Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Informations

A Simple and Eco-Sustainable Method for Sulfonylation of Amines Under Microwave Assisted Solvent-Free Conditions.

Salah Lakrout, Hacène K'tir, Aïcha Amira, Malika Berredjem and Nour-Eddine Aouf[A]

Laboratory of Applied Organic Chemistry, Bioorganic Chemistry Group, Sciences Faculty, Chemistry Department, Badji Mokhtar - Annaba University, Box 12, 23000 Annaba, Algeria

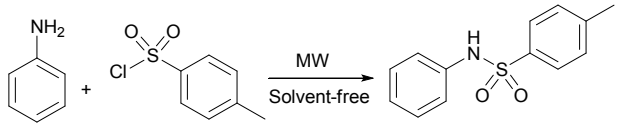
[A]Corresponding author. Email: noureddineaouf@yahoo.fr, noureddine.aouf@univ-annaba.dz

1. General:

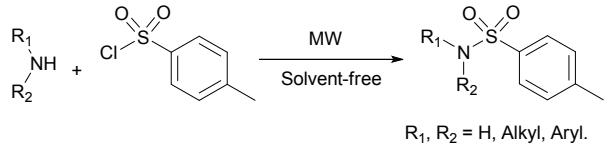
All chemicals and solvents were purchased from common commercial sources and were used as received without any further purification. All reactions were monitored by TLC on silica Merck 60 F_{254} percolated aluminum plates and were developed by spraying with ninhydrin solution. All reactions were carried out in the LG microwave *Lightwave Oven MJ3281BCS*, using 100W of microwave power at 50 °C. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Brücker spectrometer at 250, 300 or 400 MHz. Chemical shifts are reported in δ units (ppm) with TMS as reference (δ 0.00). All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Brücker at 60, 75 or 100 MHz. Chemical shifts are reported in δ units (ppm) relative to $CDCl_3$ (δ 77.0). Infrared spectra were recorded on a SHIMADZU FT-IR 8000 spectrometer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

2. Typical experimental procedure for the sulfonylation of amines:

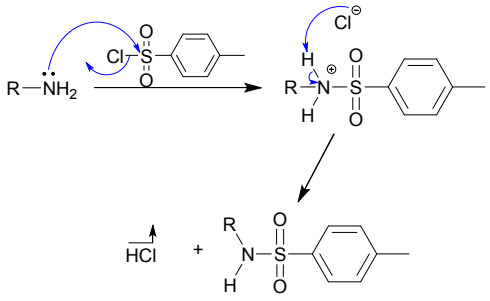
p-Toluenesulfonyl chloride (1 mmol) was added to amine (1 mmol) and the mixture was exposed to microwave irrdiation for the appropriate time. After completion of the reaction (monitored by TLC), the reaction mixture was treated with *n*-hexane (15-20 mL), and was allowed to stand at room temperature for 7-10 hours. The resulting crystals were collected by filtration, washed with *n*-hexane and dried.



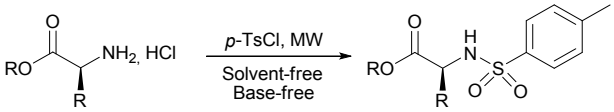
Scheme 1: Sulfonylation of aniline



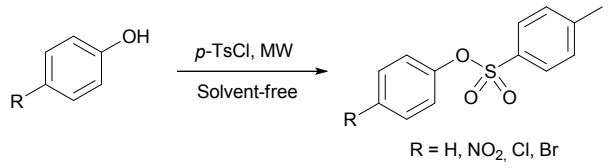
Scheme 2: Microwave assisted sulfonylation of various structurally amines.



Scheme 3: Mechanistic proposal for the sulfonylation of amines.

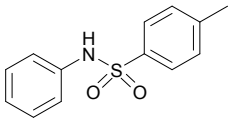


Scheme 4: Microwave assisted sulfonylation of amino acid esters hydrochloride.



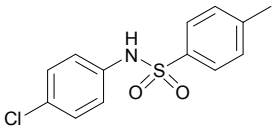
Scheme 4: Microwave assisted sulfonylation of phenols.

3. Experimental data:



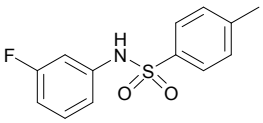
***N*-Phenyl-4-methylbenzenesulfonamide (Table 1, Entry 1a)**

(0.26 g, 97 %). mp 101.5-102.2 °C (From diethyl ether). R_f 0.63 (DCM/MeOH : 95/5). (Found: C, 63.27; H, 5.22; N, 5.56. Calc. for $C_{13}H_{13}NO_2S$: C, 63.13; H, 5.30; N, 5.66 %). ν_{max}/cm^{-1} 3288 (NH), 1602 (C=C), 1352 and 1154 (SO_2). δ_H (400 MHz, $CDCl_3$; Me_4Si) 1.74 (s, 1H, NH), 2.38 (s, 3H, CH_3), 7.08-7.32 (m, 5H, H-Ar), 7.11 (d, *J* 7.5 Hz, 2H, H-Ar), 7.67 (d, *J* 7.5 Hz, 2H, H-Ar). δ_C (100 MHz, $CDCl_3$) 21.5, 111.1, 121.1, 125.7, 126.0, 129.5, 136.7, 143.1. 149.6. M.W. 247.



***N*-(4-Chlorophenyl)-4-methylbenzenesulfonamide (Table 1, Entry 4a)**

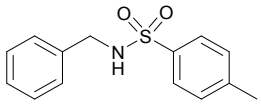
(0.20 g, 92 %). R_f 0.72 (DCM/MeOH : 95/5). (Found: C, 55.36; H, 4.33; N, 5.07. Calc. for $C_{13}H_{12}ClNO_2S$: C, 55.42; H, 4.29; N, 4.97%). ν_{max}/cm^{-1} 3397 (NH), 3032 (CH), 1609 (C=C), 1357 and 1167 (SO_2). δ_H (250 MHz, $CDCl_3$) 1.88 (s, 1H, NH), 2.40 (s, 3H, CH_3-Ar), 6.75-7.72 (m, 8H, H-Ar). δ_C (60 MHz, $CDCl_3$) 21.7, 122.9, 127.4, 129.5, 129.9, 130.9, 135.3, 135.7, 144.3. M.W. 281,5.



***N*-(3-Fluorophenyl)-4-methylbenzenesulfonamide (Table 1, Entry 6a)**

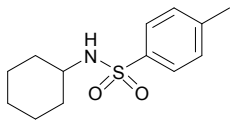
(0.22 g, 93 %). mp 101.7-103.5 °C (From diethyl ether). R_f 0.69 (DCM/MeOH : 95/5). (Found: C, 58.63; H, 4.66; N, 5.34. Calc. for $C_{13}H_{12}FNO_2S$: C, 58.85; H, 4.56; N, 5.28%).

ν_{max}/cm^{-1} 3457 (NH), 2941 (CH), 1594 (C=C), 1339 and 1107 (SO_2). δ_H (250 MHz, $CDCl_3$) 1.66 (s, 1H, NH), 2.38 (s, 3H, CH_3-Ar), 6.78-6.91 (m, 3H, H-Ar), 7.15 (m, 1H, H-Ar), 7.26 (d, *J* 7.8, 2H, H-Ar), 7.69 (d, *J* 7.8, 2H, H-Ar). δ_C (60 MHz, $CDCl_3$) 21.7, 108.5, 112.2, 116.4, 127.4, 130.0, 130.6, 130.8, 135.9, 138.3, 144.4. M.W. 265.



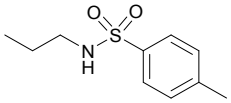
***N*-Benzyl-4-methylbenzenesulfonamide (Table 1, Entry 8a)**

(0.22 g, 89 %). mp 115.1-115.9 °C (From diethyl ether). R_f 0.68 (DCM/MeOH : 95/5). (Found: C, 64.53; H, 5.66; N, 5.51. Calc. for $C_{14}H_{15}NO_2S$: C; 64.34: H, 5.79; N, 5.36%). ν_{max}/cm^{-1} 3430 (NH), 2965 (CH), 1616 (C=C), 1316 and 1178 (SO_2). δ_H (300 MHz, $CDCl_3$) 2.38 (s, 3H, CH_3-Ar), 4.04 (d, *J* 6.1 Hz, 2H, CH_2-N), 4.78 (t, *J* 5.6 Hz, 1H, NH), 7.09-7.24 (m, 5H, H-Ar), 7.17 (d, *J* 7.5 Hz, 2H, H-Ar), 7.68 (d, *J* 7.5 Hz, 2H, H-Ar). δ_C (75 MHz, $CDCl_3$) 21.5, 47.3, 127.2, 127.9, 128.7, 129.7, 136.3, 136.9, 143.5. M.W. 261.



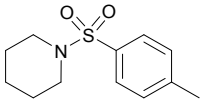
***N*-Cyclohexyl-4-methylbenzenesulfonamide (Table 1, Entry 10a)**

(0.22 g, 86%). mp 85.0-85.4 °C (From diethyl ether). R_f 0.76 (DCM/MeOH : 95/5). (Found: C, 61.81; H, 7.49; N, 5.61. Calc. for $C_{13}H_{19}NO_2S$: C, 61.63; H, 7.56; N, 5.53%). ν_{max}/cm^{-1} 3468 (NH), 3065 (CH), 1585 (C=C), 1338 and 1152 (SO_2). δ_H (300 MHz, $CDCl_3$) 1.09 (m, 4H, 2xCH_2), 1.46 (m, 2H, CH_2), 1.71 (m, 4H, 2xCH_2), 2.37 (s, 3H, CH_3-Ar), 3.04 (m, 1H, CH), 4.59 (s, 1H, NH), 7.22 (d, *J*=7.5 Hz, 2H, H-Ar), 7.71 (d, *J*=7.5 Hz, 2H, H-Ar). δ_C (75 MHz, $CDCl_3$) 21.5, 24.6, 25.1, 33.9, 52.6, 126.9, 129.6, 138.5, 143.1. M.W. 253.



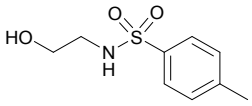
4-Methyl-*N*-propylbenzenesulfonamide (Table 1, Entry 11a)

(0.32 g, 88 %). R_f 0.53 (DCM/MeOH : 95/5). (Found: C, 56.43; H, 7.06; N, 6.88. Calc. for $C_{10}H_{15}NO_2S$: C, 56.31; H, 7.09; N, 6.57%). ν_{max}/cm^{-1} 3265 (NH), 2978 (CH), 1593 (C=C), 1372 and 1154 (SO_2). δ_H (300 MHz, $CDCl_3$) 0.81 (t, *J* 6.4 Hz, 3H, CH_3), 1.43 (m, 2H, CH_2), 2.37 (s, 3H, CH_3-Ar), 2.84 (m, 2H, CH_2-N) 5.17 (s, 1H, NH), 7.22 (d, *J* 7.5 Hz, 2H, H-Ar), 7.71 (d, *J* 7.5 Hz, 2H, H-Ar). δ_C (75 MHz, $CDCl_3$) 11.1, 21.5, 22.8, 44.9, 127.1, 129.6, 137.1, 143.2. M.W. 213.



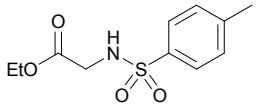
1-Tosylpiperidine (Table 1, Entry 15a)

(0.23 g, 83 %). mp 98.7-100.5 °C (From diethyl ether). R_f 0.66 (DCM/MeOH : 95/5). (Found: C, 60.43; H, 7.17; N, 5.89. Calc. for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85%). ν_{max}/cm^{-1} 3002 (CH), 1575 (C=C), 1368 and 1121 (SO_2). δ_H (250 MHz, $CDCl_3$) 1.38 (m, 2H, CH_2), 1.62 (m, 4H, 2xCH_2), 2.46 (s, 3H, CH_3-Ar), 2.99 (t, *J* 5.7, 4H, 2xCH_2-N), 7.33 (d, *J* 7.9, 2H, H-Ar), 7.65 (d, *J* 7.9, 2H, H-Ar). δ_C (60 MHz, $CDCl_3$) 21.7, 23.7, 25.3, 47.1, 127.9, 129.7, 133.6, 143.4. M.W. 239.



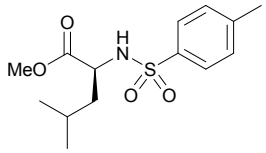
***N*-(2-Hydroxyethyl)-4-methylbenzenesulfonamide (Table 1, entry 17a)**

(0.27 g, 77 %). R_f 0.59 (DCM/MeOH : 95/5). (Found: C, 44.69; H, 5.46; N, 5.67. Calc. for $C_9H_{13}NO_3S$: C, 44.81; H, 5.39; N, 5.81%). ν_{max}/cm^{-1} 3597 (OH), 3219 (NH), 3065 (CH), 1605 (C=C), 1328, 1148 (SO_2). δ_H (250 MHz, $CDCl_3$) 2.33 (s, 3H, CH_3), 2.94 (q, 2H, *J* 4.76 Hz, CH_2-N), 3.58 (t, 2H, *J* 5.27 Hz, CH_2-O), 6.25 (t, *J* 6.09 Hz, 1H, NH), 7.22 (d, *J* 7.8 Hz, 2H, H-Ar), 7.68 (d, *J* 7.8 Hz, 2H, H-Ar). δ_C (62.89 MHz, $CDCl_3$) 21.4, 45.1, 60.9, 126.9, 129.7, 136.4, 143.4. M.W. 215.



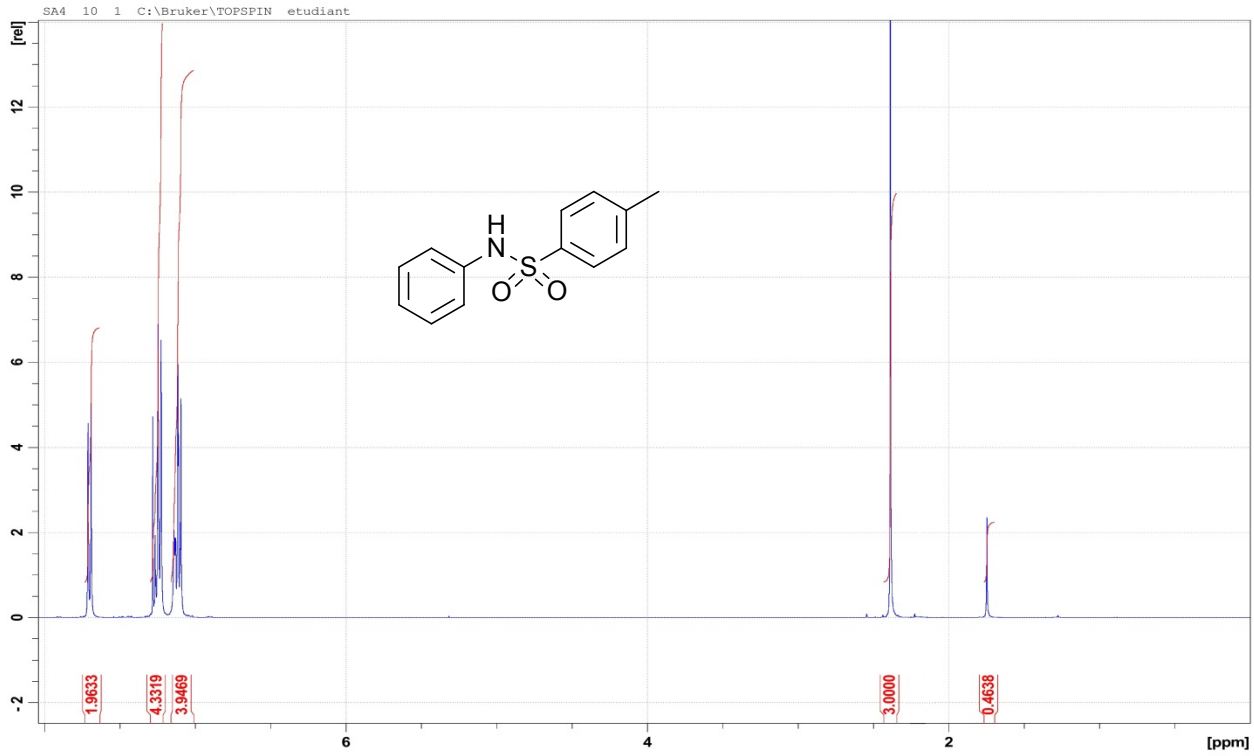
Ethyl 2-(4-methylphenylsulfonamido) acetate (Table 2, Entry 1b)

(0.16 g, 85 %). R_f 0.42 (DCM-MeOH : 95/5). (Found: C, 49.39; H, 5.66; N, 05.67. Calc. for $C_{11}H_{15}NO_4S$: C, 49.38; H, 5.35; N, 5.76%). ν_{max}/cm^{-1} 3226 (NH), 1732 (C=O), 1598 (C=C), 1372 and 1154 (SO_2). δ_H (400 MHz, $CDCl_3$) 1.18 (t, *J* 6.7 Hz, 3H, CH_3), 2.46 (s, 3H, CH_3-Ar), 3.77 (d, *J* 6.2 Hz ,2H, CH_2-N), 4.08 (q, *J* 6.9 Hz, 2H, CH_2-O), 5.12 (t, *J* 5.8 Hz, 1H, NH) 7.32 (d, *J* 7.7 Hz, 2H, H-Ar), 7.75 (d, *J* 7.7 Hz, 2H, H-Ar). δ_C (100 MHz, $CDCl_3$) 13.9, 21.5, 44.2, 61.9, 127.3, 129.8, 136.1, 143.9, 168.8. M.W. 257.

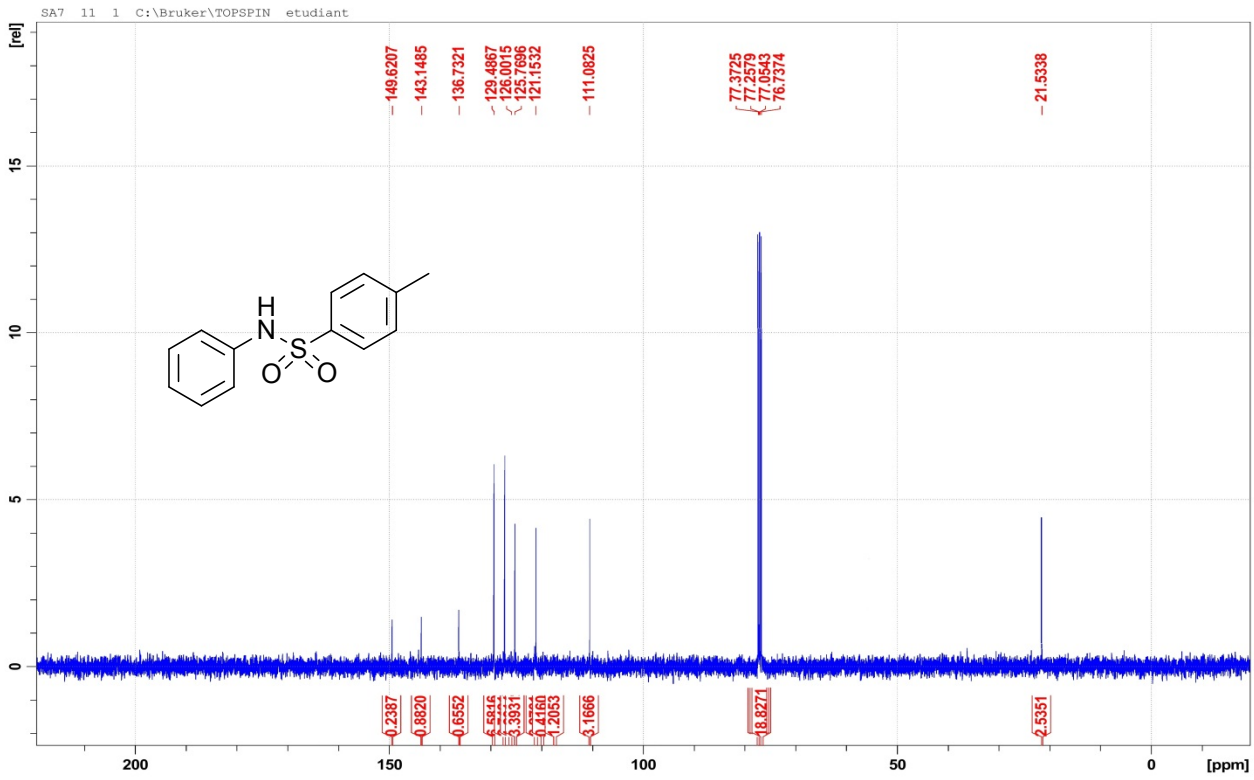


(*S*)-Methyl 4-methyl-2-(4-methylphenylsulfonamido) pentanoate (Table 2, Entry 2b)

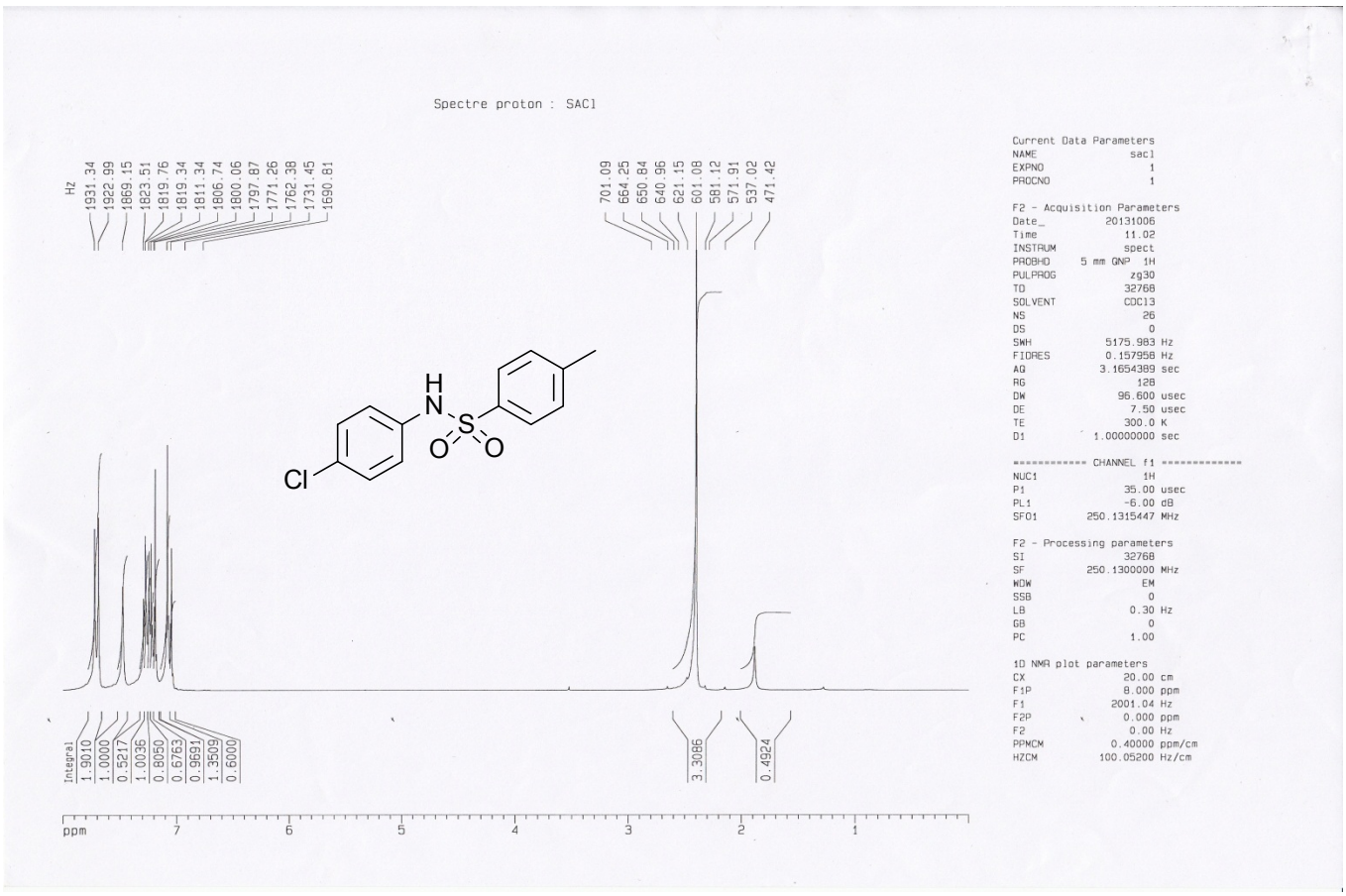
(0.13 g, 79 %). R_f 0.61 (DCM/MeOH : 95/5). (Found: C, 56.09; H, 7.16; N, 4.67. Calc. for $C_{14}H_{21}NO_4S$: C, 56.19; H, 7.02; N, 4.68%). ν_{max}/cm^{-1} 3274 (NH), 2958 (CH), 1743 (C=O), 1626 (C=C), 1338 and 1161 (SO_2). δ_H (250 MHz, $CDCl_3$) 0.94 and 0.85 (2d, *J* 6.5 Hz, 6H, 2xCH_3), 1.51 (m, 2H, $CH_{2\beta}$), 1.90 (m, 1H, $CH_{i\mathit{Pr}}$), 2.41 (s, 3H, CH_3-Ar), 3.48 (s, 3H, CH_3-O), 3.96 (m, 1H, C*H), 5.22 (d, *J* 10.1 Hz, 1H, NH), 7.22 (d, *J* 7.9 Hz, 2H, H-Ar), 7.50 (d, *J* 7.9 Hz, 2H, H-Ar). δ_C (60 MHz, $CDCl_3$) 21.4, 22.6, 24.2, 35.9, 42.2, 52.2, 54.3, 127.3, 129.5, 136.6, 143.6, 172.7. M.W. 299.



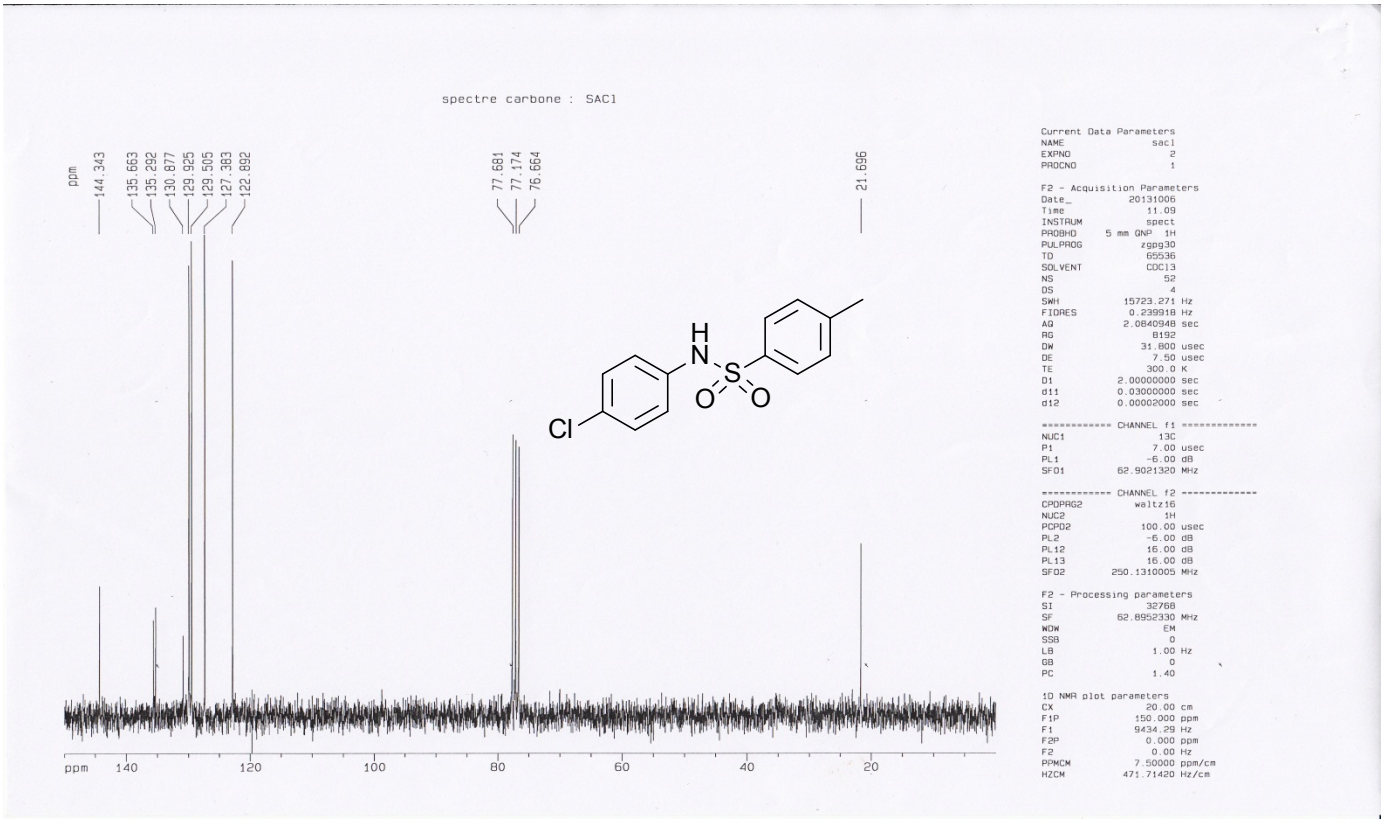
^{1}H NMR spectrum: *N*-Phenyl-4-methylbenzenesulfonamide



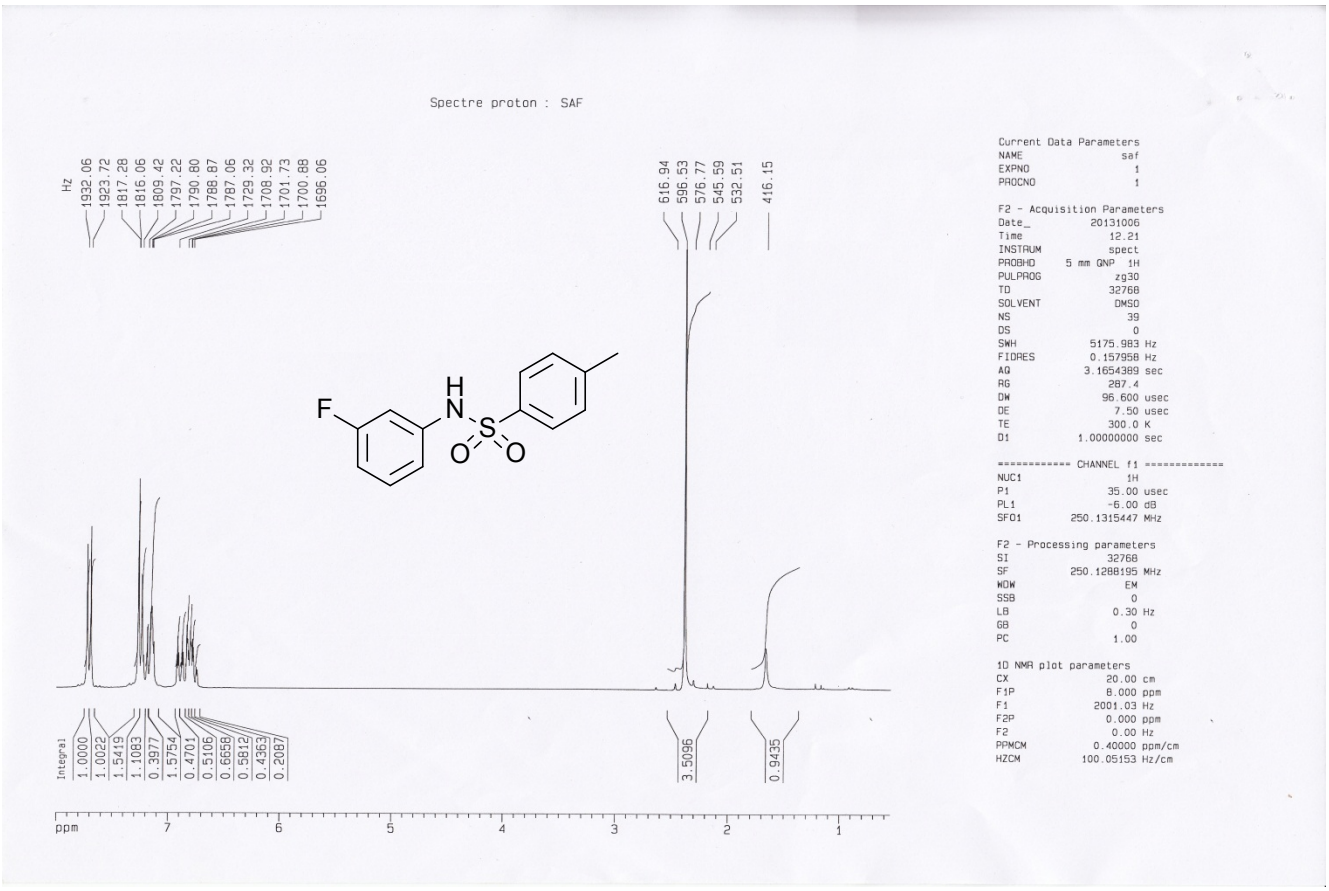
^{13}C NMR spectrum: *N*-Phenyl-4-methylbenzenesulfonamide



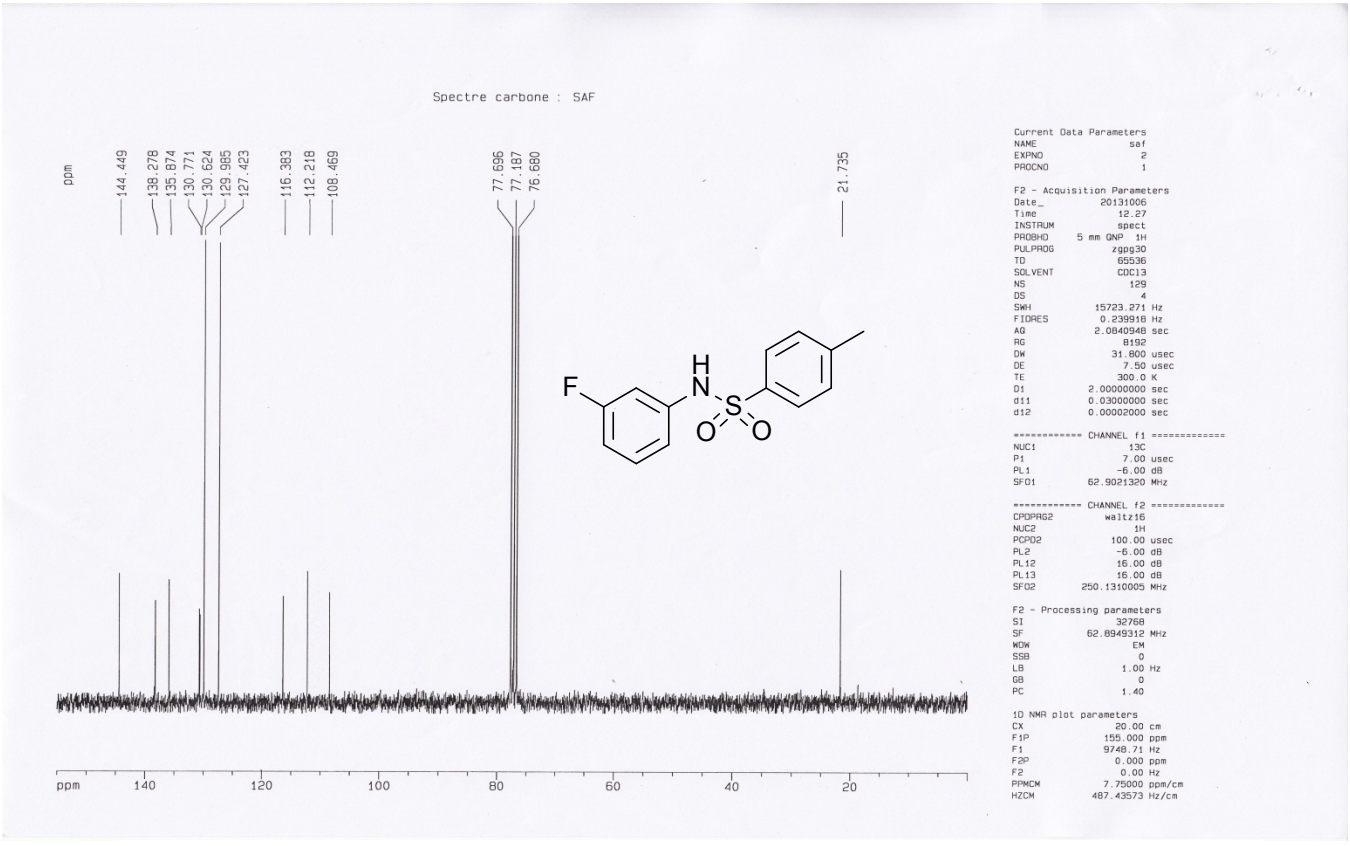
^{1}H NMR spectrum: *N*-(4-Chlorophenyl)-4-methylbenzenesulfonamide



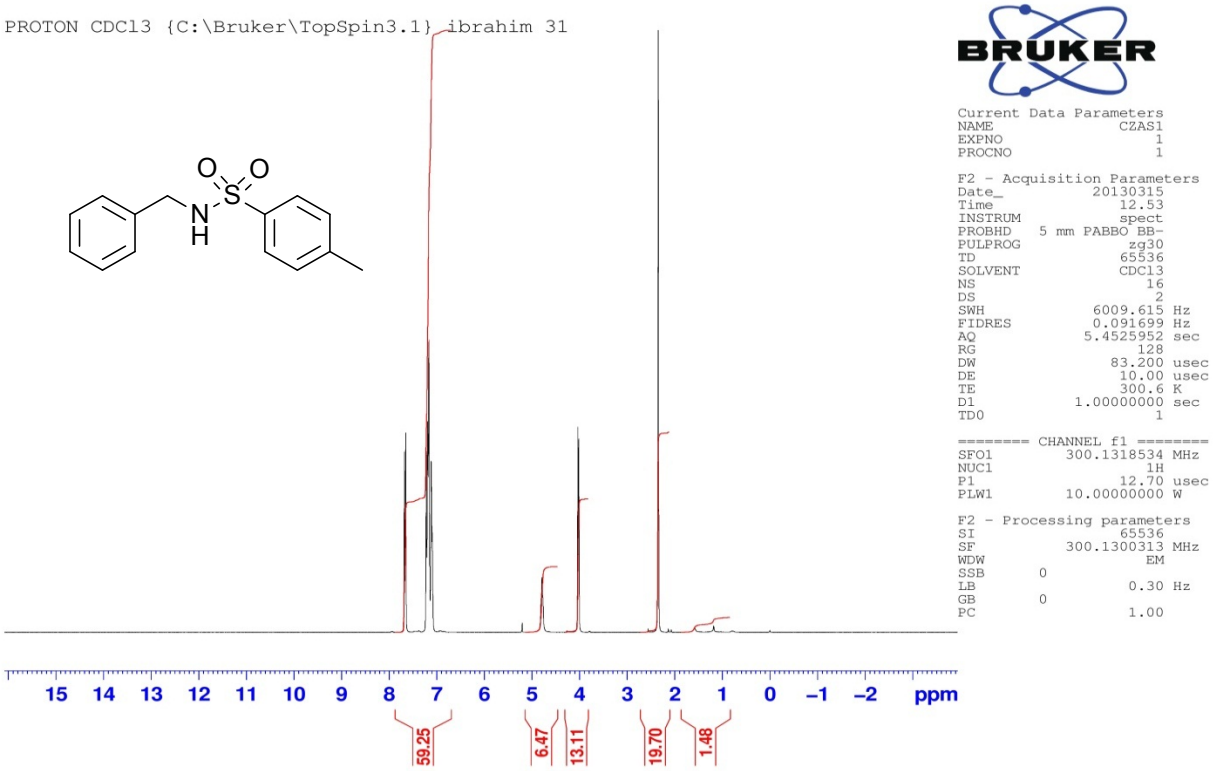
^{13}C NMR spectrum: *N*-(4-Chlorophenyl)-4-methylbenzenesulfonamide



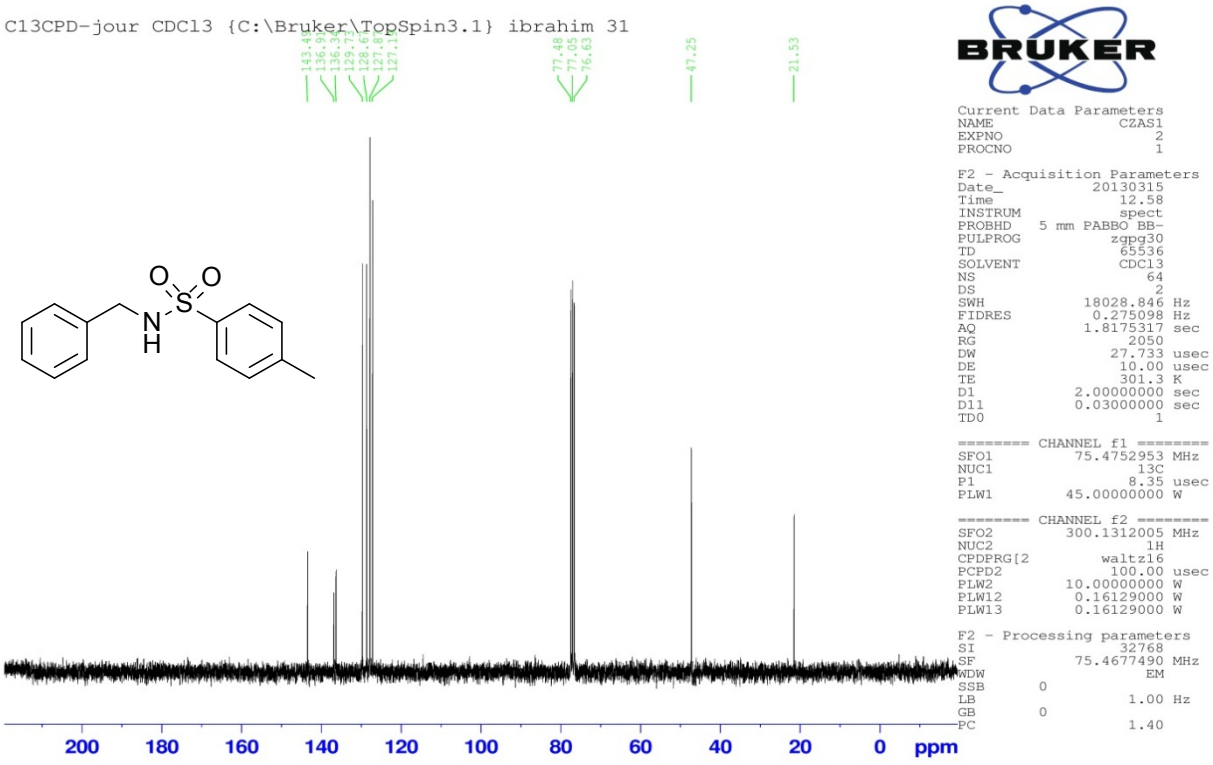
^{1}H NMR spectrum: *N*-(3-Fluorophenyl)-4-methylbenzenesulfonamide



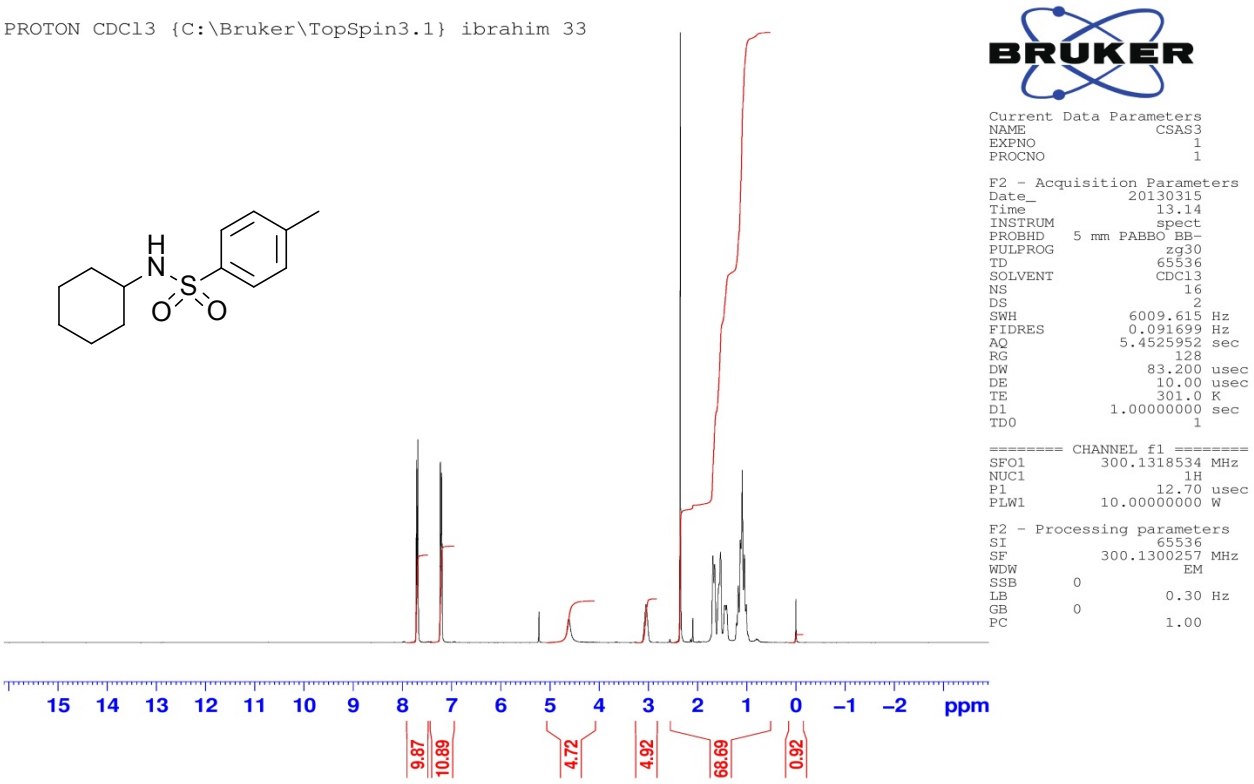
^{13}C NMR spectrum: *N*-(3-Fluorophenyl)-4-methylbenzenesulfonamide



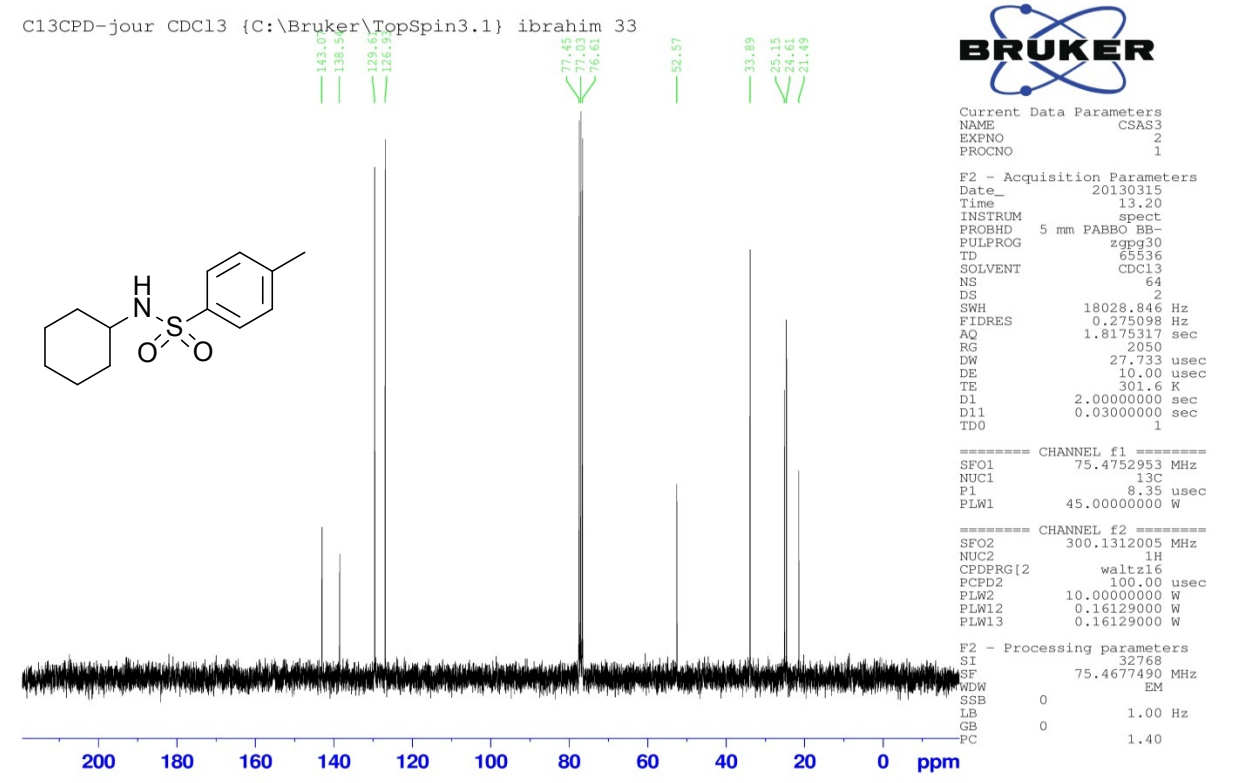
^{1}H NMR spectrum: *N*-benzyl-4-methylbenzenesulfonamide



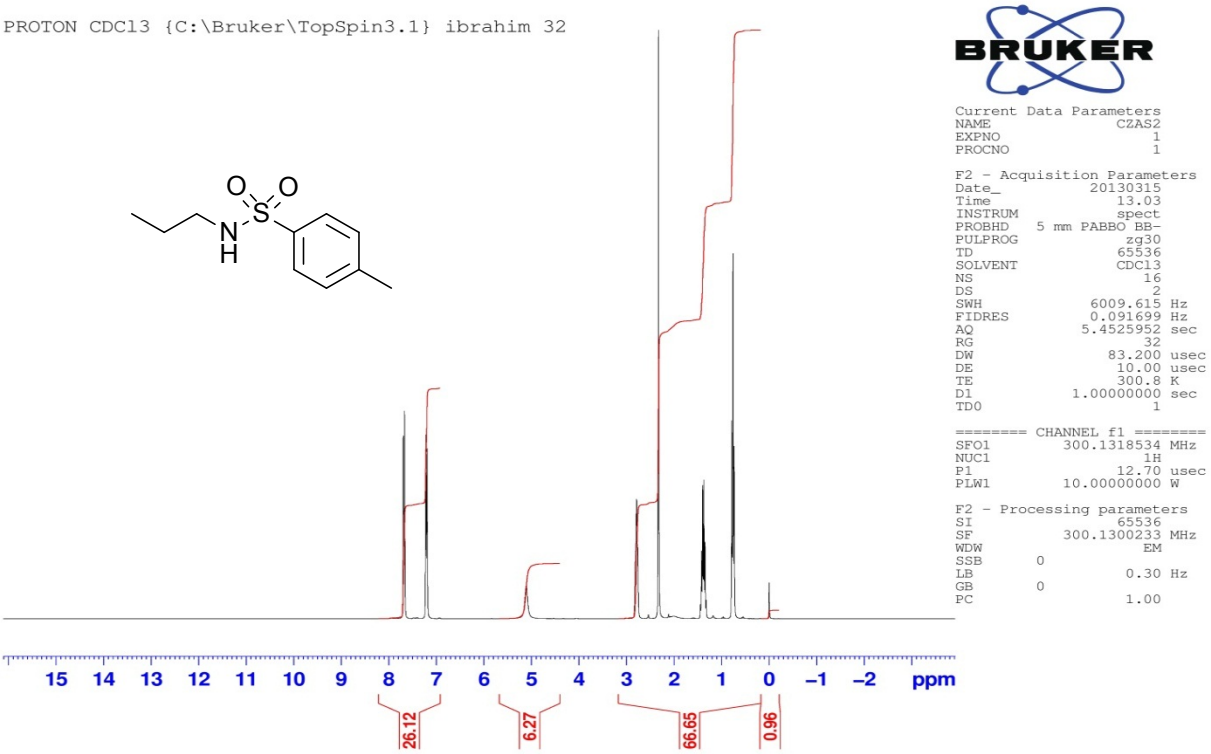
^{13}C NMR spectrum: *N*-benzyl-4-methylbenzenesulfonamide



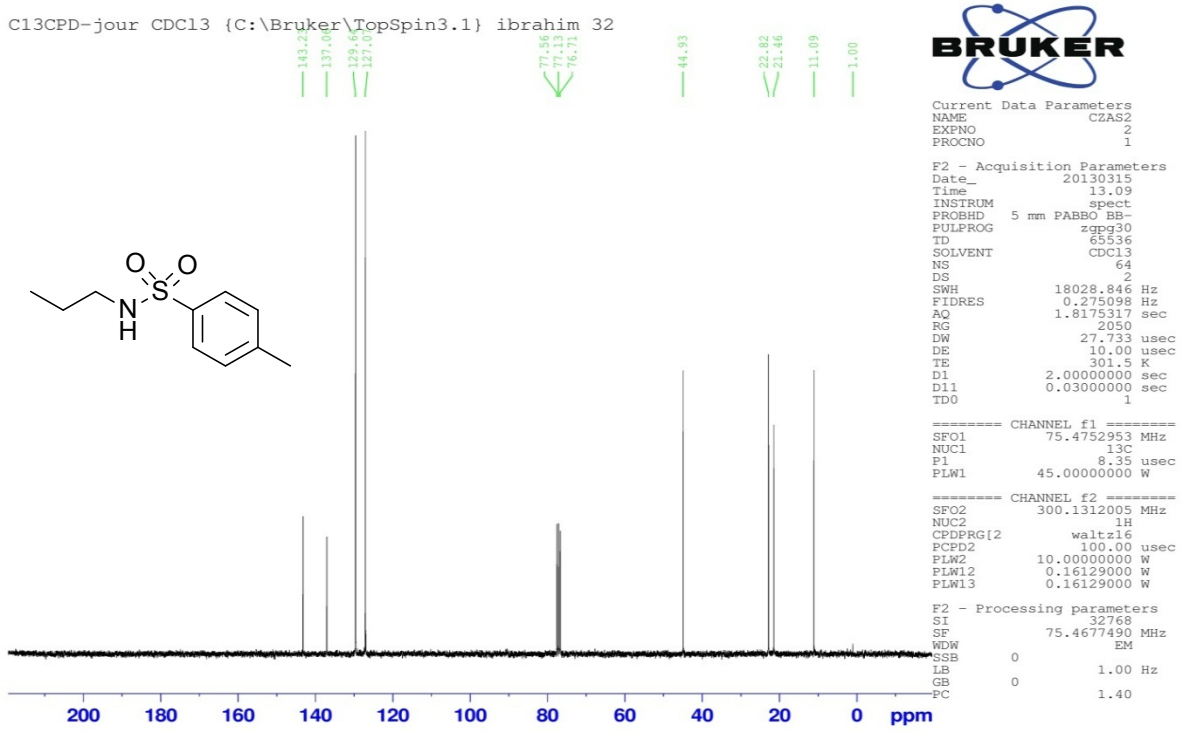
^{1}H NMR spectrum: *N*-cyclohexyl-4-methylbenzenesulfonamide



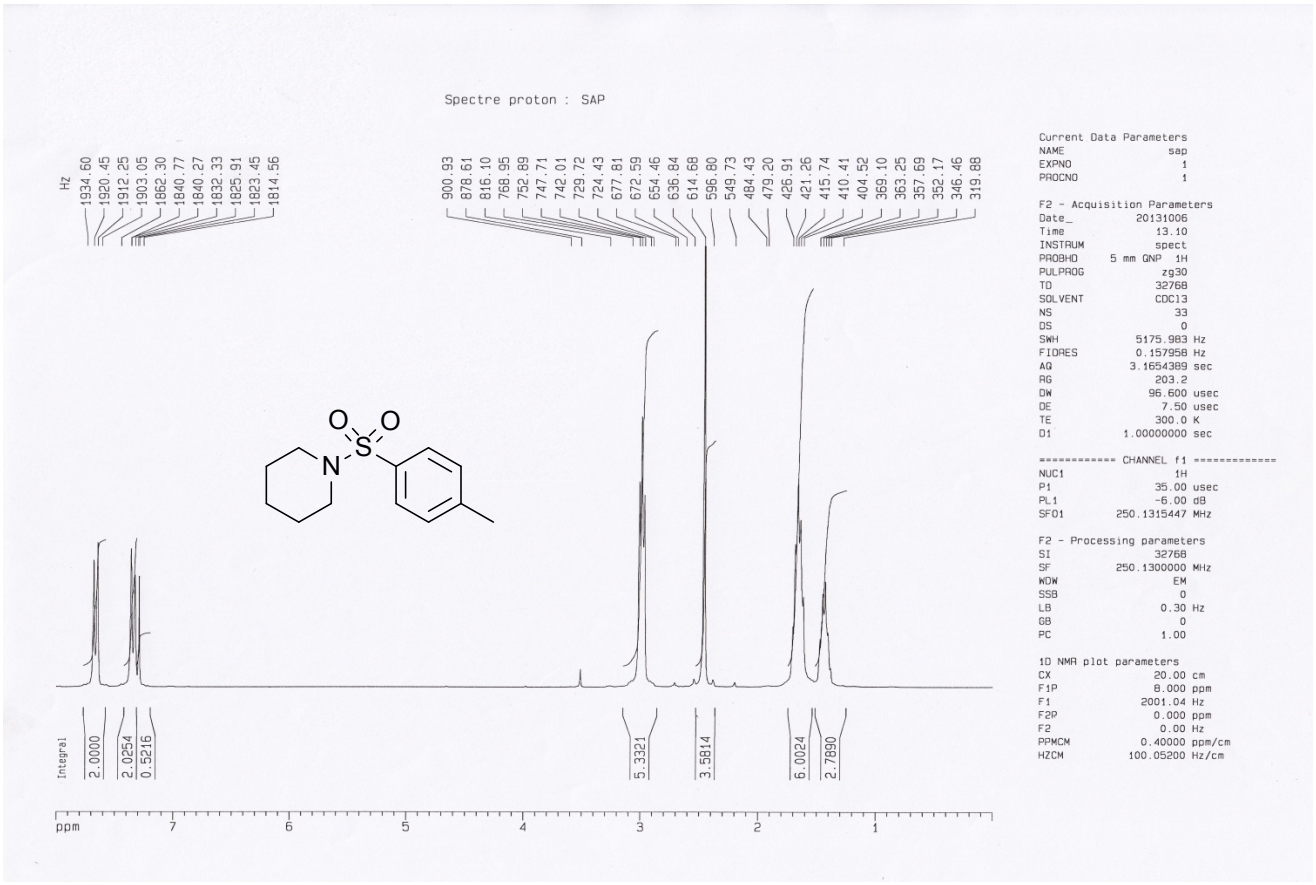
^{13}C NMR spectrum: *N*-Cyclohexyl-4-methylbenzenesulfonamide



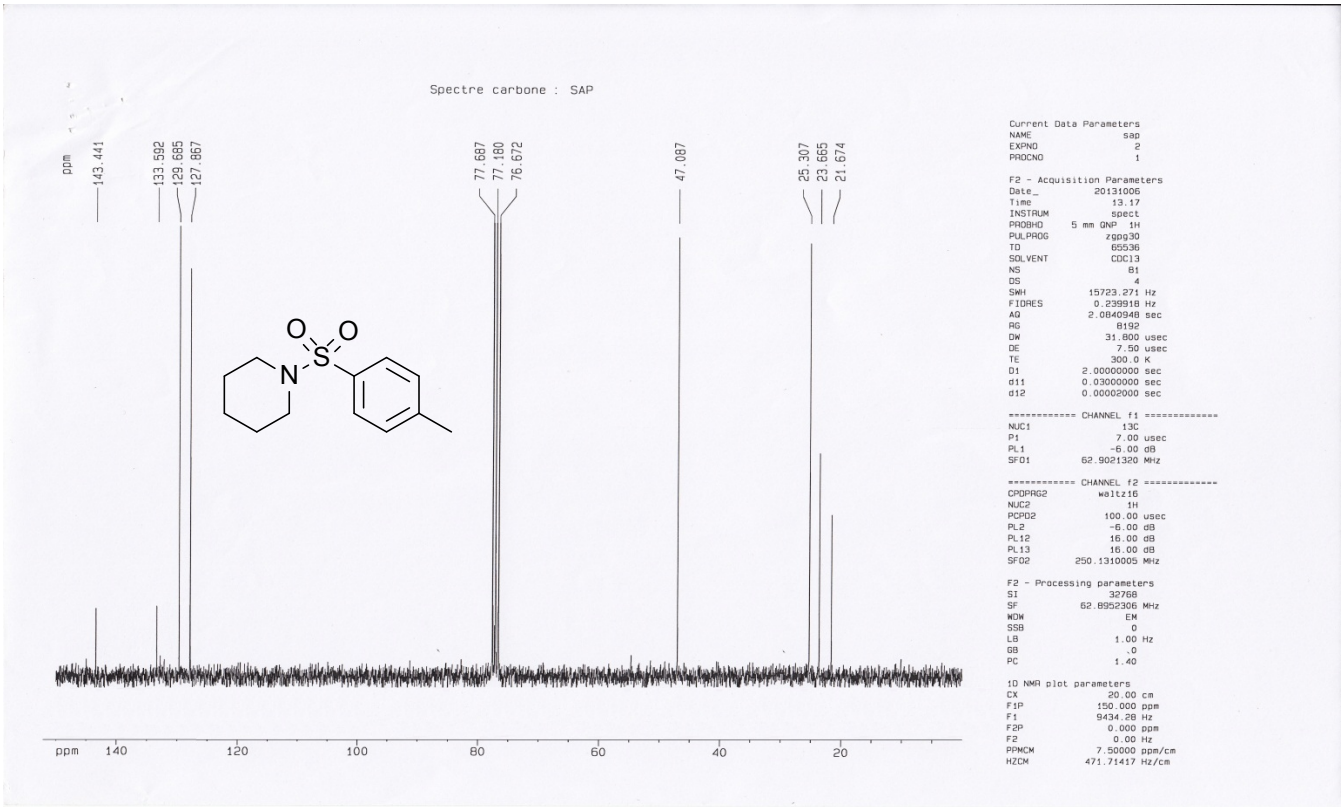
^{1}H NMR spectrum: 4-Methyl-*N*-propylbenzenesulfonamide



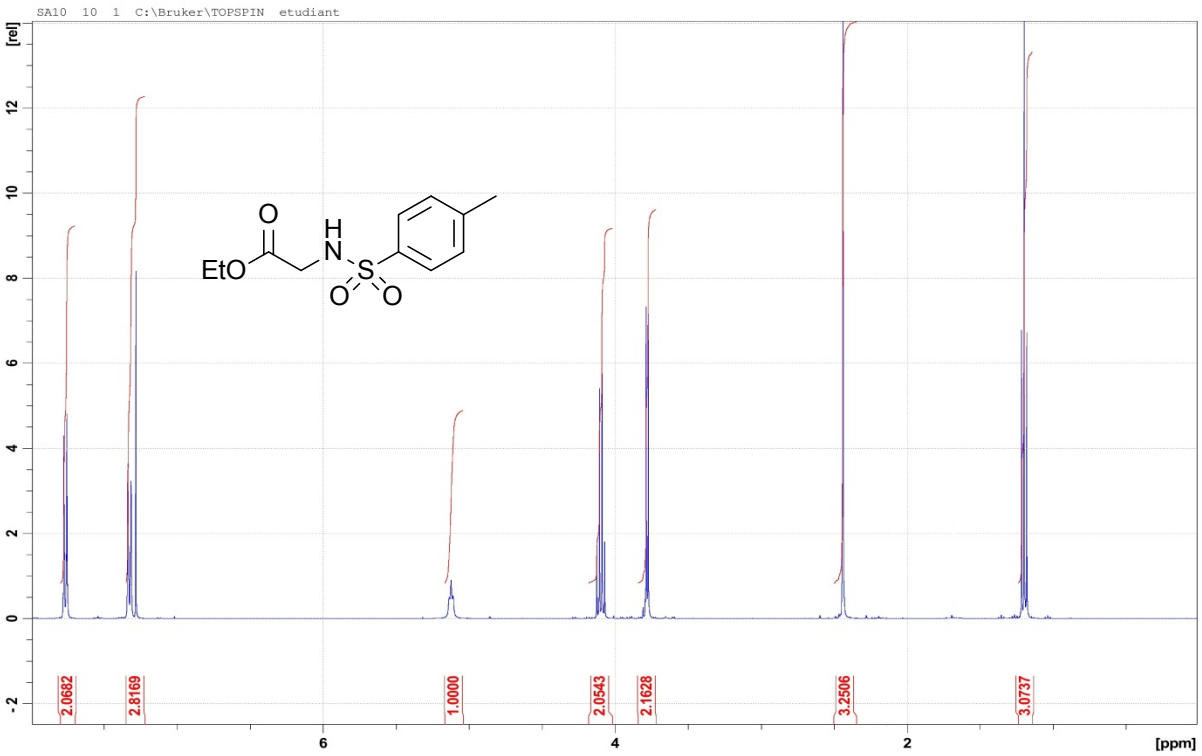
^{13}C NMR spectrum: 4-Methyl-*N*-propylbenzenesulfonamide



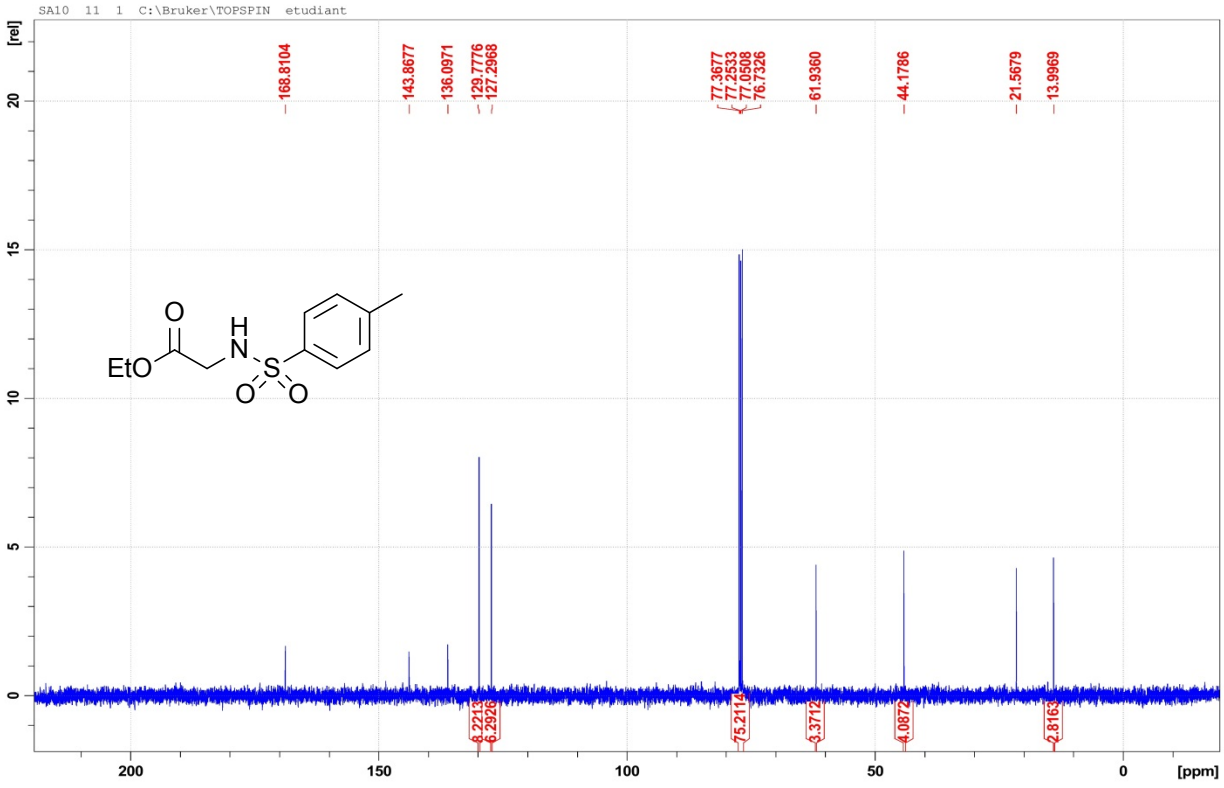
^{1}H NMR spectrum: 1-Tosylpiperidine



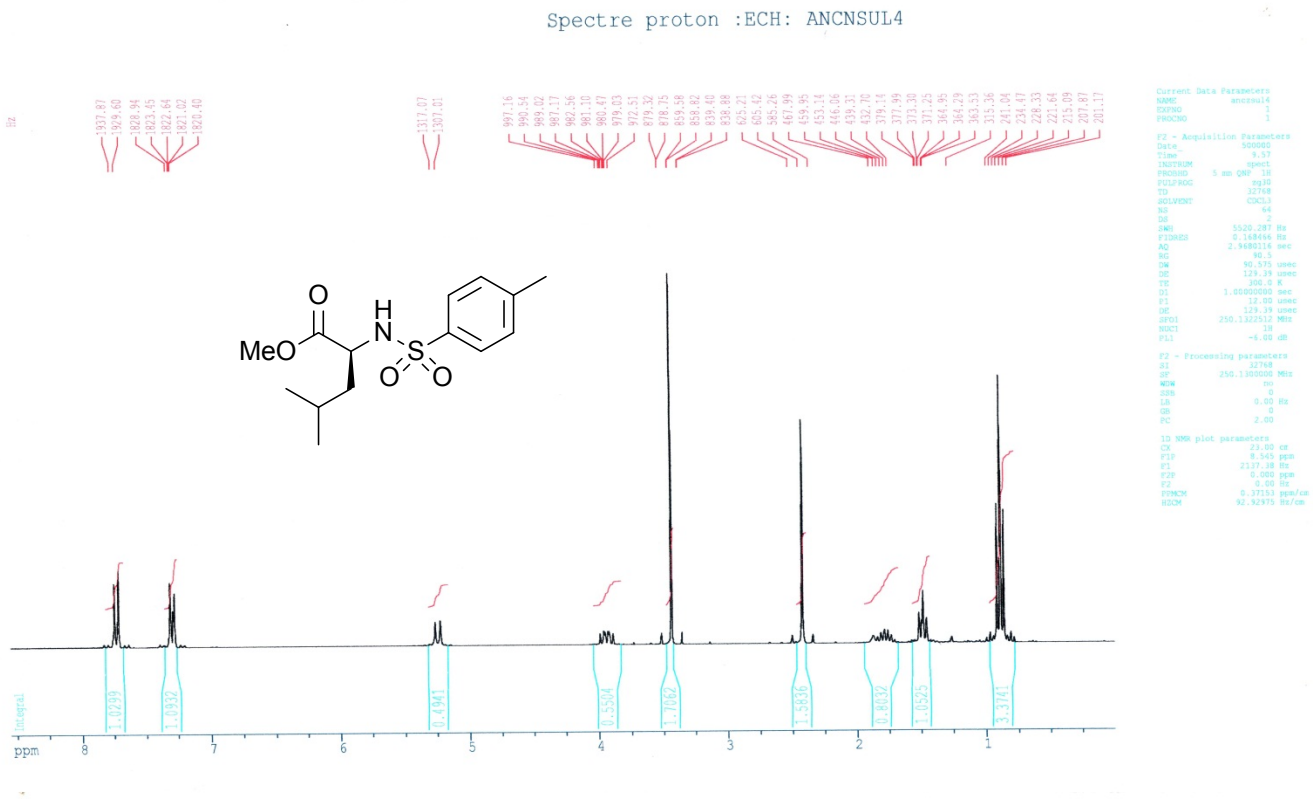
^{13}C NMR spectrum: 1-Tosylpiperidine



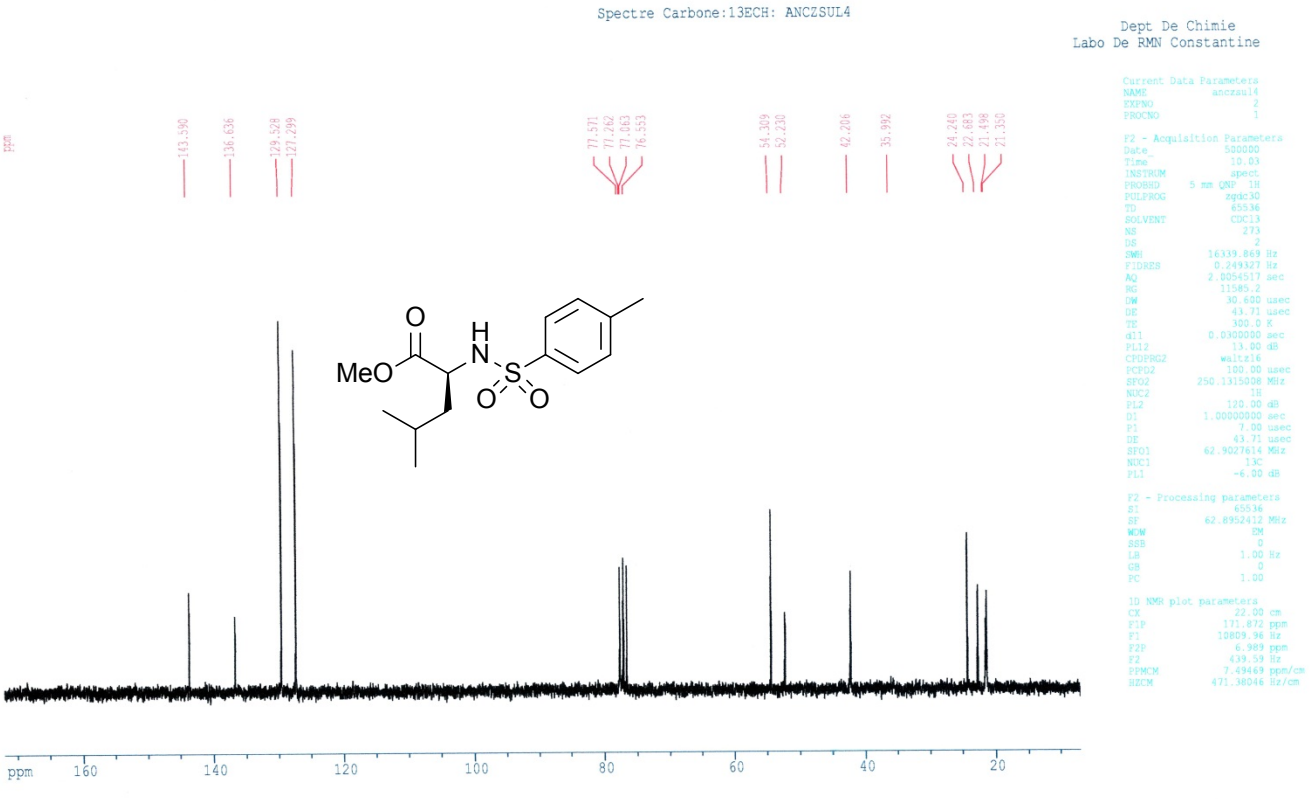
^{1}H NMR spectrum: Ethyl 2-(4-methylphenylsulfonamido) acetate



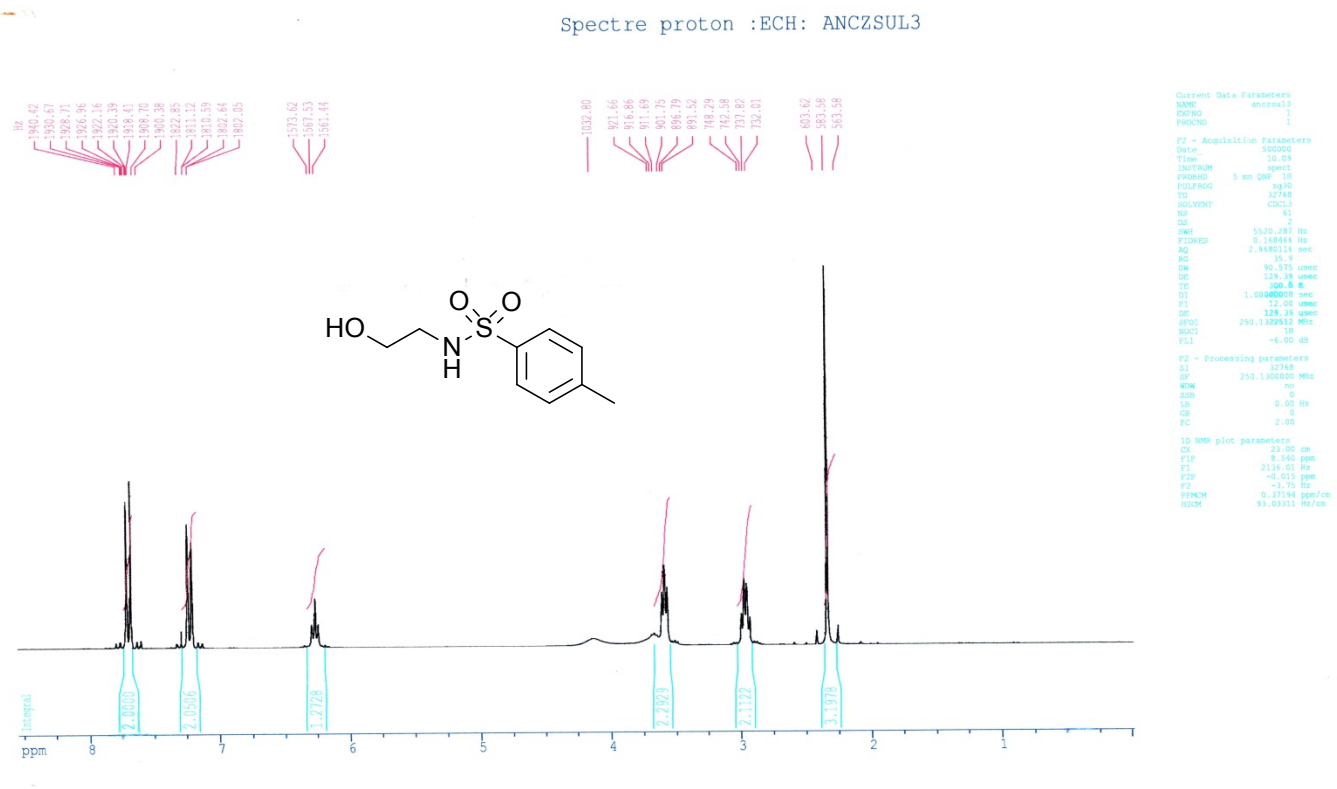
^{13}C NMR spectrum: Ethyl 2-(4-methylphenylsulfonamido) acetate



^{1}H NMR spectrum: (*S*)-Methyl 4-methyl-2-(4-methylphenylsulfonamido) pentanoate



^{13}C NMR spectrum: (*S*)-Methyl 4-methyl-2-(4-methylphenylsulfonamido) pentanoate



^{1}H NMR spectrum: *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide

^{13}C NMR spectrum: *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide