

Supporting Information

A Biomimetic Electrocatalytic System for the Atom-Economical Chemoselective Synthesis of Secondary Amines

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I. General considerations: ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer operating at 300 MHz and 75 MHz, respectively. Chemical shifts δ , are given in ppm relative to TMS and coupling constants J , in hertz. The measurements were carried out using the standard pulse-sequences. The carbon type (methyl, methylene, methine, or quaternary) was determined by DEPT experiments. Mass spectra were recorded on a ZQ 2000 Waters spectrometer, equipped with the positive electrospray mode (ES+). Chemicals were commercial products of the highest available purity and were used as supplied. Reduced catalyst **1_{red}** was synthesized in two steps from commercially available 2-nitroresorcinol.¹ The identity of known secondary amines was confirmed by ^1H and ^{13}C NMR after comparison with previously reported data: *N*-Benzyl-*N*-cyclopropylmethylamine (322 mg, 80%) (Table 1, entry 1);² *N*-Benzyl-*N*-cyclohexylmethylamine (305 mg, 60%) (Table 1, entry 2);³ *N*-benzyl-*N*-cyclohexylamine (321 mg, 68%) (Table 1, entry 3);⁴ 4-(*N*-Benzyl-2-aminoethyl)morpholine (363 mg, 66%) (Table 1, entry 4), previously described as the dihydrochloride salt;⁵ *N*-benzyl(3,3-dimethyl)butylamine (334 mg, 70%) (Table 1, entry 5);⁶ *N*-benzylhexylamine (272 mg, 57%) (Table 1, entry 6);^{6,7} *N*-benzyl-1-phenyl-2-propylamine (360 mg, 64%) (Table 1, entry 8);⁸ *N*-Benzyl-2-methoxyethylamine (293 mg, 71%) (Table 1, entry 9), previously described as the oxalate salt;⁹ Benzyl(2,2-dimethoxyethyl)amine (292 mg, 60%) (Table 1, entry 10);¹⁰ 2-Benzylaminoethanol (257 mg, 68%) (Table 1, entry 11);¹¹ (*R*)-(-)-*N*-Benzyl-2-amino-1-butanol (313 mg, 70%) (Table 1, entry 12)¹²; *N*-(4-methoxybenzyl)-3-phenylpropylamine (Table 2, entry 3);¹³ *N*-(3-phenylpropyl)-2-pyridinemethanamine (Table 2, entry 6.);¹⁴ *N*-(3-phenylpropyl)-3-pyridinemethanamine (Table 2, entry 7);¹⁵

II. General experimental procedure for the **1_{ox}-mediated **N**-alkylation of primary amines with amines:** Controlled-potential electrolysis was carried out in a cylindrical, three-electrode divided cell (9 cm diameter), using an electronic potentiostat. In the main compartment, a platinum grid (90 cm² area) served as the anode (working electrode). A platinum sheet was placed in the concentric cathodic compartment (counter electrode), which was separated from the main compartment with a glass frit. The reference electrode, to which all quoted potentials are referred, was an aqueous saturated calomel electrode (SCE). The electrolyte solution (0.1 molL⁻¹ lithium perchlorate in methanol) was poured into the anodic and the cathodic compartments, as well as into the glass tube that contained the SCE electrode. Reduced catalyst **1_{red}** (0.1 mmol) (4 mol % relative to primary aliphatic amine substrate), primary aliphatic amine substrate (2.5 mmol) together with a slight excess of alkylating amine (3.75 mmol) were added to the solution in the main compartment (250 mL),

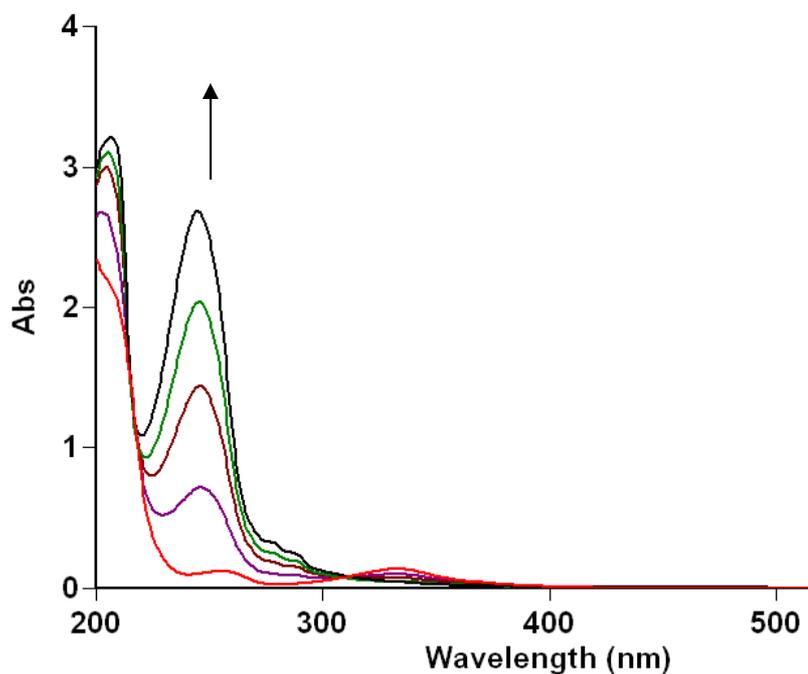
and the resulting solution was then oxidized under nitrogen, at room temperature, at + 0.6 V vs SCE (initial current 60-70 mA). After exhaustive electrolysis (3 h), the platinum anode was replaced by a mercury pool whose the potential was fixed at -1.6 V vs SCE. After 1 h, when a negligible value of the current was recorded indicating the end of the electrochemical reduction, the electrolysis solution was poured into an aqueous HCl solution (0.5 molL^{-1} , 15 mL) and MeOH was removed under reduced pressure. The resulting solution was treated with an aqueous K_2CO_3 solution (0.5 molL^{-1} , 15 mL) and extracted with CH_2Cl_2 (100 mL). The organic layer was then dried over MgSO_4 and the solvent removed under reduced pressure at 30 °C. Flash column chromatography of the residue on silica afforded the expected secondary amine.

III. References

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IV. Figure 1

a)



b)

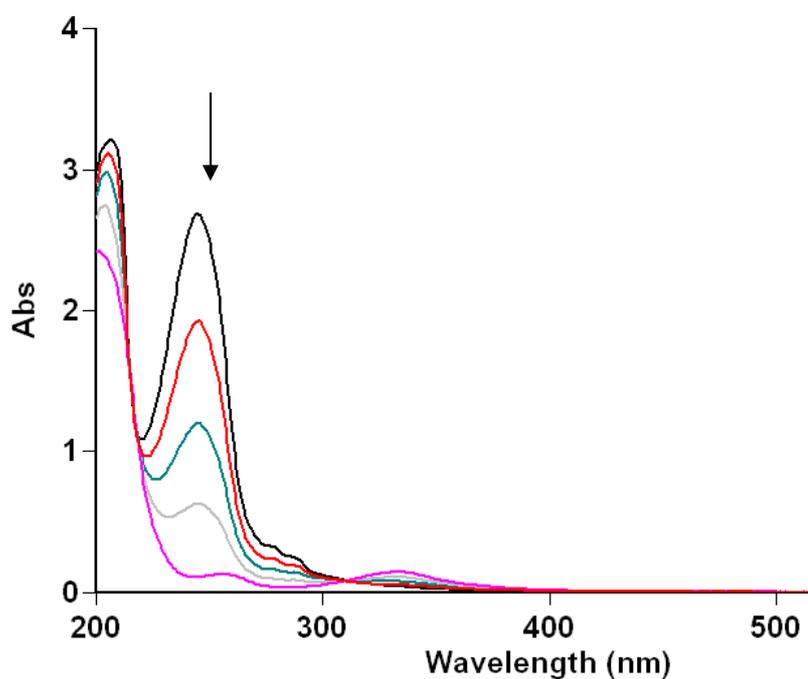


Figure 1. Spectrophotometric changes accompanying the 1_{ox} -mediated oxidation-imine formation-reduction sequence for the N-alkylation of benzylamine (2mM) with aminomethylcyclopropane (3mM) in MeOH: a) oxidation-imine formation sequence; b) imine reduction reaction. Spectra recorded: before anodic (a) or cathodic (b) controlled potential electrolysis, and after exchange of 0.5, 1.0, 1.5 and 2 mol of electrons (relative to benzylamine), respectively. Cell thickness is 0.1 cm.

V. High field ^1H NMR spectra for known secondary amines

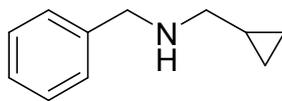
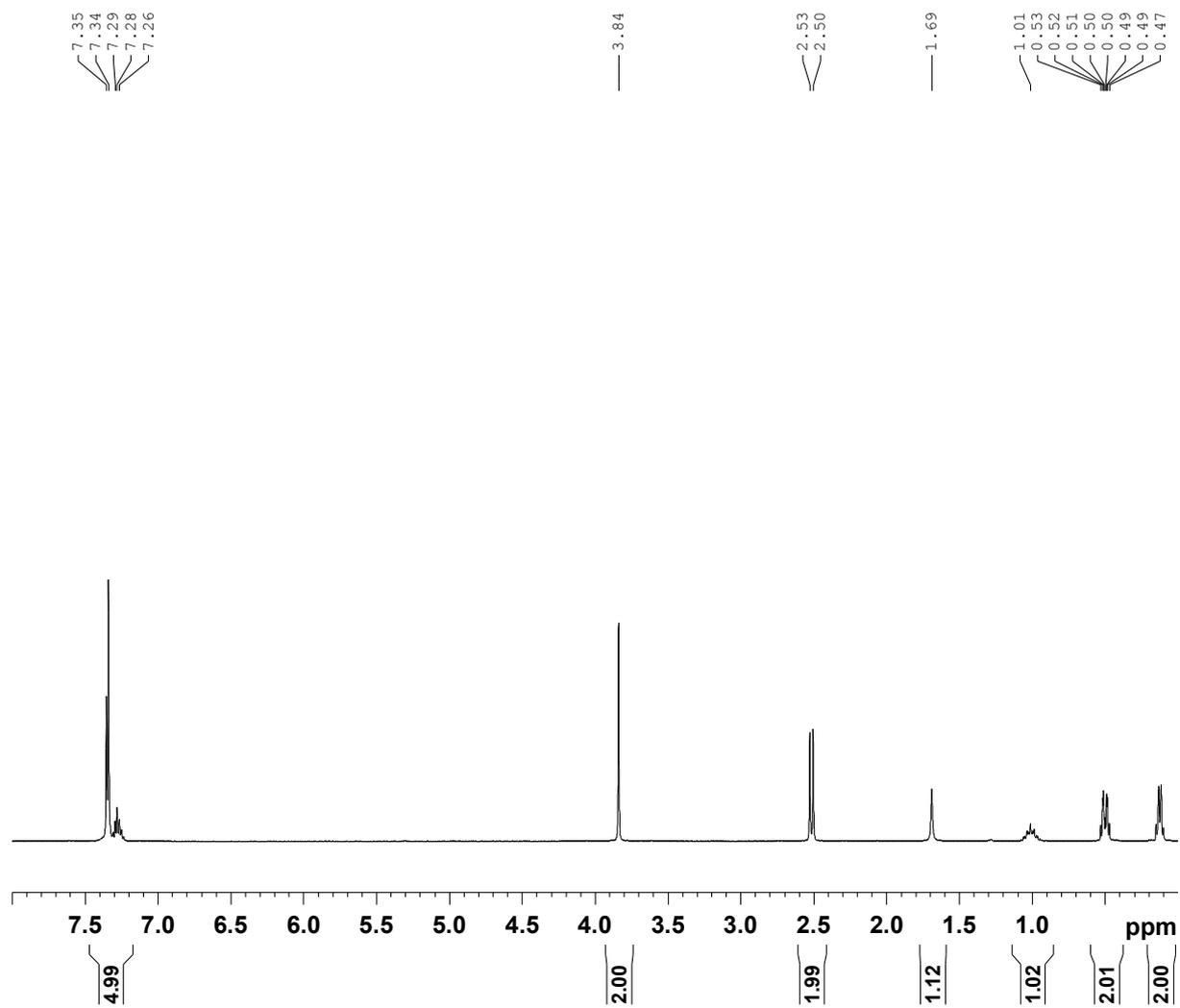


Table 1 - Entry 1



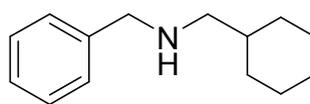
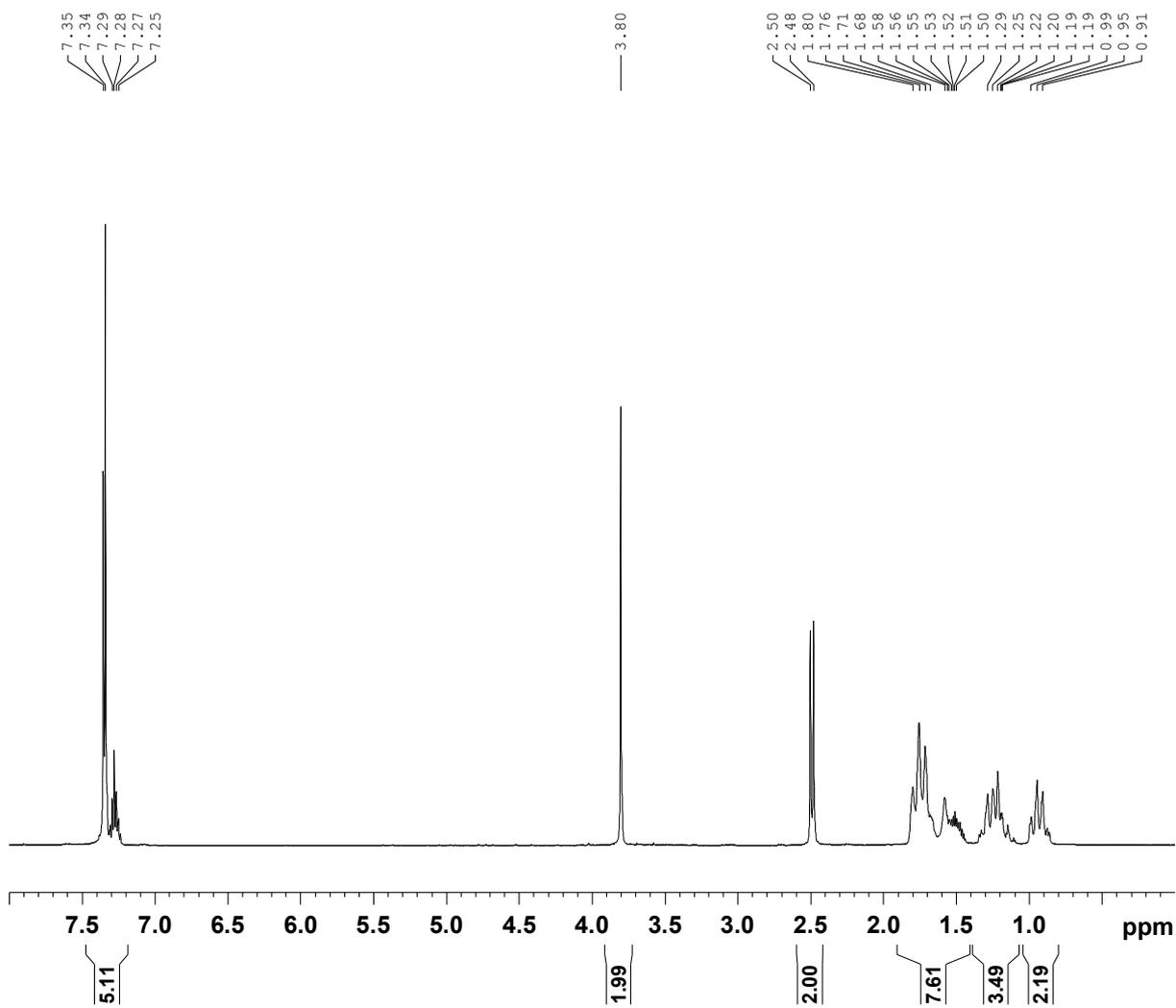


Table 1 - Entry 2



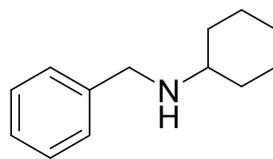
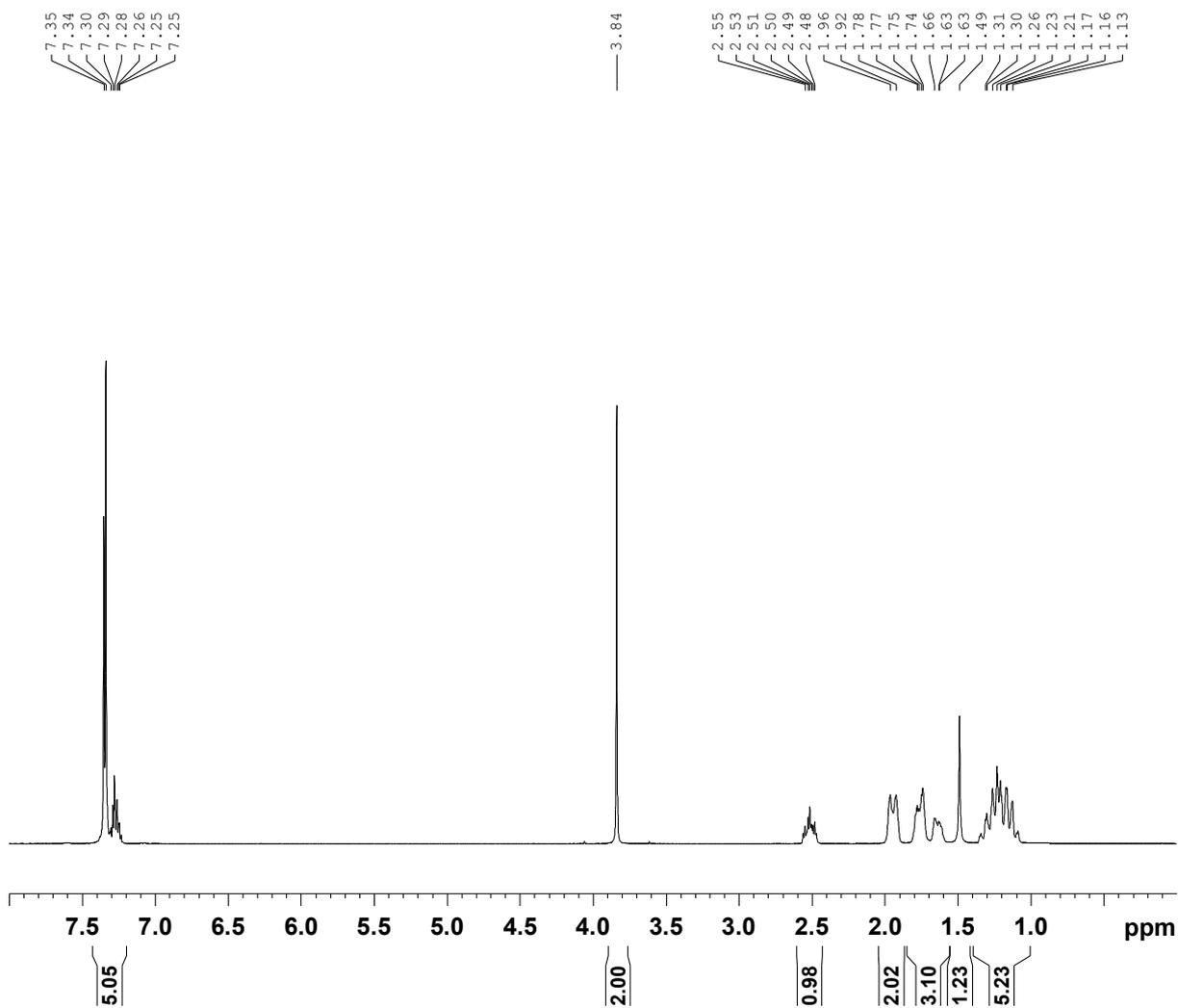


Table 1 - Entry 3



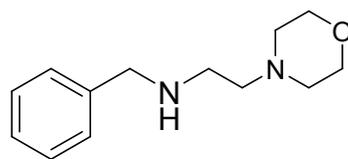
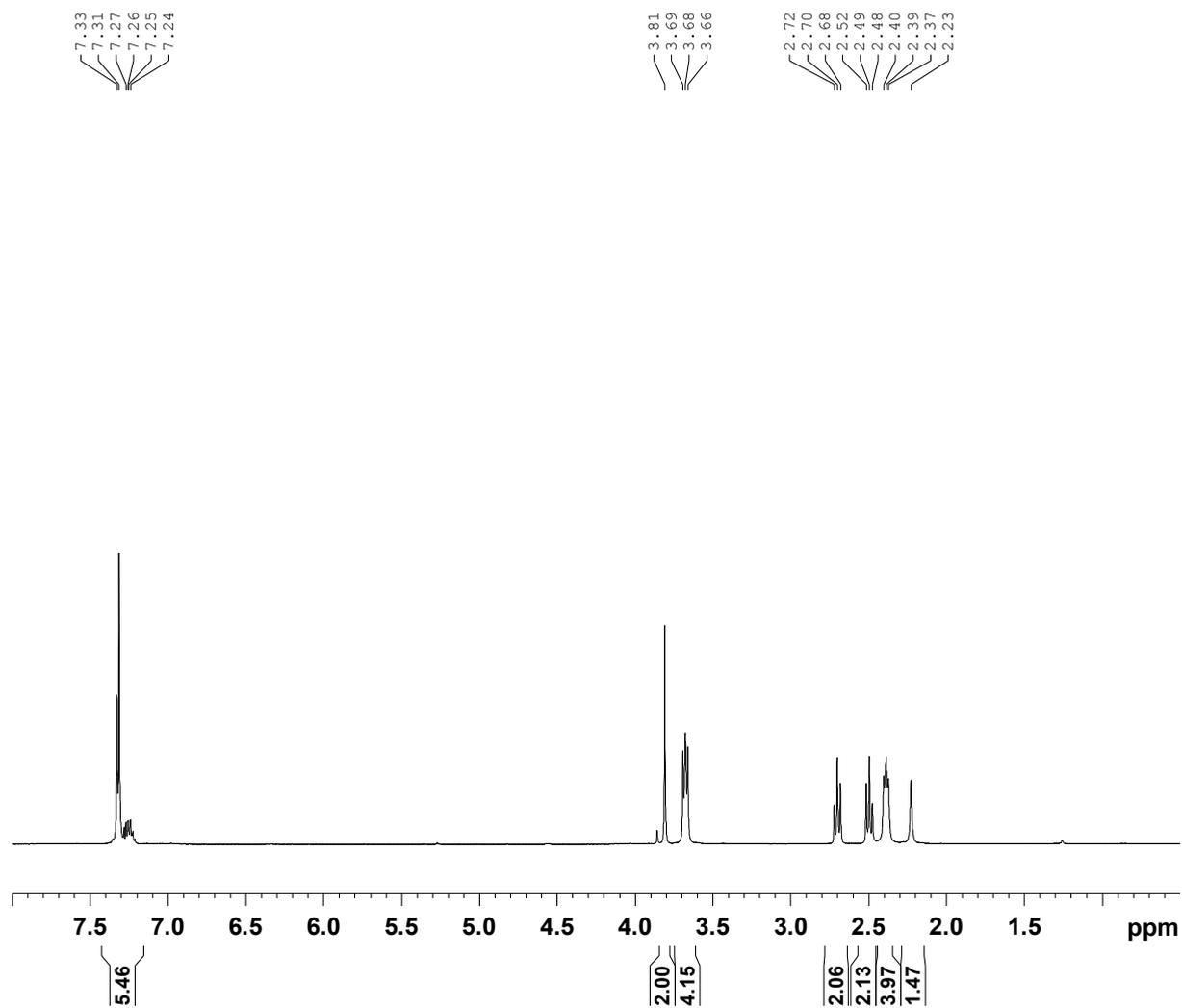


Table 1 - Entry 4



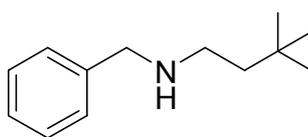
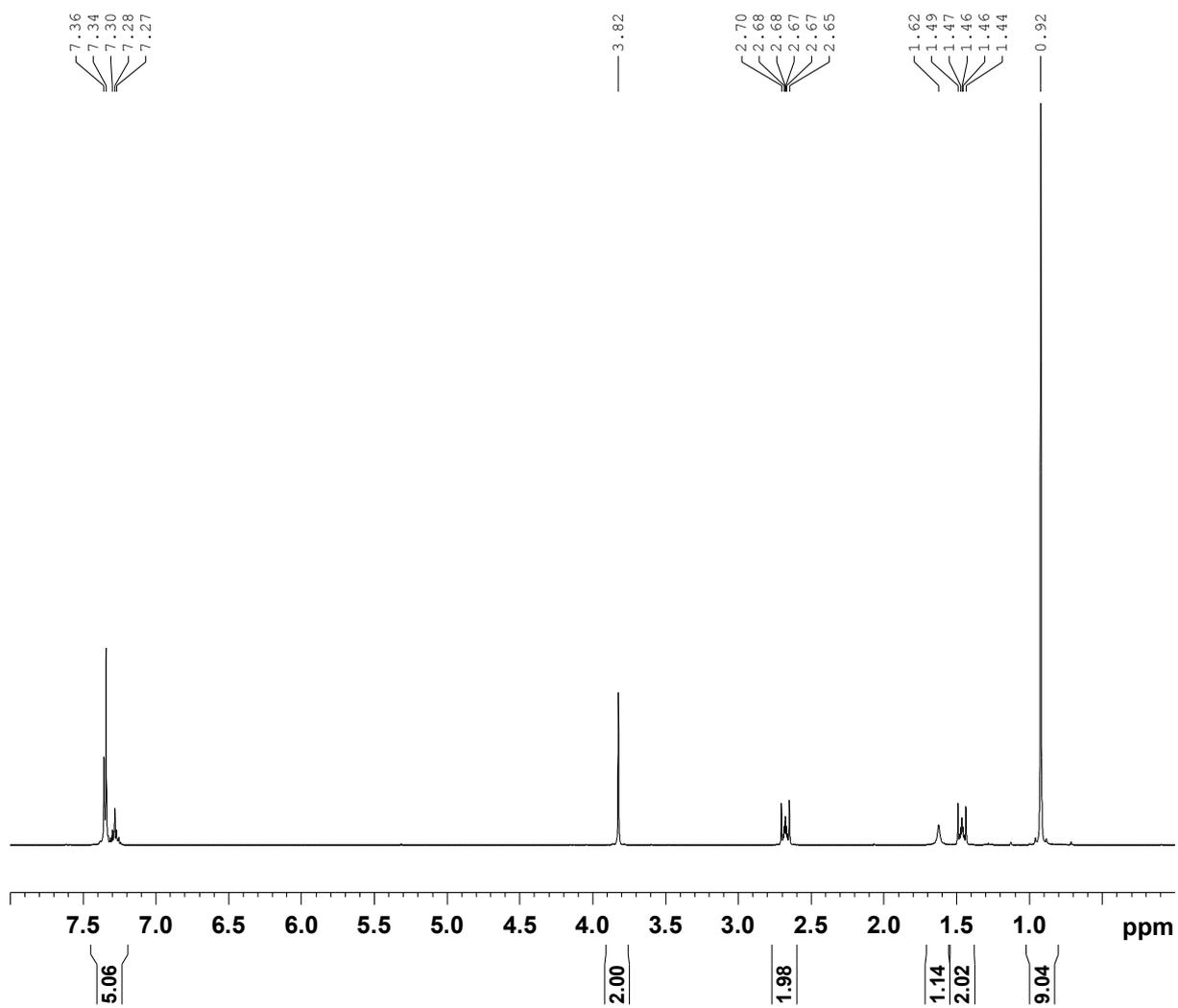


Table 1 – Entry 5



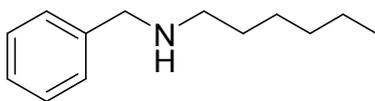
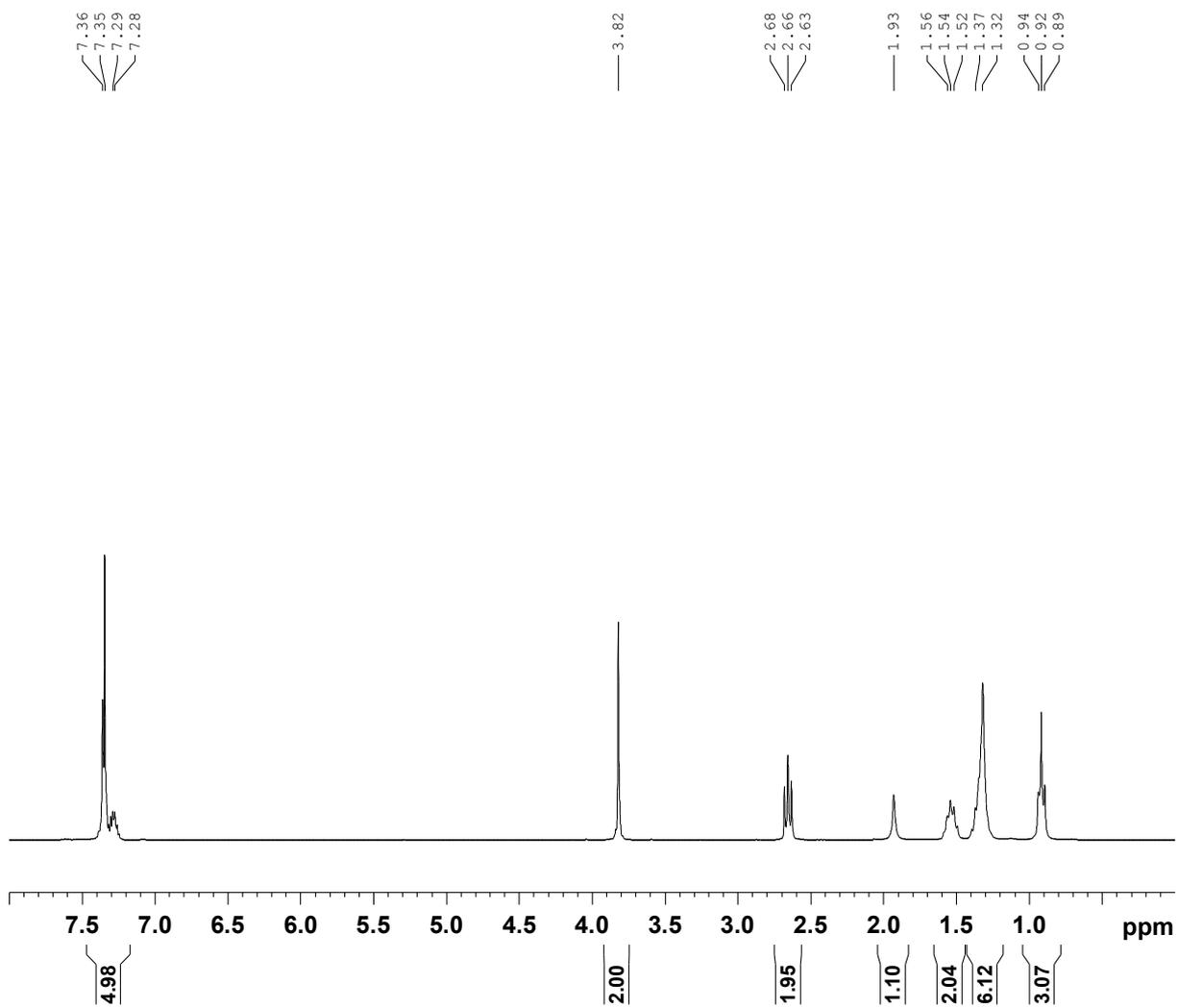


Table 1 - Entry 6



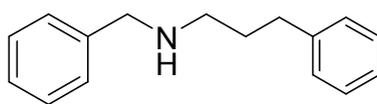
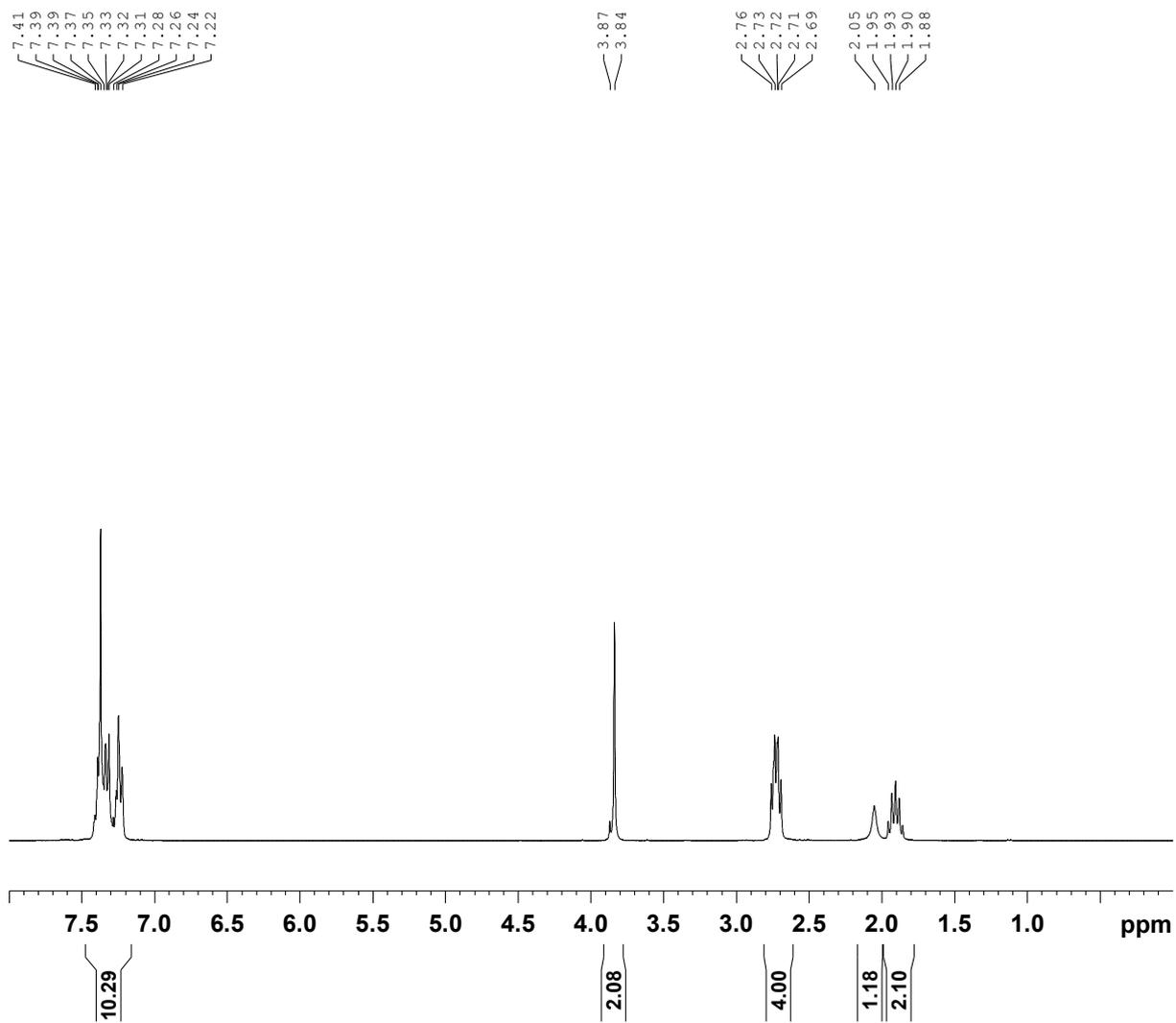


Table 1 - Entry 8



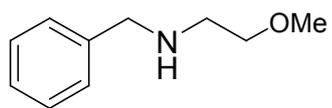
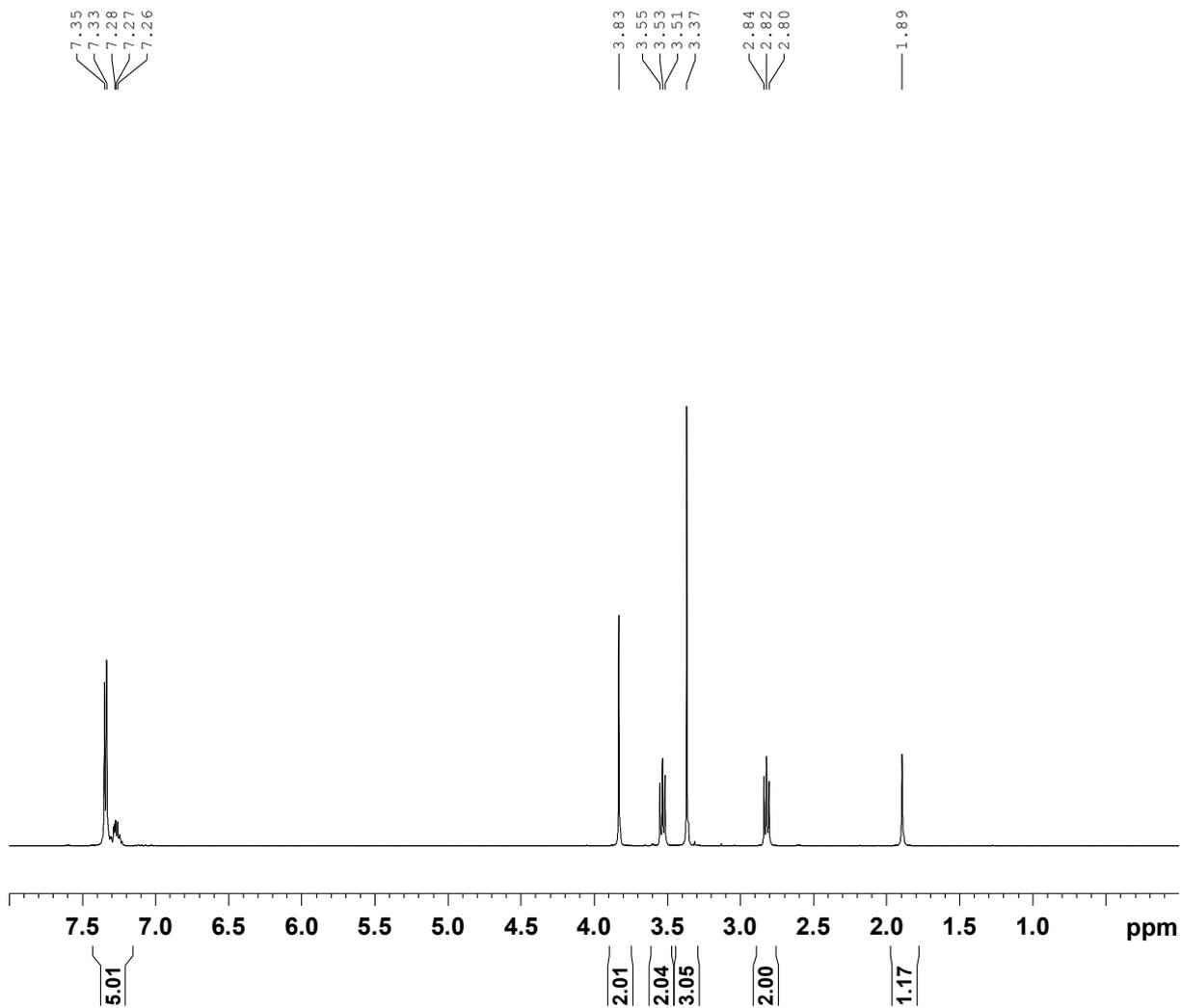


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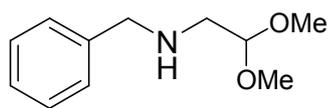
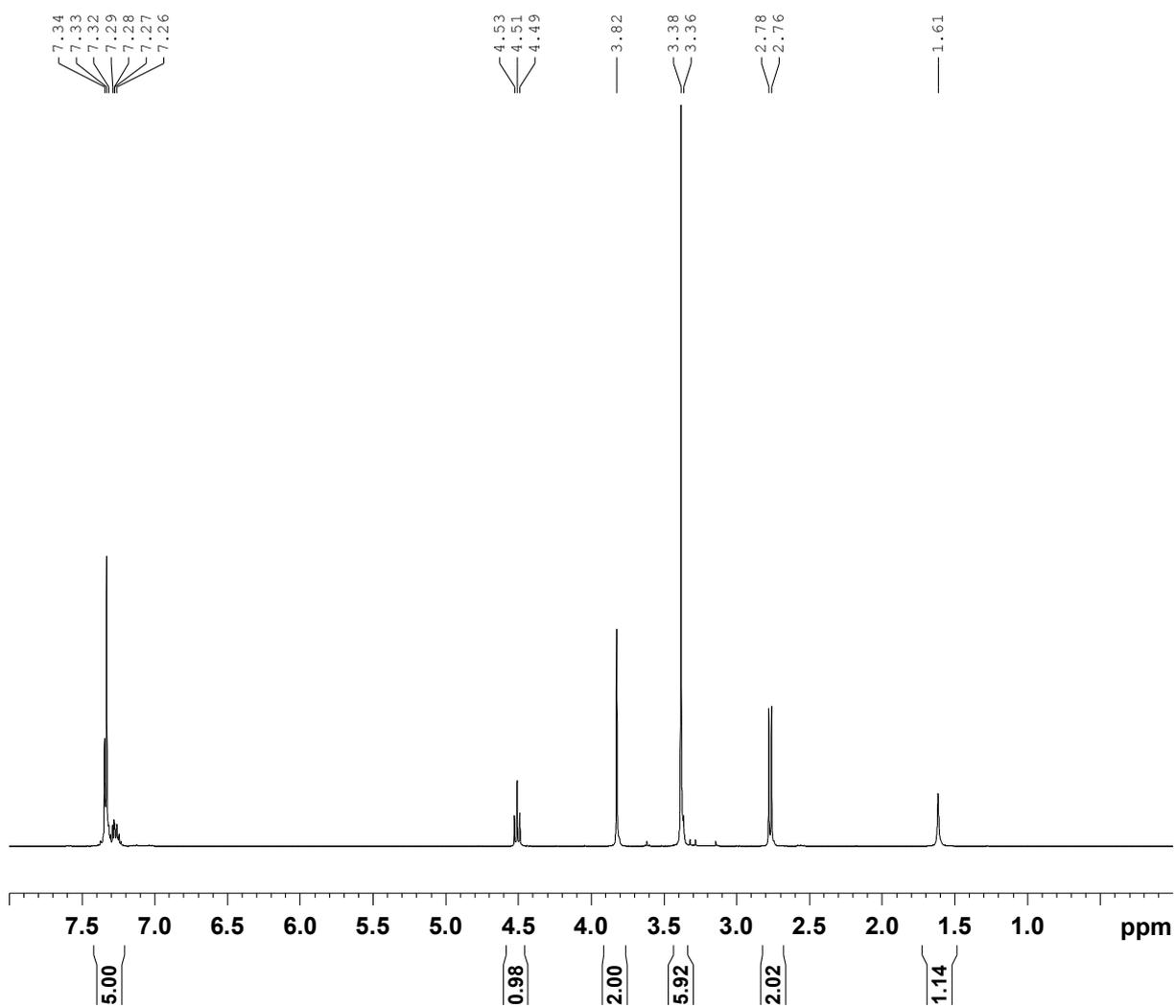


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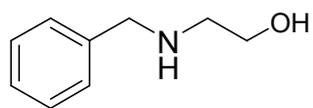
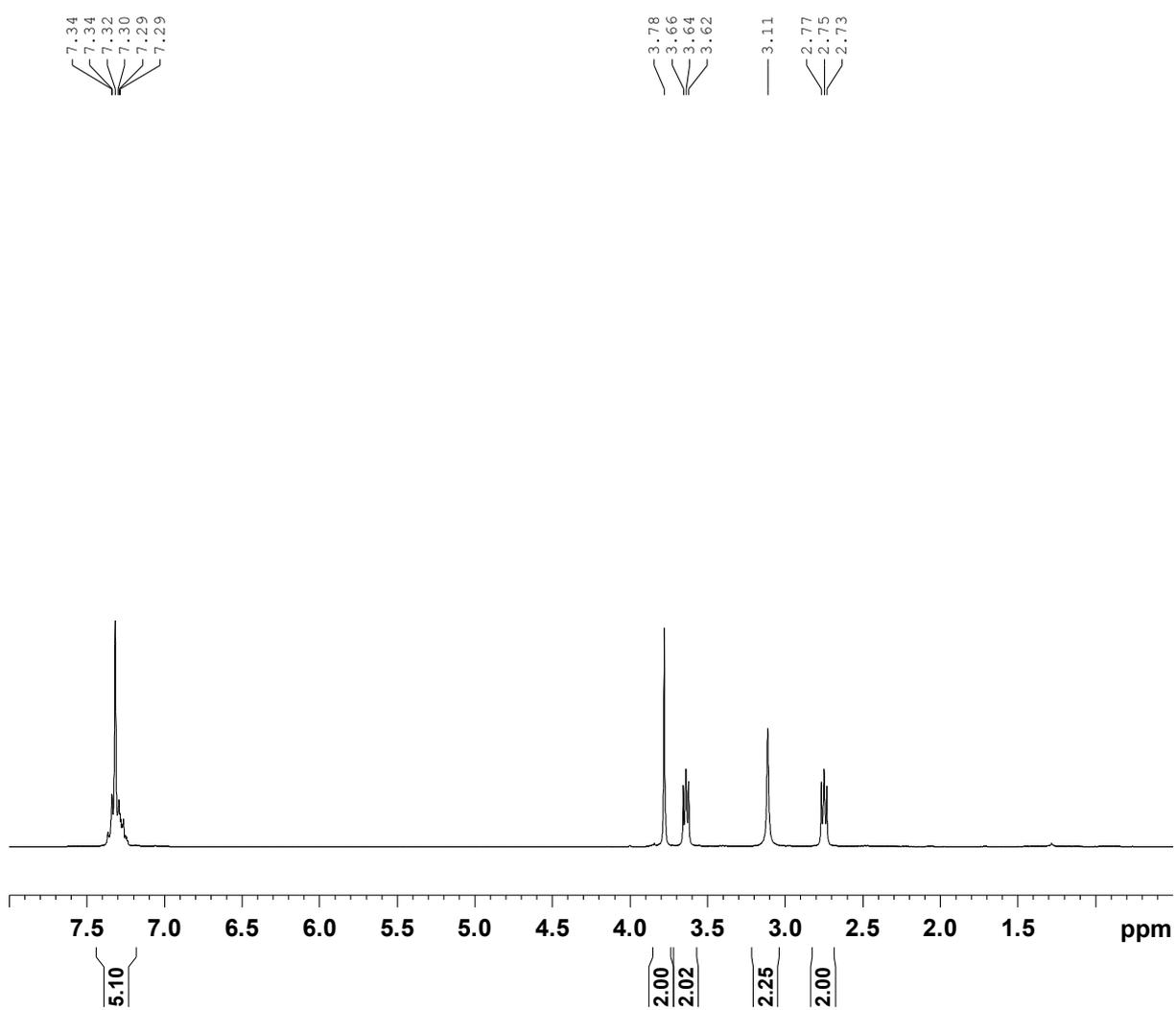


Table 1 - Entry 11



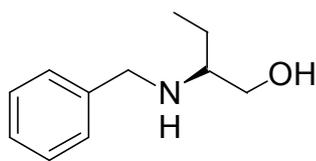
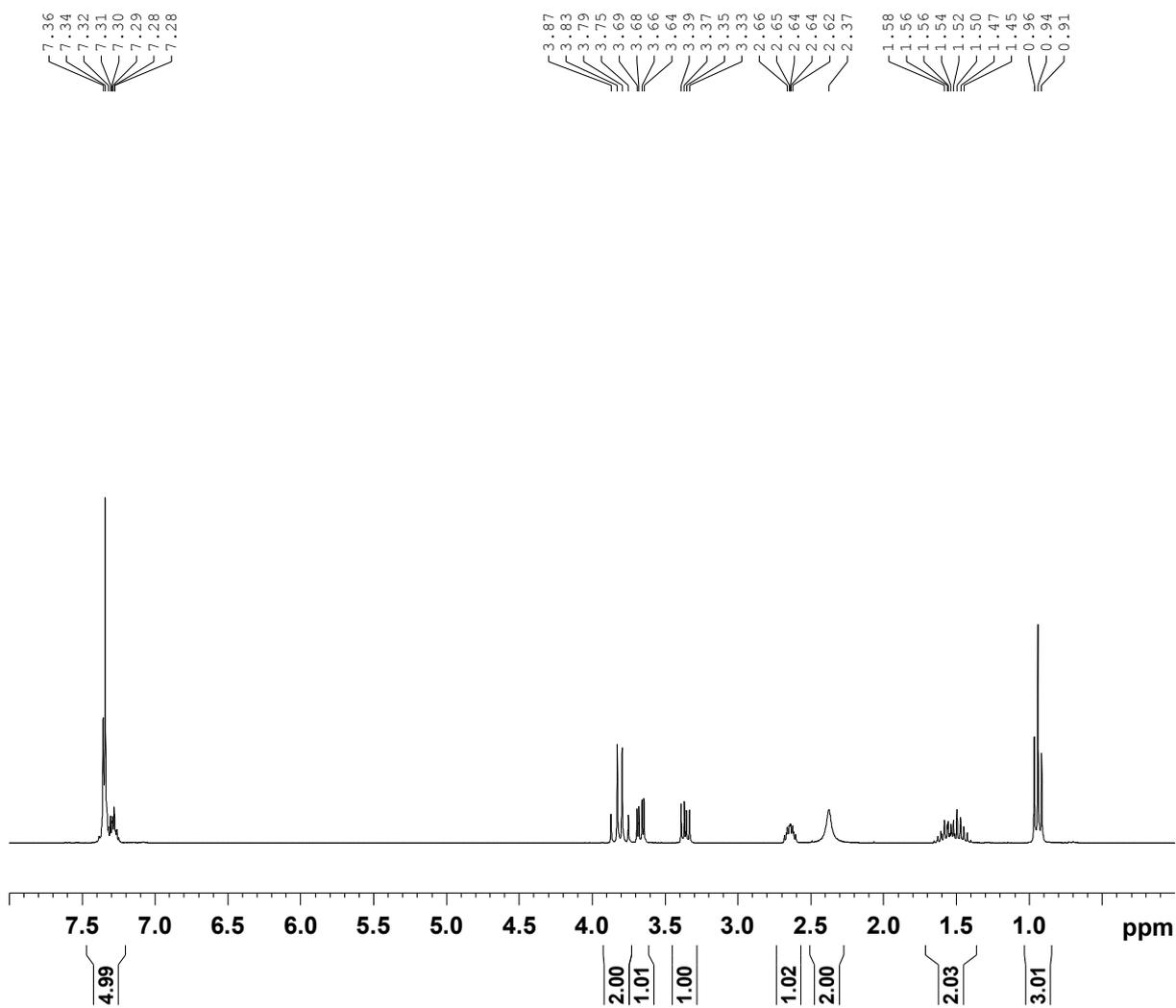


Table 1 - Entry 12



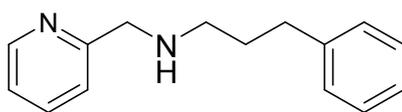
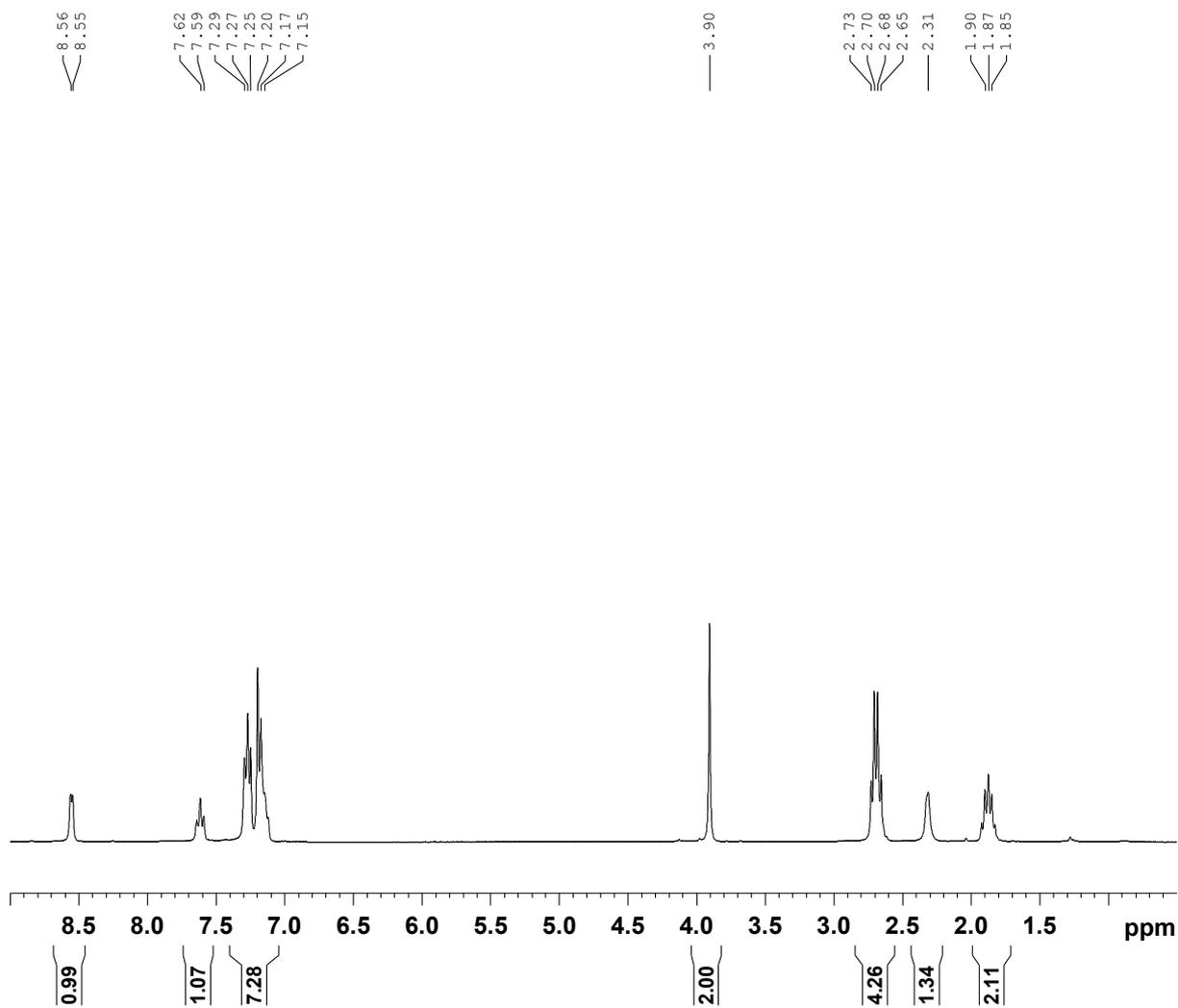


Table 2 - Entry 6



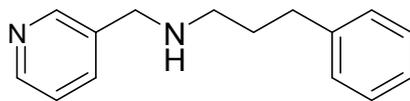
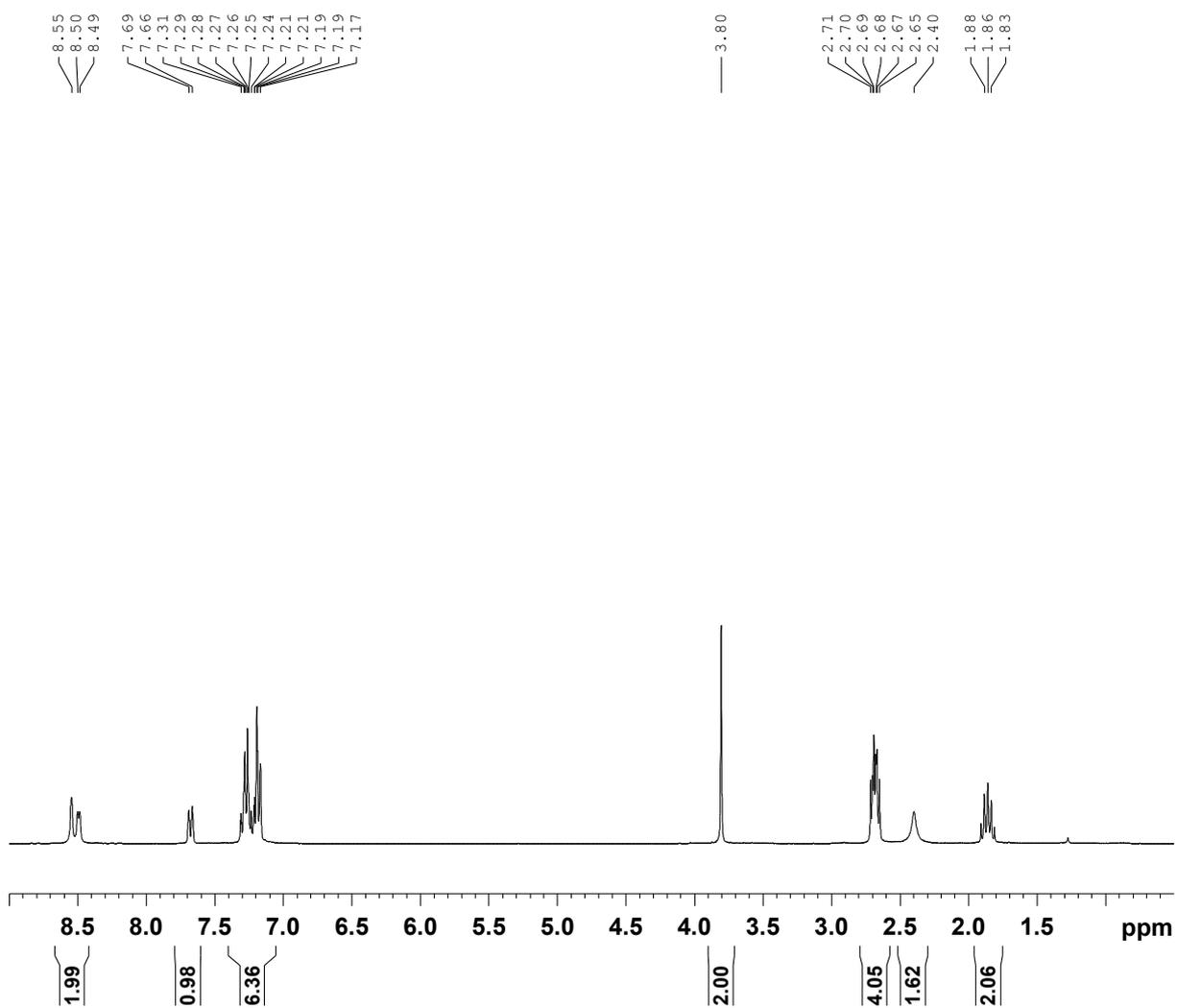
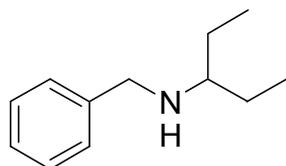


Table 2 - Entry 7



VI. Known secondary amine for which no previously NMR spectral data is available

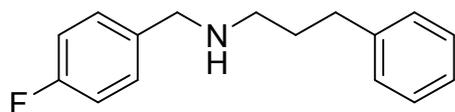
N-Benzyl-1-ethylpropylamine (Table 1 - entry 7)¹⁶



Colorless oil (226 mg, 51%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 0.93 (t, J = 7.5 Hz, 6H; CH₃), 1.55 (quintet, J = 7.5 Hz, 4H; CH₂), 2.56 (m, 1H; CH), 3.26 (s, 1H; NH), 3.88 (s, 2H; CH₂), 7.28-7.41 (m, 5H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 9.7 (CH₃), 25.0 (CH₂), 50.8 (CH₂), 59.4 (CH), 127.4 (CH), 128.5 (CH), 128.6 (CH), 138.7 (Cq).

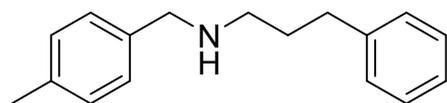
VII. Analytical data for new secondary amines

N-(4-Fluorobenzyl)-3-phenylpropylamine (Table 2 - entry 1)



Colorless oil (413 mg, 68%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 1.56 (s, 1H; NH), 1.88 (quintet, J = 7 Hz, 2H; CH₂), 2.70 (m, 4H; CH₂), 3.78 (s, 2H; CH₂), 7.05 (m, 2H; CH), 7.21-7.33 (m, 7H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 31.7 (CH₂), 33.6 (CH₂), 48.8 (CH₂), 53.2 (CH₂), 115.2 (CH), 125.8 (CH), 128.4 (CH), 129.7 (CH), 136.1 (Cq), 142.1 (Cq), 161.5 (Cq); MS (ES⁺) m/z 244 (MH⁺); Anal. Calcd for C₁₆H₁₈FN: C, 79.01; H, 7.41; N, 5.76. Found: C, 78.85; H, 7.43; N, 5.70.

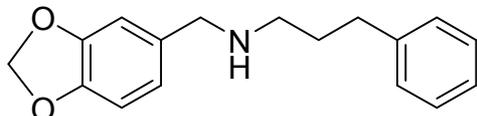
N-(4-methylbenzyl)-3-phenylpropylamine (Table 2 - entry 2)



Colorless oil (370 mg, 62%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 1.58 (s, 1H; NH), 1.88 (quintet, J = 7 Hz, 2H; CH₂), 2.38 (s, 3H; CH₃), 2.71 (m, 4H; CH₂), 3.79 (s, 2H; CH₂), 7.17-7.32 (m, 9H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 21.1 (CH₃), 31.7 (CH₂), 33.7 (CH₂), 48.9 (CH₂), 53.7 (CH₂), 125.8 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH),

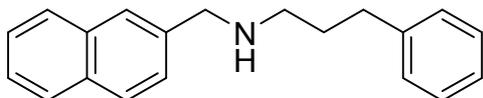
129.1 (CH), 136.5 (Cq), 137.4 (Cq), 142.2 (Cq); MS (ES+) m/z 240 (MH⁺); Anal. Calcd for C₁₇H₂₁N: C, 85.35; H, 8.78; N, 5.86. Found: C, 85.30; H, 8.76; N, 5.82.

***N*-(3,4-methylenedioxybenzyl)phenylpropylamine** (Table 2 - entry 4)



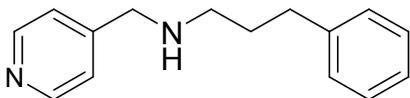
Colorless oil (457 mg, 68%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 1.40 (s, 1H; NH), 1.88 (quintet, J = 7 Hz, 2H; CH₂), 2.70 (m, 4H; CH₂), 3.73 (s, 2H; CH₂), 5.96 (s, 2H; CH₂), 6.80 (s, 2H; CH), 6.88 (s, 1H; CH), 7.22-7.33 (m, 5H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 31.6 (CH₂), 33.6 (CH₂), 48.6 (CH₂), 53.7 (CH₂), 100.9 (CH₂), 108.1 (CH), 108.8 (CH), 121.3 (CH), 125.8 (CH), 128.4 (CH), 128.5 (CH), 128.5 (CH), 134.0 (Cq), 142.1 (Cq), 146.6 (Cq), 147.8 (Cq); MS (ES+) m/z 270 (MH⁺); Anal. Calcd for C₁₇H₁₉NO₂: C, 75.84; H, 7.06; N, 5.20. Found: C, 75.90; H, 7.10; N, 5.23.

***N*-(naphthylmethyl)phenylpropylamine** (Table 2 - entry 5)



Pale yellow oil (350 mg, 51%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 1.64 (s, 1H; NH), 1.93 (q, J = 7 Hz, 2H; CH₂), 2.73 (t, J = 7 Hz, 2H; CH₂), 2.83 (t, J = 7 Hz, 2H; CH₂), 4.27 (s, 2H; CH₂), 7.21-7.35 (m, 5H; CH), 7.46-7.59 (m, 4H; CH), 7.81 (dd, J = 8 Hz, J = 1.5 Hz, 1H; CH), 7.90 (dd, J = 8 Hz, J = 1.5 Hz, 1H; CH), 8.15 (d, J = 8 Hz, 1H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 31.7 (CH₂), 33.7 (CH₂), 49.4 (CH₂), 51.7 (CH₂), 123.7 (CH), 125.4 (CH), 125.7 (CH), 125.8 (CH), 126.1 (CH), 126.2 (CH), 127.8 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 131.8 (Cq), 133.9 (Cq), 136.0 (Cq), 142.2 (Cq); MS (ES+) m/z 276 (MH⁺); Anal. Calcd for C₂₀H₂₁N: C, 87.27; H, 7.63; N, 5.09. Found: C, 87.30; H, 7.68; N, 5.10.

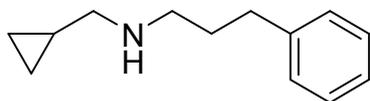
***N*-(3-phenylpropyl)-4-pyridinemethanamine** (Table 2 - entry 8)



Pale yellow oil (328 mg, 58%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 1.62 (s, 1H; NH), 1.85 (m, J = 7 Hz, 2H; CH₂), 2.67 (m, J = 7 Hz, 4H; CH₂), 3.79 (s, 2H; CH₂), 7.17-7.31 (m, 7H; CH), 8.54 (d, J = 6 Hz, 2H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 31.7

(CH₂), 33.5 (CH₂), 48.9 (CH₂), 52.7 (CH₂), 123.0 (CH), 125.9 (CH), 128.4 (CH), 142.0 (Cq), 149.6 (Cq), 149.8 (CH); MS (ES+) *m/z* 227 (MH⁺); Anal. Calcd for C₁₅H₁₈N₂: C, 79.65; H, 7.96; N, 12.39. Found: C, 79.60; H, 7.92; N, 12.35.

***N*-(cyclopropylmethyl)phenylpropylamine** (Scheme 2)



Colorless oil (227 mg, 48%). ¹H NMR (300 MHz, CDCl₃, 25°C, TMS) : δ = 0.10 (q, *J* = 4.5 Hz, 2H; CH₂), 0.50 (m, 2H; CH₂), 0.95 (m, 1H; CH), 1.43 (s, 1H; NH), 1.85 (quintet, *J* = 7.5 Hz, 2H; CH₂), 2.47 (d, *J* = 7.0 Hz, 2H; CH₂), 2.70 (m, 4H; CH₂), 7.18-7.33 (m, 5H; CH); ¹³C NMR (75 MHz, CDCl₃, 25°C, TMS) : δ = 3.5 (CH₂), 10.9 (CH), 31.4 (CH₂), 33.6 (CH₂), 49.2 (CH₂), 54.9 (CH₂), 125.8 (CH), 128.4 (CH), 141.9 (Cq); MS (ES+) *m/z* 190 (MH⁺); Anal. Calcd for C₁₃H₁₉N: C, 82.54; H, 10.05; N, 7.41. Found: C, 82.50; H, 10.00; N, 7.38.

VIII. High field ^1H NMR spectra and 1D proton-decoupled ^{13}C NMR spectra for new secondary amines and for known secondary amine for which no previously NMR spectral data is available

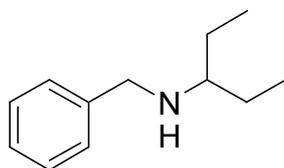
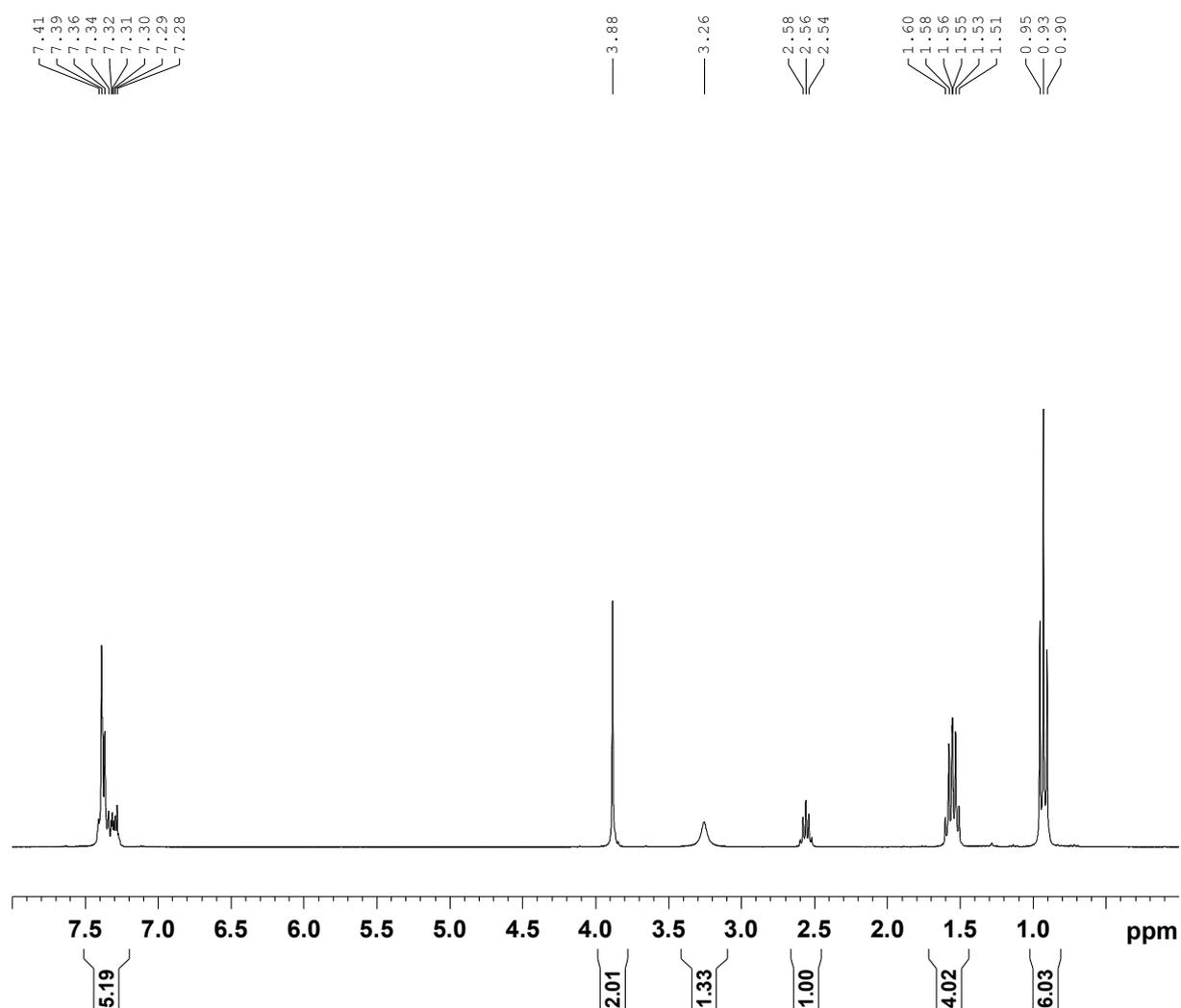


Table 1 - Entry 7



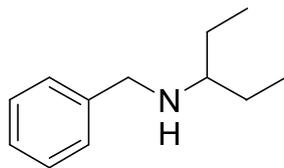
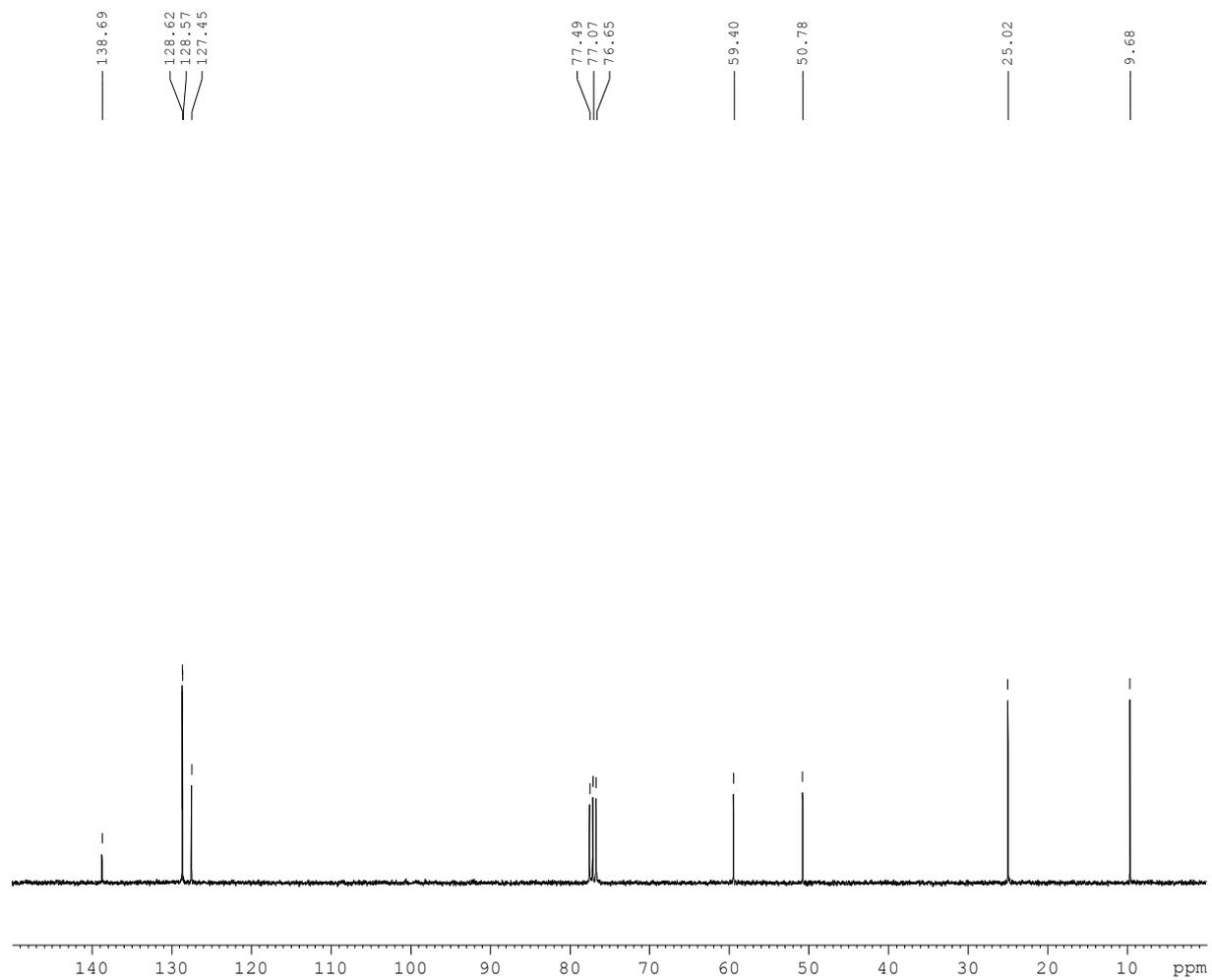


Table 1 - Entry 7



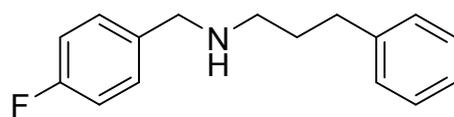
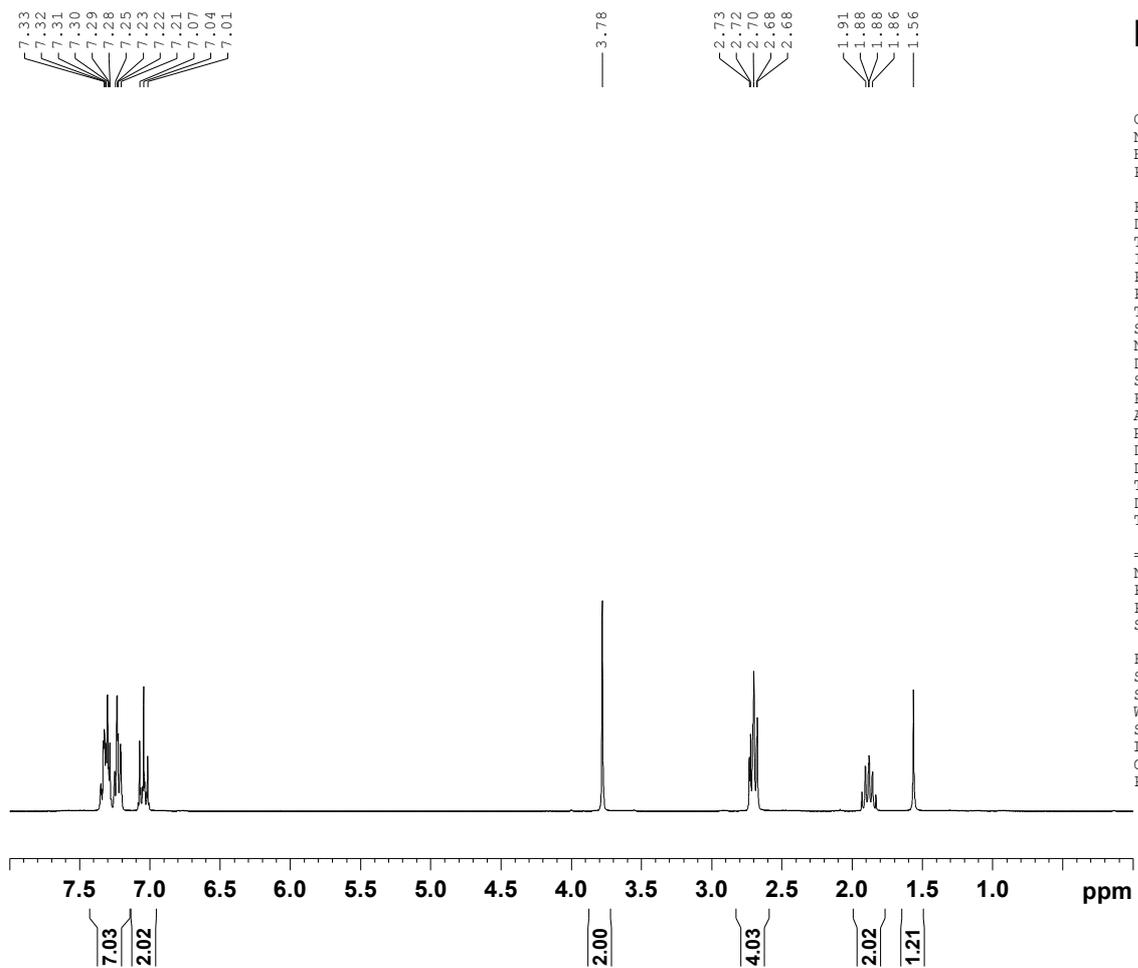


Table 2 - Entry 1



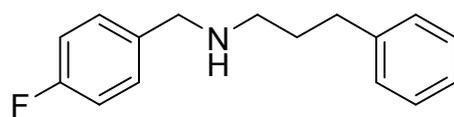
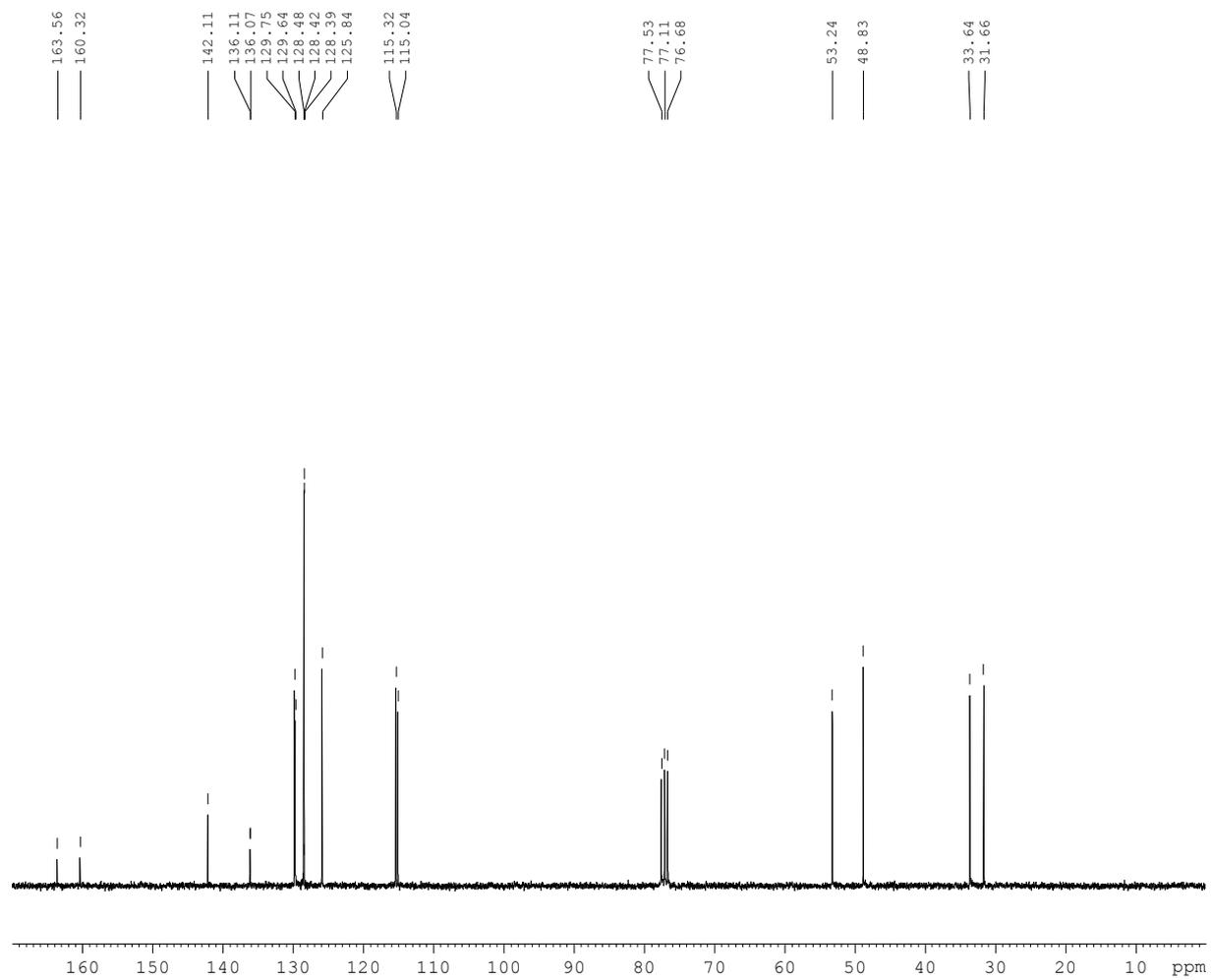


Table 2 - Entry 1



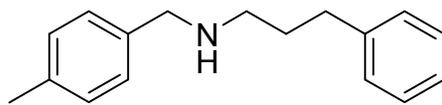
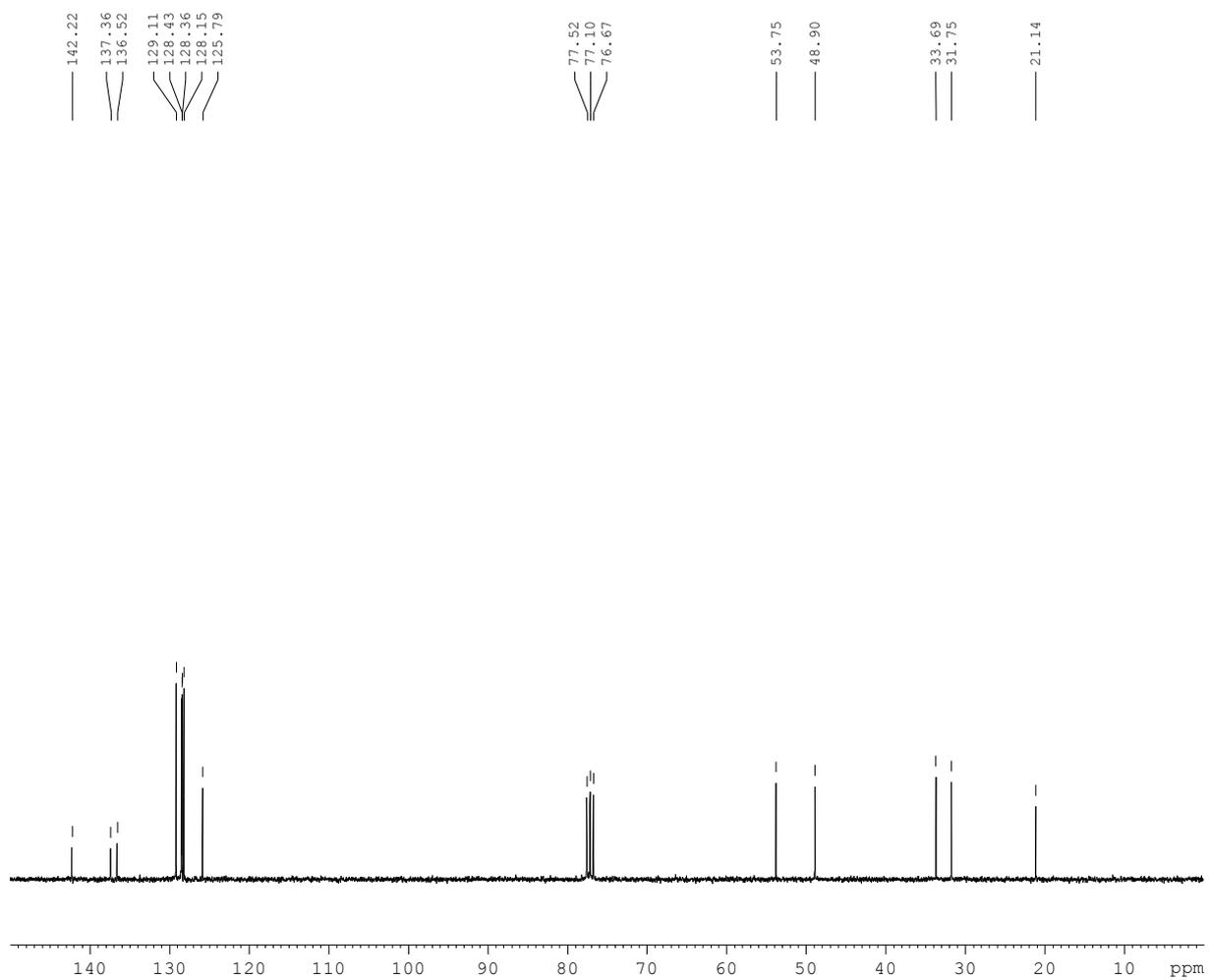


Table 2 - Entry 2



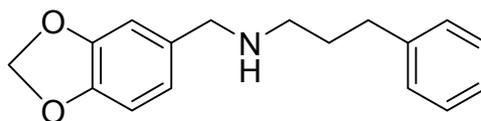
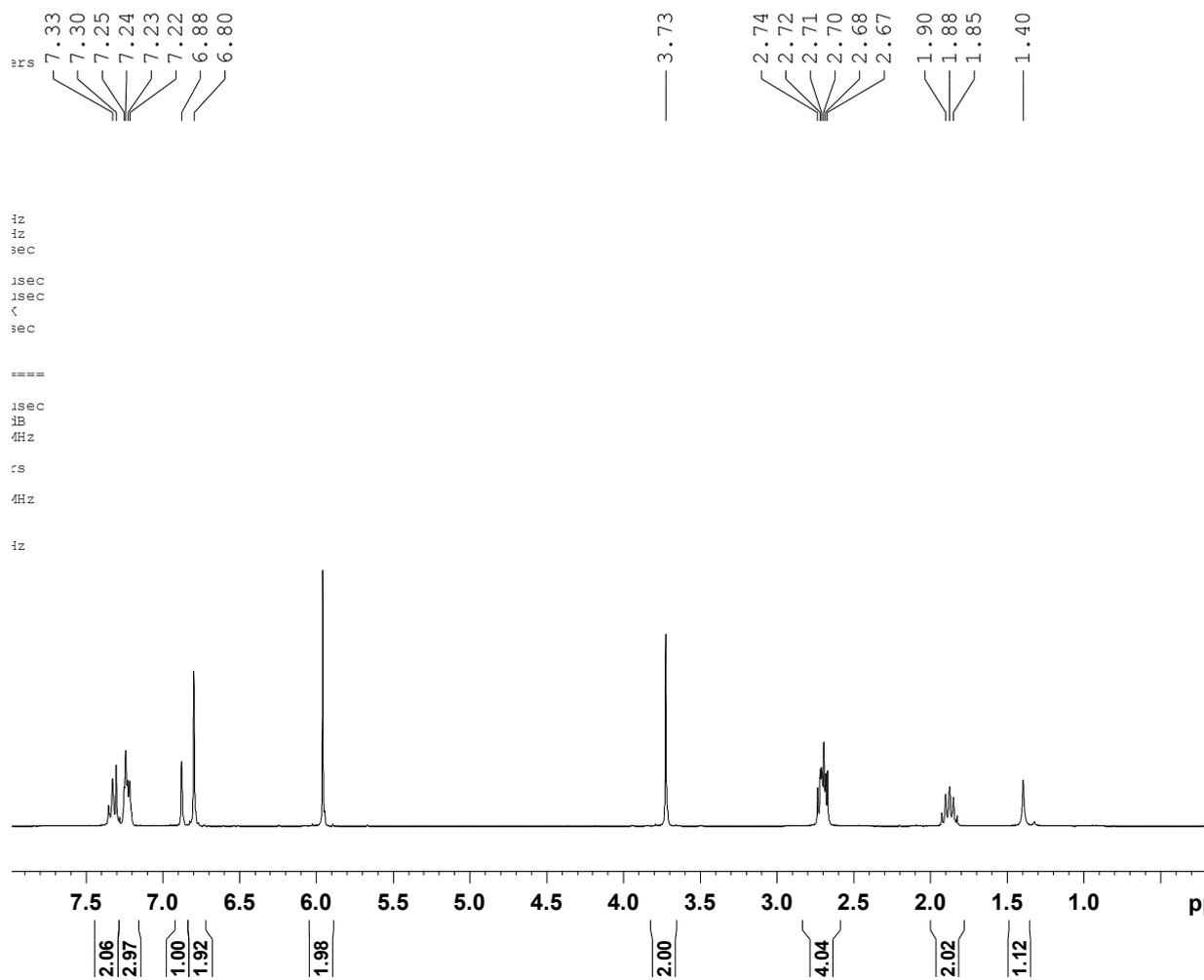


Table 2 - Entry 4



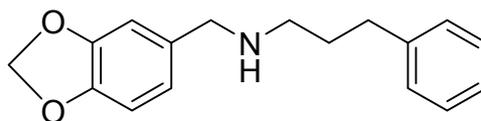
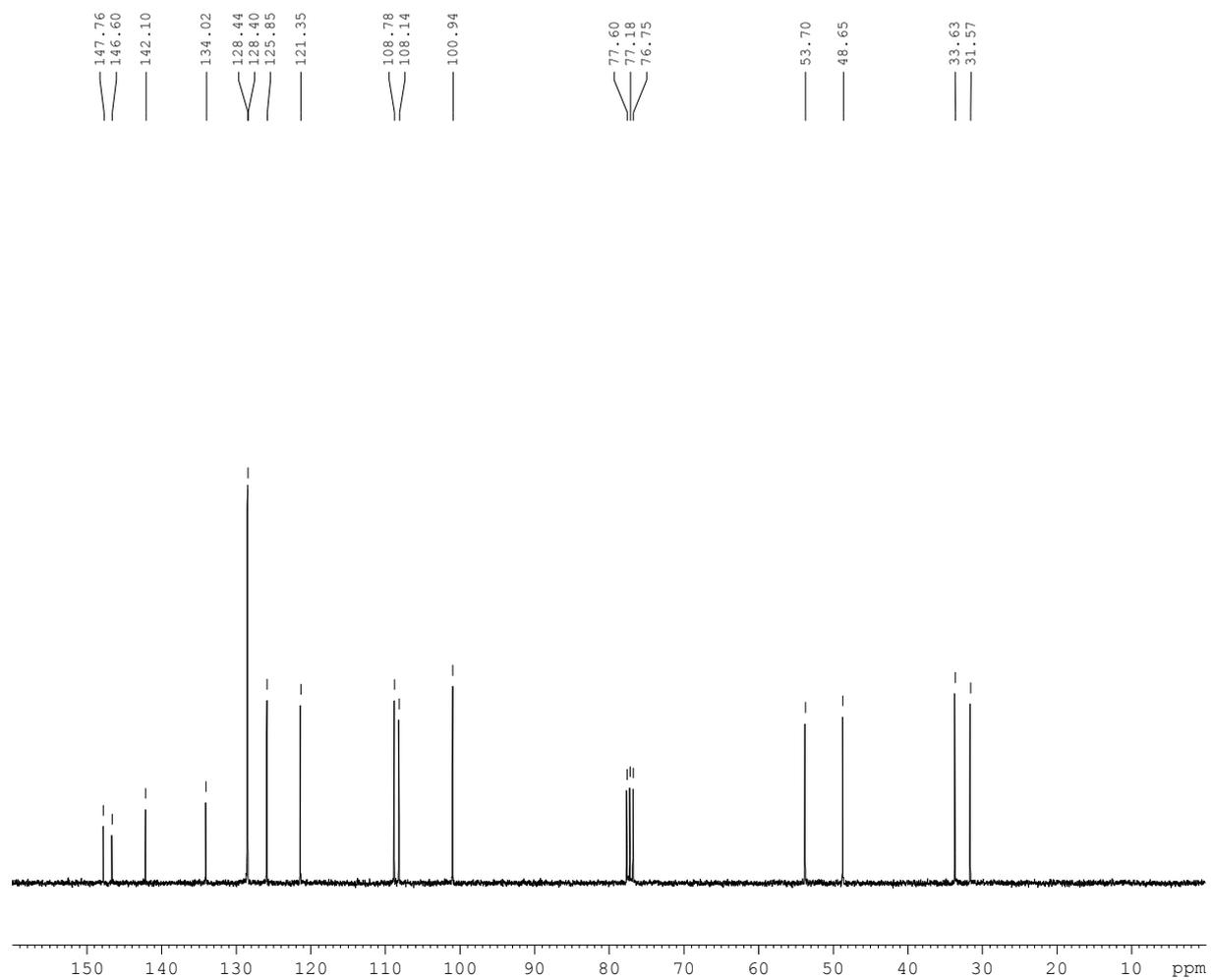


Table 2 - Entry 4



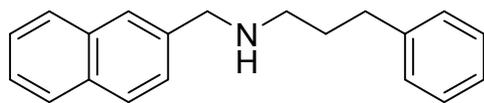
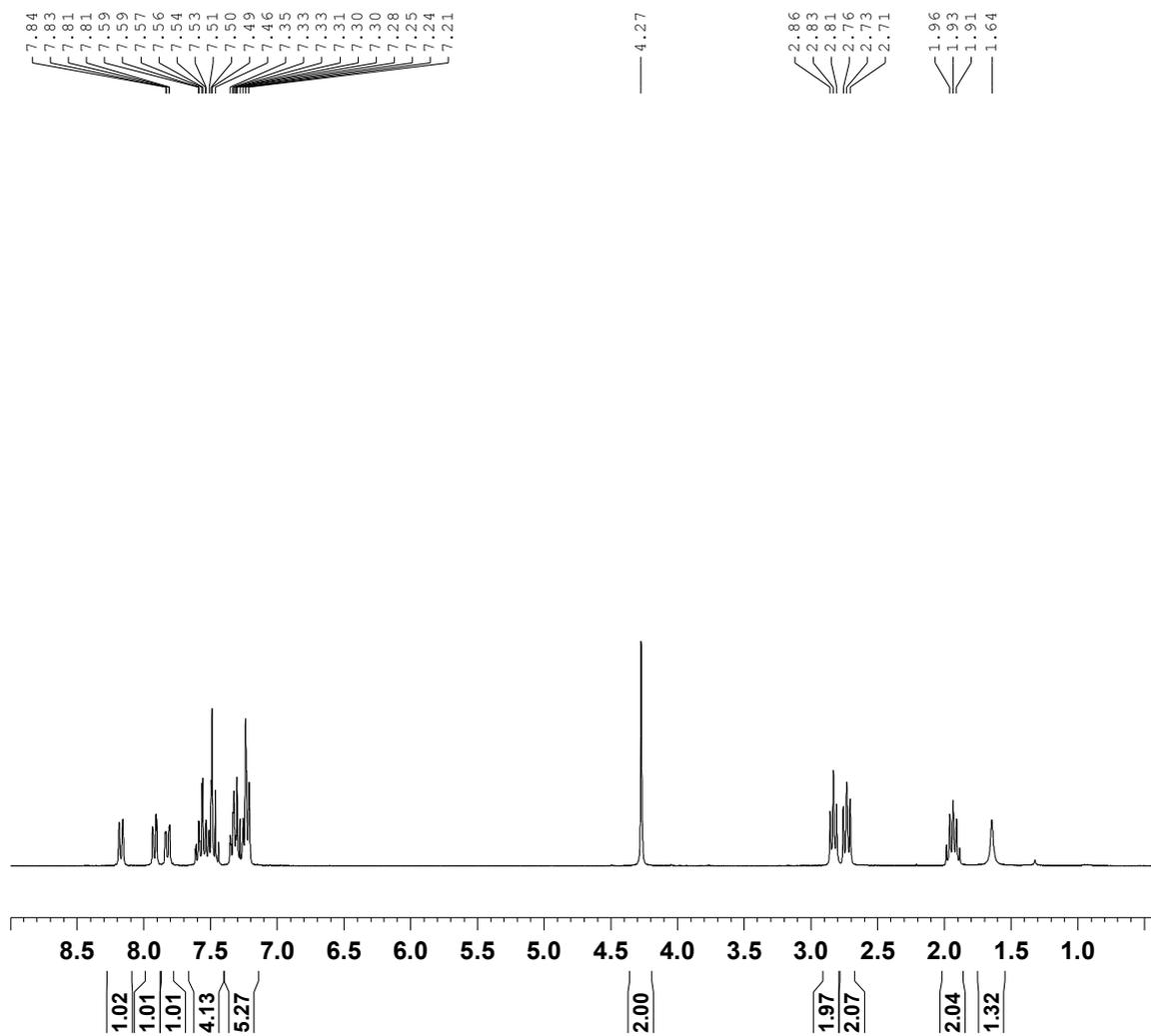


Table 2 - Entry 5



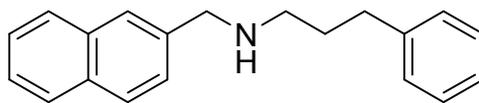
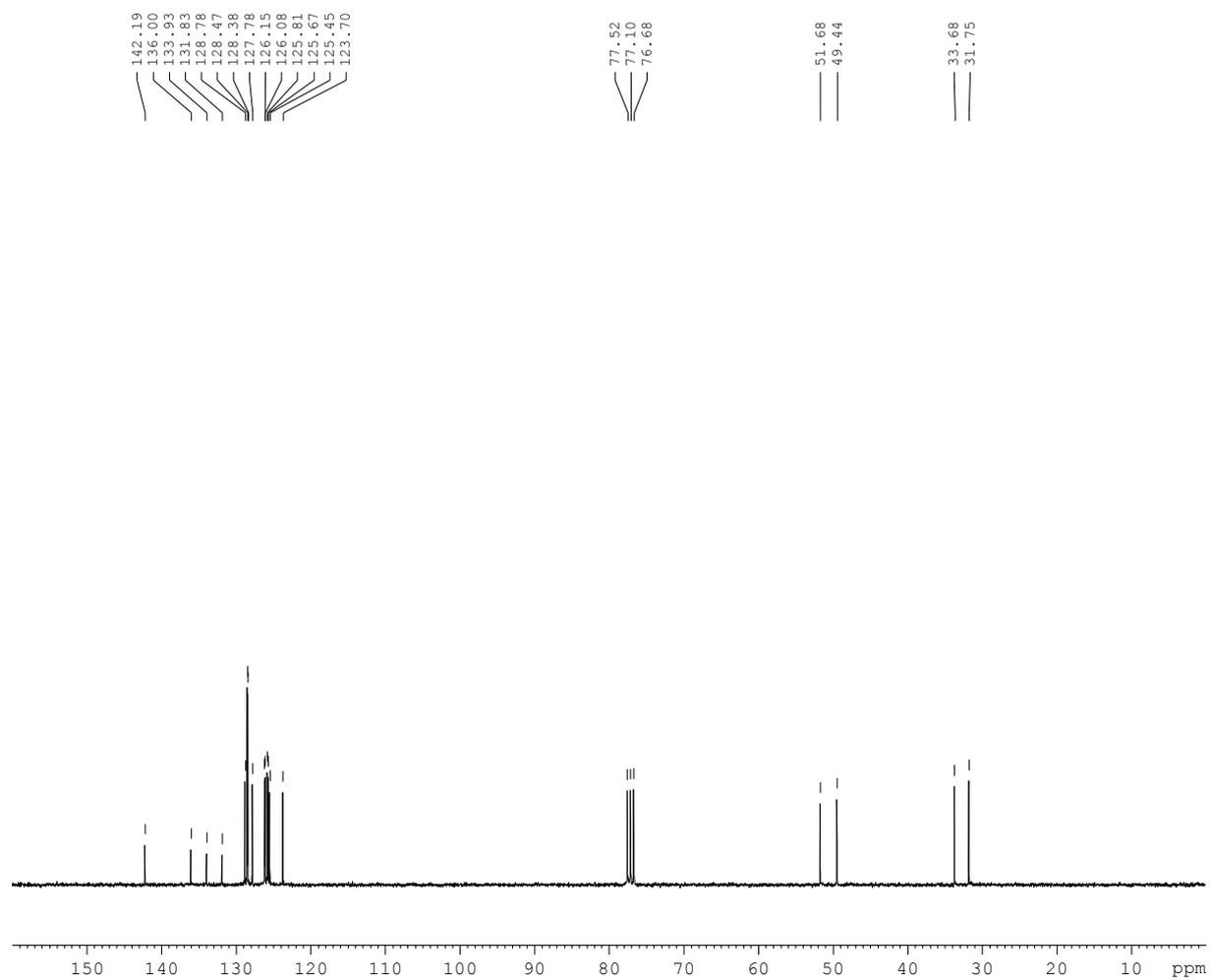


Table 2 - Entry 5



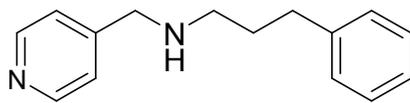
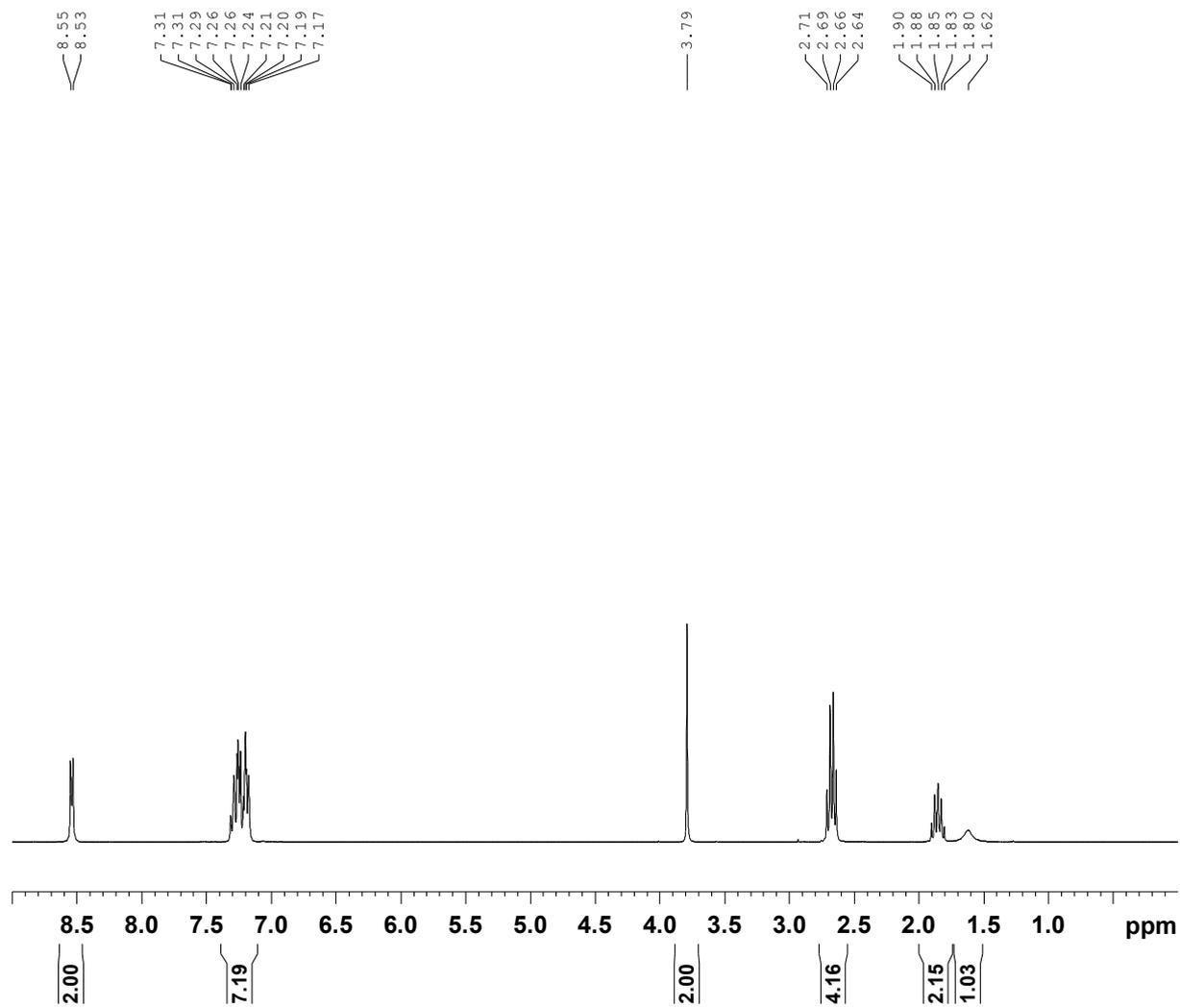


Table 2 - Entry 8



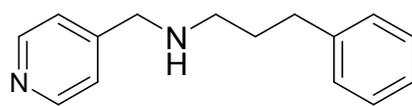
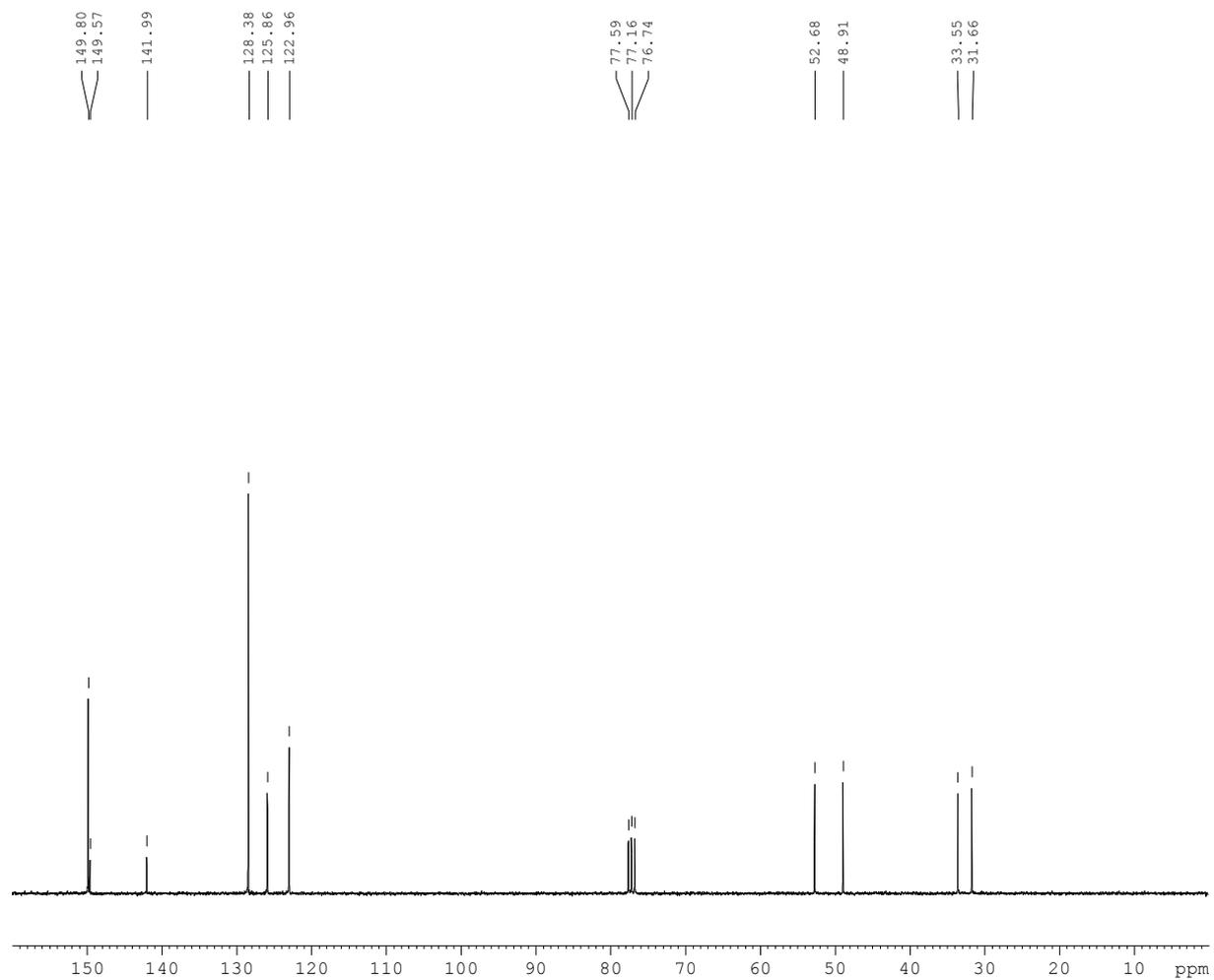
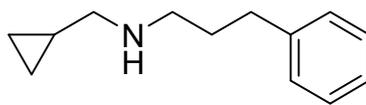
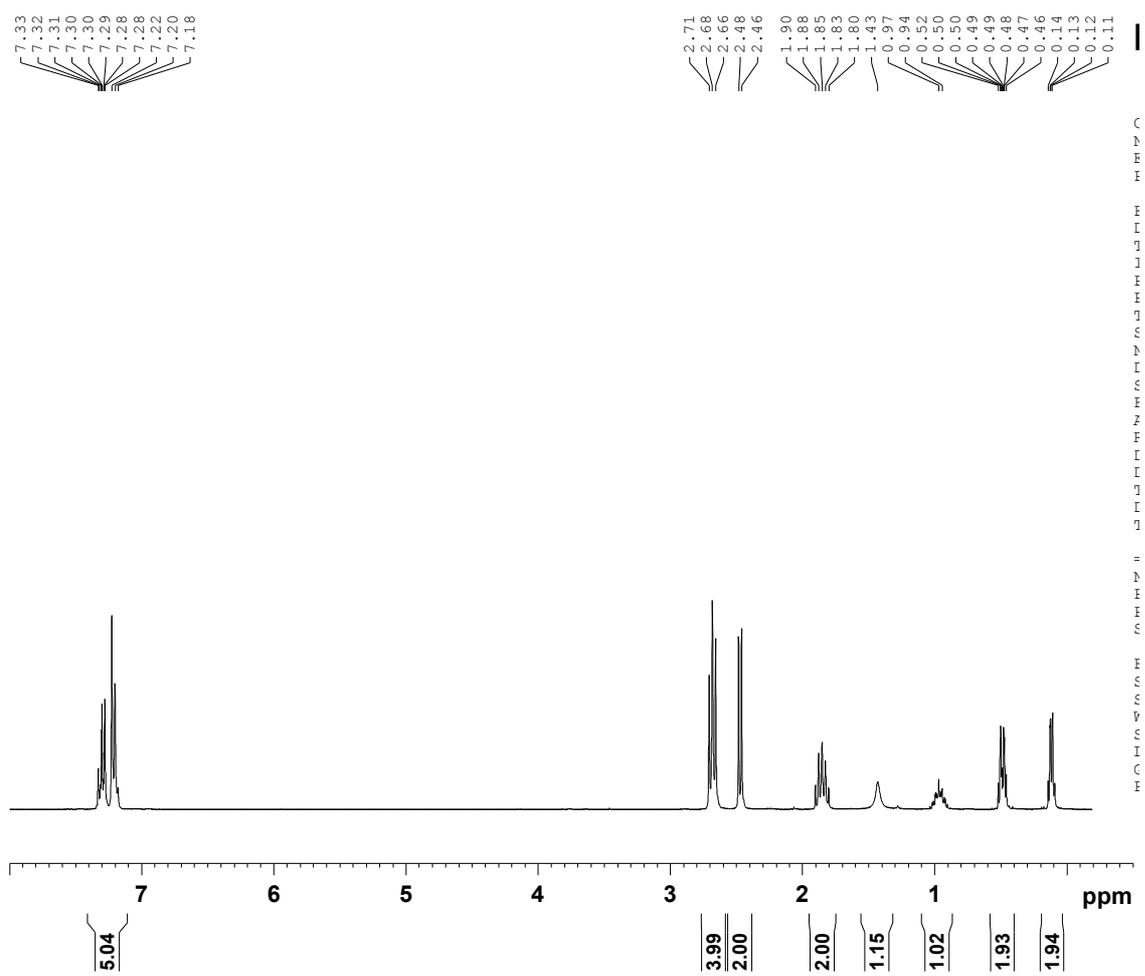


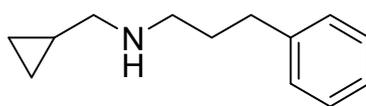
Table 2 - Entry 8





Scheme 2





Scheme 2

