

# Preparation of thioaminals in water

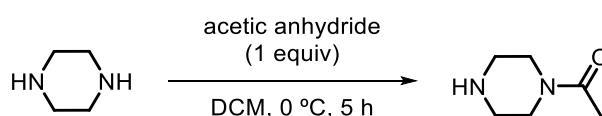
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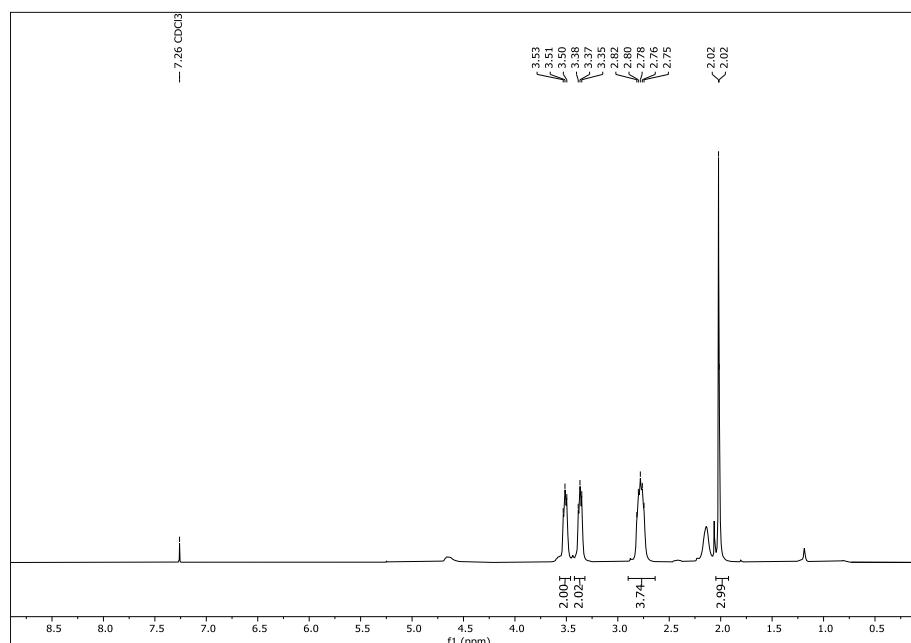
## Preparation of starting materials

### Synthesis of 1-(piperazin-1-yl)ethan-1-one



Procedure according to literature[1]: Piperazine (1.7 g, 19.74 mmol, 2 equiv) was dissolved in DCM (50 mL). The solution was cooled to 0 °C, followed by dropwise addition of acetic anhydride (0.940 mL, 9.94 mmol, 1 equiv). The reaction was allowed to stir at 0 °C for 5 hours. The reaction mixture was quenched with distilled H<sub>2</sub>O (15 mL). The organic layer was dried with MgSO<sub>4</sub> (anhyd), filtered and evaporated under reduced pressure to yield a white solid containing a mixture of monoacetylated and diacetylated piperazine in about 10:1 ratio. Monoacetylated piperazine was obtained after purification by column chromatography in silica DCM/MeOH (9:1) then DCM/MeOH (1:1). After evaporation of the desired fractions, the compound was redissolved in DCM, filtered and the solvent evaporated to yield the product as a yellow solid (0.0343g, 1.4% yield).

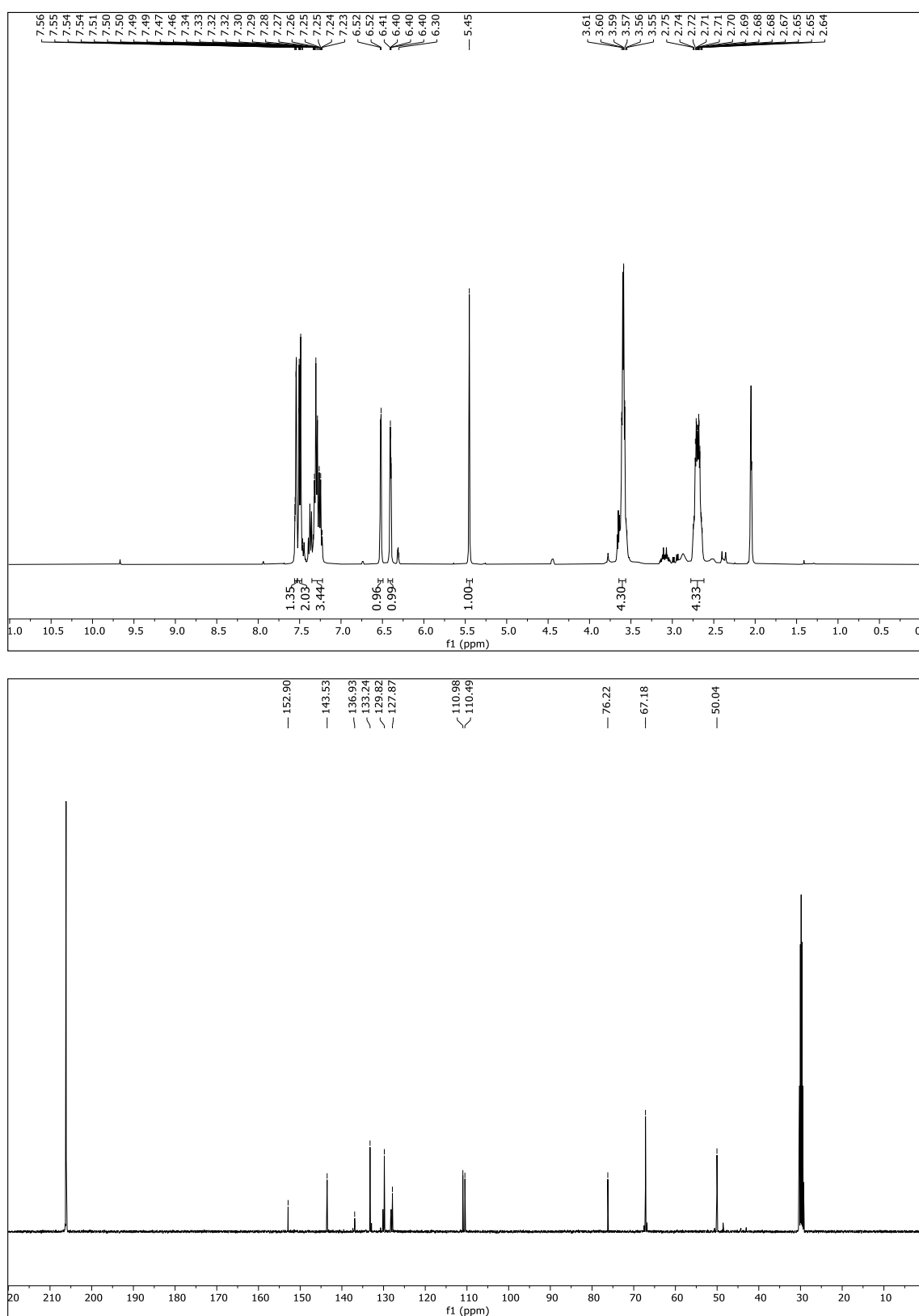
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 3.51 (t, *J* = 5.2 Hz, 2H), 3.37 (t, *J* = 5.2 Hz, 2H), 2.78 (dt, *J* = 10.7, 4.7 Hz, 4H), 2.02 (d, *J* = 1.7 Hz, 3H) ppm.



**Figure S1.** <sup>1</sup>H-NMR Spectra of 1-(piperazin-1-yl)ethan-1-one.

## NMR spectra of thioaminals

## 4-(furan-2-yl(phenylthio)methyl)morpholine (1)

Figure S2. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of 1.

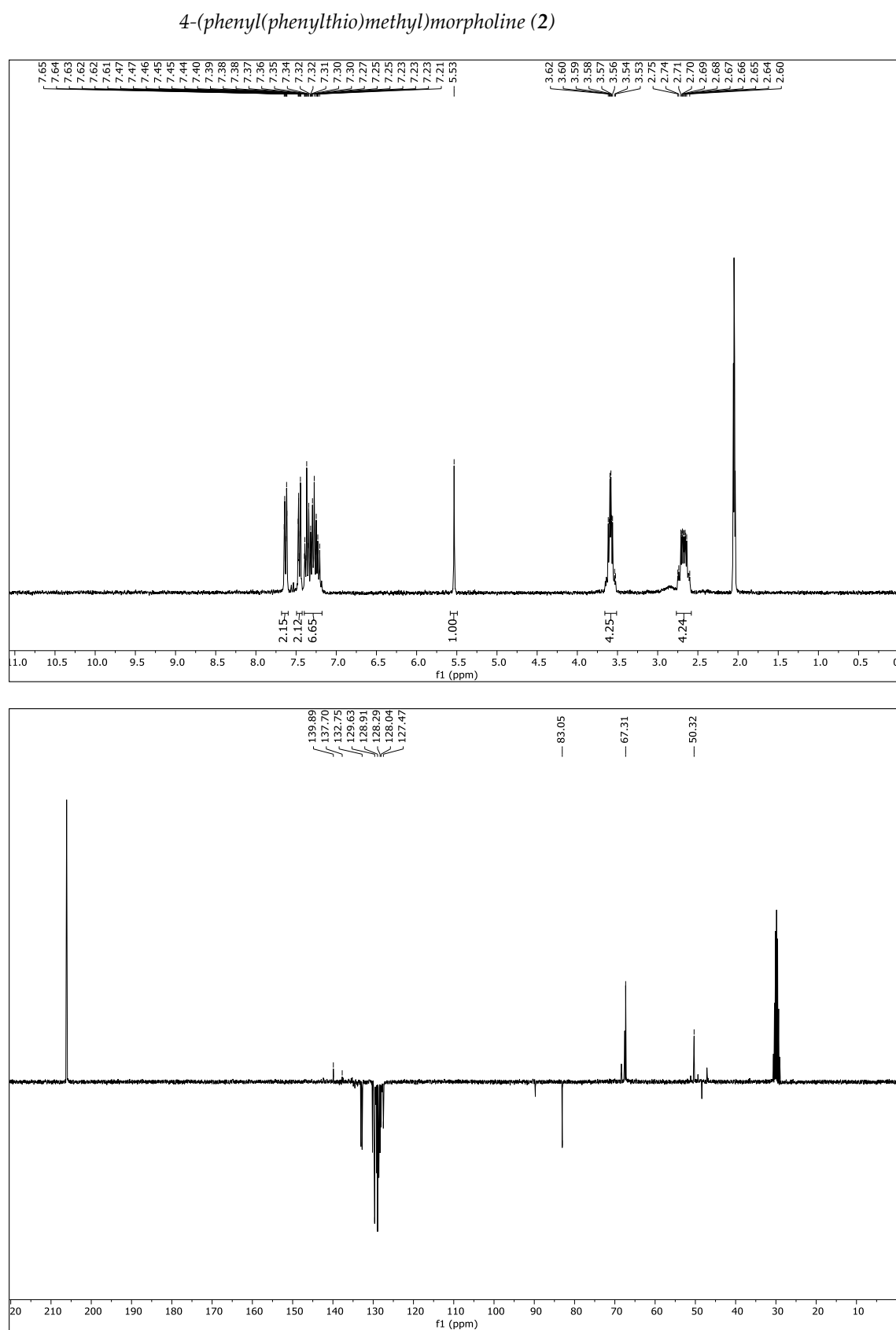
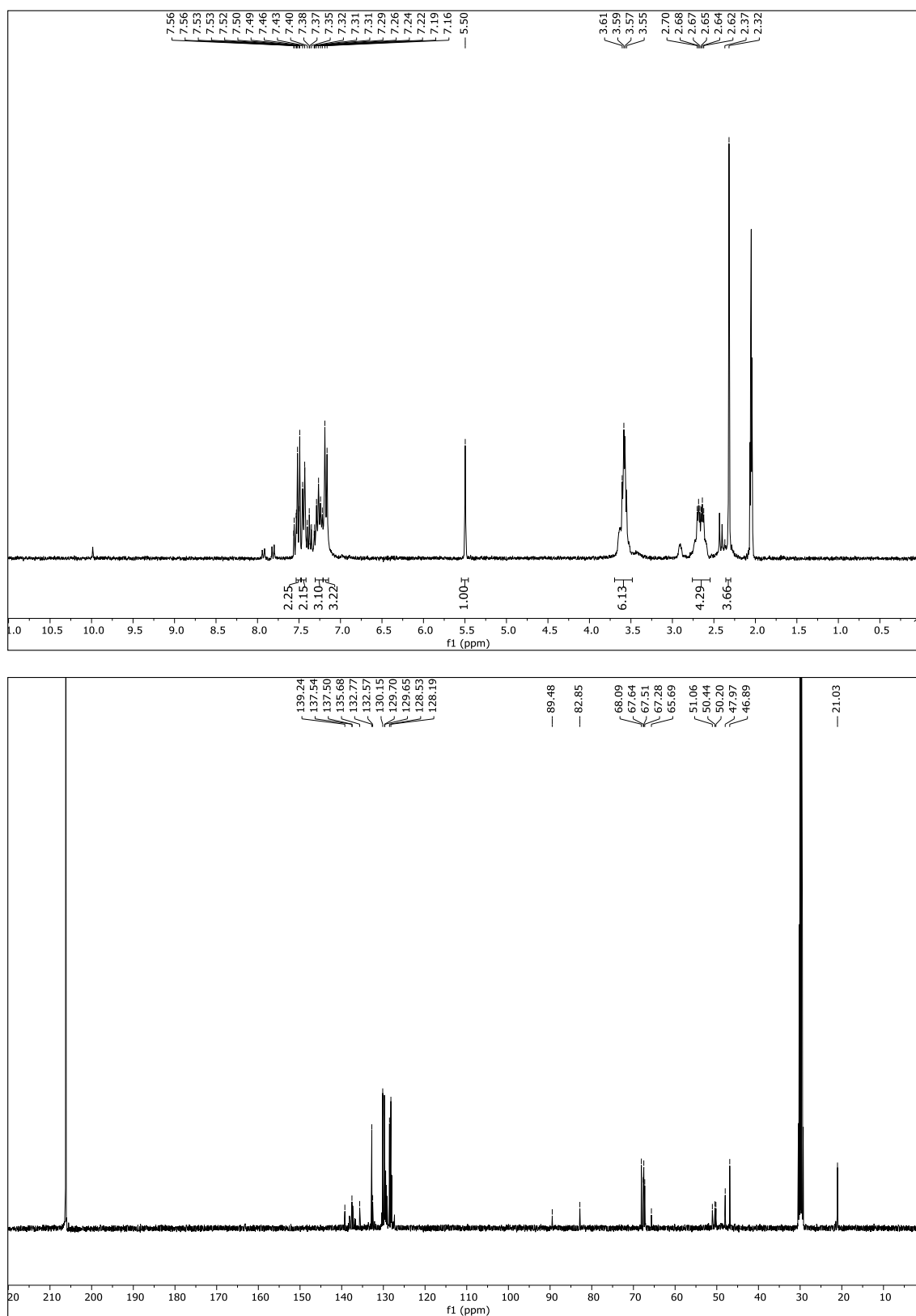


Figure S3. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of 2.

## 4-((phenylthio)(p-tolyl)methyl)morpholine (3)

Figure S4. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of 3.

4-((phenylthio)(4-(trifluoromethyl)phenyl)methyl)morpholine (**4**)

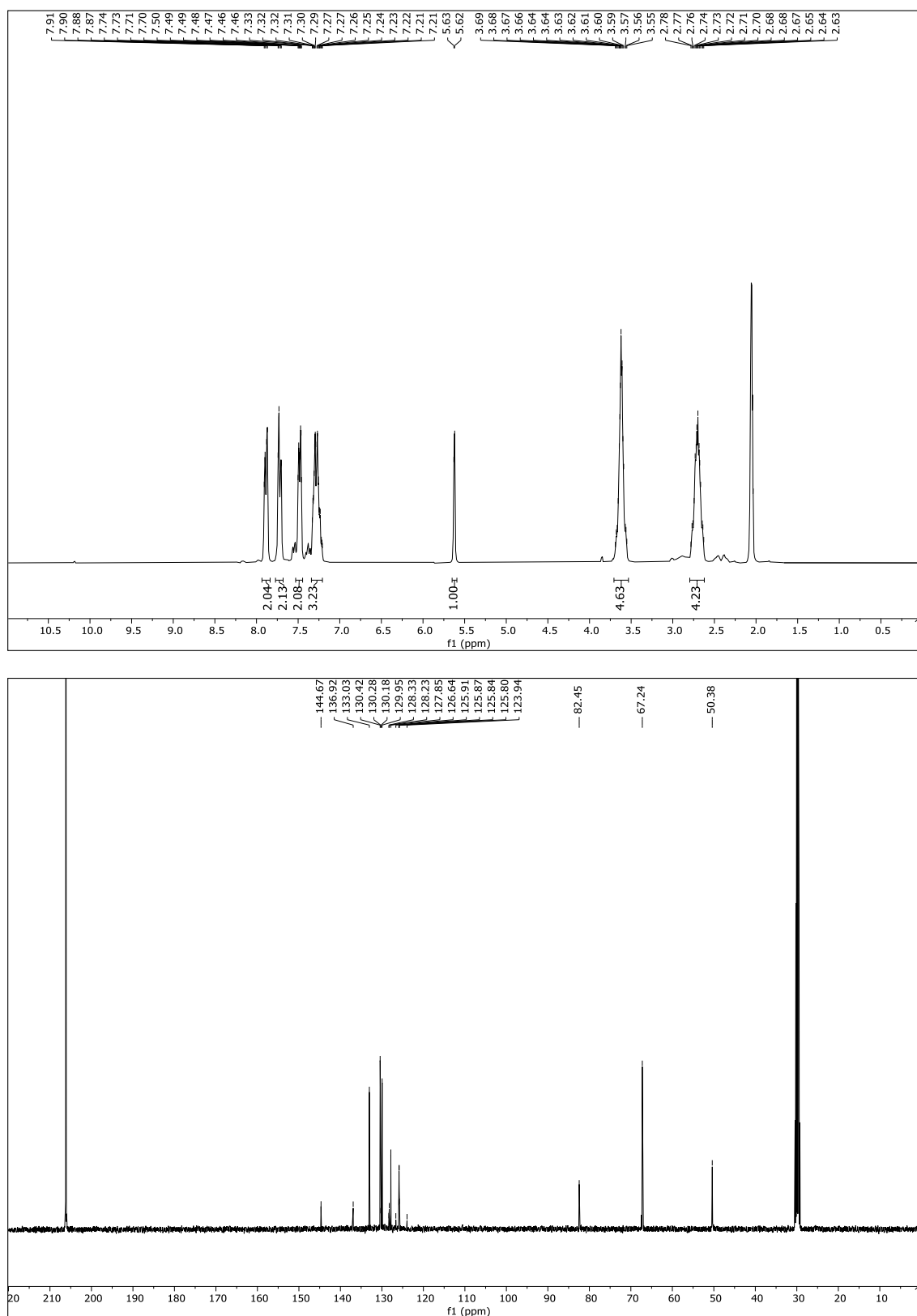
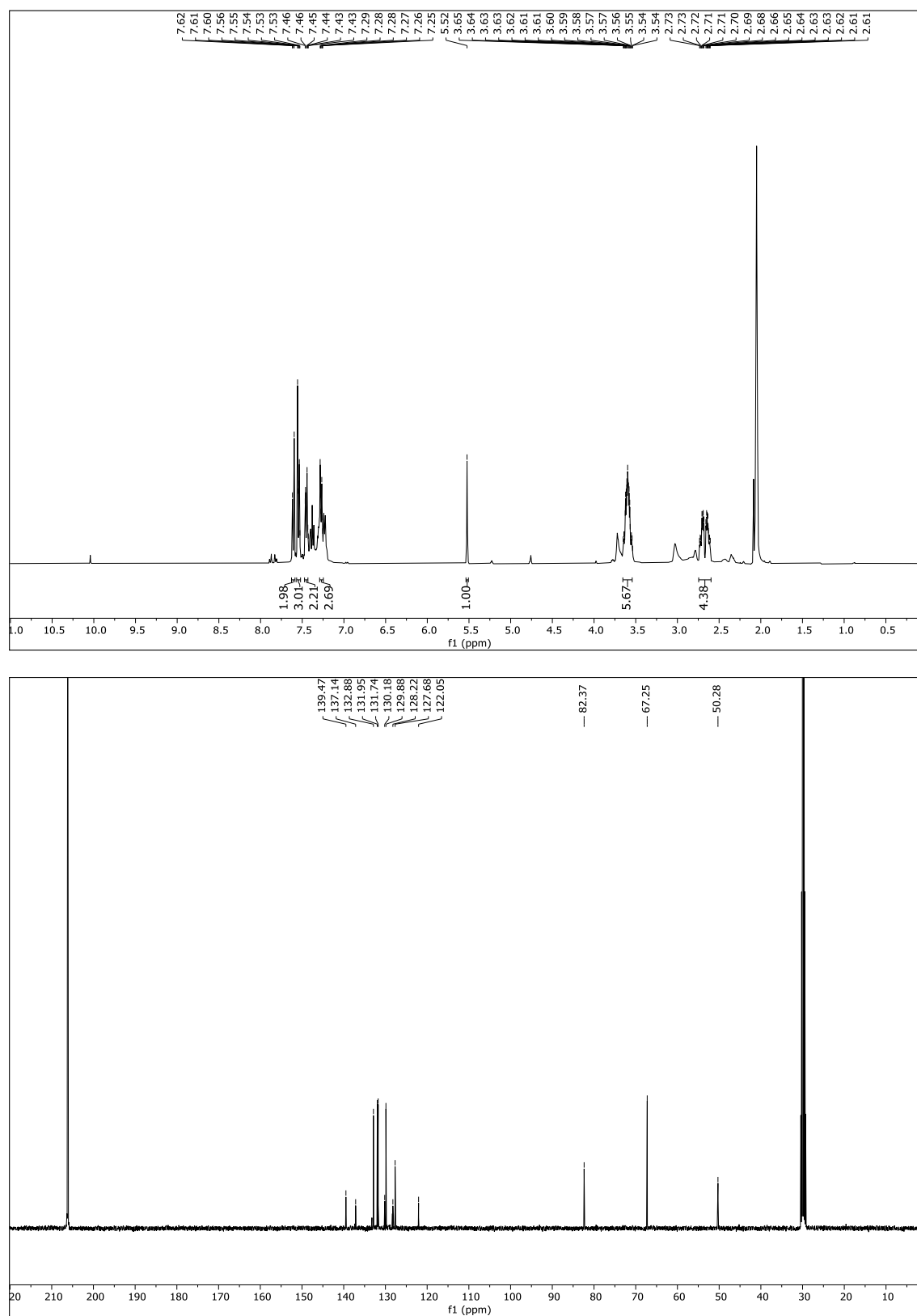
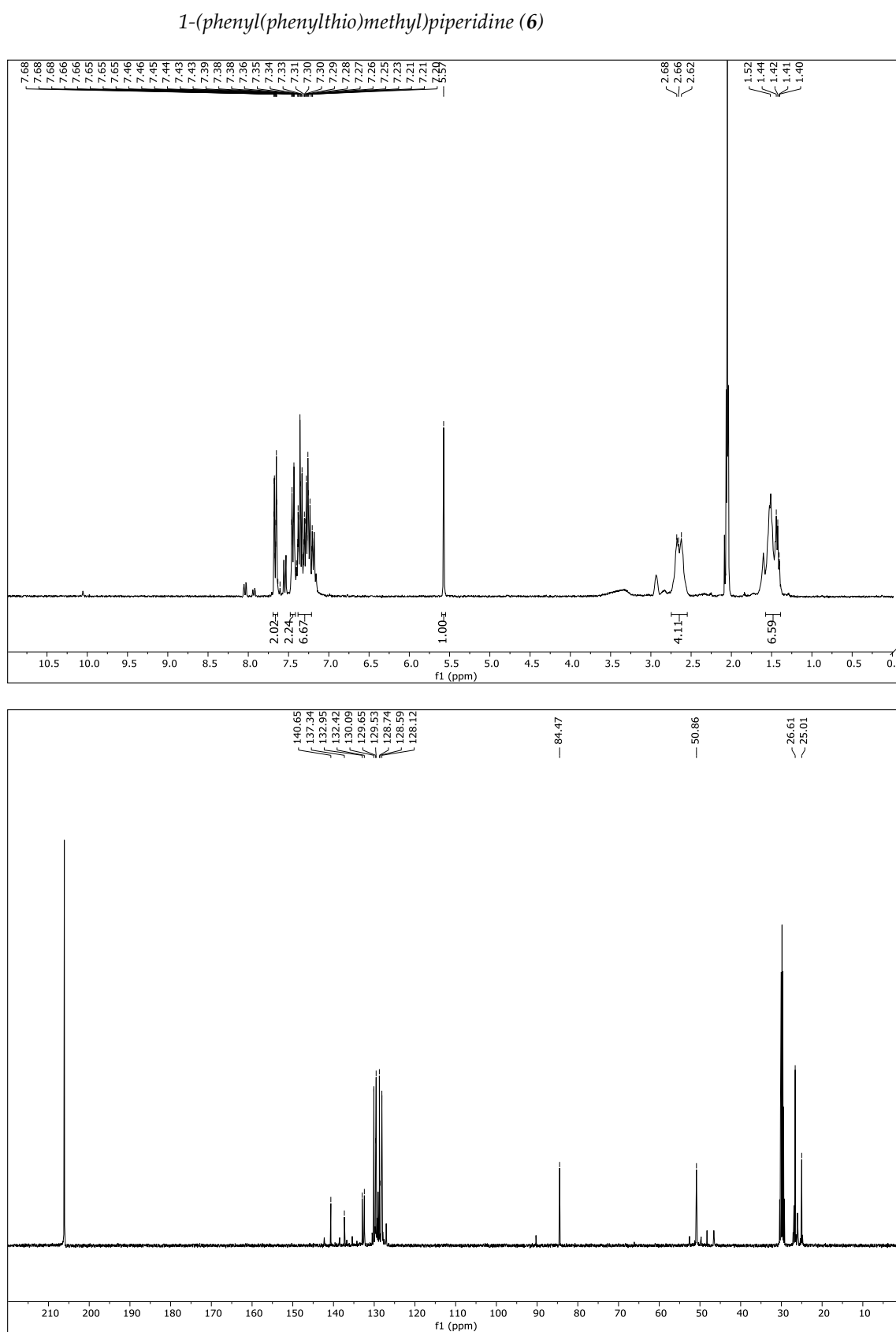


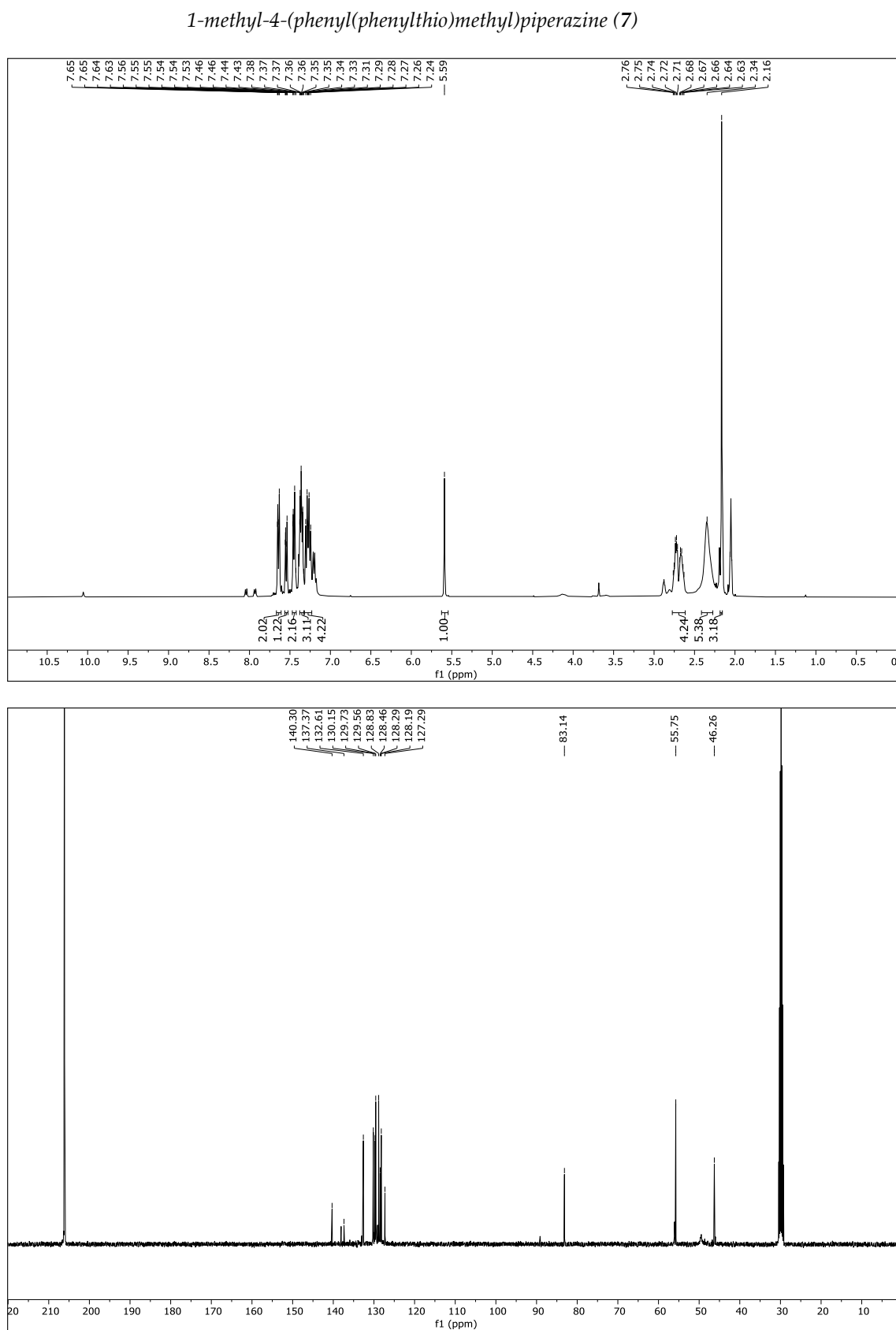
Figure S5. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of **4**.

## 4-((4-bromophenyl)(phenylthio)methyl)morpholine (5)

Figure S6.  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra of 5.

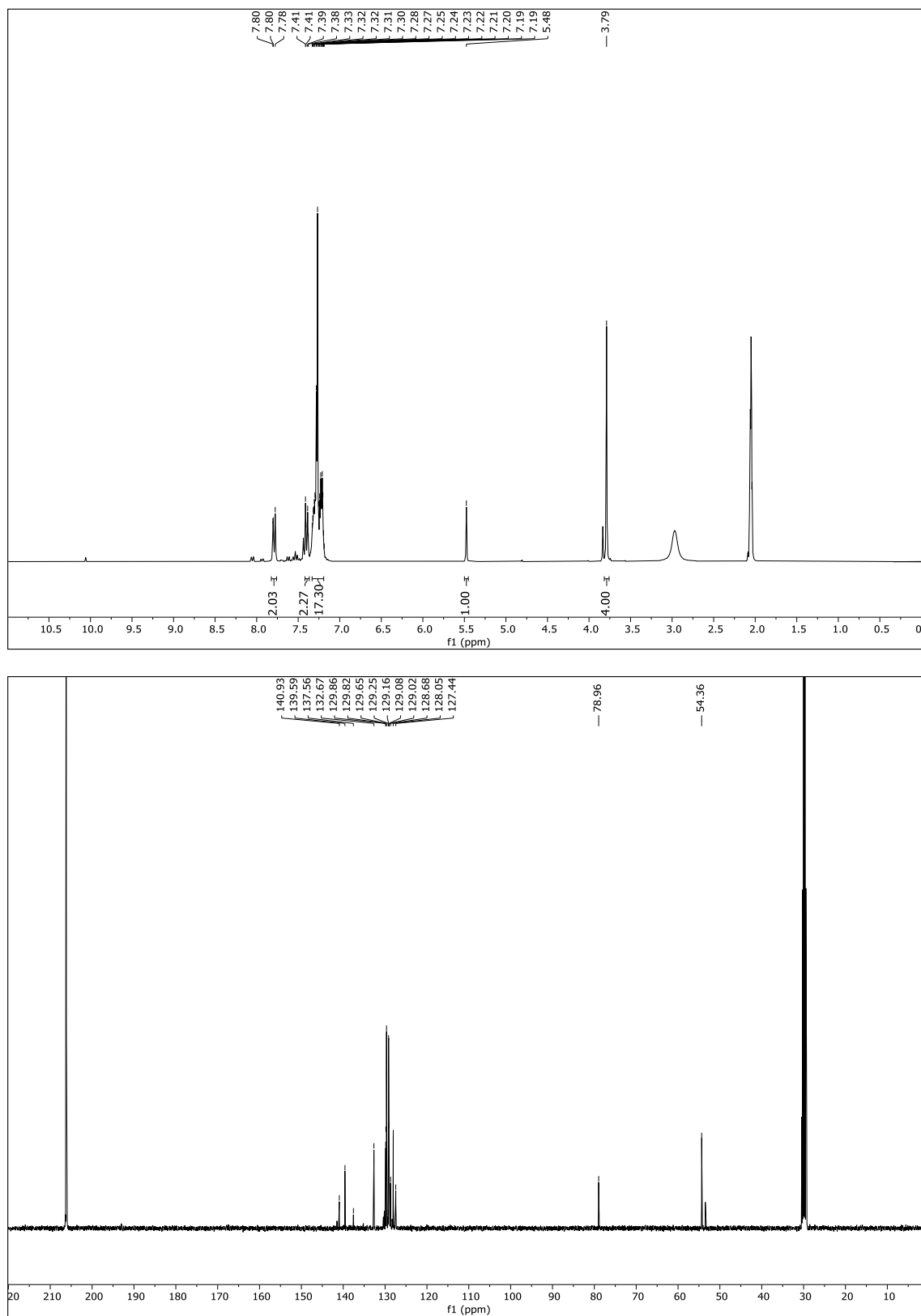


**Figure S7.**  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra of **6**. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra presented have a mixture of thioaminal **6** and products from hydrolysis, resulting from *in situ* degradation in the NMR tube.



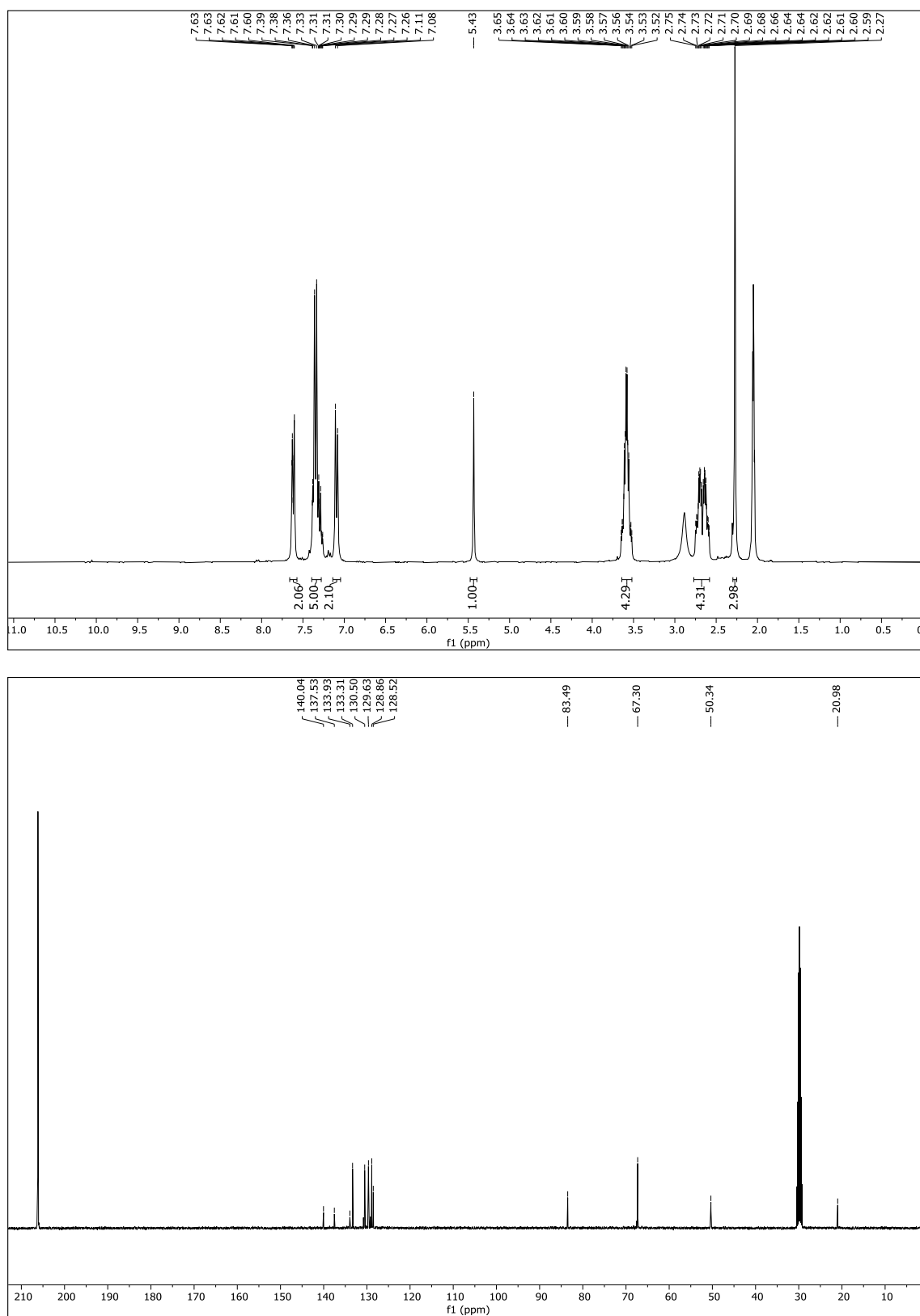
**Figure S8.** <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of **7**. The <sup>1</sup>H and <sup>13</sup>C NMR spectra presented have a mixture of thioaminal **7** and products from hydrolysis, resulting from *in situ* degradation in the NMR tube.

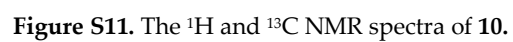


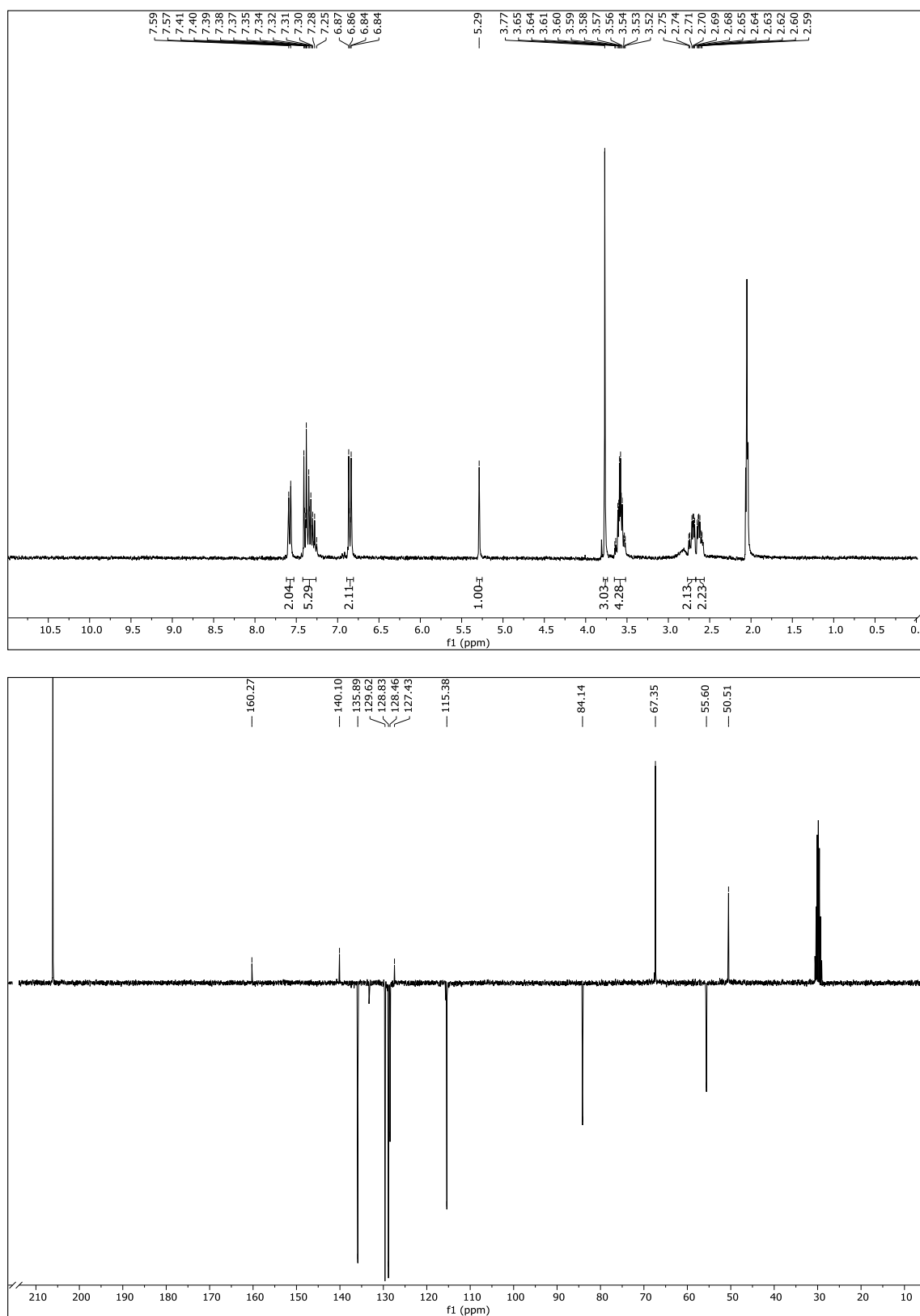
*N,N*-dibenzyl-1-phenyl-1-(phenylthio)methanamine (8)

**Figure S9.**  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra of 8. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra presented have a mixture of thioaminal 8 and products from hydrolysis, resulting from *in situ* degradation in the NMR tube.

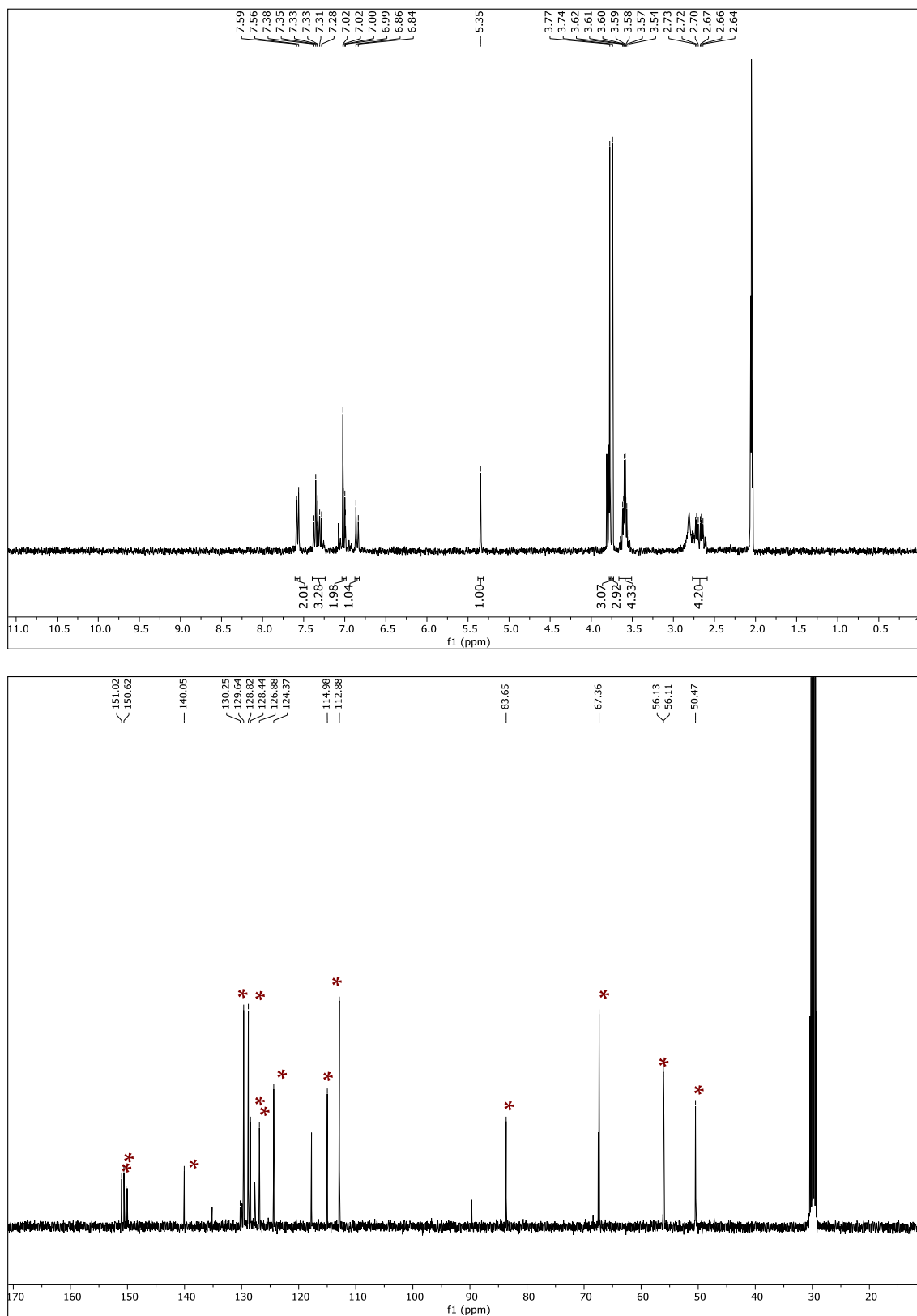
## 4-(phenyl(p-tolylthio)methyl)morpholine (9)

Figure S10. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 9.

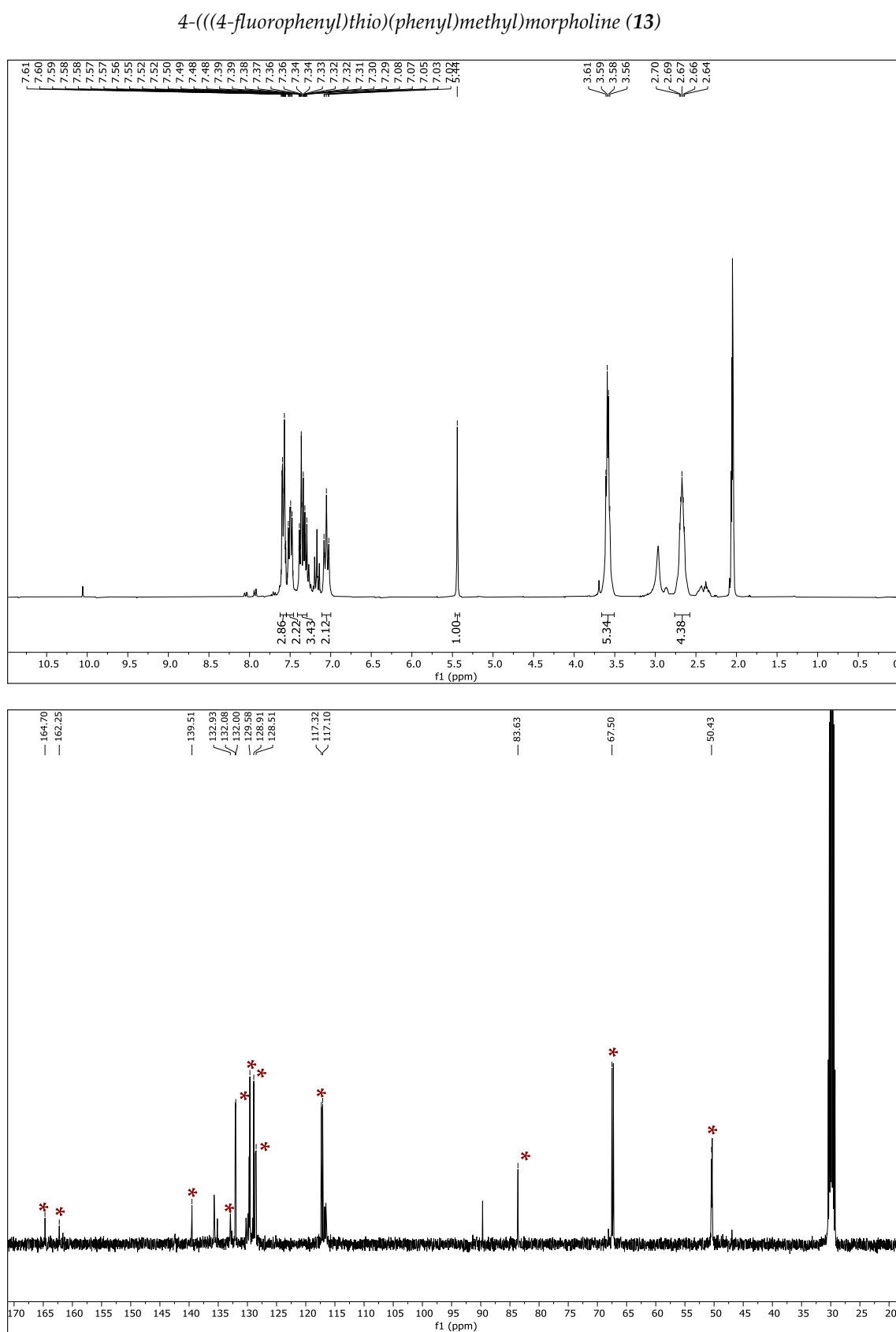


4-(((4-methoxyphenyl)thio)(phenyl)methyl)morpholine (**11**)Figure S12. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **11**.

4-(((3,4-dimethoxyphenyl)thio)(phenyl)methyl)morpholine (12)



**Figure S13.** The <sup>1</sup>H and <sup>13</sup>C NMR spectra of 12. The <sup>13</sup>C NMR spectrum presented has a mixture of thioaminal 12 and products from hydrolysis. Signals from thioaminal 9 are highlighted in the spectrum.



**Figure S14.** The <sup>1</sup>H and <sup>13</sup>C NMR spectra of **13**. The <sup>13</sup>C NMR spectrum presented has a mixture of thioaminal **13** and products from hydrolysis. Signals from thioaminal **13** are highlighted in the spectrum.

4-(((4-chlorophenyl)thio)(phenyl)methyl)morpholine (**14**)

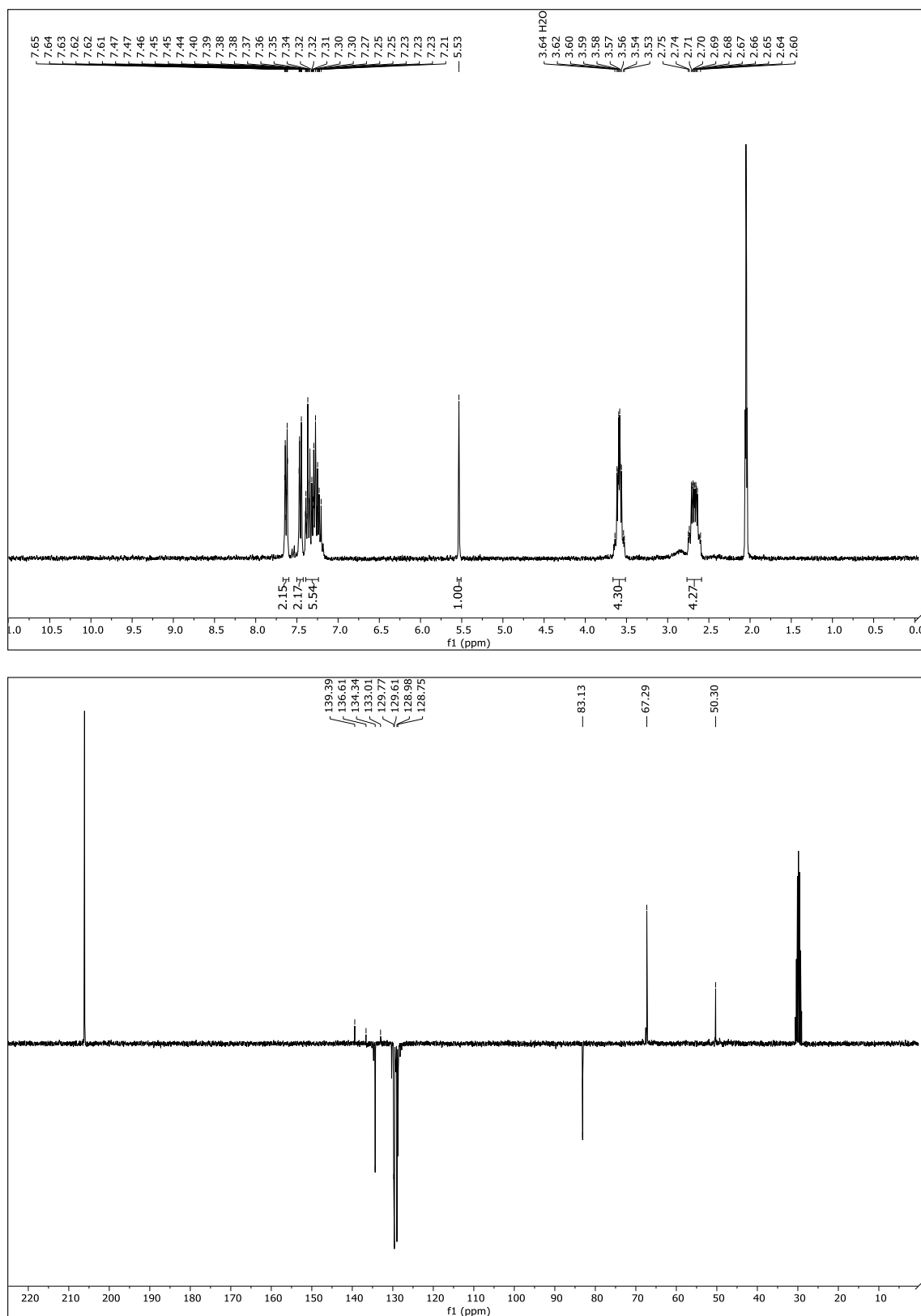
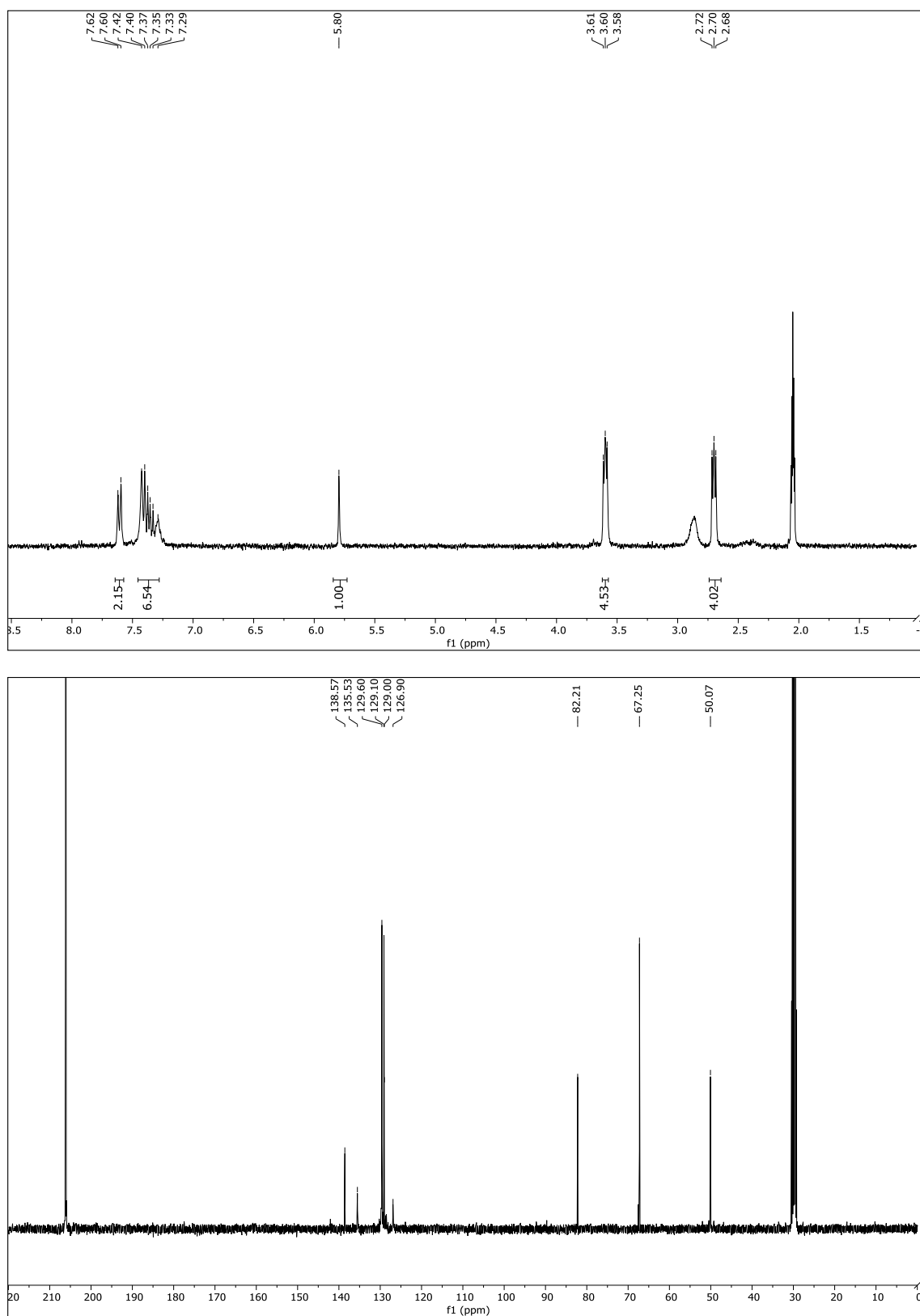


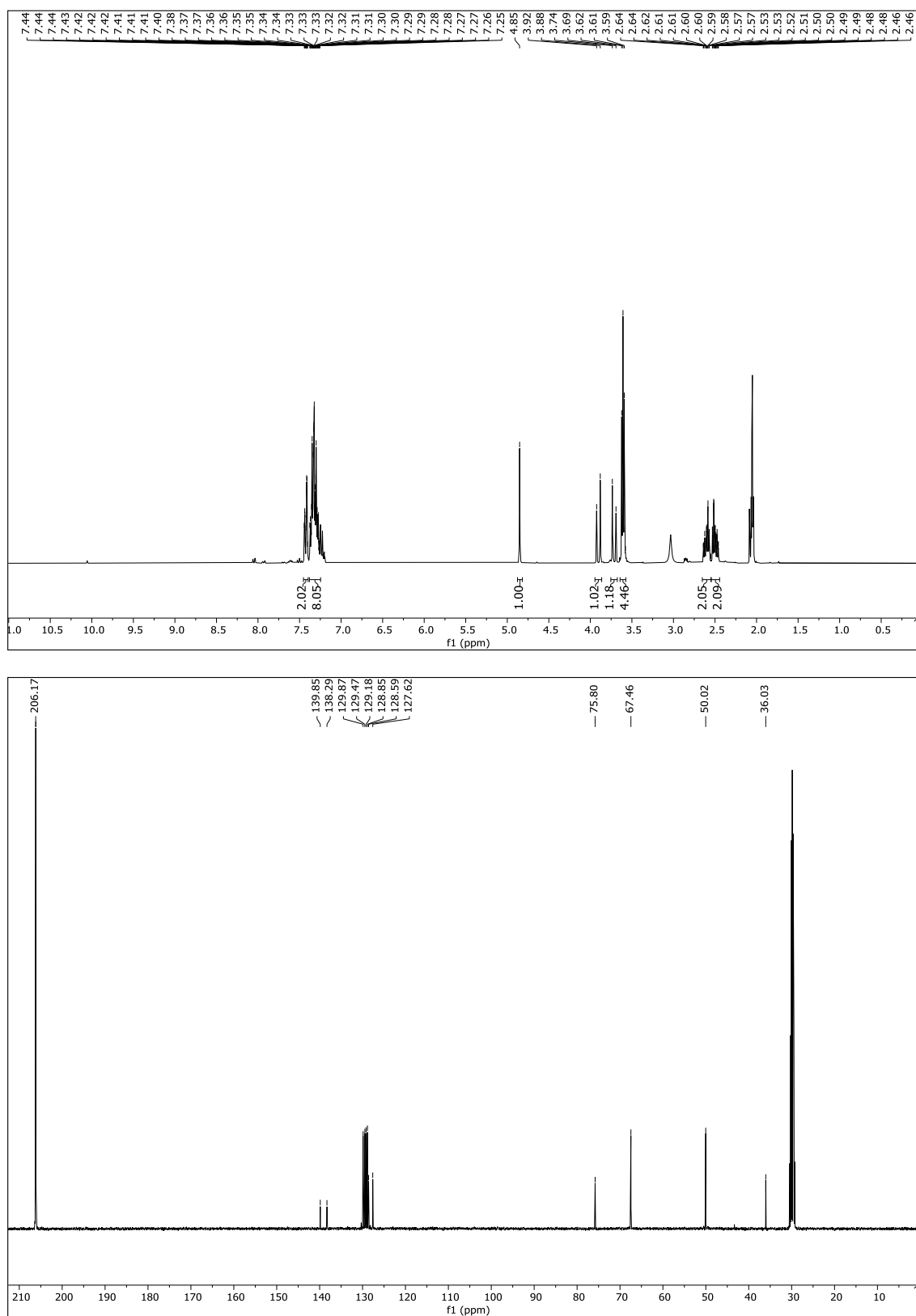
Figure S15. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **14**.

## 4-(((3,5-dichlorophenyl)thio)(phenyl)methyl)morpholine (15)

Figure S16. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 15.



## 4-((benzylthio)(phenyl)methyl)morpholine (16)

Figure S17. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 16.

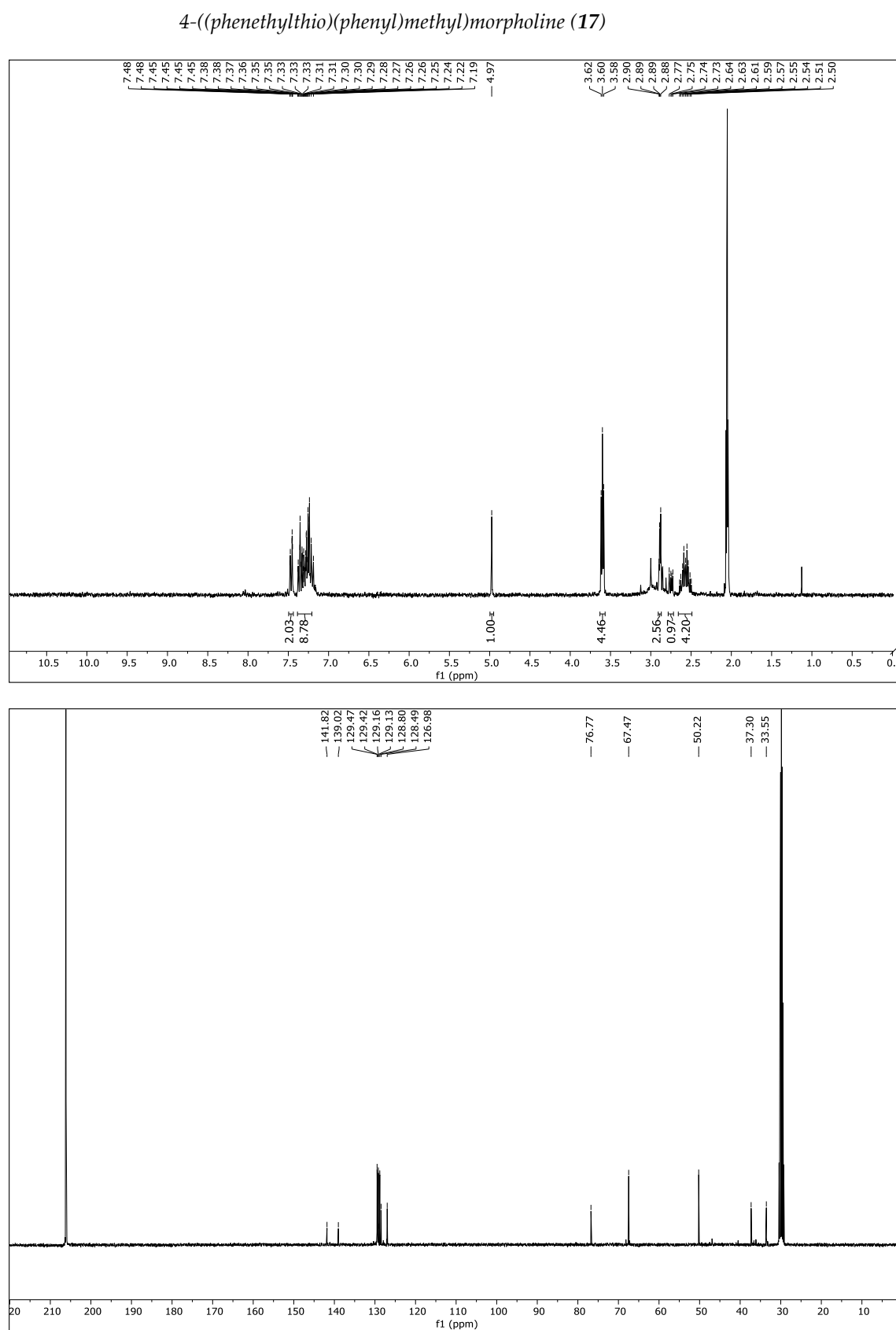
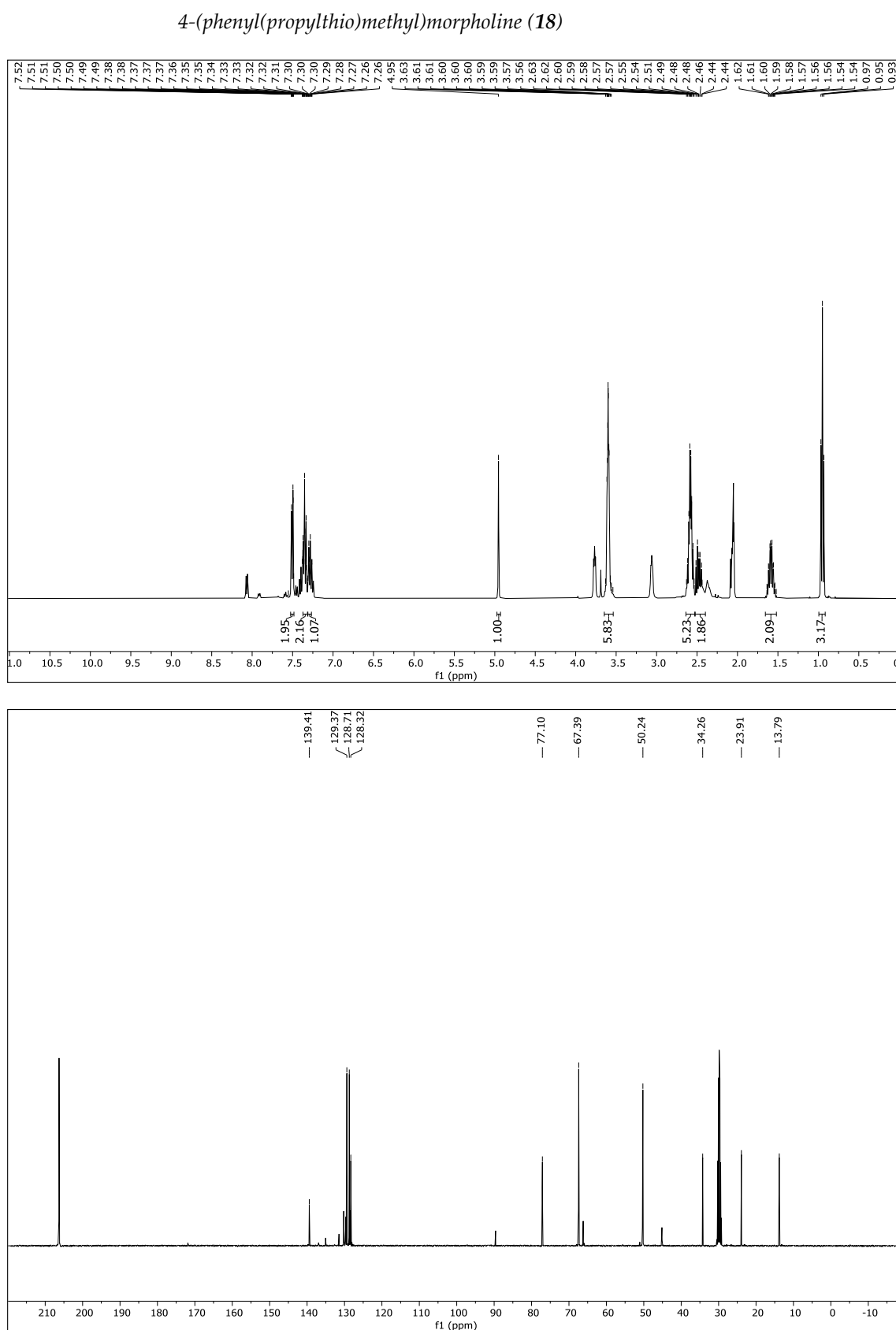
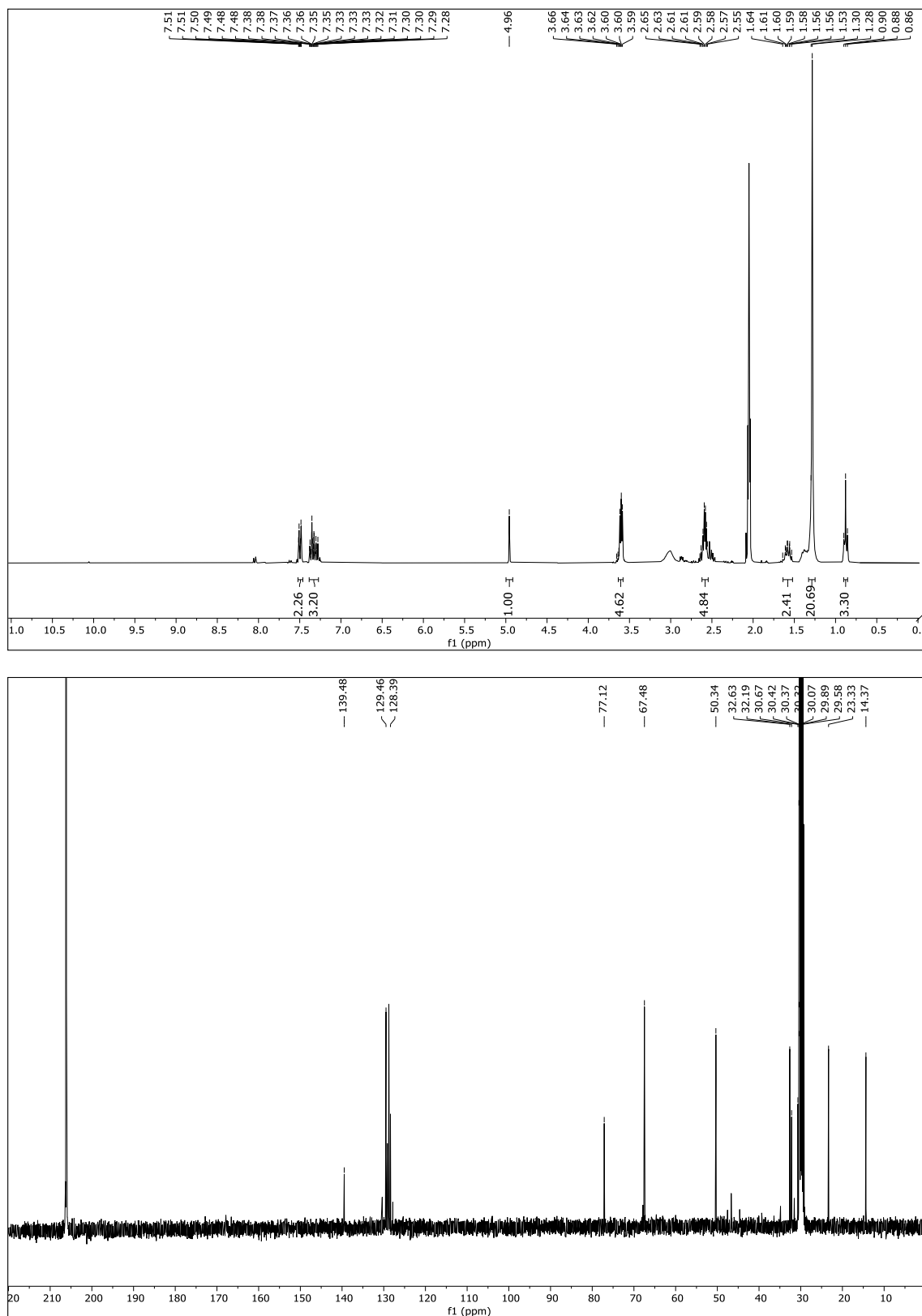


Figure S18. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 17.



**Figure S19.** The <sup>1</sup>H and <sup>13</sup>C NMR spectra of **18**. The <sup>1</sup>H and <sup>13</sup>C NMR spectra presented have a mixture of thioaminal **18** and products from hydrolysis, resulting from *in situ* degradation in the NMR tube.

*4-((dodecylthio)(phenyl)methyl)morpholine (19)*Figure S20. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 19.

## UV stability experiments

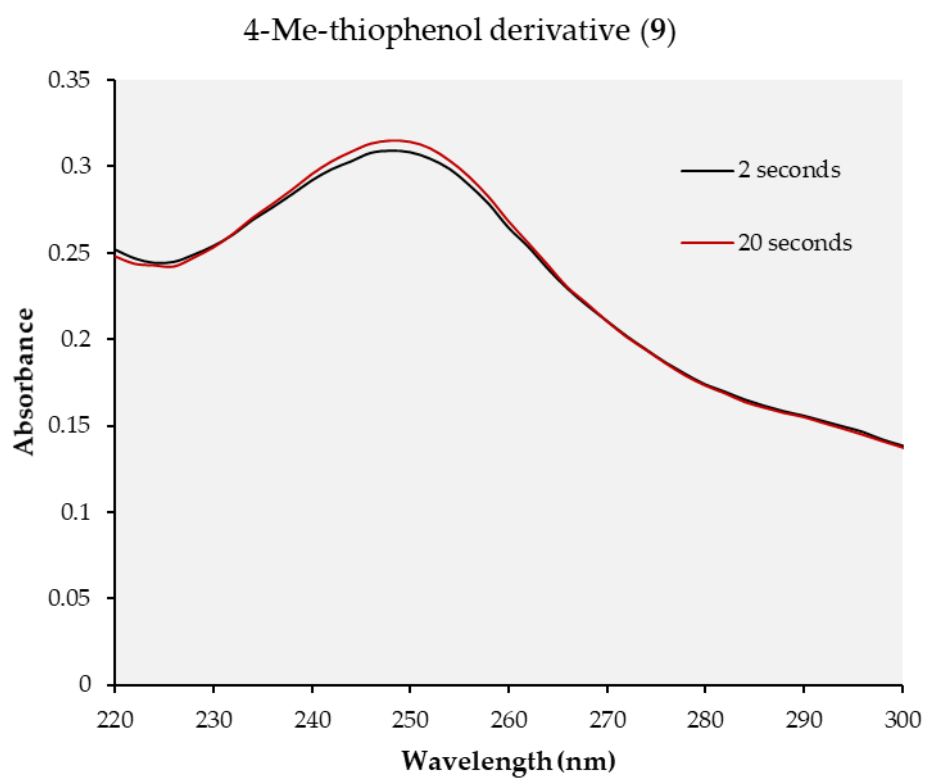


Figure S21. Variation of UV spectrum of thioaminal 9 after 20 seconds at pH 7.

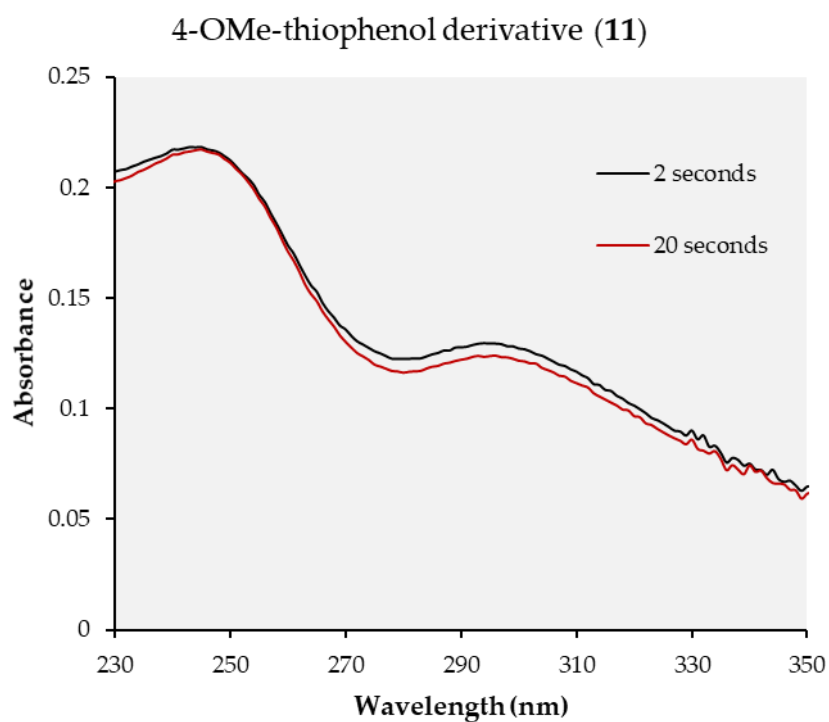
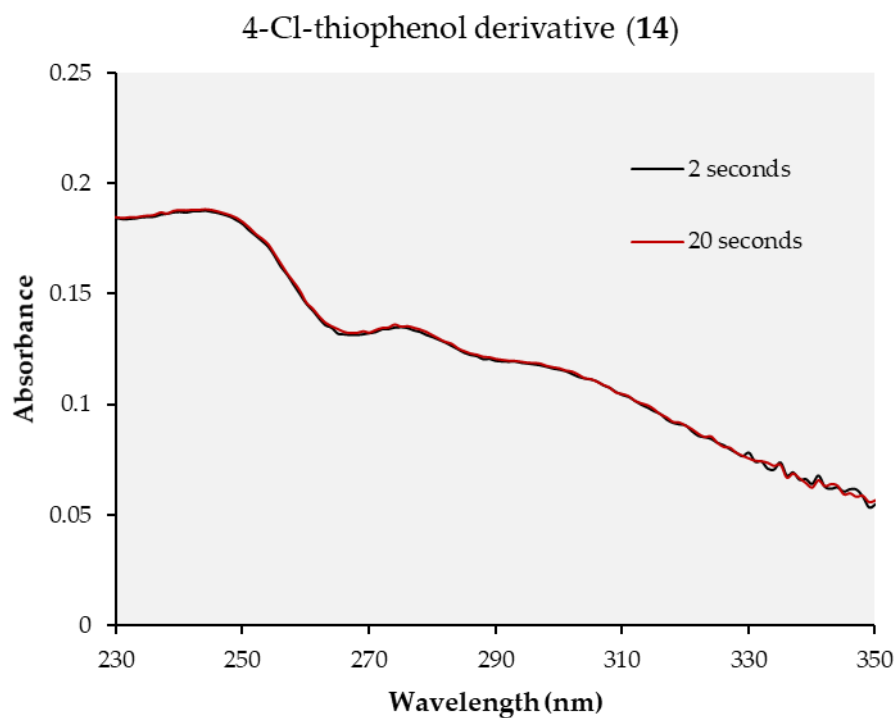


Figure S22. Variation of UV spectrum of thioaminal 11 after 20 seconds at pH 7.



**Figure S23.** Variation of UV spectrum of thioaminal **14** after 20 seconds at pH 7.

## References

1. Fawwaz, M.; Mishiro, K.; Nishii, R.; Sawazaki, I.; Shiba, K.; Kinuya, S.; Ogawa, K. Synthesis and Fundamental Evaluation of Radioiodinated Rociletinib (CO-1686) as a Probe to Lung Cancer with L858R/T790M Mutations of Epidermal Growth Factor Receptor (EGFR). *Mol.* **2020**, *25*, 2914, doi:10.3390/molecules25122914