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

Supporting Information

A Scalable Continuous Photochemical Process for the Generation of Aminopropylsulfones

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1. Materials and Methods

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Fluorochem or Sigma Aldrich and used as received.

^{1}H-NMR spectra were recorded on 400 MHz and 500 MHz instruments and are reported relative to residual solvent: $CDCl_3$ (δ 7.26 ppm) or d_6-DMSO (δ 2.50 ppm). ^{13}C-NMR spectra were recorded on the same instruments (100 and 125 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm) or d_6-DMSO (δ 39.52 ppm). ^{19}F-NMR were recorded at 376 MHz. Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for 13C{1H} NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). DEPT-135, COSY, HSQC, HMBC and NOESY experiments were used in the structural assignment.

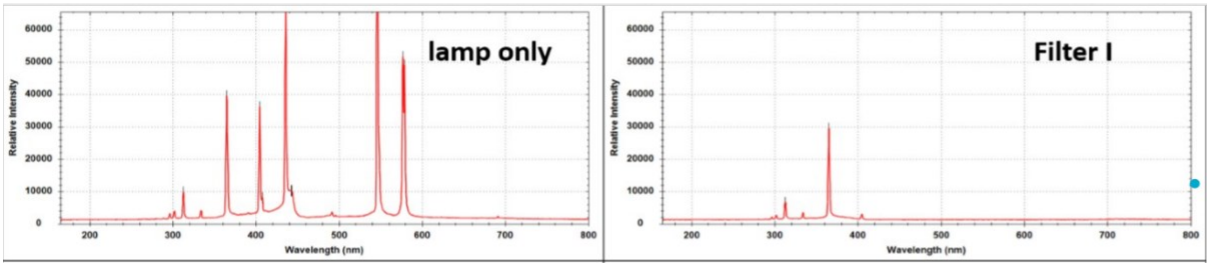
IR spectra were obtained by use of a Bruker Platinum spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal).

HPLC was performed on an Agilent 1260 Infinity II system, using a Zorbax SB-C18 column (50 °C, 50 mm length) and a gradient ranging from 95/5 to 0/100 (0.05% TFA in water – MeCN, flow rate 1.2 mL/min) over 8 minutes. The wavelength was set to either 200 nm or 250 nm.

High-resolution mass spectrometry was performed using the indicated techniques on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine-enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass.

For UV-Vis measurements a Shimadzu UV-1800 UV spectrophotometer was used. Melting points were recorded on a Stuart SMP10 melting point apparatus and are uncorrected.

Continuous flow experiments were performed on a Vapourtec E-series system with the UV150 photoreactor that is equipped with a medium-pressure Hg lamp (150 W) and use in combination with a low pass filter (see emission spectra below) or a high-power LED array (50-100 W tuneable, λ_{max} 365 nm).



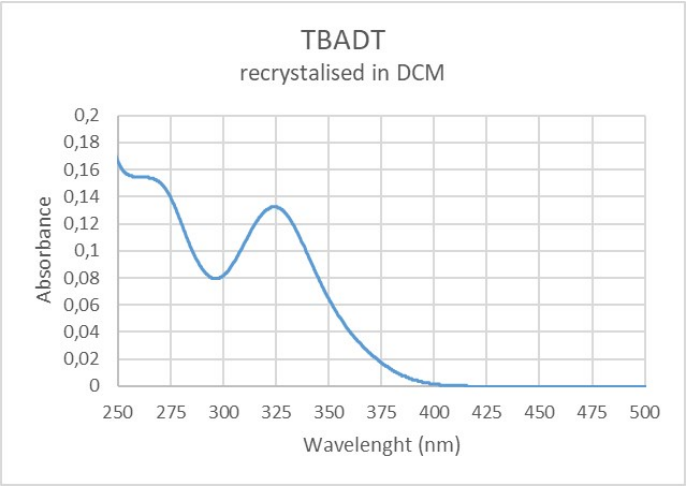
2. General procedures

2.1 Synthesis of TBADT (Tetrabutylammonium-decatungstate)[1]

Tetrabutylammonium bromide (2.4 g, 7.4 mmol) and sodium tungstate dihydrate (5.0 g, 15.0 mmol) were dissolved each in 150 mL of deionised water in two Erlenmeyer flasks and kept at 90 °C under vigorous stirring. HCl (aq., 12 M) was added dropwise to both solutions to adjust the pH to 2. The two solutions were then combined and maintained at 90 °C for 30 min under stirring. A white suspension of TBADT formed and, after cooling to room temperature, was filtered via a glass sintered funnel. The white powder was washed with water (3 × 10 mL) and then dried in a vacuum oven (40 °C, 100 mbar) overnight. The resulting white solid was suspended in dichloromethane (20 mL per gram of solid) and kept under stirring for two hours. The pure TBADT was separated from the yellow solution by filtration on a glass sintered funnel and dried in a vacuum oven (40 °C, 100 mbar) overnight.

Yield (based on the content of tungsten): 68% (3.40 g, 1.0 mmol).

[1] S. Protti, D. Ravelli, M. Fagnoni, A. Albini, *Chem. Commun.* **2009**, *47*, 7351-7353.

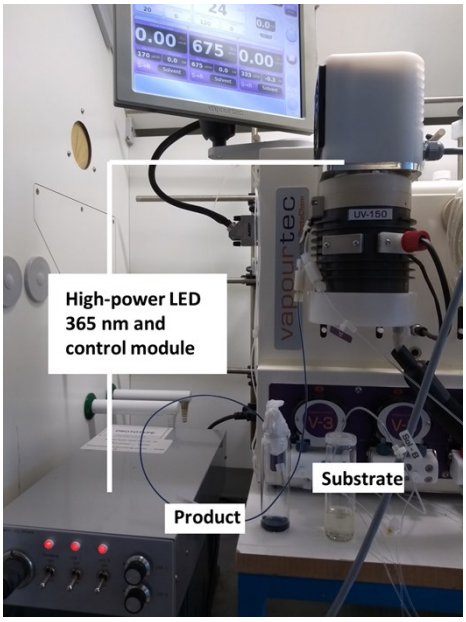


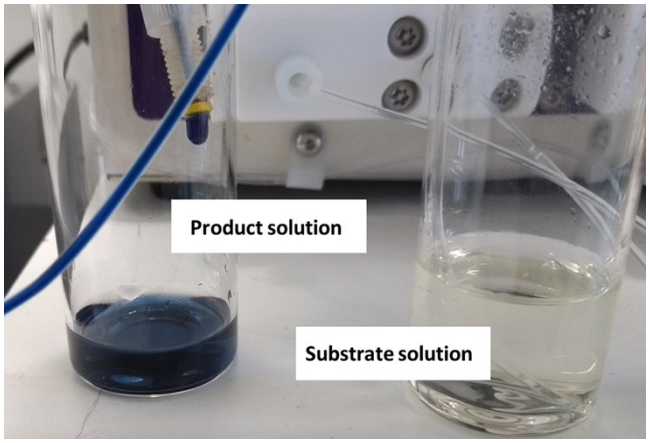
2.2 Synthesis of *N,N*-Dimethylamides

Dimethylamine hydrochloride (0.9 g, 11.0 mmol), acyl chloride (10.0 mmol) and triethylamine (2.32 g, 23.0 mmol) were dissolved in dichloromethane (20 mL) under a nitrogen atmosphere. The mixture was stirred at room temperature for 1 h, before diluting with dichloromethane (30 mL). The solution was transferred to a separating funnel and was washed with HCl (1 M, aq., 2 × 50 mL), $NaHCO_3$ sat. (25 mL) and brine (30 mL). The organic phase was dried over anhydrous sodium sulfate and filtered. The solvent was removed under vacuum to obtain the desired *N,N*-dimethylamide products.

2.3 General Procedure for Continuous Photoreaction

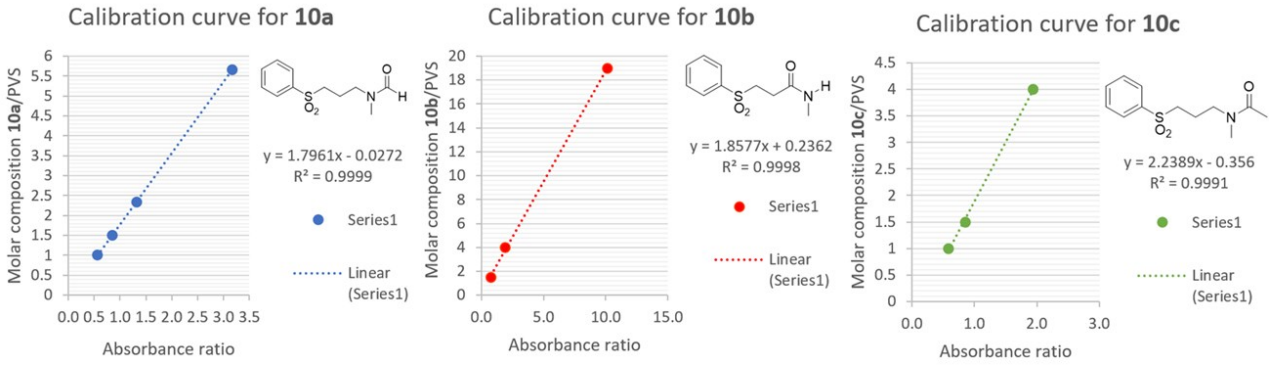
Phenyl (or ethyl) vinyl sulfone (1.0 equiv.), amide (4.0 equiv.) and tetrabutylammonium decatungstate (0.02 equiv.) were added into a vial. Acetonitrile was added to reach the concentration reported for each reaction. The solution was pumped through a 10 mL flow reactor (Vapourtec E-series) and was irradiated with a mercury medium pressure UV lamp (lamp power: 110 W, low pass filter <400 nm) or a LED lamp 365 nm (75 W). Finally, the solution was collected, and the solvent was evaporated. The residue was purified via silica gel column chromatography (eluent EtOAc/hexanes) to render the corresponding amide.





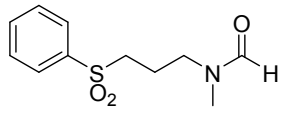
3. HPLC Yields and Calibrations for Compounds 10a, 10b and 10c

To create quantifiable HPLC data mixtures of products **10a**, **10b** and **10c** were prepared with phenyl vinyl sulfone (PVS) at known molar ratios (e.g. **10a**/PVS). These were correlated to the resulting ratios of the respective 'areas under the curve' for each HPLC chromatogram. Calibration curves were constructed as shown below for each case allowing to assess product yields by HPLC (at 250 nm).



4. Spectroscopic Data for Compounds 10a-m and 11

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)formamide **10a**



Chemical Formula: $C_{11}H_{15}NO_3S$
Molecular Weight: 241,3050

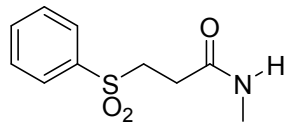
Rotameric ratio ~55:45

Red oil. Yield: 77% (1.66 g, 6.88 mmol). HPLC t_r = 3.1 min.

Both rotamers ^{1}H-NMR (300 MHz, DMSO-d_6) δ/ppm 7.86-7.95 (m, 2x3H), 7.73-7.79 (m, 2x1H), 7.64-7.70 (2x2H), 3.23-3.32 (m, 2x4H), 2.81 (s, 3H), 2.64 (s, 3H), 1.68-1.82 (m, 2x2H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ/ppm 163.2 (C), 163.0 (C), 139.3 (2xC), 134.4 (CH), 134.3 (CH), 130.0 (2CH), 129.9 (2CH), 128.1 (2x2CH), 52.8 (CH_2), 52.3 (CH_2), 47.1 (CH_2), 42.2 (CH_2), 34.3 (CH_3), 29.1 (CH_3), 21.6 (CH_2), 20.3 (CH_2).

IR (neat) v/cm^{-1}: 2928 (w), 1661 (s), 1446 (m), 1397 (m), 1302 (s), 1137 (s), 1084 (s), 731 (s), 689 (s), 594 (m), 532 (s). HR-MS (TOF ES): calculated for $C_{11}H_{16}NO_3S$ 242.0845, found 242.0846 ($M+H^+$).

N-Methyl-3-(phenylsulfonyl)propenamide **10b**



Chemical Formula: $C_{10}H_{13}NO_3S$
Molecular Weight: 227,2780

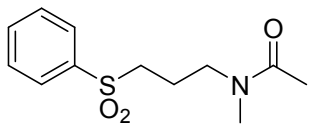
Rotameric ratio ~70:30

Light yellow oil. Yield: 78% (53 mg, 0.23 mmol). HPLC t_r = 2.1 min

Major rotamer ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 7.90 (s, 1H), 7.89-7.88 (m, 2H), 7.75 (m, 1H), 7.66 (m, 2H), 3.50 (app t, *J* = 7.6 Hz, 2H), 2.47 (d, *J* = 4.6 Hz, 3H), 2.38 (app t, *J* = 7.7 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d_6) **major rotamer** δ/ppm 169.1 (C), 139.1 (C), 134.4 (CH), 129.9 (2CH), 128.2 (2CH), 51.4 (CH_2), 28.8 (CH_2), 26.0 (CH_3).

IR (neat) v/cm^{-1}: 3305 (w), 1651 (s), 1548 (m), 1447 (m), 1412 (m), 1385 (m), 1305 (s), 1146 (s), 1085 (s), 732 (s), 688 (s), 547 (s). HR-MS (TOF ES): calculated for $C_{10}H_{14}NO_3S$ 228.0689, found 228.0692 ($M+H^+$).

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)acetamide **10c**



Chemical Formula: $C_{12}H_{17}NO_3S$
Molecular Weight: 255,3320

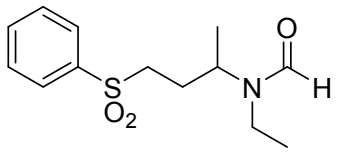
Rotameric ratio ~80:20

Yellow oil. Yield: 80% (153 mg, 0.60 mmol). HPLC t_r = 3.1 min

^{1}H-NMR (400 MHz, $CDCl_3$) **major rotamer** δ/ppm 7.93 – 7.86 (m, 2H), 7.72 – 7.56 (m, 3H), 3.48 – 3.43 (m, 2H), 3.12 – 3.06 (m, 2H), 2.99 (s, 3H), 2.06 (s, 3H), 2.04 – 1.95 (m, 2H); **minor rotamer** δ/ppm 7.93 – 7.86 (m, 2H), 7.72 – 7.56 (m, 3H), 3.48 – 3.43 (m, 2H), 3.12 – 3.06 (m, 2H), 2.87 (s, 3H), 2.08 (s, 3H), 2.04 – 1.95 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) **major rotamer** δ/ppm 170.4 (C), 139.3 (C), 134.3 (CH), 129.9 (2CH), 128.1 (2CH), 52.9 (CH_2), 45.5 (CH_2), 36.1 (CH_3), 22.1 (CH_3), 20.9 (CH_2); **minor rotamer** δ/ppm 169.7 (C), 139.3 (C), 134.3 (CH), 130.0 (2CH), 128.1 (2CH), 52.3 (CH_2), 48.4 (CH_2), 32.7 (CH_3), 21.8 (CH_3), 21.4 (CH_2).

IR (neat) v/cm^{-1}: 2928 (w), 1628(s), 1446 (m), 1407 (m), 1302 (s), 1144 (s), 1086 (m), 1015 (m), 734 (m), 691 (m), 593 (m), 534 (m). HR-MS (TOF ES): calculated for $C_{12}H_{18}NO_3S$ 256.1002, found 256.1004 ($M+H^+$).

N-Ethyl-*N*-(4-(phenylsulfonyl)butan-2-yl)acetamide **10d**



Chemical Formula: $C_{13}H_{19}NO_3S$
Molecular Weight: 269.3590

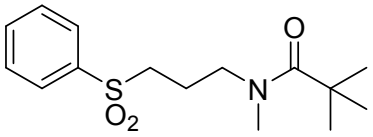
Rotameric ratio ~60:40

Light yellow oil. Yield: 49% (132 mg, 0.49 mmol). HPLC t_r = 3.9 min

Both rotamers ^{1}H-NMR (300 MHz, $CDCl_3$) δ/ppm 8.06 (s, 1H), 7.98 (s, 1H), 7.86-7.83 (m, 2x2H), 7.66-7.61 (m, 2x1H), 7.57-7.51 (m, 2x2H), 4.28-4.20 (m, 1H), 3.70-3.62 (m 1H), 3.26-3.03 (m, 3x2H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.10-1.85 (m, 2x2H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.3 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 163.3 (C), 162.5 (C), 139.0 (2xC), 134.0 (CH), 133.8 (CH), 129.5 (2CH), 129.3 (2CH), 127.9 (2x2CH), 53.6 (CH_2), 53.0 (CH_2), 52.9 (CH), 47.4 (CH), 39.3 (CH_2), 34.9 (CH_2), 27.5 (CH_2), 27.0 (CH_2), 20.5 (CH_3), 18.7 (CH_3), 17.0 (CH_3). 14.1 (CH_3).

IR (neat) v/cm^{-1}: 3975 (w), 1656 (s), 1446 (m), 1423 (m), 1302 (s), 1208 (m), 1142 (s), 1085 (s), 799 (m), 741 (m), 689 (s), 594 (m), 522 (s). HR-MS (TOF ES): calculated for $C_{13}H_{20}NO_3S$ 270.1158, found 270.1160 ($M+H^+$).

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)pivalamide **10e**



Chemical Formula: $C_{15}H_{23}NO_3S$
Molecular Weight: 297.4130

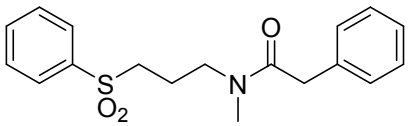
1 predominant rotamer

Yellow oil. Yield: 71% (212 mg, 0.71 mmol). HPLC t_r = 4.7 min

^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 7.88-7.85 (m, 2H), 7.75-7.71 (m, 1H), 7.66-7.62 (m, 2H), 3.28-3.22 (m, 4H), 2.88 (s, 3H), 1.74-1.67 (m, 2H), 1.10 (s, 9H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 176.6 (C), 139.3 (C), 134.3 (CH), 130.0 (2CH), 128.1 (2CH), 52.7 (CH_2), 48.1 (CH_2), 38.6 (C), 36.5 (CH_3), 28.9 ($3CH_3$), 20.9 (CH_2).

IR (neat) v/cm^{-1}: 2962 (m), 1617 (s), 1480 (m), 1447 (m), 1014 (m), 1304 (s), 1145 (s), 1086 (s), 998 (w), 958 (w), 802 (m), 746 (m), 690 (m), 595 (m), 533 (m). HR-MS (TOF ES): calculated for $C_{15}H_{24}NO_3S$ 298.1471, found 298.1474 ($M+H^+$).

N-Methyl-2-phenyl-*N*-(3-(phenylsulfonyl)propyl)acetamide **10f**



Chemical Formula: $C_{18}H_{21}NO_3S$
Molecular Weight: 331,4300

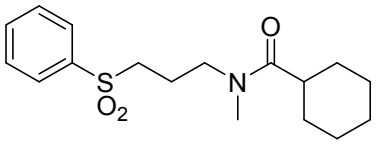
Rotameric ratio ~65:35

White powder. Yield: 76% (125 mg, 0.38 mmol). HPLC t_r = 4.8 min.

Both rotamers ^{1}H-NMR (300 MHz, DMSO-d_6) δ/ppm 7.89 – 7.85 (m, 2x2H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.67 (m , 2x2H), 7.30 – 7.13 (m, ~10H), 3.57-3.70 (m, 2x2H), 3.41 (t, *J* = 7.5 Hz, 2H), 3.31 (m, 2H), 3.26 (t, *J* = 7.7 Hz, 2H), 3.21 (m, 2H), 2.89 (s, 3H), 2.73 (s, 3H), 1.76 – 1.68 (m, 2x2H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ/ppm 171.0 (C), 170.5 (C), 139.2 (2xC), 136.1 (2xC), 134.3 (2xCH), 129.9 (2x2CH), 129.4 (2x2CH), 128.7 (2x2CH), 128.0 (2x2CH), 52.8 (CH_2), 52.2 (CH_2), 47.9 (CH_2), 45.9 (CH_2), 40.3 (CH_2), 39.6 (CH_2), 35.8 (CH_3), 33.1 (CH_3), 21.9 (CH_2), 20.8 (CH_2). Not all resonances were clearly visible.

IR (neat) v/cm^{-1}: 2931 (w), 1633 (s), 1494 (m), 1446 (m), 1400 (m), 1303 (s), 1140 (s), 1085 (s), 727 (s), 689 (s), 593 (m), 530 (s). HR-MS (TOF ES): calculated for $C_{18}H_{22}NO_3S$ 332.1315, found 332.1316 ($M+H^+$).

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)cyclohexanecarboxamide **10g**



Chemical Formula: $C_{17}H_{25}NO_3S$
Exact Mass: 323,1555

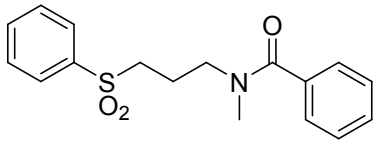
Rotameric ratio ~60:40

White powder. Yield: 48% (154 mg, 0.48 mmol). HPLC t_r = 5.1 min.

Both rotamers ^{1}H-NMR (500 MHz, DMSO-d_6) δ/ppm 7.92-7.86 (m, 4H), 7.78-7.74 (m, 2H), 7.69-7.65 (m, 4H), 3.38-3.34 (m, 4H), 3.27 (t, *J* = 7.0 Hz, 2H), 3.23-3.20 (m, 2H), 2.91 (s, 3H), 2.69 (s, 3H), 2.40-2.50 (m, 2H), 1.55-1.78 (m, ~14H), 1.44-1.49 (m, 2H), 1.05-1.30 (m, ~8H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ/ppm 175.5 (C), 175.4 (C), 139.3 (C), 139.2 (C), 134.4 (CH), 134.3 (CH), 130.0 (2CH), 129.9 (2CH), 128.1 (2x2CH), 52.9 (CH_2), 52.2 (CH_2), 47.4 (CH_2), 45.8 (CH_2), 39.5 (2CH), 35.2 (CH_3), 33.3 (CH_3), 29.8 ($2CH_2$), 29.2 ($2CH_2$), 26.0 ($2CH_2$), 25.9 (CH_2), 25.6 ($2CH_2$), 25.5 (CH_2), 22.7 (CH_2), 20.9 (CH_2); several aliphatic resonances were superimposed.

IR (neat) v/cm^{-1}: 2930 (m), 2853 (m), 1633 (s), 1445 (s), 1049 (m), 1307 (s), 1145 (s), 1030 (s), 998 (s), 739 (s), 685 (s), 593 (s), 525 (s). HR-MS (TOF ES): calculated for $C_{17}H_{26}NO_3S$ 324.1628, found 324.1629 ($M+H^+$).

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)benzamide **10h**



Chemical Formula: $C_{17}H_{19}NO_3S$
Molecular Weight: 317,4030

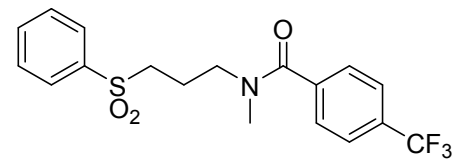
Rotameric ratio ~65:35

White powder. Yield: 60% (113 mg, 0.6 mmol). HPLC t_r = 4.5 min.

Both rotamers ^{1}H-NMR (500 MHz, DMSO-d_6) δ/ppm 7.94 (br m, 1H), 7.76 (br m, 2H), 7.67 (br m, 2H), 7.33-7.44 (m, 4H), 7.25 (br s, 1H), 3.47 (br m, 2H), 3.39 (br m, 2H), 3.24 (br m, 2H), 3.16 (br m, 2H), 2.88 (3H), 2.81 (s, 3H), 1.86 (br m, 2H) 1.72 (br m, 2H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ/ppm 170.5 (2xC), 139.5 (C), 136.9 (C), 134.4 (2CH), 129.9 (2CH), 129.8 (CH), 128.7 (2CH), 128.1 (CH), 127.3 (2CH), 52.9 (CH_2), 52.3 (CH_2), 49.3 (CH_2), 45.8 (CH_2), 37.6 (CH_3), 32.8 (CH_3), 21.9 (CH_2), 20.6 (CH_2).

IR (neat) v/cm^{-1}: 2922 (w), 1621 (s), 1447 (w), 1405 (m), 1308 (m), 1276 (m), 1145 (s), 1080 (m), 789 (m), 745 (m), 714 (s), 685 (s), 595 (s), 527 (s). HR-MS (TOF ES): calculated for $C_{17}H_{20}NO_3S$ 318.1158, found 318.1159 ($M+H^+$).

N-Methyl-*N*-(3-(phenylsulfonyl)propyl)-4-(trifluoromethyl)benzamide **10i**



Chemical Formula: $C_{18}H_{18}F_3NO_3S$
Molecular Weight: 385,4012

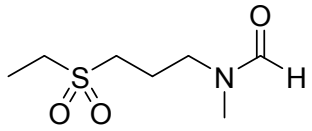
Rotameric ratio ~65:35

White solid. Yield: 70% (269 mg, 0.70 mmol). HPLC t_r= 5.4 min.

Both rotamers ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 7.91 (d, *J* = 7.3 Hz, 2H), 7.76 – 7.58 (m, >11H), 7.47 (d, *J* = 7.8 Hz, 1H), 3.47 (t, *J* = 7.0 Hz, 2H), 3.38 (t, *J* = 7.5 Hz, 2H), 3.18 (m, 4H), 2.87 (s, 3H), 2.76 (s, 3H), 1.85 (m, 2H), 1.70 (m, 2H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 169.5 (C), 141.0 (C), 139.3 (C), 134.2 (2CH), 129.9 (2CH), 128.0 (2CH), 127.7 (CH), 125.7 (2CH), 123.0 (C), 52.8 (CH_2), 52.1 (CH_2), 49.1 (CH_2), 45.8 (CH_2), 37.5 (CH_3), 32.6 (CH_3), 21.7 (CH_2). 20.5 (CH_2); some resonances were not observed ^{19}F-NMR (282 MHz, $CDCl_3$) δ/ppm -62.9 (br).

IR (neat) ν/cm^{-1}: 2927 (w), 1627 (s), 1407 (m), 1313 (s), 1276 (m), 1148 (s), 1115 (s), 1082 (s), 1062 (s), 1015 (m), 844 (s), 742 (m), 687 (m), 594 (s), 527 (s). HR-MS (TOF ES): calculated for $C_{18}H_{19}F_3NO_3S$ 386.1032, found 386.1034 ($M+H^+$). Crystal data: (CCDC2018541): for $C_{18}H_{18}SNO_3F_3$; P-1, α = 81.037(4), β = 88.297(4), γ = 87.959(4), a = 5.6871(3), b = 8.6686(4), c = 18.3693(7).

N-(3-(Ethylsulfonyl)propyl)-*N*-methylformamide **10j**



Chemical Formula: $C_7H_{15}NO_3S$
Molecular Weight: 193.2610

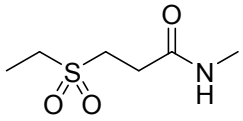
Rotameric ratio ~55:45

Light yellow oil. Yield: 70% (134 mg, 0.70 mmol). HPLC t_r = 3.5 min.

Both rotamers: ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm δ 8.06 (s, 1H), 8.04 (s, 1H), 3.48 (t, *J* = 6.9 Hz, 2H), 3.44 (t, *J* = 6.9 Hz, 2H), 2.96 (s, 3H), 2.88-3.05 (m, 4x2H), 2.86 (s, 3H), 2.18 – 2.04 (m, 2x2H), 1.40 (t, *J* = 6.9 Hz, 3H), 1.38 (t, *J* = 6.9 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 163.0 (C), 162.7 (C), 49.1 (CH_2), 48.0 (CH_2), 47.9 (CH_2), 47.7 (CH_2), 47.6 (CH_2), 42.7 (CH_2), 34.5 (CH_3), 29.3 (CH_3), 20.0 (CH_2), 19.0 (CH_2), 6.7 (CH_3), 6.6 (CH_3).

IR (neat) ν/cm^{-1}: 2942 (w), 1667 (s), 1593 (s), 1478 (m), 1457 (m), 1426(m), 1306 8m), 1195 (s), 1148 (s), 1064 (s), 916 (w), 820 (m), 729 (m). HR-MS (TOF ES): calculated for $C_7H_{16}NO_3S$ 194.0845, found 194.0851 ($M+H^+$).

3-(Ethylsulfonyl)-*N*-methylpropanamide **10k**



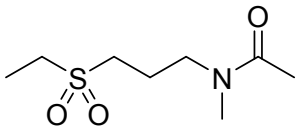
Chemical Formula: $C_6H_{13}NO_3S$
Molecular Weight: 179,2340

White solid. Yield: 90% (84 mg, 0.45 mmol). HPLC t_r = 2.0 min.

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 3.35 (t, *J* = 7.2 Hz, 2H), 3.04 (q, *J* = 7.5 Hz, 2H), 2.84 (d, *J* = 4.8 Hz, 3H), 2.72 (t, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.5 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 169.7 (C), 48.0 (CH_2), 47.5 (CH_2), 28.0 (CH_2), 26.5 (CH_3), 6.6 (CH_3).

IR (neat) ν/cm^{-1}: 3302 (m), 2935 (w), 1646 (s), 1569 (s), 1410 (m), 1304 (s), 1277 (s), 1124 (s), 1055 (m), 1012 (m), 734 (s), 550 (s), 494 (s), 448 (s). HR-MS (TOF ES): calculated for $C_6H_{14}NO_3S$ 180.0689, found 180.0690 ($M+H^+$).

N-(3-(Ethylsulfonyl)propyl)-*N*-methylacetamide **10m**



Chemical Formula: $C_8H_{17}NO_3S$
Molecular Weight: 207.2880

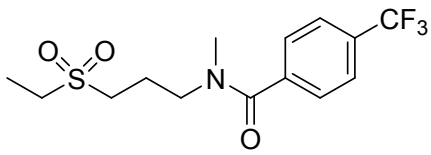
Rotameric ratio ~80:20

Colourless oil. Yield: 73% (151 mg, 0.73 mmol). HPLC t_r = 2.7 min.

Major rotamer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 3.51 (t, *J* = 6.8 Hz, 2H), 3.01 (s, 3H), 2.99 – 2.90 (m, 4H), 2.07 (s, 3H), 2.03-2.10 (m, 2H), 1.38 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 171.1 (C), 49.3 (CH_2), 47.5 (CH_2), 45.9 (CH_2), 36.1 (CH_3), 21.8 (CH_3), 19.7 (CH_2), 6.6 (CH_3).

IR (neat) ν/cm^{-1}: 2943 (w), 1619 (s), 1410 (m), 1298 (s), 1271 (s), 1126 (s), 1016 (m), 803 (m), 733 (w), 492 (w). HR-MS (TOF ES): calculated for $C_8H_{18}NO_3S$ 208.1002, found 208.1005 ($M+H^+$).

N-Methyl-*N*-(3-(propylsulfonyl)propyl)-4-(trifluoromethyl)benzamide **10m**



Chemical Formula: $C_{14}H_{18}F_3NO_3S$
Molecular Weight: 337.3572

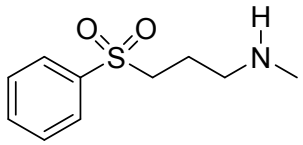
Rotameric ratio ~80:20

White powder. Yield: 82% (137 mg, 0.41 mmol). HPLC t_r = 4.6 min.

Major rotamer: ^{1}H-NMR (300 MHz, $CDCl_3$) δ/ppm 7.67 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 3.70 (t, *J* = 7.1 Hz, 2H), 3.14 – 2.99 (m, 4H), 2.98 (s, 3H), 2.22 (app p, *J* = 7.4 Hz, 2H), 1.41 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 170.5 (C), 139.5 (C), 131.6 (C), 127.3 (2CH, br), 125.6 (2CH, br), 49.3 (CH_2), 47.6 (CH_2), 46.2 (CH_2), 37.5 (CH_3), 19.3 (CH_2), 6.7 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -62.9 (s).

IR (neat) ν/cm^{-1}: 2939 (w), 1619 (s), 1405 (m), 1304 (s), 1276 (s), 1118 (s), 1066 (s), 1016 (s), 846 (m), 766 (m), 710 (m), 571 (m), 483 (m). HR-MS (TOF ES): calculated for $C_{14}H_{19}F_3NO_3S$ 338.1032, found 338.1034 ($M+H^+$).

N-Methyl-3-(phenylsulfonyl)propan-1-amine **11**



Chemical Formula: $C_{10}H_{15}NO_2S$
Molecular Weight: 213.2950

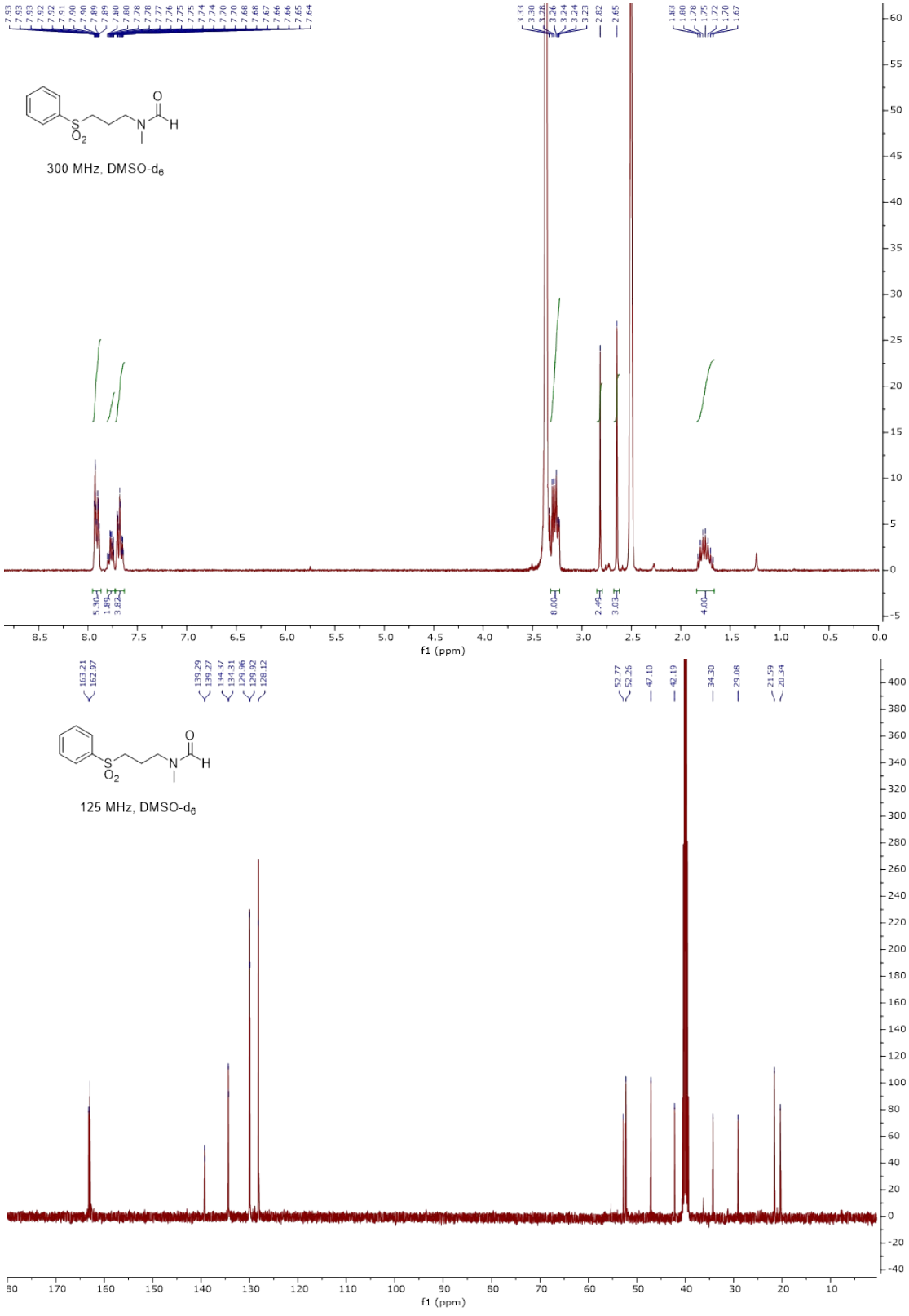
Yellow oil. Yield: 81% (2.1 g, 9.7 mmol). HPLC t_r= 1.3 min

^{1}H-NMR (300 MHz, $CDCl_3$) δ/ppm 7.95 (d, *J* = 7.5 Hz, 2H), 7.71 – 7.64 (m, 1H), 7.63 – 7.55 (m, 2H), 4.72 (br s, 1H), 3.38 – 3.27 (m, 2H), 3.01 – 2.85 (m, 2H), 2.54 (br s, 3H), 2.14 (p, *J* = 7.1 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 139.2 (C), 133.6 (CH), 129.3 (2CH), 128.0 (2CH), 54.3 (CH_2), 49.9 (CH_2), 36.2 (CH_3), 22.9 (CH_2).

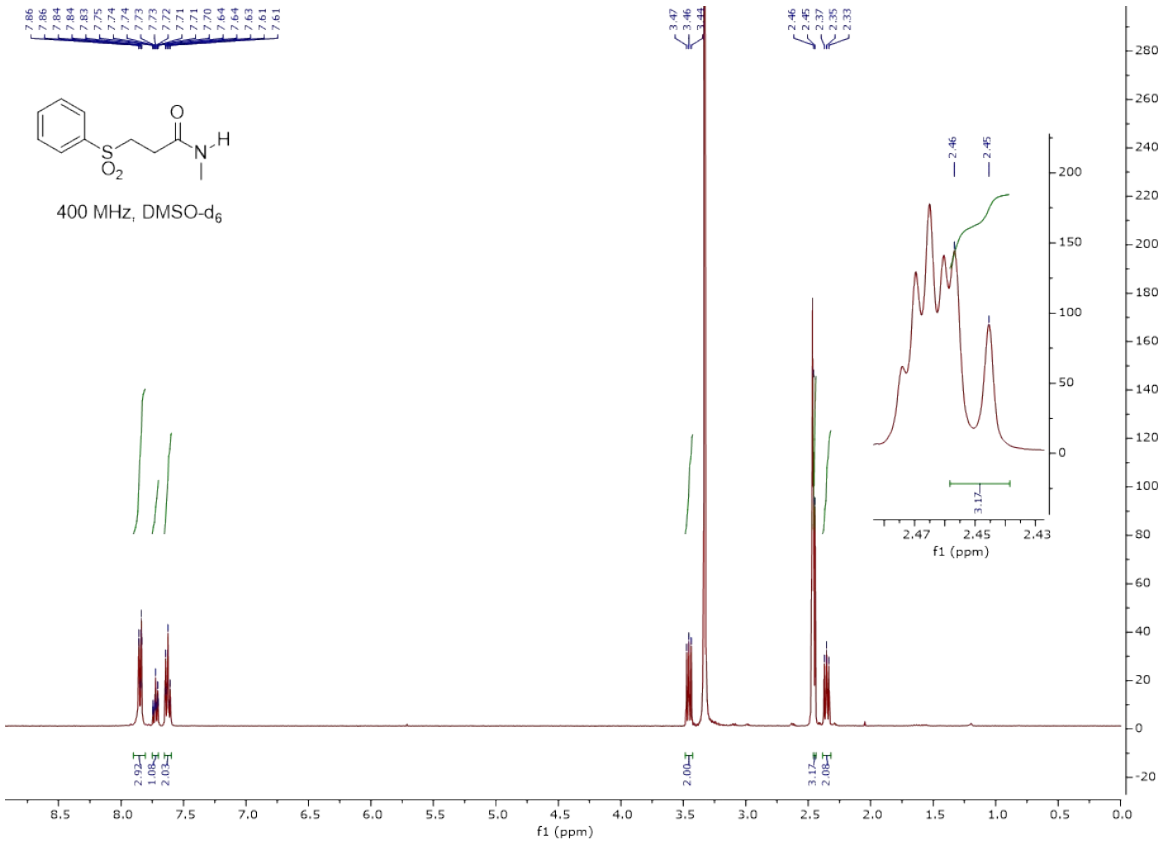
IR (neat) ν/cm^{-1}: 2944 (w), 1446 (m), 1287 (s), 1141 (s), 1085 (s), 1024 (w), 791 (w), 731 (m), 688 (s), 594 (m), 562 (m), 533 (s). HR-MS (TOF ES): calculated for $C_{10}H_{16}NO_2S$ 214.0896, found 214.0897 ($M+H^+$).

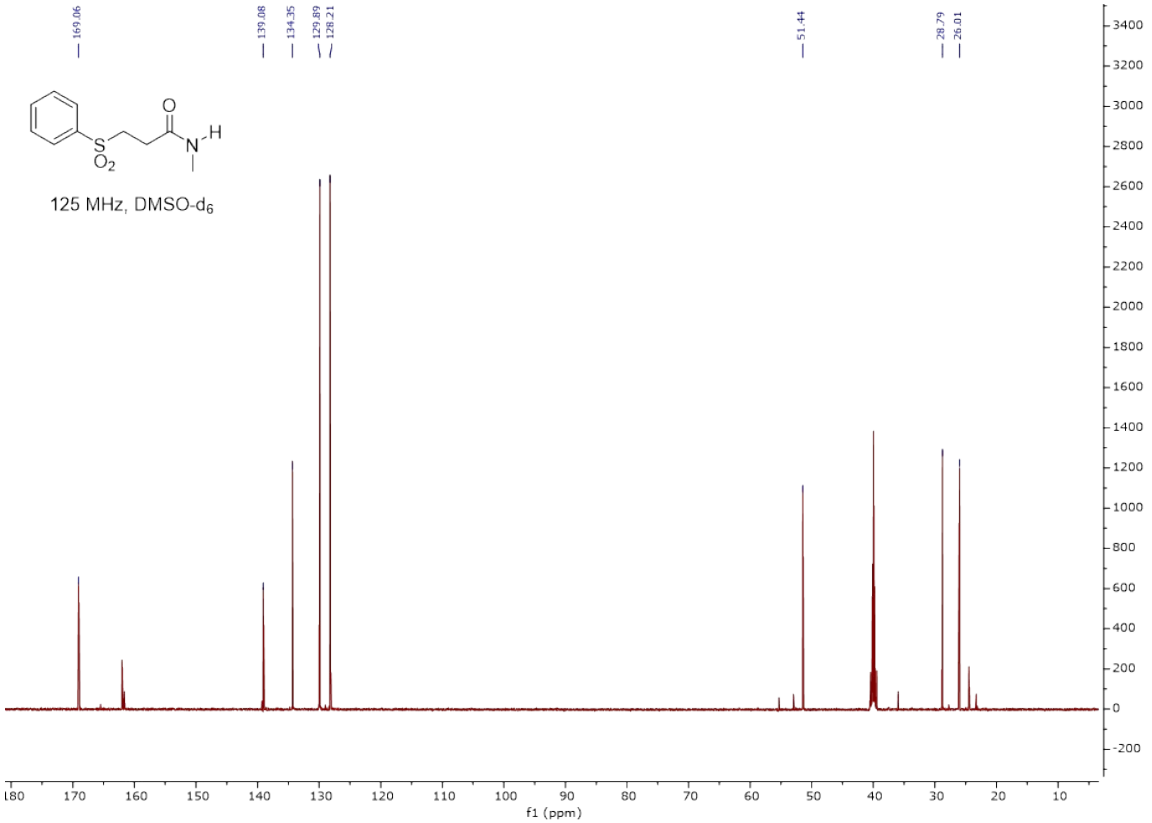
5. Copies of NMR spectra of compounds 10a-m and 11:

^{1}H and ^{13}C NMR of compound **10a**:

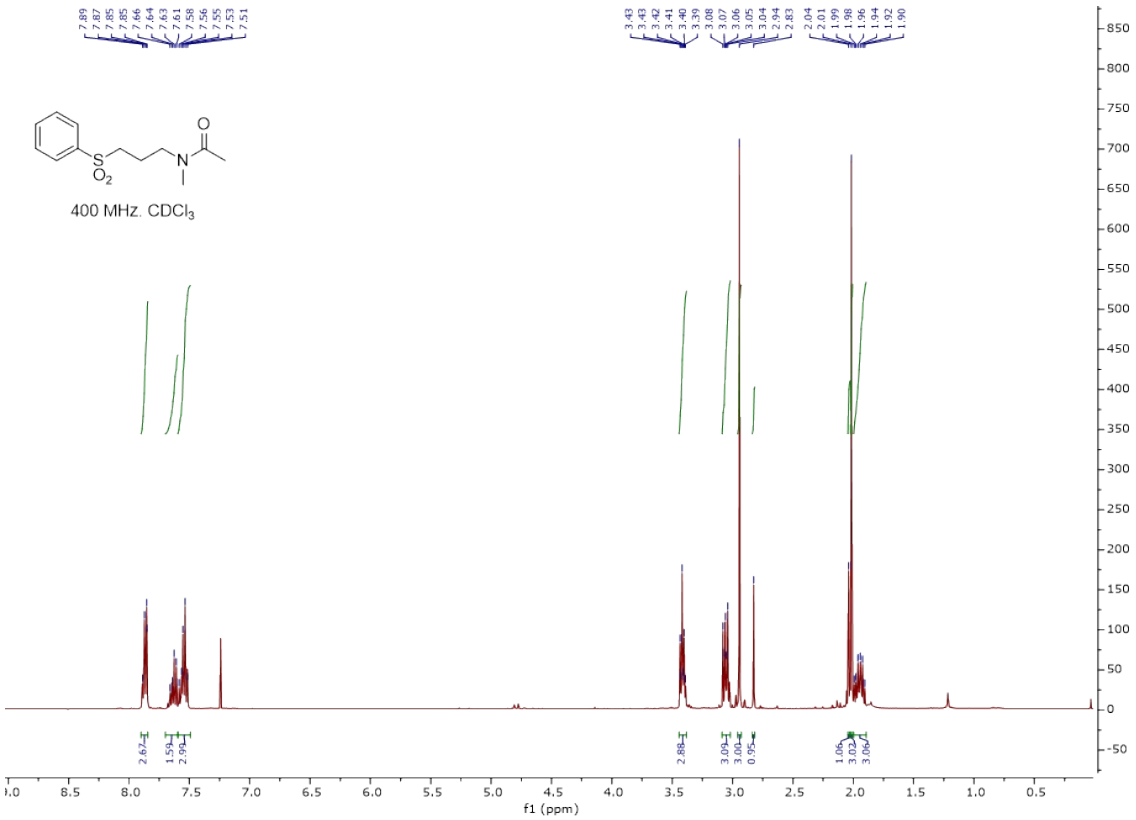


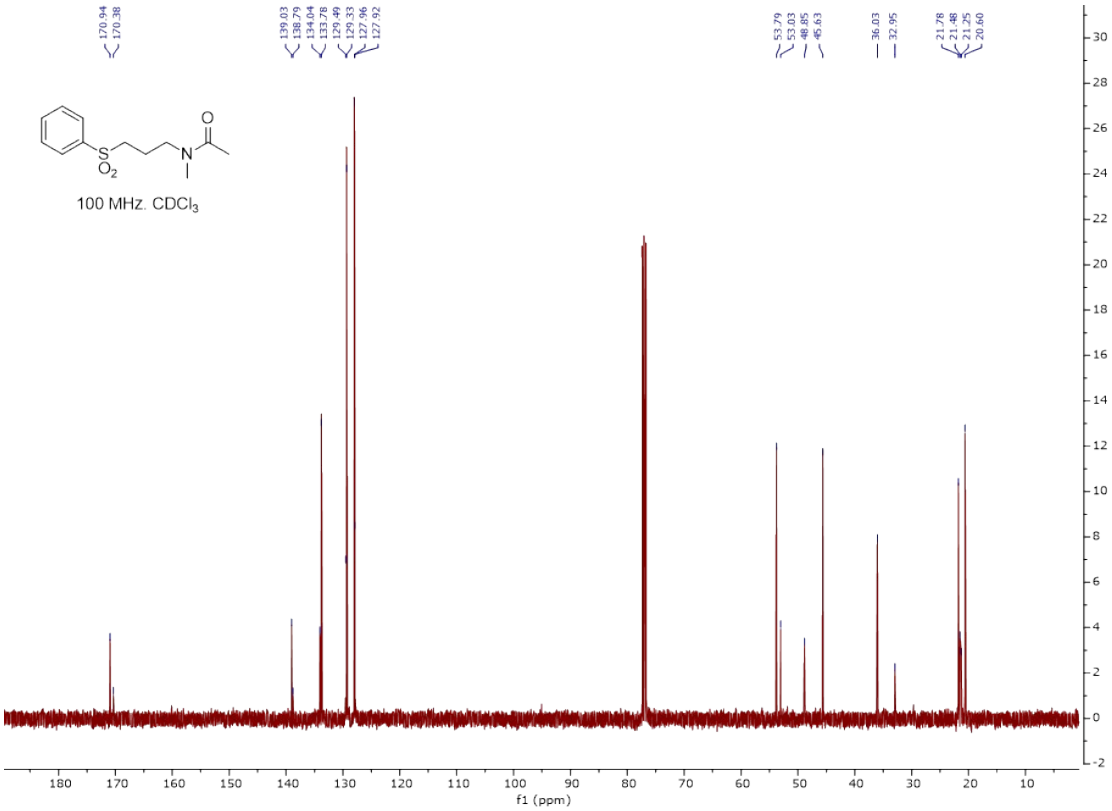
^{1}H and ^{13}C NMR of compound **10b**:



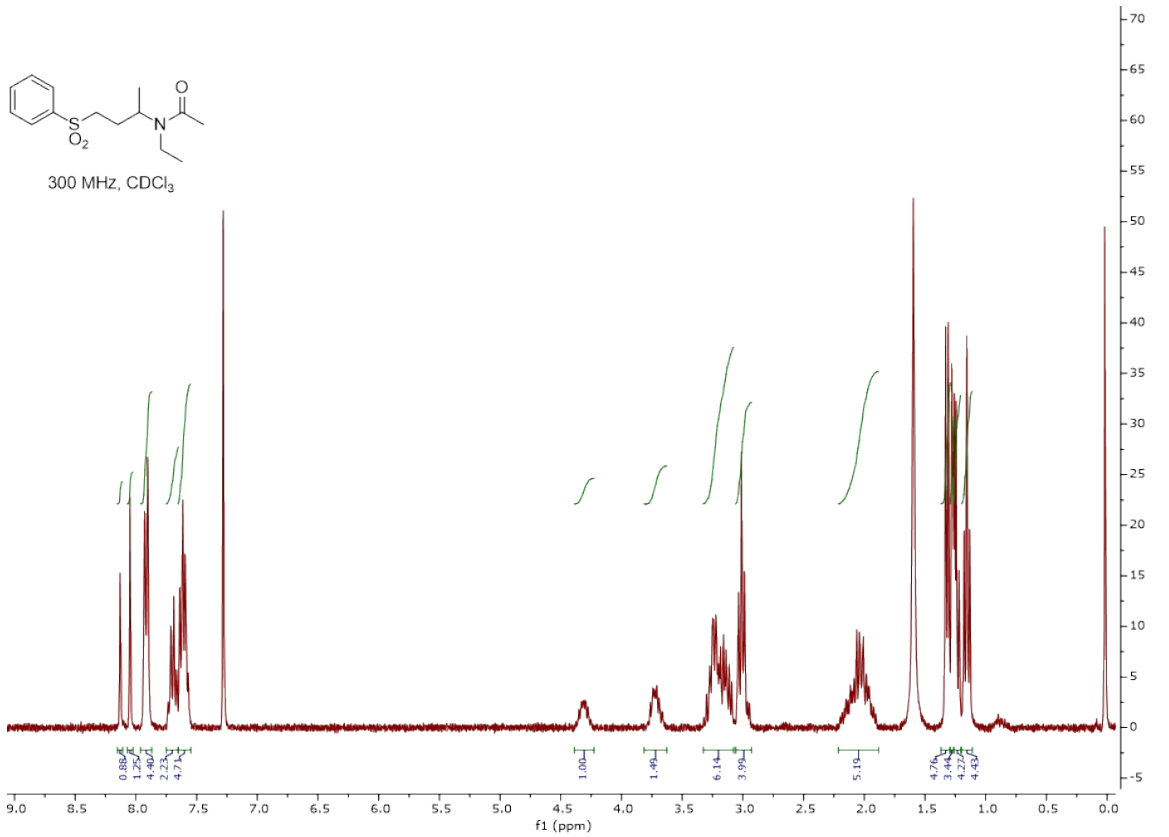


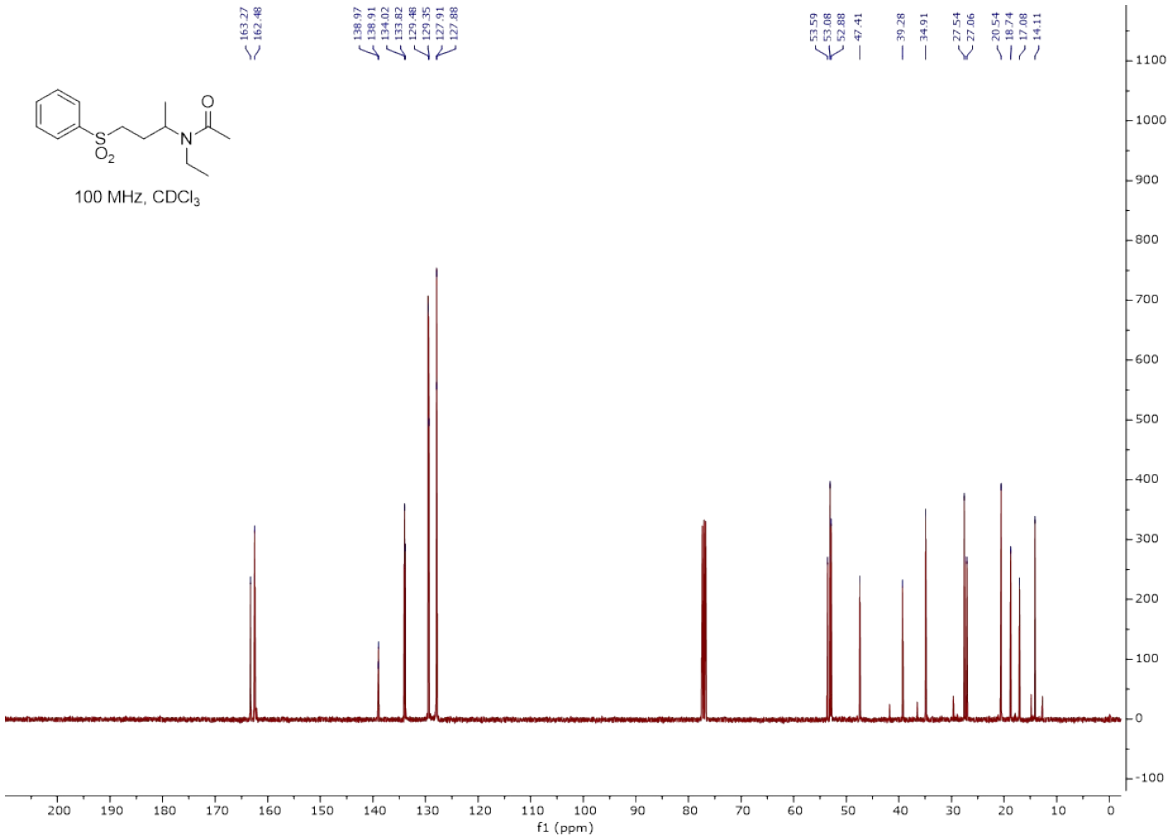
^{1}H and ^{13}C NMR of compound **10c**:



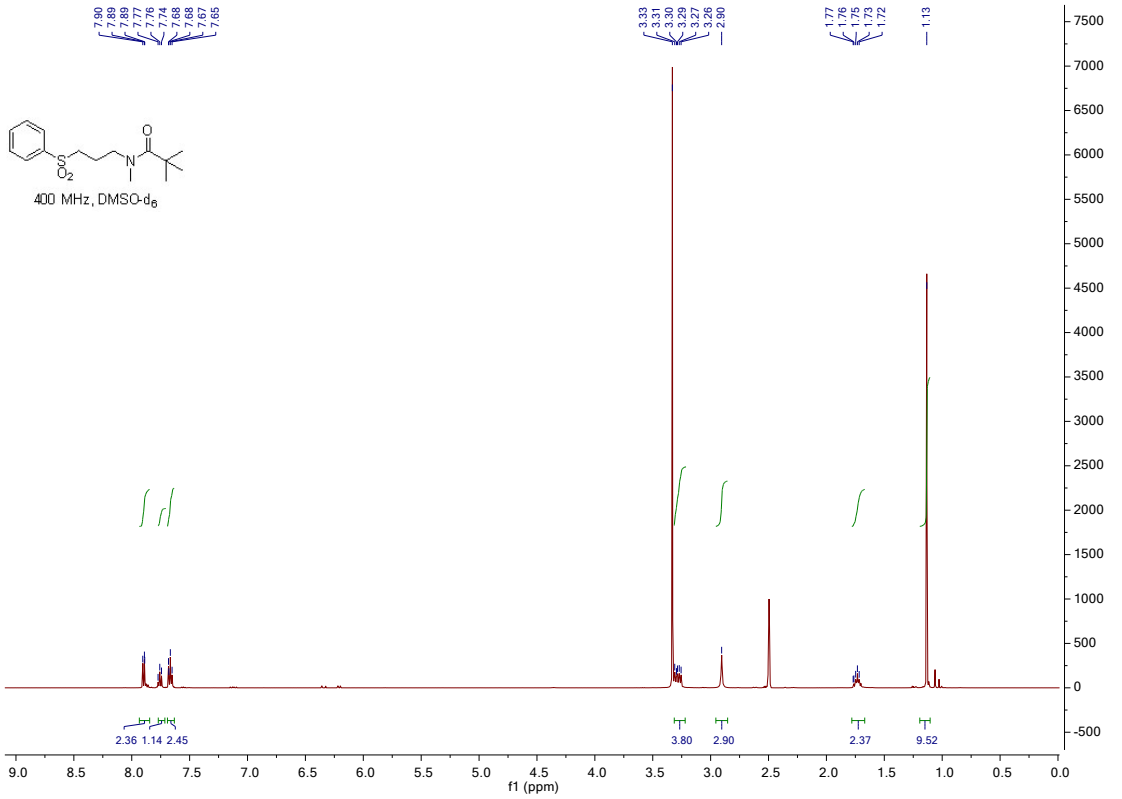


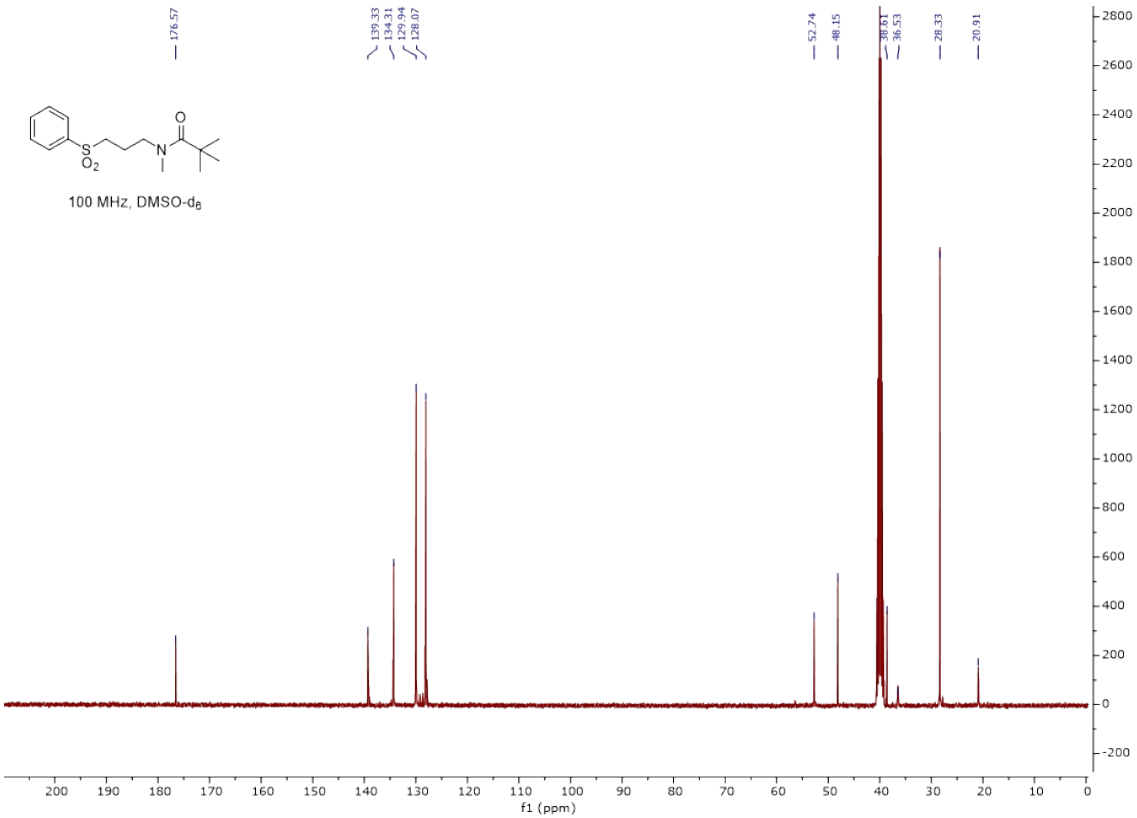
^{1}H and ^{13}C NMR of compound **10d**:



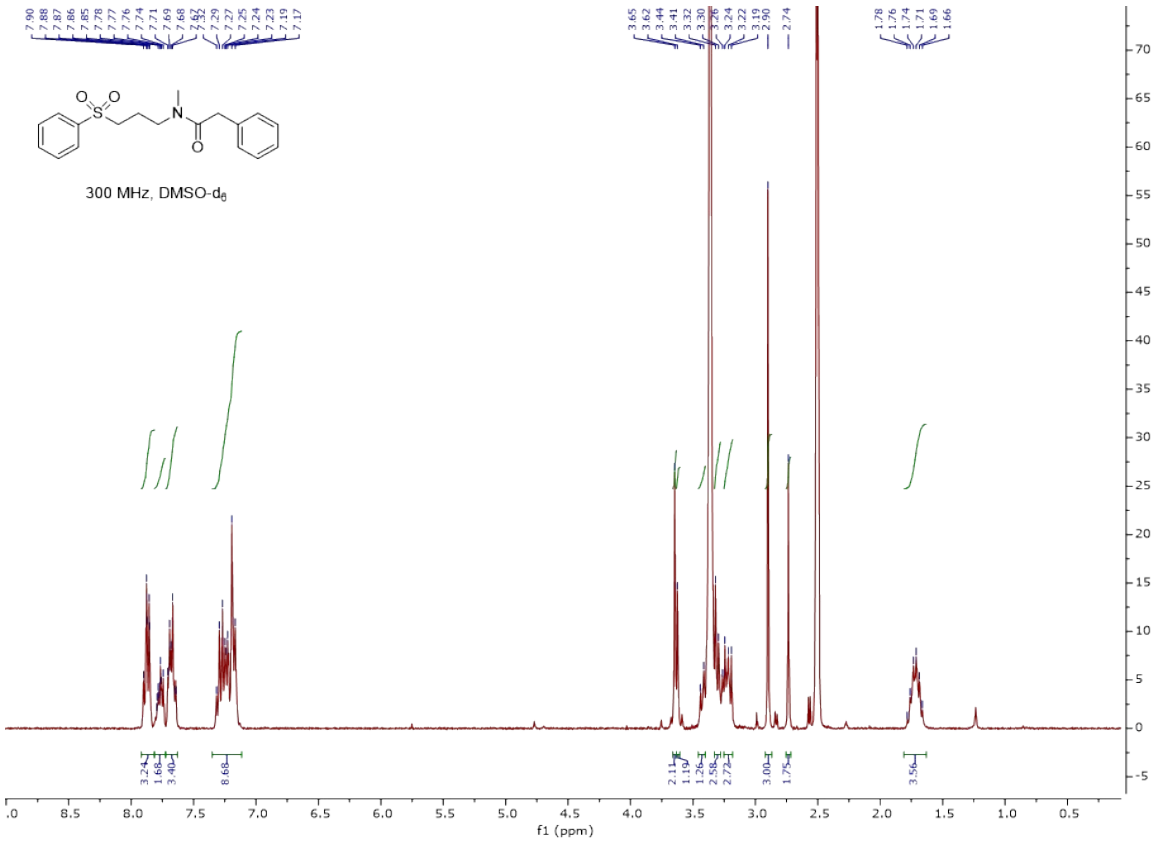


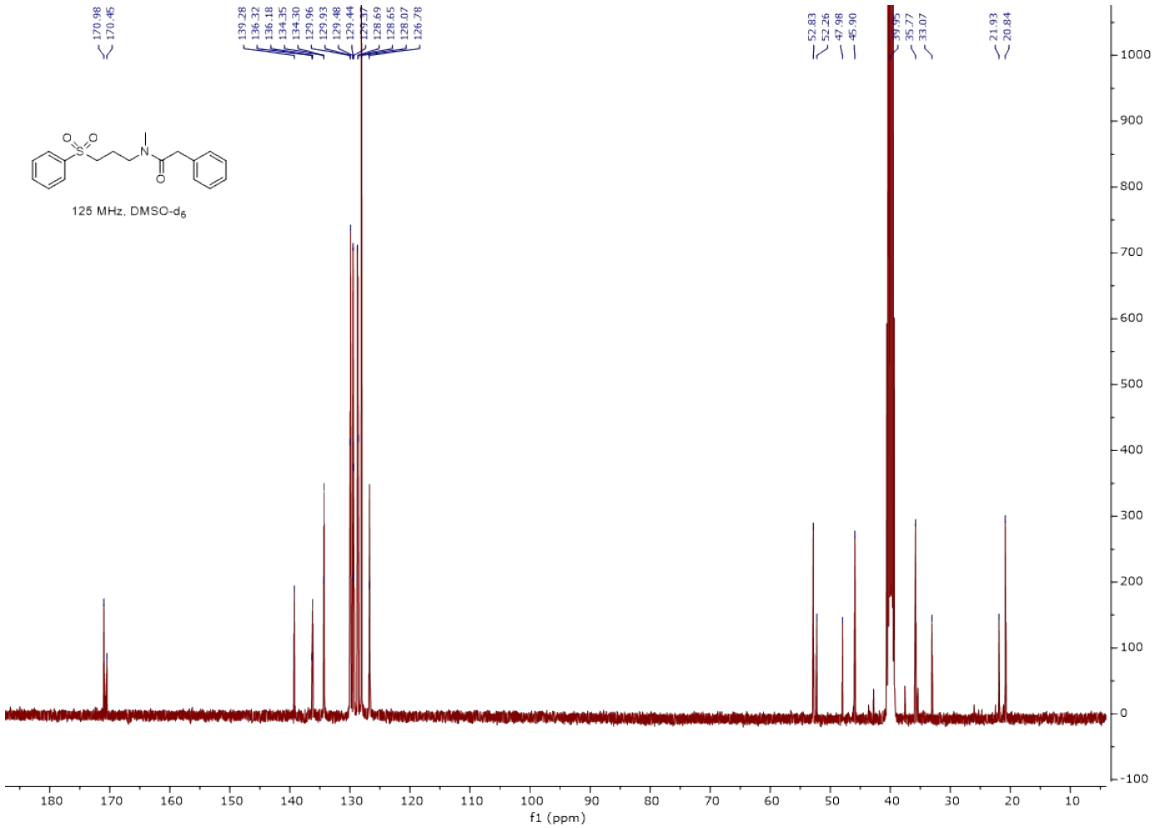
^{1}H and ^{13}C NMR of compound **10e**:



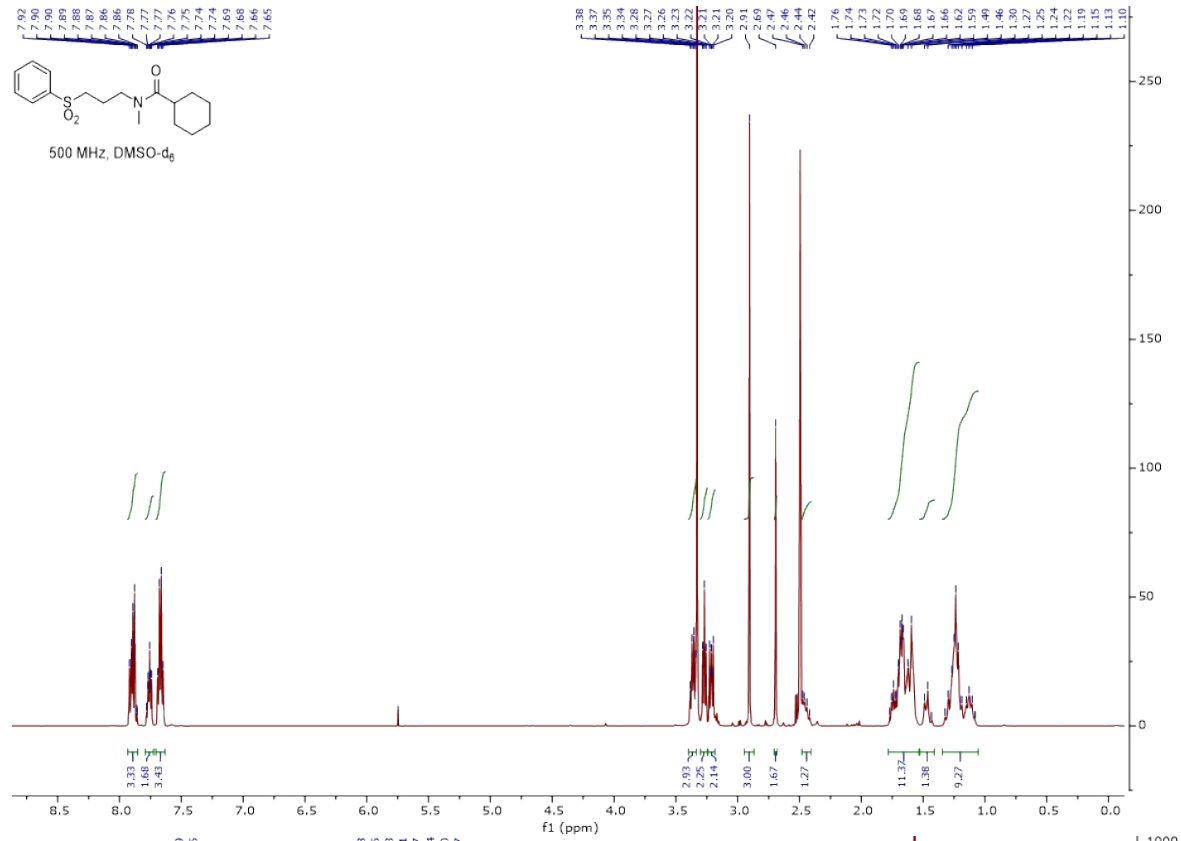


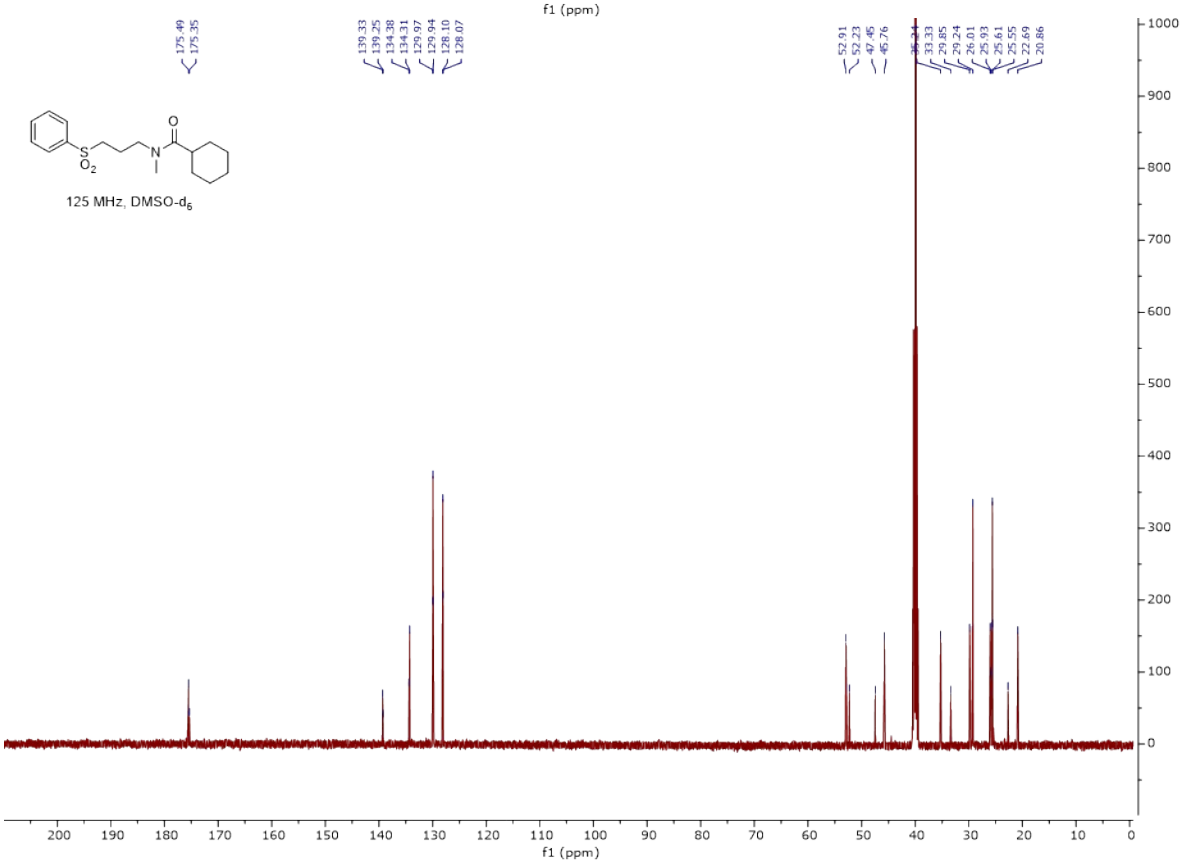
^{1}H and ^{13}C NMR of compound **10f**:



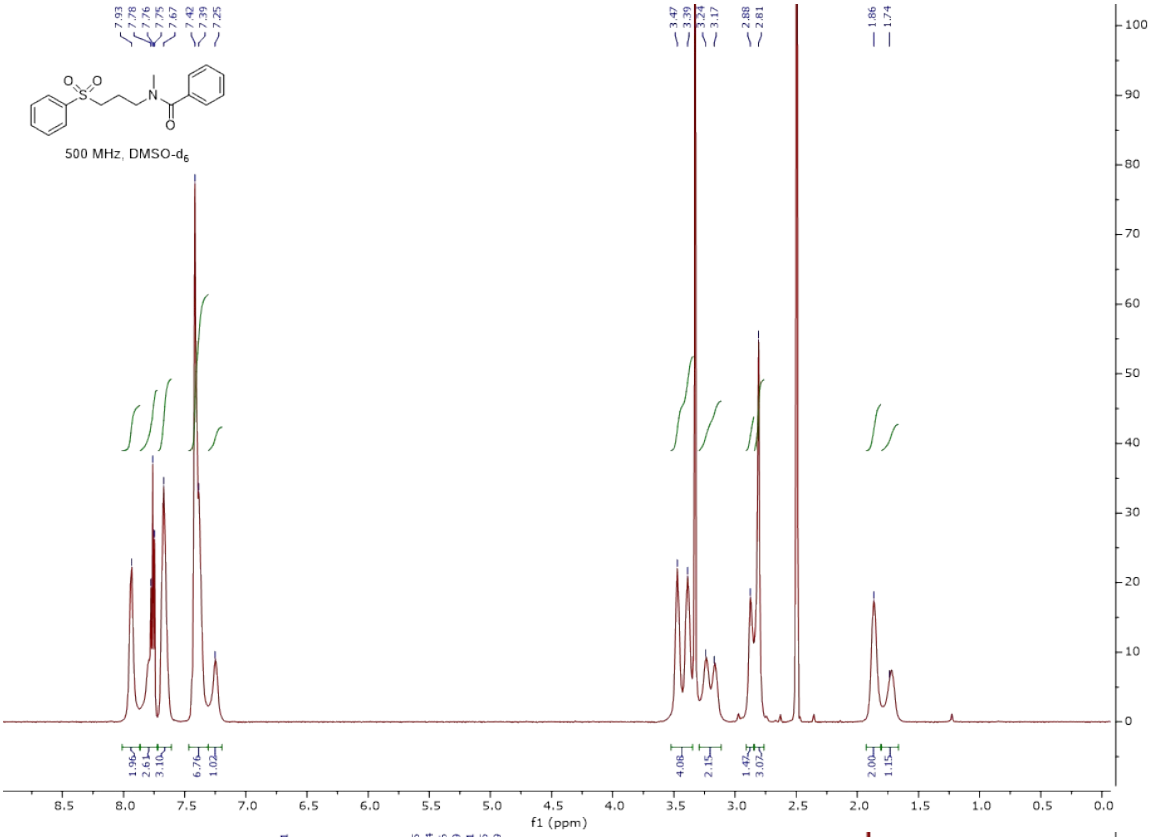


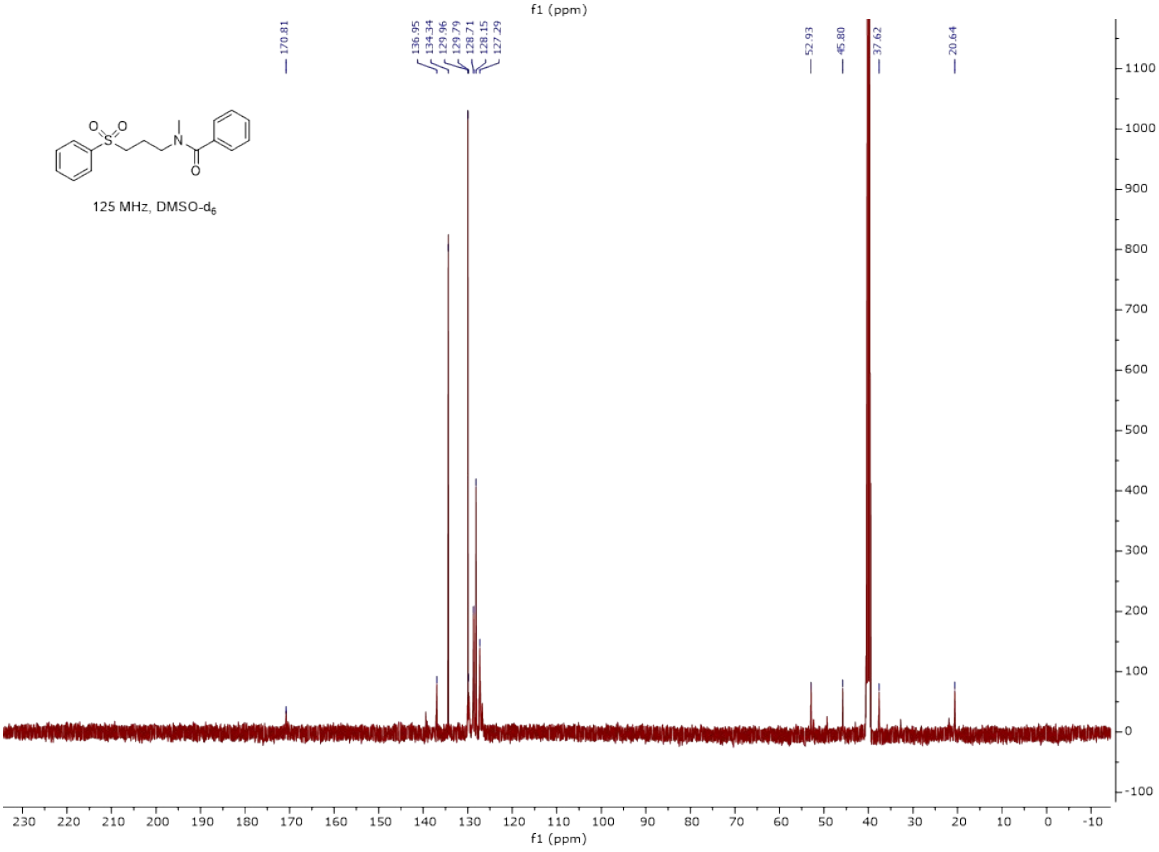
^{1}H and ^{13}C NMR of compound **10g**:

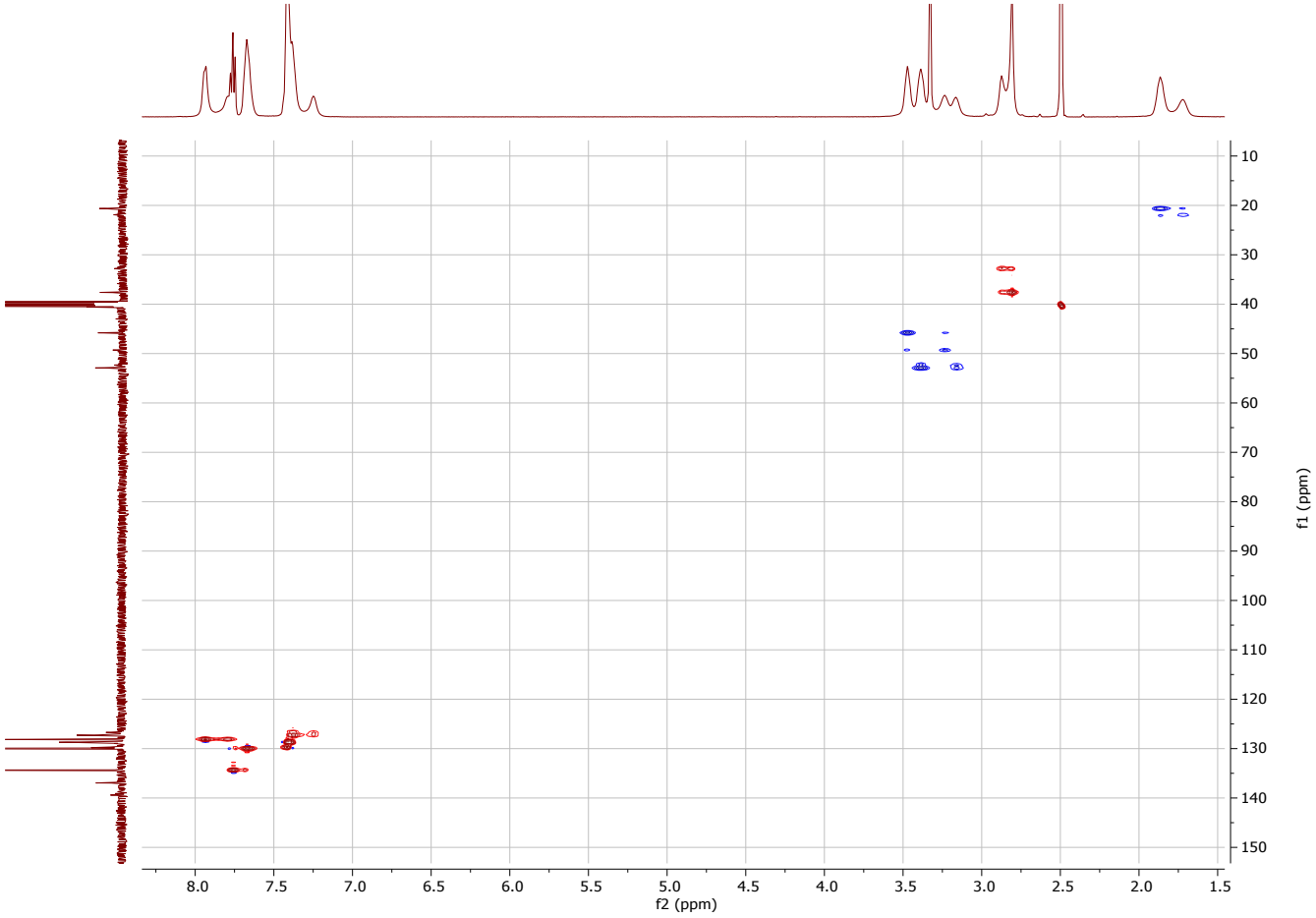




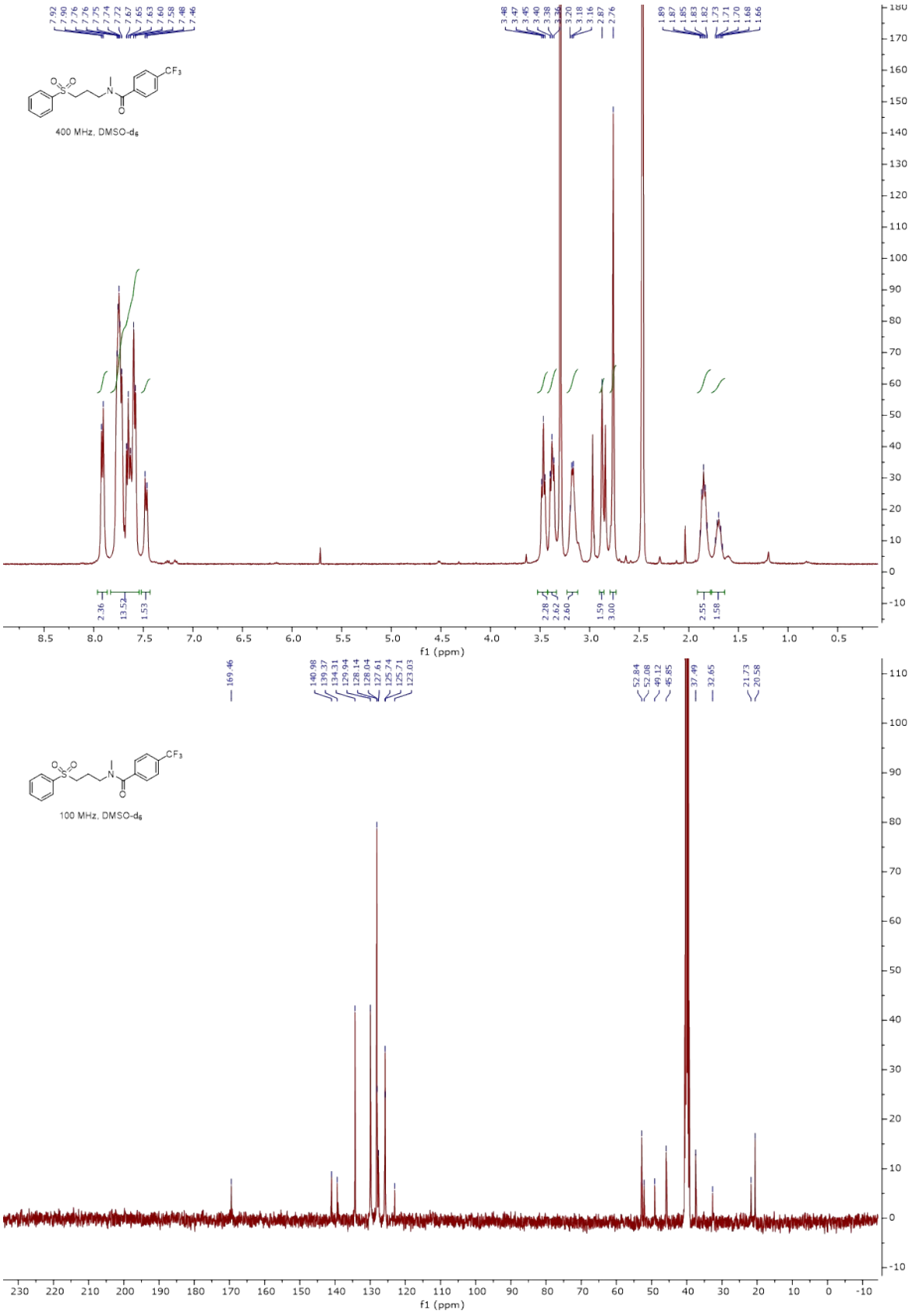
^{1}H, ^{13}C and HSQC NMR of compound **10h**:

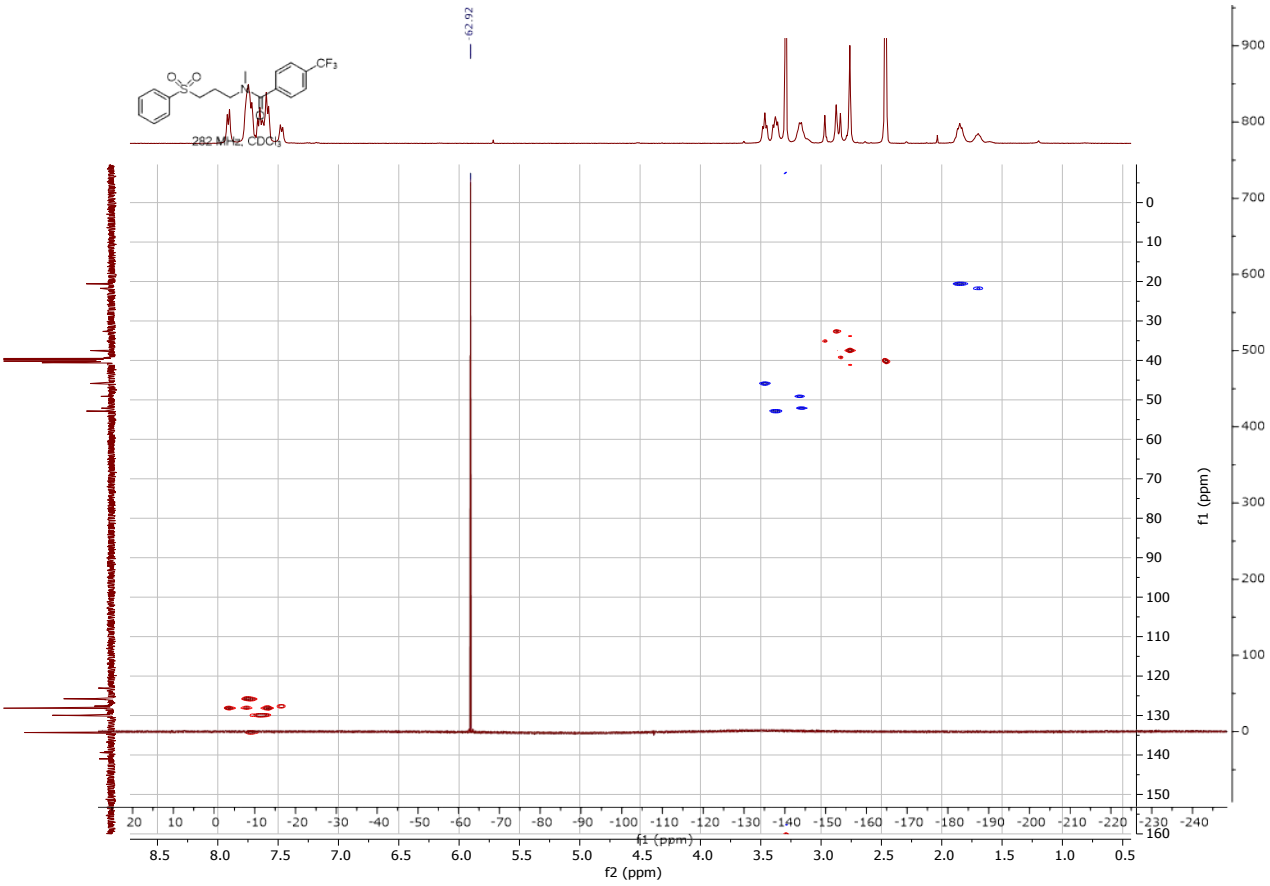




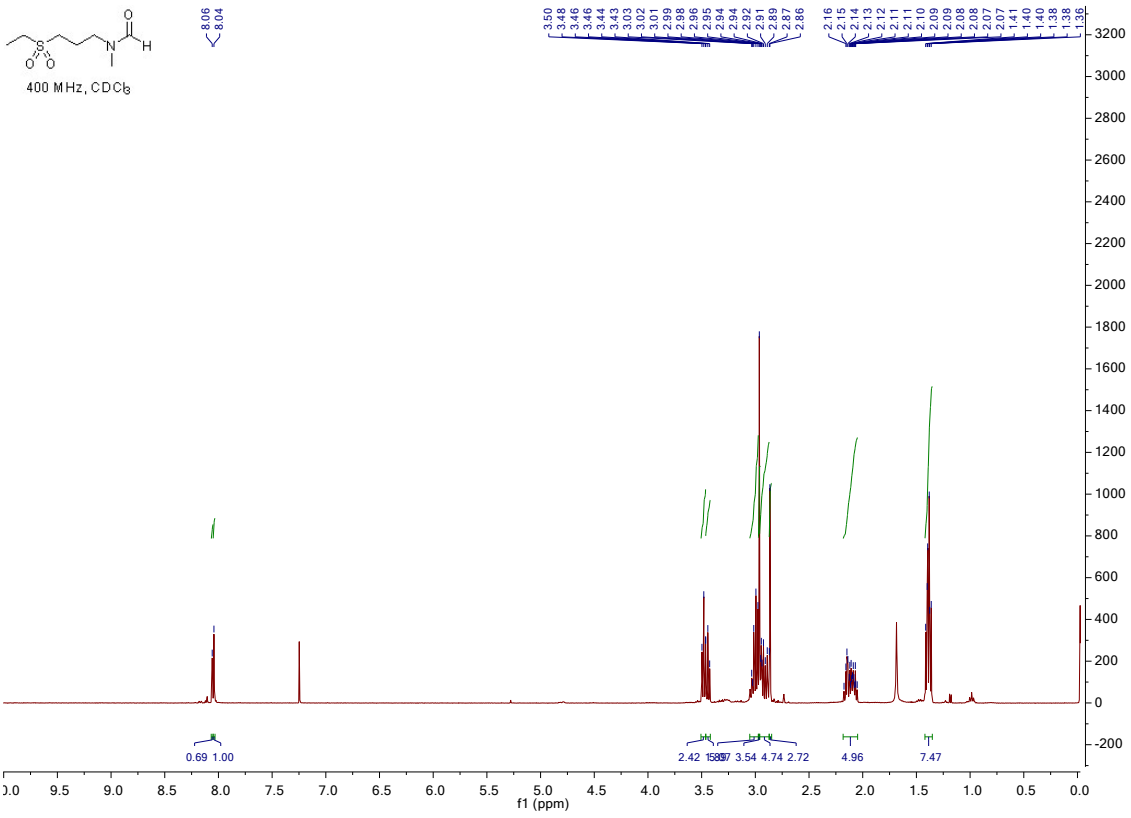

f2 (ppm)
f1 (ppm)

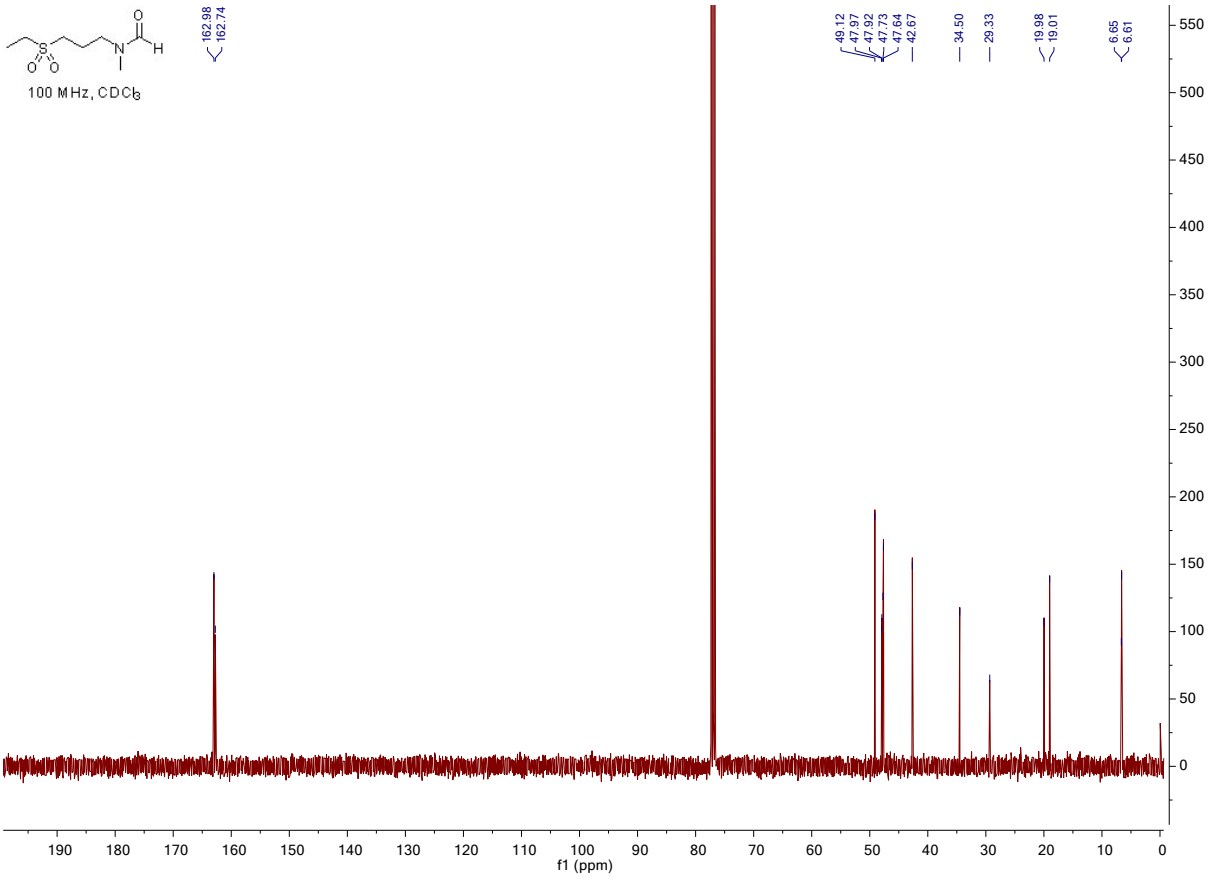
^{1}H, ^{13}C, ^{19}F and HSQC NMR of compound **10i**:

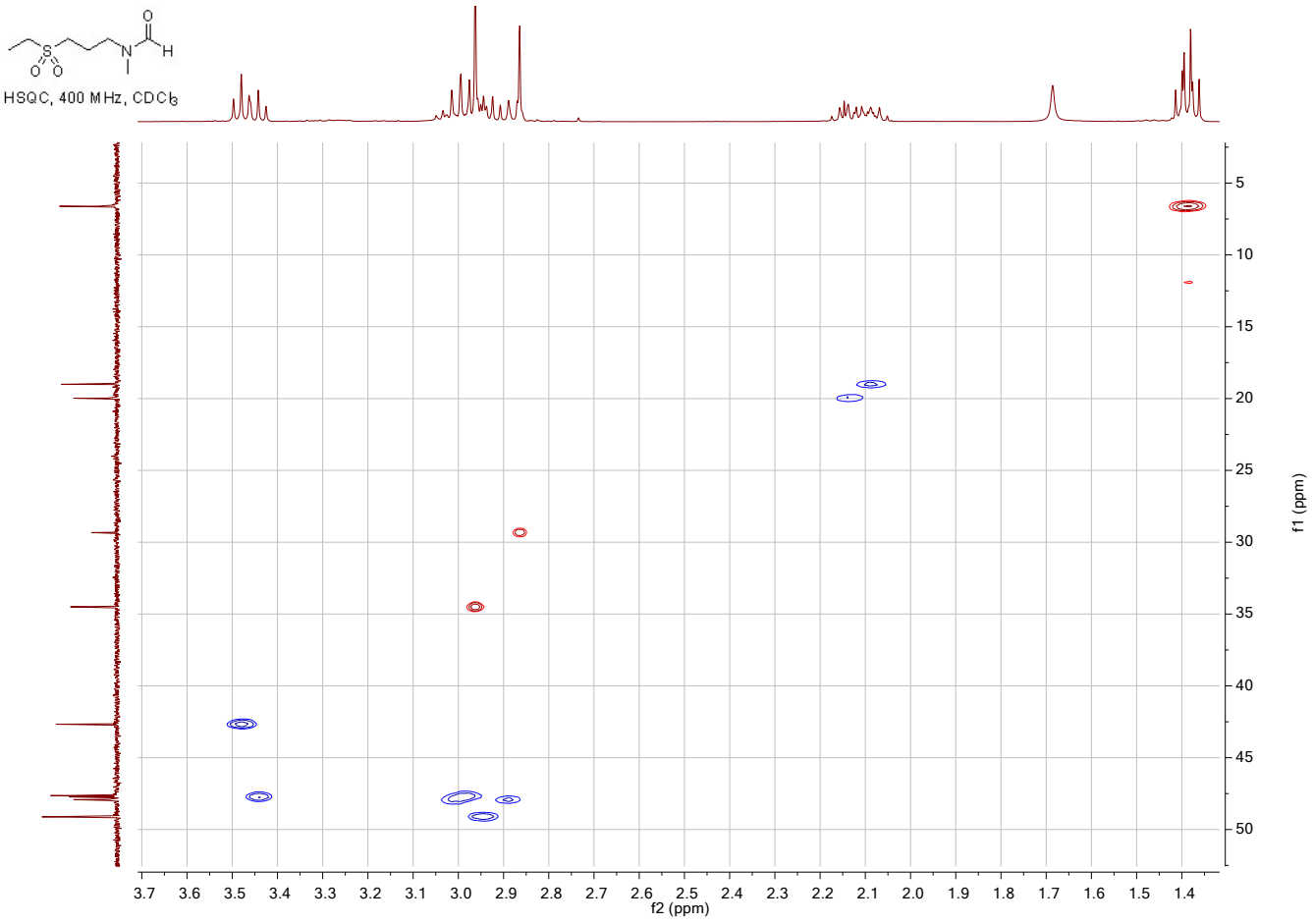




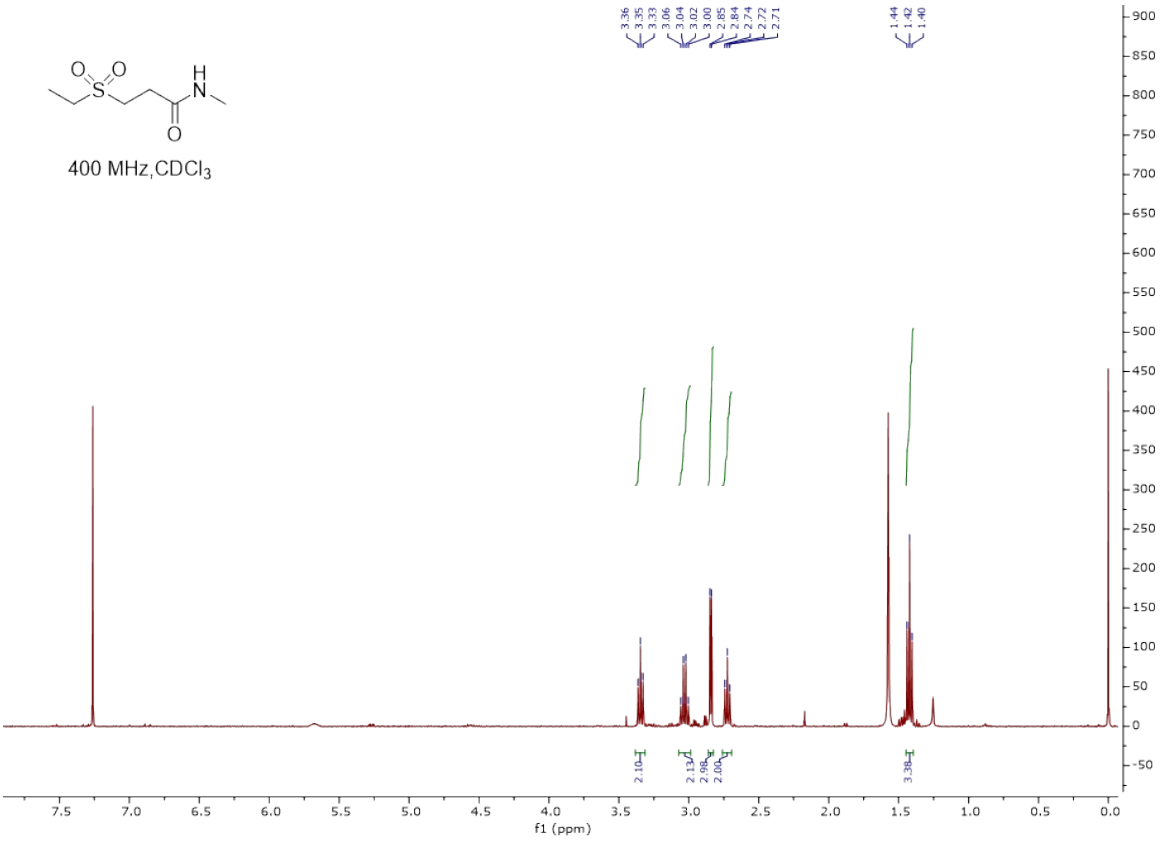
^{1}H, ^{13}C and HSQC NMR of compound **10j**:

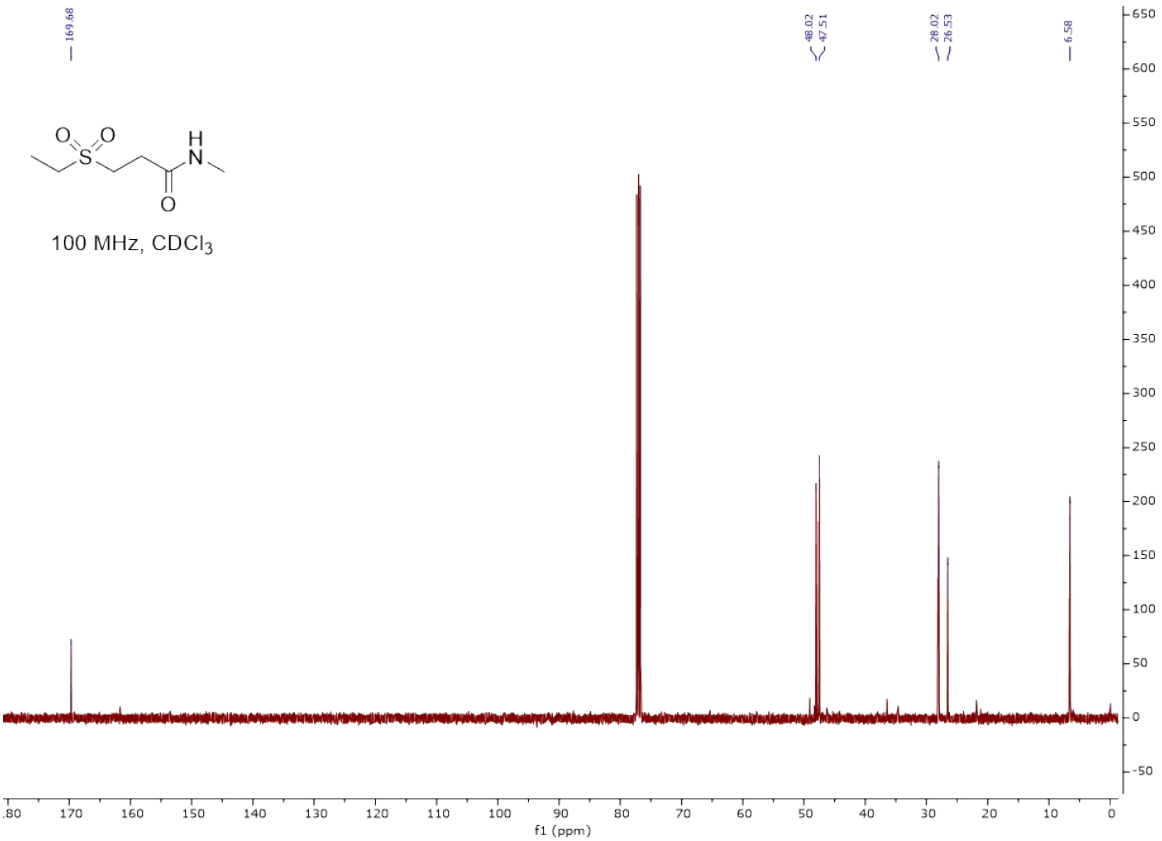

400 MHz, CDCl3
f1 (ppm)


100 MHz, CDCl3
f1 (ppm)

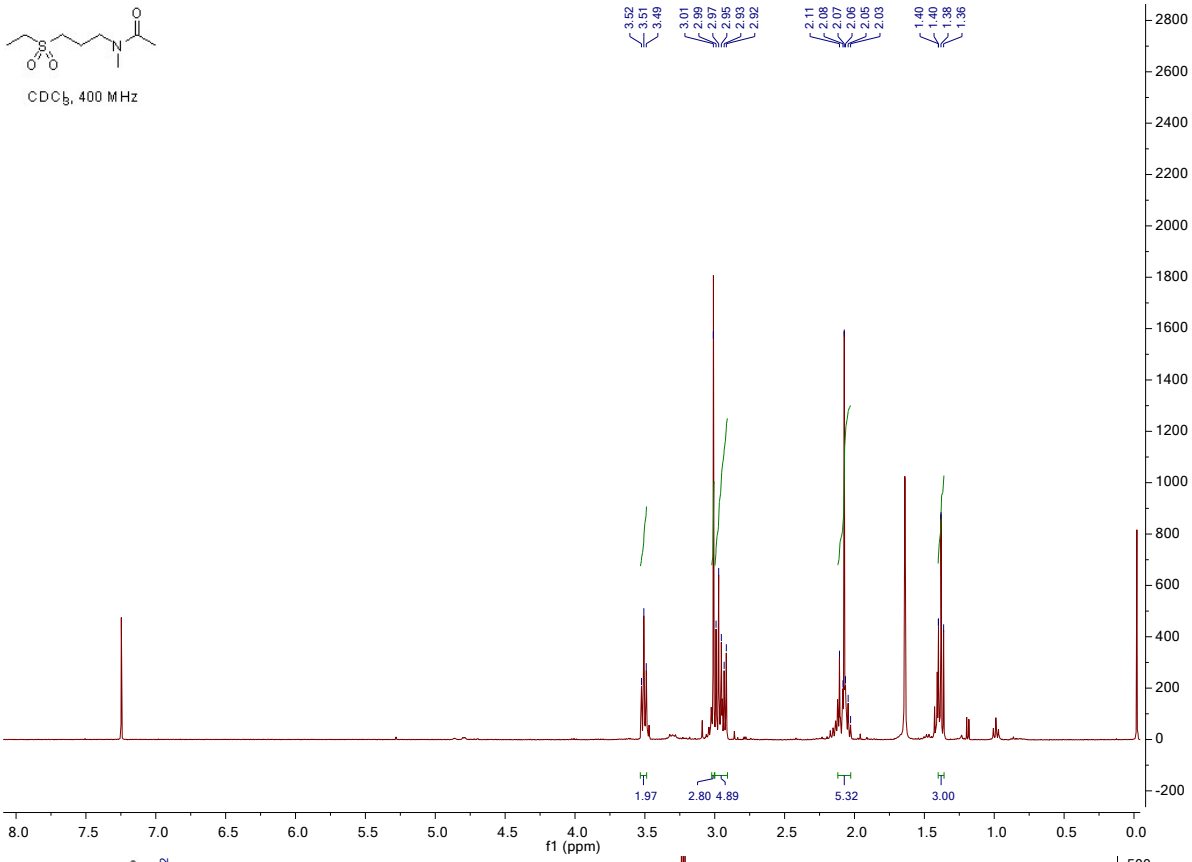


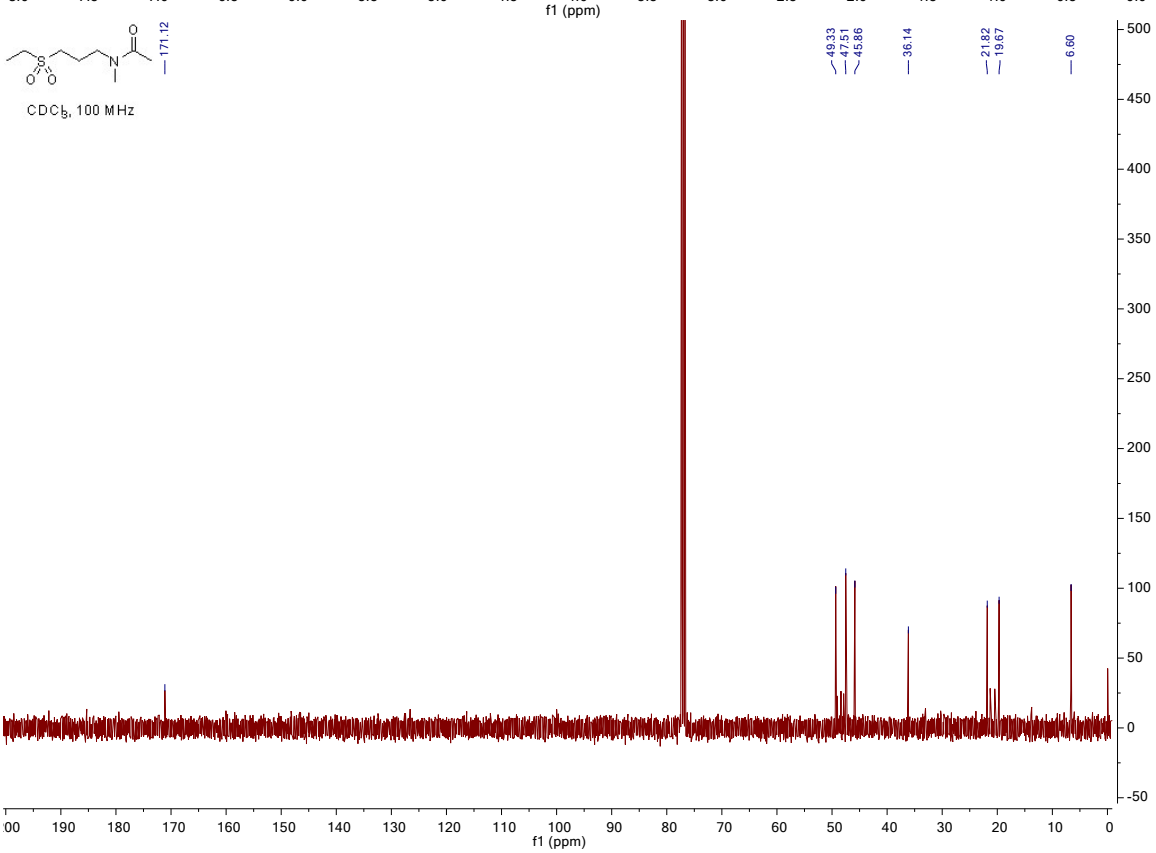
[1]H and [13]C NMR of compound **10k**:

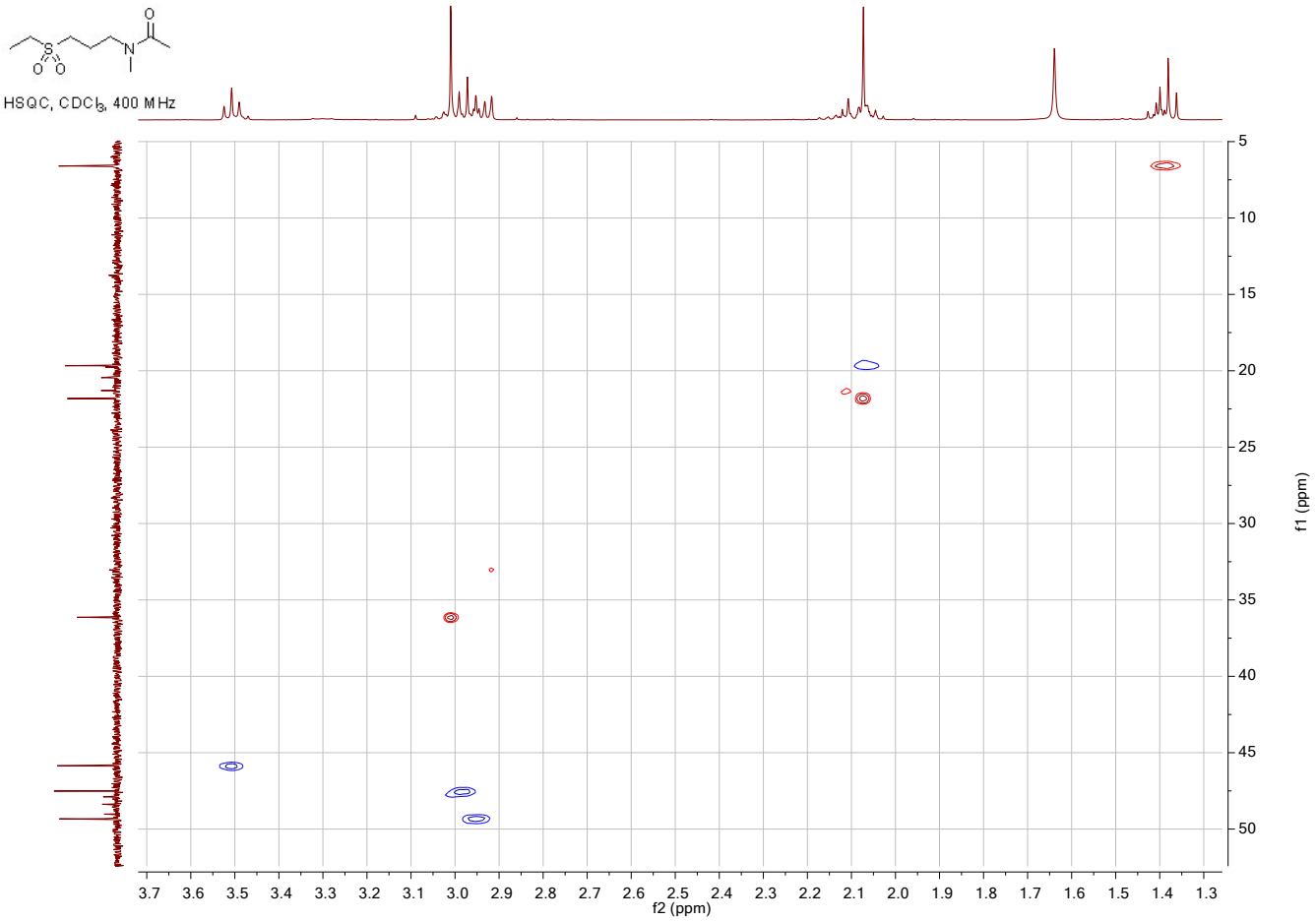




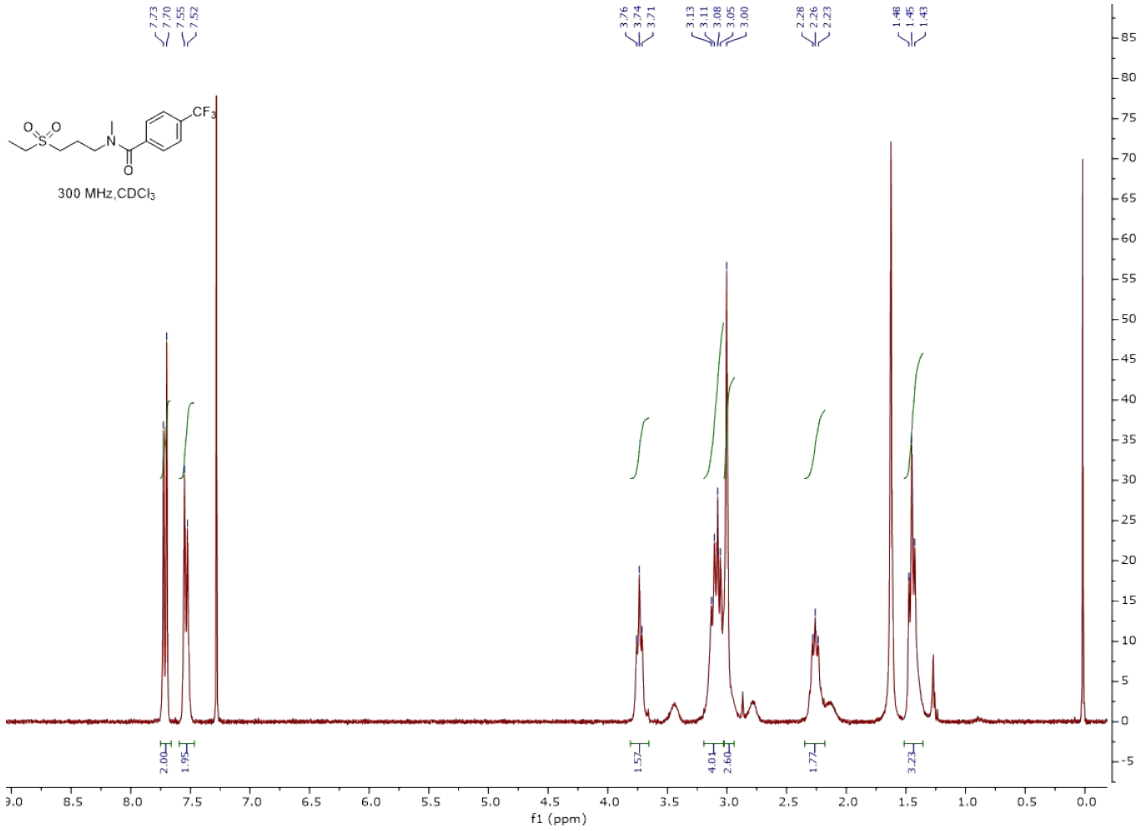
^{1}H, ^{13}C and HSQC NMR of compound **10l**:

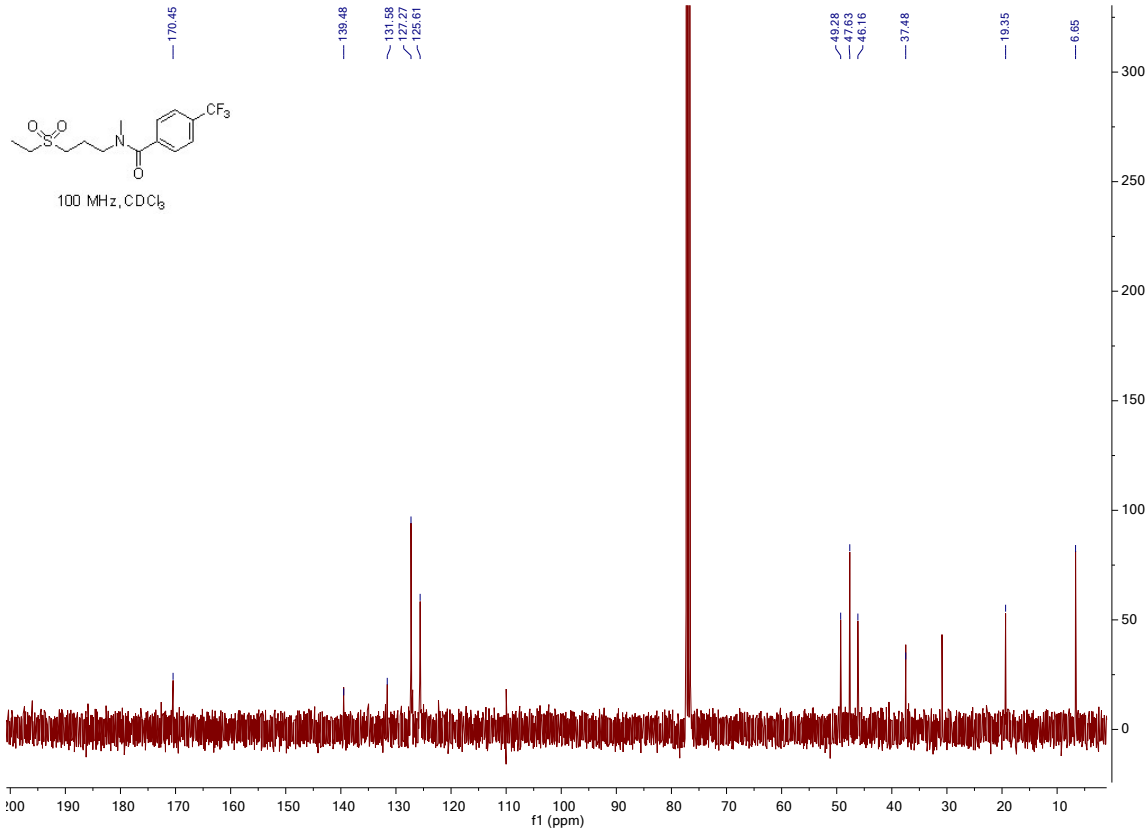

CDCl3, 400 MHz
3.52
3.51
3.49
3.01
2.99
2.97
2.95
2.93
2.92
2.11
2.08
2.07
2.06
2.05
2.03
1.40
1.40
1.38
1.36
1.97
2.80
4.89
5.32
3.00
f1 (ppm)

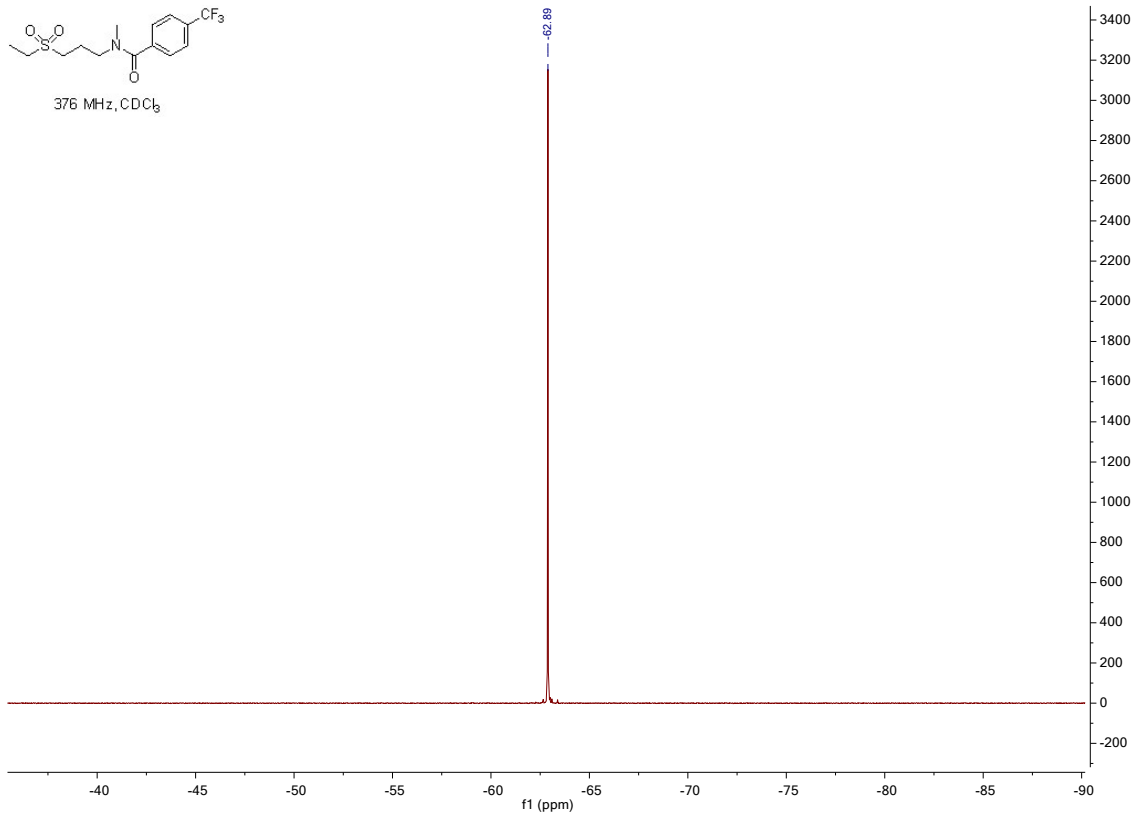

CDCl3, 100 MHz
171.12
49.33
47.51
45.86
36.14
21.82
19.67
6.60
f1 (ppm)

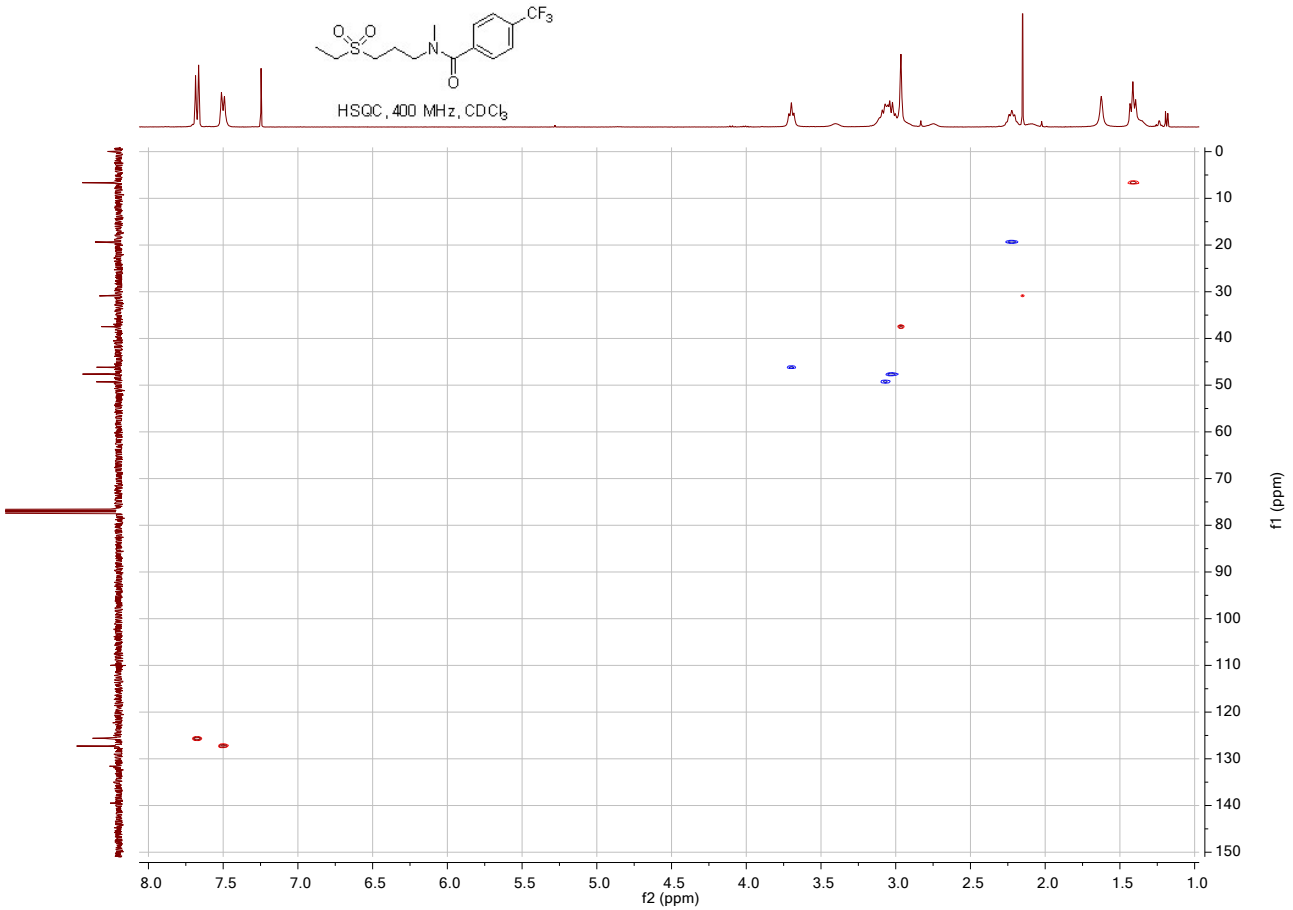

HSQC, CDCl3, 400 MHz
f2 (ppm)
f1 (ppm)

^{1}H, ^{13}C, ^{19}F and HSQC NMR of compound **10m**:






376 MHz, CDCl3
-62.89
f1 (ppm)


HSQC, 400 MHz, CDCl3
f2 (ppm)
f1 (ppm)

^{1}H and ^{13}C NMR of compound **11**: