Supplementary Information

Methylene-linked *bis*-phenylbenzimidazoles - a new scaffold to target telomeric DNA/RNA hybrid duplex

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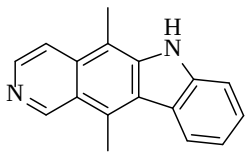
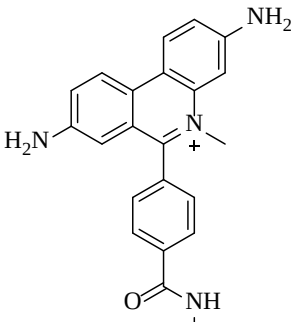
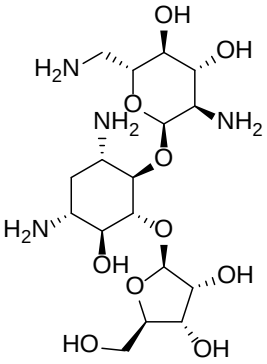
S1: Reported molecules that bind to non-telomeric DRH duplexes.[1-5]

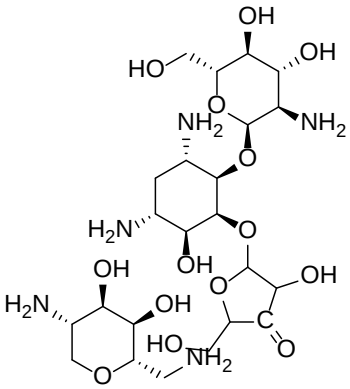


Ellipticine

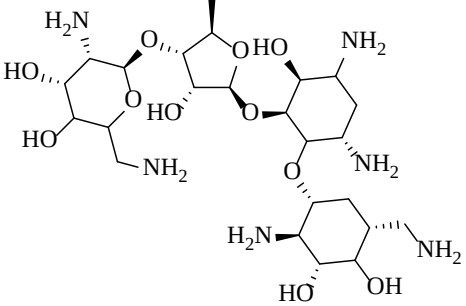




Ribostamycin



Paromomycin



Neomycin-ethidium conjugate

S2. Synthesis, Purification and Analysis

A standard method for amide coupling was employed to prepare all *bis*-amide molecules in libraries 1 to 4. The reaction was carried out using 1-hydroxybenzotriazole (HOBt) and *N*,*N*′-diisopropylcarbodiimide (DIC).[6] The HOBt/DIC-mediated amide coupling reaction was employed for all reactions due to the availability of the reagents and previous use within the research group with good yield. Additionally, most of the reactions were done with either dimethylformamide (DMF) or dichloromethane (DCM) as the solvent, because the urea by-product is soluble in DMF (easy to remove during washing) and the initial activation step is faster in nonpolar solvent like DCM.[7, 8] Initially, the activated ester was generated by treating the corresponding acid with HOBt in the presence of DIC.[9, 10] After its formation, selected diamines were added and in most cases, the reaction was completed after 14-18 h.

Every single reaction was checked by analytical thin-layer chromatography (TLC) performed on E. Merck silica gel-60 F_{254} layered plates (0.25 mm). TLC plates were visualized under UV light (254 or 360 nm) and/or by staining the plates with vanillin spray or potassium permanganate solution followed by heating.

Compounds were purified by traditional column chromatography using Merck Flash Silica Gel-60 (230-400 mesh). To get an idea of a proper solvent system, traditional TLC was done using different solvent systems to get the best separation profile. Automated flash column chromatography is an air pressure-driven hybrid of medium pressure and short column chromatography, optimized for rapid separations on the basis of UV and ELSD detection. A Reveleris® Purification System was used to purify three compounds, where the mono-adduct and bi-adduct products' retention times (*rf* value) were very close to each other. Trituration process was used to purify

crude chemical combinations with solid impurities. A solvent (either polar or non-polar) was selected in which the desired product was very soluble and the unwanted by-products were insoluble (or *vice versa*). The crude material was washed with the solvent and filtered away, leaving the purified product in solid form and any impurities in solution.

The liquid chromatography-mass spectrometry (LC-MS) technique was applied to monitor reaction progression and identification of the compounds. LC-MS was performed on a Waters Alliance 2695 with water and acetonitrile as the mobile phases. Formic acid (0.1%) was used with the acetonitrile to ensure acidic condition during the course of analysis. The gradient conditions were acetonitrile/water (95%) for 2 minutes which was increased to 50% acetonitrile over 3 minutes. The gradient was then held at 50% acetonitrile for one minute and then increased to 95% acetonitrile over 1.5 minutes. The quantity of acetonitrile was then returned to 5% over 1.5 minutes and held for 0.5 minutes. The total duration of each run was 5 and 10 minutes, which are described as **A** and **B**. The flow rate was 1 mL/min, 200 µL was split *via* a zero dead volume T-piece which passed into the mass spectrometer. The wavelength range of the UV detector was 220-400 nm. A diode array (535 scans) was functionalized with the system. A monolithic (C-18, 50X4.60 mm) column was used in the system.

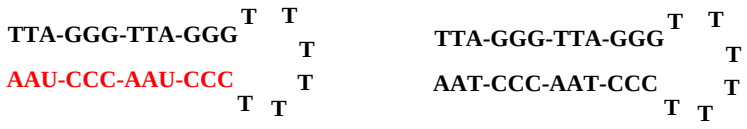
Proton NMR (^{1}H) and carbon NMR (^{13}C) were carried out on a Bruker Avance 400 MHz spectrophotometer. Chemical shifts (δ H) are cited in ppm (parts per million) and referenced to deuterated chloroform ($CDCl_3$, residual signal ^{1}H δ = 7.26, ^{13}C δ = 77.2), deuterated dimethyl sulfoxide (DMSO-d_6, residual signal ^{1}H δ = 2.54, ^{13}C δ = 40.45), deuterated methanol (MeOD, residual methanol signal ^{1}H δ = 3.31, ^{13}C δ = 49.00). Multiplicities in ^{1}H NMR spectra are quoted as s = singlet, d = doublet, t = triplet q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, td = triplet of doublets, spt = septet and br = broad. The code (0) in ^{13}C NMR spectra denotes the presence of a quaternary carbon.

High resolution mass spectra (HRMS) were obtained on a Thermo Navigator mass spectrometer coupled with liquid chromatography (LC) using electrospray ionisation (ES) and time-of-flight (TOF) mass spectrometry. Infrared spectra (IR) were recorded on a Perkin Elmer spectrum 1000 instrument.

S3. Fluorescence Resonance Energy Transfer (FRET) Assay

Stabilization of DNA/RNA hybrid duplex structures upon addition of the ligand results in an increase of melting temperature of the ligand-bound oligonucleotide. The difference in melting temperatures gives idea about the stabilizing efficiency of the ligand to the DNA structure. A 'FRET melting assay' utilizes this basic principle where an increase in temperature leads to denaturing or melting of the macromolecule, causing the distance between the probes to increase and leading to an increase in fluorescent energy. The technique has been found to be very useful in investigating various types of nucleic acid structures.[11]

The synthesized molecules were screened against the telomeric DNA/RNA hybrid (DRH) duplex, a hairpin DNA/RNA hybrid duplex was used in this experiment where the DNA strand matched the exact human telomeric repeat sequence and RNA strand counterparts with the RNA template (red colour) of telomerase enzyme (**a**). cDD; Control DNA/DNA duplex – a hairpin form of oligonucleotide sequence was used in this experiment as a control for DRH, which is similar in orientation and base pairs to DRH with the exception of replacing the RNA bases with the corresponding DNA bases (**b**).



(a) (b)

500 mL of buffer solution (100 mM K^+) was prepared with potassium hydroxide and potassium chloride and adjusted to a pH of 7.4 with cacodylic acid (50 mM and 500 mM). The buffer was stored in the freezer at -20 °C. The fluorescence-tagged oligonucleotide sequences were diluted with sterile DEPC water (DNA Grade, Fisher Scientific) to obtain 20 µM solutions. 400 nM solutions prepared by serial dilution using FRET-buffer were annealed by heating at 85 °C for 5 minutes followed by cooling to room temperature over 3-4 hours (Grant Bio PCH-2 Dry Block Heating/Cooling System). For all ligands, 5 mM stock solutions were made with dimethyl sulfoxide (≥ 99.9 %, A.C.S. spectrophotometric grade, Sigma-Aldrich). From these stock solutions, 100 µM, 10 µM, 4 µM and 2 µM working solutions were prepared by serial dilutions with FRET buffer.

For the FRET-based DNA melting assay, 50 µL of annealed DNA was added to each well of a 96-well plate (Bio-Rad Laboratories), then 50 µL of ligand solution was added to each well. Three different concentrations (10 µM, 4 µM and 2 µM) of each compound were tested in triplicate. Most commonly, pure FRET buffer instead of ligand solution was added to all wells of the first line (A) of the plate to serve as a blank. After 15 minutes of incubation at room temperature, the plate was processed in a DNA Engine Opticon (Continuous Fluorescence Detector, MJ Research) and florescence measurements taken over a temperature range from 30-100 °C at intervals of 0.5 °C. Prior to each measurement, the temperature was kept constant for 30 seconds. The incident radiation was emitted at 450-495 nm and detection measured at 515-545 nm.

The achieved data was analyzed using the program Origin – Scientific Graphing and Analysis Software (Version 7.0, OriginLab Corp.). The increases of the melting temperatures (ΔT_m) were obtained by subtracting the value of the blank from the measured values of each sample. For each concentration of every compound, the average ΔT_m was calculated from the three corresponding values and plotted against the concentration of the ligand.

***Table S1*:** FRET melting assay results for Libraries **1**, **2**, **3** and **4** molecules with telomeric DNA/RNA hybrid duplex (tDRH) and control cDD sequences.

Library	**Compound**	**ΔT_m (°C)** (SD = 0.0 - ±0.5, n = 3)			
		tDRH		**cDD**	
		2 µM	**1 µM**	**2 µM**	**1 µM**
Library-1	1	5.4	2.4	1.5	0.6
	2	5.6	2.3	3.3	0.2
	3	8.6	4.5	3.2	1.3
	4	9.5	7.2	1.3	0.8
	5	6.8	4.5	2.3	1.2
	6	8.2	6.8	1.4	0.9
Library-2	7	1.2	0.5	0.8	0.3
	8	3.6	3.2	1.2	0.6
Libray-3	9	0.6	0.2	0.1	0.1
	10	0.3	0.1	0.2	0.2
	11	0.5	0.4	0.3	0.1
	12	0.6	0.2	0.3	0.1
	13	0.3	0.2	0.2	0.0
	14	0.7	0.3	0.1	0.0
Libray-4	15	0.7	0.1	0.5	0.1
	16	0.8	0.1	0.5	0.3

	17	1.2	0.5	1.1	0.5
	18	1.0	0.3	0.7	0.2

S4. Molecular Modelling Methodology for DNA/RNA Hybrid Duplex

The DNA/RNA hybrid duplex was constructed by first using *make-na* (http://structure.usc.edu/make-na/server.html) to create the RNA strand, followed by construction of the DNA sequence (including the TTT loop) using the AMBER module *nab*. The TTT loop was then covalently linked to the DNA backbone using parameters derived in-house. All compounds were docked in the minor groove of the DNA/RNA hybrid duplex sequence using AMBER *xleap*, parm99SB and modified parmbsc0 and Gaff AMBER force field parameters. Energy minimization was then undertaken in a gradient manner by initially placing the DNA or DNA/RNA hybrid duplex under a high force constraint (*i.e.* 500 kcal mol^{-1} $Angstrom^{-2}$), which was reduced in stages to zero to enable the ligand to find its local energy minimum, followed by reduction in force in a periodic manner with a relaxation of restraints. Once in equilibrium, production simulations were run for a period of 10 ns, and atomic coordinates were saved at 1 ps intervals. Simulations involving the control DNA duplex were undertaken in an identical manner with the use of the AMBER module *nuc* to create the DNA sequence. Analysis of molecular dynamics simulations was undertaken using *VMD* [12], and all models were created using *Chimera* [13].

Figure S4.1: Below is the snapshot of a 10ns implicit solvent molecular dynamics simulation of compound **6** (blue spheres) with tDRH. Both benzimidazole moieties of the molecule intercalate the sequence; one between G4:C27 and G5:C26 (green) and the second between the A9 and A10 bases (yellow).

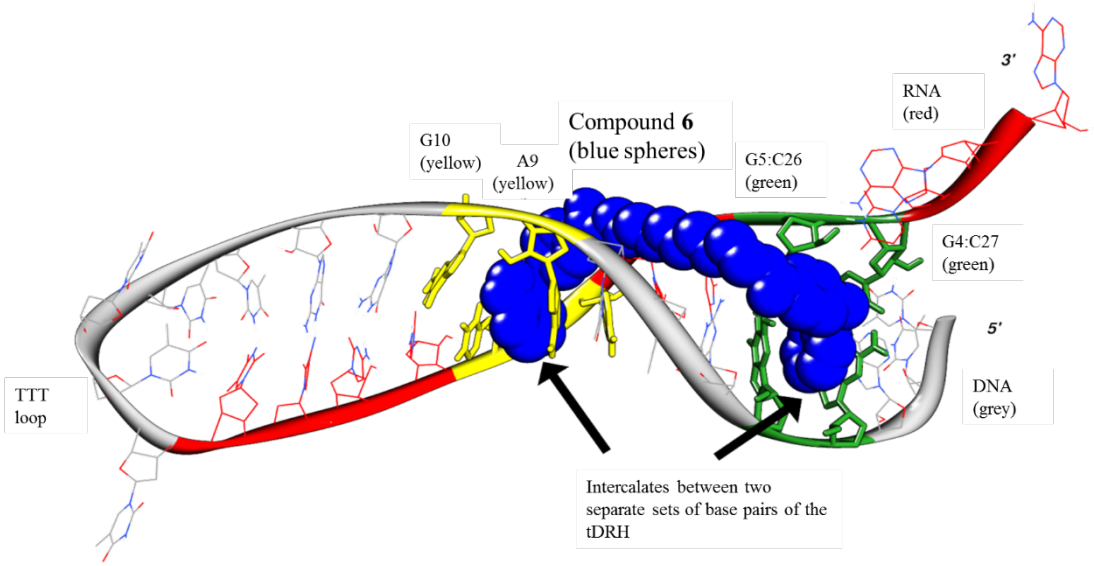


Figure S4.2: Following snapshot of a 10ns explicit solvent molecular dynamics simulation of **NSC 273829** (green spheres) shows some interaction with the tDRH sequence (**a**, grey and red) and the cDD (**b**, grey). The molecule is accommodated in each, but the shape-fit of the molecule to the tDRH is more favorable due to the different topological features of the tDRH structure.

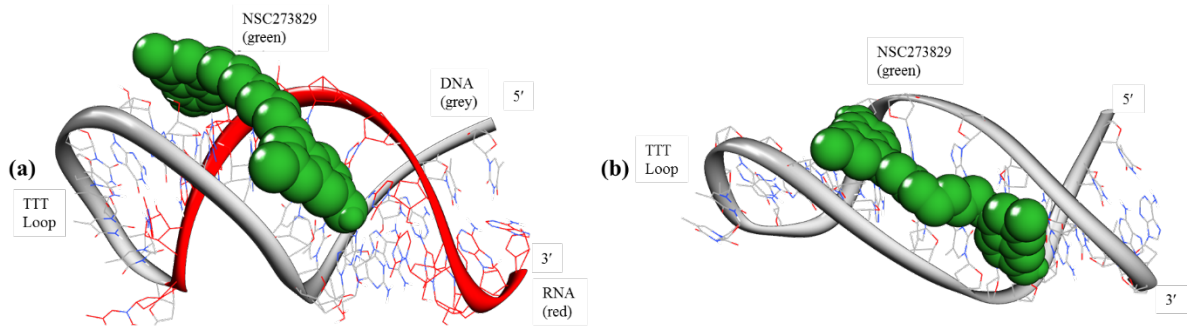


Figure S4.3: Following **s**napshot of a 10ns molecular dynamics simulation of **compound 4** (blue spheres) shows significant disorder of the RNA duplex structure (RRH, red ribbon) and benzimidazoles do not intercalate between base pairs.

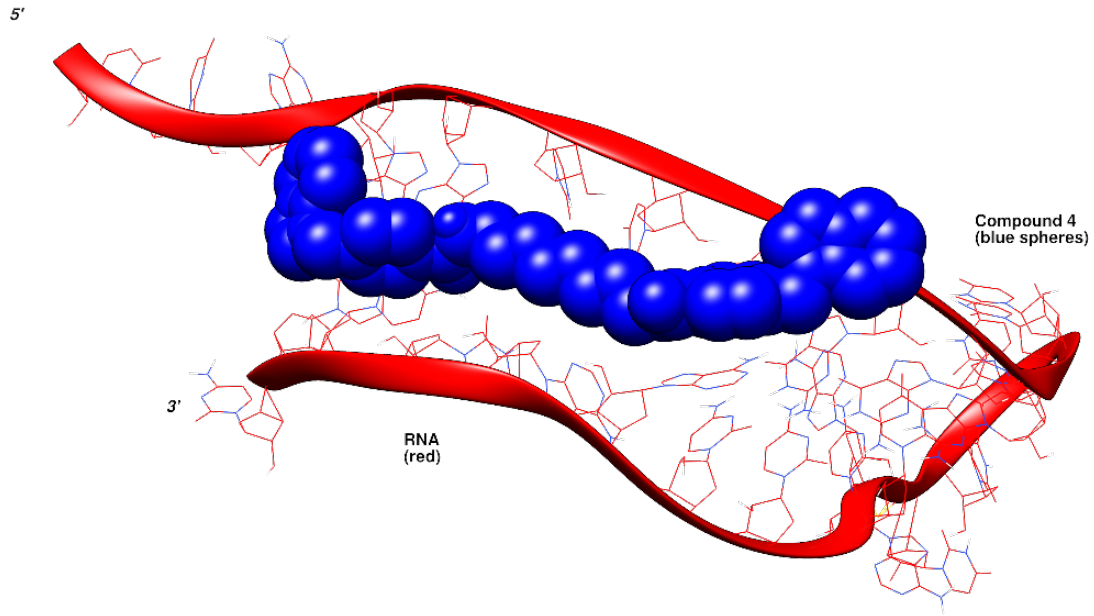
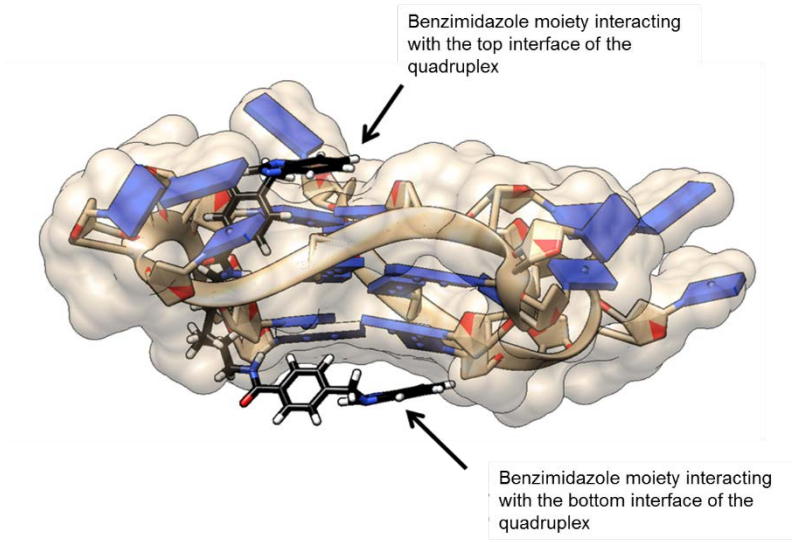


Figure S4.4: Image of the highest scoring (GBSA) docked pose of compound **3** (black) interacting with the F21T quadruplex (PDB ID: 3CDM) (blue and white). The benzimidazole moieties interact with the top and bottom faces of the quadruplex through van der Waals interactions, thus providing stabilization.



S5. Circular Dichroism (CD) Analysis[1]

The fourteen selected molecules with good and moderate selectivity towards DNA/RNA hybrid duplexes (based on preliminary FRET results and molecular modelling studies) were screened against DRH (DNA/RNA hybrid duplexes), cDD (control DNA/DNA duplexes).

Simultaneous UV absorption and CD spectra were acquired on Chirascan or Chirascan Plus spectrometers (Applied Photophysics, Leatherhead, UK). The instruments were flushed with pure nitrogen gas throughout the measurements. Far-UV spectra were recorded from 450 to 200 nm with a 1 nm spectral bandwidth, 0.5 nm stepsize and a 1 s spectrometer time-per-point. A rectangular 0.5 mm path length was employed. Unless otherwise stated, all spectra were measured at 25 °C (temperature controller made by Quantum NorthWest, Model-TC125). During data processing, a spectrum of the DNA media or solution was buffer-subtracted and Savitsky-Golay smoothing with a convolution width of 5 points applied. CD spectra were normalized for concentration and path length and expressed in terms of molar ellipticity per residue. Secondary structure analyses were performed using CDPro.

50 mM Tris (Tris(hydroxymethyl)aminomethane) was prepared, adjusted to pH 7.4 with hydrochloric acid (1 N) and labelled as 50 mM 'Tris-HCl' buffer. The oligonucleotide sequences were diluted with sterile DEPC water (DNA Grade, Fisher Scientific) to obtain 100 µM solutions. 5 µM solutions of DNA were prepared by using CD-buffer (Tris-HCl buffer). The DNA solutions were stored in the freezer at -20 °C. For all tested compounds, 5 mM stock solutions were made with dimethyl sulfoxide (≥ 99.9 %, A.C.S. spectrophotometric grade, Sigma-Aldrich). From these stock solutions, 5 µM, 10 µM, 15 µM, 20 µM and 25 µM working solutions were prepared during experimentation with DNA solutions.

For the CD-based DNA binding titration assay, 1,000 µL of respective buffer was first scanned and subsequently 1 µL of ligand was added into the same cuvette (filled with buffer) to scan one more time. Following the first step, the cuvette was cleaned properly and dried with an N_2 flow. Afterwards, 1,000 µL of DNA solution were scanned to measure the appropriate wavelength for each type of DNA sequence. After determining the proper wavelength, 1 µL of ligand solution was added into the same cuvette to make a ligand concentration of 5 µM, which was then

[1] We would like to express our gratitude to Dr Tam Bui from Biomolecular Spectroscopy Centre, Pharmaceutical Optical & Chiroptical Spectroscopy Facility, King's College London for helping with the CD analysis of the synthesised compounds.

scanned again. Subsequently, an additional 1 µL of ligand solution was added into the cuvette to make the 10 to 25 µM ligand concentrations for each scanning. CD measurements were taken at 25 °C at a wavelength of 200-450 nm.

Figure S5.1: CD spectra of **(a)** the telomeric DRH duplex, and **(b)** the control DNA duplex (cDD).

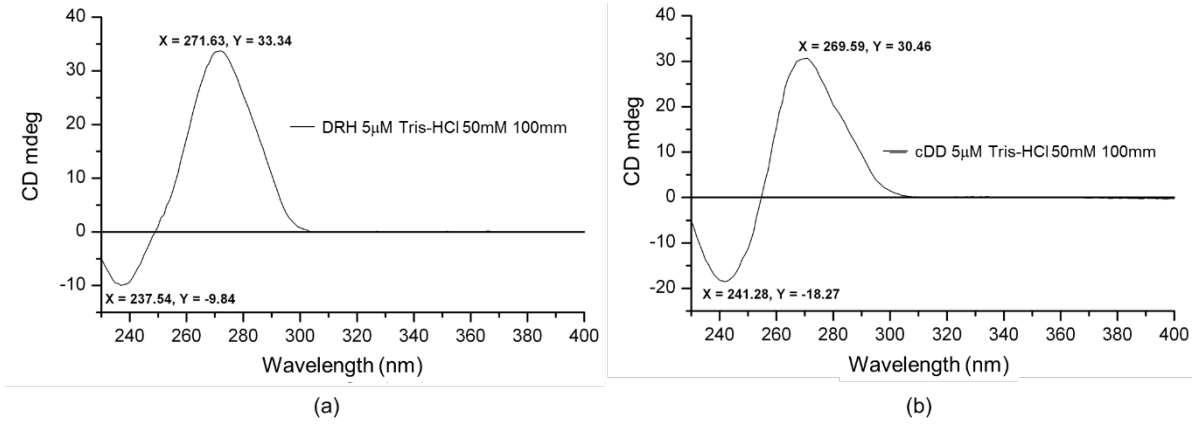


Figure S5.2: CD spectra of compound **4** (**a**) and **6** (**b**) for the control DNA duplex (cDD).

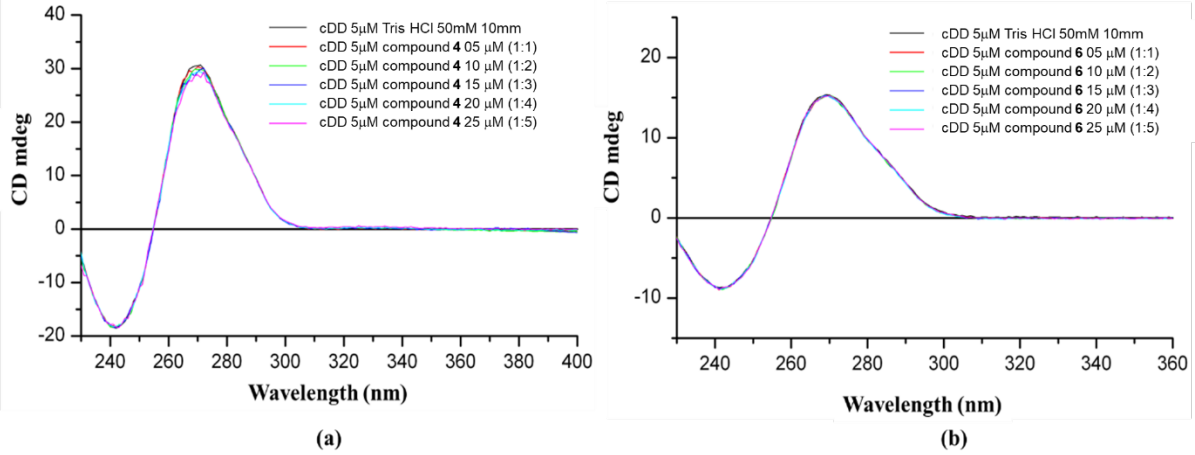


Figure S5.3: CD spectra of library-2 compounds **7** (**a**) and **8** (**b**) non-interacting with the telomeric DRH duplex sequence (5 µM) in Tris buffer (pH 7.4) at 0-5 equivalents ligand concentration.

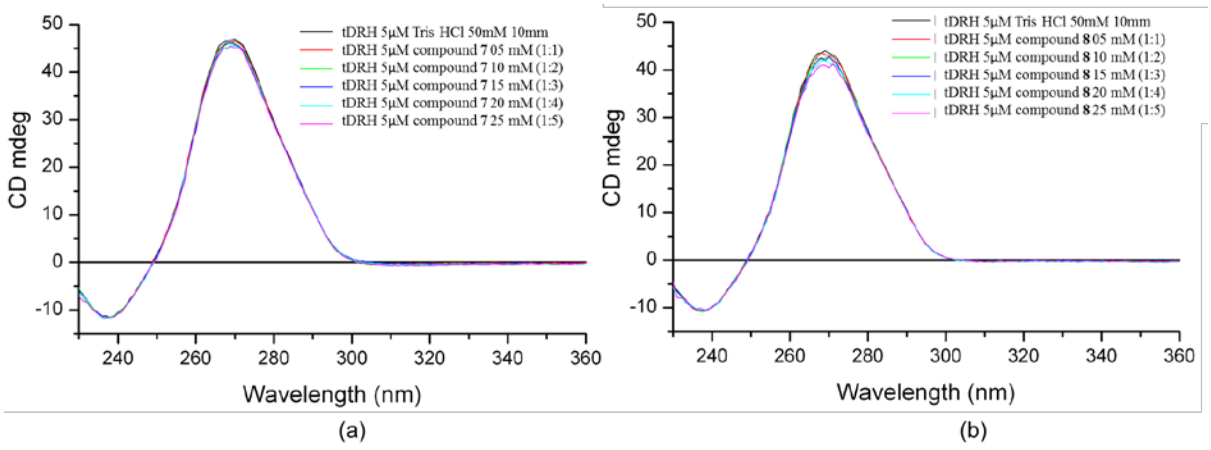
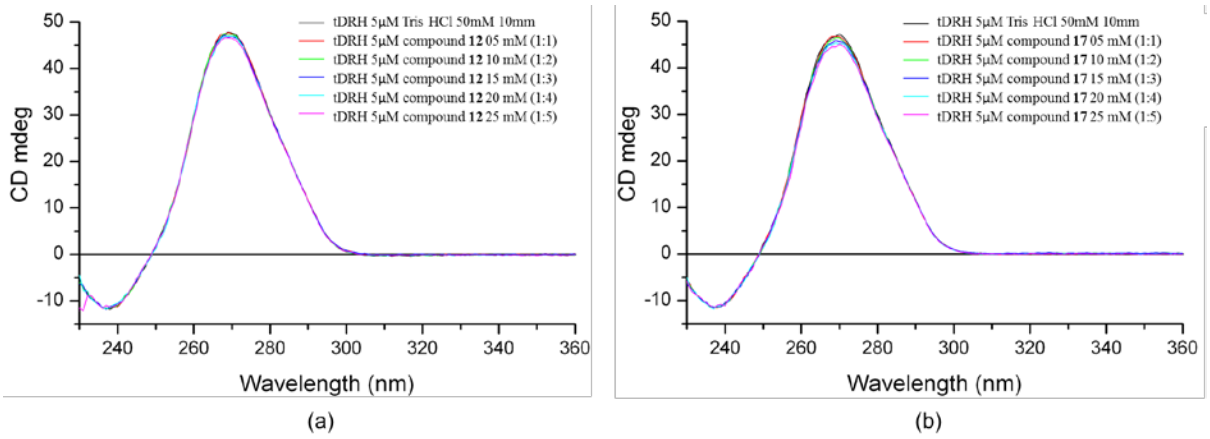
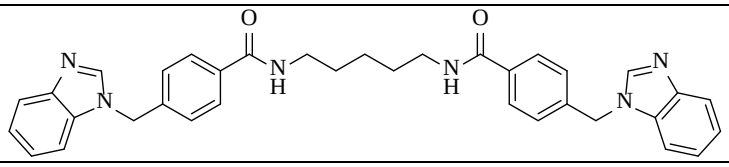
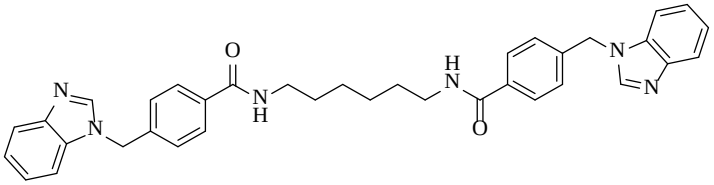
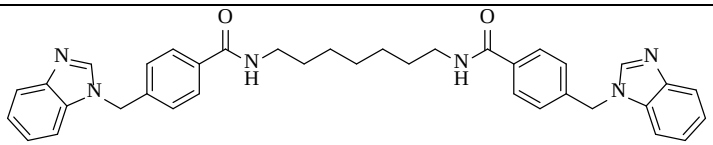
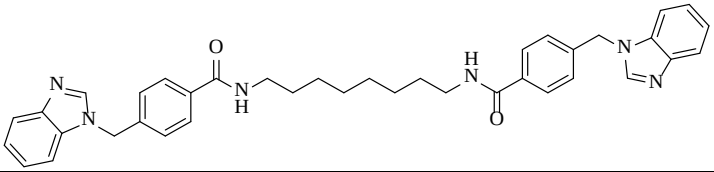
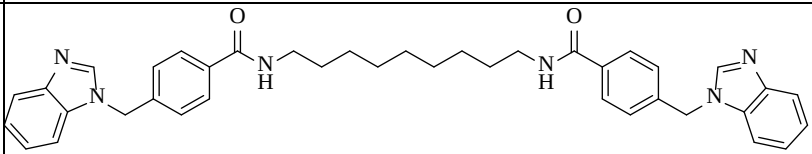
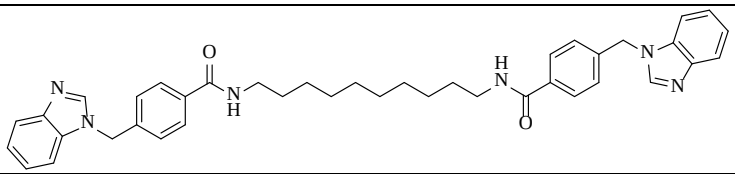


Figure S5.4: CD spectra of compounds from Libray-3 (**a**, compound **12**) and Library-4 (**b**, compound **17)** with DRH (5 µM) in Tris buffer (pH 7.4) at 0-5 equivalents ligand concentration.



S6. Synthesized molecules and their characterization

***Table S6.1: bis*-benzo[*d*]imidazole type molecules in Library 1**

Compound	Structure	Purity (%)	
		A	B
1		89	100
2		45	37
3		92	94
4		100	100
5		97	70
6		100	74

(A = 5 minute run and B = 10 minute run)

***N,N'*-(pentane-1,5-diyl)bis(4-((1*H*-benzo[*d*]imidazol-1-l)methyl)benzamide) (1),** white solid; δ_H (400 MHz, $CDCl_3$) 8.09 (s, 2 H), 7.79 (d, *J* = 7.3 Hz, 2 H), 7.83 (d, *J* = 8.6 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 4 H), 7.36-7.30 (m,

4 H), 7.12 (d, *J* = 8.6 Hz, 4 H), 6.50 (t, *J* = 6.2 Hz, 2 H), 5.38 (s, 4 H), 3.47 (q, *J* = 6.2 Hz, 4 H), 1.71-1.65 (m, 4 H), 1.48-1.43 (m, 2 H); δ_C (100 MHz, $CDCl_3$) 163.0, 145.4, 143.8, 141.3, 133.9, 130.1 (2 C), 127.9 (2 C), 127.2, 124.3, 123.8, 120.6, 110.6, 50.2, 39.1, 31.3, 24.5; υ_{max}/cm^{-1} 3268, 2936, 1638, 1616, 1540, 1504, 1456, 1385, 1364; *m/z* Observed 571.2824 $[M+H]^+$, Theoretical value 571.2816 $[C_{35}H_{34}N_6O_2+H]^+$; yield 23%

***N,N'*-(hexane-1,6-diyl)bis(4-((1*H*-benzo[*d*]imidazol-1-yl)methyl)benzamide) (2),** white solid; δ_H (400 MHz, DMSO-d_6) 8.42 (s, 2 H), 8.37 (t, *J* = 5.7 Hz, 2 H), 7.76 (d, *J* = 8.3 Hz, 4 H), 7.68-7.64 (m, 4 H), 7.35 (d, *J* = 8.3 Hz, 4 H), 7.20-7.17 (m, 4 H), 5.55 (s, 4 H), 3.22-3.17 (m, 4 H), 1.46 (br s, 4 H), 1.28 (br s, 4 H); δ_C (100 MHz, DMSO-d_6) 166.6, 144.4, 143.2, 141.7, 133.0, 130.2 (2 C), 127.5 (2 C), 127.2, 122.6, 121.9, 120.4, 110.6, 59.8, 39.7, 29.6, 26.8; υ_{max}/cm^{-1} 3285, 2935, 2359, 1641, 1569, 1540, 1456, 1436, 1363; *m/z* Observed 585.2964 $[M+H]^+$, Theoretical value 585.2973 $[C_{36}H_{36}N_6O_2+H]^+$; yield 52%.

***N,N'*-(heptane-1,7-diyl)bis(4-((1*H*-benzo[*d*]imidazol-1-l)methyl)benzamide) (3),** pale yellow solid; δ_H (400 MHz, $CDCl_3$) 7.95 (s, 2 H), 7.82-7.78 (m, 2 H), 7.75-7.70 (m, 4 H), 7.23-7.21 (m, 8 H), 7.17 (d, *J* = 8.0 Hz, 4 H), 4.20 (br s, 4 H), 3.86-3.80 (m, 2 H), 3.43-3.36 (m, 2 H), 1.56 (t, *J* = 6.5 Hz, 4 H), 1.34 (br s, 4 H), 1.21 (d, *J* = 6.5 Hz, 2 H); δ_C (101 MHz, $CDCl_3$) 166.5, 143.5, 142.8, 138.4, 134.5, 133.4, 127.3 (2 C), 126.7 (2 C), 122.9, 122.1, 120.1, 109.6, 48.1, 30.5, 28.9, 28.2, 26.2; υ_{max}/cm^{-1} 3339, 2966, 1614, 1556, 1494, 1458, 1361; *m/z* Observed 599.3123 $[M+H]^+$; Theoretical value 599.3129 $[C_{37}H_{38}N_6O_2+H]^+$; yield 83%.

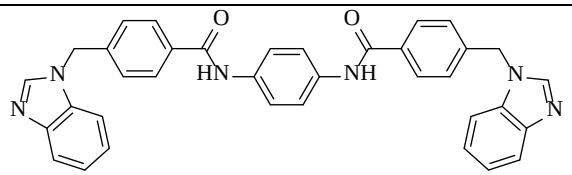
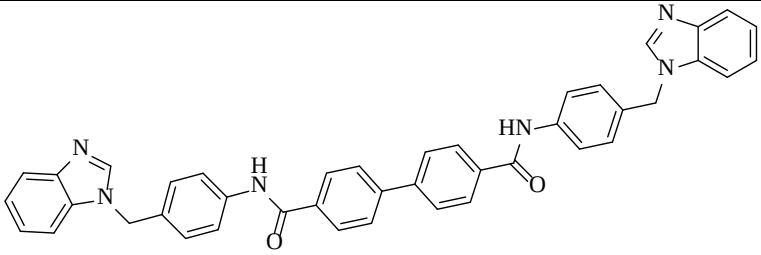
***N,N'*-(octane-1,8-diyl)bis(4-((1*H*-benzo[*d*]imidazol-1-yl)methyl)benzamide) (4),** white solid; δ_H (400 MHz, $CDCl_3$) 7.98 (s, 1 H) , 7.84 (d, *J* = 7.8 Hz, 1 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 2.5 Hz, 1 H), 7.26-7.23 (m, 2 H), 7.21 (d, *J* = 8.4 Hz, 2 H), 6.13 (t, *J* = 5.9 Hz, 1 H), 5.41 (s, 2 H), 4.00 (br s, 2 H), 3.84 (dd, *J* = 13.1, 6.6 Hz, 5 H), 3.45-3.39 (m, 2 H), 1.62-1.56 (m, 2 H), 1.34 (br s, 2 H), 1.16 (m, 15 H); δ_C (100 MHz, $CDCl_3$) 161.0, 148.1, 143.3, 142.8, 138.4, 134.2, 127.3 (2 C), 126.9 (2 C), 123.1, 122.3, 120.2, 109.6, 48.2, 39.7, 29.2, 28.6, 23.2; υ_{max}/cm^{-1}3328, 2928, 1627, 1562, 1496, 1458, 1383, 1325; *m/z* Observed 613.3268 $[M+H]^+$, Theoretical value 613.3286 $[C_{38}H_{40}N_6O_2+H]^+$; yield 74%

***N,N'*-(nonane-1,9-diyl)bis(4-((1*H*-benzo[*d*]imidazol-1-yl)methyl)benzamide) (5),** pale yellow solid, δ_H (400 MHz, $CDCl_3$) 7.97 (s, 2 H), 7.84 (d, *J* = 8.1 Hz, 4 H) 7.72 (d, *J* = 8.4 Hz, 4 H) 7.24 (td, *J* = 2.9, 1.1 Hz, 4 H) 7.21 (d, *J* = 8.1 Hz, 4 H) 6.20-6.15 (m, 2 H) 5.41 (s, 4 H) 3.87-3.83 (m, 4 H) 3.45-3.39 (m, 4 H) 1.27 (br s, 10 H); δ_C (100 MHz, $CDCl_3$) 162.2, 143.9, 142.8, 142.0, 134.1, 127.6, 127.3, 126.8, 125.5, 122.9, 120.2, 109.6, 76.9, 50.5, 36.1, 31.1, 28.6, 23.2; υ_{max}/cm^{-1} 3335, 2966, 2360, 2338, 1638, 1556, 1495, 1458, 1384, 1325; *m/z* Observed 627.3436 $[M+H]^+$, Theoretical value 627.3442 $[C_{39}H_{42}N_6O_2+H]^+$; yield 31%

***N,N'*-(decane-1,10-diyl)bis(4-((1*H*-benzo[d]imidazol-1-l)methyl)benzamide) (6),** white solid; δ_H (400 MHz, DMSO-d_6) 8.06 (s, 2 H), 7.86 (d, *J* = 8.0 Hz, 4 H), 7.68 (d, *J* = 8.3 Hz, 4 H), 7.22 (td, *J* = 2.9, 1.1 Hz, 4 H), 7.20 (d, *J* = 8.0 Hz, 4 H), 6.20-6.15 (m, 2 H), 5.41 (s, 4 H), 3.87-3.83 (m, 4 H), 3.45-3.39 (m, 4 H), 1.26 (s, 12 H); δ_C (101 MHz, DMSO-d_6) 165.9, 144.4, 143.6, 139.9.8, 134.3, 128.6, 127.7, 127.6, 122.6, 121.9, 119.6, 110.8, 47.4, 40.1, 29.2, 28.8, 26.6; υ_{max}/cm^{-1} 3336, 2924, 2850, 1639, 1616, 1543, 1492, 1438, 1369; *m/z* Observed 641.3580 $[M+H]^+$, Theoretical value 641.3599 $[C_{40}H_{44}N_6O_2+H]^+$; yield 70%

***Table S6.2: bis*-benzo[*d*]imidazole type molecules with rigid linker in Library 2**

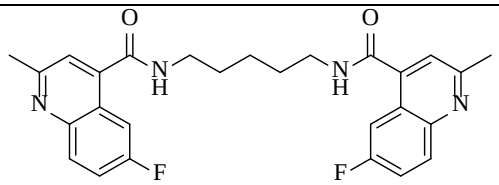
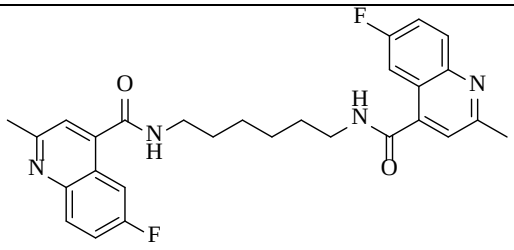
Compound	Structure	Purity (%)

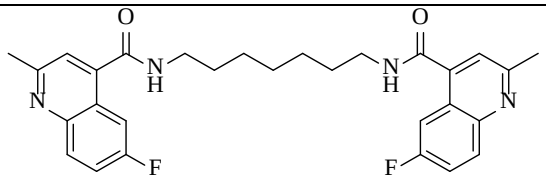
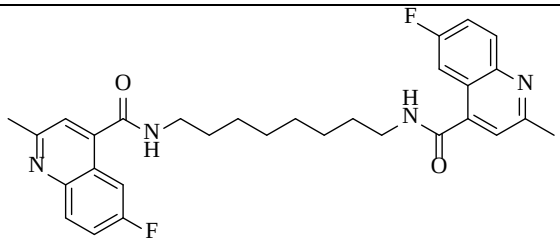
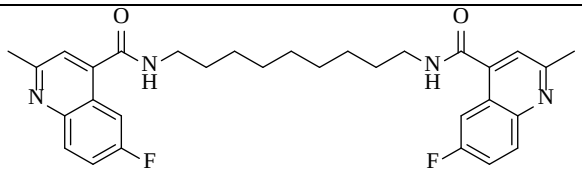
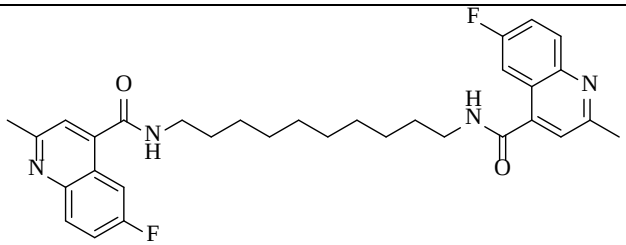
		A	B
7		100	100
8		68	74

***N,N'*-(1,4-phenylene)bis(4-((*1H*-benzo[*d*]imidazol-1-yl)methyl)benzamide) (7),** white powder; δ_H (400 MHz, DMSO-d_6) 10.19 (s, 2 H), 8.46 (s, 2 H), 7.88 (d, *J* = 8.1 Hz, 4 H), 7.71-7.64 (m, 6 H), 7.51 (d, *J* = 8.6 Hz, 2 H), 7.43 (d, *J* = 8.3 Hz, 4 H), 7.23-7.17 (m, 4 H), 5.60 (s, 4 H); δ_C (100 MHz, DMSO-d_6) 164.9, 143.9, 140.4, 134.9, 134.5, 131.8, 128.1 (2 C), 127.4 (2 C), 123.7 (2 C), 122.5, 121.7, 120.5, 110.7, 59.9; υ_{max}/cm^{-1} 3286, 3163, 3066, 2947, 1612, 1570, 1492, 1458, 1350; *m/z* Observed 577.2371 $[M+H]^+$; Theoretical value 577.2347 $[C_{36}H_{28}N_6O_2+H]^+$; yield 51%.

***N*4,*N*4'-bis(4-((1H-benzo[*d*]imidazol-1-yl)methyl)phenyl)-[1,1'-biphenyl]-4,4'-dicarboxamide (8),** white solid; δ_H (400 MHz, DMSO-d_6) 10.47 (s, 2 H), 9.69 (s, 2 H), 8.11-8.07 (m, 4 H), 7.94-7.91 (m, 4 H), 7.90-7.86 (m, 4 H), 7.85-7.82 (m, 4 H), 7.58-7.54 (m, 4 H), 7.51 (d, *J* = 8.6 Hz, 4 H), 5.72 (s, 4 H); δ_C (100 MHz, DMSO-d_6) 164.2, 144.9, 142.2, 139.6, 134.9, 134.3, 133.1, 132.9, 128.9 (2 C), 128.7 (2 C), 127.1 (2 C), 125.9, 122.6, 122.0, 120.8 (2 C), 113.4, 51.5; υ_{max}/cm^{-1} 3105, 3032, 2989, 1597, 1493, 1438, 1415, 1385, 1365; *m/z* Observed 653.2670 $[M+H]^+$; Theoretical value 653.2660 $[C_{42}H_{32}N_6O_2+H]^+$; yield 90%.

***Table S6.3: bis*-(6-fluoro-2-methylquinoline) molecules in Library 3**

Compound	Structure	Purity (%)	
		A	B
9		88	81
10		77	87

11		100	100
12		92	100
13		100	100
14		72	77

(A = 5 minute run and B = 10 minute run)

***N,N'*-(pentane-1,5-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (9),** pale yellow solid; δ_H (400 MHz, DMSO-d_6) 8.63 (dd, *J* = 8.6, 5.1 Hz, 2 H), 8.29-8.26 (m, 2 H), 7.94-7.86 (m, 2 H), 7.69-7.66 (m, 2 H), 7.42-7.34 (m, 2 H), 3.16 (t, *J* = 6.8 Hz, 4 H), 2.46 (s, 6 H), 1.60-1.56 (m, 4 H), 1.32-1.28 (m, 2 H); δ_C (100 MHz, DMSO-d_6) 166.4, 158.3, 156.9, 145.1, 142.1, 131.6, 126.6, 123.5, 120.9, 107.2, 40.0, 29.1, 23.5, 23.4; (υ_{max}/cm^{-1}) 3336, 2931, 2874, 1612, 1558, 1523, 1462, 1385, 1361; *m/z* Observed 477.2101 $[M+H]^+$; Theoretical value 477.2097 $[C_{27}H_{26}F_2N_4O_2+H]^+$; yield 37%

***N,N'*-(hexane-1,6-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (10),** white solid; δ_H (400 MHz, DMSO-d_6) 8.79-8.77 (m, 2 H), 8.03 (dd, *J* = 9.1, 5.5 Hz, 2 H), 7.84-7.76 (m, 2 H), 7.72-7.64 (m, 2 H), 7.51-7.48 (m, 2 H), 3.66-3.60 (m, 4 H), 2.71 (s, 6 H), 1.60-1.58 (m, 4 H), 1.43-1.39 (m, 4 H); δ_C (100 MHz, DMSO-d_6) 166.4, 158.3, 156.9, 145.1, 141.7, 131.6, 123.6, 123.5, 120.9, 108.7, 40.3, 29.1, 26.4, 24.8; υ_{max}/cm^{-1} 3275, 2966, 2943, 2854, 1639, 1593, 1562, 1547, 1288; *m/z* Observed 491.2252 $[M+H]^+$; Theoretical value 491.2253 $[C_{28}H_{28}F_2N_4O_2+H]^+$; yield 31%

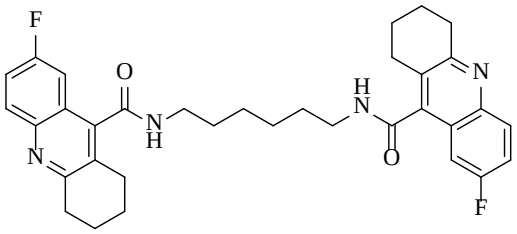
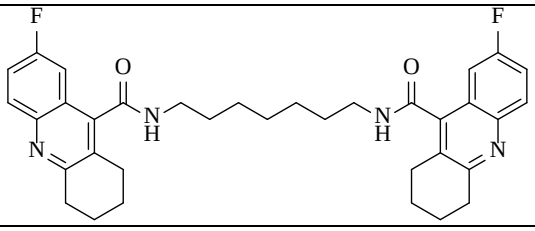
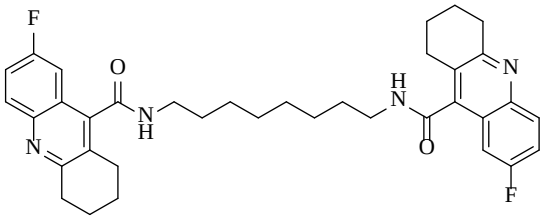
***N,N'*-(heptane-1,7-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (11),** white powder; δ_H (400 MHz, DMSO-d_6) 8.93 (dd, *J* = 9.2, 2.7 Hz, 1 H), 8.89 (dd, *J* = 9.2, 2.9 Hz, 1 H), 8.25 (br s, 2 H), 8.08 (dd, *J* = 5.0 Hz, 2.3 Hz, 2 H), 7.71 (s, 2 H), 7.42-7.39 (m, 2 H), 3.39-3.36 (m, 4 H), 2.52 (s, 6 H), 1.53-1.49 (m, 4 H), 1.26-1.23 (m, 6 H); δ_C (100 MHz, DMSO-d_6) 166.7, 161.2, 158.7, 145.3, 142.0, 131.8, 123.7, 121.1, 120.3, 120.0, 109.2, 47.4, 41.2, 29.2, 28.8, 26.9, 25.0; υ_{max}/cm^{-1} 3282, 2966, 2965, 2858, 1639, 1593, 1549, 1465; *m/z* Observed 505.2410 $[M+H]^+$; Theoretical value 505.2410 $[C_{29}H_{30}F_2N_4O_2+H]^+$; yield 25%

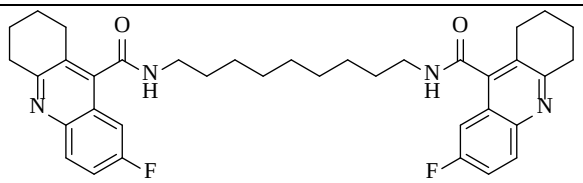
***N,N'*-(octane-1,8-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (12),** white solid; δ_H (400 MHz, DMSO-d_6) 8.78 (d, *J* = 5.0 Hz, 1 H), 8.03 (dd, *J* = 9.2, 5.7 Hz, 1 H), 7.79 (dd, *J* = 9.2, 5.7 Hz, 1 H), 7.71-7.64 (m, 2 H), 7.52-7.49 (m, 1 H), 5.48 (d, *J* = 6.6 Hz, 2 H), 3.67-3.58 (m, 2 H), 3.34-3.31 (m, 6 H), 2.69-2.66 (m, 2 H), 1.36-1.34 (m, 2 H), 1.02-0.97 (m, 12 H); δ_C (100 MHz, DMSO-d_6) 166.5, 158.5, 157.2, 145.3, 141.9, 131.8, 123.4, 121.1, 120.1, 101.5, 39.3, 29.3, 29.1, 26.8, 23.7; υ_{max}/cm^{-1} 3275, 2966, 2851, 1643, 1593, 1547, 1466, 1334; *m/z* Observed 519.2567 $[M+H]^+$; Theoretical value 519.2566 $[C_{30}H_{32}F_2N_4O_2+H]^+$; yield 92%

***N,N'*-(nonane-1,9-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (13),** white powder; δ_H (400 MHz, DMSO-d_6) 8.77 (t, *J* = 5.4 Hz, 2 H), 8.04 (dd, *J* = 9.2, 5.7 Hz, 2 H), 7.78 (d, *J* = 2.8 Hz, 1 H), 7.80 (d, *J* = 2.8 Hz, 1 H), 7.67 (td, *J* = 8.7, 2.9 Hz, 2 H), 7.50 (s, 2 H) 3.32-3.28 (m, 4 H), 2.67 (s, 6 H), 1.60-1.54 (m, 4 H), 1.34-1.30 (m, 10 H); δ_C (100 MHz, DMSO-d_6) 166.1, 158.3, 158.1, 144.9, 141.6, 131.5, 123.4, 123.2, 120.7, 108.7, 38.9, 29.0, 28.9, 28.7, 26.4, 24.6; υ_{max}/cm^{-1} 3298, 2935, 2854, 1639, 1593, 1539, 1466, 1334; *m/z* Observed 533.2716 $[M+H]^+$; Theoretical value 533.2723 $[C_{31}H_{34}F_2N_4O_2+H]^+$; yield 81%

***N,N'*-(nonane-1,9-diyl)*bis*(6-fluoro-2-methylquinoline-4-carboxamide) (14),** white powder; δ_H (400 MHz, DMSO-d_6) 8.03 (dd, *J* = 9.3, 5.3 Hz, 2 H), 7.79 (dd, *J* = 9.8, 2.8 Hz, 3 H), 7.67 (d, *J* = 8.3 Hz, 1 H), 7.47 (ddd, *J* = 9.3, 7.9, 2.9 Hz, 2 H), 6.33 (t, *J* = 5.7 Hz, 2 H), 7.31 (s, 2 H), 3.56-3.51 (m, 3 H), 2.70 (s, 6 H), 1.70-1.65 (m, 4 H), 1.46-1.39 (m, 5 H), 1.36-1.32 (m, 4 H), 1.26 (s, 2 H); ; δ_C (100 MHz, DMSO-d_6) 175.1, 168.3, 154.1, 144.8, 143.5, 130.0, 128.9, 120.8, 120.1, 104.4, 40.1, 32.0, 29.4, 28.9, 26.7, 24.8; υ_{max}/cm^{-1} 3271, 2920, 2850, 1643, 1547, 1226, 1161; m/z Observed 547.2885 $[M+H]^+$; Theoretical value 547.2879 $[C_{32}H_{36}F_2N_4O_2+H]^+$; yield 90%.

***Table S6.4: bis*-acridine molecules in Library 4**

Compound	Structure	Purity (%)	
		A	B
15		100	91
16		100	88
17		56	88

18		91	91

(A = 5 minute run and B = 10 minute run)

***N,N'*-(hexane-1,6-diyl)*bis*(7-fluoro-1,2,3,4-tetrahydroacridine-9-carboxamide) (15),** tan solid; δ_H (400 MHz, DMSO-d_6) 8.72 (t, *J* = 5.5 Hz, 2 H), 7.98 (dd, *J* = 9.3, 5.5 Hz, 2 H), 7.60 (td, *J* = 8.8, 2.8 Hz, 2 H), 7.28 (dd, *J* = 9.9, 2.9 Hz, 2 H), 3.40-3.35 (m, 4 H), 3.05-3.00 (m, 4 H), 2.85 (t, *J* = 6.2 Hz, 4 H), 1.89 (d, *J* = 5.5 Hz, 4 H), 1.85-1.80 (m, 4 H), 1.59 (d, *J* = 6.0 Hz, 4 H), 1.44 (br s, 4 H); δ_C (100 MHz, DMSO-d_6) 165.8, 158.4 (2 C), 142.9, 141.8, 131.2, 126.9, 121.1, 117.1, 107.5, 48.6, 33.2, 28.9, 28.2, 22.3, 22.0 (2 C); υ_{max}/cm^{-1} 3232, 3055, 2947, 2866, 1632, 1555, 1496, 1450; *m/z* Observed 571.2877 $[M+H]^+$; Theoretical value 571.2879 $[C_{34}H_{36}F_2N_4O_2+H]^+$; yield 55%

***N,N'*-(heptane-1,7-diyl)*bis*(7-fluoro-1,2,3,4-tetrahydroacridine-9-carboxamide) (16),** pale yellow solid; δ_H (400 MHz, DMSO-d_6) 8.73-8.69 (m, 2 H), 7.98 (dd, *J* = 9.2, 5.7 Hz, 2 H), 7.60 (td, *J* = 8.7, 2.5 Hz, 2 H), 7.28 (dd, *J* = 9.8, 2.5 Hz, 2 H), 3.05-3.00 (m, 4 H), 2.86-2.82 (m, 4 H), 1.87-1.84 (m, 4 H), 1.85-1.78 (m, 6 H), 1.61-1.56 (m, 4 H), 1.40-1.38 (m, 8 H); δ_C (100 MHz, DMSO-d_6) 165.8, 158.4 (2 C), 142.9, 141.8, 131.3, 126.9, 123.7, 119.0, 107.7, 40.1, 33.2, 28.9, 28.4, 26.5, 26.0, 22.3 (2 C); υ_{max}/cm^{-1} 3225, 3074, 2928, 2858, 1631, 1558, 1493, 1454, 1431; *m/z* Observed 585.3028 $[M+H]^+$; Theoretical value 585.3036 $[C_{35}H_{38}F_2N_4O_2+H]^+$; yield 39%

***N,N'*-(octane-1,8-diyl)*bis*(7-fluoro-1,2,3,4-tetrahydroacridine-9-carboxamide) (17),** yellow powder; δ_H (400 MHz, DMSO-d_6) 8.70 (t, *J* = 5.5 Hz, 2 H), 7.98 (dd, *J* = 9.3, 5.5 Hz, 2 H), 7.60 (td, *J* = 8.8, 2.8 Hz, 2 H), 7.27 (dd, *J* = 9.8, 2.8 Hz, 2 H), 3.66-3.59 (m, 2 H), 3.40-3.36 (m, 2 H), 3.05-3.00 (m, 4 H), 2.84 (t, *J* = 6.4 Hz, 4 H), 1.89 (d, *J* = 5.0 Hz, 4 H), 1.84-1.79 (m, 4 H), 1.57 (d, *J* = 6.8 Hz, 4 H), 1.42-1.37 (m, 8 H); ; δ_C (100 MHz, DMSO-d_6) 168.2, 164.4 (2 C), 142.9, 141.3, 131.9, 126.6, 123.3, 120.0, 105.1, 39.6, 33.8, 31.4, 27.5, 27.1, 26.4, 21.9 (2 C); υ_{max}/cm^{-1} 3336, 3271, 2858, 1628, 1554, 1493, 1454, 1442; *m/z* Observed 599.3190 $[M+H]^+$; Theoretical value 599.3192 $[C_{36}H_{40}F_2N_4O_2+H]^+$; yield 57%

***N,N'*-(nonane-1,9-diyl)*bis*(7-fluoro-1,2,3,4-tetrahydroacridine-9-carboxamide) (18),** white solid; ; δ_H (400 MHz, $CDCl_3$) 7.89 (dd, *J* = 9.2, 5.4 Hz, 2 H), 7.35 (td, *J* = 8.6, 2.6 Hz, 2 H), 7.27-7.22 (m, 2 H), 6.40 (t, *J* = 5.7 Hz, 2 H), 3.52 (q, *J* = 6.6 Hz, 4 H), 3.02-2.98 (m, 4 H), 2.83 (t, *J* = 5.2 Hz, 4 H), 1.91-1.85 (m, 4 H), 1.83-1.77 (m, 4 H), 1.69-1.63 (m, 4 H), 1.45-1.36 (m, 10 H); ; δ_C (100 MHz, $CDCl_3$) 167.6, 165.0 (2 C), 144.1, 139.2, 133.6, 127.3, 122.9, 121.1, 103.4, 40.6, 32.8, 29.8, 27.1, 26.4, 26.2, 22.2 (2 C); υ_{max}/cm^{-1} 3336, 2935, 2874, 1612, 1562, 1523, 1462, 1384, 1327; *m/z* Observed 613.3354 $[M+H]^+$; Theoretical value 613.3349 $[C_{37}H_{42}F_2N_4O_2+H]^+$; yield 74%

S7. Cytotoxicity Tests with the MTT Assay

MTT assay was done to look for cytotoxic compounds by screening "hits" from initial high-throughput drug screening for cytotoxic effects. Cytotoxicity was monitored by using 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT). A colorimetric reaction is used in this assay to measure the reducing potential of the cell. Viable cells will reduce the MTT reagent to a coloured formazan product. HeLa (Cervical cancer), MDA-

MB-231 (Triple negative breast cancer) and NCI H1975 (Non-small cell lung cancer) cell lines were used in this assay, which were obtained from the American Type Culture Collection (Manassas, VA).

The MTT assay is comprised of a number of crucial steps, from cell splitting to 96-well plate reading in a photometer. The below steps were followed to process the MTT assay for each type of cell line:

HeLa and MDA-MB231 cell lines were cultivated in Dulbecco's modified eagle medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 1% penicillin and streptomycin and 1% NEAA (200x) non-essential amino acids. NCI H1975 cell lines were grown in RPMI-1640 supplemented with 10% fetal bovine serum (FBS) and 1% penicillin and streptomycin. Three cells were maintained in an incubator at 37 °C with 5% CO_2.

Cells were passed when they are 70-80% confluent. In this process, a small number of confluent cells are transferred into a new vessel since a high density of rapidly dividing cells is related to cells going into senescence. Cells contained in a T-flask were taken out from the incubator and checked under a microscope (dead cells floated and appeared round-shaped, whereas growing cells were attached to the bottom surface in a rod-shaped and clustered fashion). Previous media was aspirated by using a vacuum pump (a sharp pointed pipette, 2 mL, was used for this purpose). 5 mL of DPBS was added to wash previous media fully and clean the T-flask, which was aspirated again to remove the floating dead cells as well. 1 mL of trypsin-EDTA was added to detach the growing cells and the flask was then incubated at 37 °C in a 5% CO_2 incubator for 2 minutes. 10 mL of DMEM was added to inactivate the trypsin; afterwards the total suspension was transferred into a falcon tube for centrifugation (2.5 minutes, 21 °C, 1.5 rpm). All the supernatant medium was aspirated out, leaving the cells at the bottom of the tube. Finally, 5 mL of DMEM was added and mixed properly and an appropriate amount of cell suspension transferred to a newly-labelled T-flask according to next passage time. Furthermore, an appropriate amount of DMEM was added into the same T-flask to make a total volume of 15 mL (in general, 15 mL is the optimum volume for the survival of cells in a T-flask). Lastly, the new T-flask was returned to the incubator (37 °C, 5% CO_2) for the next splitting schedule. Cells were passaged every 2 to 3 days. 70% ethanol was used to clean the fume hood, equipment, flask and pipette before starting any process.

In our experiments, 96-well polypropylene plates were used to seed cells and carry out the MTT experiments with tested compounds which are free of binding affinity for proteins or DNA, allowing complete sample recovery. These plates can withstand temperatures of -80 to +121°C. A haemocytometer was used to count cells, where a solution of cells was made with typan blue stain (10 µL cells/90 µL stain) to visualize the cells under an electron microscope. An appropriate amount of cell suspension was taken to make a dilution of cells with DMEM to confirm about 10^6 cells per well. Afterwards, a multichannel pipette was used to seed cells on to the plate, which was then returned for incubation at 37°C in a 5% CO_2 incubator (incubation time was varied from 24 – 72 hours).

During the addition of test compounds, the previous medium was aspirated out from every well by using sharp pipette tips and replaced with an equal amount (100 µL) of fresh medium and ligand of appropriate concentration, made from a 5 mM stock solution by using DMSO, which were then added onto the cell seeded plate. Lastly, the plate was returned for further incubation at 37°C in a 5% CO_2 incubator (incubation time was 72 hours).

After incubation of 72 hours, plates were processed to read and assay the data. Firstly, old medium was aspirated off from each well after the predetermined incubation period and subsequently each well was washed with 100 µL of medium (high glucose content but without phenol red). Then all medium was aspirated off from each well and 100 µL of previously made MTT/medium phenol red-free solution was added into each well. A further 4

hours of incubation was done at 37°C in a 5% CO_2 incubator and afterwards medium was aspirated off from each well and 100 µL of DMSO was added to dissolve the crystals formed. The plate was again incubated for 5 minutes at 37°C in a 5% CO_2 incubator and subsequently placed in a shaker for 5 minutes (500 rpm) to remove all air bubbles. Absorbance were then taken by an Infinite 200Pro plate reader at a 570 nm wavelength and the data was processed with the help of Tecan i-control application software.

Of note, MTT solution was prepared in a 1:10 dilution with phenol red-free medium; *e.g.*, 1 mL of MTT was added into 9 mL of phenol red-free medium. The final solution was filtered through a 0.2 µm filter and kept in the dark at 4°C. Such solutions can be stored for up to a month.

S8. ^{1}H-NMR, ^{13}C-NMR spectrum and HRMS spectrum

Compound 1

Compound 1

Acquisition Time (sec)	3.9584	*Comment*	Sample Ref KI-6(2)			*Date*	03 Feb 2012 01:33:52
Date Stamp	03 Feb 2012 01:33:52						
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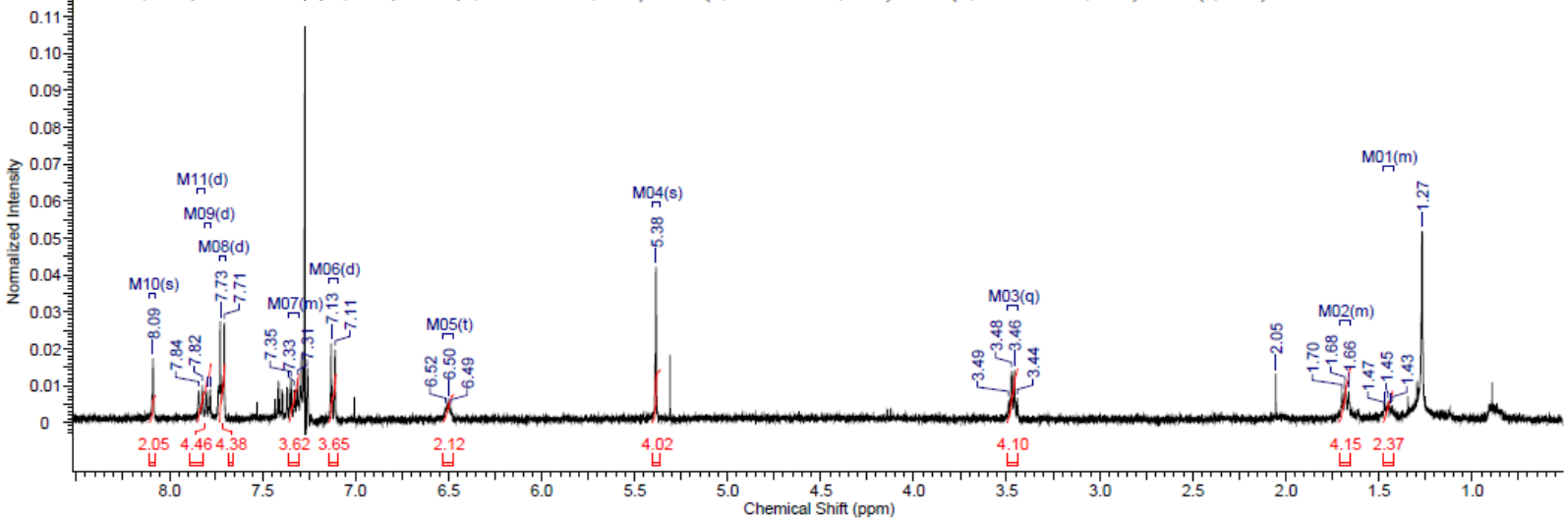
Frequency (MHz)	400.13	*Nucleus*	1H	*Number of Transients*	16	*Origin*	spect
Original Points Count	32768	*Owner*	nmr	*Points Count*	32768	*Pulse Sequence*	zg30
Receiver Gain	812.70	*SW(cyclical) (Hz)*	8278.15	*Solvent*	CHLOROFORM-d	*Spectrum Offset (Hz)*	2465.2024
Spectrum Type	STANDARD	*Sweep Width (Hz)*	8277.89	*Temperature (degree C)*	27.000		

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 1.43 - 1.48 (m, 2 H) 1.65 - 1.71 (m, 4 H) 3.47 (q, *J*=6.32 Hz, 4 H) 5.38 (s, 4 H) 6.50 (t, *J*=6.06 Hz, 2 H) 7.12 (d, *J*=8.59 Hz, 4 H) 7.30 - 7.36 (m, 4 H) 7.72 (d, *J*=8.34 Hz, 4 H) 7.83 (d, *J*=8.59 Hz, 2 H) 7.79 (d, *J*=7.33 Hz, 2 H) 8.09 (s, 2 H)

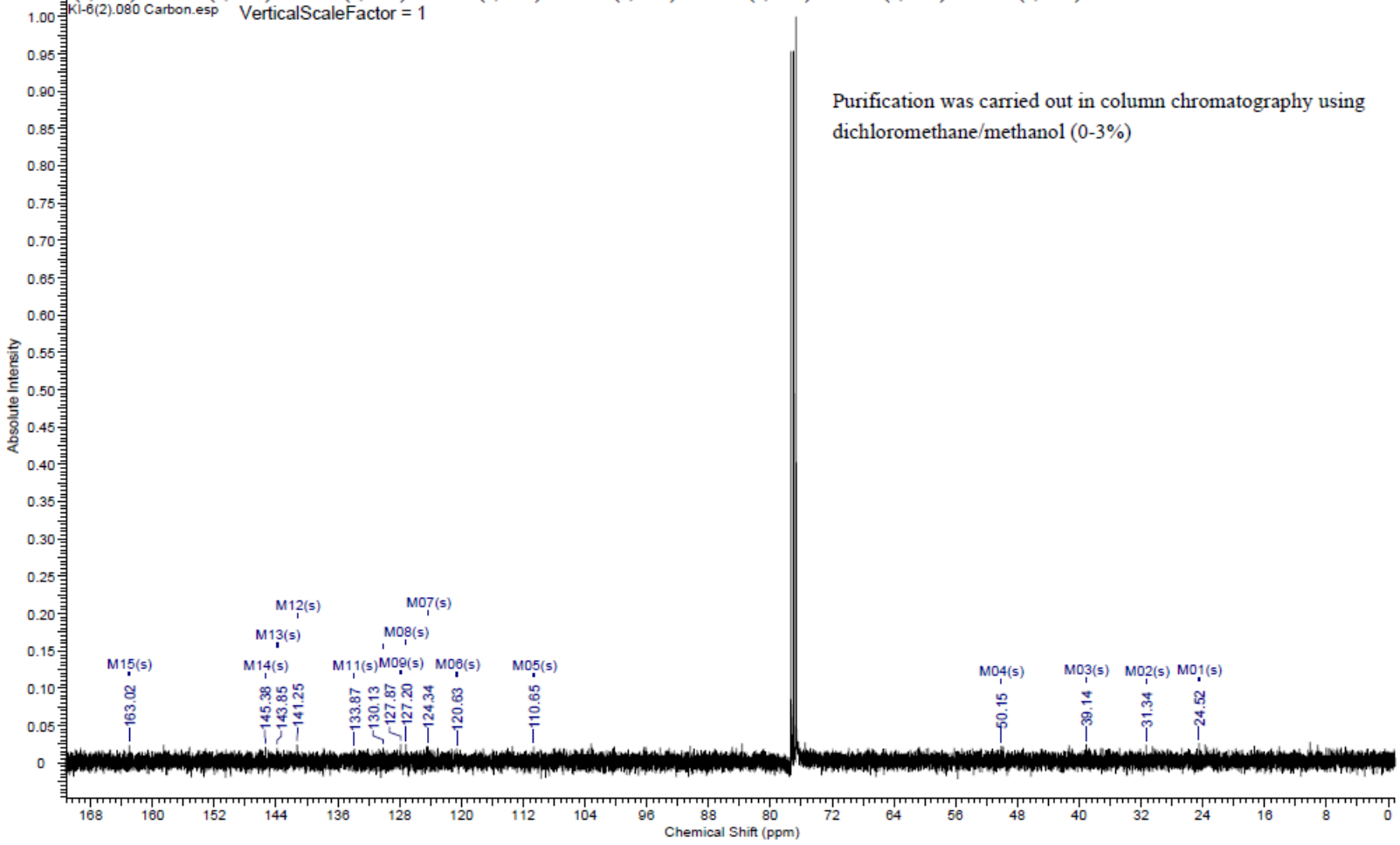


No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	1.45	2	m	-	M01	-	[1.43 .. 1.48]
2	1.68	4	m	-	M02	-	[1.65 .. 1.71]
3	3.47	4	q	6.32	M03	-	[3.44 .. 3.50]
4	5.38	4	s	-	M04	-	[5.36 .. 5.41]
5	6.50	2	t	6.06	M05	-	[6.47 .. 6.53]
6	7.12	4	d	8.59	M06	M08	[7.10 .. 7.14]

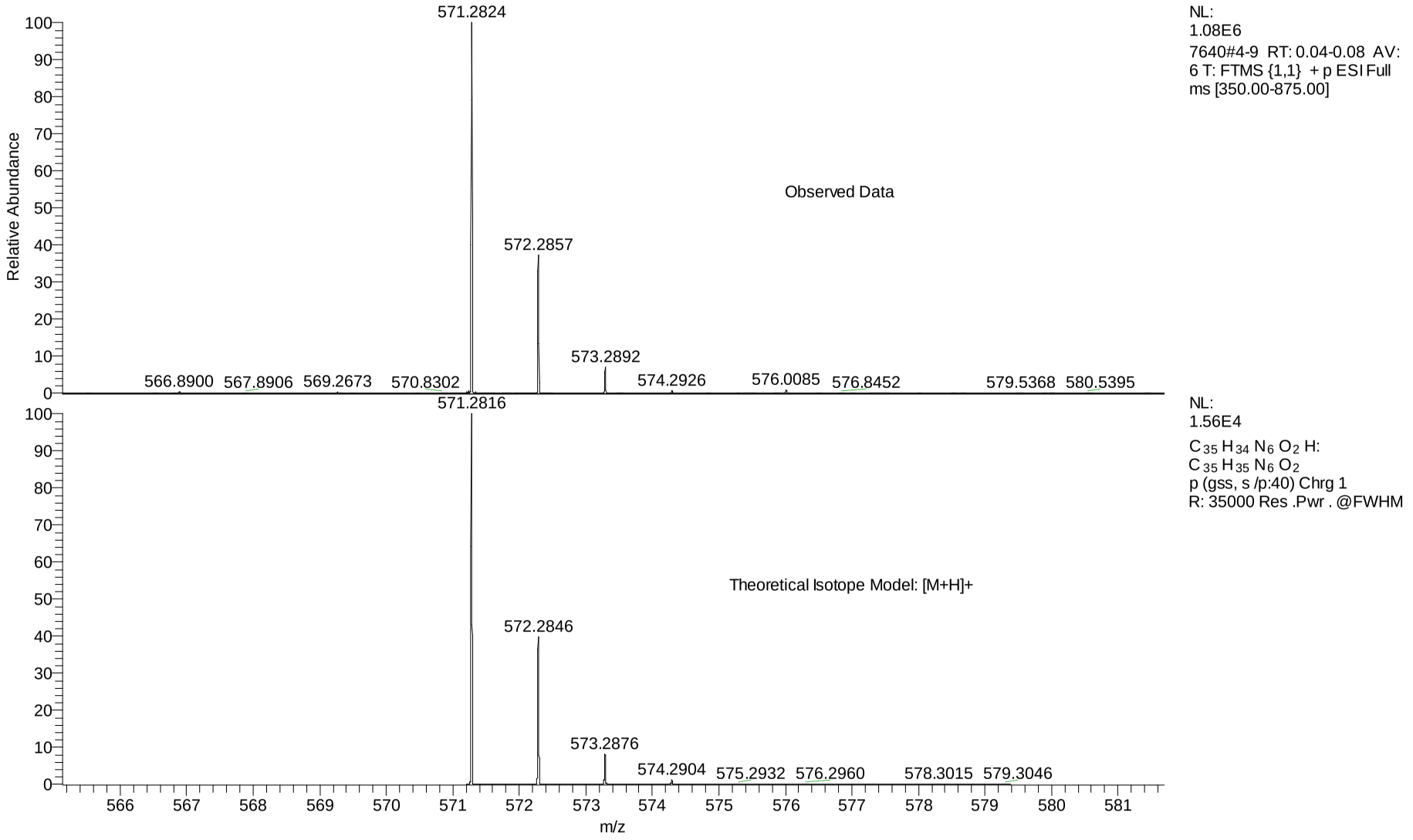
No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
7	7.33	4	m	-	M07	-	[7.30 .. 7.36]
8	7.72	4	d	8.34	M08	M06	[7.70 .. 7.73]
9	7.79	2	d	7.33	M09	-	[7.77 .. 7.81]
10	7.83	2	d	8.59	M11	-	[7.81 .. 7.85]
11	8.09	2	s	-	M10	-	[8.07 .. 8.11]

Compound 1

^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 24.52 (s, 1 C) 31.34 (s, 1 C) 39.14 (s, 1 C) 50.15 (s, 1 C) 110.65 (s, 1 C) 120.63 (s, 1 C) 124.34 (s, 1 C) 127.20 (s, 1 C) 127.87 (s, 1 C) 130.13 (s, 1 C) 133.87 (s, 1 C) 141.25 (s, 1 C) 143.85 (s, 1 C) 145.38 (s, 1 C) 163.02 (s, 1 C)



Purification was carried out in column chromatography using dichloromethane/methanol (0-3%)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Relative Abundance
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C35 H35 N6 O2
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Theoretical Isotope Model: [M+H]+
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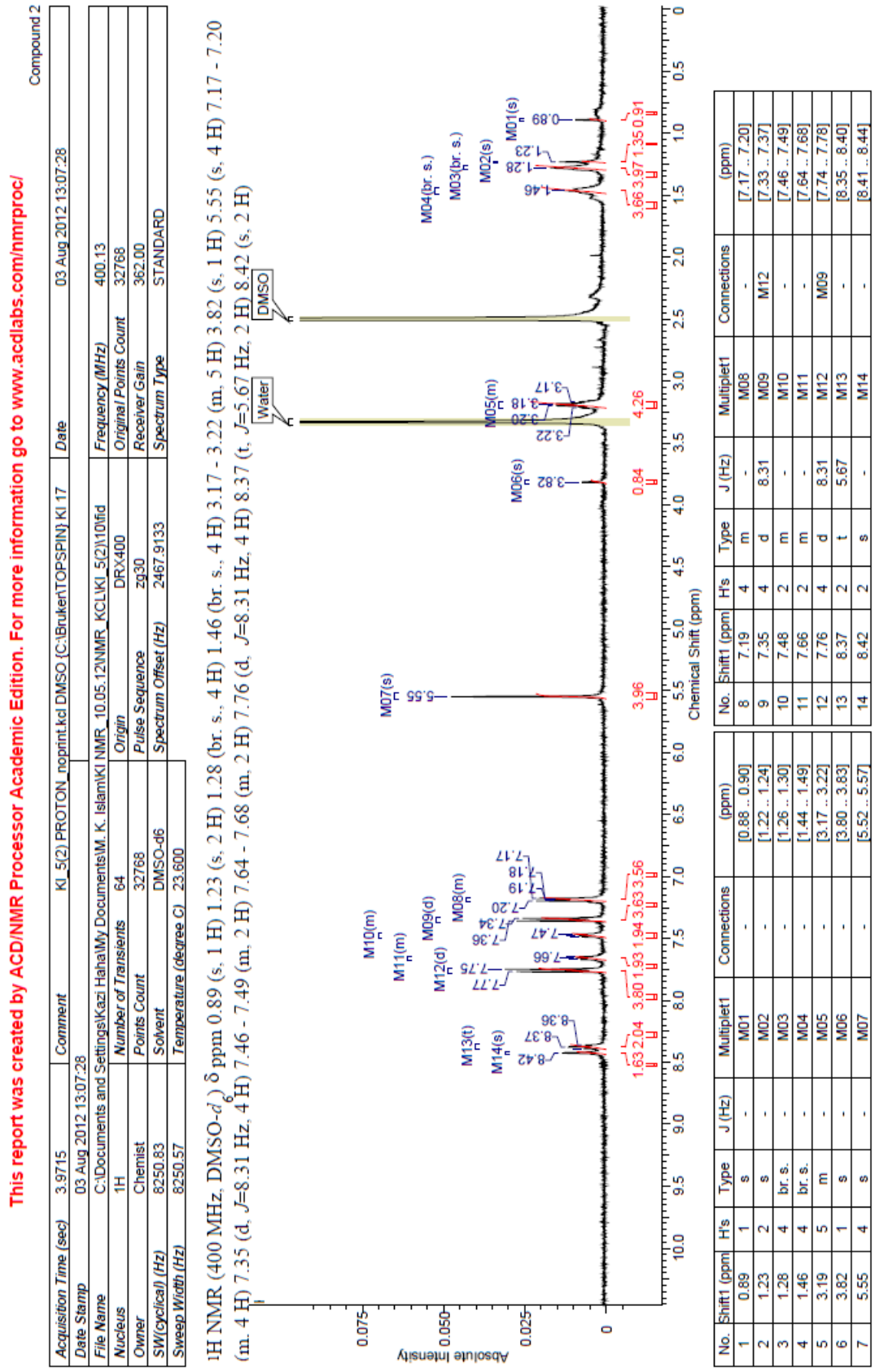
m/z

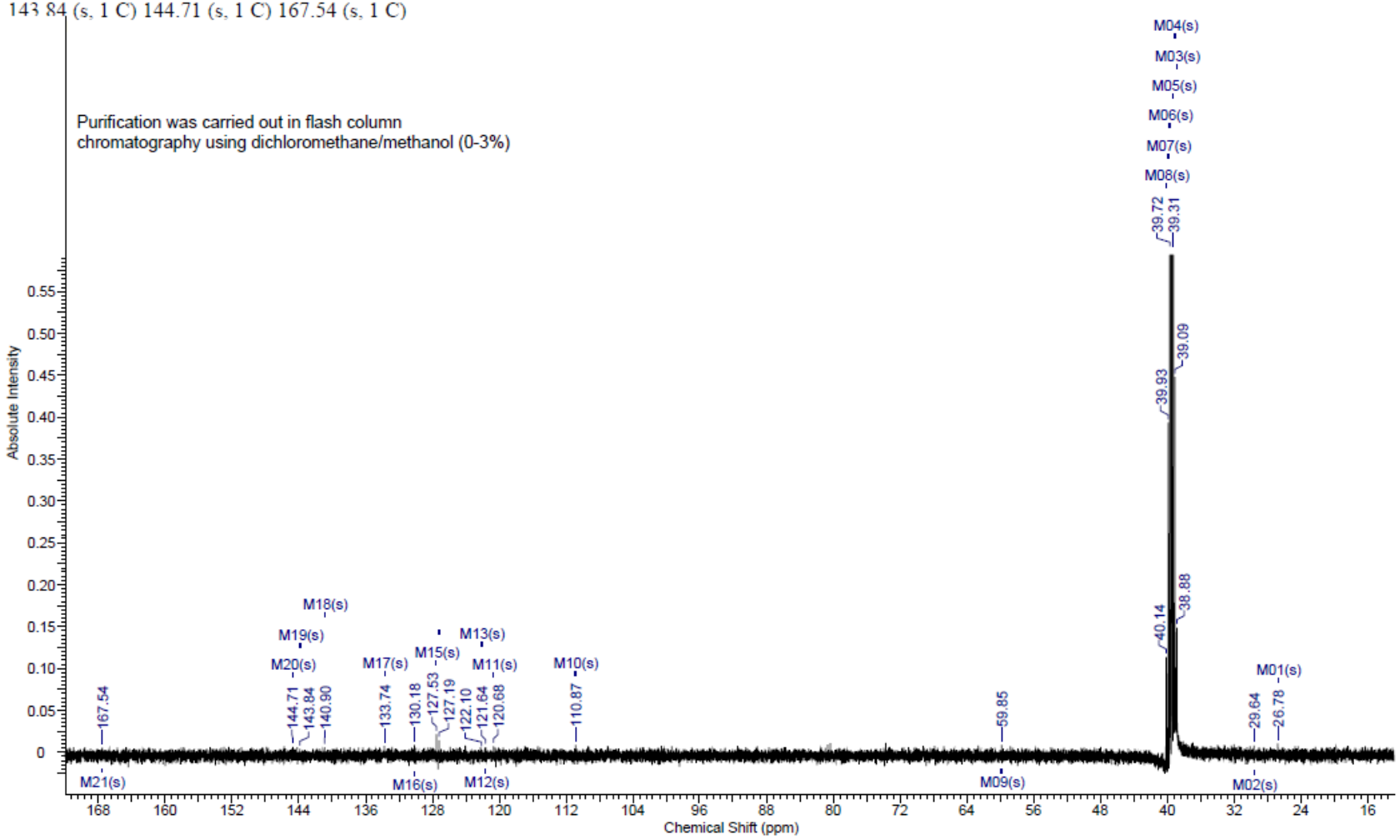
Compound 2

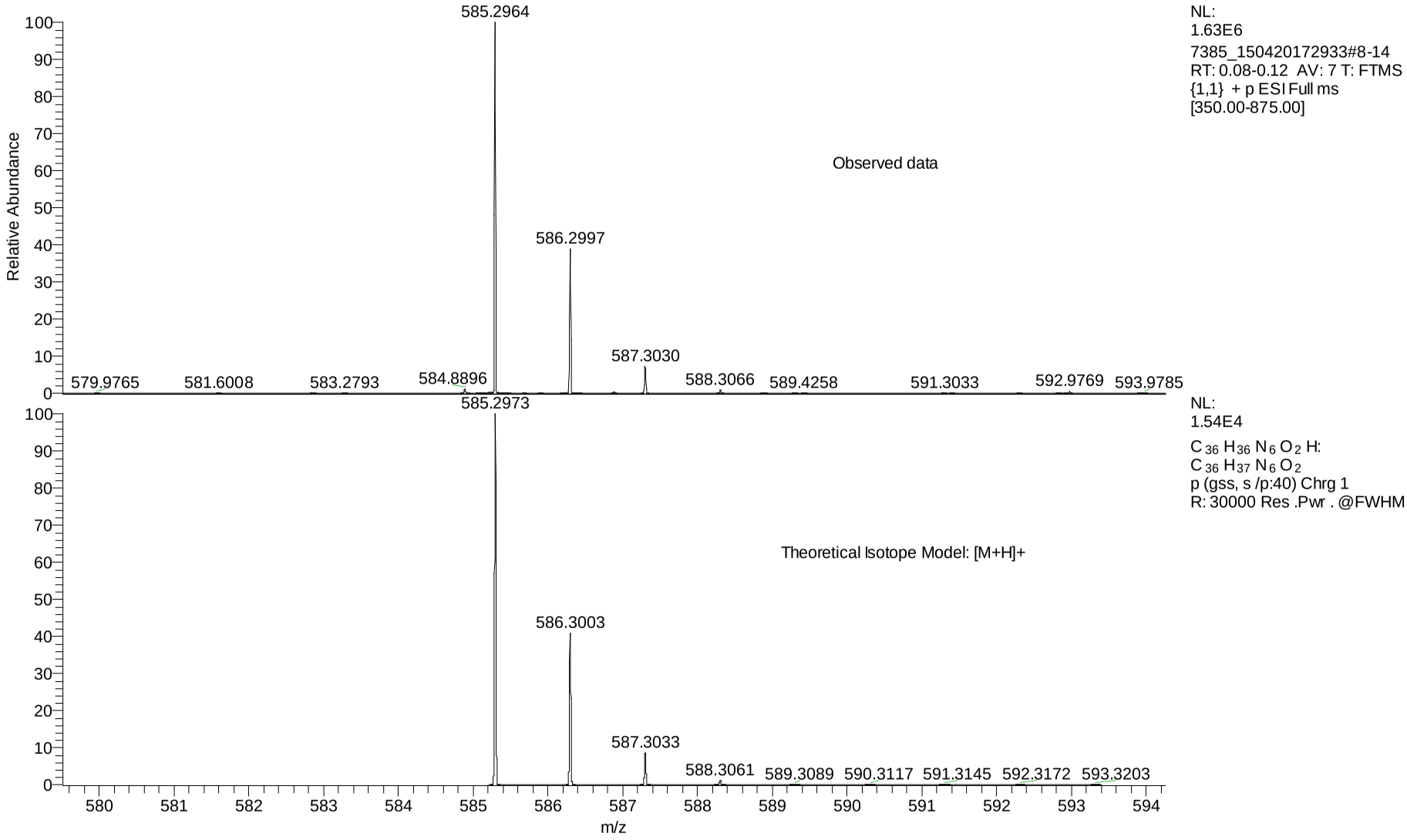


No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	0.89	1	s	-	M01	-	[0.88 .. 0.90]
2	1.23	2	s	-	M02	-	[1.22 .. 1.24]
3	1.28	4	br. s.	-	M03	-	[1.26 .. 1.30]
4	1.46	4	br. s.	-	M04	-	[1.44 .. 1.49]
5	3.19	5	m	-	M05	-	[3.17 .. 3.22]
6	3.82	1	s	-	M06	-	[3.80 .. 3.83]
7	5.55	4	s	-	M07	-	[5.52 .. 5.57]
8	7.19	4	m	-	M08	-	[7.17 .. 7.20]
9	7.35	4	d	8.31	M09	M12	[7.33 .. 7.37]
10	7.48	2	m	-	M10	-	[7.46 .. 7.49]
11	7.66	2	m	-	M11	-	[7.64 .. 7.68]
12	7.76	4	d	8.31	M12	M09	[7.74 .. 7.78]
13	8.37	2	t	5.67	M13	-	[8.35 .. 8.40]
14	8.42	2	s	-	M14	-	[8.41 .. 8.44]

Compound 2

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 26.78 (s, 1 C) 29.64 (s, 1 C) 38.88 (s, 1 C) 39.09 (s, 1 C) 39.31 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 59.85 (s, 1 C) 110.87 (s, 1 C) 120.68 (s, 1 C) 121.64 (s, 1 C) 122.10 (s, 1 C) 127.19 (s, 1 C) 127.53 (s, 1 C) 130.18 (s, 1 C) 133.74 (s, 1 C) 140.90 (s, 1 C) 143.84 (s, 1 C) 144.71 (s, 1 C) 167.54 (s, 1 C)

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Relative Abundance
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C 36 H 37 N 6 O 2
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R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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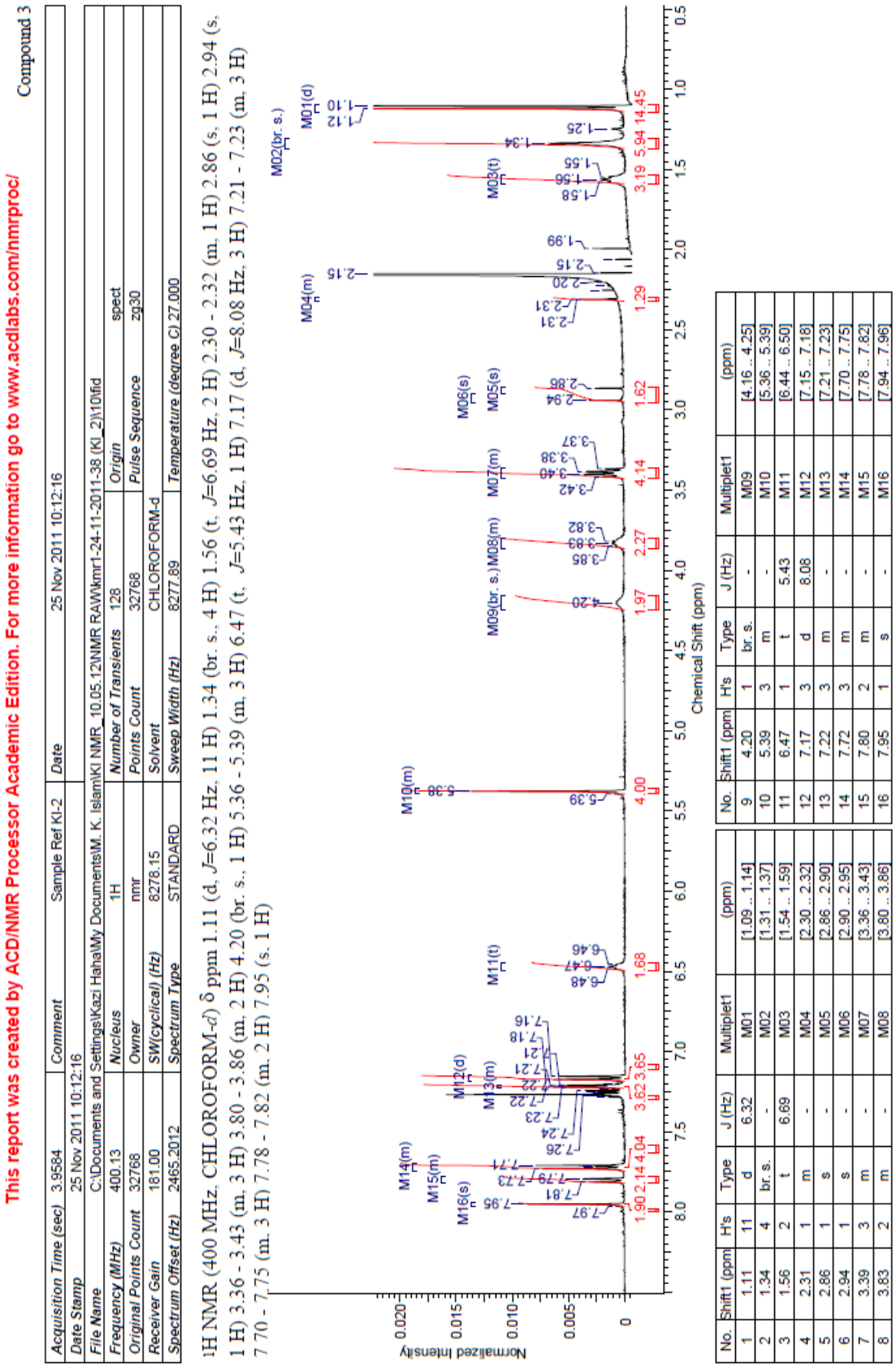
m/z

Compound 3



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Spectrum Offset (Hz)	2465.2012	Spectrum Type	STANDARD	Sweep Width (Hz)	8277.89	Temperature (degree C)	27.000

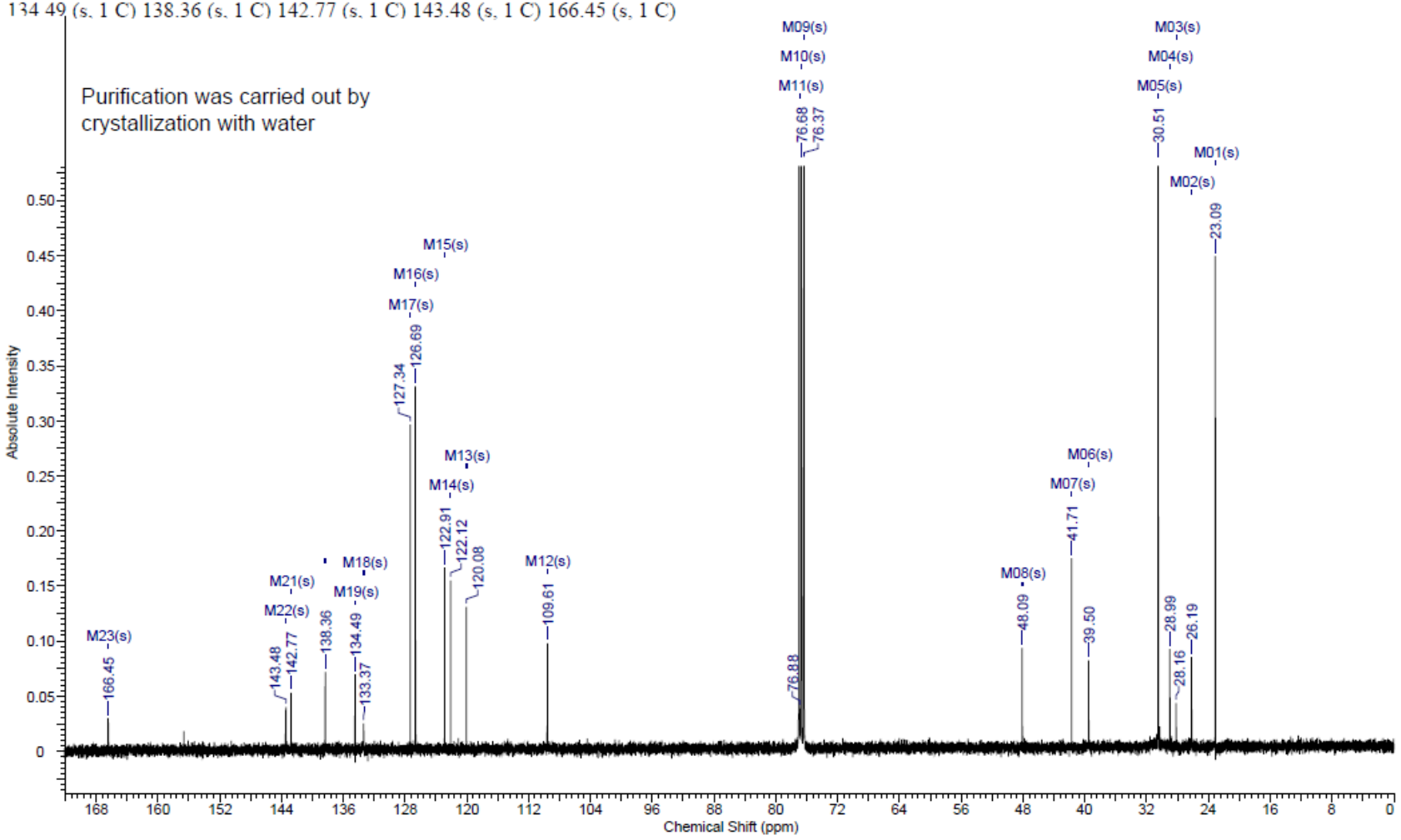
^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 1.11 (d, *J*=6.32 Hz, 11 H) 1.34 (br. s., 4 H) 1.56 (t, *J*=6.69 Hz, 2 H) 2.30 - 2.32 (m, 1 H) 2.86 (s, 1 H) 2.94 (s, 1 H) 3.36 - 3.43 (m, 3 H) 3.80 - 3.86 (m, 2 H) 4.20 (br. s., 1 H) 5.36 - 5.39 (m, 3 H) 6.47 (t, *J*=5.43 Hz, 1 H) 7.17 (d, *J*=8.08 Hz, 3 H) 7.21 - 7.23 (m, 3 H) 7.70 - 7.75 (m, 3 H) 7.78 - 7.82 (m, 2 H) 7.95 (s, 1 H)

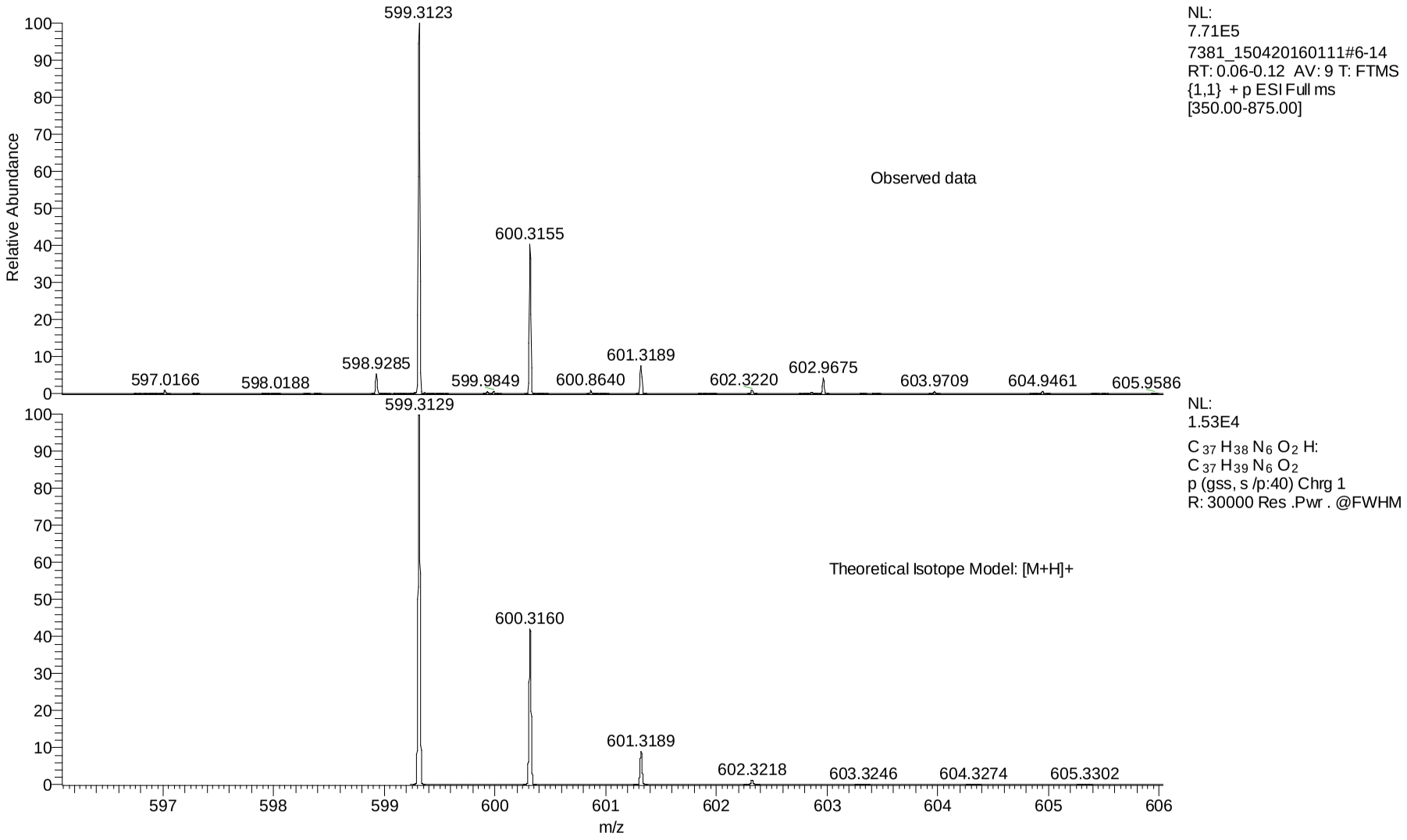
No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	(ppm)
1	1.11	11	d	6.32	M01	[1.09 .. 1.14]
2	1.34	4	br. s.	-	M02	[1.31 .. 1.37]
3	1.56	2	t	6.69	M03	[1.54 .. 1.59]
4	2.31	1	m	-	M04	[2.30 .. 2.32]
5	2.86	1	s	-	M05	[2.86 .. 2.90]
6	2.94	1	s	-	M06	[2.90 .. 2.95]
7	3.39	3	m	-	M07	[3.36 .. 3.43]
8	3.83	2	m	-	M08	[3.80 .. 3.86]

No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	(ppm)
9	4.20	1	br. s.	-	M09	[4.16 .. 4.25]
10	5.39	3	m	-	M10	[5.36 .. 5.39]
11	6.47	1	t	5.43	M11	[6.44 .. 6.50]
12	7.17	3	d	8.08	M12	[7.15 .. 7.18]
13	7.22	3	m	-	M13	[7.21 .. 7.23]
14	7.72	3	m	-	M14	[7.70 .. 7.75]
15	7.80	2	m	-	M15	[7.78 .. 7.82]
16	7.95	1	s	-	M16	[7.94 .. 7.96]

Compound 3

^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 23.09 (s, 1 C) 26.19 (s, 1 C) 28.16 (s, 1 C) 28.99 (s, 1 C) 30.51 (s, 1 C) 39.50 (s, 1 C) 41.71 (s, 1 C) 48.09 (s, 1 C) 76.37 (s, 1 C) 76.68 (s, 1 C) 76.88 (s, 1 C) 109.61 (s, 1 C) 120.08 (s, 1 C) 122.12 (s, 1 C) 122.91 (s, 1 C) 126.69 (s, 1 C) 127.34 (s, 1 C) 133.37 (s, 1 C) 134.49 (s, 1 C) 138.36 (s, 1 C) 142.77 (s, 1 C) 143.48 (s, 1 C) 166.45 (s, 1 C)

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[350.00-875.00]
Observed data
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599.9849
600.8640
602.3220
603.9709
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Relative Abundance
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NL:
1.53E4
C 37 H 38 N 6 O 2 H:
C 37 H 39 N 6 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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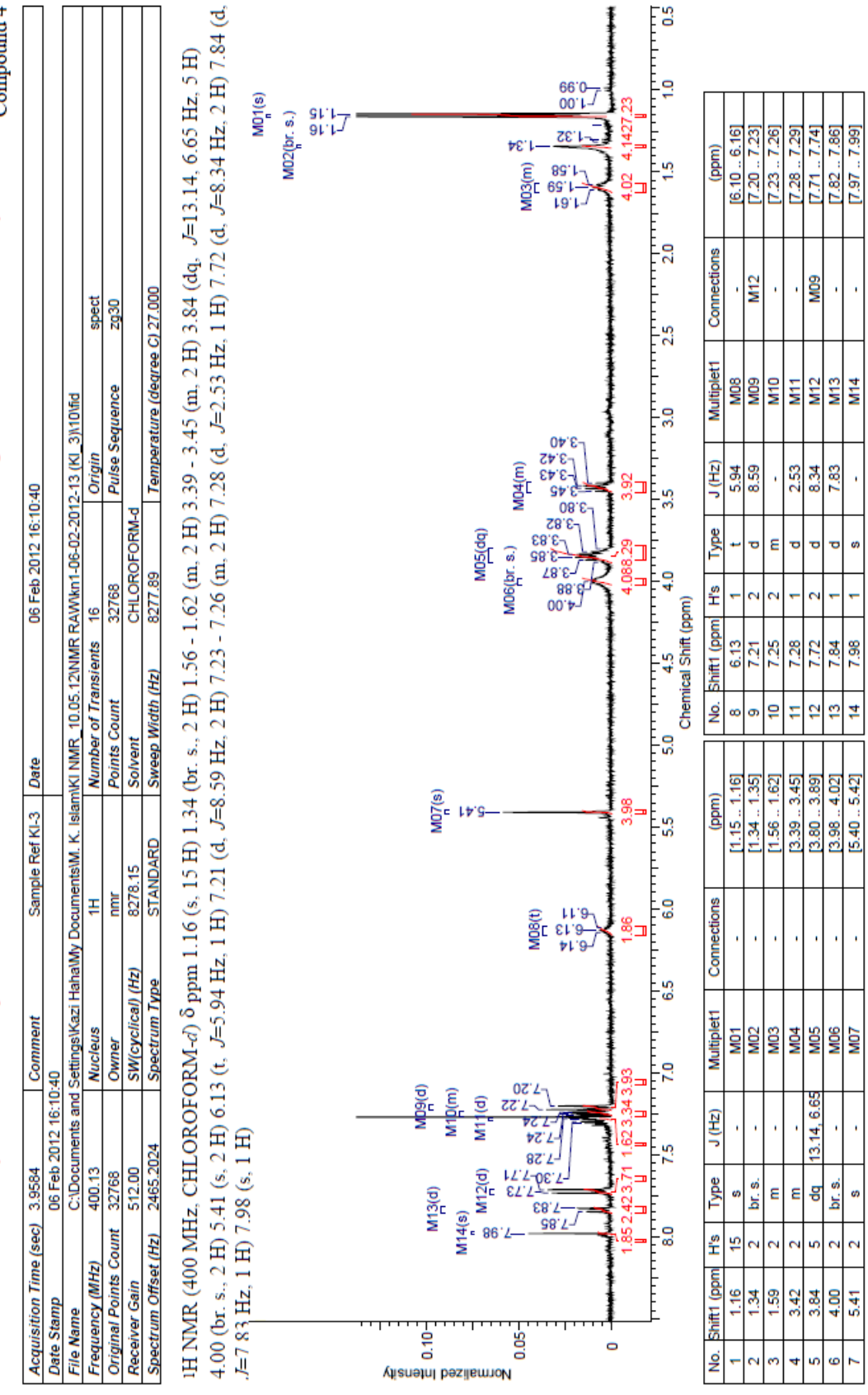
602.3218
603.3246
604.3274
605.3302
m/z

Compound 4



No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
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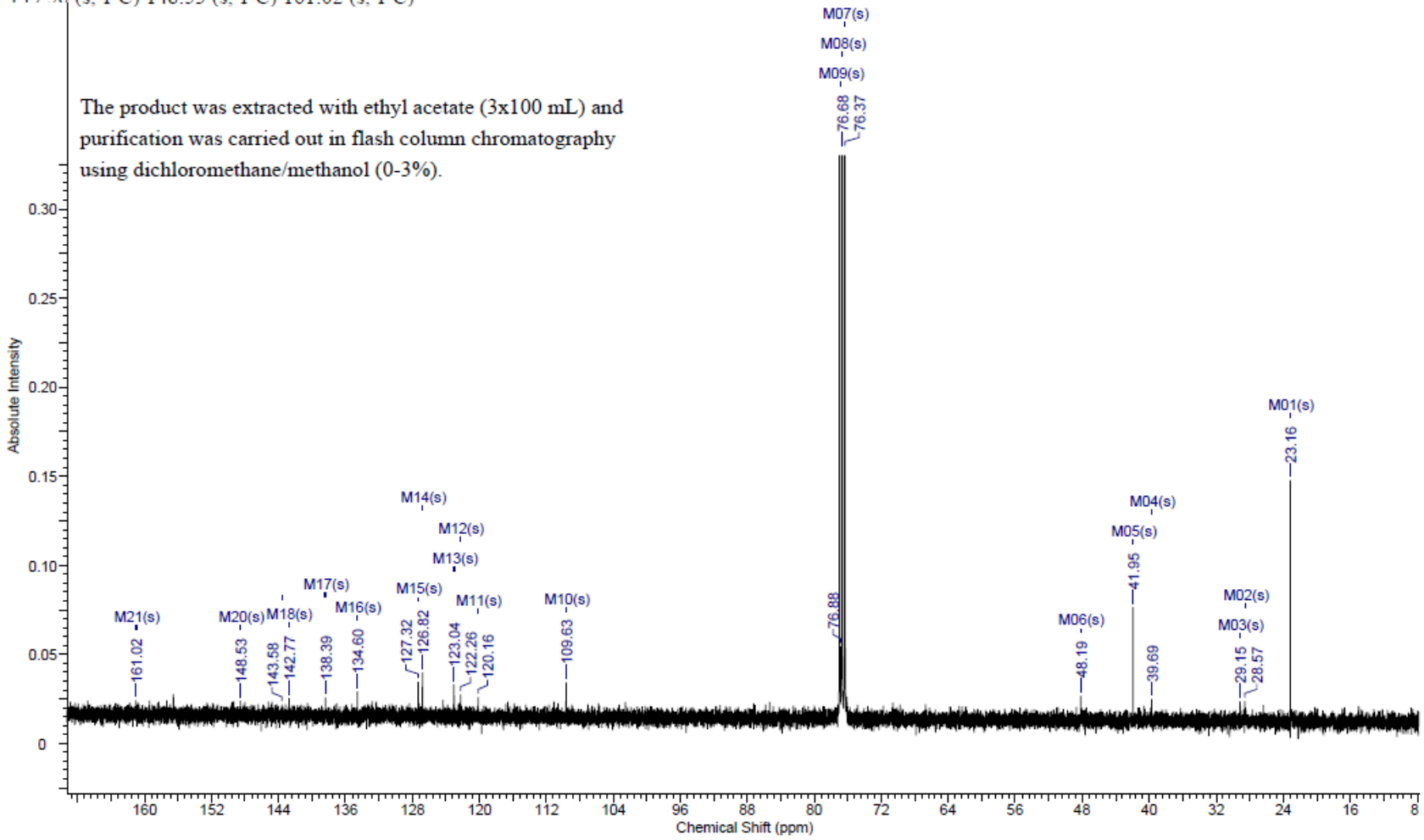
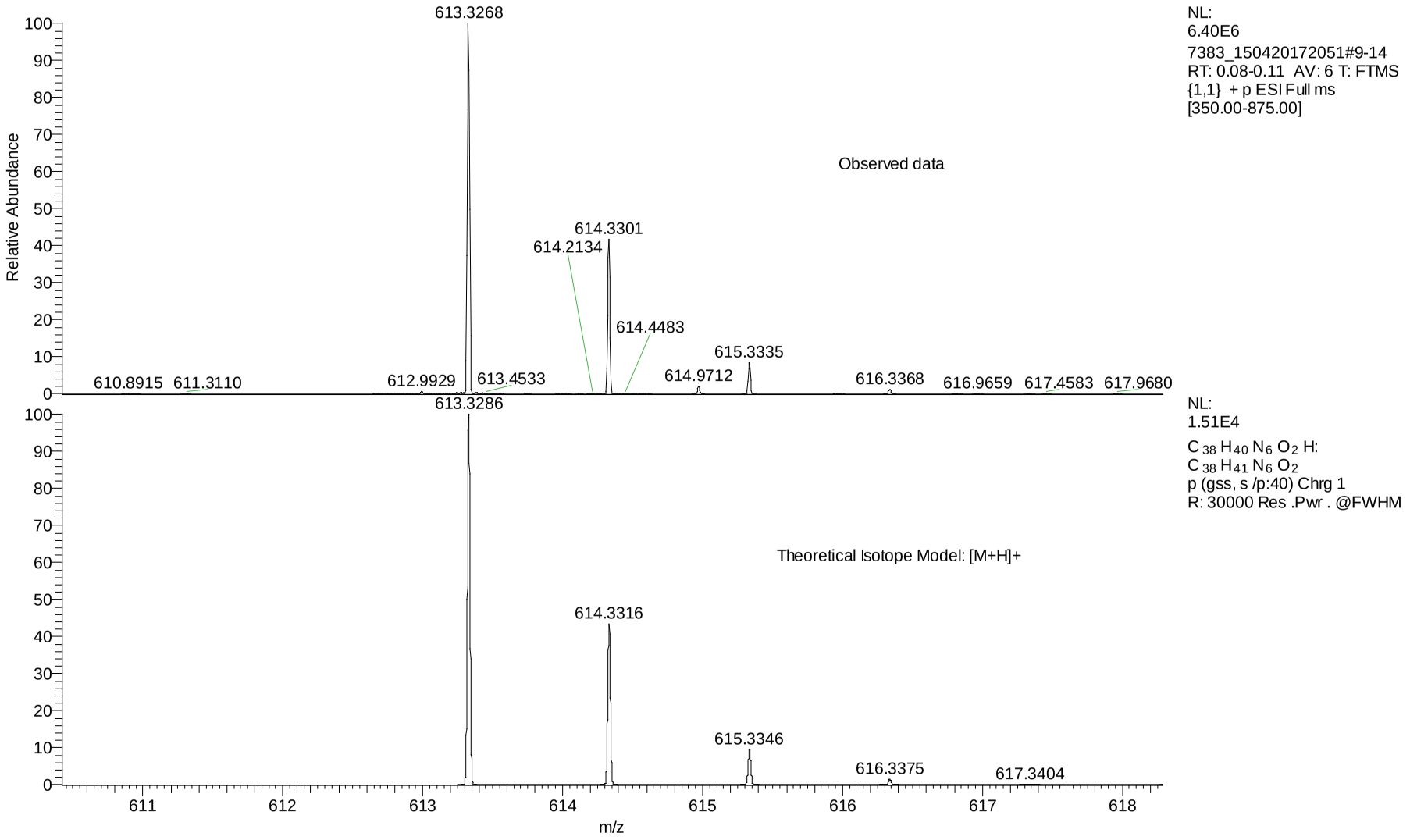
2	1.34	2	br. s.	-	M02	-	[1.34 .. 1.35]
3	1.59	2	m	-	M03	-	[1.56 .. 1.62]
4	3.42	2	m	-	M04	-	[3.39 .. 3.45]
5	3.84	5	dq	13.14, 6.65	M05	-	[3.80 .. 3.89]
6	4.00	2	br. s.	-	M06	-	[3.98 .. 4.02]
7	5.41	2	s	-	M07	-	[5.40 .. 5.42]
8	6.13	1	t	5.94	M08	-	[6.10 .. 6.16]
9	7.21	2	d	8.59	M09	M12	[7.20 .. 7.23]
10	7.25	2	m	-	M10	-	[7.23 .. 7.26]
11	7.28	1	d	2.53	M11	-	[7.28 .. 7.29]
12	7.72	2	d	8.34	M12	M09	[7.71 .. 7.74]
13	7.84	1	d	7.83	M13	-	[7.82 .. 7.86]
14	7.98	1	s	-	M14	-	[7.97 .. 7.99]

Compound 4

^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 23.16 (s, 1 C) 28.57 (s, 1 C) 29.15 (s, 1 C) 39.69 (s, 1 C) 41.95 (s, 1 C) 48.19 (s, 1 C) 76.37 (s, 1 C) 76.68 (s, 1 C) 76.88 (s, 1 C) 109.63 (s, 1 C) 120.16 (s, 1 C) 122.26 (s, 1 C) 123.04 (s, 1 C) 126.82 (s, 1 C) 127.32 (s, 1 C) 134.60 (s, 1 C) 138.39 (s, 1 C) 142.77 (s, 1 C) 143.58 (s, 1 C) 148.53 (s, 1 C) 161.02 (s, 1 C)

The product was extracted with ethyl acetate (3x100 mL) and purification was carried out in flash column chromatography using dichloromethane/methanol (0-3%).

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7383_150420172051#9-14
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{1,1} + p ESI Full ms
[350.00-875.00]
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614.4483
615.3335
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NL:
1.51E4
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R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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616.3375
617.3404
Relative Abundance
m/z
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40
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10
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612
613
614
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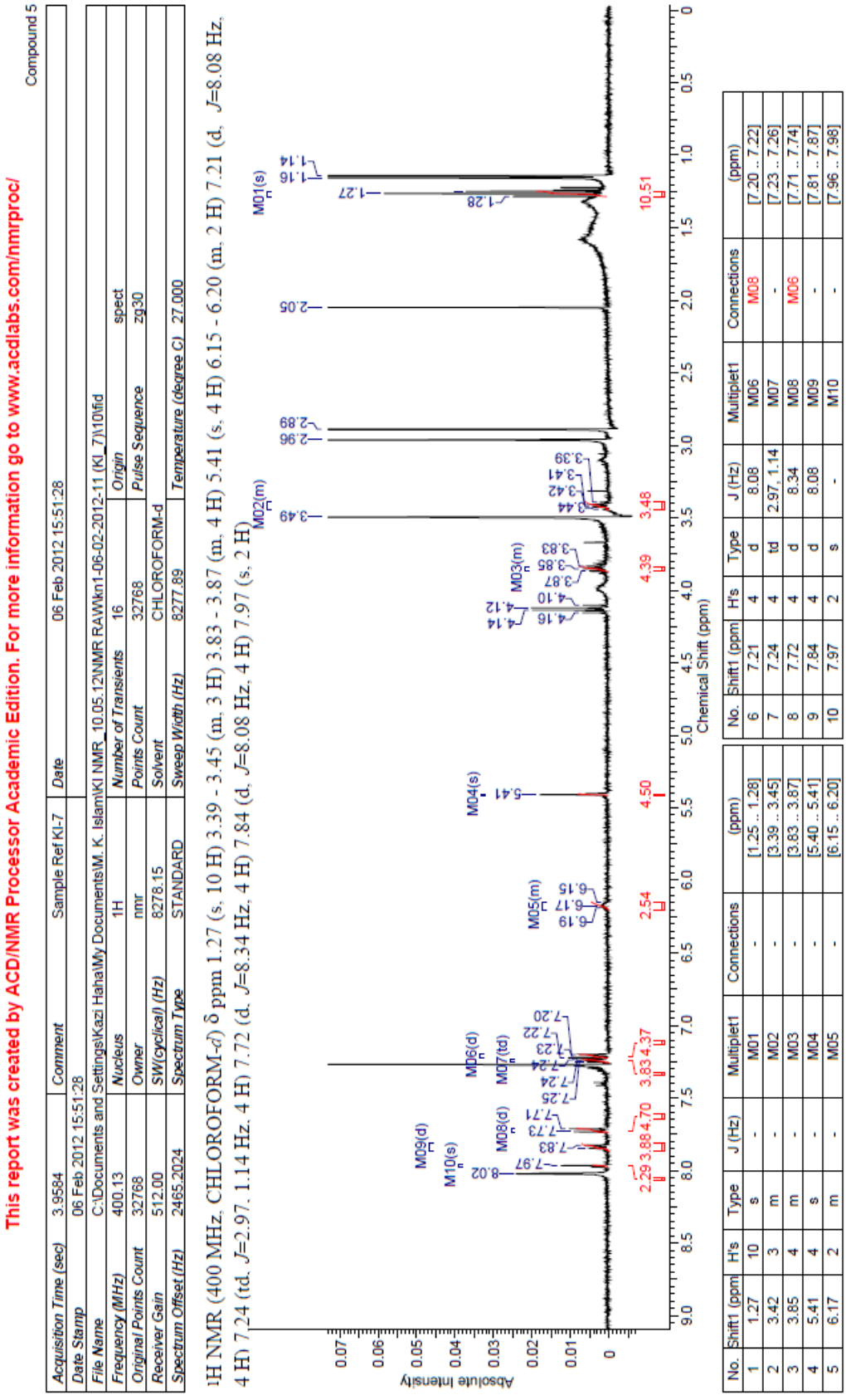
616
617
618

Compound 5


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 5
Acquisition Time (sec) 3.9584
Comment
Sample Ref KI-7
Date 06 Feb 2012 15:51:28
Date Stamp 06 Feb 2012 15:51:28
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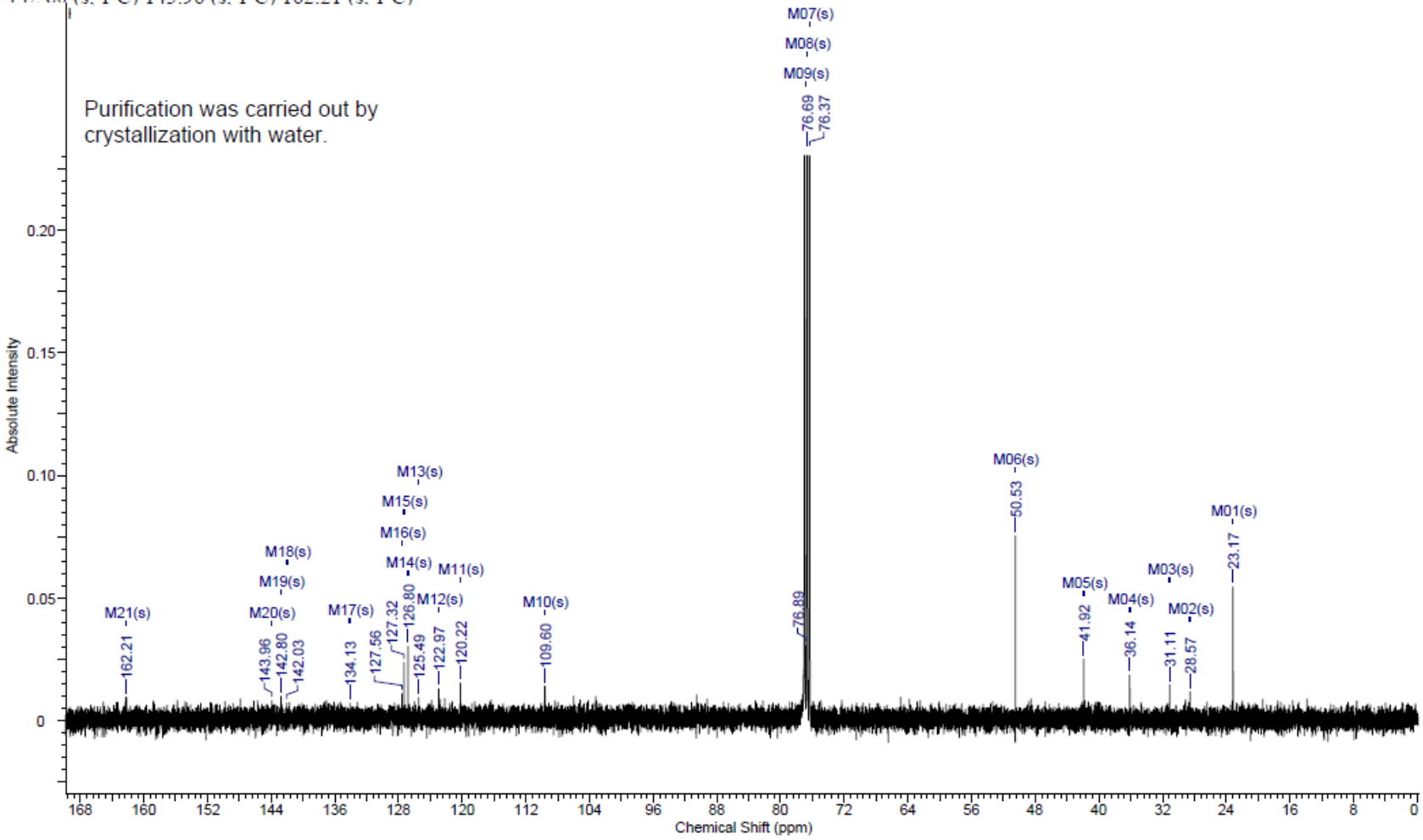
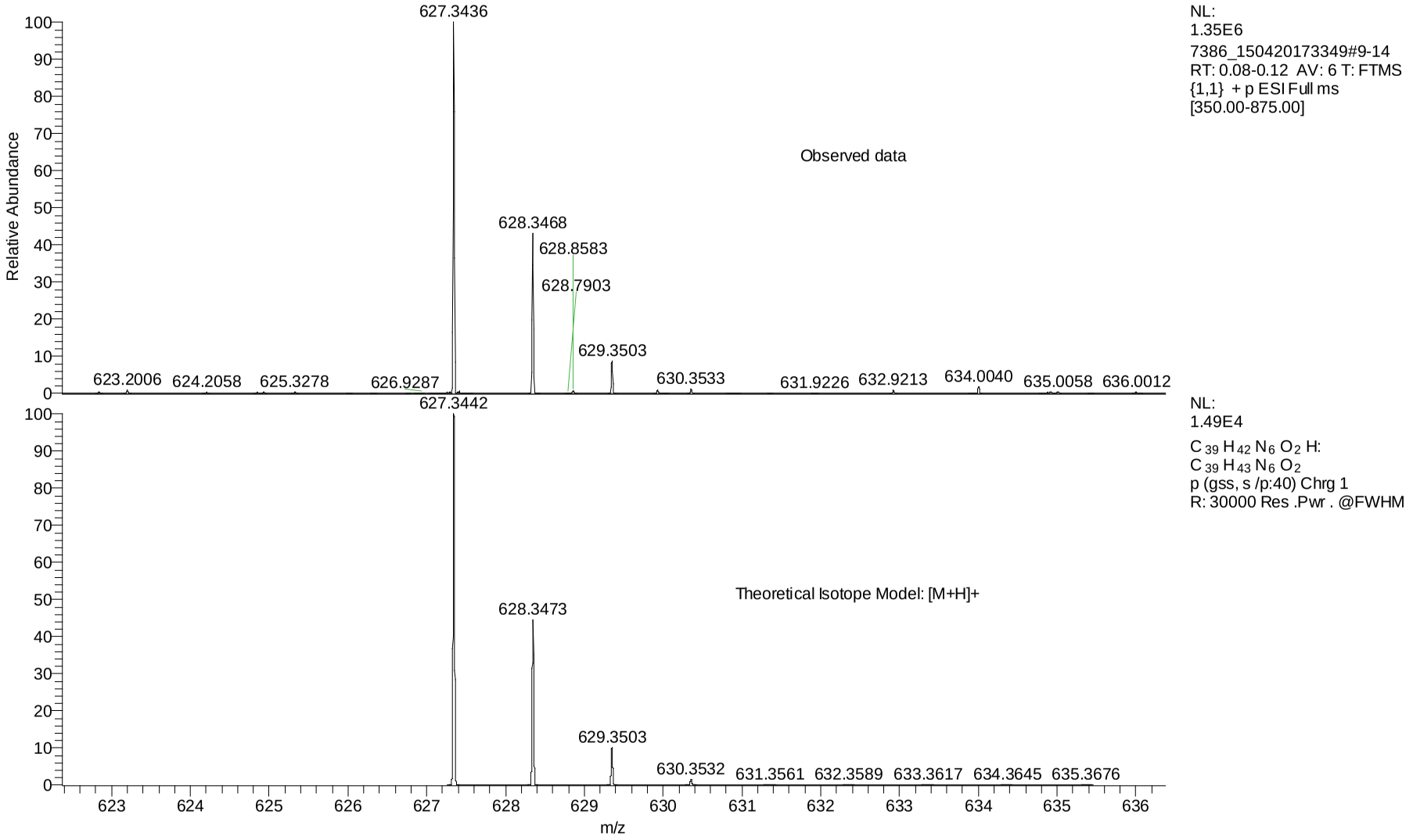
Nucleus 1H
Number of Transients 16
Origin spect
Original Points Count 32768
Owner nmr
Points Count 32768
Pulse Sequence zg30
Receiver Gain 512.00
SW(cyclical) (Hz) 8278.15
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 2465.2024
Spectrum Type STANDARD
Sweep Width (Hz) 8277.89
Temperature (degree C) 27.000
1H NMR (400 MHz, CHLOROFORM-d) δ ppm 1.27 (s, 10 H) 3.39 - 3.45 (m, 3 H) 3.83 - 3.87 (m, 4 H) 5.41 (s, 4 H) 6.15 - 6.20 (m, 2 H) 7.21 (d, J=8.08 Hz, 4 H) 7.24 (td, J=2.97, 1.14 Hz, 4 H) 7.72 (d, J=8.34 Hz, 4 H) 7.84 (d, J=8.08 Hz, 4 H) 7.97 (s, 2 H)
Absolute Intensity
Chemical Shift (ppm)
M01(s)
M02(m)
M03(m)
M04(s)
M05(m)
M06(d)
M07(td)
M08(d)
M09(d)
M10(s)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
1 1.27 10 s - M01 - [1.25 .. 1.28]
2 3.42 3 m - M02 - [3.39 .. 3.45]
3 3.85 4 m - M03 - [3.83 .. 3.87]
4 5.41 4 s - M04 - [5.40 .. 5.41]
5 6.17 2 m - M05 - [6.15 .. 6.20]
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
6 7.21 4 d 8.08 M06 M08 [7.20 .. 7.22]
7 7.24 4 td 2.97, 1.14 M07 - [7.23 .. 7.26]
8 7.72 4 d 8.34 M08 M06 [7.71 .. 7.74]
9 7.84 4 d 8.08 M09 - [7.81 .. 7.87]
10 7.97 2 s - M10 - [7.96 .. 7.98]

Compound 5

^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 23.17 (s, 1 C) 28.57 (s, 1 C) 31.11 (s, 1 C) 36.14 (s, 1 C) 41.92 (s, 1 C) 50.53 (s, 1 C) 76.37 (s, 1 C) 76.69 (s, 1 C) 76.89 (s, 1 C) 109.60 (s, 1 C) 120.22 (s, 1 C) 122.97 (s, 1 C) 125.49 (s, 1 C) 126.80 (s, 1 C) 127.32 (s, 1 C) 127.56 (s, 1 C) 134.13 (s, 1 C) 142.03 (s, 1 C) 142.80 (s, 1 C) 143.96 (s, 1 C) 162.21 (s, 1 C)

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7386_150420173349#9-14
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{1,1} + p ESI Full ms
[350.00-875.00]
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628.7903
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623.2006
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631.9226
632.9213
634.0040
635.0058
636.0012
Relative Abundance
627.3442
NL:
1.49E4
C 39 H 42 N 6 O 2 H:
C 39 H 43 N 6 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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633.3617
634.3645
635.3676
m/z

Acquisition Time (sec)	3.9715	*Comment*	KI-4 PROTON_noprint.kcl DMSO {C:\Bruker\TOPSPIN} KI 42				
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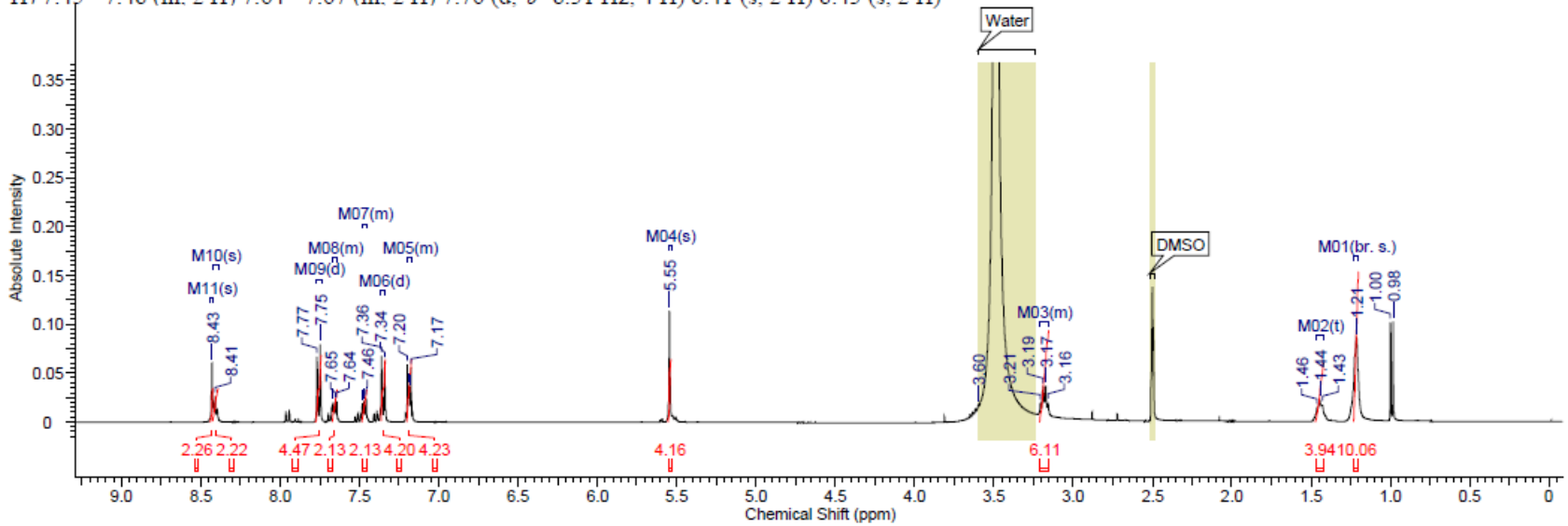
File Name	D:\KI NMR\nmr\KI_20141125\10\fid			*Frequency (MHz)*	400.13	*Nucleus*	1H
Number of Transients	512	*Origin*	DRX400	*Original Points Count*	32768	*Owner*	Chemist
Points Count	32768	*Pulse Sequence*	zg30	*Receiver Gain*	71.80	*SW(cyclical) (Hz)*	8250.83
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	2468.1650	*Spectrum Type*	STANDARD	*Sweep Width (Hz)*	8250.57
Temperature (degree C)	20.100						

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.21 (br. s., 10 H) 1.44 (t, *J*=6.42 Hz, 4 H) 3.15 - 3.21 (m, 6 H) 5.55 (s, 4 H) 7.17 - 7.20 (m, 4 H) 7.35 (d, *J*=8.31 Hz, 4 H) 7.45 - 7.48 (m, 2 H) 7.64 - 7.67 (m, 2 H) 7.76 (d, *J*=8.31 Hz, 4 H) 8.41 (s, 2 H) 8.43 (s, 2 H)

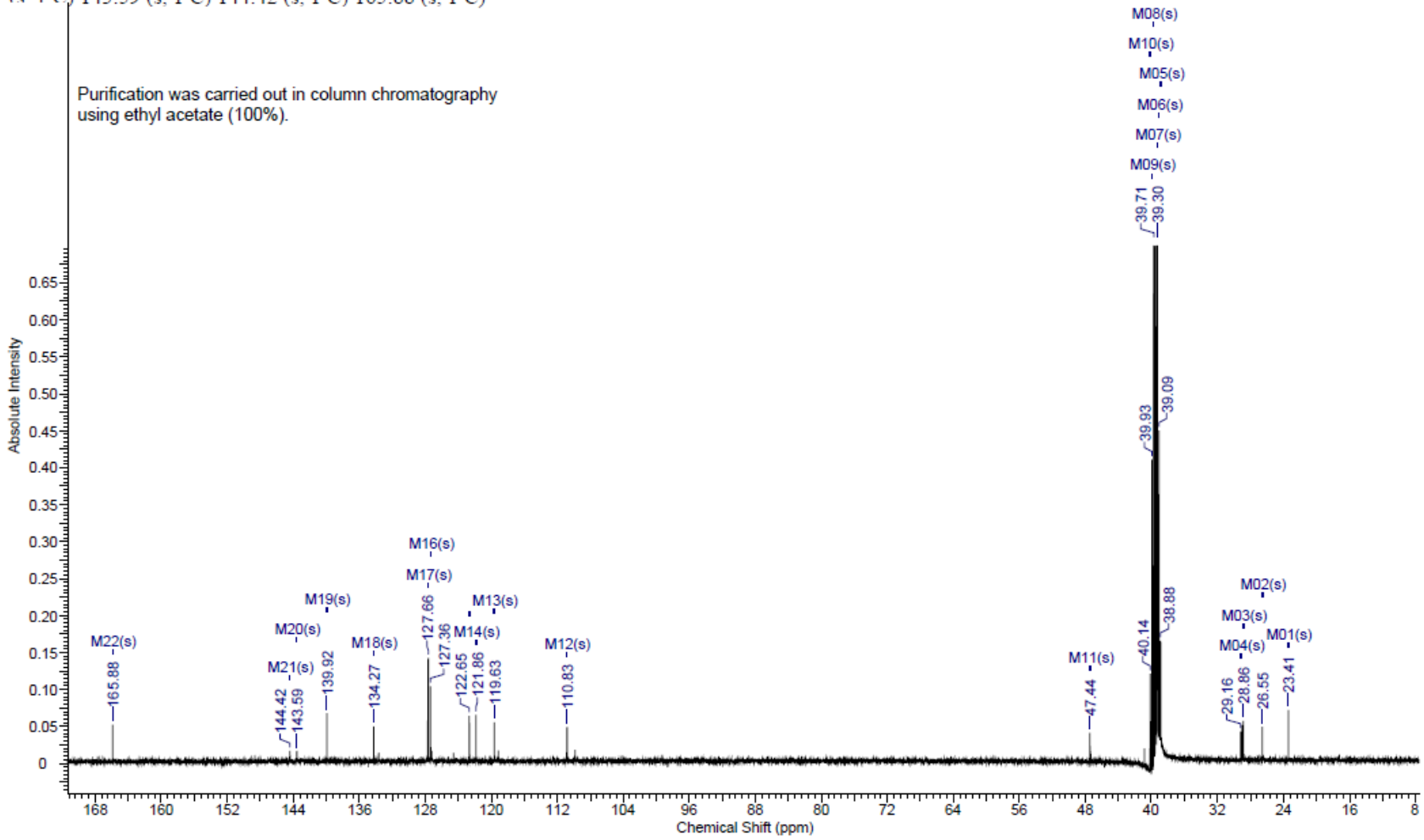


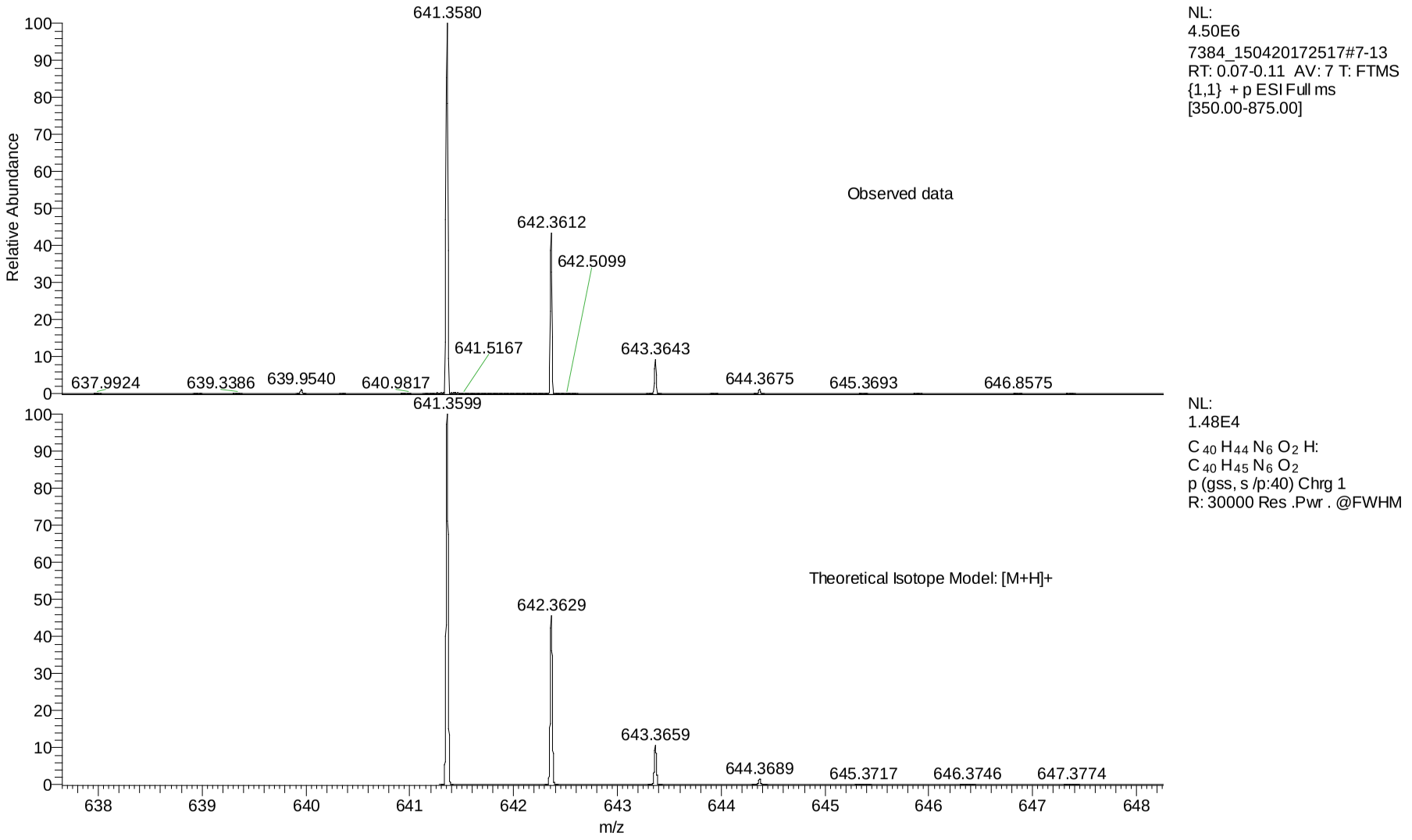
No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	1.21	10	br. s.	-	M01	-	[1.20 .. 1.23]
2	1.44	4	t	6.42	M02	-	[1.42 .. 1.47]
3	3.18	6	m	-	M03	-	[3.15 .. 3.21]
4	5.55	4	s	-	M04	-	[5.54 .. 5.55]
5	7.19	4	m	-	M05	-	[7.17 .. 7.20]
6	7.35	4	d	8.31	M06	M09	[7.34 .. 7.36]

No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
7	7.47	2	m	-	M07	-	[7.45 .. 7.48]
8	7.65	2	m	-	M08	-	[7.64 .. 7.67]
9	7.76	4	d	8.31	M09	M06	[7.74 .. 7.78]
10	8.41	2	s	-	M10	-	[8.39 .. 8.42]
11	8.43	2	s	-	M11	-	[8.42 .. 8.44]

Compound 6

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 23.41 (s, 1 C) 26.55 (s, 1 C) 28.86 (s, 1 C) 29.16 (s, 1 C) 38.88 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.71 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 47.44 (s, 1 C) 110.83 (s, 1 C) 119.63 (s, 1 C) 121.86 (s, 1 C) 122.65 (s, 1 C) 127.36 (s, 1 C) 127.66 (s, 1 C) 134.27 (s, 1 C) 139.92 (s, 1 C) 143.59 (s, 1 C) 144.42 (s, 1 C) 165.88 (s, 1 C)

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646.8575
Observed data
NL:
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7384_150420172517#7-13
RT: 0.07-0.11 AV: 7 T: FTMS
{1,1} + p ESI Full ms
[350.00-875.00]
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642.3629
643.3659
644.3689
645.3717
646.3746
647.3774
Theoretical Isotope Model: [M+H]+
NL:
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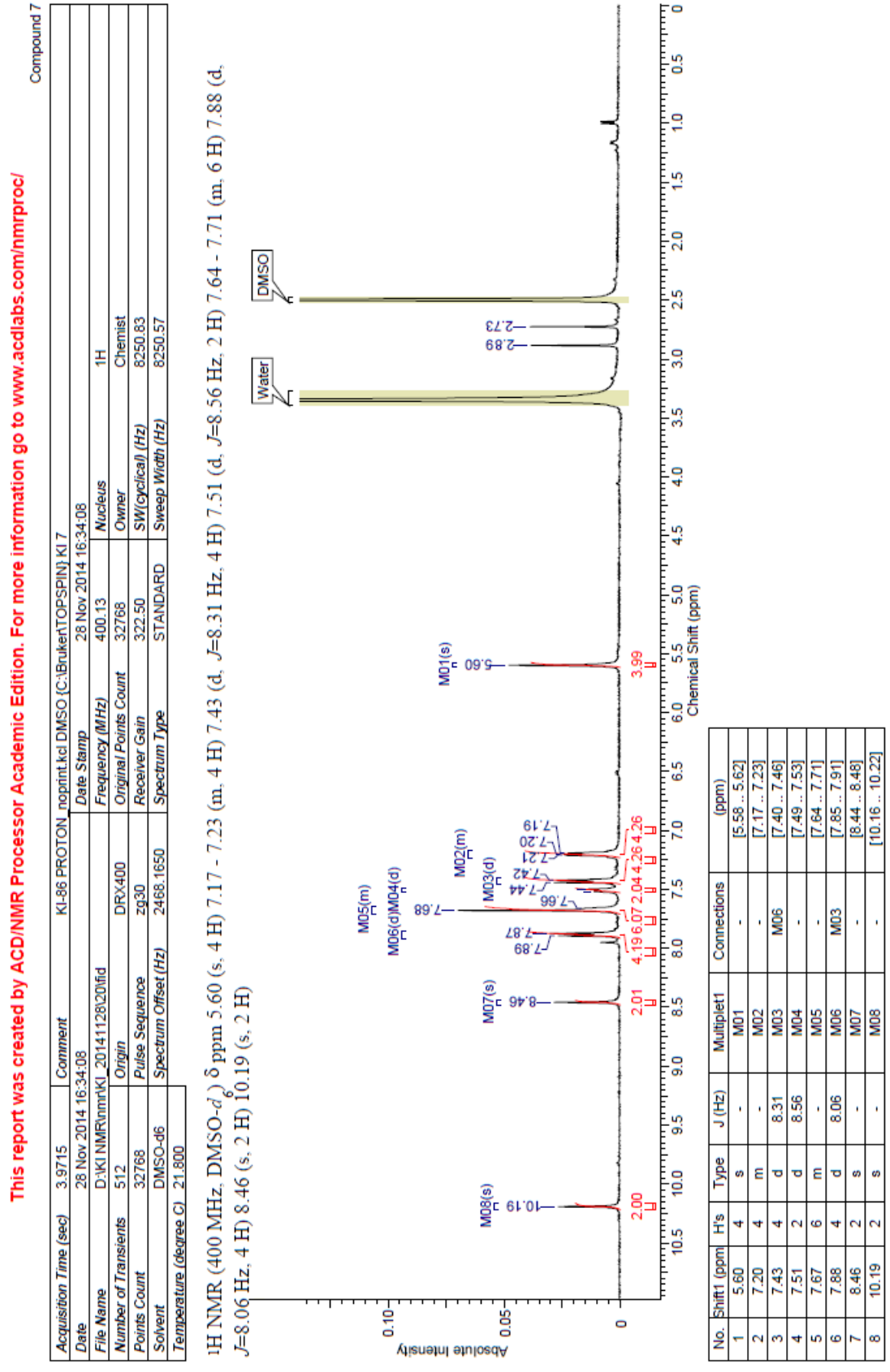
C 40 H 45 N 6 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Relative Abundance
m/z

Compound 7

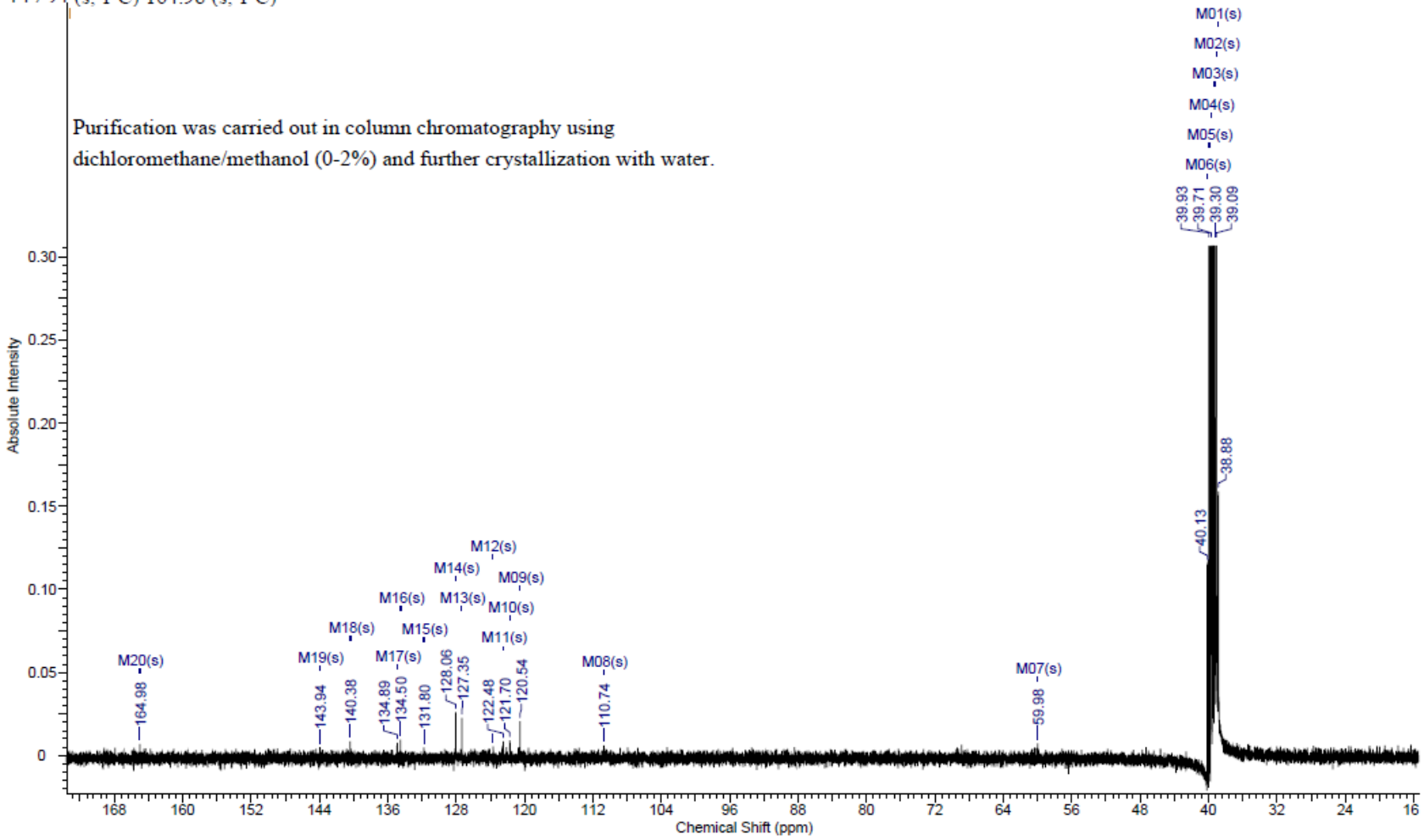


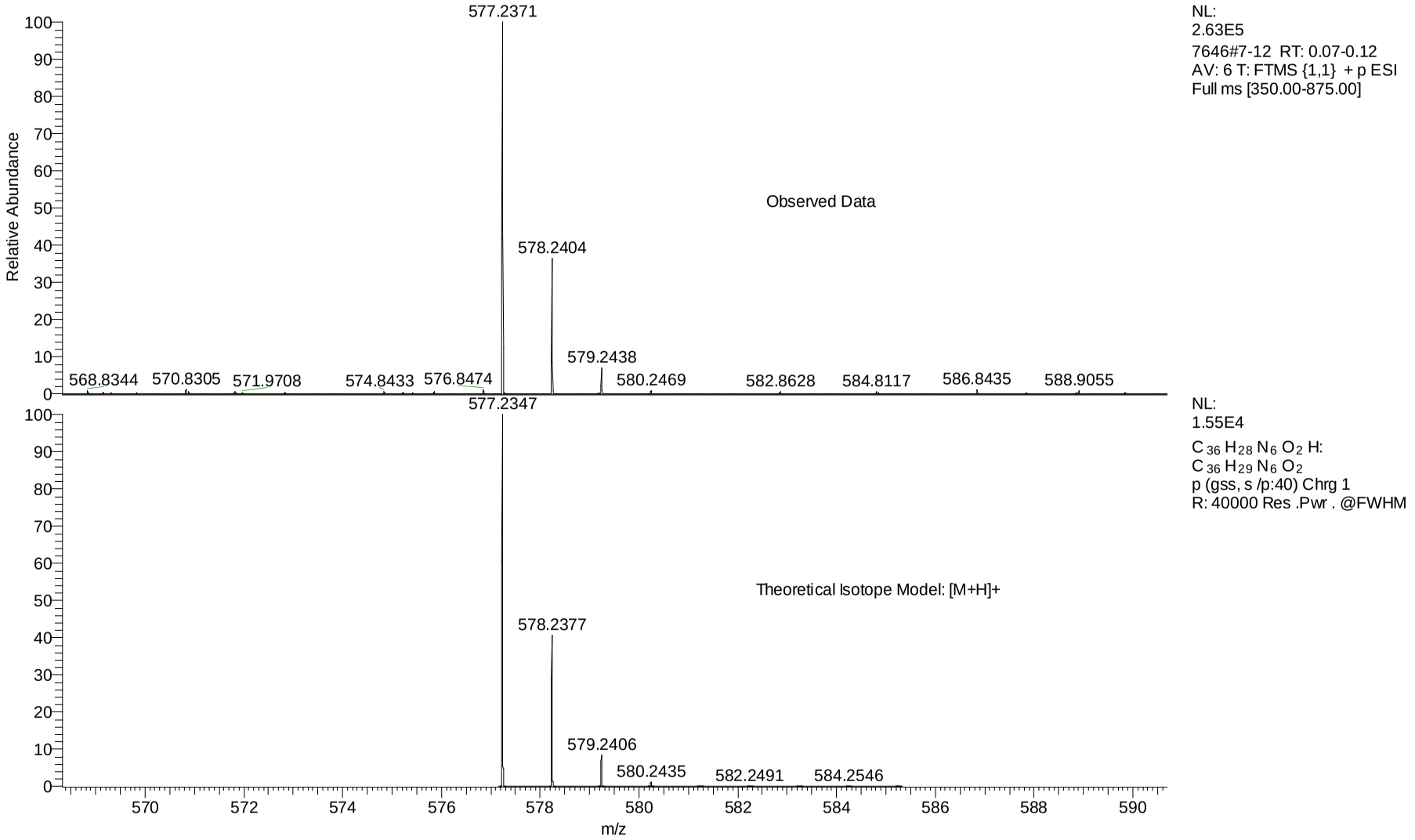
No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	5.60	4	s	-	M01	-	[5.58 .. 5.62]
2	7.20	4	m	-	M02	-	[7.17 .. 7.23]
3	7.43	4	d	8.31	M03	M06	[7.40 .. 7.46]
4	7.51	2	d	8.56	M04	-	[7.49 .. 7.53]
5	7.67	6	m	-	M05	-	[7.64 .. 7.71]
6	7.88	4	d	8.06	M06	M03	[7.85 .. 7.91]
7	8.46	2	s	-	M07	-	[8.44 .. 8.48]
8	10.19	2	s	-	M08	-	[10.16 .. 10.22]

Compound 7

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 38.88 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.71 (s, 1 C) 39.93 (s, 1 C) 40.13 (s, 1 C) 59.98 (s, 1 C) 110.74 (s, 1 C) 120.54 (s, 1 C) 121.70 (s, 1 C) 122.48 (s, 1 C) 123.70 (s, 1 C) 127.35 (s, 1 C) 128.06 (s, 1 C) 131.80 (s, 1 C) 134.50 (s, 1 C) 134.89 (s, 1 C) 140.38 (s, 1 C) 143.94 (s, 1 C) 164.98 (s, 1 C)

Purification was carried out in column chromatography using dichloromethane/methanol (0-2%) and further crystallization with water.

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AV: 6 T: FTMS {1,1} + p ESI
Full ms [350.00-875.00]
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580.2469
582.8628
584.8117
586.8435
588.9055
577.2347
NL:
1.55E4
C 36 H 28 N 6 O 2 H:
C 36 H 29 N 6 O 2
p (gss, s /p:40) Chrg 1
R: 40000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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580.2435
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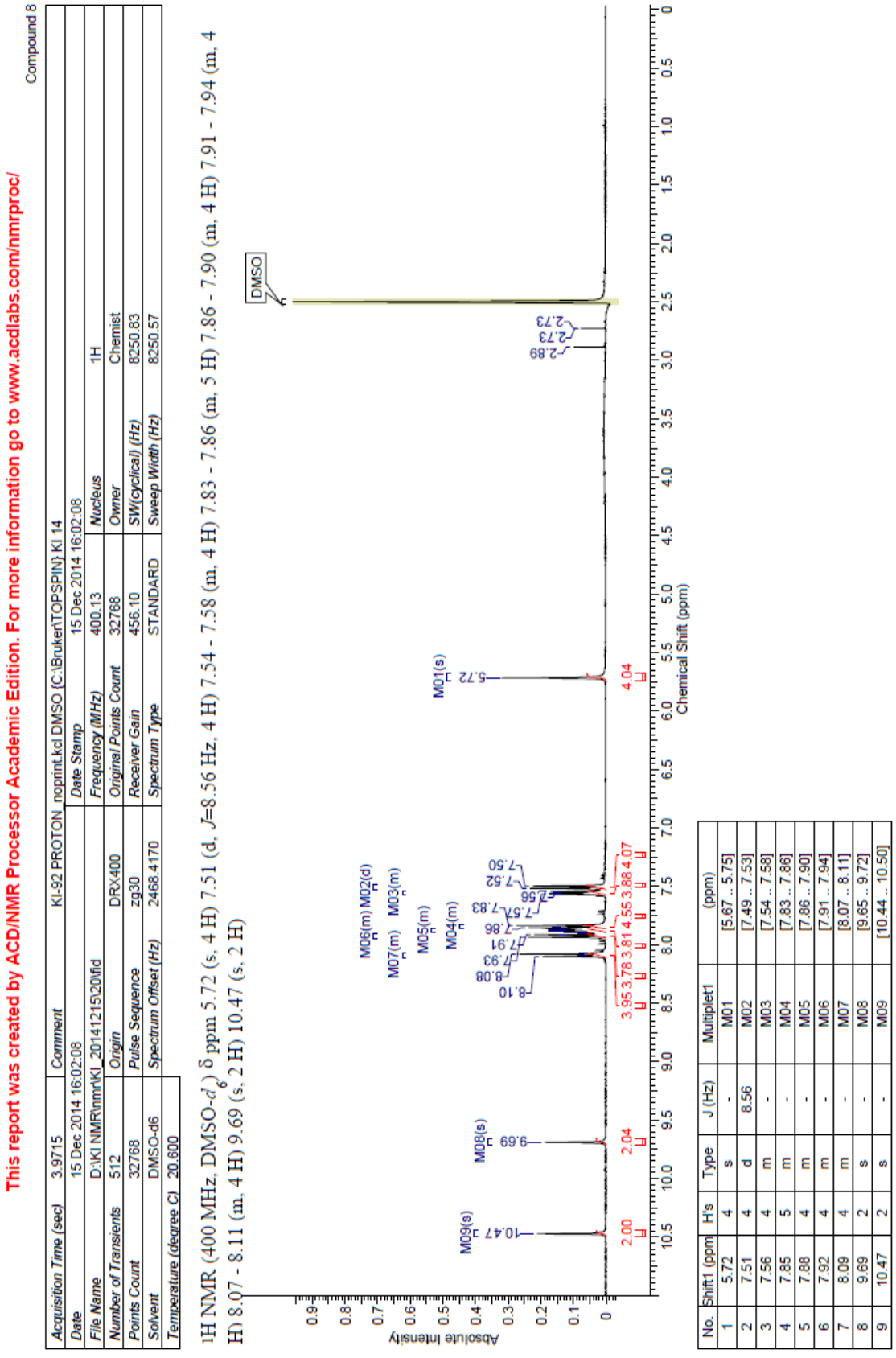
584.2546
Relative Abundance
m/z

Compound 8



No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	(ppm)
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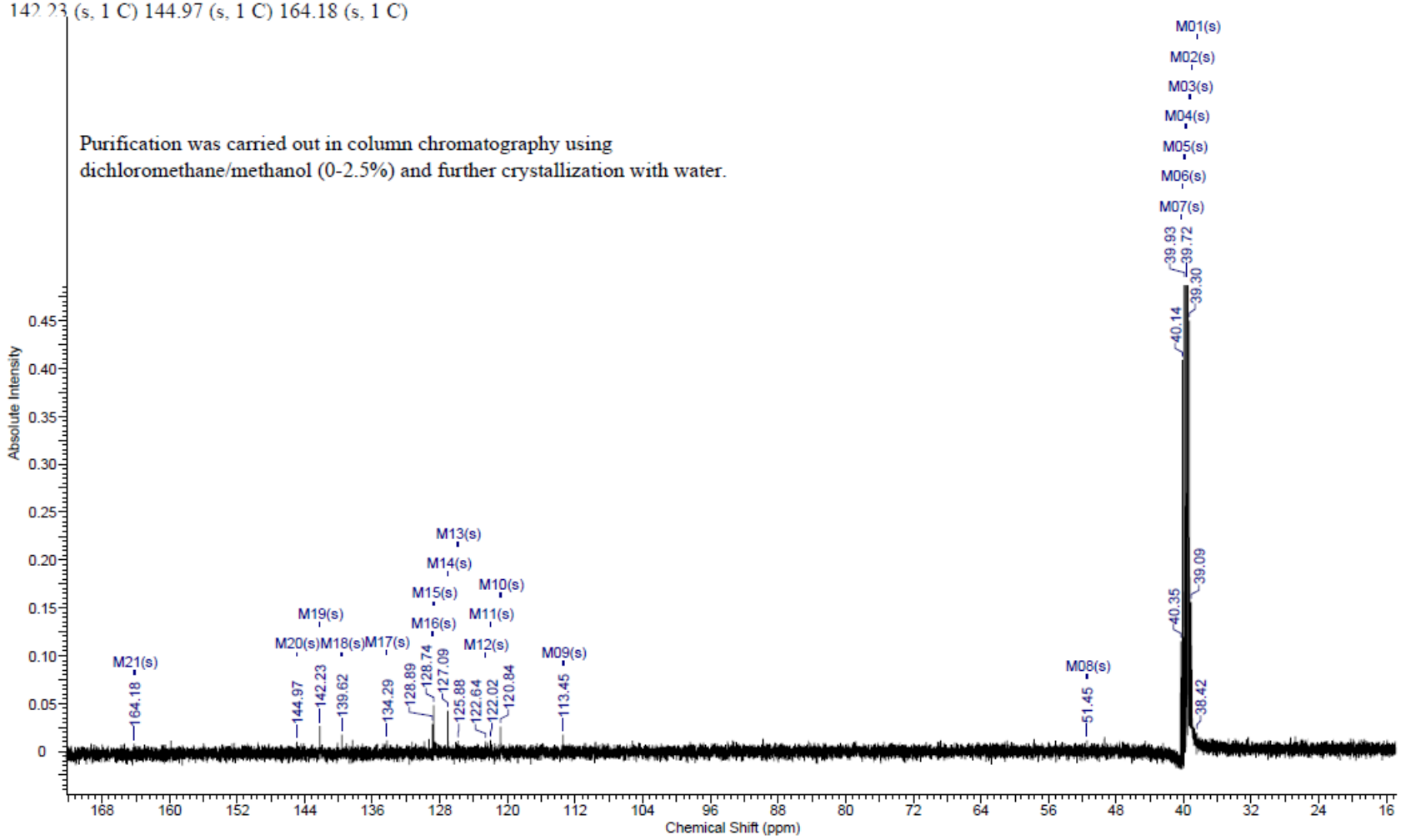
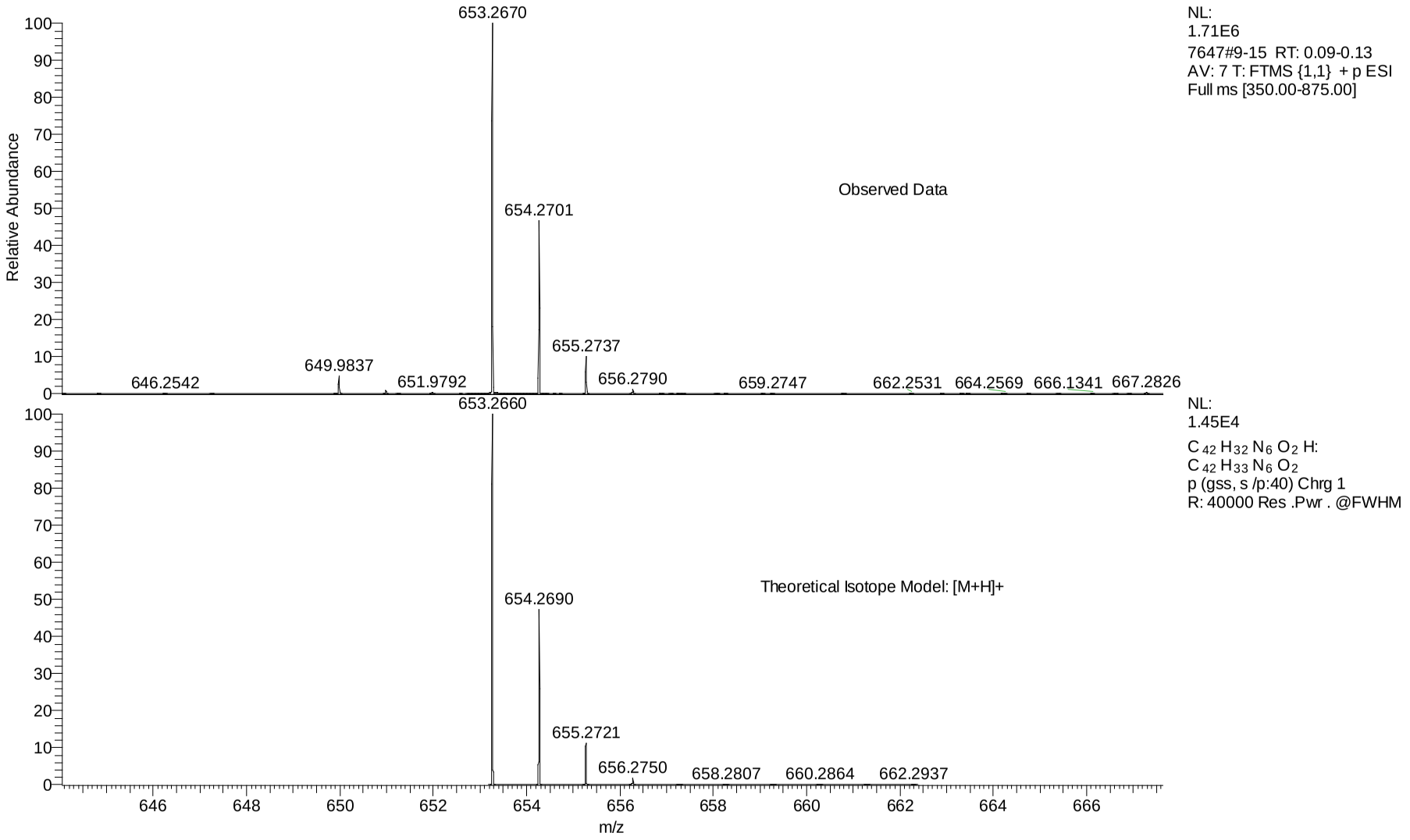
2	7.51	4	d	8.56	M02	[7.49 .. 7.53]
3	7.56	4	m	-	M03	[7.54 .. 7.58]
4	7.85	5	m	-	M04	[7.83 .. 7.86]
5	7.88	4	m	-	M05	[7.86 .. 7.90]
6	7.92	4	m	-	M06	[7.91 .. 7.94]
7	8.09	4	m	-	M07	[8.07 .. 8.11]
8	9.69	2	s	-	M08	[9.65 .. 9.72]
9	10.47	2	s	-	M09	[10.44 .. 10.50]

Compound 8

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 38.42 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 40.35 (s, 1 C) 51.45 (s, 1 C) 113.45 (s, 1 C) 120.84 (s, 1 C) 122.02 (s, 1 C) 122.64 (s, 1 C) 125.88 (s, 1 C) 127.09 (s, 1 C) 128.74 (s, 1 C) 128.89 (s, 1 C) 134.29 (s, 1 C) 139.62 (s, 1 C) 142.23 (s, 1 C) 144.97 (s, 1 C) 164.18 (s, 1 C)

Purification was carried out in column chromatography using dichloromethane/methanol (0-2.5%) and further crystallization with water.

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NL:
1.71E6
7647#9-15 RT: 0.09-0.13
AV: 7 T: FTMS {1,1} + p ESI
Full ms [350.00-875.00]
Observed Data
654.2701
655.2737
649.9837
646.2542
651.9792
656.2790
659.2747
662.2531
664.2569
666.1341
667.2826
Relative Abundance
653.2660
NL:
1.45E4
C 42 H 32 N 6 O 2 H:
C 42 H 33 N 6 O 2
p (gss, s /p:40) Chrg 1
R: 40000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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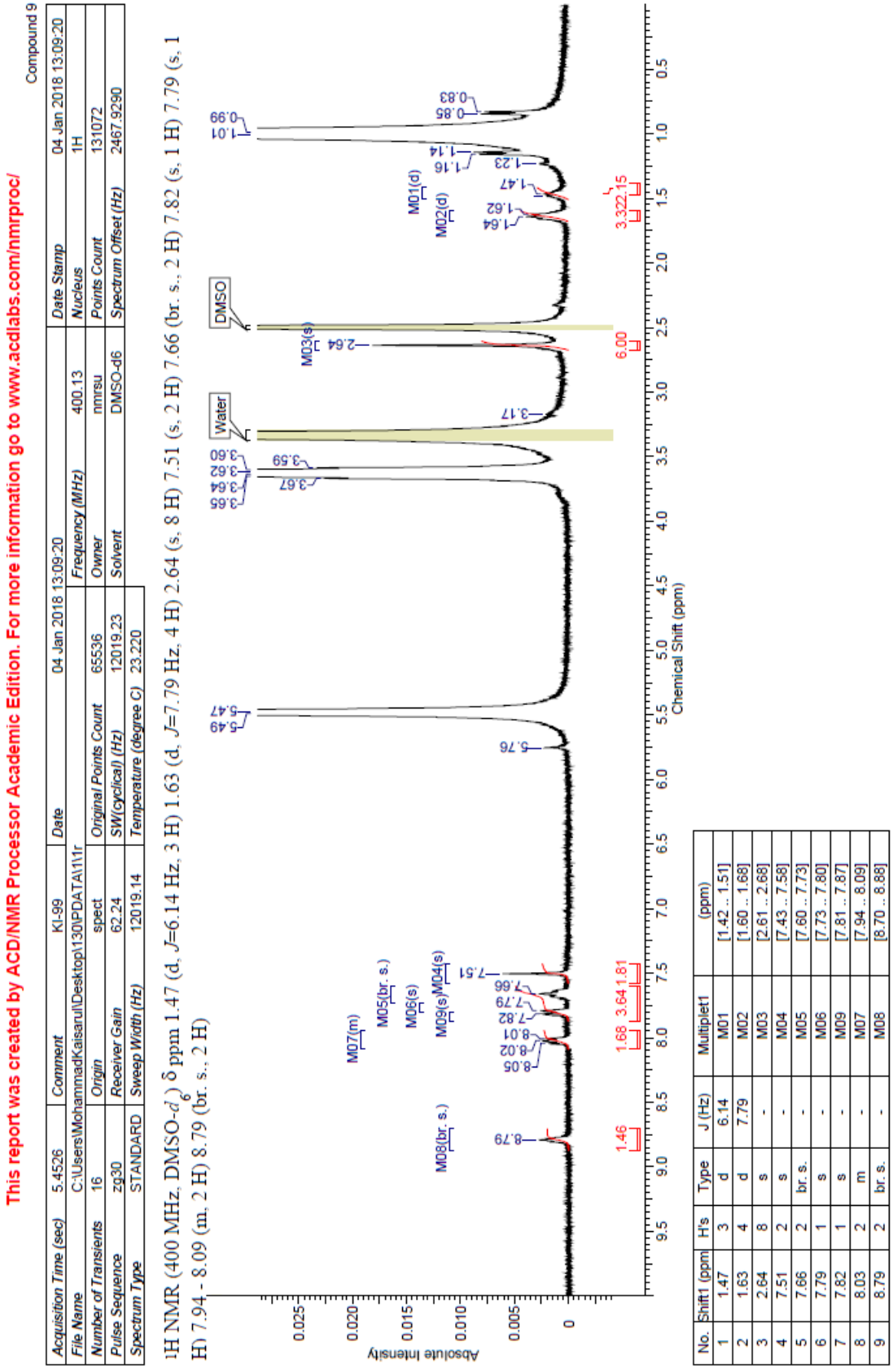
m/z

Compound 9


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 9
Acquisition Time (sec) 5.4526 Comment KI-99 Date 04 Jan 2018 13:09:20 Frequency (MHz) 400.13 Date Stamp 04 Jan 2018 13:09:20
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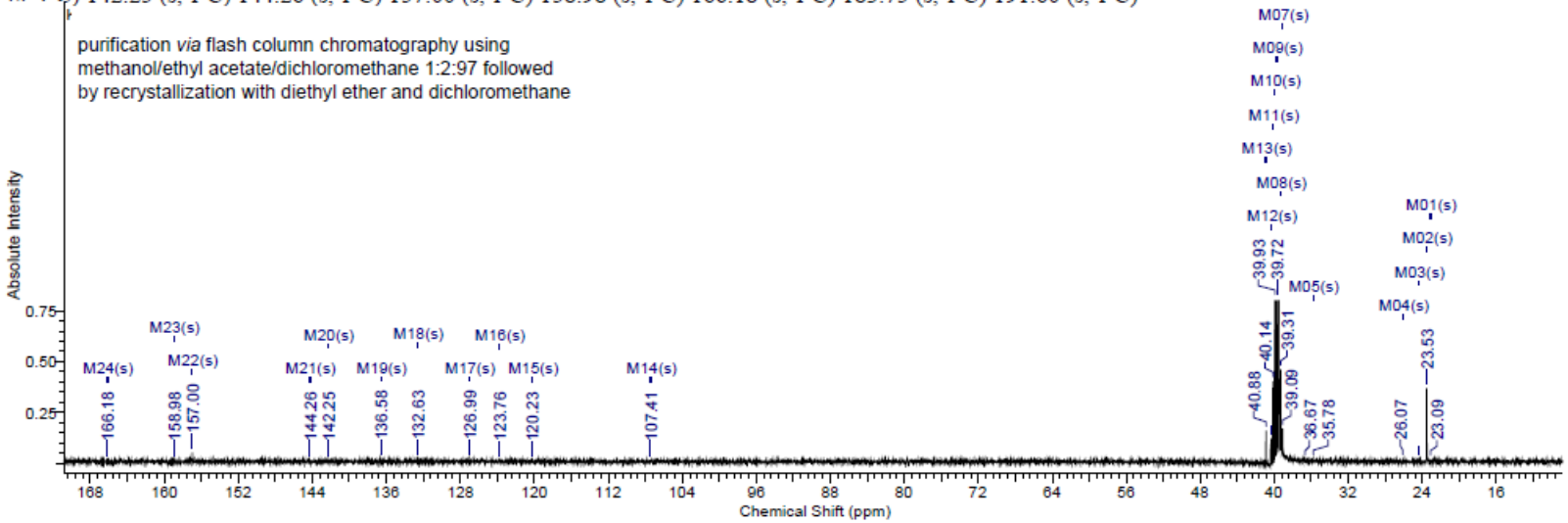
Pulse Sequence zg30 Receiver Gain 62.24 SW(cyclical) (Hz) 12019.23 Solvent DMSO-d6 Spectrum Offset (Hz) 2467.9290
Spectrum Type STANDARD Sweep Width (Hz) 12019.14 Temperature (degree C) 23.220
1H NMR (400 MHz, DMSO-d6) δ ppm 1.47 (d, J=6.14 Hz, 3 H) 1.63 (d, J=7.79 Hz, 4 H) 2.64 (s, 8 H) 7.51 (s, 2 H) 7.66 (br. s., 2 H) 7.82 (s, 1 H) 7.79 (s, 1 H) 7.94 - 8.09 (m, 2 H) 8.79 (br. s., 2 H)
Absolute Intensity
Chemical Shift (ppm)
DMSO
Water
M01(d)
M02(d)
M03(s)
M04(s)
M05(br. s.)
M06(s)
M07(m)
M08(br. s.)
M09(s)
1.46
1.68
3.64
1.81
6.00
3.32
2.15
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 (ppm)
1 1.47 3 d 6.14 M01 [1.42 ... 1.51]
2 1.63 4 d 7.79 M02 [1.60 ... 1.68]
3 2.64 8 s - M03 [2.61 ... 2.68]
4 7.51 2 s - M04 [7.43 ... 7.58]
5 7.66 2 br. s. - M05 [7.60 ... 7.73]
6 7.79 1 s - M06 [7.73 ... 7.80]
7 7.82 1 s - M09 [7.81 ... 7.87]
8 8.03 2 m - M07 [7.94 ... 8.09]
9 8.79 2 br. s. - M08 [8.70 ... 8.88]

Compound 9

Acquisition Time (sec)	1.3631	*Comment*	KI-99 C13CPD noprint.kcl DMSO (C:\Bruker\TOPSPIN) KI 36			*Date*	13 May 2015 03:14:24
Date Stamp	13 May 2015 03:14:24			*File Name*	D:\PHD STUDIES\Thesis\KI NMR\nmr\KI_20150512\41\fid		
Frequency (MHz)	100.61	*Nucleus*	13C	*Number of Transients*	2048	*Origin*	DRX400
Original Points Count	32768	*Owner*	Chemist	*Points Count*	32768	*Pulse Sequence*	zgpg30
Receiver Gain	1149.40	*SW(cyclical) (Hz)*	24038.46	*Solvent*	DMSO-d6	*Spectrum Offset (Hz)*	10036.5459
Spectrum Type	STANDARD	*Sweep Width (Hz)*	24037.73	*Temperature (degree C)*	-9.600		

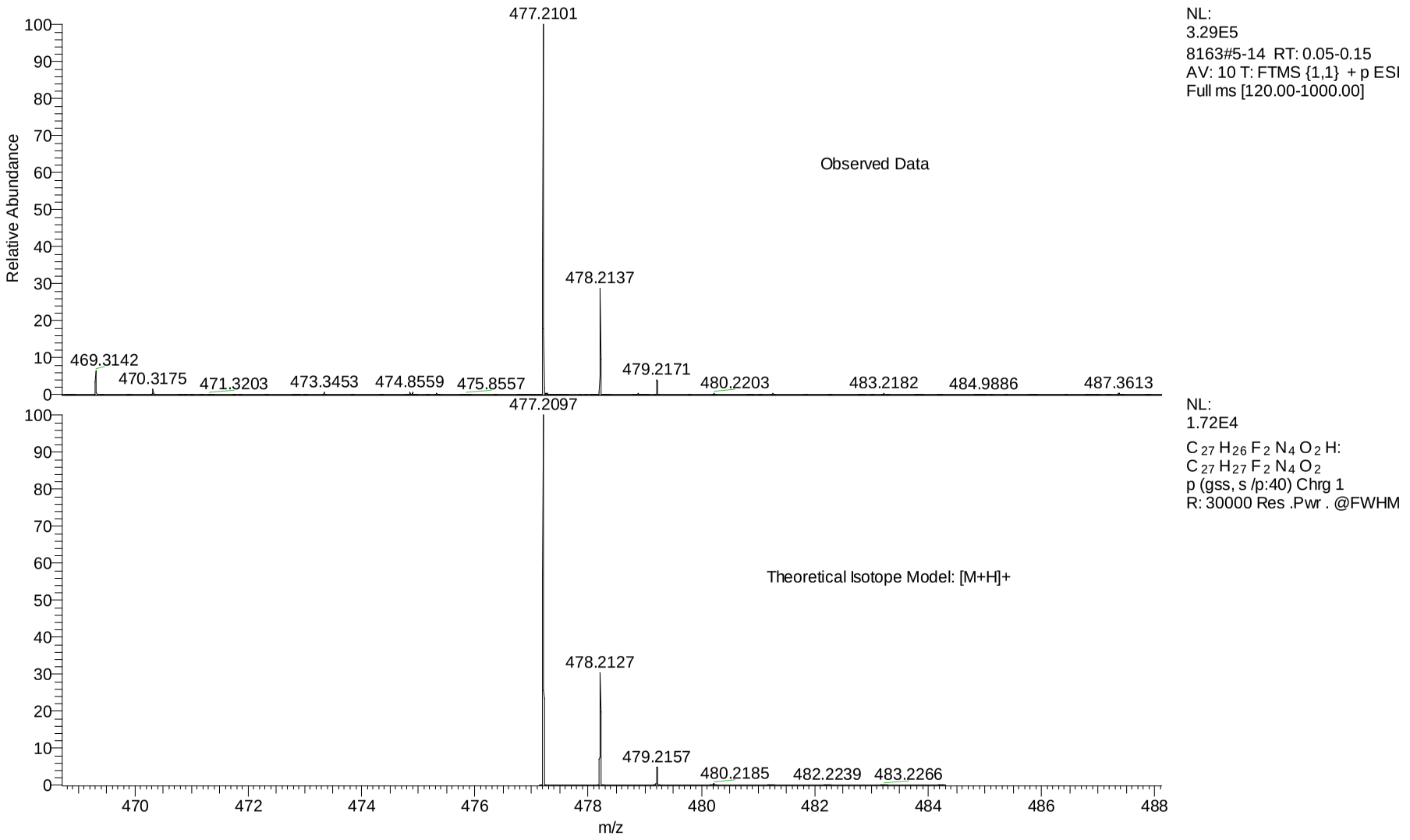
^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 23.09 (s, 1 C) 23.53 (s, 1 C) 24.32 (s, 1 C) 26.07 (s, 1 C) 35.78 (s, 1 C) 36.67 (s, 1 C) 39.09 (s, 1 C) 39.31 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 40.35 (s, 1 C) 40.88 (s, 1 C) 107.41 (s, 1 C) 120.23 (s, 1 C) 123.76 (s, 1 C) 126.99 (s, 1 C) 132.63 (s, 1 C) 136.58 (s, 1 C) 142.25 (s, 1 C) 144.26 (s, 1 C) 157.00 (s, 1 C) 158.98 (s, 1 C) 166.18 (s, 1 C) 183.75 (s, 1 C) 191.60 (s, 1 C)

purification *via* flash column chromatography using
methanol/ethyl acetate/dichloromethane 1:2:97 followed
by recrystallization with diethyl ether and dichloromethane

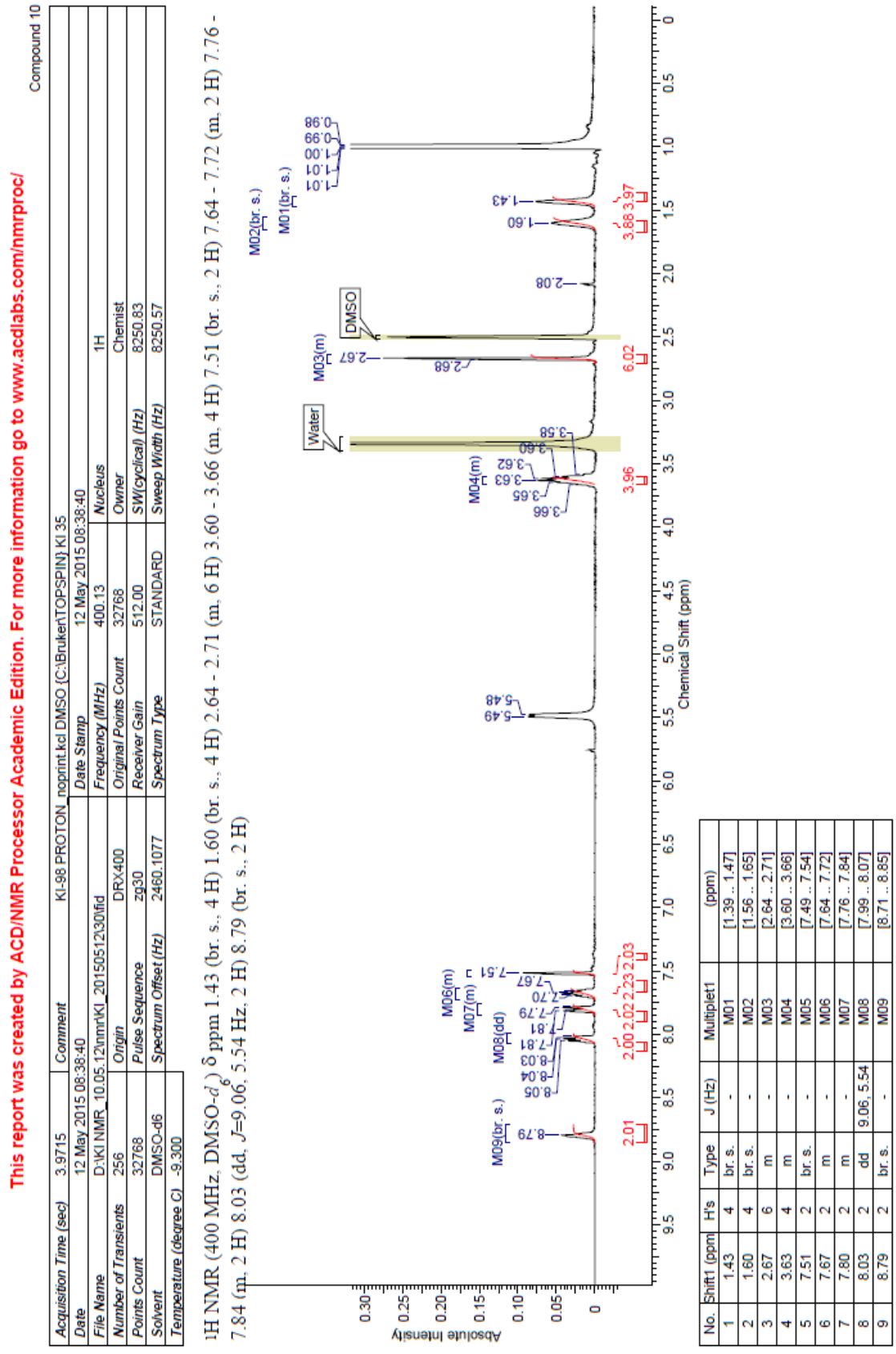


No.	Shift1 (ppm	C's	Type	Multiplet1	(ppm)
1	23.09	1	s	M01	[23.06 .. 23.12]
2	23.53	1	s	M02	[23.50 .. 23.56]
3	24.32	1	s	M03	[24.29 .. 24.35]
4	26.07	1	s	M04	[26.04 .. 26.10]
5	35.78	1	s	M05	[35.75 .. 35.81]
6	36.67	1	s	M06	[36.64 .. 36.70]
7	39.09	1	s	M07	[39.06 .. 39.12]
8	39.31	1	s	M08	[39.28 .. 39.34]
9	39.72	1	s	M09	[39.69 .. 39.75]

No.	Shift1 (ppm	C's	Type	Multiplet1	(ppm)
10	39.93	1	s	M10	[39.90 .. 39.96]
11	40.14	1	s	M11	[40.11 .. 40.17]
12	40.35	1	s	M12	[40.32 .. 40.38]
13	40.88	1	s	M13	[40.85 .. 40.91]
14	107.41	1	s	M14	[107.38 .. 107.44]
15	120.23	1	s	M15	[120.20 .. 120.26]
16	123.76	1	s	M16	[123.73 .. 123.79]
17	126.99	1	s	M17	[126.96 .. 127.02]
18	132.63	1	s	M18	[132.60 .. 132.66]


477.2101
NL:
3.29E5
8163#5-14 RT: 0.05-0.15
AV: 10 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Observed Data
Relative Abundance
478.2137
469.3142
470.3175
471.3203
473.3453
474.8559
475.8557
479.2171
480.2203
483.2182
484.9886
487.3613
477.2097
NL:
1.72E4
C 27 H 26 F 2 N 4 O 2 H:
C 27 H 27 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
478.2127
479.2157
480.2185
482.2239
483.2266
m/z

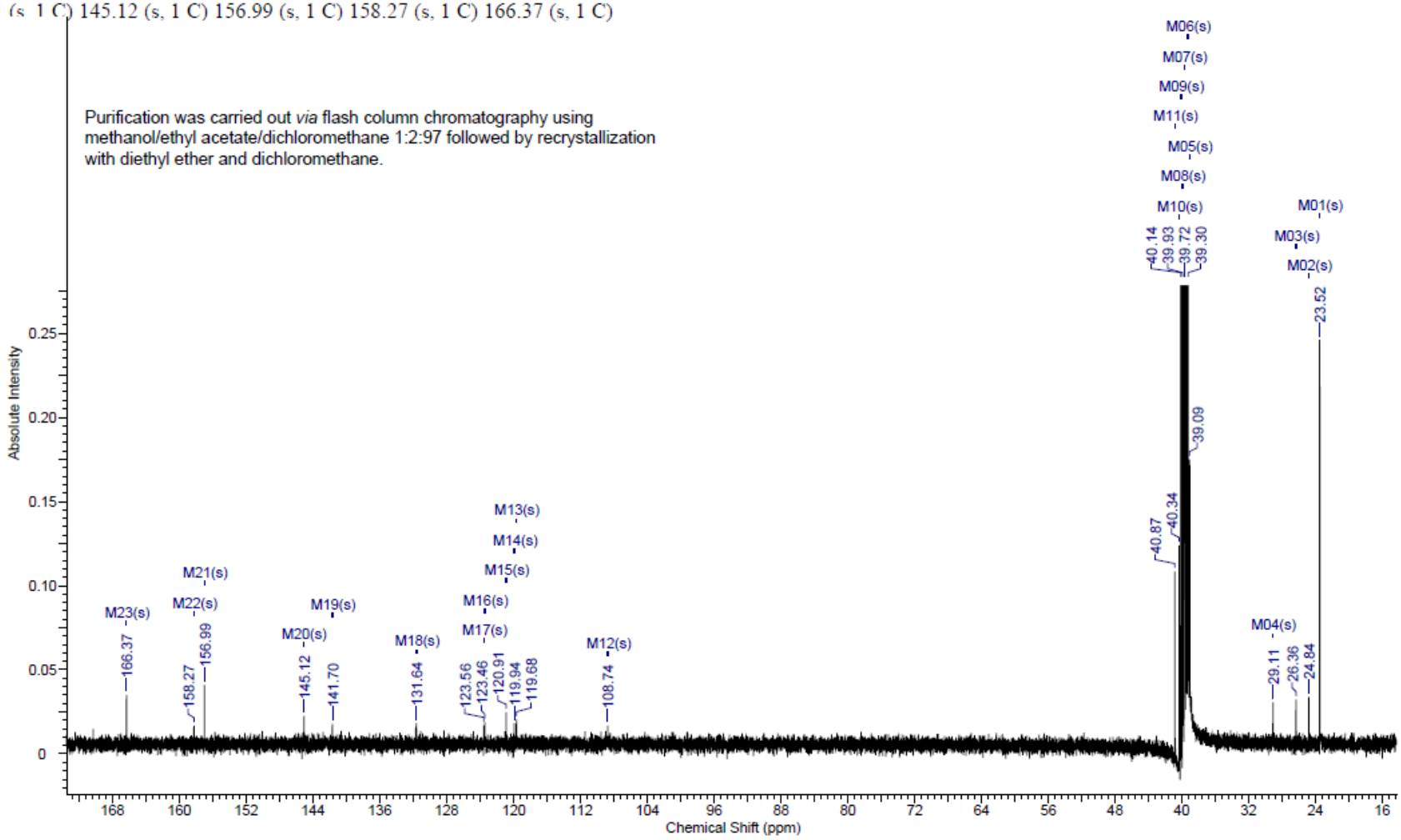
Compound 10

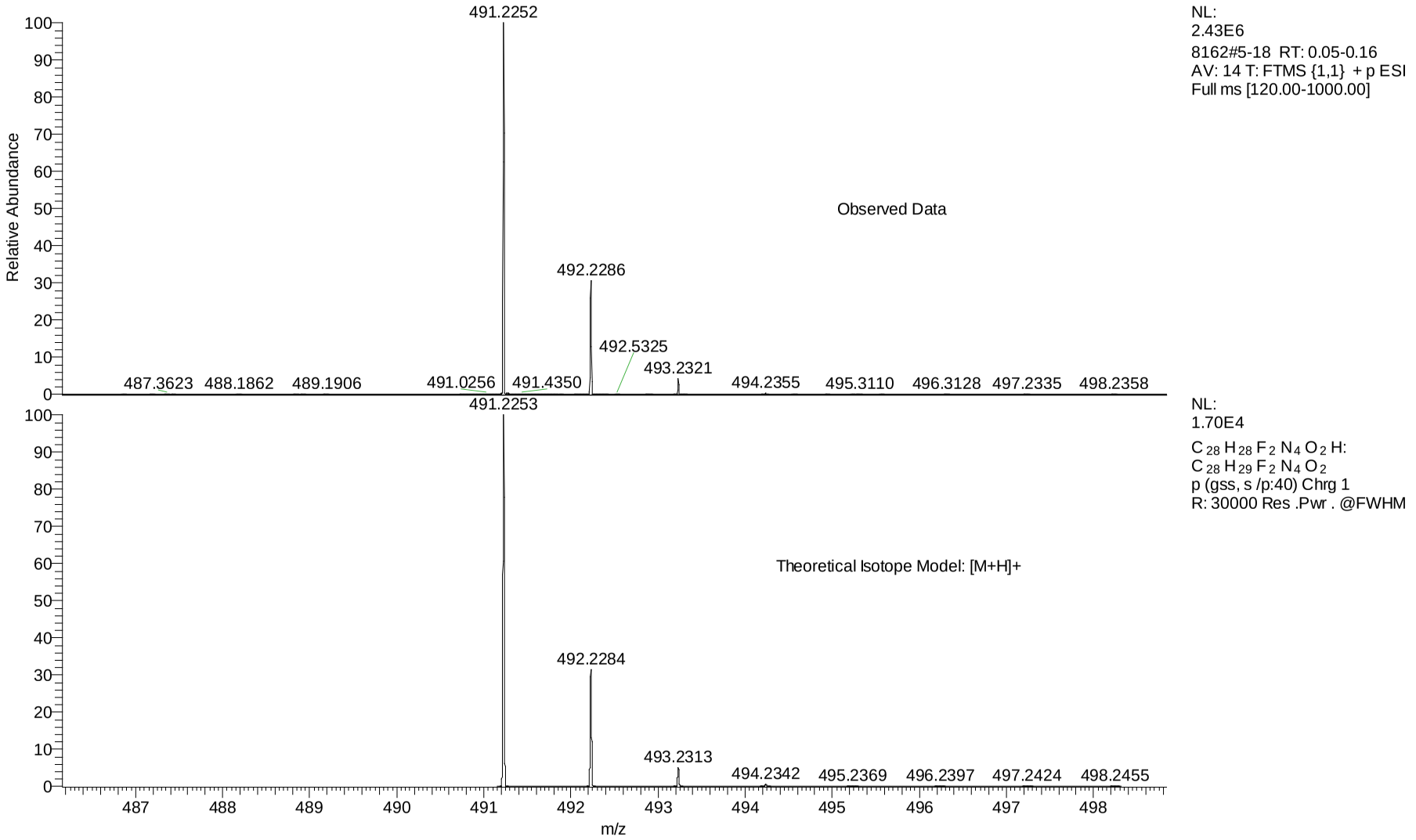

This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 10
Acquisition Time (sec) 3.9715
Comment KI-98 PROTON_noprint.kcl DMSO (C:\Bruker\TOPSPIN) KI 35
Date 12 May 2015 08:38:40
Date Stamp 12 May 2015 08:38:40
File Name D:\KI NMR_10.05.12\nmr\KI_20150512\30\fid
Frequency (MHz) 400.13
Nucleus 1H
Number of Transients 256
Origin DRX400
Original Points Count 32768
Owner Chemist
Points Count 32768
Pulse Sequence zg30
Receiver Gain 512.00
SW(cyclical) (Hz) 8250.83
Solvent DMSO-d6
Spectrum Offset (Hz) 2460.1077
Spectrum Type STANDARD
Sweep Width (Hz) 8250.57
Temperature (degree C) -9.300
1H NMR (400 MHz, DMSO-d6) δ ppm 1.43 (br. s., 4 H) 1.60 (br. s., 4 H) 2.64 - 2.71 (m, 6 H) 3.60 - 3.66 (m, 4 H) 7.51 (br. s., 2 H) 7.64 - 7.72 (m, 2 H) 7.76 - 7.84 (m, 2 H) 8.03 (dd, J=9.06, 5.54 Hz, 2 H) 8.79 (br. s., 2 H)
Absolute Intensity
Chemical Shift (ppm)
Water
DMSO
M01(br. s.)
M02(br. s.)
M03(m)
M04(m)
M06(m)
M07(m)
M08(dd)
M09(br. s.)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 (ppm)
1 1.43 4 br. s. - M01 [1.39 .. 1.47]
2 1.60 4 br. s. - M02 [1.56 .. 1.65]
3 2.67 6 m - M03 [2.64 .. 2.71]
4 3.63 4 m - M04 [3.60 .. 3.66]
5 7.51 2 br. s. - M05 [7.49 .. 7.54]
6 7.67 2 m - M06 [7.64 .. 7.72]
7 7.80 2 m - M07 [7.76 .. 7.84]
8 8.03 2 dd 9.06, 5.54 M08 [7.99 .. 8.07]
9 8.79 2 br. s. - M09 [8.71 .. 8.85]

Compound 10

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 23.52 (s, 1 C) 24.84 (s, 1 C) 26.36 (s, 1 C) 29.11 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 40.34 (s, 1 C) 40.87 (s, 1 C) 108.74 (s, 1 C) 119.68 (s, 1 C) 119.94 (s, 1 C) 120.91 (s, 1 C) 123.46 (s, 1 C) 123.56 (s, 1 C) 131.64 (s, 1 C) 141.70 (s, 1 C) 145.12 (s, 1 C) 156.99 (s, 1 C) 158.27 (s, 1 C) 166.37 (s, 1 C)

Purification was carried out *via* flash column chromatography using methanol/ethyl acetate/dichloromethane 1:2:97 followed by recrystallization with diethyl ether and dichloromethane.

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NL:
2.43E6
8162#5-18 RT: 0.05-0.16
AV: 14 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Relative Abundance
Observed Data
492.2286
492.5325
493.2321
487.3623
488.1862
489.1906
491.0256
491.4350
494.2355
495.3110
496.3128
497.2335
498.2358
491.2253
NL:
1.70E4
C 28 H 28 F 2 N 4 O 2 H:
C 28 H 29 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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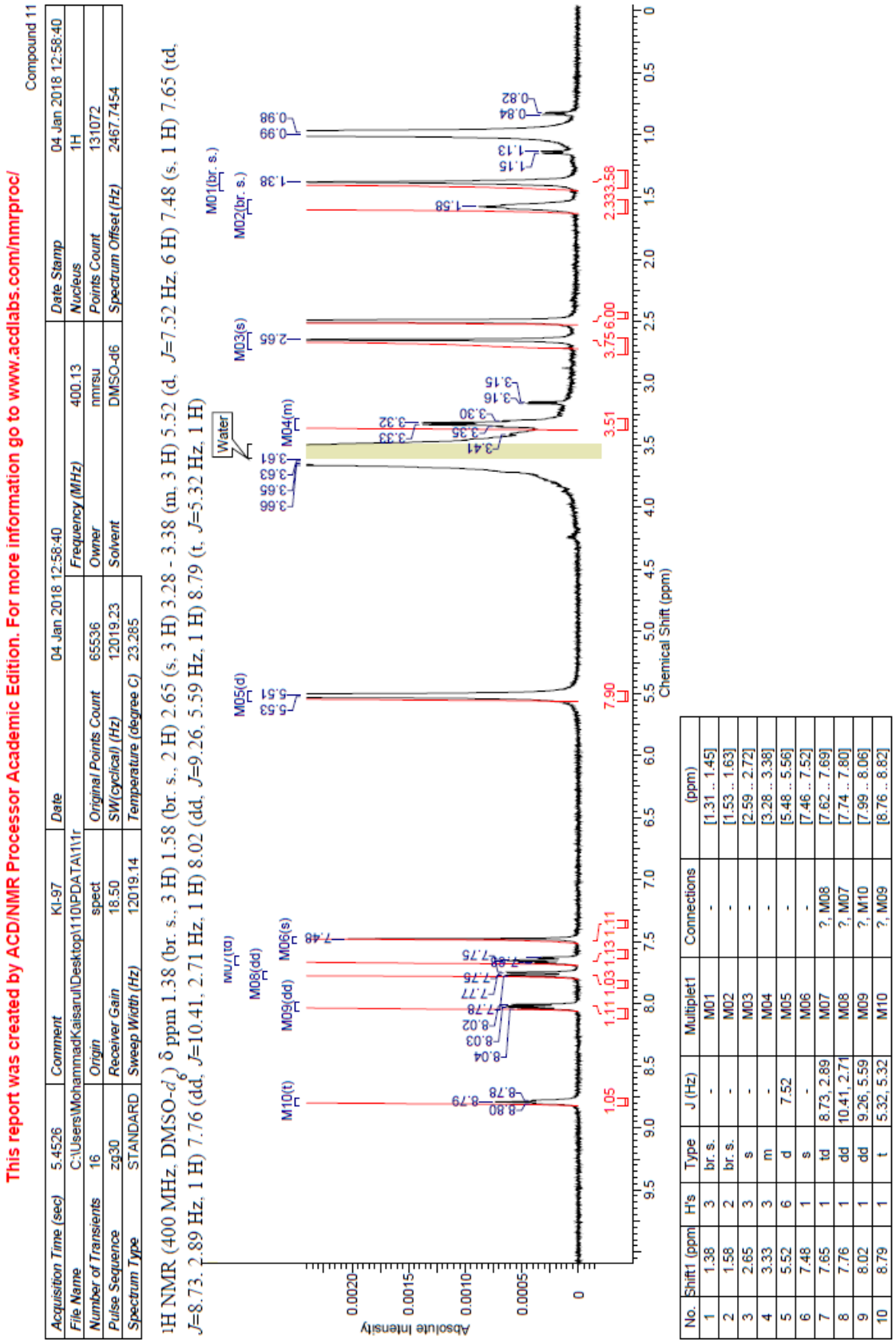
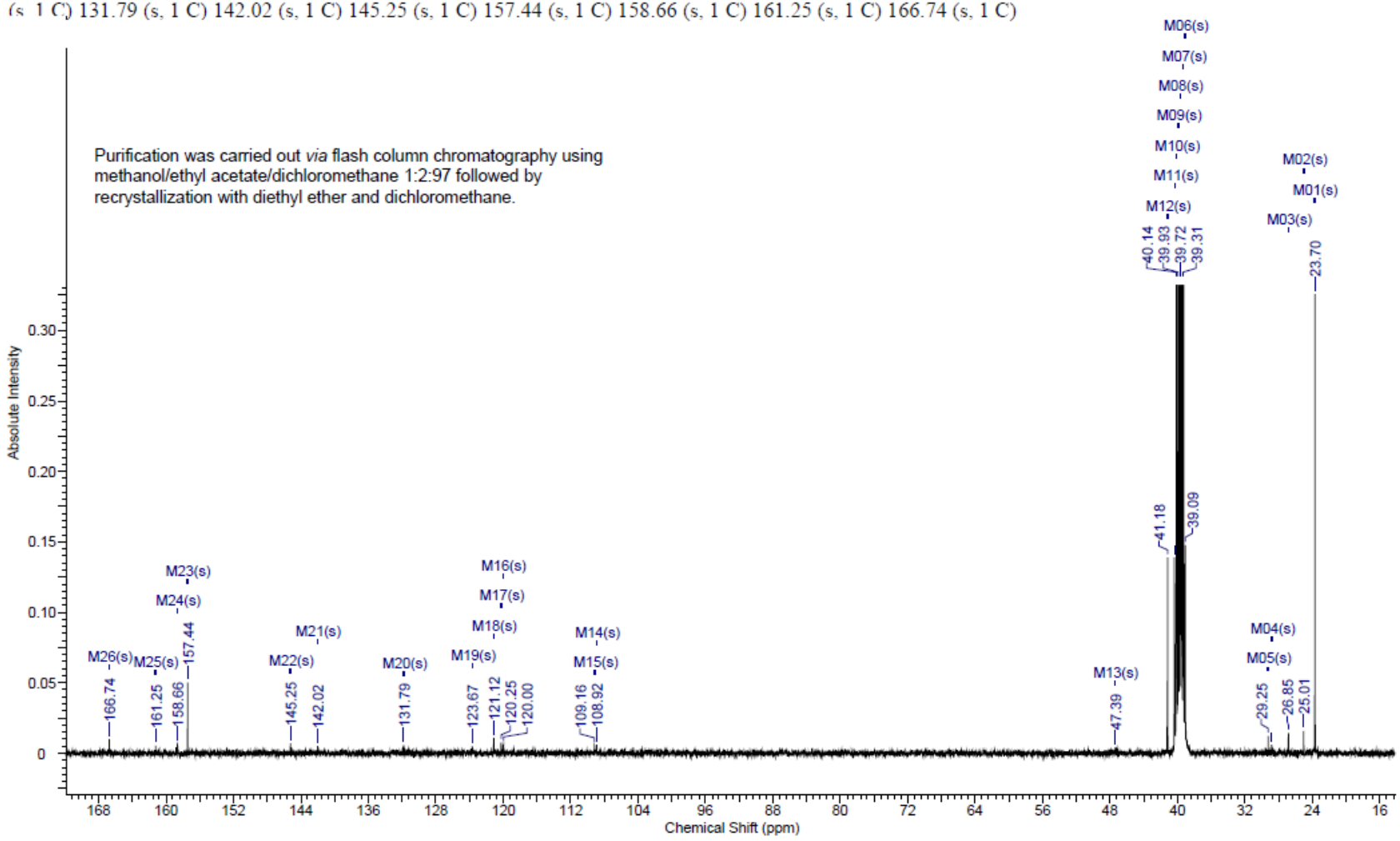
493.2313
494.2342
495.2369
496.2397
497.2424
498.2455
m/z

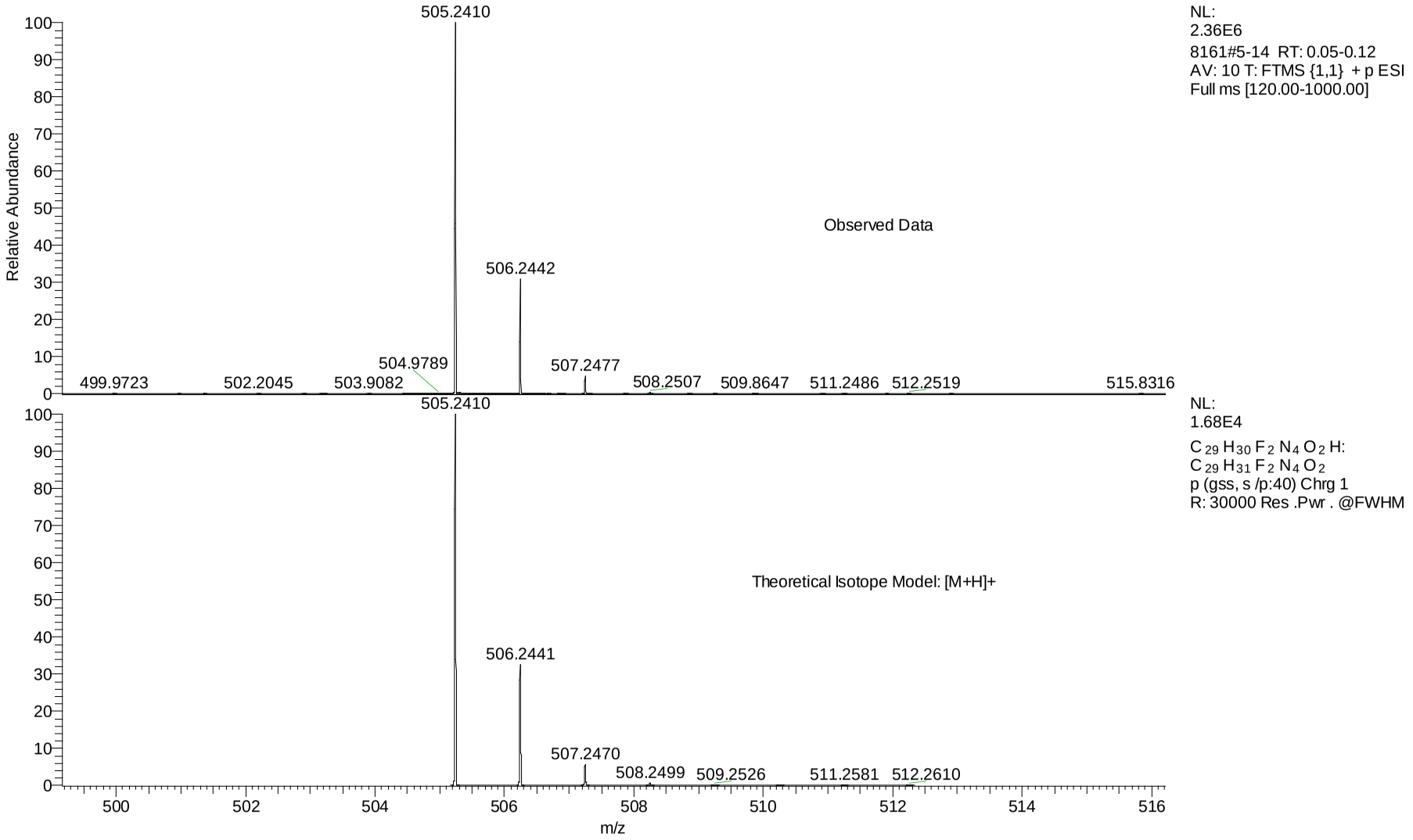
Compound 11


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 11
Acquisition Time (sec) 5.4526 Comment KI-97 Date 04 Jan 2018 12:58:40 Date Stamp 04 Jan 2018 12:58:40
File Name C:\Users\MohammmadKaisarul\Desktop\110\PDATA\1\1r Frequency (MHz) 400.13 Nucleus 1H
Number of Transients 16 Origin spect Original Points Count 65536 Owner nmrsu Points Count 131072
Pulse Sequence zg30 Receiver Gain 18.50 SW(cyclical) (Hz) 12019.23 Solvent DMSO-d6 Spectrum Offset (Hz) 2467.7454
Spectrum Type STANDARD Sweep Width (Hz) 12019.14 Temperature (degree C) 23.285
1H NMR (400 MHz, DMSO-d6) δ ppm 1.38 (br. s., 3 H) 1.58 (br. s., 2 H) 2.65 (s, 3 H) 3.28 - 3.38 (m, 3 H) 5.52 (d, J=7.52 Hz, 6 H) 7.48 (s, 1 H) 7.65 (td, J=8.73, 2.89 Hz, 1 H) 7.76 (dd, J=10.41, 2.71 Hz, 1 H) 8.02 (dd, J=9.26, 5.59 Hz, 1 H) 8.79 (t, J=5.32 Hz, 1 H)
Absolute Intensity
Chemical Shift (ppm)
Water
M01(br. s.)
M02(br. s.)
M03(s)
M04(m)
M05(d)
M06(s)
M07(td)
M08(dd)
M09(dd)
M10(t)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
1 1.38 3 br. s. - M01 - [1.31 .. 1.45]
2 1.58 2 br. s. - M02 - [1.53 .. 1.63]
3 2.65 3 s - M03 - [2.59 .. 2.72]
4 3.33 3 m - M04 - [3.28 .. 3.38]
5 5.52 6 d 7.52 M05 - [5.48 .. 5.56]
6 7.48 1 s - M06 - [7.46 .. 7.52]
7 7.65 1 td 8.73, 2.89 M07 ?, M08 [7.62 .. 7.69]
8 7.76 1 dd 10.41, 2.71 M08 ?, M07 [7.74 .. 7.80]
9 8.02 1 dd 9.26, 5.59 M09 ?, M10 [7.99 .. 8.06]
10 8.79 1 t 5.32, 5.32 M10 ?, M09 [8.76 .. 8.82]

Compound 11

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 23.70 (s, 1 C) 25.01 (s, 1 C) 26.85 (s, 1 C) 28.81 (s, 1 C) 29.25 (s, 1 C) 39.09 (s, 1 C) 39.31 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 40.35 (s, 1 C) 41.18 (s, 1 C) 47.39 (s, 1 C) 108.92 (s, 1 C) 109.16 (s, 1 C) 120.00 (s, 1 C) 120.25 (s, 1 C) 121.12 (s, 1 C) 123.67 (s, 1 C) 131.79 (s, 1 C) 142.02 (s, 1 C) 145.25 (s, 1 C) 157.44 (s, 1 C) 158.66 (s, 1 C) 161.25 (s, 1 C) 166.74 (s, 1 C)

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NL:
2.36E6
8161#5-14 RT: 0.05-0.12
AV: 10 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Relative Abundance
Observed Data
506.2442
504.9789
507.2477
499.9723
502.2045
503.9082
508.2507
509.8647
511.2486
512.2519
515.8316
505.2410
NL:
1.68E4
C 29 H 30 F 2 N 4 O 2 H:
C 29 H 31 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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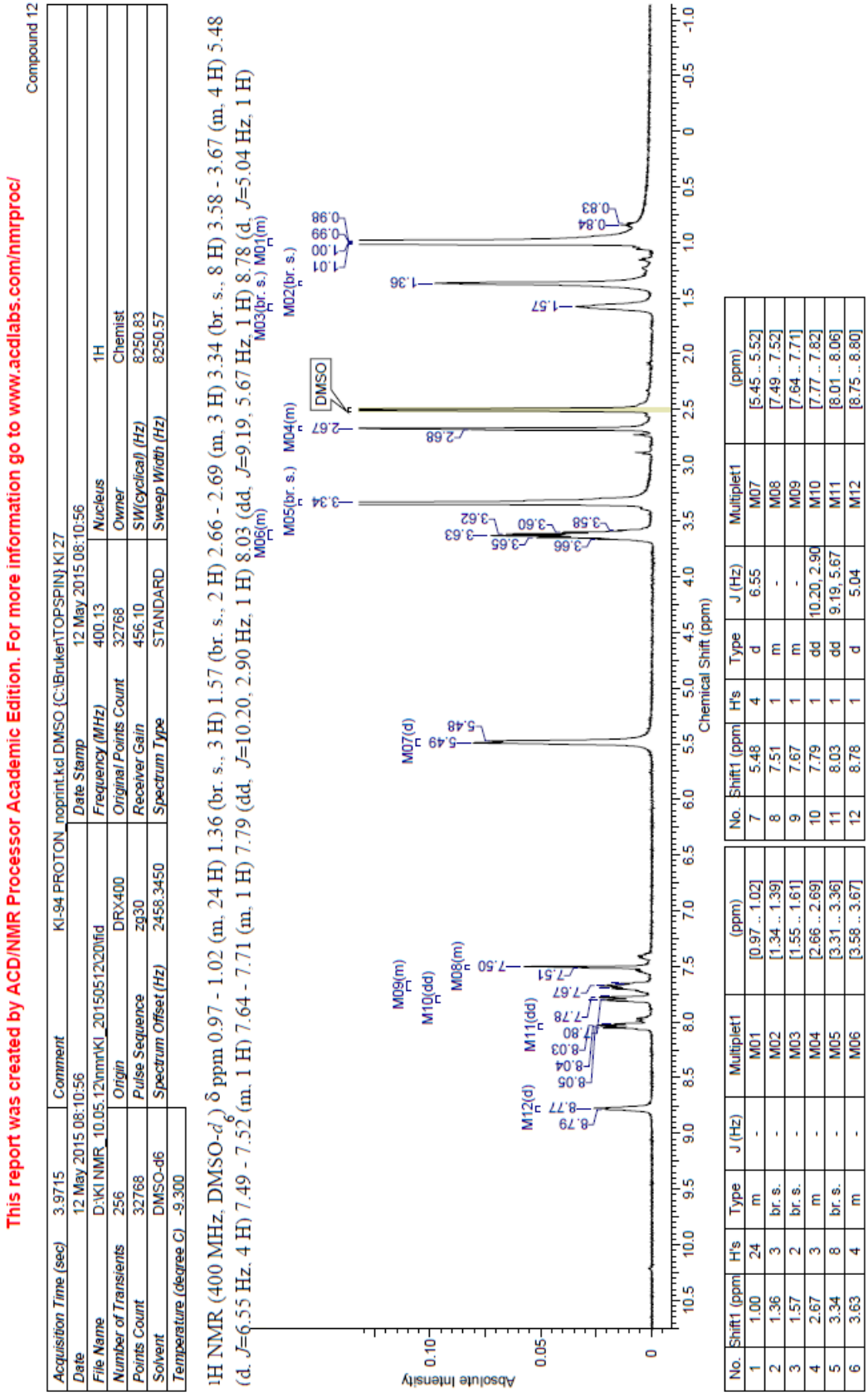
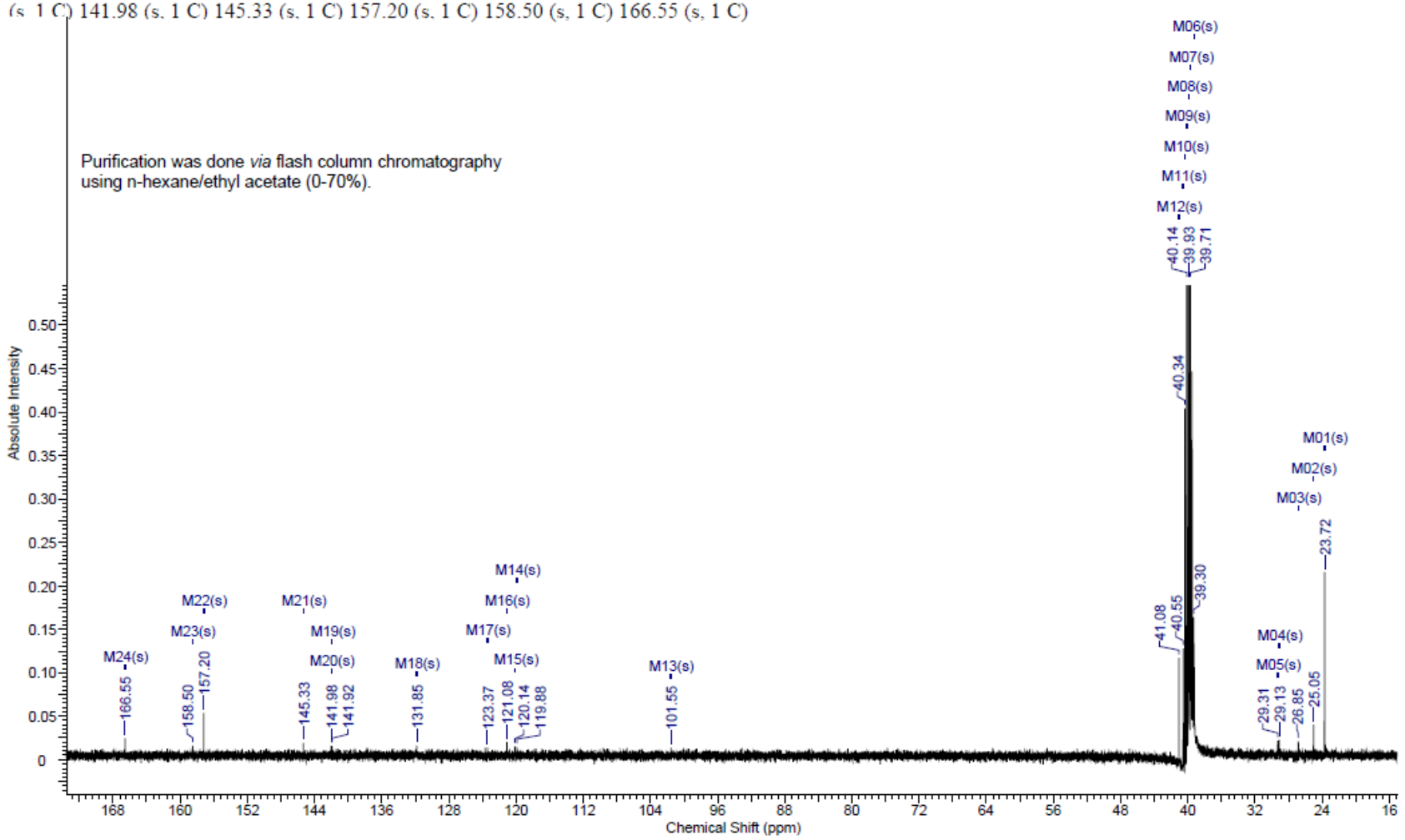
507.2470
508.2499
509.2526
511.2581
512.2610
m/z

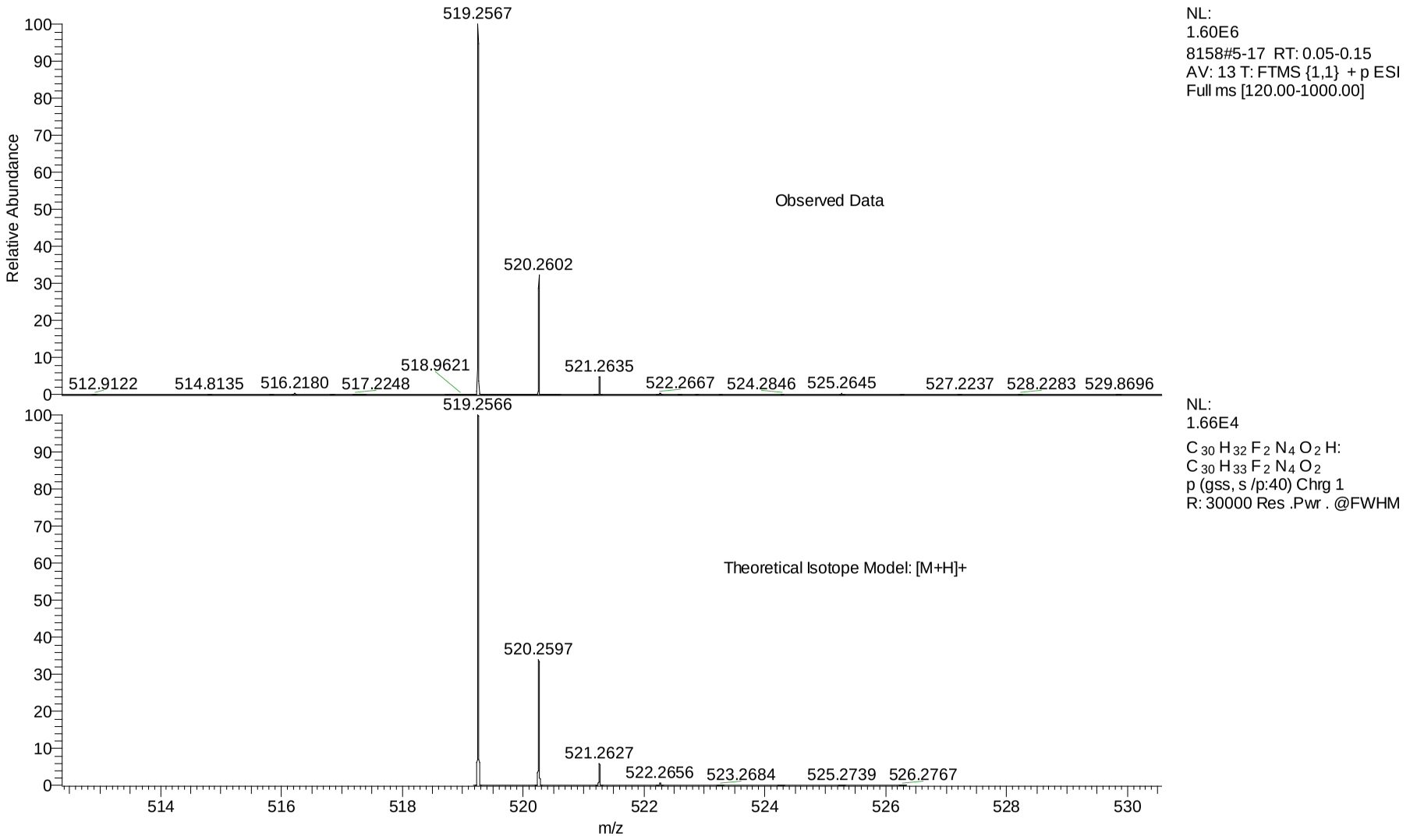
Compound 12


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 12
Acquisition Time (sec) 3.9715
Comment KI-94 PROTON_noprint.kcl DMSO (C:\Bruker\TOPSPIN) KI 27
Date 12 May 2015 08:10:56
Date Stamp 12 May 2015 08:10:56
File Name D:\KI NMR_10.05.12\nmrKI_20150512\20\fid
Frequency (MHz) 400.13
Nucleus 1H
Number of Transients 256
Origin DRX400
Original Points Count 32768
Owner Chemist
Points Count 32768
Pulse Sequence zg30
Receiver Gain 456.10
SW(cyclical) (Hz) 8250.83
Solvent DMSO-d6
Spectrum Offset (Hz) 2458.3450
Spectrum Type STANDARD
Sweep Width (Hz) 8250.57
Temperature (degree C) -9.300
1H NMR (400 MHz, DMSO-d6) δ ppm 0.97 - 1.02 (m, 24 H) 1.36 (br. s., 3 H) 1.57 (br. s., 2 H) 2.66 - 2.69 (m, 3 H) 3.34 (br. s., 8 H) 3.58 - 3.67 (m, 4 H) 5.48 (d, J=6.55 Hz, 4 H) 7.49 - 7.52 (m, 1 H) 7.64 - 7.71 (m, 1 H) 7.79 (dd, J=10.20, 2.90 Hz, 1 H) 8.03 (dd, J=9.19, 5.67 Hz, 1 H) 8.78 (d, J=5.04 Hz, 1 H)
M01(m)
M02(br. s.)
M03(br. s.)
M04(m)
M05(br. s.)
M06(m)
M07(d)
M08(m)
M09(m)
M10(dd)
M11(dd)
M12(d)
DMSO
Absolute Intensity
Chemical Shift (ppm)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 (ppm)
1 1.00 24 m - M01 [0.97 .. 1.02]
2 1.36 3 br. s. - M02 [1.34 .. 1.39]
3 1.57 2 br. s. - M03 [1.55 .. 1.61]
4 2.67 3 m - M04 [2.66 .. 2.69]
5 3.34 8 br. s. - M05 [3.31 .. 3.36]
6 3.63 4 m - M06 [3.58 .. 3.67]
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 (ppm)
7 5.48 4 d 6.55 M07 [5.45 .. 5.52]
8 7.51 1 m - M08 [7.49 .. 7.52]
9 7.67 1 m - M09 [7.64 .. 7.71]
10 7.79 1 dd 10.20, 2.90 M10 [7.77 .. 7.82]
11 8.03 1 dd 9.19, 5.67 M11 [8.01 .. 8.06]
12 8.78 1 d 5.04 M12 [8.75 .. 8.80]

Compound 12

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 23.72 (s, 1 C) 25.05 (s, 1 C) 26.85 (s, 1 C) 29.13 (s, 1 C) 29.31 (s, 1 C) 39.30 (s, 1 C) 39.71 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 40.34 (s, 1 C) 40.55 (s, 1 C) 41.08 (s, 1 C) 101.55 (s, 1 C) 119.88 (s, 1 C) 120.14 (s, 1 C) 121.08 (s, 1 C) 123.37 (s, 1 C) 131.85 (s, 1 C) 141.92 (s, 1 C) 141.98 (s, 1 C) 145.33 (s, 1 C) 157.20 (s, 1 C) 158.50 (s, 1 C) 166.55 (s, 1 C)

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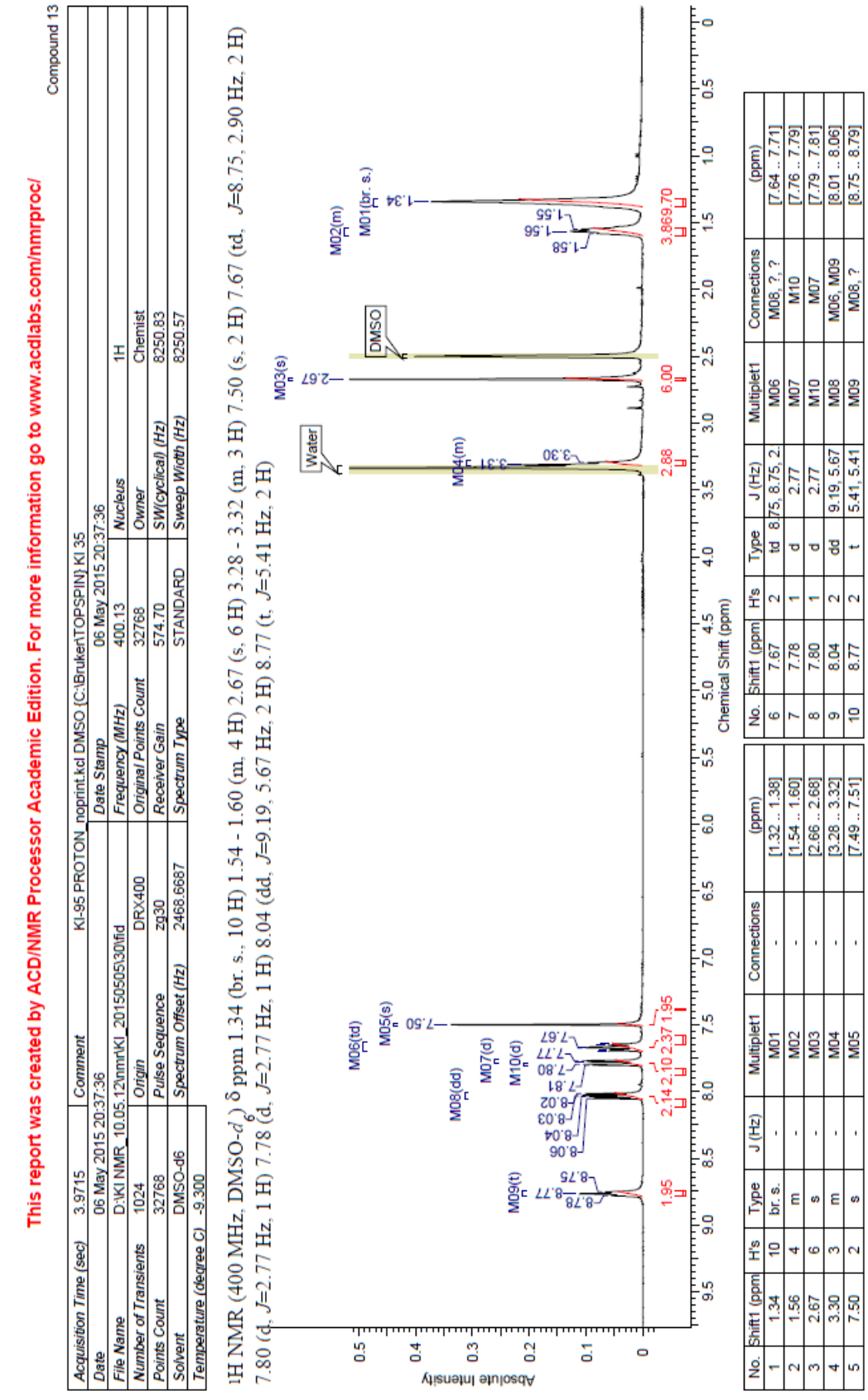
NL:
1.60E6
8158#5-17 RT: 0.05-0.15
AV: 13 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Relative Abundance
Observed Data
520.2602
518.9621
521.2635
512.9122
514.8135
516.2180
517.2248
522.2667
524.2846
525.2645
527.2237
528.2283
529.8696
519.2566
NL:
1.66E4
C 30 H 32 F 2 N 4 O 2 H:
C 30 H 33 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
520.2597
521.2627
522.2656
523.2684
525.2739
526.2767
m/z

Compound 13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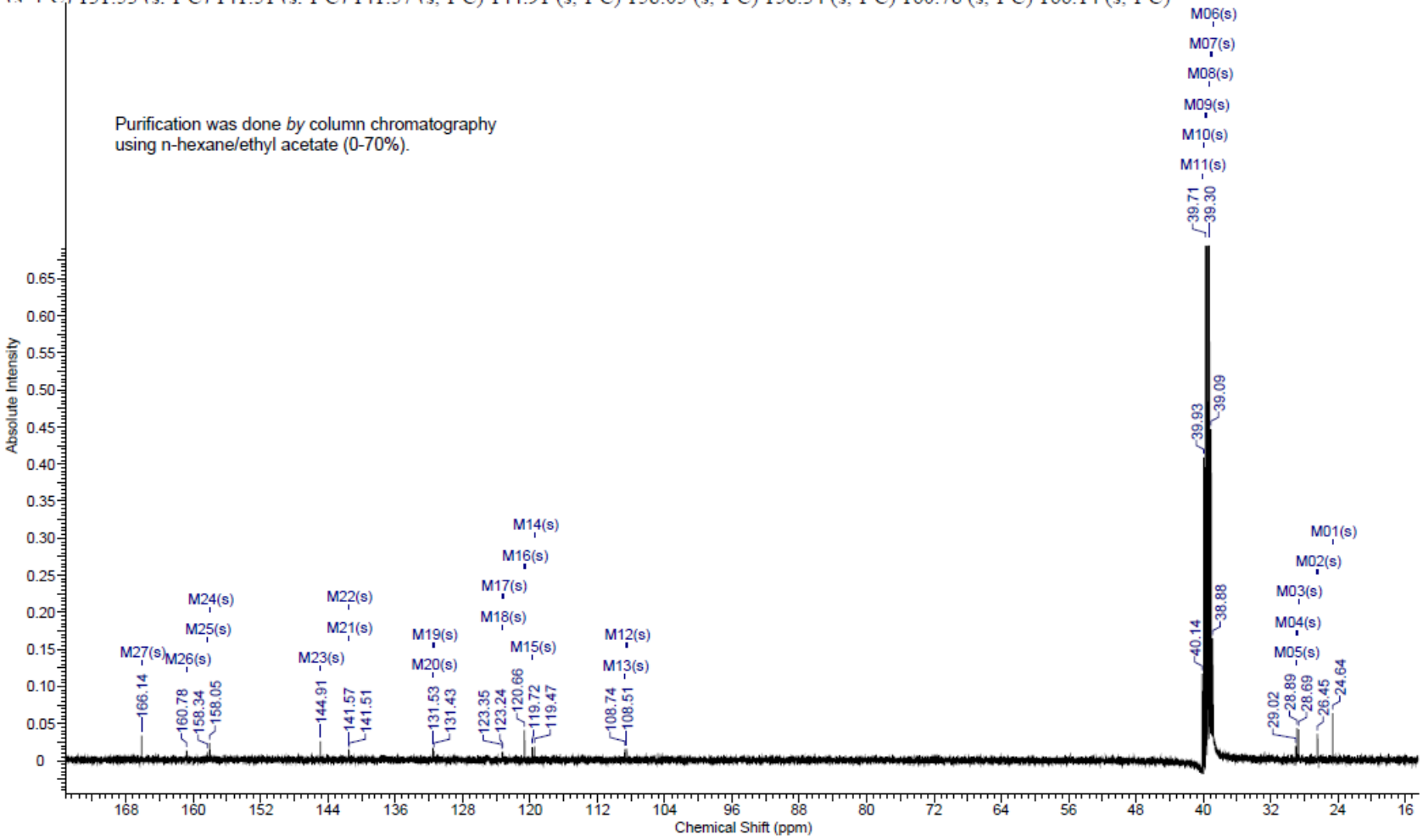
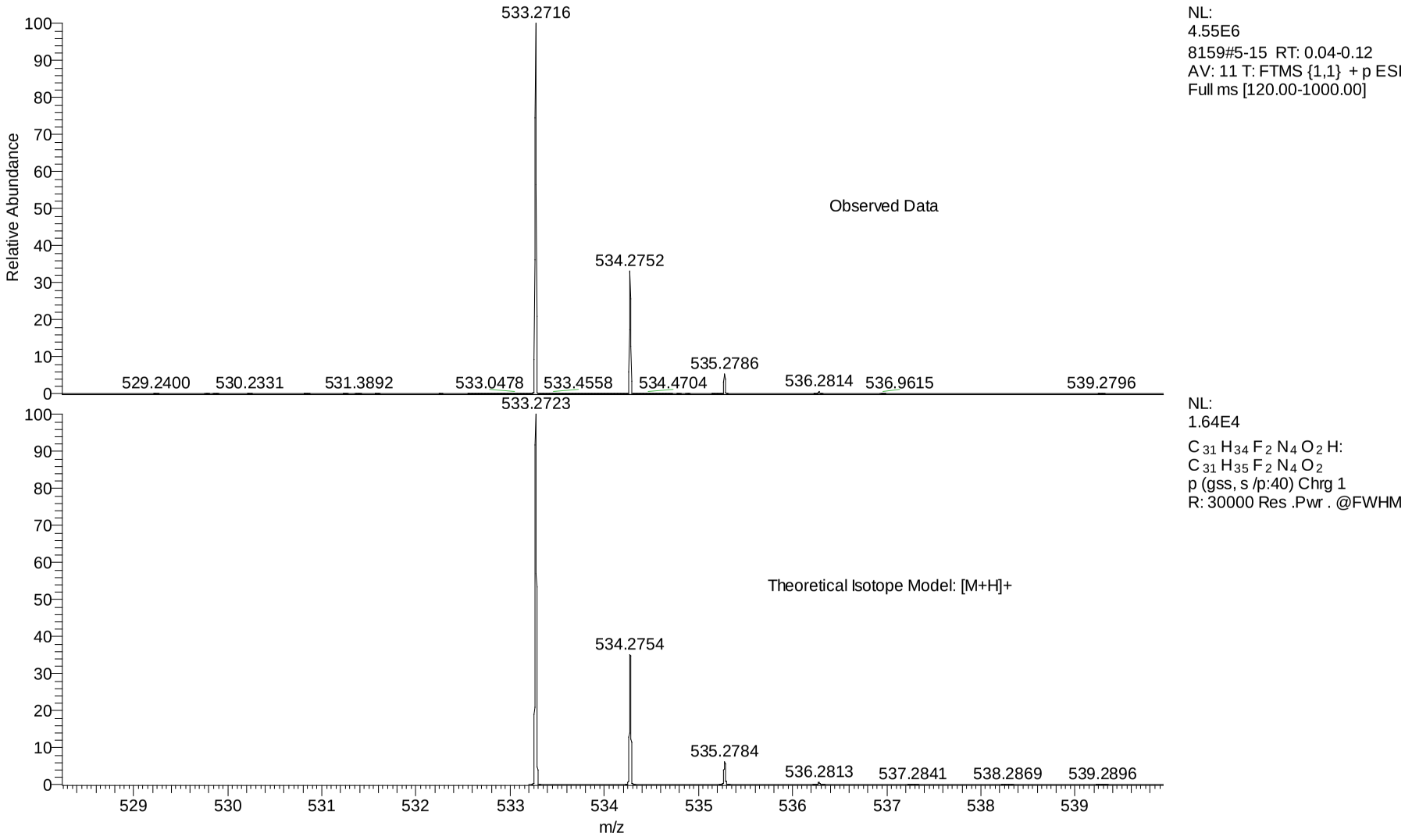
Compound 13
Acquisition Time (sec) 3.9715
Comment KI-95 PROTON_noprint.kcl DMSO (C:\Bruker\TOPSPIN) KI 35
Date 06 May 2015 20:37:36
Date Stamp 06 May 2015 20:37:36
File Name D:\KI NMR_10.05.12\nmrKI_20150505\30\fid
Frequency (MHz) 400.13
Nucleus 1H
Number of Transients 1024
Origin DRX400
Original Points Count 32768
Owner Chemist
Points Count 32768
Pulse Sequence zg30
Receiver Gain 574.70
SW(cyclical) (Hz) 8250.83
Solvent DMSO-d6
Spectrum Offset (Hz) 2468.6687
Spectrum Type STANDARD
Sweep Width (Hz) 8250.57
Temperature (degree C) -9.300
1H NMR (400 MHz, DMSO-d6) δ ppm 1.34 (br. s., 10 H) 1.54 - 1.60 (m, 4 H) 2.67 (s, 6 H) 3.28 - 3.32 (m, 3 H) 7.50 (s, 2 H) 7.67 (td, J=8.75, 2.90 Hz, 2 H) 7.80 (d, J=2.77 Hz, 1 H) 7.78 (d, J=2.77 Hz, 1 H) 8.04 (dd, J=9.19, 5.67 Hz, 2 H) 8.77 (t, J=5.41 Hz, 2 H)
Water
DMSO
M01(br. s.)
M02(m)
M03(s)
M04(m)
M05(s)
M06(td)
M07(d)
M08(dd)
M09(t)
M10(d)
Absolute Intensity
Chemical Shift (ppm)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
1 1.34 10 br. s. - M01 - [1.32 .. 1.38]
2 1.56 4 m - M02 - [1.54 .. 1.60]
3 2.67 6 s - M03 - [2.66 .. 2.68]
4 3.30 3 m - M04 - [3.28 .. 3.32]
5 7.50 2 s - M05 - [7.49 .. 7.51]
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
6 7.67 2 td 8.75, 8.75, 2. M06 M08, ?, ? [7.64 .. 7.71]
7 7.78 1 d 2.77 M07 M10 [7.76 .. 7.79]
8 7.80 1 d 2.77 M10 M07 [7.79 .. 7.81]
9 8.04 2 dd 9.19, 5.67 M08 M06, M09 [8.01 .. 8.06]
10 8.77 2 t 5.41, 5.41 M09 M08, ? [8.75 .. 8.79]

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 24.64 (s, 1 C) 26.45 (s, 1 C) 28.69 (s, 1 C) 28.89 (s, 1 C) 29.02 (s, 1 C) 38.88 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.71 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 108.51 (s, 1 C) 108.74 (s, 1 C) 119.47 (s, 1 C) 119.72 (s, 1 C) 120.66 (s, 1 C) 123.24 (s, 1 C) 123.35 (s, 1 C) 131.43 (s, 1 C) 131.53 (s, 1 C) 141.51 (s, 1 C) 141.57 (s, 1 C) 144.91 (s, 1 C) 158.05 (s, 1 C) 158.34 (s, 1 C) 160.78 (s, 1 C) 166.14 (s, 1 C)

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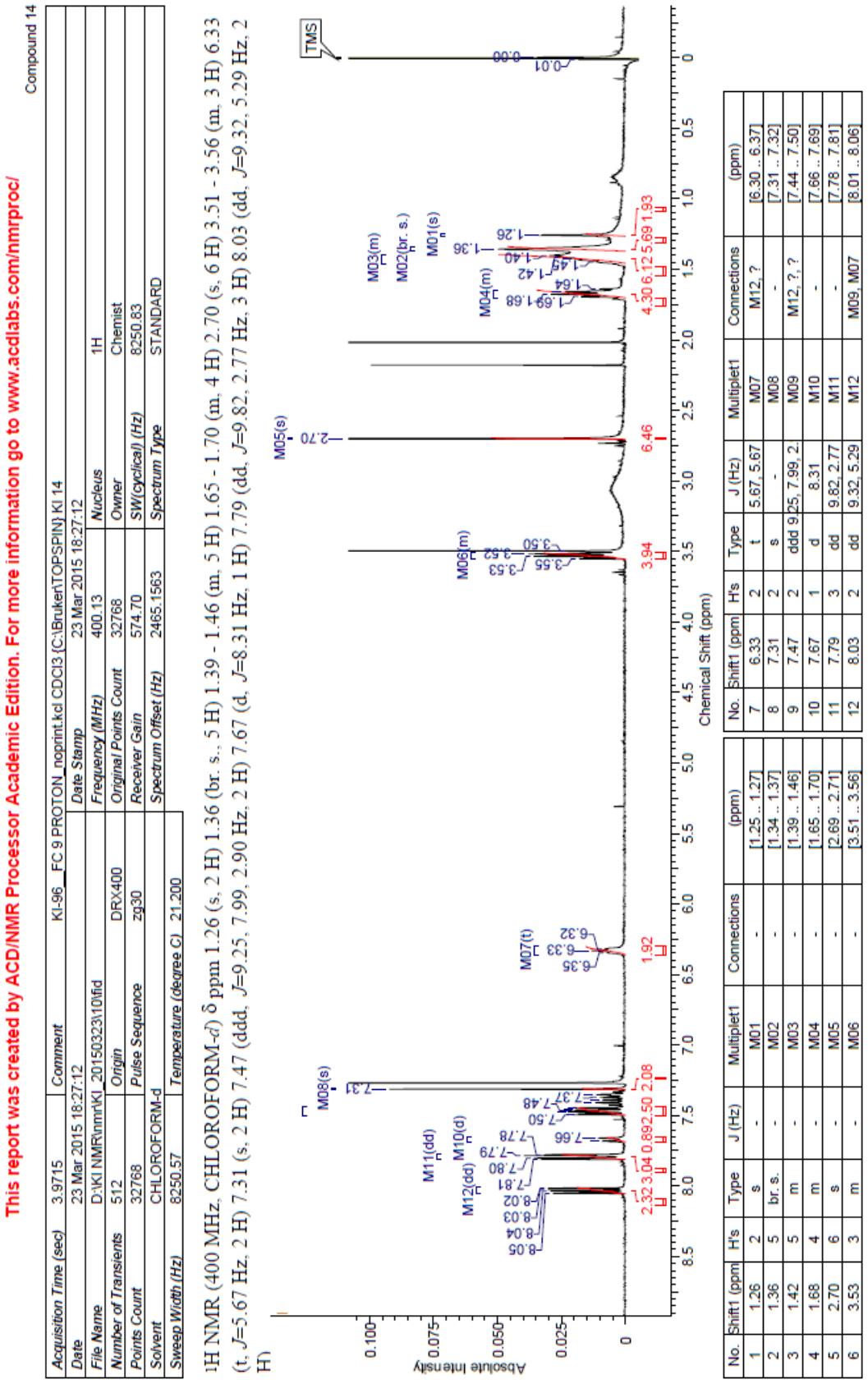
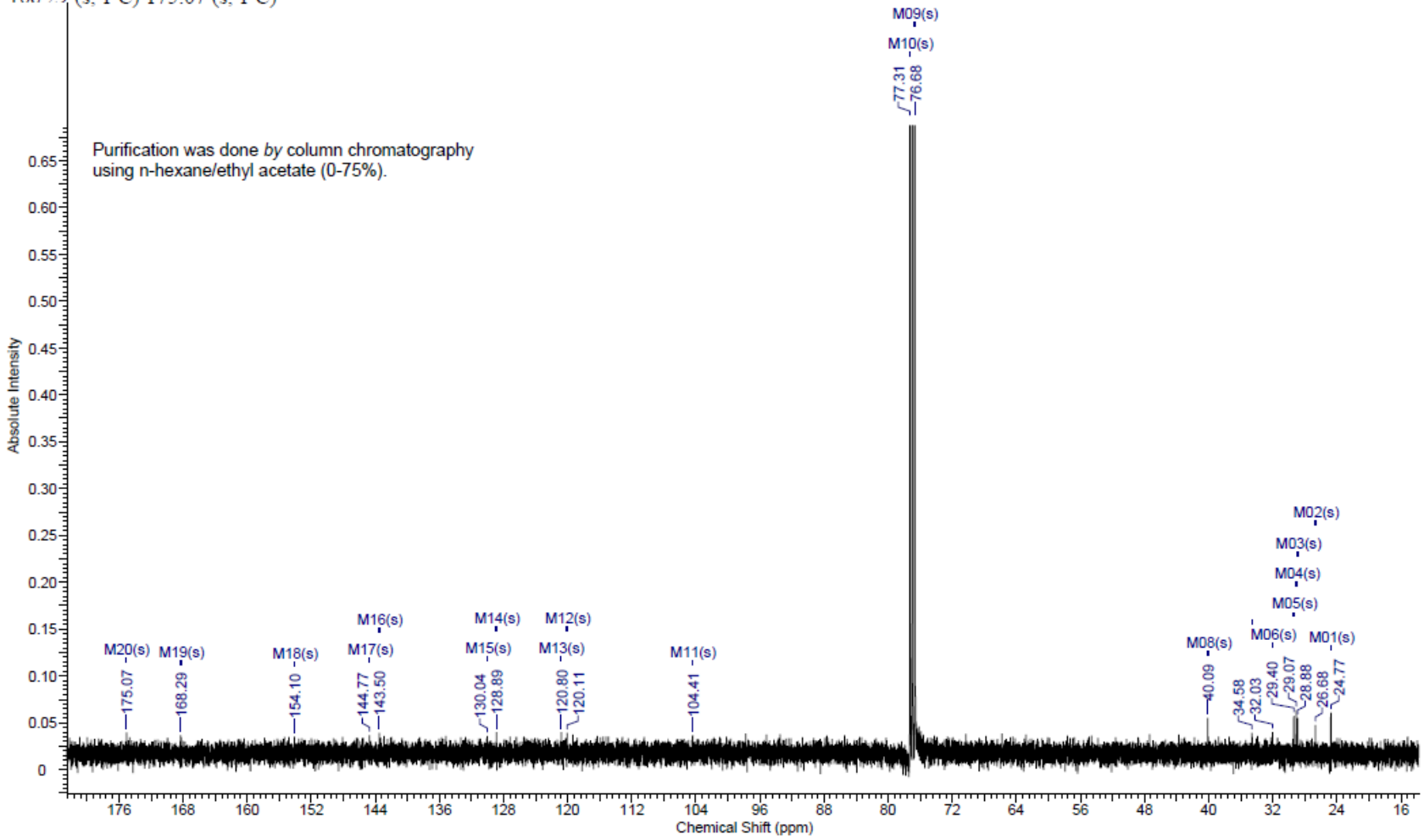
533.4558
534.4704
536.2814
536.9615
539.2796
Observed Data
NL:
4.55E6
8159#5-15 RT: 0.04-0.12
AV: 11 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
533.2723
534.2754
535.2784
536.2813
537.2841
538.2869
539.2896
Theoretical Isotope Model: [M+H]+
NL:
1.64E4
C 31 H 34 F 2 N 4 O 2 H:
C 31 H 35 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Relative Abundance
m/z

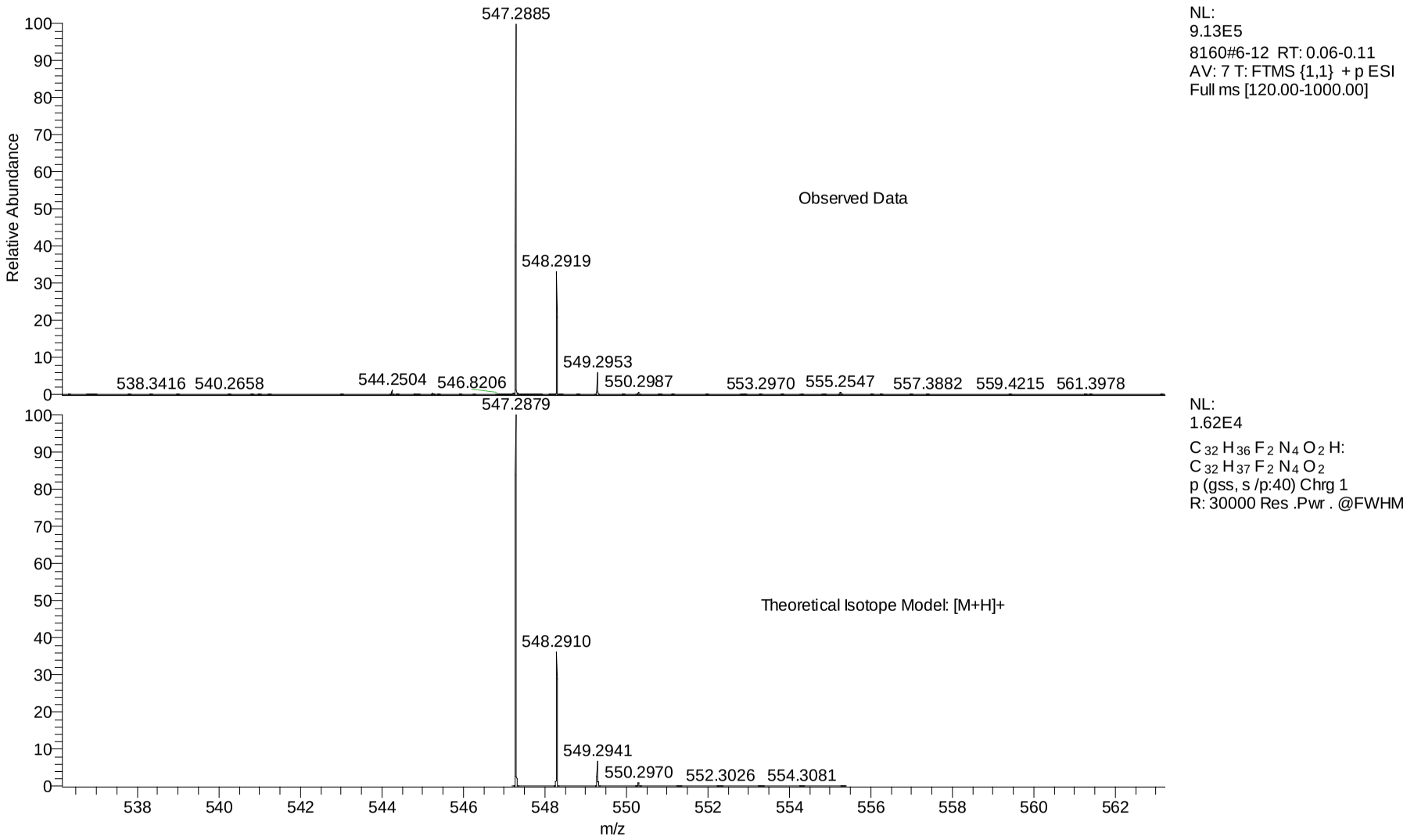
Compound 14


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
Compound 14
Acquisition Time (sec) 3.9715 Comment KI-96 FC 9 PROTON_noprint.kcl CDCl3 (C:\Bruker\TOPSPIN) KI 14
Date 23 Mar 2015 18:27:12 Date Stamp 23 Mar 2015 18:27:12
File Name D:\KI NMR\nmr\KI_20150323\10\fid Frequency (MHz) 400.13 Nucleus 1H
Number of Transients 512 Origin DRX400 Original Points Count 32768 Owner Chemist
Points Count 32768 Pulse Sequence zg30 Receiver Gain 574.70 SW(cyclical) (Hz) 8250.83
Solvent CHLOROFORM-d Spectrum Offset (Hz) 2465.1563 Spectrum Type STANDARD
Sweep Width (Hz) 8250.57 Temperature (degree C) 21.200
1H NMR (400 MHz, CHLOROFORM-d) δ ppm 1.26 (s, 2 H) 1.36 (br. s., 5 H) 1.39 - 1.46 (m, 5 H) 1.65 - 1.70 (m, 4 H) 2.70 (s, 6 H) 3.51 - 3.56 (m, 3 H) 6.33 (t, J=5.67 Hz, 2 H) 7.31 (s, 2 H) 7.47 (ddd, J=9.25, 7.99, 2.90 Hz, 2 H) 7.67 (d, J=8.31 Hz, 1 H) 7.79 (dd, J=9.82, 2.77 Hz, 3 H) 8.03 (dd, J=9.32, 5.29 Hz, 2 H)
Absolute Intensity
Chemical Shift (ppm)
TMS
M01(s)
M02(br. s.)
M03(m)
M04(m)
M05(s)
M06(m)
M07(t)
M08(s)
M09
M10(d)
M11(dd)
M12(dd)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
1 1.26 2 s - M01 - [1.25 .. 1.27]
2 1.36 5 br. s. - M02 - [1.34 .. 1.37]
3 1.42 5 m - M03 - [1.39 .. 1.46]
4 1.68 4 m - M04 - [1.65 .. 1.70]
5 2.70 6 s - M05 - [2.69 .. 2.71]
6 3.53 3 m - M06 - [3.51 .. 3.56]
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
7 6.33 2 t 5.67, 5.67 M07 M12, ? [6.30 .. 6.37]
8 7.31 2 s - M08 - [7.31 .. 7.32]
9 7.47 2 ddd 9.25, 7.99, 2. M09 M12, ?, ? [7.44 .. 7.50]
10 7.67 1 d 8.31 M10 - [7.66 .. 7.69]
11 7.79 3 dd 9.82, 2.77 M11 - [7.78 .. 7.81]
12 8.03 2 dd 9.32, 5.29 M12 M09, M07 [8.01 .. 8.06]

Compound 14

^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 24.77 (s, 1 C) 26.68 (s, 1 C) 28.88 (s, 1 C) 29.07 (s, 1 C) 29.40 (s, 1 C) 32.03 (s, 1 C) 34.58 (s, 1 C) 40.09 (s, 1 C) 76.68 (s, 1 C) 77.31 (s, 1 C) 104.41 (s, 1 C) 120.11 (s, 1 C) 120.80 (s, 1 C) 128.89 (s, 1 C) 130.04 (s, 1 C) 143.50 (s, 1 C) 144.77 (s, 1 C) 154.10 (s, 1 C) 168.29 (s, 1 C) 175.07 (s, 1 C)

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Full ms [120.00-1000.00]
Relative Abundance
Observed Data
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547.2879
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1.62E4
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C 32 H 37 F 2 N 4 O 2
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R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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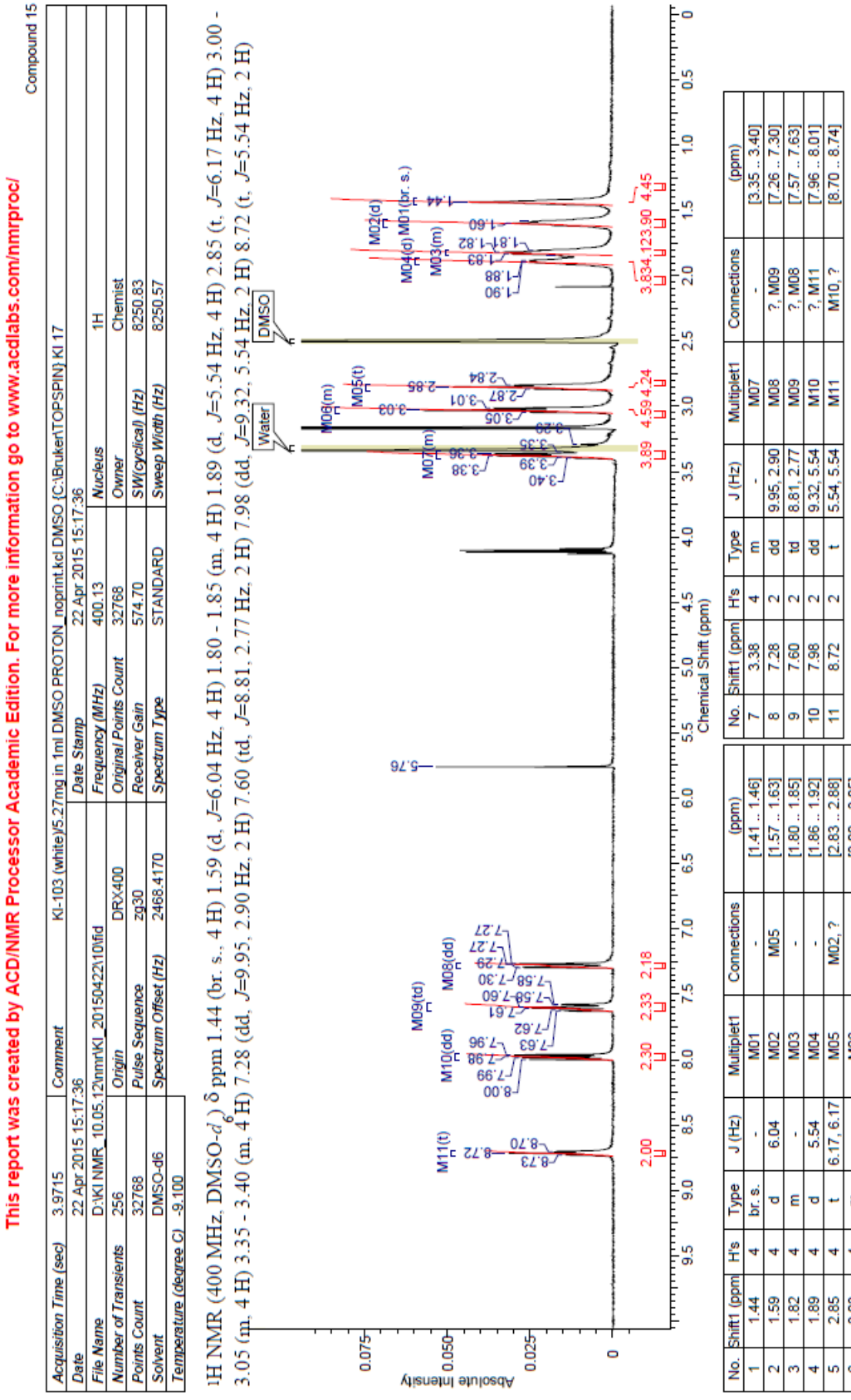
549.2941
550.2970 552.3026 554.3081
538 540 542 544 546 548 550 552 554 556 558 560 562
m/z

Compound 15

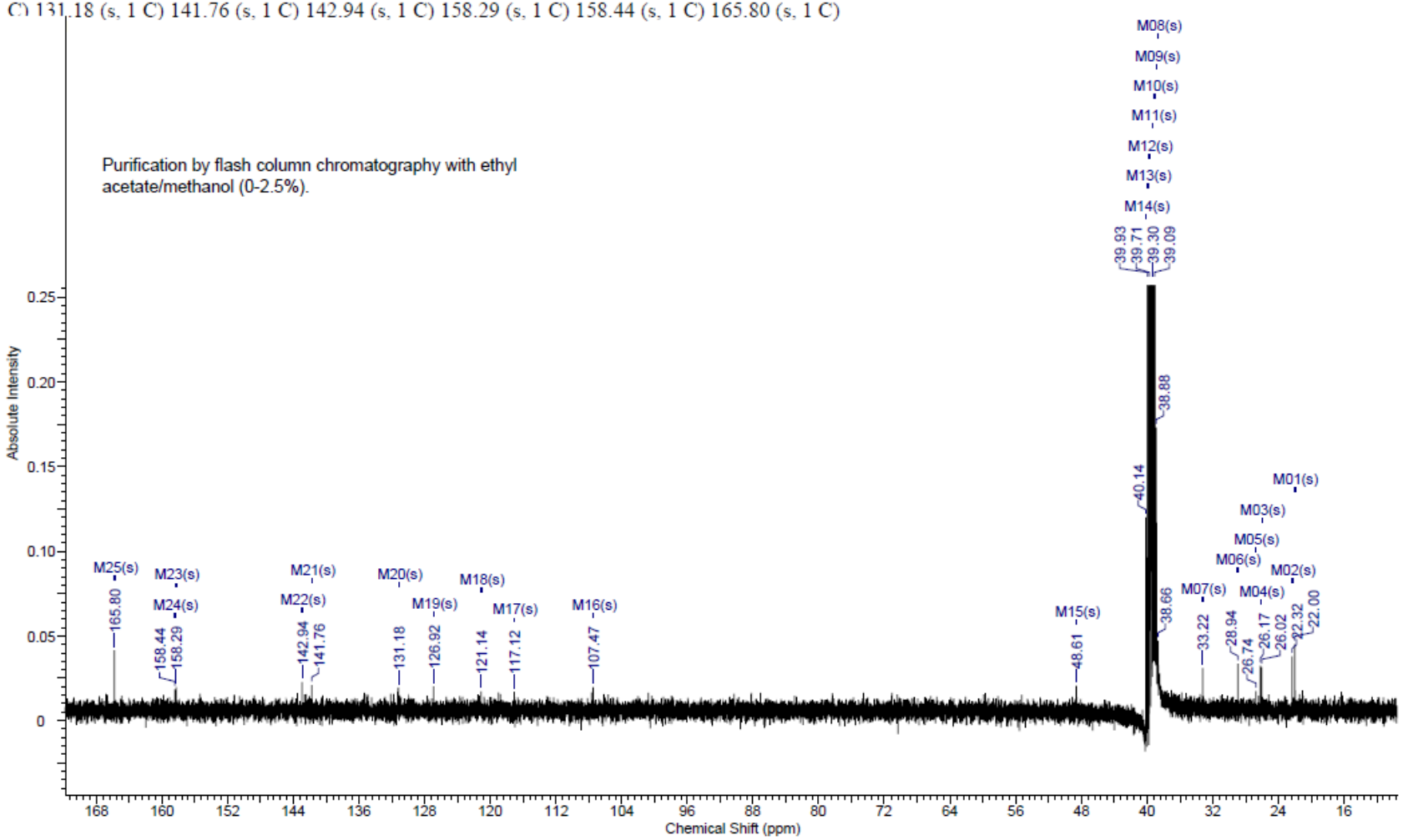


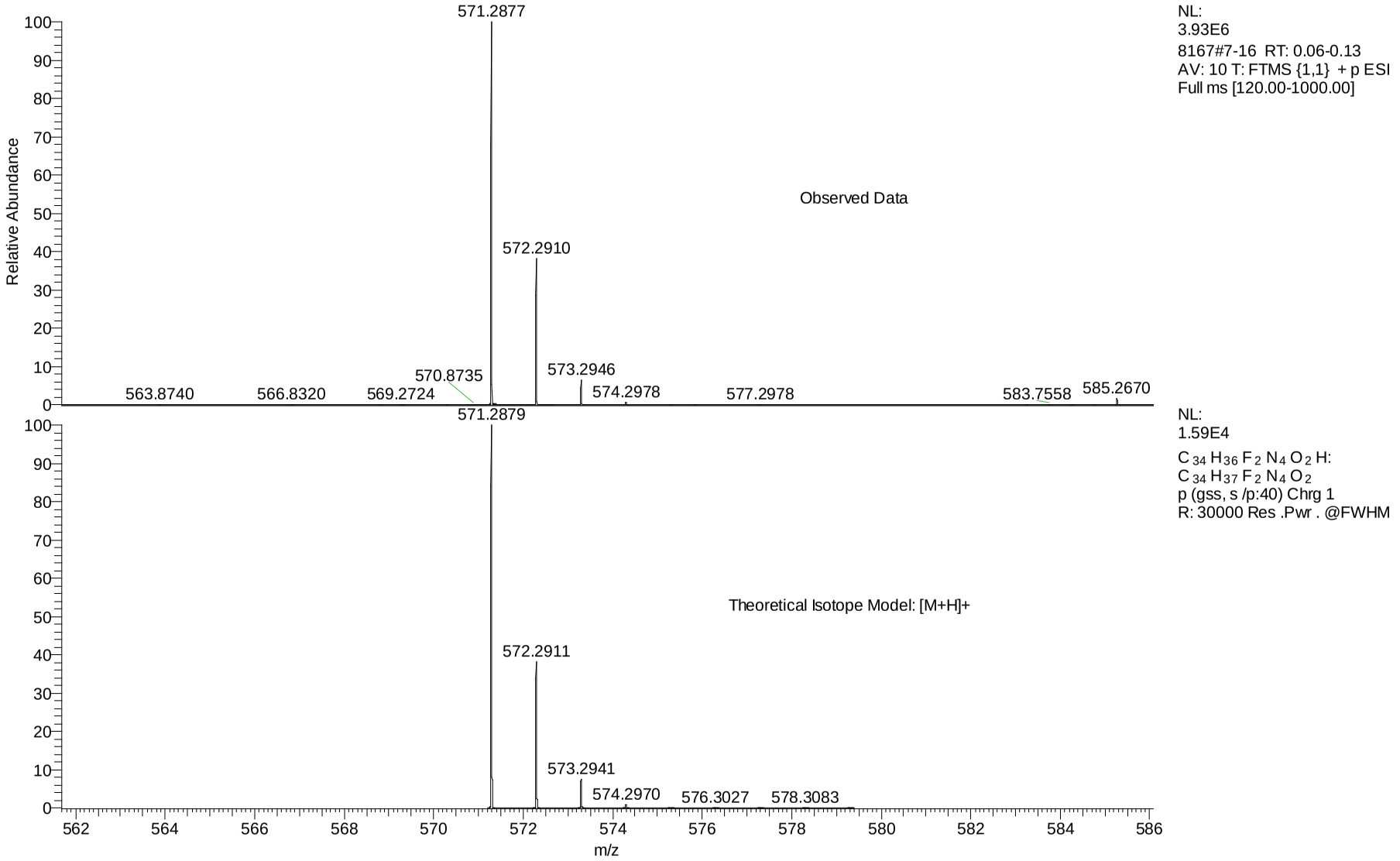
No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	1.44	4	br. s.	-	M01	-	[1.41 ... 1.46]
2	1.59	4	d	6.04	M02	M05	[1.57 ... 1.63]
3	1.82	4	m	-	M03	-	[1.80 ... 1.85]
4	1.89	4	d	5.54	M04	-	[1.86 ... 1.92]
5	2.85	4	t	6.17, 6.17	M05	M02, ?	[2.83 ... 2.88]
6	3.03	4	m	-	M06	-	[3.00 ... 3.05]

No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
7	3.38	4	m	-	M07	-	[3.35 ... 3.40]
8	7.28	2	dd	9.95, 2.90	M08	?, M09	[7.26 ... 7.30]
9	7.60	2	td	8.81, 2.77	M09	?, M08	[7.57 ... 7.63]
10	7.98	2	dd	9.32, 5.54	M10	?, M11	[7.96 ... 8.01]
11	8.72	2	t	5.54, 5.54	M11	M10, ?	[8.70 ... 8.74]

Compound 15

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 22.00 (s, 1 C) 22.32 (s, 1 C) 26.02 (s, 1 C) 26.17 (s, 1 C) 26.74 (s, 1 C) 28.94 (s, 1 C) 33.22 (s, 1 C) 38.66 (s, 1 C) 38.88 (s, 1 C) 39.09 (s, 1 C) 39.30 (s, 1 C) 39.71 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 48.61 (s, 1 C) 107.47 (s, 1 C) 117.12 (s, 1 C) 121.14 (s, 1 C) 126.92 (s, 1 C) 131.18 (s, 1 C) 141.76 (s, 1 C) 142.94 (s, 1 C) 158.29 (s, 1 C) 158.44 (s, 1 C) 165.80 (s, 1 C)

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8167#7-16 RT: 0.06-0.13
AV: 10 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Observed Data
Relative Abundance
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573.2946
574.2978
563.8740
566.8320
569.2724
577.2978
583.7558
585.2670
NL:
1.59E4
C 34 H 36 F 2 N 4 O 2 H:
C 34 H 37 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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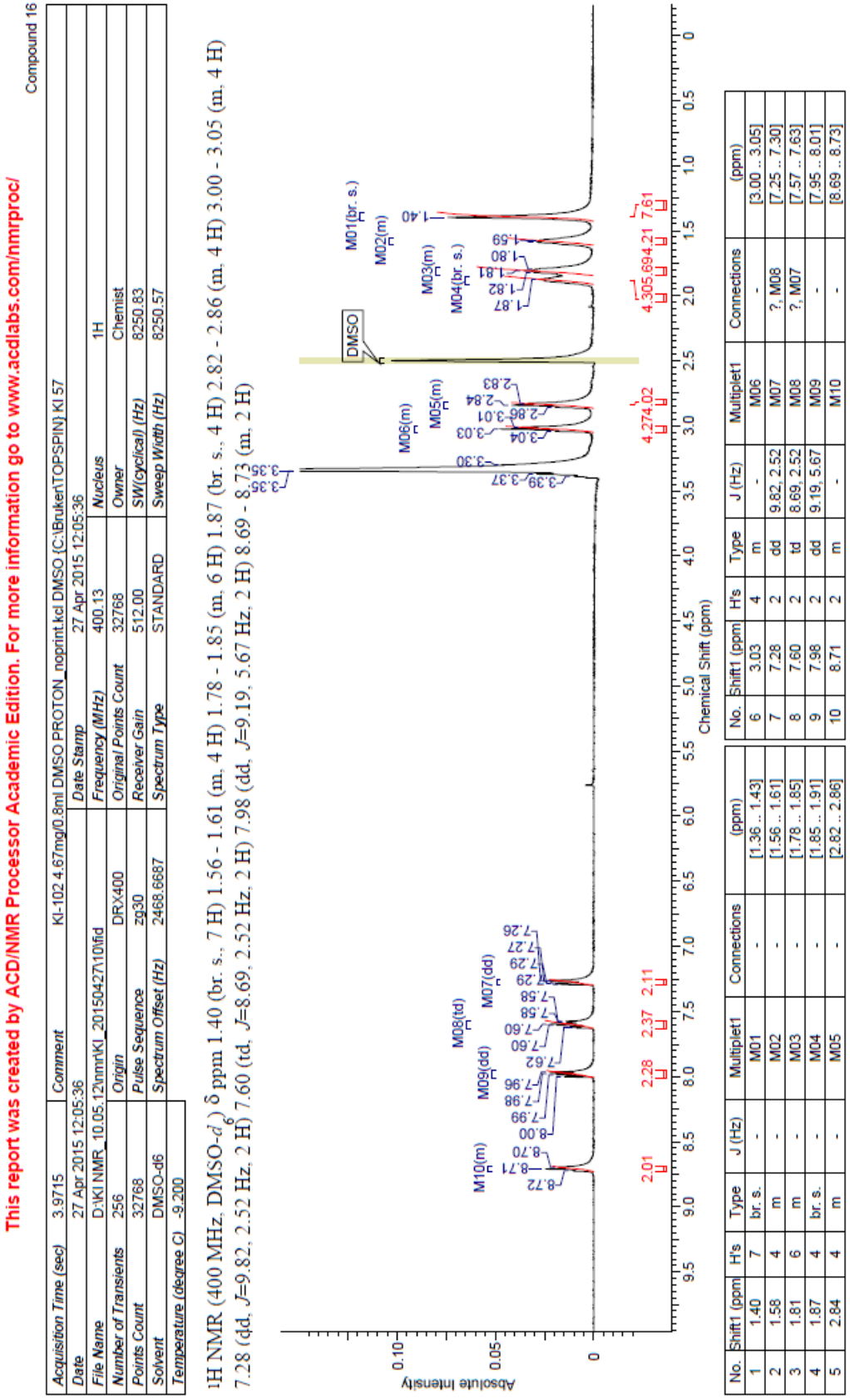
572.2911
573.2941
574.2970
576.3027
578.3083
m/z

Compound 16


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
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Acquisition Time (sec) 3.9715
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Date Stamp 27 Apr 2015 12:05:36
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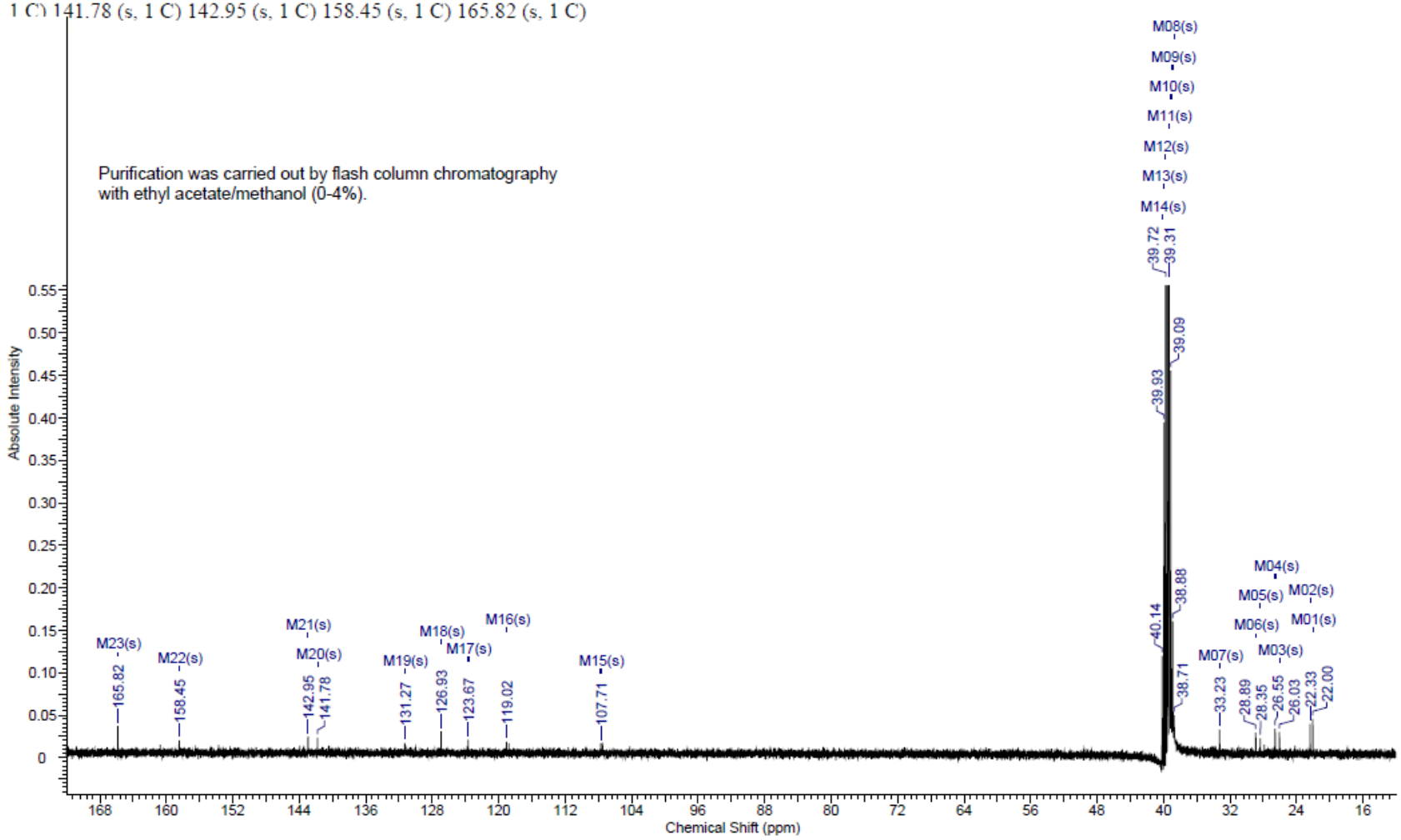
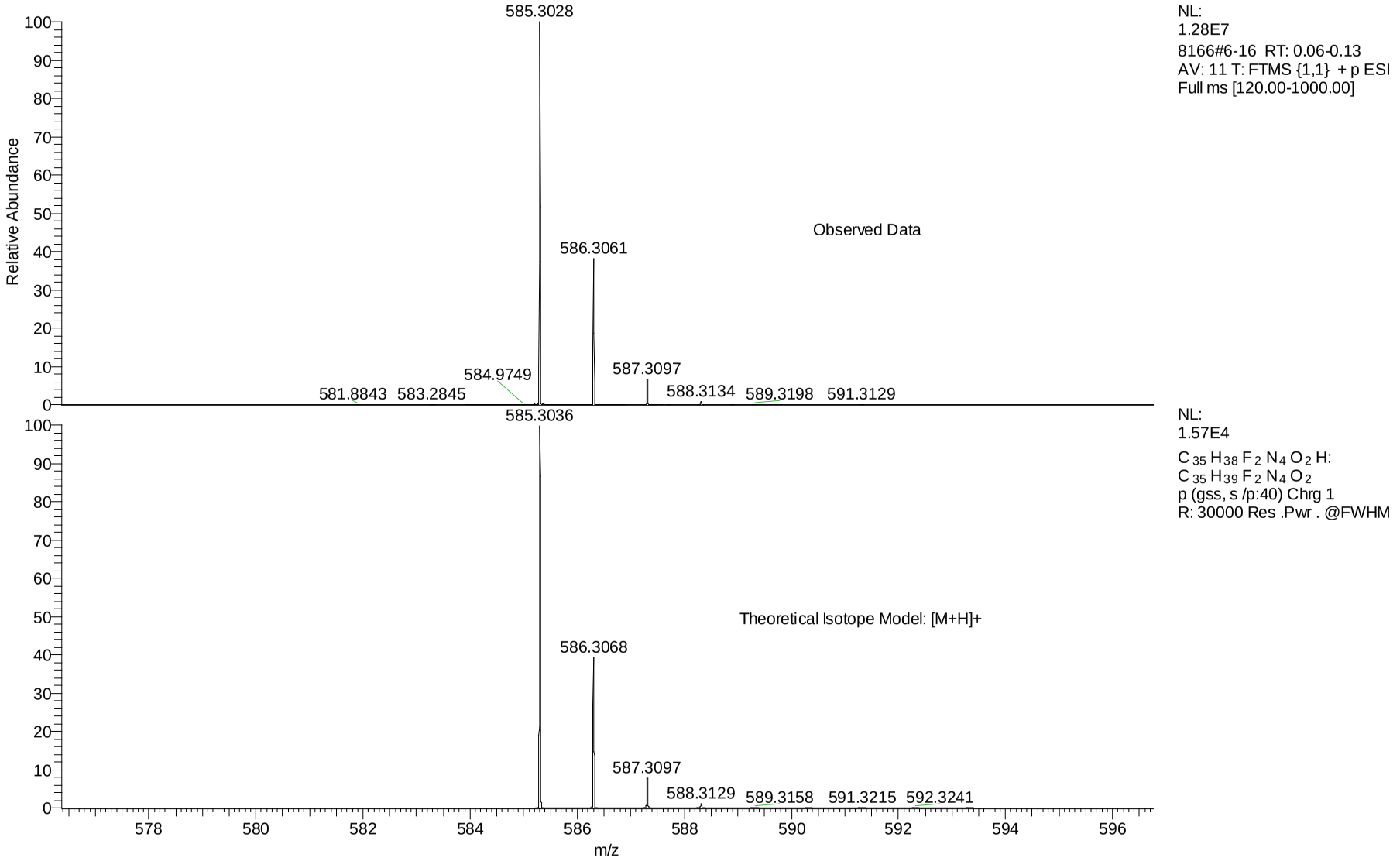
Frequency (MHz) 400.13
Nucleus 1H
Number of Transients 256
Origin DRX400
Original Points Count 32768
Owner Chemist
Points Count 32768
Pulse Sequence zg30
Receiver Gain 512.00
SW(cyclical) (Hz) 8250.83
Solvent DMSO-d6
Spectrum Offset (Hz) 2468.6687
Spectrum Type STANDARD
Sweep Width (Hz) 8250.57
Temperature (degree C) -9.200
1H NMR (400 MHz, DMSO-d6) δ ppm 1.40 (br. s., 7 H) 1.56 - 1.61 (m, 4 H) 1.78 - 1.85 (m, 6 H) 1.87 (br. s., 4 H) 2.82 - 2.86 (m, 4 H) 3.00 - 3.05 (m, 4 H) 7.28 (dd, J=9.82, 2.52 Hz, 2 H) 7.60 (td, J=8.69, 2.52 Hz, 2 H) 7.98 (dd, J=9.19, 5.67 Hz, 2 H) 8.69 - 8.73 (m, 2 H)
DMSO
M01(br. s.)
M02(m)
M03(m)
M04(br. s.)
M05(m)
M06(m)
M07(dd)
M08(td)
M09(dd)
M10(m)
Absolute Intensity
Chemical Shift (ppm)
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
1 1.40 7 br. s. - M01 - [1.36 ... 1.43]
2 1.58 4 m - M02 - [1.56 ... 1.61]
3 1.81 6 m - M03 - [1.78 ... 1.85]
4 1.87 4 br. s. - M04 - [1.85 ... 1.91]
5 2.84 4 m - M05 - [2.82 ... 2.86]
No. Shift1 (ppm) H's Type J (Hz) Multiplet1 Connections (ppm)
6 3.03 4 m - M06 - [3.00 ... 3.05]
7 7.28 2 dd 9.82, 2.52 M07 ?, M08 [7.25 ... 7.30]
8 7.60 2 td 8.69, 2.52 M08 ?, M07 [7.57 ... 7.63]
9 7.98 2 dd 9.19, 5.67 M09 - [7.95 ... 8.01]
10 8.71 2 m - M10 - [8.69 ... 8.73]

Compound 16

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 22.00 (s, 1 C) 22.33 (s, 1 C) 26.03 (s, 1 C) 26.55 (s, 1 C) 28.35 (s, 1 C) 28.89 (s, 1 C) 33.23 (s, 1 C) 38.71 (s, 1 C) 38.88 (s, 1 C) 39.09 (s, 1 C) 39.31 (s, 1 C) 39.72 (s, 1 C) 39.93 (s, 1 C) 40.14 (s, 1 C) 107.71 (s, 1 C) 119.02 (s, 1 C) 123.67 (s, 1 C) 126.93 (s, 1 C) 131.27 (s, 1 C) 141.78 (s, 1 C) 142.95 (s, 1 C) 158.45 (s, 1 C) 165.82 (s, 1 C)

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AV: 11 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
Relative Abundance
Observed Data
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587.3097
581.8843
583.2845
588.3134
589.3198
591.3129
585.3036
NL:
1.57E4
C 35 H 38 F 2 N 4 O 2 H:
C 35 H 39 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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592.3241
m/z

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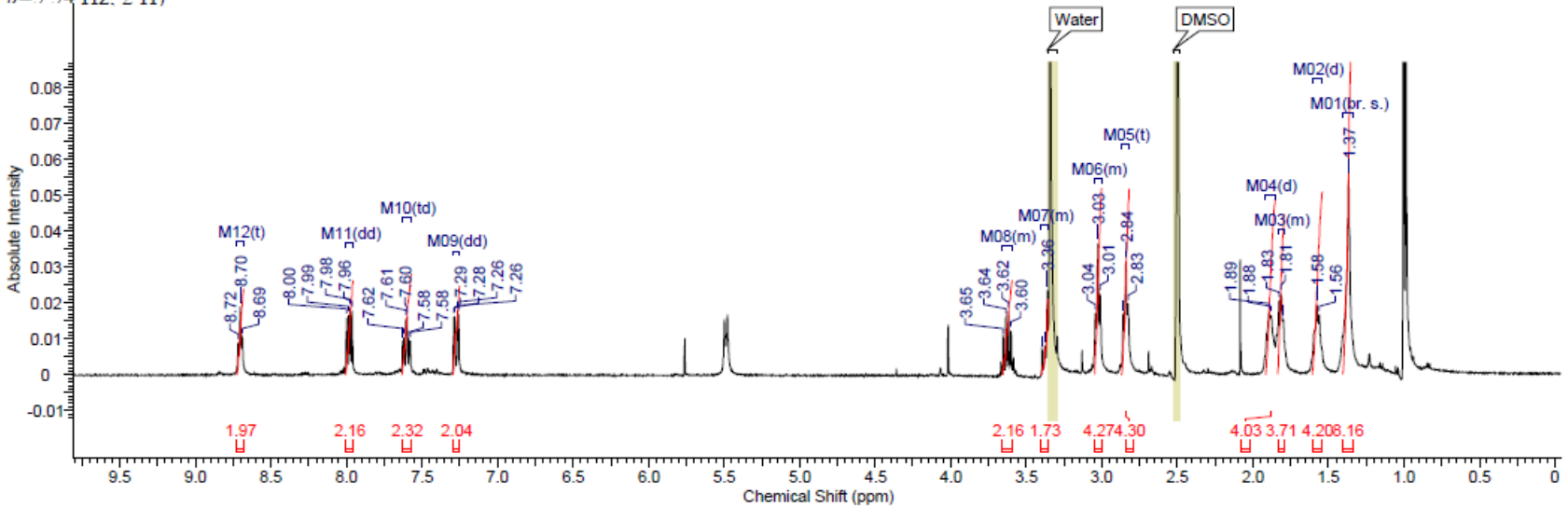
File Name	D:\KI NMR_10.05.12\nmr\KI_20150423\10\fid			*Frequency (MHz)*	400.13	*Nucleus*	1H
Number of Transients	256	*Origin*	DRX400	*Original Points Count*	32768	*Owner*	Chemist
Points Count	32768	*Pulse Sequence*	zg30	*Receiver Gain*	456.10	*SW(cyclical) (Hz)*	8250.83
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	2468.6687	*Spectrum Type*	STANDARD	*Sweep Width (Hz)*	8250.57
Temperature (degree C)	-9.400						

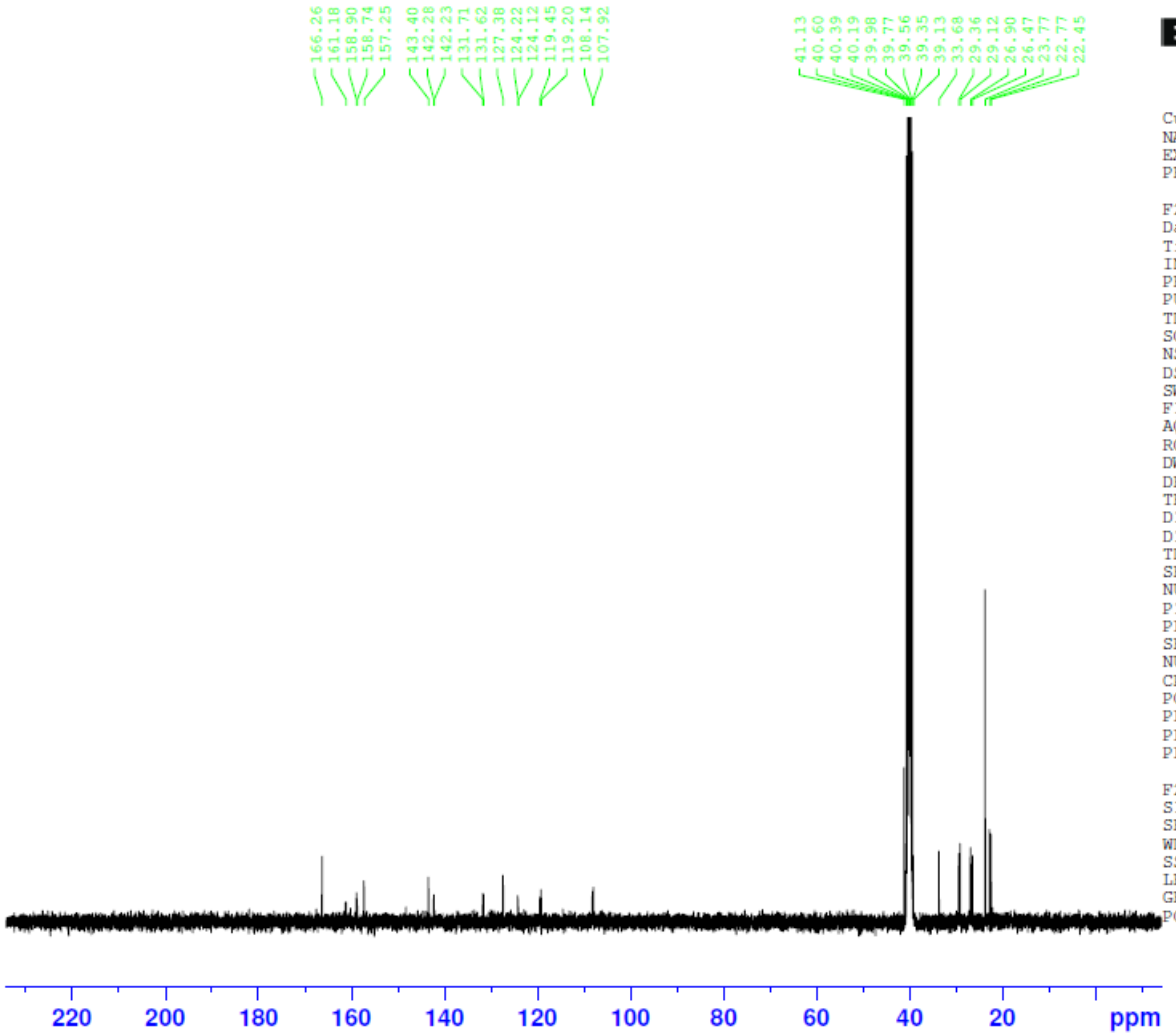
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.37 (br. s., 8 H) 1.57 (d, *J*=6.80 Hz, 4 H) 1.79 - 1.84 (m, 4 H) 1.89 (d, *J*=5.04 Hz, 4 H) 2.84 (t, *J*=6.42 Hz, 4 H) 3.00 - 3.05 (m, 4 H) 3.36 - 3.40 (m, 2 H) 3.59 - 3.66 (m, 2 H) 7.27 (dd, *J*=9.82, 2.77 Hz, 2 H) 7.60 (td, *J*=8.81, 2.77 Hz, 2 H) 7.98 (dd, *J*=9.32, 5.54 Hz, 2 H) 8.70 (t, *J*=5.54 Hz, 2 H)



No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	1.37	8	br. s.	-	M01	-	[1.34 .. 1.40]
2	1.57	4	d	6.80	M02	M05	[1.54 .. 1.61]
3	1.81	4	m	-	M03	-	[1.79 .. 1.84]
4	1.89	4	d	5.04	M04	-	[1.85 .. 1.91]
5	2.84	4	t	6.42, 6.42	M05	M02, ?	[2.82 .. 2.87]
6	3.03	4	m	-	M06	-	[3.00 .. 3.05]

No.	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
7	3.38	2	m	-	M07	-	[3.36 .. 3.40]
8	3.63	2	m	-	M08	-	[3.59 .. 3.66]
9	7.27	2	dd	9.82, 2.77	M09	?, M10	[7.25 .. 7.30]
10	7.60	2	td	8.81, 2.77	M10	?, M09	[7.57 .. 7.63]
11	7.98	2	dd	9.32, 5.54	M11	?, M12	[7.96 .. 8.00]
12	8.70	2	t	5.54, 5.54	M12	M11, ?	[8.68 .. 8.73]

Compound 17



BRUKER

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EXPNO                30
PROCNO                1

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SOLVENT             DMSO
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DE                10.12 usec
TE                296.5 K
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D11           0.03000000 sec
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NUC2                1H
CPDPRG[2         waltz64
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F2 - Processing parameters
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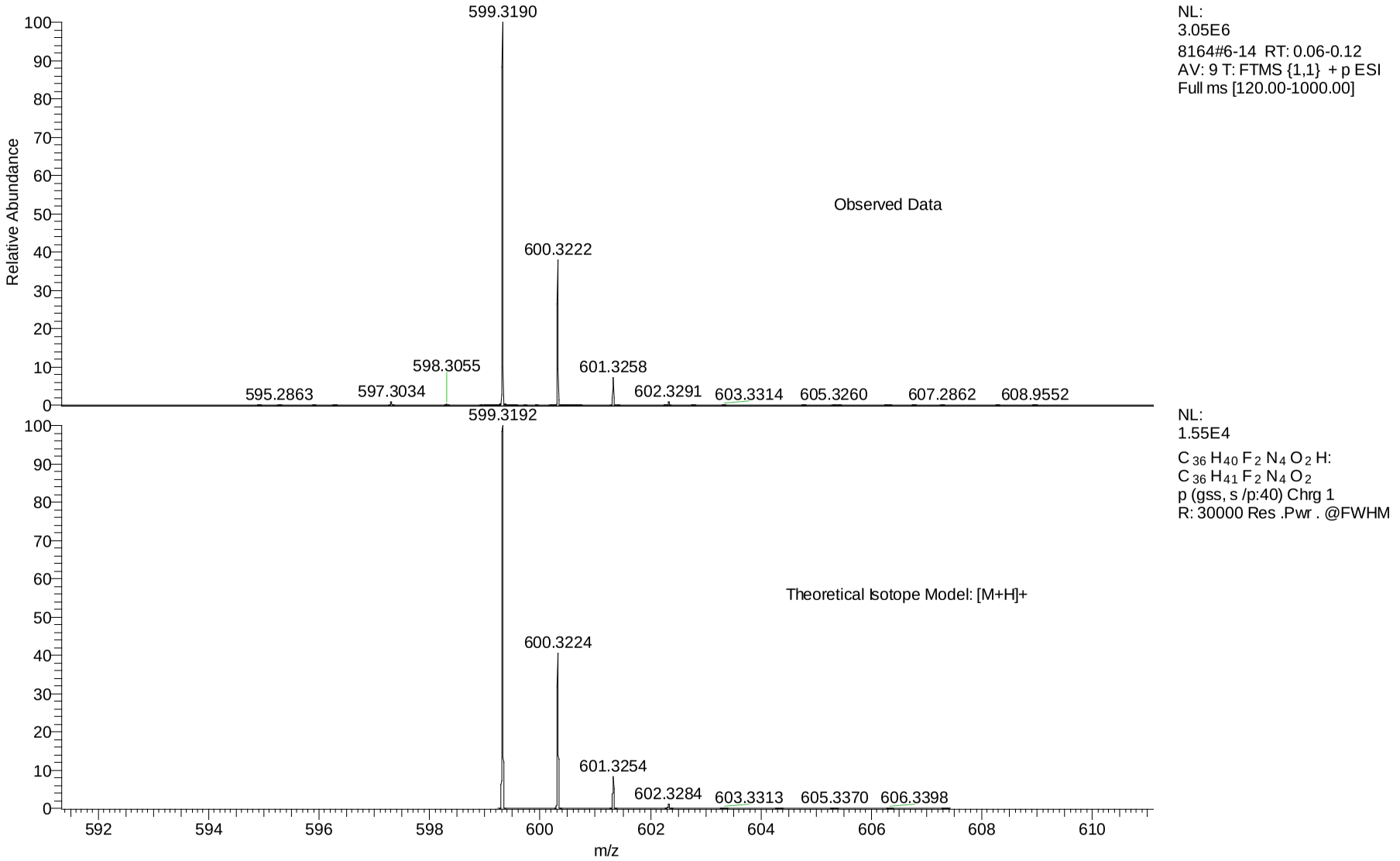
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600.3222
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605.3260
607.2862
608.9552
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C 36 H 40 F 2 N 4 O 2 H:
C 36 H 41 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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601.3254
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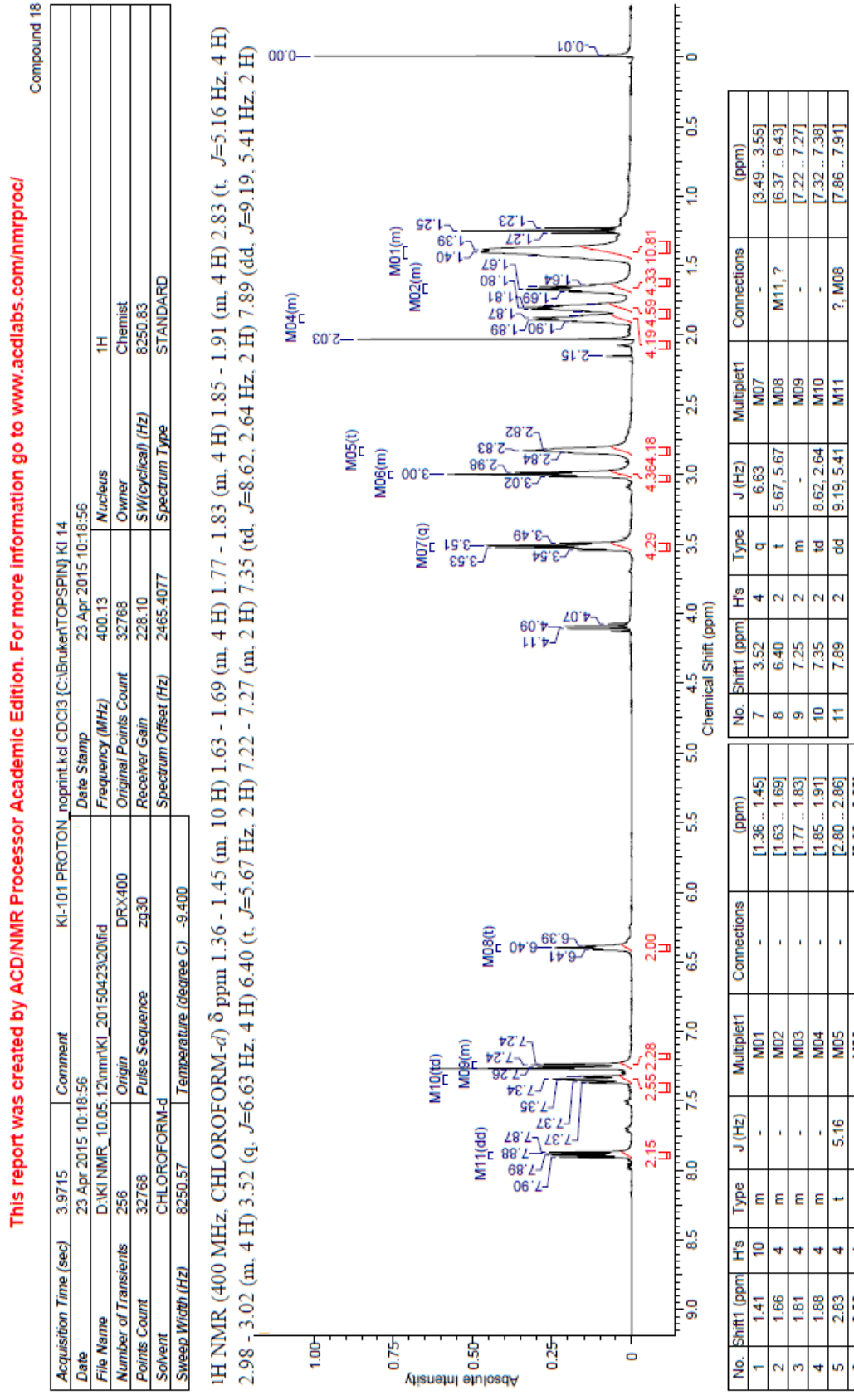
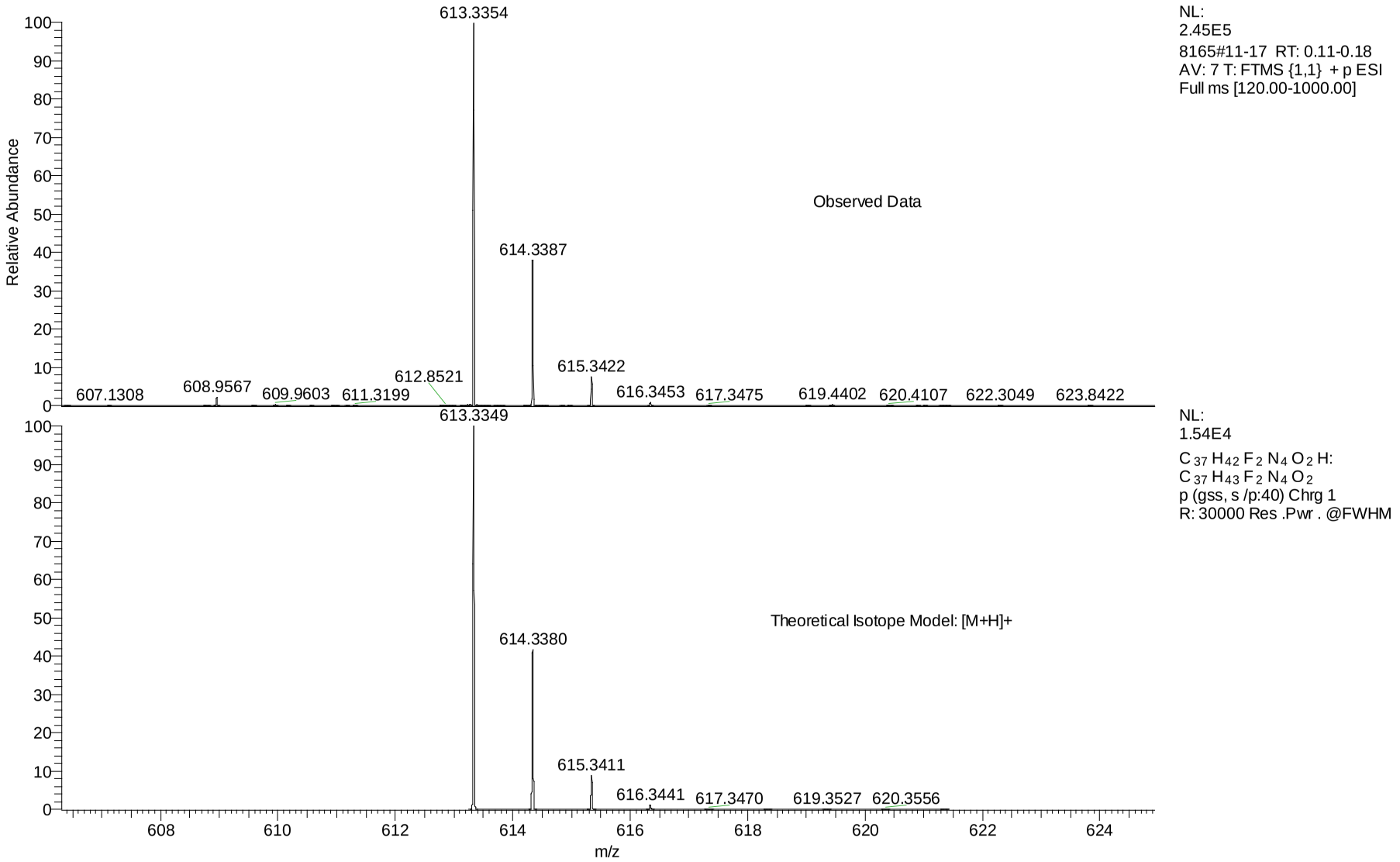
606.3398
Relative Abundance
m/z

Compound 18



No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
1	1.41	10	m	-	M01	-	[1.36 .. 1.45]
2	1.66	4	m	-	M02	-	[1.63 .. 1.69]
3	1.81	4	m	-	M03	-	[1.77 .. 1.83]
4	1.88	4	m	-	M04	-	[1.85 .. 1.91]
5	2.83	4	t	5.16	M05	-	[2.80 .. 2.86]
6	3.00	4	m	-	M06	-	[2.98 .. 3.02]

No.	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	Connections	(ppm)
7	3.52	4	q	6.63	M07	-	[3.49 .. 3.55]
8	6.40	2	t	5.67, 5.67	M08	M11, ?	[6.37 .. 6.43]
9	7.25	2	m	-	M09	-	[7.22 .. 7.27]
10	7.35	2	td	8.62, 2.64	M10	-	[7.32 .. 7.38]
11	7.89	2	dd	9.19, 5.41	M11	?, M08	[7.86 .. 7.91]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AV: 7 T: FTMS {1,1} + p ESI
Full ms [120.00-1000.00]
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619.4402
620.4107
622.3049
623.8422
Relative Abundance
613.3349
NL:
1.54E4
C 37 H 42 F 2 N 4 O 2 H:
C 37 H 43 F 2 N 4 O 2
p (gss, s /p:40) Chrg 1
R: 30000 Res .Pwr . @FWHM
Theoretical Isotope Model: [M+H]+
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615.3411
616.3441
617.3470
619.3527
620.3556
m/z

References

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