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Supporting information

Lipase catalyzed 1,2-addition of thiols to imines under mild conditions

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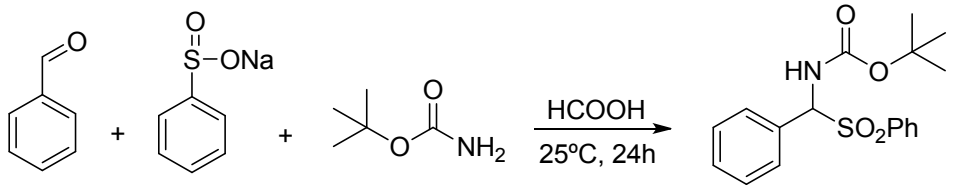
1. GENERAL PROCEDURE

All other reactions were carried out using chemical reagents and solvents without any specific treatment. The respective reactions were monitored by Thin Layer Chromatography (TLC) MACHEREY-NAGEL (SIL G / UV_{254}) and were visualized by fluorescence quenching with UV light at 254 nm. The purification of the compounds was performed by chromatography on silica gel (eluent: hexane/EtOAc, 90:10). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker (300 MHz and 75 MHz respectively) spectrometer. ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, q =quartet, m = multiplet), coupling constants (*J*) and assignment. The infrared spectra were recorded spectra were recorded on FT/IR 4100 type A spectrometer of Jasco.

2. EXPERIMENTAL PROCEDURE

2.1. General Procedure for *N*-Boc-Imines

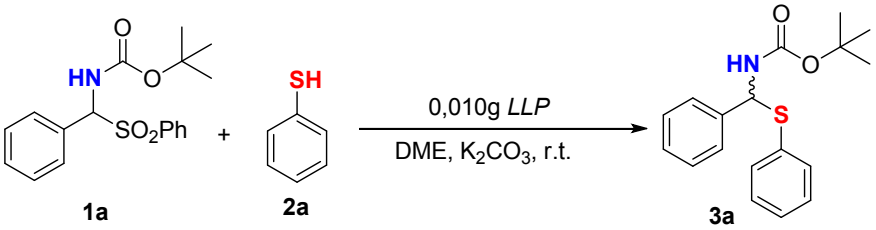


In a 50 mL bottle flask was added aldehyde (5.76 mmol), benzenesulfinic acid sodium salt (5.76 mmol), *tert*-butyl carbamate (5.76 mmol) e HCO_2H (217 µL). The mixture was magnetically stirred in CH_3OH (5 mL) and water (10 mL) at room temperature for 24 hours. After completed, the solid was filtrated and washed with ether and dried overnight (yield 95%).[1]

Previous literature reference

1 Wang**,** H. Y, Zhang, J. X, Cao, D. D and Zhao, G. Enantioselective Addition of Thiols to Imines Catalyzed by Thiourea–Quaternary Ammonium Salts**.** *ACS Catalysis,* **2013** 3 (10), 2218-2221.

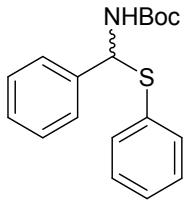
2.2. General Procedure for addition thiols to *N*-Boc-Imines



In a 25 mL bottle flask was added thiol (0.2 mmol), imine (0.1 mmol), K_2CO_3 (0.5 mmol) and 0,001g *LLP* in DME (4 mL) at room temperature. The reaction was magnetically stirred and the reaction was monitored by TLC (eluent: hexane/ EtOAc, 90:10). When the reaction was completed, the enzyme was separated by filtration off and the mixture was extracted with DCM (3x10 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, the salt was filtered off and organic phase was concentrated under reduced pressure. The product was purified by column chromatography on silica gel (eluent: hexane/ EtOAc, 90:10) to afford the product.

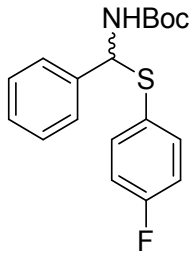
3. ^{1}H AND ^{13}C NMR SPECTRA ANALYSIS

***tert*-butyl (phenyl(phenylthio)methyl)carbamate:**



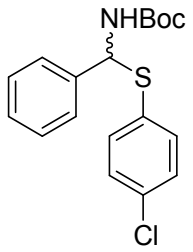
White solid. MW: 315.13 g/mol. $C_{18}H_{21}NO_2S$. **IR** (KBr) ($\nu_{máx}$ cm^{-1}): 3358, 2959, 1689, 1165, 1086, 1021, 876, 825, 798. **^{1}H NMR** (300 MHz, $CDCl_3$): δ ppm 1.35 (s, 9H), 5.22-5.25 (d, J= 9 Hz, 1H), 6.32-6.29 (d, *J*=9 Hz, 1 H), 7.30-7.52 (m, 10H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ ppm 28.17, 61.21, 126.44, 127.74, 128.01, 128.19, 128.62, 128.90, 132.93, 133.39, 139.02, 139.17, 154.21.

***tert*-butyl (((4-fluorophenyl)thio(phenyl)methyl)carbamate:**



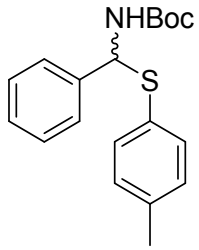
White solid. MW: 333.12 g/mol. $C_{18}H_{20}FNO_2S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3361, 1688, 1510, 1349, 1287, 1168, 1020, 882, 829. **^{1}H NMR** (300 MHz, DMSO): δ ppm 1.35 (s, 1H), 5.22-5.25 (d, *J* = 9, 1H), 6.29-6.32 (d, *J*= 9 Hz, 1H), 7.30-7.52 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ ppm 28.20, 28.92, 61.55, 115.53, 118.58, 128.30, 129.04, 132.75, 133.30, 160.77-164.05 (d, J_{C-F}= 245.25).

***tert*-butyl (((4-chlorophenyl)thio)(phenyl)methyl)carbamate:**



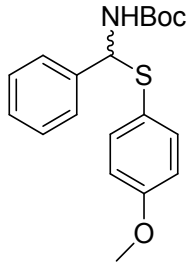
White solid, MW: 349.09 g/mol. $C_{18}H_{20}ClNO_2S$. **IR** (KBr) ($\nu_{máx}$ cm^{-1}): 3358, 1682, 1512, 1474, 1387, 1362, 1250, 1165, 1093, 1014, 883. **^{1}H NMR** (300 MHz, $CDCl_3$): δ ppm 1.35 (s, 1H), 5.22-5.25 (d, *J* = 9, 1H), 6.29-6.32 (d, *J*= 9 Hz, 1H), 7.30-7.52 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ ppm 28.18, 30.41, 61.73, 122.67, 125.63, 126.94, 127.83, 129.16, 130.07, 130.45, 130.69, 132.42, 135.70, 143.83, 155.06.

***tert*-butyl (phenyl(*p*-tolylthio)methyl)carbamate:**



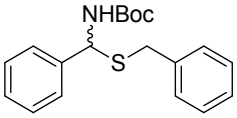
White solid. MW: 329.14 g/mol. $C_{19}H_{23}NO_2S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3352, 2966, 1682, 1505, 1250, 1047, 1021, 876, 811. **^{1}H NMR** (300 MHz, $CDCl_3$): δ ppm 1.34 (s, 9H), 2.26 (s, 3H), 5.09-5.12 (d, *J* = 9 Hz, 1H), 6.12-6.15 (d, *J*= 9 Hz, 1H), 6.97-7.50 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ ppm 21.00, 28.08, 61.46, 126.33, 127.96, 128.39, 128.45, 128.86, 129.01, 129.58, 129.72, 131.37.

***tert*-butyl (((4-methoxyphenyl)thio)(phenyl)methyl)carbamate:**



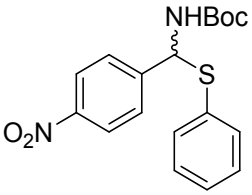
White solid. MW: 345.14 g/mol. $C_{19}H_{23}NO_3S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3367, 1681, 1586, 1490, 1362, 1290, 1168, 1026, 875, 826. **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 1.36 (s, 9H), 3.82 (s, 3H), 5.23-5.25 (d, *J* = 10 Hz, 1H), 6.14-6.16 (d, *J*= 10 Hz, 1H), 6.83-7.44 (m, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 28.25, 55.38, 62.25, 114.64, 123.15, 128.07, 128.44, 128.58, 129.02, 129.76, 132.43, 132.68, 134.46, 136.63, 139.27.

***tert*-butyl ((benzylthio)(phenyl)methyl)carbamate:**



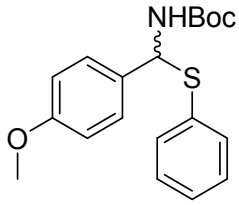
White solid. MW: 345.14 g/mol. $C_{19}H_{23}NO_2S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3367, 1681, 1586, 1490, 1362, 1290, 1168, 1026, 875, 826. **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 1.38 (s, 9H), 3.70-3.82 (m, 2H), 5.07-5.09 (d, *J*= 10 Hz), 5.77-5.83 (m, 1H), 6.87-7.29 (m, 10H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 28.24, 29.36, 58.62, 126.39, 127.00, 127.12, 127.43, 128.07, 128.36, 128.49, 128.90, 128.98, 129.42, 129.74, 139.51.

***tert*-butyl ((4-nitrophenyl)(phenylthio)methyl)carbamate:**



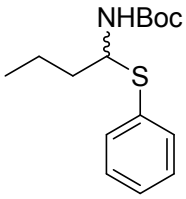
White solid. MW: 360.11 g/mol. $C_{18}H_{20}N_2O_4S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3358, 2959, 1682, 1512, 1362, 1263, 1171, 1093, 1014, 883, 825. **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 1.27 (s, 9H), 5.10-5.12 (d, *J*= 10 Hz, 1H), 6.17-6.19 (d, *J*= 10 Hz, 1H), 7.14-7.34 (m, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 28.18, 28.24, 29.71, 61.66, 126.47, 128.39, 128.75, 129.08, 129.18, 129.76, 130.79, 131.46, 134.48, 134.92, 138.73.

***tert*-butyl ((4-methoxyphenyl)(phenylthio)methyl)carbamate:**



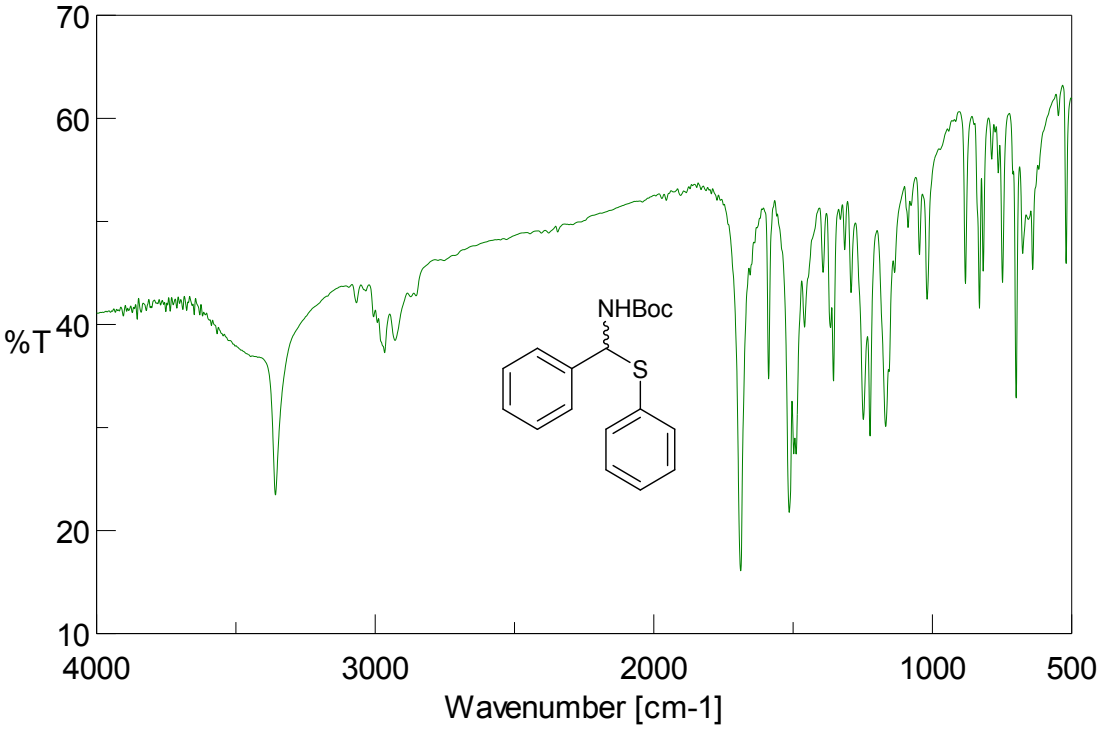
White solid. MW: 345.14 g/mol. $C_{19}H_{23}NO_3S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3352, 2966, 1689, 1617, 1505, 1250, 1165, 1014, 883, 837. **^{1}H NMR** (300 MHz, $CDCl_3$): δ ppm, 1.33 (s, 9H), 3.81 (s, 3H), 5.16-5.19 (d, *J*= 9 Hz, 1H), 6.23-6.26 (d, *J*= 9 Hz, 1H), 6.87-7.49 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ ppm 28.22, 55.35, 59.48, 111.76, 113.99, 126.73, 127.71, 128.97, 129.41, 130.22, 131.76, 132.63, 143.26, 159.31.

***tert*-butyl (1-(phenylthio)butyl)carbamate:**



White solid. MW: 281.41 g/mol. $C_{15}H_{23}NO_2S$. **IR** KBr ($\nu_{máx}$ cm^{-1}): 3367, 1681, 1586, 1490, 1362, 1290, 1168, 1026, 875, 826. **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 0.92-0.95 (m, 3H), 1.34 (s, 9H), 1.46-1.52 (m, 2H), 1.63-1.75 (m, 2H), 4.67-4.65 (d, *J*= 10 Hz, 1H), 5.12-5.17 (dd, *J*= 10 Hz, 1H), 7.26-7.47 (m, 5H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 13.54, 19.55, 28.24, 29.70, 38.35, 58.80, 127.60, 128.83, 129.06, 132.84, 133.45, 154.56.

Figure 1. FTIR spectra for the *tert*-butyl (phenyl(phenylthio)methyl)carbamate.



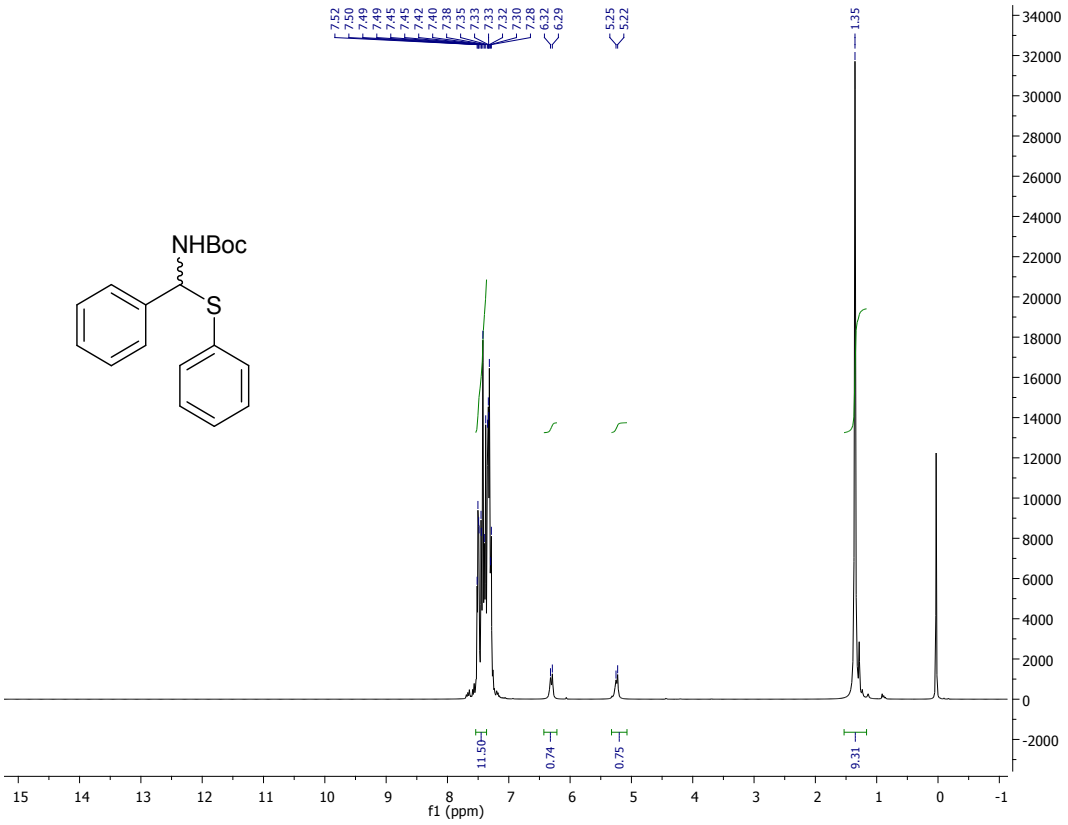


Figure 2. ^{1}H NMR spectra for the *tert*-butyl (phenyl(phenylthio)methyl)carbamate.

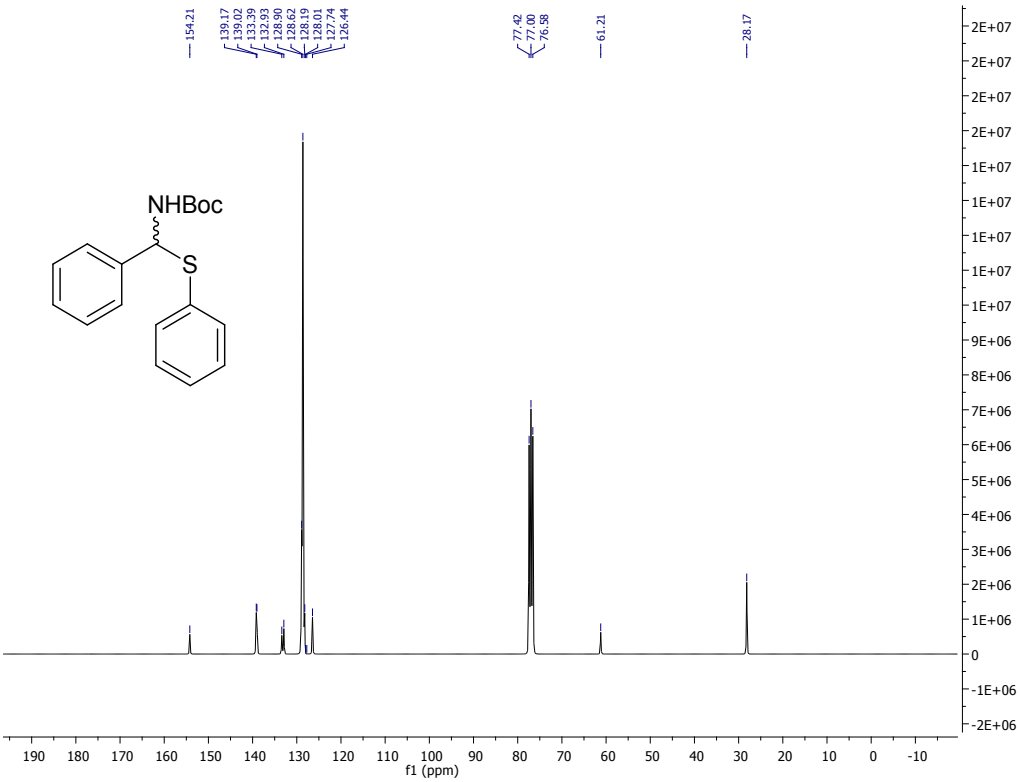


Figure 3. ^{13}C NMR spectra for the *tert*-butyl (phenyl(phenylthio)methyl)carbamate.

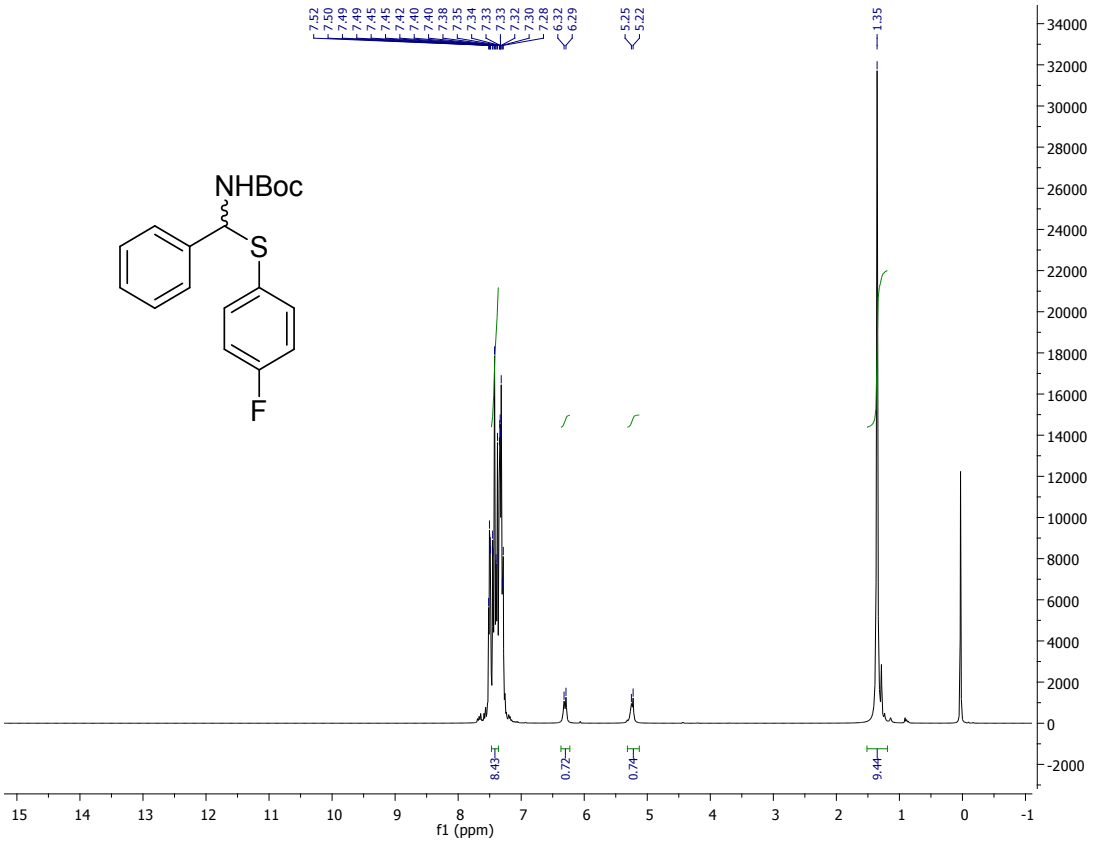


Figure 4. ^{1}H NMR spectra for the *tert*-butyl (((4-fluorophenyl)thio(phenyl)methyl)carbamate.

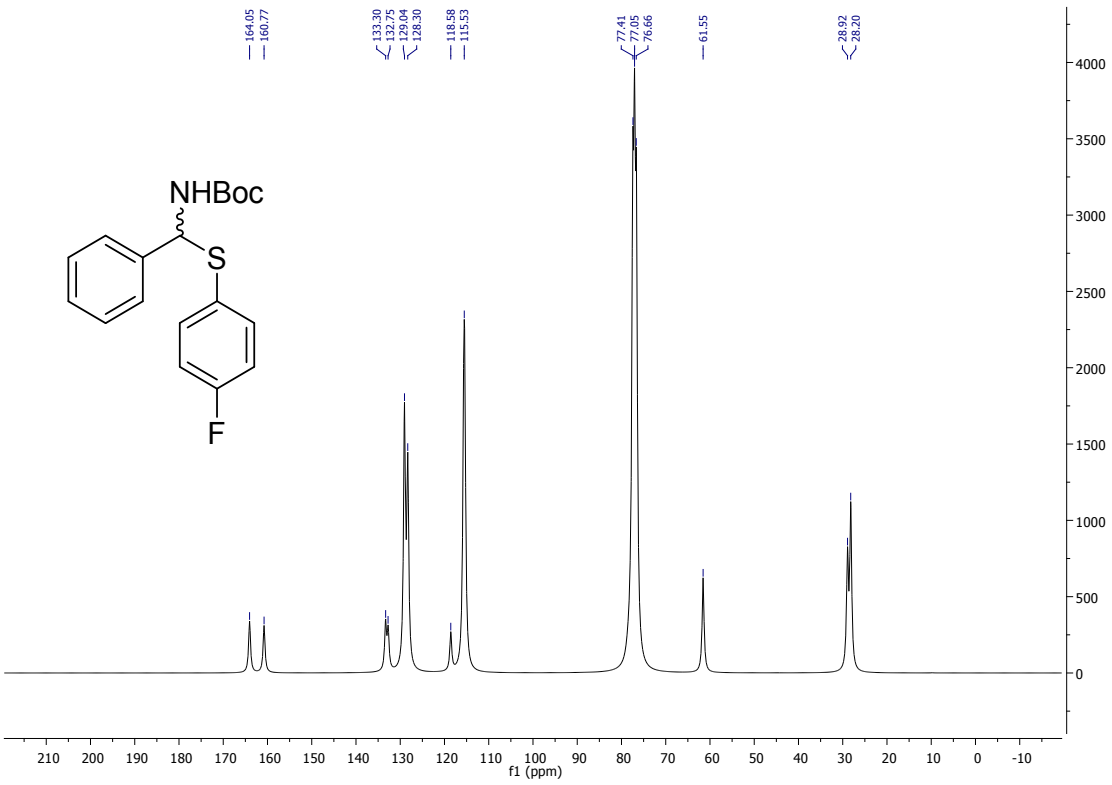


Figure 5. ^{13}C NMR spectra for the *tert*-butyl (((4-fluorophenyl)thio(phenyl)methyl)carbamate.

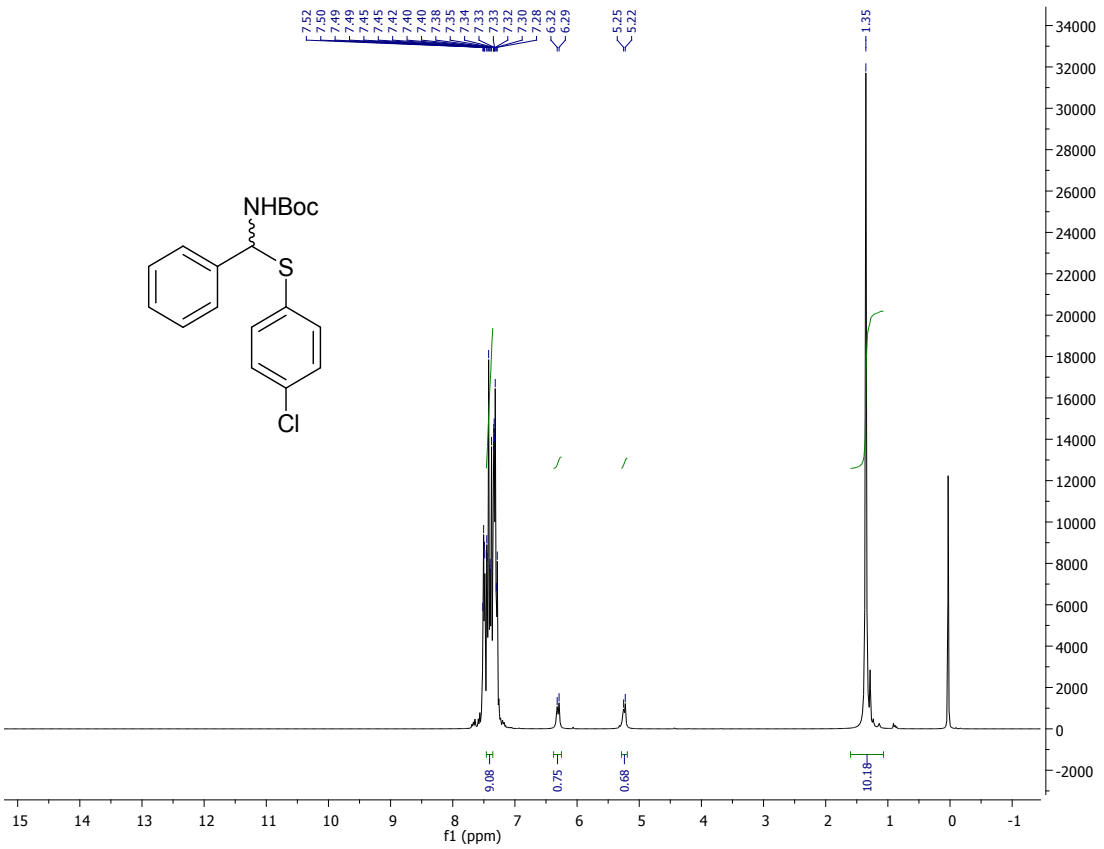


Figure 6. ^{1}H NMR spectra for the *tert*-butyl (((4-chlorophenyl)thio(phenyl)methyl)carbamate.

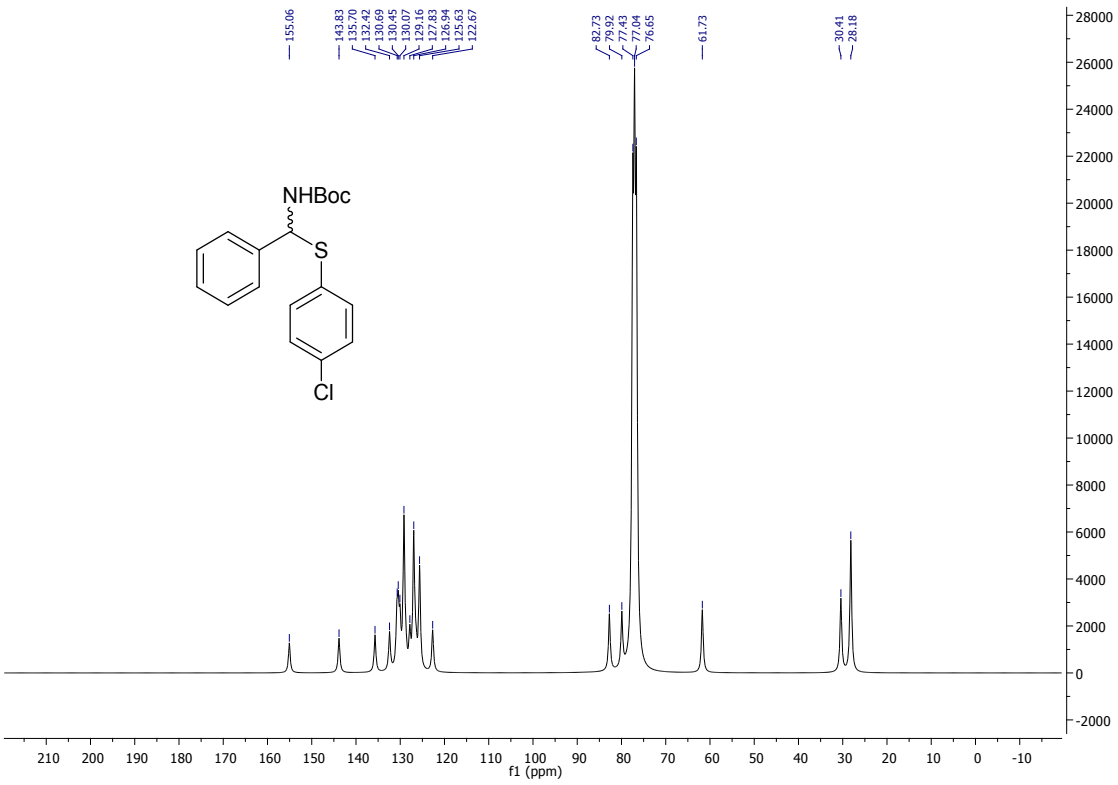


Figure 7. ^{13}C NMR spectra for the *tert*-butyl (((4-chlorophenyl)thiol(phenyl)methyl)carbamate.

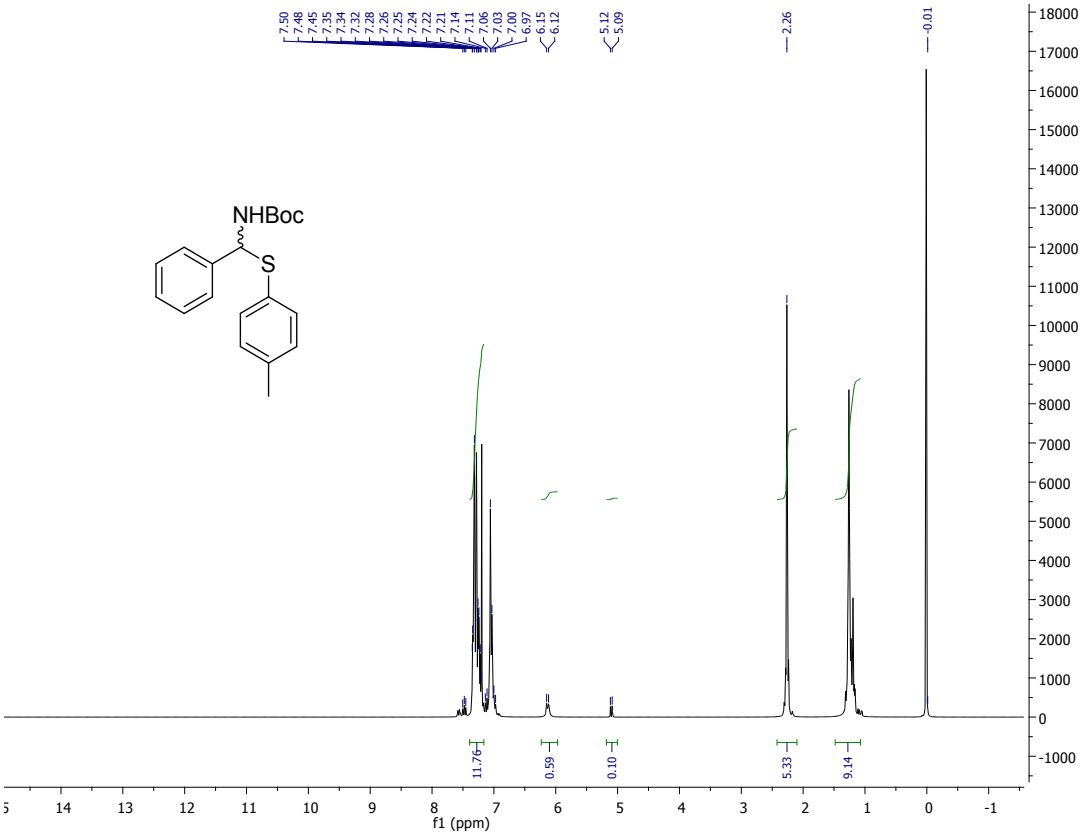


Figure 8. ^{1}H NMR spectra for the *tert*-butyl (phenyl)(p-tolylthio)methyl)carbamate.

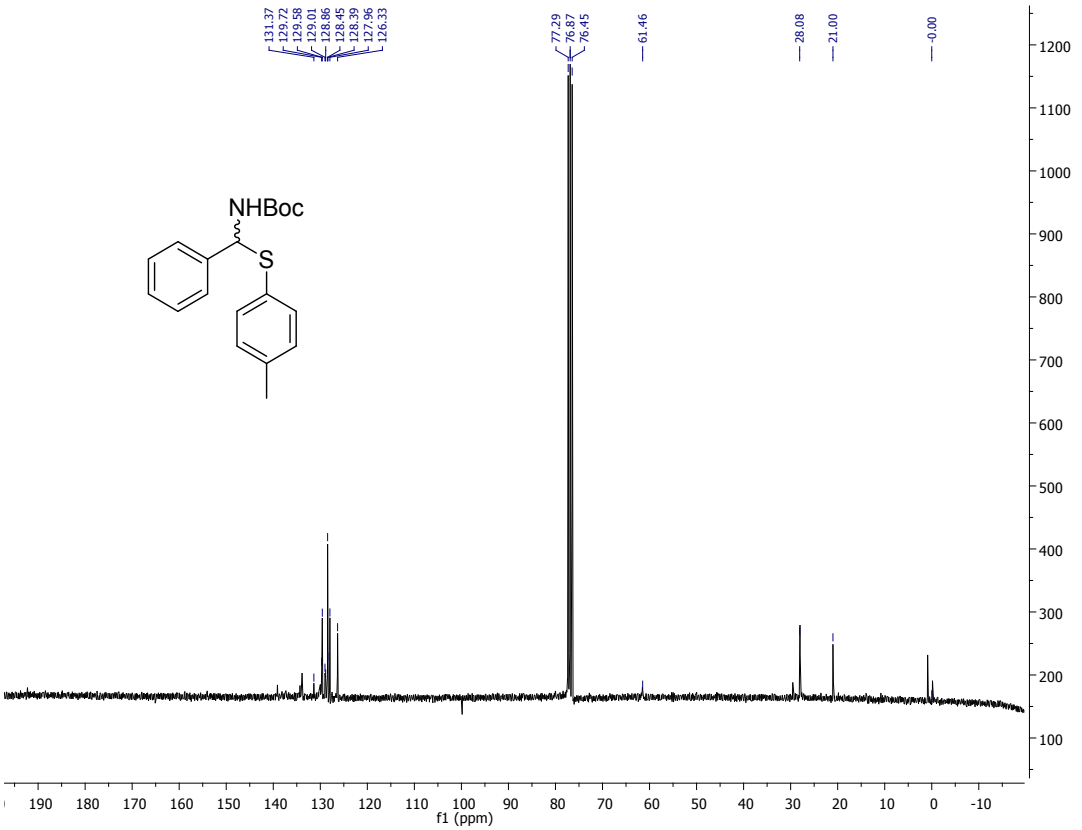


Figure 9. ^{13}C NMR spectra for the *tert*-butyl (phenyl)(p-tolylthio)methyl)carbamate.

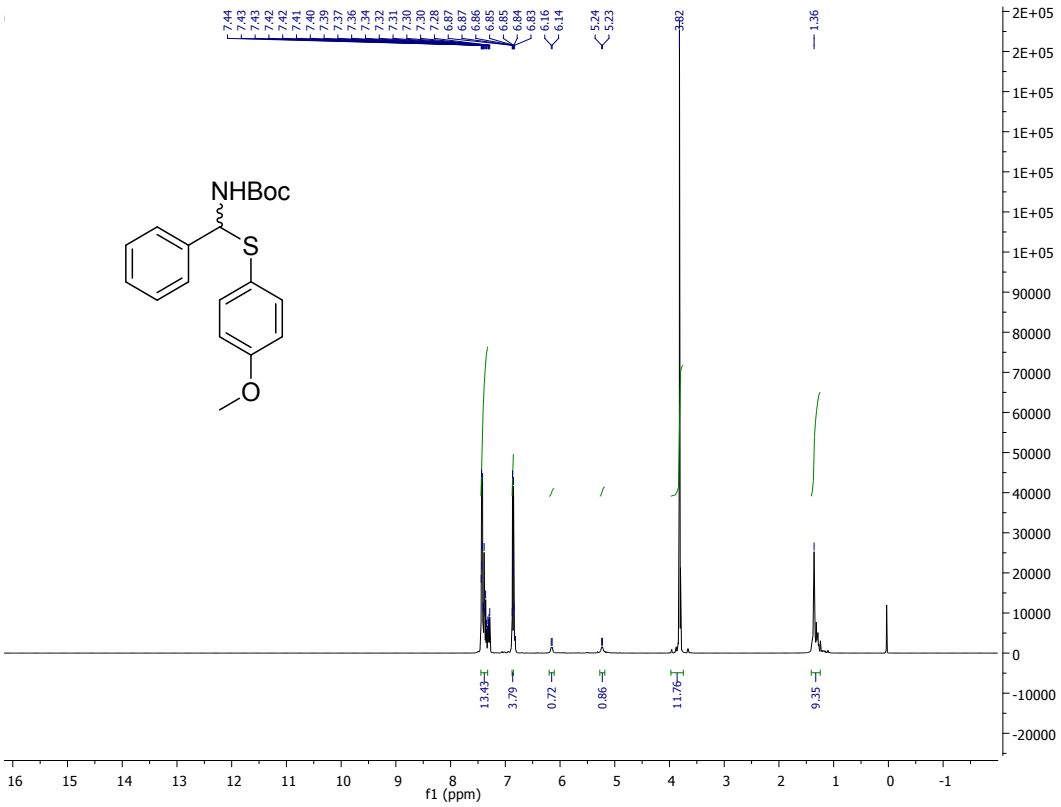


Figure 10. ^{1}H NMR spectra for the *tert*-butyl (((4-methoxyphenyl)thio)(phenyl)methyl)carbamate.

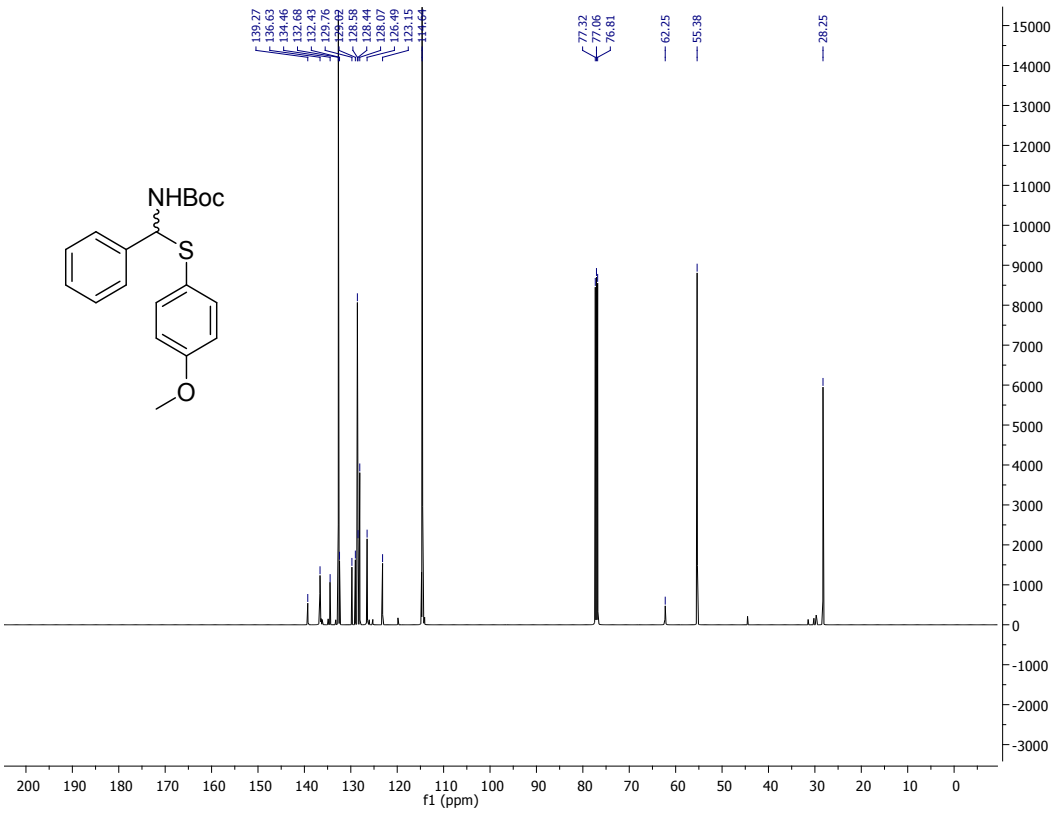


Figure 11. ^{13}C NMR spectra for the *tert*-butyl (((4-methoxyphenyl)thio)(phenyl)methyl)carbamate.

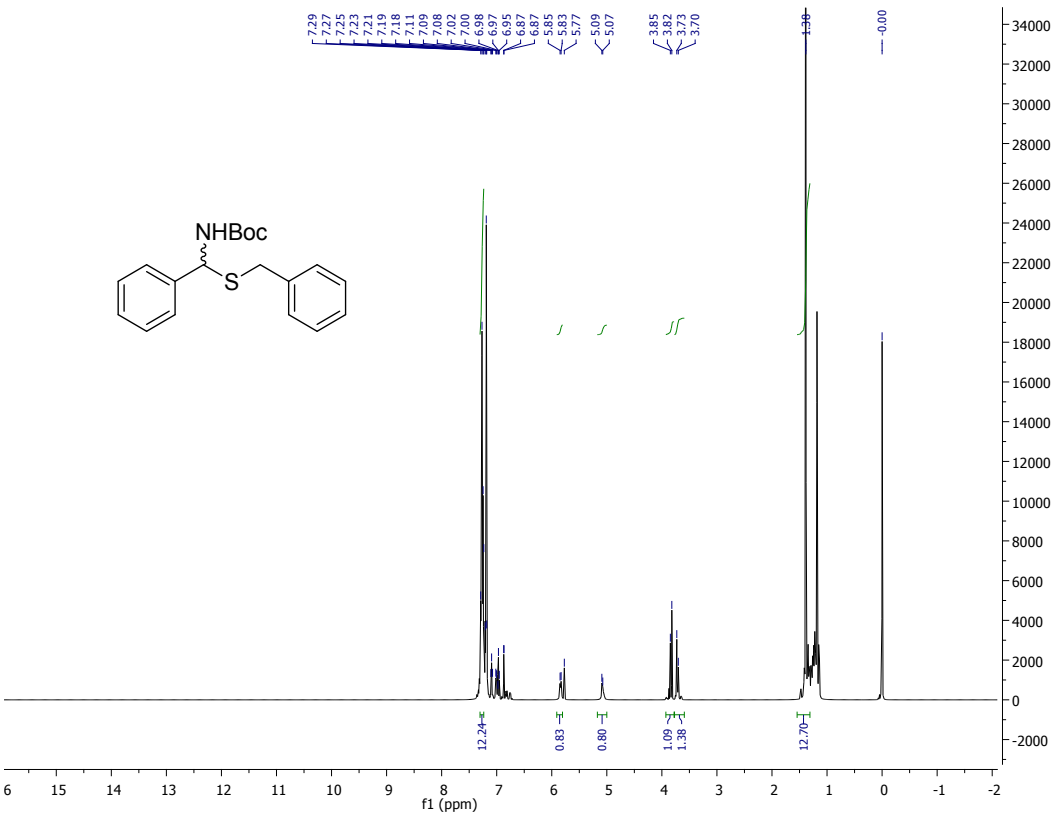


Figure 12. ^{1}H NMR spectra for the *tert*-butyl ((benzylthio)(phenyl)methyl)carbamate.

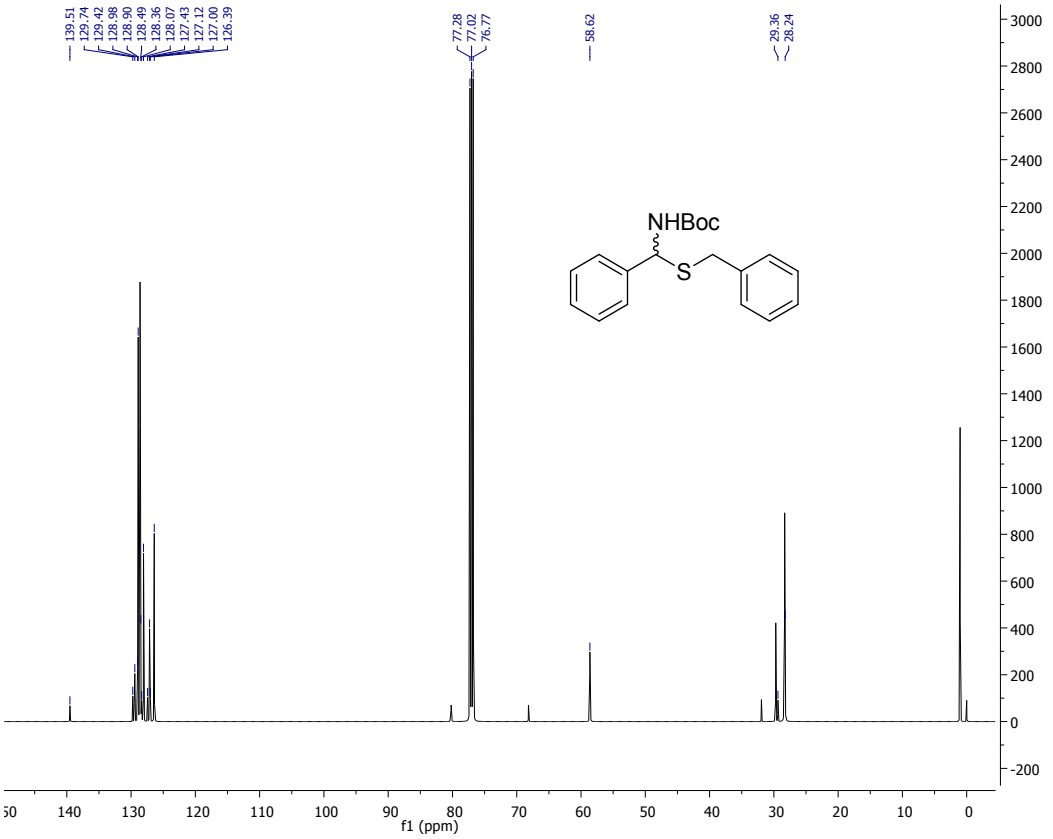


Figure 13. ^{13}C NMR spectra for the *tert*-butyl ((benzylthio)(phenyl)methyl)carbamate.

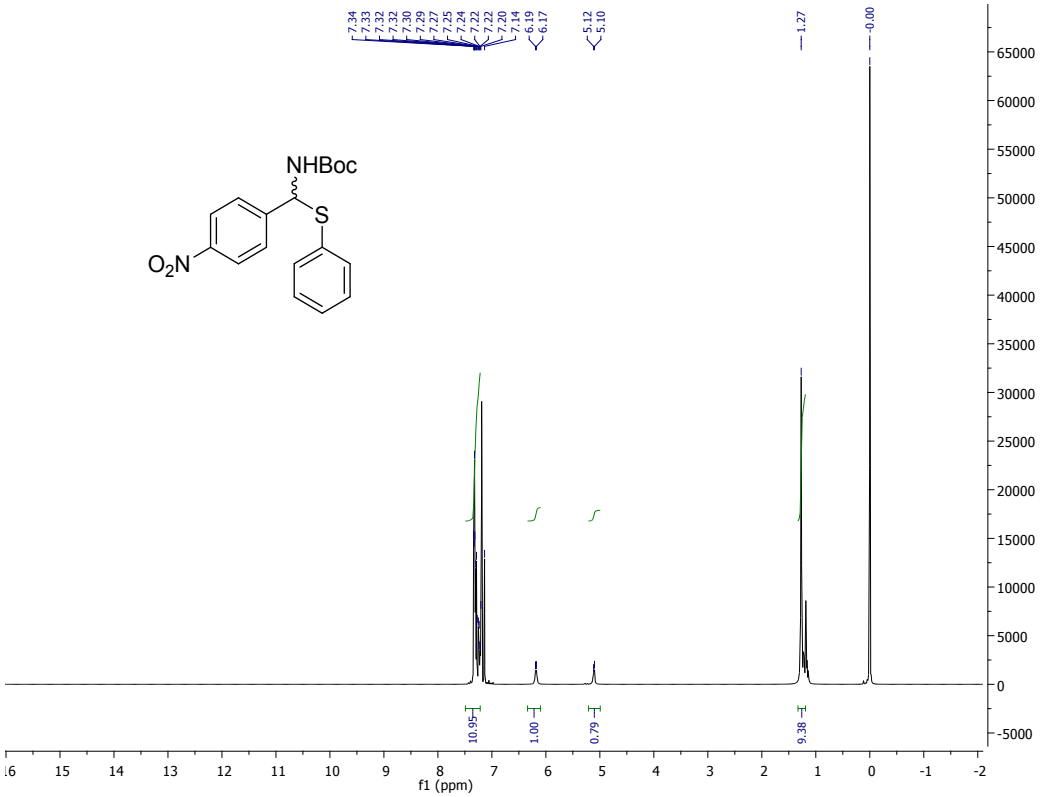


Figure 14. ^{1}H NMR spectra for the *tert*-butyl ((4-nitrophenyl)(phenylthio)methyl)carbamate.

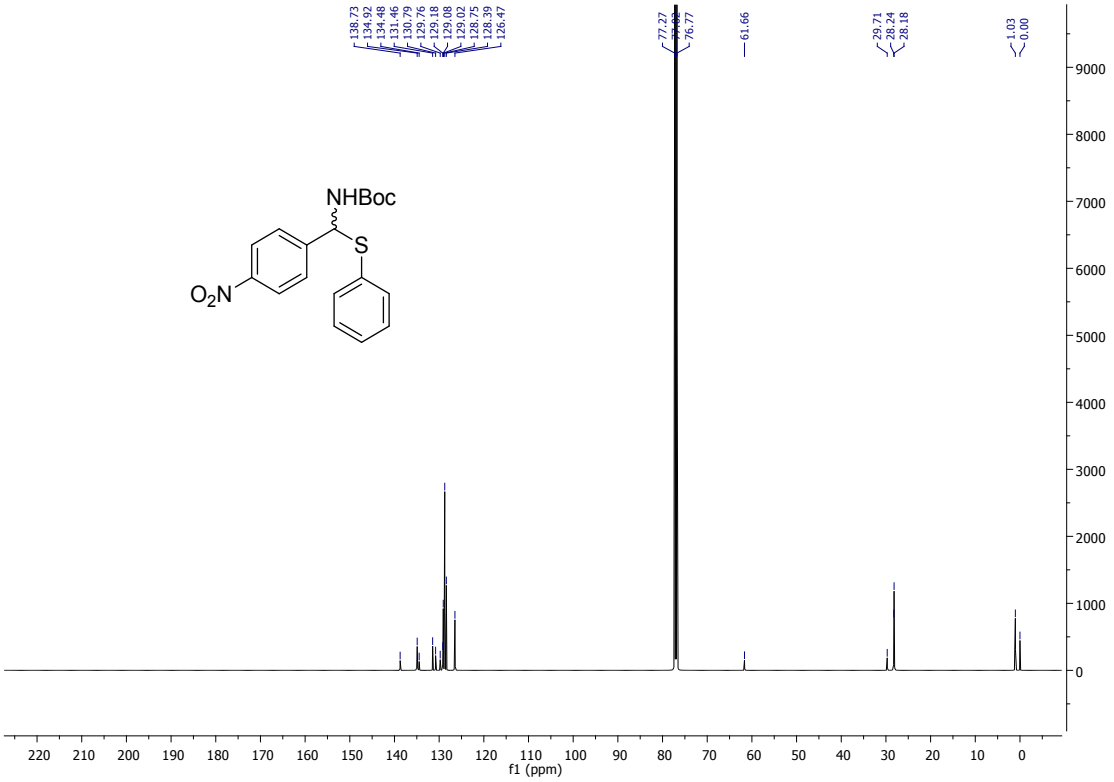


Figure 15. ^{1}H NMR spectra for the *tert*-butyl ((4-nitrophenyl)(phenylthio)methyl)carbamate.

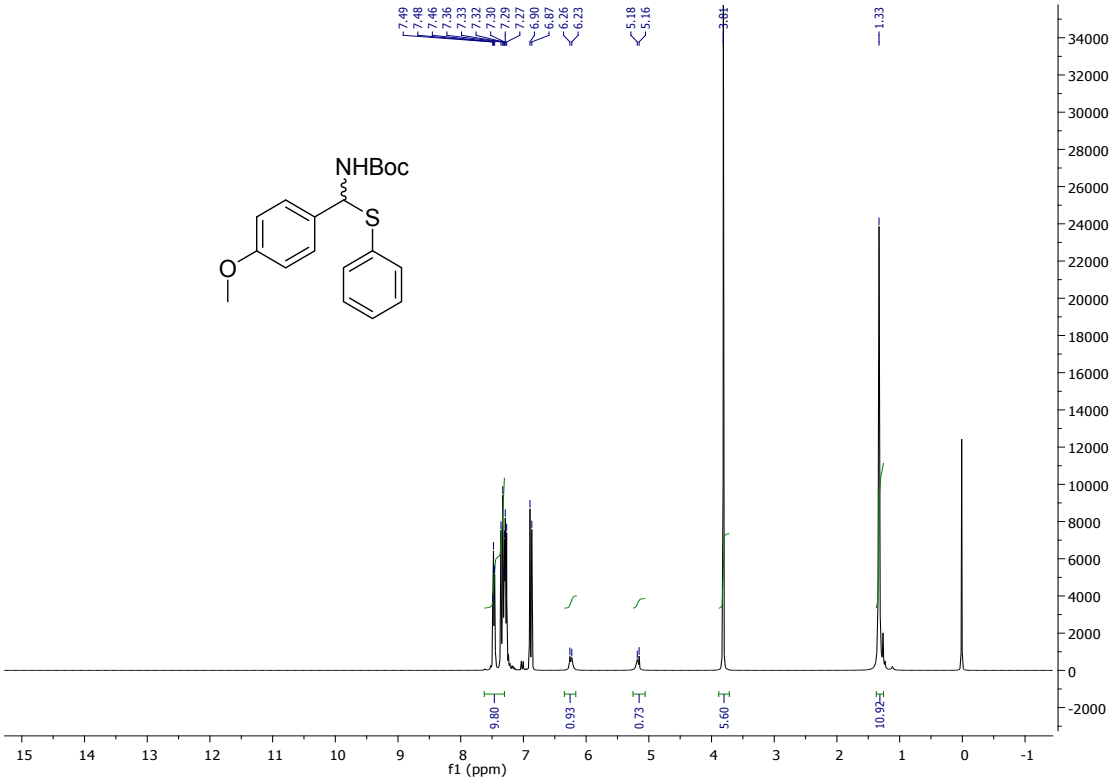


Figure 16. ^{1}H NMR spectra for the *tert*-butyl ((4-methoxyphenyl)(phenylthio)methyl)carbamate.

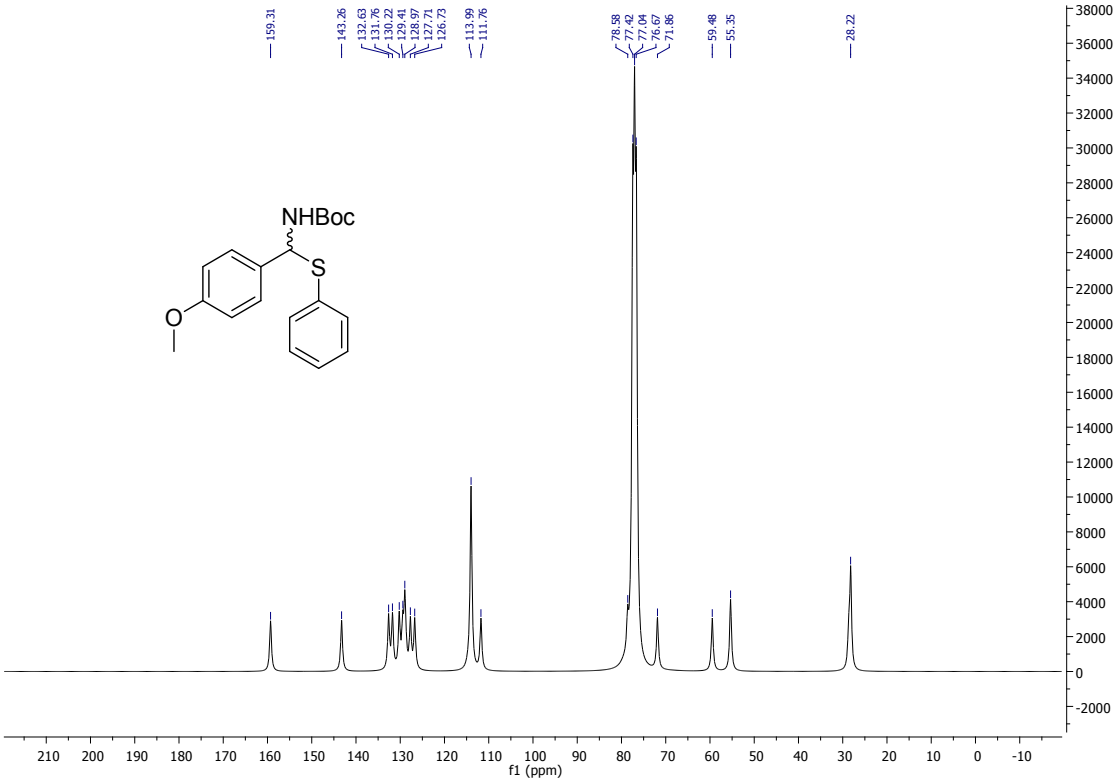


Figure 17. ^{13}CNMR spectra for the *tert*-butyl ((4-methoxyphenyl)(phenylthio)methyl)carbamate.

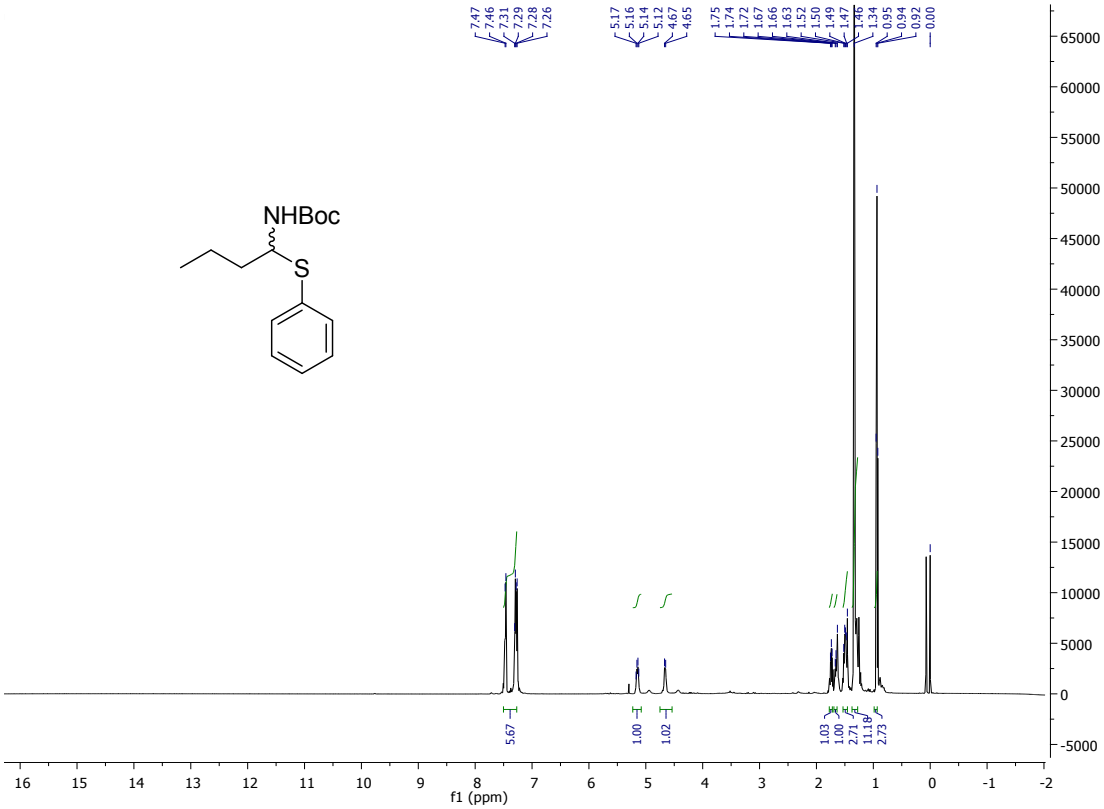


Figure 18. ^{1}H NMR spectra for the *tert*-butyl (1-(phenylthio)butyl)carbamate.

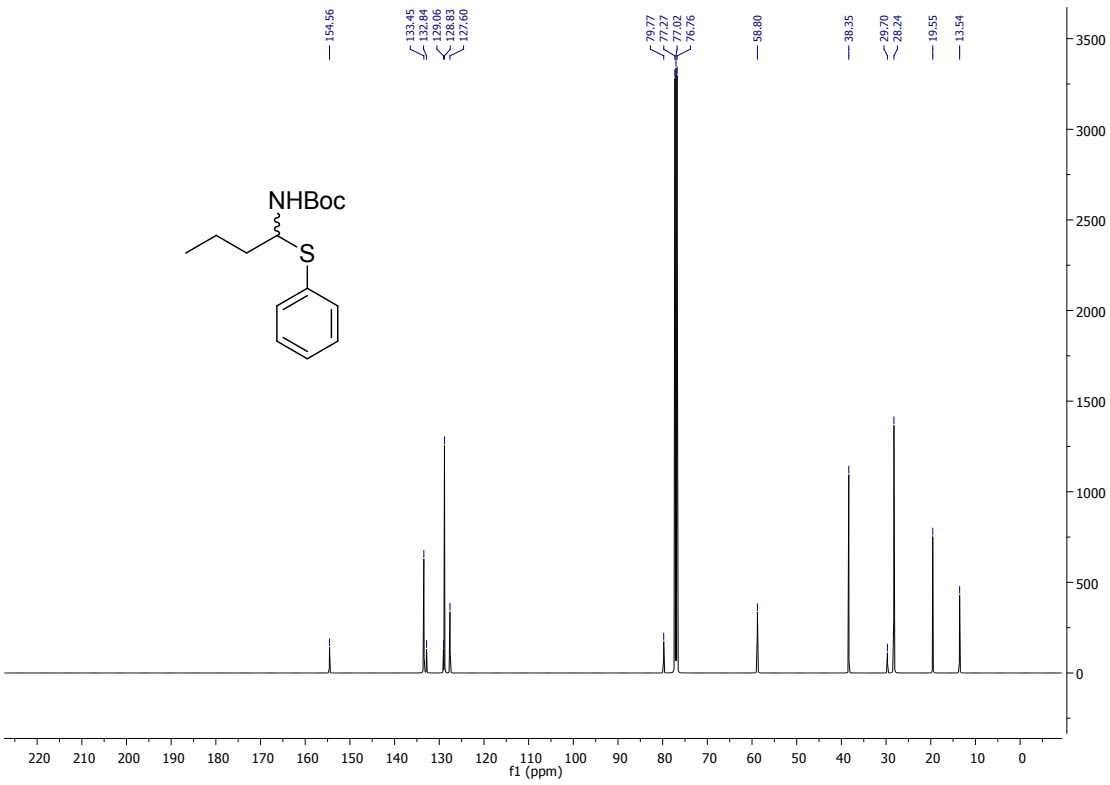


Figure 19. ^{1}H NMR spectra for the *tert*-butyl (1-(phenylthio)butyl)carbamate.