Electronic Supplementary Information (ESI)

for

Continuous-flow synthesis of fluorine-containing fine chemicals with integrated benchtop NMR analysis

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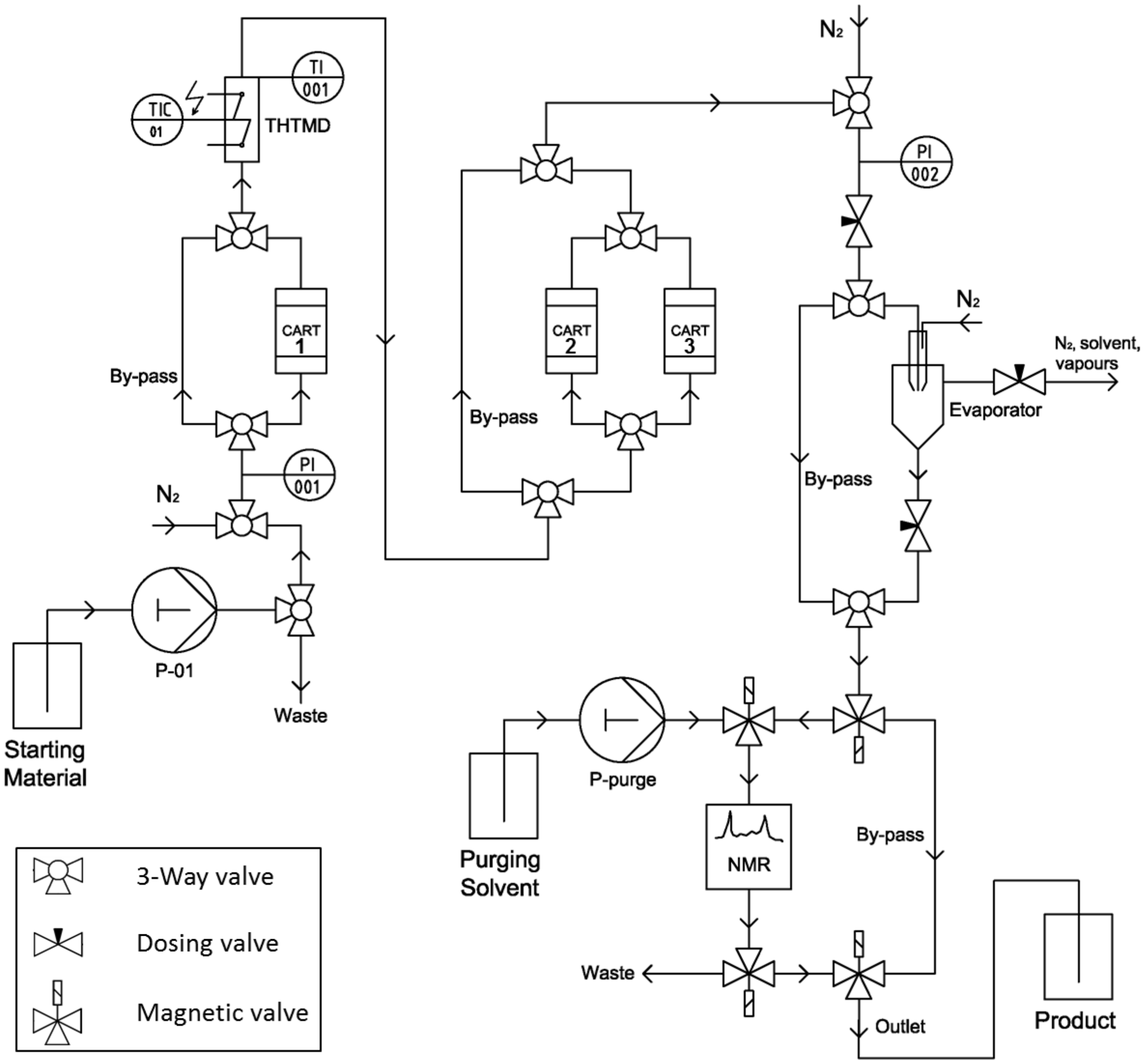
1. Lab plant flow chart with liquid control system



Scheme S1 Flow chart of THTMD-XL lab plant with integrated liquid control system and benchtop NMR analysis.

Pumps
Supplier: Knauer GmbH

P-01 Knauer Smartline P100 with 10 mL pump head
Flow rate: max. 10 mL/min
Pressure: max. 400 bar

P-purge Knauer Smartline K-501 with 10 mL pump head
Flow rate: max. 10 mL/min
Pressure: max. 400 bar

Heating cartridge in THTMD
Supplier: Hotrod®
Typ HHP 20 mm
Diameter: 20 mm, length: 200 mm, maximum power: 2500 W, voltage supply: 230 V
Integrated thermocouple: *TIC-001* NiCr-Ni Typ K

Connection cable: 1500 mm

Control unit for heating cartridge in THTMD
Supplier: Fraunhofer ICT-IMM
Voltage supply : 230 V
Integrated controller: JUMO iTRON B70.2040

Cartridges
Supplier: Fraunhofer ICT-IMM
CART1 length 5 cm, ¼" stainless steel pipe (1.4435), V = 0.8 mL
CART2 length 18 cm, 3/8" stainless steel pipe (1.4435), V = 7 mL
CART3 length 15 cm, ¼" stainless steel pipe (1.4435), V = 2.4 mL
Frits für ¼" tubes: pore size 10 µm, thickness: 1 mm, stainless steel (1.4401)
Connectors: Swagelok® 1/16'' connection nut with clamp ring

3-Way valves
Supplier: Swagelok®
Type: SS-41GXS1
1/16" connectors, stainless steel body (1.4401), Packung aus modifiziertem PTFE, working pressure: 172 bar (2500 psig), maximum temperature: +148 °C

Dosing valves
Supplier: Swagelok®
Type: SS-SS2-KZ-VH
1/8" connectors, stainless steel body 1.4401, working pressure: 137 bar, maximum temperature: +148 °C, material O-ring: Kalrez (FFKM), complete blocking not possible, dosing with micrometer screw

Flipper magnetic valves
Supplier: Bürkert
Type: 6650
3/2-Way universal passage, seal: FFKM, construction material: PEEK, voltage: 24 V, maximum pressure: 1 bar
Additional components: cable head Typ 2504 with integrated booster- and power reduction electronic, 24 V/DC, connection plate material: PEEK with UNF1/4-28-F connectors

Gas-liquid separator
Supplier: Fraunhofer ICT-IMM
Construction based upon literature data from: Ley et al. *Green Chem.*, **2013**, *15*, 2050.
Liquid feed capillary: 1/16" OD, 127 µm ID, stainless steel
Gas feed capillary: 1/8"stainless steel
Gas withdrawing capillary: ¼"stainless steel
Separator body: FEP tubing, 14 mm OD, 12 mm ID, length 100 mm
Screw connection material for separator body: Teflon

Nitrogen mass flow controller for g/l-splitter
Supplier: Bronkhorst®
Type: F-201C-FAC-22-P, S.N. M2207388B, 5 ls/min, maximum pressure: 4 bar (a), working temperature: 20 °C, signal out 0-5 V, signal in 0-5 V with control box for 5 V mass flow controller

Sensors and regulation units

a) Temperature detection (single unit)
   Supplier: TC direct
   TI-001 Typ K, diameter: 0,5 mm, length: 150 mm, material: stainless steel (1.4541), connection cable: 2000 mm with PFA isolation

b) Pressure detection
   Supplier: Landefeld
   PI-001/PI-002 MIDAS Type 1001, pressure range: 0-100 bar, material of contacting elements for measurement: stainless steel 1.4571 and 1.4542, temperature range of measuring medium: -20°C to +125 °C, voltage feed: 10-30 V DC, output signal: 4 to 20 mA

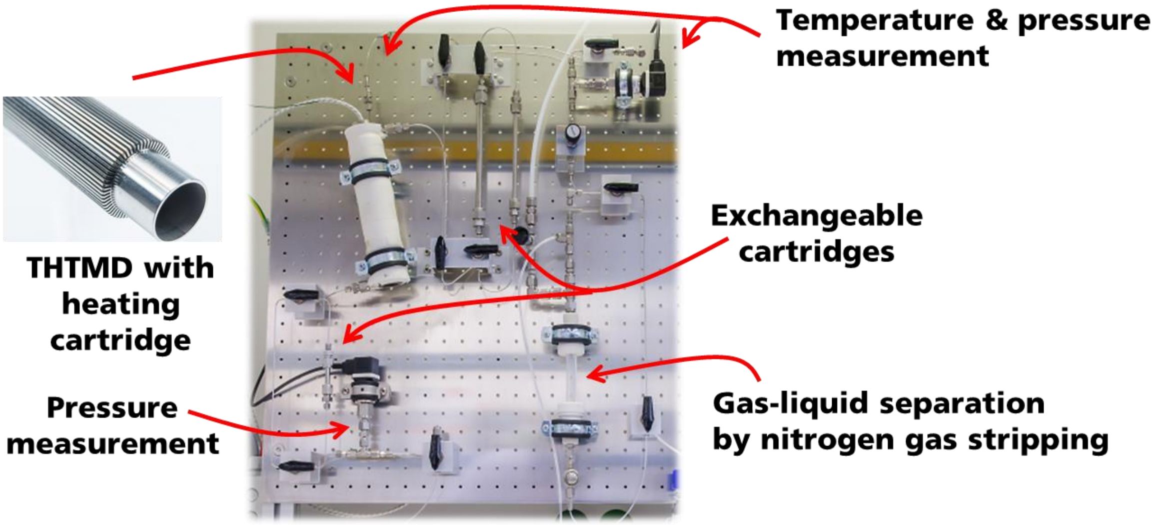


Figure S1 Detailed description of lab plant.

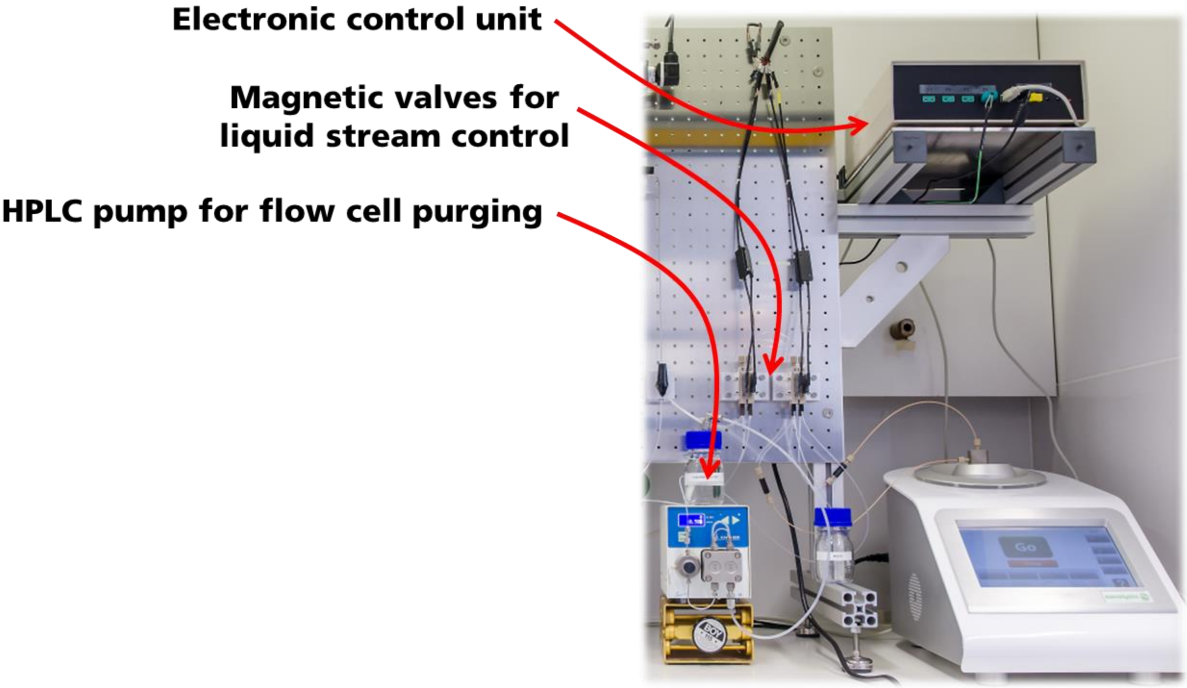


Figure S2 Detailed description of liquid control system.

2. Tube Heat Transfer Micro Device XL (THTMD-XL)

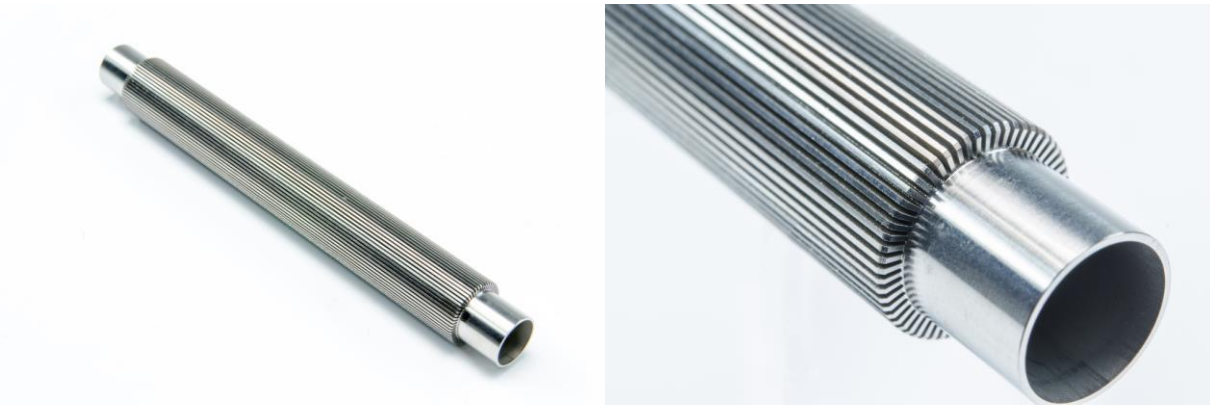


Figure S3 Microstructured inner tube in full length (left) and close-up of microstructure (right) of THTMD-XL.

3. Capillary photoreactor

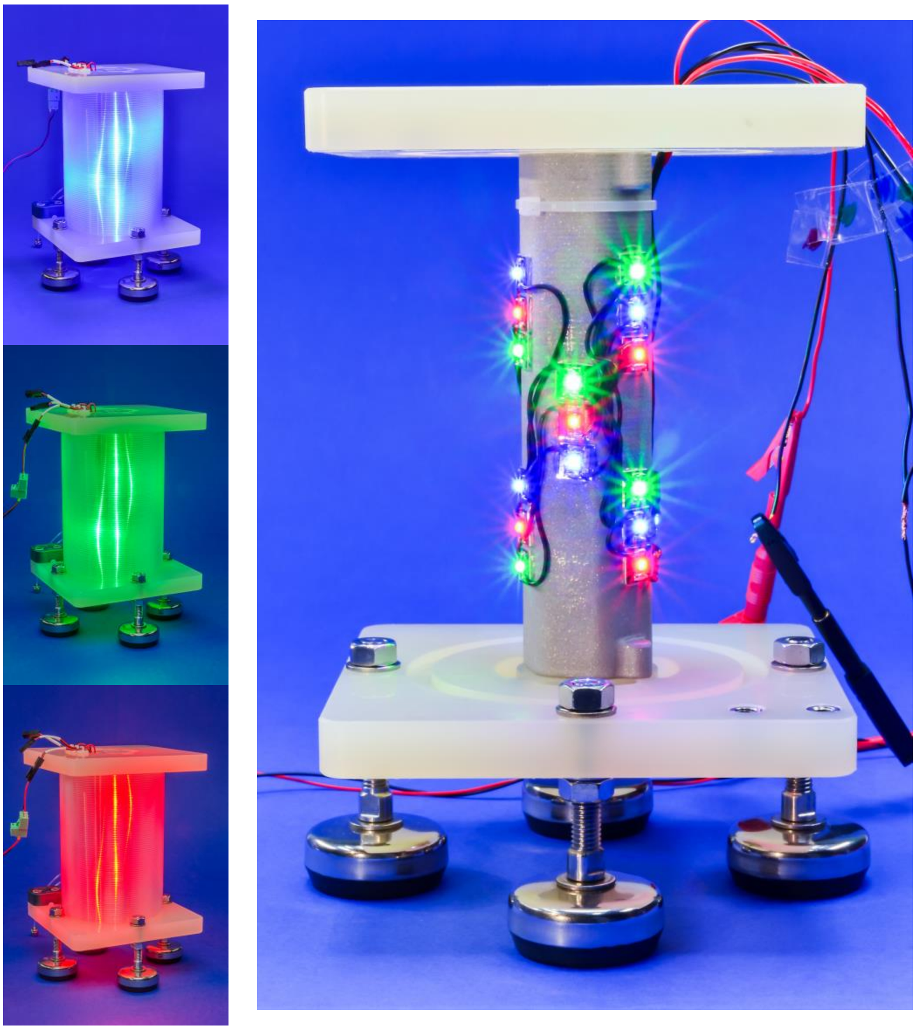


Figure S4 1st Generation of the capillary photoreactor with blue, green and red LED.

Light Emitting Diods
Supplier: Cree, Inc.
Type: XP-E series
XPEROY-L1-0000-00A01 (royal blue, 445 nm)
XPEGRN-L1-0000-00C01 (green, 520 nm)
XPERED-L1-0000-00501 (red, 630 nm)

Central Heat Exchanger and LED carrier
Supplier of CAD design: Fraunhofer ICT-IMM
External company for 3D printing (selective laser melting): FIT prototyping GmbH

Power Supply for LEDs
Supplier: Basetech GmbH
Type: BT-305

Cryostat for LED cooling
Supplier: Julabo
Type: F10 with HC E07 (control unit)

4. SNR measurement of ^{19}F NMR experiments with CF_3 signal

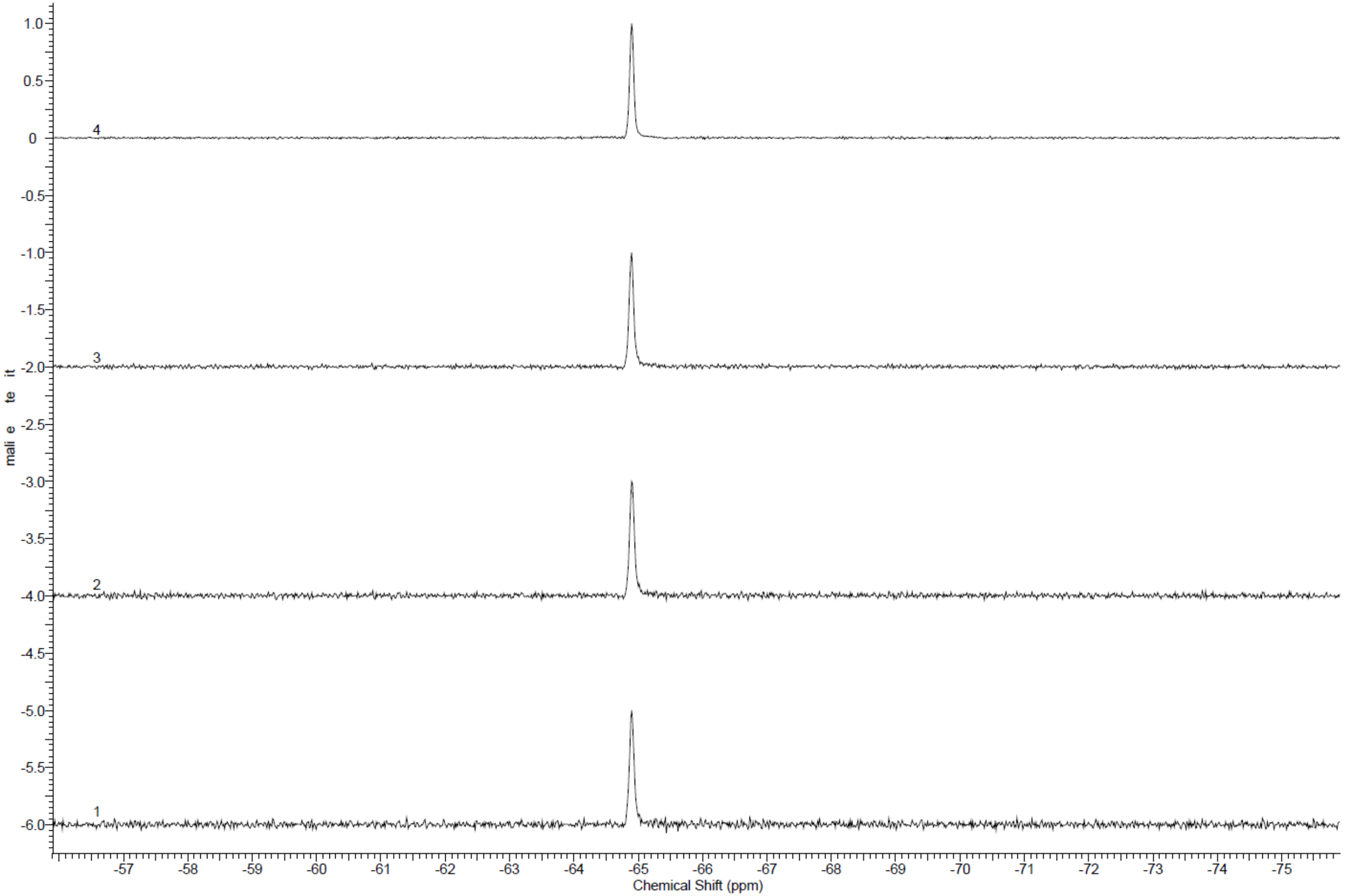


Figure S5 ^{19}F NMR spectra of 4-(trifluoromethyl) benzyl alcohol in DMSO with **$c = 0.6$ mol L^{-1}** with **$f_l = 0.5$ mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

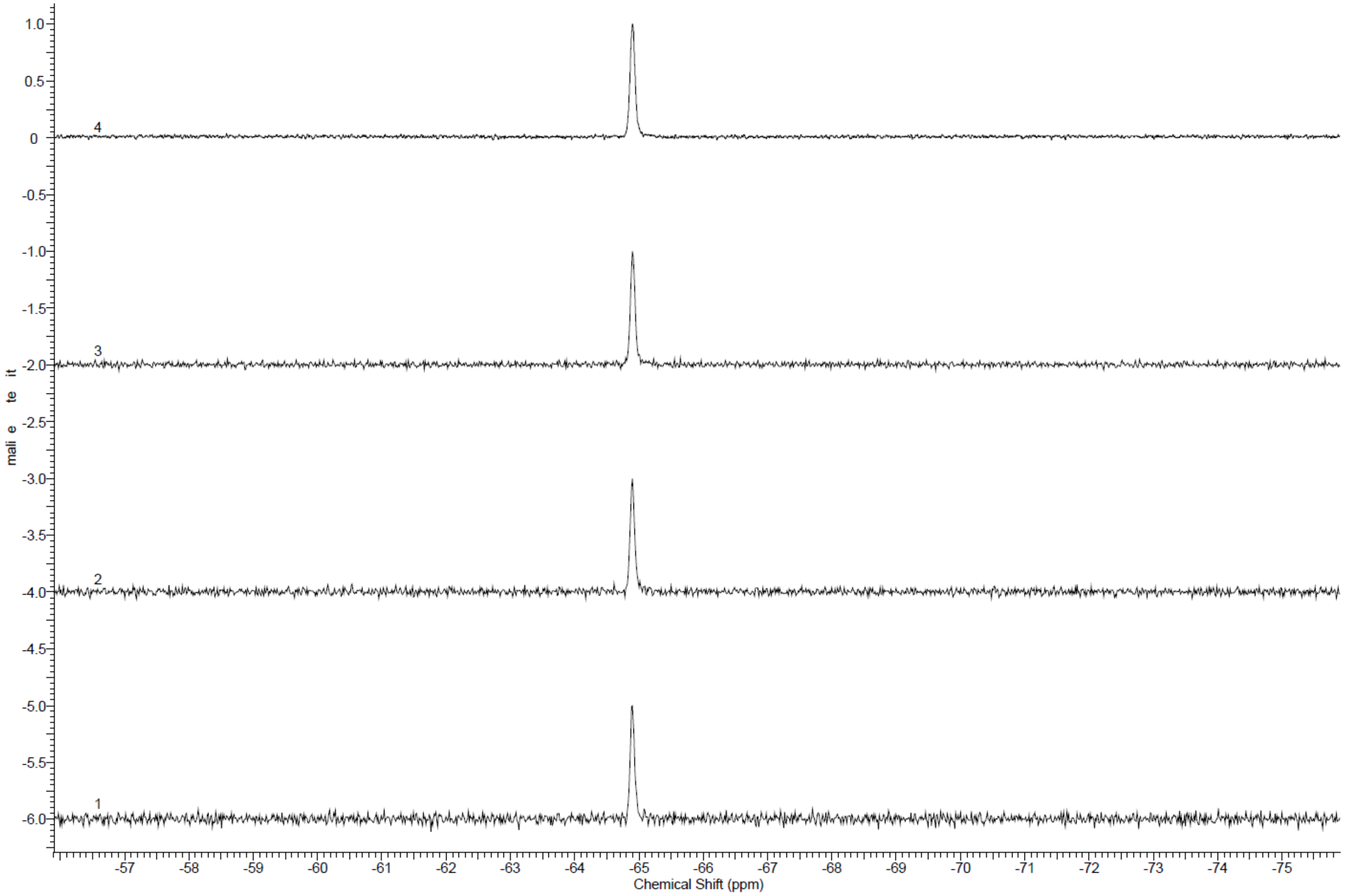


Figure S6 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with **c = 0.3 mol L^{-1}** with **f_l = 0.5 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

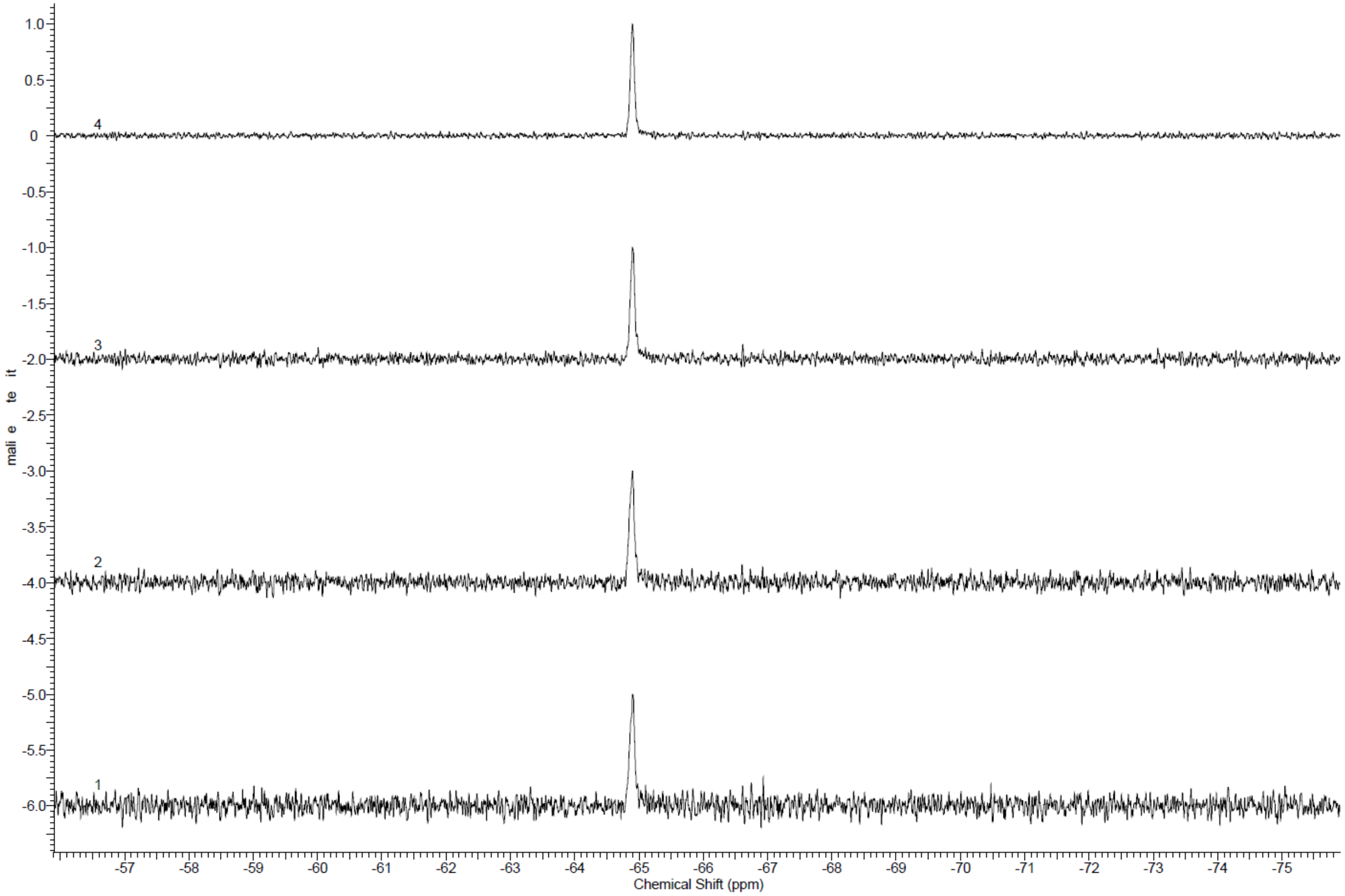


Figure S7 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with ***c* = 0.15 mol L^{-1}** with ***f*$_l$ = 0.5 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

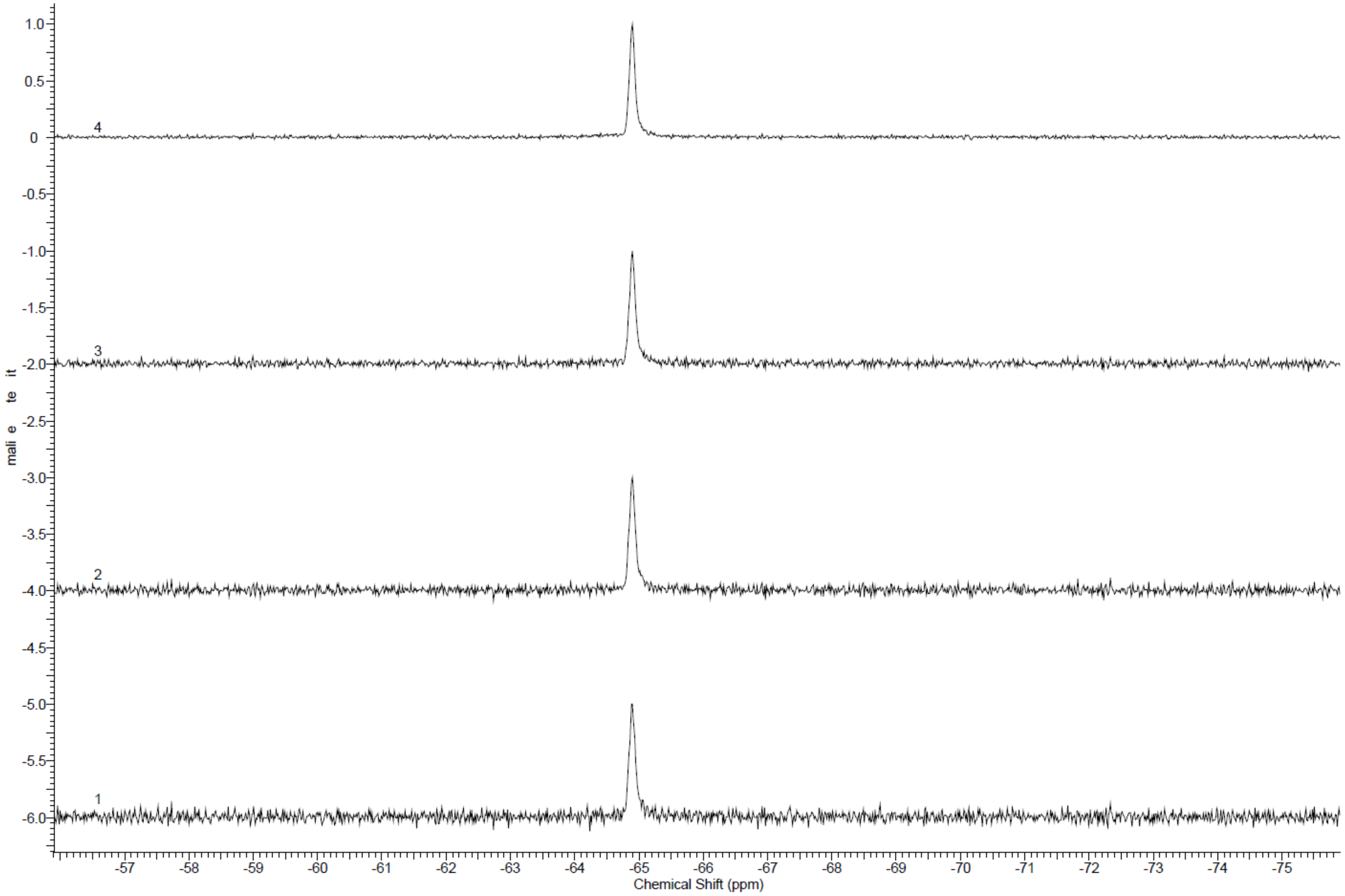


Figure S8 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with **c = 0.6 mol L^{-1}** with **f_l = 2 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

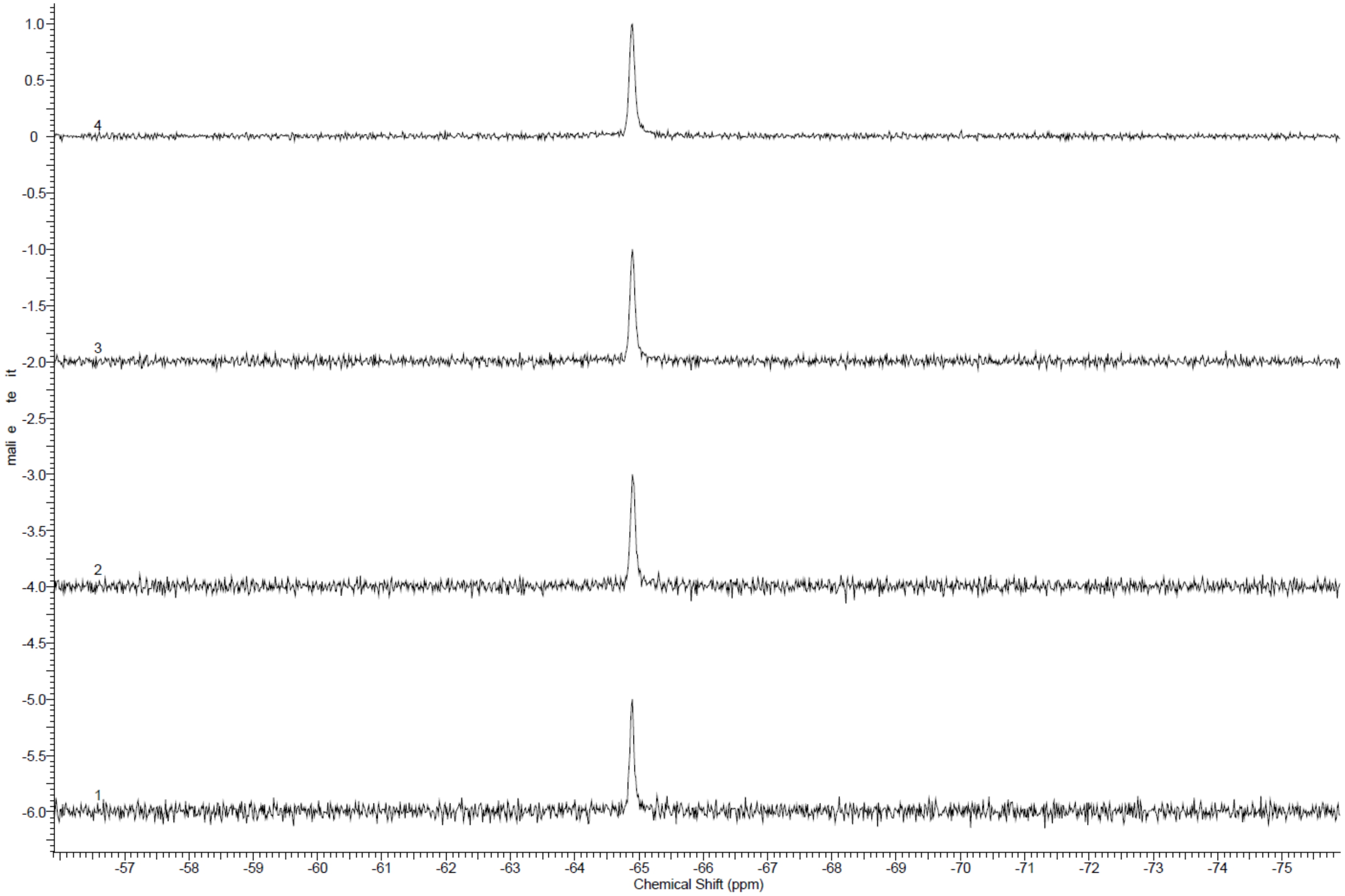


Figure S9 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with $\boldsymbol{c}$ **= 0.3 mol L^{-1}** with $\boldsymbol{f_l}$ **= 2 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

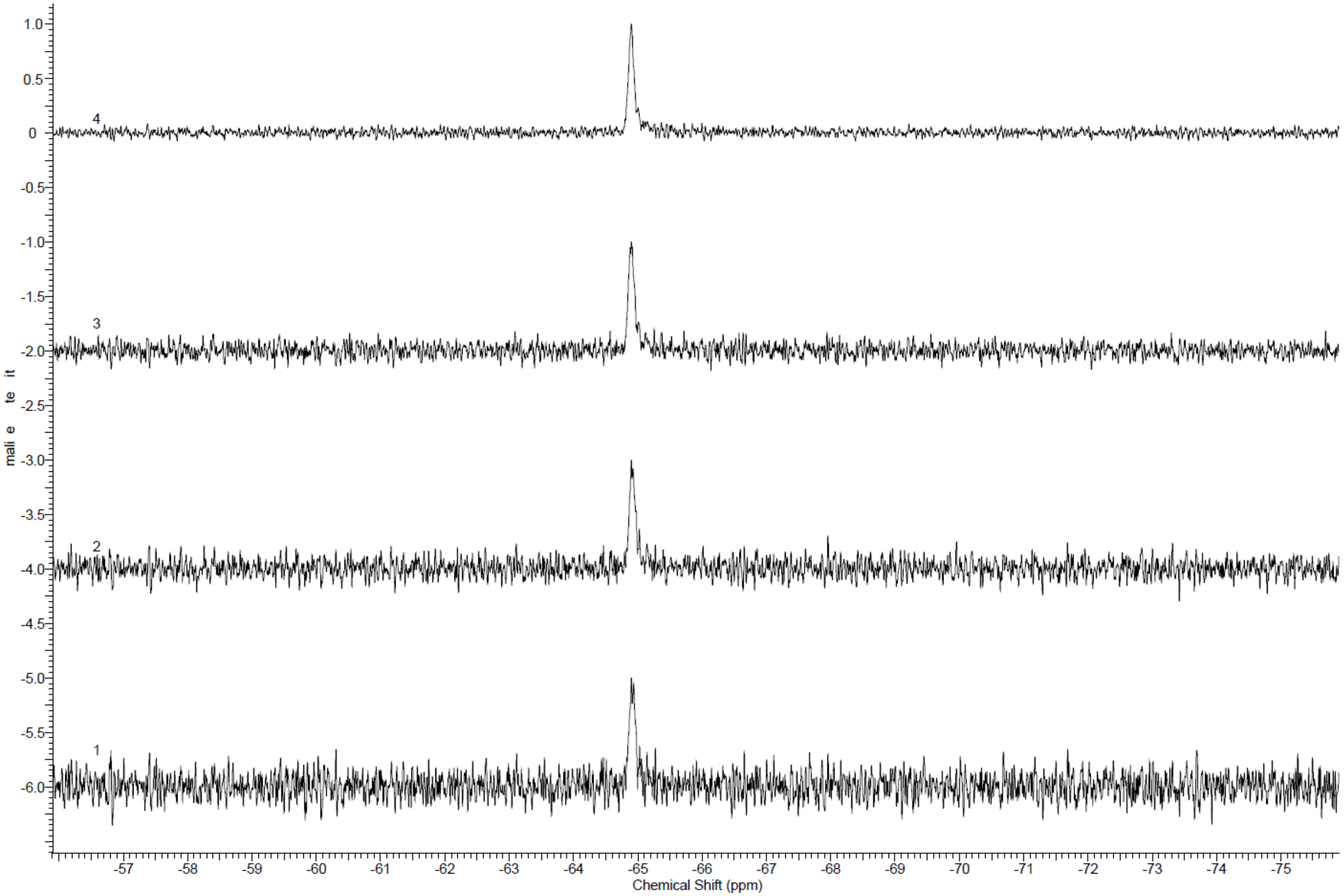


Figure S10 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with **c = 0.15 mol L^{-1}** with **f_l = 2 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

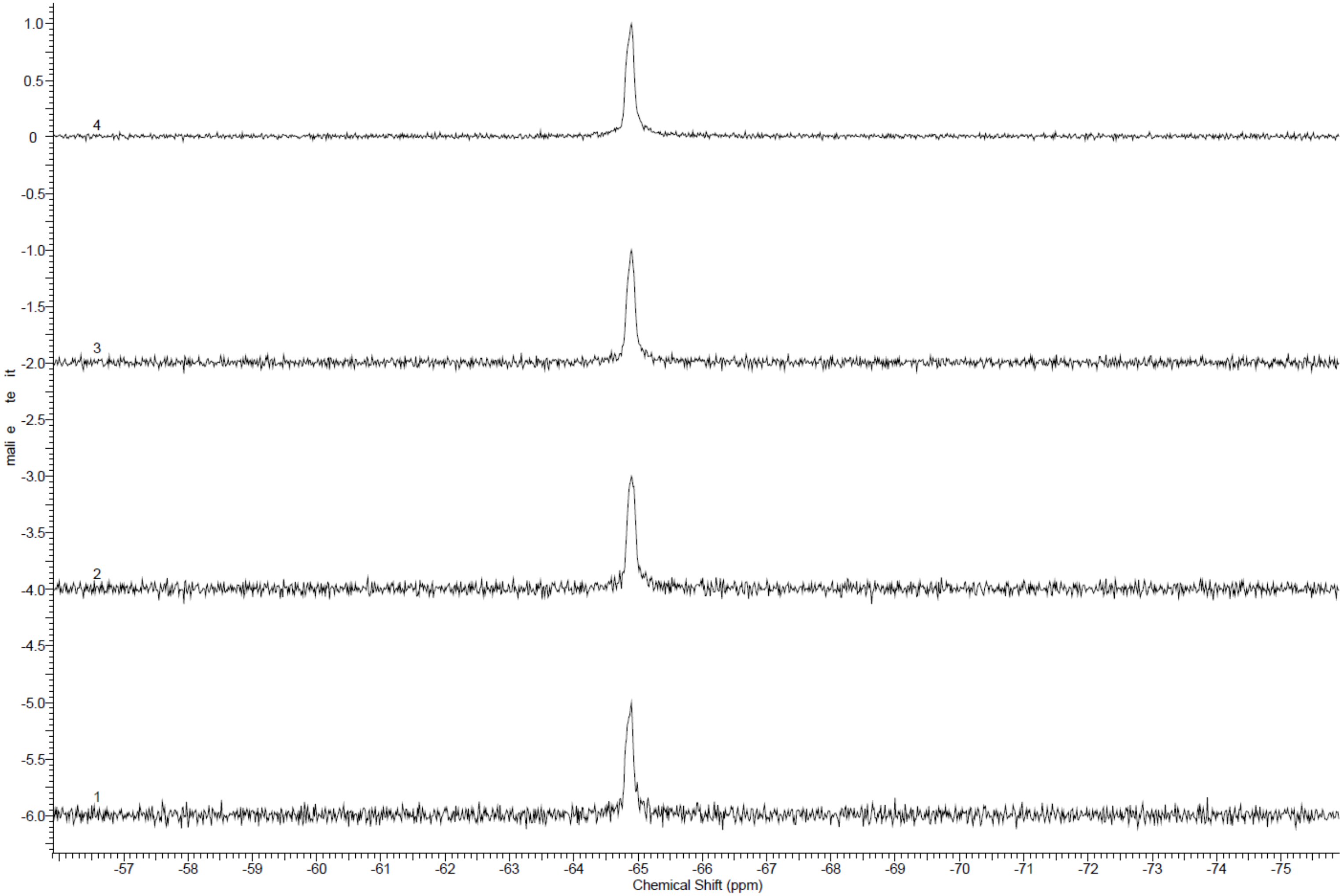


Figure S11 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with $\boldsymbol{c} \mathbf{= 0.6\ mol\ L^{-1}}$ with $\boldsymbol{f}_\mathbf{l} \mathbf{= 4\ mL\ min^{-1}}$; scan numbers from bottom to top: 4, 8, 16, 64.

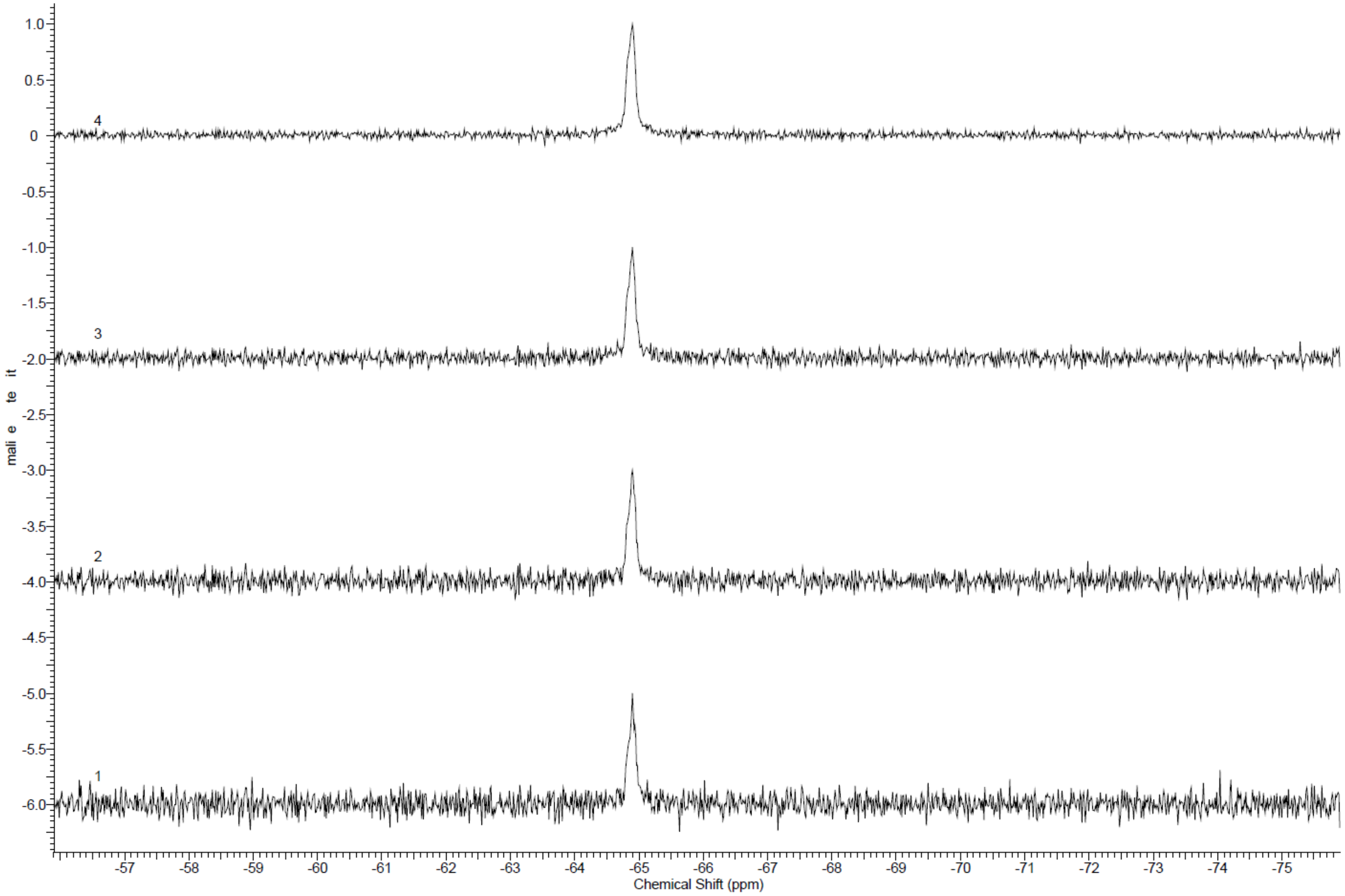


Figure S12 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with **c = 0.3 mol L^{-1}** with **f_l = 4 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

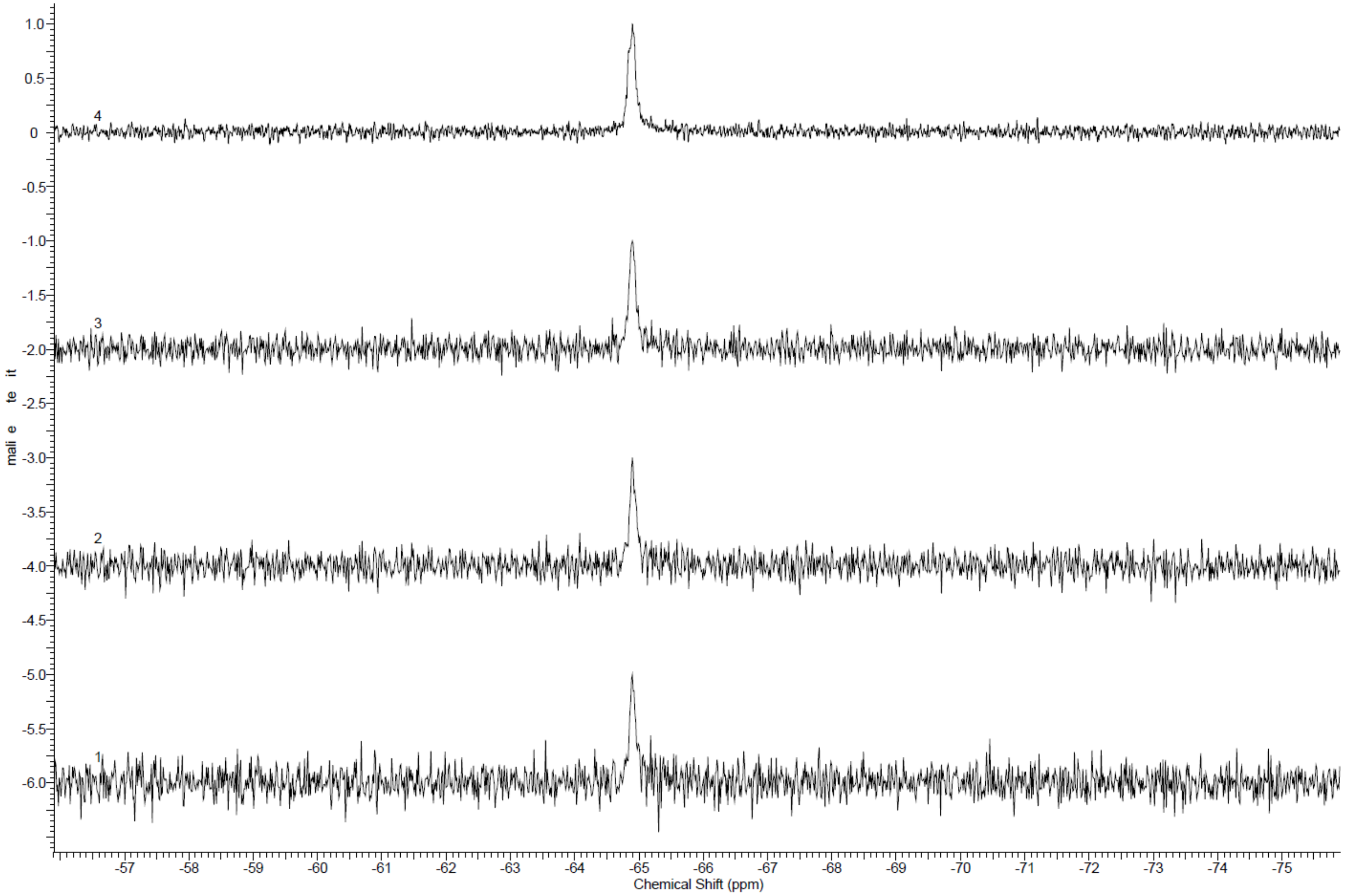
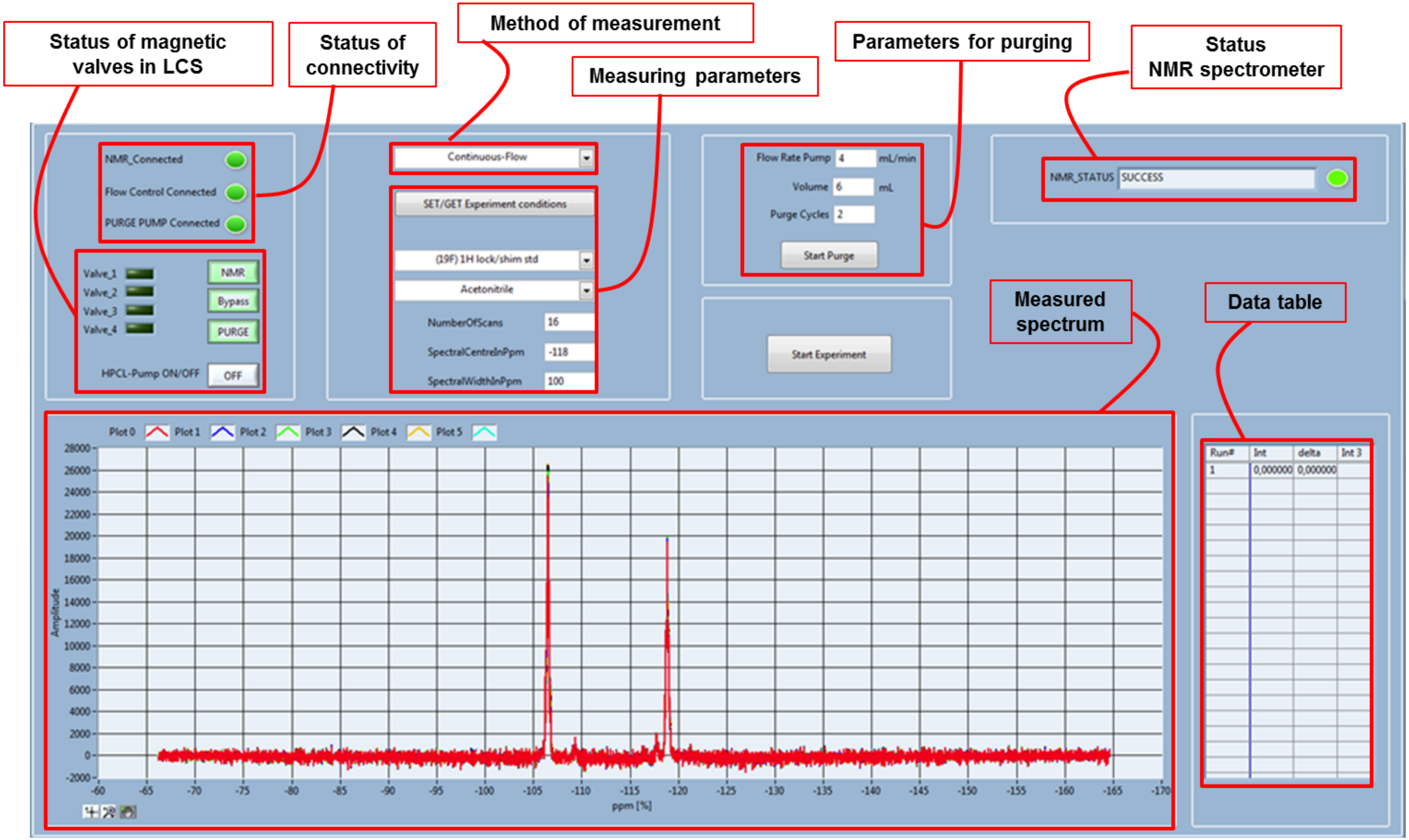


Figure S13 ^{19}F NMR spectra of 4-(trifluoromethyl)benzyl alcohol in DMSO with **c = 0.15 mol L^{-1}** with **f_l = 4 mL min^{-1}**; scan numbers from bottom to top: 4, 8, 16, 64.

5. Software interface



HPCL-Pump ON/OFF OFF

Continuous-Flow

(19F) 1H lock/shim std

Acetonitrile

NumberOfScans 16

SpectralCentreInPpm -118

SpectralWidthInPpm 100

Flow Rate Pump 4 mL/min

Volume 6 mL

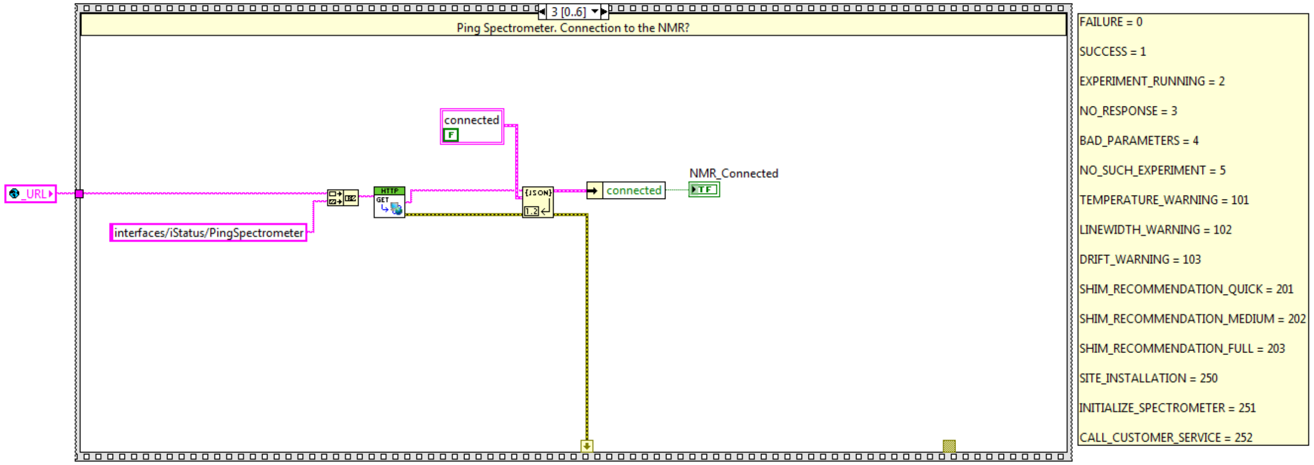
Purge Cycles 2

NMR_STATUS SUCCESS

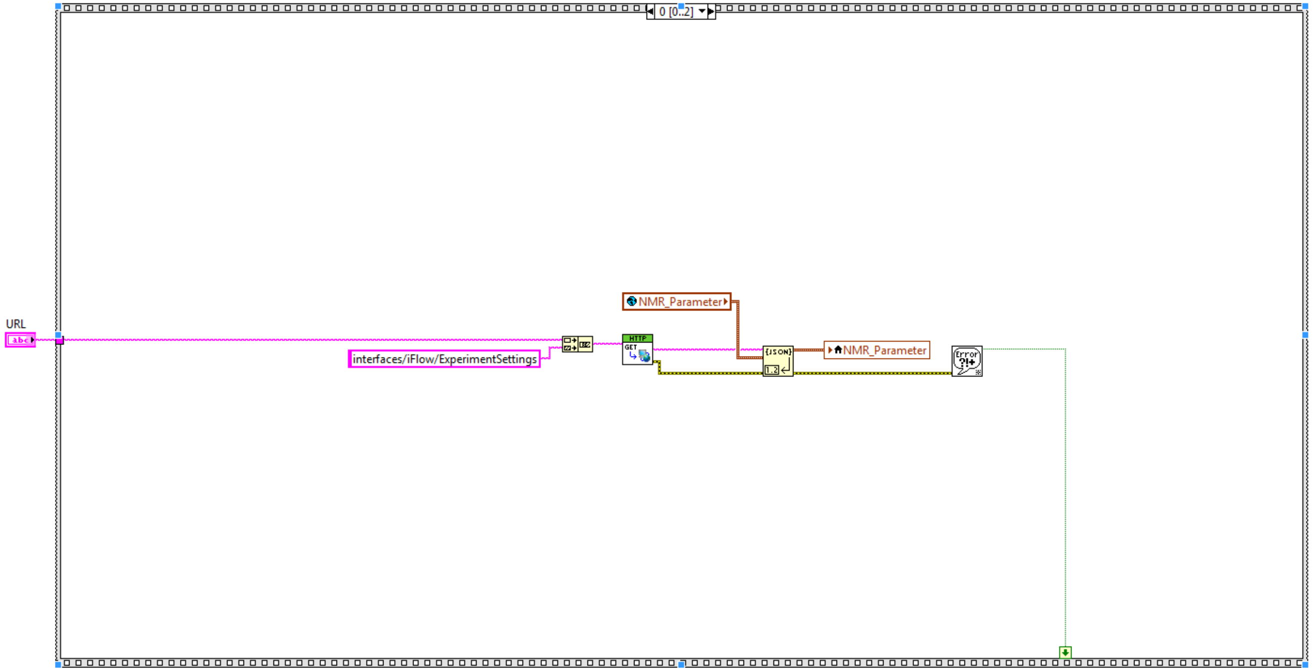
Run#	Int	delta	Int 3
1	0,000000	0,000000	

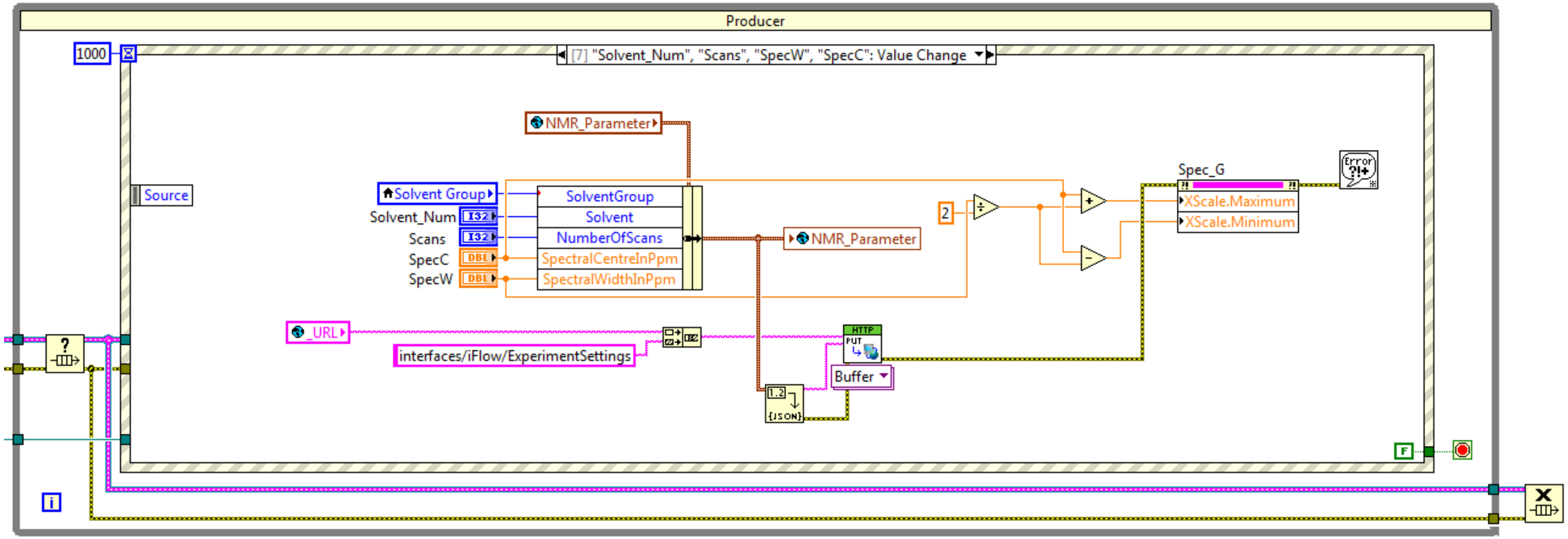
Figure S14 Front end of the LabView-based software interface for LCS and NMR spectrometer control.

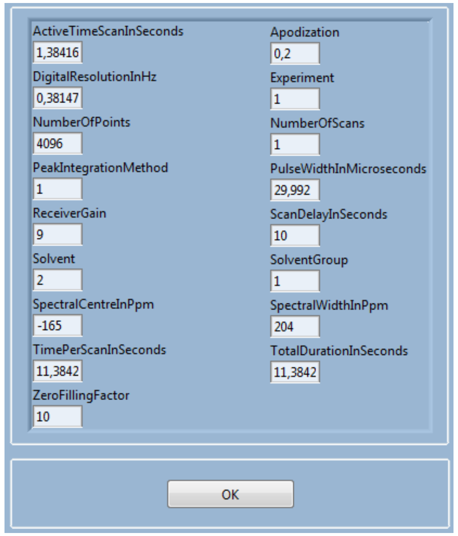
a. Electronic communication with NMR spectrometer via LabView



FAILURE = 0
SUCCESS = 1
EXPERIMENT_RUNNING = 2
NO_RESPONSE = 3
BAD_PARAMETERS = 4
NO_SUCH_EXPERIMENT = 5
TEMPERATURE_WARNING = 101
LINEWIDTH_WARNING = 102
DRIFT_WARNING = 103
SHIM_RECOMMENDATION_QUICK = 201
SHIM_RECOMMENDATION_MEDIUM = 202
SHIM_RECOMMENDATION_FULL = 203
SITE_INSTALLATION = 250
INITIALIZE_SPECTROMETER = 251
CALL_CUSTOMER_SERVICE = 252







ActiveTimeScanInSeconds
1,38416

DigitalResolutionInHz
0,38147

NumberOfPoints
4096

PeakIntegrationMethod
1

ReceiverGain
9

Solvent
2

SpectralCentreInPpm
-165

TimePerScanInSeconds
11,3842

ZeroFillingFactor
10

Apodization
0,2

Experiment
1

NumberOfScans
1

PulseWidthInMicroseconds
29,992

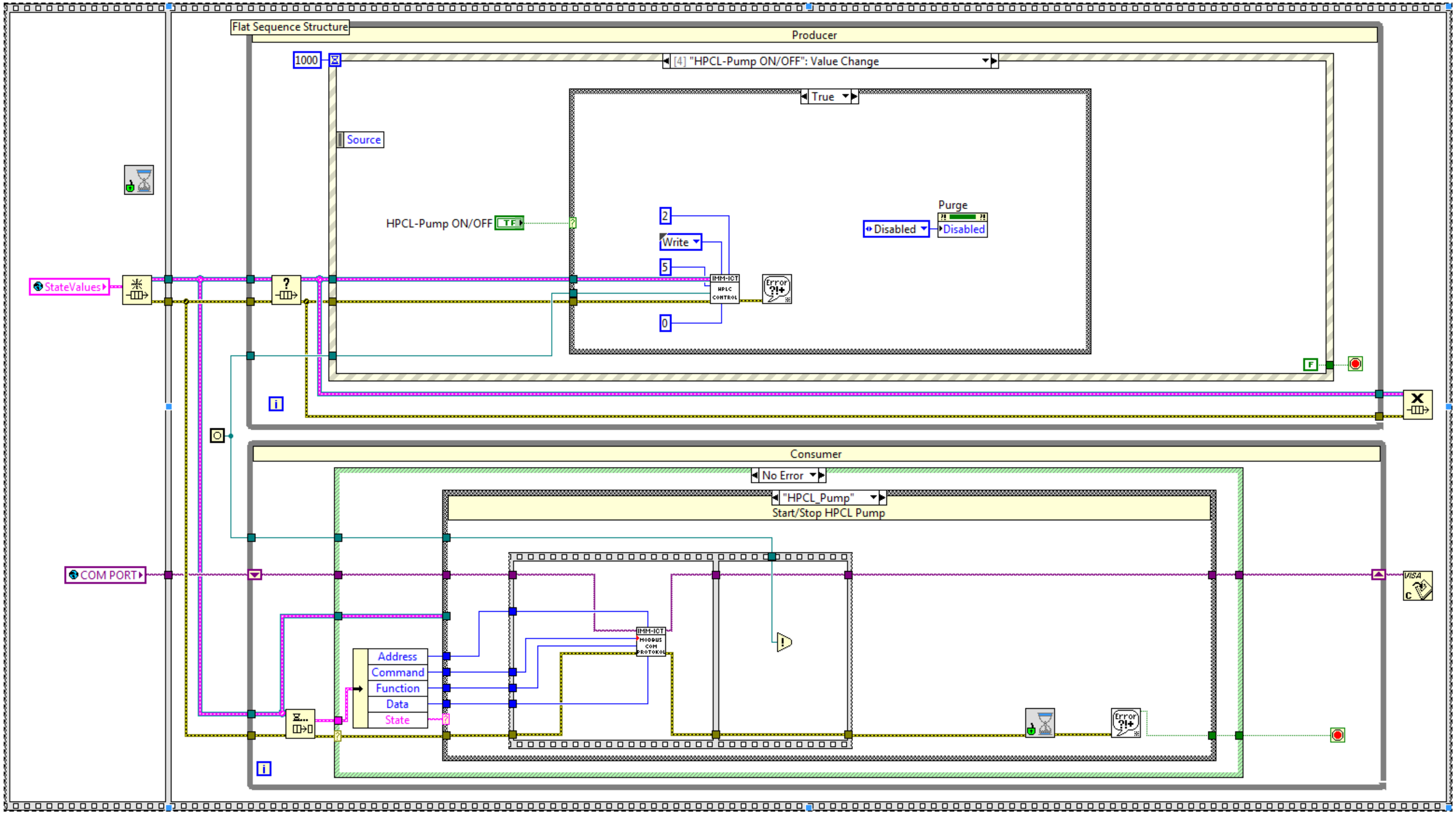
ScanDelayInSeconds
10

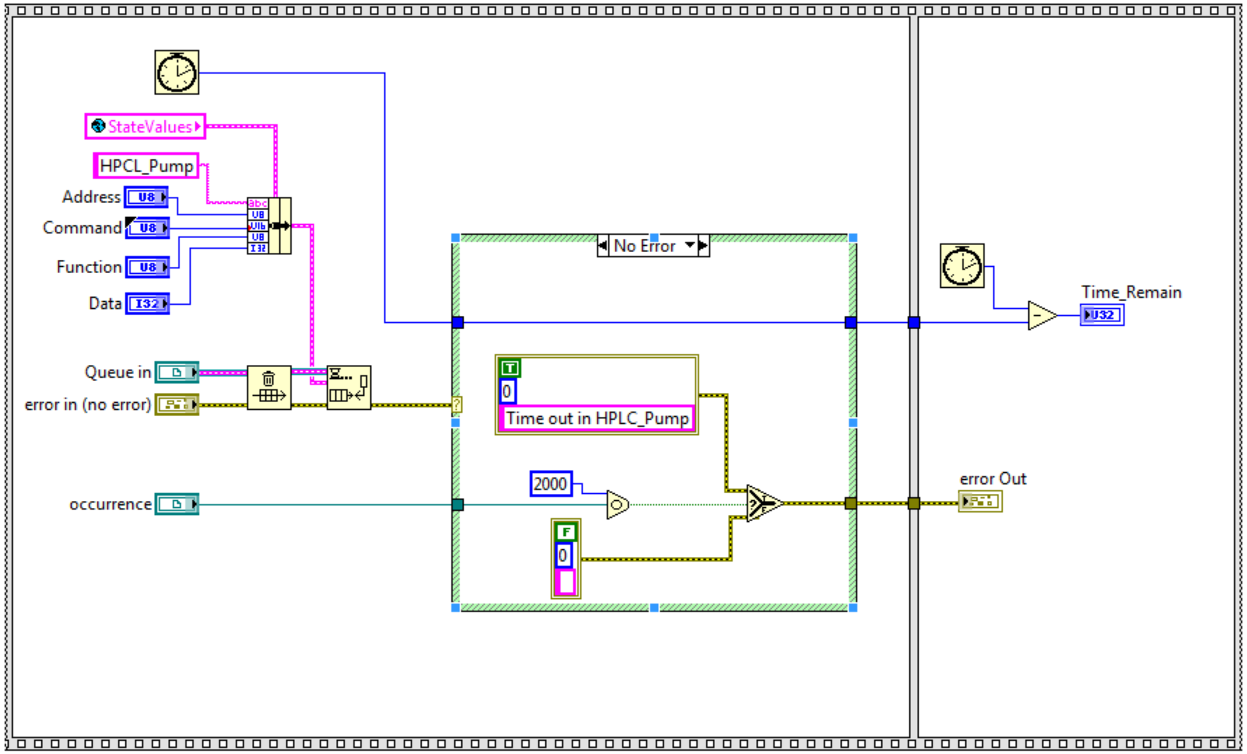
SolventGroup
1

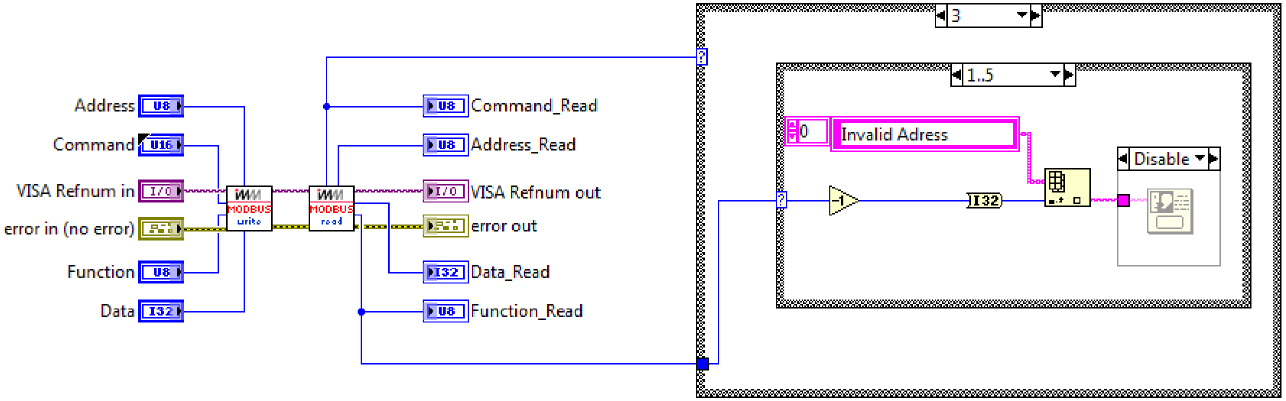
SpectralWidthInPpm
204

TotalDurationInSeconds
11,3842

b. Electronic communication with HPLC pump and magnetic valves via LabView




StateValues
HPCL_Pump
Address
Command
Function
Data
Queue in
error in (no error)
occurrence
No Error
T
0
Time out in HPLC_Pump
2000
F
0
Time_Remain
error Out


3
Address
Command
VISA Refnum in
error in (no error)
Function
Data
MODBUS write
MODBUS read
Command_Read
Address_Read
VISA Refnum out
error out
Data_Read
Function_Read
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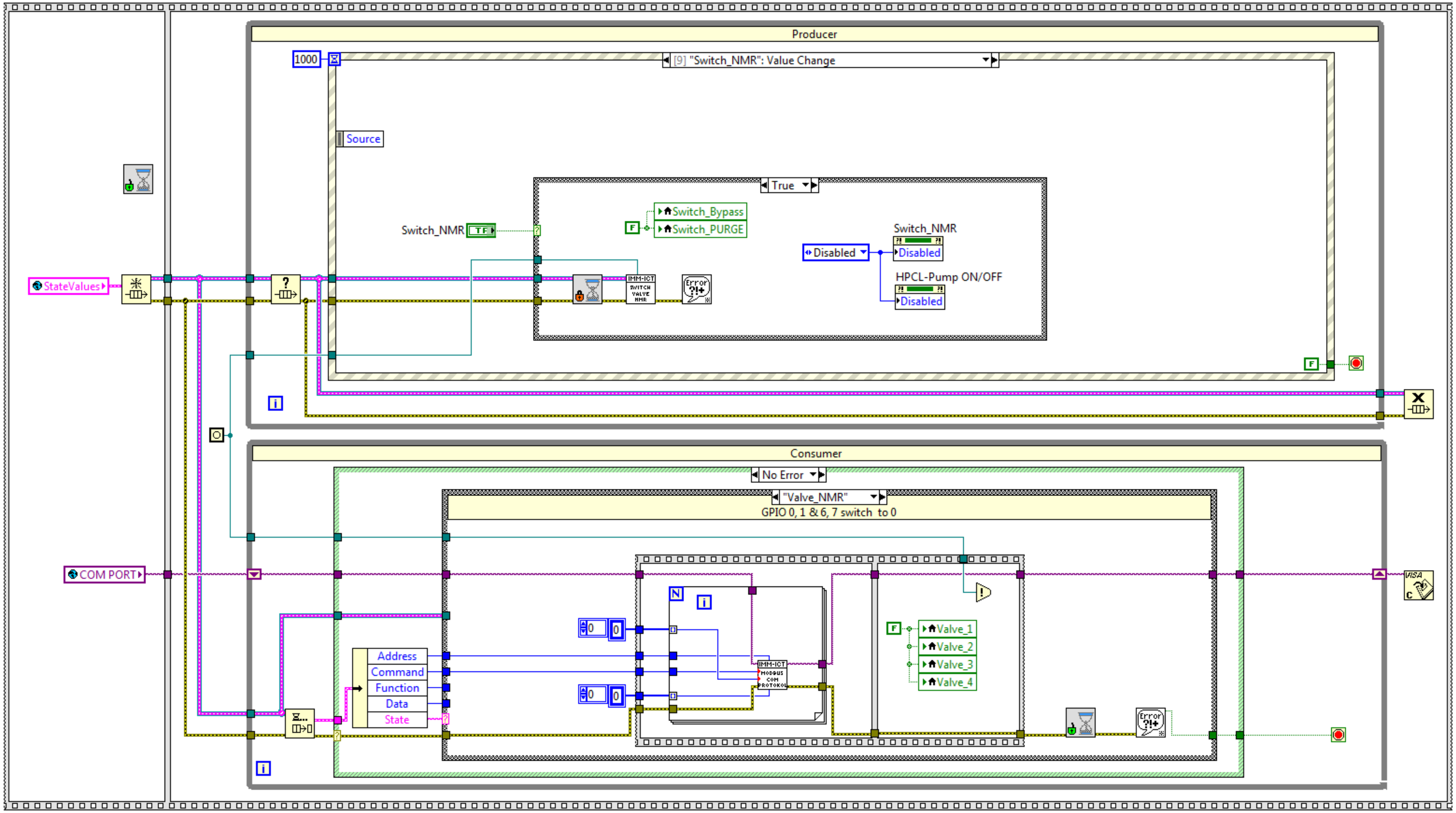
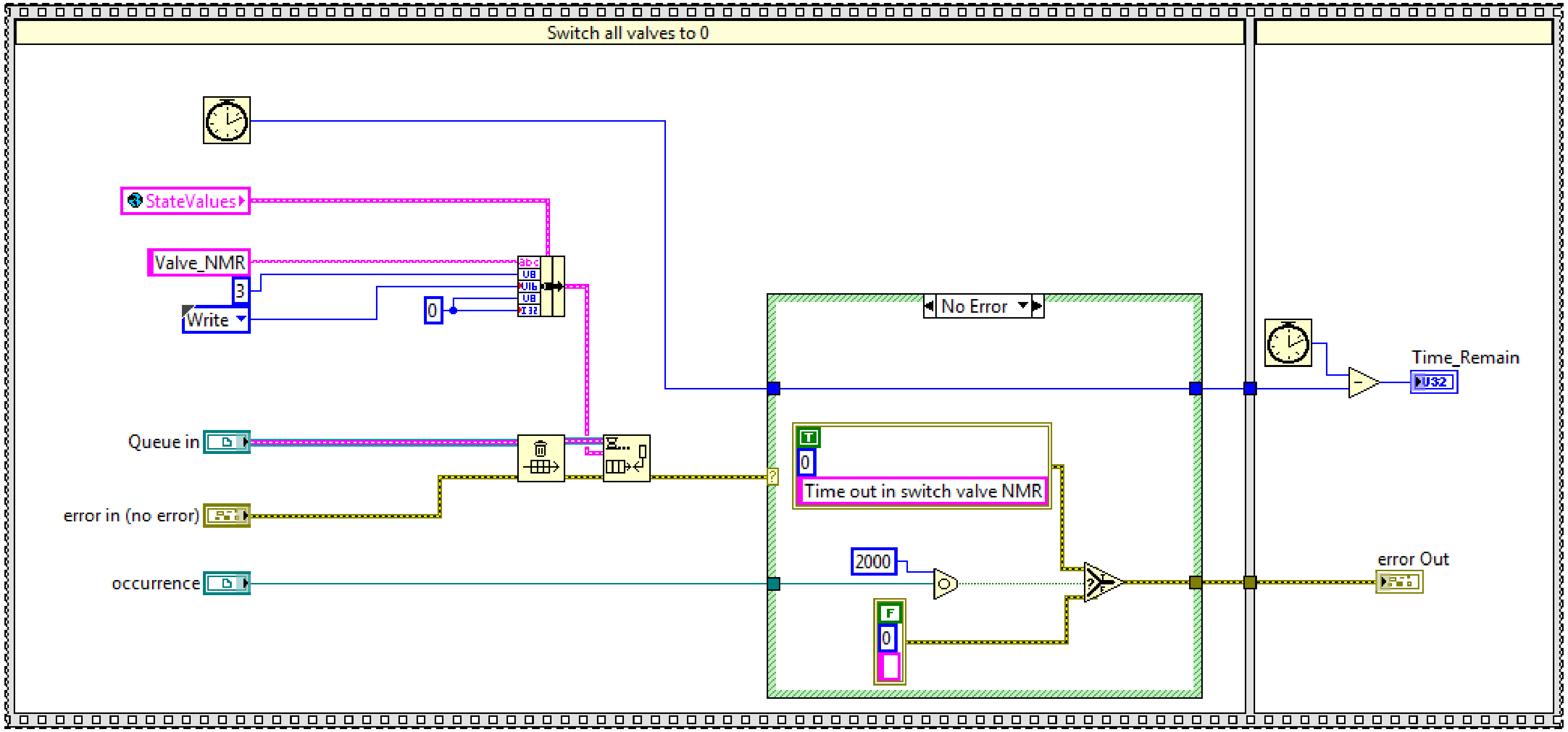
0
Invalid Adress
I32
Disable


Producer
1000
[9] "Switch_NMR": Value Change
Source
True
Switch_NMR
Switch_Bypass
Switch_PURGE
F
IMM-ICT SWITCH VALVE NMR
Error ?!+
Disabled
Switch_NMR
Disabled
HPCL-Pump ON/OFF
Disabled
StateValues
F
i
Consumer
No Error
"Valve_NMR"
GPIO 0, 1 & 6, 7 switch to 0
COM PORT
N
i
0
0
0
0
IMM-ICT MODBUS COM PROTOKOL
F
Valve_1
Valve_2
Valve_3
Valve_4
Address
Command
Function
Data
State
Error ?!+
VISA
i


Switch all valves to 0
StateValues
Valve_NMR
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Write
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Queue in
error in (no error)
occurrence
No Error
T
0
Time out in switch valve NMR
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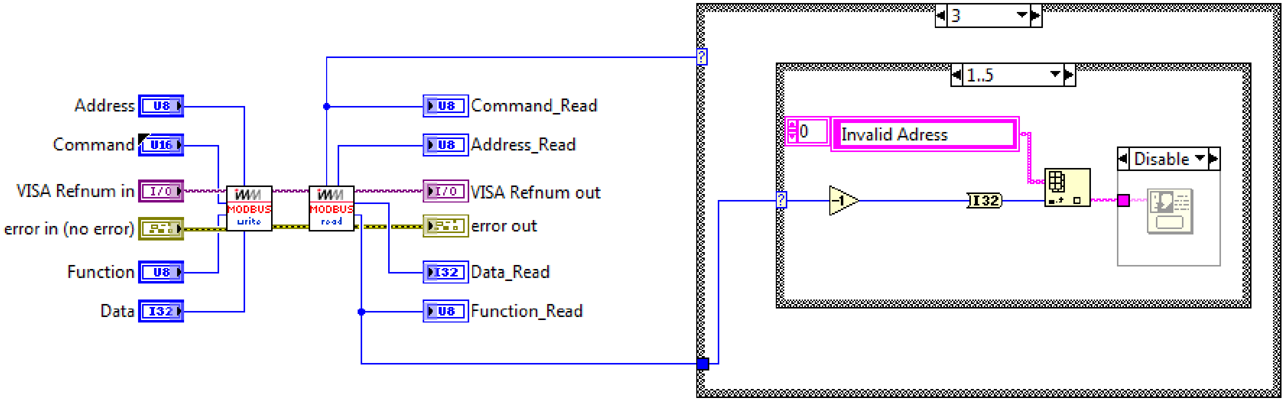
F
0
Time_Remain
U32
error Out


Address
Command
VISA Refnum in
error in (no error)
Function
Data
U8
U16
I/O
I32
MODBUS write
MODBUS read
Command_Read
Address_Read
VISA Refnum out
error out
Data_Read
Function_Read
3
1..5
0
Invalid Adress
-1
I32
Disable

6. Experimental

Online- and offline-NMR spectroscopy

^{1}H and ^{19}F NMR spectra were recorded with a NMReady-60e benchtop NMR spectrometer (Nanalysis Corp.) with Larmor frequencies of 58.63 MHz for ^{1}H and 55.17 MHz for ^{19}F. High-resolution ^{1}H and ^{13}C spectra were recorded with an Avance III HD 300 NMR spectrometer (Bruker BioSpin GmbH) with Larmor frequencies of 300.13 MHz for ^{1}H and 75.48 MHz for ^{13}C.

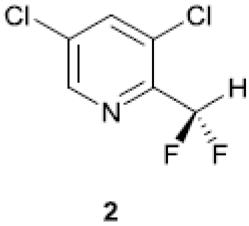
Glassware from Norell Inc. was used for standard NMR tubes and for the manufacturing of the flow cell. Deuterated solvents were purchased from Deutero GmbH. NMR spectra were processed with ACD/NMR Processor software (academic edition) from ACD/Labs.

Chemical shifts are reported relative $SiMe_4$ (^{1}H: $\delta = 0.00$ ppm) and $CFCl_3$ (^{19}F: $\delta = 0.00$ ppm). As internal standards the residual DMSO-d_6 solvent proton signal (2.50 ppm) was used.

Krapcho decarboxylation

10.8 g (0.04 mol, 1 eq) Ethyl (3,5-dichloropyridin-2-yl)(difluoro)acetate (**1**) was dissolved in a DMSO-water mixture (97/3, v/v; 100 mL) and lithium chloride (3.39 g, 0.08 mol, 2 eq) was added. The suspension was stirred at room temperature until all LiCl has dissolved resulting in a clear and colourless solution.

The substrate solution was pumped with various flow rates and at various temperatures through the THTMD, the gas-liquid splitter and into the flow cell for online NMR analysis. The dark brown reaction solution was collected in one vessel and stirred into cold water (200 mL). The resulting suspension was extracted with ethyl acetate (3 x 80 mL). The organic phases were combined, washed with water (2x 50 mL) and dried with Na_2SO_4. The solvent was evaporated at 40 °C under reduced pressure and subjected to flash chromatography with cyclohexane as eluent. The purified product was used for ^{1}H NMR analysis in standard NMR tubes with DMSO-d_6 as solvent.



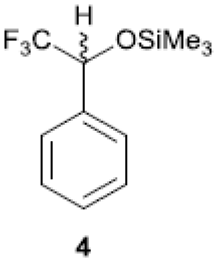
2

^{1}H-NMR (300 MHz; DMSO-d_6): δ 8.75 (d, $J = 2.2$ Hz, 1H), 8.46 (d, $J = 1.8$ Hz, 1H), 7.19 (t, $J = 53.2$ Hz, 1H); ^{13}C NMR (75 MHz; DMSO-d_6): δ 146.7 (CH), 146.1 (t, $J = 23.1$, C), 138.4 (CH), 133.7 (C), 130.3 (C), 111.8 (t, $J = 239.9$ Hz, CH).[1,2]

Ruppert-Prakash reaction with TMS-CF_3

Benzaldehyde (1.77 g, 0.017 mol, 1 eq) and TMS-CF_3 (2.84 g, 0.02 mol, 1.2 eq) were mixed with 100 mL DMSO resulting in a clear and colourless solution.

The substrate solution was pumped at various temperatures through the THTMD and analysed online with the benchtop NMR spectrometer. The slightly yellow reaction solution was collected in one vessel and stirred into cold water (200 mL). The resulting suspension was extracted with dichloromethane (3 x 80 mL). The organic phases were combined, washed with water (2x 50 mL) and dried with Na_2SO_4. The solvent was evaporated at 40 °C under reduced pressure and subjected to flash chromatography with cyclohexane as eluent. The purified product was used for ^{1}H NMR analysis in standard NMR tubes with DMSO-d_6 as solvent.



4

^{1}H-NMR (300 MHz; DMSO-d_6): δ 7.52-7.48 (m, 2H), 7.44-7.36 (m, 3H), 5.40 (q, *J* = 6.9 Hz, 1H), 0.07 (s, 9H); ^{13}C NMR (75 MHz; DMSO-d_6): δ 135.5 (C), 129.1 (CH), 128.3 (CH), 127.5 (CH), 124.5 (q, *J* = 282.8 Hz, C), 71.6 (q, *J* = 30.8 Hz, CH), -0.34 (CH_3).[3]

Ruppert-Prakash reaction with TMS-C_2F_5

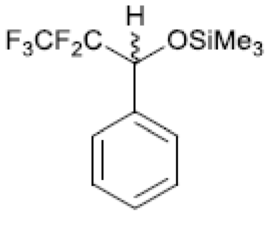
Method 1:

Benzaldehyde (1.77 g, 0.017 mol, 1 eq) and TMS-C_2F_5 (3.84 g, 0.02 mol, 1.2 eq) were mixed with 100 mL DMSO resulting in a clear and colourless solution. Vigorous stirring was necessary in this case for breaking the binary phase system between DMSO and TMS-C_2F_5. The substrate solution was used as described above for the Ruppert-Prakash reaction with TMS-CF_3.

Method 2:

Benzaldehyde (1.77 g, 0.017 mol, 1 eq) and TMS-C_2F_5 (3.84 g, 0.02 mol, 1.2 eq) were each mixed with 50 mL DMSO resulting in clear and colourless solution. Vigorous stirring was necessary for the DMSO / TMS-C_2F_5 mixture for breaking the binary phase system between the two liquids.

Both solutions were pumped separately with two HPLC pumps into a static T-piece mixer and via the cartridge – reactor – cartridge cascade of the lab plant into the flow cells for NMR analysis. The flow rates of both HPLC pumps were kept equal so that a constant substrate concentration of 0.2 M was given throughout the complete runtime. During the run time various temperatures were applied at the THTMD.



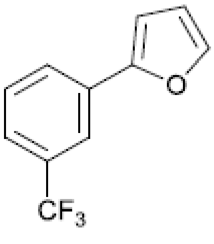
5

^{1}H-NMR (300 MHz; DMSO-d$_6$): δ 7.52-7.49 (m, 2H), 7.43-7.38 (m, 3H), 5.40 (dd, *J* = 19.7 Hz, 5.2 Hz, 1H), 0.01 (s, 9H); ^{13}C NMR (75 MHz; DMSO-d$_6$): δ 134.6 (C), 129.2 (CH), 128.2 (CH), 128.1 (CH), 119.0 (qt, *J* = 288.3 Hz, 36.3 Hz C), 113.0 (tq, *J* = 261.9 Hz, 35.2 Hz), 71.0 (dd, *J* = 30.1 Hz, 21.5 Hz, CH), 0.52 (CH$_3$).[3,4]

Dye-sensitized C-H arylation of furan with a trifluoromethylated diazonium salt

3-(Trifluoromethyl)phenyl diazonium tetrafluoroborate (5.2 g, 0.02 mol, 1 eq) was dissolved in DMSO (50 mL). Eosin Y (138.4 mg, 0.2 mmol, 0.01 eq) was dissolved in a solvent mixture of DMSO and furan (35.5/14.5, v/v).

Both reaction solutions were pumped separately with two HPLC pumps into a static T-piece mixer and via the capillary microreactor and the gas-liquid splitter into the flow cells for online NMR analysis. The flow rates of both HPLC pumps were kept equal so that a constant substrate concentration of 0.2 M was given throughout the complete runtime. The dark yellow reaction solution was collected in one vessel and stirred into cold water (200 mL). The resulting suspension was extracted with ethyl acetate (3 x 80 mL). The organic phases were combined, washed with water (2x 50 mL) and dried with Na_2SO_4. The solvent was evaporated at 40 °C under reduced pressure and subjected to flash chromatography with cyclohexane as eluent. The purified product was used for ^{1}H NMR analysis in standard NMR tubes with DMSO-d$_6$ as solvent.



7

^{1}H-NMR (300 MHz; **CDCl$_3$**): δ 7.94 (br.s, 1H), 7.86-7.82 (m, 1H), 7.55-7.50 (m, 3H), 6.75 (dd, *J* = 3.44 Hz, 0.69 Hz, 1H), 6.52 (dd, *J* = 3.44 Hz, 1.83 Hz, 1H); ^{13}C NMR (75 MHz; CDCl$_3$): δ 152.4 (C), 142.8 (CH), 131.1 (q, *J* = 31.9 Hz, C), 129.1 (CH), 126.7 (CH), 124.1 (q, *J* = 272.9 Hz, C), 123.7 (q, *J* = 3.3 Hz, CH), 120.5 (q, *J* = 3.3 Hz, CH), 111.9 (CH), 106.3 (CH).[5]

^{1}H-NMR (300 MHz; **DMSO-d$_6$**): δ 7.96-7.93 (m, 2H), 7.77 (dd, *J* = 1.83 Hz, 0.73 Hz, 1H), 7.63-7.55 (m, 2H), 7.13 (dd, *J* = 3.3 Hz, 0.73 Hz, 1H), 6.61 (dd, *J* = 3.3 Hz, 1.83 Hz, 1H); ^{13}C NMR (75 MHz; DMSO-d$_6$): δ 151.9 (C), 144.1 (CH), 131.7 (C), 130.4 (CH), 130.3 (q, *J* = 31.9 Hz, C), 127.4 (CH), 124.5 (q, *J* = 271.8 Hz, C), 124.0 (q, *J* = 3.3 Hz, CH), 120.0 (q, *J* = 3.3 Hz, CH), 112.7 (CH), 108.0 (CH).

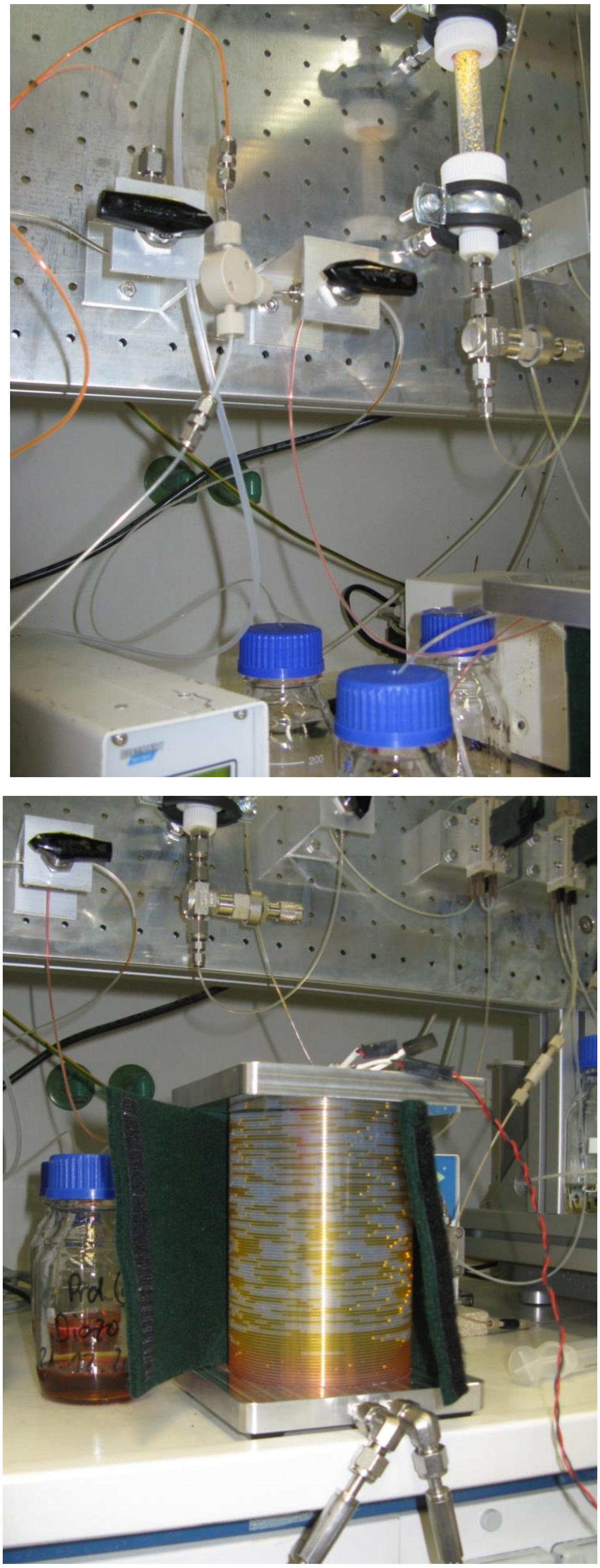
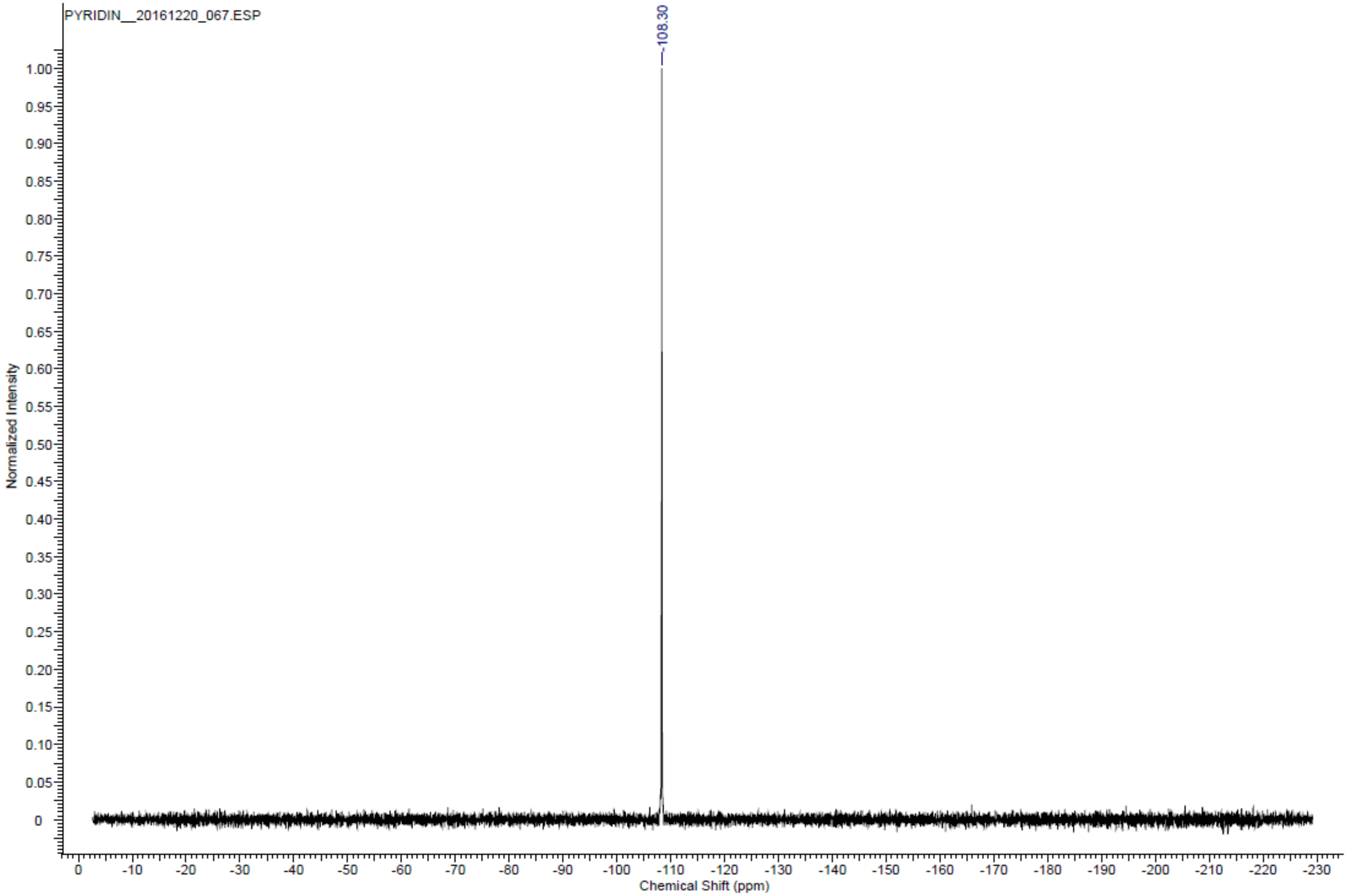
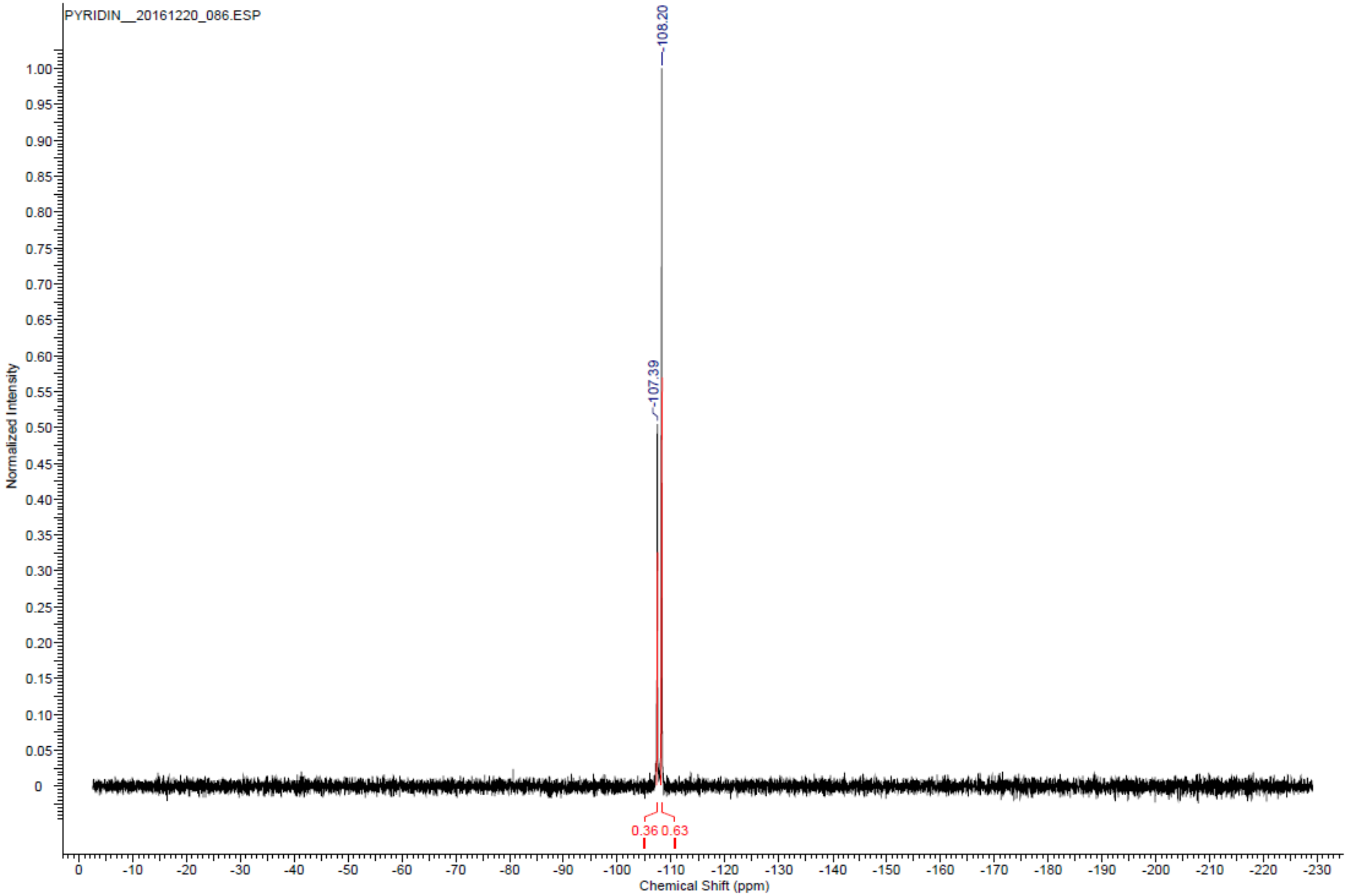
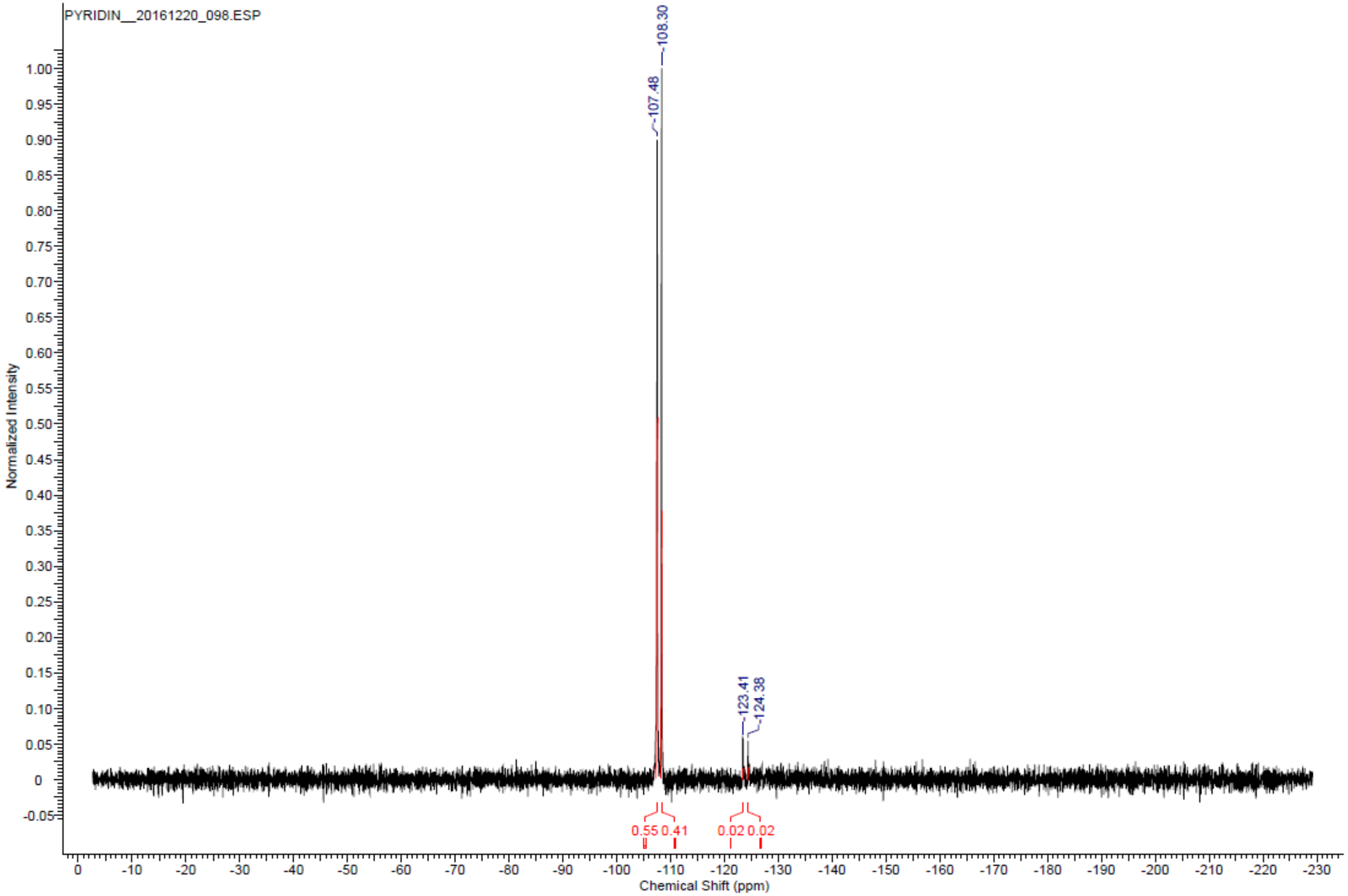


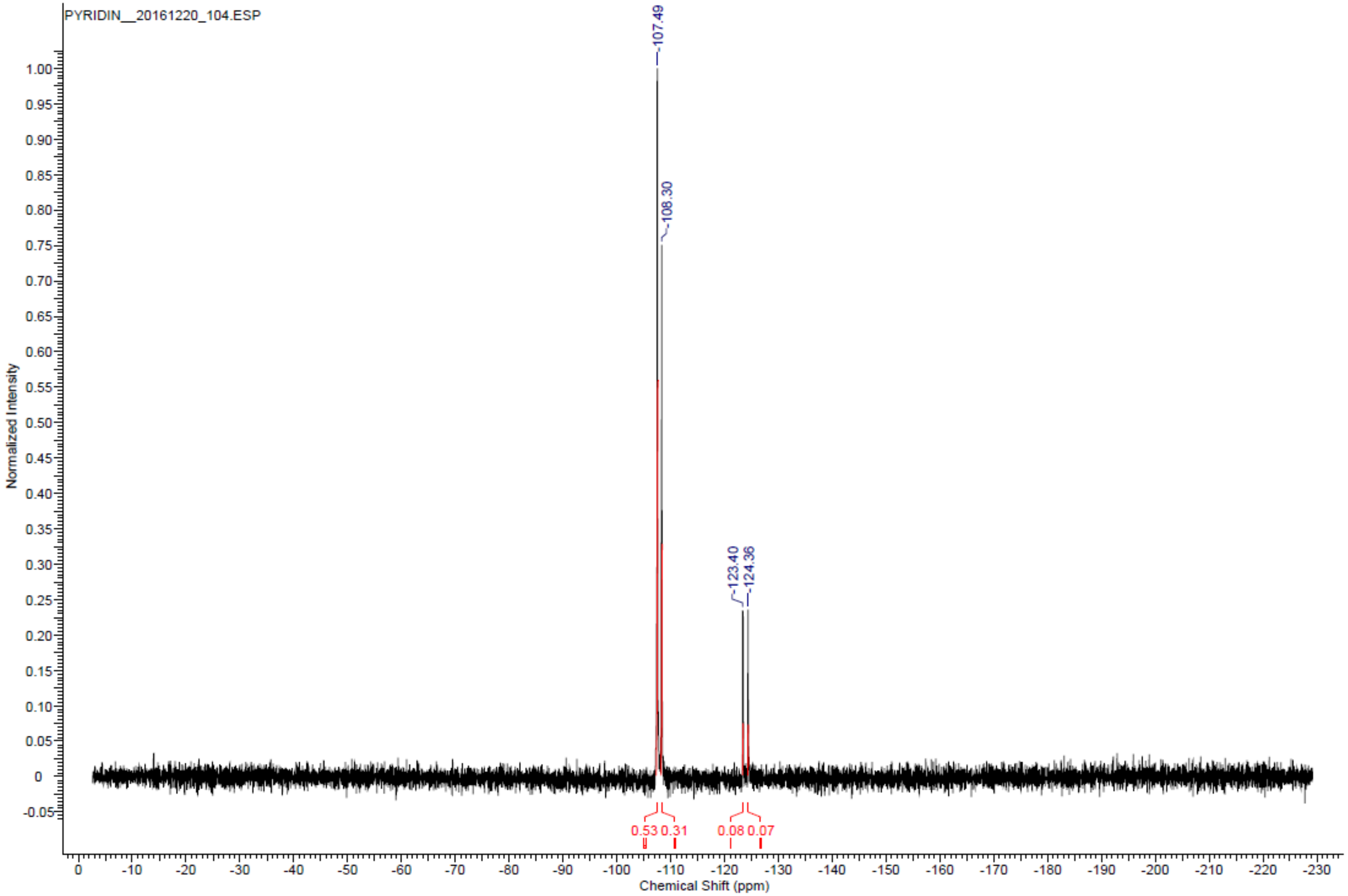
Figure S 15 Top: Static T-mixer with incoming orange Eosin Y solution and colourless substrate solution resulting in deep pink solution; Bottom: colour change of the substrate solution from deep pink (bottom part of the reactor) to dark yellow upon irradiation with green light. Formation of gas slugs due to the expulsion of molecular nitrogen during the reaction. Internal light source is switched off for taking the picture.

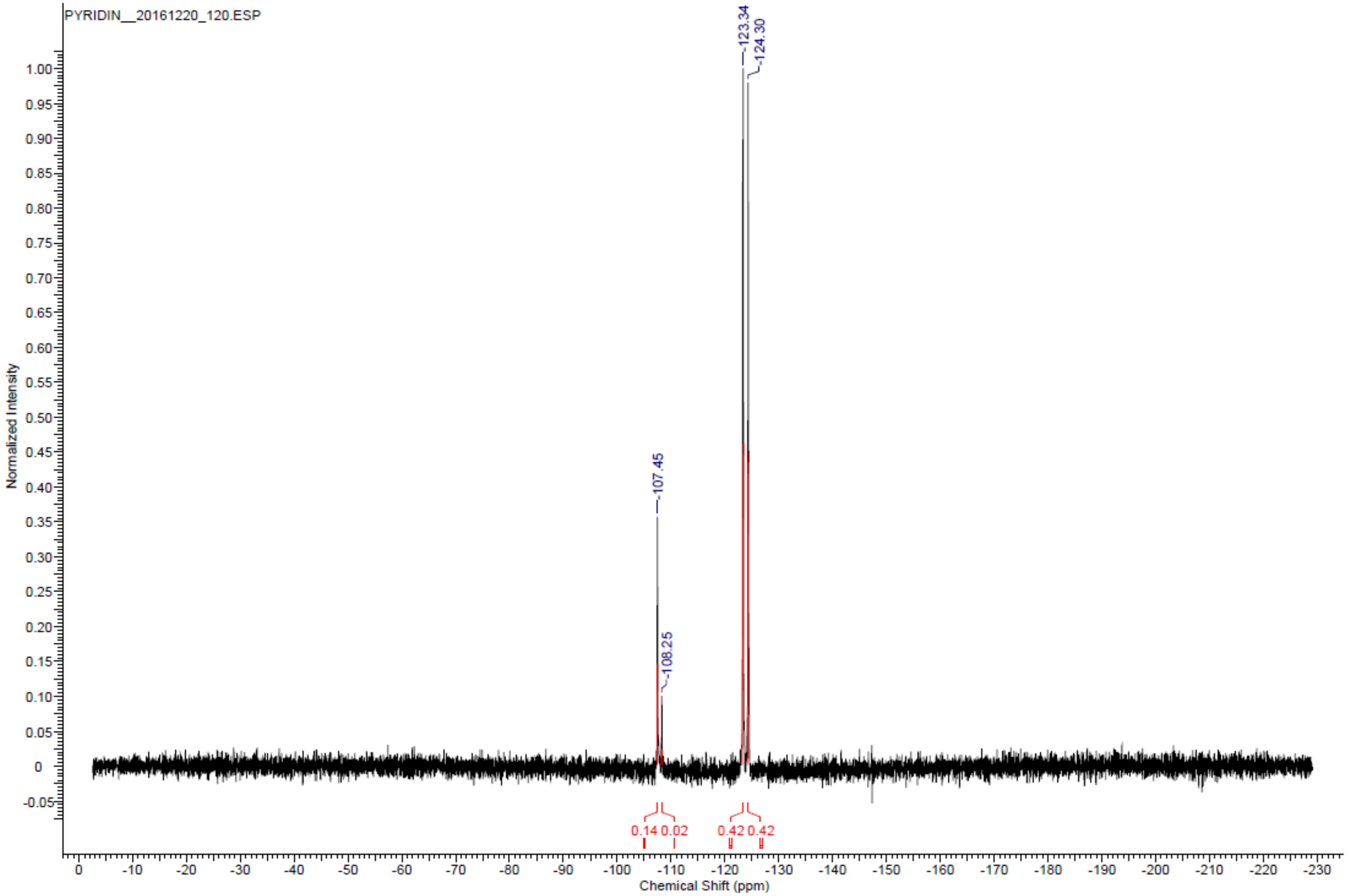
7. ^{19}F NMR spectra of Krapcho decarboxylation in continuous-flow

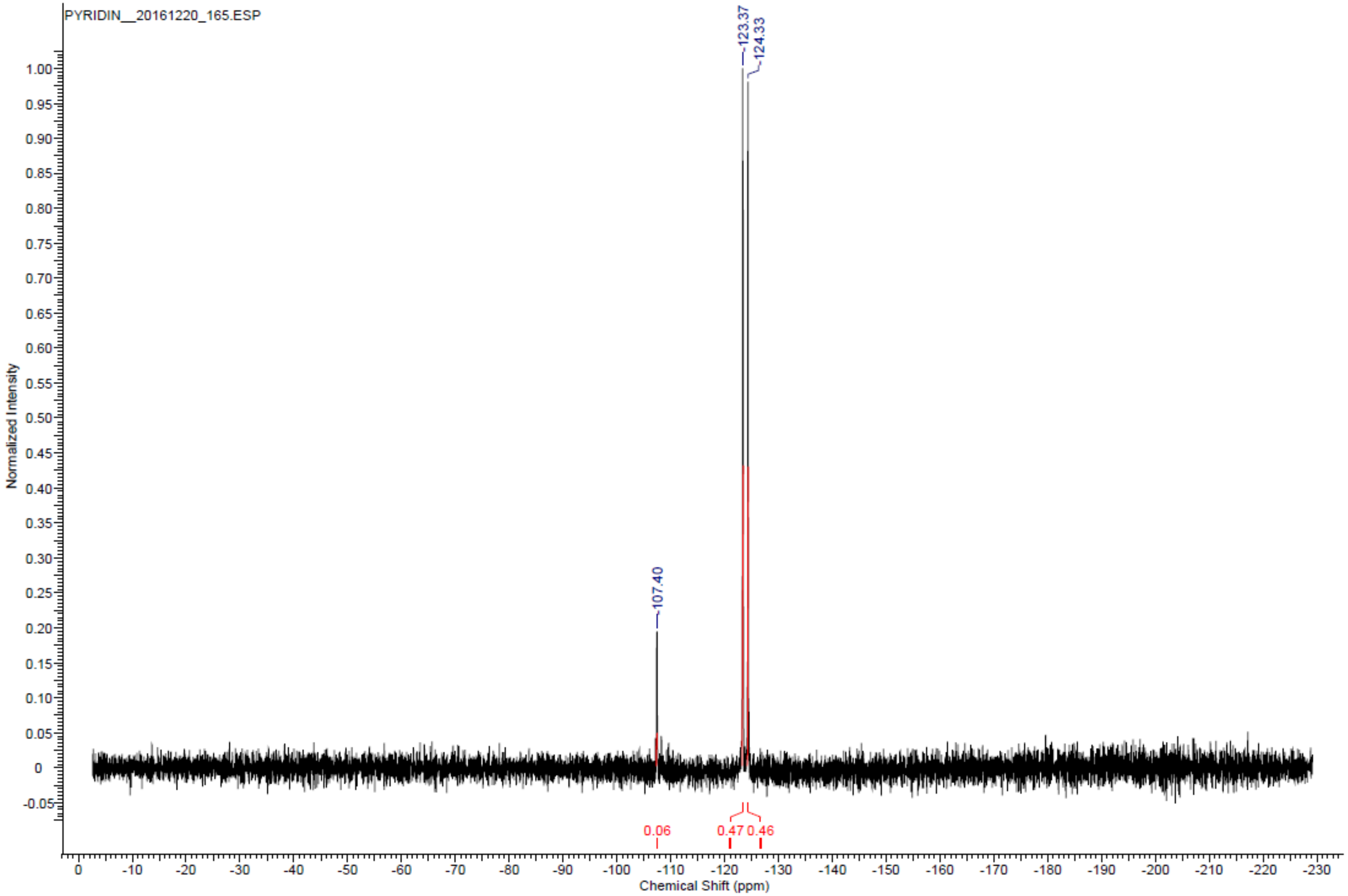



PYRIDIN__20161220_086.ESP
-108.20
-107.39
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.36
0.63
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

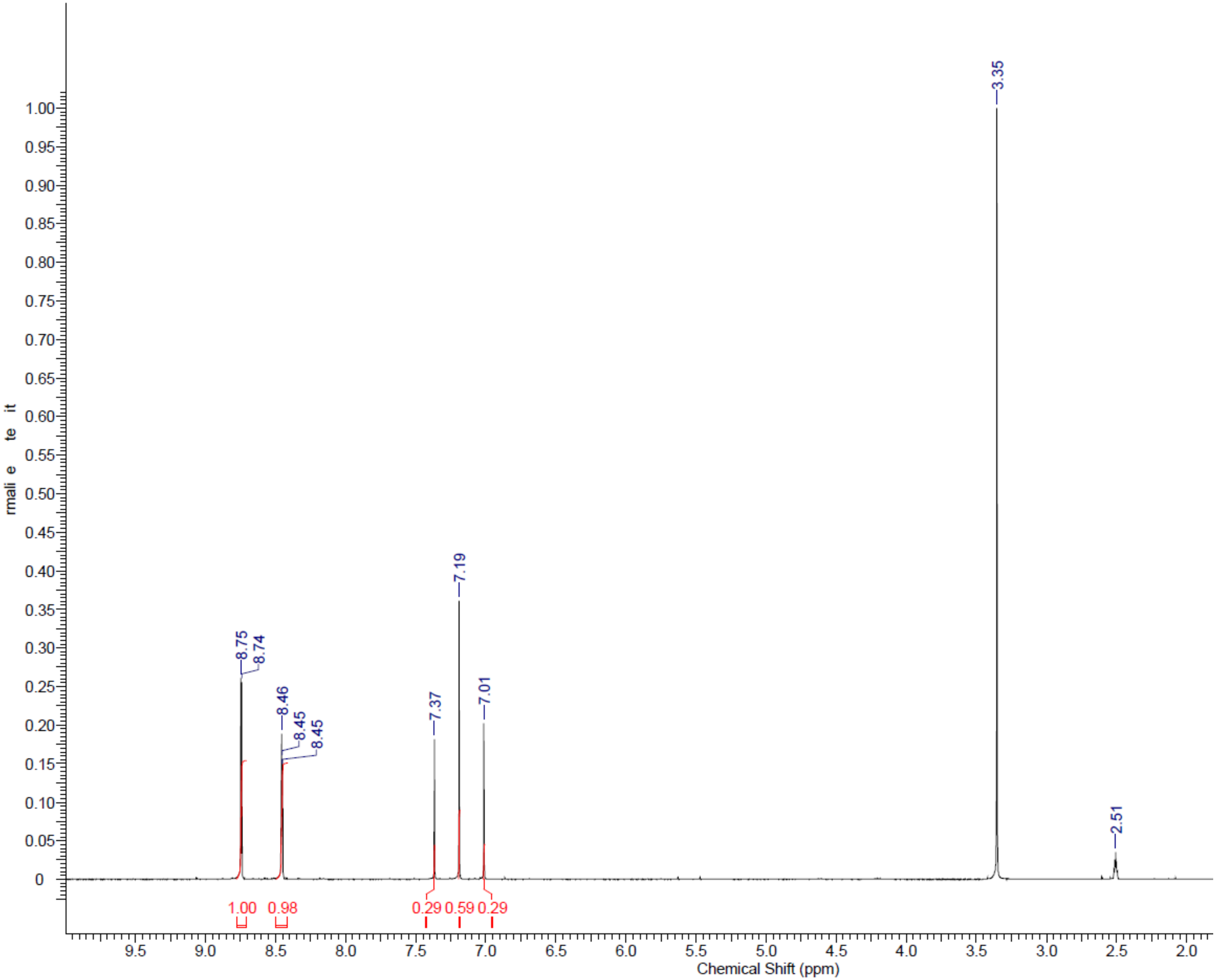

PYRIDIN__20161220_098.ESP
108.30
107.48
123.41
124.38
0.55
0.41
0.02
0.02
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

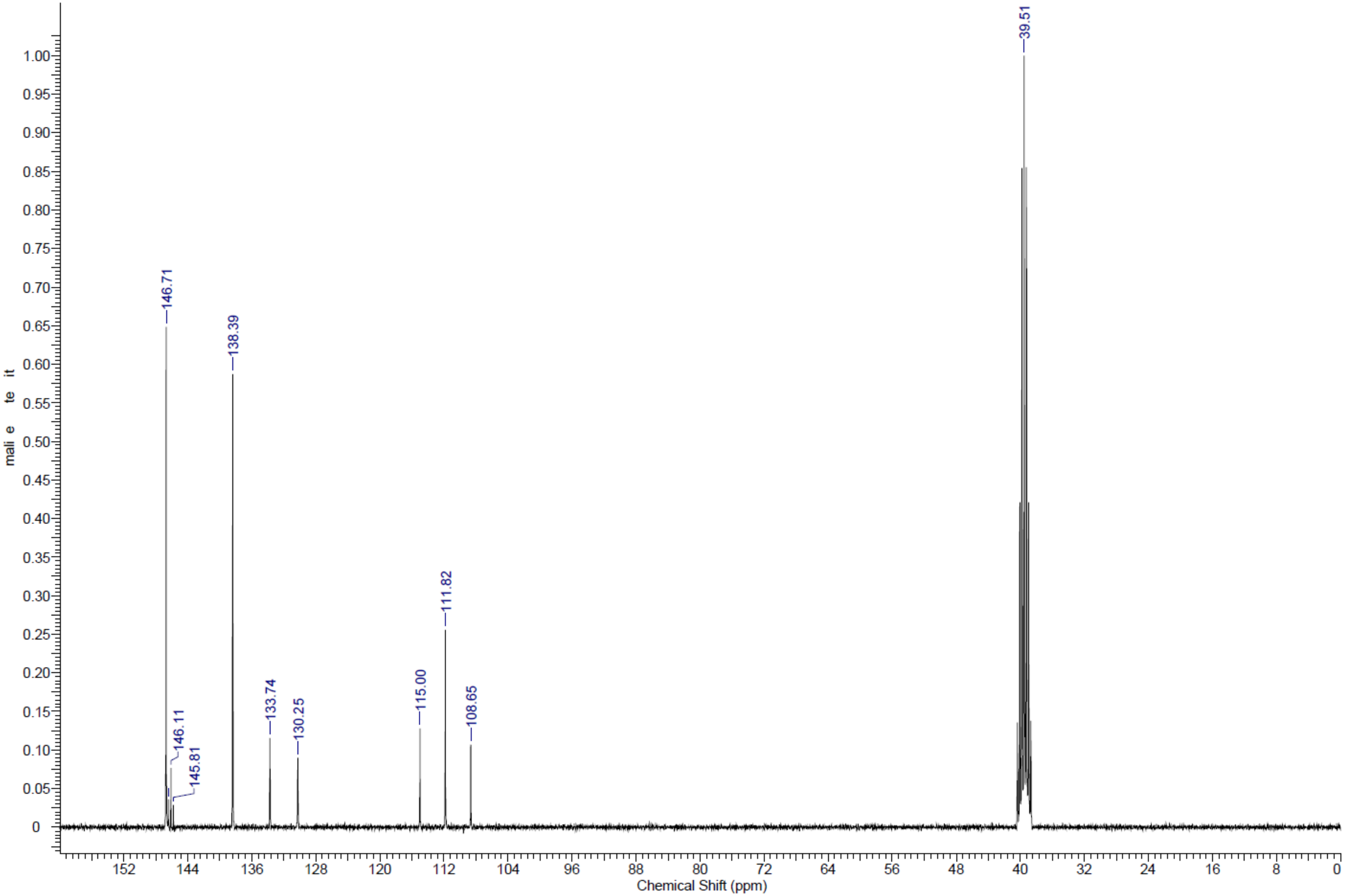

PYRIDIN__20161220_104.ESP
-107.49
-108.30
-123.40
-124.36
0.53
0.31
0.08
0.07
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)


PYRIDIN__20161220_120.ESP
-123.34
-124.30
-107.45
-108.25
0.14
0.02
0.42
0.42
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

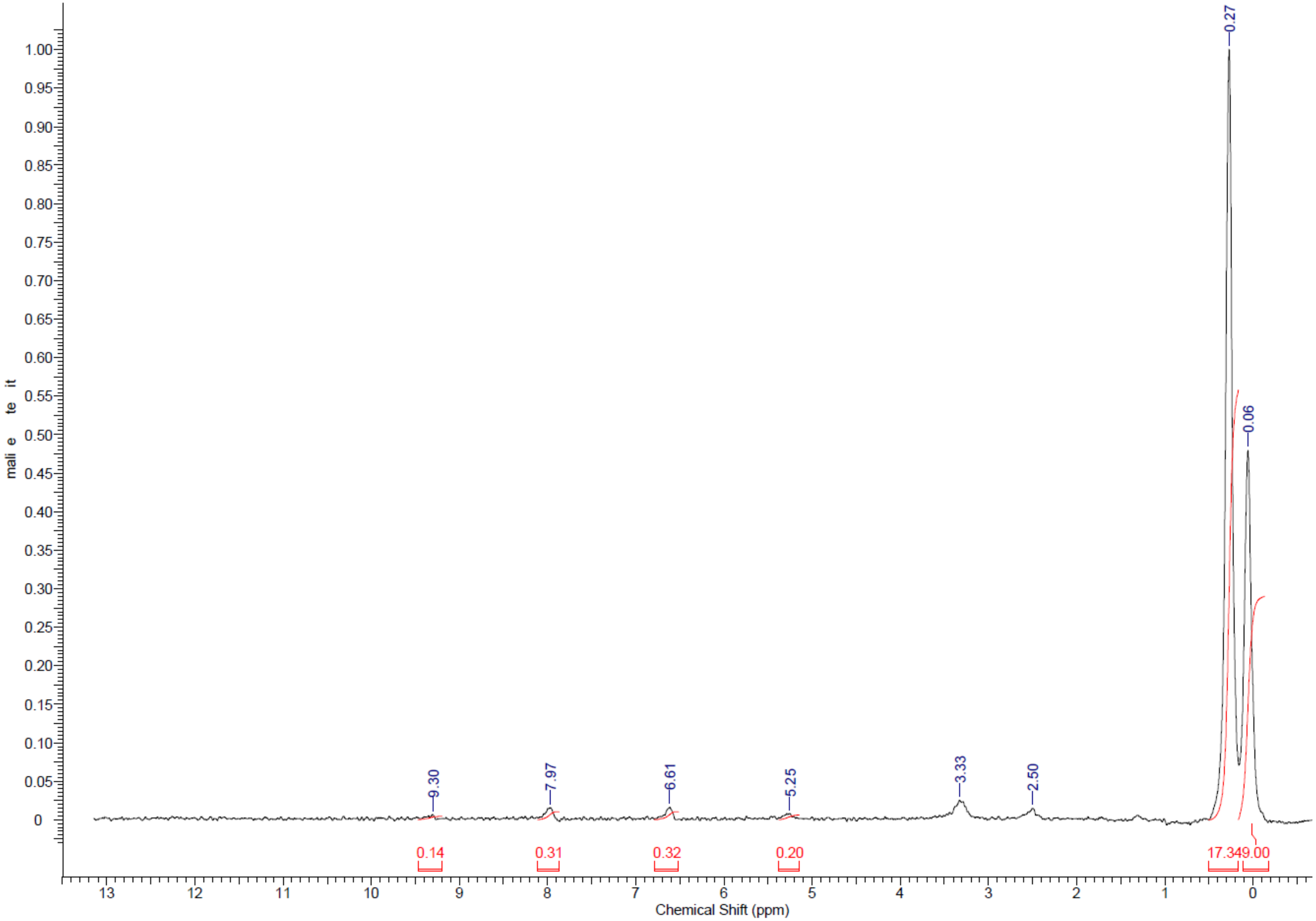

PYRIDIN__20161220_165.ESP
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
107.40
123.37
124.33
0.06
0.47
0.46
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

8. High-resolution ^1H / ^{13}C NMR spectrum of purified 2 (DMSO-d_6)

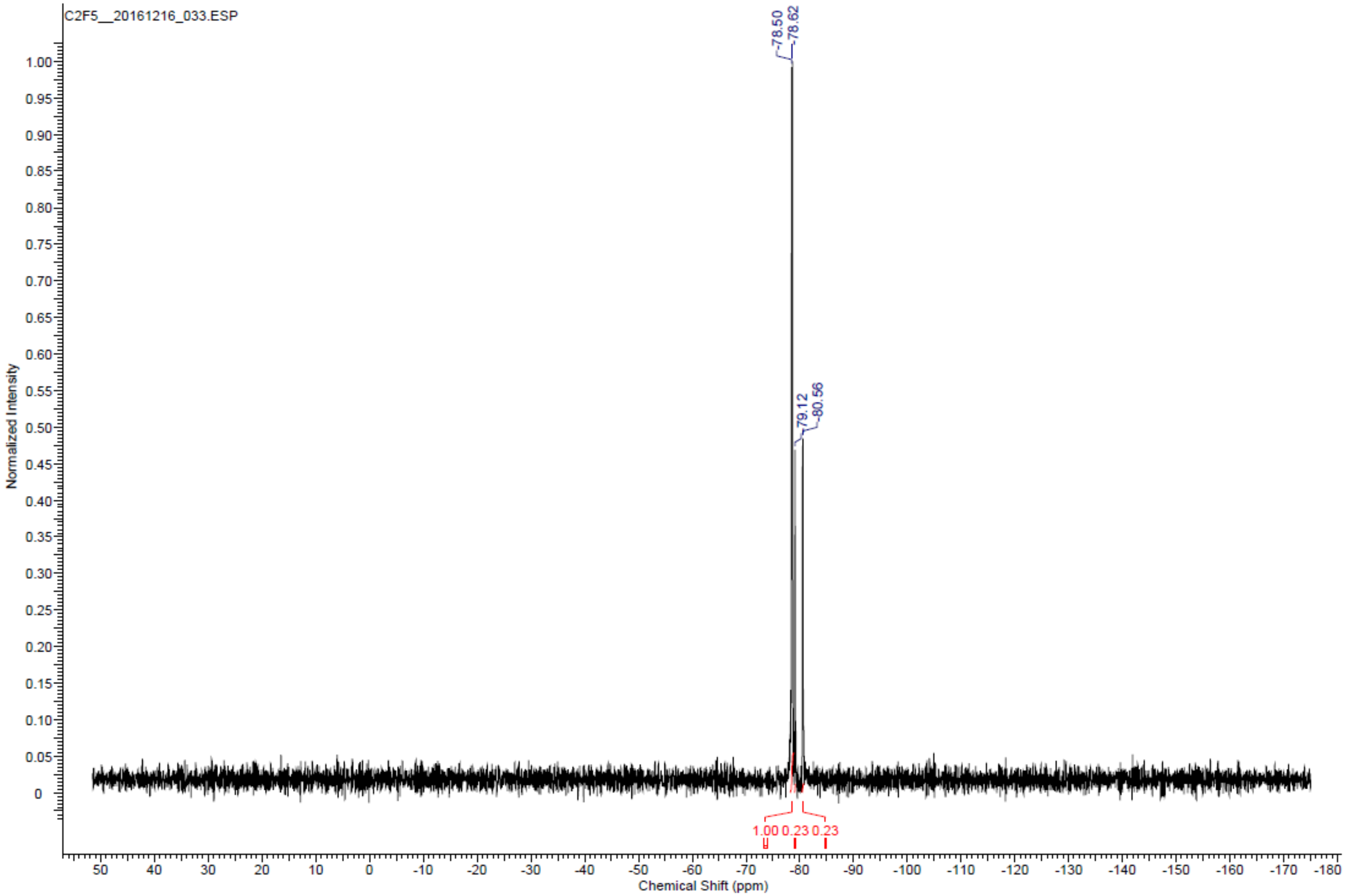


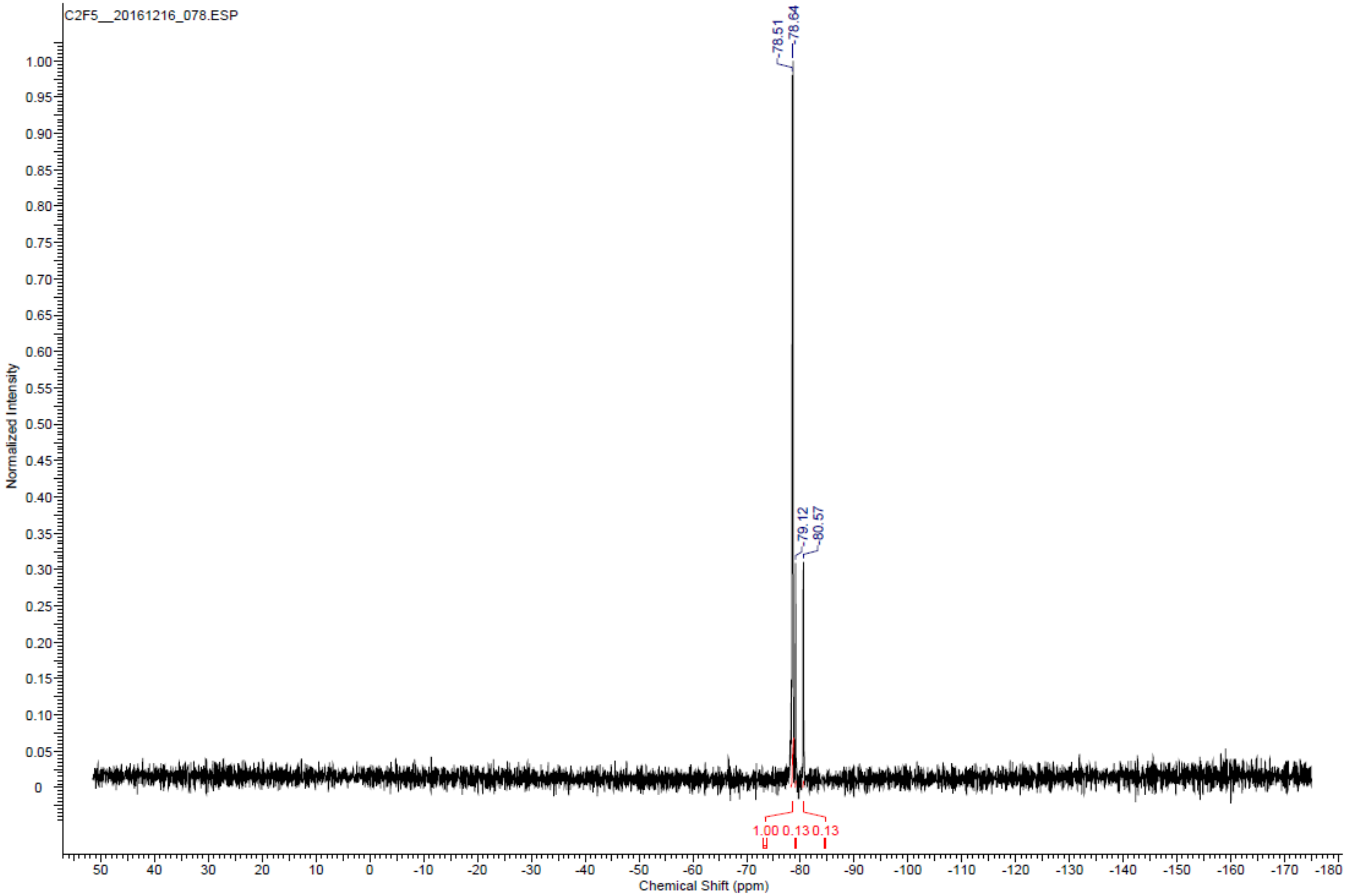

146.71
146.11
145.81
138.39
133.74
130.25
115.00
111.82
108.65
39.51
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

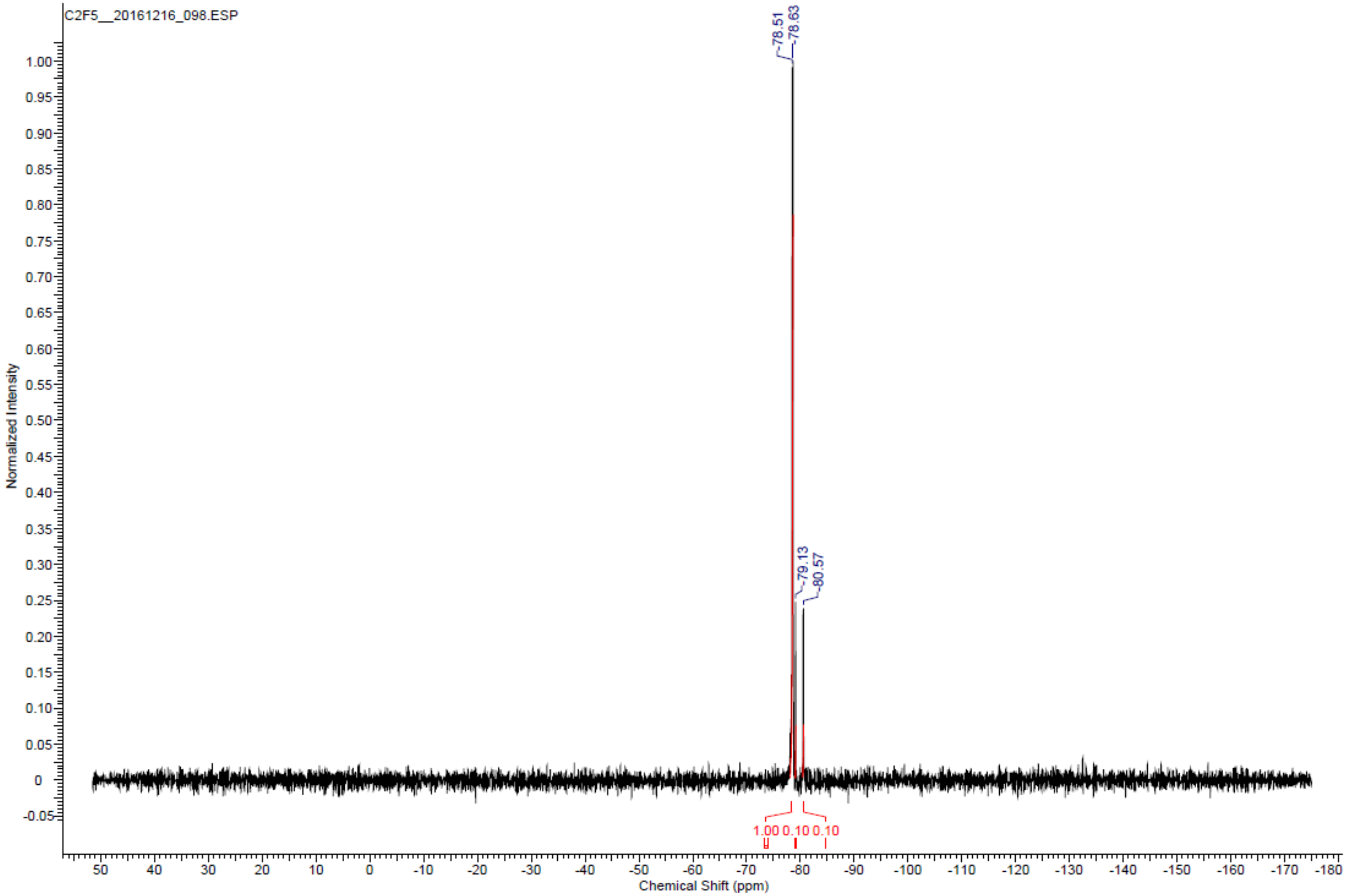
9. ^{1}H NMR spectrum of partly hydrolysed TMS-CF$_3$ in DMSO-d$_6$



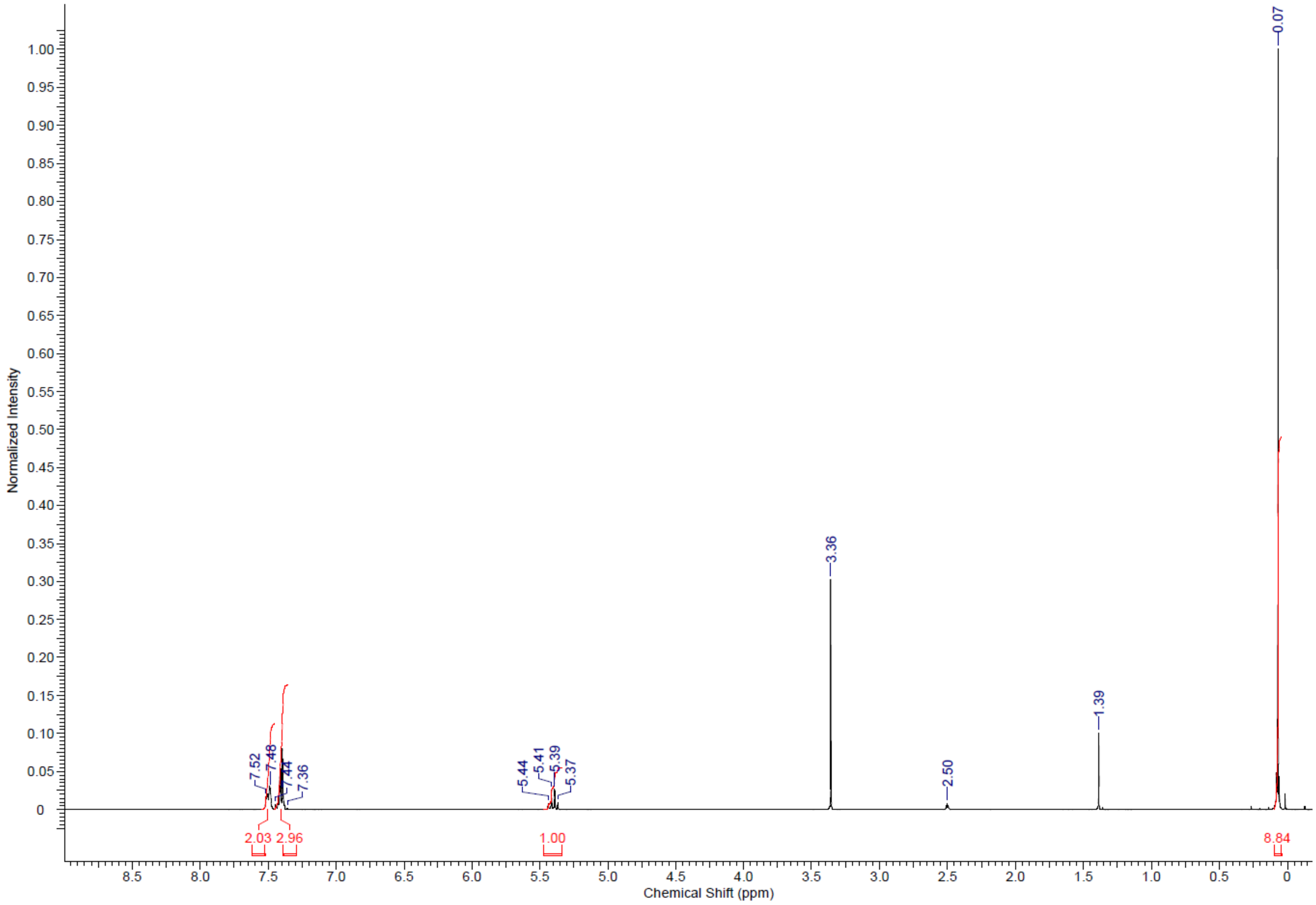
10. ^{19}F NMR spectra of Ruppert-Prakash reaction with TMS-CF_3 in continuous-flow (non-dried DMSO)

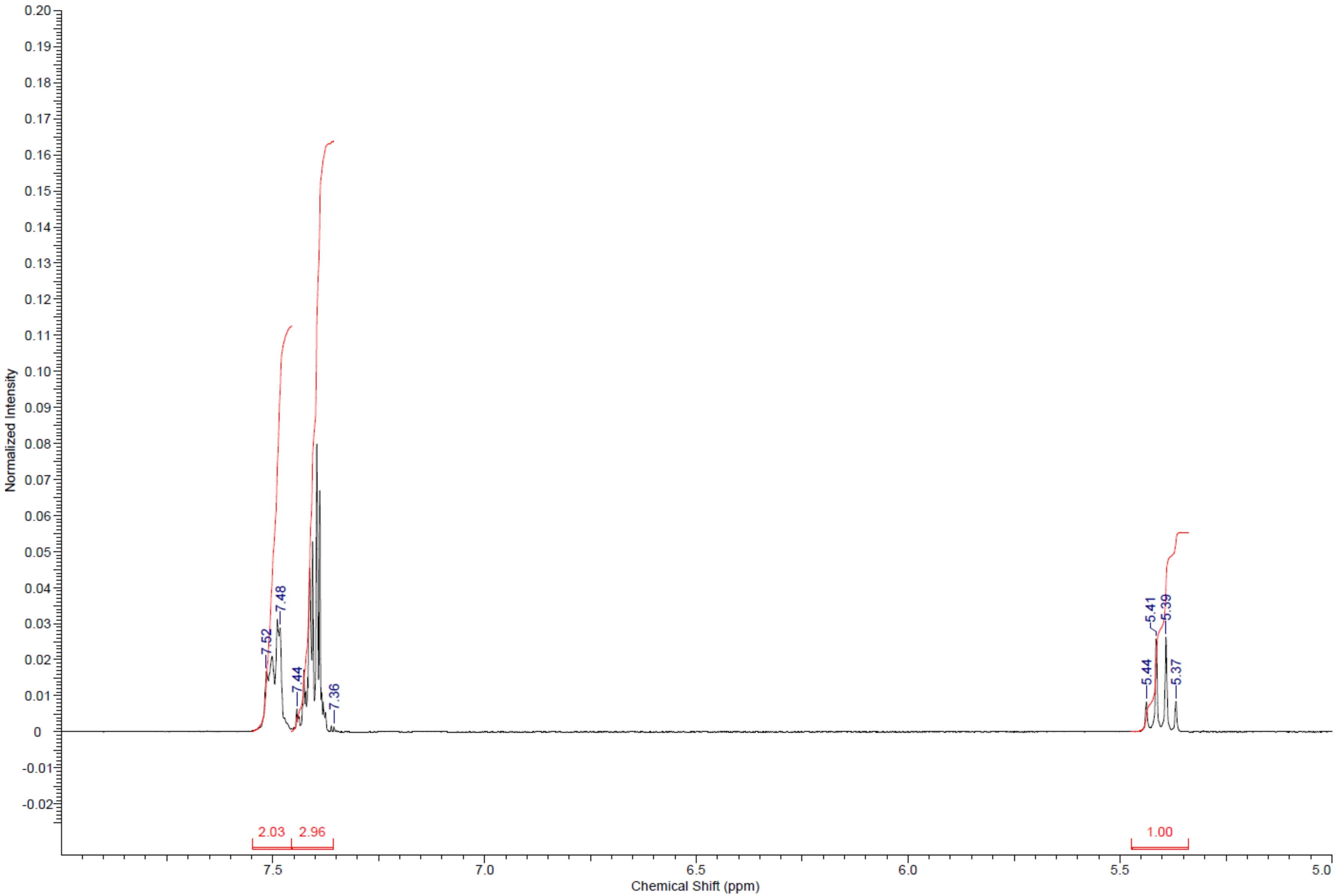


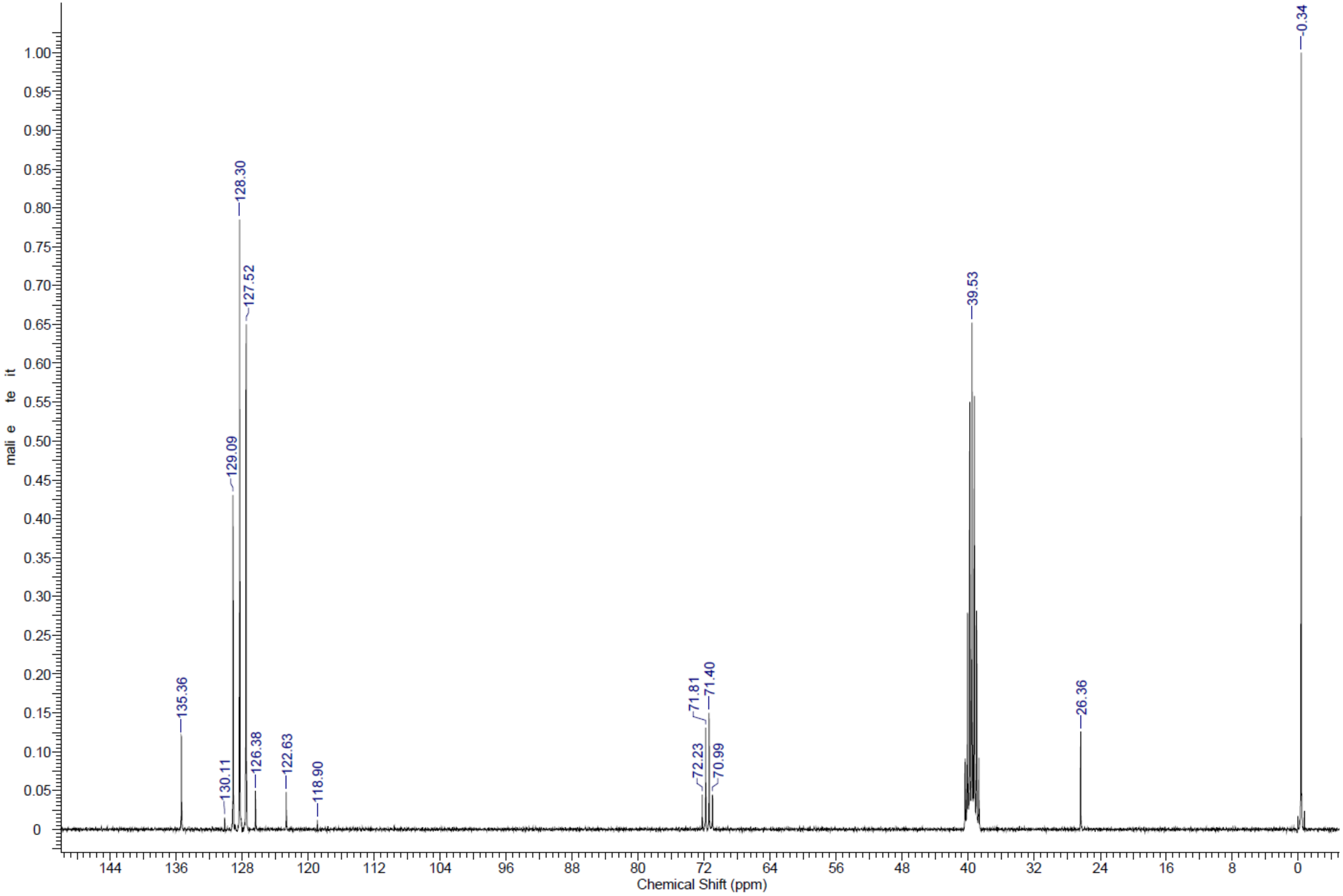

C2F5__20161216_078.ESP
-78.51
-78.64
-79.12
-80.57
1.00
0.13
0.13
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
Chemical Shift (ppm)


C2F5__20161216_098.ESP
-78.51
-78.63
-79.13
-80.57
1.00
0.10
0.10
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
Chemical Shift (ppm)

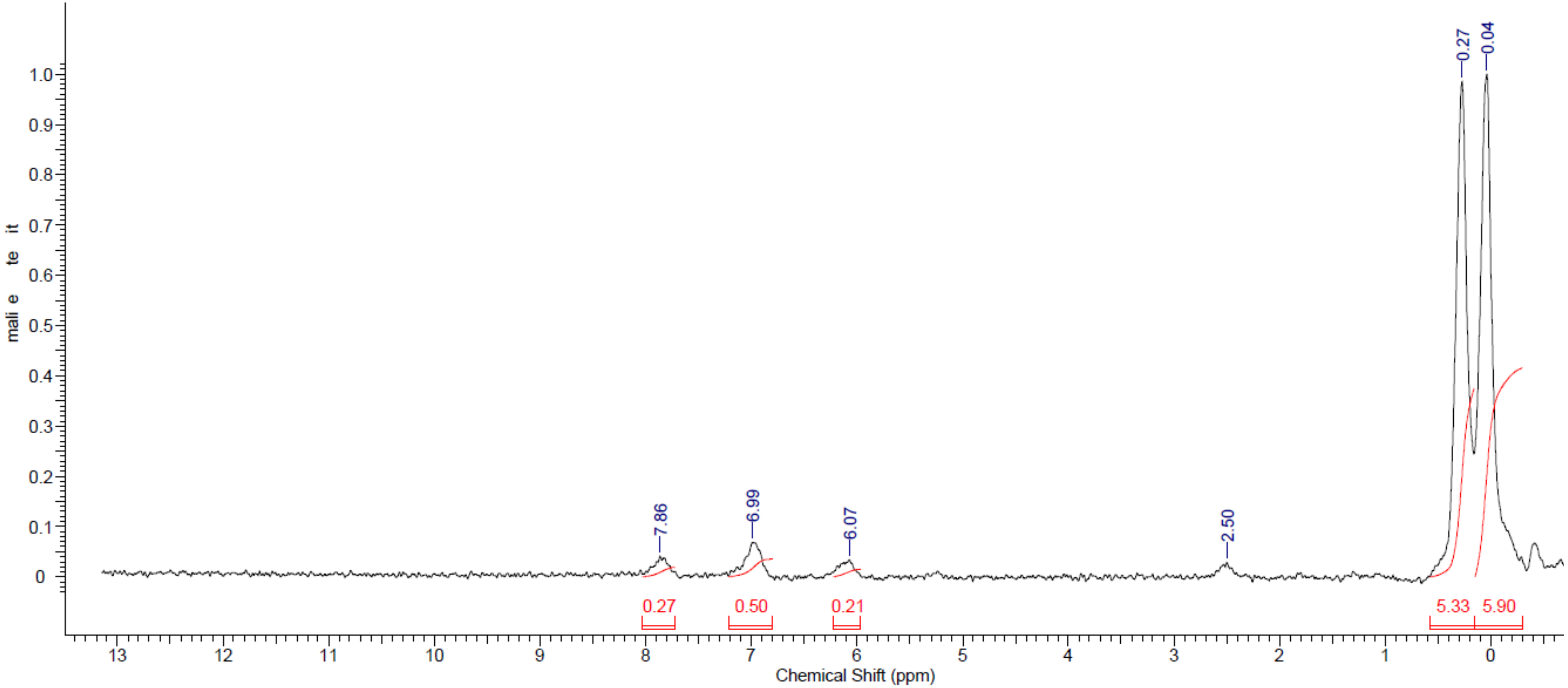
11. High-resolution ^{1}H / ^{13}C NMR spectra of purified 4 (DMSO-d$_6$)



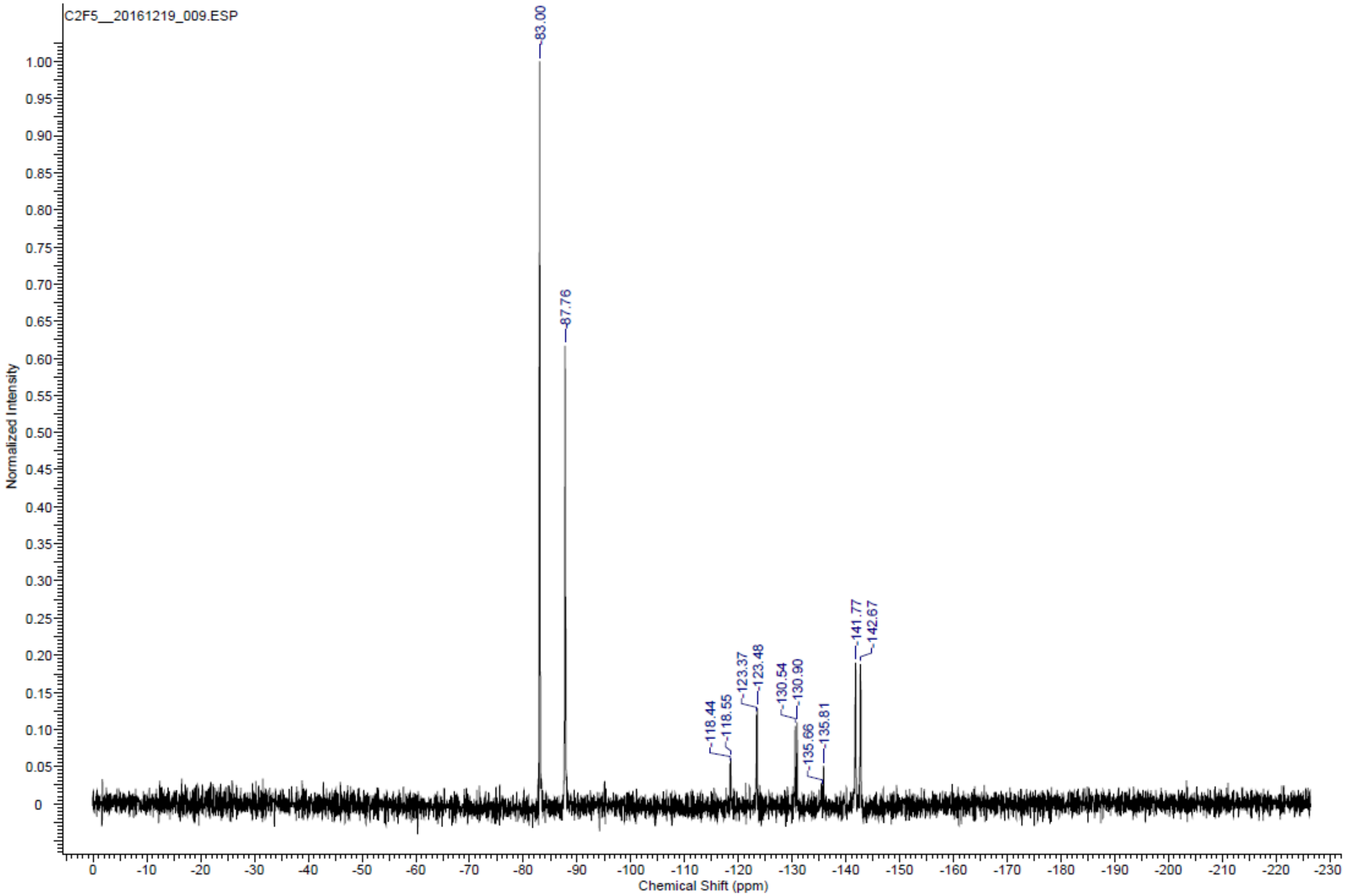

Normalized Intensity
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
-0.02
7.52
7.48
7.44
7.36
5.44
5.41
5.39
5.37
2.03
2.96
1.00
7.5
7.0
6.5
6.0
5.5
5.0
Chemical Shift (ppm)

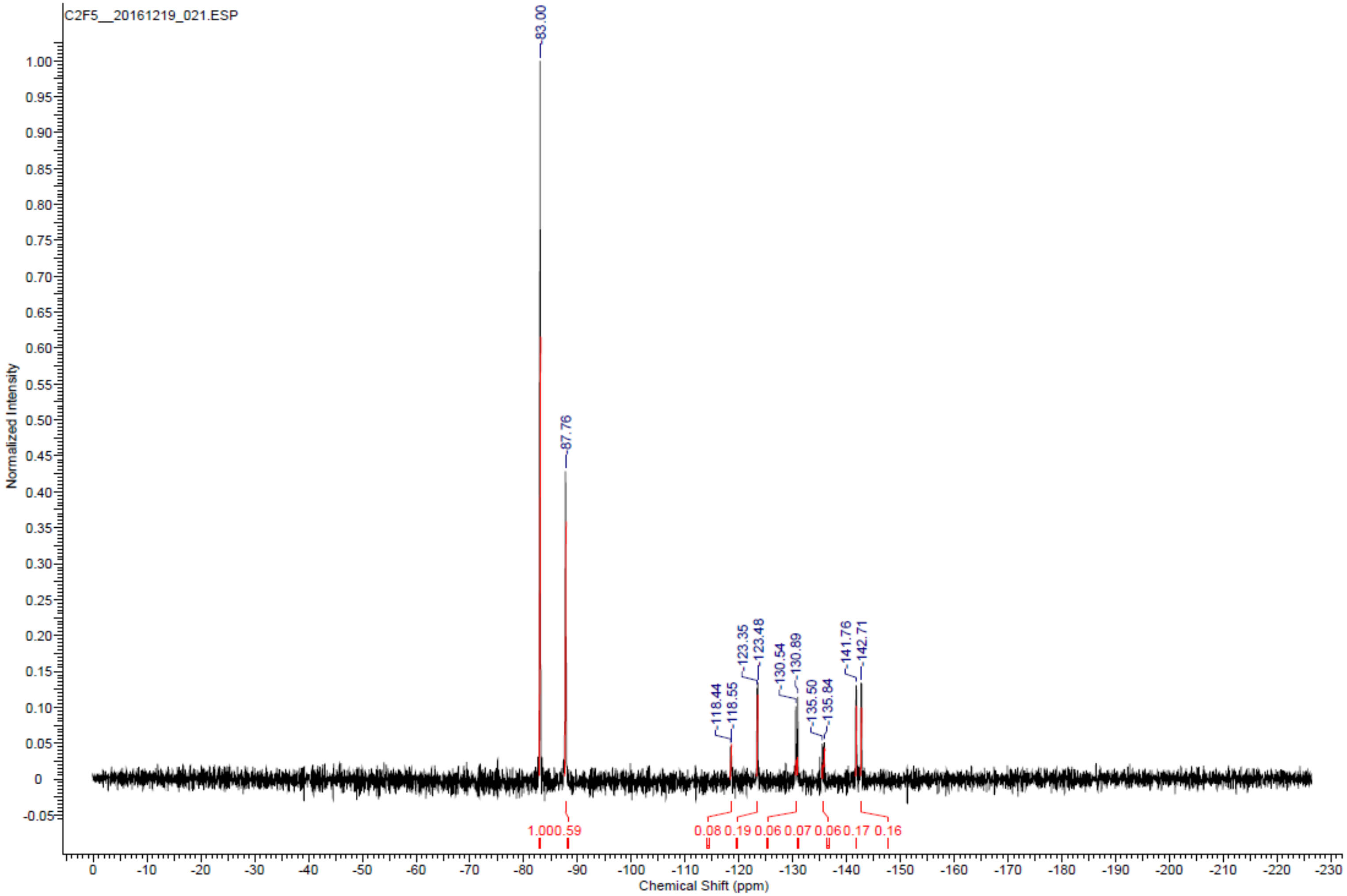

135.36
130.11
129.09
128.30
127.52
126.38
122.63
118.90
72.23
71.81
71.40
70.99
39.53
26.36
-0.34
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
mali e te it
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

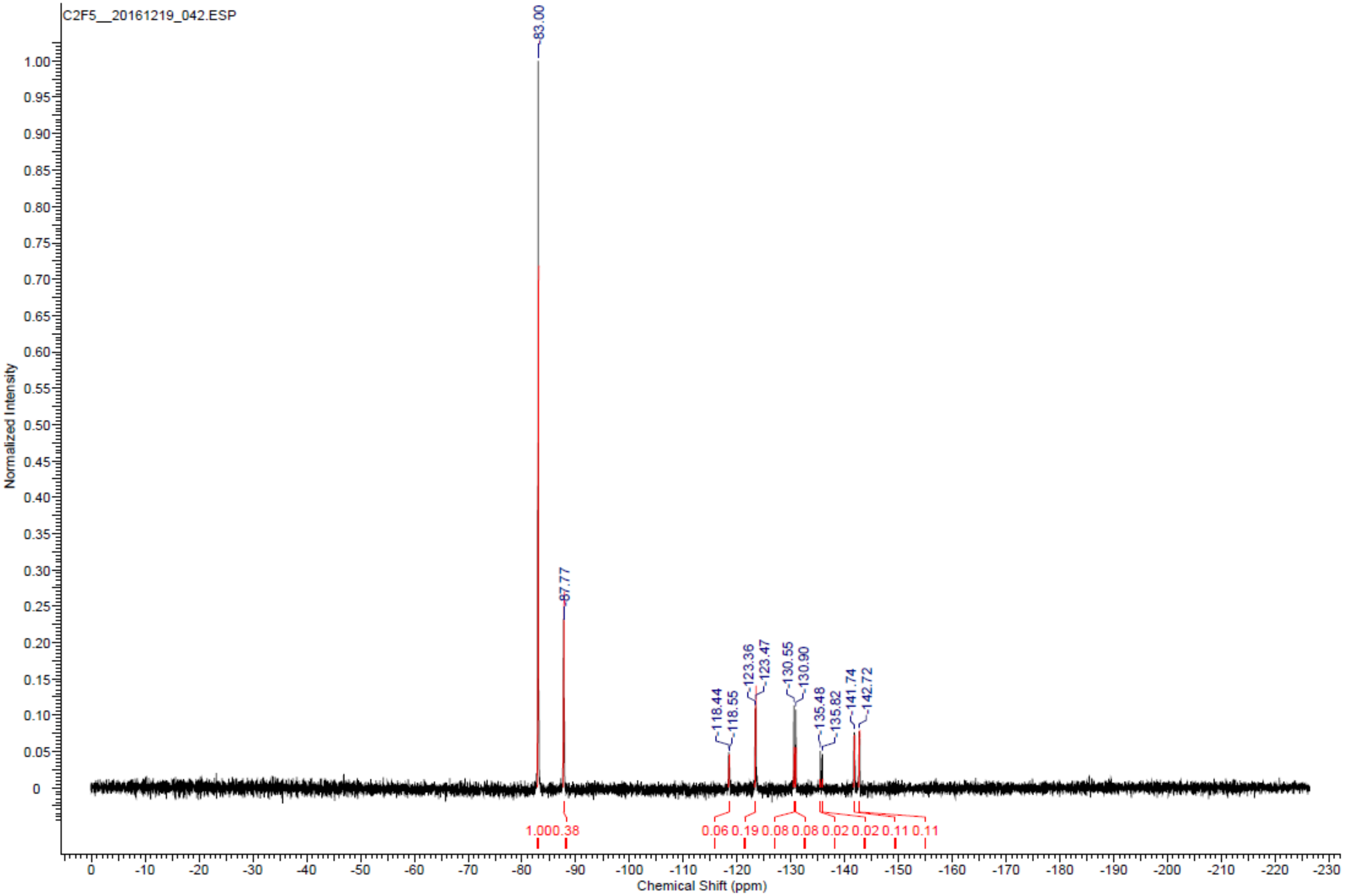
12. ^1H NMR spectrum of partly hydrolysed TMS-C_2F_5 in DMSO-d_6



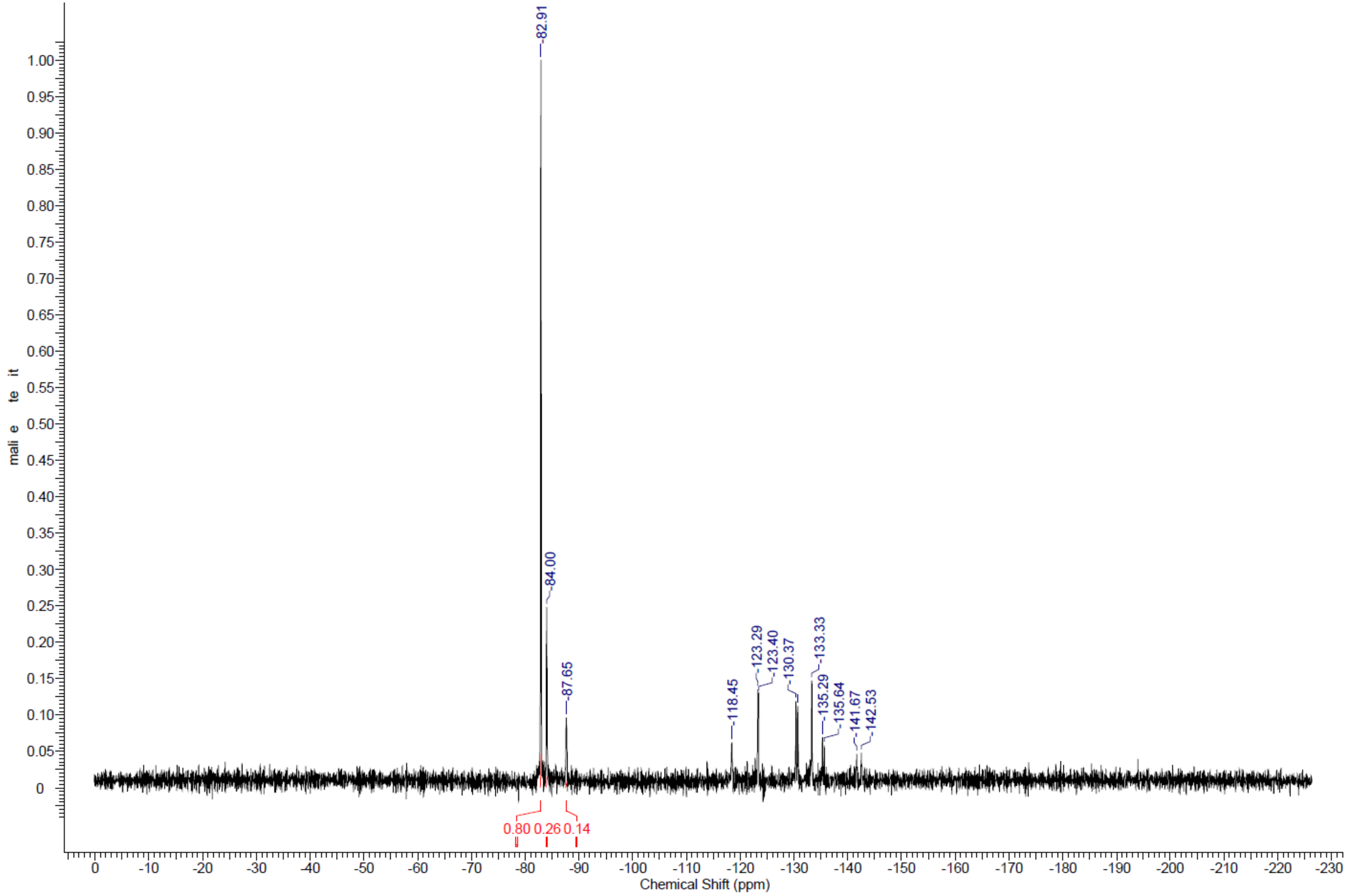
13. ^{19}F NMR spectra of Ruppert-Prakash reaction with TMS-C_2F_5 in continuous-flow (non-dried DMSO)

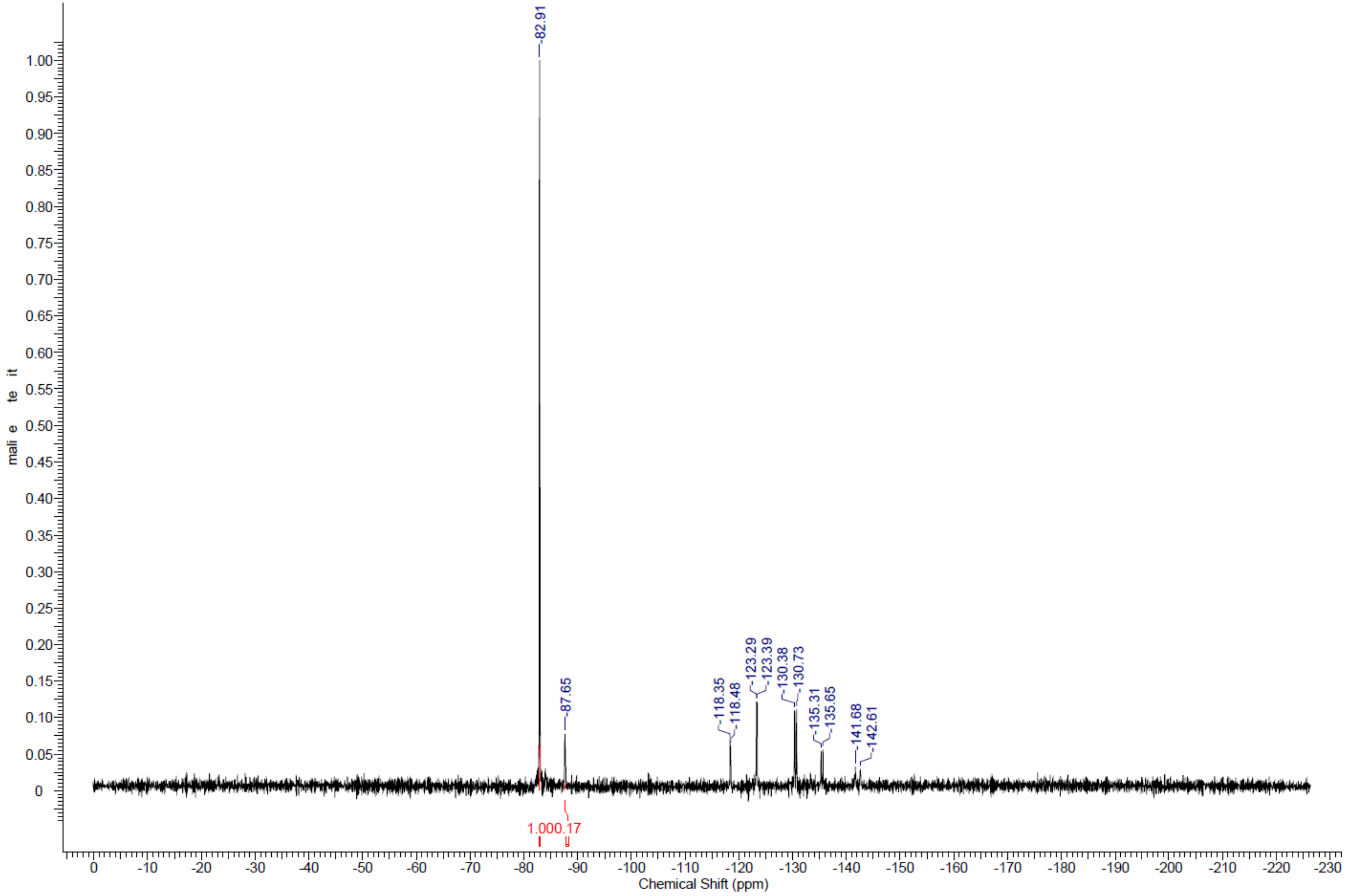



C2F5__20161219_021.ESP
-83.00
-87.76
-118.44
-118.55
-123.35
-123.48
-130.54
-130.89
-135.50
-135.84
-141.76
-142.71
1.00
0.59
0.08
0.19
0.06
0.07
0.06
0.17
0.16
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

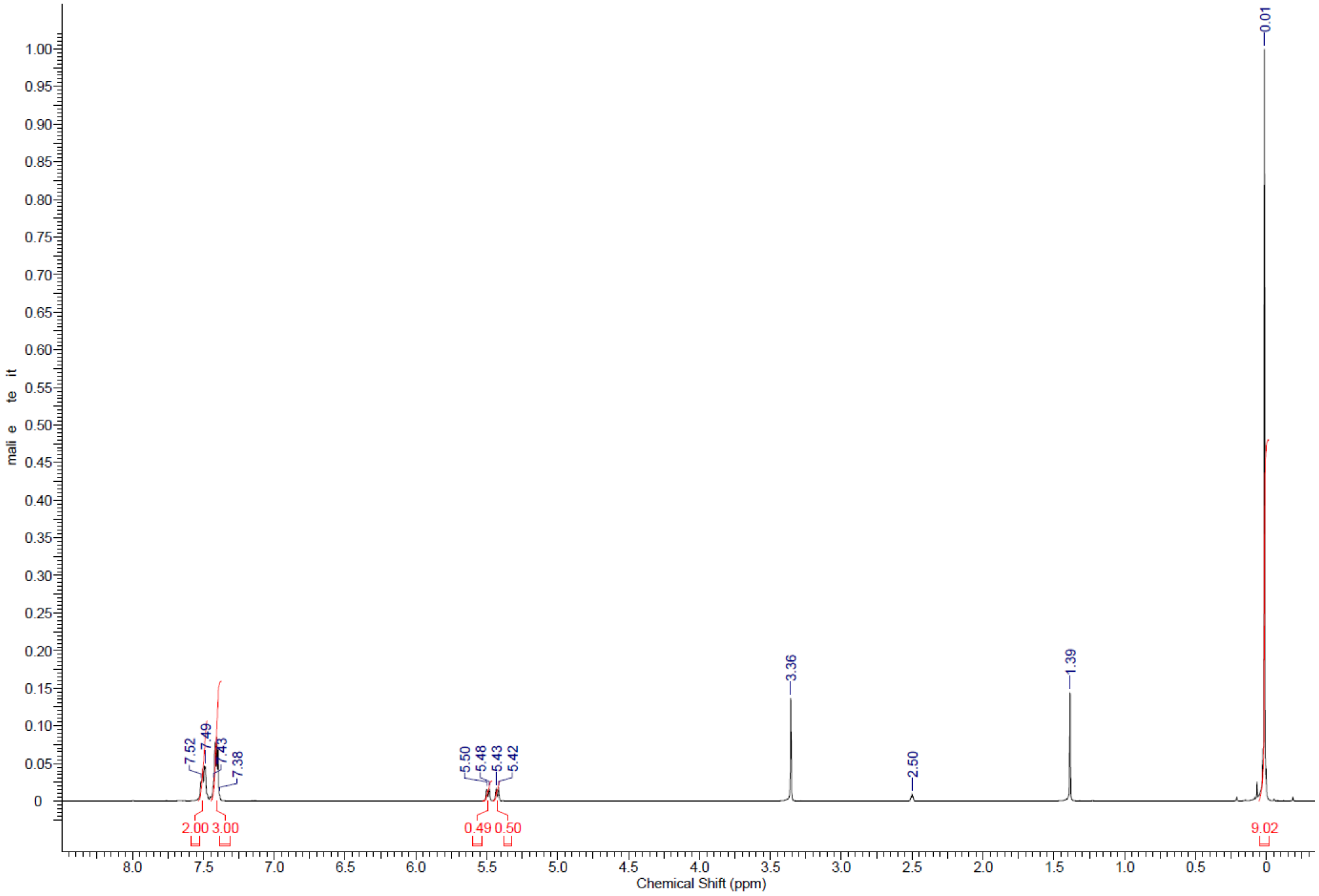

C2F5__20161219_042.ESP
-83.00
-87.77
-118.44
-118.55
-123.36
-123.47
-130.55
-130.90
-135.48
-135.82
-141.74
-142.72
1.00
0.38
0.06
0.19
0.08
0.08
0.02
0.02
0.11
0.11
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

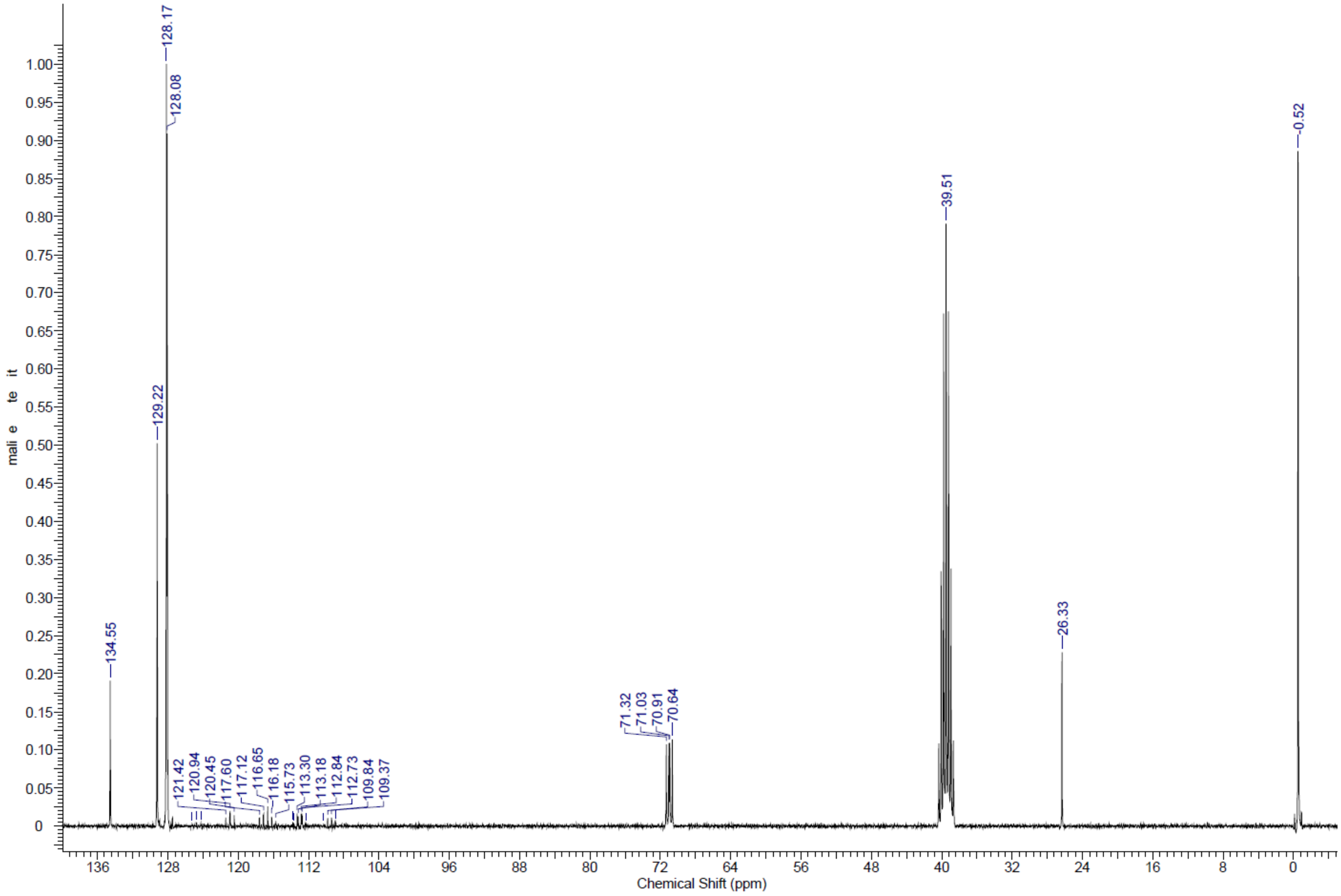
14. ^{19}F NMR spectra of Ruppert-Prakash reaction with TMS-C_2F_5 in continuous-flow (dry DMSO)

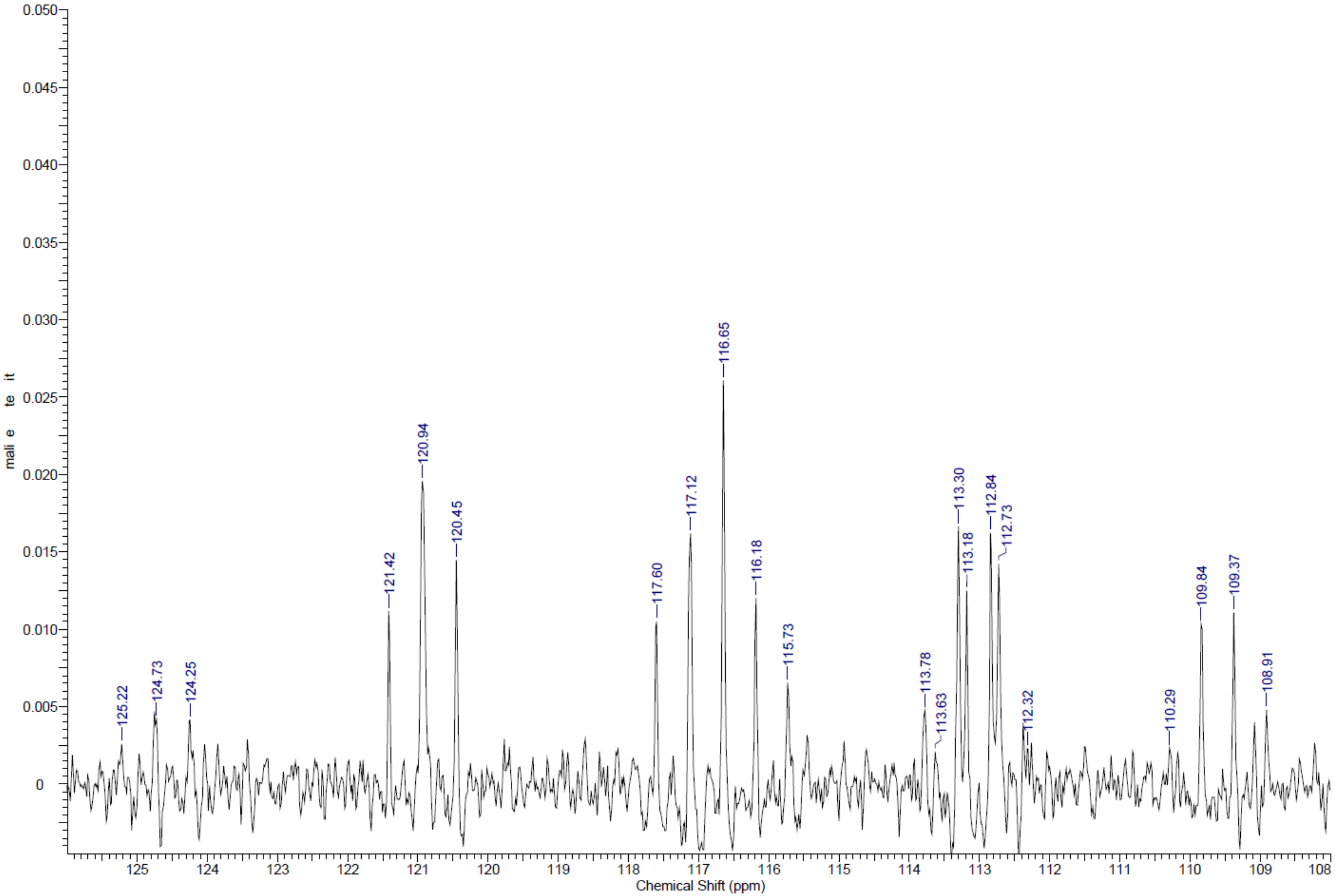



-82.91
-87.65
-118.35
-118.48
-123.29
-123.39
-130.38
-130.73
-135.31
-135.65
-141.68
-142.61
1.00
0.17
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

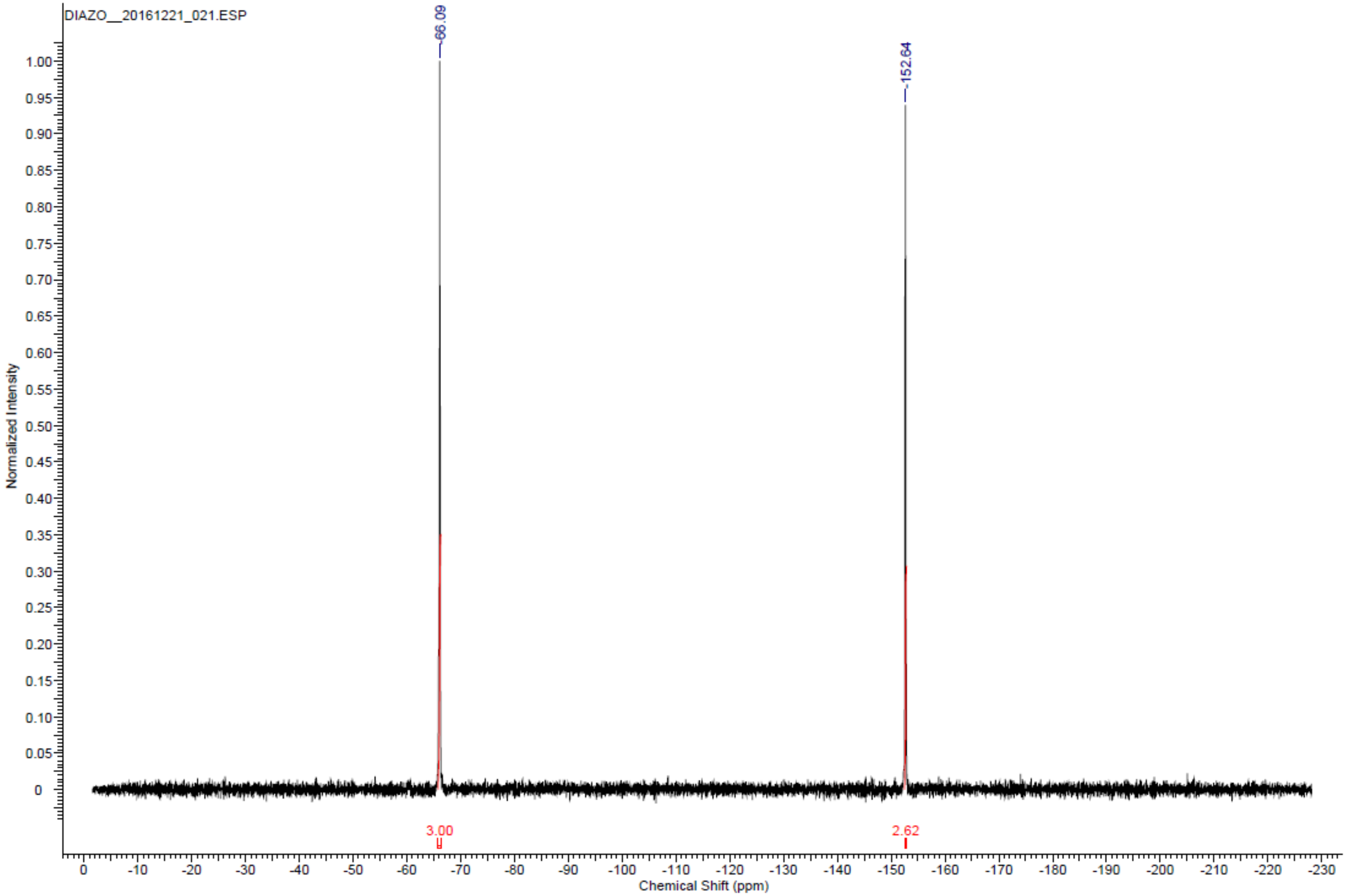
15. High-resolution ^{1}H / ^{13}C NMR spectra of purified 5 (DMSO-d_6)

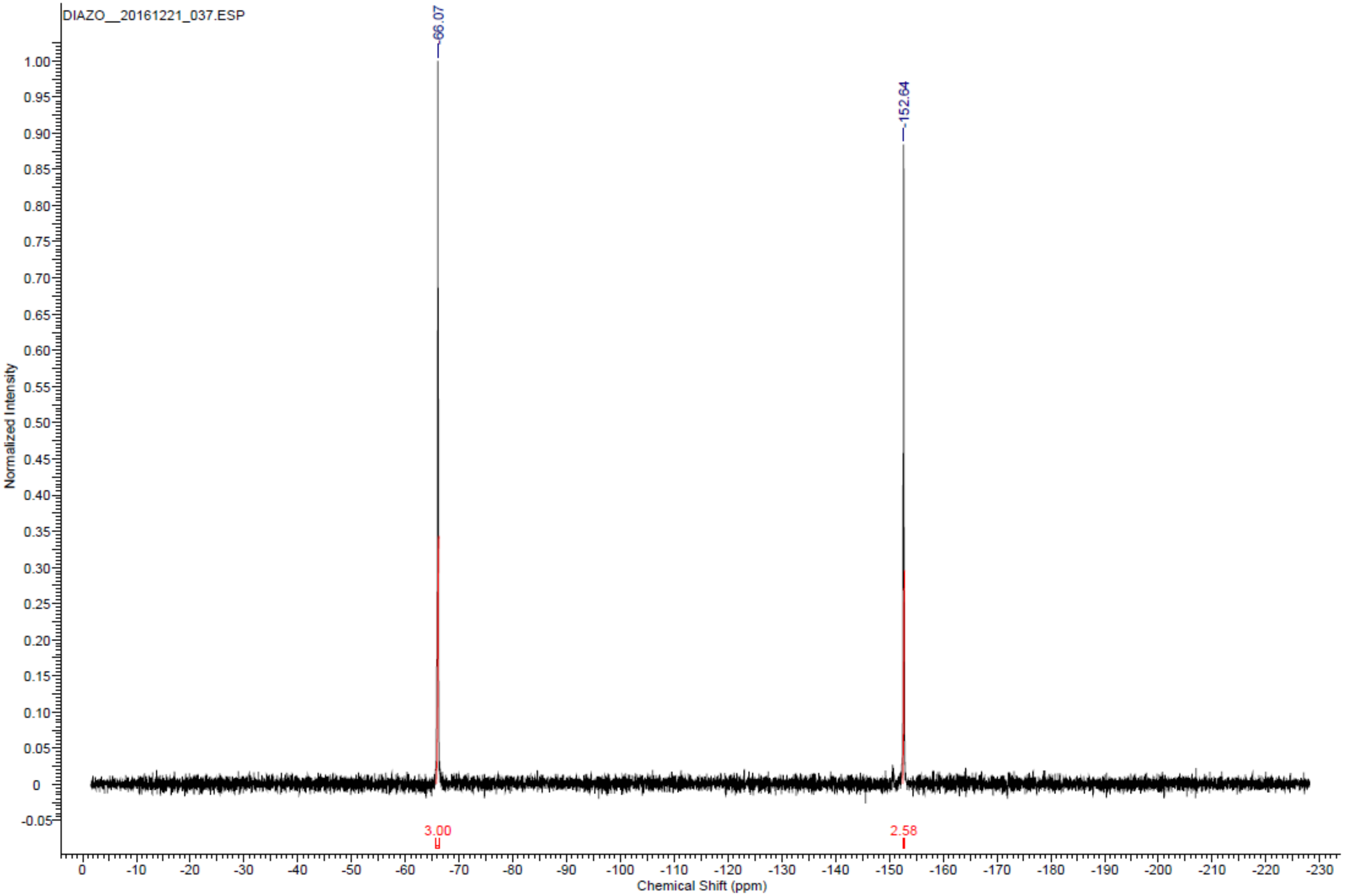


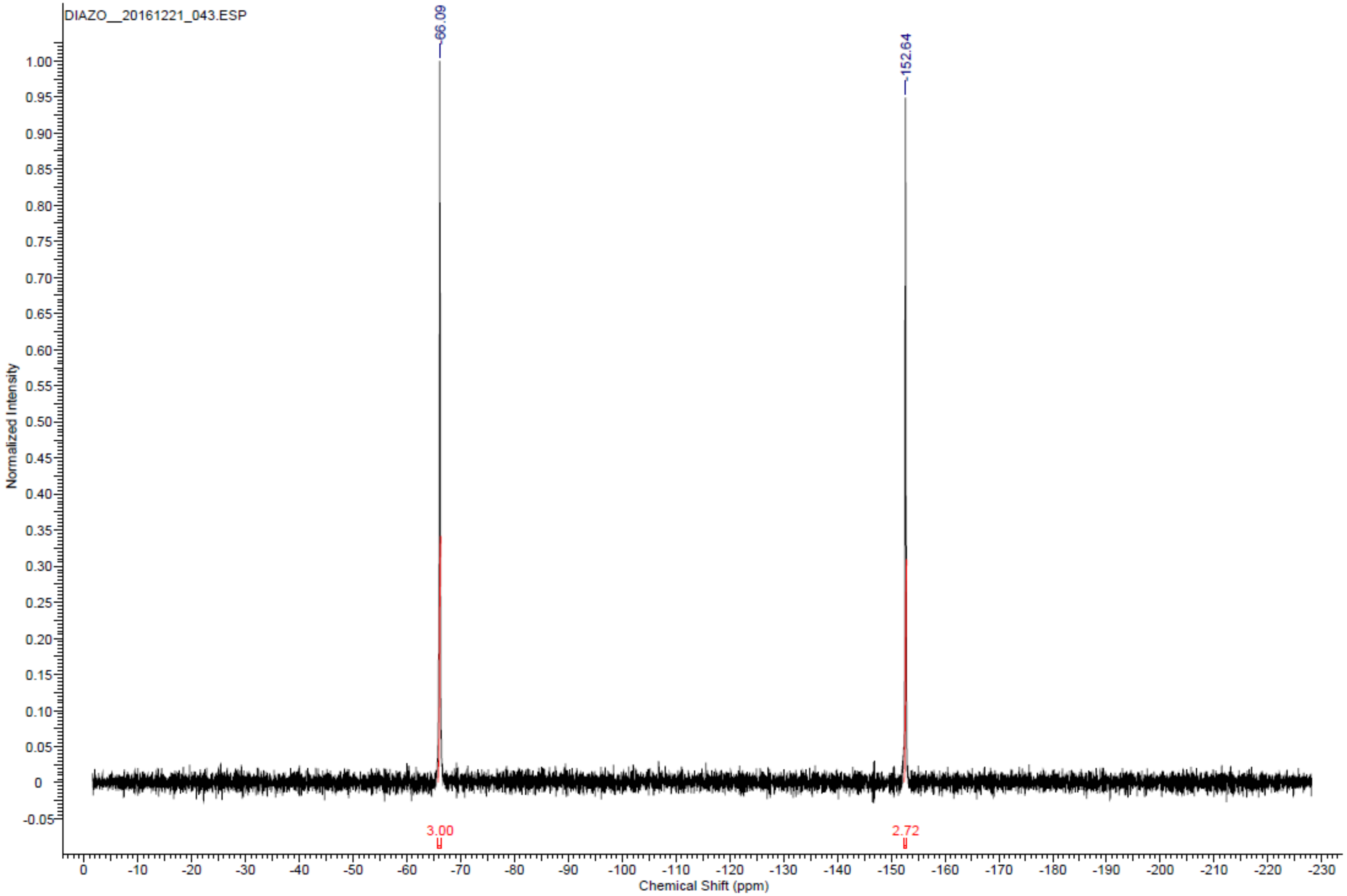

128.17
128.08
129.22
134.55
121.42
120.94
120.45
117.60
117.12
116.65
116.18
115.73
113.30
113.18
112.84
112.73
109.84
109.37
71.32
71.03
70.91
70.64
39.51
26.33
-0.52
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

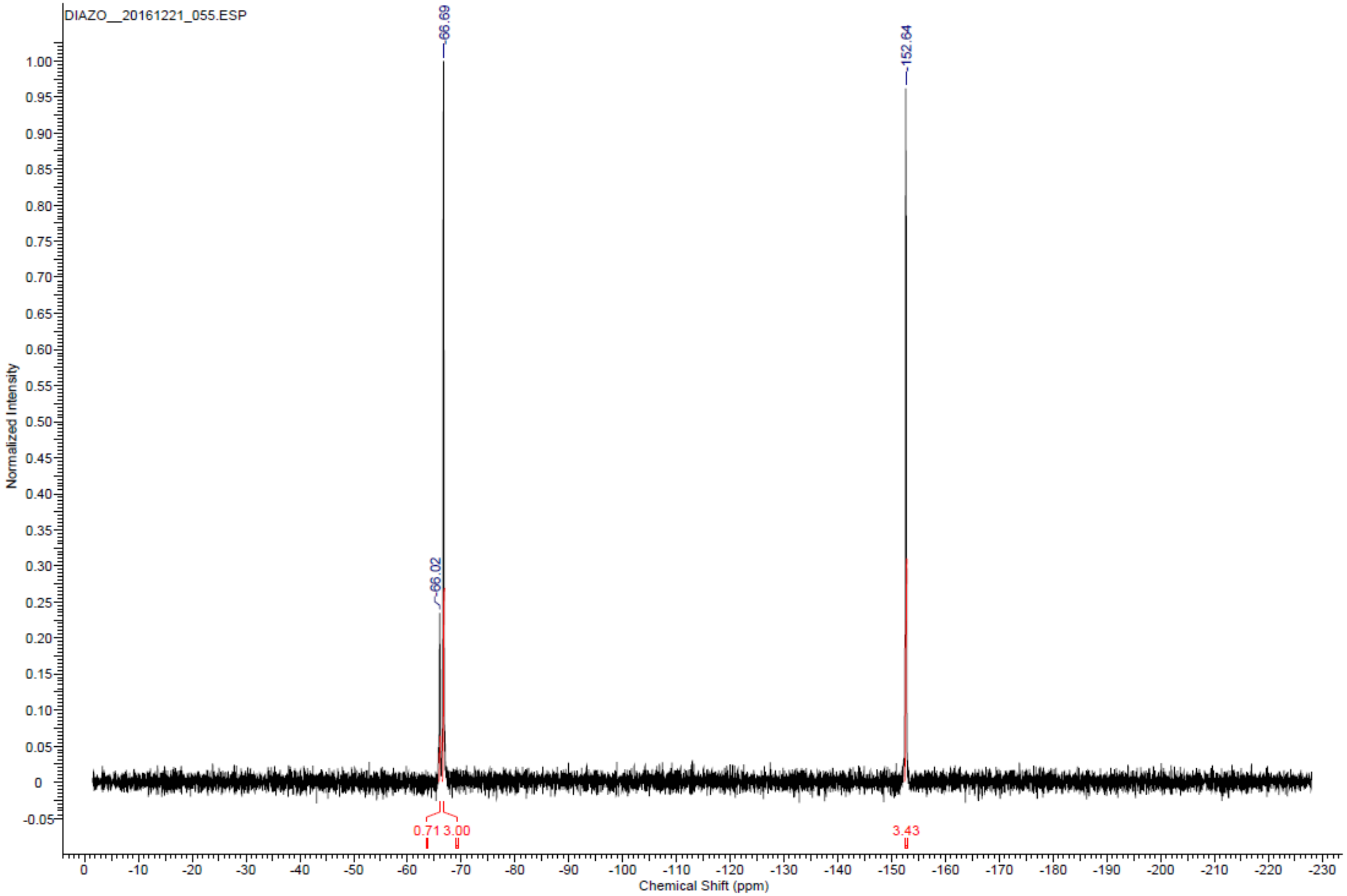

0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0
mali e te it
125.22
124.73
124.25
121.42
120.94
120.45
117.60
117.12
116.65
116.18
115.73
113.78
113.63
113.30
113.18
112.84
112.73
112.32
110.29
109.84
109.37
108.91
125
124
123
122
121
120
119
118
117
116
115
114
113
112
111
110
109
108
Chemical Shift (ppm)

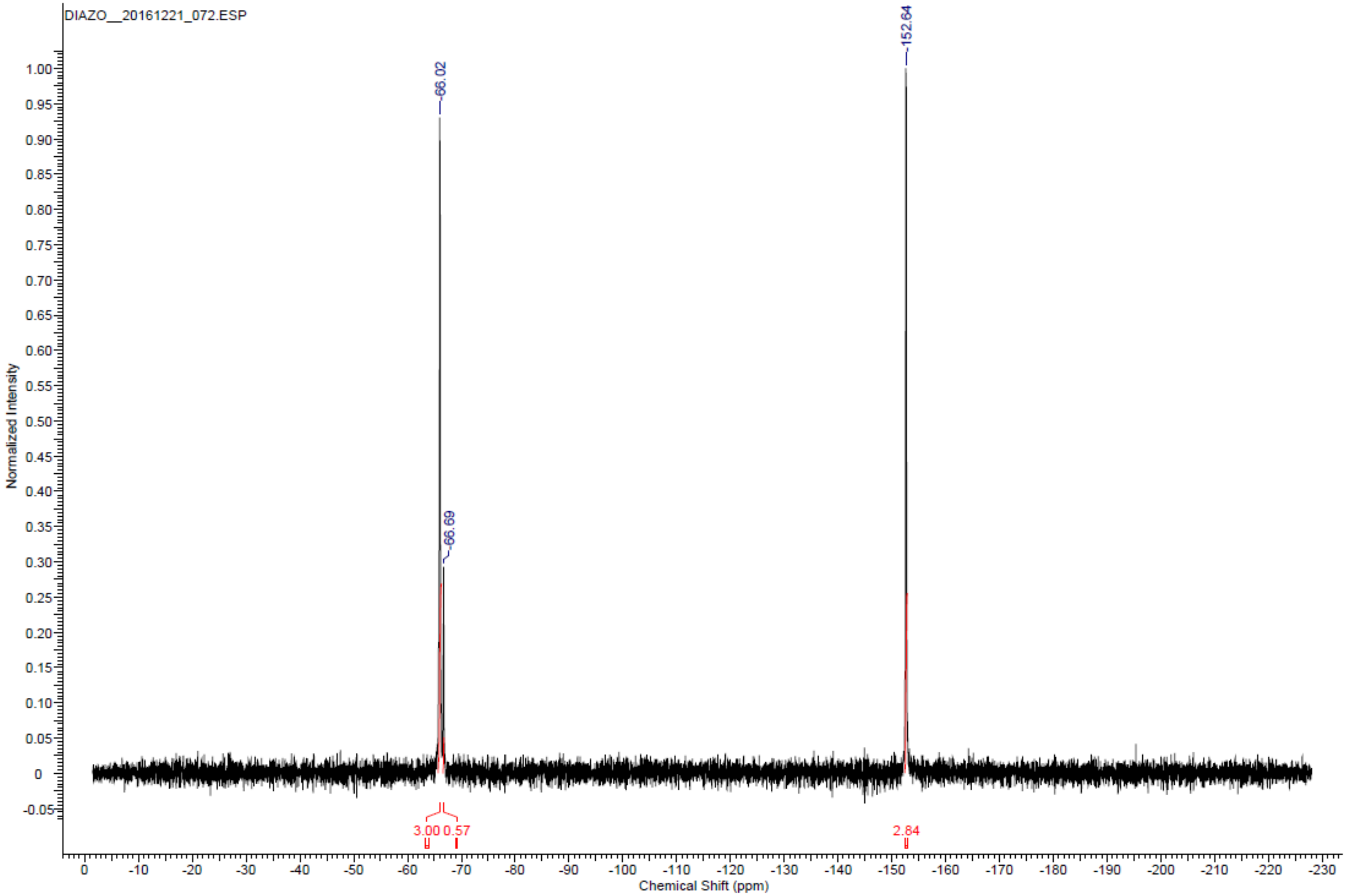
16. ^{19}F NMR spectra of dye-sensitized C-H arylation in continuous-flow



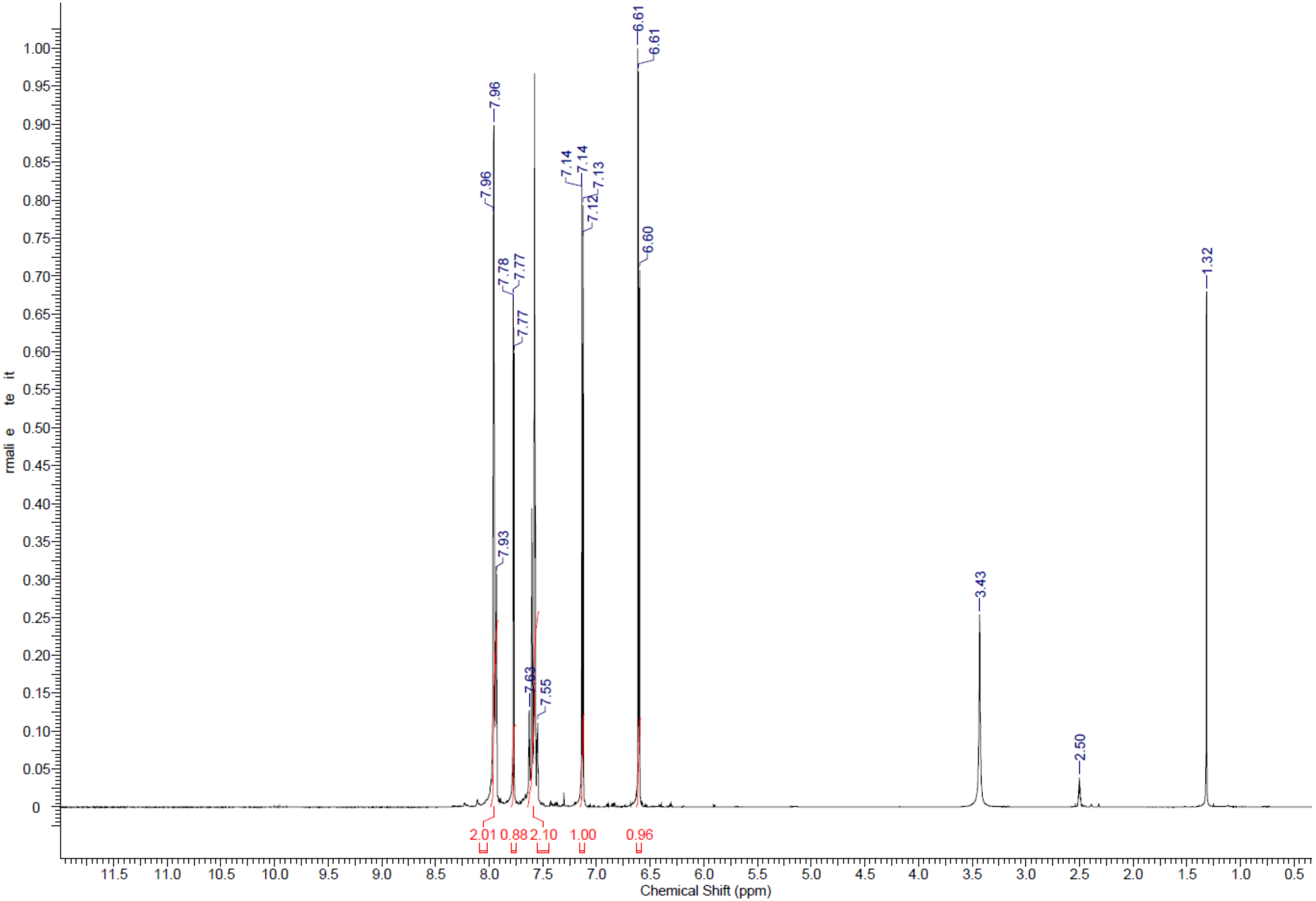

DIAZO__20161221_037.ESP
-66.07
-152.64
3.00
2.58
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

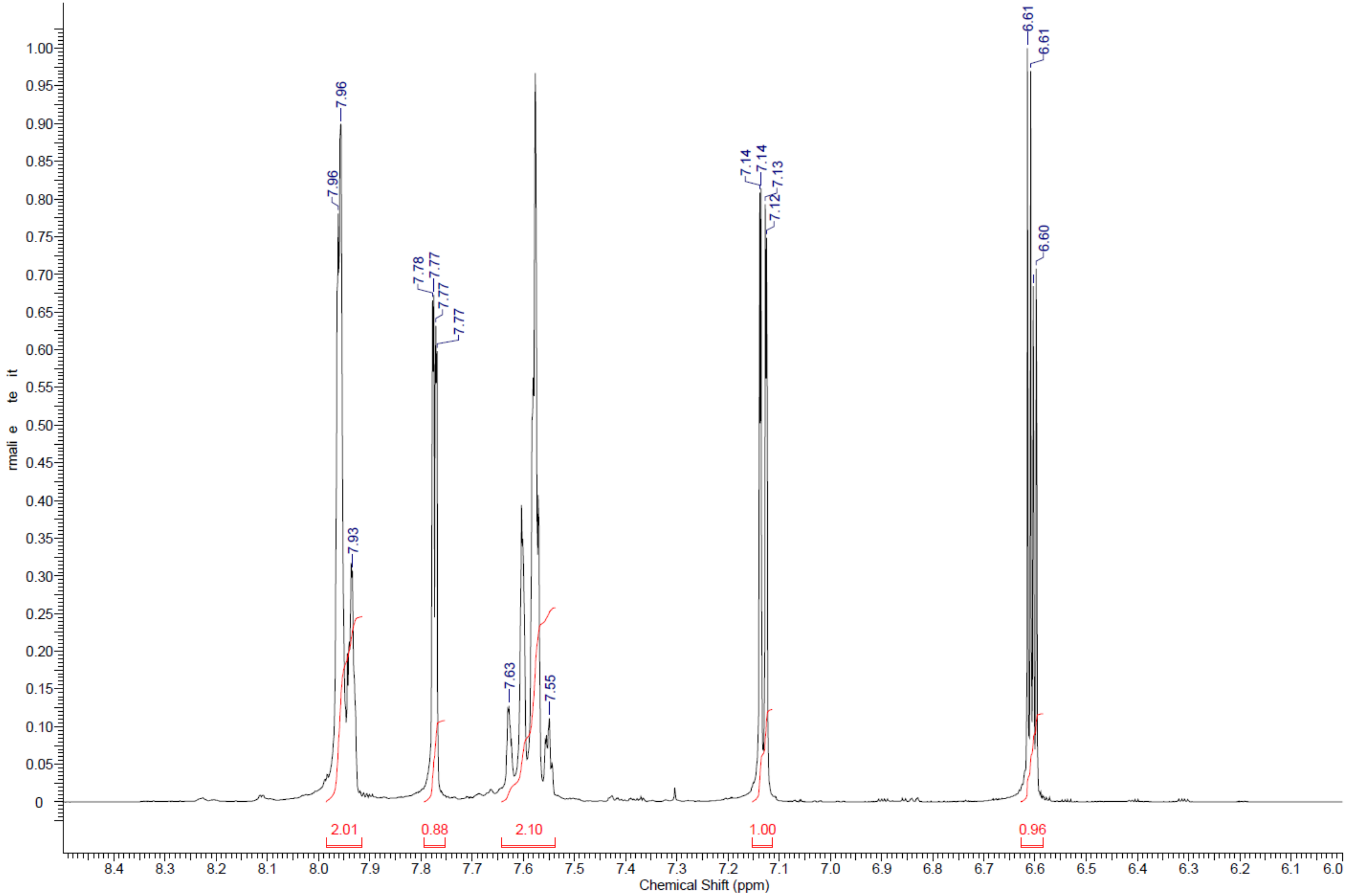

DIAZO__20161221_043.ESP
-66.09
-152.64
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
3.00
2.72
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

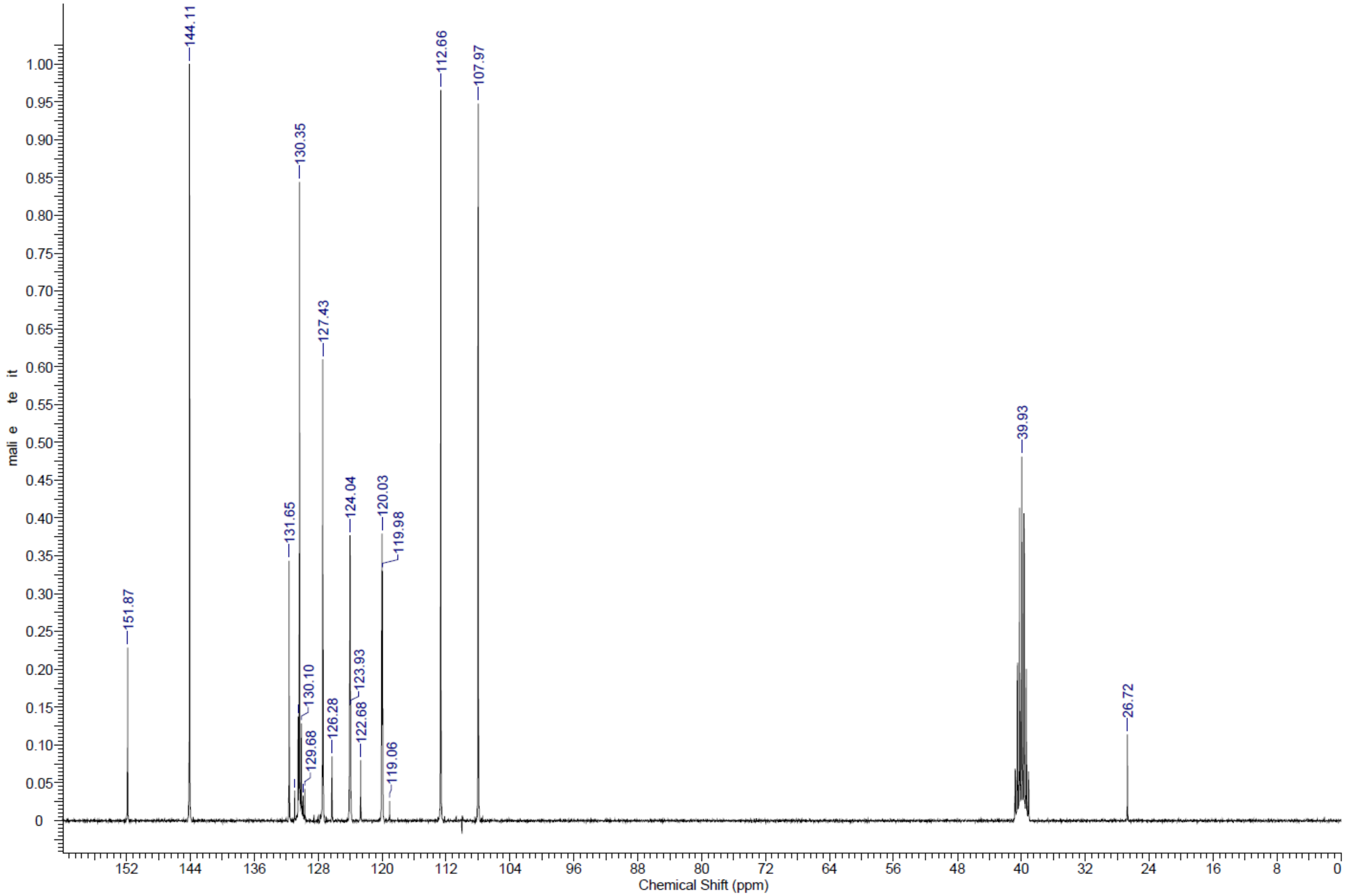

DIAZO__20161221_055.ESP
-66.69
-152.64
-66.02
0.71
3.00
3.43
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

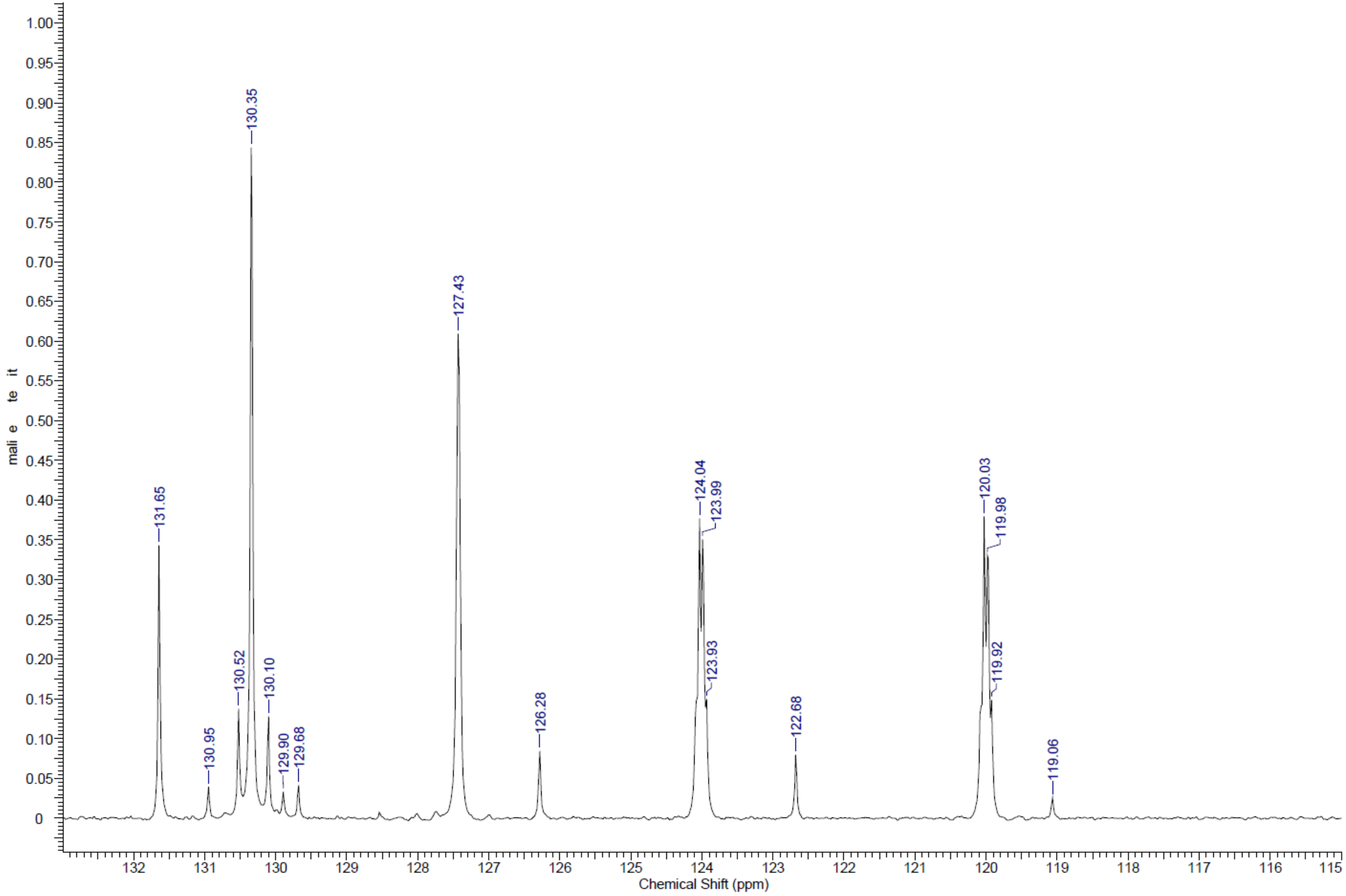

DIAZO__20161221_072.ESP
-66.02
-66.69
-152.64
3.00
0.57
2.84
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
Chemical Shift (ppm)

17. High-resolution ^{1}H / ^{13}C NMR spectrum of purified 7 (DMSO-d$_6$)

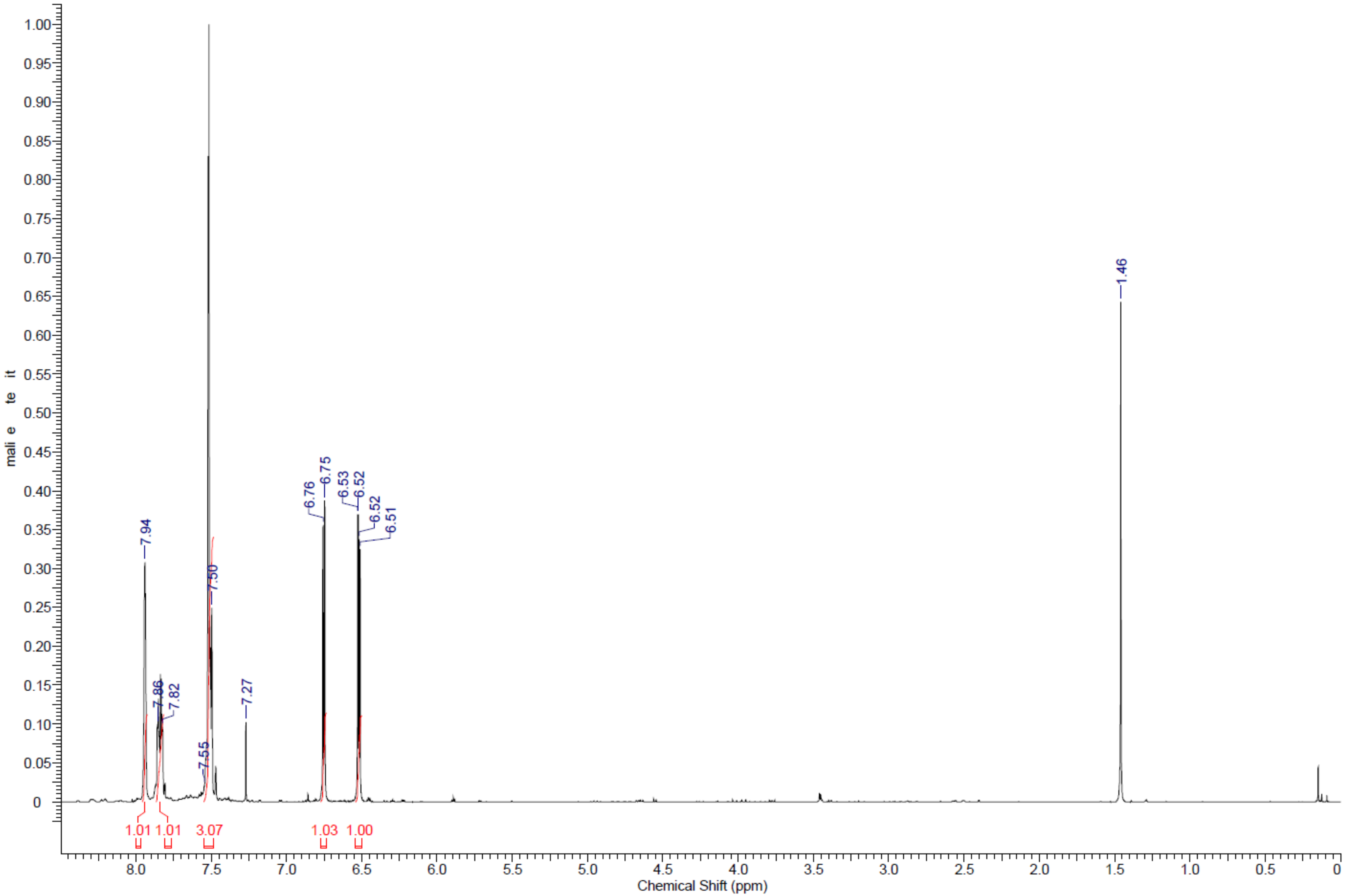


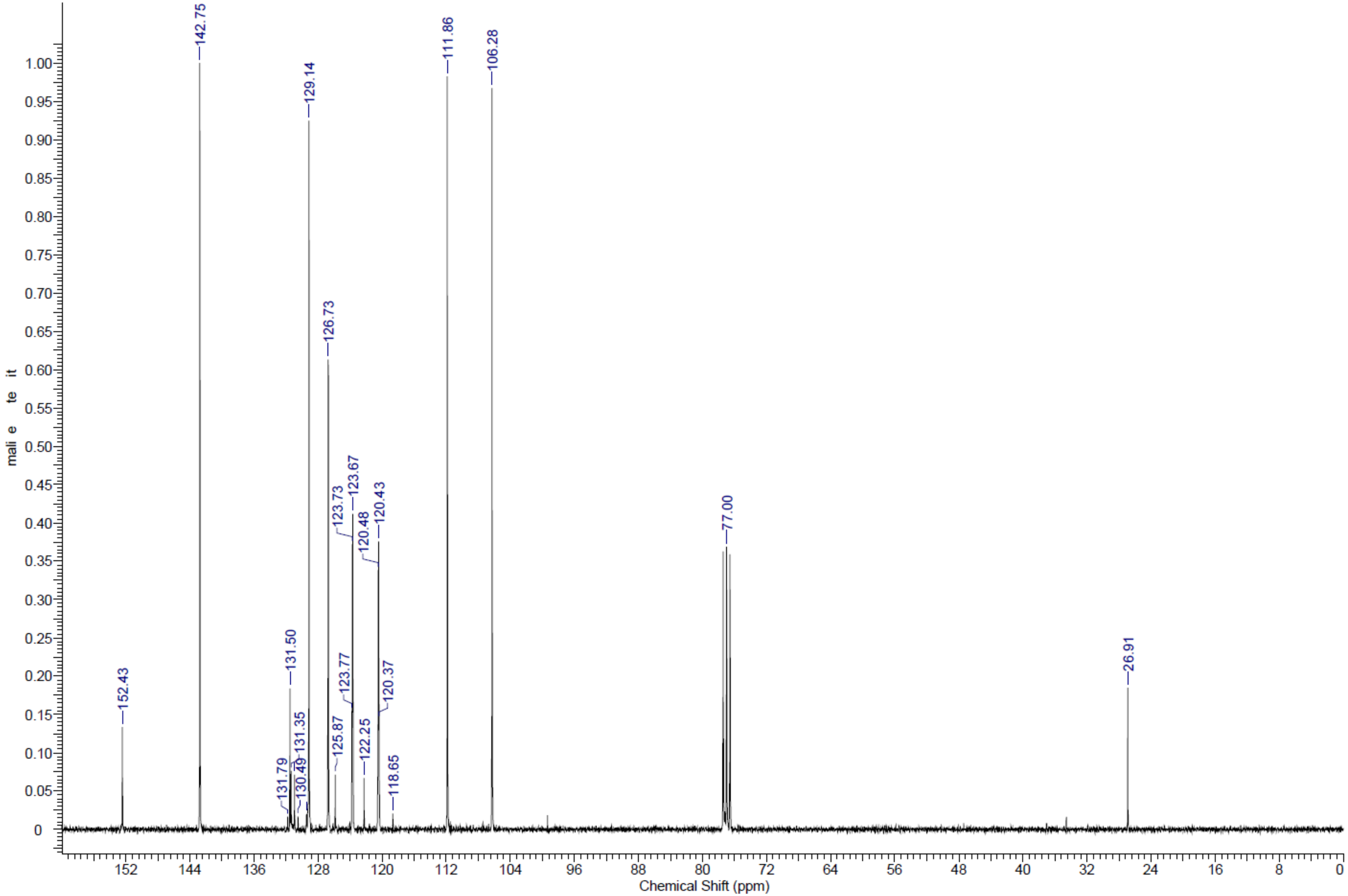

7.96
7.96
7.93
7.78
7.77
7.77
7.77
7.63
7.55
7.14
7.14
7.13
7.12
6.61
6.61
6.60
2.01
0.88
2.10
1.00
0.96
rmali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
6.3
6.2
6.1
6.0
Chemical Shift (ppm)

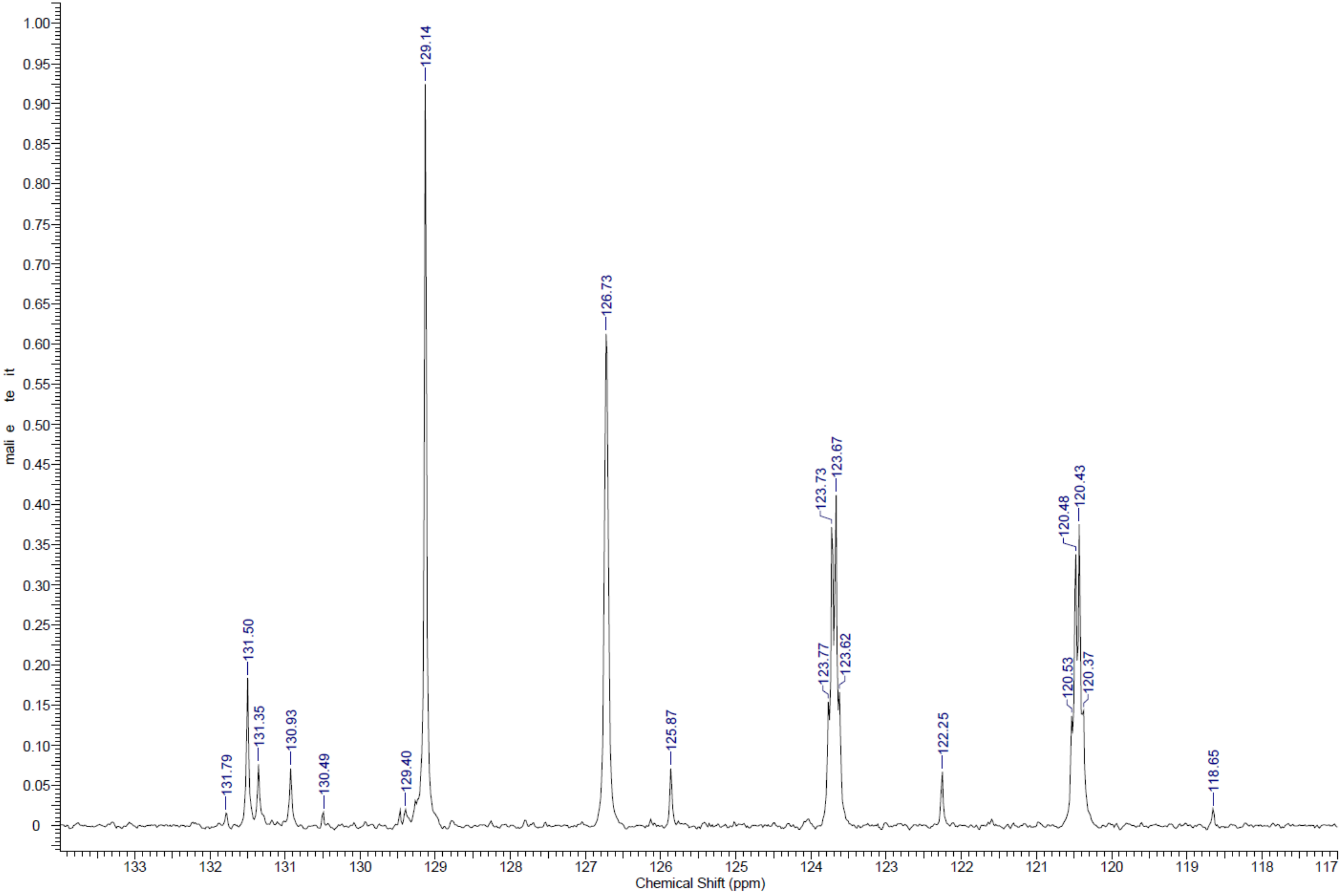

151.87
144.11
131.65
130.35
130.10
129.68
127.43
126.28
124.04
123.93
122.68
120.03
119.98
119.06
112.66
107.97
39.93
26.72
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


131.65
130.95
130.52
130.35
130.10
129.90
129.68
127.43
126.28
124.04
123.99
123.93
122.68
120.03
119.98
119.92
119.06
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
132
131
130
129
128
127
126
125
124
123
122
121
120
119
118
117
116
115
Chemical Shift (ppm)

18. High-resolution ^{1}H NMR spectrum of purified 7 (300 MHz, $CDCl_3$)




152.43
142.75
131.79
131.50
131.35
130.49
129.14
126.73
125.87
123.77
123.73
123.67
122.25
120.48
120.43
120.37
118.65
111.86
106.28
77.00
26.91
mali e te it
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


131.79
131.50
131.35
130.93
130.49
129.40
129.14
126.73
125.87
123.77
123.73
123.67
123.62
122.25
120.53
120.48
120.43
120.37
118.65
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
mali e te it
133
132
131
130
129
128
127
126
125
124
123
122
121
120
119
118
117
Chemical Shift (ppm)

19. References

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