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Oxidative β-C–H Sulfonylation of Cyclic Amines

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Abstract: A transition metal-free strategy for the dehydrogenative β-sulfonylation of tertiary cyclic amines is described. *N*-iodosuccinimide facilitates regioselective oxidative sulfonylation at C–H bonds positioned β to the nitrogen atom of tertiary amines, installing enaminyl sulfone functionality in cyclic systems. Mild reaction conditions, broad functional group tolerance and a wide substrate scope are demonstrated. The nucleophilic character of the enaminyl sulfone is harnessed, demonstrating potential application for scaffold diversification.

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General Experimental

Solvents and Reagents

Unless otherwise stated:

- Reactions were carried out under an atmosphere of nitrogen at room temperature, and glassware was not dried beforehand. Solvents used were anhydrous.
- Solvents and reagents were purchased from commercial suppliers or obtained from GlaxoSmithKline's internal compound storage and used as received without further purification.
- Reactions were monitored by liquid chromatography-mass spectroscopy (LCMS) and Nuclear Magnetic Resonance (NMR).

Where materials were synthesized in-house, full procedures or literature references to procedures are provided.

Chromatography

Thin layer chromatography (TLC) was carried out using plastic-backed 50 precoated silica plates (particle size 0.2 mm). Spots were visualized by ultraviolet (UV) light (λ_{max} = 254 nm or 365 nm) and then stained with potassium permanganate solution followed by gentle heating. Normal phase silica gel chromatography was carried out using the Teledyne ISCO CombiFlash® Rf+ apparatus with RediSep® silica cartridges. Reverse phase chromatography was carried out using Teledyne ISCO CombiFlash® Rf+ apparatus with Biotage® SNAP KP-C18-HS cartridges.

Liquid Chromatography-Mass Spectrometry (LCMS)

LCMS analysis was carried out on an H_2Os Acquity UPLC instrument equipped with a BEH column (50 mm x 2.1 mm, 1.7 µm packing diameter) and H_2Os micromass ZQ MS using alternate-scan positive and negative electrospray. Analytes were detected as a summed UV wavelength of 210 – 350 nm. Two liquid phase methods were used: was a high pH method:

> **Method A – High pH**: 40 °C, 1 mL/min flow rate. Gradient elution with the as the eluents as (A) 10 mM aqueous ammonium bicarbonate solution, adjusted to pH 10 with 0.88 M aqueous ammonia and (B) acetonitrile. Gradient conditions were initially 1% B, increasing linearly to 97% B over 1.5 min, remaining at 97% B for 0.4 min then increasing to 100% B over 0.1 min.
>
> **Method B** – **Low pH**: 40 °C, 1 mL/min flow rate. Gradient elution with the as the eluents as (A) H_2O containing 0.1% volume/volume (v/v) formic acid and (B) acetonitrile containing 0.1% (v/v) formic acid. Gradient conditions were initially 1% B, increasing linearly to 97% B over 1.5 min, remaining at 97% B for 0.4 min then increasing to 100% B over 0.1 min.

Nuclear Magnetic Resonance (NMR) Spectroscopy

Proton (^{1}H), carbon (^{13}C) and fluorine (^{19}F) spectra were recorded in deuterated solvents at ambient temperature using standard pulse methods on any of the following spectrometers and signal frequencies: Bruker AV-400 (^{1}H = 400 MHz, ^{13}C = 101 MHz) and Bruker AV-600 (^{1}H = 600 MHz, ^{13}C = 151 MHz). Chemical shifts (δ) are reported in ppm and are referenced to the following solvent peaks: $CDCl_3$ (^{1}H = 7.27 ppm, ^{13}C = 77.0 ppm), DMSO-d_6 (^{1}H = 2.50 ppm, ^{13}C = 39.5 ppm) and CD_2Cl_2 (^{1}H = 5.32 ppm, ^{13}C = 53.8 ppm). Peak assignments were made on the basis of chemical shifts, integrations, and coupling constants using COSY, DEPT, HSQC, HMBC, NOESY and ROESY where appropriate. Coupling constants (*J*) are reported in, and quoted to the nearest 0.01 Hz for ^{1}H and 0.1 Hz for ^{13}C, and multiplicities are described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sxt), br. (broad) and multiplet (m).

Infrared (IR) Spectroscopy

IR spectra were recorded using a Perkin Elmer Spectrum 1 machine. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}).

High Resolution Mass Spectrometry (HRMS)

High-resolution mass spectra were recorded on one of two systems:

System A: Micromass Q-Tof Ultima hybrid quadrupole time-of-flight mass spectrometer, with analytes separated on an Agilent 1100 Liquid Chromatograph equipped with a Phenomenex Luna C18 (2) reversed phase column (100 mm x 2.1 mm, 3 µm packing diameter). LC conditions were 0.5 mL/min flow rate, 35 °C, injection volume 2–5 µL, using a gradient elution with (A) H2O containing 0.1% (v/v) formic acid and (B) acetonitrile containing 0.1% (v/v) formic acid. Gradient conditions were initially 5% B, increasing linearly to 100% B over 6 min, remaining at 100% B for 2.5 min then decreasing linearly to 5% B over 1 min followed by an equilibration period of 2.5 min prior to the next injection.

System B: Waters XEVO G2-XS quadrupole time-of-flight mass spectrometer, with analytes separated on an Acquity UPLC CSH C18 column (100mm x 2.1mm, 1.7µm packing diameter). LC conditions were 0.8 mL/min flow rate, 50 °C, injection volume 0.2 µL, using a gradient elution with (A) H2O containing 0.1% (v/v) formic acid and (B) acetonitrile containing 0.1% (v/v) formic acid. Gradient conditions were initially 3% B, increasing linearly to 100% B over 8.5 min, remaining at 100% B for 0.5 min then decreasing linearly to 3% B over 0.5 min followed by an equilibration period of 0.5 min prior to the next injection.

Mass to charge ratios (m/z) are reported in Daltons.

Mass-Directed Automated Preparation (MDAP)

MDAP was carried out using a Waters ZQ MS, using alternate-scan positive and negative electrospray and a summed UV wavelength of 210–350 nm. Two liquid phase methods were used:

Formic – Xselect C18 column (150 mm x 30 mm, 5 µm packing diameter, 40 mL/min flow rate). Gradient elution occurred at ambient temperature with the eluents as (A) H_2O containing 0.1% volume/volume (v/v) formic acid and (B) acetonitrile containing 0.1% (v/v) formic acid.

High pH – Xselect C18 column (150 mm x 30 mm, 5 µm packing diameter, 40 mL/min flow rate). Gradient elution occurred at ambient temperature with the eluents as (A) 10 mM aqueous ammonium bicarbonate solution, adjusted to pH 10 with aqueous ammonia and (B) acetonitrile.

The elution gradients used were at a flow rate of 40 mL/min over 20 or 30 min depending on separation:

Method A	5-30% B
Method B	15-55% B
Method C	30-85% B
Method D	50-99% B
Method E	80-99% B

Hydrophobic frit cartridges by ISOLUTE® contain a frit which is selectively permeable to organic solutions. These are separated from aqueous phase under gravity. Various cartridge sizes were used.

Oxidative *β*-C–H sulfonylation

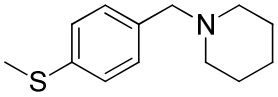
Table S1: Optimization of conditions

Entry	Eq **1a**	Equiv *p*-TolSO$_2$Na	Equiv [O]	Reaction conditions[a]	**%2a**[b]
1	1	3	4, NIS	RT, 0.5 h actv[c], 3h, 2:1 THF[d]:water, 5 eq $NaHCO_3$	43
2	1	3	4, NIS	RT, 0.5 h actv, 3h, 2:1 DMSO:water, 5 eq $NaHCO_3$	38
3	1	3	4, NIS	RT, 0.5 h actv, 3h, 2:1 DCM:water, 5 eq $NaHCO_3$	28
4	1	3	4, NIS	RT, 0.5 h actv, 3h, 2:1 EtOH:water, 5 eq $NaHCO_3$	-
5	1	3	4, NIS	RT, 0.5 h actv, 3h, THF[d]	22
6	1	3	4, NIS	RT, 0.5 h actv, 3h, MeTHF	11
7	1	3	4, NIS	RT, 0.5 h actv, 3h, DMF	27
8	1	3	4, NIS	RT, 0.5 h actv, 2h, MeCN	27
9	1	3	4, NIS	RT, 0.5 h actv, 2h, DCM	27
10	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO	60
11	1	3	4, NIS	15 °C, 0.5 h actv, 24h, DMSO	48
12	1	3	4, NIS	45 °C, 0.5 h actv, 2h, DMSO	38
13	1	3	4, NIS	60 °C, 0.5 h actv, 2h, DMSO	-
14	1	3	4, NIS	RT, 0.5 h actv, 10min, DMSO	40
15	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO, 0.025 M	33
16	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO, 0.5 M	51
17	1	3	4, I_2	RT, 0.5 h actv, 2h, DMSO	trace
18	1	3	4, NBS	RT, 0.5 h actv, 2h, DMSO	10
19	1	3	4, NCS	RT, 0.5 h actv, 2h, DMSO	-
20	1	3	4, ICl	RT, 0.5 h actv, 2h, DMSO	-
21	1	3	4, NIS	RT, 2 h, DMSO	trace
22	1	3	4, NIS	RT, 0.5 h rev-actv[e], 2h, DMSO	trace
23	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO, slow addition of RSO_2Na	trace
24[f]	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO	36
25[g]	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO	71
26	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO, N_2	76
27	1	3	4, NIS	RT, 0.5 h actv, 2h, DMSO, N_2, dark	81
28	1	1.5	4, NIS	RT, 0.5 h actv, 2h, DMSO, N_2, dark	31

29	1	3	4, NIS	RT, 0.5 h actv, 2h, THF[h], N_2, dark	95
30	1	3	4, NIS	RT, 0.5 h actv, 2h, 2-MeTHF, N_2, dark	65
31	1	1.5	3, NIS	RT, 0.5 h actv, 2h, THF[h], N_2, dark	53
32	***1***	***1.5***	***4, NIS***	***RT, 0.5 h actv, 2h, THF[h], N_2, dark***	***90***
33	1	1.5[i]	4, NIS	RT, 0.5 h actv, 2h, THF[h], N_2, dark	71

[a]Reaction conditions: **1a** (1.0 eq), [O], solvent, 0.5 h, *then* *p*-TolSO$_2$Na, solvent (0.063 M), T, 2h. [b]% conversion to **2a** measured by analysis of the crude material against 3,4,5-trichloropyridine as an internal standard. [c]"actv" refers to the pre-stirring of oxidant with **1a**. [d]THF contained 250 ppm BHT radical inhibitor. [e]"rev-actv" refers to the pre-stirring of oxidant with *p*-TolSO$_2$Na. [f]Reaction carried on 35 mg of **1a** scale. [g]Reaction carried on 500 mg of **1a** scale. [h]THF was inhibitor-free. [i] *p*-TolSO$_2$Li was used as the sulfinate salt instead.

Synthesis of starting materials



1-(4-(Methylthio)benzyl)piperidine 3c

$MgSO_4$ (0.85 g, 7.05 mmol) was added to a solution of piperidine (1.16 mL, 11.7 mmol), 4-(methylthio)benzaldehyde (1.56 mL, 11.7 mmol) and DIPEA (6.15 ml, 35.2 mmol) in THF (30 mL). The resulting suspension was stirred at RT for 5 min before addition of sodium triacetoxyborohydride (4.98 g, 23.5 mmol). The resulting reaction mixture was stirred at RT for 20 h. The reaction solvent was removed *in vacuo*, and the residue was suspended in DCM (20 mL). The solution was washed with sat. aq. $NaHCO_3$ (20 mL), the aqueous layer washed with DCM (20 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography using 0-20% 3:1 EtOAc:EtOH (with 1% Et_3N modifier)/cyclohexane as the eluent, to afford **3c** (1.90 g, 73 % yield) as a yellow oil.

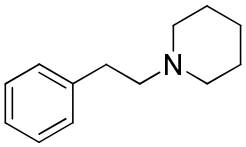
LCMS (High pH, UV, ESI) R_t = 1.27 min, $[M+H]^+$ m/z = 222.1

^1H NMR (400 MHz, $CDCl_3$) δ 7.19-7.27 (m, 4H), 3.43 (s, 2H), 2.49 (s, 3H), 2.33-2.41 (m, 4H), 1.57 (quin, *J*=5.6, 4H), 1.39-1.48 (m, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 135.8, 129.7, 126.7, 63.3, 54.4, 26.0, 24.4, 16.1

ν_{max} (thin film): 2932, 1493, 1343

HRMS: Calculated for $C_{13}H_{20}NS$ $[M+H]^+$ m/z = 222.1316, found m/z = 222.1318 (0.9 ppm).



1-Phenethylpiperidine 3e

$MgSO_4$ (0.85 g, 7.05 mmol) was added to a solution of piperidine (1.16 mL, 11.7 mmol), 2-phenylacetaldehyde (1.41 g, 11.7 mmol) and DIPEA (6.15 ml, 35.2 mmol) in THF (75 mL). The resulting suspension was stirred at RT for 5 min before addition of sodium triacetoxyborohydride (4.98 g, 23.5 mmol). The resulting reaction mixture was stirred at RT for 20 h. The reaction solvent was removed *in vacuo*, and the residue was suspended in DCM (20 mL). The solution was washed with sat. aq. $NaHCO_3$ (20 mL), the aqueous layer washed with DCM (20 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography using 0-20% 3:1 EtOAc:EtOH (with % Et_3N modifier)/cyclohexane as the eluent, to afford **3e** (0.31 g, 14 % yield) as a yellow oil.

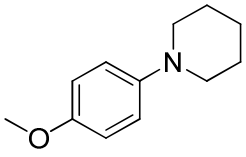
LCMS (High pH, UV, ESI) R_t = 1.12 min, $[M+H]^+$ m/z = 190.2

^1H NMR (400 MHz, CD_2Cl_2) δ 7.23-7.30 (m, 2H), 7.14-7.22 (m, 3H), 2.72-2.80 (m, 2H), 2.48-2.55 (m, 2H), 2.36-2.48 (m, 4H), 1.57 (dt, *J*=11.2, 5.5, 4H), 1.39-1.48 (m, 2H)

^{13}C NMR (101 MHz, CD_2Cl_2) δ 141.7, 129.3, 128.8, 126.3, 61.8, 55.1, 34.1, 26.7, 25.2

ν_{max} (thin film): 2932, 1452, 1154

HRMS: Calculated for $C_{13}H_{20}N$ $[M+H]^+$ m/z = 190.1596, found m/z = 190.1601 (2.6 ppm).



1-(4-Methoxyphenyl)piperidine 3m

A solution of 4-methoxyaniline (1.00 g, 8.12 mmol) in MeCN (9 mL) was added to a mixture of 1,5-dibromopentane (2.28 mL, 16.2 mmol) and potassium carbonate (4.5 g, 32.5 mmol) in MeCN (16 mL), and the reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was filtered through a sintered funnel, and the filtrate was concentrated *in vacuo*. The crude material was purified by silica gel chromatography using 0-30% 3:1 EtOAc:EtOH (with 1% Et_3N modifier)/cyclohexane as the eluent to afford **3m** (0.86 g, 55 %) as a yellow oil.

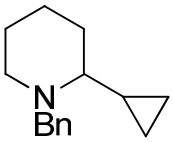
LCMS (High pH, UV, ESI) R_t = 1.17 min, $[M+H]^+$ m/z = 192.1

^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.85-6.90 (m, 2H), 6.77-6.82 (m, 2H), 3.74 (s, 3H), 3.00 (t, *J*=5.6, 4H), 1.70 (quin, *J*=5.7, 4H), 1.50-1.58 (m, 2H)

^{13}C NMR (101 MHz, CD_2Cl_2) δ 154.1, 147.7, 119.1, 114.8, 56.0, 52.7, 26.8, 24.9

ν_{max} (thin film): 2929, 1508, 1231, 1039

HRMS: Calculated for $C_{12}H_{18}NO$ $[M+H]^+$ m/z = 192.1388, found m/z = 192.1392 (2.1 ppm).



1-Benzyl-2-cyclopropylpiperidine 3p

A mixture of 2-cyclopropylpiperidine (210 mg, 1.70 mmol), benzyl bromide (185 µL, 1.56 mmol) and potassium carbonate (650 mg, 4.70 mmol) were heated to 80 °C for 16 h. The crude reaction mixture was filtered through a sintered funnel, and the filtrate concentrated under reduced pressure. The crude material was purified by silica gel chromatography using 0-30% TBME/cyclohexane as the eluant, to afford **3p** (199.9 mg, 60%) as a yellow oil.

LCMS (Method A, UV, ESI) R_t = 1.41 min, $[M+H]^+$ 216.2

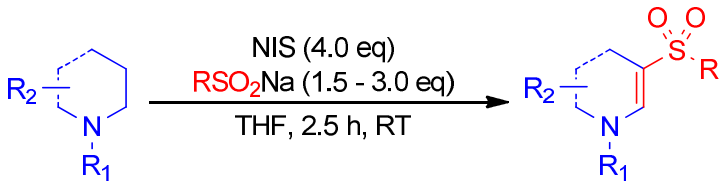
^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.25-7.34 (m, 4H), 7.17-7.23 (m, 1H), 4.50 (d, *J*=13.7 Hz, 1H), 3.02 (d, *J*=13.4 Hz, 1H), 2.64 (dtd, *J*=11.6, 4.0, 1.5 Hz, 1H), 1.82 (td, *J*=10.9, 3.1 Hz, 1H), 1.71-1.78 (m, 1H), 1.66 (dquin, *J*=12.2, 4.0 Hz, 1H), 1.39-1.47 (m, 2H), 1.28-1.39 (m, 2H), 1.22 (qt, *J*=11.0, 3.4 Hz, 1H), 0.76 (qt, *J*=8.4, 4.9 Hz, 1H), 0.62 (dddd, *J*=9.3, 7.9, 5.6, 4.2 Hz, 1H), 0.37-0.46 (m, 1H), 0.27 (dt, *J*=13.4, 5.1 Hz, 1H), 0.03 (td, *J*=9.5, 5.0 Hz, 1H)

^{13}C NMR (DMSO-d_6, 101 MHz): δ 140.4, 128.3, 128.0, 126.3, 67.0, 58.0, 51.6, 32.2, 25.2, 23.7, 14.5, 7.5, 1.1

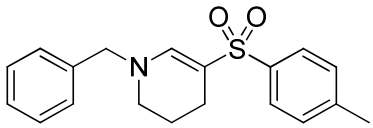
IR ν_{max} (cm^{-1}) (thin film): 2932, 1495

HRMS: Calculated for $C_{15}H_{22}N$ 216.1752, found $[M+H]^+$: 216.1753 (0.5 ppm).

General procedure.



Amine **1** or **3** (1.0 eq) was added to a solution of *N*-iodosuccinimide (4.0 eq) in degassed inhibitor-free THF (0.11 M) shielded from light, and the resultant reaction mixture was stirred at RT for 30 min. This reaction mixture was then transferred *via* syringe to a suspension of sodium sulfinate salt (1.5 eq) in inhibitor-free THF (0.29 M), shielded from light, and inhibitor-free THF was used to wash the first reaction vial to ensure complete transfer to give a resulting reaction concentration of 0.063 M. The reaction was stirred at RT for 2 h. Upon completion of the reaction, the reaction mixture was quenched with saturated aqueous sodium thiosulfate (10 mL) and saturated aqueous sodium bicarbonate (10 mL). The solution was extracted in ethyl acetate (2 x 20 mL) and the combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. Conversion to product was quantified *via* ^{1}H NMR analysis of the crude material together with a known amount of internal standard 3,4,5-trichloropyridine (aryl 2H singlet at 8.51 ppm in $CDCl_3$) or dibromomethane (2H singlet at 4.92 ppm in $CDCl_3$). The crude material was then purified as described to afford enaminyl sulfone **2** or **4**.



1-Benzyl-5-tosyl-1,2,3,4-tetrahydropyridine 2a

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.132 mmol) as a standard showed 90% conversion to **2a**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2a** (157.4 mg, 84%) as an off-white solid.

LCMS (High pH, UV, ESI) R_t = 1.23 min, $[M+H]^+$ m/z = 328.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63 (d, *J*=8.3, 2H), 7.54 (s, 1H), 7.34-7.42 (m, 4H), 7.28-7.33 (m, 1H), 7.26 (d, *J*=8.3, 2H), 4.43 (s, 2H), 2.94 (t, *J*=5.4, 2H), 2.38 (s, 3H), 2.00 (t, *J*=6.0, 2H), 1.64 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 144.4, 141.9, 140.2, 137.2, 129.5, 128.6, 127.5, 127.5, 126.1, 99.4, 58.1, 44.6, 20.9, 20.4, 19.3

ν_{max} (thin film): 2936, 1618, 1280, 1134, 1094

HRMS: Calculated for $C_{19}H_{22}NO_2S$ $[M+H]^+$ m/z = 328.1371, found m/z = 328.1374 (0.9 ppm).

5.4 mmol scale preparation of 2a:

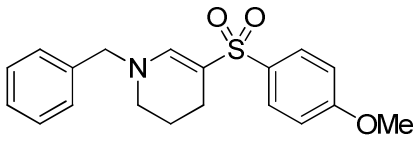
N-iodosuccinimide (4.88 g, 21.7 mmol) was reacted with 1-benzylpiperidine (0.95 g, 5.42 mmol) and sodium 4-methylbenzenesulfinate (1.45 g, 8.13 mmol) in THF (86 mL) as per the

general procedure. The crude material was purified by silica gel chromatography using 0-50% EtOAc/cyclohexane as the eluent to afford **2a** (1.33 g, 75%) as an off-white solid.

LCMS (High pH, UV, ESI) R_t = 1.22 min, $[M+H]^+$ m/z = 328.1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J*=8.3, 2H), 7.51 (s, 1H), 7.25-7.40 (m, 5H), 7.18-7.23 (m, *J*=8.2, 1.6, 2H), 4.30 (s, 2H), 2.92-3.01 (m, *J*=5.6, 5.6, 1H), 2.41 (s, 3H), 2.17 (t, *J*=6.2, 2H), 1.76 (quin, *J*=6.0, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 142.3, 139.8, 136.5, 129.4, 128.8, 127.9, 127.5, 126.9, 101.1, 59.7, 45.0, 21.5, 21.0, 19.7



1-Benzyl-5-((4-methoxyphenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2b

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-methoxybenzenesulfinate (222 mg, 1.15 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.130 mmol) as a standard showed 68% conversion to **2b**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2b** (120.8 mg, 62%) as a white solid.

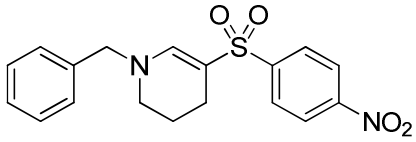
LCMS (High pH, UV, ESI) R_t = 1.17 min, $[M+H]^+$ m/z = 344.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (d, *J*=8.8, 2H), 7.51 (s, 1H), 7.38 (t, *J*=7.1, 2H), 7.30 (tt, *J*=7.3, 2.2, 1H), 7.25 (d, *J*=8.1, 2H), 7.07 (d, *J*=8.8, 2H), 4.41 (s, 2H), 3.83 (s, 3H), 2.93 (t, *J*=5.4, 2H), 1.99 (t, *J*=6.1, 2H), 1.63 (quin, *J*=5.8, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 161.7, 144.0, 137.3, 134.7, 128.6, 128.2, 127.5, 127.5, 114.2, 99.9, 58.1, 55.5, 44.6, 20.4, 19.3

ν_{max} (thin film): 2929, 1620, 1497, 1277, 1256, 1133, 1094

HRMS: Calculated for $C_{19}H_{22}NO_3S$ $[M+H]^+$ m/z = 344.1320, found m/z = 344.1322 (0.6 ppm).



1-Benzyl-5-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2c

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-nitrobenzenesulfinate (179 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.136 mmol) as a standard showed 71% conversion to **2c**. The crude material was purified by silica gel chromatography using 0-25% EtOAc/cyclohexane as the eluent to afford **2c** (128.1 mg, 63%) as a yellow solid.

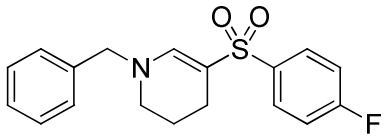
LCMS (High pH, UV, ESI) R_t = 1.20 min, $[M+H]^+$ m/z = 359.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (d, *J*=9.0, 2H), 7.99 (d, *J*=9.0, 2H), 7.68 (s, 1H), 7.35-7.41 (m, 2H), 7.31 (tt, *J*=7.3, 2.2, 1H), 7.26 (d, *J*=8.3, 2H), 4.47 (s, 2H), 2.97 (t, *J*=5.4, 2H), 2.05 (t, *J*=6.1, 2H), 1.65 (quin, *J*=5.8, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 149.1, 148.8, 146.2, 136.9, 128.6, 127.6, 127.5, 127.5, 124.5, 97.2, 58.3, 44.6, 20.2, 19.2

ν_{max} (thin film): 2935, 1615, 1525, 1347, 1293, 1136, 1094

HRMS: Calculated for $C_{18}H_{19}N_2O_4S$ $[M+H]^+$ m/z = 359.1066, found m/z = 359.1066 (0 ppm).



1-Benzyl-5-((4-fluorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2d

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-fluorobenzenesulfinate (156 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.136 mmol) as a standard showed 69% conversion to **2d**. The crude material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **2d** (104.4 mg, 55%) as an off-white solid.

LCMS (High pH, UV, ESI) R_t = 1.19 min, $[M+H]^+$ m/z = 332.1

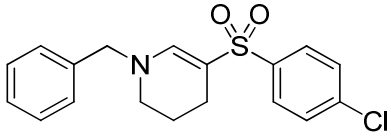
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77-7.83 (m, 2H), 7.58 (s, 1H), 7.35-7.42 (m, 4H), 7.30 (tt, *J*=7.3, 2.2, 1H), 7.25 (d, *J*=8.3, 2H), 4.43 (s, 2H), 2.94 (t, *J*=5.4, 2H), 2.01 (t, *J*=6.1, 2H), 1.64 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.7 (d, $^1J_{C-F}$=253.1), 144.8, 139.5 (d, $^4J_{C-F}$=2.9), 137.0, 129.0 (d, $^3J_{C-F}$=9.5), 128.6, 127.5 (2C), 116.1 (d, $^2J_{C-F}$=22.0), 98.7, 58.1, 44.5, 20.3, 19.3

^{19}F NMR ($CDCl_3$, 376MHz): δ -107.34 (s, 1F)

ν_{max} (thin film): 2935, 1619, 1493, 1282, 1135, 1094

HRMS: Calculated for $C_{18}H_{19}FNO_2S$ $[M+H]^+$ m/z = 332.1121, found m/z = 332.1120 (-0.3 ppm).



1-Benzyl-5-((4-chlorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2e

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-chlorobenzenesulfinate (170 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.112 mmol) as a standard showed 78% conversion to **2e**. The crude material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **2e** (124.7 mg, 63%) as an off-white solid.

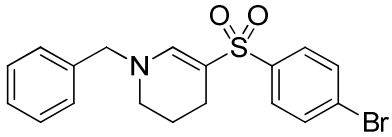
LCMS (High pH, UV, ESI) R_t = 1.27 min, $[M+H]^+$ m/z = 348.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71-7.77 (m, 2H), 7.60-7.65 (m, 2H), 7.59 (s, 1H), 7.35-7.41 (m, 2H), 7.28-7.34 (m, 1H), 7.25 (d, *J*=6.8, 2H), 4.44 (s, 2H), 2.94 (t, *J*=5.9, 2H), 2.01 (t, *J*=6.0, 2H), 1.64 ppm (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 145.1, 142.0, 137.1, 136.5, 129.1, 128.6, 128.0, 127.7, 127.5, 98.3, 58.2, 44.6, 20.3, 19.3

v_{max} (thin film): 2940, 1616, 1273, 1171, 1136, 1093, 1010

HRMS: Calculated for $C_{18}H_{19}ClNO_2S$ $[M+H]^+$ m/z = 348.0825, found m/z = 348.0827 (0.6 ppm).



1-Benzyl-5-((4-bromophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2f

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 4-bromobenzenesulfinate dihydrate (239 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.123 mmol) as a standard showed 98% conversion to **2f**. The crude material was purified by silica gel chromatography using 0-15% EtOAc/cyclohexane as the eluent to afford **2f** (177.6 mg, 79%) as an off-white solid.

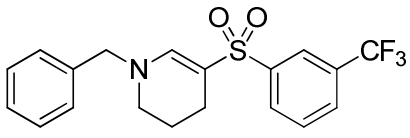
LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ m/z = 391.9 (^{79}Br), 393.9 (^{81}Br)

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75-7.79 (m, 2H), 7.63-7.70 (m, 2H), 7.59 (s, 1H), 7.35-7.40 (m, 2H), 7.27-7.33 (m, 1H), 7.23-7.27 (m, 2H), 4.44 (s, 2H), 2.94 (t, *J*=5.6, 2H), 2.01 (t, *J*=6.0, 2H), 1.64 ppm (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 145.1, 142.4, 137.1, 132.1, 128.6, 128.1, 127.5, 125.4, 111.4, 98.3, 58.2, 44.5, 20.3, 19.2

v_{max} (thin film): 2935, 1616, 1172, 1133, 1093, 1008

HRMS: Calculated for $C_{18}H_{19}BrNO_2S$ [M+H] m/z = 392.0320, found m/z = 392.0317 (-0.8 ppm).



1-Benzyl-5-((3-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2g

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 3-(trifluoromethyl)benzenesulfinate (199 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.147 mmol) as a standard showed 91% conversion to **2g**. The crude

material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **2g** (174.5 mg, 80%) as a white solid.

LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ m/z = 382.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03-8.10 (m, 1H), 7.94-8.01 (m, 2H), 7.79-7.87 (m, 1H), 7.69 (s, 1H), 7.33-7.40 (m, 2H), 7.28-7.33 (m, 1H), 7.24-7.27 (m, 2H), 4.46 (s, 2H), 2.96 (t, *J*=5.4, 2H), 2.03 (t, *J*=6.1, 2H), 1.64 (quin, *J*=5.8, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 145.9, 144.6, 137.0, 130.7, 130.1, 129.7 (q, $^2J_{C-F}$=32.3), 128.6, 128.4 (q, $^3J_{C-F}$=3.7), 127.5, 127.5, 122.3 (q, $^3J_{C-F}$=4.2), 122.1 (q, $^1J_{C-F}$=272.9), 97.5, 58.2, 44.5, 20.3, 19.2

^{19}F NMR ($CDCl_3$, 376MHz): δ -62.75 (s, 1F)

v_{max} (thin film): 2929, 2850, 1617, 1427, 1326

HRMS: Calculated for $C_{19}H_{19}F_3NO_2S$ $[M+H]^+$ m/z = 382.1089, found m/z = 382.1092 (0.8 ppm).

3.75 mmol scale preparation of 2g:

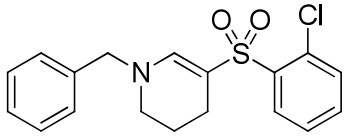
N-iodosuccinimide (3.38 g, 15.0 mmol) was reacted with 1-benzylpiperidine (0.66 g, 3.75 mmol) and sodium 3-(trifluoromethyl)benzenesulfinate (1.31 g, 5.63 mmol) in THF (36.5 mL) as per the general procedure. The crude material was purified by silica gel chromatography using 20-50% EtOAc/cyclohexane as the eluent to afford **2g** (0.99 g, 70%) as an white solid.

LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ m/z = 382.1

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.05 (d, *J*=7.8, 1H), 7.78 (d, *J*=8.1, 1H), 7.60-7.67 (m, 1H), 7.56 (s, 1H), 7.30-7.42 (m, 3H), 7.21 (d, *J*=6.4, 2H), 4.35 (s, 2H), 2.96-3.04 (t, *J*=5.7, 2H), 2.19 (t, *J*=6.2, 2H), 1.80 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 144.2, 136.1, 131.5 (q, $^2J_{C-F}$=33.0), 130.0, 129.5, 128.9, 128.3 (q, $^3J_{C-F}$=3.7), 128.1, 127.4, 123.8 (q, $^3J_{C-F}$=3.9), 123.4 (q, $^1J_{C-F}$=272.2), 99.5, 59.9, 45.0, 20.9, 19.6

^{19}F NMR ($CDCl_3$, 376MHz): δ -62.75 (s, 1F)



1-Benzyl-5-((2-chlorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2h

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium 2-chlorobenzenesulfinate (170 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.138 mmol) as a standard showed 73% conversion to **2h**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2h** (124.3 mg, 63%) as a yellow solid.

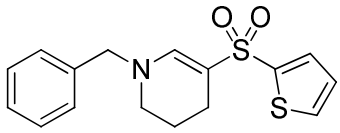
LCMS (High pH, UV, ESI) R_t = 1.23 min, $[M+H]^+$ m/z = 348.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, *J*=7.6, 1H), 7.57-7.65 (m, 3H), 7.50-7.56 (m, 1H), 7.36-7.42 (m, 2H), 7.26-7.34 (m, 3H), 4.49 (s, 2H), 3.00 (t, *J*=5.4, 2H), 1.94 (t, *J*=6.1, 2H), 1.64 (quin, *J*=5.8, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 147.2, 138.7, 137.1, 133.6, 131.9, 130.7, 130.5, 128.6, 127.6, 127.5, 127.4, 95.9, 58.3, 44.7, 20.4, 19.2

v_{max} (thin film): 2919, 1618, 1453, 1296, 1139

HRMS: Calculated for $C_{18}H_{19}ClNO_2S$ $[M+H]^+$ m/z = 348.0825, found m/z = 348.0825 (0 ppm).



1-Benzyl-5-(thiophen-2-ylsulfonyl)-1,2,3,4-tetrahydropyridine 2i

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium thiophene-2-sulfinate (146 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.153 mmol) as a standard showed 80% conversion to **2i**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2i** (132.1 mg, 73%) as a colourless oil.

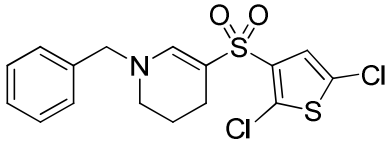
LCMS (High pH, UV, ESI) R_t = 1.15 min, $[M+H]^+$ m/z = 320.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (dd, *J*=5.0, 1.3, 1H), 7.57 (s, 1H), 7.49 (dd, *J*=3.7, 1.2, 1H), 7.35-7.40 (m, 2H), 7.28-7.33 (m, 1H), 7.23-7.27 (m, 2H), 7.13 (dd, *J*=5.1, 3.7, 1H), 4.45 (s, 2H), 2.97 (t, *J*=5.4, 2H), 2.10 (t, *J*=6.1, 2H), 1.68 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 145.3, 144.6, 137.1, 131.9, 130.5, 128.6, 127.6, 127.5, 127.5, 99.5, 58.1, 44.6, 20.3, 19.3

v_{max} (thin film): 2935. 1617, 1293, 1127, 1019

HRMS: Calculated for $C_{16}H_{18}NO_2S_2$ $[M+H]^+$ m/z = 320.0779, found m/z = 320.0781 (0.6 ppm).



1-Benzyl-5-((2,5-dichlorothiophen-3-yl)sulfonyl)-1,2,3,4-tetrahydropyridine 2j

N-iodosuccinimide (180 mg, 0.80 mmol) was reacted with 1-benzylpiperidine (35 mg, 0.20 mmol) and sodium 2,5-dichlorothiophene-3-sulfinate (96 mg, 0.40 mmol) in THF (3 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.113 mmol) as a standard showed 66% conversion to **2j**. The crude material was purified by silica gel chromatography using 0-40% TBME/cyclohexane as the eluent to afford **2j** (50.6 mg, 65%) as an off-white gum.

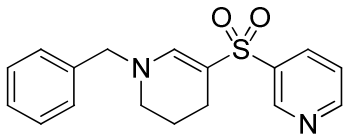
LCMS (High pH, UV, ESI) R_t = 1.37 min, $[M+H]^+$ m/z = 388.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (s, 1H), 7.35-7.40 (m, 2H), 7.28-7.33 (m, 1H), 7.24-7.28 (m, 3H), 4.47 (s, 2H), 3.01 (t, *J*=5.4, 2H), 2.09 (t, *J*=6.1, 2H), 1.69 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 146.4, 139.5, 136.9, 128.6, 127.6, 127.3, 127.0, 125.6 (2C), 97.5, 58.3, 44.7, 20.3, 19.1

ν_{max} (thin film): 2929, 1615, 1424, 1316, 1120, 1038

HRMS: Calculated for $C_{16}H_{16}Cl_2NO_2S_2$ [M+H] m/z = 388.0000, found m/z = 387.9997 (-0.8 ppm).



3-((1-Benzyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)pyridine 2k

N-iodosuccinimide (180 mg, 0.80 mmol) was reacted with 1-benzylpiperidine (35 mg, 0.20 mmol) and pyridine-3-sulfinic acid hydrochloride (75 mg, 0.42 mmol) in THF (3 mL) as per the general procedure, with the following modifications: sodium hydride (60 wt% in mineral oil, 35.4 mg, 0.884 mmol) was mixed with the sulfinic acid hydrochloride in THF (0.5 mL) to generate sodium pyridine-3-sulfinate *in situ*. The vial was then sealed and the suspension left to stir for 10 minutes at RT under a positive pressure of N_2 gas before the amine-iodination reaction solution was injected into the vial containing the sulfinate mixture, and the reaction stirred at RT for 2 h. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.171 mmol) as a standard showed 55% conversion to **2k**. The crude material was purified by silica gel chromatography using 80-100% TBME/cyclohexane as the eluent to afford **2k** (32.2 mg, 51%) as a colourless oil.

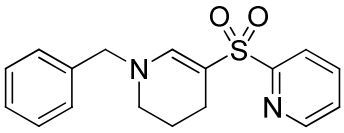
LCMS (High pH, UV, ESI) R_t = 0.99 min, $[M+H]^+$ m/z = 315.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.90 (dd, *J*=2.3, 0.6, 1H), 8.77 (dd, *J*=4.8, 1.6, 1H), 8.12 (ddd, *J*=8.1, 2.4, 1.6, 1H), 7.65 (s, 1H), 7.60 (ddd, *J*=8.1, 4.9, 0.7, 1H), 7.35-7.40 (m, 2H), 7.28-7.33 (m, 1H), 7.24-7.28 (m, 2H), 4.46 (s, 2H), 2.96 (t, *J*=5.4, 2H), 2.05 (t, *J*=6.1, 2H), 1.65 (quin, *J*=6.1, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 152.3, 146.8, 145.7, 139.3, 137.0, 134.0, 128.6, 127.5, 124.1, 111.5, 98.0, 58.2, 44.6, 20.3, 19.2

ν_{max} (thin film): 2935, 1616, 1292, 1142, 1103, 1014

HRMS: Calculated for $C_{17}H_{19}N_2O_2S$ $[M+H]^+$ m/z = 315.1167, found m/z = 315.1165 (-0.6 ppm).



2-((1-Benzyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)pyridine 2l

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium pyridine-2-sulfinate[1] (293 mg, 1.14 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against dibromomethane (0.215 mmol) as a standard showed 22% conversion to **2l**. The crude material was purified by silica gel chromatography using 0-80% 3:1 EtOAc:EtOH (with 1% Et_3N modifier)/cyclohexane as the eluent to afford **2l** (43.1 mg, 24%) as an orange oil.

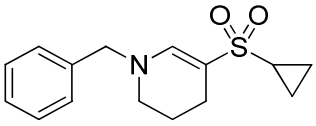
LCMS (High pH, UV, ESI) R_t = 1.00 min, $[M+H]^+$ m/z = 315.0

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.72 (ddd, *J*=4.6, 1.7, 0.7, 1H), 8.06 (dt, *J*=7.8, 1.0, 1H), 7.88 (td, *J*=7.7, 1.7, 1H), 7.60 (s, 1H), 7.43 (ddd, *J*=7.6, 4.7, 1.3, 1H), 7.29-7.39 (m, 3H), 7.21-7.25 (m, 2H), 4.34 (s, 2H), 2.97-3.01 (m, 2H), 2.31 (t, *J*=6.1, 2H), 1.80 (dt, *J*=11.8, 6.0, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 150.0, 146.6, 137.6, 136.3, 128.8, 128.0, 127.7, 125.7, 121.6, 97.9, 59.9, 45.0, 21.0, 20.0

ν_{max} (thin film): 2931, 1616, 1315, 1110

HRMS: Calculated for $C_{17}H_{19}N_2O_2S$ $[M+H]^+$ m/z = 315.1167, found m/z = 315.1165 (-0.6 ppm).



1-Benzyl-5-(cyclopropylsulfonyl)-1,2,3,4-tetrahydropyridine 2m

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylpiperidine (100 mg, 0.57 mmol) and sodium cyclopropanesulfinate (146 mg, 1.15 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.121 mmol) as a standard showed 74% conversion to **2m**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2m** (107.2 mg, 68%) as a yellow oil.

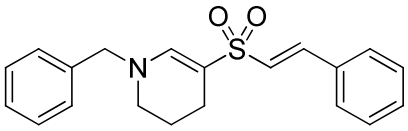
LCMS (High pH, UV, ESI) R_t = 1.02 min, $[M+H]^+$ m/z = 278.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.35-7.41 (m, 2H), 7.28-7.34 (m, 1H), 7.23-7.28 (m, 3H), 4.38 (s, 2H), 2.99 (t, *J*=5.4, 2H), 2.44-2.49 (m, *J*=2.2, 1H), 2.25 (t, *J*=6.1, 2H), 1.77 (quin, *J*=5.9, 2H), 0.83-0.92 (m, 4H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 143.8, 137.4, 128.5, 127.5, 127.4, 100.0, 58.0, 44.6, 31.0, 20.6, 19.9, 4.1

ν_{max} (thin film): 2929, 1621, 1275, 1118

HRMS: Calculated for $C_{15}H_{20}NO_2S$ $[M+H]^+$ m/z = 278.1215, found m/z = 278.1217 (0.7 ppm).



(*E*)-1-Benzyl-5-(styrylsulfonyl)-1,2,3,4-tetrahydropyridine 2n

N-iodosuccinimide (180 mg, 0.80 mmol) was reacted with 1-benzylpiperidine (35 mg, 0.20 mmol) and sodium (*E*)-stryrylsulfinate[2] (76 wt%, 75 mg, 0.30 mmol) in THF (3 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.098 mmol) as a standard showed 57% conversion to **2n**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **2n** (32.0 mg, 47%) as an orange solid.

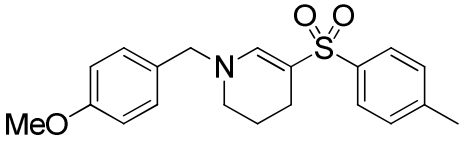
LCMS (High pH, UV, ESI) R_t = 1.23 min, $[M+H]^+$ m/z = 340.1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.52 (m, 2H), 7.29-7.46 (m, 8H), 7.22 (dd, *J*=8.1, 1.5, 2H), 6.72 (d, *J*=15.4, 1H), 4.32 (s, 2H), 3.02 (t, *J*=5.6, 2H), 2.29 (t, *J*=6.2, 2H), 1.86 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 139.5, 136.4, 133.4, 130.2, 128.9, 128.9, 128.1, 128.0, 127.9, 127.5, 99.8, 59.8, 45.1, 21.1, 19.5

ν_{max} (thin film): 2931, 1615, 1276, 1117

HRMS: Calculated for $C_{20}H_{22}NO_2S$ $[M+H]^+$ m/z = 340.1371, found m/z = 340.1367 (-1.2 ppm).



1-(4-Methoxybenzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4a

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-(4-methoxybenzyl)piperidine[3] (117 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.159 mmol) as a standard showed 84% conversion to **4a**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4a** (161.9 mg, 79%) as a white solid.

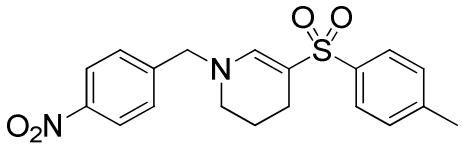
LCMS (High pH, UV, ESI) R_t = 1.22 min, $[M+H]^+$ m/z = 358.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, *J*=8.1, 2H), 7.51 (s, 1H), 7.35 (d, *J*=8.1, 2H), 7.19 (d, *J*=8.8, 2H), 6.93 (d, *J*=8.8, 2H), 4.33 (s, 2H), 3.75 (s, 3H), 2.91 (t, *J*=5.4, 2H), 2.37 (s, 3H), 1.97 (t, *J*=6.1, 2H), 1.61 (quin, *J*=6.1, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 158.7, 144.2, 141.8, 140.2, 129.4 (2C), 129.0, 126.1, 114.0, 99.1, 57.6, 55.0, 44.3, 20.9, 20.4, 19.4

ν_{max} (thin film): 2934, 1619, 1513, 1280, 1249, 1172, 1134, 1093

HRMS: Calculated for $C_{20}H_{24}NO_3S$ $[M+H]^+$ m/z = 358.1477, found m/z = 358.1479 (0.6 ppm).



1-(4-Nitrobenzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4b

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-(4-nitrobenzyl)piperidine[3] (126 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.217 mmol) as a standard showed 79% conversion to **4b**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4b** (138.8 mg, 65%) as a yellow solid.

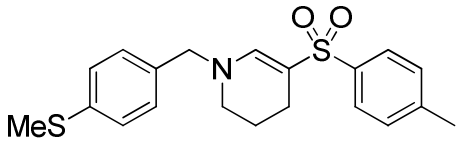
LCMS (High pH, UV, ESI) R_t = 1.19 min, $[M+H]^+$ m/z = 373.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, *J*=8.8, 2H), 7.63 (d, *J*=8.1, 2H), 7.58 (s, 1H), 7.53 (d, *J*=8.8, 2H), 7.37 (d, *J*=8.1, 2H), 4.60 (s, 2H), 2.95 (t, *J*=5.4, 2H), 2.38 (s, 3H), 2.01 (t, *J*=6.1, 2H), 1.66 (quin, *J*=5.8, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 146.9, 145.4, 144.3, 142.0, 140.0, 129.5, 128.6, 126.2, 123.7, 100.4, 57.2, 44.8, 20.9, 20.4, 19.3

v_{max} (thin film): 2935, 1622, 1520, 1345, 1280, 1136, 1094, 1014

HRMS: Calculated for $C_{19}H_{21}N_2O_4S$ $[M+H]^+$ m/z = 373.1222, found m/z = 373.1221 (-0.3 ppm).



1-(4-(Methylthio)benzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4c

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with **3c** (126 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.121 mmol) as a standard showed 87% conversion to **4c**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4c** (178.3 mg, 84%) as an off-white solid.

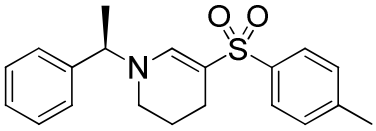
LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ m/z = 374.2

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, *J*=8.3, 2H), 7.52 (s, 1H), 7.36 (d, *J*=8.1, 2H), 7.26 (d, *J*=8.3, 2H), 7.20 (d, *J*=8.6, 2H), 4.37 (s, 2H), 2.91 (t, *J*=5.4, 2H), 2.47 (s, 3H), 2.37 (s, 3H), 1.98 (t, *J*=6.1, 2H), 1.62 (quin, *J*=5.6, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 144.2, 141.9, 140.1, 137.3, 133.8, 129.5, 128.3, 126.1, 126.1, 99.4, 57.6, 44.5, 20.9, 20.4, 19.3, 14.6

v_{max} (thin film): 2919, 1619, 1280, 1135, 1093, 1013

HRMS: Calculated for $C_{20}H_{24}NO_2S_2$ $[M+H]^+$ m/z = 374.1248, found m/z = 374.1248 (0 ppm).



(*R*)-1-(1-Phenylethyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4d

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with (*R*)-1-(1-phenylethyl)piperidine[3] (108 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.158 mmol) as a standard showed 96% conversion to **4d**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4d** (182.2 mg, 94%) as a white solid.

LCMS (High pH, UV, ESI) R_t = 1.26 min, $[M+H]^+$ m/z = 342.0

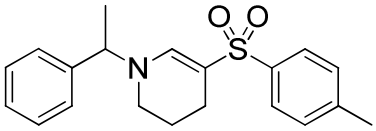
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.62 (d, *J*=8.3, 2H), 7.53 (s, 1H), 7.33-7.41 (m, 4H), 7.26-7.32 (m, 3H), 4.68 (q, *J*=6.8, 1H), 2.93 (ddd, *J*=12.7, 7.6, 3.9, 1H), 2.82 (ddd, *J*=12.7, 6.6, 3.9, 1H), 2.36 (s, 3H), 1.99 (t, *J*=6.1, 2H), 1.54-1.66 (m, 2H), 1.52 (d, *J*=7.1, 3H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 142.4, 141.8, 141.0, 140.1, 129.4, 128.5, 127.4, 126.4, 126.1, 99.4, 61.3, 42.4, 20.8, 20.4, 19.8, 18.1

ν_{max} (thin film): 2929, 1615, 1280, 1134, 1092

HRMS: Calculated for $C_{20}H_{24}NO_2S$ $[M+H]^+$ m/z = 342.1528, found m/z = 342.1529 (0.3 ppm).

Chiral HPLC (25 cm Chiralpak AD, 10% EtOH/*n*-heptane, 1.0 mL/min, detection at 215 nm) R_t = 18.7 min (major) and 21.0 min (minor), *ee* = 99.4%.



1-(1-Phenylethyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4db

N-iodosuccinimide (270 mg, 1.20 mmol) was reacted with 1-(1-phenylethyl)piperidine[3] (57 mg, 0.30 mmol) and sodium 4-methylbenzenesulfinate (80 mg, 0.45 mmol) in THF (5 mL) as per the general procedure. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4db** (41.5 mg, 41%) as an orange oil.

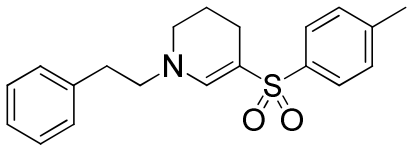
LCMS (High pH, UV, ESI) R_t = 1.27 min, $[M+H]^+$ m/z = 342.1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J*=8.3, 2H), 7.63 (s, 1H), 7.33-7.39 (m, 2H), 7.26-7.32 (m, 3H), 7.23 (d, *J*=7.1, 2H), 4.45 (q, *J*=7.0, 1H), 2.81-2.98 (m, 2H), 2.42 (s, 3H), 2.17 (t, *J*=6.2, 2H), 1.67-1.74 (m, 2H), 1.61 (d, *J*=7.1, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.2, 142.0, 140.9, 139.9, 129.4, 128.8, 127.7, 126.9, 126.4, 100.7, 62.7, 43.3, 21.5, 21.1, 20.2, 18.9

ν_{max} (thin film): 2932, 1611, 1277, 1131

HRMS: Calculated for $C_{20}H_{24}NO_2S$ $[M+H]^+$ m/z = 342.1528, found m/z = 342.1526 (-0.6 ppm).



1-Phenethyl-5-tosyl-1,2,3,4-tetrahydropyridine 4e

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with **3e** (108 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.155 mmol) as a standard showed 81% conversion to **4e**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4e** (136.0 mg, 70%) as a white solid.

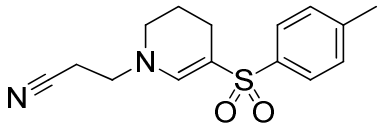
LCMS (High pH, UV, ESI) R_t = 1.24 min, $[M+H]^+$ m/z = 342.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41 (d, *J*=8.1, 2H), 7.23-7.33 (m, 7H), 7.06 (s, 1H), 3.47 (t, *J*=6.8, 2H), 3.07 (t, *J*=5.4, 2H), 2.79 (t, *J*=6.8, 2H), 2.37 (s, 3H), 1.90 (t, *J*=6.1, 2H), 1.61 (quin, *J*=6.1, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 144.2, 141.7, 140.1, 138.7, 129.3, 128.9, 128.3, 126.1 (2C), 97.4, 56.1, 44.5, 34.0, 20.8, 20.3, 19.3

ν_{max} (thin film): 2929, 1619, 1278, 1134, 1095

HRMS: Calculated for $C_{20}H_{24}NO_2S$ $[M+H]^+$ m/z = 342.1528, found m/z = 342.1533 (1.5 ppm).



3-(5-Tosyl-3,4-dihydropyridin-1-yl)propanenitrile 4f

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 3-(piperidin-1-yl)propanenitrile (79 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure, with the following modification: solution 1 was stirred for 60 min before being transferred. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.164 mmol) as a standard showed 84% conversion to **4f**. The crude material was purified by reverse phase chromatography using 0-50% MeCN/10 mM ammonium bicarbonate as the eluent to afford **4f** (120.7 mg, 73%) as a white solid.

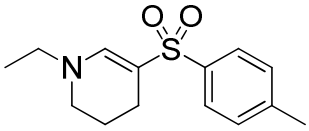
LCMS (High pH, UV, ESI) R_t = 0.93 min, $[M+H]^+$ m/z = 291.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, *J*=8.3, 2H), 7.38 (s, 1H), 7.33 (d, *J*=7.8, 2H), 3.52 (t, *J*=6.4, 2H), 3.09 (t, *J*=5.4, 2H), 2.78 (t, *J*=6.4, 2H), 2.36 (s, 3H), 1.98 (t, *J*=6.1, 2H), 1.67 (quin, *J*=5.9, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 144.4, 142.5, 140.5, 129.9, 126.7, 119.5, 100.5, 50.7, 44.9, 21.4, 20.9, 19.8, 17.2

ν_{max} (thin film): 2936, 1621, 1277, 1135, 1095

HRMS: Calculated for $C_{15}H_{19}N_2O_2S$ $[M+H]^+$ m/z = 291.1167, found m/z = 291.1175 (2.7 ppm).



1-Ethyl-5-tosyl-1,2,3,4-tetrahydropyridine 4g

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-ethylpiperidine (64.6 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure, with the following modification: solution 1 was stirred for 60 min before being transferred. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.110 mmol) as a standard showed 95% conversion to **4g**. The crude material was purified by silica gel chromatography using 0-20% (3:1 EtOAc-EtOH, 1% Et_3N modifier)/cyclohexane as the eluent to afford **4g** (136.8 mg, 90%) as a white solid.

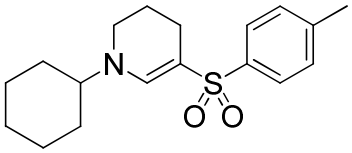
LCMS (High pH, UV, ESI) R_t = 1.07 min, $[M+H]^+$ m/z = 266.2

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, *J*=8.1, 2H), 7.33 (d, *J*=8.1, 2H), 7.28 (s, 1H), 3.23 (q, *J*=7.3, 2H), 3.03 (t, *J*=5.4, 2H), 2.36 (s, 3H), 1.99 (t, *J*=6.1, 2H), 1.66 (quin, *J*=5.9, 2H), 1.08 (t, *J*=7.1, 3H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 143.7, 141.7, 140.3, 129.4, 126.1, 98.2, 49.4, 44.0, 20.8, 20.5, 19.4, 13.6

ν_{max} (thin film): 2933, 1618, 1280, 1136, 1095

HRMS: Calculated for $C_{14}H_{20}NO_2S$ $[M+H]^+$ m/z = 266.1215, found m/z = 266.1215 (0 ppm).



1-Cyclohexyl-5-tosyl-1,2,3,4-tetrahydropyridine 4h

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-cyclohexylpiperidine (96 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.107 mmol) as a standard showed 93% conversion to **4h**. The crude material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **4h** (155.5 mg, 85%) as a white solid.

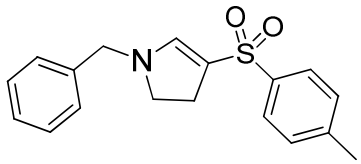
LCMS (High pH, UV, ESI) R_t = 1.32 min, $[M+H]^+$ m/z = 320.2

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, *J*=8.1, 2H), 7.33 (d, *J*=8.1, 2H), 7.29 (s, 1H), 3.12 (tt, *J*=11.5, 3.2, 1H), 3.05 (t, *J*=5.4, 2H), 2.36 (s, 3H), 2.00 (t, *J*=6.1, 2H), 1.73 (t, *J*=13.6, 4H), 1.63 (quin, *J*=6.0, 2H), 1.58 (d, *J*=12.7, 1H), 1.39 (qd, *J*=12.7, 3.9, 2H), 1.26 (qt, *J*=12.7, 2.9, 2H), 1.09 (qt, *J*=13.0, 3.2, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 142.3, 141.7, 140.3, 129.4, 126.1, 98.0, 62.7, 42.2, 30.7, 25.0, 24.8, 20.8, 20.8, 20.0

ν_{max} (thin film): 2930, 1615, 1280, 1132, 1093

HRMS: Calculated for $C_{18}H_{26}NO_2S$ $[M+H]^+$ m/z = 320.1684, found m/z = 320.1682 (-0.6 ppm).



1-Benzyl-4-tosyl-2,3-dihydro-pyrrole 4i

N-iodosuccinimide (558 mg, 2.48 mmol) was reacted with 1-benzylpyrrolidine (100 mg, 0.62 mmol) and sodium 4-methylbenzenesulfinate (166 mg, 0.93 mmol) in THF (9 mL) as per the general procedure, with the following modification: solution 1 was stirred for 60 minutes before being transferred. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4n** (43.1 mg, 22%) as a green gum.

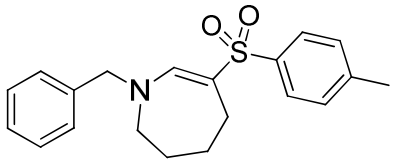
LCMS (High pH, UV, ESI) R_t = 1.18 min, $[M+H]^+$ m/z = 314.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.62 (d, *J*=8.3, 2H), 7.40 (s, 1H), 7.34-7.39 (m, 4H), 7.29-7.32 (m, 1H), 7.25-7.28 (m, 2H), 4.30 (s, 2H), 3.33 (t, *J*=10.3, 2H), 2.51-2.53 (m, 2H), 2.37 (s, 3H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 151.7, 142.1, 140.0, 136.6, 129.6, 128.5, 128.0, 127.5, 125.9, 104.6, 52.8, 51.0, 27.2, 20.9

ν_{max} (thin film): 2924, 1578, 1301, 1138, 1091

HRMS: Calculated for $C_{18}H_{20}NO_2S$ $[M+H]^+$ m/z = 314.1215, found m/z = 314.1213 (-0.6 ppm).



1-Benzyl-6-tosyl-2,3,4,5-tetrahydro-azepine 4j

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with 1-benzylazepane[3] (108 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (306 mg, 1.71 mmol) as per the general procedure, with the following modification: DMSO (9 mL) was used as the reaction solvent. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.114 mmol) as a standard showed 23% conversion to **4j**. The crude material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **4j** (37.1 mg, 19%) as a clear oil.

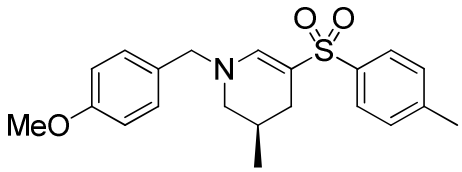
LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ m/z = 342.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.62 (d, *J*=8.3, 2H), 7.51 (s, 1H), 7.28-7.42 (m, 7H), 4.45 (s, 2H), 3.17 (t, *J*=5.4, 2H), 2.38 (s, 3H), 2.19 (t, *J*=6.4, 2H), 1.46-1.62 ppm (m, 4H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 148.1, 142.0, 139.9, 137.9, 129.4, 128.6, 127.5, 127.4, 126.4, 104.4, 61.3, 51.6, 27.5, 26.2, 25.7, 20.9

ν_{max} (thin film): 2920, 1634, 1280, 1135, 1088

HRMS: Calculated for $C_{20}H_{24}NO_2S$ $[M+H]^+$ m/z = 342.1528, found m/z = 342.1526 (-0.6 ppm).



(*R*)-1-(4-Methoxybenzyl)-3-methyl-5-tosyl-1,2,3,4-tetrahydropyridine 4k

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with (*R*)-1-(4-methoxybenzyl)-3-methylpiperidine[3] (108 mg, 0.49 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.165 mmol) as a standard showed 58% conversion to **4k**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4k** (92.9 mg, 51%) as an off-white solid.

LCMS (High pH, UV, ESI) R_t = 1.28 min, $[M+H]^+$ m/z = 372.1

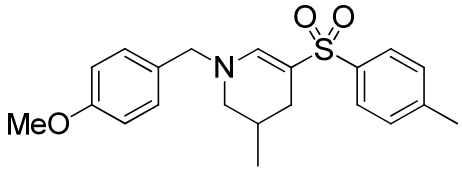
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, *J*=8.3, 2H), 7.52 (s, 1H), 7.35 (d, *J*=8.1, 2H), 7.19 (d, *J*=8.6, 2H), 6.93 (d, *J*=8.6, 2H), 4.37 (d, *J*=14.7, 1H), 4.30 (d, *J*=14.7, 1H), 3.75 (s, 3H), 2.93 (ddd, *J*=12.7, 3.7, 1.7, 1H), 2.51-2.55 (m, 1H), 2.36 (s, 3H), 2.09 (ddd, *J*=9.8, 4.9, 1.2, 1H), 1.65-1.77 (m, 1H), 1.58 (dd, *J*=15.2, 8.8, 1H), 0.77 (d, *J*=6.6, 3H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 158.7, 143.8, 141.8, 140.2, 129.4, 129.1, 129.0, 126.1, 113.9, 98.9, 57.5, 55.0, 50.7, 27.3, 25.6, 20.9, 18.0

ν_{max} (thin film): 2919, 1619, 1513, 1281, 1249, 1134, 1088

HRMS: Calculated for $C_{21}H_{26}NO_3S$ $[M+H]^+$ m/z = 372.1633, found m/z = 372.1638 (1.3 ppm).

Chiral HPLC (25 cm Chiralpak AD, 40% EtOH/*n*-heptane, 1.0 mL/min, detection at 215 nm) R_t = 8.6 min, *ee* >99%.



1-(4-Methoxybenzyl)-3-methyl-5-tosyl-1,2,3,4-tetrahydropyridine 4kb

N-iodosuccinimide (270 mg, 1.20 mmol) was reacted with (*R*)-1-(4-methoxybenzyl)-3-methylpiperidine[3] (66 mg, 0.30 mmol) and sodium 4-methylbenzenesulfinate (80 mg, 0.45 mmol) in THF (5 mL) as per the general procedure. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4kb** (40.6 mg, 36%) as an orange oil.

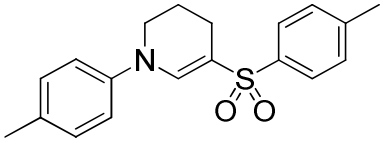
LCMS (High pH, UV, ESI) R_t = 1.28 min, $[M+H]^+$ m/z = 372.1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J*=8.3, 2H), 7.50 (d, *J*=1.0, 1H), 7.28 (d, *J*=8.1, 2H), 7.14 (d, *J*=8.8, 2H), 6.90 (d, *J*=8.8, 2H), 4.26 (s, 2H), 3.83 (s, 3H), 2.90 (ddd, *J*=12.2, 3.9, 2.2, 1H), 2.55 (dd, *J*=12.5, 9.3, 1H), 2.43 (s, 3H), 2.28 (ddd, *J*=14.9, 4.4, 2.0, 1H), 1.81-1.91 (m, 1H), 1.74 (dd, *J*=15.7, 9.3, 1H), 0.88 (d, *J*=6.6, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 143.7, 142.3, 139.8, 129.4, 128.9, 128.4, 126.9, 114.2, 100.7, 59.1, 55.3, 51.4, 27.7, 26.4, 21.5, 18.5

v_{max} (thin film): 2924, 1617, 1512, 1132

HRMS: Calculated for $C_{21}H_{26}NO_3S$ $[M+H]^+$ m/z = 372.1633, found m/z = 372.1635 (0.5 ppm).



1-(*p*-Tolyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4l

N-iodosuccinimide (180 mg, 0.80 mmol) was reacted with 1-(*p*-tolyl)piperidine[3] (35 mg, 0.20 mmol) and sodium 4-methylbenzenesulfinate (53.4 mg, 0.30 mmol) in THF (3 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.083 mmol) as a standard showed 49% conversion to **4l**. The crude material was purified by silica gel chromatography using 0-20% EtOAc/cyclohexane as the eluent to afford **4l** (33.1 mg, 51%) as an off-white solid.

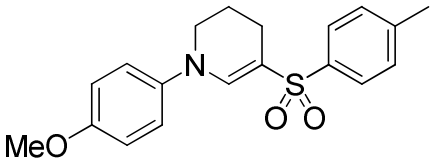
LCMS (High pH, UV, ESI) R_t = 1.31 min, $[M+H]^+$ m/z = 328.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, *J*=8.1, 2H), 7.66 (s, 1H), 7.38 (d, *J*=8.1, 2H), 7.19 (d, *J*=8.1, 2H), 7.09 (d, *J*=8.6, 2H), 3.53 (t, *J*=5.4, 2H), 2.38 (s, 3H), 2.28 (s, 3H), 2.12 (t, *J*=6.1, 2H), 1.84 (quin, *J*=6.1, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 142.7, 139.0, 138.7, 132.2, 131.2, 129.8, 129.6, 126.6, 117.6, 106.6, 45.3, 20.9, 20.6, 20.1, 19.6

v_{max} (thin film): 2929, 1623, 1514, 1283, 1142, 1100

HRMS: Calculated for $C_{19}H_{22}NO_2S$ $[M+H]^+$ m/z = 328.1371, found m/z = 328.1372 (0.3 ppm).



1-(4-methoxyphenyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4m

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with **3m** (109 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4m** (120.8 mg, 27%) as a white solid.

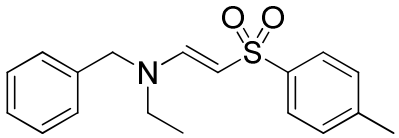
LCMS (High pH, UV, ESI) R_t = 1.22 min, $[M+H]^+$ m/z = 344.0

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, *J*=8.3, 2H), 7.59 (s, 1H), 7.37 (d, *J*=8.1, 2H), 7.14 (d, *J*=9.0, 2H), 6.95 (d, *J*=9.0, 2H), 3.74 (s, 3H), 3.51 (t, *J*=5.4, 2H), 2.38 (s, 3H), 2.11 (t, *J*=6.1, 2H), 1.83 (quin, *J*=5.7, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 155.6, 142.4, 139.4, 139.2, 138.8, 129.6, 126.6, 119.6, 114.6, 105.6, 55.3, 45.9, 20.9, 20.6, 19.5

v_{max} (thin film): 2935, 1620, 1512, 1246, 1141, 1102

HRMS: Calculated for $C_{19}H_{22}NO_3S$ $[M+H]^+$ m/z = 344.1320, found m/z = 344.1322 (0.6 ppm).



(*E*)-*N*-Benzyl-*N*-ethyl-2-tosylethen-1-amine 4n

N-iodosuccinimide (513 mg, 2.28 mmol) was reacted with *N*-benzyl-*N*-ethylethanamine (93 mg, 0.57 mmol) and sodium 4-methylbenzenesulfinate (153 mg, 0.86 mmol) in THF (9 mL) as per the general procedure, with the following modification: the amine-iodination reaction solution was stirred for 60 minutes before being transferred. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.169 mmol) as a standard showed 62% conversion to **4n** The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4n** (88.5 mg, 47%) as a yellow gum.

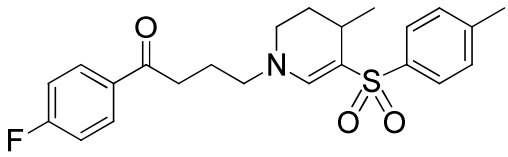
LCMS (High pH, UV, ESI) R_t = 1.19 min, $[M+H]^+$ m/z = 316.0

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.64 (br. s, 2H), 7.47 (d, *J*=12.7, 1H), 7.17-7.40 (m, 7H), 5.17 (br. s., 1H), 4.27-4.55 (m, 2H), 3.34 (br. s., 1H), 3.05 (br. s., 1H), 2.37 (s, 3H), 0.82-1.22 (m, 3H)

^{13}C NMR (151 MHz, DMSO-d_6) δ 149.8, 142.9, 141.5, 137.4, 129.3, 128.5, 127.7, 127.0, 125.5, 92.1, 57.3, 42.1, 20.8, 10.4

ν_{max} (thin film): 2976, 1613, 1280, 1134, 1081

HRMS: Calculated for $C_{18}H_{22}NO_2S$ $[M+H]^+$ m/z = 316.1371, found m/z = 316.1376 (1.6 ppm).



1-(4-Fluorophenyl)-4-(4-methyl-5-tosyl-3,4-dihydropyridin-1-yl)butan-1-one 4o

N-iodosuccinimide (126 mg, 0.56 mmol) was reacted with melperone hydrochloride (42 mg, 0.14 mmol) and sodium 4-methylbenzenesulfinate (37 mg, 0.21 mmol) in THF (3 mL) as per the general procedure, with the following modification: solution 1 was stirred for 60 minutes before being transferred to the sulfinate. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent to afford **4o** (20.0 mg, 34%) as a white solid.

LCMS (High pH, UV, ESI) R_t = 1.28 min, $[M+H]^+$ m/z = 416.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01-8.07 (m, 2H), 7.55 (d, *J*=8.3, 2H), 7.33-7.39 (m, 2H), 7.32 (s, 1H), 7.27 (d, *J*=8.1, 2H), 3.31-3.41 (m, 2H), 3.09 (dd, *J*=8.8, 3.2, 2H), 3.02 (t, *J*=7.0, 2H), 2.34 (s, 3H), 2.26-2.32 (m, 1H), 1.81-1.94 (m, 2H), 1.53 (dq, *J*=13.0, 2.4, 1H), 1.33-1.44 (m, 1H), 0.88 ppm (d, *J*=6.8, 3H)

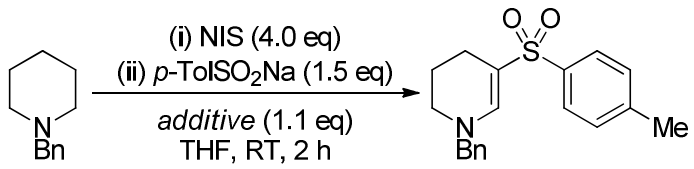
^{13}C NMR (101 MHz, DMSO-d_6) δ 198.4, 165.4 (d, $^1J_{C-F}$=250.2), 145.0, 142.1, 141.9, 133.8 (d, $^4J_{C-F}$=2.2), 131.3 (d, $^3J_{C-F}$=8.8), 129.8, 129.6, 126.6, 116.2 (d, $^2J_{C-F}$=21.3), 103.5, 54.8, 35.2, 28.0, 24.9, 22.9, 22.0, 21.4

^{19}F NMR ($CDCl_3$, 376 MHz): δ -104.78 (s, 1F)

ν_{max} (thin film): 2927, 1685, 1614, 1278, 1133, 1087, 667

HRMS: Calculated for $C_{23}H_{27}NO_3FS$ $[M+H]^+$ m/z = 416.1696, found m/z = 416.1694 (-0.5 ppm).

Table S2: Radical control experiments



1a **2a**

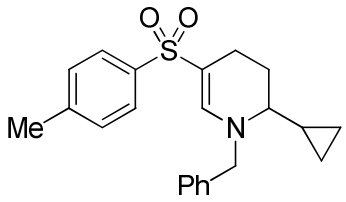
Entry	Additive	Amount of 3,4,5-Trichloropyridine	Conversion to 2a
1	BHT	0.125 mmol	77%
2	Catechol	0.118 mmol	29%
3	TEMPO	0.127 mmol	0%

Amine **1** (100 mg, 0.57 mmol) was added to a solution of *N*-iodosuccinimide (514 mg, 2.28 mmol) in degassed inhibitor-free THF (5 mL) shielded from light, and the resultant reaction mixture was stirred at RT for 30 min. This reaction mixture was then transferred *via* syringe to a suspension of sodium sulfinate salt (153 mg, 0.86 mmol) and additive (0.63 mmol, 1.1 eq) in inhibitor-free THF (1 mL), shielded from light, and inhibitor-free THF (1 mL) was used to wash the first reaction vial to ensure complete transfer to give a resulting reaction concentration of 0.063 M. The reaction was stirred at RT for 2 h. Upon completion of the reaction, the reaction mixture was quenched with saturated aqueous sodium thiosulfate (10 mL) and saturated aqueous sodium bicarbonate (10 mL). The solution was extracted in ethyl acetate (2 x 10 mL) and the combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was analyzed by ^{1}H NMR against 3,4,5-trichloropyridine (amounts as described in Table S2), which showed little inhibition of the reaction by BHT, significant inhibition by catechol, and total inhibition of formation of **2a** by TEMPO.

1-Benzyl-2-cyclopropyl-5-tosyl-1,2,3,4-tetrahydropyridine 4p$^{\alpha}$ and 1-benzyl-6-cyclopropyl-5-tosyl-1,2,3,4-tetrahydropyridine 4p$^{\beta}$

N-iodosuccinimide (180 mg, 0.80 mmol) was reacted with **3p** (43 mg, 0.20 mmol) and sodium 4-methylbenzenesulfinate (53.4 mg, 0.30 mmol) in THF (3 mL) as per the general procedure. ^{1}H NMR analysis of the crude material against 3,4,5-trichloropyridine (0.055 mmol) as a standard (10.1 mg, 0.055 mmol) showed 27% conversion to **4p$^{\alpha}$** and 20% conversion to **4p$^{\beta}$**. The crude material was purified by silica gel chromatography using 0-30% EtOAc/cyclohexane as the eluent, to afford **4p$^{\alpha}$** (18.1 mg, 25%) as an brown oil, and **4p$^{\beta}$** (11.7 mg, 16%) as an orange oil.

1-Benzyl-2-cyclopropyl-5-tosyl-1,2,3,4-tetrahydropyridine 4p$^{\alpha}$



LCMS (Method A, UV, ESI) R_t = 1.35 min, $[M+H]^+$ 368.1

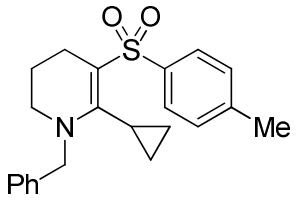
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J*=8.3, 2H), 7.49 (s, 1H), 7.26-7.37 (m, 5H), 7.18 (d, *J*=6.8, 2H), 4.59 (d, *J*=15.2 Hz, 1H), 4.44 (d, *J*=15.9, 1H), 2.42 (s, 3H), 2.18-2.35 (m, 3H), 1.84-1.92 (m, 1H), 1.52-1.64 (m, 1H), 0.73-0.84 (m, 1H), 0.55-0.64 (m, 1H), 0.39 (tt, *J*=8.7, 5.2, 1H), 0.25 (dq, *J*=9.9, 4.9, 1H), -0.07 (dq, *J*=9.8, 5.0, 1H)

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.8, 142.2, 139.9, 137.1, 129.4, 128.8, 127.7, 127.2, 126.8, 100.9, 58.1, 57.7, 26.2, 21.4, 17.2, 13.4, 5.7, 0.3

IR v_{max} (cm^{-1}) (thin film): 2923, 1614, 1132

HRMS: Calculated for $C_{22}H_{26}NO_2S$ $[M+H]^+$: 368.1684, found $[M+H]^+$ 368.1680 (-1.1 ppm).

1-Benzyl-6-cyclopropyl-5-tosyl-1,2,3,4-tetrahydropyridine 4p$^{\beta}$



LCMS (High pH, UV, ESI) R_t = 1.33 min, $[M+H]^+$ 368.1

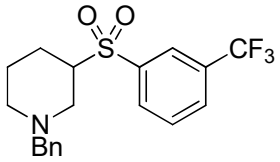
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J*=8.3, 2H), 7.28-7.38 (m, 5H), 7.16 (d, *J*=7.1, 2H), 4.61 (s, 2H), 2.95 (t, *J*=5.4, 2H), 2.46 (t, *J*=6.2, 2H), 2.42 (s, 3H), 1.69-1.79 (m, 3H), 0.89-0.95 (m, 2H), 0.63-0.72 (m, 2H)

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.8, 142.3, 141.6, 138.0, 129.2, 128.7, 127.2, 126.8, 126.7, 108.9, 55.0, 48.1, 26.0, 21.5, 21.2, 12.6, 10.0

IR v_{max} (cm^{-1}) (thin film): 2927, 1733, 1620, 1135

HRMS: Calculated for $C_{22}H_{26}NO_2S$ $[M+H]^+$: 368.1684, found $[M+H]^+$ 368.1672 (-3.3 ppm).

Diversification of enaminyl sulfone scaffolds



1-Benzyl-3-((3-(trifluoromethyl)phenyl)sulfonyl)piperidine 5

A solution of **2g** (191mg, 0.50 mmol) in trifluoroacetic acid (2.5 ml) was stirred at 60 °C for 10 min. A solution of triethylsilane (160 µl, 1.00 mmol) in trifluoroacetic acid (2.5 mL) was then added dropwise, and the reaction stirred at 60 °C for 60 h. The reaction was cooled to RT, and the solvents were evaporated *in vacuo*, and the crude residue was basified with aqueous 2M sodium hydroxide (5 mL), diluted with water (5 mL) and extracted into DCM (2 x 10 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-60% EtOAc/cyclohexane as the eluent, to afford **5** (174 mg, 91%) as a white solid.

LCMS (Low pH, UV, ESI) R_t = 0.74 min, $[M+H]^+$ 384.1

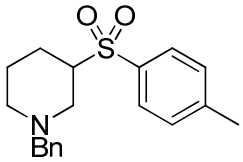
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.06 (d, *J*=7.8, 1H), 7.93 (d, *J*=7.8, 1H), 7.72 (t, *J*=7.8, 1H), 7.19-7.34 (m, 5H), 3.54 (dd, *J*=17.9, 13.2, 2H), 3.25 (ddt, *J*=15.1, 7.6, 3.7, 1H), 3.12-3.19 (m, 1H), 2.83 (br. d, *J*=11.7, 1H), 2.19 (t, *J*=10.9, 1H), 2.03-2.10 (m, 1H), 1.93 (td, *J*=11.6, 2.8, 1H), 1.77-1.84 (m, 1H), 1.46-1.63 (m, 2H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.9, 137.3, 132.1, 132.0 (q $^2J_{C-F}$=33.7), 130.4 (q $^3J_{C-F}$=3.7), 129.9, 128.9, 128.3, 127.3, 125.9 (q, $^3J_{C-F}$=3.7), 123.0 (q, $^1J_{C-F}$=272.2), 63.0, 61.7, 52.6, 51.9, 24.2, 23.9

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.82 (s, 3F)

ν_{max} (cm^{-1}) (thin film): 2954, 1610, 1328, 1141

HRMS: Calculated for $C_{19}H_{21}NO_2SF_3$ $[M+H]^+$ m/z = 384.1245, found m/z = 384.1246 (0.3 ppm).



1-Benzyl-3-tosylpiperidine 6

A mixture of **2a** (50 mg, 0.15 mmol), 10% Pd/C (16 mg, 0.015 mmol, 10 mol%) and acetic acid (1.5 mL) were added to one chamber of COware apparatus under a flow of nitrogen. This first reaction chamber was sealed, and granular zinc (110 mg, 1.68 mmol) and aqueous HCl (2M, 1 mL, 2.00 mmol) were added to the second chamber under flow of nitrogen. The nitrogen line was removed, the second reaction was sealed, and the first reaction chamber was heated to 70 °C for 16 h under an atmosphere of hydrogen at a pressure of approximately 2.9 atm (in addition to the 1 atm of nitrogen already in the flask). On complete conversion of starting material the reaction was cooled to RT and the pressure was released under flow of nitrogen. The reaction mixture was passed through a pad of Celite® and flushed with methanol, and the filtrate was concentrated *in vacuo*. The crude product was then diluted with water and basified with 2M sodium hydroxide and extracted into DCM (5 x 10 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*, affording **6** (45.5 mg, 90%) as a colourless oil.

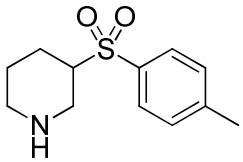
LCMS (Low pH, UV, ESI) R_t = 0.62 min, $[M+H]^+$ 330.1

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J*=8.3, 2H), 7.35 (d, *J*=8.3, 2H), 7.22-7.33 (m, 5H), 3.57 (d, *J*=13.0, 1H), 3.47 (d, *J*=13.7, 1H), 3.15-3.26 (m, 2H), 2.80 (br. d, *J*=11.2, 1H), 2.47 (s, 3H), 2.17 (t, *J*=12.5, 1H), 2.02-2.09 (m, 1H), 1.87 (td, *J*=11.5, 2.7, 1H), 1.71-1.79 (m, *J*=6.4, 1H), 1.41-1.60 (m, 2H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.6, 137.6, 134.5, 129.7, 128.9, 128.8, 128.2, 127.1, 63.0, 61.6, 52.5, 52.4, 24.3, 24.0, 21.6

ν_{max} (cm^{-1}) (thin film): 2953, 1597, 1314, 1142

HRMS: Calculated for $C_{19}H_{24}NO_2S$ $[M+H]^+$ m/z = 330.1528, found m/z = 330.1529 (0.3 ppm).



3-Tosylpiperidine 7

2a (50.4 mg, 0.15 mmol) in AcOH (5 mL) was passed at 1 mL/min through a ThalesNano H-Cube Pro™ hydrogenation flow apparatus using a Pd/C (10 wt%) catalyst at 70 °C and 25 bar pressure. The product line fed back into the reactant solution, ensuring cycling of the reaction solution and the reaction mixture was cycled for 40 min. After full conversion of starting material the system was flushed for 10 min at 1 mL/min, and the resulting solution was concentrated under flow of nitrogen. The concentrated material was then basified with aqueous 2M sodium hydroxide (10 mL) and extracted into DCM (5 x 15 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo* to afford **7** (28.0 mg, 76 % yield) as a colourless oil.

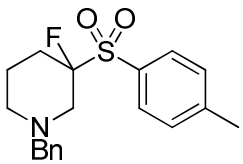
LCMS (Low pH, UV, ESI) R_t = 0.43 min, $[M+H]^+$ 240.2

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.72 (d, *J*=8.3, 2H), 7.48 (d, *J*=8.3, 2H), 3.02-3.15 (m, 2H), 2.75-2.84 (m, 1H), 2.45-2.48 (m, 1H), 2.42-2.44 (m, 3H), 2.28 (td, *J*=12.3, 2.8, 1H), 1.90-1.98 (m, 1H), 1.59-1.67 (m, 1H), 1.44 (qd, *J*=12.0, 4.2, 1H), 1.23-1.37 (m, 2H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 144.4, 134.3, 129.8, 128.4, 60.5, 45.2, 45.0, 25.0, 23.9, 21.0

ν_{max} (cm^{-1}) (thin film): 3323, 2940, 1596, 1142

HRMS: Calculated for $C_{12}H_{18}NO_2S$ $[M+H]^+$ m/z = 240.1058, found m/z = 240.1058 (0.0 ppm).



1-Benzyl-3-fluoro-3-tosylpiperidine 9

2a (260 mg, 0.79 mmol) and 2,6-dichloro-1-fluoropyridin-1-ium trifluoromethanesulfonate, **8**, (530 mg, 1.68 mmol) were dissolved in THF (8 mL) and stirred at RT for 1 h, at which point borane tetrahydrafuranoate (1 M, 0.8 mL, 0.80 mmol) was then added, and the reaction stirred for 2 h at RT. The reaction was quenched with water (10 mL) and diluted with sat. brine (10 mL) and extracted into DCM (3 x 30 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel

chromatography using 0-60% TBME/cyclohexane as the eluent to afford **9** (208.1 mg, 75 % yield) as a grey solid.

LCMS (High pH, UV, ESI) R_t = 1.29 min, $[M+H]^+$ 348.1

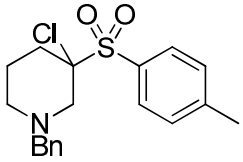
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.72 (d, *J*=8.3, 2H), 7.50 (d, *J*=8.3, 2H), 7.28-7.34 (m, 2H), 7.23-7.28 (m, 3H), 3.55 (dd, *J*=24.0, 13.2, 2H), 2.86-2.96 (m, 1H), 2.73-2.80 (m, 1H), 2.60 (d, *J*=12.5, 1H), 2.44 (s, 3H), 2.04-2.12 (m, 1H), 1.86-2.03 (m, 1H), 1.67-1.84 (m, 2H), 1.54-1.67 (m, 1H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 145.9, 137.2, 130.0, 129.9, 129.9, 128.8, 128.1, 127.0, 105.4 (d, $^1J_{C-F}$=220.8), 61.2, 52.7 (d, $^2J_{C-F}$=19.1), 51.1, 26.6 (d, $^2J_{C-F}$=20.5), 21.1, 20.2

^{19}F NMR (376 MHz, DMSO-d_6): δ -156.47 (s, 1F)

ν_{max} (cm^{-1}) (thin film): 2966, 1596, 1321, 1154

HRMS: Calculated for $C_{19}H_{23}NO_2SF$ $[M+H]^+$ m/z = 348.1434, found m/z = 348.1435 (0.3 ppm).



1-Benzyl-3-chloro-3-tosylpiperidine 10

A solution of **2a** (250 mg, 0.76 mmol) and *N*-chlorosuccinimide (recrystallized from water, 112 mg, 0.84 mmol) in THF (7 mL) was stirred at RT for 15 min, at which point borane tetrahydrafuranoate (1 M, 1 mL, 1.0 mmol) was added dropwise (10 min), and the reaction stirred at RT for 3 h. The reaction was quenched with water (15 mL) and stirred at RT for 5 min, and extracted into DCM (3 x 25 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-50% TBME/cyclohexane as the eluent. Trituration of the isolated colourless oil from Et_2O afforded **10** (236.9 mg, 85 % yield) as a white solid.

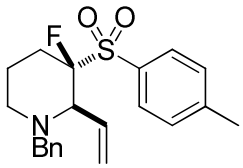
LCMS (High pH, UV, ESI) R_t = 1.37 min, $[M+H]^+$ 364.1

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.77 (d, *J*=8.3, 2H), 7.50 (d, *J*=8.3, 2H), 7.21-7.36 (m, 5H), 3.63 (d, *J*=13.4, 1H), 3.53 (d, *J*=13.4, 1H), 2.92 (dt, *J*=11.9, 2.0, 1H), 2.79-2.85 (m, 1H), 2.64 (d, *J*=12.0, 1H), 2.44 (s, 3H), 2.09-2.20 (m, 1H), 1.96-2.05 (m, 1H), 1.81-1.90 (m, 1H), 1.68-1.78 (m, 2H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 145.8, 137.4, 130.8, 129.9, 129.7, 128.6, 128.1, 127.0, 85.0, 61.2, 56.4, 51.7, 31.0, 21.1, 20.8

ν_{max} (cm^{-1}) (thin film): 2969, 1596, 1320, 1157

HRMS: Calculated for $C_{19}H_{23}NO_2SCl$ $[M+H]^+$ m/z = 364.1138, found m/z = 364.1136 (-0.5 ppm).



***trans*-(2*R*,3*S*)-1-Benzyl-3-fluoro-3-tosyl-2-vinylpiperidine 11a**[4]

2a (33 mg, 0.10 mmol) and **8** (recrystallized from MeCN-Et_2O, 35 mg, 0.11 mmol) were dissolved in THF (8 mL) and stirred at RT for 10 min, at which point vinylmagnesium bromide (1M in THF, 0.13 mL, 0.13 mmol) was added dropwise and the reaction was stirred at RT for 1.5 h. The reaction was then cooled over ice-water and the reaction was quenched with water (5 mL), and stirred for 10 min. The crude material was diluted with saturated aqueous sodium bicarbonate (5 mL) and brine (5 mL) and extracted into DCM (3 x 15 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-20% TBME/cyclohexane as the eluent, affording **11a** (27.9 mg, 74%) as a white solid.

LCMS (High pH, UV, ESI) R_t = 1.45 min, $[M+H]^+$ 374.2

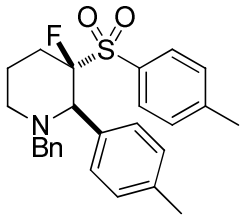
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.71 (d, *J*=7.6, 2H), 7.46 (d, *J*=8.3, 2H), 7.30-7.38 (m, 4H), 7.23-7.28 (m, 1H), 6.02 (dt, *J*=17.1, 9.8, 1H), 5.39 (dd, *J*=10.3, 2.0, 1H), 5.21 (dd, *J*=17.0, 2.1, 1H), 3.81 (t, *J*=8.8, 1H), 3.64 (d, *J*=13.9, 1H), 3.47 (d, *J*=13.9, 1H), 2.59 (ddd, *J*=12.2, 9.3, 3.2, 1H), 2.43 (s, 3H), 2.32-2.40 (m, *J*=7.1, 2.4, 1H), 2.03-2.15 (m, 1H), 1.83-2.03 (m, 2H), 1.59-1.68 (m, 1H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 145.8, 139.1, 132.2, 130.5 (d, $^3J_{C-F}$=1.5), 130.3, 129.8 (d, $^3J_{C-F}$=2.2), 128.9, 128.6, 127.3, 123.1, 106.2 (d, $^1J_{C-F}$=220.8), 64.0 (d, $^2J_{C-F}$=22.0), 58.0, 46.0, 27.3 (d, $^2J_{C-F}$=19.1), 21.6, 21.4

^{19}F NMR (376 MHz, DMSO-d_6): δ -144.52 (s, 1F)

ν_{max} (cm^{-1}) (thin film): 2921, 1596, 1324, 1152

HRMS: Calculated for $C_{21}H_{25}NO_2SF$ $[M+H]^+$ m/z = 374.1590, found m/z = 374.1589 (-0.3 ppm).



***trans*-(2*R*,3*S*)-1-Benzyl-3-fluoro-2-(*p*-tolyl)-3-tosylpiperidine 11b**[4]

2a (259 mg, 0.79 mmol) and **8** (recrystallized from MeCN-Et_2O, 275 mg, 0.87 mmol) were dissolved in THF (4 mL) and stirred at RT for 10 min, at which point *p*-tolylmagnesium bromide (1M in THF, 1.0 mL, 1.00 mmol) was added dropwise and the reaction was stirred at RT for 1.5 h. The reaction was then cooled over ice-water and the reaction was quenched with water (5 mL), and stirred for 10 min. The crude material was diluted with saturated aqueous sodium bicarbonate (5 mL) and brine (5 mL) and extracted into DCM (3 x 15 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-20% TBME/cyclohexane as the eluent, and the resulting colourless oil was triturated from Et_2O to afford **11b** (279.3 mg, 81%) as a white solid.

LCMS (High pH, UV, ESI) R_t = 1.58 min, $[M+H]^+$ 438.2

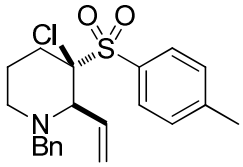
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (dd, *J*=8.3, 1.2, 2H), 7.32 (dd, *J*=8.1, 2.0, 2H), 7.21-7.26 (m, 2H), 7.15-7.20 (m, 3H), 7.07 (d, *J*=8.3, 2H), 6.95 (d, *J*=8.3, 2H), 3.96 (d, *J*=26.2, 1H), 3.57 (d, *J*=13.7, 1H), 2.96 (d, *J*=11.5, 1H), 2.77 (d, *J*=13.7, 1H), 2.37 (s, 3H), 2.27 (s, 3H), 2.23-2.32 (m, 1H), 1.98-2.17 (m, 2H), 1.91 (qt, *J*=12.7, 3.5, 1H), 1.69-1.76 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.0, 139.4, 138.2, 132.8, 131.9 (d, $^1J_{C-F}$=205.4), 130.9, 129.7, 129.7, 128.8, 128.7, 128.4, 128.1, 126.7, 68.8 (d, $^2J_{C-F}$=16.1), 58.3, 51.8, 29.9 (d, $^2J_{C-F}$=20.5), 21.6, 21.1, 20.7

^{19}F NMR (376 MHz, $CDCl_3$): δ -163.05 (s, 1F)

ν_{max} (cm^{-1}) (thin film): 2949, 1595, 1326, 1152

HRMS: Calculated for $C_{26}H_{29}NO_2SF$ $[M+H]^+$ m/z = 438.1903, found m/z = 438.1904 (0.2 ppm).



***cis*-(2*R*,3*R*)-1-Benzyl-3-chloro-3-tosyl-2-vinylpiperidine 11c**[4]

2a (33 mg, 0.10 mmol) and *N*-chlorosuccinimide (recrystallized from water, 15 mg, 0.11 mmol) were dissolved in THF (1 mL) and stirred at RT for 10 min, at which point vinylmagnesium bromide (1M in THF, 0.13 mL, 0.13 mmol) was added dropwise and the reaction was stirred at RT for 4.5 h. The reaction was then cooled over ice-water and the reaction was quenched with water (5 mL), and stirred for 10 min. The crude material was diluted with saturated aqueous sodium bicarbonate (5 mL) and brine (5 mL) and extracted into DCM (3 x 15 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-20% TBME/cyclohexane as the eluent, and the resulting colourless oil was triturated from Et_2O to afford **11c** (33.1 mg, 84%) as a white solid.

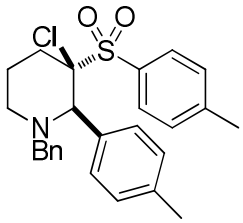
LCMS (High pH, UV, ESI) R_t = 1.49 min, $[M+H]^+$ 390.1

^{1}H NMR (400MHz, DMSO-d_6): δ 7.79 (d, *J*=8.6, 2H), 7.49 (d, *J*=8.3, 2H), 7.28-7.33 (m, 4H), 7.20-7.26 (m, 1H), 5.91 (ddd, *J*=16.9, 10.6, 8.9, 1H), 5.43 (q, *J*=2.0, 1H), 5.39 (dd, *J*=9.5, 1.7, 1H), 3.92 (d, *J*=14.2, 1H), 3.69 (d, *J*=9.0, 1H), 3.24 (d, *J*=13.9, 1H), 2.62-2.70 (m, 1H), 2.44 (s, 3H), 2.21-2.30 (m, 1H), 2.14 (ddd, *J*=13.2, 9.8, 2.9, 1H), 1.57-1.78 (m, 3H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 145.9, 139.7, 133.7, 132.3, 131.4, 130.0, 128.7, 128.6, 127.2, 122.7, 88.4, 67.7, 57.3, 49.4, 34.6, 21.6, 21.3

ν_{max} (cm^{-1}) (thin film): 2924, 1597, 1325, 1151

HRMS: Calculated for $C_{21}H_{25}NO_2SCl$ $[M+H]^+$ m/z = 390.1295, found m/z = 390.1294 (-0.3 ppm).



***cis*-(2*R*,3*R*)-1-Benzyl-3-chloro-2-(*p*-tolyl)-3-tosylpiperidine 11d**[4]

2a (33 mg, 0.10 mmol) and *N*-chlorosuccinimide (recrystallized from water, 15 mg, 0.11 mmol) were dissolved in THF (1 mL) and stirred at RT for 10 min, at which point *p*-tolylmagnesium bromide (1M in THF, 0.13 mL, 0.13 mmol) was added dropwise and the reaction was stirred at RT for 1.5 h. The reaction was then cooled over ice-water and the reaction was quenched with water (5 mL), and stirred for 10 min. The crude material was diluted with saturated

aqueous sodium bicarbonate (5 mL) and brine (5 mL) and extracted into DCM (3 x 15 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by silica gel chromatography with 0-20% TBME/cyclohexane as the eluent to afford **11d** (29.0 mg, 63%) as a colourless oil.

LCMS (High pH, UV, ESI) R_t = 1.61 min, $[M+H]^+$ 454.2

^{1}H NMR (400MHz, DMSO-d_6): δ 7.60 (d, *J*=8.6, 2H), 7.47 (d, *J*=9.0, 2H), 7.38 (d, *J*=8.3, 2H), 7.25-7.32 (m, 2H), 7.17-7.24 (m, 3H), 7.12 (d, *J*=8.6, 2H), 4.20 (s, 1H), 3.49 (d, *J*=13.9, 1H), 2.77-2.86 (m, 2H), 2.40 (s, 3H), 2.32-2.37 (m, 1H), 2.30 (s, 3H), 2.13 (td, *J*=12.1, 3.2, 1H), 1.60-1.82 (m, 3H)

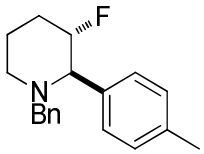
^{13}C NMR (101 MHz, DMSO-d_6): δ 145.7, 139.4, 138.0, 133.9, 132.0, 131.2, 129.7, 128.7, 128.7, 128.5, 127.2, 125.6, 89.4, 69.0, 57.7, 52.1, 36.1, 21.6, 21.2, 21.2

ν_{max} (cm^{-1}) (thin film): 2922, 1597, 1315, 1144

HRMS: Calculated for $C_{26}H_{29}NO_2SCl$ $[M+H]^+$ m/z = 454.1608, found m/z = 454.1608 (0.0 ppm).

trans-1-Benzyl-3-fluoro-2-(*p*-tolyl)piperidine 13, and cis-1-Benzyl-3-fluoro-2-(p-tolyl)piperidine 13b

A mixture of magnesium powder (49 mg, 2.01 mmol) and **11b** (22 mg, 0.05 mmol) was sonicated under an atmosphere of nitrogen for 1 min. Methanol (1 mL) was then added, and the reaction mixture was stirred at RT for 20 h under a positive pressure of nitrogen. The reaction mixture was filtered through a 1g Isolute NH2 SPE column and flushed with methanol. The elute was concentrated *in vacuo*, and ^{19}F NMR analysis showed a diastereomeric ratio of 6:1 for **13**:**13b**, based on the peaks at 177.8 and 195.3 ppm, respectively. The crude material was purified by high pH MDAP (Method E), to afford **13** (9.8 mg, 69%) as a white solid, and **13b** (0.4 mg, 3%) as a colourless oil.



trans-1-Benzyl-3-fluoro-2-(p-tolyl)piperidine 13

LCMS (High pH, UV, ESI) R_t = 1.52 min, $[M+H]^+$ 284.2

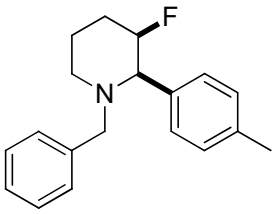
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J*=8.1, 2H), 7.17-7.30 (m, 7H), 4.47 (dtd, *J*=47.7, 9.5, 5.1 Hz, 1H), 3.75 (d, *J*=13.7, 1H), 3.13 (dd, *J*=8.7, 6.7, 1H), 2.83-2.96 (m, 2H), 2.35 (s, 3H), 2.21-2.29 (m, 1H), 1.97 (td, *J*=11.6, 2.7, 1H), 1.69-1.77 (m, 1H), 1.57-1.62 (m, 1H), 1.52-1.57 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 139.4, 137.5, 137.4, 129.3, 128.5, 128.5, 128.1, 126.7, 93.9 (d, $^1J_{C-F}$=173.9), 72.7 (d, $^2J_{C-F}$=22.0), 58.6, 52.0, 31.3 (d, $^2J_{C-F}$=18.3), 22.6 (d, $^3J_{C-F}$=12.5), 21.2

^{19}F NMR (376 MHz, $CDCl_3$): δ -177.79 (s, 1F)

ν_{max} (cm^{-1}) (thin film): 2945, 2796, 1514, 1352

HRMS: Calculated for $C_{19}H_{23}NF$ $[M+H]^+$ m/z = 284.1815, found m/z = 284.1814 (-0.4 ppm).



***cis*-1-Benzyl-3-fluoro-2-(*p*-tolyl)piperidine 13b**

LCMS (High pH, UV, ESI) R_t = 1.49 min, $[M+H]^+$ 284.2

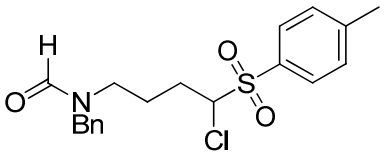
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.39 (d, *J*=7.3 Hz, 2H), 7.30 (t, *J*=7.7 Hz, 2H), 7.20-7.26 (m, 3H), 7.17 (d, *J*=8.1 Hz, 2H), 4.57 (d, *J*=47.3 Hz, 1H), 3.65 (d, *J*=13.6 Hz, 1H), 3.36 (d, *J*=31.2 Hz, 1H), 2.86 (d, *J*=13.9 Hz, 2H), 2.29 (s, 3H), 1.98-2.05 (m, 2H), 1.78 (qt, *J*=13.2, 3.7 Hz, 1H), 1.67 (dtdd, J=45.1, 13.9, 4.0, 1.8 Hz, 1H), 1.45-1.51 (m, 1H)

^{13}C NMR (151 MHz, DMSO-d6): δ 138.7, 137.3, 136.3, 128.7, 128.5, 128.2, 128.1, 126.7, 89.9 (d, $^1J_{C-F}$=178.0) 69.1 (d, $^2J_{C-F}$=16.6), 58.6, 51.8, 29.2 (d, $^2J_{C-F}$=22.1), 20.6, 19.5

^{19}F NMR (376 MHz, $CDCl_3$): δ -195.31 (s, 1F)

ν_{max} (cm^{-1}) (thin film): 2929, 1670, 1453, 1139

HRMS: Calculated for $C_{19}H_{23}NF$ $[M+H]^+$ m/z = 284.1815, found m/z = 284.1813 (-0.7 ppm).



***N*-Benzyl-*N*-(4-chloro-4-tosylbutyl)formamide 14**

2a (33 mg, 0.10 mmol) and *N*-chlorosuccinimide (20 mg, 0.15 mmol) were dissolved in THF (1.0 mL) and stirred at RT for 2 h, at which aqueous potassium hydroxide (1 M, 0.20 mL, 0.20 mmol) was added and the reaction stirred at RT for 24 h. The reaction mixture was diluted with water (5 mL) and extracted into DCM (3 x 10 mL). The combined organic layers were passed through a hydrophobic frit and concentrated *in vacuo*. The crude material was purified by reverse phase chromatography using 10-95% MeCN/10mM ammonium bicarbonate as the eluent to afford **14** (27.8 mg, 73%) as a yellow gum.

LCMS (High pH, UV, ESI) R_t = 1.14 min, $[M+H]^+$ 280.1

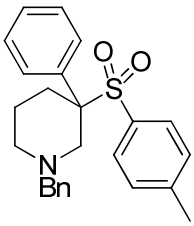
^{1}H NMR (400MHz, DMSO-d_6, 120 °C): δ 8.24 (br. s., 1H), 7.80 (d, *J*=8.3, 2H), 7.49 (d, *J*=8.3, 2H), 7.18-7.40 (m, 5H), 5.25 (dd, *J*=8.8, 3.7, 1H), 4.44 (s, 2H), 3.25 (br. s., 2H), 2.46 (s, 3H), 2.09-2.24 (m, 1H), 1.62-1.83 (m, 3H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 163.2, 163.0, 145.6, 145.5, 137.1, 137.0, 132.0, 131.9, 129.8, 129.8, 129.4, 129.4, 128.6, 128.4, 127.6, 127.6, 127.1, 73.5, 73.4, 50.0, 45.1, 44.3, 40.2, 27.5, 27.1, 24.1, 22.8, 21.1

More than the expected number of ^{13}C signals because restricted rotation led to formation of a mixture of rotamers at RT.

ν_{max} (cm^{-1}) (thin film): 3392 (br), 2923, 2257, 1663

HRMS: Calculated for $C_{19}H_{23}NO_3SCl$ $[M+H]^+$ m/z = 380.1087, found m/z = 380.1087 (0.0 ppm).



1-Benzyl-3-phenyl-3-tosylpiperidine 15

Copper(II) triflate (1.8 mg, 5.0 µmol, 10 mol%) and three 3Å molecular sieves were placed under an atmosphere of nitrogen and heated to 200 °C under vacuum for 2 h, and then cooled to RT and placed back under a nitrogen atmosphere. The catalyst solution was then treated with a solution containing **2a** (16 mg, 0.05 mmol), diphenyliodonium triflate (52.6 mg, 0.12 mmol) and three 3Å molecular sieves in DCM (1.0 ml), and the reaction mixture was stirred at RT for 5 d. Sodium borohydride (3.7 mg, 0.10 mmol) and methanol (0.1 ml) were added to the reaction mixture and the reaction stirred at RT for 1 h. Water (2 mL) was added to quench the reaction, and the crude material was extracted into DCM (2 x 5 mL). The combined organic layer was passed through a hydrophobic frit and concentrated under flow of nitrogen. The crude material was purified by formic MDAP (method B), affording **15** (4.4 mg, 22%) as a yellow oil.

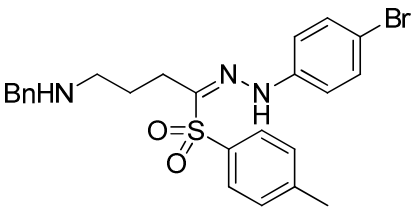
LCMS (High pH, UV, ESI) R_t = 1.43 min, $[M+H]^+$ 406.2

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.16-7.34 (m, 10H), 7.11 (d, *J*=8.3, 2H), 7.06 (d, *J*=7.6, 2H), 3.49-3.54 (m, 2H), 3.42-3.49 (m, 2H), 2.64-2.71 (m, 1H), 2.57 (dd, *J*=13.8, 3.1, 1H), 2.35 (s, 3H), 1.92-2.04 (m, 2H), 1.56-1.65 (m, 1H), 1.24 (qt, *J*=13.4, 3.7, 1H)

^{13}C NMR (101 MHz, DMSO-d_6): δ 144.9, 138.0, 133.3, 132.4, 130.3, 130.1, 129.7, 129.5, 128.4, 128.4, 127.9, 127.6, 69.2, 62.5, 54.6, 53.6, 28.0, 21.7, 21.5

ν_{max} (cm^{-1}) (thin film): 2926, 1597, 1313, 1143

HRMS: Calculated for $C_{25}H_{28}NO_2S$ $[M+H]^+$ m/z = 406.1827, found m/z = 406.1842 (0.2 ppm).



***N*-Benzyl-4-(2-(4-bromophenyl)hydrazono)-4-tosylbutan-1-amine 16**

Trifluoroacetic acid (7.5 µL, 0.10 mmol) was added to a solution of **2a** (32 mg, 0.10 mmol) and 4-bromobenzenediazonium tetrafluoroborate (29 mg, 0.11 mmol) in MeOH (1 mL). The reaction mixture was stirred at RT for 8 h, then concentrated *in vacuo*. The crude material was purified by high pH MDAP (Method E), to afford **16** (27 mg, 55%) as an orange gum.

LCMS (High pH, UV, ESI) R_t = 1.48 min, $[M+H]^+$ 500.1 (^{79}Br), 502.1 (^{81}Br)

^{1}H NMR (600 MHz, DMSO-d_6): δ 7.78 (d, *J*=8.1, 2H), 7.46 (d, *J*=8.1, 2H), 7.30-7.36 (m, 6H), 7.23-7.27 (m, 1H), 6.79 (d, *J*=8.8, 2H), 3.66 (s, 2H), 2.72 (t, *J*=7.3, 2H), 2.44 (t, *J*=6.4, 2H), 2.42 (s, 3H), 1.72 (quin, *J*=7.0, 2H)

The amine and aza protons underwent exchange in the wet deuterated solvent, therefore were not observed.

^{13}C NMR (151 MHz, DMSO-d_6): δ 145.2, 144.1, 143.3, 140.1, 136.3, 131.7, 129.8, 128.1, 128.1, 128.0, 126.6, 115.3, 112.3, 52.1, 46.4, 25.5, 22.6, 21.0

ν_{max} (cm^{-1}) (thin film): 3304, 2922, 1583, 1487, 1144

HRMS: Calculated for $C_{24}H_{27}N_3O_2SBr$ $[M+H]^+$ m/z = 500.1007, found m/z = 500.1010 (0.6 ppm).

References

[1] T. Markovic, B. N. Rocke, D. C. Blakemore, V. Mascitti, M. C. Willis, Chem. Sci. 2017, 8, 4437–4442.

[2] Prepared by stirring (*E*)-styrylsulfinic acid (1.0 eq) and sodium hydroxide (1.0 eq) in 1:1 EtOH:H_2O (6 mL) and stirring at RT for 3 h. The EtOH was evaporated, and the crude material was diluted with water (15 mL), washed with EtOAc (3 x 15 mL) and the aqueous layer was concentrated *in vacuo* and dried in a vacuum oven overnight to afford sodium (*E*)-styrylsulfinate as an off-white solid (76 wt%).

[3] R. J. Griffiths, G. A. Burley, E. P. A. Talbot, Org. Lett. 2017, 19, 870–873.

[4] Compound naming based on Cahn-Ingold-Prelog rules for functional group priorities.

NMR spectra of synthesized compounds

Reaction optimization

Table S1, entry 32, $CDCl_3$

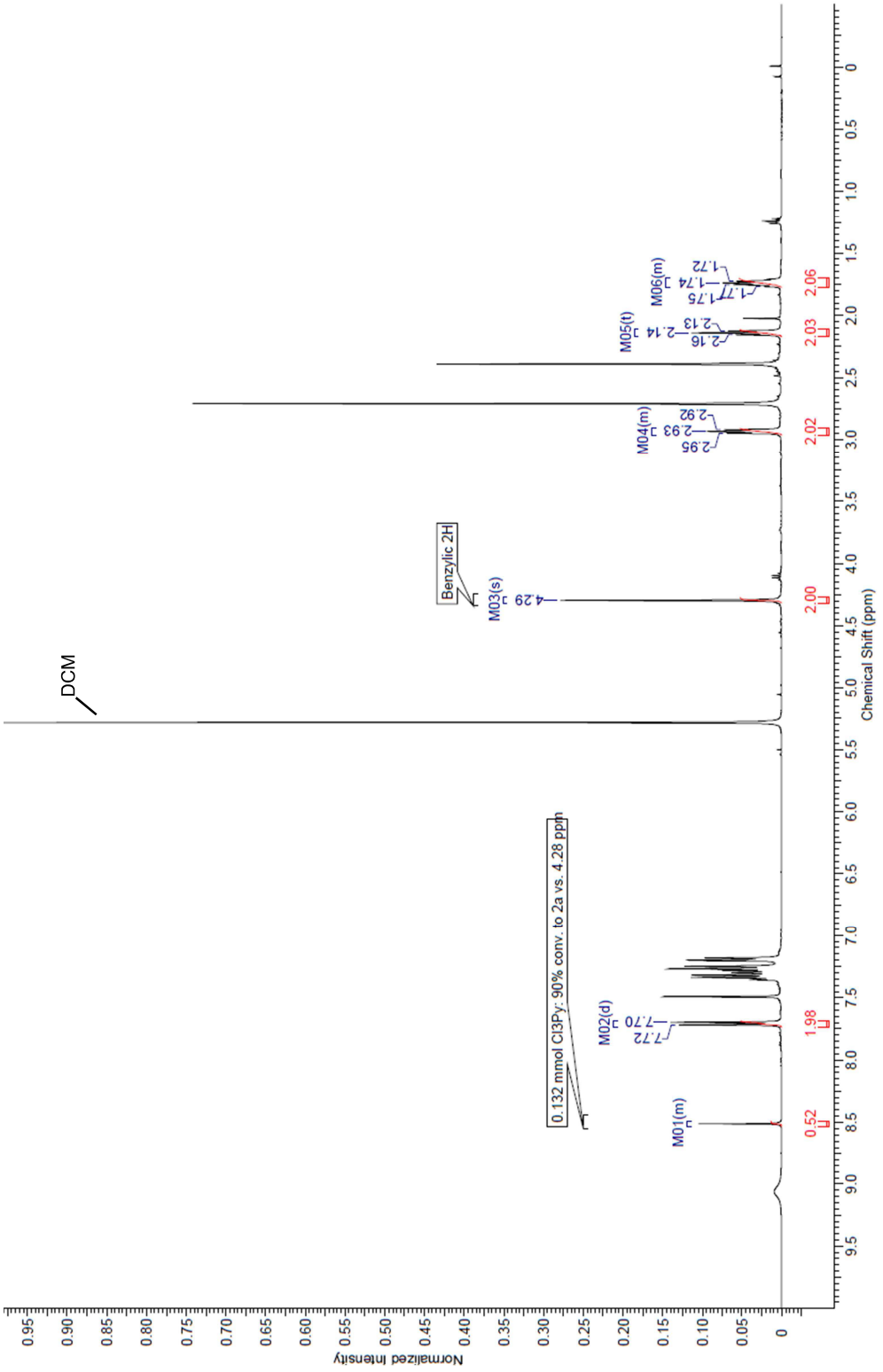
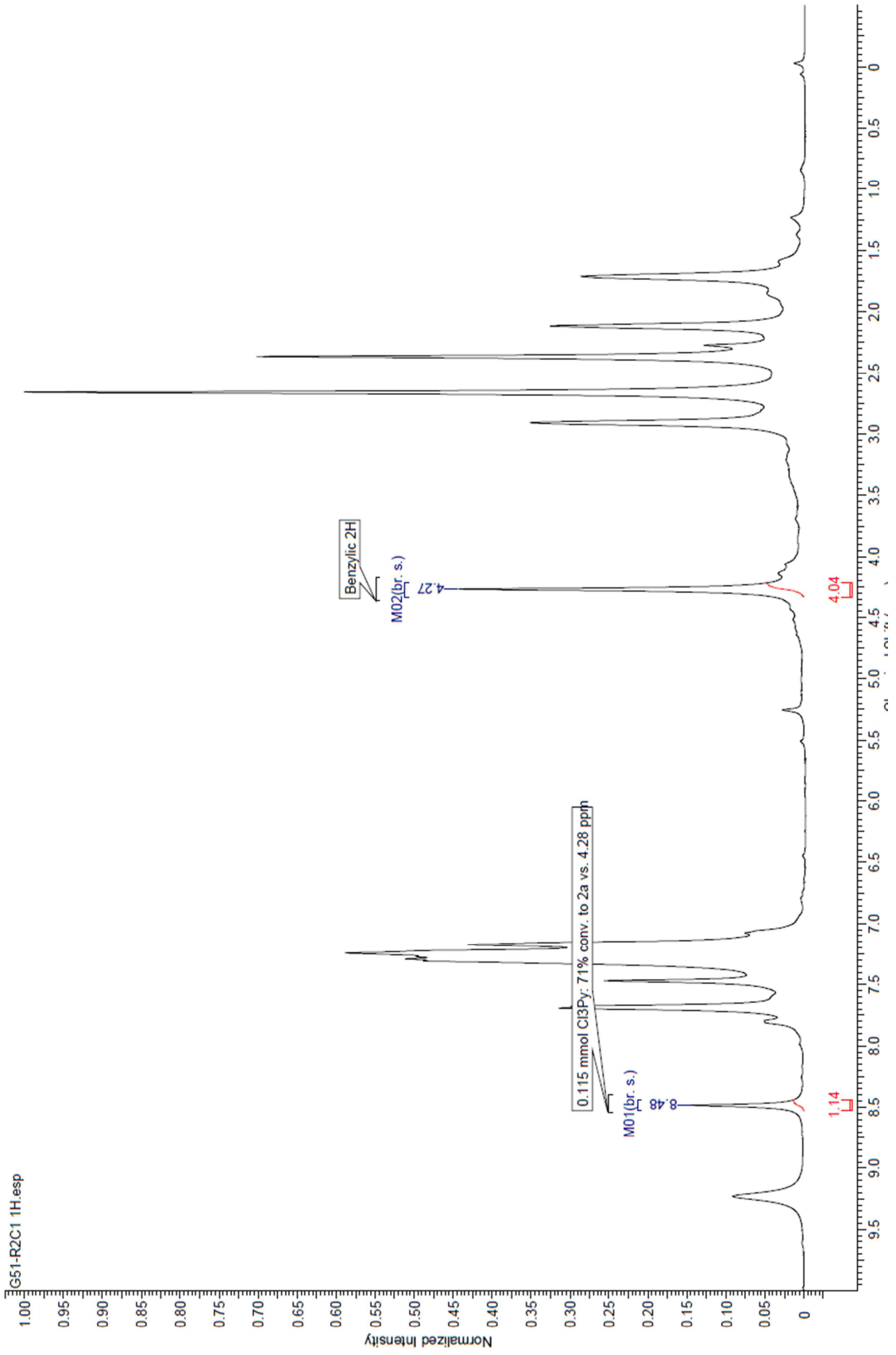
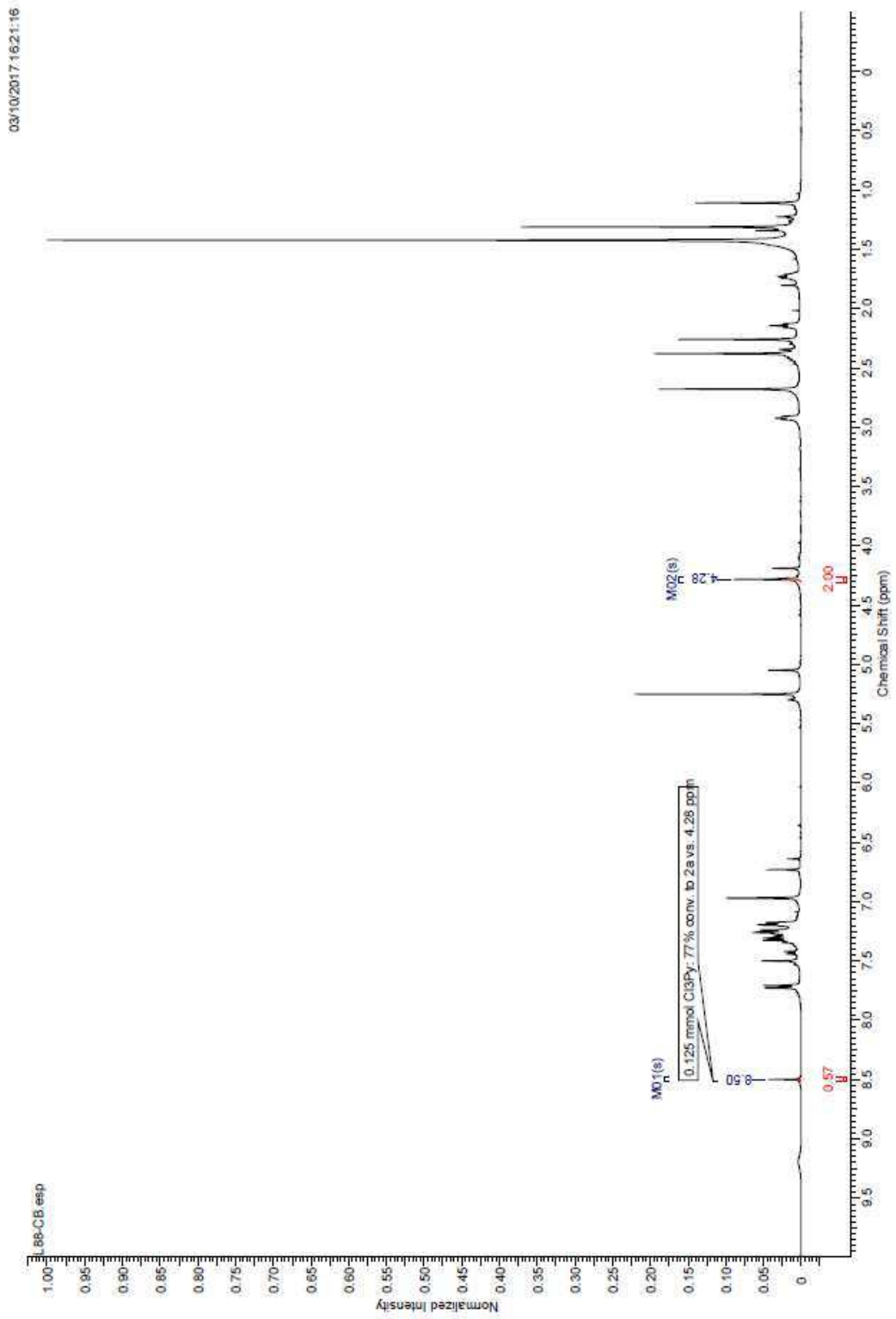


Table S1, entry 33, $CDCl_3$

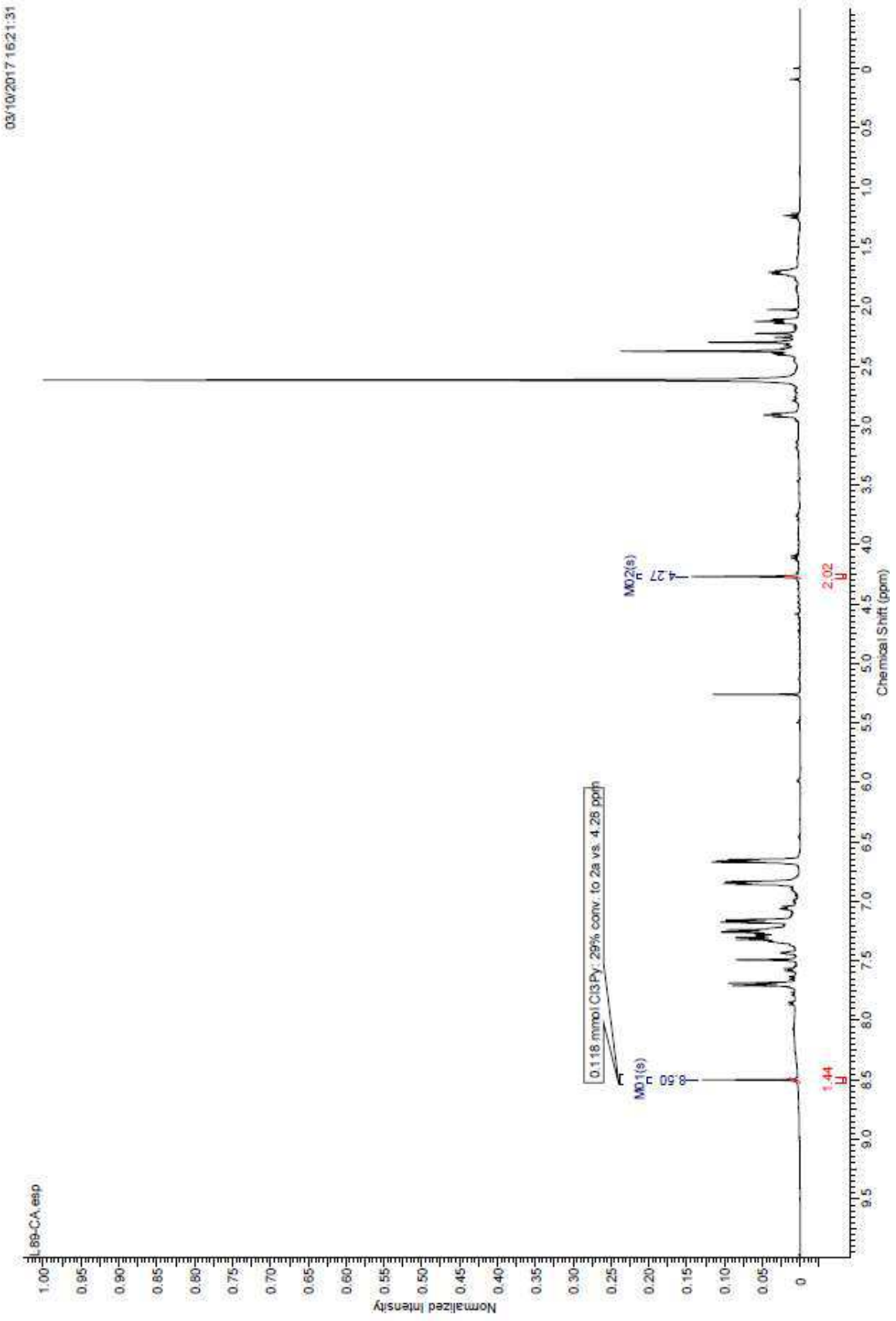


Radical control experiments

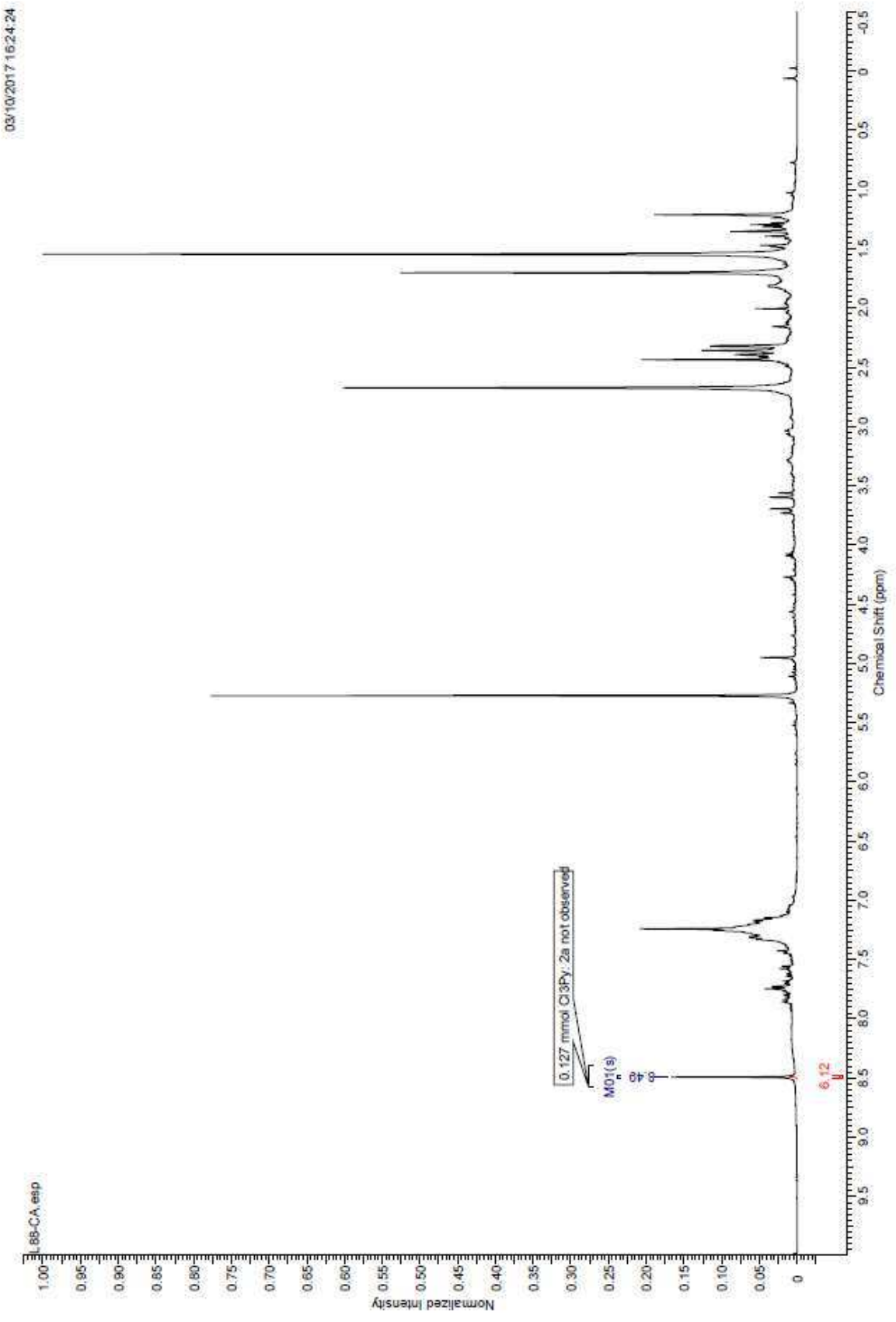
With BHT additive, $CDCl_3$



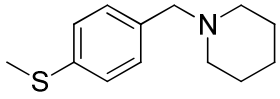
With catechol additive, $CDCl_3$



With TEMPO additive, $CDCl_3$

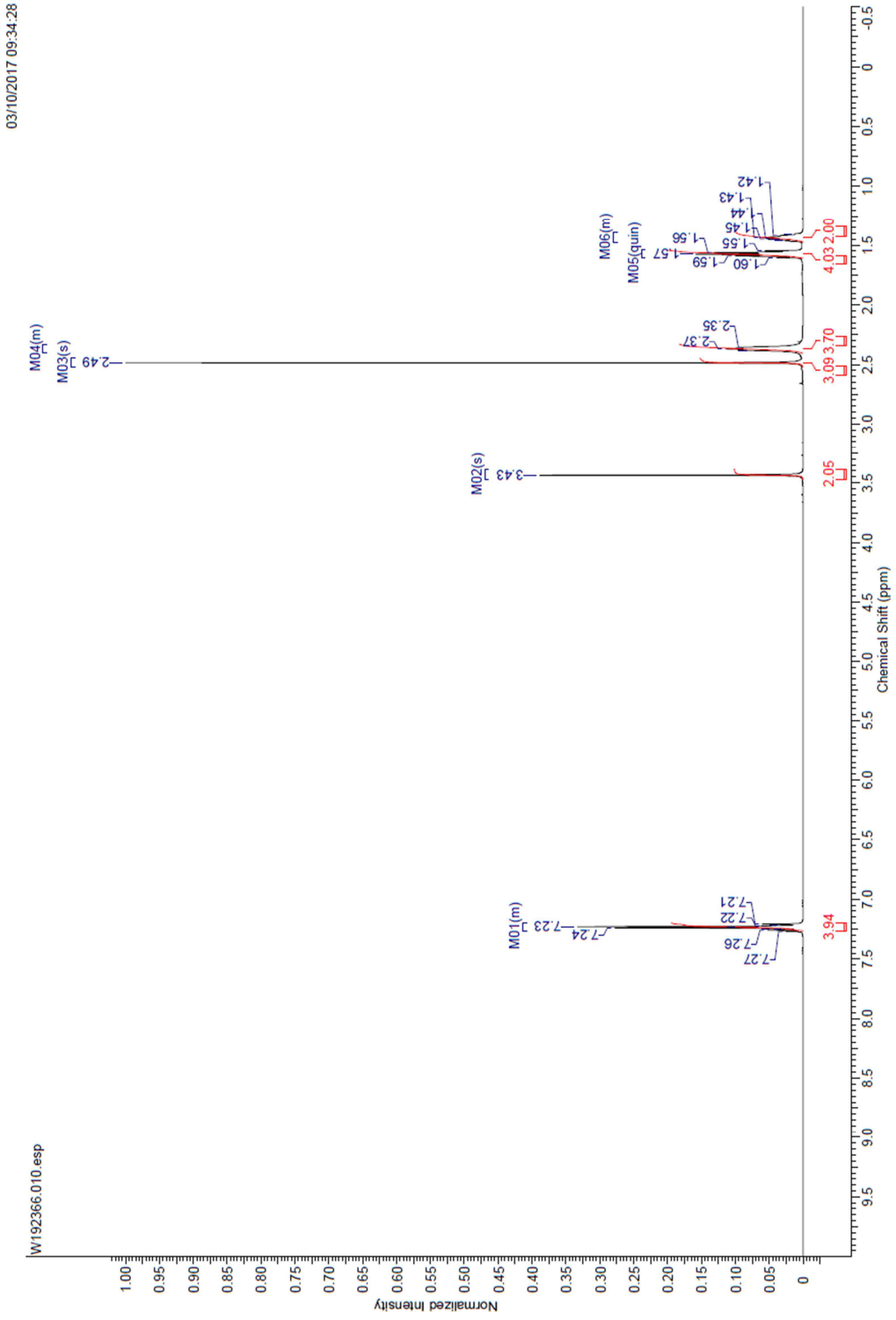


Synthesized starting materials

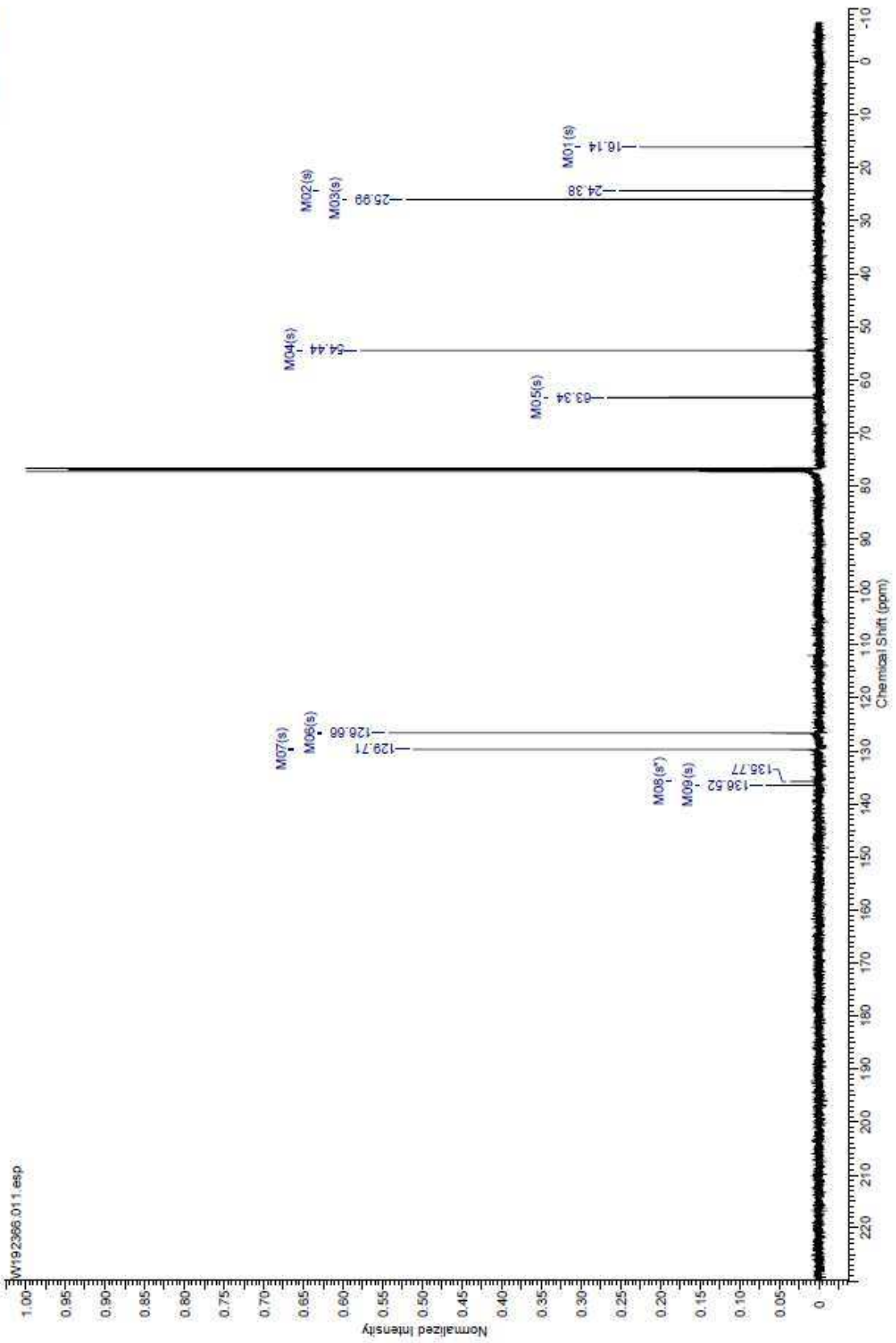


1-(4-(Methylthio)benzyl)piperidine 3c

^{1}H, $CDCl_3$



^{13}C, $CDCl_3$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M08(s*)
M09(s)
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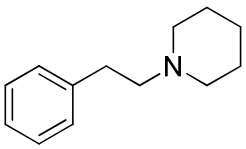
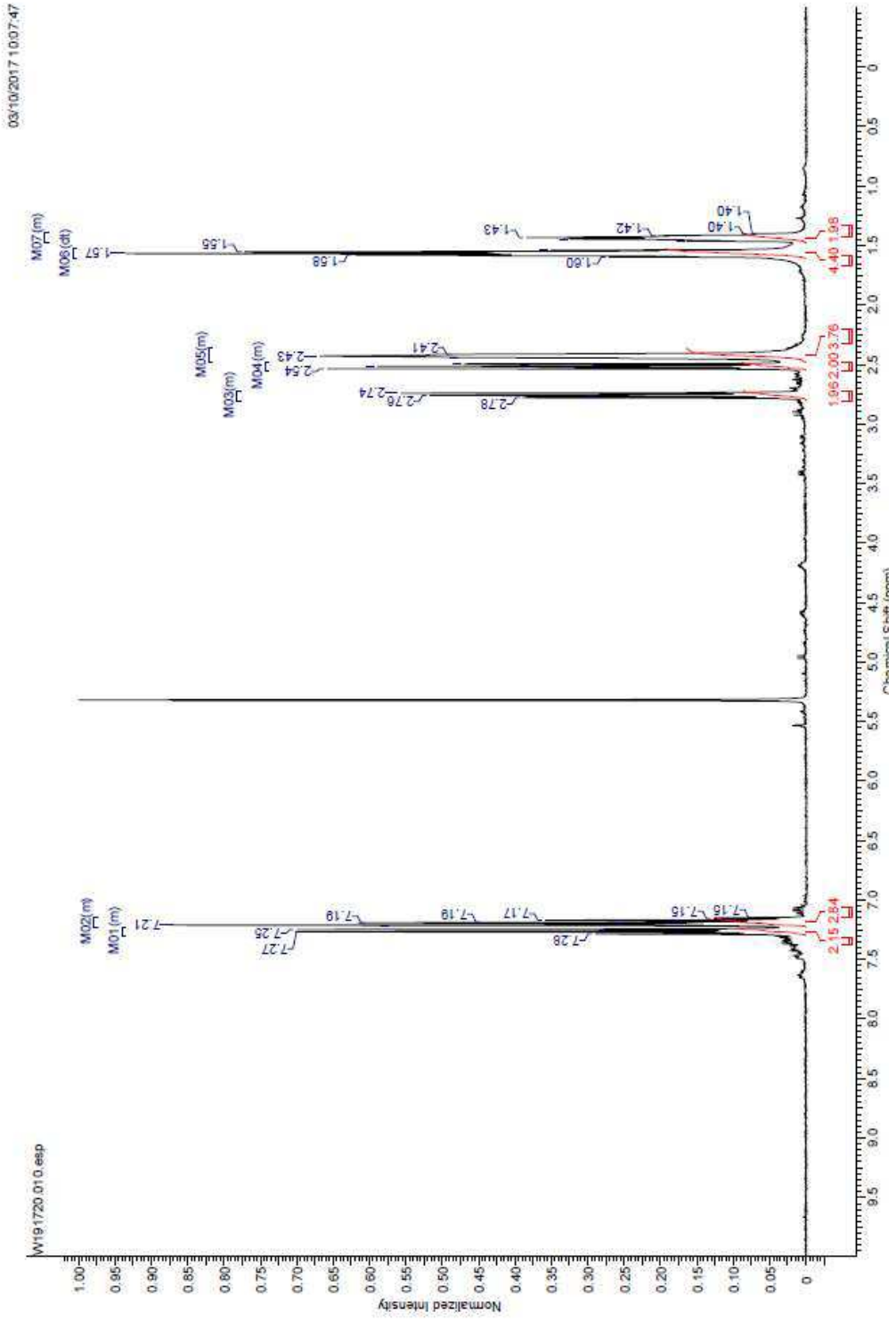
136.77

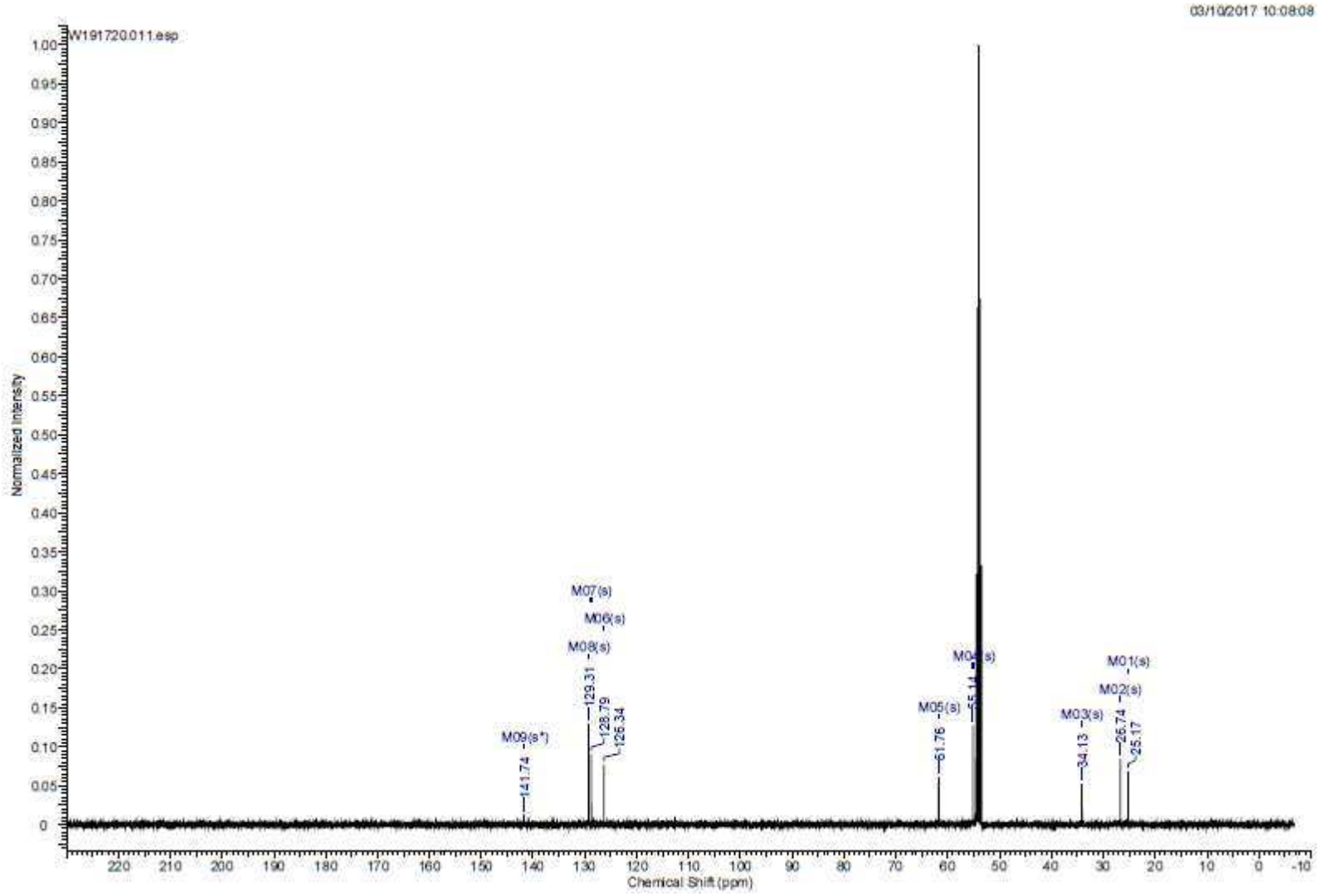


1-Phenethylpiperidine 3e

^{1}H, CD_2Cl_2



^{13}C, CD_2Cl_2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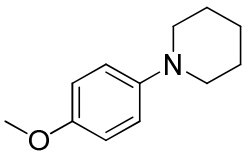
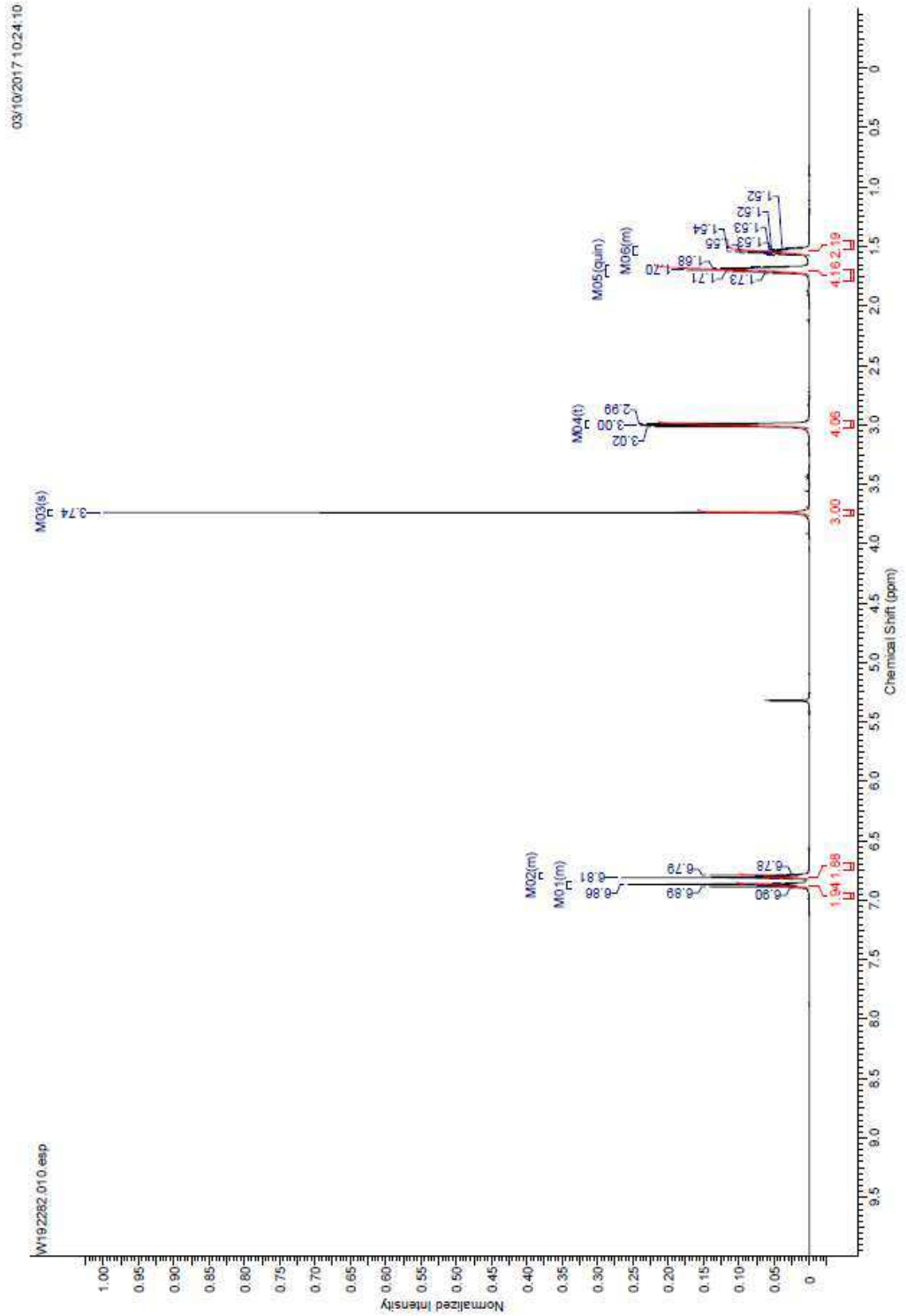
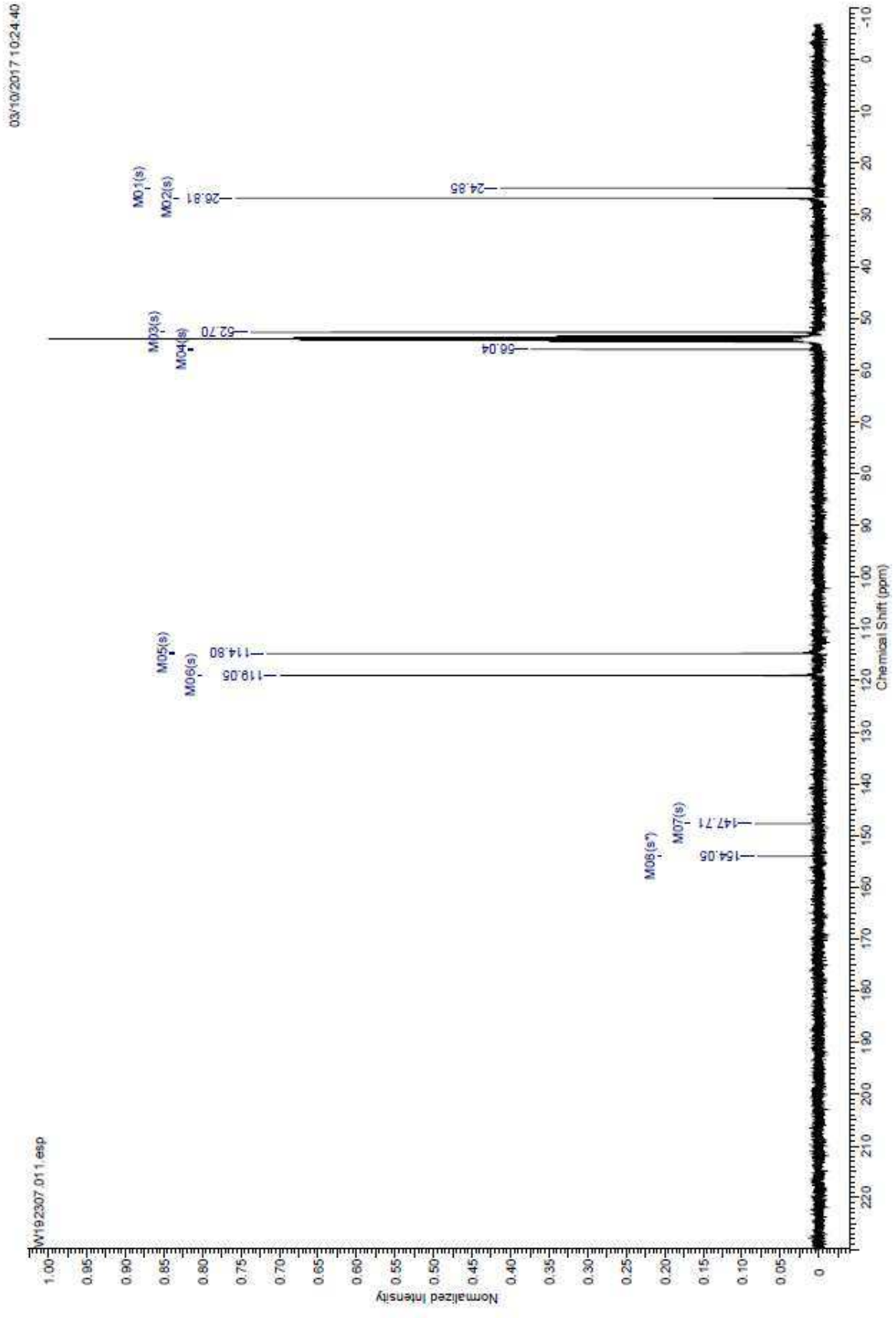


1-(4-Methoxyphenyl)piperidine 3m

^{1}H, CD_2Cl_2



^{13}C, CD_2Cl_2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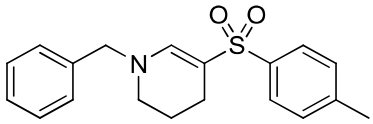
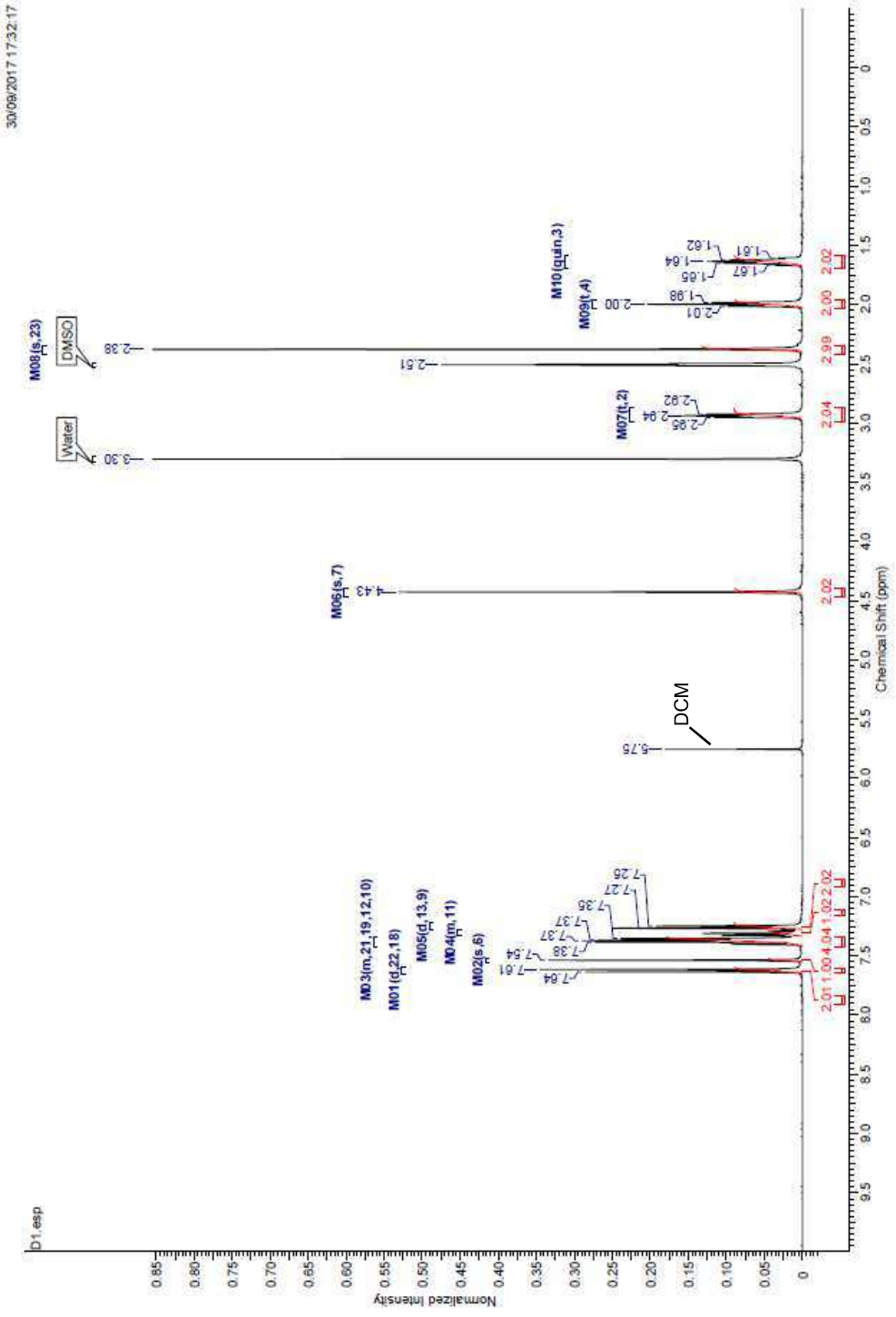
Oxidative β-C–H sulfonylation of amines



1-Benzyl-5-tosyl-1,2,3,4-tetrahydropyridine 2a

^{1}H, DMSO-*d*$_6$



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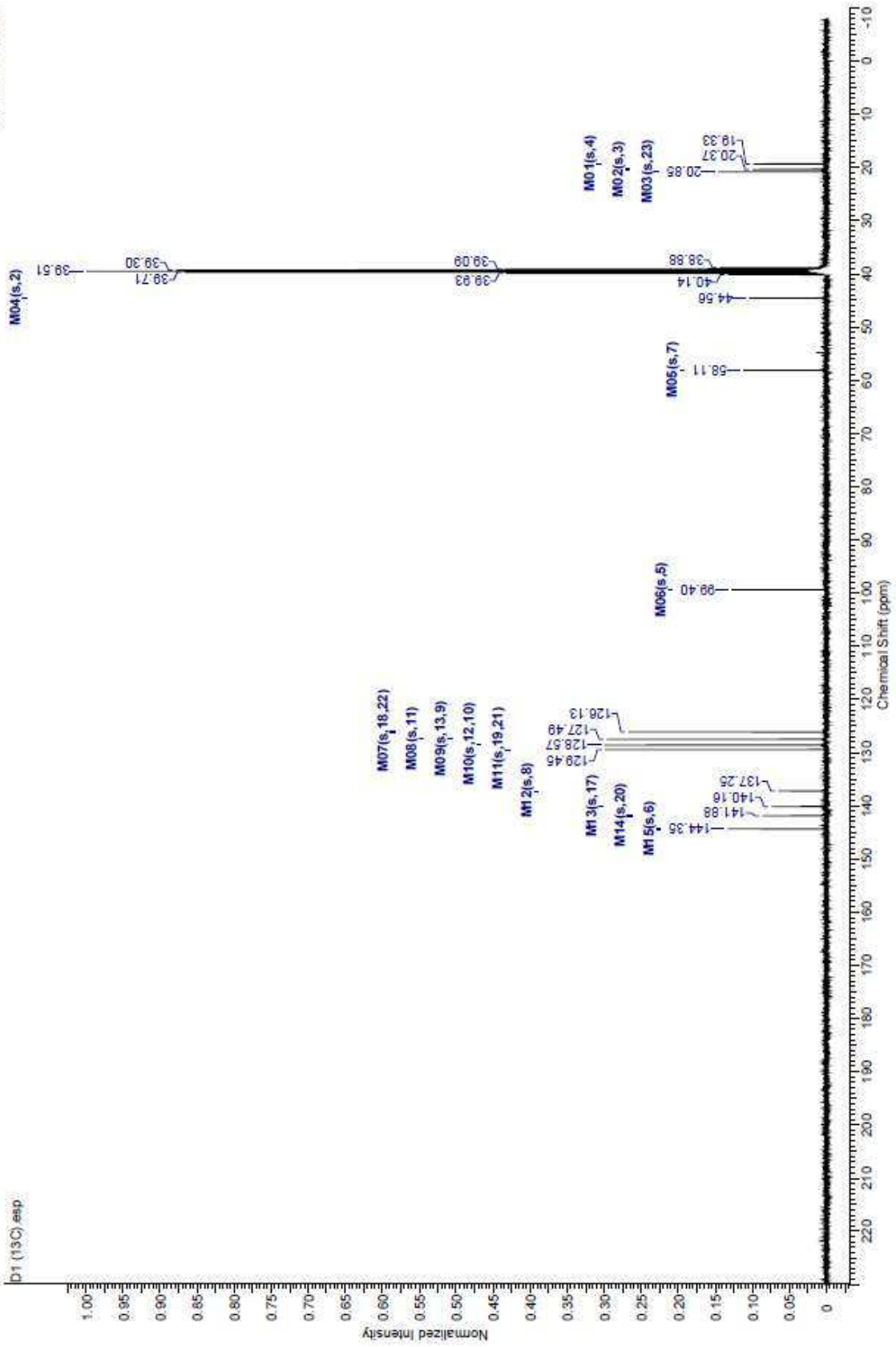
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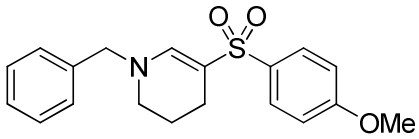
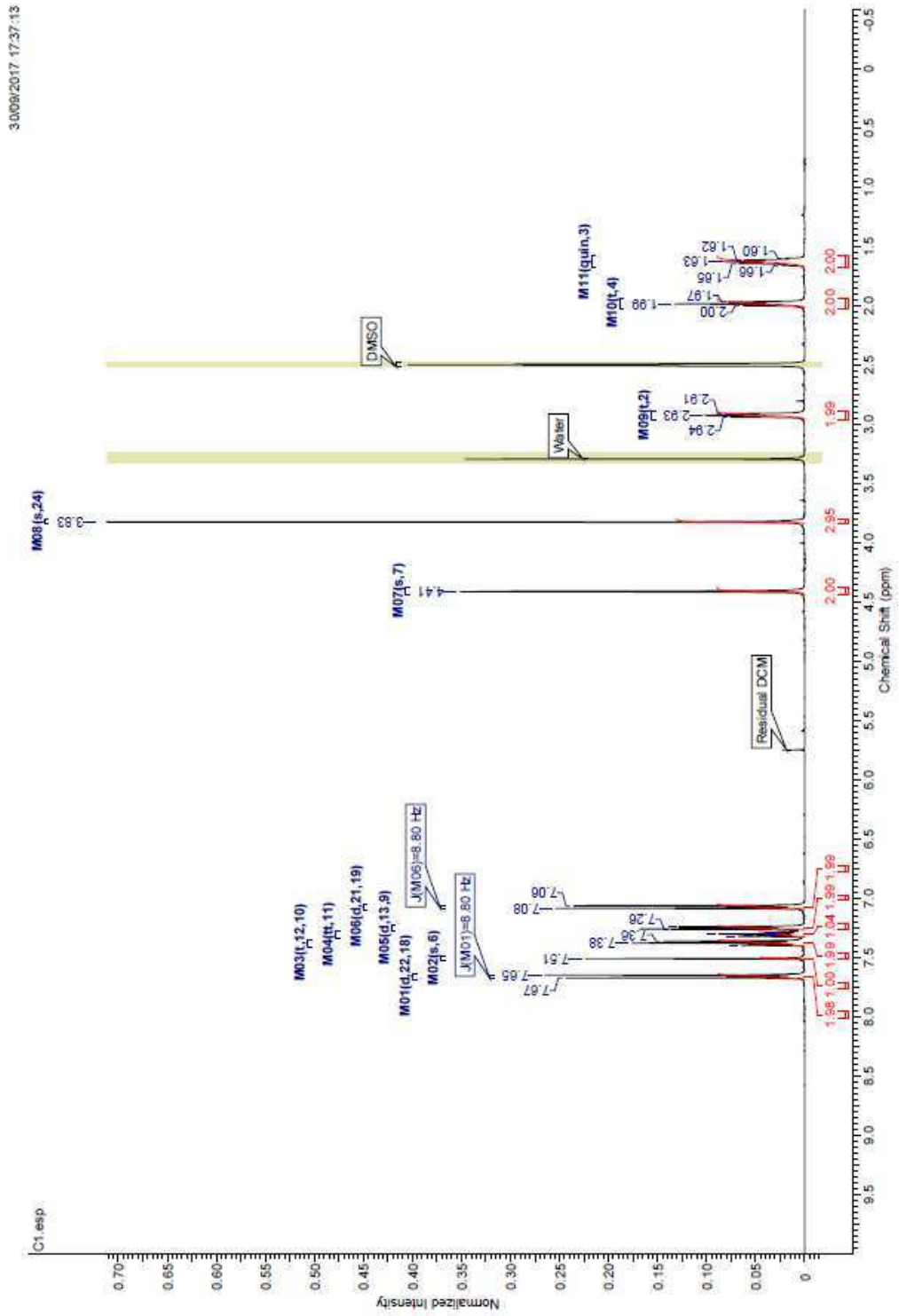


1-Benzyl-5-((4-methoxyphenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2b

^{1}H, DMSO-*d*$_6$



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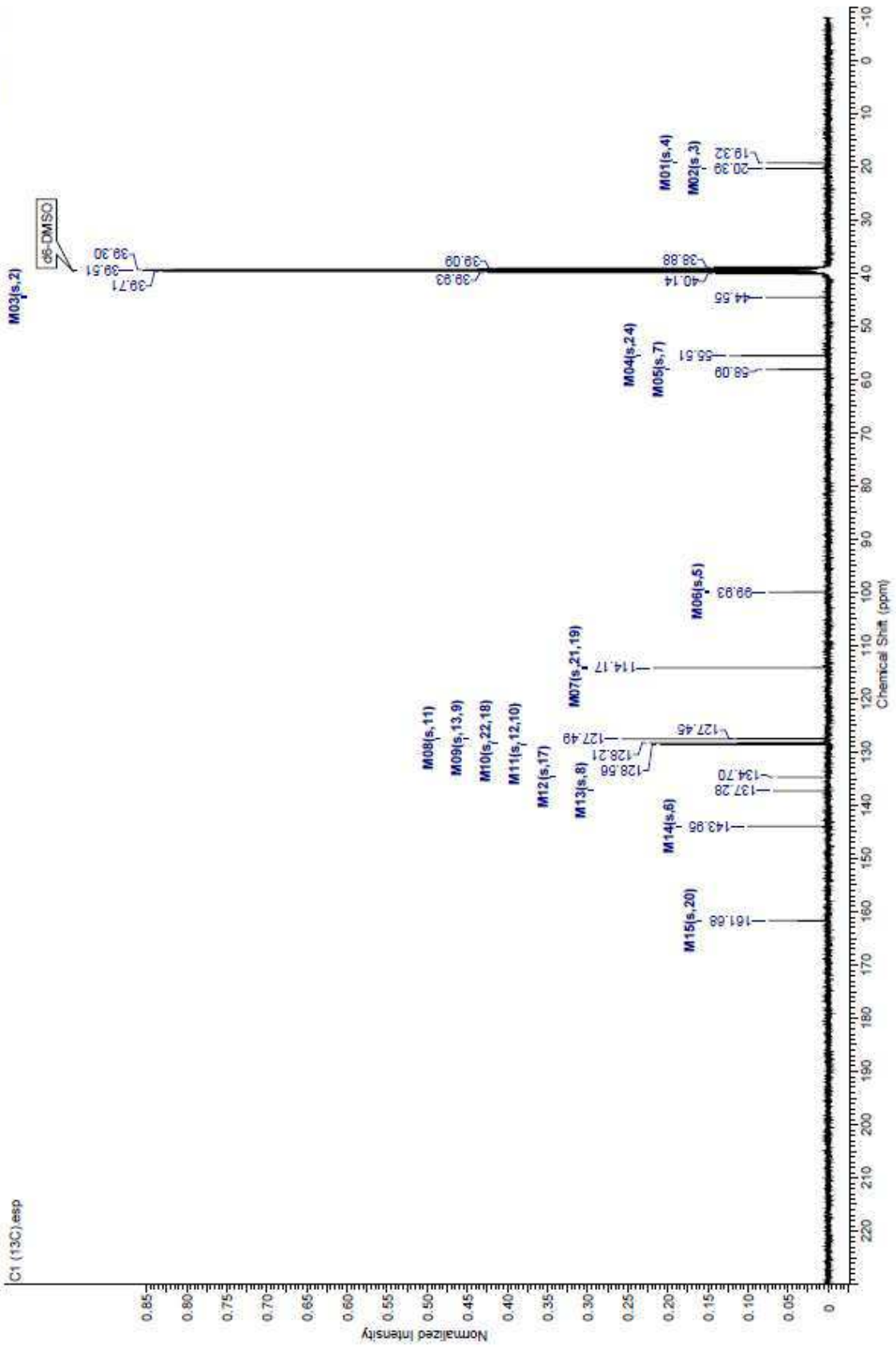
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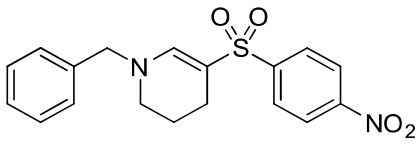
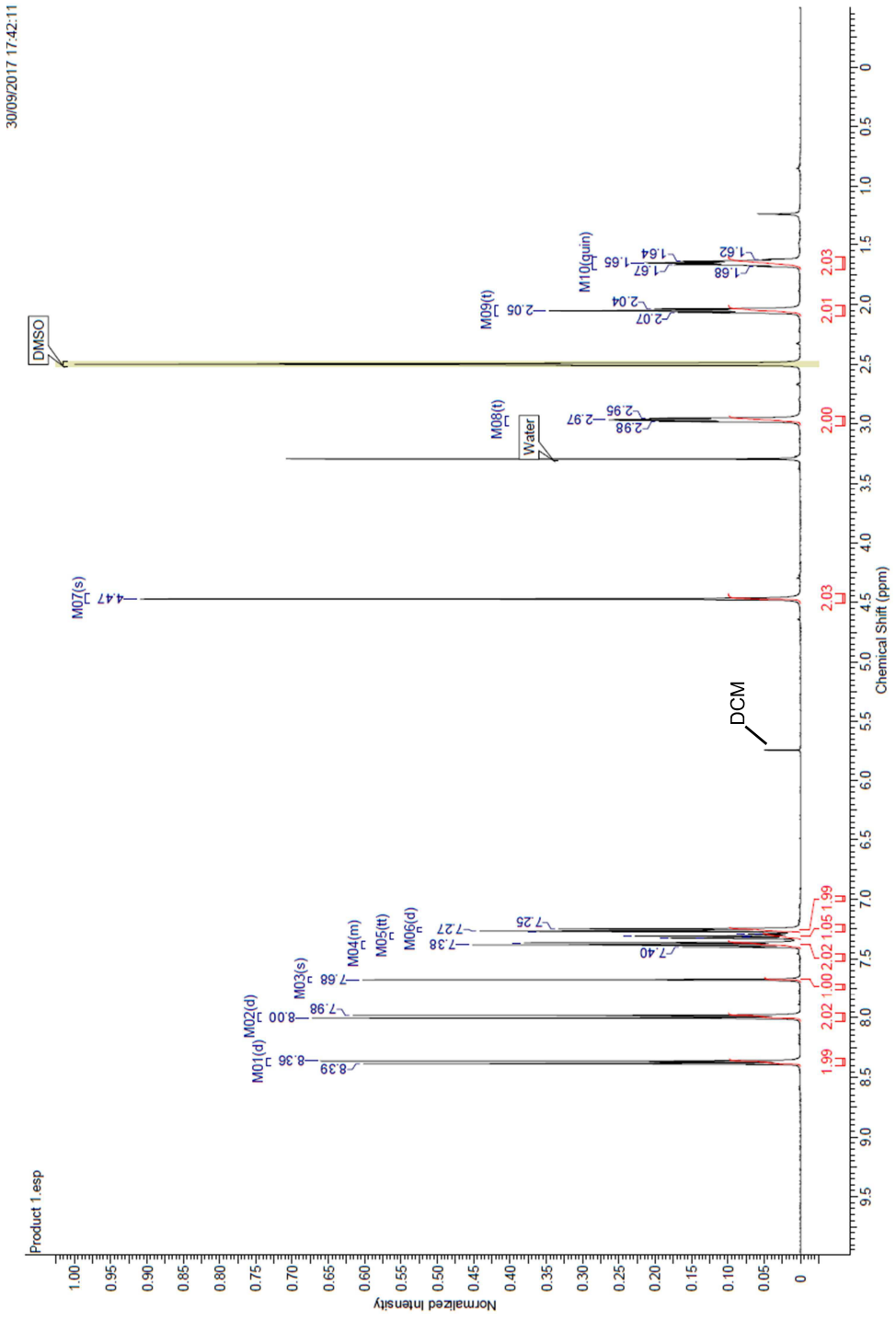
Normalized Intensity

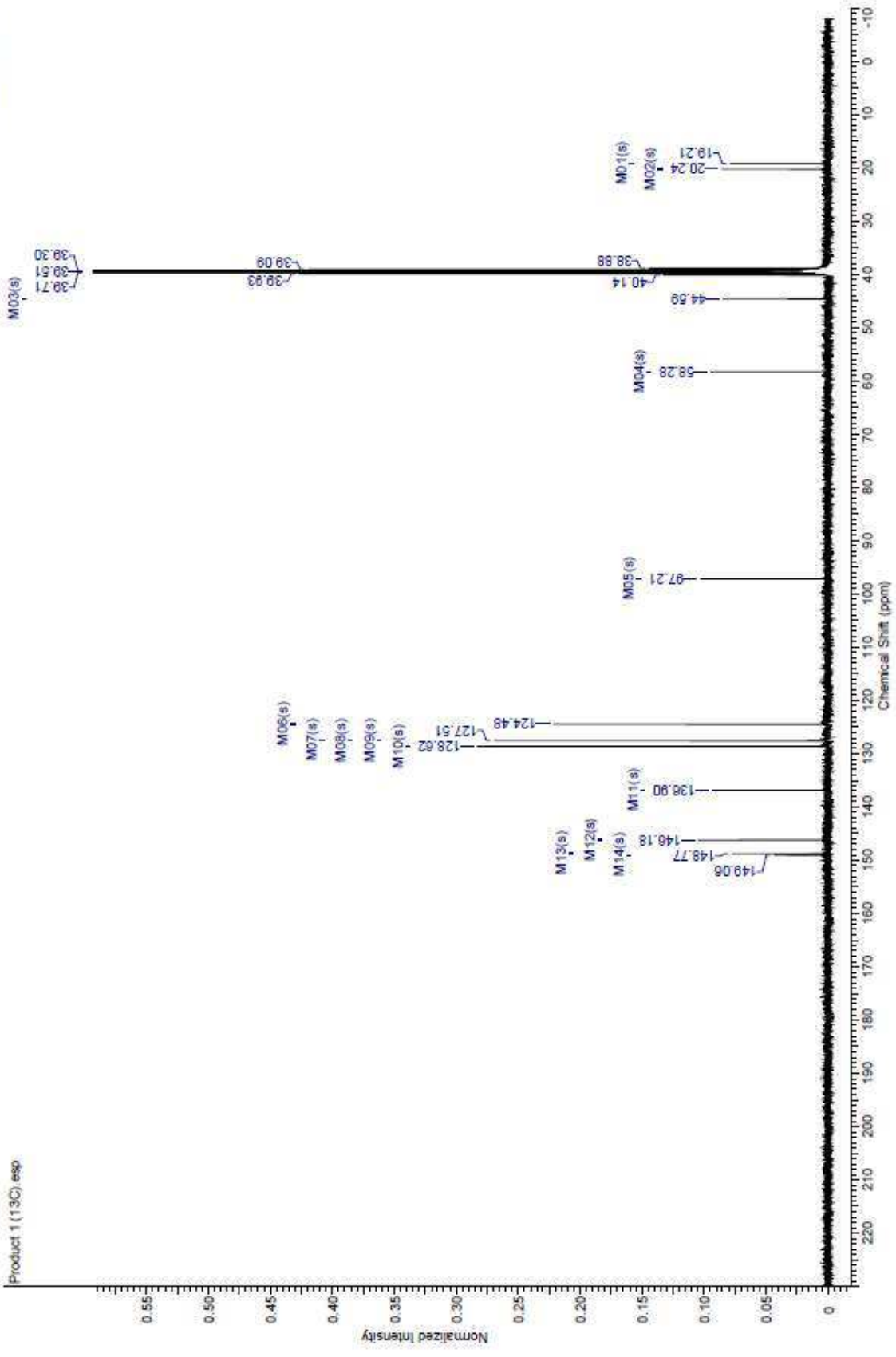


1-Benzyl-5-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2c

^{1}H, DMSO-*d*$_6$



^{13}C, DMSO-d_6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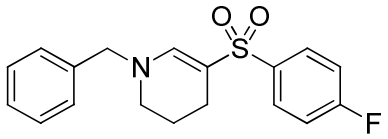
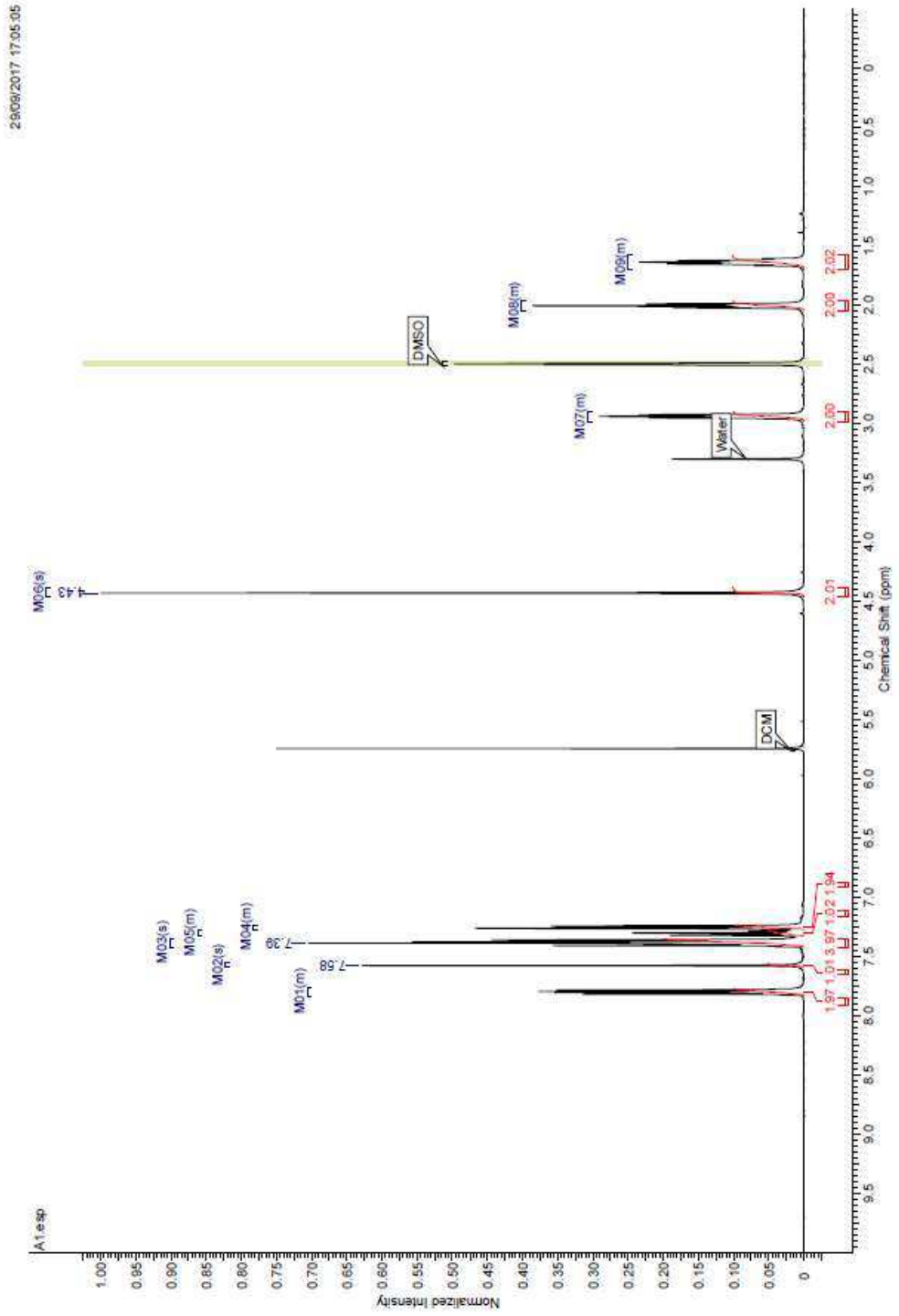
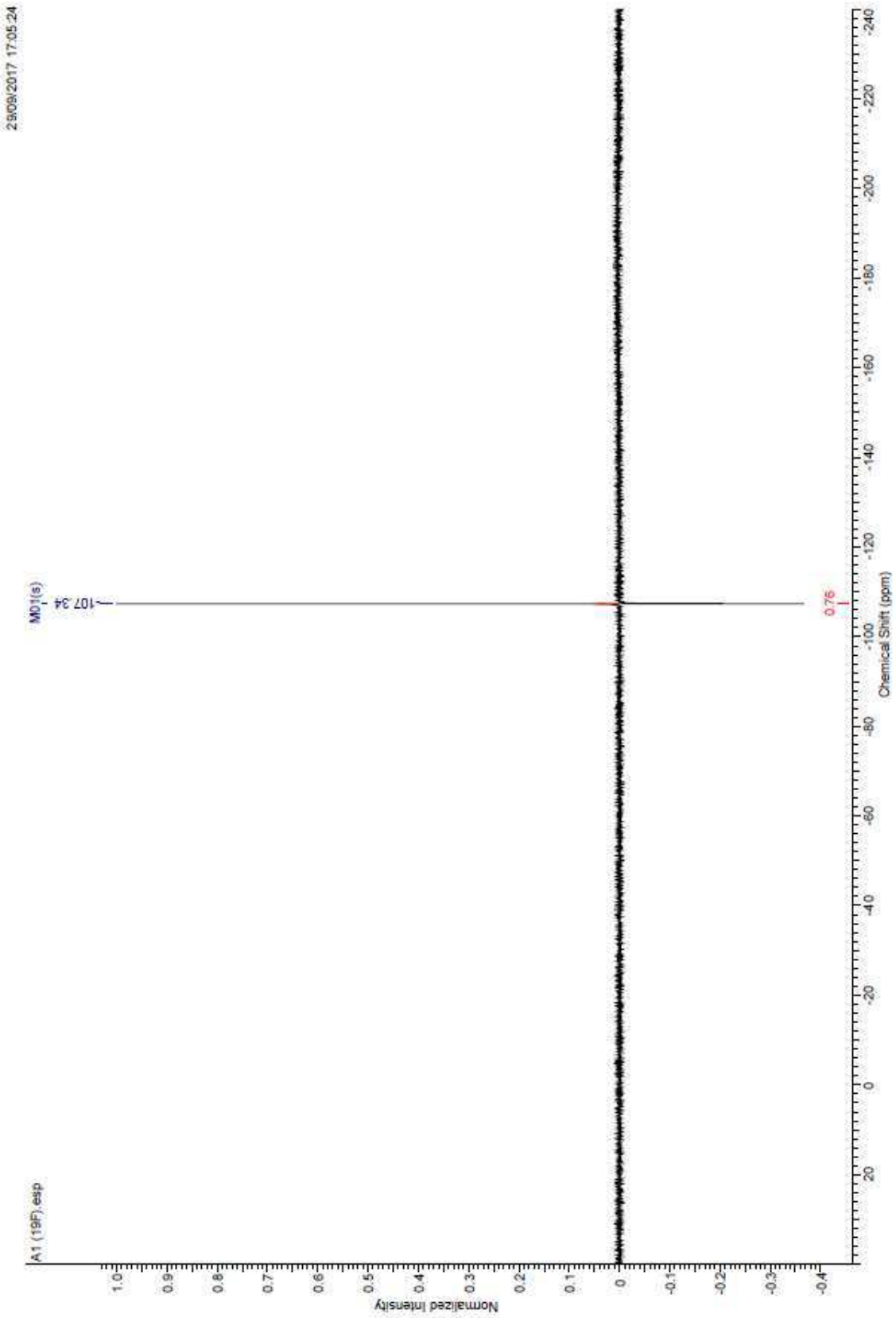


1-Benzyl-5-((4-fluorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2d

^{1}H, DMSO-*d*$_6$



^{19}F, $CDCl_3$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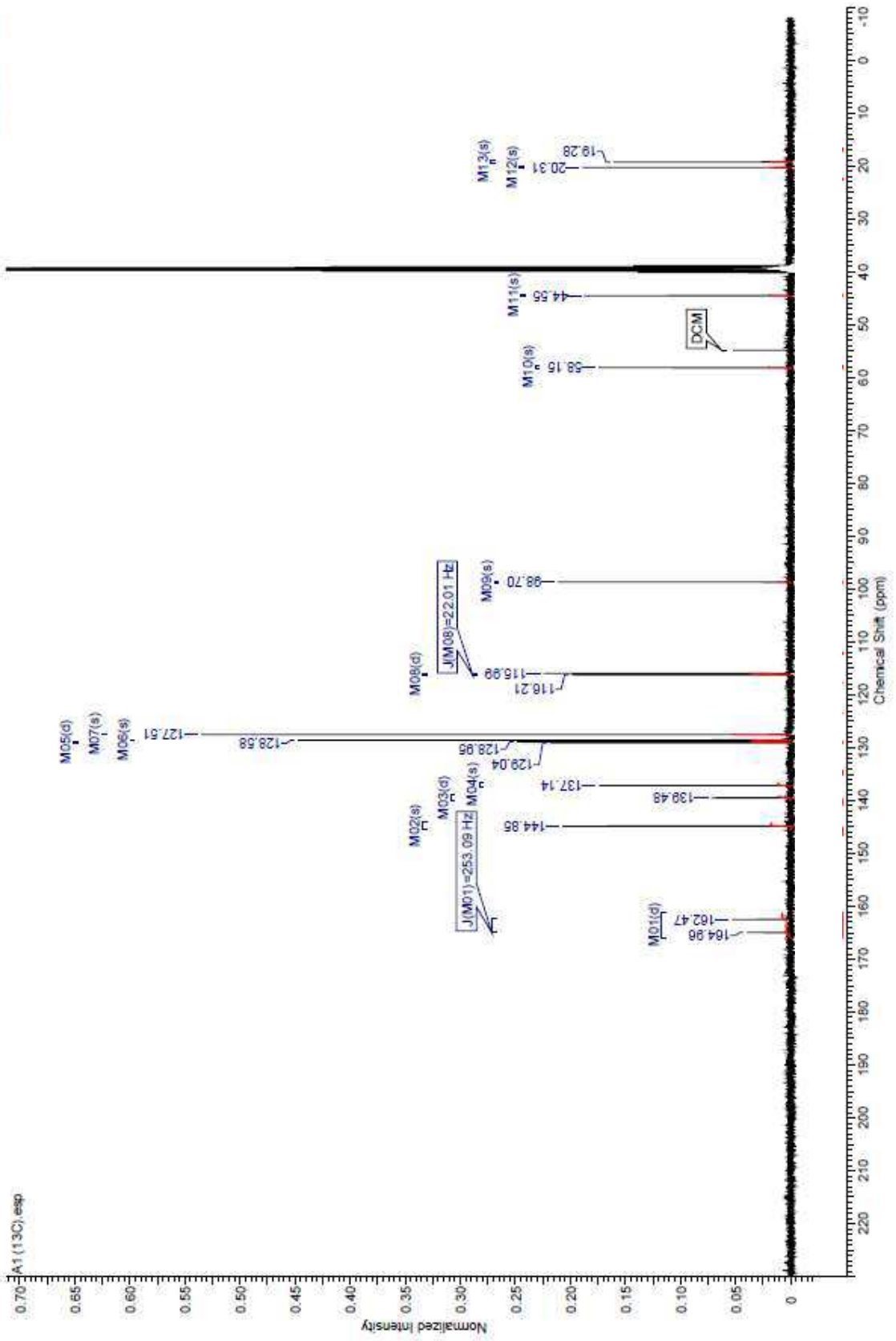
Normalized Intensity
Chemical Shift (ppm)

^{13}C, DMSO-d_6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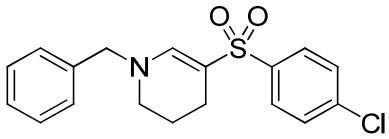
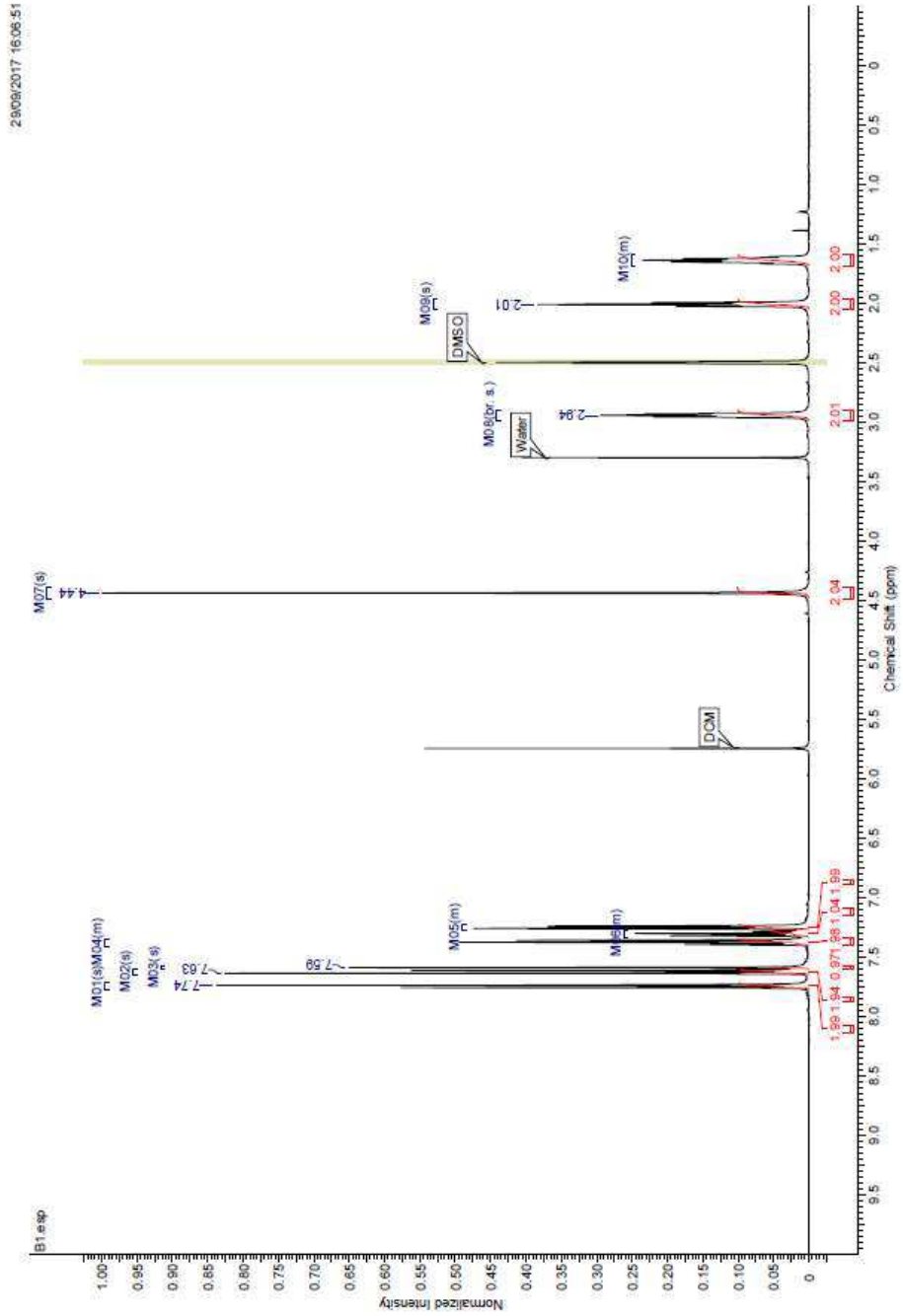
162.47
164.96

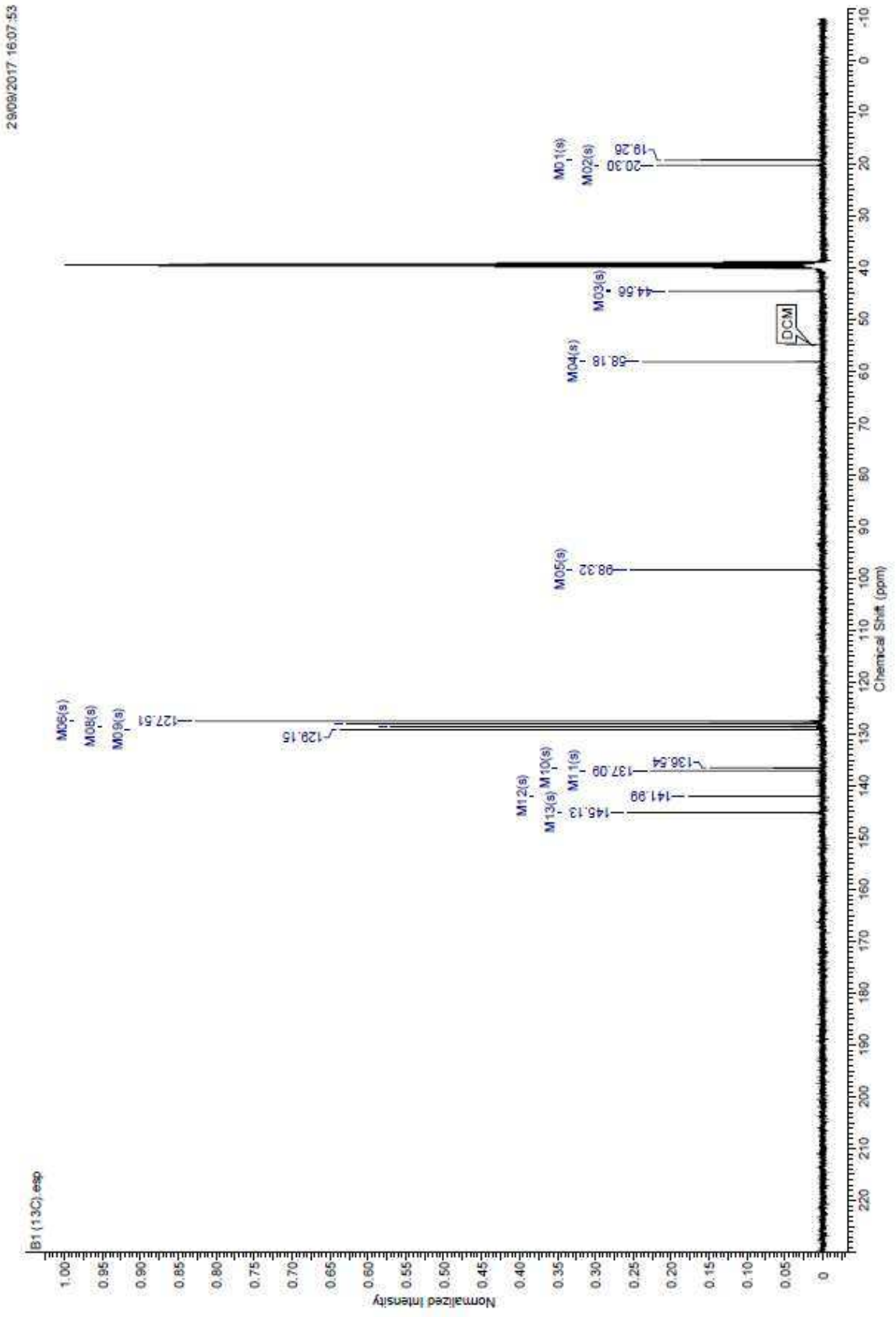


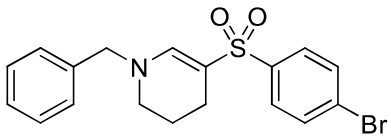
1-Benzyl-5-((4-chlorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2e

^{1}H, DMSO-*d*$_6$



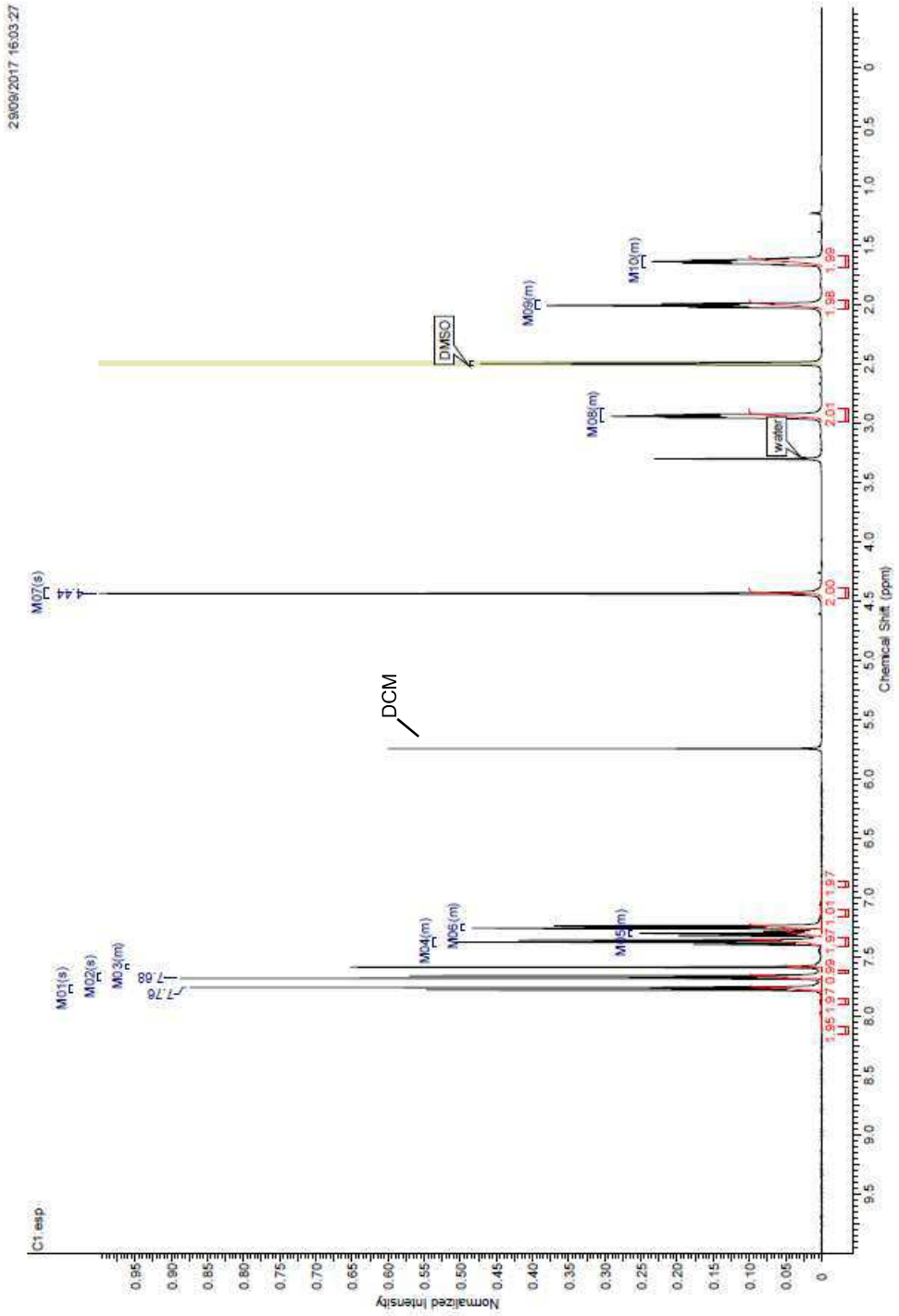
^{13}C, DMSO-d_6


29/09/2017 16:07:53
B1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
19.26
20.30
44.66
58.18
88.32
127.51
128.15
136.54
137.09
141.99
145.13
DCM

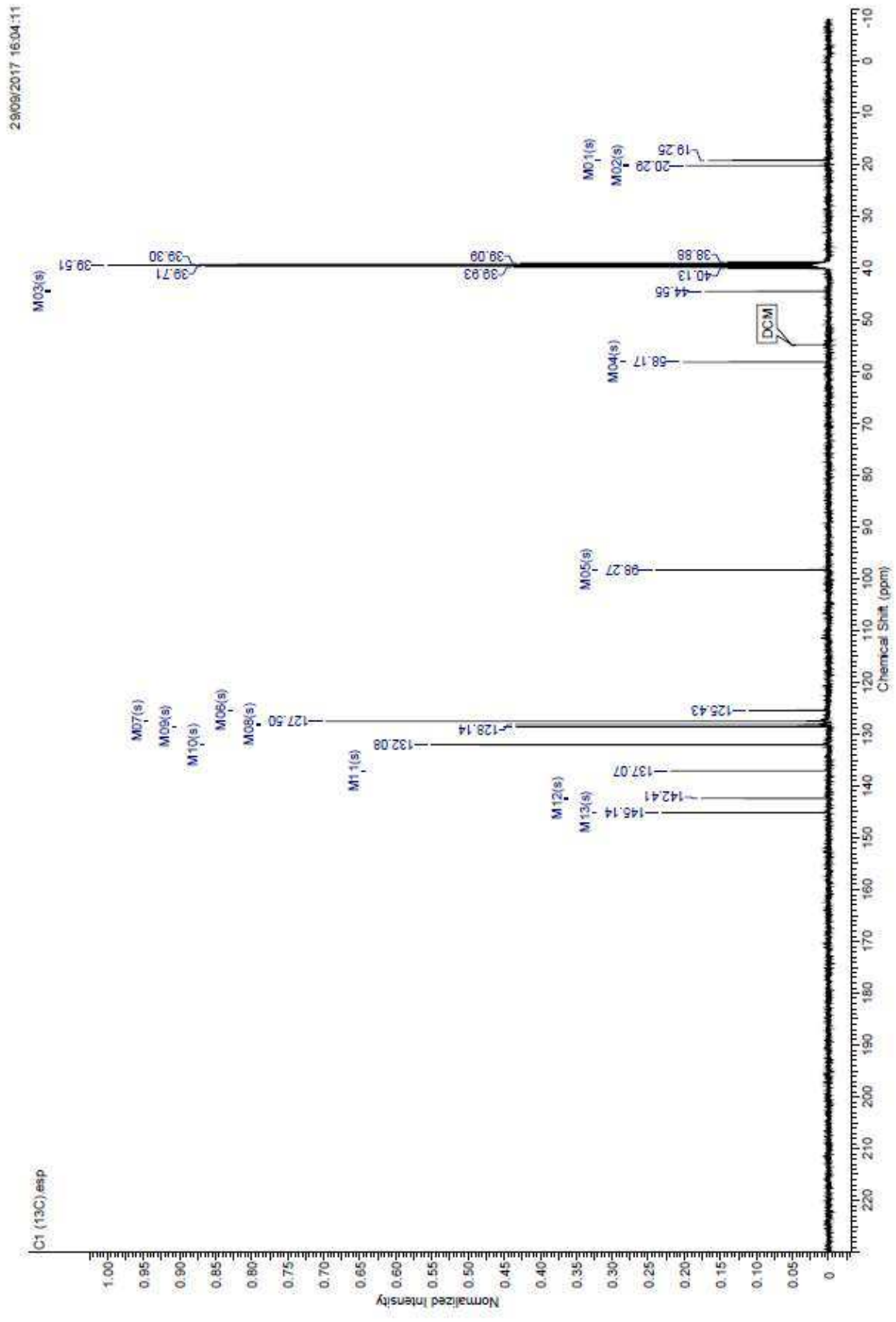


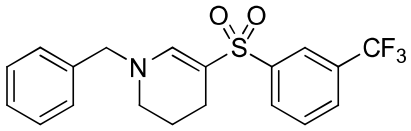
1-Benzyl-5-((4-bromophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2f

^{1}H, DMSO-*d*$_6$



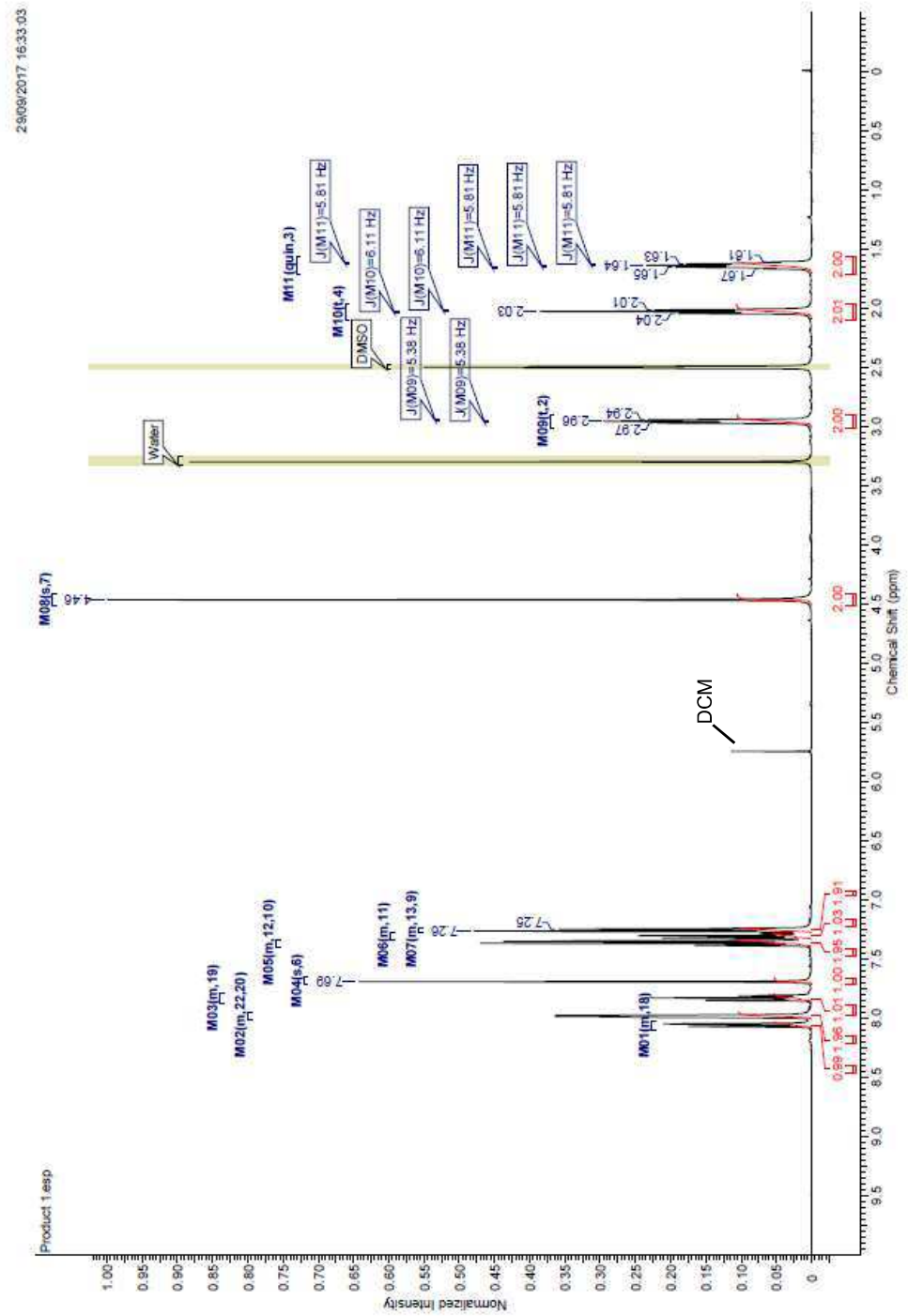
^{13}C, DMSO-d_6


29/09/2017 16:04:11
C1 (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
DCM
19.25
20.29
38.88
39.09
39.30
39.51
39.71
39.93
40.13
44.66
58.17
98.27
125.43
127.50
128.14
132.08
137.07
142.41
146.14

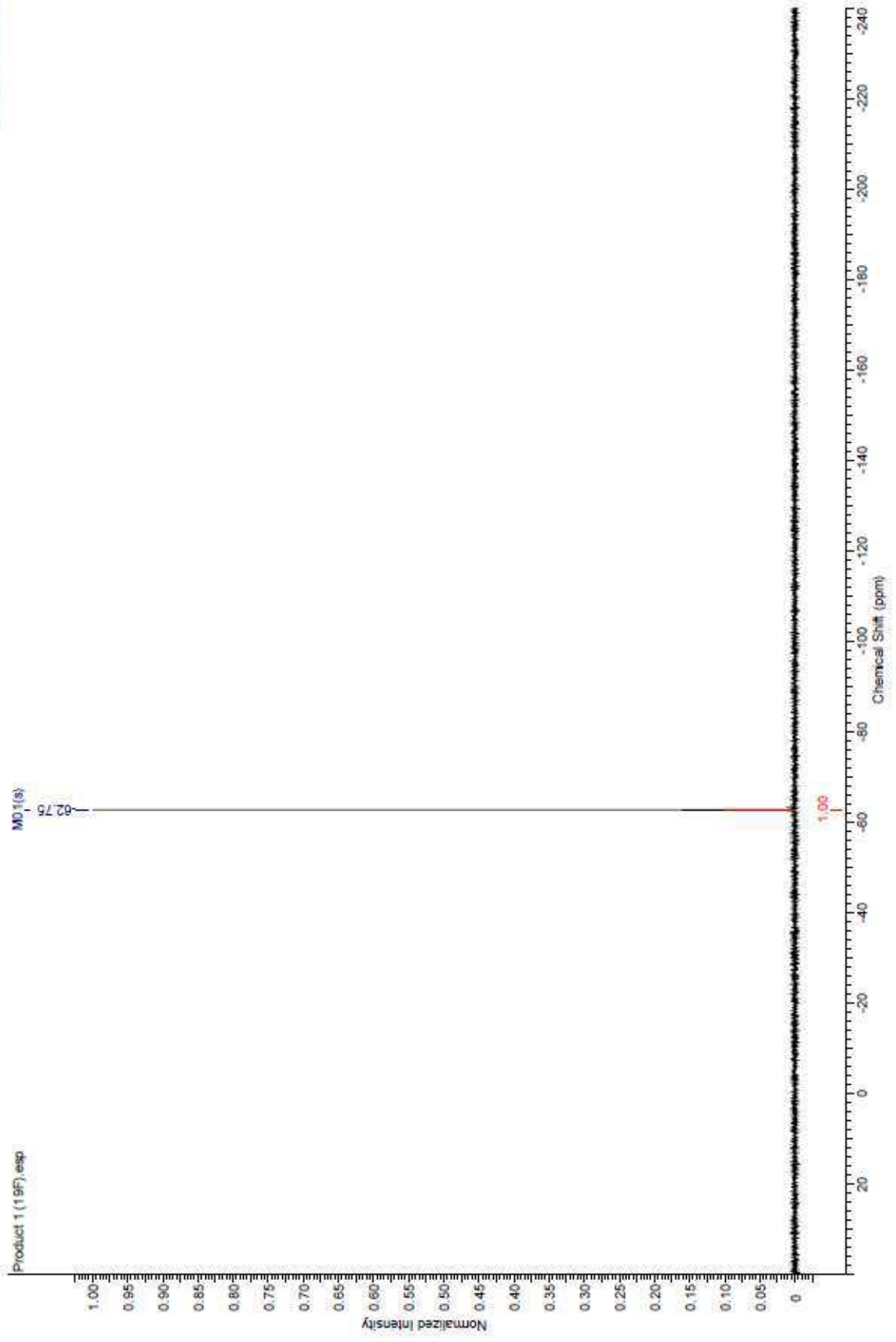


1-Benzyl-5-((3-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2g

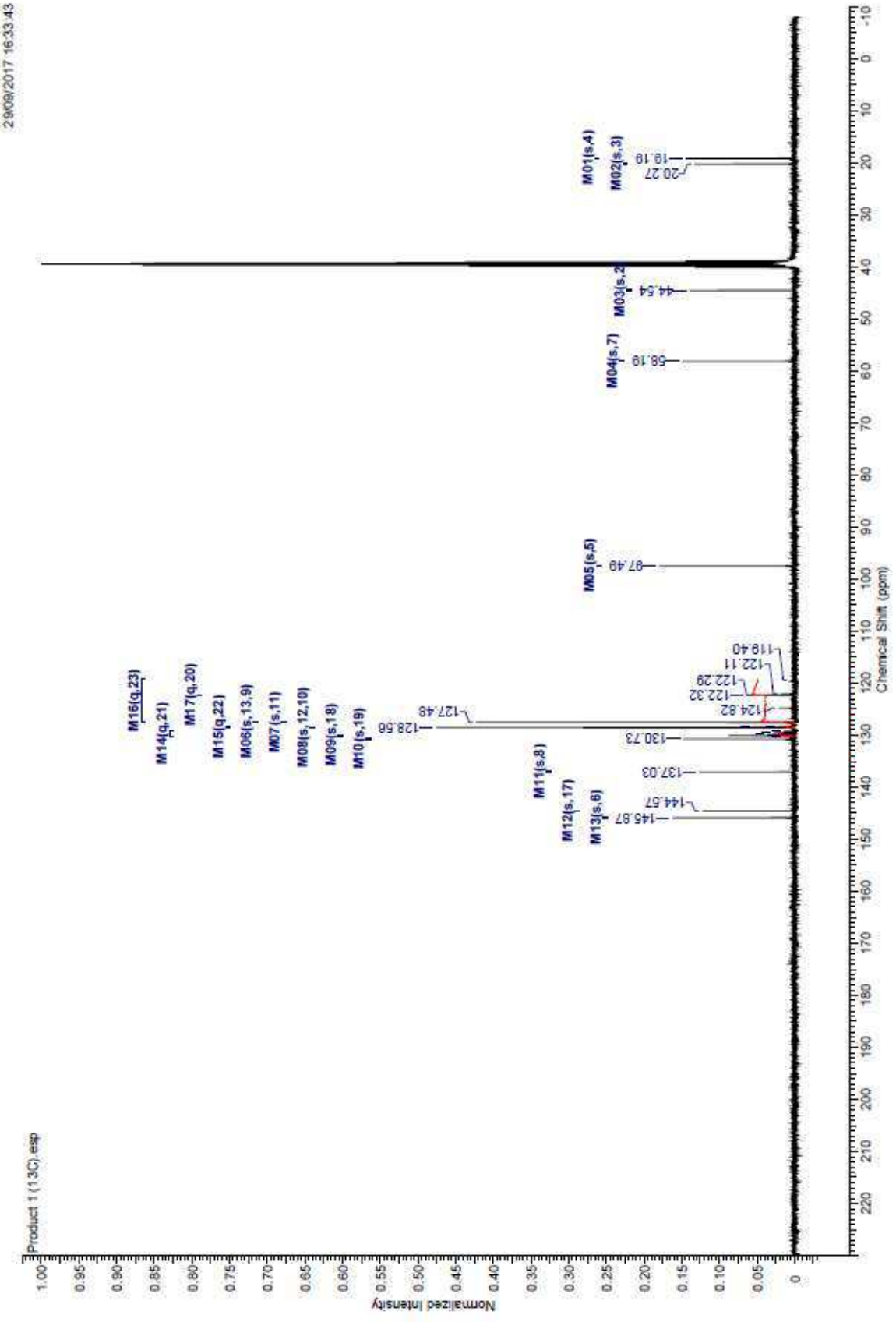
^{1}H, DMSO-*d*$_6$

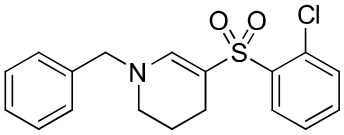


^{19}F, $CDCl_3$


29/09/2017 16:33:19
Product 1 (19F).esp
MD1(s)
-62.75
1.00
Normalized Intensity
Chemical Shift (ppm)

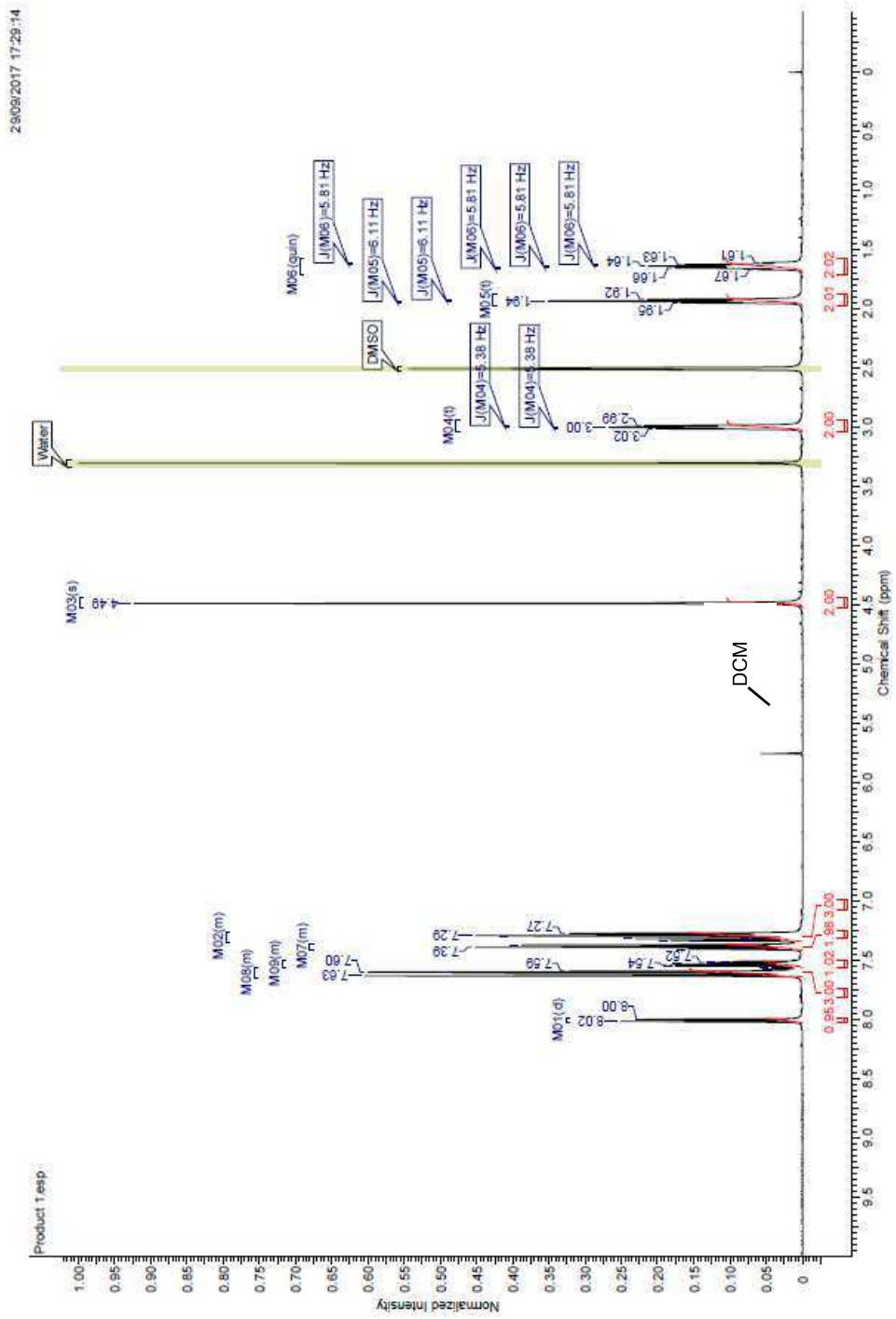
^{13}C, DMSO-d_6


29/09/2017 16:33:43
Product 1 (13C).esp
M01(s,4)
M02(s,3)
M03(s,2)
M04(s,7)
M05(s,5)
M06(s,13,9)
M07(s,11)
M08(s,12,10)
M09(s,18)
M10(s,19)
M11(s,8)
M12(s,17)
M13(s,6)
M14(q,21)
M15(q,22)
M16(q,23)
M17(q,20)
19.19
20.27
44.54
58.19
97.49
118.40
122.11
122.29
122.32
124.82
127.48
128.58
130.73
137.03
144.57
145.87
Chemical Shift (ppm)
Normalized Intensity

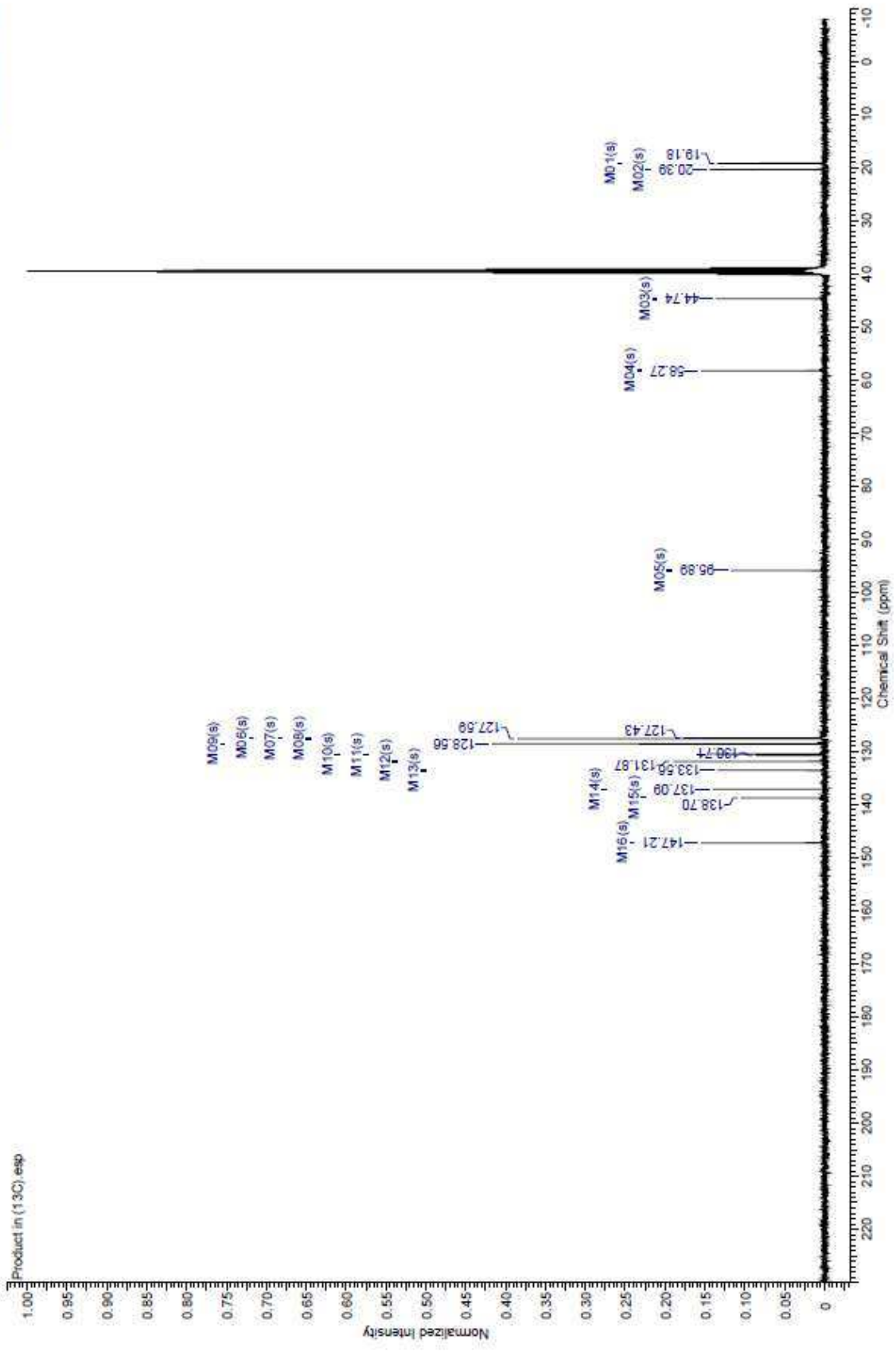


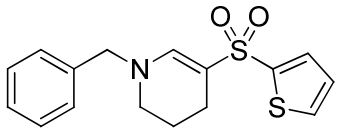
1-Benzyl-5-((2-chlorophenyl)sulfonyl)-1,2,3,4-tetrahydropyridine 2h

^{1}H, DMSO-*d*$_6$



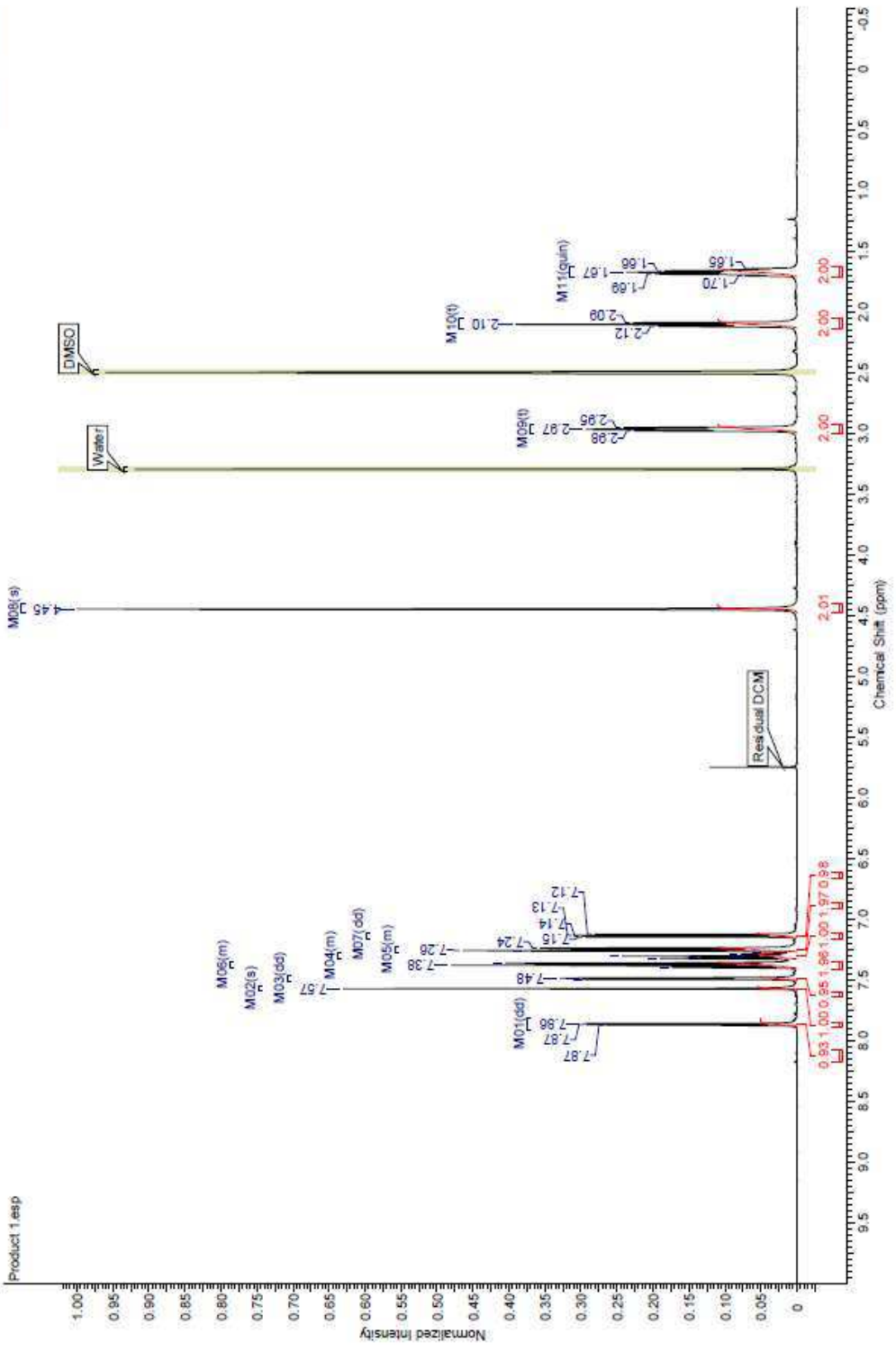
^{13}C, DMSO-d_6


29/09/2017 17:30:44
Product in (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
19.18
20.39
44.74
58.27
86.89
127.43
127.59
128.56
130.74
131.87
133.56
137.09
138.70
147.21

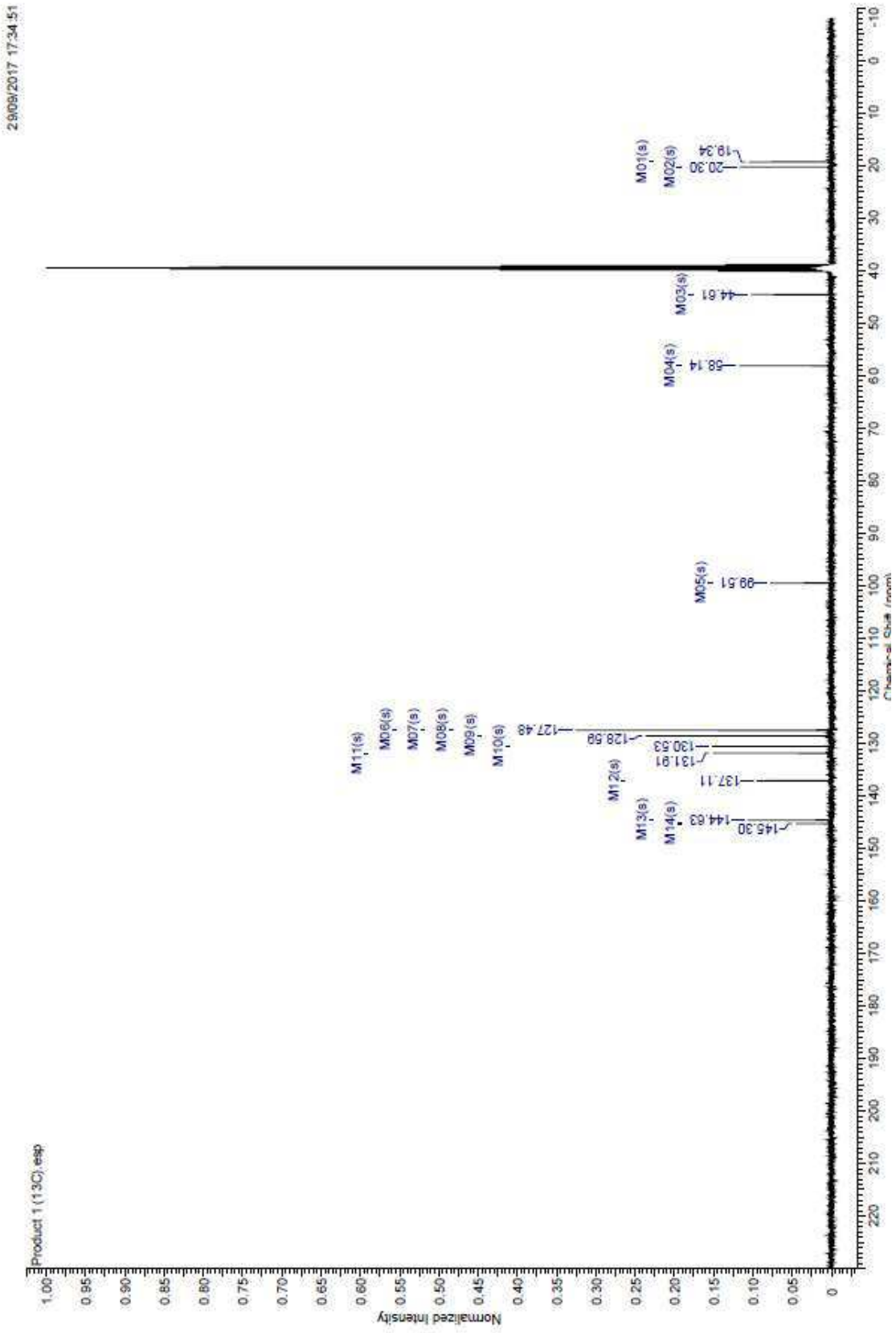


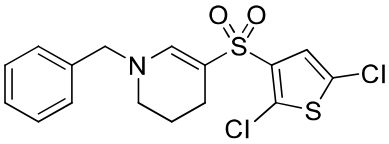
1-Benzyl-5-(thiophen-2-ylsulfonyl)-1,2,3,4-tetrahydropyridine 2i

^{1}H, DMSO-*d*$_6$



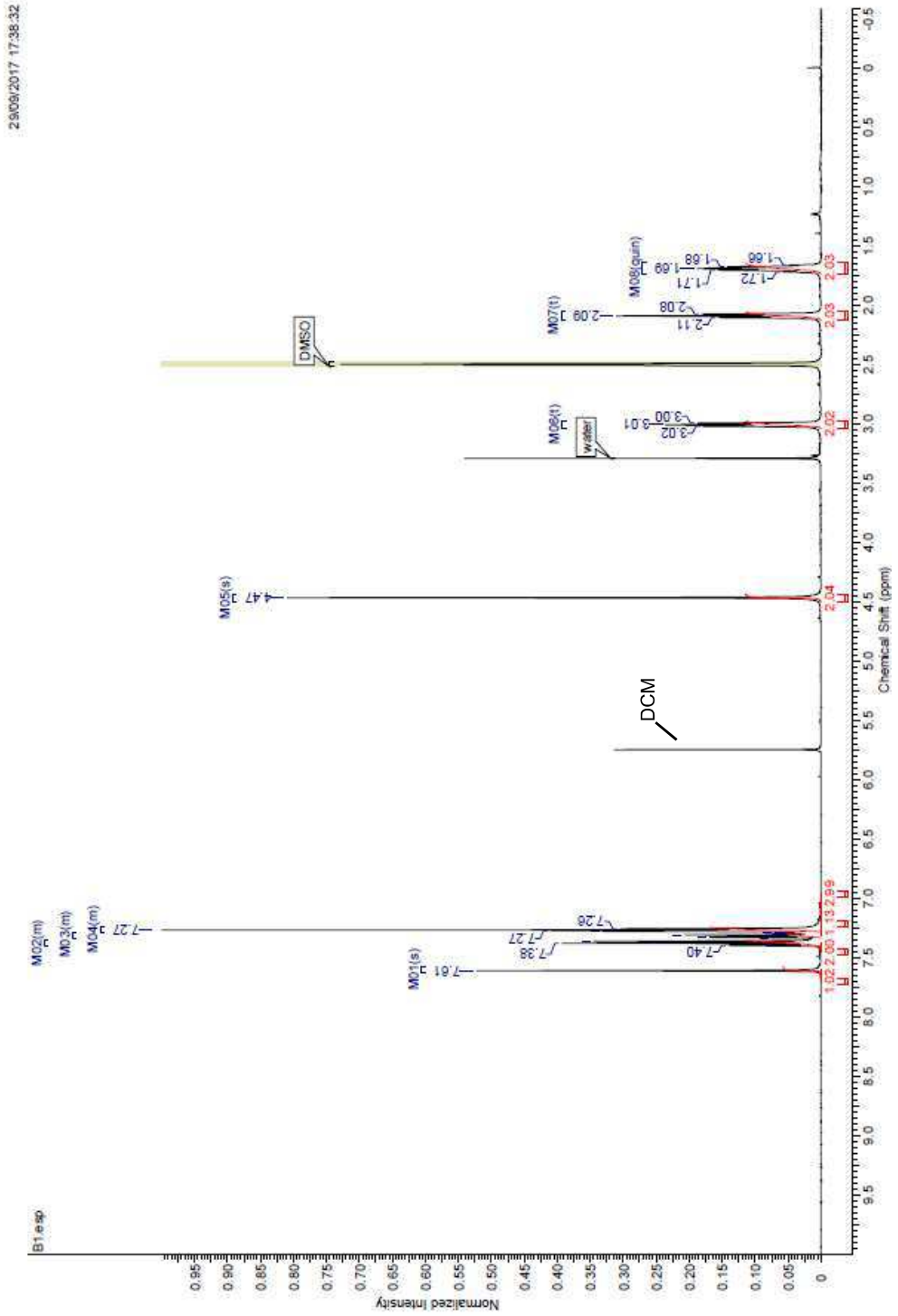
^{13}C, DMSO-d_6


29/09/2017 17:34:51
Product 1 (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
19.34
20.30
44.61
58.14
99.51
127.48
128.58
130.53
131.91
137.11
144.63
145.30

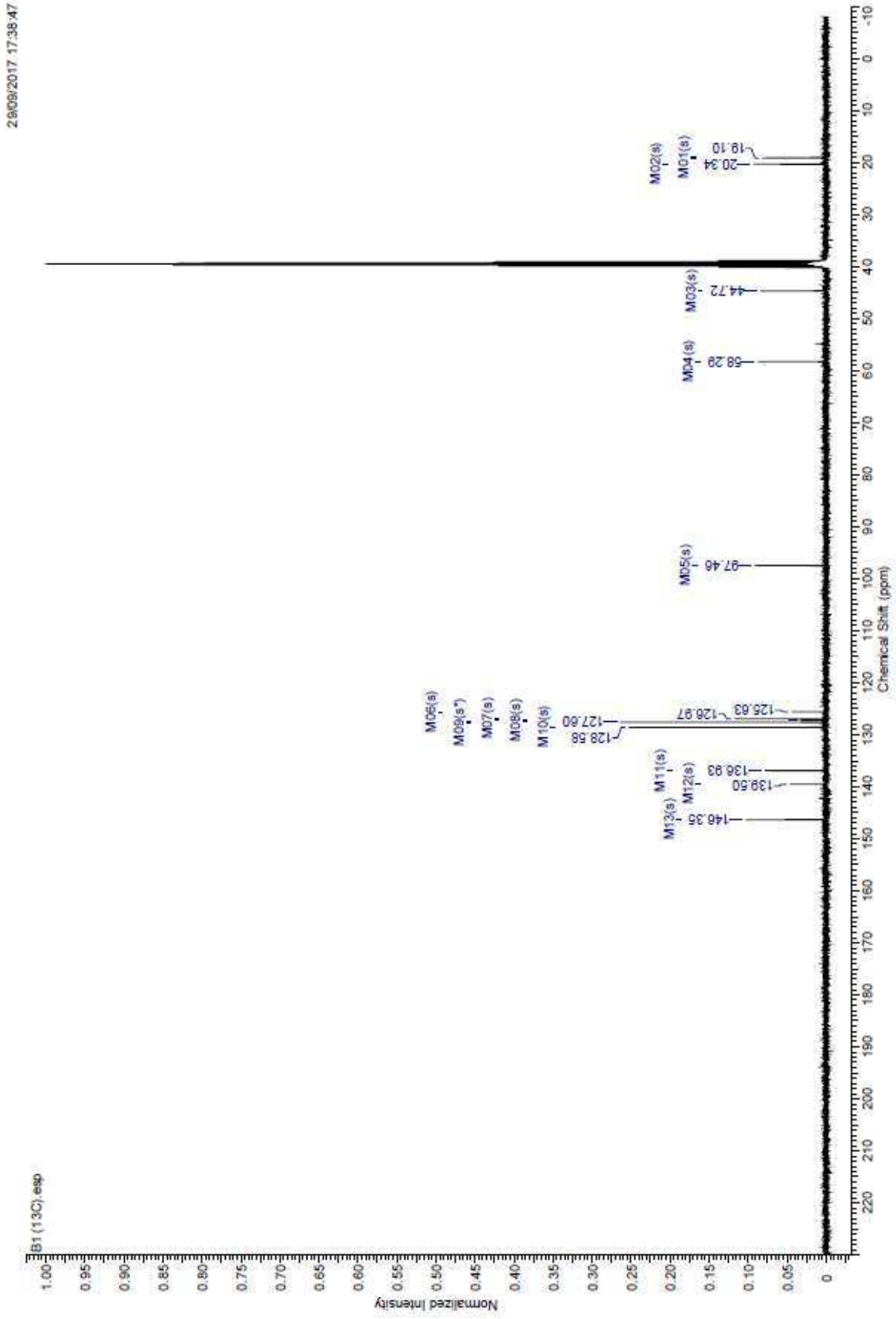


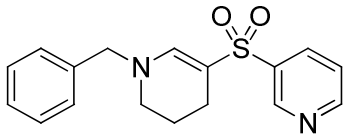
1-Benzyl-5-((2,5-dichlorothiophen-3-yl)sulfonyl)-1,2,3,4-tetrahydropyridine 2j

^{1}H, DMSO-*d*$_6$



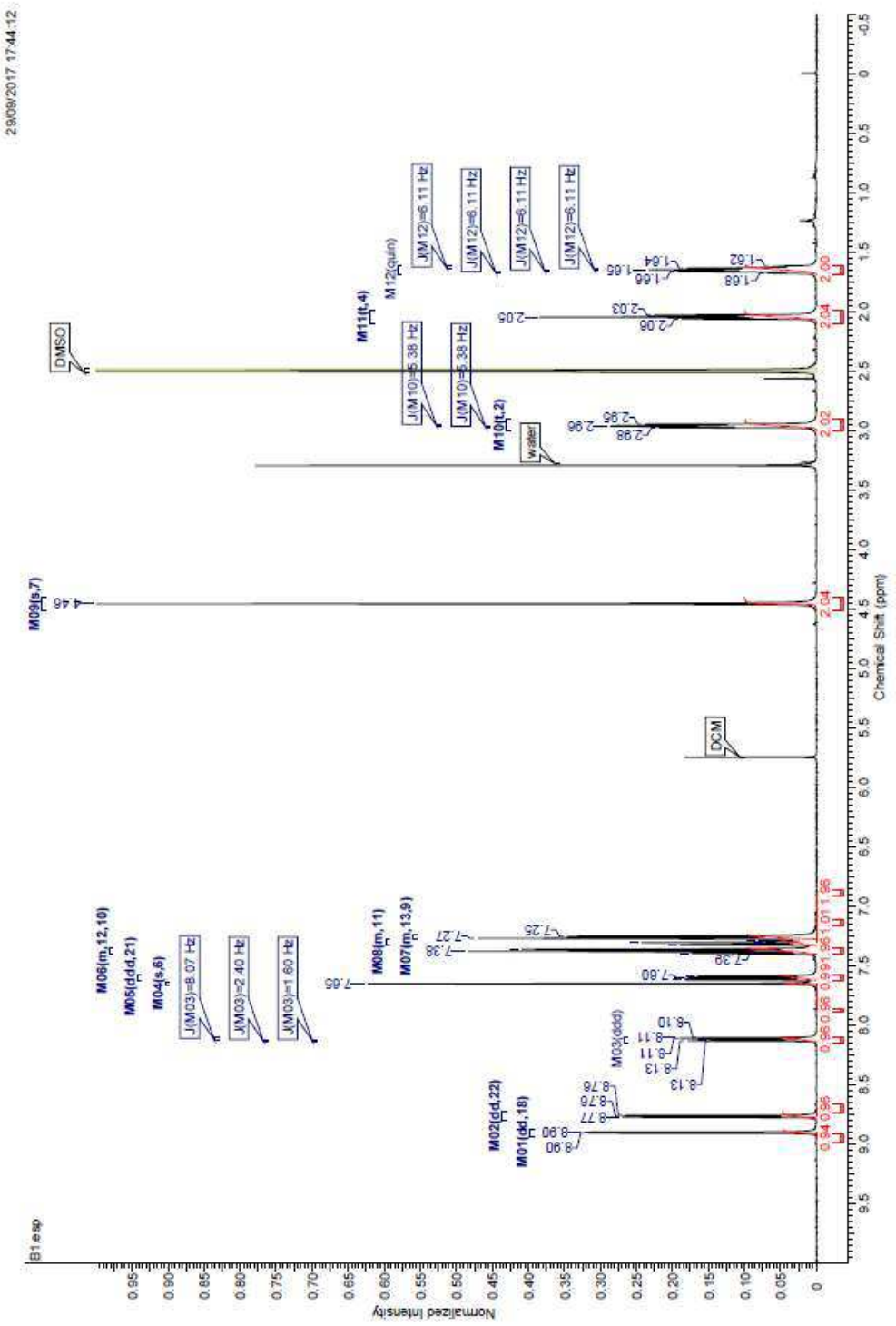
^{13}C, DMSO-d_6


29/09/2017 17:38:47
B1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
19.10
20.34
44.72
58.29
97.46
125.63
126.97
127.60
128.58
136.93
139.60
146.35
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s*)
M10(s)
M11(s)
M12(s)
M13(s)

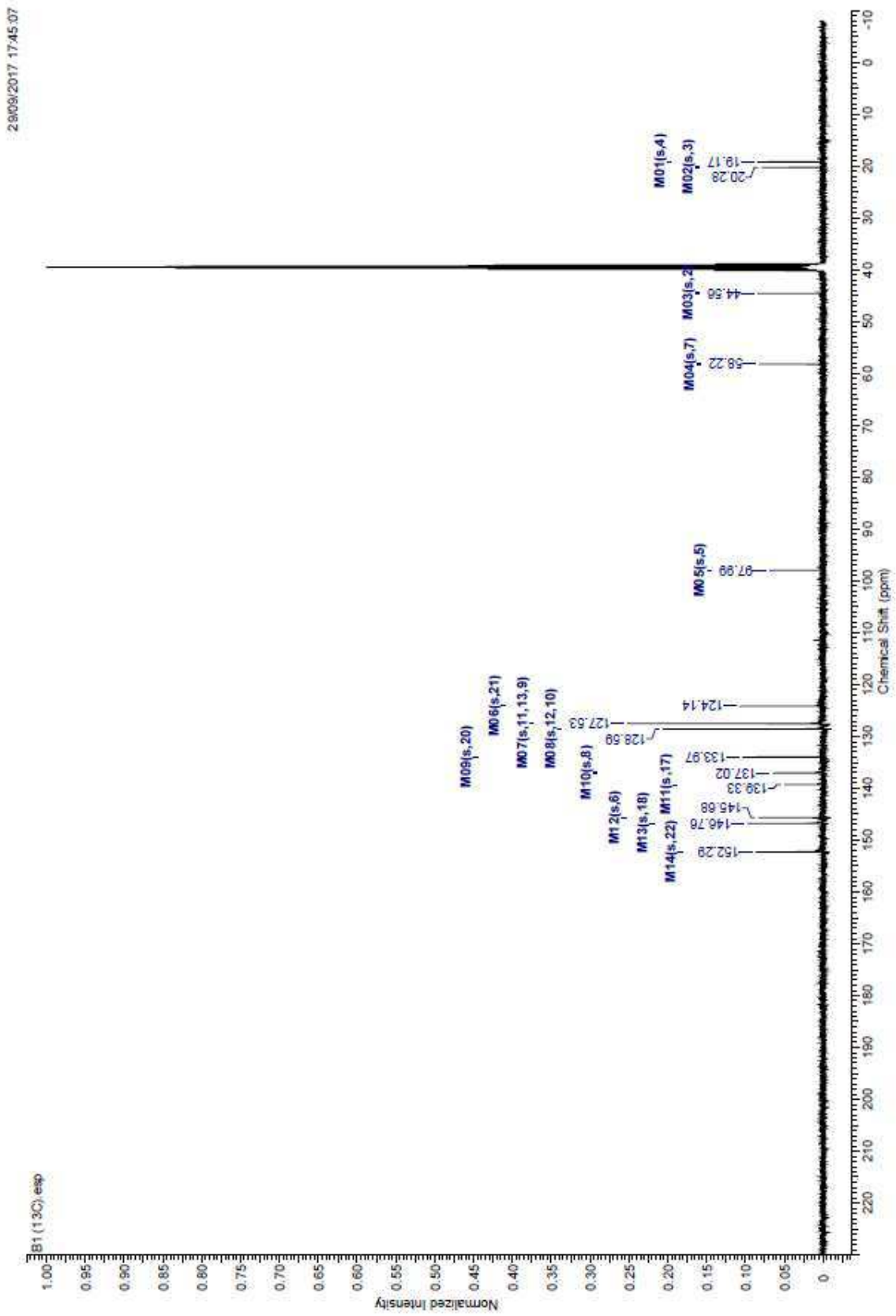


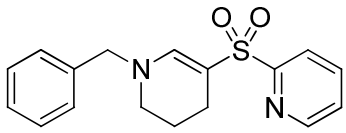
3-((1-Benzyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)pyridine 2k

^{1}H, DMSO-*d*$_6$



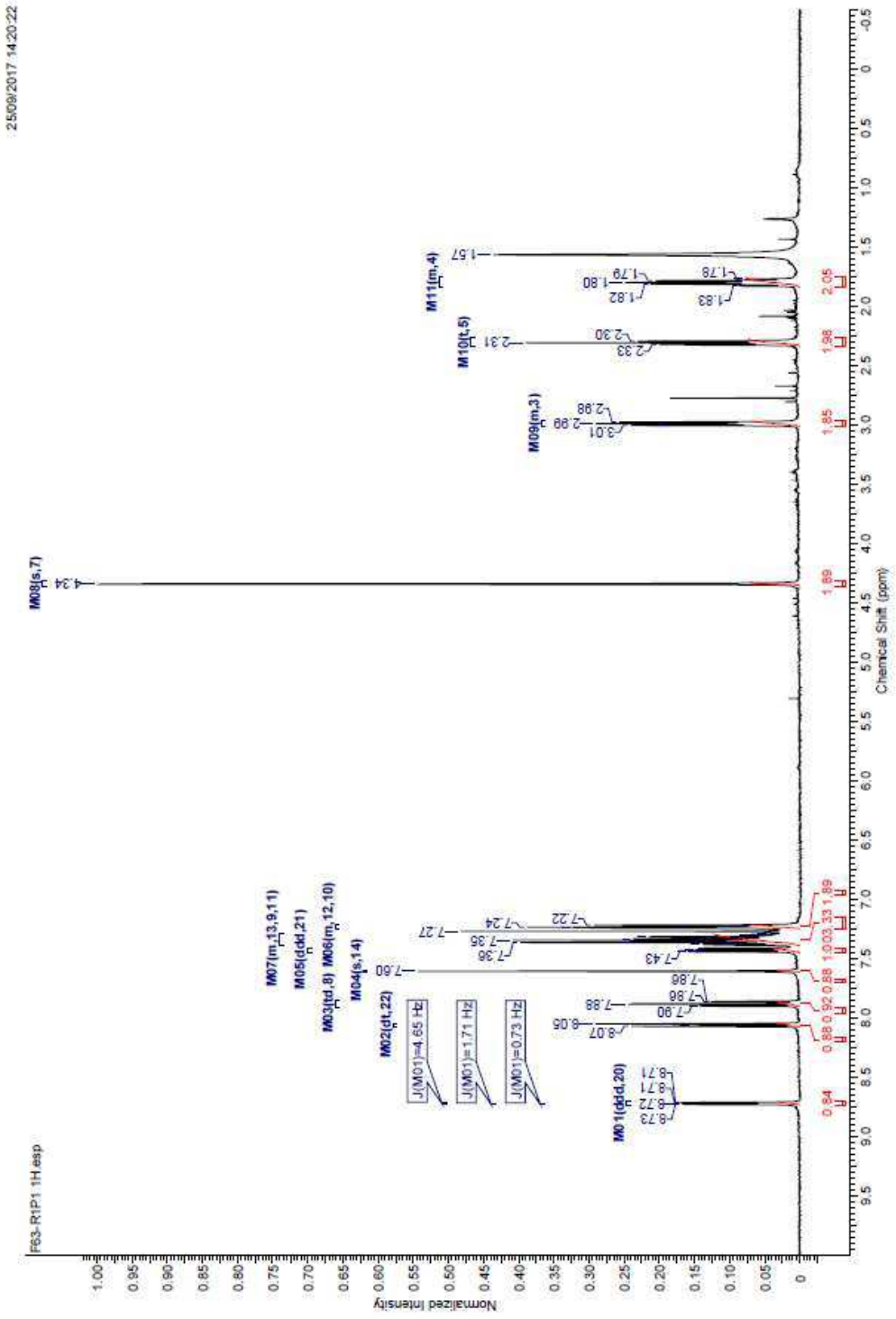
^{13}C, DMSO-*d*$_6$


29/09/2017 17:45:07
B1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M01(s,4)
M02(s,3)
M03(s,2)
M04(s,7)
M05(s,5)
M06(s,21)
M07(s,11,13,9)
M08(s,12,10)
M09(s,20)
M10(s,8)
M11(s,17)
M12(s,6)
M13(s,18)
M14(s,22)
19.17
20.28
44.56
58.22
97.99
124.14
127.53
128.59
133.97
137.02
139.33
145.68
146.76
152.29

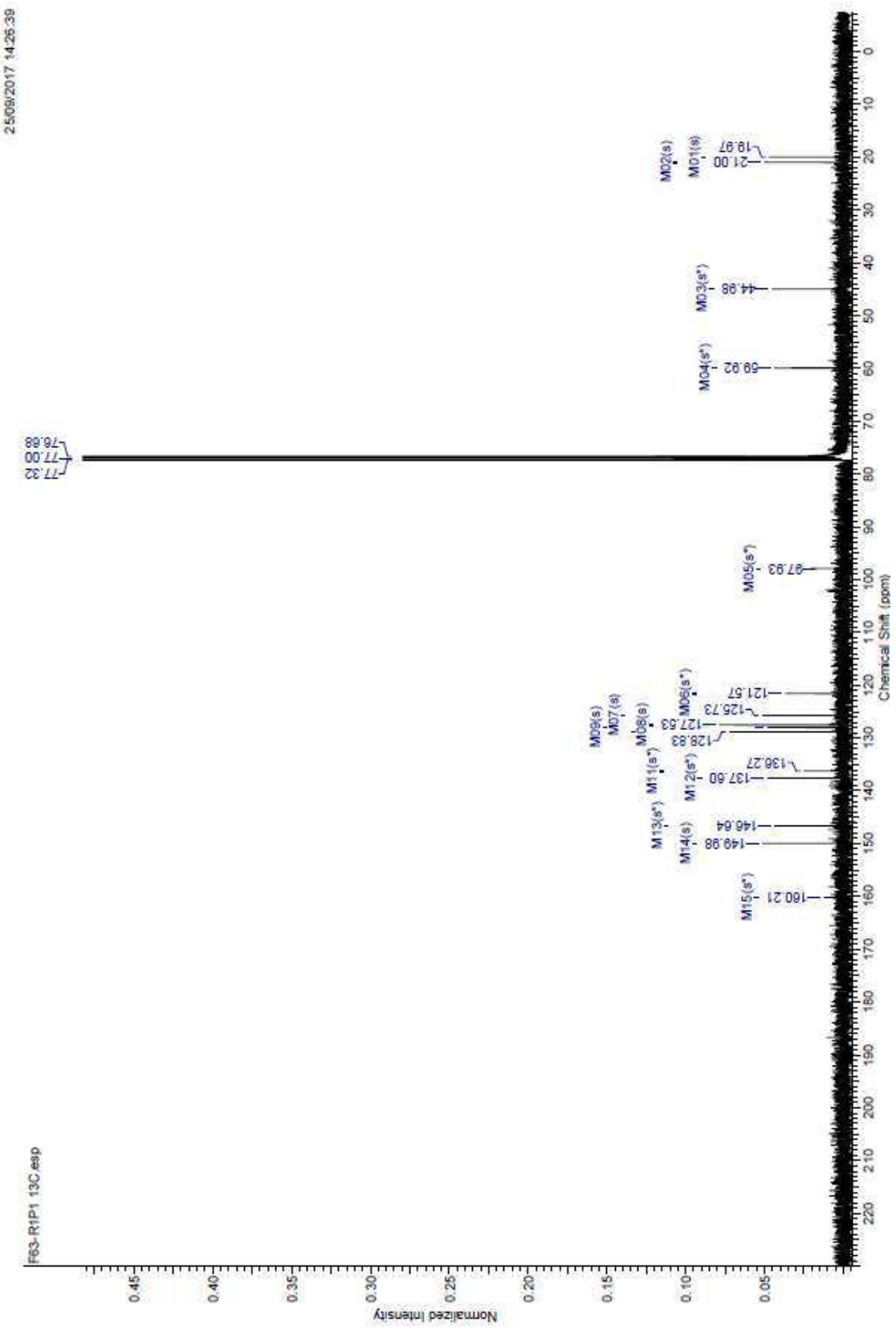


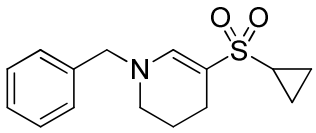
2-((1-Benzyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)pyridine 2l

^{1}H, $CDCl_3$



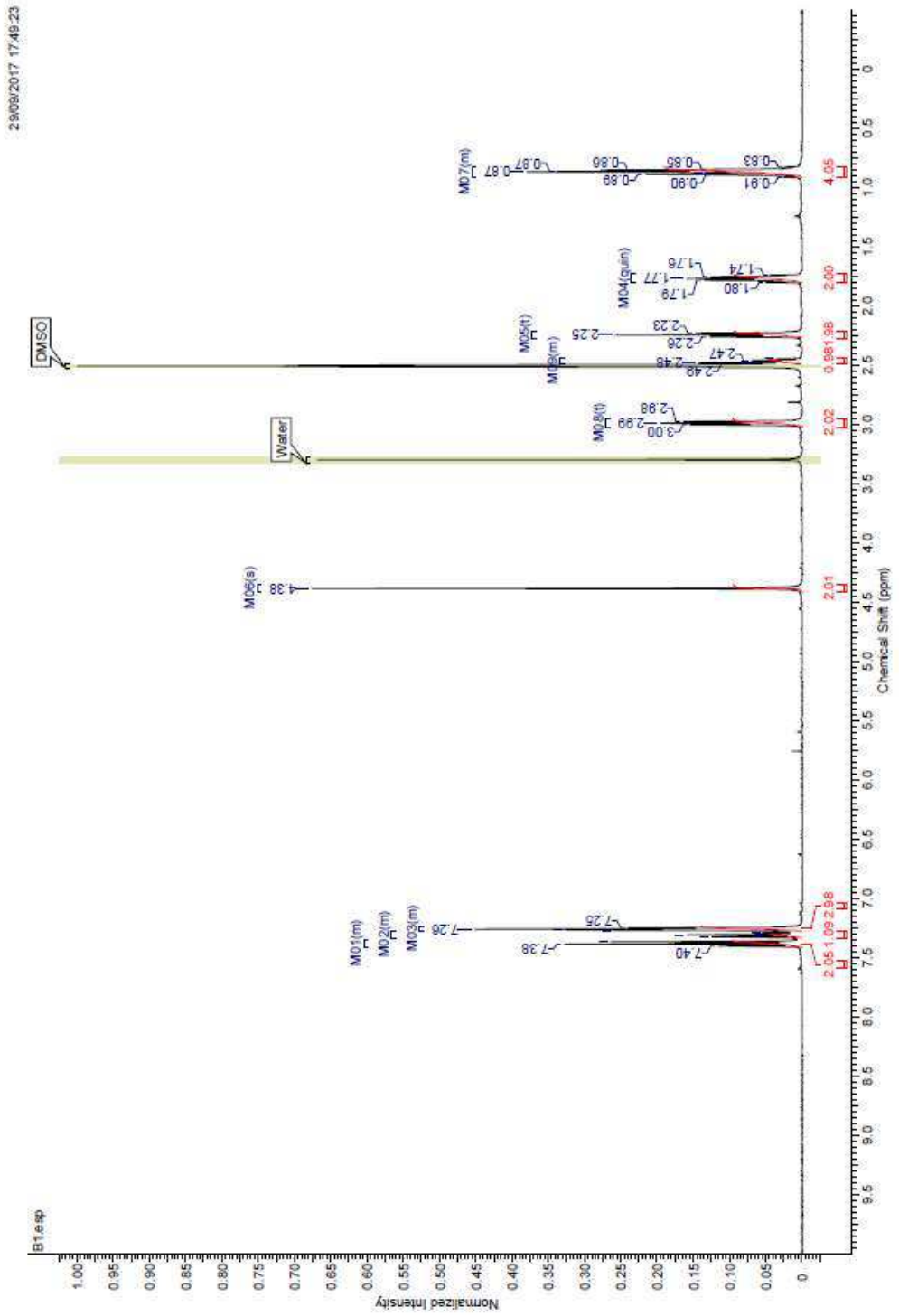
^{13}C, $CDCl_3$


25/09/2017 14:26:39
F63-R1P1 13C.esp
Normalized Intensity
Chemical Shift (ppm)
77.32
77.00
76.68
M01(s)
M02(s)
M03(s*)
M04(s*)
M05(s*)
M06(s*)
M07(s)
M08(s)
M09(s)
M10(s*)
M11(s*)
M12(s*)
M13(s*)
M14(s)
M15(s*)
19.97
21.00
44.98
69.92
87.93
121.57
125.73
127.63
128.83
136.27
137.60
140.64
149.98
160.21

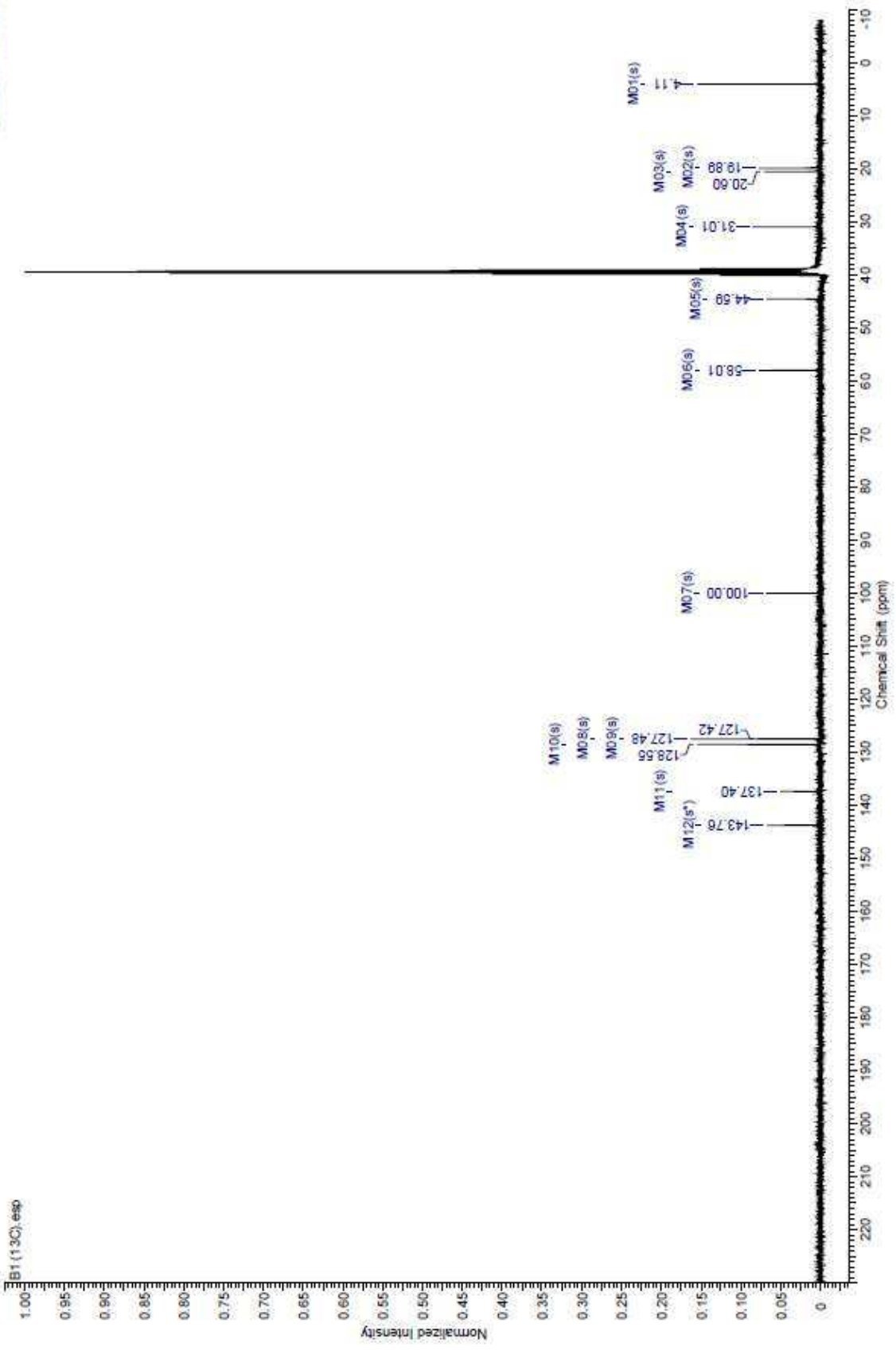


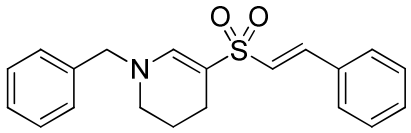
1-Benzyl-5-(cyclopropylsulfonyl)-1,2,3,4-tetrahydropyridine 2m

^{1}H, DMSO-*d*$_6$



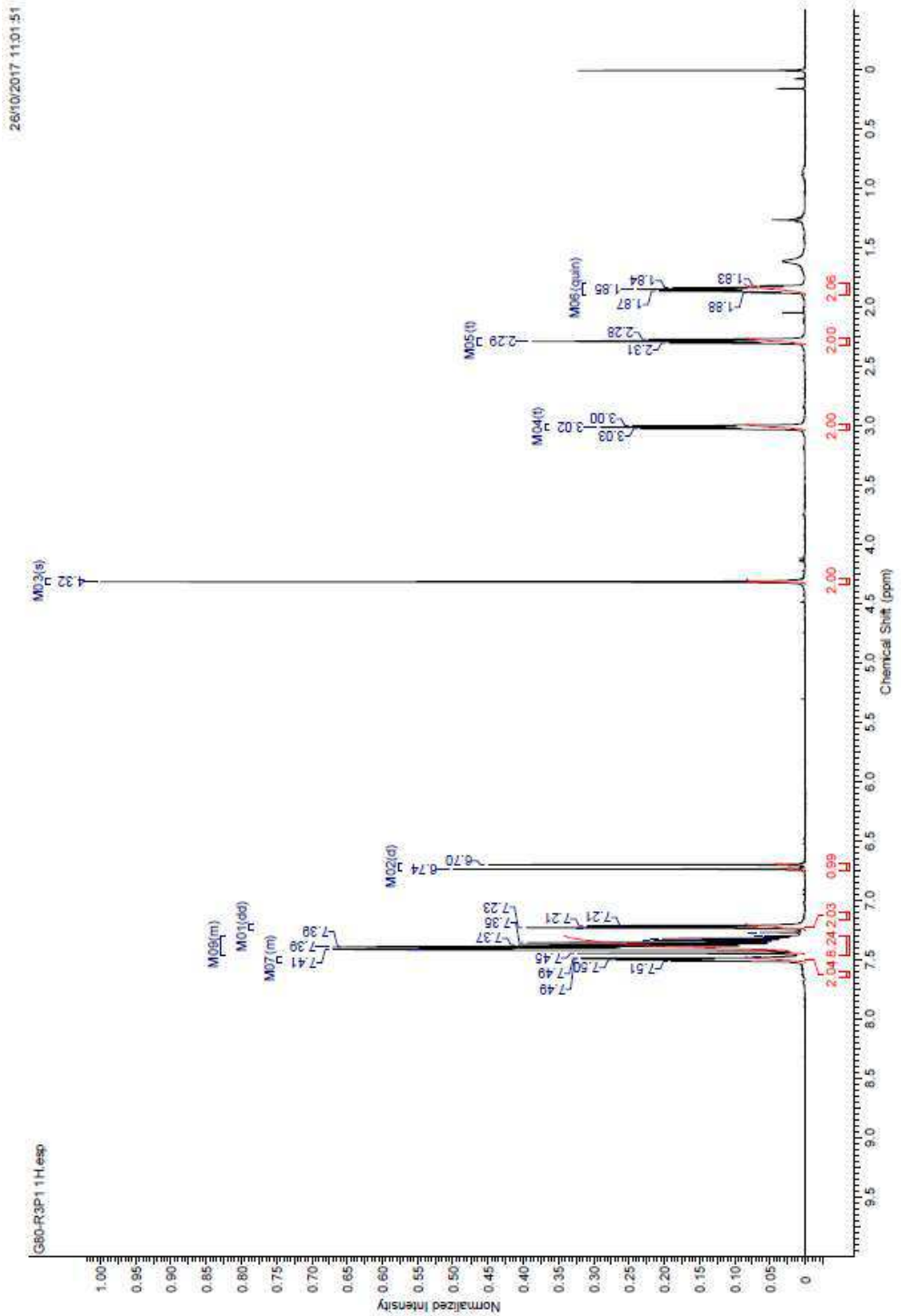
^{13}C, DMSO-d_6


29/09/2017 17:50:45
B1 (13C), esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
4.11
M02(s)
18.89
M03(s)
20.60
M04(s)
31.01
M05(s)
44.59
M06(s)
58.01
M07(s)
100.00
M08(s)
127.42
M09(s)
127.48
M10(s)
128.55
M11(s)
137.40
M12(s*)
143.76

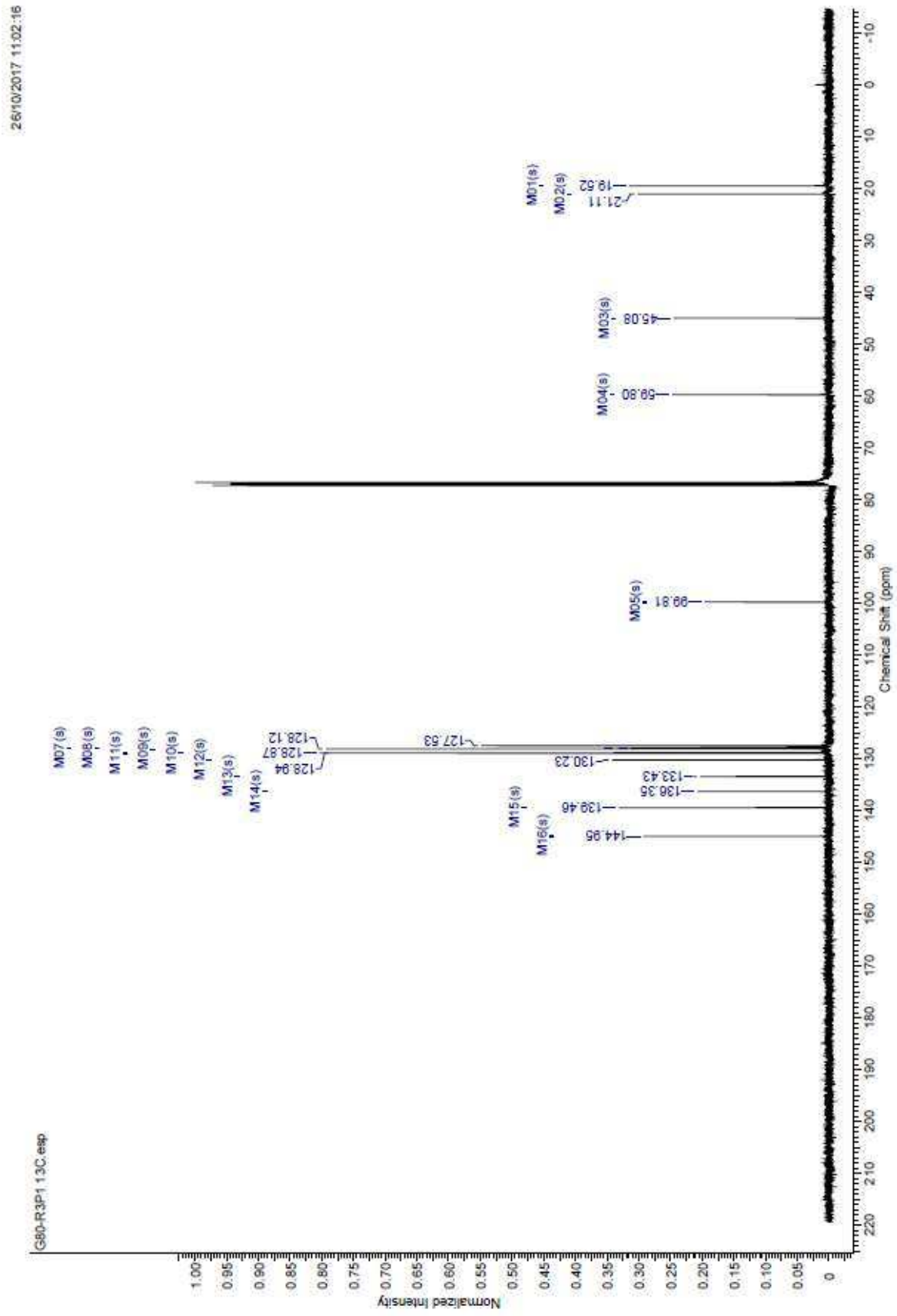


(*E*)-1-Benzyl-5-(styrylsulfonyl)-1,2,3,4-tetrahydropyridine 2n

^{1}H, $CDCl_3$



^{13}C, $CDCl_3$


26/10/2017 11:02:16
G80-R3P1 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
19.52
21.11
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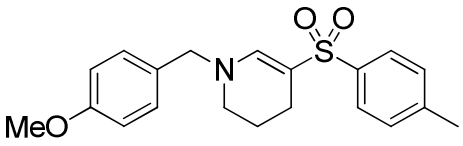
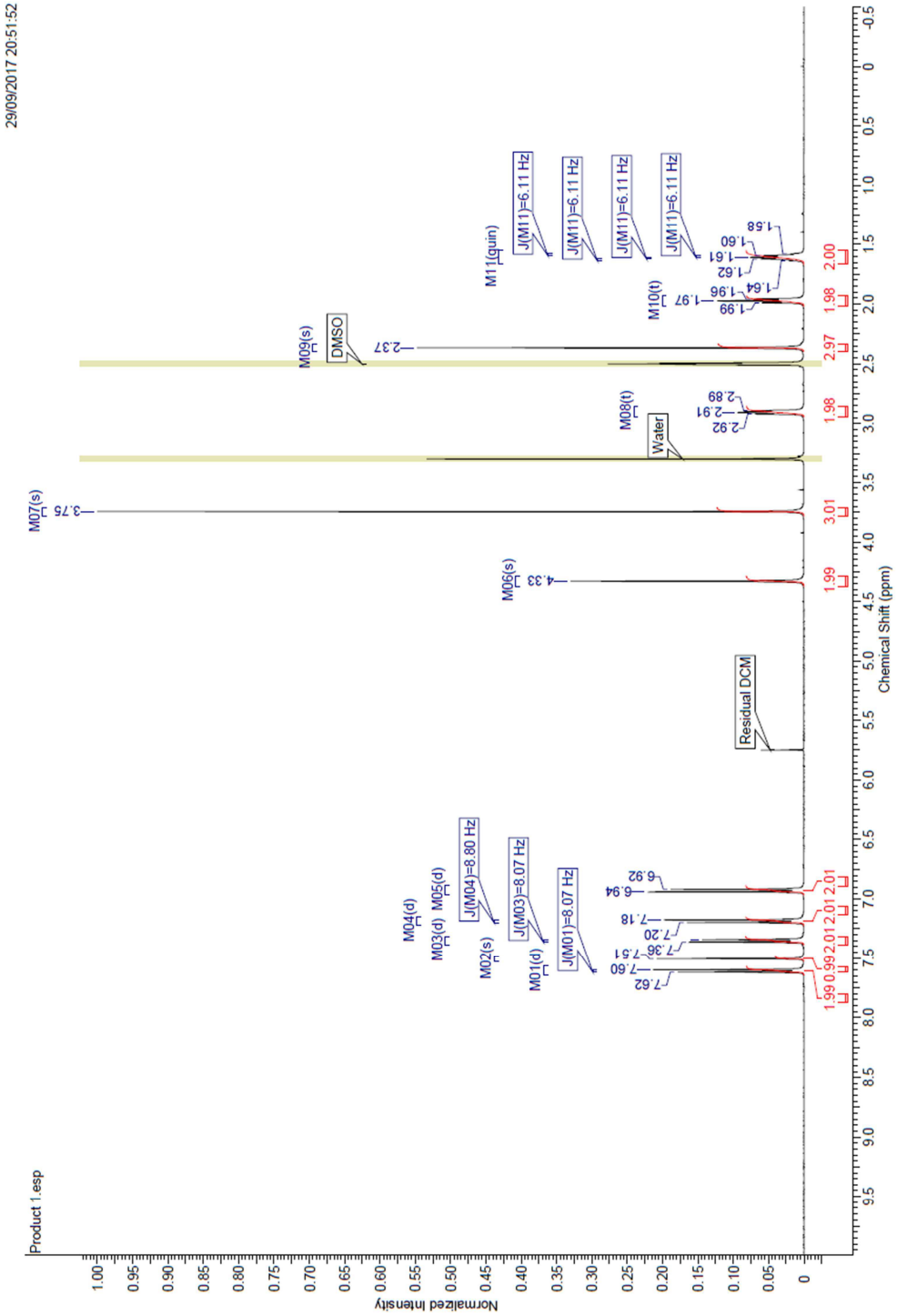
128.94
130.23
133.43
136.35
139.46
144.85

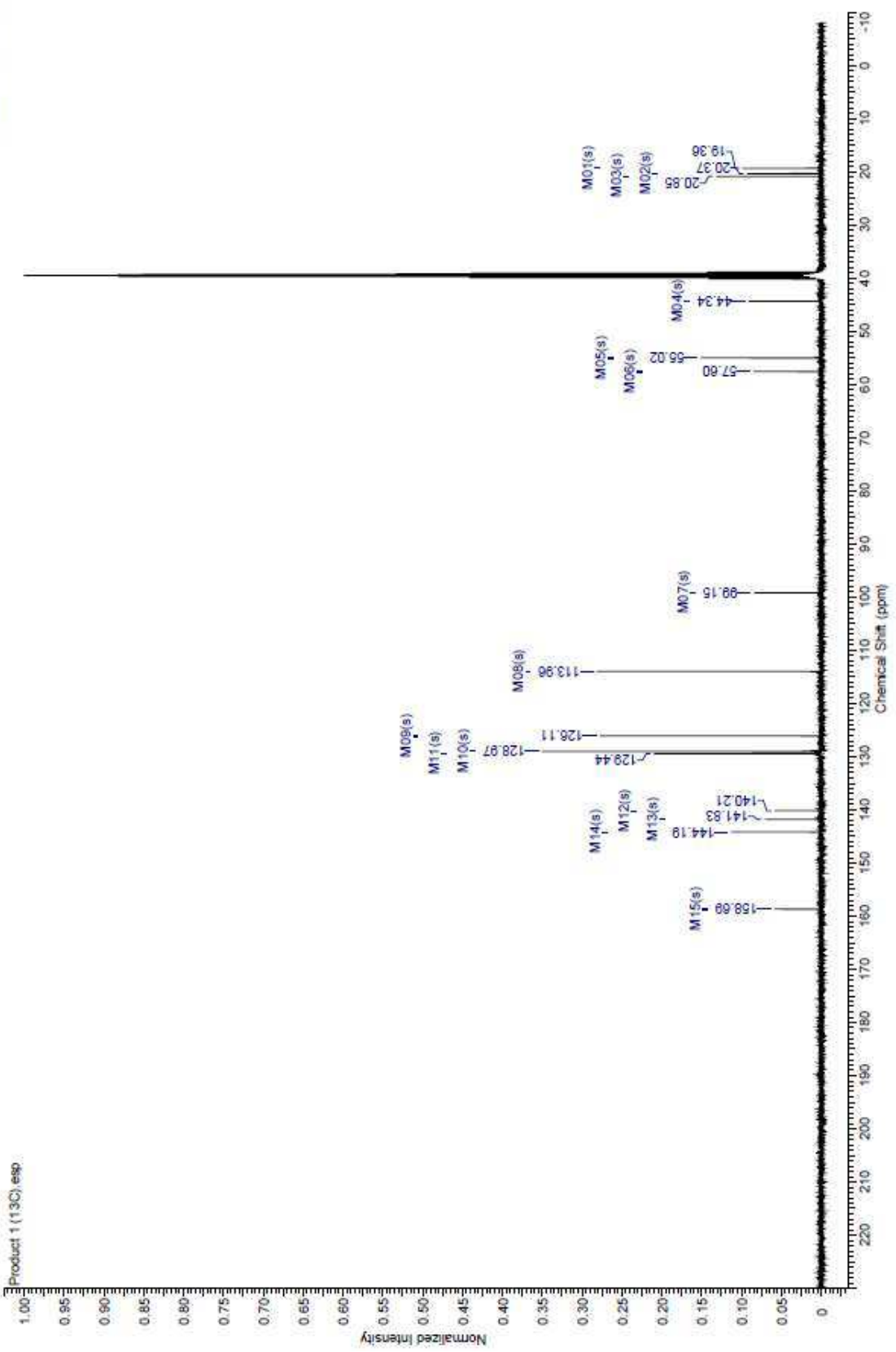


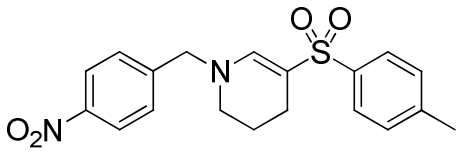
1-(4-Methoxybenzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4a

^{1}H, DMSO-d_6



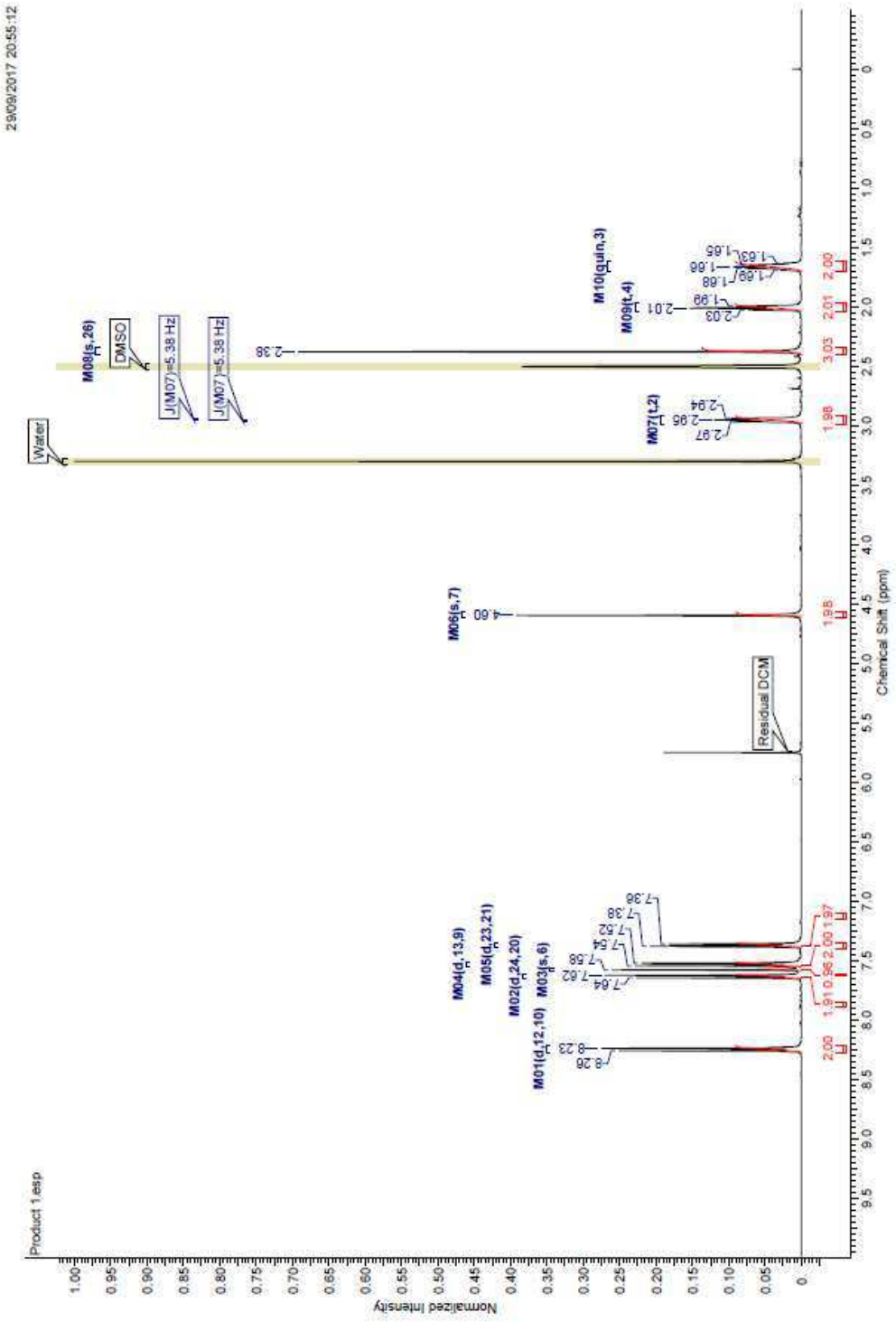
^{13}C, DMSO-d_6


29/09/2017 20:53:03
Product 1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M03(s)
M02(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M11(s)
M10(s)
M14(s)
M12(s)
M13(s)
M15(s)
19.36
20.37
20.85
44.34
55.02
57.60
99.15
113.96
126.11
128.97
129.44
140.21
141.83
144.19
158.69

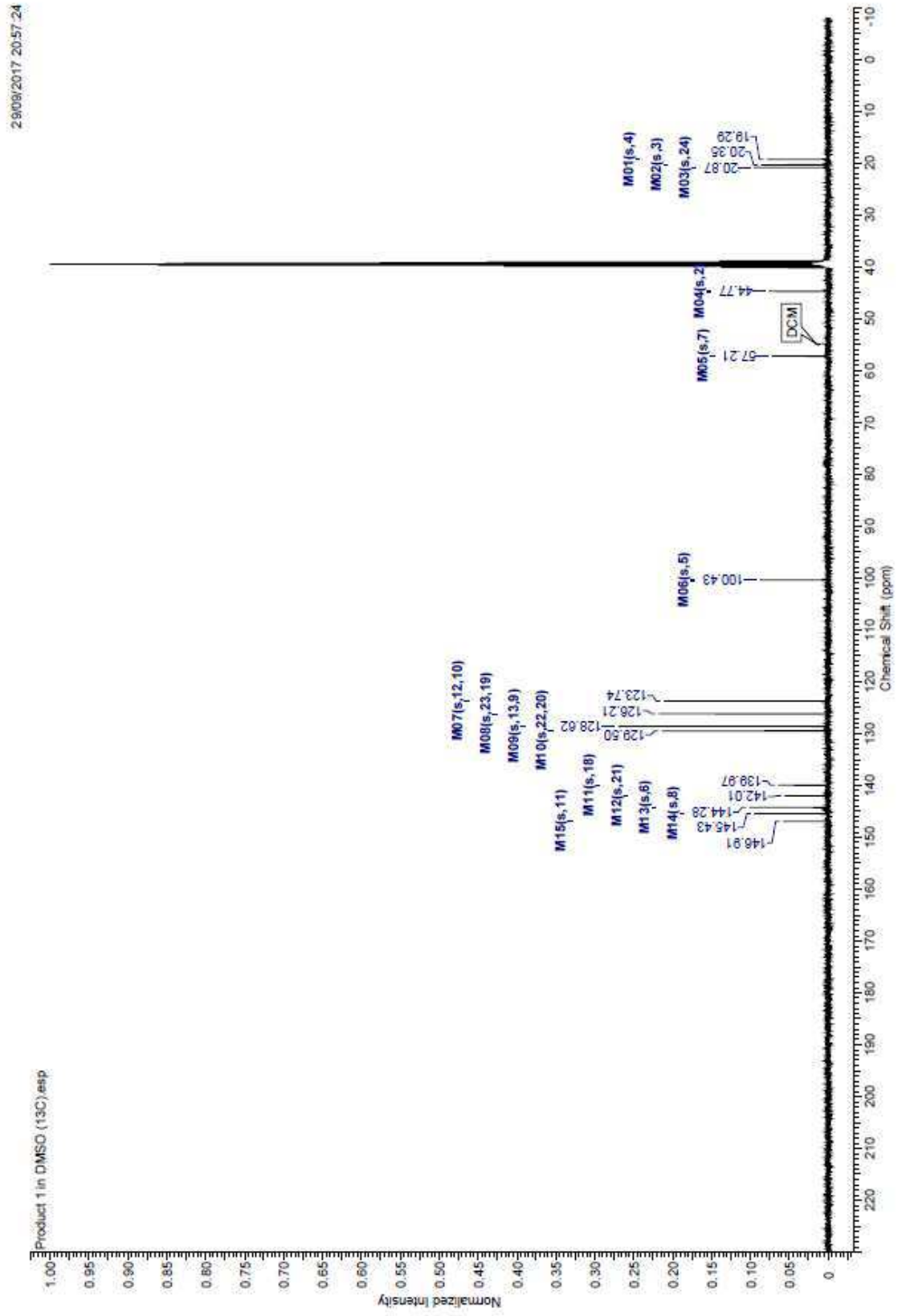


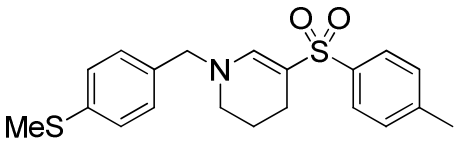
1-(4-Nitrobenzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4b

^{1}H, DMSO-*d*$_6$



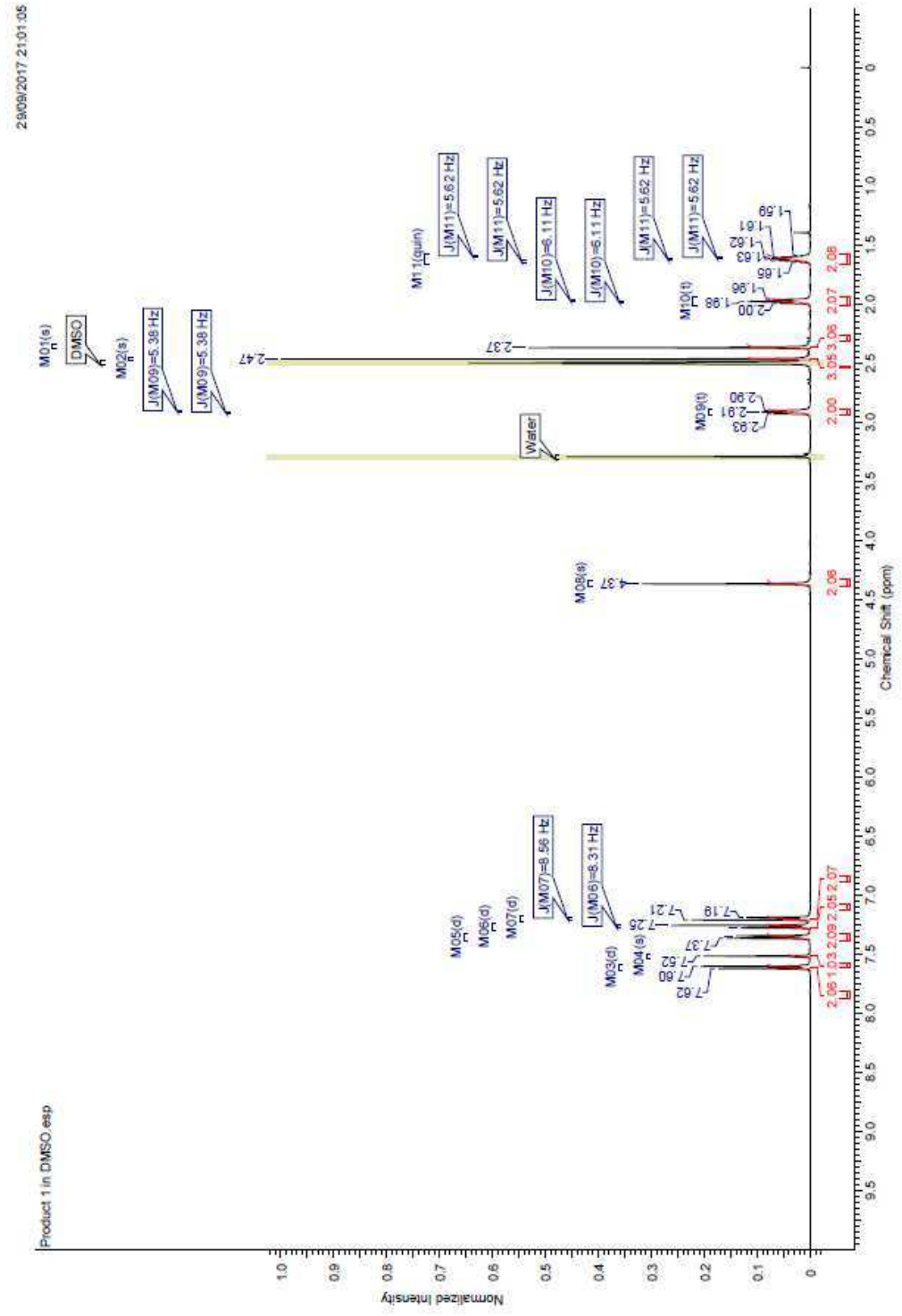
^{13}C, DMSO-d_6


29/09/2017 20:57:24
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s,4)
M02(s,3)
M03(s,24)
M04(s,2)
M05(s,7)
M06(s,5)
M07(s,12,10)
M08(s,23,19)
M09(s,13,9)
M10(s,22,20)
M11(s,18)
M12(s,21)
M13(s,6)
M14(s,8)
M15(s,11)
19.29
20.35
20.87
44.77
57.21
DCM
100.43
123.74
126.21
128.50
128.62
139.87
142.01
144.28
145.43
146.91

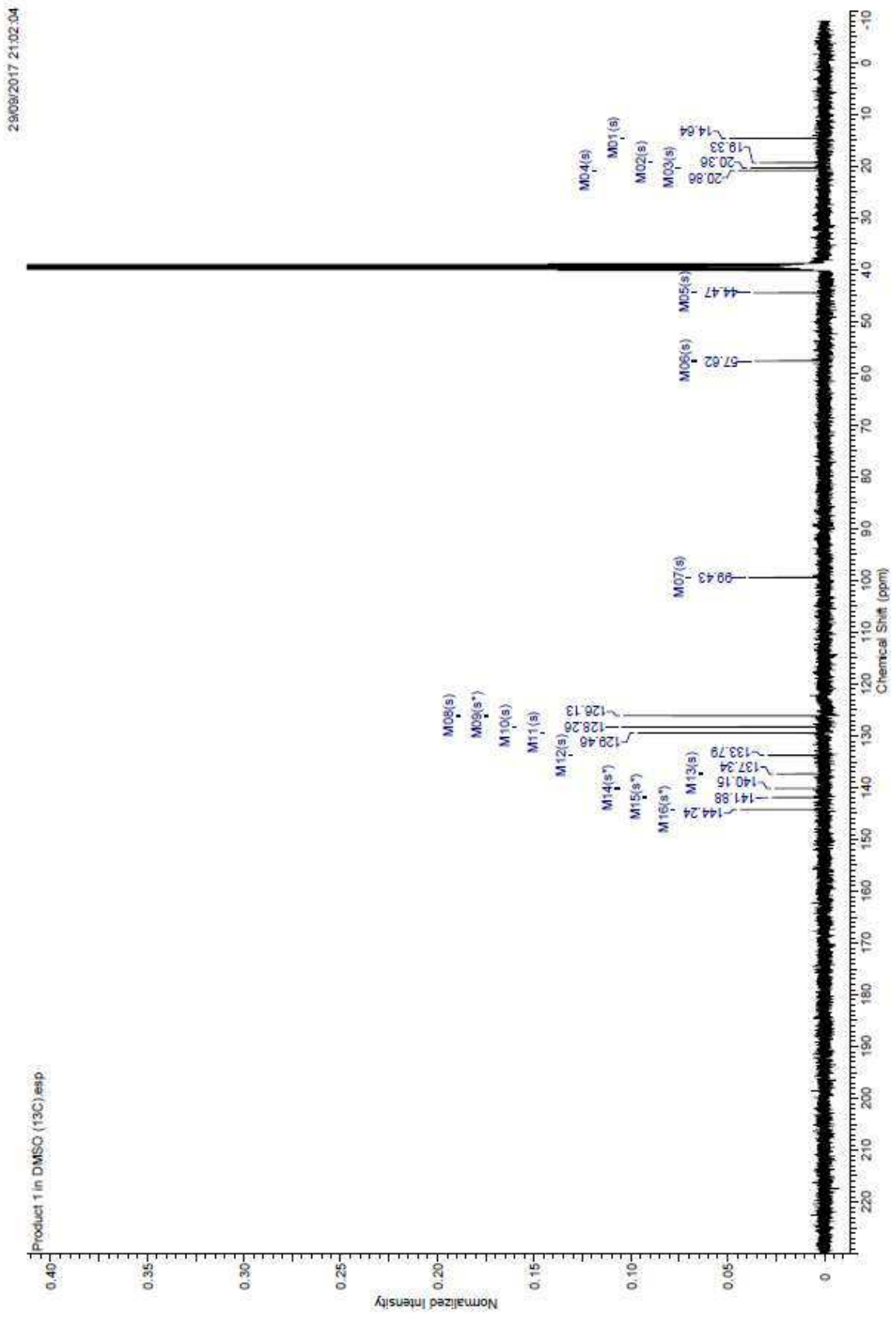


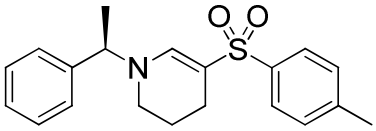
1-(4-(Methylthio)benzyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4c

^{1}H, DMSO-*d*$_6$



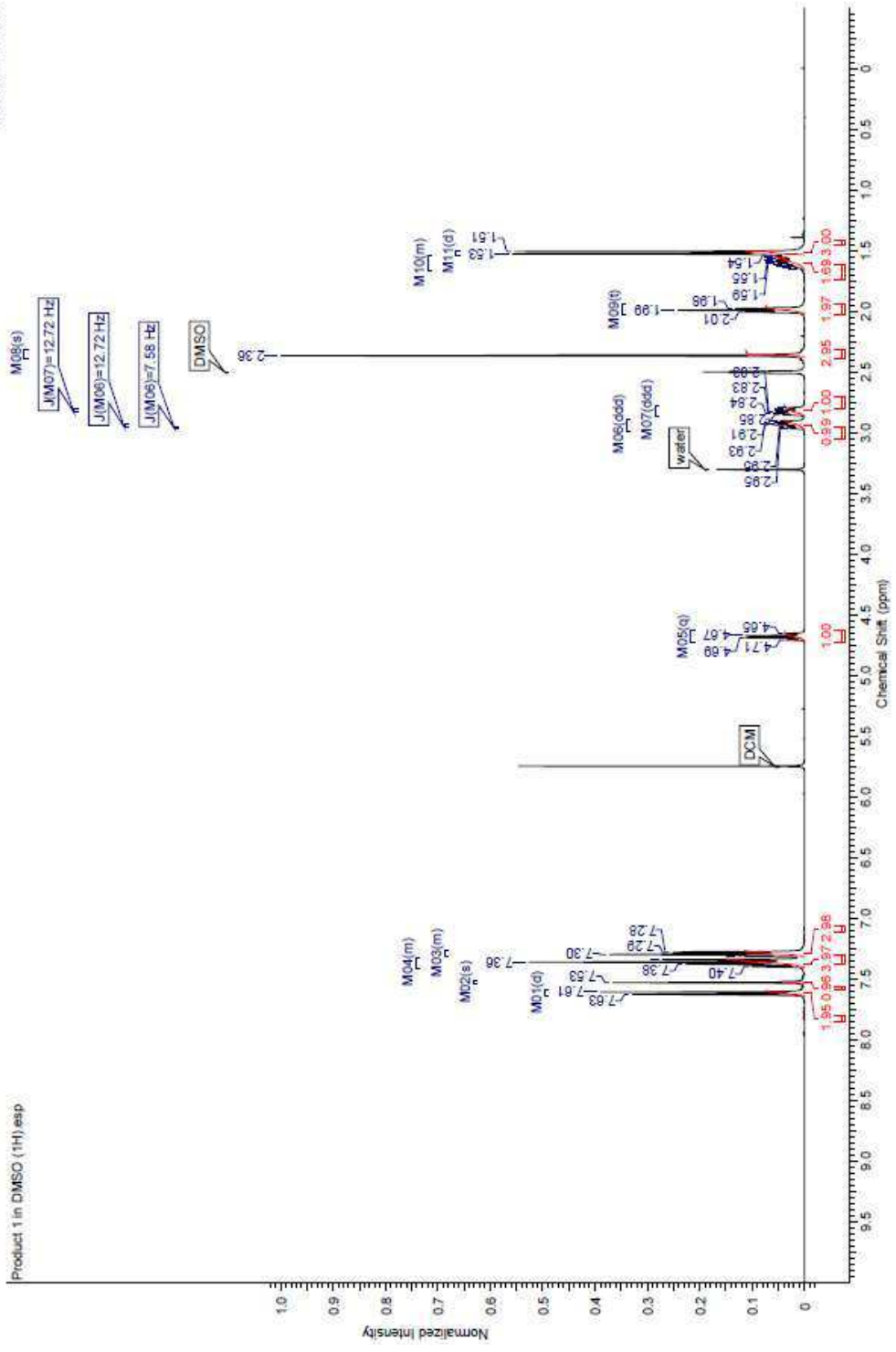
^{13}C, DMSO-d_6


29/09/2017 21:02:04
Product 1 in DMSO (13C) esp
Normalized Intensity
Chemical Shift (ppm)
14.64
19.33
20.36
20.86
44.47
57.62
89.43
126.13
128.29
129.46
133.79
137.34
140.15
141.88
144.24
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s*)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s*)
M15(s*)
M16(s*)

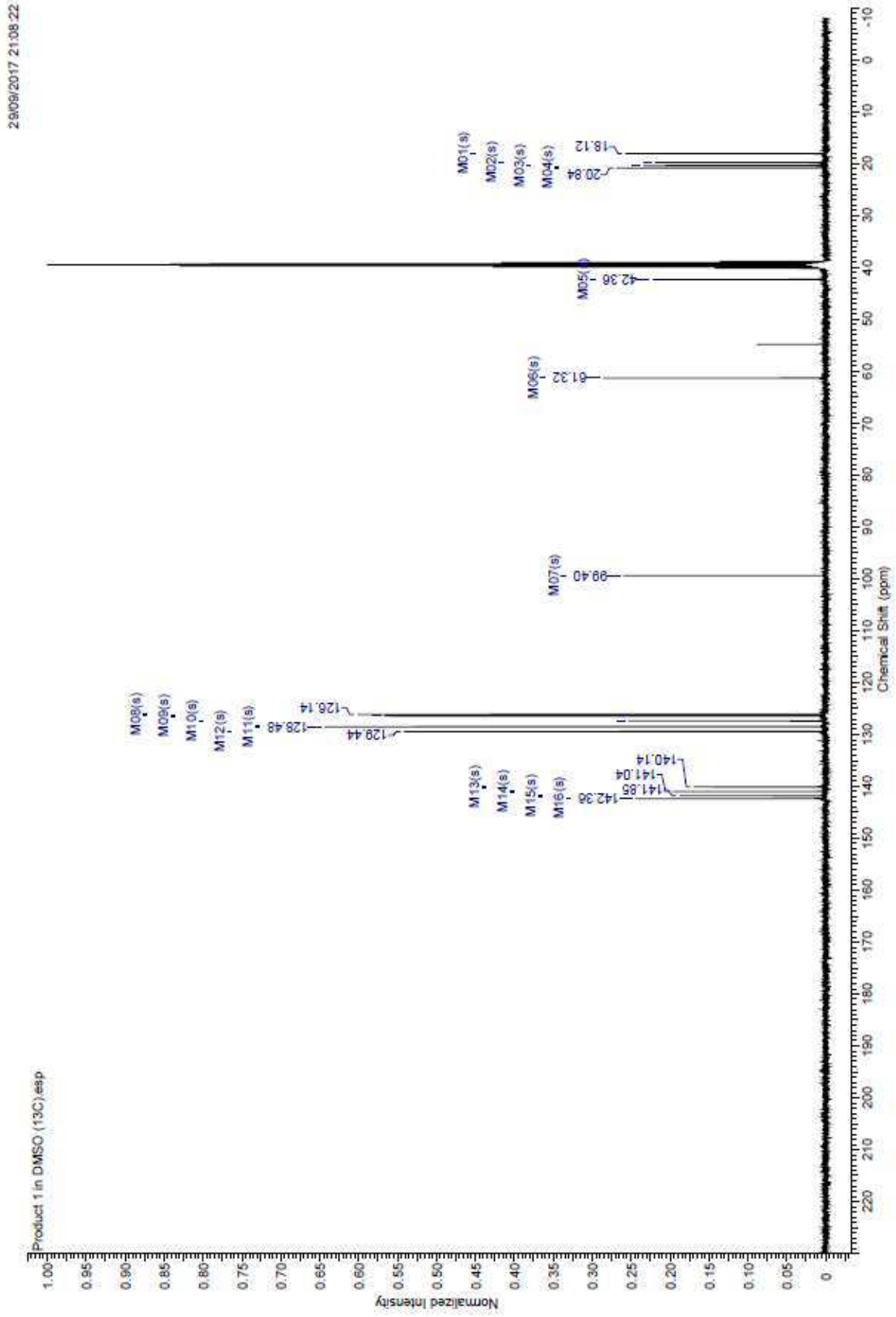


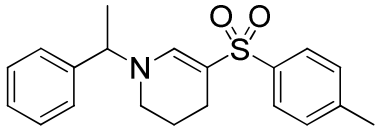
(*R*)-1-(1-Phenylethyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4d

^{1}H, DMSO-d_6



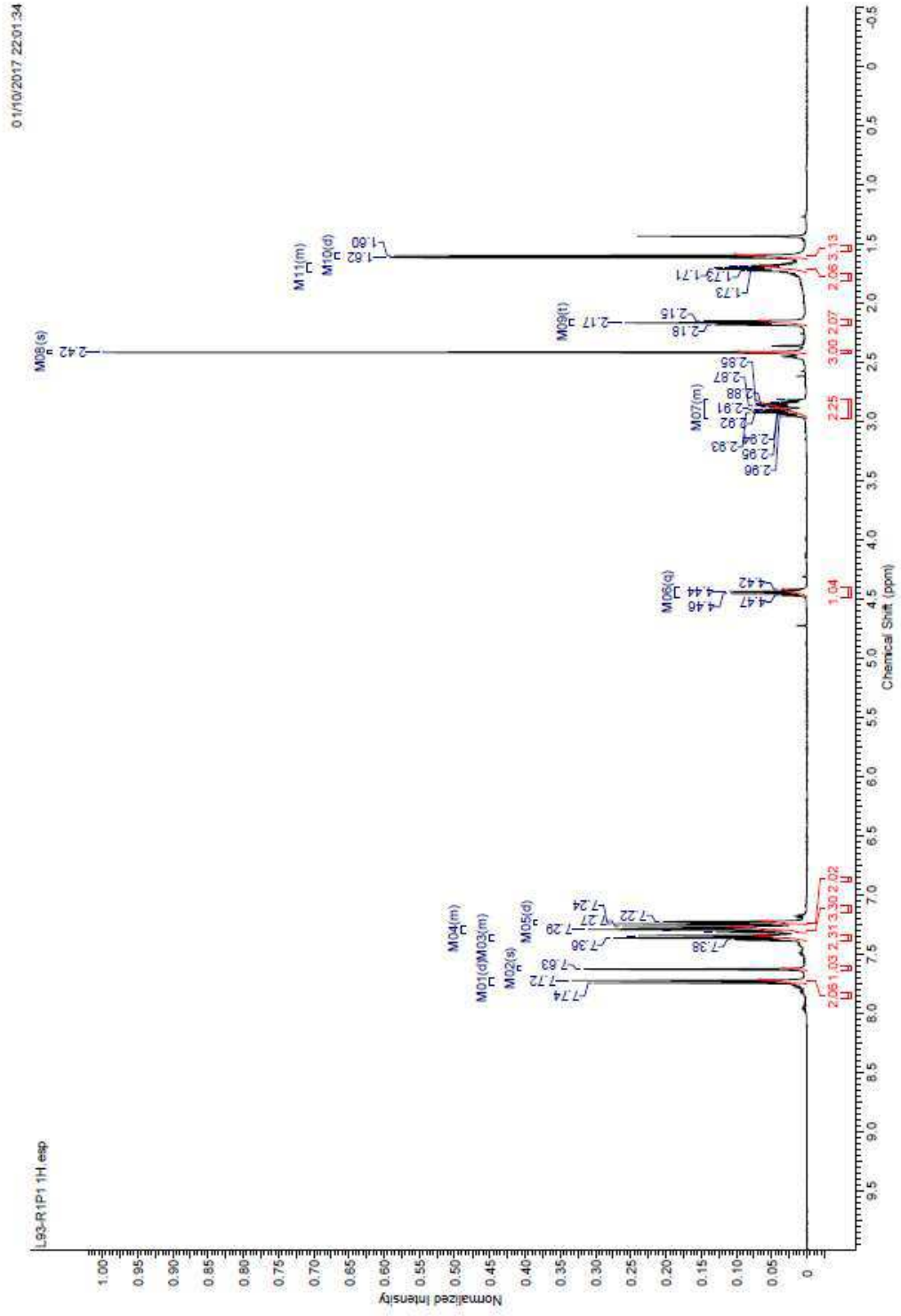
^{13}C, DMSO-d_6


29/09/2017 21:08:22
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
18.12
20.84
42.36
61.32
99.40
126.14
128.48
129.44
140.14
141.04
141.85
142.36

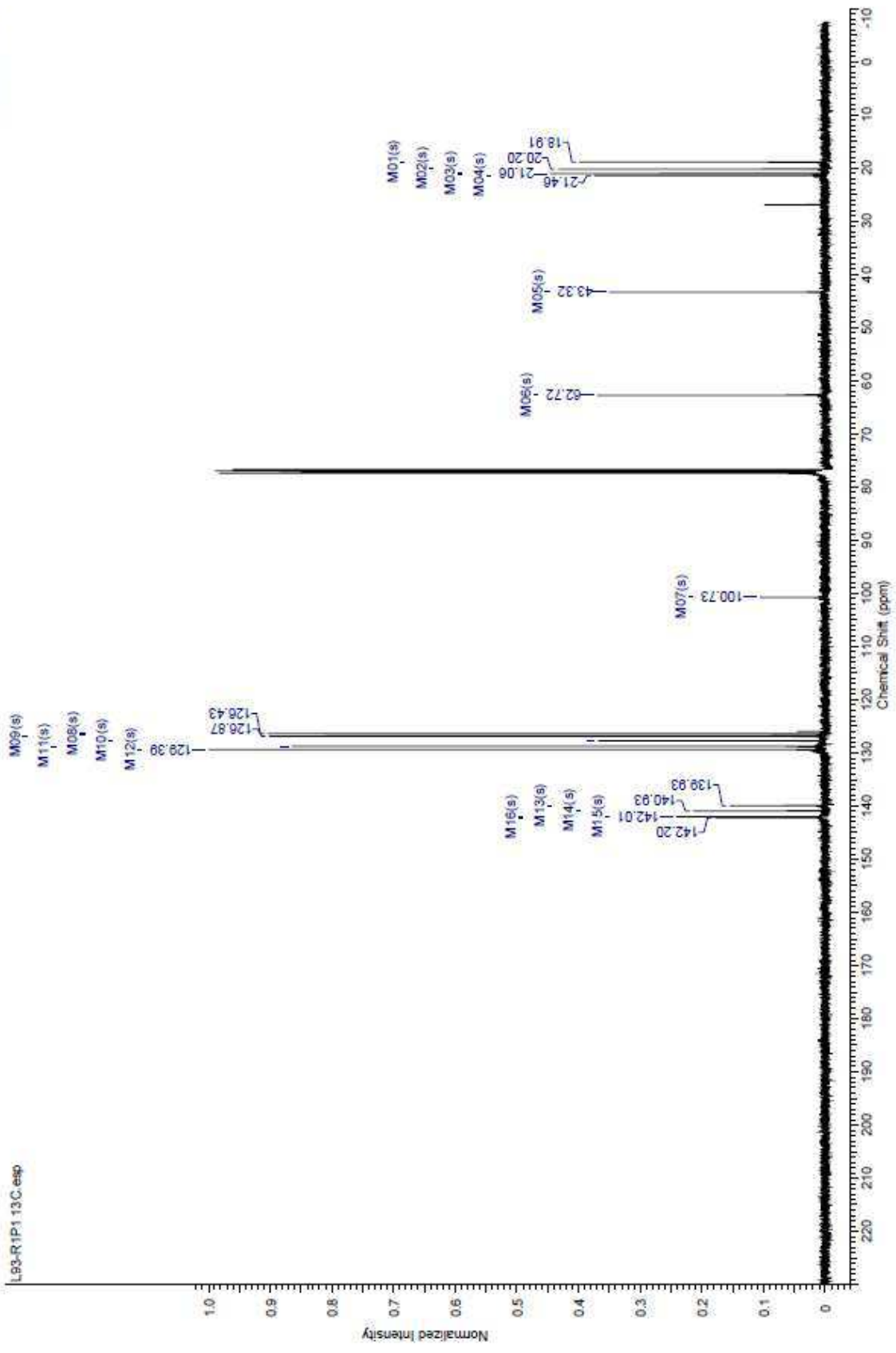


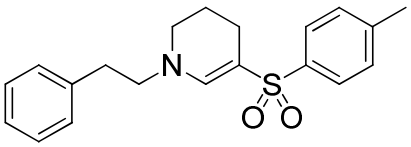
1-(1-Phenylethyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4db

^{1}H, $CDCl_3$



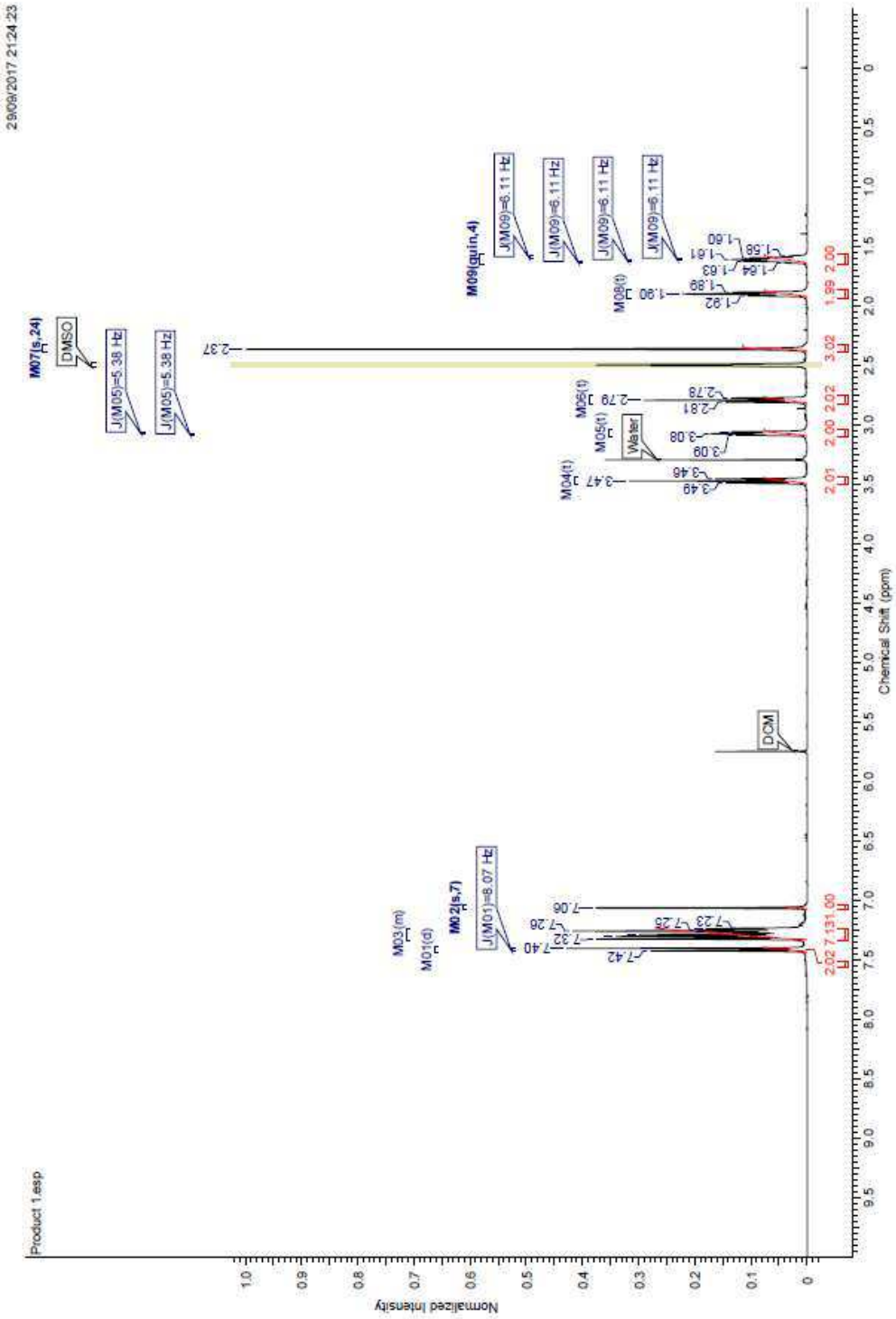
^{13}C, $CDCl_3$


01/10/2017 22:06:16
L93-R1P1 13C esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
18.91
20.20
21.06
21.46
43.32
62.72
100.73
126.43
126.87
129.39
139.93
140.93
142.01
142.20

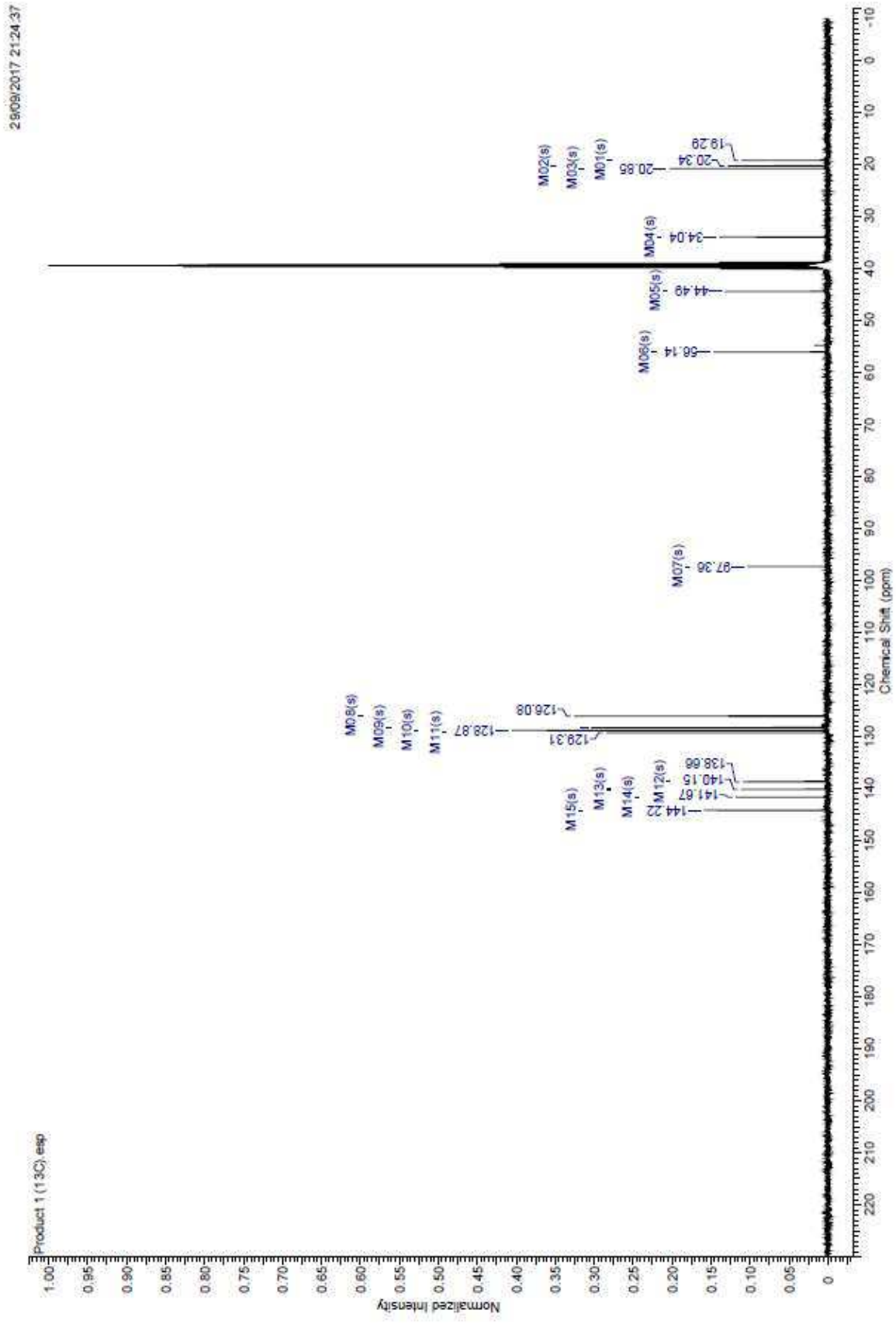


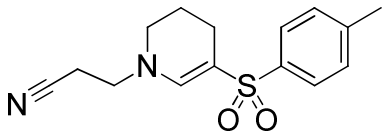
1-Phenethyl-5-tosyl-1,2,3,4-tetrahydropyridine 4e

^{1}H, DMSO-*d*$_6$



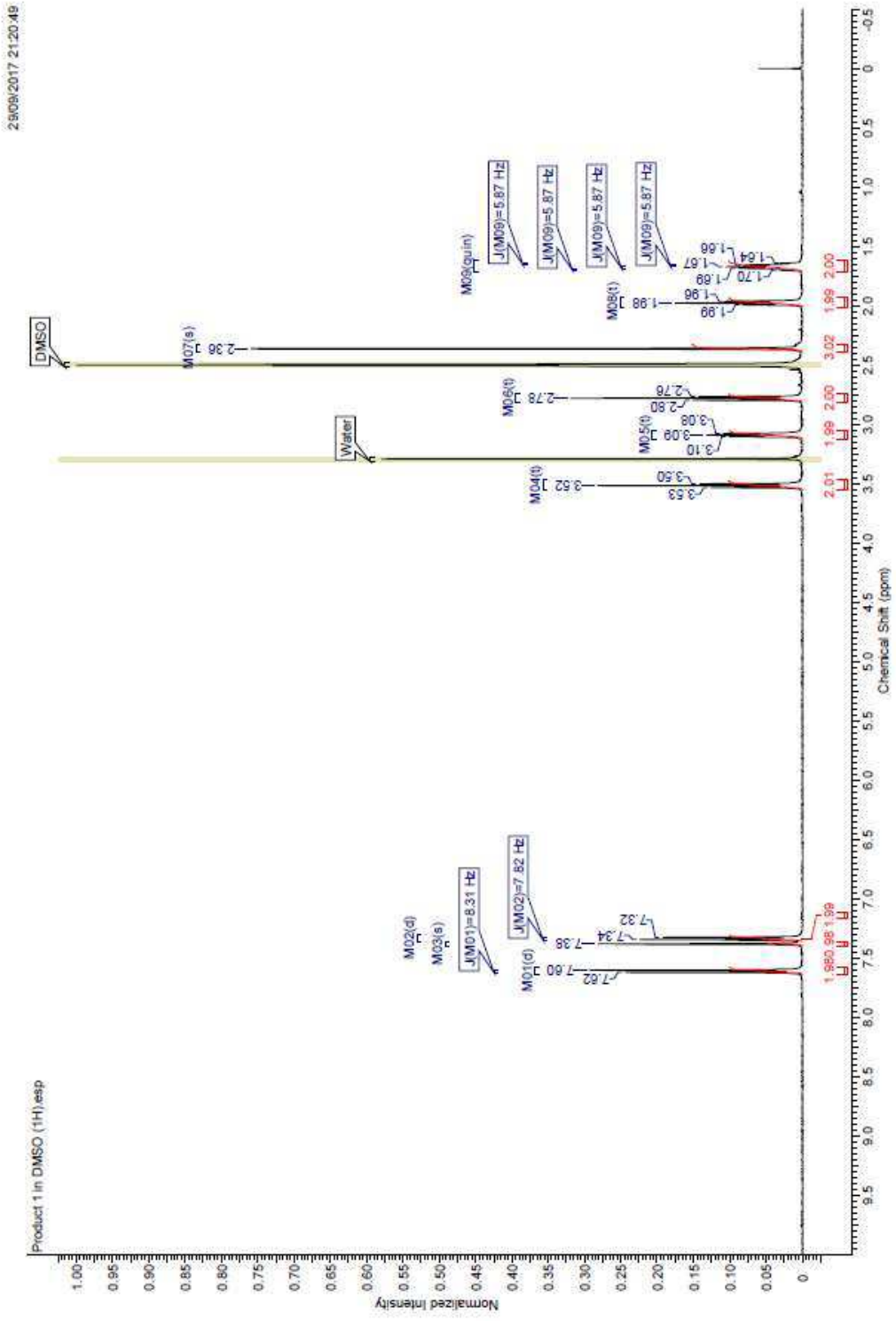
^{13}C, DMSO-d_6


29/09/2017 21:24:37
Product 1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
19.29
20.34
20.85
34.04
44.49
56.14
97.36
126.08
128.31
128.87
138.66
140.15
141.67
144.22

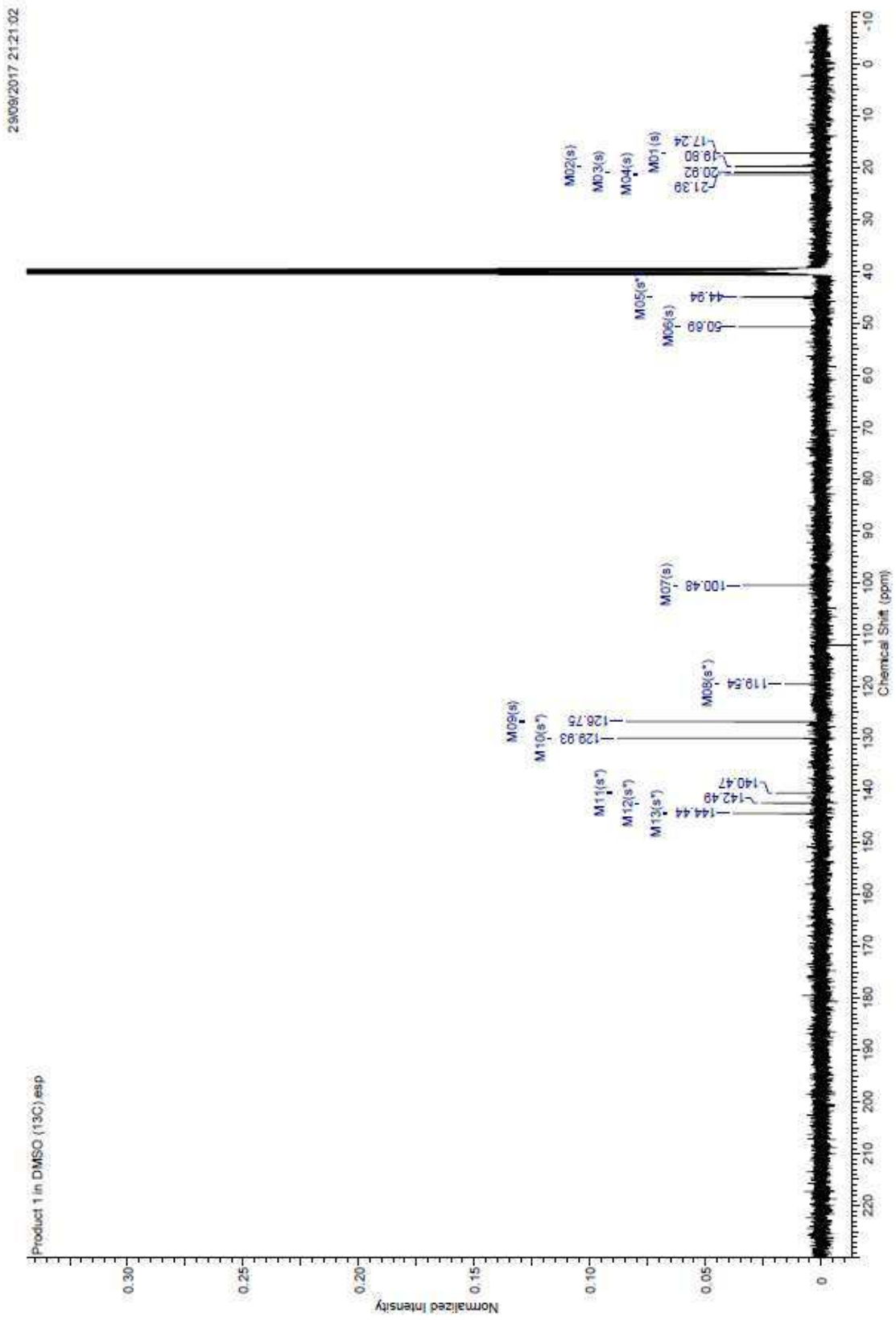


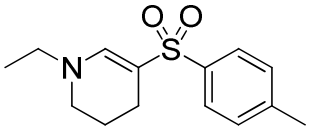
3-(5-Tosyl-3,4-dihydropyridin-1(2*H*)-yl)propanenitrile 4f

^{1}H, DMSO-d_6



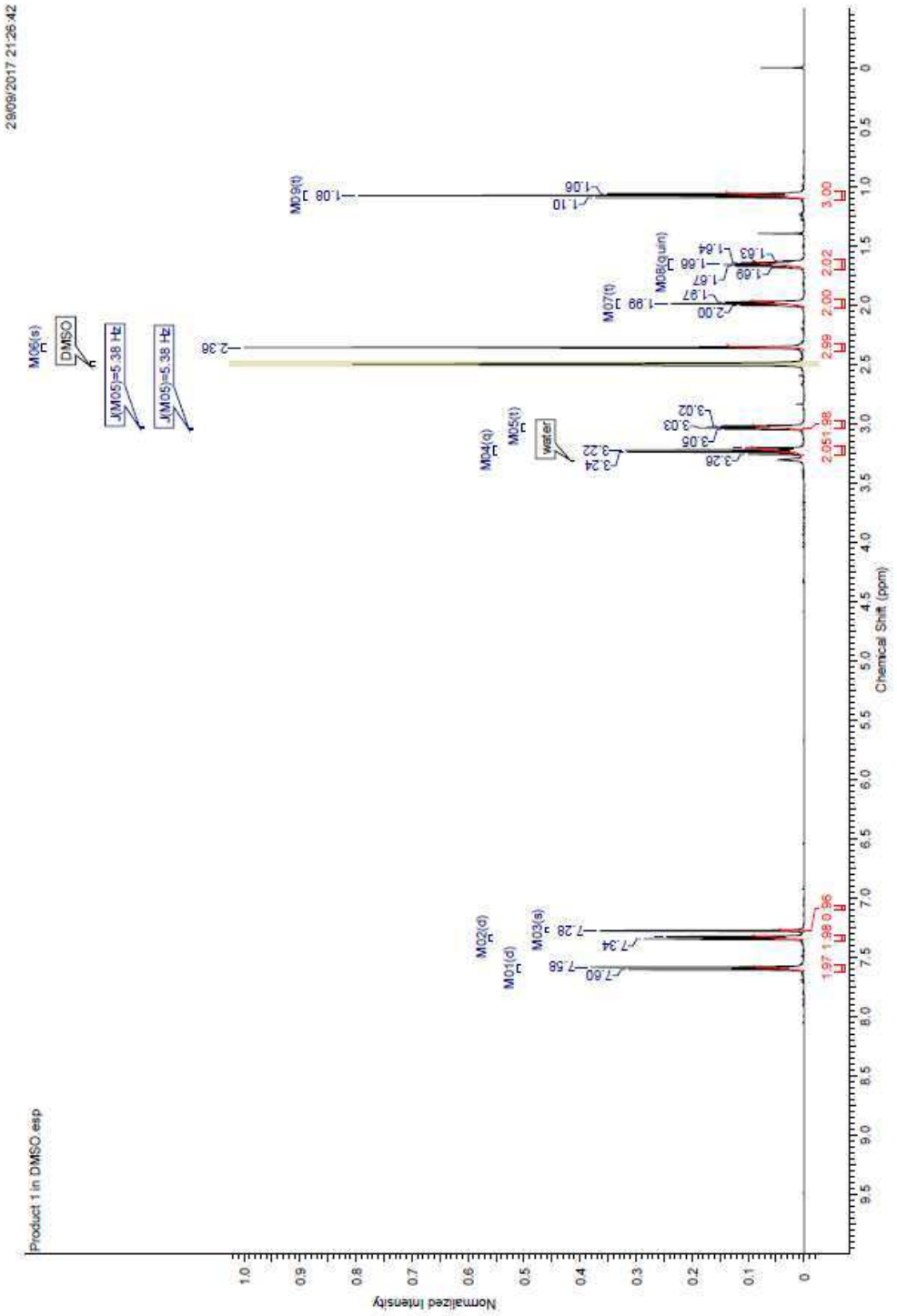
^{13}C, DMSO-d_6


29/09/2017 21:21:02
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s*)
M06(s)
M07(s)
M08(s*)
M09(s)
M10(s*)
M11(s*)
M12(s*)
M13(s*)
21.39
20.92
19.80
17.24
44.94
50.69
100.48
118.54
126.75
129.93
140.47
142.49
144.44

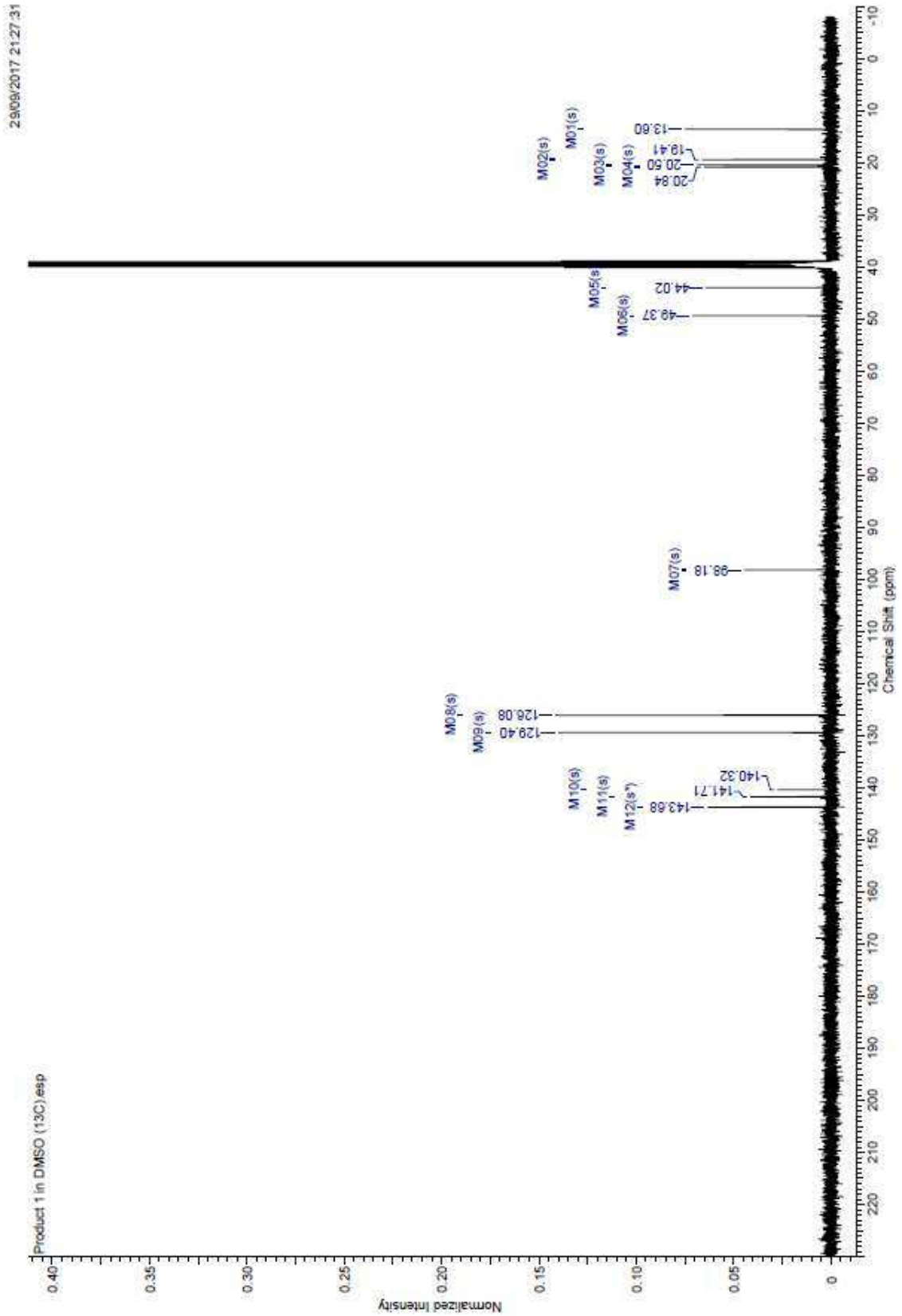


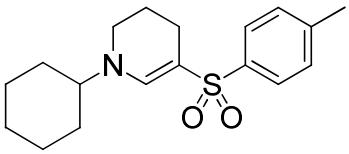
1-Ethyl-5-tosyl-1,2,3,4-tetrahydropyridine 4g

^{1}H, DMSO-*d*$_6$



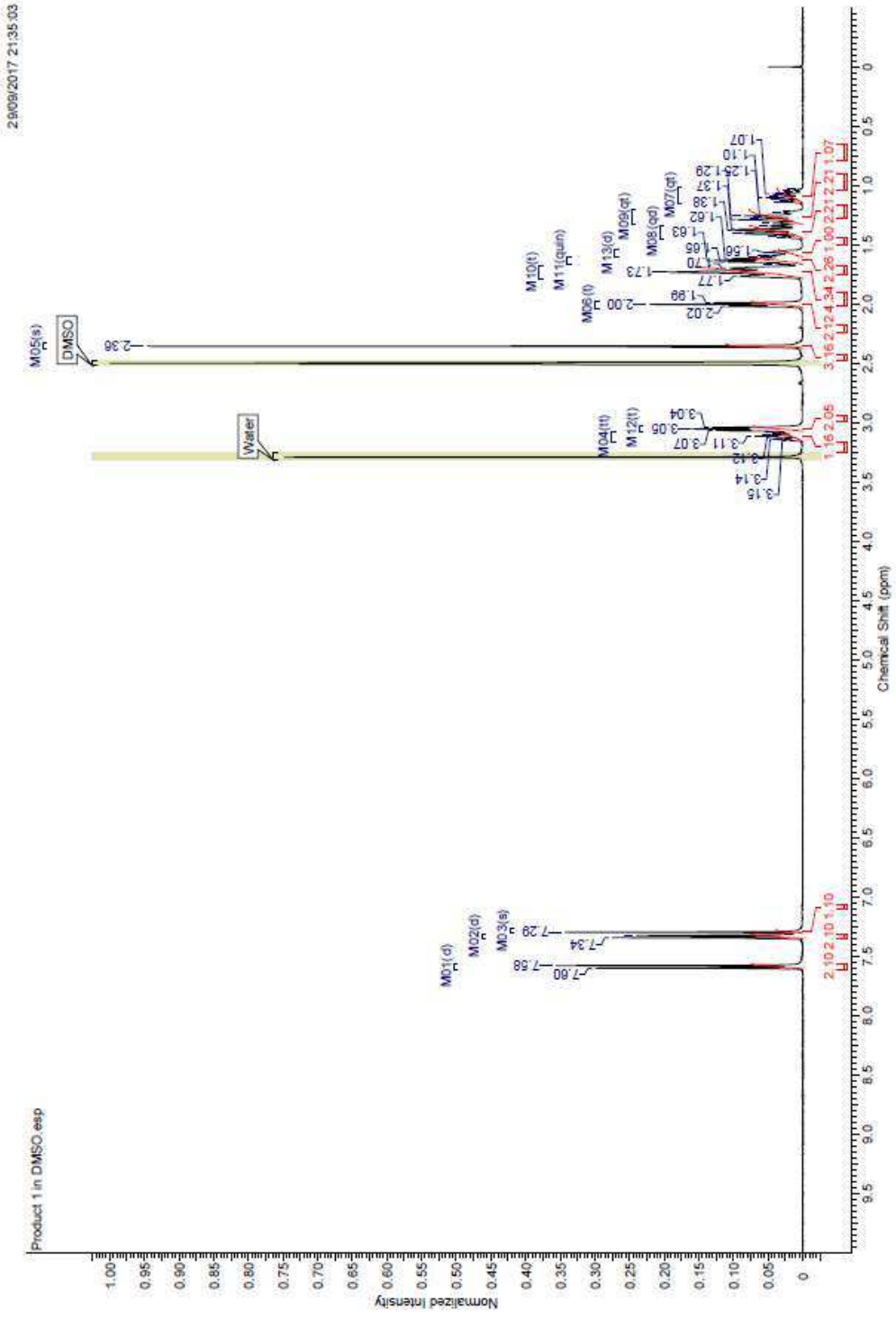
^{13}C, DMSO-d_6


29/09/2017 21:27:31
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s*)
13.60
19.41
20.50
20.84
44.02
49.37
98.18
126.08
129.40
140.32
141.71
143.68

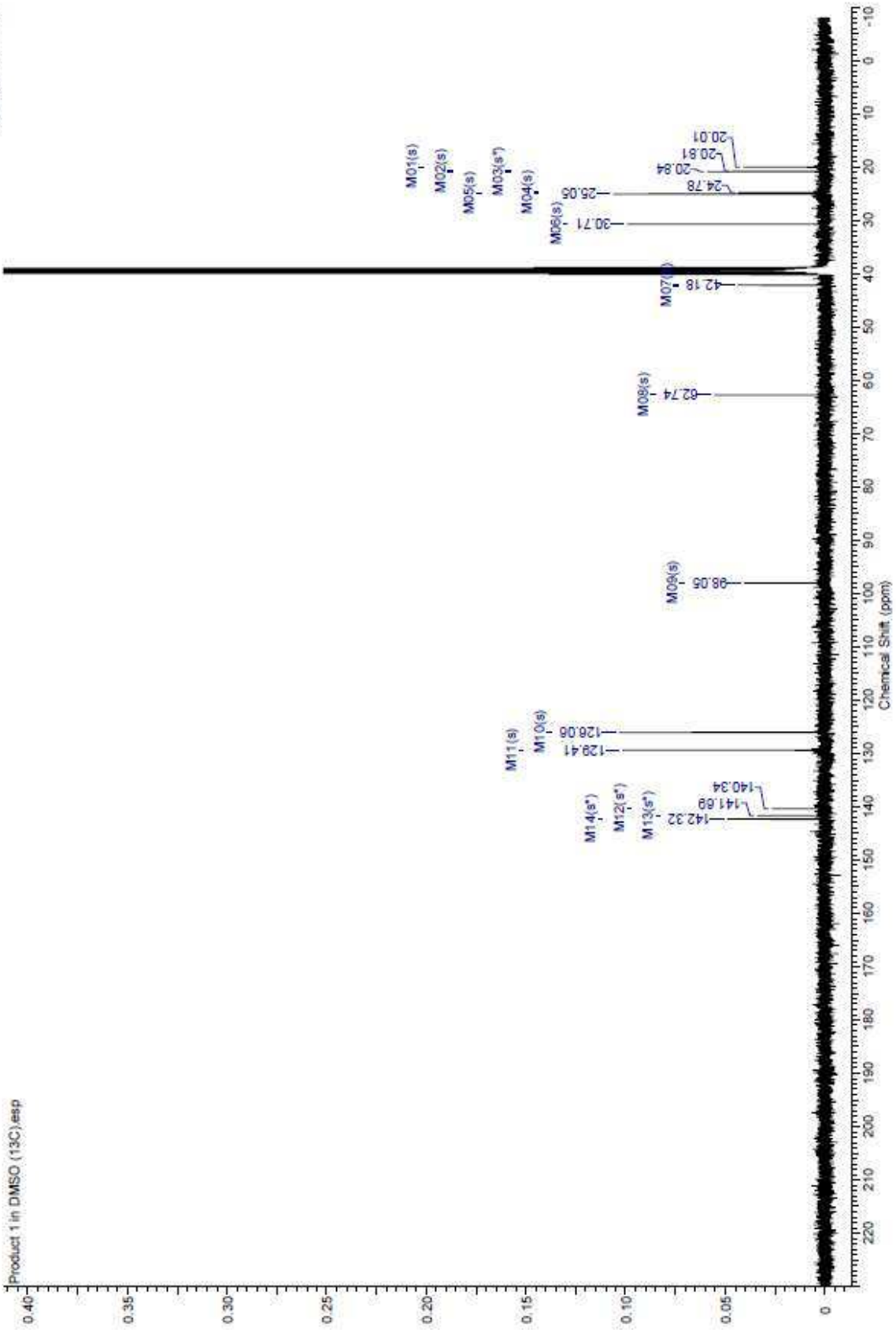


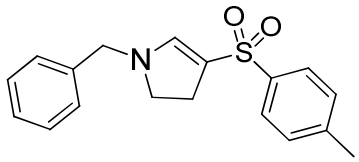
1-Cyclohexyl-5-tosyl-1,2,3,4-tetrahydropyridine 4h

^{1}H, DMSO-*d*$_6$



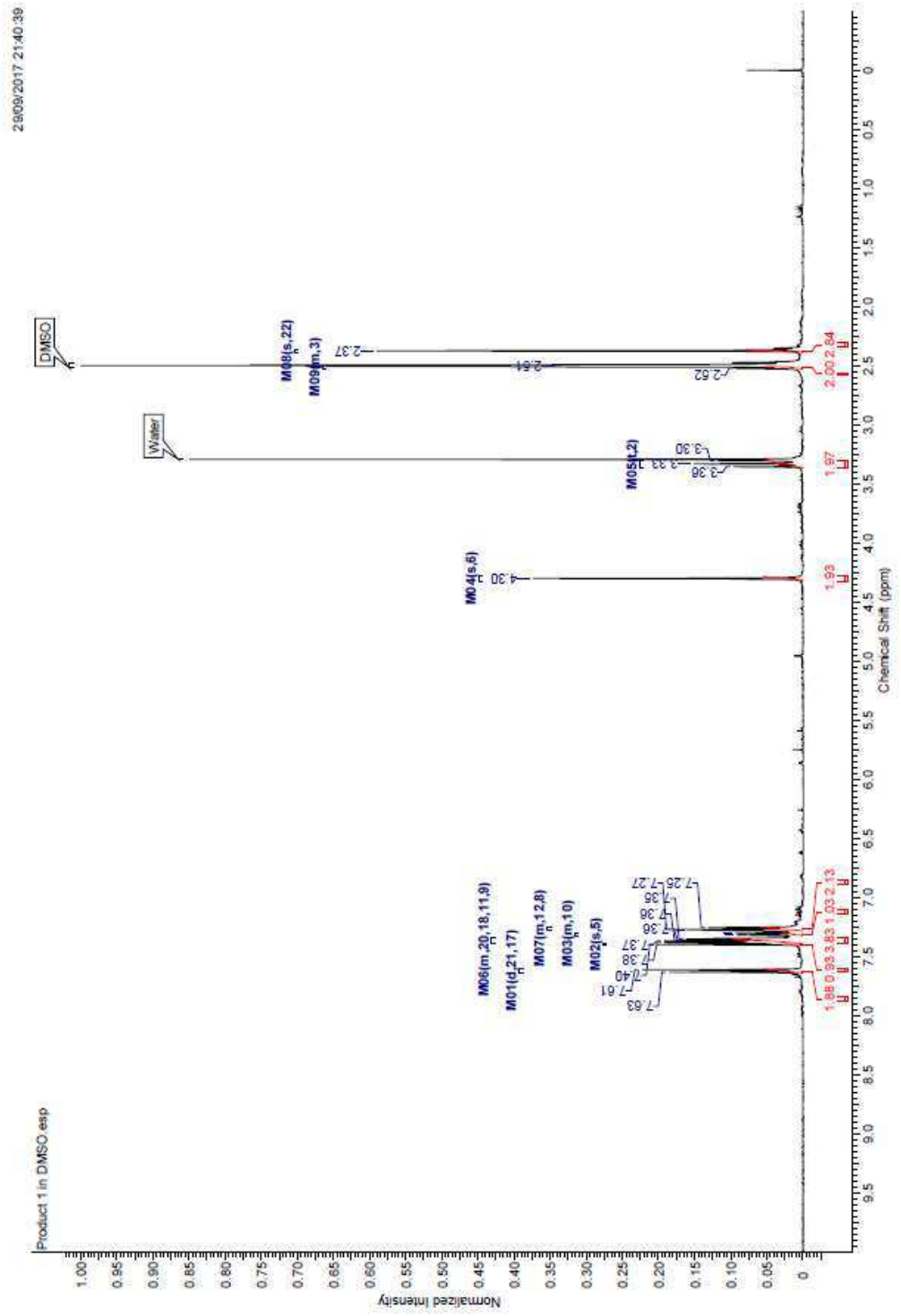
^{13}C, DMSO-d_6


29/09/2017 21:35:57
Product 1 in DMSO (13C).esp
M01(s)
M02(s)
M05(s)
M03(s*)
M04(s)
M06(s)
M07(s)
M08(s)
M09(s)
M11(s)
M10(s)
M14(s*)
M12(s*)
M13(s*)
20.01
20.81
20.84
24.78
25.05
30.71
42.18
62.74
98.05
126.06
128.41
140.34
141.69
142.32
Chemical Shift (ppm)

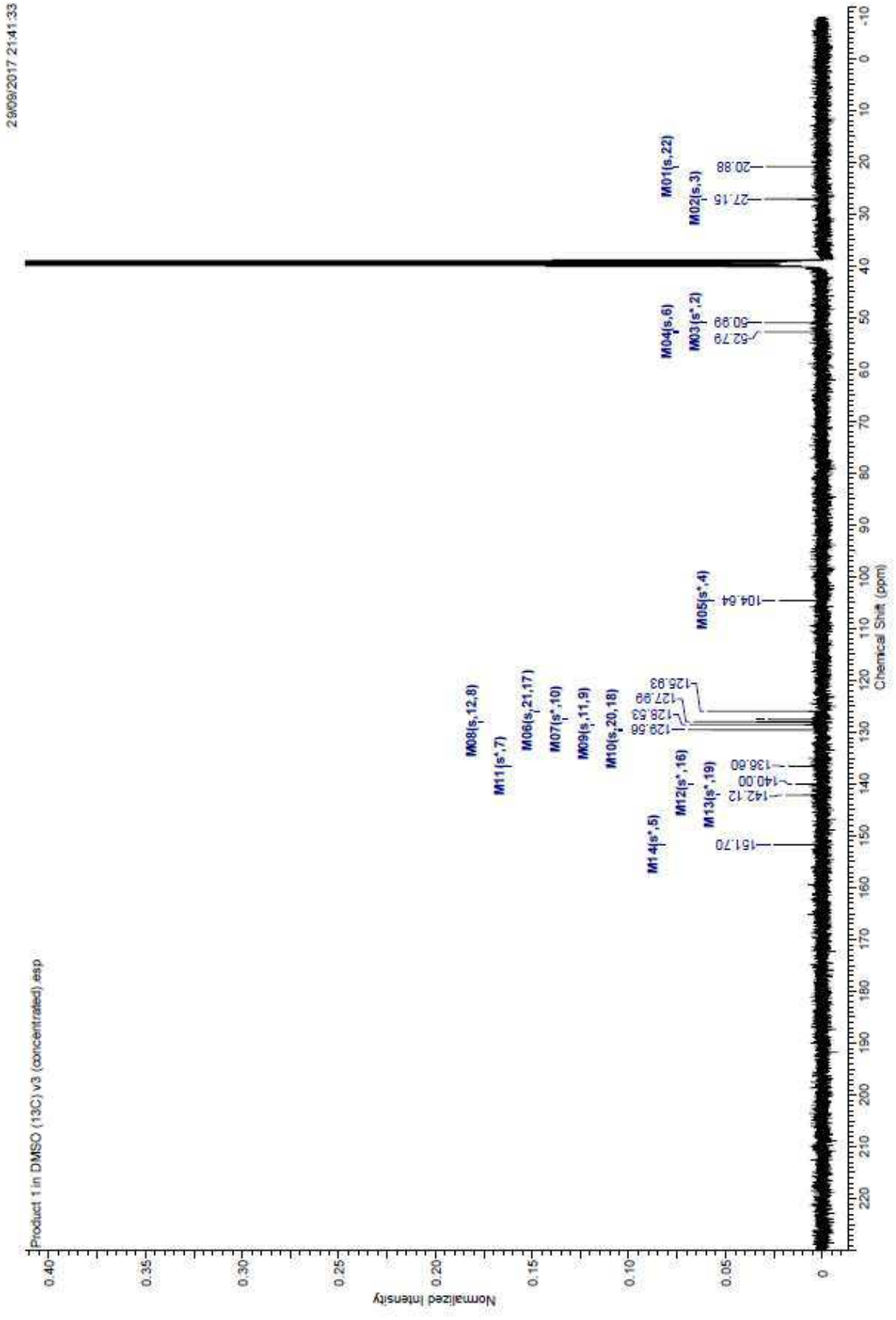


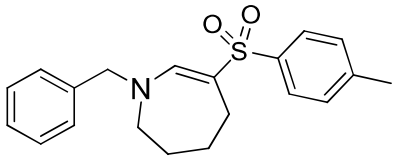
1-Benzyl-4-tosyl-2,3-dihydro-1H-pyrrole 4i

^{1}H, DMSO-*d*$_6$



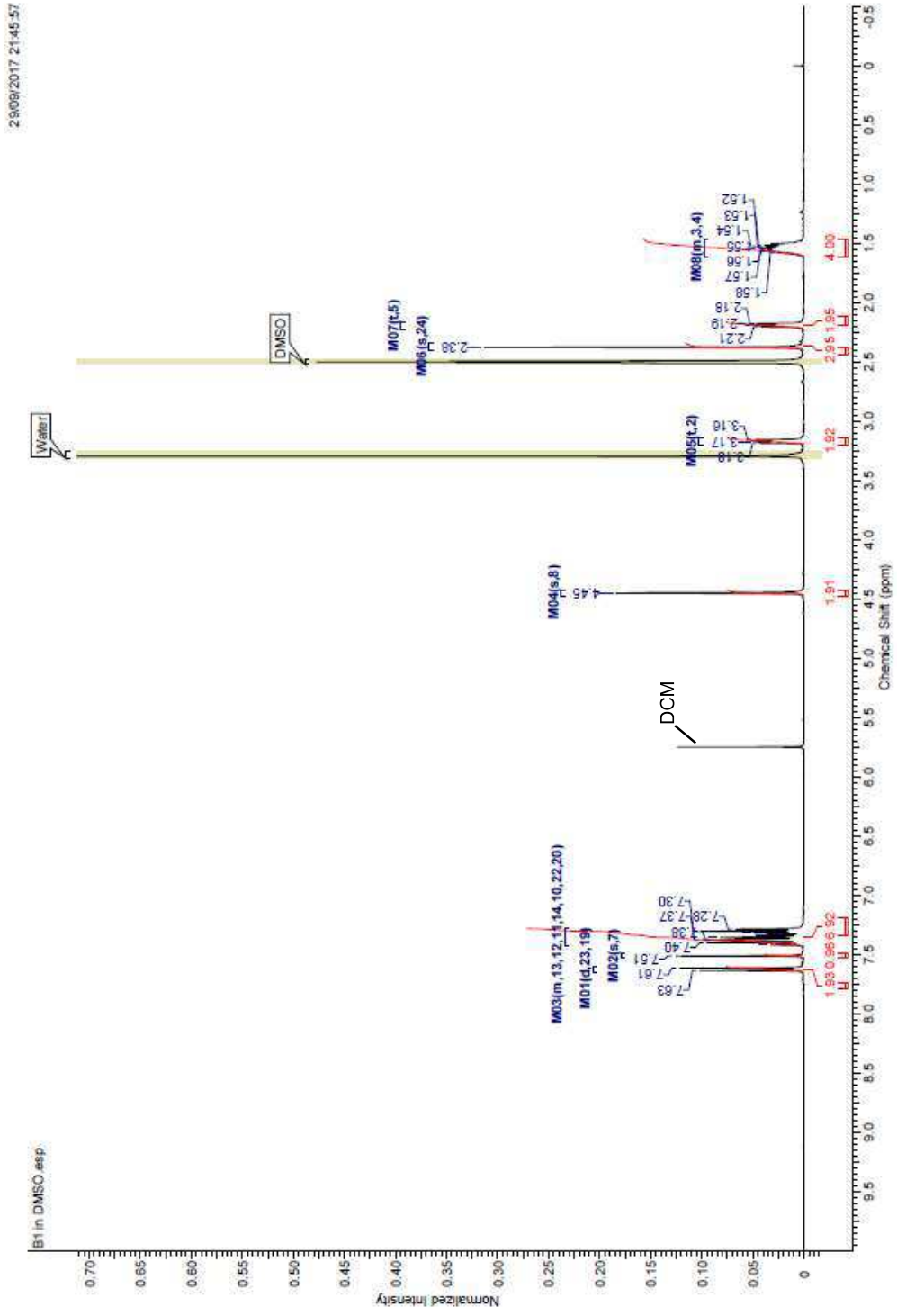
^{13}C, DMSO-d_6


29/09/2017 21:41:33
Product 1 in DMSO (13C) v3 (concentrated).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s,22)
M02(s,3)
M03(s*,2)
M04(s,6)
M05(s*,4)
M06(s,21,17)
M07(s*,10)
M08(s,12,8)
M09(s,11,9)
M10(s,20,18)
M11(s*,7)
M12(s*,16)
M13(s*,19)
M14(s*,5)
20.88
27.15
50.99
52.79
104.64
125.83
127.99
128.53
129.56
136.60
140.00
142.12
151.70

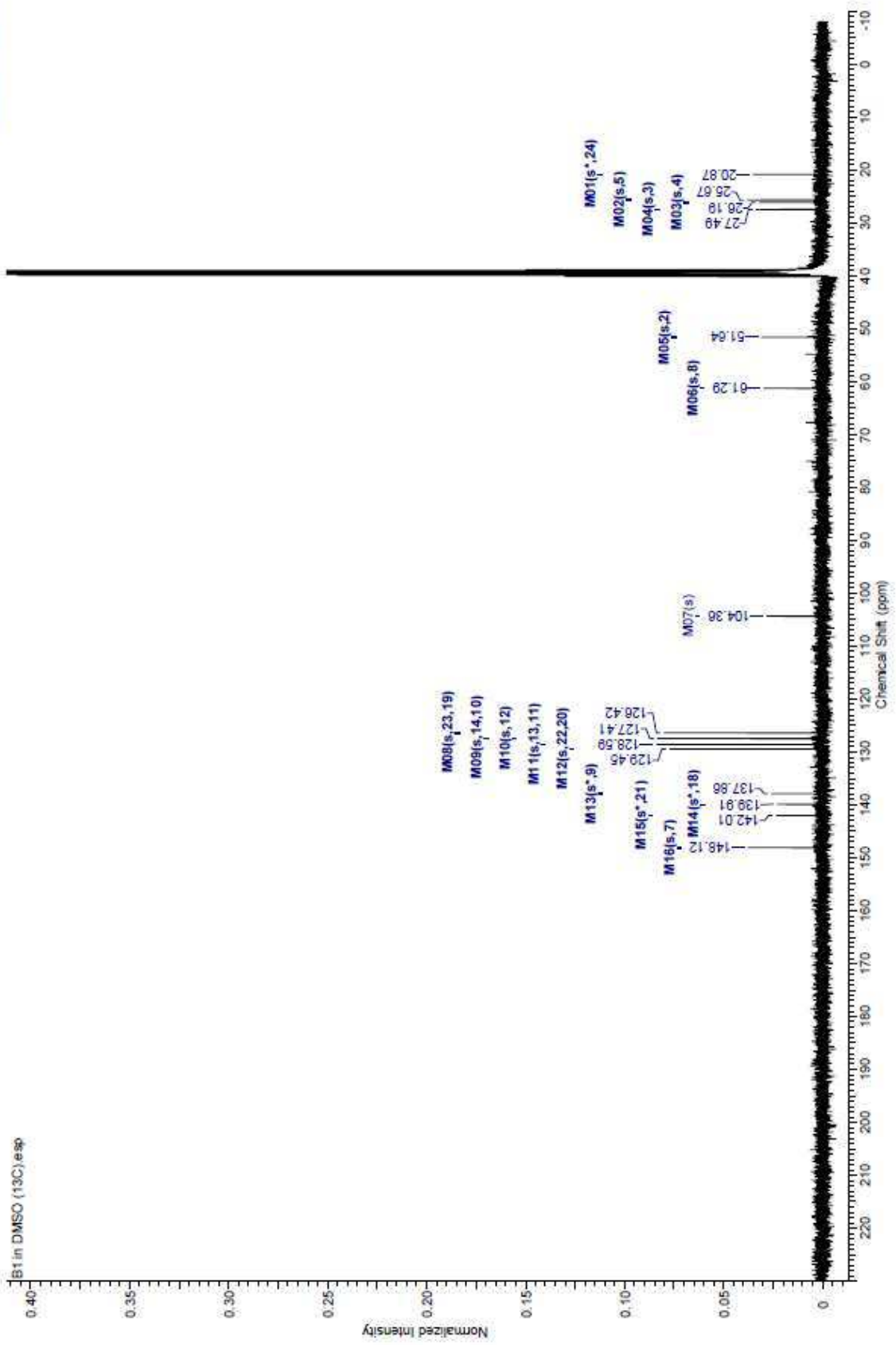


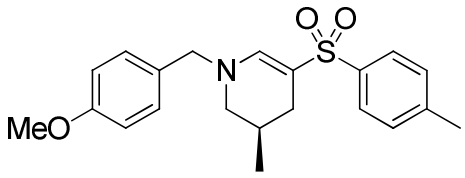
1-benzyl-6-tosyl-2,3,4,5-tetrahydro-1H-azepine 4j

^{1}H, DMSO-*d*$_6$



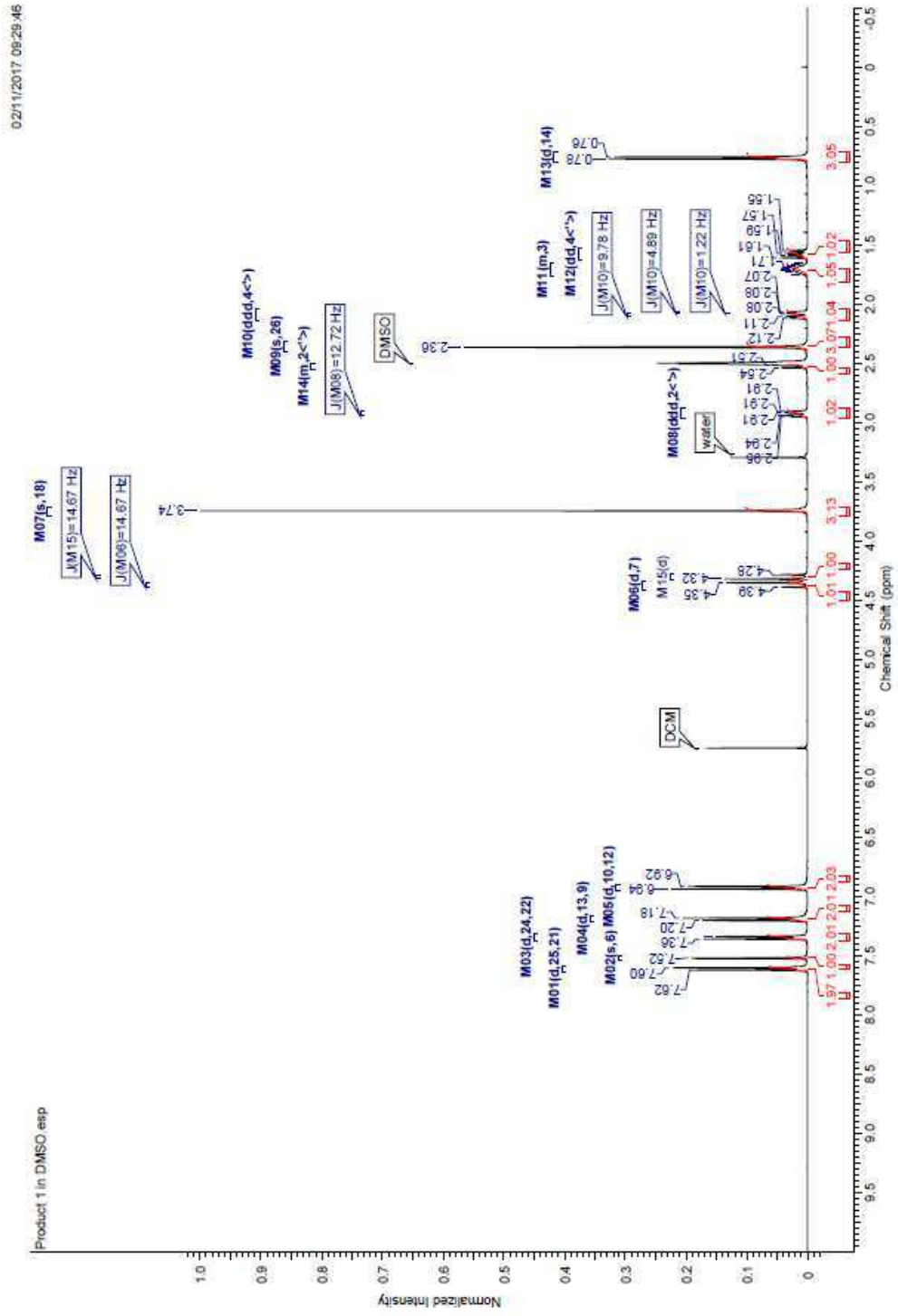
^{13}C, DMSO-d_6


29/09/2017 21:46:52
B1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s*,24)
M02(s,5)
M04(s,3)
M03(s,4)
M05(s,2)
M06(s,8)
M07(s)
M08(s,23,19)
M09(s,14,10)
M10(s,12)
M11(s,13,11)
M12(s,22,20)
M13(s*,9)
M15(s*,21)
M14(s*,18)
M16(s,7)
20.87
25.67
26.18
27.49
51.64
61.29
104.36
126.42
127.41
128.59
129.45
137.86
139.91
142.01
148.12

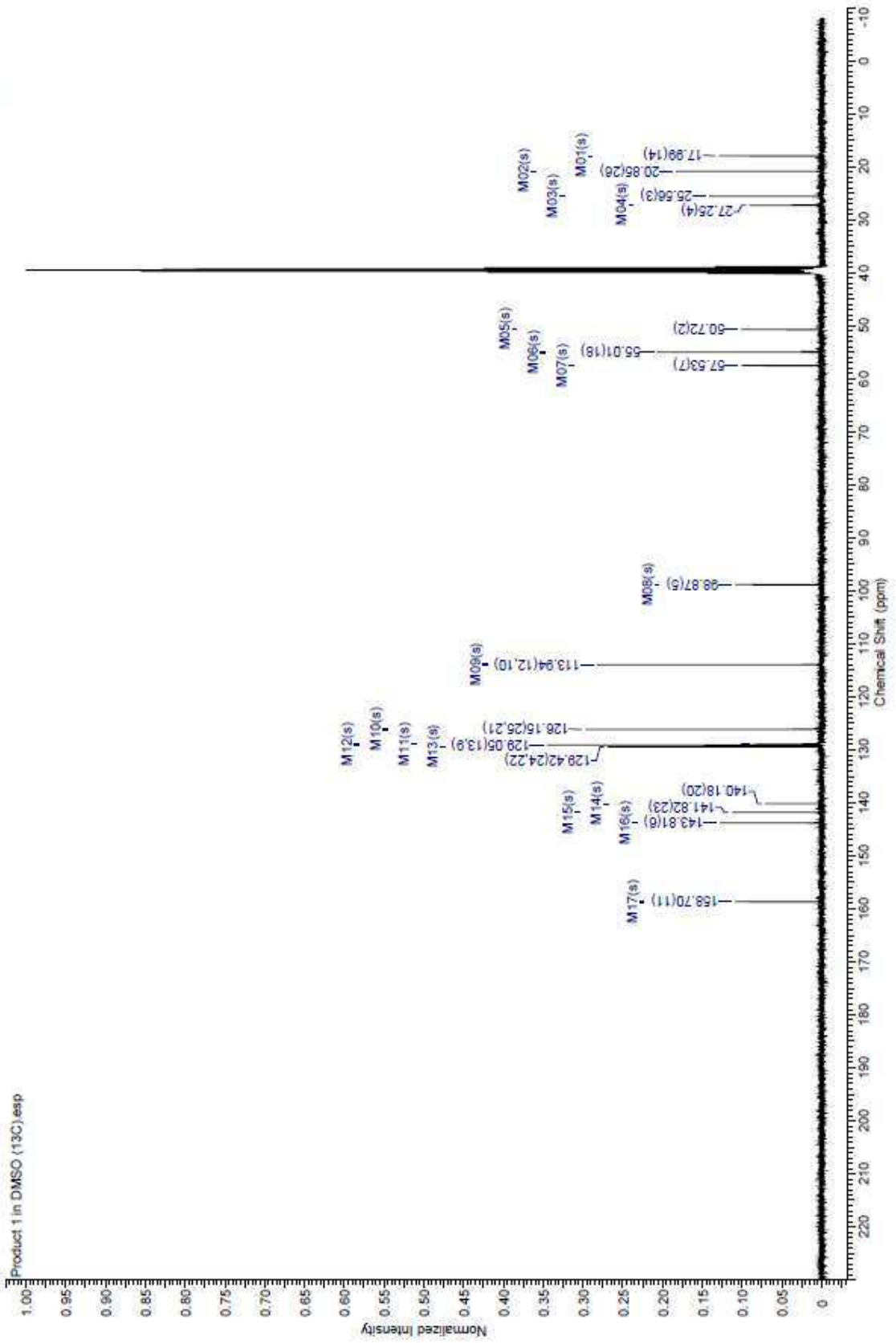


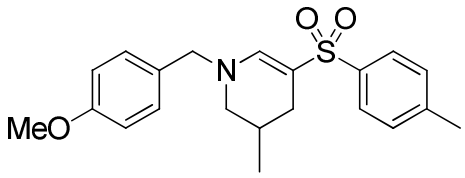
(*R*)-1-(4-Methoxybenzyl)-3-methyl-5-tosyl-1,2,3,4-tetrahydropyridine 4k

^{1}H, DMSO-*d*$_6$



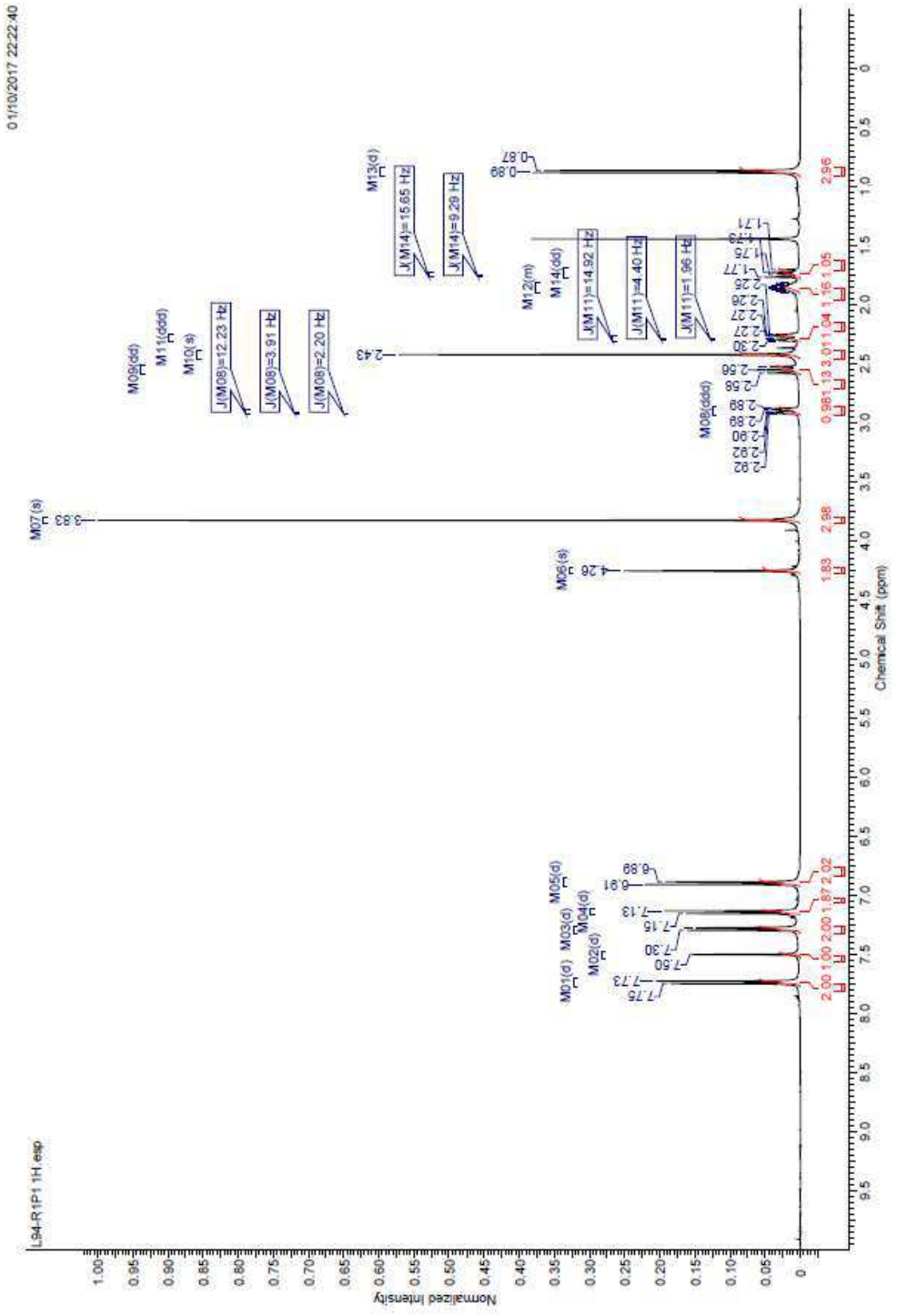
^{13}C, DMSO-d_6


30/09/2017 07:50:21
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
17.99(14)
20.86(26)
25.56(3)
27.25(4)
60.72(2)
57.53(7)
56.01(16)
98.87(5)
113.94(12.10)
129.05(13.9)
128.42(24.22)
126.15(25.21)
140.18(20)
141.82(23)
143.81(6)
158.70(11)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
M17(s)

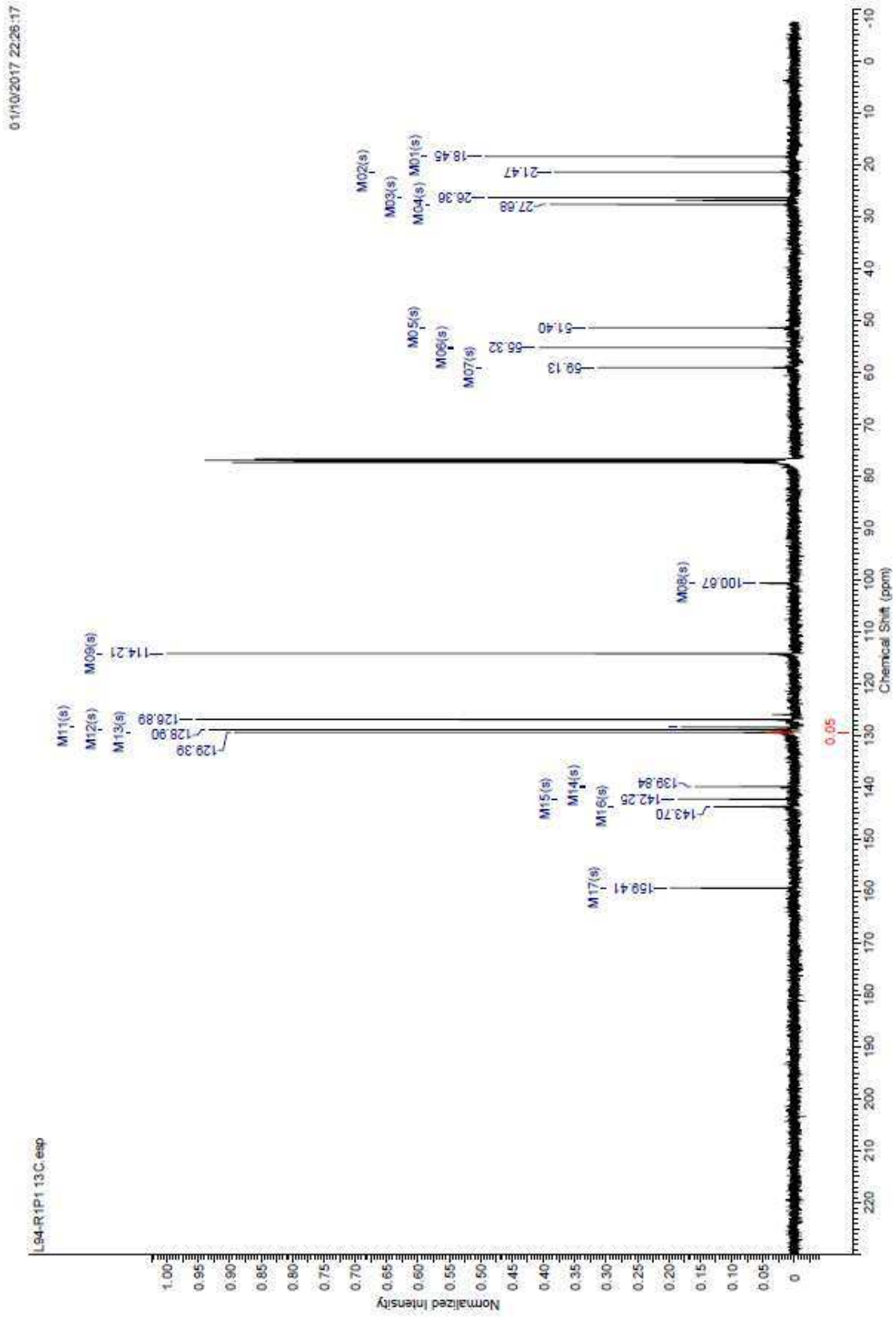


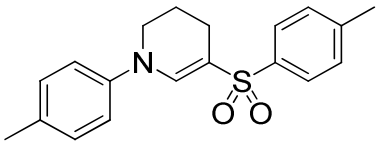
1-(4-Methoxybenzyl)-3-methyl-5-tosyl-1,2,3,4-tetrahydropyridine 4kb

^{1}H, $CDCl_3$



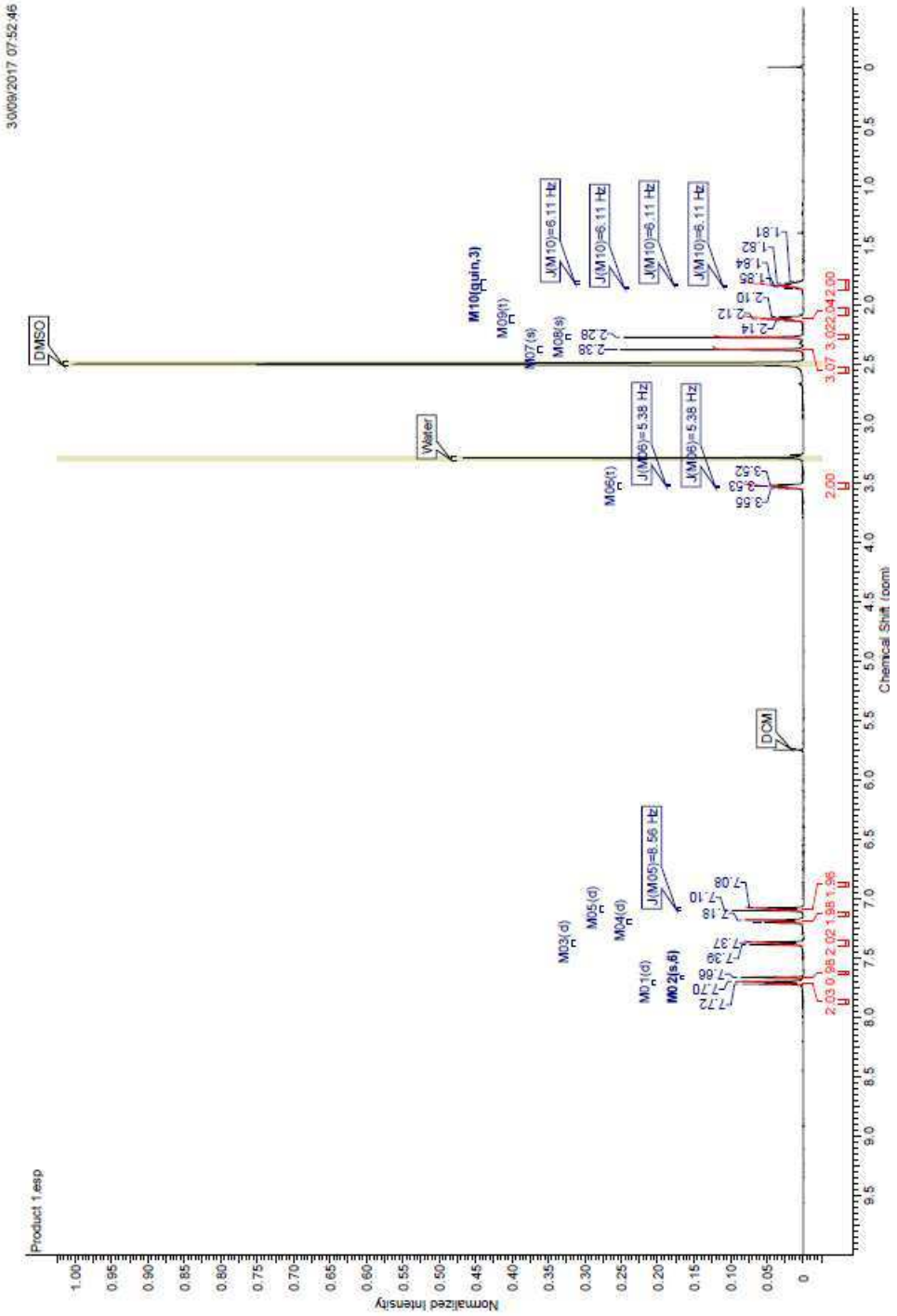
^{13}C, $CDCl_3$


01/10/2017 22:26:17
L94-R1P1 13C esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s)
M17(s)
18.45
21.47
26.38
27.68
51.40
55.32
59.13
100.67
114.21
126.89
128.90
129.39
139.84
142.26
143.70
159.41
0.05

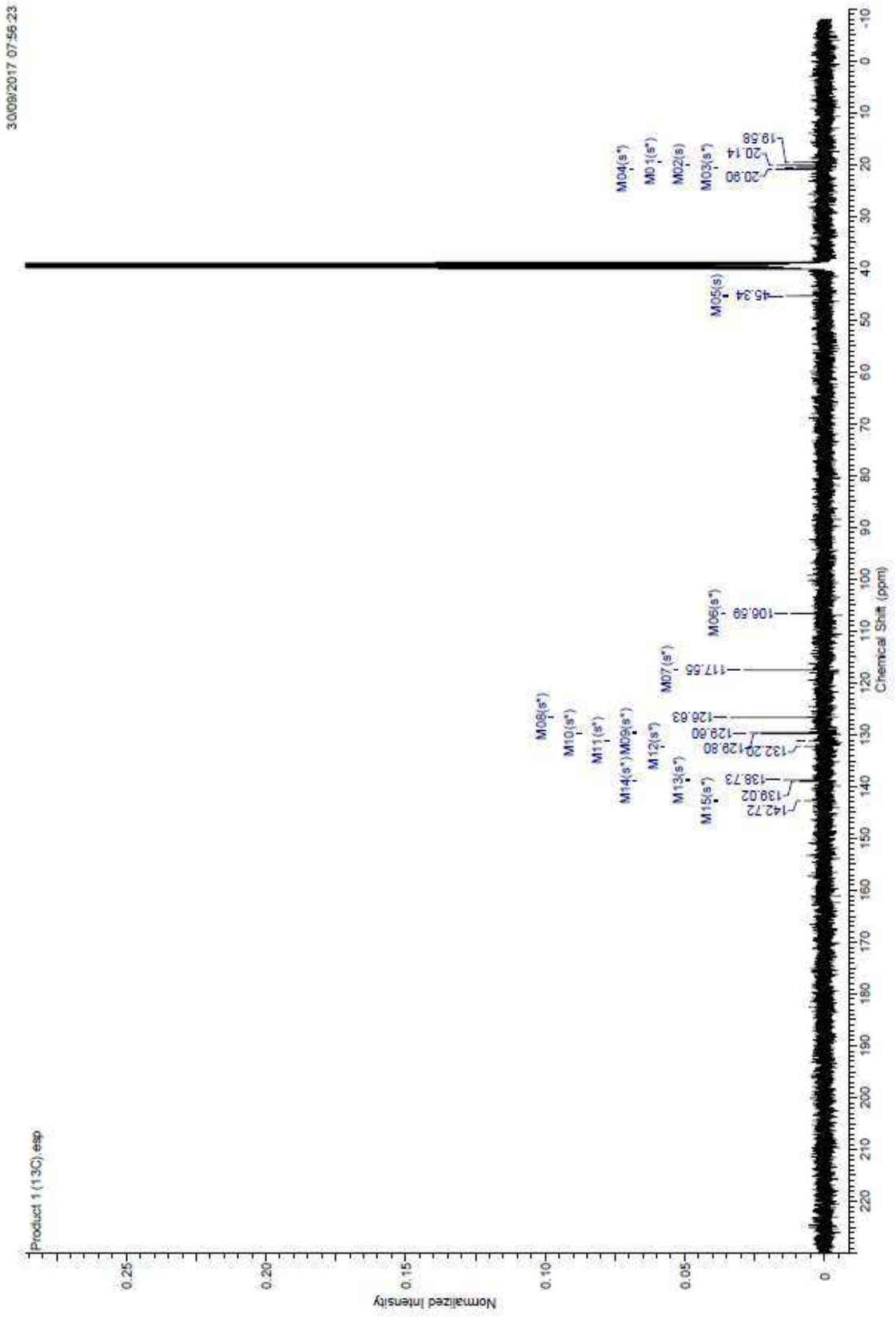


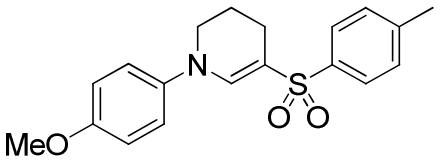
1-(*p*-Tolyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4l

^{1}H, DMSO-d_6



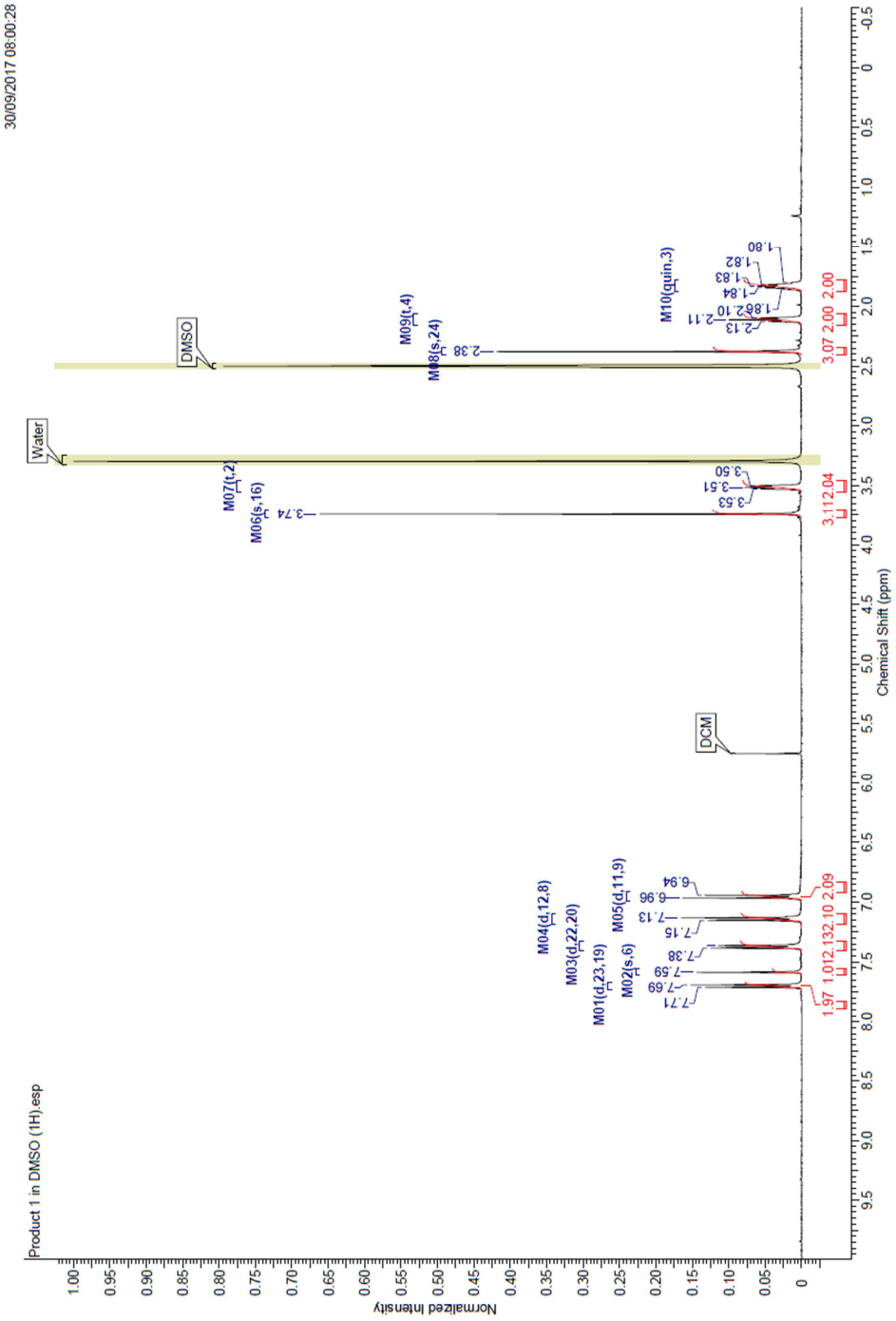
^{13}C, DMSO-d_6


30/09/2017 07:56:23
Product 1 (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M04(s*)
M01(s*)
M02(s)
M03(s*)
20.90
20.14
19.58
M05(s)
45.34
M06(s*)
106.59
M07(s*)
117.55
M08(s*)
M10(s*)
M11(s*)
M14(s*)M09(s*)
M12(s*)
M13(s*)
M15(s*)
126.63
129.80
129.80
132.20
138.73
139.02
142.72

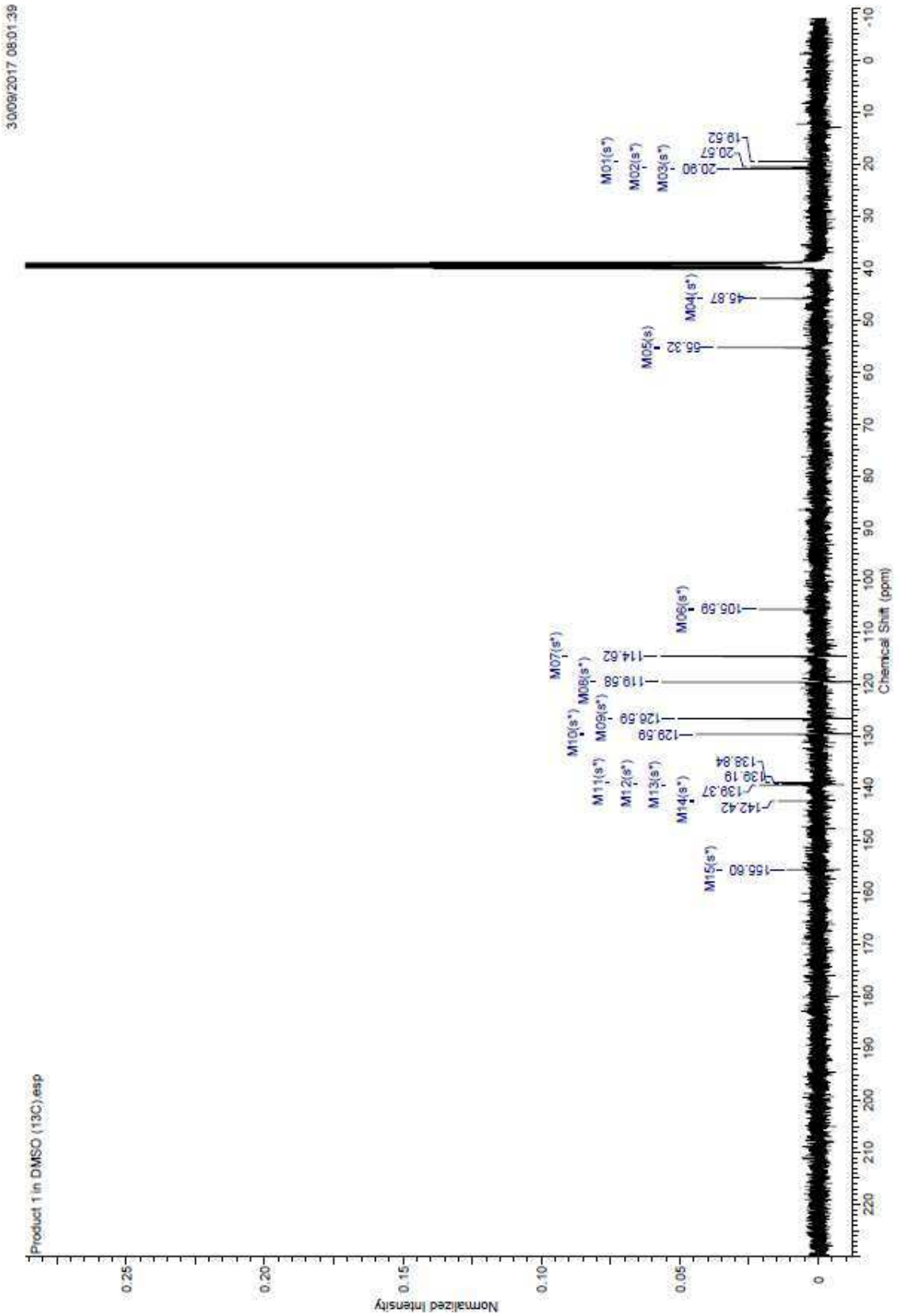


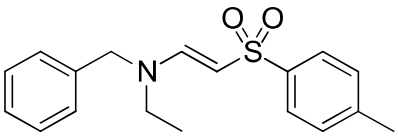
1-(4-methoxyphenyl)-5-tosyl-1,2,3,4-tetrahydropyridine 4m

^{1}H, DMSO-*d*$_6$



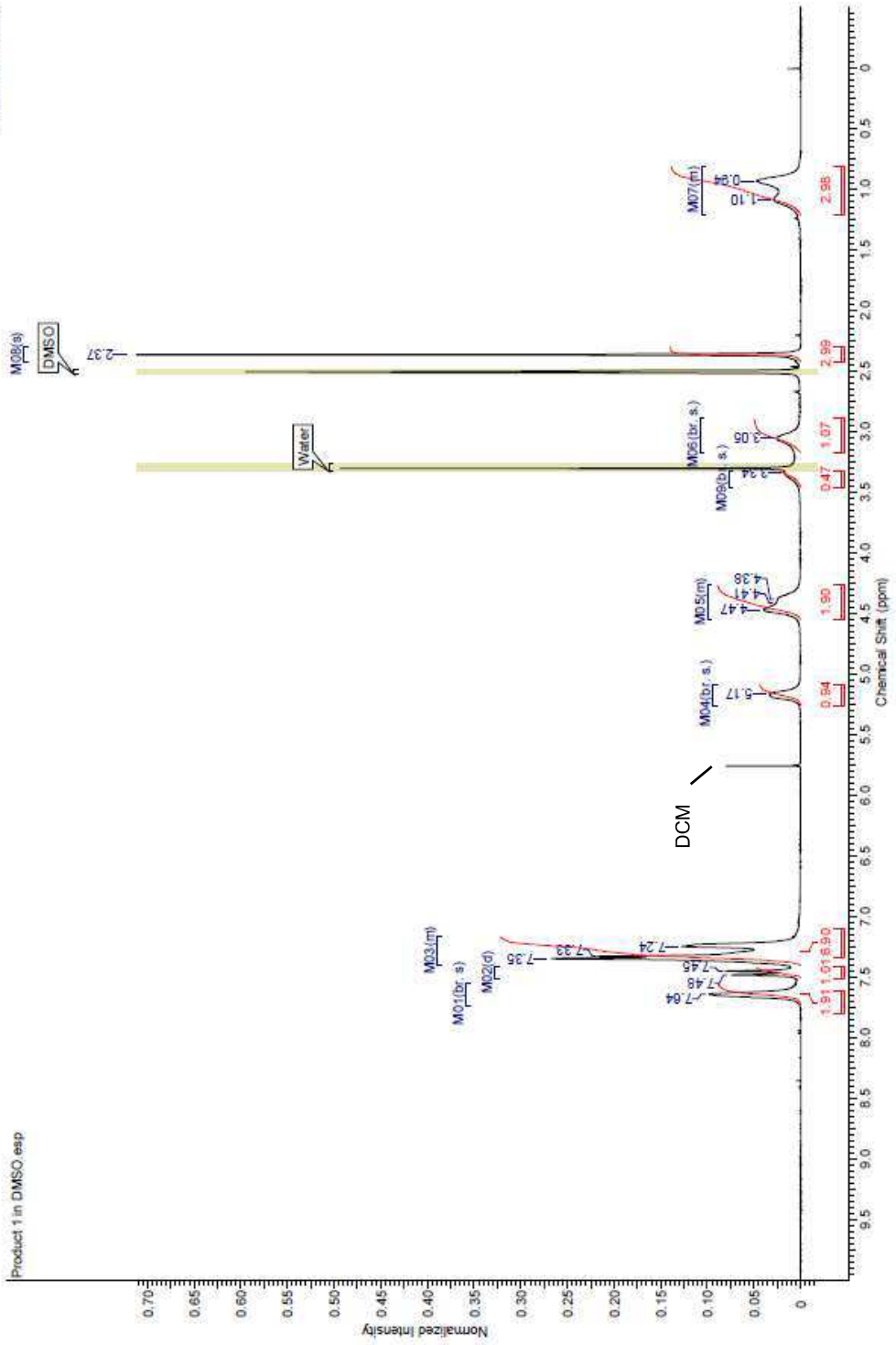
^{13}C, DMSO-d_6


30/09/2017 08:01:39
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
19.52
20.57
20.90
45.87
55.32
105.59
114.62
119.58
126.59
129.59
138.84
139.19
139.37
142.42
156.60
M01(s*)
M02(s*)
M03(s*)
M04(s*)
M05(s)
M06(s*)
M07(s*)
M08(s*)
M09(s*)
M10(s*)
M11(s*)
M12(s*)
M13(s*)
M14(s*)
M15(s*)

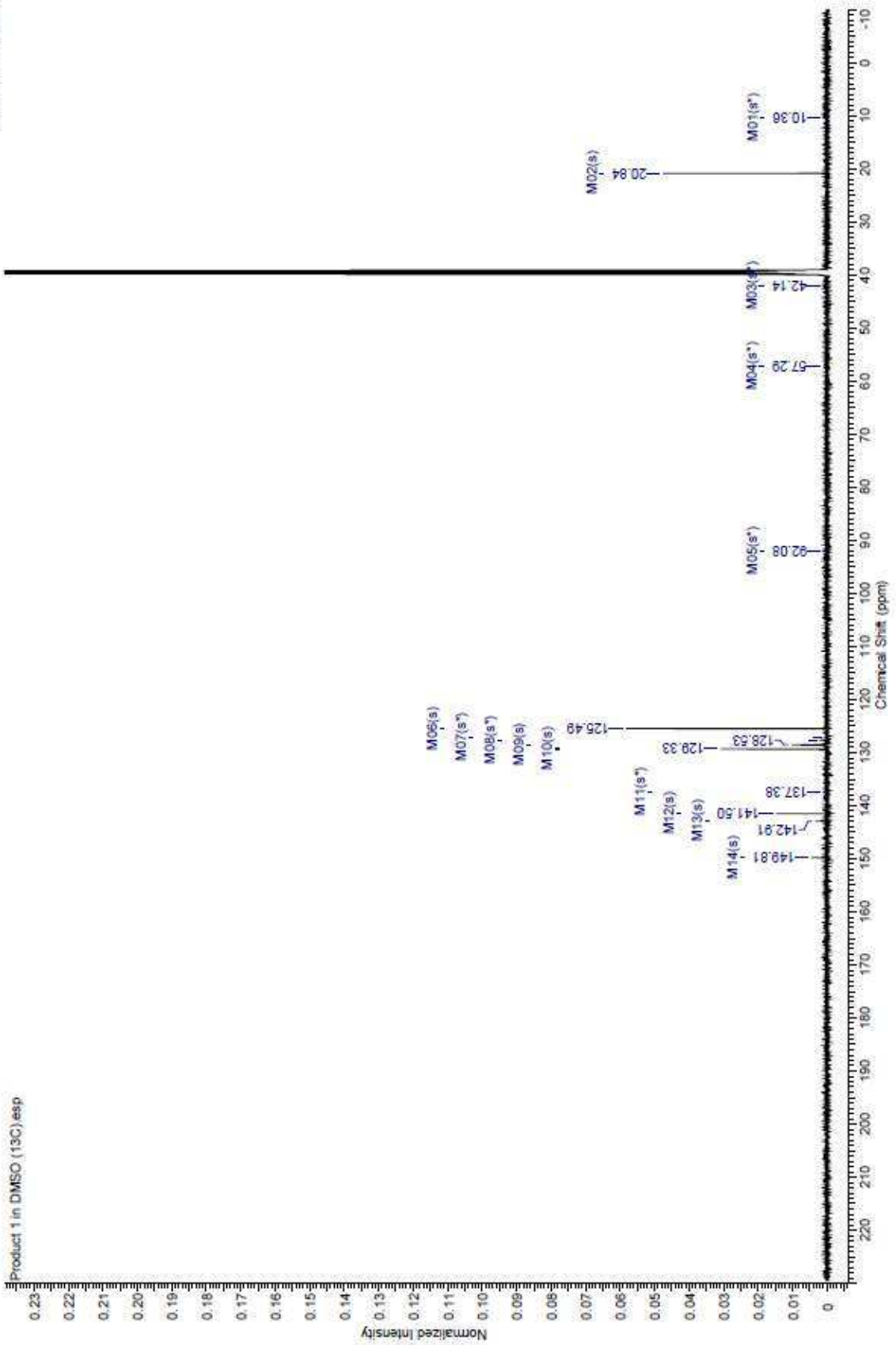


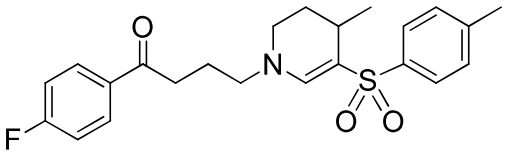
(*E*)-*N*-Benzyl-*N*-ethyl-2-tosylethen-1-amine 4n

^{1}H, DMSO-d_6



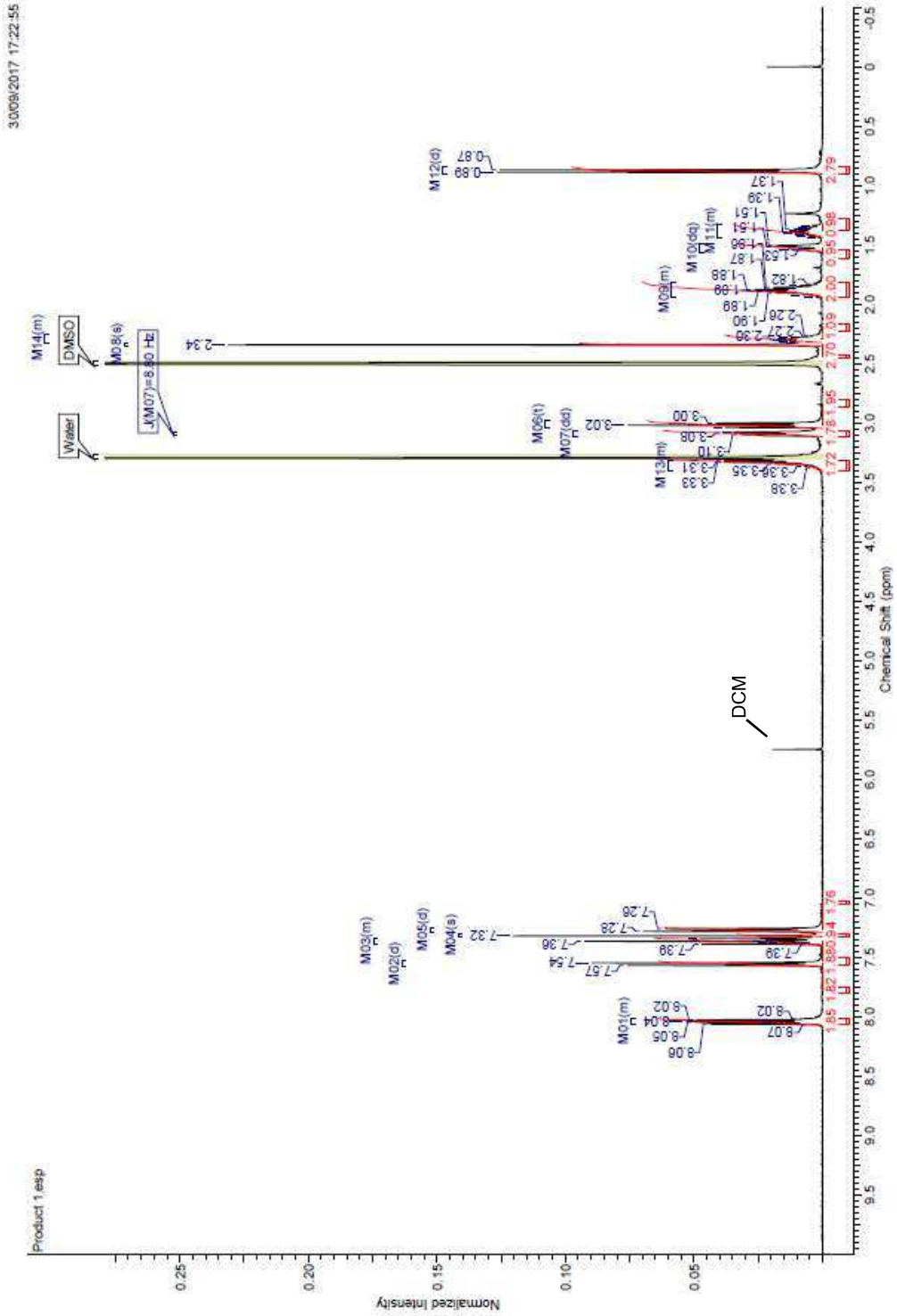
^{13}C, DMSO-d_6


30/09/2017 08:29:06
Product 1 in DMSO (13C).esp
Normalized Intensity
Chemical Shift (ppm)
M01(s*)
M02(s)
M03(s*)
M04(s*)
M05(s*)
M06(s)
M07(s*)
M08(s*)
M09(s)
M10(s)
M11(s*)
M12(s)
M13(s)
M14(s)
10.36
20.84
42.14
57.29
92.08
125.49
128.33
128.53
137.38
141.50
142.91
149.81

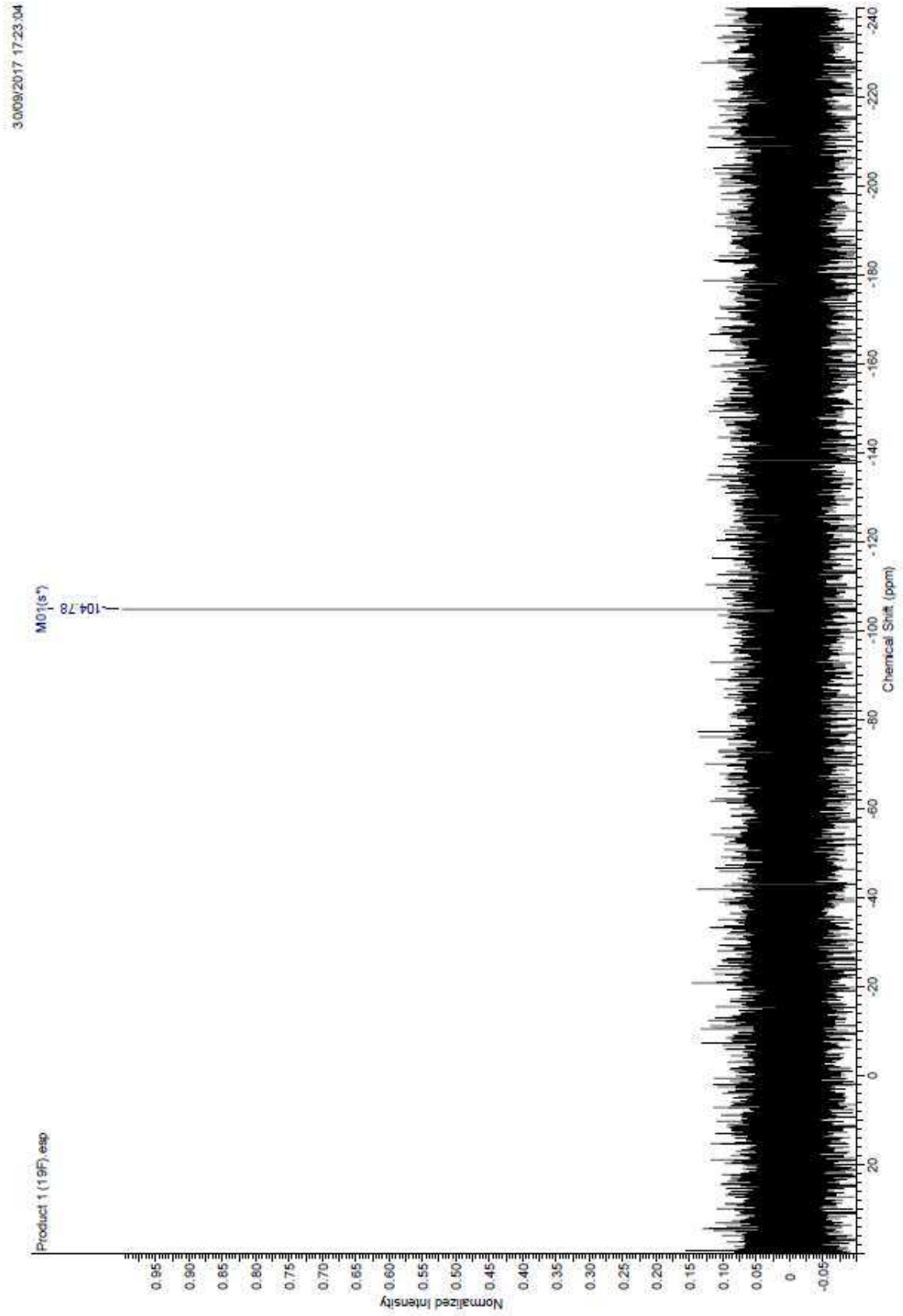


1-(4-Fluorophenyl)-4-(4-methyl-5-tosyl-3,4-dihydropyridin-1(2*H*)-yl)butan-1-one 4o

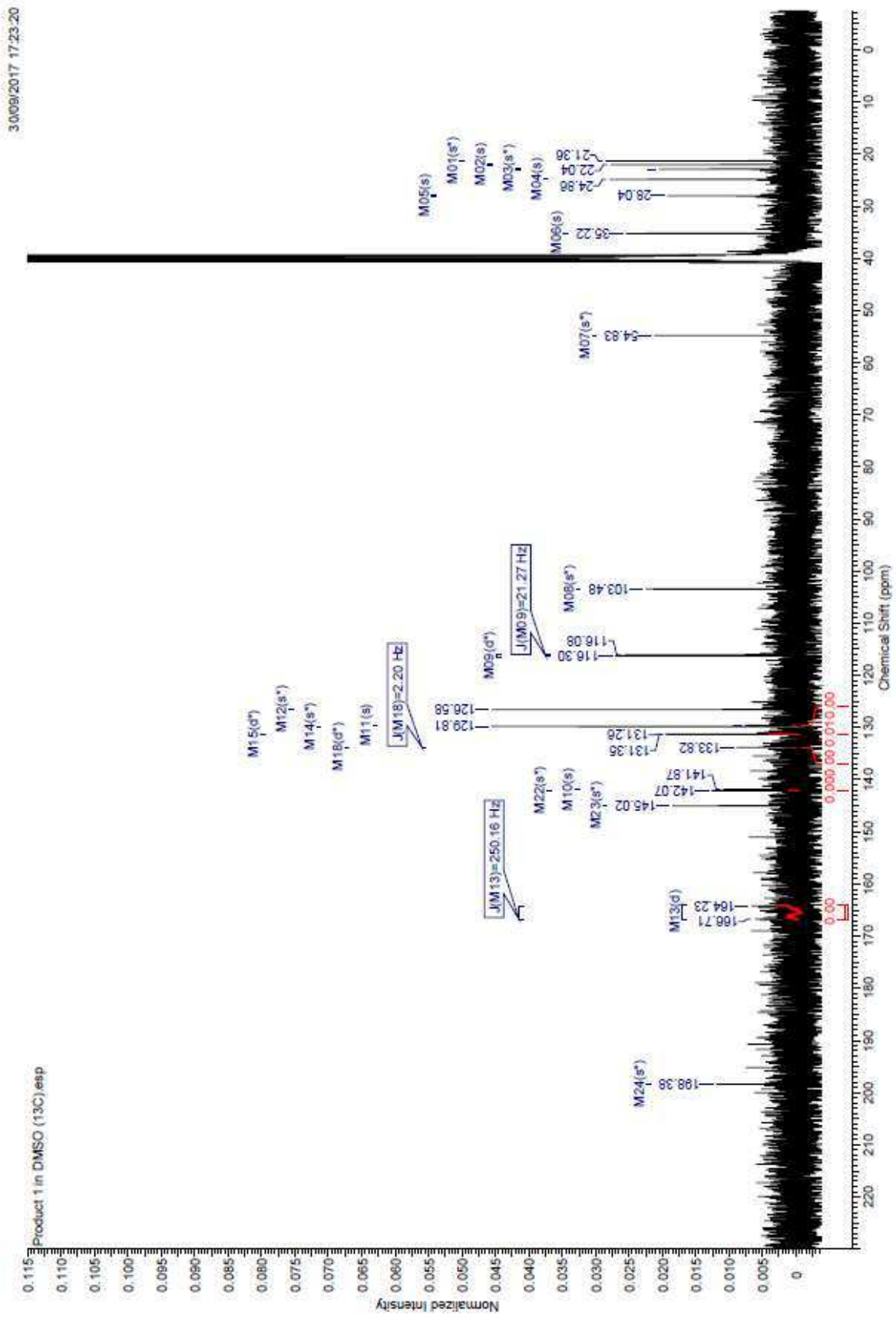
^{1}H, DMSO-d_6

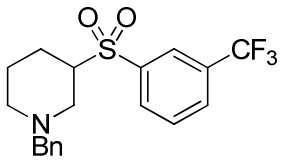


^{19}F, $CDCl_3$


3/09/2017 17:23:04
M01(ss*)
-104.78
Product 1 (19F).esp
Normalized Intensity
Chemical Shift (ppm)

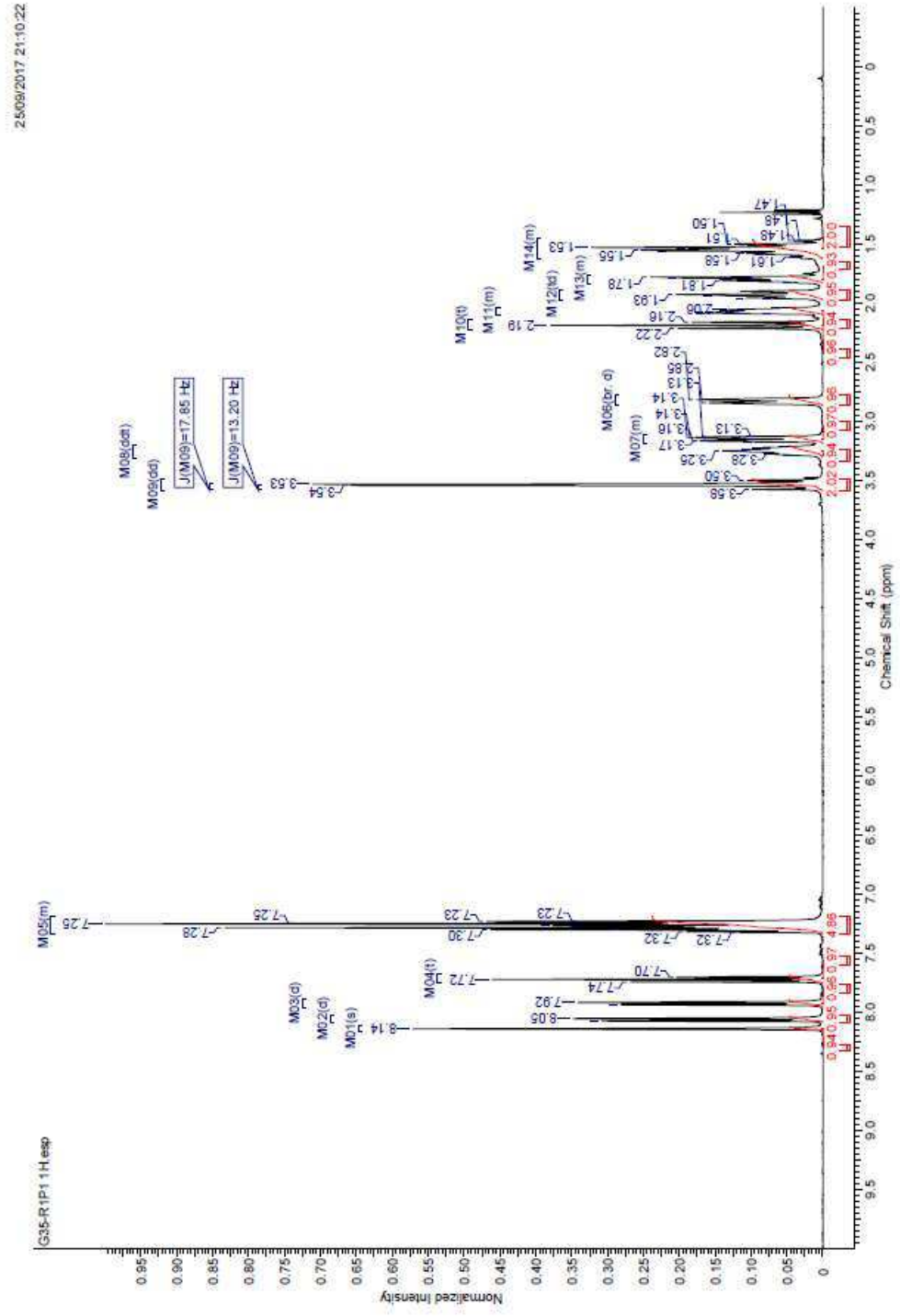
^{13}C, DMSO-d_6


30/09/2017 17:23:20
Product 1 in DMSO (13C) esp
Normalized Intensity
Chemical Shift (ppm)
M05(s)
M01(s*)
M02(s)
M03(s*)
M04(s)
M06(s)
M07(s*)
M08(s*)
M09(d*)
J(M09)=21.27 Hz
M15(d*)
M12(s*)
M14(s*)
M16(d*)
M11(s)
J(M18)=2.20 Hz
M22(s*)
M10(s)
M23(s*)
J(M13)=250.16 Hz
M13(d)
M24(s*)
21.36
22.04
24.86
28.04
35.22
54.83
103.48
116.30
116.08
126.58
129.81
131.26
131.35
133.82
141.87
142.07
145.02
164.23
166.71
198.38

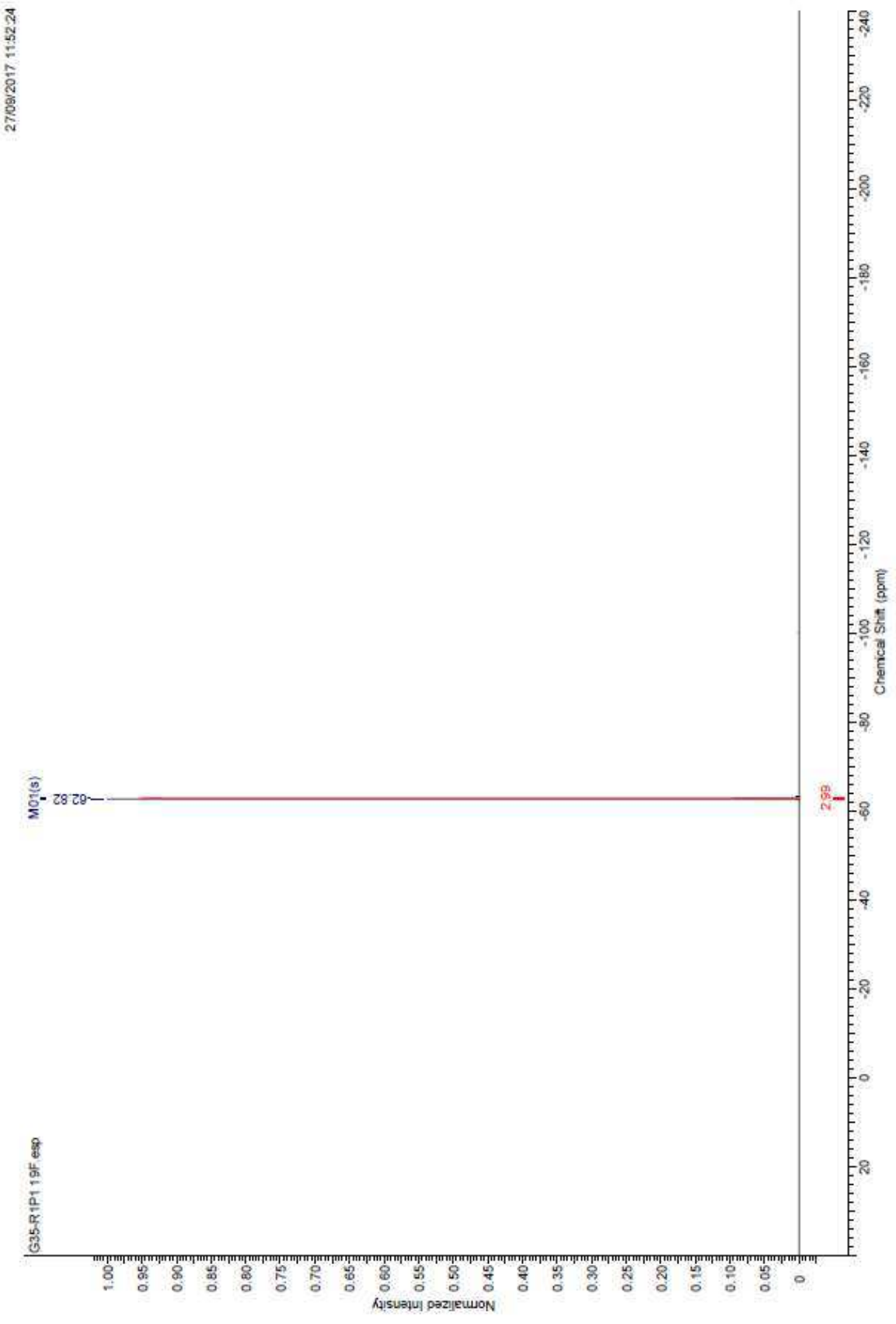


1-Benzyl-3-((3-(trifluoromethyl)phenyl)sulfonyl)piperidine 5

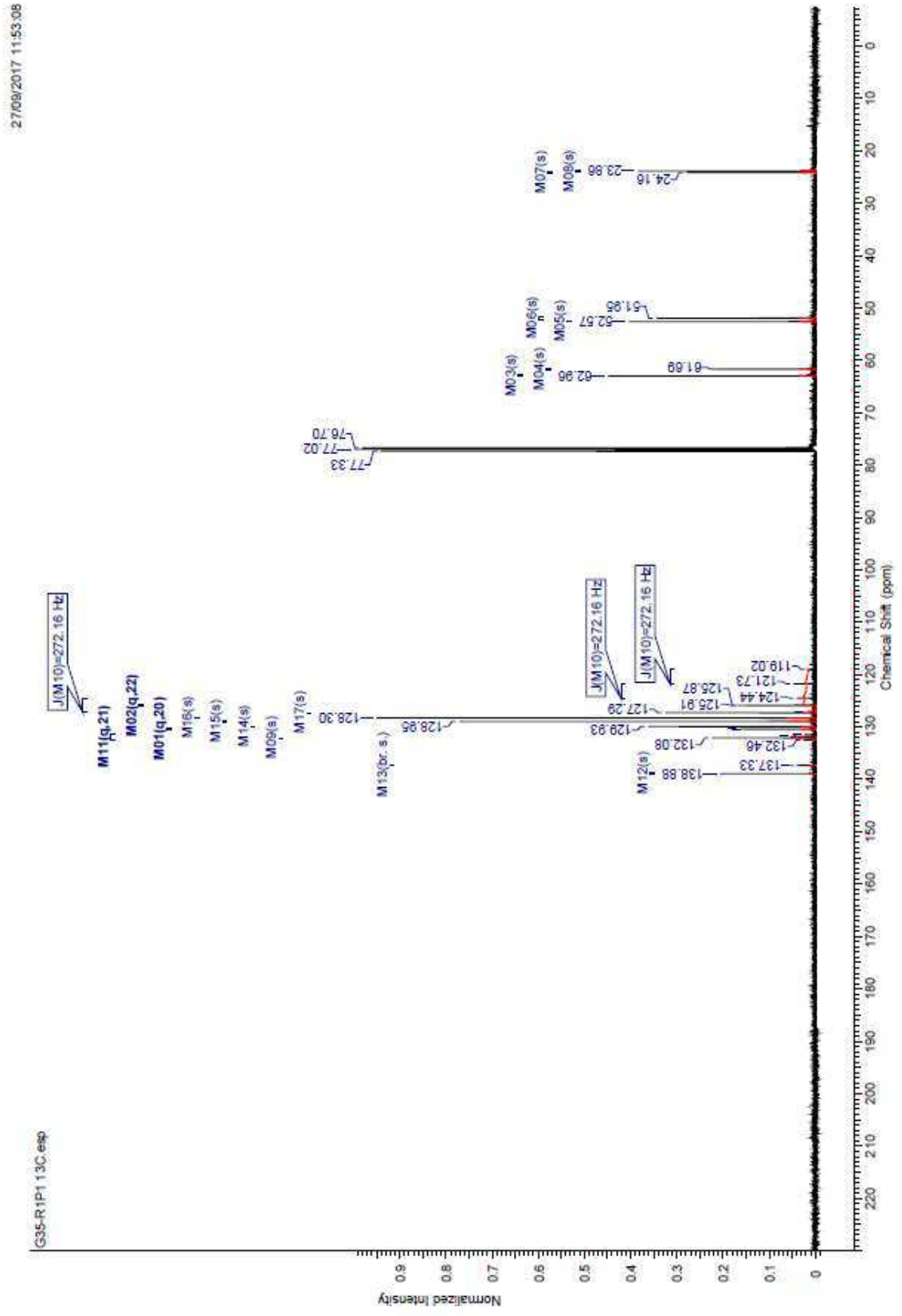
^{1}H, $CDCl_3$



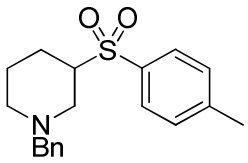
^{19}F, $CDCl_3$


27/09/2017 11:52:24
G35-R1P1 19F esp
M01(s)
-62.82
2.99
Normalized Intensity
Chemical Shift (ppm)

^{13}C, $CDCl_3$

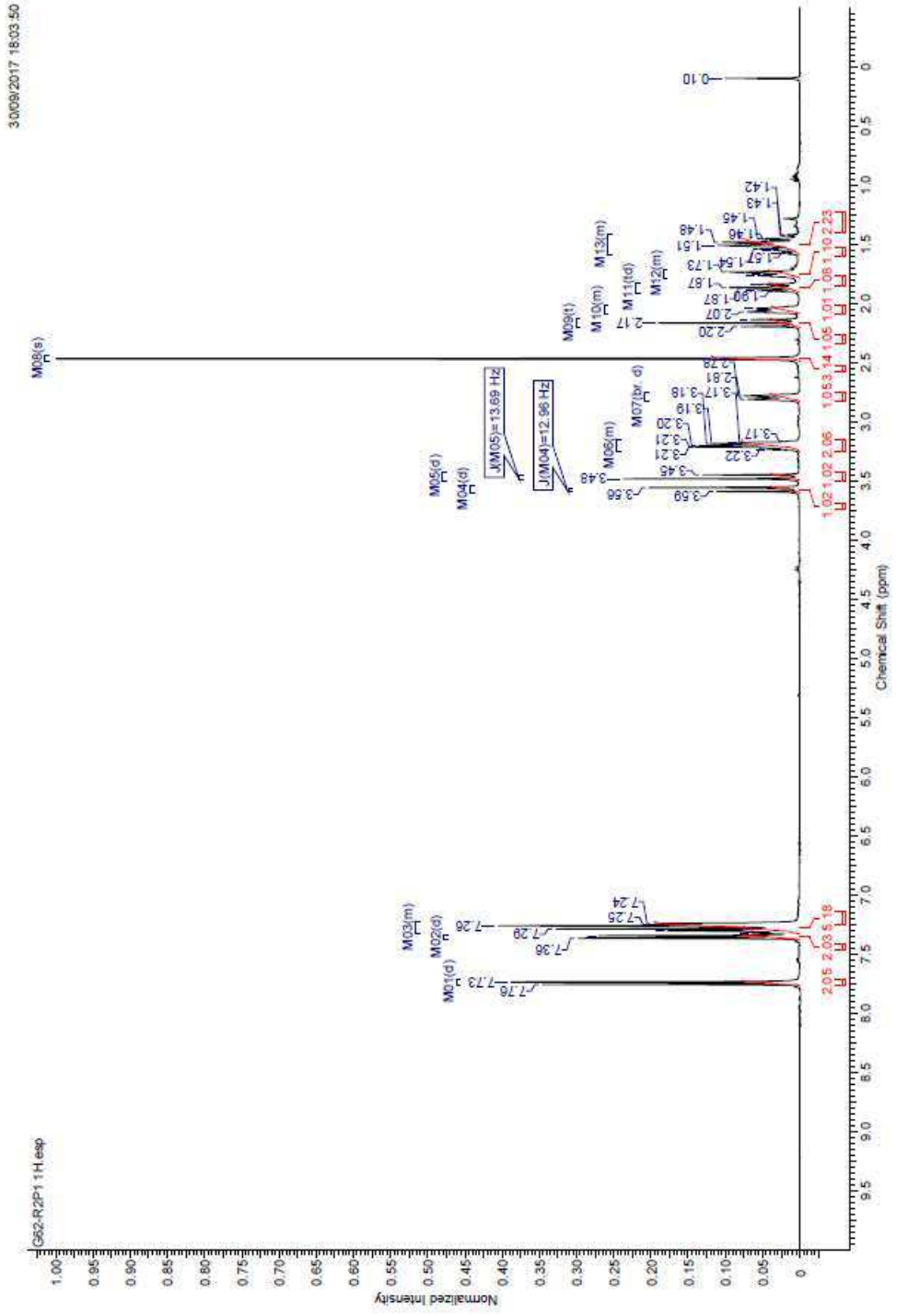

27/09/2017 11:53:08
G35-R1P1 13C.esp
J(M10)=272.16 Hz
M11(q,21)
M02(q,22)
M01(q,20)
M16(s)
M15(s)
M14(s)
M09(s)
M17(s)
M13(br. s.)
M12(s)
M07(s)
M08(s)
M03(s)
M04(s)
M06(s)
M05(s)
24.16
23.86
51.86
52.57
61.69
62.96
76.70
77.02
77.33
119.02
121.73
124.44
125.87
125.91
127.29
128.30
128.95
129.93
132.08
132.46
137.33
138.88
Normalized Intensity
Chemical Shift (ppm)

Diversification of enaminyl sulfone scaffolds

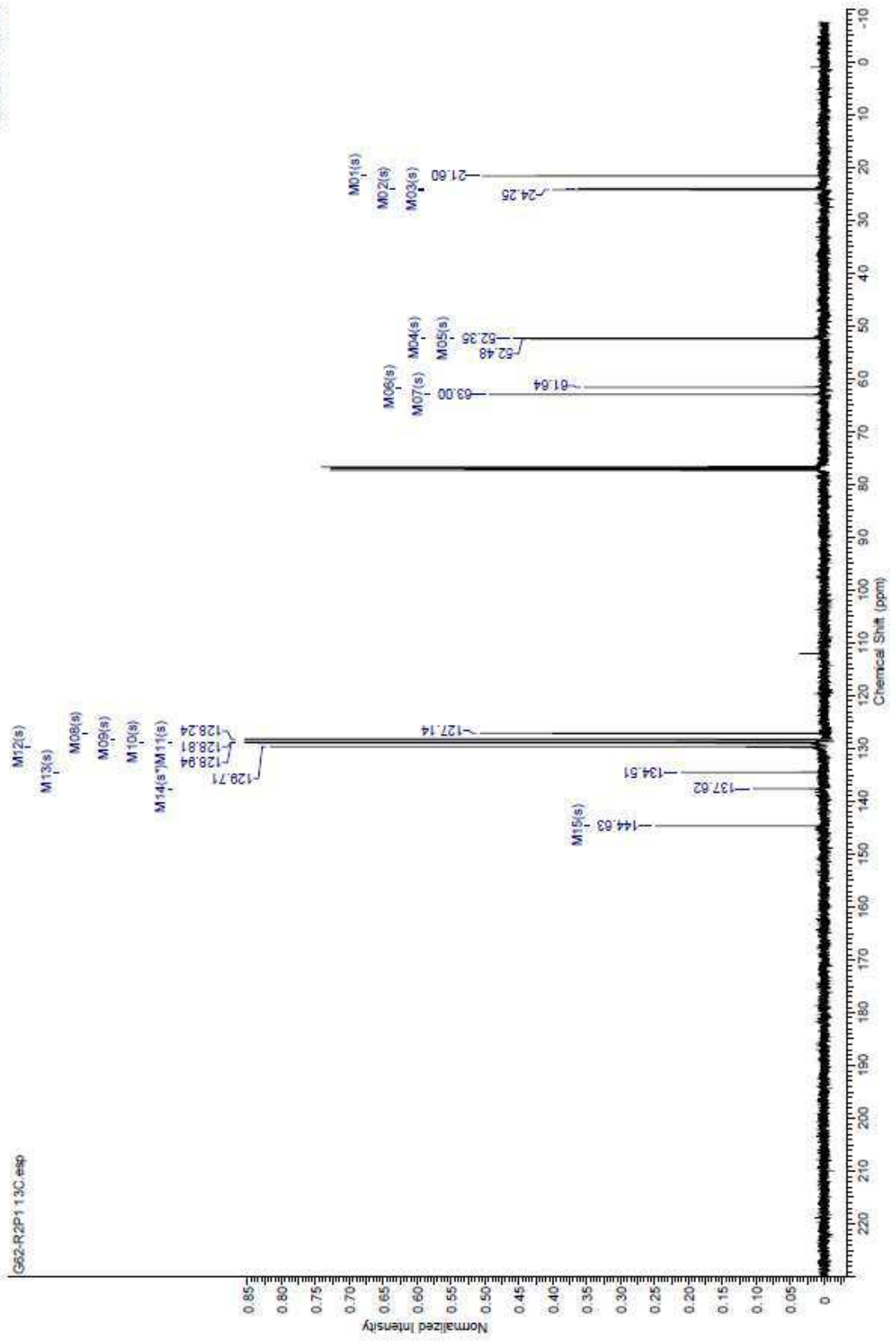


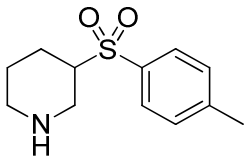
1-Benzyl-3-tosylpiperidine 6

^{1}H, $CDCl_3$



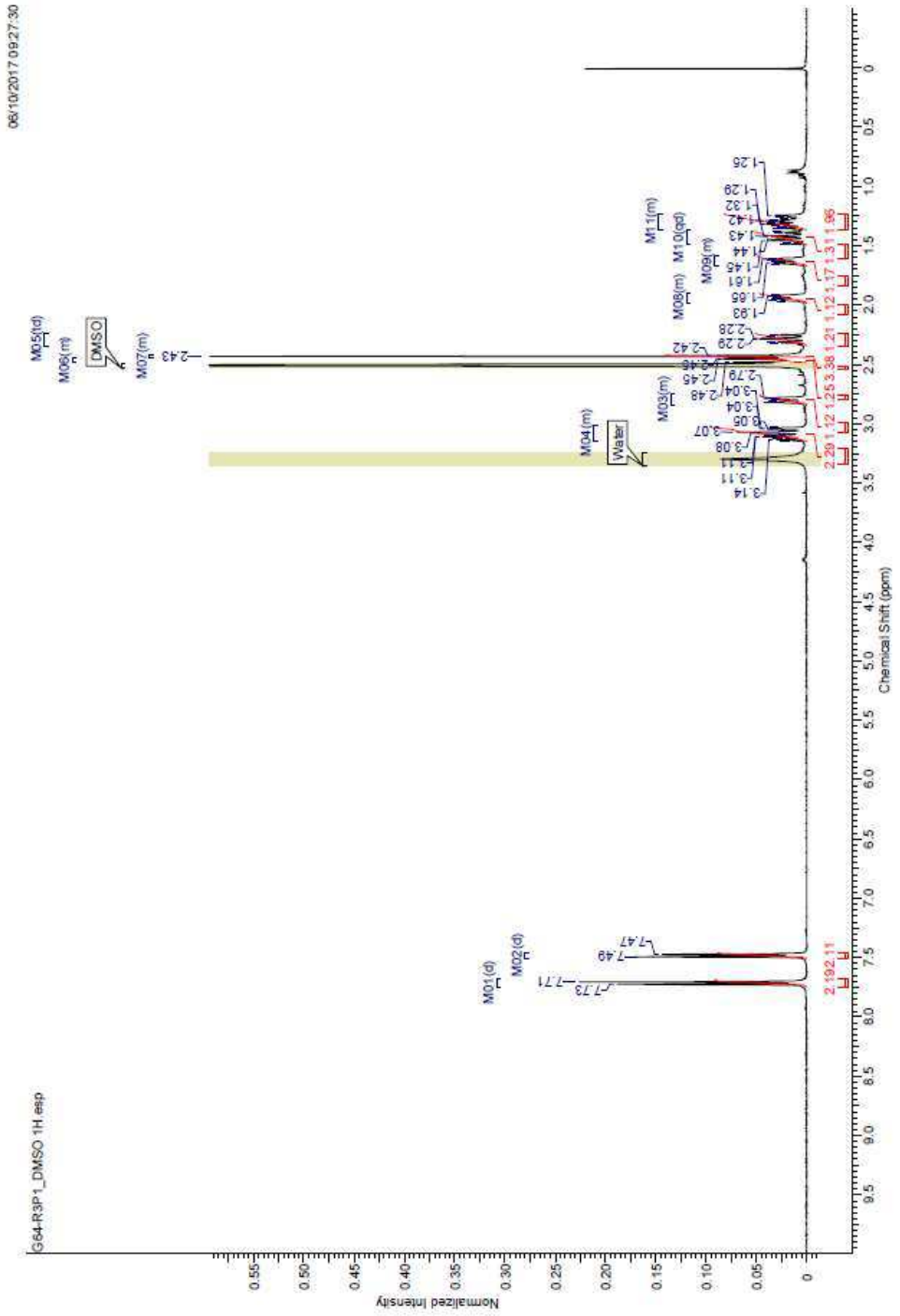
^{13}C, $CDCl_3$


30/09/2017 18:05:14
G62-R2P1 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
21.60
24.25
52.48
52.35
61.64
63.00
127.14
128.24
128.81
128.94
129.71
134.51
137.62
144.63

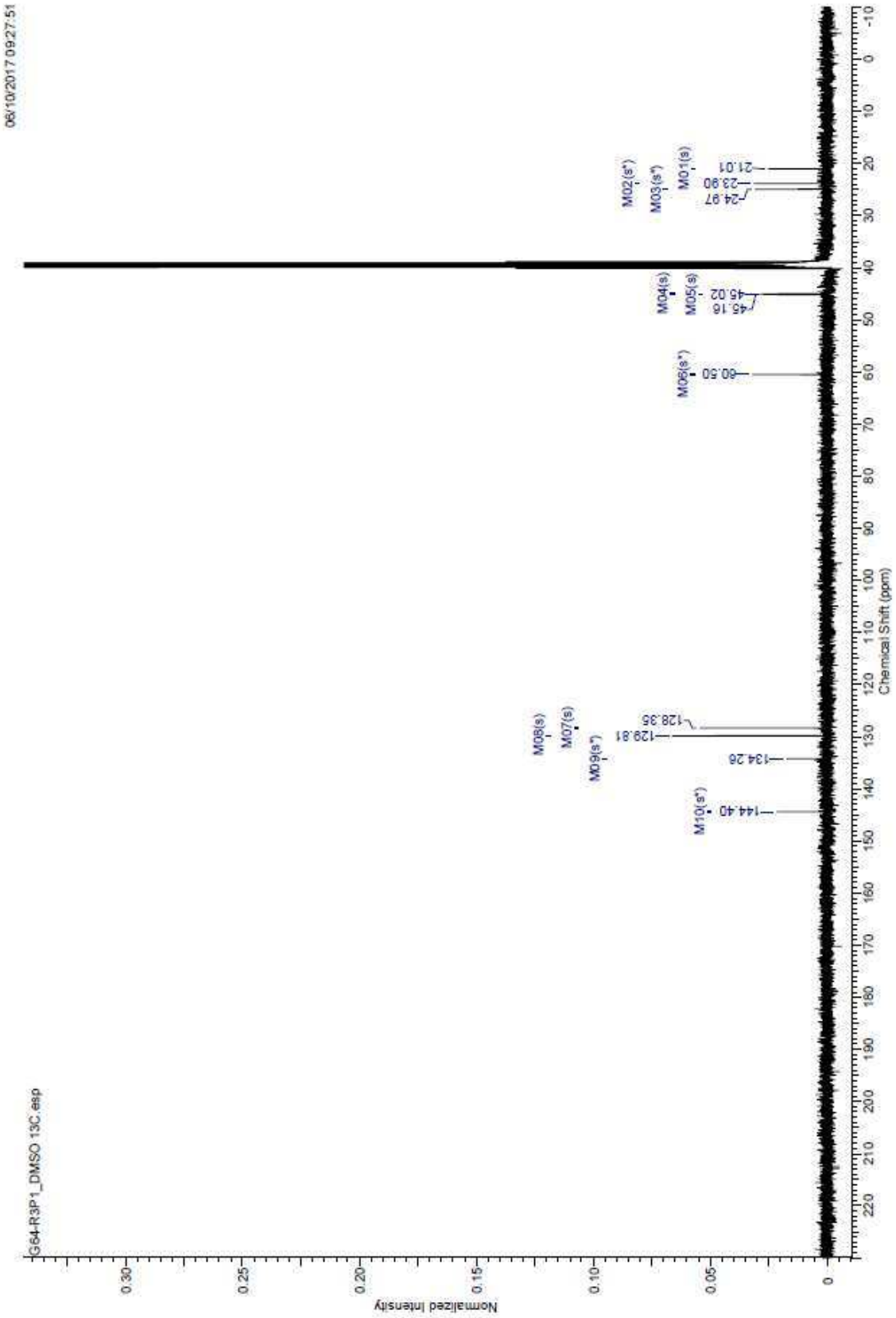


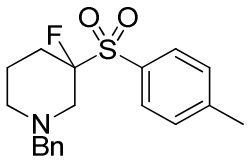
3-Tosylpiperidine 7

^{1}H, DMSO-*d*$_6$



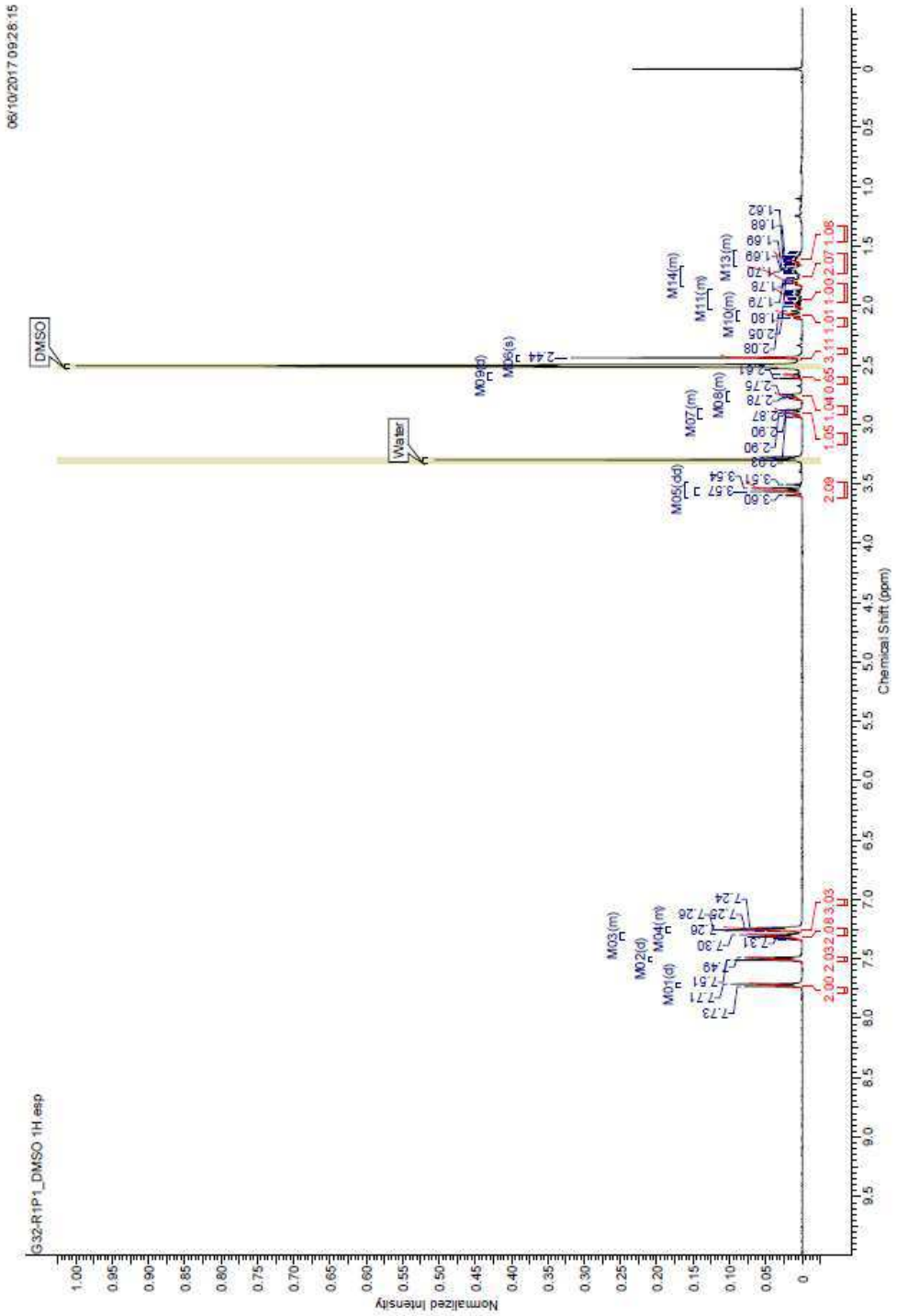
^{13}C, DMSO-d_6


06/10/2017 09:27:51
G64-R3P1_DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s*)
M03(s*)
M04(s)
M05(s)
M06(s*)
M07(s)
M08(s)
M09(s*)
M10(s*)
21.01
23.90
24.97
45.16
46.02
60.50
128.35
129.81
134.26
144.40

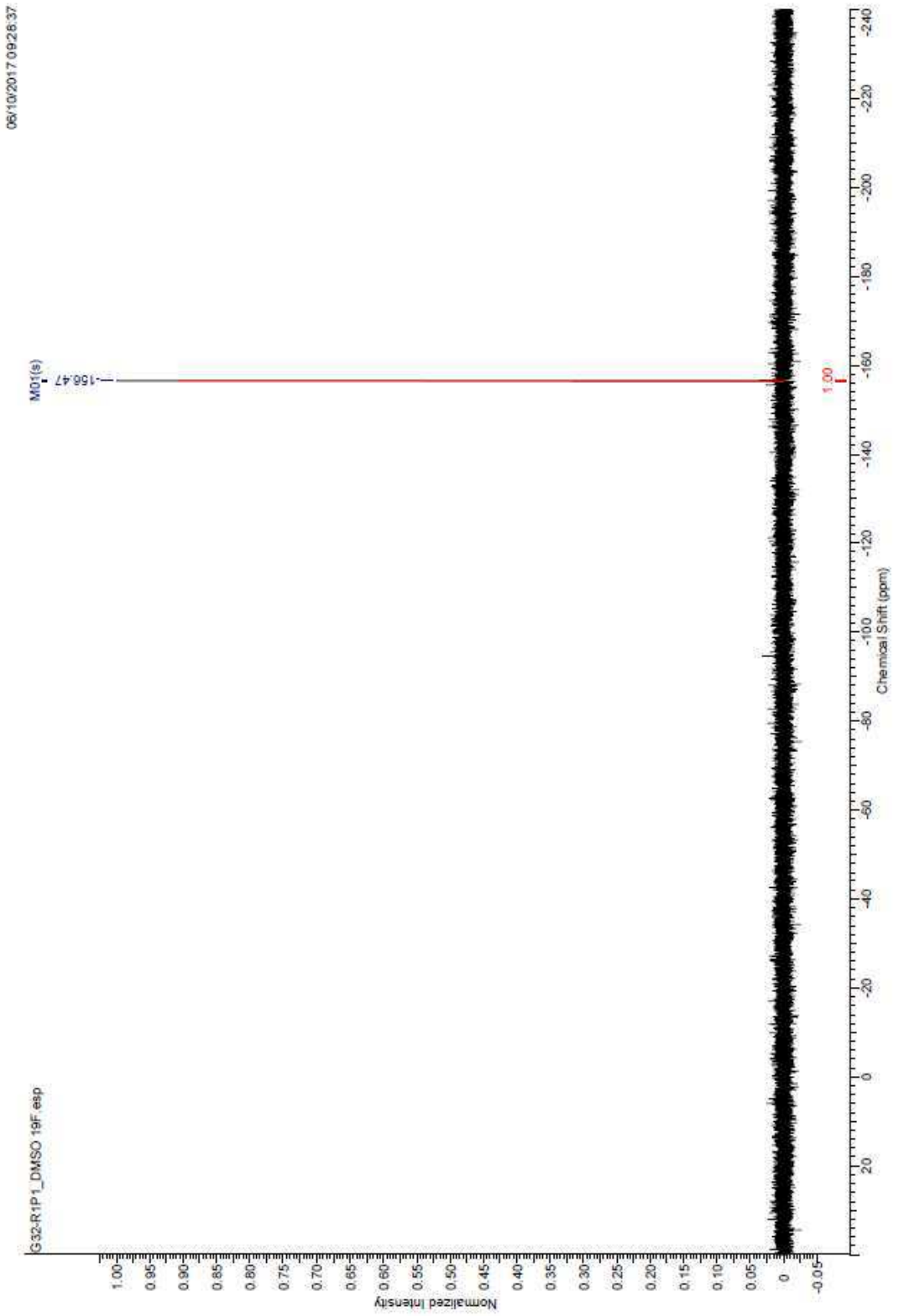


1-Benzyl-3-fluoro-3-tosylpiperidine 9

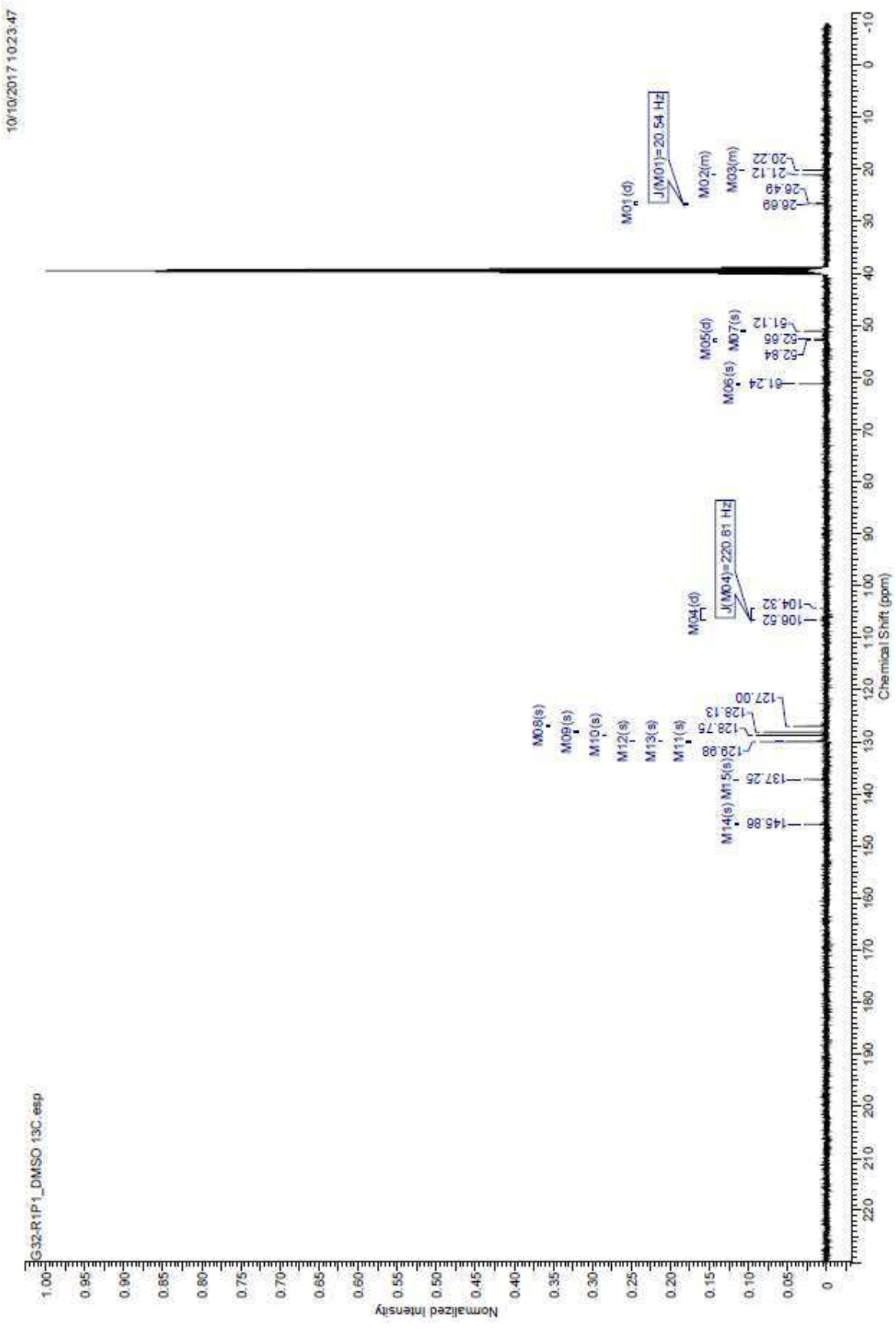
^{1}H, DMSO-*d*$_6$

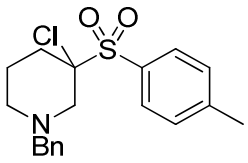


^{19}F, DMSO-d_6


06/10/2017 09:26:37
M01(s)
-156.47
1.00
G32-R1P1_DMSO 19F.esp
Normalized Intensity
Chemical Shift (ppm)

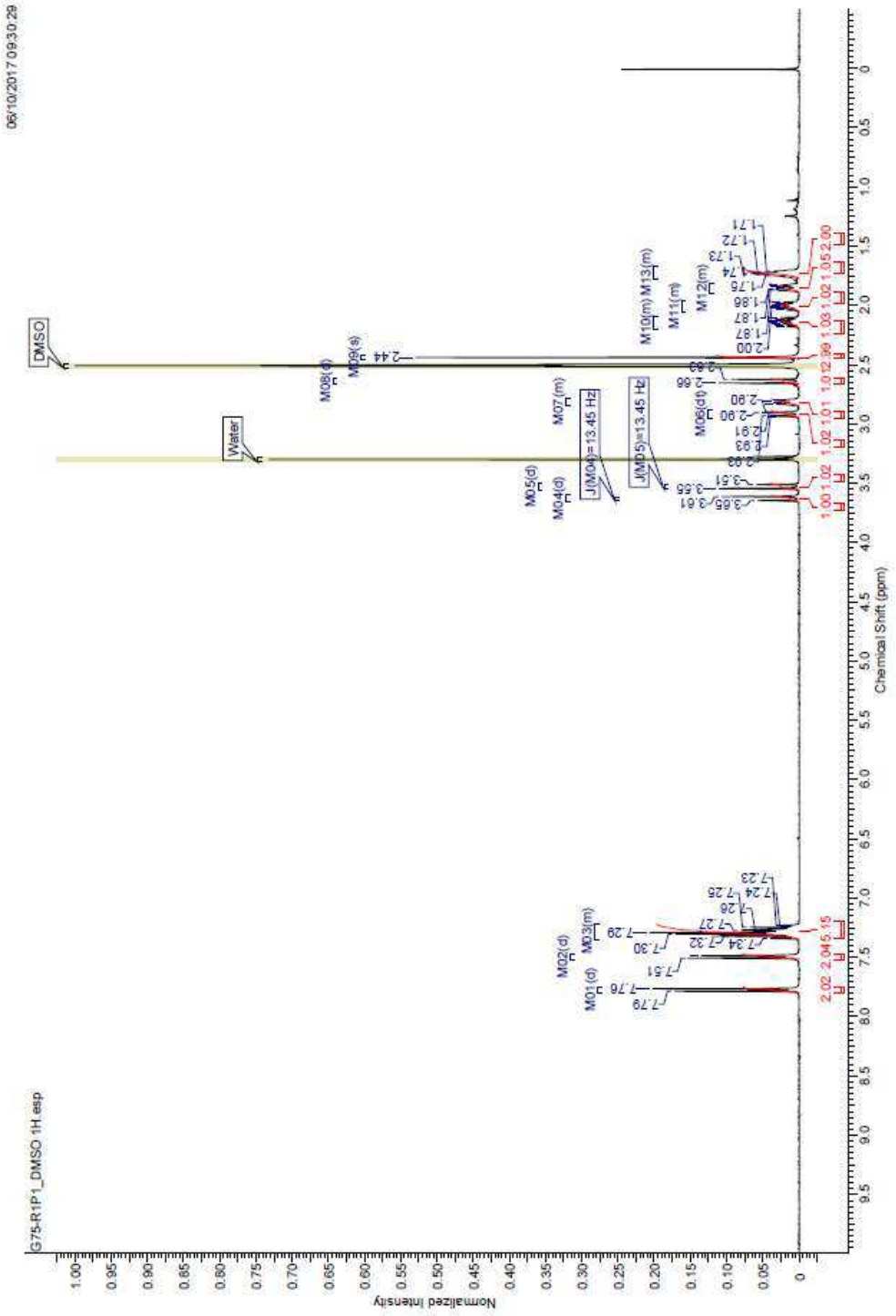
^{13}C, DMSO-d_6


10/10/2017 10:23:47
G32-R1P1_DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(d)
J(M01)=20.54 Hz
M02(m)
M03(m)
M04(d)
J(M04)=220.61 Hz
M05(d)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
26.89
26.49
21.12
20.22
61.24
62.84
62.66
61.12
104.32
106.52
127.00
128.13
128.75
128.98
137.25
145.86

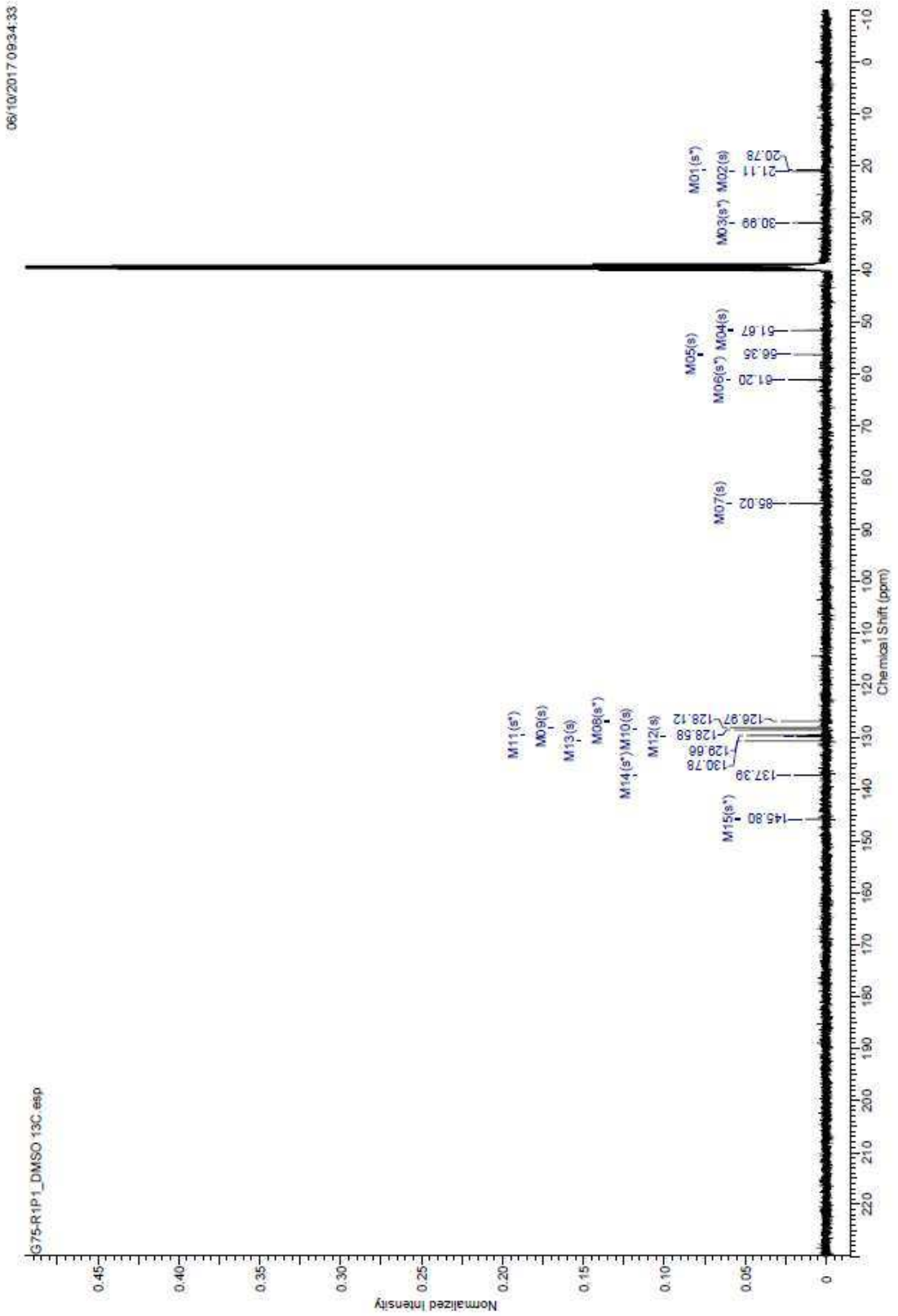


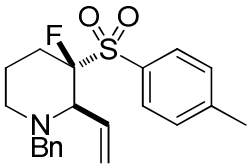
1-Benzyl-3-chloro-3-tosylpiperidine 10

^{1}H, DMSO-*d*$_6$



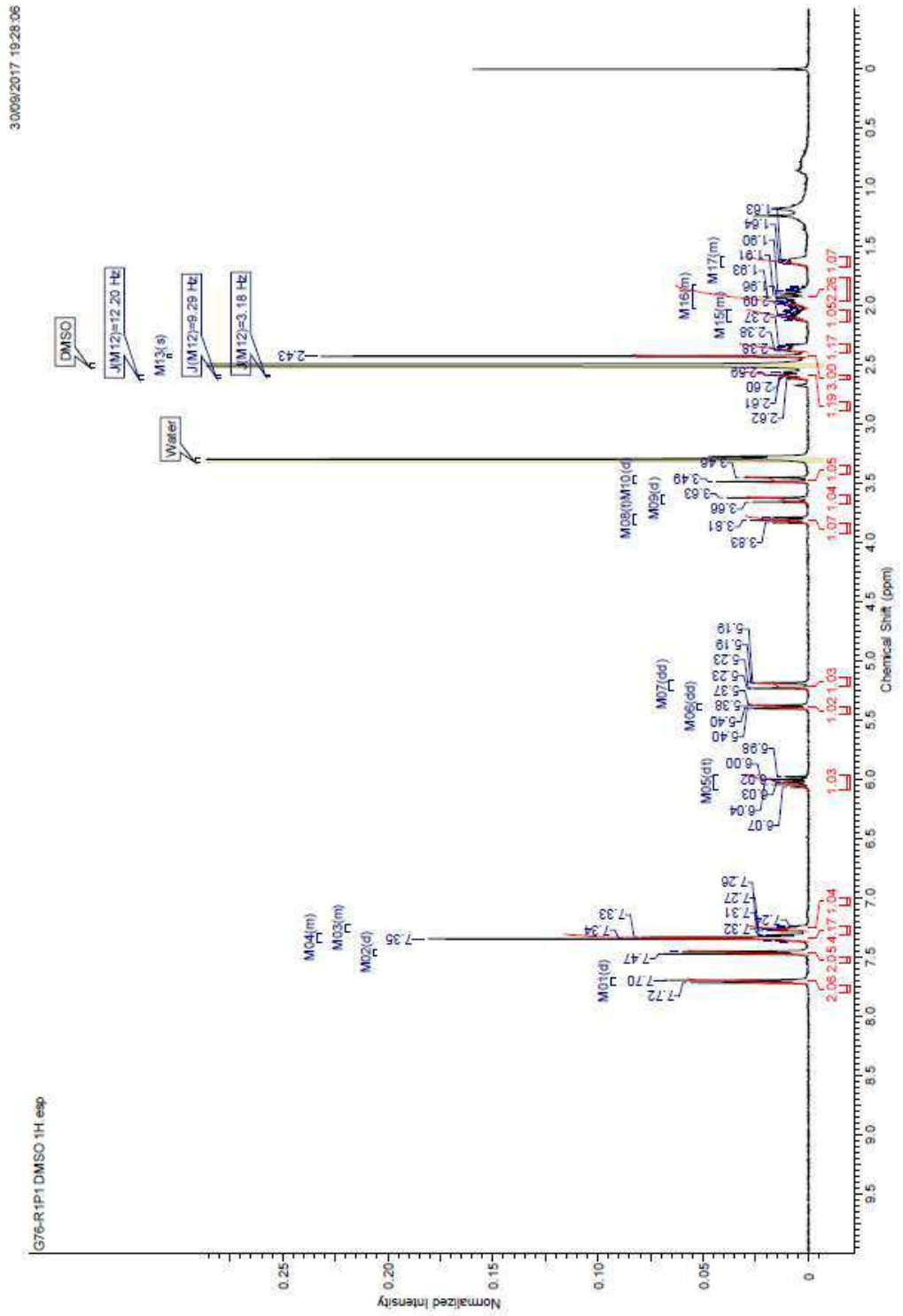
^{13}C, DMSO-d_6


06/10/2017 09:34:33
G75-R1P1_DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s*)
M02(s)
M03(s*)
M04(s)
M05(s)
M06(s*)
M07(s)
M08(s*)
M09(s)
M10(s)
M11(s*)
M12(s)
M13(s)
M14(s*)
M15(s*)
20.78
21.11
30.99
51.67
56.35
61.20
85.02
126.97
128.12
128.58
129.66
130.78
137.39
145.80

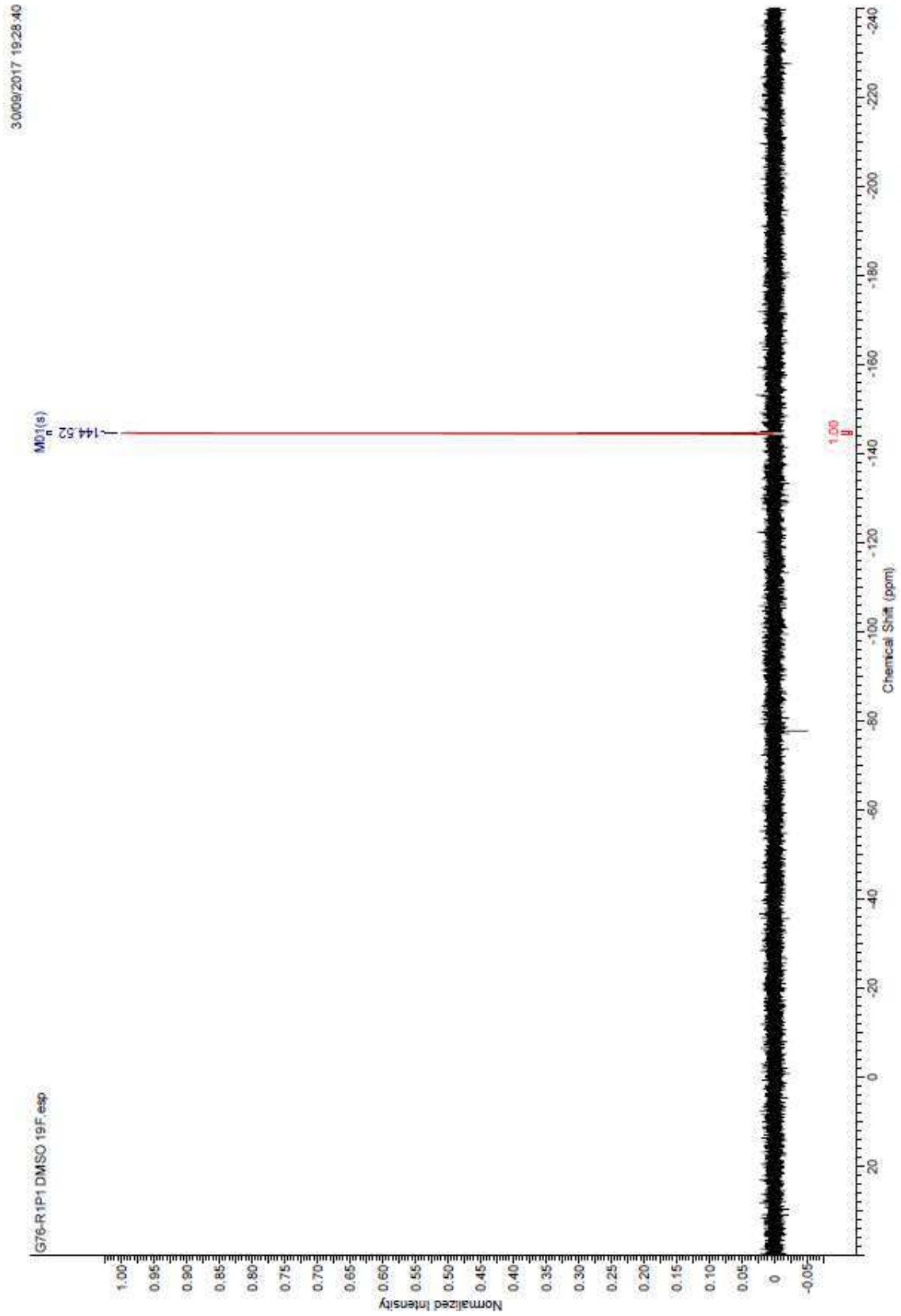


***rel*-(2*R*,3*S*)-1-Benzyl-3-fluoro-3-tosyl-2-vinylpiperidine 11a**

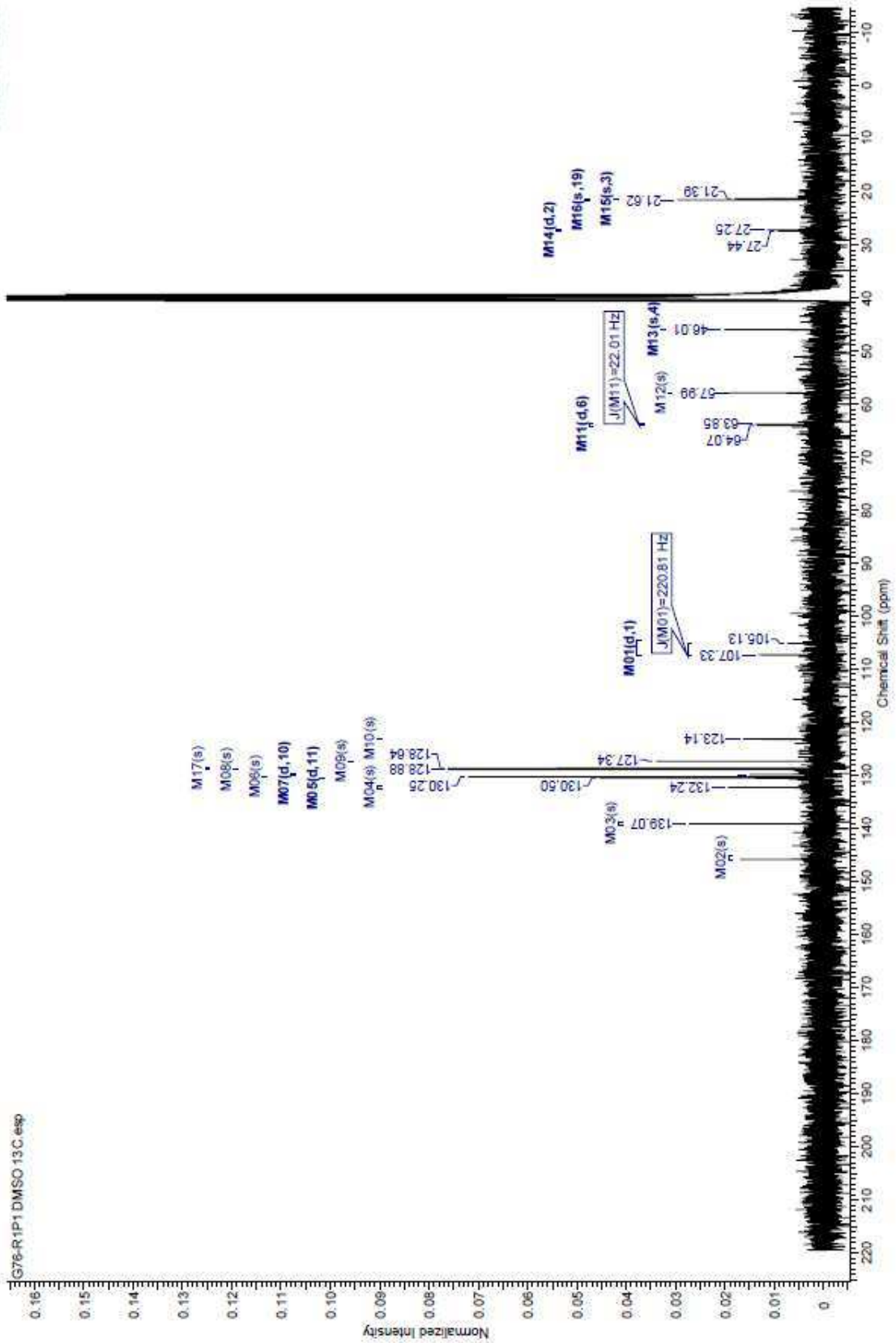
^{1}H, DMSO-d_6



^{19}F, DMSO-d_6

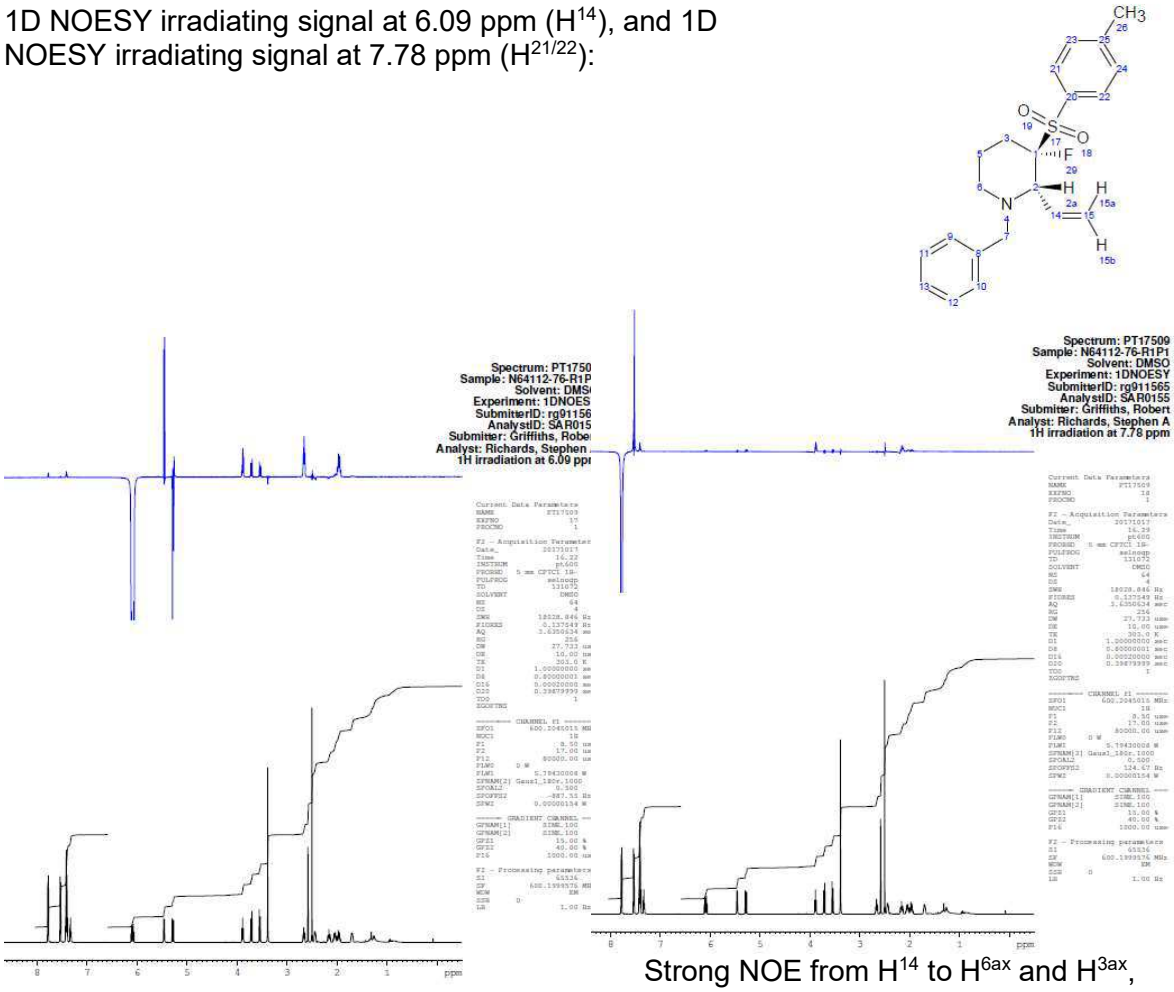

30/09/2017 19:28:40
M01(s)
144.52
1.00
G76-R1P1 DMSO 19F.esp
Normalized Intensity
Chemical Shift (ppm)

^{13}C, DMSO-d_6

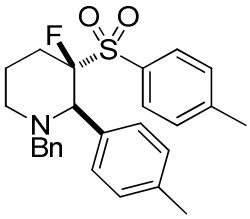

30/09/2017 19:29:00
G76-R1P1 DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M14(d,2)
M16(s,19)
M15(s,3)
21.62
21.39
27.44
27.25
M13(s,4)
46.01
M12(s)
57.99
M11(d,6)
J(M11)=22.01 Hz
63.85
64.07
M01(d,1)
J(M01)=220.81 Hz
105.13
107.33
123.14
127.34
128.64
128.88
130.25
130.50
132.24
139.07
M03(s)
M02(s)
M17(s)
M08(s)
M06(s)
M07(d,10)
M05(d,11)
M09(s)
M04(s) M10(s)

1D NOESY

1D NOESY irradiating signal at 6.09 ppm (H^{14}), and 1D NOESY irradiating signal at 7.78 ppm ($H^{21/22}$):

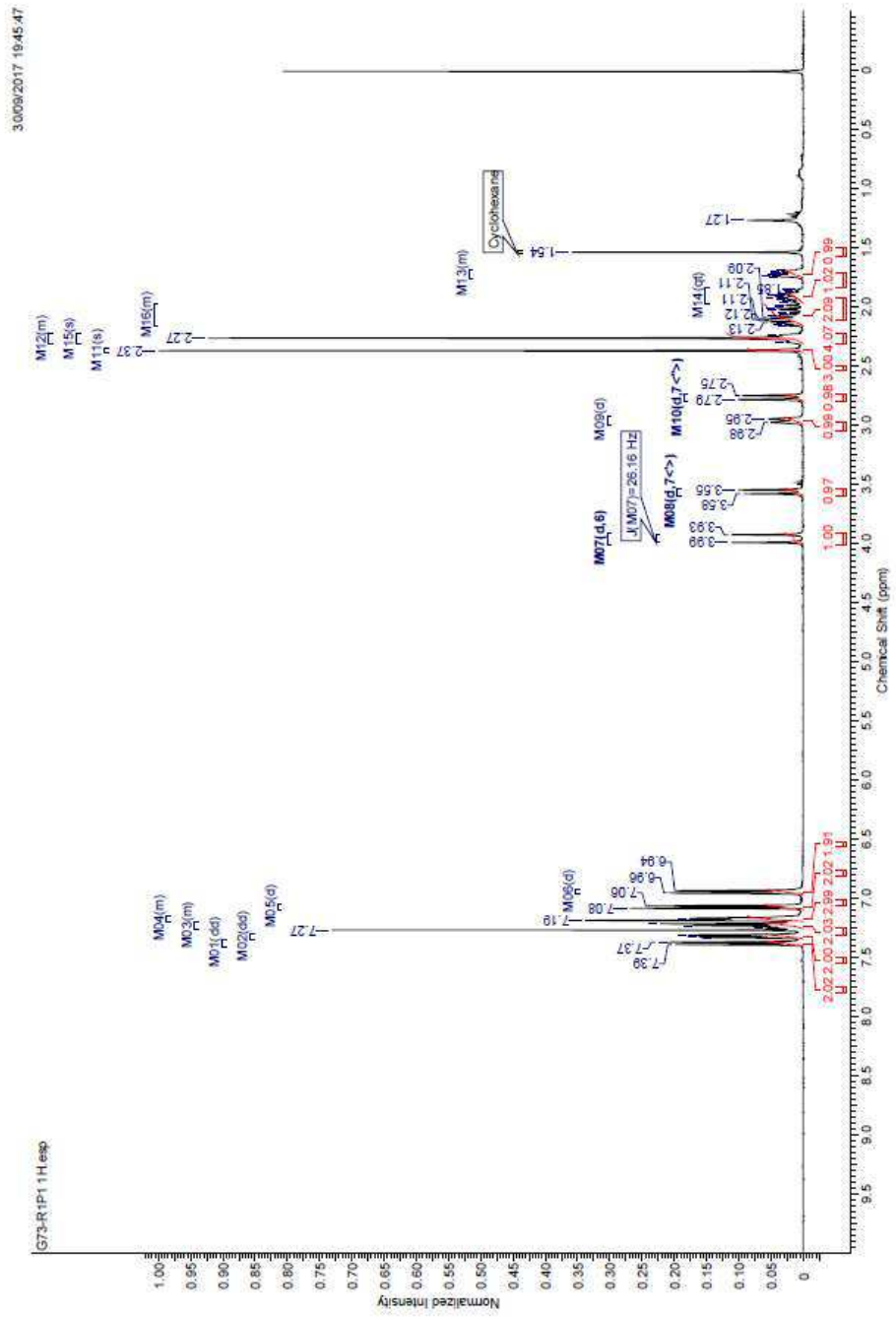


Strong NOE from H^{14} to H^{6ax} and H^{3ax}, suggesting vinyl group is axial. Also strong NOE from aryl protons $H^{21/22}$ to H^{5ax} and H^{3eq}, suggesting tosyl group is also axial. The size of F coupling to H^2 (8.7 Hz) and to H^3 (approximately 14 Hz to both) agrees with these NOEs. This reflects the dihedral angle between the fluorine atom and these protons. Note that a 180° angle would give rise to a much larger coupling (25-35 Hz).

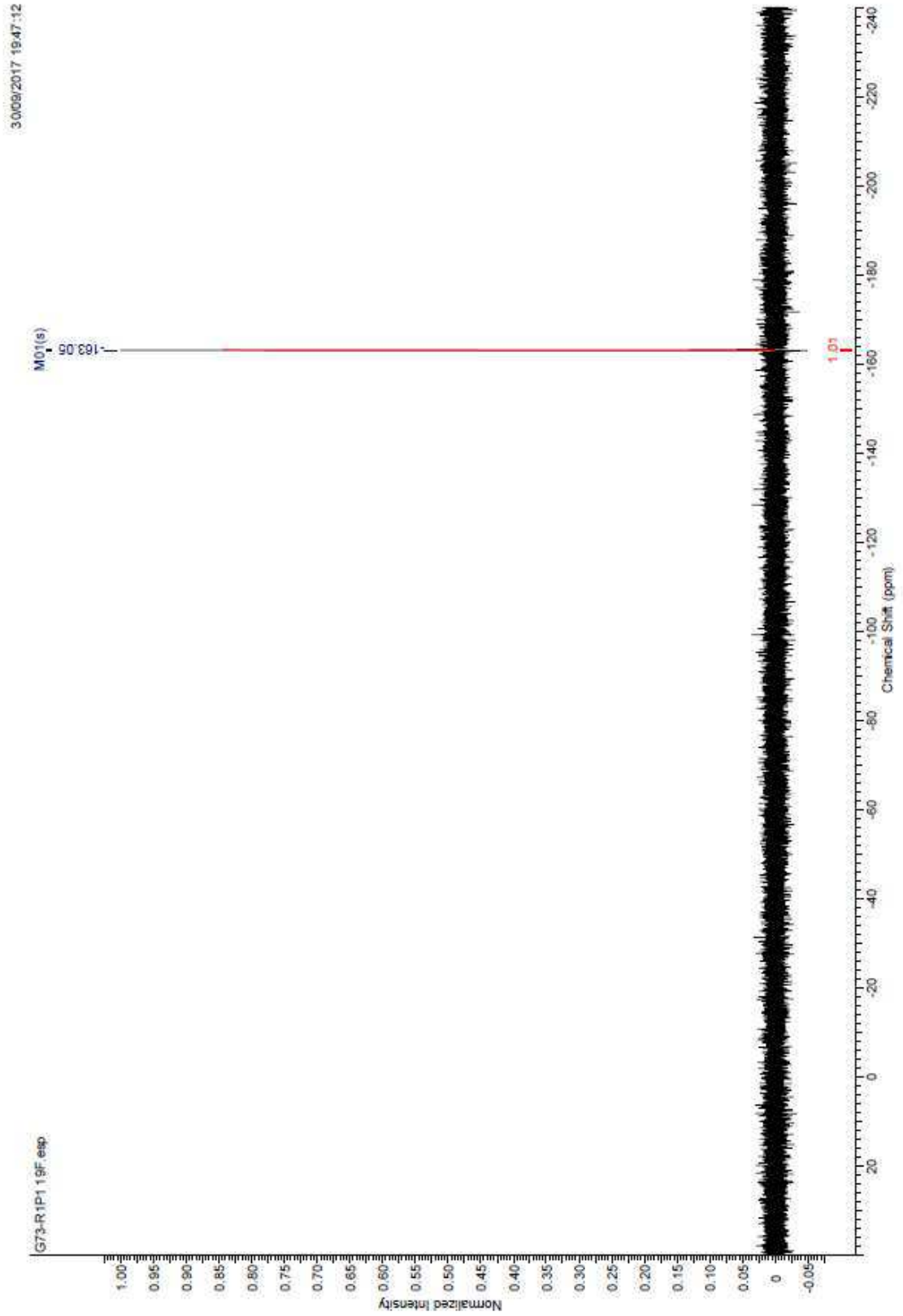


***rel*-(2*R*,3*S*)-1-Benzyl-3-fluoro-2-(*p*-tolyl)-3-tosylpiperidine 11b**

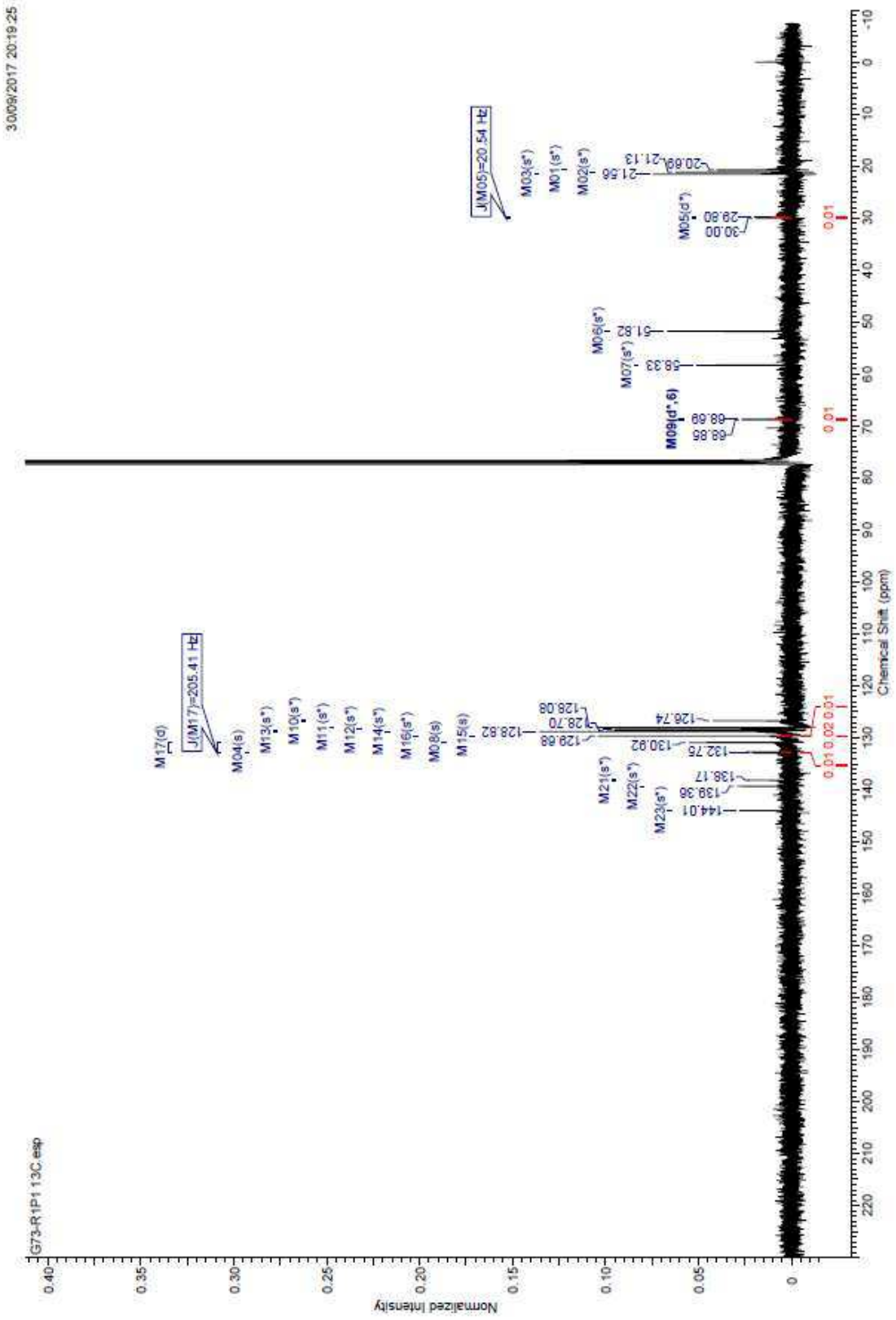
^{1}H, $CDCl_3$

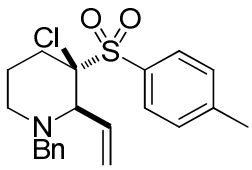


^{19}F, $CDCl_3$


30/09/2017 19:47:12
M01(s)
-163.06
1.01
G73-R1P1 19F esp
Normalized Intensity
Chemical Shift (ppm)

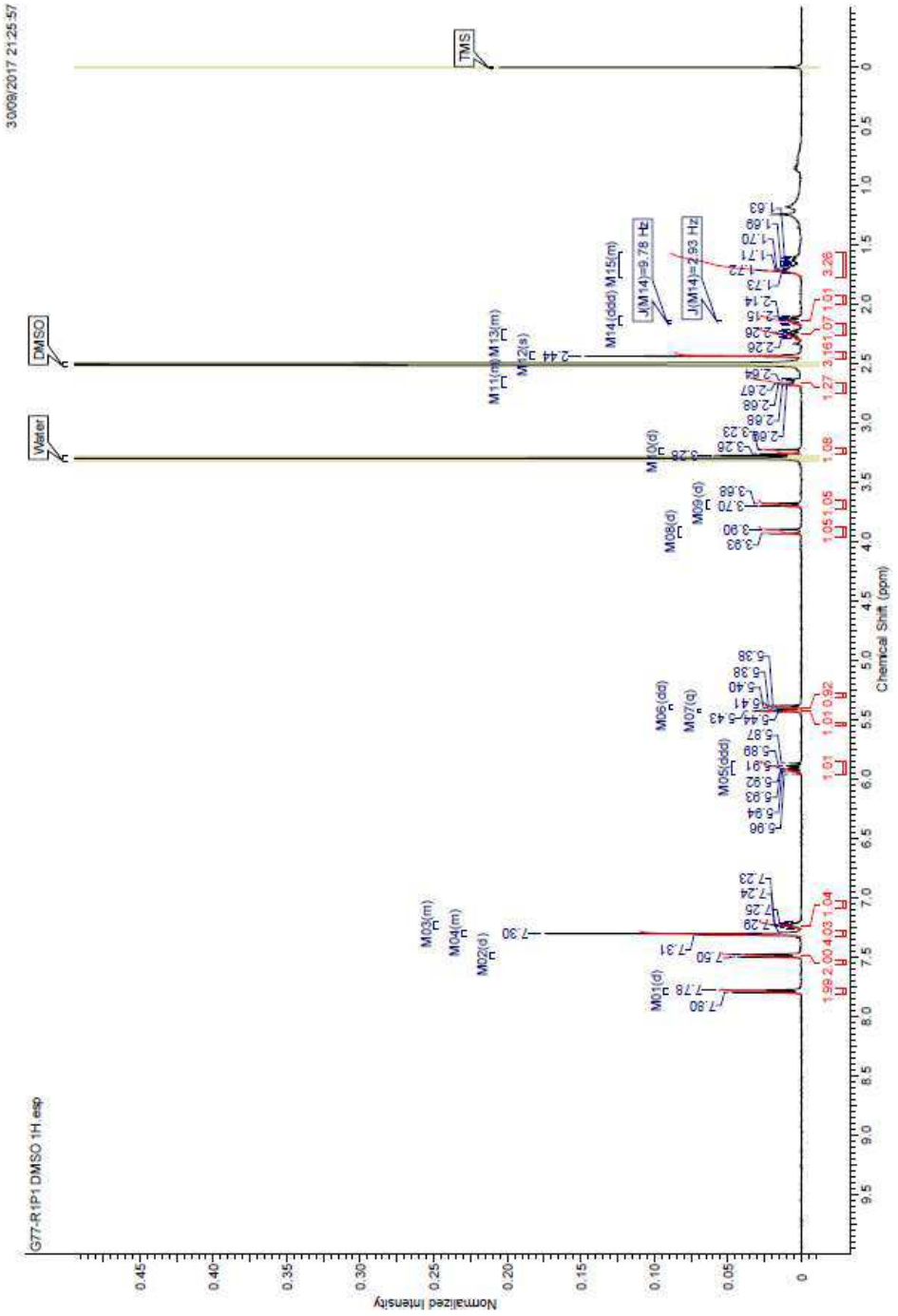
^{13}C, $CDCl_3$


30/09/2017 20:19:25
G73-R1P1 13C.esp
J(M17)=205.41 Hz
J(M05)=20.54 Hz
M17(d)
M04(s)
M13(s*)
M10(s*)
M11(s*)
M12(s*)
M14(s*)
M16(s*)
M08(s)
M15(s)
M21(s*)
M22(s*)
M23(s*)
M03(s*)
M01(s*)
M02(s*)
M05(d*)
M06(s*)
M07(s*)
M09(d*,6)
128.82
128.68
128.70
128.08
126.74
132.76
130.92
138.17
139.36
144.01
68.86
68.69
58.33
51.82
30.00
29.80
21.66
21.13
20.89
0.01
0.01
0.01 0.02 0.01
Normalized Intensity
Chemical Shift (ppm)

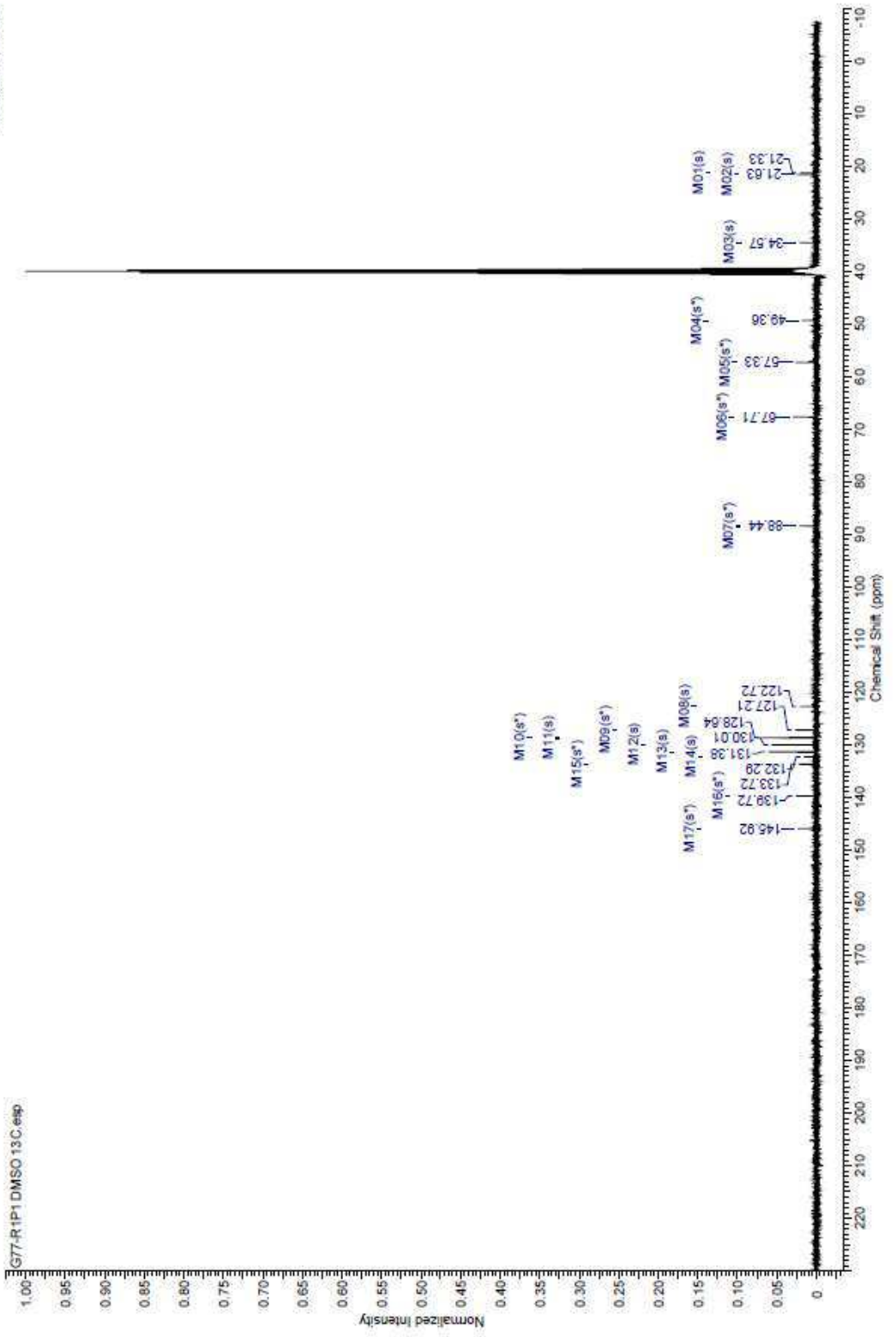


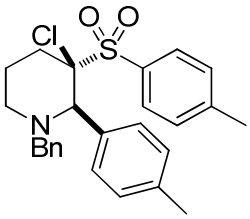
***rel*-(2*R*,3*R*)-1-Benzyl-3-chloro-3-tosyl-2-vinylpiperidine 11c**

^{1}H, DMSO-d_6



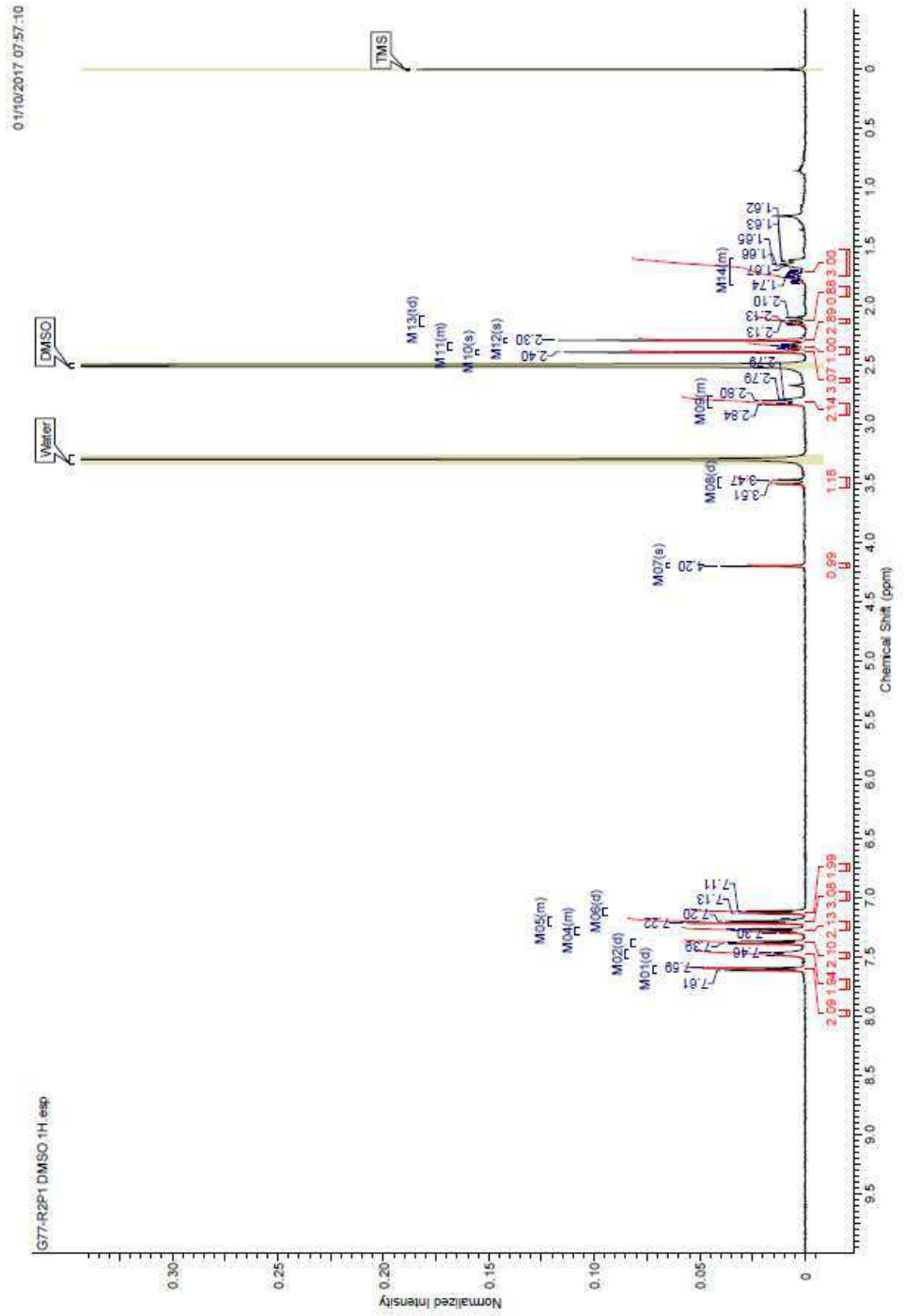
^{13}C, DMSO-d_6


30/09/2017 21:26:30
G77-R1P1 DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s*)
M05(s*)
M06(s*)
M07(s*)
M08(s)
M09(s*)
M10(s*)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s*)
M16(s*)
M17(s*)
21.33
21.63
34.57
49.36
67.33
67.71
88.44
122.72
127.21
128.64
130.01
131.38
132.29
133.72
139.72
145.82

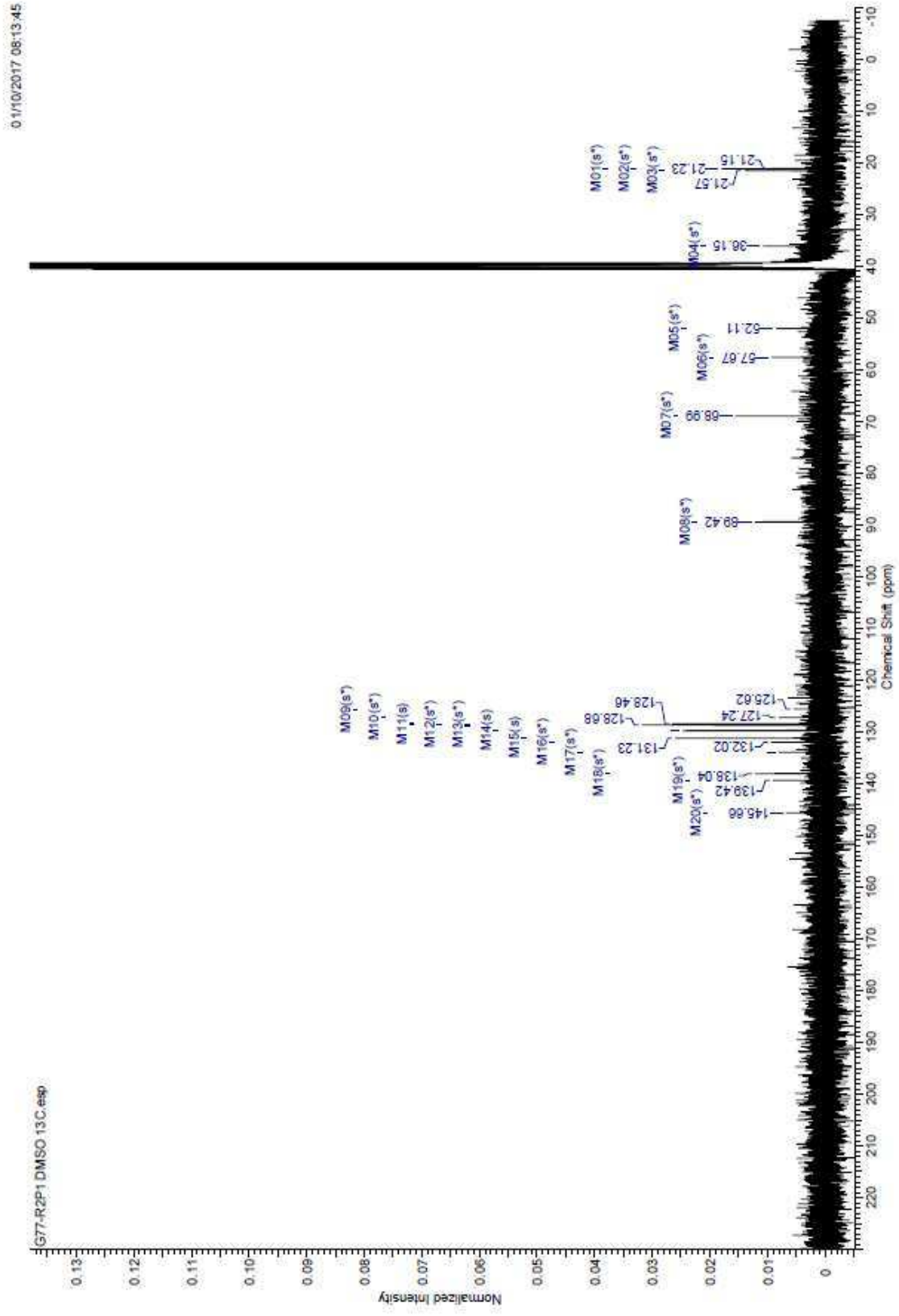


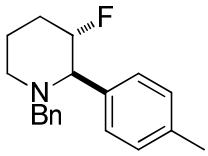
***rel*-(2*R*,3*R*)-1-Benzyl-3-chloro-2-(*p*-tolyl)-3-tosylpiperidine 11d**

^{1}H, DMSO-d_6



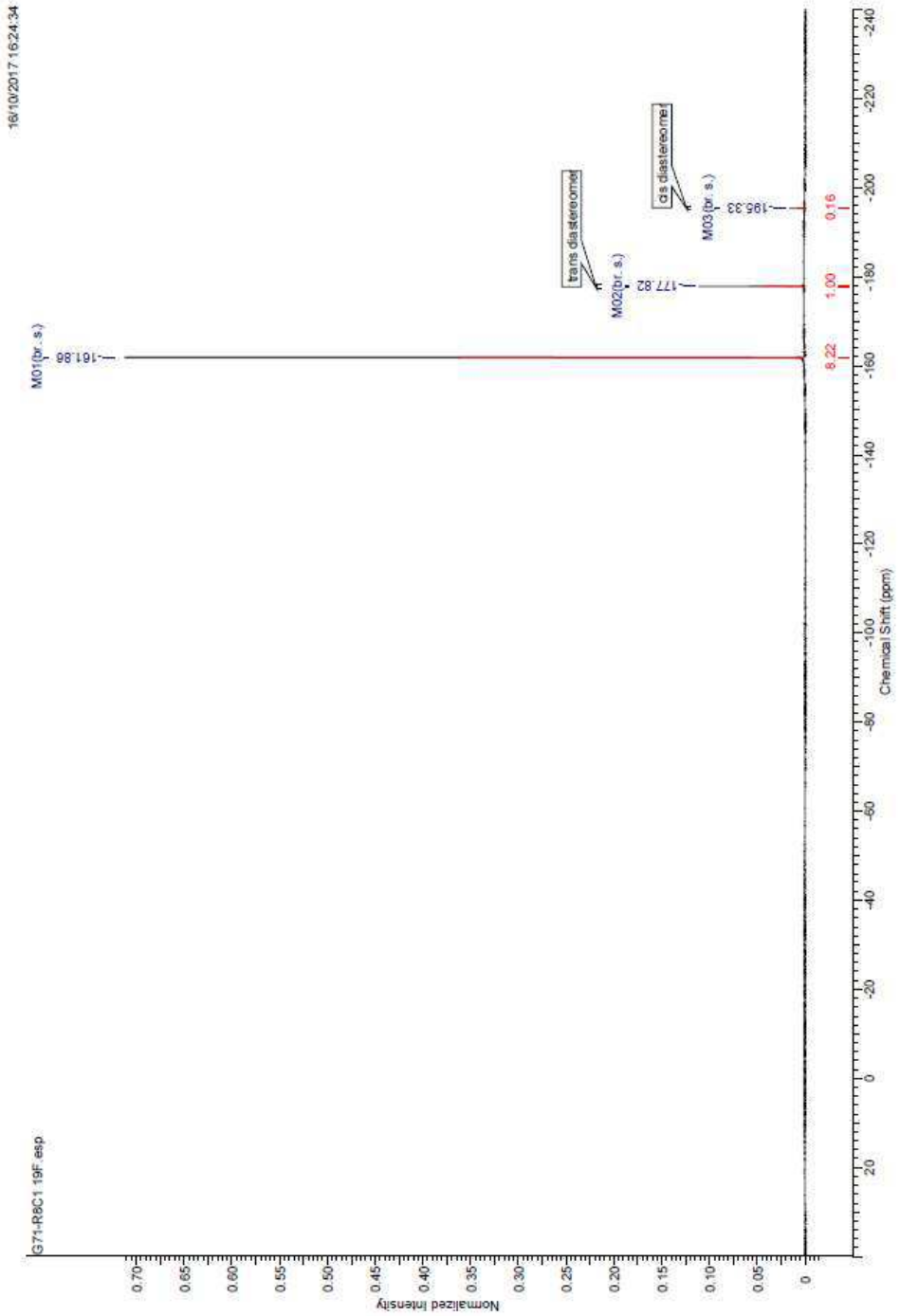
^{13}C, DMSO-d_6


01/10/2017 08:13:45
G77-R2P1 DMSO 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s*)
M02(s*)
M03(s*)
M04(s*)
M05(s*)
M06(s*)
M07(s*)
M08(s*)
M09(s*)
M10(s*)
M11(s)
M12(s*)
M13(s*)
M14(s)
M15(s)
M16(s*)
M17(s*)
M18(s*)
M19(s*)
M20(s*)
21.15
21.23
21.57
39.15
52.11
57.67
68.99
89.42
125.62
127.24
128.46
128.68
131.23
132.02
138.04
138.42
145.66

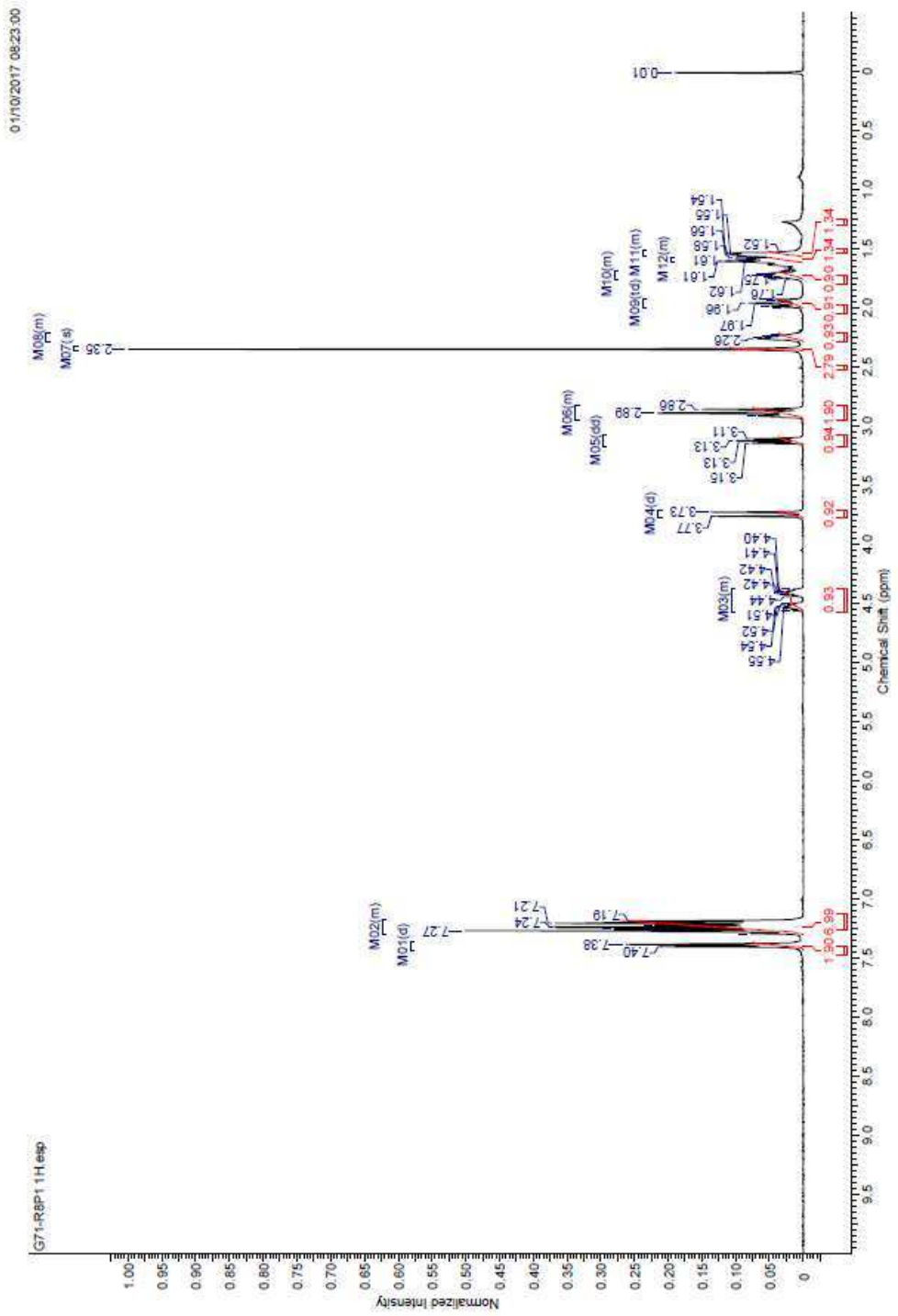


***trans*-1-Benzyl-3-fluoro-2-(*p*-tolyl)piperidine 13**

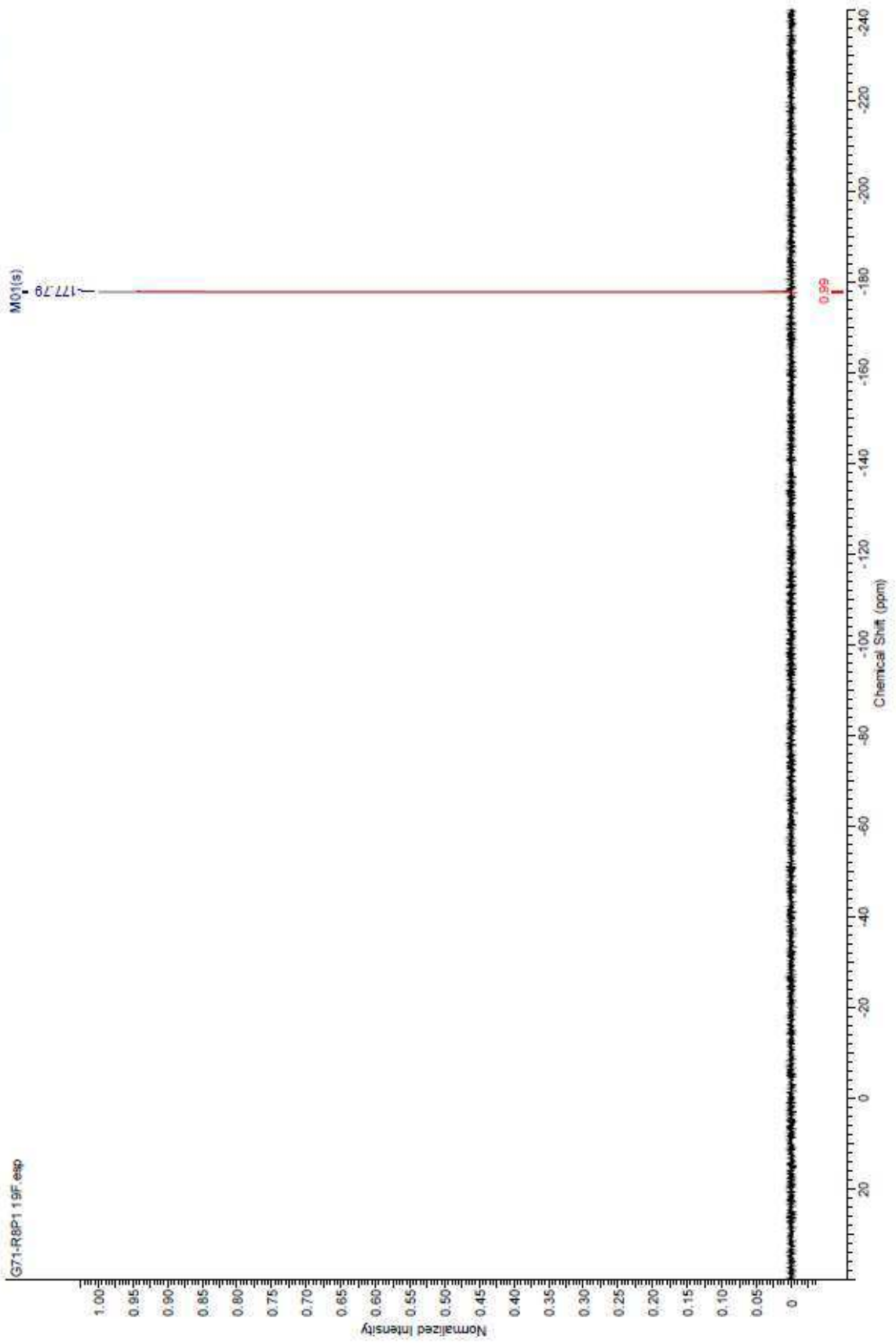
^{19}F NMR of crude material, $CDCl_3$



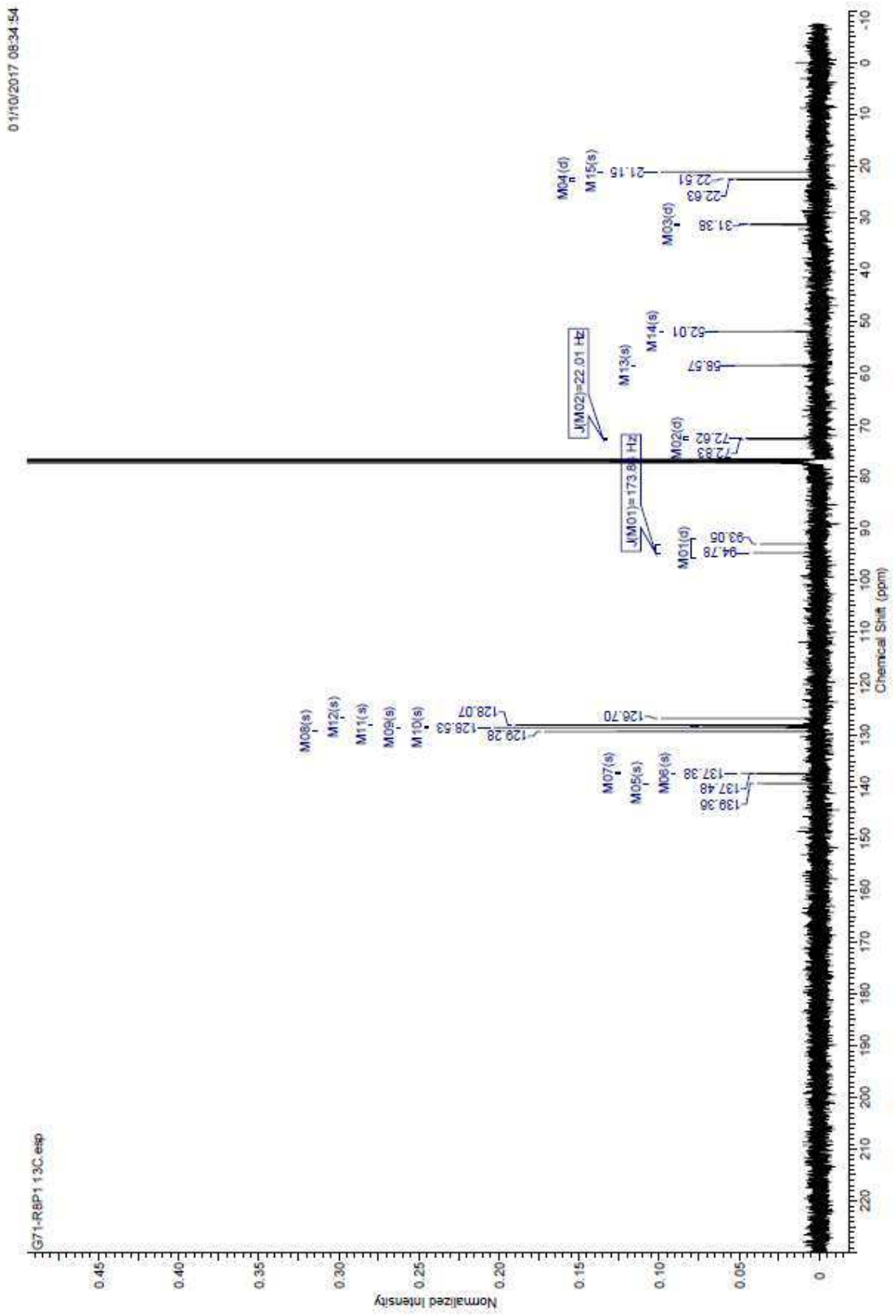
^1H, $CDCl_3$

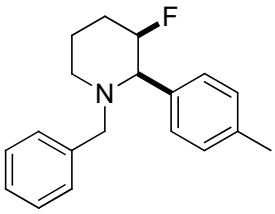

01/10/2017 08:23:00
G71-RBP1 1H.esp
Chemical Shift (ppm)
Normalized Intensity

^{19}F, $CDCl_3$


01/10/2017 08:23:17
M01(s)
-177.79
0.99
G71-R8P1 19F esp
Normalized Intensity
Chemical Shift (ppm)

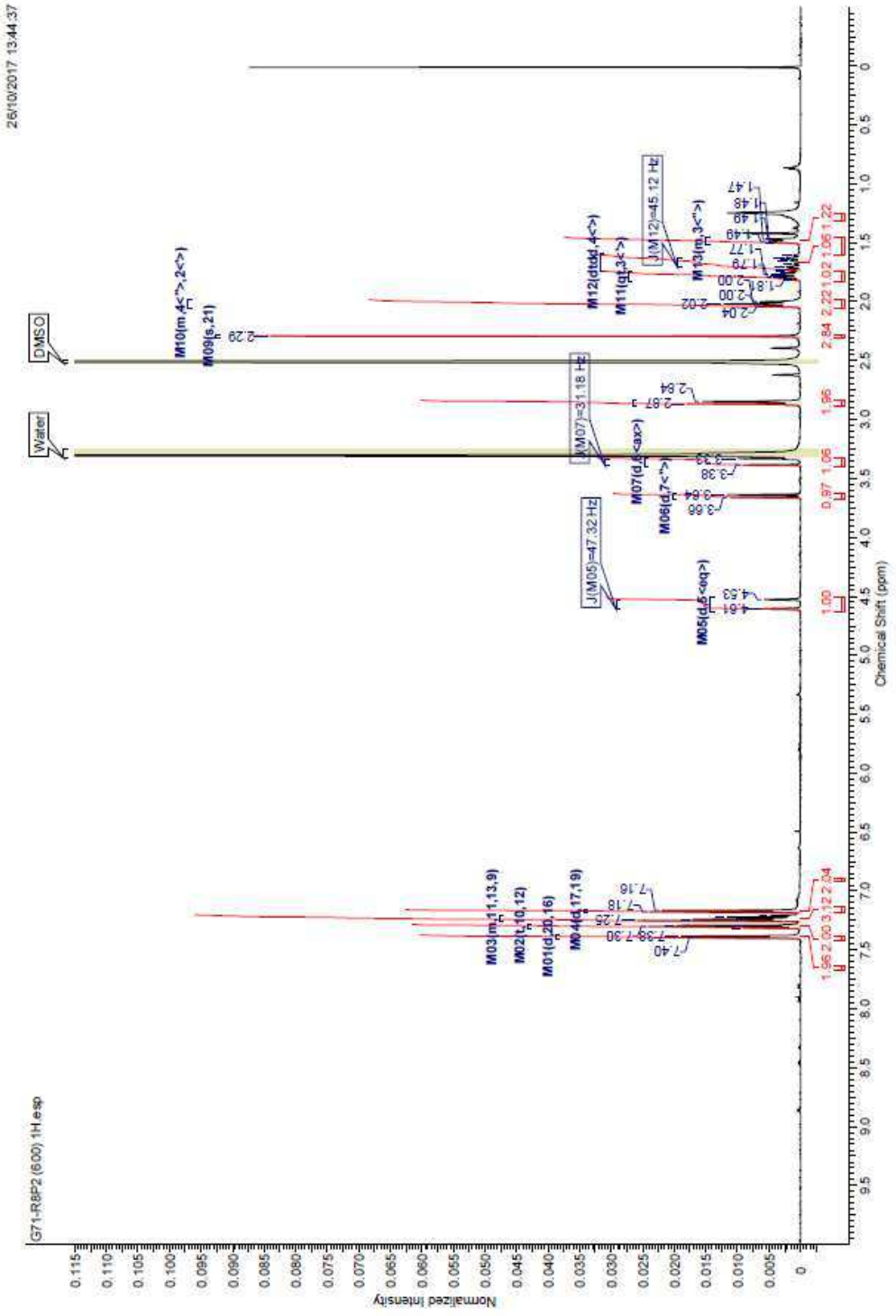
^{13}C, $CDCl_3$


01/10/2017 08:34:54
G71-R8P1 13C.esp
Normalized Intensity
Chemical Shift (ppm)
J(M01)=173.8 Hz
J(M02)=22.01 Hz
M01(d)
M02(d)
M03(d)
M04(d)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
94.78
93.05
72.83
72.62
62.01
58.57
31.38
22.63
22.51
21.15
139.36
137.48
137.38
129.28
128.53
128.07
126.70

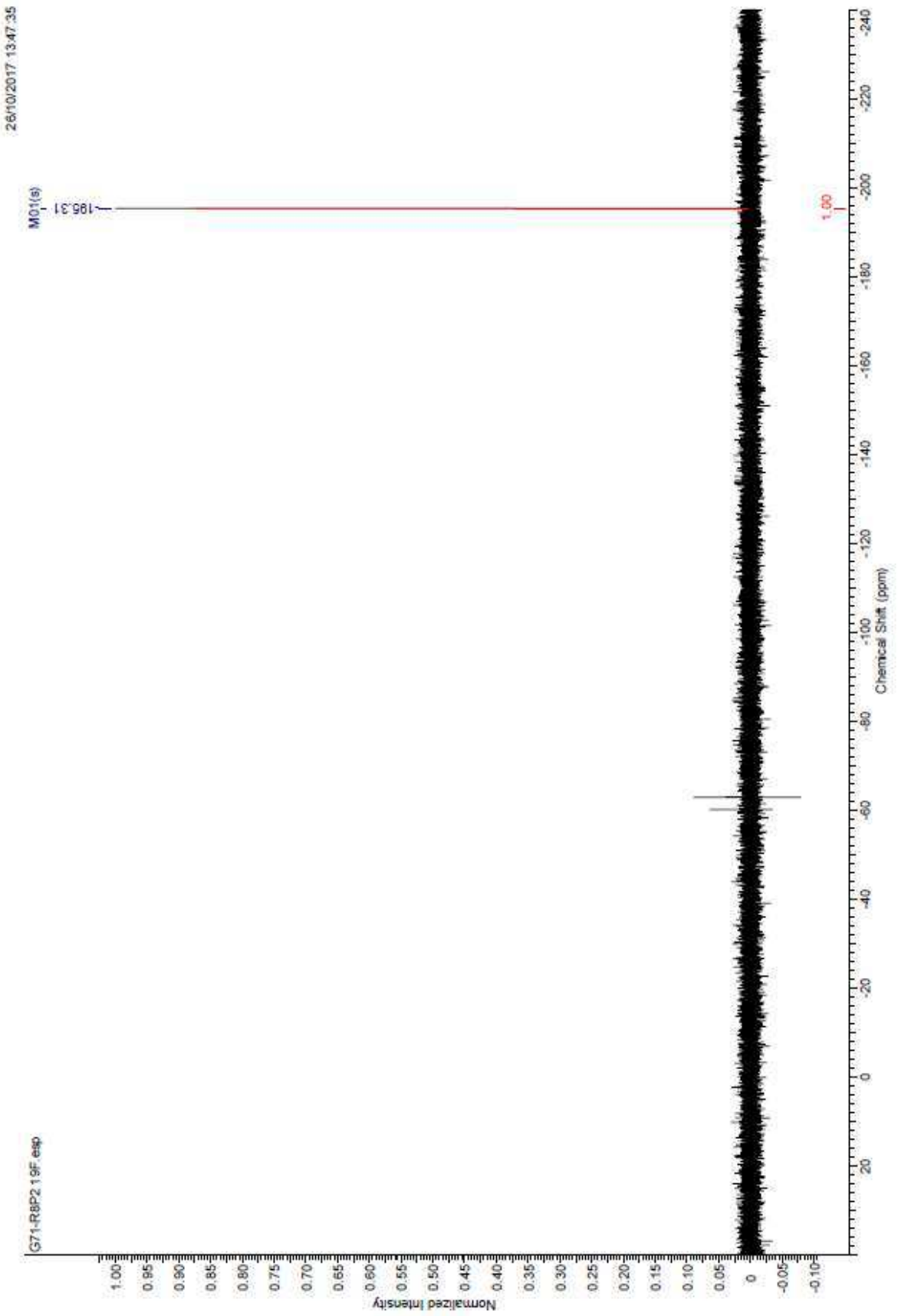


***cis*-1-Benzyl-3-fluoro-2-(*p*-tolyl)piperidine 13b**

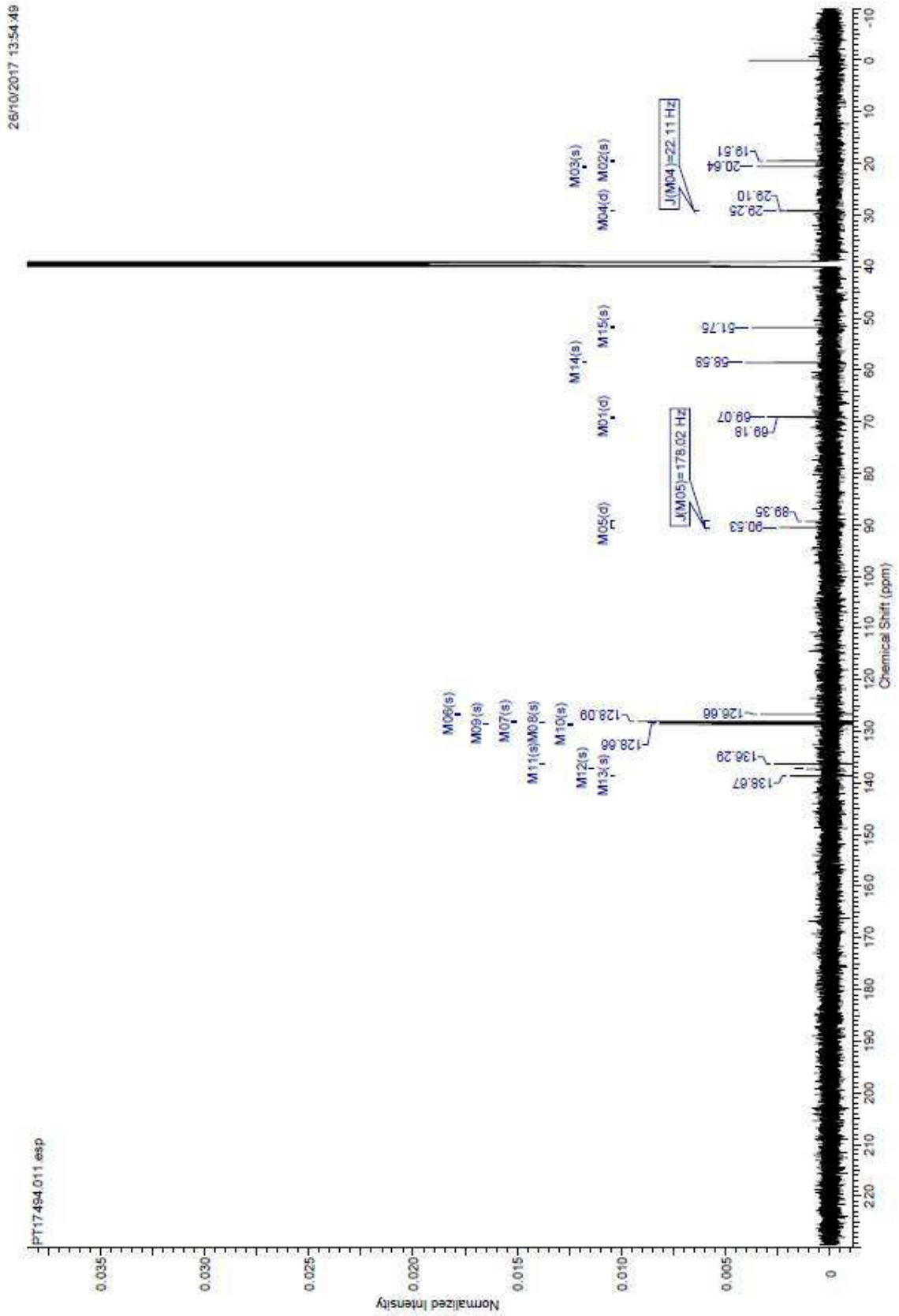
^{1}H NMR, DMSO-d_6

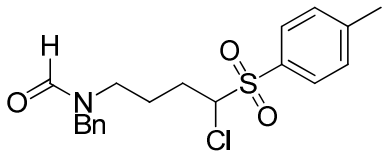


^{19}F NMR, $CDCl_3$



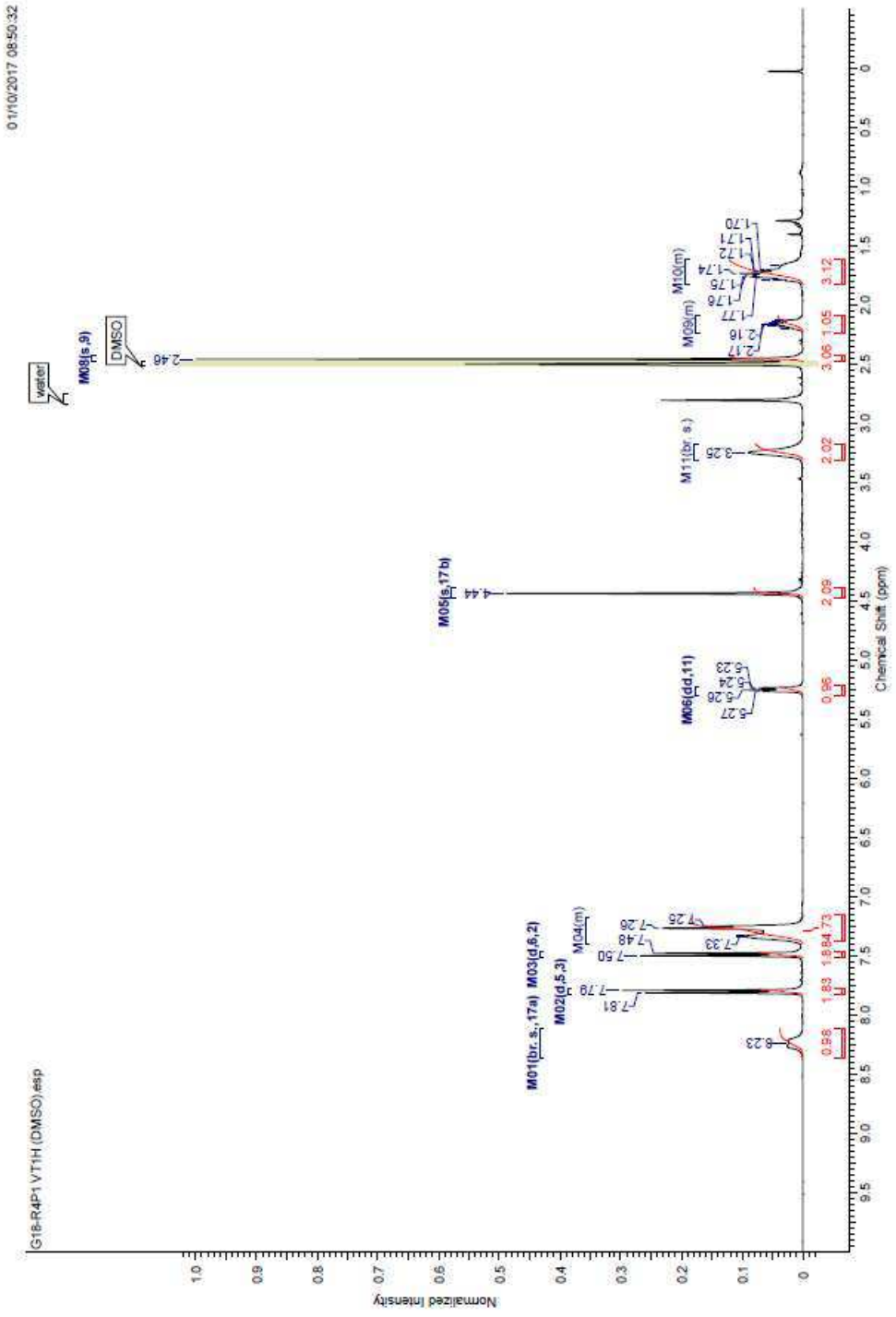
^{13}C NMR, DMSO-d_6


26/10/2017 13:54:49
PT17494.011.esp
Normalized Intensity
Chemical Shift (ppm)
M03(s)
M02(s)
M04(d)
J(M04)=22.11 Hz
M14(s)
M15(s)
M01(d)
J(M05)=178.02 Hz
M05(d)
M06(s)
M09(s)
M07(s)
M11(s)M08(s)
M10(s)
M12(s)
M13(s)
20.64
19.51
29.25
29.10
51.75
58.58
69.18
69.07
89.35
90.53
128.66
128.09
128.66
136.29
138.67

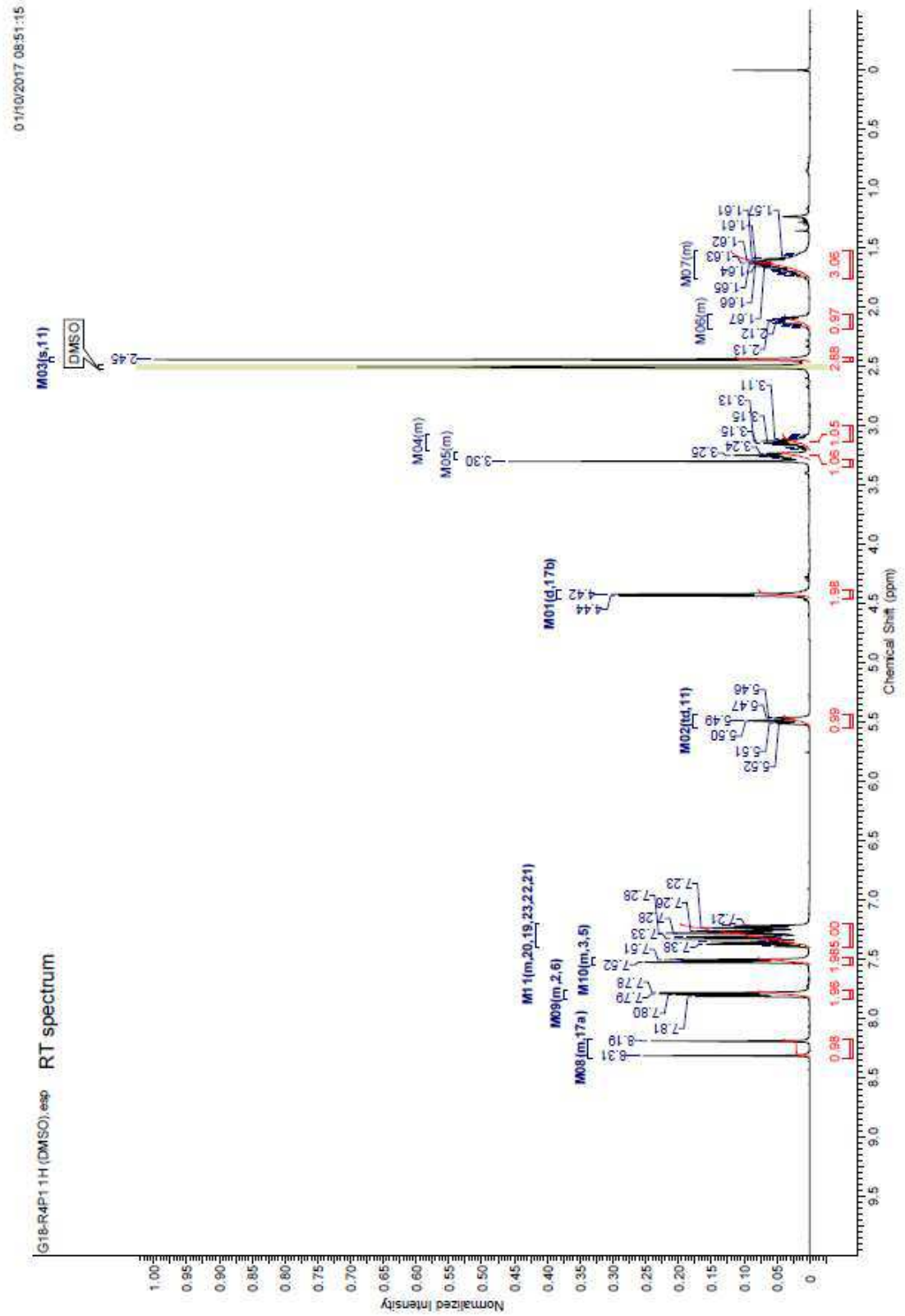


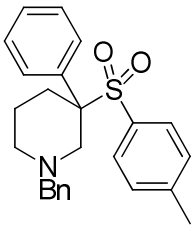
***N*-Benzyl-*N*-(4-chloro-4-tosylbutyl)formamide 14**

^{1}H, DMSO-d_6



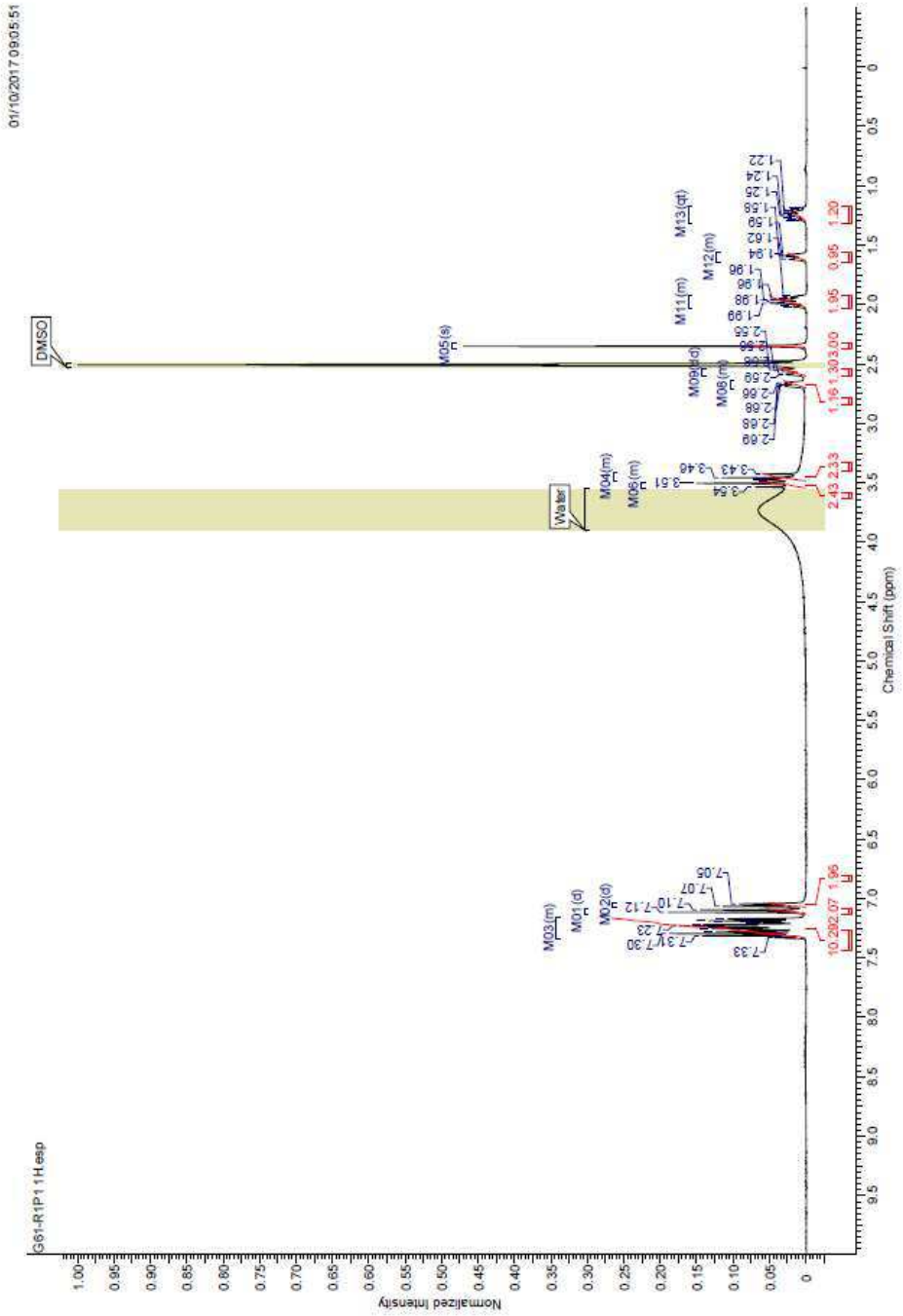
^{13}C, DMSO-d_6


01/10/2017 08:51:15
G18-R4P11H (DMSO).esp
RT spectrum
M03(s,11)
DMSO
2.45
M04(m)
M05(m)
3.30
M01(d,17b)
4.42
4.44
M02(td,11)
5.46
5.47
5.49
5.50
5.51
5.52
M11(m,20,19,23,22,21)
M09(m,2,6)
M10(m,3,5)
M08(m,17a)
6.31
8.19
7.81
7.80
7.79
7.78
7.62
7.61
7.38
7.36
7.33
7.28
7.28
7.23
7.21
M07(m)
M06(m)
1.57
1.61
1.61
1.62
1.63
1.64
1.65
1.66
1.67
2.12
2.13
3.11
3.13
3.15
3.15
3.24
3.25
1.98
0.99
1.96
1.95
5.00
0.98
2.88
0.97
3.05
1.06
1.05
Normalized Intensity
Chemical Shift (ppm)

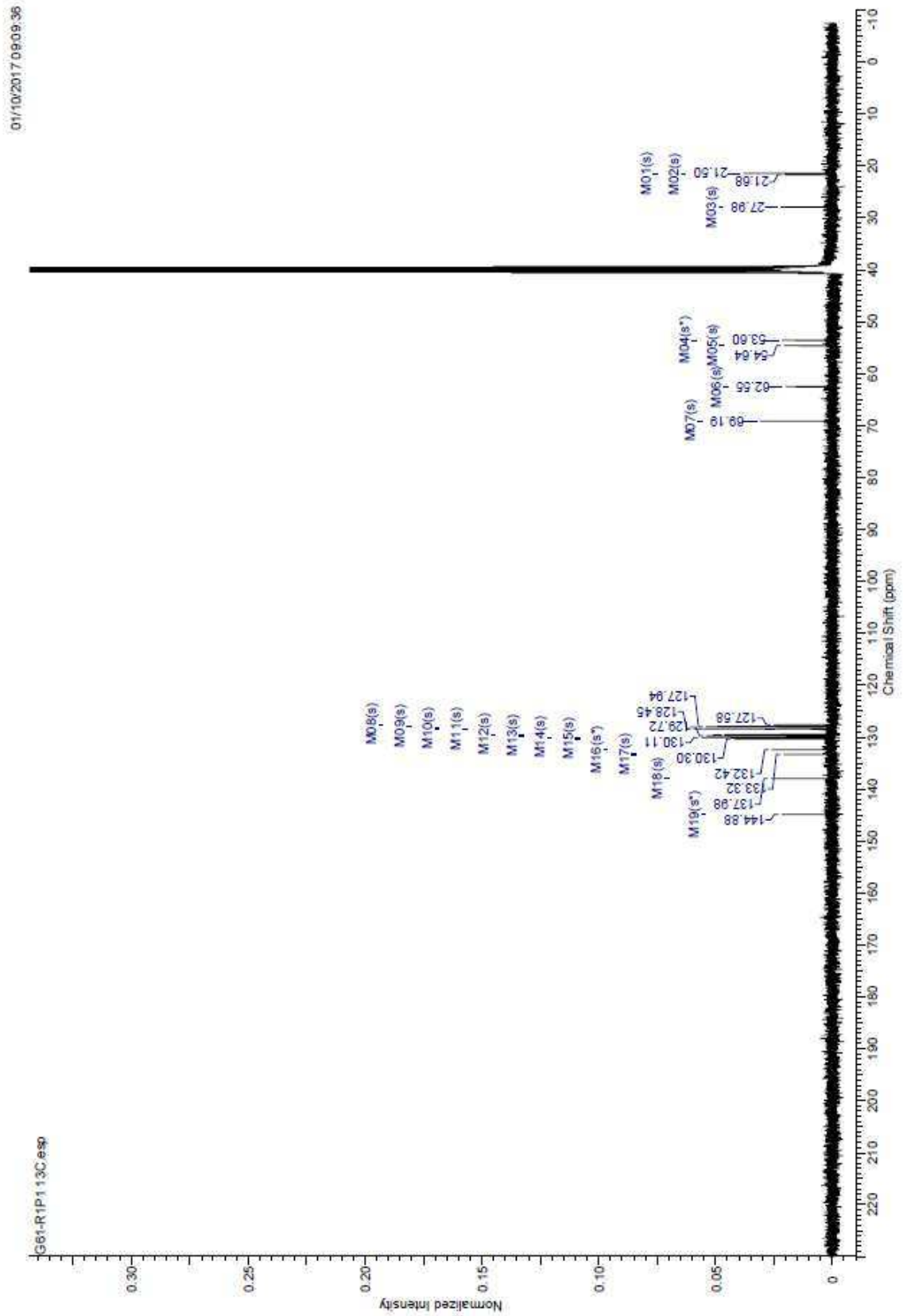


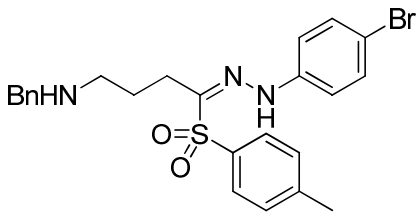
1-Benzyl-3-phenyl-3-tosylpiperidine 15

^{1}H, DMSO-d_6



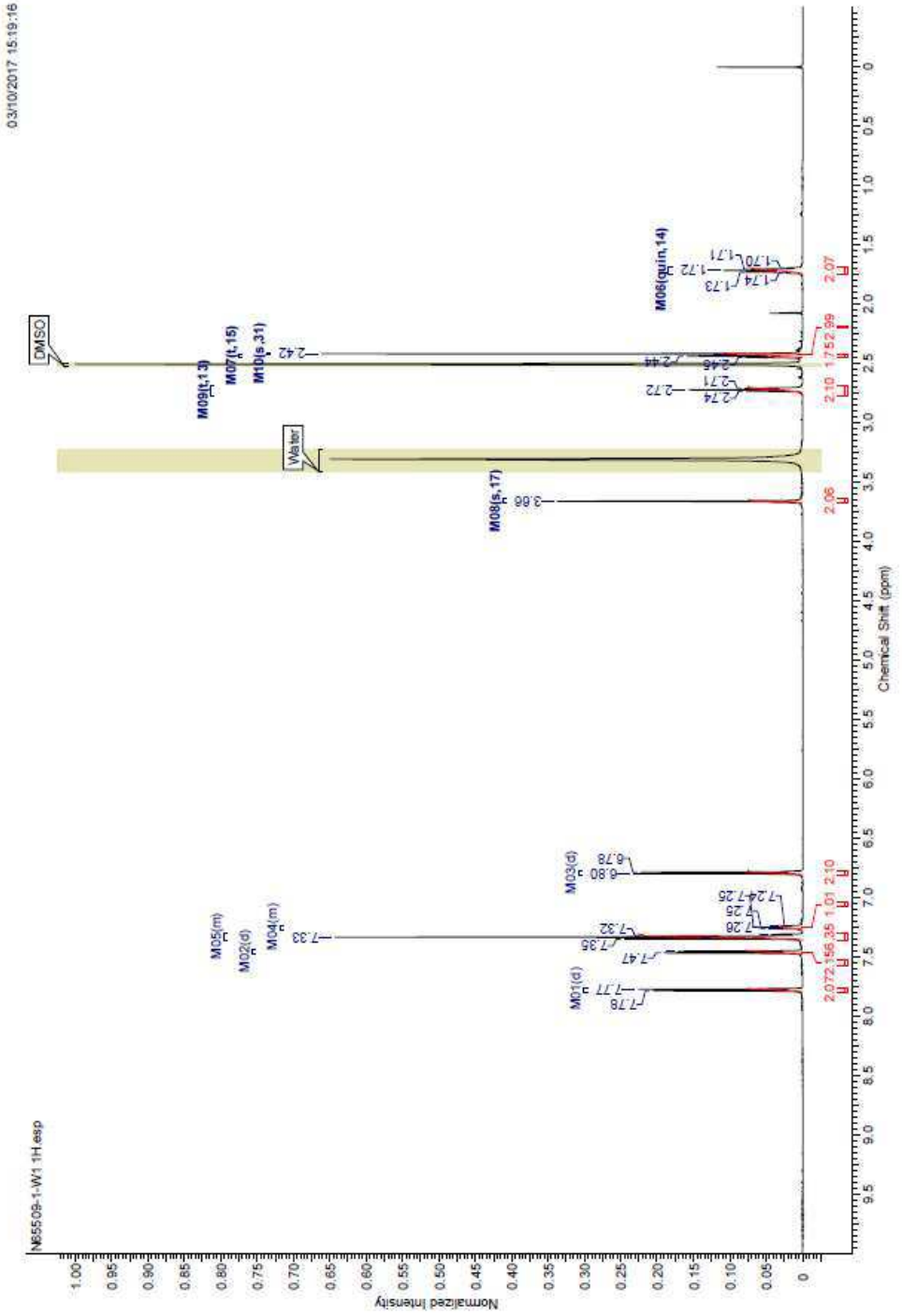
^{13}C, DMSO-d_6


01/10/2017 09:09:36
G61-R1P1113C.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(s)
M04(s*)
M05(s)
M06(s)
M07(s)
M08(s)
M09(s)
M10(s)
M11(s)
M12(s)
M13(s)
M14(s)
M15(s)
M16(s*)
M17(s)
M18(s)
M19(s*)
21.68
21.60
27.98
53.60
54.64
62.55
69.19
127.58
127.94
128.45
129.72
130.11
130.30
132.42
133.32
137.98
144.88

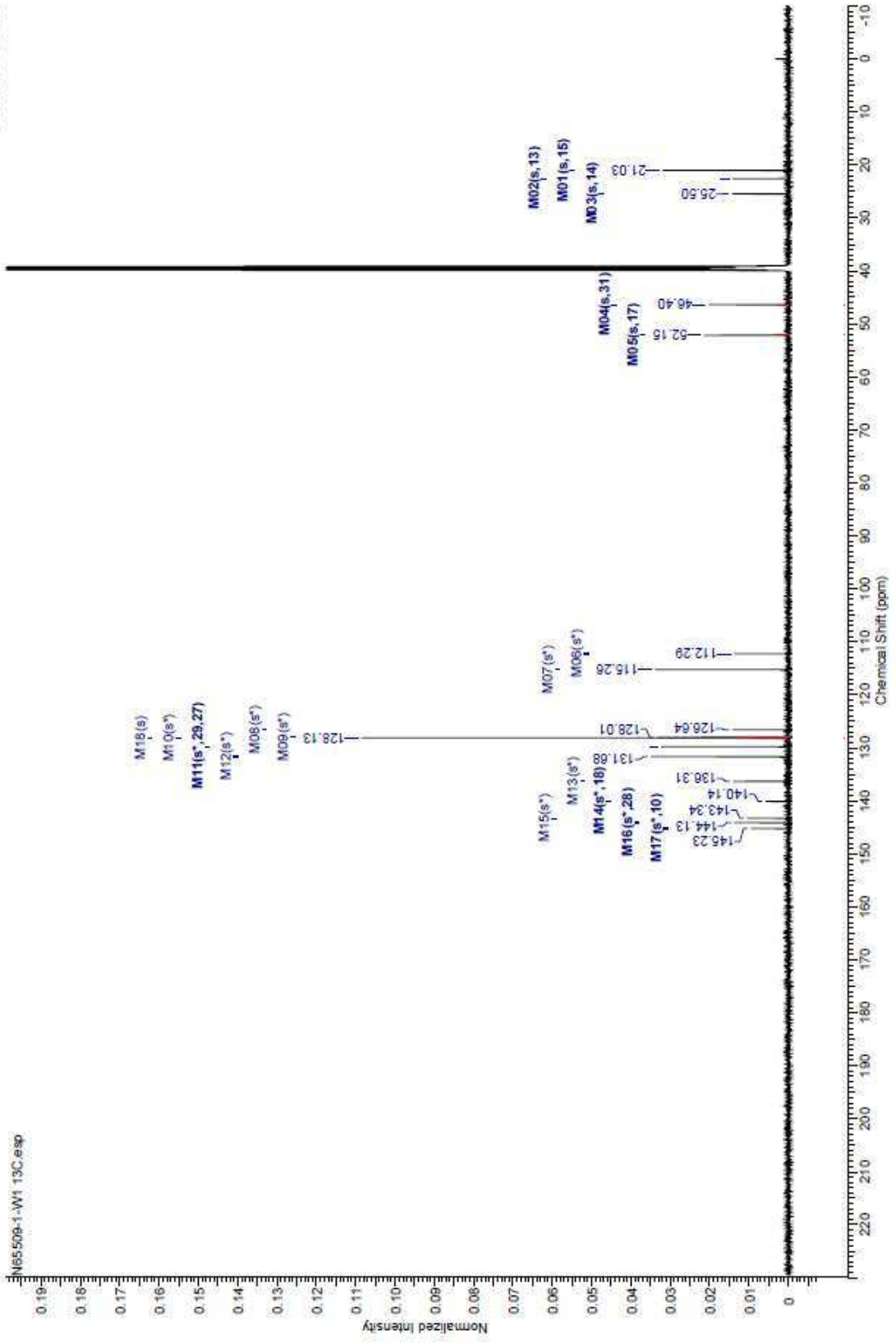


***N*-Benzyl-4-(2-(4-bromophenyl)hydrazono)-4-tosylbutan-1-amine 16**

^{1}H, DMSO-*d*$_6$



^{13}C, DMSO-d_6


03/10/2017 15:19:41
M65.509-1-W1 13C.esp
Normalized Intensity
Chemical Shift (ppm)
M02(s,13)
M01(s,15)
M03(s,14)
21.03
25.60
M04(s,31)
M05(s,17)
46.40
52.15
M18(s)
M10(s*)
M11(s*,29.27)
M12(s*)
M08(s*)
M09(s*)
128.13
M07(s*)
M06(s*)
112.29
116.26
126.64
128.01
131.88
M15(s*)
M13(s*)
M14(s*,18)
M16(s*,28)
M17(s*,10)
136.31
140.14
143.34
144.13
145.23