Chemoselective Reduction of Nitroaromatics in Water at Room Temperature

Supporting Information

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Contents:

General Methods

Chemicals. All commercially available reagents were stored as directed and used without further purification. Zinc dust (<10 μm) was obtained from Acros Organics (catalog # 198340010) and stored in a glove box under argon atmosphere. A 1-2 weeks supply was kept outside the glove box in a tightly sealed vial, but no special precautions were taken to avoid exposure to air. TPGS-750-M (CAS# 1309573-60-1) was synthesized according to the previously reported procedure.[1] A stock solution of 2% TPGS-750-M in water by weight was prepared in bulk from deionized water, and stored under air at rt until required, matching the commercially available formulation (Aldrich catalog #733857). Nitrated natural products were synthesized according to a literature procedure,[2] with individual isomers isolated by flash chromatography.

Equipment and Instrumentation. Reactions were performed on 1 mL scale, using 5 mL Biotage round bottom microwave vials stirred with 1/8 inch by 1/2 inch Fisher Scientific octaganol stir bars at 800 rpm, unless otherwise noted. Reaction progress was monitored by TLC using Merck KGaA Silica gel 60 F_{254} plates, and by GC using an Agilent 7890A gas chromatograph coupled to an FID or a 5975C VL mass selective detector. Products requiring isolation were purified by column chromatography utilizing Silicycle Silia-P 60 Å flash silica gel, or on a Biotage SP4 automated flash chromatography system. NMR spectra were obtained using a Varian Unity Inova 500 MHz NMR spectrometer in $CDCl_3$ unless otherwise noted, and processed via ACDLabs NMR Processor.

General Procedure for the Reduction of Aromatic Nitro Compounds. To a 5 mL round bottom vial equipped with a magnetic stir bar was added nitroarene (0.5 mmol) and ammonium chloride (0.6 mmol, 1.2 equiv), followed by 2 wt. % TPGS-750-M stock solution (1.0 mL), washing down the sides of the vial. The mixture was stirred for approximately 1 min to distribute and dissolve starting nitroarene. Zinc dust (2.5 mmol, 5.0 equiv) was added in a single batch to the resulting stirred emulsion, and the reaction was allowed to continue stirring at rt. Reaction progress was monitored by TLC / GC-MS. Upon complete disappearance of starting material and any nitroso or hydroxylamine intermediates visible by GC-MS (generally between 0.5 and 6 hours), the reaction was filtered through a 1 cm silica gel plug to remove water and zinc solids, and eluted by a minimal volume of EtOAc (generally between 5 and 10 mL). Alternately, the completed reaction was extracted three times by a minimum volume (generally 250 to 500 μL) of EtOAc or diethyl ether, and dried over anhydrous sodium sulfate. The resulting organic solution was concentrated *in vacuo*, and analyzed by GC-MS and NMR spectrometry, without further purification unless otherwise noted.

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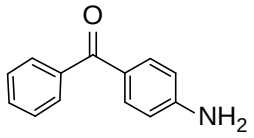
[1] Lipshutz, B. H.; Ghorai, S.; Abela, A. R.; Moser, R.; NIshikata, T.; Duplais, C.; Krasovskiv, A.; Gaston, R. D.; Gadwood, R. C.; *J. Org. Chem.* **2011**, 76, 4379.
[2] Wahba, A. E.; Peng, J.; Hamann, M. T. *Tetrahedron Lett.* **2009**, *50*, 3901.

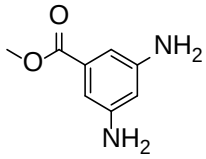
Experimental Procedures and Characterization

4-Aminobenzeophenone (1b, CAS# 1137-41-3)



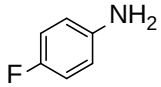
4-Nitrobenzophenone **1** (115 mg, 0.5 mmol), ammonium chloride (33 mg, 1.2 equiv), and zinc dust (160 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as a yellow solid (99 mg, 0.502 mmol, 99%). Spectral data matched that reported in the literature for 4-aminobenzophenone.[3] M^+ = 197; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (td, *J* = 2.30, 8.82 Hz, 2H), 7.72 - 7.75 (m, 2H), 7.55 (tt, *J* = 1.80, 7.50 Hz, 1H), 7.46 (tt, *J* = 1.30, 7.70 Hz, 2H), 6.84 - 6.91 (m, 2H).

Methyl 3,5-diaminobenzoate (2b, CAS# 1949-55-9)



Methyl 3-amino-5-nitrobenzoate **2** (98 mg, 0.5 mmol), ammonium chloride (30 mg, 1.2 equiv), and zinc dust (150 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as yellow needles (81.3 mg, 0.490 mmol, 98%). Spectral data matched that reported in the literature for methyl 3,5-diaminobenzoate.[4] M+ = 166; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (s, 2H), 6.18 (s, 1H), 3.85 (s, 3H).

4-Fluoroaniline (3b, CAS# 371-40-4)



4-Fluoronitrobenzene **3** (69 mg, 0.5 mmol), ammonium chloride (30 mg, 1.2 equiv), and zinc dust (151 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as a yellow oil (52 mg, 0.468 mmol, 96%). Spectral data matched that reported for 4-fluoroaniline.[5] M^+ = 111; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 - 6.88 (m, 2H), 6.60- 6.64 (m, 2H), 3.35 (br.s, 2H).

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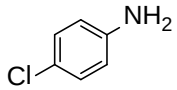
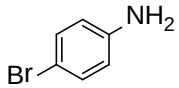
[3] Mannam, S., *Tetrahedron: Asymm.* **2009**, 20, 497
[4] Boije af Gennas, G., *J. Med. Chem.* **2009**, 52, 3969
[5] Wu, Z, *Eur. J. Org. Chem.* **2010**, 10, 1854

4-Chloroaniline (4b, CAS# 106-47-8)



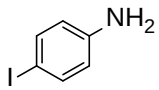
4-Chloronitrobenzene **4** (78 mg, 0.5 mmol), ammonium chloride (31 mg, 1.2 equiv), and zinc dust (150 mg, 5 equiv) were reacted for 5 h following the general procedure, yielding the product as tan crystals (60.5 mg, 0.476 mmol, 96%). Spectral data matched that reported in the literature for 4-chloroaniline.[6] M^+ = 127; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 – 7.10 (d, *J* = 8.04 Hz, 2H), 6.60 - 6.61 (d, *J* = 8.04 Hz, 2H), 3.64 (br.s, 2H).

4-Bromoaniline (5b, CAS# 106-40-1)



Following the general procedure, 4-bromonitrobenzene **5** (101 mg, 0.5 mmol), ammonium chloride (32 mg, 1.2 equiv), and zinc dust (150 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding 4-bromoaniline as orange crystals (79 mg, 0.476 mmol, 97%). Spectral data matched that reported in the literature for 4-bromoaniline.[7] M^+ = 171/173; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.22 – 7.25 (dt, *J* = 8.82, 3.10 Hz, 2H), 6.55 - 6.58 (dt, *J* = 8.82, 3.10 Hz, 2H), 3.53 (br.s, 2H).

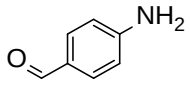
4-**Iodooaniline (6b, CAS# 540-37-4)**



4-Iodonitrobenzene **6** (126 mg, 0.5 mmol), ammonium chloride (31 mg, 1.2 equiv), and zinc dust (149 mg, 5 equiv) were reacted for 3 h following the general procedure, yielding the product as tan crystals (106 mg, 0.484 mmol, 96%). Spectral data matched that reported in the literature for 4-iodoaniline.[8] M^+ = 219; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 - 7.41 (d, *J* = 8.05, 2H), 6.46 - 6.48(d, *J* = 8.05, 2H), 2.88 (br.s, 2H).

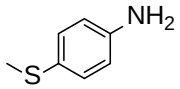
[6] Maddani, M. R., *Tetrahedron* **2010**, 66, 329
[7] Kamal, A., *Chemistry* **2009**, 15, 7215
[8] Ribeiro da Silva, M. A. V., *Chem. Phys. Lett.* **2006**, 422, 565

4-Aminobenzaldehyde (7b, CAS# 556-18-3)



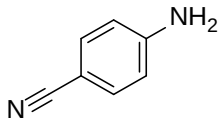
4-Nitrobenzaldehyde **7** (76mg, 0.5 mmol), ammonium chloride (29 mg, 1.2 equiv), and zinc dust (159 mg, 5 equiv) were reacted for 3 h following the general procedure and extracted by a minimal volume of diethyl ether, yielding the product as an orange solution showing a single signal by GCMS analysis. Product was then isolated via precipitation as the HCl salt by the addition of concentrated hydrochloric acid to the ether extract, followed by filtration, yielding very dark orange solid. (72 mg, 0.458 mmol, 92%). Spectral data matched that reported in the literature for 4-aminobenzaldehyde.[9] Note: Product appears stable in dilute organic solution but polymerizes upon concentration. M^+ = 121; ^{1}H NMR (500 MHz, D_2O) δ 9.85 (s, 1H), 7.98 (d, *J* = 8.30 Hz, 2H), 7.42 (d, *J* = 8.30 Hz, 2H), 3.65 (br.s, 2H).

4-(Methylthio)aniline (8b, CAS# 104-96-1)



4-(Methylthio)nitrobenzene **8** (84 mg, 0.5 mmol), ammonium chloride (33 mg, 1.2 equiv), and zinc dust (150 mg, 5 equiv) were reacted for 6 h following the general procedure, yielding the product as a yellow oil (67 mg, 0.483 mmol, 97%). Spectral data matched that reported in the literature for 4-(methyl-thio)anline.[10] M^+ = 139; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.56 Hz, 2H), 6.63 (d, *J* = 8.56 Hz, 2H), 3.35 - 3.51 (m, 2H), 2.41 (s, 3H).

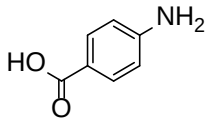
4-Aminobenzonitrile (9b, CAS# 873-74-5)



4-Nitrobenzonitrile **9** (73 mg, 0.5 mmol), ammonium chloride (31 mg, 1.2 equiv), and zinc dust (151 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as amber crystals (56.8 mg, 0.481 mmol, 98%). Spectral data matched that reported in the literature for 4-aminobenzonitrile.[11] M^+ = 118; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (td, *J* = 2.10, 6.80 Hz, 2H), 6.64 (td, *J* = 2.08, 6.75 Hz, 2H), 4.17 (br.s, 2H).

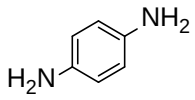
[9] Chen, Y., *Nature Chem.* **2011**, 3, 146
[10] Vo, G. D., *J. Am. Chem. Soc.* **2009**, 131, 11049
[11] von Bilow, R., *Zeitschrift fuer Naturforschung, B: Chem. Sci.* **2004**, 59, 1471

4-Aminobenzoic acid (10b, CAS# 150-13-0)



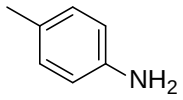
4-Nitrobenzoic acid **10** (83 mg, 0.5 mmol), ammonium chloride (32 mg, 1.2 equiv), and zinc dust (162 mg, 5 equiv) were reacted for 6 h following the general procedure. Upon full conversion, the pH was lowered using concentrated HCl, followed by extraction by EtOAc, and concentration *in vacuo*, yielding the desired product as off white crystals (64 mg, 0.467 mmol, 94%). Spectral data matched that reported in the literature for 4-aminobenzoic acid.[12] M^+ = 137; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.56, 2H), 6.65 (d, *J* = 8.56, 2H).

1,4-Benzenediamine (11b, CAS# 106-50-3)



4-Nitroaniline **11** (68 mg, 0.5 mmol), ammonium chloride (53 mg, 2.0 equiv), and zinc dust (152 mg, 5 equiv) were reacted for 1 h following the general procedure, and isolated by extraction with EtOAc, yielding purple crystals (53 mg, 0.489 mmol, 98%). Spectral data matched that reported in the literature for 1,4-benzenediamine.[13] M^+ = 108; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 4H), 3.33 (br.s, 4H).

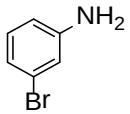
p-Aminotoluene (12b, CAS# 106-49-0)



4-Nitrotoluene **12** (67 mg, 0.489 mmol), ammonium chloride (32 mg, 1.2 equiv), and zinc dust (148 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the expected product as a beige solid (49 mg, 0.457 mmol, 94%). Spectral data matched that reported in the literature for p-toluidine.[14] M+ = 107; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 0.50, 8.56 Hz, 2H), 6.63 (td, *J* = 2.90, 8.30 Hz, 2H), 3.54 (br.s, 2H), 2.27 (s, 3H).

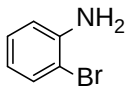
[12] Jimenez, V., *Tetrahedron* **2005**, 61, 5449
[13] Gao, X., J. Org. Chem. **2008**, 73, 6864
[14] Tseplin, E. E.; Tseplina, S. N.; Tuimedov, G. M.; Khvostenko, O. G. *Optics and Spectroscopy* **2009**, *107,* 244.

3-Bromoaniline (13b, CAS# 591-19-5)



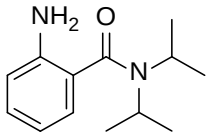
3-Bromonitrobenzene **13** (100 mg, 0.5 mmol), ammonium chloride (35 mg, 1.2 equiv), and zinc dust (163 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as orange crystals (81 mg, 0.471 mmol, 95%). Spectral data matched that reported in the literature for 3-bromoaniline.[15] M^+ = 171/173; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (t, *J* = 8.04 Hz, 1H), 6.87 (ddd, *J* = 0.91, 1.82, 7.92 Hz, 1H), 6.84 (t, *J* = 1.95 Hz, 1H), 6.59 (ddd, *J* = 0.91, 2.21, 8.04 Hz, 1H), 3.61 (br.s, 2H).

2-Bromoaniline (14b, CAS# 615-36-1)



2-Bromonitrobenzene **14** (101 mg, 0.5 mmol), ammonium chloride (31 mg, 1.2 equiv), and zinc dust (159 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as a dark yellow oil (79 mg, 0.459 mmol, 92%). Spectral data matched that reported in the literature for 2-bromoaniline.[16] M^+ = 171/173; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 1.30, 8.04 Hz, 1H), 7.10 (dt, *J* = 1.43, 7.59 Hz, 1H), 6.76 (dd, *J* = 1.43, 7.92 Hz, 1H), 6.62 (dt, *J* = 1.56, 7.66 Hz, 1H), 4.07 (br.s, 2H).

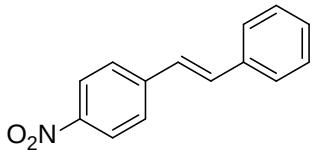
2-Amino-*N,N*-diisopropylbenzamide (15b, CAS# 103794-66-7)



4-Nitro-*N,N*-diisopropylbenzamide **15** (124 mg, 0.5 mmol), ammonium chloride (52 mg, 2.0 equiv), and zinc dust (157 mg, 5 equiv) were reacted for 3 h following the general procedure, yielding the product as off-white crystals (104 mg, 0.463 mmol, 94%). Spectral data matched that reported in the literature for 2-amino-*N,N*-diisopropylbenzamide.[17] M^+ = 220; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (td, *J* = 7.79, 1.56 Hz, 1H), 6.99 (dd, *J* = 7.40, 1.43 Hz, 1H), 6.67 - 6.74 (m, 2H), 3.55 - 4.00 (m, 1H), 1.35 (br. s., 7 H).

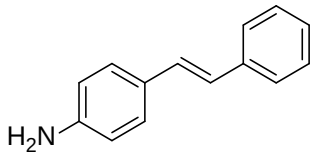
[15] Sharma, U., *Adv. Synth. Catal.* **2010**, 352, 1834
[16] Xu, H., *J. Org. Chem.* **2011**, 76, 2296
[17] Clayden, J., *J. Am. Chem. Soc.* **2008**, 130, 15193

4-Nitrostilbene (16, CAS# 4003-94-5)



Catalyst $Pd[P(t\text{-}Bu)_3]_2$ (10.3 mg, 0.02 mmol) and 4-iodo-nitrobenzene (149 mg, 1.0 mmol) were added under argon to a 5.0 mL microwave vial equipped with a large stir bar and sealed with a rubber septa. An aliquot of 2.5% TPGS-750-M in water solution (2.0 mL), triethylamine (420 uL, 3.0 mmol), and styrene (110 mg, 2.0 mmol) were added by syringe, and the resulting mixture was allowed to stir under argon at rt for 18 h. Upon disappearance of starting material by TLC, reaction mixture was filtered through a bed of silica gel and eluted by EtOAc to collect the coupled material. The resulting crude solid was purified by flash chromatography (2-25% EtOAc in Hexanes) and concentrated *in vacuo*, to afford the desired coupled product as a pale yellow solid (198 mg, 0.880 mmol, 88% yield). Spectral data matched that reported in the literature for 4-nitrostilbene.[18] M^+ = 225; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (ddd, *J* = 1.80, 2.60, 8.80 Hz, 2H), 7.64 (ddd, *J* = 1.80, 2.59, 8.82 Hz, 2H), 7.55 (ddd, *J* = 1.80, 2.60, 7.50 Hz, 5H), 7.40 (tt, *J* = 1.60, 7.80 Hz, 3H), 7.34 (tt, *J* = 2.10, 7.30 Hz, 1H), 7.27 (d, *J* = 15.60 Hz, 1H), 7.15 (d, *J* = 16.30 Hz, 1H).

4-Aminostilbene (16b, CAS# 834-24-2)

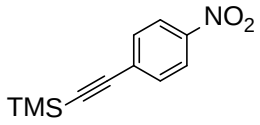


4-Nitrostilbene **16** (111 mg, 0.493 mmol) and ammonium chloride (31mg, 1.2 equiv.) were added to a 5 mL vial equipped with a large Teflon coated stirbar, followed by 2% TPGS-750-M / H_2O solution (1 mL) and zinc dust (131 mg, 4 equiv.). Reaction was stirred at rt for 2 h, at which point TLC analysis showed complete disappearance of starting material. The reaction was filtered through a bed of silica gel and eluted by EtOAc to collect the crude product, which was further purified by flash chromatography (10-50% EtOAc / hexanes), yielding the desired isolated product as a beige solid (89 mg, 0.456 mmol, 92%). Spectral data matched that reported in the literature for 4-aminostilbene.[19] Note: Added heat or extended reaction time can lead to undesired over reduction of the alkene bond. M^+ = 195; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 0.78, 8.04 Hz, 2H), 7.31 - 7.36 (m, 4H), 7.18 - 7.24 (m, 1H), 7.03 (d, *J* = 16.30 Hz, 1H), 6.92 (d, *J* = 16.60 Hz, 1H), 6.63 - 6.72 (m, 2H), 3.74 (br.s, 2H).

[18] Baruwati, B., Guin, D., Manorama, S. V. *Org. Lett.* **2007**, 9, 5377

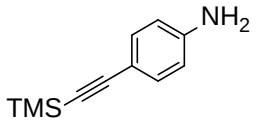
[19] Sorribes, I., Wienhoefer, G., Vicent, C., Junge, K., Llusar, R., Beller, M., *Angew. Chemie Int. Ed.* **2012**, 51, 7794

Trimethyl((4-nitrophenyl)ethynyl)silane (17, CAS# 899445-56-8)



4-Iodonitrobenzene (1244 mg, 5 mmol), trimethylsilylacetylene (0.78 mL, 5.5 mmol), CuI (20 mg, 0.1 mmol), and palladium (tetrakis)triphenylphosphine (58 mg, 0.05 mmol) were dissolved in a 1:1 mixture of triethylamine and dry THF (10 mL). The mixture was stirred overnight at rt, until GCMS showed complete disappearance of starting material. The reaction was concentrated *in vacuo*, and the residue was purified by flash chromatography (5-25% EtOAc in hexanes) yielding the product as pale yellow needles (516 mg, 94%). Alternately, the product was recrystallized from hexanes, affording similar purity while avoiding chromatography. Spectral data is consistent with literature reports of trimethyl((4-nitrophenyl)ethynyl)silane.[20] M^+ = 219; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.82 Hz, 2H), 7.57 - 7.62 (m, 2H), 0.27 (s, 9H).

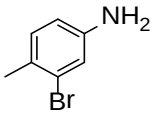
4-((Trimethylsilyl)ethynyl)aniline (17b, CAS# 75867-39-9)



Trimethyl((4-nitrophenyl)ethynyl)silane **17** (106 mg, 0.5 mmol), was reacted with ammonium chloride (35 mg, 1.2 equiv) and zinc dust (158 mg, 5 equiv) for 6 h following the general procedure, yielding the product as peach colored needles (90 mg, 0.476 mmol, 99%). Spectral data matched that expected for 4-((trimethylsilyl)ethynyl)-aniline. M^+ = 189; mp 93-95 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (td, *J* = 2.60, 8.56 Hz, 1H), 6.64 (td, *J* = 2.60, 8.56 Hz, 1H), 4.14 (br.s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.73, 133.34, 114.49, 112.49, 105.95, 91.34, -.011

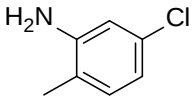
[20] Ruano, J. L. G., Aleman, J., Paredes, C. G., *Org. Lett.*, **2006,** 8, 2683

3-Bromo-4-methylaniline (18b, CAS# 7745-91-7)



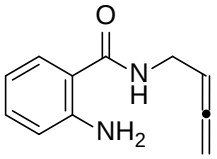
3-Bromo-4-methylnitrobenzene **18** (107 mg, 0.5 mmol), ammonium chloride (29 mg, 1.2 equiv), and zinc dust (150 mg, 5 equiv) were reacted for 4 h following the general procedure, yielding the product as a yellow solid (90 mg, 0.484 mmol, 98%). Spectral data matched that reported in the literature for 3-bromo-4-methylaniline.[21] M^+ =185/187; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, *J* = 8.04 Hz, 1H), 6.90 (d, *J* = 2.34 Hz, 1H), 6.54 (dd, *J* = 2.34, 8.04 Hz, 1H), 3.34 (br.s, 2H), 2.28 (s, 3H).

5-Chloro-2-methylaniline (19b, CAS# 95-79-4)



4-Chloro-2-nitrotoluene **19** (85 mg, 0.495 mmol), ammonium chloride (32 mg, 1.2 equiv), and zinc dust (170 mg, 5 equiv) were reacted for 3 h following the general procedure, yielding the product as a yellow oil (68 mg, 0.480 mmol, 97%). Spectral data matched that reported in the literature for 5-chloro-2-methylaniline.[22] M^+ = 141/143; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, *J* = 8.30 Hz, 1H), 6.64 - 6.68 (m, 2H), 3.65 (br.s, 2H), 2.12 (s, 3H).

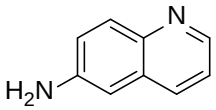
2-Amino-*N*-(propa-1,2-dien-1-yl)benzamide (20b)



2-Nitro-*N*-(buta-2,3-dien-1-yl)benzamide **20** (49.2 mg, 0.23 mmol), ammonium chloride (42 mg, 2.0 equiv) and zinc dust (79 mg, 5 equiv) were reacted for 0.5 h in a 2% aqueous solution of TPGS-750-M (0.5 mL), yielding the product as an off white solid (42.8 mg, 0.227 mmol, 99%). Spectroscopy is consistent with the expected 2-amino-*N*-(propa-1,2-dien-1-yl)benzamide product. Note: rapid reaction compared to other examples and mildly exothermic. Product fluorescent under UV light, no flight on GCMS, ESI/TOF M^+ = 211.11 (188.12 + sodium ion); mp 92-94 °C, ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.35 (dd, *J* = 1.30, 8.04 Hz, 1H), 7.22 (ddd, *J* = 1.56, 7.07, 8.24 Hz, 1H), 6.60 - 6.73 (m, 2H), 6.26 (br.s, 1H), 5.54 (br.s, 2H), 5.27 - 5.38 (m, 1H), 4.90 (td, *J* = 3.37, 6.75 Hz, 1H), 3.99 (tt, *J* = 3.37, 5.71 Hz, 2H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ 207.89, 168.80, 148.85, 132.20, 127.04, 116.99, 116.31, 115.75, 88.06, 77.37, 37.43.

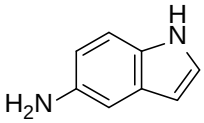
[21] Trunz, B. B.; *Eur. J. Med. Chem.* **2011**, 46, 1524
[22] Owen, W. S., *Mikrochimica et Ichnoanalytica Acta* **1963**, 19

6-Quinolinamine (24b, CAS# 580-15-4)



6-Nitroquinoline **24** (87 mg, 0.5 mmol), ammonium chloride (33 mg, 1.2 equiv), and zinc dust (158 mg, 5 equiv) were reacted for 6 h following the general procedure, yielding the product as a yellow crystalline solid (69.6 mg, 0.483 mmol, 97%). Spectral data matched that reported in the literature for 6-quinolinamine.[23] M^+ = 144; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 1.56, 4.15 Hz, 1H), 7.90 (d, *J* = 9.08 Hz, 1H), 7.87 (d, *J* = 8.05 Hz, 1H), 7.25 (dd, *J* = 4.28, 8.17 Hz, 1H), 7.14 (dd, *J* = 2.47, 8.95 Hz, 1H), 6.87 (d, *J* = 2.60 Hz, 1H), 3.87 (br.s, 2H).

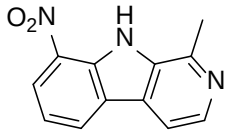
5-Aminoindole (25b, CAS# 5192-03-0)



5-Nitroindole **25** (80 mg, 0.5 mmol), ammonium chloride (33 mg, 1.2 equiv), and zinc dust (157 mg, 5 equiv) were reacted for 6 h following the general procedure, and isolated from a silica plug eluted by 1% MeOH in CH_2Cl_2, yielding the product as peach colored solid (64 mg, 0.485 mmol, 98%). Spectral data matched that reported in the literature for 5-aminoindole.[24] M^+ = 132; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (br.s, 1H), 7.20 (td, *J* = 0.80, 8.30 Hz, 1H), 7.13 (t, *J* = 2.72 Hz, 1H), 6.93 - 6.97 (m, 1H), 6.67 (dd, *J* = 2.21, 8.43 Hz, 1H), 6.37 (ddd, *J* = 1.04, 2.08, 3.11 Hz, 1H), 3.51 (br.s, 2H).

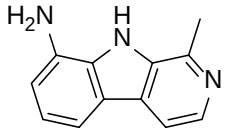
[23] Lundgren, R. J., *Angew. Chemie, Int. Ed.* **2010**, 49, 4071
[24] Sharma, U., *Adv. Synth. Catal.* **2010**, 352, 1834

8-Nitroharmane (26, CAS# 102207-02-3)



Commercially available harmane (Sigma-Aldrich catalog # 103276) was nitrated according to a literature procedure.[25] To a 10 mL round bottom flask was added harmane (102 mg, 0.560 mmol), and trifluoroacetic acid (3 mL). The solution was stirred in an ice bath at 0 °C for 5 min. Sodium nitrate (25 mg, 1.0 equiv) was added in a single batch, and the reaction was allowed to warm to rt with stirring. After 3 h, the reaction was quenched by the addition of ice, followed by ammonium hydroxide. The product was isolated by EtOAc extraction, and purification by flash chromatography (CH_2Cl_2/MeOH), yielded the desired product as a yellow oil (81 mg, 357 mmol, 64%). Spectral data matched that reported in the literature for 8-nitroharmane.[25] M^+ = 227; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.94 (br.s, 1H), 8.42 - 8.50 (m, 3H), 7.84 (d, *J* = 5.45 Hz, 1H), 7.39 (t, *J* = 7.80, 1H), 2.91 (s, 3H).

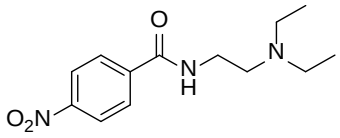
8-Aminoharmane (26b, CAS# 102206-92-8)



8-Nitroharmane **26** (57 mg, 0.25 mmol), ammonium chloride (28 mg, 2 equiv), and zinc dust (84 mg, 5 equiv) were reacted in 2 wt. % TPGS-750-M stock solution (0.5 mL) for 8 h, yielding the product as a yellow crystalline solid (43 mg, 0.218 mmol, 88%). Spectral data matched that expected for 8-aminoharmane with no further purification needed. M^+ = 197; mp decomp at 145 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.06 (br.s, 1H), 8.28 (d, *J* = 5.45 Hz, 1H), 7.76 (d, *J* = 5.45 Hz, 1H), 7.56 (dd, *J* = 7.92, 0.65 Hz, 1H), 7.12 (s, 1H), 6.89 (dd, *J* = 7.53, 0.52 Hz, 1H), 3.51 (br.s, 2H), 2.66 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.43, 137.80, 134.95, 132.41, 131.10, 129.38, 122.63, 121.00, 113.52, 113.31, 112.21, 19.93.

[25] Wahba, A. E., *Tetrahedron Lett.* **2009**, 50, 3901

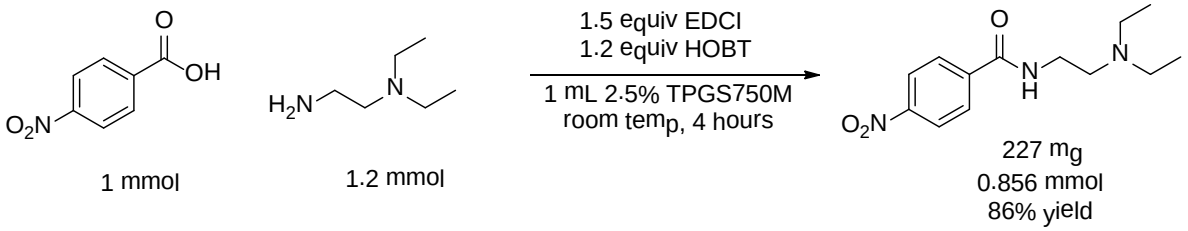
N-(2-(Diethylamino)ethyl)-4-nitrobenzamide (29, CAS# 1664-62-4)



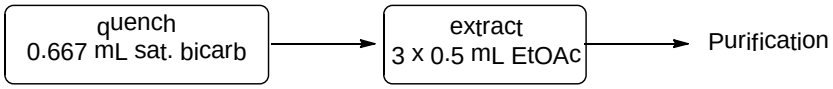
To a 5 mL round bottom vial was added nitrobenzoic acid **27** (167 mg, 1 mmol), EDCI (238 mg, 1.5 equiv) and 182 mg HOBt (182 mg, 1.2 equiv). TPGS-750-M stock solution (2 wt. %, 1 mL) was added and the reaction was stirred for approximately 1 min to form an emulsion, at which point *N,N*-diethyl-ethylenediamine **28** (125 mg, 1.1 equiv) was added in a single portion. Stirring was continued for 4 h at rt, at which time GCMS analysis showed full conversion. The reaction was quenched by a saturated solution of sodium bicarbonate (667 µL), extracted three times by EtOAc (3 x 500 µL), dried over anhydrous sodium sulfate, and concentrated *in vacuo* yielding the coupled product as a viscous yellow oil (227 mg, 0.856 mmol, 86%). Spectral data matched that reported in the literature for *N*-(2-(diethylamino)ethyl)-4-nitrobenzamide.[26] M^+ = 266 (key fragment at 193); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (dt, *J* = 8.8, 2.1 Hz, 2H), 7.93 (dt, *J*=8.8, 2.1 Hz, 2H), 7.10 (br.s, 1H), 3.50 (dt, *J* = 6.2, 5.2 Hz, 2H), 2.67 (t, *J* = 6.0 Hz, 2H), 2.58 (q, *J* = 7.1 Hz, 4H), 1.04 (t, *J* = 7.1 Hz, 6H).

E Factor Calculations:

Reaction



Workup



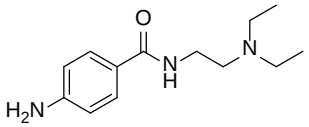
1.00g Water (TPGS)
1.33g EtOAc
\+ 0.67g Water (bicarb)
3.00g Solvent Waste

E-Factor = 3.00 / 0.227 = **13**

Organics E-Factor = 1.33 / 0.227 = **6**

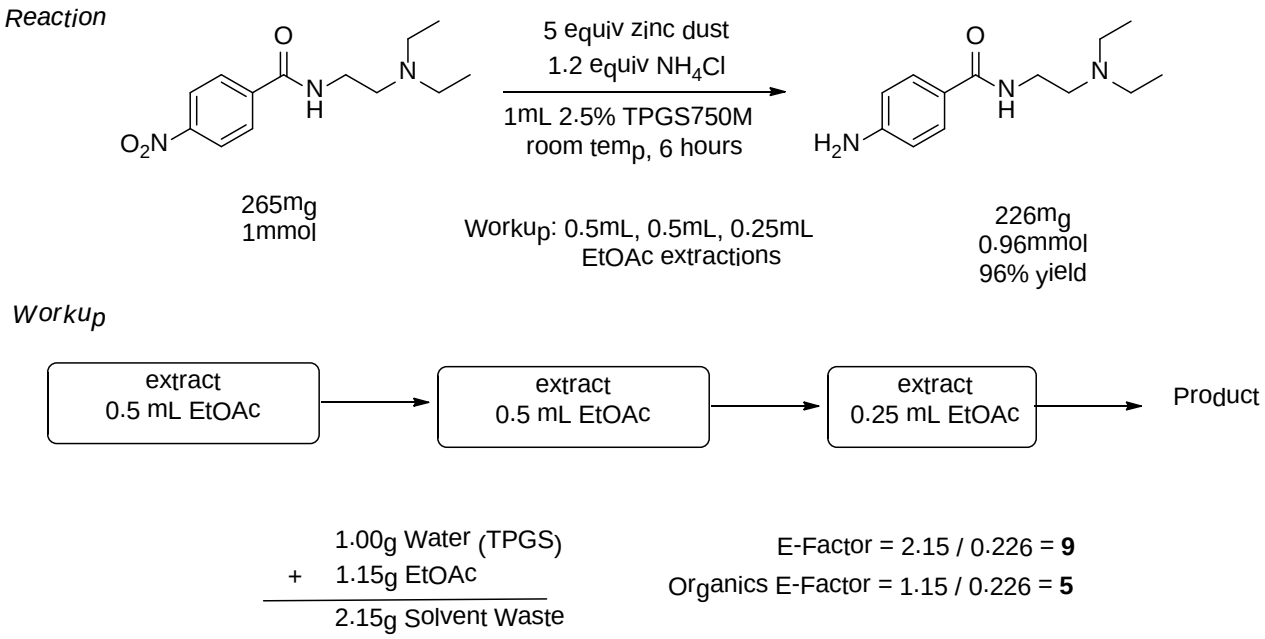
[26] Shannon, S. K., Peacock, M. J., Kates, S. A., Barany, G., *J. of Comb. Chem.* **2003**, 5, 860

Procainamide (30, CAS# 51-06-9)



N-(2-(Diethylamino)ethyl)-4-nitrobenzamide **29** (265 mg, 1.0 mmol), ammonium chloride (61 mg, 1.2 equiv), and zinc dust (314 mg, 5 equiv) were reacted in an aqueous solution of TPGS-750-M (1 mL, 2 weight %) at rt for 6 h, at which point TLC and GCMS analysis showed complete conversion. Three extractions by a minimal volume of EtOAc (500 µL, 500 µL, 250 µL) and concentration *in vacuo* yielded the expected product as a pale yellow solid (226 mg, 0.962 mmol, 96%). Spectral data matched that reported in the literature for procainamide active pharmaceutical ingredient.[27] M^+ = 235; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1(br. s., 1H), 7.72 (d, *J* = 8.81 Hz, 2H), 6.59 (d, *J* = 8.68 Hz, 2H), 3.80 (t, *J* = 5.12 Hz, 2H), 3.23 (t, *J* = 5.10 Hz 2H), 3.03 - 3.20 (m, 4H), 1.32-1.35 (t, *J* = 7.26 Hz, 6H).

E Factor Calculations:

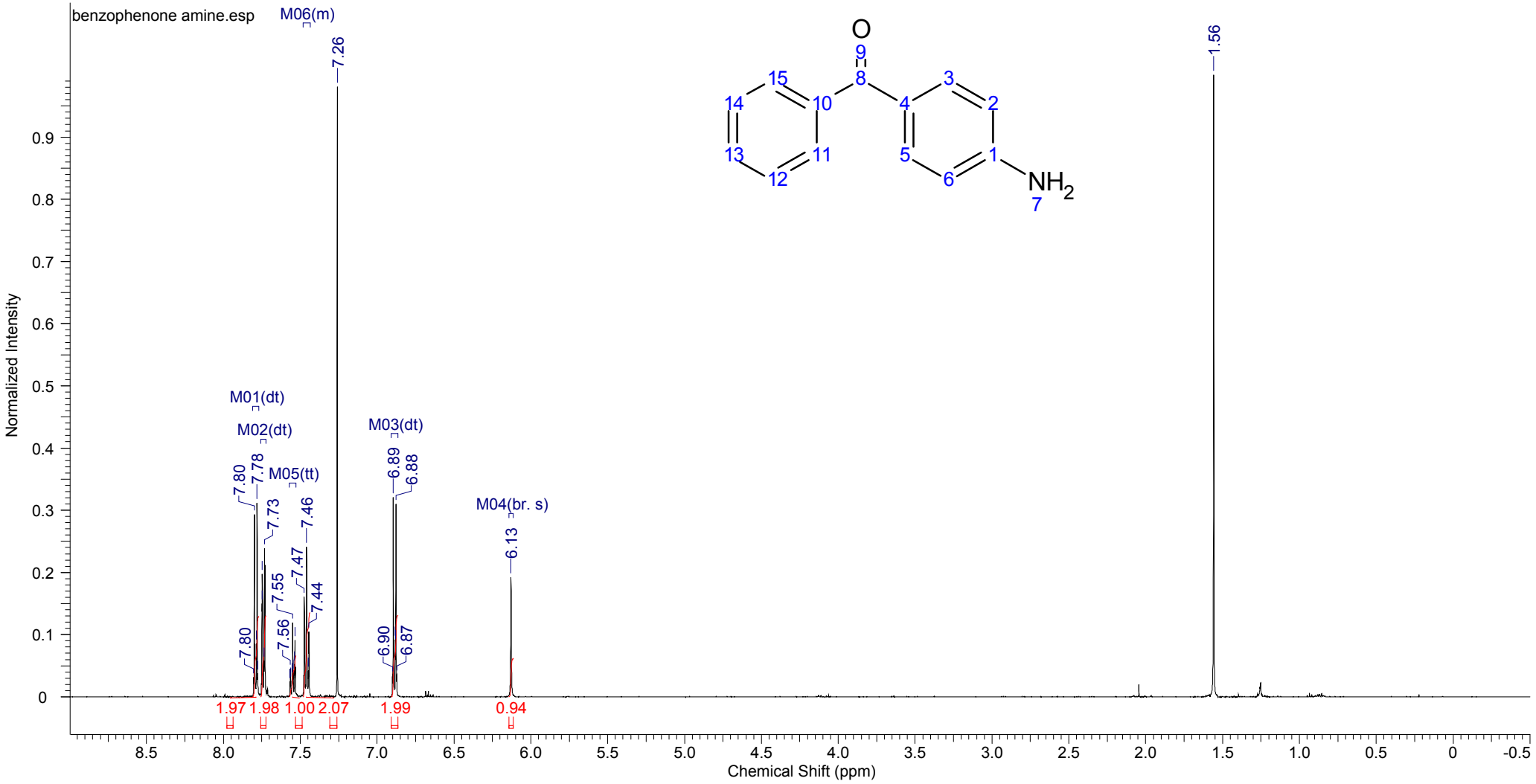


[27] Li, Q., Guo, D., Qian, H., Liu, Y., *Eur. J. Org. Chem.* **2012** , 21, 3962

Formula $C_{13}H_{11}NO$	FW	197.2325

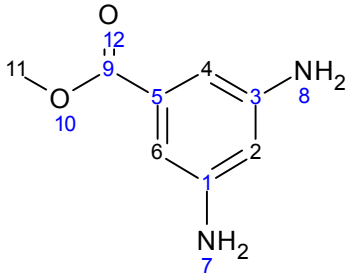
Acquisition Time (sec)	2.5001	**Comment**	Nitrobenzophenone Reduction			**Date**	Sep 16 2013
Date Stamp	Sep 16 2013	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0024-001.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	16	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	42.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

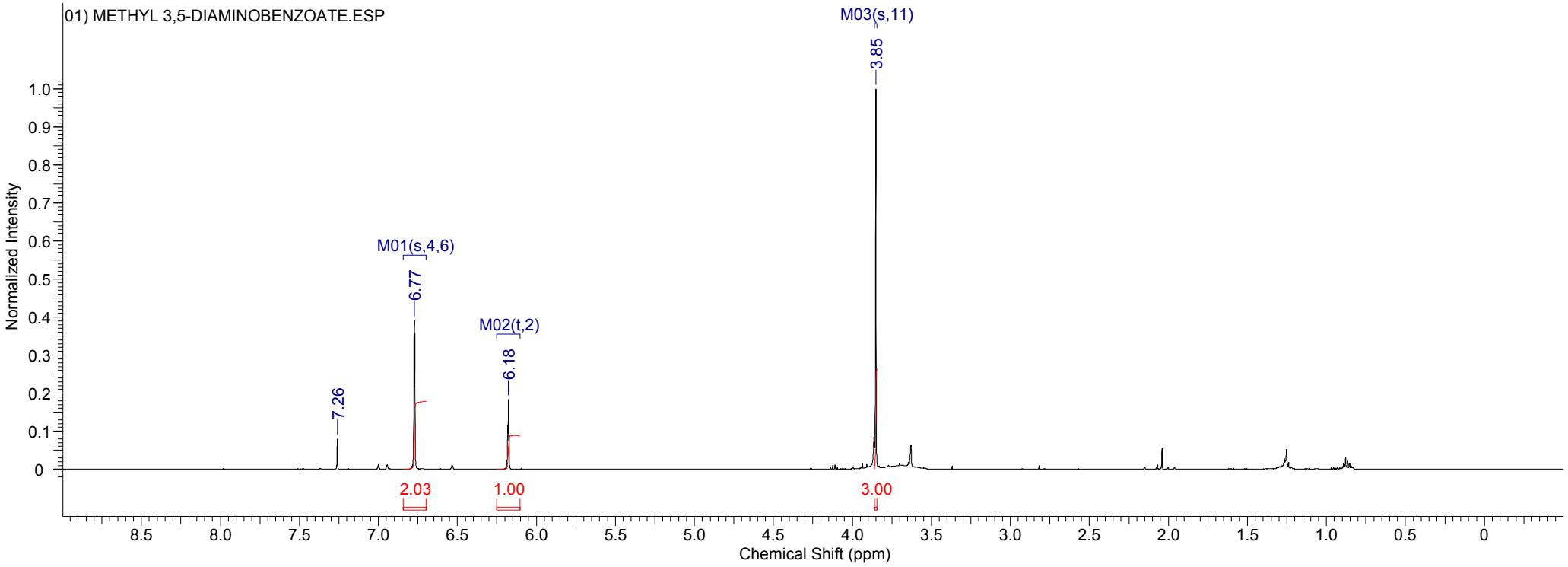
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.79 (td, J = 2.10, 8.82 Hz, 2H), 7.74 (td, J = 1.30, 7.01 Hz, 2H), 7.55 (tt, J = 1.80, 7.50 Hz, 1H), 7.44 - 7.48 (m, J = 1.60, 1.60, 7.80, 7.80 Hz, 2H), 6.89 (td, J = 1.80, 8.82 Hz, 2H), 6.13 (br. s, 2H)



Formula $C_8H_{10}N_2O_2$		***FW***	166.1772				
Acquisition Time (sec)	2.5001	***Comment***	After silica plug	***Date***	May 14 2012	***Date Stamp***	May 14 2012
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0028-CR.FID\FID					***Frequency (MHz)***	499.86
Nucleus	1H	***Number of Transients***	16	***Original Points Count***	21259	***Points Count***	32768
Pulse Sequence	s2pul	***Receiver Gain***	36.00	***Solvent***	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	8503.40	***Temperature (degree C)***	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.77 (s, 2H), 6.18 (t, J = 2.08 Hz, 1H), 3.85 (s, 3H)

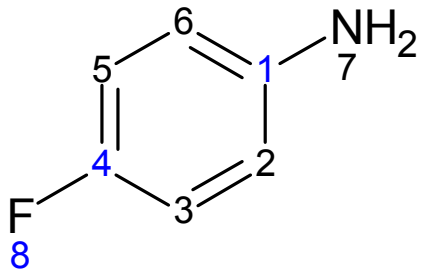


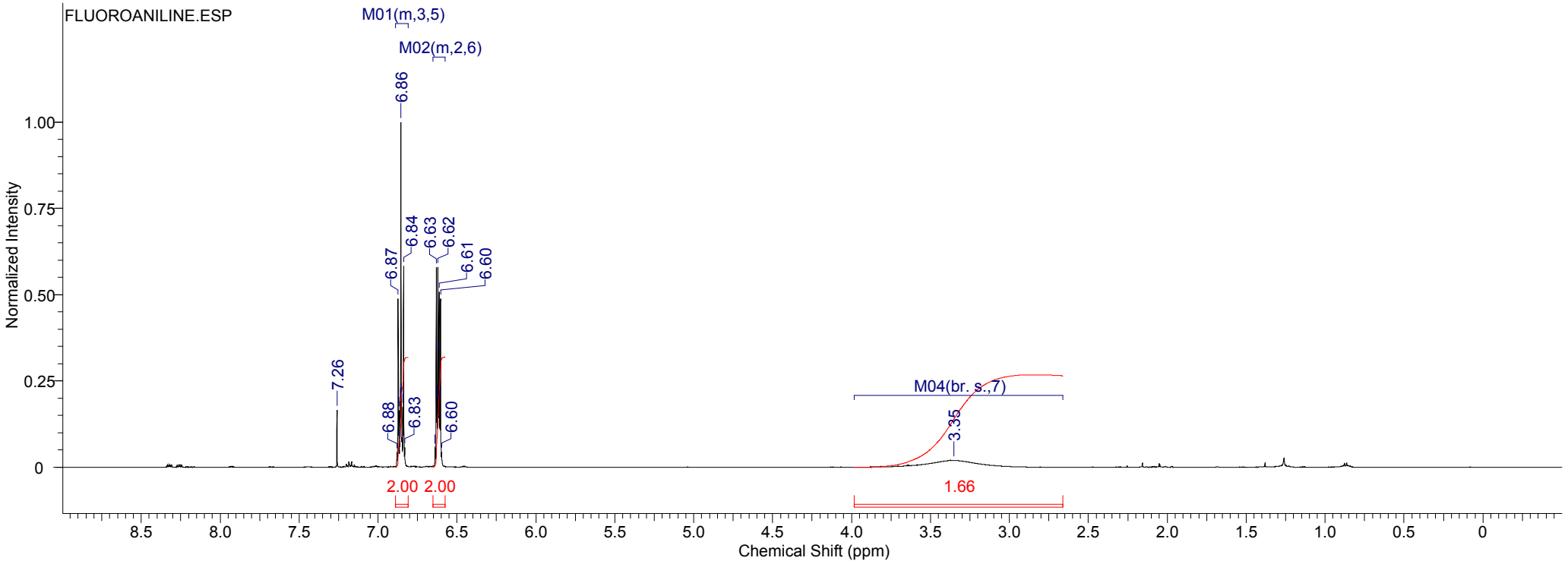


Formula	C_6H_6FN	FW	111.1169

Acquisition Time (sec)	2.5001	Comment	STANDARD 1H OBSERVE - profile			Date	Jul 20 2012
Date Stamp	Jul 20 2012	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0033-CR2.FID\FID				
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	16	Original Points Count	21259
Points Count	32768	Pulse Sequence	s2pul	Receiver Gain	36.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.81 - 6.89 (m, 2H), 6.57 - 6.65 (m, 2H), 3.35 (br. s., 2H)

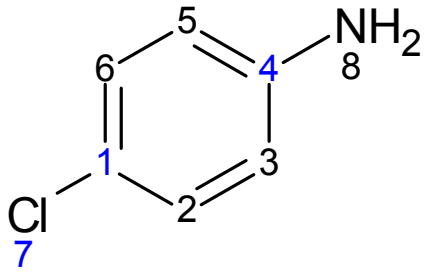


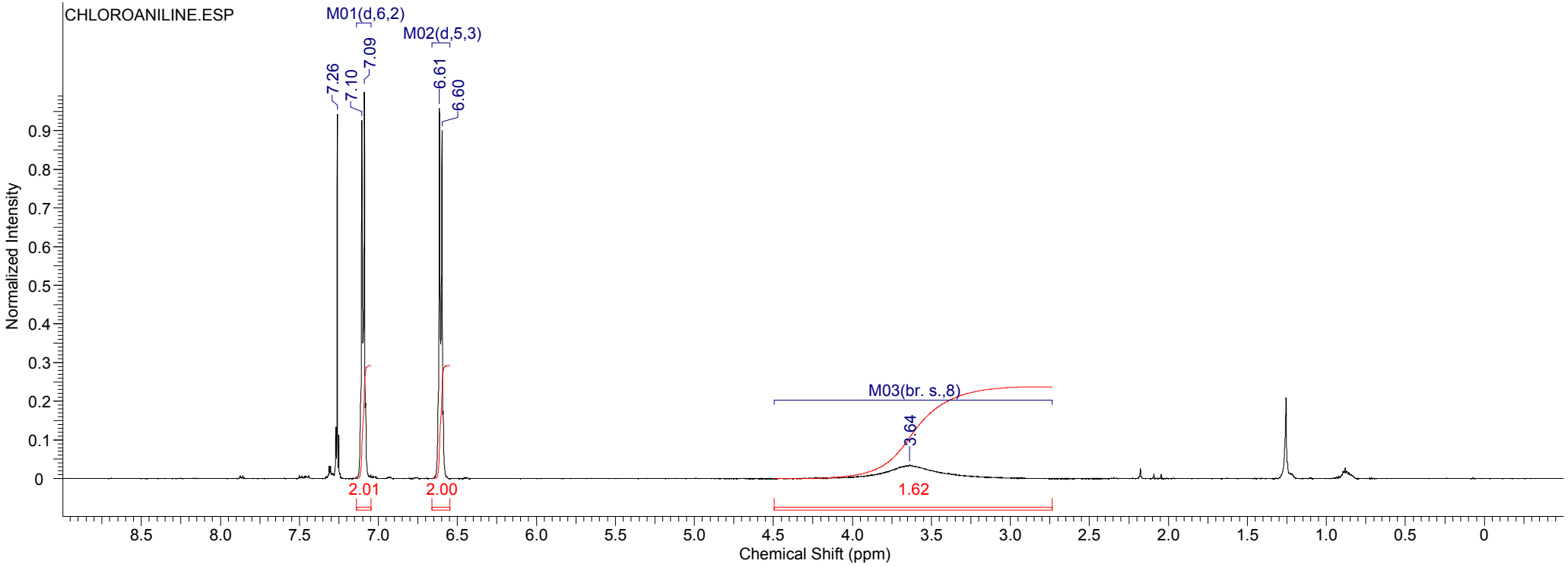


Formula	C_6H_6ClN	FW	127.5715

Acquisition Time (sec)	2.5001	Comment	crude 4-chloro-aniline			Date	Jun 1 2012
Date Stamp	Jun 1 2012	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0032-A-CR.FID\FID				
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	32	Original Points Count	21259
Points Count	32768	Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.10 (d, J = 8.04 Hz, 2H), 6.61 (d, J = 8.30 Hz, 2H), 3.64 (br. s., 2H)

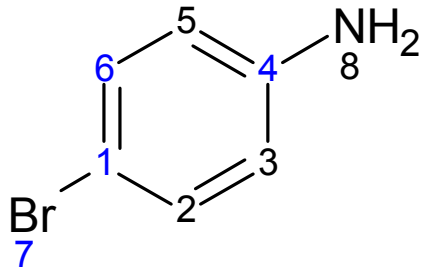


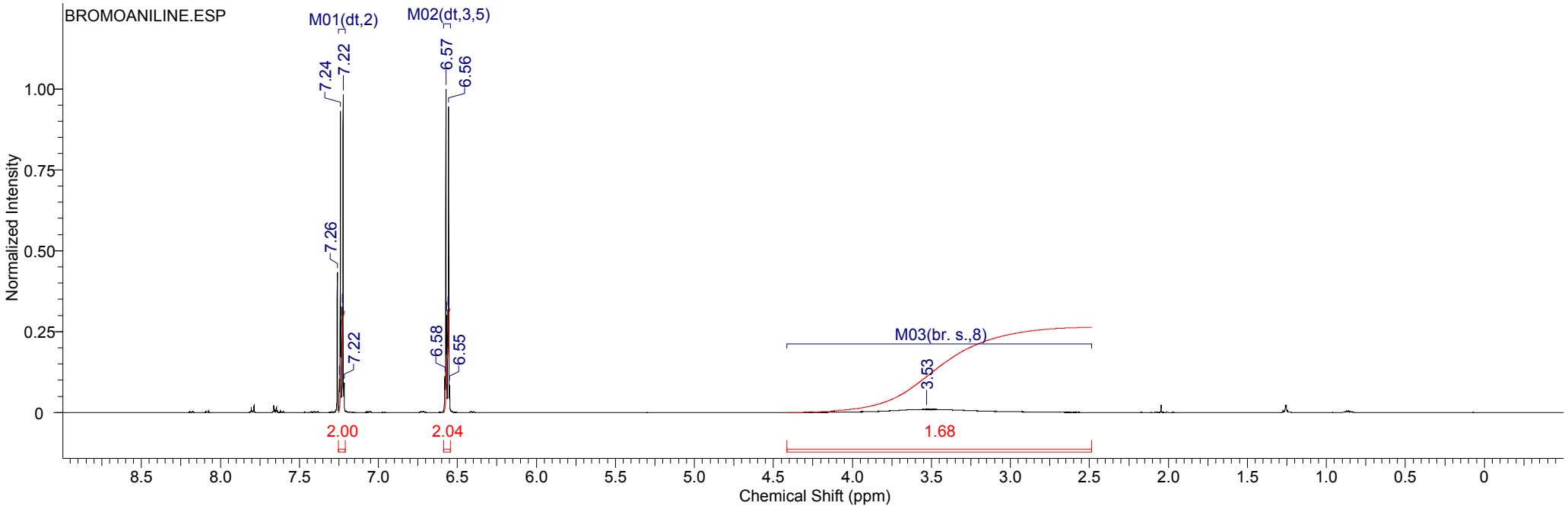


Formula	C_6H_6BrN	FW	172.0225

Acquisition Time (sec)	2.5001	Date	Jul 20 2012	Date Stamp	Jul 20 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0034-CR2.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.23 (td, J = 3.10, 8.82 Hz, 2H), 6.56 (td, J = 3.10, 8.82 Hz, 2H), 3.53 (br. s., 2H)

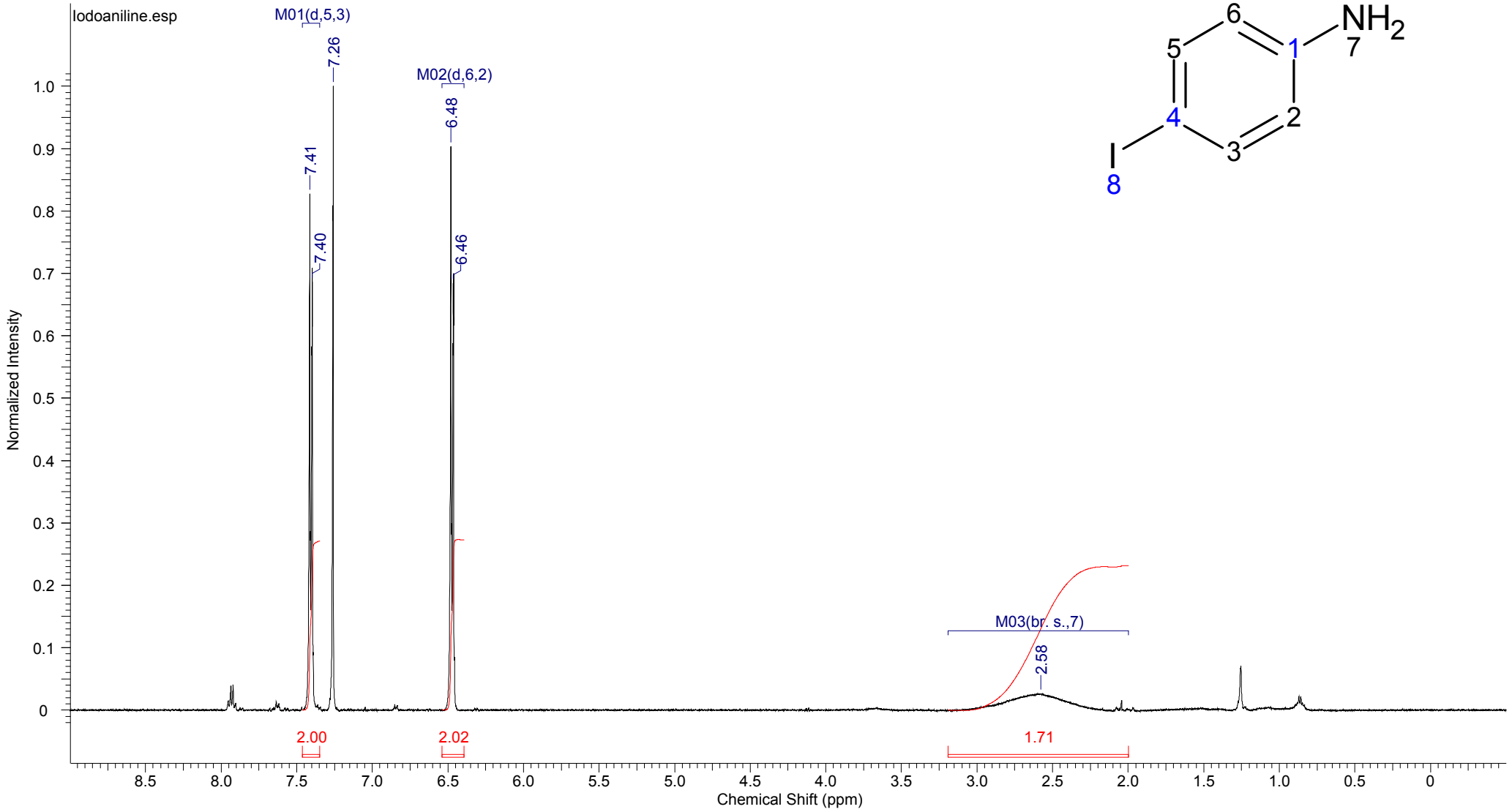




Formula	C_6H_6IN	FW	219.0230

Acquisition Time (sec)	2.5001	**Comment**	Iodide rerun 5eq Zn 1eq NH4Cl			**Date**	Jun 6 2012
Date Stamp	Jun 6 2012	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0038-CR.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	16	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	42.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2495.3828	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

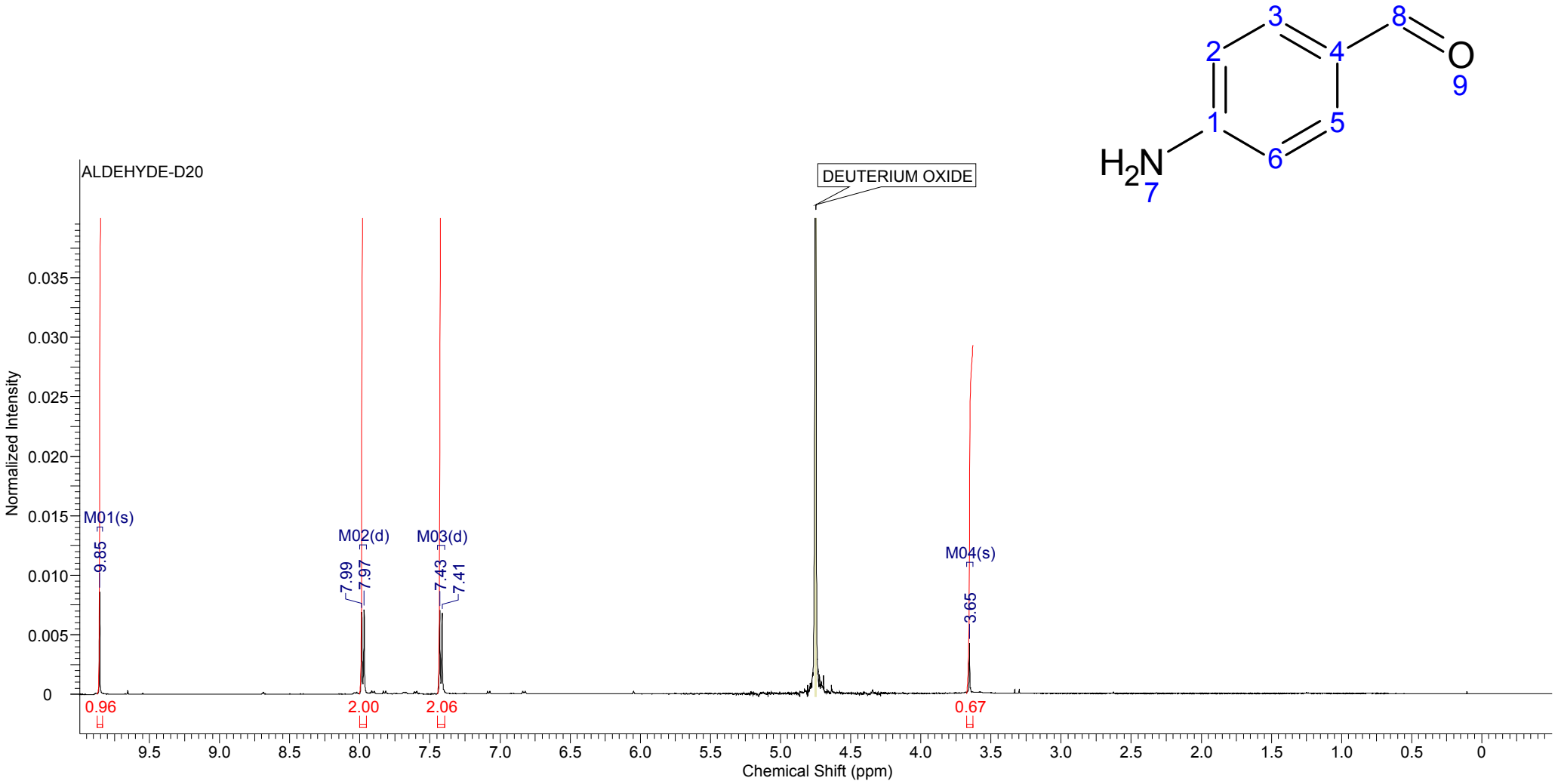
^{1}H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.41 (d, *J*=8.05 Hz, 2 H), 6.47 (d, *J*=8.04 Hz, 2 H), 2.58 (br. s., 2 H)



Formula	C_7H_7NO	FW	121.1366

Acquisition Time (sec)	2.5001	Comment				Date	Oct 22 2013
Date Stamp	Oct 22 2013	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\ALDEHYDE-D20.FID\FID				
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	32	Original Points Count	21259
Points Count	32768	Pulse Sequence	s2pul	Receiver Gain	36.00	Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	2544.4438	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

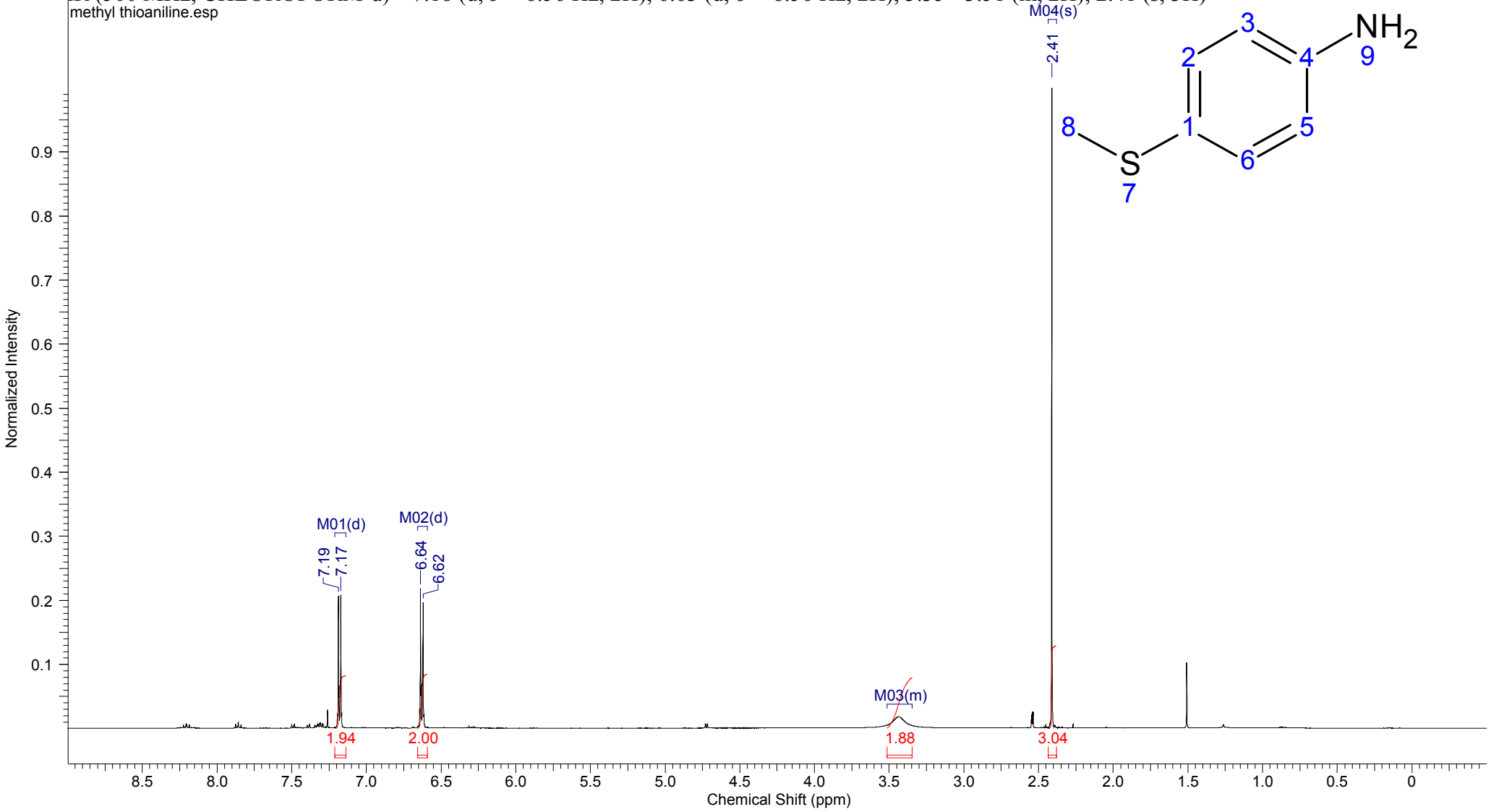
^{1}H NMR (500 MHz, DEUTERIUM OXIDE) δ 9.85 (s, 1H), 7.98 (d, J = 8.30 Hz, 2H), 7.42 (d, J = 8.30 Hz, 2H), 3.65 (s, 2H)



Formula	C_7H_9NS	FW	139.2181

Acquisition Time (sec)	2.5001	Date	Jul 12 2012	Date Stamp	Jul 12 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0049-CR.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	32.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

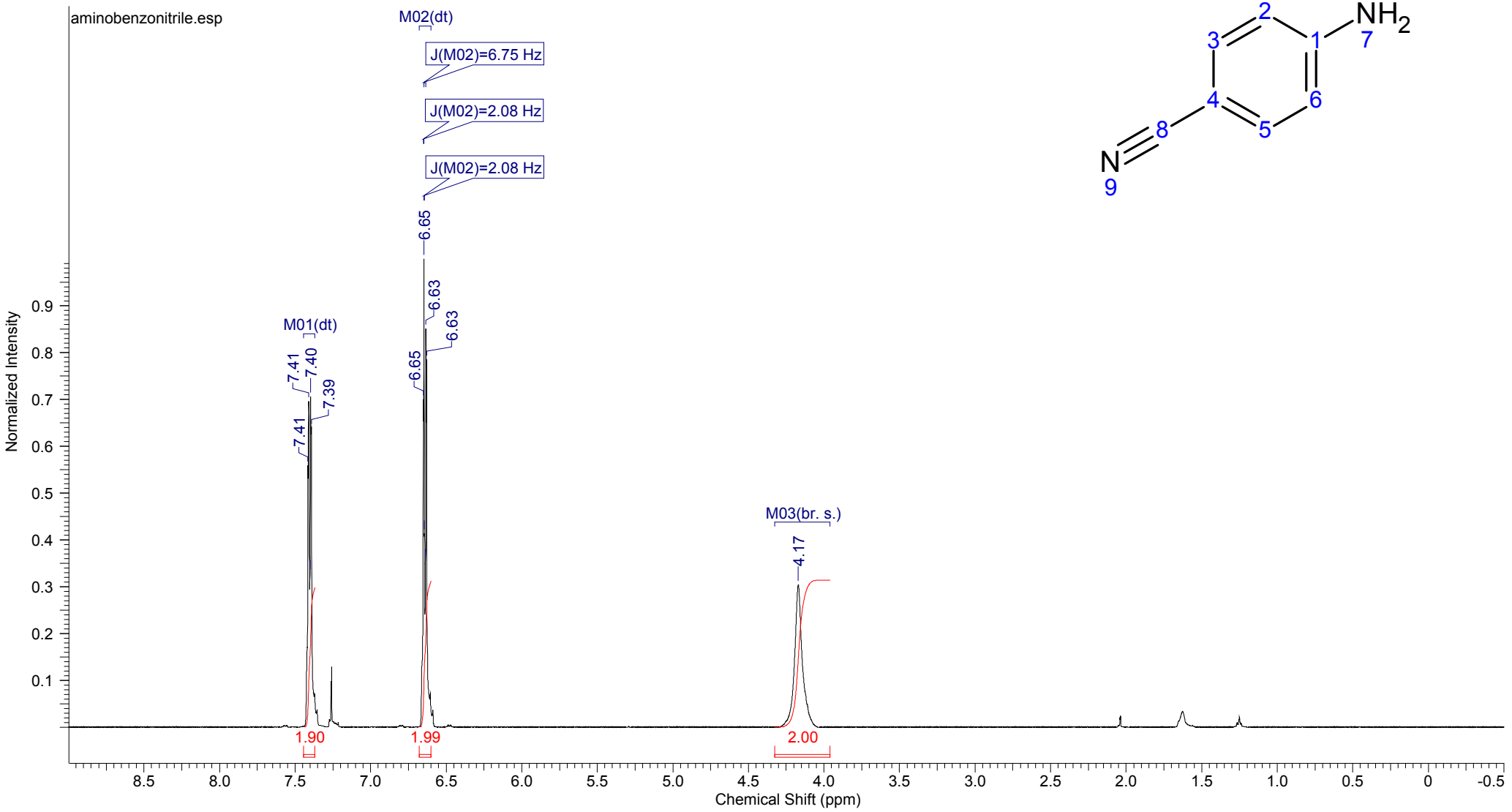
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.18 (d, J = 8.56 Hz, 2H), 6.63 (d, J = 8.56 Hz, 2H), 3.35 - 3.51 (m, 2H), 2.41 (s, 3H)



Formula $C_7H_6N_2$	FW	118.1359

Acquisition Time (sec)	2.5001	**Comment**	aminobenzonitrile rerun			**Date**	Aug 30 2013
Date Stamp	Aug 30 2013	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\AMINO-BENZONITRILE.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	16	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	36.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

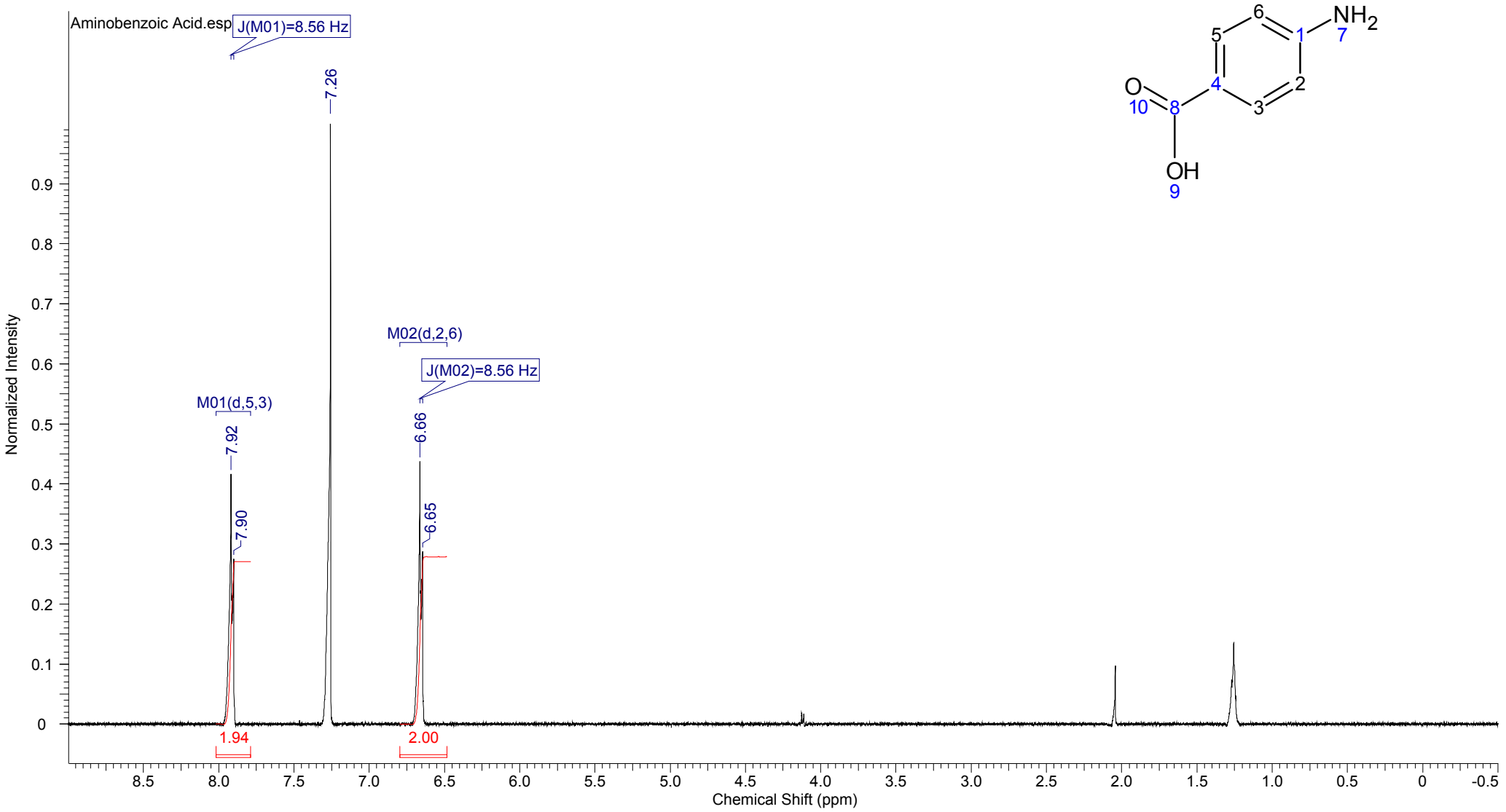
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.40 (td, J = 2.10, 6.80 Hz, 2H), 6.64 (td, J = 2.08, 6.75 Hz, 2H), 4.17 (br. s., 2H)



Formula $C_7H_7NO_2$	FW	137.1360

Acquisition Time (sec)	2.5001	**Date**	Aug 29 2013	**Date Stamp**	Aug 29 2013		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\AMINOBENZOIC_ACID.FID\FID					**Frequency (MHz)**	499.86
Nucleus	1H	**Number of Transients**	8	**Original Points Count**	21259	**Points Count**	32768
Pulse Sequence	s2pul	**Receiver Gain**	42.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

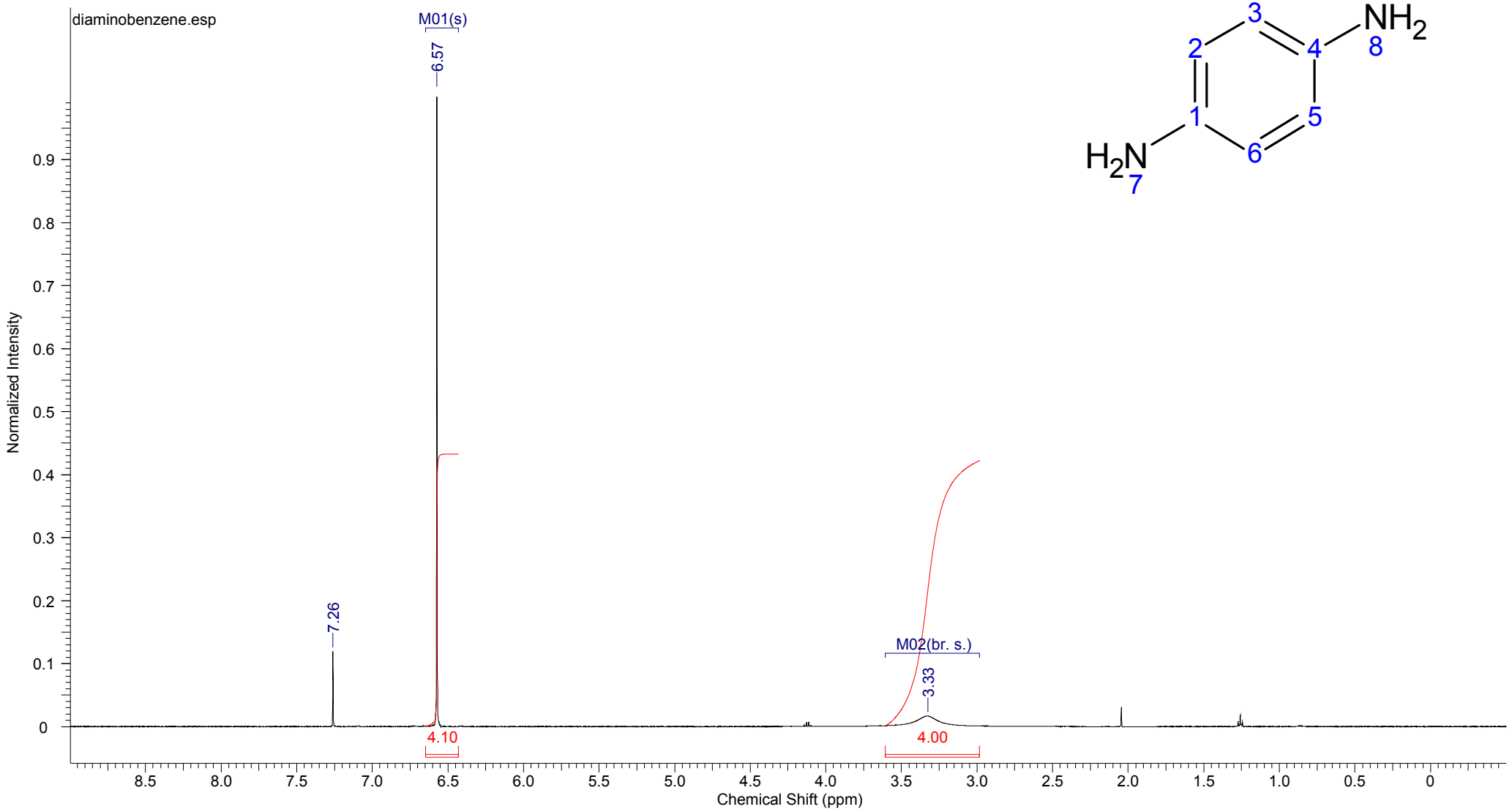
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.91 (d, J = 8.56 Hz, 2H), 6.65 (d, J = 8.56 Hz, 2H)



Formula $C_6H_8N_2$	FW	108.1411

Acquisition Time (sec)	2.5001	Date	Jul 23 2012	Date Stamp	Jul 23 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0050-CR.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

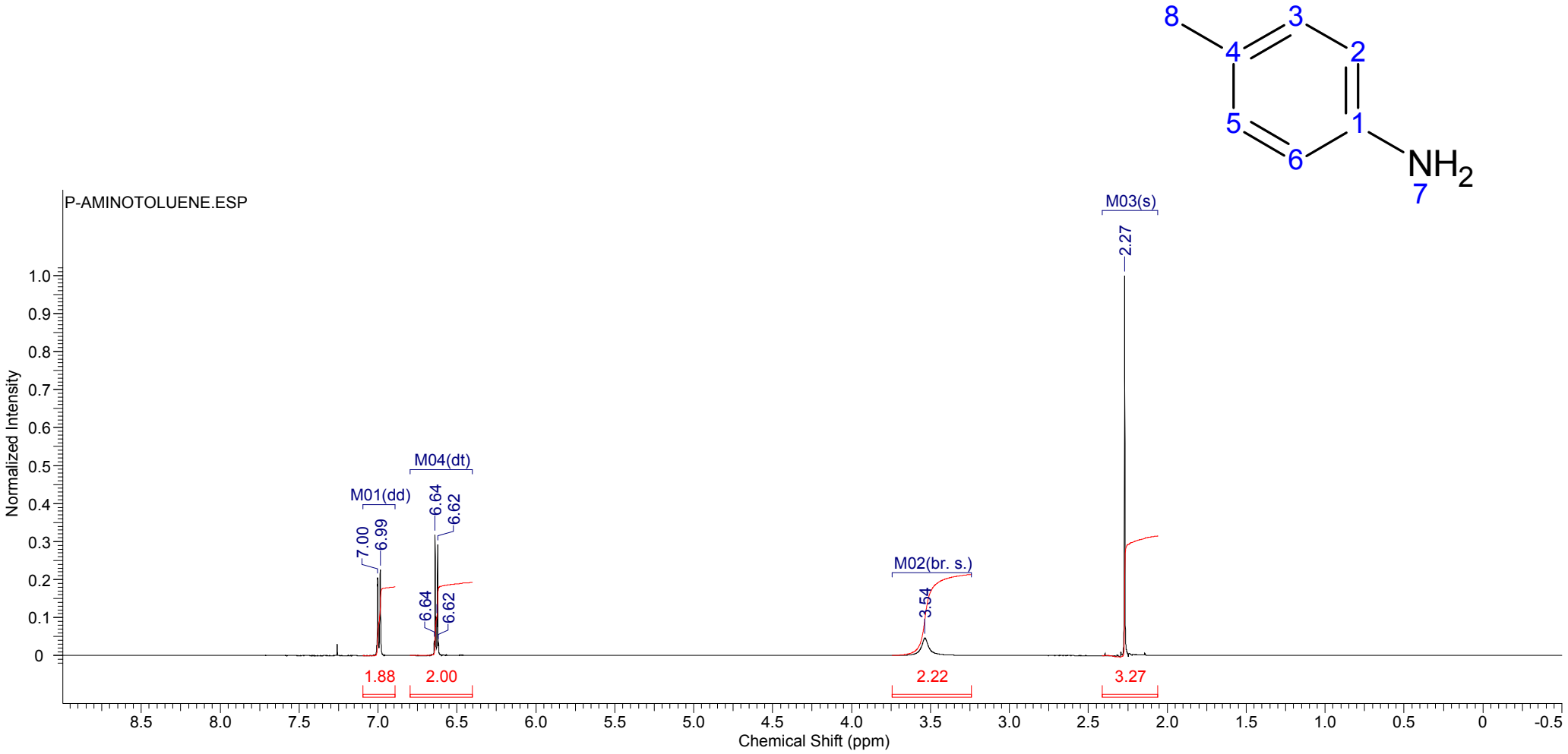
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.57 (s, 4H), 3.33 (br. s., 4H)



Formula C_7H_9N	FW	107.1531

Acquisition Time (sec)	2.5001	**Comment**	nitrotoluene product			**Date**	Sep 9 2013
Date Stamp	Sep 9 2013	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0062-001.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	8	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	30.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

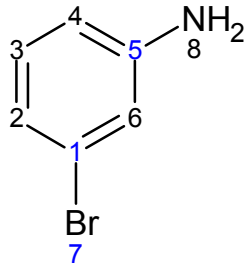
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.99 (dd, J = 0.50, 8.56 Hz, 2H), 6.63 (td, J = 2.90, 8.30 Hz, 2H), 3.54 (br. s., 2H), 2.27 (s, 3H)

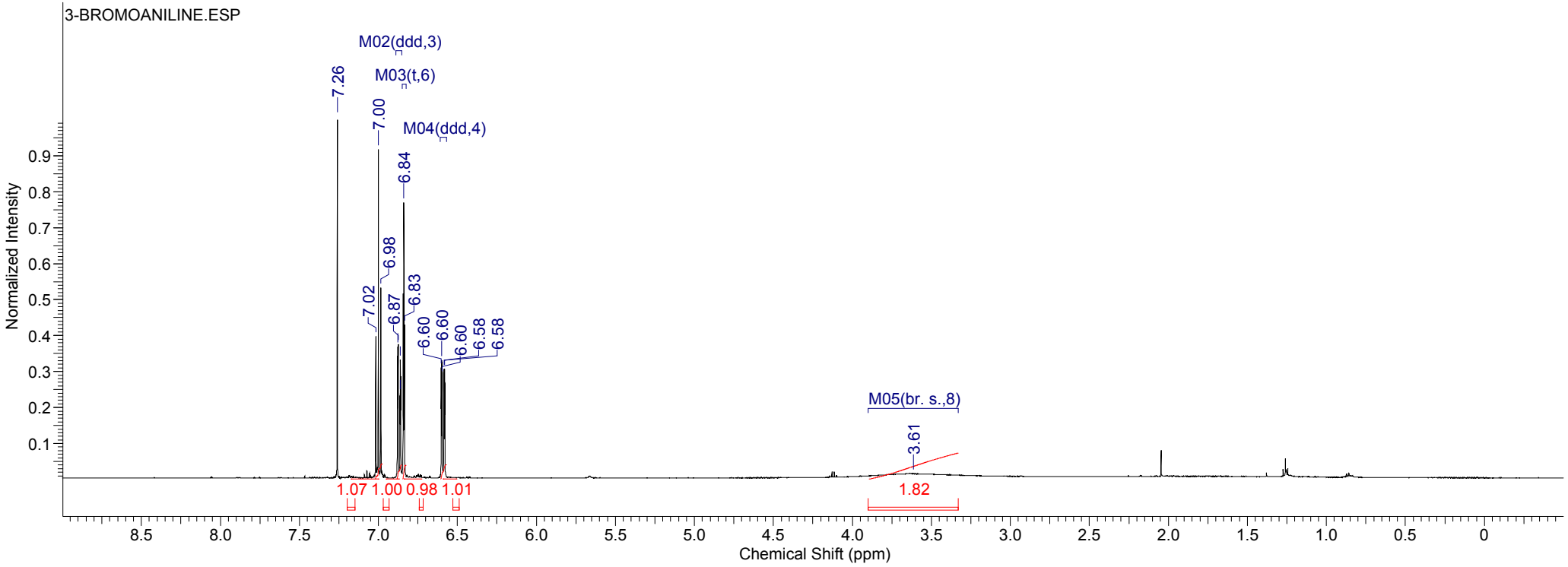


Formula	C_6H_6BrN	FW	172.0225

Acquisition Time (sec)	2.5001	Date	Jul 5 2012	Date Stamp	Jul 5 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0055-CR.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.00 (t, J = 8.00 Hz, 1H), 6.87 (ddd, J = 0.91, 1.82, 7.92 Hz, 1H), 6.84 (t, J = 1.95 Hz, 1H), 6.59 (ddd, J = 0.91, 2.21, 8.04 Hz, 1H), 3.61 (br. s., 2H)

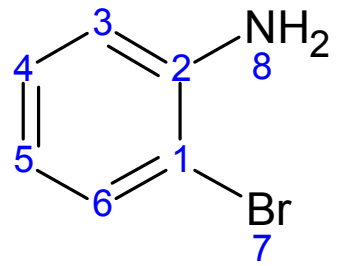


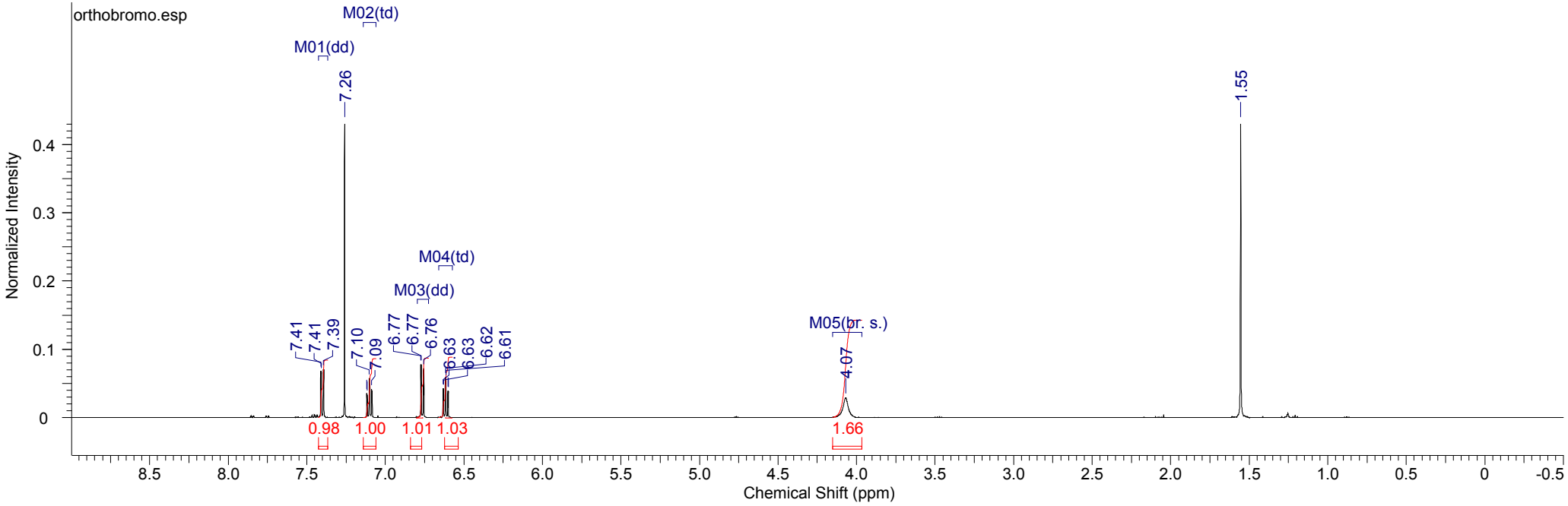


Formula	C_6H_6BrN	FW	172.0225

Acquisition Time (sec)	2.5001	Date	Oct 23 2013	Date Stamp	Oct 23 2013		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\O-BROMO.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	32	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.40 (dd, *J* = 1.30, 8.04 Hz, 1H), 7.10 (dt, *J* = 1.43, 7.59 Hz, 1H), 6.76 (dd, *J* = 1.43, 7.92 Hz, 1H), 6.62 (dt, *J* = 1.56, 7.66 Hz, 1H), 4.07 (br. s., 2H)

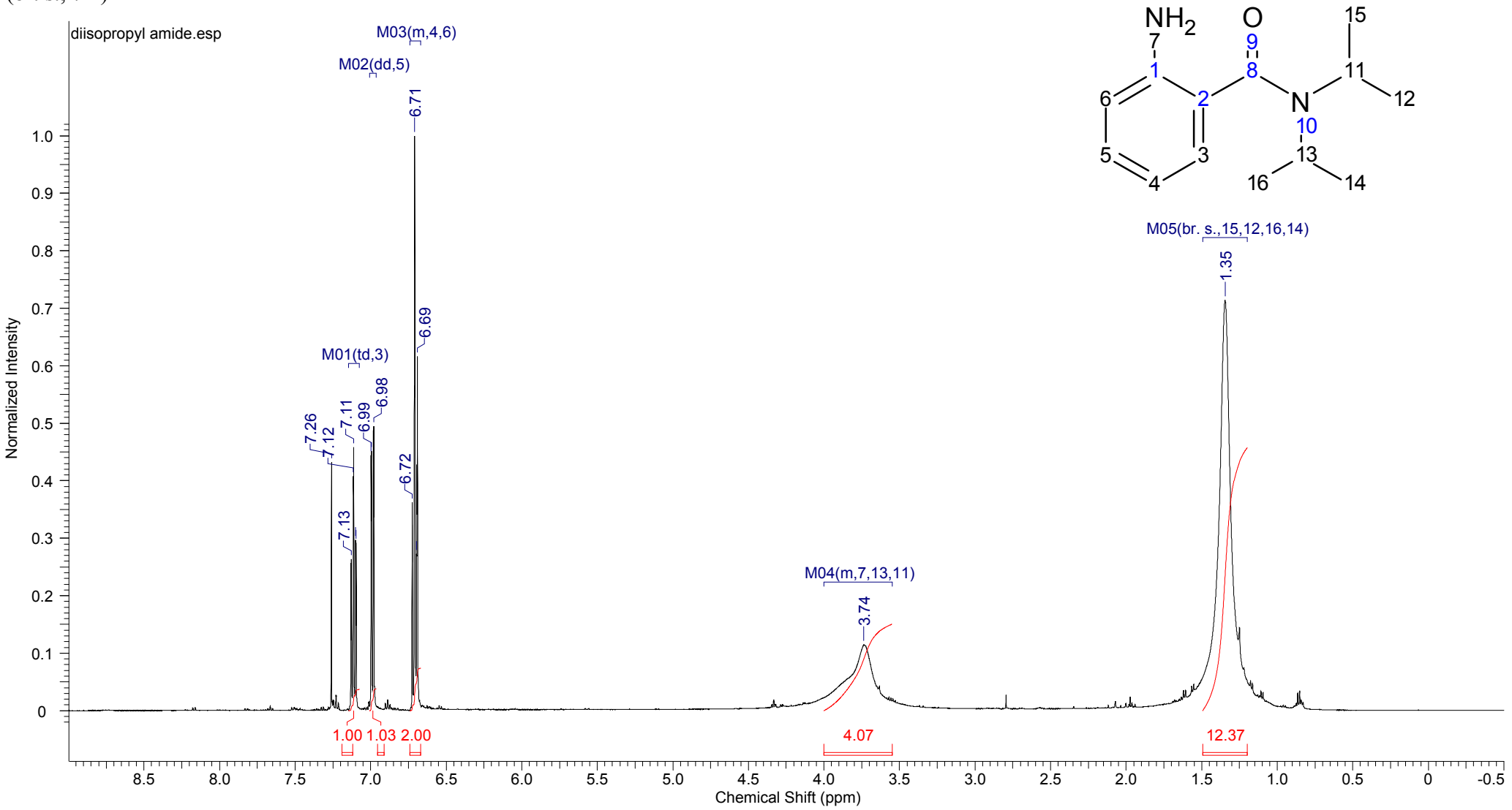




Formula	$C_{13}H_{20}NO_2$	FW	220.3107

Acquisition Time (sec)	2.5001	Date	Aug 2 2013	Date Stamp	Aug 2 2013	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\2046-CR.FID\FID		
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	30.00	Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	2494.9937
Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE				

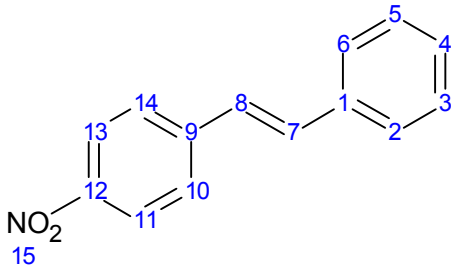
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.11 (dt, *J* = 1.56, 7.79 Hz, 1H), 6.99 (dd, *J* = 1.43, 7.40 Hz, 1H), 6.67 - 6.74 (m, 2H), 3.55 - 4.00 (m, 1H), 1.35 (br. s., 7H)

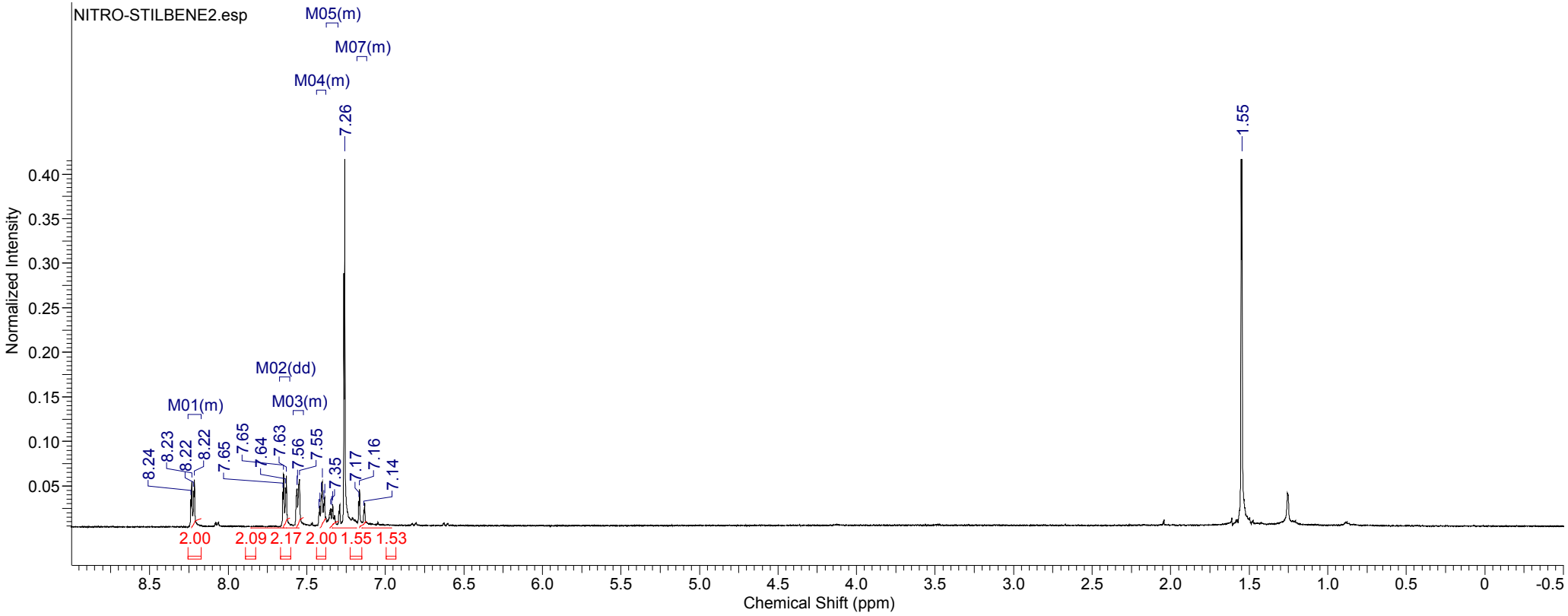


Formula	$C_{14}H_{11}NO_2$	FW	225.2426

Acquisition Time (sec)	2.5001	**Comment**	heck product	**Date**	Oct 23 2013	**Date Stamp**	Oct 23 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\NITRO-STILBENE.FID\FID					**Frequency (MHz)**	499.86
Nucleus	1H	**Number of Transients**	32	**Original Points Count**	21259	**Points Count**	32768
Pulse Sequence	s2pul	**Receiver Gain**	42.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 8.17 - 8.26 (m, 2H), 7.64 (dd, J = 2.85, 8.82 Hz, 2H), 7.52 - 7.59 (m, 2H), 7.38 - 7.44 (m, 2H), 7.30 - 7.38 (m, 2H), 7.12 - 7.18 (m, 2H)

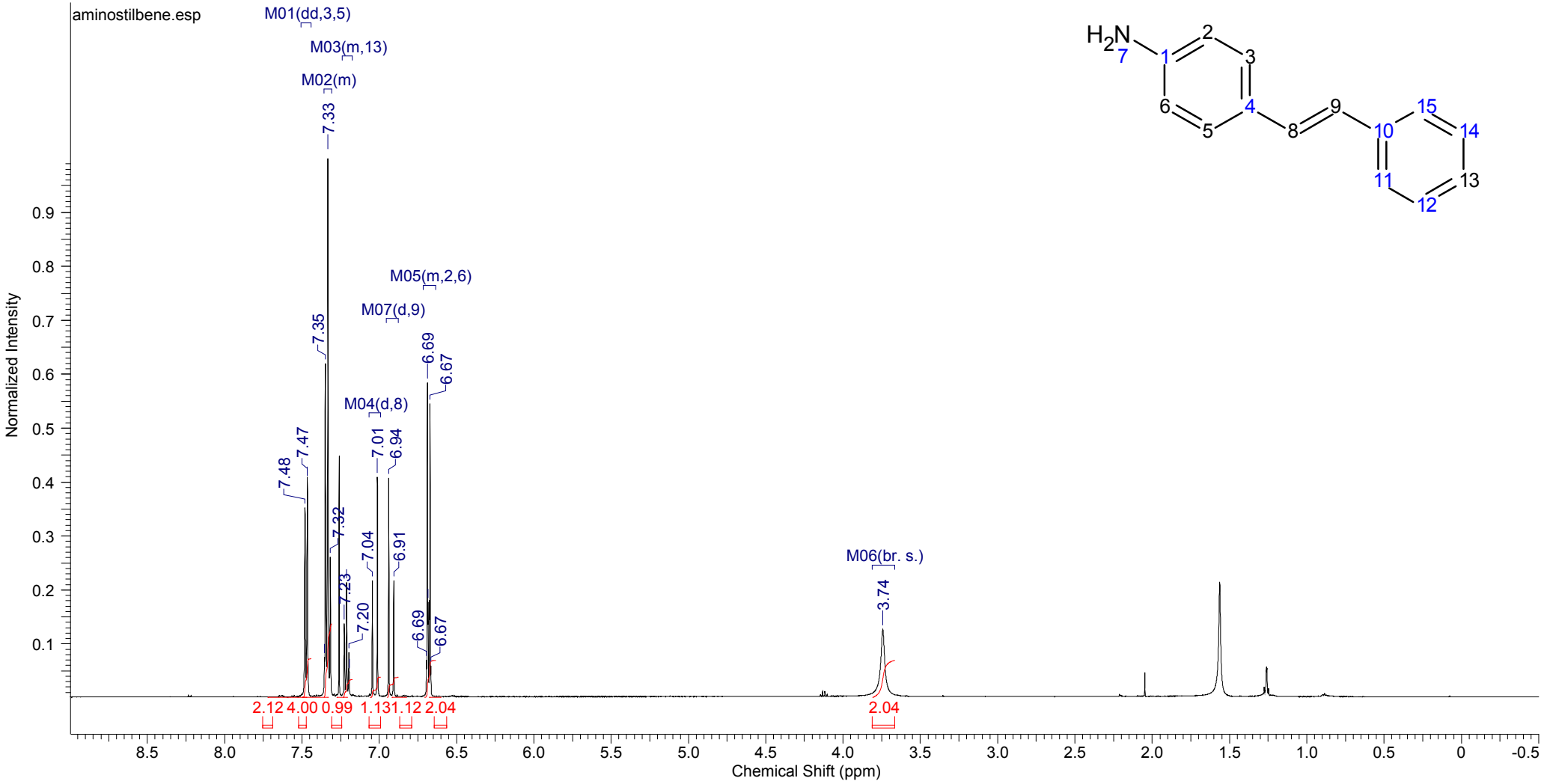




Formula $C_{14}H_{13}N$	FW	195.2597

Acquisition Time (sec)	2.5001	**Comment**	major product	**Date**	Oct 2 2013	**Date Stamp**	Oct 2 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\3062-001.FID\FID					**Frequency (MHz)**	499.86
Nucleus	1H	**Number of Transients**	16	**Original Points Count**	21259	**Points Count**	32768
Pulse Sequence	s2pul	**Receiver Gain**	42.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

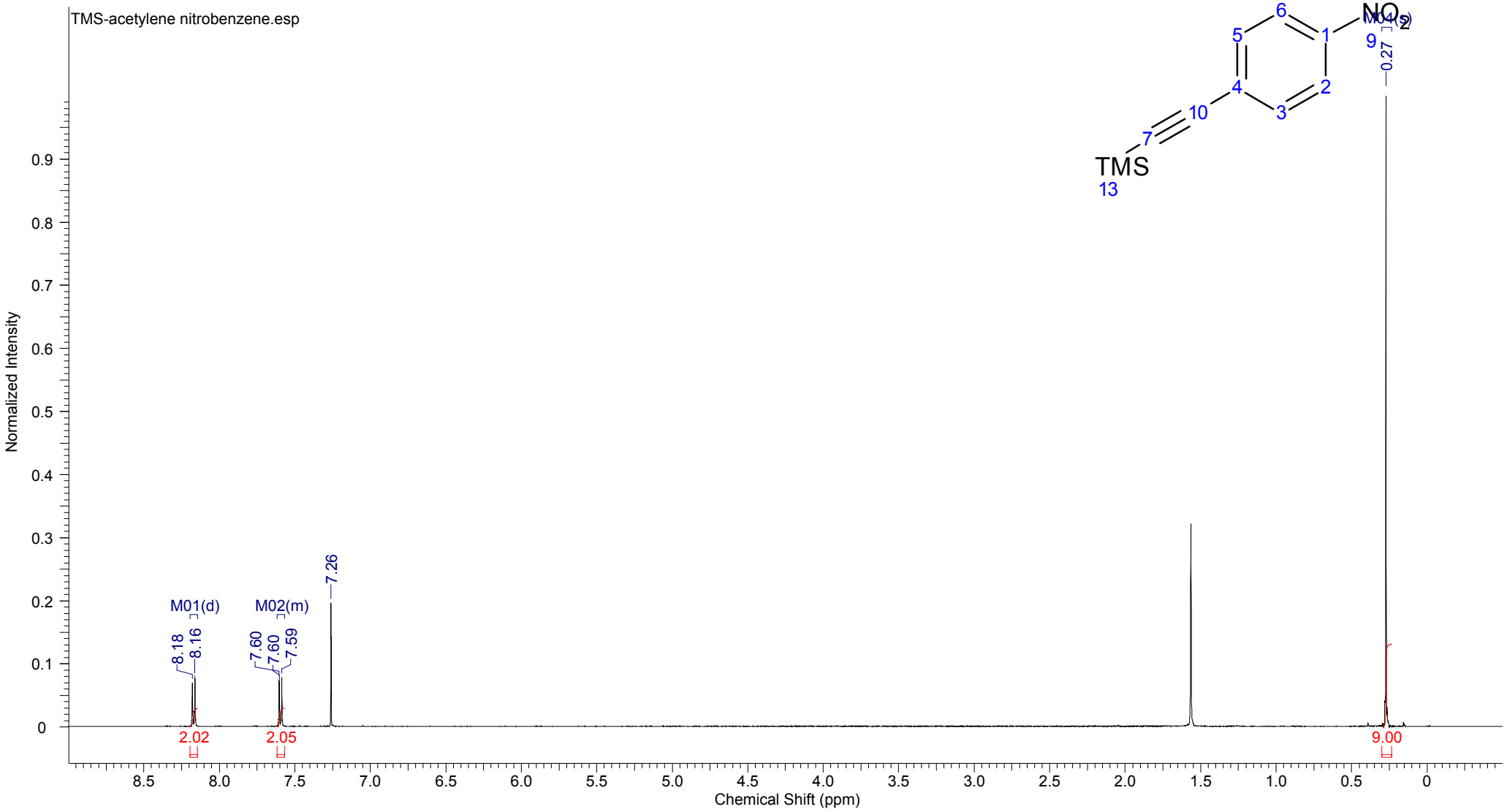
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.47 (dd, J = 0.78, 8.04 Hz, 2H), 7.31 - 7.36 (m, 4H), 7.18 - 7.24 (m, 1H), 7.03 (d, J = 16.30 Hz, 1H), 6.92 (d, J = 16.60 Hz, 1H), 6.63 - 6.72 (m, 2H), 3.74 (br. s., 2H)



Formula	$C_{11}H_{13}NO_2Si$	FW	219.3120

Acquisition Time (sec)	2.5001	Date	Jul 12 2012	Date Stamp	Jul 12 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0051-CR.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	8	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

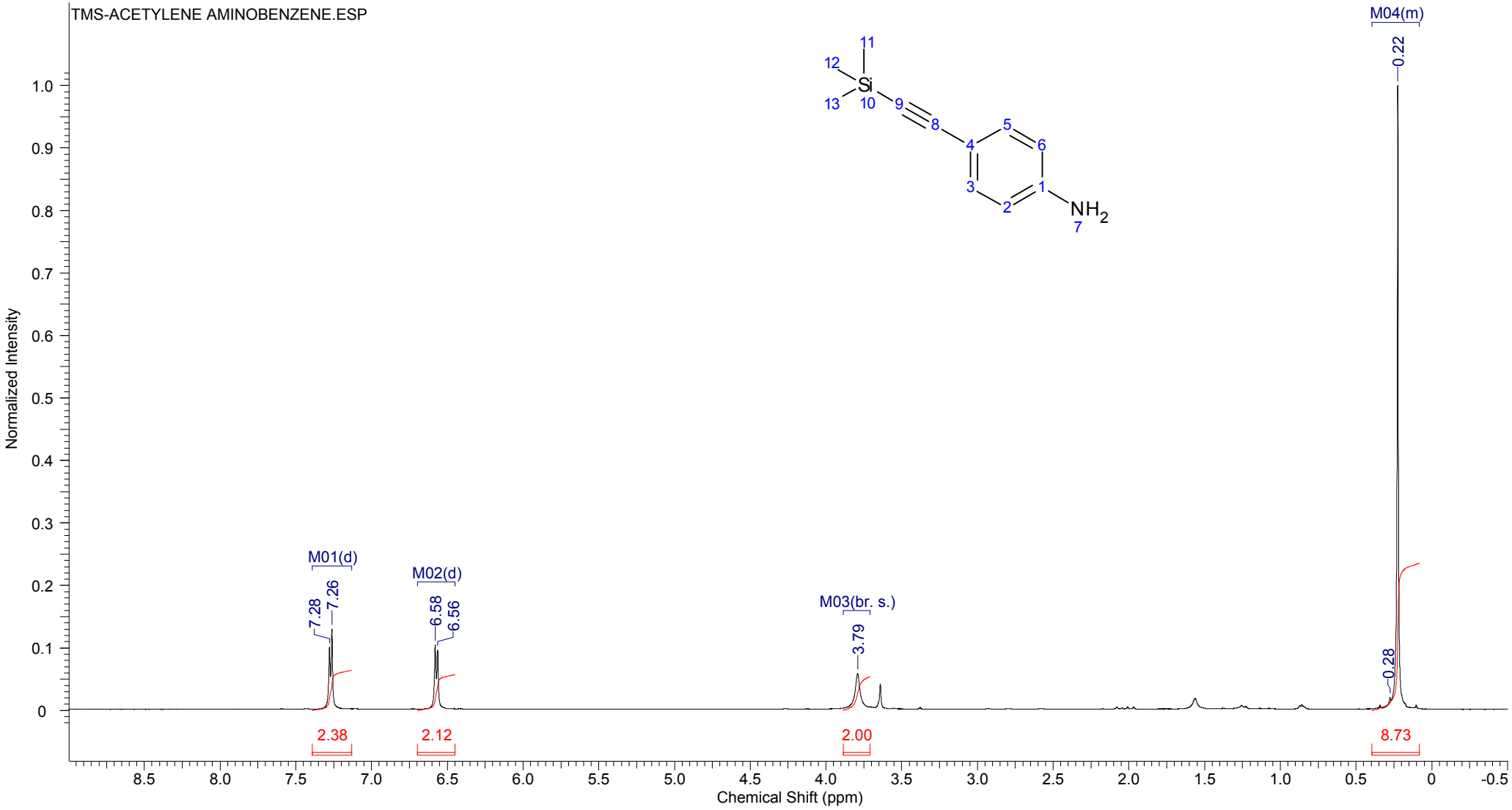
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 8.17 (d, J = 8.82 Hz, 2H), 7.57 - 7.62 (m, 2H), 0.27 (s, 9H)



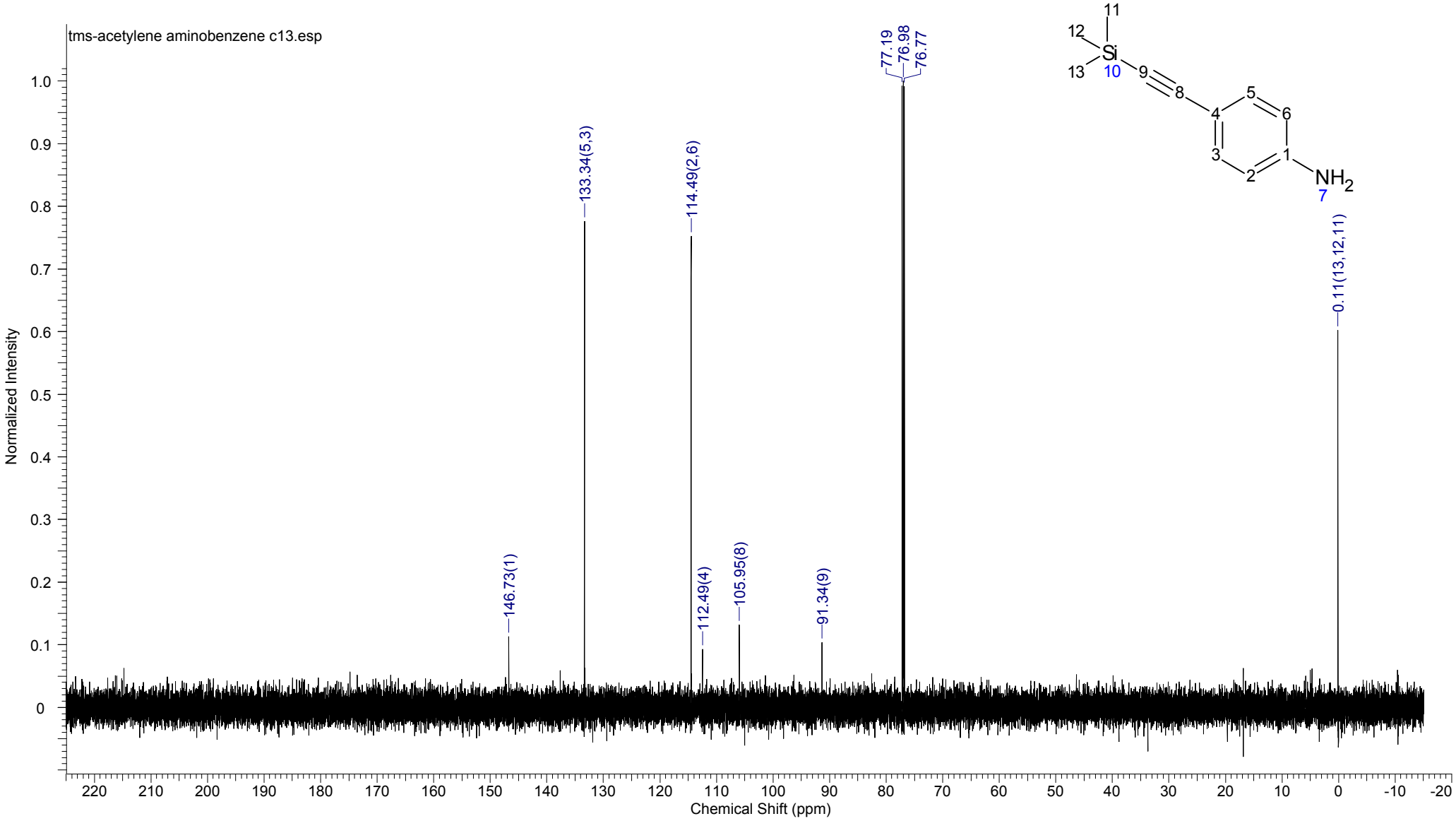
Formula	$C_{11}H_{15}NSi$	FW	189.3290

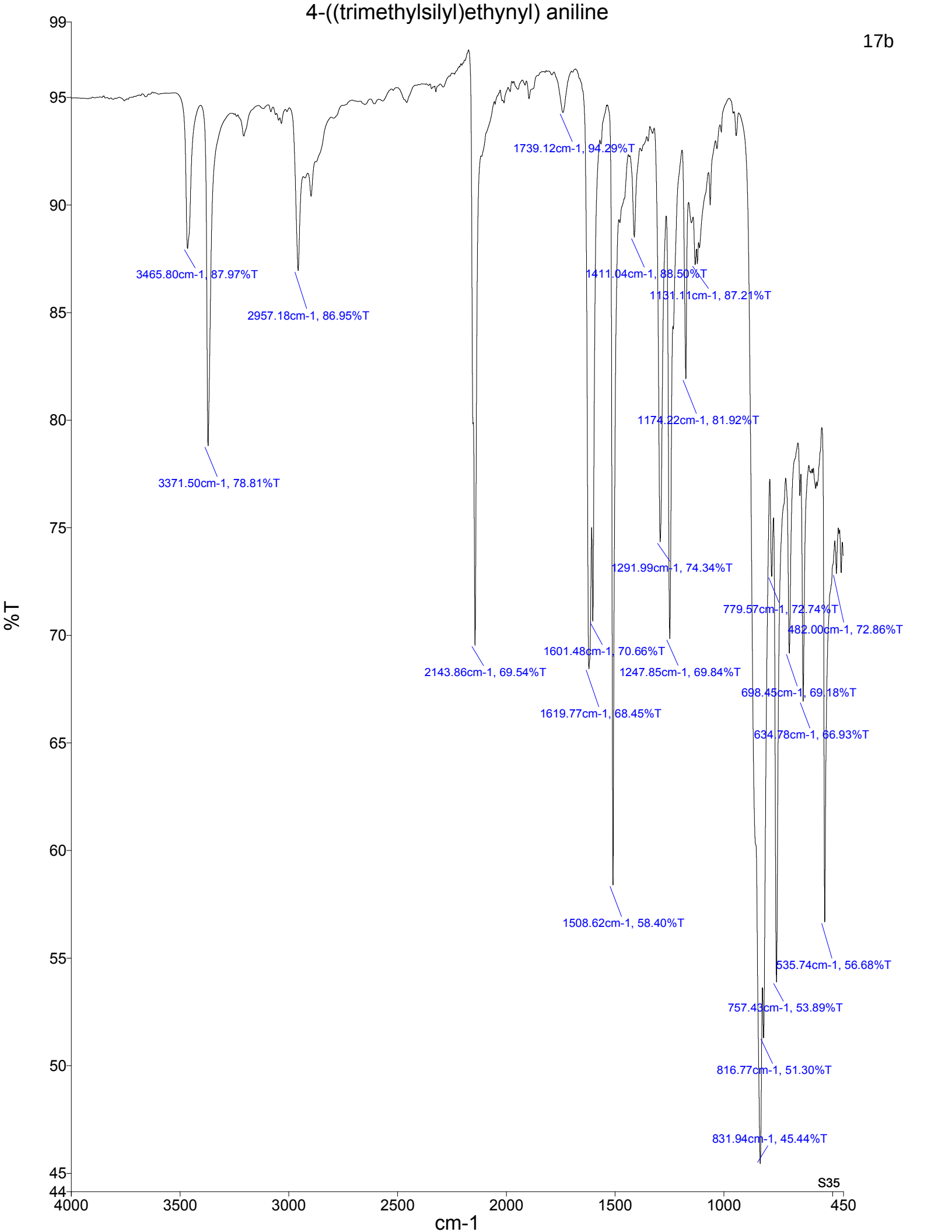
Acquisition Time (sec)	2.5001	**Comment**	tms-acetylene-nitrobenzene product			**Date**	Sep 13 2013
Date Stamp	Sep 13 2013	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0065-CR.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	16	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	38.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.27 (d, J = 8.30 Hz, 2H), 6.57 (d, J = 8.30 Hz, 2H), 3.79 (br. s., 2H), 0.08 - 0.40 (m, 9H)



Formula $C_{11}H_{15}NSi$	***FW***	189.3290					
Acquisition Time (sec)	1.2987	***Comment***	Std carbon	***Date***	Sep 13 2013	***Date Stamp***	Sep 13 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0065-C13.FID\FID					***Frequency (MHz)***	150.79
Nucleus	13C						
Number of Transients	256	***Original Points Count***	47013	***Points Count***	65536	***Pulse Sequence***	s2pul
Receiver Gain	30.00						
Solvent	CHLOROFORM-d			***Spectrum Offset (Hz)***	15831.6172	***Spectrum Type***	STANDARD
Sweep Width (Hz)	36199.09						
Temperature (degree C)	25.000						




4-((trimethylsilyl)ethynyl) aniline
17b
%T
cm-1
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2957.18cm-1, 86.95%T
3371.50cm-1, 78.81%T
1739.12cm-1, 94.29%T
1411.04cm-1, 88.50%T
1131.11cm-1, 87.21%T
1174.22cm-1, 81.92%T
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698.45cm-1, 69.18%T
1619.77cm-1, 68.45%T
634.78cm-1, 66.93%T
1508.62cm-1, 58.40%T
535.74cm-1, 56.68%T
757.43cm-1, 53.89%T
816.77cm-1, 51.30%T
831.94cm-1, 45.44%T
S35

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Operator   :
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Sample Name:
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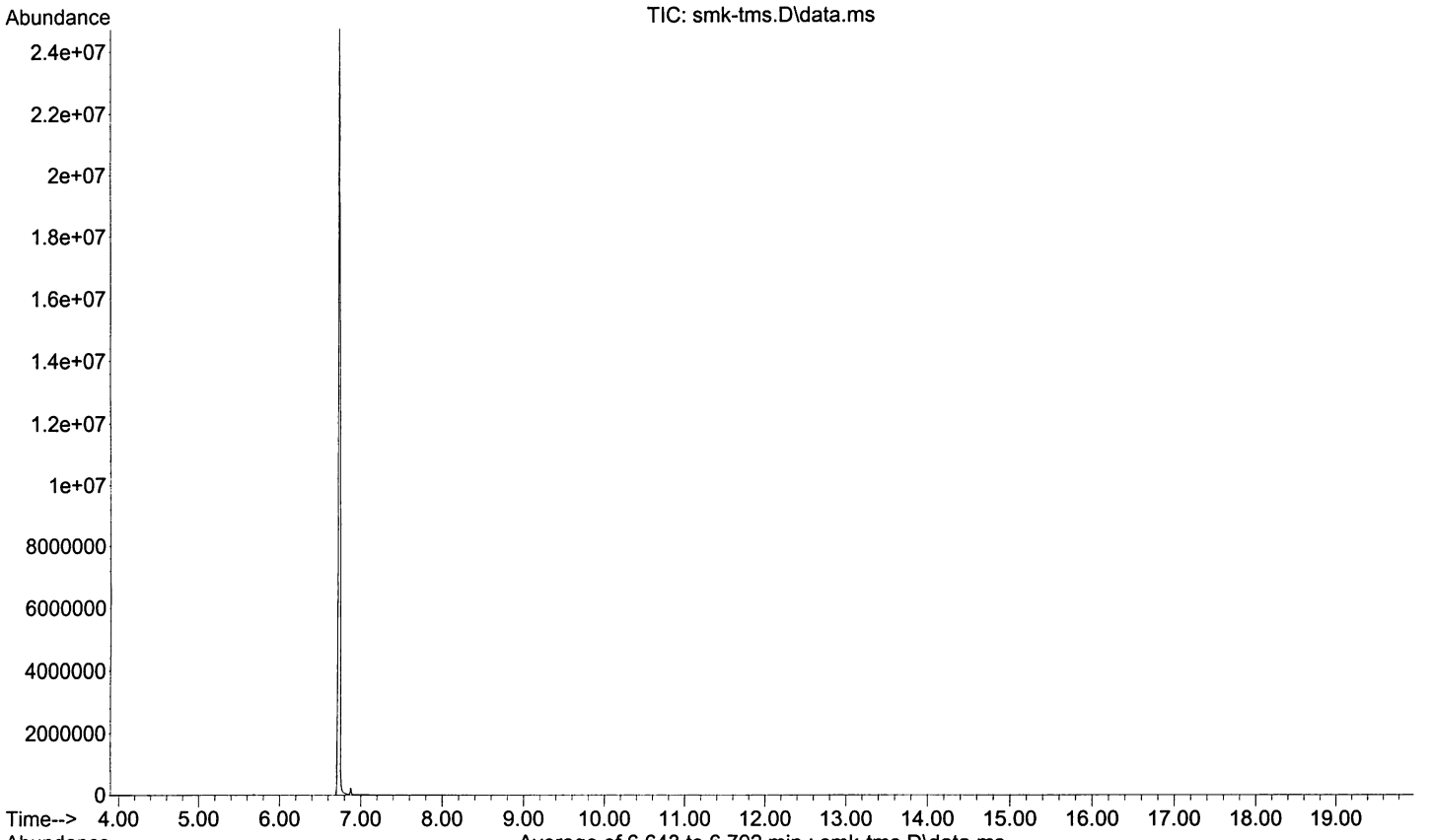
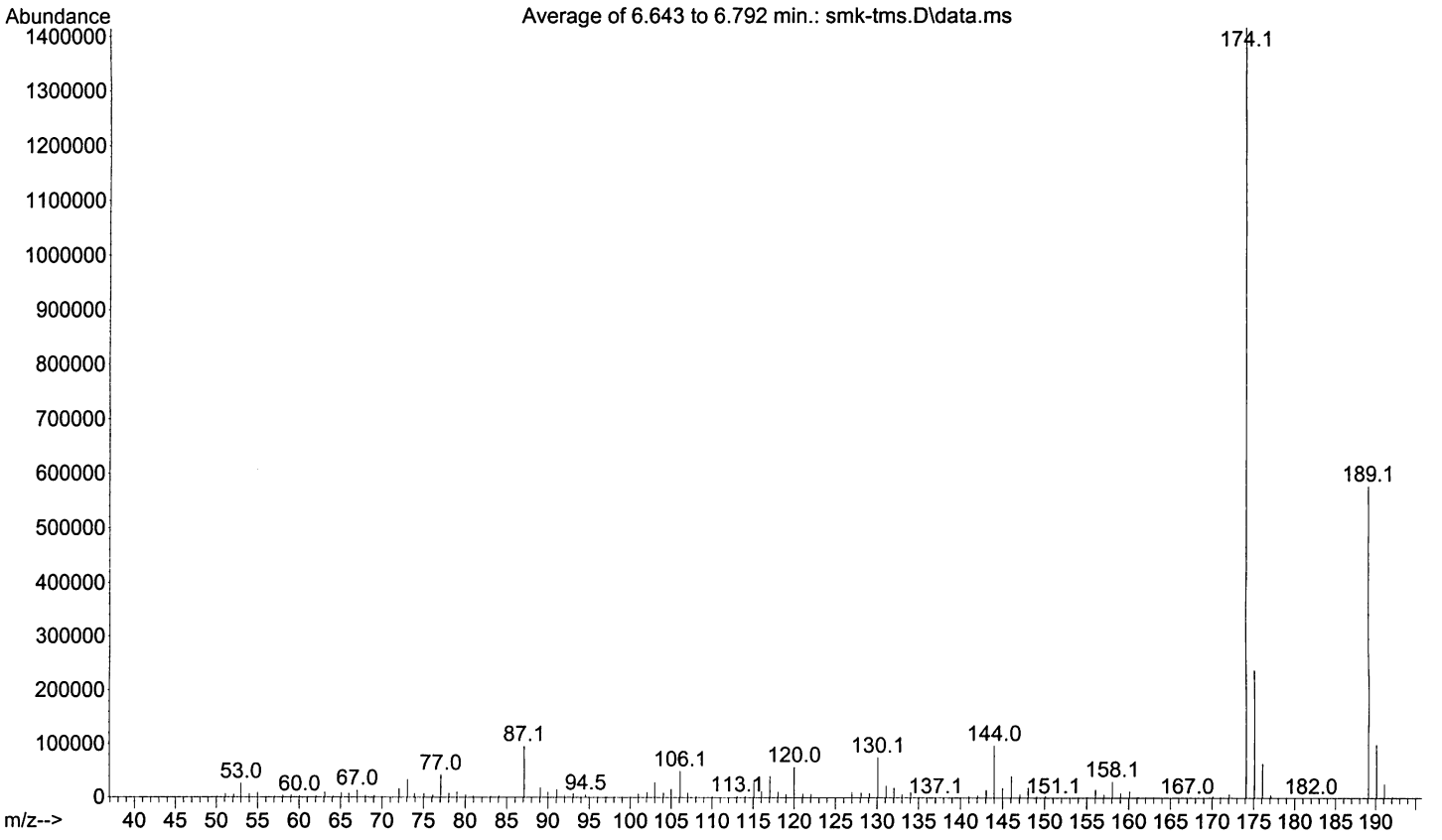
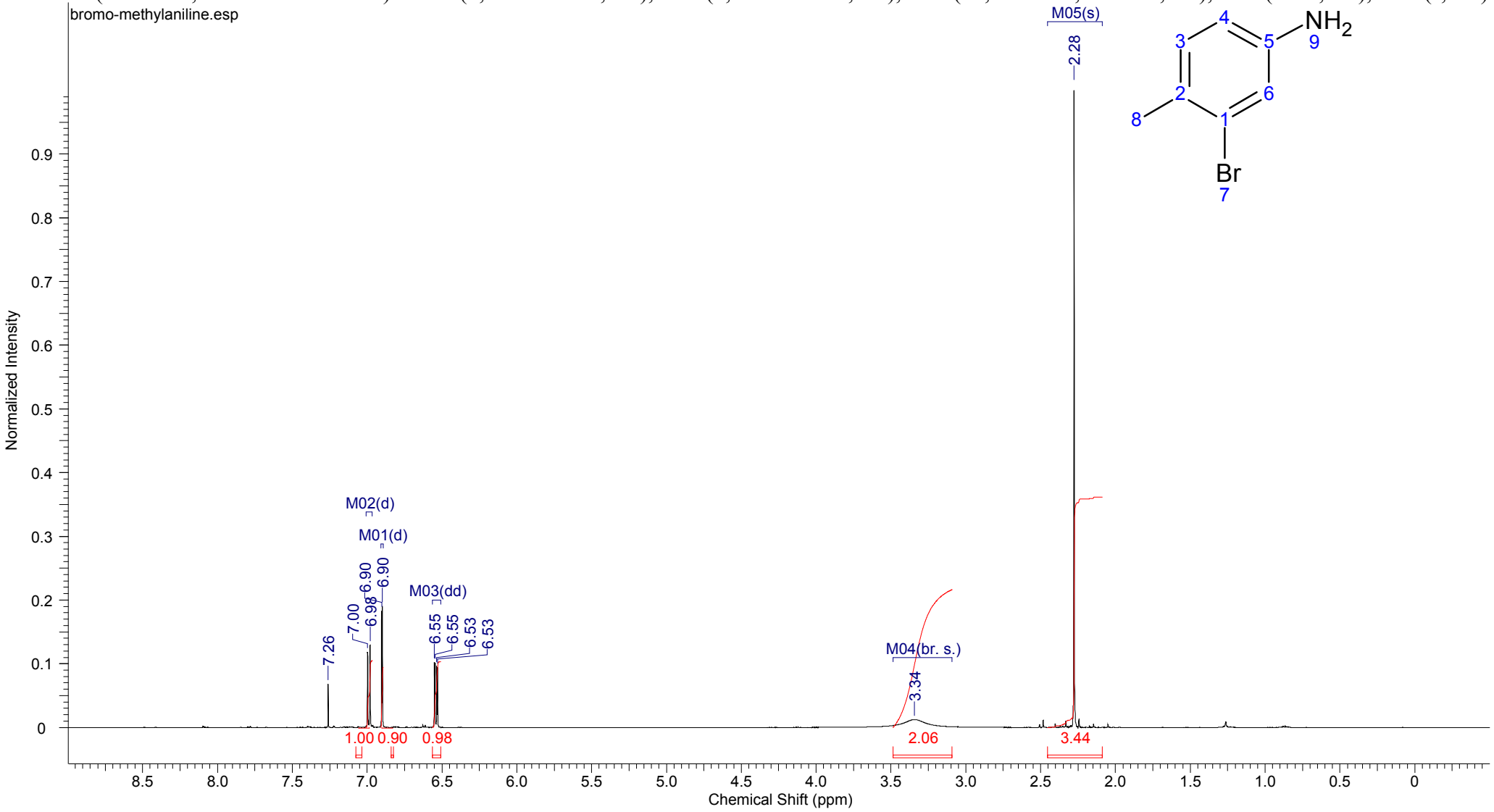




Formula	C_7H_8BrN	FW	186.0491

Acquisition Time (sec)	2.5001	Date	Jun 21 2012	Date Stamp	Jun 21 2012		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\0047-CR.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	36.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2495.3828	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

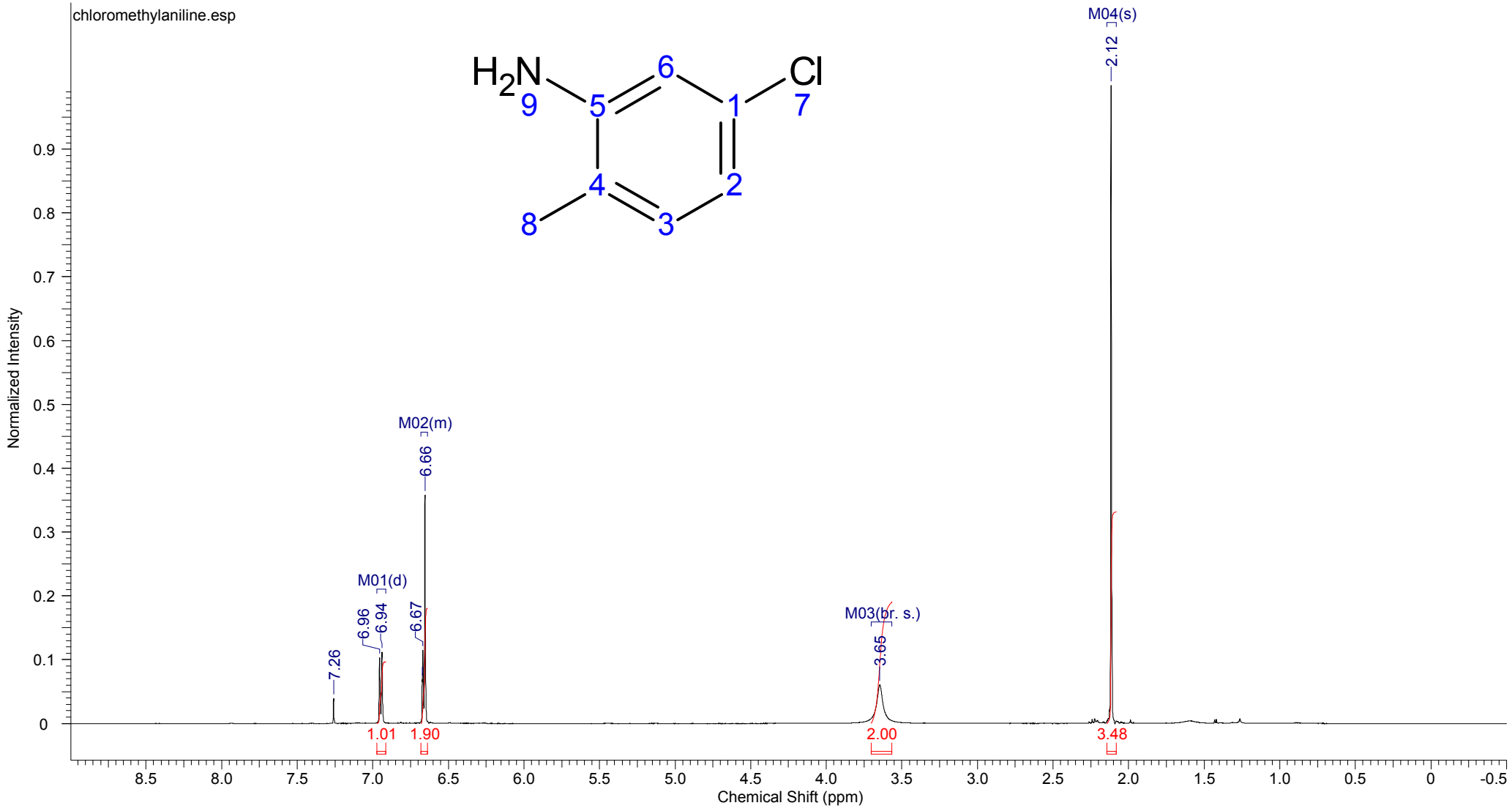
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.99 (d, J = 8.04 Hz, 1H), 6.90 (d, J = 2.34 Hz, 1H), 6.54 (dd, J = 2.34, 8.04 Hz, 1H), 3.34 (br. s., 2H), 2.28 (s, 3H)



Formula	C_7H_8ClN	FW	141.5981

Acquisition Time (sec)	2.5001	**Comment**	bromo methyl	**Date**	Sep 9 2013	**Date Stamp**	Sep 9 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\3048-001.FID\FID					**Frequency (MHz)**	499.86
Nucleus	1H	**Number of Transients**	16	**Original Points Count**	21259	**Points Count**	32768
Pulse Sequence	s2pul	**Receiver Gain**	36.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

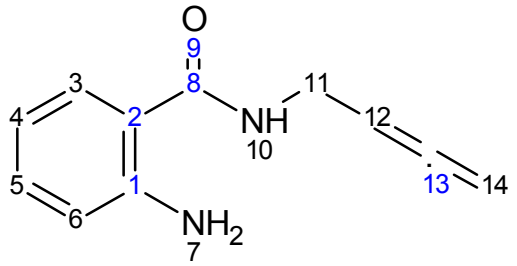
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 6.95 (d, J = 8.30 Hz, 1H), 6.64 - 6.68 (m, 2H), 3.65 (br. s., 2H), 2.12 (s, 3H)

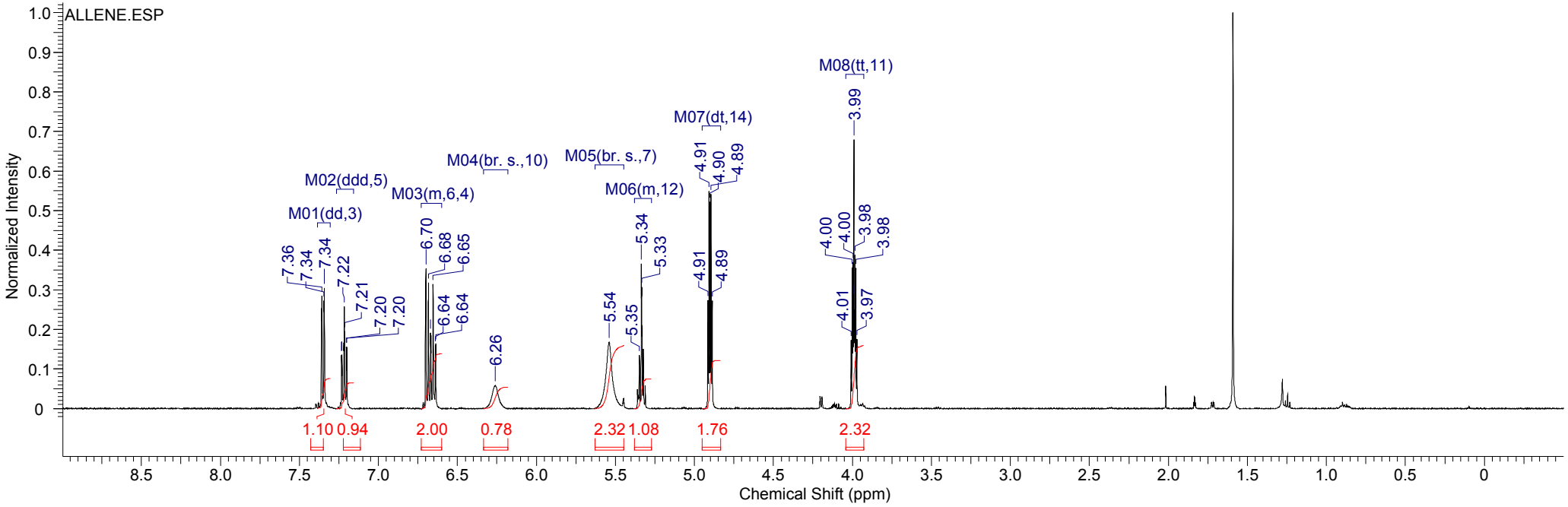


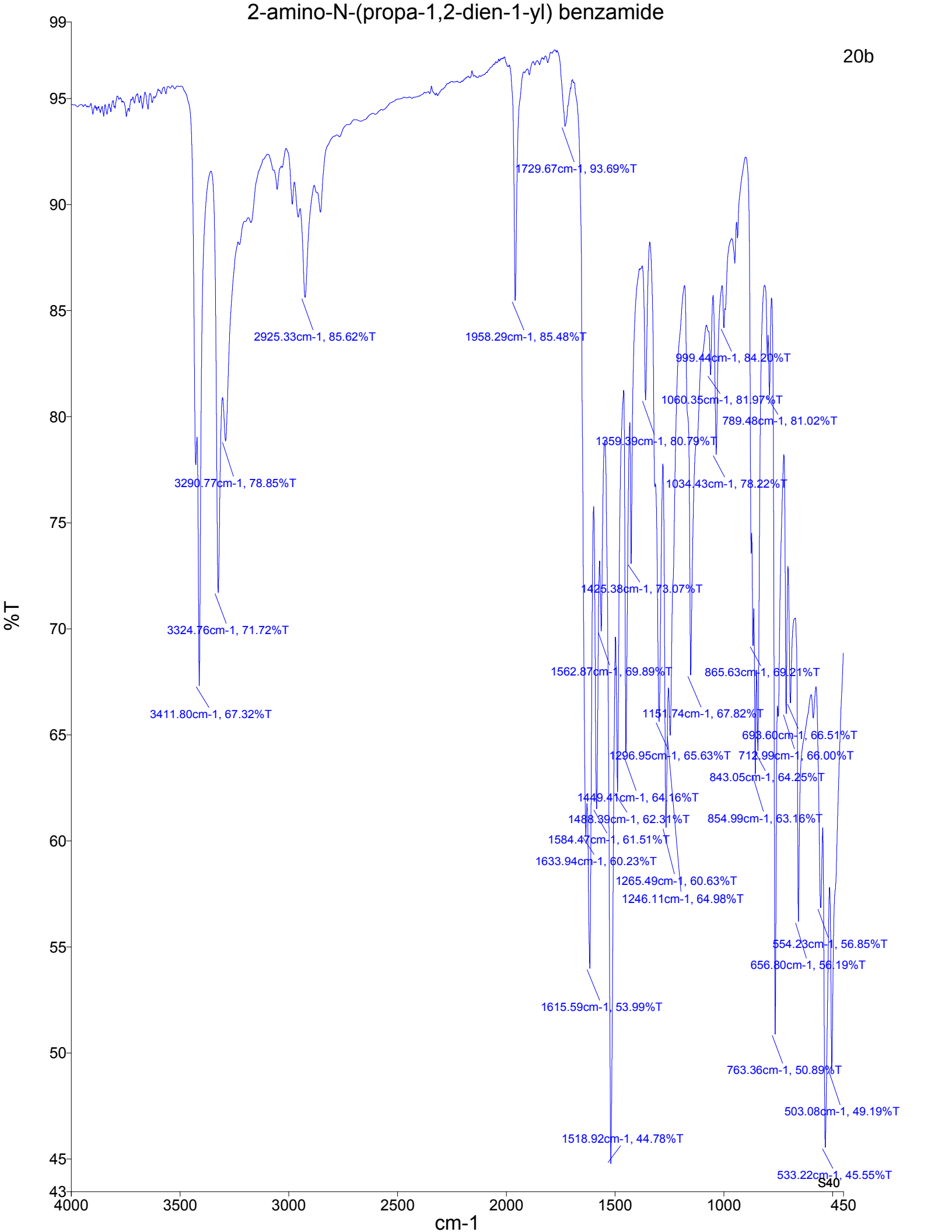
Formula	$C_{10}H_{12}N_2O$?	FW	176.2151+?

Acquisition Time (sec)	2.5001	Date	Jul 25 2013	Date Stamp	Jul 25 2013		
File Name	C:\USERS\SEAN\DESKTOP\MH_BDP_2066_2ND_CD2CL2.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	12	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	38.00	Solvent	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	2494.9937	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, DICHLOROMETHANE-d_2) δ 7.35 (dd, J = 1.30, 8.04 Hz, 1H), 7.22 (ddd, J = 1.56, 7.07, 8.24 Hz, 1H), 6.60 - 6.73 (m, 2H), 6.26 (br. s., 1H), 5.54 (br. s., 2H), 5.27 - 5.38 (m, 1H), 4.90 (td, J = 3.37, 6.75 Hz, 1H), 3.99 (tt, J = 3.37, 5.71 Hz, 2H)

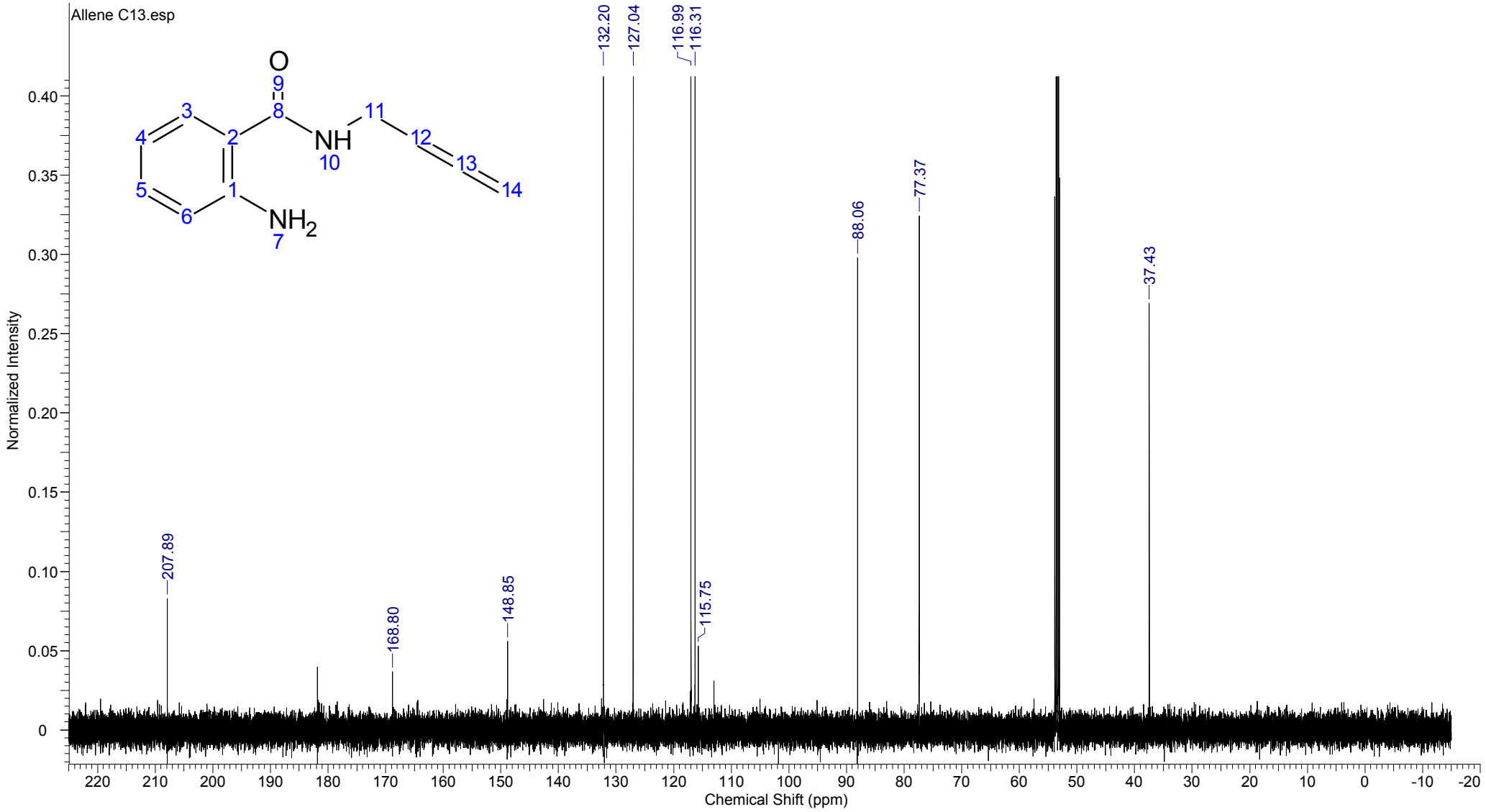





2-amino-N-(propa-1,2-dien-1-yl) benzamide
20b
%T
cm-1
99
95
90
85
80
75
70
65
60
55
50
45
43
4000
3500
3000
2500
2000
1500
1000
450
3411.80cm-1, 67.32%T
3324.76cm-1, 71.72%T
3290.77cm-1, 78.85%T
2925.33cm-1, 85.62%T
1729.67cm-1, 93.69%T
1958.29cm-1, 85.48%T
1615.59cm-1, 53.99%T
1633.94cm-1, 60.23%T
1584.47cm-1, 61.51%T
1562.87cm-1, 69.89%T
1518.92cm-1, 44.78%T
1488.39cm-1, 62.31%T
1449.41cm-1, 64.16%T
1425.38cm-1, 73.07%T
1359.39cm-1, 80.79%T
1296.95cm-1, 65.63%T
1265.49cm-1, 60.63%T
1246.11cm-1, 64.98%T
1151.74cm-1, 67.82%T
1060.35cm-1, 81.97%T
1034.43cm-1, 78.22%T
999.44cm-1, 84.20%T
865.63cm-1, 69.21%T
854.99cm-1, 63.16%T
843.05cm-1, 64.25%T
789.48cm-1, 81.02%T
763.36cm-1, 50.89%T
712.99cm-1, 66.00%T
698.60cm-1, 66.51%T
656.80cm-1, 56.19%T
554.23cm-1, 56.85%T
533.22cm-1, 45.55%T
503.08cm-1, 49.19%T
S40

Formula $C_{11}H_{12}N_2O$	FW	188.2258

Acquisition Time (sec)	1.3026	**Comment**	Std carbon	**Date**	Jul 25 2013	**Date Stamp**	Jul 25 2013
File Name	C:\USERS\SEAN\DESKTOP\MH_BDP_2066_C13_2ND_CD2CL2.FID\FID					**Frequency (MHz)**	125.70
Nucleus	13C	**Number of Transients**	604	**Original Points Count**	39295	**Points Count**	65536
Pulse Sequence	s2pul	**Receiver Gain**	46.00	**Solvent**	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	13197.3711	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	30165.91	**Temperature (degree C)**	AMBIENT TEMPERATURE



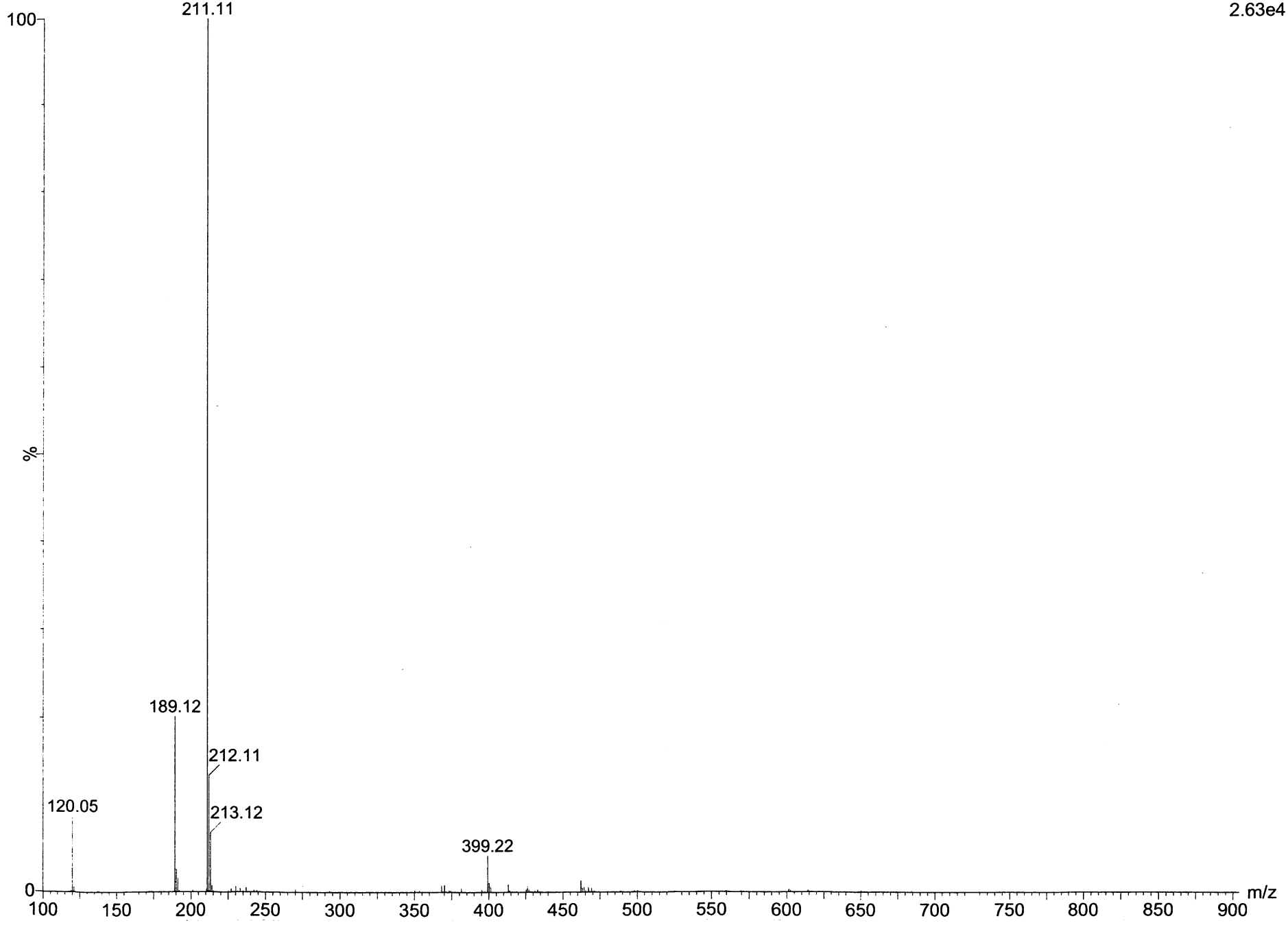
Hageman/Lipshutz, MH-BDP-2066, mw 188; ESI+/TOF

LIP072213MB 443 (8.396) Sm (SG, 4x3.00); Cm (427:651-2:257x2.000)

UCSB CHEM BIOCHEM QTOF2

TOF MS ES+

2.63e4



Single Mass Analysis

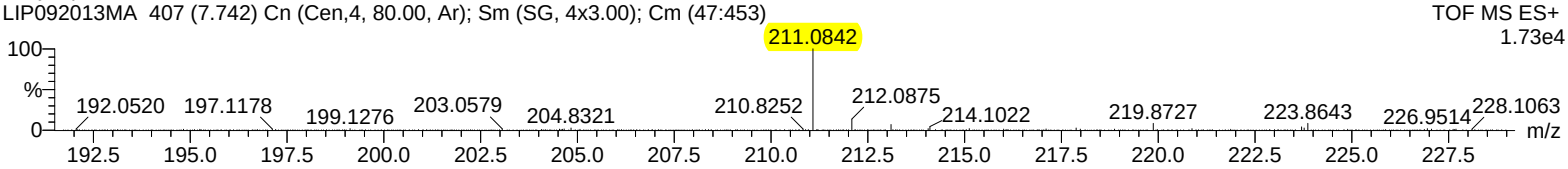
20b

Tolerance = 3.0 mDa / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
403 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-10 O: 0-10 Na: 0-1

Kelly/Lipshutz, SMK-3042-001, mw 188, ESI+
LIP092013MA 407 (7.742) Cn (Cen,4, 80.00, Ar); Sm (SG, 4x3.00); Cm (47:453)

UCSB CHEM BIOCHEM QTOF2
TOF MS ES+
1.73e4

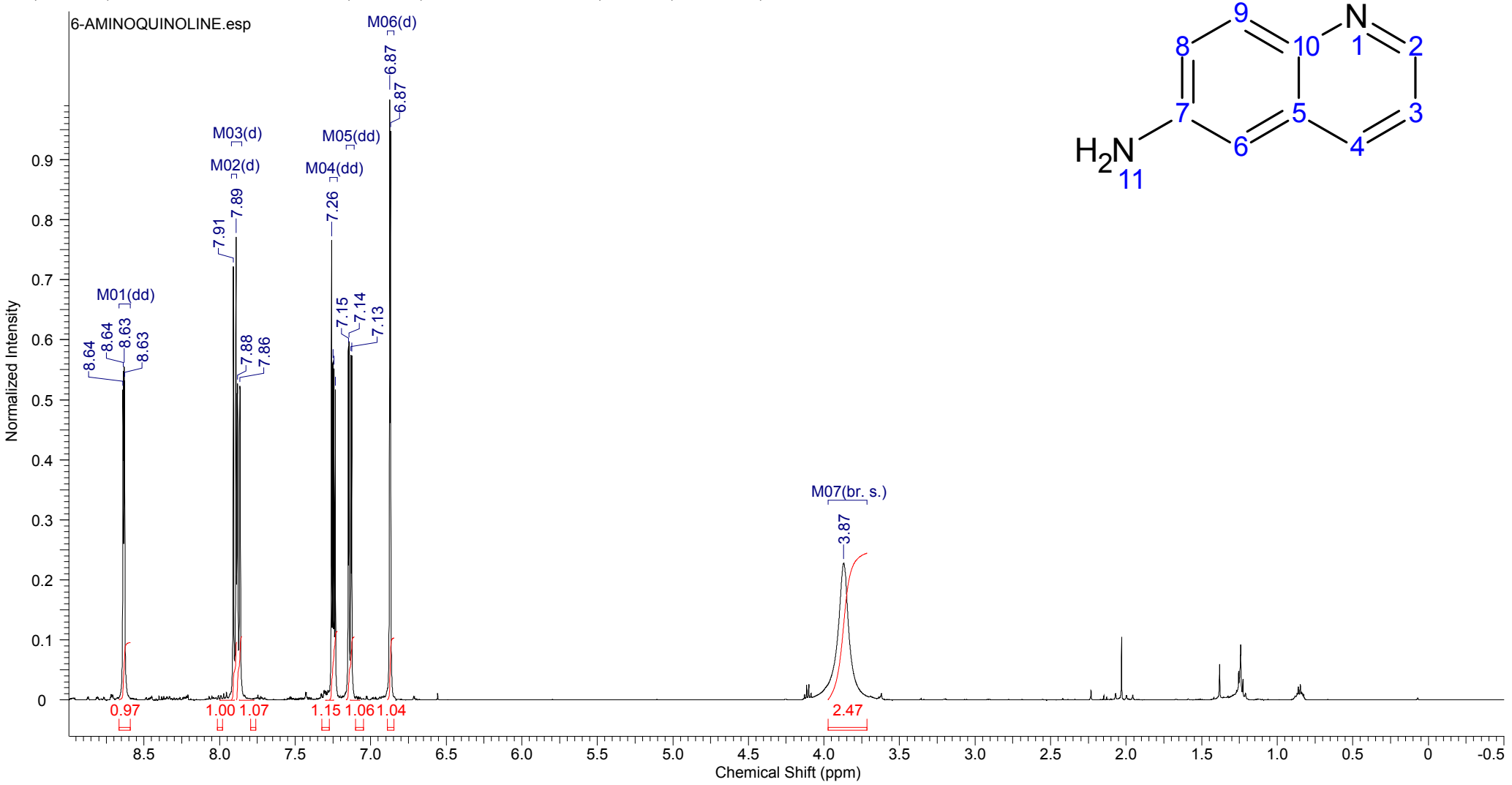


Minimum:				-1.5		
Maximum:		3.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
211.0842	211.0847	-0.5	-2.4	6.5	441.8	C11 H12 N2 O Na
	211.0831	1.1	5.2	5.5	473.7	C8 H11 N4 O3
	211.0818	2.4	11.4	0.5	513.4	C7 H15 O7
	211.0871	-2.9	-13.7	9.5	428.6	C13 H11 N2 O

Formula $C_9H_8N_2$	FW	144.1732

Acquisition Time (sec)	2.5001	Date	Aug 3 2013	Date Stamp	Aug 3 2013		
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\6-AMINOQUINOLINE.FID\FID					Frequency (MHz)	499.86
Nucleus	1H	Number of Transients	16	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	36.00	Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

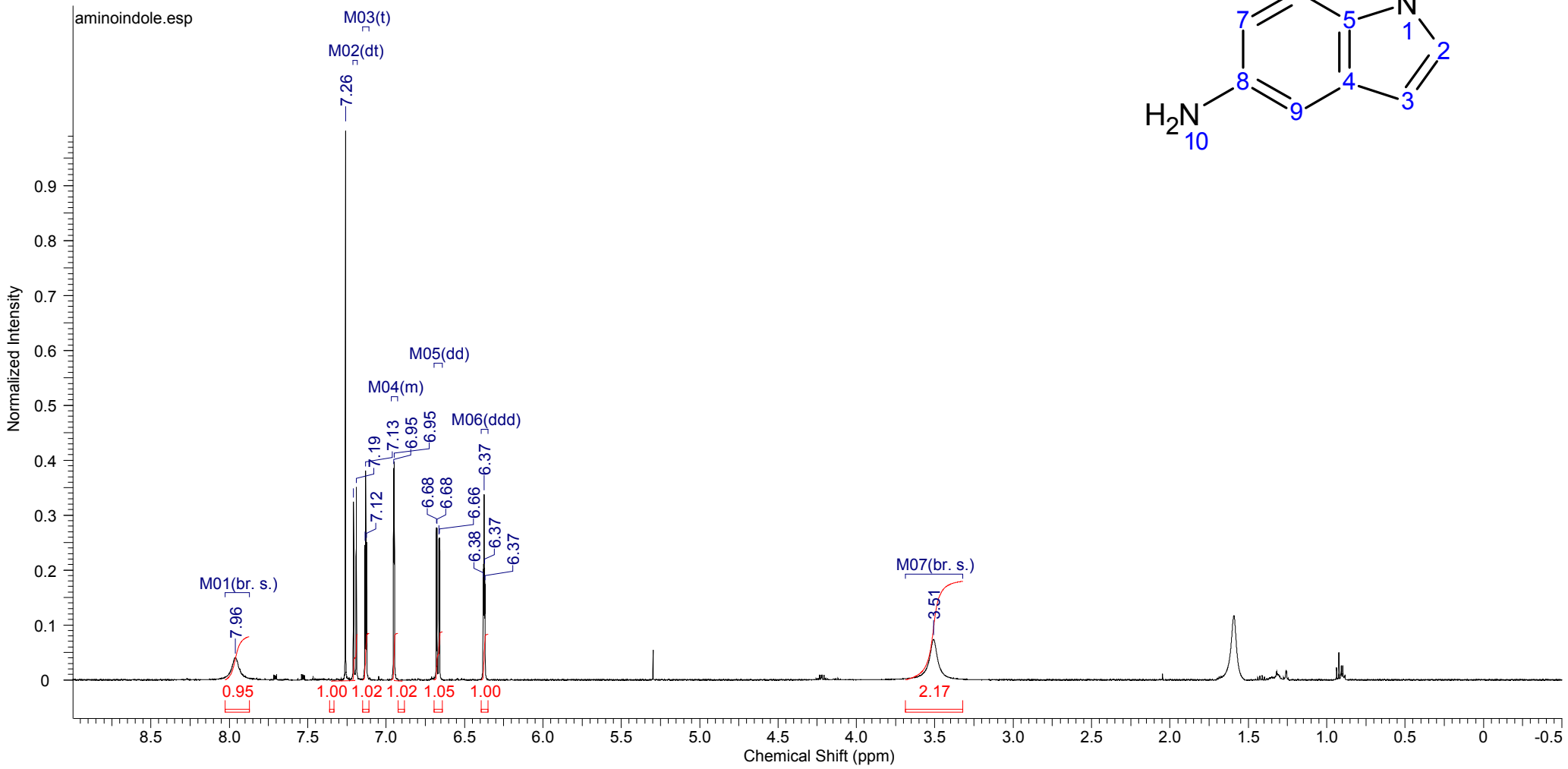
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 8.63 (dd, J = 1.56, 4.15 Hz, 1H), 7.90 (d, J = 9.08 Hz, 1H), 7.87 (d, J = 8.05 Hz, 1H), 7.25 (dd, J = 4.28, 8.17 Hz, 1H), 7.14 (dd, J = 2.47, 8.95 Hz, 1H), 6.87 (d, J = 2.60 Hz, 1H), 3.87 (br. s., 2H)



Formula $C_8H_8N_2$	FW	132.1625

Acquisition Time (sec)	2.5001	Comment	nitroindole product - flash column			Date	Sep 24 2013
Date Stamp	Sep 24 2013	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PAPER\3078-001.FID\FID				
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	16	Original Points Count	21259
Points Count	32768	Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE

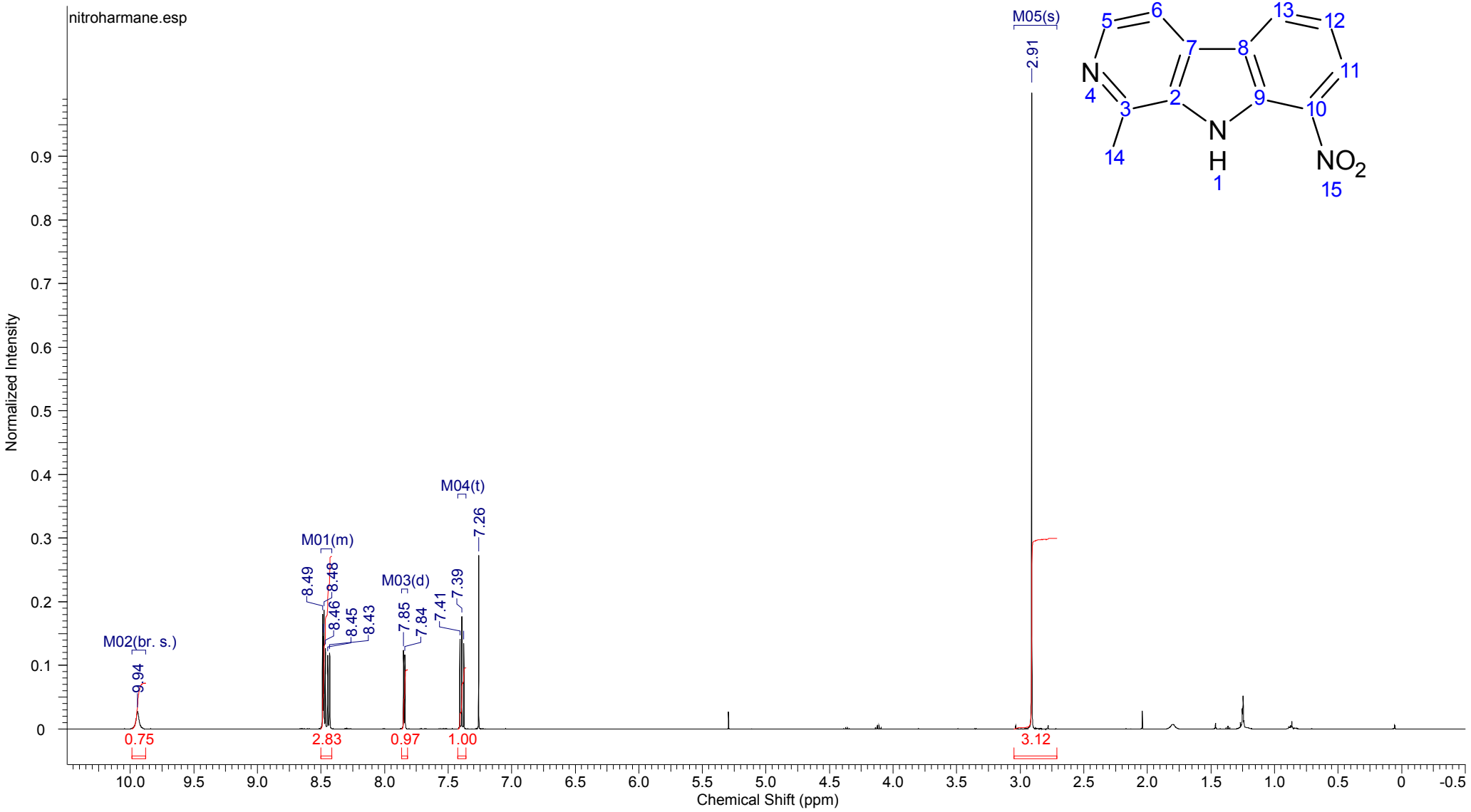
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 7.96 (br. s., 1H), 7.20 (td, J = 0.80, 8.30 Hz, 1H), 7.13 (t, J = 2.72 Hz, 1H), 6.93 - 6.97 (m, 1H), 6.67 (dd, J = 2.21, 8.43 Hz, 1H), 6.37 (ddd, J = 1.04, 2.08, 3.11 Hz, 1H), 3.51 (br. s., 2H)



Formula $C_{12}H_9N_3O_2$	FW	227.2188

Acquisition Time (sec)	2.5001	Date	Aug 15 2013	Date Stamp	Aug 15 2013	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\HAR1.FID\FID		
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	8	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	2494.9937
Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE				

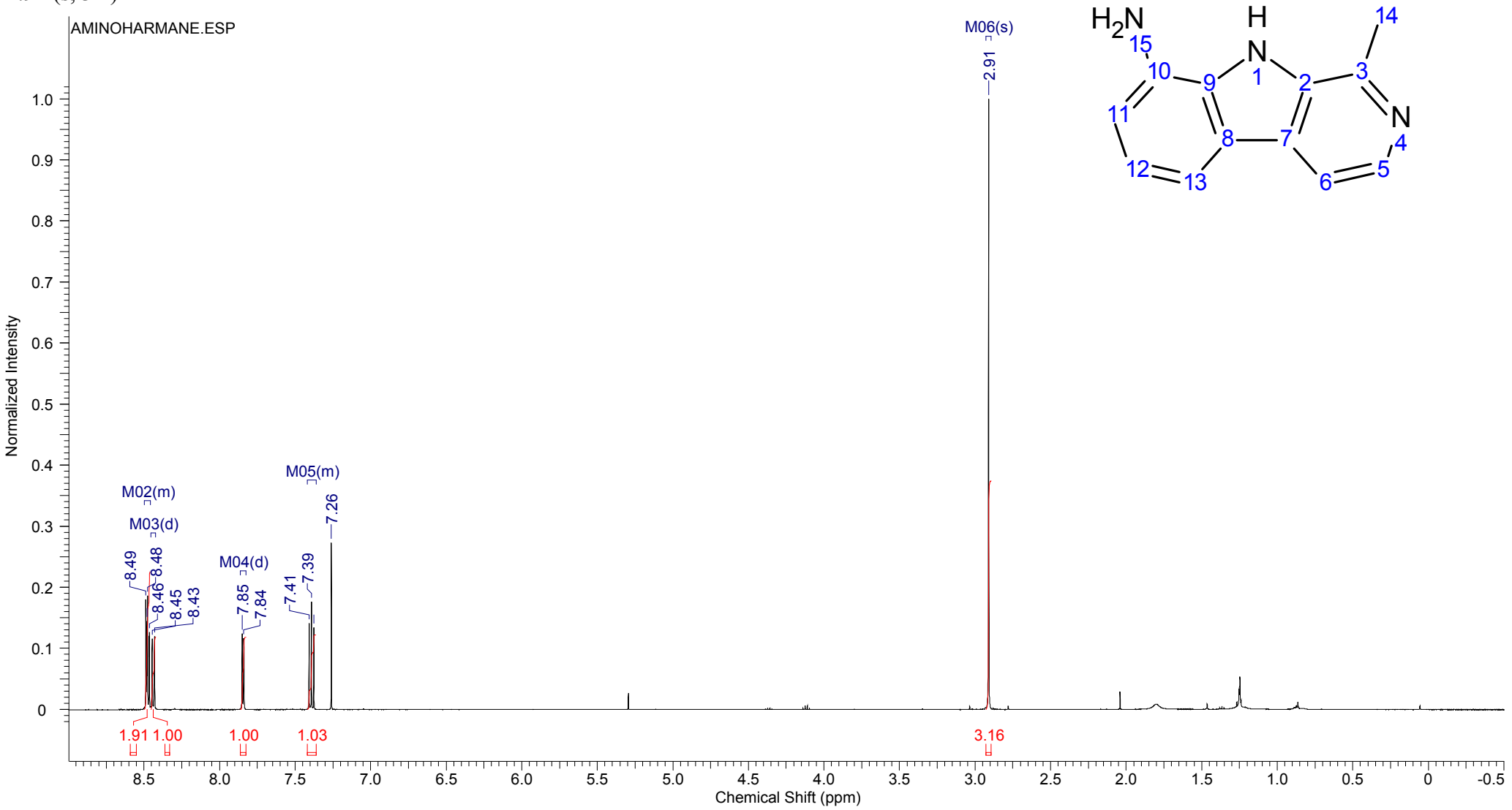
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 9.94 (br. s., 1H), 8.42 - 8.50 (m, 3H), 7.84 (d, J = 5.45 Hz, 1H), 7.39 (t, J = 7.80 Hz, 1H), 2.91 (s, 3H)



Formula	$C_{12}H_{11}N_3$	FW	197.2358

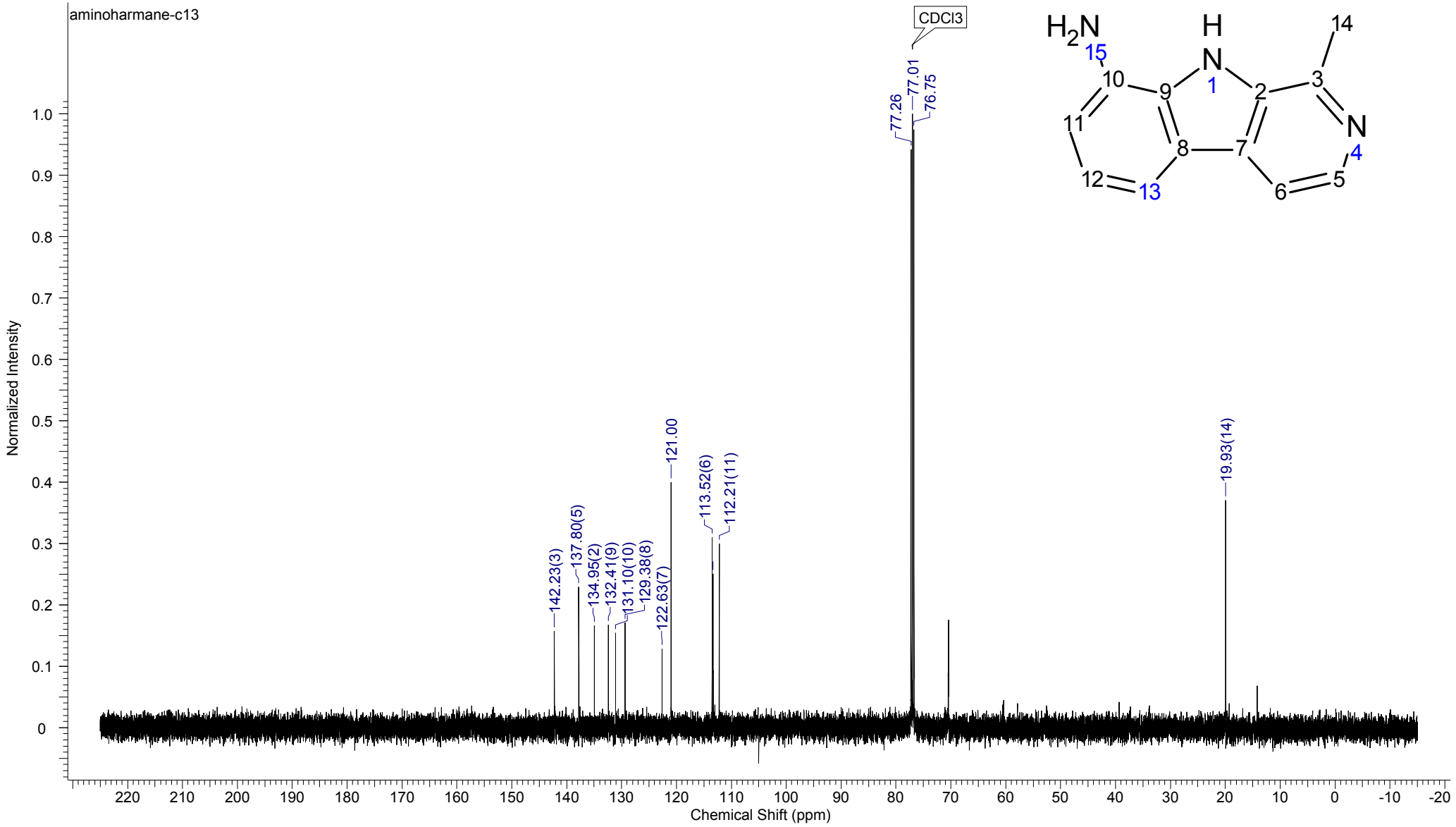
Acquisition Time (sec)	2.5001	Date	Aug 15 2013	Date Stamp	Aug 15 2013	File Name	C:\USERS\SEAN\DOCUMENTS\NMR\HAR1.FID\FID		
Frequency (MHz)	499.86	Nucleus	1H	Number of Transients	8	Original Points Count	21259	Points Count	32768
Pulse Sequence	s2pul	Receiver Gain	42.00	Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	2494.9937
Spectrum Type	STANDARD	Sweep Width (Hz)	8503.40	Temperature (degree C)	AMBIENT TEMPERATURE				

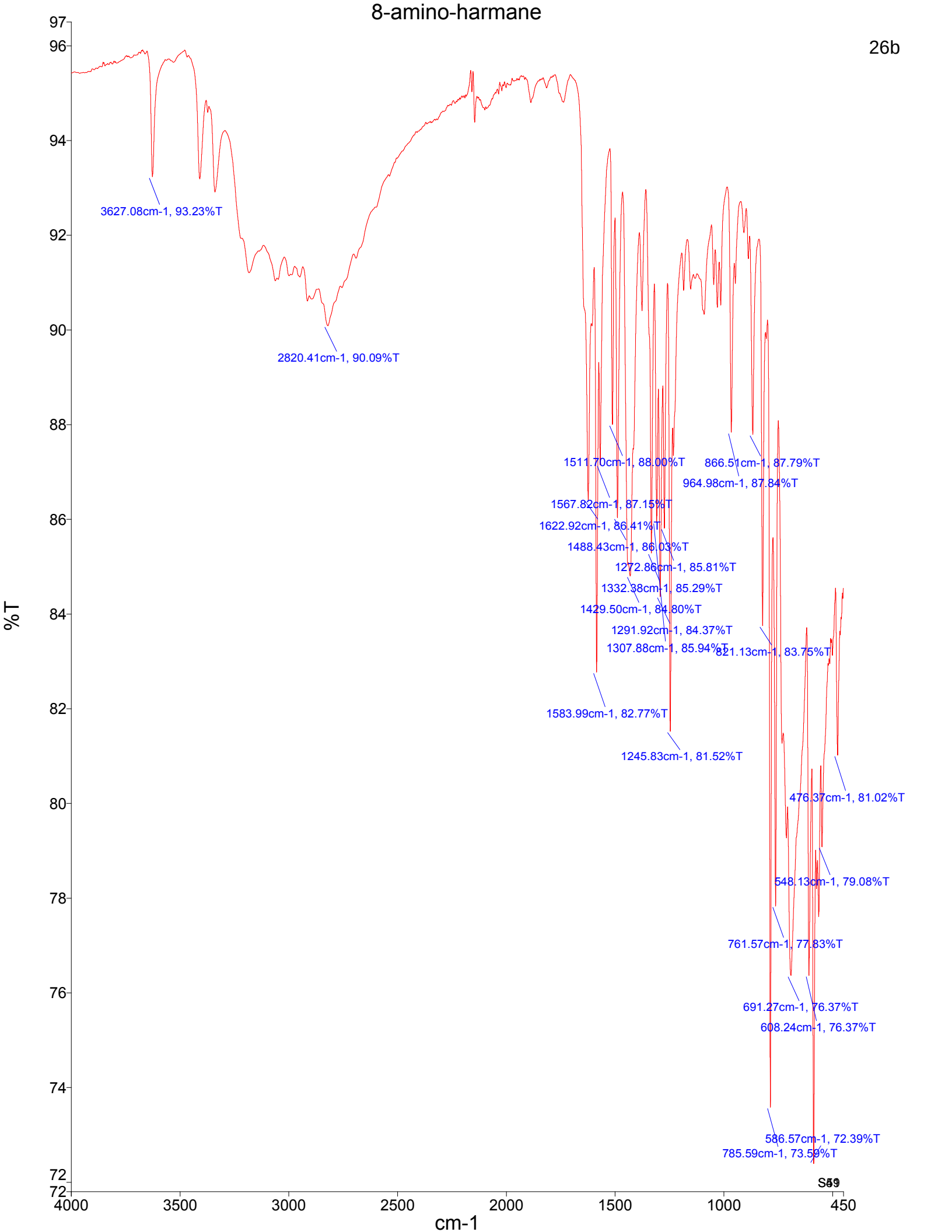
^{1}H NMR (500 MHz, CHLOROFORM-d) δ 9.94 (br. s., 1H), 8.46 - 8.50 (m, 2H), 8.44 (d, J = 7.53 Hz, 1H), 7.84 (d, J = 5.45 Hz, 1H), 7.36 - 7.42 (m, 1H), 2.91 (s, 3H)



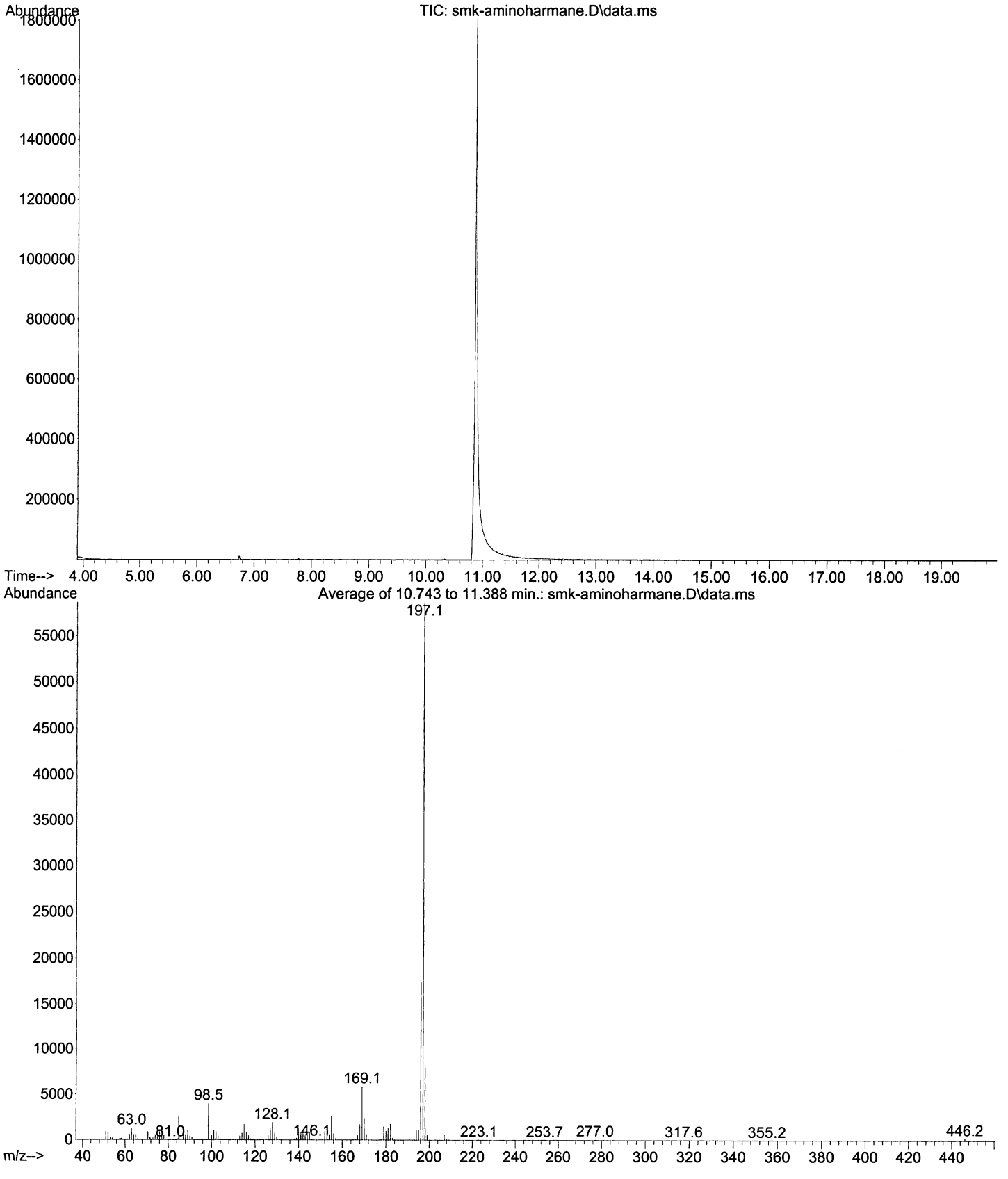
Formula	$C_{12}H_{11}N_3$	FW	197.2358

Acquisition Time (sec)	1.3026	**Comment**	Std carbon	**Date**	Aug 29 2013	**Date Stamp**	Aug 29 2013
File Name	C:\Users\Sean\Documents\NMR\aminoharmane-c13.fid\fid			**Frequency (MHz)**	125.70	**Nucleus**	13C
Number of Transients	256	**Original Points Count**	39295	**Points Count**	65536	**Pulse Sequence**	s2pul
Receiver Gain	46.00	**Solvent**	CHLOROFORM-d			**Spectrum Offset (Hz)**	13197.3711
Spectrum Type	STANDARD	**Sweep Width (Hz)**	30165.91	**Temperature (degree C)**	AMBIENT TEMPERATURE		




8-amino-harmane
26b
%T
cm-1
97
96
94
92
90
88
86
84
82
80
78
76
74
72
4000
3500
3000
2500
2000
1500
1000
450
3627.08cm-1, 93.23%T
2820.41cm-1, 90.09%T
1511.70cm-1, 88.00%T
866.51cm-1, 87.79%T
964.98cm-1, 87.84%T
1567.82cm-1, 87.15%T
1622.92cm-1, 86.41%T
1488.43cm-1, 86.03%T
1272.86cm-1, 85.81%T
1332.38cm-1, 85.29%T
1429.50cm-1, 84.80%T
1291.92cm-1, 84.37%T
1307.88cm-1, 85.94%T
821.13cm-1, 83.75%T
1583.99cm-1, 82.77%T
1245.83cm-1, 81.52%T
476.37cm-1, 81.02%T
548.13cm-1, 79.08%T
761.57cm-1, 77.83%T
691.27cm-1, 76.37%T
608.24cm-1, 76.37%T
586.57cm-1, 72.39%T
785.59cm-1, 73.59%T

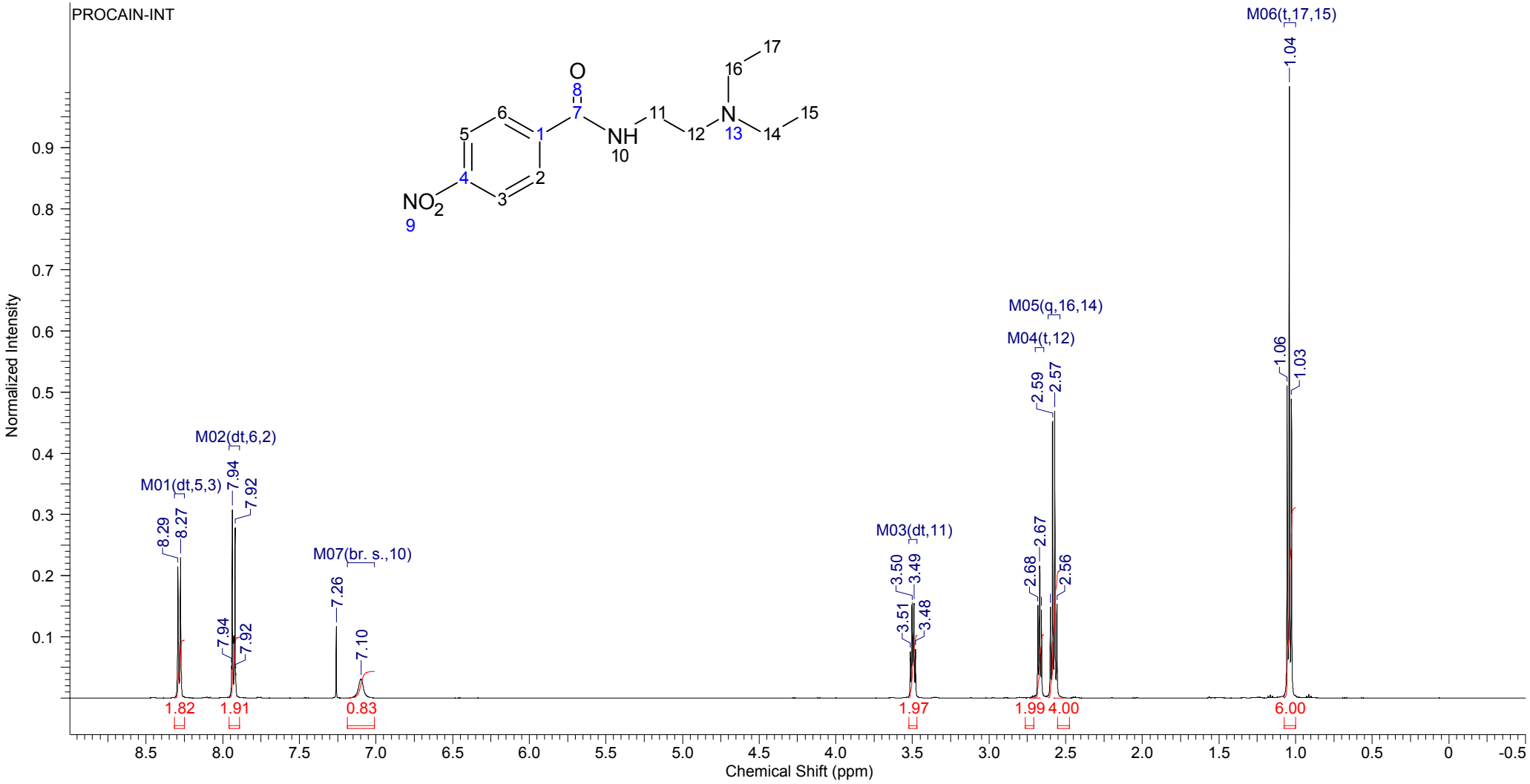
```
File       :C:\msdchem\New Column-110725\AutoSampler\smk-aminoharmane.D
Operator   :
Acquired   : 13 Sep 2013  13:02     using AcqMethod 70-250-20M-LD.M
Instrument :    GCMS1
Sample Name:
Misc Info  :
Vial Number: 1
```



Formula $C_{13}H_{19}N_3O_3$	FW	265.3083

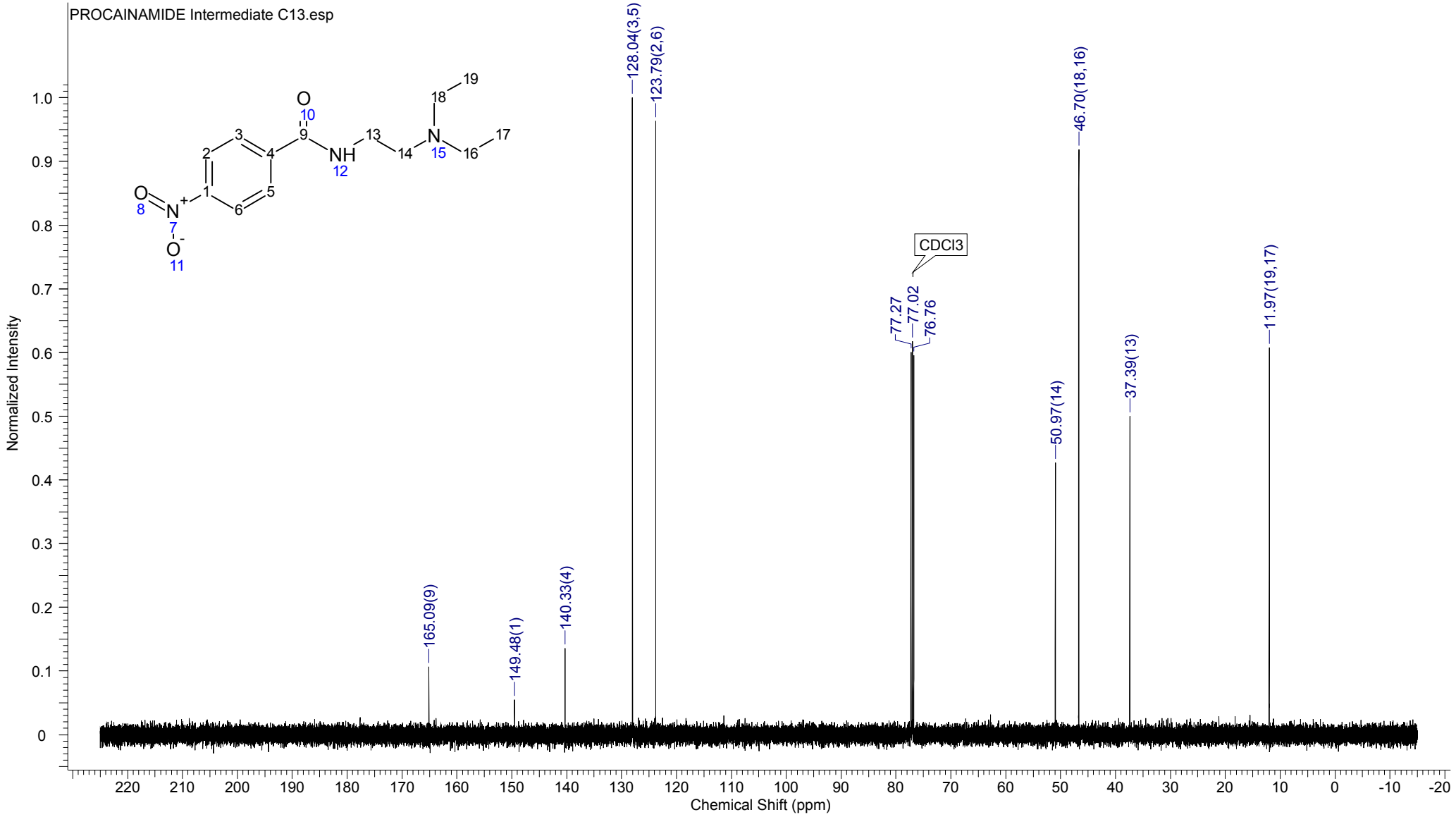
Acquisition Time (sec)	2.5001	**Comment**	Nitro intermediate			**Date**	Sep 6 2013
Date Stamp	Sep 6 2013	**File Name**	C:\USERS\SEAN\DOCUMENTS\NMR\PROCAIN-INT.FID\FID				
Frequency (MHz)	499.86	**Nucleus**	1H	**Number of Transients**	32	**Original Points Count**	21259
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	36.00	**Solvent**	CHLOROFORM-d
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 8.28 (dt, *J*=8.80, 2.10 Hz, 2 H), 7.93 (dt, *J*=8.80, 2.10 Hz, 2 H), 7.10 (br. s., 1 H), 3.50 (dt, *J*=6.20, 5.20 Hz, 2 H), 2.67 (t, *J*=5.97 Hz, 2 H), 2.58 (q, *J*=7.09 Hz, 4 H), 1.04 (t, *J*=7.14 Hz, 6 H)



Formula $C_{13}H_{19}N_3O_3$	FW	265.3083

Acquisition Time (sec)	1.3026	**Comment**	Std carbon	**Date**	Sep 6 2013	**Date Stamp**	Sep 6 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PROCAINAMIDE-INT-C13.FID\FID					**Frequency (MHz)**	125.70
Nucleus	13C	**Number of Transients**	64	**Original Points Count**	39295	**Points Count**	65536
Pulse Sequence	s2pul	**Receiver Gain**	46.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	13197.3711	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	30165.91	**Temperature (degree C)**	AMBIENT TEMPERATURE



Formula $C_{13}H_{21}N_3O$	FW	235.3253

Acquisition Time (sec)	2.5001	**Date**	Sep 6 2013	**Date Stamp**	Sep 6 2013
File Name	C:\USERS\SEAN\DOCUMENTS\NMR\PROCAINAMIDE.FID\FID			**Frequency (MHz)**	499.86
Nucleus	1H	**Number of Transients**	16	**Original Points Count**	21259	**Points Count**	32768
Pulse Sequence	s2pul	**Receiver Gain**	30.00	**Solvent**	CHLOROFORM-d		
Spectrum Offset (Hz)	2494.9937	**Spectrum Type**	STANDARD	**Sweep Width (Hz)**	8503.40	**Temperature (degree C)**	AMBIENT TEMPERATURE

^{1}H NMR (500 MHz, CHLOROFORM-*d*) δ ppm 7.60 (dt, *J*=8.82, 2.60 Hz, 2 H), 6.76 (br. s., 1 H), 6.64 (dt, *J*=8.56, 2.60 Hz, 2 H), 3.97 (br. s., 2 H), 3.44 (dt, *J*=6.23, 5.40 Hz, 2 H), 2.62 (t, *J*=5.97 Hz, 2 H), 2.55 (q, *J*=7.01 Hz, 4 H), 1.02 (t, *J*=7.14 Hz, 6 H)