Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Hydrogenation of Functionalised Pyridines with a Rhodium Oxide Catalyst under Mild Conditions

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1. General Information

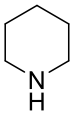
Chemicals were purchased from Sigma-Aldrich, Alfa Aesar or Fluorochem and used without further purification. NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer with TMS as the internal standard. The hydrogenation reactions were carried out using 12 mL glass vials provided by Kimble in a Parr autoclave (Figure 1). For the volatile compounds, the yields have been calculated using NMR and an internal standard. For the reactions that appear to have completed based on NMR analysis, the yield is recorded as >99%. In the cases where there are diastereoisomers present, the analytical data corresponds to the major isomer, unless stated otherwise. For compounds with lower than 30% yield (i.e. **2r, 6f, 10a, 10b** and **12a**), the NMR yield was calculated from the amount of starting material that remained and the product was assigned tentatively based on the NMR spectra and comparison with the literature. All of the NMR spectra can be found in Section 4.

2. General Procedure

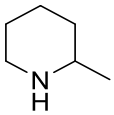
Pyridine (0.79 mmol., 1 eq.) and rhodium (iii) oxide (1.0 mg, 0.5 mol%) were added to a glass vial equipped with a stirrer bar. Trifluoroethanol (1 mL) was added and the mixture was briefly flushed with nitrogen. The sample vial was added to an autoclave and purged with hydrogen three times. Once the autoclave had been charged with hydrogen (5 bar), the reaction mixture was heated to 40 ^{o}C and stirred for the allocated amount of time. Thereafter the autoclave was removed from the heat source and the pressure carefully released in a fumehood once at room temperature. An internal standard (1,3,5-trimethoxybenzene, 0.33 equiv. or maleic acid, 0.50 equiv.) was added to the crude mixture, which was then partially concentrated *in vacuo*. The NMR solvent was added to the mixture and filtered through celite prior to analysis. For isolated compounds, no internal standard was added and the reaction mixture was filtered through celite prior to removing the solvent. There was no requirment for further purification.

Figure 1 - Hydrogenation reaction setup

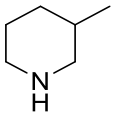
3. Analytical Data



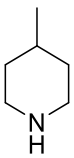
Piperidine (2a)[1,2]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80 – 2.71 (broad m, 4H), 1.61 – 1.43 (broad m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.23, 26.10, 24.15. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



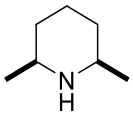
2-Methylpiperidine (2b)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 (broad d, *J* = 12.7 Hz, 1H), 2.67 – 2.51 (broad m, 2H), 1.83 – 1.74 (broad m, 1H), 1.70 – 1.55 (m, 2H), 1.44 – 1.27 (m, 2H), 1.12 – 0.99 (m, 1H overlapped), 1.05 (d, *J* = 6.3 Hz, 3H overlapped). ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.03, 46.16, 33.84, 25.24, 24.07, 21.77. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

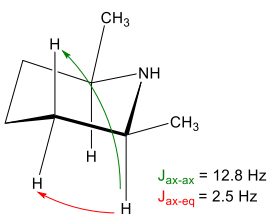


3-Methylpiperidine (2c)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 – 2.88 (broad m, 2H), 2.46 (td, *J* = 12.4, 2.9 Hz, 1H), 2.15 (dd, J = 12.0 Hz, 1H), 1.82 – 1.73 (broad m, 1H), 1.70 – 1.62 (m, 1H), 1.57 – 1.36 (m, 2H), 1.08 – 0.97 (m, 1H), 0.83 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 53.53, 45.83, 32.97, 31.77, 26.06, 19.40. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

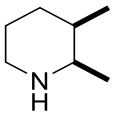


4-Methylpiperidine (2d)[1,3]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (broad d, *J* = 12.6 Hz, 2H), 2.54 (broad t, *J* = 12.4 Hz, 2H), 1.64 (broad d, *J* = 13.2 Hz, 2H), 1.56 – 1.41 (broad m, 1H), 1.12 – 0.98 (m, 2H), 0.91 (d, *J* = 6.5 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 45.82, 34.63, 30.66, 22.06. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

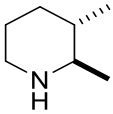




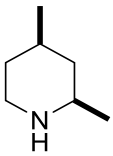
***cis*-2,6-Dimethylpiperidine (2e)**[1,3,4]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (dqd, *J* = 12.8, 6.4, 2.5 Hz, 2H), 1.81 – 1.70 (m, 1H), 1.63 – 1.56 (m, 2H), 1.36 (qt, *J* = 13.2, 3.9 Hz, 1H), 1.05 (d, *J* = 6.4 Hz, 6H overlapped), 1.11 – 0.91 (m, 2H overlapped). ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.38, 33.04, 24.06, 21.57. 97% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



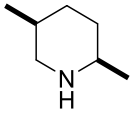
***cis*-2,3-Dimethylpiperidine (*cis* 2f)**[5,6]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 – 2.84 (m, 2H), 2.65 – 2.54 (m, 1H overlapped with minor isomer), 1.79 – 1.69 (m, 1H), 1.62 – 1.47 (m, 3H overlapped with minor isomer), 1.43 – 1.34 (m, 1H overlapped with minor isomer), 1.00 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 7.1 Hz, 3H overlapped with minor isomer). ^{13}C NMR (101 MHz, $CDCl_3$) δ 53.15, 43.36, 32.63, 29.39, 21.96, 16.02, 13.34. 86% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

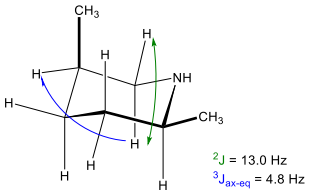


***trans*-2,3-Dimethylpiperidine (*trans* 2f)**[5,6]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (ddt, *J* = 12.4, 4.0, 2.0 Hz, 1H), 2.65 – 2.53 (m, 1H overlapped with major isomer), 2.24 – 2.15 (m, 1H), 1.79 – 1.69 (m, 1H overalapped with major isomer), 1.69 – 1.60 (m, 2H), 1.47 – 1.43 (m, 1H), 1.43 – 1.34 (m, 1H overlapped with major isomer), 1.06 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 7.1 Hz, 3H overlapped with major isomer). ^{13}C NMR (101 MHz, $CDCl_3$) δ 58.16, 46.21, 38.05, 33.17, 26.06, 19.36, 18.57. 14% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

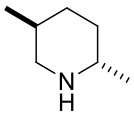


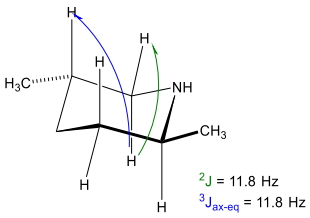
***cis*–2,4-Dimethylpiperidine (2g)**[5]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (ddd, *J* = 12.5, 4.1, 2.2 Hz, 1H), 2.63 – 2.52 (m, 1H overlapped), 2.56 (td, *J* = 12.6, 2.7 Hz, 1H overlapped), 1.67 – 1.54 (m, 2H), 1.52 – 1.38 (m, 1H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.95 (dd, *J* = 11.8, 4.5 Hz, 1H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.74 – 0.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 51.90, 46.15, 42.89, 34.07, 30.99, 22.14, 22.07. 87% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). The *trans* product was assigned (13%) based on the literature.[5]



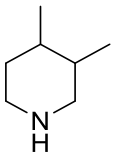


***cis*-2,5-Dimethylpiperidine (*cis* 2h)**[5,7]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 – 2.71 (m, 2H), 2.62 (dd, *J* = 13.0, 4.8 Hz, 1H), 1.72 – 1.64 (m, 1H overlapped with minor isomer), 1.64 – 1.57 (m, 1H), 1.57 – 1.48 (m, 1H), 1.49 – 1.37 (m, 1H overlapped with minor isomer), 1.39 – 1.26 (m, 1H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 53.75, 51.70, 34.13, 29.42, 28.81, 21.83, 19.11. 60% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). ^{13}C NMR tentatively assigned using literature.[5]

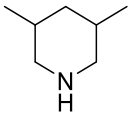




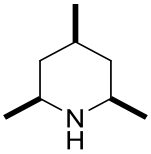
***trans*-2,5-Dimethylpiperidine (*trans* 2h)** [5,7]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.93 (ddd, *J* = 12.3, 3.7, 2.1 Hz, 1H), 2.58 – 2.48 (m, 1H), 2.20 (broad t, *J* = 11.8 Hz, 1H), 1.80 – 1.72 (m, 1H), 1.72 – 1.64 (m, 1H overlapped with major isomer), 1.49 – 1.37 (m, 1H overlapped with major isomer), 1.16 – 1.06 (m, 1H), 1.08 – 1.01 (m, 1H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 50.04, 49.54, 33.19, 31.20, 28.29, 20.11, 17.24. 40% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). ^{13}C NMR tentatively assigned using literature.[5]

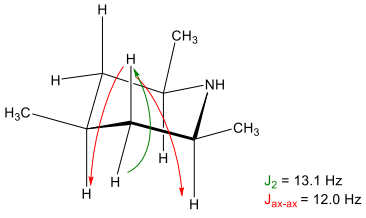


3,4-Dimethylpiperidine (2i): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 – 2.82 (broad m, 1H), 2.74 – 2.57 (broad m, 2H), 1.85 – 1.67 (broad m, 2H), 1.58 – 1.45 (m, 1H), 1.44 – 1.33 (m, 1H), 1.11 – 1.04 (m, 1H), 0.89 (d, *J* = 7.1 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H). ~6% NMR yield calculated from the remaining starting material, product assigned tentatively based on the chemical shift, splitting and integration.

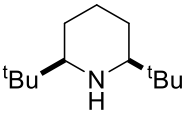


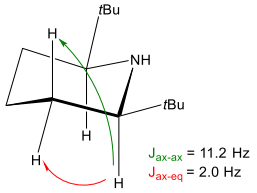
3,5-Dimethylpiperidine (2j)[2,8]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92 (broad d, *J* = 12.0 Hz, 2H), 2.05 (broad t, *J* = 11.8 Hz, 2H), 1.76 (broad d, *J* = 13.1 Hz, 1H), 1.62 – 1.45 (broad m, 2H), 0.83 (d, *J* = 6.5 Hz, 6H), 0.66 (broad q, *J* = 12.0 Hz, 1H).<7% NMR yield calculated from the remaining starting material, product assigned tentatively based on the chemical shift, splitting,integration and literature.[2,8]



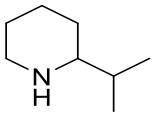


***cis*-2,4,6-Trimethylpiperidine (2k)**[7]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.73 – 2.60 (broad m, 2H), 1.58 (broad d, *J* = 13.1 Hz, 2H), 1.51 – 1.39 (broad m, 1H), 1.02 (d, *J* = 6.4 Hz, 6H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.61 (q, *J* = 12.0 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 51.88, 41.99, 30.81, 21.70, 21.59. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

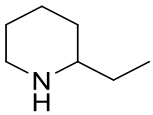




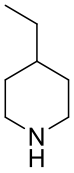
***cis*-2,6-Di-*tert*-butylpiperidine (2m)**[7]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (dd, *J* = 11.2, 2.0 Hz, 2H), 1.94 – 1.86 (m, 1H), 1.73 – 1.60 (m, 2H), 1.32 (qt, *J* = 13.0, 4.0 Hz, 1H), 1.13 – 0.99 (m, 2H), 0.91 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 68.50, 33.41, 26.34, 26.27, 25.50. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



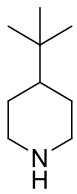
2-Isopropylpiperidine (2n)[9]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.09 – 2.97 (broad m, 1H), 2.56 (td, *J* = 12.0, 2.9 Hz, 1H), 2.17 (ddd, *J* = 11.0, 6.6, 2.5 Hz, 1H), 1.85 – 1.75 (broad m, 1H), 1.73 – 1.66 (broad m, 1H), 1.63 – 1.48 (m, 2H), 1.41 – 1.24 (m, 2H), 1.11 – 0.99 (m, 1H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 62.75, 46.87, 32.61, 28.37, 25.66, 24.43, 18.96, 18.25. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



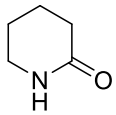
2-Ethylpiperidine (2p)[6]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 (broad d, *J* = 11.7 Hz, 1H), 2.63 – 2.53 (brm, 1H), 2.39 – 2.27 (m, 1H), 1.83 – 1.65 (m, 2H), 1.63 – 1.53 (m, 1H), 1.42 – 1.23 (m, 4H), 1.08 – 0.96 (m, 1H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 58.21, 46.54, 31.48, 29.35, 25.74, 24.26, 9.92. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



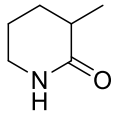
4-Ethylpiperidine (2q)[10]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 (broad d, *J* = 12.7 Hz, 2H), 2.56 (broad t, *J* = 12.4 Hz, 2H), 1.74 (broad d, *J* = 13.4 Hz, 2H), 1.31 – 1.18 (broad m, 3H), 1.11 – 0.98 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 45.57, 37.09, 31.98, 29.27, 10.50. 98% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



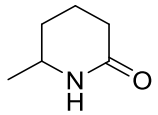
4-*tert*-Butylpiperidine (2r)[11]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.07 (broad d, *J* = 11.7 Hz, 2H), 2.50 (broad t, *J* = 11.5 Hz, 2H), 1.72 – 1.64 (broad m, 2H), 1.15 – 1.09 (broad m, 2H), 1.05 – 1.00 (broad m, 1H), 0.82 (s, 9H). 11% NMR yield calculated from the remaining starting material, product assigned tentatively based on the chemical shift, splitting, integration and literature.[11]



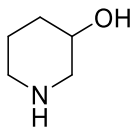
2-Piperidone (4a)[8,12]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (bs, 1H) 3.30 – 3.22 (broad m, 2H), 2.34 – 2.25 (broad m, 2H), 1.81 – 1.66 (broad m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.55, 42.04, 31.03, 21.92, 20.48. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



3-Methylpiperidin-2-one (4b)[13]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (bs, 1H), 3.35 – 3.24 (m, 2H), 2.50 – 2.29 (m, 1H), 2.01 – 1.91 (m, 1H), 1.90 – 1.80 (m, 1H), 1.79 – 1.65 (m, 1H), 1.56 – 1.42 (m, 1H), 1.23 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.89, 42.58, 35.99, 29.23, 21.35, 17.47. HRMS: Calculated $[M+H]^+$ 114.0913; found $[M+H]^+$ 114.0914. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). 93% isolated yield.

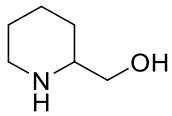


6-Methylpiperidin-2-one (4c)[12]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (bs, 1H), 3.49 – 3.39 (broad m, 1H), 2.34 – 2.12 (broad m, 2H), 1.90 – 1.77 (broad m, 2H), 1.71 – 1.55 (broad m, 1H), 1.35 – 1.22 (m, 1H), 1.12 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.56, 48.92, 30.08, 29.64, 21.76, 18.92. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

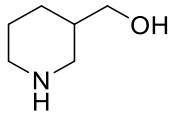


3-Hydroxypiperidine (4d)[14]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 – 3.62 (broad m, 1H), 2.97 – 2.87 (broad m, 1H), 2.80 – 2.70 (broad m, 1H), 2.69 – 2.60 (broad m, 1H), 2.60 – 2.52 (m, 1H), 1.93 – 1.81 (broad m, 1H), 1.81 – 1.70 (broad m, 1H), 1.56 – 1.36 (broad m, 2H). ^{13}C

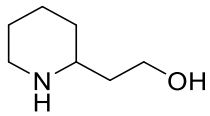
NMR (101 MHz, $CDCl_3$) δ 66.13, 52.39, 45.49, 32.34, 23.13. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



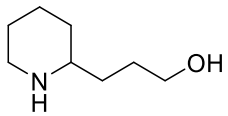
Piperidin-2-ylmethanol (4e)[15–18]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 – 3.48 (m, 1H), 3.44 – 3.30 (m, 1H), 3.04 (broad d, *J* = 11.4 Hz, 1H), 2.69 – 2.50 (broad m, 2H), 1.86 – 1.73 (broad m, 1H), 1.68 – 1.47 (m, 2H), 1.46 – 1.27 (m, 2H), 1.18 – 1.02 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 65.70, 57.60, 45.64, 27.37, 25.18, 23.42. 76% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



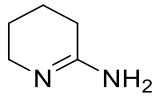
Piperidin-3-ylmethanol (4f)[19]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 – 3.38 (m, 1H), 3.36 – 3.29 (m, 1H), 3.06 (broad d, *J* = 12.0 Hz, 1H), 2.94 (broad d, *J* = 12.2 Hz, 1H), 2.52 – 2.42 (broad m, 1H), 2.24 (broad t, *J* = 11.5 Hz, 1H), 1.79 – 1.54 (broad m, 3H), 1.50 – 1.35 (broad m, 1H), 1.11 – 0.98 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 65.44, 48.37, 45.61, 38.69, 26.61, 24.76. 86% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



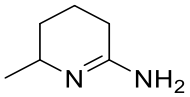
2-Piperidineethanol (4g)[20]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 – 3.59 (m, 2H overlapped with internal standard), 2.97 (broad d, *J* = 12.4 Hz, 1H), 2.70 – 2.60 (broad m, 1H), 2.60 – 2.50 (m, 1H), 1.81 – 1.71 (broad m, 1H), 1.66 – 1.50 (m, 4H), 1.43 – 1.25 (m, 2H), 1.20 – 1.04 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 60.37, 55.84, 46.02, 37.53, 31.75, 25.29, 23.88. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



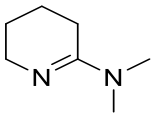
3-(Piperidin-2-yl)propan-1-ol (4h)[21,22]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 – 3.44 (m, 2H), 2.99 (broad d, *J* = 12.5 Hz, 1H), 2.55 (broad t, *J* = 11.9 Hz, 1H), 2.46 – 2.37 (broad m, 1H), 1.82 – 1.74 (broad m, 1H), 1.71 – 1.63 (broad m, 1H), 1.63 – 1.55 (broad m, 2H), 1.55 – 1.39 (m, 2H), 1.39 – 1.22 (m, 3H), 1.13 – 1.00 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 62.27, 56.48, 46.03, 34.04, 32.11, 29.13, 25.68, 24.10. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



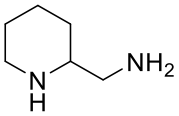
3,4,5,6-Tetrahydropyridin-2-amine (6a)[23]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 – 3.21 (broad m, 2H), 2.34 – 2.26 (broad m, 2H), 1.78 – 1.59 (broad m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.98, 42.78, 26.40, 21.25, 18.88. 83% NMR yield (5 hours) and 65% NMR yield (16 hours) using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



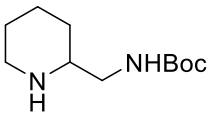
6-Methyl-3,4,5,6-tetrahydropyridin-2-amine (6b)[24]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 – 3.39 (broad m, 1H), 2.49 – 2.28 (m, 2H), 1.95 – 1.80 (broad m, 2H), 1.72 – 1.57 (broad m, 1H), 1.39 – 1.25 (m, 1H), 1.21 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.36, 48.85, 28.55, 25.63, 20.76, 16.87. 73% NMR yield (5 hours) and 62% NMR yield (16 hours) using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



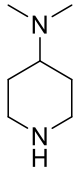
***N,N*-Dimethyl-3,4,5,6-tetrahydropyridin-2-amine (6c)**[25]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 – 3.28 (broad m, 2H), 2.87 (s, 6H), 2.38 – 2.18 (broad m, 2H), 1.75 – 1.66 (broad m, 2H). 1.60 – 1.48 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.29, 42.44, 36.31, 25.12, 19.70, 17.86. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



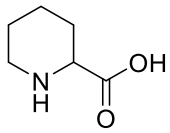
Piperidin-2-ylmethanamine (6d) [26]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.02 (broad d, *J* = 11.3 Hz, 1H), 2.67 – 2.61 (m, 1H), 2.61 – 2.48 (m, 2H), 2.48 – 2.40 (m, 1H), 1.82 – 1.73 (broad m, 1H), 1.64 – 1.54 (m, 2H), 1.42 – 1.28 (m, 2H), 1.11 – 0.98 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 58.33, 46.69, 46.28, 29.51, 25.59, 23.78. 55% NMR yield calculated from the remaining startingra material, product assigned tentatively based on the chemical shift, splitting,integration and literature.[27]



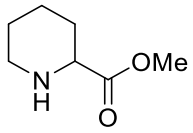
***tert*-Butyl (piperidin-2-ylmethyl)carbamate (6e)**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (bs, 1H), 3.18 – 3.07 (m, 1H), 3.06 – 2.98 (m, 1H), 2.93 – 2.84 (m 1H), 2.64 – 2.52 (m, 2H), 1.95 (bs, 1H), 1.80 – 1.69 (broad m, 1H), 1.62 – 1.51 (m, 2H), 1.40 (s, 9H overlapped), 1.44 – 1.28 (m, 2H overlapped), 1.10 – 0.98 (m, 1H). ^{13}C NMR (101 MHz, MeOD) δ 157.10, 78.62, 56.33, 45.98, 45.59, 29.39, 27.42, 25.36, 23.90. HRMS: Calculated $[M+H]^+$ 215.1754; found $[M+H]^+$ 215.1754. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). 72% isolated yield.



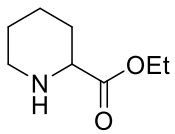
***N,N*-Dimethylpiperidin-4-amine (6f)[1]:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (broad d, *J* = 12.9 Hz, 2H), 2.53 (broad t, *J* = 12.5 Hz, 2H), 2.32 – 2.12 (m, 1H overlapped), 2.24 (s, 6H overlapped), 1.85 (broad d, *J* = 12.7 Hz, 2H), 1.39 – 1.25 (m, 2H). 17% NMR yield calculated from the remaining starting material, product assigned tentatively based on the chemical shift, splitting, integration and literature.[1]



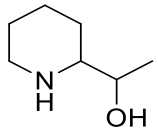
Piperidine-2-carboxylic acid (8a)[28]: ^{1}H NMR (400 MHz, MeOD) δ 3.27 (broad d, *J* = 10.8 Hz, 1H), 3.16 (broad d, *J* = 13.3 Hz, 1H), 2.78 (broad t, *J* = 11.9 Hz, 1H), 2.06 (broad d, *J* = 13.6 Hz, 1H), 1.77 – 1.58 (broad m, 2H), 1.58 – 1.33 (m, 3H). ^{13}C NMR (101 MHz, MeOD) δ 174.34, 60.54, 44.74, 28.13, 23.60, 23.21. HRMS: Calculated $[M+H]^+$ 130.0863; found $[M+H]^+$ 130.0863. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). 95% isolated yield.



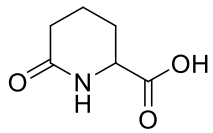
Methyl piperidine-2-carboxylate (8b)[29]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.41 – 3.29 (broad m, 1H), 3.08 – 2.98 (broad m, 1H), 2.67 – 2.56 (broad m, 1H), 2.06 – 1.93 (broad m, 1H), 1.85 – 1.73 (broad m, 1H), 1.67 – 1.55 (broad m, 1H), 1.54 – 1.32 (broad m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.16, 57.88, 51.78, 44.67, 28.47, 24.56, 23.05. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



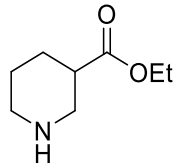
Ethyl piperidine-2-carboxylate (8c)[30]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (q, *J* = 7.0 Hz, 2H), 3.32 – 3.22 (broad m, 1H), 3.07 – 2.95 (broad m, 1H), 2.65 – 2.53 (broad m, 1H), 1.99 – 1.90 (broad m, 1H), 1.78 – 1.69 (broad m, 1H), 1.60 – 1.49 (broad m, 1H), 1.49 – 1.31 (m, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.13, 60.94, 58.11, 45.12, 28.79, 25.22, 23.67, 13.88. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



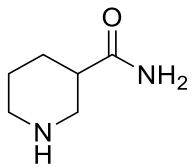
1-(Piperidin-2-yl)ethan-1-ol (8d)[31,32]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 – 3.66 (m, 1H overlapped with internal standard), 3.09 – 3.00 (broad m, 1H), 2.63 – 2.53 (m, 1H), 2.44 (broad d, *J* = 11.2 Hz, 1H), 1.88 – 1.74 (broad m, 1H), 1.68 – 1.54 (broad m, 2H), 1.42 – 1.27 (m, 2H), 1.27 – 1.15 (m, 1H), 1.15 – 1.00 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 77.27, 61.42, 46.53, 26.17, 25.41, 24.16, 18.52. >99% NMR yield (mixture of both diasterioisomers with d.r. 37:13) using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



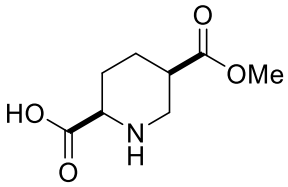
6-Oxopiperidine-2-carboxylic acid (8e)[12]: ^{1}H NMR (400 MHz, D_2O) δ 4.18 (broad t, *J* = 6.1 Hz, 1H), 2.34 – 2.27 (m, 2H), 2.13 – 2.04 (m, 1H), 1.92 – 1.83 (m, 1H), 1.79 – 1.69 (m, 2H).^{13}C NMR (101 MHz, D_2O) δ 175.71, 175.65, 54.17, 29.91, 24.40, 17.84. >99% NMR yield using internal standard (maleic acid, 0.5 eq.).

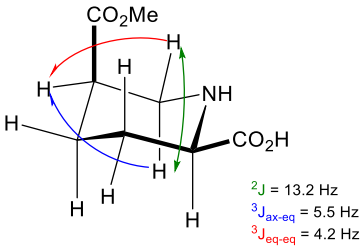


Ethyl piperidine-3-carboxylate (8f)[33]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (q, *J* = 6.9 Hz, 2H), 3.02 (broad d, *J* = 12.3 Hz, 1H), 2.87 – 2.70 (m, 2H), 2.58 (broad t, *J* = 11.2 Hz, 1H), 2.44 – 2.34 (broad m, 1H), 1.98 – 1.88 (broad m, 1H), 1.70 – 1.56 (m, 2H), 1.48 – 1.35 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.26, 60.59, 47.37, 45.57, 41.52, 26.85, 24.67, 13.96. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

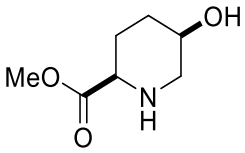


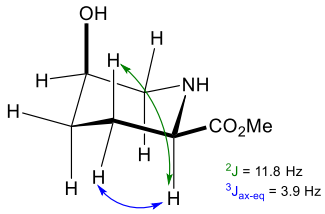
3-Piperidinecarboxamide (8g)[14]: ^{1}H NMR (400 MHz, MeOD) δ 3.05 (dd, *J* = 12.4, 3.0 Hz, 1H), 2.99 – 2.89 (m, 1H), 2.69 (dd, *J* = 12.3, 10.6 Hz, 1H), 2.57 (td, *J* = 12.1, 2.9 Hz, 1H), 2.39 (tt, *J* = 10.5, 3.7 Hz, 1H), 1.98 – 1.90 (m, 1H), 1.76 – 1.67 (m, 1H), 1.67 – 1.57 (m, 1H), 1.57 – 1.45 (m, 1H). ^{13}C NMR (101 MHz, MeOD) δ 178.52, 48.08, 45.35, 43.07, 27.63, 24.78. >99% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.). 93% isolated yield.



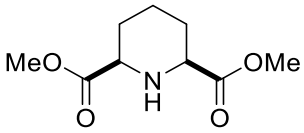


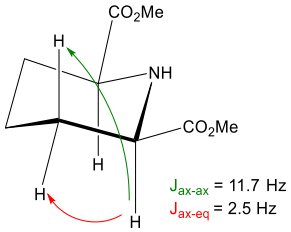
***cis*-5-(Methoxycarbonyl)piperidine-2-carboxylic acid (8h)**[34]: ^{1}H NMR (400 MHz, D_2O) δ 3.79 – 3.73 (m, 1H overlapped), 3.77 (s, 3H overlapped), 3.65 (dd, *J* = 13.2, 5.5 Hz, 1H), 3.33 (dd, *J* = 13.2, 4.2 Hz, 1H), 3.05 – 2.97 (m, 1H), 2.16 – 2.06 (m, 1H), 2.06 – 1.97 (m, 2H), 1.97 – 1.85 (m, 1H). ^{13}C NMR (101 MHz, D_2O) δ 174.61, 173.34, 57.53, 52.77, 42.79, 36.76, 23.42, 23.14. HRMS: Calculated $[M+H]^+$ 188.0917; found $[M+H]^+$ 118.0917. 92% isolated yield (mixture of both diasteriosomers with d.r. 50:7).



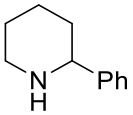


***cis*-Methyl-5-hydroxypiperidine-2-carboxylate (8i)**[35]: ^{1}H NMR (400 MHz, D_2O) δ 4.15 – 4.03 (broad m, 1H), 3.96 (dd, *J* = 11.8, 3.9 Hz, 1H), 3.71 (s, 3H), 3.31 – 3.20 (m, 1H), 3.16 – 3.08 (m, 1H), 2.14 – 1.90 (m, 2H), 1.87 – 1.66 (m, 2H). ^{13}C NMR (101 MHz, D_2O) δ 173.91, 61.39, 58.58, 58.32, 48.11, 28.16, 21.11.76% NMR yield (24 hours) using internal standard (maleic acid, 0.5 eq.).

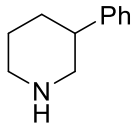




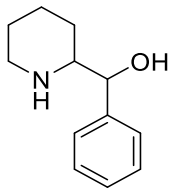
Dimethyl-piperidine-2,6-dicarboxylate (8j)[10]: ^{1}H NMR (400 MHz, MeOD) δ 3.76 (s, 6H), 3.43 (dd, *J* = 11.7, 2.5 Hz, 2H), 2.07 – 1.94 (m, 3H), 1.66 – 1.51 (m, 1H), 1.45 – 1.31 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 172.90, 57.72, 51.16, 28.01, 23.60. HRMS: Calculated $[M+H]^+$ 202.1074; found $[M+H]^+$ 202.1075. 97% isolated yield (mixture of both diasteriosomers with d.r. 100:9).



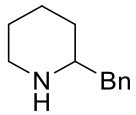
2-Phenylpiperidine (10a)[36]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.22 (m, 5H), 3.61 (broad d, *J* = 10.0 Hz, 1H), 3.19 (broad d, *J* = 11.8 Hz, 1H), 2.80 (broad t, *J* = 11.0 Hz, 1H), 2.00 – 1.50 (broad m, 6H). ~30% Yield tentatively calculated from the remaining starting material and significant peaks that correspond to the product (see Figure 83), product assigned tentatively based on the chemical shift, splitting, integration and literature.[36]



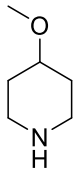
3-Phenylpiperidine (10b)[3]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.18 (m, 5H), 3.21 – 2.95 (m, 2H), 2.75 – 2.45 (m, 3H), 2.09 – 1.55 (broad m, 4H). ~17% Yield tentatively calculated from the remaining starting material and significant peaks that correspond to the product (see Figure 84), product assigned tentatively based on the chemical shift, splitting, integration and literature.[3]



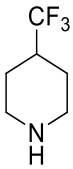
Phenyl(piperidin-2-yl)methanol (10c)[37]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.21 (m, 5H), 4.58 (d, *J* = 5.1 Hz, 1H), 3.06 – 2.88 (m, 1H), 2.75 – 2.45 (m, 2H), 1.84 – 1.73 (broad m, 1H), 1.73 – 1.63 (broad m, 1H), 1.63 – 1.51 (broad m, 1H), 1.41 – 1.11 (broad m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.70, 128.36, 127.61, 126.43, 76.11, 61.85, 46.51, 26.19, 25.84, 24.04. >99% NMR yield (mixture of both diasterioisomers with d.r. 4:1) using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



2-Benzylpiperidine (10d)[3]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.29 – 7.19 (m, 3H), 3.00 (broad d, *J* = 12.1 Hz, 1H), 2.77 – 2.68 (m, 2H), 2.67 – 2.59 (m, 1H), 2.57 – 2.49 (m, 1H), 1.86 – 1.77 (broad m, 1H), 1.77 – 1.68 (broad m, 1H), 1.66 – 1.57 (broad m, 1H), 1.52 – 1.39 (m, 1H), 1.39 – 1.31 (m, 1H), 1.31 – 1.18 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.61, 129.23, 128.54, 126.41, 58.19, 46.77, 43.21, 32.20, 25.60, 24.50. 75% NMR yield using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).



4-Methoxypiperidine (12a)[33]: ^{1}H NMR (400 MHz, chloroform-d) δ 3.36 – 3.25 (m, 1H overlapped) 3.32 (s, 3H overlapped), 3.02 (broad d, *J* = 13.0 Hz, 2H), 2.57 (broad t, *J* = 11.2 Hz, 2H), 1.91 (broad d, *J* = 10.9 Hz, 2H), 1.47 – 1.32 (broad m, 2H). 19% NMR yield (4 hours) calculated from the remaining starting material, product assigned tentatively based on the chemical shift, splitting, integration and literature.[33]



4-(Trifluoromethyl)piperidine (12b)[38]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (broad d, *J* = 13.0 Hz, 2H), 2.55 (td, *J* = 12.7, 2.5 Hz, 2H), 2.24 – 2.03 (m, 1H), 1.83 (broad d, *J* = 13.4 Hz, 2H), 1.42 (qd, *J* = 12.7, 4.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 126.94 (q, *J* = 278.0 Hz, overlapped with solvent), 44.36, 40.03 (q, *J* = 27.6 Hz), 24.78. >99% NMR yield (4 hours) using internal standard (1,3,5-trimethoxybenzene, 0.33 eq.).

4. ^{1}H and ^{13}C NMR Spectra

NMR spectra were collected of crude pruduct which contain solvent (trifluoroethanol) and internal standard (1,35-trimethoxybenzene, unless stated otherwise). These are labelled in the spectra for piperidine **2a** (Figure 1 and Figure 2) but are omitted in the rest of the spectra. Residual trifluoroethanol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.98, 3.86. ^{13}C NMR (101 MHz, $CDCl_3$) δ 124.54, 77.00. Internal Standard (1,3,5-trimethoxybenzene, 0.33 eq.): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (s, 1H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.45, 92.93, 55.18.

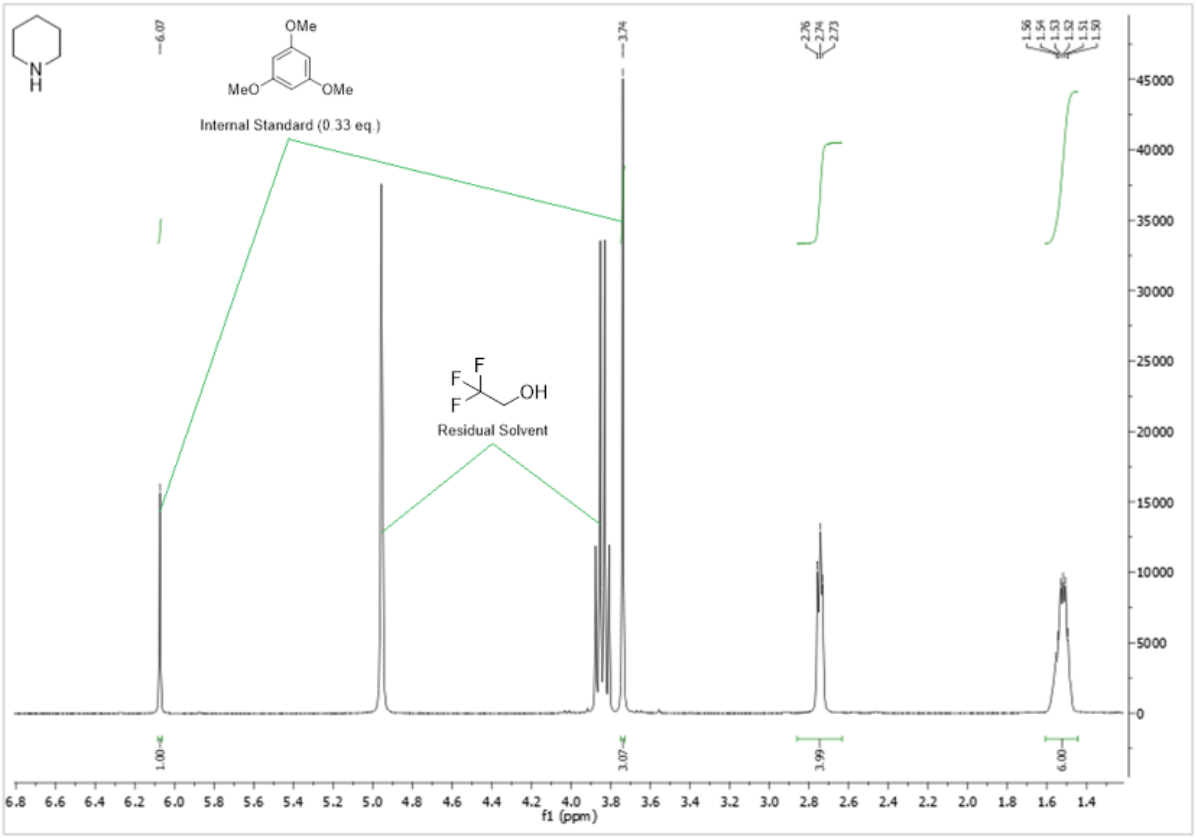


Figure 2 - ^{1}H NMR of piperidine (2a) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

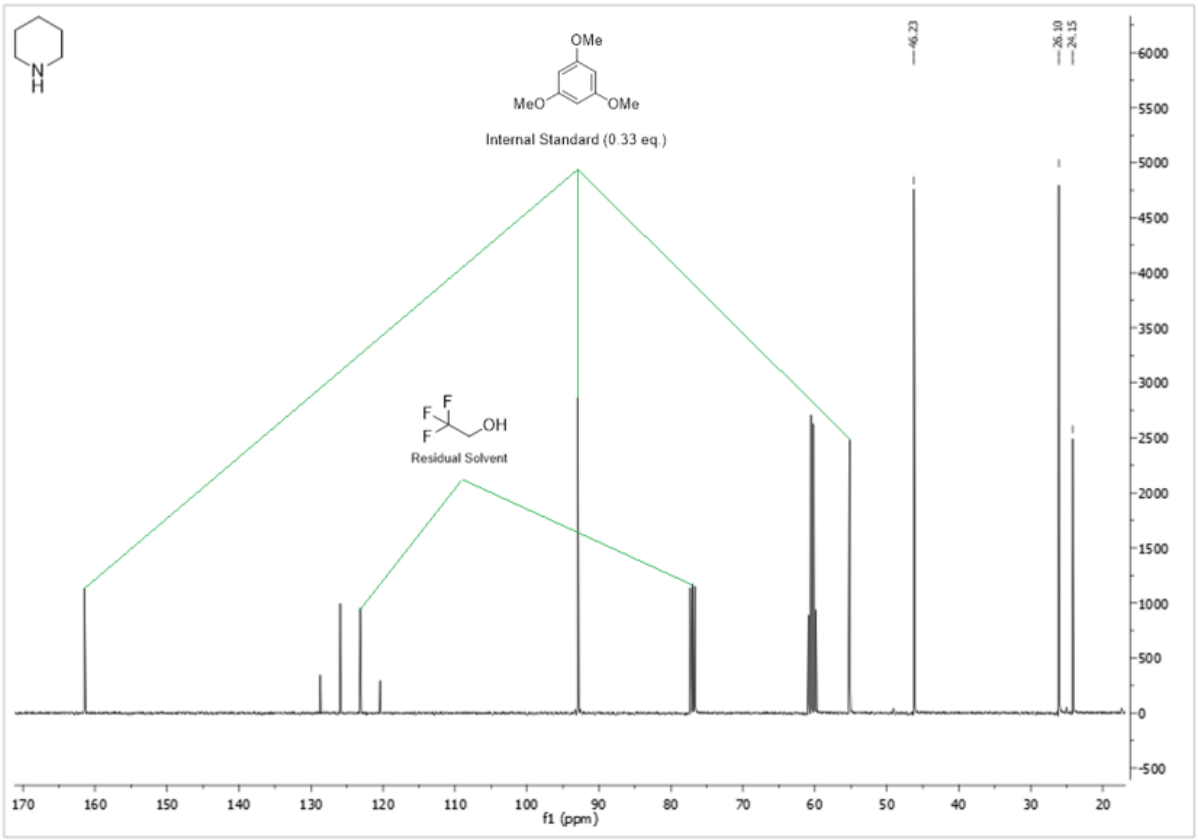


Figure 3 - ^{13}C NMR of piperidine (2a) in CDCl3. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

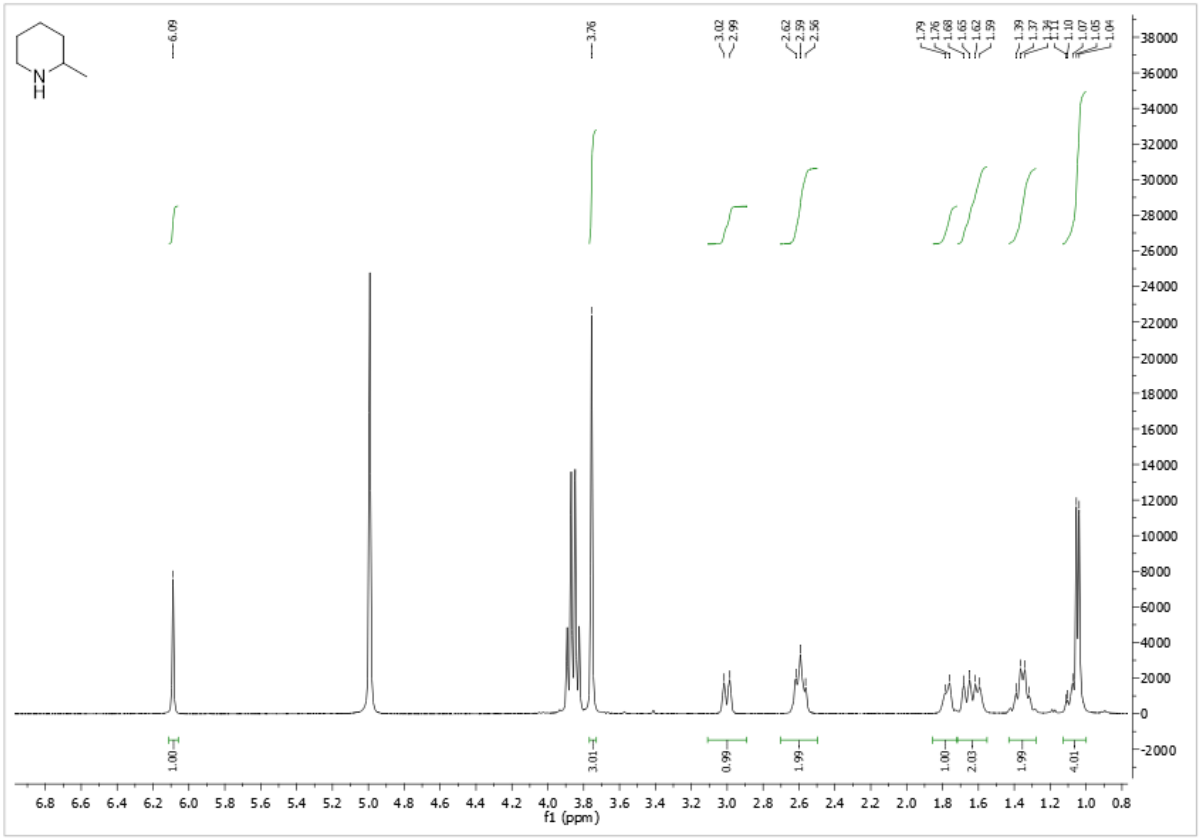


Figure 4 - ^{1}H NMR of 2- methylpiperidine (2b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

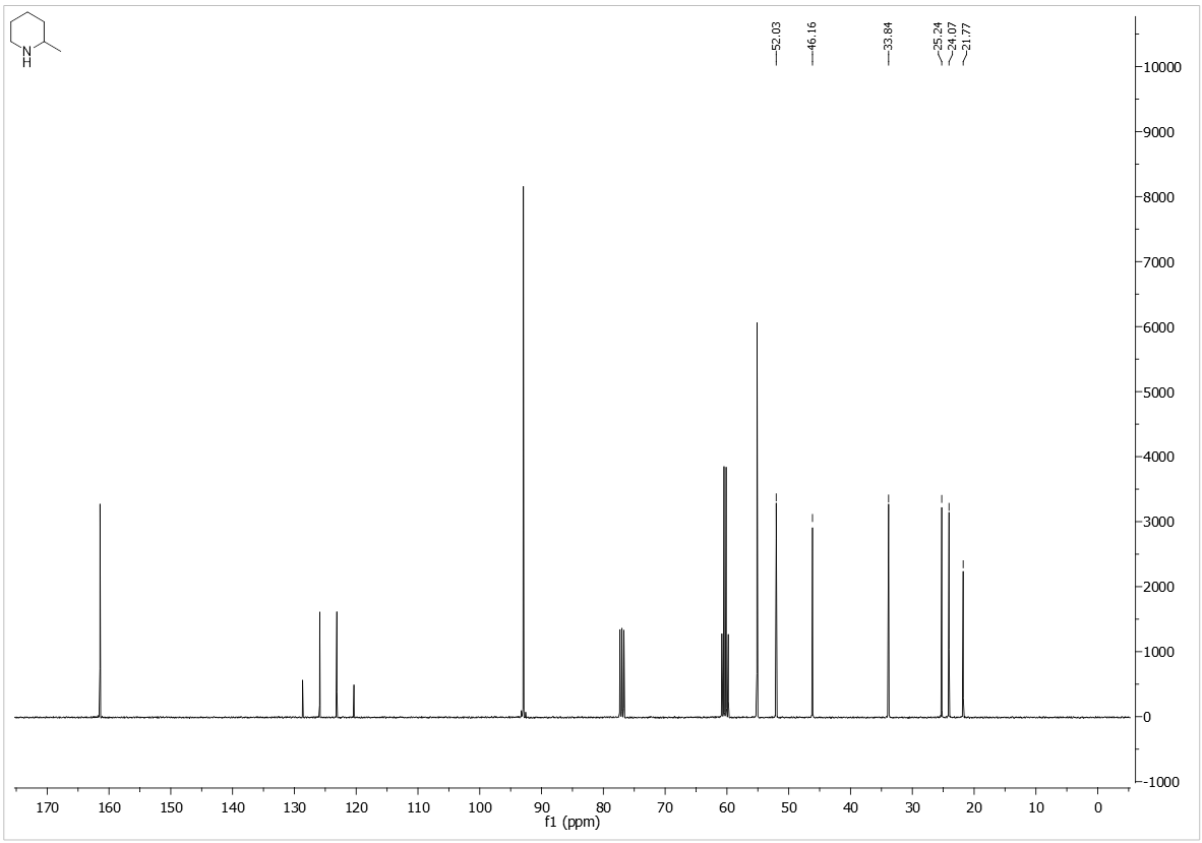


Figure 5 - ^{13}C NMR of 2-methylpiperidine (2b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

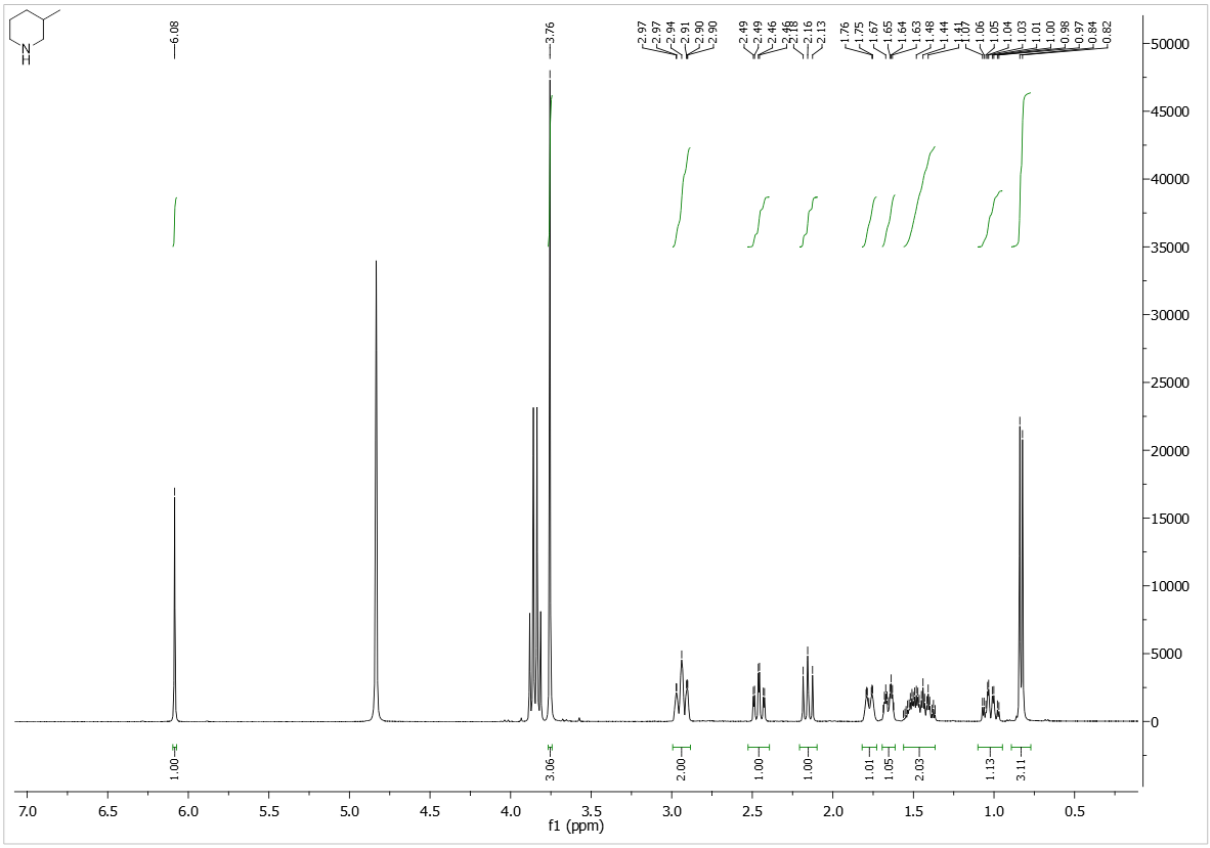


Figure 6 - ^{1}H NMR of 3-methylpiperidine (2c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

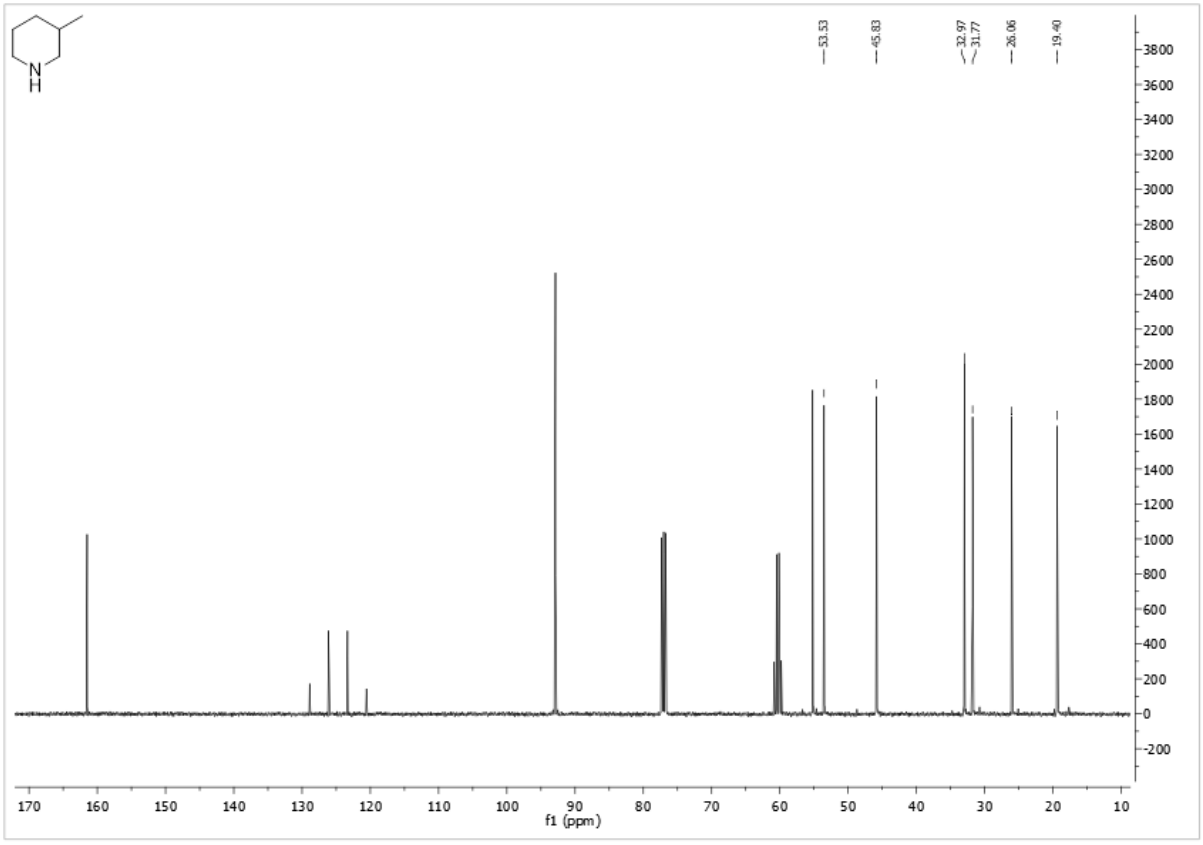


Figure 7 - ^{13}C NMR of 3-methylpiperidine (2c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

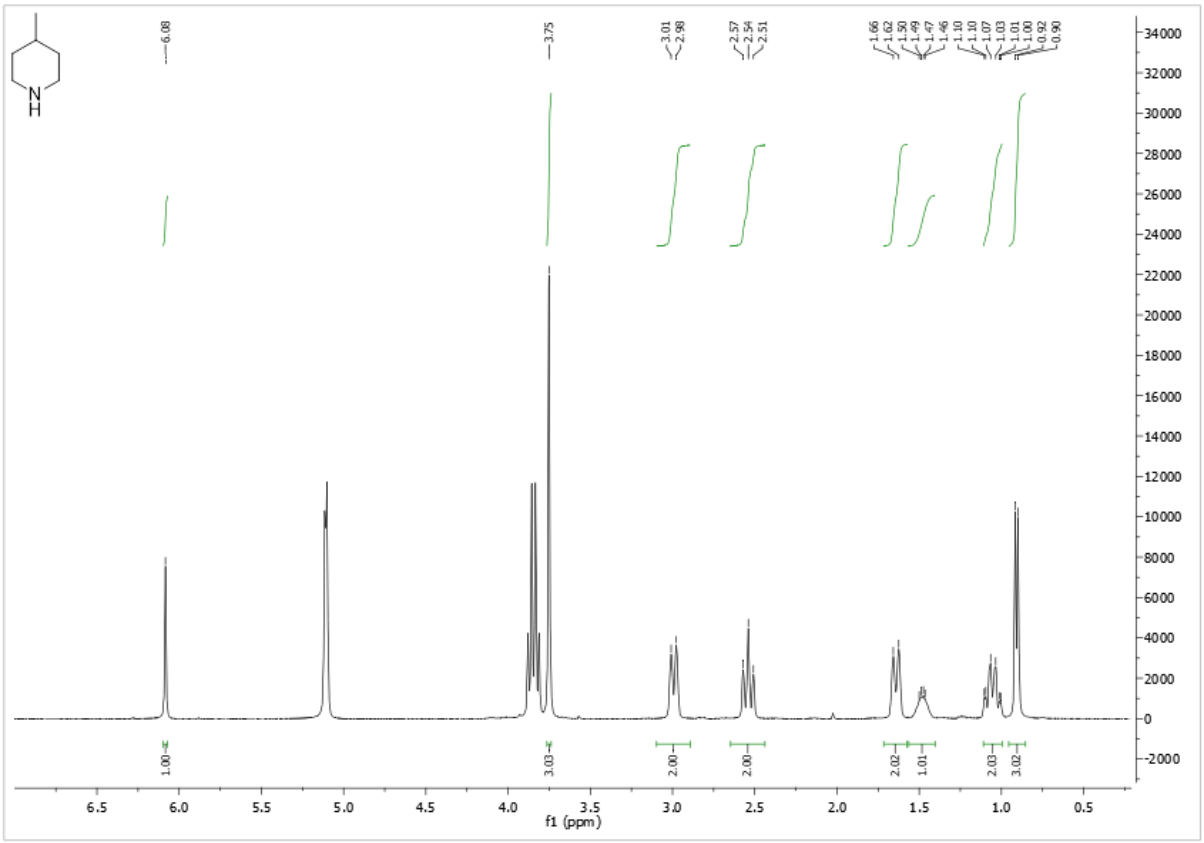


Figure 8 - ^{1}H NMR of 4-methylpiperidine (2d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

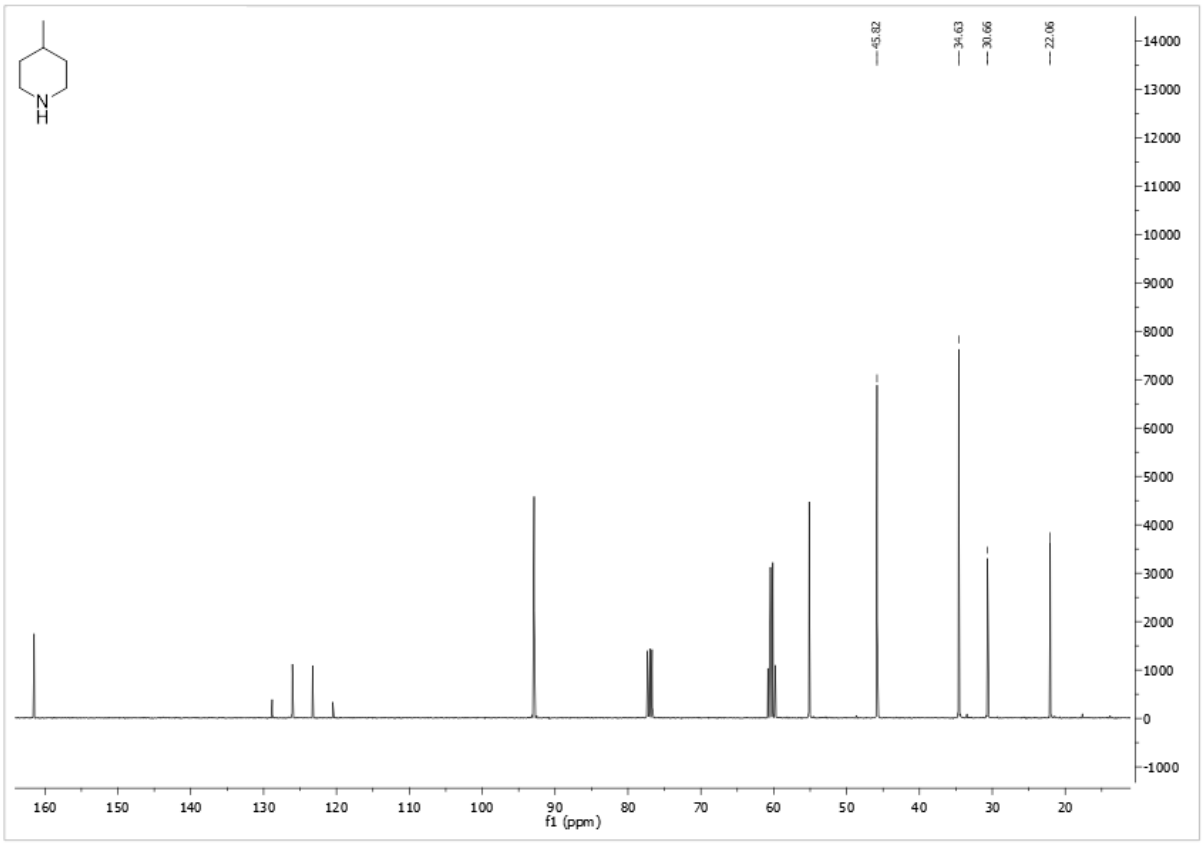


Figure 9 - ^{13}C NMR of 4-methylpiperidine (2d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

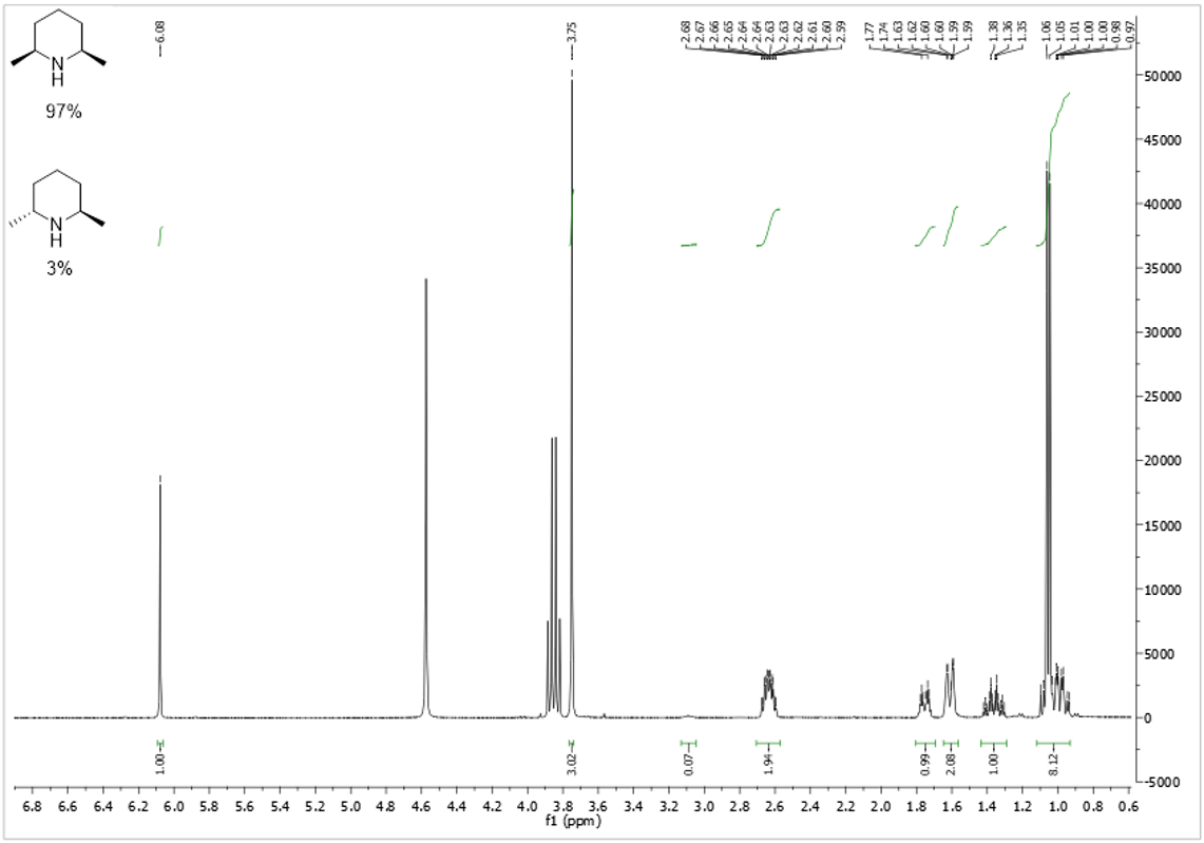


Figure 10 - ^{1}H NMR of 2,6-dimethylpiperidine (2e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

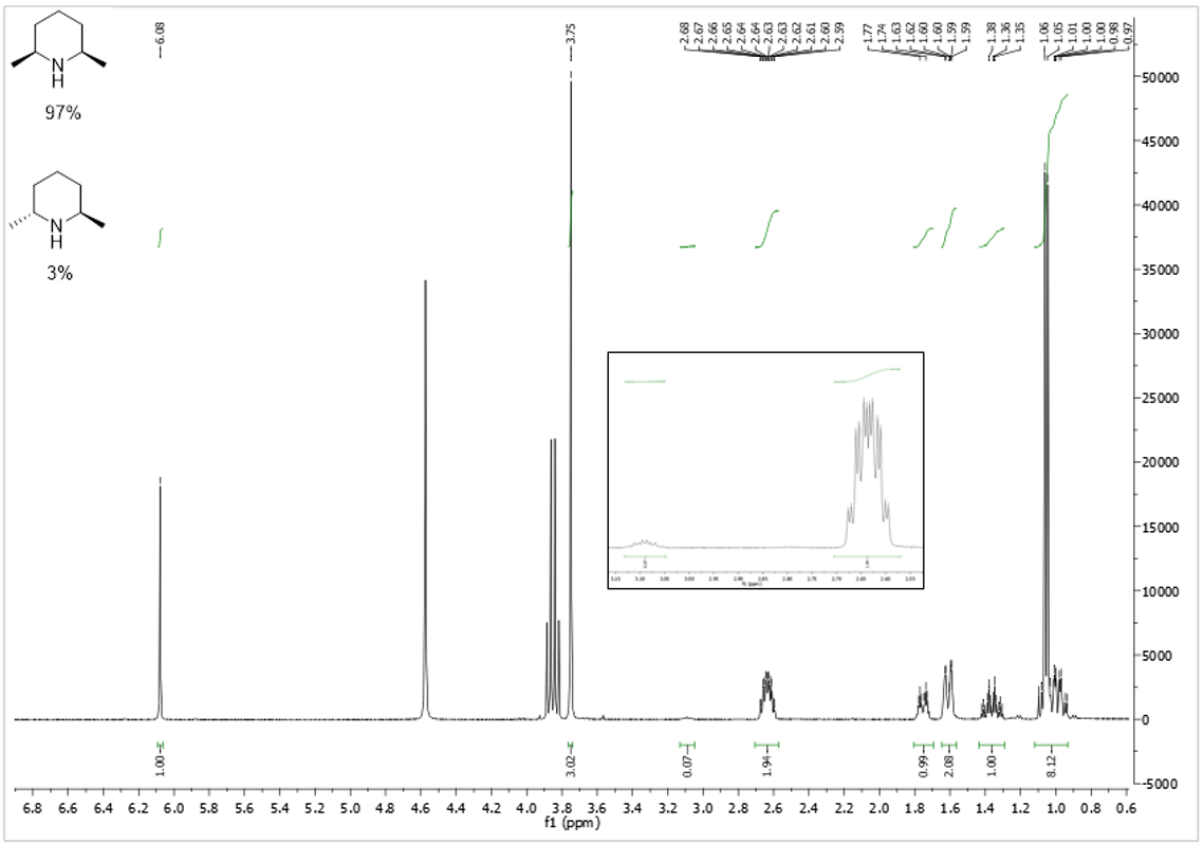


Figure 11 - ^{1}H NMR of 2,6-dimethylpiperidine (2e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows presnce of two diastereoisomers.

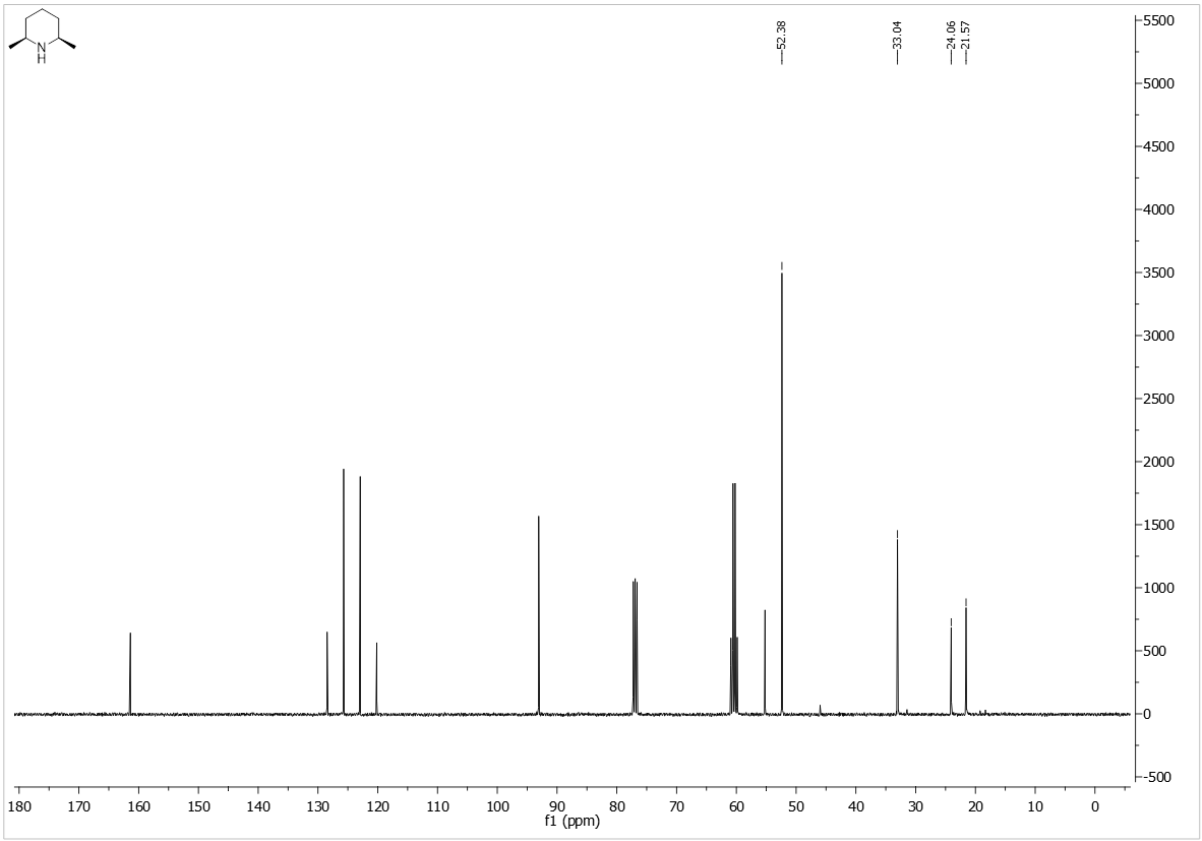


Figure 12 - ^{13}C NMR of 2,6-dimethylpiperidine (2e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

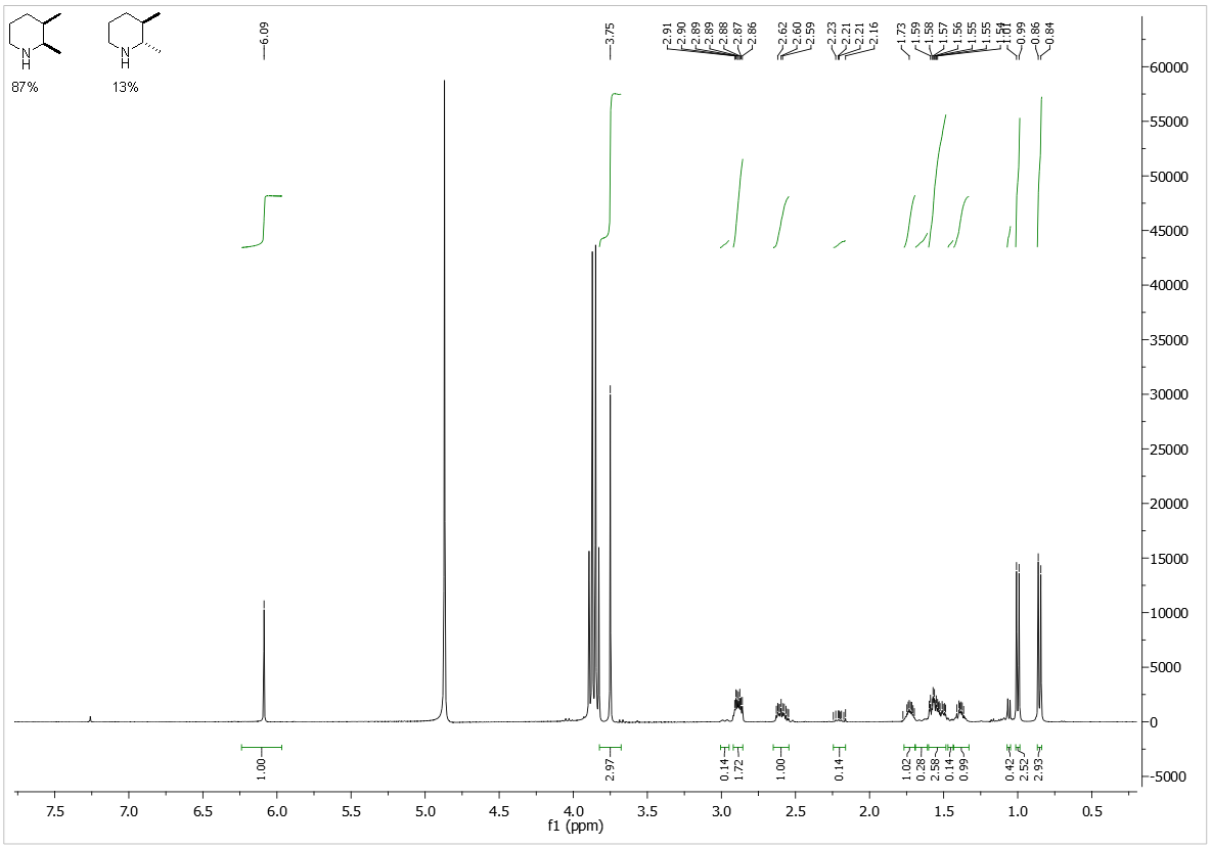


Figure 13 - ^{1}H NMR of 2,3-dimethylpiperidine (2f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

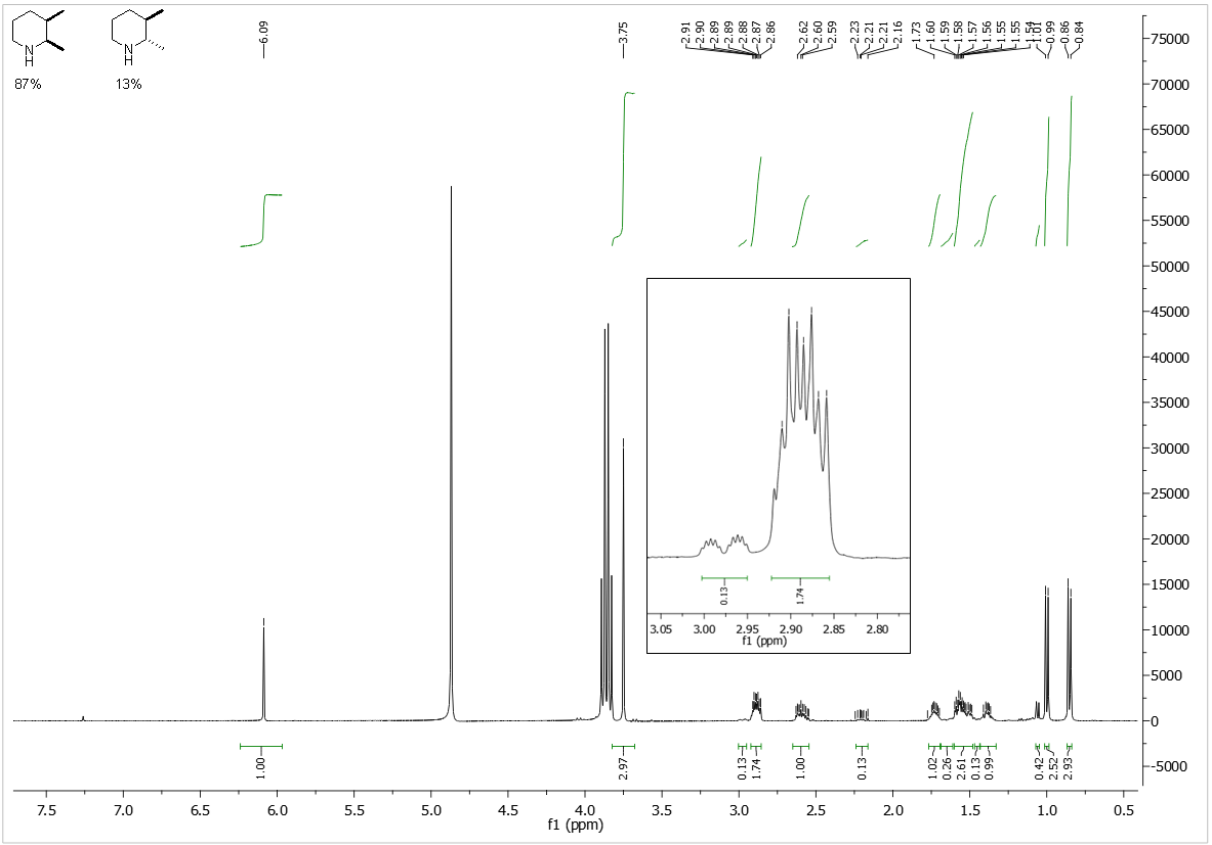


Figure 14 - ^{1}H NMR of 2,3-dimethylpiperidine (2f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows presnce of two diastereoisomers.

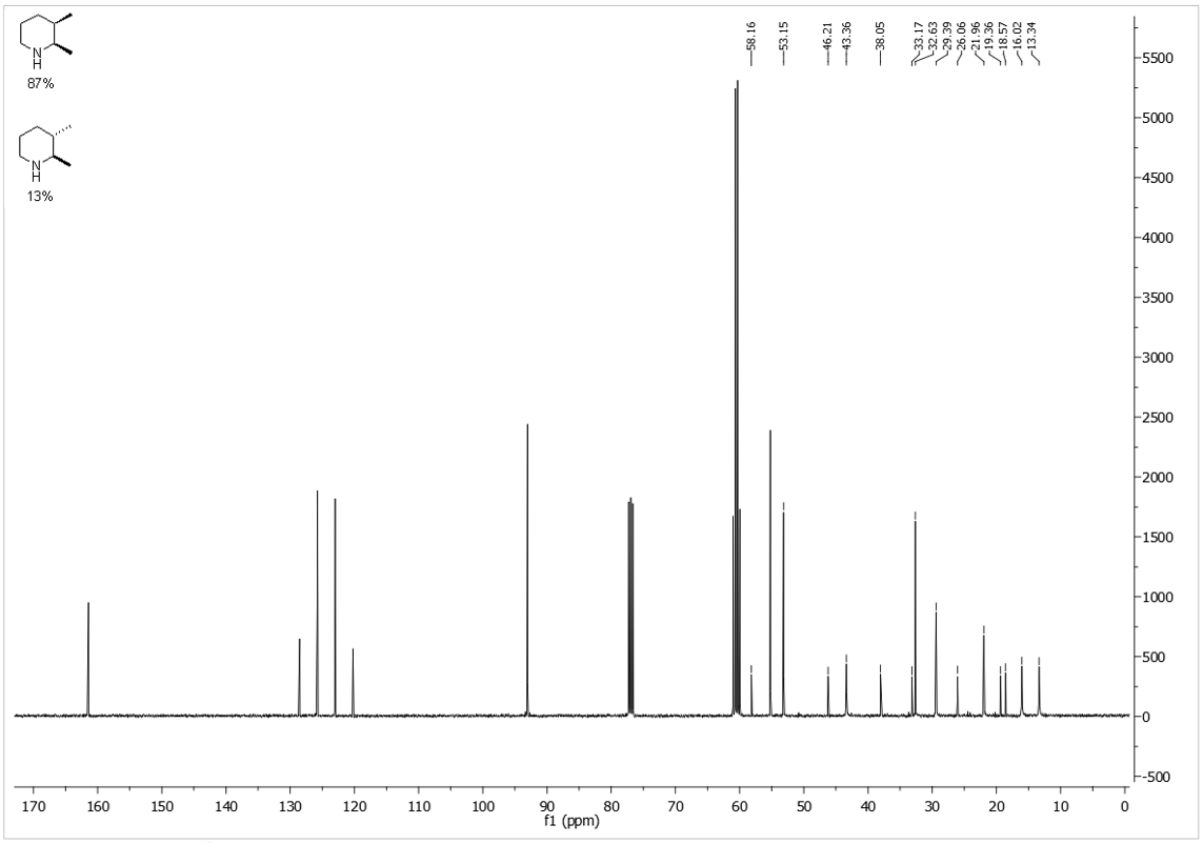


Figure 15 - ^{13}C NMR of 2,3-dimethylpiperidine (2f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

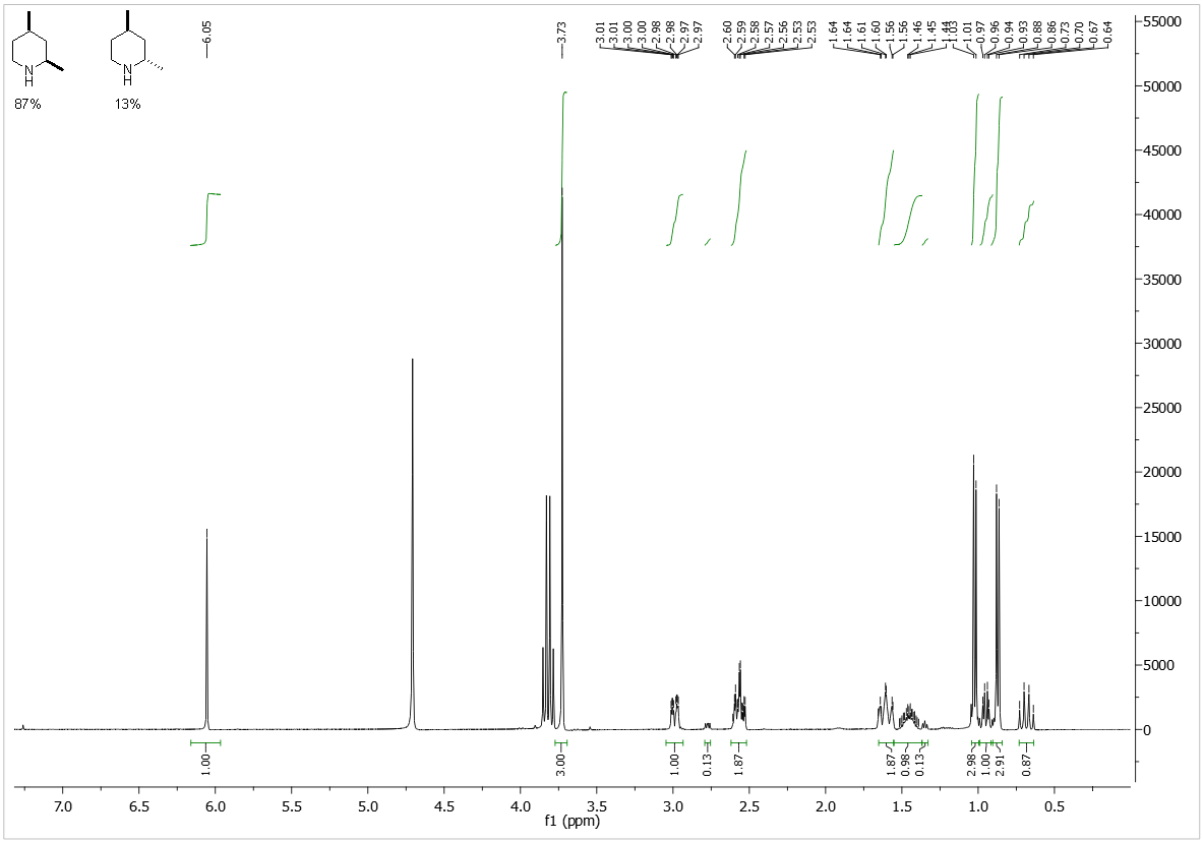


Figure 16 - ^{1}H NMR of 2,4-dimethylpiperidine (2g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

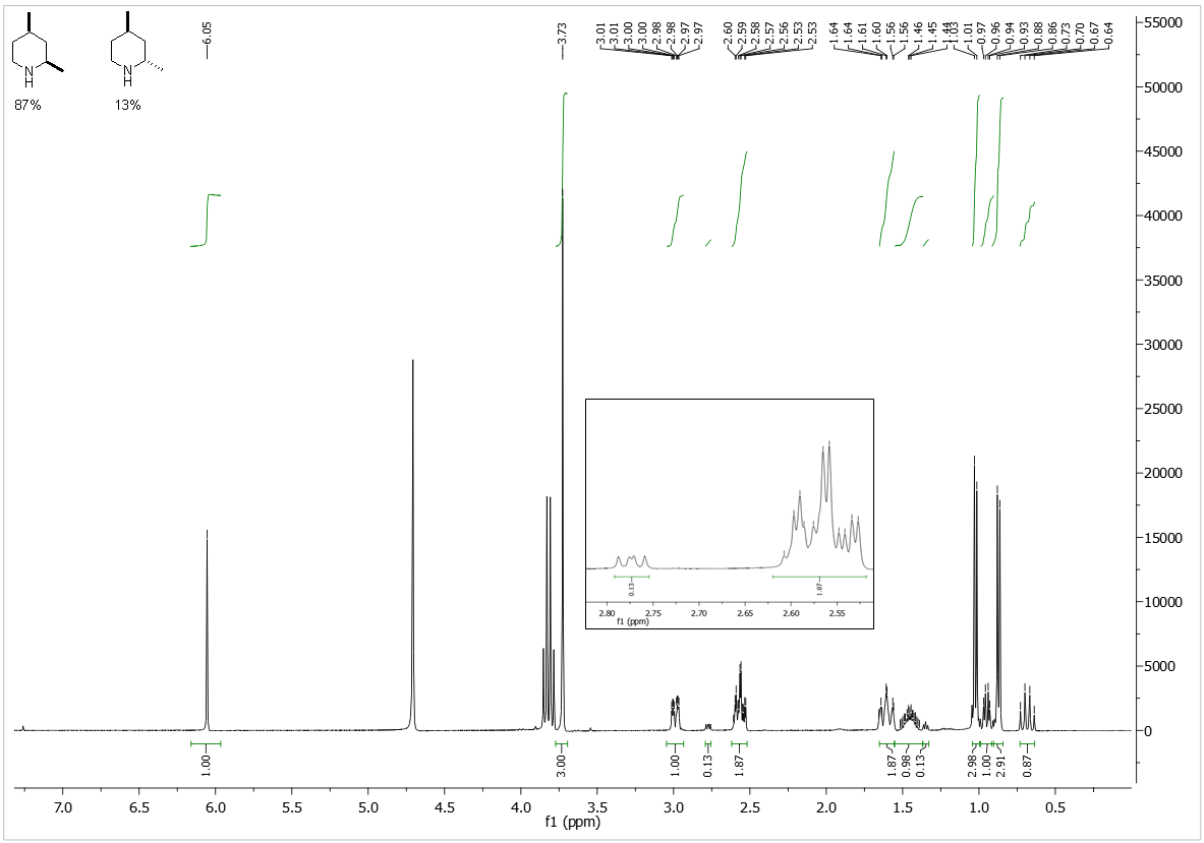


Figure 17 - ^{1}H NMR of 2,4-dimethylpiperidine (2g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows presence of both diastereisomers.

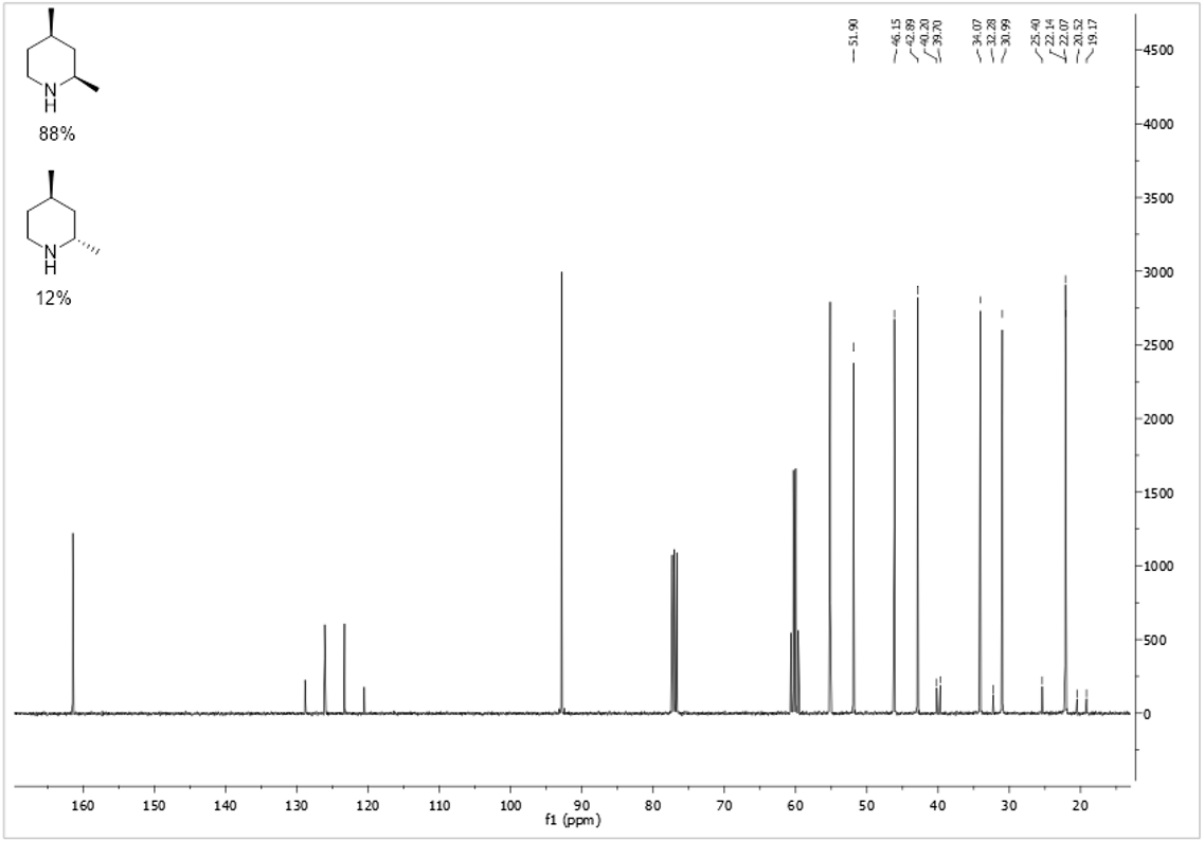


Figure 18 - ^{13}C NMR of 2,4-dimethylpiperidine (2g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

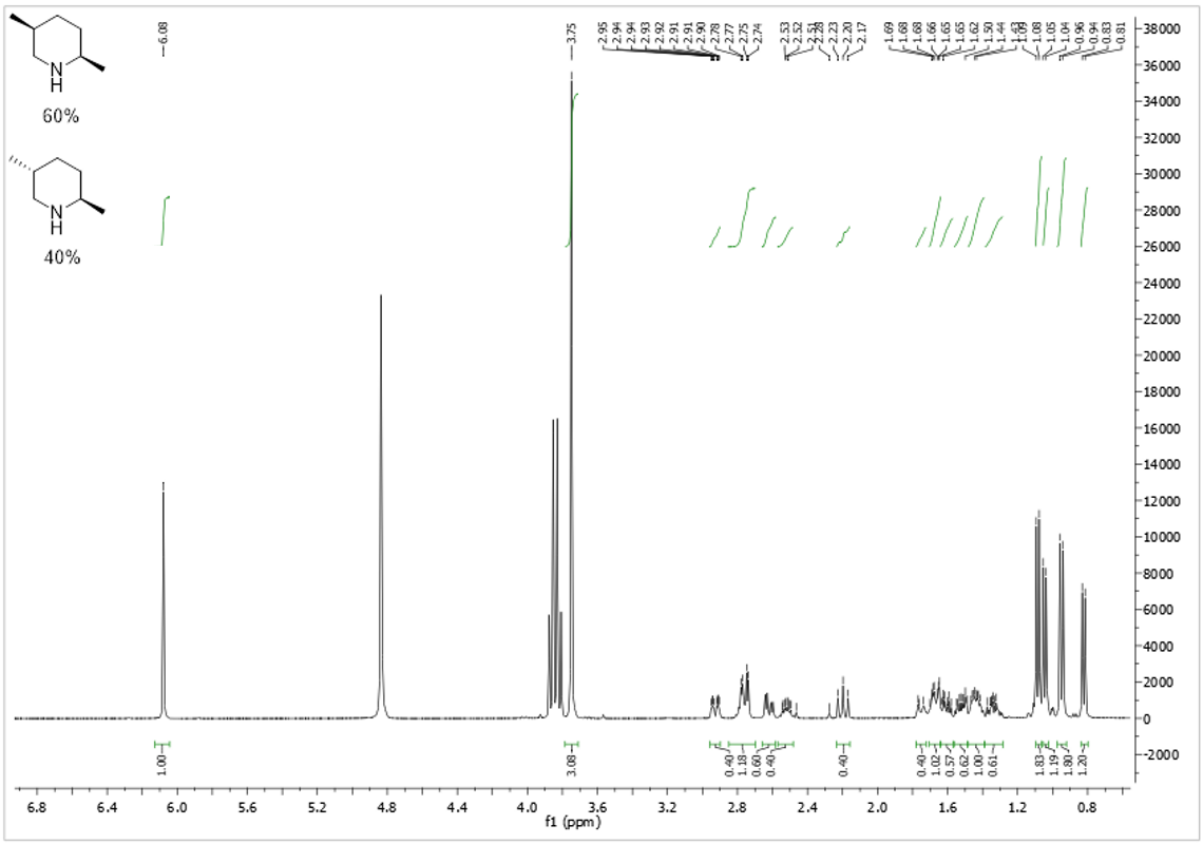


Figure 19 - ^{1}H NMR of 2,5-dimethylpiperidine (2h) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

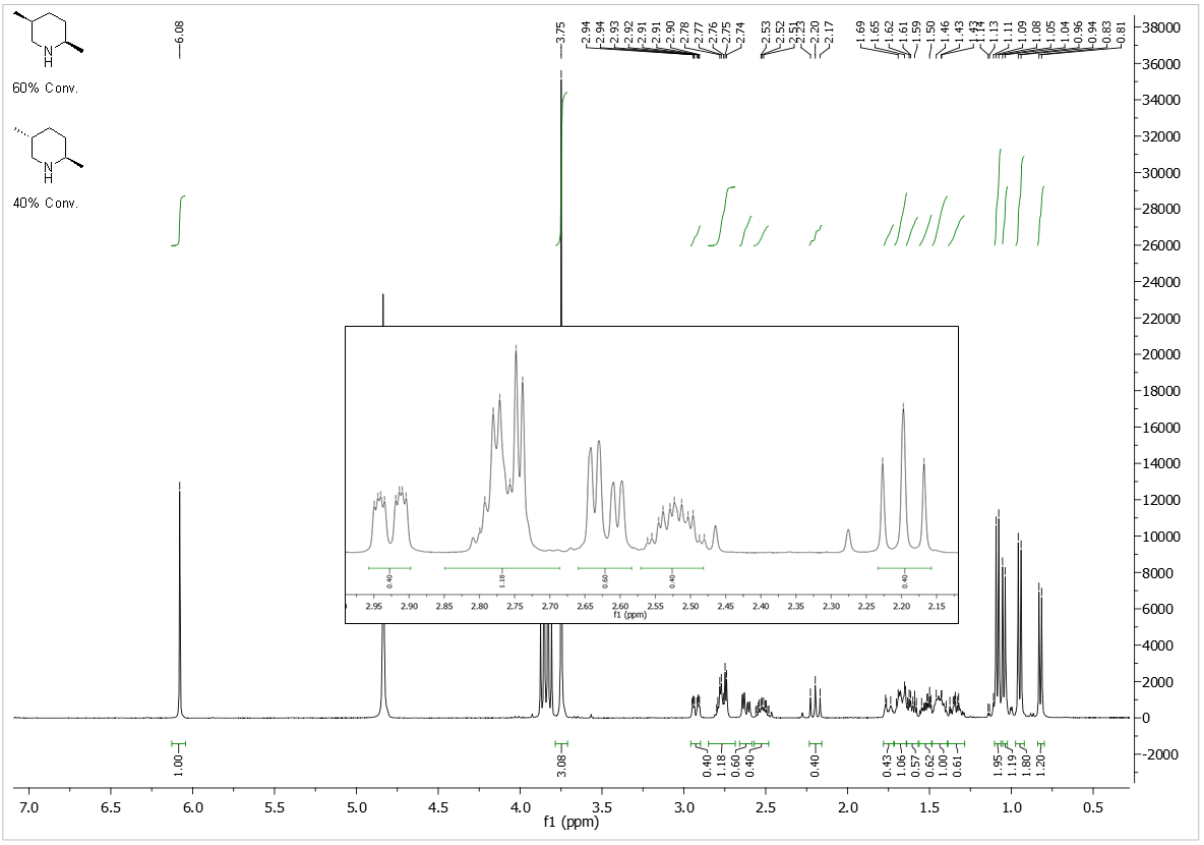


Figure 20 - ^{1}H NMR of 2,5-dimethylpiperidine (2h) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Trans product at 2.93ppm,2.52ppm and 2.20ppm and cis product at 2.75ppm (2H) and 2.62ppm.

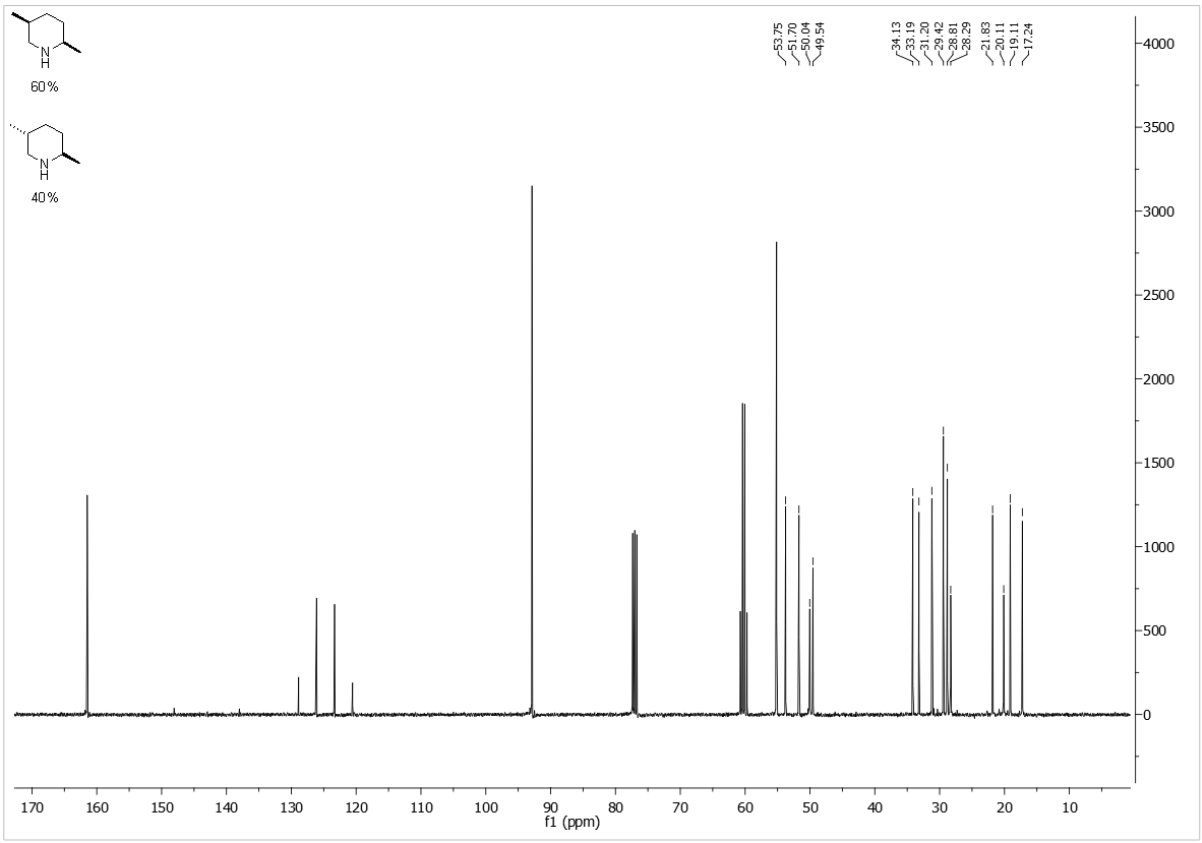


Figure 21 - ^{13}C NMR of 2,5-dimethylpiperidine (2h) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

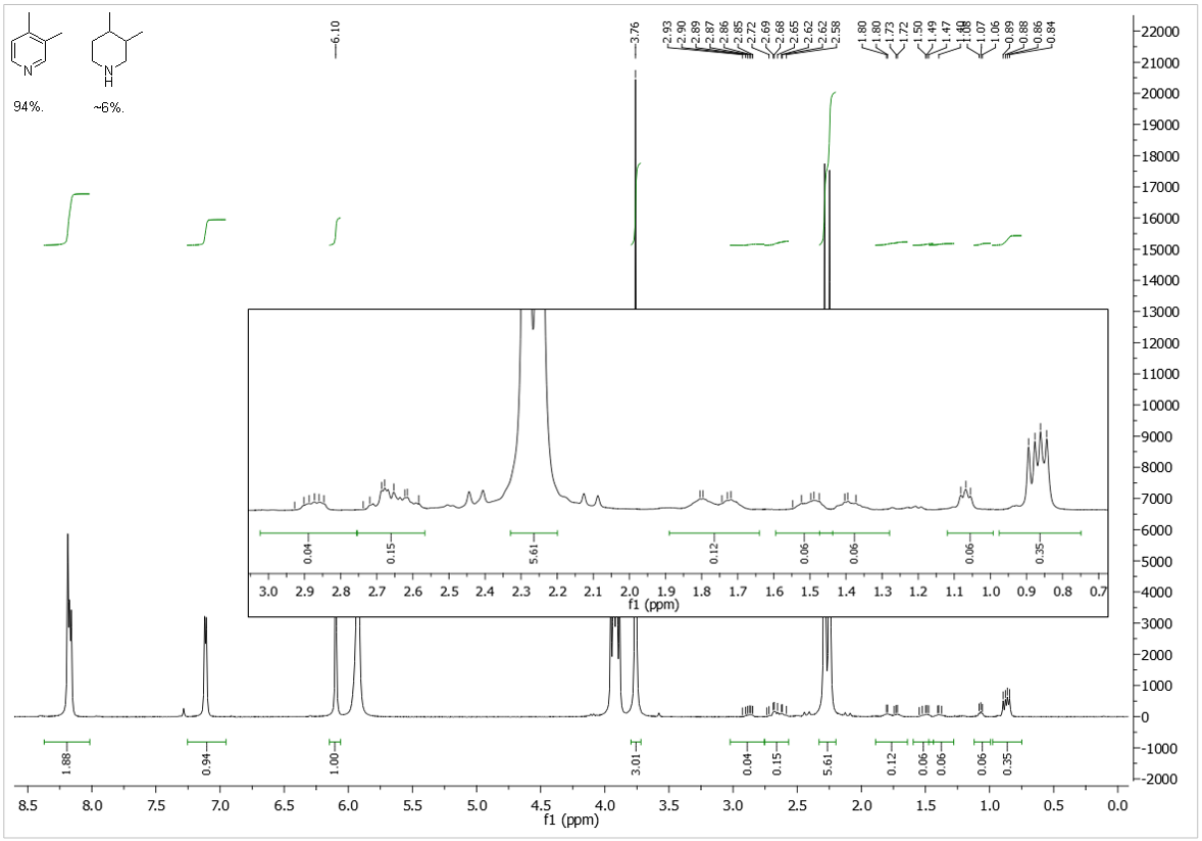


Figure 22 - ^{1}H NMR of 3,4-dimethylpiperidine (2i) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Yield calculated from the remaining starting material and the product is assigned only tentatively based on the approximate chemical shift, splitting and integration.

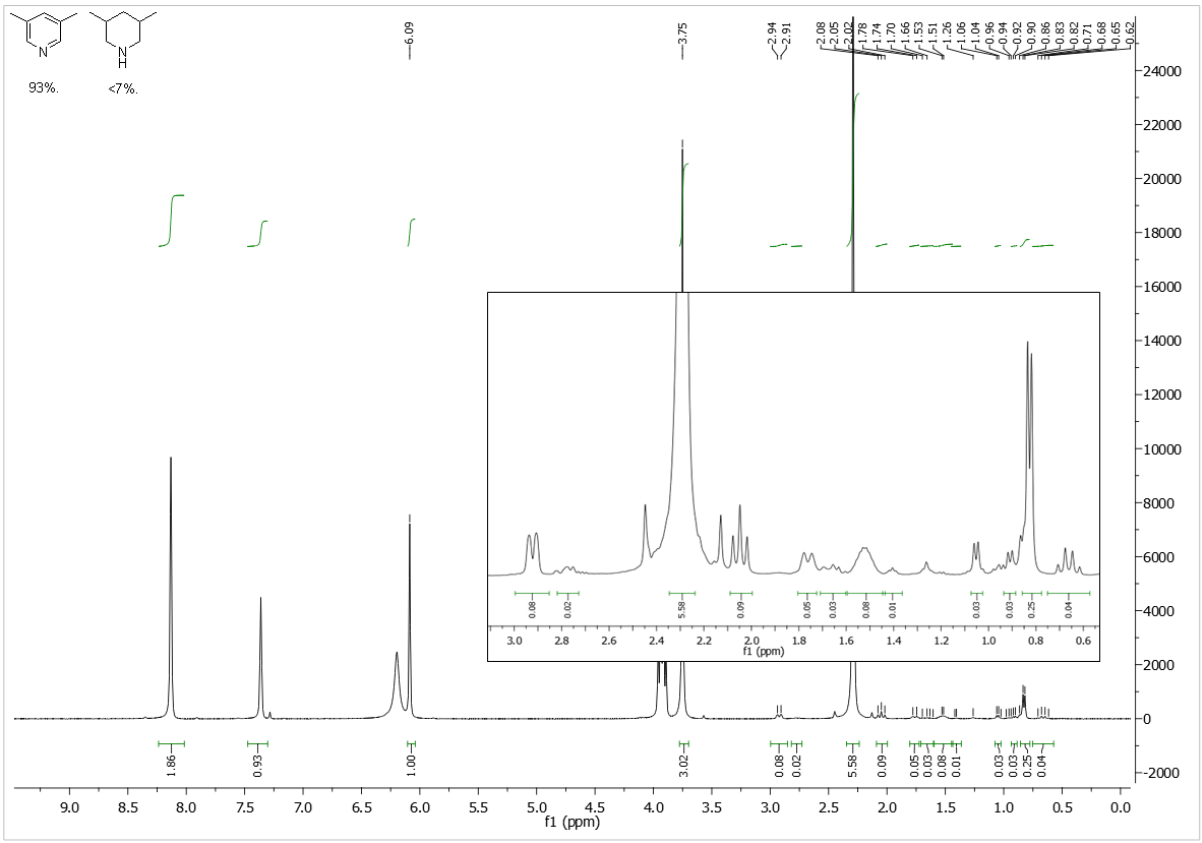


Figure 23 - ^{1}H NMR of 3,5-dimethylpiperidine (2j) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Yield calculated from the remaining starting material and the product is assigned only tentatively based on the chemical shift, splitting and integration. Inset suggests the presence of two diastereoisomers.

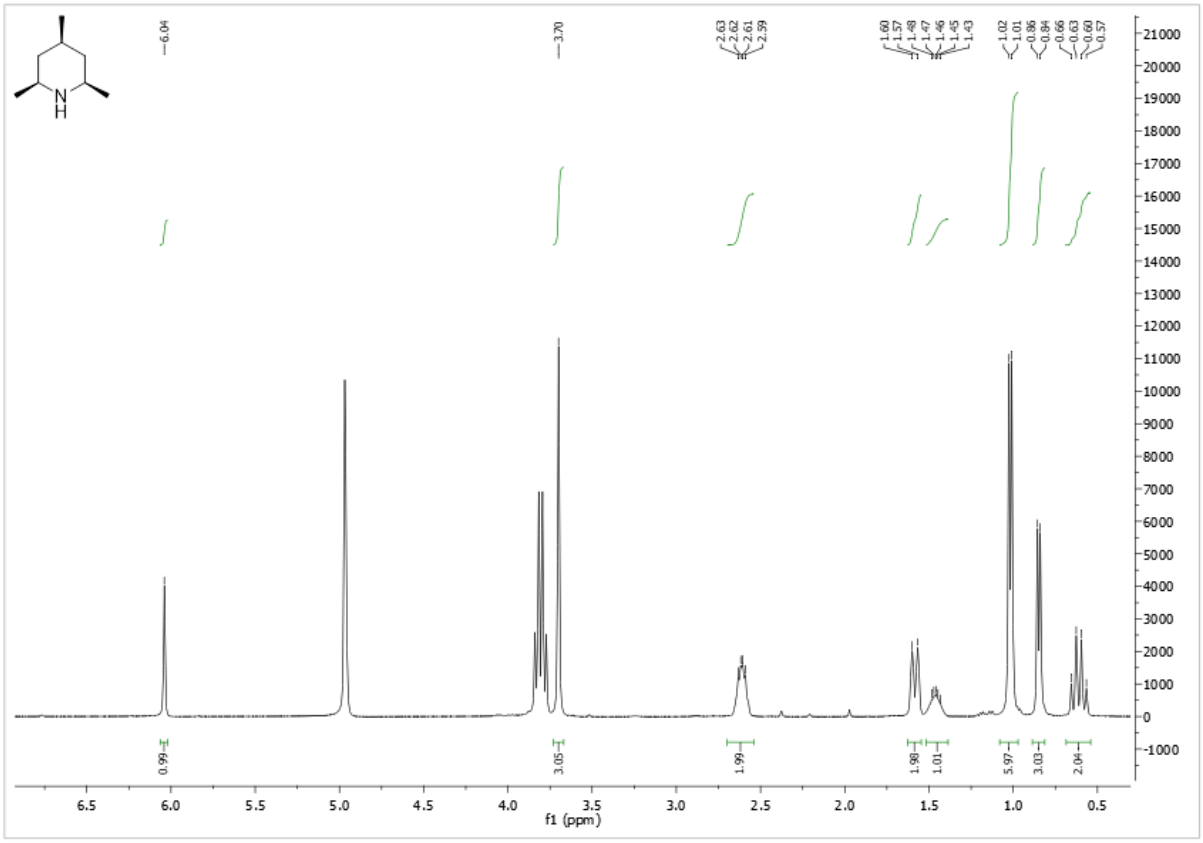


Figure 24 - ^{1}H NMR of 2,4,6-trimethylpiperidine (2k) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) as internal standard.

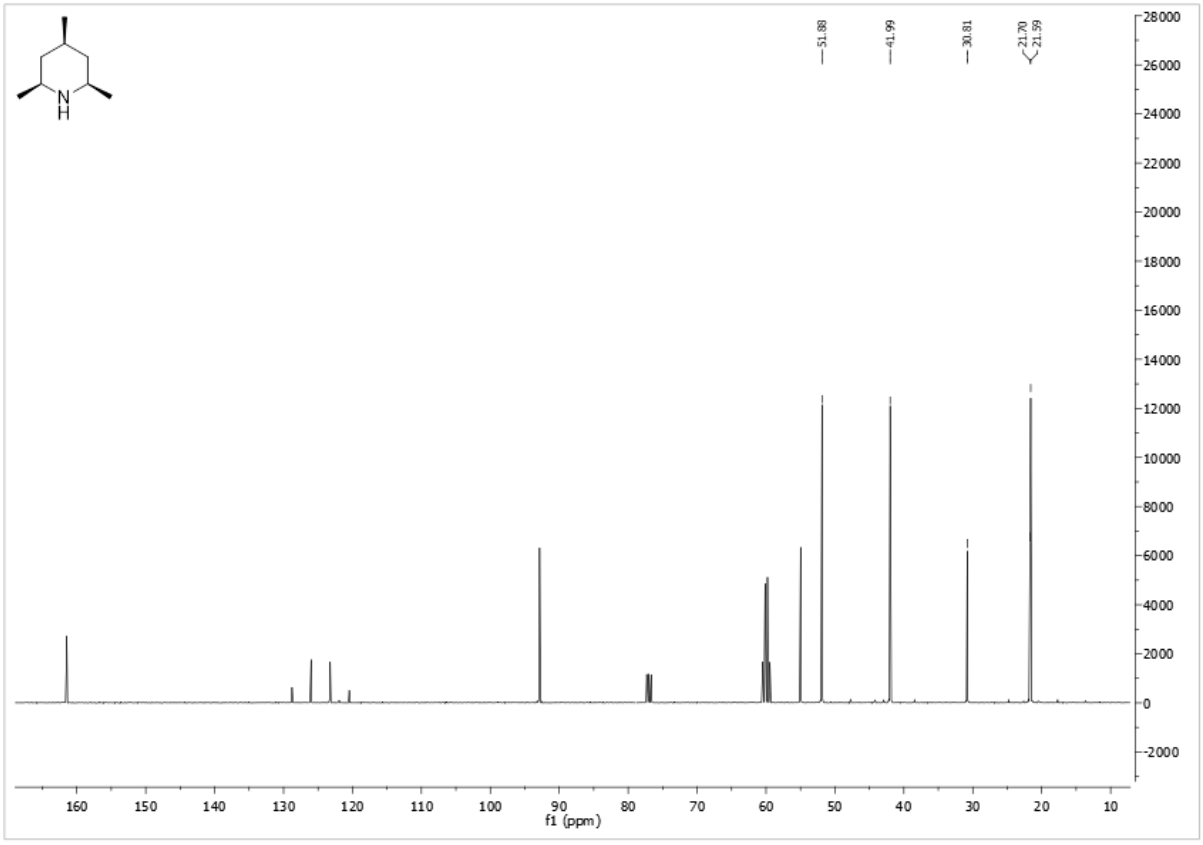


Figure 25 - ^{13}C NMR of 2,4,6-trimethylpiperidine (2k) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

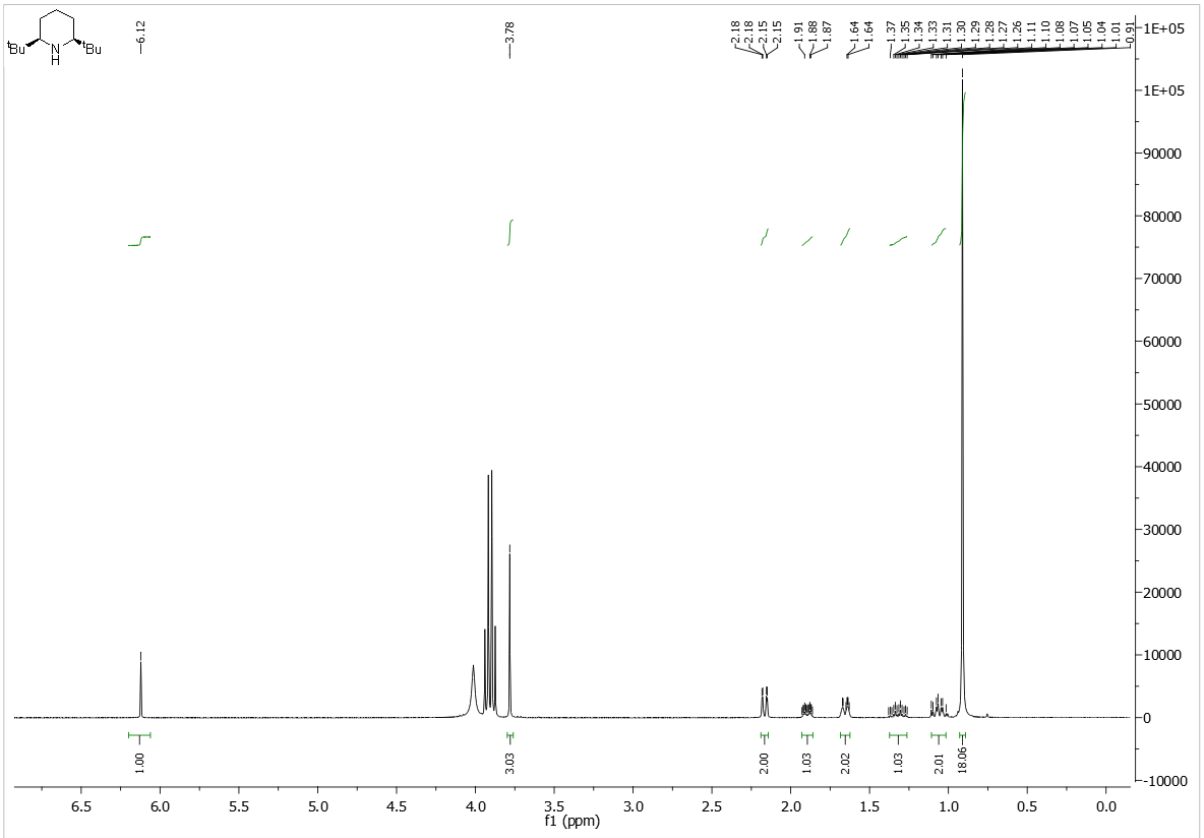


Figure 26 - ^{1}H NMR of 2,6-di-tert-butylpiperidine (2m) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

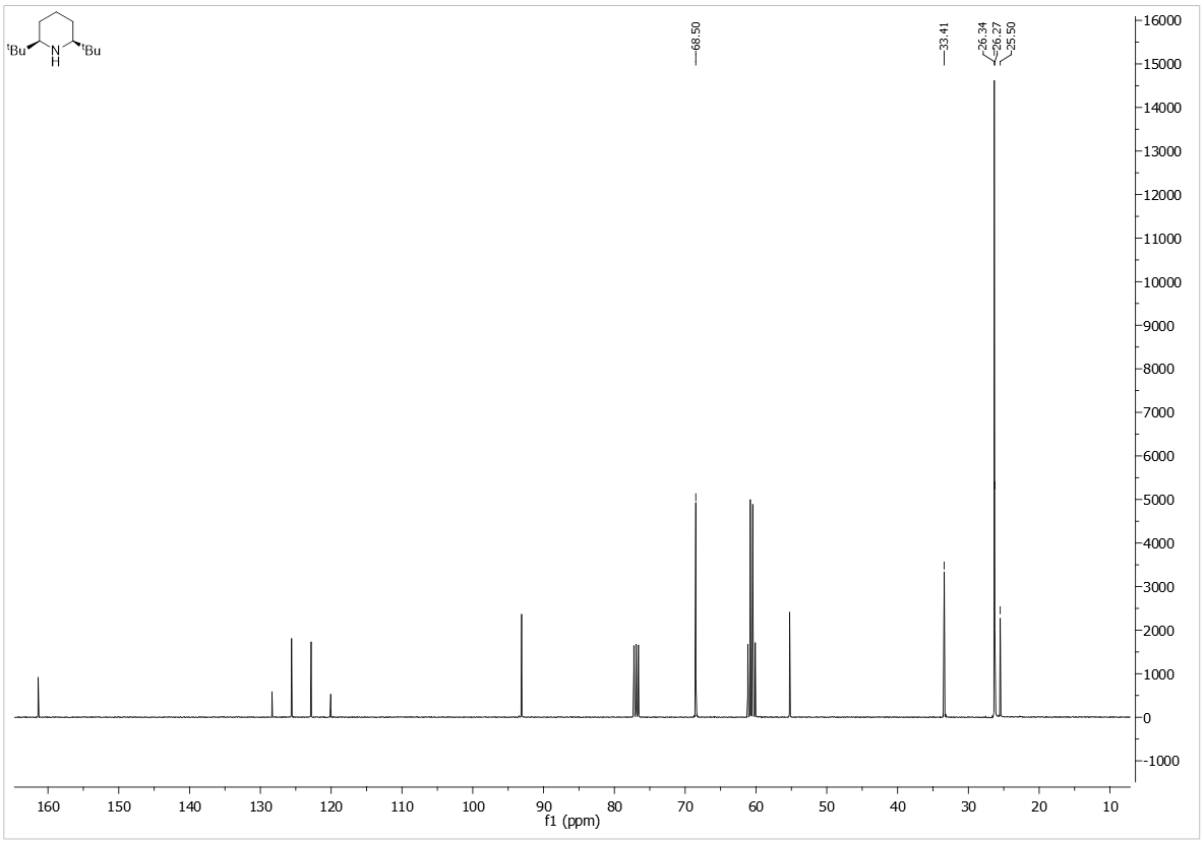


Figure 27 - ^{13}C NMR of 2,6-di-tert-butylpiperidine (2m) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

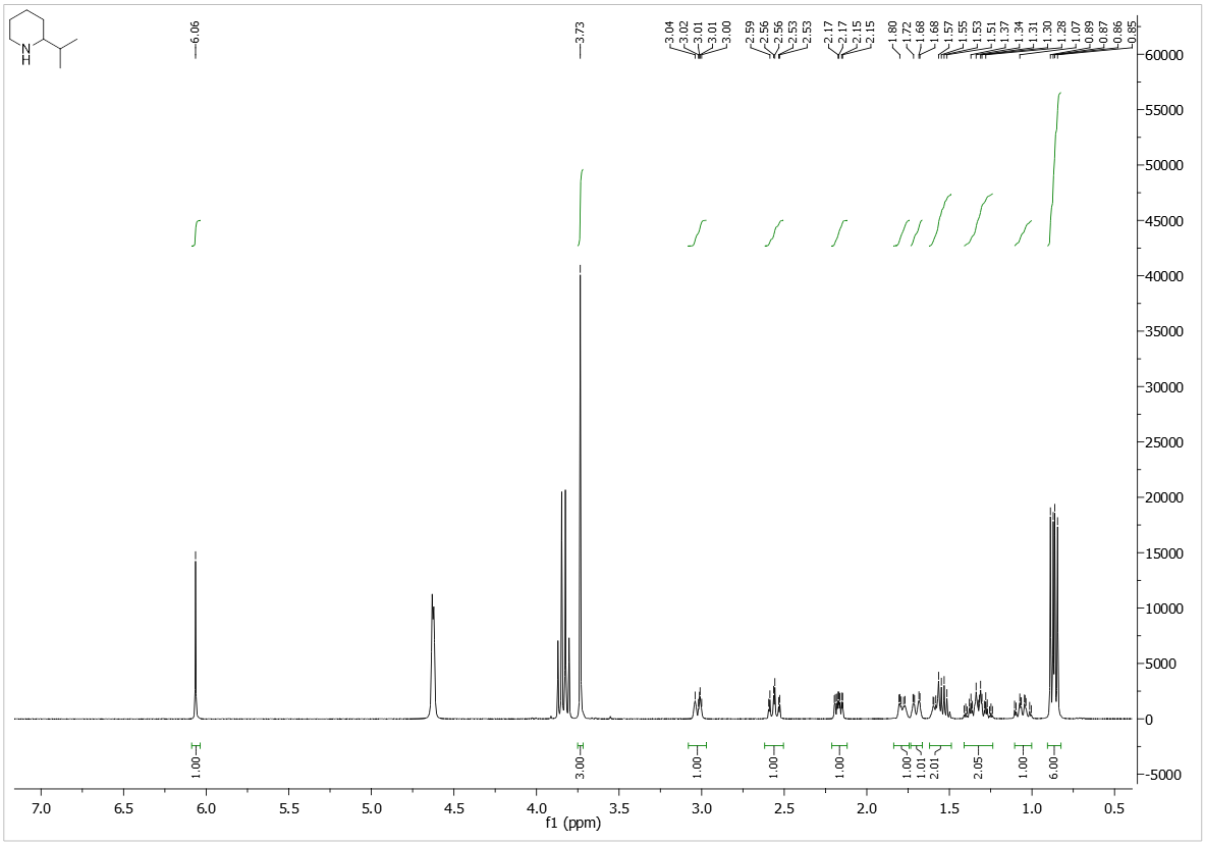


Figure 28 - ^{1}H NMR of 2-isopropylpiperidine (2n) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

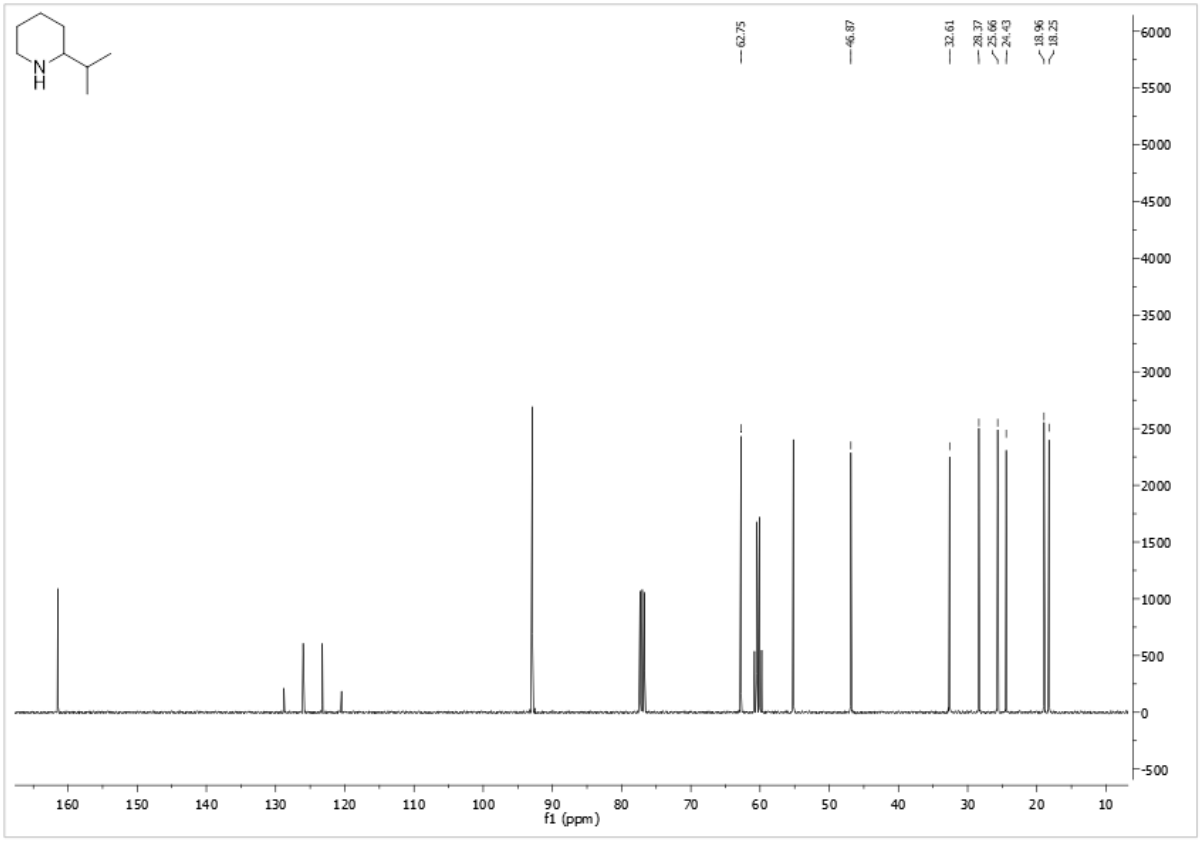


Figure 29 - ^{13}C NMR of 2-isopropylpiperidine (2n) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

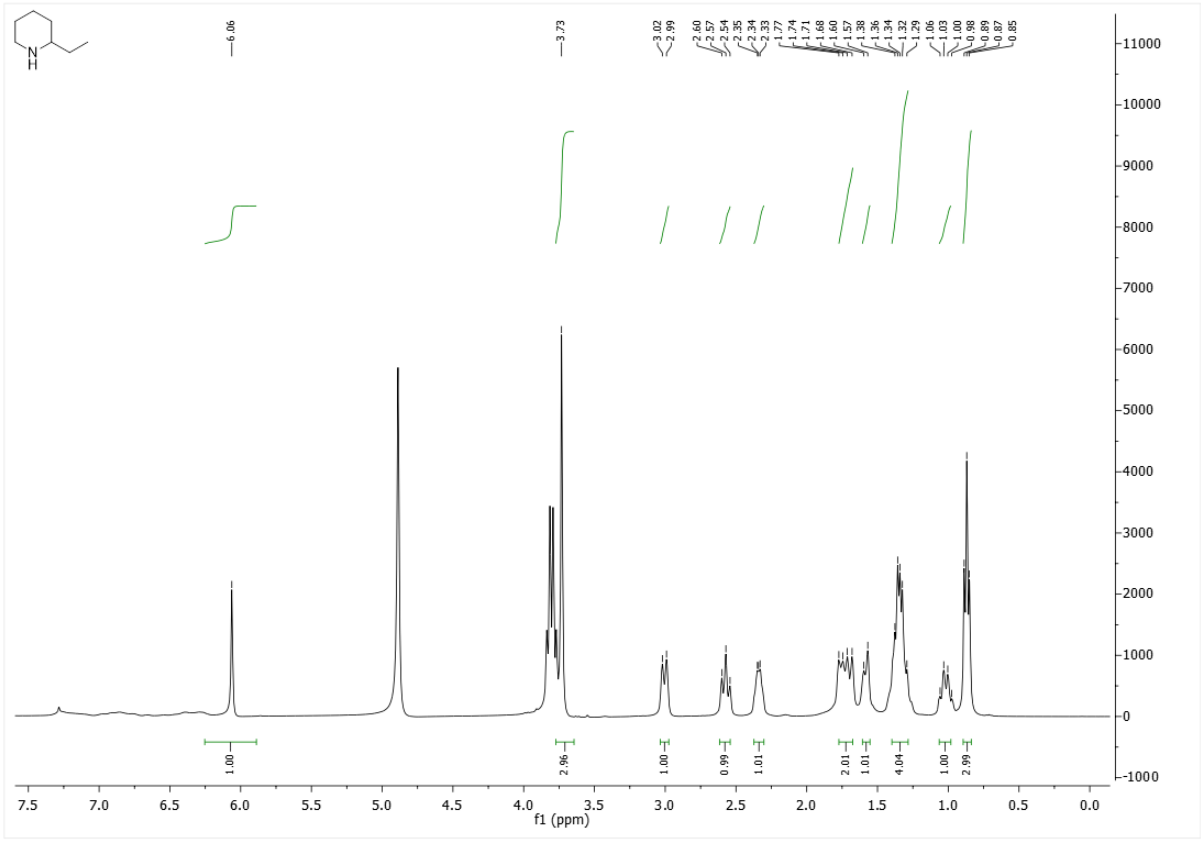


Figure 30 - ^{1}H NMR of 2-ethylpiperidine (2p) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

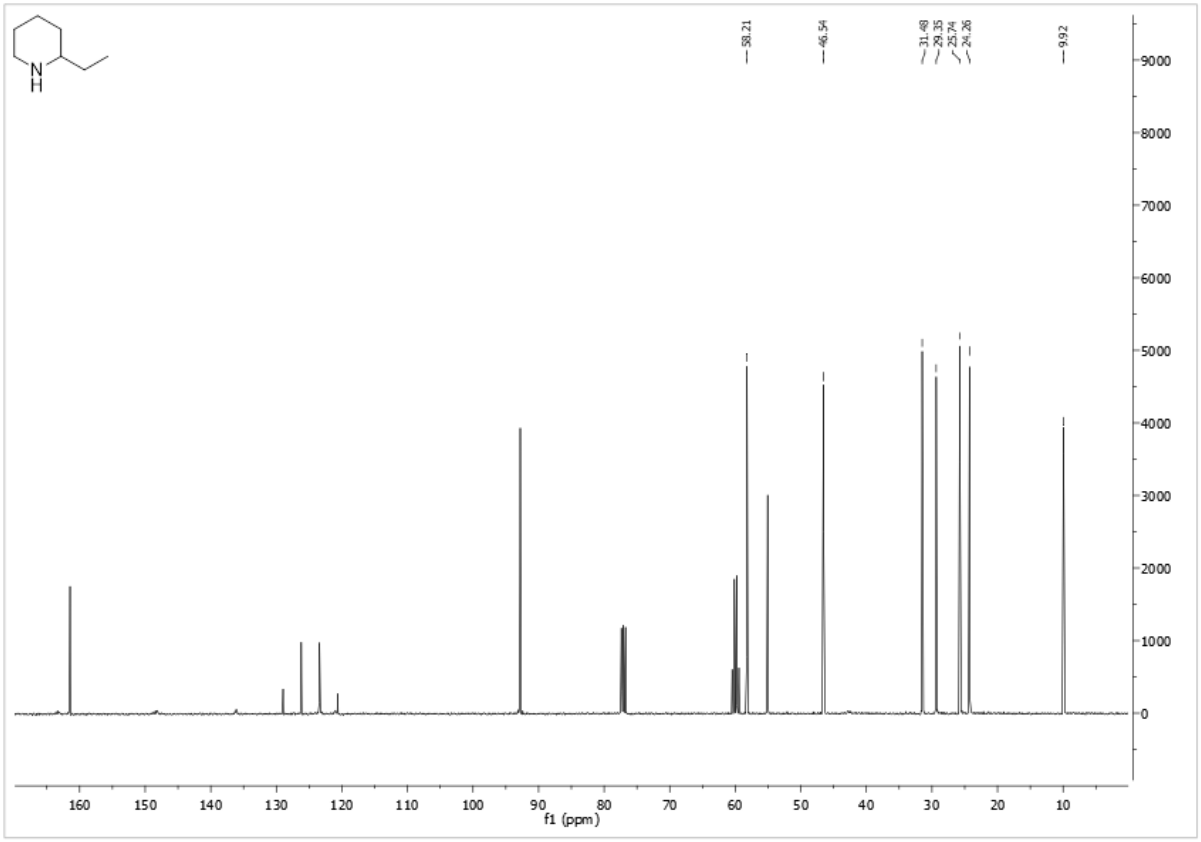


Figure 31 - ^{13}C NMR of 2-ethylpiperidine (2p) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

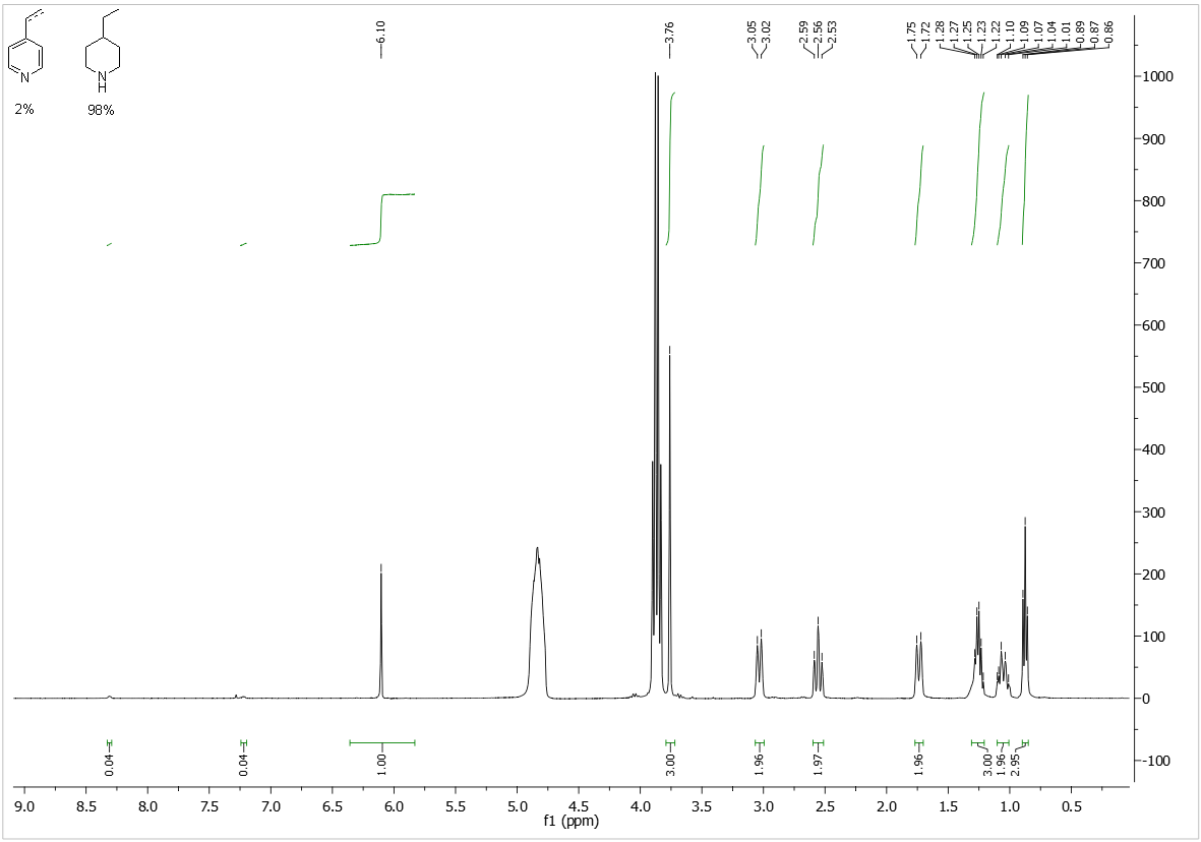


Figure 32 - ^{1}H NMR of 4-ethylpiperidine (2q) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

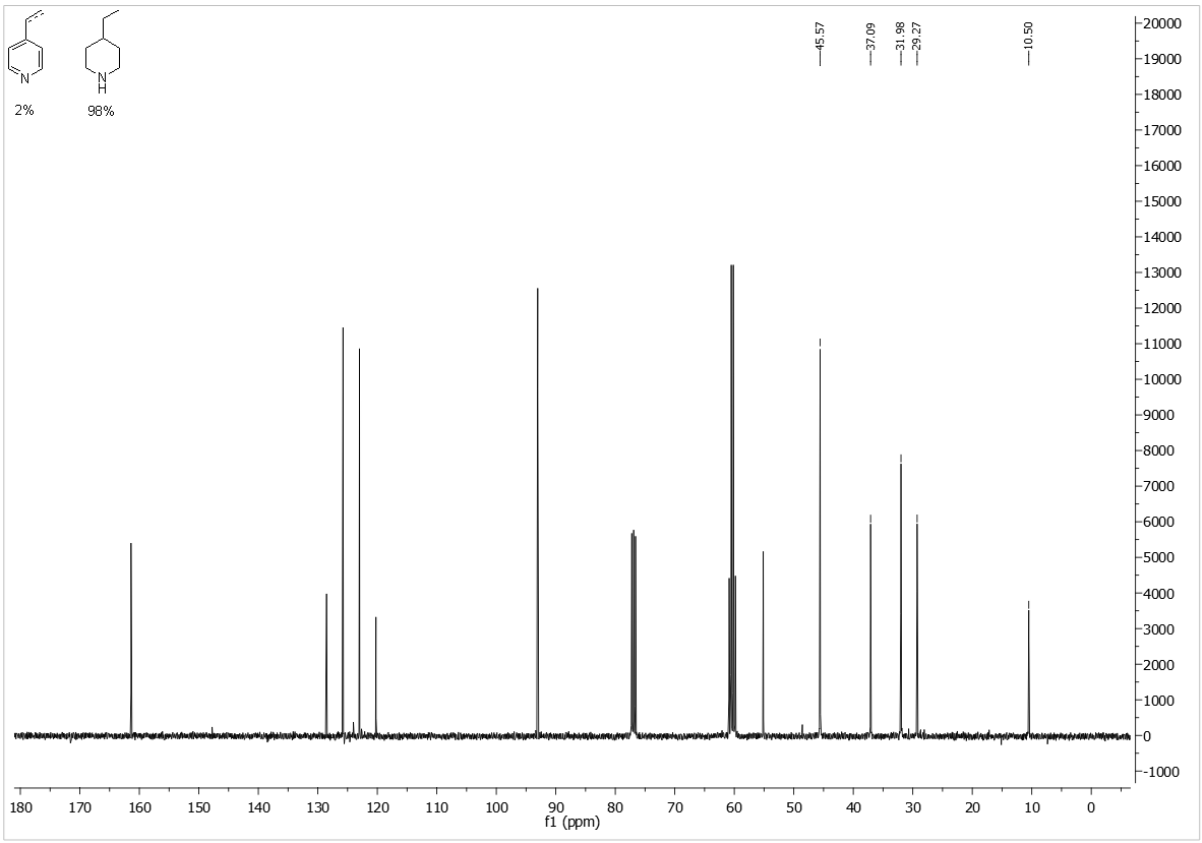


Figure 33 - ^{13}C NMR of 4-ethylpiperidine (2q) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

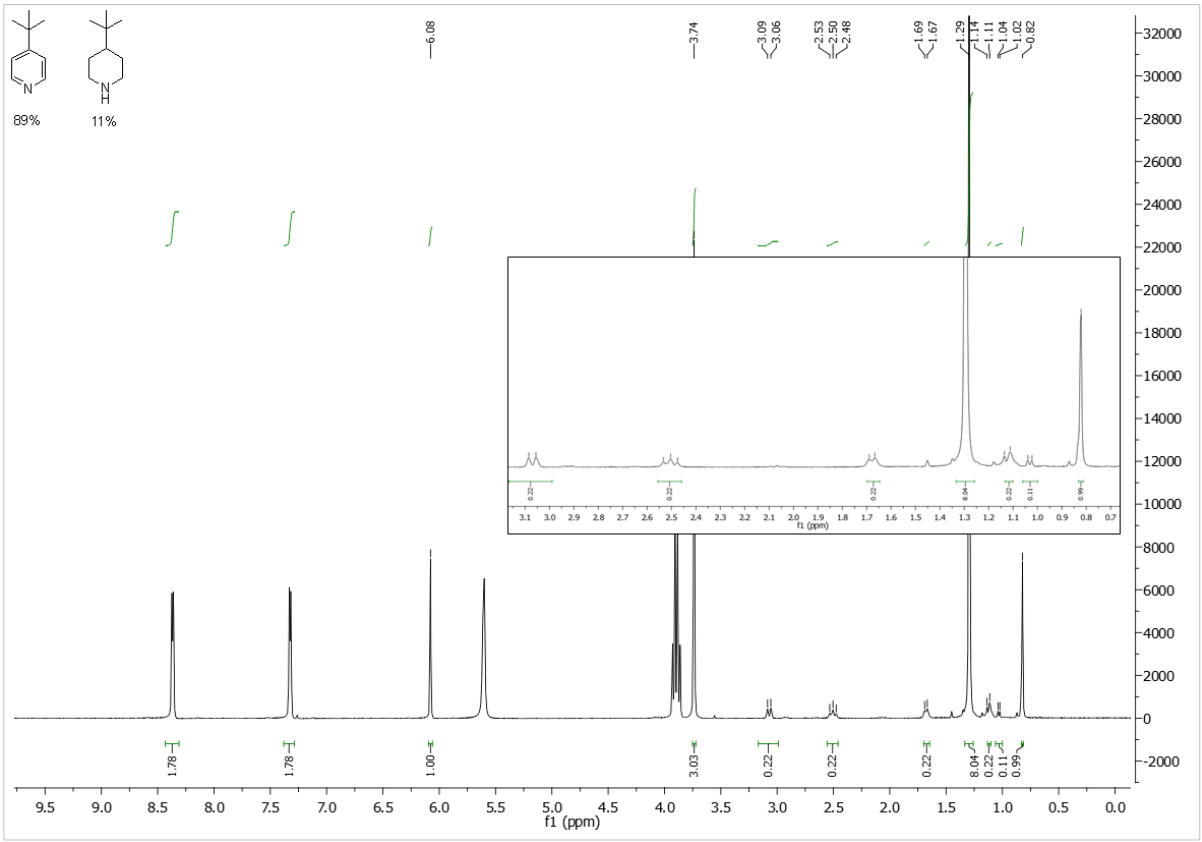


Figure 34 - ^{1}H NMR of 4-tert-butylpiperidine (2r) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Yield calculated from the remaining starting material and the product has been assigned tentatively based on the chemical shift, splitting and integration.

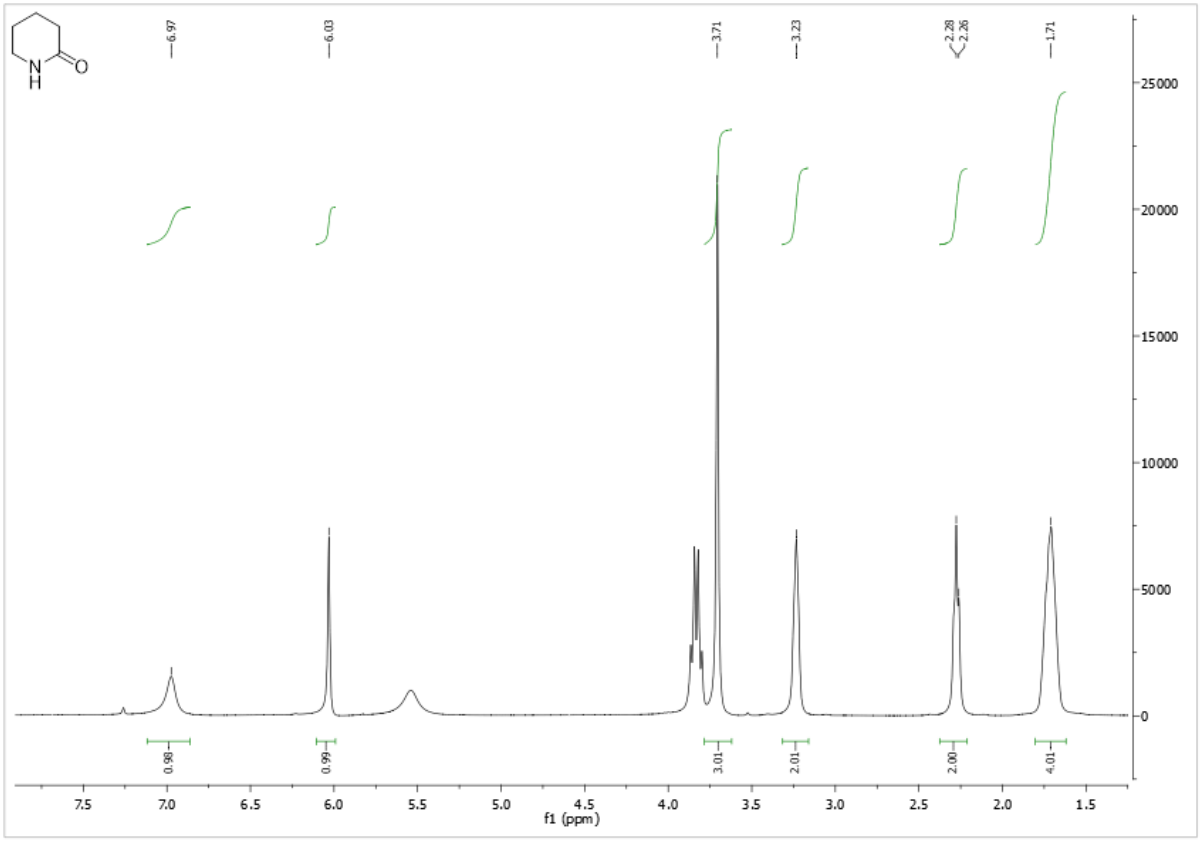


Figure 35 - ^{1}H NMR of 2-piperidone (4a) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

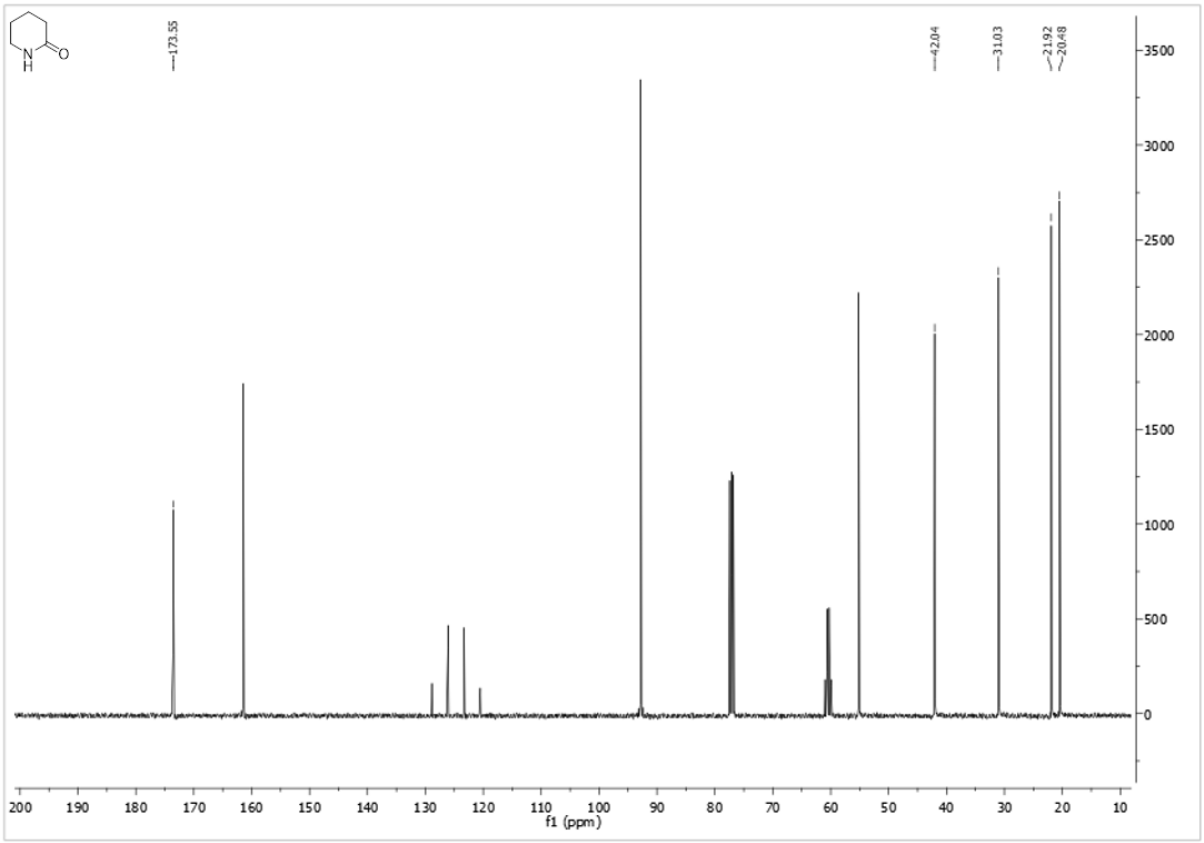


Figure 36 - ^{13}C NMR of 2-piperidone (4a) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

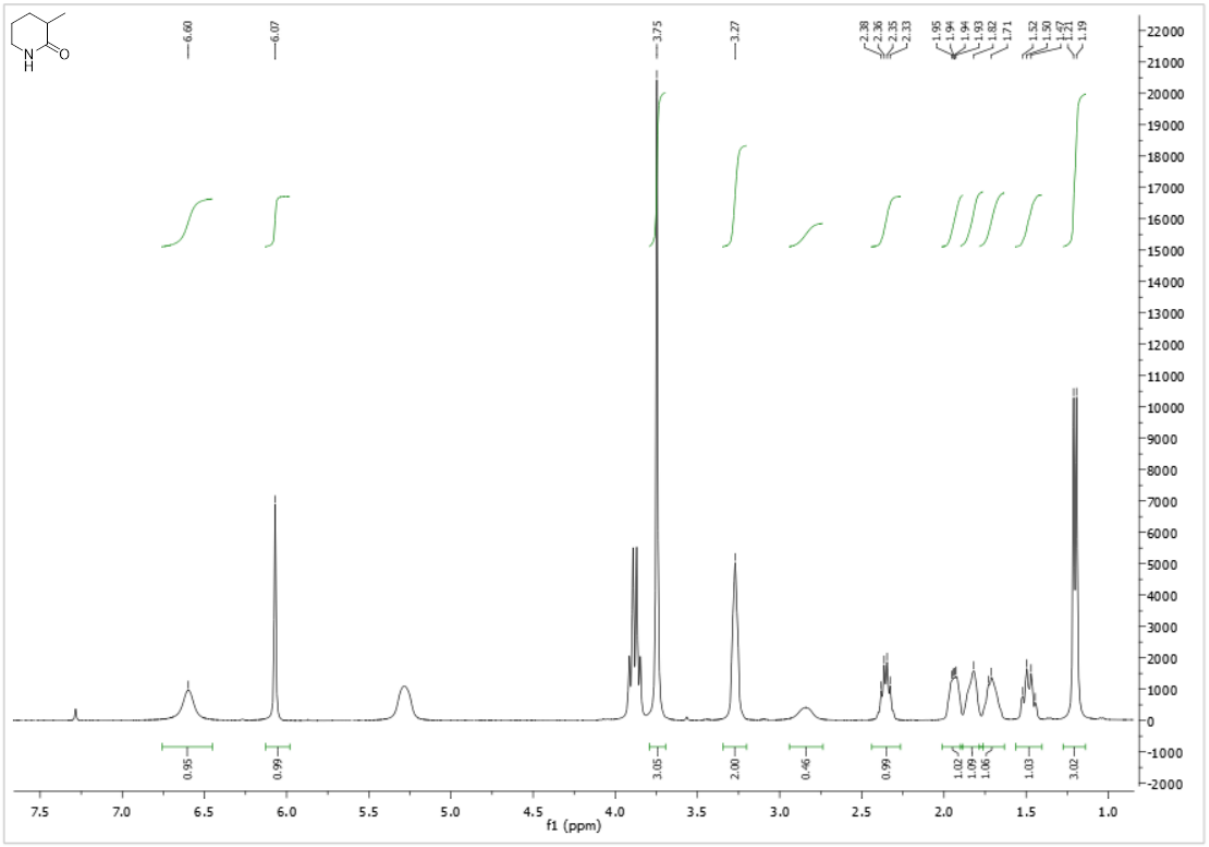


Figure 37 - ^{1}H NMR of 3-methylpiperin-2-one (4b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

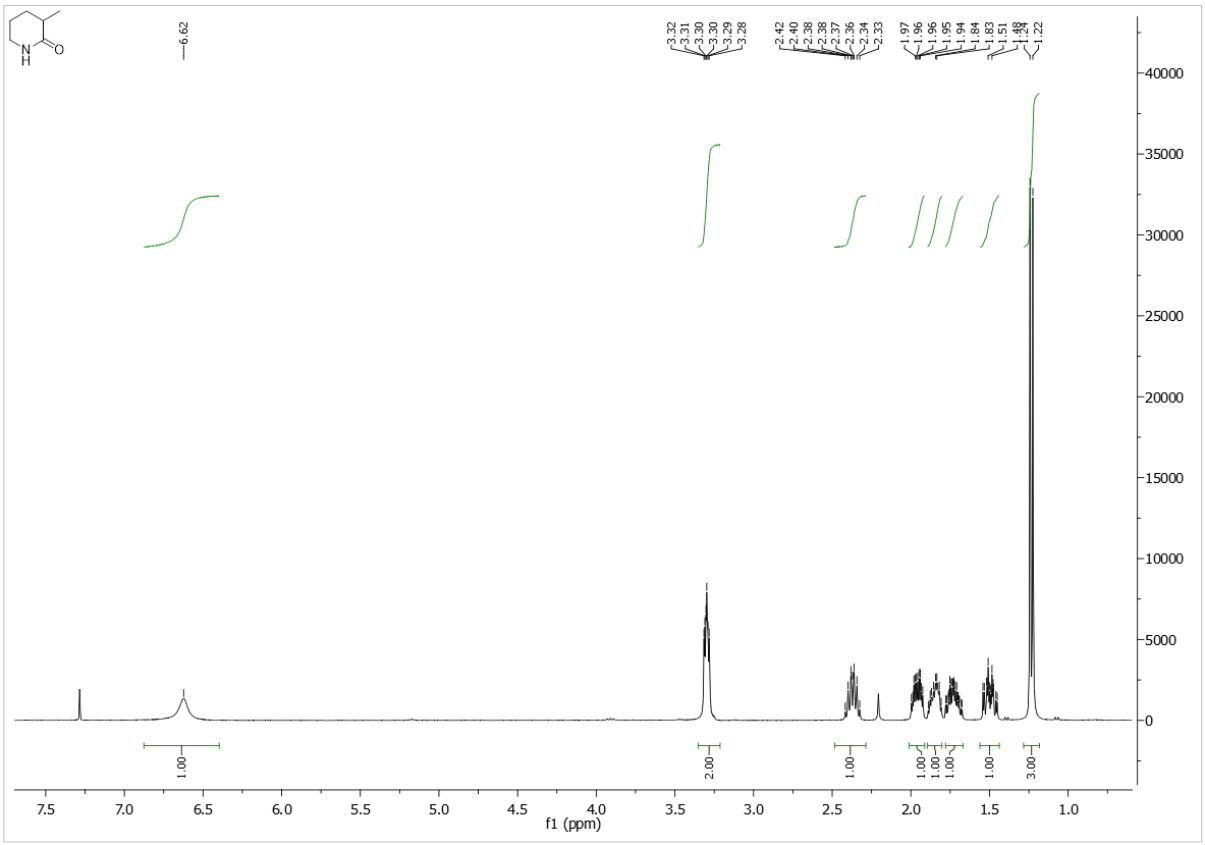


Figure 38 - ^{1}H NMR of purified 3-methylpiperin-2-one (4b) in $CDCl_3$.

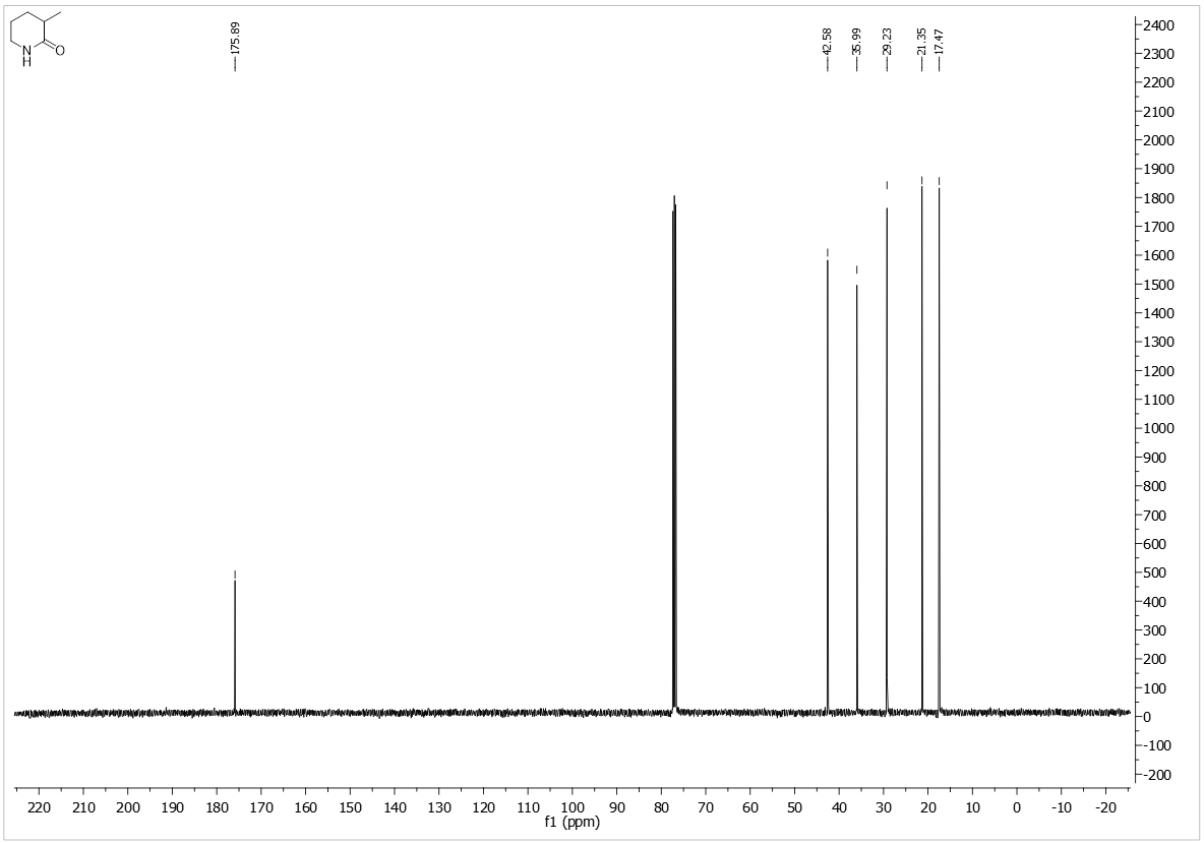


Figure 39 - ^{13}C NMR of purified 3-methylpiperin-2-one (4b) in $CDCl_3$.

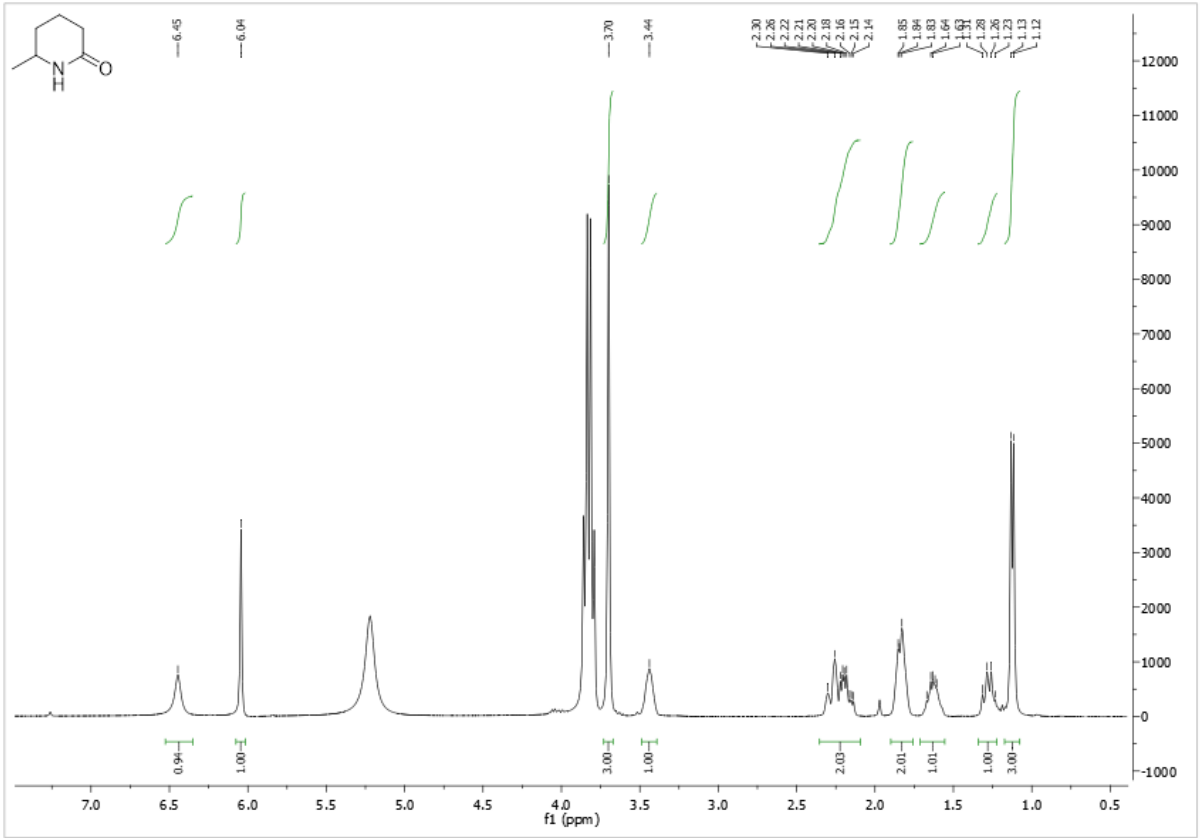


Figure 40 - ^{1}H NMR of 6-methylpiperin-2-one (4c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

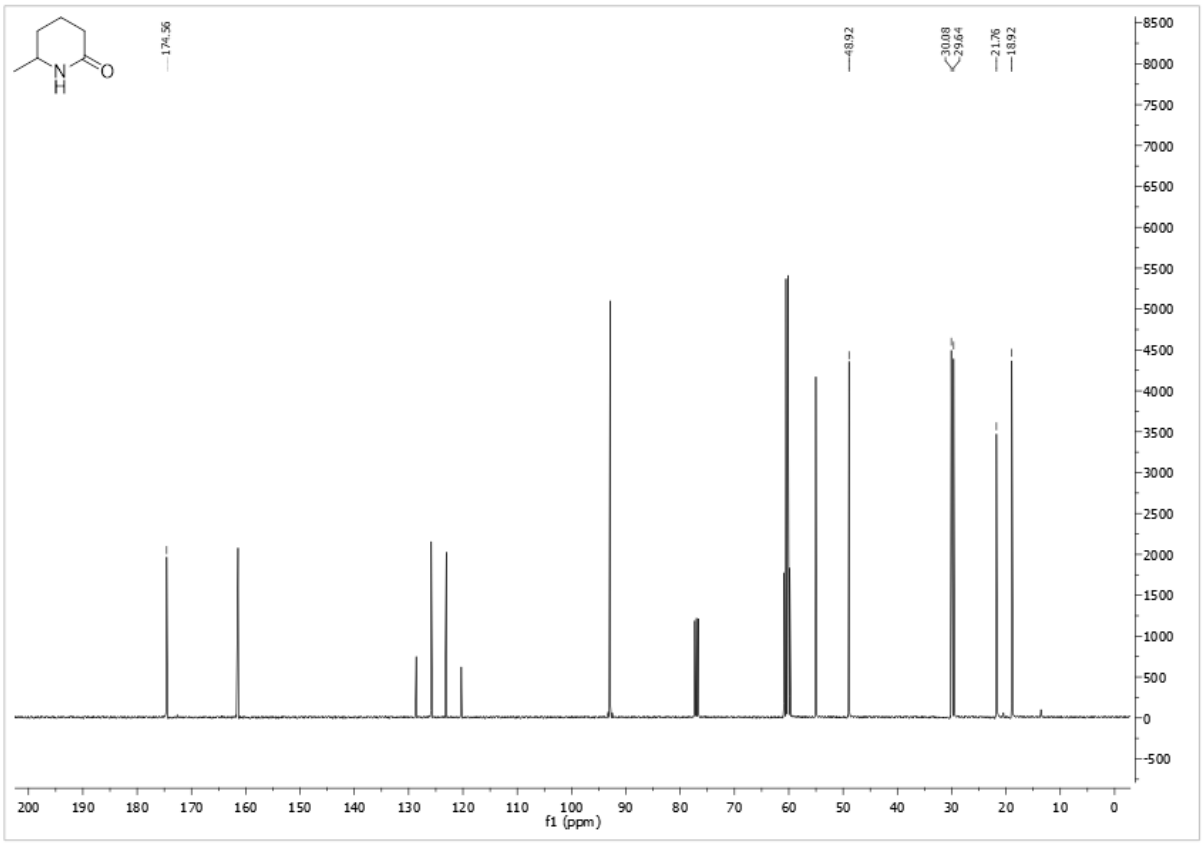


Figure 41 - ^{13}C NMR of 6-methylpiperin-2-one (4c) in CDCl3. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

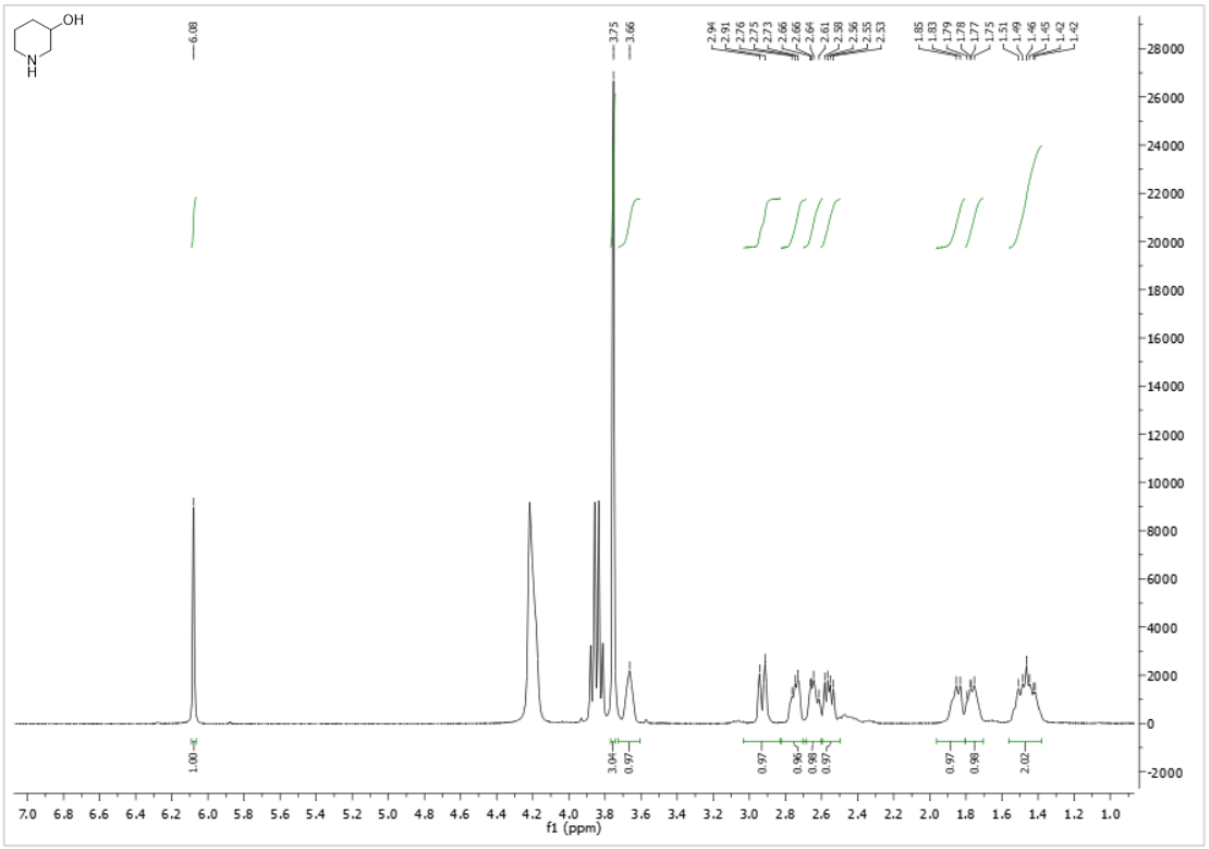


Figure 42 - ^{1}H NMR of 3-hydroxypiperidine (4d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

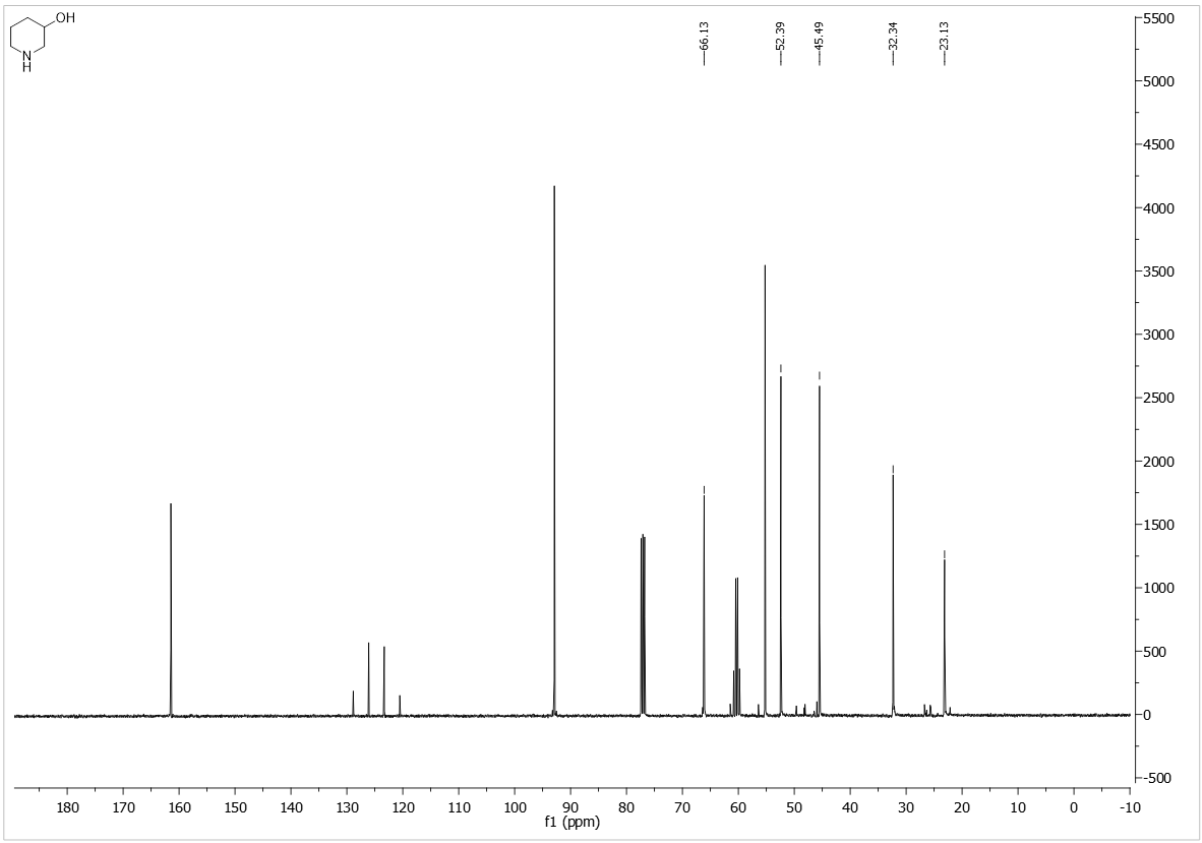


Figure 43 - ^{13}C NMR of 3-hydroxypiperidine (4d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

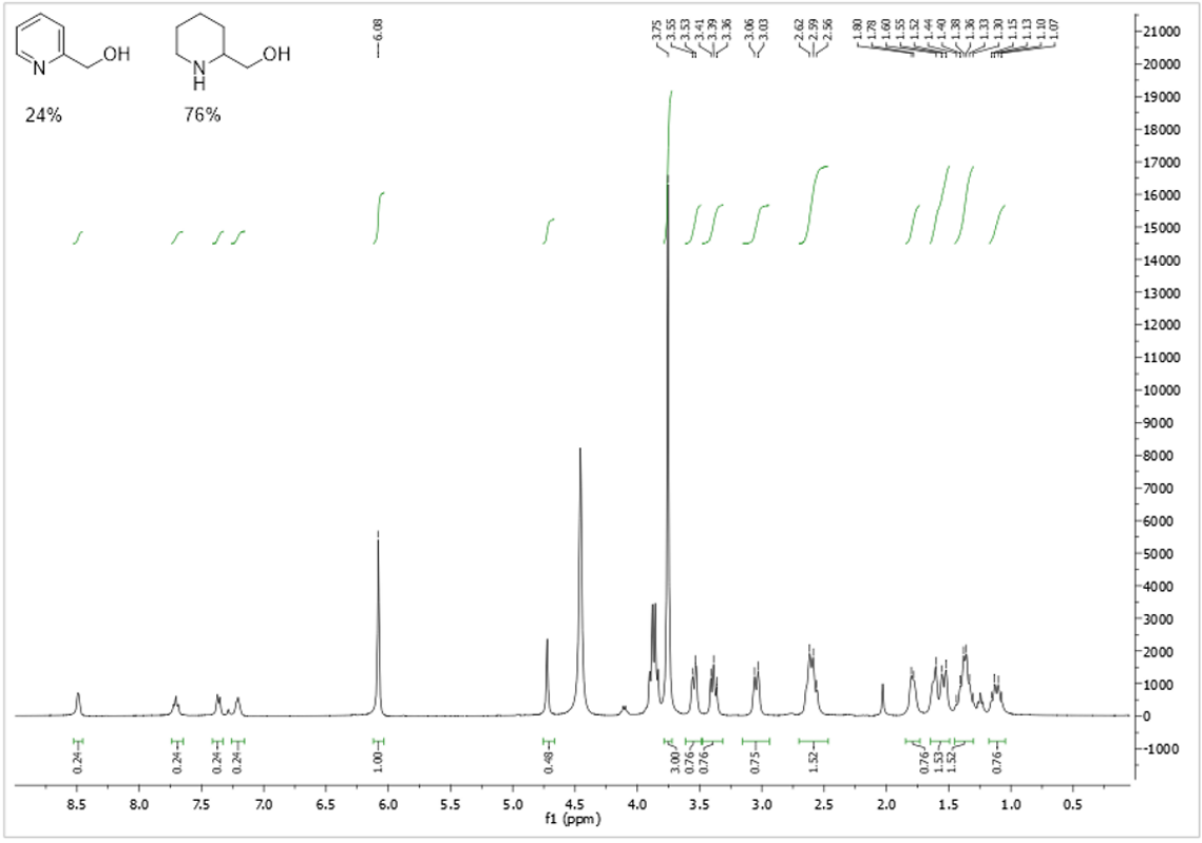


Figure 44 - ^{1}H NMR of 2-piperidinemethanol (4e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

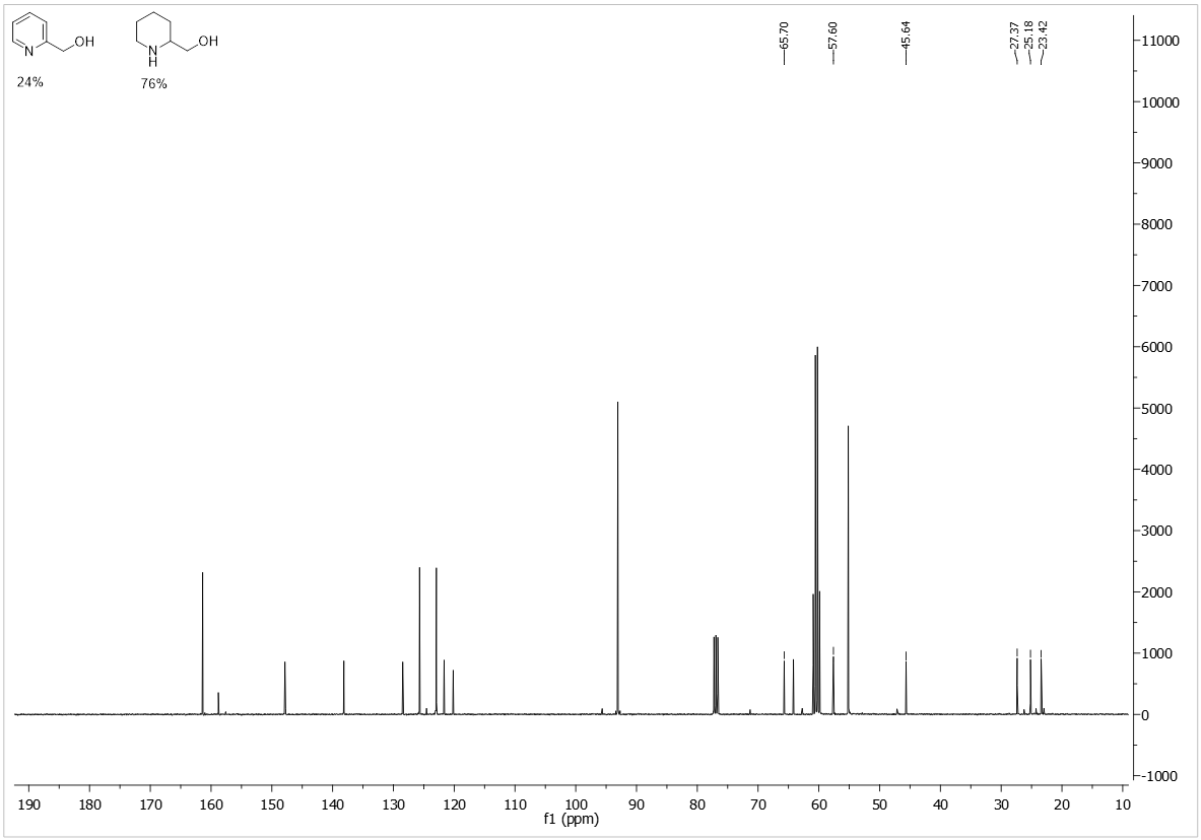


Figure 45 - ^{13}C NMR of 2-piperidinemethanol (4e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

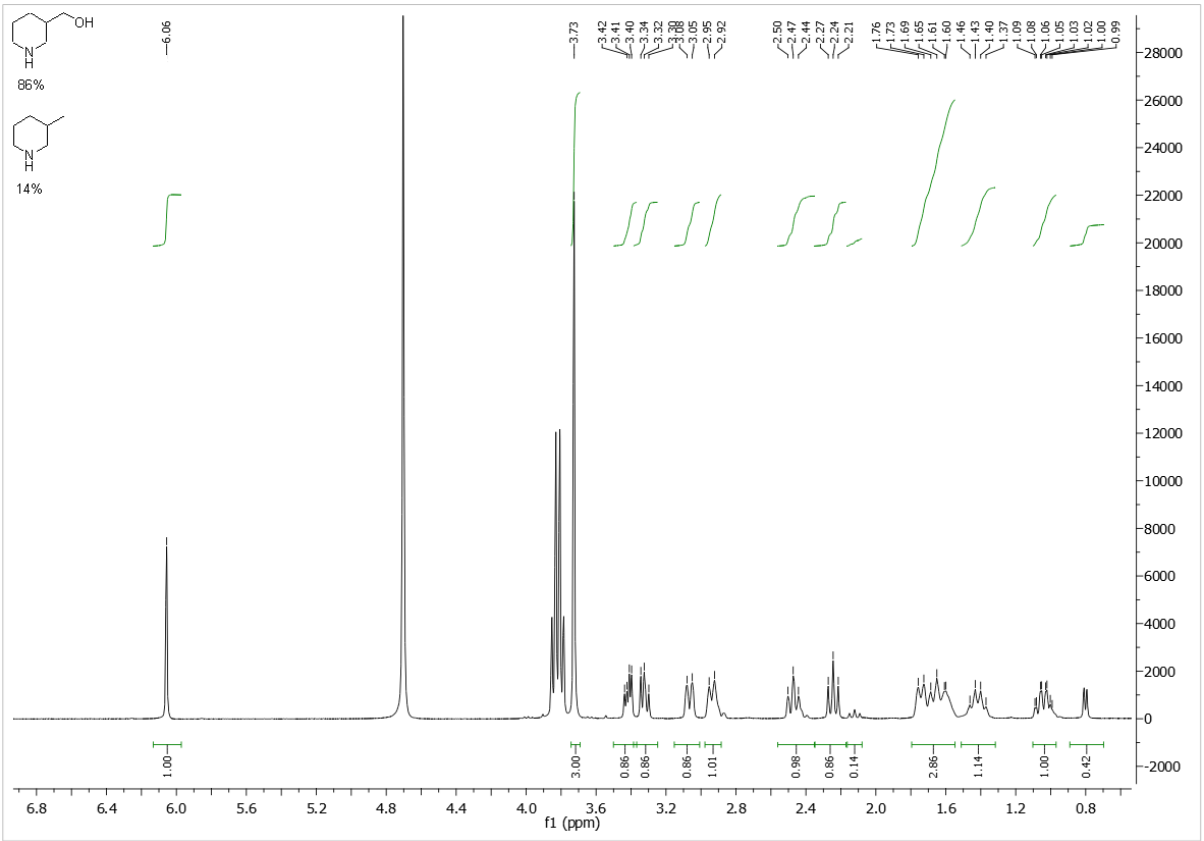


*Figure 46 - ^{1}H NMR of 3-piperidinemethanol (4f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. 86% desired product and 14% 3-methyl piperidine (**2c**), compare with Figure 5.*

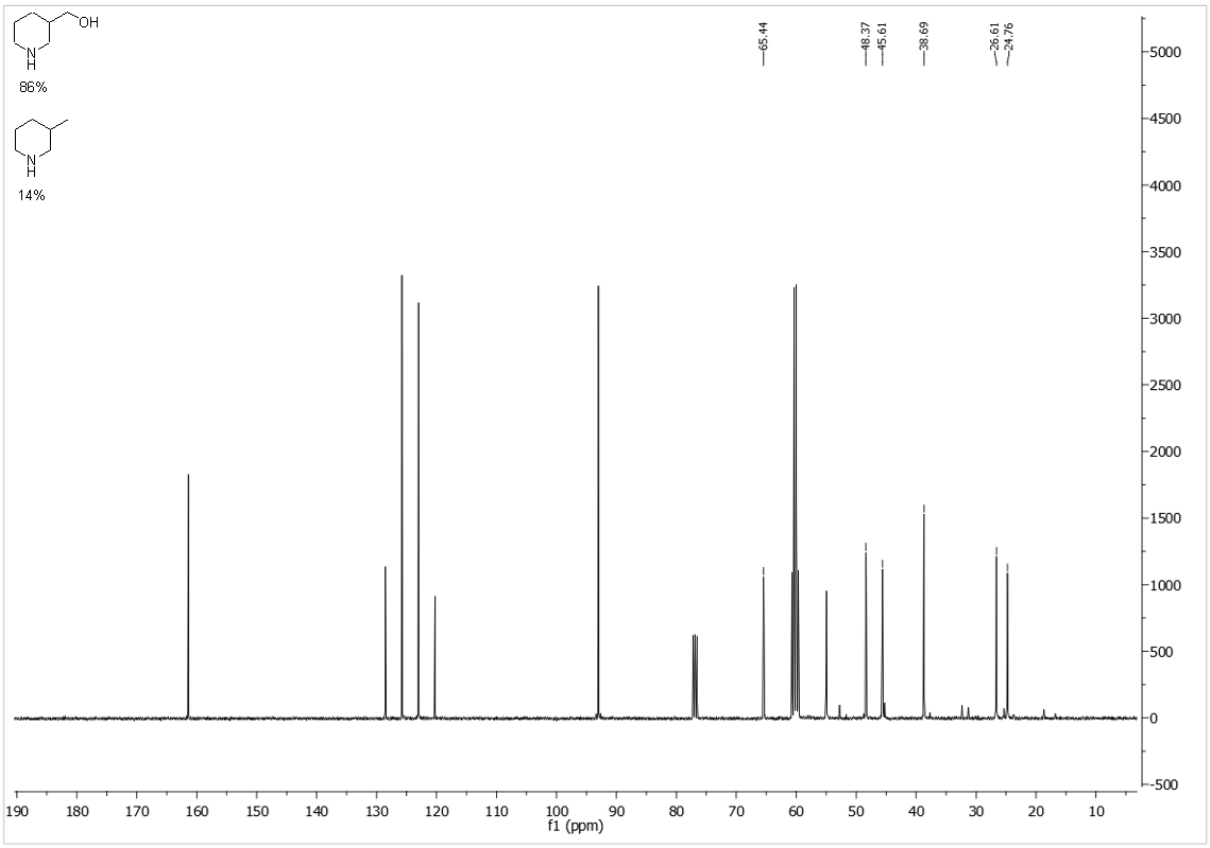


Figure 47 - ^{13}C NMR of 3-piperidinemethanol (4f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

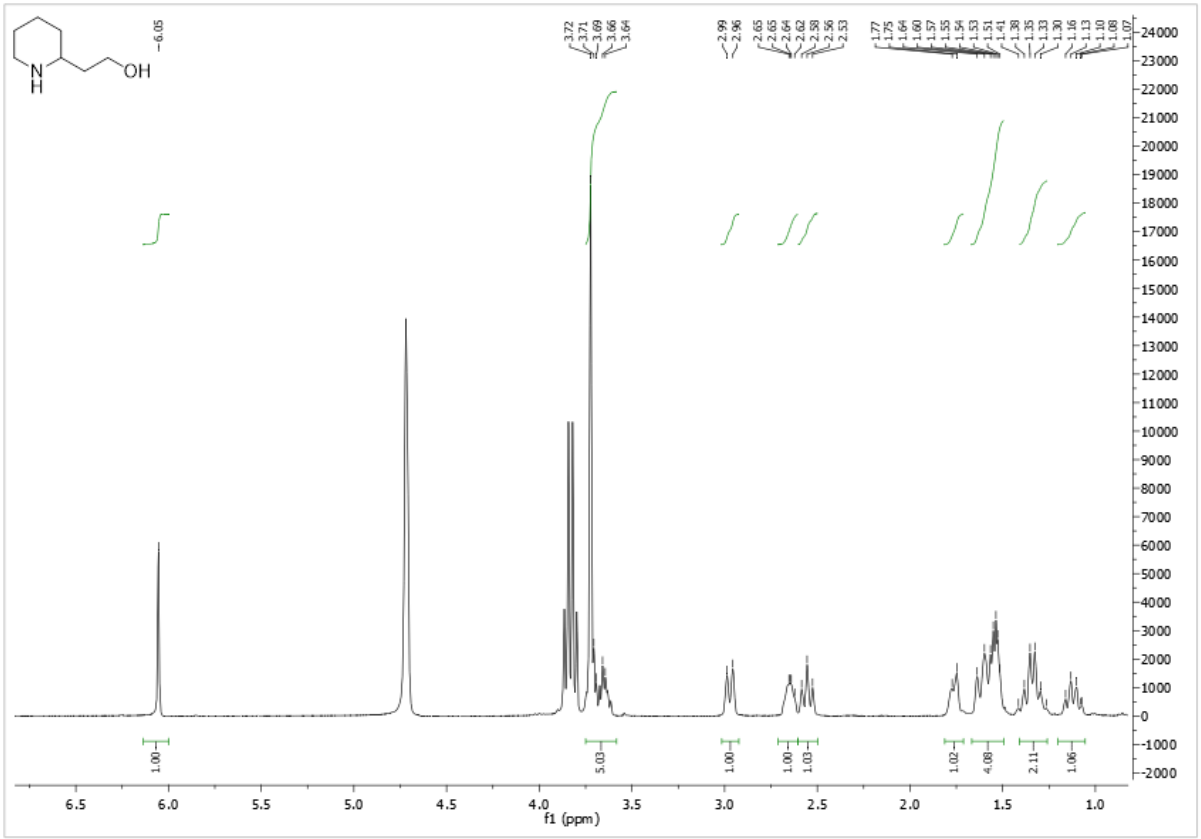


Figure 48 - ^{1}H NMR of 2-piperidineethanol (4g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

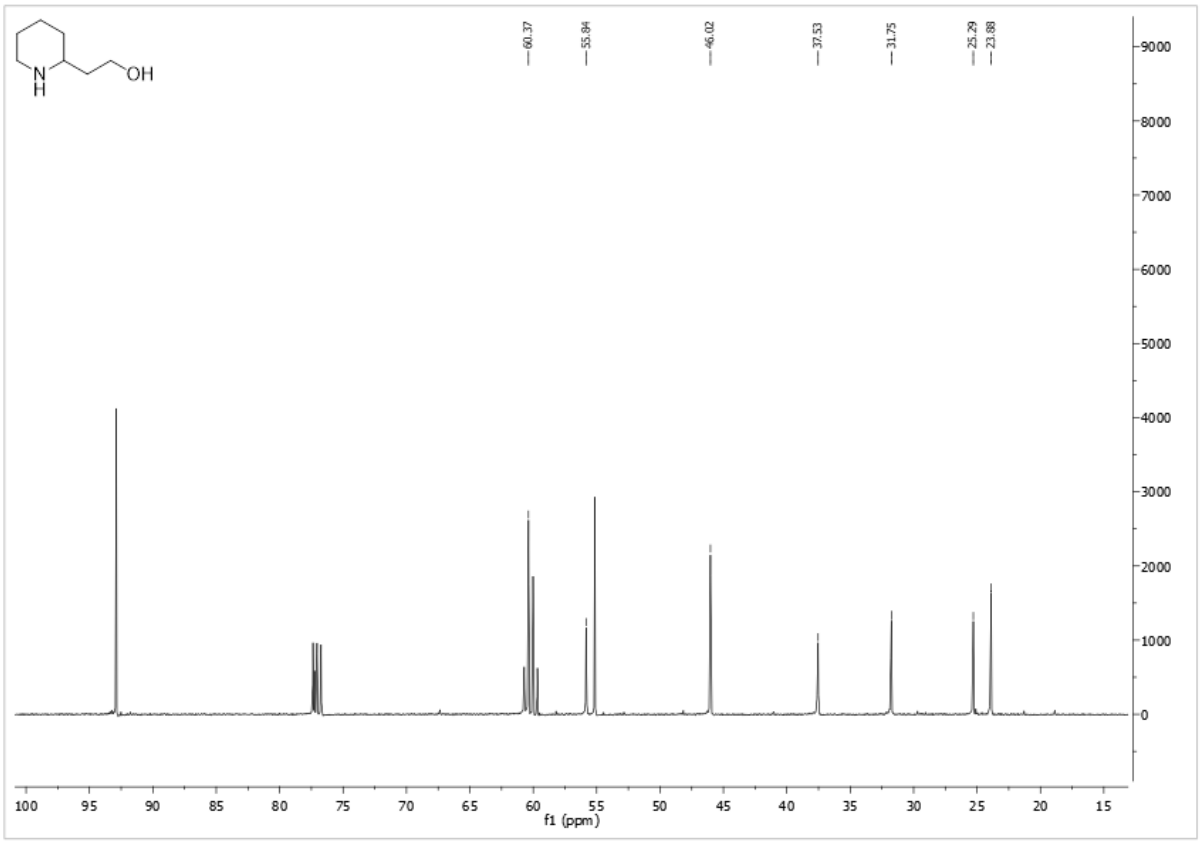


Figure 49 - ^{13}C NMR of 2-piperidineethanol (4g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

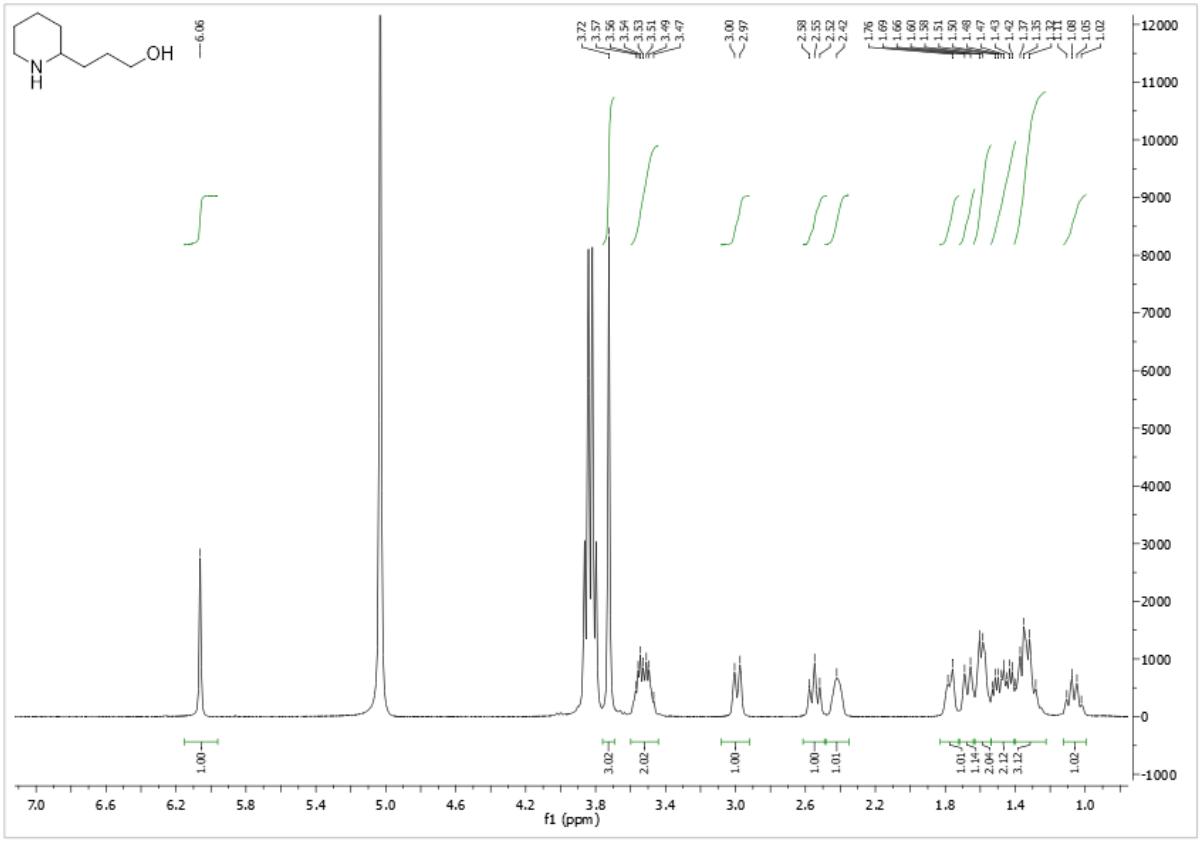


Figure 50 - ^{1}H NMR of 3-(piperidin-2-yl)propan-1-ol (4h) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

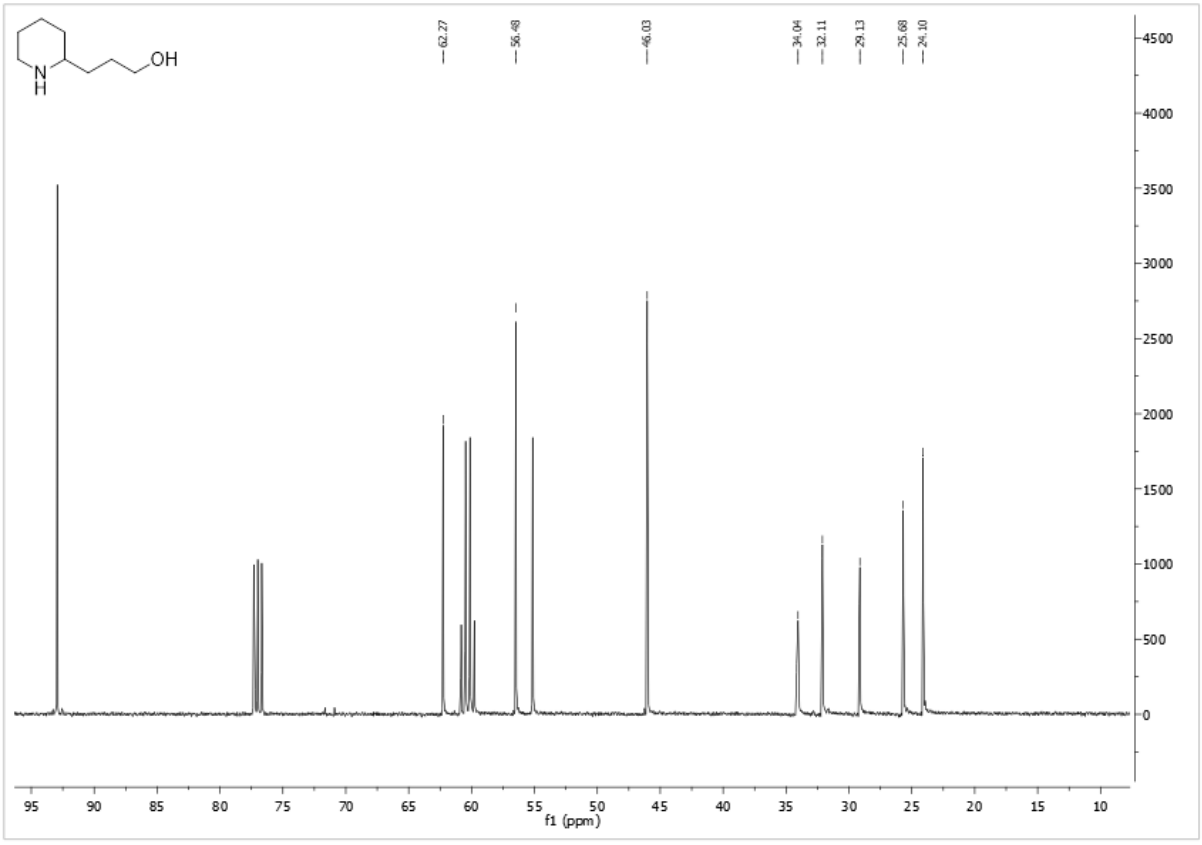


Figure 51 - ^{13}C NMR of 3-(piperidin-2-yl)propan-1-ol (4h) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

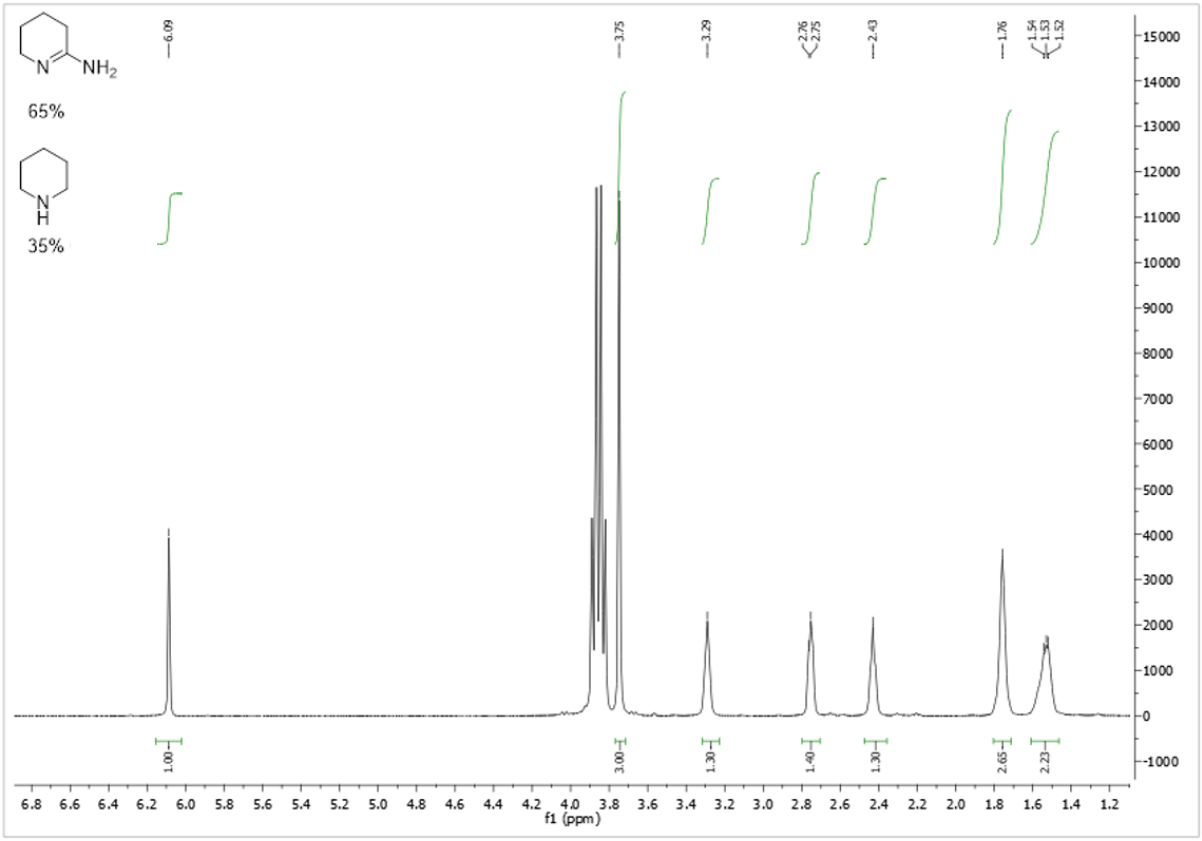


Figure 52 – ^{1}H NMR of 3,4,5,6-tetrahydropyridin-2-amine (6a) in $CDCl_3$ after 16 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

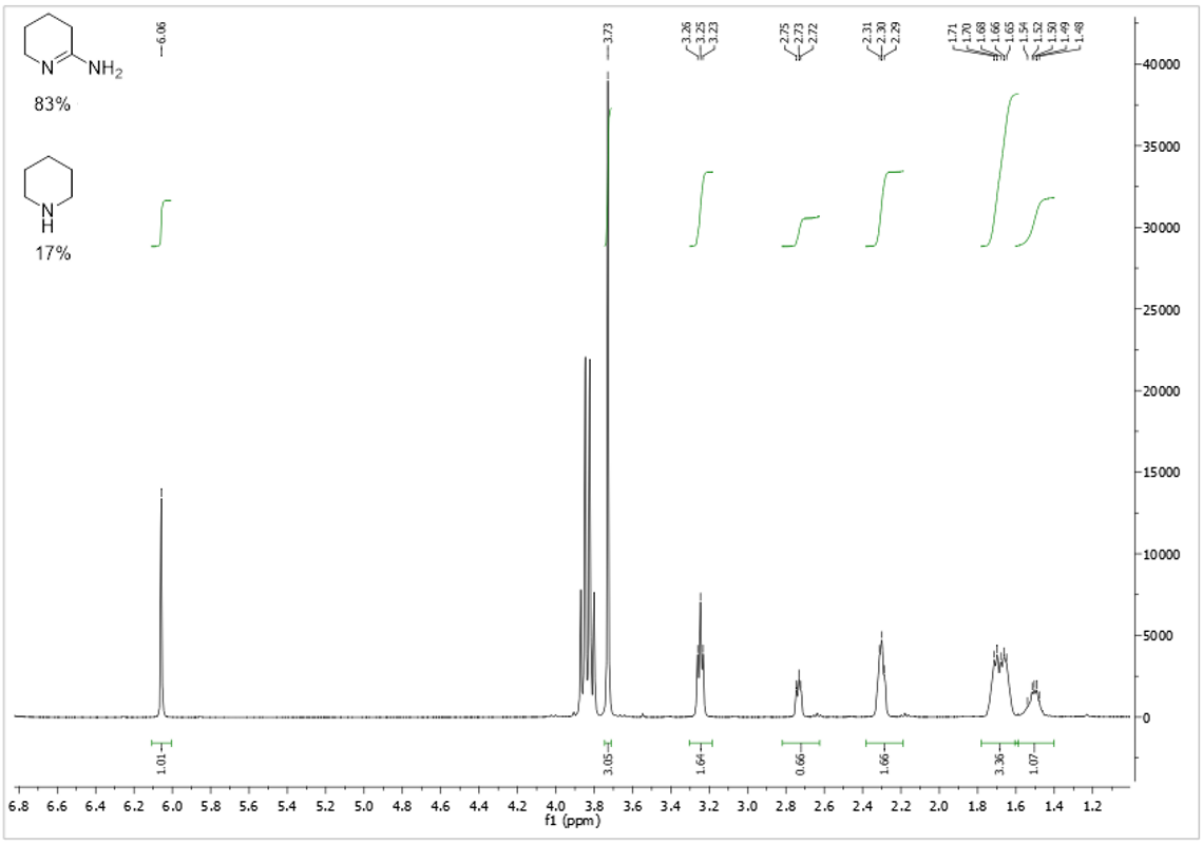


Figure 53 - ^{1}H NMR of 3,4,5,6-tetrahydropyridin-2-amine (6a) in $CDCl_3$ after 5 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

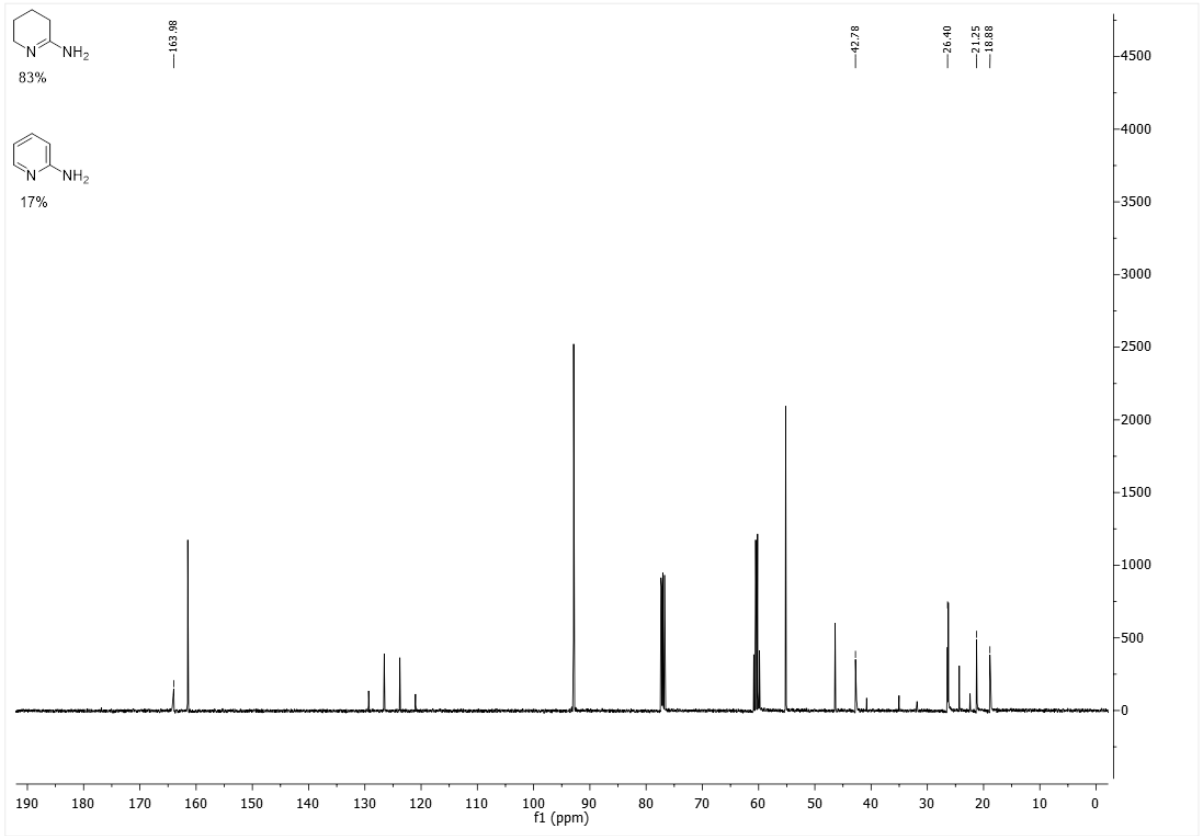


Figure 54 - ^{13}C NMR of 3,4,5,6-tetrahydropyridin-2-amine (6a) in $CDCl_3$ after 5 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

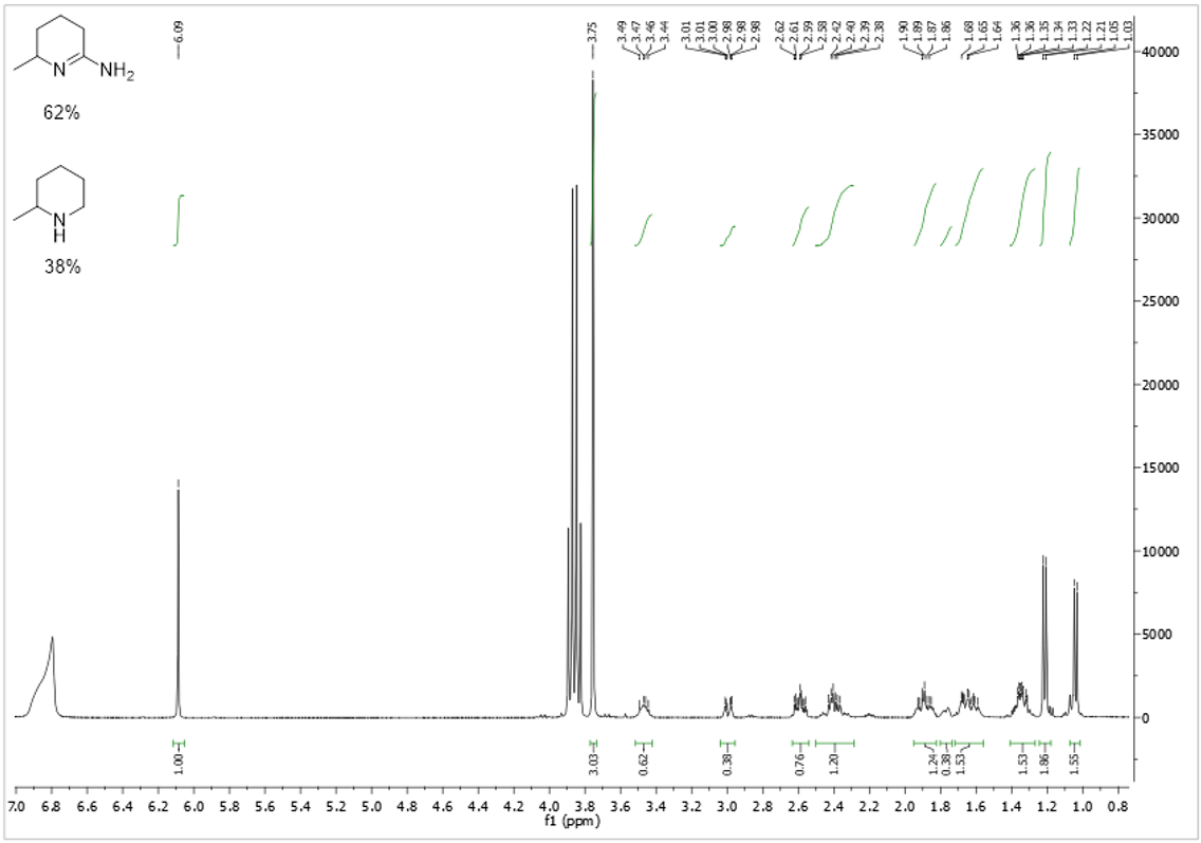


Figure 55 - ^{1}H NMR of 6-methyl-3,4,5,6-tetrahydropyridin-2-amine (6b) in $CDCl_3$ for 16 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

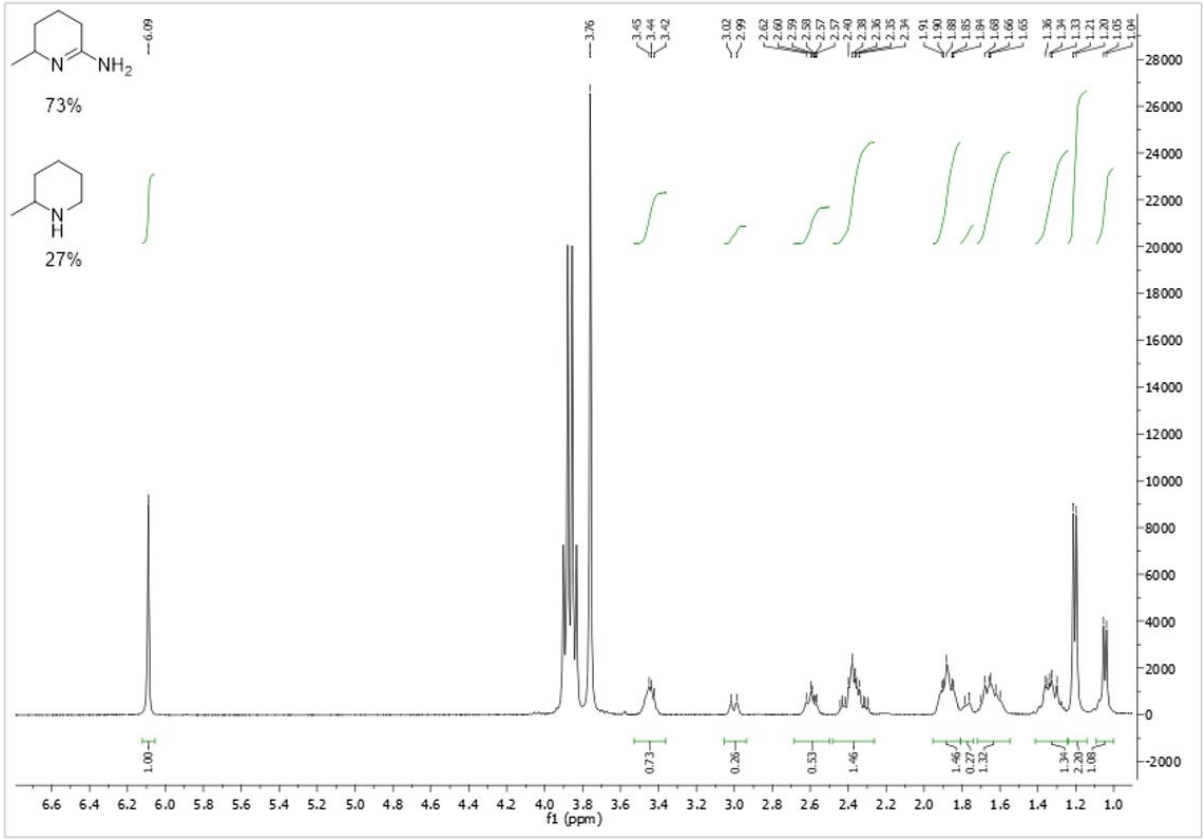


Figure 56 - ^{1}H NMR of 6-methyl-3,4,5,6-tetrahydropyridin-2-amine (6b) in CDCl3 for 5 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

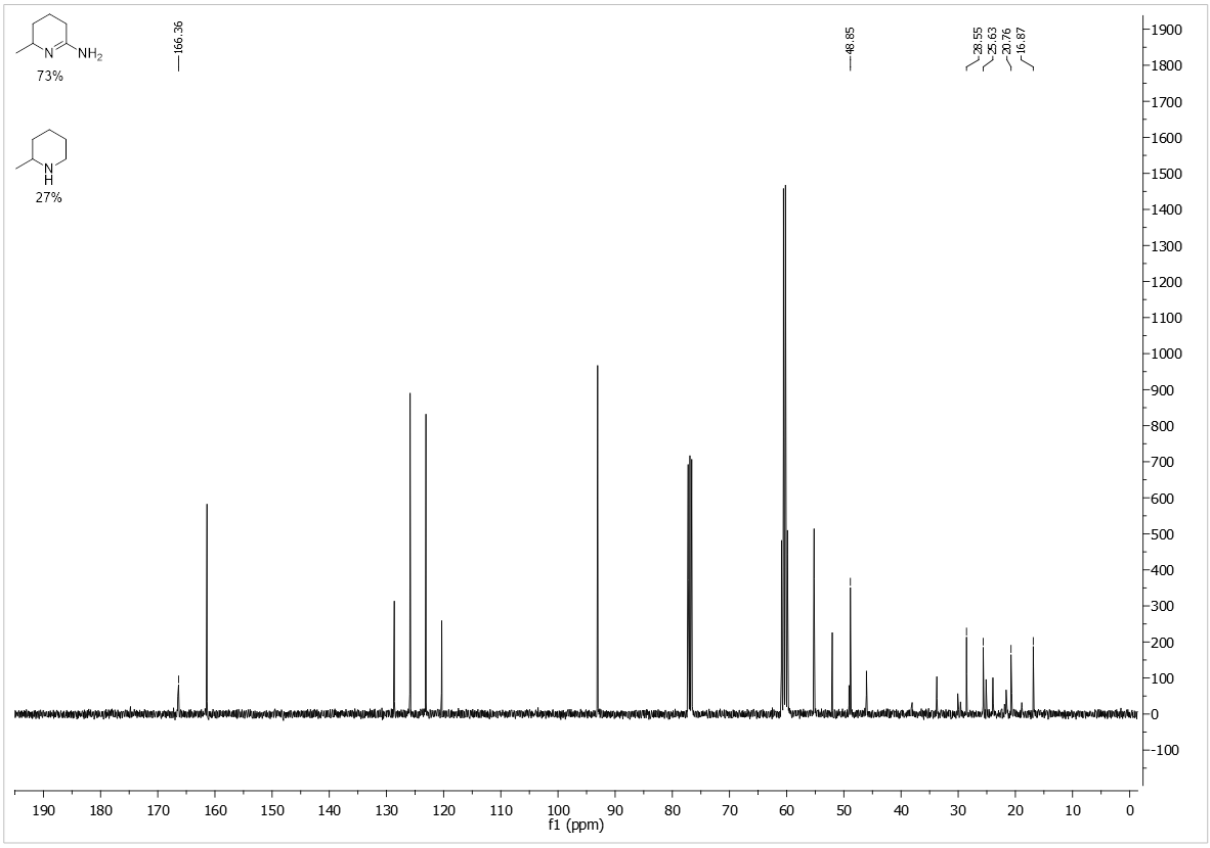


Figure 57 - ^{13}C NMR of 6-methyl-3,4,5,6-tetrahydropyridin-2-amine (6b) in $CDCl_3$ for 5 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

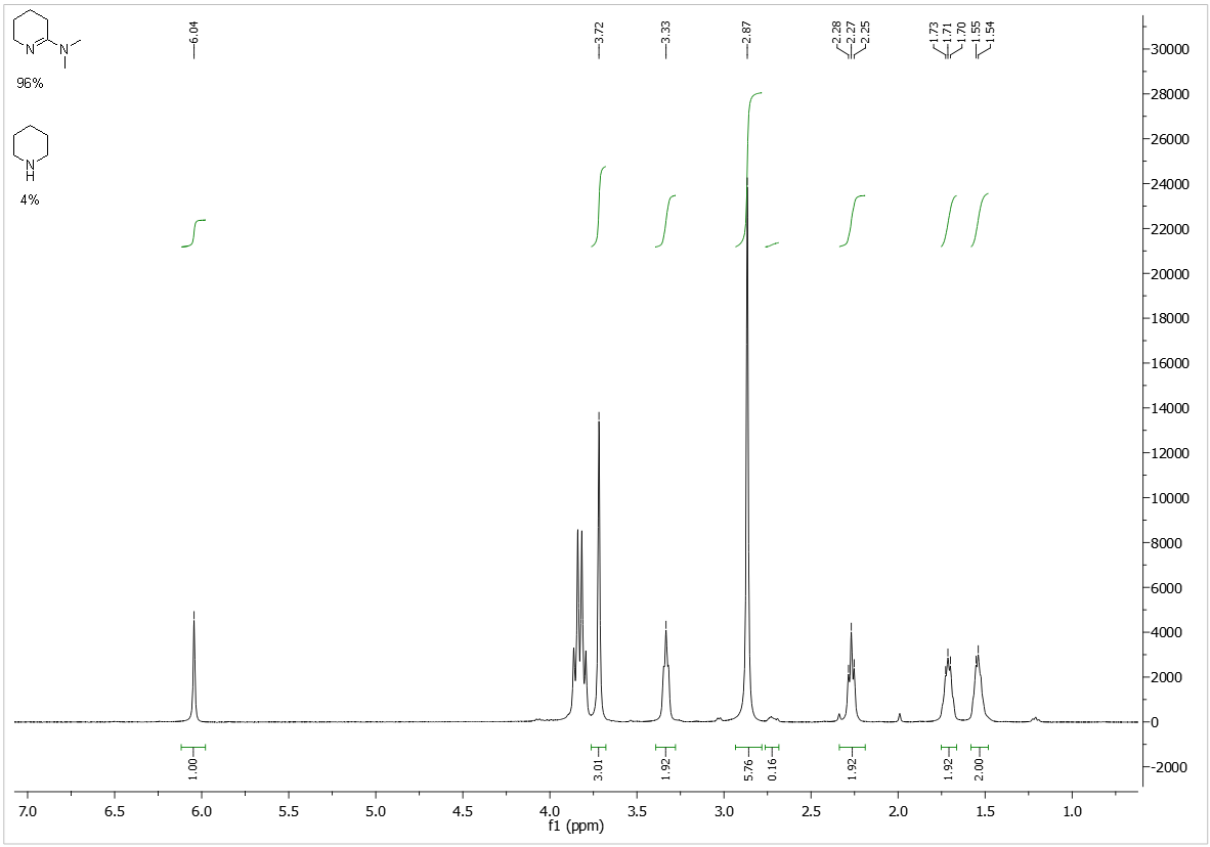


Figure 58 - ^{1}H NMR of N,N-dimethyl-3,4,5,6-tetrahydropyridin-2-amine (6c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

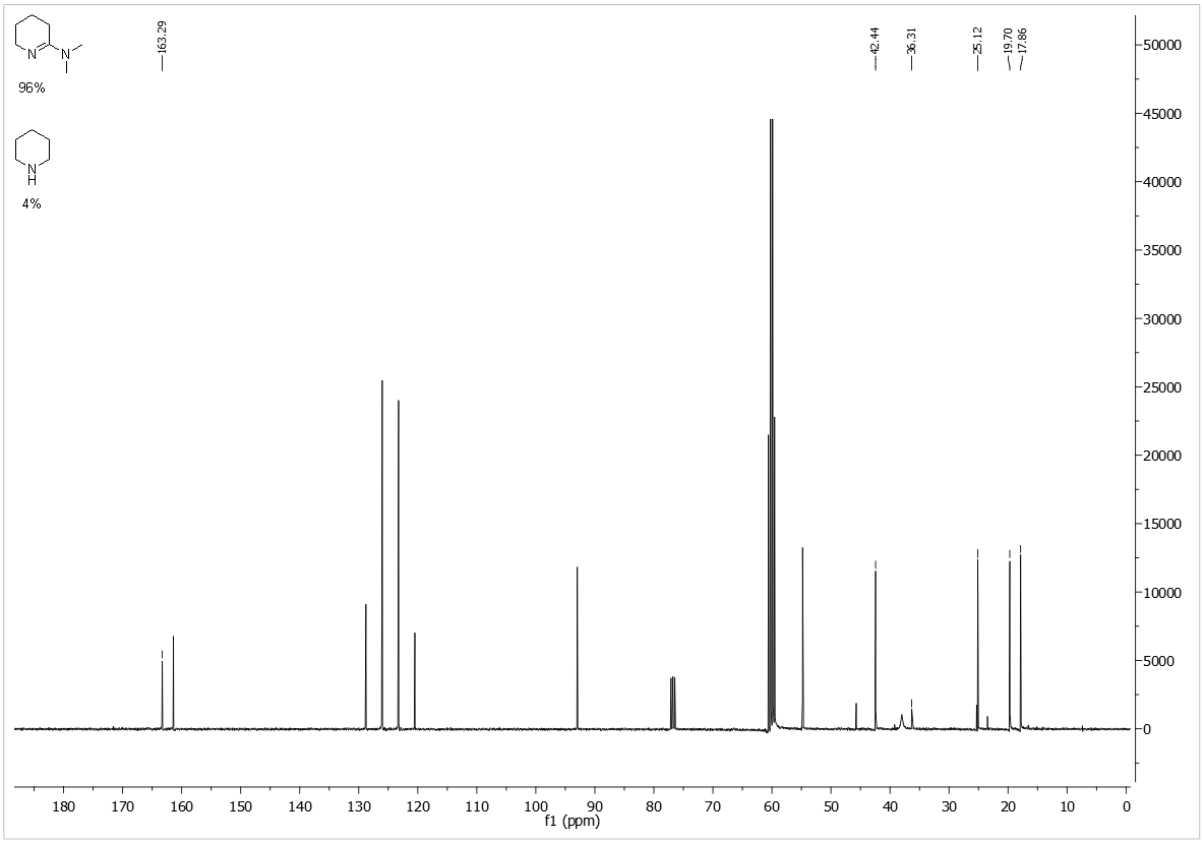


Figure 59 - ^{13}C NMR of N,N-dimethyl-3,4,5,6-tetrahydropyridin-2-amine (6c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

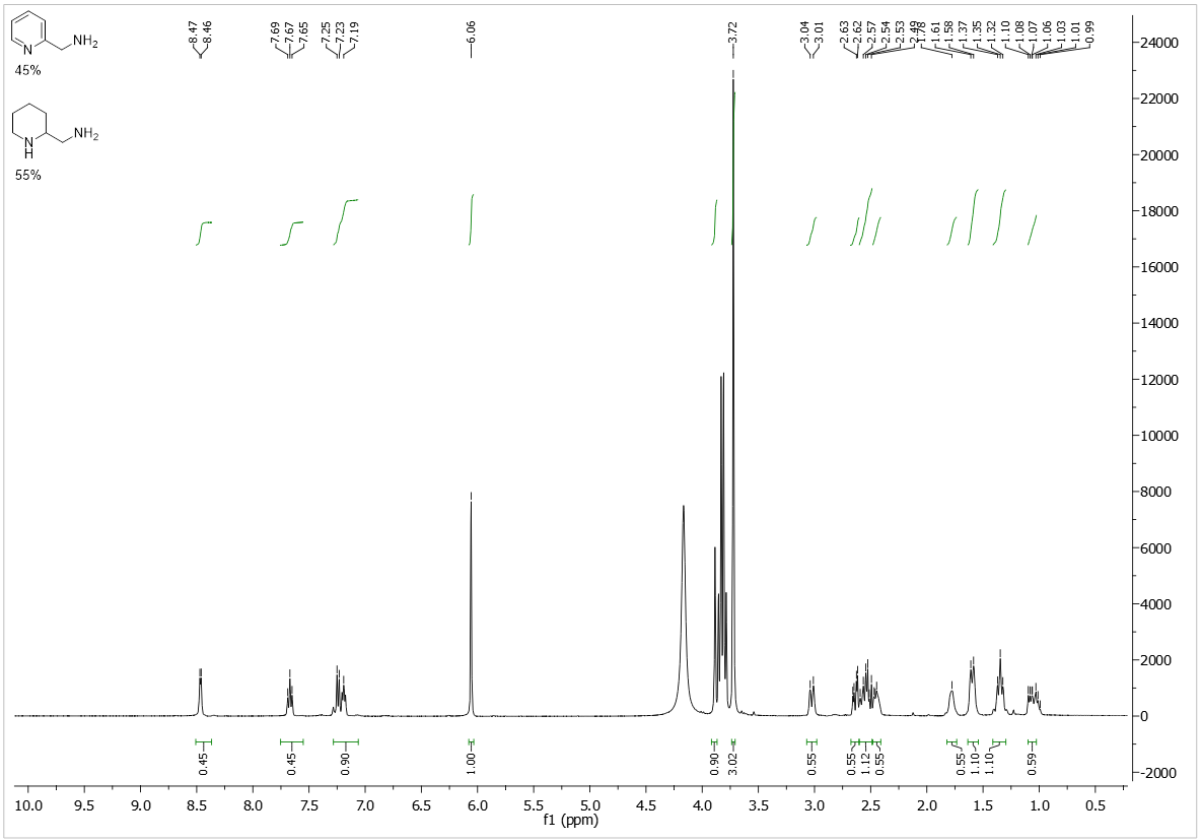


Figure 60 - ^{1}H NMR of piperidin-2-ylmethanamine (6d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

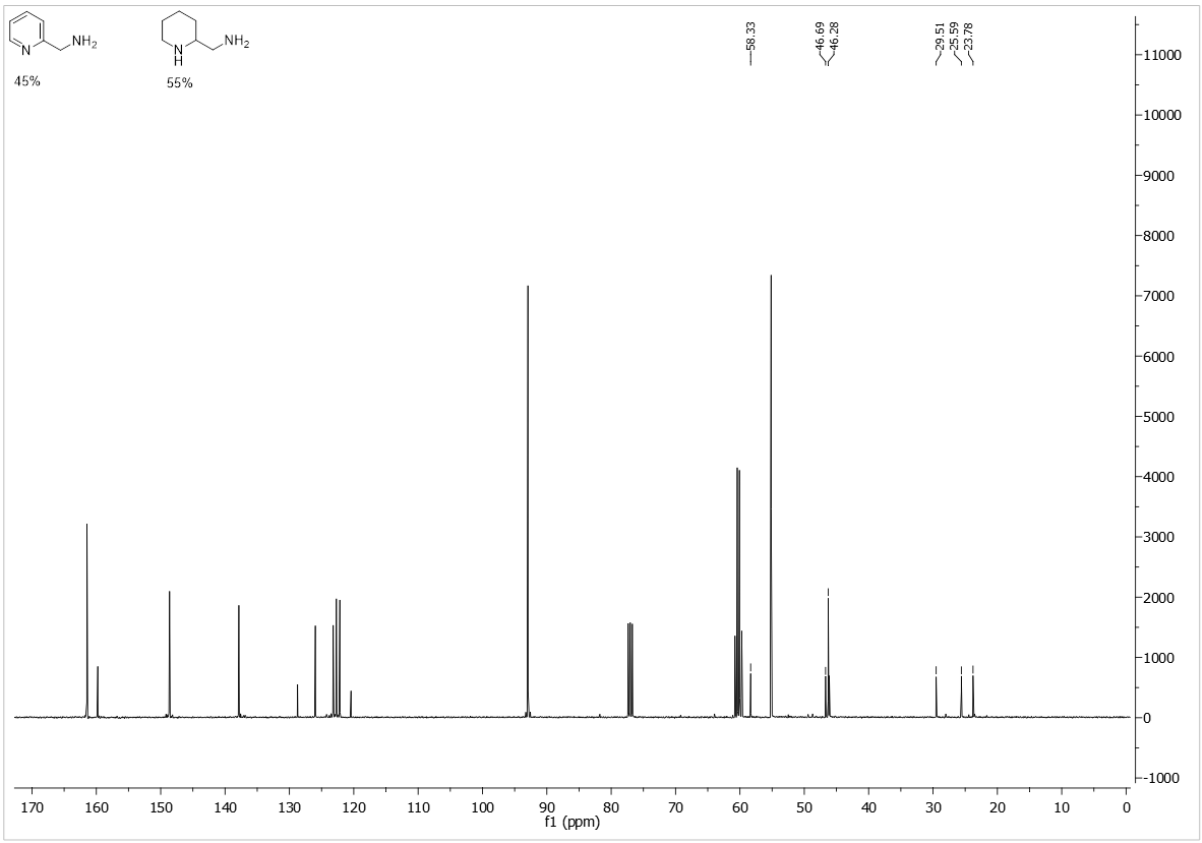


Figure 61 - ^{13}C NMR of piperidin-2-ylmethanamine (6d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

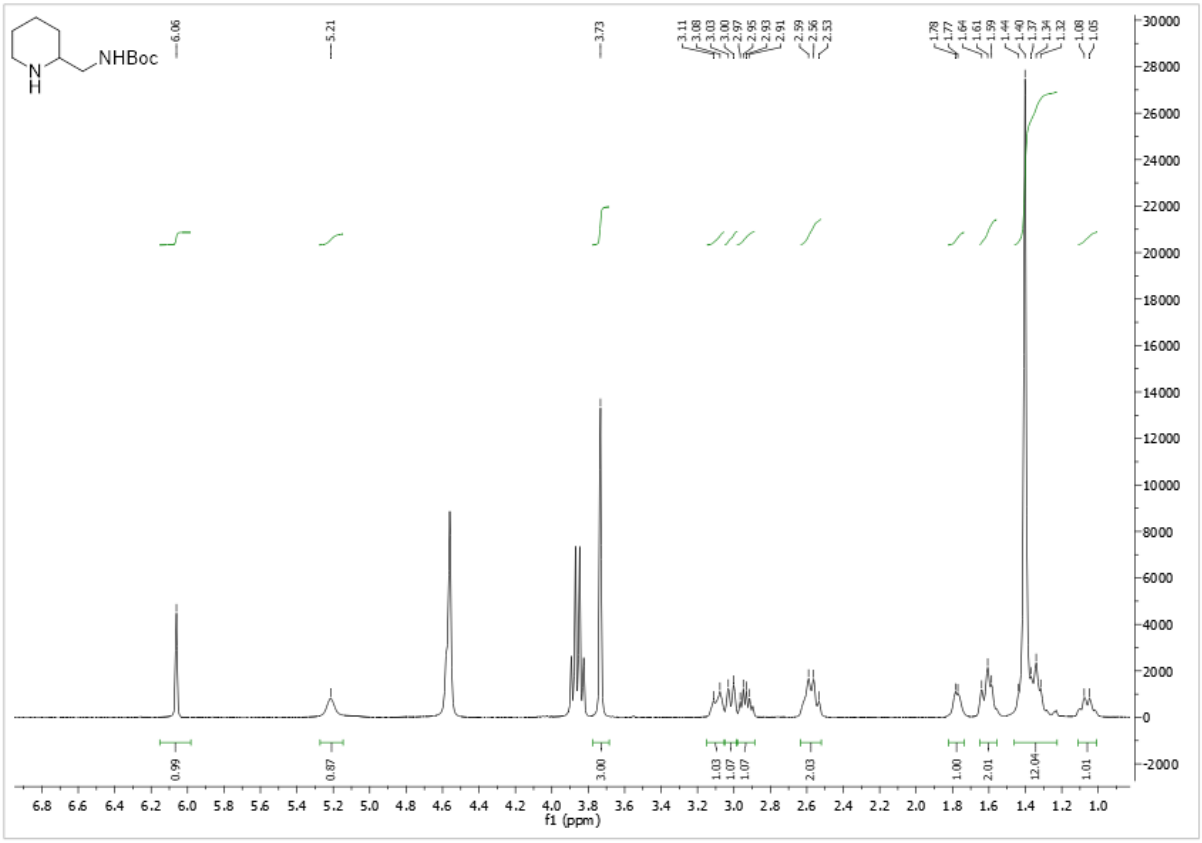


Figure 62 - ^{1}H NMR of tert-butyl (piperidin-2-ylmethyl)carbamate (6e) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

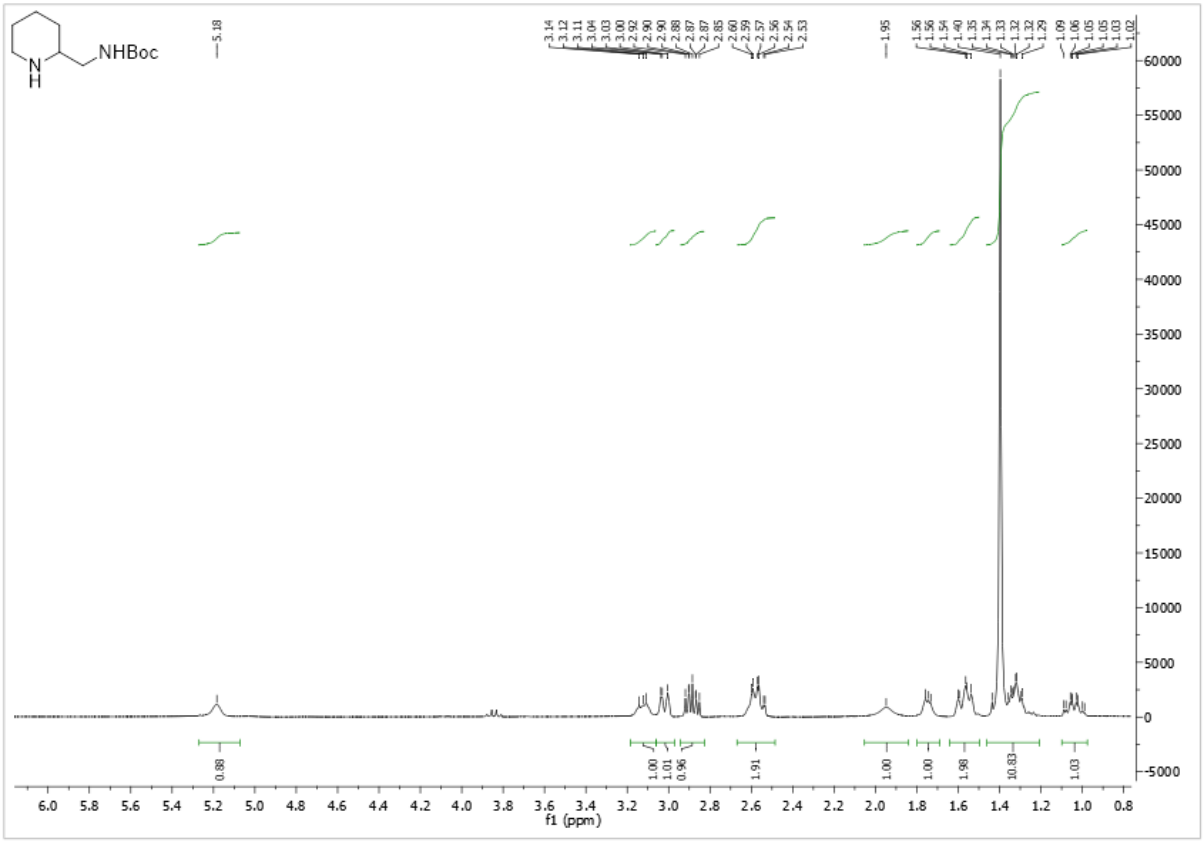


Figure 63 – ^{1}H NMR of purified tert-butyl (piperidin-2-ylmethyl)carbamate (6e) in $CDCl_3$.

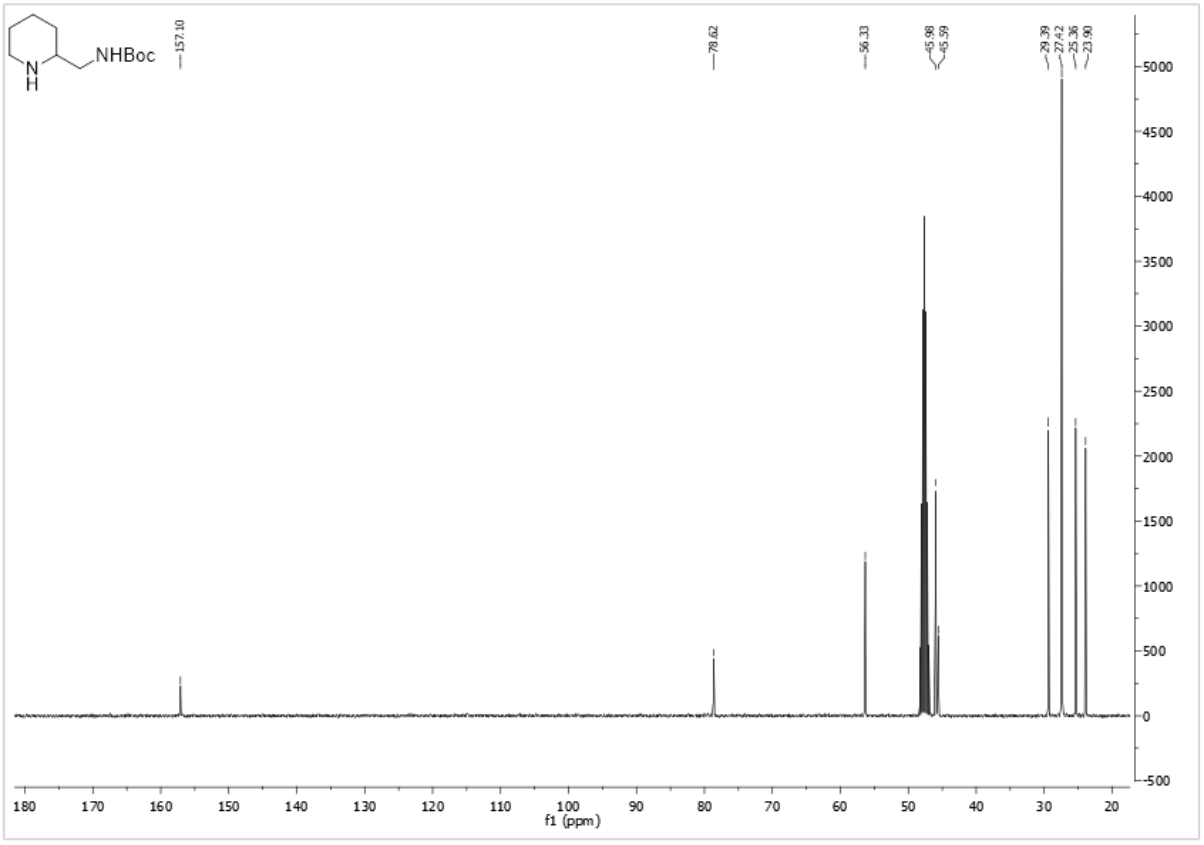


Figure 64 - ^{13}C NMR of purified tert-butyl (piperidin-2-ylmethyl)carbamate (6e) in $CDCl_3$.

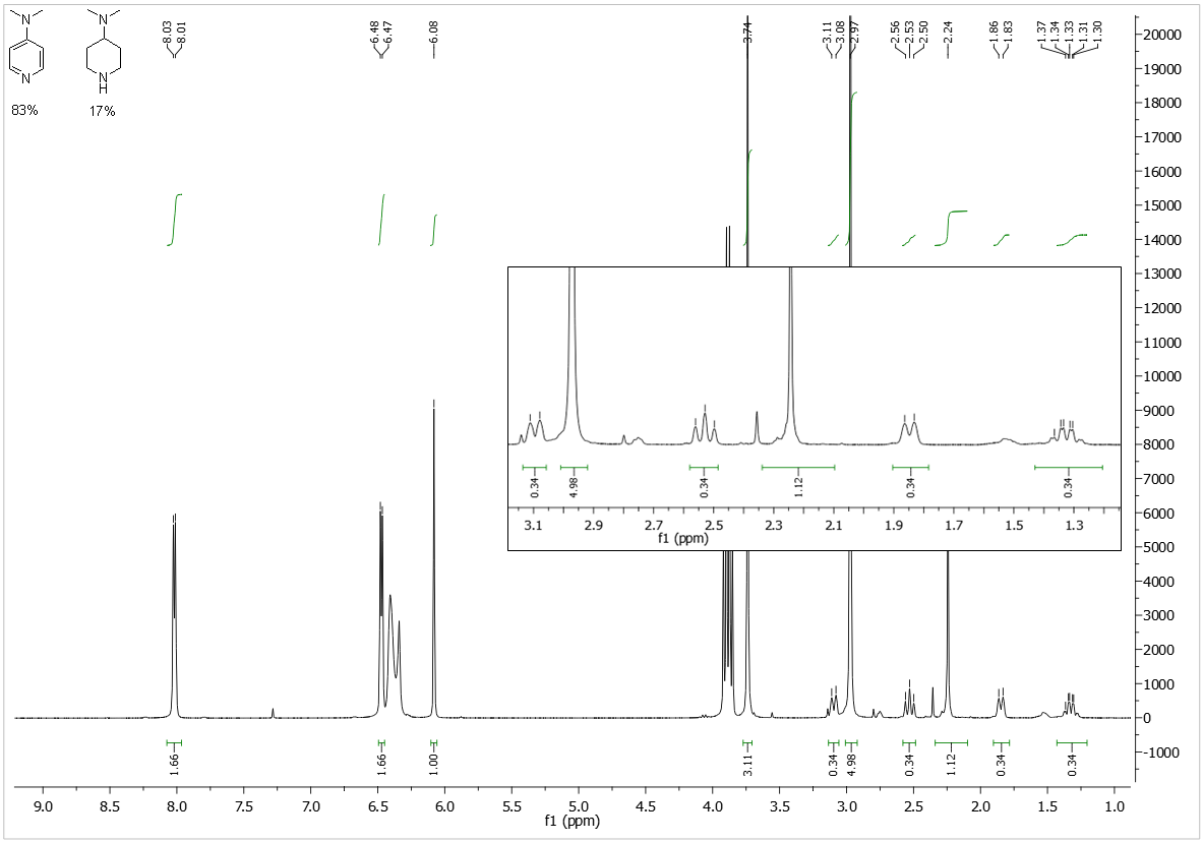


Figure 65 - ^{1}H NMR of N,N-dimethylpiperidin-4-amine (6f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Yield calculated from the remaining starting material and the product has been assigned tentatively based on the chemical shift, splitting and integration.

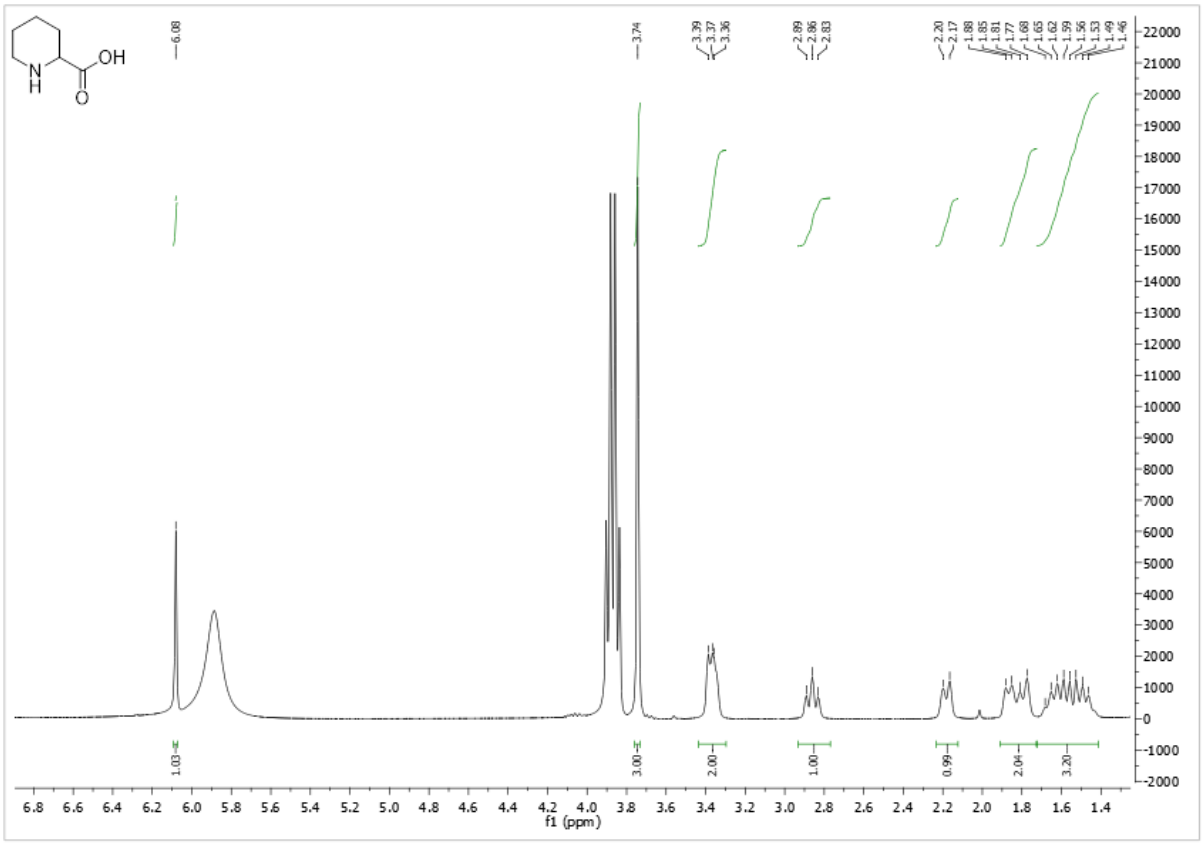


Figure 66 - ^{1}H NMR of piperidine-2-carboxylic acid (8a) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

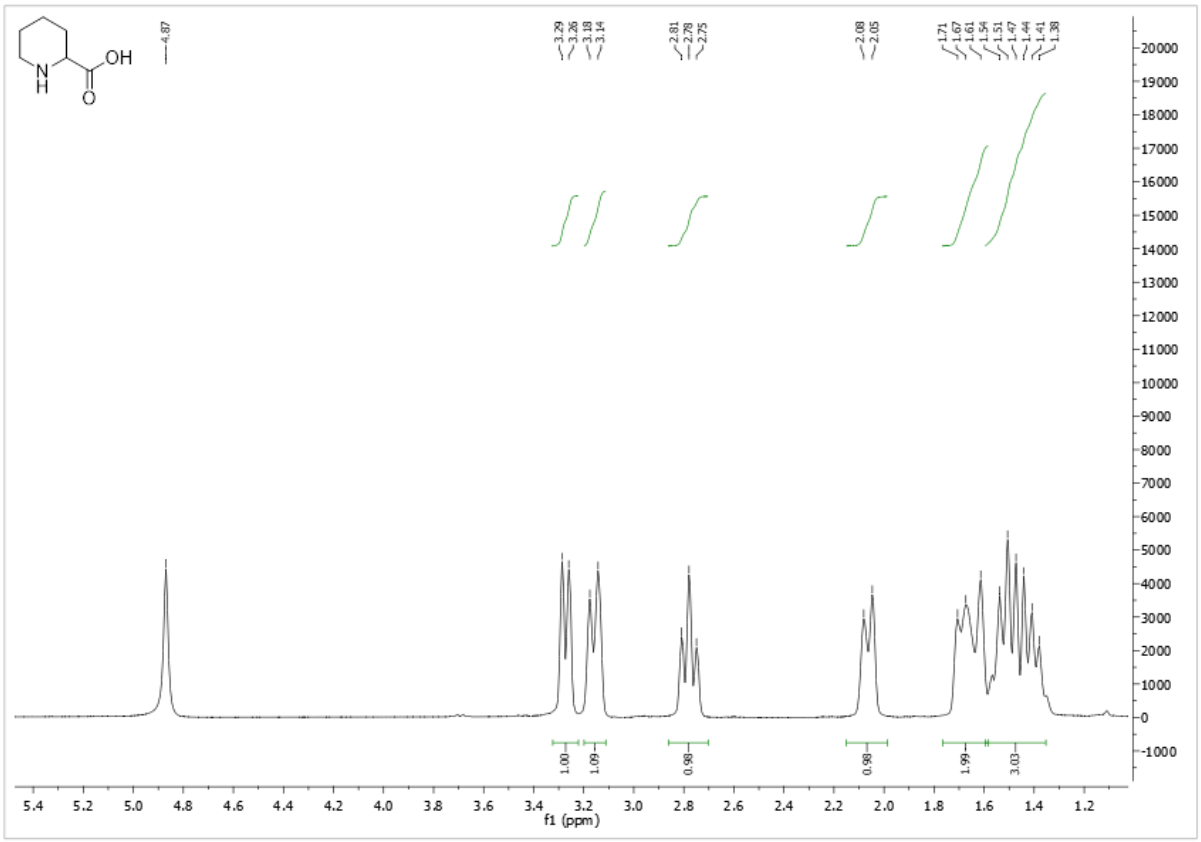


Figure 67 - ^{1}H NMR of purified piperidine-2-carboxylic acid (8a) in MeOD.

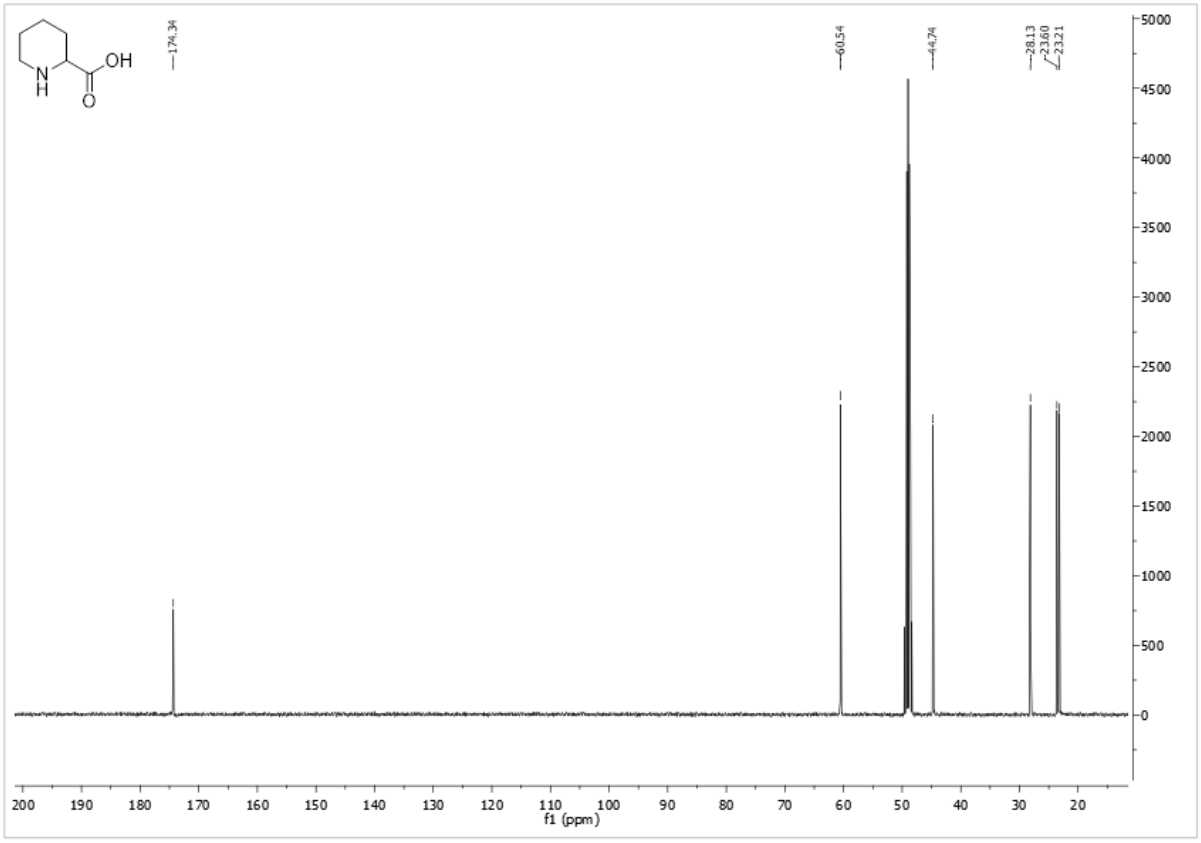


Figure 68 - ^{13}C NMR of purified piperidine-2-carboxylic acid (8a) in MeOD.

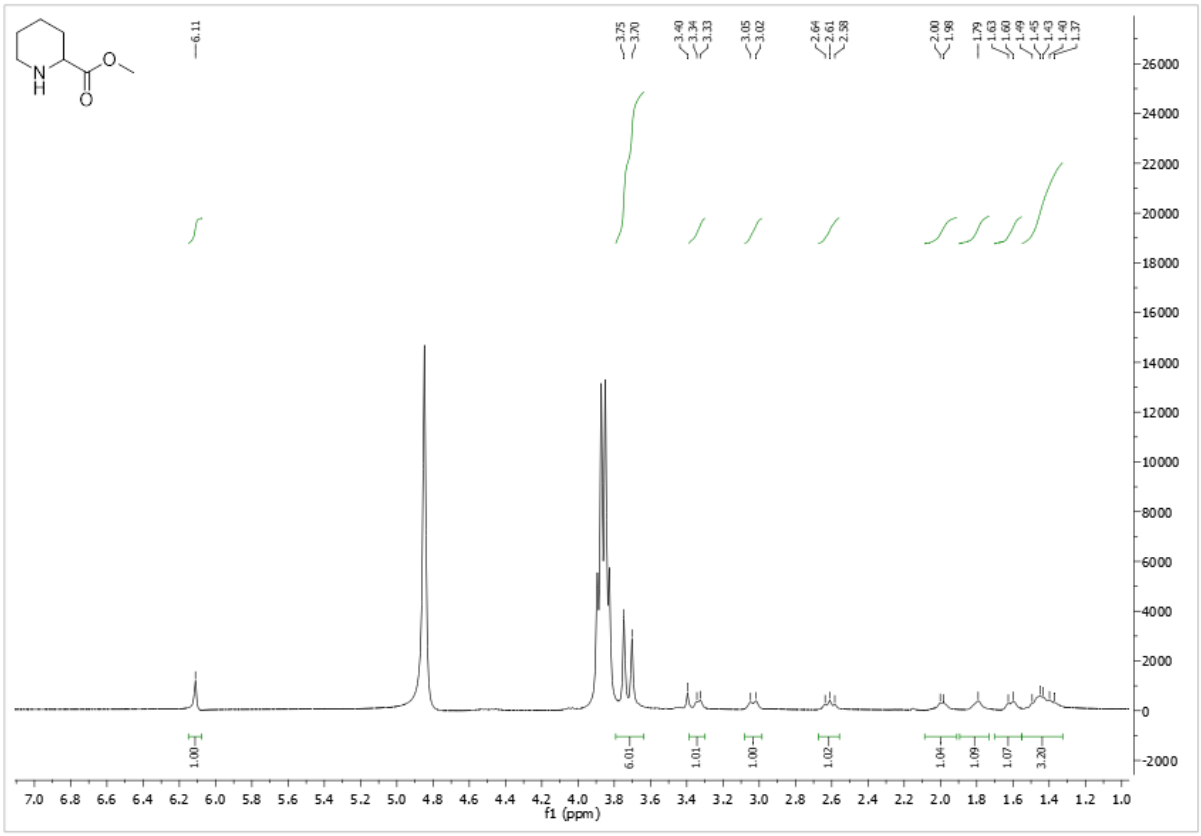


Figure 69 - ^{1}H NMR of methyl piperidine-2-carboxylate (8b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

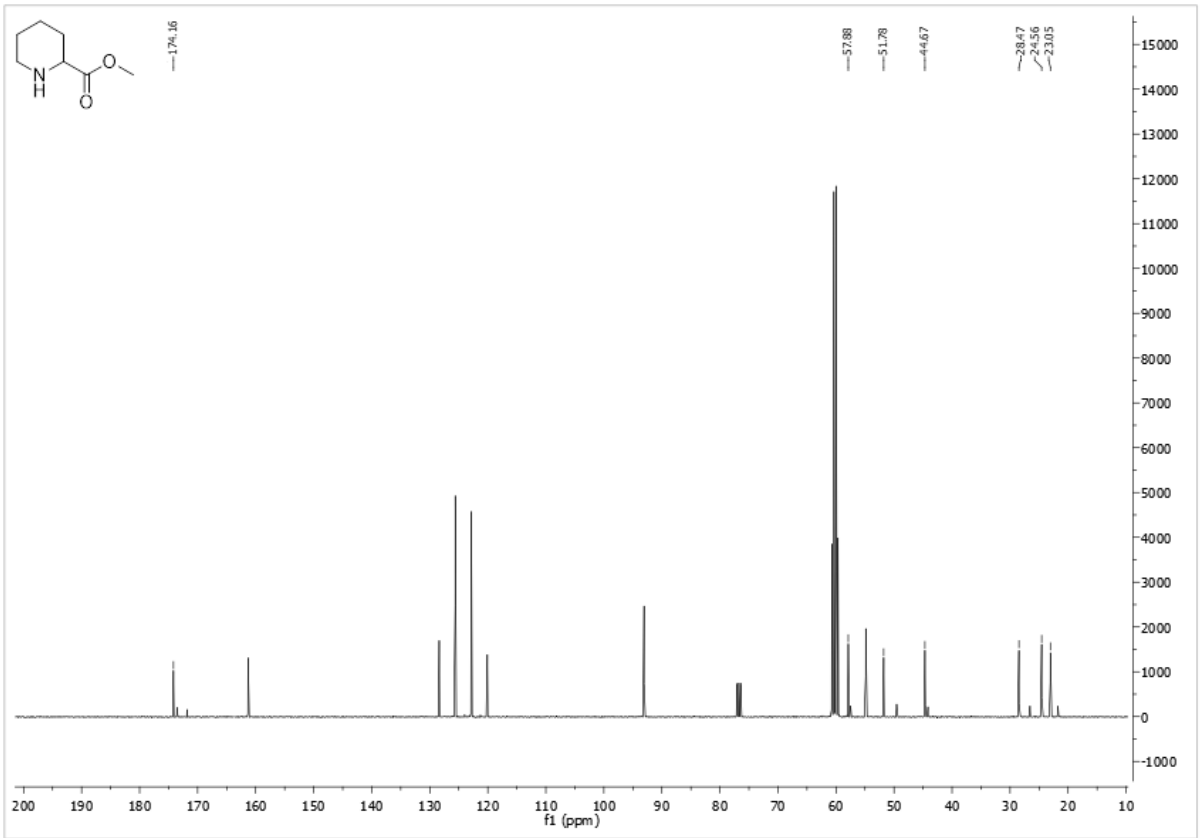


Figure 70 - ^{13}C NMR of methyl piperidine-2-carboxylate (8b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

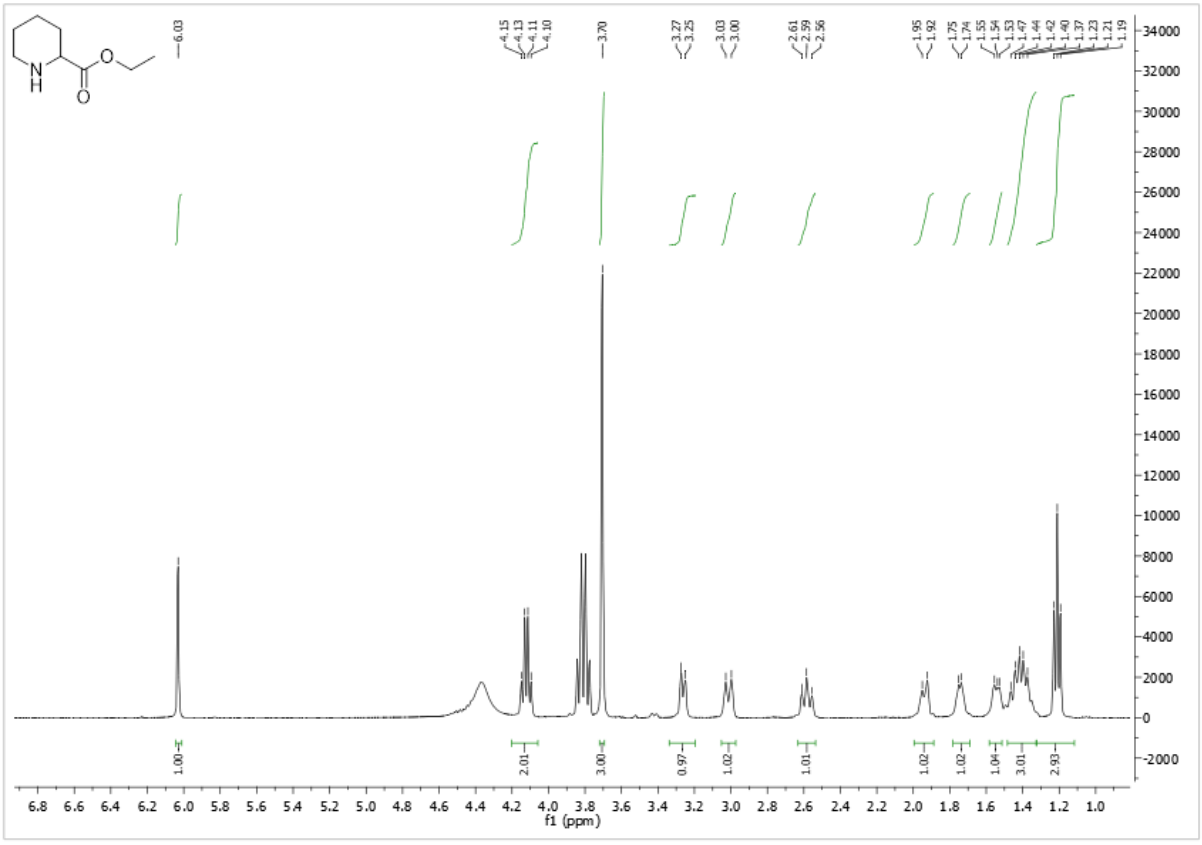


Figure 71 - ^{1}H NMR of ethyl piperidine-2-carboxylate (8c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

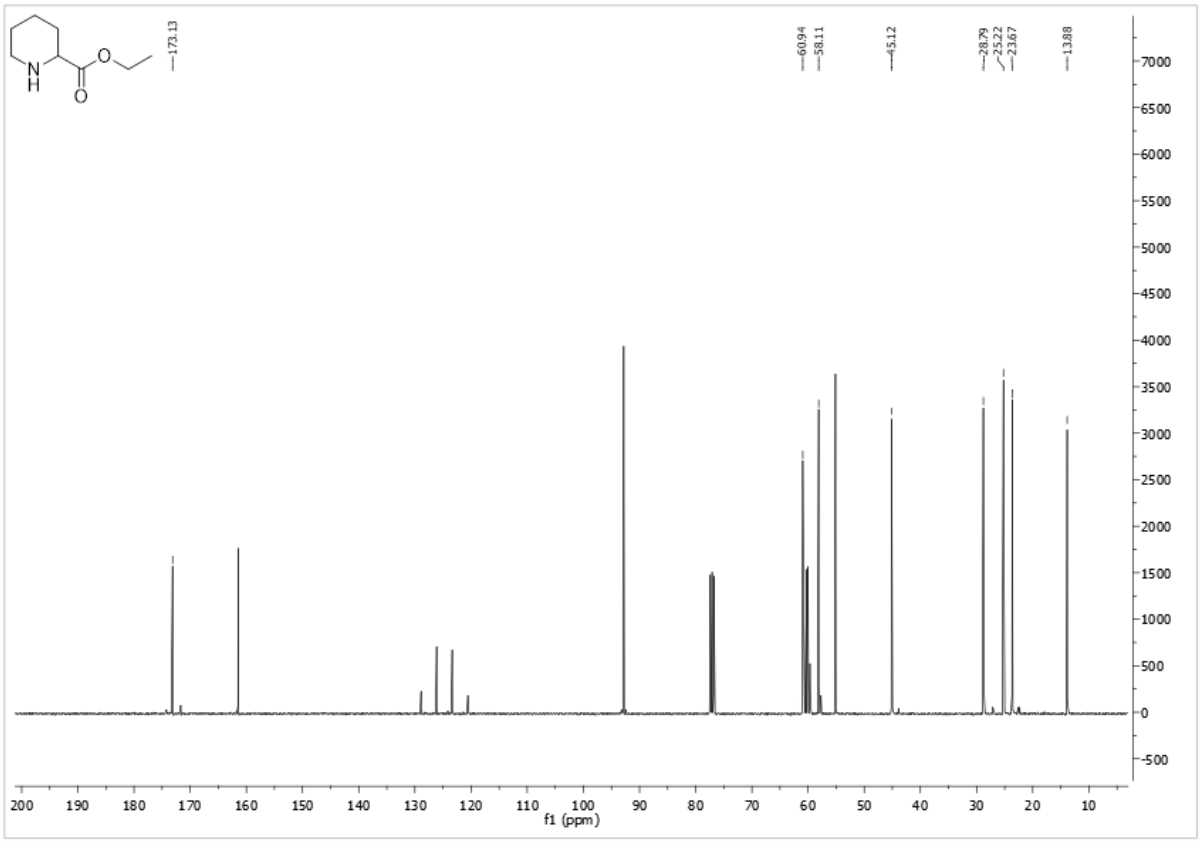


Figure 72 - ^{13}C NMR of ethyl piperidine-2-carboxylate (8c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

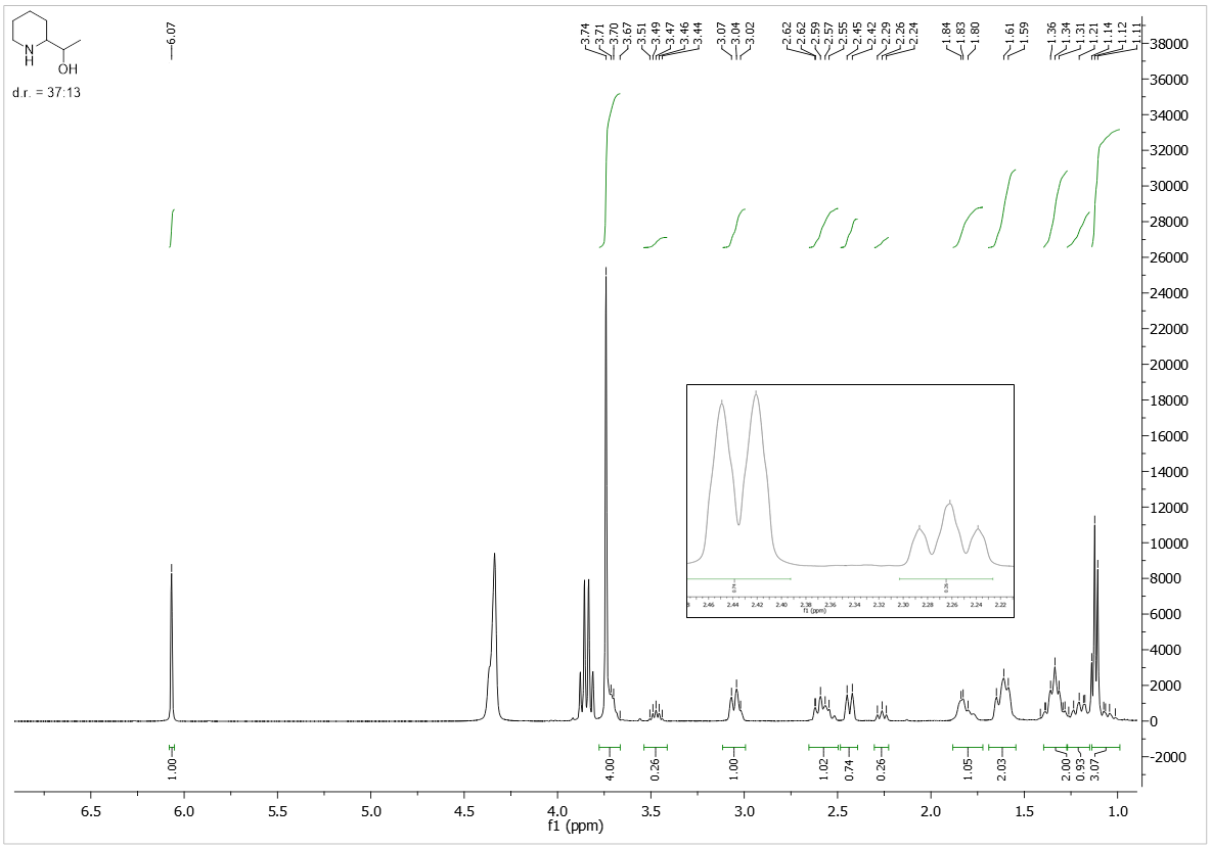


Figure 73 - ^{1}H NMR of 1-(piperidin-2-yl)ethan-1-ol (8d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows the presecnce of two diasteroisomers at 2.44ppm and 2.26ppm.

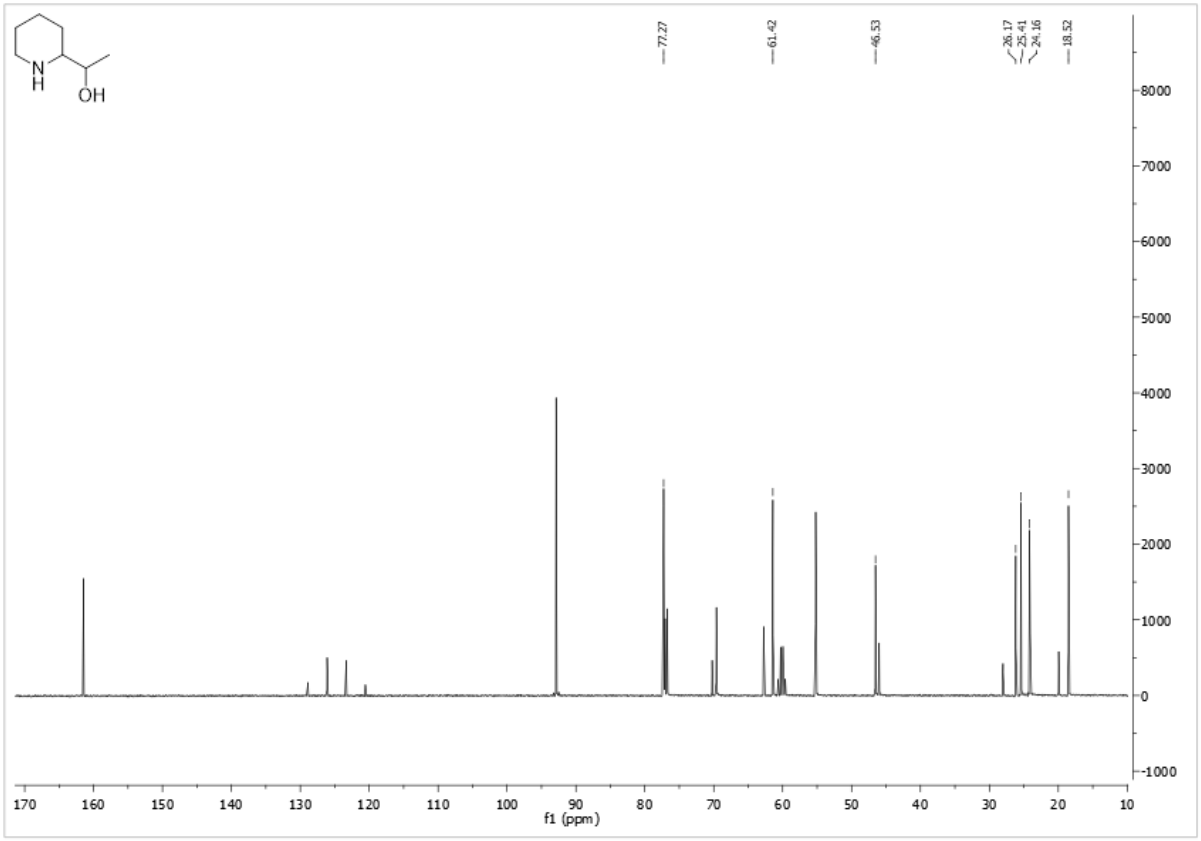


Figure 74 - ^{13}C NMR of 1-(piperidin-2-yl)ethan-1-ol (8d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

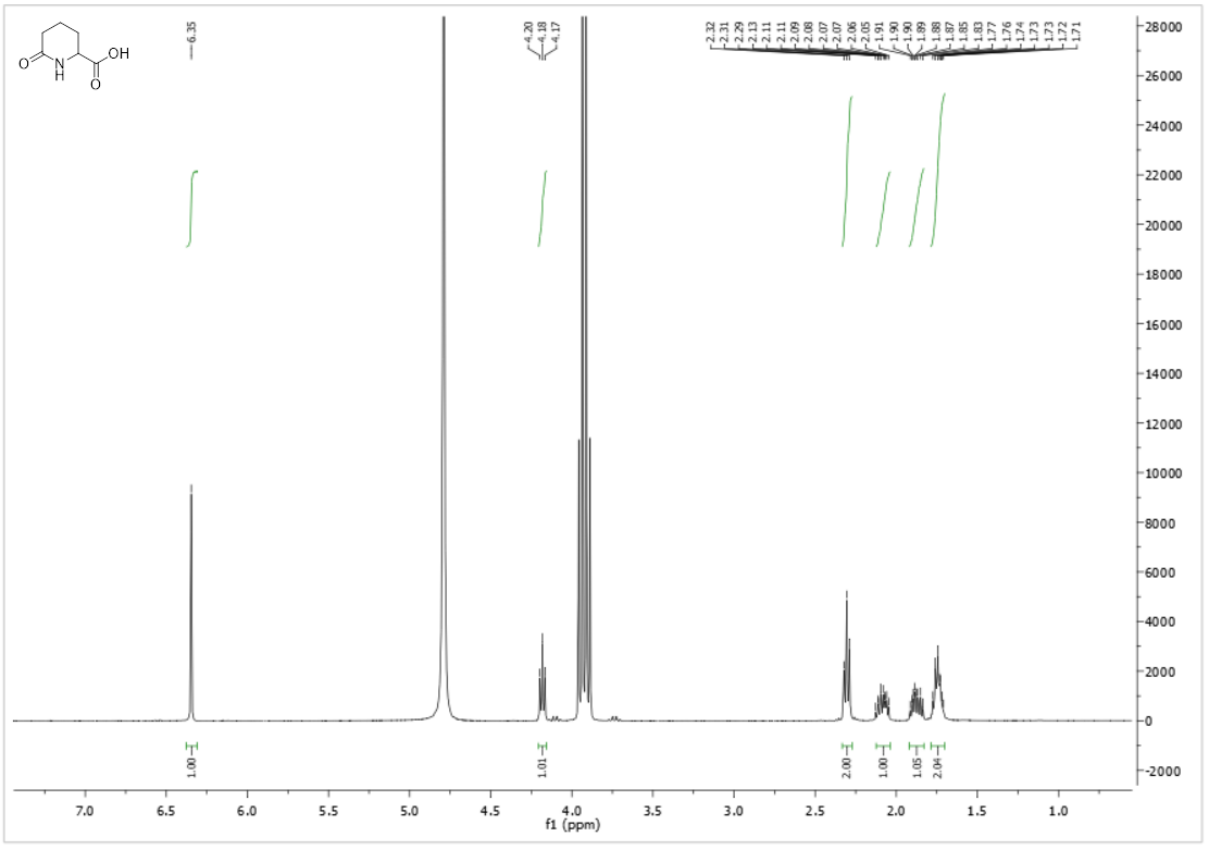


Figure 75 - ^{1}H NMR of 6-oxopiperidine-2-carboxylic acid (8e) in D_2O. Maleic acid (0.5 eq., δ 6.35 (s, 1H)) used as internal standard.

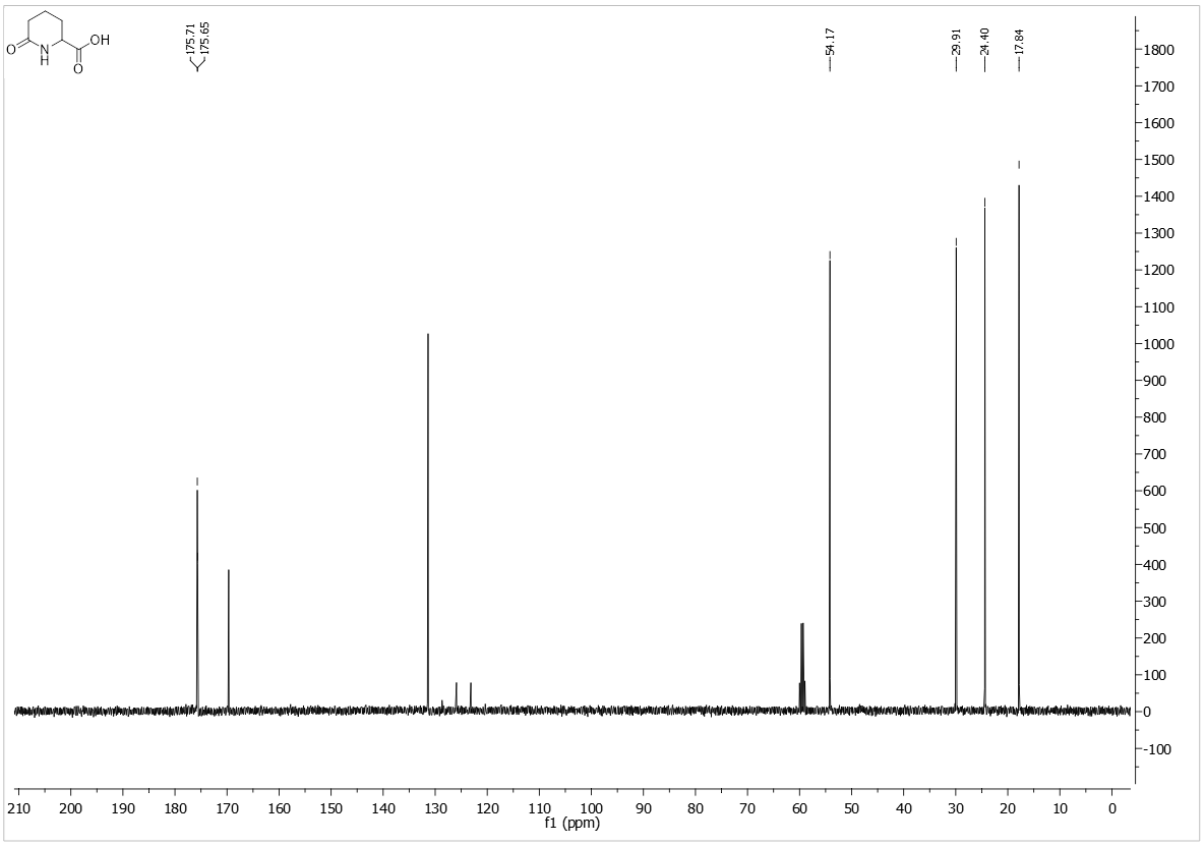


Figure 76 - ^{13}C NMR of 6-oxopiperidine-2-carboxylic acid (8e) in D_2O. Maleic acid (0.5 eq.) used as internal standard.

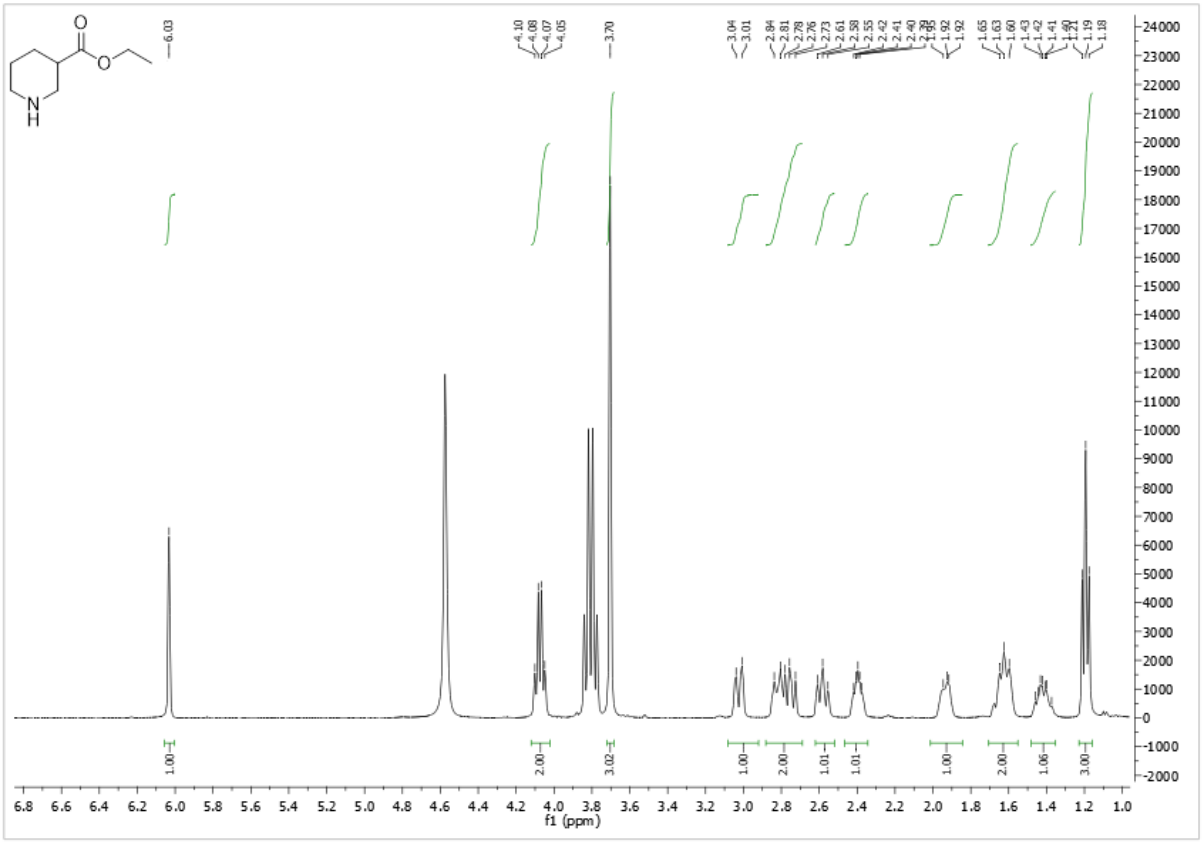


Figure 77 - ^{1}H NMR of ethyl piperidine-3-carboxylate (8f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

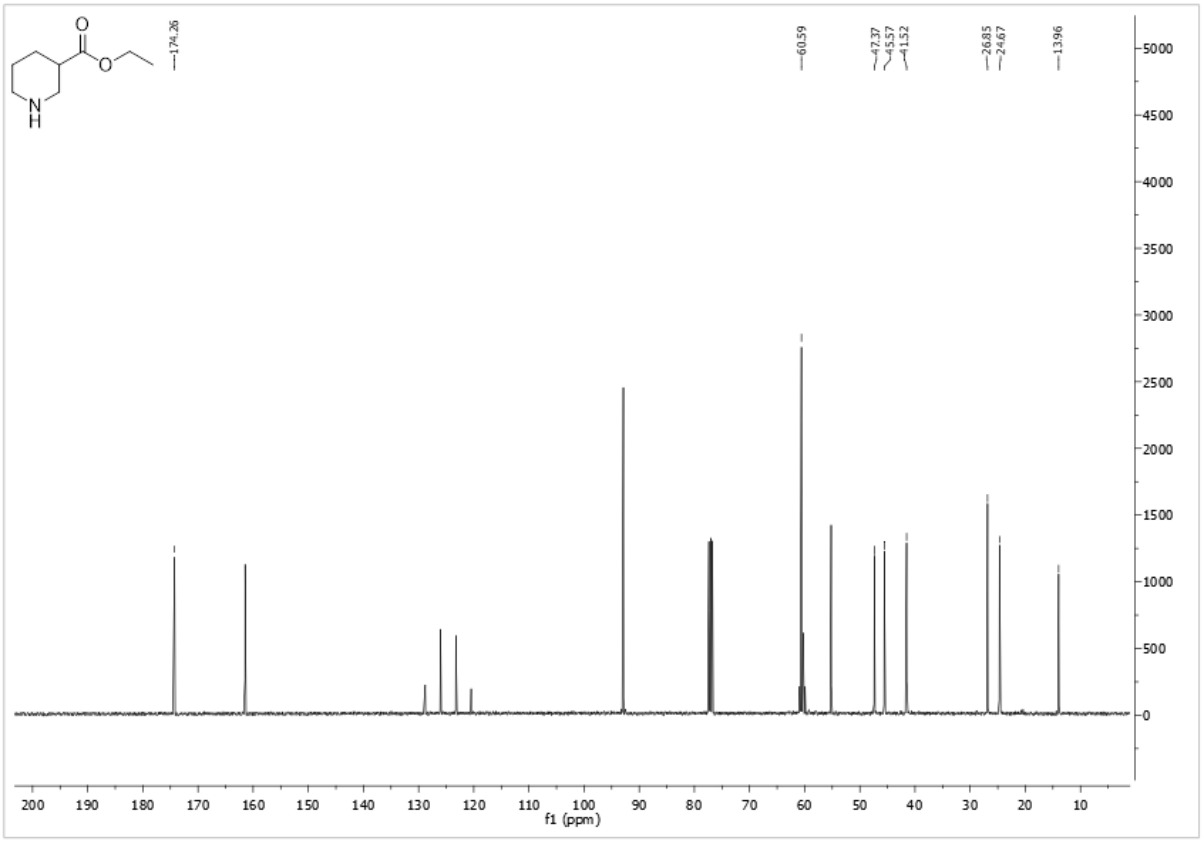


Figure 78 - ^{13}C NMR of ethyl piperidine-3-carboxylate (8f) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

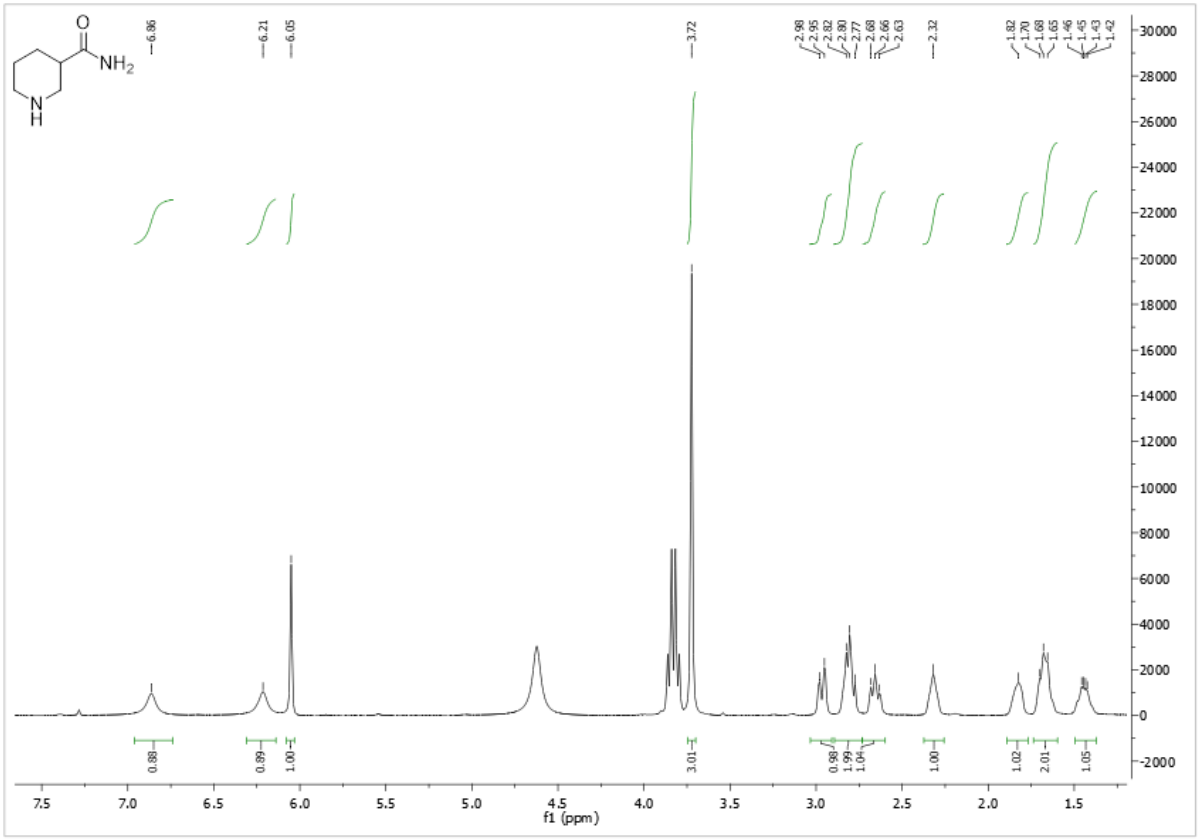


Figure 79 - ^{1}H NMR of piperidine-3-carboxamide (8g) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

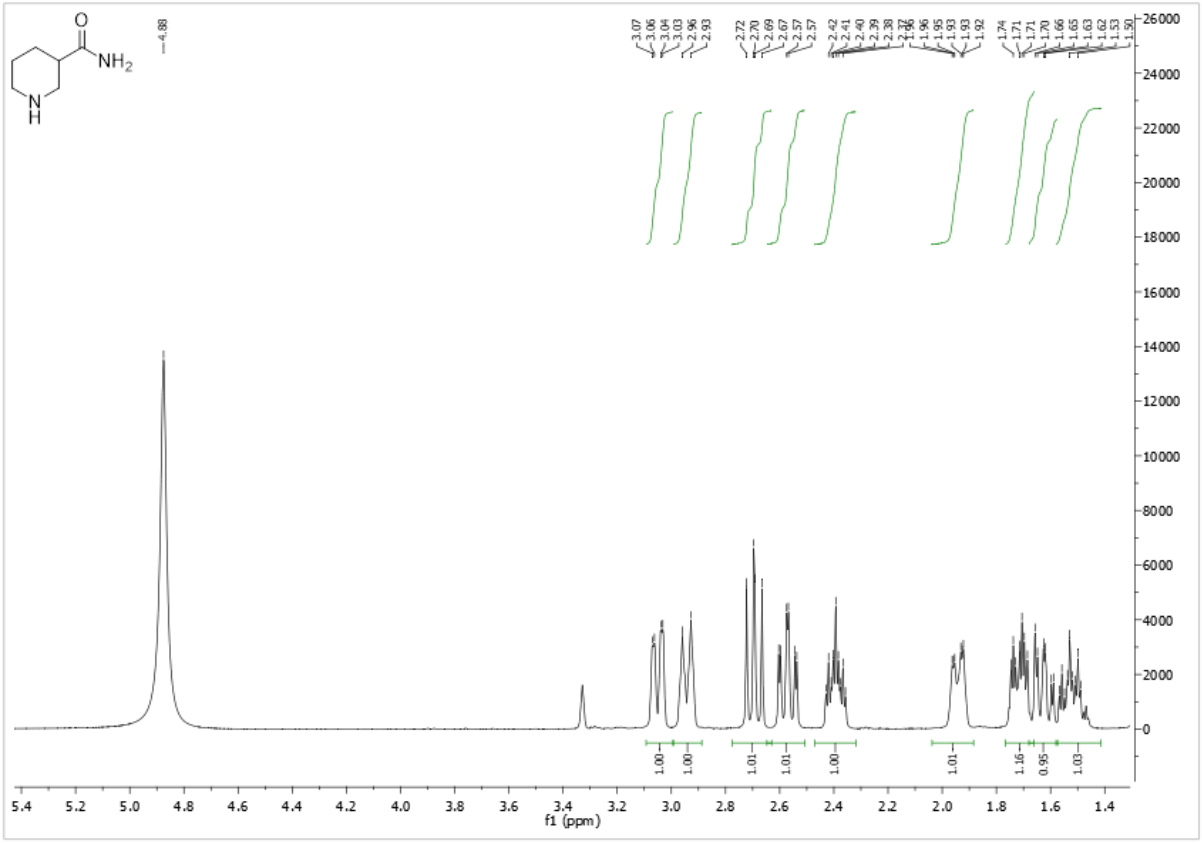


Figure 80 - ^{1}H NMR of purified piperidine-3-carboxamide (8g) in MeOD.

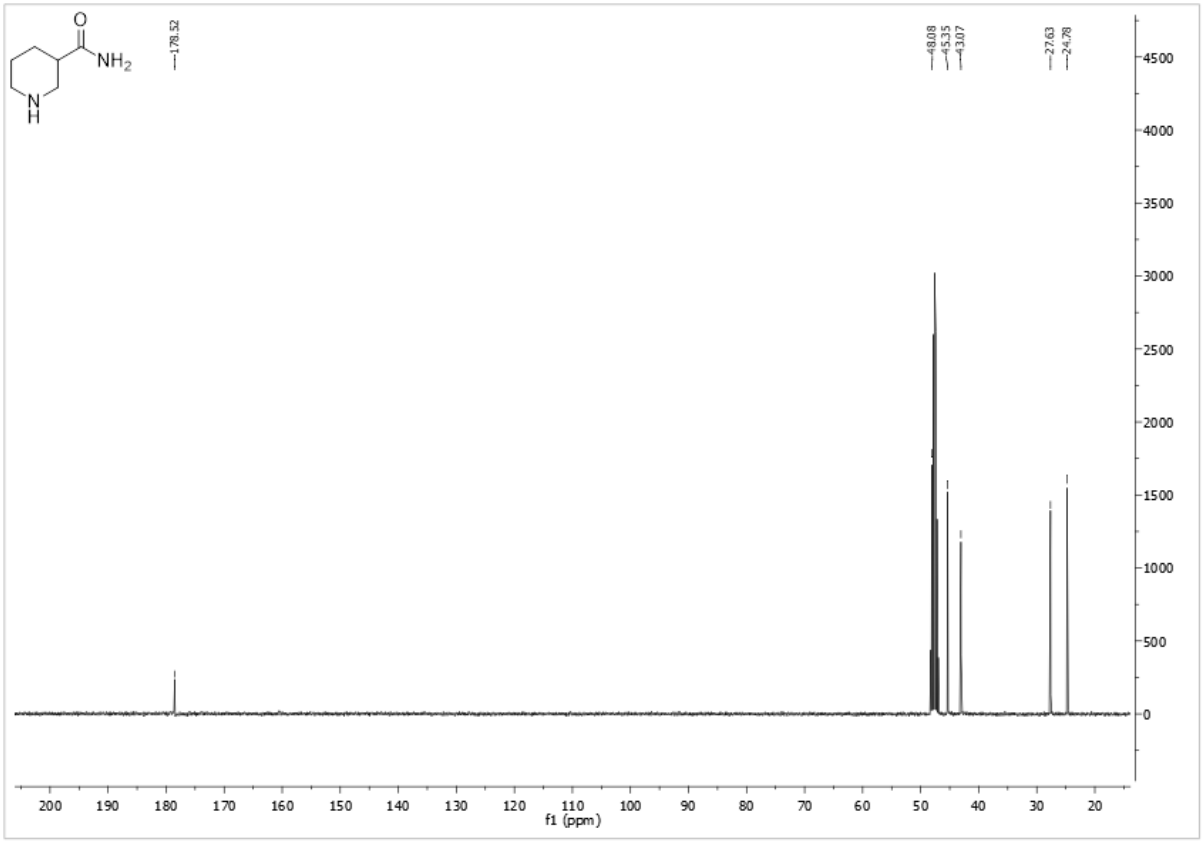


Figure 81 - ^{13}C NMR of purified piperidine-3-carboxamide (8g) in MeOD.

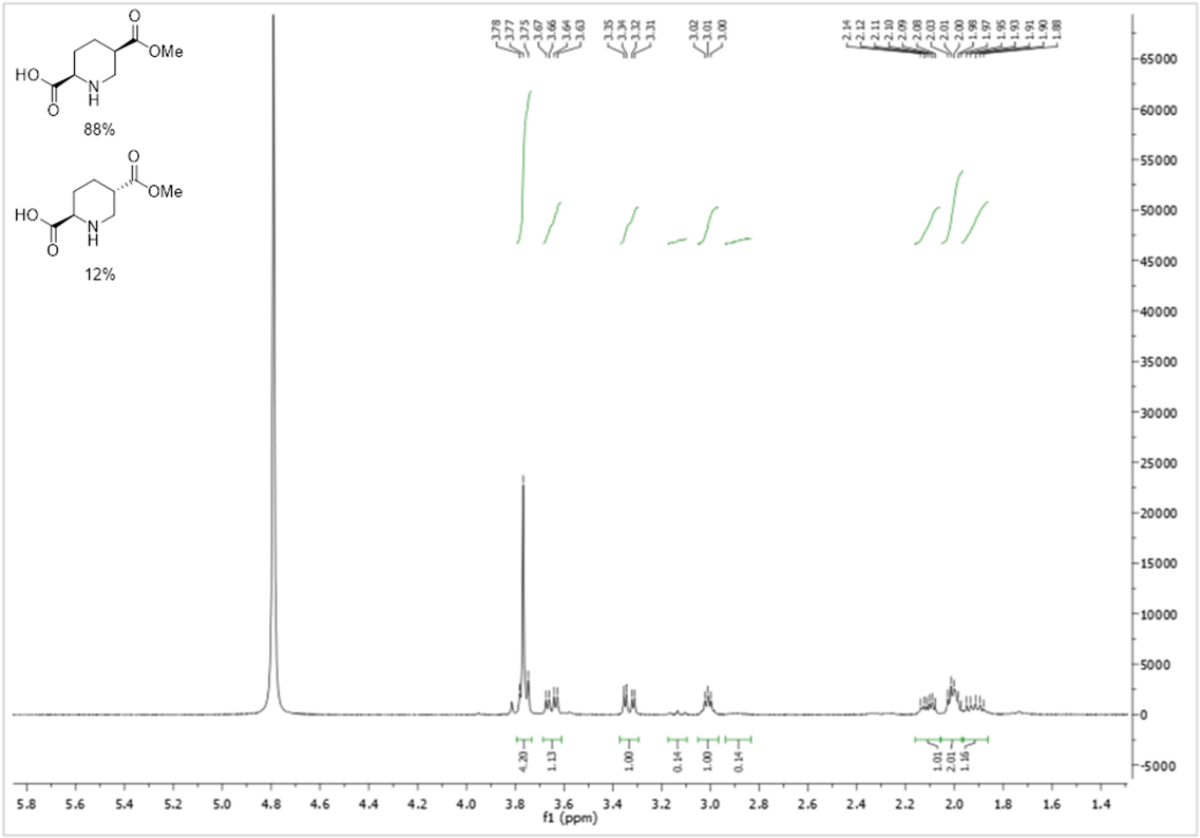


Figure 82 - ^{1}H NMR of purified 5-(methoxycarbonyl)piperidine-2-carboxylic acid (8h) in D_2O.

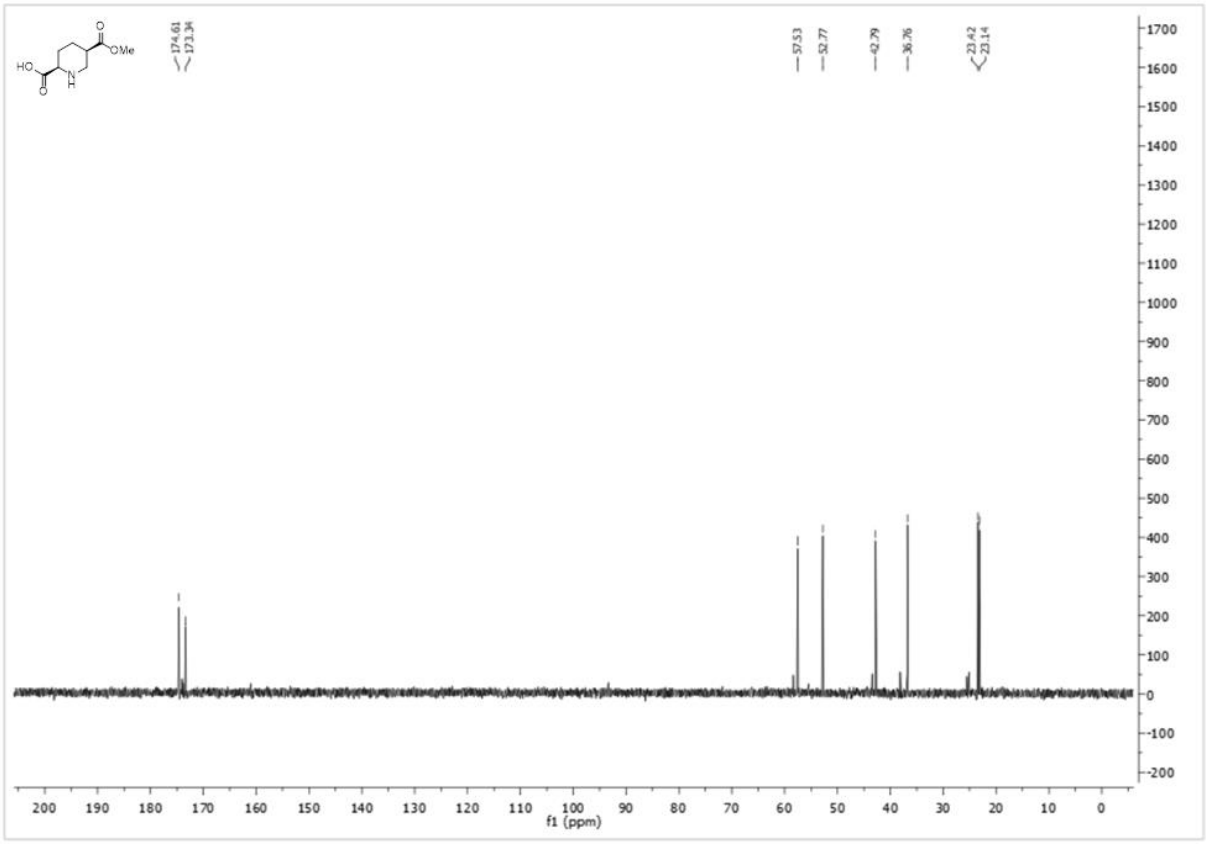


Figure 83 - ^{13}C NMR of purified 5-(methoxycarbonyl)piperidine-2-carboxylic acid (8h) in D_2O.

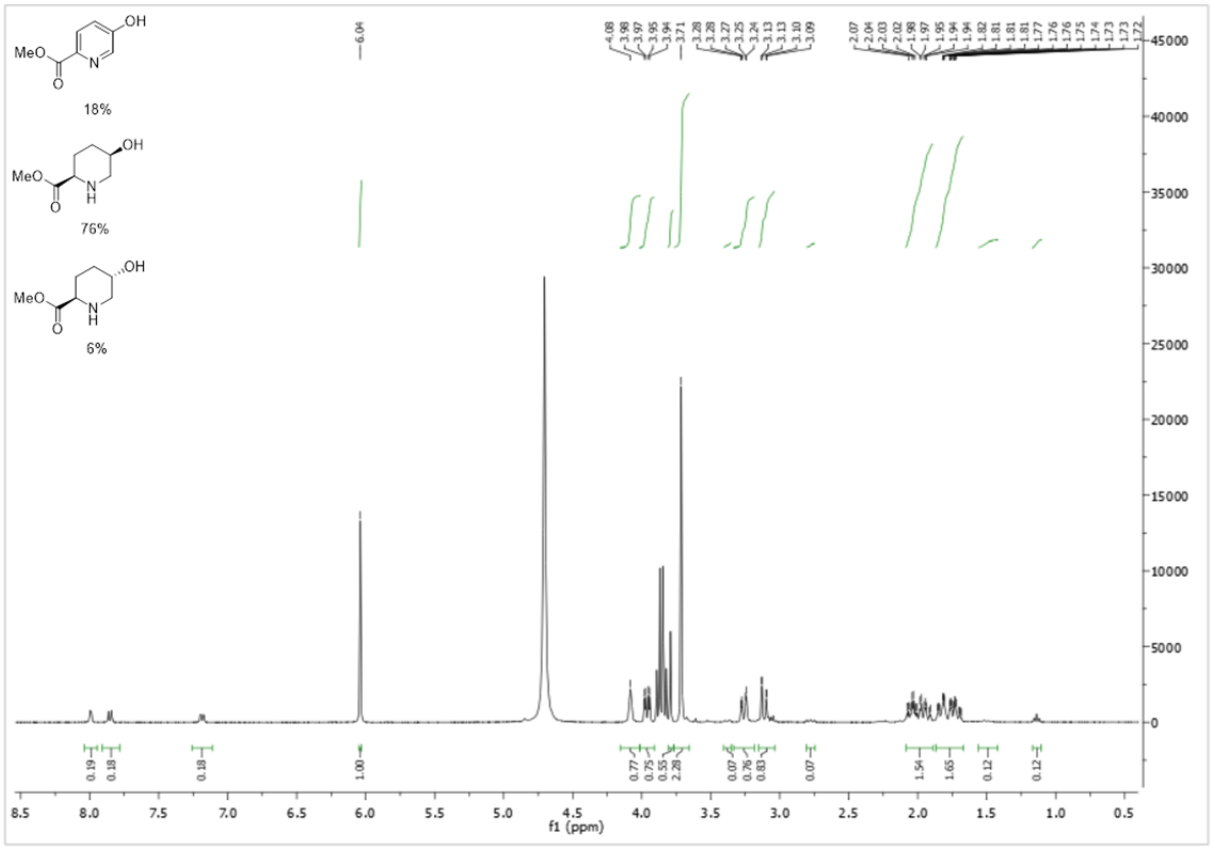


Figure 84 - ^{1}H NMR of methyl-5-hydroxypiperidine-2-carboxylate (8i) in D_2O after 24 hours. Maleic Acid (0.5 eq., δ 6.04 (s, 1H)) used as internal standard.

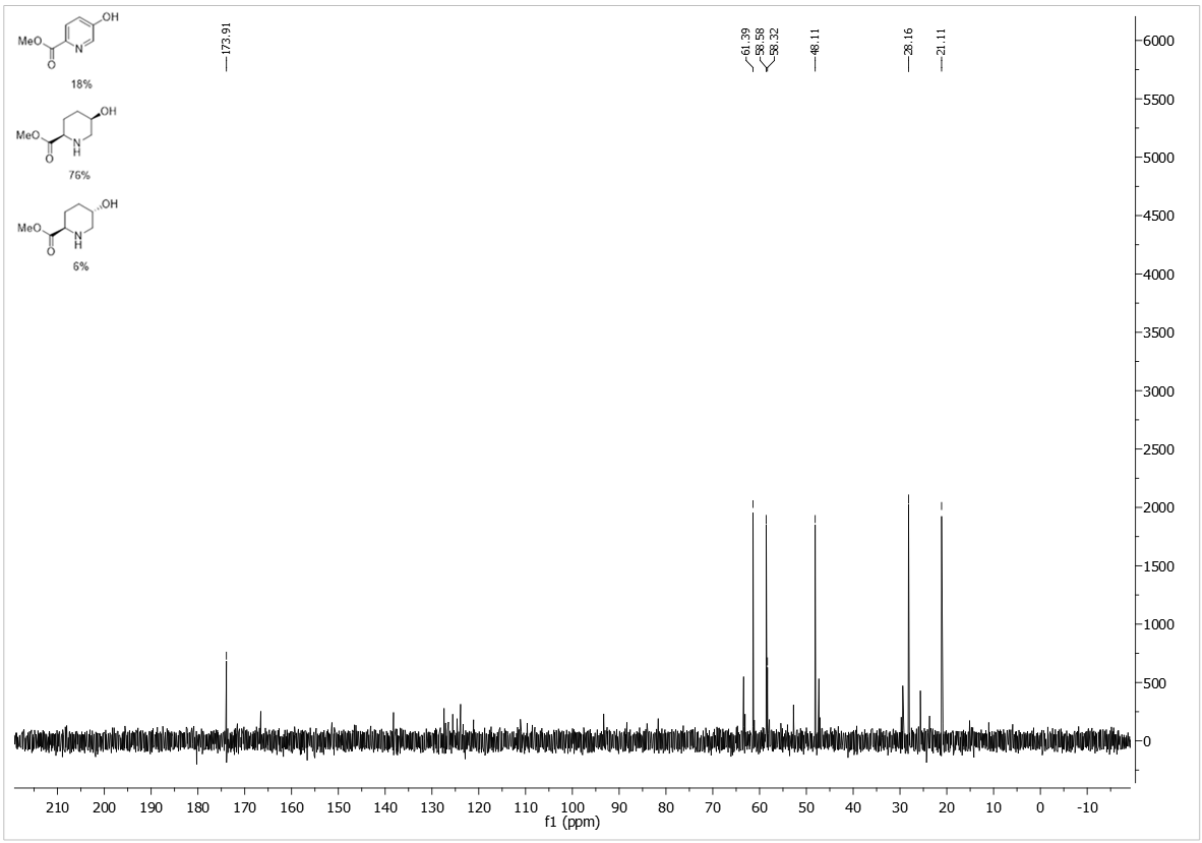


Figure 85 - ^{13}C NMR of methyl-5-hydroxypiperidine-2-carboxylate (8i) in D_2O after 24 hours. Maleic Acid (0.5 eq.) used as internal standard.

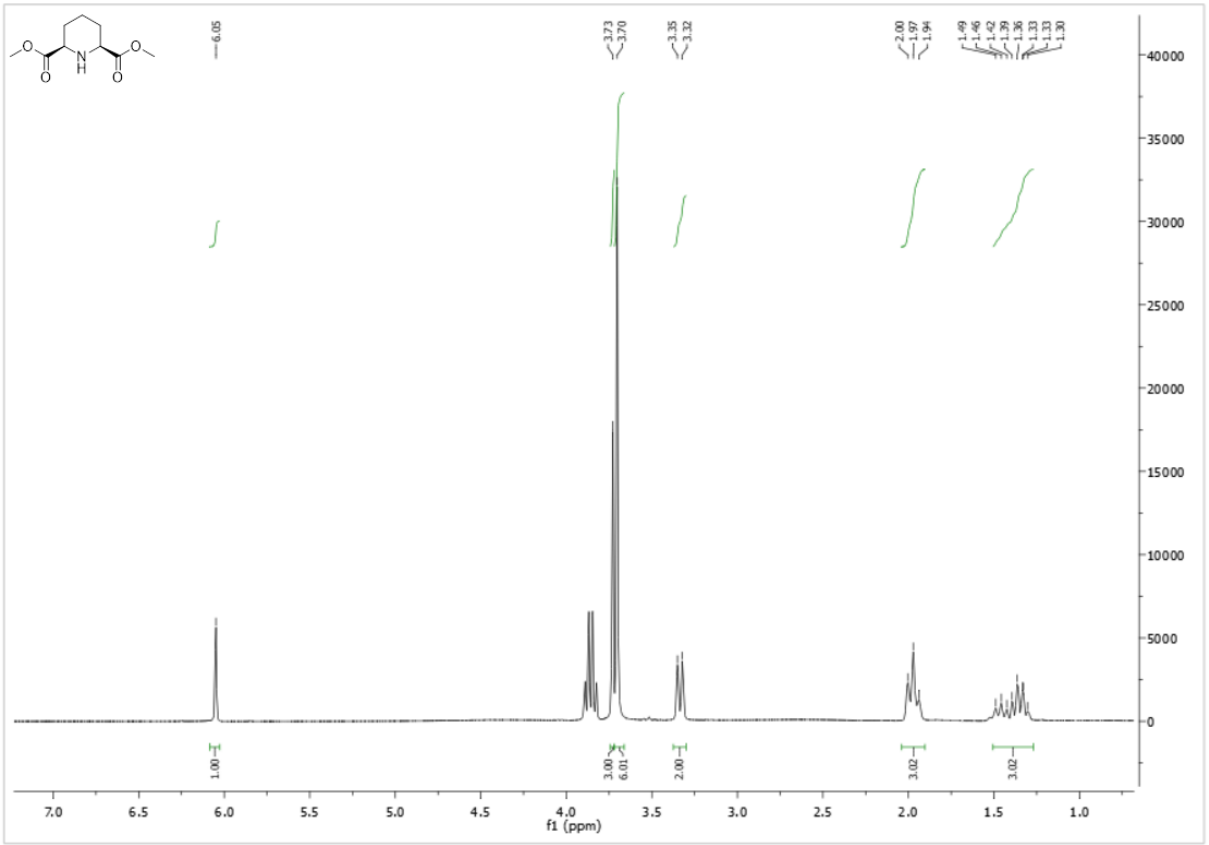


Figure 86 - ^{1}H NMR of dimethyl-piperidine-2,6-dicarboxylate (8j) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

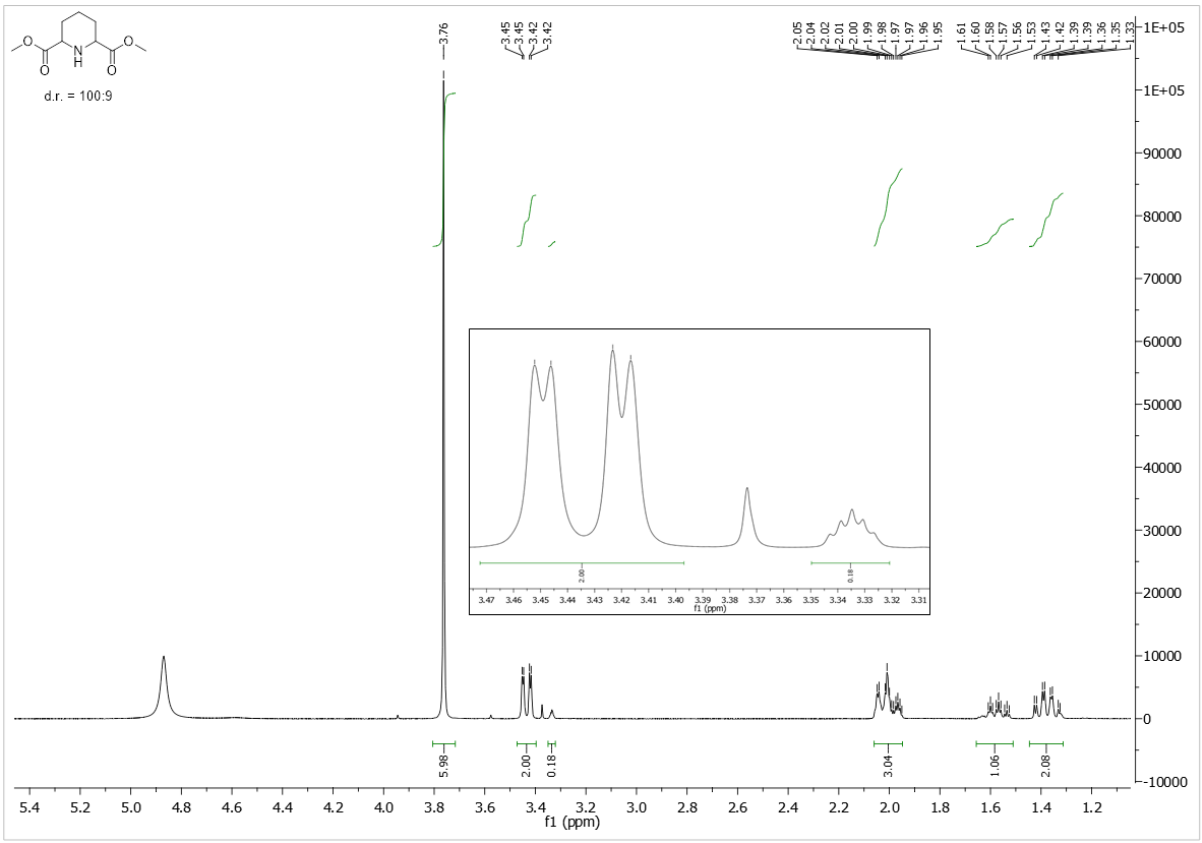


Figure 87 - ^{1}H NMR of purified dimethyl-piperidine-2,6-dicarboxylate (8j) in MeOD. Inset shows presence of two diastereoisomers with cis at 3.43ppm and trans at 3.33 ppm.

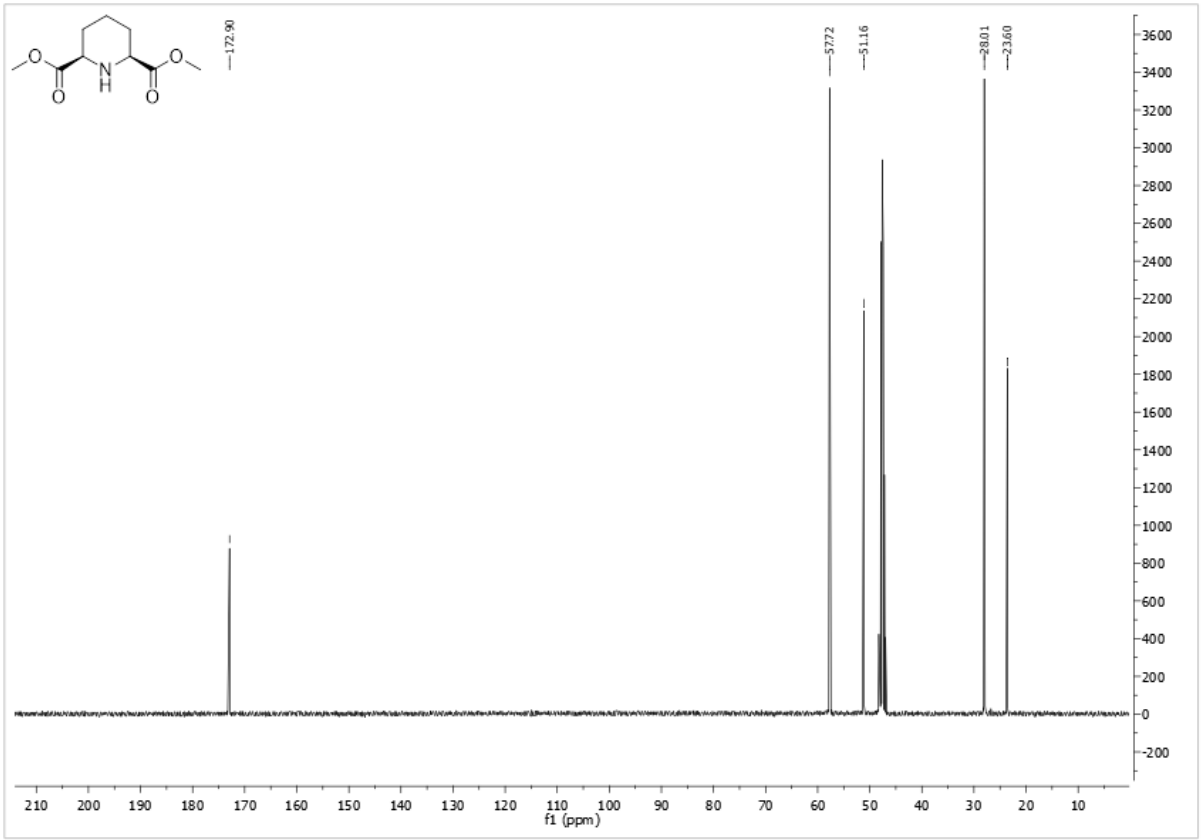


Figure 88 - ^{13}C NMR of purified dimethyl-piperidine-2,6-dicarboxylate (8j) in MeOD.

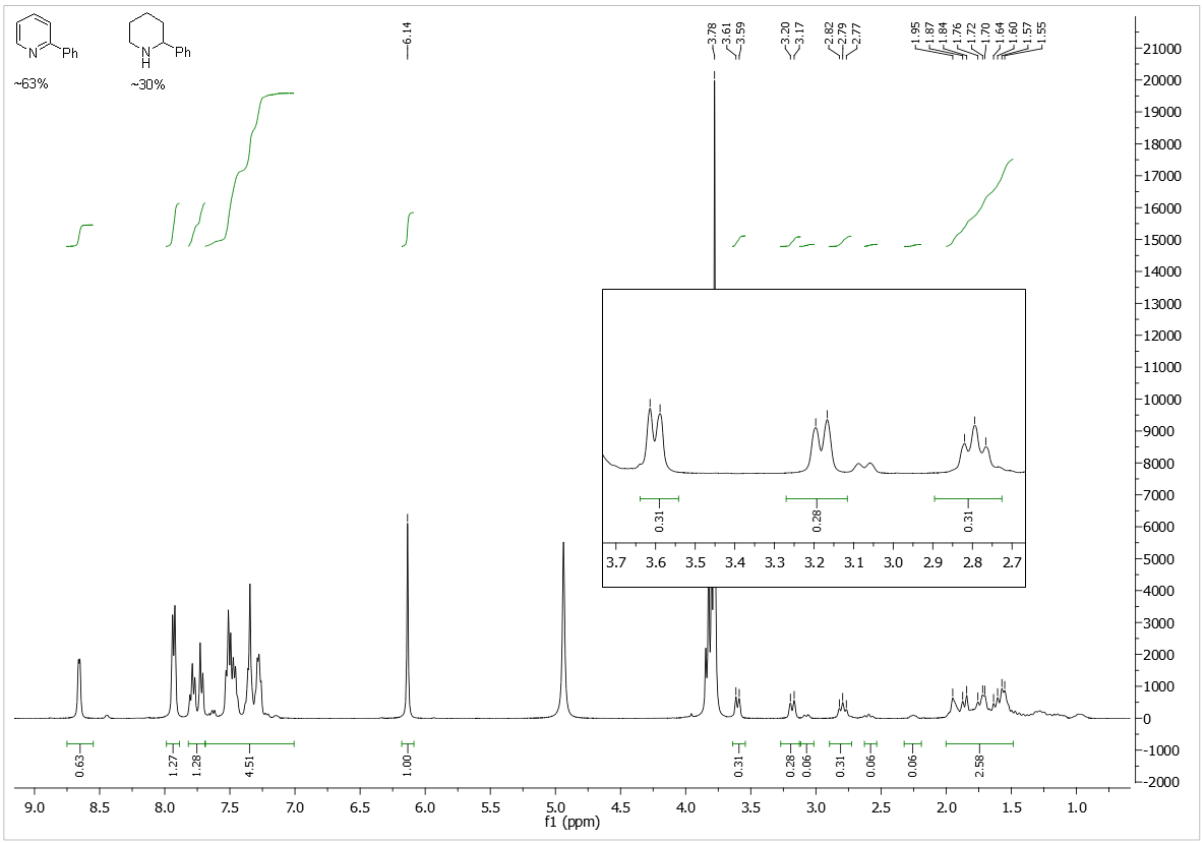


Figure 89 - ^{1}H NMR of 2-phenylpiperidine (10a) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows peaks used to tentatively calculate the yield and assign the product.

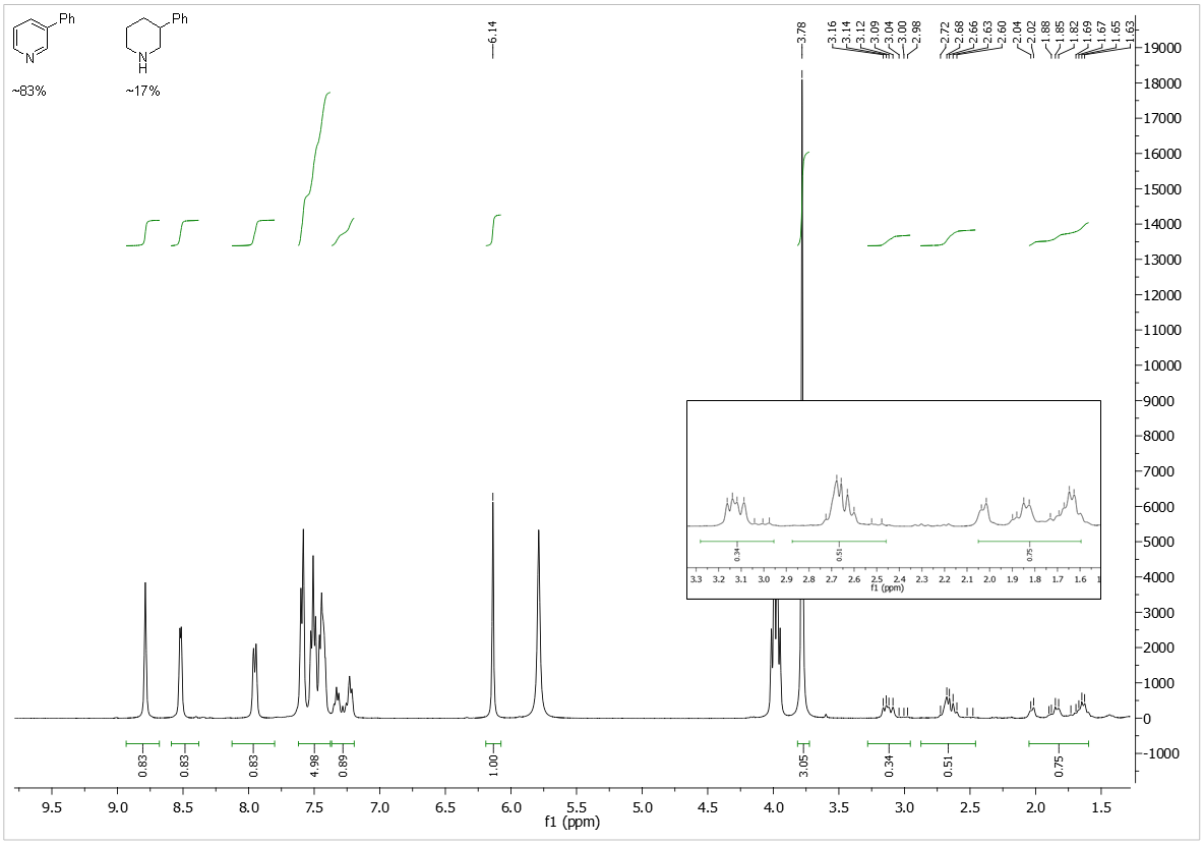


Figure 90 - ^{1}H NMR of 3-phenylpiperidine (10b) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

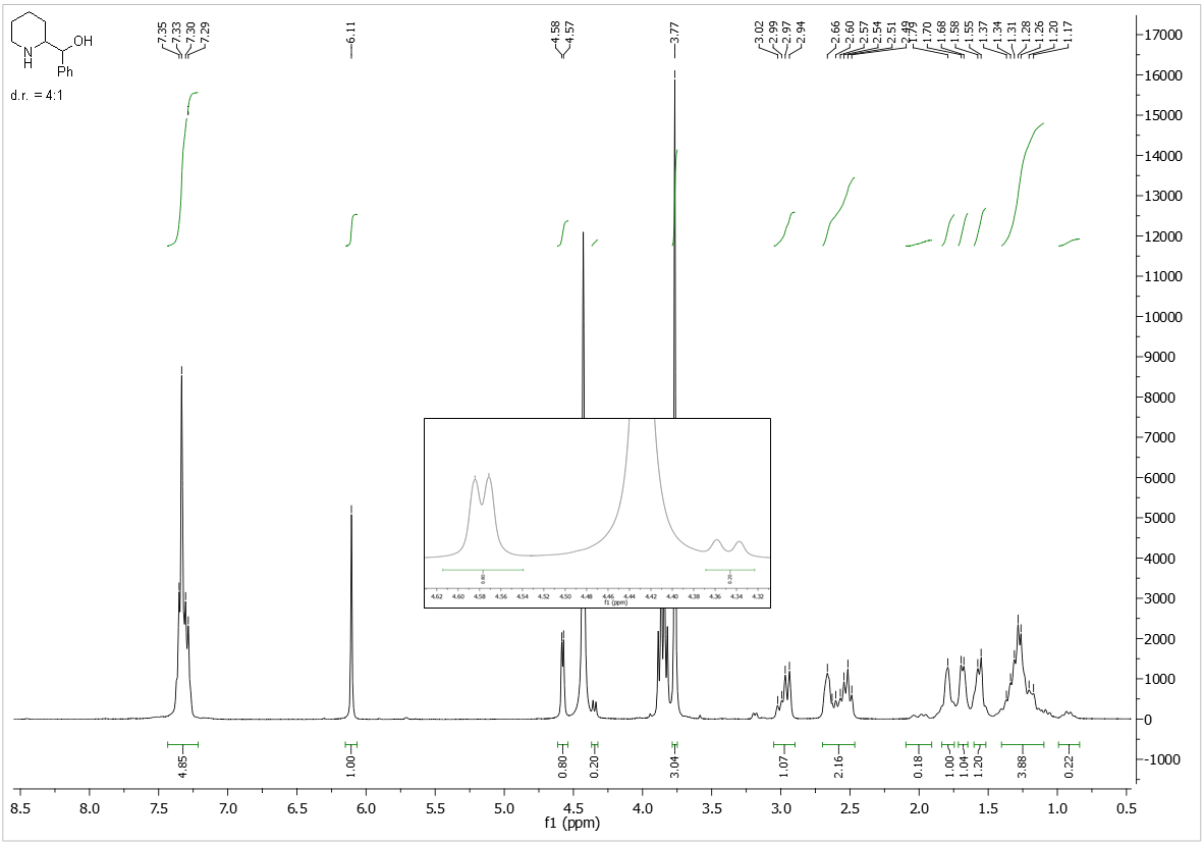


Figure 91 - ^{1}H NMR of phenyl(piperidin-2-yl)methanol (10c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard. Inset shows presence of two diastereoisomers at 4.58ppm and 4.34 ppm.

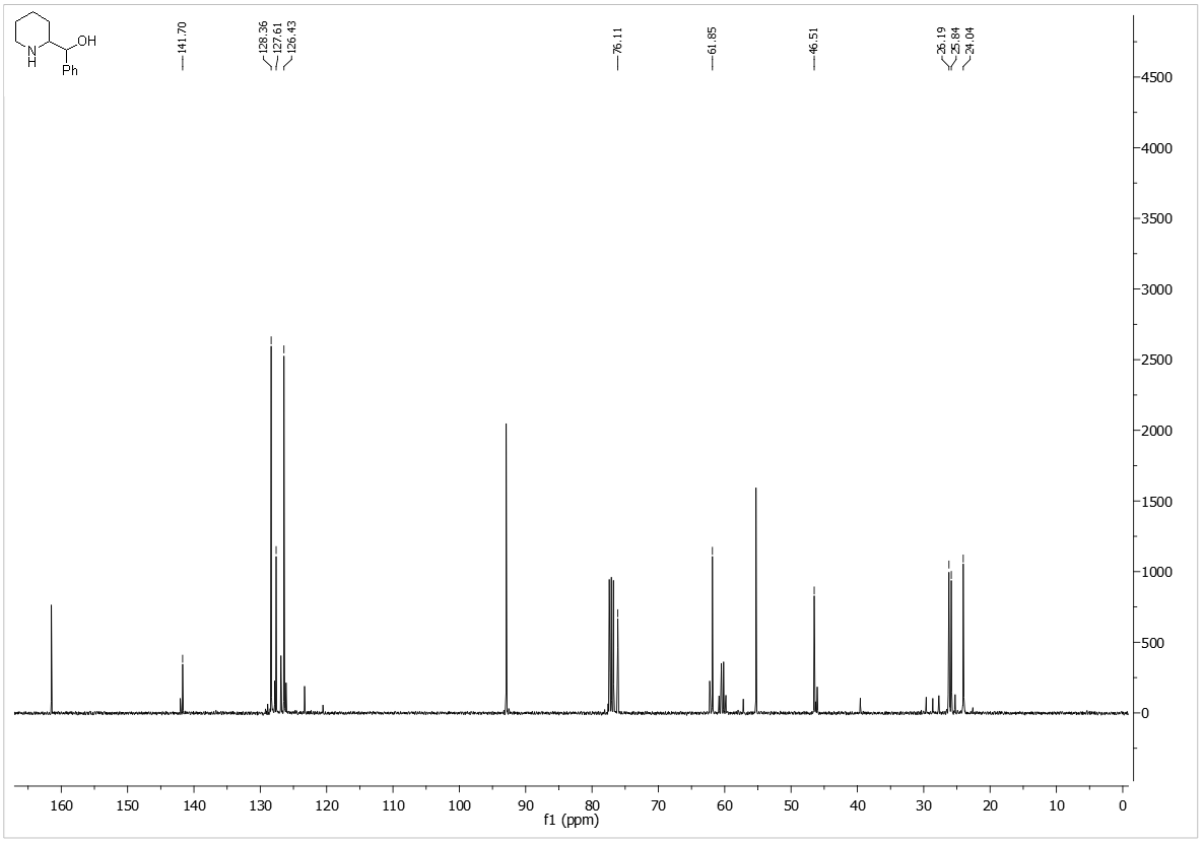


Figure 92 - ^{13}C NMR of phenyl(piperidin-2-yl)methanol (10c) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

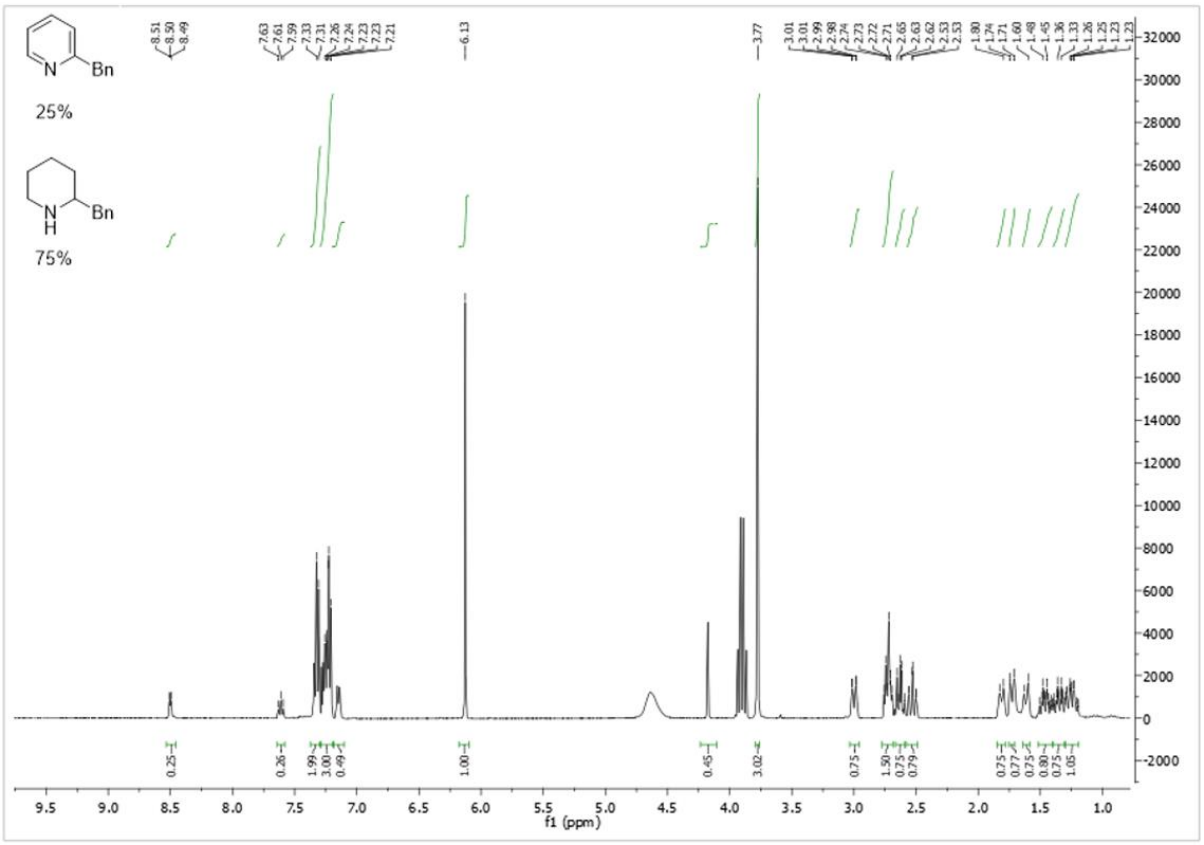


Figure 93 - ^{1}H NMR of 2-benzylpiperidine (10d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

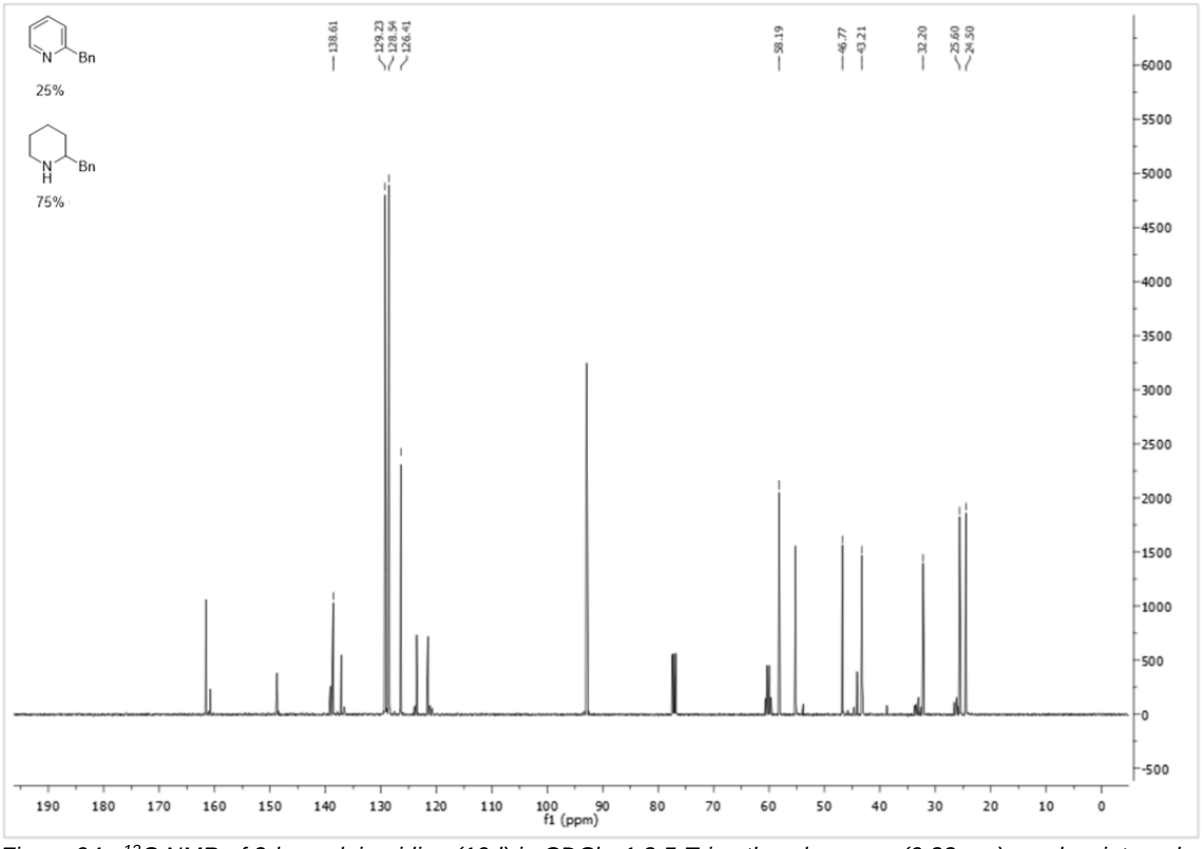


Figure 94 - ^{13}C NMR of 2-benzylpiperidine (10d) in $CDCl_3$. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

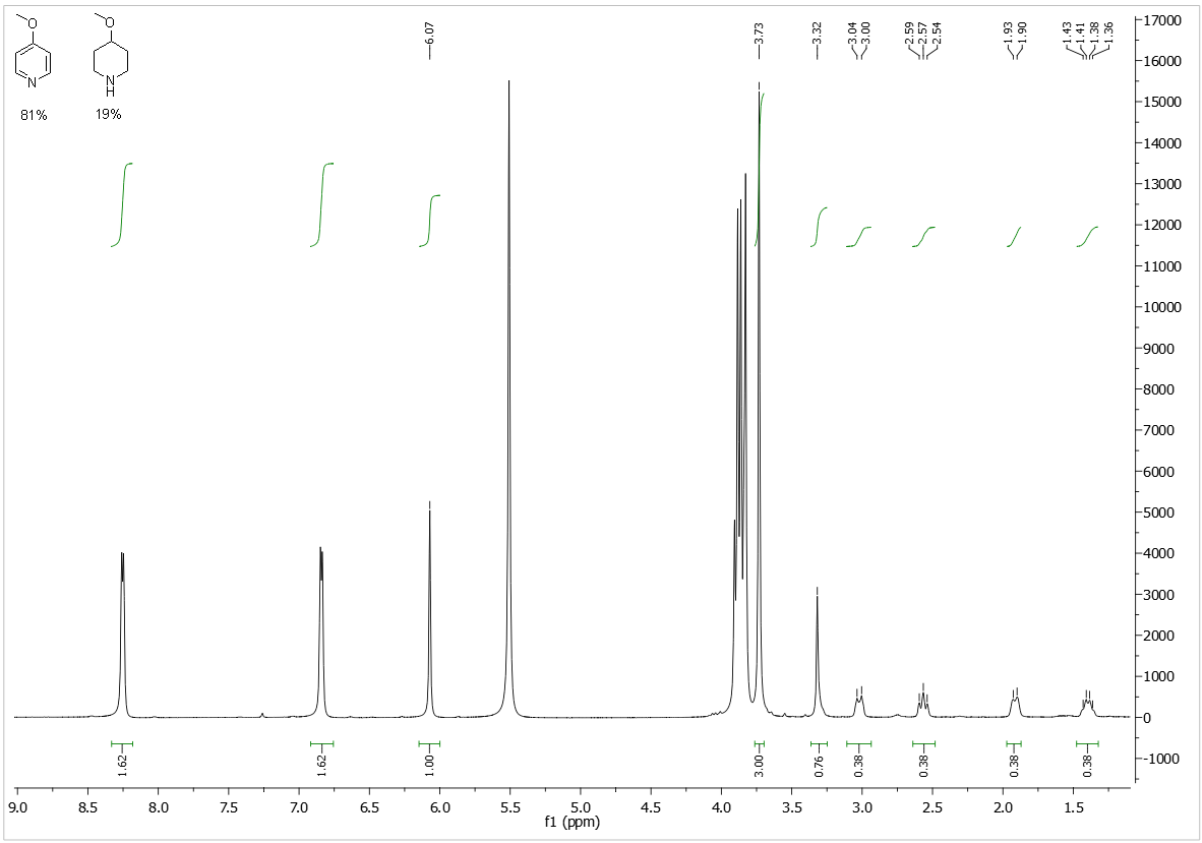


Figure 95 - ^{1}H NMR of 4-methoxypiperidine (12a) in $CDCl_3$ after 4 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

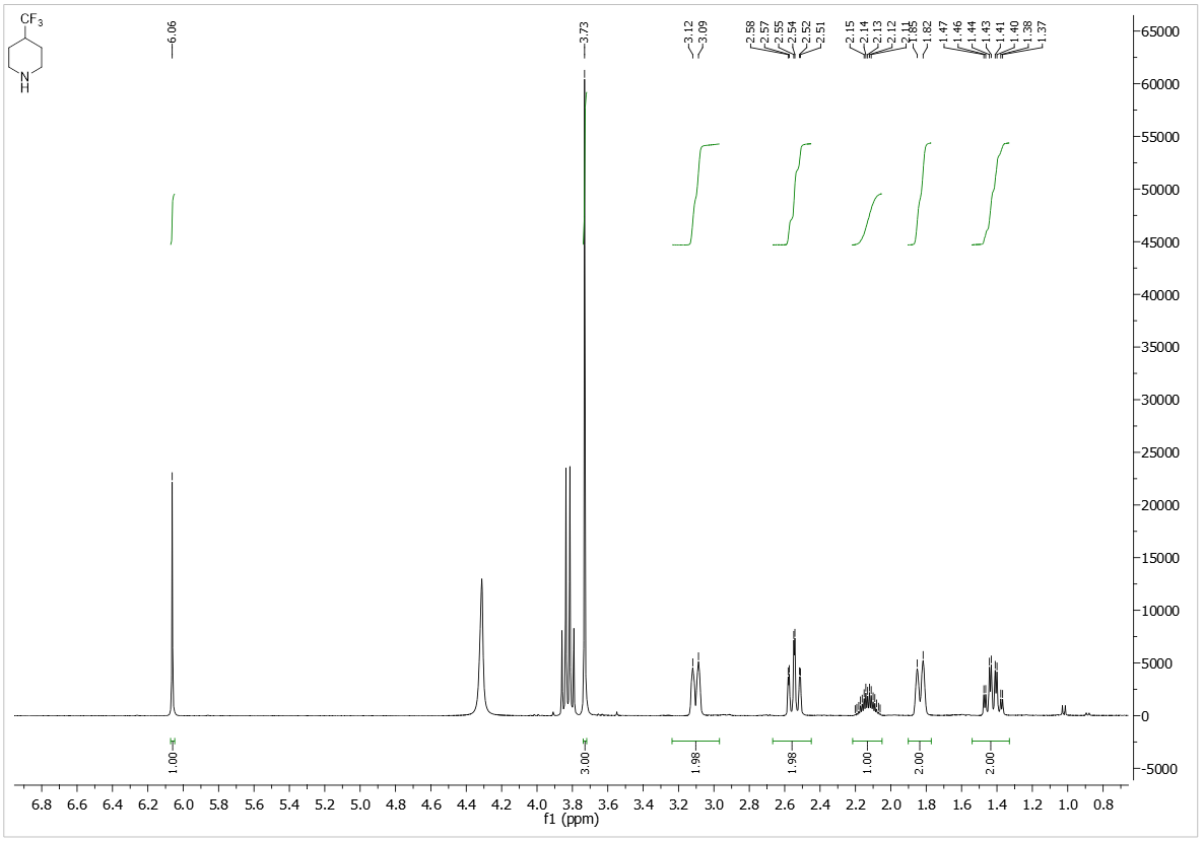


Figure 96 - ^{1}H NMR of 4-(trifluoromethyl)piperidine (12b) in $CDCl_3$ after 4 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

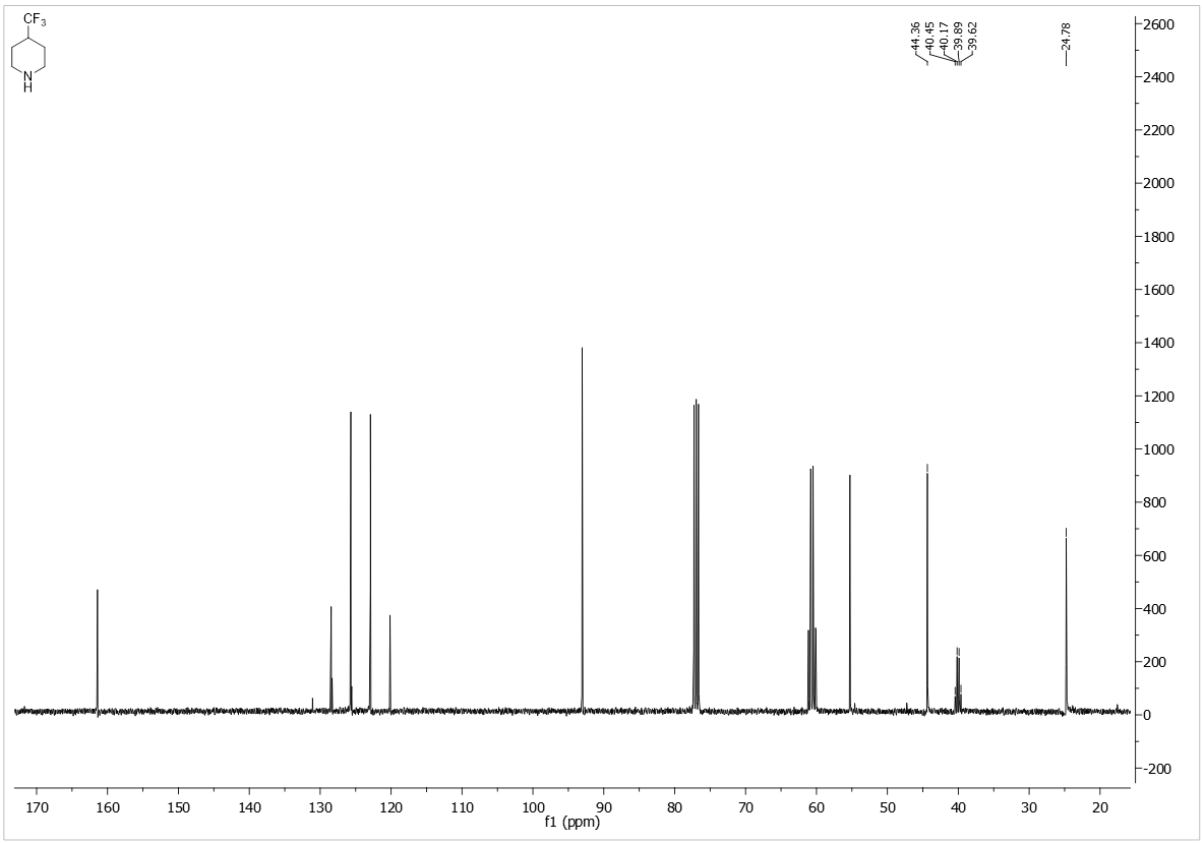


Figure 97 - ^{13}C NMR of 4-(trifluoromethyl)piperidine (12b) in $CDCl_3$ after 4 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

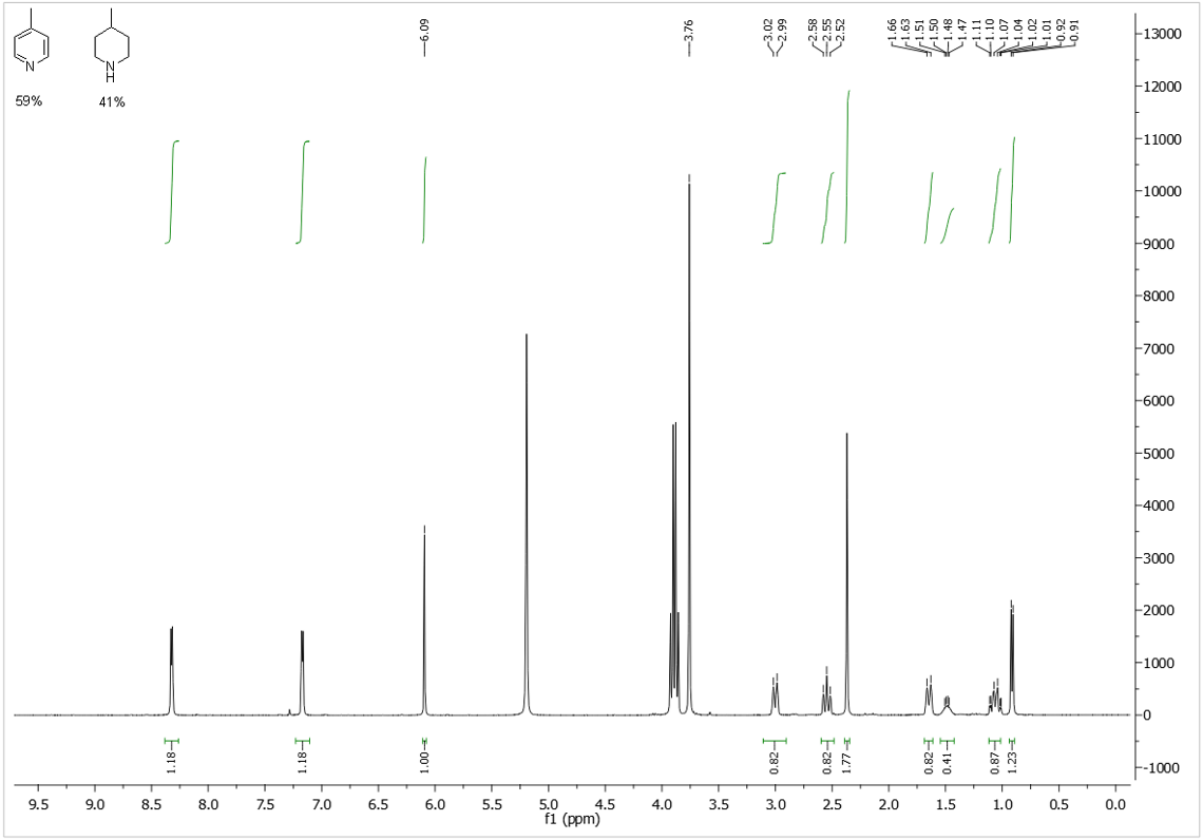


Figure 98 - ^{1}H NMR of 4-methylpiperidine (2d) in $CDCl_3$ after 4 hours. 1,3,5-Trimethoxybenzene (0.33 eq.) used as internal standard.

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