Supporting information for:

A Scalable Route to Fibrinolysis Inhibitor AZD6564

Søren M. Andersen[a], *Martin Bollmark*[b], *Robert Engqvist*[b], *Christofer Fredriksson*[c], *Staffan Karlsson*[d], *Catarina Liljeholm*[c], *Henrik Sörensen**[d]

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[b]SP Process Development, Box 36, SE-151 21 Södertälje, Sweden

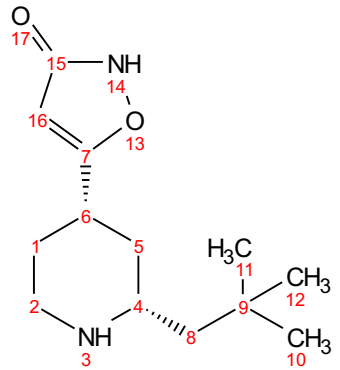
[c] Pharmaceutical Development, Global Medicines Development, AstraZeneca R & D Mölndal, S-431 83 Mölndal, Sweden

[d]Medicinal Chemistry, Cardiovascular & Metabolic Diseases iMed, AstraZeneca R & D Mölndal, S-431 83 Mölndal, Sweden

henrik.sorensen@astrazeneca.com

Contents:

Book Reference: EN06958-29-001
Analytical Number: SN1045263272
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 400.03MHz (nmr2)
Spinner: 34
Experiment Name: Proton_day
#Scans: 16
Solvent: MeOD
Parameters:
Date: Thu Oct 03 12:31:32 CEST 2013
Extension:



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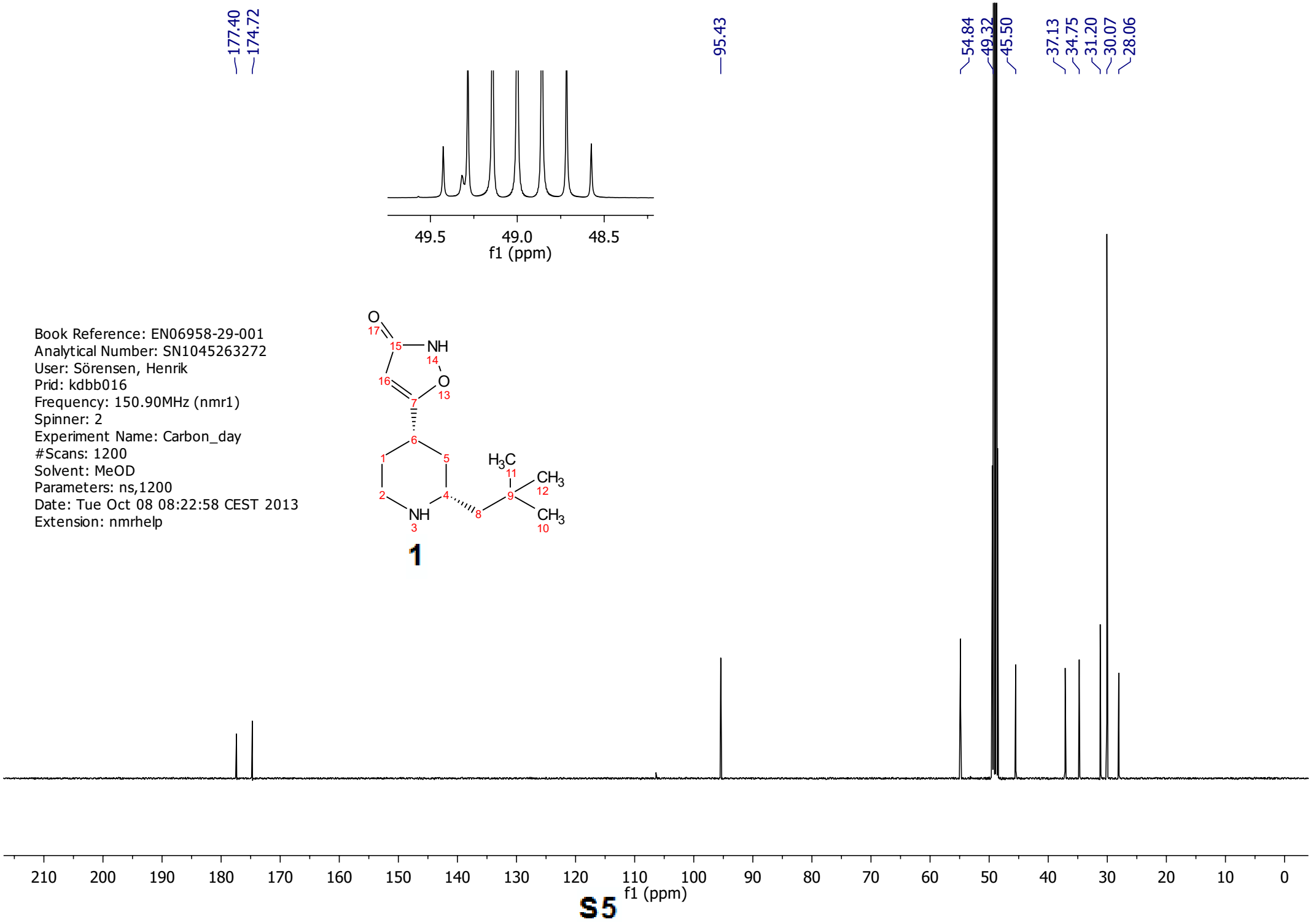
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54.84
49.32
45.50
37.13
34.75
31.20
30.07
28.06
49.5
49.0
48.5
f1 (ppm)
Book Reference: EN06958-29-001
Analytical Number: SN1045263272
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 150.90MHz (nmr1)
Spinner: 2
Experiment Name: Carbon_day
#Scans: 1200
Solvent: MeOD
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Date: Tue Oct 08 08:22:58 CEST 2013
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NH
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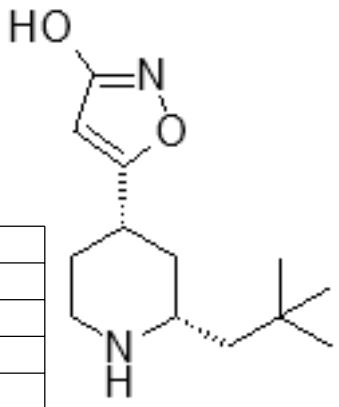
16
O
13
7
6
1
5
H3C
11
CH3
12
2
4
9
8
NH
3
CH3
10
1
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

AstraZeneca **EnantioBase** Analysis Report

Sample Information

Sample ID	Compound name	Project name
SN1014430621	AZ13212451	NOFI



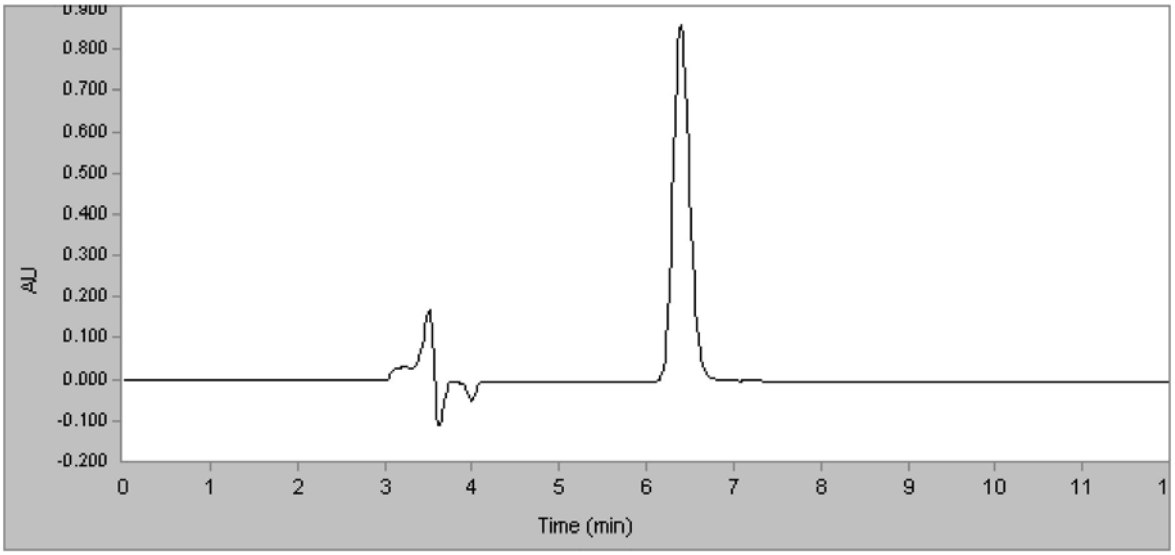
1

Analytical Conditions

Column	Dimensions (mm)	Particle Size (µm)
Chiralpak IC	250 * 4.6	5
Mobile Phase		
Heptan/IPA/FA 60/40/0.1		
Flow (ml/min)	**Detection (nm)**	**Temperature (C)**
1 ml/min	PDA 220.0 nm	RT
Comment		

Analytical Result

UV Chromatogram

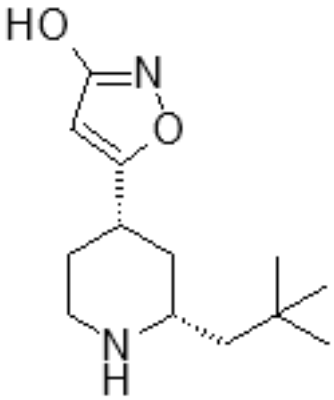


Retention Time	Area	Area %	K'	N	USP Resolution
2.967	0		0.000		
5.137	2489		0.731		
6.398	11434238		1.156		4.253837e+000

ee: 99.9%

Chemist Signature

Print Date
2009-06-13



1

Purity Analysis and Accurate Mass Report

Submitter: Henrik Sörensen

Sample ID: SN1014430621

Compound Name: AZ13212451

Project: NOFI

Results

SN1014430621: Your sample was 99% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

Instrumental setup

Column	Acquity UPLC™ BEH C18 100mm×2.1mm, 1.7µm particles
Temperature	60ºC
Gradient	2% ACN to 95% ACN in 6 minutes; 47mM NH_4 6.5mm NH_4HCO_3, pH 10
Flow	0.8 mL/min
Injection volume	3 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Waters LCTP
Lockmass	Leucine Enkephaline C28H37N5O7

Comments

Signature: _____ Date: 2009-07-02

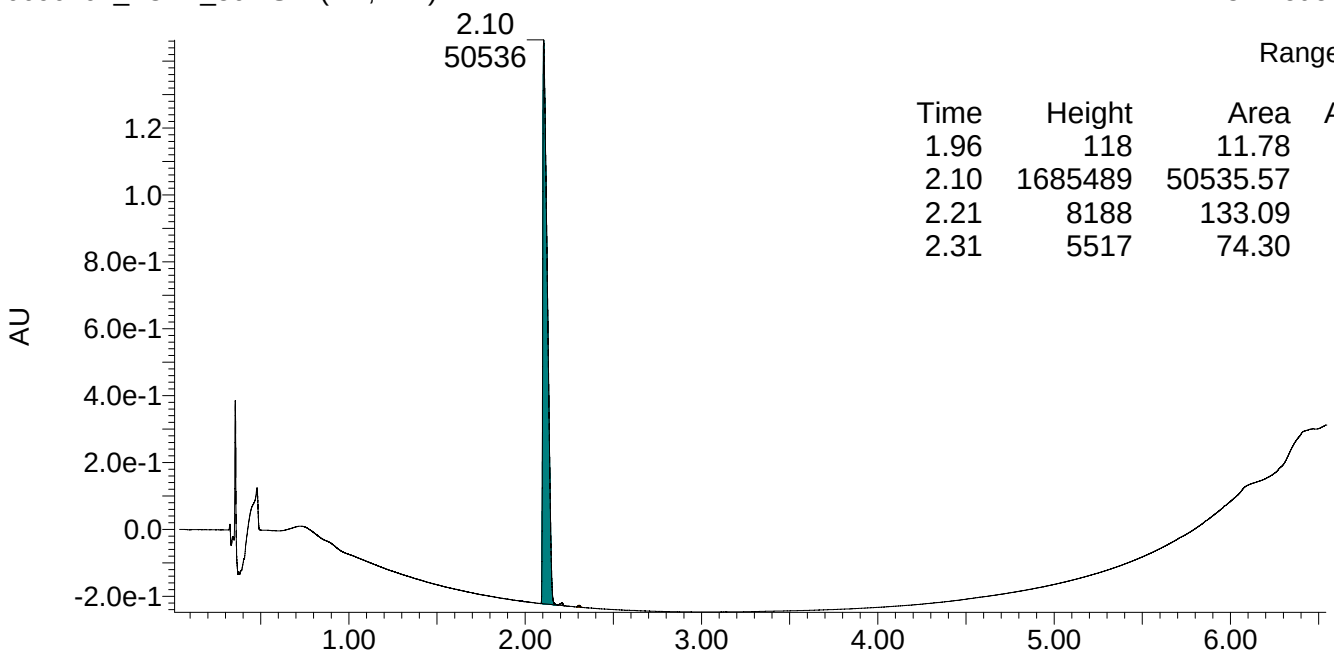
Stina Kiellarson
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

SN1014430621 **AZ13212451** **Henrik Sörensen**

20090701_LCTP_504 Sm (Mn, 2x2)

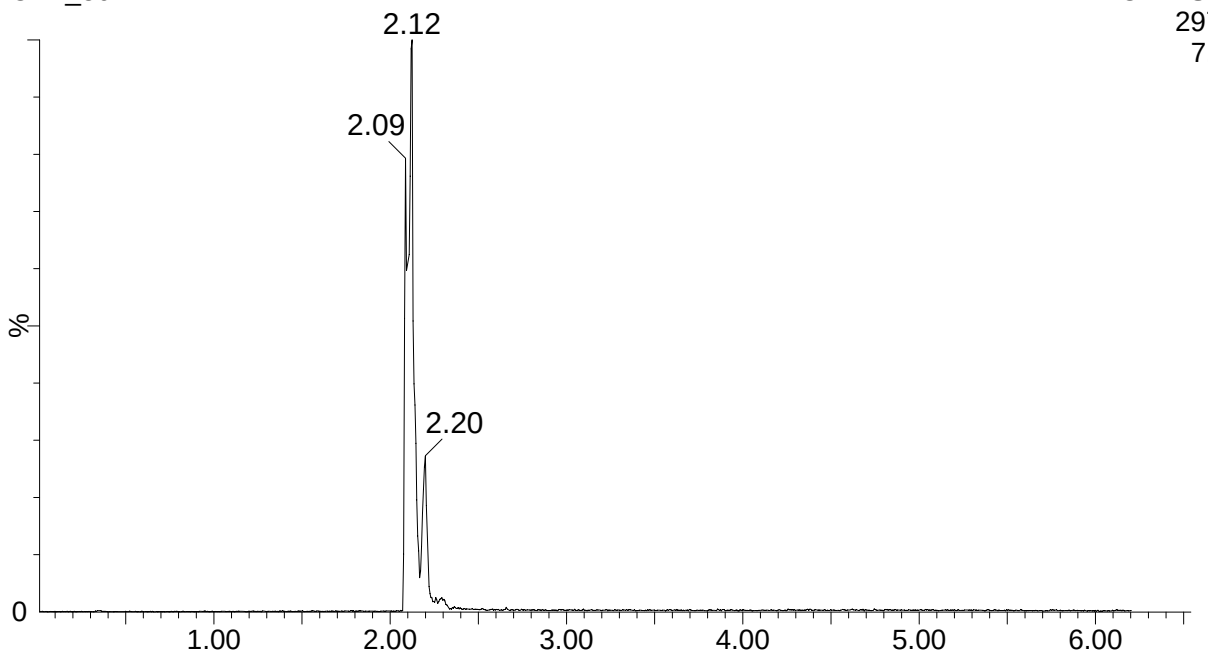
3: Diode Array
210
Range: 1.71

Time	Height	Area	Area%
1.96	118	11.78	0.02
2.10	1685489	50535.57	99.57
2.21	8188	133.09	0.26
2.31	5517	74.30	0.15



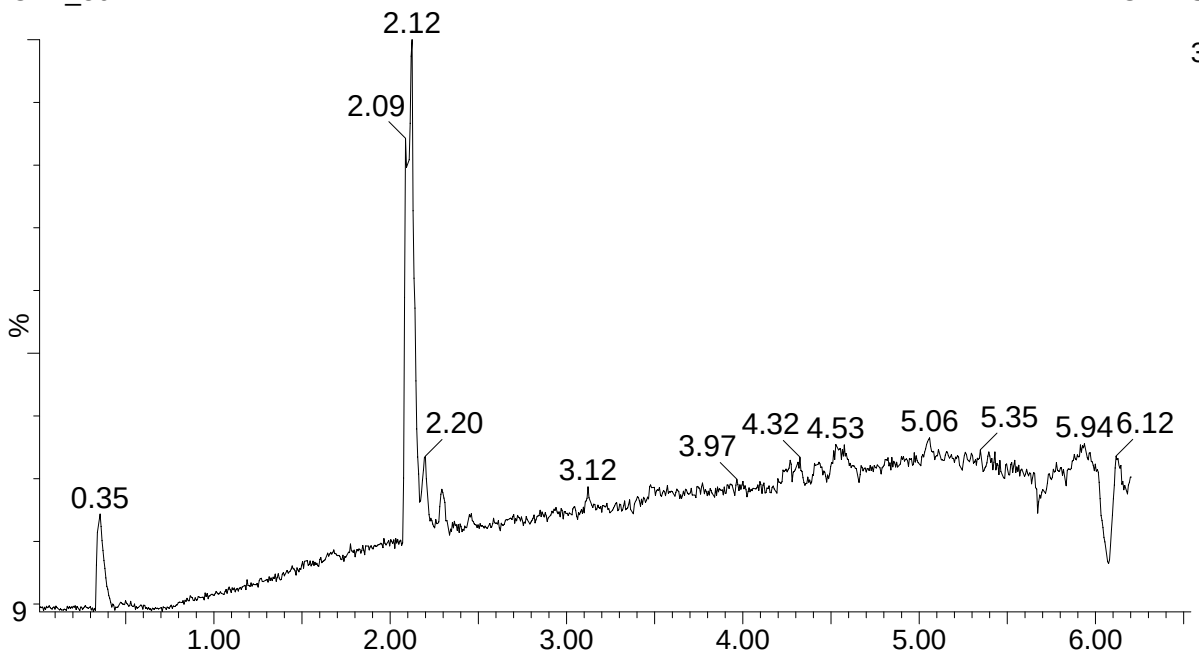
20090701_LCTP_504

1: TOF MS ES+
297.182
7.62e3



20090701_LCTP_504

1: TOF MS ES+
TIC
3.74e4

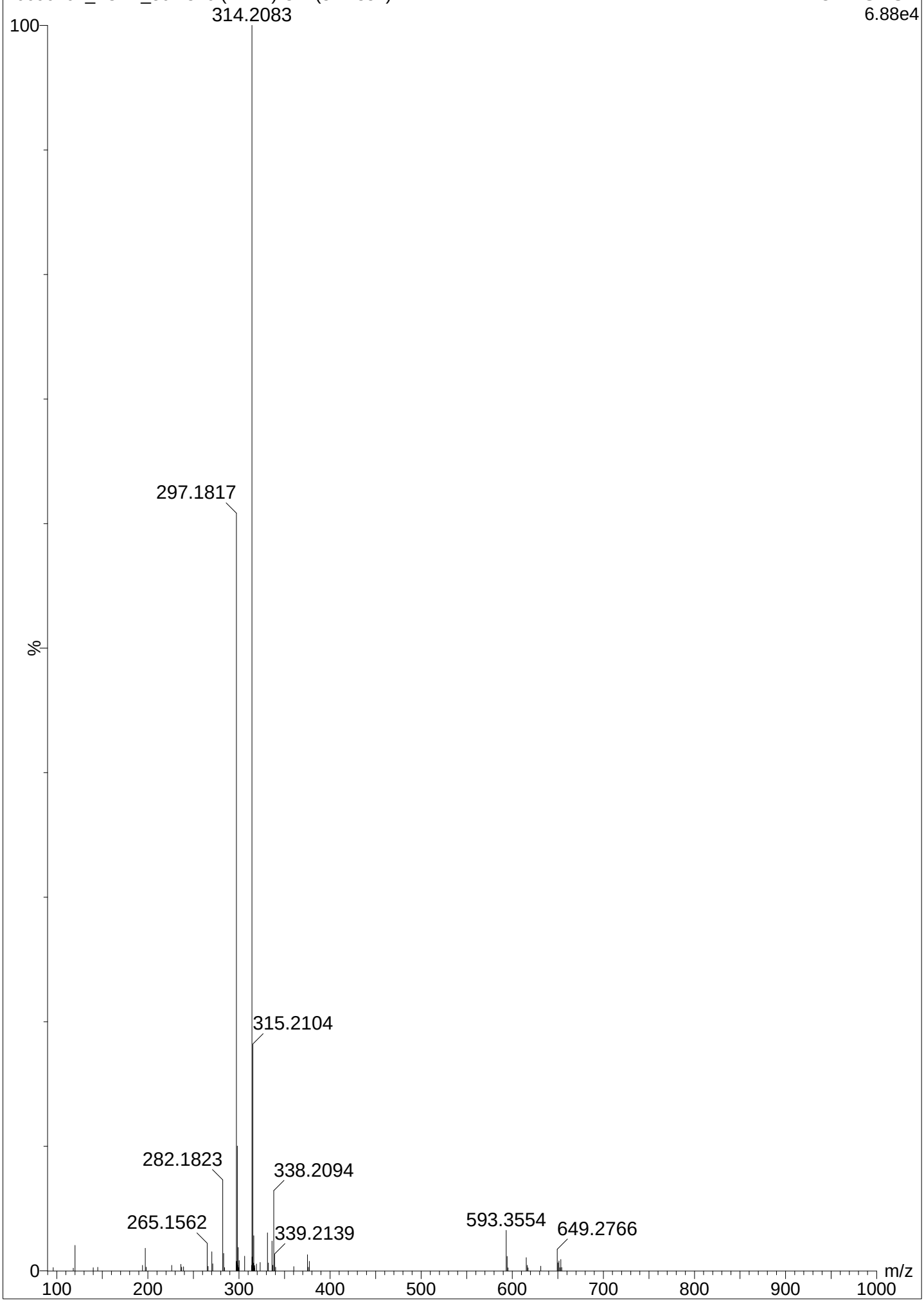


SN1014430621 **AZ13212451** **Henrik Sörensen**

20090701_LCTP_504 346 (2.124) Cm (342:352)

1: TOF MS ES+

6.88e4



Single Mass Analysis

Tolerance = 30.0 PPM / DBE: min = -0.5, max = 50.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

1 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

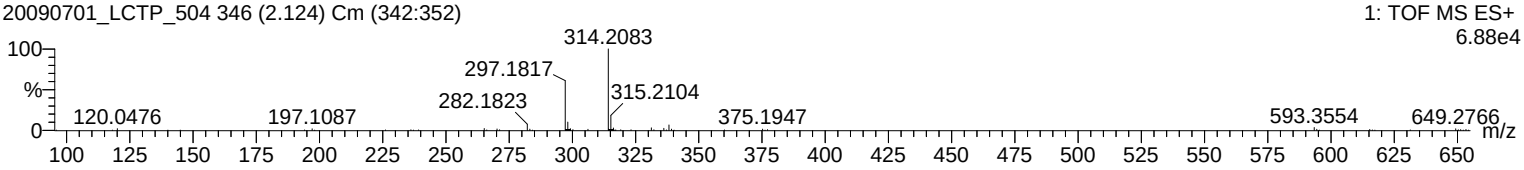
Elements Used:

C: 15-15 H: 24-25 N: 2-2 O: 4-4

SN1014430621 AZ13212451 Henrik Sörensen

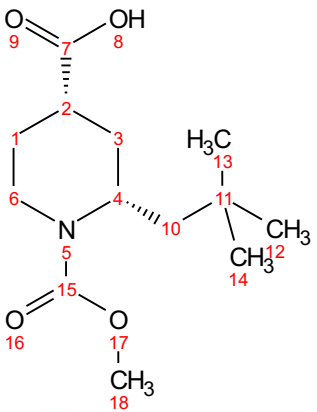
20090701_LCTP_504 346 (2.124) Cm (342:352) 1: TOF MS ES+

6.88e4



Minimum:				-0.5		
Maximum:		200.0	30.0	50.0		
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Formula**
297.1817	297.1814	0.3	1.0	4.5	65.8	C15 H25 N2 O4

Book Reference: EN06958-31-001
Analytical Number: SN1045263390
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 400.03MHz (nmr2)
Spinner: 45
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Mon Oct 07 16:54:38 CEST 2013
Extension:



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Book Reference: EN06953-31-001
Analytical Number: SN1043263390
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 100.59MHz (nmr2)
Spinner: 45
Experiment Name: Carbon_night
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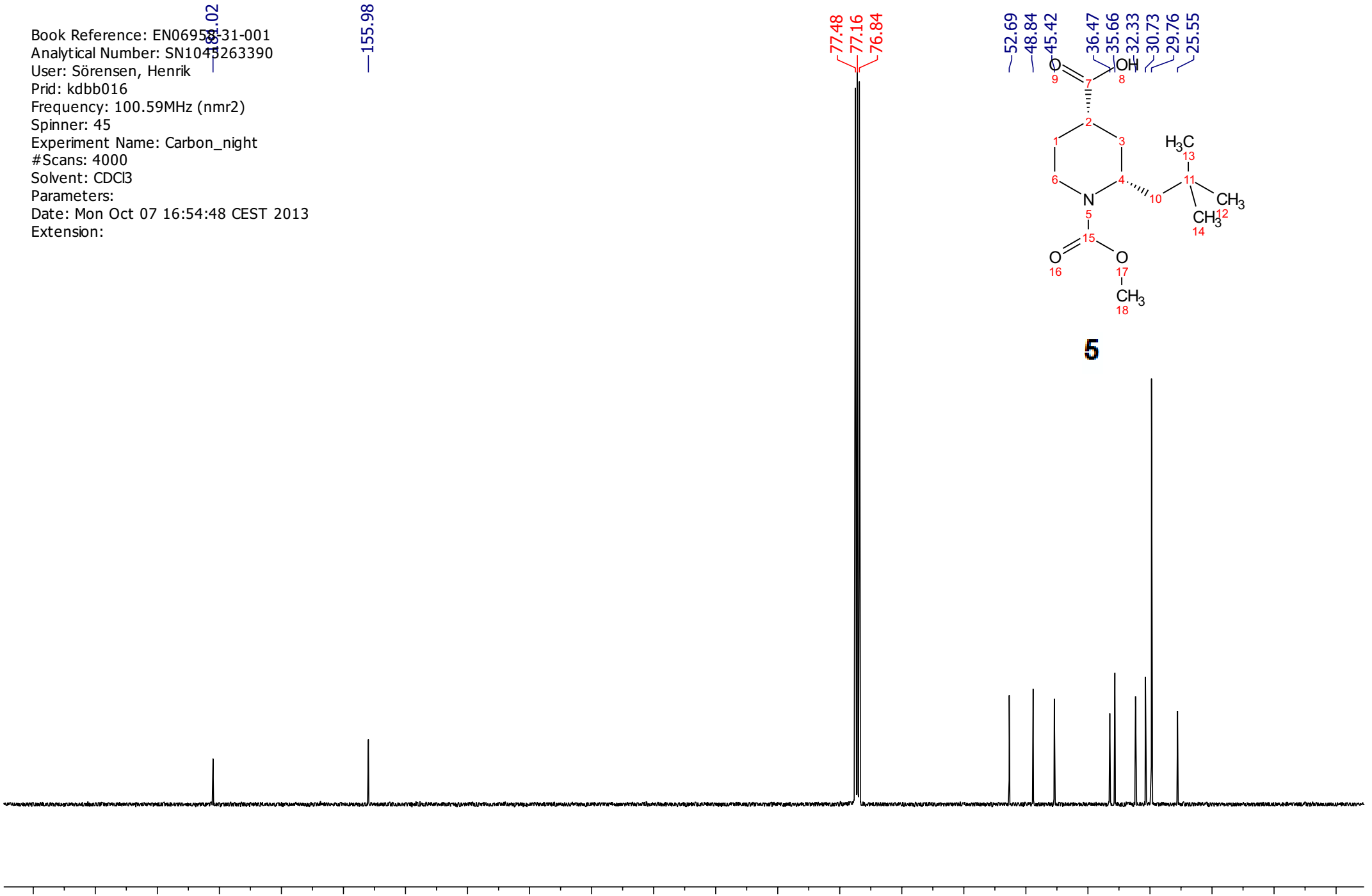
Solvent: CDCl3
Parameters:
Date: Mon Oct 07 16:54:48 CEST 2013
Extension:



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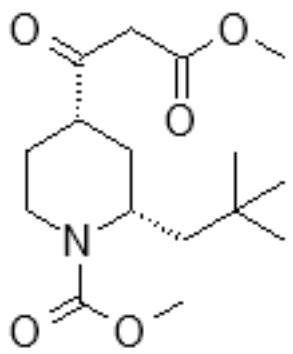
Sample_Id SN1014430517;
EN EN02629-35-001;
filename SN1014430517_rotavap_h1nmr_1;
experiment h1nmr;
operator Henrik Sorensen;
chemist Henrik Sorensen;
automation SMS;
Sample# 58;
prid kdbb016;
date Jun 9 2009;
solvent cdcl3;
hostname nmr2;
NMR Spectrometer 400 MHz;
probe auto_x_400;
nt 16;
ct 16;
site AstraZeneca R&D Molndal;



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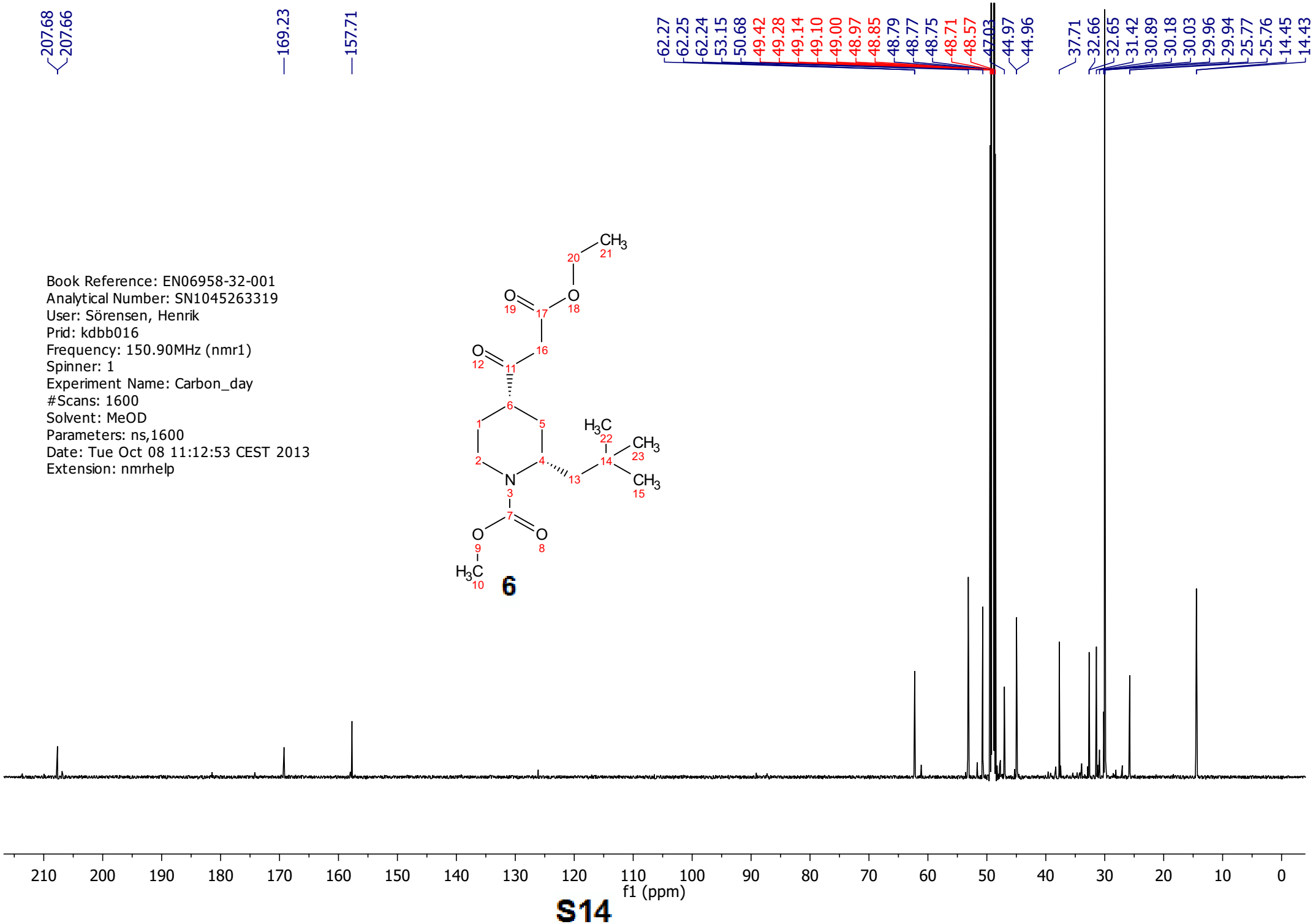
207.68
207.66
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157.71
62.27
62.25
62.24
53.15
50.68
49.42
49.28
49.14
49.10
49.00
48.97
48.85
48.79
48.77
48.75
48.71
48.57
47.03
44.97
44.96
37.71
32.66
32.65
31.42
30.89
30.18
30.03
29.96
29.94
25.77
25.76
14.45
14.43
Book Reference: EN06958-32-001
Analytical Number: SN1045263319
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 150.90MHz (nmr1)
Spinner: 1
Experiment Name: Carbon_day
#Scans: 1600
Solvent: MeOD
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Date: Tue Oct 08 11:12:53 CEST 2013
Extension: nmrhelp
6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

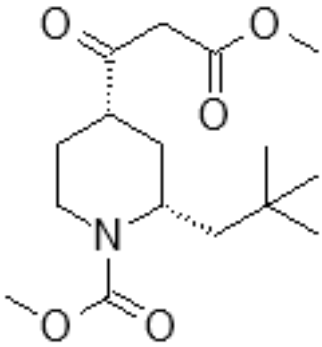
Purity Analysis and Accurate Mass Report

Submitter: Henrik Sörensen

Sample ID: SN1014430517

Compound Name: AZ13212294

Project: NOFI



6

Results

Your sample was 87% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

The main impurity (11% at UV 210nm) did not ionize in ES+. As target compound has low absorbtion coefficient, this impurity might be overestimated when based on UV data.

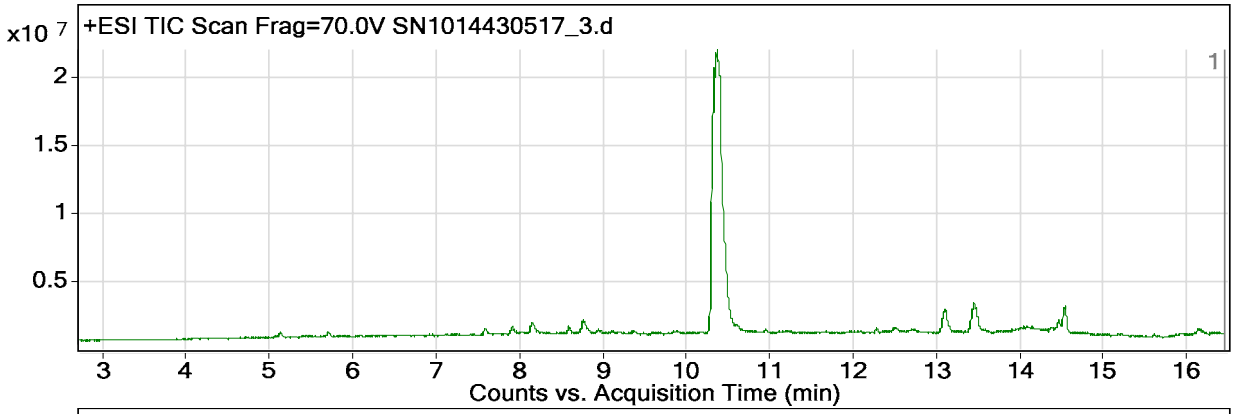
Instrumental setup

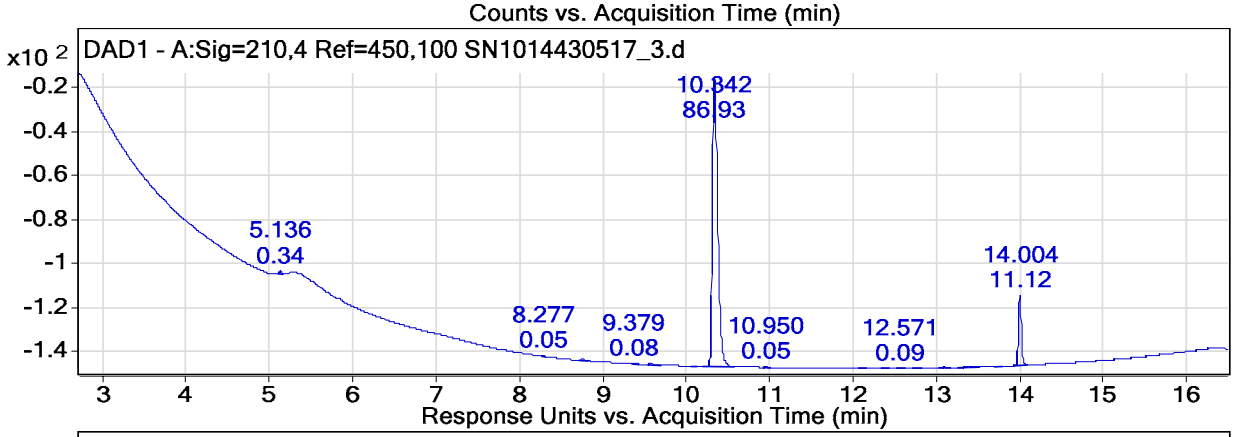
Column	Aquity UPLC BEH C18, 2.1mm×100mm, 1.7µm particles
Temperature	50ºC
Gradient	4% ACN to 95% ACN in 16 minutes.; 40 mM ammonia 6 mM ammonium carbonate, pH 10
Flow	0.54 ml/min
Injection volume	6 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Q-TOF 6530 Agilent

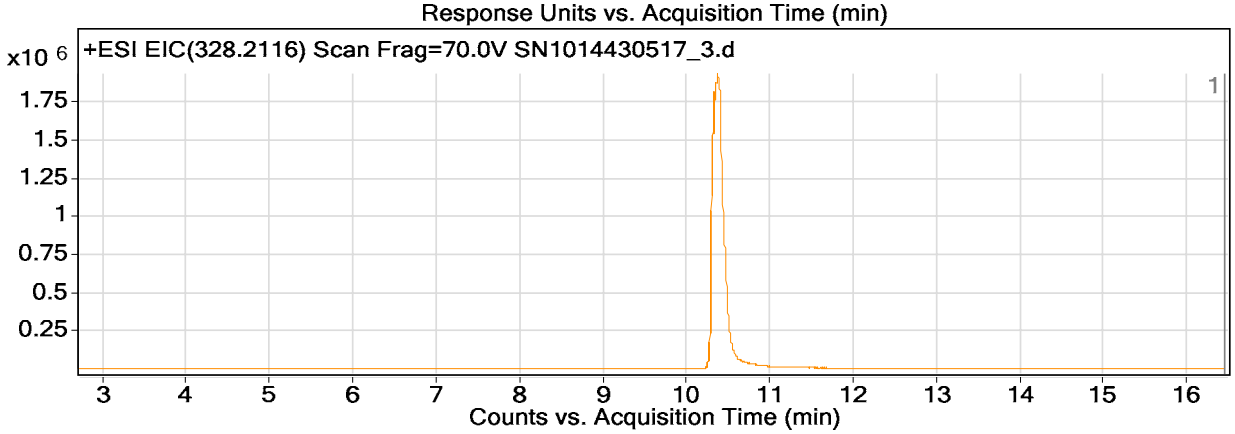
Gustaf Hulthe
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

Date: 2009-06-10

Qualitative Plot Window Report



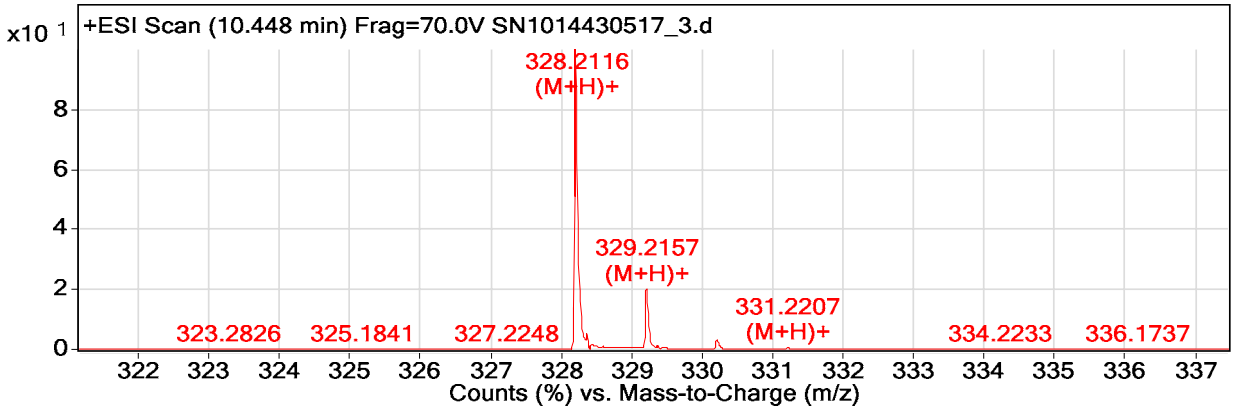




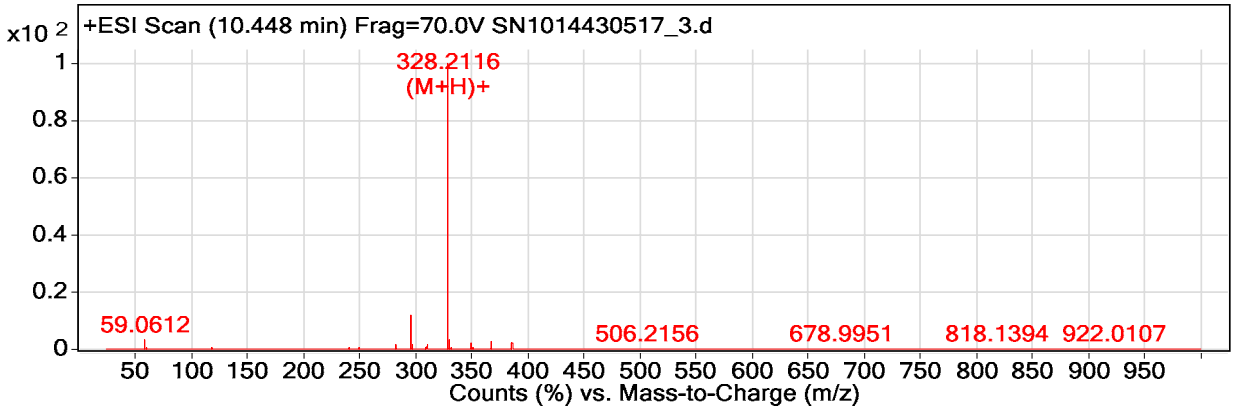
Peaks: DAD1 - A:Sig=210,4 Ref=450,100 (SN1014430517_3.d)

Peak	RT	Area	Height	Width	Area Sum%
1	5.136	2.3	1.42	0.026	0.34
2	8.277	0.31	0.14	0.036	0.05
3	8.76	2.21	0.75	0.045	0.33
4	9.379	0.52	0.19	0.04	0.08
5	9.578	1.79	0.5	0.049	0.27
6	10.091	0.38	0.17	0.035	0.06
7	10.226	0.32	0.16	0.033	0.05
8	10.342	584.82	131.57	0.069	86.93
9	10.95	0.37	0.15	0.038	0.05
10	12.102	0.45	0.18	0.036	0.07
11	12.384	0.57	0.2	0.041	0.09
12	12.571	0.59	0.22	0.041	0.09
13	12.756	0.32	0.09	0.052	0.05
14	13.101	0.66	0.18	0.051	0.1
15	13.353	0.51	0.16	0.048	0.08
16	13.456	1.42	0.34	0.063	0.21
17	13.75	0.4	0.16	0.035	0.06
18	14.004	74.78	31.45	0.037	11.12

Qualitative Plot Window Report



Qualitative Plot Window Report



MS Formula Results: + Scan (10.448 min) (SN1014430517_3.d)

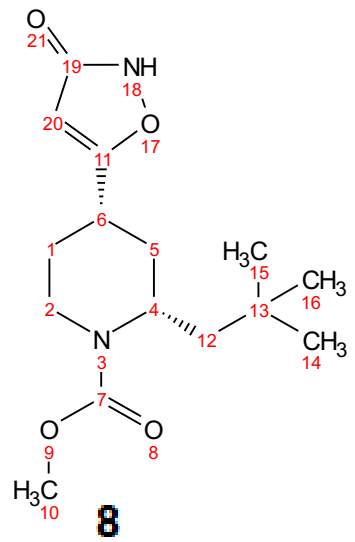
m/z	Ion	Formula	Abundance
328.2116	(M+H)+	C17 H30 N O5	1026782.8

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C17 H29 N O5	C17 H30 N O5	328.2118	99.31		327.2044	327.2046	0.64	0.64	98.9	98.65	99.88	328.2116	4

Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	81.72	328.2116	328.2118	0.66	80.7
2	20.47	19.29	15.76	329.2157	329.2151	-1.63	16.52
3	3.08	2.79	2.28	330.2182	330.2176	-1.97	2.48
4	0.37	0.3	0.24	331.2207	331.2202	-1.46	0.3

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C21 H26 F N O	C21 H27 F N O	328.2071	76.99		327.2044	327.1998	-13.82	13.82	93	98.73	56.51	328.2116	9
☐	C24 H25 N	C24 H26 N	328.206	64.71		327.2044	327.1987	-17.31	17.31	76.16	98.74	40.83	328.2116	13

Book Reference: EN06958-28-001
Analytical Number: SN1045263168
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 400.03MHz (nmr2)
Spinner: 62
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Thu Oct 03 12:15:02 CEST 2013
Extension:

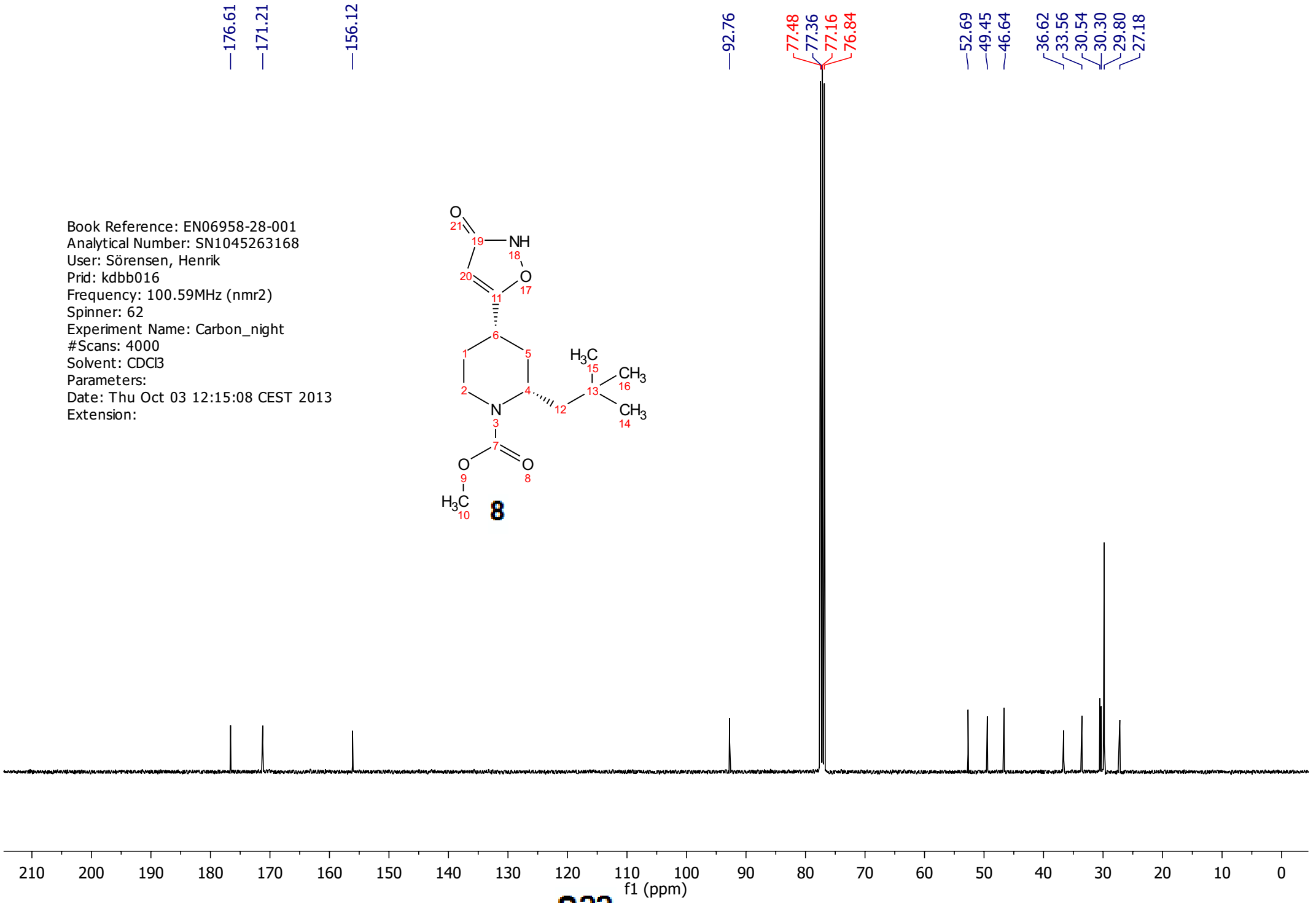


8

0.97 1.00 1.00 2.97 0.98 0.98 1.99 1.98 1.00 0.99 8.95

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

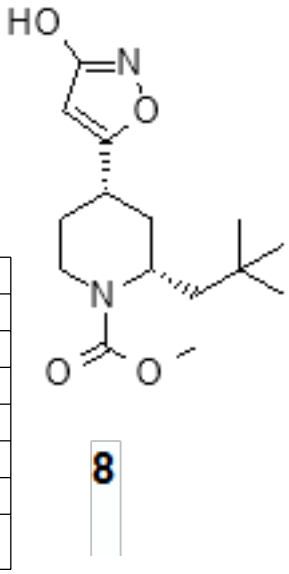
f1 (ppm)


176.61
171.21
156.12
92.76
77.48
77.36
77.16
76.84
52.69
49.45
46.64
36.62
33.56
30.54
30.30
29.80
27.18
Book Reference: EN06958-28-001
Analytical Number: SN1045263168
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 100.59MHz (nmr2)
Spinner: 62
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Thu Oct 03 12:15:08 CEST 2013
Extension:
8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

AstraZeneca **EnantioBase** Analysis Report

Sample Information

Sample ID	Compound name	Project name
SN1014430621	AZ13212451	NOFI

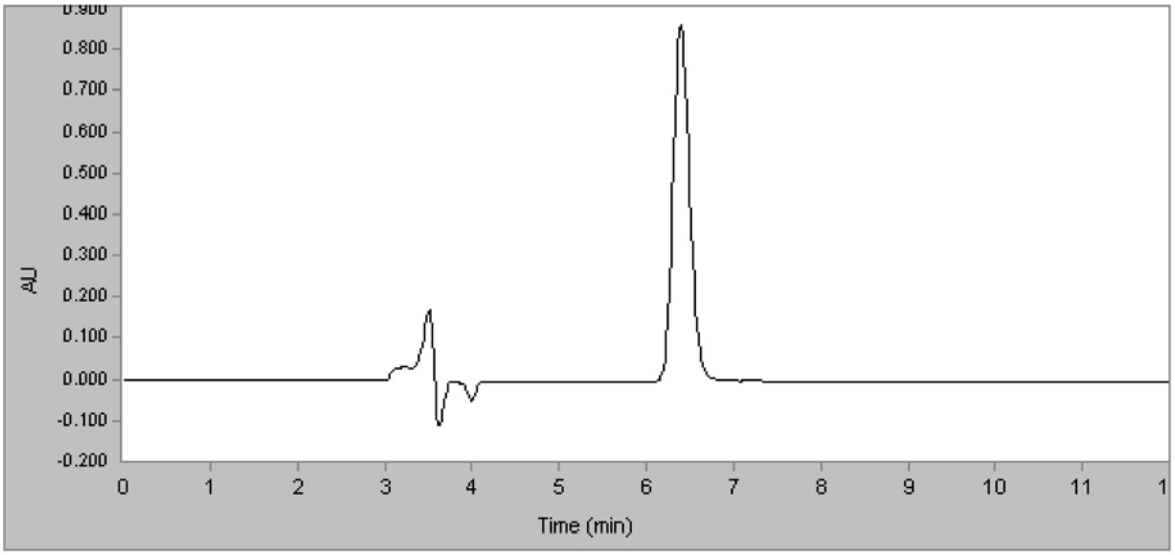


Analytical Conditions

Column	Dimensions (mm)	Particle Size (µm)
Chiralpak IC	250 * 4.6	5
Mobile Phase		
Heptan/IPA/FA 60/40/0.1		
Flow (ml/min)	**Detection (nm)**	**Temperature (C)**
1 ml/min	PDA 220.0 nm	RT
Comment		

Analytical Result

UV Chromatogram

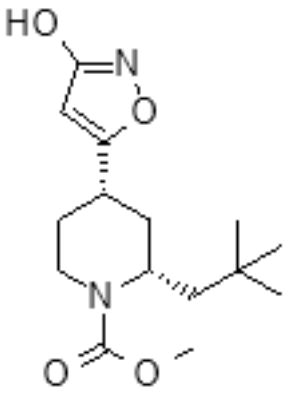


Retention Time	Area	Area %	K'	N	USP Resolution
2.967	0		0.000		
5.137	2489		0.731		
6.398	11434238		1.156		4.253837e+000

ee: 99.9%

Chemist Signature

Print Date
2009-06-13



Purity Analysis and Accurate Mass Report

Submitter: Henrik Sörensen

Sample ID: SN1014430621

Compound Name: AZ13212451

Project: NOFI

8

Results

SN1014430621: Your sample was 99% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

Instrumental setup

Column	Acquity UPLC™ BEH C18 100mm×2.1mm, 1.7µm particles
Temperature	60ºC
Gradient	2% ACN to 95% ACN in 6 minutes; 47mM NH_4 6.5mm NH_4HCO_3, pH 10
Flow	0.8 mL/min
Injection volume	3 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Waters LCTP
Lockmass	Leucine Enkephaline C28H37N5O7

Comments

Signature: _____ Date: 2009-07-02

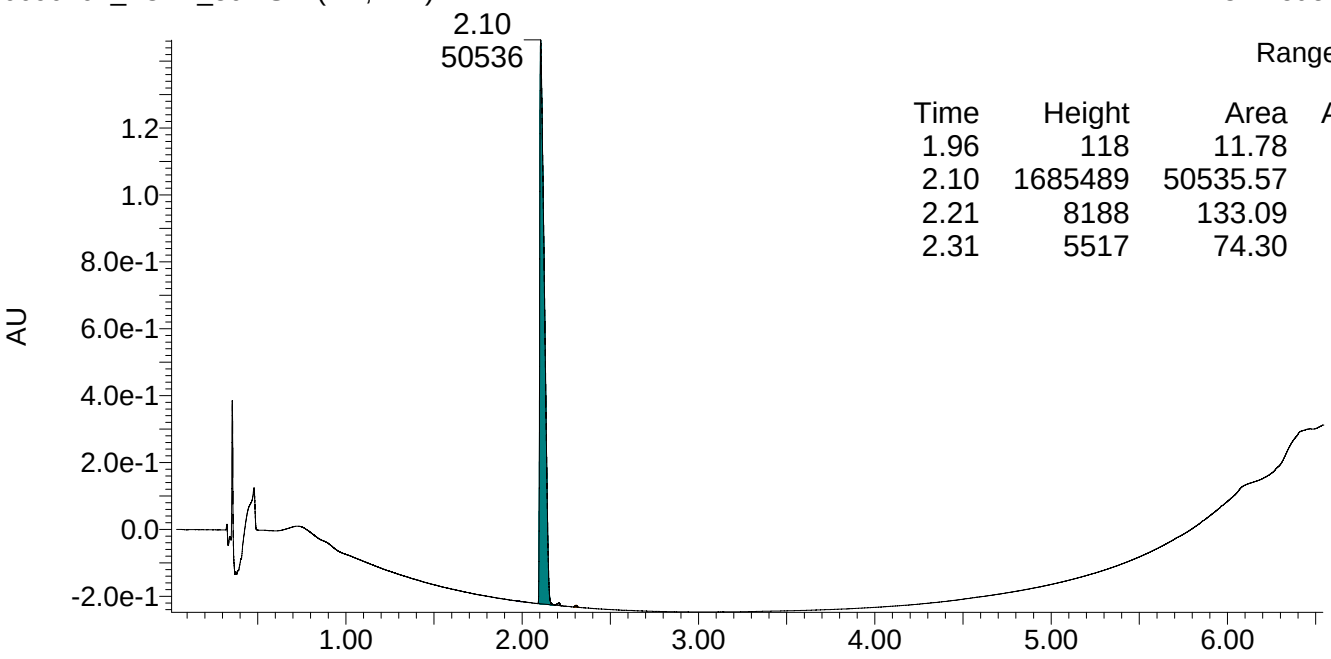
Stina Kiellarson
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

SN1014430621 **AZ13212451** **Henrik Sörensen**

20090701_LCTP_504 Sm (Mn, 2x2)

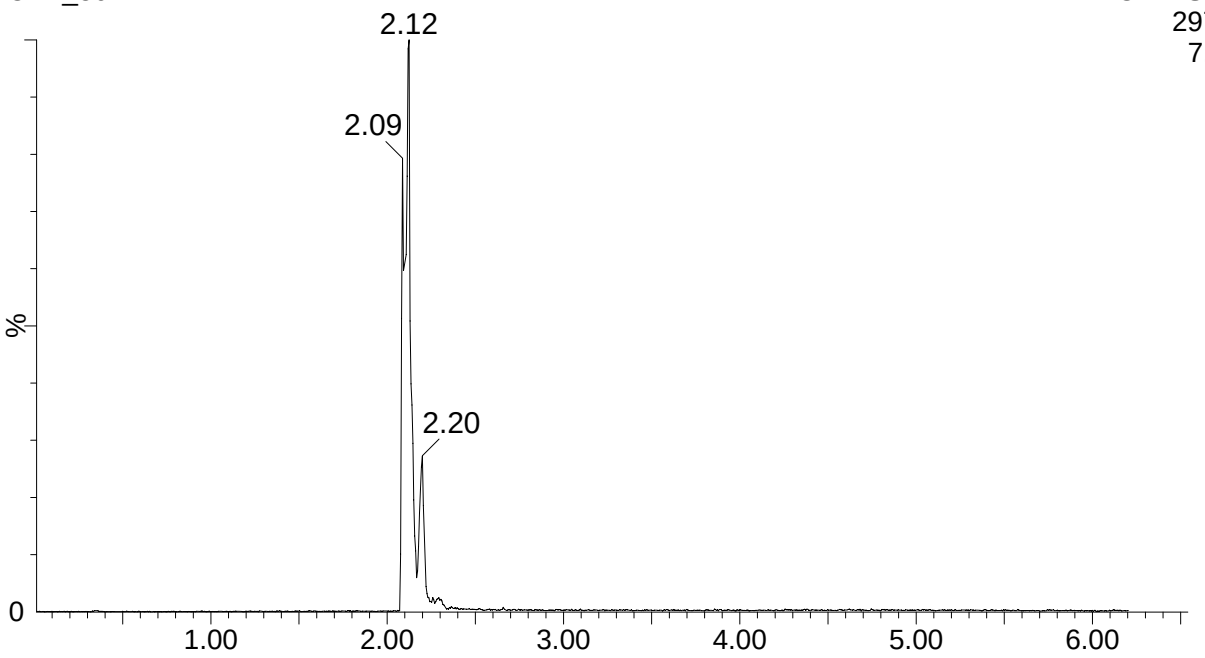
3: Diode Array
210
Range: 1.71

Time	Height	Area	Area%
1.96	118	11.78	0.02
2.10	1685489	50535.57	99.57
2.21	8188	133.09	0.26
2.31	5517	74.30	0.15



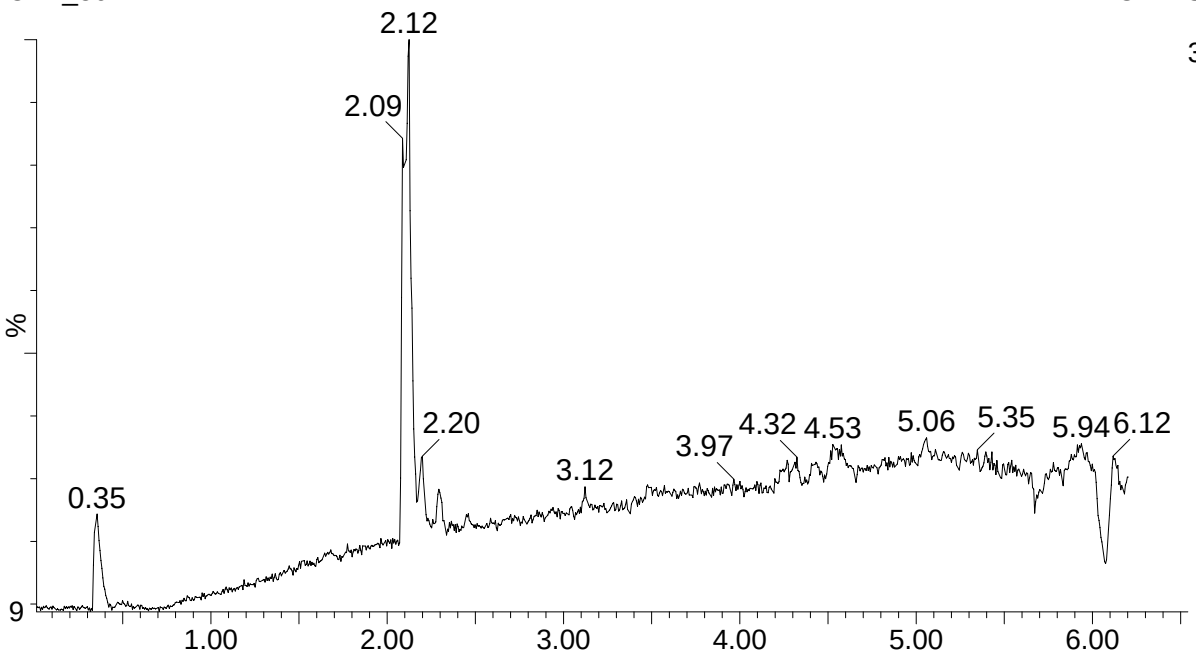
20090701_LCTP_504

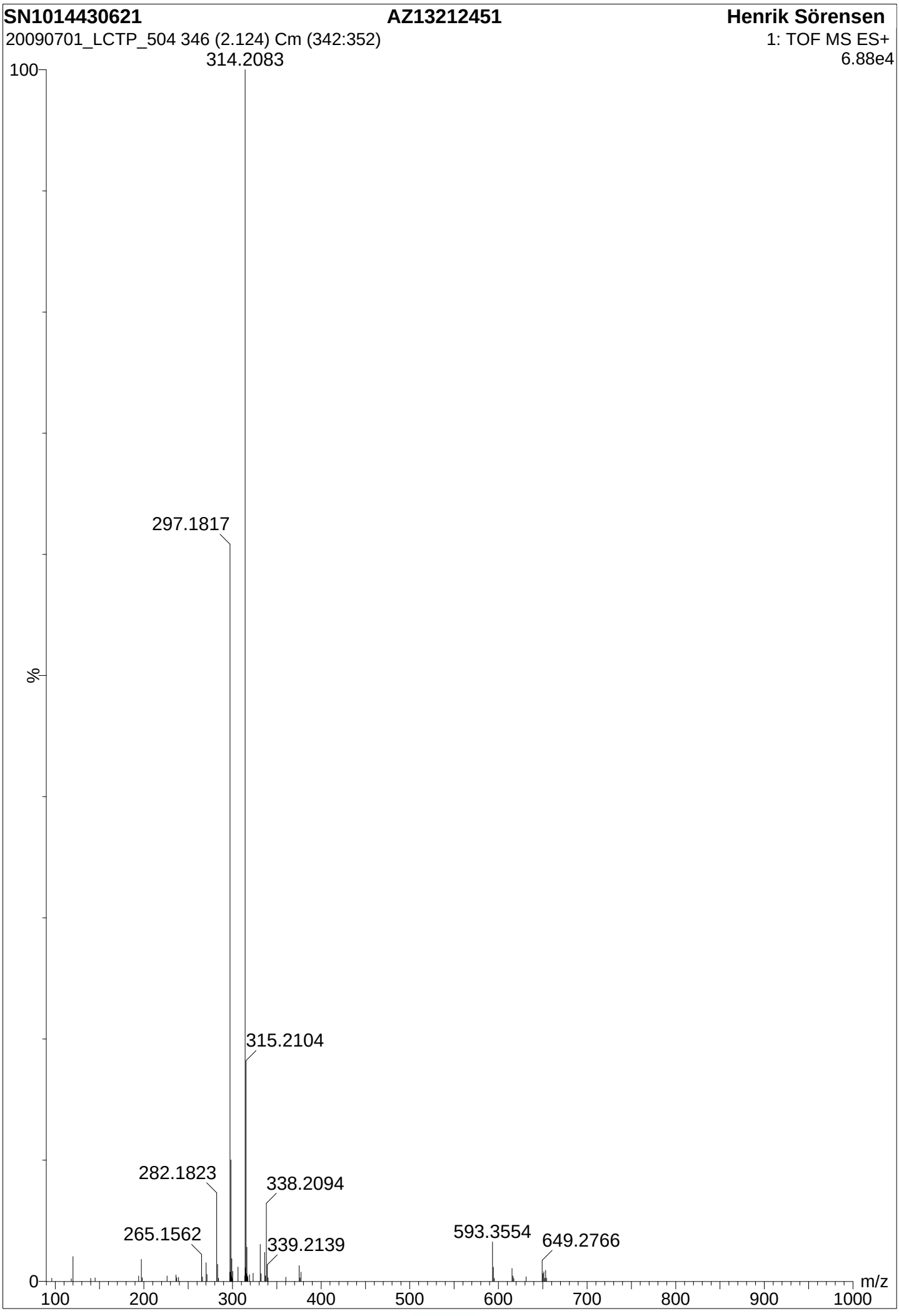
1: TOF MS ES+
297.182
7.62e3



20090701_LCTP_504

1: TOF MS ES+
TIC
3.74e4




SN1014430621
AZ13212451
Henrik Sörensen
20090701_LCTP_504 346 (2.124) Cm (342:352)
1: TOF MS ES+
6.88e4
314.2083
297.1817
315.2104
282.1823
338.2094
265.1562
339.2139
593.3554
649.2766
100
%
0
100
200
300
400
500
600
700
800
900
1000
m/z

Single Mass Analysis

Tolerance = 30.0 PPM / DBE: min = -0.5, max = 50.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

1 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

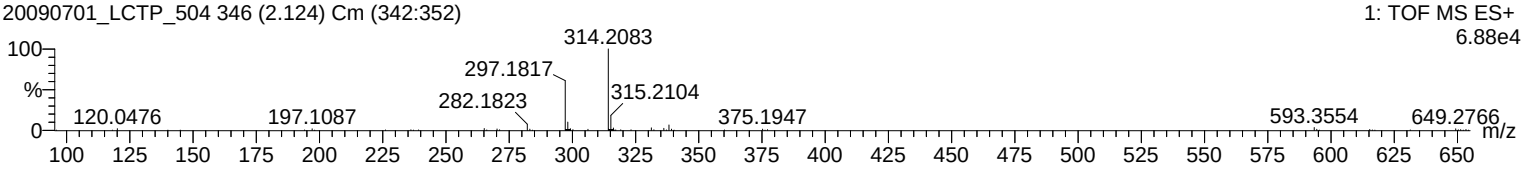
Elements Used:

C: 15-15 H: 24-25 N: 2-2 O: 4-4

SN1014430621 AZ13212451 Henrik Sörensen

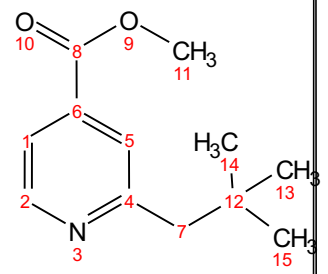
20090701_LCTP_504 346 (2.124) Cm (342:352) 1: TOF MS ES+

6.88e4

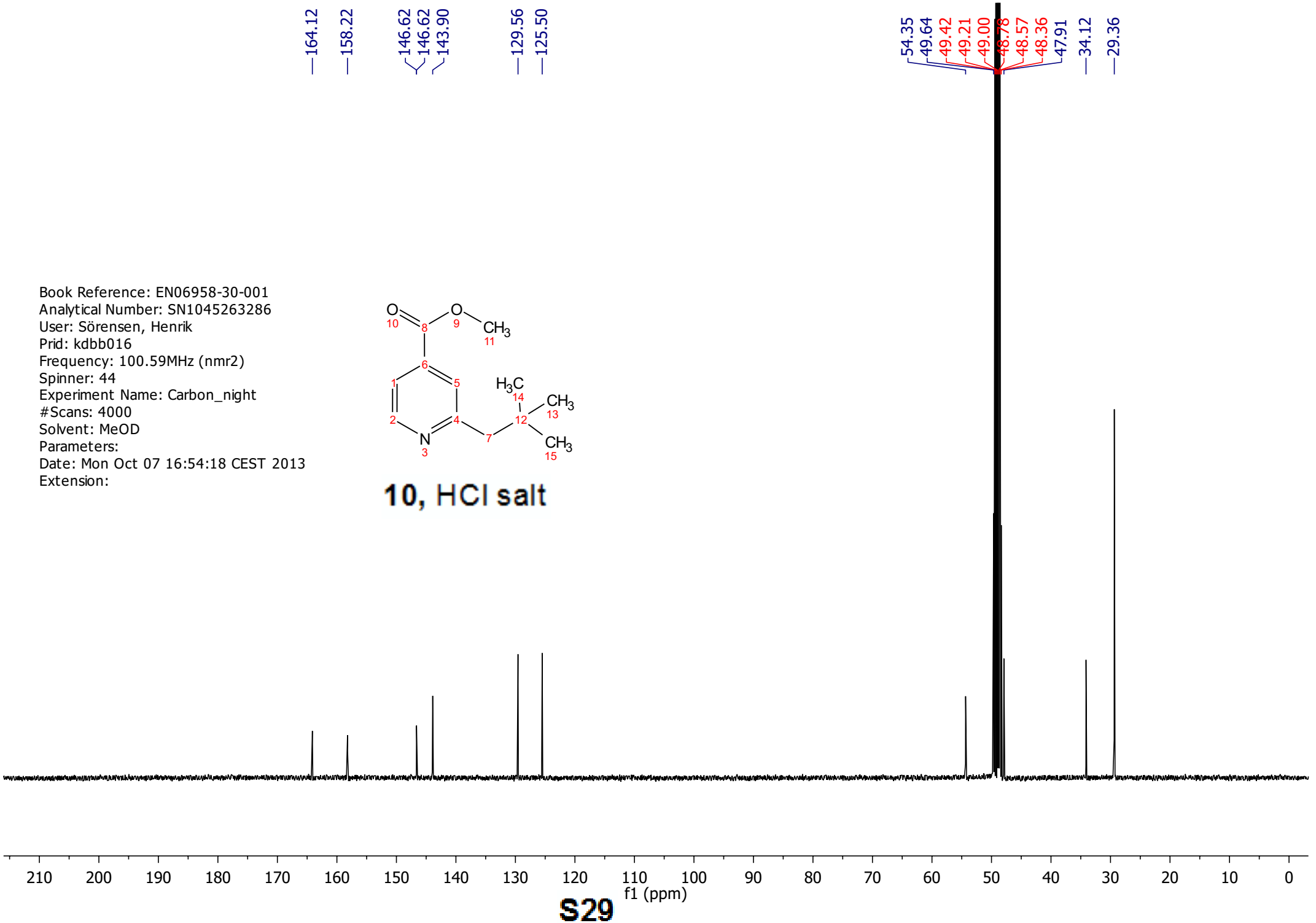


Minimum:				-0.5		
Maximum:		200.0	30.0	50.0		
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Formula**
297.1817	297.1814	0.3	1.0	4.5	65.8	C15 H25 N2 O4

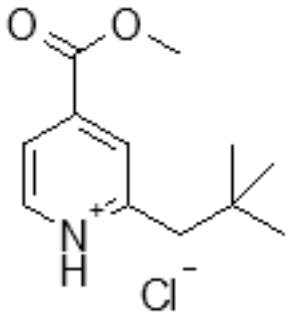
Book Reference: EN06958-30-001
Analytical Number: SN1045263286
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 400.03MHz (nmr2)
Spinner: 44
Experiment Name: Proton_day
#Scans: 16
Solvent: MeOD
Parameters:
Date: Mon Oct 07 16:54:01 CEST 2013
Extension:



10, HCl salt


164.12
158.22
146.62
146.62
143.90
129.56
125.50
54.35
49.64
49.42
49.21
49.00
48.78
48.57
48.36
47.91
34.12
29.36
Book Reference: EN06958-30-001
Analytical Number: SN1045263286
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 100.59MHz (nmr2)
Spinner: 44
Experiment Name: Carbon_night
#Scans: 4000
Solvent: MeOD
Parameters:
Date: Mon Oct 07 16:54:18 CEST 2013
Extension:
10, HCl salt
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Purity Analysis and Accurate Mass Report



Submitter: Henrik Sörensen

Sample ID: SN1014429979

Compound Name: AZ13162519

Project: NOFI

Results

10, HCl salt

Your sample was 97.9% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

The two largest impurities are:

10.45 min	**1.1%**	**222.1489**	**C13 H19 N O2**
13.10 min	**0.6%**	**264.1958**	**C16 H25 N O2**

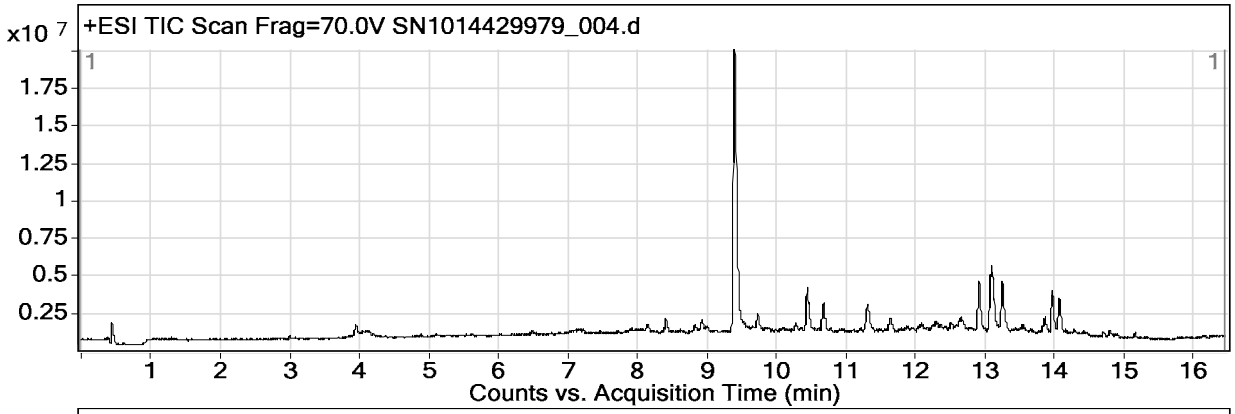
Instrumental setup

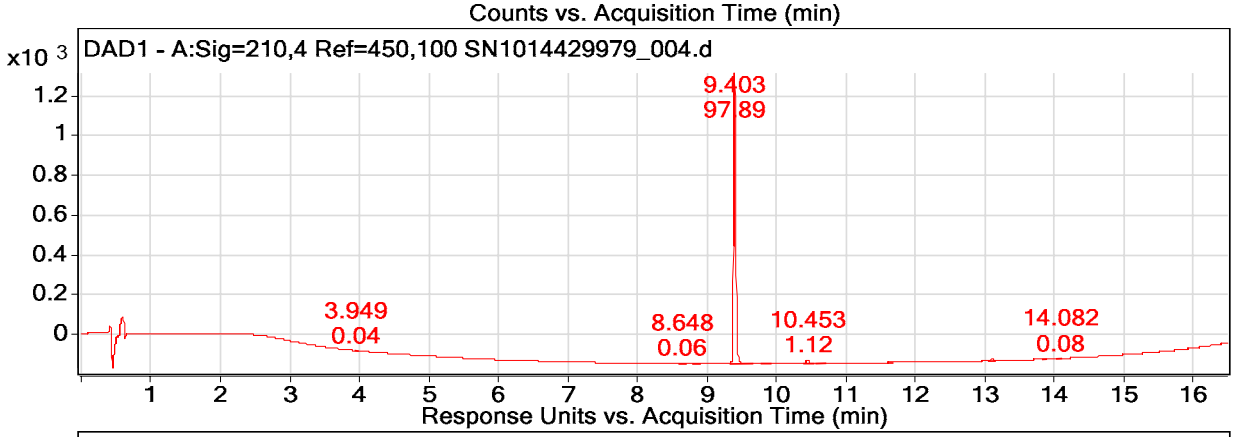
Column	Aquity UPLC BEH C18, 2.1mm×100mm, 1.7µm particles
Temperature	50ºC
Gradient	4% ACN to 95% ACN in 16 minutes.; 40 mM ammonia 6 mM ammonium carbonate, pH 10
Flow	0.54 ml/min
Injection volume	5 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Q-TOF 6530 Agilent

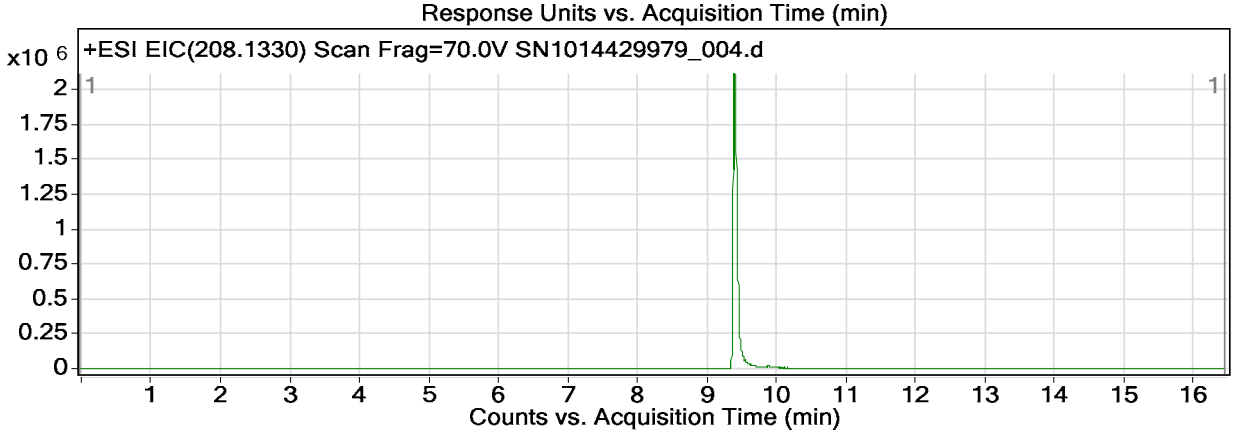
Gustaf Hulthe
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

Date: 2009-05-19

Qualitative Plot Window Report



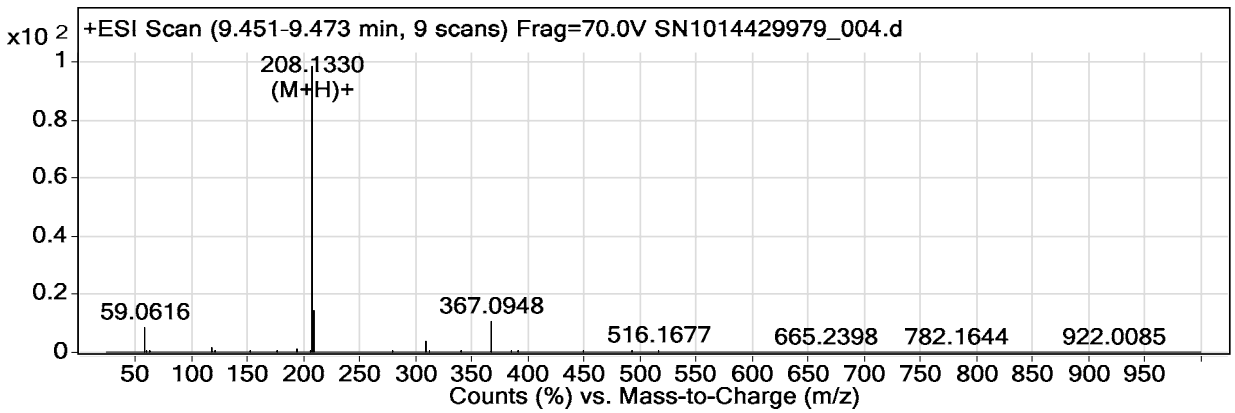




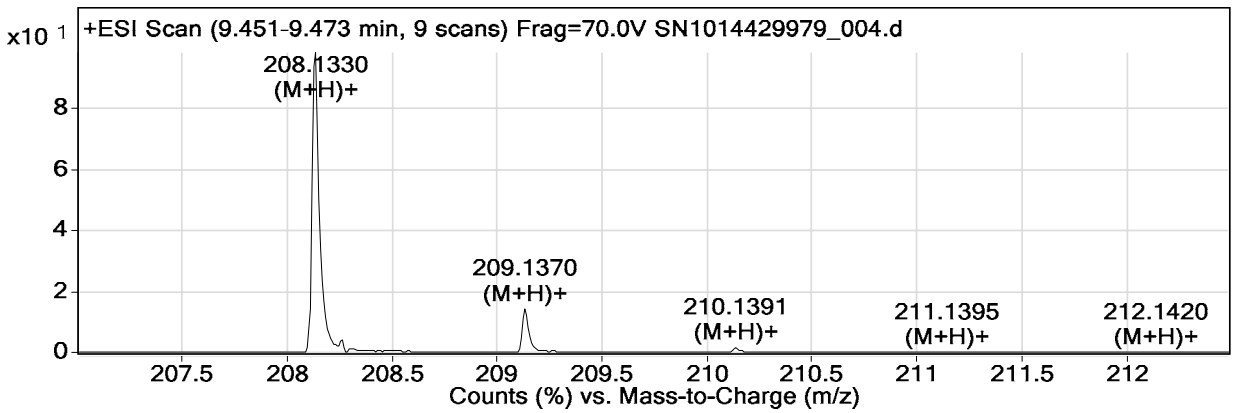
Peaks: DAD1 - A:Sig=210,4 Ref=450,100 (SN1014429979_004.d)

Peak	RT	Area	Height	Width	Area Sum%
1	3.949	1.51	0.87	0.027	0.04
2	8.648	2.33	0.98	0.038	0.06
3	8.833	0.75	0.26	0.045	0.02
4	9.403	3586.06	1464.77	0.038	97.89
5	9.886	1.77	0.7	0.038	0.05
6	10.453	41	16.83	0.037	1.12
7	10.672	2.23	0.89	0.039	0.06
8	11.645	1.53	0.61	0.04	0.04
9	13.104	22.26	9.15	0.038	0.61
10	13.876	0.87	0.36	0.037	0.02
11	14.082	2.97	1.29	0.037	0.08

Qualitative Plot Window Report



Qualitative Plot Window Report



MS Formula Results: + Scan (9.451-9.473 min) (SN1014429979_004.d)

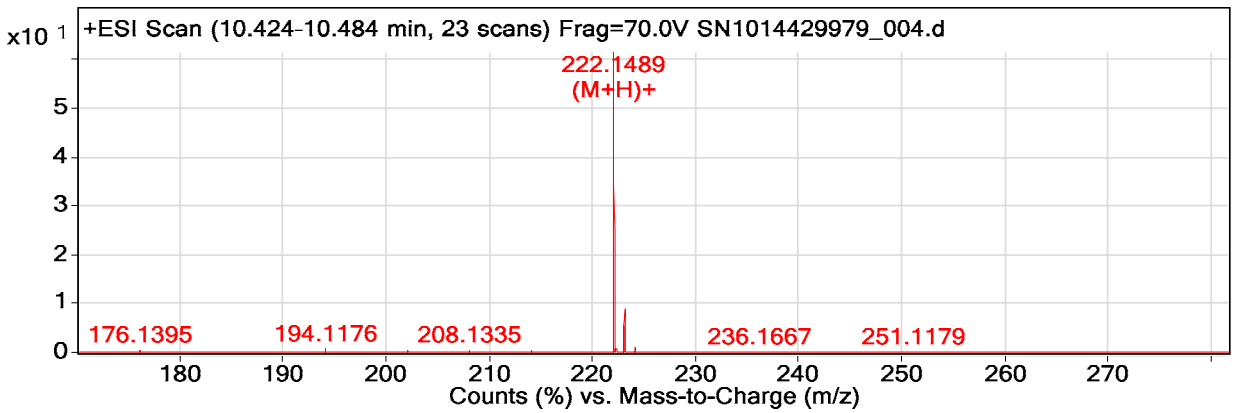
m/z	Ion	Formula	Abundance
208.133	(M+H)+	C12 H18 N O2	485729.1

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C12 H17 N O2	C12 H18 N O2	208.1332	98.13		207.1257	207.1259	0.94	0.94	99.48	93.88	99.45	208.133	5

Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	86.97	208.133	208.1332	0.95	86.38
2	14.35	13.63	11.85	209.137	209.1364	-2.63	12.39
3	1.31	1.27	1.1	210.1391	210.1389	-0.95	1.13
4	0.11	0.09	0.08	211.1395	211.1415	9.63	0.09

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C9 H18 F N O3	C9 H19 F N O3	208.1343	83.16		207.1257	207.1271	6.46	6.46	84.76	93.35	77.12	208.133	1
☐	C7 H18 Cl N5	C7 H19 Cl N5	208.1323	61.16		207.1257	207.1251	-3.2	3.2	0.02	69.23	93.81	208.133	1

Qualitative Plot Window Report



MS Formula Results: + Scan (10.424-10.484 min) (SN1014429979_004.d)

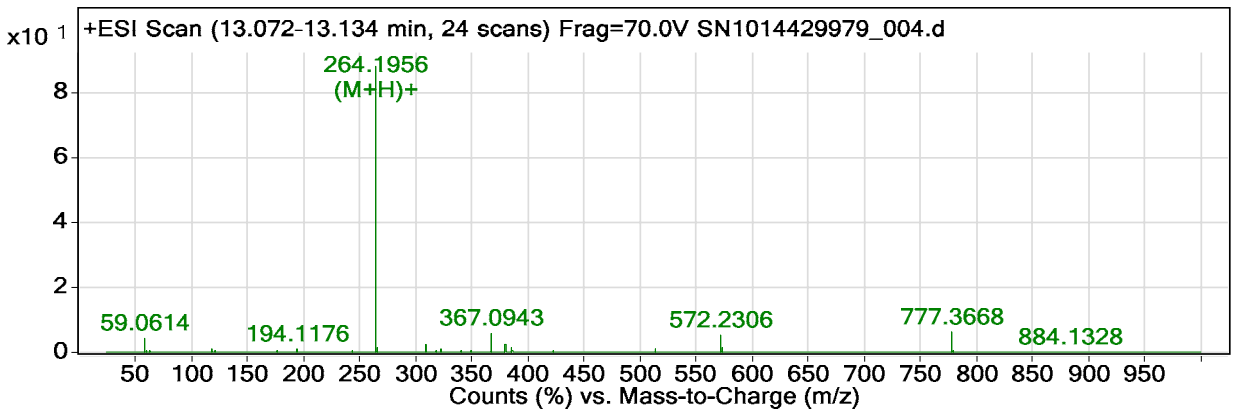
m/z	Ion	Formula	Abundance
222.1489	(M+H)+	C13 H20 N O2	298104.7

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C13 H19 N O2	C13 H20 N O2	222.1489	99.37		221.1416	221.1416	-0.03	0.03	99.96	97.41	100	222.1489	5

Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	86.02	222.1489	222.1489	-0.02	85.84
2	14.92	14.73	12.67	223.1526	223.1521	-2.18	12.81
3	1.44	1.42	1.22	224.1545	224.1547	1.02	1.24
4	0.13	0.1	0.09	225.1568	225.1573	2.08	0.11

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C10 H20 F N O3	C10 H21 F N O3	222.15	88.19		221.1416	221.1427	5.14	5.14	88.74	97.16	83.38	222.1489	1
☐	C8 H20 Cl N5	C8 H21 Cl N5	222.148	61		221.1416	221.1407	-3.91	3.91	0.02	76.15	90.02	222.1489	1

Qualitative Plot Window Report



MS Formula Results: + Scan (13.072-13.134 min) (SN1014429979_004.d)

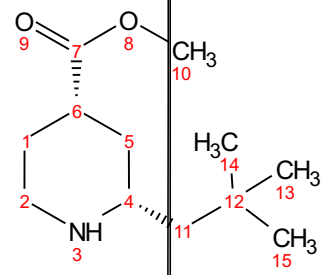
m/z	Ion	Formula	Abundance
264.1956	(M+H)+	C16 H26 N O2	429273.1

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C16 H25 N O2	C16 H26 N O2	264.1958	97.9		263.1884	263.1885	0.6	0.6	98.98	93.03	99.68	264.1956	5

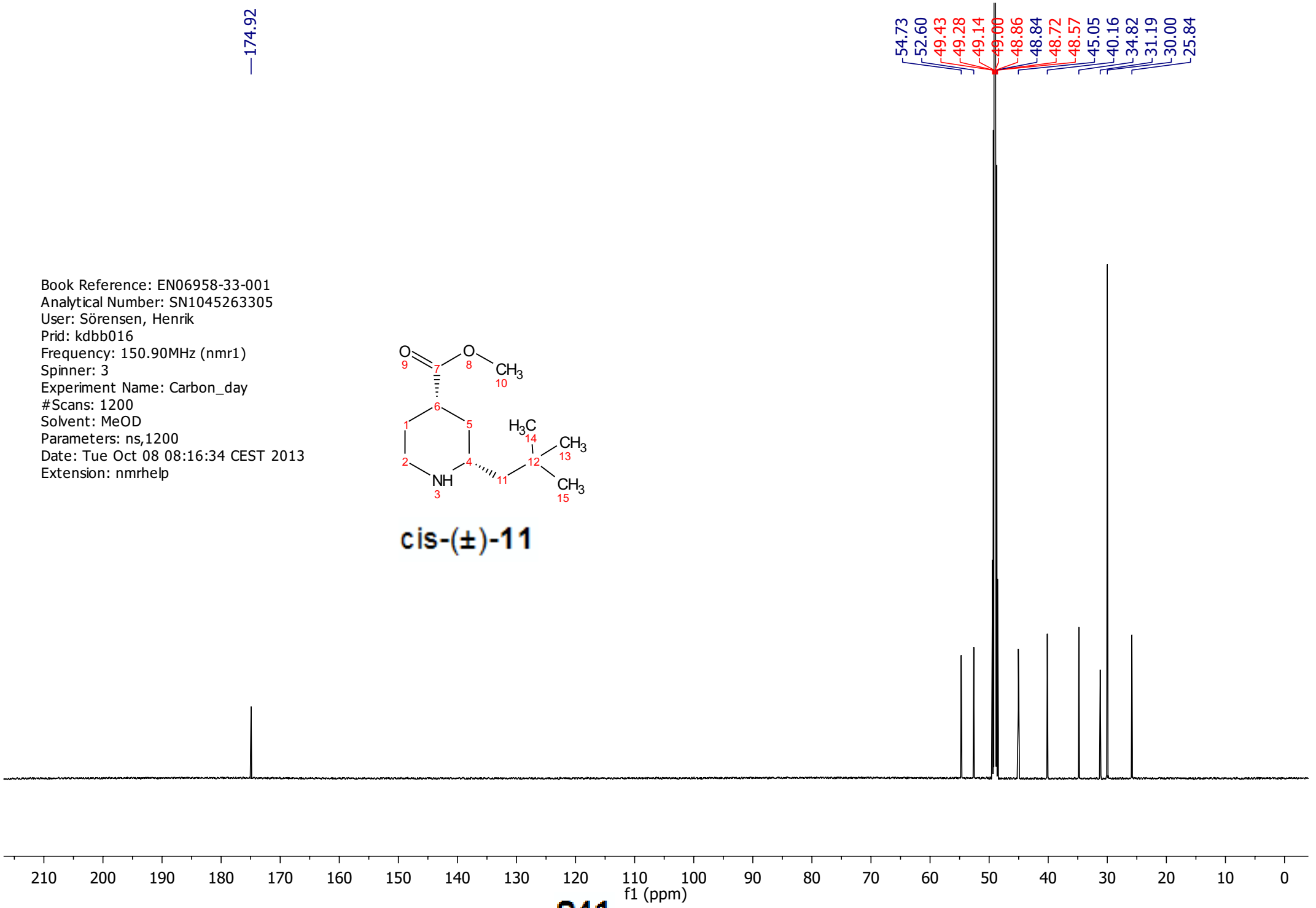
Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	83.23	264.1956	264.1958	0.62	82.5
2	19.12	18.05	15.02	265.1998	265.1991	-2.59	15.78
3	1.92	1.94	1.62	266.2024	266.2019	-1.96	1.59
4	0.16	0.16	0.13	267.2039	267.2045	2.3	0.13

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C13 H26 F N O3	C13 H27 F N O3	264.1969	84.63		263.1884	263.1897	4.94	4.94	84.75	92.73	80.5	264.1956	1
☐	C11 H26 Cl N5	C11 H27 Cl N5	264.195	61.1		263.1884	263.1877	-2.67	2.67	0.03	68.84	93.87	264.1956	1

Book Reference: EN06958-33-001
Analytical Number: SN1045263305
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 600.13MHz (nmr1)
Spinner: 3
Experiment Name: Proton_day
#Scans: 16
Solvent: MeOD
Parameters:
Date: Tue Oct 08 15:35:23 CEST 2013
Extension: nmrhelp



cis-(±)-11


174.92
54.73
52.60
49.43
49.28
49.14
49.00
48.86
48.84
48.72
48.57
45.05
40.16
34.82
31.19
30.00
25.84
Book Reference: EN06958-33-001
Analytical Number: SN1045263305
User: Sörensen, Henrik
Prid: kdbb016
Frequency: 150.90MHz (nmr1)
Spinner: 3
Experiment Name: Carbon_day
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Solvent: MeOD
Parameters: ns,1200
Date: Tue Oct 08 08:16:34 CEST 2013
Extension: nmrhelp
O
9
O
8
CH3
10
7
6
1
5
H3C
14
CH3
13
2
4
12
NH
3
11
CH3
15
cis-(±)-11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

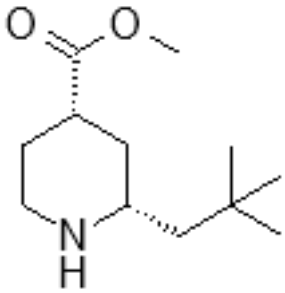
Purity Analysis and Accurate Mass Report

Submitter: Henrik Sörensen

Sample ID: SN1014430248

Compound Name: AZ13210702

Project: NOFI



cis-(±)-11

Results

Your sample was 98.7% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

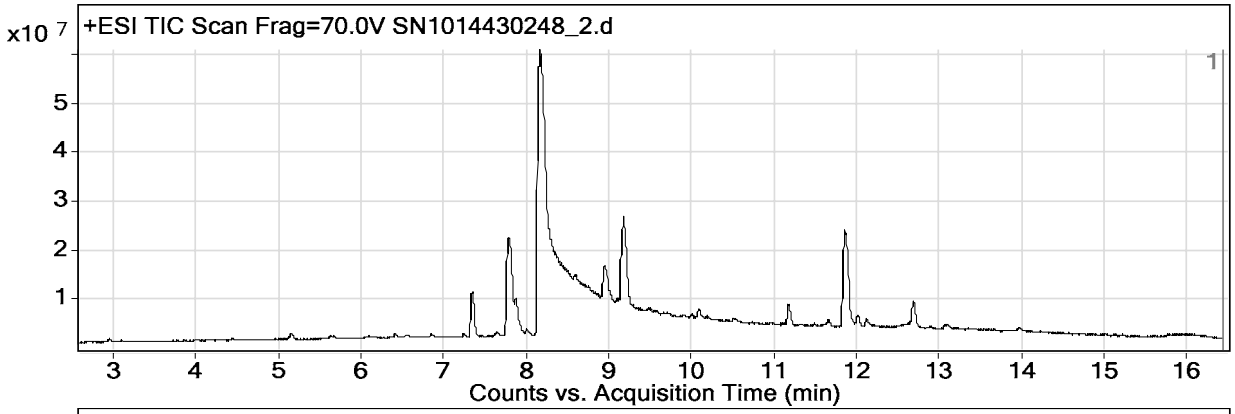
Instrumental setup

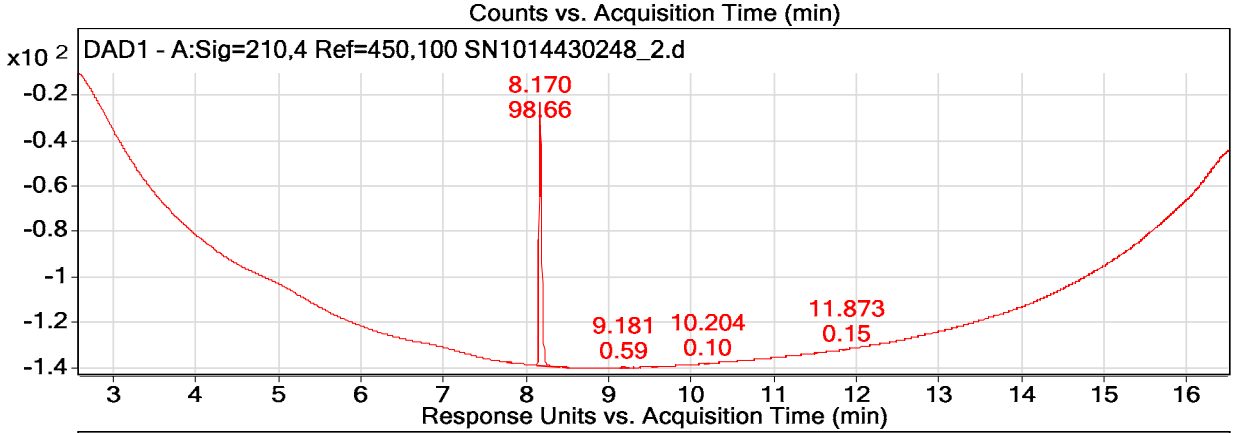
Column	Aquity UPLC BEH C18, 2.1mm×100mm, 1.7µm particles
Temperature	50ºC
Gradient	4% ACN to 95% ACN in 16 minutes.; 40 mM ammonia 6 mM ammonium carbonate, pH 10
Flow	0.55 ml/min
Injection volume	5 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Q-TOF 6530 Agilent

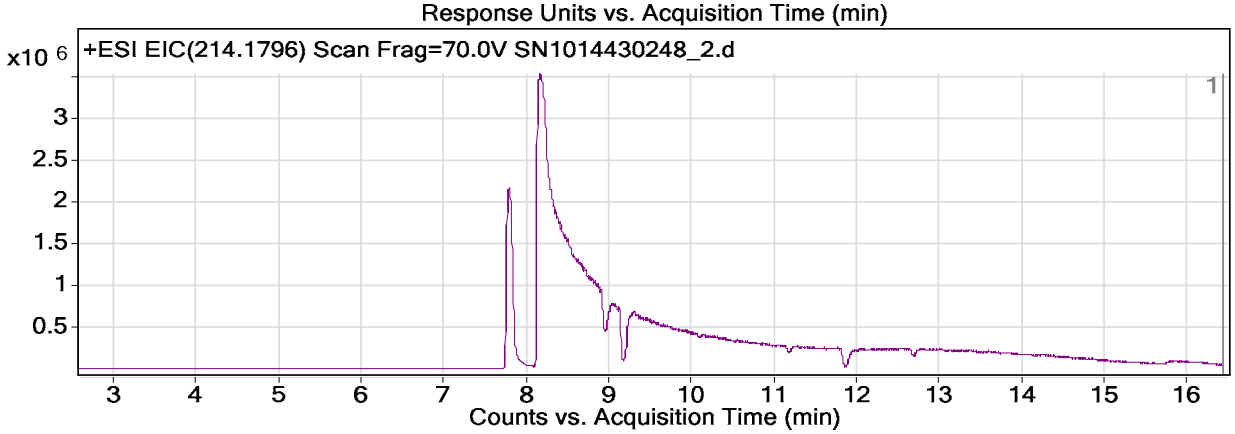
Gustaf Hulthe
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

Date: 2009-05-20

Qualitative Plot Window Report



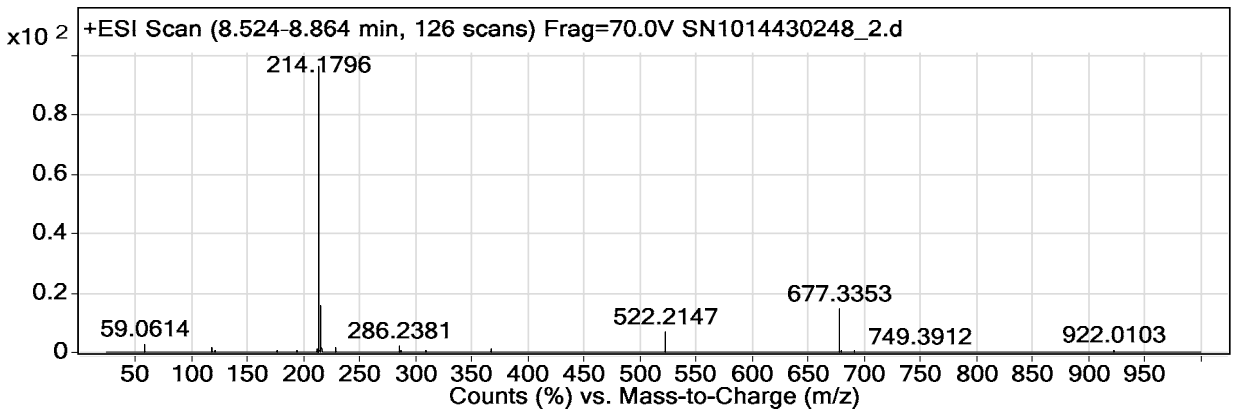




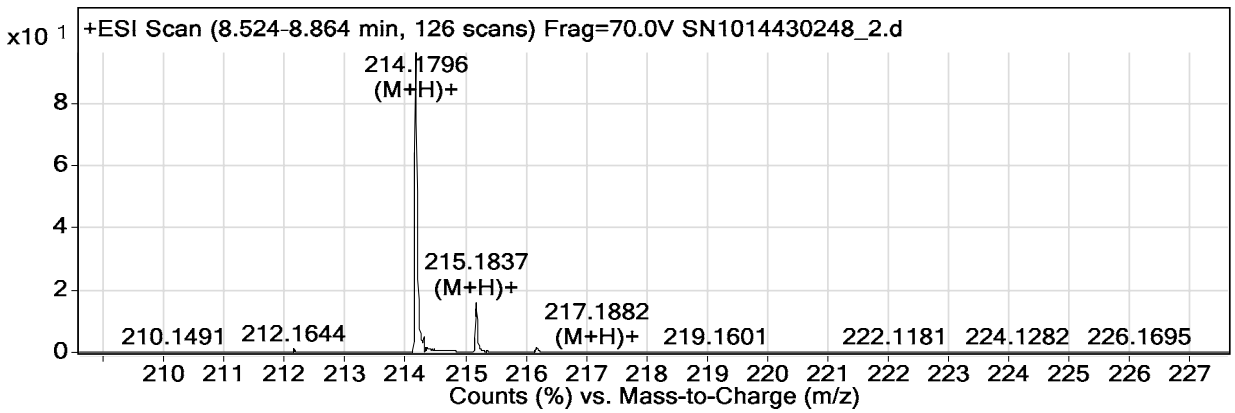
Peaks: DAD1 - A:Sig=210,4 Ref=450,100 (SN1014430248_2.d)

Peak	RT	Area	Height	Width	Area Sum%
1	7.79	0.71	0.34	0.034	0.24
2	8.17	288.66	115.92	0.038	98.66
3	8.46	0.2	0.08	0.037	0.07
4	9.181	1.73	0.79	0.035	0.59
5	9.557	0.28	0.1	0.04	0.09
6	10.204	0.28	0.11	0.042	0.1
7	11.518	0.26	0.17	0.026	0.09
8	11.873	0.45	0.2	0.038	0.15

Qualitative Plot Window Report



Qualitative Plot Window Report



MS Formula Results: + Scan (8.524-8.864 min) (SN1014430248_2.d)

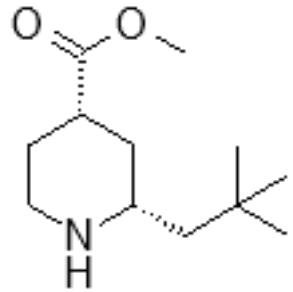
m/z	Ion	Formula	Abundance
214.1796	(M+H)+	C12 H24 N O2	1259968.4

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C12 H23 N O2	C12 H24 N O2	214.1802	94.91		213.1723	213.1729	2.56	2.56	95.48	92.39	95.82	214.1796	2

Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	86.98	214.1796	214.1802	2.56	85.22
2	15.85	13.7	11.91	215.1837	215.1834	-1.39	13.51
3	1.49	1.28	1.11	216.1859	216.1859	0.13	1.27

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C8 H19 N7	C8 H20 N7	214.1775	64.73		213.1723	213.1702	-10.06	10.06	81.63	70.4	51.76	214.1796	3

Sample_Id SN1014430248;
EN EN02629-29-001;
filename SN1014430248_efter_bas_h1nmr_1;
experiment h1nmr;
operator Henrik Sorensen;
chemist Henrik Sorensen;
automation SMS;
Sample# 61;
prid kdbb016;
date May 19 2009;
solvent cdcl3;
hostname nmr2;
NMR Spectrometer 400 MHz;
probe auto_x_400;
nt 16;
ct 16;
site AstraZeneca R&D Molndal;



(2R,4S)-**11**

Sample_Id SN1014430248;
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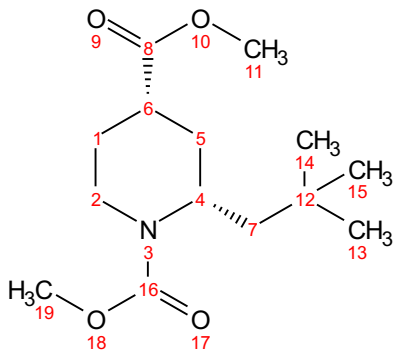
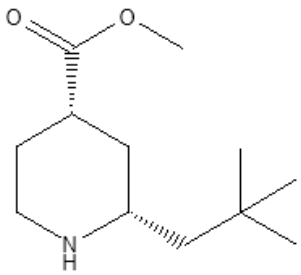
filename SN1014430248_efter_bas_c13nmr_1;
experiment c13nmr;
operator Henrik Sorensen;
chemist Henrik Sorensen;
automation SMS;
Sample# 62;
prid kdbb016;
date May 19 2009;
solvent cdcl3;
hostname nmr2;
NMR Spectrometer 400 MHz;
probe auto_x_400;
nt 300;
ct 300;
site AstraZeneca R&D Molndal;



(2R,4S)-**11**

AstraZeneca **EnantioBase** Analysis Report



(2R,4S)-**11**

Sample Information

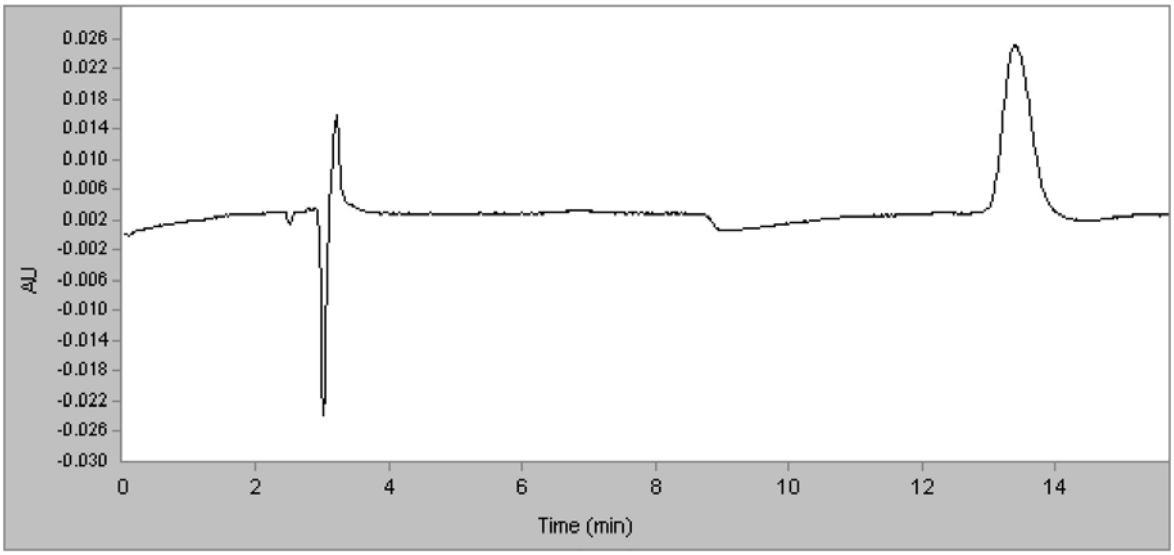
Sample ID	Compound name	Project name
SN1014430248	AZ13210702	NOFI

Analytical Conditions

Column	Dimensions (mm)	Particle Size (µm)
Chirobiotic V2	4.6 * 250 mm	5
Mobile Phase		
MeOH/HOAc/TEA 100/0.1/0.025		
Flow (ml/min)	**Detection (nm)**	**Temperature (C)**
1 ml/min	PDA 220.0 nm	RT
Comment		
Optical rotation: +23.8 (c 0.5, ACN)		

Analytical Result

UV Chromatogram



Retention Time	Area	Area %	K'	N	USP Resolution
2.883	1997	0.30	0.000	13545	
13.000	3635	0.55	3.509		
13.398	657489	99.15	3.647	5050	

ee: 98.9%

Chemist Signature

Print Date
2009-06-03

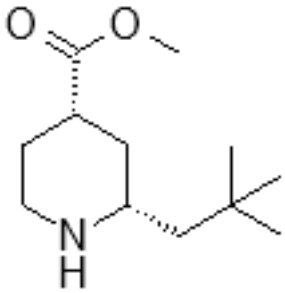
Purity Analysis and Accurate Mass Report

Submitter: Henrik Sörensen

Sample ID: SN1014430248

Compound Name: AZ13210702

Project: NOFI



(2R,4S)-**11**

Results

Your sample was 98.7% pure (UV 210 nm) and the measured mass confirmed the elemental composition (within 5 ppm).

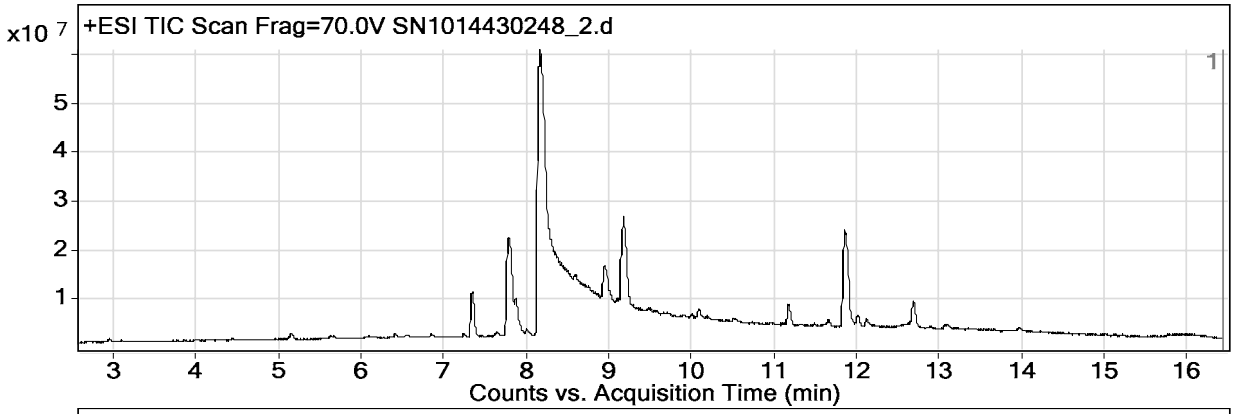
Instrumental setup

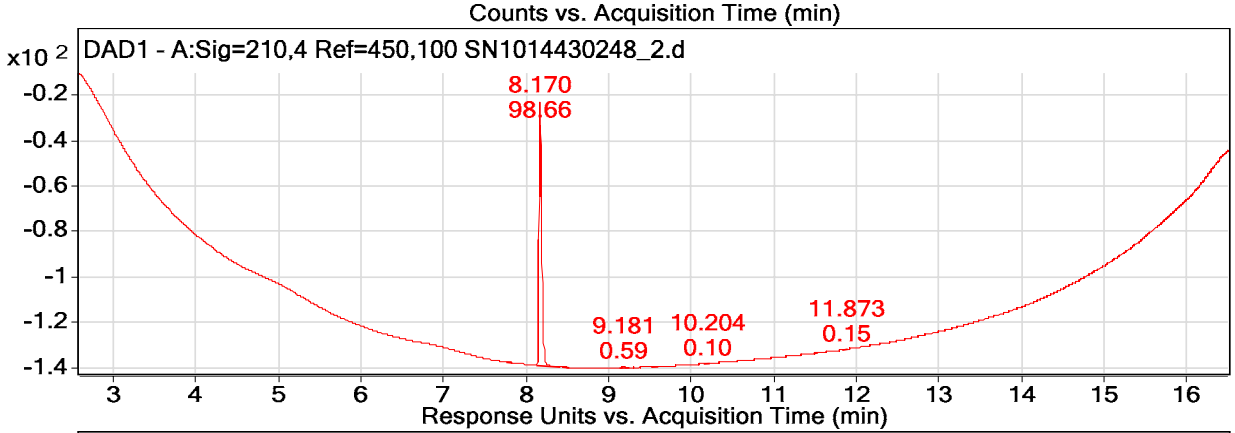
Column	Aquity UPLC BEH C18, 2.1mm×100mm, 1.7µm particles
Temperature	50ºC
Gradient	4% ACN to 95% ACN in 16 minutes.; 40 mM ammonia 6 mM ammonium carbonate, pH 10
Flow	0.55 ml/min
Injection volume	5 µL
Purity	Relative Absorbance at 210 nm
Ionization mode	ESI+
Mass spectrometer	Q-TOF 6530 Agilent

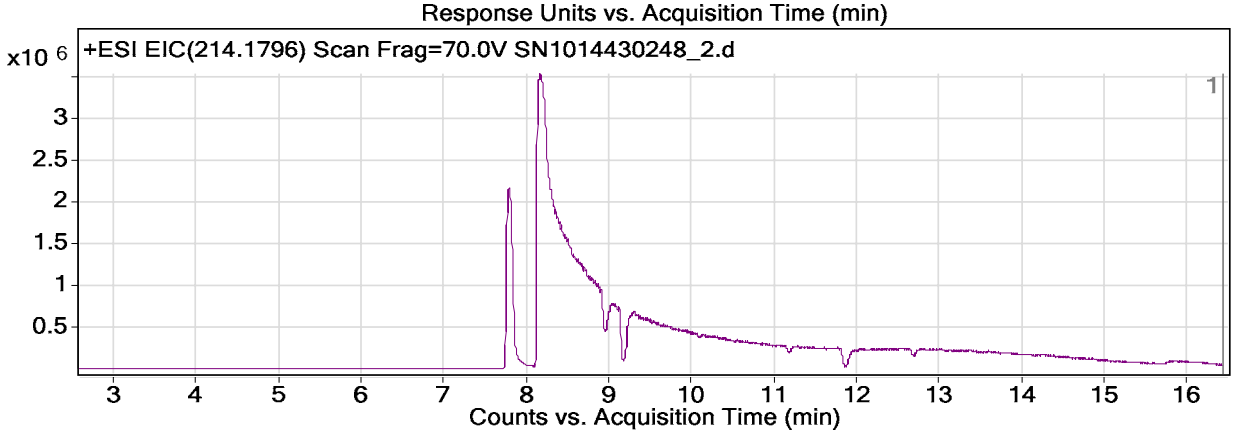
Gustaf Hulthe
Medicinal Chemistry
AstraZeneca R&D Mölndal
SE-431 83 Mölndal, Sweden

Date: 2009-05-20

Qualitative Plot Window Report



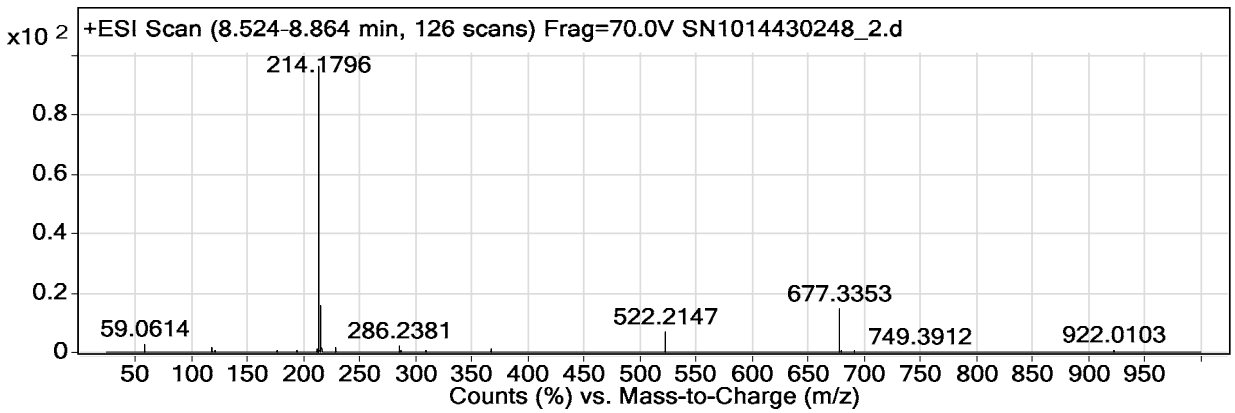




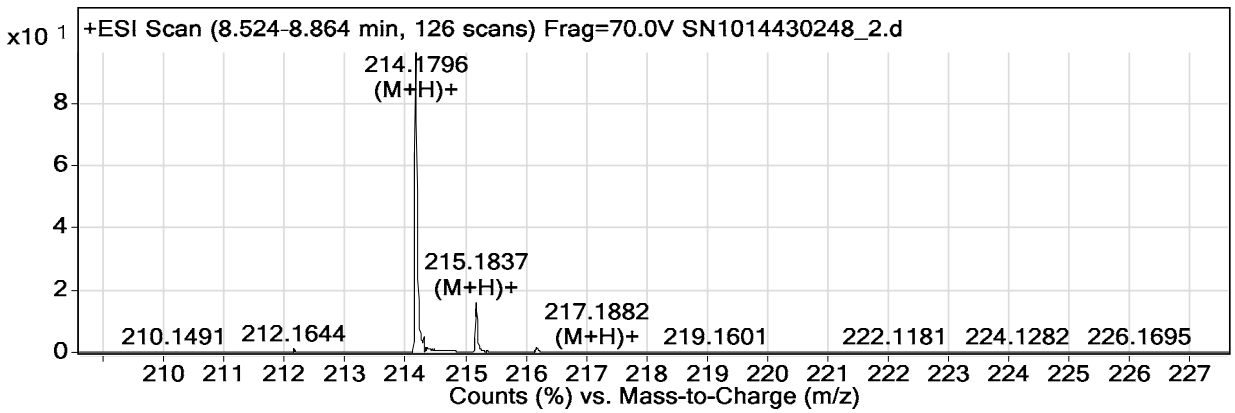
Peaks: DAD1 - A:Sig=210,4 Ref=450,100 (SN1014430248_2.d)

Peak	RT	Area	Height	Width	Area Sum%
1	7.79	0.71	0.34	0.034	0.24
2	8.17	288.66	115.92	0.038	98.66
3	8.46	0.2	0.08	0.037	0.07
4	9.181	1.73	0.79	0.035	0.59
5	9.557	0.28	0.1	0.04	0.09
6	10.204	0.28	0.11	0.042	0.1
7	11.518	0.26	0.17	0.026	0.09
8	11.873	0.45	0.2	0.038	0.15

Qualitative Plot Window Report



Qualitative Plot Window Report



MS Formula Results: + Scan (8.524-8.864 min) (SN1014430248_2.d)

m/z	Ion	Formula	Abundance
214.1796	(M+H)+	C12 H24 N O2	1259968.4

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☑	C12 H23 N O2	C12 H24 N O2	214.1802	94.91		213.1723	213.1729	2.56	2.56	95.48	92.39	95.82	214.1796	2

Isotope	Abund%	Calc Abund%	Calc Abund	m/z	Calc m/z	Diff (ppm)	Abund Su
1	100	100	86.98	214.1796	214.1802	2.56	85.22
2	15.85	13.7	11.91	215.1837	215.1834	-1.39	13.51
3	1.49	1.28	1.11	216.1859	216.1859	0.13	1.27

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross Scor	Mass	Calc Mass	Diff (pp	Abs Diff	Abund Matc	Spacing Matc	Mass Match	m/z	DBE
☐	C8 H19 N7	C8 H20 N7	214.1775	64.73		213.1723	213.1702	-10.06	10.06	81.63	70.4	51.76	214.1796	3