# Borrowing hydrogen in water and ionic liquids: Iridium-catalyzed alkylation of amines with alcohols

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## Supporting Information

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## I. General considerations

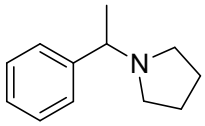
All the reactions were carried out under a nitrogen atmosphere with dried solvents. Silica gel plates ($GF_{254}$) were used for TLC monitoring and silica gel (230-400 mesh) was used for flash column chromatography. The following chemicals were purchased from Aldrich and used as received: all the amines and the alcohol. $[Cp^*IrI_2]_2$ was prepared according to literature procedures.[1] All solvents were dry and degassed before use. The $^1H$, $^{13}C$ and $^{19}F$ NMR spectra were recorded on Bruker Avance 300 instruments with TMS as the internal standard. The mass spectra were run on a microTOF electrospray time of flight (ESI-TOF) coupled to an Agilent 1200 LC system. IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrometer with selected absorbances quoted as υ in $cm^{-1}$. Melting points were carried out on a Gallenkamp MF-370 hot stage melting point apparatus.

## II. Representative procedure for the alkylation of 1-phenylethanamine with 1,4-butanediol:

To an oven dried, nitrogen purged carousel tube containing $[IrCp^*I_2]_2$ (11.7 mg, 0.01 mmol) were added the representative diol (1 mmol), 1-phenylethanamine (1 mmol, 127 µL) followed by deionised and degassed water (2 mL).

The reaction mixture was then heated to 115 °C at reflux for 15 h to 20 h. After the required time, the crude mixture is extracted 3 times with ethyl acetate, dried over magnesium sulfate, and then the solvent was removed under vacuum. The resulting residue was purified by column chromatography to give the desired product.

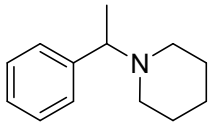
**1-(1-Phenylethyl)pyrrolidine (compound 17):** [2]




According to the representative procedure **II**, using butane-1,4-diol (1 mmol, 87µL), and the title compound was obtained by flash chromatography eluting with (EtOAc/Hexane: 1/10) to give a colourless oil (135 mg, 77%); $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.31-7.13 (m, 5H), 3.13 (q, $J$ = 6.6 Hz, 1H), 2.52-2.47 (m, 2H), 2.33-2.30 (m, 2H), 1.71-1.69 (m, 4H), 1.35 (d, $J$ = 6.6 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ

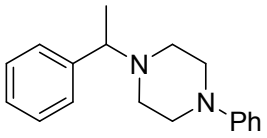
145.5, 128.3, 128.2, 127.2, 126.8, 65.9, 52.9, 23.4, 23.1; HRMS calcd for $C_{12}H_{17}NH^+$: 176.1439; Found: 176.1435.

**1-(1-Phenylethyl)piperidine (compound 18)[2]**



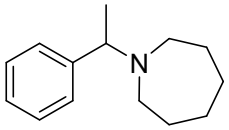
According to the representative method, using 1-phenylethanamine (1 mmol, 127 µL), pentane-1,5-diol (1 mmol, 105 µL), and the title compound was obtained by flash chromatography eluting with hexane then (EtOAc/Hexane; 1/10) to give a colourless oil (180 mg, 95%). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.27-7.16 (m, 5H), 3.35 (q, $J$ = 6.6 Hz, 1H), 2.39-2.28 (m, 6H), 1.54-1.48 (m, 4H), 1.33 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 143.9, 127.9, 127.7, 126.6, 65.1, 51.5, 26.2, 24.6, 19.3; HRMS calcd for $C_{13}H_{19}NH^+$: 190.1595; Found: 190.1589.

**1-Phenyl-4-(1-phenylethyl)piperazine (compound 19):[3]**



According to the representative procedure **II**, using 2,2'-(phenylazanediyl)diethanol, (1 mmol, 181 mg), and the title compound was obtained by flash chromatography eluting with (EtOAc/Hexane: 1/5) to give a white solid (181 mg, 68%); mp 42-49 °C; $\upsilon_{max}$ /cm$^{-1}$: 3057, 3027, 2952, 2903, 2873, 2812, 2766; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.27-7.12 (m, 7H), 6.83-6.72 (m, 3H), 3.31 (q, $J$ = 8.2 Hz, 1H), 3.08 (t, $J$ = 6.0 Hz, 4H), 2.62-2.41 (m, 4H), 1.32 (d, $J$ = 8.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 151.4, 143.9, 129.0, 128.4, 128.3, 127.6, 126.9, 126.6, 119.5, 115.9, 64.9, 50.6, 49.3, 19.9; HRMS calcd for $C_{18}H_{22}N_2H^+$: 267.1862; Found: 267.1855.

**1-(1-Phenylethyl)azepane (compound 20):** [2]



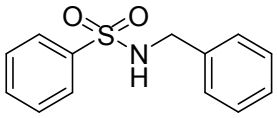

According to the representative procedure **II**, using hexane-1,6-diol (1 mmol, 118 mg), and the title compound was obtained by flash chromatography eluting with (EtOAc/Hexane: 1/10) to give a colourless oil (114 mg, 56%); $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.35-7.18 (m, 5H), 3.77 (q, $J$ = 6.9 Hz, 1H), 2.64 (br, s, 4H), 1.54 (br, s, 8H), 1.36 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 128.4, 128.3, 128.0, 127.7, 126.8, 126.6, 63.5, 52.0, 28.3, 27.0, 18.2; HRMS calcd for $C_{14}H_{21}NH^{+}$: 204.1753; Found: 204.1742.

## III. Representative procedure for the alkylation of sulfonamides with benzyl alcohol:

To an oven dried, nitrogen purged carousel tube containing $[IrCp^*I_2]_2$ (11.7 mg, 0.01 mmol), $K_2CO_3$ (138 mg, 1 eq), were added the representative sulfonamide (1mmol), benzylalcohol (1.2 mmol, 125 μL) followed by the deionised and degassed water (2 mL).

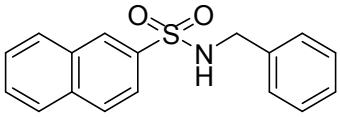
The reaction mixture was then heated to 115 °C at reflux for 20 h to 23 h depending on the sulfonamide used. After the required time, the crude mixture was extracted 3 times with ethyl acetate, dried over magnesium sulfate, then the solvent was removed under vacuum. The resulting residue was purified by column chromatography to give the desired product.

**_N_-Benzylbenzenesulfonamide (compound 23):** [2]



According to the representative procedure **III** using benzenesulfonamide (1 mmol, 157 mg), and the title compound was obtained by flash chromatography eluting with (MeOH/DCM; 2/98) to give a white solid (138 mg, 56%); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, $J$ = 8.7 Hz, 2H), 7.62-7.48 (m, 3H), 7.28-7.17 (m, 5H), 4.70 (br, s, 1H), 4.15 (d, $J$ = 6.3 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 143.1, 139.9, 136.1, 132.7, 129.1, 128.7, 127.9, 127.8, 127.1, 47.3; HRMS calcd for $C_{13}H_{13}NO_2SH^+$: 248.0743; Found: 248.0739.

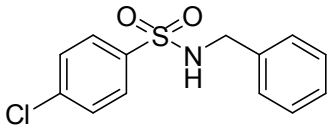
**_N_-Benzylnaphthalene-2-sulfonamide (compound 24):** [2]



According to the representative procedure **III**, using naphthalene-2-sulfonamide (1 mmol, 207 mg), and the title compound was obtained by flash chromatography eluting with (MeOH/DCM; 2/98) to give a white solid (172 mg, 58%); $^1$H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.64-7.48 (m, 4H), 7.35-7.25 (m, 2H), 6.92-76.85 (m, 5H), 4.49 (br, s, 1H), 3.84 (d, $J$ = 6.3 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 136.6,

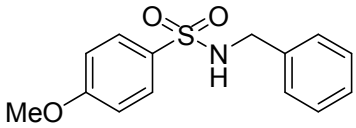
136.1, 134.8, 132.1, 129.5, 129.2, 128.8, 128.6, 127.9, 127.8, 127.5, 122.3, 47.4; HRMS calcd for $C_{17}H_{15}NO_2SH^+$: 298.0902; Found: 298.0901.

***N*-Benzyl-4-chlorobenzenesulfonamide (compound 25):** [2]



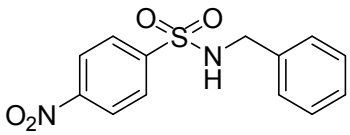
According to the representative procedure **III**, using 4-chlorobenzenesulfonamide (1 mmol, 191 mg), and the title compound was obtained by flash chromatography eluting with (MeOH/DCM; 2/98) to give a white solid (208 mg, 74%); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, $J$ = 8.7 Hz, 2H), 7.40 (dd, $J$ = 8.4 Hz, $J$ = 1.8 Hz, 2H), 7.23-7.10 (m, 5H), 4.73 (br, s, 1H), 4.09 (d, $J$ = 6.0 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 139.1, 138.4, 135.7, 129.3, 128.6, 128.4, 127.9, 127.7, 47.2; HRMS calcd for $C_{13}H_{12}ClNO_2SH^+$: 304.0175; Found: 304.0170.

***N*-Benzyl-4-methoxybenzenesulfonamide (compound 26):** [2]



According to the representative procedure **III**, using 4-methoxybenzenesulfonamide (1 mmol, 187 mg), and the title compound was obtained by flash chromatography eluting with (MeOH/DCM; 2/98) to give a white solid (197 mg, 71%); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, $J$ = 9.0 Hz, 2H), 7.29-7.17 (m, 5H), 6.97 (d, $J$ = 9.0 Hz, 2H), 4.60 (br, s, 1H), 4.22 (d, $J$ = 6.3 Hz, 2H), 3.88 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 162.9, 155.9, 136.3, 131.4, 129.3, 128.7, 127.9, 127.8, 114.3, 55.6, 47.3; HRMS calcd for $C_{14}H_{15}NO_3SH^+$: 278.0850; Found: 278.0847.

***N*-Benzyl-4-nitrobenzenesulfonamide (compound 27):** [2]

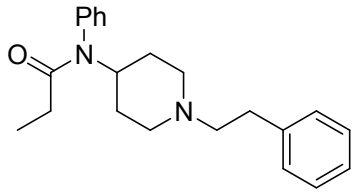


According to the representative procedure **III**, using 4-nitrobenzenesulfonamide (1 mmol, 202 mg), and the title compound was obtained by flash chromatography

eluting with (MeOH/DCM; 2/98) to give a colourless solid (73 mg, 25%); $^{1}$H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, $J$ = 8.7 Hz, 2H), 7.98 (d, $J$ = 8.7 Hz, 2H), 7.27-7.15 (m, 5H), 4.92 (br, s, 1H), 4.23 (d, $J$ = 6.0 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.0, 165.6, 146.0, 135.4, 128.8, 128.3, 127.8, 124.3, 47.4; HRMS calcd for $C_{13}H_{12}N_2O_4SH^+$: 315.0415; Found: 315.0409.

## IV. Preparation of Fentanyl:

### *N*-(1-Phenethylpiperidin-4-yl)-*N*-phenylpropionamide (compound 9): [4]



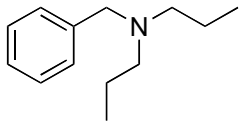

To an oven dried, nitrogen purged carousel tube containing $[IrCp^*I_2]_2$ (23.3 mg, 2 mol%) were added *N*-phenyl-*N*-(piperidin-4-yl)propionamide (1 mmol, 232 mg), 2-phenylethanol (1.2 mmol, 143µL) followed by the deionised and degassed water (2 mL).

The reaction mixture was then heated to 115 °C for 24 h. After the required time, the crude mixture is extracted 3 times with ethyl acetate, dried over magnesium sulfate, and then the solvent was removed under vacuum. The resulting residue was purified by column chromatography (EtOAc/Hexane: 1/10) then (EtOAc/Hexane: 1/5) to give the product as a white solid in reasonable yields. (219 mg, 65%); $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.43-7.07 (m, 10H), 4.74-4.65 (m, 1H), 3.01 (br, d, $J$ = 11.7 Hz, 2H), 2.77-2.71 (m, 2H), 2.57-2.54 (m, 2H), 2.17 (br, t, $J$ = 12 Hz, 2H), 1.93 (q, $J$ = 7.5 Hz, 2H), 1.81 (br, d, $J$ = 12.0 Hz, 2H), 1.45 (br, q, $J$ = 12.0 Hz, 2H), 1.02 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.5, 140.2, 138.8, 130.4, 129.3, 128.6, 128.3, 128.2, 126.0, 60.4, 53.0, 52.1, 33.8, 30.5, 28.5, 9.6; HRMS calcd for $C_{22}H_{28}N_2OH^+$: 337.2279; Found: 337.2277.

## V. Representative procedure for the *N*-alkylation of primary and secondary amines in ionic liquid

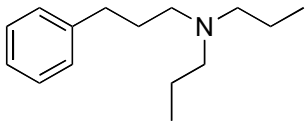
$[Cp^*IrI_2]_2$ (11.6 mg, 0.01 mmol) was placed in an oven dried carousel tube and placed under an inert atmosphere of nitrogen. $[BMIM]PF_6$ (0.5 mL) was added followed by the alcohol (1 mmol) and primary or secondary amine (1 mmol). The tube was then heated at 115 °C for 3-24 h before cooling to room temperature. Ethyl actetate was added and the crude extracted three times with diethylether. The organic portions were combined and the solvent removed under vacuum. Conversions were determined by analysis of the crude $^1$H NMR spectra and th following compound further purified.

**_N_-Benzyl-_N_-propylpropan-1-amine (compound 36):[2]**




The title compound was prepared according to the representative procedure and obtained by Kugelrohr distillation to give a colourless oil (156 mg, 82%); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.30-7.10 (m, 5H), 3.49 (s, 2H), 2.30 (m, 4H), 1.42 (m, 4H), 0.79 (t, $J$ = 7.3 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 128.82, 128.07, 126.60, 58.66, 55.87, 20.20, 11.92.

**3-phenyl-*N*,*N*-dipropylpropan-1-amine (compound 38):**




The title compound was prepared according to the representative procedure and was obtained by flash chromatography eluting with (EtOAc/Hexane: 1/10) to give a colourless oil (138 mg, 63%); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.23-7.04 (m, 5H), 2.54 (t, $J$ = 7.7 Hz, 2H), 2.38 (t, $J$ = 7.2 Hz, 2H), 2.29 (m, 4H), 1.68 (m, 2H), 1.36 (m, 4H), 0.79 (t, $J$ = 7.3 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 142.60, 128.43, 128.32, 125.67, 56.31, 53.88, 33.92, 29.05, 20.33, 12.08.

## VI. Representative procedure for the reaction of alcohol with $HNMe_2$ in ionic liquid

$[Cp^*IrI_2]_2$ (11.6 mg, 0.01 mmol) was placed in an oven dried carousel tube and placed under an inert atmosphere of nitrogen. [BMIM]$PF_6$ (0.5 mL) was added followed by the alcohol (1 mmol) and the dimethylamine (40% solution in $H_2O$, 1.2 mmol, 0.15 mL). The tube was then heated at 115 °C for 3 h before cooling to room temperature. Ethyl actetate was added and the crude extracted three times with diethylether. The combined organics were dried with $MgSO_4$ and concentrated under reduced pressure. Conversions were determined by analysis of the crude $^1$H NMR spectra.

## VII. References:


[1] A. J. Blacker, M. J. Stirling, and M. I. Page, *Org. Proc. Res. Dev*., 2007, **11**, 642-648

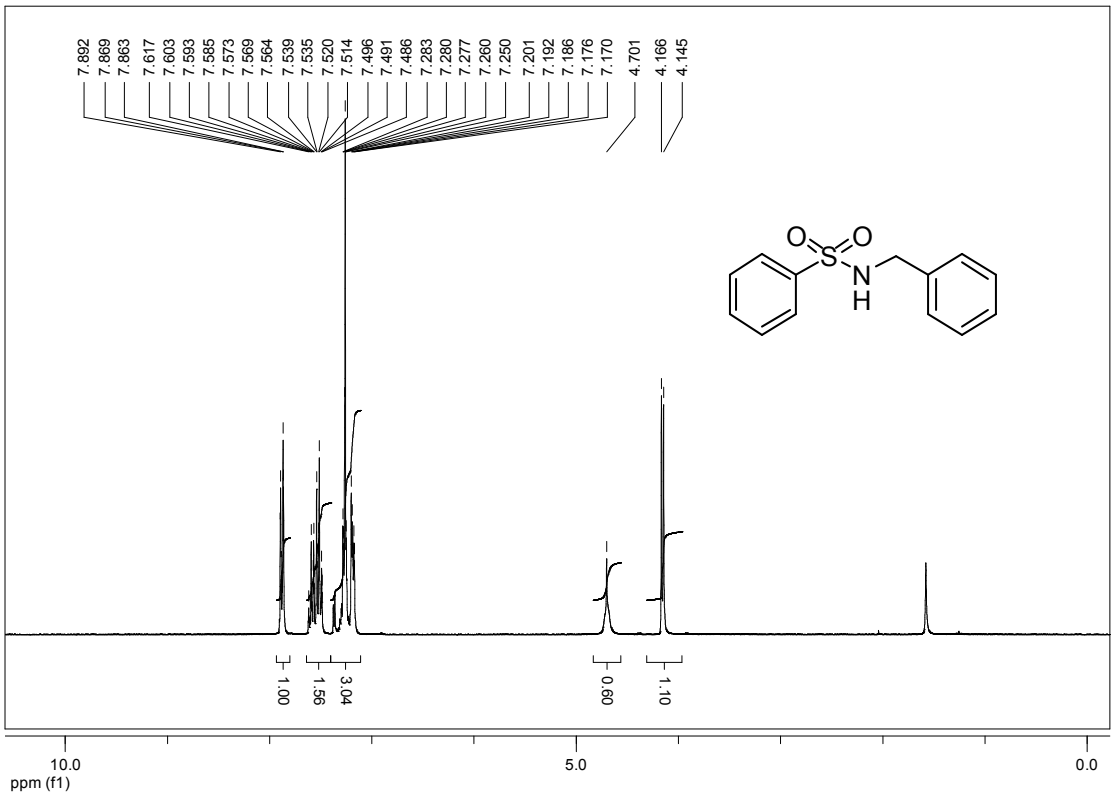
[2] M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc.*, 2009, **131**, 1766-1774.

[3] M. Utsunomiya and J. F. Hartwig, *J. Am. Chem. Soc.*, 2003, **125** (47), 14286-14287

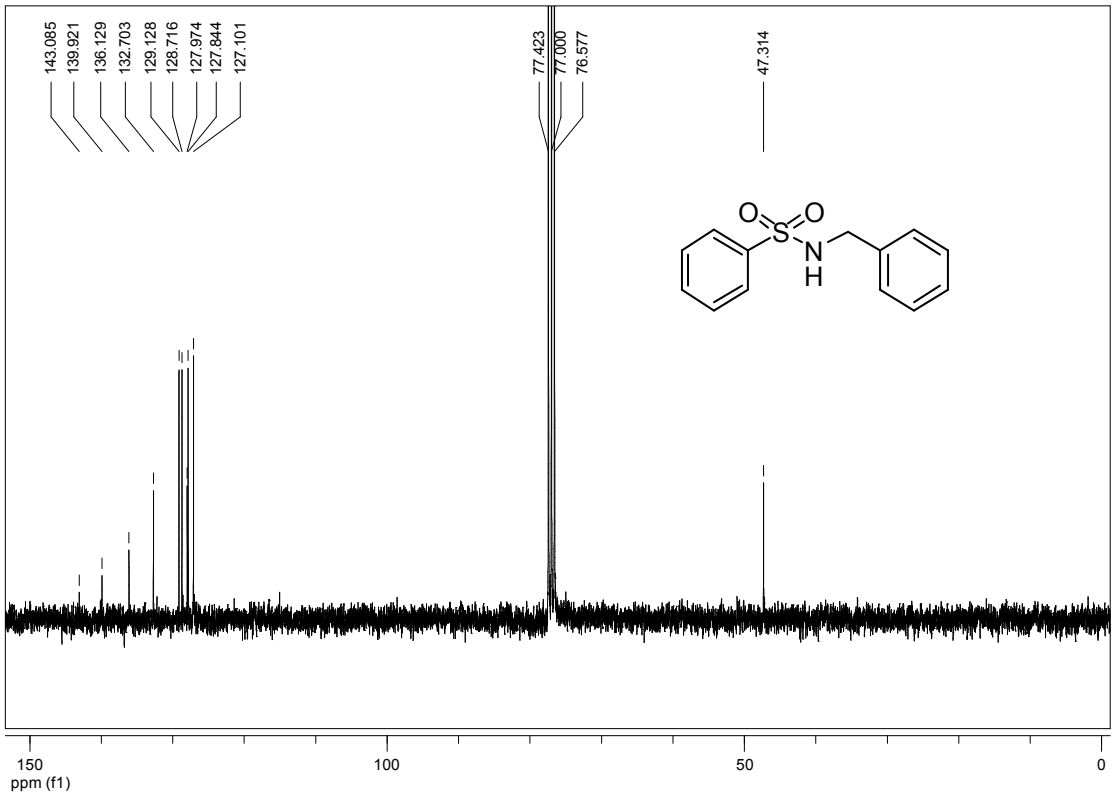
[4] P. K. Gupta, K. Ganesan, P. K. Gutch, L. Manral, and D. K. Dubey, *J. Chem. Eng. Data*, 2008, **53**, 841-845; M. L. Jimeno, I. Alkorta, C. Cano, N. Jagerovic, P. Goya, J. Elguero, C. Foces-foces, *Chem. Pharm. Bull*., 2003, **51** (8), 929-934.

## VIII. $^{1}$H NMR and $^{13}$C NMR spectra

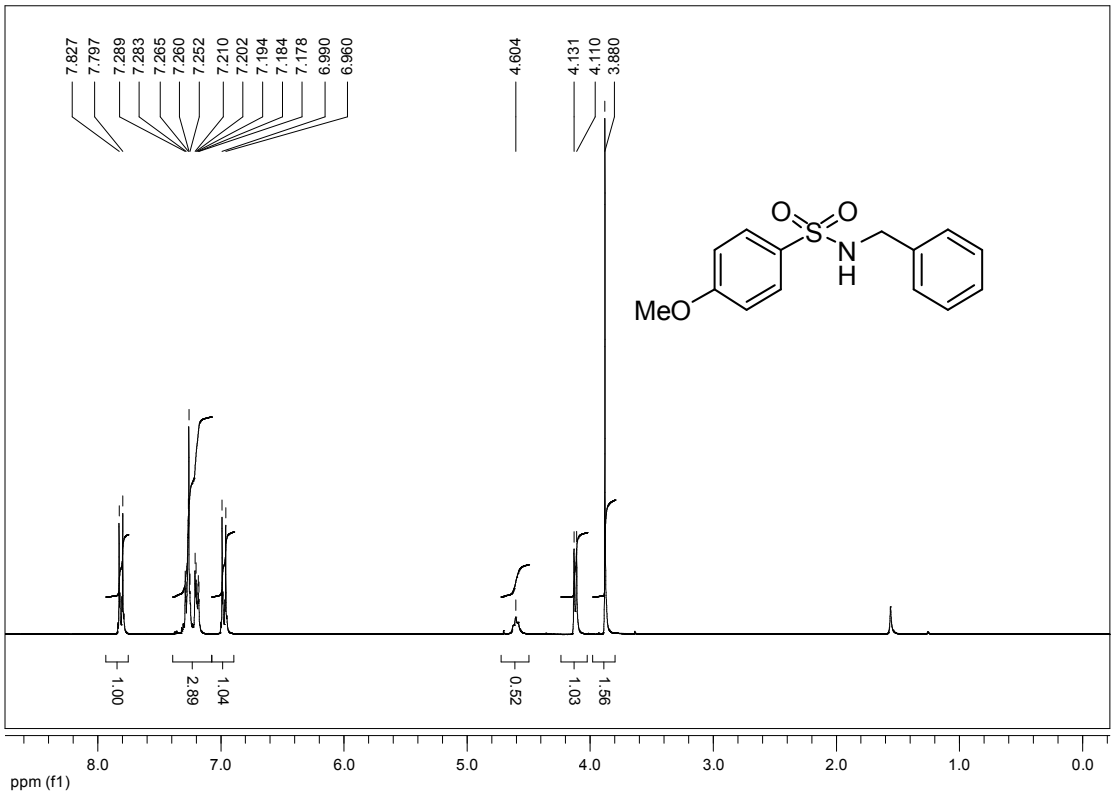
### $^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzylbenzenesulfonamide (compound 23)



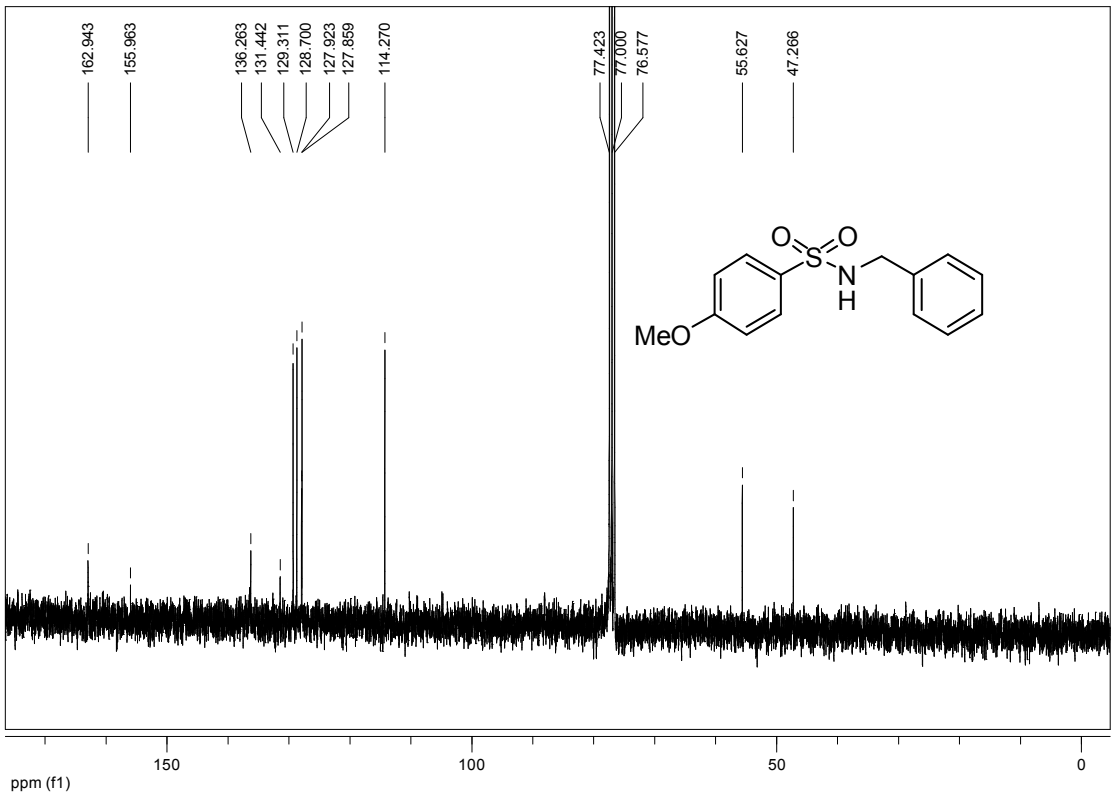

### $^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzylbenzenesulfonamide (compound 23)



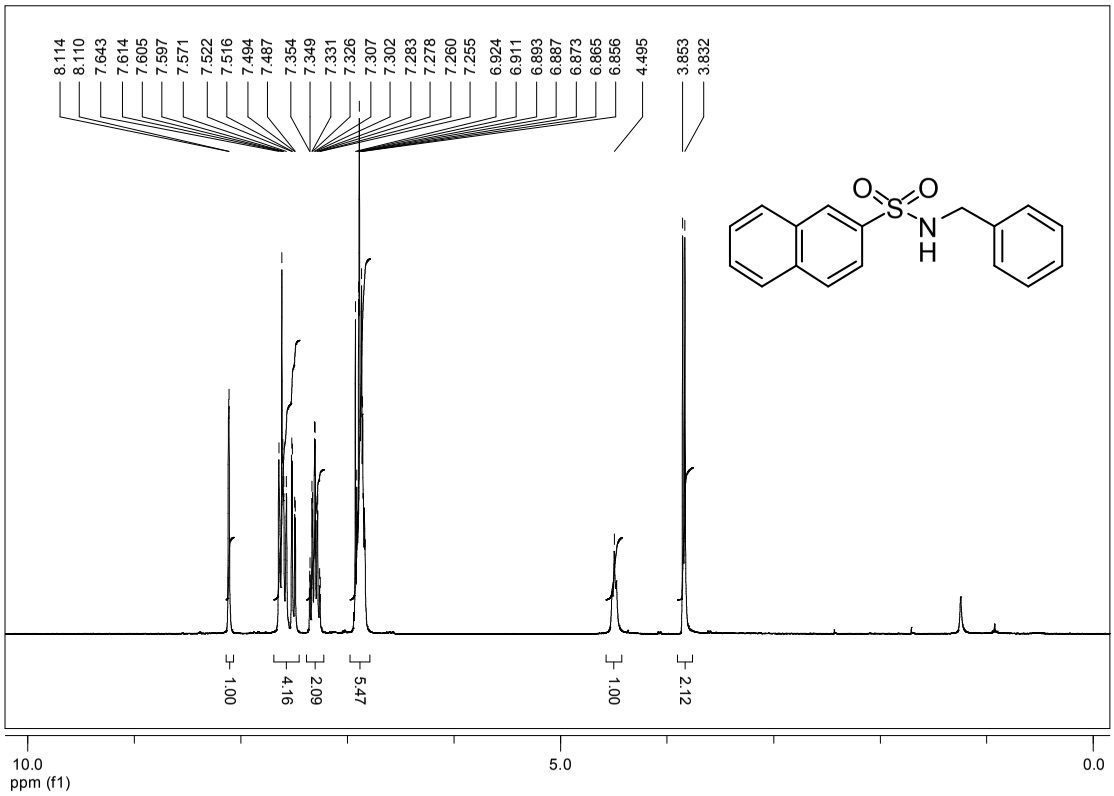
**$^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzyl-4-methoxybenzenesulfonamide (compound 26)**



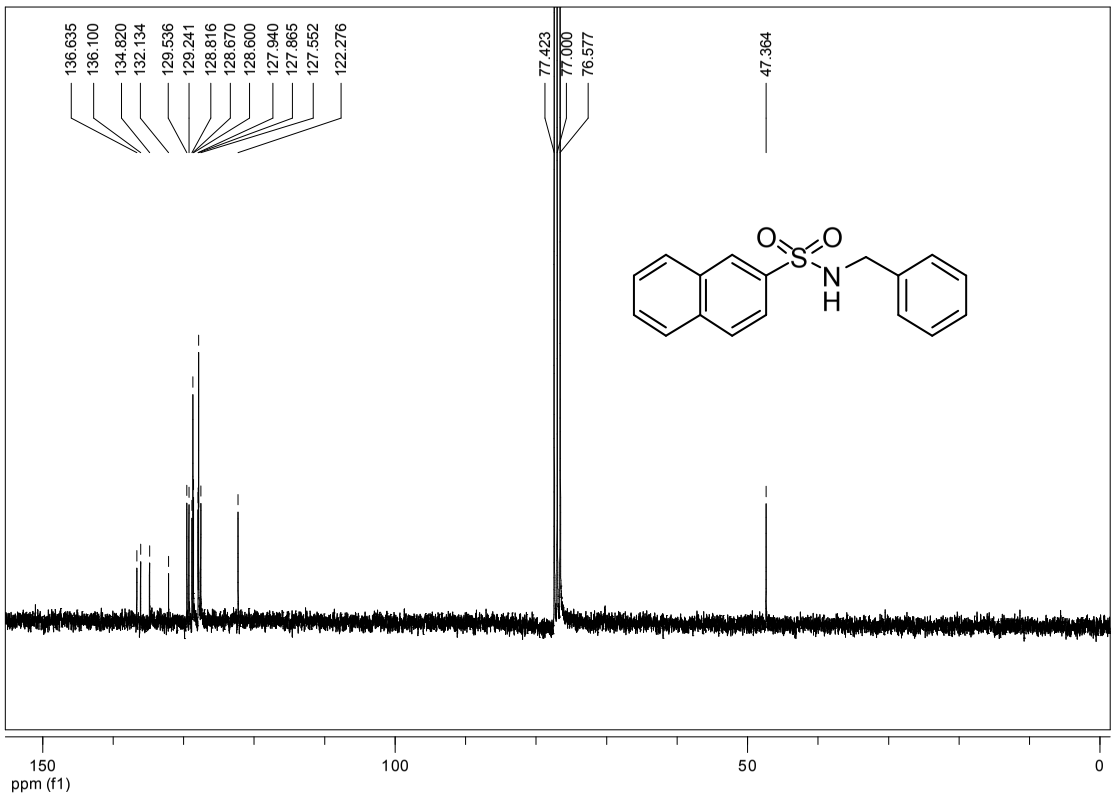

**$^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzyl-4-methoxybenzenesulfonamide (compound 26)**



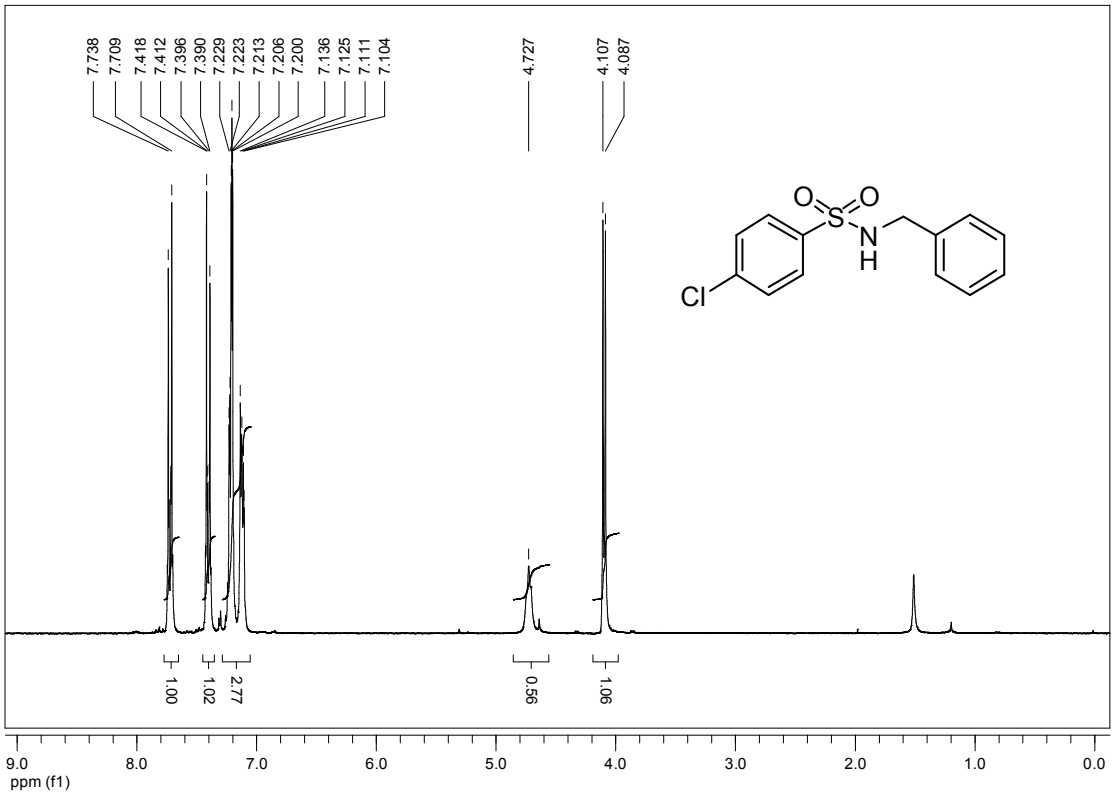
**$^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzylnaphthalene-2-sulfonamide (compound 24)**



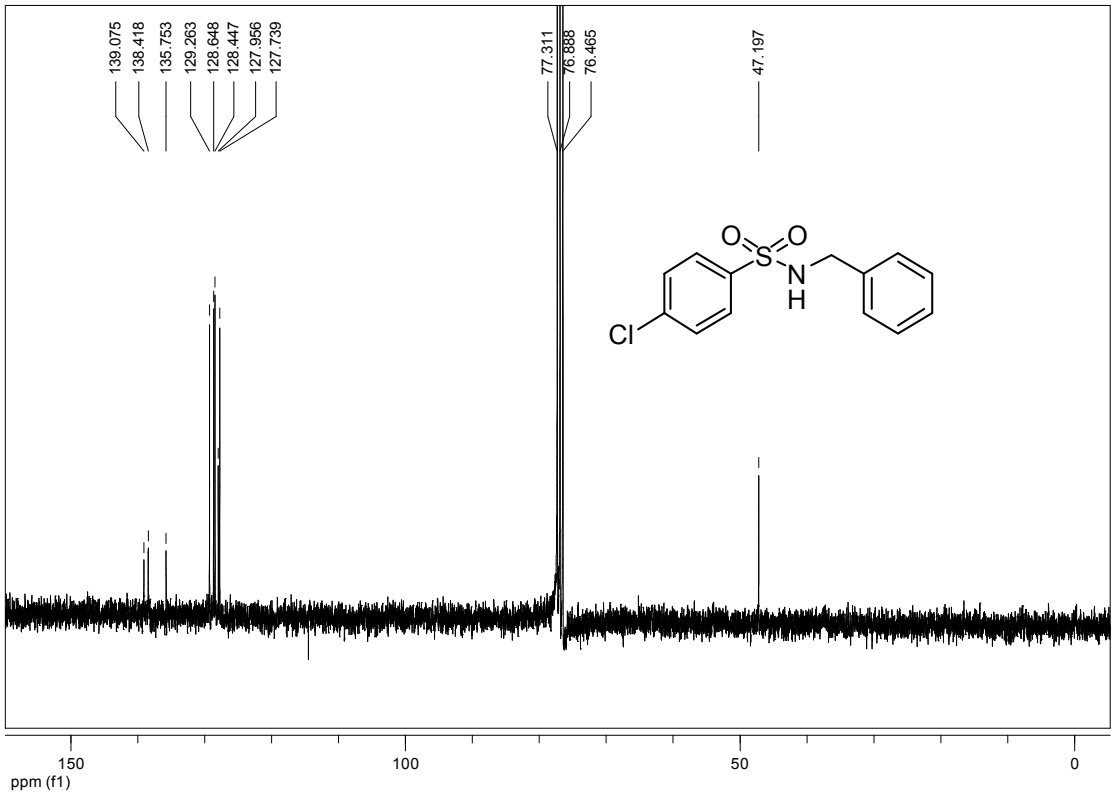

**$^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzylnaphthalene-2-sulfonamide (compound 24)**



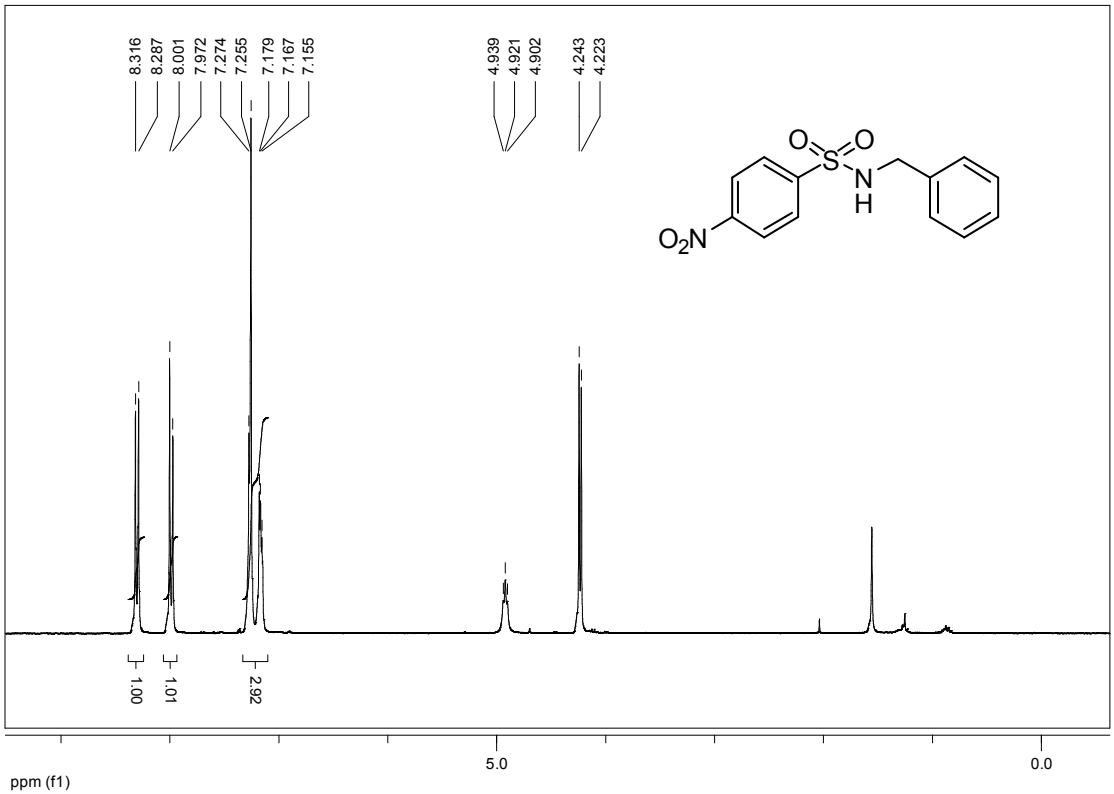
**$^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzyl-4-chlorobenzenesulfonamide (compound 25)**



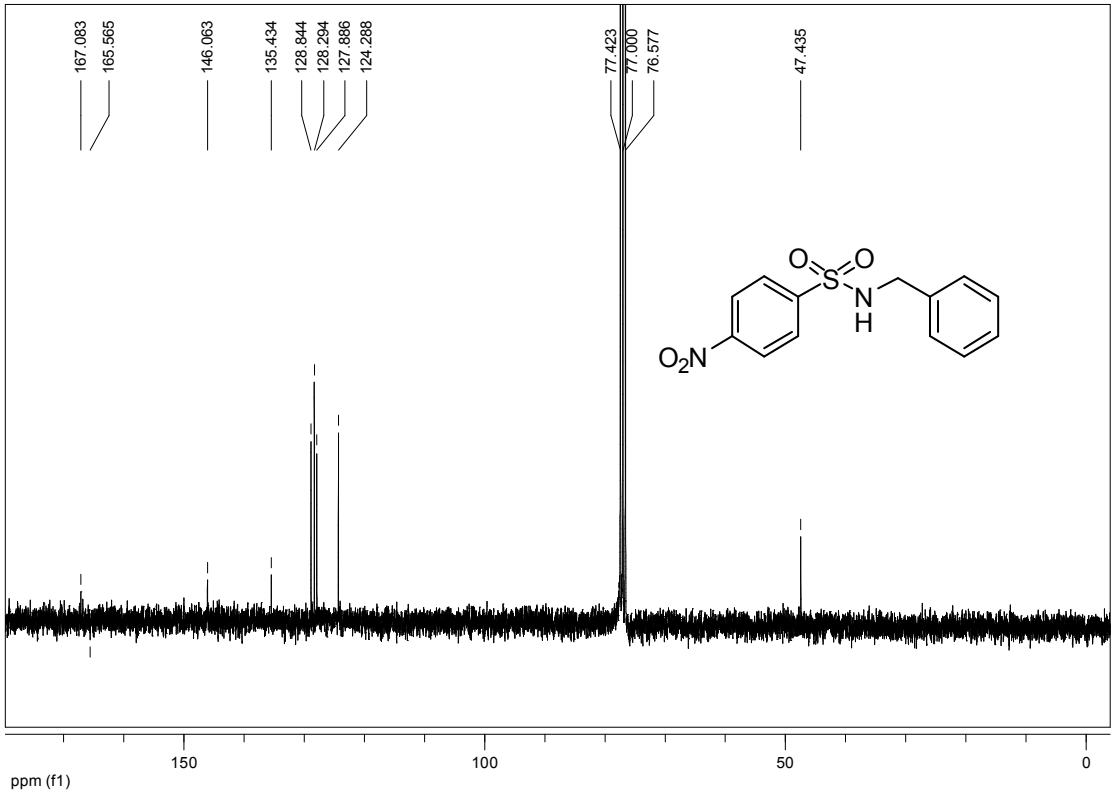

**$^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzyl-4-chlorobenzenesulfonamide (compound 25)**



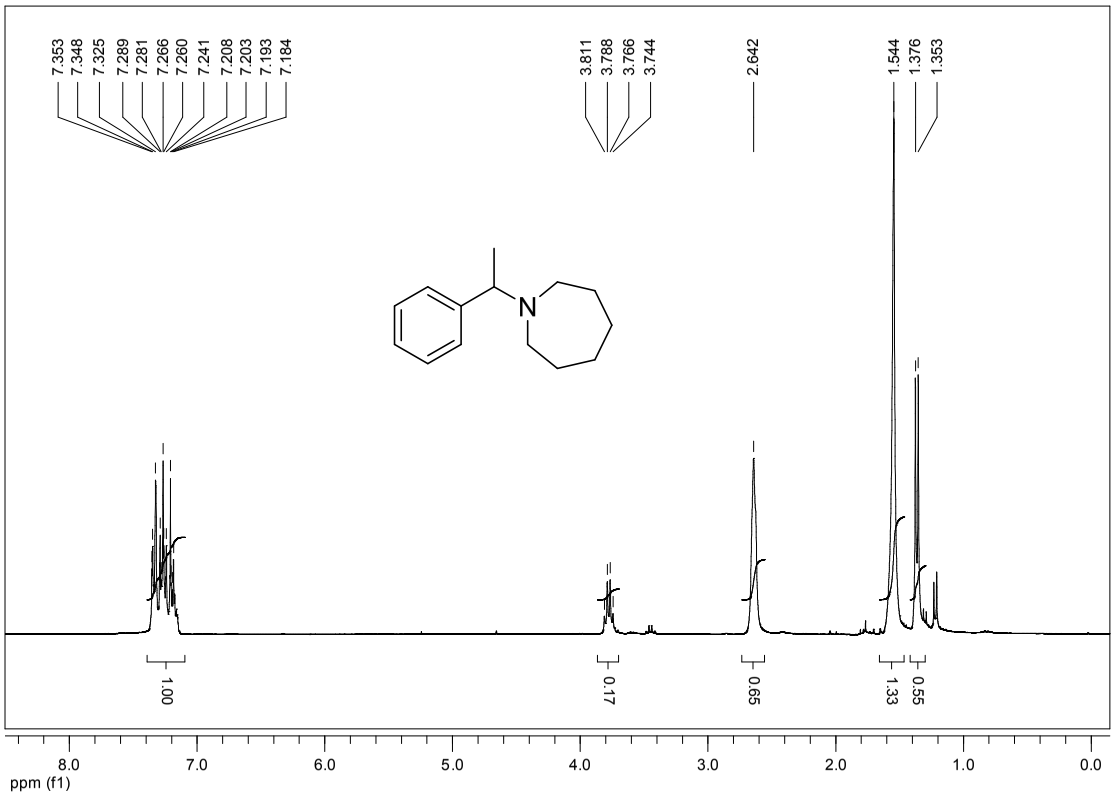
**$^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzyl-4-nitrobenzenesulfonamide (compound 27)**



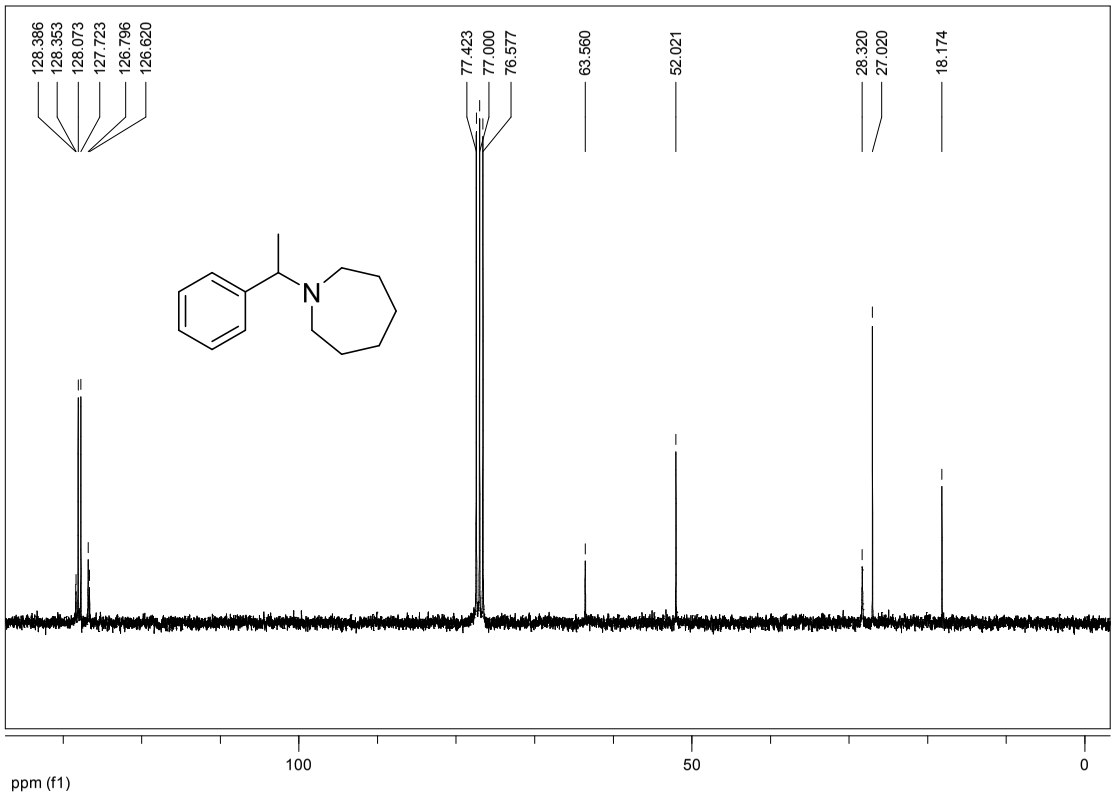

**$^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzyl-4-nitrobenzenesulfonamide (compound 27)**



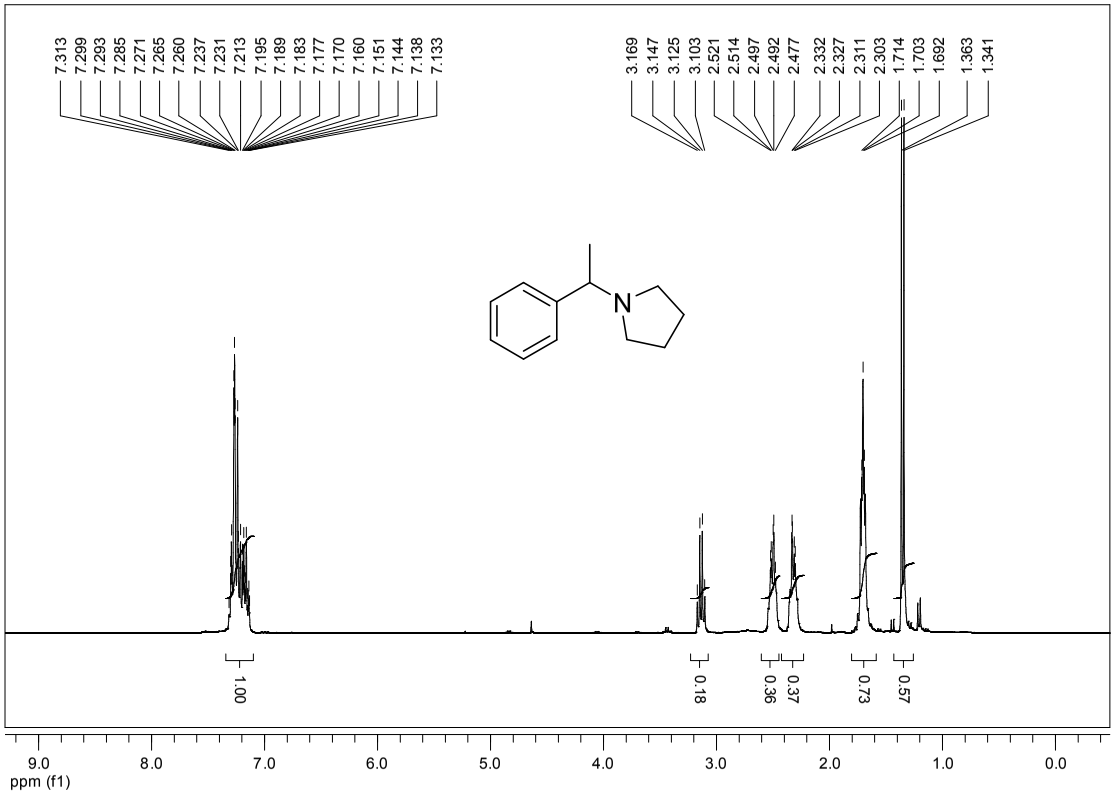
**$^{1}$H NMR (300 MHz, $CDCl_3$): 1-(1-Phenylethyl)azepane (compound 20)**



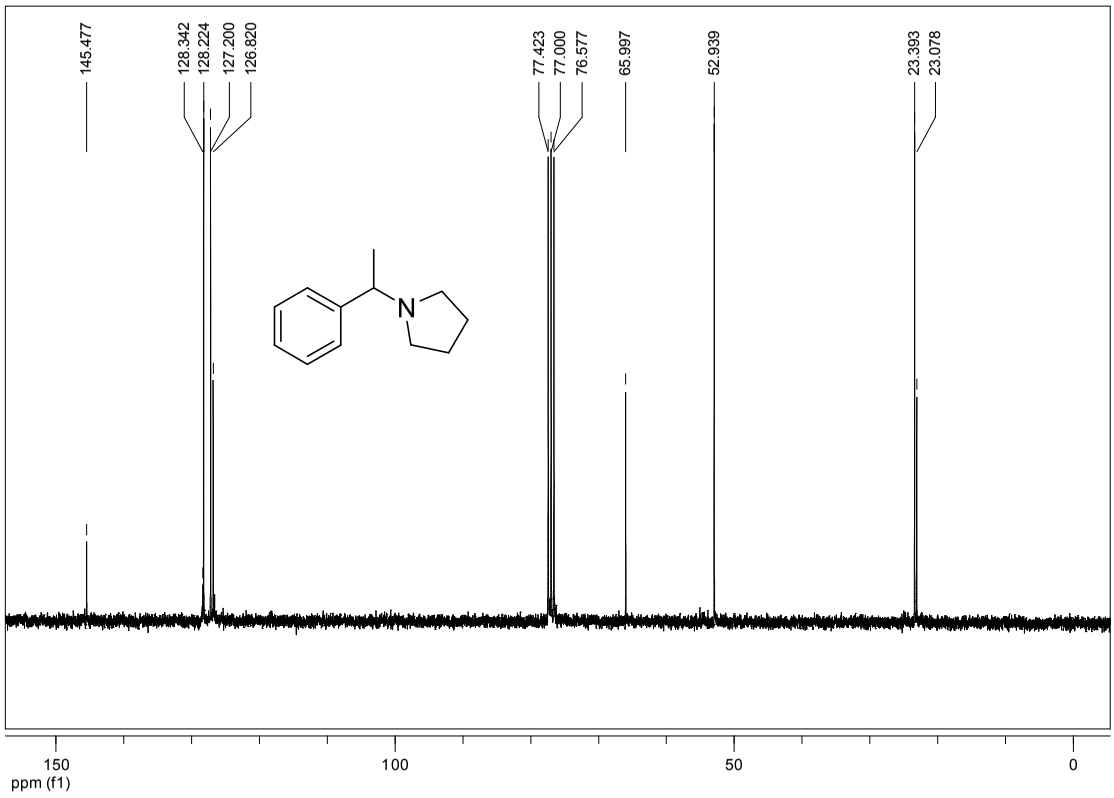

**$^{13}$C NMR (75 MHz, $CDCl_3$): 1-(1-Phenylethyl)azepane (compound 20)**



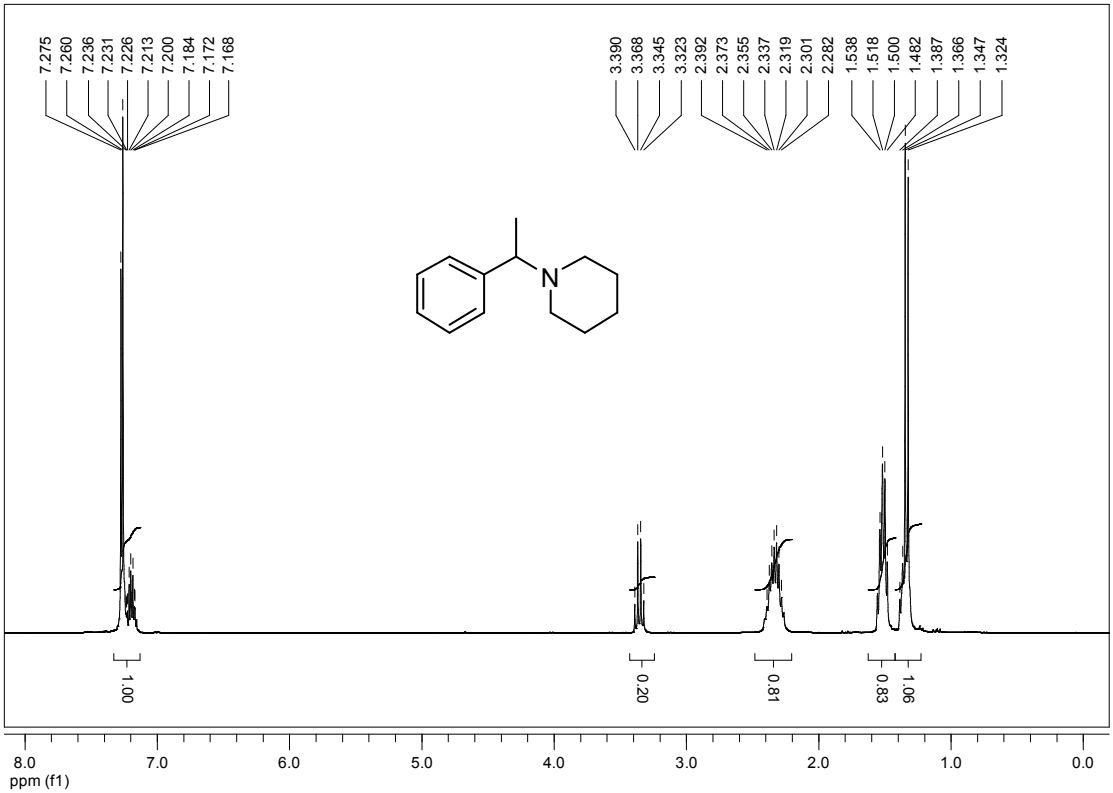
**$^{1}$H NMR (300 MHz, $CDCl_3$): 1-(1-Phenylethyl)pyrrolidine (compound 17)**



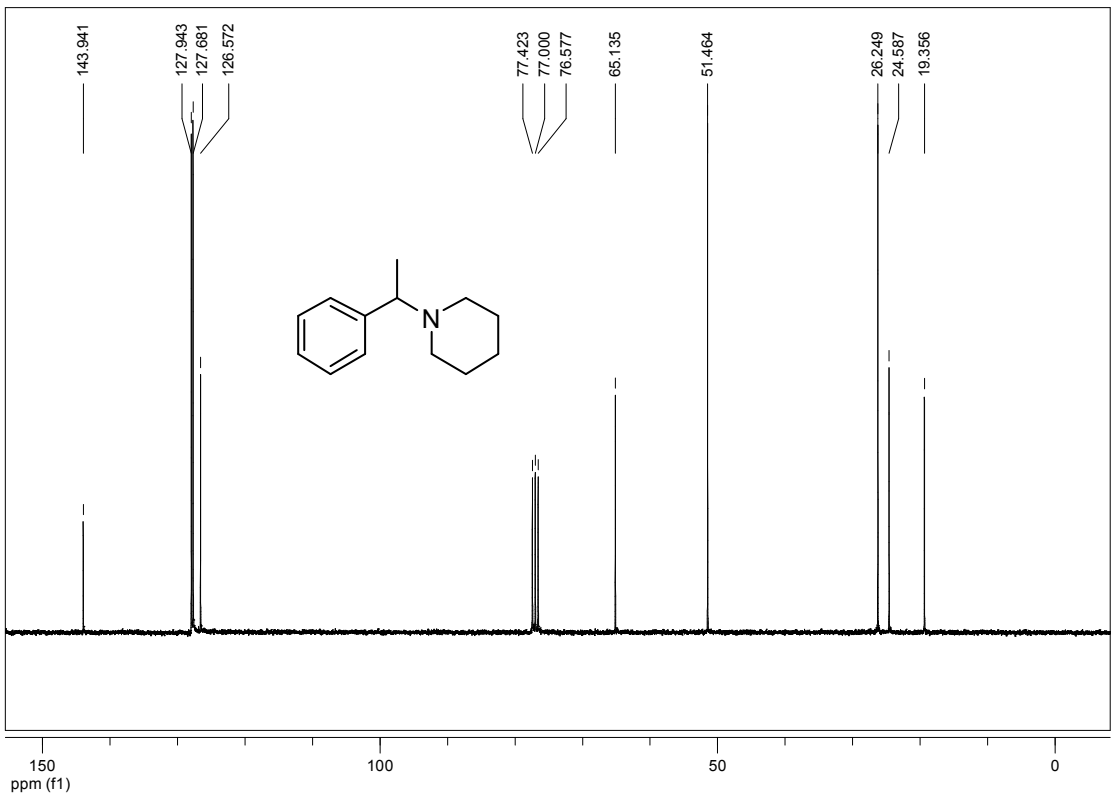

**$^{13}$C NMR (75 MHz, $CDCl_3$): 1-(1-Phenylethyl)pyrrolidine (compound 17)**



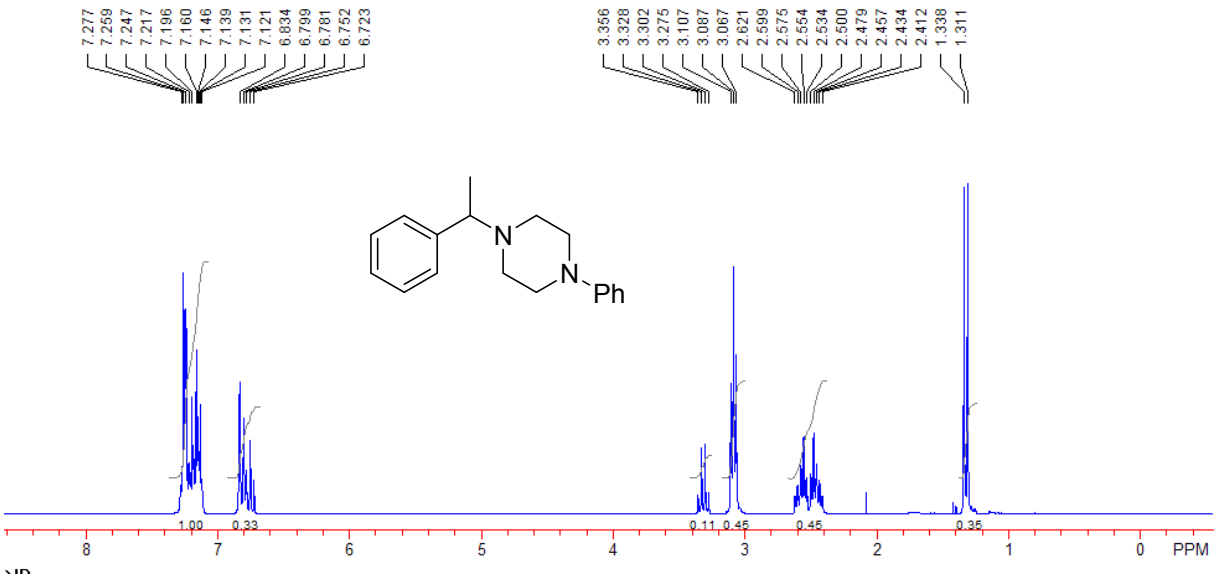
**$^{1}$H NMR (300 MHz, $CDCl_3$): 1-(1-Phenylethyl)piperidine (compound 18)**



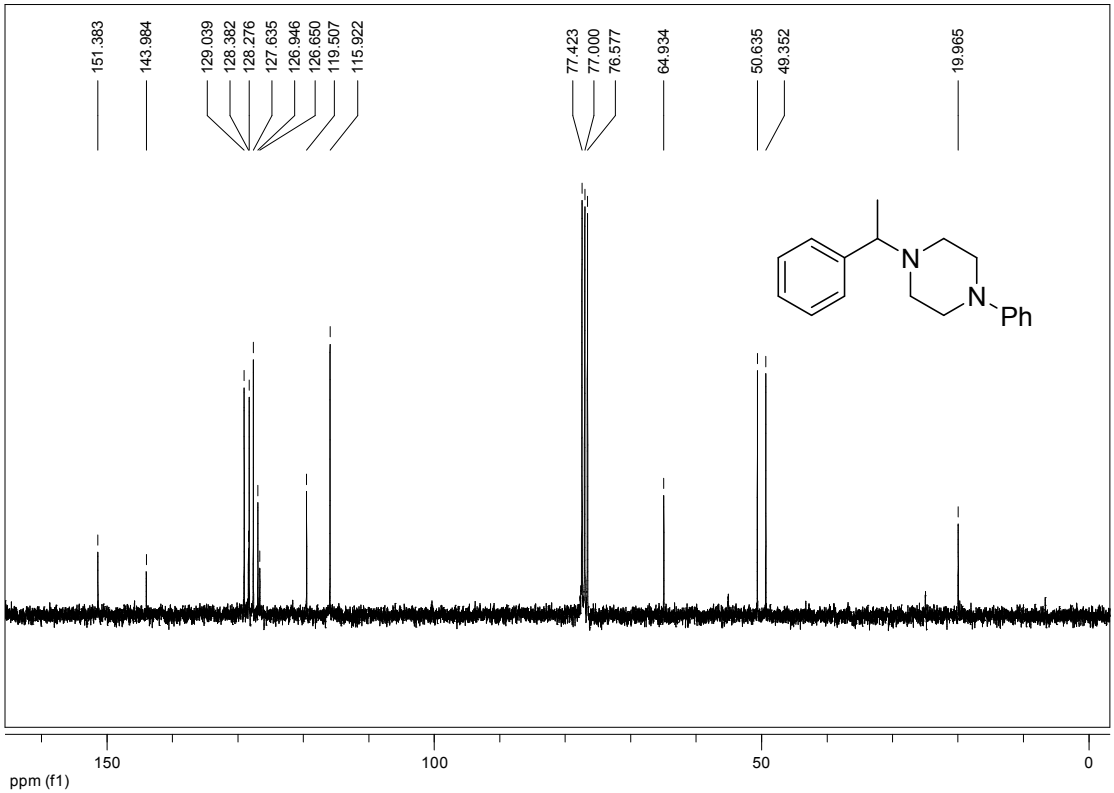

**$^{13}$C NMR (75 MHz, $CDCl_3$): 1-(1-Phenylethyl)piperidine (compound 18)**



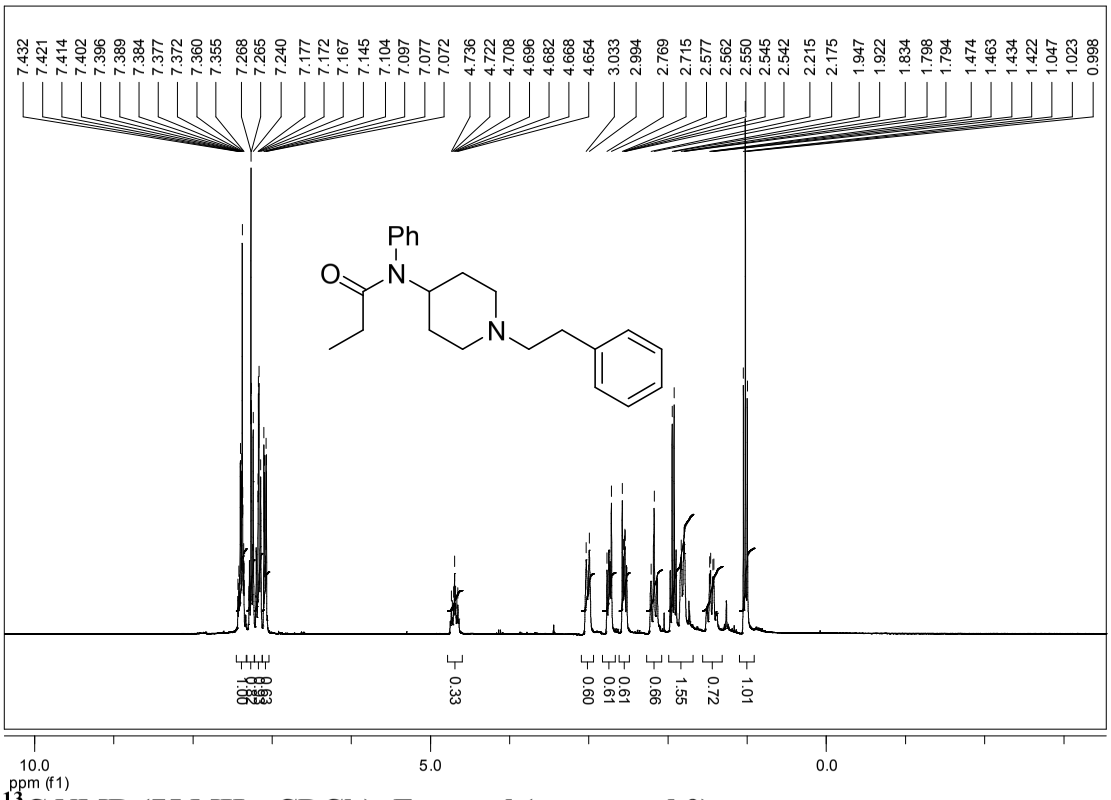
**$^{1}$H NMR (300 MHz, $CDCl_3$): 1-Phenyl-4-(1-phenylethyl)piperazine (compound 19)**



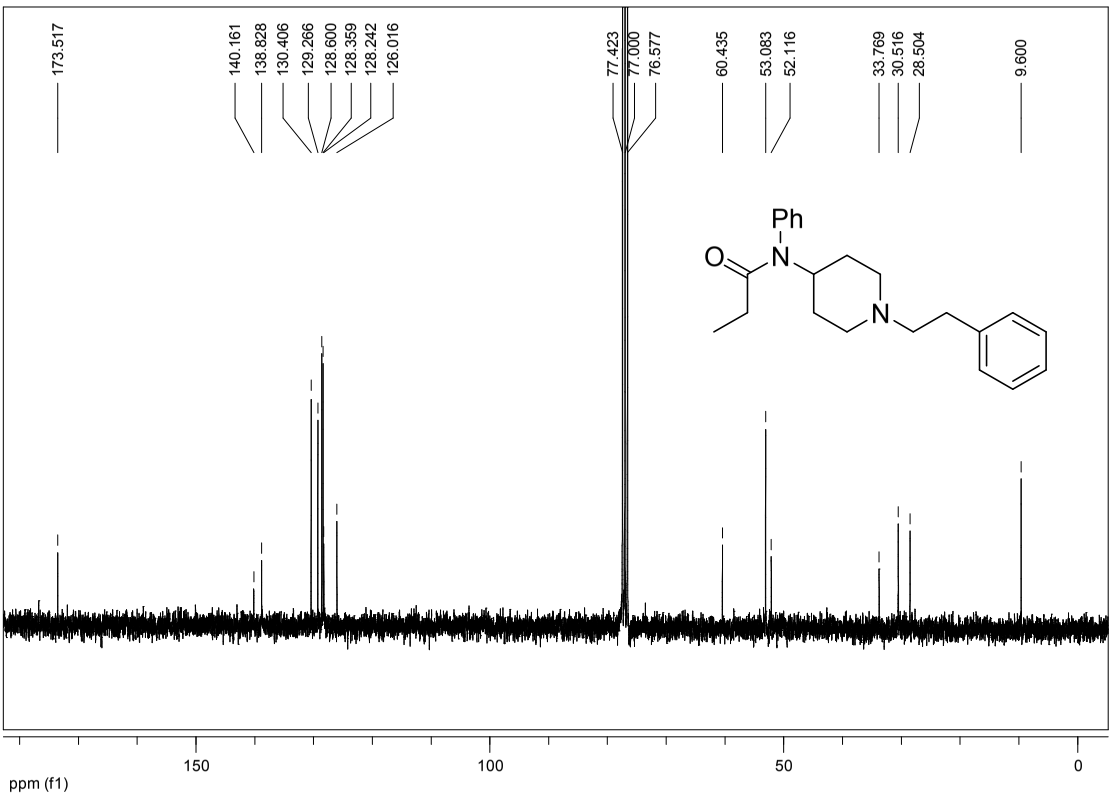

**$^{13}$C NMR (75 MHz, $CDCl_3$): 1-Phenyl-4-(1-phenylethyl)piperazine (compound 19)**



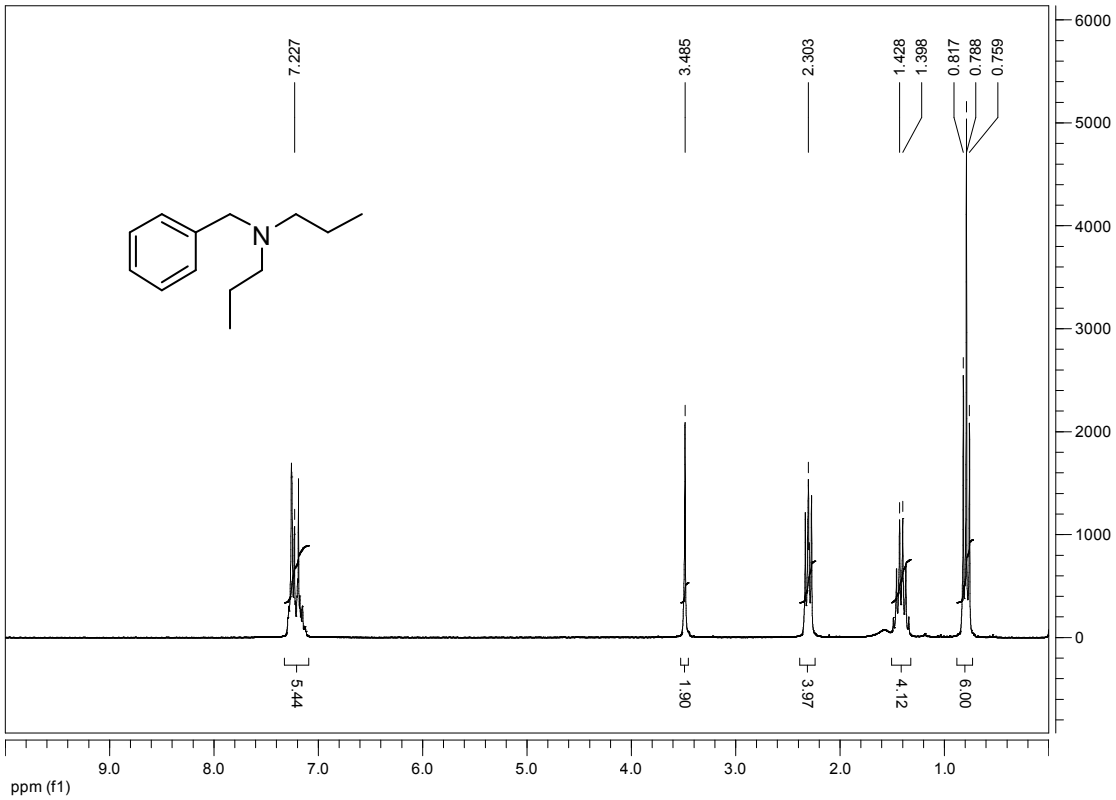
**$^{1}$H NMR (300 MHz, $CDCl_3$): Fentanyl (compound 9)**



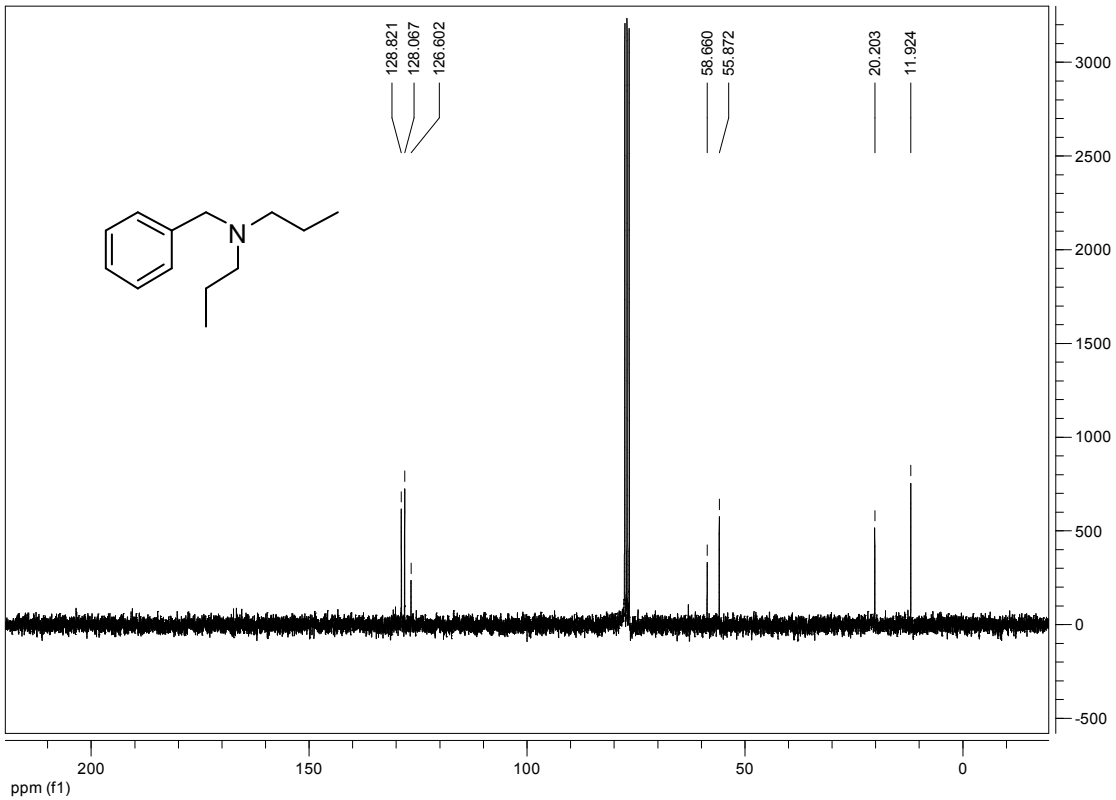

**$^{13}$C NMR (75 MHz, $CDCl_3$): Fentanyl (compound 9)**



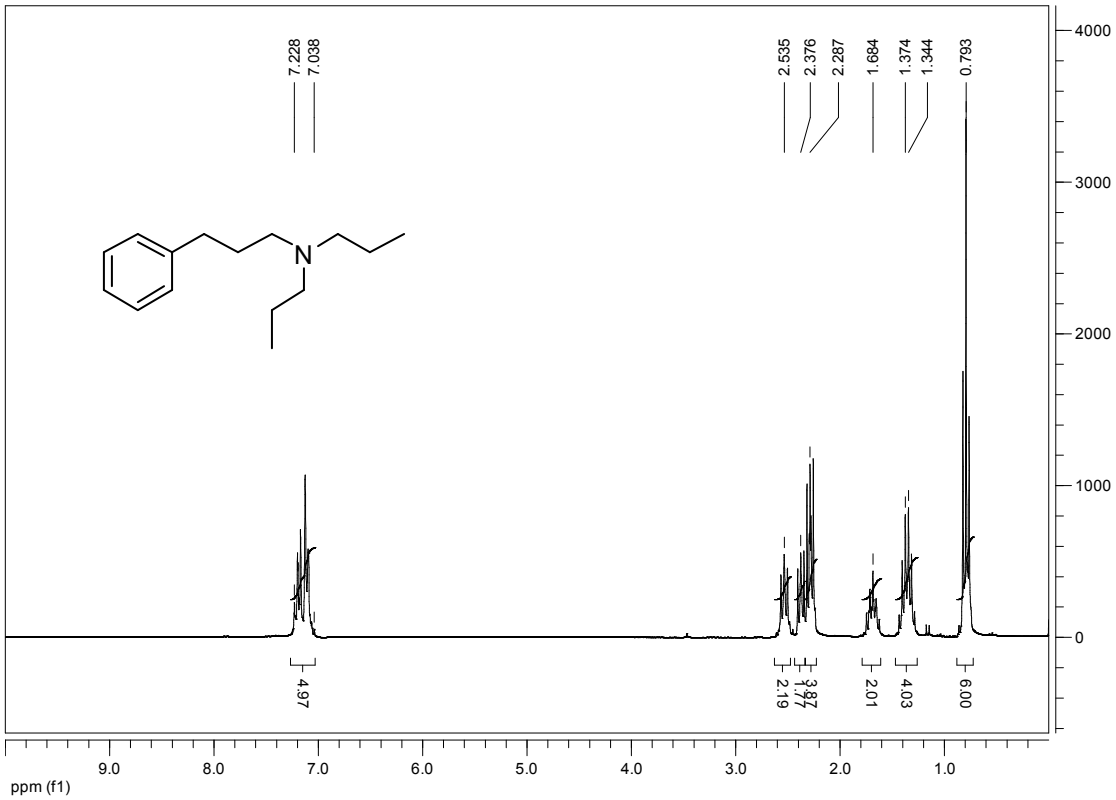
**$^{1}$H NMR (300 MHz, $CDCl_3$): *N*-Benzyl-*N*-propylpropan-1-amine (compound 36)**




**$^{13}$C NMR (75 MHz, $CDCl_3$): *N*-Benzyl-*N*-propylpropan-1-amine (compound 36)**



**$^{1}$H NMR (300 MHz, $CDCl_3$): 3-Phenyl-*N*,*N*-dipropylpropan-1-amine (compound 38)**




**$^{13}$C NMR (75 MHz, $CDCl_3$): 3-P|henyl-*N*,*N*-dipropylpropan-1-amine (compound 38)**