Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information: Copper-catalysed reductive amination of nitriles and organic-group reductions using dimethylamine borane

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doi:

Table of contents:

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General experimental data:

All reactions requiring an anhydrous, inert atmosphere were carried out under a nitrogen atmosphere using a nitrogen purged Radley's carousel tubes. Unless preparative details are provided, all reagents were purchased from commercial suppliers Acros Organics, Sigma Aldrich, Alfa Aesar, Lancaster or TCI UK and used without further purification. Thin layer chromatography was carried out on aluminium or plastic backed silica plates, purchased from Fisher. The plates were visualised under UV (254 nm) light, followed by staining with phosphomolybdic acid dip or potassium permanganate and gentle heating. During compound separations, column chromatography was carried out using 60 micron dry silica purchased from Aldrich. Organic layers were routinely dried with anhydrous $MgSO_4$ and concentrated using a Büchi rotary evaporator.

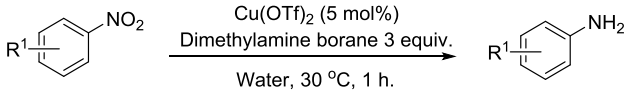
^{1}H NMR / ^{13}C NMR spectra were run in $CDCl_3$ or d6-DMSO (≥99.5% deuterated) purchased from Fluorochem, on a Bruker Avance 300 (300 MHz). Any chemical shifts (δ) are reported as parts per million (ppm) with reference to tetramethylsilane (TMS) (δH = 0.00 ppm) unless otherwise stated. The coupling constants (*J*) are reported in Hz and signal multiplicities are reported as; singlet (s) , doublet (d), triplet (t), quartet (q), quintet (qu), sextet (sext.) doublet of doublets (dd), doublet of triplets (dt), triplet of triplets (tt), multiplet (m), or broad singlet (br. s).

For mass spectrometry data aquisition a micrOTOF electrospray time-of-flight (ESI-TOF) mass spectrometer (Bruker Daltonik, GmbH, Bremen, Germany) was used; this was coupled to an Agilent 1200 LC system (Agilent Technologies, Waldbronn, Germany). The LC system was used as an autosampler only. 10 µL of sample was injected into a 30:70 flow of water:acetonitrile at 0.3 mL/min to the mass spectrometer. For each acquisition 10 µL of a calibrant of 5 mM sodium formate was injected after the sample. The observed mass and isotope pattern matched the corresponding theoretical values as calculated from the expected elemental formula.

Infra-red spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer, using a Universal ATR accessory for sampling, with relevant absorbances quoted as ν in cm^{-1}. Optical rotations were measured on an AA-10 Automatic Polarimeter.

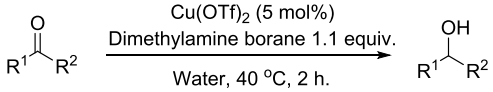
General Procedures

Procedure for the reduction of aromatic nitro compounds: (1)



To an oven dried Radleys tube was added copper(II) triflate (0.0543 g, 0.15 mmol) followed by deionised water (3 mL) then the substrate (3.0 mmol). Dimethylamine borane (0.530 g, 9 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 30 °C for 1 h with stirring. After this time the reactions were briefly allowed to cool, diluted with DCM (25 mL) and separated from NaOH (10 mL, 2M) and brine (10 mL). The aqueous layer was washed two further times with DCM (10 mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the product.

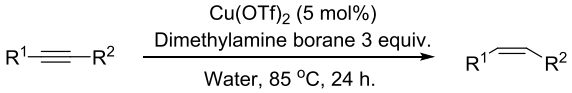
Procedure for the reduction of carbonyl compounds: (2)



To an oven dried Radleys tube was added copper(II) triflate (0.0543 g, 0.15 mmol) followed by deionised water (3 mL) then the substrate (3.0 mmol). Dimethylamine borane (0.0641 g, 1.1 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 40 °C for 2 h with stirring. After this time the reactions were

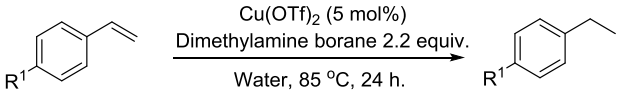
briefly allowed to cool, diluted with DCM (25 mL) and separated from brine (30 mL). The aqueous layer was washed two further times with DCM (10 mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the product.

Procedure for the reduction of alkyne compounds: (3)



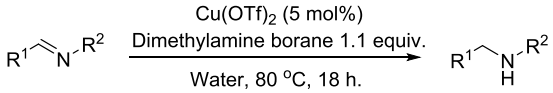
To an oven dried Radleys tube was added copper(II) triflate (0.0543 g, 0.15 mmol) followed by deionised water (3 mL) then the substrate (3.0 mmol). Dimethylamine borane (0.1944 g, 3.3 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 85 °C for 24 h with stirring. After this time the reactions were briefly allowed to cool, diluted with DCM (25 mL) and separated from brine (30 mL). The aqueous layer was washed two further times with DCM (10 mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. The product was separated by column chromatography with hexanes through silica.

Procedure for the reduction of alkenes compounds: (4)



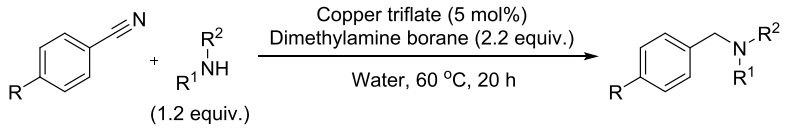
To an oven dried Radleys tube was added copper(II) triflate (0.0543 g, 0.15 mmol) followed by deionised water (1.5 mL) then the substrate (3.0 mmol). Dimethylamine borane (0.3888 g, 6.6 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 85 °C for 24 h with stirring. After this time the reactions were briefly allowed to cool, diluted with DCM (25 mL) and separated from brine (30 mL). The aqueous layer was washed two further times with DCM (10 mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. The product was separated by column chromatography with hexanes through silica.

Procedure for the reduction of imine compounds: (5)



To an oven dried Radleys tube was added copper(II) triflate (0.0181 g, 0.05 mmol) followed by deionised water (1 mL) then the substrate (3.0 mmol). Dimethylamine borane (0.0641 g, 1.1 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 80 °C for 18 h with stirring. After this time the reactions were briefly allowed to cool, diluted with DCM (25 mL) and separated from brine (30 mL). The aqueous layer was washed two further times with DCM (10 mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. The product was dissolved in a minimal amount of ether and ethereal HCl (2M, 2 mL) was added to form the salt which was precipitated out and collected by filtration after washing with Et2O (20 mL).

Procedure for the amination of nitriles: (6)

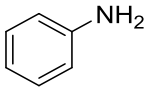


To an oven dried Radleys tube was added copper(II) triflate (0.543 g, 0.15 mmol) followed by deionised water (3 mL) then the amine (3.6 mmol). The solution was allowed to mix and then the nitrile specie was added (3.0 mmol). Dimethylamine borane (0.3889 g, 6.6 mmol) was added and the tube lids attached but not sealed. The reactions were heated at 60 °C for 20 h with stirring. After this time the reactions were briefly allowed to cool, diluted with DCM (25 mL) and separated from brine (30 mL). The aqueous layer was washed two further times with DCM (10mL) and the organic layers were collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. Nitrile was separated from the product by means of a silica gel plug.

Isolated Compounds:

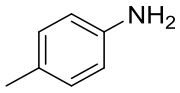
[n.b.] Compounds marked * are commercially available through Sigma Aldrich and the data collected matches their reported data.

Aniline: *



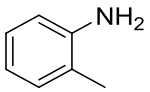
The title compound was formed following representative procedure 1. 4-Nitrobenzene (0.308 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.530 g, 9.0 mmol) was added. The compound was purified by washing to give a yellow crystalline solid in a 0.242 g (86 %) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 3.69 (2H, br s, -NH_2), 6.74 (2H, d, J = 8.7 Hz, aromatic), 6.86 (1H, t, J = 7.2 Hz, aromatic), 7.25 (2H, t, J = 8.1 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 115.24, 118.57, 129.42.
ESI -MS of $[C_6H_7N]^+$; theoretical m/z of $[M+H]^+$ = 94.066, measured m/z of $[M+H]^+$ = 94.065. Consistent with the literature data supplied from a commercial source.

4-Aminotoluene: *



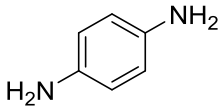
The title compound was formed following representative procedure 1. 4-Nitrotoluene (0.411 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.530 g, 9.0 mmol) was added. The compound was purified by washing to give a yellow crystalline solid in a 0.393 g (100%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 2.33 (3H, s, CH_3-Ph), 3.64 (2H, br s, Ph-NH_2), 6.66 (2H, d, J = 8.4 Hz, aromatic), 7.04 (2H, d, J = 8.4 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 20.59, 44.41, 115.47, 129.56, 144.06.
ESI -MS of $[C_7H_9N]^+$; theoretical m/z of $[M+H]^+$ = 108.081, measured m/z of $[M+H]^+$ = 108.082. Consistent with the literature data supplied from a commercial source.

2-Aminotoluene: *



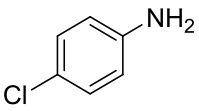
The title compound was formed following representative procedure 1. 2-Nitrotoluene (0.354 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.530 g, 9.0 mmol) was added. The compound was purified by washing to give a yellow liquid in a 0.276 g (86%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 2.20 (3H, s, CH_3-Ph), 3.49 (2H, br s, Ph-NH_2), 6.69-6.67 (2H, m, aromatic), 7.05-7.10 (2H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 17.43, 115.08, 118.46, 122.55, 126.72, 130.44, 144.58.
ESI -MS of $[C_7H_9N]^+$; theoretical m/z of $[M+H]^+$ = 108.081, measured m/z of $[M+H]^+$ = 108.082. Consistent with the literature data supplied from a commercial source.

1,4-Diaminobenzene: *



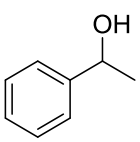
The title compound was formed following representative procedure 1. 4-Nitroaniline (0.414 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.530 g, 9.0 mmol) was added. The compound was purified by washing to give a dark red solid in a 0.113 g (34 %) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 3.35 (4H, br s, -NH_2), 6.57 (4H, s, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 116.55, 138.59.
ESI -MS of $[C_6H_8N_2]^+$; theoretical m/z of $[M+H]^+$ = 109.076, measured m/z of $[M+H]^+$ = 109.077. Consistent with the literature data supplied from a commercial source.

4-Chloroaniline: *



The title compound was formed following representative procedure 1. 4-Chloro nitrotoluene (0.473 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.530 g, 9.0 mmol) was added. The compound was purified by washing to give yellow crystals in a 0.358 g (94%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 3.50 (2H, br s, Ph-NH_2), 6.51 (2H, dt, J = 3.3 Hz, J = 8.7 Hz, aromatic), 7.01 (2H,dt, J = 3.3 Hz, J = 8.7 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 116.29, 122.97, 129.33, 144.63.
ESI -MS of $[C_6H_6NCl]^+$; theoretical m/z of $[M+H]^+$ = 128.027, measured m/z of $[M+H]^+$ = 128.028. Consistent with the literature data supplied from a commercial source.

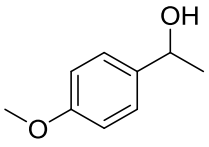
1-Phenyl ethanol: [1]



The title compound was formed following representative procedure 2. Acetophenone (0.350 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified

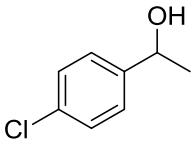
by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a colourless liquid in a 0.364 g (99%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.47 (3H, d, J = 6.6 Hz, CH_3-CH-OH), 2.69 (1H, br s, CH-OH), 4.83 (1H, q, J = 6.6 Hz, CH_3-CH-OH), 7.23-7.39 (5H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 24.89, 70.19, 125.88, 127.44, 128.45, 145.39.
ESI -MS of $[C_8H_{10}O]^+$; theoretical m/z of $[M-H_2O+H]^+$ = 105.070, measured m/z of $[M-H_2O+H]^+$ = 105.070.

4'-Methoxy-1-phenylethanol: [2]



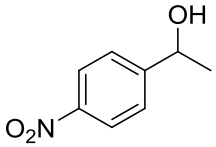
The title compound was formed following representative procedure 2. 4-Methoxy acetophenone (0.457 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a yellow liquid in a 0.362 g (79%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.46 (3H, d, J = 7.5 Hz, CH_3-CH-OH), 2.14 (1H, br s, CH-OH), 3.79 (3H, s, CH_3-O-Ph), 4.82 (1H, q, J = 6.6 Hz, CH_3-CH-OH), 6.87 (2H, d, J = 8.4 Hz, aromatic), 7.28 (2H, d, J = 7.5 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 25.05, 55.30, 69.93, 113.82, 126.71, 138.06, 158.92.
ESI -MS of $[C_9H_{12}O_2]^+$; theoretical m/z of $[M+H]^+$ = 175.074, measured m/z of $[M+H]^+$ = 175.073.

4'-Chloro-1-phenylethanol: *



The title compound was formed following representative procedure 2. 4-Chloro acetophenone (0.389 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a clear liquid in a 0.469 g (99%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.42 (3H, d, J = 6.3 Hz, CH_3-CH-OH), 2.66 (1H, br s, CH-OH), 4.80 (1H, m, CH_3-CH-OH), 7.23-7.33 (4H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 25.24, 69.10, 126.73, 127.81, 133.09, 143, 84.
ESI -MS of $[C_8H_9OCl]^+$; theoretical m/z of $[M-H_2O+H]^+$ = 139.031, measured m/z of $[M-H_2O+H]^+$ = 139.033. Consistent with the literature data supplied from a commercial source.

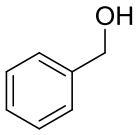
4'-Nitro-1-phenylethanol: [2]



The title compound was formed following representative procedure 2. 4-Nitro acetophenone (0.496 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a yellow solid in a 0.194 g (39%) yield.

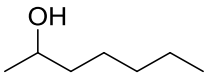
1H NMR (300 MHz, $CDCl_3$) δ = 1.51 (3H, d, J = 6.6 Hz, CH_3-CH-OH), 2.07 (1H, br s, CH-OH), 5.01 (1H, q, J = 6.3 Hz, CH_3-CH-OH), 7.53 (2H, d, J = 9.0 Hz, aromatic) 8.18 (2H, d, J = 8.7 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 25.64, 69.77, 123.32, 125.94, 146.91, 152.84.
ESI -MS of $[C_8H_9NO_3]^+$; theoretical m/z of $[M+H]^+$ = 190.048, measured m/z of $[M+H]^+$ = 190.047.

Benzyl alcohol: *



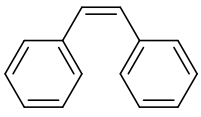
The title compound was formed following representative procedure 2. Benzaldehyde (0.306 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a pale yellow liquid in a 0.243 g (75%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 3.27 (1H, br s, CH_2-OH), 4.62 (2H, s, Ph-CH_2-OH), 7.26-7.39 (5H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 45.06, 65.28, 127.02, 128.52, 130.01, 140.89.
ESI -MS of $[C_7H_8O]^+$; theoretical m/z of $[M-H_2O+H]^+$= 91.054, measured m/z of $[M-H_2O+H]^+$= 91.054.
Consistent with the literature data supplied from a commercial source.

2-Heptanol: *



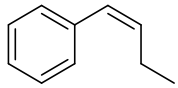
The title compound was formed following representative procedure 2. 2-Heptanone (0.418 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The compound was purified by washing followed by column chromatography eluted by a mixture of ethyl acetate and pentane to give a yellow liquid in a 0.294 g (84%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 0.82 (3H, t, CH_2-CH_2-CH_3), 1.10 (3H, d, J = 6.0 Hz, CH_3-CH-OH), 1.17-1.45 (8H, m, aliphatic chain), 2.14 (1H, br s, CH-OH), 3.70 (1H, q, J = 5.1 Hz, CH_3-CH-OH).
13C NMR (75.5 MHz, $CDCl_3$) δ = 13.69, 21.92, 23.35, 25.31, 31.68, 39.16, 67.97.
ESI -MS of $[C_7H_{16}O]^+$; theoretical m/z of $[M-H_2O+H]^+$ = 99.117, measured m/z of $[M-H_2O+H]^+$ = 99.117. Consistent with the literature data supplied from a commercial source.

Cis-stilbene: *



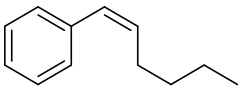
The title compound was formed following representative procedure 3. Bis-phenyl acetylene (0.535 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.389 g, 6.6 mmol) was added. The compound was purified by washing to give a clear liquid in a 0.523 g (97%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 6.72 (2H, t, J = 3.3 Hz, PhCH-CH-), 7.26-7.38 (10H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 127.27, 128.38, 129.04, 130.41, 137.39.
IR: υ = 1600.05 (C=C stretch). Consistent with the literature data supplied from a commercial source.

1-Phenylbutene: [3]



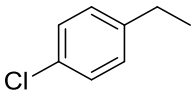
The title compound was formed following representative procedure 3. 1-Phenyl butyne (0.426 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.389 g, 6.6 mmol) was added. The compound was purified by washing to give a yellow liquid in a 0.397 g (98%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.14 (3H, t, J = 7.5 Hz, CH_3-CH_2-CH-), 2.43 (2H, m, CH_3-CH_2-CH-) 5.66-5.77 (1H, m, CH_2-CH=CH-), 6.46 (1H, d, J = 13.0 Hz, CH=CH-Ph), 7.26-7.44 (5H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 14.46, 21.91, 125.94, 128.19, 128.83, 134.50, 137.89.
IR: υ = 1601.23 (C=C stretch).

1-Phenylhexene: [4]



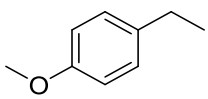
The title compound was formed following representative procedure 3. 1-Phenyl hexyne (0.528 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.389 g, 6.6 mmol) was added. The compound was purified by washing to give a clear liquid in a 0.421 g (88%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 0.94 (3H, t, J = 6.0 Hz, CH_3-CH_2-CH_2-), 1.36-1.53 (4H, m, CH_3-CH_2-CH_2-), 2.37 (2H, q, J = 7.2 Hz, CH_2-CH_2-CH_2-CH-), 5.66-5.75 (1H, m, CH_2-CH=CH-), 6.45 (1H, d, J = 13.0 Hz, CH=CH-Ph), 7.21-7.39 (5H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 14.06, 22.70, 28.62, 32.35, 126.46, 128.15, 128.72, 128.81, 133.23137.87.
IR: υ = 1600.22 (C=C stretch).

4-Ethyl chlorobenzene: *



The title compound was formed following representative procedure 4. 4-Chloro styrene (0.36 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.389 g, 6.6 mmol) was added. The product and remaining starting material were separated from the reaction mixture by washing to give a clear liquid in a 0.285 g yield of which 71% was determined to be the product by analysis of NMR spectroscopy.
1H NMR (300 MHz, $CDCl_3$) δ = 1.23 (3H, t, J = 7.5 Hz, CH_3-CH_2-Ph), 2.62 (2H, q, J = 7.5 Hz, CH_3-CH_2-Ph), 7.24-7.36 (4H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 15.59, 28.29, 127.28, 128.32, 129.25, 135.69. Consistent with the literature data supplied from a commercial source.

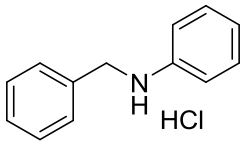
4-Ethyl methoxybenzene: *



The title compound was formed following representative procedure 4. 4-Methoxy styrene (0.399 mL, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.389 g, 6.6 mmol) was added. The product and remaining

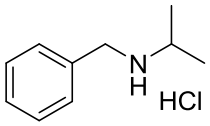
starting material were separated from the reaction mixture by washing to give a mauve liquid in a 0.362 g yield of which 72% was determined to be the product by analysis of NMR spectroscopy.
1H NMR (300 MHz, $CDCl_3$) δ = 1.29 (3H, t, J = 7.8 Hz, CH_3-CH_2-Ph), 2.65 (2H, q, J = 7.5 Hz, CH_3-CH_2-Ph), 6.91 (2H, d, J = 8.4 Hz, aromatic), 7.19 (2H, d, J = 8.7 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 15.22, 27.85, 55.16, 113.56, 128.57, 135.64, 157.71. Consistent with the literature data supplied from a commercial source.

N-Benzyl aniline hydrochloride: *



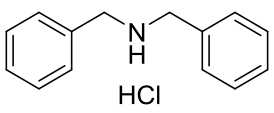
The title compound was formed following representative procedure 5. *N*-Benzylidine aniline (0.181 g, 1.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The product and remaining starting material were separated from the reaction mixture by washing, dissolving in a minimal amount of ether and acidification with ethereal HCl to give a pale precipitate. This was filtered, washed with ether and dried to give the product in a 0.182 g (83%) yield.
1H NMR (300 MHz, DMSO) δ = 4.44 (2H, s, Ph-CH_2-NH), 7.13-7.25 (3H, m, aromatic), 7.28-7.36 (5H, m, aromatic), 7.44-7.47 (2H, d, J = 7.8 Hz), 7.56 (1H, br s, NH).
13C NMR (75.5 MHz, DMSO) δ = 52.08, 120.97, 125.76, 128.64, 128.73, 129.76, 129.96, 134.18.
ESI -MS of $[C_{13}H_{13}N]^+$; theoretical m/z of $[M+H]^+$ =184.113, measured m/z of $[M+H]^+$ = 184.113. Consistent with the literature data supplied from a commercial source.

N-Isopropyl benzylamine: [2]



The title compound was formed following representative procedure 5. *N*-Benzylidine isopropylamine (0.441 g, 3.0 mmol) was used as the substrate to which dimethylamine borane (0.1923 g, 3.3 mmol) was added. The product and remaining starting material were separated from the reaction mixture by washing, dissolving in a minimal amount of ether and acidification with ethereal HCl to give a white precipitate. This was filtered, washed with ether and dried to give the product in a 0.343 g (70%) yield.
1H NMR (300 MHz, DMSO) δ = 1.28 (6H, d, J = 6.3 Hz, CH_3-CH), 3.23 (1H, br s, CH_3-CH), 4.09 (2H, s, Ph-CH_2), 7.35-7.45 (3H, m, aromatic), 7.55-7.59 (2H, m, aromatic), 9.19 (1H, br, s, NH).
13C NMR (75.5 MHz, DMSO) δ = 18.89, 47.46, 49.69, 128.98, 129.14, 130.33, 132.68.
ESI -MS of $[C_{10}H_{16}N]^+$; theoretical m/z of $[M+H]^+$ = 151.136, measured m/z of $[M+H]^+$= 151.133

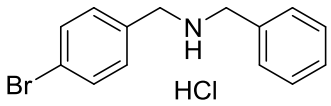
Dibenzylamine hydrochloride: [1]



The title compound was formed following representative procedure 5. *N*-Benzylidine benzylamine (0.195 g, 1.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The product and remaining starting material were separated from the reaction mixture by washing, dissolving in a minimal amount

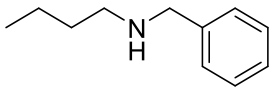
of ether and acidification with ethereal HCl to give a white precipitate. This was filtered, washed with ether and dried to give the product in a 0.151 g (65%) yield.
1H NMR (300 MHz, DMSO) δ = 4.10 (4H, m, (N-CH2-Ph)2), 7.34-7.62 (10H, m, aromatic), 9.88 (H, br s, NH).
13C NMR (75.5 MHz, DMSO) δ = 49.87, 122.66, 130.52, 131.81, 132.85.
ESI -MS of [C14H15N]+; theoretical m/z of [M+H]+ =198.128, measured m/z of [M+H]+ = 198.130.

N-Benzyl-4-bromobenzylamine: *



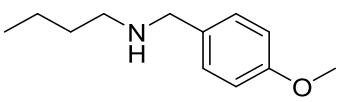
The title compound was formed following representative procedure 5. *N*-4-Bromo benzylidine benzylamine (0.274 g, 1.0 mmol) was used as the substrate to which dimethylamine borane (0.064 g, 1.1 mmol) was added. The product and remaining starting material were separated from the reaction mixture by washing, dissolving in a minimal amount of ether and acidification with ethereal HCl to give a white precipitate. This was filtered, washed with ether and dried to give the product in a 0.273 g (87%) yield.
1H NMR (300 MHz, DMSO) δ = 4.55 (2H, s, Ph-CH2-N), 4.57 (2H, s, Ph-CH2-N), 6.52 (1H, br s, NH), 7.03 (2H, t, J = 8.7 Hz, aromatic), 7.24-7.33 (5H, m, aromatic), 7.71-7.77 (2H, m, aromatic).
13C NMR (75.5 MHz, DMSO) δ = 49.27, 49.98, 122.64, 128.90, 129.20, 130.55, 131.38, 131.78, 132.25, 132.88.
ESI -MS of $[C_{14}H_{14}NBr]^+$; theoretical m/z of $[M+H]^+$ =276.039, measured m/z of $[M+H]^+$= 276.038. Consistent with the literature data supplied from a commercial source.

N-Benzylbutylamine: [5]



The title compound was formed following representative procedure 6. Butylamine (0.356 mL, 3.6 mmol) was used as the nucleophile and was added to benzonitrile (0.309 mL, 3.0 mmol). Dimethylamine borane (0.389 g, 6.6 mmol) was added and the reaction allowed to react for 20 h. Upon completion of the reaction the organic layer was extracted by DCM from water and the aqueous layer washed a further two times with DCM. After purification the product was isolated in a 0.230 g (47%) yield.
1H NMR (300 MHz, CDCl3) δ = 0.92 (3H, t, J = 7.2 Hz, CH3-CH2), 1.29-1.56 (4H, m, aliphatic), 1.77 (1H, br s, NH), 2.64 (2H, t, J = 7.2 Hz, NH-CH2), 3.80 (2H, s, Ph-CH2), 7.27-7.41 (5H, m, aromatic).
13C NMR (75.5 MHz, CDCl3) δ = 14.07, 27.52, 32.18, 49.16, 54.06, 126.94, 128.20, 128.42, 140.36.
ESI -MS of $[C_{11}H_{17}N]^+$; theoretical m/z of $[M+H]^+$ = 164.144, measured m/z of $[M+H]^+$ = 164.146.

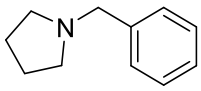
N-Butyl-4-methoxybenzylamine: [6]



The title compound was formed following representative procedure 6. Butylamine (0.356 mL, 3.6 mmol) was used as the nucleophile and was added to 4-methoxy-benzonitrile (0.400 g, 3.0 mmol). Dimethylamine borane (0.389 g, 6.6 mmol) was added and the reaction allowed to react for 20 h. Upon completion of the reaction the organic layer was extracted by DCM from water and the aqueous layer washed a further two times with DCM. After purification the product was isolated in a 0.460 g (76%) yield.

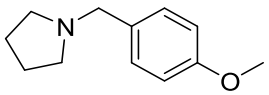
1H NMR (300 MHz, $CDCl_3$) δ = 0.90 (3H, t, J = 7.2 Hz, CH_3-CH_2), 1.27-1.54 (4H, m, aliphatic), 2.30 (1H, br s, NH), 2.60 (2H, t, J = 7.2 Hz, NH-CH_2), 3.71 (2H, s, Ph-CH_2), 3.77 (3H, s, CH_3-O-Ph), 6.84 (2H, d, J = 8.4 Hz, aromatic), 7.23 (2H, d, J = 8.4 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 14.06, 20.51, 32.02, 48.94, 53.32, 55.23, 113.76, 129.38, 129.63, 132.22, 158.63.
ESI -MS of $[C_{12}H_{19}NO]^+$; theoretical m/z of $[M+H]^+$ = 194.154, measured m/z of $[M+H]^+$ = 194.155.

N-Benzylpyrrolidine: [7]



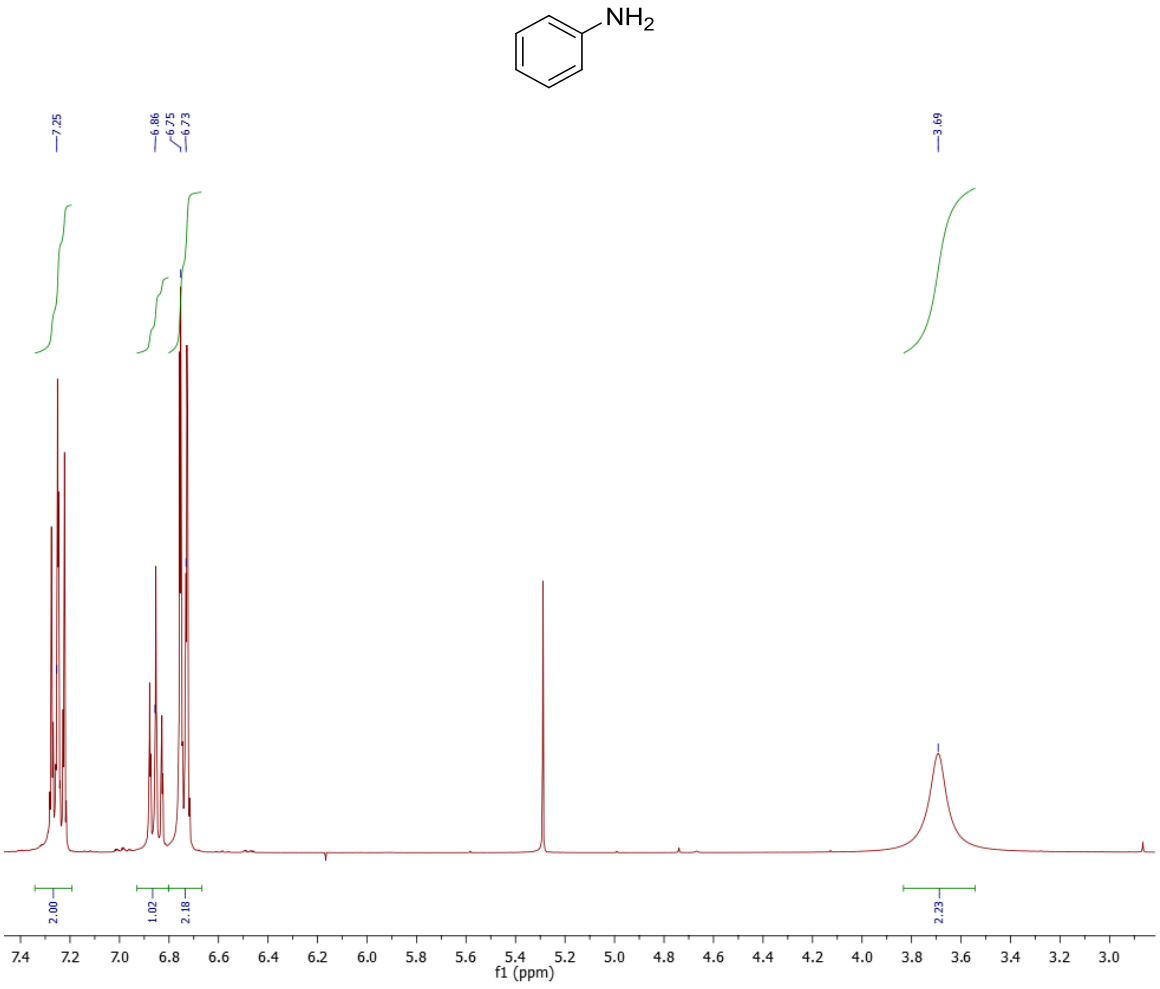
The title compound was formed following representative procedure 6. Pyrrolidine (0.296 mL, 3.6 mmol) was used as the nucleophile and was added to benzonitrile (0.309 mL, 3.0 mmol). Dimethylamine borane (0.389 g, 6.6 mmol) was added and the reaction allowed to react for 20 h. Upon completion of the reaction the organic layer was extracted by DCM from water and the aqueous layer washed a further two times with DCM. After purification the product was isolated in a 0.400 g (72%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.80 (4H, m, CH_2-CH_2-N), 2.53 (4H, m, CH_2-CH_2-N), 3.63 (2H, s, Ph-CH_2), 7.29-7.41 (5H, m, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 23.44, 54.19, 60.70, 127.01, 128.27, 129.02, 139.22.
ESI -MS of $[C_{11}H_{15}N]^+$; theoretical m/z of $[M+H]^+$ = 162.129, measured m/z of $[M+H]^+$ = 162.130.

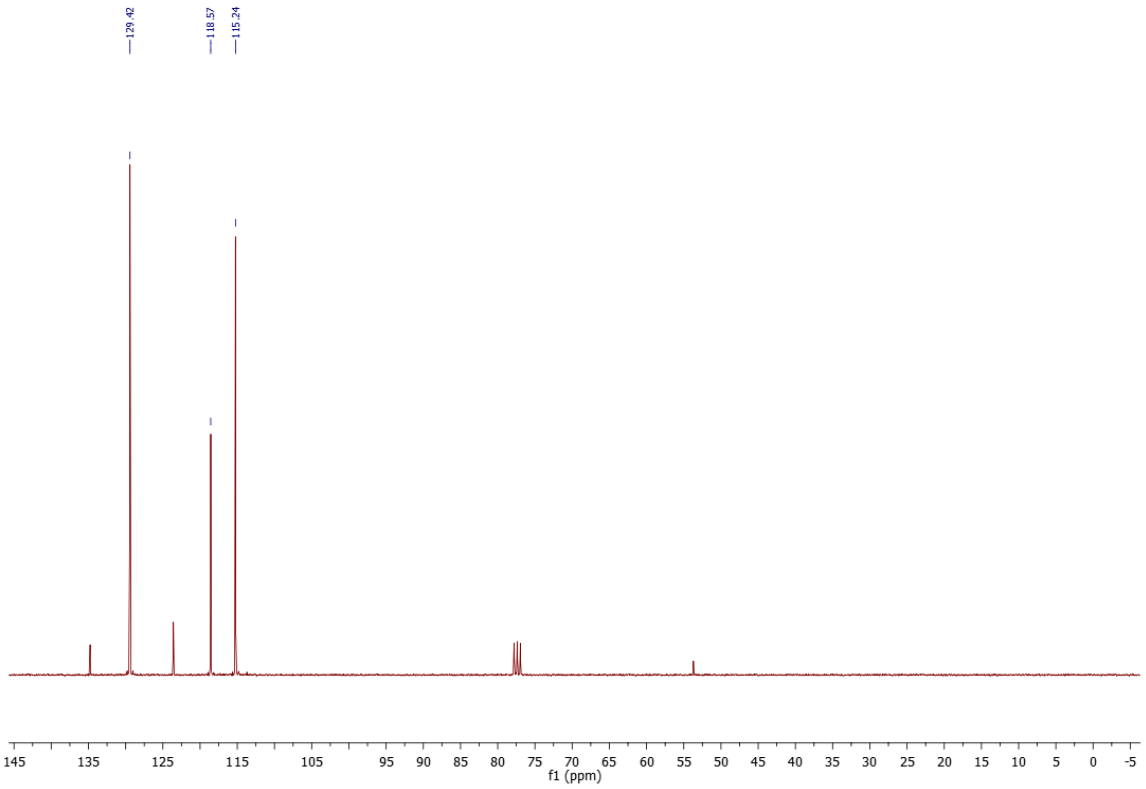
N-4-Methoxybenzylpyrrolidine: [7]

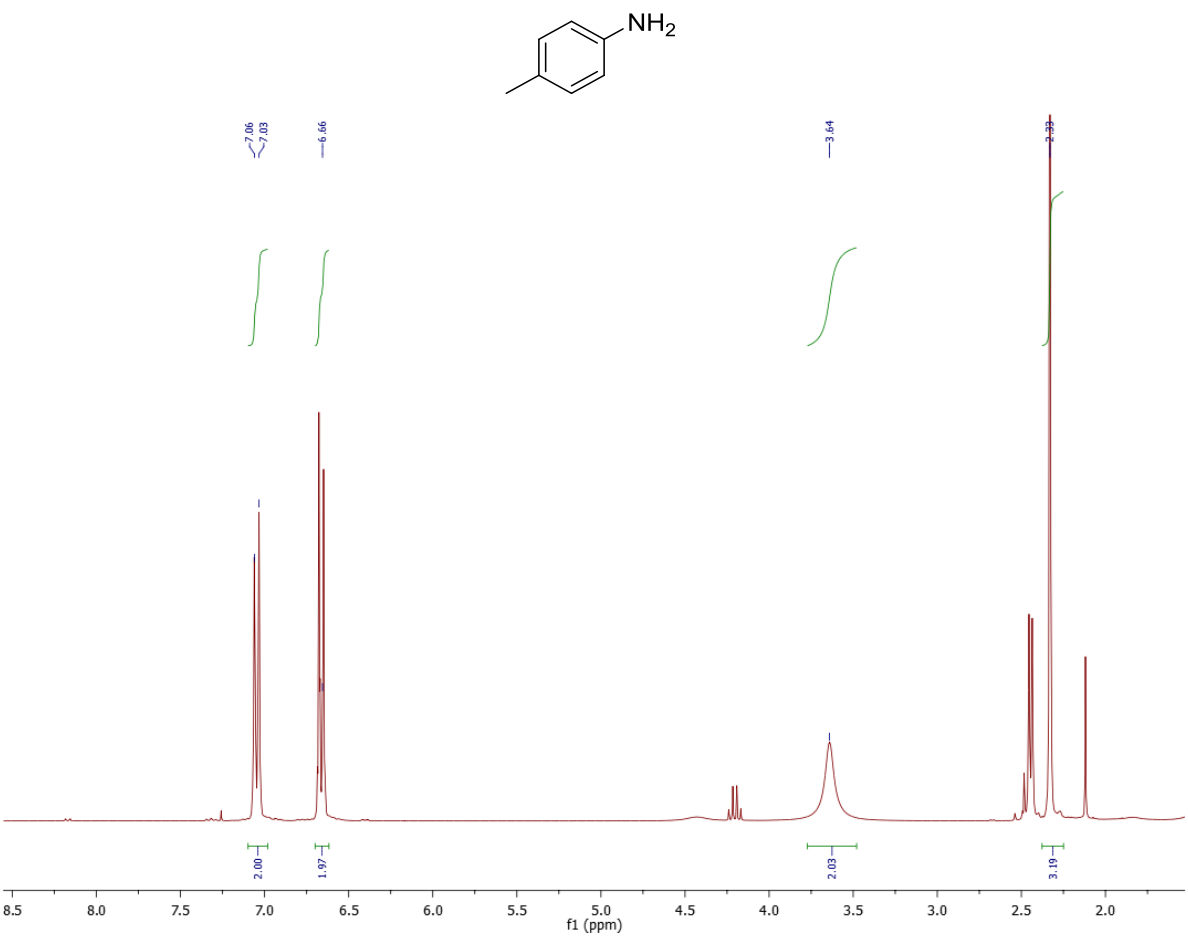


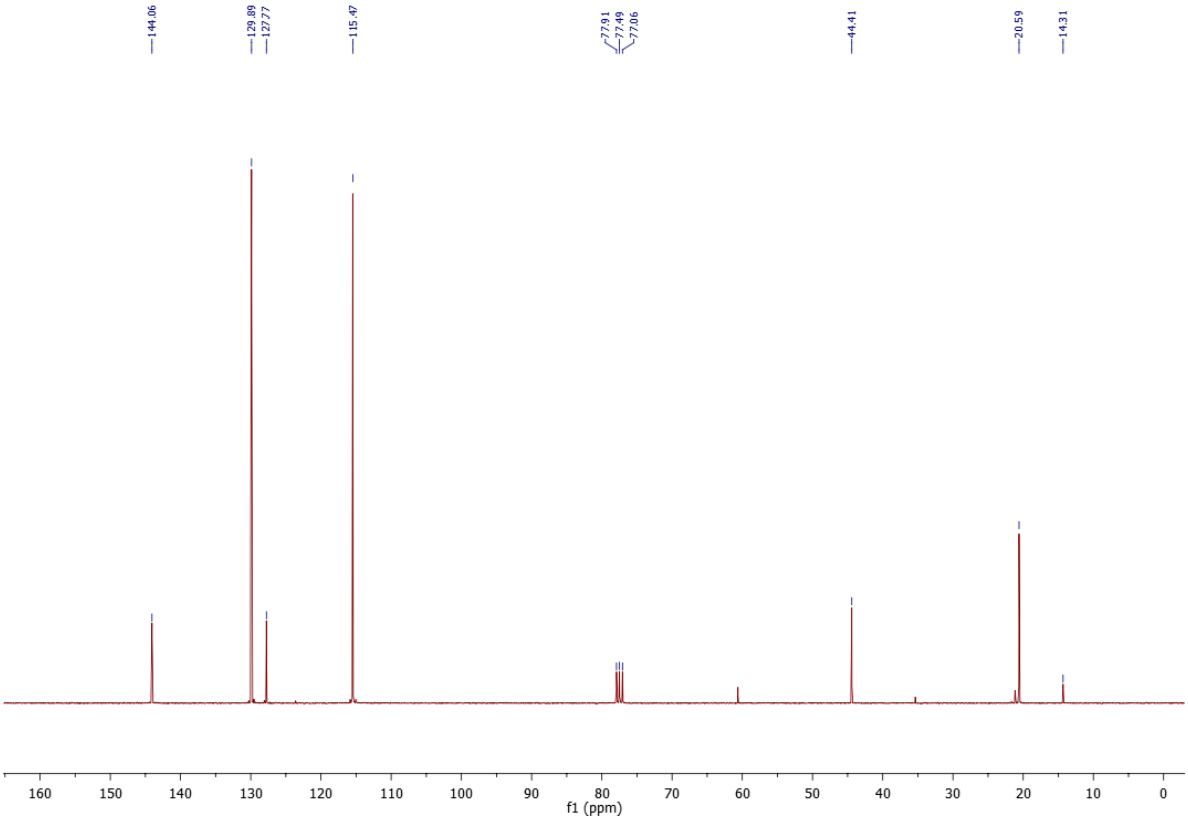
The title compound was formed following a slight modification on representative procedure 6. Pyrrolidine (0.320 mL, 3.9 mmol) was used as the nucleophile and was added to 4-methoxybenzonitrile (0.400 g, 3.0 mmol). Dimethylamine borane (0.389 g, 6.6 mmol) was added and the reaction allowed to react at 45 °C for 20 h. Upon completion of the reaction the organic layer was extracted by DCM from water and the aqueous layer washed a further two times with DCM. After purification the product was isolated in a 0.461 g (80%) yield.
1H NMR (300 MHz, $CDCl_3$) δ = 1.77 (4H, m, CH_2-CH_2-N), 2.46 (4H, m, CH_2-CH_2-N), 3.54 (2H, s, Ph-CH_2), 3.78 (3H, s, CH_3-O-Ph), 6.83 (2H, d, J = 8.7 Hz, aromatic), 7.24 (2H, d, J = 8.7 Hz, aromatic).
13C NMR (75.5 MHz, $CDCl_3$) δ = 23.37, 54.02, 55.24, 60.10, 113.55, 130.03, 131.54, 158.11.
ESI -MS of $[C_{12}H_{17}NO]^+$; theoretical m/z of $[M+H]^+$ = 192.139, measured m/z of $[M+H]^+$ = 192.138.

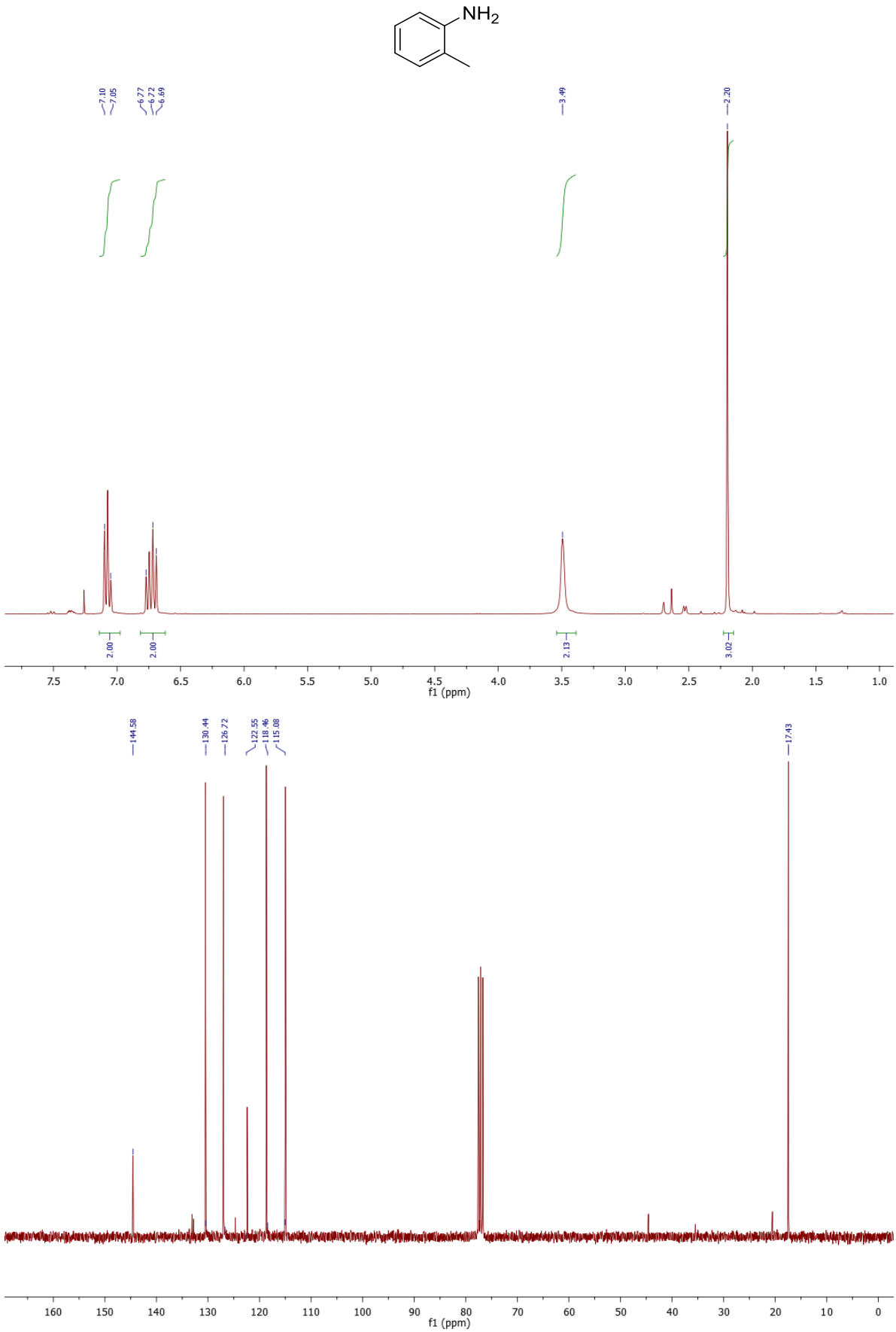
Spectra:

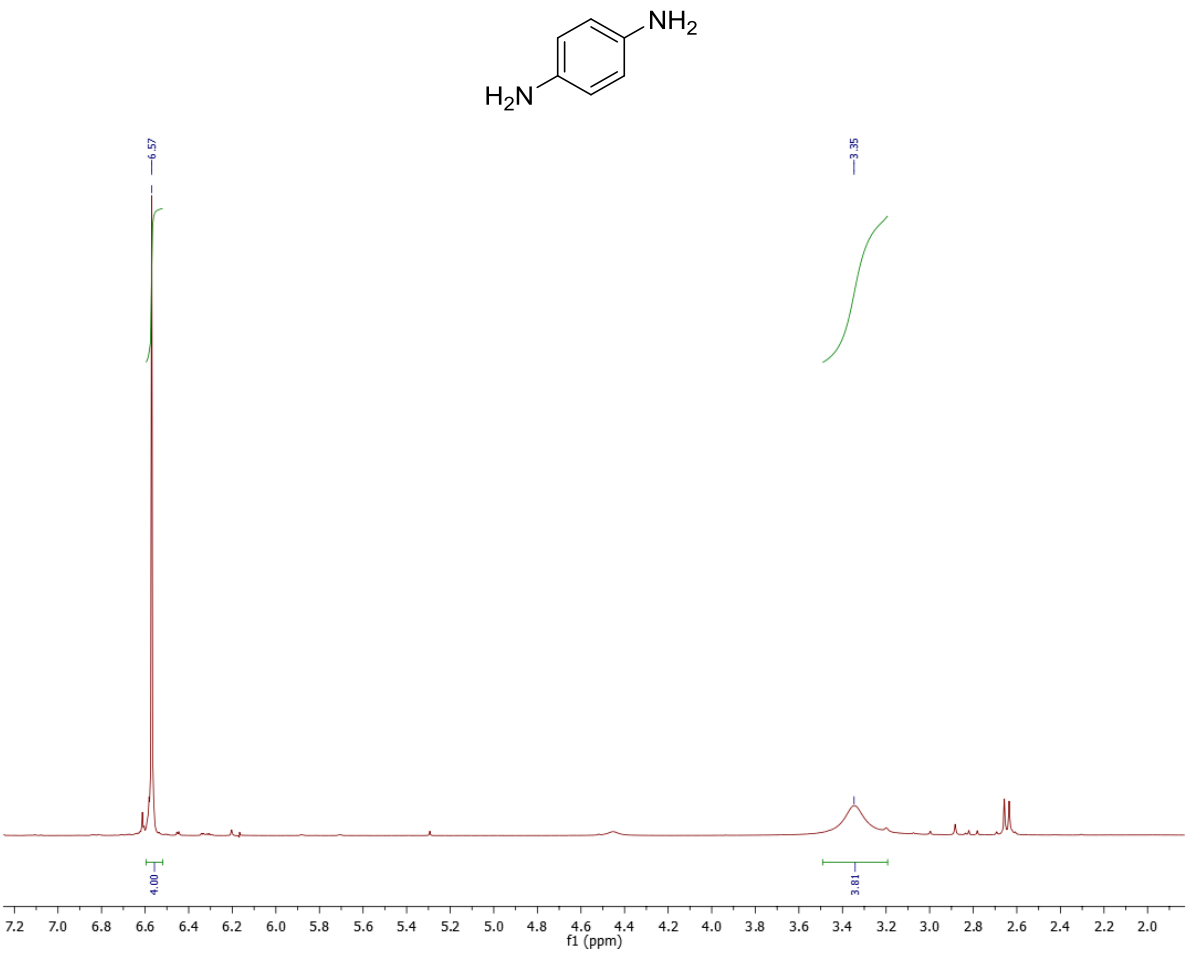

NH2
7.25
6.86
6.75
6.73
3.69
2.00
1.02
2.18
2.23
f1 (ppm)

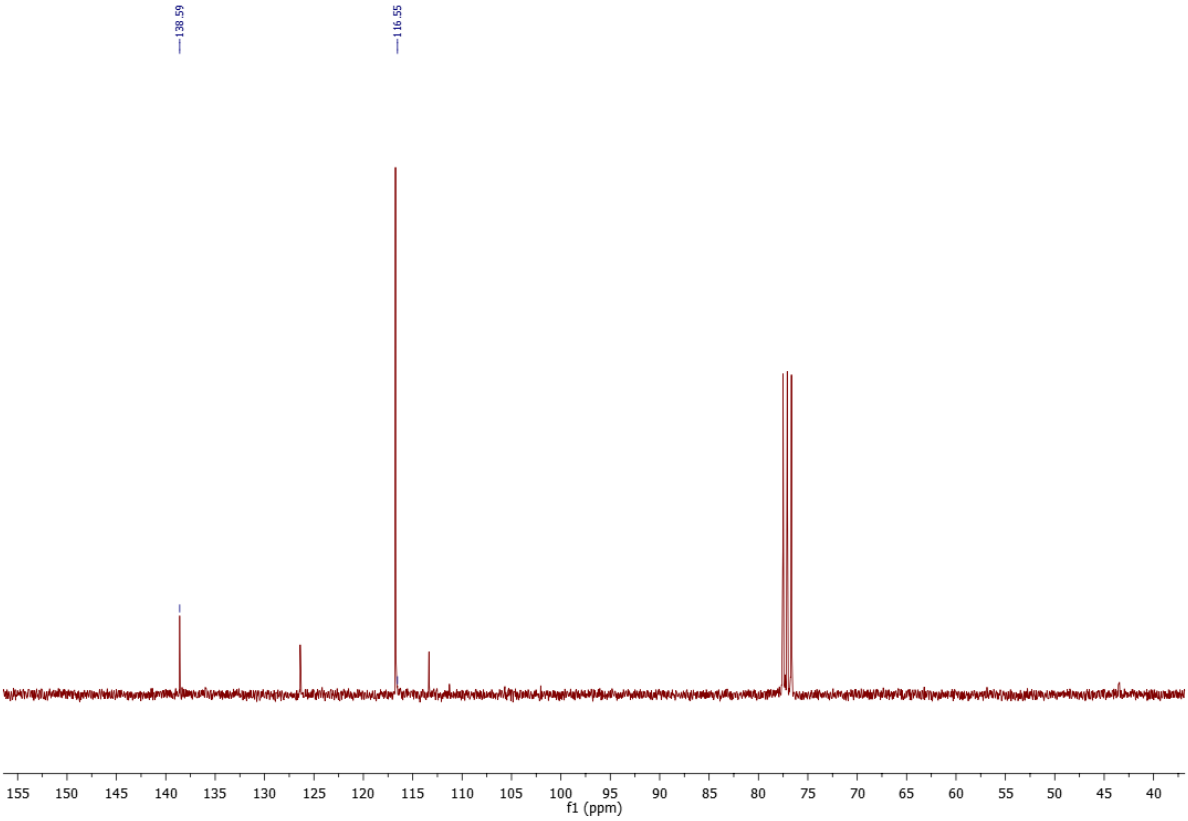

129.42
118.57
115.24
f1 (ppm)

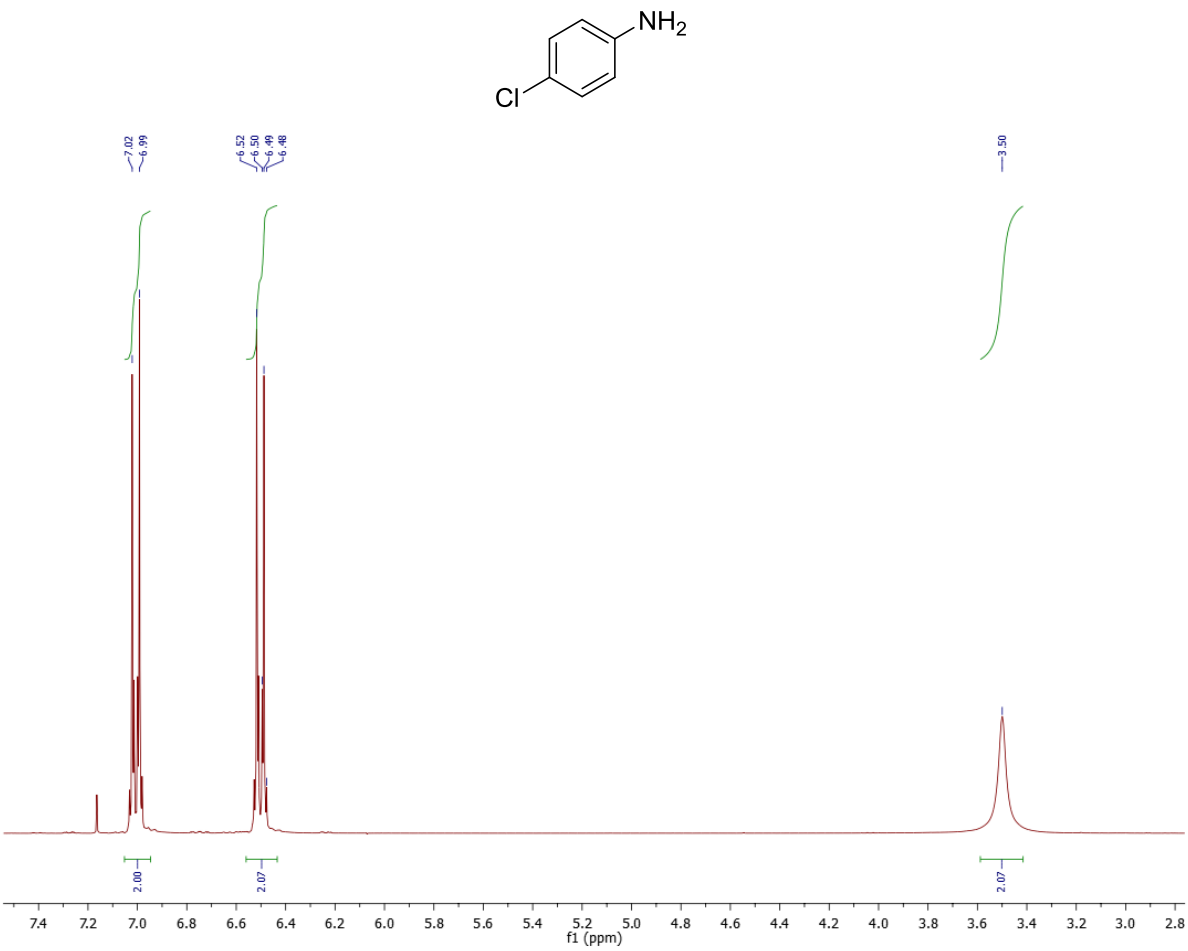

NH2
7.06
7.03
6.66
3.64
2.33
2.00
1.97
2.03
3.19
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

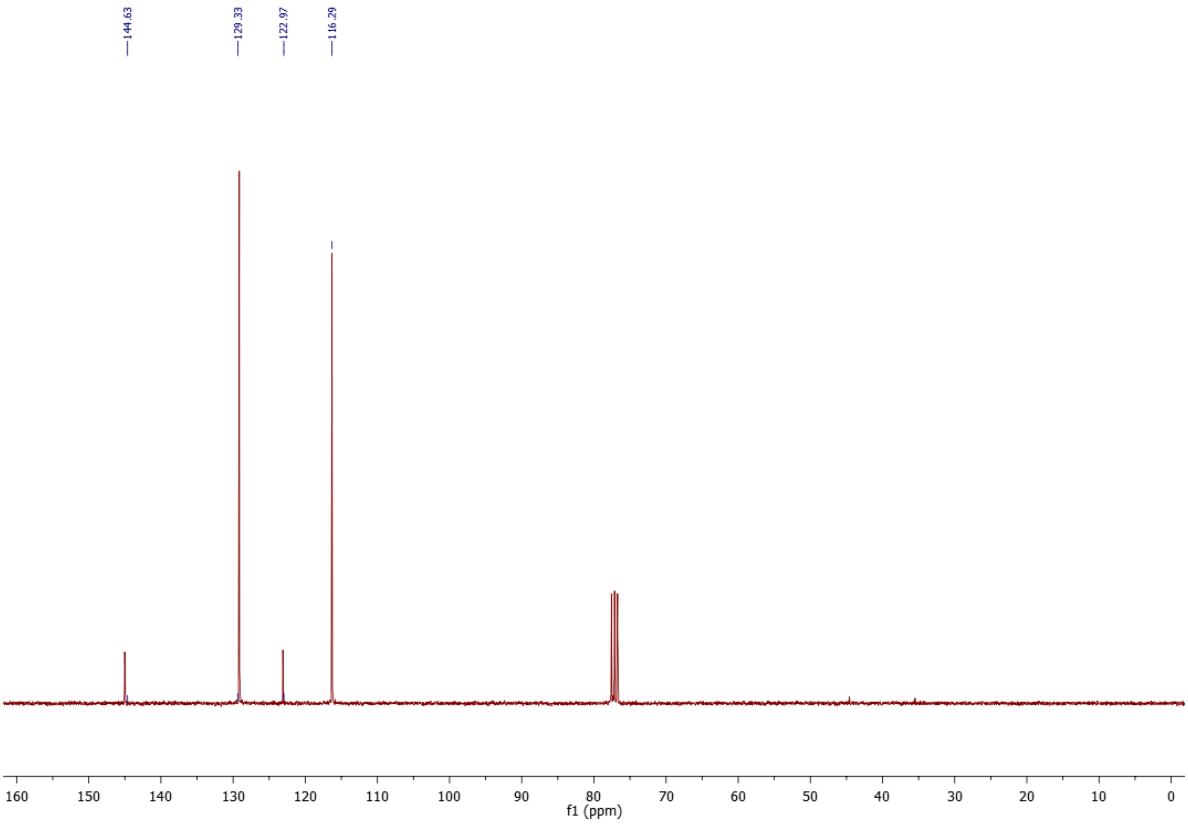

144.06
129.89
127.77
115.47
77.91
77.49
77.06
44.41
20.59
14.31
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

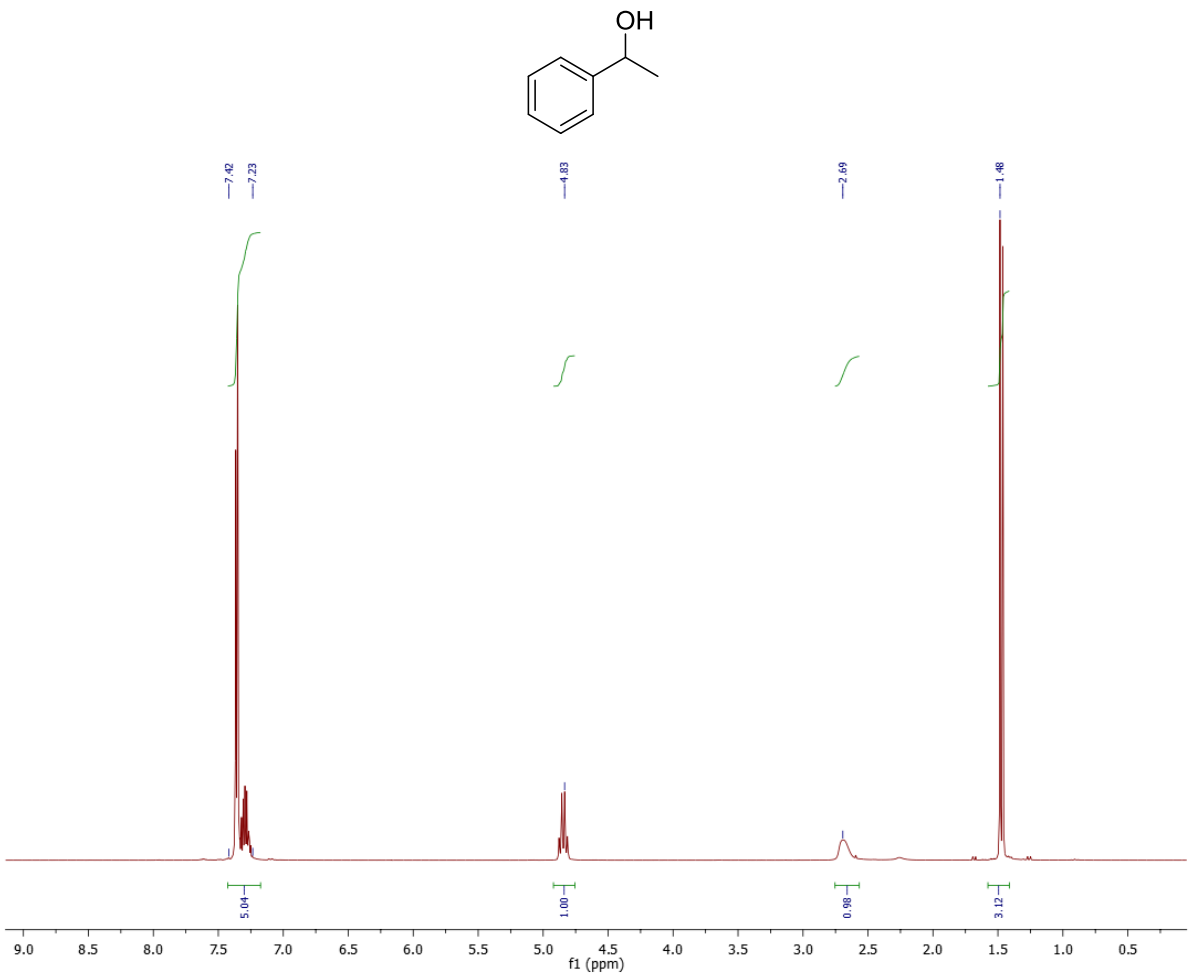

NH2
7.10
7.05
6.77
6.72
6.69
3.49
2.20
2.00
2.00
2.13
3.02
f1 (ppm)
144.58
130.44
126.72
122.55
118.46
115.08
17.43
f1 (ppm)

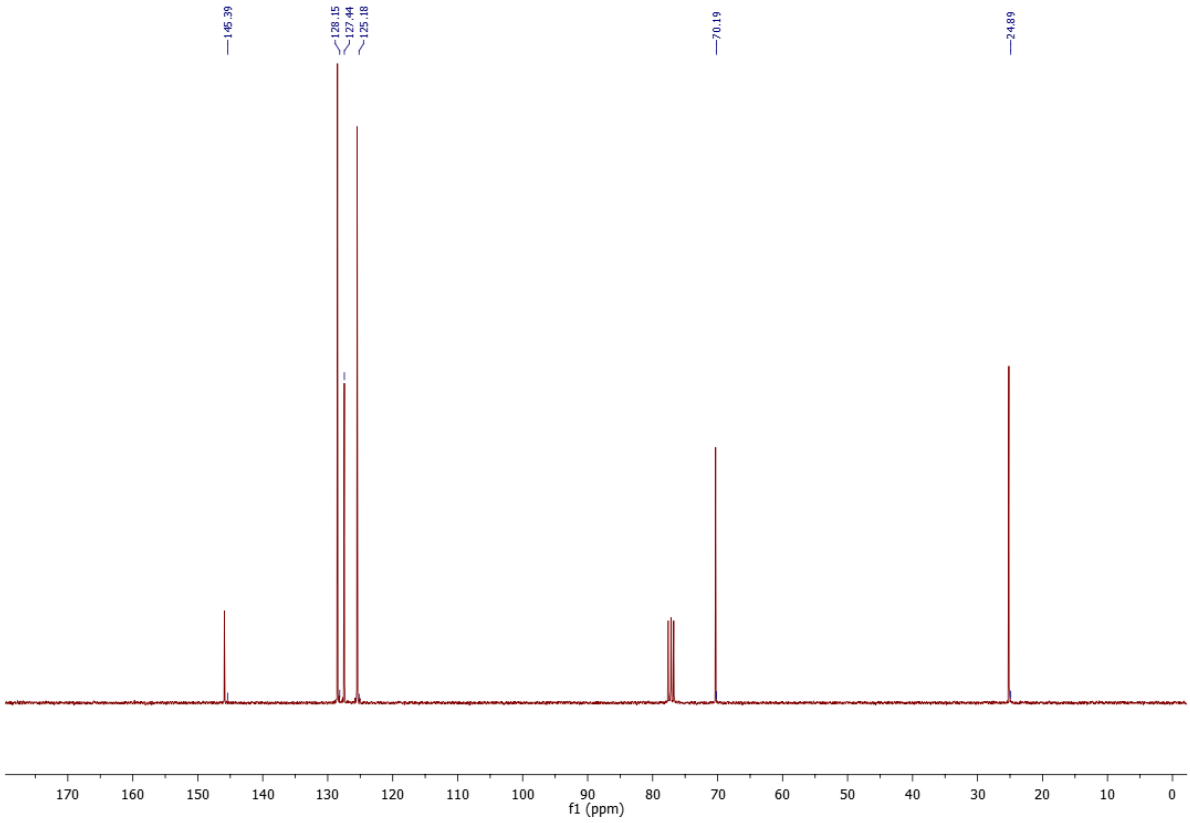

NH2
H2N
6.57
3.35
4.00
3.81
7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)

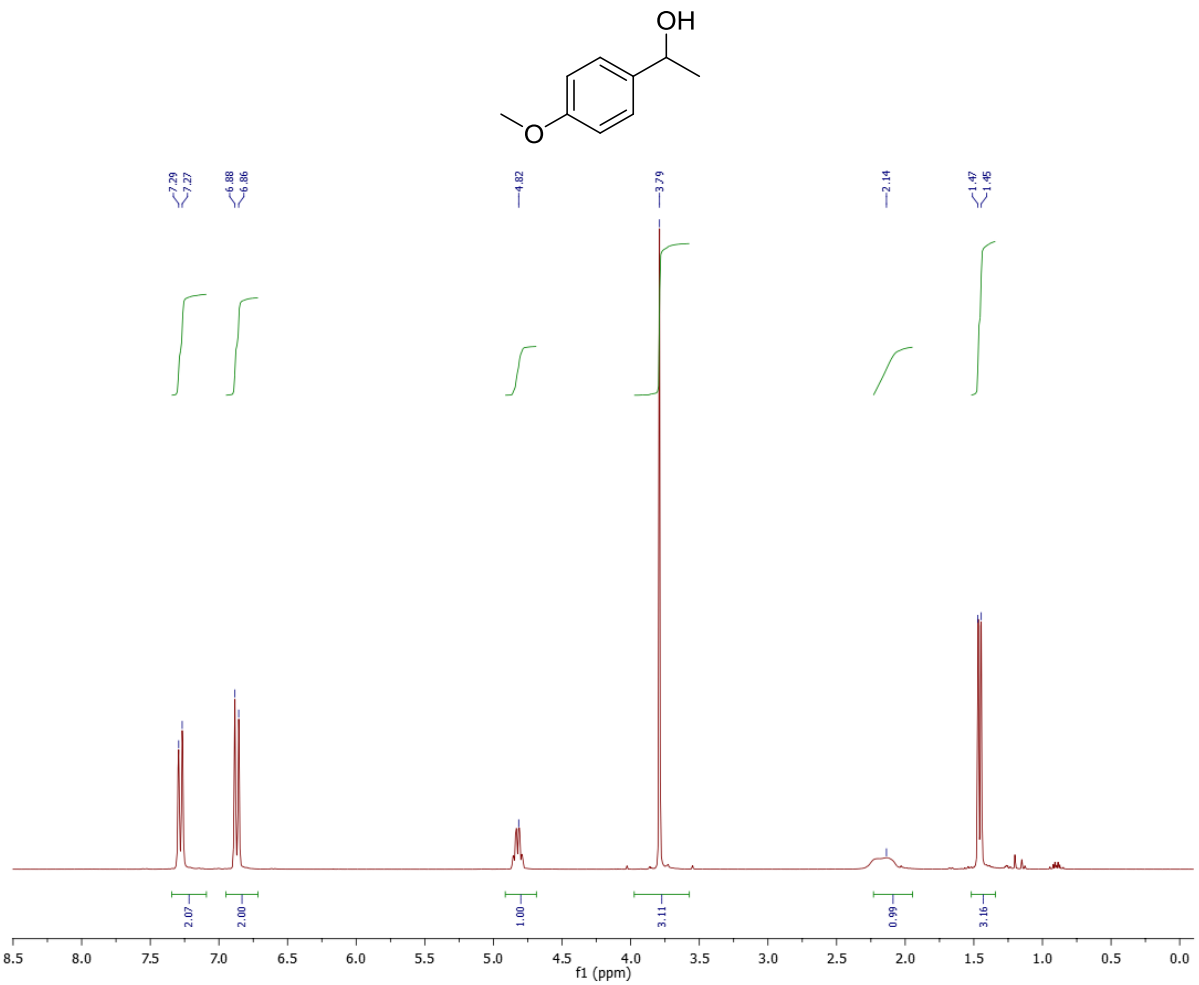

138.59
116.55
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40
f1 (ppm)

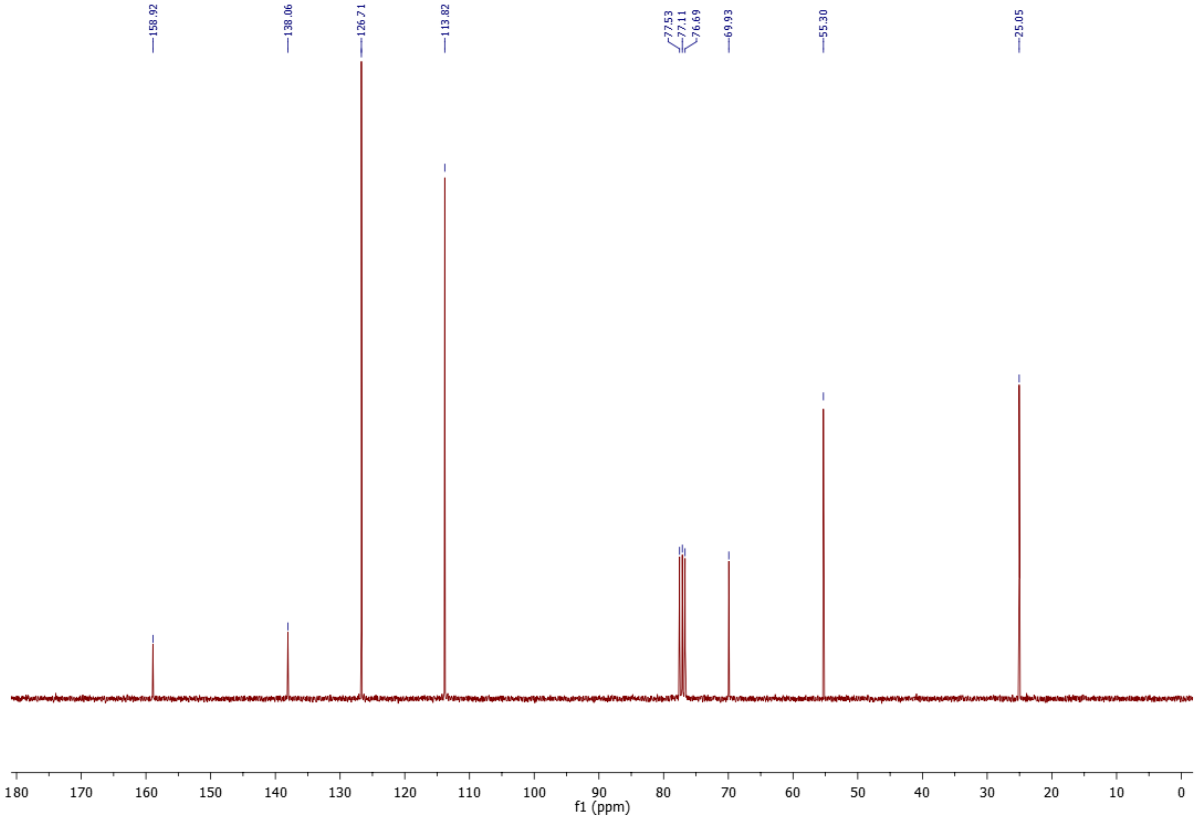

NH2
Cl
7.02
6.99
6.52
6.50
6.49
6.48
3.50
2.00
2.07
2.07
f1 (ppm)

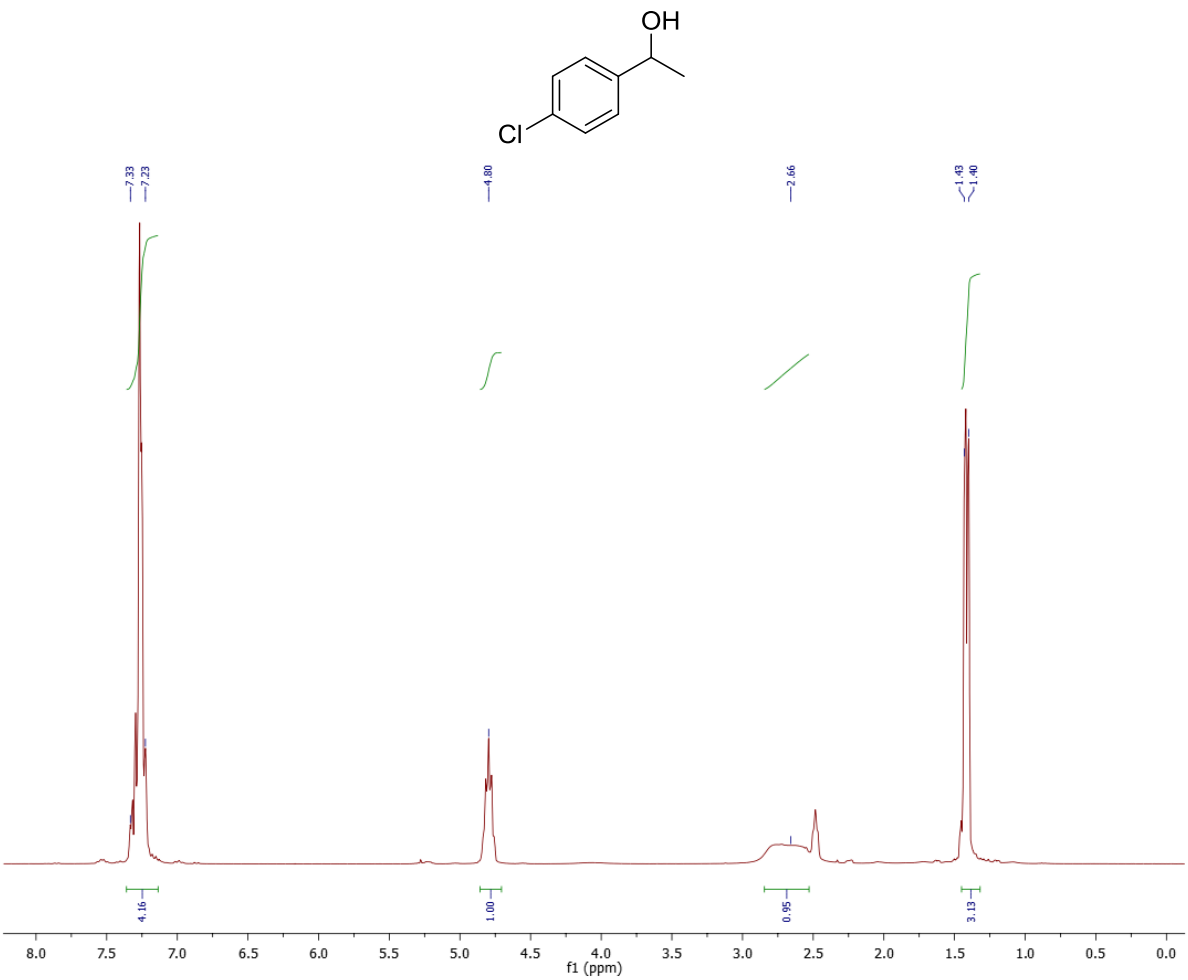

144.63
129.33
122.97
116.29
f1 (ppm)

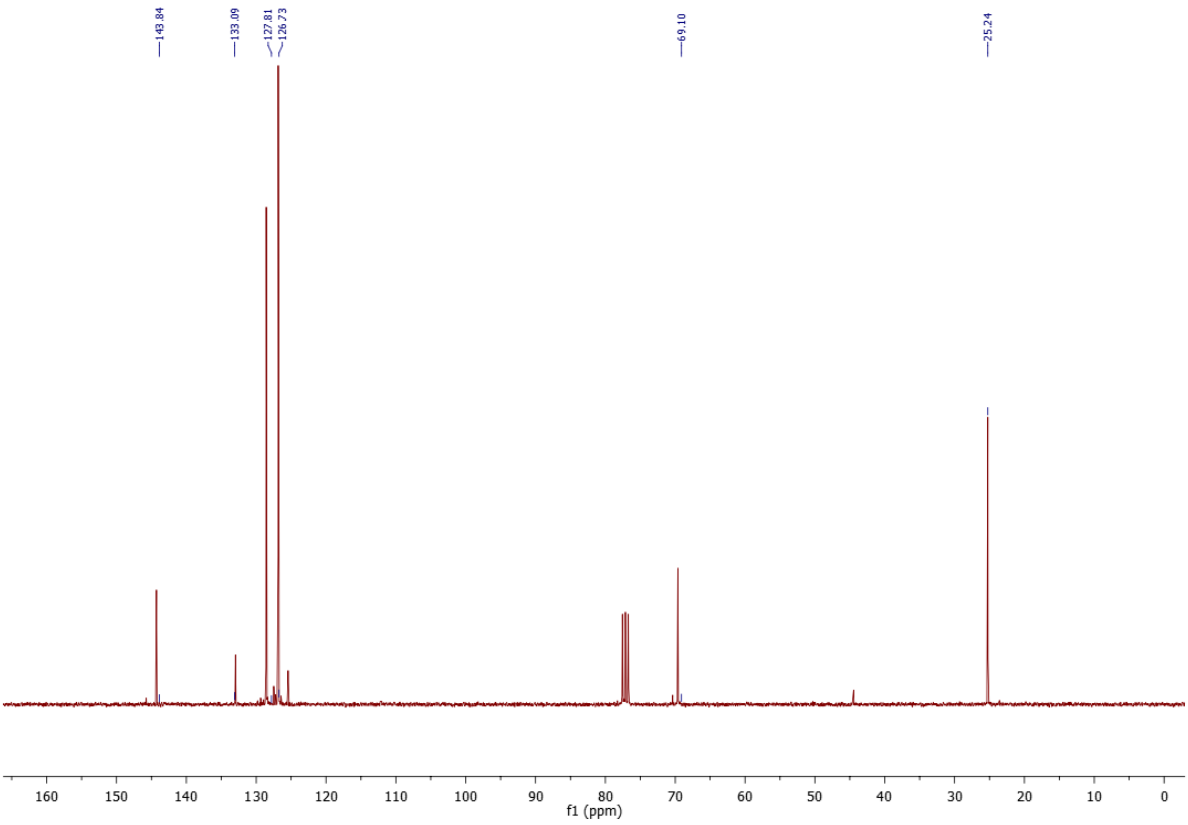

OH
7.42
7.23
4.83
2.69
1.48
5.04
1.00
0.98
3.12
f1 (ppm)

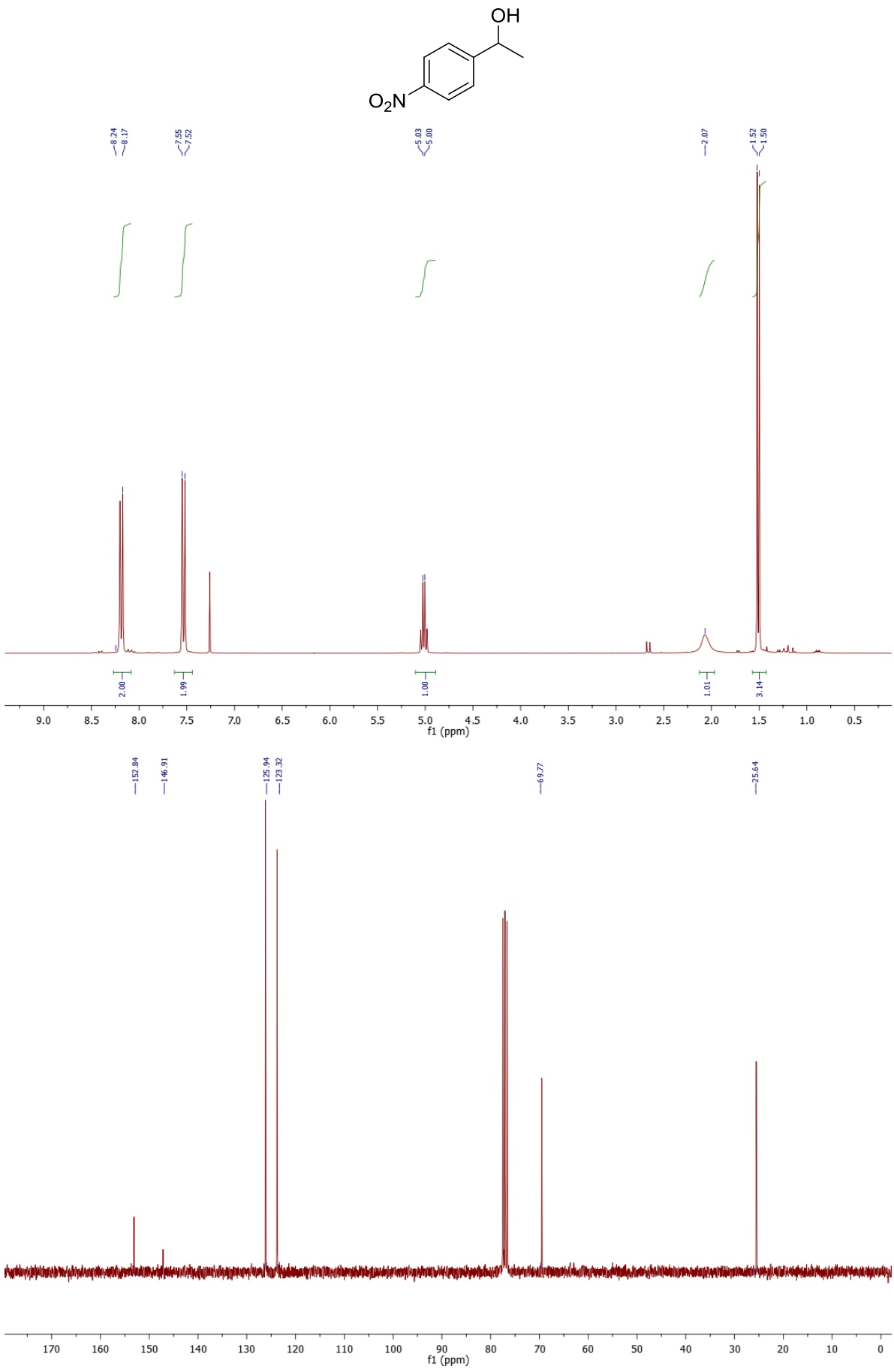

145.39
128.15
127.44
125.18
70.19
24.89
f1 (ppm)


OH
O
7.29
7.27
6.88
6.86
4.82
3.79
2.14
1.47
1.45
2.07
2.00
1.00
3.11
0.99
3.16
f1 (ppm)


158.92
138.06
126.71
113.82
77.53
77.11
76.69
69.93
55.30
25.05
f1 (ppm)


OH
Cl
7.33
7.23
4.80
2.66
1.48
1.40
4.16
1.00
0.95
3.13
f1 (ppm)


143.84
133.09
127.81
126.73
69.10
25.24
f1 (ppm)


OH
O2N
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8.17
7.55
7.52
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5.00
2.07
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1.50
2.00
1.99
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3.14
f1 (ppm)
152.84
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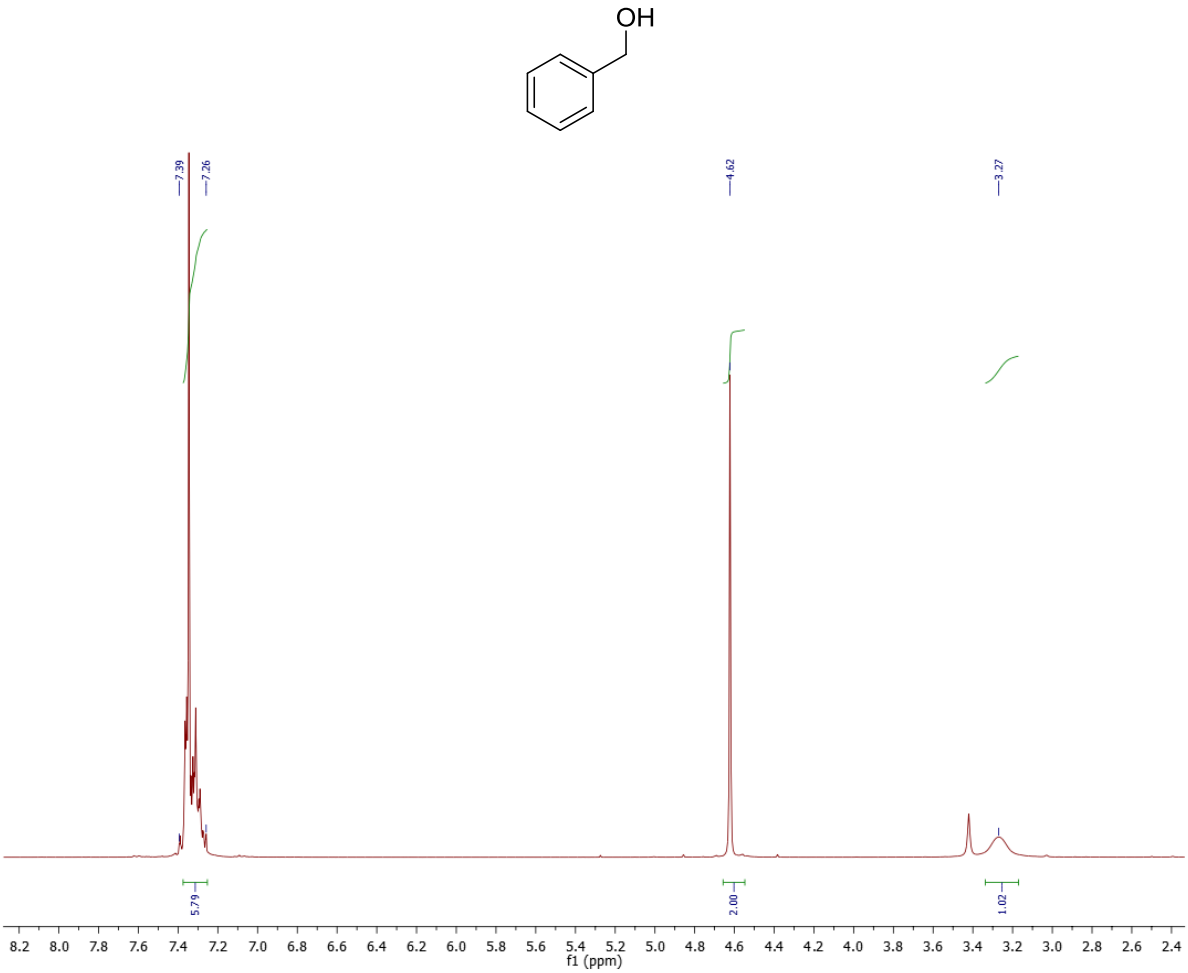
125.94
123.32
69.77
25.64
f1 (ppm)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3.27
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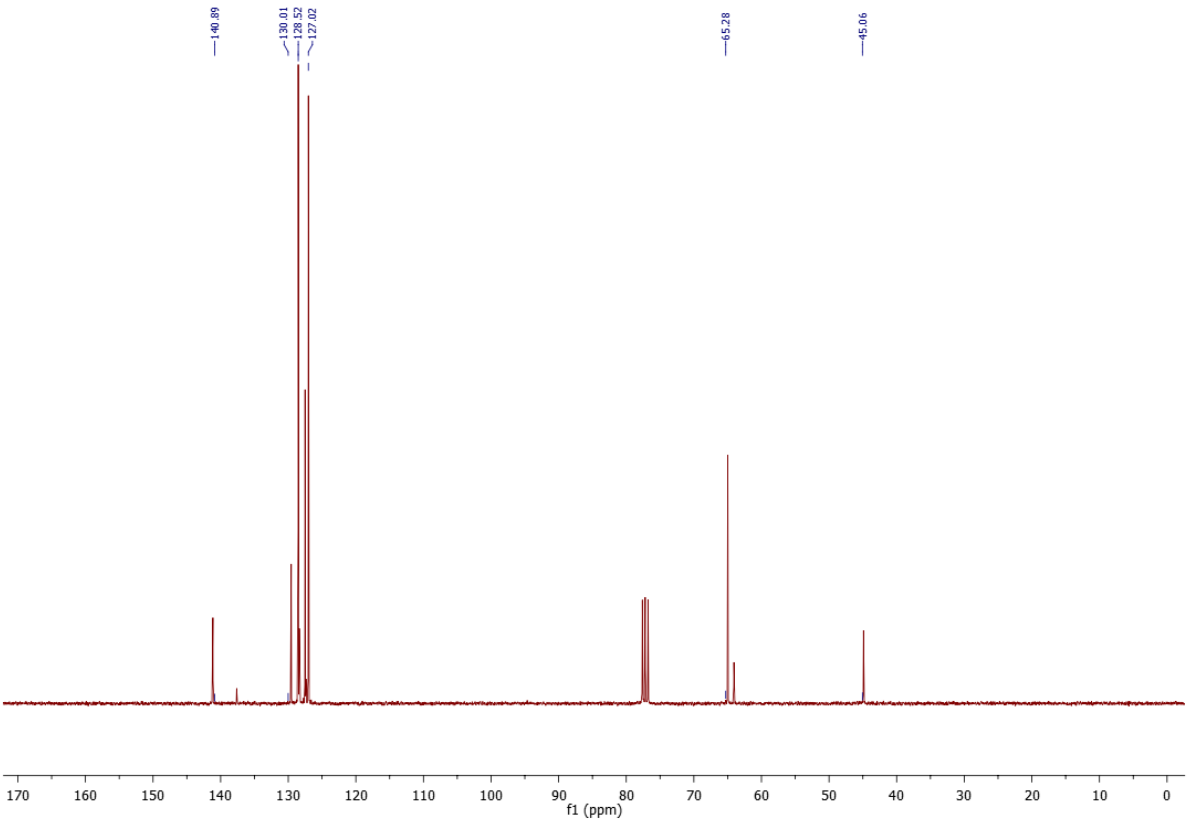
1.02
f1 (ppm)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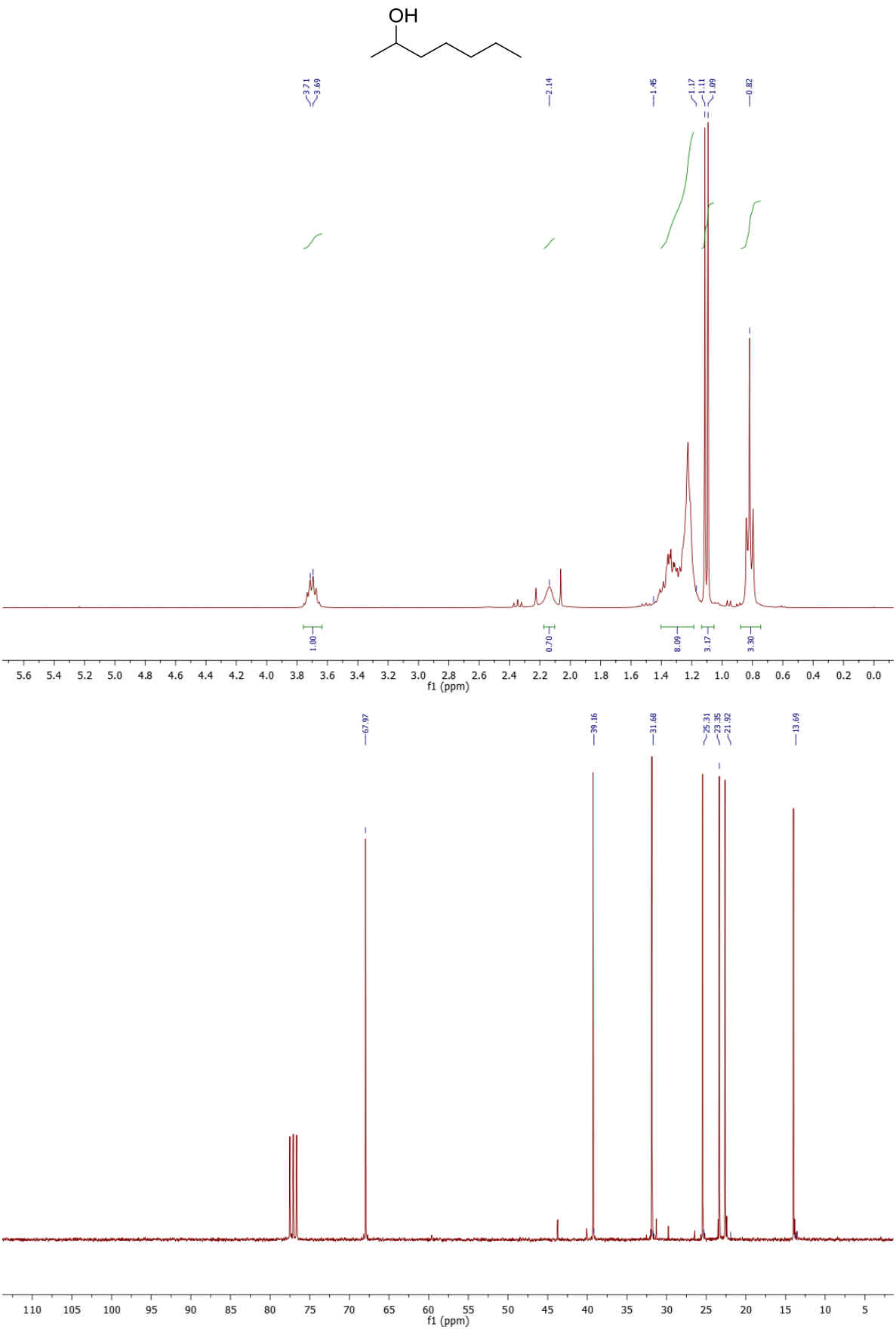
130.01
128.52
127.02
65.28
45.06
f1 (ppm)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1.17
1.11
1.09
0.82
1.00
0.70
8.09
3.17
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f1 (ppm)
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39.16
31.68
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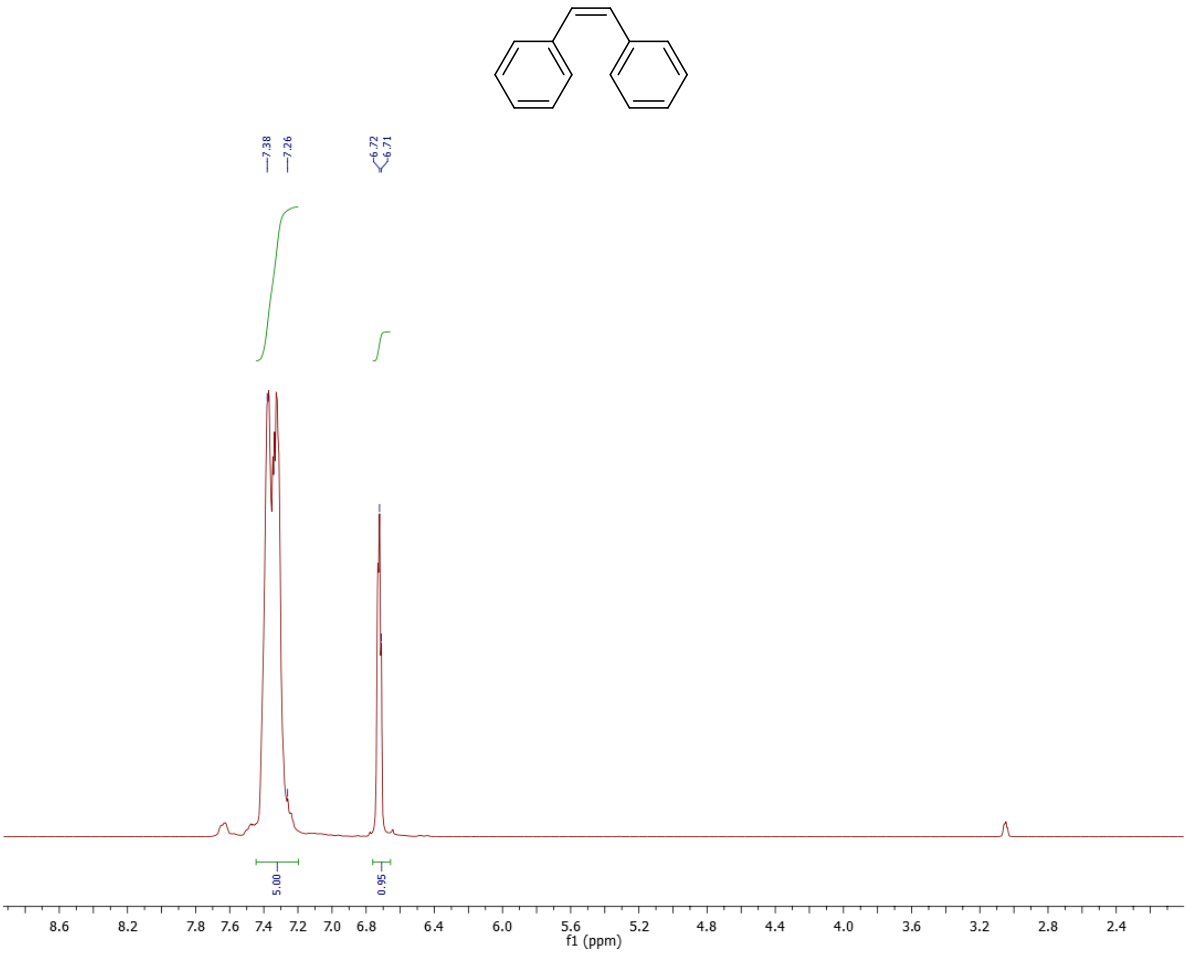
23.35
21.92
13.69
f1 (ppm)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7.26
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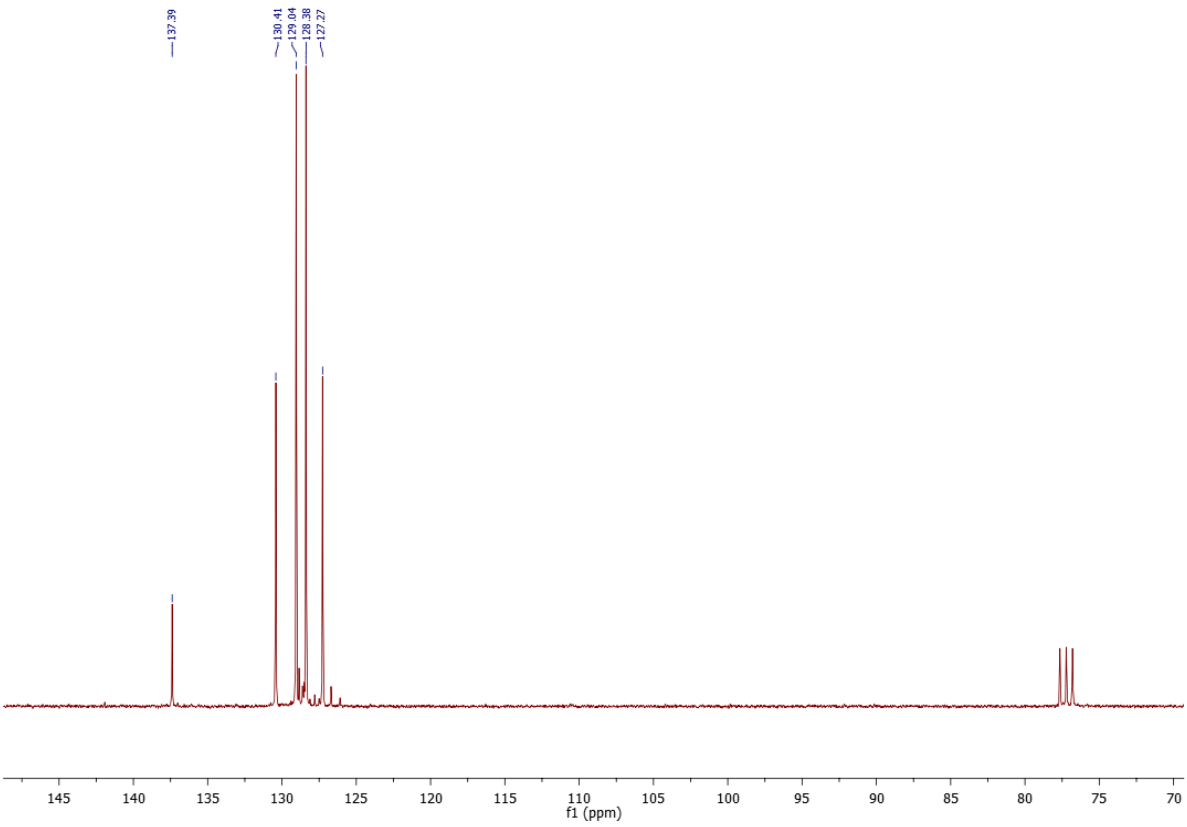
0.95
8.6
8.2
7.8
7.6
7.4
7.2
7.0
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
f1 (ppm)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140
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120
115
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95
90
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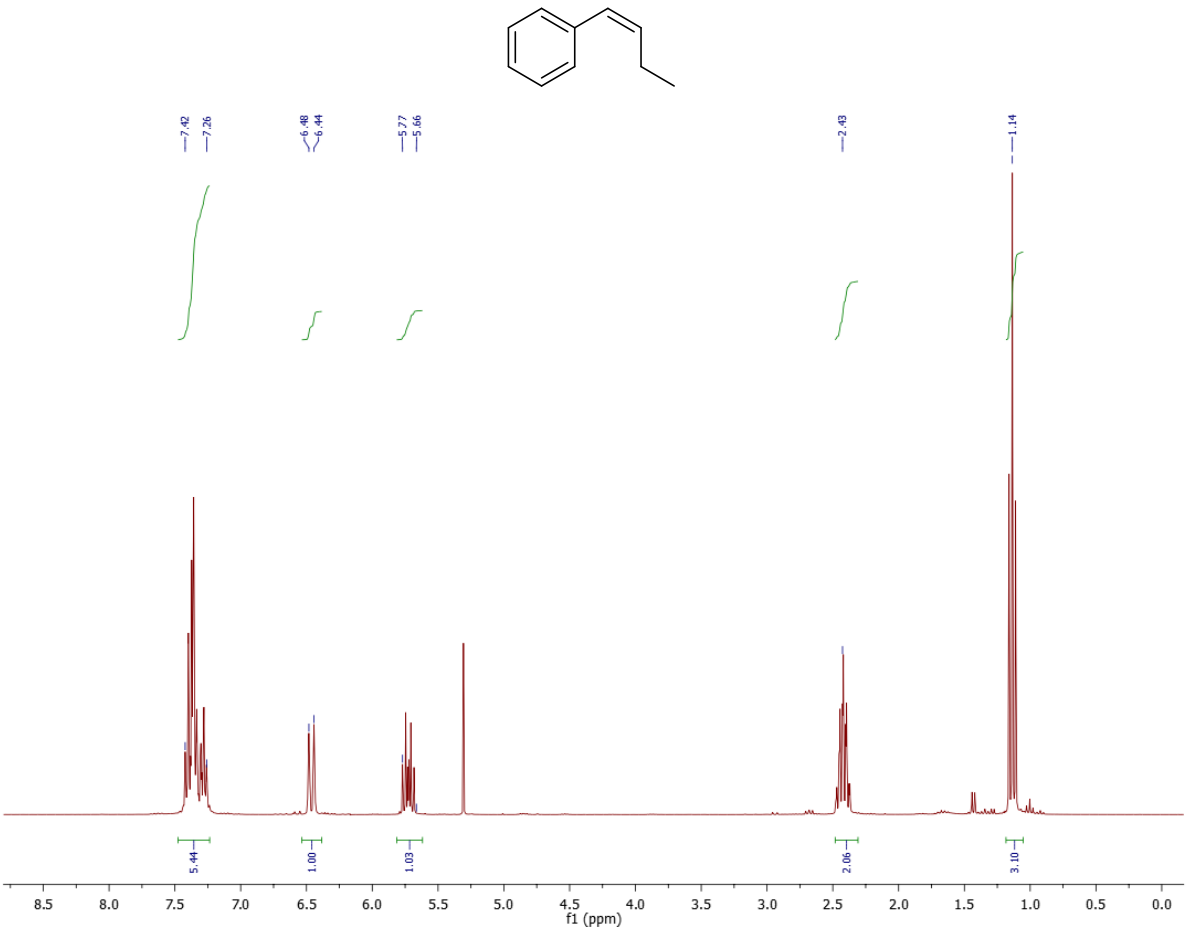
80
75
70
f1 (ppm)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1.14
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1.03
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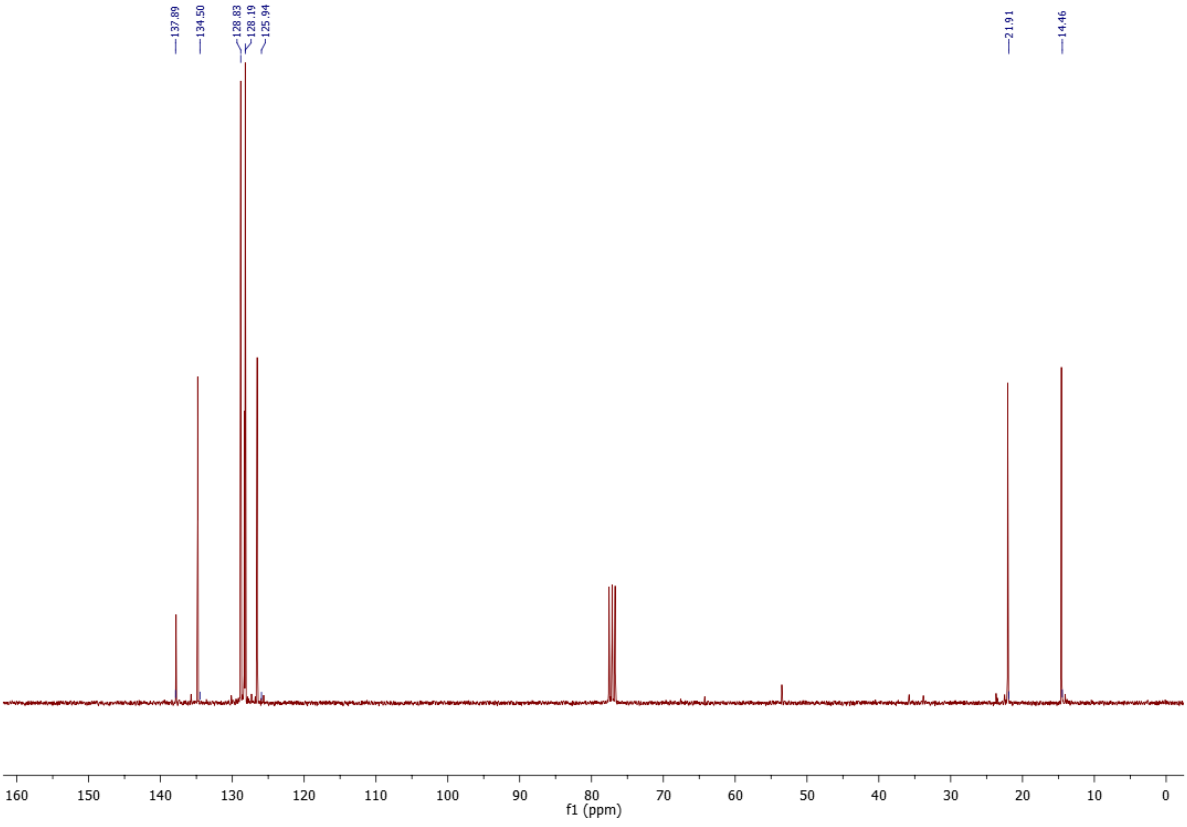
3.10
f1 (ppm)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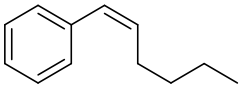

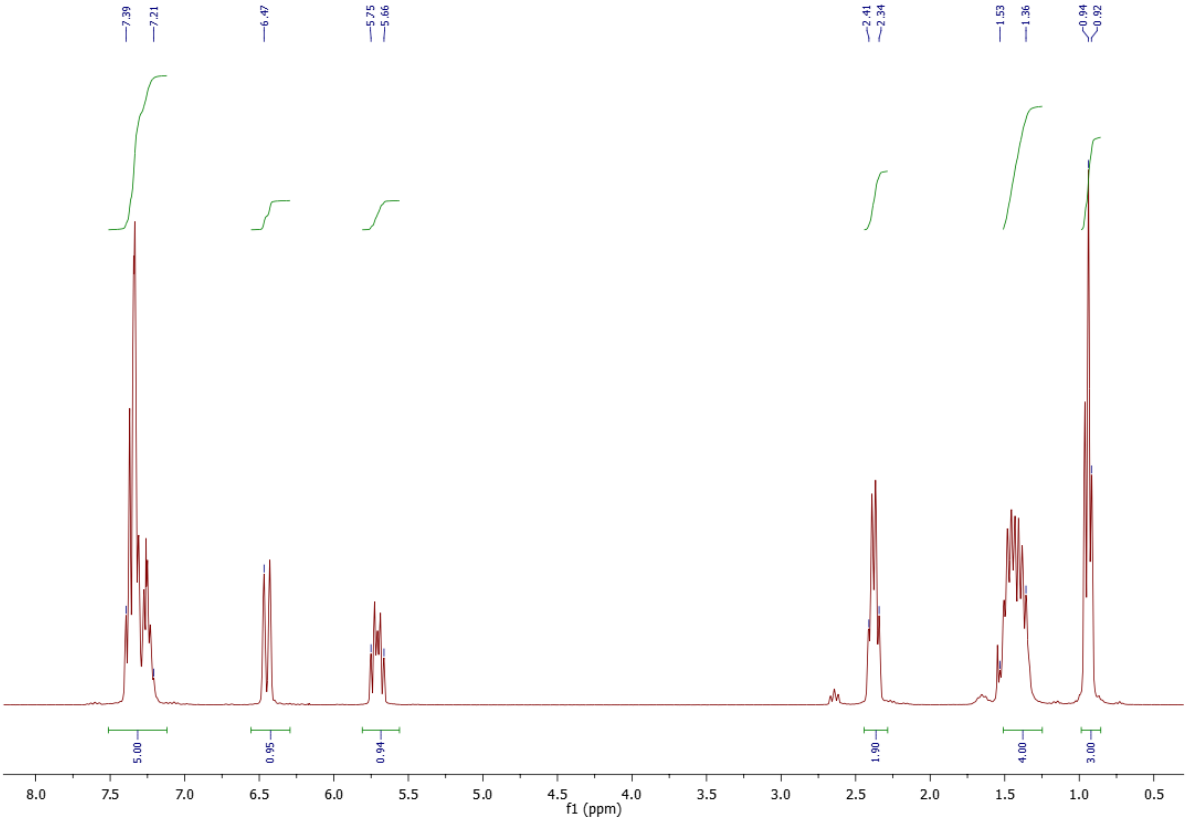
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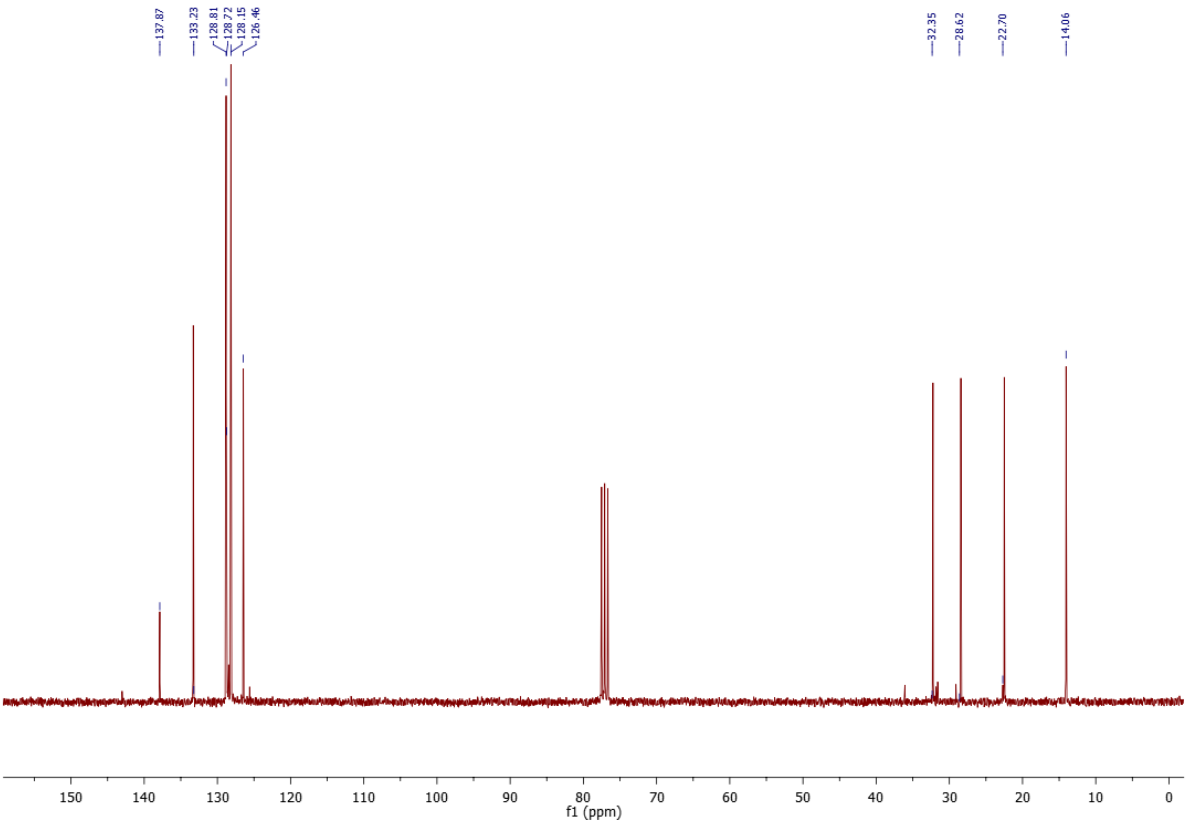
7.21
6.47
5.75
5.66
2.41
2.34
1.53
1.36
0.94
0.92
5.00
0.95
0.94
1.90
4.00
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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128.81
128.72
128.15
126.46
32.35
28.62
22.70
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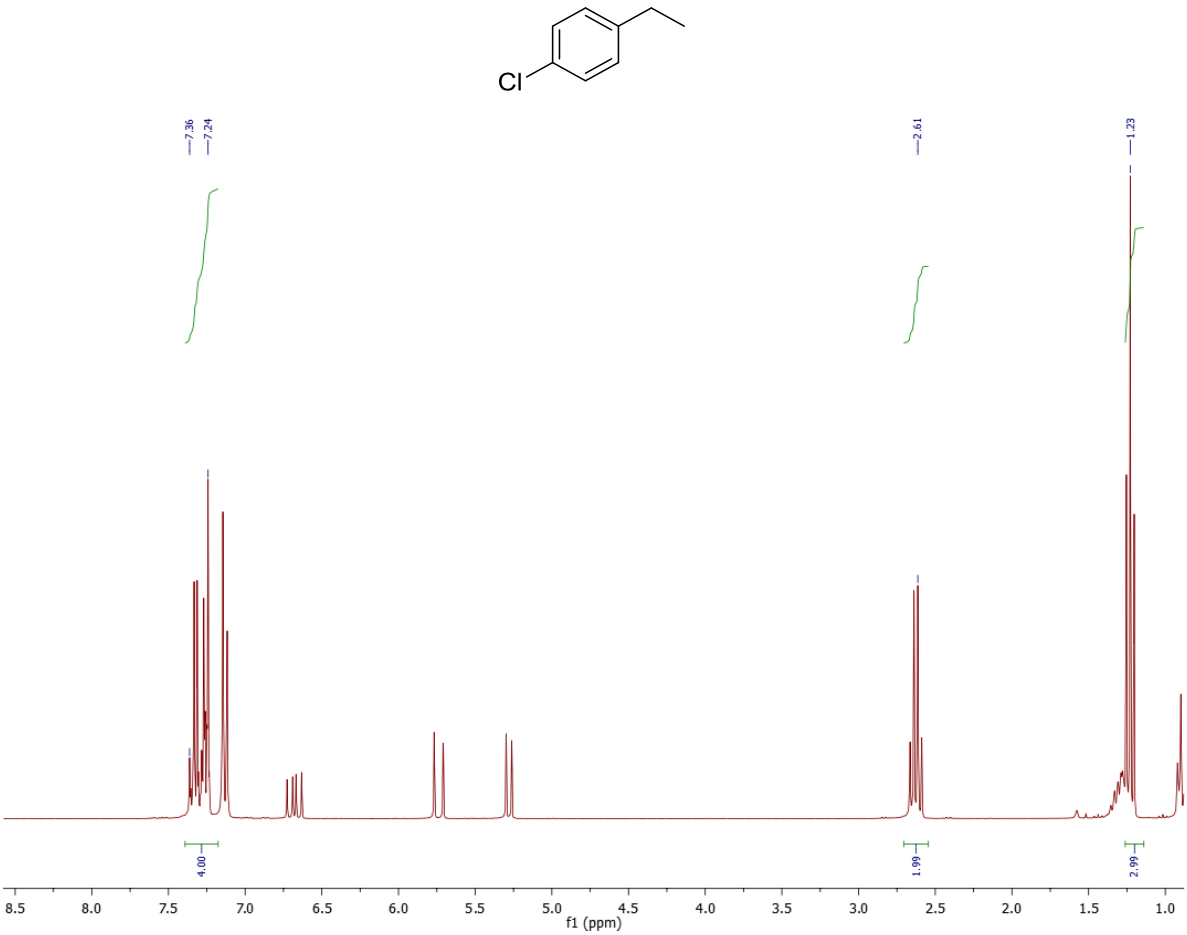
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Cl
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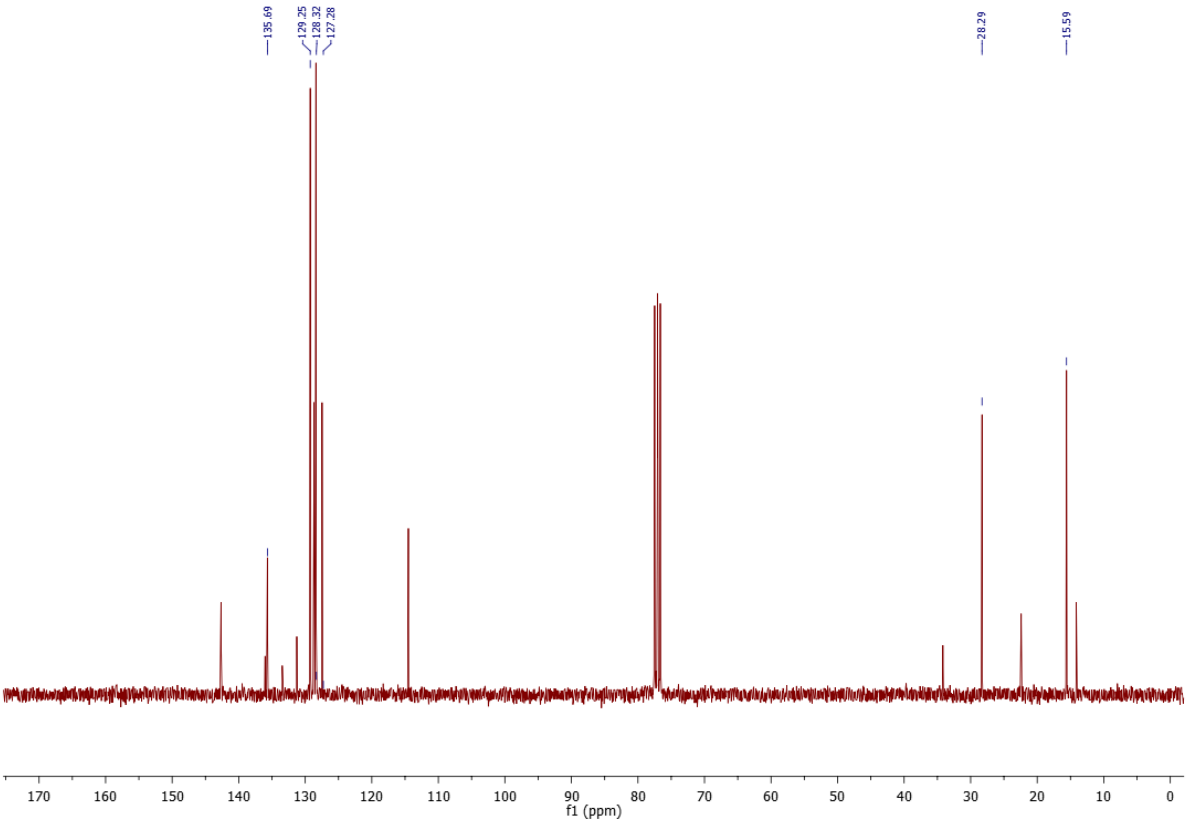
7.24
2.61
1.23
4.00
1.99
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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129.25
128.32
127.28
28.29
15.59
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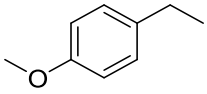
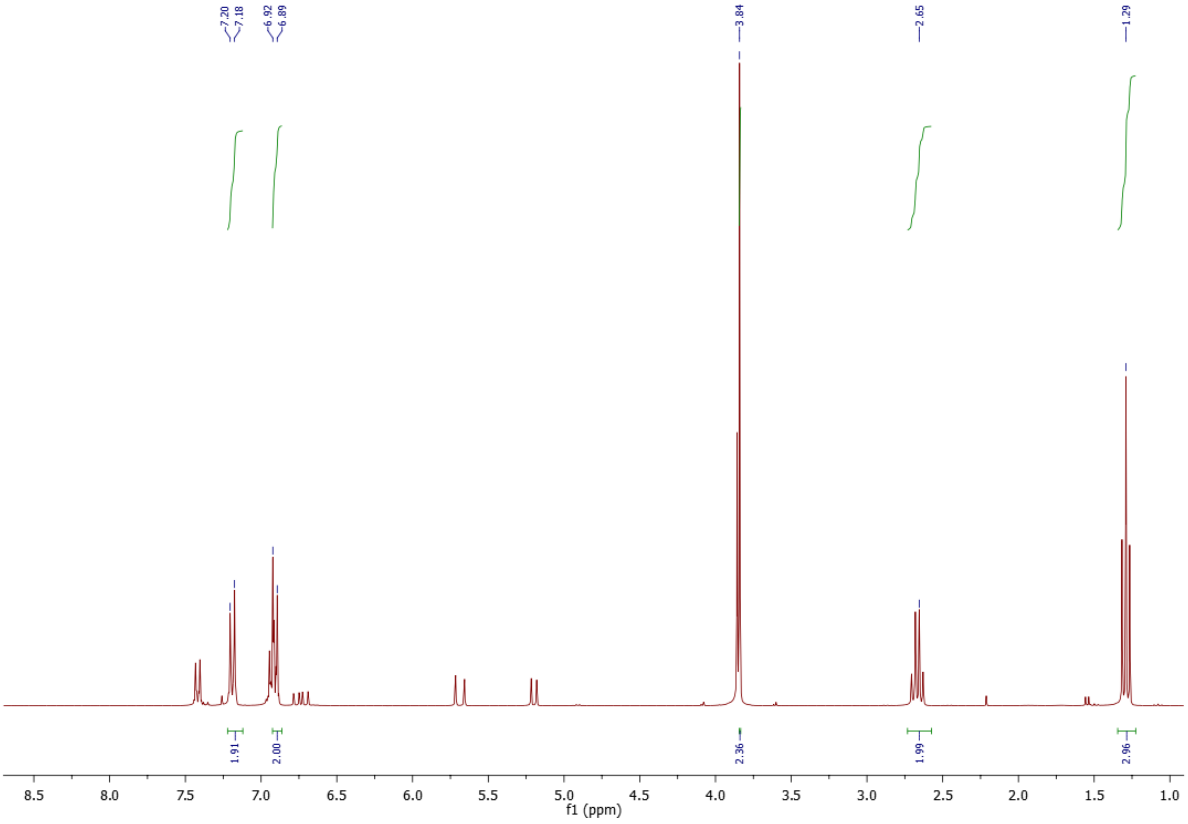
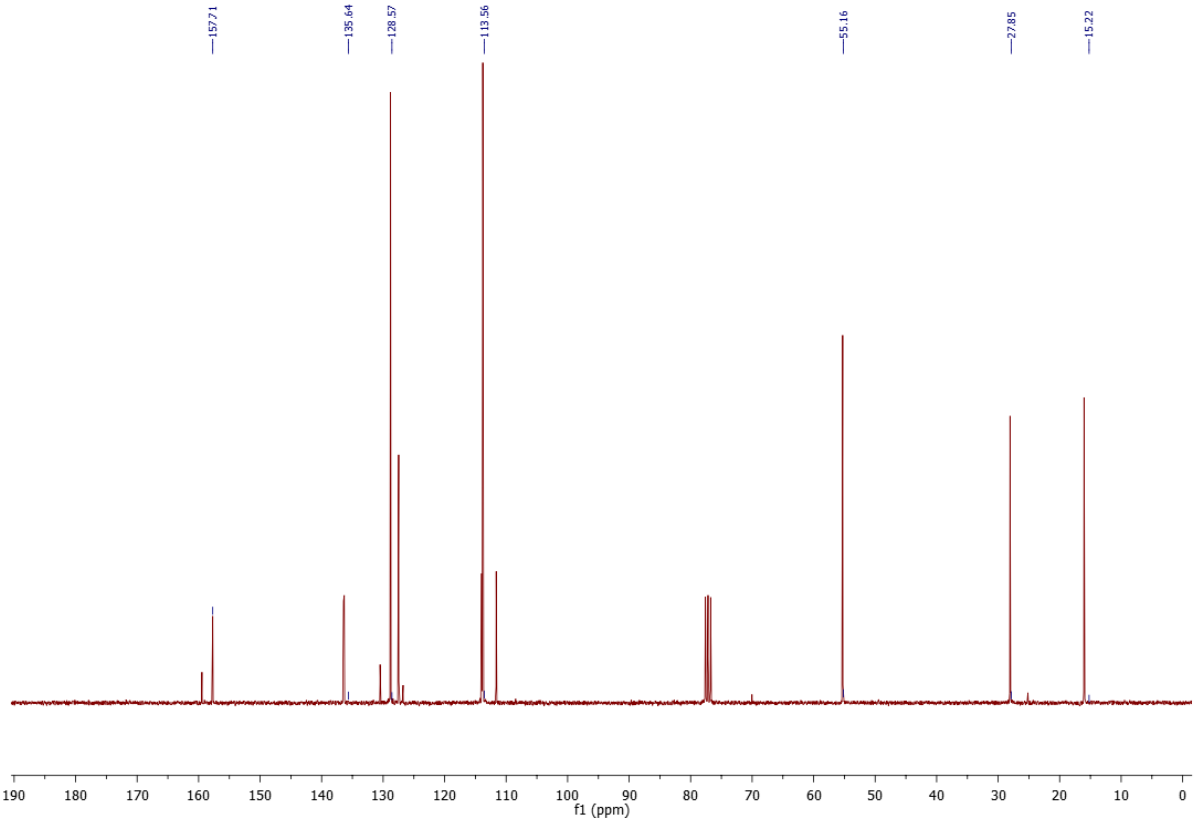
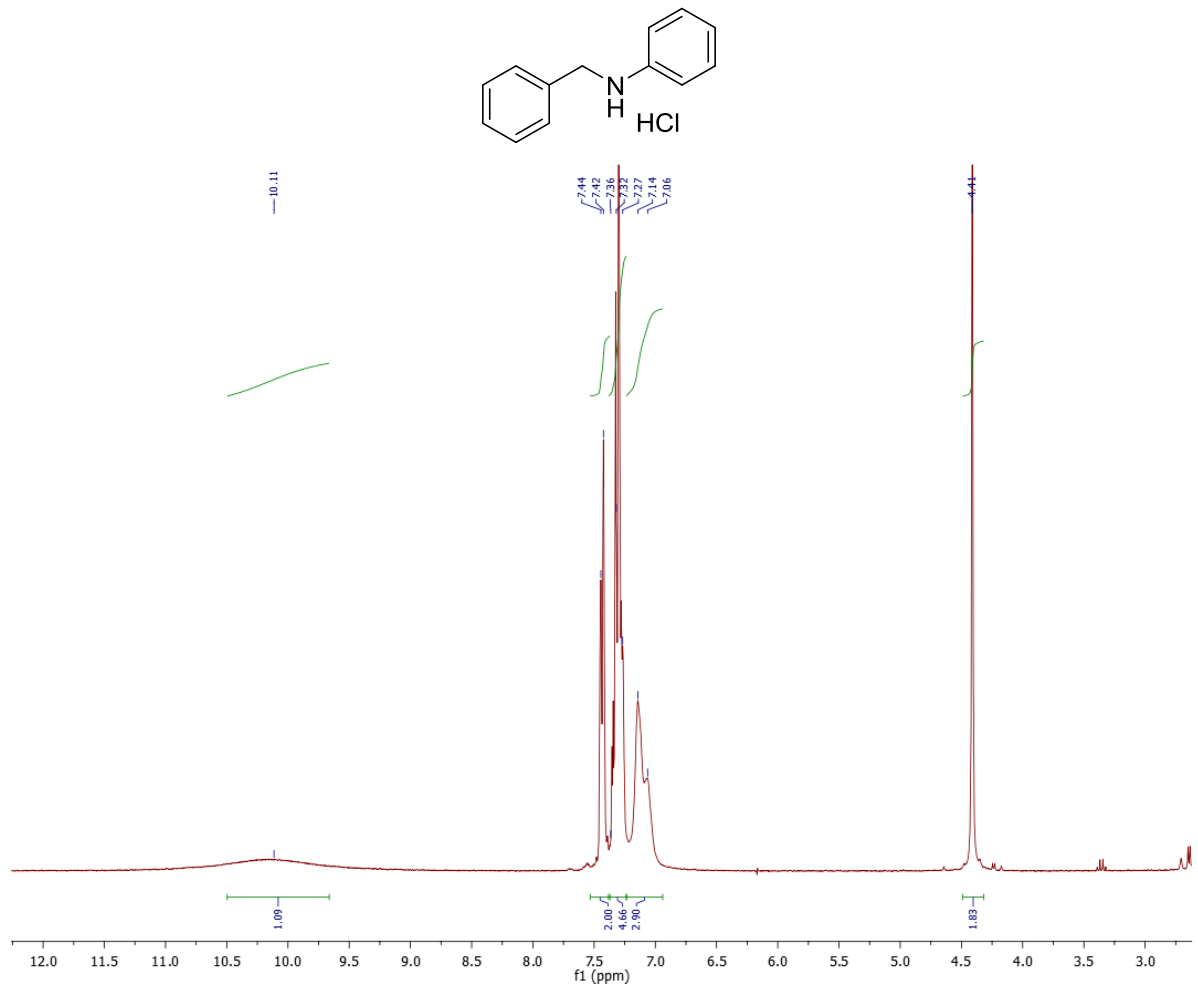
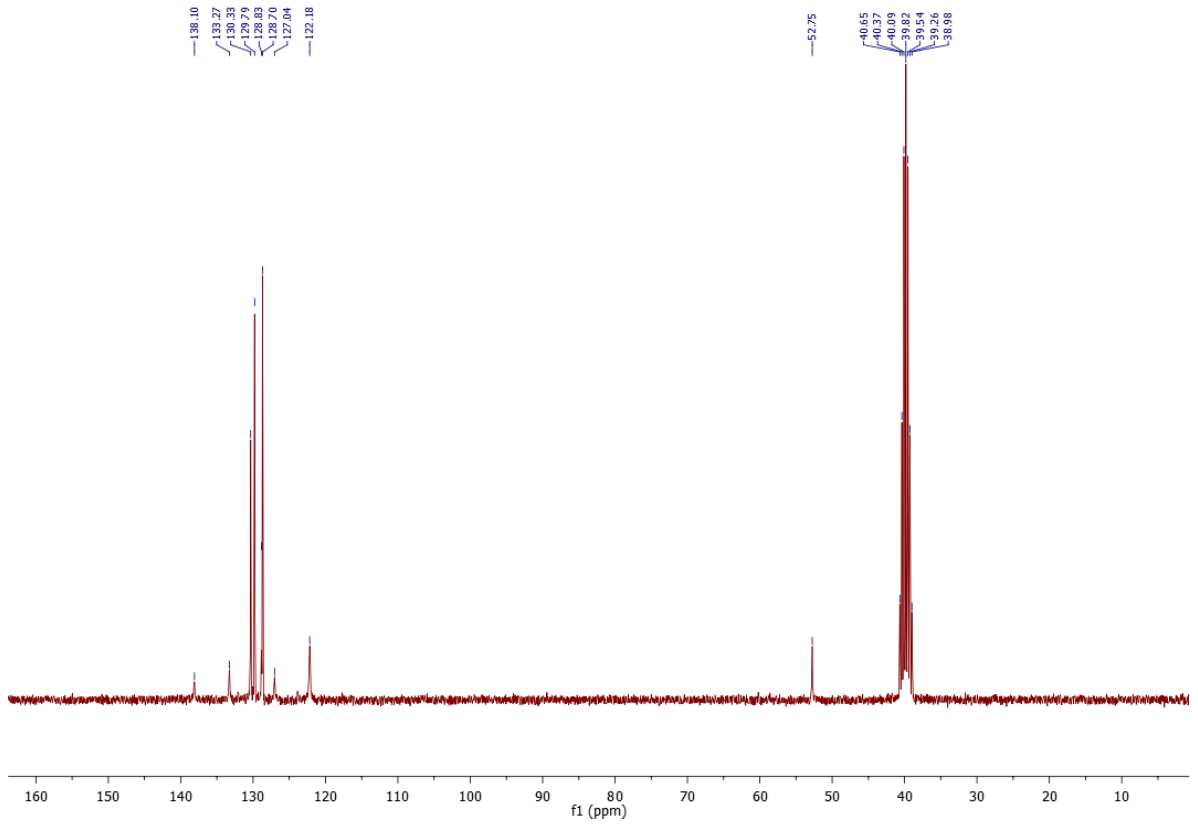
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

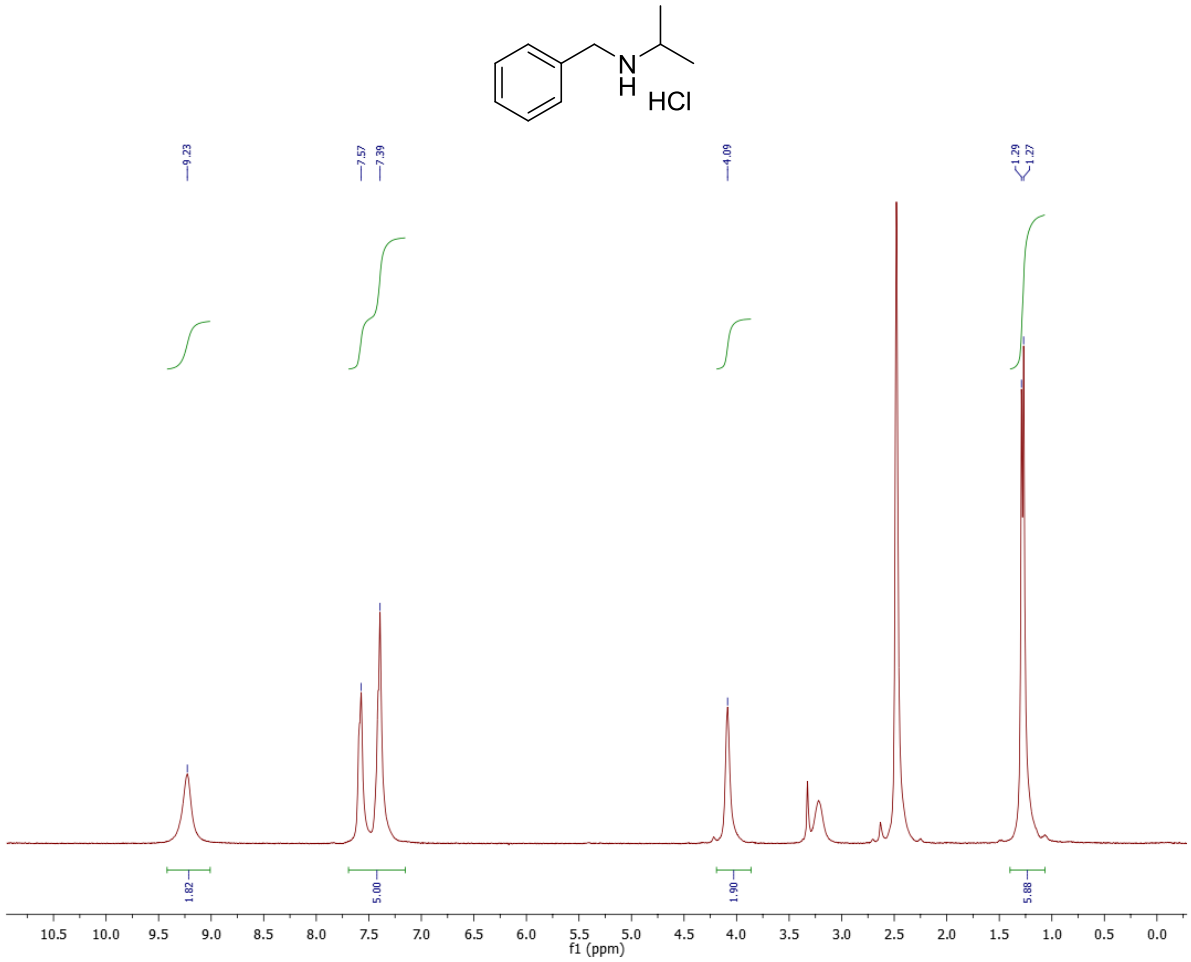

O


7.20
7.18
6.92
6.89
3.84
2.65
1.29
1.91
2.00
2.36
1.99
2.96
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


157.71
135.64
128.57
113.56
55.16
27.85
15.22
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
H
HCl
10.11
7.44
7.42
7.36
7.32
7.27
7.14
7.06
4.41
1.09
2.00
4.66
2.90
1.83
f1 (ppm)


138.10
133.27
130.33
129.79
128.83
128.70
127.04
122.18
52.75
40.65
40.37
40.09
39.82
39.54
39.26
38.98
f1 (ppm)


N
H
HCl
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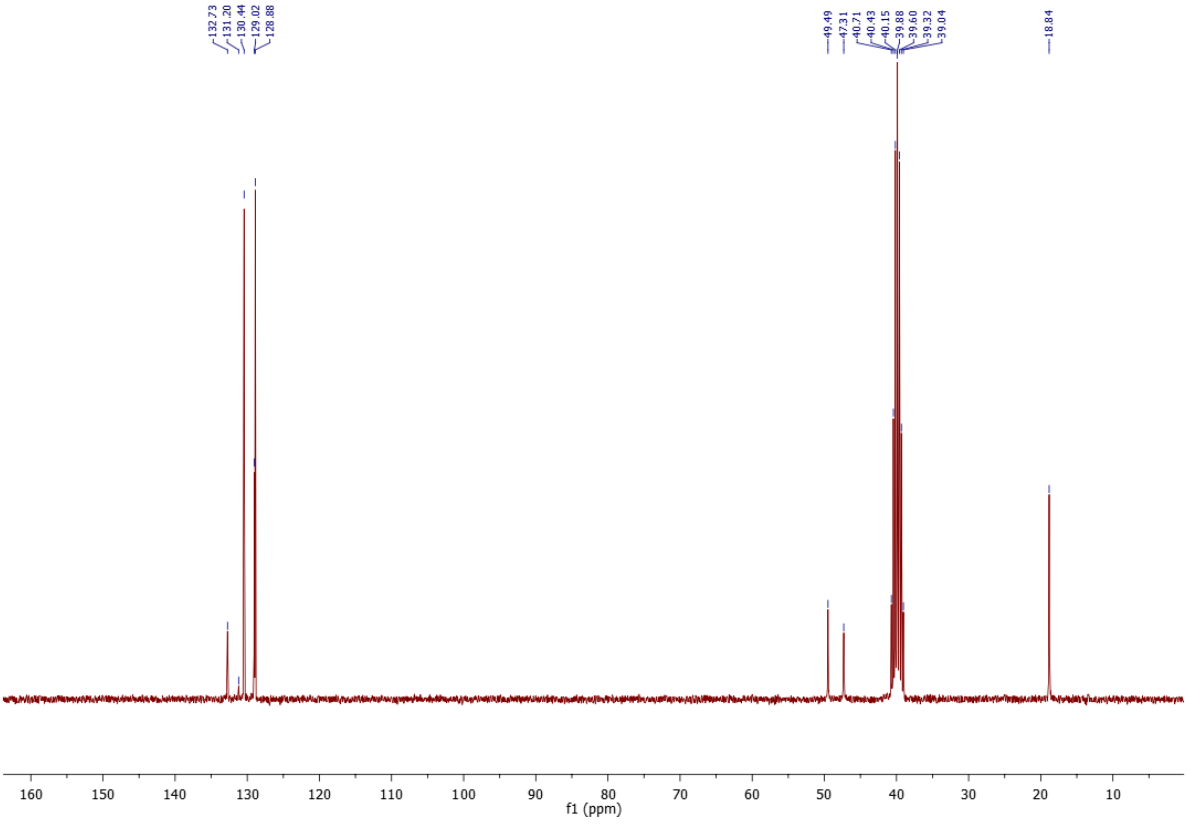
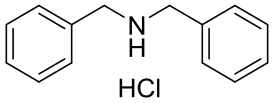
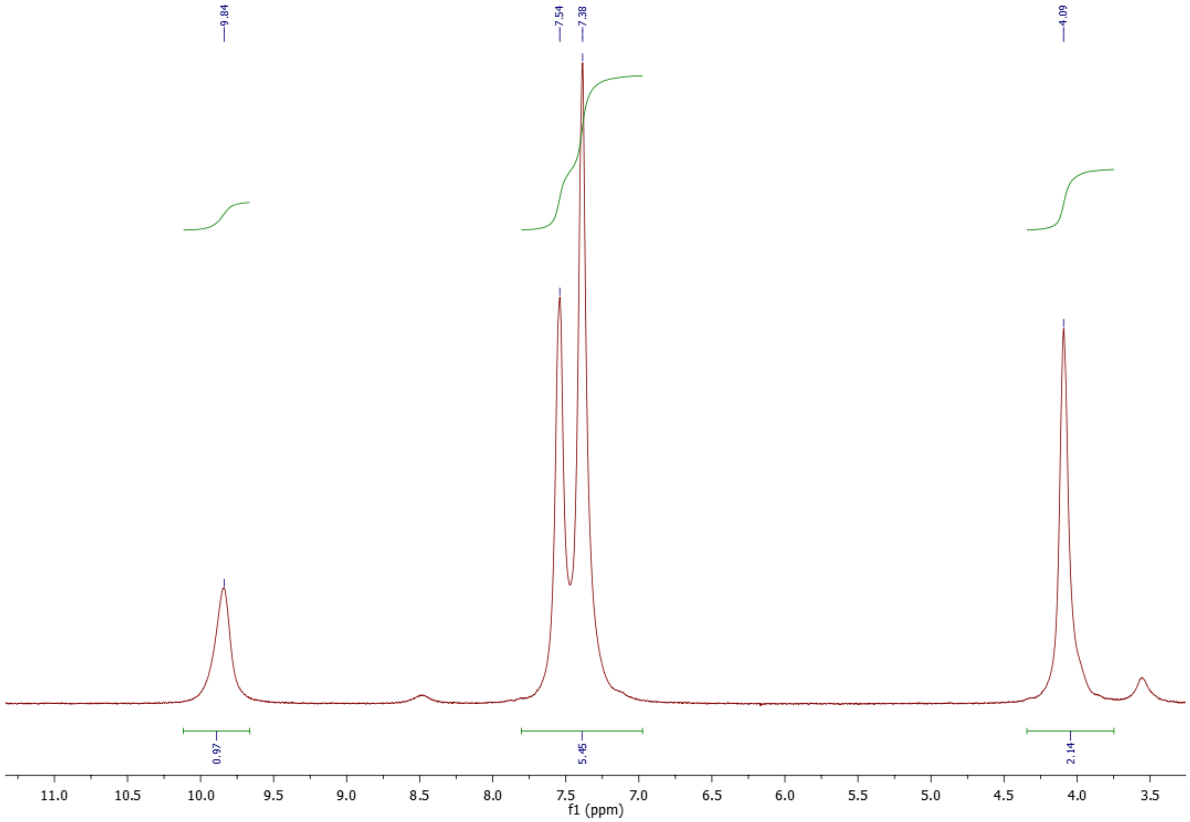
7.57
7.39
4.09
1.29
1.27
1.82
5.00
1.90
5.88
f1 (ppm)


132.73
131.20
130.44
129.02
128.88
49.49
47.31
40.71
40.43
40.15
39.88
39.60
39.32
39.04
18.84
f1 (ppm)


N
H
HCl


9.84
7.54
7.38
4.09
0.97
5.45
2.14
11.0
10.5
10.0
9.5
9.0
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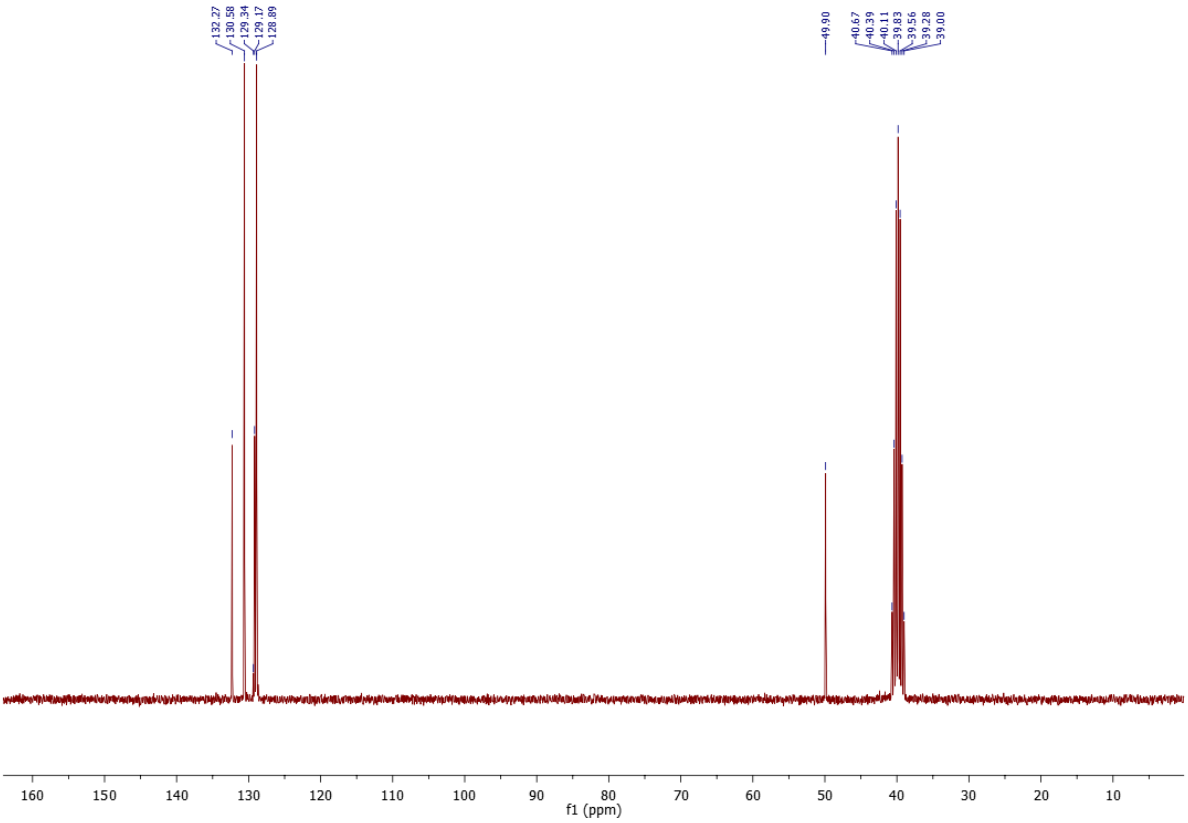
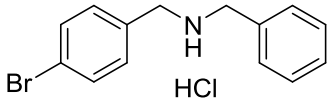
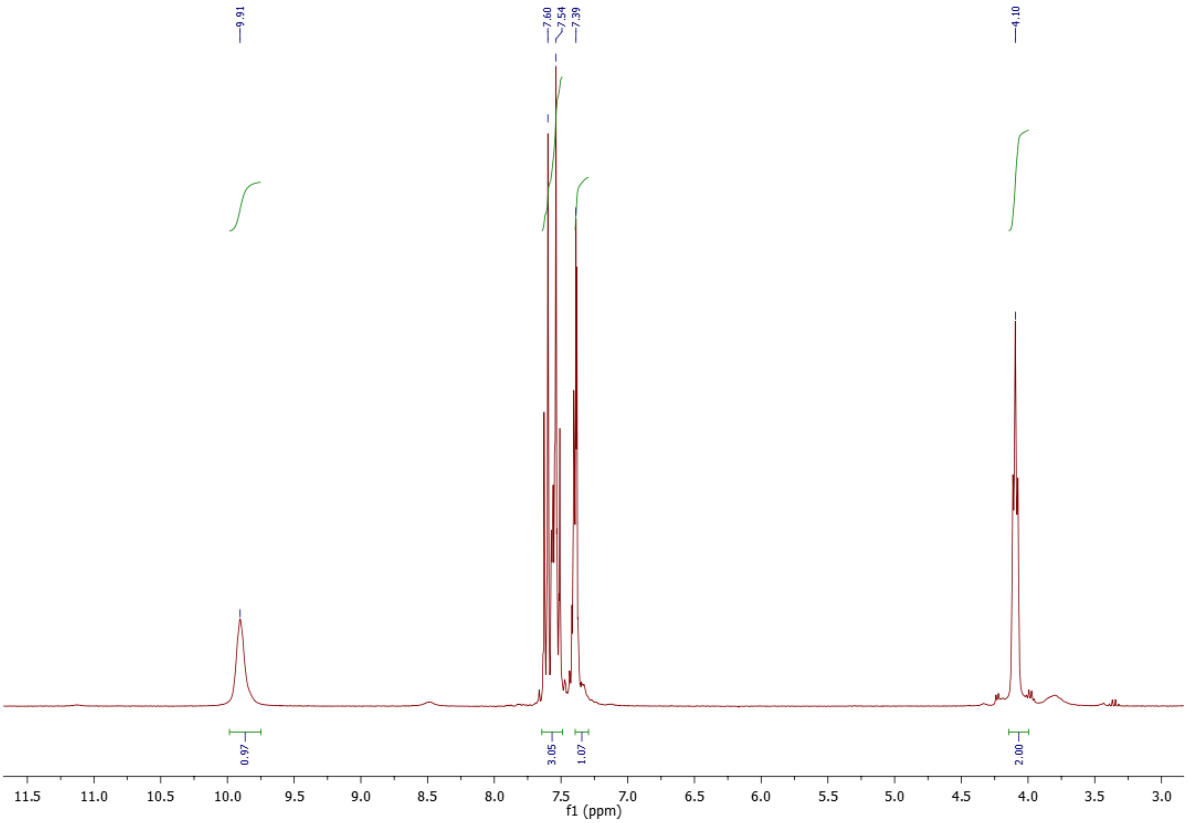
5.0
4.5
4.0
3.5
f1 (ppm)


132.27
130.58
129.34
129.17
128.89
49.90
40.67
40.39
40.11
39.83
39.56
39.28
39.00
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Br
N
H
HCl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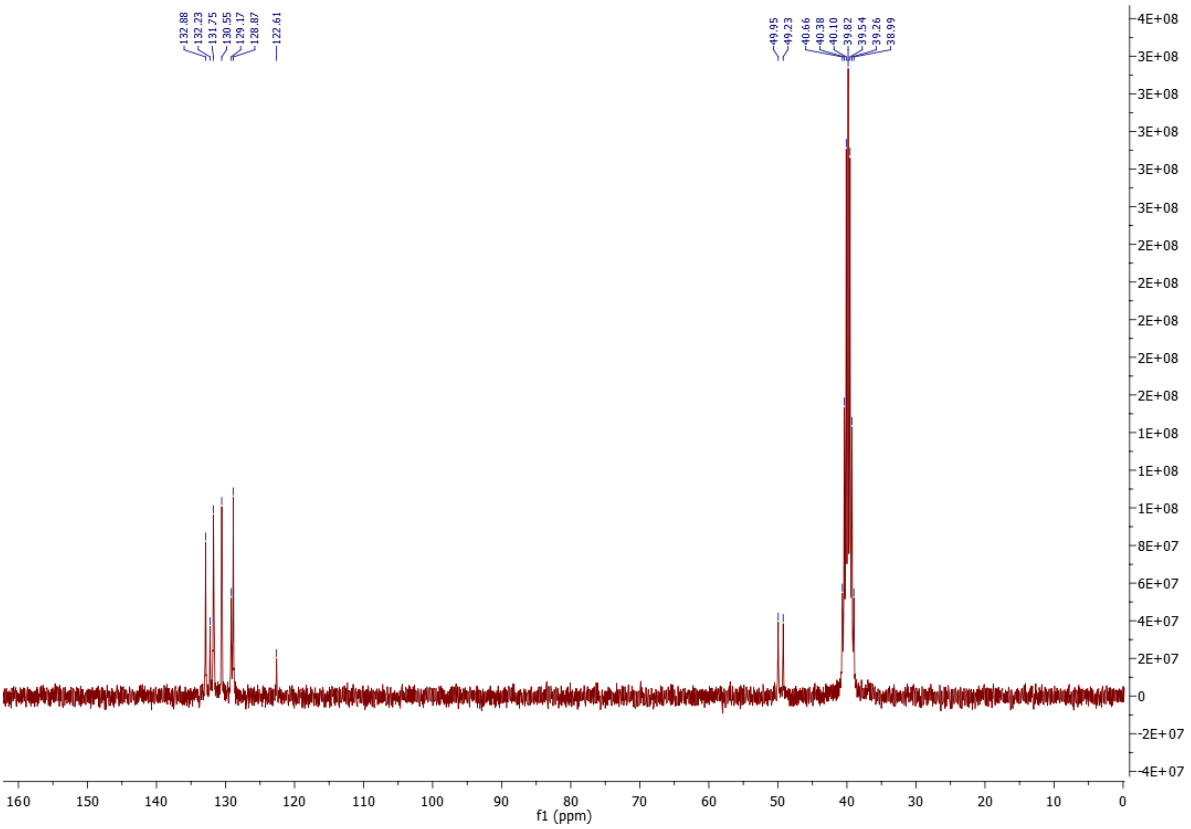
7.39
4.10
0.97
3.05
1.07
2.00
f1 (ppm)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132.23
131.75
130.55
129.17
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122.61
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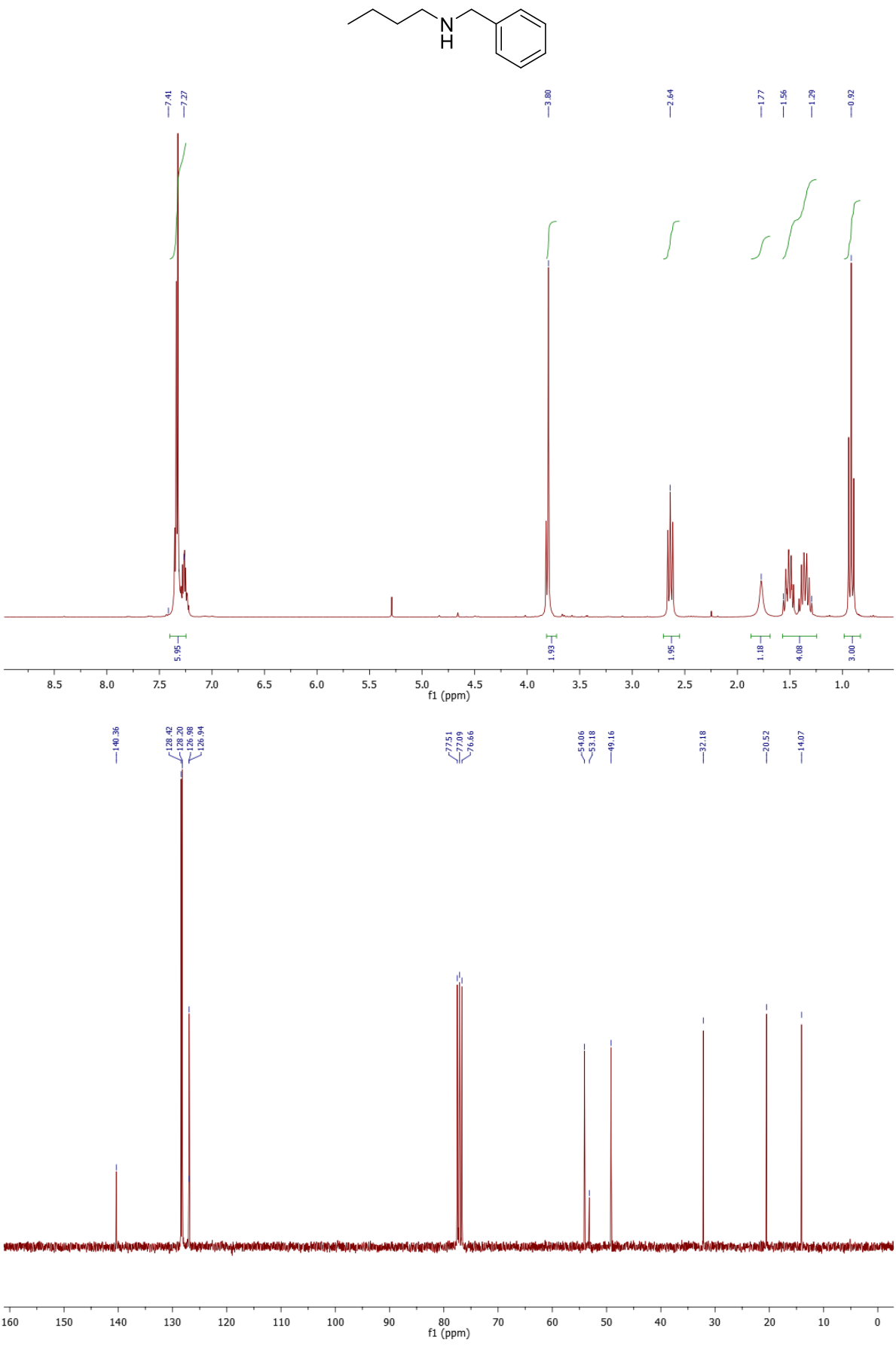
49.23
40.66
40.38
40.10
39.82
39.54
39.26
38.99
f1 (ppm)


7.41
7.27
3.80
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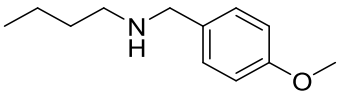
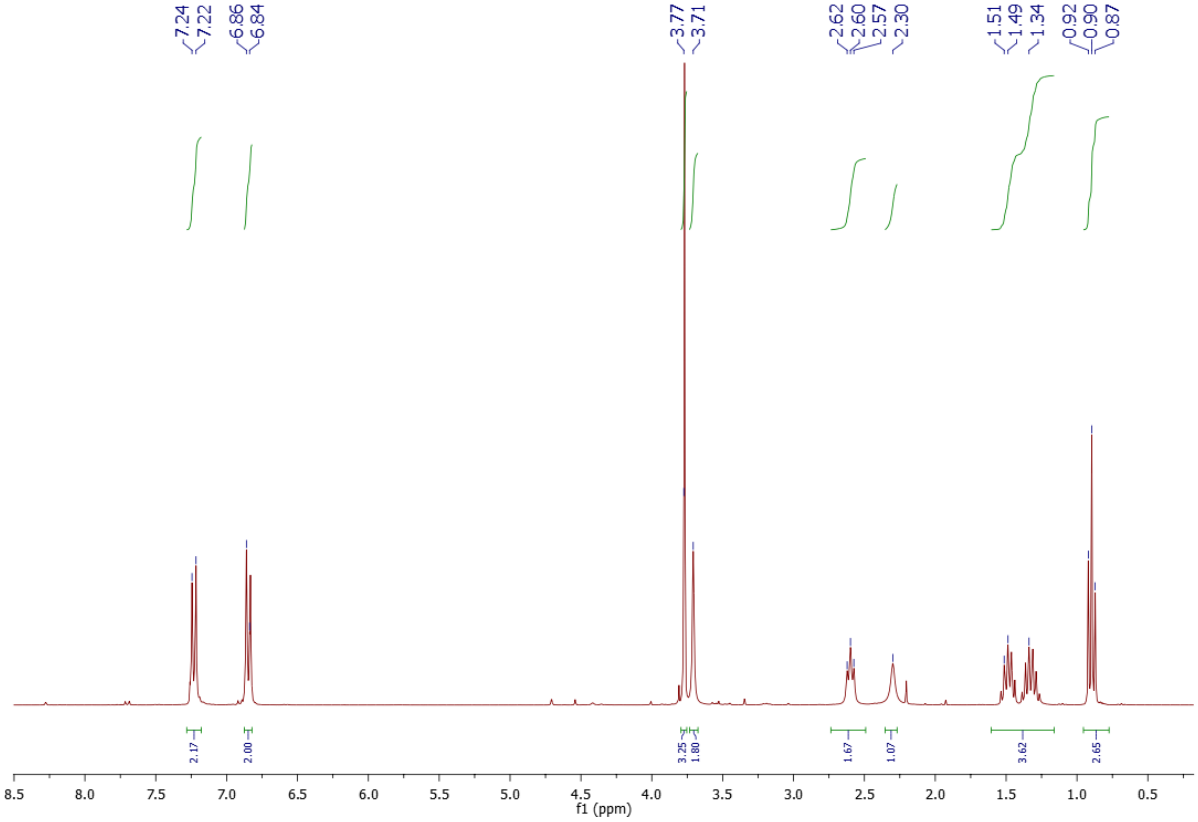
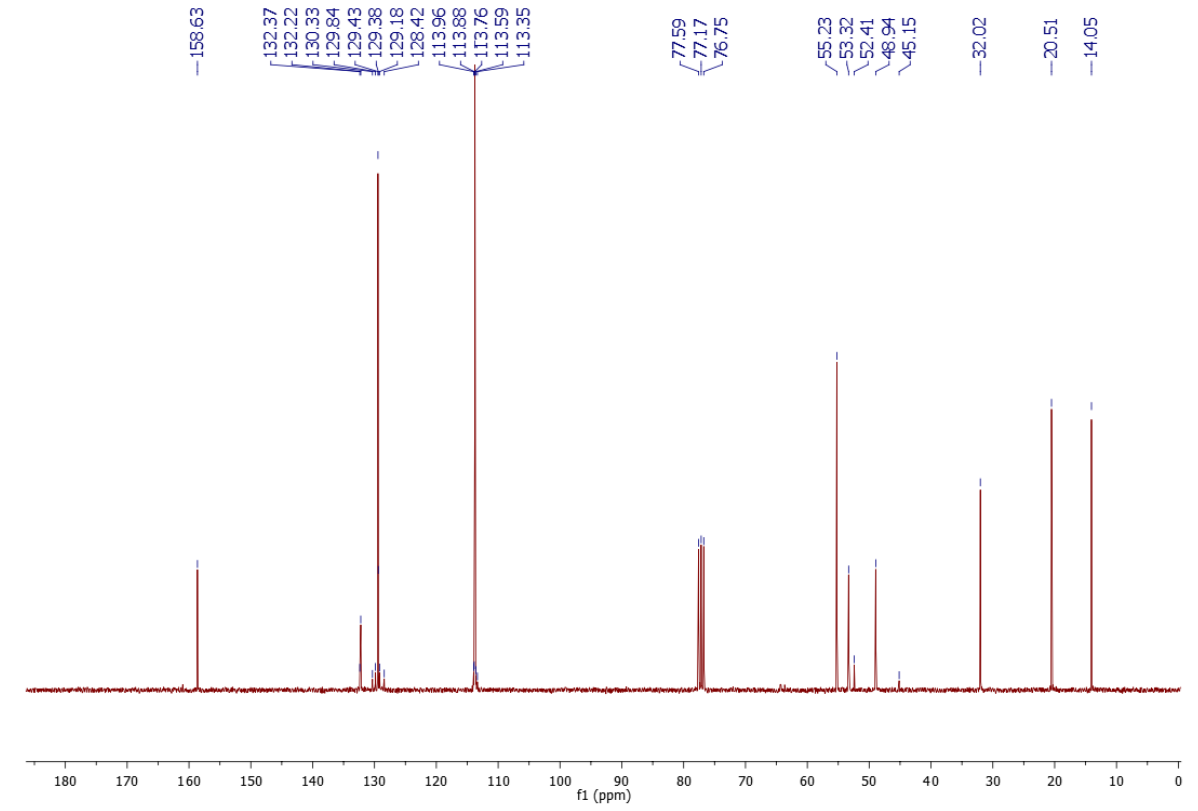
1.77
1.56
1.29
0.92
5.95
1.93
1.95
1.18
4.08
3.00
f1 (ppm)
140.36
128.42
128.20
126.98
126.94
77.51
77.09
76.66
54.06
53.18
49.16
32.18
20.52
14.07
f1 (ppm)




7.24
7.22
6.86
6.84
3.77
3.71
2.62
2.60
2.57
2.30
1.51
1.49
1.34
0.92
0.90
0.87
2.17
2.00
3.25
1.80
1.67
1.07
3.62
2.65
f1 (ppm)


158.63
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132.22
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129.84
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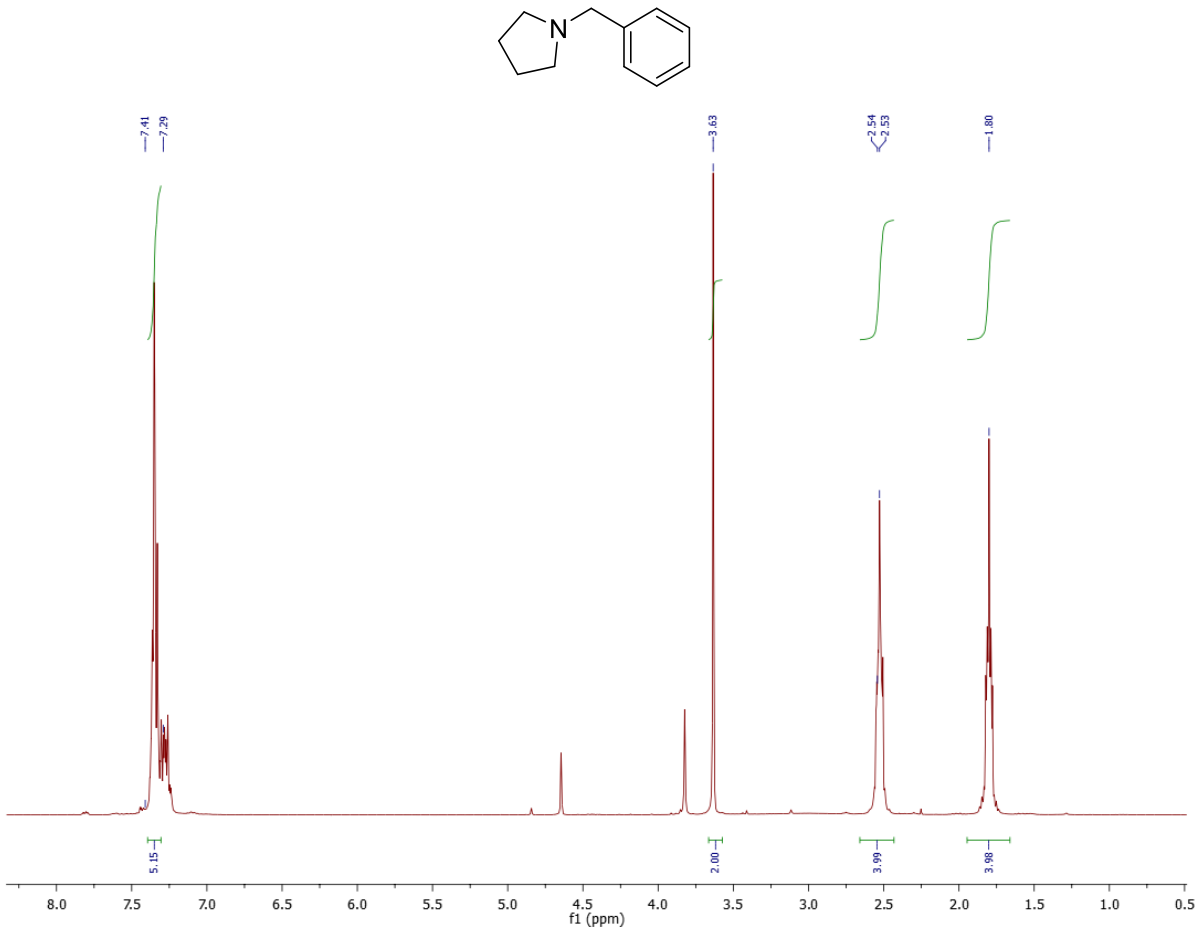
129.18
128.42
113.96
113.88
113.76
113.59
113.35
77.59
77.17
76.75
55.23
53.32
52.41
48.94
45.15
32.02
20.51
14.05
f1 (ppm)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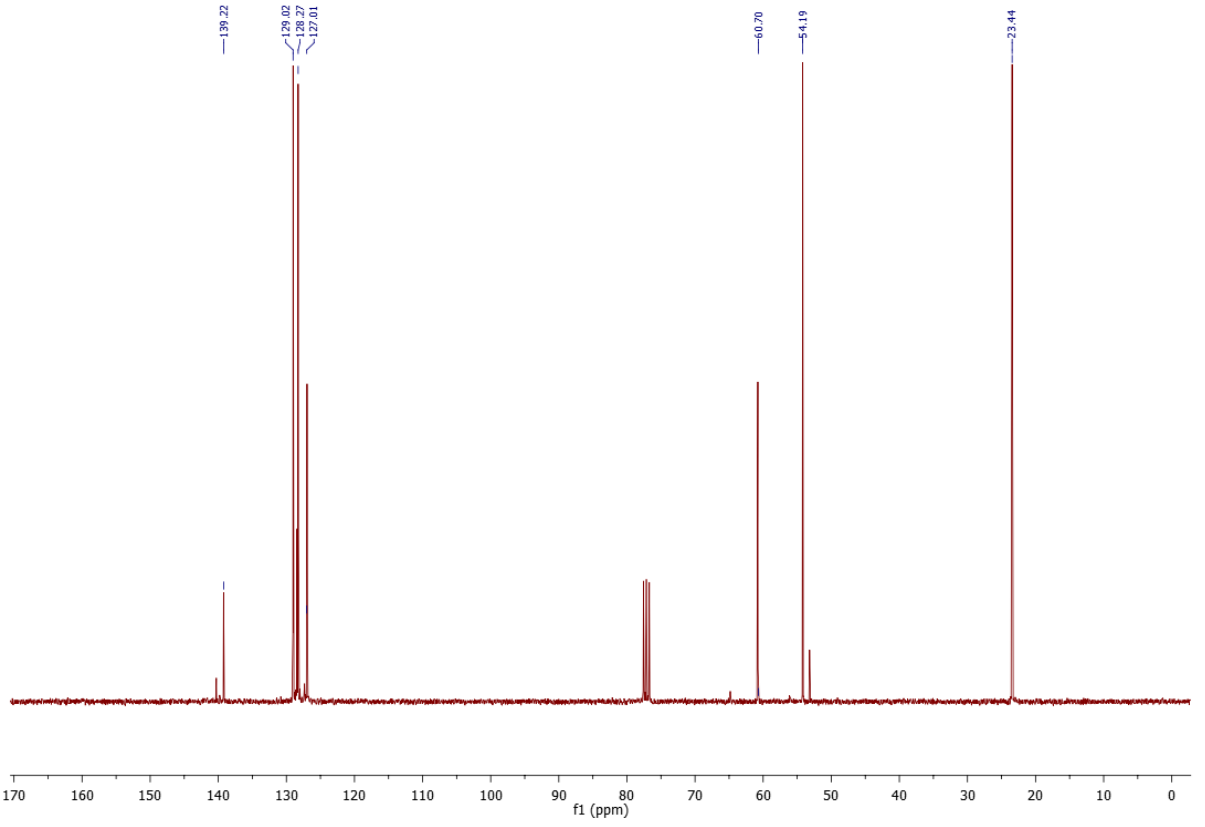
7.29
3.63
2.54
2.53
1.80
5.15
2.00
3.99
3.88
f1 (ppm)


139.22
129.02
128.27
127.01
60.70
54.19
23.44
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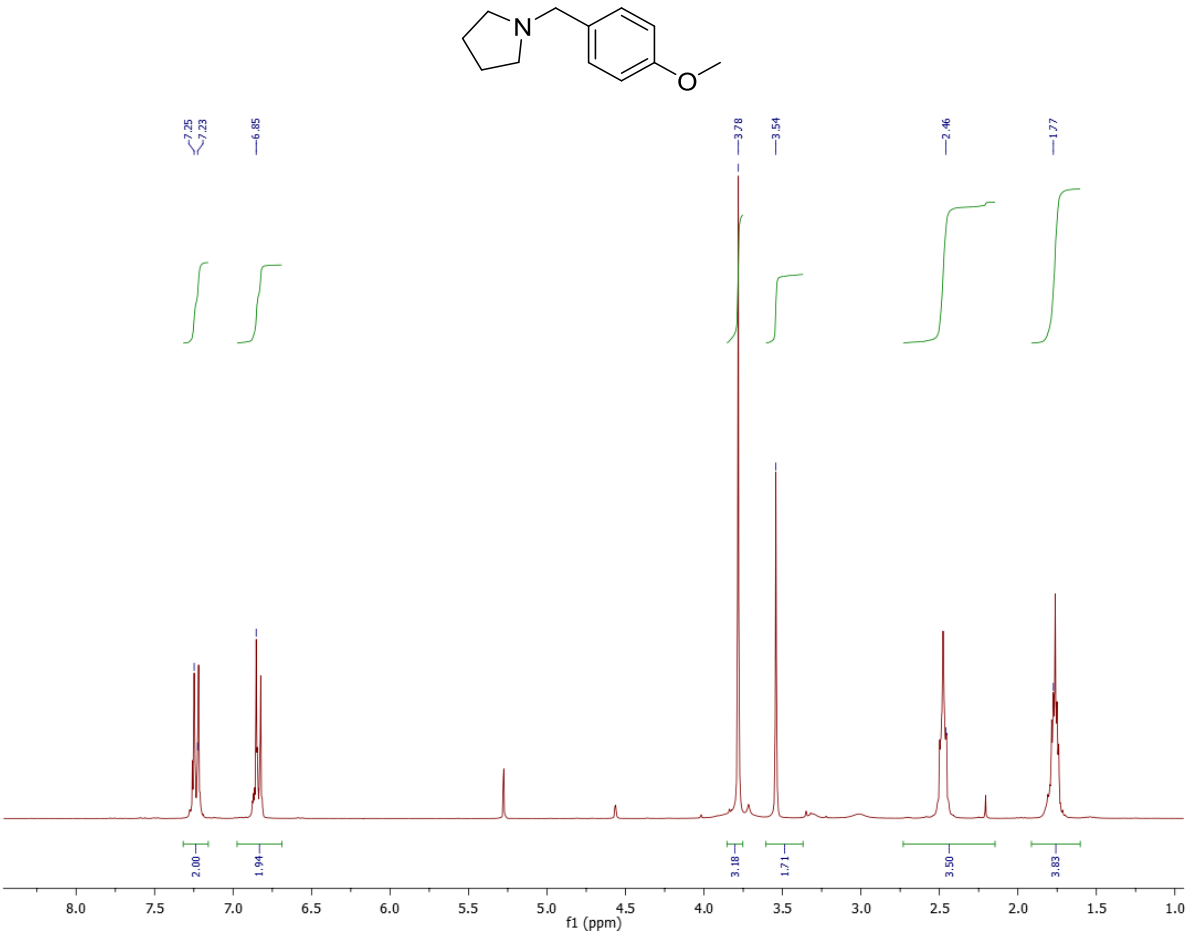
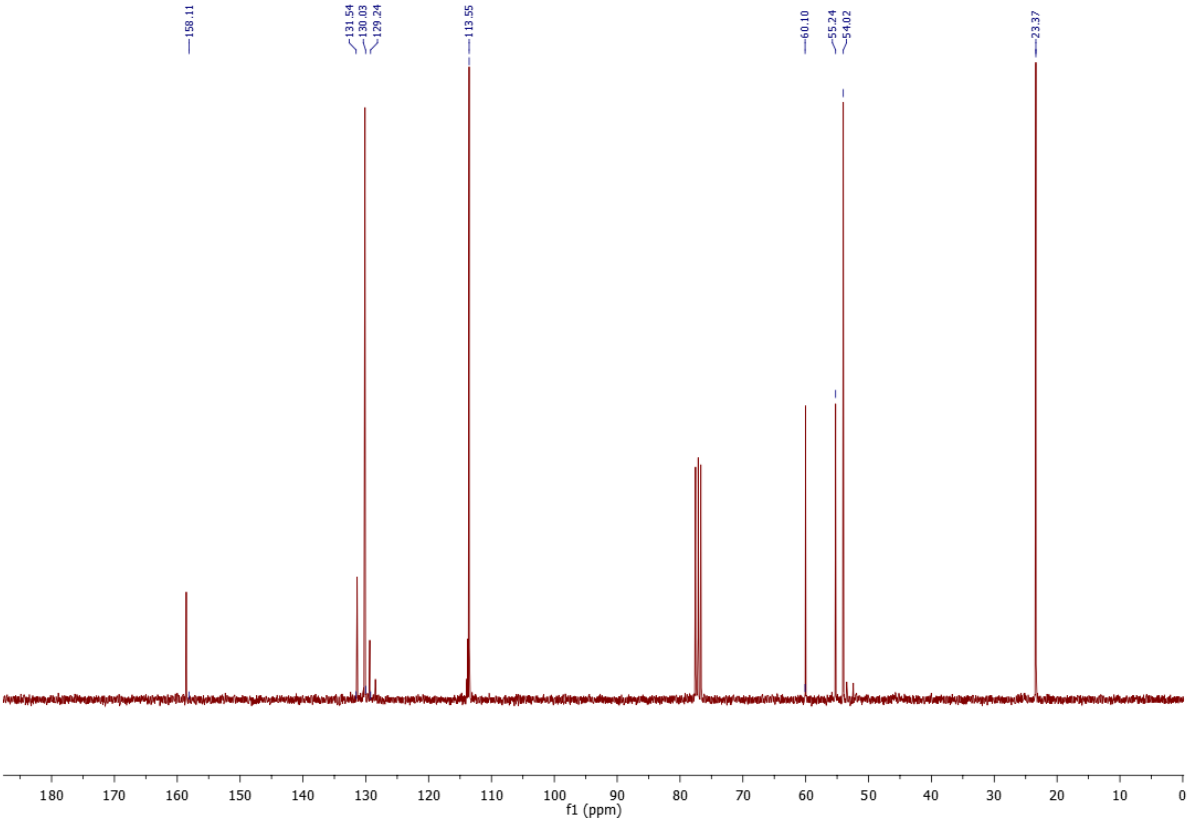
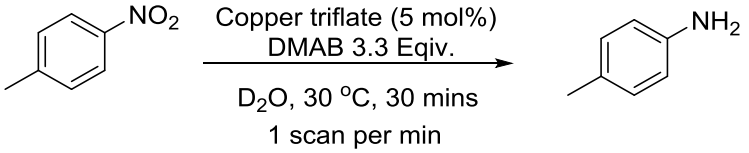

7.25
7.23
6.85
3.78
3.54
2.46
1.77
2.00
1.94
3.18
1.71
3.50
3.83
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


158.11
131.54
130.03
129.24
113.55
60.10
55.24
54.02
23.37
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Details for the mechanistic NMR experiment:



Relative ratios of the three components as judged by ^{1}H NMR.

Time (min)	% Starting Material	% Intermediate	% Product
1	100	0	0
2	100	0	0
3	100	0	0
4	100	0	0
5	100	0	0
6	100	0	0
7	100	0	0
8	100	0	0
9	100	0	0
10	100	0	0
11	100	0	0
12	100	0	0
13	81	19	0
14	62	38	0
15	60	40	0
16	60	40	0
17	63	37	0
18	63	37	0
19	58	0	42
20	0	0	100
21	0	0	100
22	0	0	100
23	0	0	100
24	0	0	100
25	0	0	100
26	0	0	100

References:

1 T. Nixon, M. K. Whittlesey, J.M.J. Williams, *Tetrahedron Lett.,* 2011, **52,** 6652.

2 S. Abbina, S. Bian, C. Oian, G. Du., *ACS Catal.* 2013, **3,** 678.

3 T. Gieshoff, A. Welther, M. Kessler, M. Prechtl, A. Jacobi von Wangelin., *Chem. Commun.,* 2014, **50,** 2261.

4 C-C, Tai, M-S. Yu, Y-L. Chen, W-H. Chuang, T_H. Lin, G. Yap, T-G. Ong, Tiow-Gan,, *Chem. Commun.*, 2014, **50,** 4344.

5 S. Sharma, J. Lynch, A. Sobolewska, P. Plucinski, R. Watson, J.M.J. Williams., *Catal. Sci. Technol.* 2013, **3,** 85.

6 A. Volkov, E. Buitrago, H. Adolfsson., *Eur. J. Org. Chem.* 2013, **11,** 2066

7 G. Molander, P. Gormisky, D. Sandrock., *J. Org. Chem.,* 2008, **73,** 2052.

8 C-Y. Tsai, R. Sung ,B.R. Zhuang, K. Sung, *Tetrahedron*, 2010, **66,** 6869.