A Ruthenium-catalyzed, atom-economical synthesis of nitrogen heterocycles

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Supporting Information

Materials and Methods:

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Reaction solvents were dried using J. C. Meyer's Solvent Purification System passing through activated alumina prior to use. All other reagents were purchase from commercial sources and used without further purification, unless otherwise indicated.

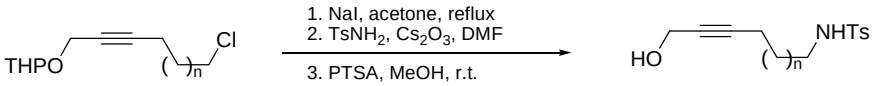
Flash Chromatography was performed using SiliCycle SilicaFlash F 60 40-60 μm 60 Å silica gel. Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC-Glasfolien, Kieselgel 60 F254) and visualized with UV light and potassium permanganate stain. Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) data were acquired on a Varian Gemini 300 (300 MHz), Mercury 400 (400 MHz), Varian 400 (400 MHz), or on a Varian Unity Inova-500 (500 MHz) spectrometer. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) data were acquired at 100 MHz on a Mercury 400 or at 125 MHz on a Varian Unity Inova 500 spectrometer. Chemical shifts are reported in delta (δ) units, part per million (ppm) relative to deuterochloroform (7.26 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C). Infrared (IR) data were recorded as films on potassium bromide (KBr) pellets on a Thermo Scientific Nicolet IR 100 FT-IR spectrometer. High resolution mass spectra were obtained from Stanford University on a Micromass Q-Tof API US Mass Spectrometer using positive electrospray ionization (+ESI). Elemental analyses were conducted by M-H-W Laboratories, Phoenix, Az.

Abbreviations:
Me = methyl
Et = ethyl
Ph = phenyl
Ind = indenyl
EA = ethyl acetate
PE = petroleum ether

Experimental procedures

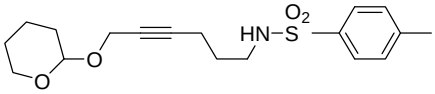
Substrates

General procedure



n=1 **NHTs-5**
n=2 **NHTs-6**

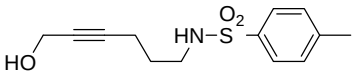
In a 25 mL flask, the chloroalkane[1] (430 mg, 2 mmol, 1 eq) is dissolved in 10 mL of acetone and NaI (1.05 g, 7 mmol, 3.5 eq) are added. The ensuing suspension is heated to reflux overnight. 15 mL of water are added to the reaction mixture which is then extracted by 3x 15 mL of ether. The combined yellow organic layers are washed with 5% Na_2S_2O3 solution, washed with brine, dried ($MgSO_4$) and concentrated. The light yellow oil thus obtained is pure enough for the subsequent step.
In a flame-dried 25 mL flask, the iodide is dissolved in 8 mL dry DMF. Then, $TsNH_2$ (2.4 mmol, 1.2 eq) is added followed by cesium carbonate (2.4 mmol, 1.2 eq) and the mixture is heated to 60°C for 8 h. After cooling, 5 mL of saturated aqueous NH_4Cl are added, followed by 10 mL of ether. The aqueous layer is extracted with 3x10 mL of ether and the combined organic layers are washed with 2x10 mL of brine. The ensuing organic extracts are then dried ($MgSO_4$) and concentrated. The resulting residue can be purified by chromatography (silica, PE/EA 4:1) or used crude in the deprotection (*vide* example towards **5a**).



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dm, *J* = 8.0 Hz, 2H), 7.29 (dm, *J* = 7.5 Hz, 2H), 4.87-4.84 (m, 1H), 4.75 (t, *J* = 3.4 Hz, 1H), 4.25-4.10 (m, 2H), 3.84-3.78 (m, 1H), 3.53-3.48 (m, 1H),3.03 (q, *J* = 6.4 Hz, 2H), 2.42 (s, 3H), 2.26-2.21 (m, 2H), 1.82-1.48 (m, 8H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.3, 136.9, 129.7, 127.0, 96.8, 84.8, 62.0, 54.5, 42.2, 30.2, 28.2, 25.3, 21.5, 19.0, 16.1.

The protected tosylamine is dissolved in enough methanol to make a 0.1 M solution. Then, 10 mol% PTSA is added and stirring is continued at room temperature for 3 h. At this stage, saturated aqueous $NaHCO_3$ is added, followed by ether. Extraction of the aqueous layer with 3 portions of ether, followed by drying ($MgSO_4$) and concentration affords a residue, which can be purified by short-path chromatography (silica, PE/EA 2:1) to afford typically 60-70% overall yields of **5a-6a** substrates.

[1] Haynes, R. K.; Lambert, D. E.; Parafiniuk, K. A.; Schober, P. A.; Turner, S. G. *Austr. J. Chem.* **1987**, *40*, 273



5a

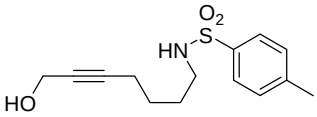
5a

IR ($CHCl_3$): 3435 (br), 2943, 2123, 1641, 1432, 1322, 1157 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dm, *J* = 8.4 Hz, 2H), 7.30 (dm, *J* = 7.5 Hz, 2H), 5.06 (t, *J* = 6 Hz, 1H), 4.19 (t, *J* = 2 Hz, 2H), 3.05 (q, *J* = 6.8 Hz, 2H), 2.42 (s, 3H), 2.27-2.23 (m, 2H), 1.66 (quin, *J* = 6.8 Hz, 2H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.7, 137.0, 130.0, 127.3, 84.9, 80.0, 51.4, 42.4, 28.3, 21.8, 16.3.

HRMS: Calculated for $C_{13}H_{17}NO_3NaS$: 290.0827. Found: 290.0828.



5e

5e

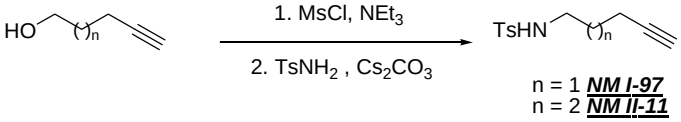
IR ($CHCl_3$): 3433 (br), 2947, 2120, 1645, 1433, 1322, 1158 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.76 (dm, *J* = 7.4 Hz, 2H), 7.31 (dm, *J* = 7.5 Hz, 2H), 4.95 (br s, 1H), 4.22 (s, 2H), 2.95 (q, *J* = 5.7 Hz, 2H), 2.43 (s, 3H), 2.21-2.17 (m, 2H), 1.61-1.58 (m, 2H), 1.52-1.49 (m, 2 H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.4, 136.7, 129.7, 127.0, 85.5, 79.1, 51.2, 42.6, 28.5, 25.2, 21.5, 18.2.

HRMS: Calculated for $C_{14}H_{19}NO_3NaS$: 304.0983. Found: 304.0981.

Preparation of N-tosylalkynyl amines

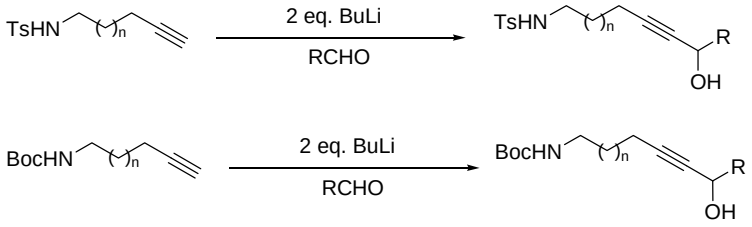


Sample procedure

In a flame-dried 100 mL flask kept under Argon, pent-4-ynol (10 mmol, 1 eq) is dissolved in 40 mL of dichloromethane. To this solution, triethylamine (30 mmol, 3 eq) is added and the resulting mixture is cooled to 0° C. Then, methanesulfonyl chloride (14 mmol, 1.4 eq) is added dropwise, causing the reaction mixture to turn from light yellow to a turbid orange mixture. After stirring for 3 hours, 15 mL of water are added. Following phase separation, the aqueous layer is extracted with 3x15 mL of dichloromethane and the combined organic extracts are washed with 2x20 mL of brine. The ensuing organic extracts are then dried ($MgSO_4$) and concentrated. The crude orange oil thus obtained is directly dissolved in 20 mL DMF. Then,

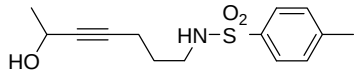
$TsNH_2$ (16 mmol, 1.6 eq) and Cs_2CO_3 (12 mmol, 1.2 eq) are sequentially added and the mixture is heated to 120° C. After completion (TLC monitoring), the reaction mixture is cooled down to room temperature and 15 mL saturated aqueous NH_4Cl are added, followed by 10 mL of ether. The aqueous layer is extracted with 3x10 mL of ether and the combined organic layers are washed with 2x10 mL of brine. The ensuing organic extracts are then dried ($MgSO_4$) and concentrated. The resulting residue is purified by chromatography (silica, PE/EA 4:1 to 1:2) to afford typically 45-55% yields of product. NMR data match those previously reported for these compounds (cf. *J. Am. Chem. Soc.* **2007**, *129*, 3794).

Addition to aldehydes



General procedure

In a flame-dried 25 mL flask kept under Argon, the alkynyl amine (1 mmol, 1 eq) is dissolved in 4 mL of THF and cooled down to -78 °C. To this solution is added dropwise *n*-BuLi (2.2 mmol, 2.2 eq) and stirring is continued at the same temperature for 1 hour. At this point, the corresponding aldehyde is added neat (5 mmol, 5 eq) and the mixture is gradually warmed to room temperature before quenching with 15 mL saturated aqueous NH_4Cl, followed by 10 mL of ether. Extractive workup followed by chromatography then affords the pure amino alcohols.



NM I-99

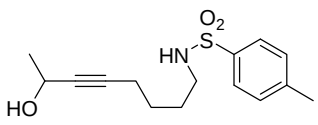
5b

IR ($CHCl_3$): 3430, 3291, 2936, 1657, 1597, 1431, 1329, 1157 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2H), 7.31 (dm, *J* = 8.4 Hz, 2H), 5.11 (t, *J* = 6.4 Hz, 1H), 4.46 (tq, *J* = 6.4, 2.0 Hz, 1H), 3.06 (q, *J* = 6.8 Hz, 2H), 2.43 (s, 3H), 2.08-2.04 (m, 2H), 2.04 (br s, 1H), 1.66 (quin, *J* = 6.8 Hz, 2H), 1.39 (d, *J* = 6.4 Hz, 3H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.7, 137.1, 130.0, 127.4, 84.0, 83.1, 58.6, 42.5, 28.3, 24.8, 21.8, 16.2.

HRMS: Calculated for $C_{14}H_{19}NO_3NaS$: 304.0983. Found: 304.0981.



NM II-15

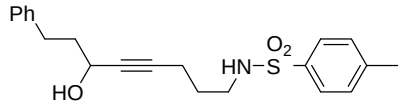
6f

IR ($CHCl_3$): 3430, 3201, 2974, 2936, 1657, 1598, 1431, 1329, 1157cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.19 (m, 1H), 4.47 (qm, *J* = 6.8, 1H), 2.92 (q, *J* = 6.7 Hz, 2H), 2.43 (s, 3H), 2.16 (dt, *J* = 6.8, 1.8 Hz, 2H), 2.05 (d, *J* = 7.2 Hz, 1H), 1.59 (quin, *J* = 6.8 Hz, 2H), 1.49 (quin, *J* = 6.8 Hz, 2H), 1.39 (d, *J* = 6.4 Hz, 3H), 1.28-1.19 (m, 2H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.3, 137.0, 129.6, 127.0, 83.5, 82.9, 58.3, 42.5, 28.4, 25.2, 24.5, 21.4, 18.0.

HRMS: Calculated for $C_{15}H_{21}NO_3NaS$: 318.1140. Found: 318.1141.



NM II-4

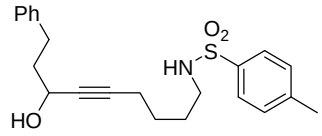
5c

IR ($CHCl_3$): 3422, 2936, 2872, 2366, 2334, 1649, 1496, 1451, 1330, 1157 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.75 (dm, *J* = 8.5 Hz, 2H), 7.29-7.26 (m, 4H), 7.20-7.17 (m, 3H), 4.99 (t, *J* = 6.25 Hz, 1H), 4.31 (tm, *J* = 6.5 Hz, 1H), 3.06 (q, *J* = 6.5 Hz, 2H), 2.74 (t, *J* = 8.0 Hz, 2H), 2.40 (s, 3H), 2.36 (d, *J* = 4.5 Hz, 1H), 2.26 (dt, *J* = 6.8, 2.0 Hz, 2H), 1.99-1.92 (m, 2H), 1.67 (quin, *J* = 6.9 Hz, 2H).

^{13}C – NMR (125 MHz, $CDCl_3$): δ = 143.4, 141.3, 136.8, 129.7, 128.4, 128.4, 127.0, 125.9, 84.0, 82.4, 61.8, 42.1, 39.4, 31.4, 28.1, 21.5, 16.0.

HRMS: Calculated for $C_{21}H_{25}NO_3NaS$: 394.1453. Found: 394.1451.



NM II-18

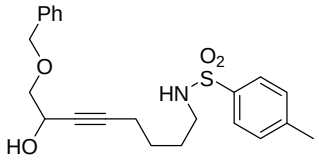
5q

IR ($CHCl_3$): 3418, 2937, 2348, 2233, 1638, 1597, 1469, 1306, 1157 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dm, *J* = 8.3 Hz, 2H), 7.32-7.26 (m, 4H), 7.22-7.18 (m, 3H), 4.70 (br s, 1H), 4.33 (tm, *J* = 6.5 Hz, 1H), 2.96 (q, *J* = 6.7 Hz, 2H), 2.76 (tm, *J* = 7.9 Hz, 3H), 2.42 (s, 3H), 2.20 (dt, *J* = 6.7, 1.8 Hz, 2H), 2.03-1.92 (m, 2H), 1.63-1.57 (m, 2H), 1.54-1.47 (m, 2H).

^{13}C – NMR (125 MHz, $CDCl_3$): δ = 143.4, 141.4, 136.8, 129.7, 129.0, 128.4, 127.0, 125.9, 84.9, 81.8, 61.8, 42.6, 39.5, 31.4, 28.6, 25.8, 21.5, 18.2.

HRMS: Calculated for $C_{22}H_{27}NO_3NaS$: 408.1609. Found: 408.1609.



NM II-24

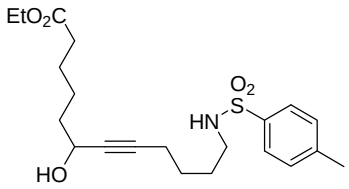
5h

IR ($CHCl_3$): 3430, 2928, 2859, 2234, 2090, 1650, 1458, 1341, 1162, 1094 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.73 (dm, *J* = 8.3 Hz, 2H), 7.38-7.28 (m, 7H), 4.86 (br s, 1H), 4.61-4.54 (m, 1H), 4.57 (d, *J* = 2.8 Hz, 2H), 3.60-3.48 (AB m, 2H), 2.90 (q, *J* = 6.6 Hz, 2H), 2.77 (br s, 1H), 2.41 (s, 3H), 2.15 (dt, *J* = 6.4, 1.8 Hz, 2H), 2.03-1.92 (m, 2H), 1.58-1.43 (m, 4H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.3, 137.6, 136.8, 129.6, 128.4, 127.8, 127.7, 127.0, 94.3, 85.5, 78.4, 73.8, 73.2, 73.2, 71.3, 61.8, 61.7, 42.5, 28.4, 25.1, 21.4, 18.1.

HRMS: Calculated for $C_{14}H_{19}NO_3NaS$: 424.1559. Found: 424.1556.



NM II-30

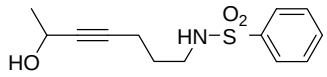
5d

IR ($CHCl_3$): 3423, 2941, 2864, 1725, 1711, 1660, 1636, 1446, 1340, 1168 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dm, *J* = 8.3 Hz, 2H), 7.30 (dm, *J* = 8.0 Hz, 2H), 4.97 (t, *J* = 6.3 Hz, 1H), 4.30 (t, *J* = 6.5 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.05 (q, *J* = 6.6 Hz, 2H), 2.42 (s, 3H), 2.30 (t, *J* = 7.4, 2H), 2.25 (dt, *J* = 6.8, 1.9 Hz, 1H), 1.70-1.45 (m, 8 H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 173.8, 143.4, 136.9, 129.7, 127.0, 94.4, 83.8, 82.5, 62.2, 60.3, 42.1, 37.5, 34.1, 28.1, 24.6, 24.5, 21.5, 15.9, 14.2.

HRMS: Calculated for $C_{20}H_{29}NO_5NaS$: 418.1664. Found: 418.1660.



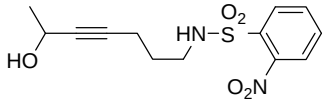
NM II-21

7i

IR ($CHCl_3$): 3432, 2935, 2858, 2372, 1661, 1140, 1028 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.89-7.86 (m, 2H), 7.60-7.49 (m, 3H), 5.10 (br s, 1H), 4.46 (qm, *J* = 6.4 Hz, 1H), 3.07 (q, *J* = 6.4 Hz, 2H), 2.32 (br s, 1H), 2.23 (dt, *J* = 6.8, 2.0 Hz, 2H), 1.66 (quin, *J* = 6.4 Hz, 2H), 1.38 (d, *J* = 6.4 Hz, 3H).

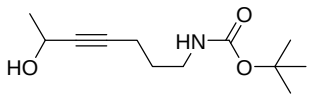
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 139.8, 132.6, 129.1, 127.0, 83.7, 82.8, 58.3, 42.2, 28.0, 24.5, 15.9.
HRMS: Calculated for $C_{13}H_{17}NO_3NaS$: 290.0827. Found: 290.0822.



NM II-34

7i

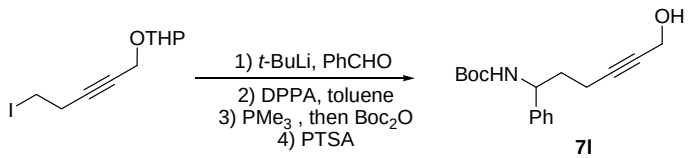
IR ($CHCl_3$): 3392, 2921, 1640, 1543, 1416, 1332, 1163 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.14-8.11 (m, 1H), 7.87-7.84 (m, 1H), 7.77-7.71 (m, 2H), 5.55 (t, *J* = 6.3 Hz, 1H), 4.47 (qm, *J* = 6.0 Hz, 1H), 3.22 (q, *J* = 6.4 Hz, 2H), 2.28 (dt, *J* = 6.6, 2.0 Hz, 2H), 2.21 (br s, 1H), 1.73 (quin, *J* = 6.8 Hz, 2H), 1.39 (d, *J* = 6.8 Hz, 3H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 147.9, 133.6, 133.5, 132.8, 131.0, 125.4, 83.8, 82.4, 58.4, 42.8, 28.1, 24.5, 15.9.
HRMS: Calculated for $C_{13}H_{16}N_2O_5NaS$: 335.1137. Found: 335.1137.



NM II-71

7k

IR ($CHCl_3$): 3390, 2982, 2926, 2350, 2082, 1691, 1640, 1522, 1377, 1254, 1165 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 4.74 (br s, 1H), 4.47 (qm, *J* = 6.5 Hz, 1H), 3.22 (q, *J* = 6.4 Hz, 2H), 2.56 (br s, 1H), 2.24 (dt, *J* = 6.7, 2.0 Hz, 2H) 1.66 (quin, *J* = 7.0 Hz, 2H), 1.42 (s, 9H), 1.39 (d, *J* = 6.5 Hz, 3H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 155.9, 83.3, 83.2, 79.3, 58.3, 39.6, 28.5, 228.4, 24.5, 16.1.
HRMS: Calculated for $C_{12}H_{21}NO_3Na$: 250.1419. Found: 250.1421.



7l

The iodide[2] (1.47 g, 5.00 mmol) was dissolved in freshly distilled ether (50 mL) in a 250-ml flask. The solution was cooled to -78°C and *t*-BuLI (1.7 M in pentane, 6.47 mL, 11.0 mmol) was added. The mixture was stirred at the same temperature for 30 min and freshly distilled benzaldehyde (1.02 mL, 1.06 g, 10.0 mmol) was added via syringe. The mixture was allowed to

[2] Nishibayashi, Y.; Milton, M. D.; Inada, Y.; Yoshikawa, M.; Wakiji, I.; Hidai, M.; Uemura, S. *Chem. Eur. J.* **2005**, *11*, 1433

warm to room temperature and was quenched at -78°C with acetic acid (1.2 eq); upon warming back to room temperature water was added. Following aqueous workup and chromatographic purification, the intermediate alcohol (930 mg, 67% yield) was carried forward without complete characterization.

^{1}H NMR (300 MHz, CDCI3): δ = 7.36-7.25 (m, 5H), 4.82 (dd, *J* = 7.9, 5.1 Hz, 2H), 4.30 (dt, *J* = 15.3, 2.2 Hz, 1H), 4.20 (dd, J = 15.2, 2.1 Hz, 1H), 3.88-3.80 (m, 1H), 3.56-3.49 (m, 1H), 2.41-2.27 (m, 2H), 2.02-1.51 (m, 9H)

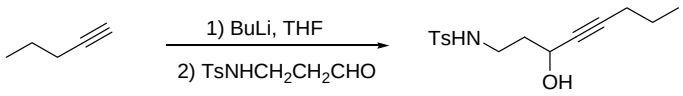
The previous alcohol (685 mg, 2.50 mmol) was dissolved in freshly distilled toluene (3 mL) and the solution was cooled in an ice bath. Diphenylphosphorazidate (648 μL, 3.00 mmol) and DBU (449 μL, 3.00 mmol) were added and the mixture was stirred at 0 °C for 2 h. The mixture was allowed to warm to room temperature and stirring was continued for 48 h. The reaction was worked up with water (10 mL) and ether (3xl0 mL) and the combined extracts were dried over magnesium sulfate. Removal ofthe solvent under reduced pressure and flash chromatography on silica gel (10:1 PE: EA) gave 663 mg of clear oil (89% yield). This intermediate was carried forward without complete characterization.

IR(film): 2944, 2870, 2096, 1455, 1346, 1247, 1202, 1118, 1024, 903, 872, 762 cm^{-1}.
^{1}H NMR (300 MHz, CDCI3): δ = 7.42-7.30 (m, 5H), 4.82 (t, *J* = 3.2 Hz, 1H), 4.62 (dd, *J* = 8.2, 6.4 Hz, 1H), 4.32 (dt, *J* =15.3, 2.2 Hz, 1H), 4.22 (dt, *J* =15.3, 2.1 Hz, 1H), 3.89-3.82 (m, 1H), 3.58-3.51 (m, 1H), 2.38-2.1.9 (m, 2H), 2.07-1.52 (m, 8H).
^{13}C NMR (75 MHz, CDCI3) δ = 139.1, 128.9 (2), 128.4, 126.9 (2), 96.7, 84.7, 77.0, 64.8, 61.9, 54.4, 34.8, 30.1, 25.2, 18.9, 15.7.

To the above azide (599 mg, 2.00 mmol) in THF (10 mL) and water (5 mL) was added trimethyl phosphine (2.40 mL, 1.0M, 2.40 mmol). After stirring 4 h, triethylamine (1 mL) and di-t-butyl dicarbonate (524 mg, 2.40 mmol) were added and the mixture was stirred overnight. The solvent was removed under vacuum and the residue was taken up in methanol. Catalytic PTSA was added and the mixture was stirred 2 h at room temperature. Removal of the solvent under vacuum and flash chromatography on silica (1:1 hexanes: ethyl acetate) gave 480 mg white solid (83% yield).

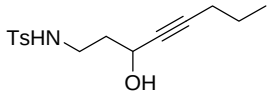
IR(film): 3331, 2978, 2932, 2225,1689, 1526, 1367, 1251, 1168, 1026, 701 cm^{-1}.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37-7.26 (m, 5H), 4.91 (br s, 1H), 4.82 (br s, 1H), 4.23 (s, 2H), 2.24 (d, J = 7.1 Hz, 2H), 1.98 (d, J =6.6 Hz, 1H), 1.61 (s, 1H), 1.42 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.2, 141.9, 128.6 (2), 127.3, 126.3 (2), 84.8, 79.7 (2), 53.9, 51.0, 35.3, 28.3 (3), 15.8.
HRMS: Calculated for $C_{13}H_{15}NO_3$ (M^+ - C_4H_8): 233.1052. Found 233.1057.

Piperidinone substrates



Sample procedure: ***8a*** (***NM II-33)***

In a flame-dried 25 mL flask, 1-hexyne (0.26 mL, 2.6 mmol, 3eq) are dissolved in 8 mL dry THF and cooled to -78 °C. To this solution is added BuLi (1.1 mL of a 2.5M hexanes solution, 2.7 mmol, 3.1eq) and stirring is continued at this temperature for 1 hour. Then, the N-tosylaldehyde (200 mg, 0.88 mmol, 1eq) dissolved in 4 mL dry THF is added dropwise. After addition is completed, the reaction is slowly warmed up to room temperature. After reaching room temperature, 5 mL of saturated aqueous NH_4Cl are added, followed by 5 mL of ether. Following conventional extractive workup, purification by chromatography (silica, PE/AcEt 4:1 to 1:1) affords 143 mg (55% yield) of the aminoalcohol.



NM II - 33

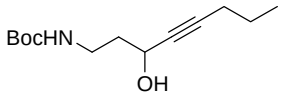
8a

IR ($CHCl_3$): 3417, 3257, 2957, 2127, 1654, 1437, 1328, 1169 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.4 Hz, 2H), 7.29 (dd, *J* = 8.0, 0.4 Hz, 7H), 5.26 (t, *J* = 6.0 Hz, 1H), 4.48 (br s, 1H), 3.13 (apparent dsext, *J* = 6.4 Hz, 2H), 2.43 (s, 3H), 2.33 (d, *J* = 4.0 Hz, 1H), 2.12 (tm, *J* = 7.2 Hz, 2H), 1.91-1.76 (m, 2H), 1.52-1.43 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 143.6, 137.0, 129.9, 127.4, 86.8, 80.3, 61.4, 40.3, 36.8, 22.1, 21.8, 20.8, 13.7.

HRMS: Calculated for $C_{15}H_{21}NO_3NaS$: 318.1140. Found: 318.1138.



NM III - 40

8b

IR ($CHCl_3$): 3411, 2968, 2358, 2121, 1653, 1522 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.04 (br s, 1H), 4.40 (br s, 1H), 3.46-3.41 (m, 1H), 3.35 (apparent sext, *J* = 6.5 Hz, 1H), 3.23-3.14 (m, 1H), 2.12 (dt, *J* = 7.2, 2.0 Hz, 2H), 1.79 (q, *J* = 6.2 Hz, 2H), 1.47 (sext, *J* = 7.2 Hz, 2H), 1.38 (s, 9H), 0.92 (t, *J* = 7.2 Hz, 3H).

^{13}C – NMR (100 MHz, $CDCl_3$): δ = 156.6, 85.3, 80.7, 79.3, 60.0, 38.0, 36.8, 28.3, 28.2, 21.9, 20.5, 13.4.

HRMS: Calculated for $C_{13}H_{23}NO_3Na$: 264.1576. Found: 264.1577.

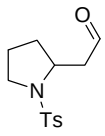
Tandem Redox isomerisation/Cyclisation

General procedure

The substrate is dissolved in enough dry THF to make a 0.1 M solution, in a flame-dried flask fitted with reflux condenser. To this solution is then added the ruthenium catalyst (3 mol%) and CSA (5 mol%), and the resulting reddish mixture is stirred at room temperature from 5 minutes.

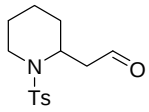
At this stage, indium triflate (3 mol%) is added and the solution is brought to reflux in a preheated oil bath. After 1 h stirring, the mixture is filtered through a plug of florisil, rinsing with ether. The filtrate is concentrated and purified by chromatography (silica gel, PE/EA 2:1 to 1:1).
NB: In the case of piperidine formation, 10 mol% CSA were used instead.

NM I-60



NM I-60

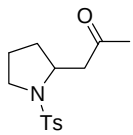
6a
IR: 3267, 2957, 2924, 2360, 1720 (sh), 1597, 1451, 1341, 1158, 1092 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.80 (s, 1H), 7.72 (dm, *J* = 8.0 Hz, 2H), 7.31 (dm, *J* = 7.5 Hz, 2H), 4.00 (sept, *J* = 4.5 Hz , 1H) 3.46-3.41 (m, 1H), 3.20-3.09 (m, 2H), 2.74 (qd, *J* = 5.4, 1.5 Hz, 1H), 2.43 (s, 3H), 1.86-1.73 (m, 2H), 1.58-1.47 (m, 2H).
^{13}C – NMR (125 MHz, $CDCl_3$): δ = 200.7, 143.7, 133.8, 129.8, 127.6, 54.8, 50.9, 49.0, 32.0, 23.9, 21.5.
HRMS: Calculated for $C_{13}H_{17}NO_3NaS$: 290.0827. Found: 290.0826.



NM I-74

CAS: 934472-39-6

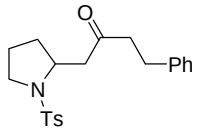
6e
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.68 (t, *J* = 2.0 Hz, 1H), 7.71 (dm, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 4.68-4.64 (m, 1H), 3.80 (dm, *J* = 12.0 Hz , 1H), 2.94 (dt, *J* = 12.7, 2.5 Hz, 1H), 2.67-2.65 (m, 2H), 2.42 (s, 3H), 1.57-1.42 (m, 4H), 1.32-1.24 (m, 2H).
^{13}C – NMR (125 MHz, $CDCl_3$): δ = 200.1, 143.3, 137.9, 129.8, 127.0, 47.6, 43.9, 41.0, 27.8, 24.3, 21.5, 18.3.
HRMS: Calculated for $C_{14}H_{19}NO_3NaS$: 304.0983. Found: 304.0983.



NM II-3

6b

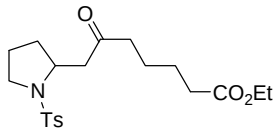
IR: 3435, 2957, 2862, 2145, 1729, 1654, 1603, 1339, 1156 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.5 Hz, 2H), 7.31 (dd, *J* = 8.0, 0.5 Hz, 2H), 3.90 (sept, *J* = 3.5 Hz, 1H), 3.45-3.40 (m, 1H), 3.23 (dd, *J* = 17.8, 3.2 Hz, 1H), 3.06 (ddd, *J* = 10.0, 7.5, 7.5 Hz, 1H), 2.42 (s, 3H), 2.16 (s, 3H), 1.83-1.67 (m, 2H), 1.54-1.43 (m, 2H).
^{13}C – NMR (125 MHz, $CDCl_3$): δ = 207.2, 143.5, 133.7, 129.7, 127.6, 55.8, 50.6, 49.1, 32.0, 30.5, 23.7, 21.5.
HRMS: Calculated for $C_{14}H_{19}NO_3NaS$: 304.0983. Found: 304.0985.



NM II-6

6c

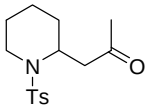
IR ($CHCl_3$): 3423, 3024, 2936, 2859, 1709, 1604, 1492, 1457, 1334, 1158, 1087 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.69 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.33-7.26 (m, 4H), 7.21-7.18 (m, 3H), 3.95-3.89 (m, 1H), 3.43-3.38 (m, 1H), 3.20 (dd, *J* = 17.4, 3.2 Hz, 1H), 3.09-3.03 (m, 1H), 2.92-2.85 (m, 2H), 2.85-2.68 (m, 2H), 2.43 (s, 3H), 1.80-1.65 (m, 2H), 1.51-1.40 (m, 2H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 208.4, 143.5, 140.8, 133.7, 129.7, 128.5, 128.3, 127.6, 126.1, 55.8, 49.9, 49.1, 44.7, 32.0, 29.6, 23.7, 21.5.
HRMS: Calculated for $C_{21}H_{25}NO_3NaS$: 394.1453. Found: 394.1453.



NM II-32

6d

IR ($CHCl_3$): 3407, 2933, 2873, 2358, 1735, 1712, 1663, 1599, 1456, 1380, 1344, 1178 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.10 (q, *J* = 7.0 Hz, 2H), 3.94-3.89 (m, 1H), 3.43 (ddd, *J* = 10.5, 5.5, 5.5 Hz, 1H), 3.20 (dd, *J* = 17.5, 3.0 Hz, 1H), 3.08 (ddd, *J* = 10.0, 7.0, 7.0 Hz, 1H), 2.63 (dd, *J* = 18.0, 9.5 Hz, 1H), 2.52-2.40 (m, 1H), 2.43 (s, 3H), 2.31 (t, *J* = 6.5 Hz, 2H), 1.83-1.69 (m, 2H), 1.62-1.61 (m, 5H), 1.54-1.44 (m, 2H), 1.25 (t, *J* = 7.5 Hz, 3H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 208.9, 173.4, 143.5, 133.7, 129.7, 127.6, 60.3, 55.9, 49.7, 49.1, 42.9, 34.0, 32.1, 24.4, 23.8, 23.0, 21.5, 14.2.
HRMS: Calculated for $C_{20}H_{29}NO_5NaS$: 418.1664. Found: 418.1658.

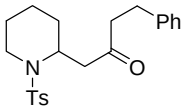


NM II-17

CAS: 227018-74-8

6f

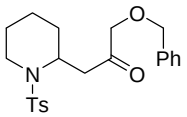
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.71 (dm, *J* = 8.3 Hz, 2H), 7.30-7.27 (m, 2H), 4.52 (dd, *J* = 8.8, 4.3 Hz, 1H), 3.78 (dm, *J* = 13.8 Hz, 1H), 2.94 (dt, *J* = 13.7, 2.4 Hz, 1H), 2.79 (dd, *J* = 16.3, 9.3 Hz, 1H), 2.60 (dd, *J* = 16.3, 4.6 Hz, 1H), 2.42 (s, 3H), 2.13 (s, 3H), 1.55-1.22 (m, 6H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 206.0, 143.1, 138.0, 129.7, 127.0, 48.6, 43.9, 41.2, 30.2, 27.6, 24.5, 21.5, 18.3.



NM II-22

6g

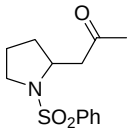
IR ($CHCl_3$): 2934, 2853, 2362, 1715, 1597, 1498, 1454, 1342, 1149, 1093 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.69 (dt, *J* = 8.4, 1.8 Hz, 2H), 7.30-7.25 (m, 4H), 7.21-7.16 (m, 3H), 4.52-4.48 (m, 1H), 3.76 (dm, *J* = 13.6 Hz, 1H), 2.94-2.84 (m, 3H), 2.75-2.68 (m, 3H), 2.54 (dd, *J* = 8.0 Hz, 4.6 Hz, 2H), 2.41 (s, 3H), 1.53-1.23 (m, 6H).
^{13}C – NMR (100 MHz, $CDCl_3$): δ = 207.3, 143.1, 140.8, 138.0, 129.7, 128.5, 128.3, 127.0, 126.1, 48.7, 44.6, 43.2, 41.2, 29.6, 27.7, 24.5, 21.5, 18.3.
HRMS: Calculated for $C_{22}H_{27}NO_3NaS$: 408.1609. Found: 408.1612.



NM II-26

6h

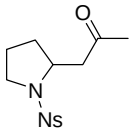
IR ($CHCl_3$): 3422, 2934, 2863, 2126, 1722, 1652, 1338, 1165 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.68 (dt, *J* = 8.5, 2.0 Hz, 2H), 7.39-7.30 (m, 5H), 7.27-7.25 (m, 2H), 4.59-4.54 (m, 1H), 4.57 (d, *J* = 2.0 Hz, 2H), 4.01 (ddd, *J* = 16.5, 16.4 Hz, 2H), 3.81-3.78 (m, 1H), 2.95 (dt, *J* = 13.0, 2.5 Hz, 1H), 2.84 (dd, *J* = 16.0, 8.3 Hz, 1H), 2.65 (dd, *J* = 16.0, 5.0 Hz, 1H), 2.40 (s, 3H), 1.53-1.39 (m, 5H), 1.33-1.25 (m, 1H).
^{13}C – NMR (125 MHz, $CDCl_3$): δ = 206.4, 143.1, 138.0, 137.0, 129.7, 128.5, 128.0, 127.9, 127.0, 75.1, 73.4, 48.6, 41.1, 39.4, 27.9, 24.5, 21.5, 18.3.
HRMS: Calculated for $C_{22}H_{27}NO_4NaS$: 424.1559. Found: 424.1559.



NM II-23

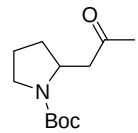
6i

IR ($CHCl_3$): 3407, 2976, 2885, 1715, 1454, 1411, 1345, 1163, 1102, 1047 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.83-7.81 (m, 2H), 7.61-7.58 (m, 1H), 7.54-7.51 (m, 2H), 3.95-3.90 (m, 1H), 3.46-3.42 (m, 1H), 3.23 (dd, *J* = 17.75, 3.25 Hz, 1H), 3.08 (ddd, *J* = 14.0, 7.5, 7.0 Hz, 1H), 2.67 (dd, *J* = 17.5, 9.5 Hz, 1H), 2.16 (s, 3H), 1.82-1.69 (m, 2H), 1.55-1.42 (m, 2H).
^{13}C–NMR (125 MHz, $CDCl_3$): δ = 207.1, 136.6, 132.7, 129.1, 127.5, 55.8, 50.5, 49.1, 32.0, 30.5, 23.7.
HRMS: Calculated for $C_{13}H_{17}NO_3NaS$: 290.0827. Found: 290.0829.



6j

IR: 3579, 3415, 2918, 2121, 1712, 1649, 1549, 1379, 1172, 1115 cm^{-1}.
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 7.5, 2.5 Hz, 1H), 7.73-7.67 (m, 1H), 7.58 (dd, *J* = 7.5, 2.5 Hz, 2H), 4.27-4.22 (m, 1H), 3.50-3.46 (m, 1H), 3.43-3.38 (m, 1H), 3.18 (dd, *J* = 17.75, 3.25 Hz, 1H), 2.64 (dd, *J* = 17.75, 9.75 Hz, 1H), 2.16 (s, 3H), 2.10-2.02 (m, 1H), 1.91-1.83 (m, 1H), 1.80-1.73 (m, 1H), 1.70-1.64 (m, 1H).
^{13}C – NMR (125 MHz, $CDCl_3$): δ = 206.7, 148.6, 133.7, 131.4, 131.1, 130.7, 123.9, 56.0, 49.6, 49.1, 32.2, 30.5, 23.8.
HRMS: Calculated for $C_{13}H_{16}N_2O_5NaS$: 335.0678. Found: 335.0677.

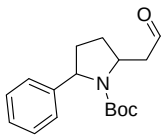


NM II-73

CAS: 86953-89-1

6k

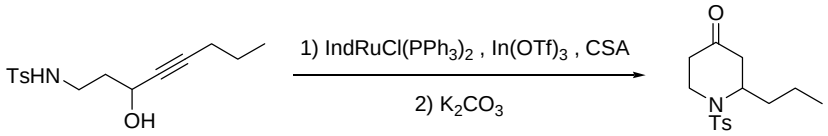
Data is in agreement with the published reference (*J.Org.Chem.* **1983**, *48*, 4058).
IR ($CHCl_3$): 3582, 3452, 2964, 2873, 2347, 1690, 1651, 1450, 1391, 1170 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.13 (br s, 1H), 3.30-3.29 (br m, 2H), 3.01 (dd, *J* = 16.0 Hz, 1H), 2.43-2.35 (m, 1H), 2.14 (s, 3H), 2.05 (dddd, *J* = 12.4, 8.0, 8.0, 7.9 Hz, 1H), 1.80 (quint, *J* = 8.0 Jz, 2H), 1.65-1.60 (m, 1H), 1.44 (s, 9H).



6l

NMR data is given for the major diastereomer.
IR(film): 2976, 1723, 1689, 1391, 1367, 1169, 1120, 701.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.83 (t, *J* =2.0 Hz, 1H), 7.35-7.09 (m, 5H), 4.86 (d, *J* = 8.0 Hz), 4.66-4.60 (m, IH), 3.12 (ddd, *J* = 16.2, 4.6, 1.9 Hz, 1H), 2.54 (ddd, *J* =16.3, 8.2, 2.0 Hz), 2.39-2.16 (m, 2H), 1.81-1.75 (m, 1H), 1.65-1.58 (m, 1H), 1.13 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$) δ = 200.7, 154.0, 144.7, 128.2 (2), 126.6, 125.1 (2), 79.7, 61.6, 53.1, 48.4, 32.6, 28.4, 28.0 (3).
HRMS: Calculated for $C_{16}H_{23}NO_2$ (M^+ - CO): 261.1729. Found 261.1726.

Piperidinones

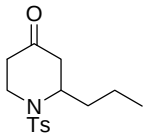


NM II-40

9a (NM II-40)
The aminoalcohol (50 mg, 0.17 mmol, 1eq) is subjected to the standard procedure for redox isomerisation. After 3h, near complete conversion to the amino-enone is observed.

Aminoenone: ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.5, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.80 (ddd, *J* = 14.0, 7.0 Hz, 1H), 6.02 (d, *J* = 16.0, 1.3 Hz, 1H), 5.19 (t, *J* = 6.5 Hz, 1H), 3.18 (q, *J* = 6.0 Hz, 2H), 2.78 (t, *J* = 5.8 Hz, 2H), 2.42 (s, 3H), 2.18 (dq, *J* = 7.0, 1.5 Hz, 2H), 1.47 (sext, *J* = 7.25 Hz, 2H), 0.93 (t, *J* = 7.25 Hz, 3H).

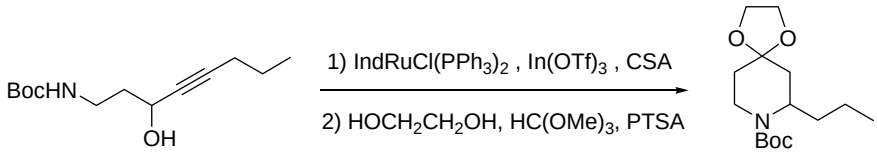
At this stage, the mixture is cooled down to room temperature. Then, 1 mL MeOH is added to the reaction mixture, followed by K_2CO_3 (24 mg, 0.17 mmol, 1 eq) and stirring is continued at room temperature for 12 hours. After filtration over a pad of Florisil, 5 mL of saturated aqueous NH_4Cl and 10 mL of ether are added. Following conventional extractive workup, purification by chromatography (silica, PE/AcEt 4:1 to 1:1) affords 26 mg of the piperidinone (52% yield).



NM II-40

IR ($CHCl_3$): 3414, 2955, 2362, 2338, 1715, 1601, 1353, 1165, 1093 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.77 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.31 (dm, *J* = 8.0 Hz, 2H), 4.43-4.37 (m, 1H), 4.13 (tq, *J* = 7.6, 2.0 Hz, 1H), 3.30-3.23 (m, 1H), 2.50 (dd, *J* = 13.6, 6.6 Hz,

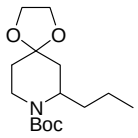
1H), 2.44 (s, 3H), 2.41-2.34 (m, 1H), 2.21 (dm, *J* = 8.0 Hz, 1H), 1.42-1.22 (m, 6H), 0.84 (t, *J* = 7.6 Hz, 3H).
^{13}C–NMR (100 MHz, $CDCl_3$): δ = 206.7, 143.8, 137.5, 129.9, 127.0, 54.3, 45.3, 40.3, 40.0, 34.3, 21.5, 19.0, 13.5.
HRMS: Calculated for $C_{15}H_{21}NO_3NaS$: 318.1140. Found: 318.1141.



NM III-44

9b (NM III-44)

The aminoalcohol (45 mg, 0.186 mmol, 1eq) is subjected to the standard procedure for redox isomerisation. After 2h, complete conversion to the amino-enone is observed.
At this stage, the mixture is cooled down to room temperature. Then, PTSA (35 mg, 0.186 mmol, 1 eq), followed by ethylene glycol (20 μL, 0.37 mmol, 2 eq) and trimethyl orthoformate (40 μl, 0.37 mmol, 2 eq) stirring is continued at room temperature for 2 hours. After filtration over a pad of Florisil, 5 mL of saturated aqueous $NaHCO_3$ and 10 mL of ether are added. Following conventional extractive workup, purification by chromatography (silica, PE/AcEt 4:1 to 1:1) affords 32 mg of the protected piperidinone (62% yield).

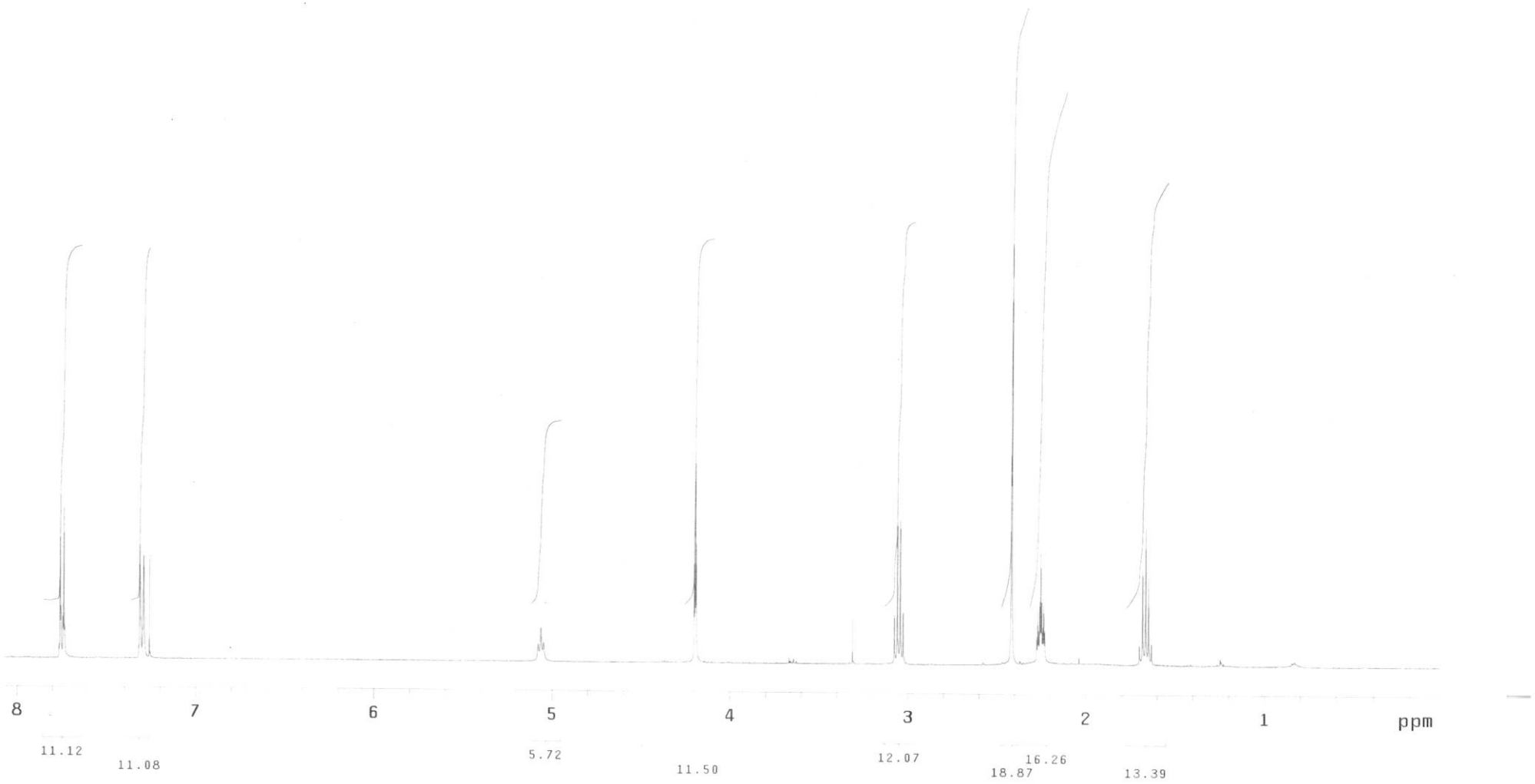


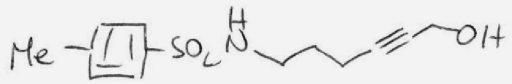
NM III-44

IR ($CHCl_3$): 34073416, 2960, 2922, 2871, 1687, 1414, 1370, 1250, 1174, 1116 cm^{-1}.
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.34-4.29 (m, 1H), 4.09-3.97 (m, 5H), 3.02-2.95 (m, 1H), 1.86-1.76 (m, 2H), 1.67-1.58 (m, 4H), 1.45 (s, 9H), 1.31-1.20 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H).
^{13}C–NMR (100 MHz, $CDCl_3$): δ = 154.8, 107.4, 79.4, 64.6, 63.7, 50.4, 36.9, 34.7, 33.3, 19.8, 14.0.
HRMS: Calculated for $C_{15}H_{27}NO_4Na$: 308.1838. Found: 308.1838.

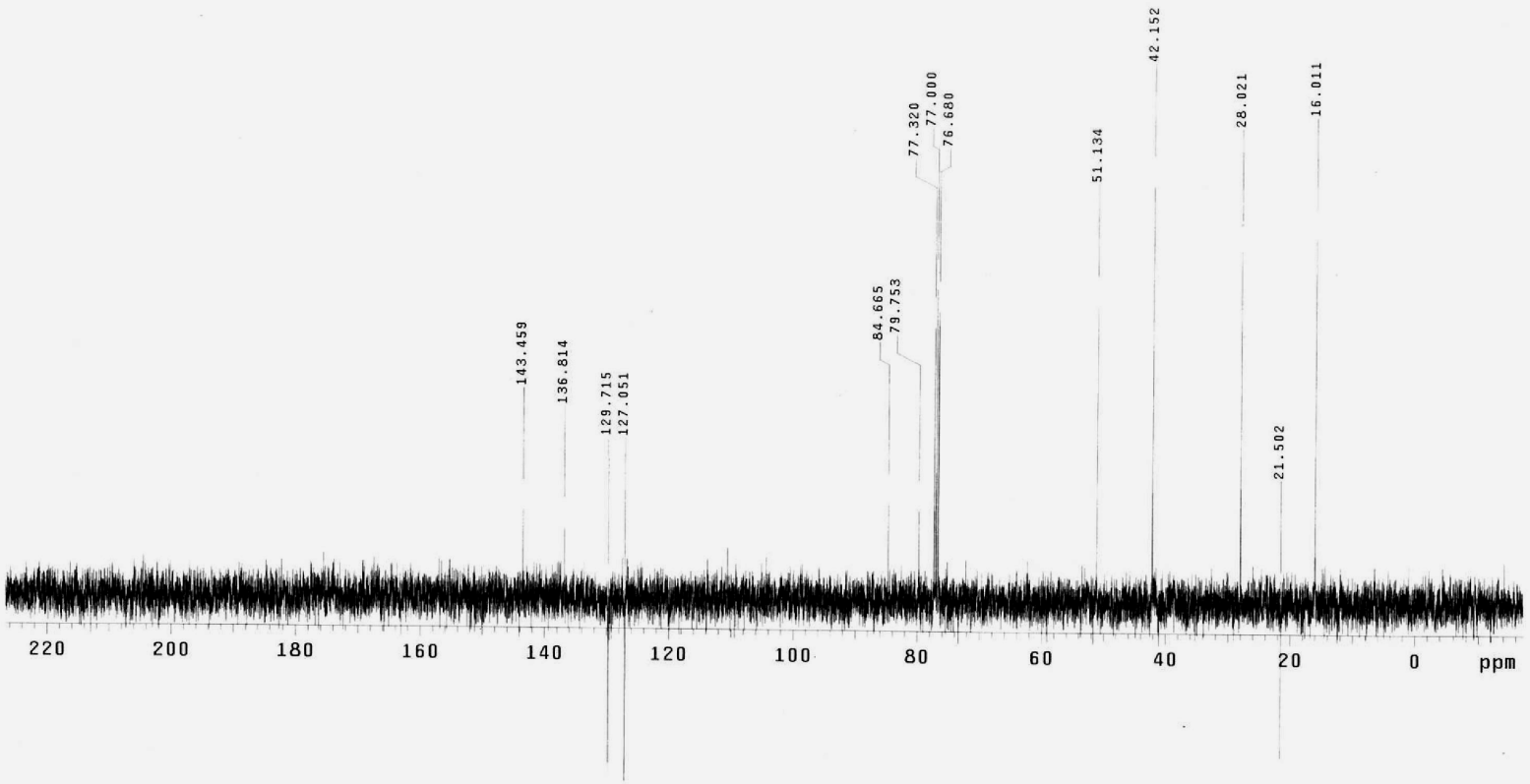
Copies of Spectra

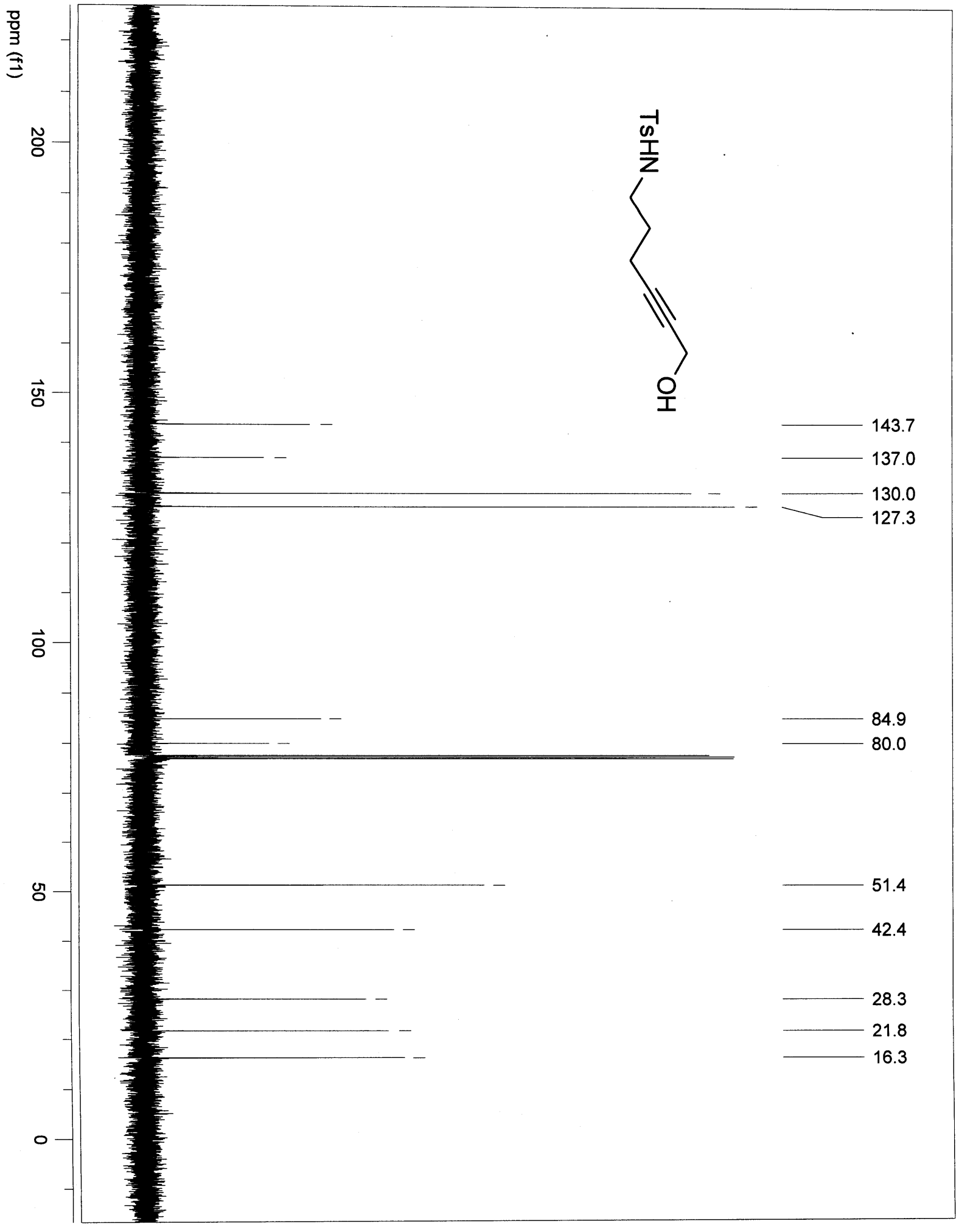
NMI-48





APT Spectrum




ppm (f1)
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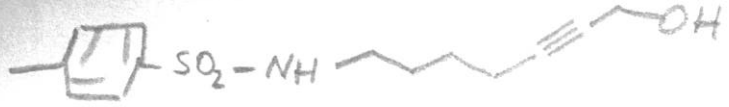
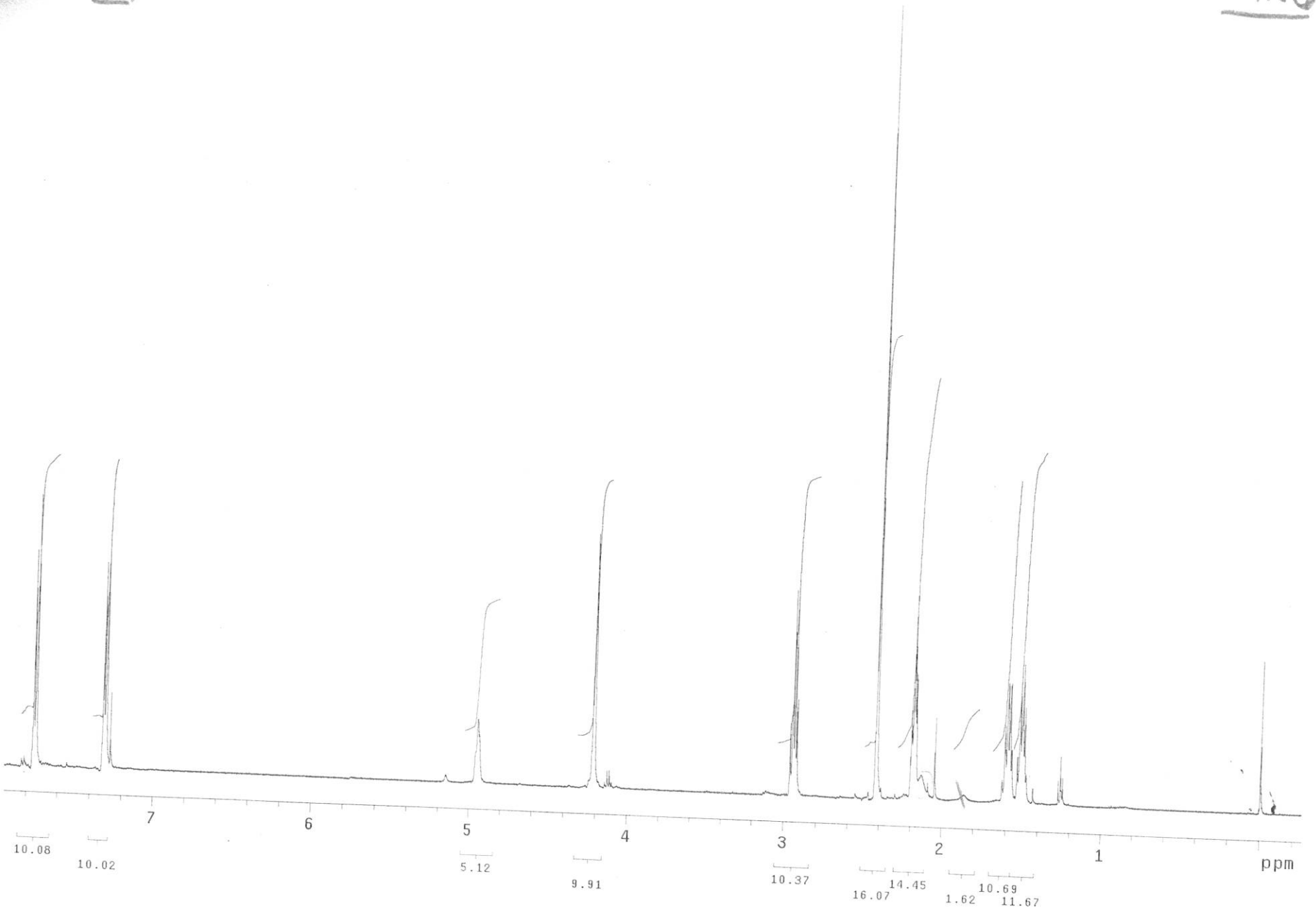
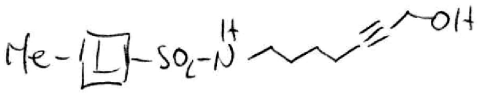
150
100
50
0
TsHN
OH
143.7
137.0
130.0
127.3
84.9
80.0
51.4
42.4
28.3
21.8
16.3

NMJ-6

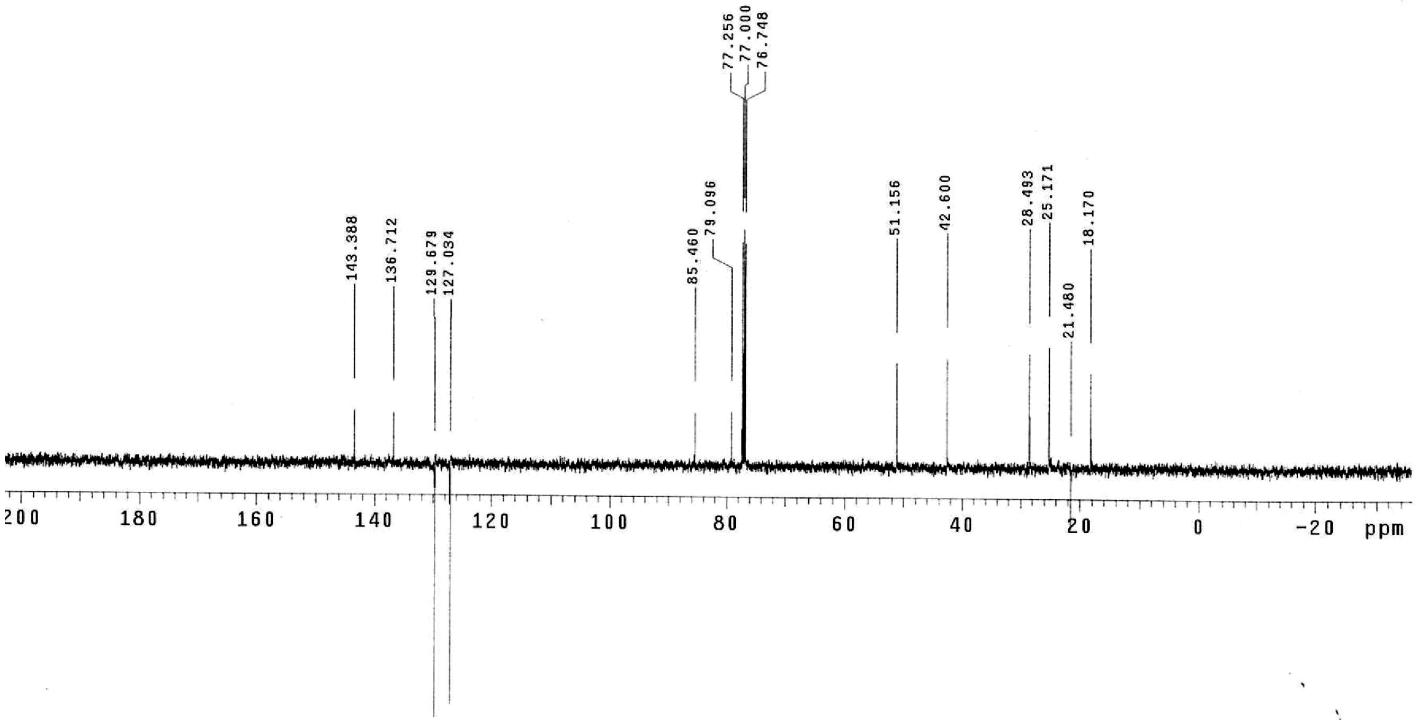
NHTs6

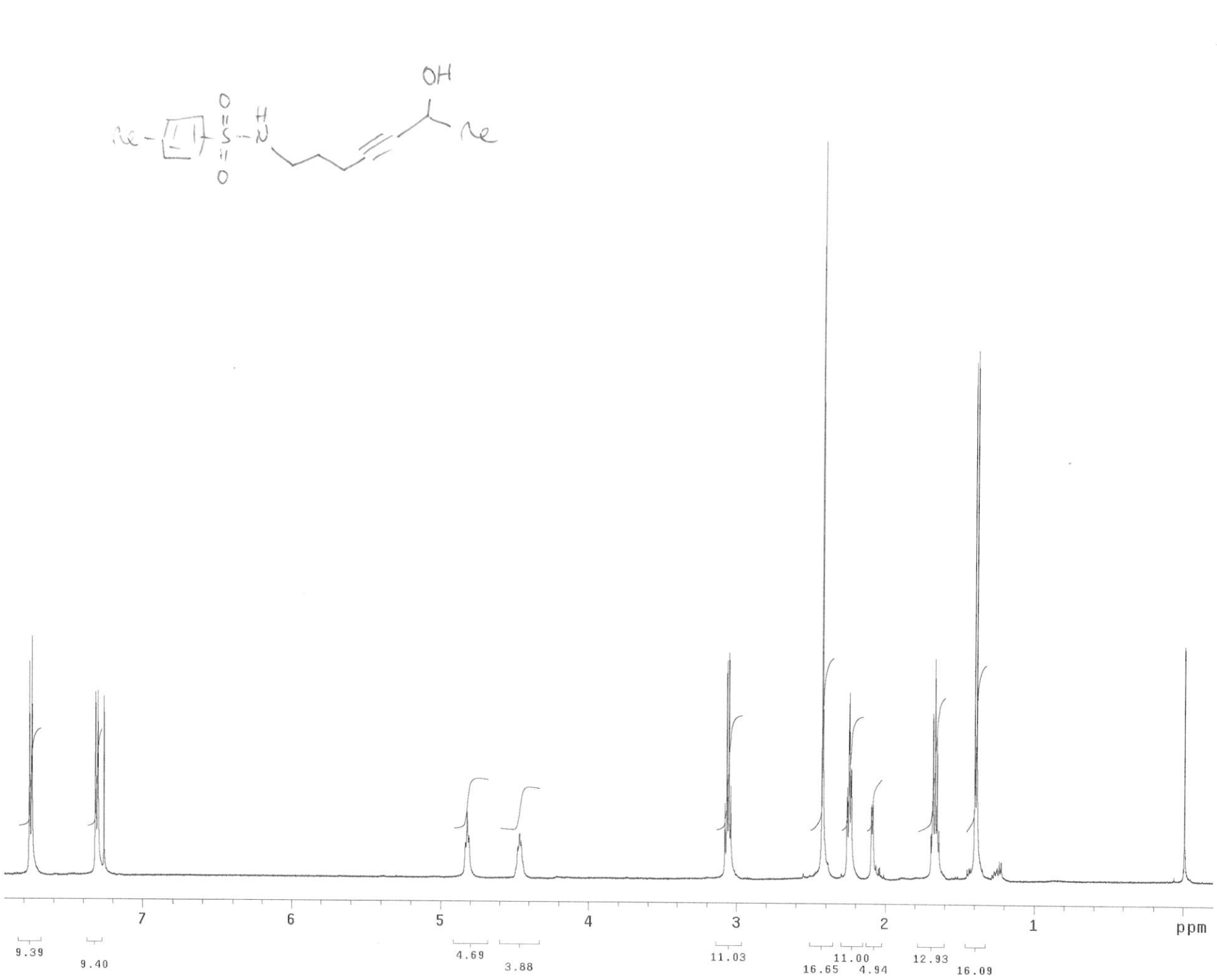

SO2-NH
OH

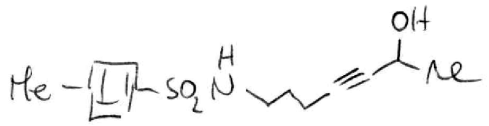

7
6
5
4
3
2
1
ppm
10.08
10.02
5.12
9.91
10.37
16.07
14.45
1.62
10.69
11.67



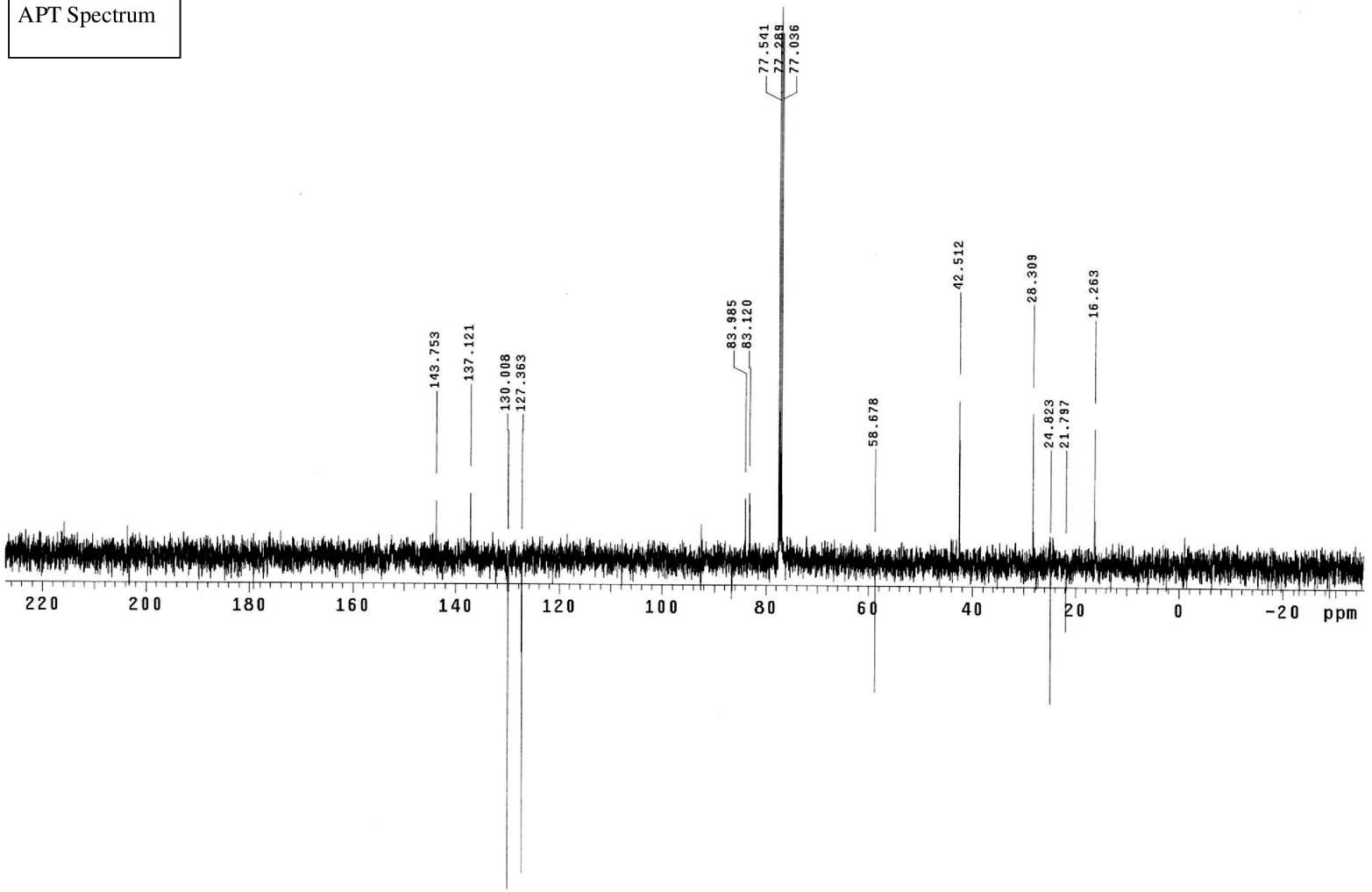
APT Spectrum

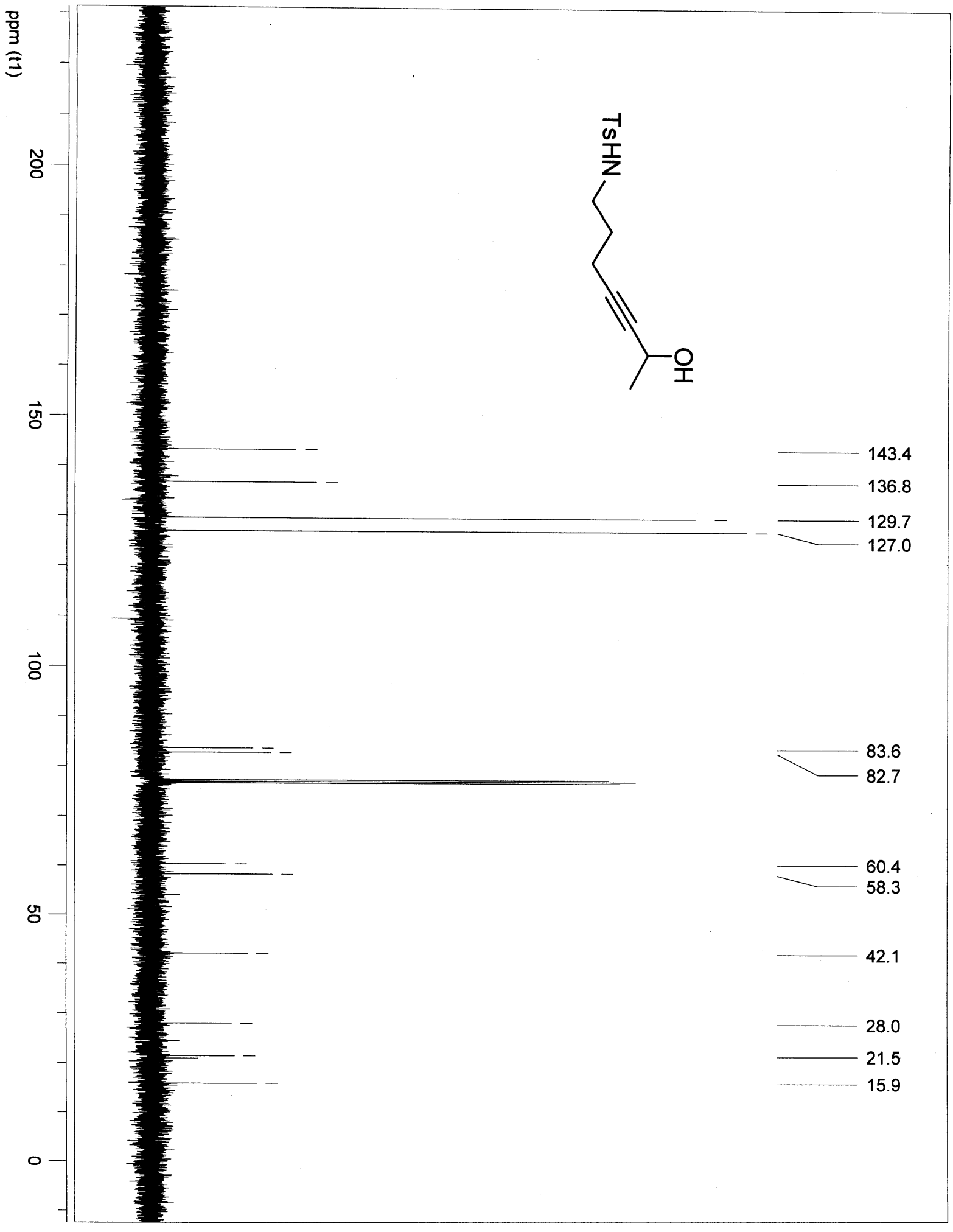



OH
Me
Me
7
6
5
4
3
2
1
ppm
9.39
9.40
4.69
3.88
11.03
16.65
11.00
4.94
12.93
16.09



APT Spectrum




ppm (t1)
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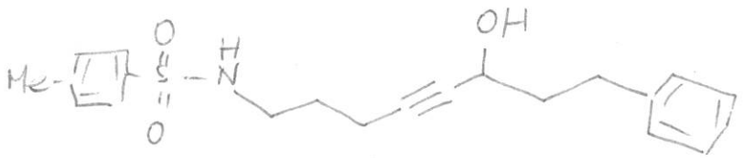
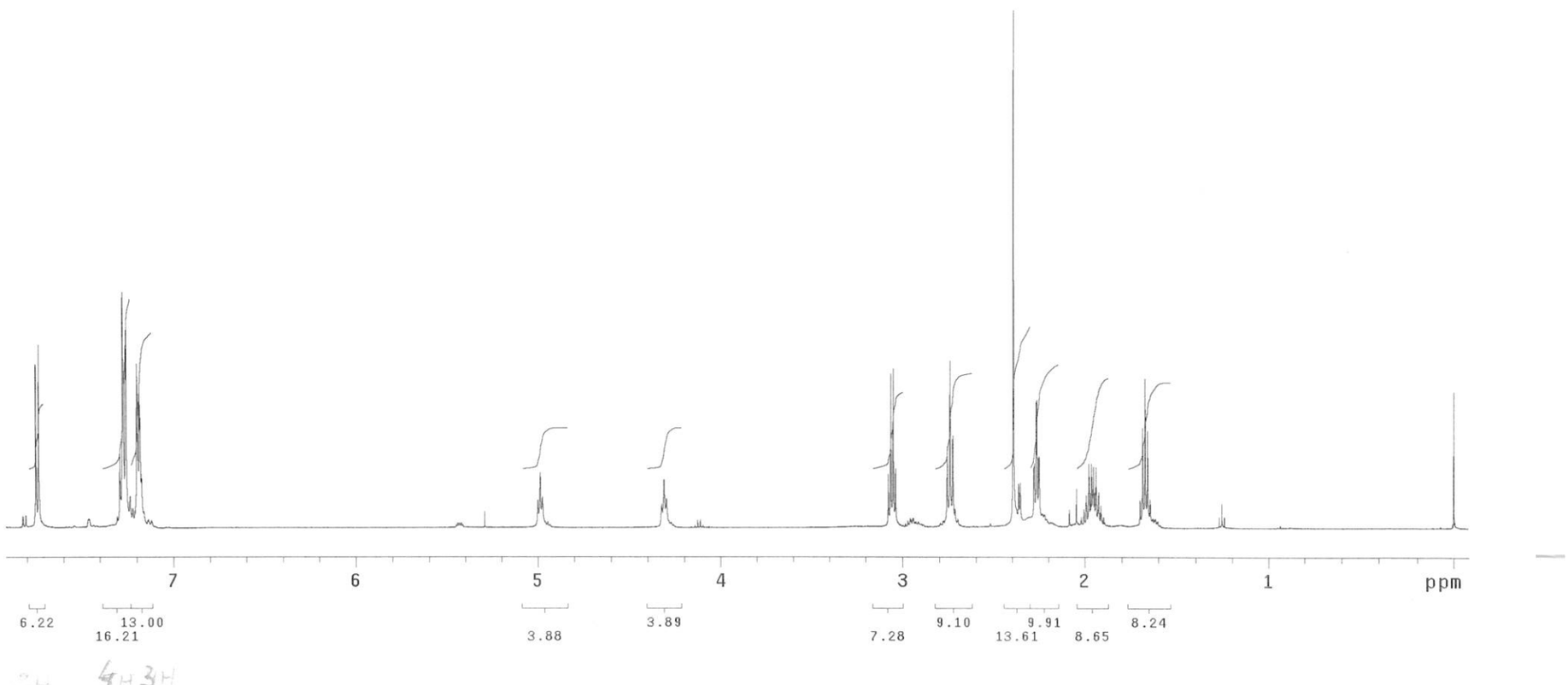
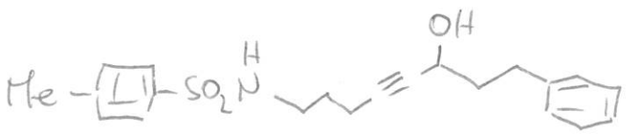
150
100
50
0
TsHN
OH
143.4
136.8
129.7
127.0
83.6
82.7
60.4
58.3
42.1
28.0
21.5
15.9

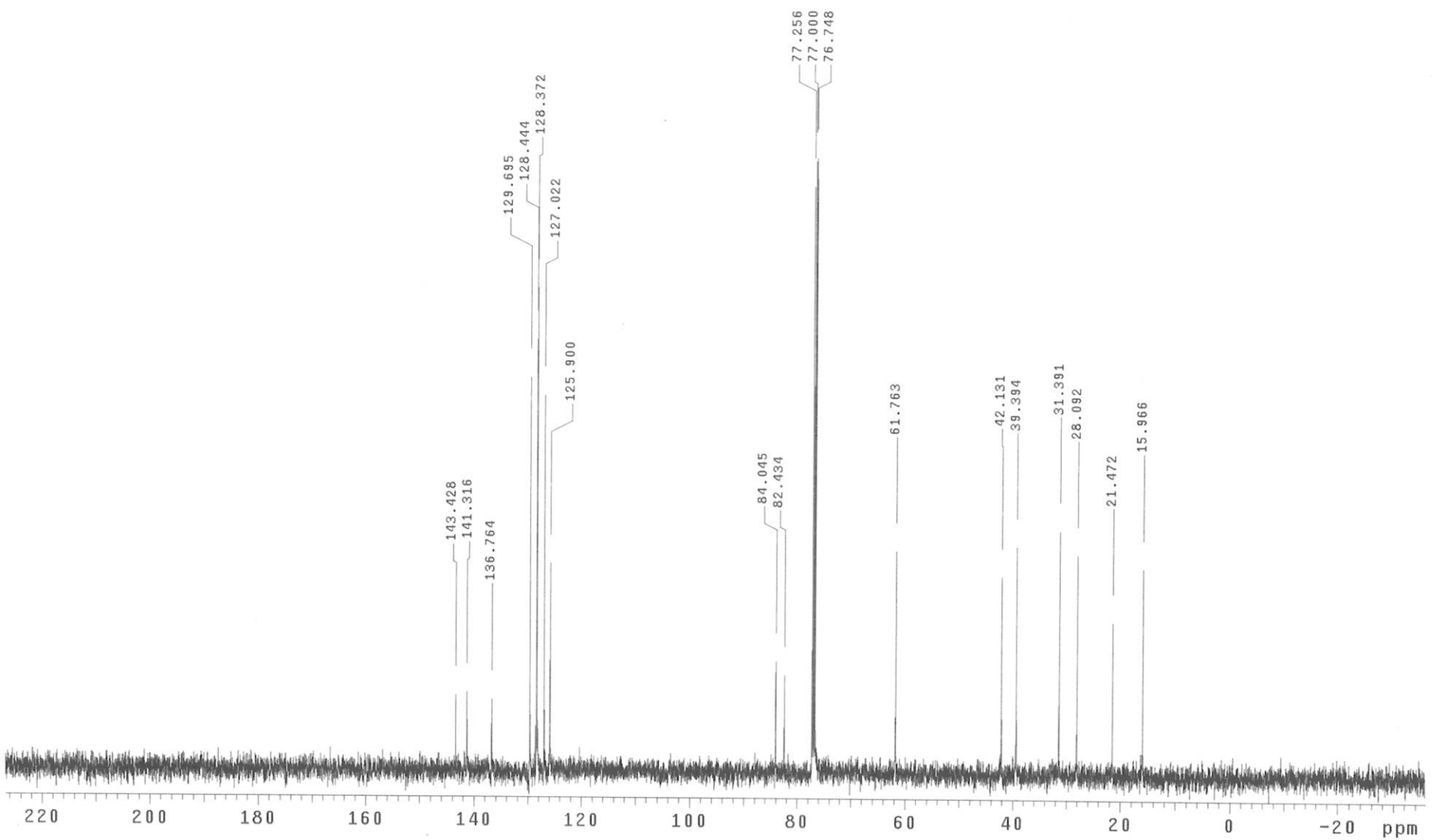
500


OH
Me
O
S
O
H
N


7
6
5
4
3
2
1
ppm
6.22
16.21
13.00
3.88
3.89
7.28
9.10
13.61
9.91
8.65
8.24

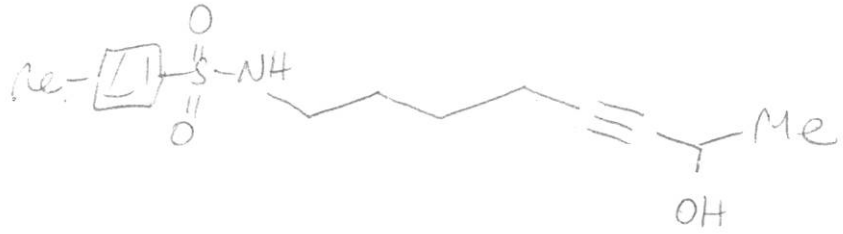
2H 4H 3H


OH
H
N
Me
SO2


143.428
141.316
136.764
129.695
128.444
128.372
127.022
125.900
84.045
82.434
77.256
77.000
76.748
61.763
42.131
39.394
31.391
28.092
21.472
15.966
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

400

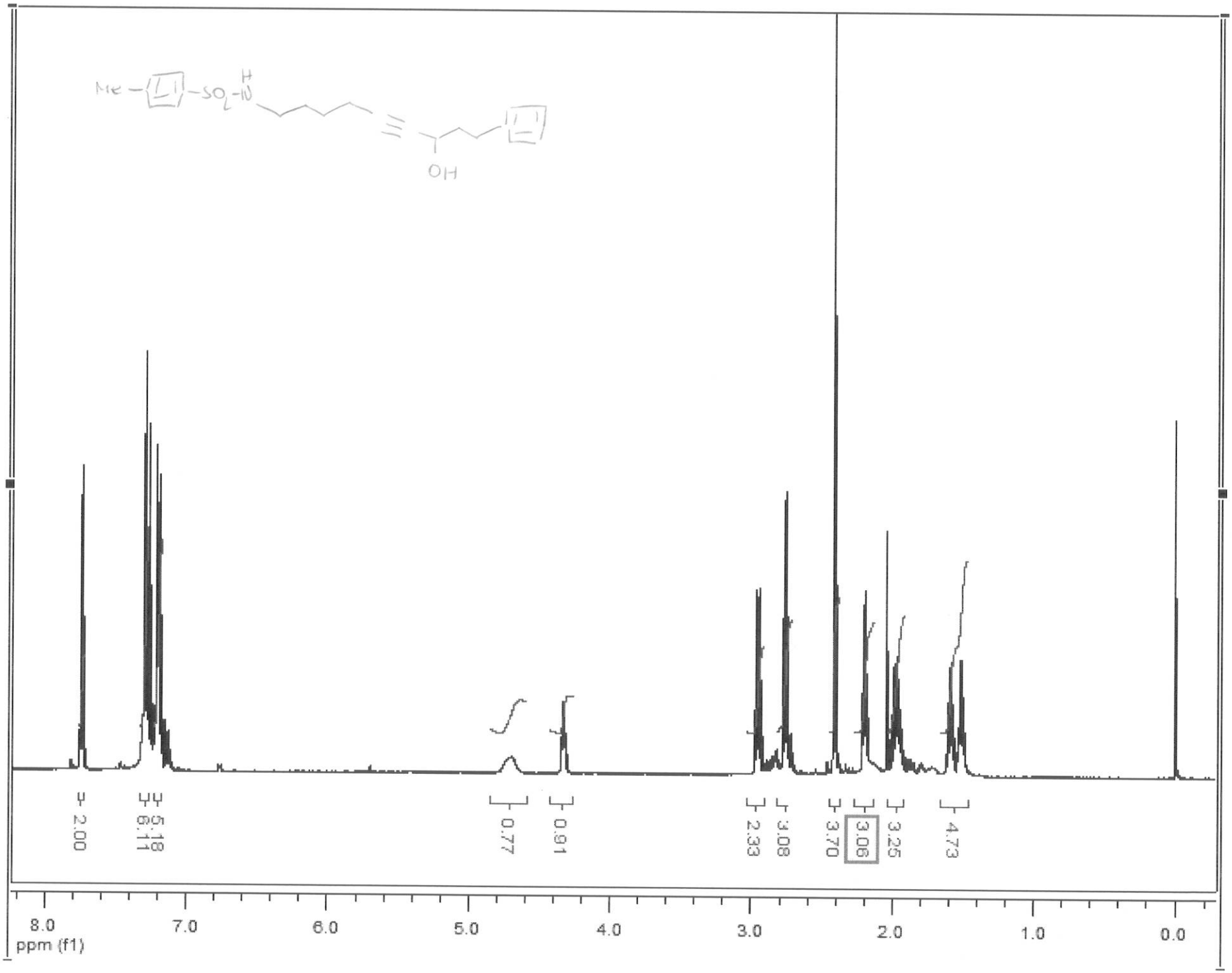
NMR-1

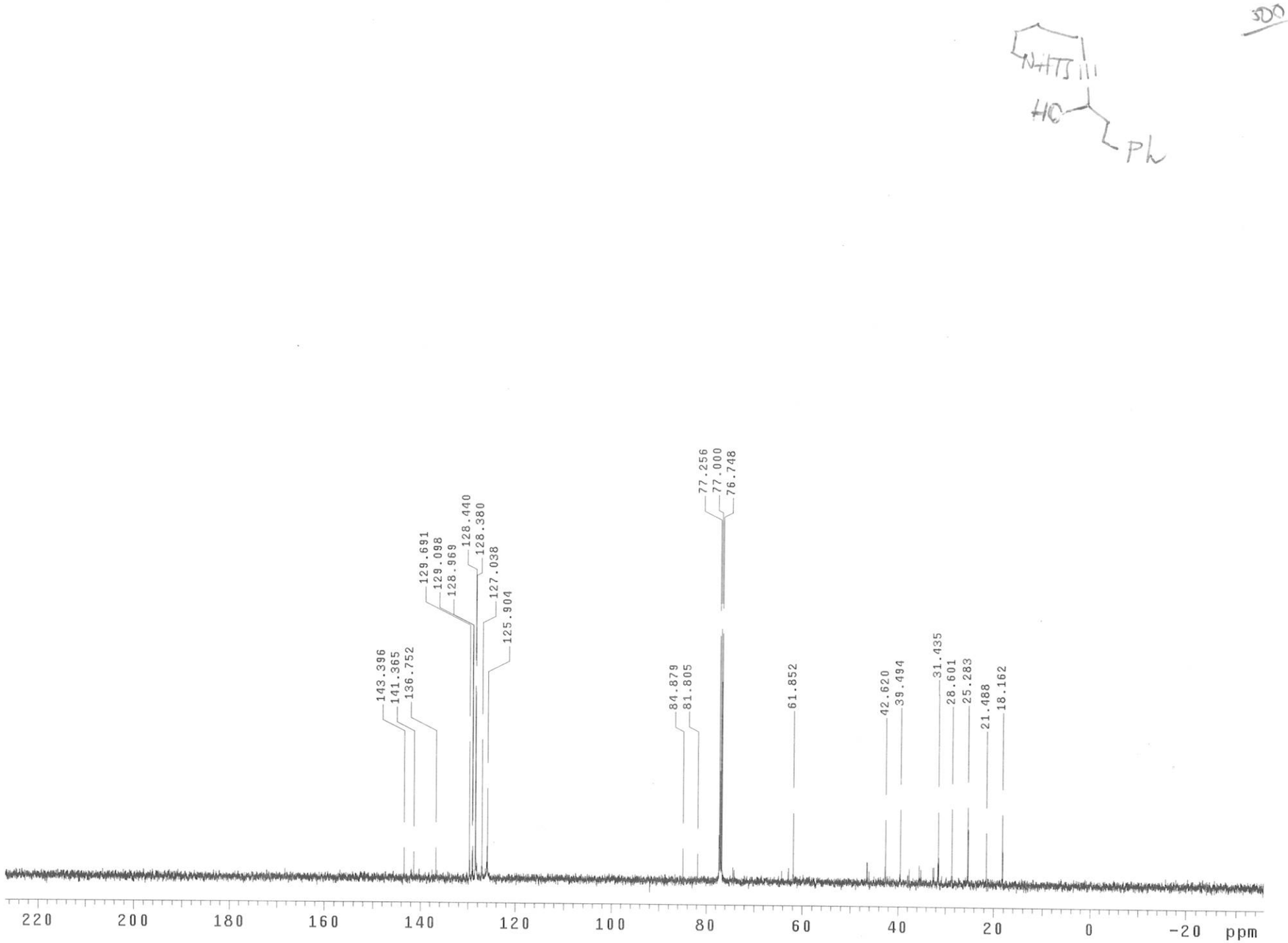

Me
NH
Me
OH

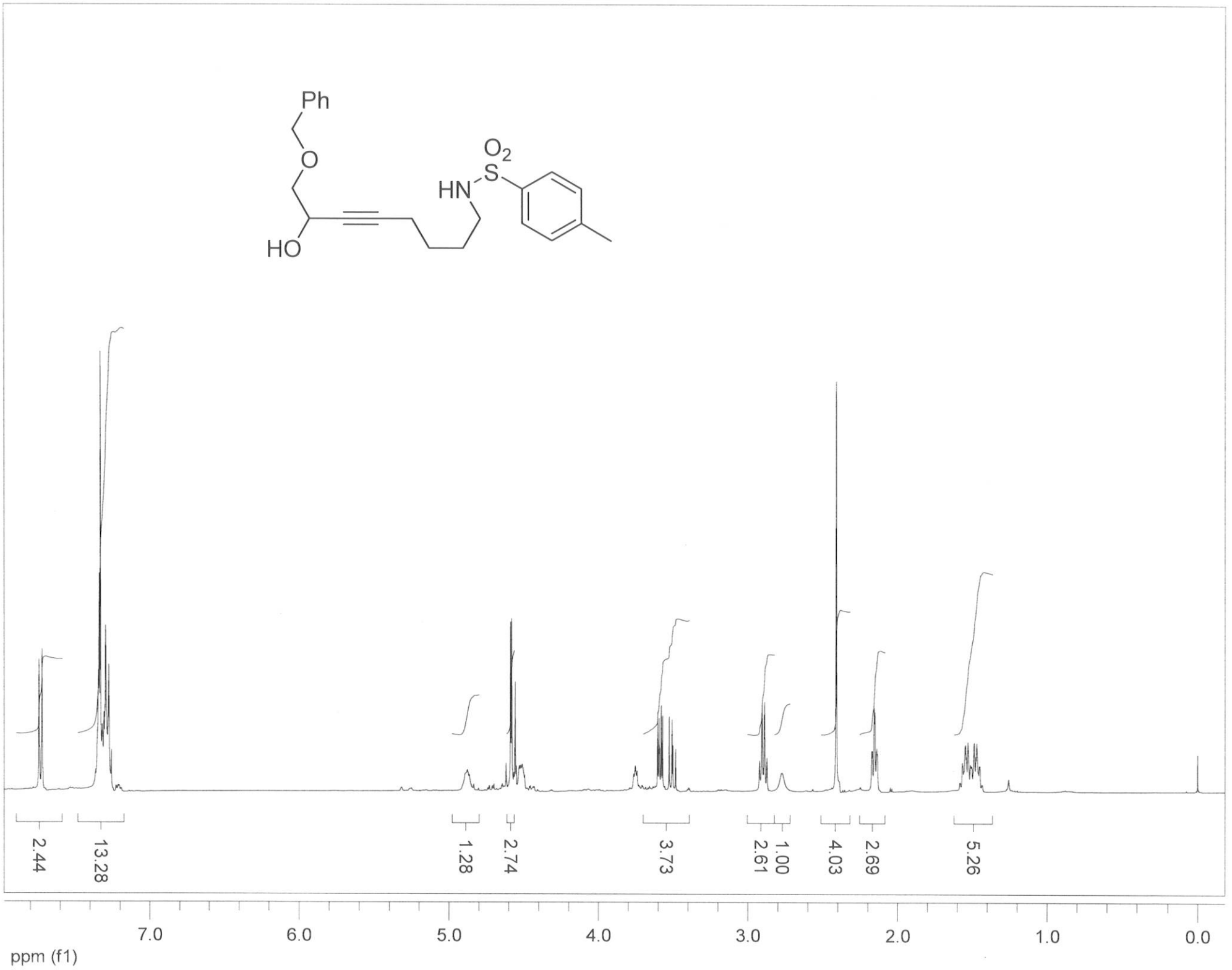
8
7
6
5
4
3
2
1
ppm
8.63
9.09
4.79
3.91
9.17
14.30
9.50
4.00
9.33
8.36
9.53
9.38

143.280
136.697
129.614
126.983
83.499
82.923
77.326
77.000
76.689
58.254
42.548
28.428
25.197
24.545
21.428
18.031
200
180
160
140
120
100
80
60
40
20
0
ppm

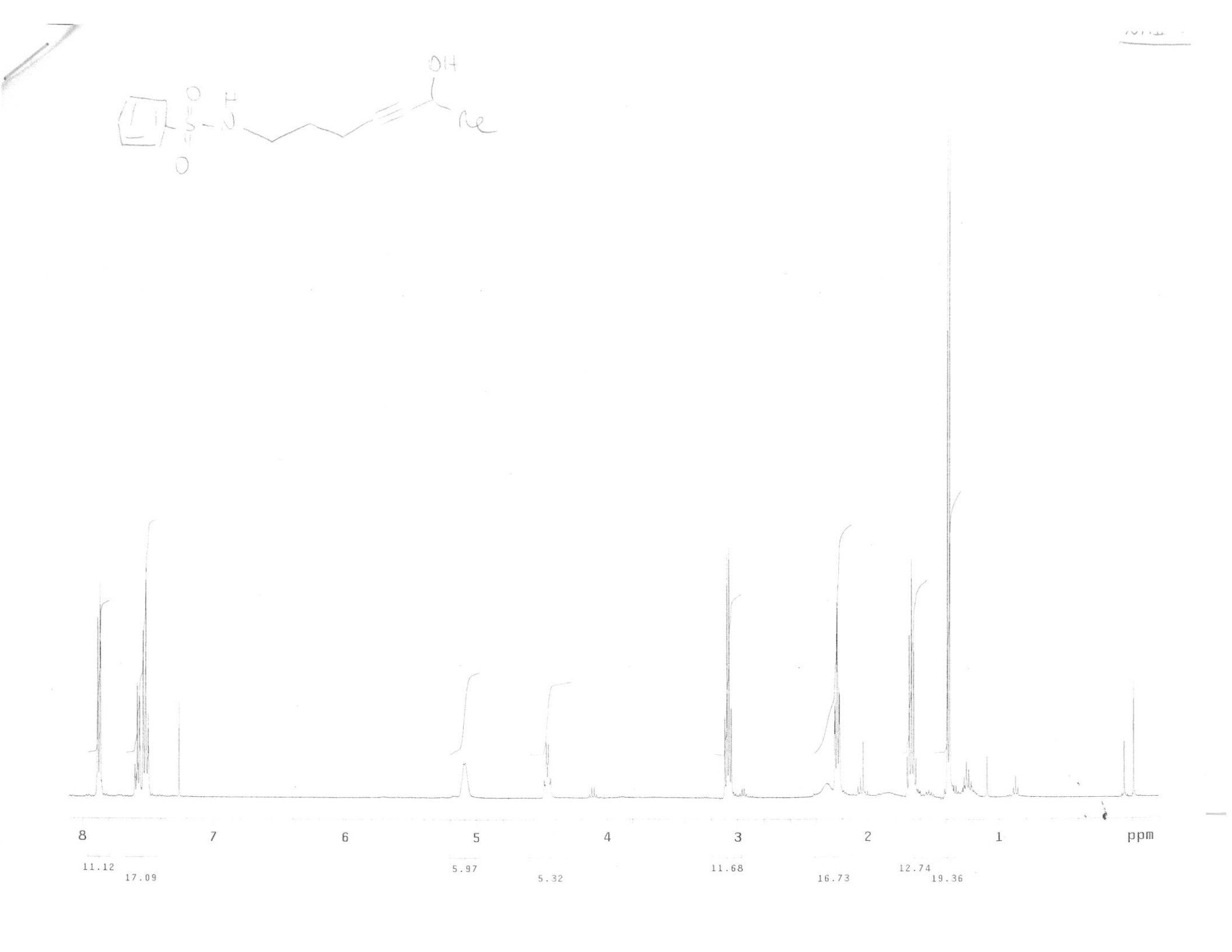
H
N
Me
OH

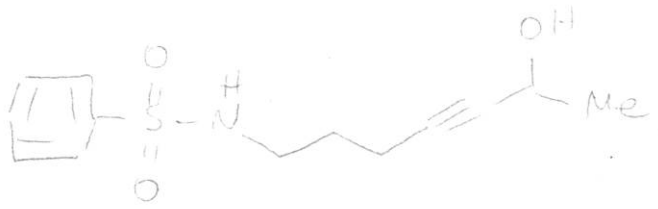

Me
SO2
N
H
OH
2.00
5.18
6.11
0.77
0.91
2.33
3.08
3.70
3.06
3.25
4.73
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


NHTs
HO
Ph
300
143.396
141.365
136.752
129.691
129.098
128.969
128.440
128.380
127.038
125.904
84.879
81.805
77.256
77.000
76.748
61.852
42.620
39.494
31.435
28.601
25.283
21.488
18.162
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

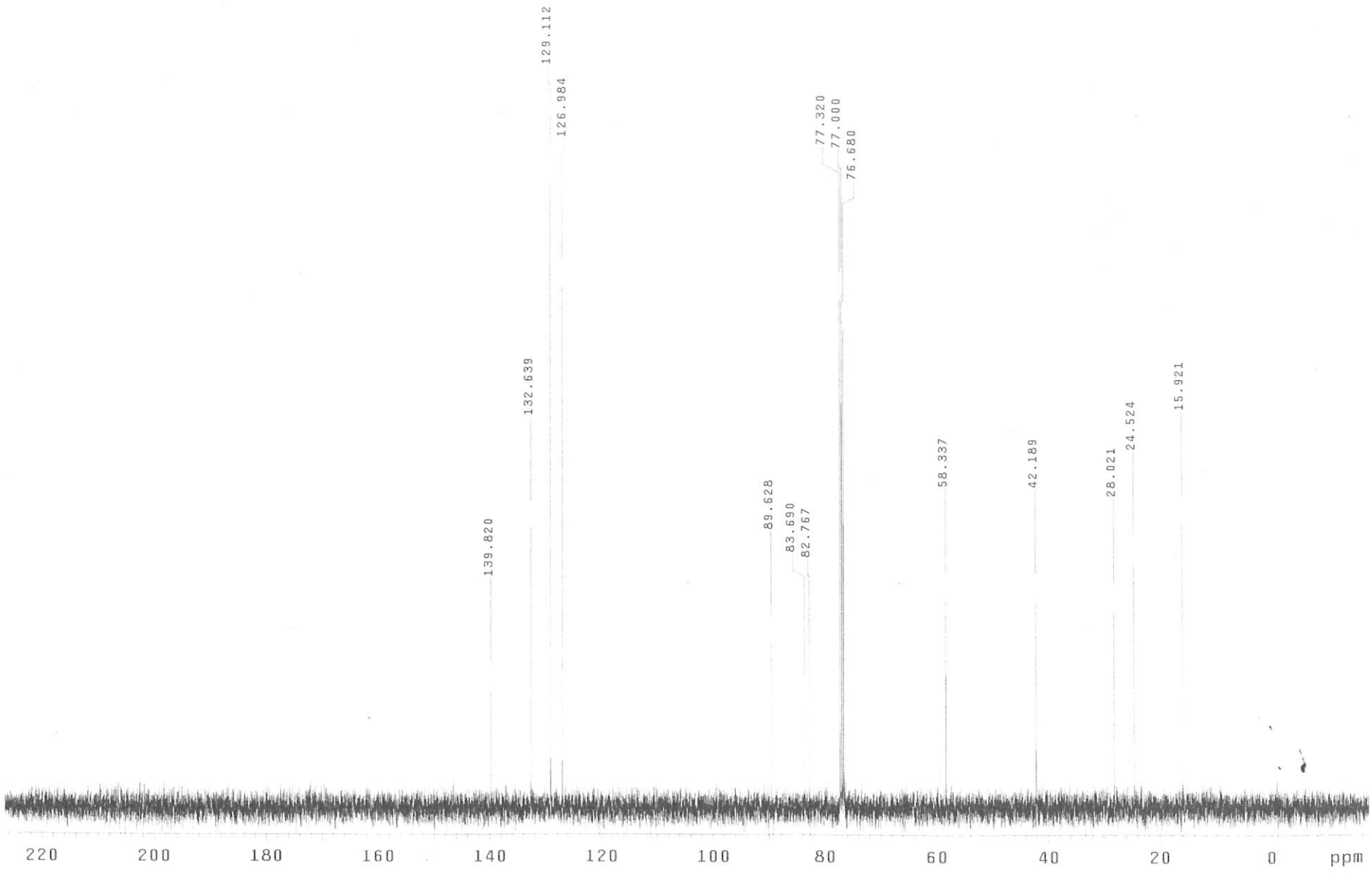

Ph
O
HO
HN
O2
S
2.44
13.28
1.28
2.74
3.73
2.61
1.00
4.03
2.69
5.26
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

ppm (f1)
200
150
100
50
0
HO
O
Ph
HN
S
O2
143.259
137.571
136.771
129.610
128.388
127.780
127.722
126.983
94.340
85.498
78.431
77.319
77.000
76.682
73.834
73.244
73.172
71.275
61.762
61.663
42.525
28.457
25.091
21.446
18.103


OH
O
H
N
S
O
8
7
6
5
4
3
2
1
ppm
11.12
17.09
5.97
5.32
11.68
16.73
12.74
19.36


OH
O
S
H
N
Me
O

180 mg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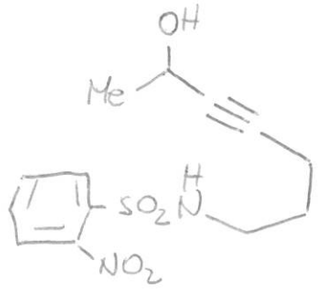
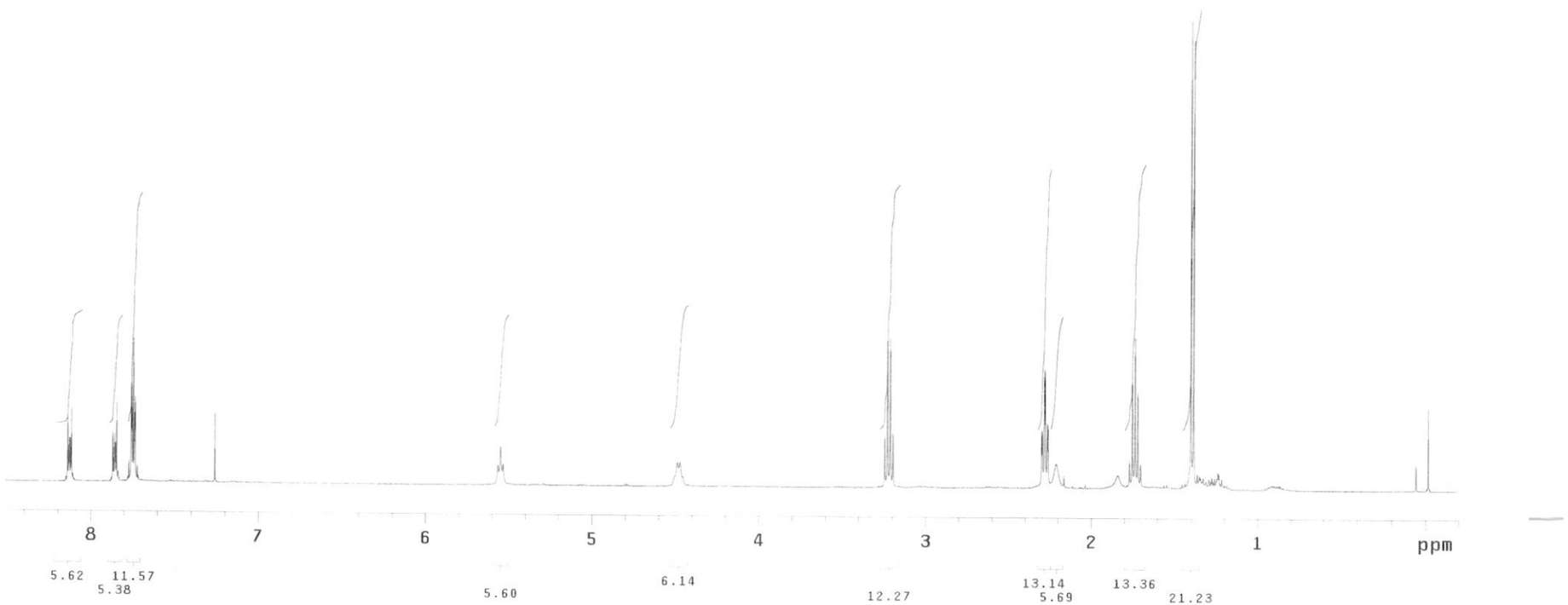
126.984
89.628
83.690
82.767
77.320
77.000
76.680
58.337
42.189
28.021
24.524
15.921
220
200
180
160
140
120
100
80
60
40
20
0
ppm

NM111-34


OH
Me
H
N
SO2
NO2

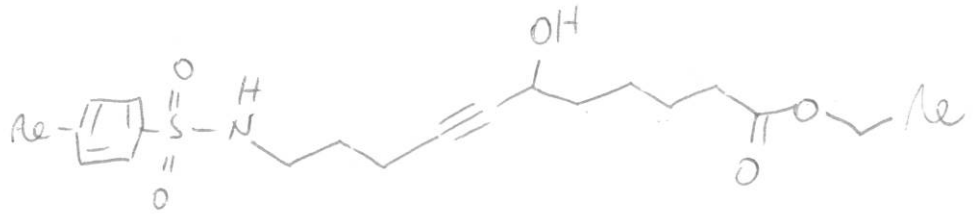

8
7
6
5
4
3
2
1
ppm
5.62
11.57
5.38
5.60
6.14
12.27
13.14
5.69
13.36
21.23

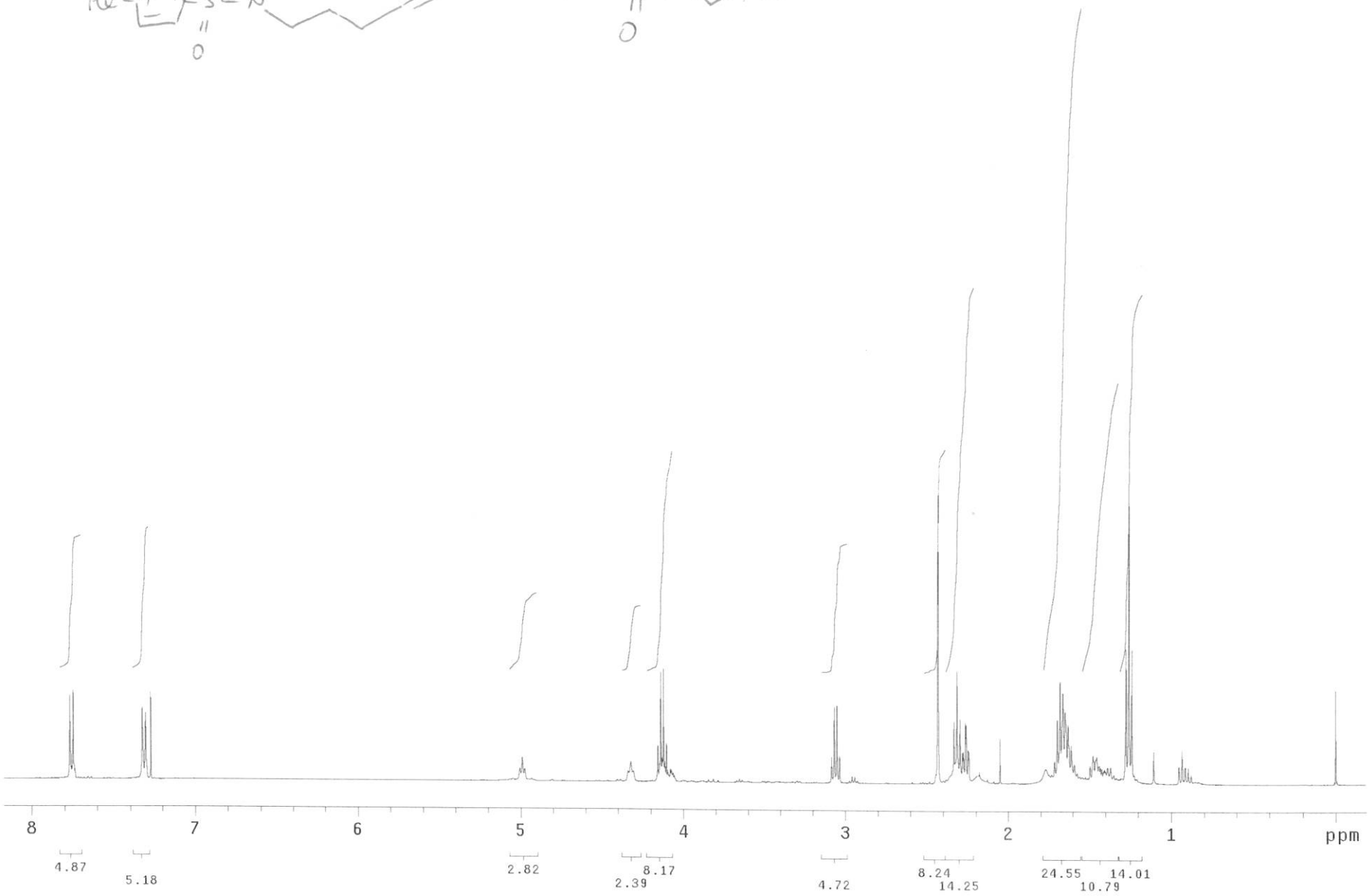
147.942
133.594
133.542
132.835
131.019
125.349
89.606
83.765
82.432
77.320
77.000
76.680
65.800
60.390
58.329
42.746
28.145
24.484
21.016
15.919
15.197
14.125
220
200
180
160
140
120
100
80
60
40
20
0
ppm

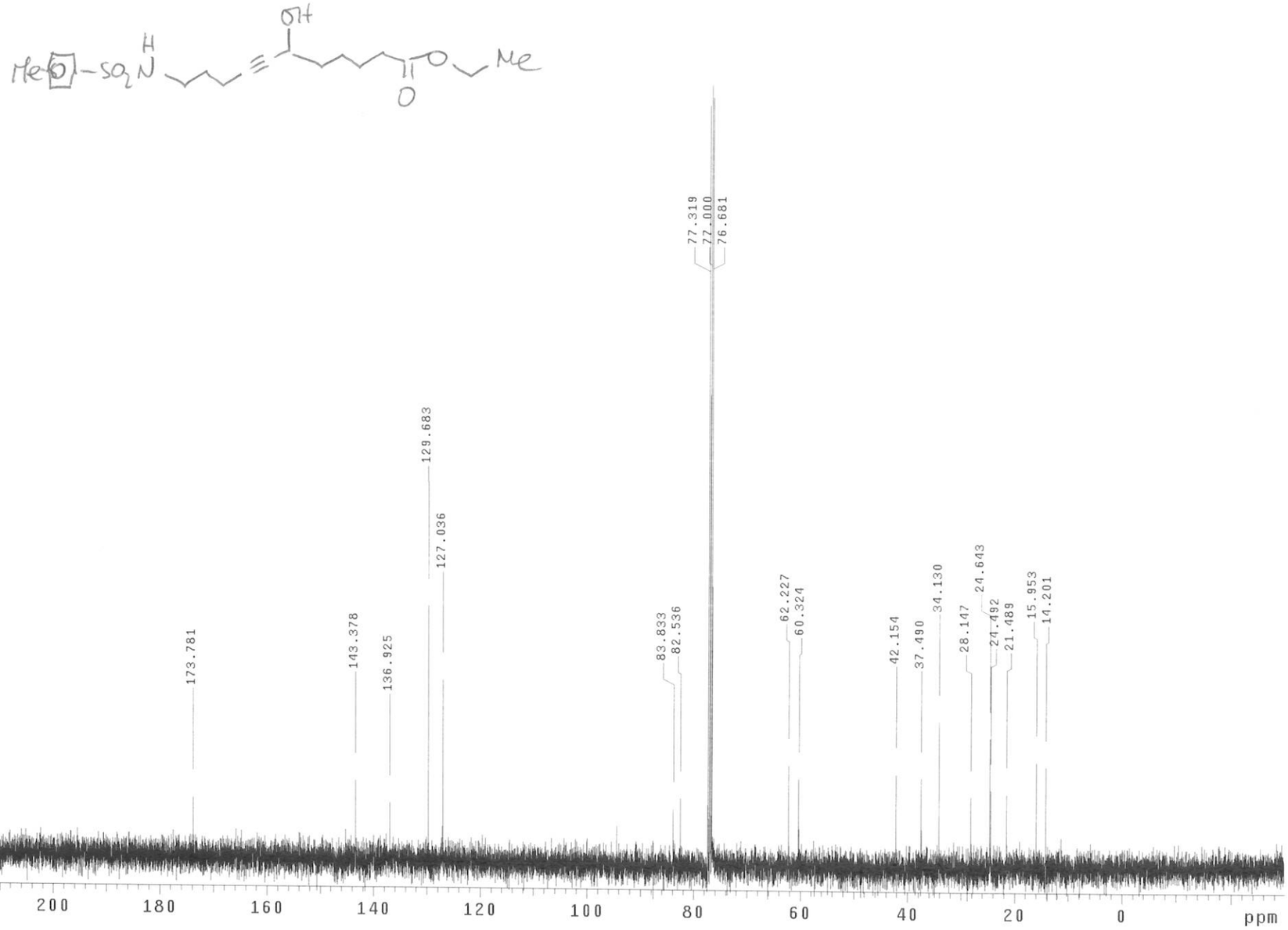
H
N
OH

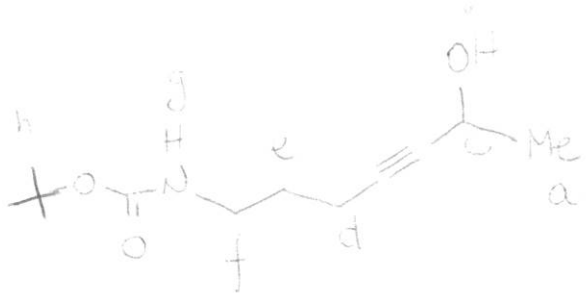
400

II-30


OH
H
N
S
O
O
O
O
Me
Me

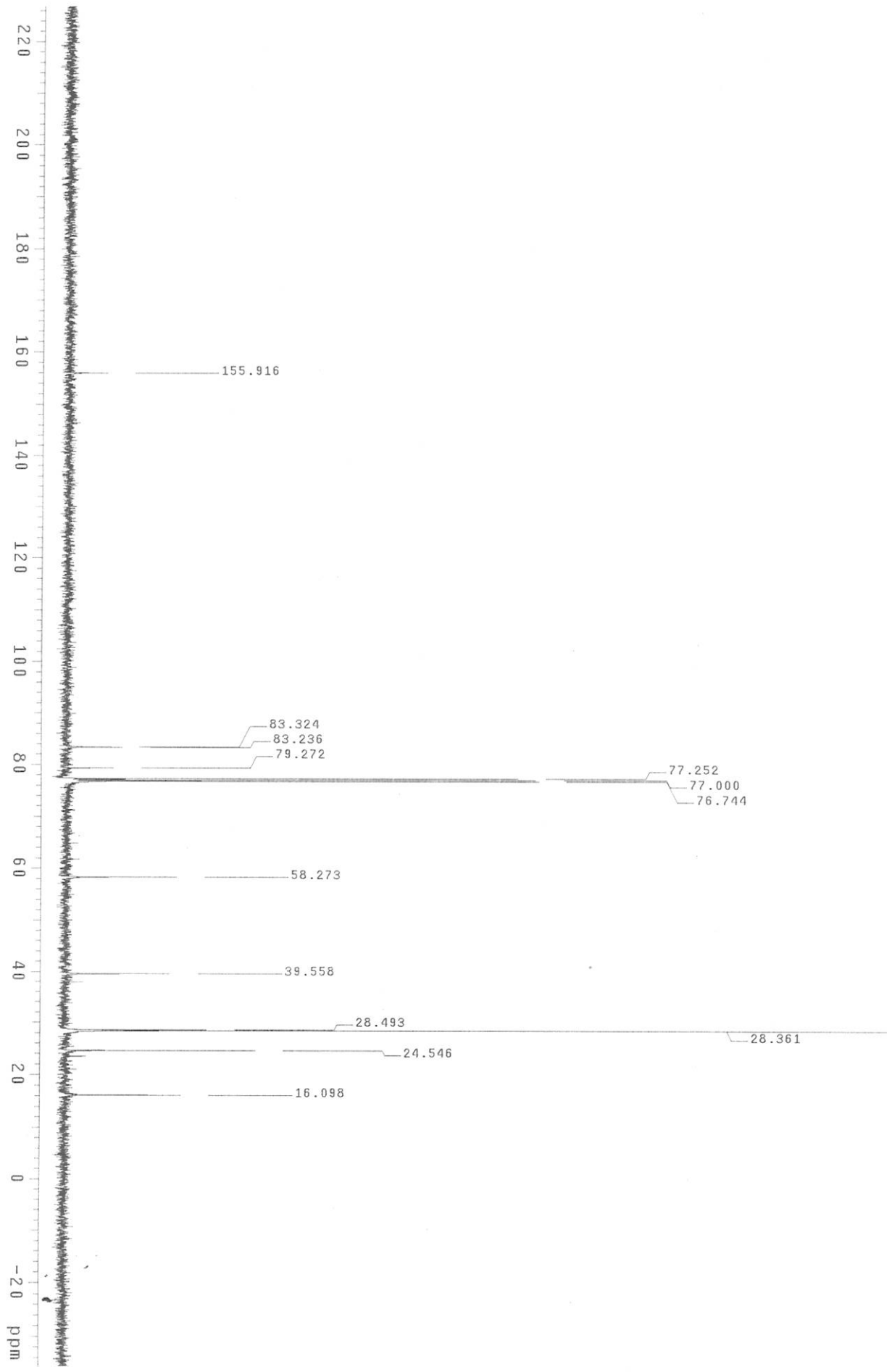

8
7
6
5
4
3
2
1
ppm
4.87
5.18
2.82
2.39
8.17
4.72
8.24
14.25
24.55
14.01
10.79

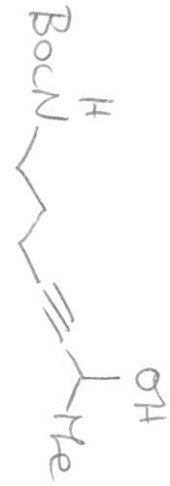

77.319
77.000
76.681
173.781
143.378
136.925
129.683
127.036
83.833
82.536
62.227
60.324
42.154
37.490
34.130
28.147
24.643
24.492
21.489
15.953
14.201
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
g
H
N
e
Me
a
O
O
f
d

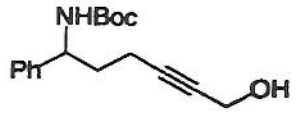
500

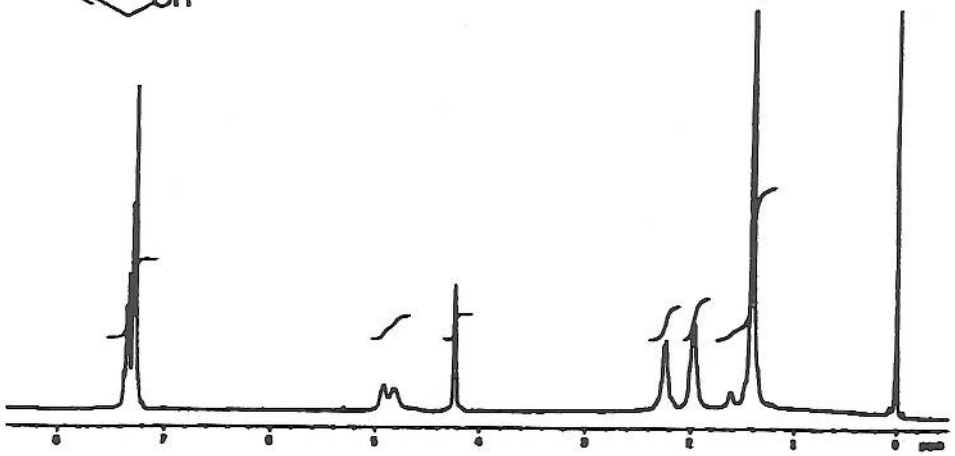
a+h
g
c
f
b
d
e
7
6
5
4
3
2
1
ppm
3.90
4.12
9.80
2.94
9.96
10.01
59.28

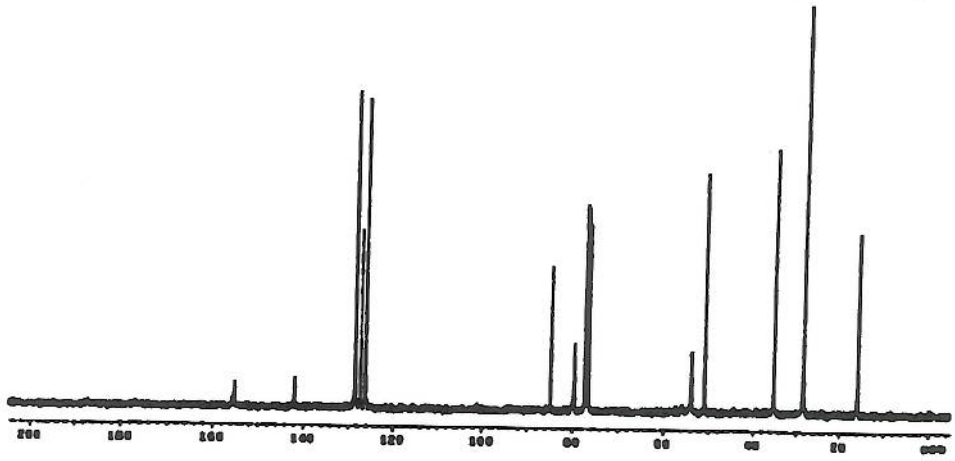

155.916
83.324
83.236
79.272
77.252
77.000
76.744
58.273
39.558
28.493
28.361
24.546
16.098
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

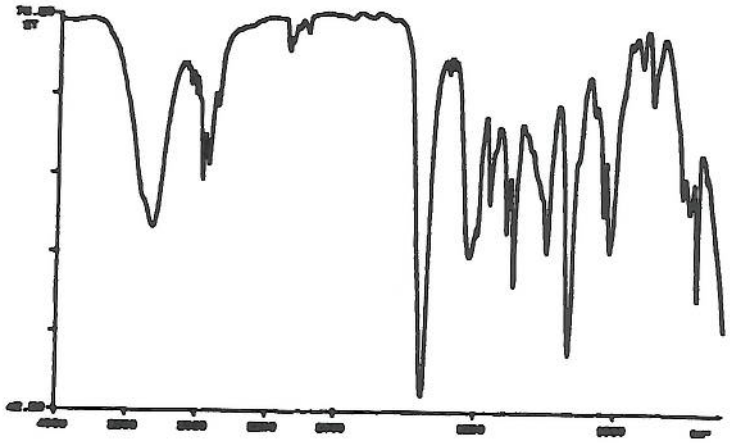

H
BocN
OH
Me

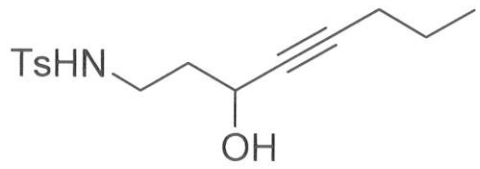
N-*t*-BOC-6-Amino-6-phenyl-2-hexyn-1-ol **(3.43)**









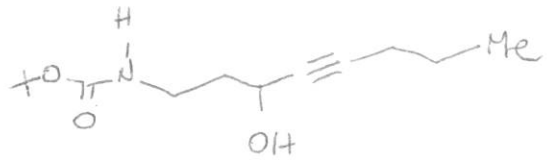

TsHN
OH

NM II - 33

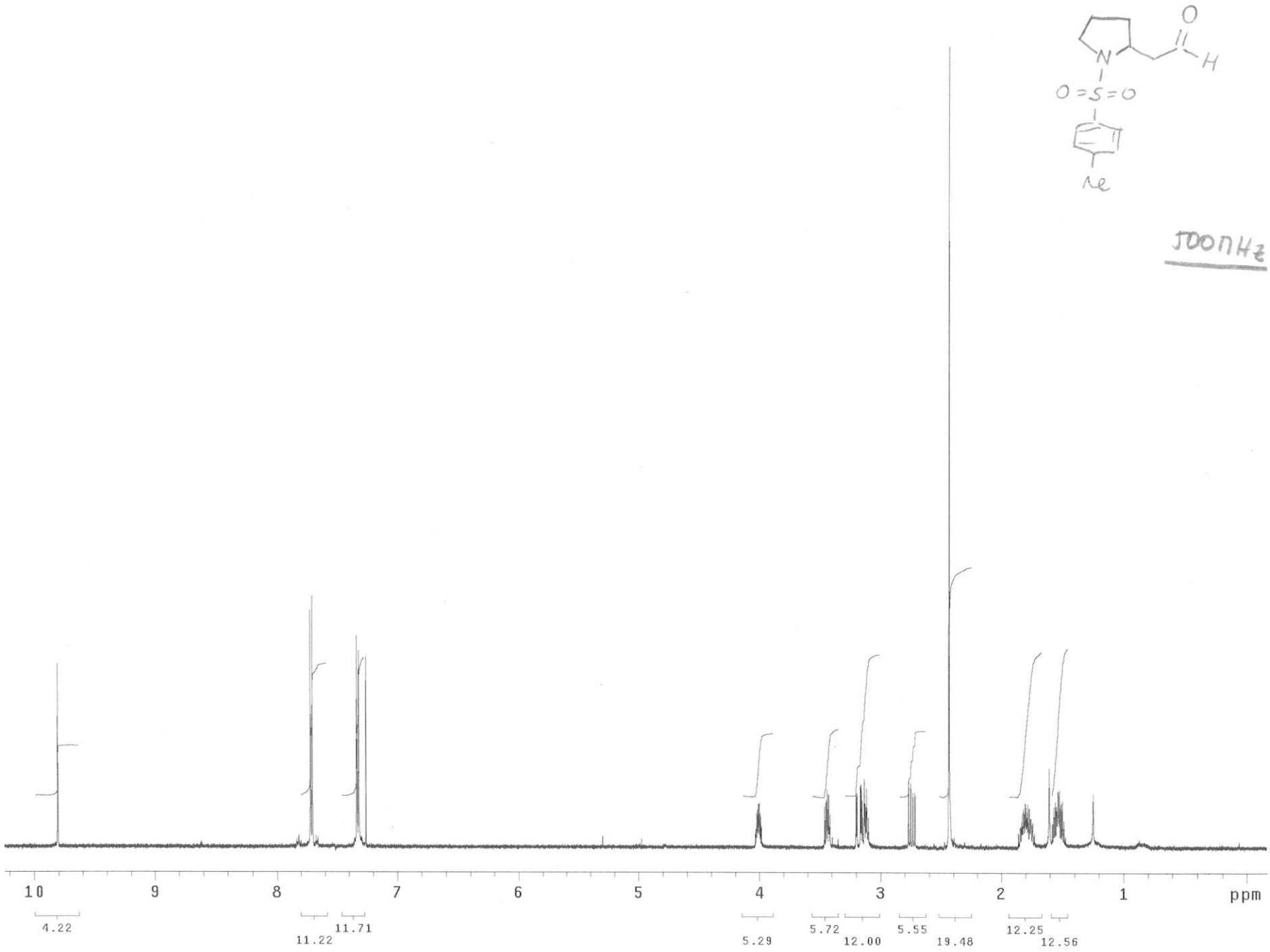
2.01
2.20
0.99
0.93
2.11
3.34
0.93
2.00
2.40
1.92
3.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

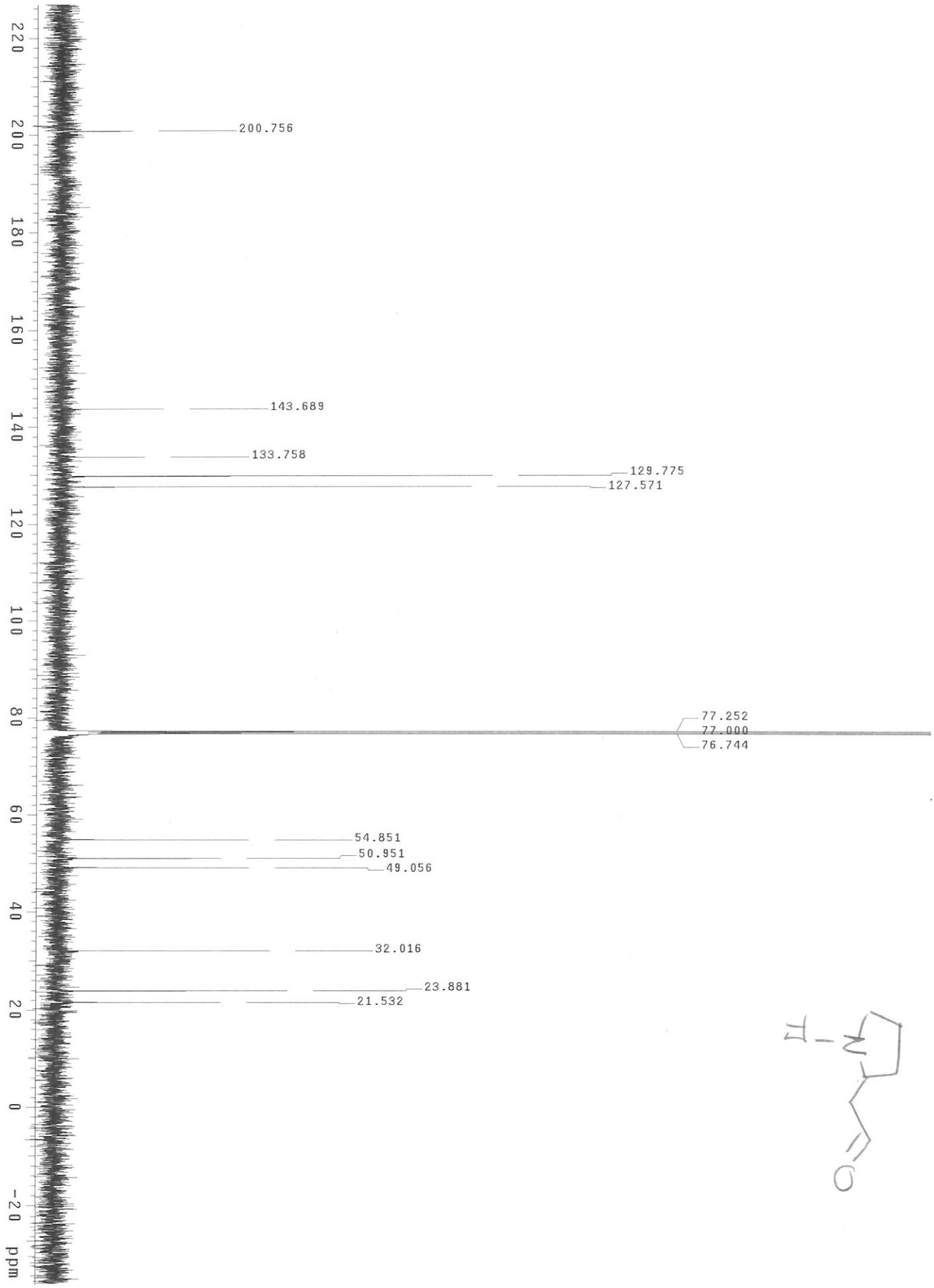
ppm (f1)
200
150
100
50
0
TsHN
OH
NM II - 33
143.290
136.687
129.643
127.080
86.473
80.000
77.318
77.000
76.683
61.088
40.069
36.507
21.868
21.479
20.507
13.420

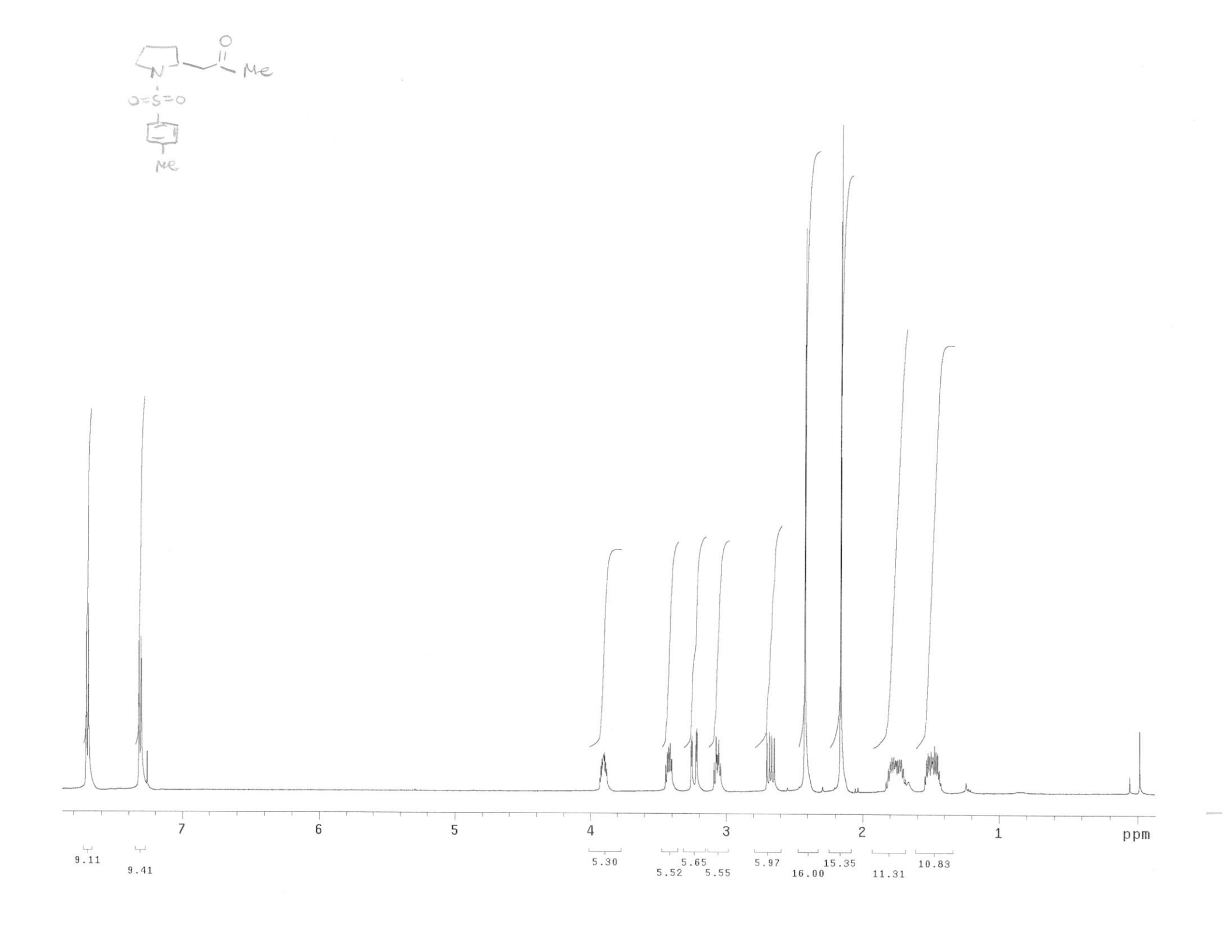
NM111-40



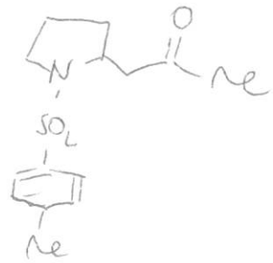
156.567
85.275
80.728
79.322
77.313
77.000
76.680
60.078
38.058
36.807
28.264
28.235
21.902
20.547
13.381
220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
N
H
O=S=O
Me
500MHz
10
9
8
7
6
5
4
3
2
1
ppm
4.22
11.22
11.71
5.29
5.72
12.00
5.55
19.48
12.25
12.56

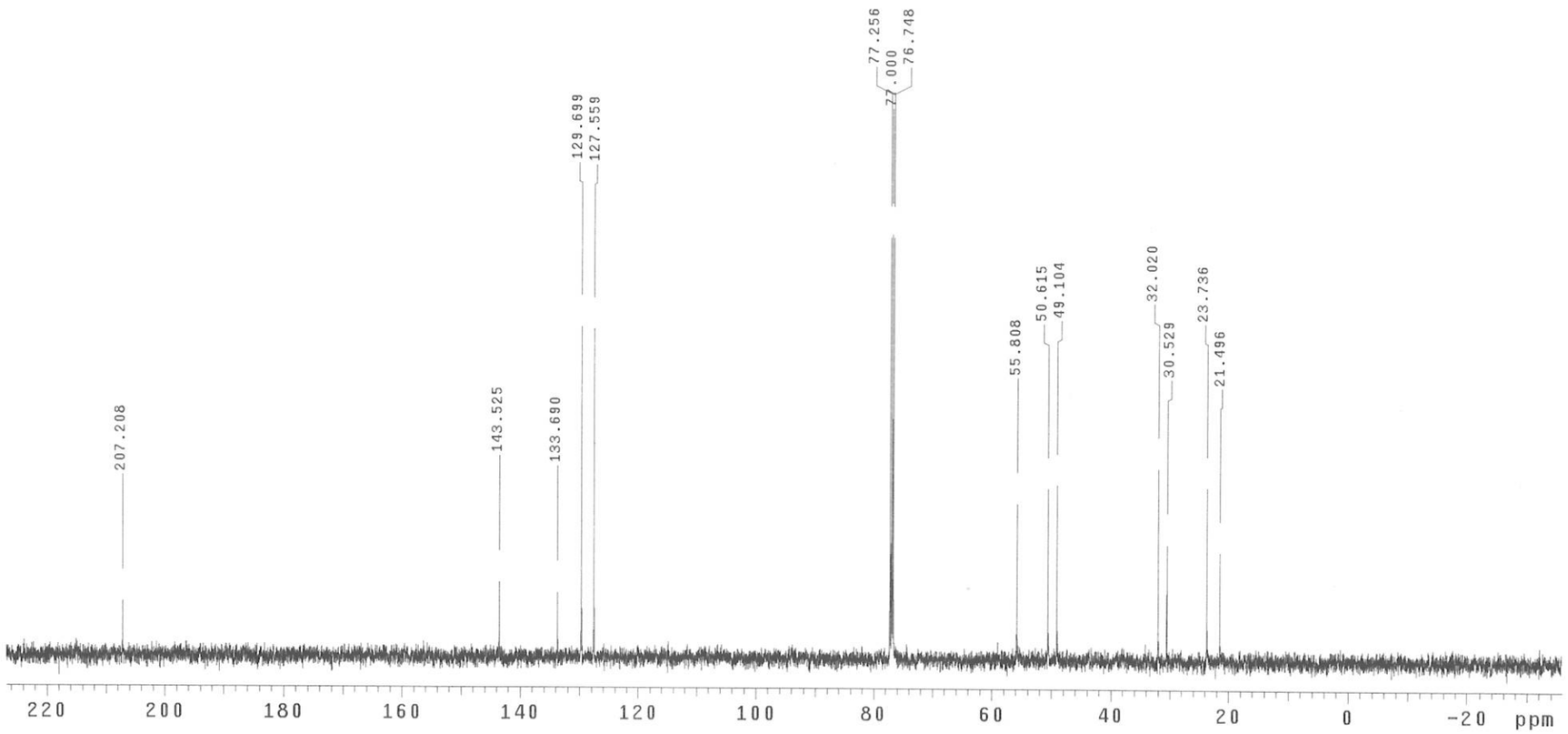

220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
200.756
143.689
133.758
129.775
127.571
77.252
77.000
76.744
54.851
50.951
49.056
32.016
23.881
21.532
H
N
O


Me
O=S=O
Me
7
6
5
4
3
2
1
ppm
9.11
9.41
5.30
5.52
5.65
5.55
5.97
16.00
15.35
11.31
10.83

500

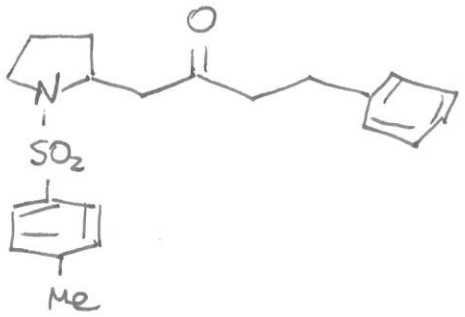


IMII-3

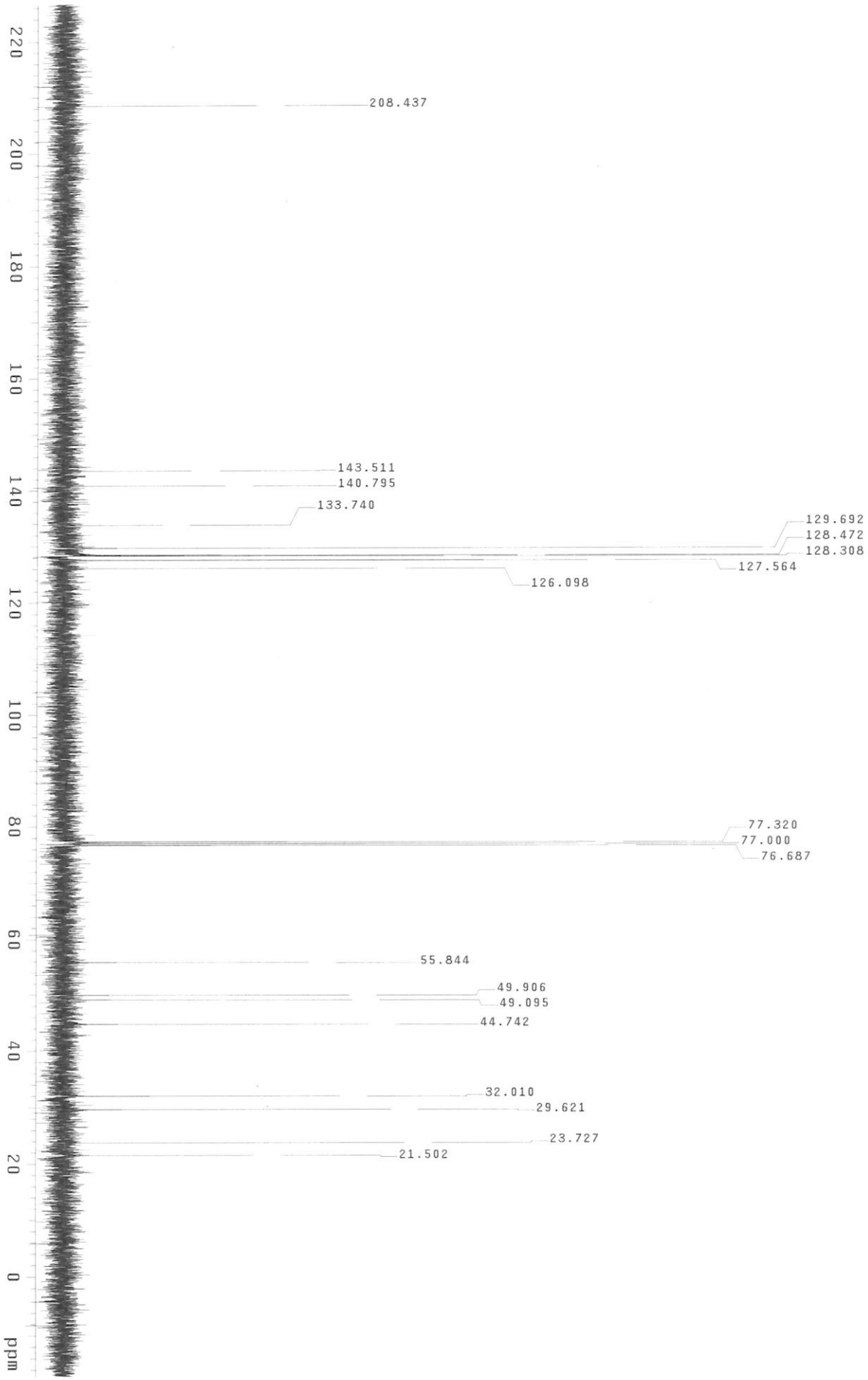

207.208
143.525
133.690
129.699
127.559
77.256
77.000
76.748
55.808
50.615
49.104
32.020
30.529
23.736
21.496
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

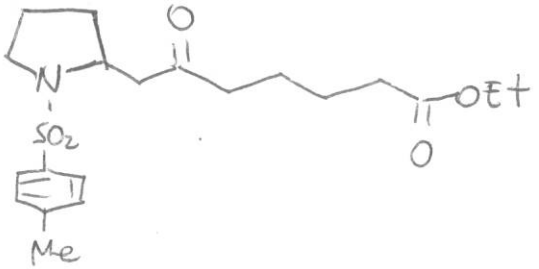
400

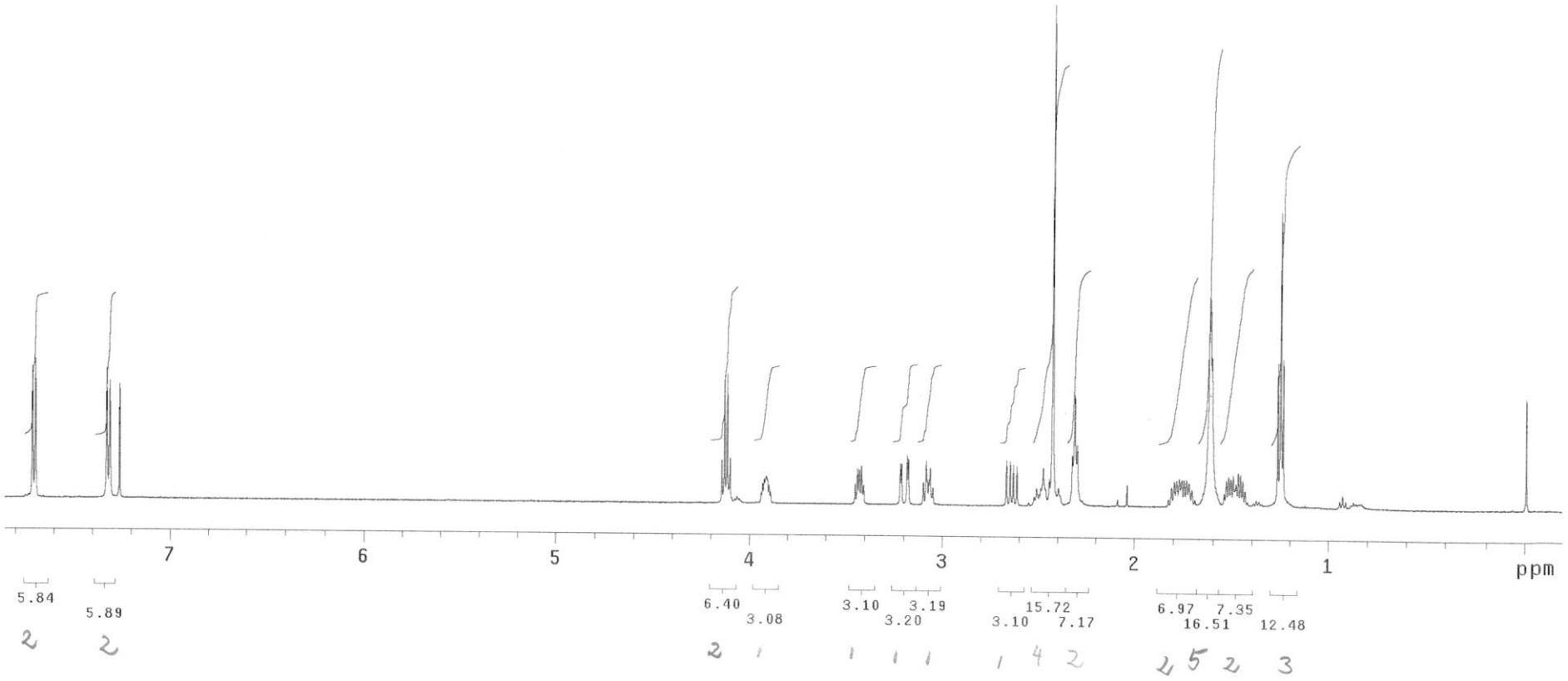
II-6

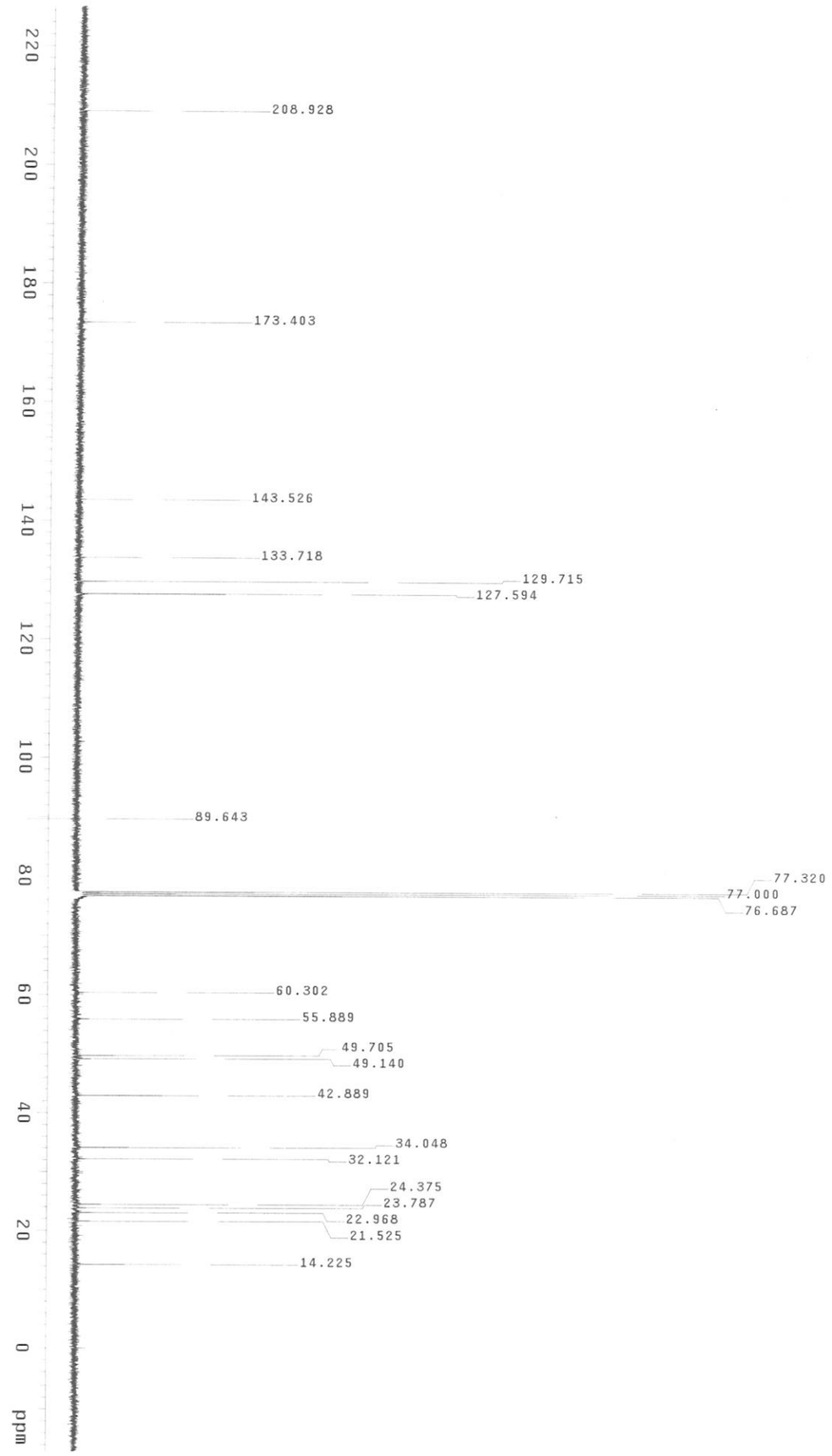

O
N
SO2
Me

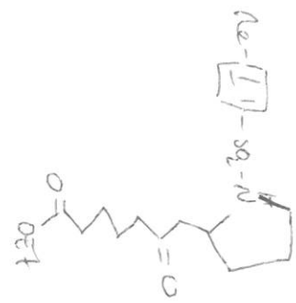
7
6
5
4
3
2
1
ppm
7.44
11.02
15.74
3.95
4.02
4.15
8.31
11.59
4.10
8.01
4.17
9.33
8.16


208.437
143.511
140.795
133.740
129.692
128.472
128.308
127.564
126.098
77.320
77.000
76.687
55.844
49.906
49.095
44.742
32.010
29.621
23.727
21.502
220
200
180
160
140
120
100
80
60
40
20
0
ppm

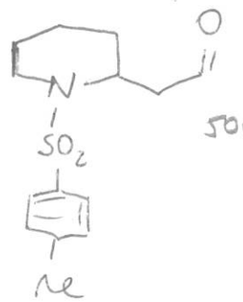

O
N
SO2
OEt
O
Me


7
6
5
4
3
2
1
ppm
5.84
5.89
6.40
3.08
3.10
3.19
3.20
3.10
15.72
7.17
6.97
7.35
16.51
12.48
2
2
2
1
1
1
1
4
2
2
5
2
3

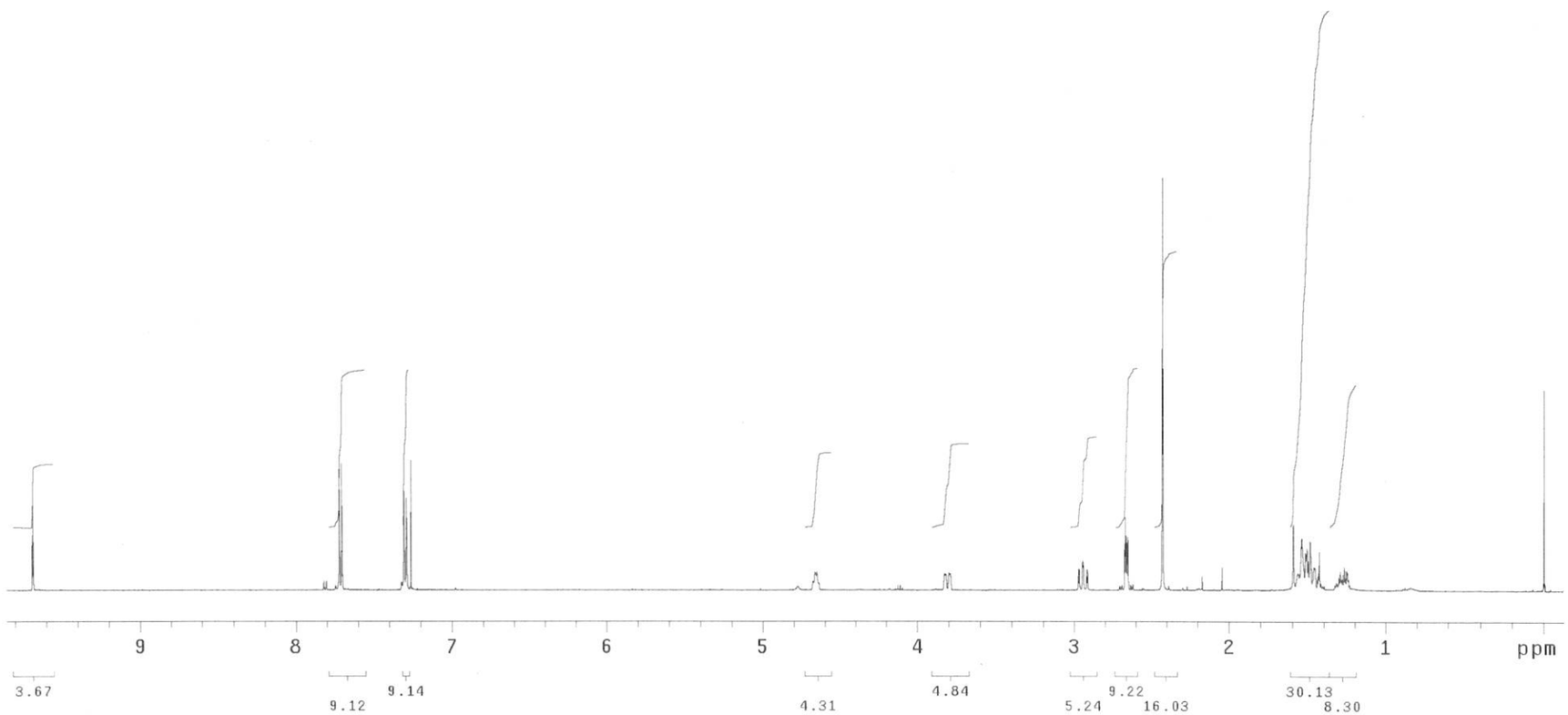

208.928
173.403
143.526
133.718
129.715
127.594
89.643
77.320
77.000
76.687
60.302
55.889
49.705
49.140
42.889
34.048
32.121
24.375
23.787
22.968
21.525
14.225
220
200
180
160
140
120
100
80
60
40
20
0
ppm

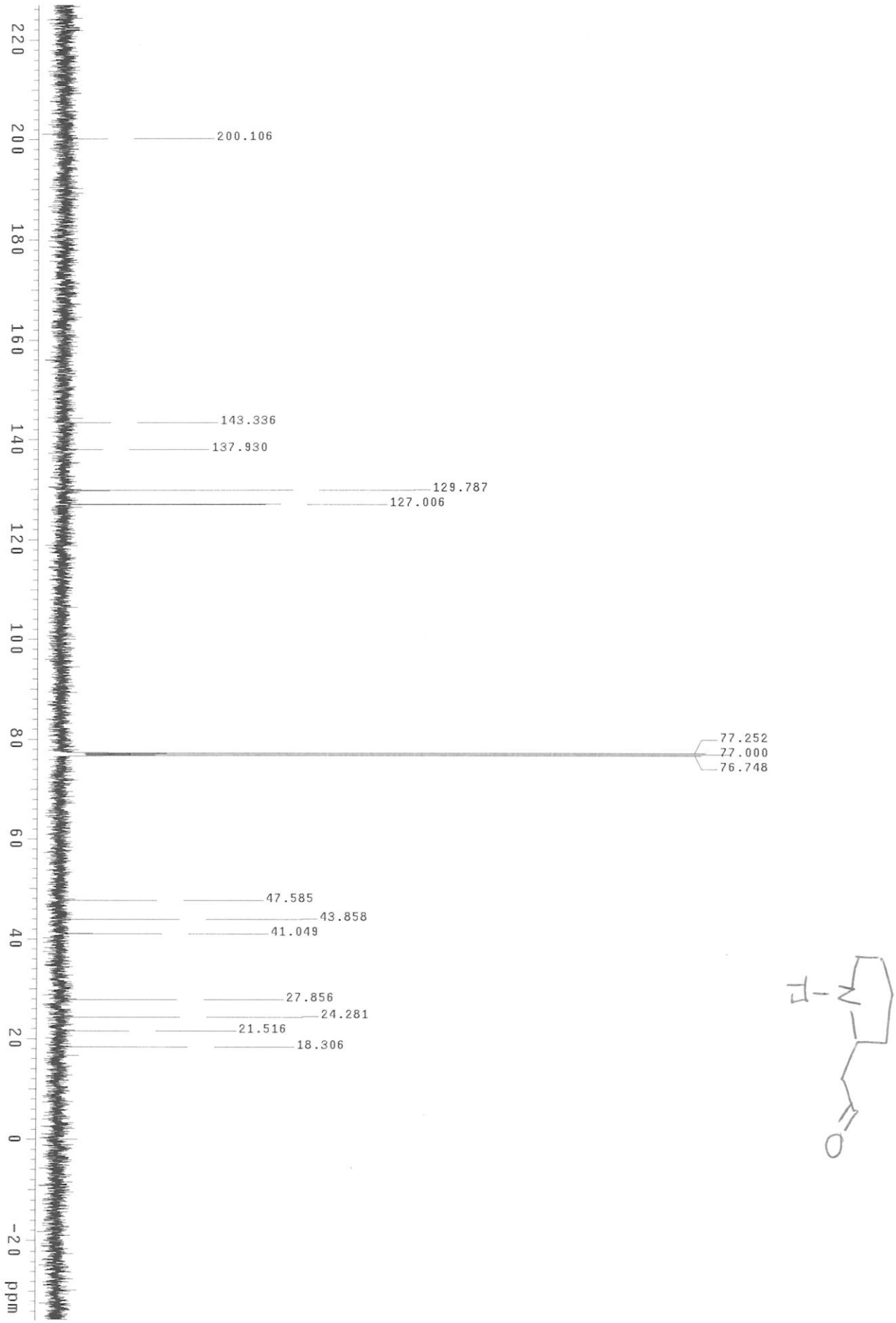

Re-[1]-sq-N
O
EtO
O

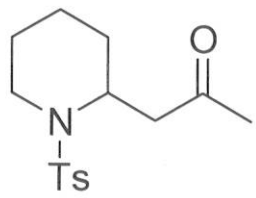
NHTs6



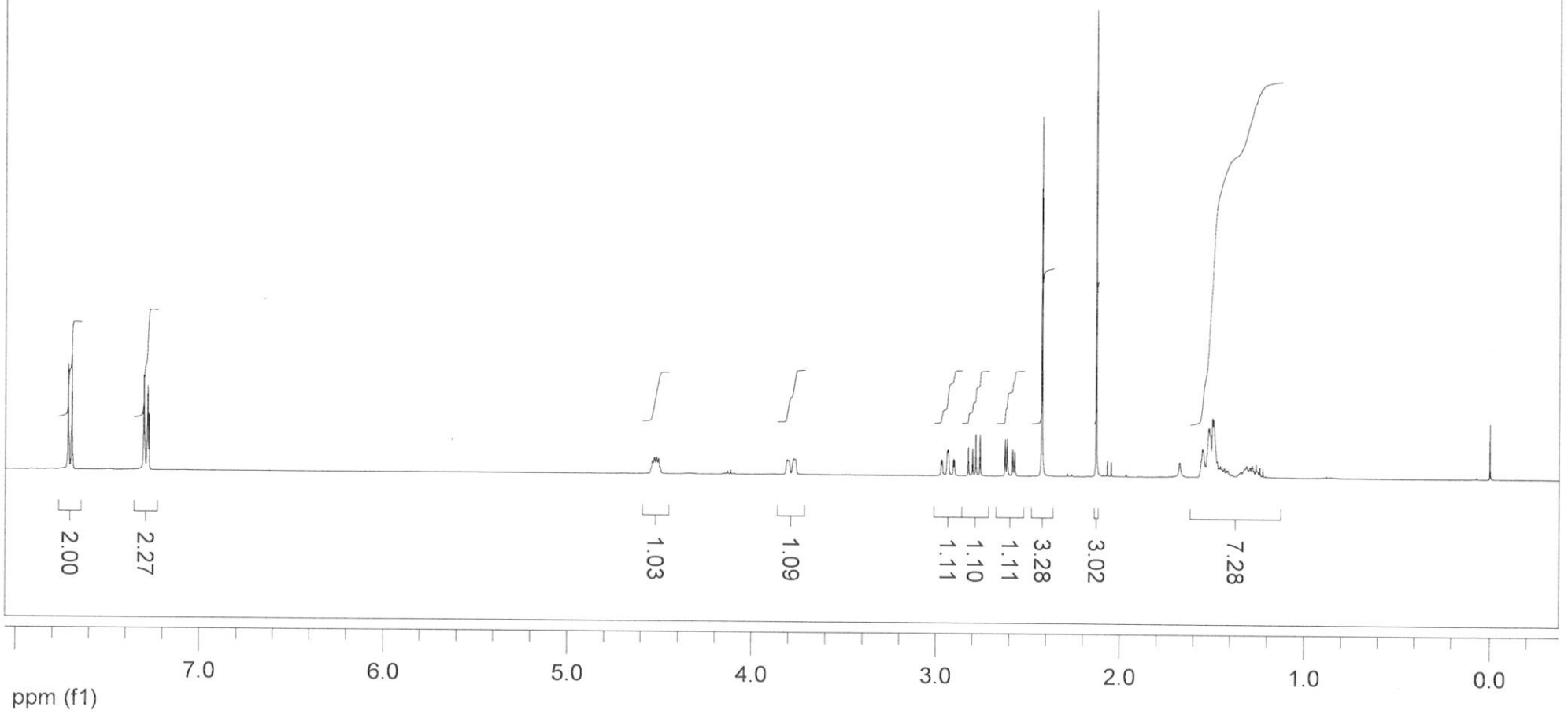
500MHz

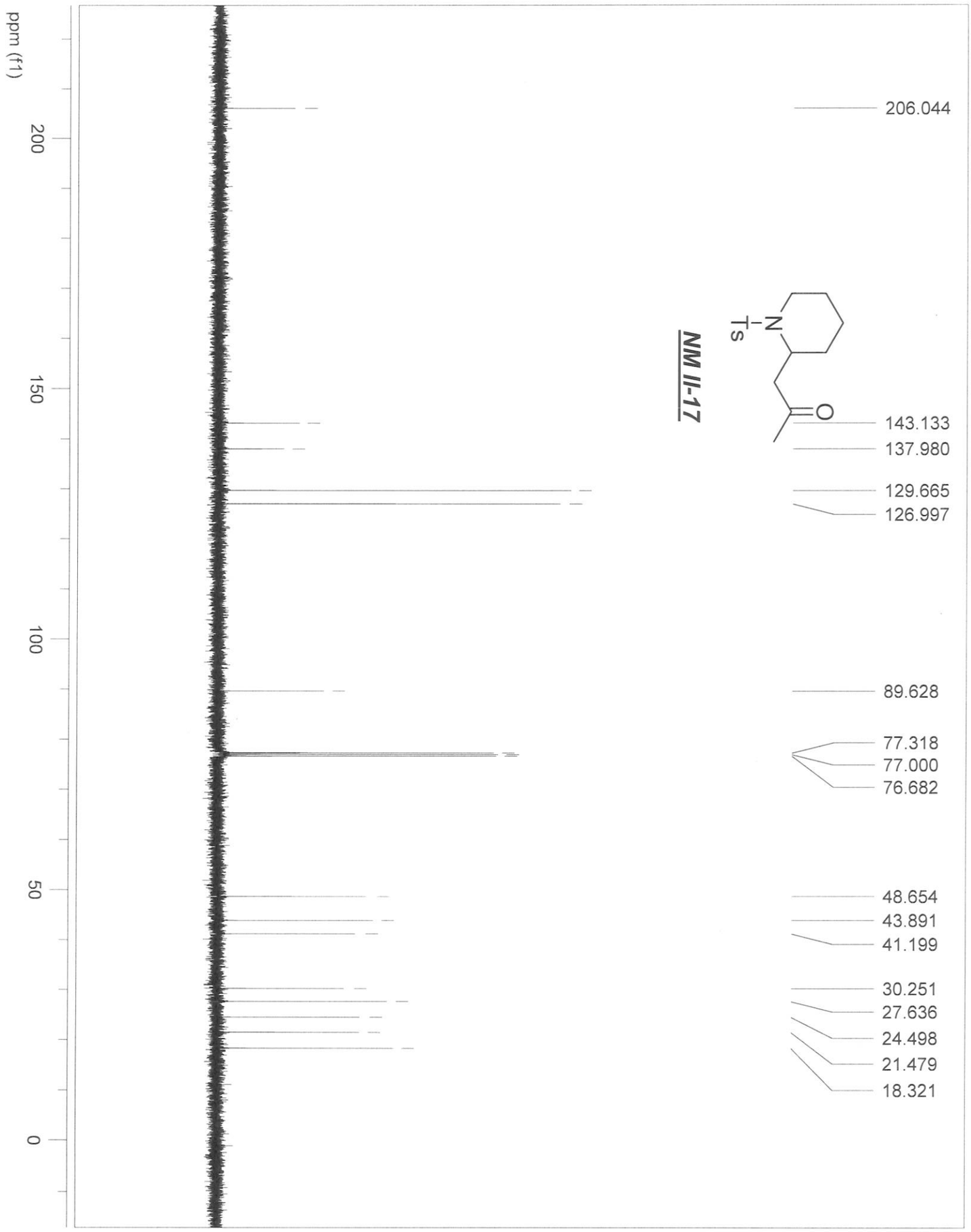



220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
200.106
143.336
137.930
129.787
127.006
77.252
77.000
76.748
47.585
43.858
41.049
27.856
24.281
21.516
18.306
H
N
O

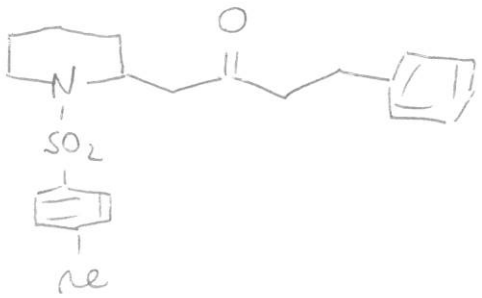

O
N
Ts

NM II-17

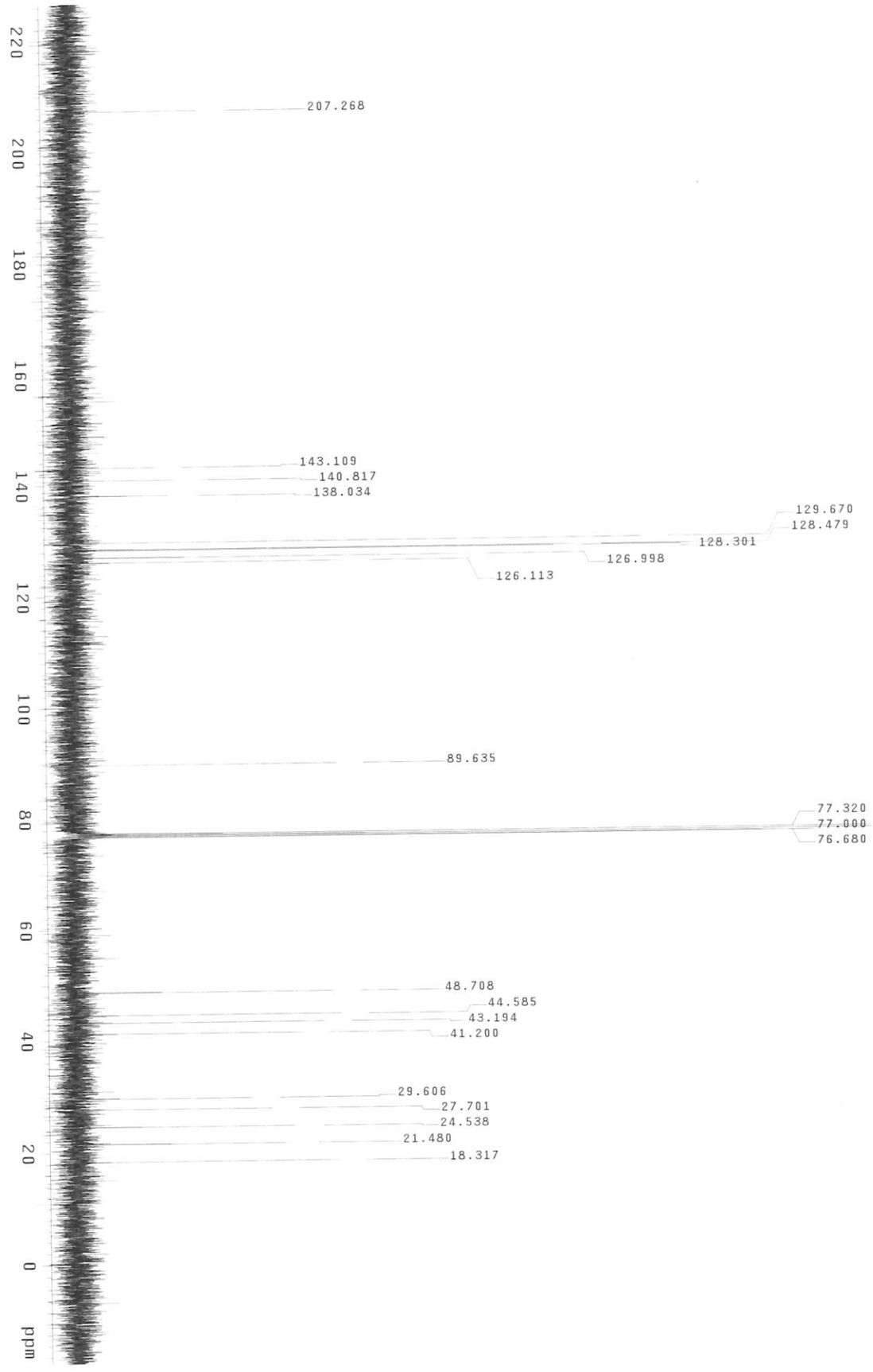

2.00
2.27
1.03
1.09
1.11
1.10
1.11
3.28
3.02
7.28
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

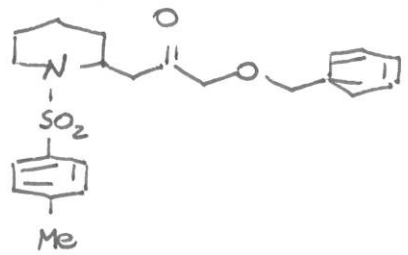

ppm (f1)
200
150
100
50
0
206.044
143.133
137.980
129.665
126.997
89.628
77.318
77.000
76.682
48.654
43.891
41.199
30.251
27.636
24.498
21.479
18.321
NM II-17
N
Ts
O

NMR-22A
(40mg)


O
N
SO2
Me

7
6
5
4
3
2
1
ppm
6.82
10.67
15.27
3.55
3.72
11.20
10.84
11.09
3.96
22.88
2
4
3
1
1
3
3
1
3
9H


220
200
180
160
140
120
100
80
60
40
20
0
ppm
207.268
143.109
140.817
138.034
129.670
128.479
128.301
126.998
126.113
89.635
77.320
77.000
76.680
48.708
44.585
43.194
41.200
29.606
27.701
24.538
21.480
18.317


O
N
SO2
Me

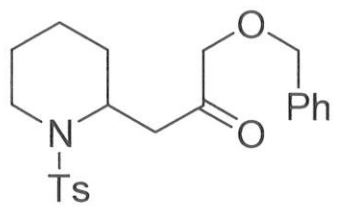
8
7
6
5
4
3
2
1
ppm
6.55
7.85
14.92
11.23
7.62
4.02
3.85
3.84
3.85
10.89
19.55
5.83

206.404

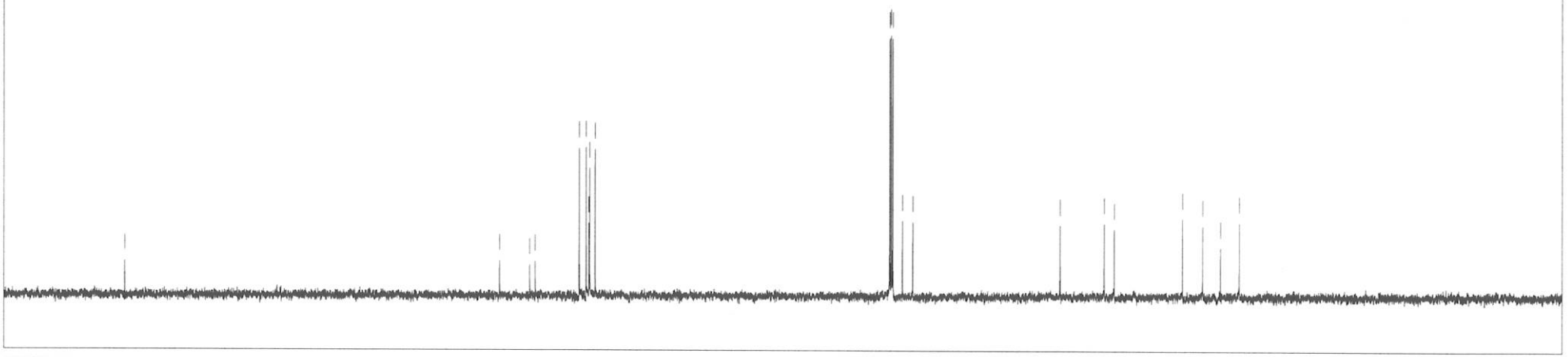
143.094
137.983
137.052
129.656
128.503
128.021
127.914
126.996

77.254
77.000
76.746
75.127
73.396

48.586
41.137
39.420
27.888
24.480
21.479
18.333



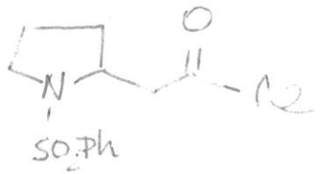
NM II-26

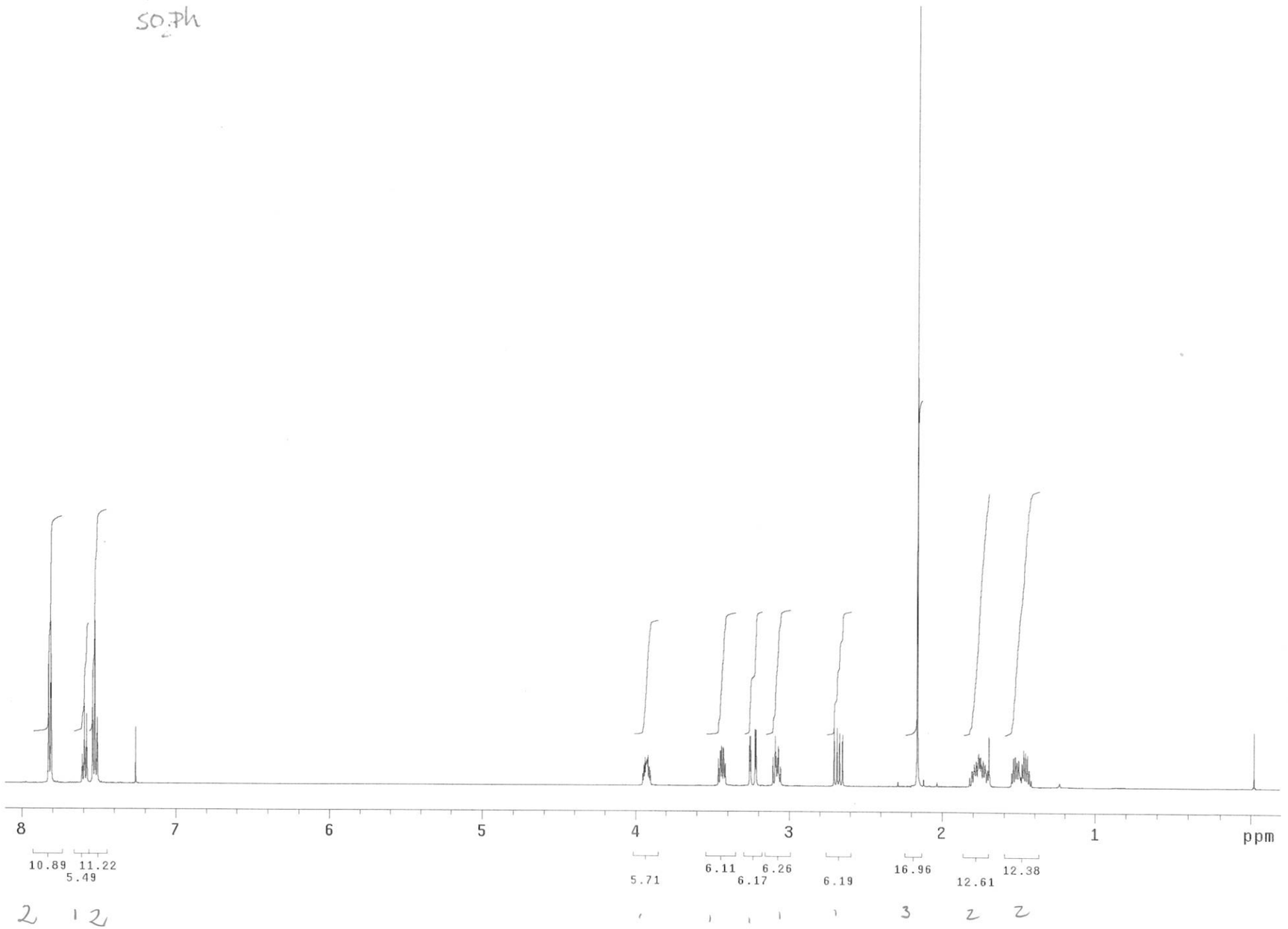


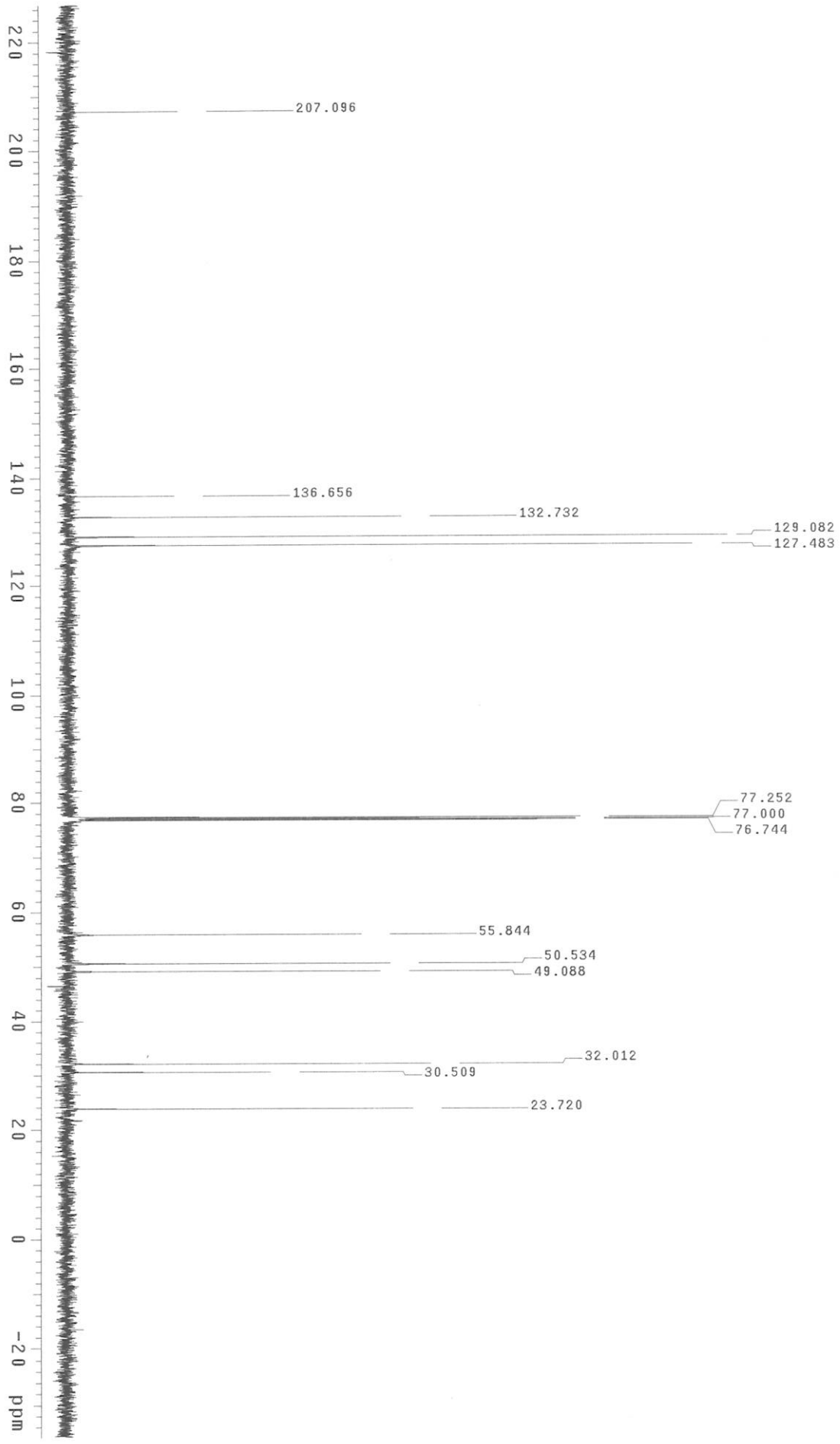
200
150
100
50
0

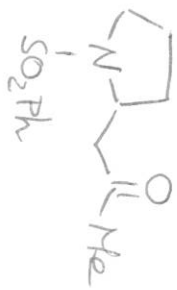
ppm (f1)

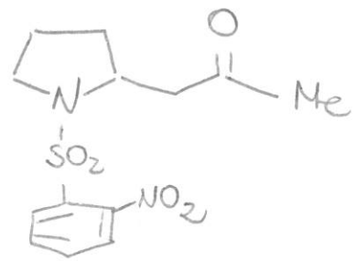
MN 11-23

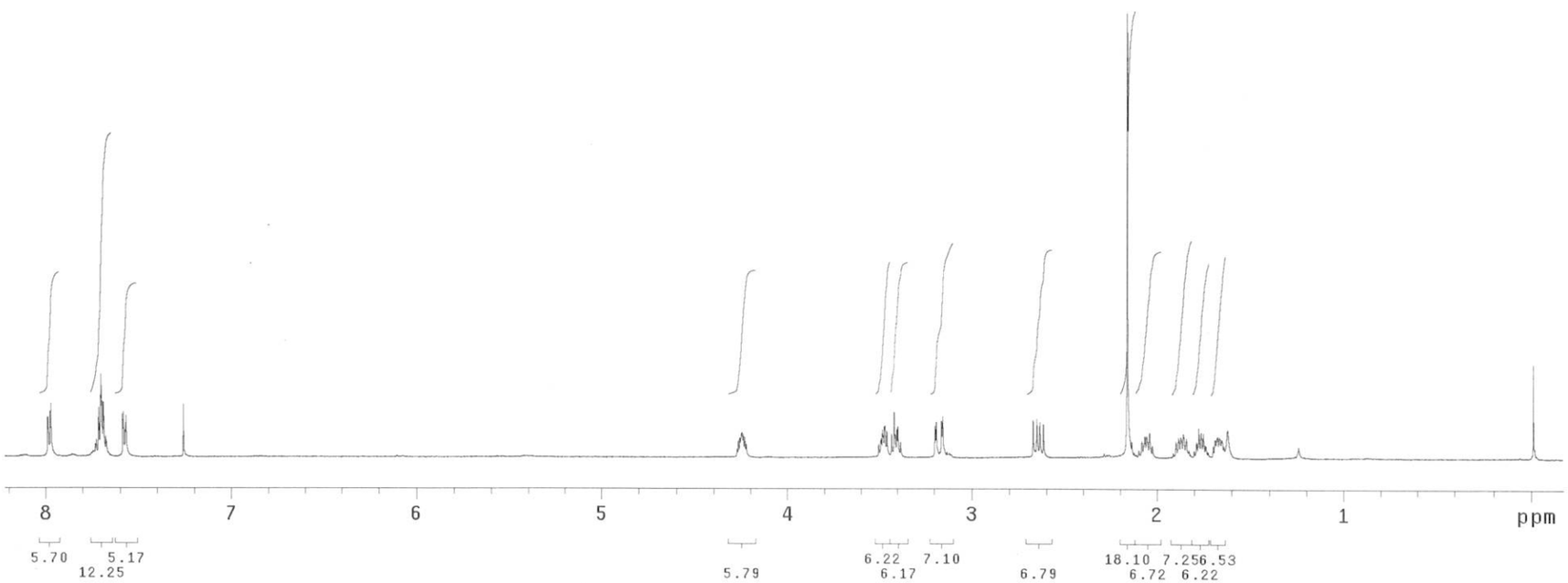

O
N
SO2Ph

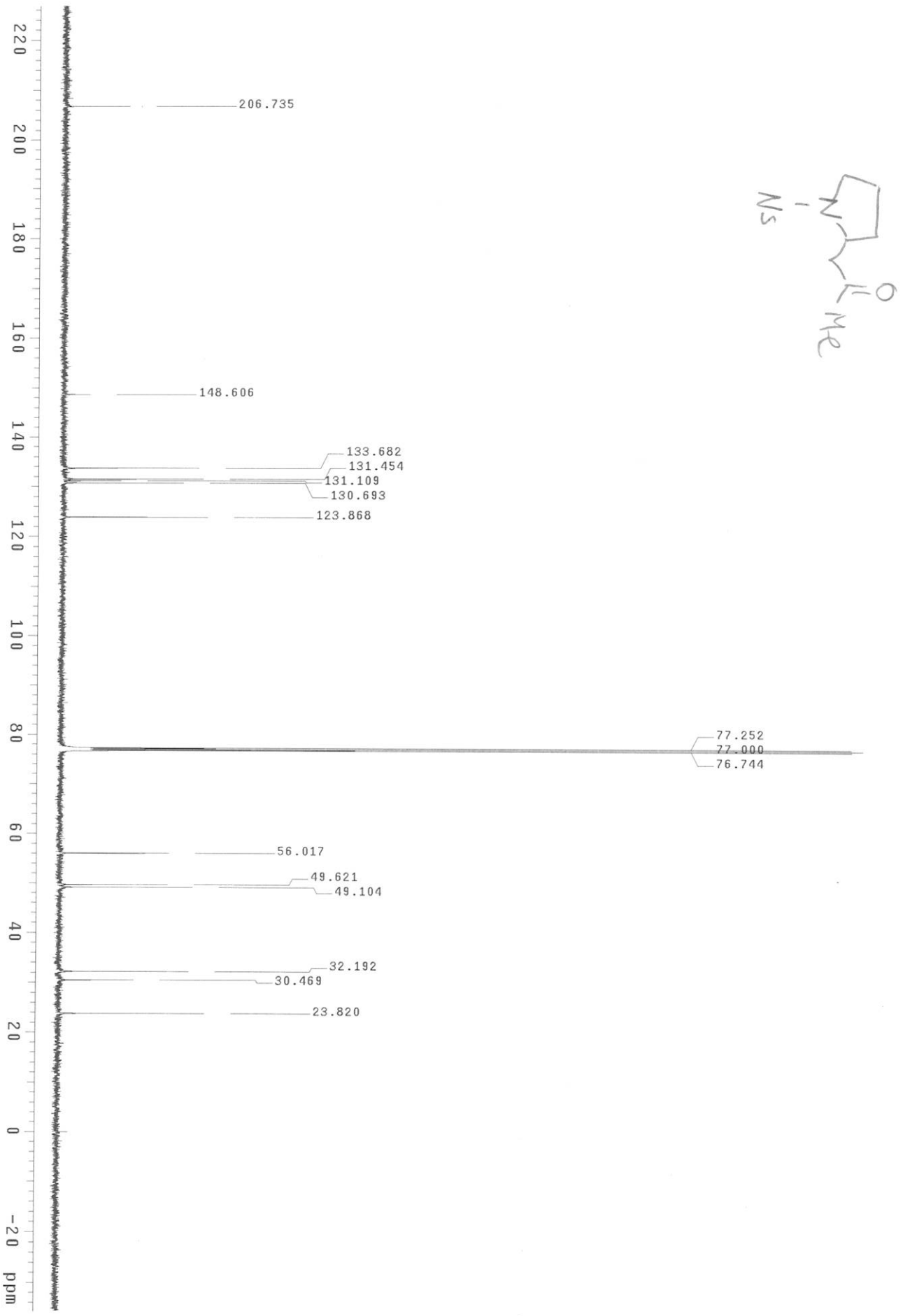

8
7
6
5
4
3
2
1
ppm
10.89
11.22
5.49
5.71
6.11
6.17
6.26
6.19
16.96
12.61
12.38
2
1
2
3
2
2

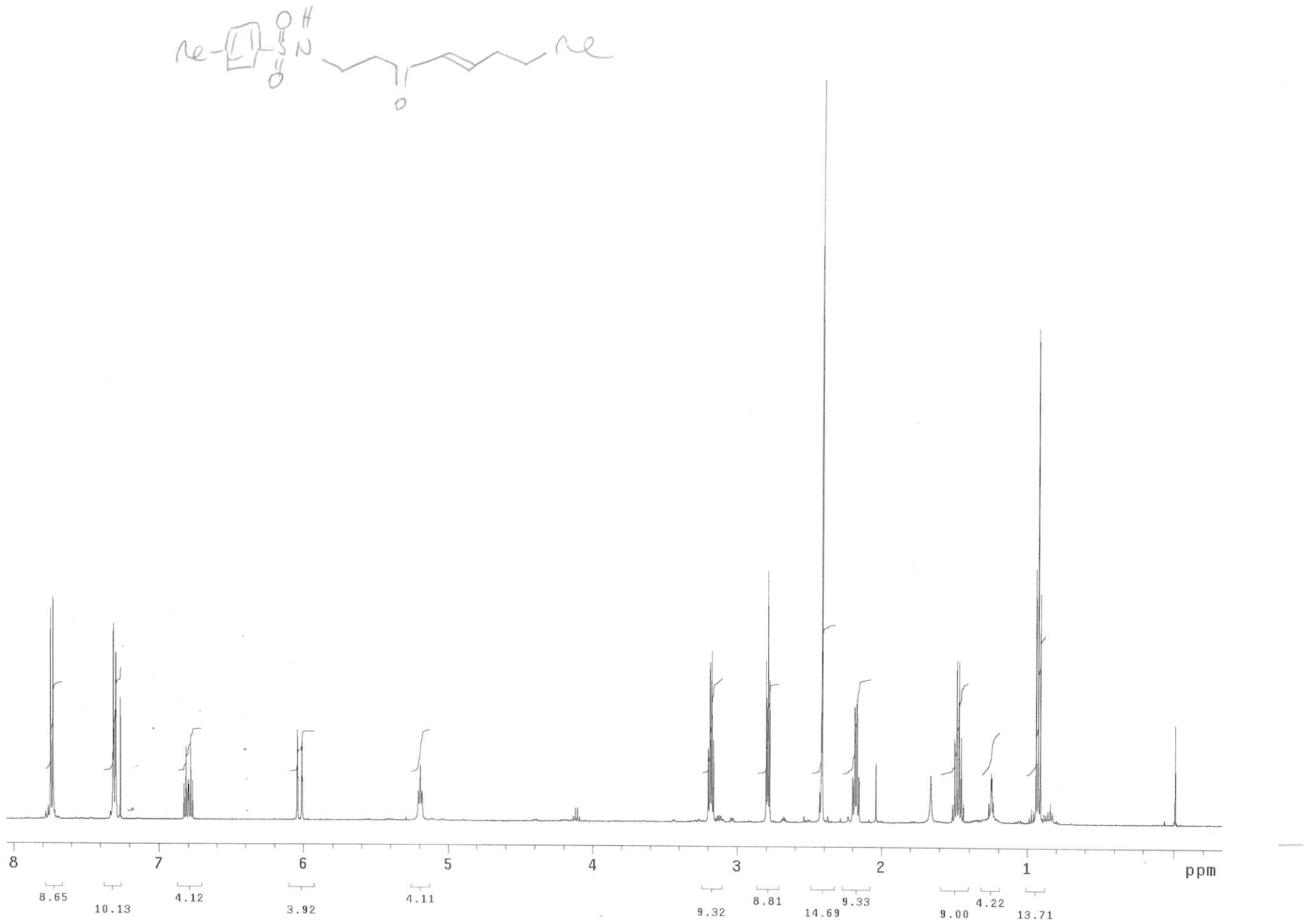

220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
207.096
136.656
132.732
129.082
127.483
77.252
77.000
76.744
55.844
50.534
49.088
32.012
30.509
23.720

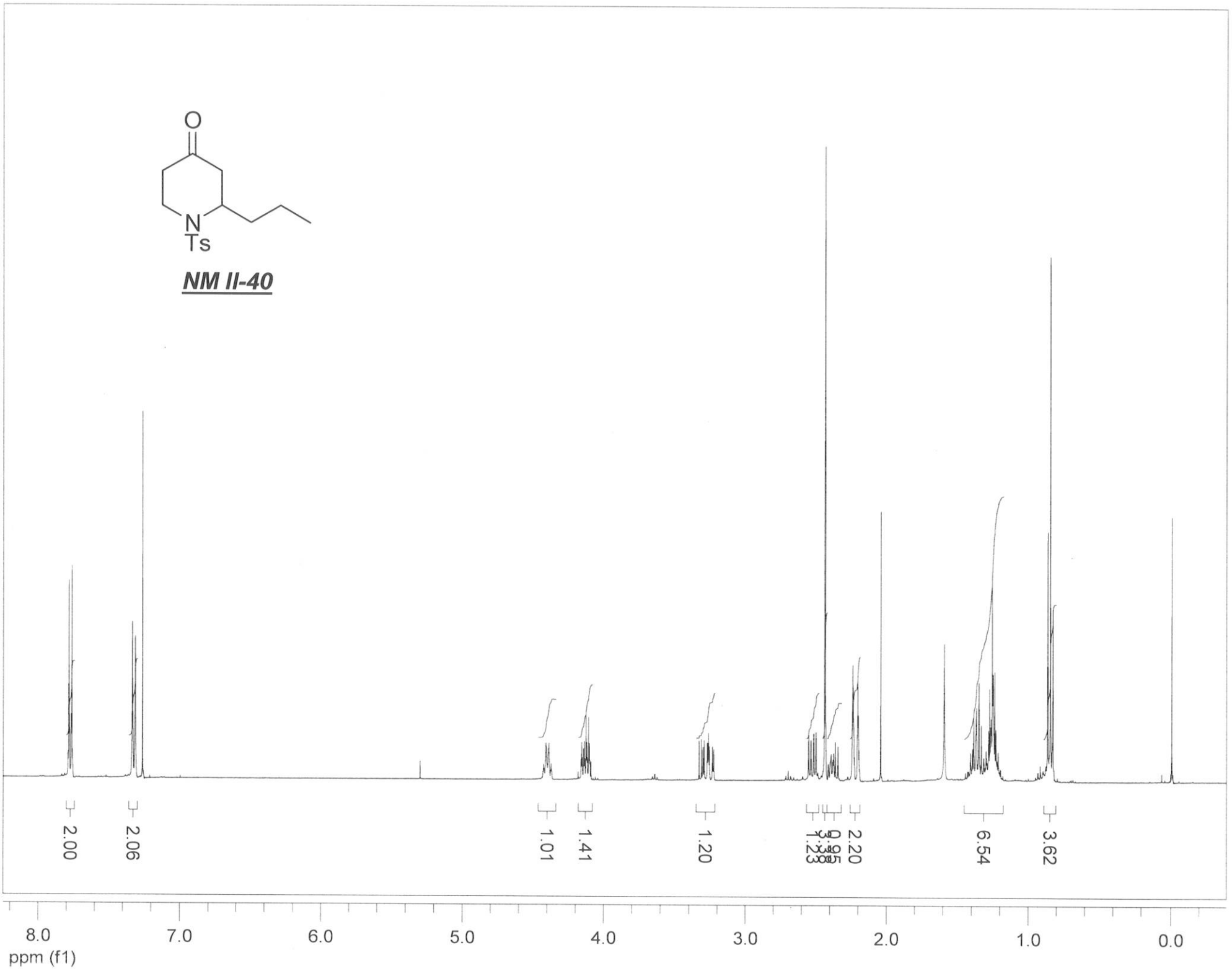

N
SO2Ph
O
Me

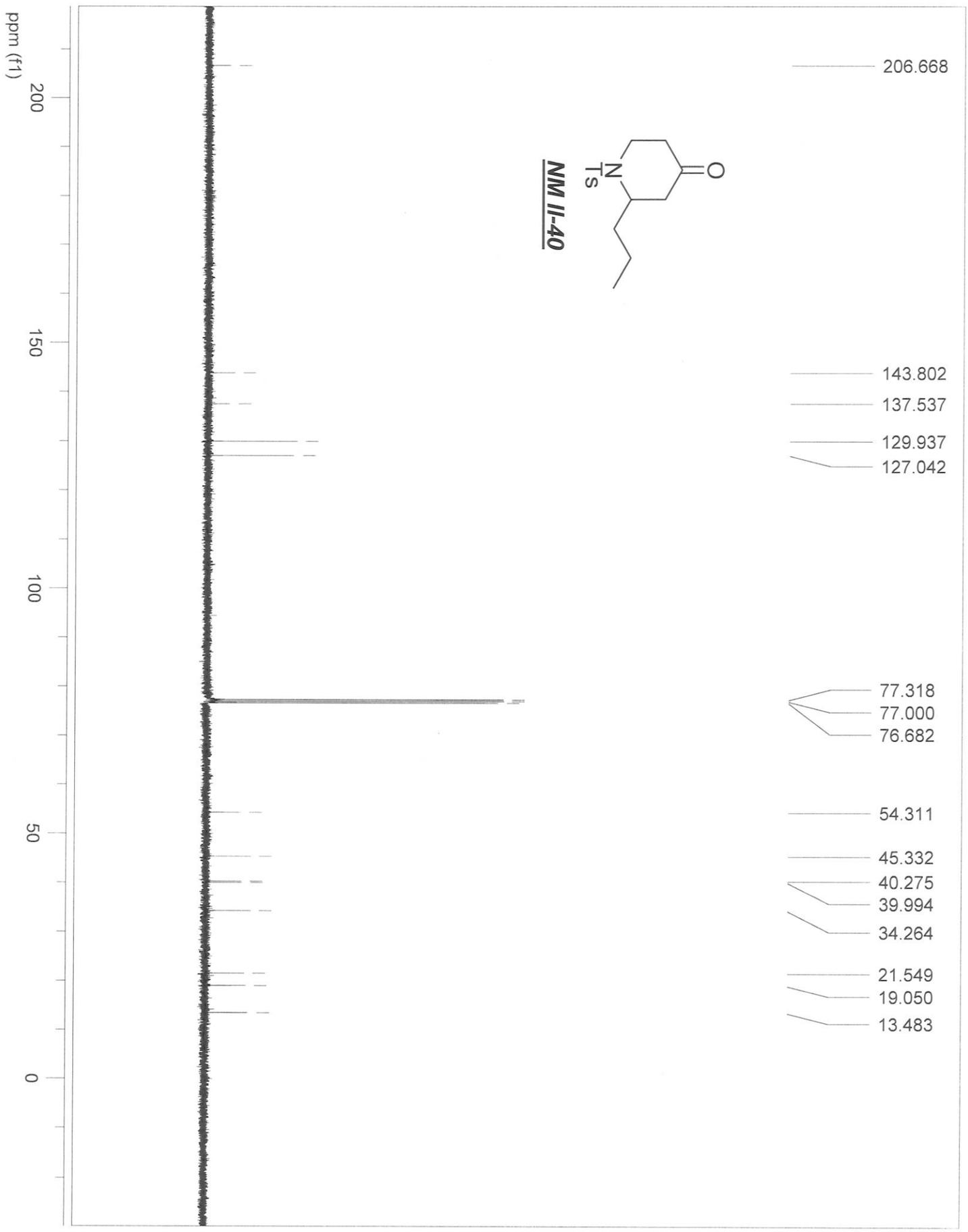

O
N
Me
SO2
NO2

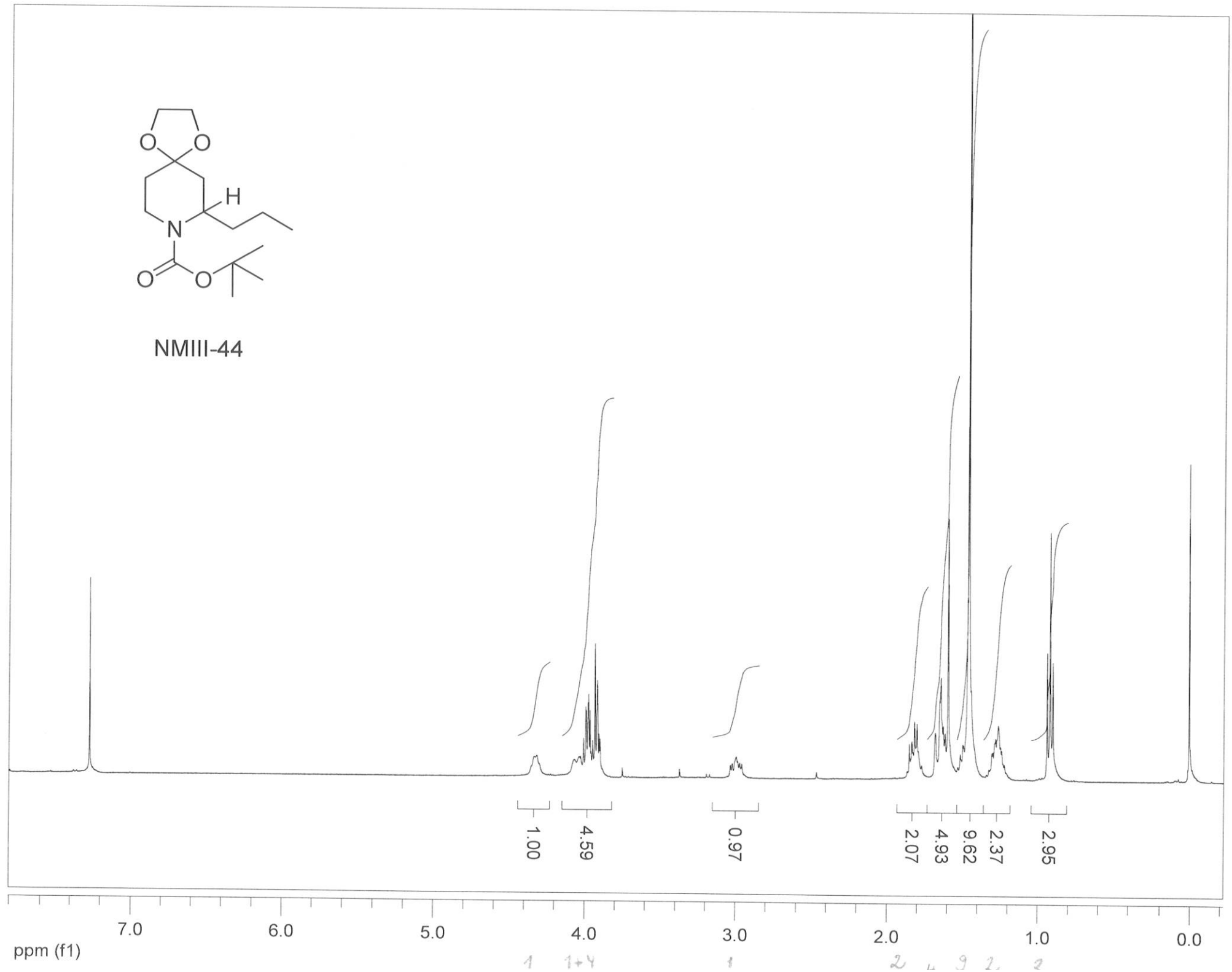

8
7
6
5
4
3
2
1
ppm
5.70
5.17
12.25
5.79
6.22
6.17
7.10
6.79
18.10
6.72
7.25
6.22
6.53

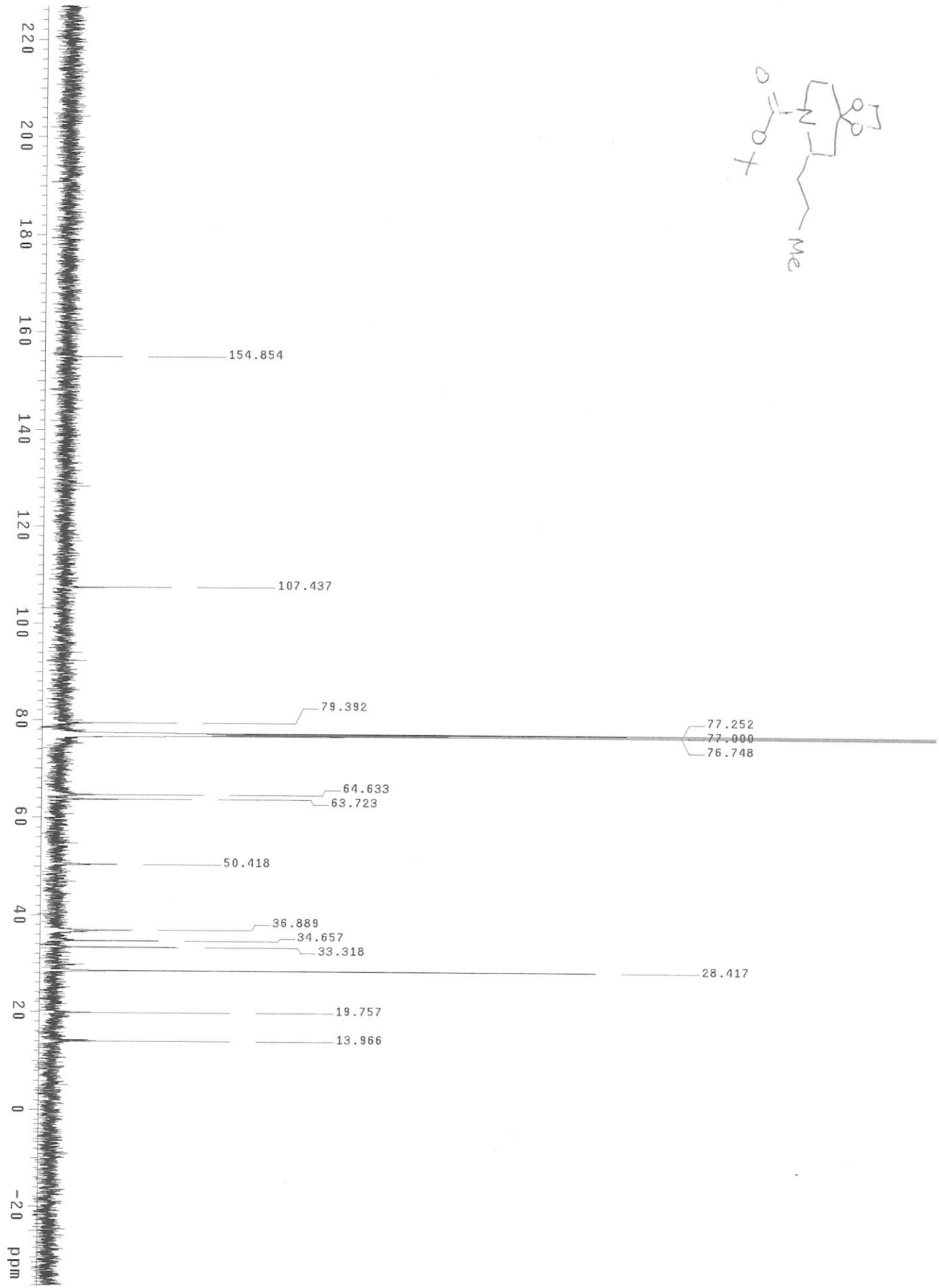

206.735
148.606
133.682
131.454
131.109
130.693
123.868
77.252
77.000
76.744
56.017
49.621
49.104
32.192
30.469
23.820
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
Ns
N
O
Me


8
7
6
5
4
3
2
1
ppm
8.65
10.13
4.12
3.92
4.11
9.32
8.81
14.69
9.33
9.00
4.22
13.71


O
N
Ts
NM II-40
2.00
2.06
1.01
1.41
1.20
2.20
6.54
3.62
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


ppm (f1)
200
150
100
50
0
206.668
143.802
137.537
129.937
127.042
77.318
77.000
76.682
54.311
45.332
40.275
39.994
34.264
21.549
19.050
13.483
NM II-40
N
Ts
O


O
O
H
N
O
O
NMIII-44
1.00
4.59
0.97
2.07
4.93
9.62
2.37
2.95
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
154.854
107.437
79.392
77.252
77.000
76.748
64.633
63.723
50.418
36.889
34.657
33.318
28.417
19.757
13.966
Me

N-t-BOC-2-(2-Oxoethyl)-5-phenyltetrahydropyrrolidine (3.44)