SUPPORTING INFORMATION

Auxiliary-Assisted Palladium-Catalyzed Arylation and Alkylation of sp^2 and sp^3 Carbon-Hydrogen Bonds

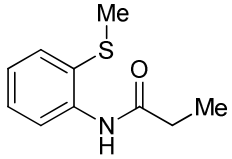
Dmitry Shabashov and Olafs Daugulis*

Department of Chemistry, University of Houston, Houston TX 77204-5003

Experimental Section

General considerations. The coupling reactions were performed without special precautions in 2-dram screw-cap vials. Flash chromatography was performed on 60 Å silica gel (Sorbent Technologies). GC analyses were performed on a Shimadzu GC-2010 chromatograph equipped with a Restek column (Rtx®-5, 15 m, 0.25 mm ID). The ^{1}H and ^{13}C NMR spectra were recorded on a GE QE-300, JEOL ECX400P or ECA500 spectrometers using TMS or solvent peak as a standard. Melting points were measured on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlab Inc. of Norcross, GA. IR-spectra were obtained using a ThermoNicolet Avatar 370 FT-IR instrument. Chemicals were used as received. The following starting materials are known: 8-(butyrylamino)quinoline,[1] 8-(cyclohexylcarbonylamino)quinoline,[1] 8-(propionylamino)quinoline,[2] 8-(pivaloylamino)quinoline,[3] (2-dimethylamino)-*N*-propionylaniline,[4] *N*-propionyl-*N',N'*-dimethylethylenediamine.[5]

SYNTHESIS OF STARTING AMIDES



2-Methylthio-*N*-propionylaniline (Table 1, entry 1): 2-Methylthioaniline (3.0 g, 21.5 mmol) and Et_3N (3.1 mL, 22.2 mmol) were dissolved in dichloromethane (20 mL) followed by dropwise addition of propionic acid anhydride (2.8 mL, 21.5 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with 1M HCl, once with saturated aqueous $NaHCO_3$, and once with water. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 4.15 g (99%) of white crystals, mp 56-57 ^{o}C (EtOAc/hexanes), R_f=0.25 (EtOAc/toluene 1/15). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.40-8.28 (m, 2H) 7.51-7.45 (m, 1H) 7.34-7.25 (m, 1H) 7.10-7.02 (m, 1H) 2.48 (q, 2H, *J*= 7.6 Hz) 2.38 (s, 3H) 1.29 (t, 3H, *J*= 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 172.1, 138.5, 133.0, 129.0, 125.2, 124.3, 120.7, 31.2, 19.0, 9.8. FT-IR (neat, cm^{-1}) υ 3223, 1659. Anal. calcd. for $C_{10}H_{13}NOS$: C 61.50, H 6.71, N 7.17. Found: C 61.72, H 6.62, N 7.21.

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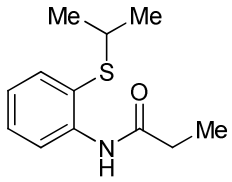
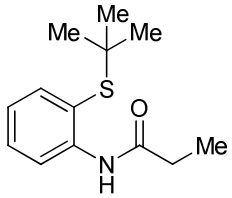
[1] Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154.
[2] Pagani, G.; Baruffini, A.; Caccialanza, G. *Farmaco, Edizione Scientifica* **1971**, *26*, 118.
[3] Lee, J. C., Jr.; Müller, B.; Pregosin, P.; Yap, G. P. A.; Rheingold, A. L.; Crabtree, R. H. *Inorg. Chem.* **1995**, *34*, 6295.
[4] Smith, C. W.; Rasmunssen, R. S.; Ballard, S. A. *J. Am. Chem. Soc.* **1949**, *71*, 1082.
[5] Khromov-Borisov, N. V.; Aleksandrova, L. N.; Danilov, A. F.; Shelkovnikov, S. A. *Khim. Farmatsev. Zh.* **1984**, *18*, 689.



2-Isopropylthio-*N*-propionylaniline (Table 1, entry 3): 2-Isopropylthioaniline[6] (3.9 g, 23.2 mmol) and Et_3N (4.3 mL, 31 mmol) were dissolved in dichloromethane (30 mL) followed by dropwise addition of propionyl chloride (2.3 mL, 26.3 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed once with 1M HCl and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 5.06 g (98%) of oil, R_f=0.46 (EtOAc/hexanes 1/4). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.71 (br s, 1H) 8.47 (d, 1H, *J*= 8.3 Hz) 7.51 (dd, 1H, *J*= 7.7, 1.6 Hz) 7.38-7.32 (m, 1H) 7.03 (d, 1H, *J*= 7.6, 7.5, 1.4 Hz) 3.14 (sept, 1H, *J*= 6.8 Hz) 2.47 (q, 2H, *J*= 7.6 Hz) 1.29 (t, 3H, *J*= 7.6 Hz) 1.25 (d, 3H, *J*= 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 172.0, 140.6, 136.7, 130.2, 123.7, 121.5, 119.9, 40.7, 31.3, 23.4, 9.9. FT-IR (neat, cm^{-1}) υ 3346, 1695. Anal. calcd. for $C_{12}H_{17}NOS$: C 64.53, H 7.67, N 6.27. Found: C 64.45, H 7.53, N 6.31.



2-*t*-Butylthio-*N*-propionylaniline (Table 1, entry 4): 2-*t*-Butylthioaniline[7] (1.3 g, 7.17 mmol) and Et_3N (1.1 mL, 7.89 mmol) were dissolved in dichloromethane (15 mL) followed by dropwise addition of propionic acid anhydride (1.0 mL, 7.5 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed once with aqueous HCl (pH ~2) and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 1.56 g (92%) of oil, R_f=0.49 (EtOAc/hexanes 1/4). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.91 (br s, 1H) 8.54 (dd, 1H, *J*= 8.3, 1.2 Hz) 7.50 (dd, 1H, *J*= 7.7, 1.7 Hz) 7.43-7.36 (m, 1H) 7.04 (ddd, 1H, *J*= 7.6, 7.6, 1.4 Hz) 2.46 (q, 2H, *J*= 7.6 Hz) 1.30 (s, 9H) 1.28 (t, 3H, *J*= 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 171.9, 141.7, 138.8, 131.0, 123.3, 120.0, 119.7, 48.5, 31.4, 31.1, 9.9. FT-IR (neat, cm^{-1}) υ 3340, 1697. Anal. calcd. for $C_{13}H_{19}NOS$: C 65.78, H 8.07, N 5.90. Found: C 65.49, H 8.04, N 6.08.

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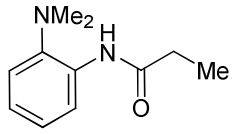
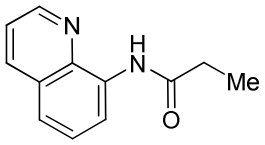
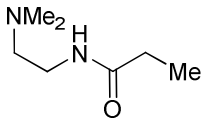
[6] Hodson, S. J.; Bishop, M. J.; Speake, J. D.; Navas, F., III; Garrison, D. T.; Bigham, E. C.; Saussy, D. L., Jr.; Liacos, J. A.; Irving, P. E.; Gobel, M. J.; Sherman, B. W. *J. Med. Chem.* **2002**, *45*, 2229.
[7] Montanari, S.; Paradisi, C.; Scorrano, G. *J. Org Chem.* **1991**, *56*, 4274.



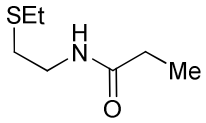
2-Dimethylamino-*N*-propionylaniline (Table 1, entry 5) is known.[4] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.49 (br s, 1H) 8.37 (d, 1H, *J*= 8.1 Hz) 7.19-7.08 (m, 2H) 7.07-7.00 (m, 1H) 2.64 (s, 6H) 2.46 (q, 2H, *J*= 7.6 Hz) 1.28 (t, 3H, *J*= 7.6 Hz).



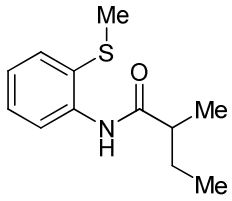
8-(*N*-Propionylamino)quinoline (Table 1, entry 6) is known.[2] ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.83 (br s, 1H) 8.82-8.77 (m, 2H) 8.16 (dd, 1H, *J*= 8.3, 1.5 Hz) 7.58-7.43 (m, 4H) 2.61 (q, 2H, *J*= 7.6 Hz) 1.34 (t, 3H, *J*= 7.6 Hz).



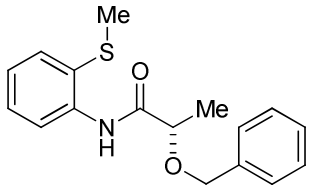
***N,N*-Dimethyl-*N'*-propionylethylenediamine (Table 1, entry 7)** is known.[5] ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.05 (br s, 1H) 3.36-3.29 (m, 2H) 2.41 (t, 2H, *J*= 5.9 Hz) 2.23 (s, 6H) 2.21 (q, 2H, *J*= 7.6 Hz) 1.16 (t, 3H, *J*= 7.6 Hz).



2-Ethylthio-*N*-propionylethylamine (Table 1, entry 8): 2-Ethylthioethylamine (1.0 g, 9.5 mmol) and Et_3N (1.4 mL, 10.0 mmol) were dissolved in dichloromethane (20 mL) followed by dropwise addition of propionic acid anhydride (1.2 mL, 9.5 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed once with 1M HCl and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 1.38 g (90%) of oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 5.85 (br s, 1H) 3.46 (q, 2H, *J*= 6.3 Hz) 2.68 (t, 3H, *J*= 6.3 Hz) 2.56 (q, 2H, *J*= 7.4 Hz) 2.23 (q, 2H, *J*= 7.6 Hz) 1.27 (t, 3H, *J*= 7.4 Hz) 1.17 (t, 3H, *J*= 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 174.1, 38.4, 31.5, 29.8, 25.7, 14.9, 10.0. FT-IR (neat, cm^{-1}) υ 3297, 1647. Anal. calcd. for $C_7H_{15}NOS$: C 52.13, H 9.38, N 8.69. Found: C 51.75, H 9.48, N 8.59.



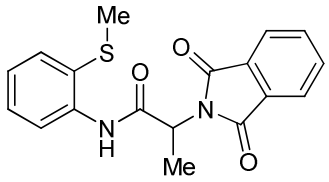
***N*-(2-Methylbutyryl)-2-methylthioaniline (Table 2, entry 3):** 2-Methylthioaniline (2.0 g, 14.4 mmol) and Et_3N (2.2 mL, 15.8 mmol) were dissolved in dichloromethane (30 mL) followed by dropwise addition of 2-methylbutyryl chloride (1.8 mL, 14.4 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with 1M HCl and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 3.18 g (99%) of white crystals, mp 49-50 ^oC (pentane), R_f=0.20 (EtOAc/toluene 1/50). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.41-8.33 (m, 2H) 7.49 (dd, 1H, *J*= 7.7, 1.4 Hz) 7.34-7.27 (m, 1H) 7.06 (ddd, 1H, *J*= 7.6, 7.6, 1.3 Hz) 2.44-2.31 (m, 4H) 1.88-1.72 (m, 1H) 1.64-1.49 (m, 1H) 1.28 (d, 3H, *J*= 6.9 Hz) 1.00 (t, 3H, *J*= 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 174.9, 138.6, 133.1, 129.1, 125.2, 124.3, 120.8, 44.6, 27.6, 19.1, 17.6, 12.1. FT-IR (neat, cm^{-1}) υ 3230, 1656. Anal. calcd. for $C_{12}H_{17}NOS$: C 64.53, H 7.67, N 6.27. Found: C 64.57, H 7.68, N 6.26.



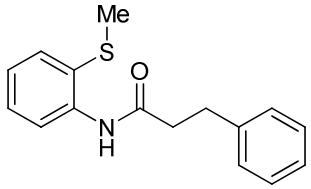
***N*-(2-(*S*)-Benzyloxypropionyl)-2-methylthioaniline (Table 2, entry 4):** 2-Methylthioaniline (0.77 g, 5.5 mmol) and Et_3N (1.0 mL, 7.2 mmol) were dissolved in dichloromethane (10 mL) followed by dropwise addition of (*S*)-2-benzyloxypropionyl chloride[8] solution in dichloromethane (5 mL). Acid chloride was prepared from (*S*)-2-benzyloxypropionic acid (1.1 g, 6.1 mmol) according to a reported procedure.[9] The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with 0.1M HCl and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 1.56 g (93%) of oil, 81% ee (Chiralcel OD-H, 10% iPrOH-Hex, 1.0 mL/min, 254 nm, 7.24 min minor, 10.35 min major), R_f=0.17 (EtOAc/toluene 1/50). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 9.64 (br s, 1H) 8.40 (dd, 1H, *J*= 8.2, 1.3 Hz) 7.49 (dd, 1H, *J*= 7.7, 1.6 Hz) 7.47-7.42 (m, 2H) 7.41-7.27 (m, 4H) 7.08 (ddd, 1H, *J*= 7.6, 7.6, 1.4 Hz) 4.75-4.65 (m, 2H) 4.13 (q, 1H, *J*= 6.8 Hz) 2.31 (s, 3H) 1.55 (d, 3H, *J*= 6.8 Hz). ^{13}C

[8] Auge, C.; David, S.; Gauthron, C.; Malleron, A.; Cavaye, B. *New J. Chem.* **1988**, *12*, 733.
[9] Mayer, S. C.; Ramanjulu, J.; Vera, M. D.; Pfizenmayer, A. J.; Joullié, M. M. *J. Org. Chem.* **1994**, *59*, 5192.

NMR (100 MHz, $CDCl_3$, ppm) δ 171.7, 138.1, 137.3, 133.2, 129.0, 128.7, 128.3, 128.0, 126.0, 124.7, 120.5, 76.8, 72.3, 18.9, 18.7. FT-IR (neat, cm^{-1}) υ 3317, 1692. Anal. calcd. for $C_{17}H_{19}NO_2S$: C 67.74, H 6.35, N 4.65. Found: C 67.63, H 6.26, N 4.83.



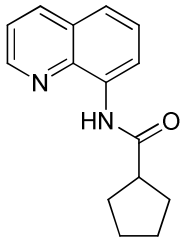
***N*-(2-Phthalimidopropionyl)-2-methylthioaniline (Table 2, entry 5):** 2-Methylthioaniline (2.3 g, 16.6 mmol) and 2,6-lutidine (2.3 mL, 19.9 mmol) were dissolved in dichloromethane (30 mL) followed by dropwise addition of 2-phthalimidopropionyl chloride solution in dichloromethane (10 mL). Acid chloride was prepared from 2-phthalimidopropionic acid[10] (4.0 g, 18.2 mmol) according to a reported procedure.[11] The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with 1M HCl and once with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 5.02 g (89%) of brownish crystals, mp 135-136 ^oC (EtOAc/hexanes), R_f=0.27 (EtOAc/toluene 1/15). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.94 (br s, 1H) 8.33 (d, 1H, *J*= 8.2 Hz) 7.93-7.87 (m, 2H) 7.80-7.74 (m, 2H) 7.46 (dd, 1H, *J*= 7.8, 1.3 Hz) 7.32-7.27 (m, 1H) 7.05 (ddd, 1H, *J*= 7.6, 7.6, 1.3 Hz) 5.15 (q, 1H, *J*= 7.3 Hz) 2.26 (s, 3H) 1.87 (d, 3H, *J*= 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 167.8, 167.2, 138.2, 134.5, 133.7, 132.0, 129.5, 125.4, 124.8, 123.7, 120.6, 50.2, 19.3, 15.2. FT-IR (neat, cm^{-1}) υ 3275, 1710, 1666. Anal. calcd. for $C_{18}H_{16}N_2O_3S$: C 63.51, H 4.74, N 8.23. Found: C 63.25, H 4.72, N 8.18.



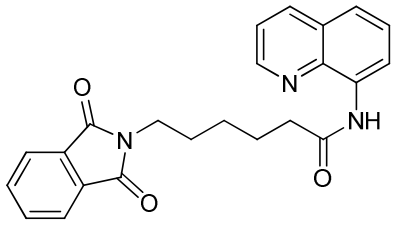
***N*-(Hydrocinnamoyl)-2-methylthioaniline (Table 2, entry 7):** 2-Methylthioaniline (2.0 g, 14.4 mmol) and Et_3N (2.2 mL, 15.8 mmol) were dissolved in dichloromethane (30 mL) followed by dropwise addition of hydrocinnamoyl chloride (2.1 mL, 14.4 mmol). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with 1M HCl and once with saturated $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent

[10] Billman, J. H.; Harting, W. F. *J. Am. Chem. Soc.* **1948**, *70*, 1473.
[11] Ma, T.; Gao, Q.; Chen, Z.; Wang, L.; Liu, G. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1079.

gave 3.9 g (99%) of white crystals, mp 73-74 ^{o}C (EtOAc/hexanes), R_f=0.12 (EtOAc/toluene 1/50). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.33 (d, 1H, *J*= 8.2 Hz) 8.24 (br s, 1H) 7.46 (d, 1H, *J*= 7.7 Hz) 7.34-7.17 (m, 6H) 7.05 (dd, 1H, *J*= 7.5, 7.5 Hz) 3.13-3.05 (m, 2H) 2.79-2.71 (m, 2H) 2.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.6, 140.7, 138.4, 133.1, 129.1, 128.8, 128.5, 126.5, 125.3, 124.5, 120.8, 39.8, 31.6, 19.0. FT-IR (neat, cm^{-1}) υ 3272, 1655. Anal. calcd. for $C_{16}H_{17}NOS$: C 70.81, H 6.31, N 5.16. Found: C 70.92, H 6.28, N 5.18.



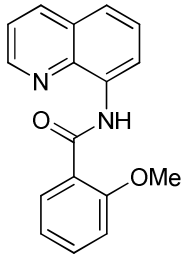
***N*-(Cyclopentanecarbonyl)-8-aminoquinoline (Table 3, entry 6):** 8-Aminoquinoline (1.7 g, 11.8 mmol) and Et_3N (2.2 mL, 15.8 mmol) were dissolved in dichloromethane (20 mL) followed by dropwise addition of cyclopentanecarbonyl chloride solution in dichloromethane (10 mL). Acid chloride was prepared from cyclopentanecarboxylic acid (2.0 g, 17.5 mmol).[12] The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with water and twice with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 2.8 g (99%) of brownish crystals, mp 84-85 ^{o}C (hexanes), R_f=0.17 (EtOAc/toluene 1/50). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.88 (br s, 1H) 8.83-8.77 (m, 2H) 8.16 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.58-7.43 (m, 3H) 2.96 (quintet, 1H, *J*= 8.2 Hz) 2.13-1.92 (m, 4H) 1.91-1.77 (m, 2H) 1.75-1.60 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 175.2, 148.2, 138.5, 136.5, 134.9, 128.1, 127.6, 121.7, 121.4, 116.5, 47.6, 30.8, 26.2. FT-IR (neat, cm^{-1}) υ 3349, 1677. Anal. calcd. for $C_{15}H_{16}N_2O$: C 74.97, H 6.71, N 11.66. Found: C 74.88, H 6.75, N 11.67.



***N*-(6-Phthalimidohexanoyl)-8-aminoquinoline (Table 3, entry 7):** 8-Aminoquinoline (1.5 g, 10.4 mmol) and Et_3N (1.9 mL, 13.5 mmol) were dissolved in dichloromethane (20 mL) followed by dropwise addition of phthalimidohexanoyl chloride in dichloromethane (10 mL). Acid chloride was

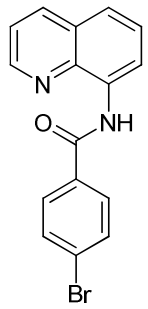
[12] Tromm, P.; Heimgartner, H. *Helv. Chim. Acta* **1988**, *71*, 2071.

prepared from phthalimidohexanoic acid[13] (3.0 g, 11.5 mmol) according to a published procedure.[13] The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with water and twice with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent followed by purification by flash chromatography (EtOAc/hexanes 1/1 to 2/1) gave 3.4 g (85%) of yellowish crystals, mp 111-112 ^oC (EtOAc/hexanes), R_f=0.44 (EtOAc/hexanes 1/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 9.79 (br s, 1H) 8.80 (dd, 1H, *J*= 4.2, 1.8 Hz) 8.75 (dd, 1H, *J*= 7.2, 1.7 Hz) 8.15 (dd, 1H, *J*= 8.3, 1.6 Hz) 7.86-7.80 (m, 2H) 7.73-7.67 (m, 2H) 7.55-7.47 (m, 2H) 2.98 (dd, 1H, *J*= 8.2, 4.1 Hz) 3.72 (t, 2H, *J*= 7.3 Hz) 2.57 (t, 2H, *J*= 7.6 Hz) 1.93-1.83 (m, 2H) 1.82-1.73 (m, 2H) 1.56-1.46 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 171.6, 168.6, 148.3, 138.5, 136.5, 134.7, 134.0, 132.3, 128.1, 127.6, 123.3, 121.7, 121.5, 116.6, 38.1, 38.0, 28.6, 26.7, 25.3. FT-IR (neat, cm^{-1}) υ 3296, 1770, 1703. Anal. calcd. for $C_{23}H_{21}N_3O_3$: C 71.30, H 5.46, N 10.85. Found: C 71.17, H 5.30, N 10.77.

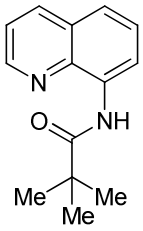


***N*-(2-Methoxybenzoyl)-8-aminoquinoline (Table 3, entry 8):** 8-Aminoquinoline (1.8 g, 12.5 mmol) and Et_3N (2.0 mL, 14.4 mmol) were dissolved in dichloromethane (25 mL) followed by dropwise addition of 2-methoxybenzoyl chloride solution in dichloromethane (10 mL). Acid chloride was prepared from 2-methoxybenzoic acid (2.0 g, 13.1 mmol).[14] The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with water and twice with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 3.5 g (99%) of crystalline material, mp 120-121 ^oC (EtOAc/hexanes), R_f=0.22 (EtOAc/hexane 1/4). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 12.3 (br s, 1H) 9.04 (dd, 1H, *J*= 7.6, 1.4 Hz) 8.84 (dd, 1H, *J*= 4.2, 1.7 Hz) 8.36 (dd, 1H, *J*= 7.9, 1.8 Hz) 8.13 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.60-7.45 (m, 4H) 7.42 (dd, 1H, *J*= 8.3, 4.2 Hz) 7.16-7.09 (m, 1H) 7.07-7.03 (m, 1H) 4.17 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 163.8, 157.9, 148.4, 139.4, 136.4, 135.9, 133.3, 132.5, 128.3, 127.7, 122.5, 121.6, 121.4, 117.5, 111.8, 56.3. FT-IR (neat, cm^{-1}) υ 3251, 1651. Anal. calcd. for $C_{17}H_{14}N_2O_2$: C 73.37, H 5.07, N 10.07. Found: C 73.36, H 5.02, N 10.08.

[13] Granados, R.; Alvarez, M.; Lopez-Calahorra, F.; Salas, M. *Synthesis* **1983**, 329.
[14] Hattori, T.; Suzuki, T.; Hayashizaka, N.; Koike, N.; Miyano, S. *Bull. Chem. Soc. Jp.* **1993**, *66*, 3034.



***N*-(4-Bromobenzoyl)-8-aminoquinoline (Table 4, entry 3):** 8-Aminoquinoline (1.5 g, 10.4 mmol) and Et_3N (1.5 mL, 10.9 mmol) were dissolved in dichloromethane (20 mL) followed by dropwise addition of 4-bromobenzoyl chloride (2.4 g, 10.9 mmol) solution in dichloromethane (10 mL). The resulting mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed twice with water and twice with saturated aqueous $NaHCO_3$. Organic layer was dried over $MgSO_4$. Evaporation of solvent gave 3.38 g (99%) of crystalline material, mp 134-135 ^oC (EtOAc/hexanes), R_f=0.40 (EtOAc/hexanes 1/4). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 10.73 (br s, 1H) 8.91 (dd, 1H, *J*= 7.1, 1.9 Hz) 8.86 (dd, 1H, *J*= 4.2, 1.7 Hz) 8.21 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.98-7.93 (m, 2H) 7.72-7,67 (m, 2H) 7.64-7.54 (m, 2H) 7.50 (dd, 3H, *J*= 8.3, 4.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 164.6, 148.6, 139.0, 136.7, 134.6, 134.3, 132.3, 129.1, 128.3, 127.7, 126.8, 122.1, 121.9, 116.9. FT-IR (neat, cm^{-1}) υ 3334, 1674. Anal. calcd. for $C_{16}H_{11}BrN_2O$: C 58.74, H 3.39, N 8.56. Found: C 58.65, H 3.22, N 8.36.



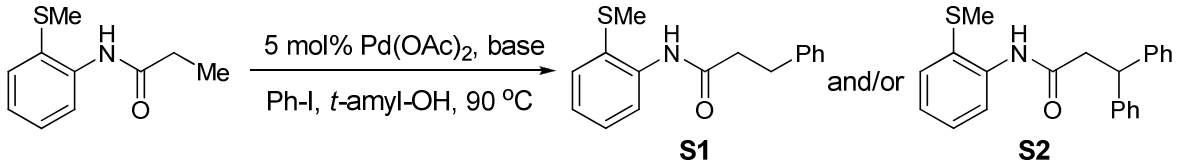
***N*-Pivaloyl-8-aminoquinoline (12)** is known.[3] ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 10.39 (br s, 1H) 8.84-8.78 (m, 2H) 8.16 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.57-7.43 (m, 4H) 1.44 (s, 9H).

OPTIMIZATION OF BASE

General procedure

Amide (0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), base (1.75 mmol), and phenyl iodide (428 mg, 2.1 mmol) were reacted at 90 ^oC for 18.5 hours. GC conversions are presented in **Table S1** and show the amount of starting material consumed (e.g. 98% conversion means that 2% of starting material remains and 98% is converted to a mixture of **S1** and **S2**). Ratio of mono/diarylation products are given in parentheses.

Table S1. Base Optimization



S1 **S2**

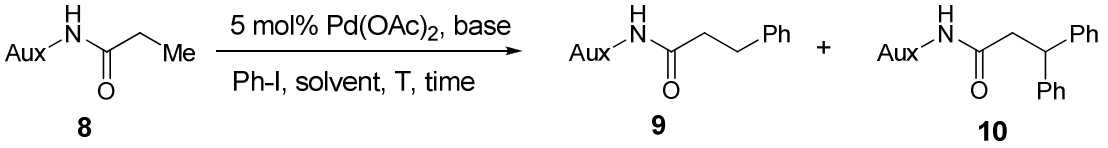
Base	GC conversion (S1:S2)
K_2CO_3	98% (2.4:1)
K_3PO_4	80% (12.5:1)
KOAc	24% (**S1** only)
Cs_2CO_3	5% (**S1** only)
CsOAc	43% (**S1** only)
Na_2CO_3	14% (37.2:1)

AUXILIARY OPTIMIZATION STUDIES

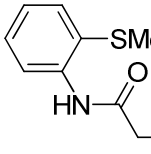
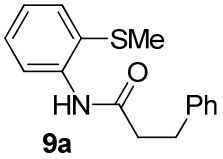
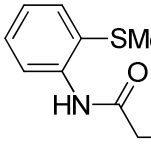
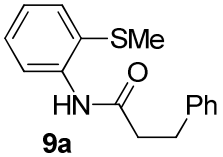
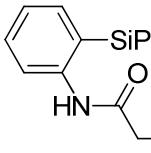
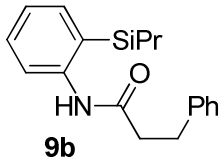
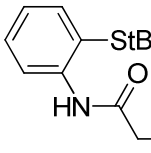
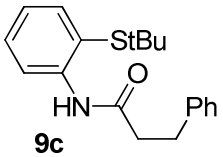
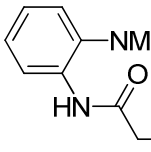
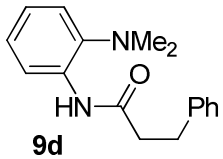
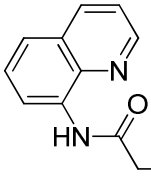
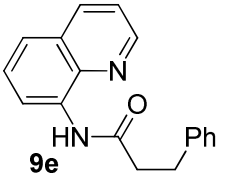
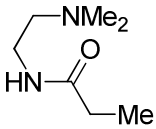
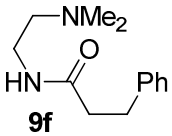
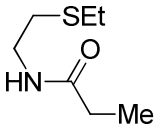
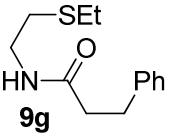
General procedure

Amide (0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), base (1.75 mmol), and phenyl iodide (428 mg, 2.1 mmol) were reacted under conditions indicated in Table S2. Then, ethyl acetate was added to the reaction mixture followed by washing with brine. Organic extract was dried over $MgSO_4$ and evaporated. Residue was dried under vacuum to remove traces of solvent. The aliquot was taken to determine ratios of products and starting material by NMR against dichloroethane internal standard.

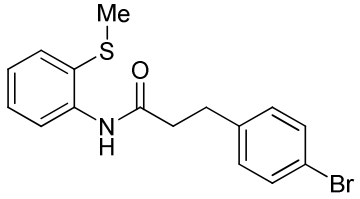
Table S2. Auxiliary Optimization Studies



8 **9** **10**

Entry	Substrate	Conditions	Product	Yield
1		K_2CO_3 *t*-Amyl-OH 90 °C, 14h	 **9a**	55% **9a** 22% **10a**
2		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 90 °C, 17h	 **9a**	84% **9a** 13% **10a**
3		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 90 °C, 21h	 **9b**	59% **9b** 8% **10b**
4		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 90 °C, 21h	 **9c**	19% **9c**
5		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 110 °C, 18h	 **9d**	61% **9d** 6% **10d**
6		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 110 °C, 13h	 **9e**	66% **9e** 17% **10e**
7		K_3PO_4 *t*-Amyl-OH/H_2O (4/1) 90 °C, 14h	 **9f**	45% **9f**
8		K_2CO_3 *t*-Amyl-OH/H_2O (4/1) 90 °C, 21h	 **9g**	10% **9g**

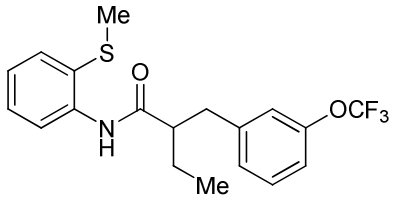
ARYLATION OF PRIMARY C-H BONDS



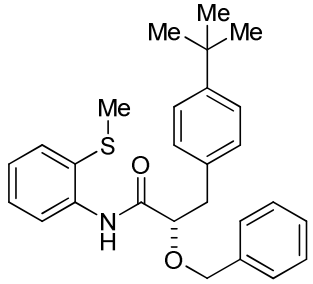
***N*-(3-(4-Bromophenyl)-propionyl)-2-methylthioaniline (Table 2, entry 1):** *N*-Propionyl-2-methylthioaniline (137 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), and 4-bromoiodobenzene (792 mg, 2.8 mmol) were dissolved in *t*-amyl alcohol and water (5:2) mixture (0.7 mL). Resulting solution was heated for 27 h at 90 ^oC. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) and washed with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 100/1 to 50/1 to 25/1) gave 147 mg (60%) of a crystalline material, mp 101-102 ^oC (EtOAc/hexanes), R_f=0.15 (toluene/EtOAc 50/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.30 (d, 1H, *J*= 8.1 Hz) 8.19 (br s, 1H) 7.48-7.38 (m, 3H) 7.32-7.25 (m, 1H) 7.16-7.11 (m, 2H) 7.06 (t, 1H, *J*= 7.5 Hz) 3.03 (t, 2H, *J*= 7.6 Hz) 2.71 (t, 2H, *J*= 7.6 Hz) 2.28 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.1, 139.8, 138.3, 133.1, 131.8, 130.4, 129.1, 125.4, 124.7, 120.9, 120.4, 39.5, 31.0, 19.1. FT-IR (neat, cm^{-1}) υ 3256, 1658. Anal. calcd. for $C_{16}H_{16}BrNOS$: C 54.86, H 4.60, N 4.00. Found: C 54.68, H 4.65, N 4.04. Diarylated product was isolated in 33 mg (9%) yield. R_f=0.22 (toluene/EtOAc 50/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.24-8.13 (m, 2H) 7.48-7.38 (m, 5H) 7.30-7.22 (m, 1H, overlaps with solvent signal) 7.17-7.10 (m, 4H) 7.09-7.02 (m, 1H) 4.64 (t, 1H, *J*= 7.6 Hz) 3.09 (d, 2H, *J*= 7.6 Hz) 2.21 (s, 3H).

Reaction in acetonitrile solvent

N-Propionyl-2-methylthioaniline (137 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), and 4-bromoiodobenzene (594 mg, 2.1 mmol) were dissolved in acetonitrile (0.7 mL). Resulting solution was heated for 26 h at 90 ^oC. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) and washed with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 50/1 to 30/1) gave 133 mg (54%) of a crystalline material.

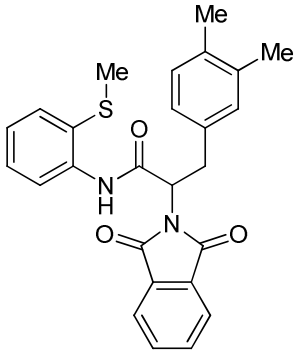


***N*-(2-Ethyl-3-(3-trifluoromethoxyphenyl)-propionyl)-2-methylthioaniline (Table 2, entry 3):** *N*-(2-Methyl-propionyl)-2-methylthioaniline (156 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (222 mg, 1.61 mmol), and 3-trifluoromethoxyiodobenzene (605 mg, 2.1 mmol) were dissolved in *t*-amyl alcohol and water (8:2) mixture (1.0 mL). Resulting solution was heated for 23.5 h at 90 ^oC. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) followed by washing with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 100/1 to 50/1) gave 165 mg of crude material, which was further purified by preparative TLC (toluene/EtOAc 75/1) to give 160 mg (60%) of crystalline material, mp 88-89 ^oC (EtOAc/hexanes), R_f=0.26 (toluene/EtOAc 50/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.28 (d, 1H, *J*= 8.2 Hz) 8.09 (br s, 1H) 7.43 (dd, 1H, *J*= 7.8, 1.4 Hz) 7.31-7.23 (m, 3H) 7.17-7.13 (m, 1H) 7.11-7.00 (m, 2H) 3.08 (dd, 1H, *J*= 13.5, 9.4 Hz) 2.83 (dd, 1H, *J*= 13.5, 5.4 Hz) 2.50-2.39 (m, 1H) 2.15 (s, 3H) 1.93-1.77 (m, 1H) 1.74-1.58 (m, 1H) 1.03 (t, 3H, *J*= 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 173.0, 149.6, 142.3, 138.2, 133.2, 130.0, 129.1, 127.6, 125.4, 124.6, 121.6, 120.9, 120.6 (q, $J_{C\text{-}F}$= 257.2 Hz), 119.0, 53.3, 38.8, 26.4, 18.8, 12.2. FT-IR (neat, cm^{-1}) υ 3250, 1655. Anal. calcd. for $C_{19}H_{20}F_3NO_2S$: C 59.52, H 5.26, N 3.65. Found: C 59.53, H 5.14, N 3.63.



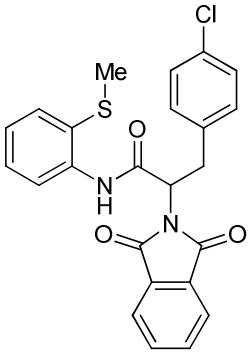
***N*-(2-(*S*)-Benzyloxy-3-(4-*tert*-butylphenyl)-propionyl)-2-methylthioaniline (Table 2, entry 4):** *N*-(2-(*S*)-Benzyloxy-propionyl)-2-methylthioaniline (151 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), K_2CO_3 (173 mg, 1.25 mmol), and 4-*t*-butyliodobenzene (520 mg, 2.0 mmol) were dissolved in *t*-amyl alcohol (0.5 mL). Resulting solution was heated for 22 h at 90 ^oC. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) followed by washing with

brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 100/1 to 50/1) gave 147 mg of crude material, which was further purified by preparative TLC (toluene/EtOAc 50/1) to give 136 mg (65%) of colorless oil, 75% ee (Chiralcel OD-H, 10% iPrOH-Hex, 1.0 mL/min, detection at 254 nm. Retention times: 5.99 min minor, 8.35 min major enantiomers). R_f=0.25 (toluene/EtOAc 50/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.52 (br s, 1H) 8.38 (dd, 1H, *J*= 8.3, 1.3 Hz) 7.46 (dd, 1H, *J*= 7.8, 1.5 Hz) 7.34-7.19 (m, 10H) 7.07 (dt, 1H, *J*= 7.6, 1.4 Hz) 4.68 (d, 1H, *J*= 11.7 Hz) 4.50 (d, 1H, *J*= 11.7 Hz) 4.22 (dd, 1H, *J*= 7.7, 3.7 Hz) 3.26 (dd, 1H, *J*= 14.2, 3.7 Hz) 3.04 (dd, 1H, *J*= 14.2, 7.7 Hz) 2.12 (s, 3H) 1.29 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.5, 149.6, 138.1, 137.1, 134.2, 133.3, 129.6, 129.1, 128.5, 128.1, 128.0, 126.0, 125.4, 124.7, 120.5, 81.6, 73.3, 38.9, 34.6, 31.6, 18.8. FT-IR (neat, cm^{-1}) υ 3322, 1689.

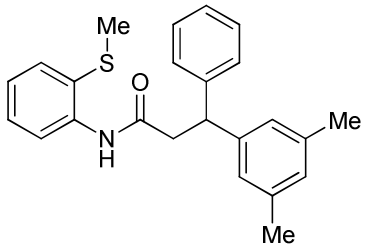


***N*-(3-(3,4-Dimethylphenyl)-2-phthalimidopropionyl)-2-methylthioaniline (Table 2, entry 5):** *N*-(2-Phthalimidopropionyl)-2-methylthioaniline (170 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), CsOAc (240 mg, 1.25 mmol), and 3,4-dimethyliodobenzene (464 mg, 2.0 mmol) were added to dry toluene (0.5 mL). Resulting solution was heated for 11 h at 110 ^{o}C. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) followed by washing with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 50/1 to 30/1) gave 175 mg (79%) of a crystalline material, mp 126-127 ^{o}C (EtOAc/hexanes), R_f=0.21 (EtOAc/hexanes 1/4). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.95 (br s, 1H) 8.34 (d, 1H, *J*= 8.2 Hz) 7.86-7.80 (m, 2H) 7.76-7.69 (m, 2H) 7.45 (dd, 1H, *J*= 7.8, 1.5 Hz) 7.33-7.27 (m, 1H) 7.06 (dt, 1H, *J*= Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 168.0, 166.7, 138.2, 137.0, 135.3, 134.5, 134.1, 133.6, 131.7, 130.4, 130.1, 129.3, 126.3, 125.7, 124.9, 123.7, 120.8,

56.6, 34.2, 19.8, 19.5, 19.2. FT-IR (neat, cm^{-1}) υ 3362, 1705, 1693. Anal. calcd. for $C_{26}H_{24}N_2O_3S$: C 70.25, H 5.44, N 6.30. Found: C 70.34, H 5.26, N 6.26.



***N*-(3-(4-Chlorophenyl)-2-phthalimidopropionyl)-2-methylthioaniline (Table 2, entry 6):** *N*-(2-Phthalimido-propionyl)-2-methylthioaniline (170 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), CsOAc (240 mg, 1.25 mmol), and 4-chloroiodobenzene (477 mg, 2.0 mmol) were dissolved in dry toluene (0.5 mL). Resulting solution was heated for 18.5 h at 110 ^oC. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) followed by washing with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (hexanes/EtOAc 7/1 to 5/1 to 3/1) followed by purification on preparative TLC (hexanes/EtOAc 2/1) gave 134 mg (60%) of a crystalline material, mp 97-98 ^oC (EtOAc/hexanes), R_f=0.21 (toluene/EtOAc 50/1). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.94 (br s, 1H) 8.33 (d, 1H, *J*= 8.1 Hz) 7.86-7.80 (m, 2H) 7.77-7.72 (m, 2H) 7.47-7.42 (m, 1H) 7.34-7.28 (m, 1H) 7.20-7.13 (m, 4H) 7.06 (ddd, 1H, *J*= 7.6, 7.6, 1.3 Hz) 5.27 (dd, 1H, *J*= 10.3, 6.4 Hz) 3.75-3.63 (m, 2H) 2.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.9, 166.3, 138.0, 135.4, 134.7, 133.7, 133.0, 131.4, 130.5, 129.5, 129.1, 125.6, 125.1, 123.9, 120.7, 56.2, 33.9, 19.3. FT-IR (neat, cm^{-1}) υ 3273, 1717, 1675. Anal. calcd. for $C_{24}H_{19}ClN_2O_3S$: C 63.92, H 4.25, N 6.21. Found: C 63.66, H 4.29, N 5.99.

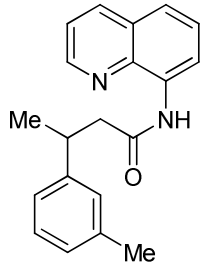


***N*-(3-(3,5-Dimethylphenyl)-3-phenylpropionyl)-2-methylthioaniline (Table 2, entry 7):** *N*-(3-Phenylpropionyl)-2-methylthioaniline (190 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), pivalic acid (14 mg, 0.14 mmol), and 3,5-dimethyliodobenzene (650 mg, 2.8

mmol) were dissolved in *t*-amyl alcohol (0.7 mL). Resulting solution was heated for 39 h at 90 ^{o}C. After cooling to room temperature, reaction mixture was diluted with ethyl acetate (15 mL) followed by washing with brine. Layers were separated and aqueous layer was washed with ethyl acetate once. Combined organic layers were dried over $MgSO_4$. Filtration, evaporation and purification of residue by flash chromatography (toluene/EtOAc 100/1 to 50/1) gave 124 mg (47%) of a crystalline material, mp 120-121 ^{o}C (EtOAc/hexanes), R_f=0.21 (toluene/EtOAc 50/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.25 (d, 1H, *J*= 8.2 Hz) 8.20 (br s, 1H) 7.42 (dd, 1H, *J*= 7.8, 1.4 Hz) 7.30-7.14 (m, 6H) 7.02 (t, 1H, *J*= 7.6 Hz) 6.91 (s, 2H) 6.82 (s, 1H) 4.60 (t, 1H, *J*= 7.7 Hz) 3.13 (d, 2H, *J*= 7.7 Hz) 2.25 (s, 6H) 2.15 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 169.7, 144.0, 143.5, 138.6, 138.3, 133.4, 129.1, 128.8, 128.6, 127.9, 126.7, 125.7, 125.2, 124.5, 120.8, 47.6, 44.9, 21.6, 19.1. FT-IR (neat, cm^{-1}) υ 3232, 1643. Anal. calcd. for $C_{24}H_{25}NOS$: C 76.76, H 6.71, N 3.73. Found: C 76.66, H 6.65, N 3.71.

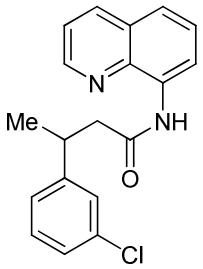
ARYLATION OF SECONDARY C-H BONDS:

General procedure: A 2-dram screw-cap vial was charged with $Pd(OAc)_2$ (5 mol%), aryl iodide (3-4 equiv), and substrate. The vial was transferred to the glove box, where it was charged with Cs_3PO_4 (2.3-3.3 equiv). *t*-Amyl alcohol (0.7 mL) solvent was added outside the glove box and the resulting mixture was stirred and heated at 90-110 ^{o}C for 7-25 h. The conversion was monitored by GC. After completion of reaction, ethyl acetate was added to reaction mixture followed by extraction with water. Aqueous layer was washed once with ethyl acetate. Combined organic extracts were dried over $MgSO_4$. Filtration and evaporation under reduced pressure followed by purification by flash chromatography gave products.

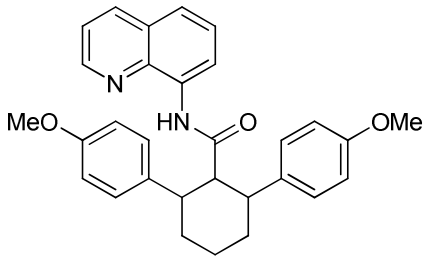


***N*-(3-(3-Methylphenyl)-butyryl)-8-aminoquinoline (Table 3, entry 1):** The general procedure was followed using *N*-butyryl-8-aminoquinoline (150 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (795 mg, 1.61 mmol), and 3-methyliodobenzene (458 mg, 2.1 mmol). Resulting mixture

was heated for 7 h at 90 °C. Flash chromatography (toluene/EtOAc 70/1 to 50/1) gave 168 mg (79%) of a colorless oil, R_f=0.50 (toluene/EtOAc 15/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.73 (br s, 1H) 8.79-8.75 (m, 2H) 8.15 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.56-7.46 (m, 2H) 7.45 (dd, 1H, *J*= 8.3, 4.3 Hz) 7.23-7.11 (m, 3H) 7.03-6.98 (m, 1H) 3.52-3.39 (m, 1H) 2.89 (dd, 1H, *J*= 14.5, 6.5 Hz) 2.75 (dd, 1H, *J*= 14.5, 8.5 Hz) 2.32 (s, 3H) 1.40 (d, 3H, *J*= 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.6, 148.2, 146.1, 138.5, 138.3, 136.5, 134.7, 128.7, 128.1, 127.8, 127.6, 127.4, 124.0, 121.7, 121.6, 116.6, 47.1, 37.0, 22.1, 21.7. FT-IR (neat, cm^{-1}) υ 3347, 1685. Anal. calcd. for $C_{20}H_{20}N_2O$: C 78.92, H 6.62, N 9.20. Found: C 78.98, H 6.49, N 9.17.

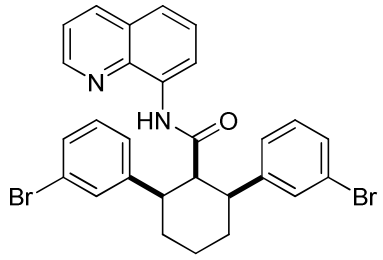


***N*-(3-(3-Chlorophenyl)-butyryl)-8-aminoquinoline (Table 3, entry 2):** The general procedure was followed using *N*-butyryl-8-aminoquinoline (150 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (795 mg, 1.61 mmol), and 3-chloroiodobenzene (501 mg, 2.1 mmol). Resulting mixture was heated for 10 h at 90 °C. Flash chromatography (toluene/EtOAc 70/1 to 50/1) gave 185 mg (81%) of a colorless oil, R_f=0.46 (toluene/EtOAc 15/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.72 (br s, 1H) 8.78 (dd, 1H, *J*= 4.3, 1.6 Hz) 8.74 (dd, 1H, *J*= 6.7, 2.2 Hz) 8.15 (dd, 1H, *J*= 8.3, 1.6 Hz) 7.56-7.48 (m, 2H) 7.45 (dd, 1H, *J*= 8.3, 4.2 Hz) 7.35-7.32 (m, 1H) 7.23-7.14 (m, 3H) 3.55-3.42 (m, 1H) 2.87 (dd, 1H, *J*= 14.6, 6.8 Hz) 2.76 (dd, 1H, *J*= 14.6, 8.0 Hz) 1.40 (d, 3H, *J*= 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.1, 148.3, 148.2, 138.5, 136.5, 134.6, 134.5, 130.1, 128.1, 127.6, 127.2, 126.8, 125.5, 121.8, 121.7, 116.7, 46.8, 36.8, 21.9. FT-IR (neat, cm^{-1}) υ 3361, 1686. Anal. calcd. for $C_{19}H_{17}ClN_2O$: C 70.26, H 5.28, N 8.62. Found: C 70.46, H 5.21, N 8.60.



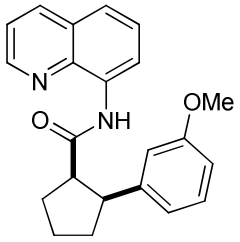
8-(2,6-Di-(4-methoxyphenyl)-cyclohexanecarboxamido)-quinoline (Table 3, entries 3 and 4): The general procedure was followed using 8-cyclohexanecarboxamidoquinoline (178 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (1.14 g, 2.31 mmol), and 4-methoxyiodobenzene (655 mg, 2.8 mmol). Resulting mixture was heated for 12 h at 90 ^oC. Flash chromatography (toluene/EtOAc 30/1 to 15/1) gave 206 mg (63%) of a white crystalline material (*all-cis* isomer) and 52 mg (16%) of another white crystalline material (*trans-cis* isomer). ^1H NMR of both products are identical with previously published data.[15]

8-(Cyclohexanecarboxamido)quinoline (178 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), AgOAc (292 mg, 1.75 mmol), and 4-iodoanisole (655 mg, 2.8 mmol) were stirred at 90 °C for 4.5 hours. Purification by flash chromatography (EtOAc/toluene 1/40 to 1/20) gave 226 mg (69%) of the all-*cis* diarylated product as a colorless crystalline material and 44 mg (13%) of *trans* diarylated product.

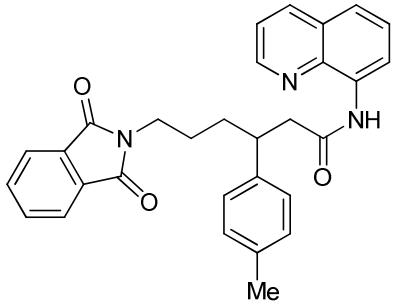


8-(2,6-Di-(3-bromophenyl)-cyclohexanecarboxamido)-quinoline (Table 3, entry 5): The general procedure was followed using 8-cyclohexanecarboxamidoquinoline (178 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (1.14 g, 2.31 mmol), and 3-bromoiodobenzene (792 mg, 2.8 mmol). Resulting mixture was heated for 12 h at 90 ^oC. Flash chromatography (toluene/EtOAc 100/1) gave 204 mg (52%) of a white crystalline material (*all-cis* isomer), mp 163-164 ^oC (EtOAc/hexanes), R_f=0.61 (toluene/EtOAc 50/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.67 (br s, 1H) 8.54 (dd, 1H, *J*= 4.3, 1.5 Hz) 8.45 (dd, 1H, *J*= 7.2, 1.6 Hz) 8.00 (dd, 1H, *J*= 8.2, 1.5 Hz) 7.50-7.47(m, 2H) 7.45-7.34 (m, 2H) 7.31 (dd, 1H, *J*= 8.2, 4.2 Hz) 7.26-7.20 (m, 2H) 7.08-7.03 (m, 2H) 6.92 (dd, 2H, *J*= 7.2, 7.2 Hz) . ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.3, 147.7, 146.4, 138.2, 136.0, 133.9, 131.1, 130.0, 129.7, 127.7, 127.2, 126.1, 122.6, 121.4, 116.4, 56.6, 47.6, 26.5, 25.5. Signal for one aromatic carbon could not be detected. FT-IR (neat, cm^{-1}) υ 3353, 1678. Anal. calcd. for $C_{28}H_{24}Br_2N_2O$: C 59.59, H 4.29, N 4.96. Found: C 59.43, H 4.22, N 4.89.

[15] Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154.



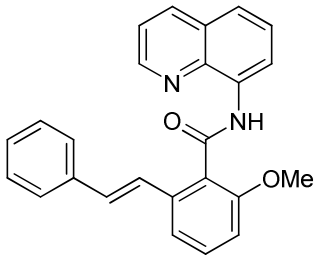
8-(2-(3-Methoxyphenyl)-cyclopentanecarboxamido)-quinoline (Table 3, entry 6): The general procedure was followed using 8-cyclopentanecarboxamidoquinoline (168 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (1.04 g, 2.1 mmol), and 3-methoxyiodobenzene (655 mg, 2.8 mmol). Resulting mixture was heated for 23 h at 110 ^oC. Flash chromatography (toluene/EtOAc 50/1 to 30/1) followed by preparative TLC (EtOAc/hexanes 1/4) gave 127 mg (52%) of a colorless oil, R_f=0.10 (toluene/EtOAc 50/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 9.32 (s, 1H) 8.66 (dd, 1H, *J*= 4.1, 1.7 Hz) 8.55 (dd, 1H, *J*= 7.0, 2.0 Hz) 8.04 (dd, 1H, *J*= 8.3, 1.4 Hz) 7.44-7.33 (m, 3H) 6.97-6.91 (m, 1H) 6.88-6.81 (m, 2H) 6.41-6.36 (m, 1H) 3.53 (s, 3H) 3.54-3.44 (m, 1H, overlaps with methyl group signal) 3.34-3.25 (m, 1H) 2.44-2.00 (m, 5H) 1.88-1.75 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 173.1, 159.5, 147.9, 143.0, 138.4, 136.2, 134.6, 129.2, 127.9, 127.4, 121.4, 121.1, 120.5, 116.2, 113.5, 112.3, 55.1, 53.2, 50.5, 31.0, 28.6, 24.6. FT-IR (neat, cm^{-1}) υ 3359, 1682. Anal. calcd. for $C_{22}H_{22}N_2O_2$: C 76.28, H 6.40, N 8.09. Found: C 76.38, H 6.42, N 8.07. Relative stereochemistry was deduced from NOE experiments.



***N*-((3-(4-Methylphenyl)-6-phthalimido)-hexanoyl)-8-aminoquinoline (Table 3, entry 7):** The general procedure was followed using *N*-(6-phthalimidohexanoyl)-8-aminoquinoline (271 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), Cs_3PO_4 (795 mg, 1.61 mmol), and 4-methyliodobenzene (458 mg, 2.1 mmol). Resulting mixture was heated for 25 h at 90 ^oC. Flash chromatography (EtOAc/hexanes 1/4 to 1/2) gave 256 mg (76%) of a crystalline material, mp 113-114 ^oC (EtOAc/hexanes), R_f=0.53 (hexane/EtOAc 1/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 9.66 (s, 1H) 8.75 (dd, 1H, *J*= 4.2, 1.7 Hz) 8.67 (dd, 1H, *J*= 6.1, 2.9 Hz) 8.12 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.80-7.73 (m, 2H) 7.69-7.63 (m, 2H) 7.48-7.40 (m, 3H) 7.18-7.14 (m, 2H) 7.08-7.04 (m, 2H) 3.63 (t, 2H, *J*=

7.2 Hz) 3.34-3.23 (m, 1H) 2.82 (d, 2H, *J*= 7.4 Hz) 2.25 (s, 3H) 1.93-1.45 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.2, 168.4, 148.1, 140.5, 138.3, 136.3, 136.1, 134.5, 133.8, 132.2, 129.4, 127.9, 127.5, 127.4, 123.1, 121.6, 121.4, 116.5, 45.8, 41.9, 38.0, 33.5, 26.7, 21.1. FT-IR (neat, cm^{-1}) υ 3351, 1706. Anal. calcd. for $C_{30}H_{27}N_3O_3$: C 75.45, H 5.70, N 8.80. Found: C 74.78, H 5.75, N 8.70.

ALKENYLATION OF sp^2 C-H BONDS

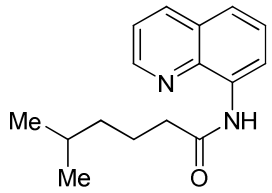


***N*-(6-Styryl-2-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 8):** The vial was charged with *N*-(2-methoxybenzoyl)-8-aminoquinoline (195 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), AgOAc (175 mg, 1.05 mmol), and 2-iodostyrene (322 mg, 1.4 mmol) and resulting mixture was heated for 8 h at 90 ^oC without solvent. After reaction was completed, reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a pad of Celite. Filtrate was evaporated under reduced pressure and residue was dried under vacuum to remove residual solvents. Further purification by flash chromatography (toluene/EtOAc 30/1) followed by separation by preparative TLC (EtOAc/hexanes 1/4) gave 170 mg (64%) of a crystalline material, mp 143-144 ^oC (EtOAc/hexanes), R_f=0.18 (hexane/EtOAc 4/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 10.16 (s, 1H) 9.06 (dd, 1H, *J*= 7.4, 1.5 Hz) 8.71 (dd, 1H, *J*= 4.2, 1.6 Hz) 8.16 (dd, 1H, *J*= 8.3, 1.6 Hz) 7.65-7.53 (m, 2H) 7.45-7.38 (m, 7H) 7.29-7.13 (m, 3H) 6.94-6.89 (m, 1H) 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.1, 156.8, 148.3, 138.7, 137.2, 137.0, 136.4, 134.9, 131.7, 130.5, 128.6, 128.1, 127.9, 127.6, 127.0, 126.2, 125.6, 121.9, 121.7, 118.1, 117.0, 110.2, 56.1. FT-IR (neat, cm^{-1}) υ 3350, 1665. Anal. calcd. for $C_{25}H_{20}N_2O_2$: C 78.93, H 5.30, N 7.36. Found: C 78.76, H 5.18, N 7.38.

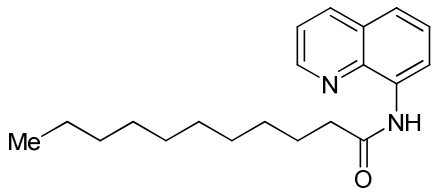
ALKYLATION OF C-H BONDS

General procedure: A 2-dram screw-cap vial was charged with $Pd(OAc)_2$ (5 mol%), K_2CO_3 (2.5 equiv), substrate (1 equiv), pivalic acid (20 mol%), and alkyl iodide (3-4 equiv). The *t*-amyl alcohol

(0.7 mL) solvent was added and the resulting mixture was stirred and heated at 100-110 ^{o}C for 12-26 h. The conversion was monitored by GC. After completion of reaction, ethyl acetate was added to reaction mixture followed by extraction with water. Aqueous layer was washed once with ethyl acetate. Combined organic extracts were dried over $MgSO_4$. Filtration and evaporation under reduced pressure followed by purification by flash chromatography gave products.

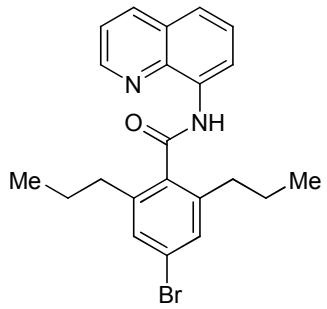


***N*-(5-Methylhexanoyl)-8-aminoquinoline (Table 4, entry 1):** The general procedure was followed using *N*-propionyl-8-aminoquinoline (140 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), pivalic acid (14 mg, 0.14 mmol), and 2-methyliodopropane (240 μL, 2.1 mmol). Resulting mixture was heated for 22 h at 110 ^{o}C. Flash chromatography (toluene/EtOAc 50/1 to 25/1) gave 104 mg (58%) of a colorless oil, R_f=0.19 (toluene/EtOAc 50/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.82 (s, 1H) 8.83-8.78 (m, 2H) 8.17 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.58-7.43 (m, 3H) 2.55 (t, 2H, *J*= 7.6 Hz) 1.89-1.77 (m, 2H) 1.63 (septet, 2H, *J*= 6.7 Hz) 1.37-1.28 (m, 2H) 0.92 (d, 6H, *J*= 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 172.1, 148.3, 138.5, 136.5, 134.8, 128.1, 127.6, 121.7, 121.5, 116.6, 38.7, 28.1, 23.8, 22.7. Signal for one aliphatic carbon could not be detected. FT-IR (neat, cm^{-1}) υ 3353, 1687. Anal. calcd. for $C_{16}H_{20}N_2O$: C 74.97, H 7.86, N 10.93. Found: C 74.83, H 7.91, N 10.93.

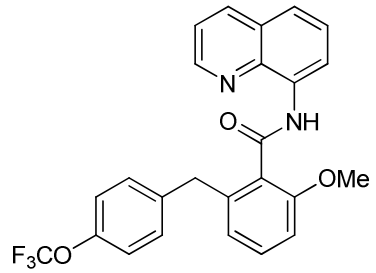


***N*-Undecanoyl-8-aminoquinoline (Table 4, entry 2):** The general procedure was followed using *N*-propionyl-8-aminoquinoline (140 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), pivalic acid (14 mg, 0.14 mmol), and 1-iodooctane (380 μL, 2.1 mmol). Resulting mixture was heated for 26 h at 110 ^{o}C. Flash chromatography (toluene/EtOAc 50/1 to 25/1) gave 103 mg (47%) of a colorless oil, R_f=0.20 (toluene/EtOAc 50/1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.82 (br s, 1H) 8.83-8.78 (m, 2H) 8.17 (dd, 1H, *J*= 8.2, 1.7 Hz) 7.58-7.43 (m, 3H) 2.57 (t, 2H, *J*= 7.6 Hz) 1.88-1.77 (m, 3H) 1.49-1.22 (m, 13H) 0.87 (t, 3H, *J*= 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 172.1, 148.3, 138.5, 136.5, 134.8, 128.1, 127.6, 121.7, 121.5, 116.6, 38.5, 32.1, 29.8, 29.7, 29.6,

29.5, 25.9, 22.9, 14.3. Signal for one aliphatic carbon could not be detected. FT-IR (neat, cm^{-1}) υ 3360, 1690. Anal. calcd. for $C_{20}H_{28}N_2O$: C 76.88, H 9.03, N 8.97. Found: C 76.34, H 8.97, N 8.85.

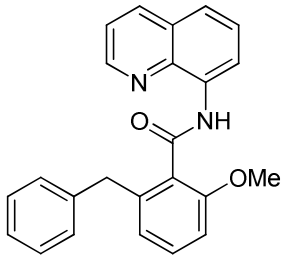


***N*-(4-Bromo-2,6-dipropylbenzoyl)-8-aminoquinoline (Table 4, entry 3):** The general procedure was followed using *N*-(4-bromobenzoyl)-8-aminoquinoline (229 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (339 mg, 2.45 mmol), pivalic acid (14 mg, 0.14 mmol), and 1-iodopropane (273 μL, 2.8 mmol). Resulting mixture was heated for 12.5 h at 110 ^oC. Flash chromatography (EtOAc/hexanes 1/15 to 1/7) gave 223 mg (77%) of a crystalline material, mp 122-123 ^oC (EtOAc/hexanes), R_f=0.34 (hexane/EtOAc 10/1). ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 9.89 (br s, 1H) 8.95 (dd, 1H, *J*= 6.8, 2.1 Hz) 8.74 (dd, 1H, *J*= 4.2, 1.7 Hz) 8.19 (dd, 1H, *J*= 8.3, 1.7 Hz) 7.65-7.56 (m, 2H) 7.45 (dd, 1H, *J*= 8.3, 4.3 Hz) 7.30 (s, 2H) 2.69-2.62 (m, 2H) 1.76-1.62 (m, 4H) 0.88 (t, 6H, *J*= 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 168.1, 148.6, 141.7, 138.7, 136.7, 136.5, 134.4, 129.9, 128.2, 127.6, 123.3, 122.3, 121.9, 117.0, 35.5, 24.6, 14.2. FT-IR (neat, cm^{-1}) υ 3334, 1677. Anal. calcd. for $C_{22}H_{23}BrN_2O$: C 64.24, H 5.64, N 6.81. Found: C 64.45, H 5.52, N 6.67.



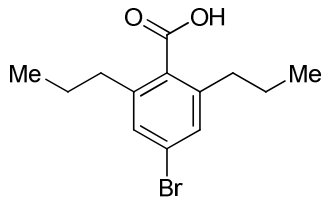
***N*-(2-Methoxy-6-(4-trifluoromethoxybenzyl)-benzoyl)-8-aminoquinoline (Table 4, entry 4):** The general procedure was followed using *N*-(2-methoxybenzoyl)-8-aminoquinoline (195 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), pivalic acid (14 mg, 0.14 mmol), and 4-trifluoromethoxybenzyl bromide (336 μL, 2.1 mmol). Resulting mixture was heated for 12 h at 110 ^oC. Flash chromatography (toluene/EtOAc 30/1 to 15/1) gave 143 mg (45%) of a crystalline material, mp 118-119 ^oC (EtOAc/hexanes), R_f=0.46 (toluene/EtOAc 15/1). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 9.93 (br s, 1H) 8.95 (dd, 1H, *J*= 7.2, 1.8 Hz) 8.68 (dd, 1H, *J*= 4.3, 1.7 Hz) 8.16

(dd, 1H, *J*= 8.3, 1.6 Hz) 7.62-7.51 (m, 2H) 7.42 (dd, 1H, *J*= 8.3, 4.3 Hz) 7.38-7.31 (m, 1H) 7.22-7.17 (m, 2H) 6.94-6.83 (m, 4H) 4.12 (s, 2H) 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 166.3, 156.9, 148.3, 147.7, 140.1, 139.4, 138.7, 136.5, 134.8, 130.7, 130.5, 128.2, 127.6, 127.3, 122.8, 122.0, 121.8, 121.0, 120.6 (q, $J_{C\text{-}F}$= 256.8 Hz) 116.9, 109.6, 56.1, 38.6. FT-IR (neat, cm^{-1}) υ 3346, 1664.

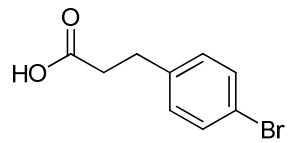


***N*-(2-Methoxy-6-(4-benzyl)-benzoyl)-8-aminoquinoline (Table 4, entry 5):** The general procedure was followed using *N*-(2-methoxybenzoyl)-8-aminoquinoline (195 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), K_2CO_3 (242 mg, 1.75 mmol), pivalic acid (14 mg, 0.14 mmol), and 4-trifluoromethoxybenzyl bromide (336 μL, 2.1 mmol). Resulting mixture was heated for 12 h at 100 ^{o}C. Flash chromatography (toluene/EtOAc 30/1 to 15/1) gave 165 mg (64%) of a crystalline material, mp 142-143 ^{o}C (EtOAc/hexanes), R_f=0.46 (toluene/EtOAc 15/1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 9.98 (br s, 1H) 8.98 (dd, 1H, *J*= 7.4, 1.6 Hz) 8.69 (dd, 1H, *J*= 4.2, 1.6 Hz) 8.15 (dd, 1H, *J*= 8.3, 1.6 Hz) 7.62-7.51 (m, 2H) 7.42 (dd, 1H, *J*= 8.3, 4.2 Hz) 7.31 (t, 1H, *J*= 8.0 Hz) 7.22-7.17 (m, 1H) 7.15-7.07 (m, 1H) 7.05-6.98 (m, 1H) 6.89-6.80 (m, 2H) 4.13 (s, 2H) 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 166.5, 156.7, 148.2, 140.7, 140.5, 138.7, 136.4, 134.9, 130.5, 129.3, 128.5, 128.1, 127.6, 127.3, 126.1, 122.8, 121.8, 121.7, 116.9, 109.2, 56.0, 39.1. FT-IR (neat, cm^{-1}) υ 3347, 1664. Anal. calcd. for $C_{24}H_{20}N_2O_2$: C 78.24, H 5.47, N 7.60. Found: C 77.96, H 5.41, N 7.50.

HYDROLYSIS OF AMIDES



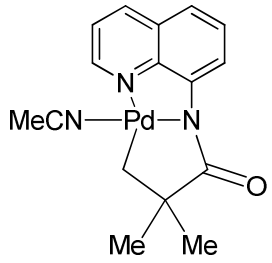
4-Bromo-2,6-dipropylbenzoic acid: *N*-(4-Bromo-2,6-dipropylbenzoyl)-8-aminoquinoline (100 mg, 0.24 mmol) was heated in aqueous 40% H_2SO_4 (0.5 mL) at 120 ^oC for 24 hours. After completion, reaction mixture was extracted with Et_2O (3 x 10 mL). Combined organic layers were dried over $MgSO_4$. Evaporation resulted in 65 mg (95%) of a crystalline material, mp 91-92 ^oC (EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.26 (s, 2H, overlaps with solvent peak) 2.68-2.62 (m, 4H) 1.72-1.61 (m, 4H) 0.96 (t, 6H, *J*= 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 175.2, 142.1, 131.3, 130.2, 124.2, 35.9, 24.6, 14.2. FT-IR (neat, cm^{-1}) υ 1692. Anal. calcd. for $C_{13}H_{17}BrO_2$: C 54.75, H 6.01. Found: C 55.04, H 6.04.



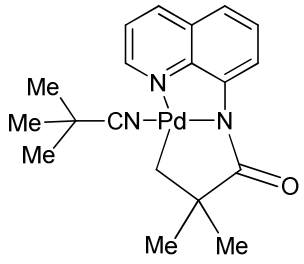
3-(4-Bromophenyl)propionic acid:[16] *N*-(3-(4-Bromophenyl)-propionyl)-2-methylthioaniline (120 mg, 0.34 mmol) and NaOH (96 mg, 2.4 mmol) were heated in ethanol (0.7 mL) for 3 hours at 70 ^oC. After completion, water was added to the reaction mixture followed by extraction with ether (3 x 5 mL). These ether extracts were discarded. Aqueous layer was acidified with 1N $NaHSO_4$ until pH~2 followed by extraction with ether (3 x 10 mL). Ether extracts from acidified aqueous layer were combined and dried over $MgSO_4$. Evaporation of solvent gave 70 mg (90%) of crystalline material. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 11.45 (br s, 1H) 7.44-7.39 (m, 2H) 7.11-7.06 (m, 2H) 2.91 (t, 2H, *J*= 7.6 Hz) 2.66 (t, 2H, *J*= 7.6 Hz).

[16] Adamczyk, M.; Watt, D. S.; Netzel, D. A. *J. Org. Chem.* **1984**, *49*, 4226.

SYNTHESIS OF PALLADACYCLES

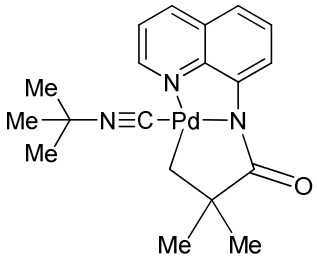


Palladacycle 13: *N*-Pivaloyl-8-aminoquinoline (685 mg, 3.0 mmol) and $Pd(OAc)_2$ (673 mg, 3.0 mmol) were heated for 4 hours in acetonitrile (6.0 mL) at 60 ^oC in a Kontes flask. After completion, sufficient amount of toluene was added to the suspension to dissolve the precipitate (ca. 10 mL). The resulting solution was filtered through a pad of Celite. Filtrate was evaporated in vacuum to give 1.11 g (99%) of yellowish-green crystals. ^1H NMR (500 MHz, CD_2C_2, ppm) δ 9.02 (dd, 1H, *J*= 8.0, 0.7 Hz) 8.42 (dd, 1H, *J*= 4.6, 1.4 Hz) 8.23 (dd, 1H, *J*= 8.4, 1.2 Hz) 7.46 (t, 1H, *J*= 8.0 Hz) 7.39 (dd, 1H, *J*= 8.4, 4.6 Hz) 7.28 (d, 1H *J*= 8.2 Hz) 2.34 (s, 3H) 1.80 (s, 2H) 1.20 (s, 6H). ^{13}C NMR (125 MHz, CD_2Cl_2, ppm) δ 189.4, 148.2, 146.5, 145.2, 138.3, 130.3, 129.2, 121.1, 120.5, 119.5, 118.4, 49.6, 30.3, 25.0, 3.8. Anal. calcd. for $C_{16}H_{17}N_3OPd$: C 51.42, H 4.58, N 11.24. Found: C 51.05, H 4.40, N 10.83. Single crystals for X-ray studies were grown by slow diffusion of pentane into dichloromethane solution of **13** at -20 ^oC.

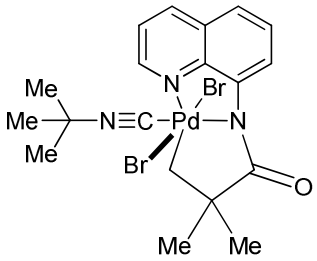


Palladacycle 14: *N*-Pivaloyl-8-aminoquinoline (342 mg, 1.5 mmol) and $Pd(OAc)_2$ (337 mg, 1.5 mmol) were heated for 3 hours in pivalonitrile (3.0 mL) at 60 ^oC in a Kontes flask. After completion, sufficient amount of toluene was added to the suspension to dissolve the precipitate (ca. 10 mL). The resulting solution was filtered through a pad of Celite. Filtrate was evaporated in vacuum to give 619 mg (99%) of yellowish-green crystals. For further purification complex can be recrystallized from toluene/hexanes at -20 ^oC. ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 9.14 (d, 1H, *J*= 7.9 Hz) 8.33 (dd, 1H, *J*= 4.6, 1.4 Hz) 8.20 (dd, 1H, *J*= 8.3, 1.3 Hz) 7.48 (t, 1H, *J*= 8.0 Hz) 7.36 (dd, 1H, *J*= 8.2, 4.6 Hz) 7.28-7.25 (m, 1H) 1.84 (s, 2H) 1.53 (s, 9H) 1.29 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 189.8, 147.8, 145.6, 145.3, 138.1, 130.0, 129.4, 127.6, 121.2, 120.7, 118.4, 49.7,

30.4, 29.9, 28.4, 25.5. Anal. calcd. for $C_{19}H_{23}N_3OPd$: C 54.88, H 5.58, N 10.11. Found: C 54.70, H 5.60, N 9.85.



Palladacycle 15: Complex **13** (400 mg, 1.07 mmol) was dissolved in toluene (10 mL) followed by slow addition of *t*-butylisonitrile (605 μL, 5.35 mmol). The color of solution changed to orange. Resulting solution was stirred overnight. The solution was filtered through a pad of Celite. Filtrate was evaporated in vacuum to give 443 mg (99%) of yellowish-green crystals. ^{1}H NMR (500 MHz, CD_2Cl_2, ppm) δ 9.00 (dd, 1H, *J*= 8.0, 1.1 Hz) 8.51 (dd, 1H, *J*= 4.6, 1.6 Hz) 8.26 (dd, 1H, *J*= 8.4, 1.5 Hz) 7.49 (t, 1H, *J*= 8.0 Hz) 7.41 (dd, 1H, *J*= 8.4, 4.6 Hz) 7.30 (dd, 1H, *J*= 8.1, 1.1 Hz) 1.90 (s, 2H) 1.59 (s, 9H) 1.23 (s, 6H). ^{13}C NMR (125 MHz, CD_2Cl_2, ppm) δ 188.5, 148.5, 148.4, 146.0, 138.5, 137.9 (t, isonitrile carbon), 130.4, 129.5, 121.3, 120.3, 118.4, 57.9 (t, quaternary carbon in *t*-Bu), 50.8, 30.75, 30.72, 24.8. Anal. calcd. for $C_{16}H_{17}N_3OPd$: C 54.88, H 5.58, N 10.11. Found: C 54.68, H 5.48, N 9.97.



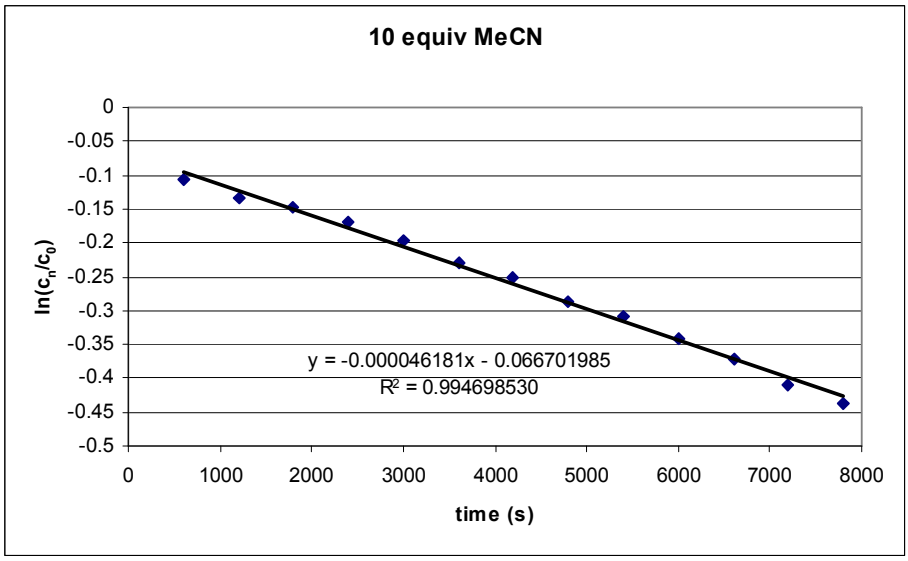
Palladacycle 16: Complex **15** (60 mg, 0.14 mmol) was dissolved in dichloromethane (1.6 mL) and resulting yellowish solution was cooled to -78 ^{o}C followed by dropwise addition of bromine solution in dichloromethane (220 μL, 0.65 M). The resulting dark green solution was stirred for 30 min at that temperature. The solvent was evaporated and dark green residue was dried under vacuum in temperature range between -20 – 0 ^{o}C. After drying, residue was recrystallized from dichloromethane-pentane at -20 ^{o}C affording 79 mg (85%) of **16** (contains dichloromethane in crystal lattice). ^{1}H NMR (500 MHz, CD_2Cl_2, -30 ^{o}C, ppm) δ 9.12 (d, 1H, *J*= 7.7 Hz) 8.74 (dd, 1H, *J*= 4.6, 1.3 Hz) 8.34 (dd, 1H, *J*= 8.3, 1.0 Hz) 7.62-7.54 (m, 2H) 7.50 (d, 1H, *J*= 8.3 Hz) 4.80 (s, 2H) 1.70 (s, 9H) 1.40 (s, 6H). ^{13}C NMR (125 MHz, CD_2Cl_2, -30 ^{o}C, ppm) δ 182.0, 147.5, 145.2, 143.5, 139.1, 130.5, 129.4, 123.1, 122.5, 121.1, 61.1, 56.1 (t, quaternary carbon in *t*-Bu), 53.2, 30.1, 28.4.

Signal for isonitrile group carbon could not be detected. Single crystals for X-ray studies were grown by slow diffusion of pentane into dichloromethane solution of **15** at -20 ^{o}C.

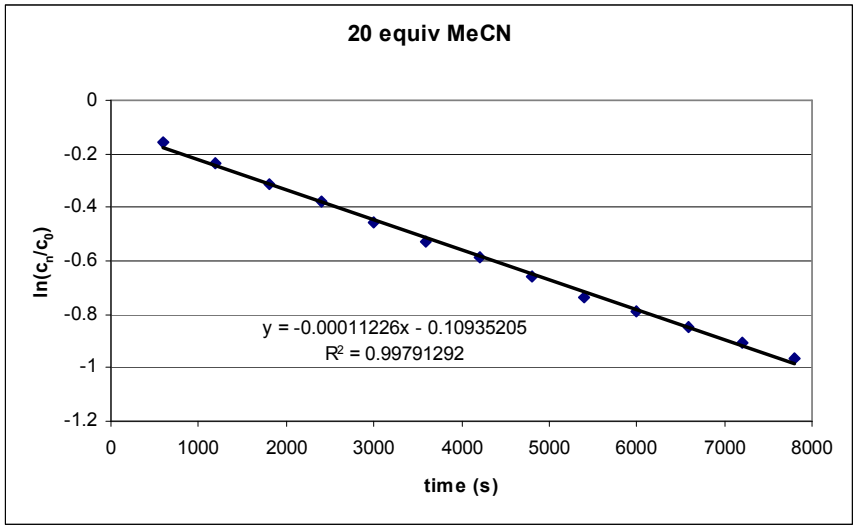
LIGAND EXCHANGE EXPERIMENT

The above reaction was followed by NMR at -35 ^{o}C. Complex **14** was subjected to reaction with 10 and 20 equiv of MeCN. The decay of *t*BuCN ligand *t*-butyl group signal (1.53 ppm) was monitored. The following rate constants were obtained.

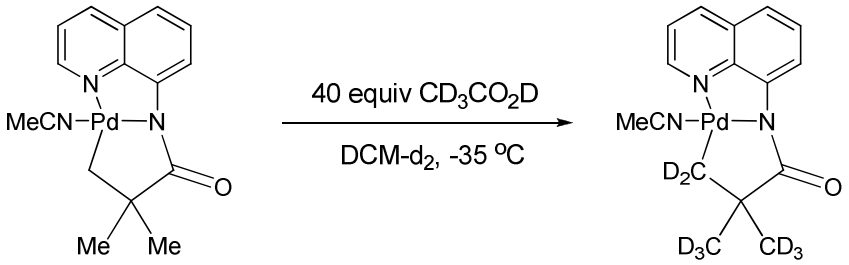
Using 10 equiv MeCN: $k_{obs}=4.6x10^{-5}$ s^{-1}.



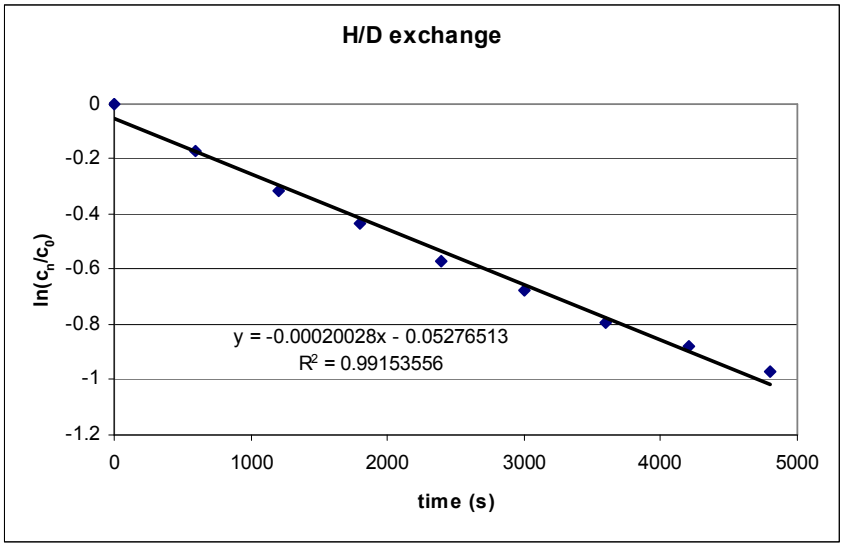
Using 20 equiv MeCN: $k_{obs}=1.1x10^{-4}$ s^{-1}.



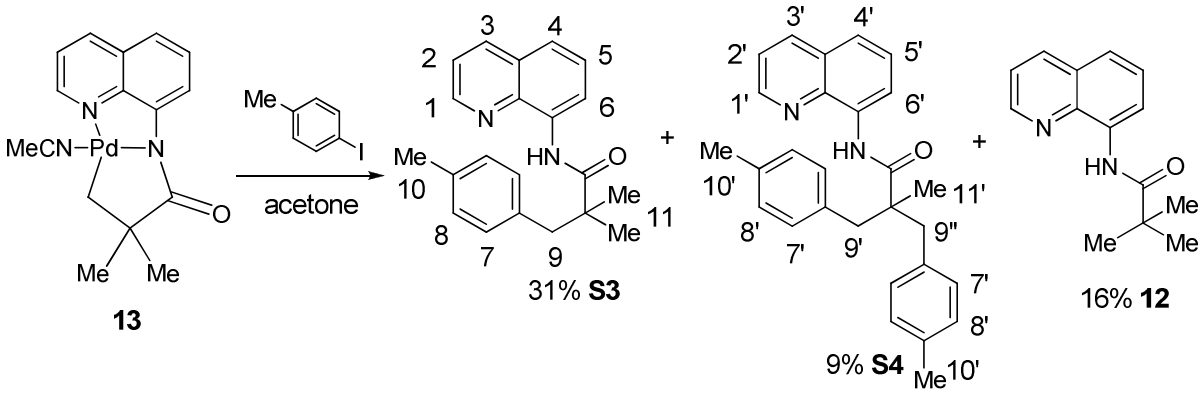
H/D EXCHANGE EXPERIMENT



The above reaction was followed by NMR at -35 ^{o}C. Complex **13** was subjected to reaction with 40equiv of CD_3CO_2D. The decay of methylene group signal (1.82 ppm) was monitored. The following rate constant and activation energy was obtained: $k_{obs}=2.0x10^{-4}$ s^{-1}, $\Delta G^{\ddagger}=18$ kcal/mol.

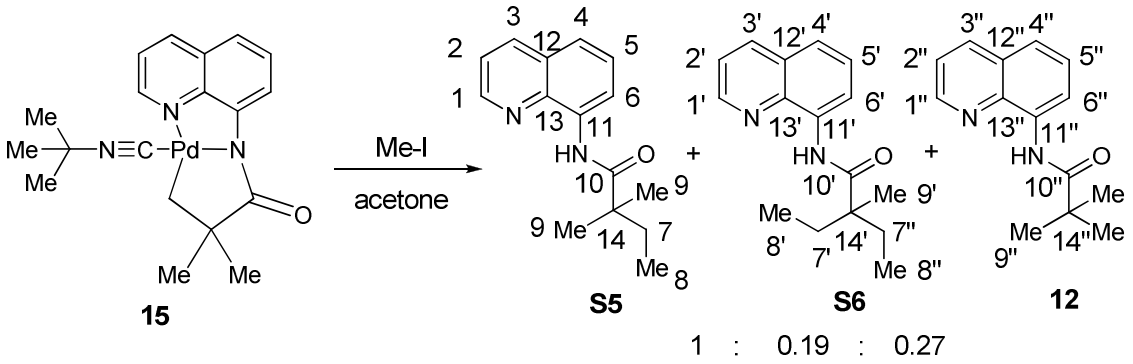


REACTIONS OF COMPLEXES 13 AND 15



Complex **13** (30 mg, 0.08 mmol) and p-tolyliodide (87 mg, 0.40 mmol) were dissolved in acetone (1.0 mL) followed by stirring at room temperature for 40 hours. The reaction mixture was diluted with dichloromethane (2.0 mL) followed by addition of excess of aqueous HI. Resulting solution was stirred for one hour and basified by solid $NaHCO_3$. Extraction with dichloromethane (3 x 10 mL), drying combined organic layers over $MgSO_4$ followed by evaporation of solvent afforded a crude mixture of products. Separation by preparative TLC (toluene/EtOAc 70/1) gave 8 mg (31%) of monoarylated product **S3**, ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.16 (br s, 1H, N*H*) 8.82 (dd, 1H, *J*= 7.5, 1.4 Hz, Ar-*H6*) 8.74 (dd, 1H, *J*= 4.2, 1.6 Hz, Ar-*H1*) 8.14 (dd, 1H, *J*= 8.2, 1.6 Hz, Ar-*H3*) 7.57-7.47 (m, 2H, Ar-*H4*+*H5*) 7.42 (dd, 1H, *J*= 8.2, 4.2 Hz, Ar-*H2*) 7.11-7.05 (m, 2H, Ar-*H7*) 7.03-6.97 (m, 2H, Ar-*H8*) 3.00 (s, 2H, *H9*) 2.24 (s, 3H, *H10*) 1.40 (s, 6H, *H11*); 3 mg (9%) of diarylated product **S4**, ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 9.92 (br s, 1H, N*H*) 8.85 (dd, 1H, *J*= 7.7, 1.3 Hz,

Ar-*H6'*) 8.63 (dd, 1H, *J*= 4.2, 1.5 Hz, Ar-*H1'*) 8.11 (dd, 1H, *J*= 8.2, 1.6 Hz, Ar-*H3'*) 7.57-7.46 (m, 2H, Ar-*H4'+H5'*) 7.37 (dd, 1H, *J*= 8.2, 4.2 Hz, Ar-*H2'*) 7.10-7.05 (m, 4H, Ar-*H7'*) 6.98-6.93 (m, 4H, Ar-*H8'*) 3.41 (d, 2H, *J*= 13.4 Hz, *H9'* or *H9"*) 2.74 (dd, 2H, *J*= 13.4 Hz, *H9'* or *H9"*) 2.20 (s, 6H, *H10'*) 1.28 (s, 3H, *H11'*) and 3 mg (16%) of **12**.



Complex **15** (40 mg, 0.096 mmol) and CH_3I (60 μL, 0.96 mmol) were dissolved in acetone (0.5 mL) and stirred at room temperature for 111 hours. The reaction mixture was diluted with dichloromethane (2.0 mL) followed by addition of excess of aqueous HI. Resulting solution was stirred for one hour and basified by solid $NaHCO_3$. Extraction with dichloromethane (3 x 10 mL), drying combined organic layers over $MgSO_4$ followed by evaporation of solvent afforded a crude mixture of products. Purification by preparative TLC (toluene/EtOAc 70/1) gave inseparable mixture of **S5** as major component, **S6**, and **12** as detected by NMR. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) *δ* 10.23 (br s, 3H, N*H*) 8.86-8.77 (m, 6H, Ar-*H6,H1*, Ar-*H6',H1'*, Ar-*H6",H1"*) 8.15 (dd, 3H, *J* = 8.3, 1.5 Hz, Ar-*H3*, Ar-*H3'*, Ar-*H3"*) 7.58-7.42 (m, 6H, Ar-*H4,H5,H2*, Ar-*H4',H5',H2'*, Ar-*H4",H5",H2"*) 1.93-1.84 (m, 2H, *H7'* or *H7"*) 1.77 (q, 2H, *J* = 7.3 Hz, *H7*) 1.69-1.60 (m, 2H, *H7'* or *H7"* overlaps with residual water signal) 1.43 (s, 9H, *H9"*) 1.40 (s, 6H, *H9*) 1.36 (s, 3H, *H9'*) 0.96 (t, 3H, *J* = 7.3 Hz, *H8*) 0.94 (t, 6H, *J* = 7.3 Hz, *H8'* and *H8"*).^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ* 177.5 (*C11"*), 176.9 (*C11*), 176.2 (*C11'*), 148.4 (*C1, C1', C1"*), 139.0 (*C11, C11', C11"*), 136.5 (*C3, C3', C3"*), 134.9 (*C13, C13', C13"*), 128.1 (*C12, C12', C12"*), 127.7 (*C5, C5', C5"*), 121.7 (*C2, C2', C2"*), 121.4 (*C4, C4', C4"*), 116.4 (*C6, C6', C6"*), 48.2 (*C14'*), 44.3 (*C14*), 40.6 (*C14"*), 34.3 (*C7*), 32.7 (*C7'*), 27.9 (*C9"*), 25.3 (*C9*), 20.4 (*C9'*), 9.5 (*C8*), 9.2 (*C8'*).

X-RAY DATA

All measurements were made with a Siemens SMART platform diffractometer equipped with a 4K CCD APEX II detector. A hemisphere of data (1271 frames at 6 cm detector distance) was collected using a narrow-frame algorithm with scan widths of 0.30\% in omega and an exposure time of 25 s/frame. The data were integrated using the Bruker-Nonius SAINT program, with the intensities corrected for Lorentz factor, polarization, air absorption, and absorption due to variation in the path length through the detector faceplate. A psi scan absorption correction was applied based on the entire data set. Redundant reflections were averaged. Final cell constants were refined using 4697 reflections having I>10\s(I), and these, along with other information pertinent to data collection and refinement, are listed in Table S3. The Laue symmetry was determined to be -1, and the space group was shown to be either P1 or P-1. The asymmetric unit consists of two independent molecules.

Acknowledgment for use of MRSEC/TCSUH Facilities:

This work made use of MRSEC/TCSUH Shared Experimental Facilities supported by the National Science Foundation under Award Number DMR-9632667 and the Texas Center for Superconductivity at the University of Houston.

Table S3. Crystal Data and Structure Refinement for 13.

Empirical formula	$C_{16}H_{17}N_3OPd$
Formula weight	373.73
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 9.0923(12) Å alpha = 84.402(2) deg.
	b = 10.9151(14) Å beta = 88.593(2) deg.
	c = 15.353(2) Å gamma = 89.179(2) deg.
Volume	1515.8(3) Å^3
Z, Calculated density	4, 1.638 Mg/m^3
Absorption coefficient	1.226 mm^-1
F(000)	752

Crystal color and shape	Orange block
Crystal size	0.30 x 0.20 x 0.15 mm
Theta range for data collection	1.87 to 25.06 deg.
Limiting indices	-10<=h<=10, -12<=k<=13, 0<=l<=18
Reflections collected/unique	5157/4156 [R(int) = 0.0380]
Completeness to theta = 25.06	96.2 %
Absorption correction	Empirical
Max. and min. transmission	0.9856 and 0.6505
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5157 / 0 / 383
Goodness-of-fit on F^2	1.151
Final R indices [I>4sigma(I)]	R1 = 0.0388, wR2 = 0.1279
R indices (all data)	R1 = 0.0524, wR2 = 0.1110

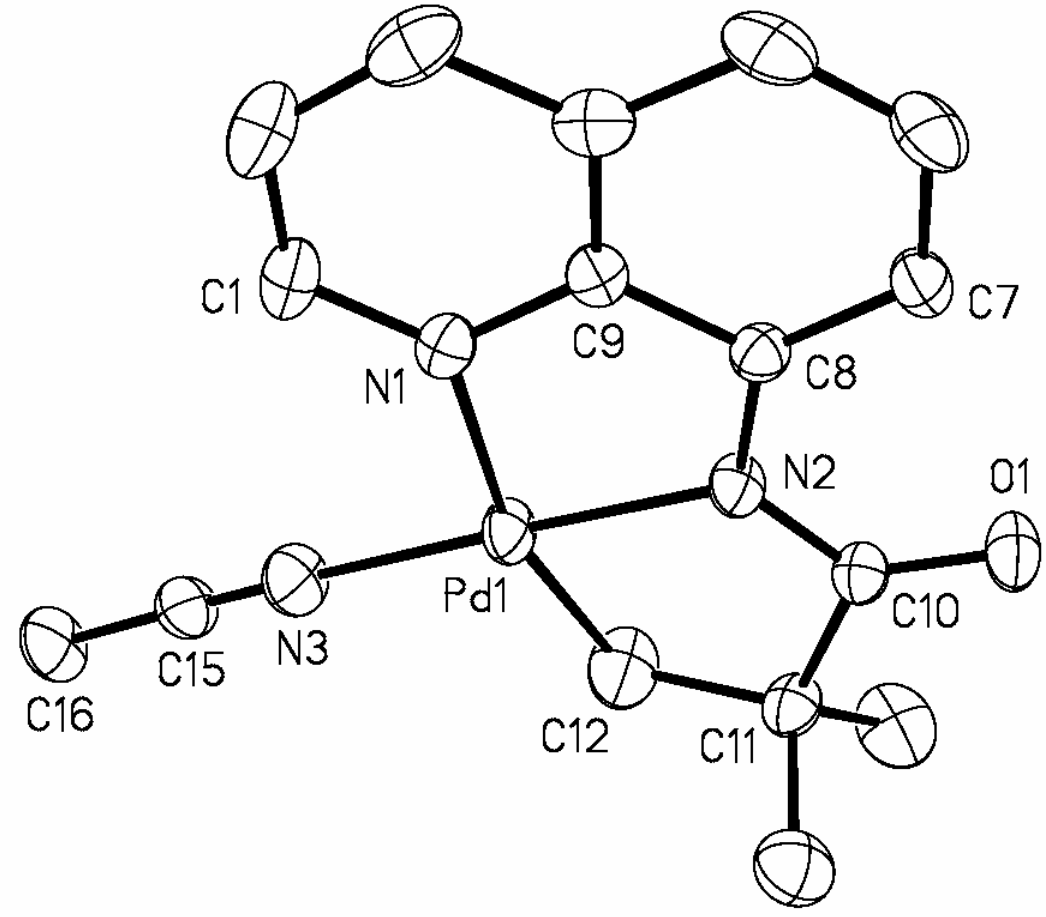


Figure S1. ORTEP view of palladacycle **13**.

All measurements were made with a Siemens SMART platform diffractometer equipped with a 4K CCD APEX II detector. A hemisphere of data (1271 frames at 6 cm detector distance) was collected using a narrow-frame algorithm with scan widths of 0.30\% in omega and an exposure time of 30 s/frame. The data were integrated using the Bruker-Nonius SAINT program, with the intensities corrected for Lorentz factor, polarization, air absorption, and absorption due to variation in the path length through the detector faceplate. A psi scan absorption correction was applied based on the entire data set. Redundant reflections were averaged. Final cell constants were refined using 4193 reflections having I>10\s(I), and these, along with other information pertinent to data collection and refinement, are listed in Table S4. The Laue symmetry was determined to be -1, and the space group was shown to be either P1 or P-1. In the final refinement there was only one residual peak greater than 0.5 e/A3. This peak refined as approximately three electrons, at about 1.7 A distance from C5 but at a very odd angle. Since this does not make chemical sense, the peak is thought to be attributable to a small satellite attached to the main sample crystal which could not be safely removed. This artifact was ignored in the final refinement.

Acknowledgment for use of MRSEC/TCSUH Facilities:

This work made use of MRSEC/TCSUH Shared Experimental Facilities supported by the National Science Foundation under Award Number DMR-9632667 and the Texas Center for Superconductivity at the University of Houston.

Table S4. Crystal Data and Structure Refinement for 16.

Empirical formula	$C_{20}H_{25}Br_2Cl_2N_3OPd$
Formula weight	660.55
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 9.9480(9) Å alpha = 94.143(1) deg.
	b = 10.5972(9) Å beta = 96.995(1) deg.
	c = 11.8562(10) Å gamma = 96.737(1) deg.
Volume	1227.27(18) Å ^3

Z, Calculated density	2, 1.788 Mg/m^3
Absorption coefficient	4.246 mm^-1
F(000)	648
Crystal color and shape	Very dark green block
Crystal size	0.45 x 0.40 x 0.30 mm
Theta range for data collection	1.74 to 25.07 deg.
Limiting indices	-11<=h<=11, -12<=k<=12, 0<=l<=14
Reflections collected/unique	4279/3477 [R(int) = 0.0332]
Completeness to theta = 25.07	98.2 %
Absorption correction	Empirical
Max. and min. transmission	0.9856 and 0.6505
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4279 / 0 / 262
Goodness-of-fit on F^2	1.008
Final R indices [I>4sigma(I)]	R1 = 0.0286, wR2 = 0.0822
R indices (all data)	R1 = 0.0337, wR2 = 0.0786

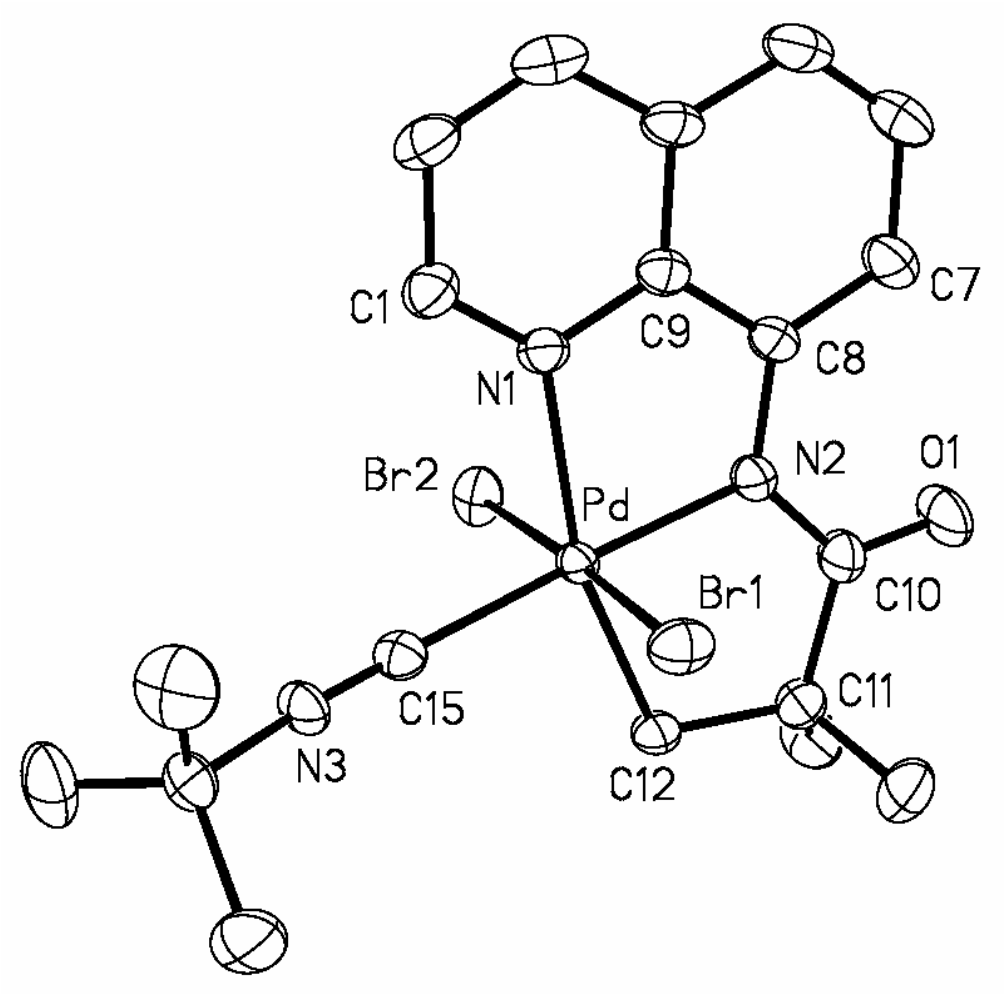
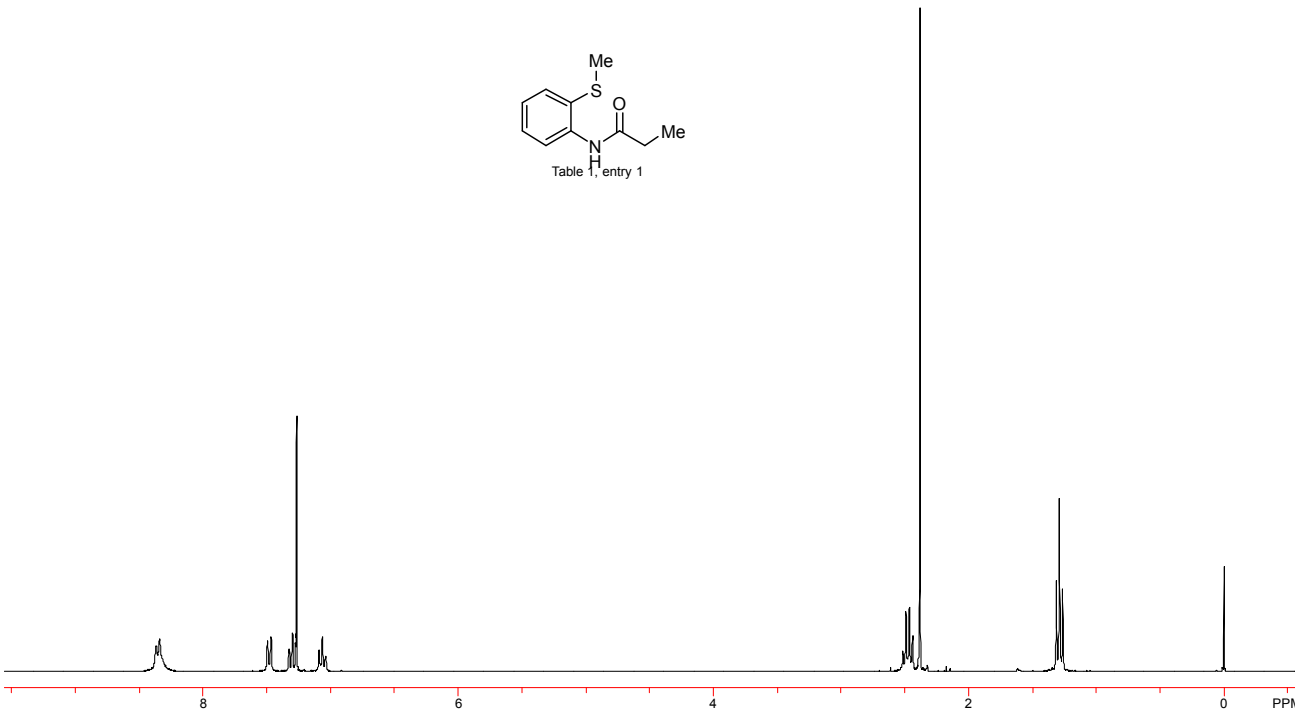


Figure S2. ORTEP view of palladium(IV) dibromide complex **16**.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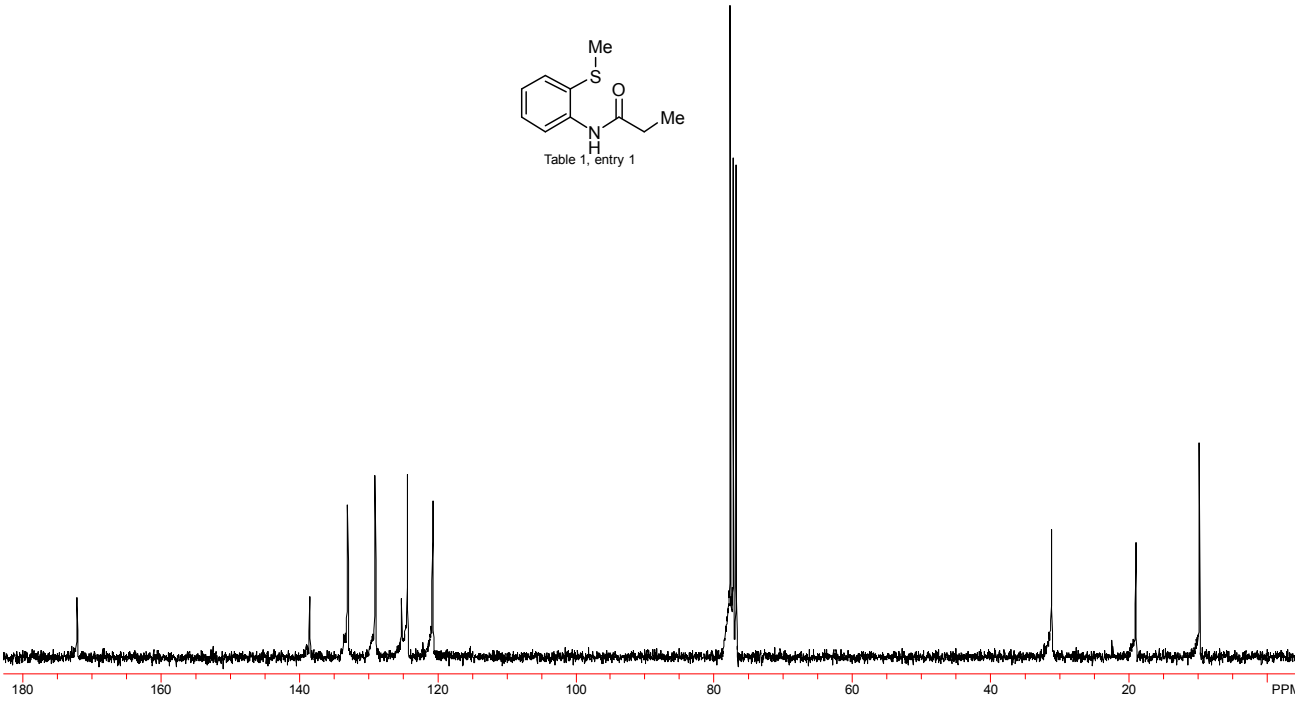
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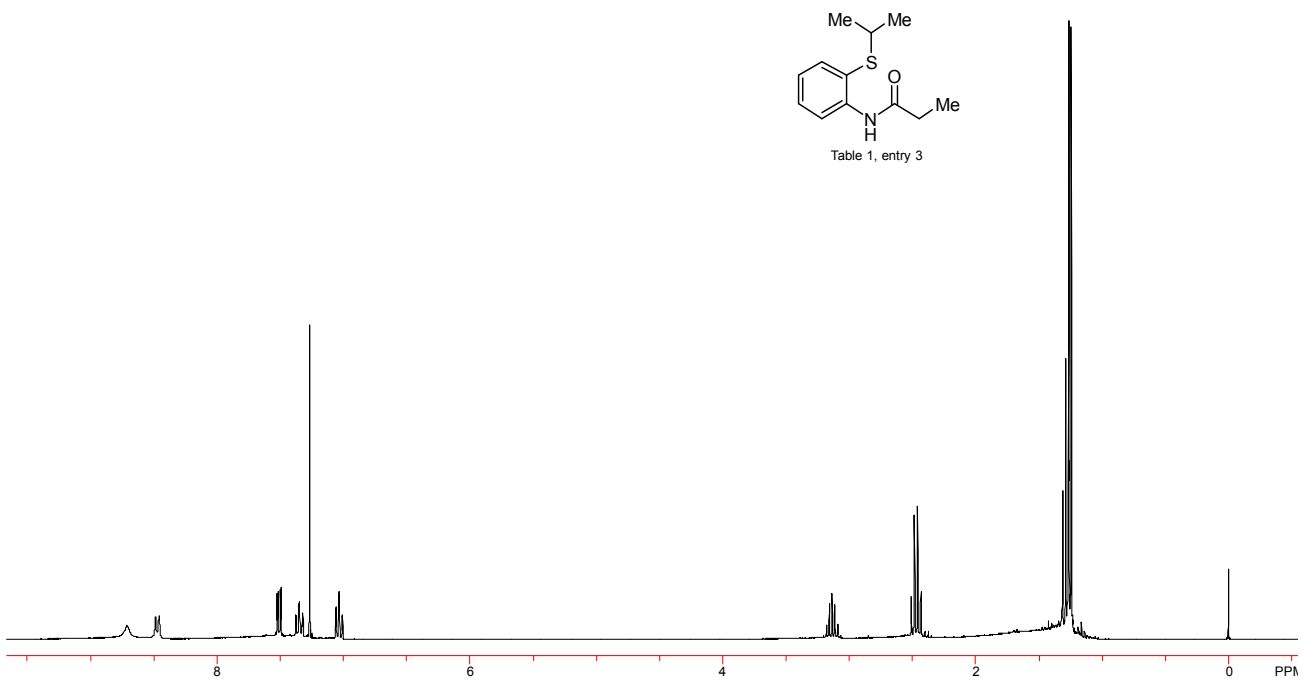

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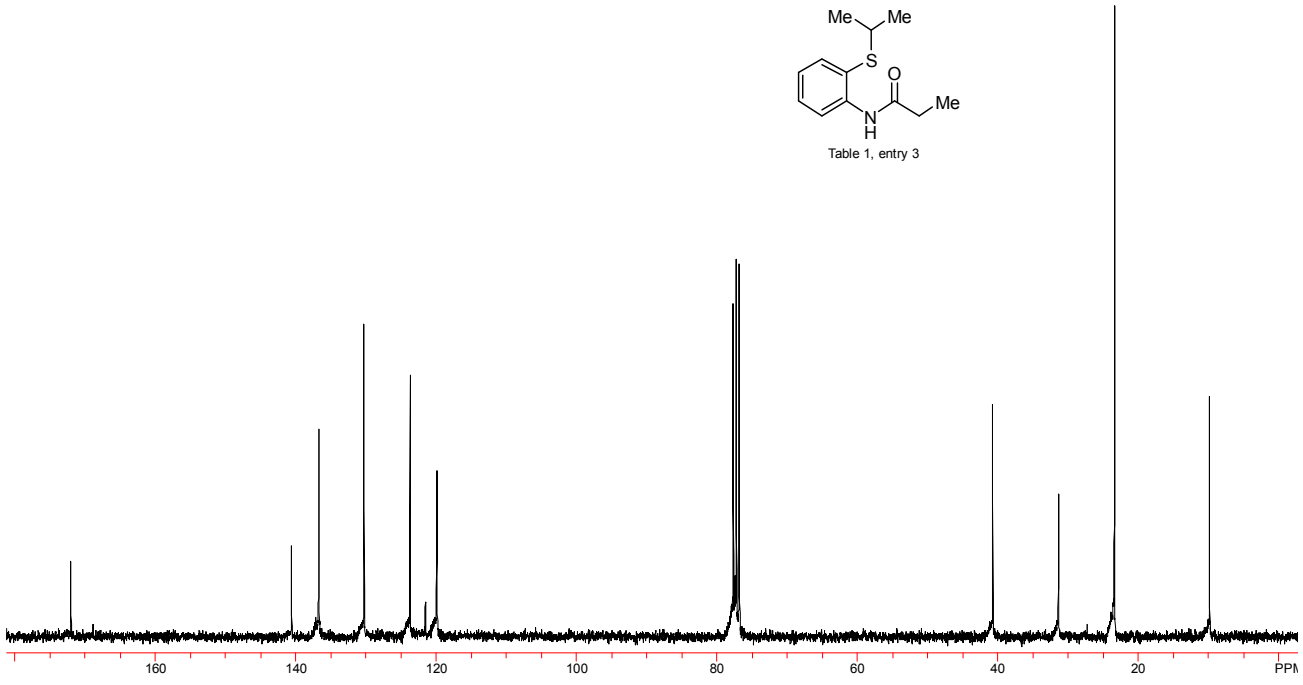

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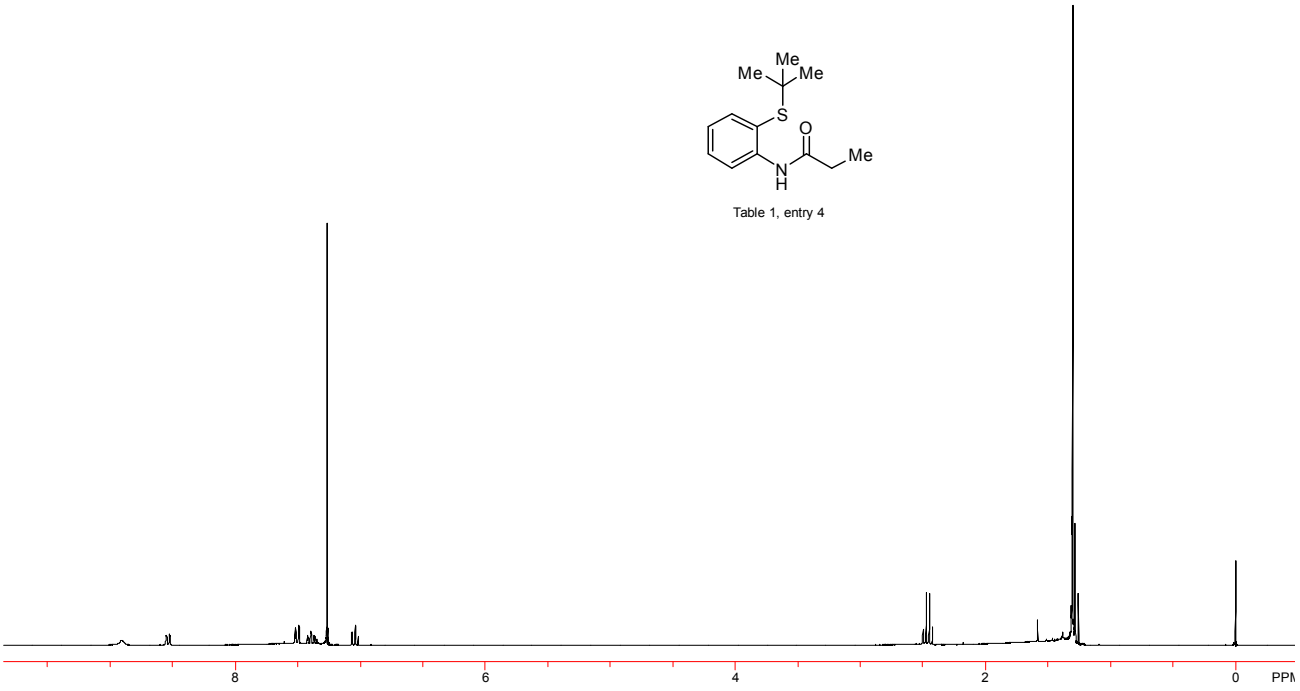

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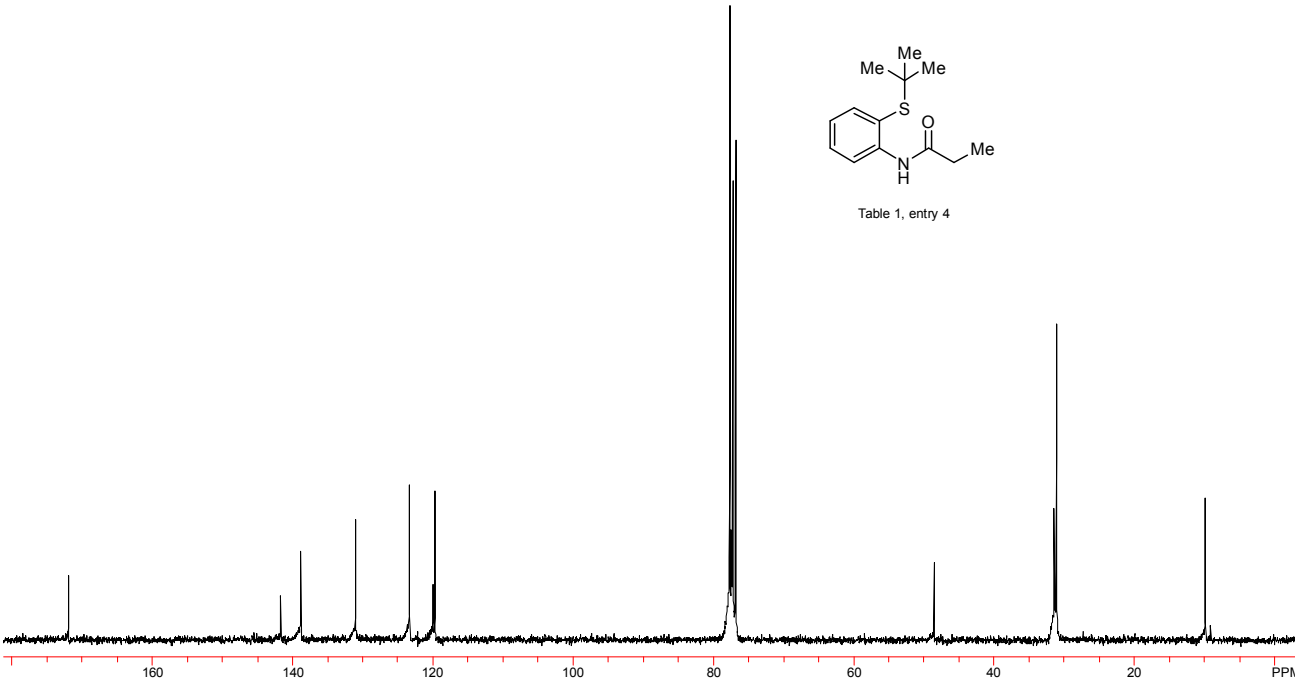

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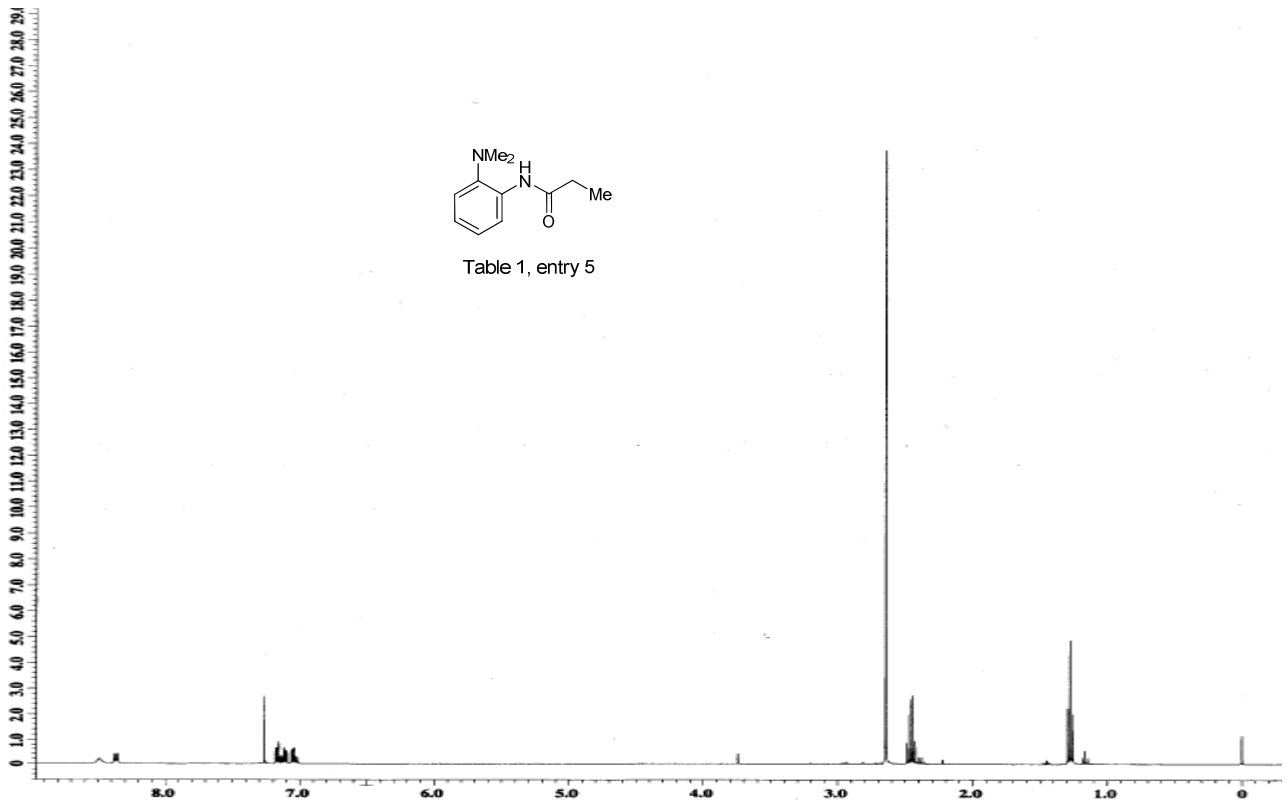

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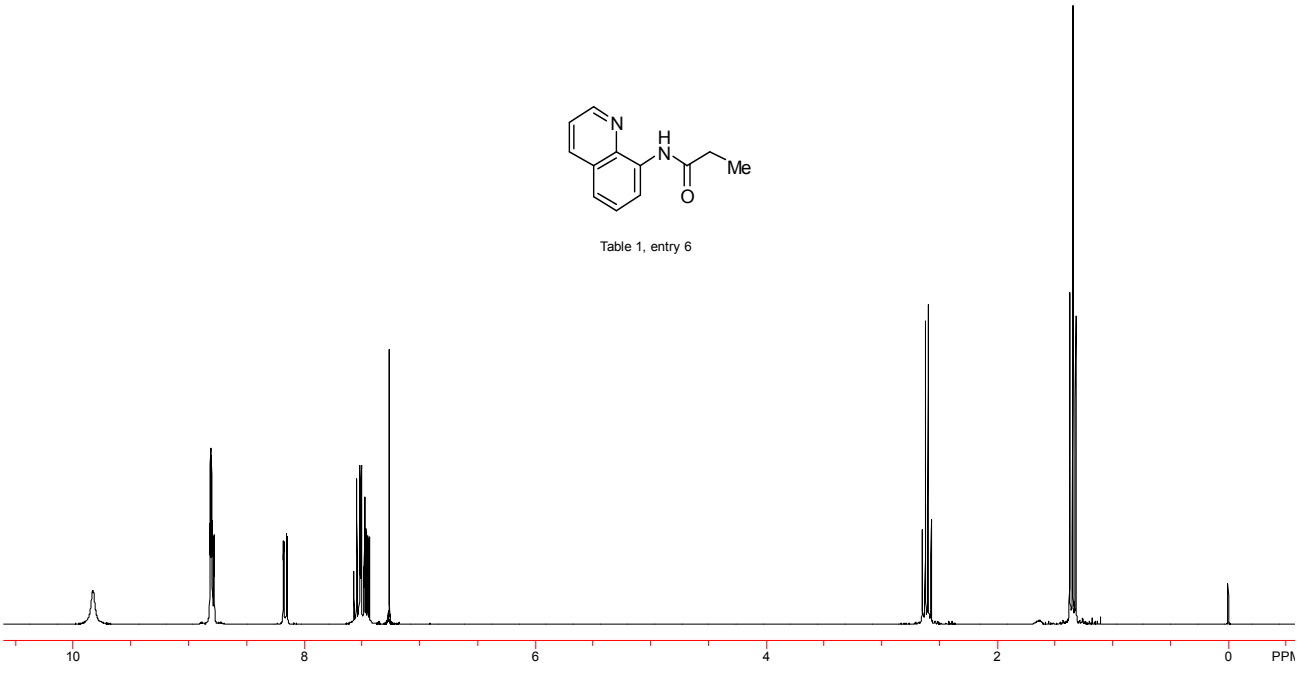

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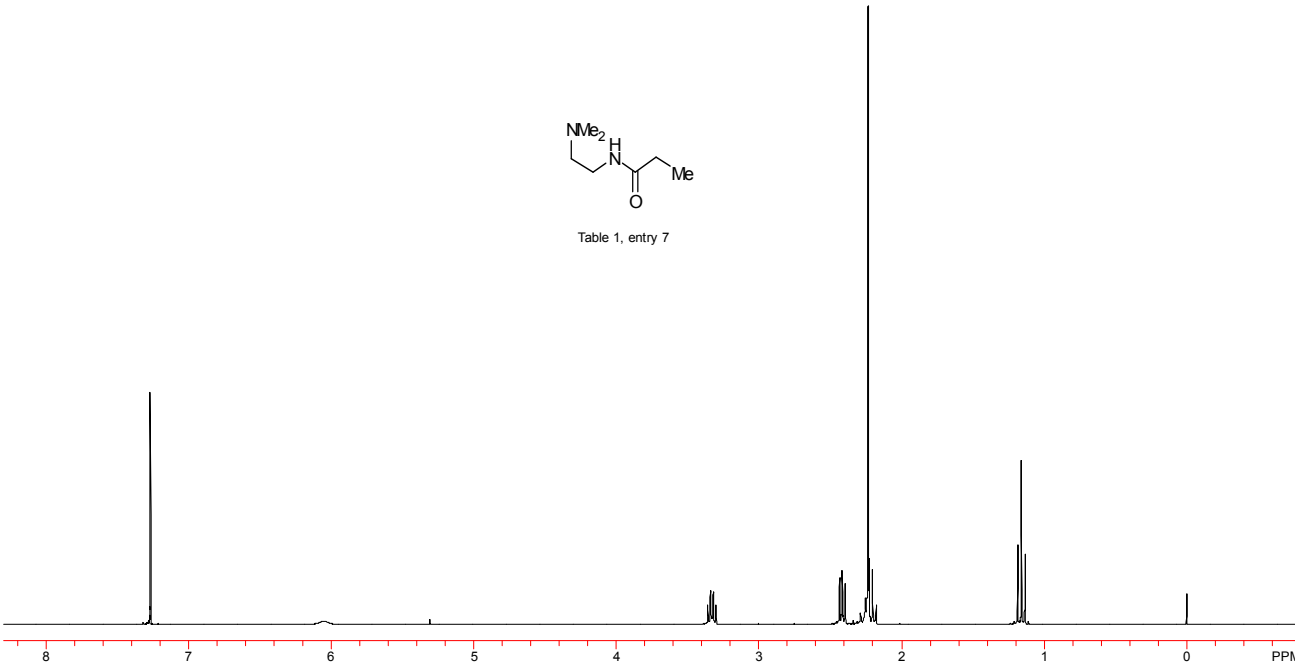

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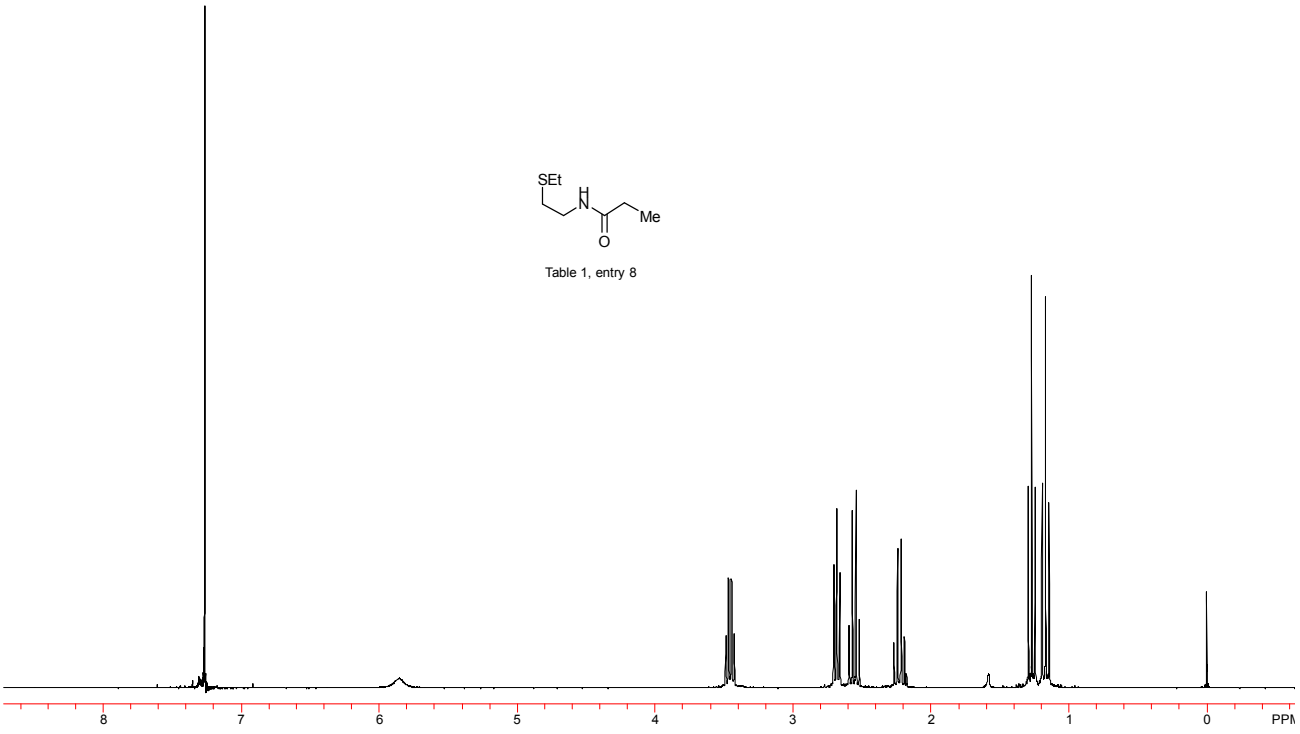

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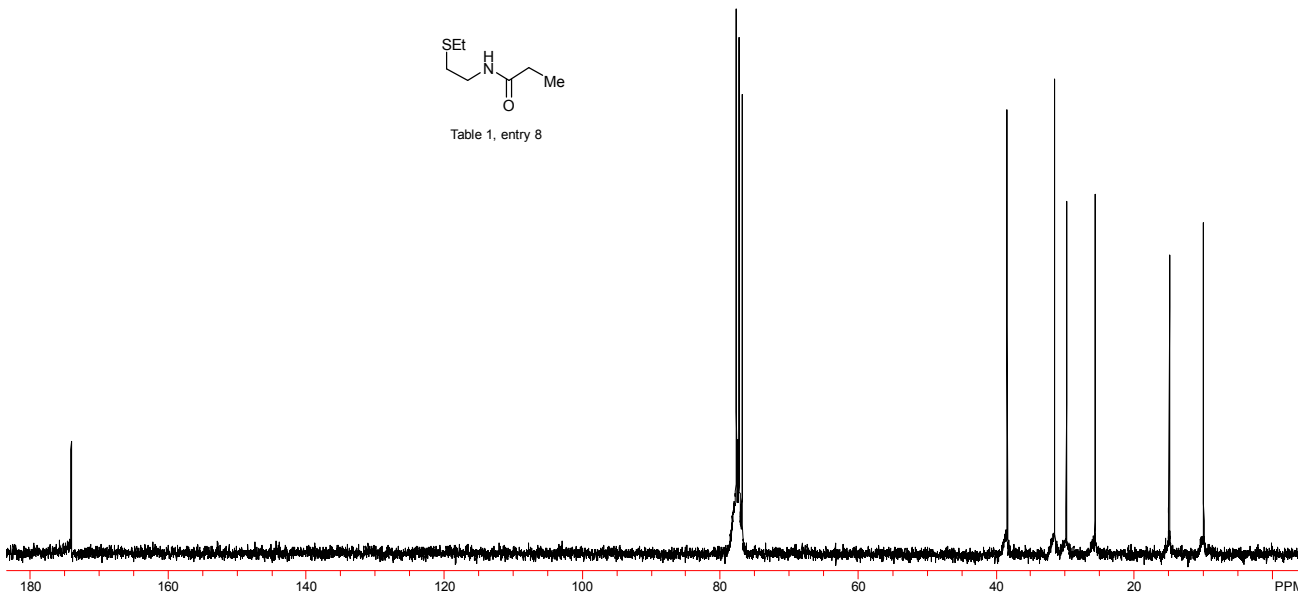

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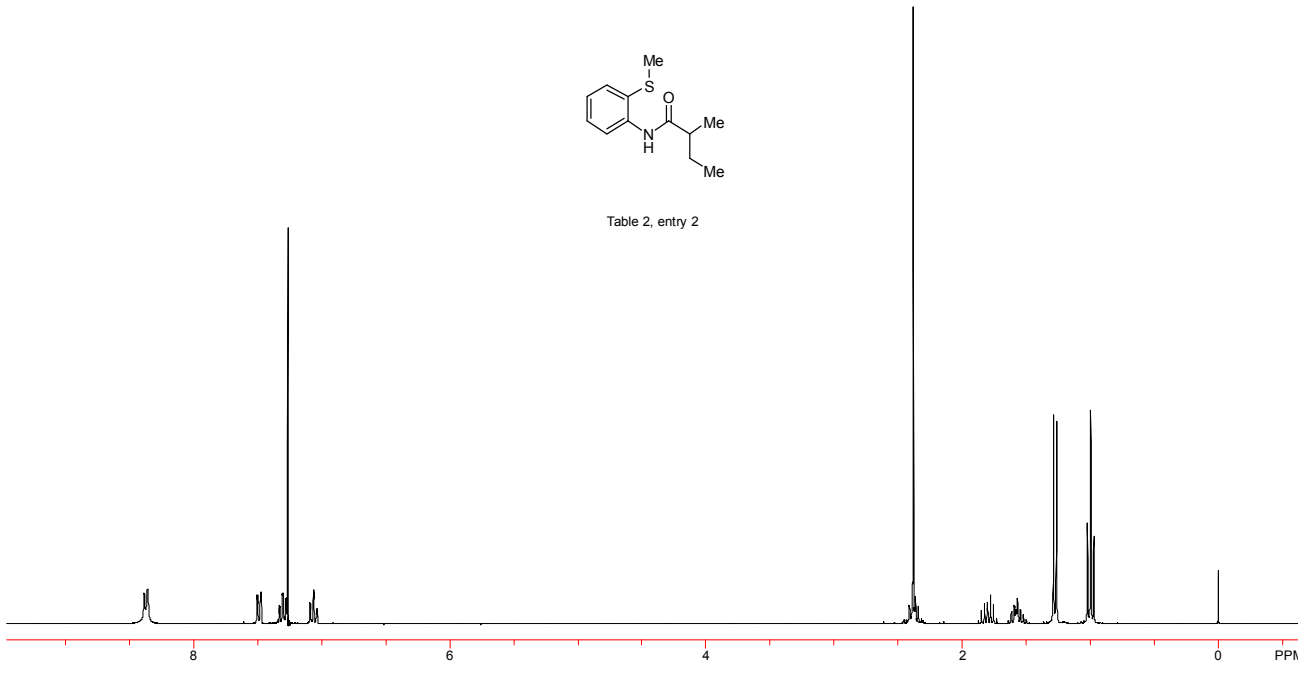

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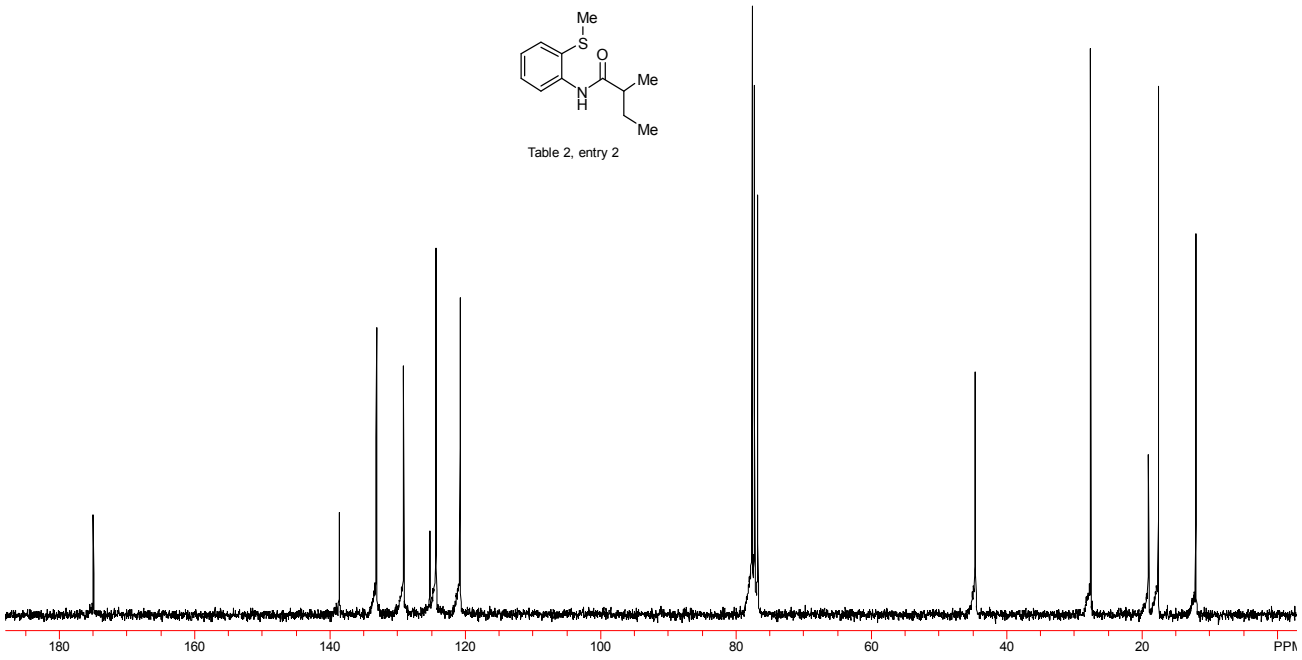

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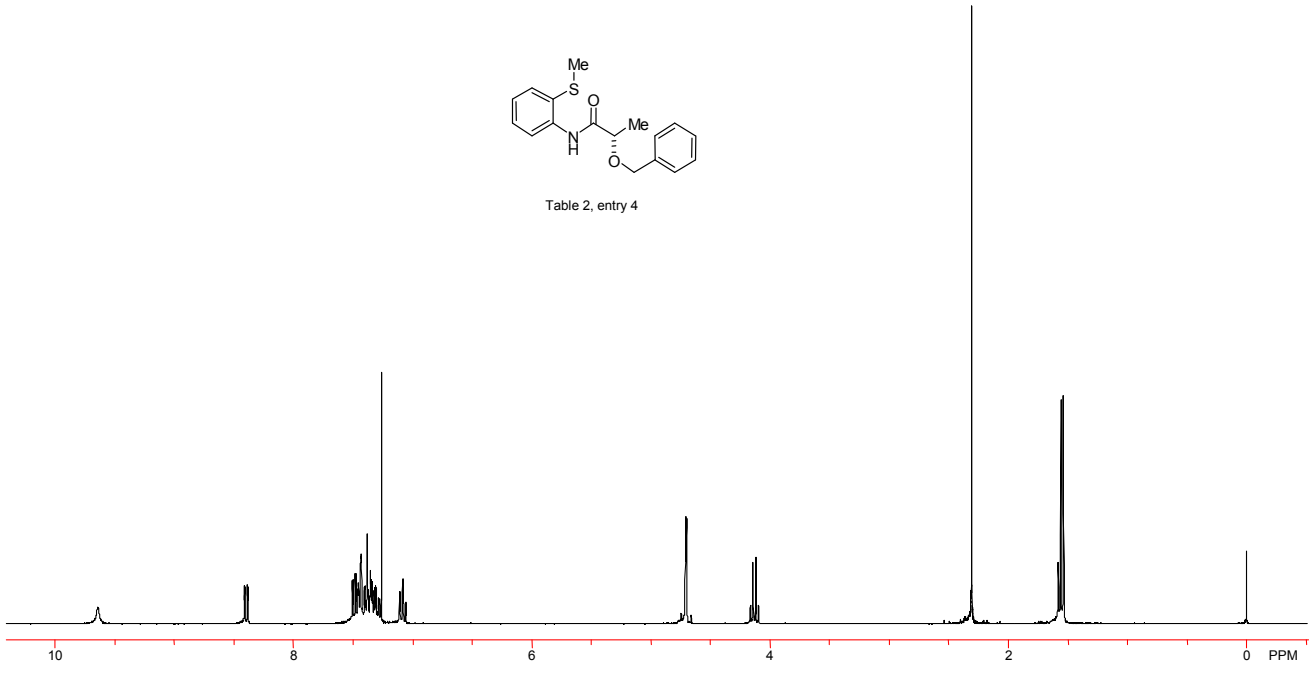

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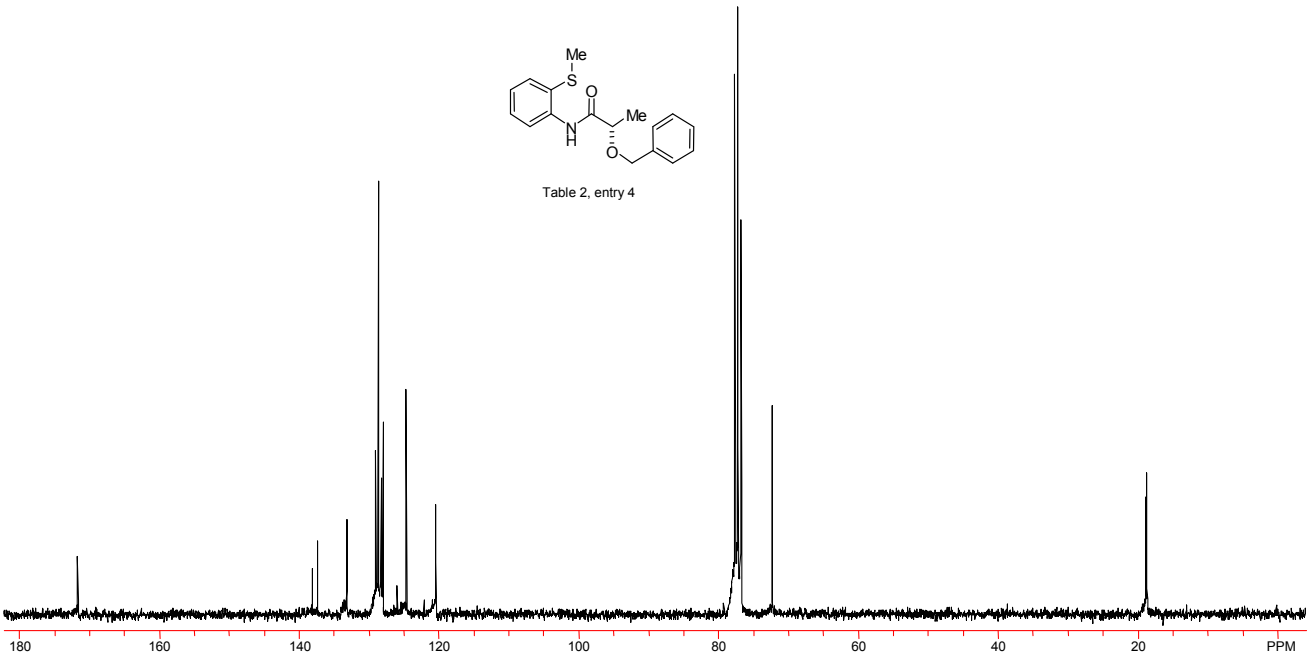

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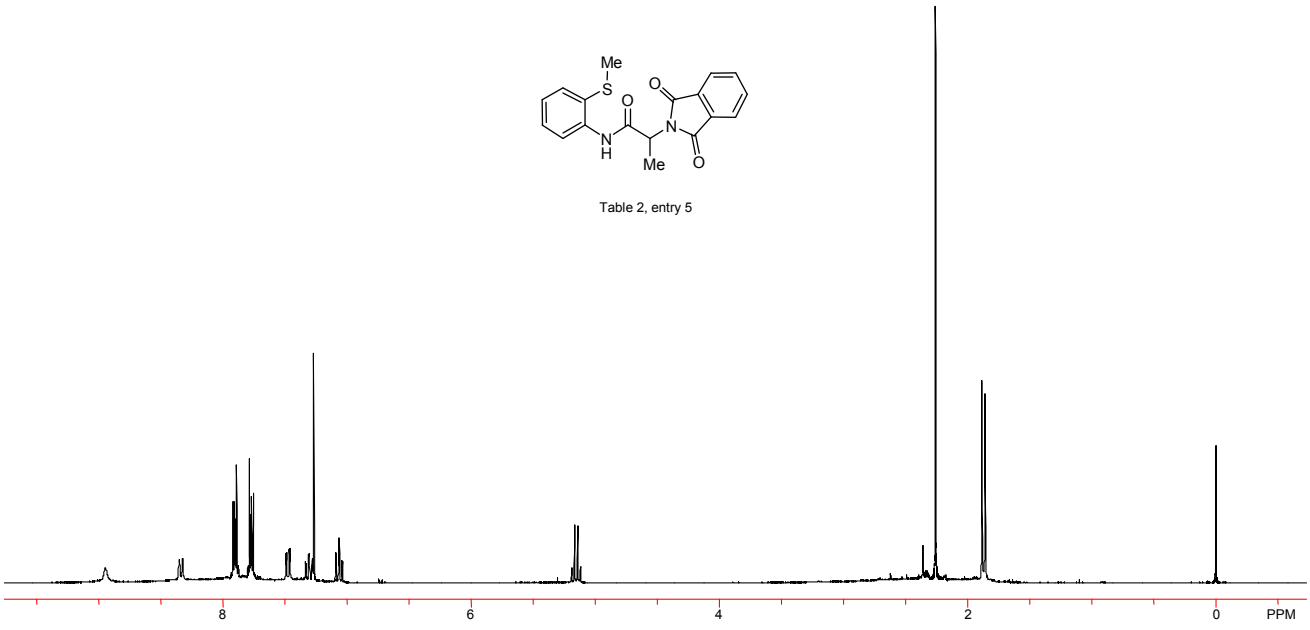

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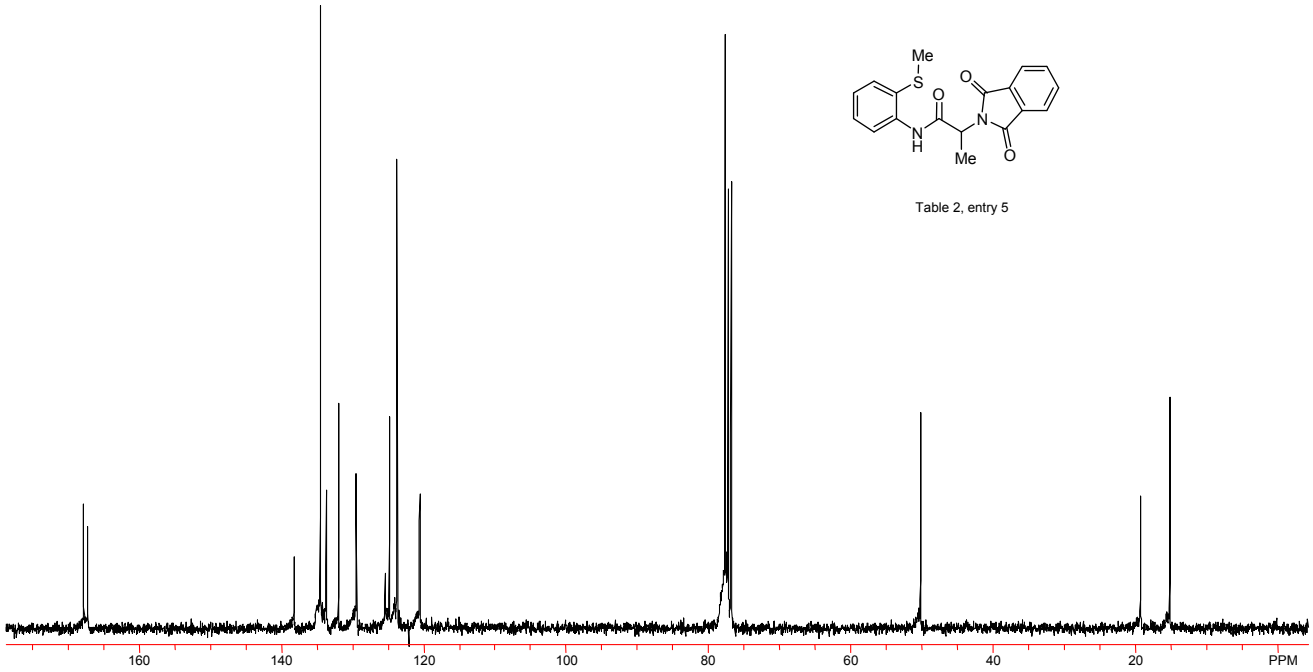

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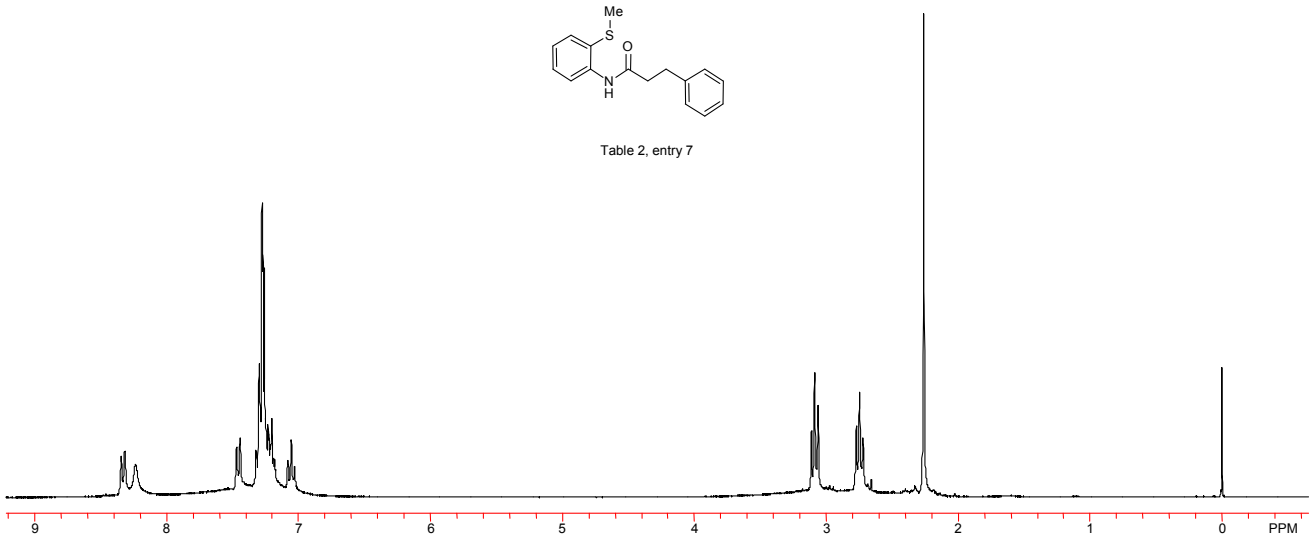

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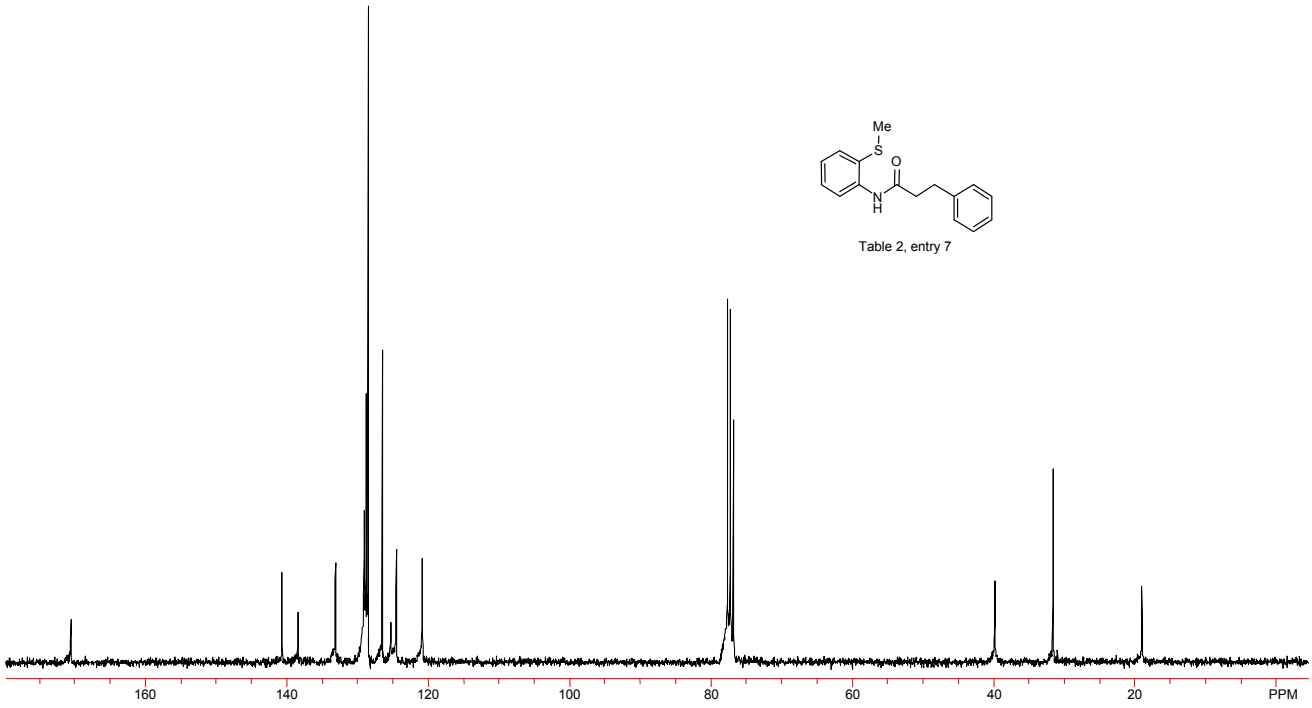

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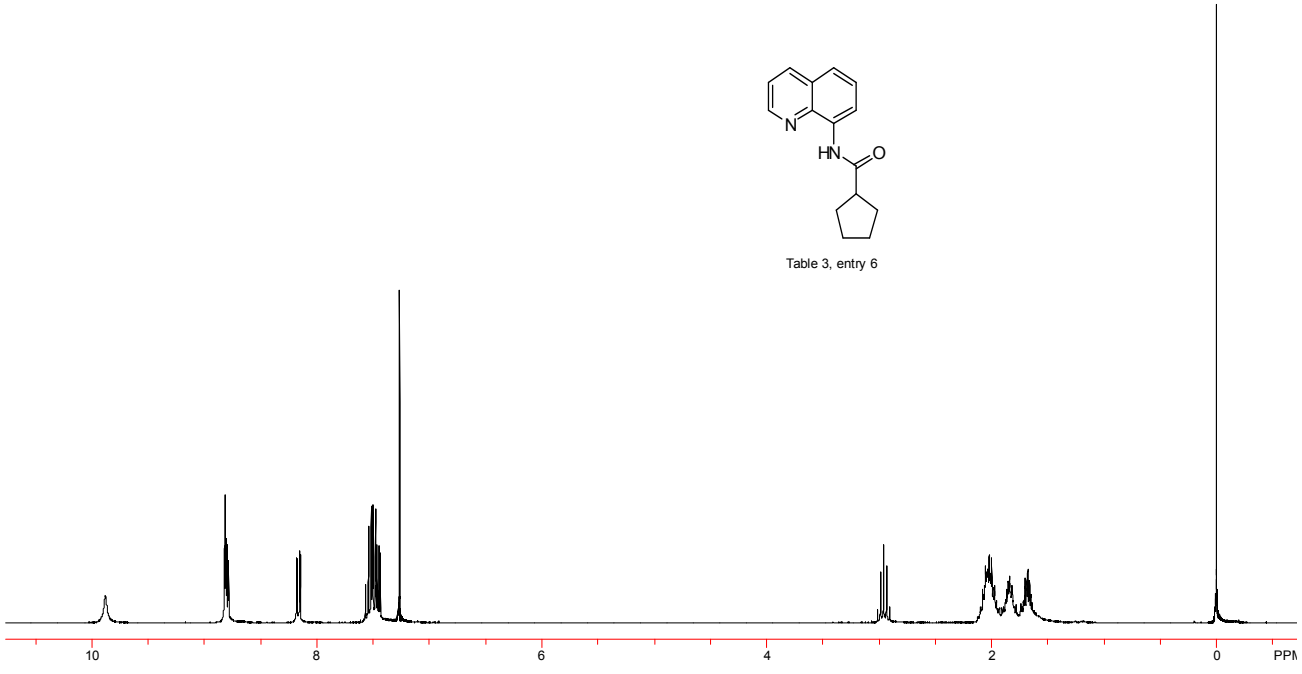

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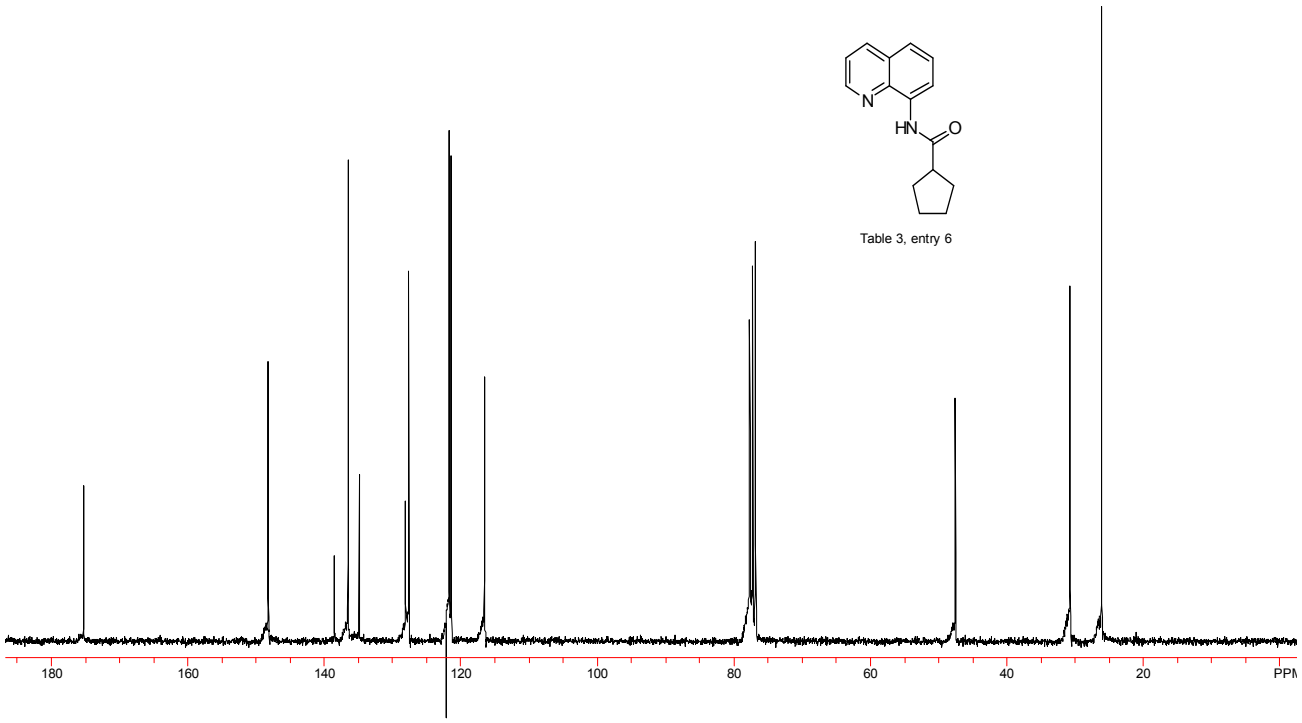

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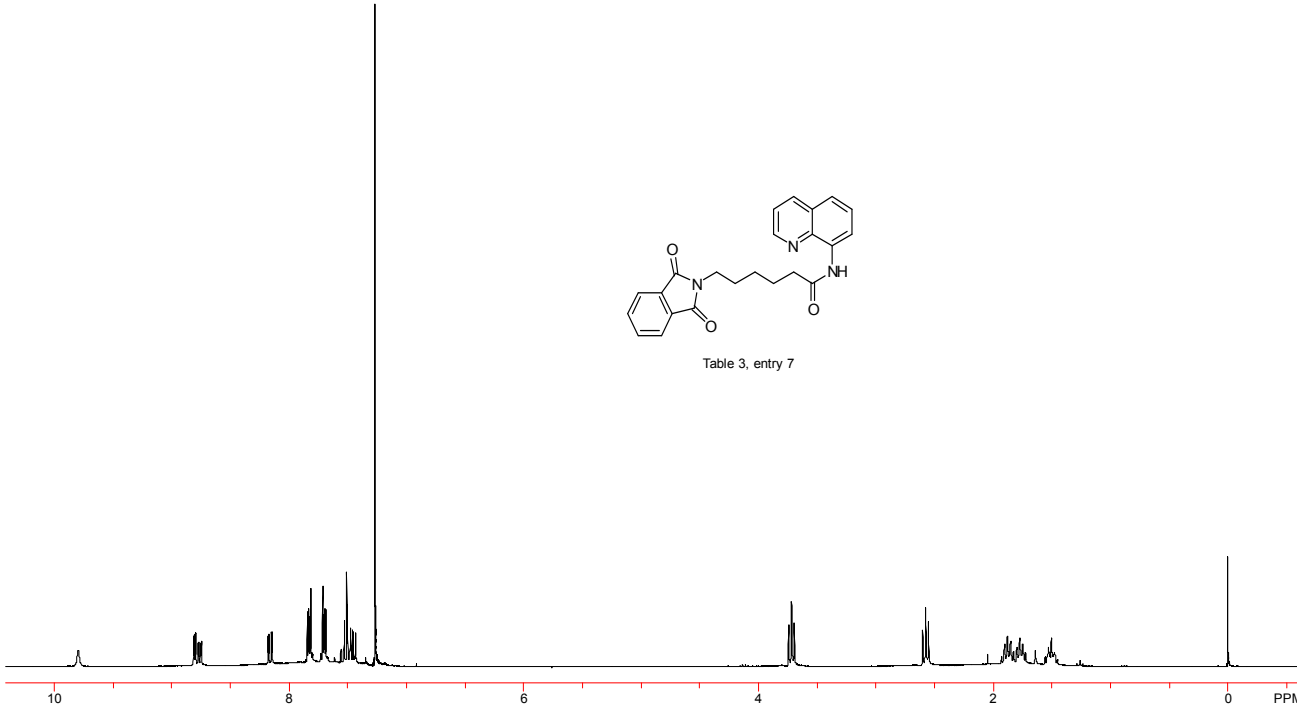

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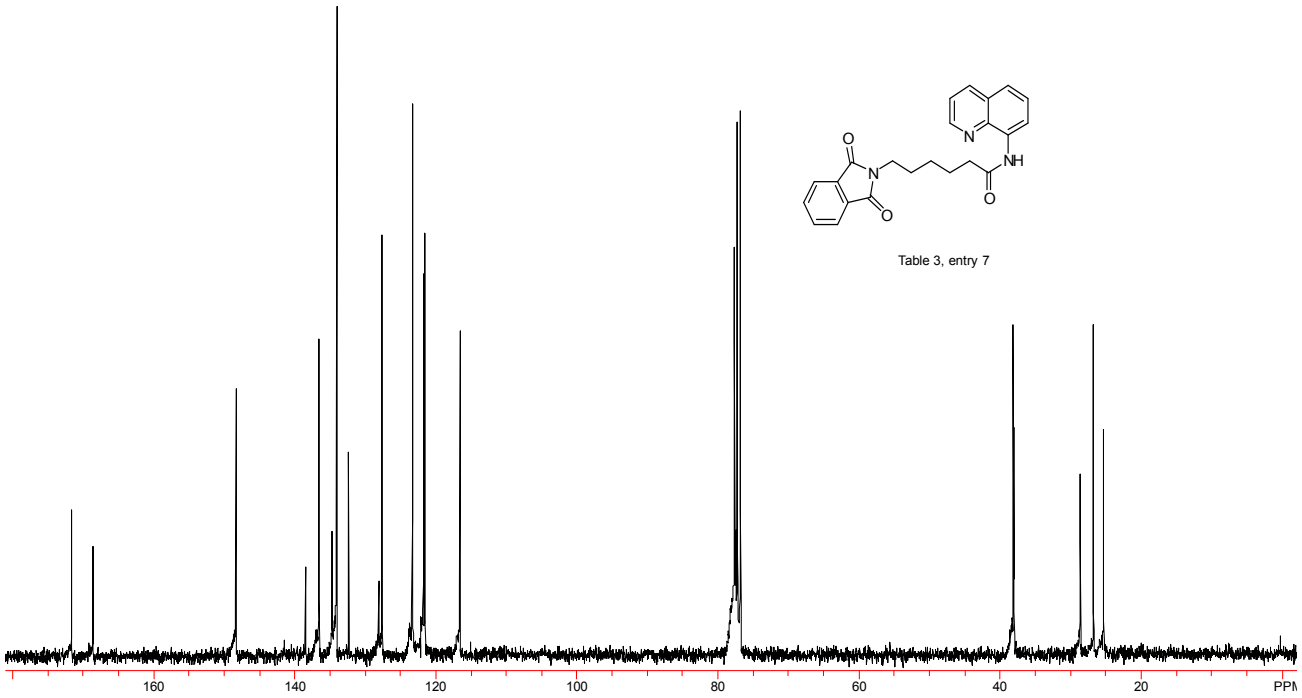

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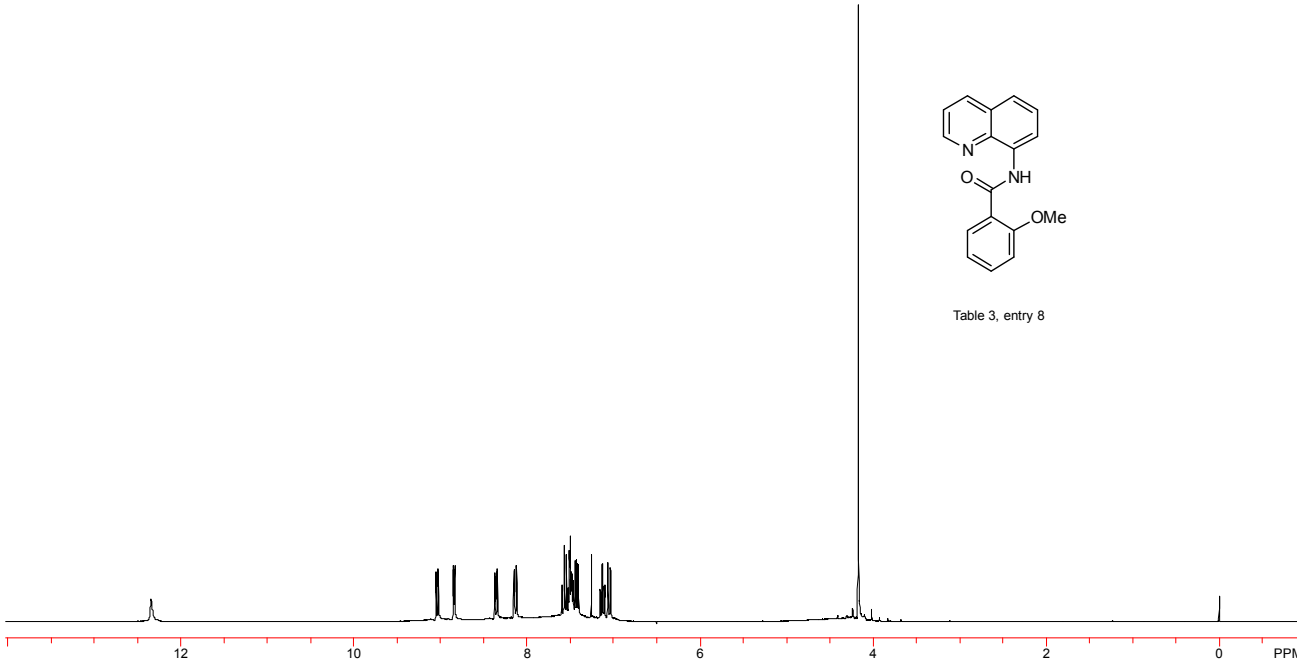

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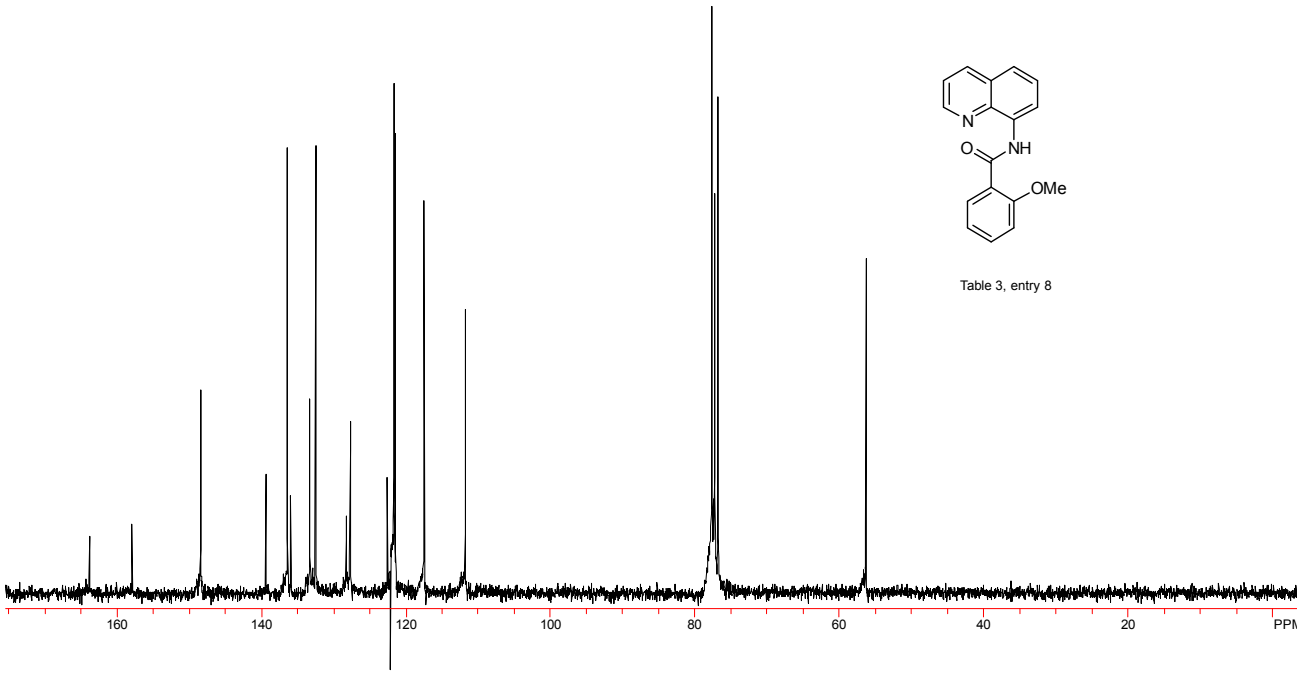

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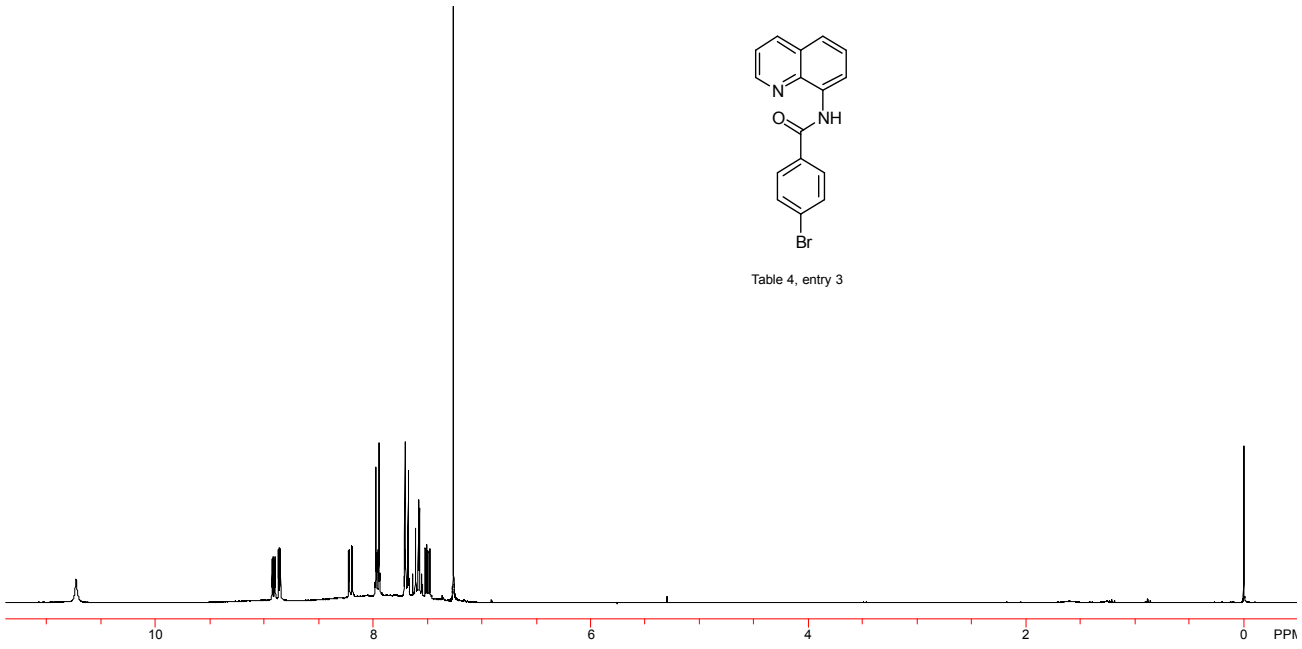

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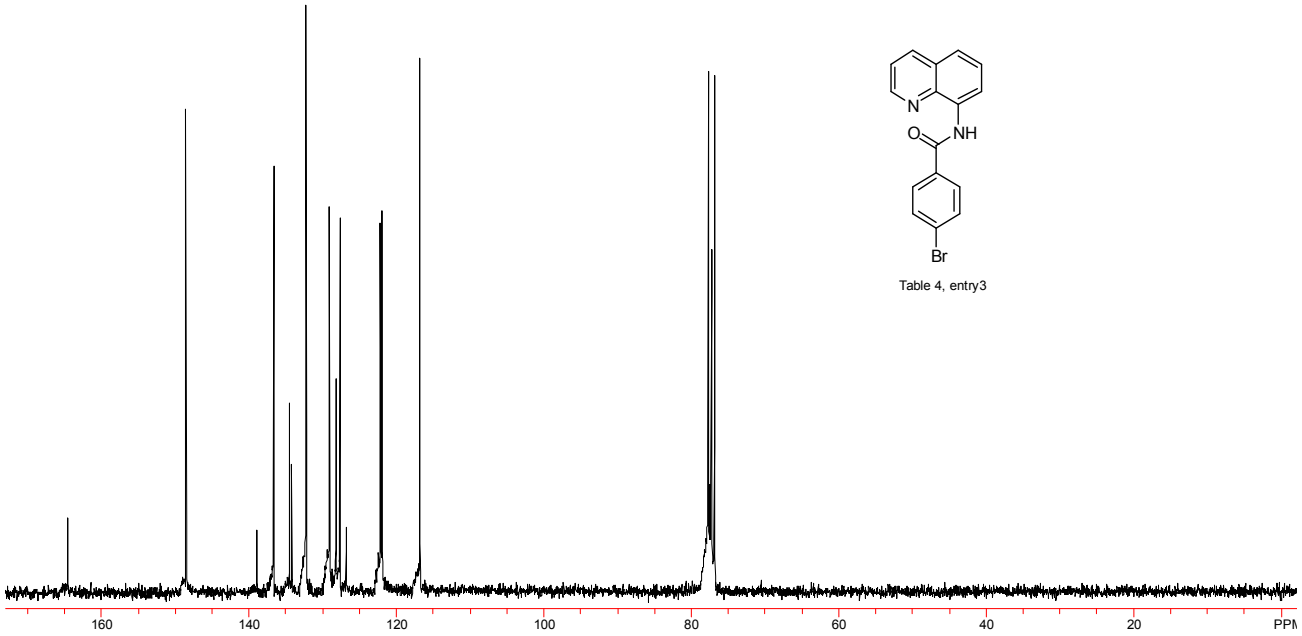

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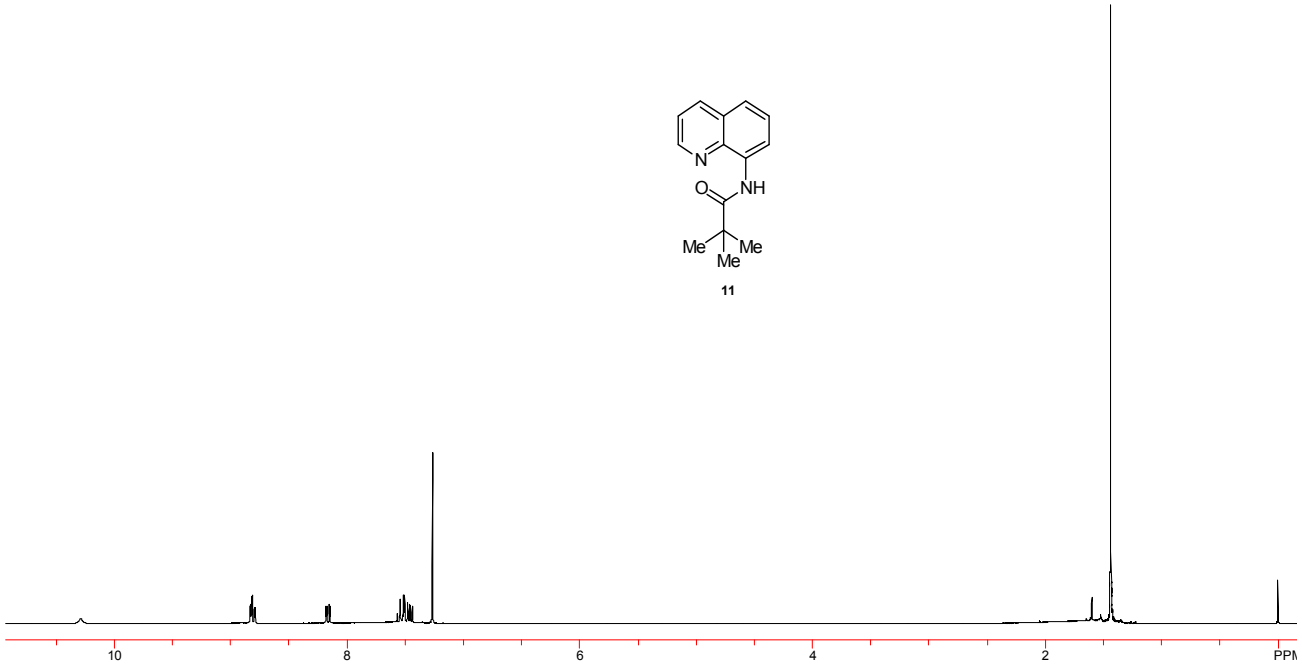

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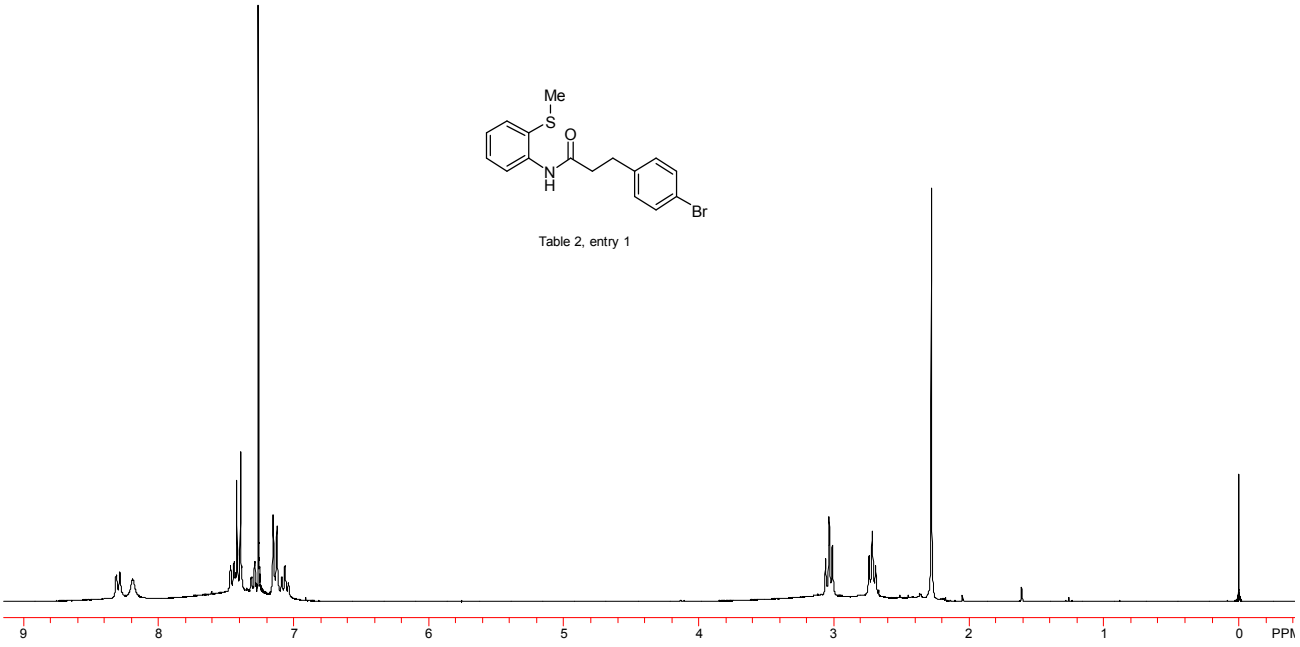
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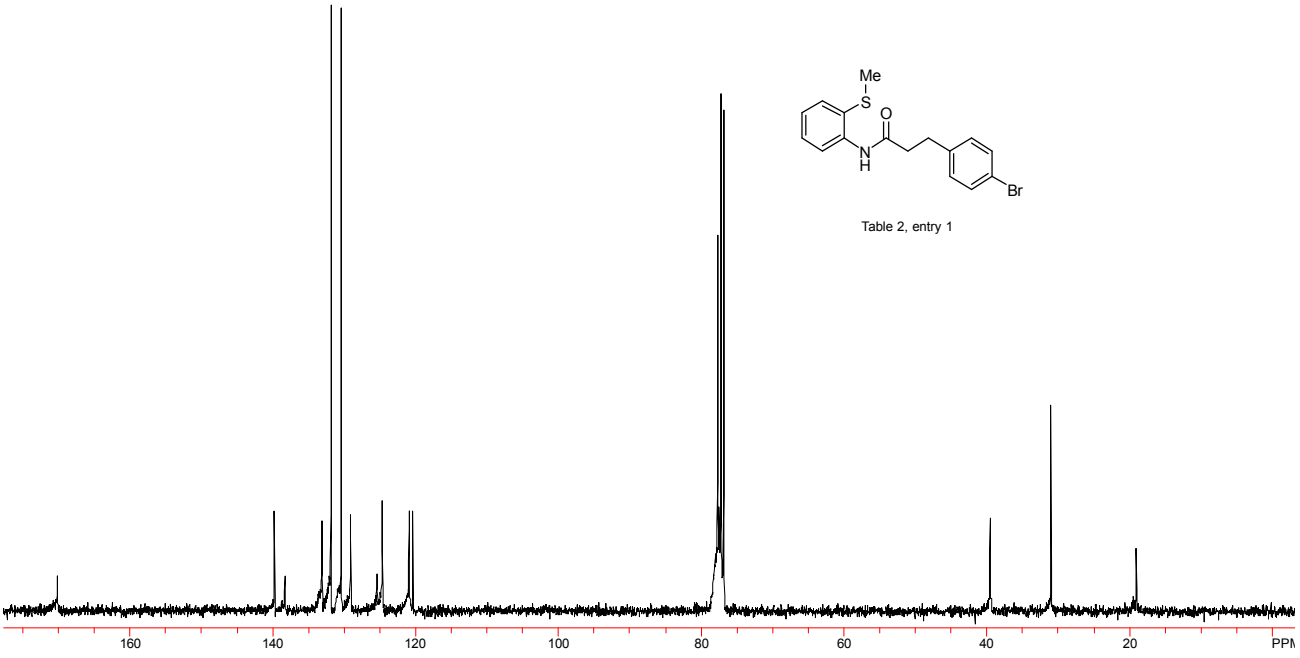
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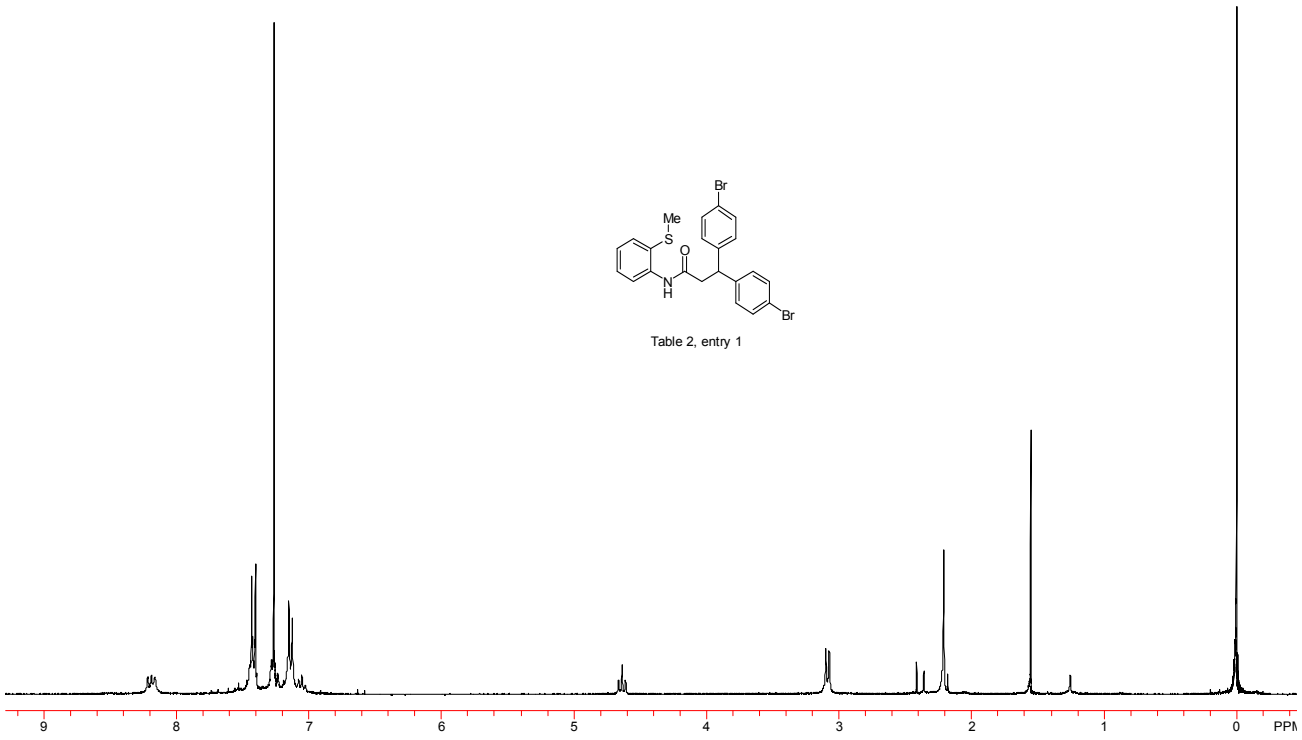

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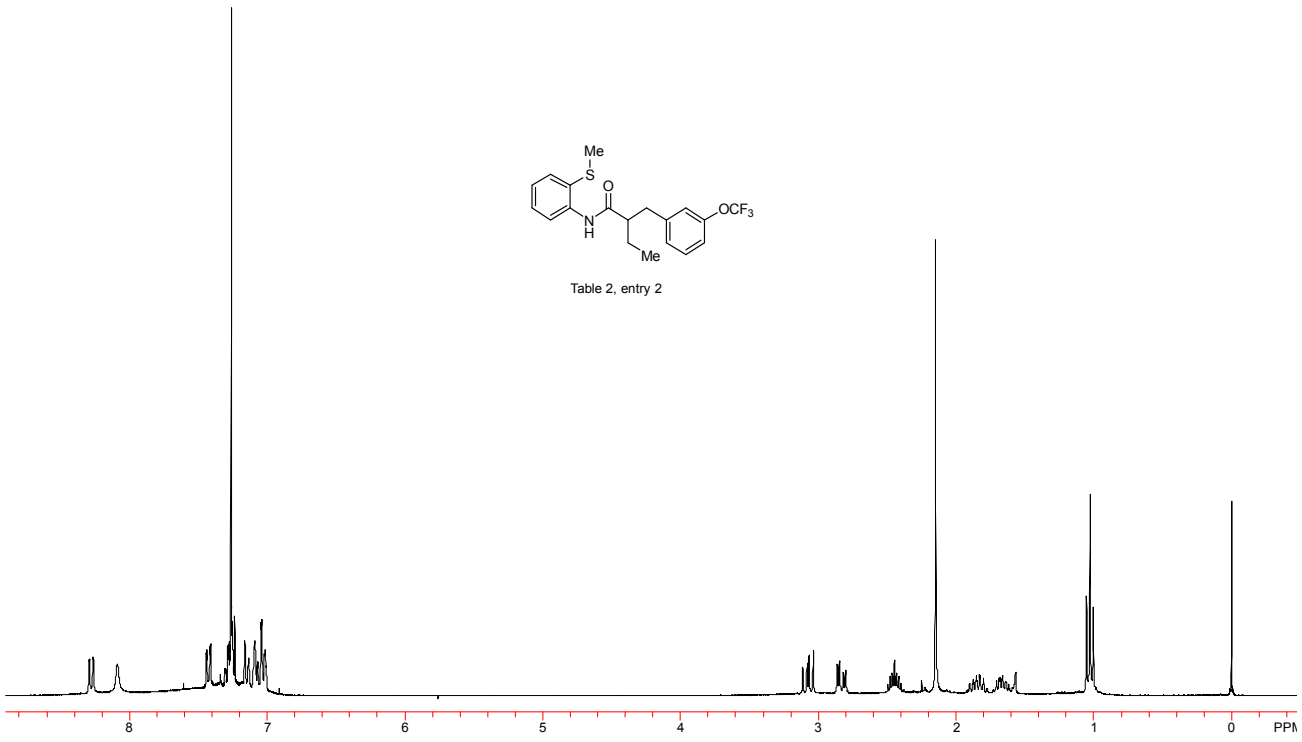

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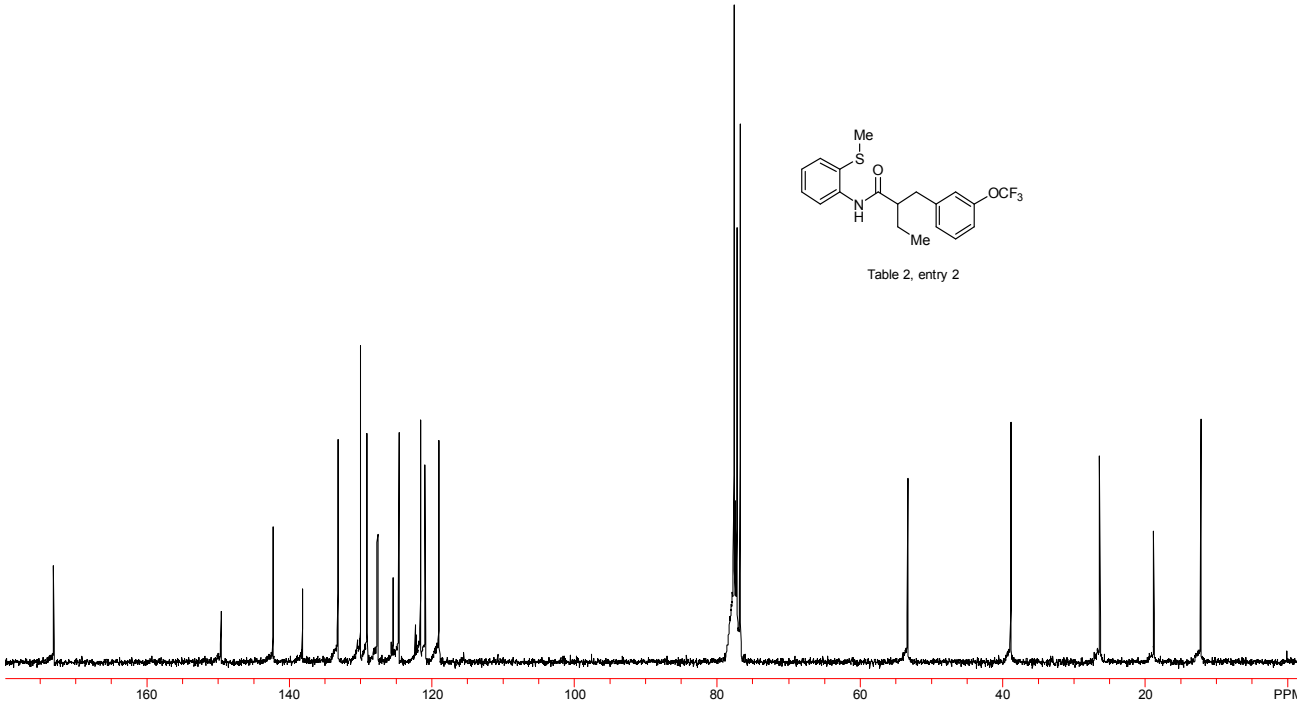

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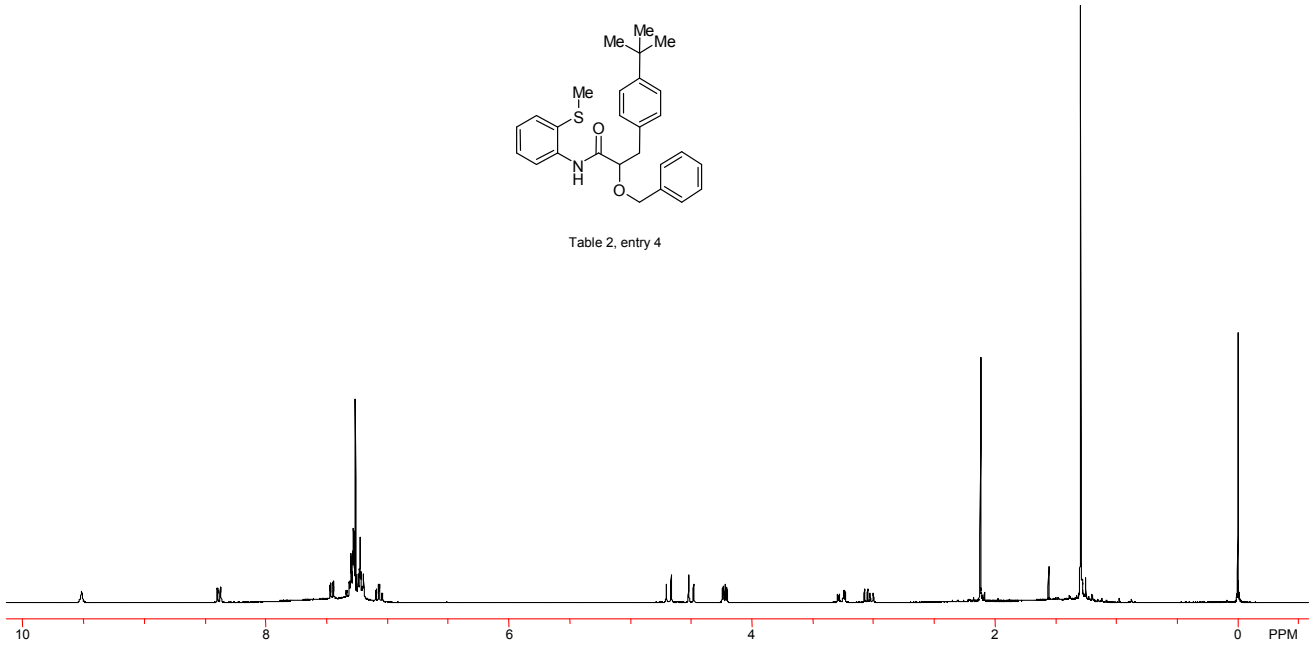

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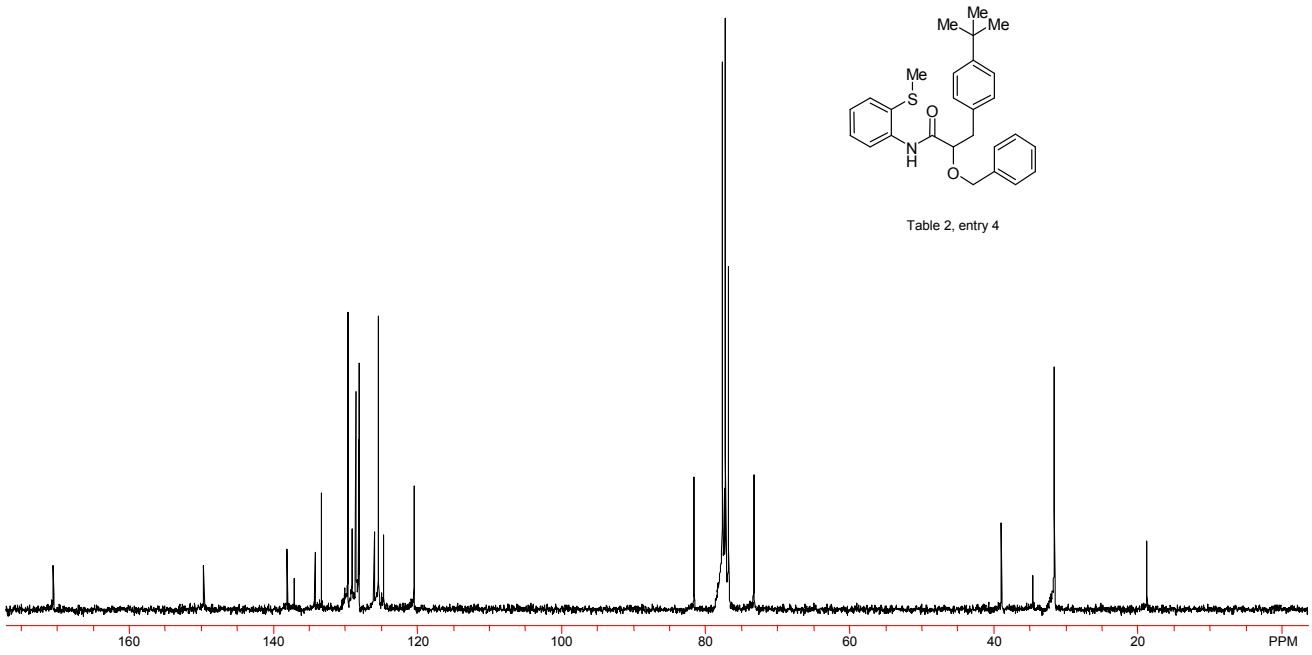

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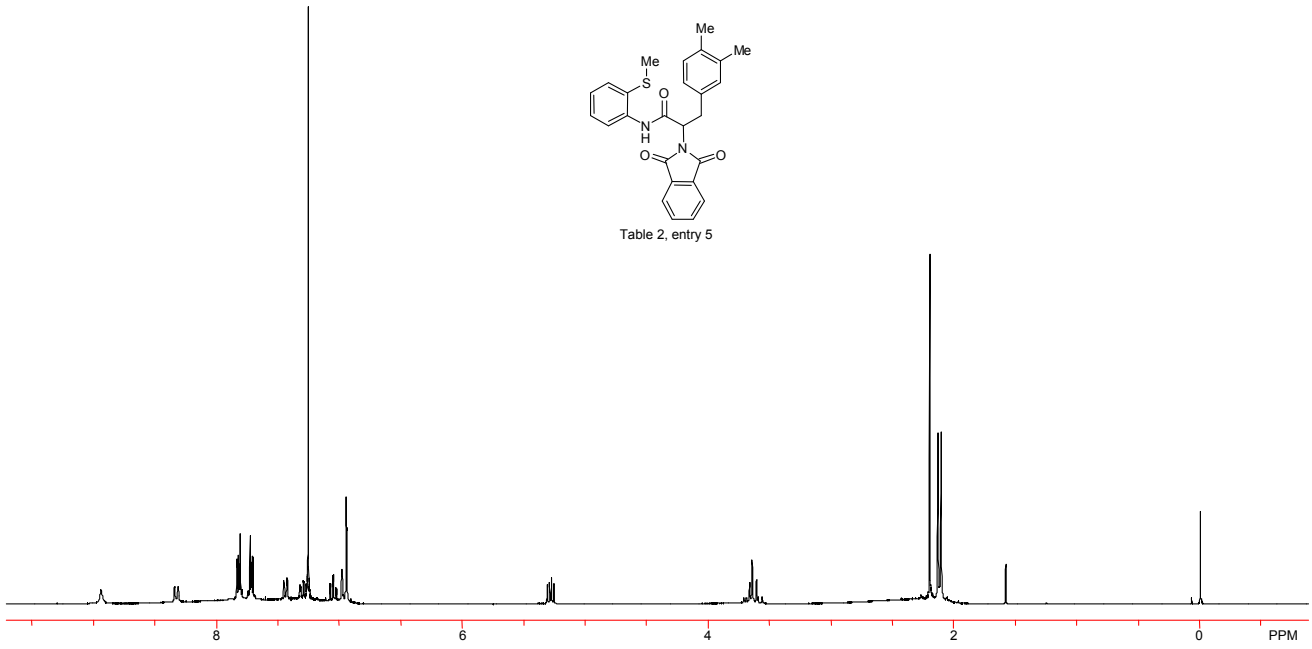

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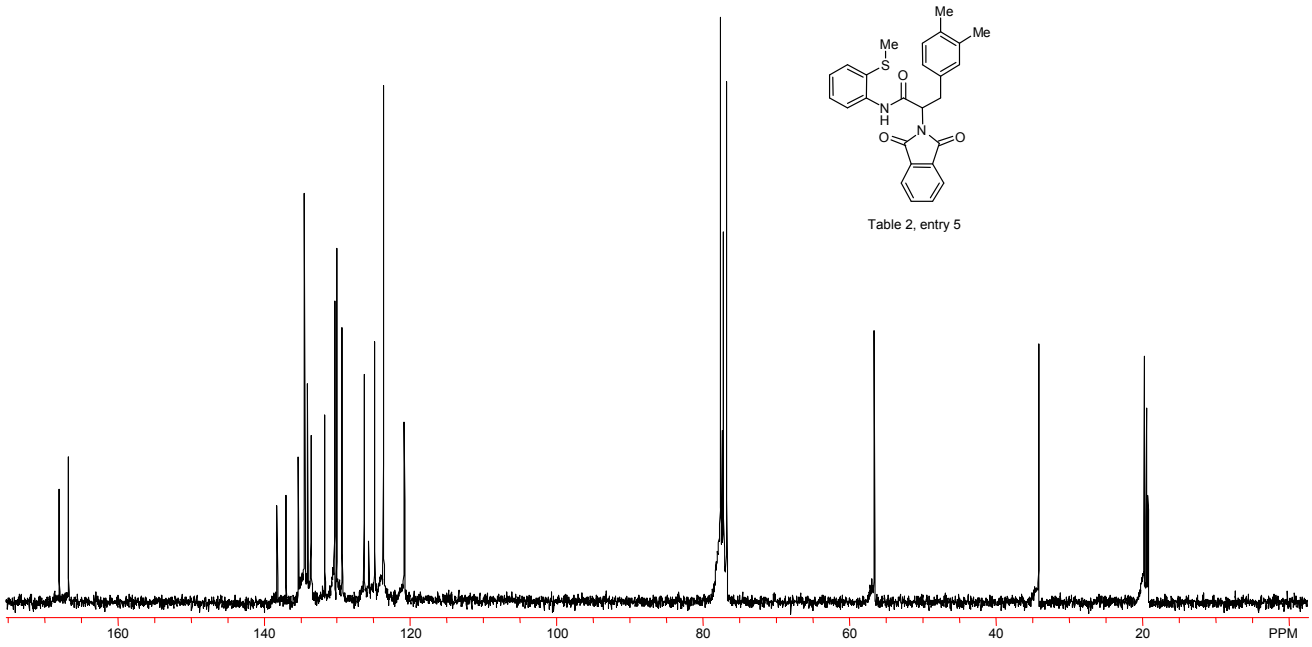

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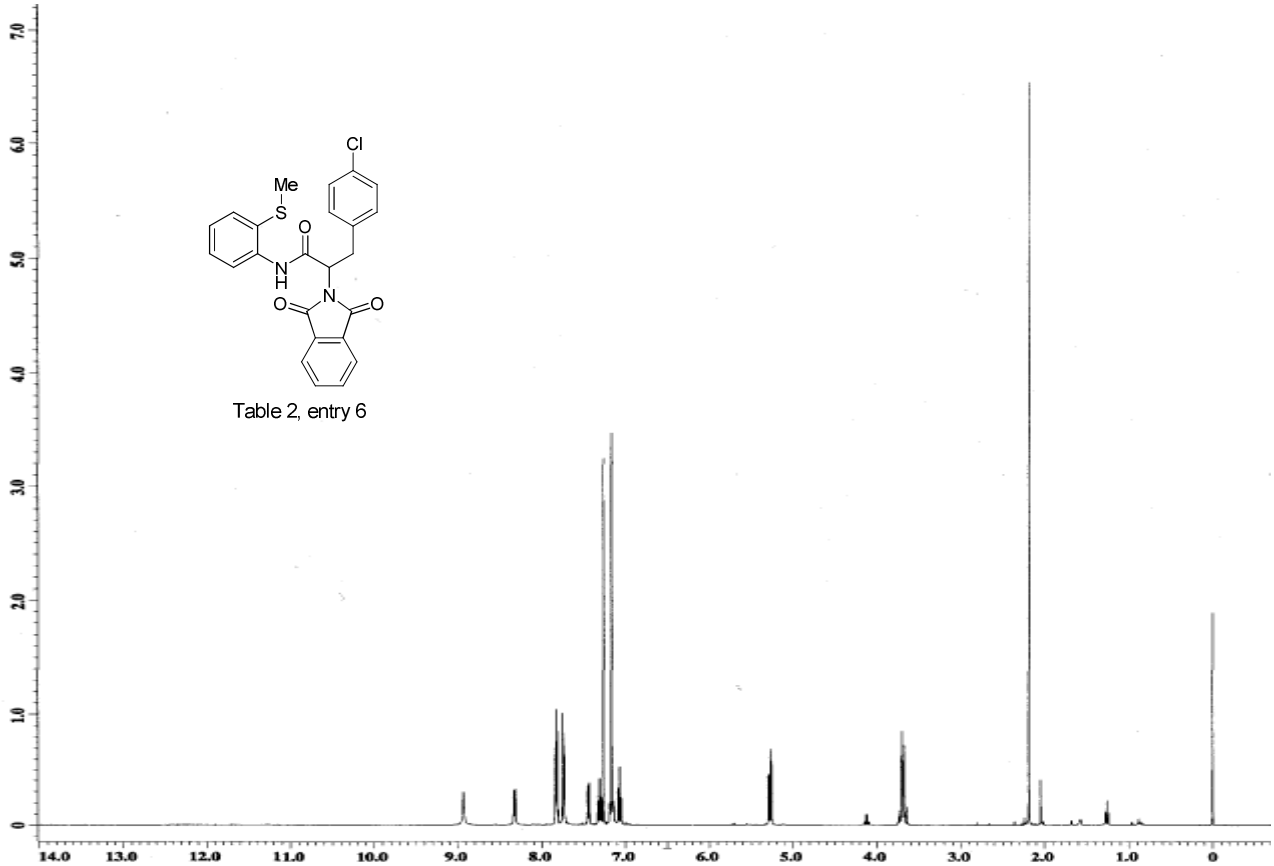

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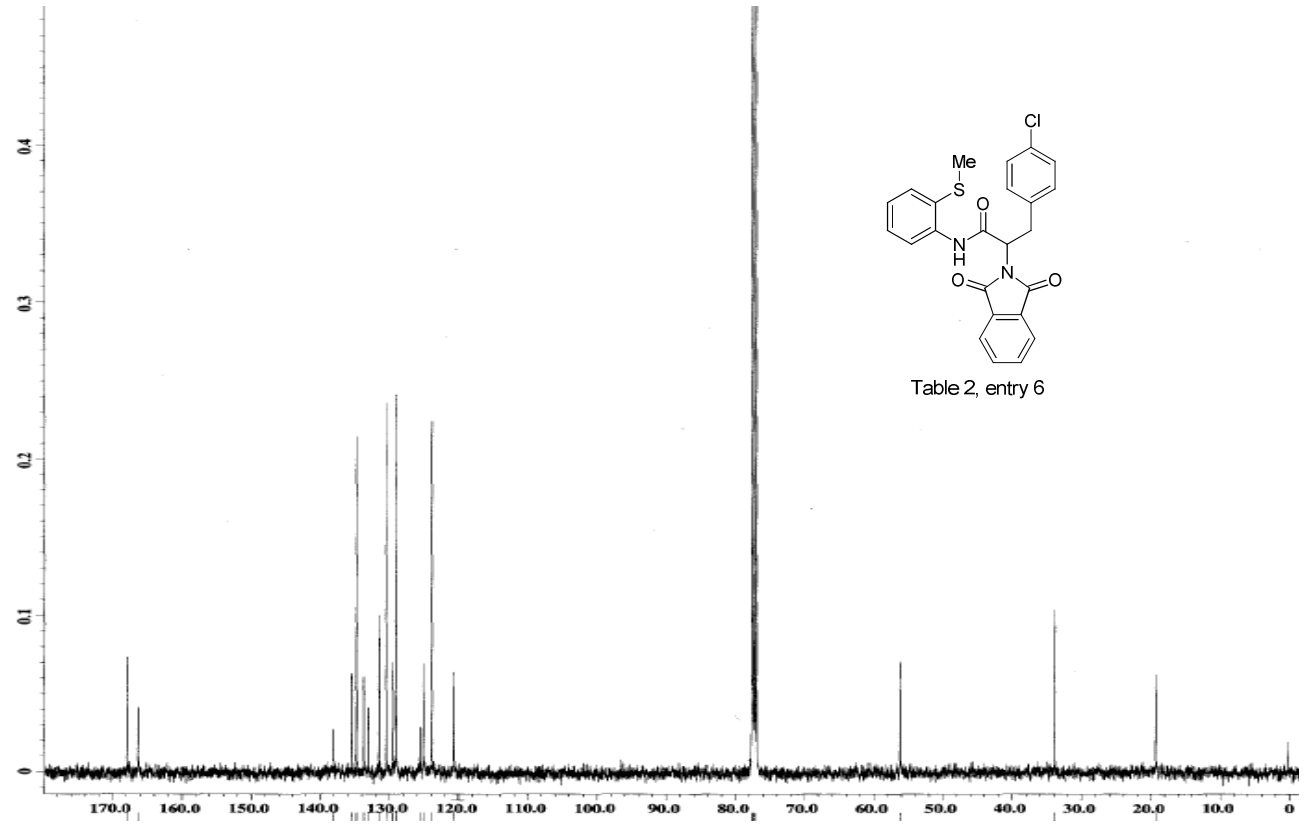

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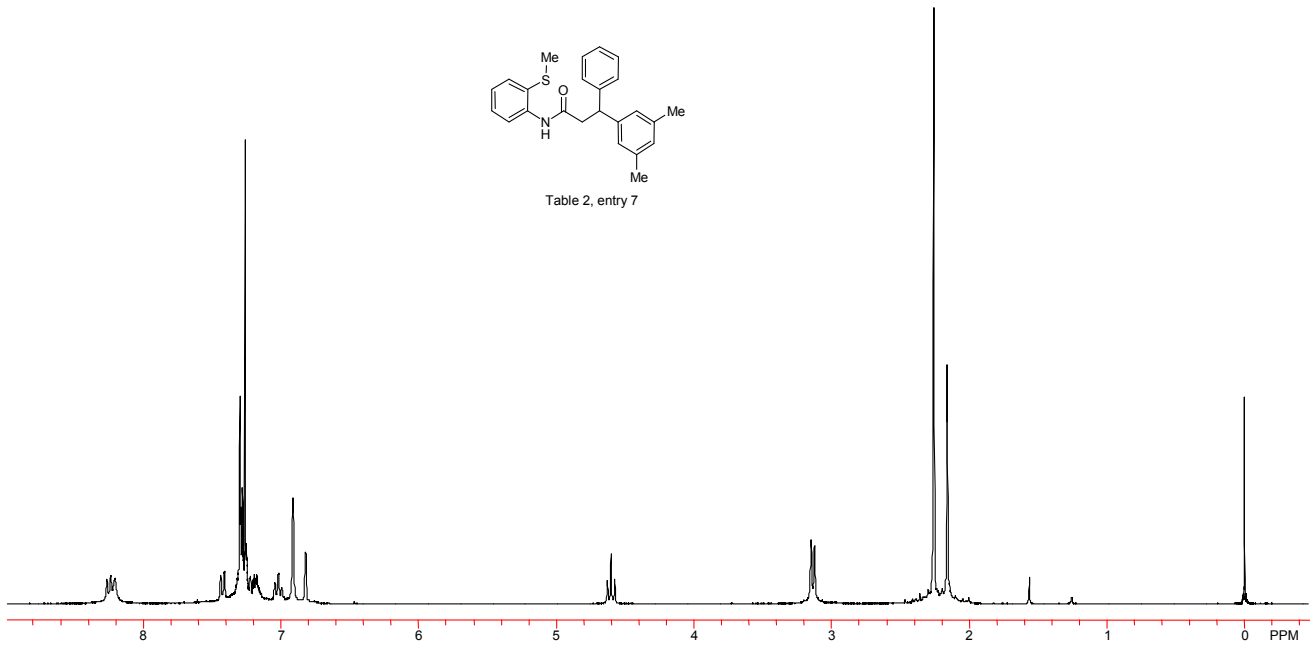

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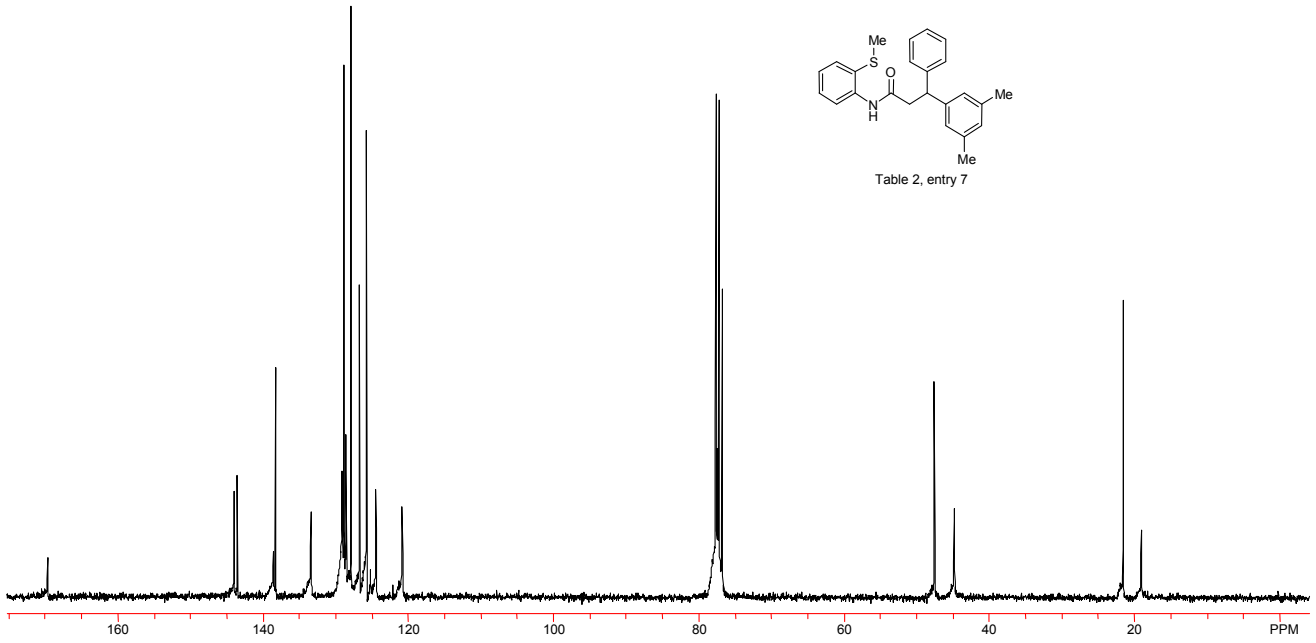

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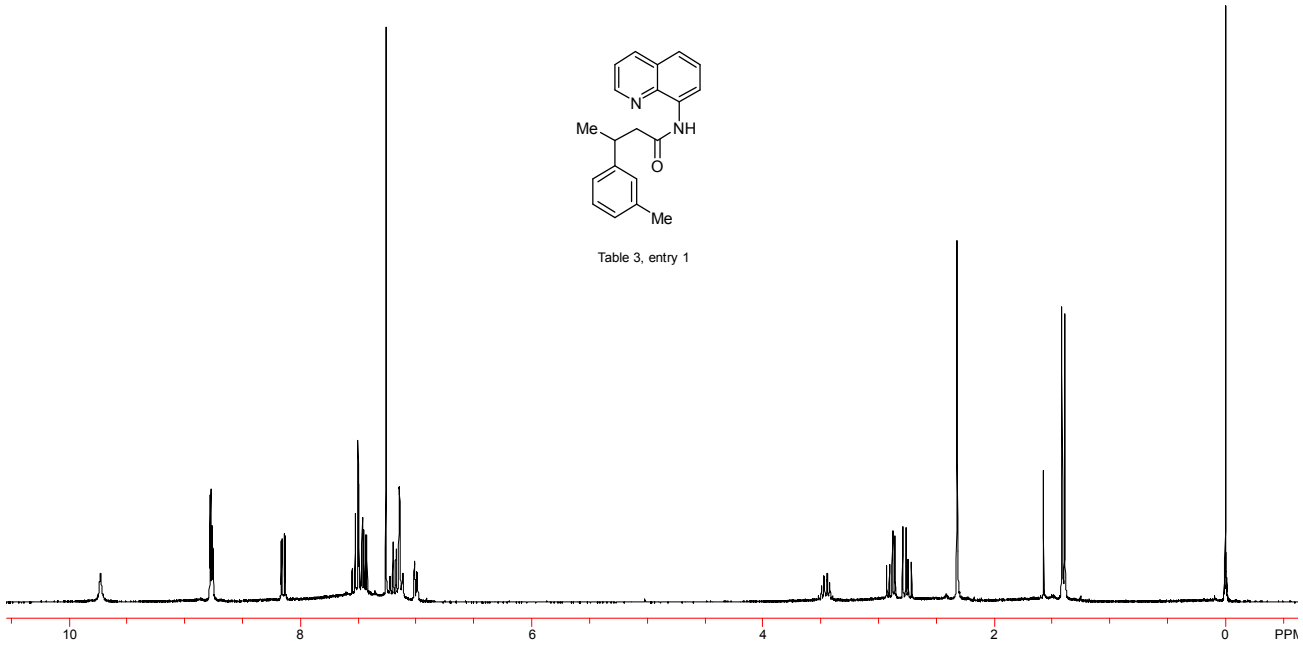

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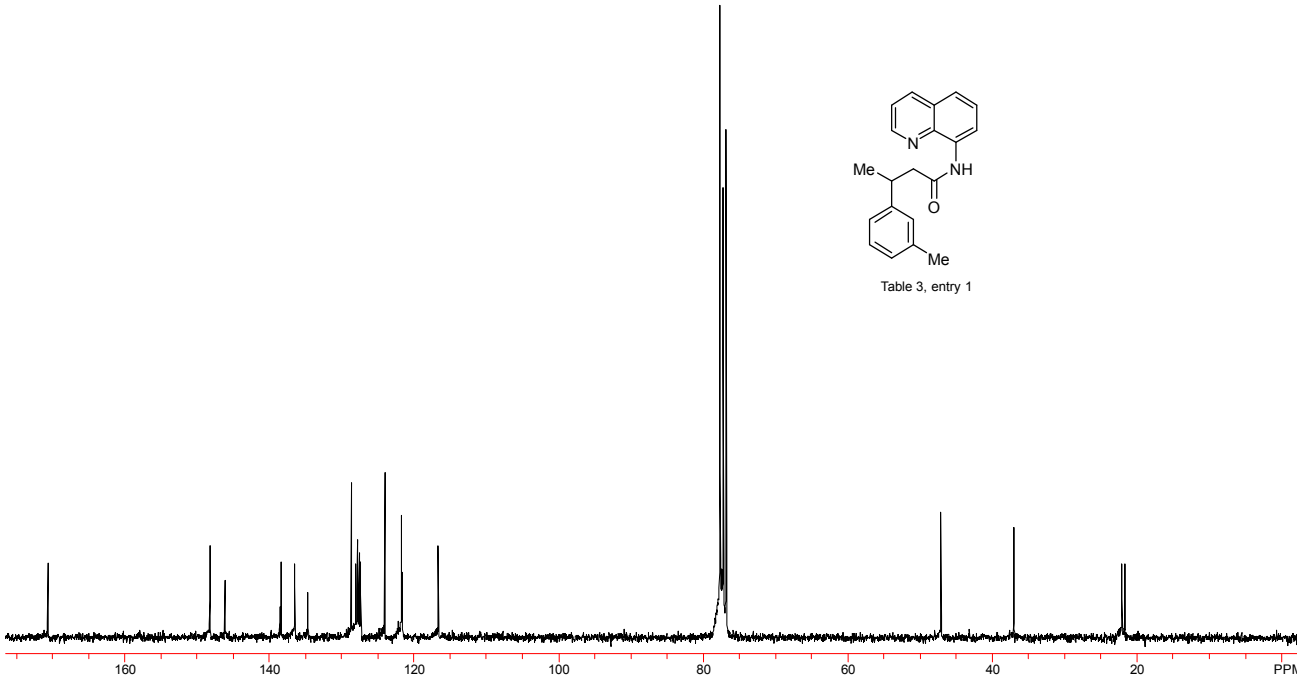

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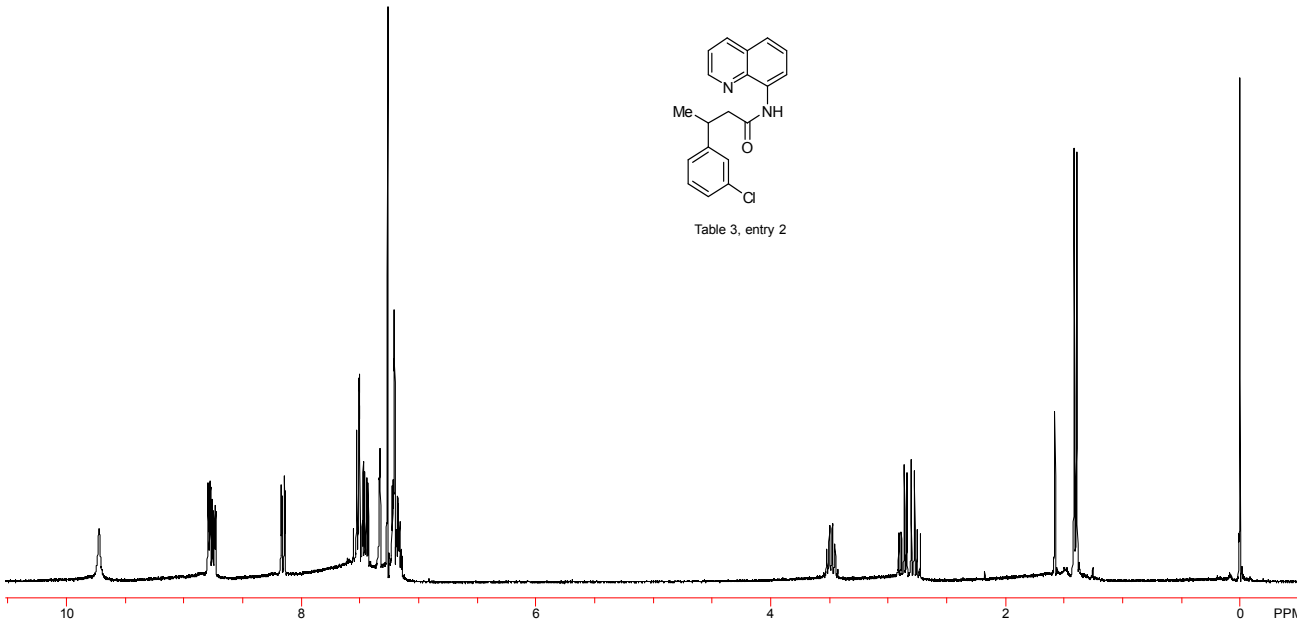

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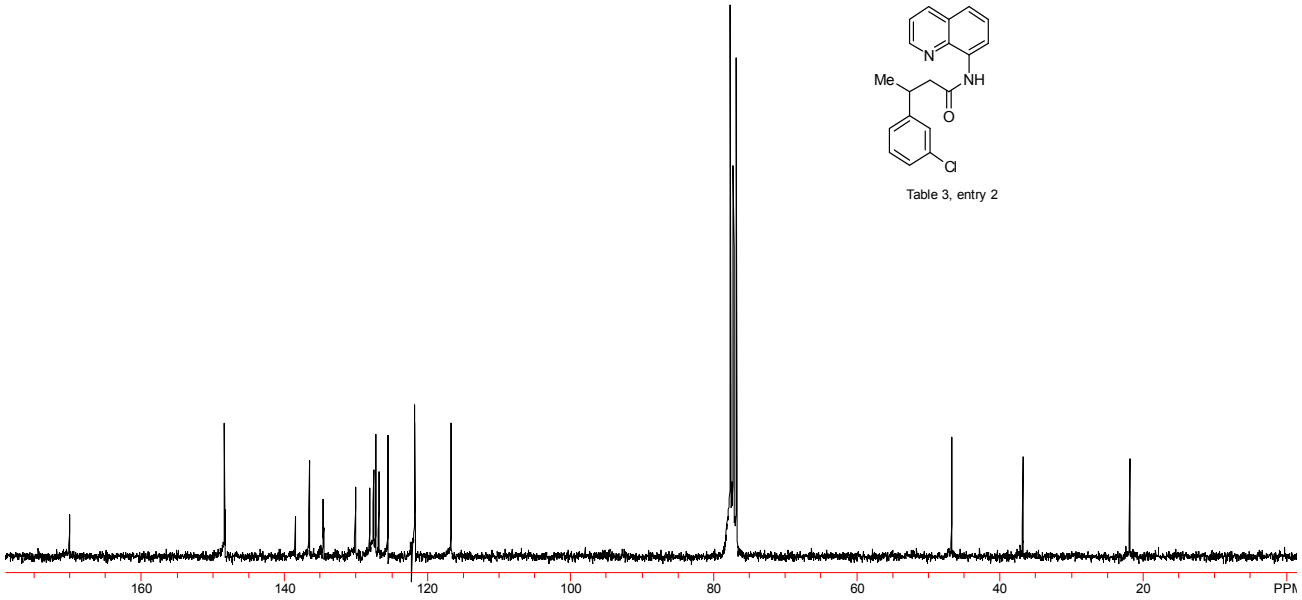

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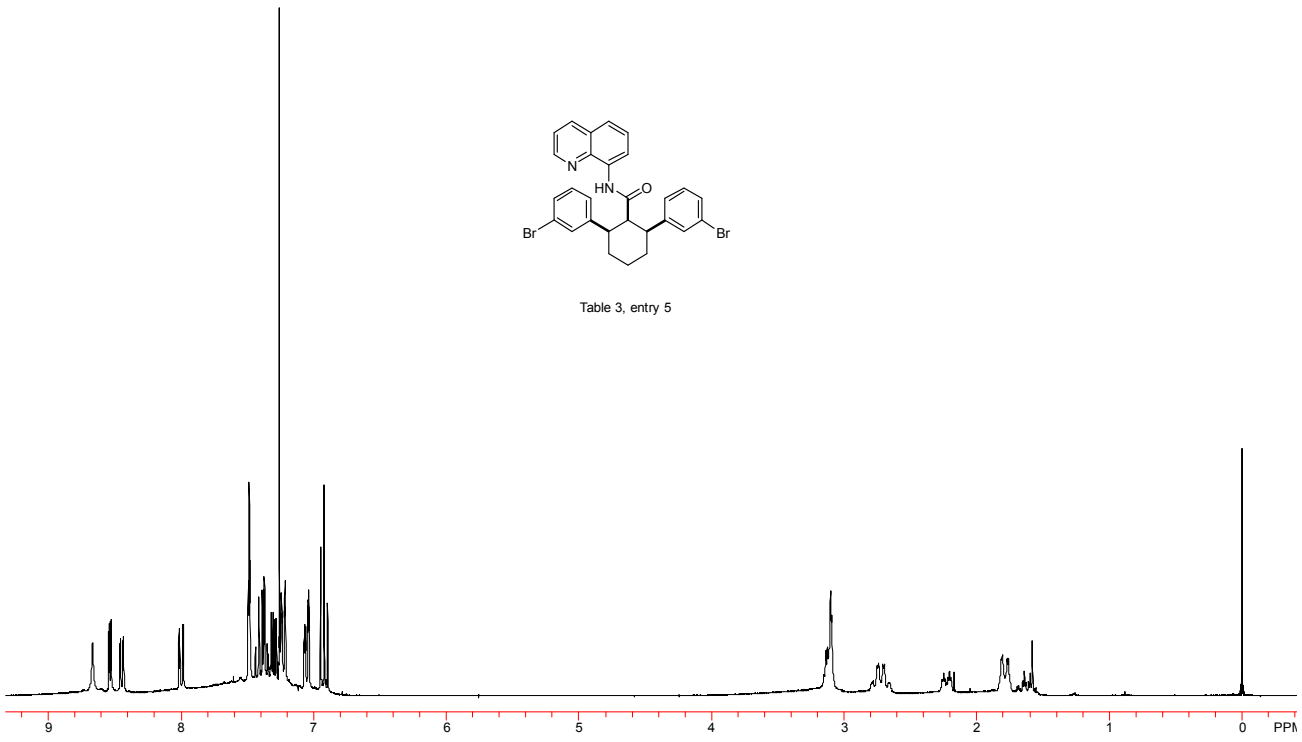

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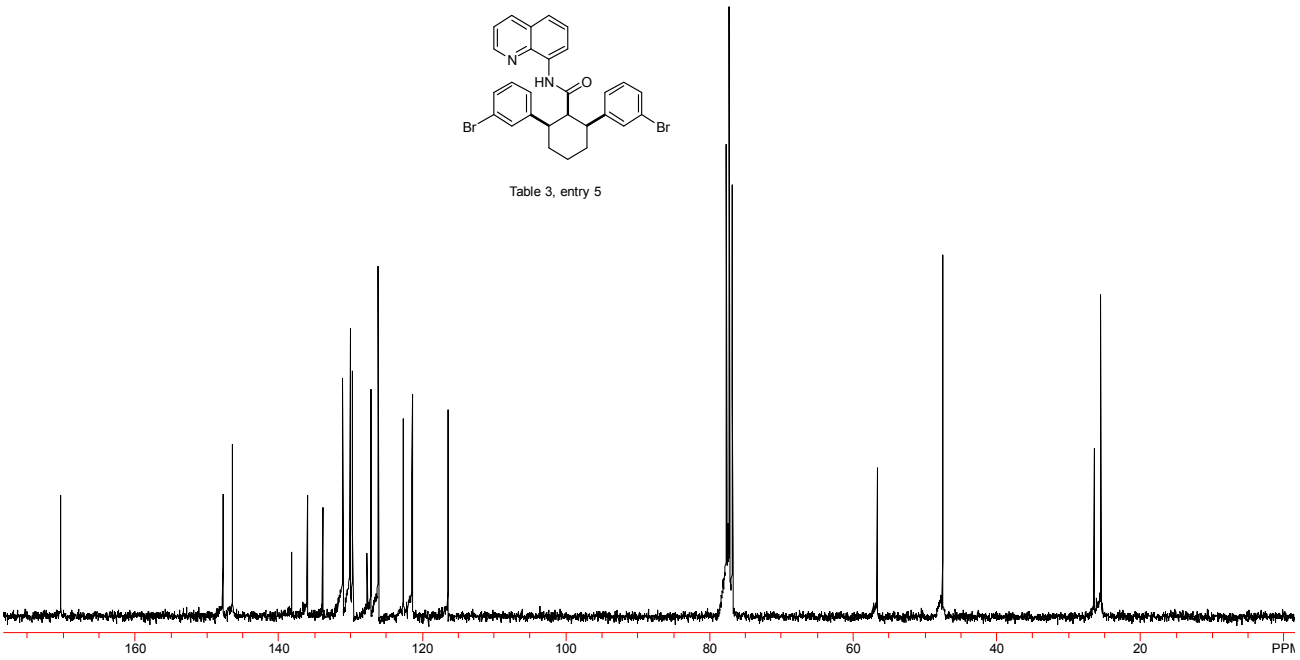

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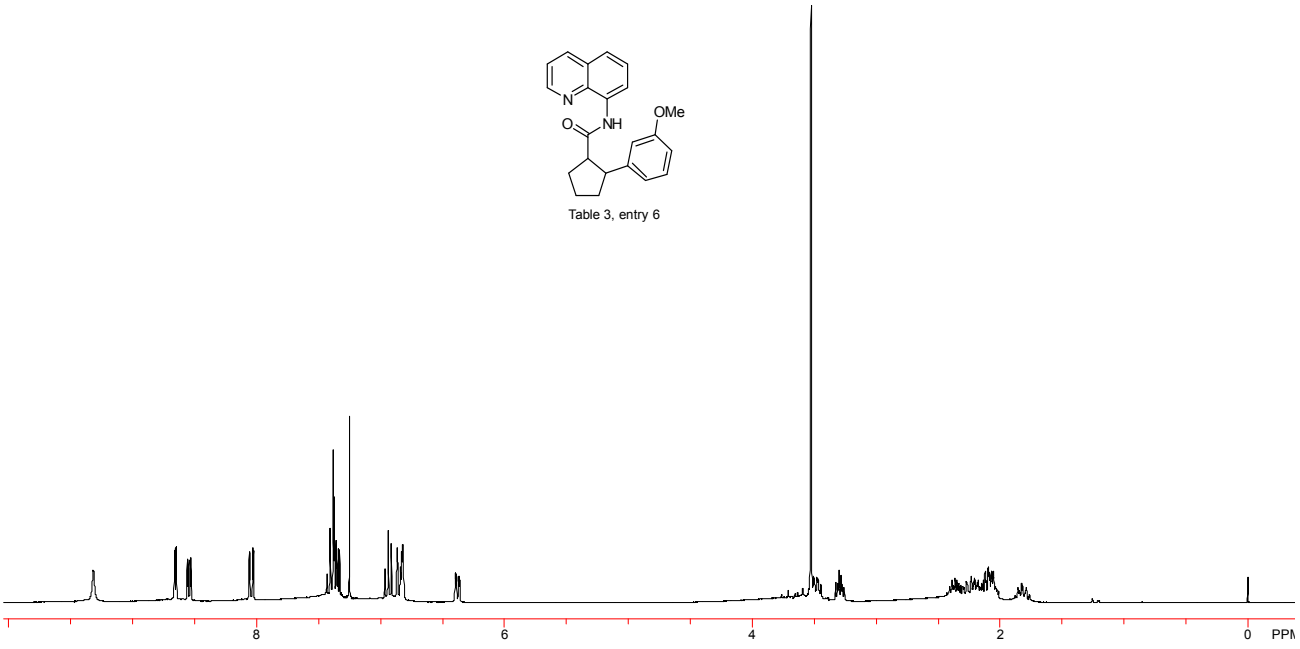

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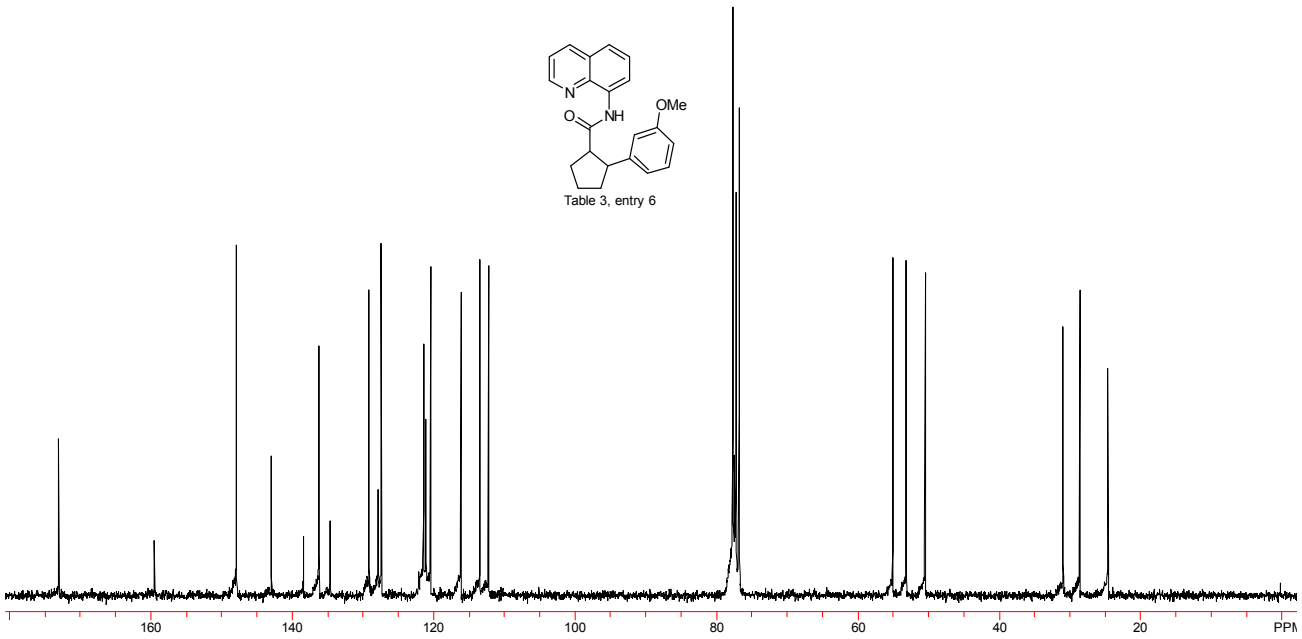

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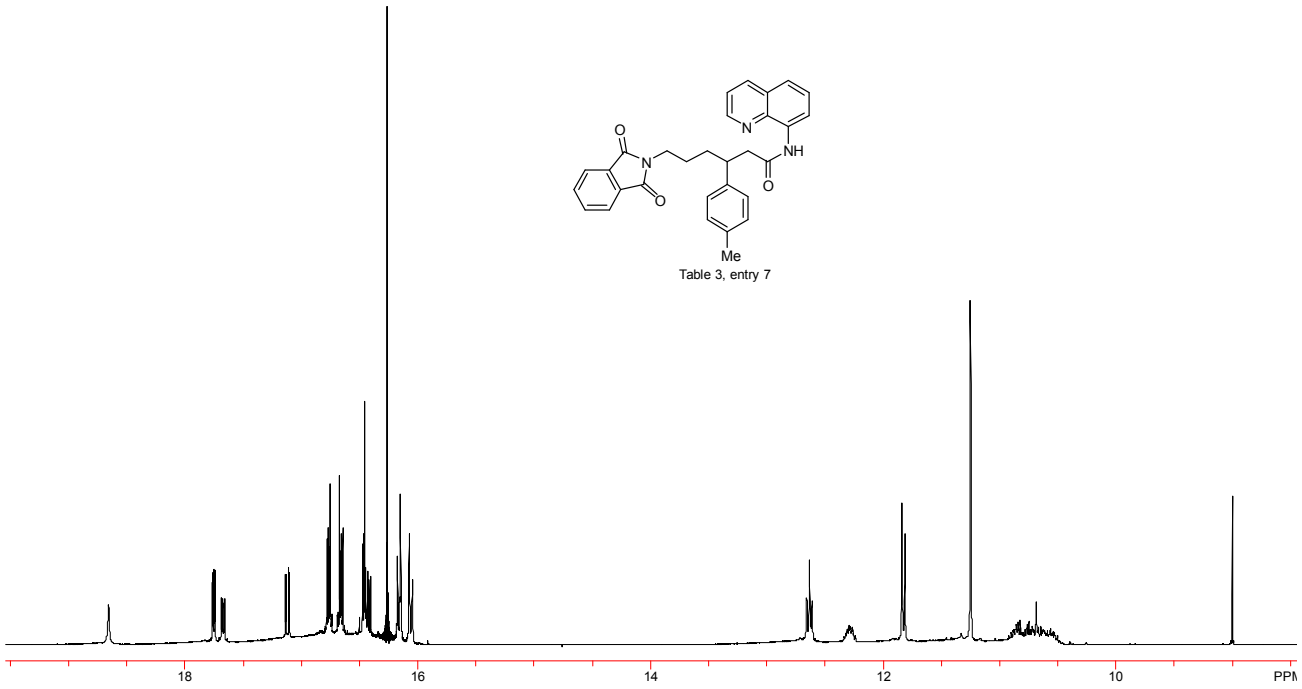

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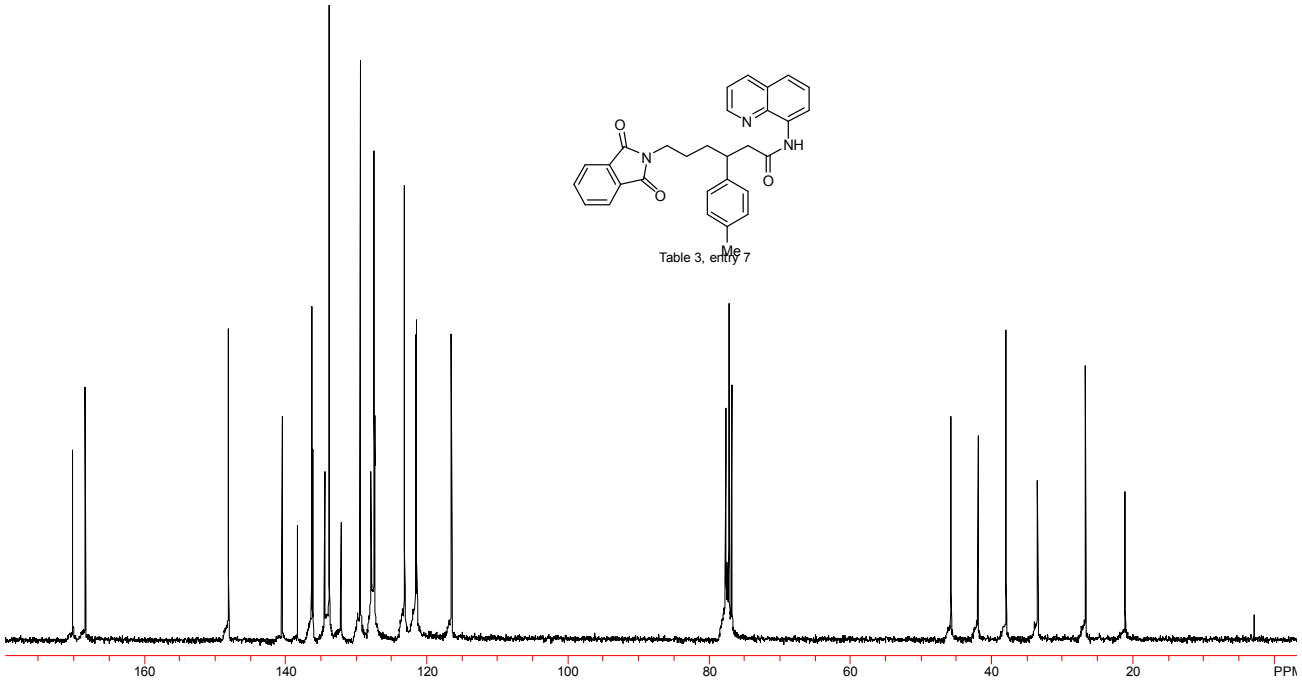

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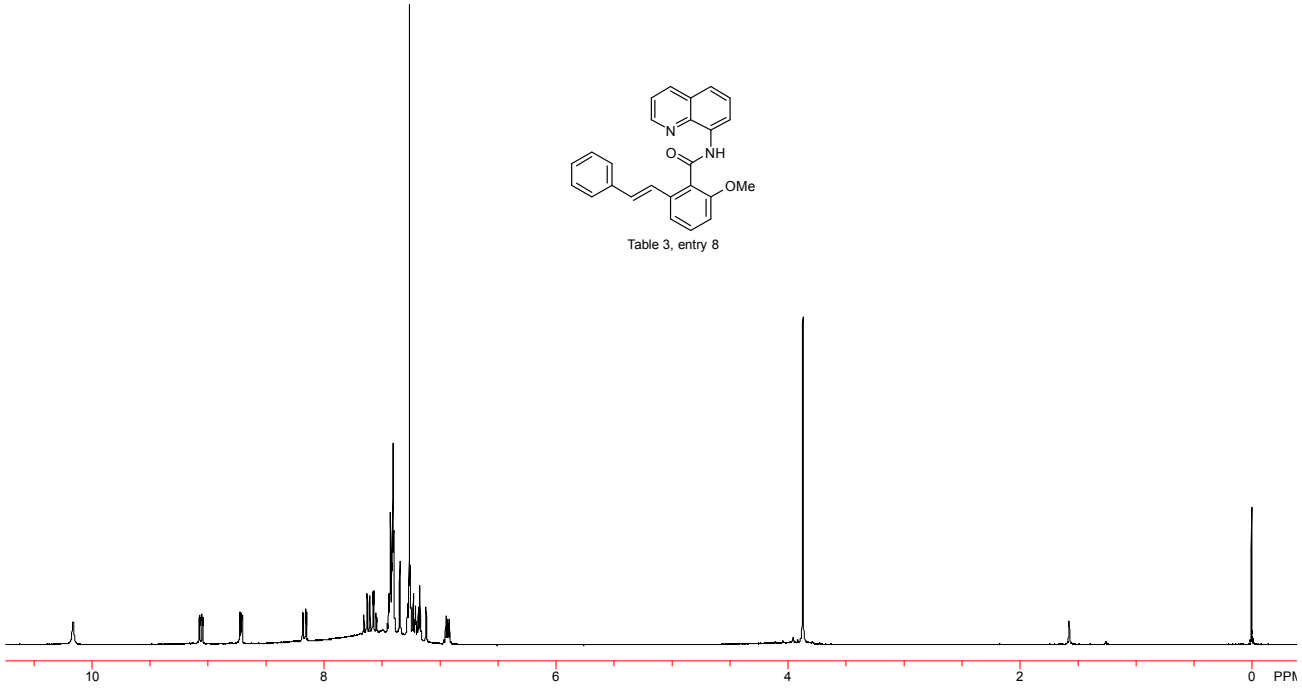

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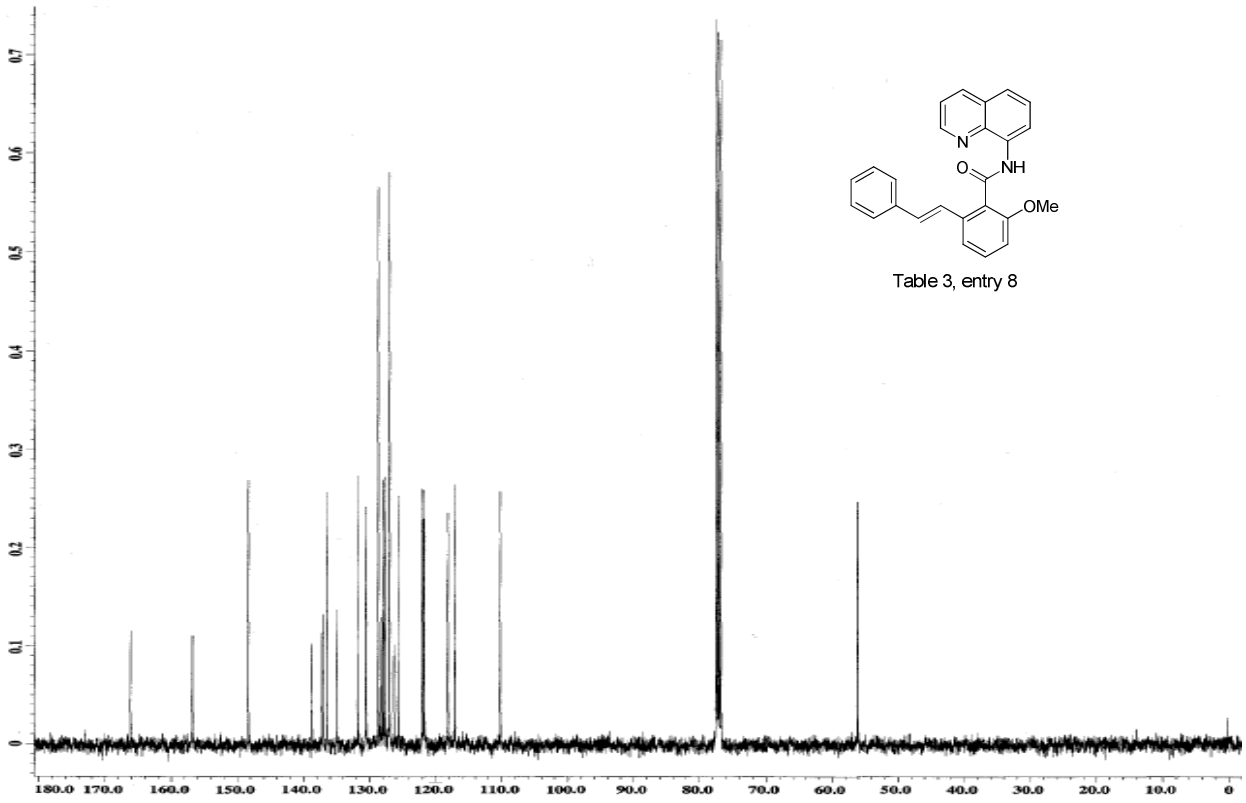

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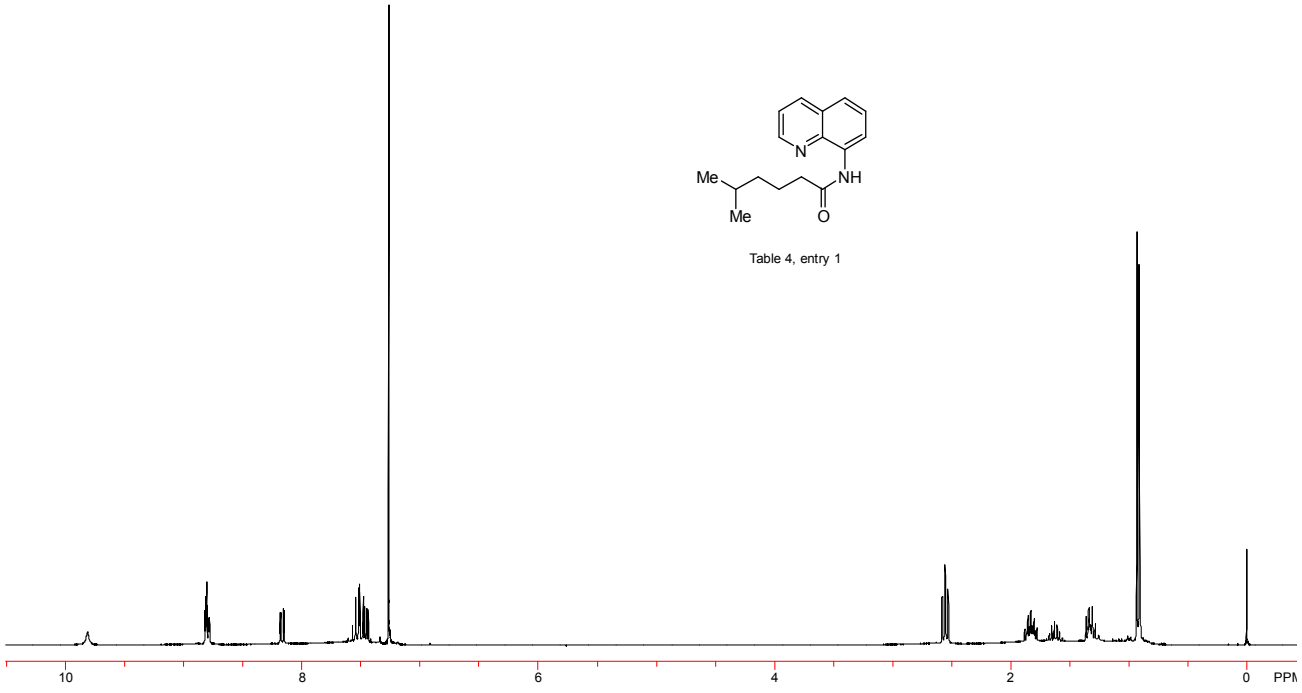

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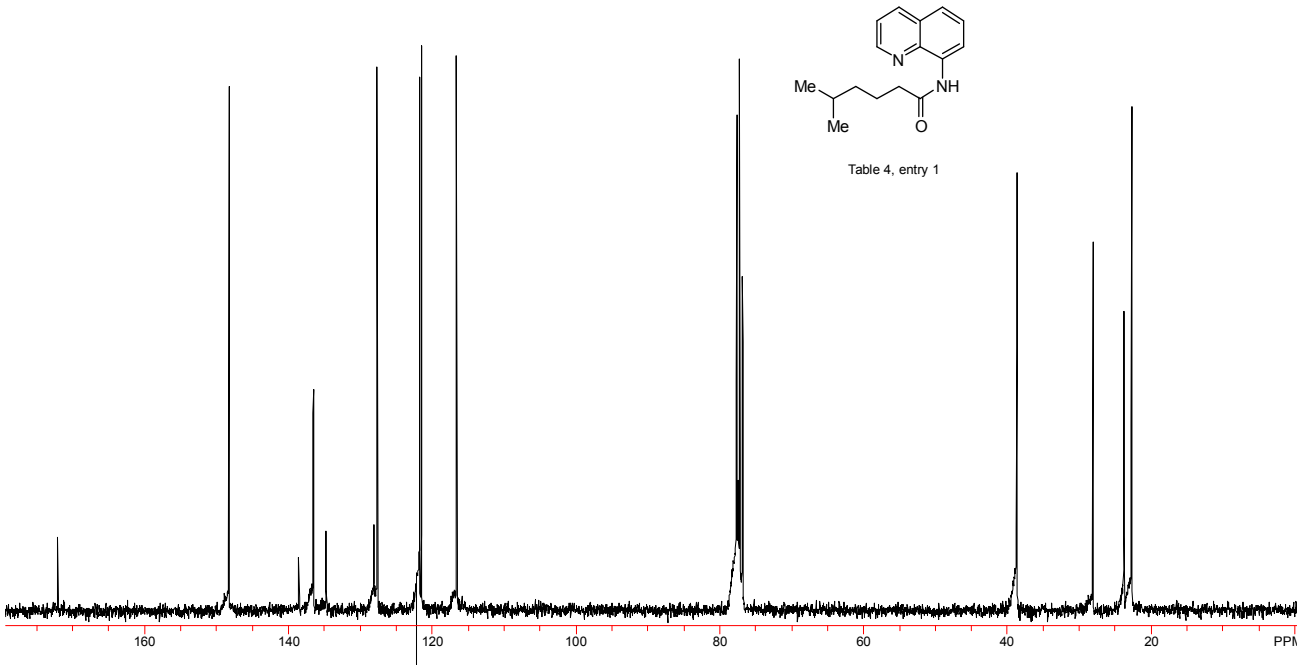

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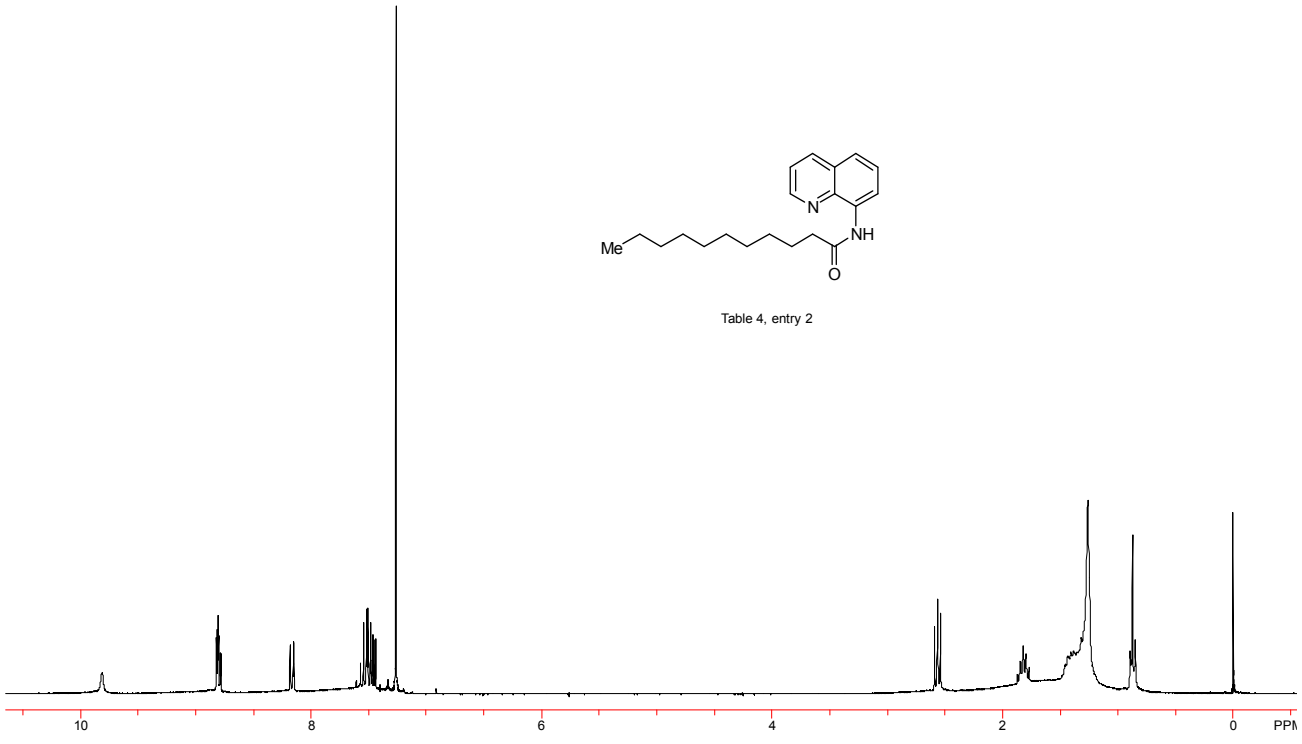

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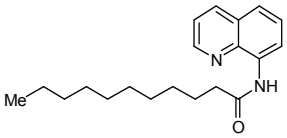

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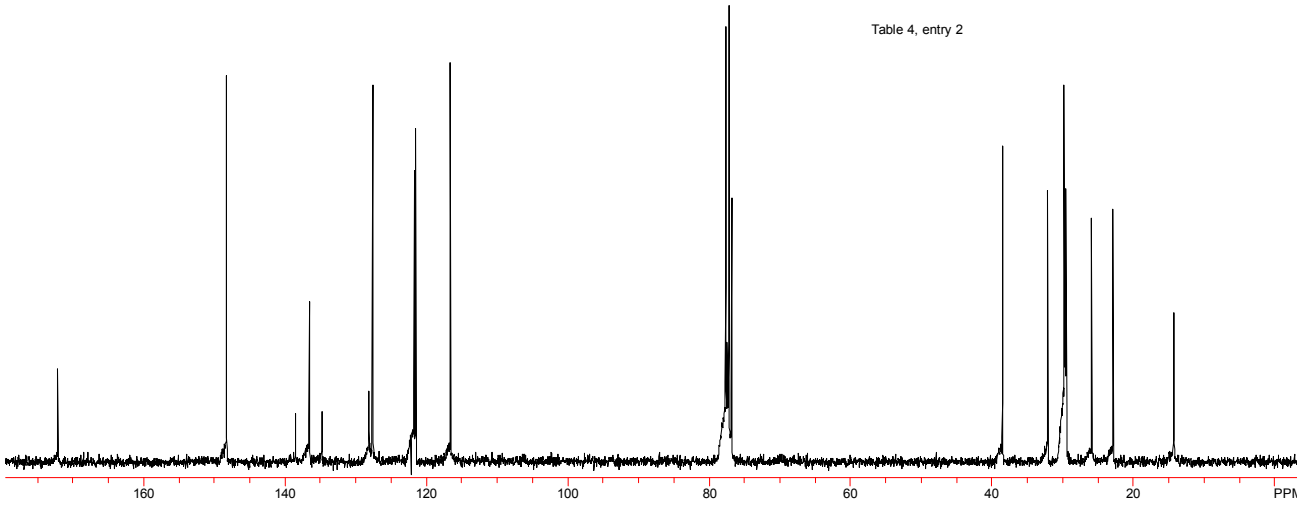

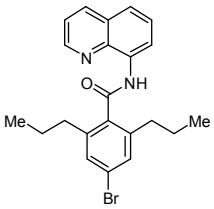

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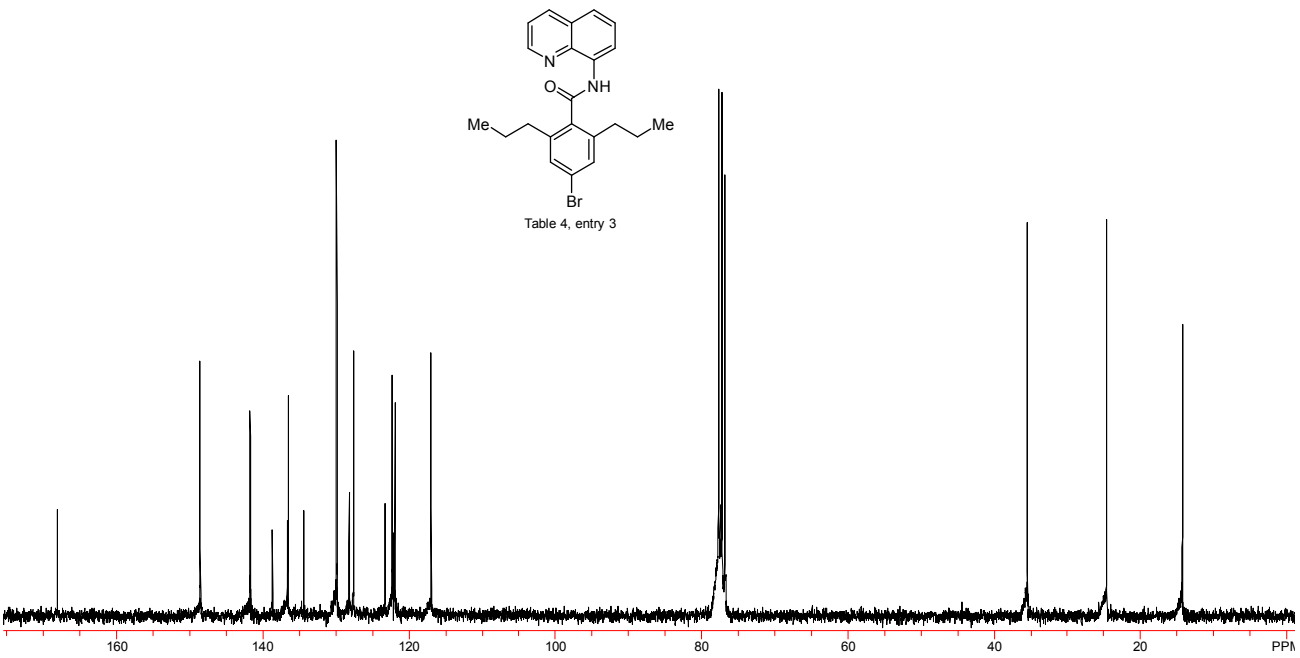

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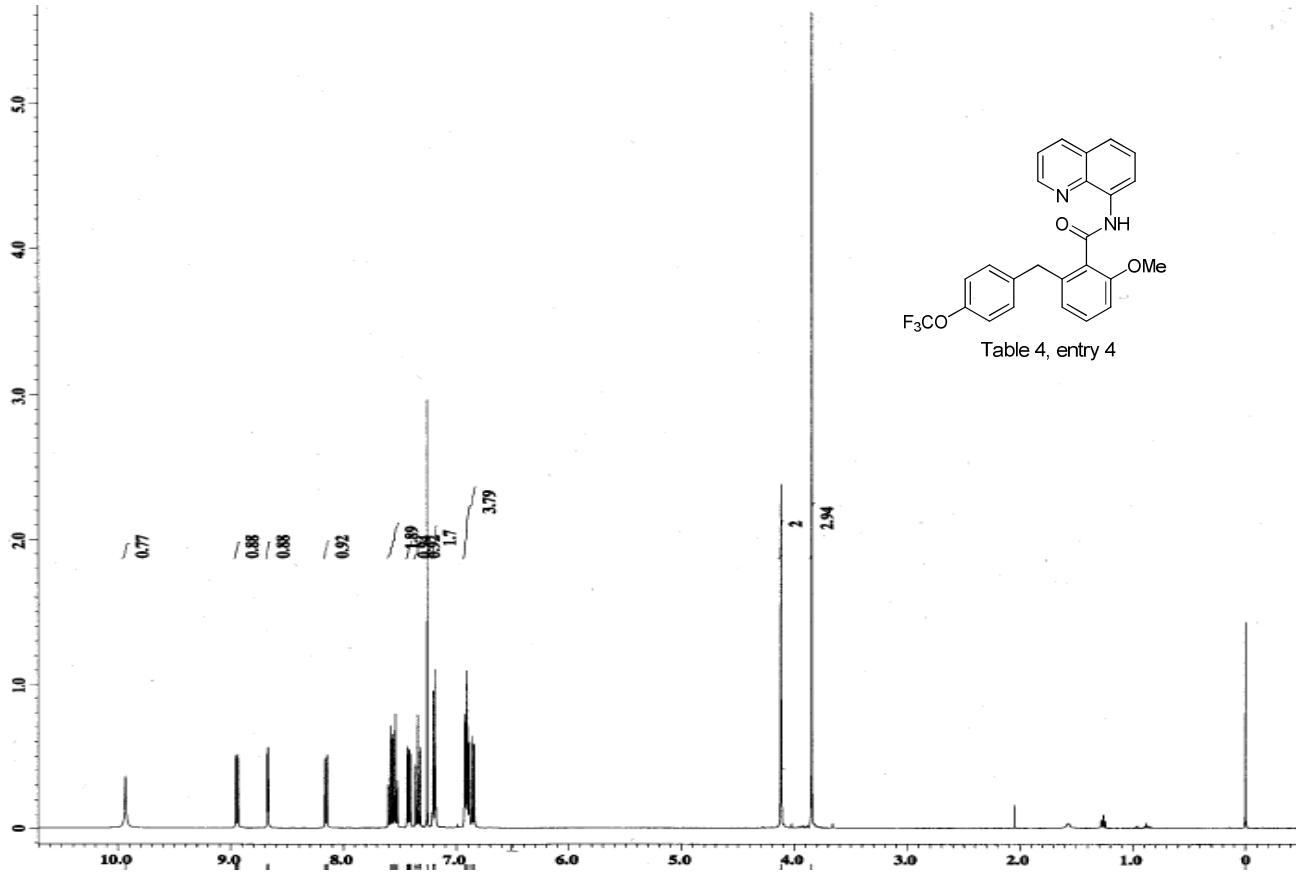

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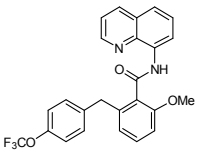

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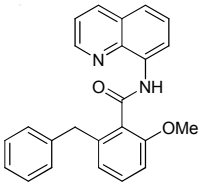

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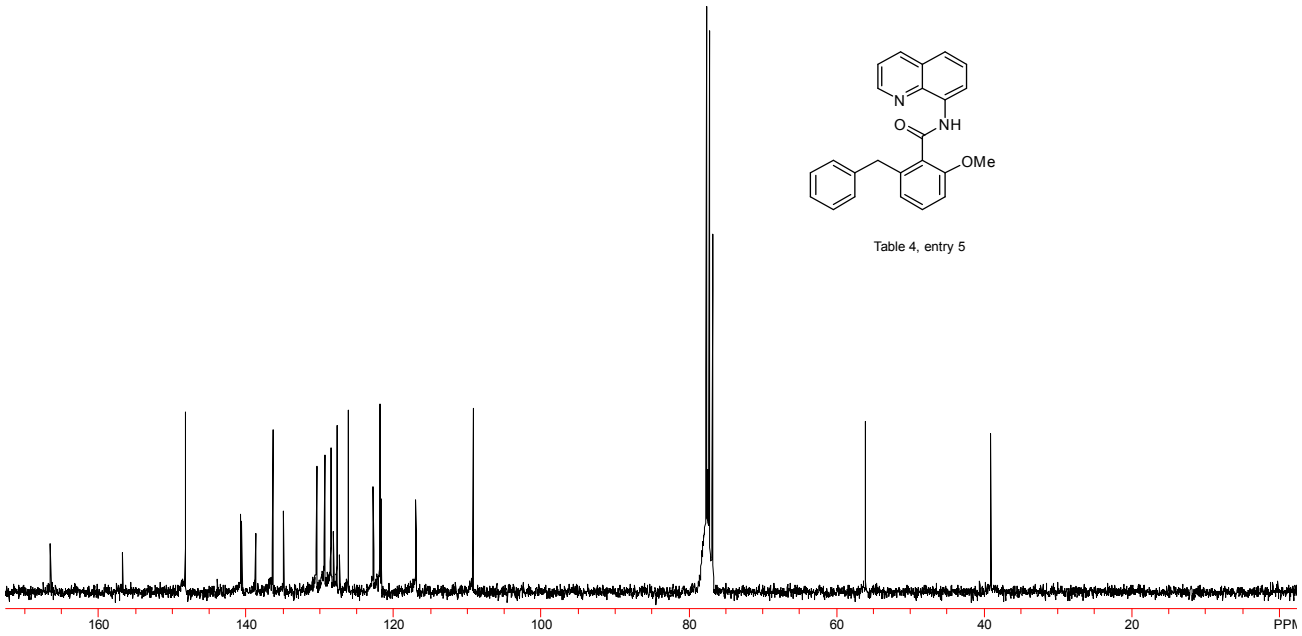

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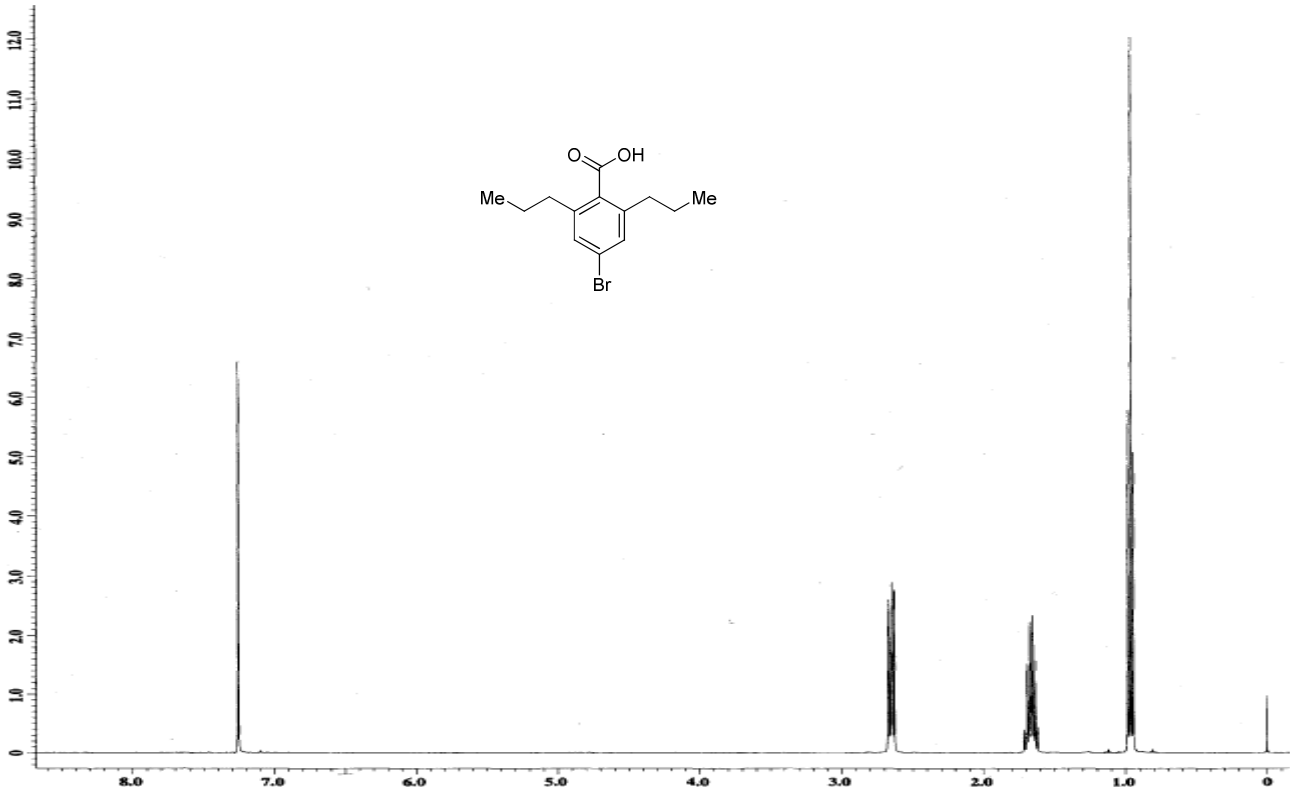

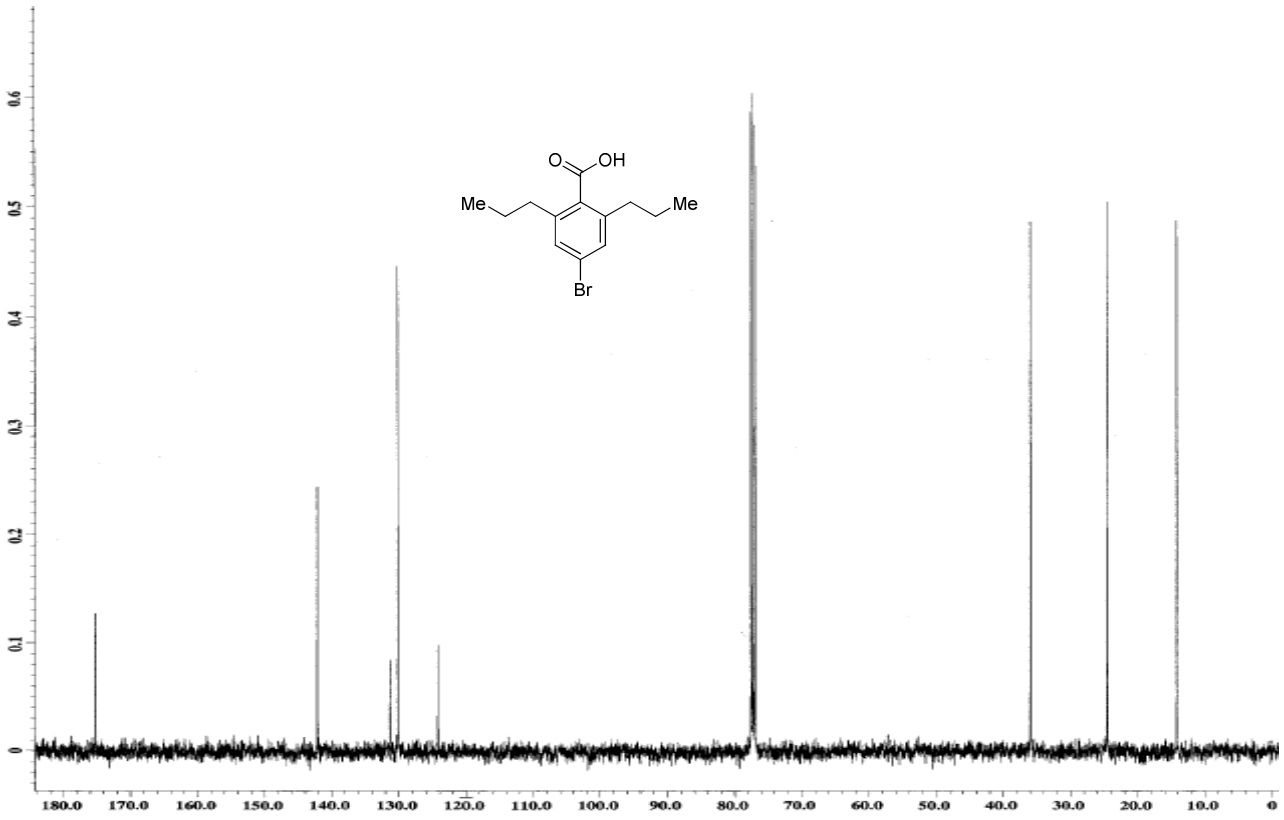
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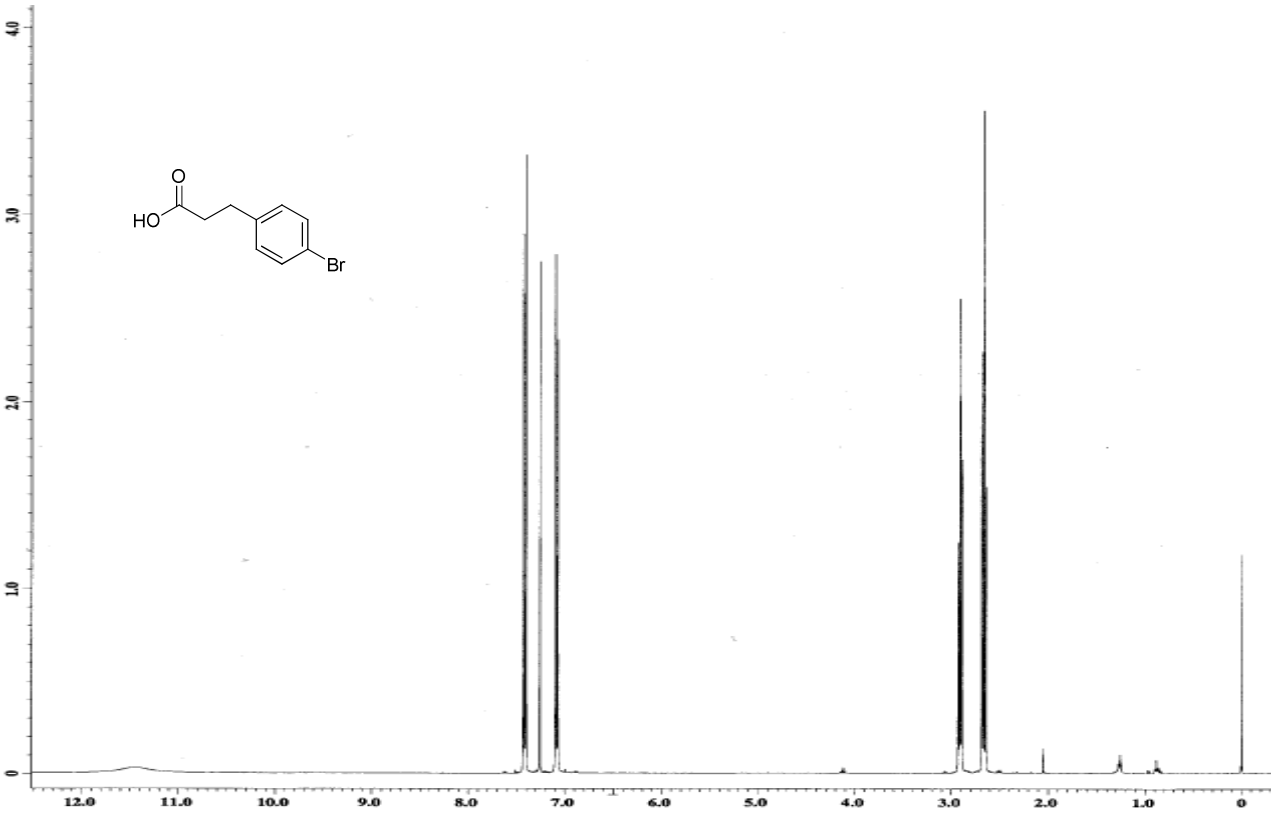
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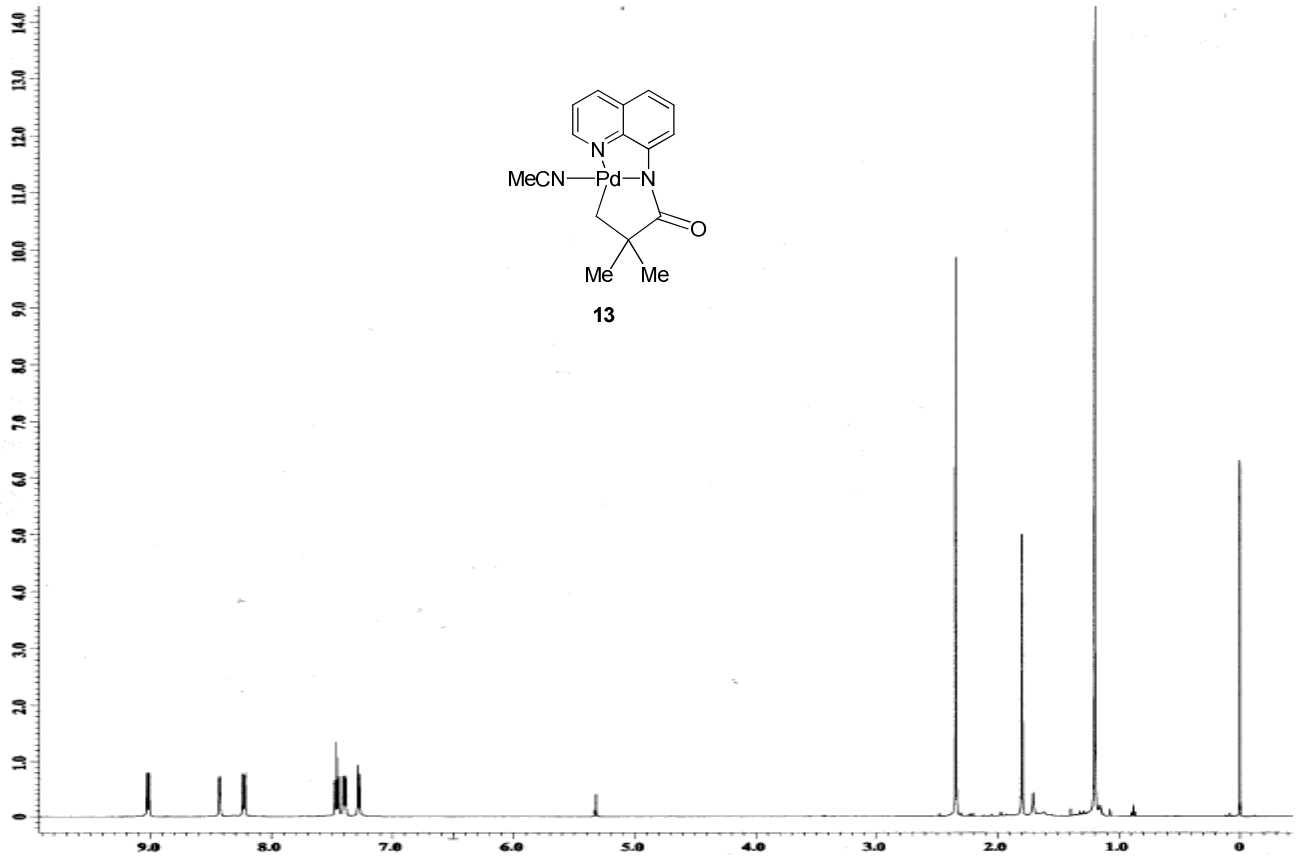

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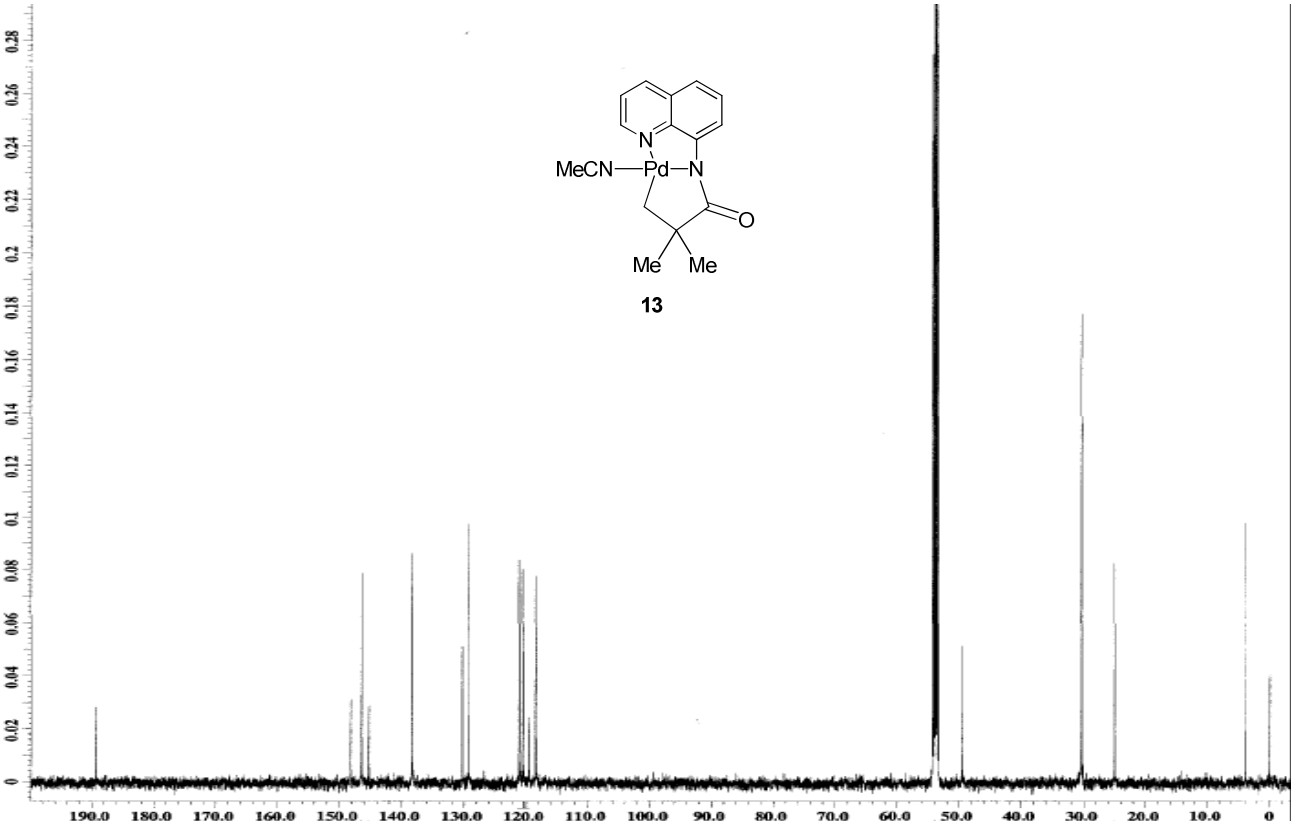

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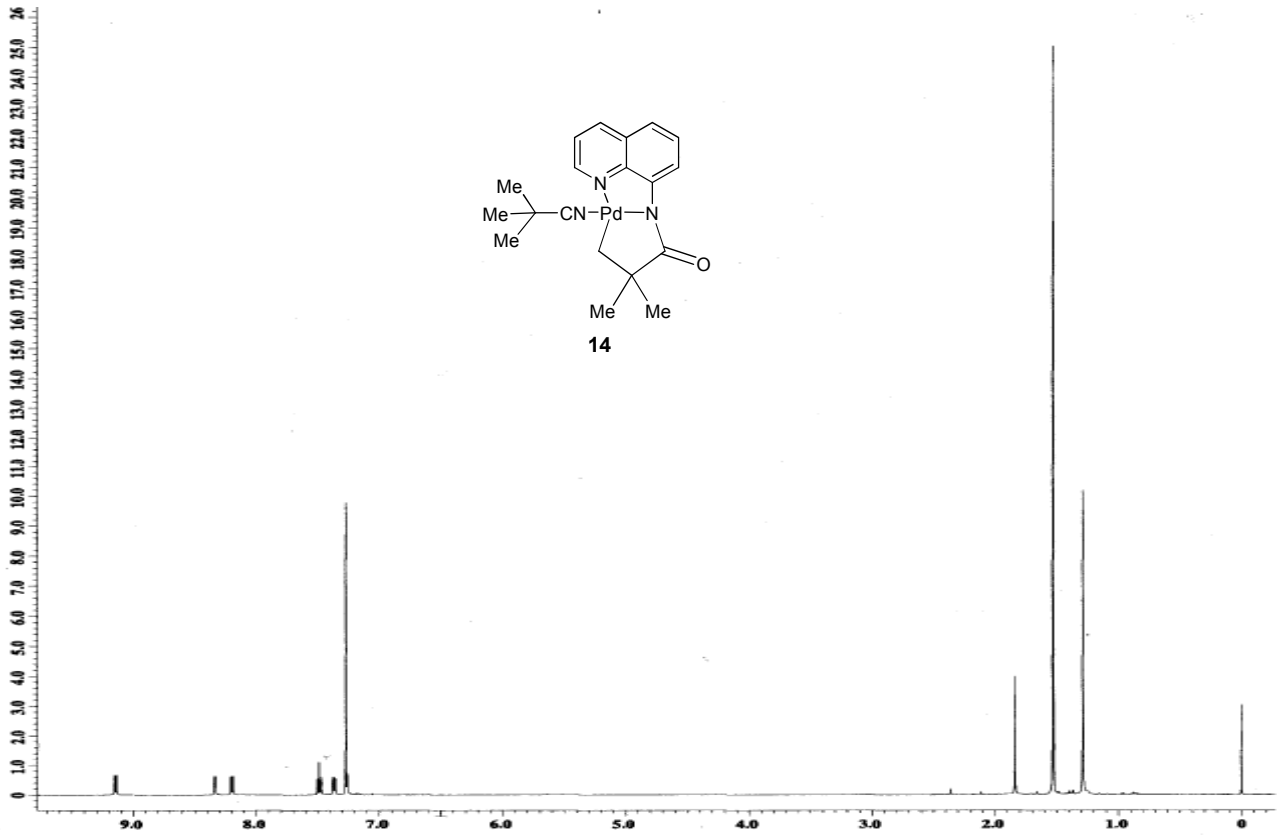

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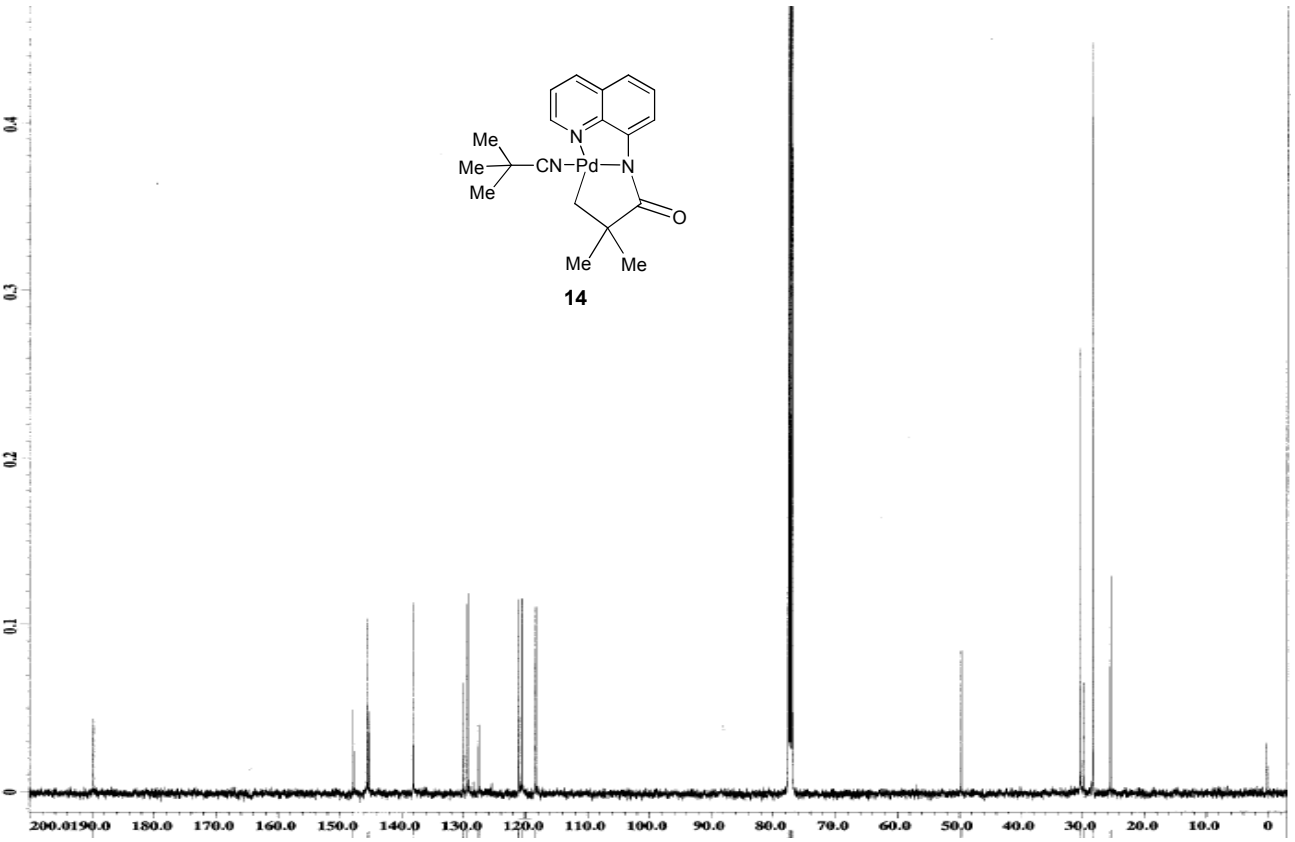

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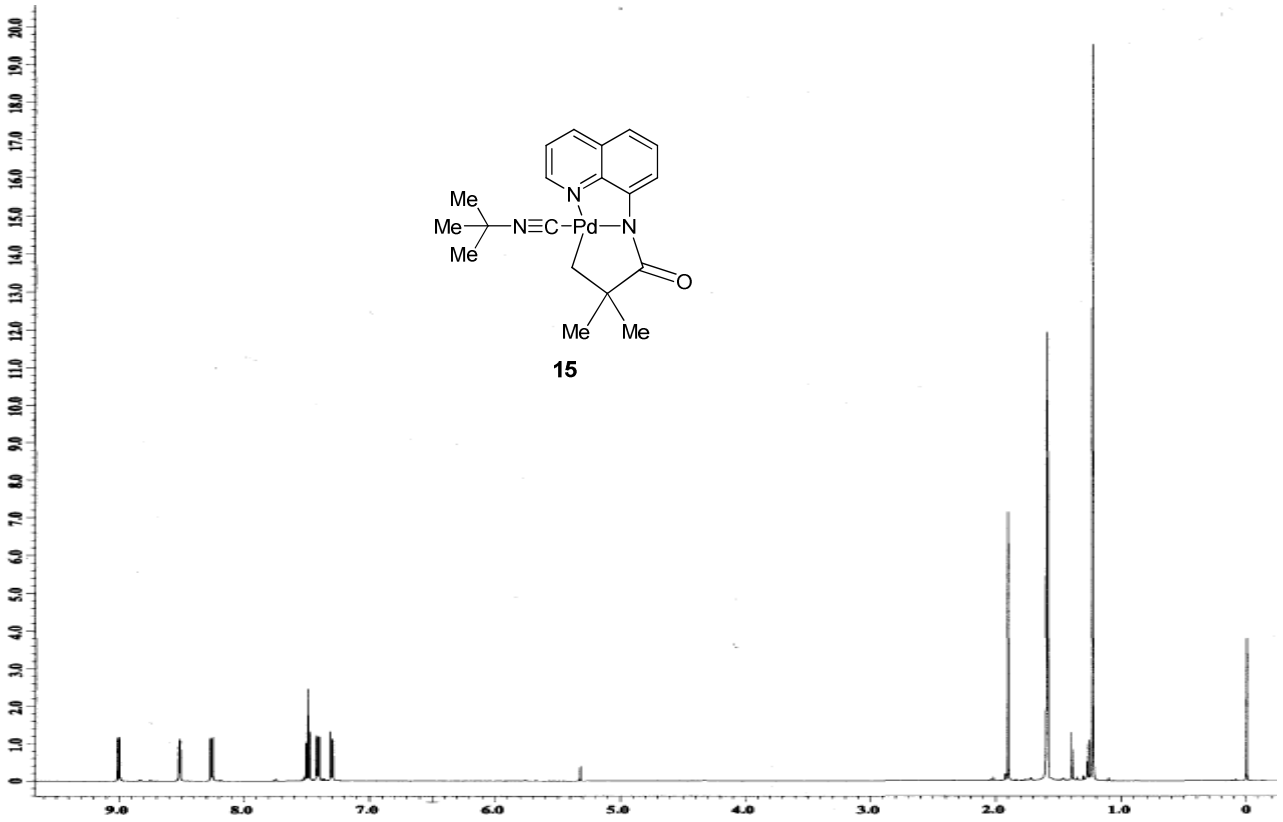

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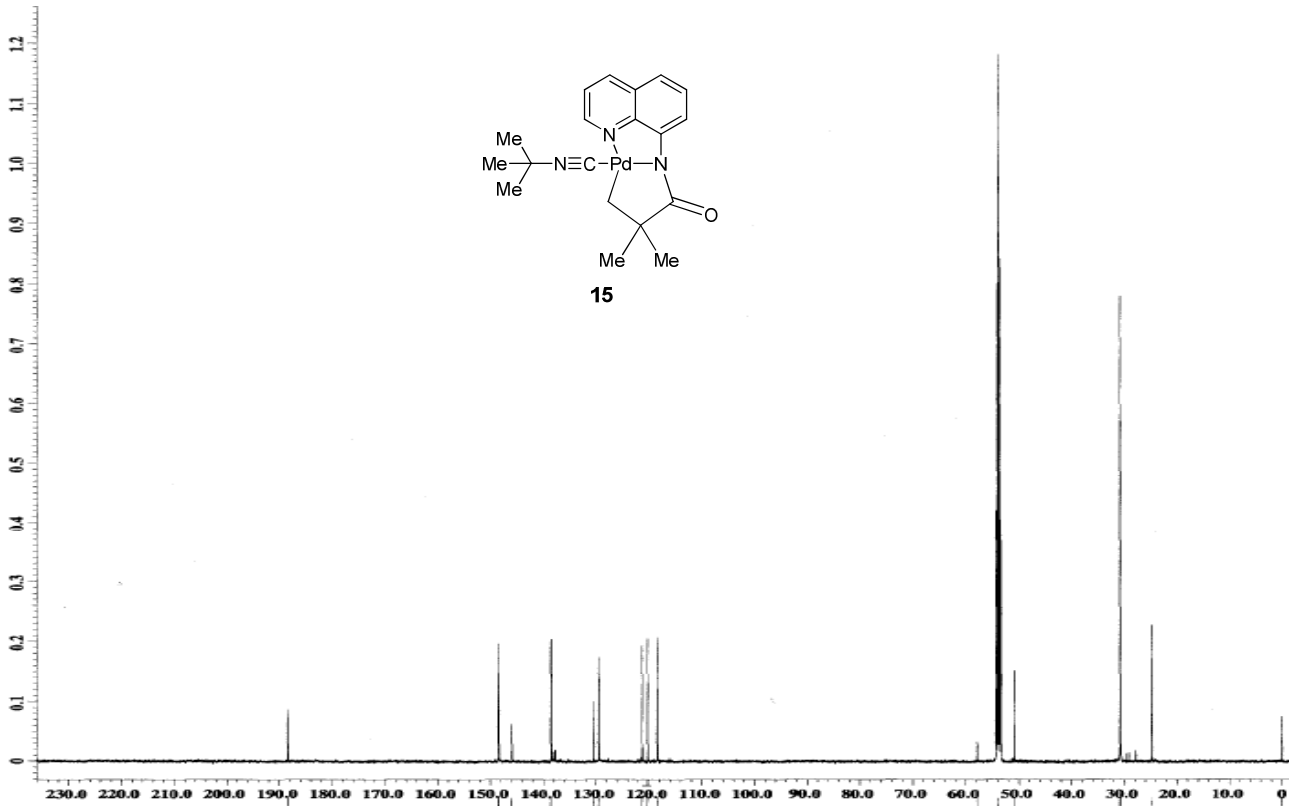

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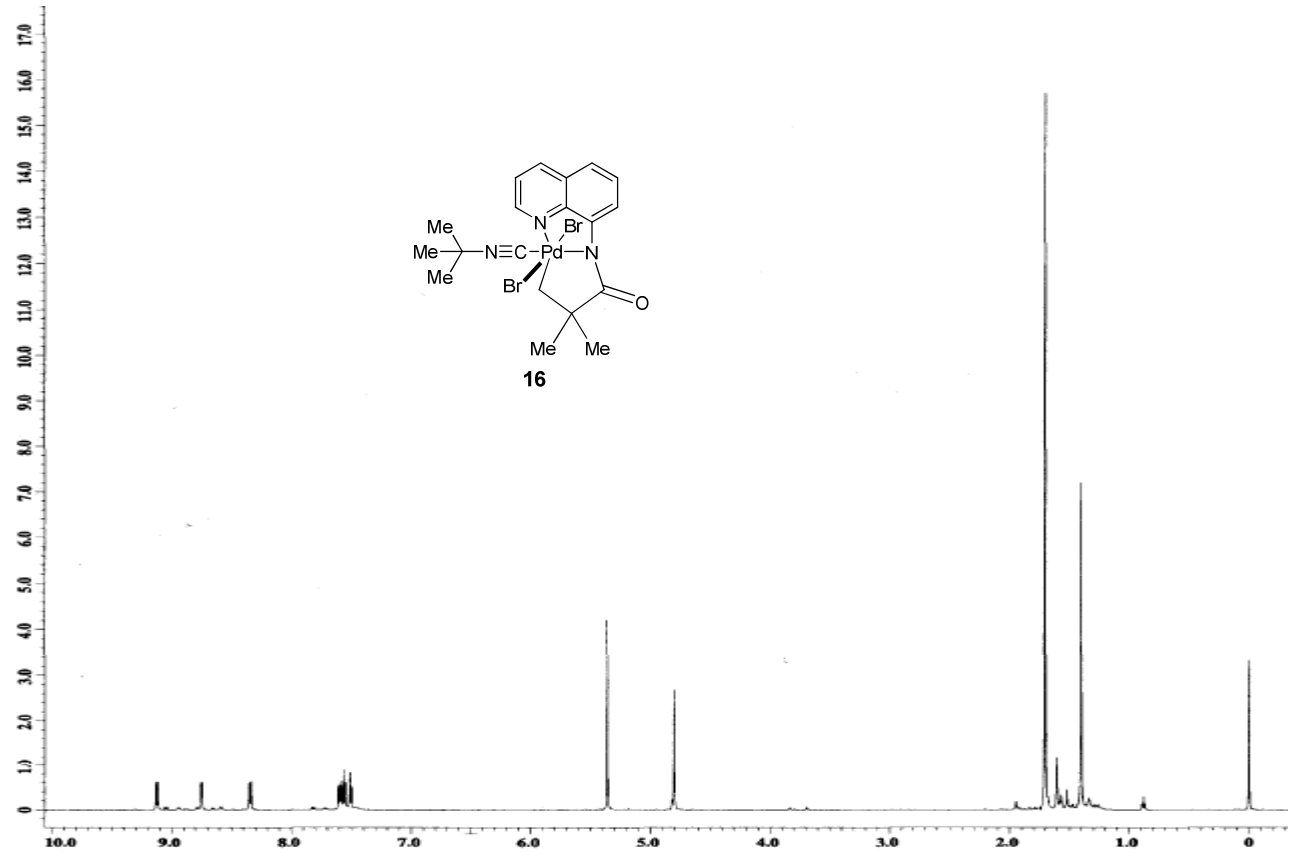

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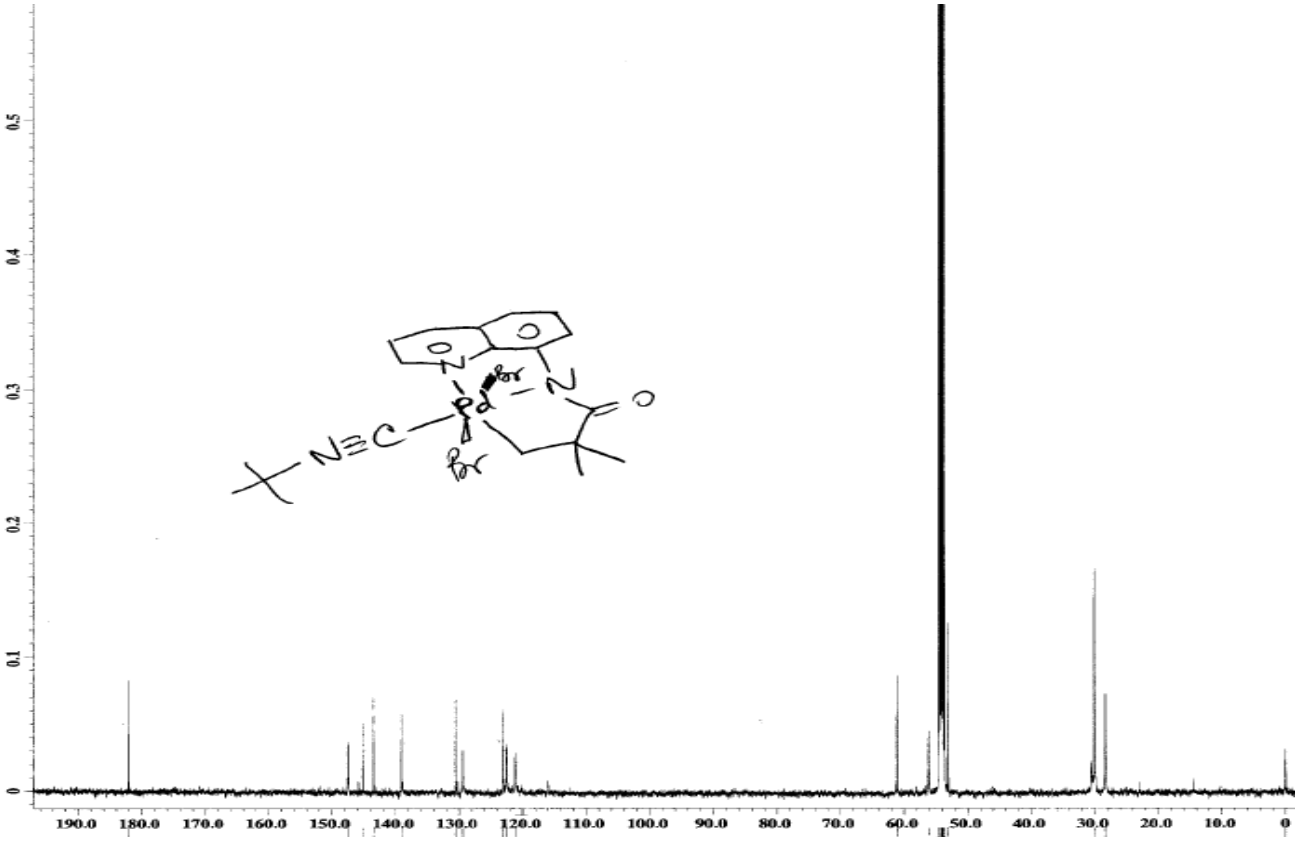

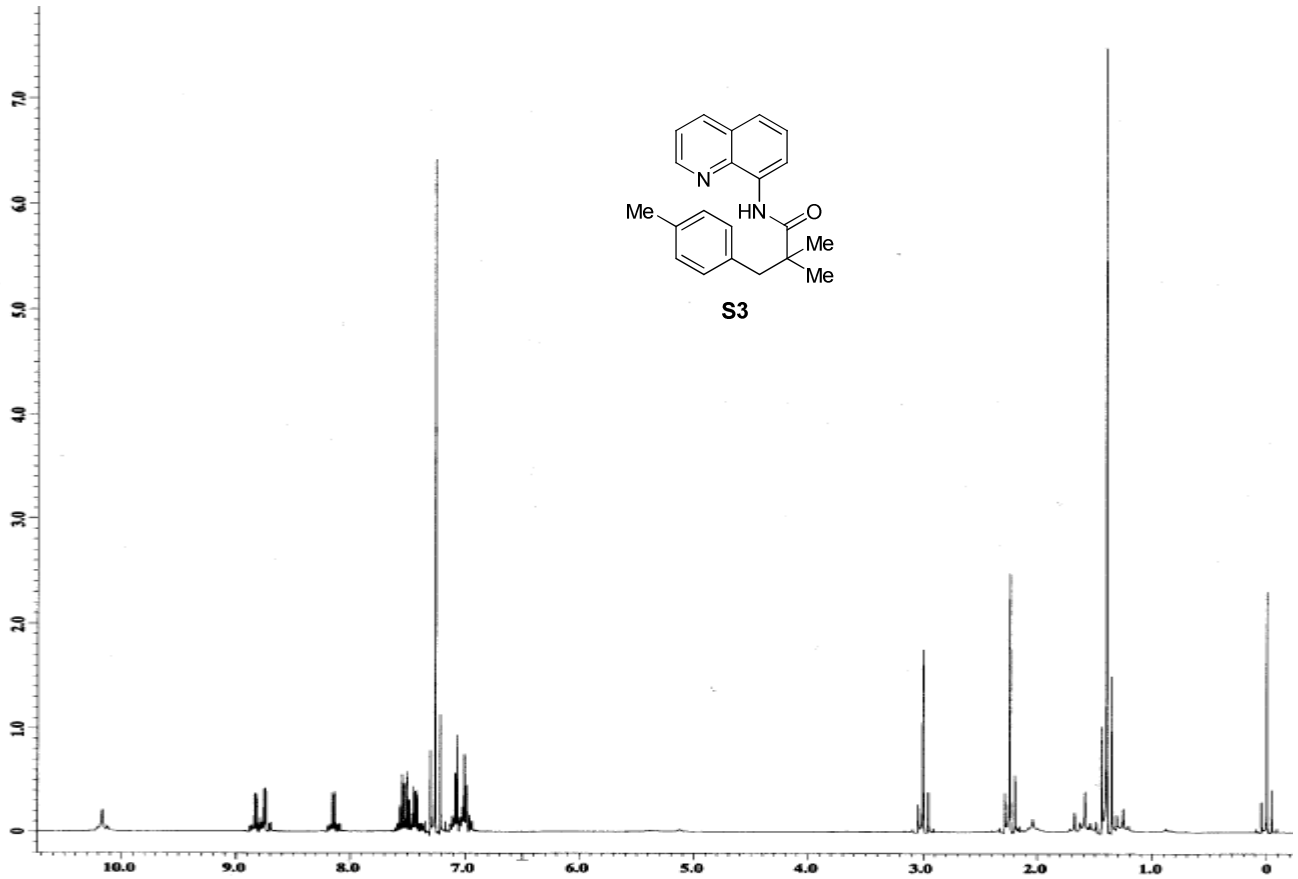

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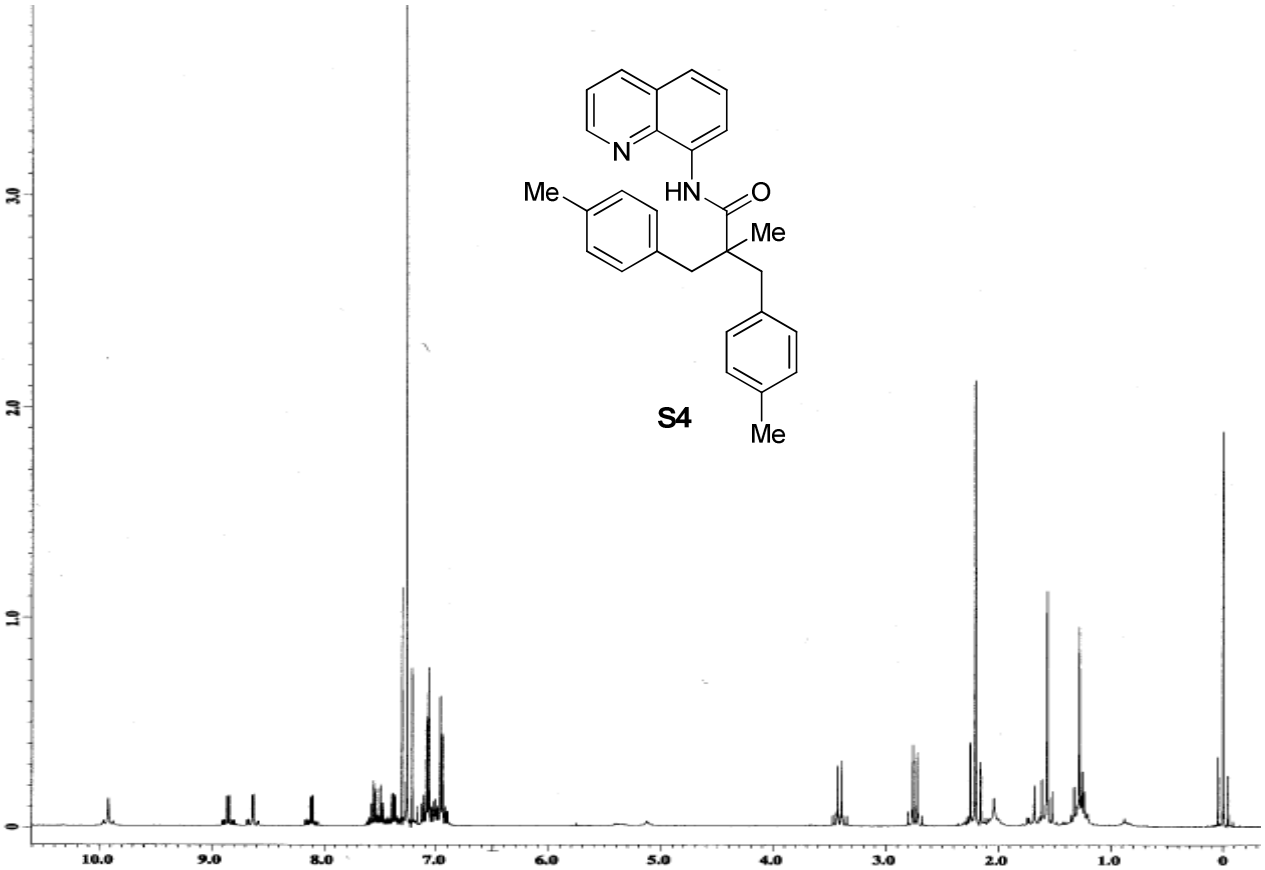

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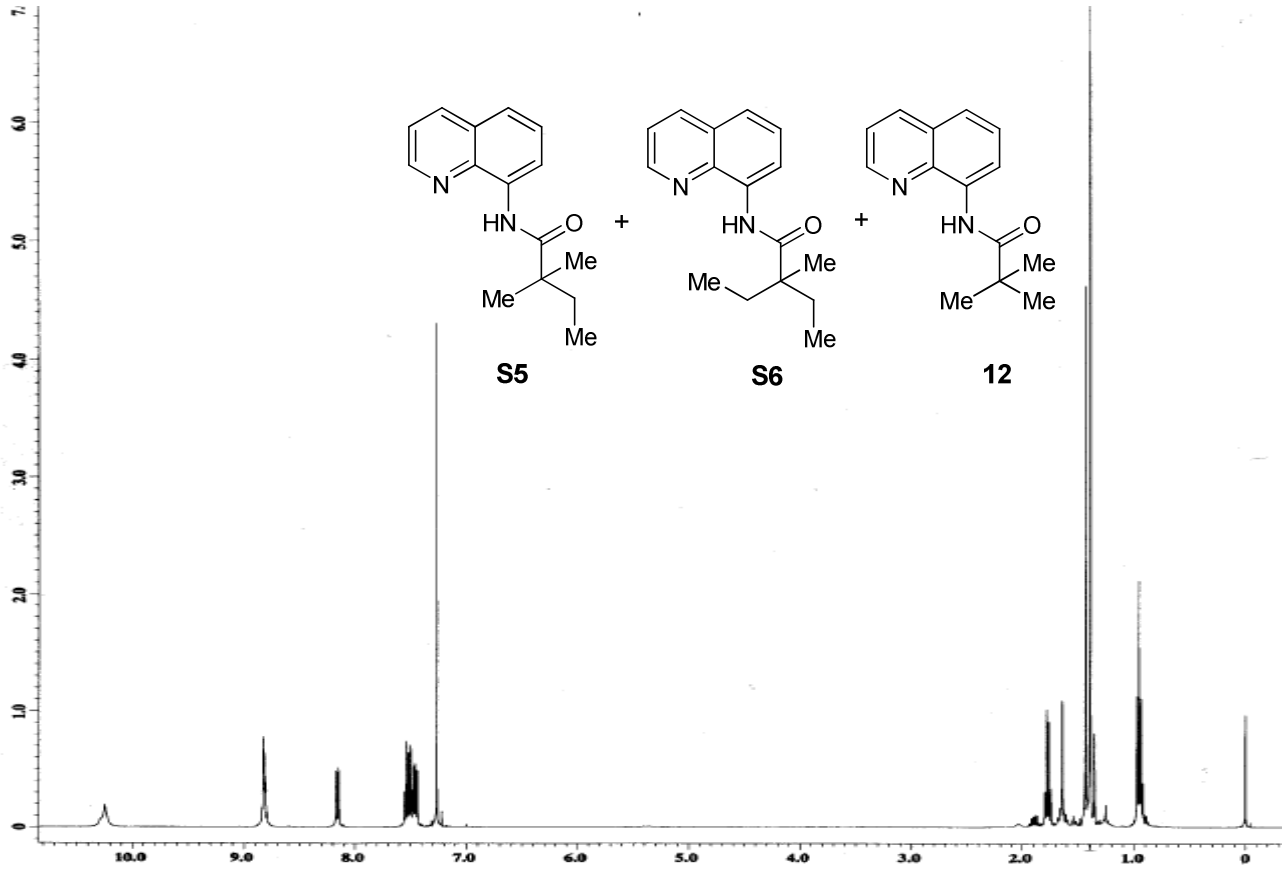
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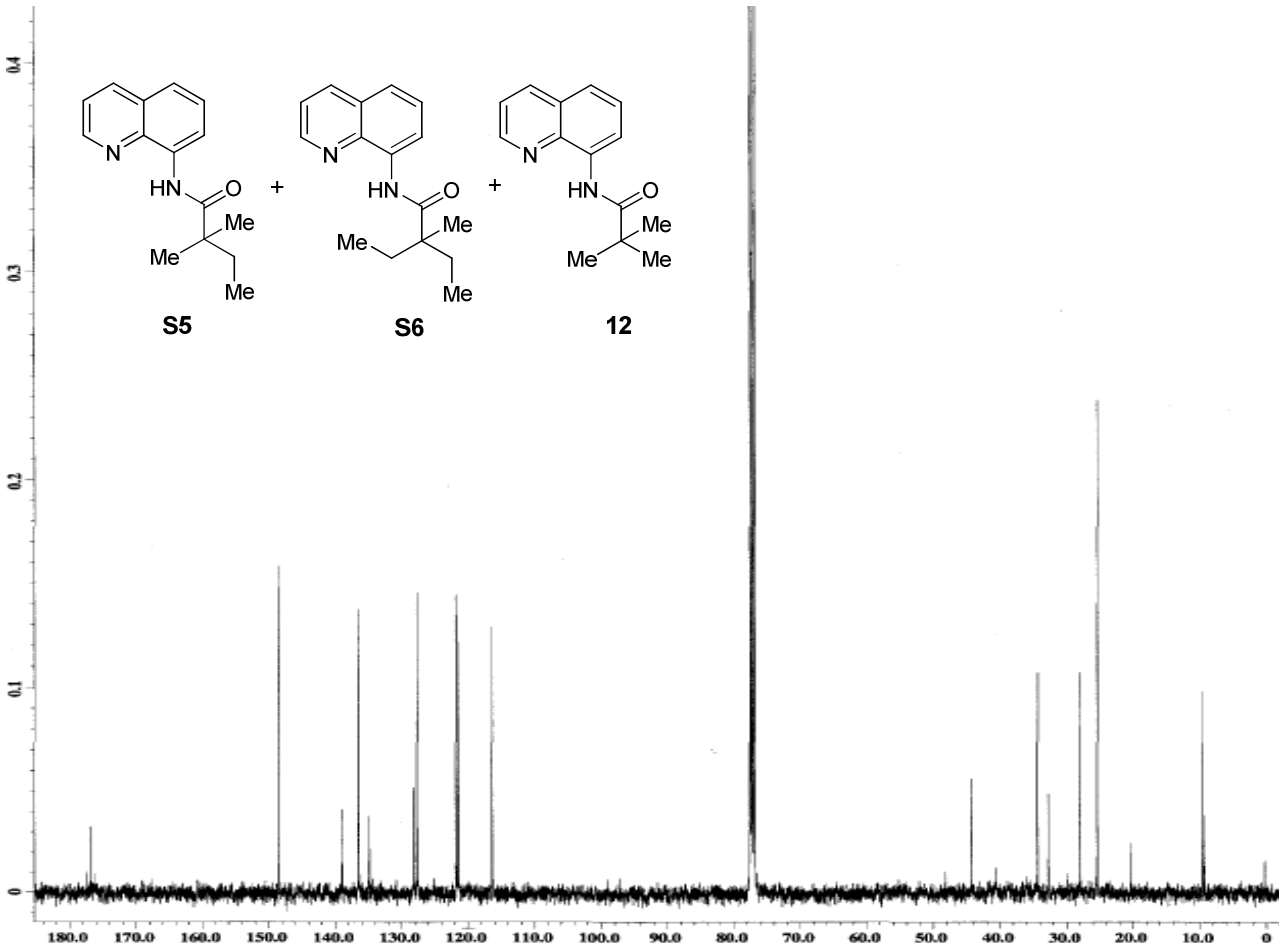
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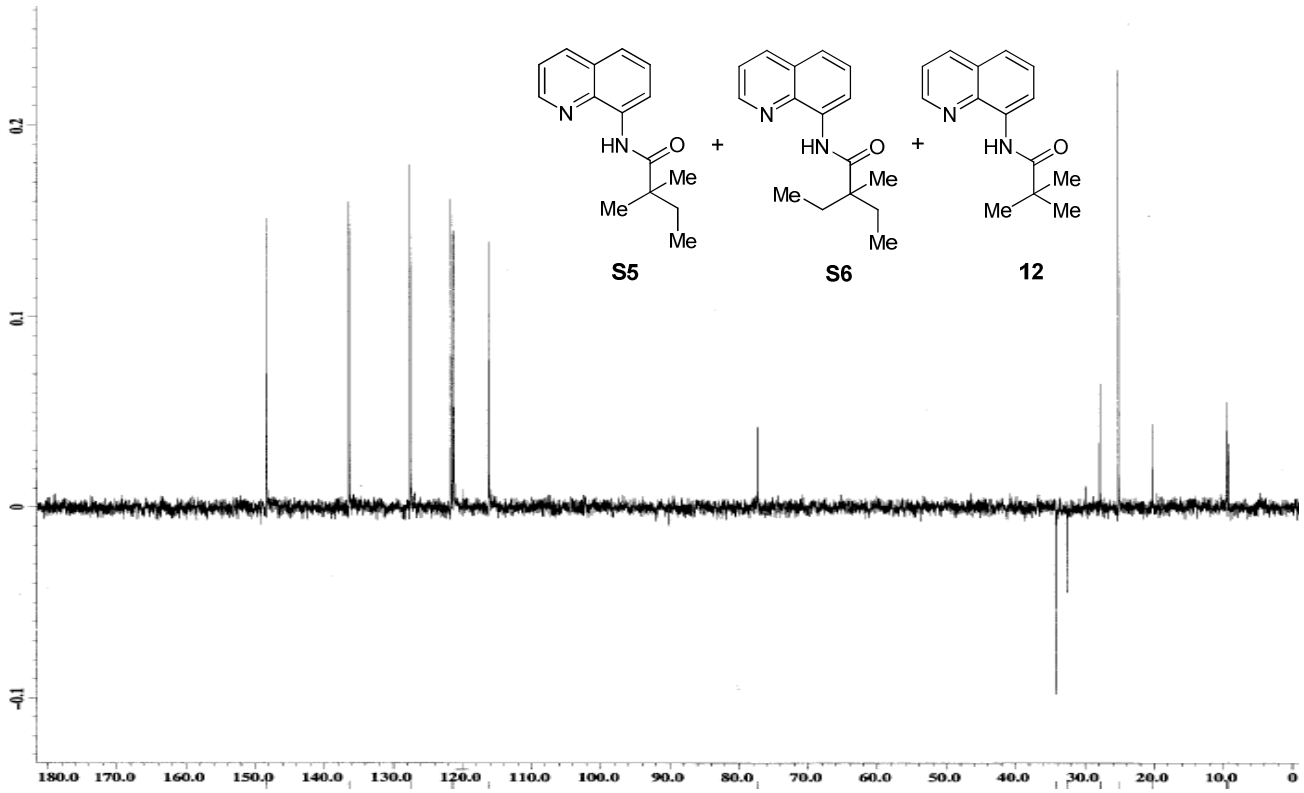
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