Electronic Supplementary Information (ESI)

C-S Cross-Coupling of Thiols with Aryl Iodides under Ligand Free Conditions Using Nano Copper Oxide as a Recyclable Catalyst in Ionic Liquid

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Experimental Section

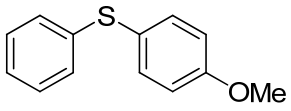
Materials and Methods. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3OD at 400 MHz, 300 MHz and 200 MHz or at 100 MHz, 75 MHz and 50 MHz respectively. Chemical shifts (ä) are reported in ppm relative to the TMS (^{1}H NMR) and to the solvent (^{13}C NMR). Mass spectra were obtained using an instrument with an electrospray ionization source (ESIMS). Column chromatography was performed using Merck Silica Gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck Silica Gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, ninhidrin, or acidic vanillin. The yields of the coupled products included in all tables refer to isolated yields. The ionic liquids were prepared according to the literature.[1]

General procedure for the coupling of aryl iodides with thiols: In a Schlenck tube under argon atmosphere CuO nanoparticles (0.055 mmol, 10 mol%) followed by thiol (0.5 mmol) and Cs_2CO_3 (0.6 mmol, 1.2 equiv) were added to a solution of aryl iodides (0.55 mmol) in [bmmim]BF_4 (1.0 mL). The mixture was stirred at 110 ^{o}C for the appropriate time. The progress of the reaction was monitored by TLC. After, the reaction was complete, the product was extracted by successive washing with diethyl ether (5 x 8 mL) and drying over $MgSO_4$. The solvent was then removed under vacuum to give the crude products, which were purified by column chromatography on silica gel.

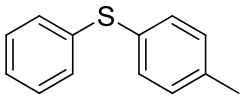
Recyclability Experiments. The CuO nanopowders and solvent [bmmim]BF_4can be recycled without loss of activity (Fig. 1). After completion of the reaction workup, the reaction mixture was treated with ethanol, and filtered through a Teflon membrane. The CuO nanopowder was recovered from the membrane by washing with water and collected by further centrifugation and drying under vacuum. It was reused for the reactions in the next three runs, and no loss of activity was observed, providing the product in high yields. After the work-up, the [bmmim]$BF_4$was recovered, dissolved in 5 mL of acetone and filtered through a celite pad to remove the CuO. The solution was dried over $MgSO_4$ and the volatiles were removed under vacuum. The recovered ionic liquid was reused for the next reaction.

Characterization data for compounds 3a-3o (table 4)

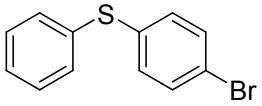
4-methoxyphenyl phenyl sulfide (Table 4 entry 1).[2] The general procedure was used to convert 4-iodoanisol and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.82 Hz, 2H), 7.27-7.08 (m, 5H), 6.88 (*J* = 8.82 Hz, 2H), 3.80 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.76, 138.53, 135.27, 128.84, 128.14, 125.68, 124.24, 114.91, 55.26 ppm.



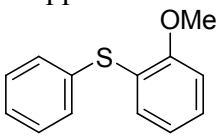
4-methylphenyl phenyl sulfide (Table 4, entry 2).[2] The general procedure was used to convert 4-iodotoluene and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.29-7.13 (m, 7H), 7.11 (d, *J* = 7.82 Hz, 2H), 2,31 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 137.51, 137.07, 132.20, 131.24, 130.00, 129.72, 128.97, 126.33, 21.06 ppm.



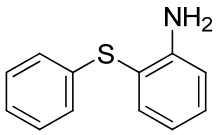
4-bromophenyl phenyl sulfide (Table 4, entry 3).[3] The general procedure was used to convert 1-bromo-4-iodobenzene and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7,51-7.11 (m, 9H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 136.96, 135.42, 134.76, 132.14, 131.99, 131.46, 129.29, 128.99, 127.47, 127.43, 127.07, 120.78 ppm.



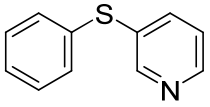
2-methoxyphenyl phenyl sulfide (Table 4, entry 4).[2] The general procedure was used to convert 2-iodoanisol and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.36-7.18 (m, 6H), 7.07 (dd, J^1 = 7.49 Hz, J^2 = 1.76 Hz, 1H), 6.90-6.81 (m, 2H), 3.85 (s, 3H) ppm. **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 157.11, 134.31, 131.42, 131.27, 129.00, 128.21, 126.91, 123.83, 121.08, 110.68, 55.69 ppm.



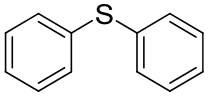
2-Phenylsulfanylaniline (Table 4, entry 5).[3] The general procedure was used to convert 2-iodoaniline and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.0:1.0] as the eluent) gave the analytically pure product as a pale yellow oil. Yield: 97%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.47-7.42 (m, 1H), 7.26-7.04 (m, 6H), 6.78-6.70 (m, 2H), 3.99 (br, 2H) ppm. **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 148.74, 137.41, 136.73, 131.08, 128.93, 126.35, 125.33, 118.67, 115.29, 114.23 ppm.



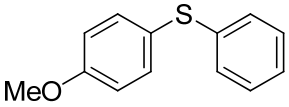
3-(phenylthio)pyridine (Table 4, entry 6). The general procedure was used to convert 3-iodopyridine and benzenethiol to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.0:1.0] as the eluent) gave the analytically pure product as a colorless oil. Yield: 96%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 8.54 (s, 1H), 8.45-8.43 (m, 1H), 7.61-7.55 (m, 1H), 7.39-7.27 (m, 5H), 7.20-7.16 (m, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 150.80, 147.61, 137.73, 133.74, 131.60, 129.35, 127.71, 123.77 ppm. **HRMS-ESI**: *m/z* calcd for $C_{11}H_9NS$ $[M + H]^+$ 188,0534; found 188.0529.



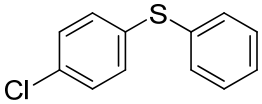
diphenyl sulfide (Table 4, entry 7).[2] The general procedure was used to convert idobenzene and benzenethiol to the title product. Purification by flash chromatography (hexane as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.35-7.14 (m, 10H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 135.71, 130.94, 129.09, 126.93 ppm.



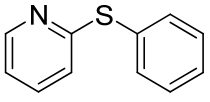
4-methoxyphenyl phenyl sulfide (Table 4, entry 8).[2] The general procedure was used to convert 4-methoxybenzenethiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.82 Hz, 2H), 7.27-7.08 (m, 5H), 6.88 (*J* = 8.82 Hz, 2H), 3.80 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.76, 138.53, 135.27, 128.84, 128.14, 125.68, 124.24, 114.91, 55.26 ppm.



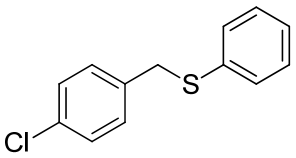
4-chlorophenyl phenyl sulfide (Table 4, entry 9).[4] The general procedure was used to convert 4-chlorobenzenethiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.35-7.23 (m, 9H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 135.06, 134.59, 132.92, 131.94, 131.25, 129.27, 129.24,127.36 ppm.



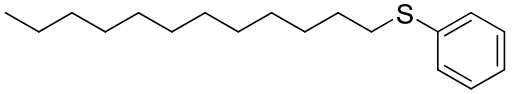
2-(phenylthio)pyridine (Table 4, entry 10).[2] The general procedure was used to convert pyridine-3-thiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a colorless oil. Yield: 80%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 8.43-8.40 (m, 1H), 7.61-7.57 (m, 2H), 7.44-7.39 (m, 4H), 7.02-6.95 (m, 1H), 6.89-6.85 (m, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 161.44, 149.45, 136.64, 134.84, 130.95, 129.54, 129.00, 121.28, 119.80 ppm.



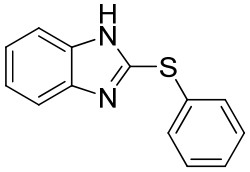
4-chlorobenzyl phenyl sulfide (Table 4, entry 11).[5] The general procedure was used to convert 4-chlorobenzylthiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a white solid. Yield: 99%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.31-7.12 (m, 9H), 4.05 (s, 2H) ppm. **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 136.08, 132.87, 130.62, 130.20, 130.06, 128.87, 128.59, 126.63, 38.48 ppm.



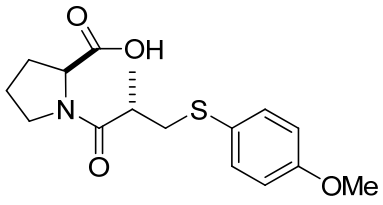
dodecyl phenyl sulfide (Table 4, entry 12).[6] The general procedure was used to convert 1-dodecanethiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [9.5:0.5] as the eluent) gave the analytically pure product as a white solid. Yield: 76%; **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.34-7.14 (m, 5H), 2.90 (t, *J* = 7.49 Hz, 2H), 1.71-1.55 (m, 2H), 1.25 (s, 18H), 0.88 (t, *J* = 6.80 Hz, 3H) ppm. **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 137.19, 128.73, 125.53, 33.49, 31.89, 29.62, 29.56, 29.48, 29.33, 29.14, 29.09, 28.82, 22.67, 14.10 ppm.



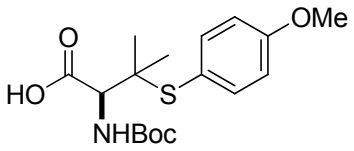
benzimidazole phenyl sulfide (Table 4, entry 13). The general procedure was used to convert 2-benzimidazolethiol and iodobenzene to the title product. Purification by flash chromatography (hexane / ethyl acetate [8.0:2.0] as the eluent) gave the analytically pure product as a white solid. Yield: 80%; **^{1}H NMR** (300 MHz, CD_3OD): δ = 7.52-7.45 (m, 4H), 7.42-7.34 (m, 3H), 7.24-7.18 (m, 2H) ppm. **^{13}C NMR** (75 MHz, CD_3OD): δ = 149.30, 133.05, 132.39, 130.78, 129.71, 123.93 ppm. **HRMS-ESI**: *m/z* calcd for $C_{13}H_{10}N_2S$ $[M + H]^+$ 227,0643; found 227.0635.



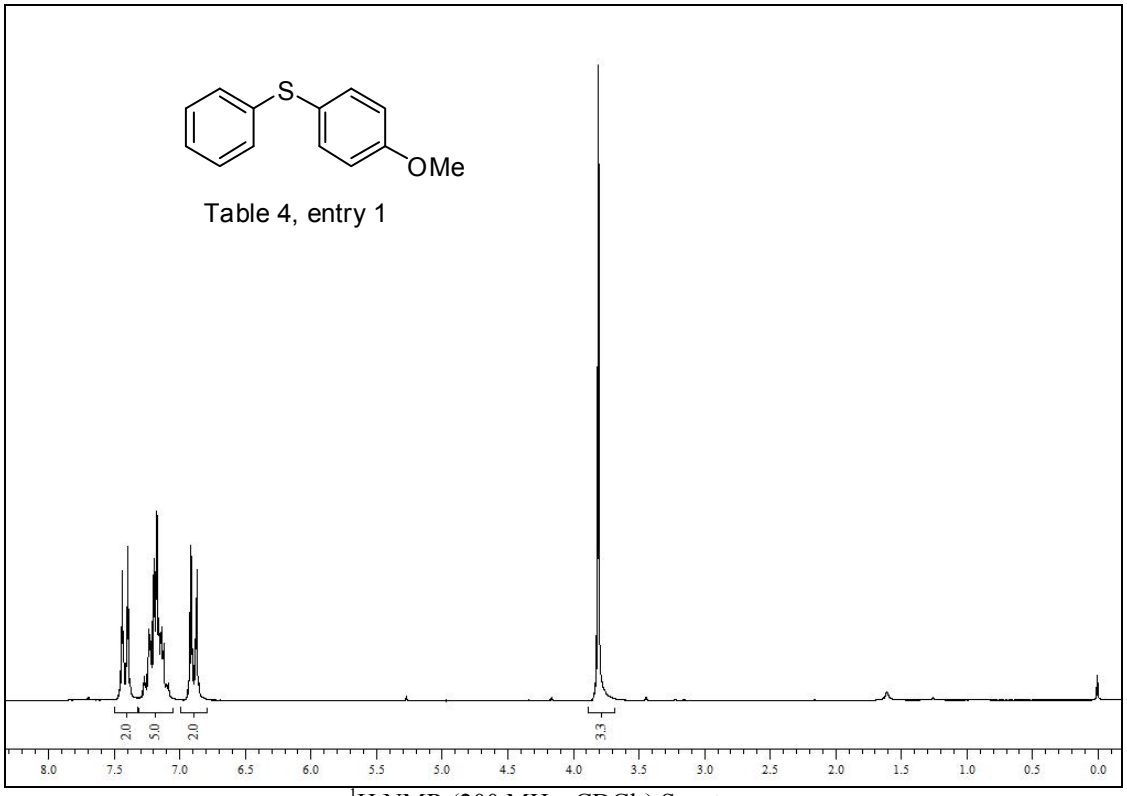
(S)-1-((S)-3-(4-methoxyphenylthio)-2-methylpropanoyl)pyrrolidine-2-carboxylic acid (Table 4, entry 14). The general procedure was used to convert (S)-1-((S)-3-mercapto-2-methylpropanoyl)pyrrolidine-2-carboxylic acid and 4-iodoanisol to the title product. Purification by flash chromatography (chloroform / methanol [8.0:2.0] as the eluent) gave the analytically pure product as a slightly yellow oil. Yield: 70%; $[\alpha_D]$ = -177.1° (*c* = 0.35; CH_2Cl_2); **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 8.37-8.34 (br 1H), 7.35-7.28 (m, 2H), 6.84 (d, *J* = 8.80 Hz, 2H), 4.50-4.46 (m, 1H), 3.79 (s, 3H), 3.52-3.15 (m, 3H), 2.87-2.70 (m, 2H), 2.26-1.89 (m, 4H), 1.21 (d, *J* = 6.60 Hz, 3H) ppm. **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 175.60, 173.93, 158.95, 133.08, 125.67, 114.52, 59.24, 55.26, 47.19, 38.83, 38.26, 27.92, 24.55, 16.95 ppm. **HRMS-ESI**: *m/z* calcd for $C_{16}H_{21}NO_4S$ $[M + Na]^+$ 346,1089; found 346.1079.



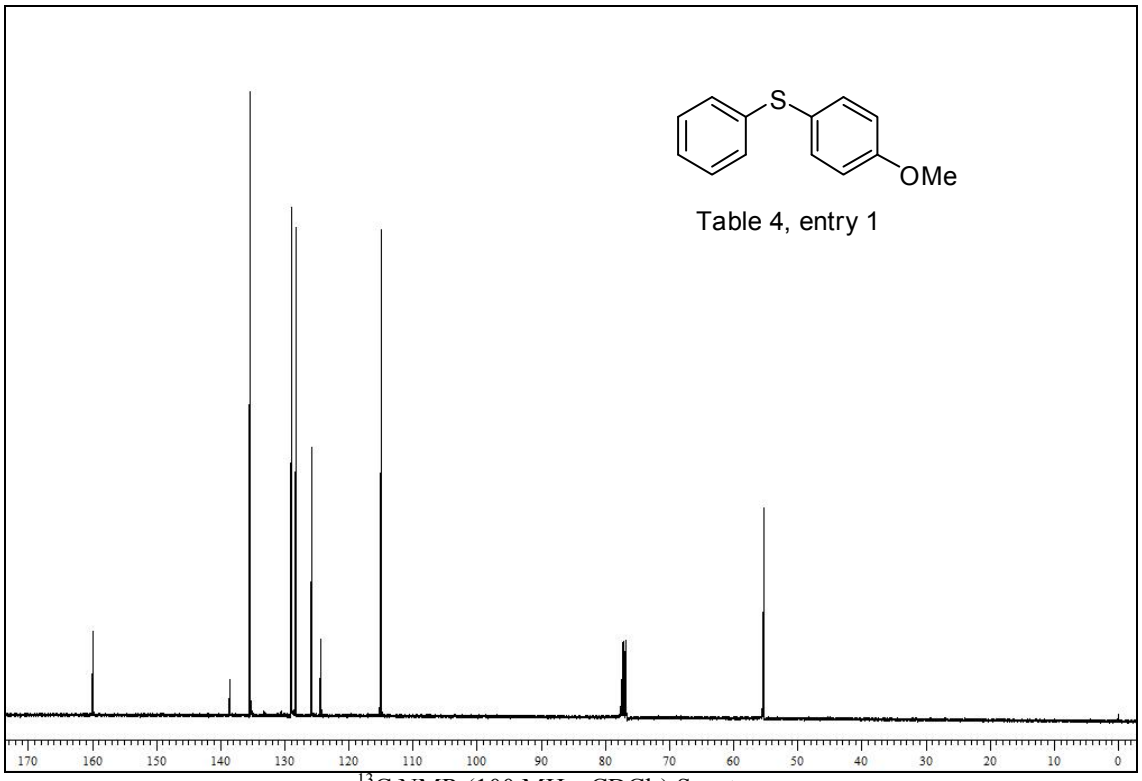
(S)-2-(tert-butoxycarbonylamino)-3-(4-methoxyphenylthio)-3-methylbutanoic acid (Table 4, entry 15). The general procedure was used to convert (S)-2-(tert-butoxycarbonylamino)-3-mercapto-3-methylbutanoic acid and 4-iodoanisol to the title product. Purification by flash chromatography (hexane / ethyl acetate [8.0:2.0] as the eluent) gave the analytically pure product as a slightly yellow oil. Yield: 53%; $[\alpha_D] = +12.4°$ (*c* = 0.31; CH_2Cl_2); **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 9.45-9.43 (br, 1H), 7.47 (d, *J* = 8.80 Hz, 2H), 6.84 (d, *J* = 8.56 Hz, 2H), 5.43-5.40 (m, 1H), 4.14-4.11 (m, 1H), 3.79 (s, 3H), 1.44 (s, 9H), 1.33 (s, 6H) ppm. **^{13}C NMR** (100 MHz, CD_3OD): δ = 173.76, 162.26, 157.55, 140.24, 122.70, 115.26, 80.78, 62.08, 55.80, 50.56, 28.71, 27.33, 25.35 ppm. **HRMS-ESI**: *m/z* calcd for $C_{17}H_{25}NO_5S$ $[M + Na]^+$ 378,1351; found 378.1342.



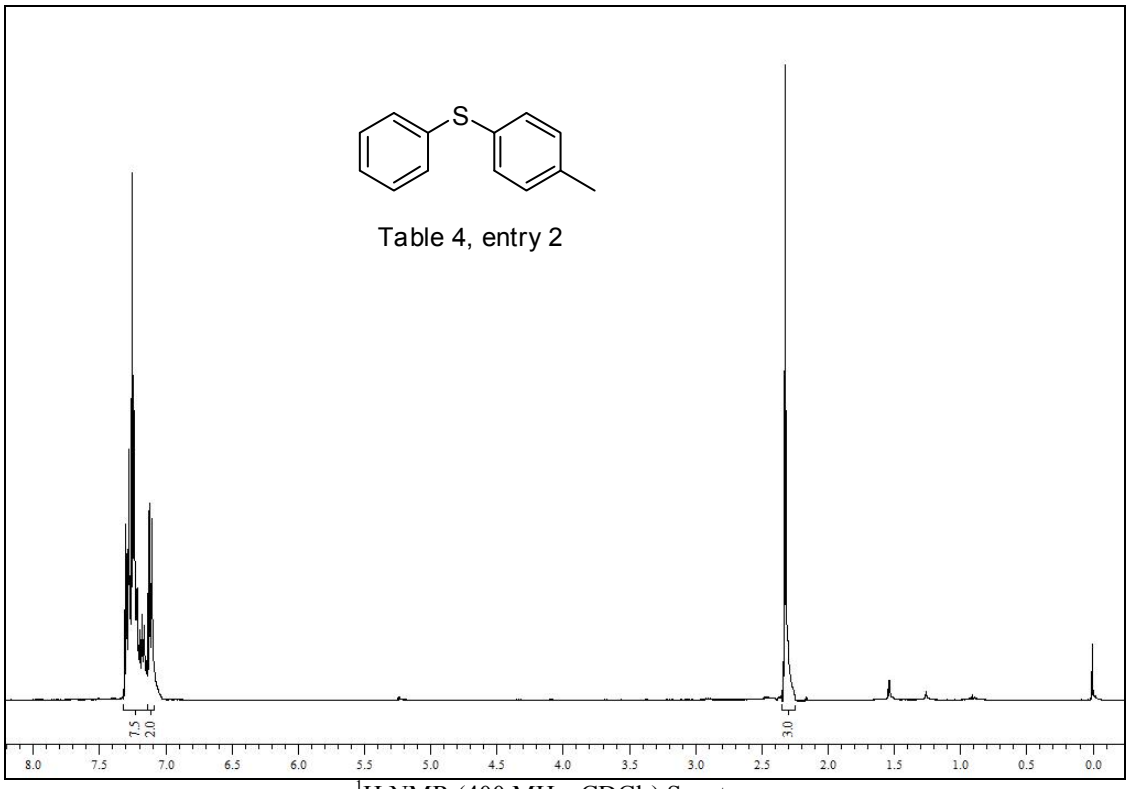
^{1}H and ^{13}C NMR Spectra of Products



^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



^{13}C NMR (100 MHz, $CDCl_3$) Spectrum.



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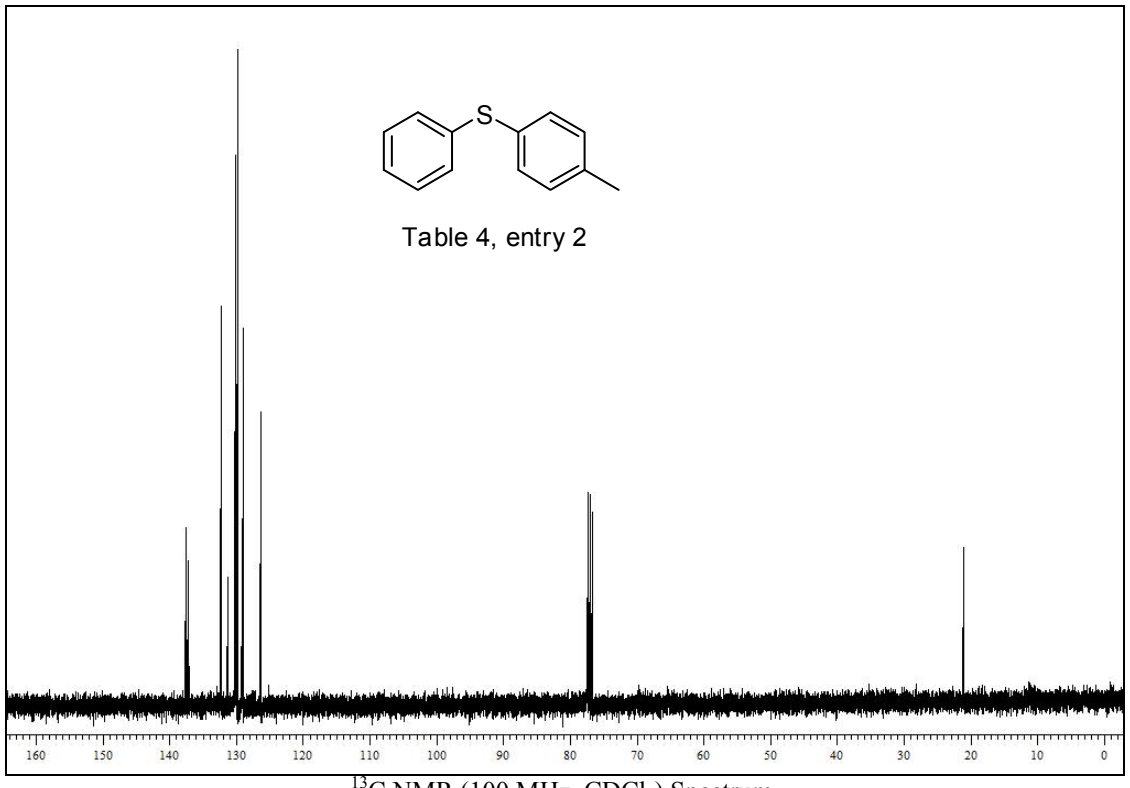

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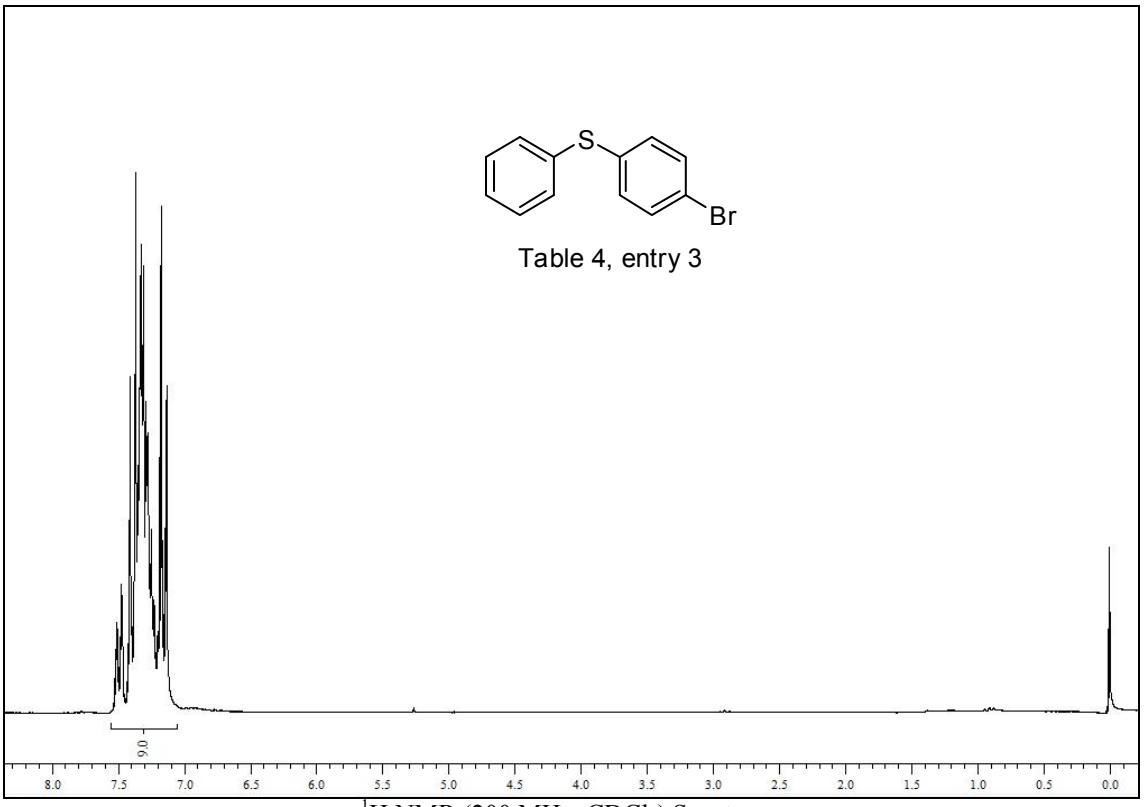

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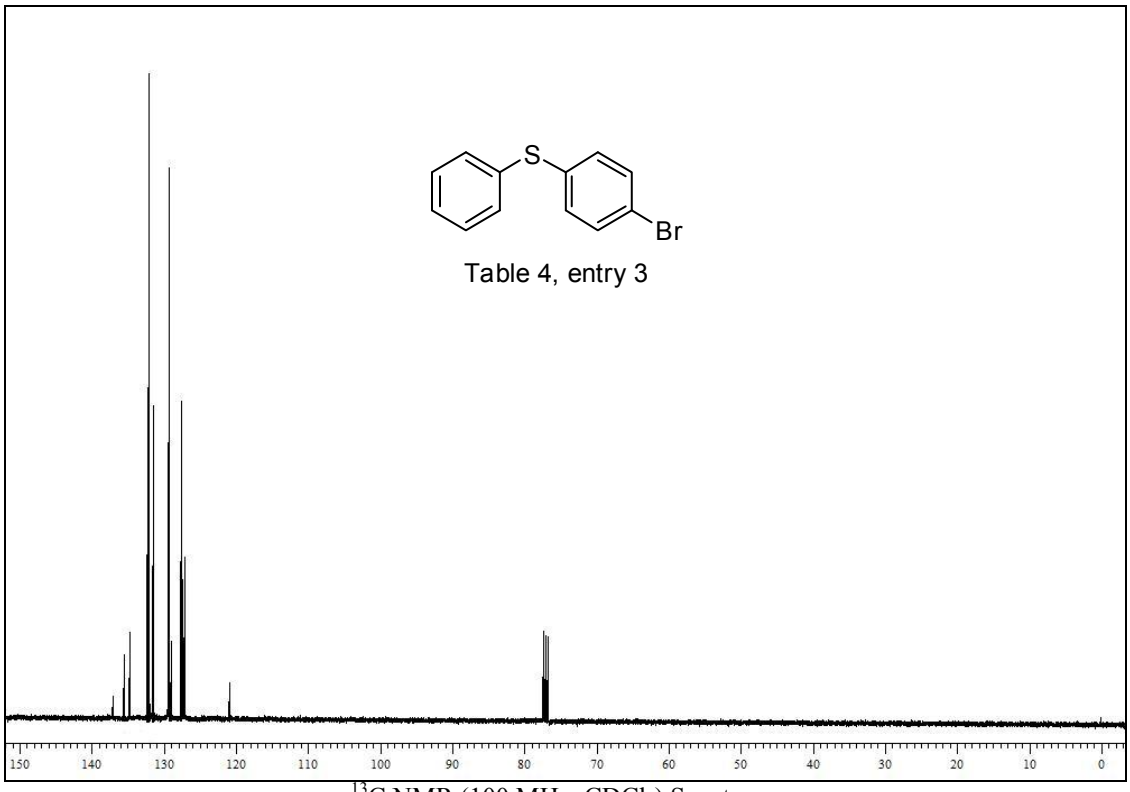

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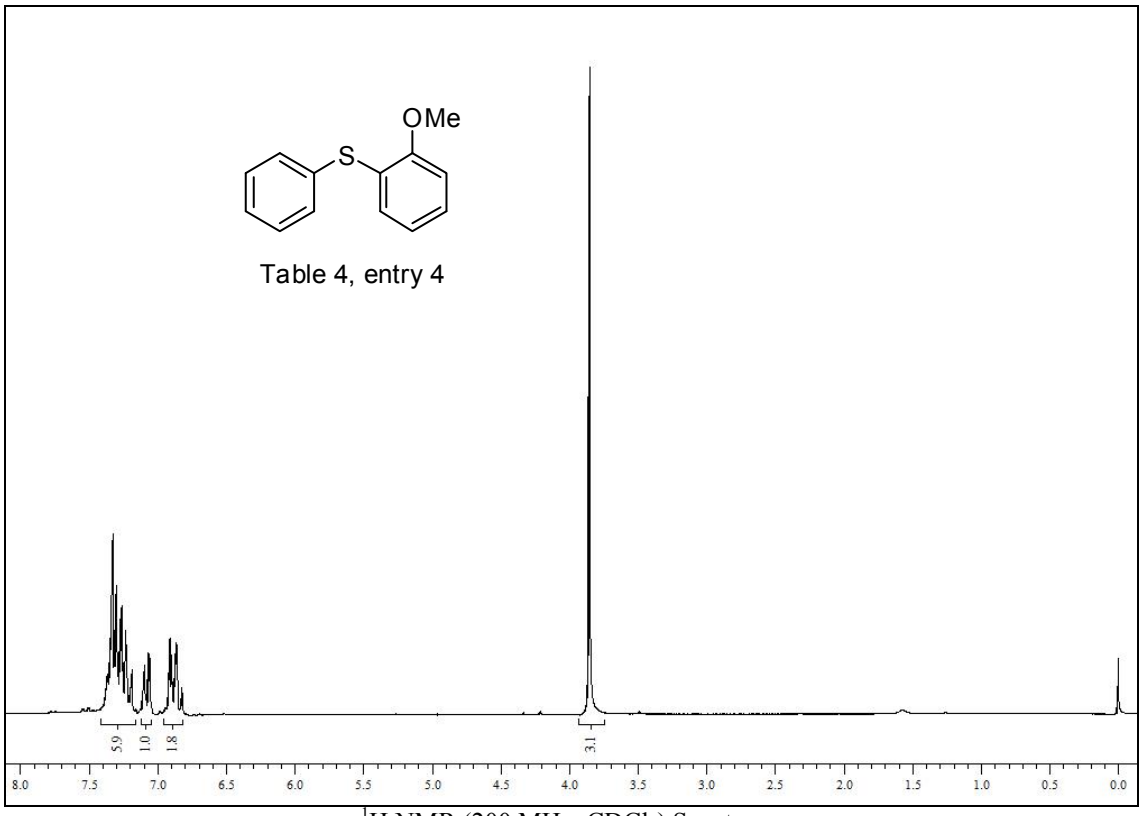

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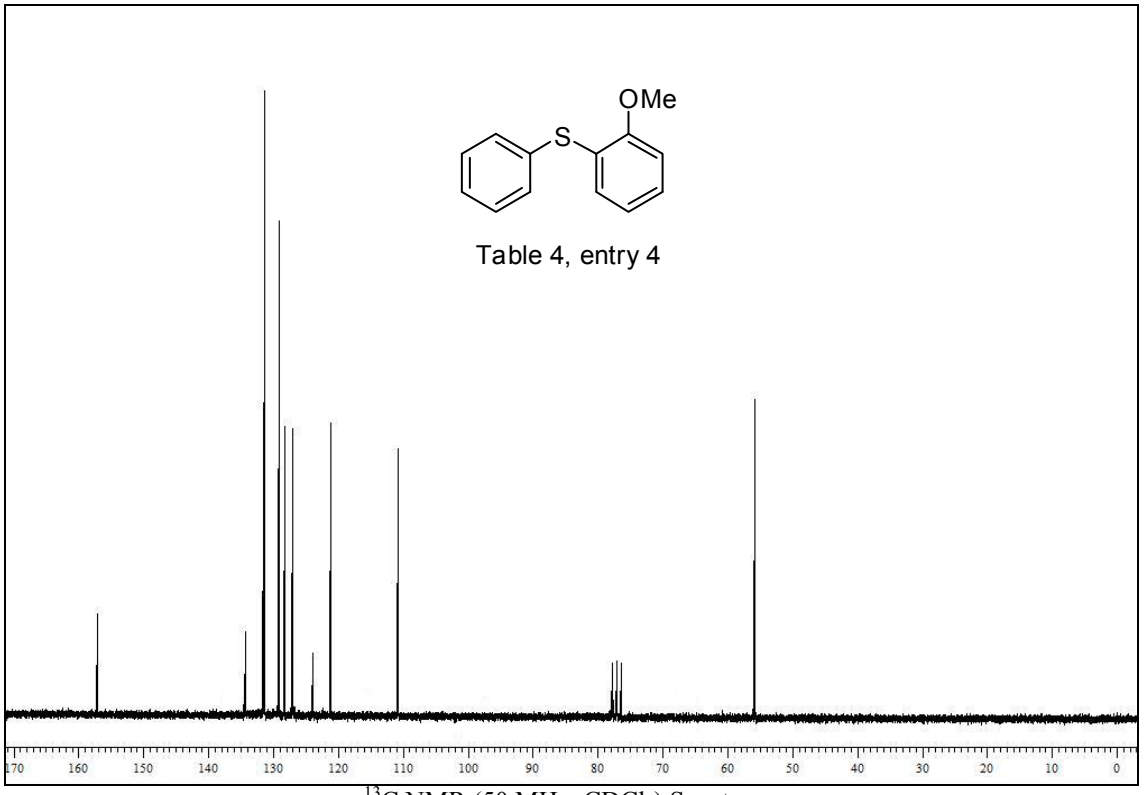

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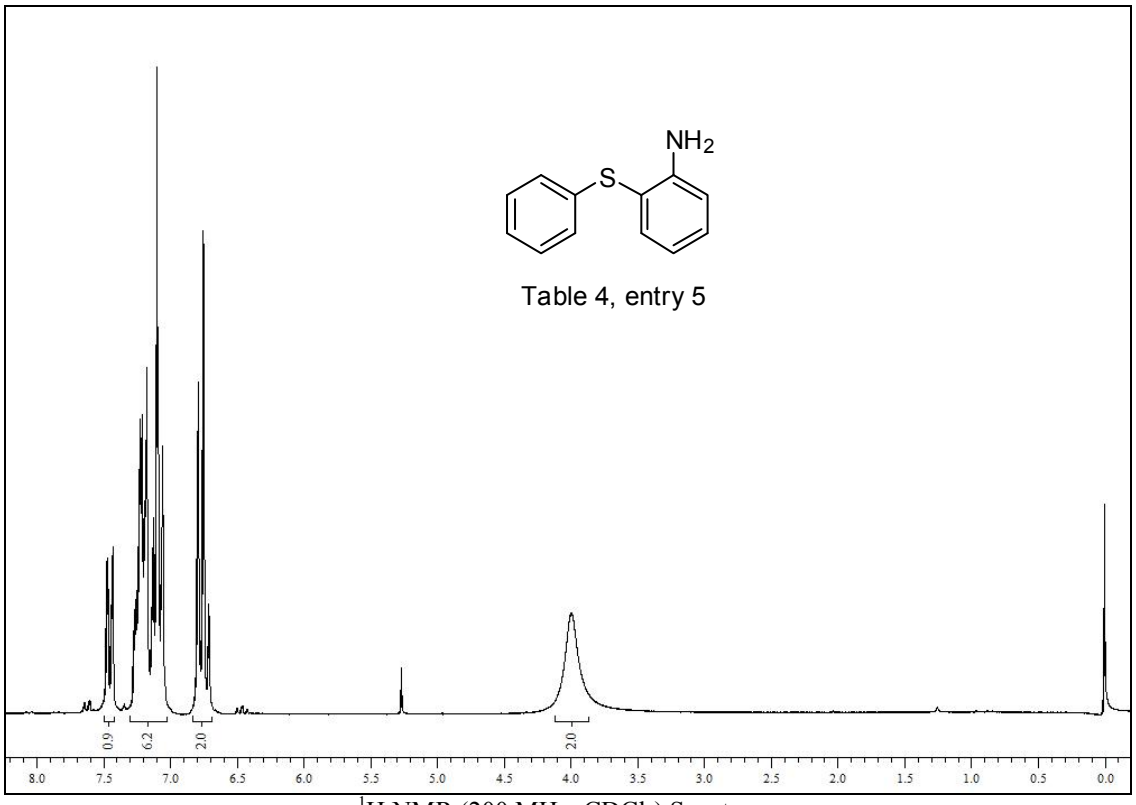

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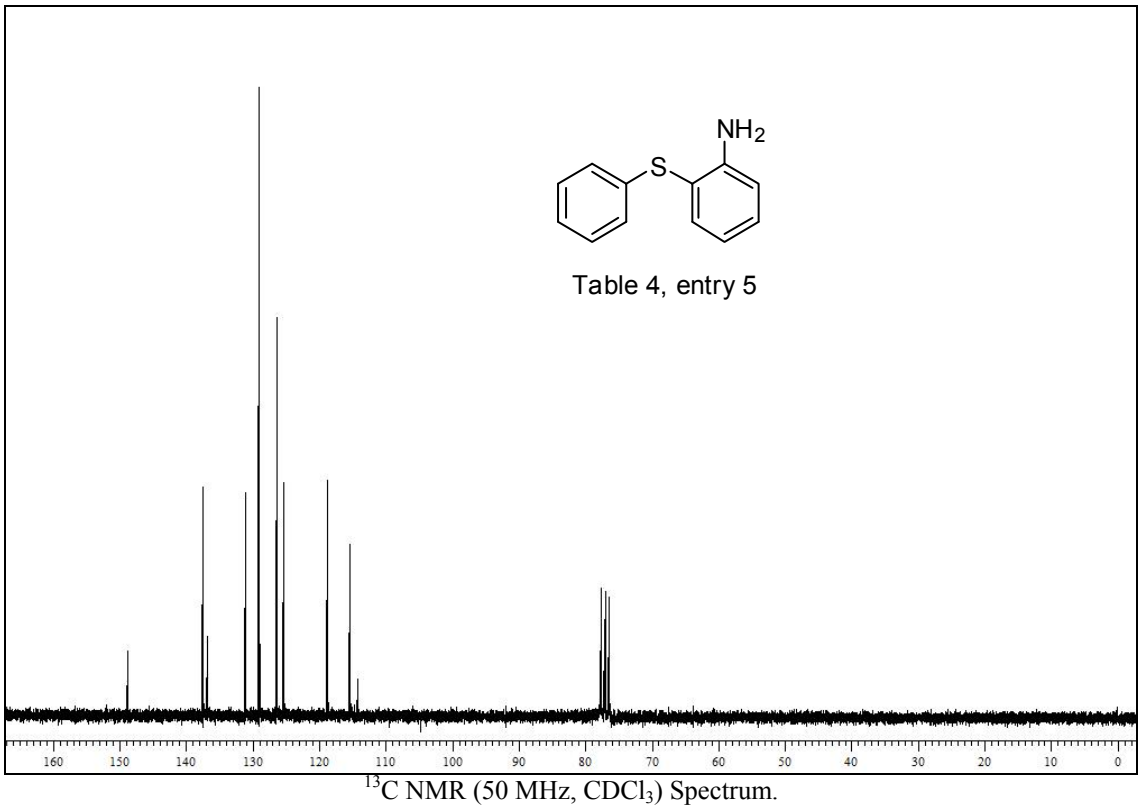

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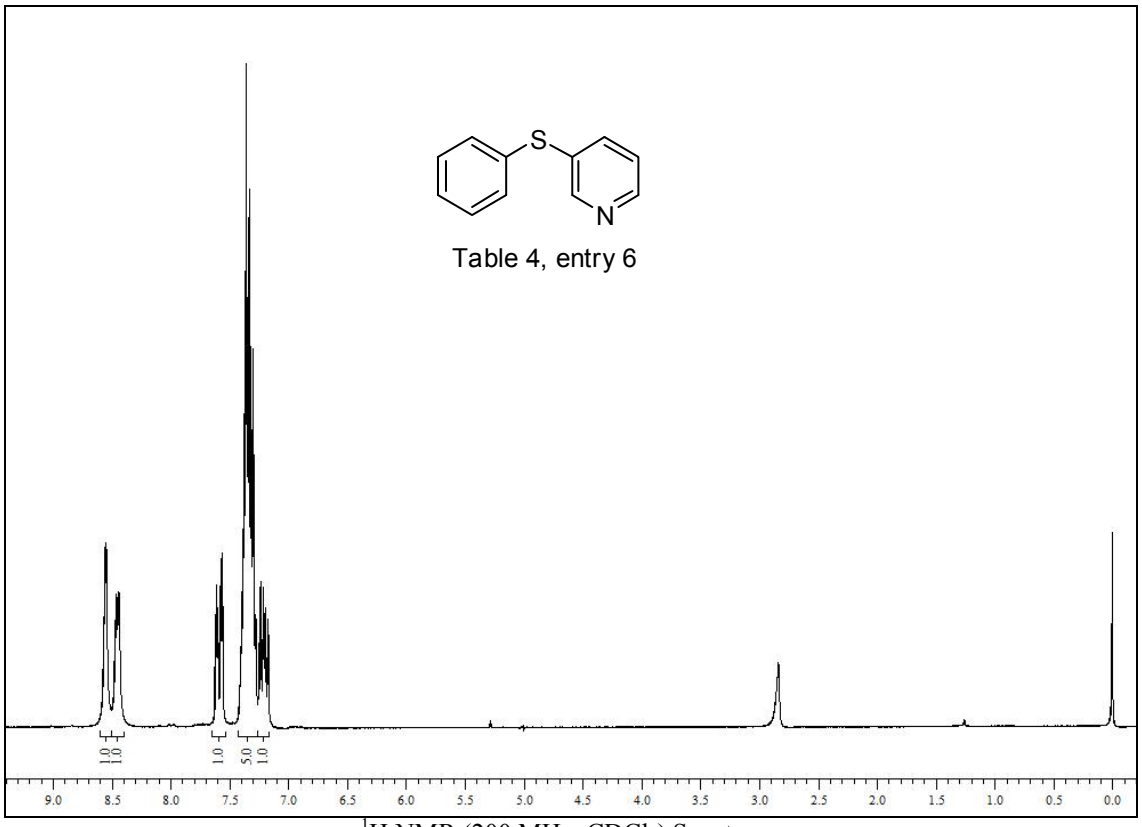
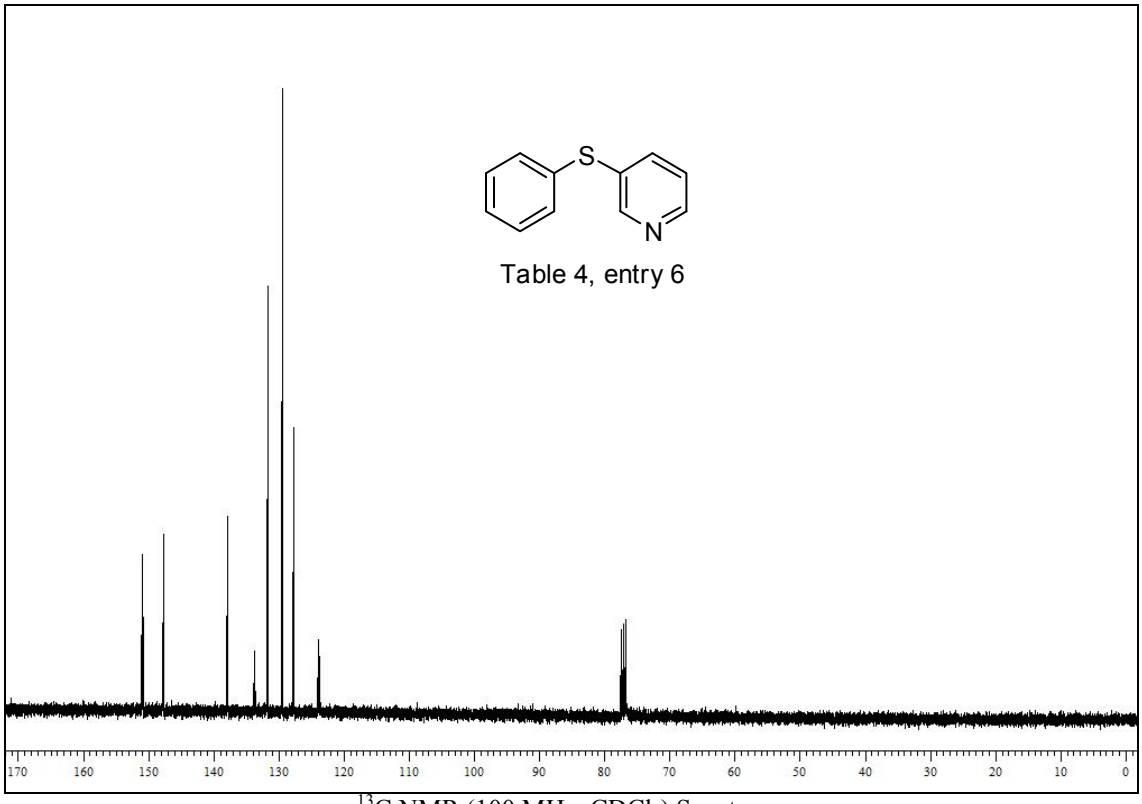
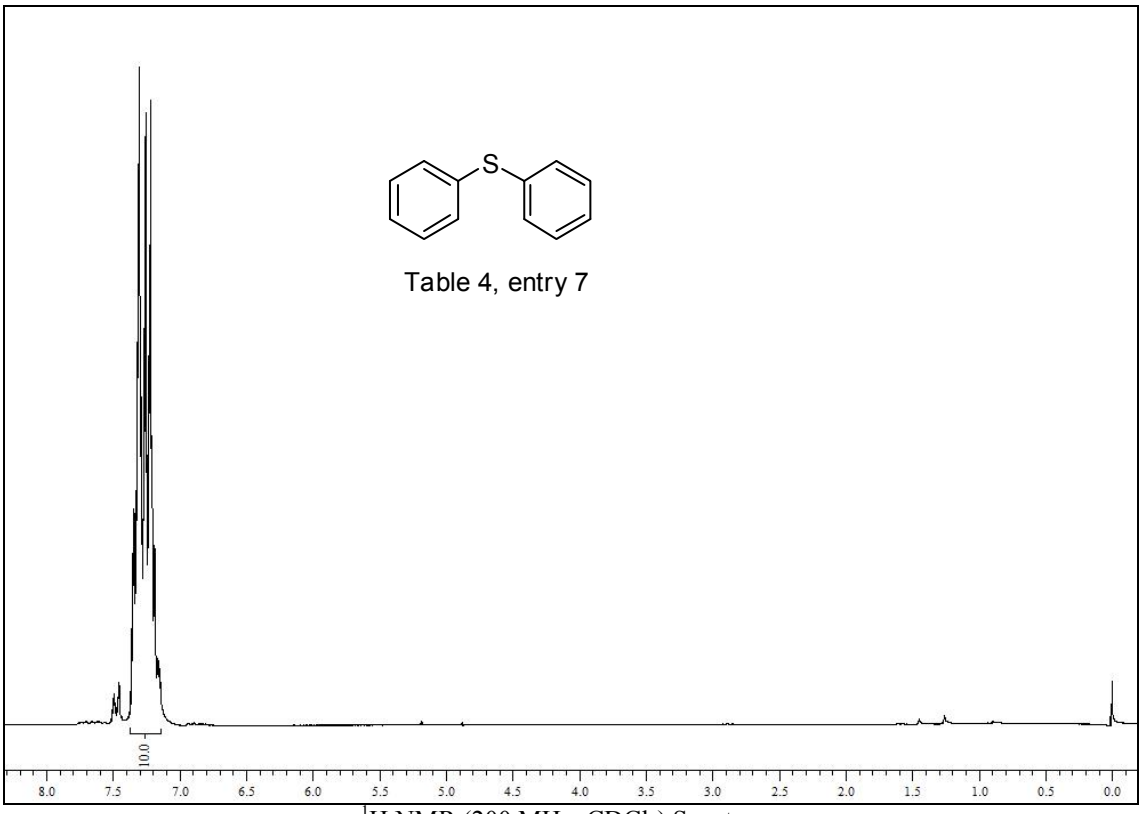


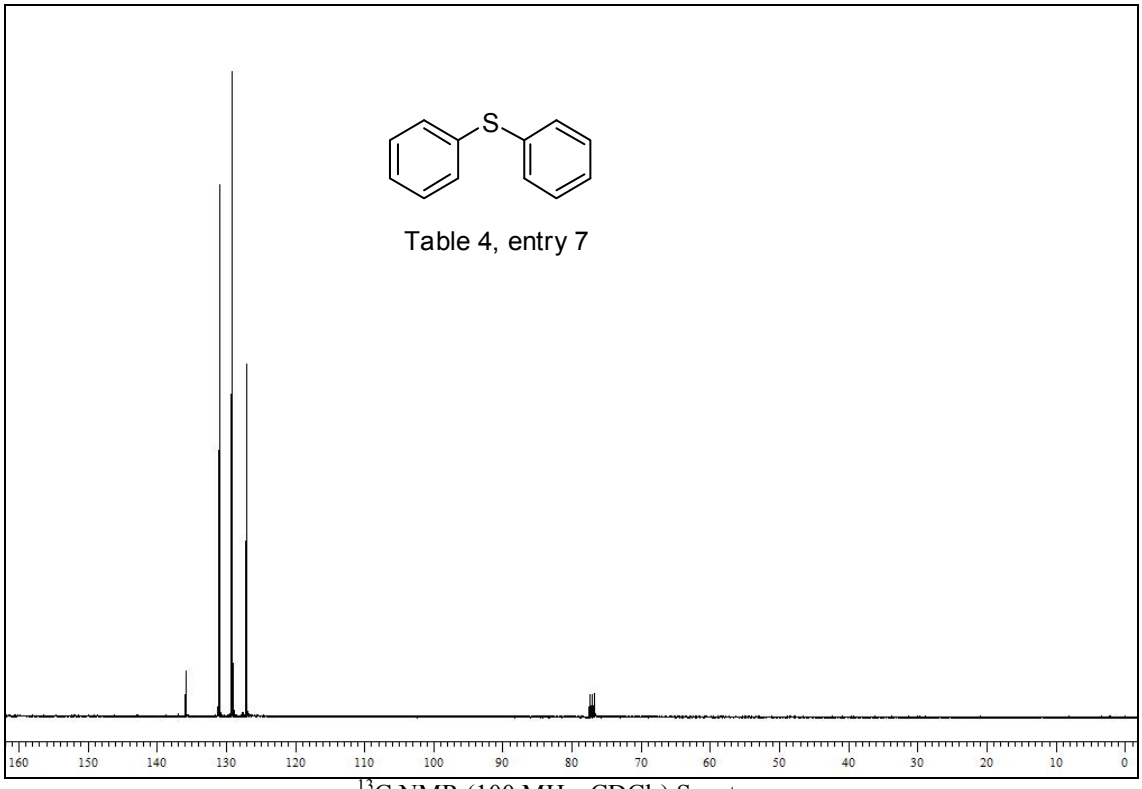
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



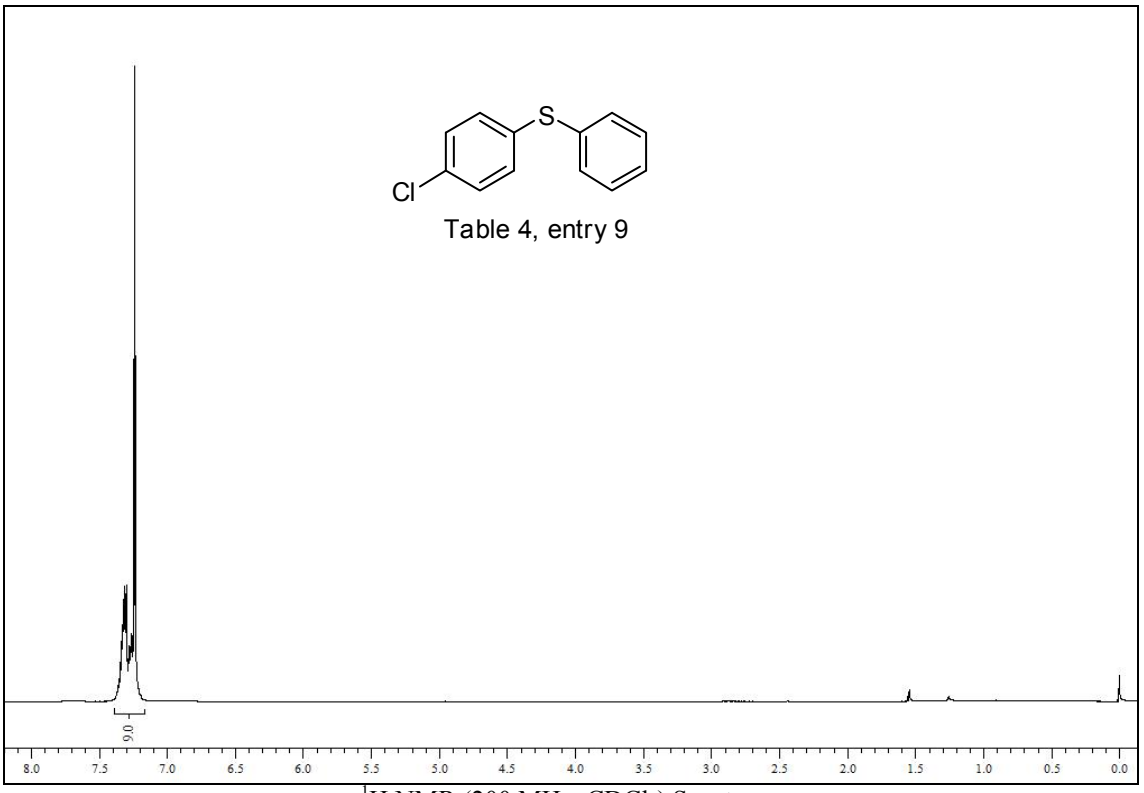
^{13}C NMR (100 MHz, $CDCl_3$) Spectrum.



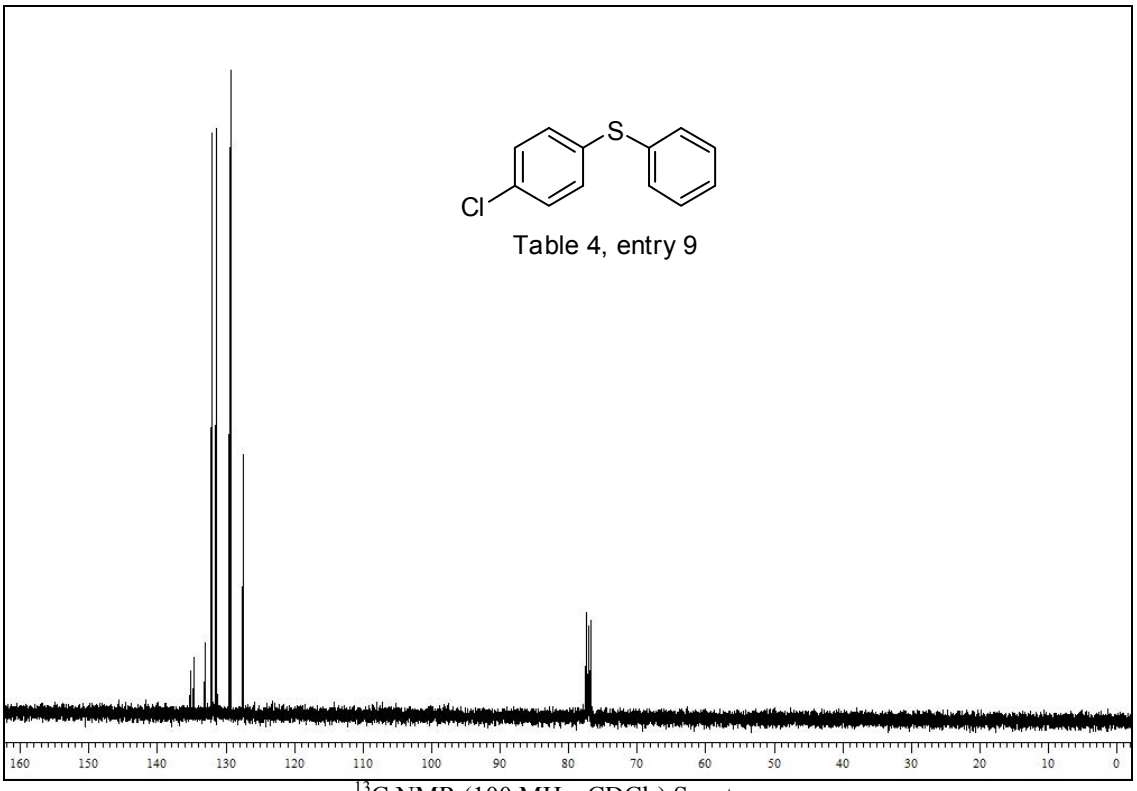
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



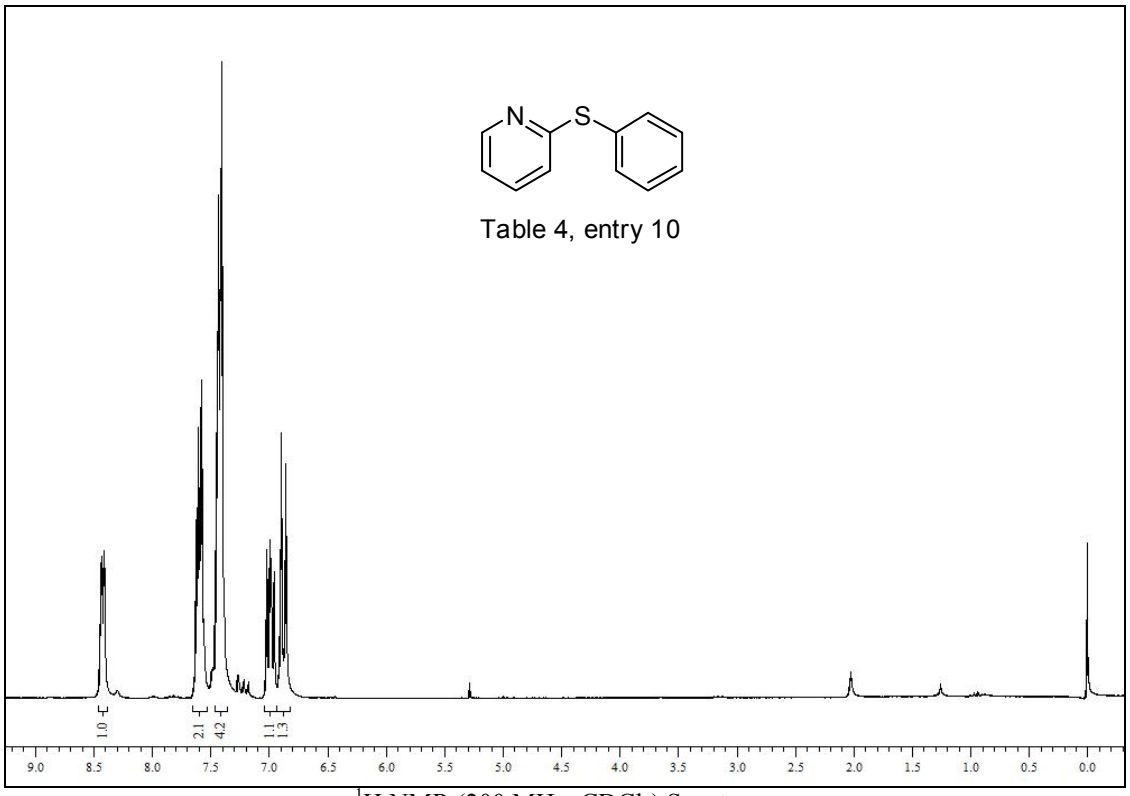
^{13}C NMR (100 MHz, $CDCl_3$) Spectrum.



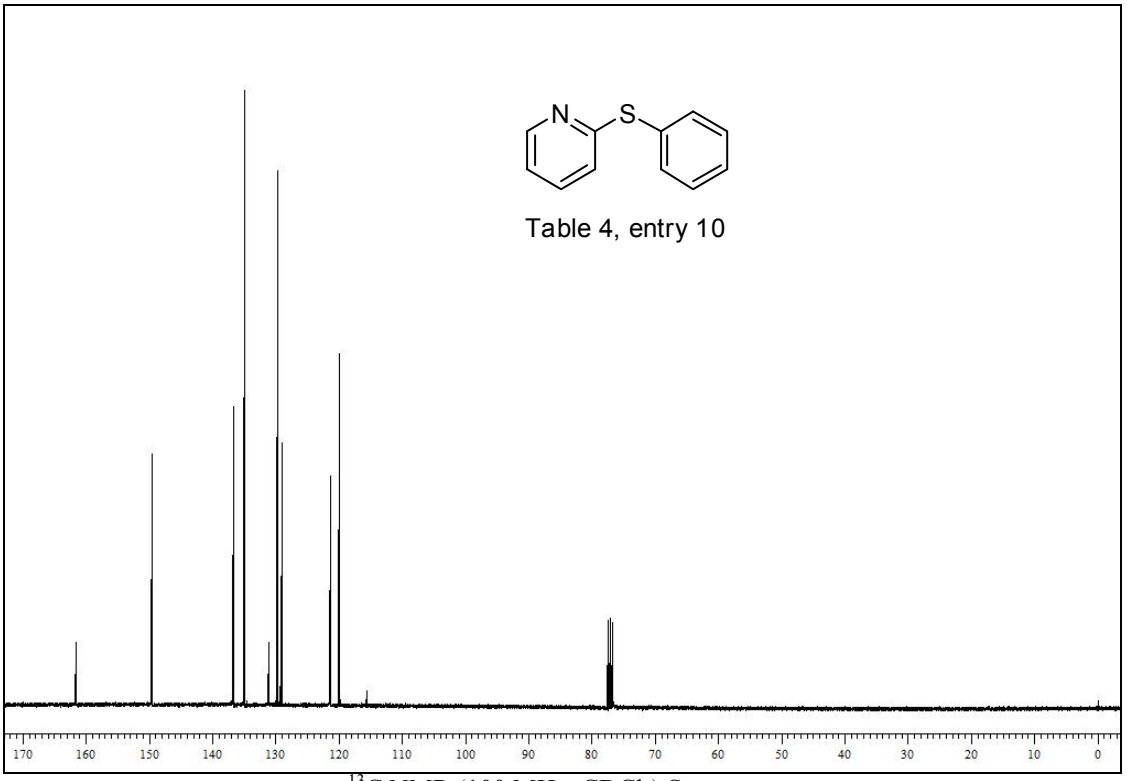
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



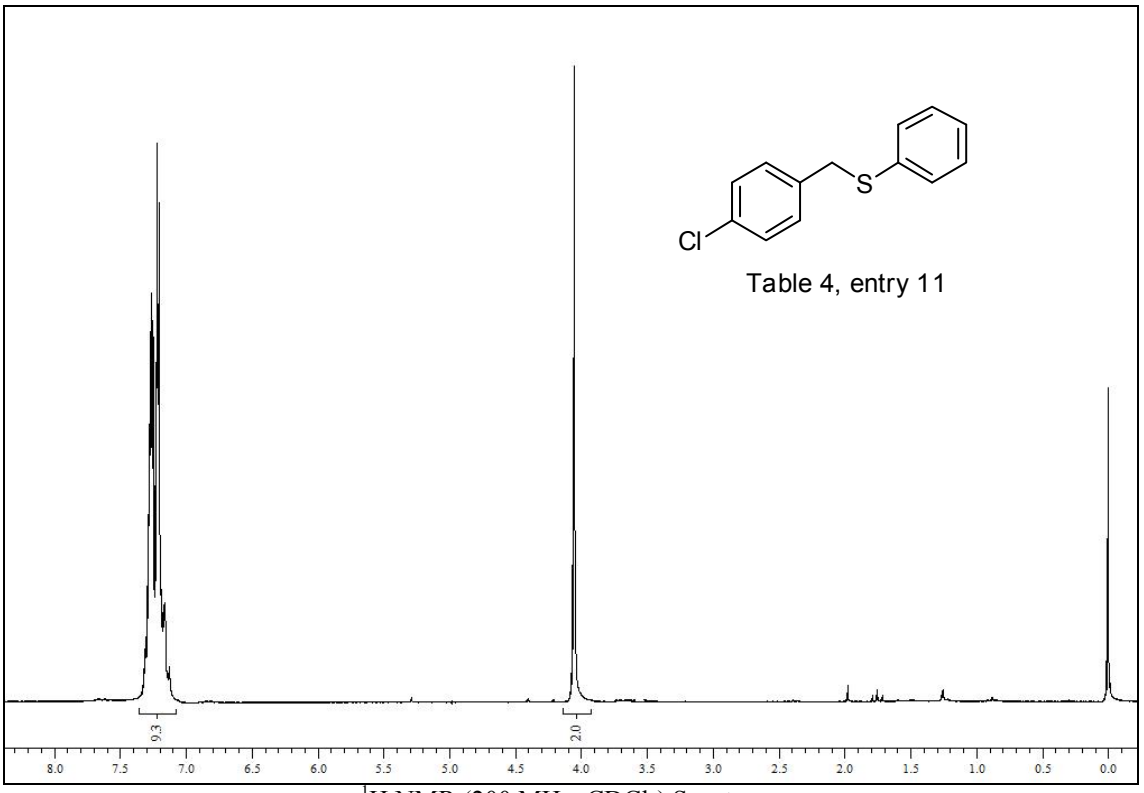
^{13}C NMR (100 MHz, $CDCl_3$) Spectrum.



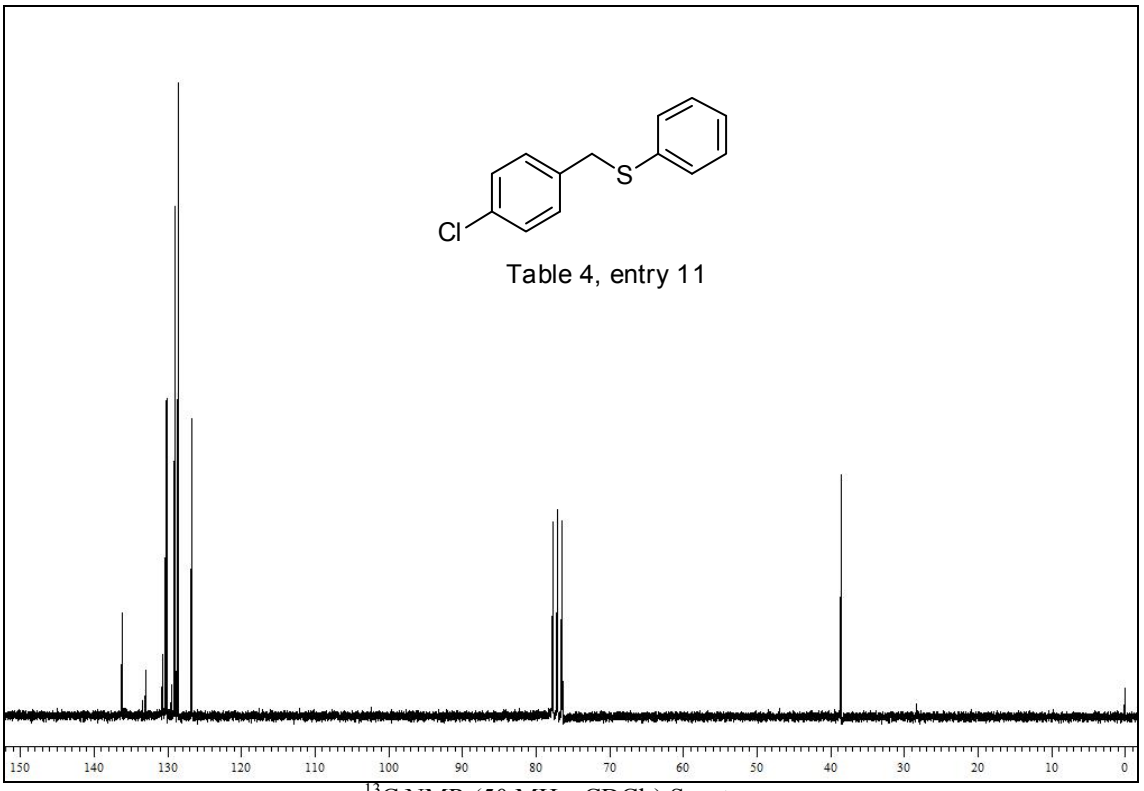
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



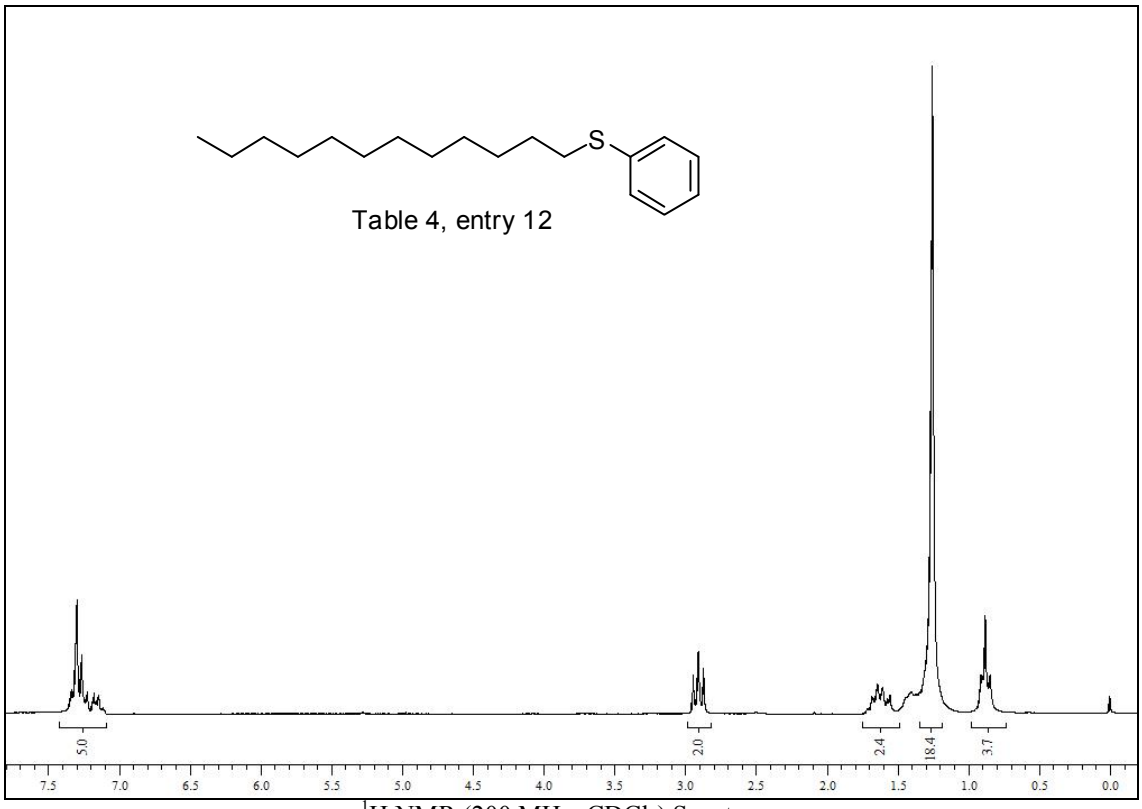
^{13}C NMR (100 MHz, $CDCl_3$) Spectrum.



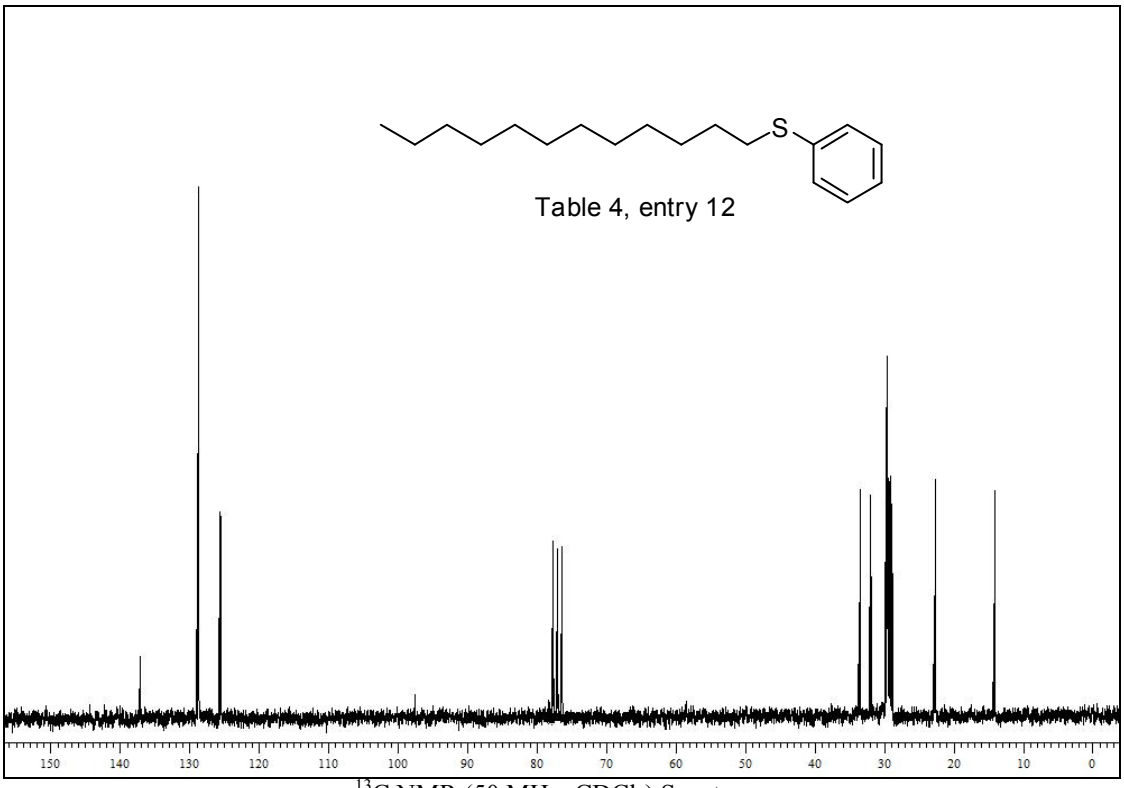
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



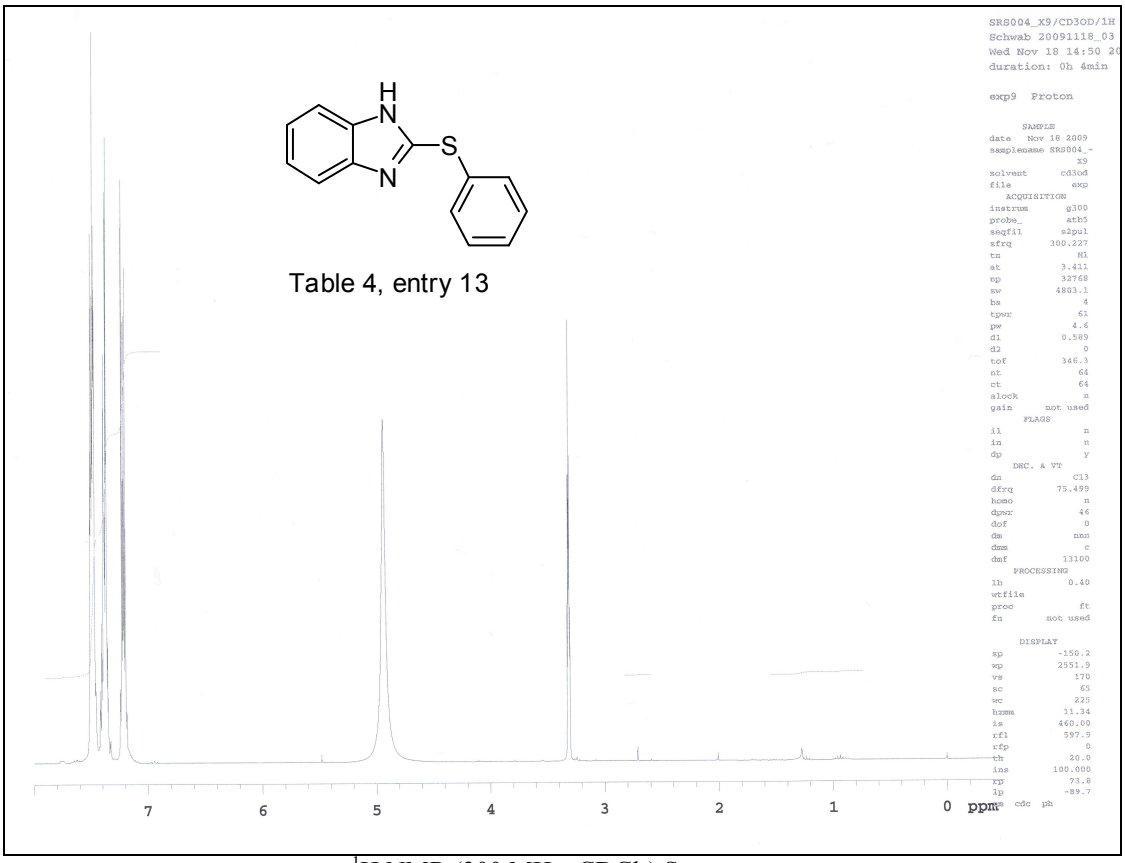
^{13}C NMR (50 MHz, $CDCl_3$) Spectrum.



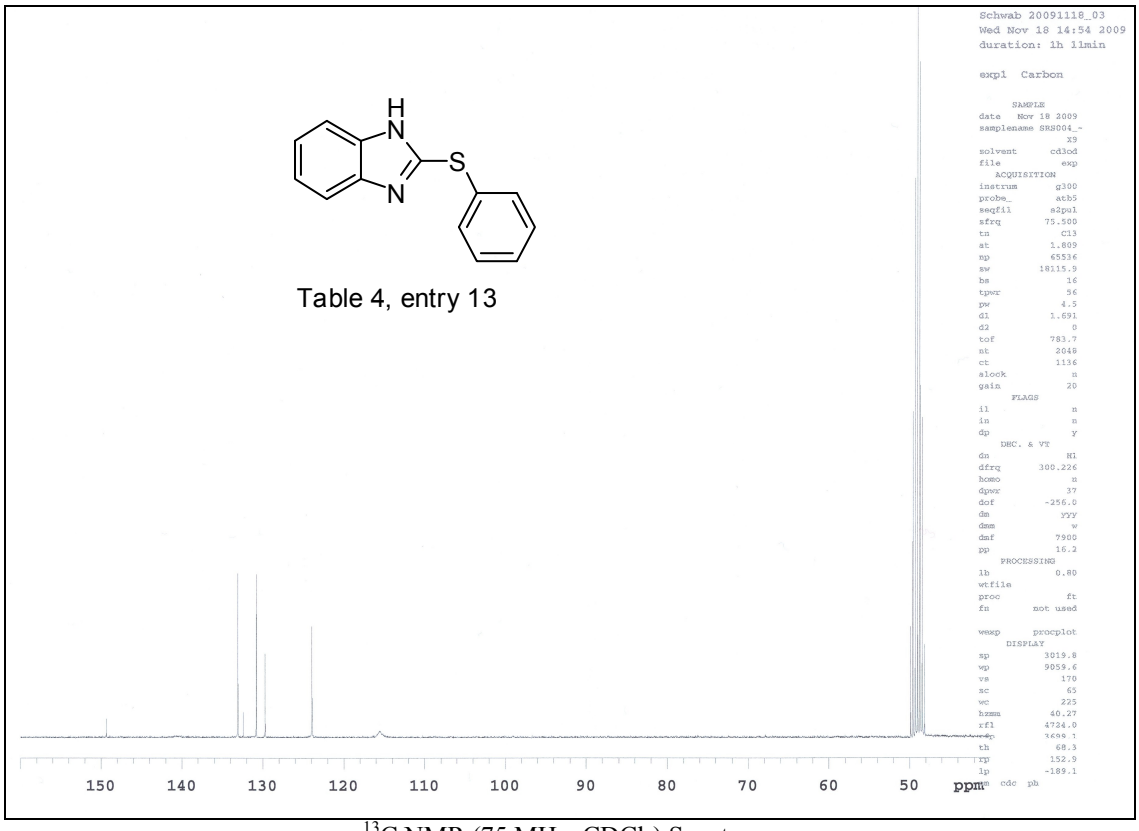
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



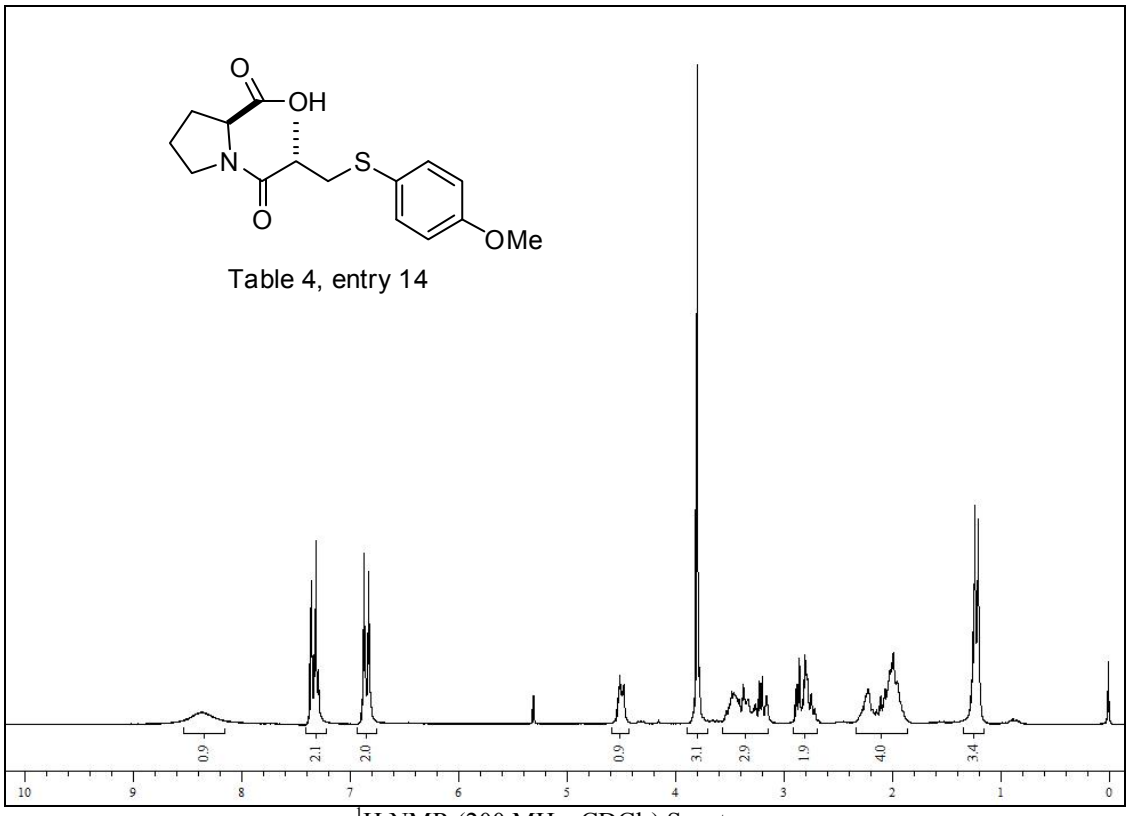
^{13}C NMR (50 MHz, $CDCl_3$) Spectrum.



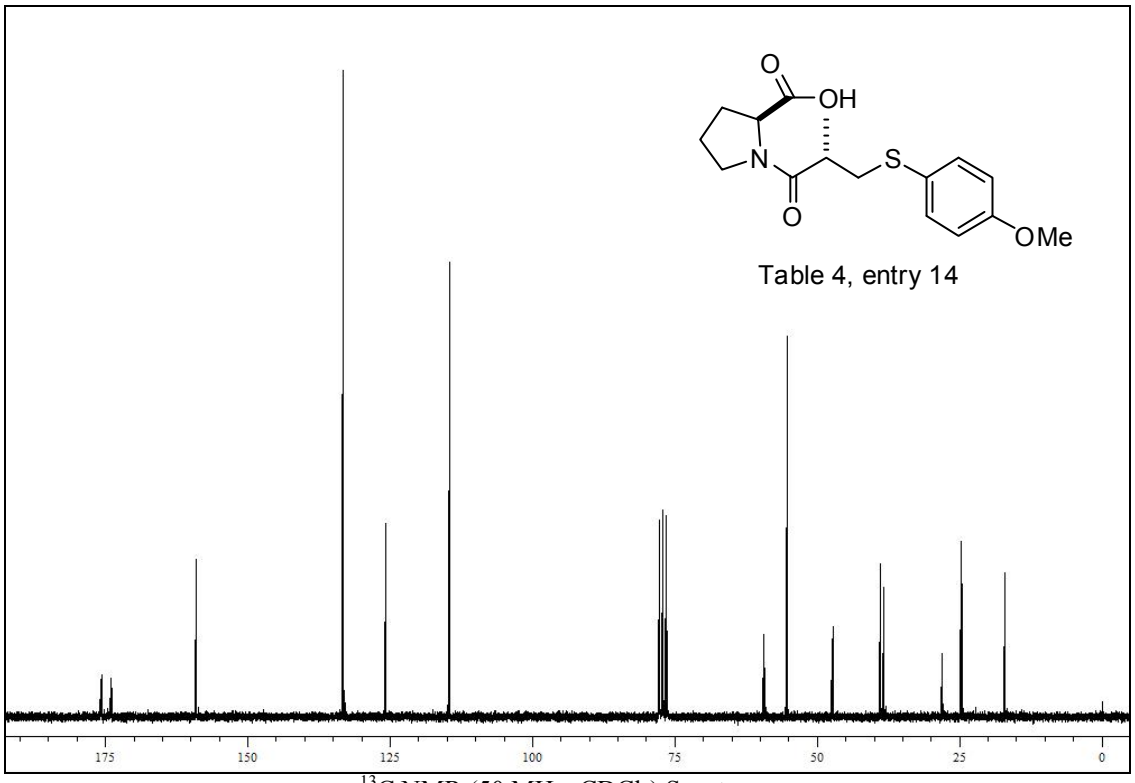
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum.



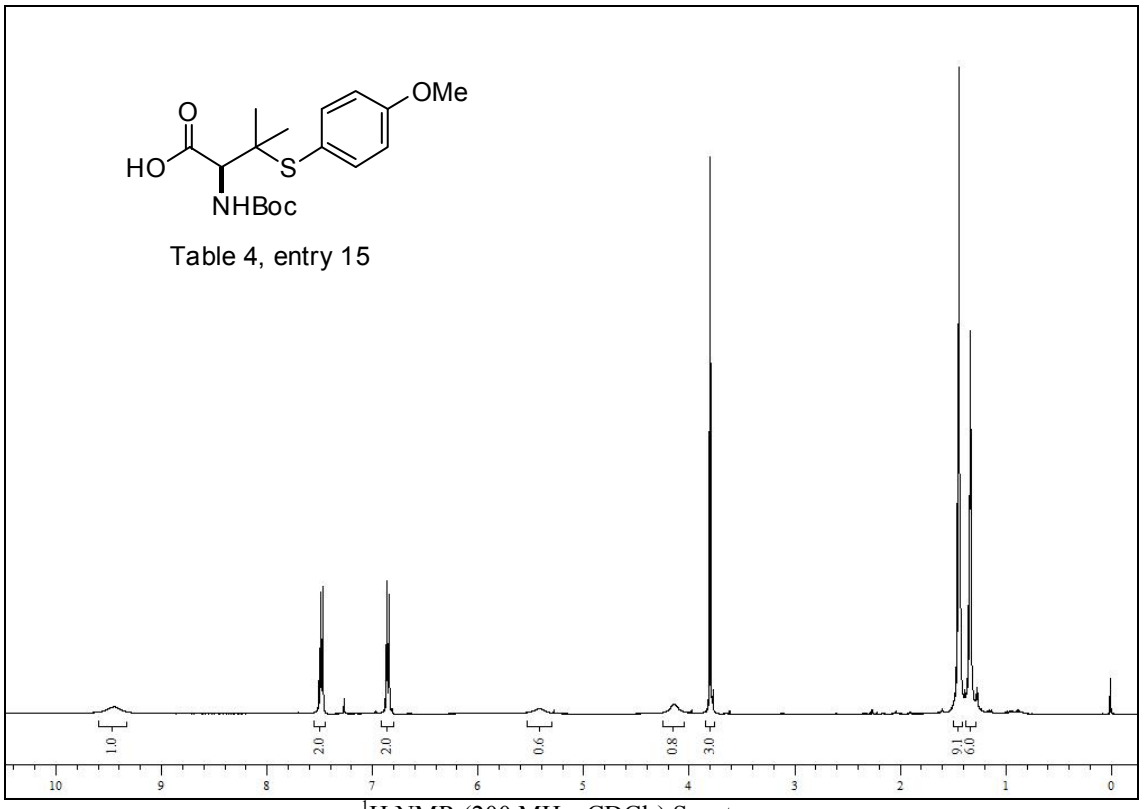
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum.



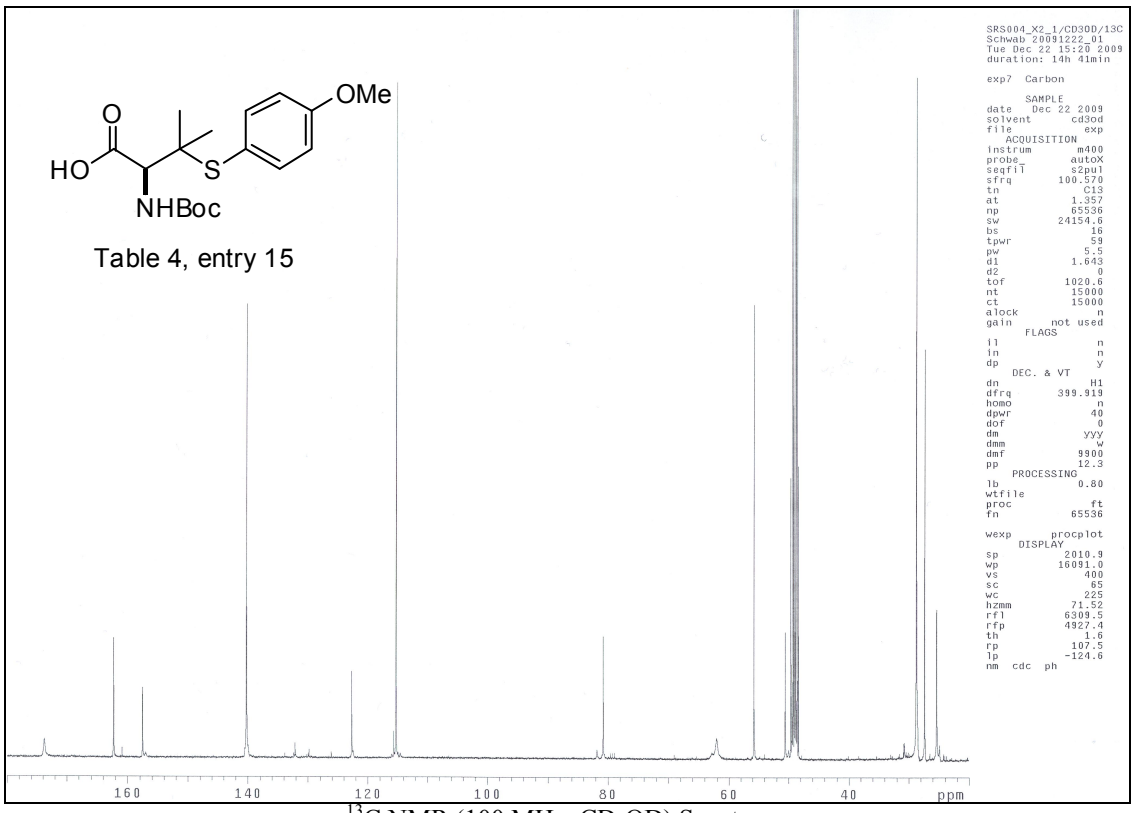
^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



^{13}C NMR (50 MHz, $CDCl_3$) Spectrum.



^{1}H NMR (200 MHz, $CDCl_3$) Spectrum.



^{13}C NMR (100 MHz, CD_3OD) Spectrum.

References

[1] C. C. Cassol, G. Ebeling, B. Ferrera and J. Dupont, *Adv. Synth. Catal.,* 2006, ***348***, 243.
[2] Y.-C. Wong, T. T. Jayanth and C.-H. Cheng, *Org. Lett.,* 2006, ***8***, 5613.
[3] E. Sperotto, G. P. M. van Klink, J. G. de Vries and G. van Koten, *J. Org. Chem*., 2008, ***73***, 5625.
[4] T. Ishiyama, M. Mori, A. Suzuki and N. Miyaura, *J. Organomet. Chem*., 1996, ***525***, 225.
[5] M. M.-Screttas and C. G. Screttas, *J. Org. Chem*., 1977, ***42***, 1462.
[6] S. D. Pastor and E. T. Hessell, J. Org. Chem. 1985, ***50***, 4812.