

Characterization of the Synthetic Cannabinoid XLR11 and Fluoroalkyl Analogs

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Part 1:

Data provided by Cayman Chemical Company, including:

Background

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- Figure 2. XLR-11 FTIR
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Part 2:

Data provided by the United States Army Criminal Investigation Laboratory (USACIL), including:

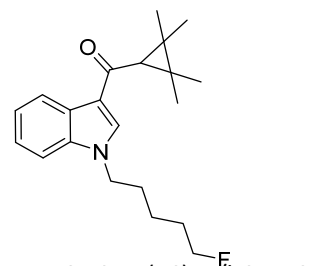
- Figure 17. GC Separation of the fluoroalkyl isomers of XLR-11
- Figure 18. XLR-11 GCMS
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- Figure 20. XLR-11 +ESI-MS
- Figure 21. XLR-11 ATR-FTIR
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References

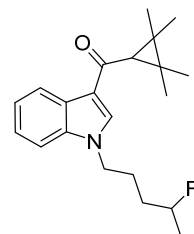
External Links

Compounds

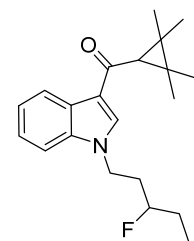
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Formal Name: (1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
Synonyms: 5-fluoro-UR144
CAS Registry No.: 1364933-54-9
MF: C₂₁H₂₈FNO
FW: 329.50
SMILES: O=C(C1C(C)(C)C1(C)C)C2=CN(CCCCCF)C3=CC=CC=C32
InChI Key: PXLDPUUMIHVLEC-UHFFFAOYSA-N
InChI: InChI=1S/C21H28FNO/c1-20(2)19(21(20,3)4)18(24)16-14-23(13-9-5-8-12-22)17-11-7-6-10-15(16)17/h6-7,10-11,14,19H,5,8-9,12-13H2,1-4H3



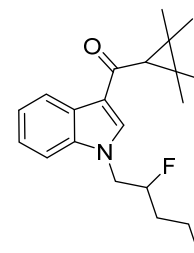
Name: XLR11-N-(4-fluoropentyl) isomer
Formal Name: (1-(4-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
Synonyms: 4-fluoro-UR144
CAS Registry No.: N/A
MF: C₂₁H₂₈FNO
FW: 329.50
SMILES: O=C(C1=CN(C2=CC=CC=C21)CCCC(F)C)C3C(C)(C3(C)C)C
InChI Key: ROEZBBZNFJXHOC-UHFFFAOYSA-N
InChI: InChI=1S/C21H28FNO/c1-14(22)9-8-12-23-13-16(15-10-6-7-11-17(15)23)18(24)19-20(2,3)21(19,4)5/h6-7,10-11,13-14,19H,8-9,12H2,1-5H3



Name: XLR11-N-(3-fluoropentyl) isomer
Formal Name: (1-(3-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
Synonyms: 3-fluoro-UR144
CAS Registry No.: N/A
MF: C₂₁H₂₈FNO
FW: 329.50
SMILES: O=C(C1=CN(C2=CC=CC=C21)CCC(F)CC)C3C(C)(C3(C)C)C
InChI Key: FAFWRNLRDMHCOR-UHFFFAOYSA-N
InChI: InChI=1S/C21H28FNO/c1-6-14(22)11-12-23-13-16(15-9-7-8-10-17(15)23)18(24)19-20(2,3)21(19,4)5/h7-10,13-14,19H,6,11-12H2,1-5H3



Name: XLR11-N-(2-fluoropentyl) isomer
Formal Name: (1-(2-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
Synonyms: 2-fluoro-UR144
CAS Registry No.: N/A
MF: C₂₁H₂₈FNO
FW: 329.50
SMILES: O=C(C1=CN(C2=CC=CC=C21)CC(F)CCC)C3C(C)(C3(C)C)C
InChI Key: QWKOFFDPSCMXAL-UHFFFAOYSA-N
InChI: InChI=1S/C21H28FNO/c1-6-9-14(22)12-23-13-16(15-10-7-8-11-17(15)23)18(24)19-20(2,3)21(19,4)5/h7-8,10-11,13-14,19H,6,9,12H2,1-5H3



Background

XLR11 is tetramethylcyclopropylethanoyl indole analog of AM2201 which is a known abused synthetic cannabinoid^{1,2} and specifically listed in the Synthetic Drug Abuse Prevention Act of 2012.³ It is related to UR-144 and other structurally similar compounds described in a patent from Abbott Laboratories⁴ which had been originally developed as CB2 receptor ligands for the treatment of pain. A recent epidemiological report associates acute kidney injury with XLR-11 exposure.⁵ The fluoroalkyl analogs of XLR11 are also expected to have similar biological activity to XLR11 and may be substituted to evade detection in crime labs.

Operator : PDK
Acquired : 10 Apr 2012 10:25 using AcqMethod CAY_DRUG_CATH.M
Instrument : Instrument #1
Sample Name: XLR11
Misc Info : 30mx0.32mm, 0.5u Rtx-5MS, 50C-30C/min-300C
Vial Number: 4

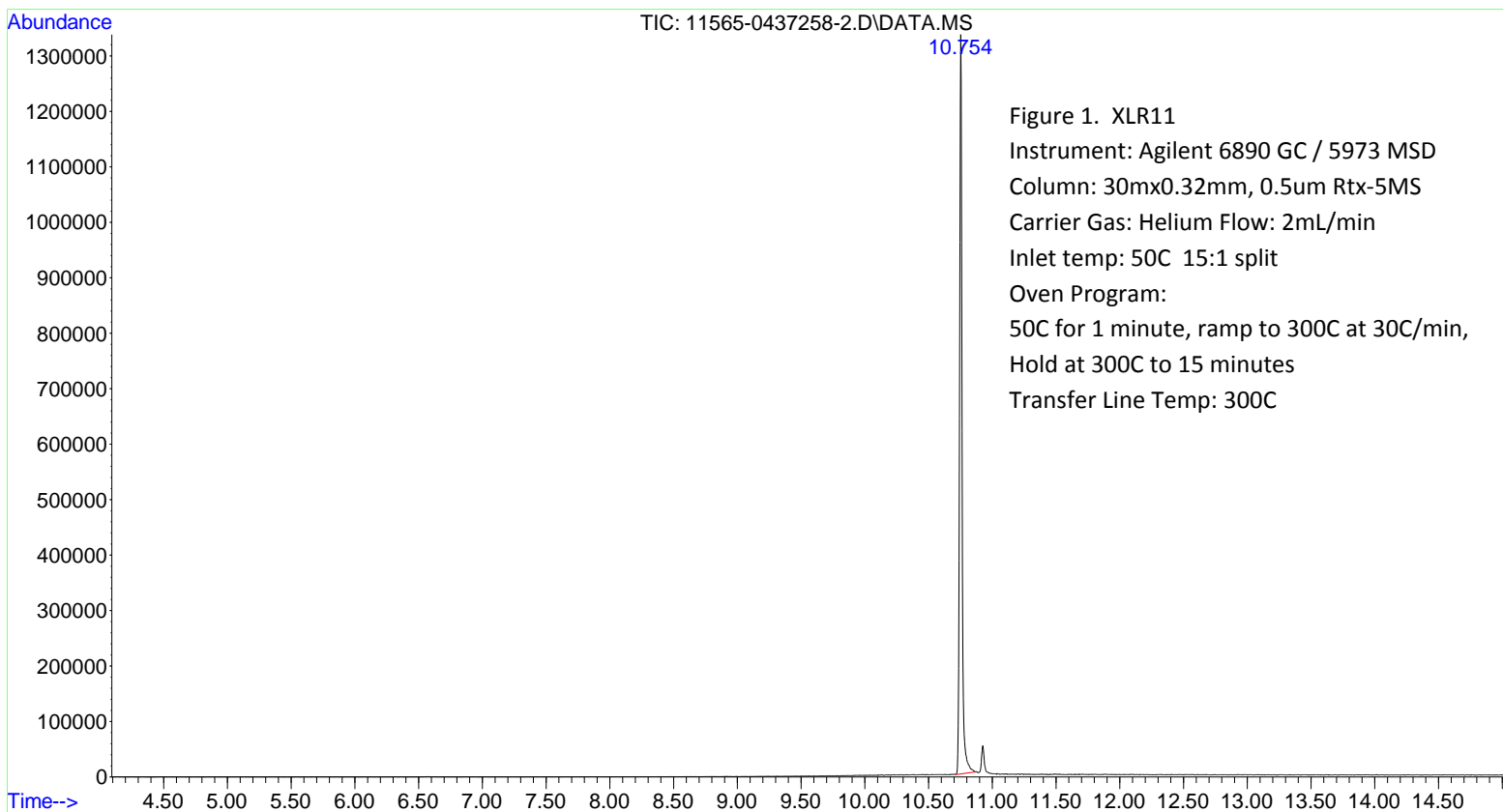
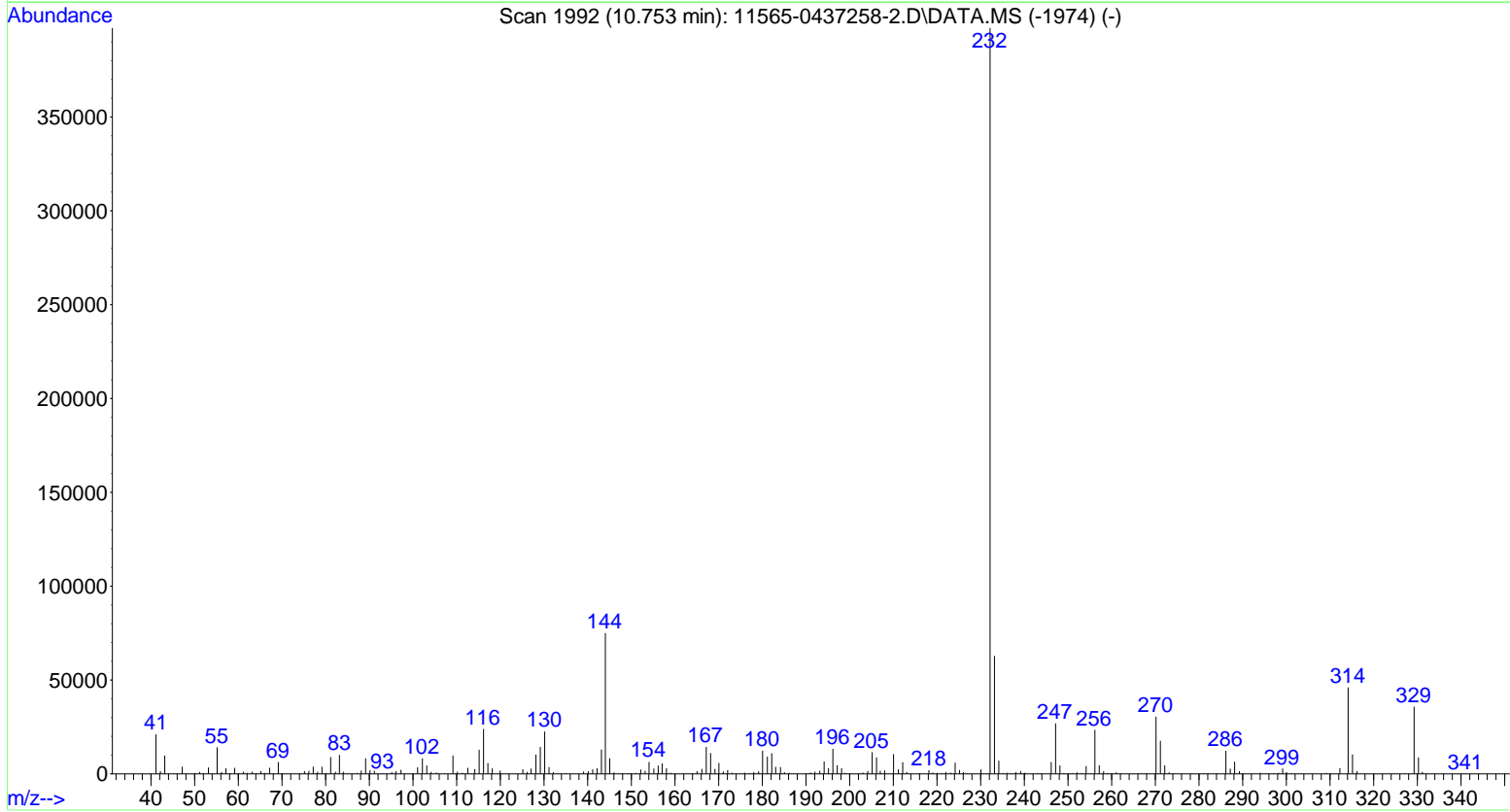


Figure 1. XLR11
Instrument: Agilent 6890 GC / 5973 MSD
Column: 30mx0.32mm, 0.5um Rtx-5MS
Carrier Gas: Helium Flow: 2mL/min
Inlet temp: 50C 15:1 split
Oven Program:
50C for 1 minute, ramp to 300C at 30C/min,
Hold at 300C to 15 minutes
Transfer Line Temp: 300C



PerkinElmer Spectrum Version 10.03.02
Tuesday, April 03, 2012 3:24 PM

Administrator
Tuesday, April 03, 2012 3:24 PM

Analyst
Date

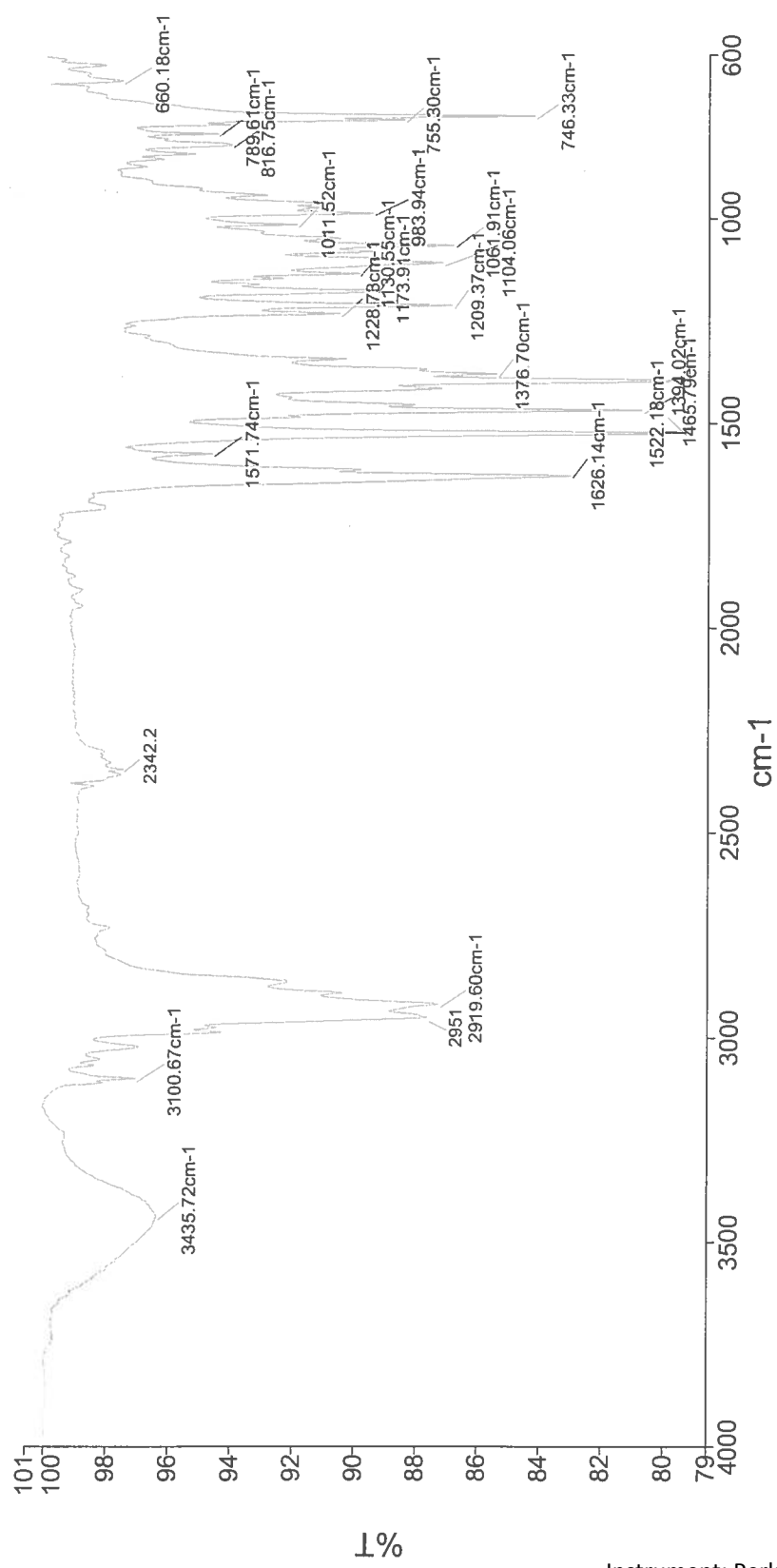


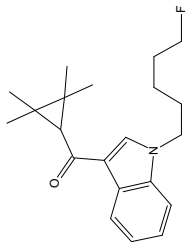
Figure 2
XLR11

QC04378_1_1 XLR11; Cat# 11565; QC04378; pellet

Instrument: Perkin Elmer Spectrum 65
4500 - 650 cm-1
resolution 4cm-1
16 scans
Sample Preparation: KBr pellet



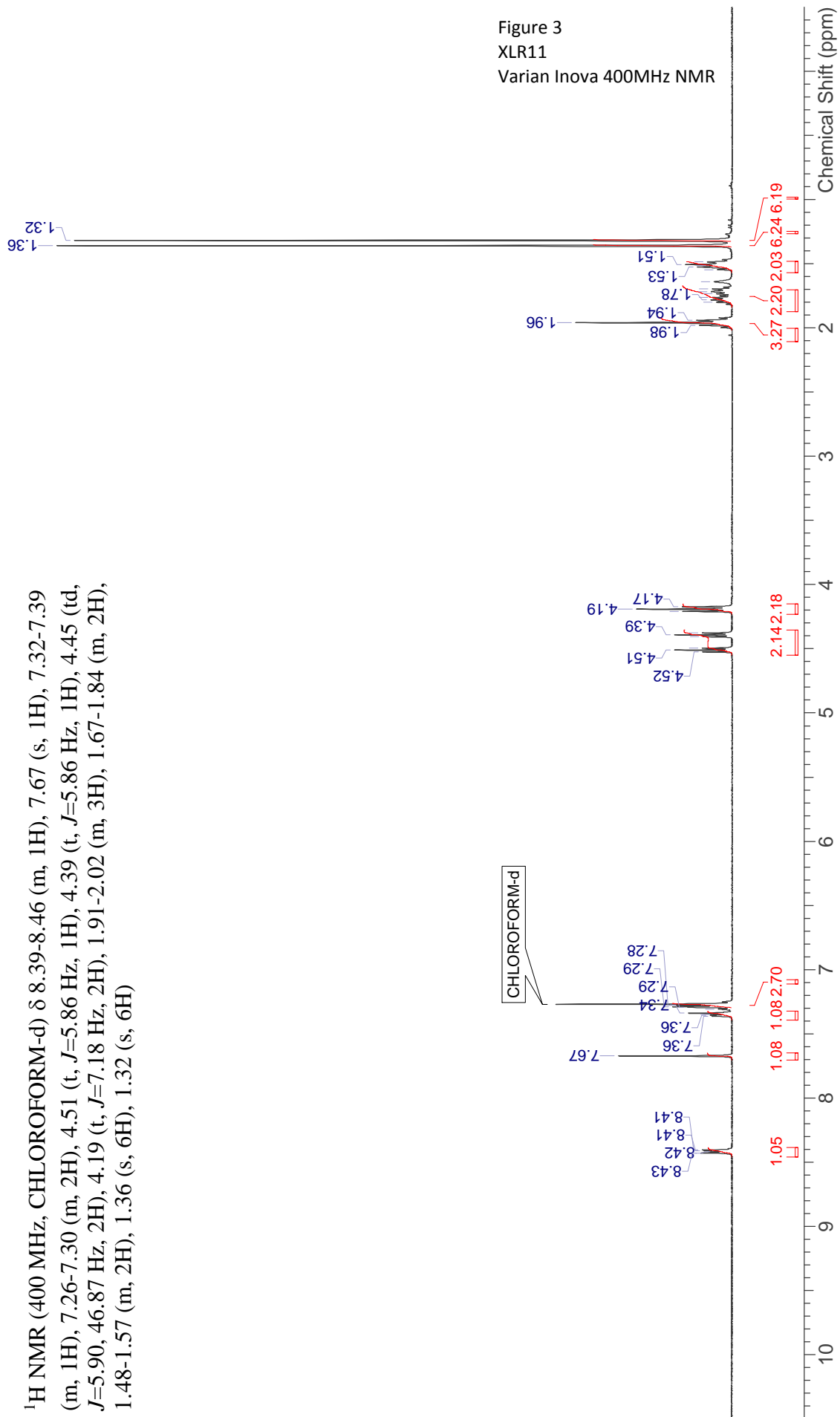
XLR11
Item #11565
Batch #0437258

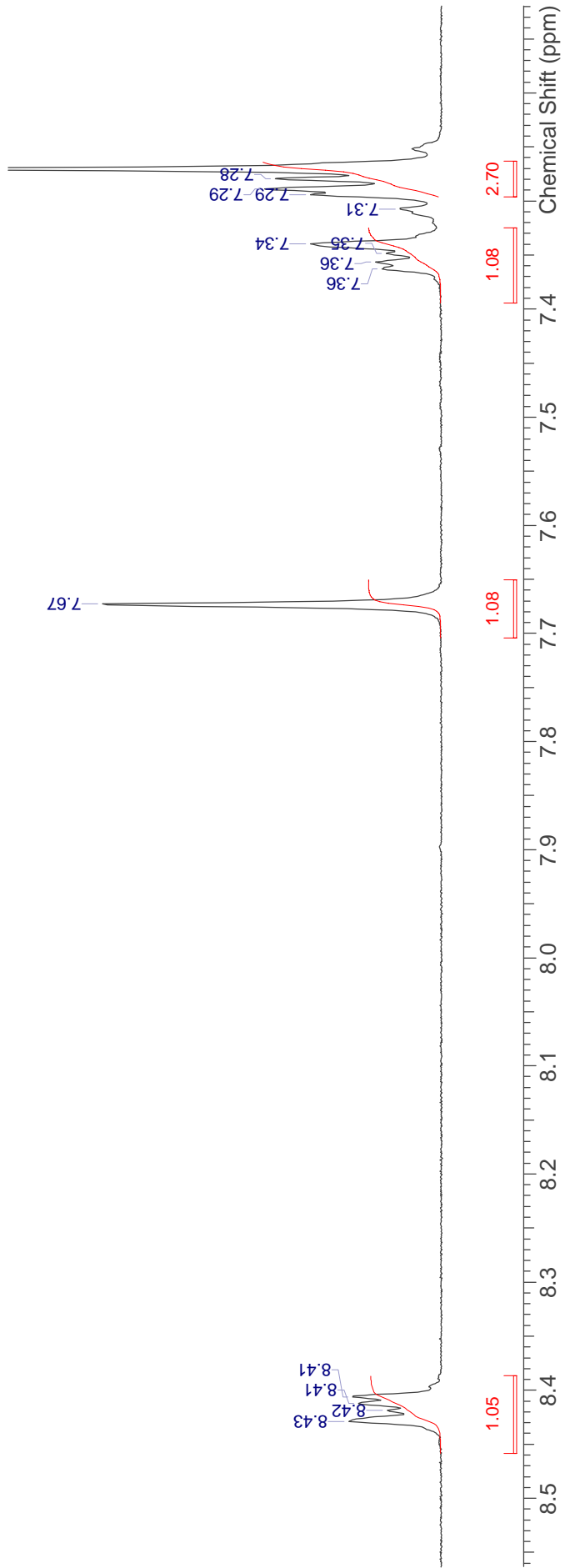


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Date	Mar 30 2012	Nucleus	1H
Solvent	CHLOROFORM-d	Comment	RMS-1088-115
		Frequency (MHz)	399.97
		Number of Transients	64

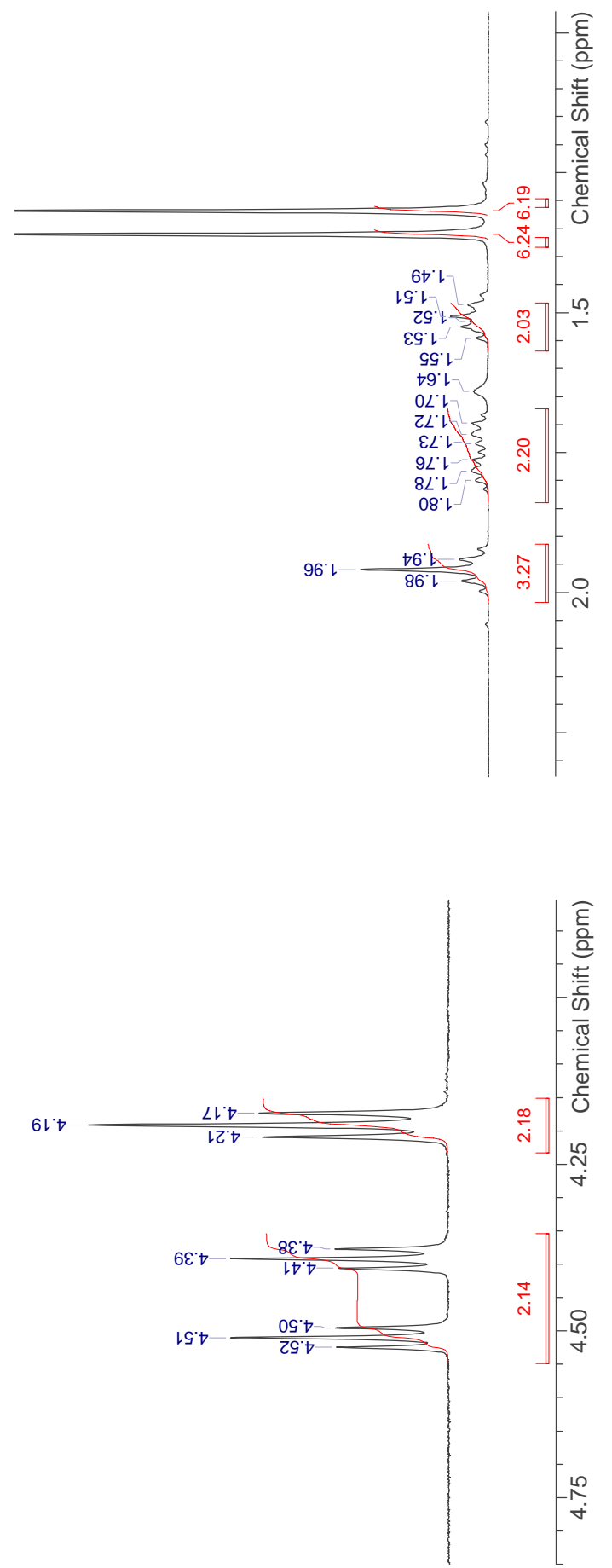
¹H NMR (400 MHz, CHLOROFORM-d) δ 8.39-8.46 (m, 1H), 7.67 (s, 1H), 7.32-7.39 (m, 1H), 7.26-7.30 (m, 2H), 4.51 (t, *J*=5.86 Hz, 1H), 4.39 (t, *J*=5.86 Hz, 1H), 4.45 (td, *J*=5.90, 46.87 Hz, 2H), 4.19 (t, *J*=7.18 Hz, 2H), 1.91-2.02 (m, 3H), 1.67-1.84 (m, 2H), 1.48-1.57 (m, 2H), 1.36 (s, 6H), 1.32 (s, 6H)

Figure 3
 XLR11
 Varian Inova 400MHz NMR





6/29



05/14/13

XLR11

4/3/2012 2:23:37 PM

C:\MassSpecData\2012\11565_QC04378
NUTRALAPCIPOSHIFLO

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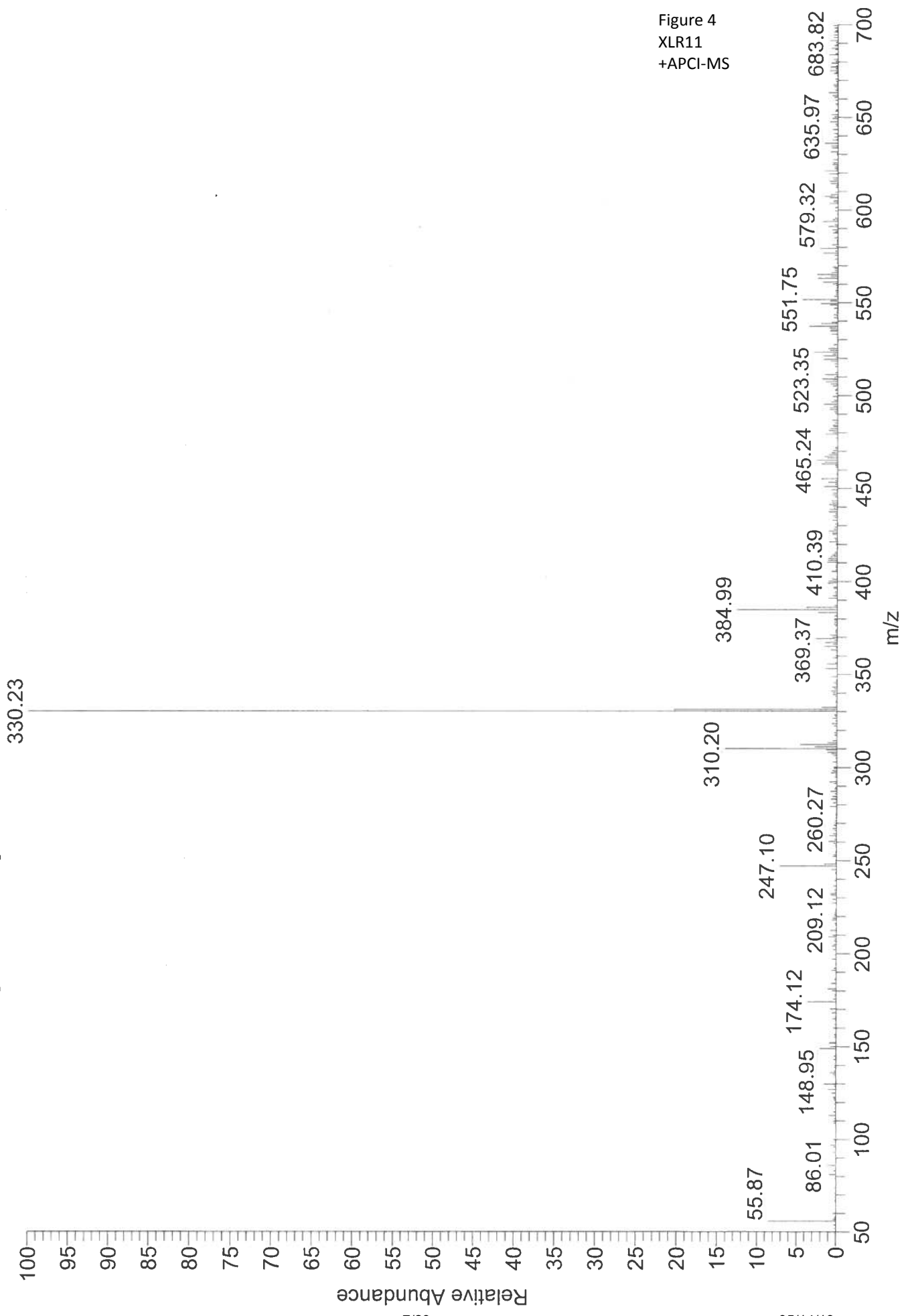


Figure 4
XLR11
+APCI-MS

Operator : PDK
Acquired : 17 Sep 2012 15:20 using AcqMethod CAY_DRUG_CATH.M
Instrument : Instrument #1
Sample Name: XLR11 N-(4-fluoropentyl) isomer
Misc Info : 30mx0.32mm, 0.5u Rtx-5MS, 50C-30C/min-300C
Vial Number: 3

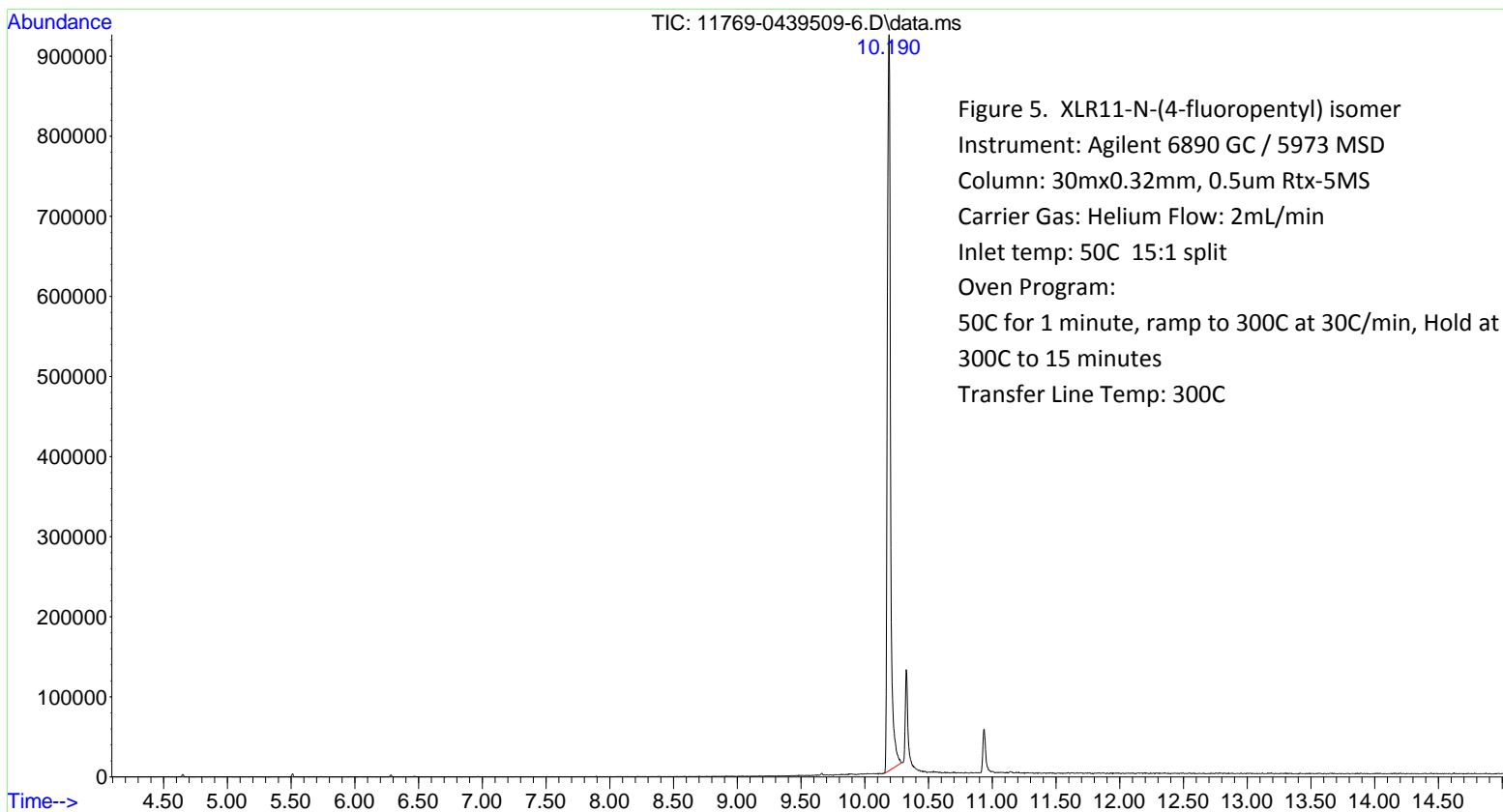


Figure 5. XLR11-N-(4-fluoropentyl) isomer
Instrument: Agilent 6890 GC / 5973 MSD
Column: 30mx0.32mm, 0.5um Rtx-5MS
Carrier Gas: Helium Flow: 2mL/min
Inlet temp: 50C 15:1 split
Oven Program:
50C for 1 minute, ramp to 300C at 30C/min, Hold at 300C to 15 minutes
Transfer Line Temp: 300C

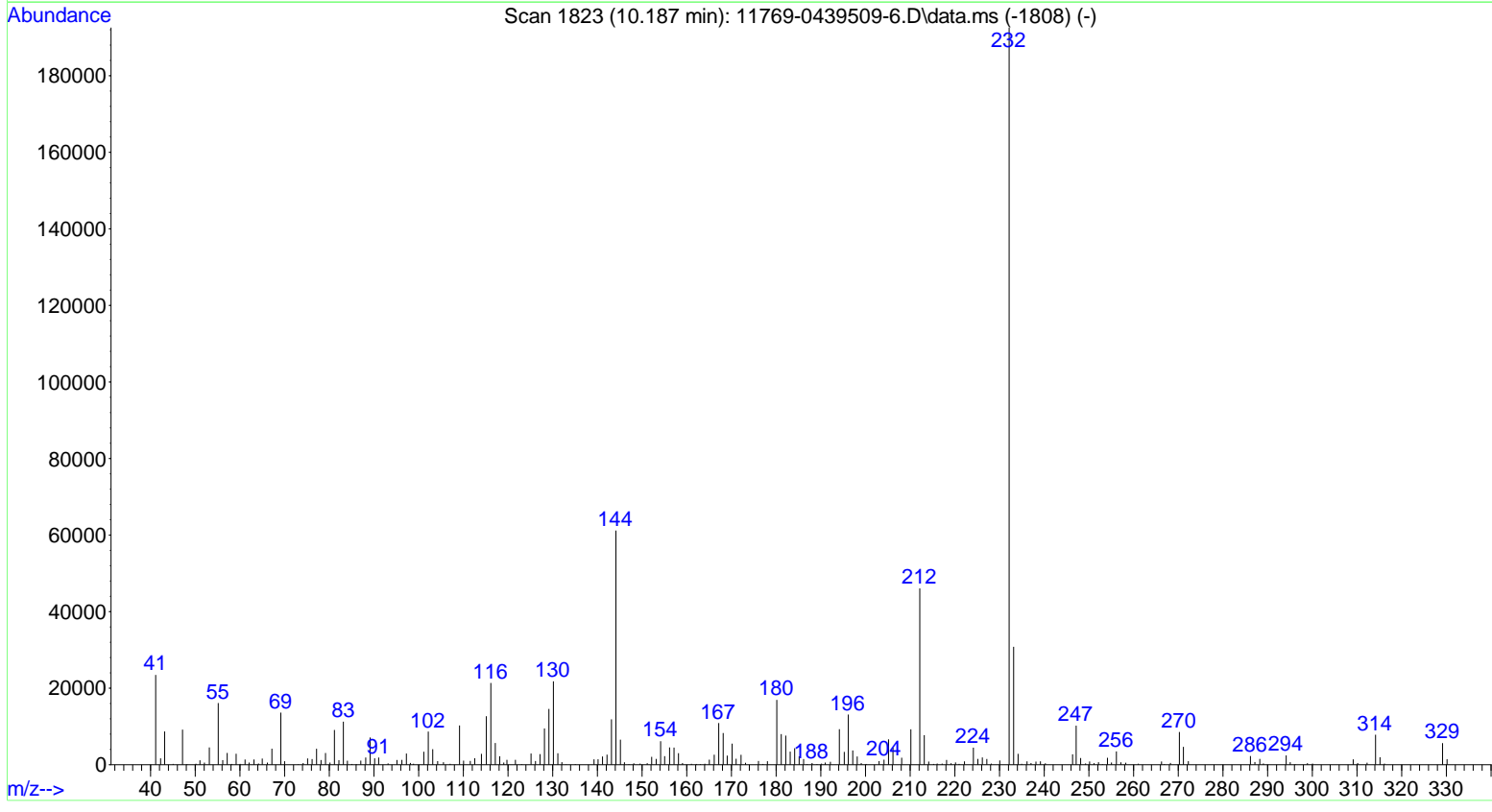
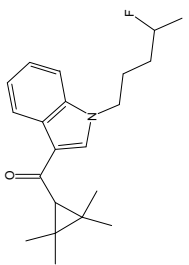
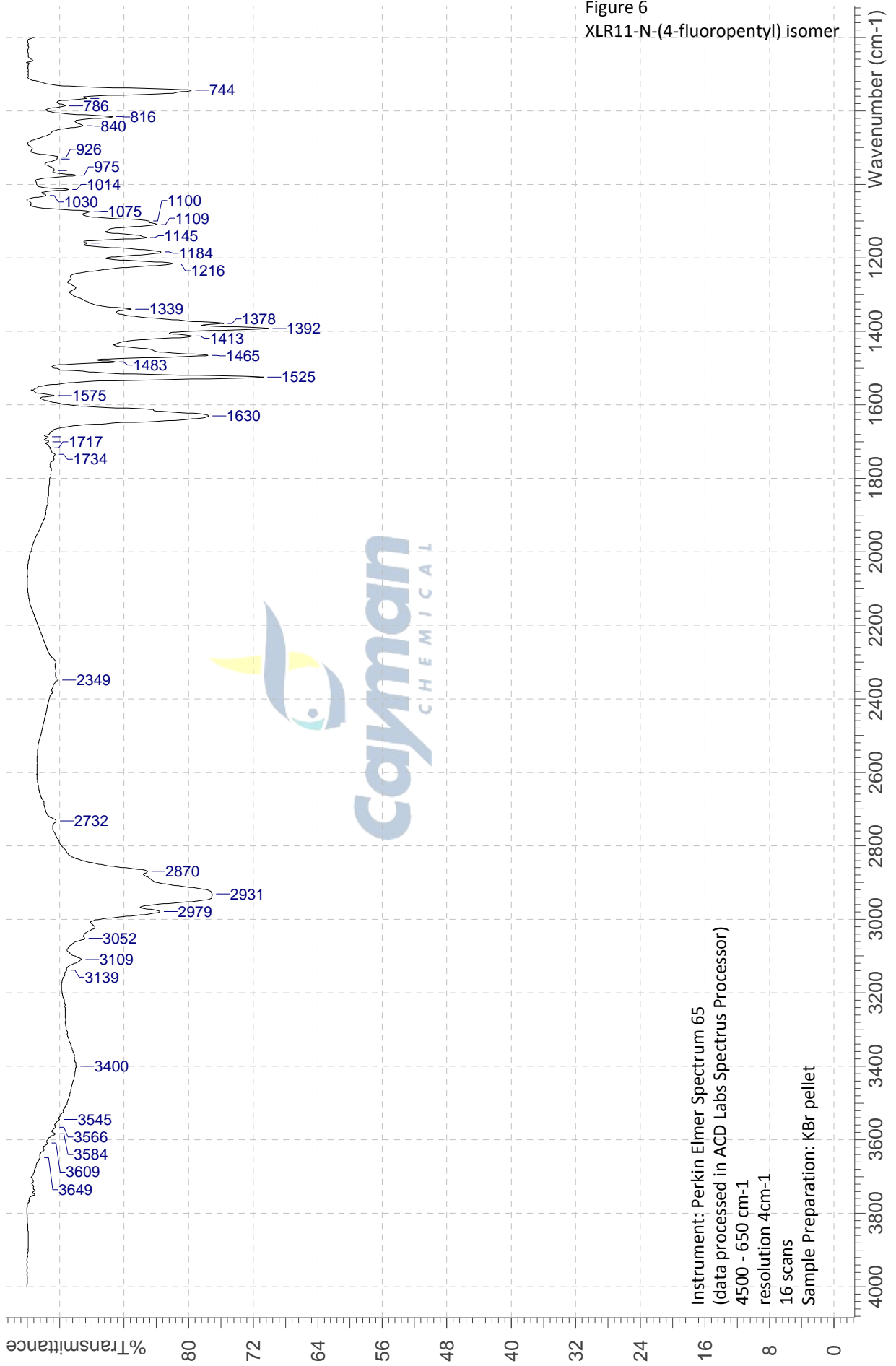


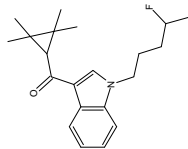
Figure 6
XLR11-N-(4-fluoropentyl) isomer



XLR11 N-(4-fluoropentyl) isomer
Item # 11769
Lot # 0439509



Instrument: Perkin Elmer Spectrum 65
(data processed in ACD Labs Spectrus Processor)
4500 - 650 cm-1
resolution 4cm-1
16 scans
Sample Preparation: KBr pellet



XLR11 N-(4-fluoropentyl) isomer

Item #11769

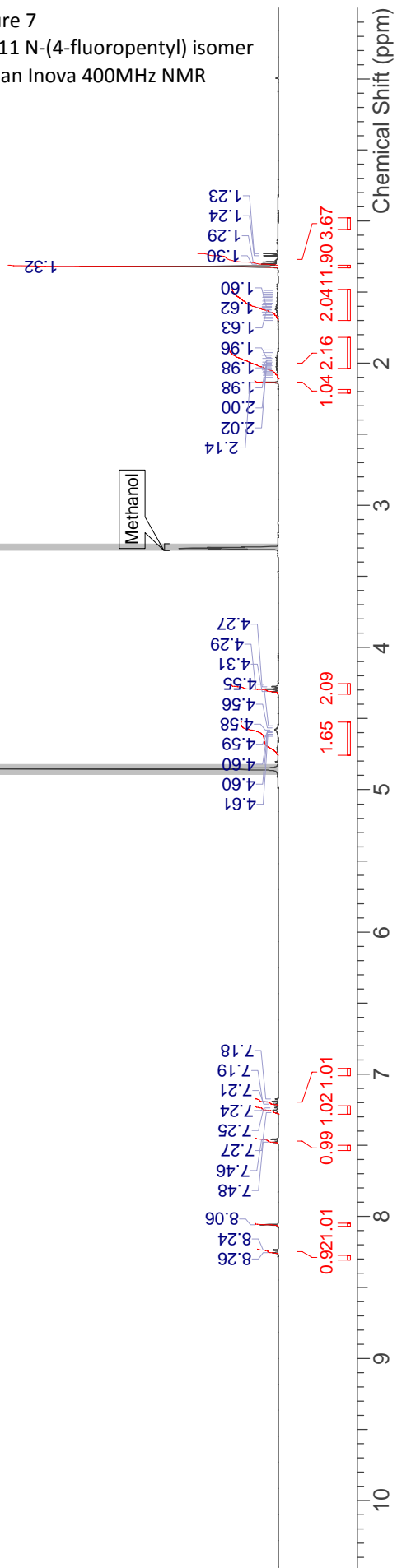
Batch #0439509

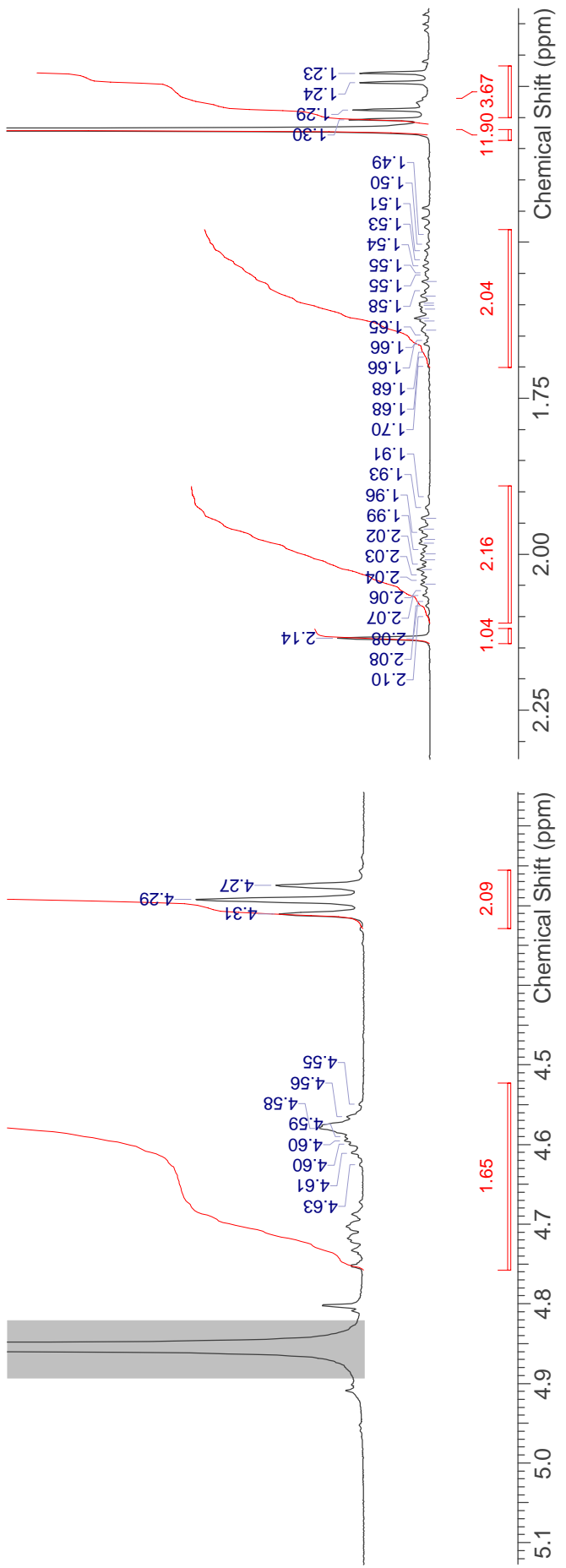


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Solvent	METHANOL-d4	Comment XLR11 N-(4-fluoropentyl) isomer Item 11769 Batch 0439509
Number of Transients	512	

¹H NMR (400 MHz, METHANOL-d₄) δ 8.25 (d, J=7.32 Hz, 1H), 8.06 (s, 2H), 7.47 (d, J=7.90 Hz, 1H), 7.26 (dd, J=7.30 Hz, 1H), 7.19 (dd, J=7.30, 7.90 Hz, 1H), 4.52-4.76 (m, 1H), 4.29 (t, J=7.14 Hz, 2H), 2.14 (s, 1H), 1.89-2.11 (m, 2H), 1.48-1.70 (m, 2H), 1.32 (s, 12H), 1.23-1.31 (m, 3H)

Figure 7
XLR11 N-(4-fluoropentyl) isomer
Varian Inova 400MHz NMR





XLR11 N-(4-fluoropentyl) isomer

6/21/2012 2:15:44 PM

C:\MassSpecData\2012\11769_QC04798
Nutralapciphiflo

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T: ITMS + c APCI corona Full ms [65.00-600.00]

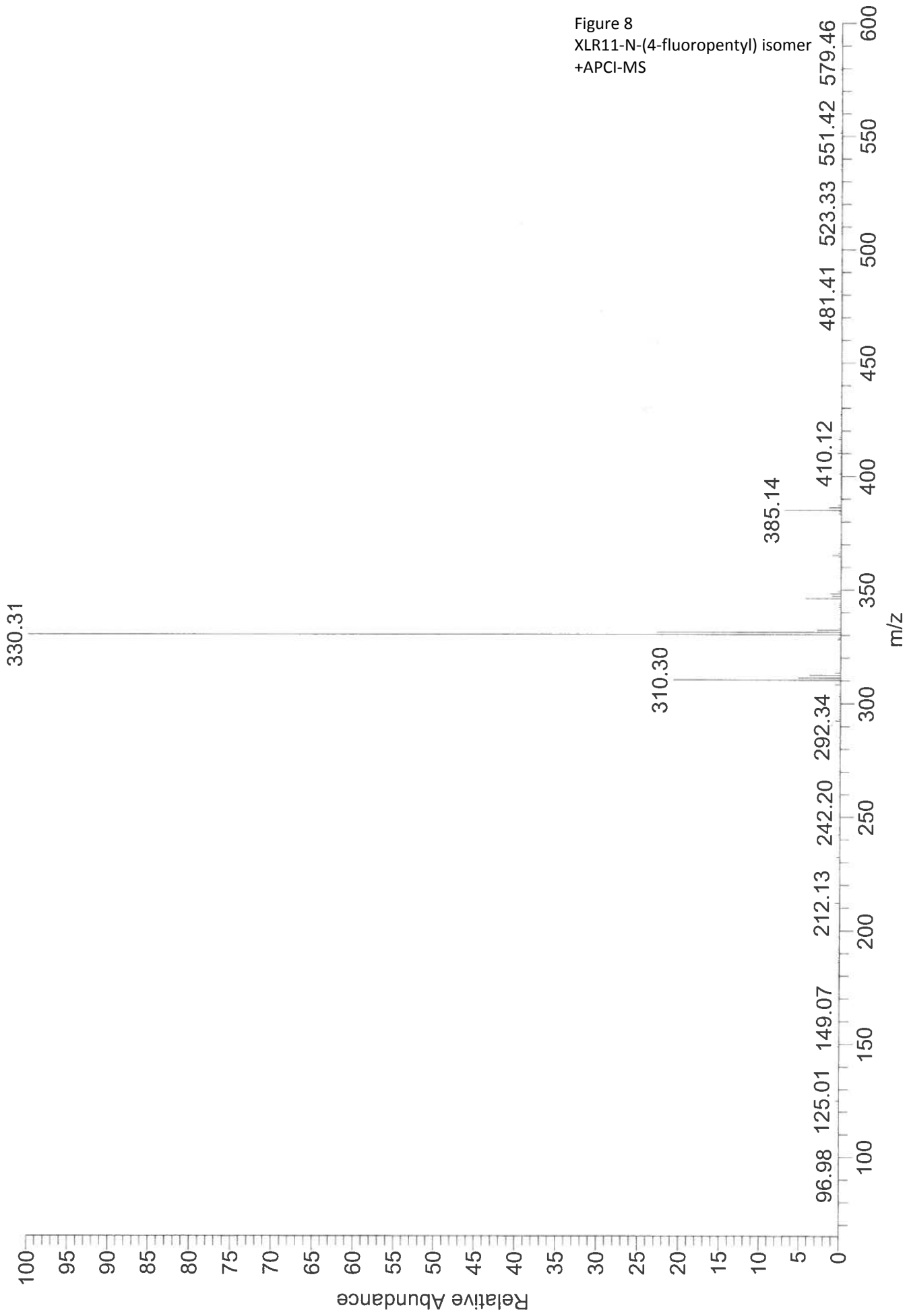


Figure 8
XLR11-N-(4-fluoropentyl) isomer
+APCI-MS

Operator : PDK
Acquired : 20 Aug 2012 14:55 using AcqMethod CAY_DRUG_CATH.M
Instrument : Instrument #1
Sample Name: XLR11 N-(3-fluoropentyl) isomer
Misc Info : 30mx0.32mm, 0.5u Rtx-5MS, 50C-30C/min-300C
Vial Number: 7

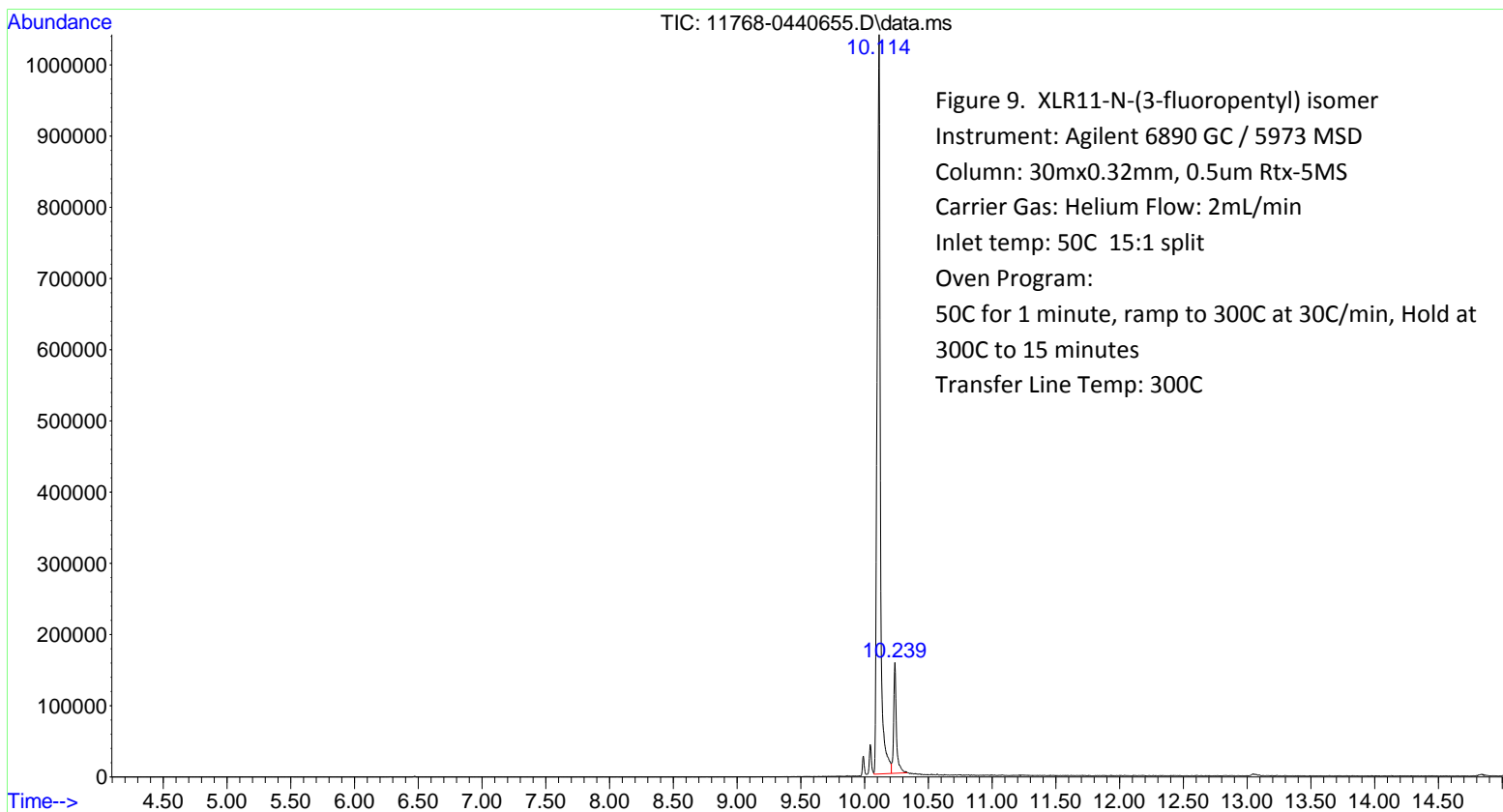
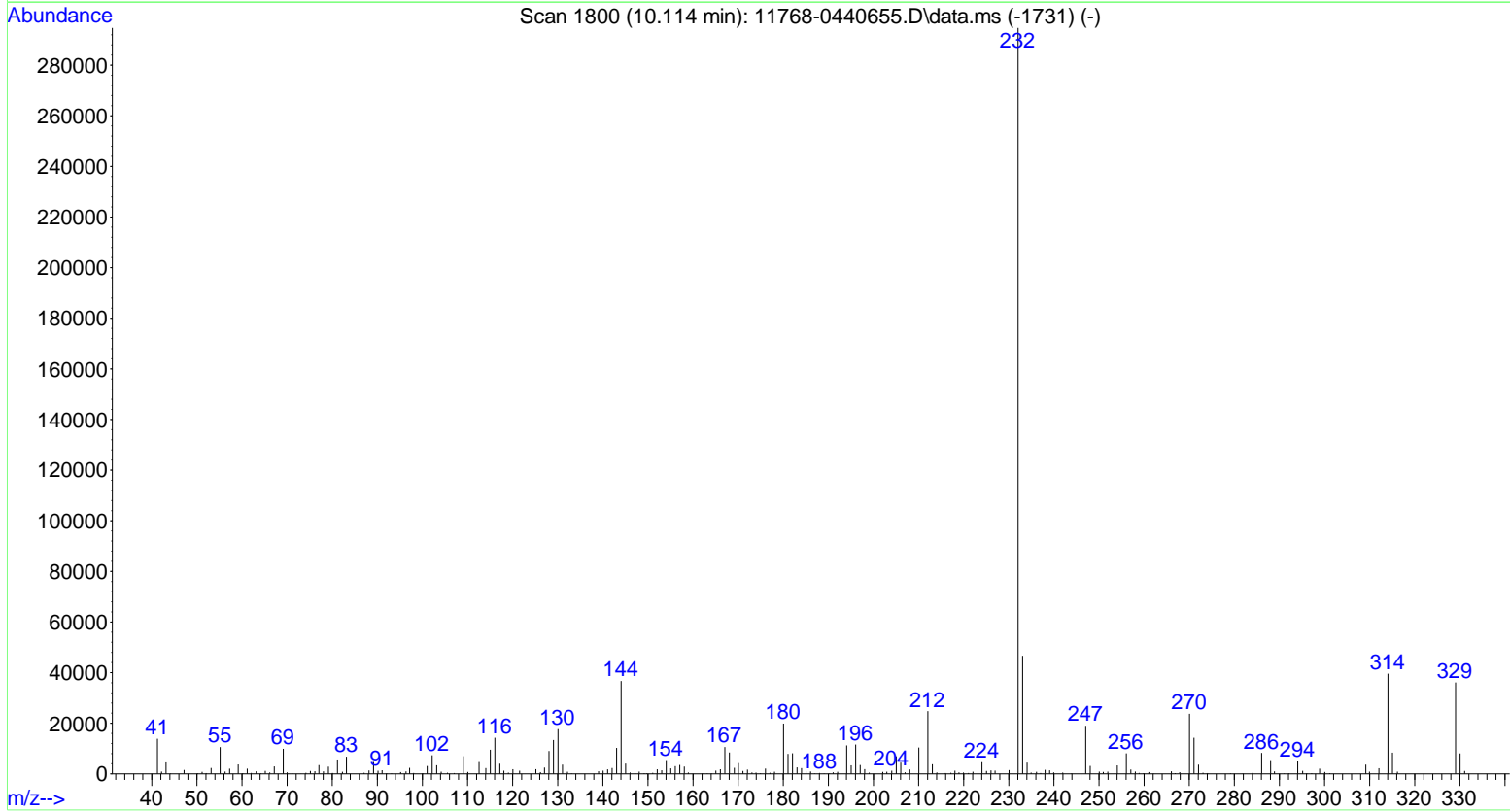
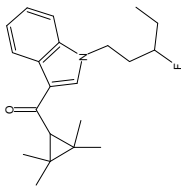


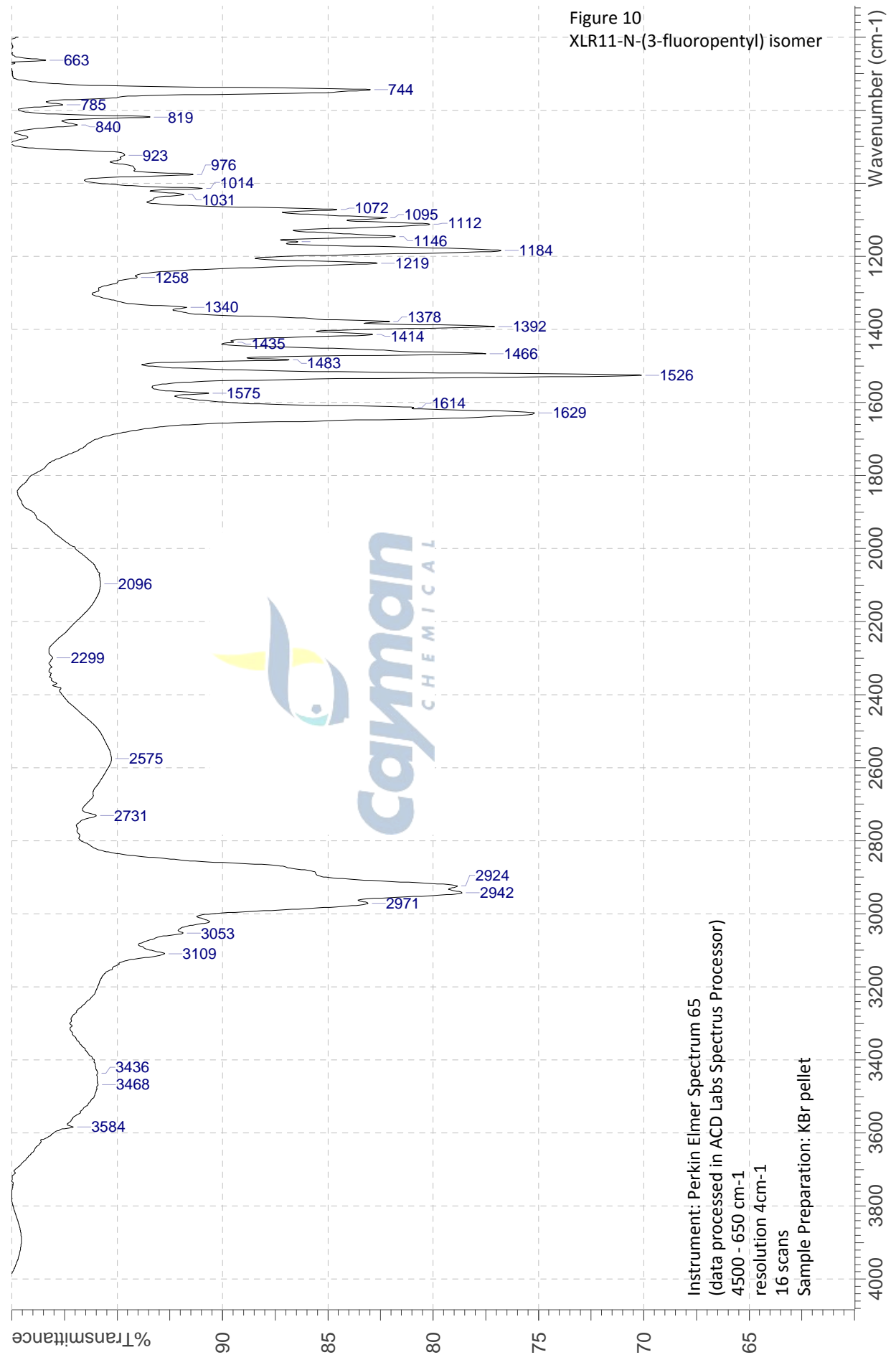
Figure 9. XLR11-N-(3-fluoropentyl) isomer
Instrument: Agilent 6890 GC / 5973 MSD
Column: 30mx0.32mm, 0.5um Rtx-5MS
Carrier Gas: Helium Flow: 2mL/min
Inlet temp: 50C 15:1 split
Oven Program:
50C for 1 minute, ramp to 300C at 30C/min, Hold at
300C to 15 minutes
Transfer Line Temp: 300C





XLR11 N-(3-fluoropentyl) isomer
Item # 11768
Lot # 0440655

Figure 10
XLR11-N-(3-fluoropentyl) isomer



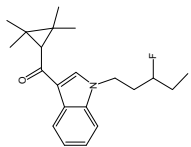
Instrument: Perkin Elmer Spectrum 65
(data processed in ACD Labs Spectrus Processor)
4500 - 650 cm-1
resolution 4cm-1
16 scans
Sample Preparation: KBr pellet



XLR11 N-(3-fluoropentyl) isomer

Item #11768

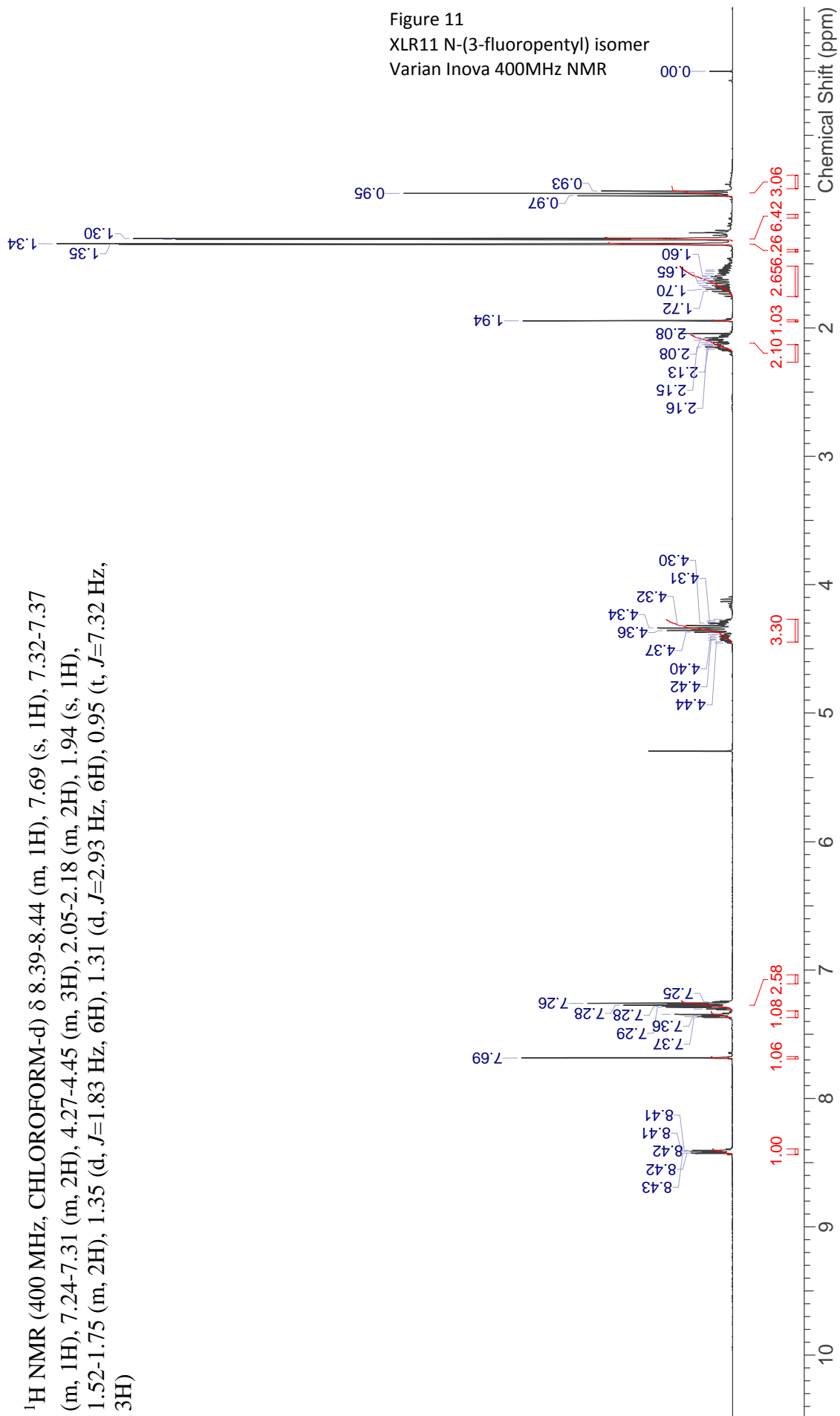
Batch #0440655

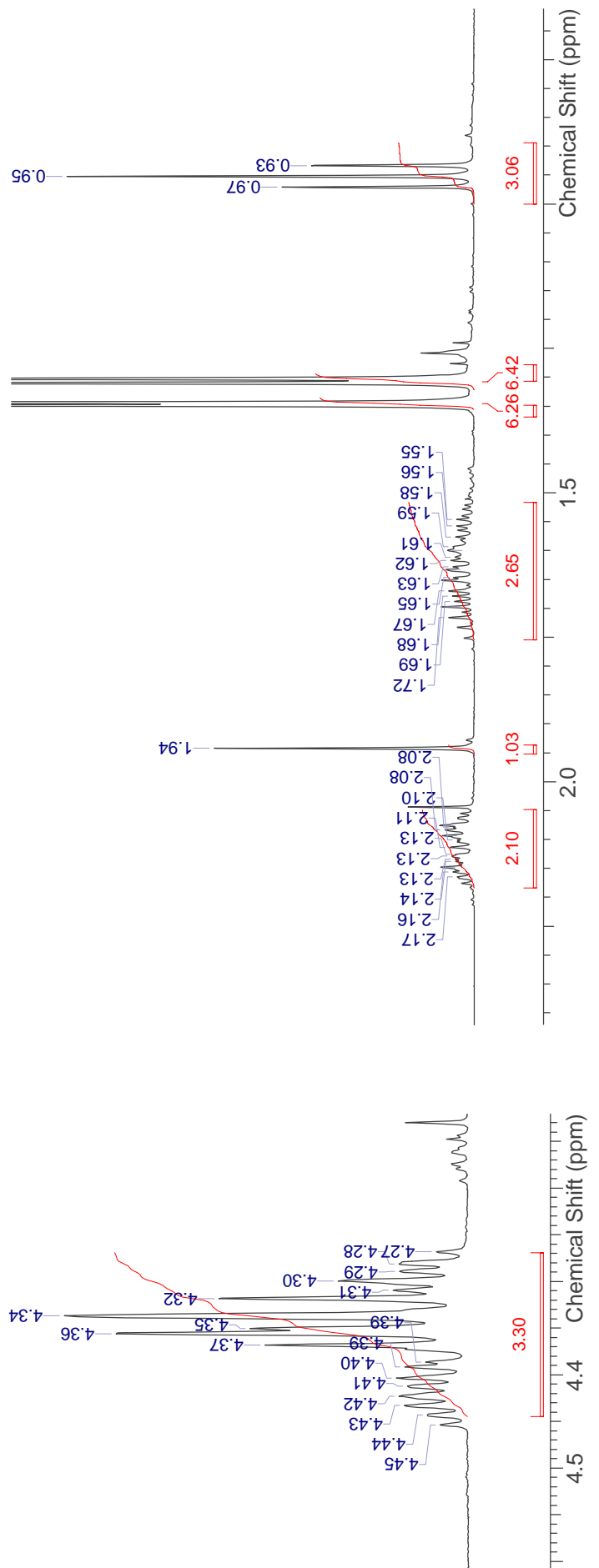
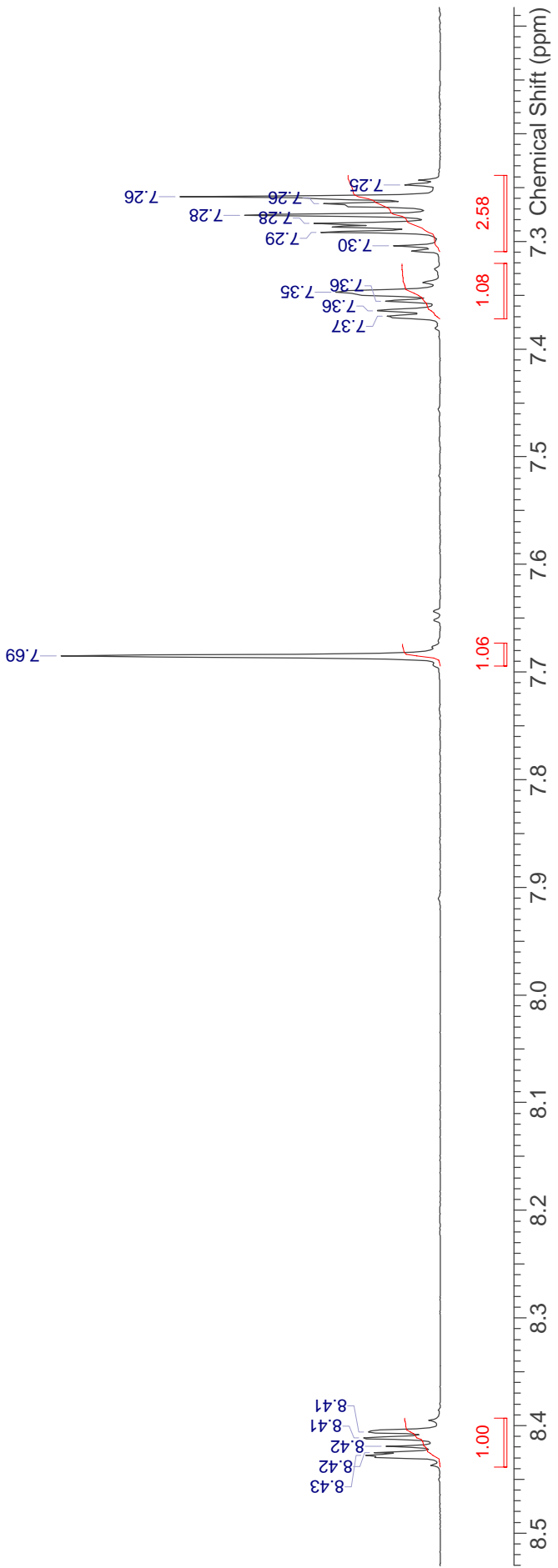


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Date	Aug 3 2012	Nucleus	¹ H
Solvent	CHLOROFORM-d	Number of Transients	64
		Frequency (MHz)	399.97

¹H NMR (400 MHz, CHLOROFORM-d) δ 8.39-8.44 (m, 1H), 7.69 (s, 1H), 7.32-7.37 (m, 1H), 7.24-7.31 (m, 2H), 4.27-4.45 (m, 3H), 2.05-2.18 (m, 2H), 1.94 (s, 1H), 1.52-1.75 (m, 2H), 1.35 (d, *J*=1.83 Hz, 6H), 1.31 (d, *J*=2.93 Hz, 6H), 0.95 (t, *J*=7.32 Hz, 3H)

Figure 11
XLR11 N-(3-fluoropentyl) isomer
Varian Inova 400MHz NMR





XLR11 N-(3-fluoropentyl) isomer

8/7/2012 2:43:39 PM

C:\MassSpecData\2012\11768_QC05011
NUTRALAPCIPOSHIFLO

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330.23

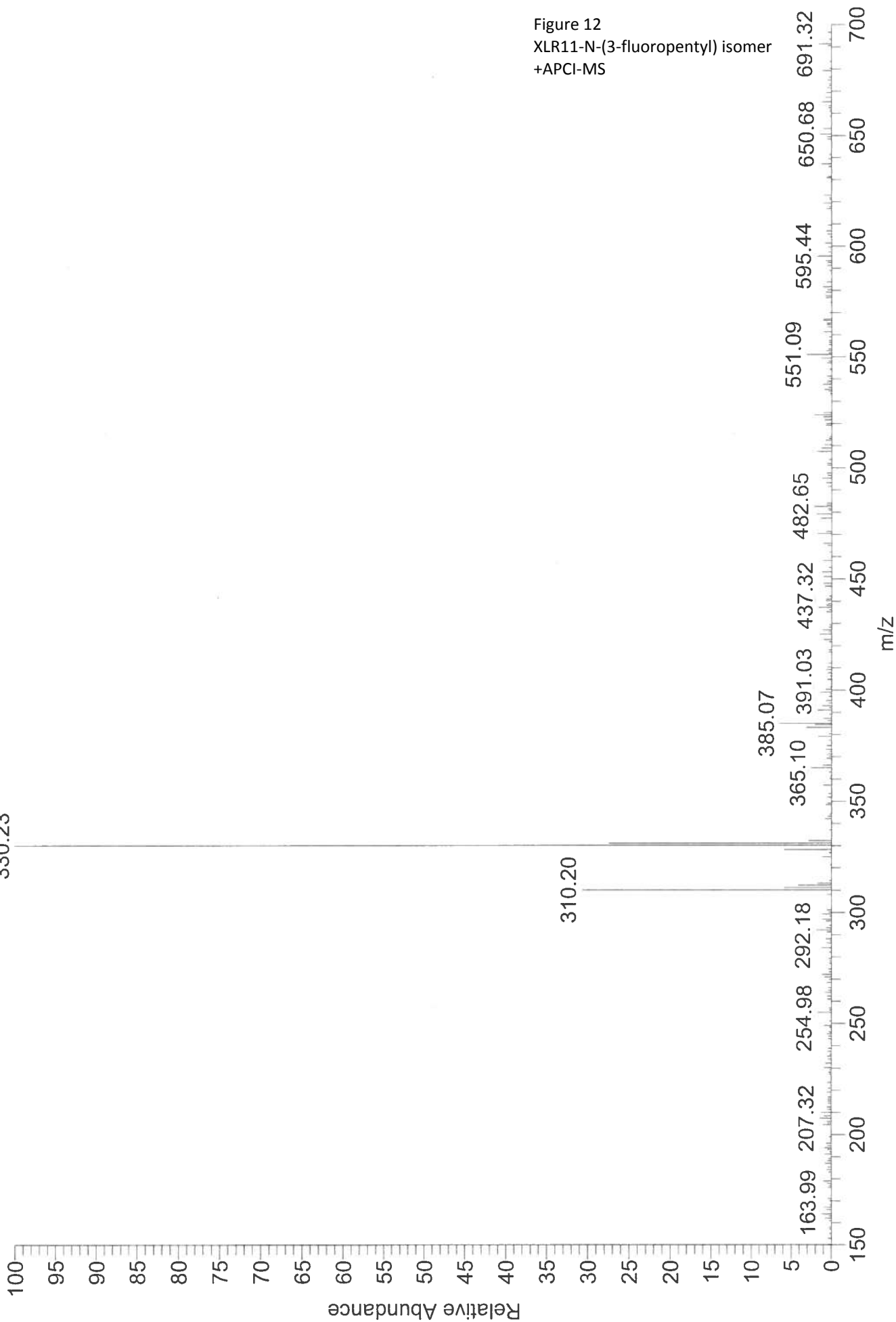


Figure 12
XLR11-N-(3-fluoropentyl) isomer
+APCI-MS

Operator : PDK
Acquired : 20 Aug 2012 14:30 using AcqMethod CAY_DRUG_CATH.M
Instrument : Instrument #1
Sample Name: XLR11 N-(2-fluoropentyl) isomer
Misc Info : 30mx0.32mm, 0.5u Rtx-5MS, 50C-30C/min-300C
Vial Number: 6

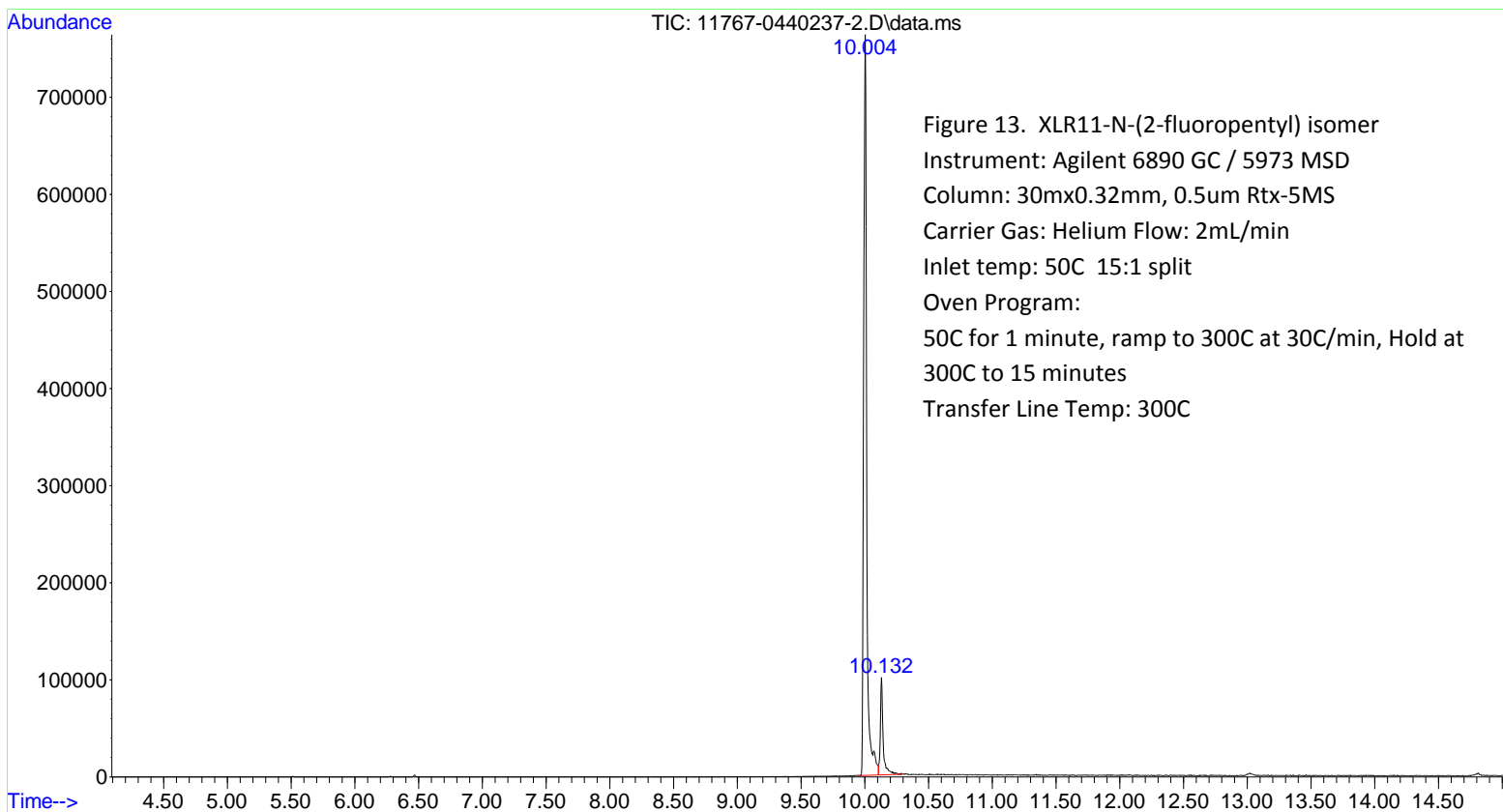


Figure 13. XLR11-N-(2-fluoropentyl) isomer
Instrument: Agilent 6890 GC / 5973 MSD
Column: 30mx0.32mm, 0.5um Rtx-5MS
Carrier Gas: Helium Flow: 2mL/min
Inlet temp: 50C 15:1 split
Oven Program:
50C for 1 minute, ramp to 300C at 30C/min, Hold at 300C to 15 minutes
Transfer Line Temp: 300C

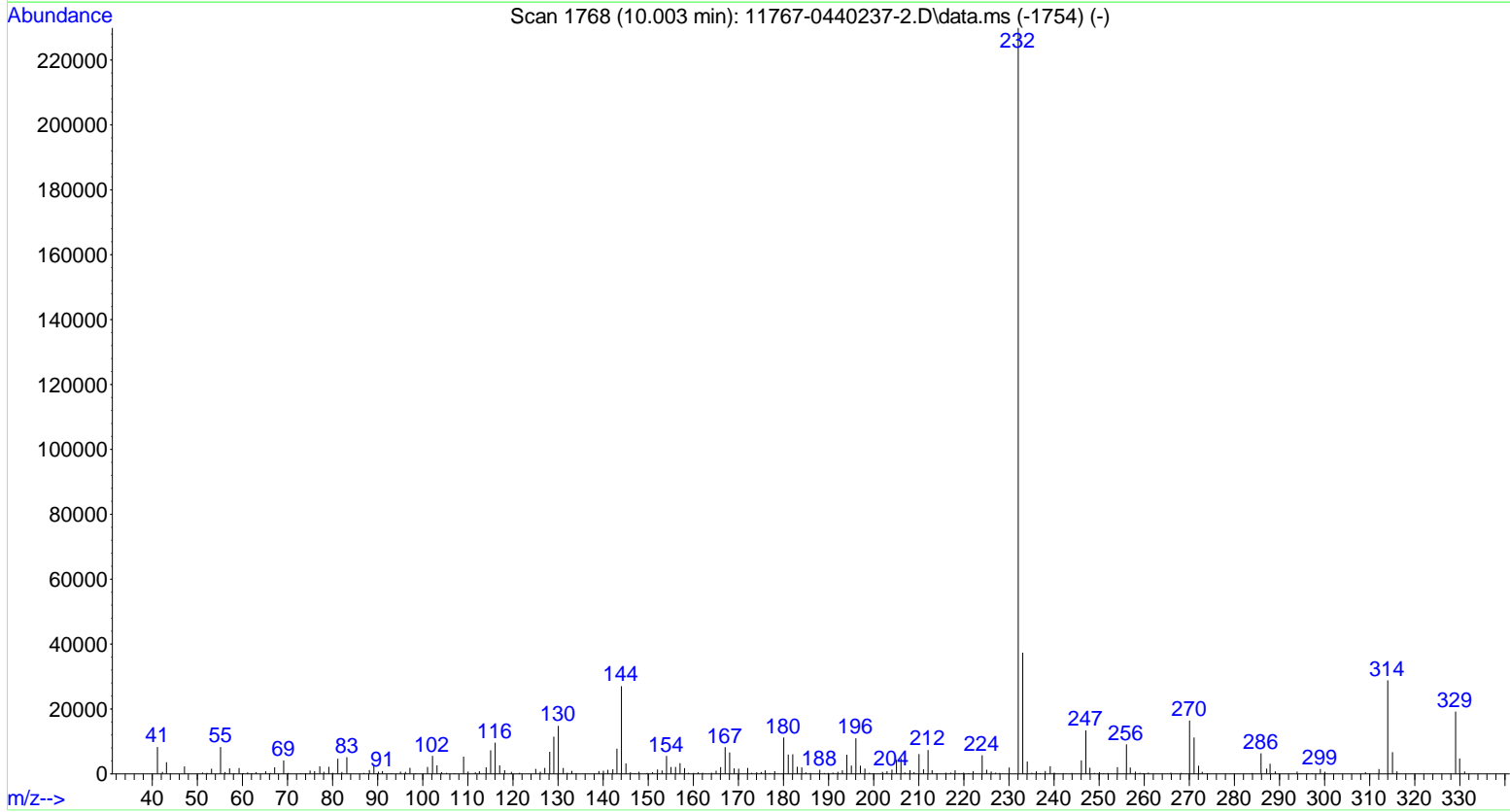
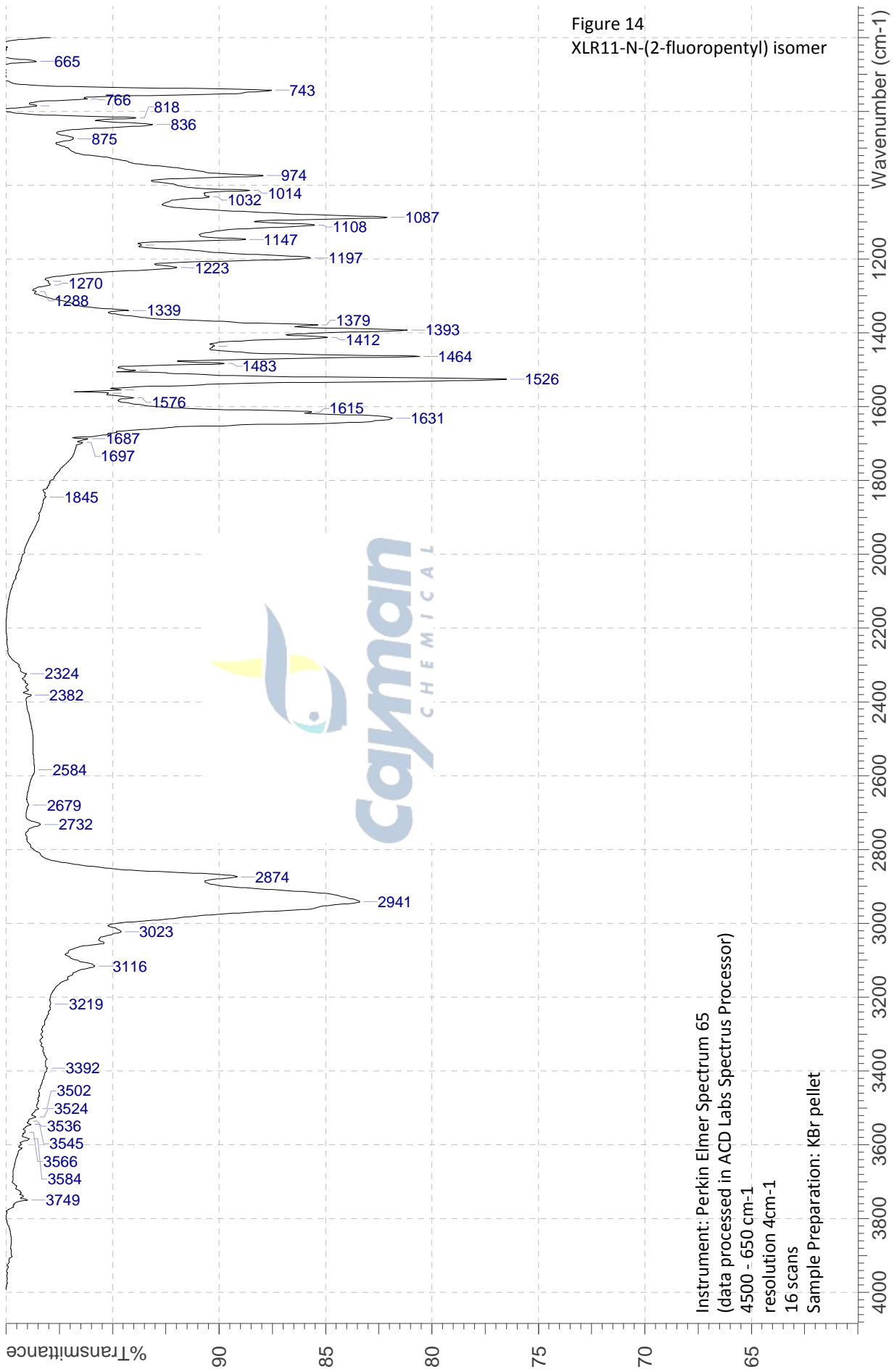
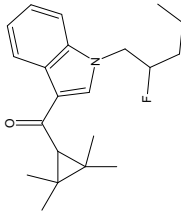


Figure 14
XLR11-N-(2-fluoropentyl) isomer



XLR11 N-(2-fluoropentyl) isomer
Item # 11767
Lot # 0440237

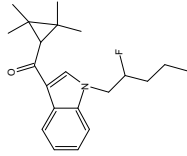
Instrument: Perkin Elmer Spectrum 65
(data processed in ACD Labs Spectrus Processor)
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resolution 4cm-1
16 scans
Sample Preparation: KBr pellet



XLR11 N-(2-fluoropentyl) isomer

Item #111767

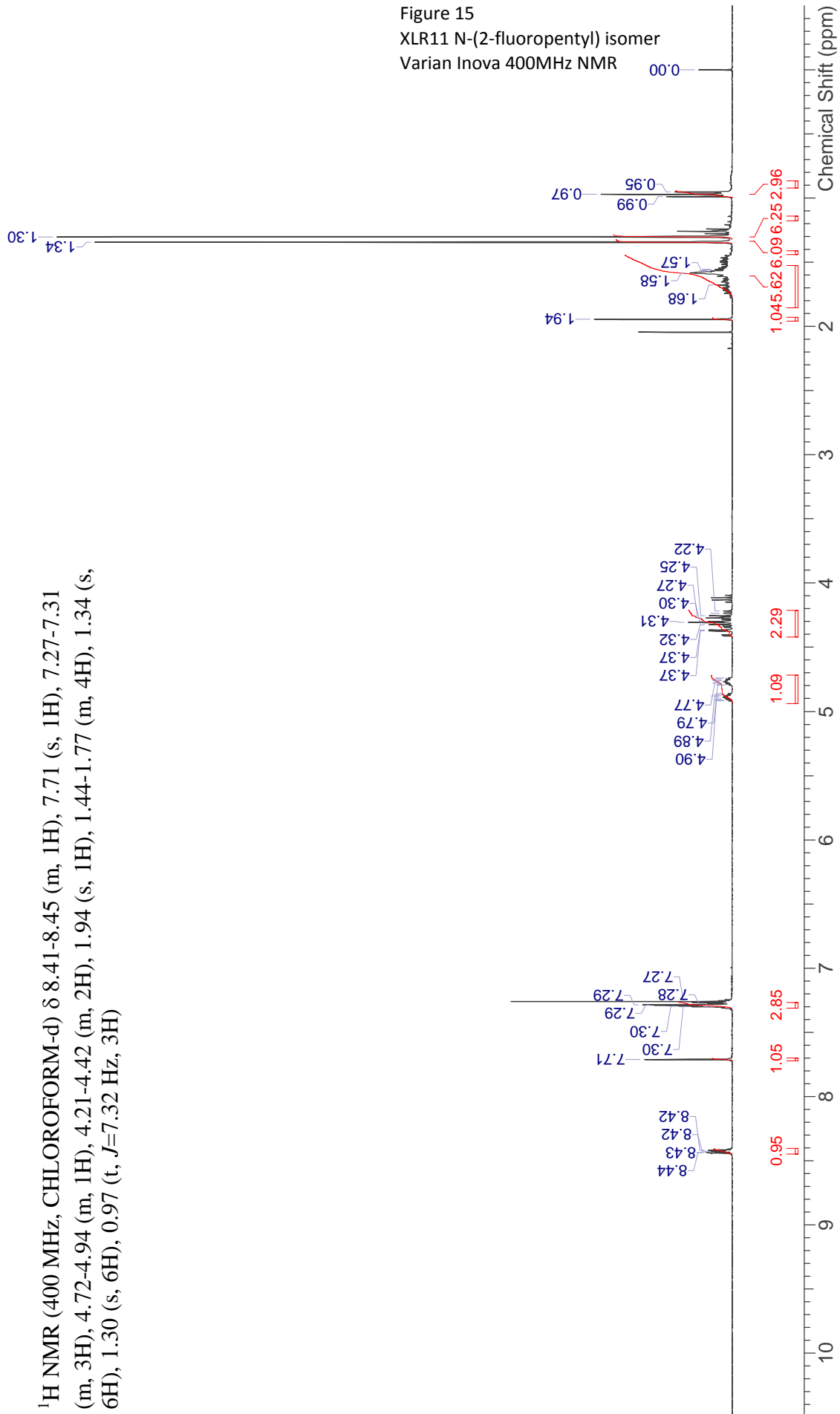
Batch #0440237

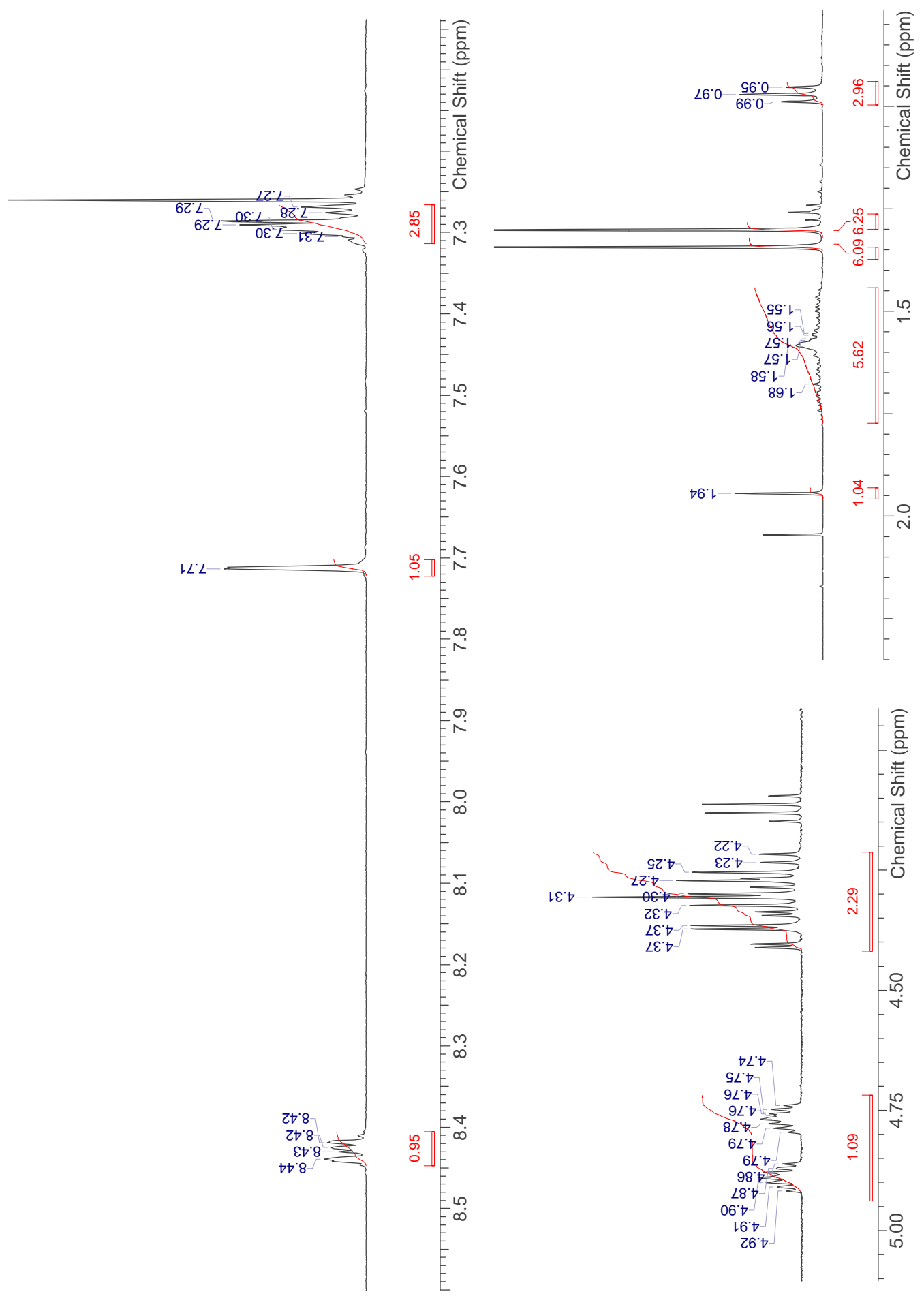


File Name	\\sulfur\private\inmdata\SK2-197_20-28_20120720_01\SK2-197_20-28_20120720_001.fid\fid	
Date	Jul 20 2012	Frequency (MHz) 399.97
Solvent	CHLOROFORM-d	
	Nucleus 1H	
	Number of Transients 64	

¹H NMR (400 MHz, CHLOROFORM-d) δ 8.41-8.45 (m, 1H), 7.71 (s, 1H), 7.27-7.31 (m, 3H), 4.72-4.94 (m, 1H), 4.21-4.42 (m, 2H), 1.94 (s, 1H), 1.44-1.77 (m, 4H), 1.34 (s, 6H), 1.30 (s, 6H), 0.97 (t, J=7.32 Hz, 3H)

Figure 15
XLR11 N-(2-fluoropentyl) isomer
Varian Inova 400MHz NMR





XLR11 N-(2-fluoropentyl) isomer

7/23/2012 12:58:54 PM

C:\MassSpecData\2012\11767_QC04957
NUTRALAPCIPOSHIFLO

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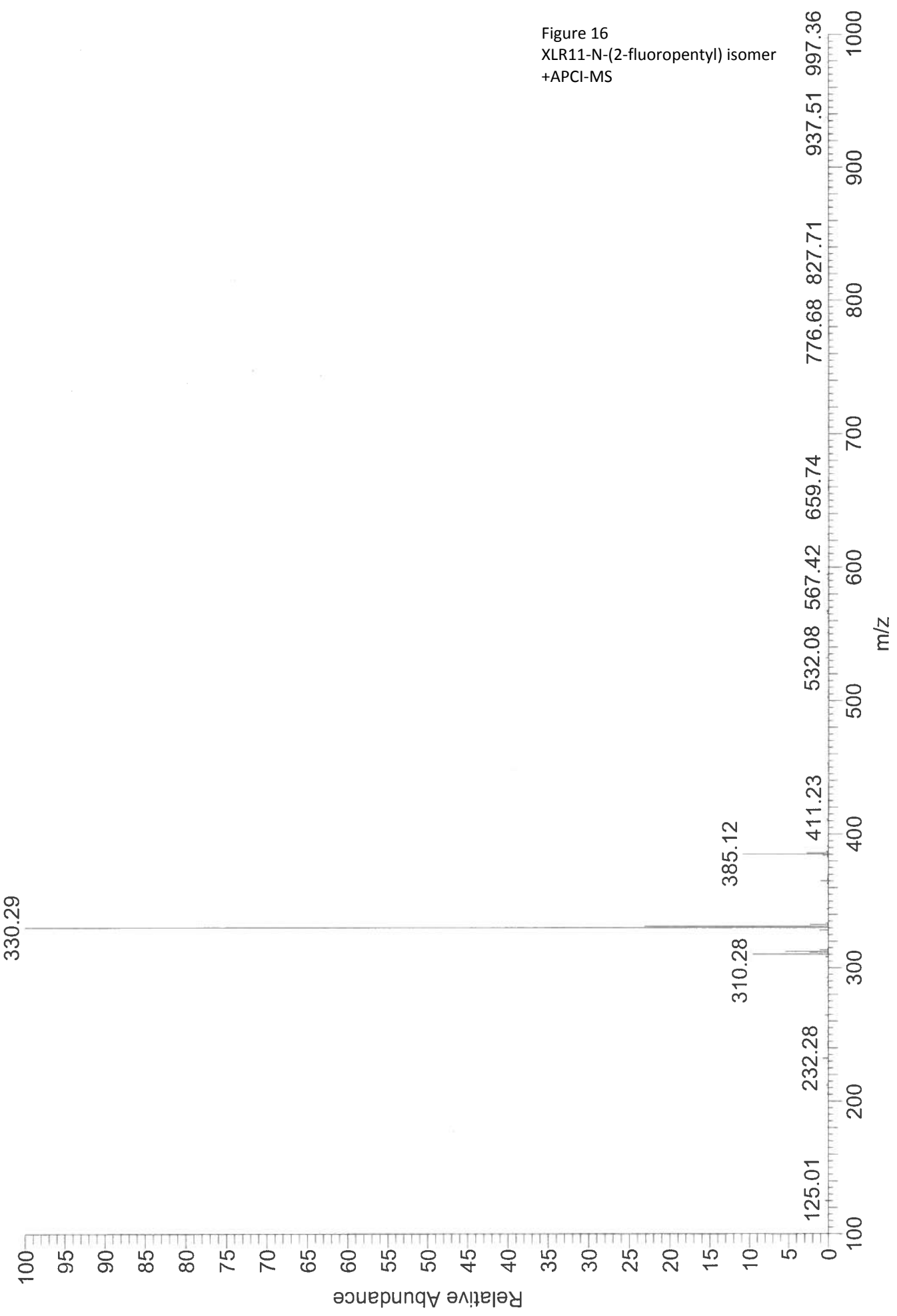
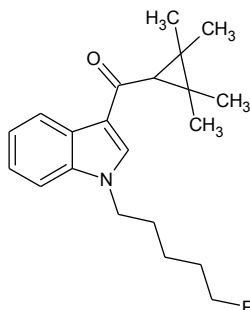


Figure 16
XLR11-N-(2-fluoropentyl) isomer
+APCI-MS

XLR11



Synonyms: (1-(5-fluoropentyl)-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone

CAS #: 1364933-54-9

Source: Cayman Chemicals (Lot #0437258-46)

2-Fluoro Isomer Lot #0440237-14

3-Fluoro Isomer Lot #0440655-13

4-Fluoro Isomer Lot #0439509-19

Appearance: White powder

Chemical Formula: C₂₁H₂₈FNO

GAS CHROMATOGRAPHY/MASS SPECTROMETRY:

Sample preparation: Extracted powder with methanol to yield a concentration of ~ 1 mg/mL in methanol.

Instrument: Agilent gas chromatograph (7890A)/ mass spectrometer (5975C)

GC Parameters:

Column: HP-5MS; 30m x 0.250mm x 0.25 micron

Carrier gas: Helium

Oven program:

1) 240°C initial temperature for 1.0 min.

2) Ramp to 300°C at 30°C/min

3) Hold at 300°C for 11 min.

Injection parameters:

Split ratio: 100:1, 1 microliter injected

MS Parameters:

Temperatures: Injector 250° C

MSD transfer line: 290°C

MS Source: 230°C

MS Quad: 150°C

Mass scan range: 34-550 amu

Threshold: 150

Tune file: atune.u

<u>Compound</u>	<u>Retention time (min)</u>	<u>Relative retention time</u>
XLR11	3.178	1.000
2-Fluoro isomer XLR11	2.913	0.917
3-Fluoro isomer XLR11	2.953	0.929
4-Fluoro isomer XLR11	3.012	0.948

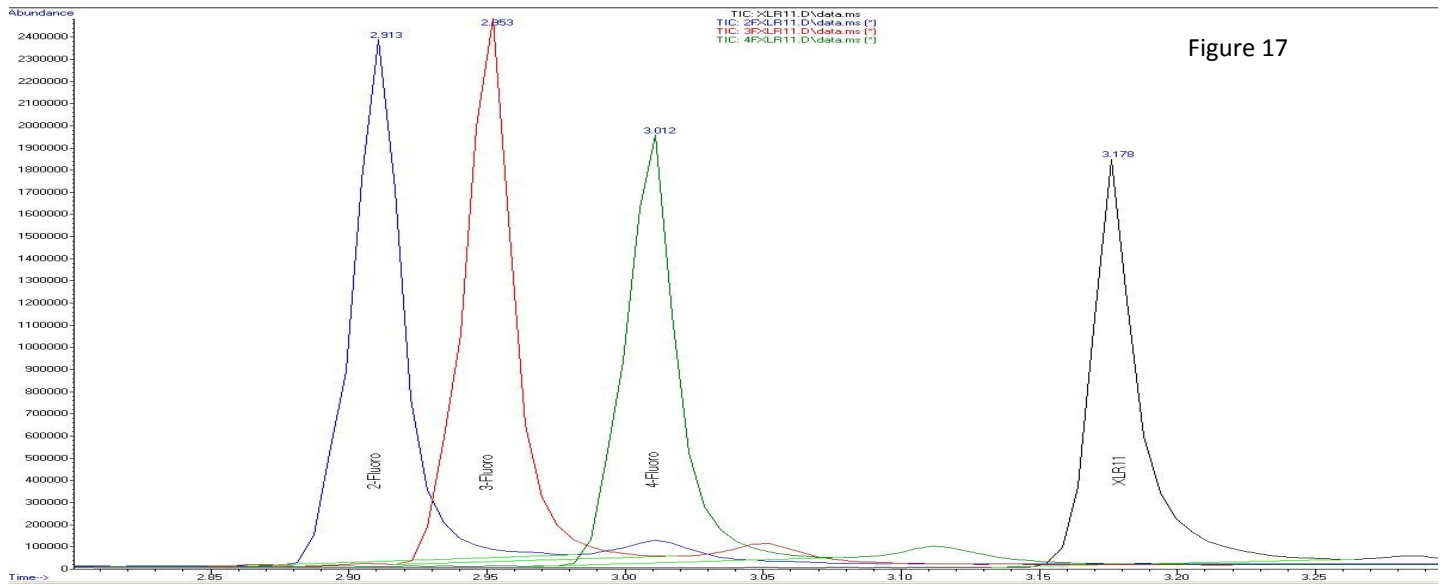


Figure 17

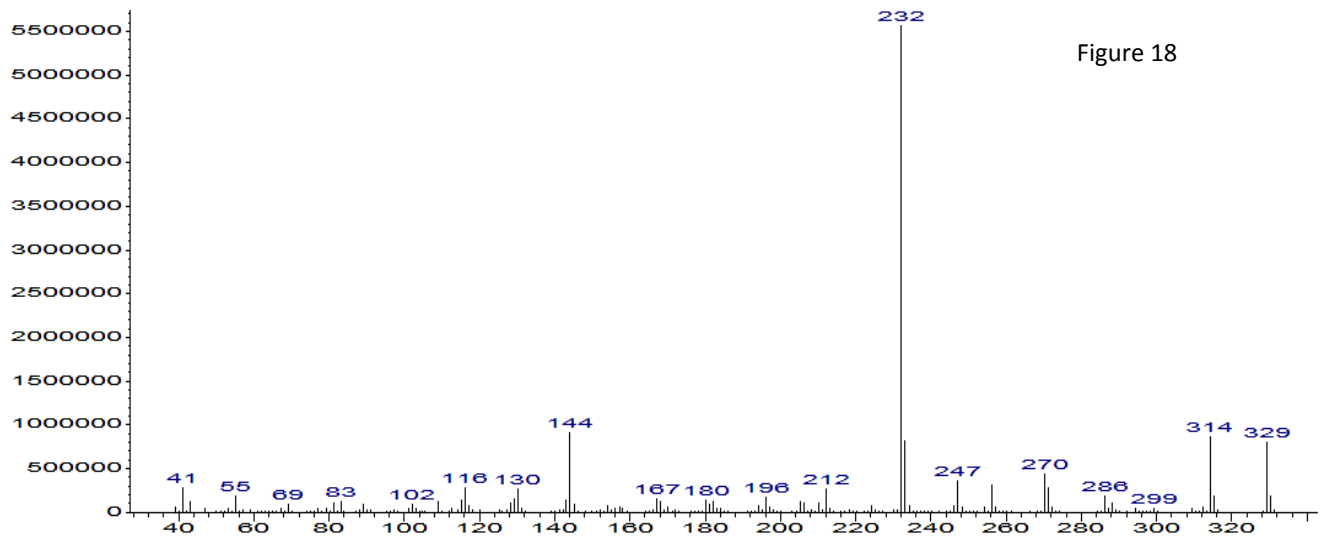
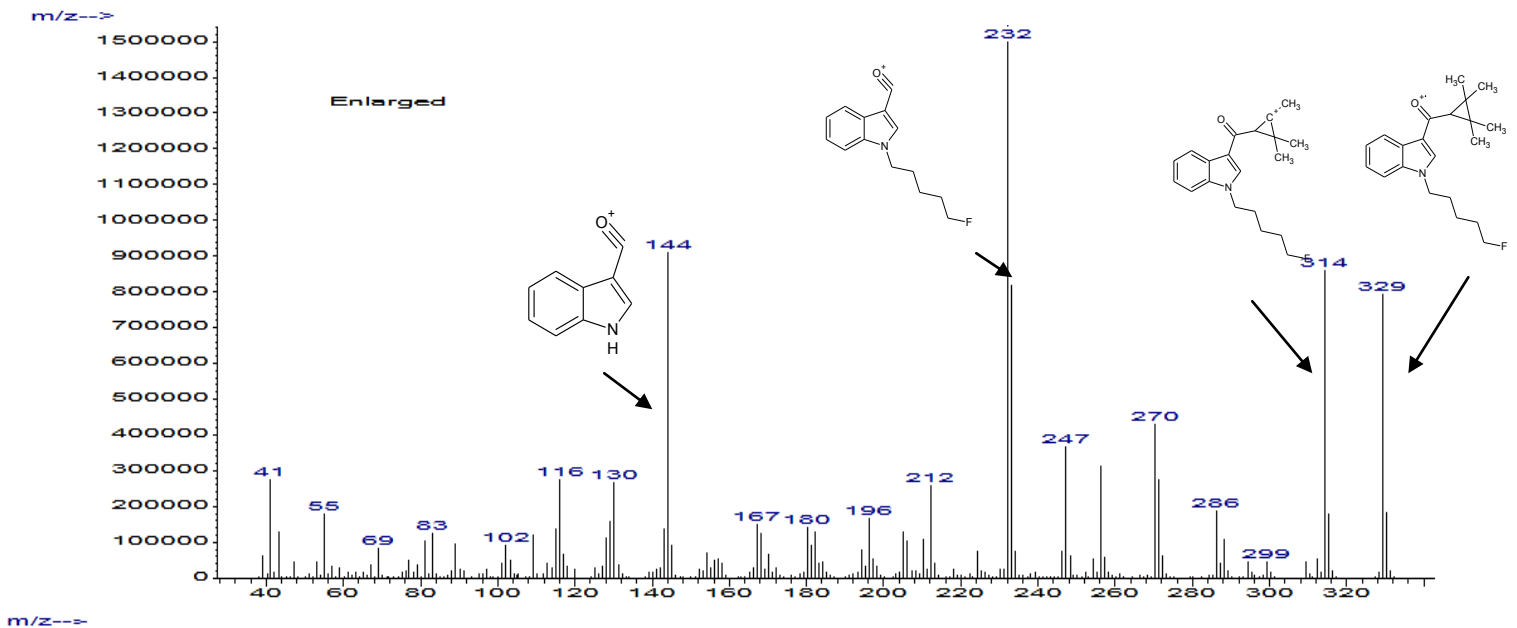


Figure 18



2.2 LIQUID CHROMATOGRAPHY/ULTRAVIOLET SPECTROSCOPY/MASS SPECTROMETRY:

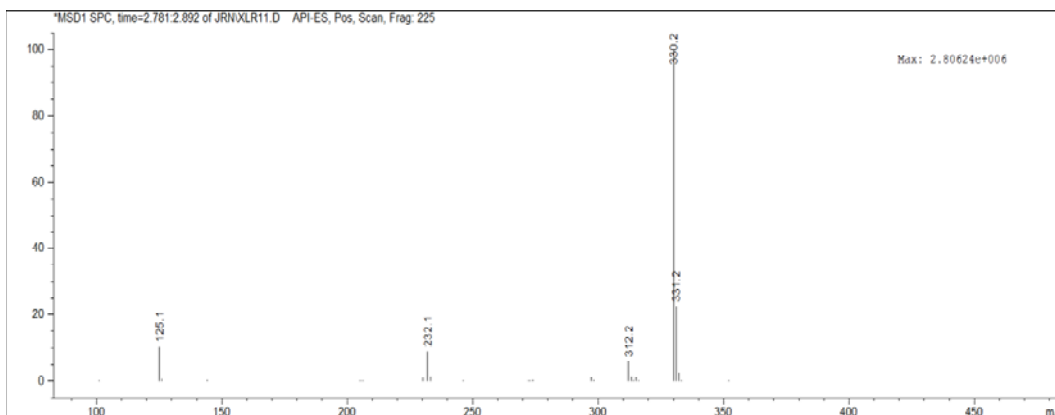
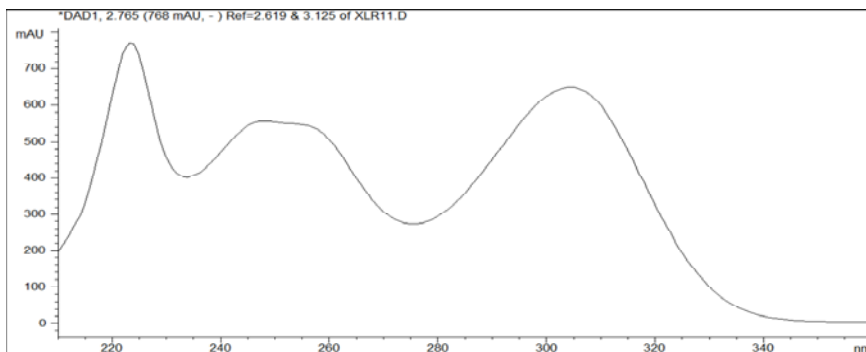
Instrument:	Agilent 1100 LC/UV/MSD
LC parameters	Column: Hypersil Gold 50 x 2.1mm; 1.9 micron
	Column compartment: 50°C
	Mobile phase: A: 15mM ammonium acetate buffer B: Acetonitrile
	Flow: 500 microliters/minute
	Gradient:

Time (min)	0.00	3.50	3.51	5.50	5.51	10.00
% B	55	55	60	60	55	55

UV parameters:	Scan: 220-360nm
	Step: 1.0nm
	Threshold: 1.000 mAu
	Split: 4 nm

MS Parameters:	Scan: 100-500 amu
	Fragmentor: 225V
	Gain: 1.00
	Threshold: 500
	Step: 0.10

Retention time:	2.766 min (UV)
	2.837 min (MS)



2.3 INFRARED SPECTROSCOPY (Attenuated Total Reflectance):

Instrument:

Thermo Nicolet 6700 FTIR with smart iTR diamond ATR attachment

Scan Parameters:

Number of scans: 32

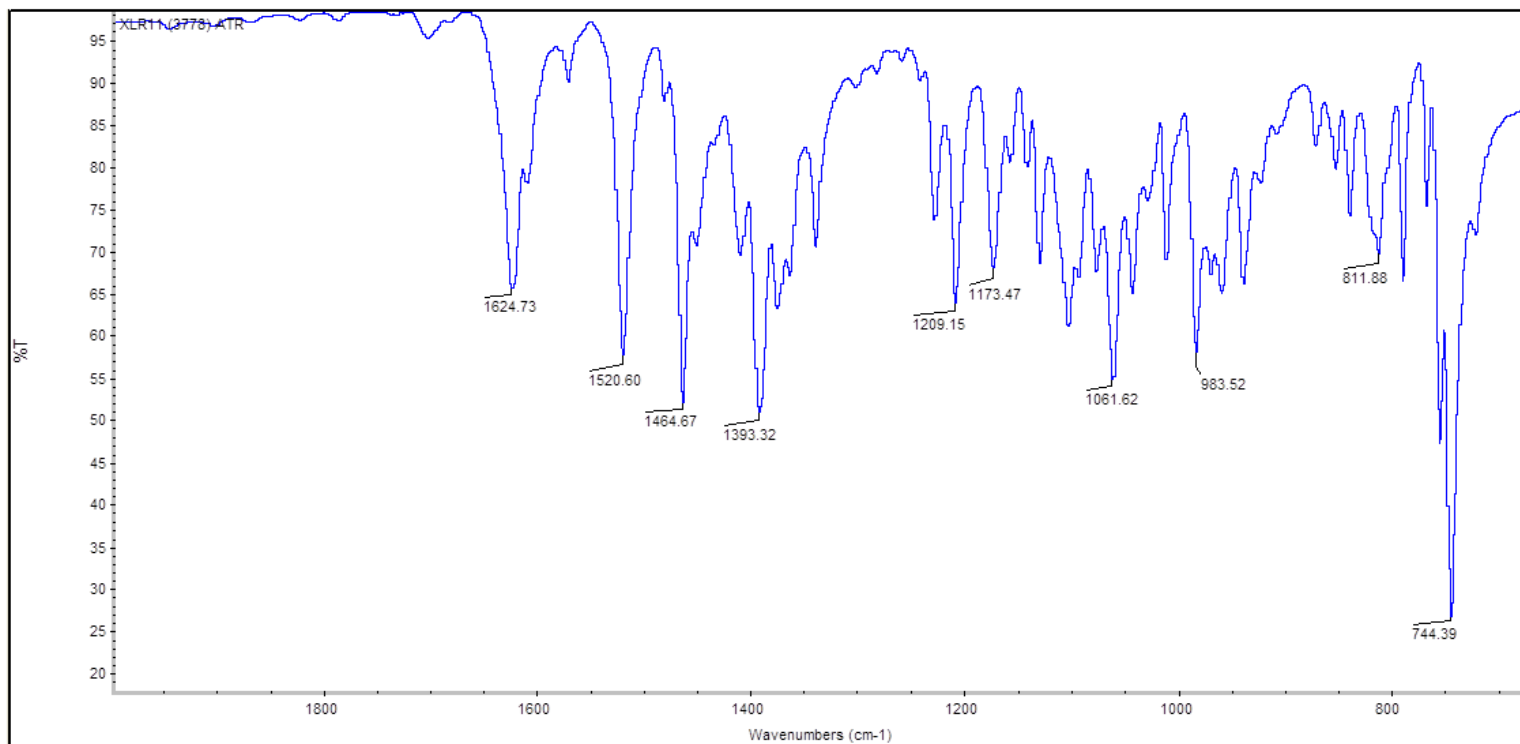
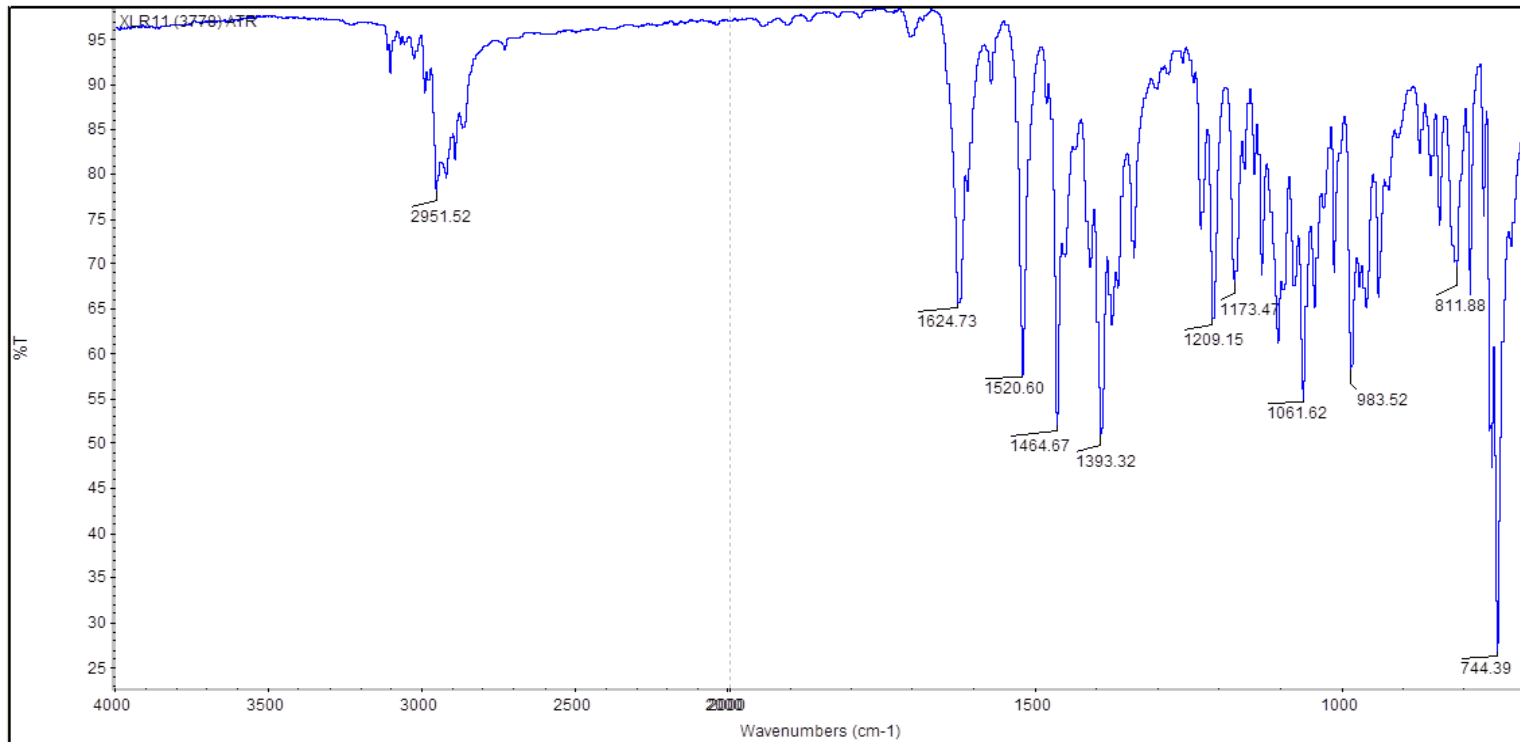
Number of background scans: 32

Resolution: 4

Sample gain: Autogain

Aperture: 74

Figure 21 USACIL ATR-FTIR of XLR11



2.4 INFRARED SPECTROSCOPY (solid phase):

Instrument:

Spectra Analysis DiscoverIR-GC

Parameters:

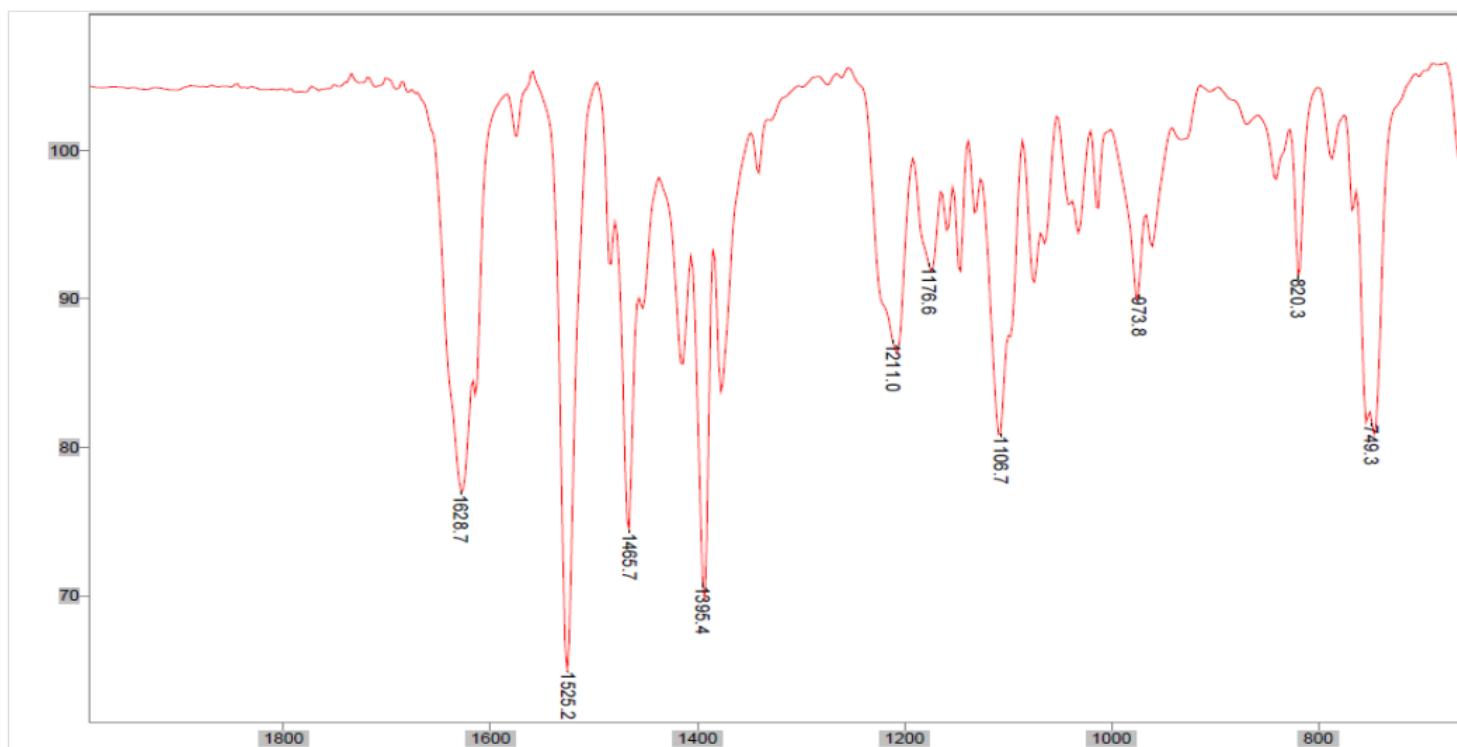
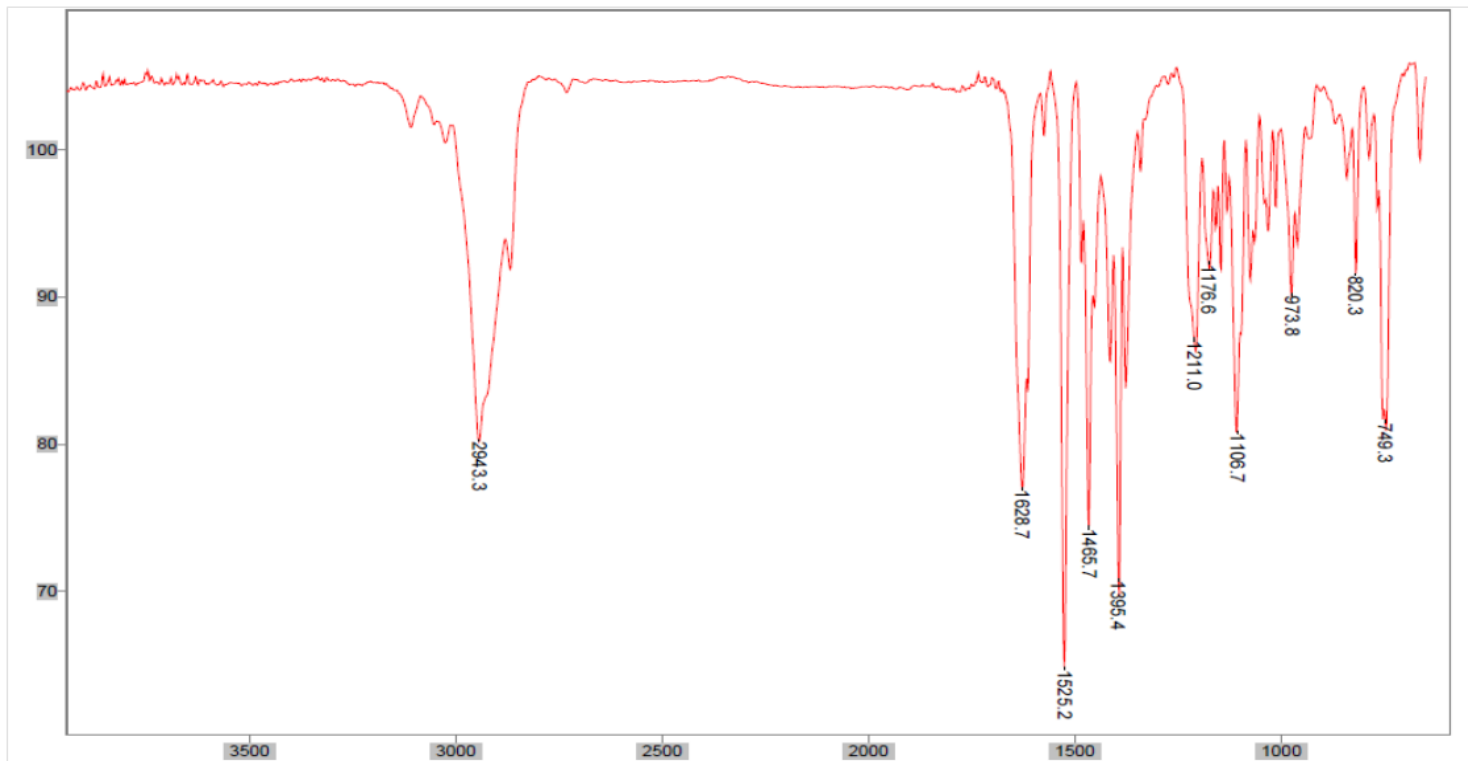
Transfer line: 250° C

Oven: 250° C

Restrictor: 250° C

Disk: -40° C

Figure 22 USACIL GC-IR of XLR11



2.5 RAMAN SPECTROSCOPY:

Instrument:

Parameters:

ThermoNicolet 6700 FTIR with XNR FT-Raman module

Number of sample scans: 32

Resolution: 4.000

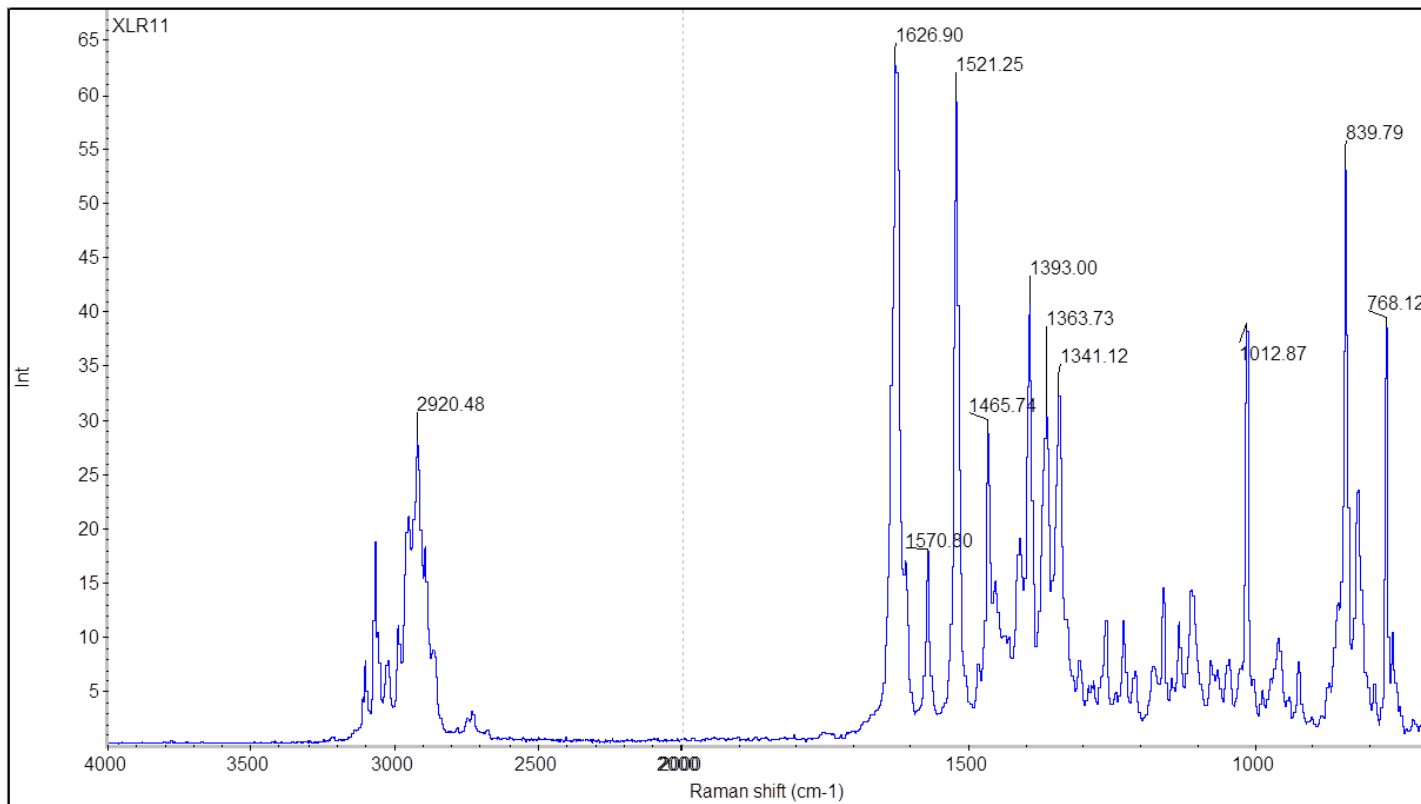
Sample gain: 4.0

Aperture: 59.00

Detector: InGaAs (Indium Gallium Arsenide)

Beamsplitter: CaF2 (Calcium Fluoride)

Figure 23



References

1. Kavanagh, P., Grigoryev, A., Savchuk, S., Mikhura, I. and Formanovsky, A. (2013), UR-144 in products sold *via* the Internet: Identification of related compounds and characterization of pyrolysis products. *Drug Test Analysis*. doi: 10.1002/dta.1456
2. Shevyrin, V., Melkozerov, V., Nevero, A., Eltsov, O., Morzherin, Y., Shafran, Y., Identification and analytical properties of new synthetic cannabimimetics bearing a 2,2,3,3-tetramethylcyclopropanecarbonyl moiety. *Forensic Sci Int*. 2013 Mar 10;226(1-3):62-73. doi:10.1016/j.forsciint.2012.12.009. Epub 2012 Dec 30.
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4. WO application 2006069196, Pace JM, Tietje K, Dart MJ, Meyer MD, "3-Cycloalkylcarbonyl indoles as cannabinoid receptor ligands", published 2006-06-29, assigned to Abbott Laboratories
5. "Acute Kidney Injury Associated with Synthetic Cannabinoid Use — Multiple States, 2012". US Centre for Disease Control. 15 Feb 2013.

External Links

[DEA SWGDRUG XLR-11 Monograph](#)

[Forendex XLR11 page](#)

[XLR-11 Wikipedia page](#)