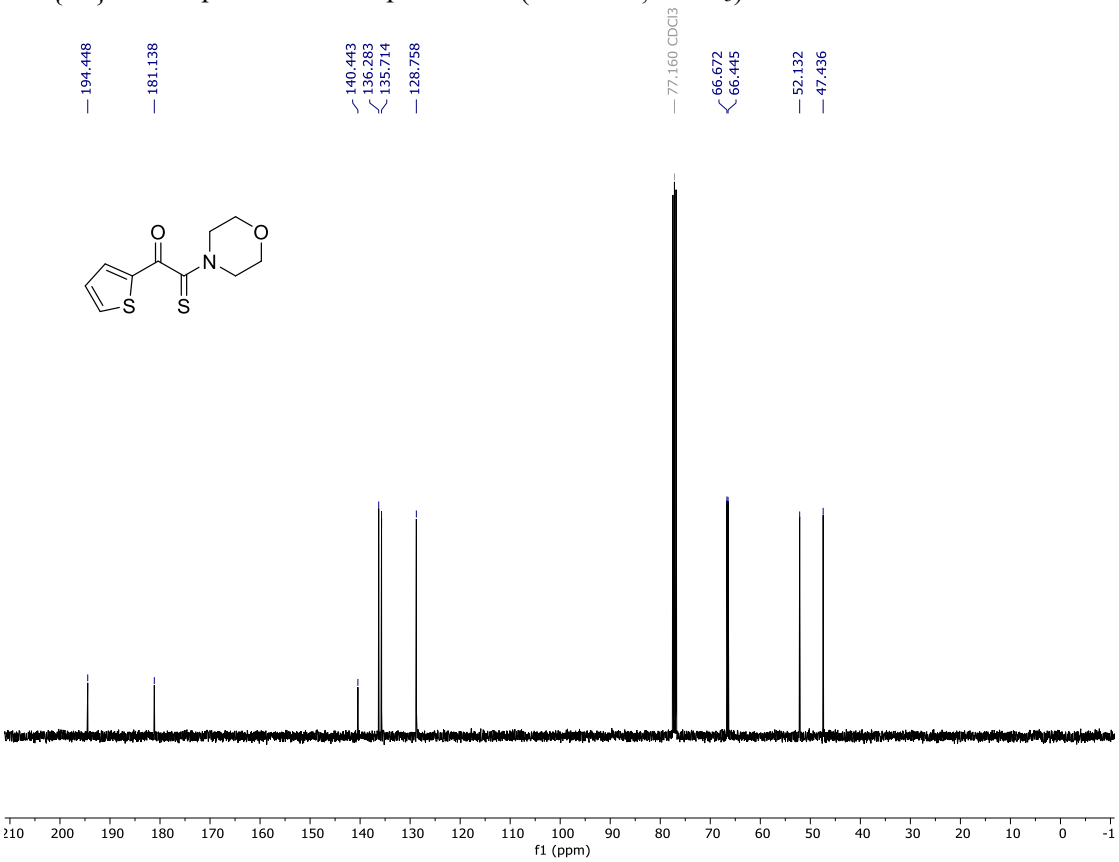
^{13}C {^{1}H} NMR spectrum of compound **3ja** (101 MHz, $CDCl_3$)



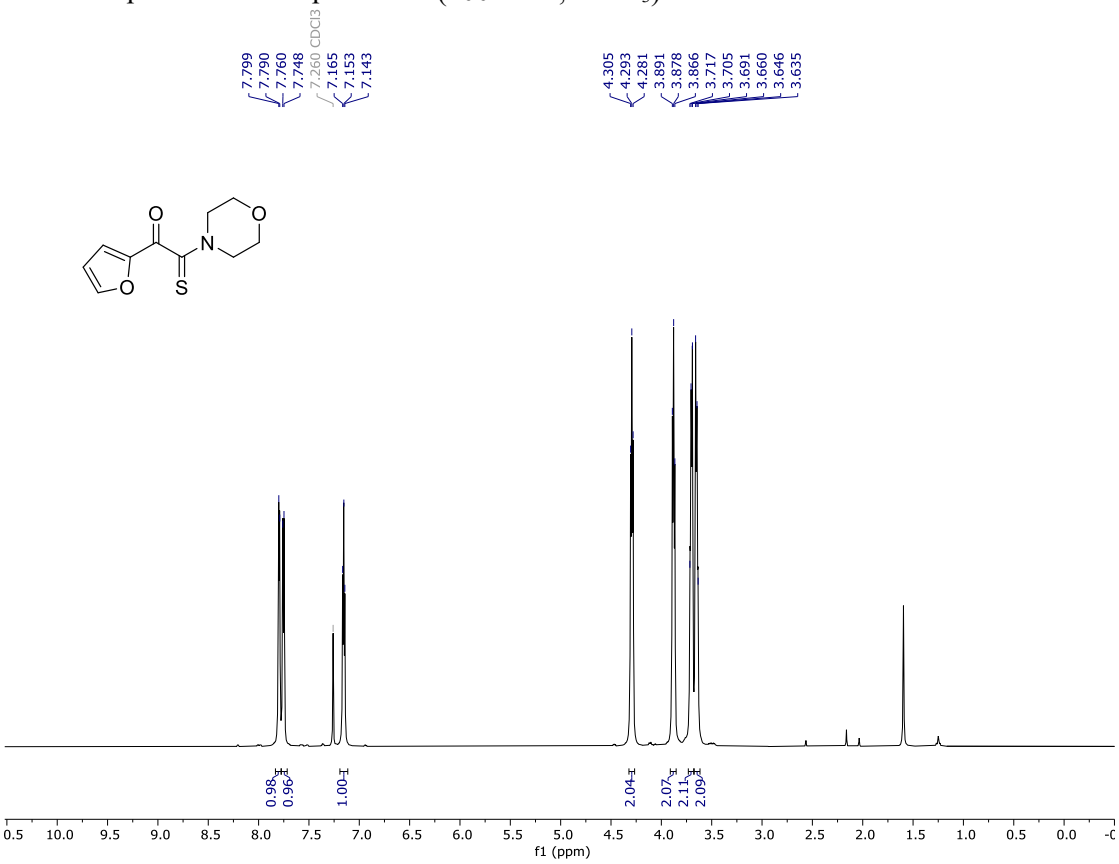
^{1}H NMR spectrum of compound **3ka** (400 MHz, $CDCl_3$)



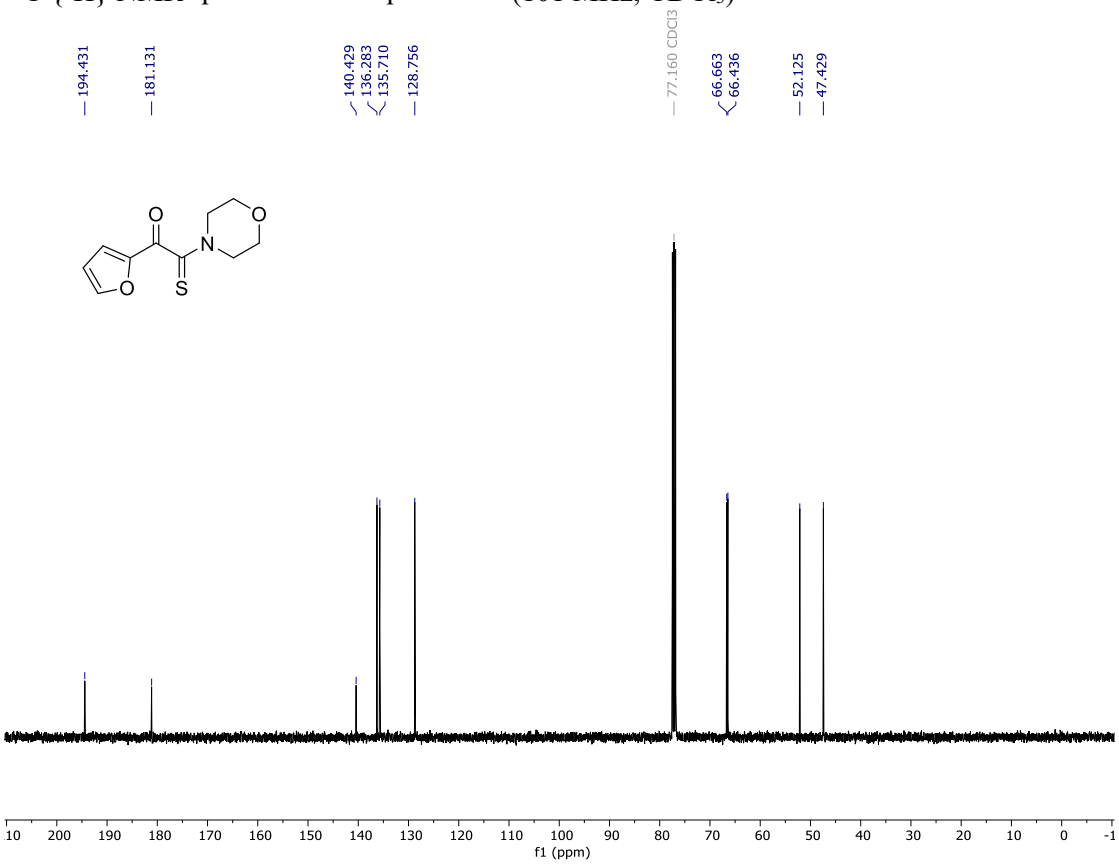
^{13}C {^{1}H} NMR spectrum of compound **3ka** (101 MHz, $CDCl_3$)



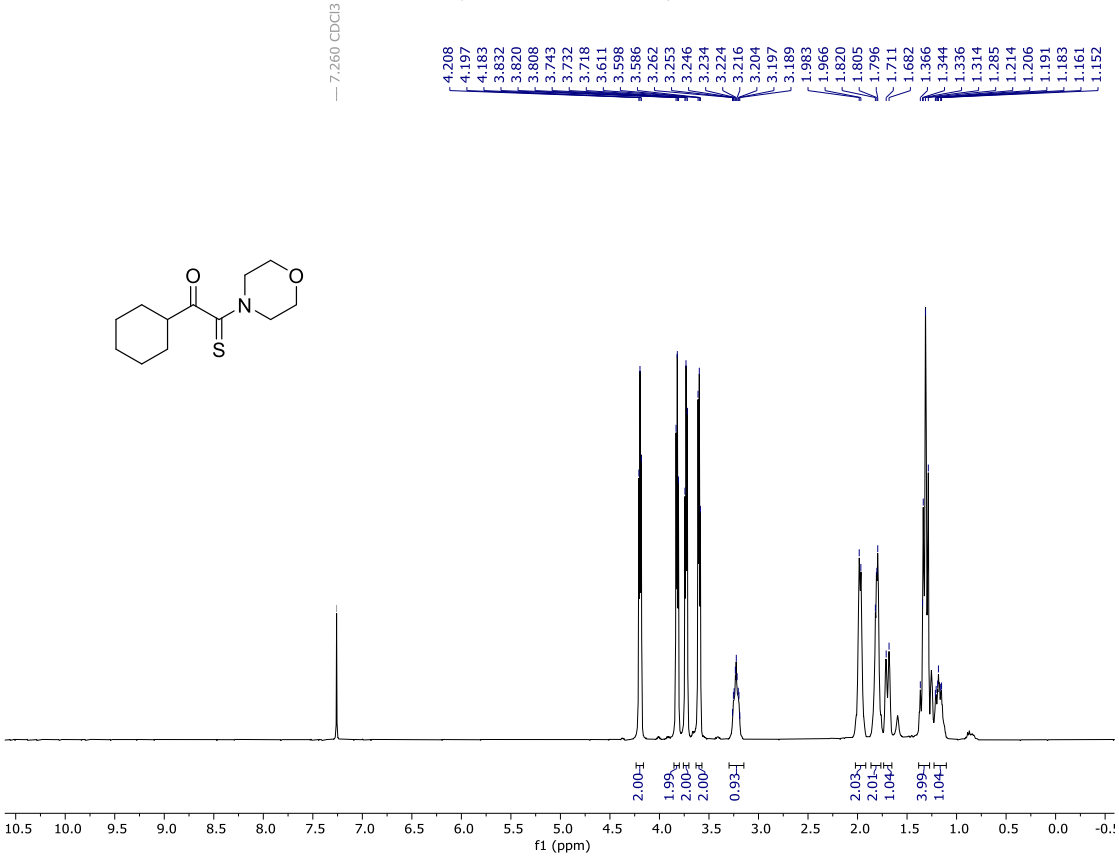
^{1}H NMR spectrum of compound **3la** (400 MHz, $CDCl_3$)



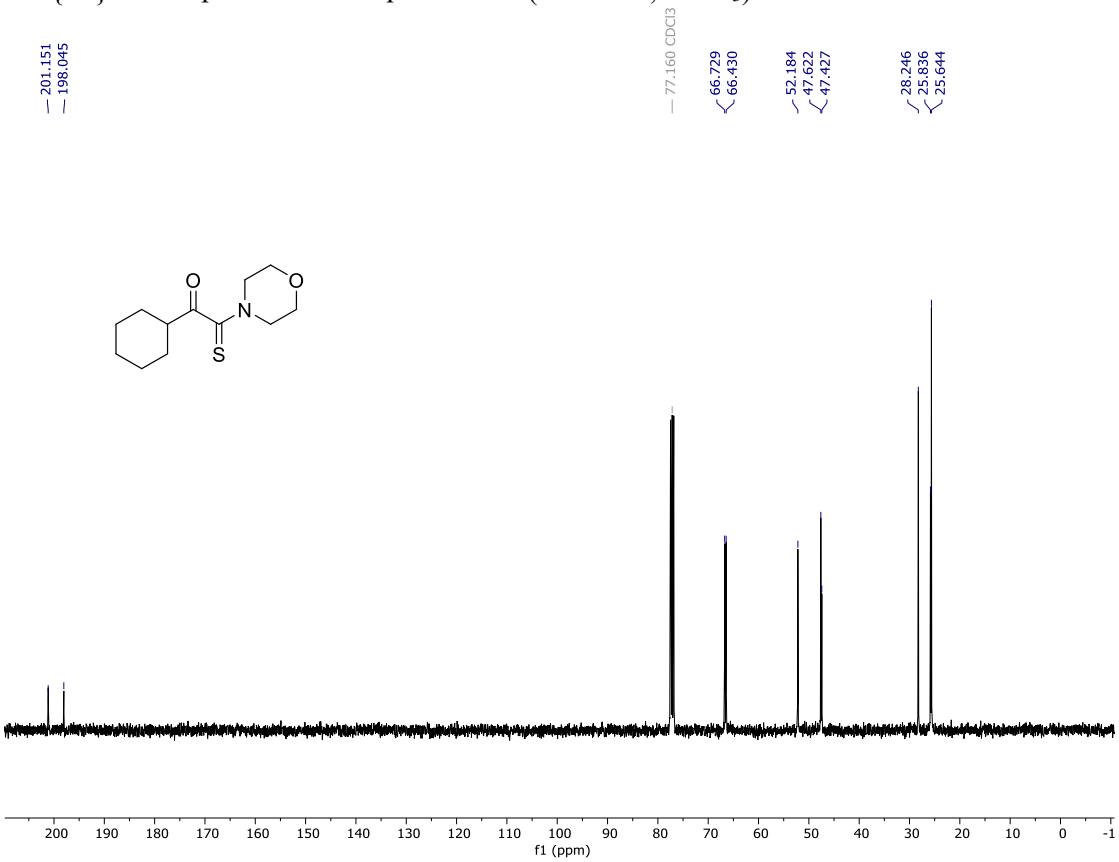
^{13}C {^{1}H} NMR spectrum of compound **3la** (101 MHz, $CDCl_3$)



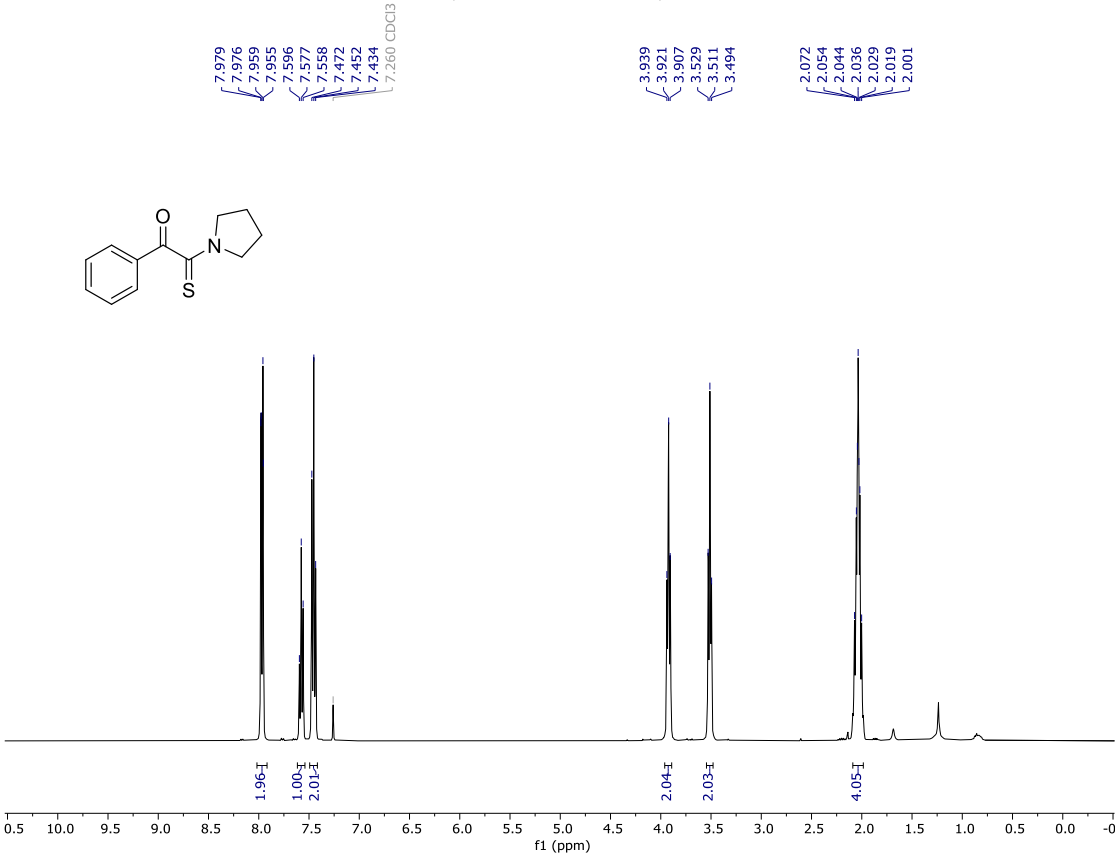
^{1}H NMR spectrum of compound **3ma** (400 MHz, $CDCl_3$)



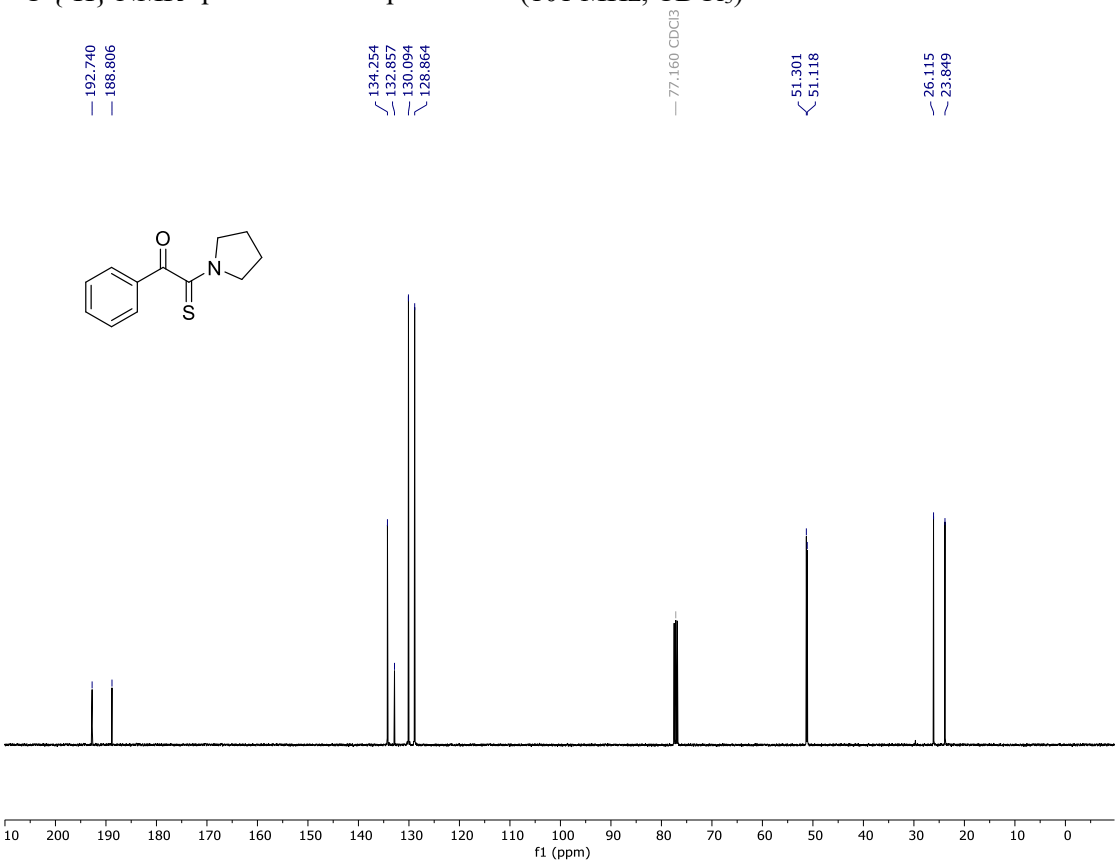
^{13}C {^{1}H} NMR spectrum of compound **3ma** (101 MHz, $CDCl_3$)



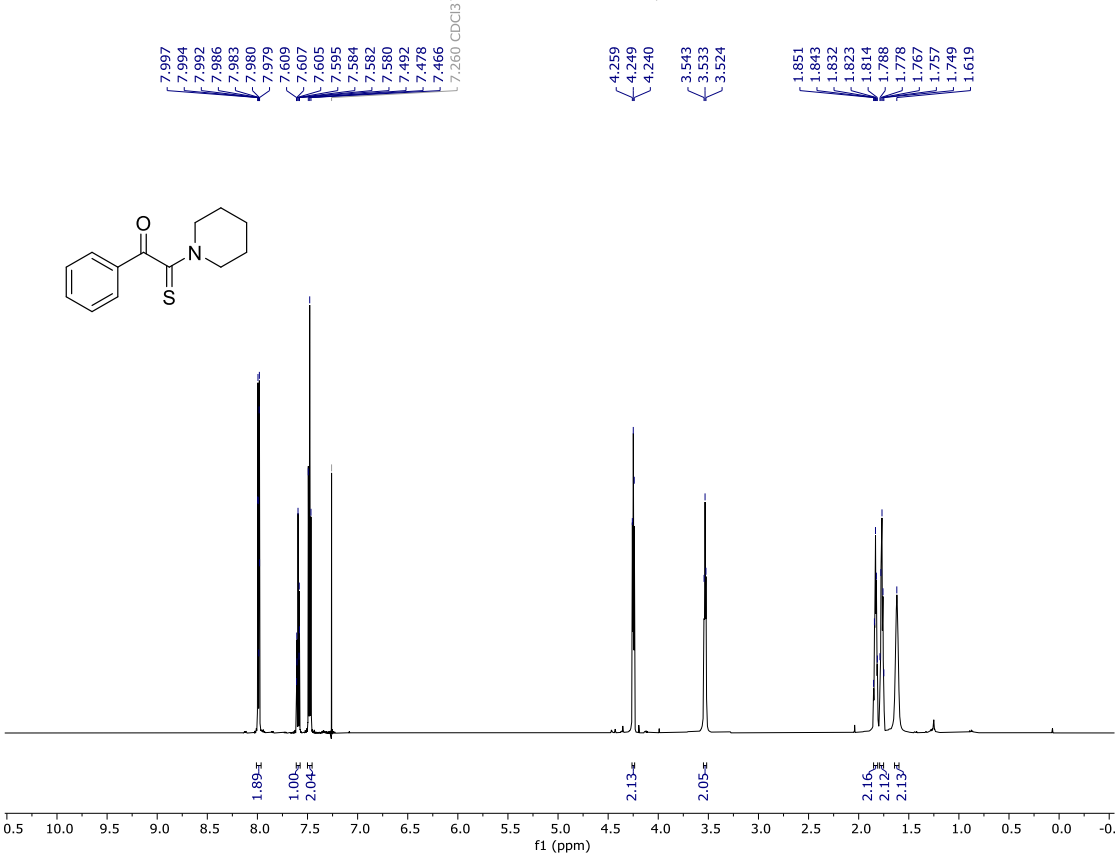
^{1}H NMR spectrum of compound **3ab** (400 MHz, $CDCl_3$)



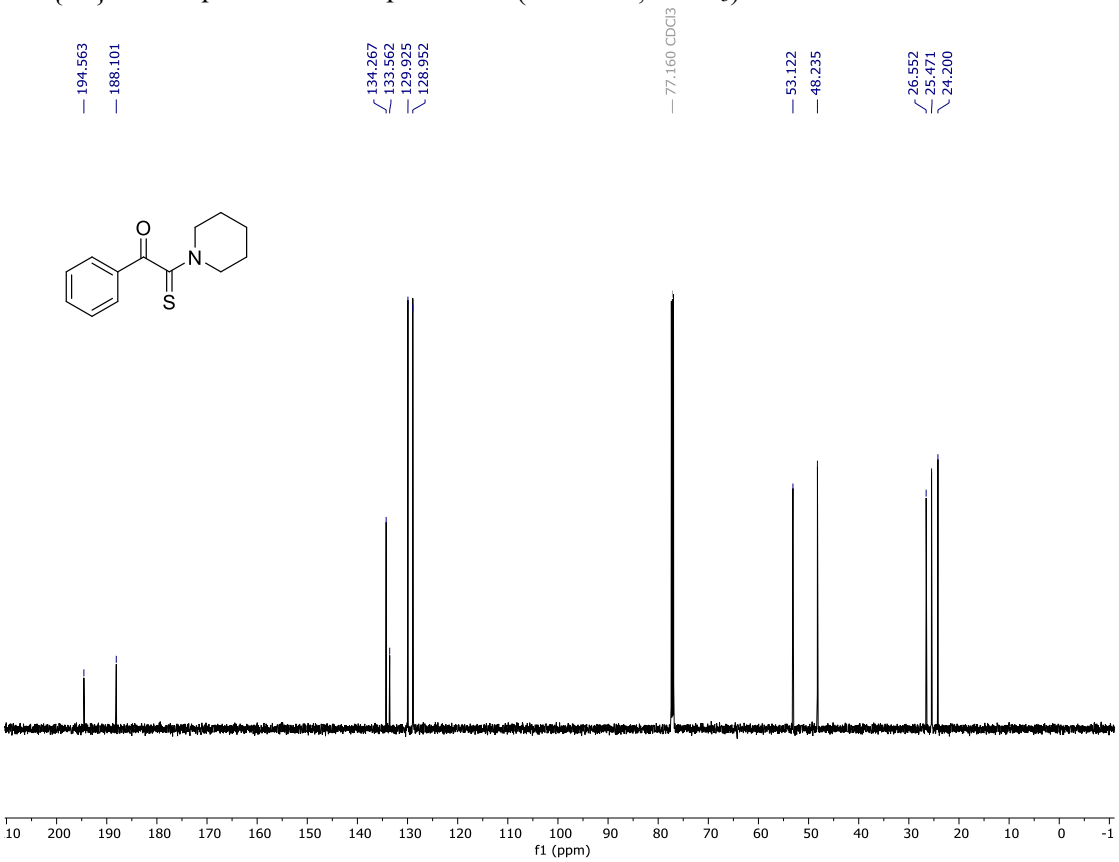
^{13}C {^{1}H} NMR spectrum of compound **3ab** (101 MHz, $CDCl_3$)



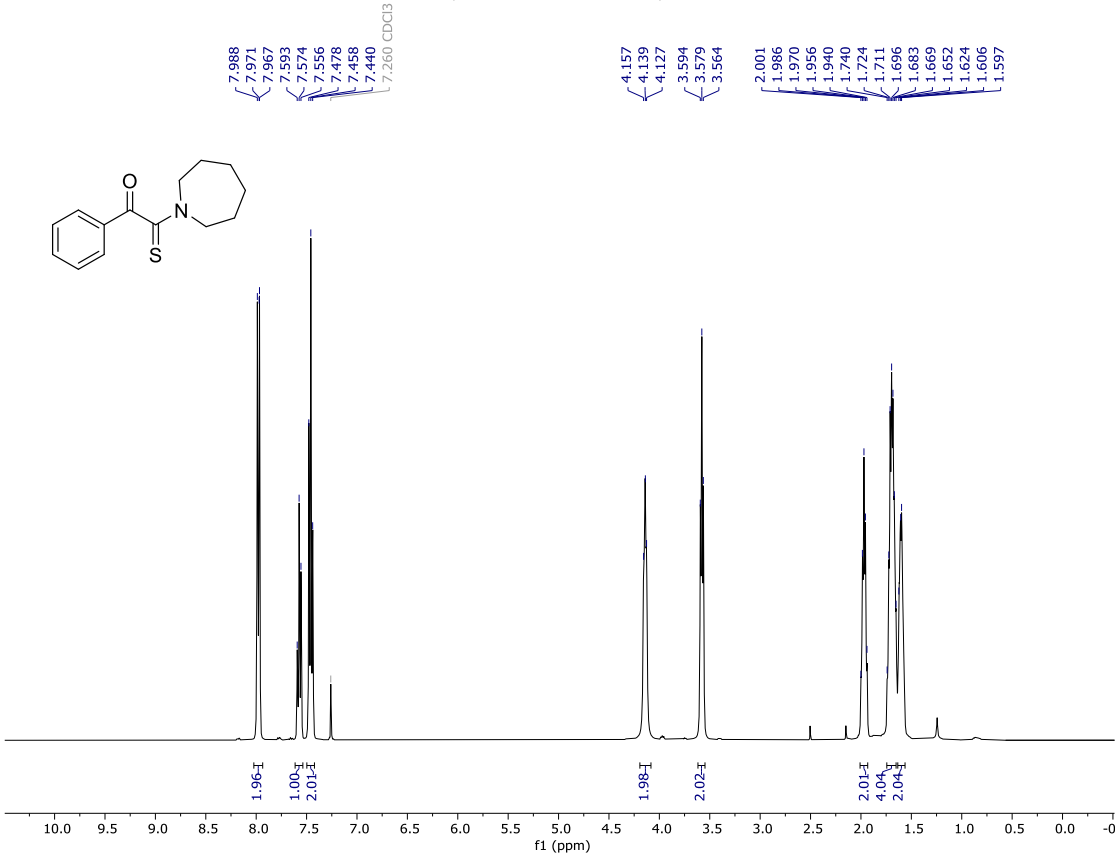
^{1}H NMR spectrum of compound **3ac** (600 MHz, $CDCl_3$)



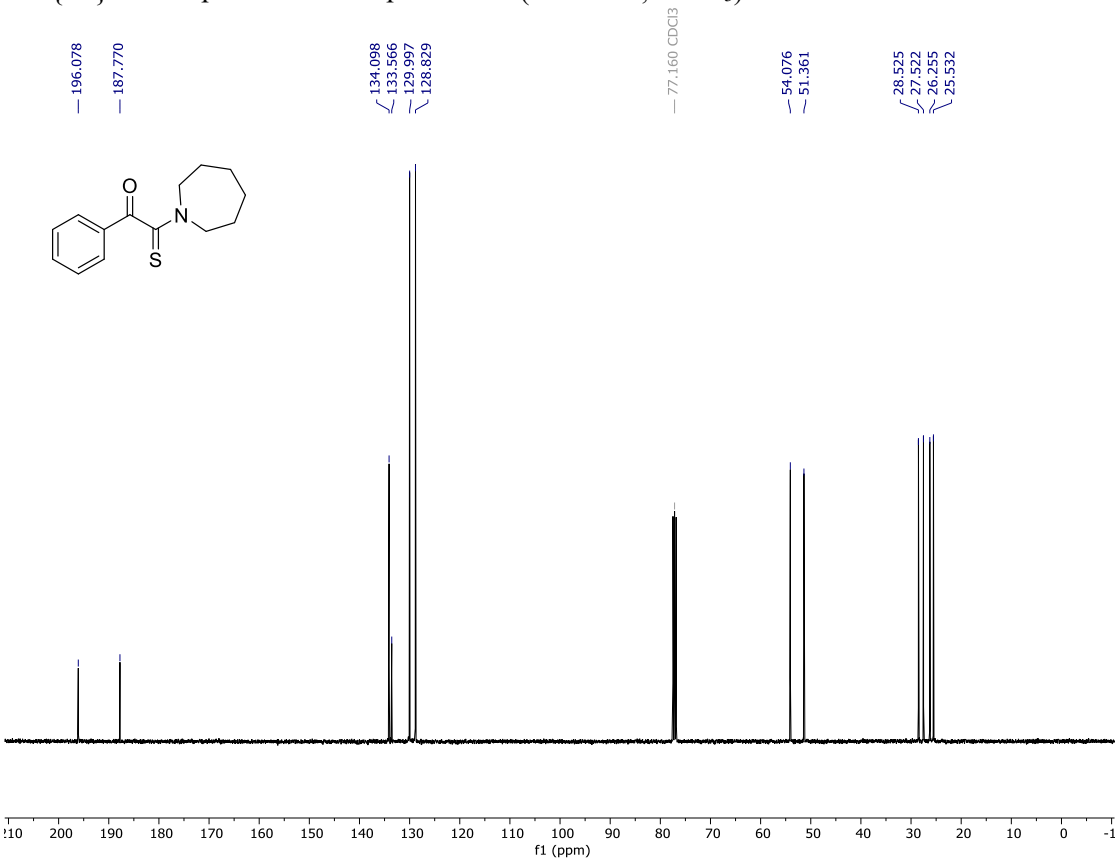
^{13}C {^{1}H} NMR spectrum of compound **3ac** (151 MHz, $CDCl_3$)



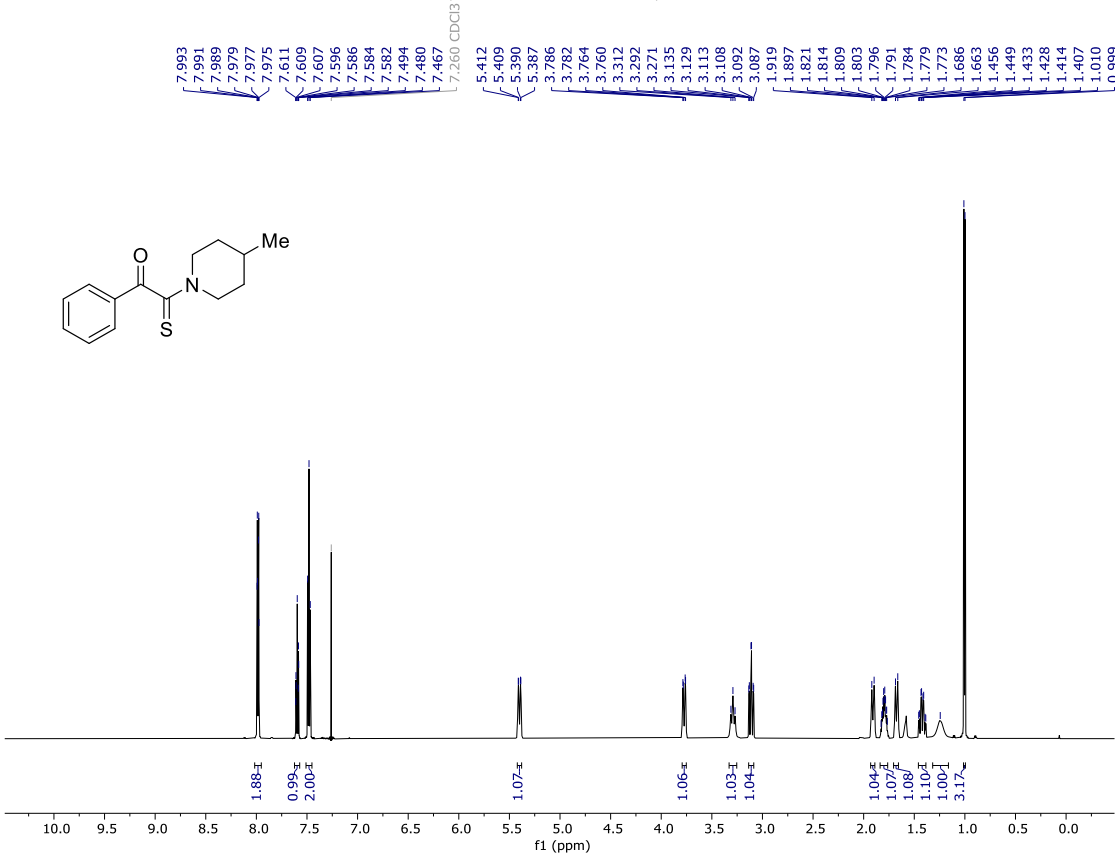
^{1}H NMR spectrum of compound **3ad** (400 MHz, $CDCl_3$)



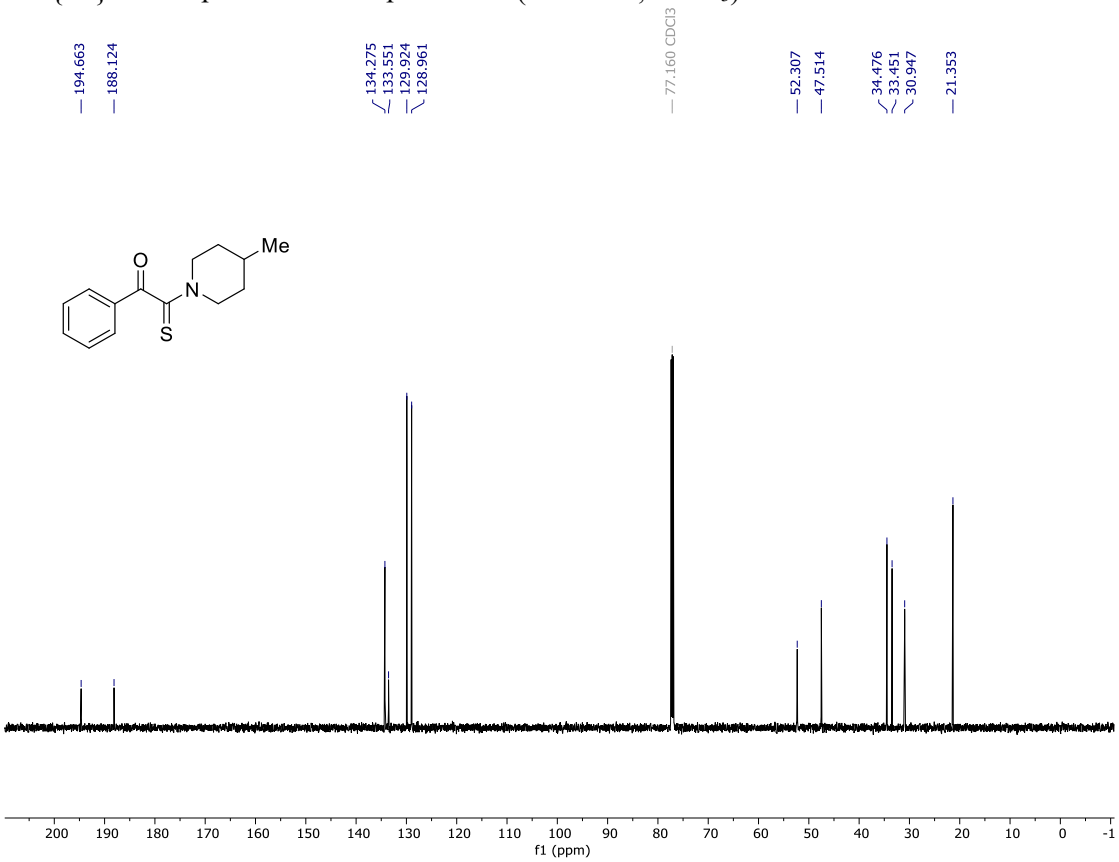
^{13}C {^{1}H} NMR spectrum of compound **3ad** (101 MHz, $CDCl_3$)



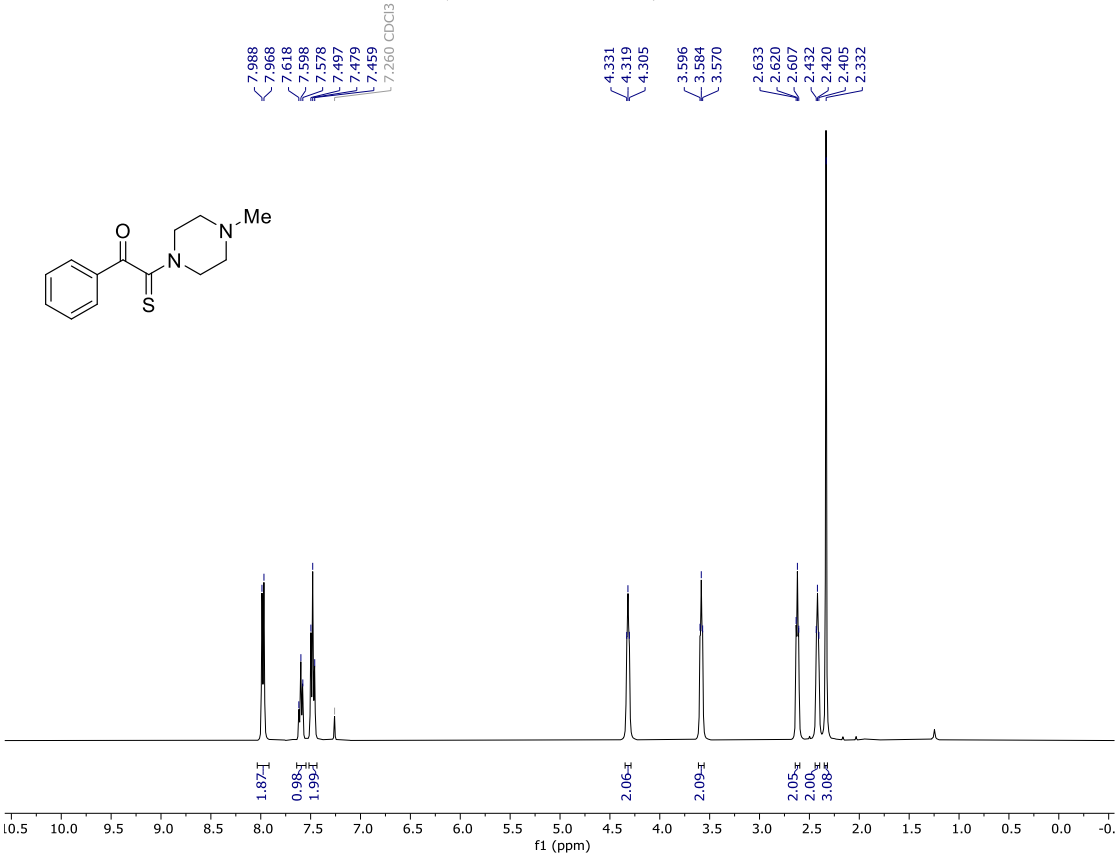
^{1}H NMR spectrum of compound **3ae** (600 MHz, $CDCl_3$)



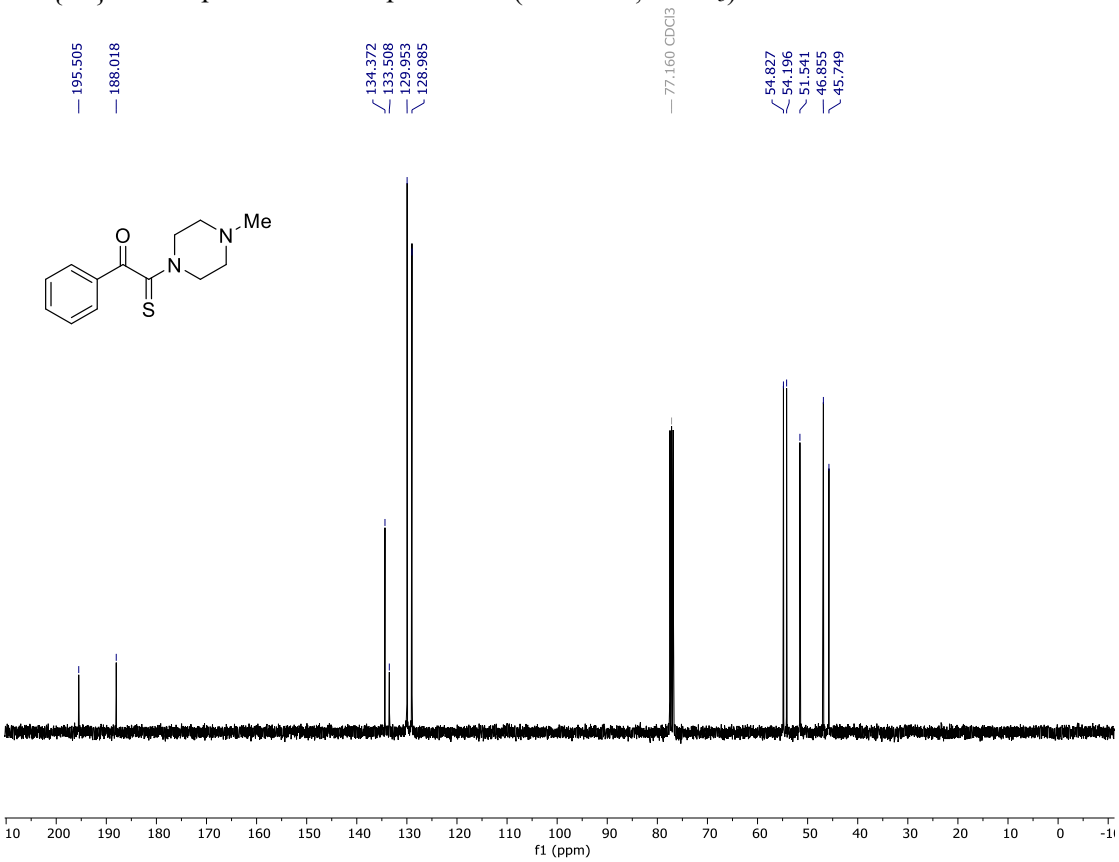
^{13}C {^{1}H} NMR spectrum of compound **3ae** (151 MHz, $CDCl_3$)



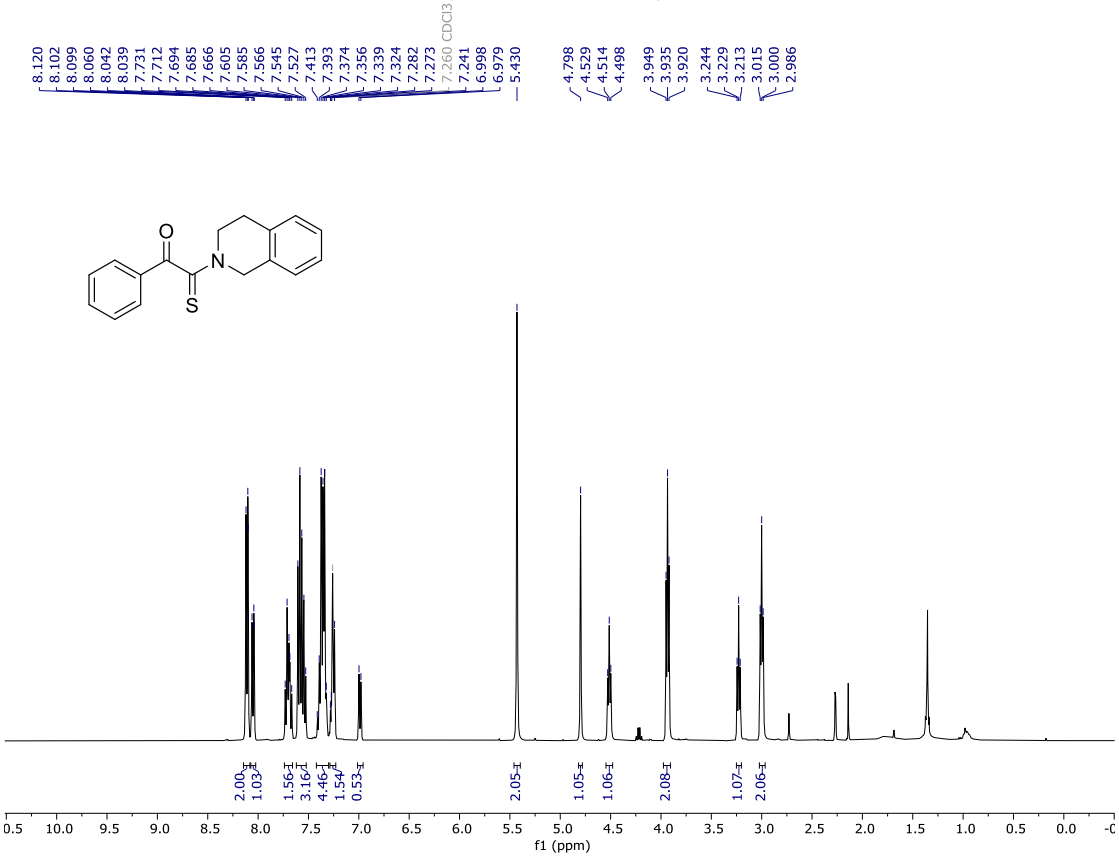
^{1}H NMR spectrum of compound **3af** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR spectrum of compound **3af** (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound **3ag** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR spectrum of compound **3ag** (101 MHz, $CDCl_3$)