

Supporting Information

Inhibitors of Src Homology-2 Domain containing Protein Tyrosine Phosphatase-2 (Shp2) Based on Oxindole Scaffolds

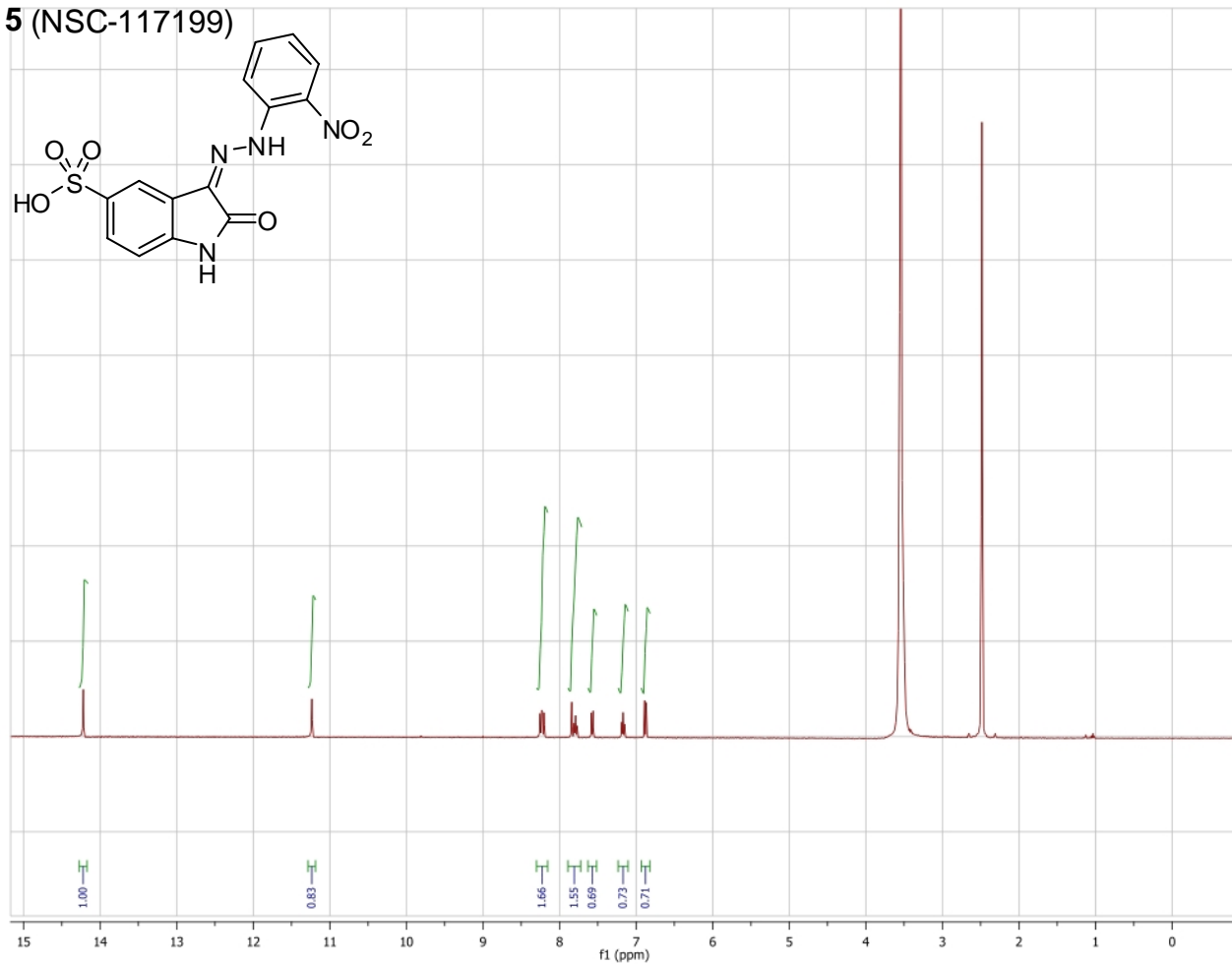
Harshani R. Lawrence,* Roberta Pireddu, Liwei Chen, Yunting Luo, Shen-Shu Sung, Ann Marie Szymanski, Richard Yip, Wayne C. Guida, Saïd M. Sebtì, Jie Wu and Nicholas J. Lawrence*

Moffitt Cancer Center, Tampa, FL

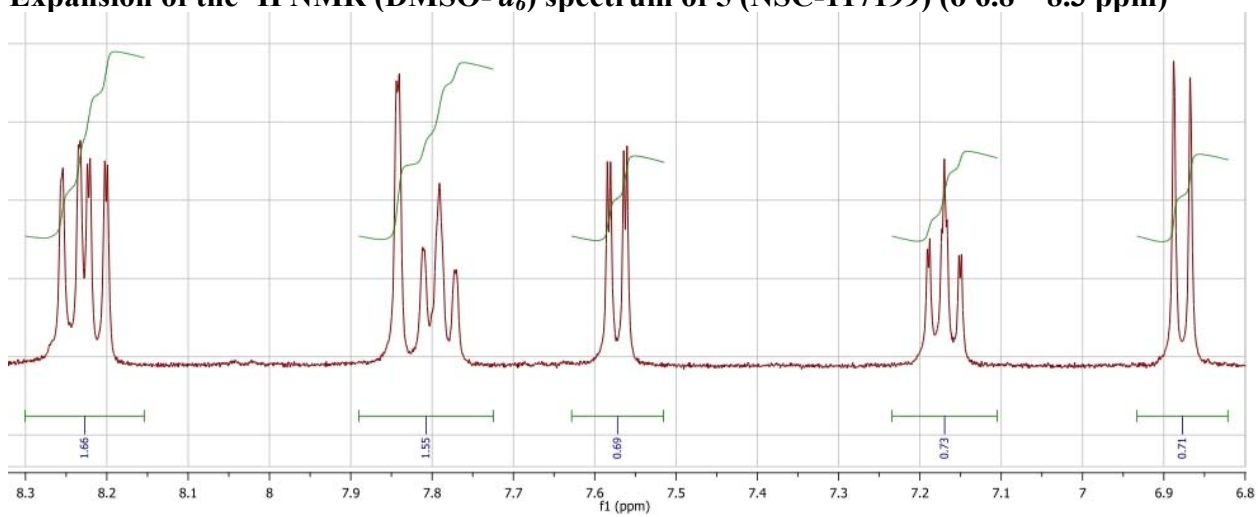
Contents.

Characterization data, mass and NMR spectra and HPLC traces of compounds **5** (NSC-117199), **10a-r**, **14a-b**, **17** and **18a-e**, nOe and COSY data for **5** and **18c**, and a description of the molecular modeling studies.

5 (NSC-117199)



Expansion of the ¹H NMR (DMSO-*d*₆) spectrum of 5 (NSC-117199) (δ 6.8 – 8.3 ppm)



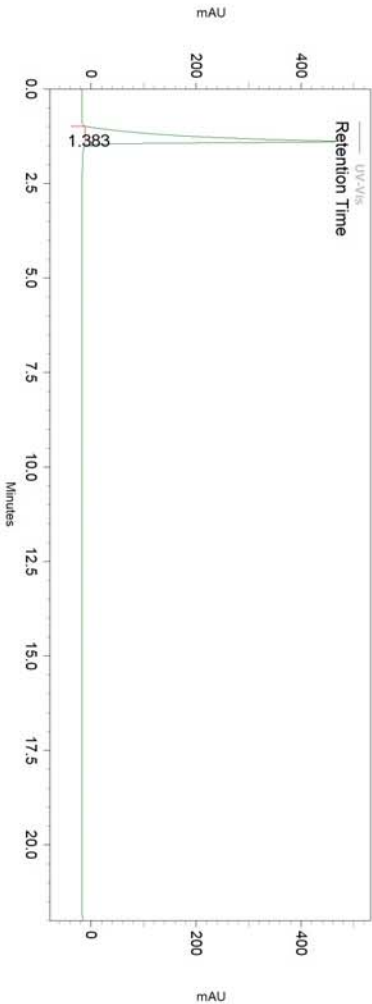
HPLC of 5 (NSC-117199)

Area Percent Report

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Page 1 of 1 Data File: C:\HPLC
Printed: 7/10/2007 5:02:22 PM

Analyst: System
Sample ID: HL1-056
Vial: N/A
Injection Volume: 0



UV-Vis Results				
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Totals		5119966	100.000	

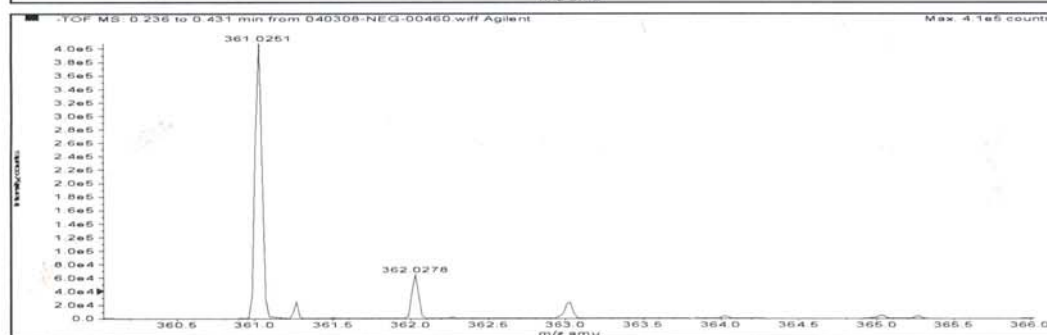
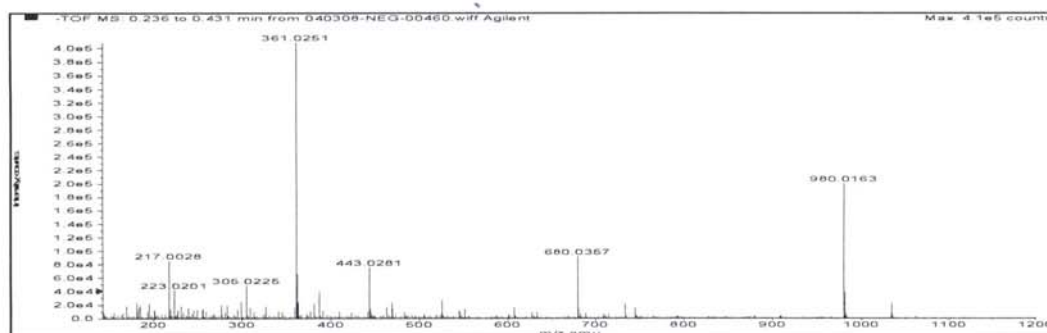
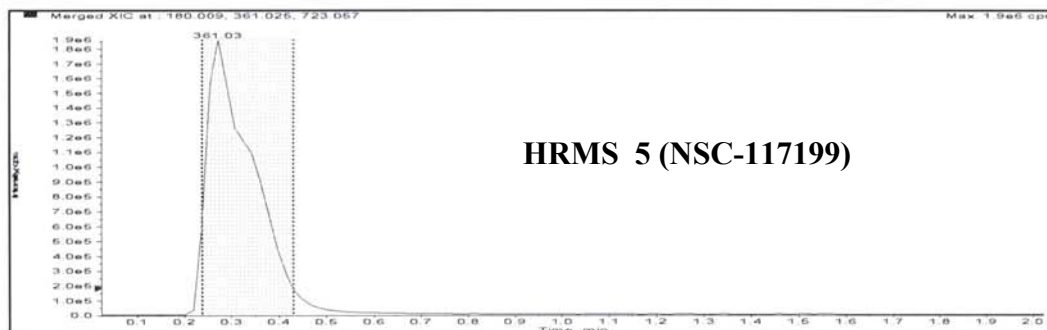
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Sequence: C:\HPLC\data\Danabc.seq
Software Version: Version 3.1.7

Empirical Formula Confirmation Report

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Sample Name: NSC117199 Sample Location: P1-E-02 Sample Id: NSC117199 Operator: EasyAccess
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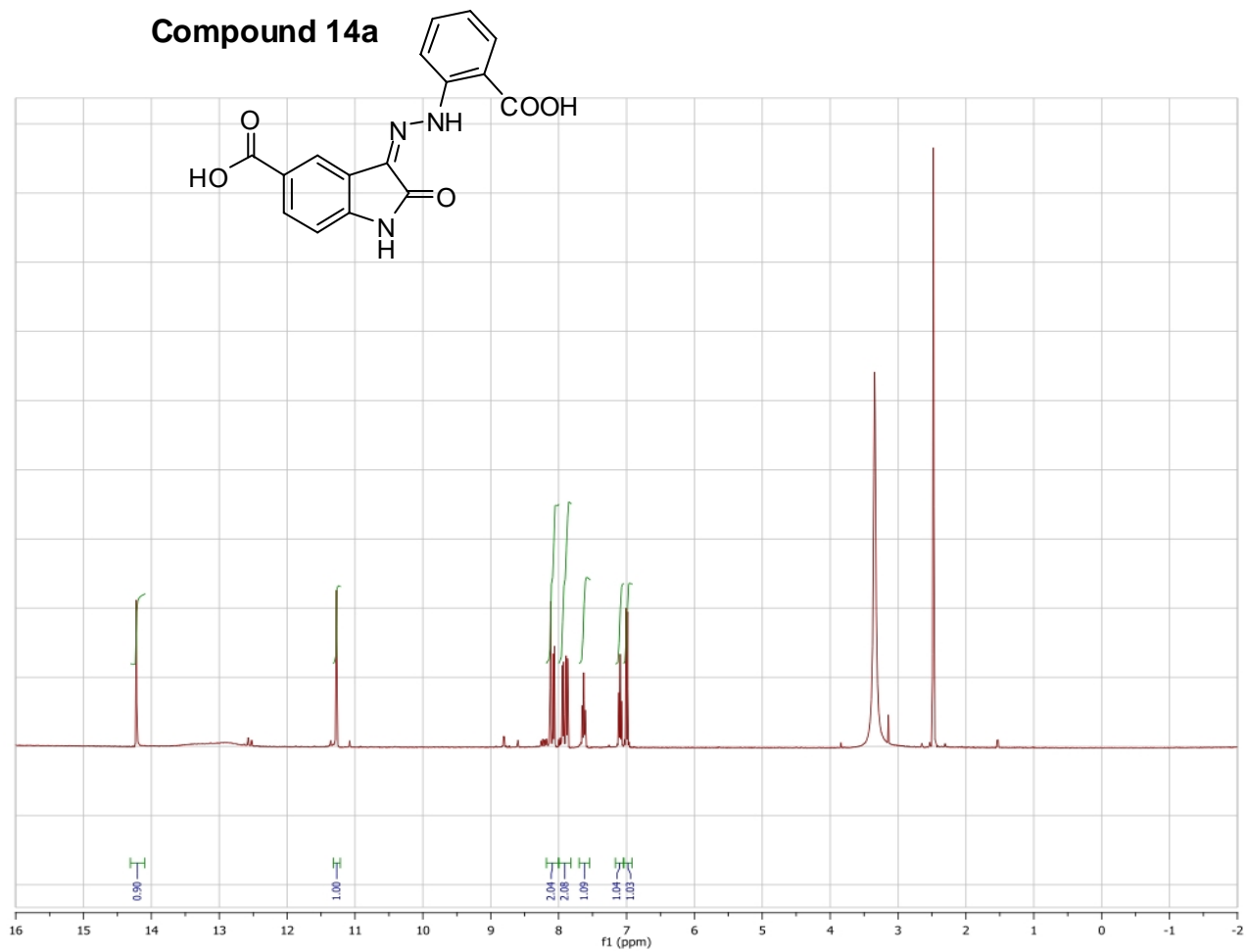
Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C14H10N4O6S	--	362.03210	0.27	1.24999 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	409551.10	361.02483	361.02507	0.24452	0.68	--

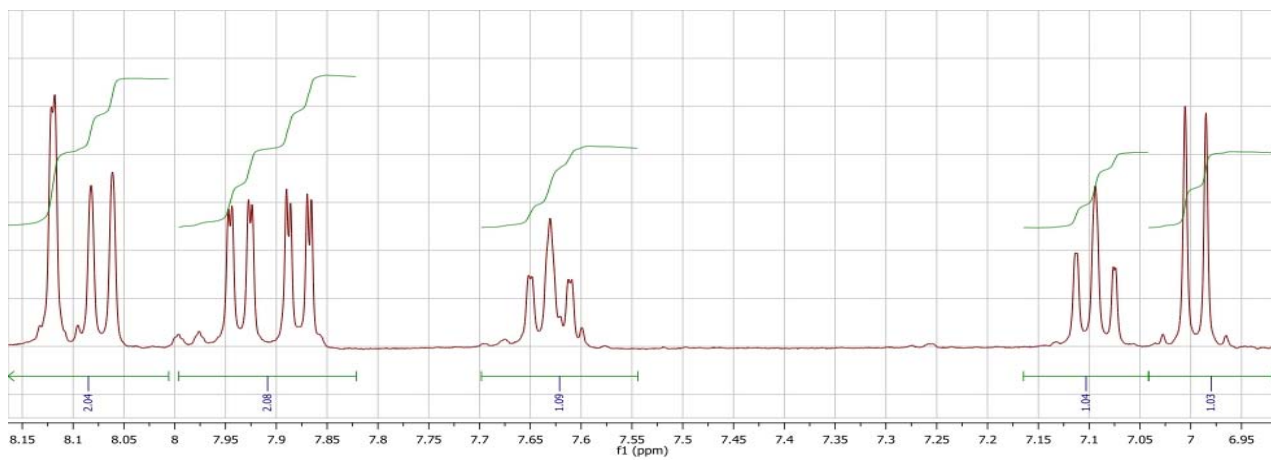
Tuesday, March 04, 2008

14:53:49 PM

Compound 14a



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 14a (δ 6.9 – 8.2 ppm)



HPLC 14a

Area Percent Report

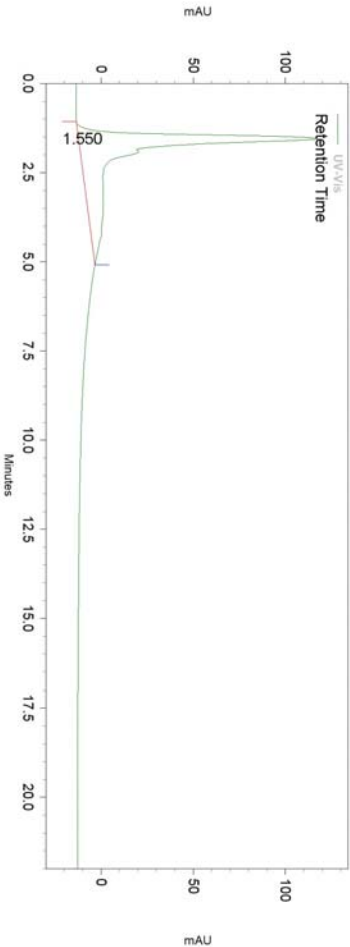
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Page 1 of 1 Data File: C:\HPLC
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Analyst: System
Sample ID: h12522

Vial: N/A

Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
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Totals		4034859	100.000	

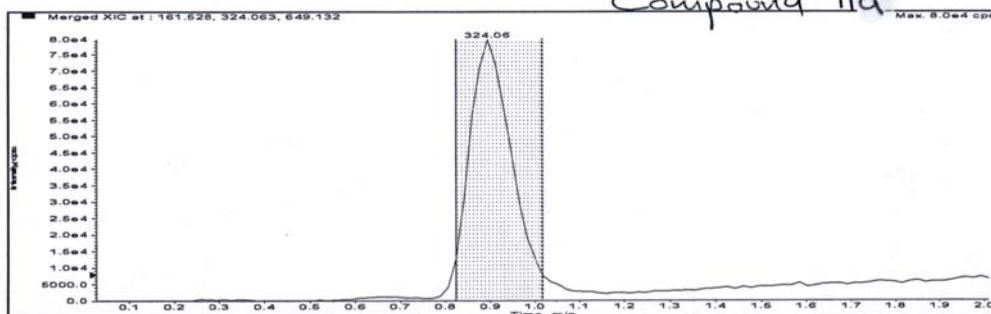
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Software Version: Version 3.1.7

HRMS 14a

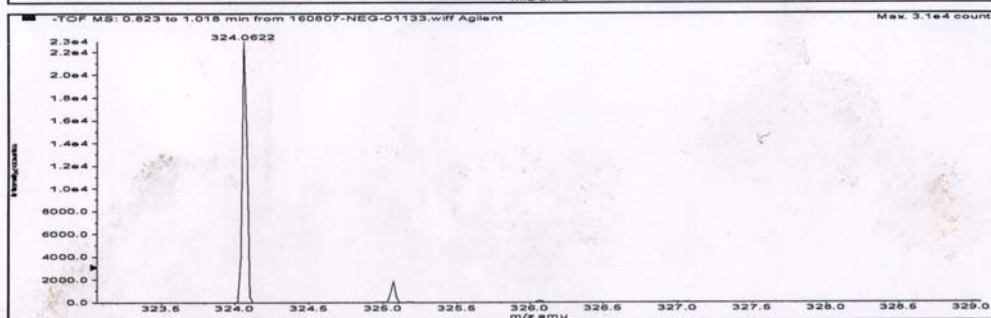
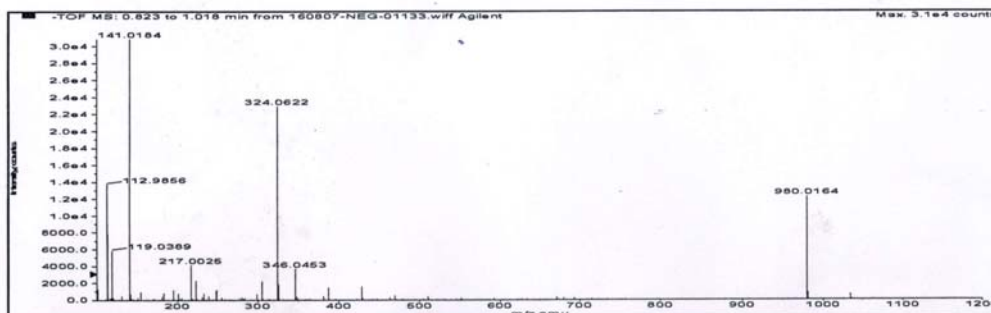
Empirical Formula Confirmation Report

Page 1 of 1

Sample Name: HL2-052-2 Sample Location: P1-B-05 Sample Id: HL2-052-2 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\08-07\Data\160807-NEG-01133.wiff Acq Time: August 16 2007 05:10:17 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml



Merged XIC, Period#: 1 Experiment#: 1

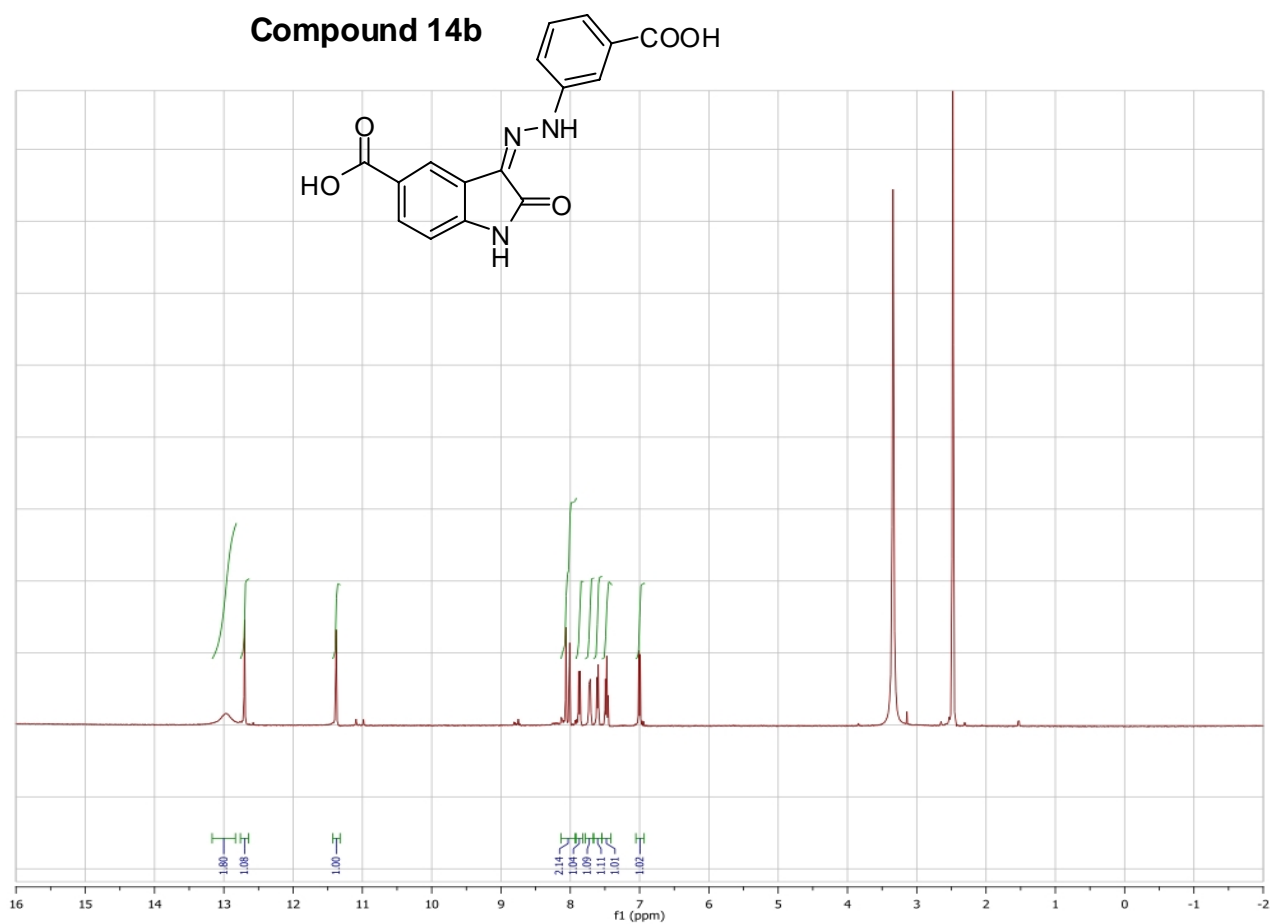


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C16H11N3O5	--	325.06987	0.89	5.19140 E5	--

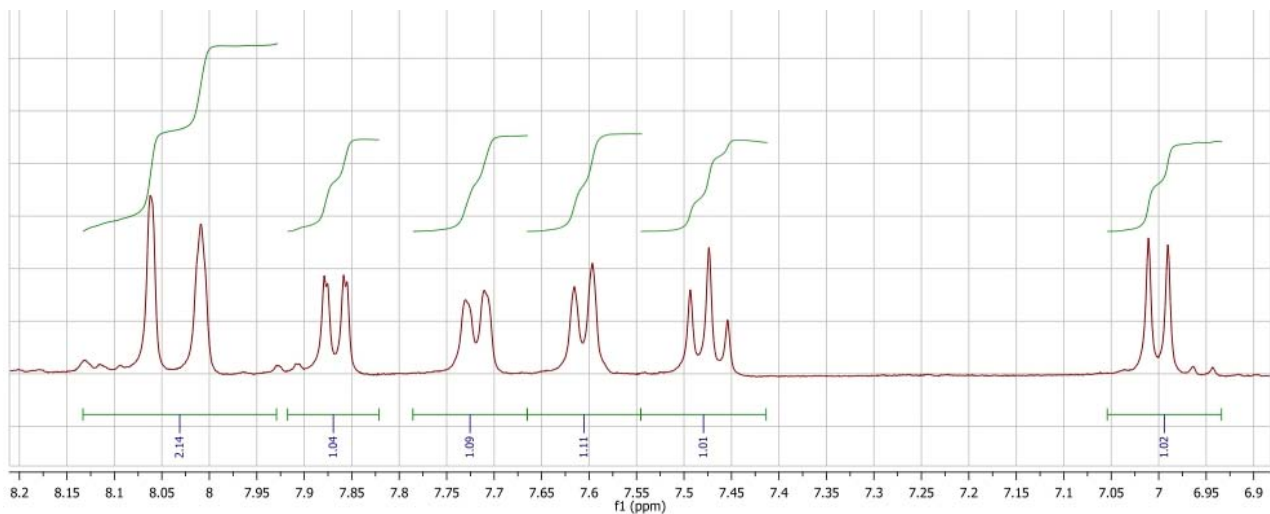
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	23392.48	324.06259	324.06224	-0.35504	-1.10	--

Thursday, August 16, 2007

17:12:26 PM



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 14b (δ 6.9 – 8.2 ppm)



Area Percent Report

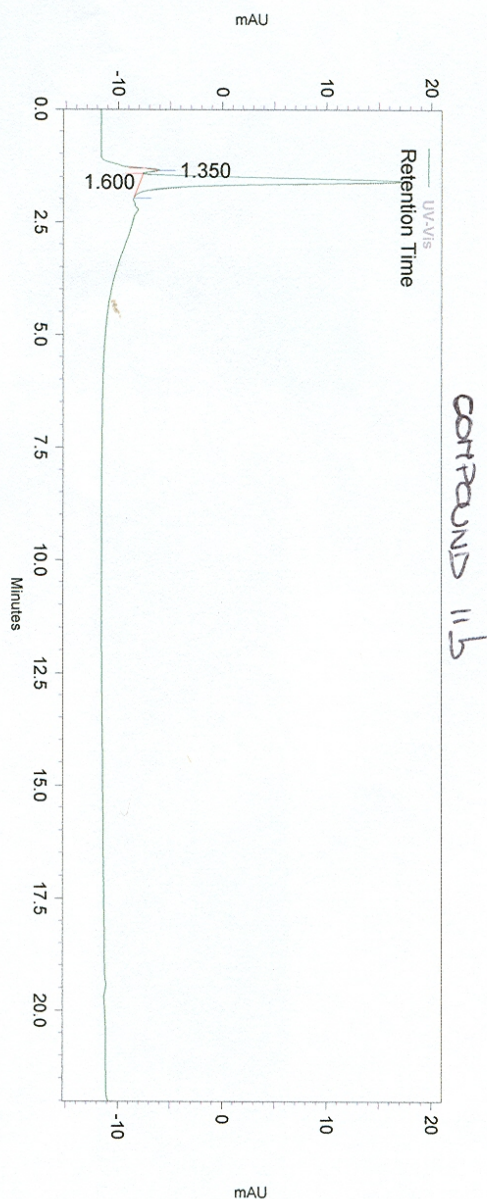
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Page 1 of 2 Data File: C:\HPL
Printed: 7/3/2007 2:55:23 PM

Analyst: System
Sample ID: hl2522

Vial: N/A

Injection Volume: 0



HPLC 14b

UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	1.350	1062	0.428	MM
	1.600	247261	99.572	MM

Totals		248323	100.000	
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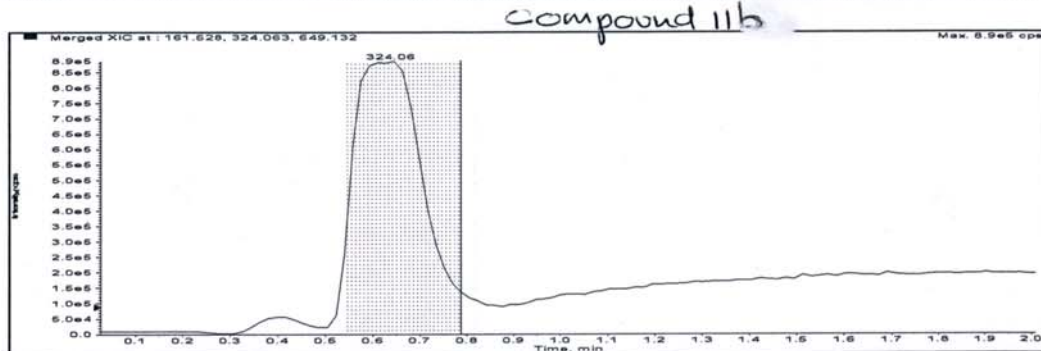
Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\80MeOH20H2O\1.722min.met
Sequence: C:\HPLC data\Danabc.seq
Software Version: Version 3.1.7

HRMS of 14b

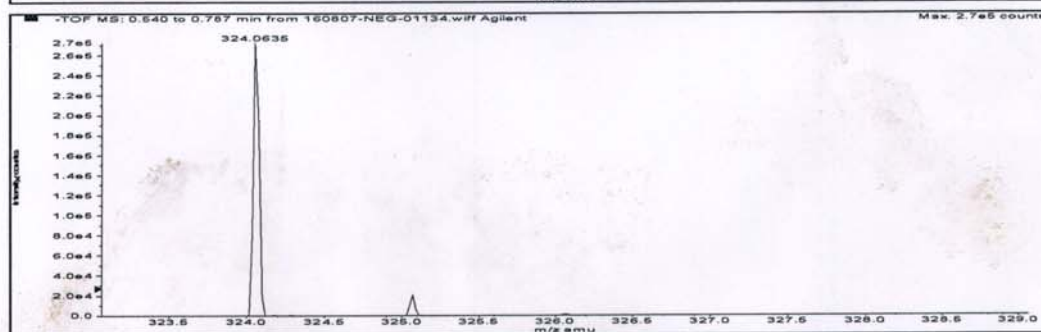
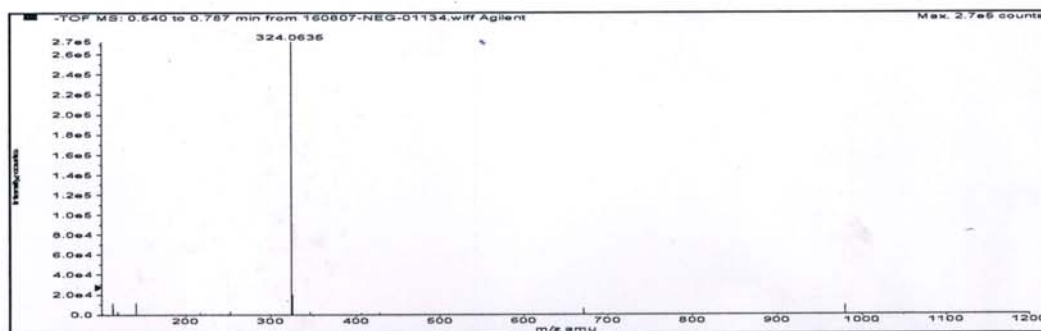
Empirical Formula Confirmation Report

Page 1 of 1

Sample Name: HL2-052-3 Sample Location: P1-B-06 Sample Id: HL2-052-3 Operator: EasyAccess
 Data File Name: D:\PE Sciex Data\Projects\chemist08-07\Data\160807-NEG-01134.wiff Acq Time: August 16 2007. 05:13:15 PM
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Merged XIC, Period#: 1 Experiment#: 1

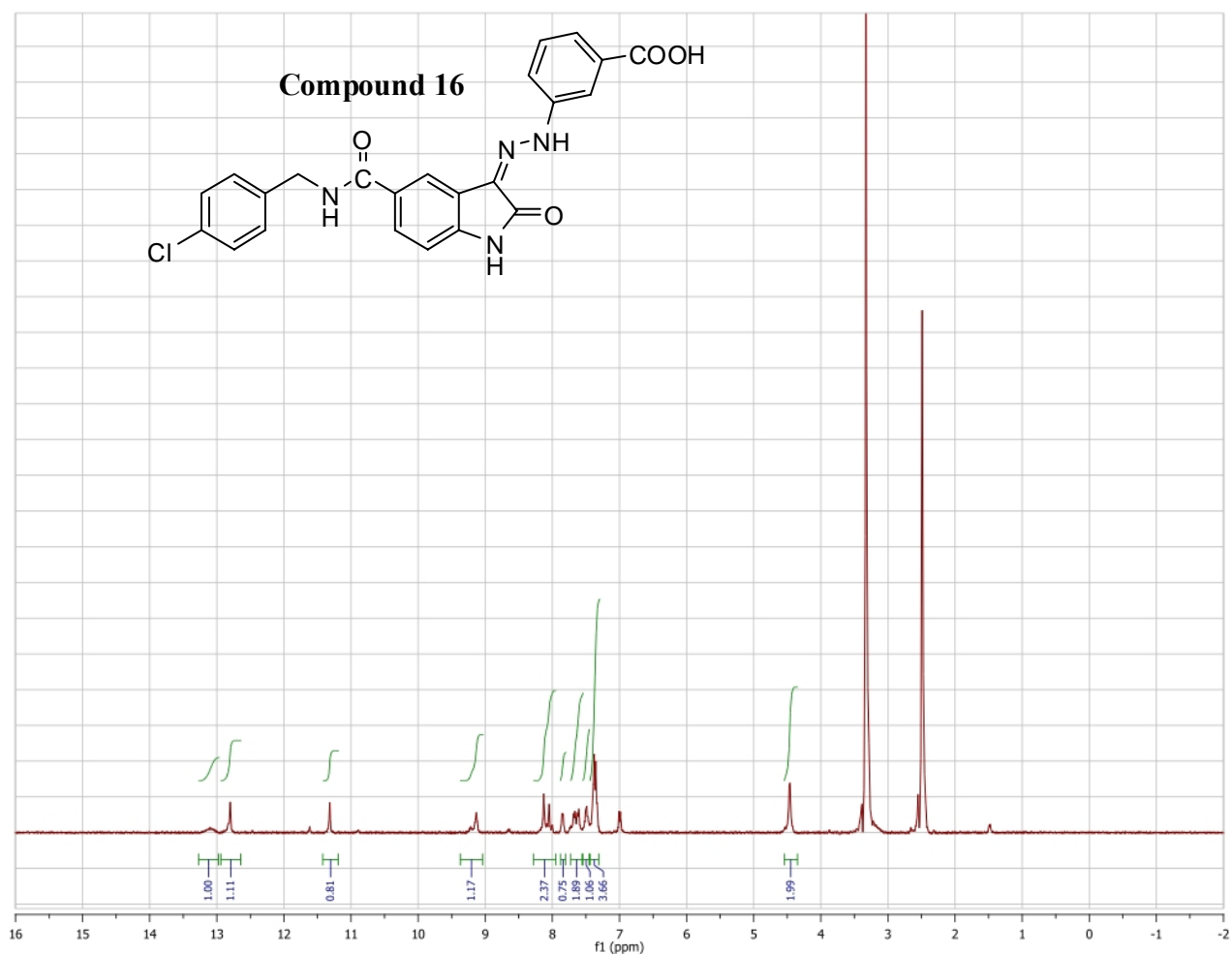


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C16H11N3O5	--	325.06987	0.64	8.42726 E6	--

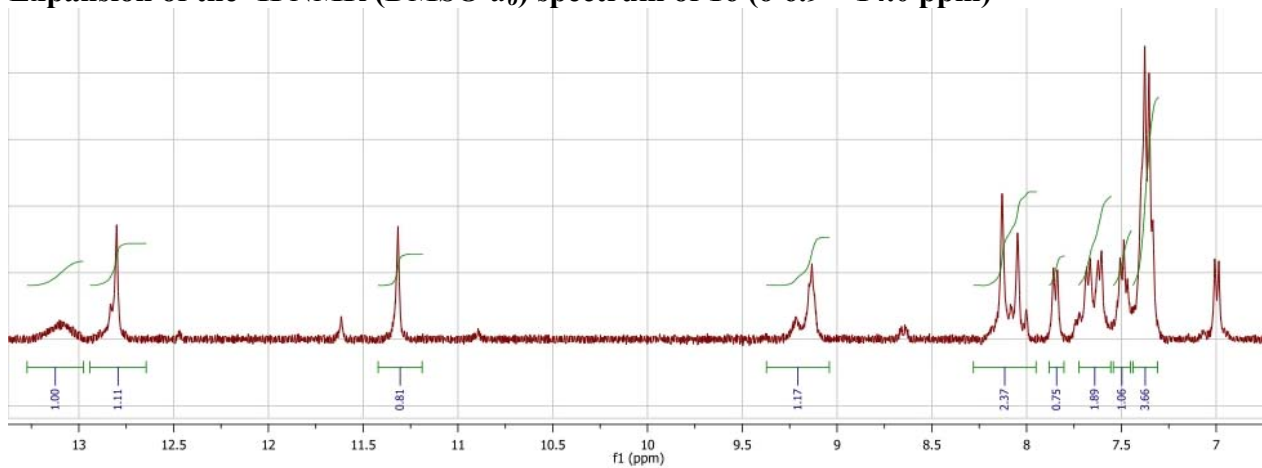
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	278788.41	324.06259	324.06352	0.92378	2.85	--

Thursday, August 16, 2007

17:15:26 PM



Expansion of the ¹H NMR (DMSO-*d*₆) spectrum of 16 (δ 6.9 – 14.0 ppm)



HPLC 16

Area Percent Report

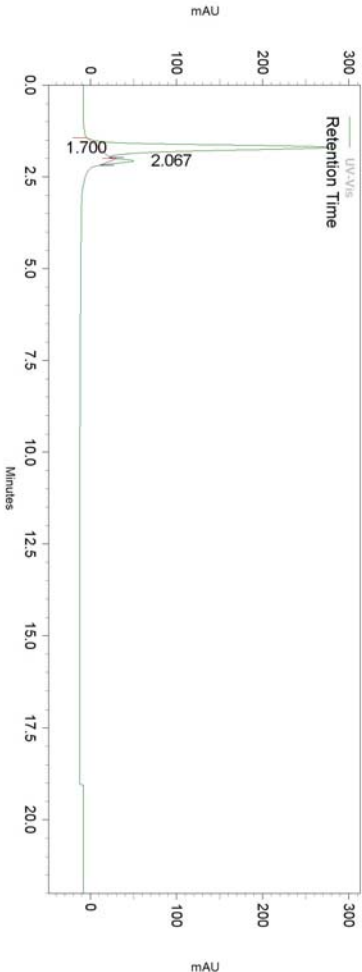
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Page 1 of 2 Data File: C:\HPLC
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Analyst: System
Sample ID: hl2522

Vial: N/A

Injection Volume: 0

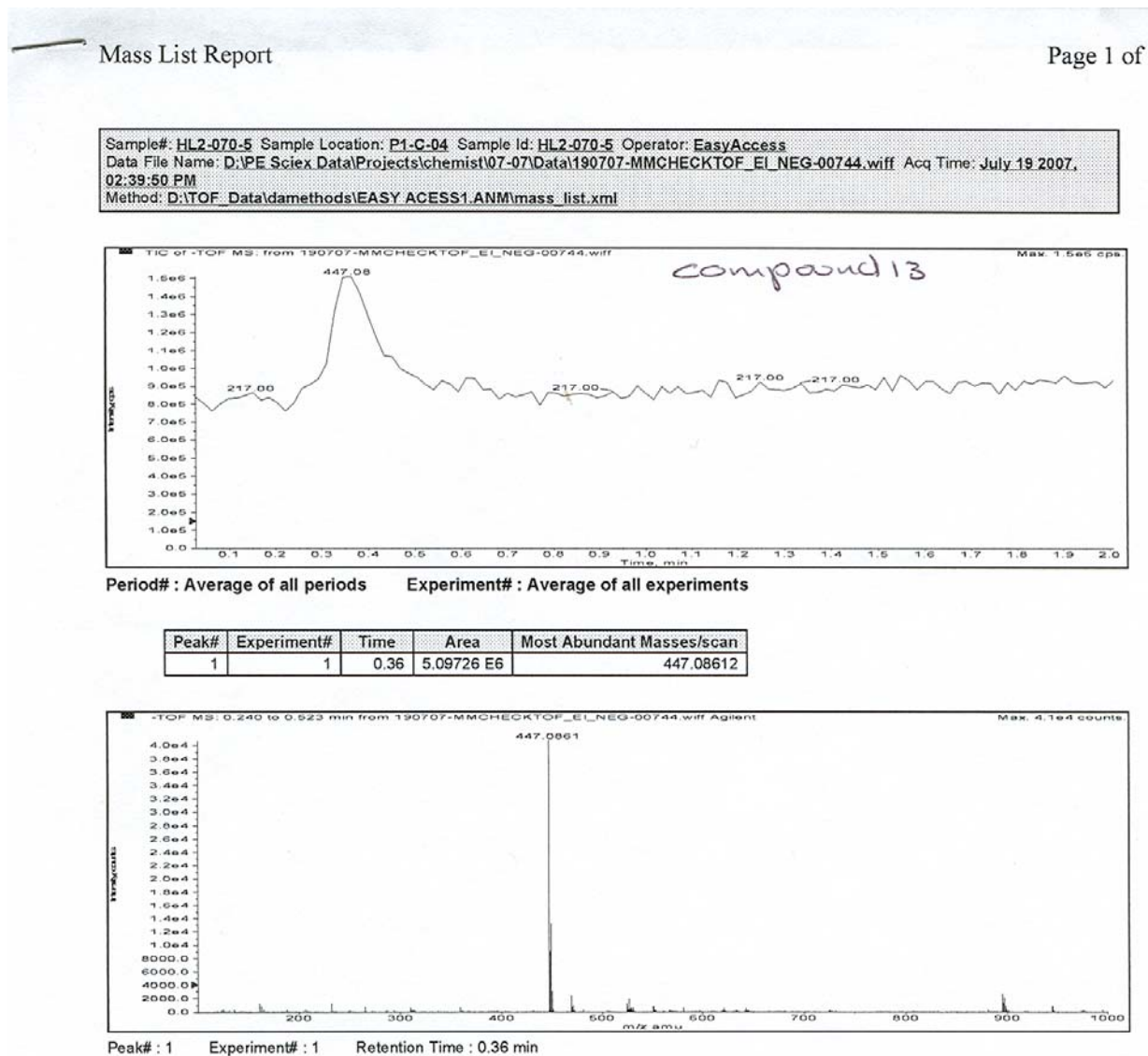


UV-Vis Results

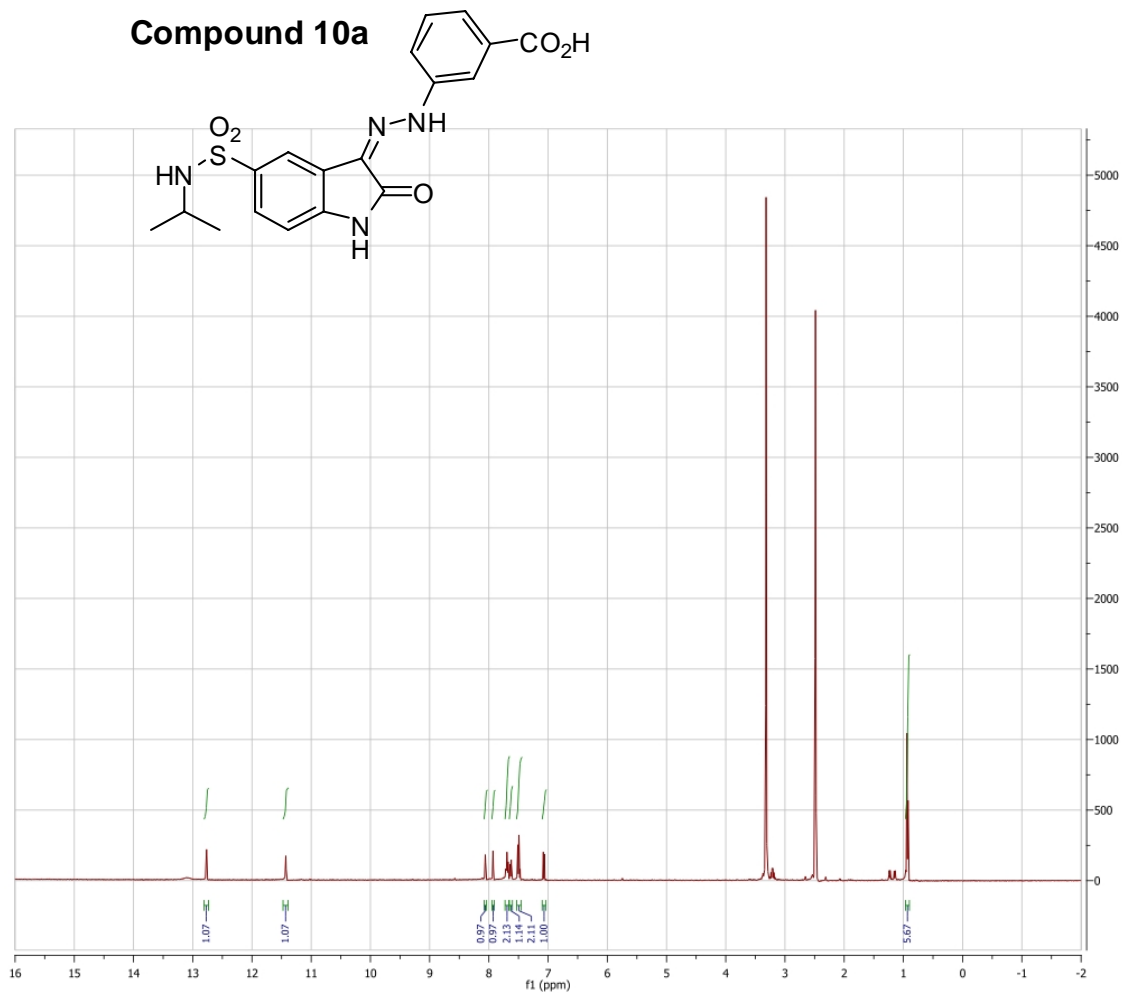
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Totals		2912288	100.000	

Instrument Name: HPLC Software Version: Version 3.1.7
Acquisition Method: C:\EZStart\Projects\Default\Method\80MeOH20H2O\1.522min.met
Sequence: C:\HPLC\data\Dan\abc.seq

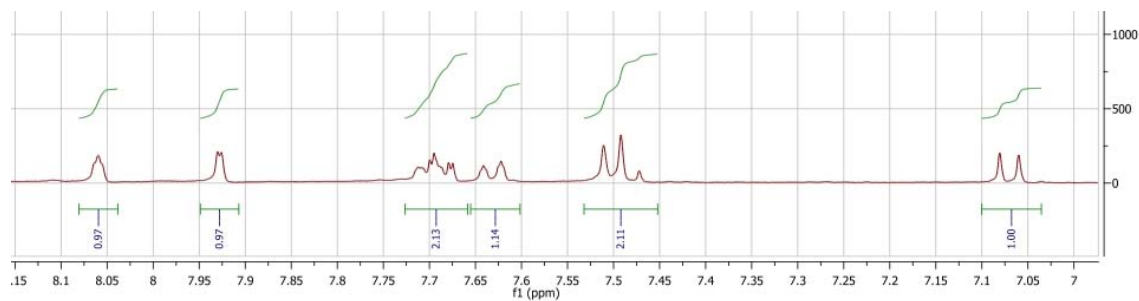
HRMS 16



Compound 10a



Expansion of the ¹H NMR (DMSO-*d*₆) spectrum of 10a (δ 7.0 – 8.2 ppm)



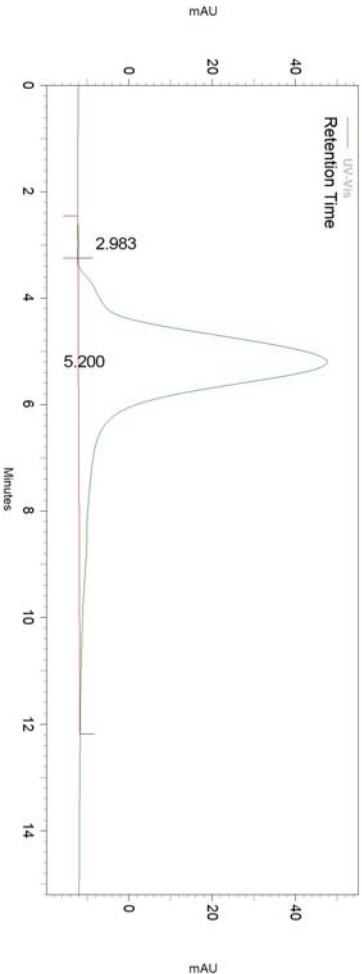
HPLC 10a

Area Percent Report

data\Robert\rpm297 method II\System4-10-2007 4-48-04 PM.dat
Acquired: 4/10/2007 4:48:28 PM

Page 1 of 2 Data File: C:\HPLC
Printed: 4/10/2007 5:12:23 PM

Analyst: System
Sample ID: rpm297 method II Vial: N/A Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	2.983	4027	0.084	BV
	5.200	478252	99.916	VB

Totals		4792279	100.000	
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Instrument Name: HPLC Software Version: Version 3.1.7
Acquisition Method: C:\EZStart\Projects\Default\Method\meoh-h2075-25 0.4 fl.met
Sequence: C:\HPLC data\Dan\abc.seq

HRMS 10a

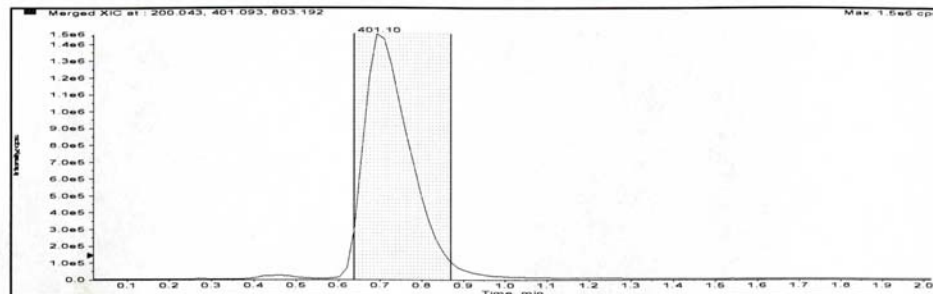
Empirical Formula Confirmation Report

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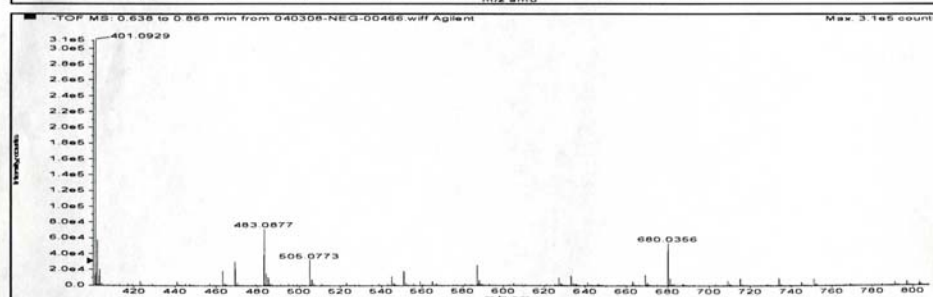
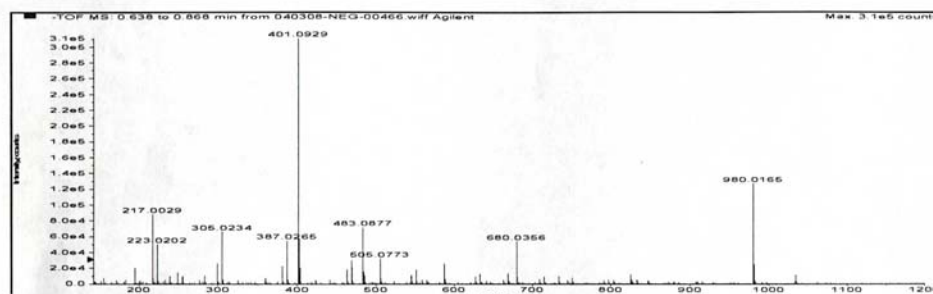
Compound 7a

Sample Name: RPM297-7a Sample Location: P1-E-08 Sample Id: RPM297-7a Operator: EasyAccess
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Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

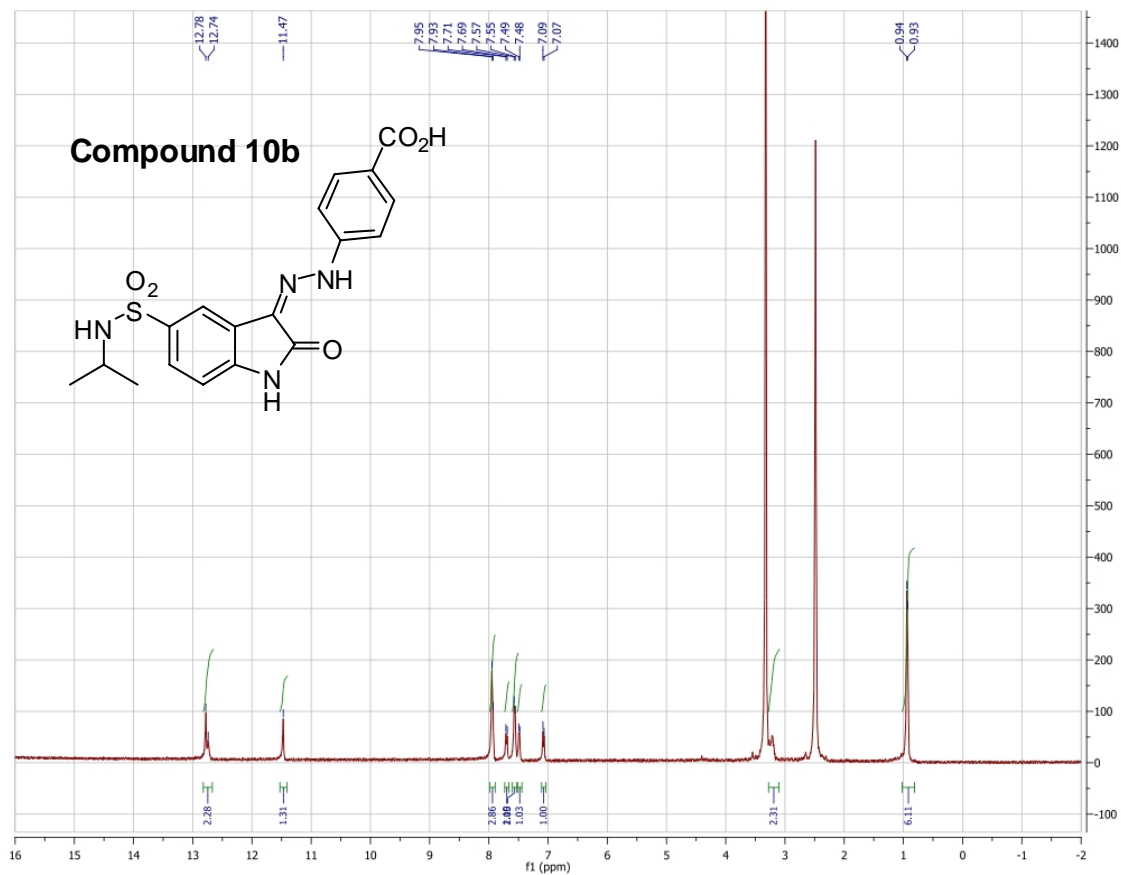


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C18H18N4O5S	--	402.09979	0.70	1.12477 E7	--

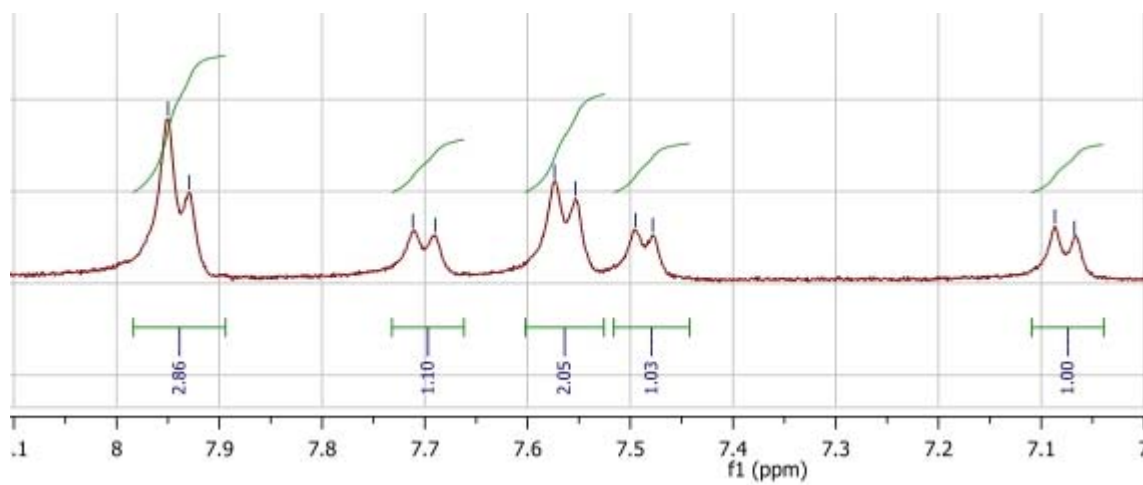
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	311592.36	401.09251	401.09290	0.38940	0.97	--
[2M-H]-	5212.62	803.19230	803.19233	0.02433	0.03	--

Tuesday, March 04, 2008

15:12:46 PM



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 10b (δ 7.0 – 8.1 ppm)



HPLC 10b

Area Percent Report

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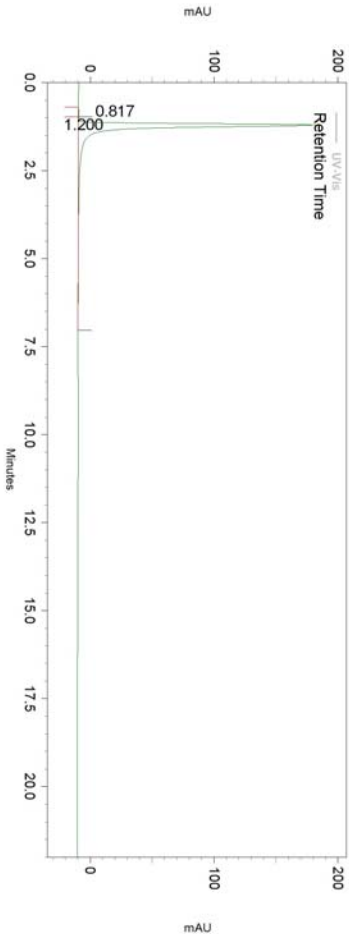
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Page 1 of 2 Data File: C:\HPLC

Analyst: System
Sample ID: RPTM739a

Vial: N/A

Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.817	2139	0.125	BV
	1.200	1704888	99.875	VB

Totals		1707027	100.000	
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Instrument Name: HPLC
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Software Version: Version 3.1.7

HRMS 10b

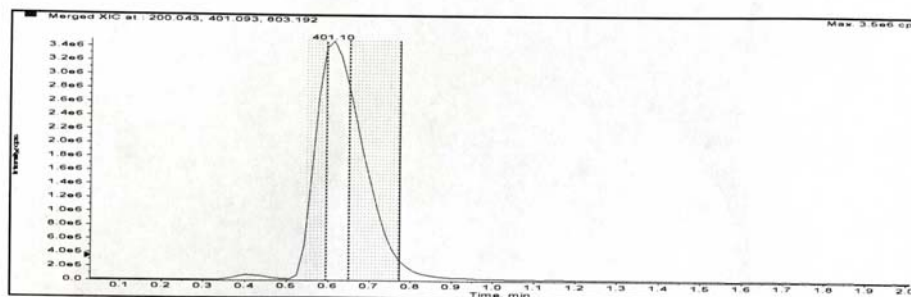
Empirical Formula Confirmation Report

CatRound 7b

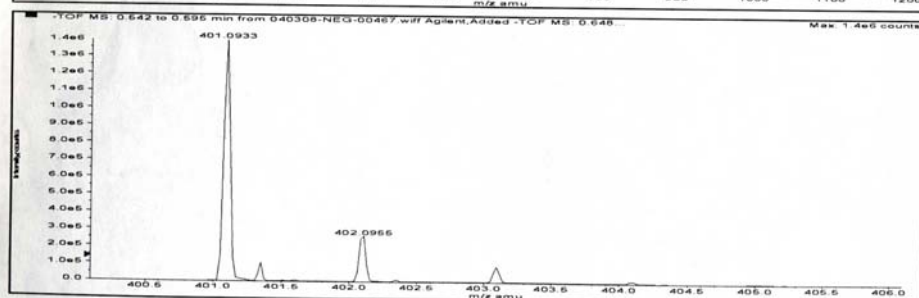
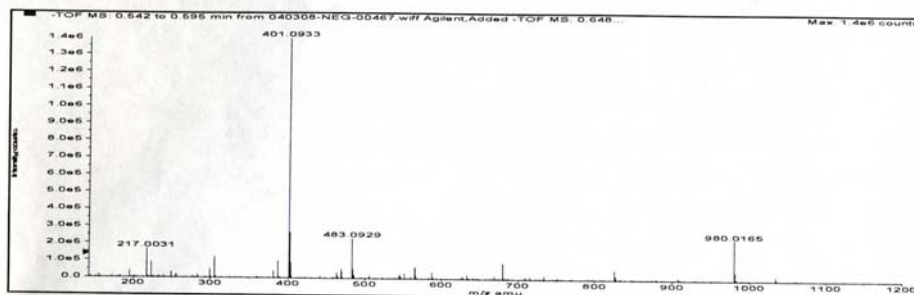
Page 1 of 1

Sample Name: RPM739-7b Sample Location: P1-E-09 Sample Id: RPM739-7b Operator: EasyAccess
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One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

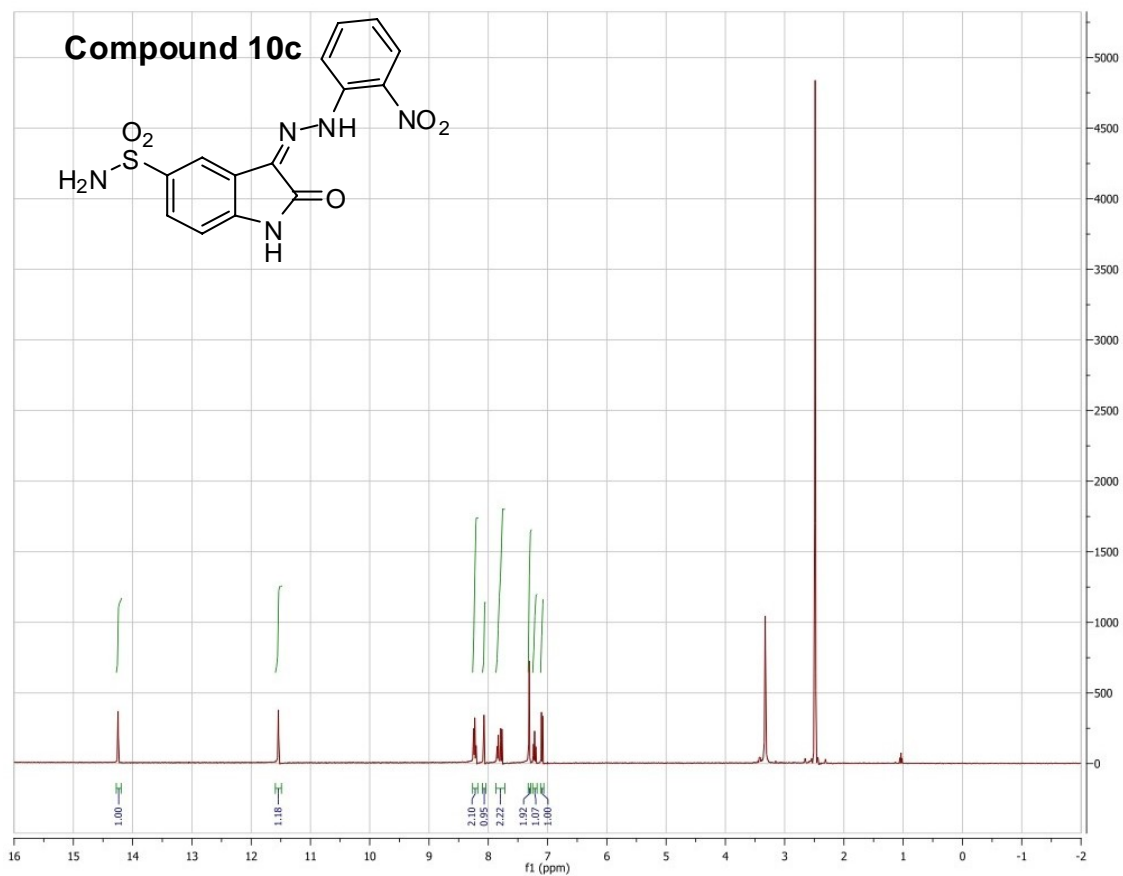


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C18H18N4O5S	--	402.09979	0.61	2.76704 E7	--

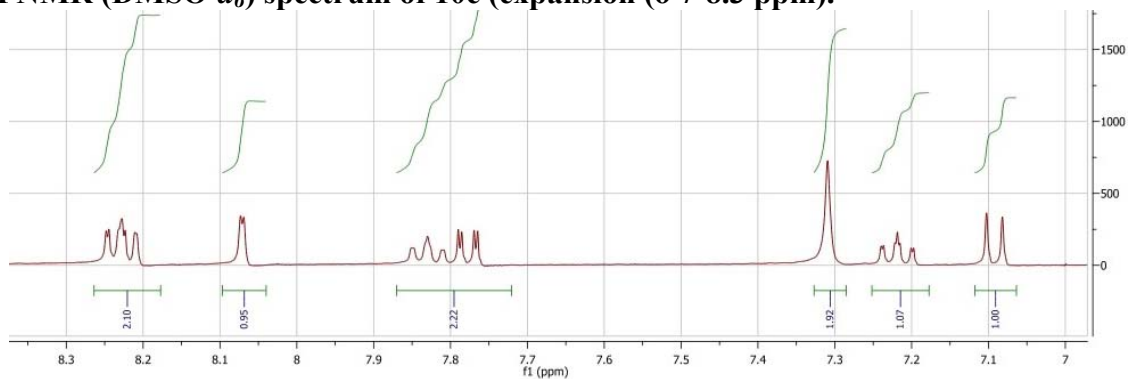
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H] ⁻	1396496.48	401.09251	401.09328	0.76761	1.91	--

Tuesday, March 04, 2008

15:15:46 PM



^1H NMR (DMSO- d_6) spectrum of 10c (expansion (δ 7-8.3 ppm)).



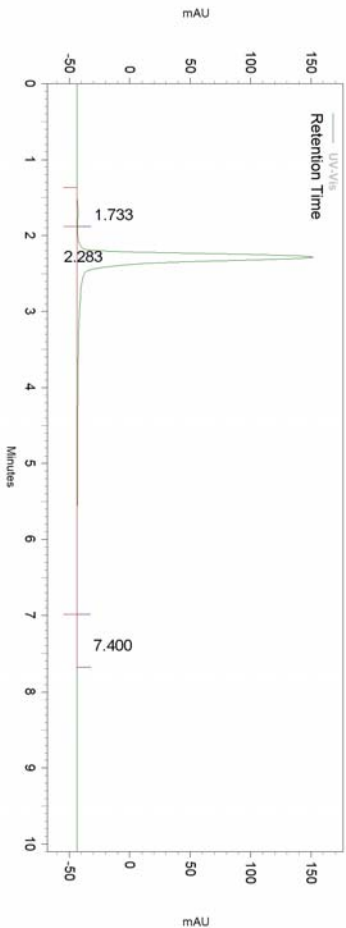
HPLC 10c

Area Percent Report

data\Robert\pm134 ch3cn 90 h2o 10\System4-4-2007 6-20-30 PM.dat
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Page 1 of 2 Data File: C:\HPLC
Printed: 4/4/2007 6:31:26 PM

Analyst: System
Sample ID: rpm134 ch3cn 90 h2o 10 Vial: N/A Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	1.733	10940	0.654	BV
	2.283	1659724	99.285	VV
	7.400	1014	0.061	VB
Totals				

Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\90CH3CN10H2O.fl 0.75 10min.mnt
Sequence: C:\HPLC\data\Danabc.seq
Software Version: Version 3.1.7

HRMS 10c

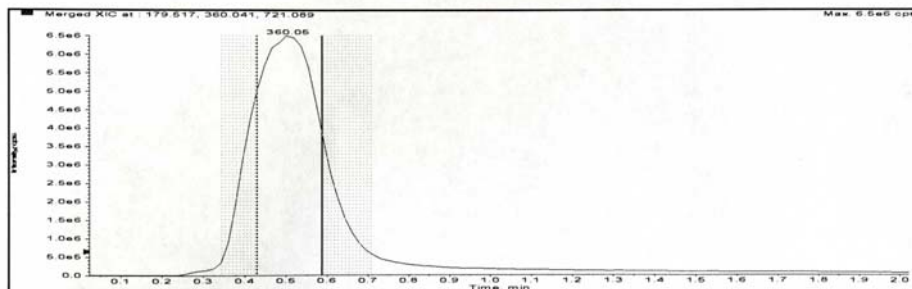
Empirical Formula Confirmation Report

Page 1 of 1

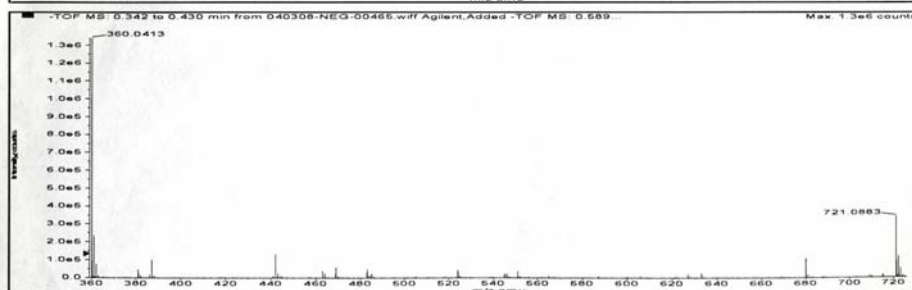
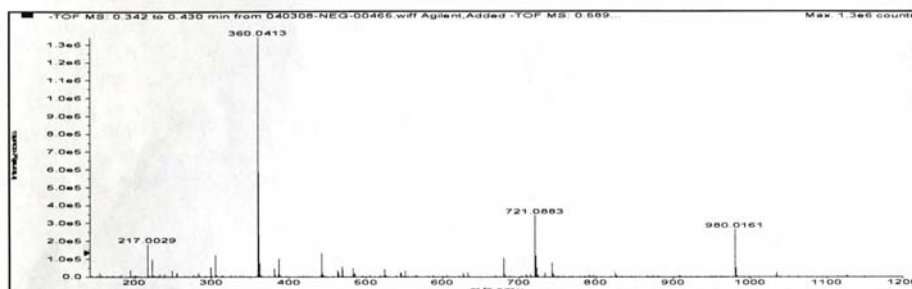
Compound 7c

Sample Name: RPM134-7c Sample Location: P1-E-07 Sample Id: RPM134-7d Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00465.wiff Acq Time: March 04 2008, 03:07:32 PM
Method: D:\TOF_Data\methods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period#: 1 Experiment#: 1

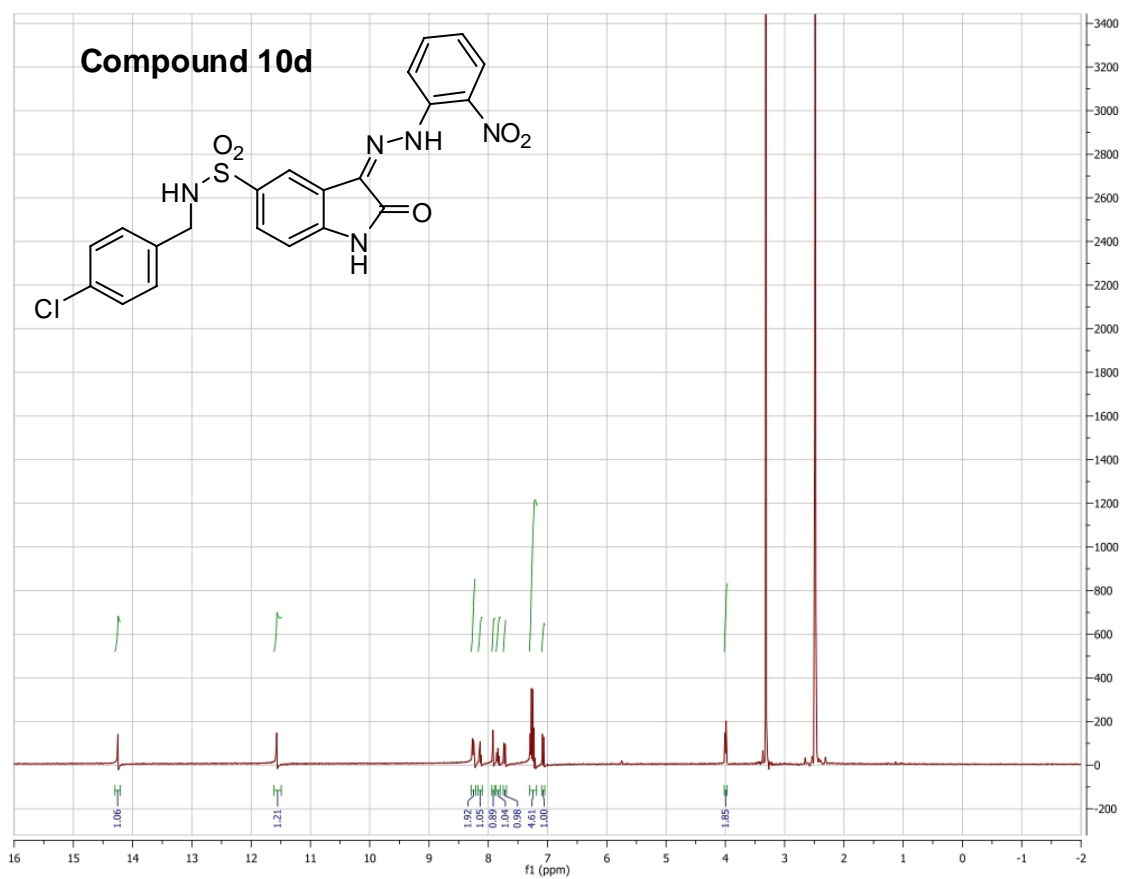


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C14H11N5O5S	--	361.04809	0.51	8.15407 E7	--

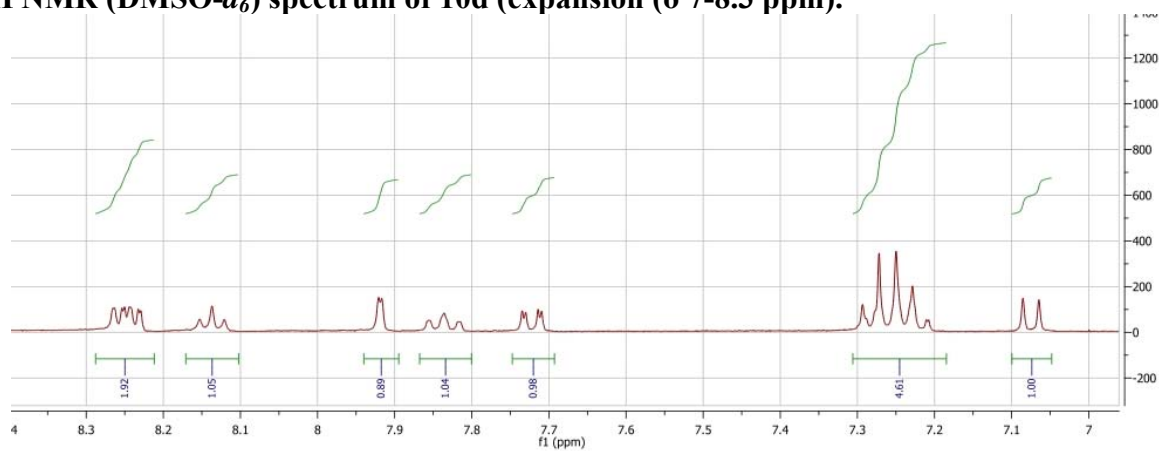
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	1376928.96	360.04081	360.04127	0.45996	1.28	--
[2M-H]-	350278.59	721.08890	721.08833	-0.57493	-0.80	--

Tuesday, March 04, 2008

15:09:45 PM



¹H NMR (DMSO-*d*₆) spectrum of 10d (expansion (δ 7-8.3 ppm)).



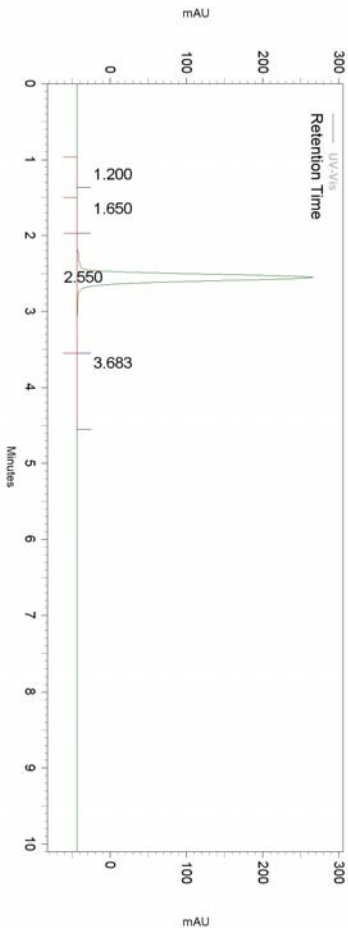
HPLC 10d

Area Percent Report

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Acquired: 4/4/2007 7:04:18 PM
Page 1 of 2 Data File: C:\HPLC

Printed: 4/4/2007 7:14:51 PM

Analyt: System
Sample ID: RPMM39 I
Vial: N/A
Injection Volume: 0



UV-Vis Results			
Name	Retention Time	Area	Area Percent

Integration Codes			
	1.200	307	0.015
	1.650	1335	0.065
	2.550	2038563	99.751
	3.683	3441	0.168

Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\90CH3CN10H2O fl 0.75 10min.mnt
Sequence: C:\HPLC\data\Danabc.seq
Software Version: Version 3.1.7

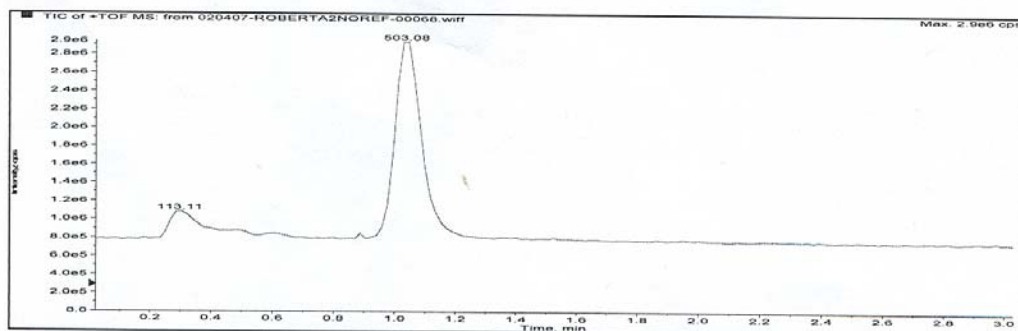
HRMS 10d

Mass List Report

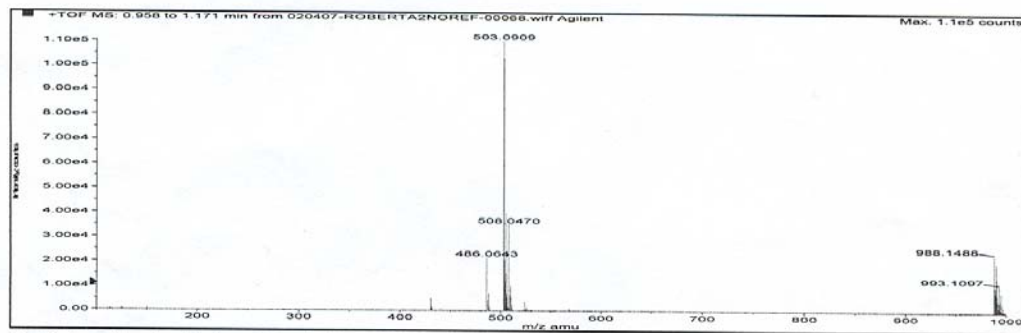
COMPOUND 7c

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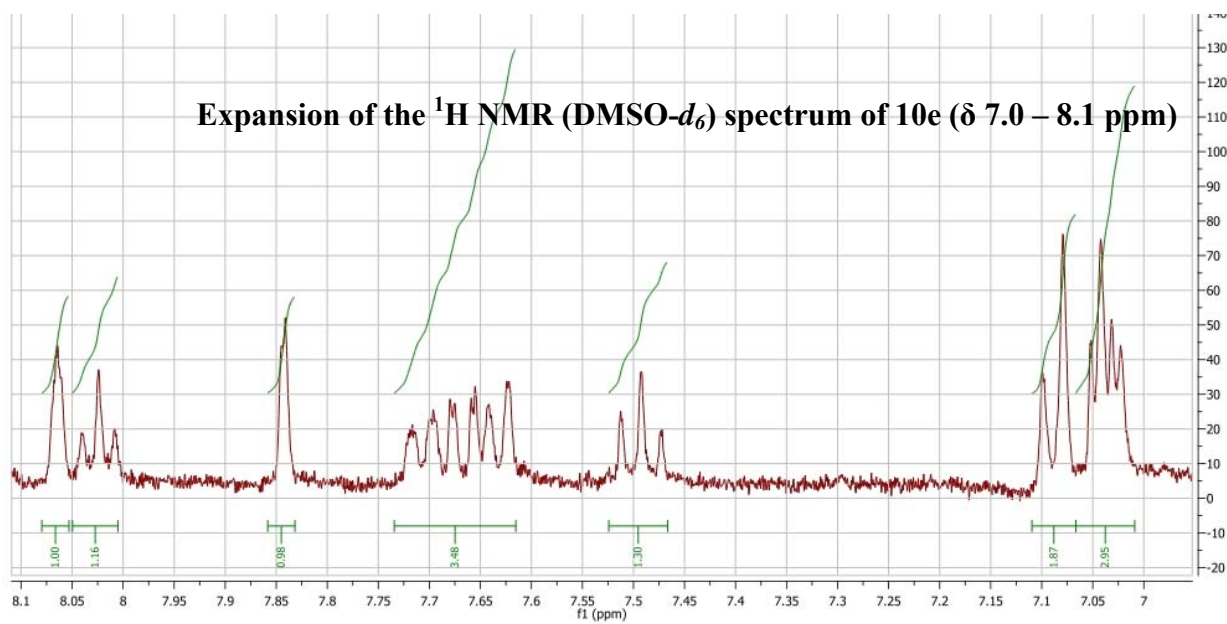
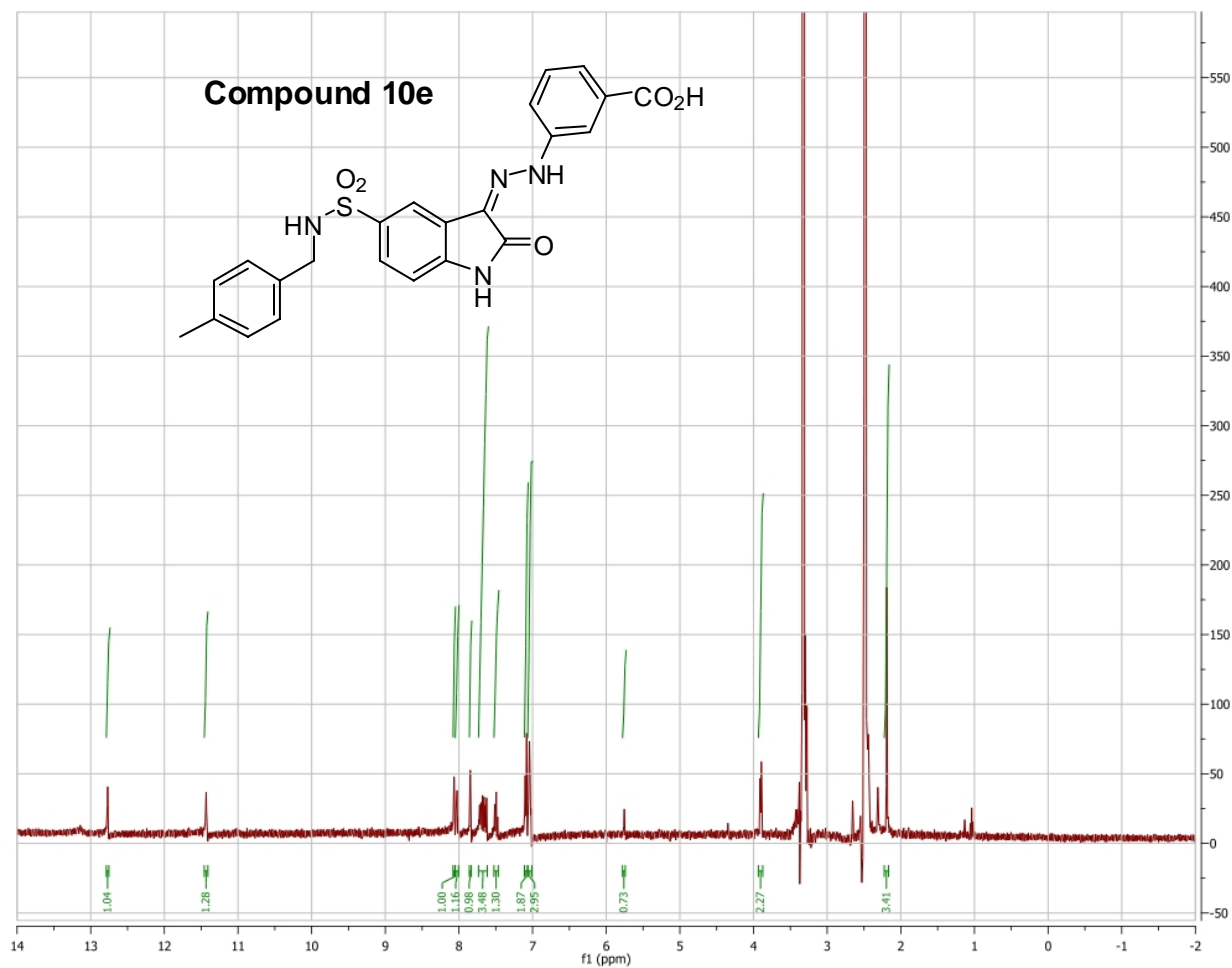
Sample#: rpm139 Sample Location: P1-F-01 Sample Id: rpm139 Operator: EasyAccess
Data File Name: D:\PE_Sciex_Data\Projects\chemist\04-07\Data\020407-ROBERTA2NOREF-00068.wiff Acq Time: April 02 2007, 03:39:33 PM
Method: D:\TOF_Data\methods\EASY ACCESS.ANM\mass_list.xml



Peak#	Experiment#	Time	Area	Most Abundant Masses/scan
1	1	1.04	1.29958 E7	503.09092



Peak#: 1 Experiment#: 1 Retention Time: 1.04 min



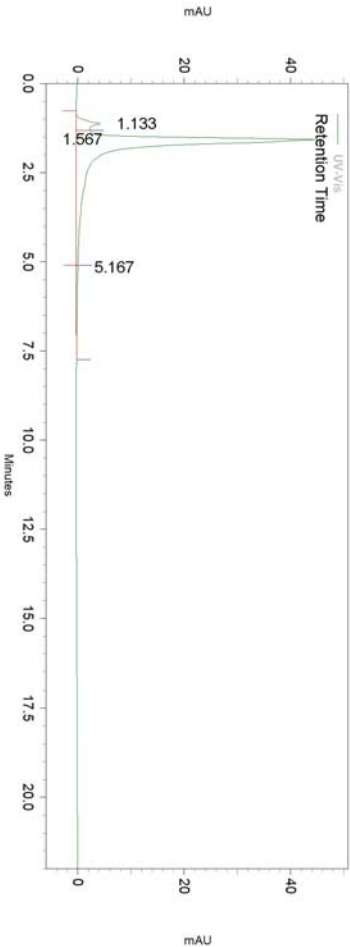
HPLC 10e

Area Percent Report

data\Yunting\YL1-165\System10-16-2007 5-18-38 PM.dat
Acquired: 10/16/2007 5:19:13 PM

Page 1 of 2 Data File: C:\HPLC
Printed: 10/16/2007 5:56:23 PM

Analyst: System
Sample ID: YL1-165
Vial: N/A
Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	1.133	57274	6.053	BV
	1.567	870590	92.007	VV
	5.167	18361	1.940	VB
Totals				

Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\MeOH90CH3CN10for1.0-21min.met
Sequence: C:\HPLC\data\Dan\abc.seq
Software Version: Version 3.1.7

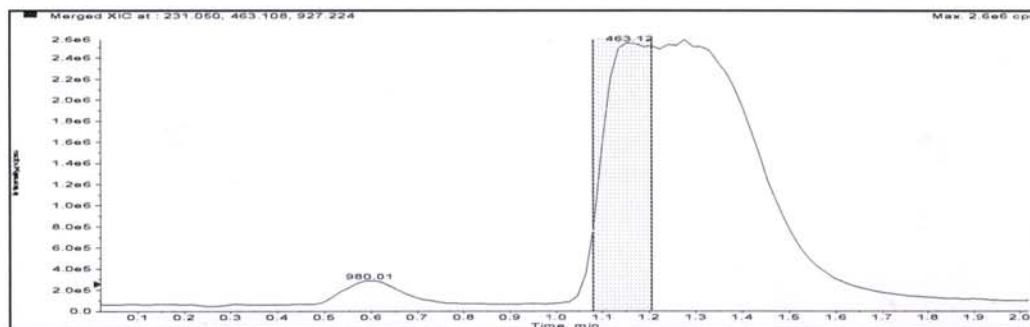
HRMS 10e

Empirical Formula Confirmation Report

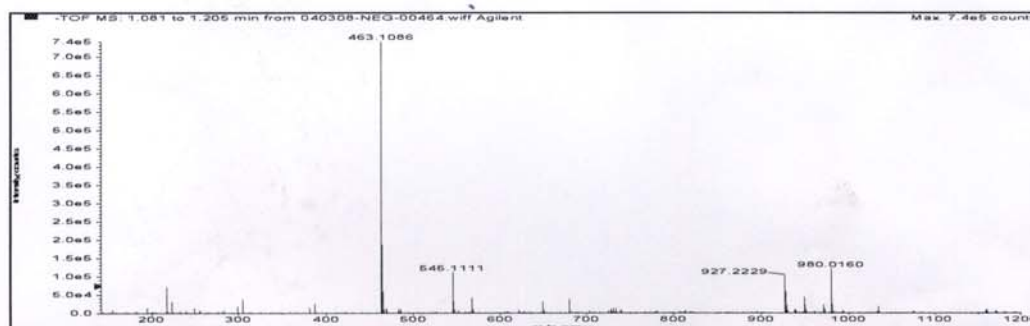
Page 1 of 1

Sample Name: YL1-165 Sample Location: P1-E-06 Sample Id: YL1-165 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00464.wiff Acq Time: March 04 2008, 03:04:31 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period#: 1 Experiment#: 1

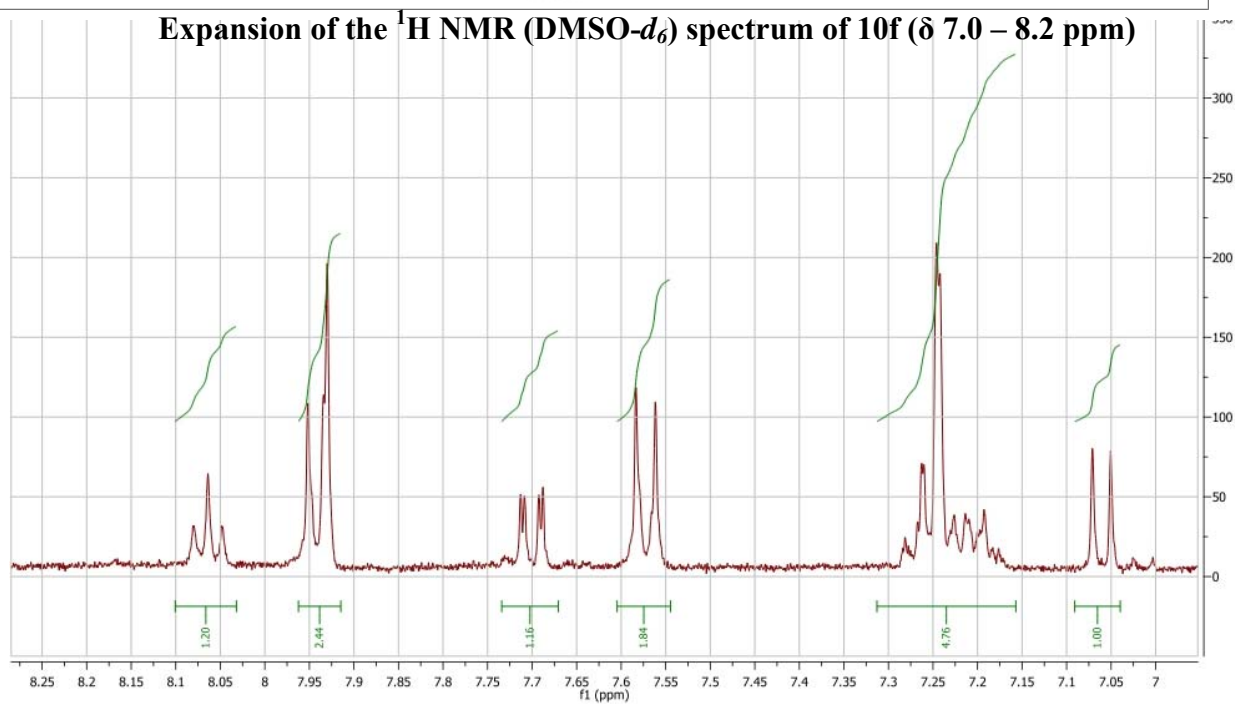
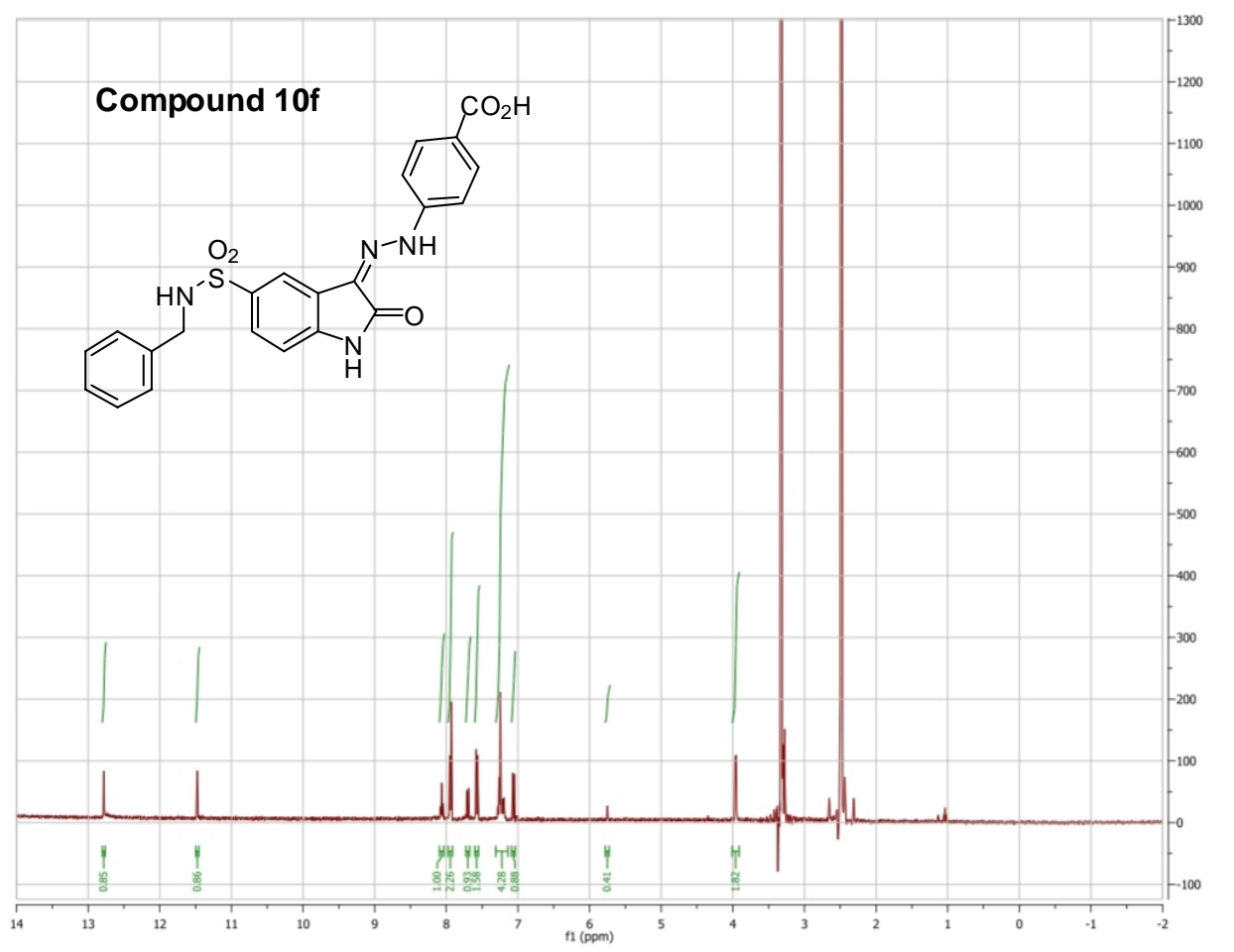


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C23H20N4O5S	--	464.11544	1.16	6.20222 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	755869.66	463.10816	463.10865	0.48311	1.04	--
[2M-H]-	101897.20	927.22360	927.22291	-0.69289	-0.75	--

Tuesday, March 04, 2008

15:06:44 PM



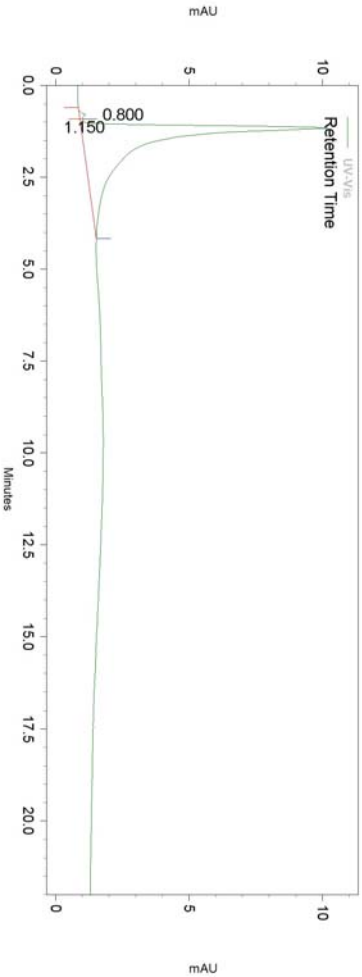
HPLC 10f

Area Percent Report

data\Yuning\YL1-162\System10-22-2007 4-26-48 PM.dat
Acquired: 10/22/2007 4:27:15 PM

Page 1 of 2 Data File: C:\HPLC
Printed: 10/22/2007 4:49:36 PM

Analyst: System
Sample ID: YL1-162
Vial: N/A
Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.800	1769	0.664	BV
	1.150	264762	99.336	VB

Totals		266531	100.000	
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Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\McOH90CH3CN10fr1.5-21min.met
Sequence: C:\HPLC\data\Danabc.seq
Software Version: Version 3.1.7

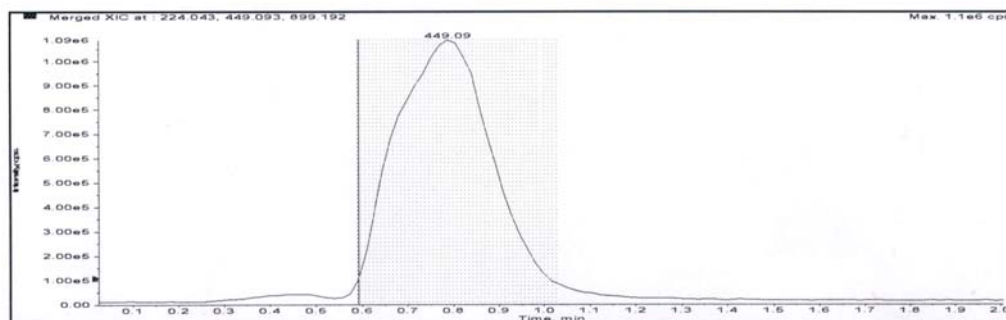
HRMS 10f

Empirical Formula Confirmation Report

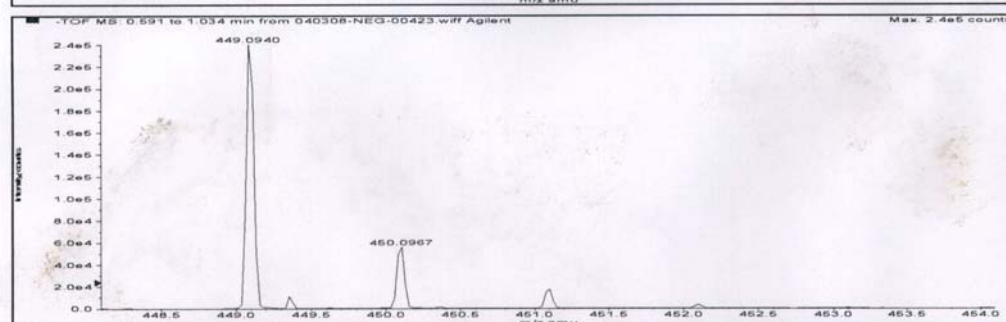
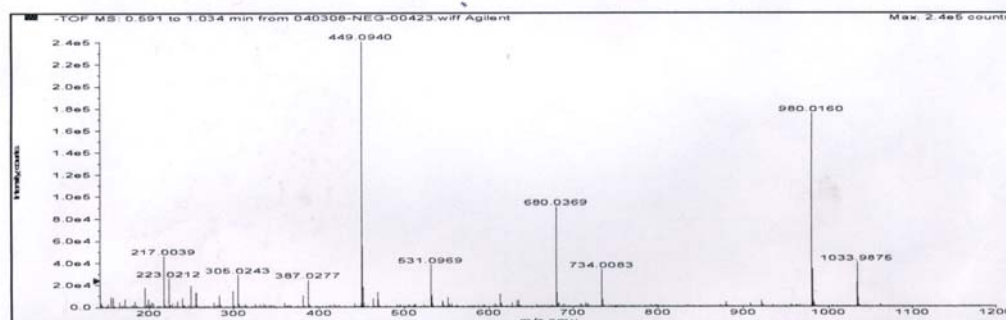
Page 1 of 1

Sample Name: YL1-162 Sample Location: P1-A-01 Sample Id: YL1-162 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00423.wiff Acq Time: March 04 2008, 12:07:31 PM
Method: D:\TOF_Data\amethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period#: 1 Experiment#: 1

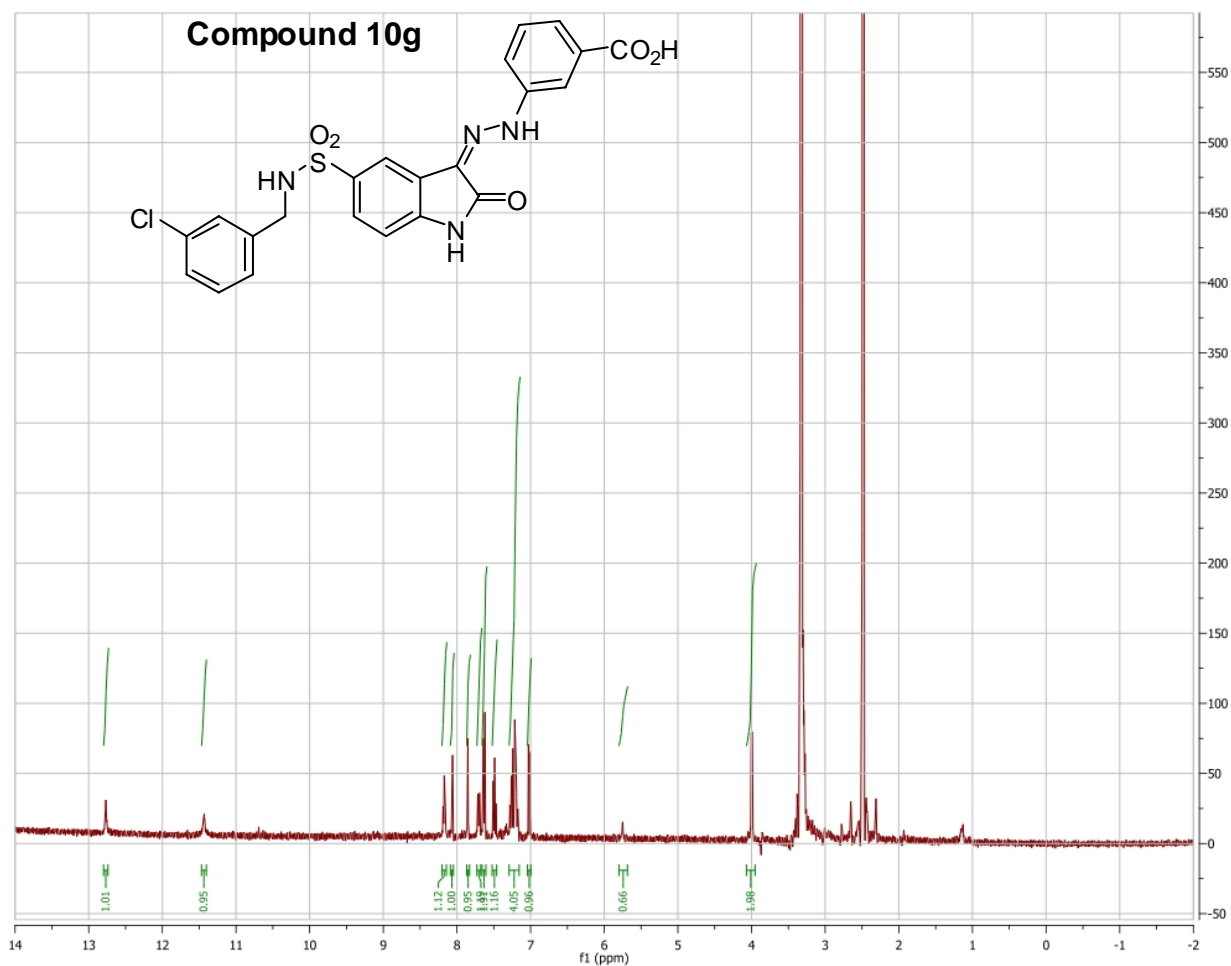


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H18N4O5S	--	450.09979	0.79	1.61046 E7	--

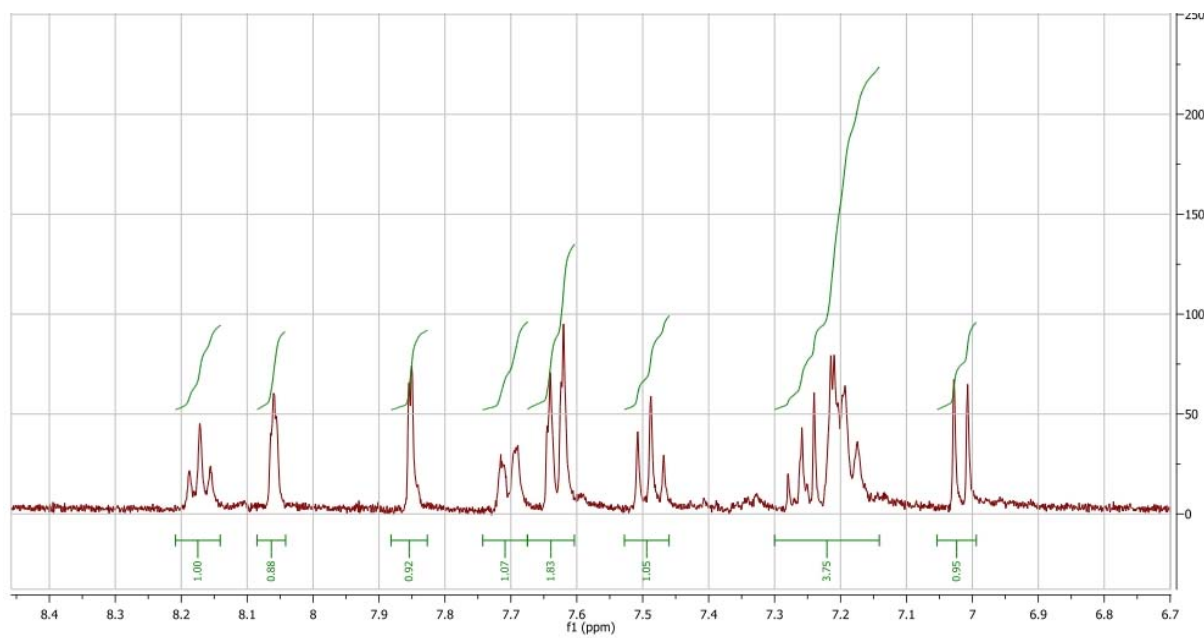
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	249165.16	449.09251	449.09404	1.52622	3.40	--

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12:09:46 PM



Expansion of the ¹H NMR (DMSO-*d*₆) spectrum of 10g (δ 6.7 – 8.4 ppm)



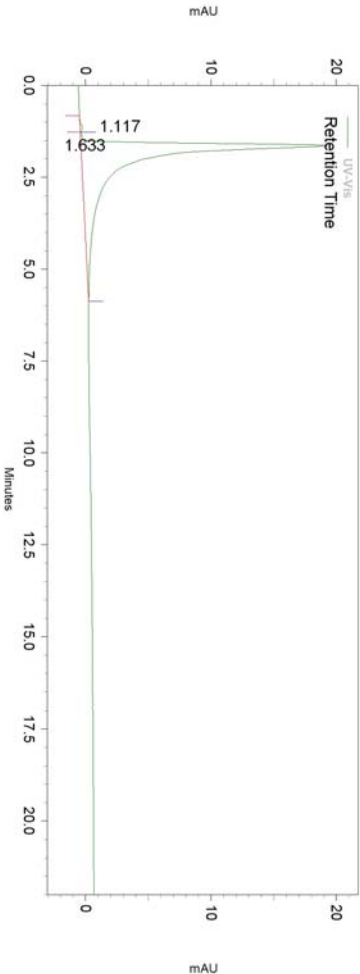
HPLC 10g

Area Percent Report

data\Yuning\YL1-168-2\System10-22-2007 2-48-50 PM.dat
Acquired: 10/22/2007 2:49:29 PM

Page 1 of 2 Data File: C:\HPLC
Printed: 10/22/2007 3:19:53 PM

Analyst: System
Sample ID: YL1-168-2 Vial: N/A Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	1.117	2100	0.395	BV
	1.633	529752	99.605	VB

Totals		531852	100.000	
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Instrument Name: HPLC Software Version: Version 3.1.7
Acquisition Method: C:\EZStart\Projects\Default\Method\MeOH90CH3CN10Fr1.0-21min.met
Sequence: C:\HPLC\data\Danabc.seq

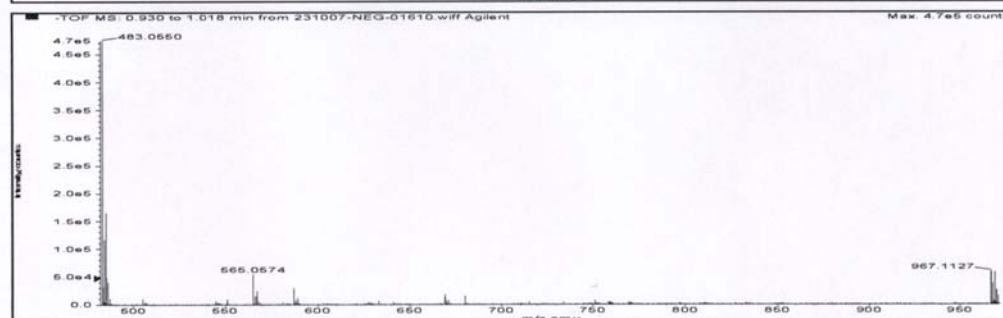
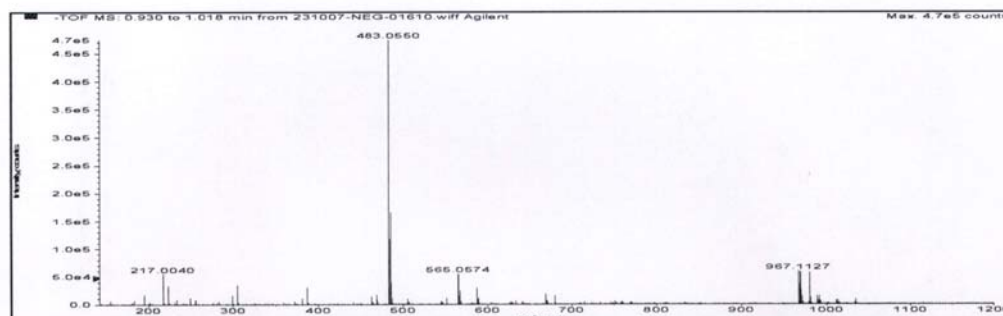
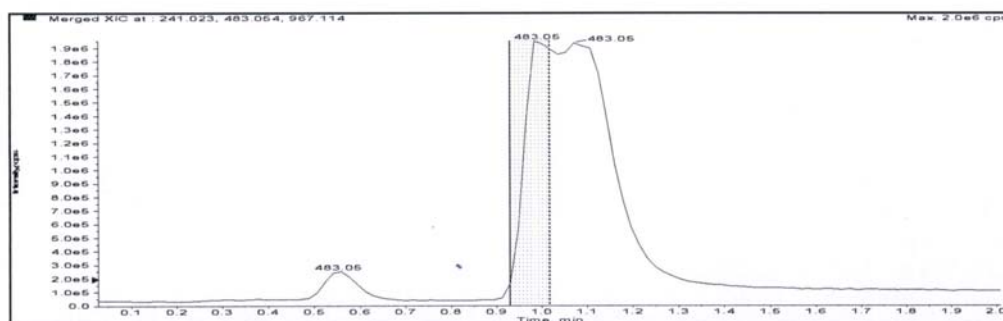
HRMS 10g

Empirical Formula Confirmation Report

Page 1 of 1

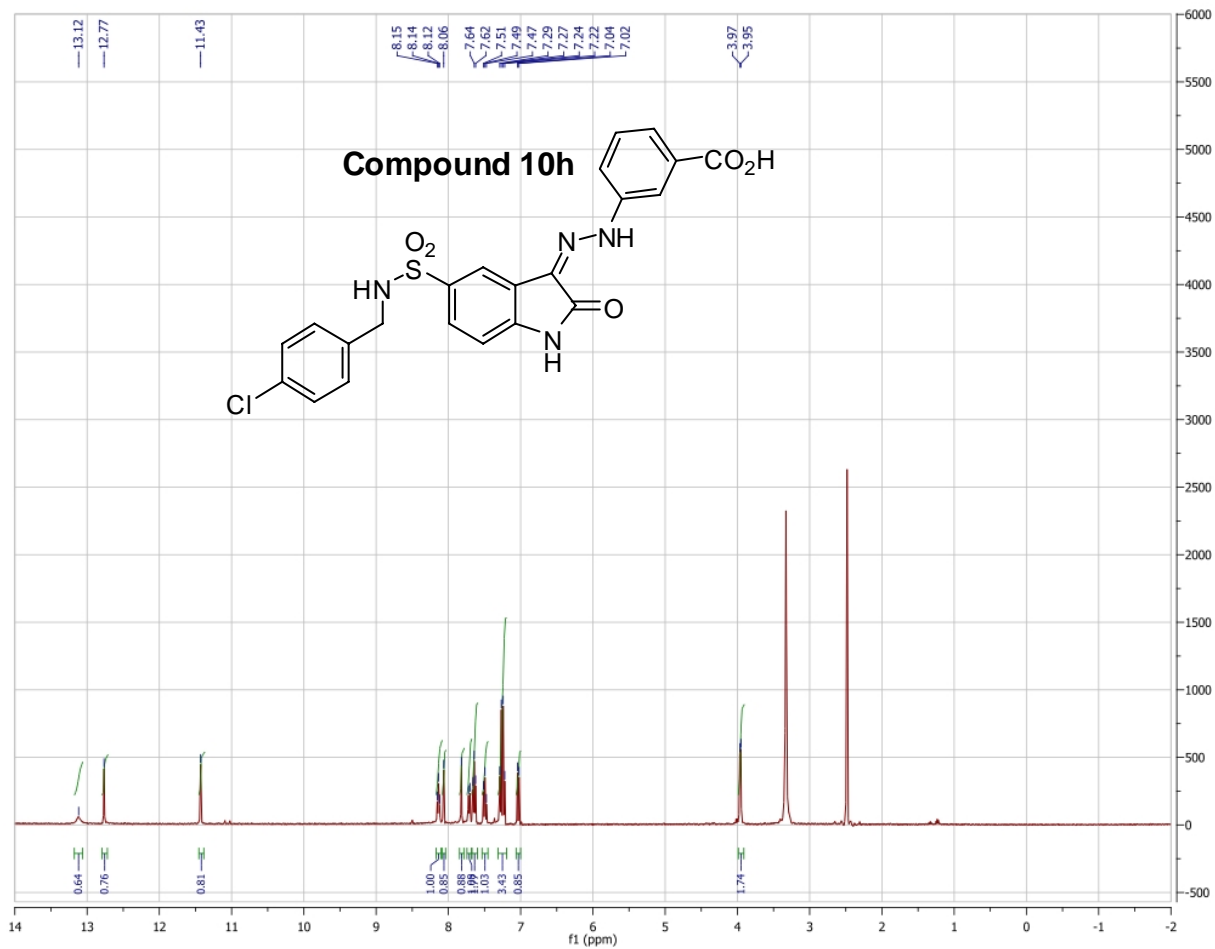
Sample Name: YL1-168-2 Sample Location: P1-A-99 Sample Id: YL1-168-2 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\10-07\Data\231007-NEG-01610.wiff Acq Time: October 23 2007, 11:01:41 AM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.

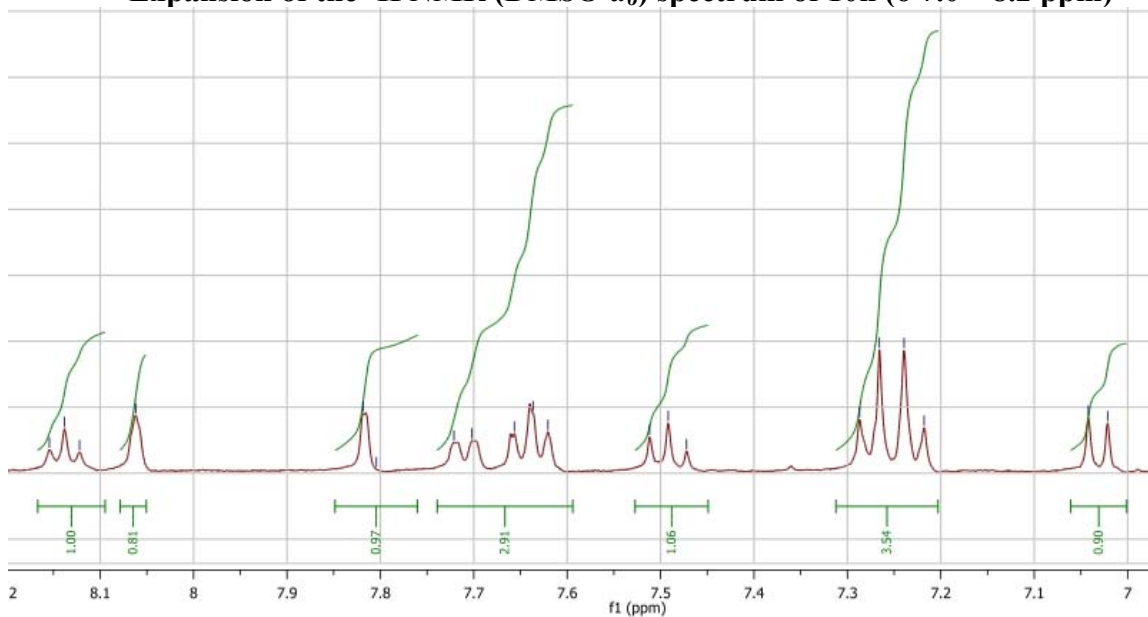


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17CIN4O5S	--	484.06082	0.99	8.92037 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	477852.28	483.05354	483.05504	1.50313	3.11	--
[2M-H]-	60135.58	967.11436	967.11270	-1.65583	-1.71	--



Expansion of the ^1H NMR ($\text{DMSO}-d_6$) spectrum of 10h (δ 7.0 – 8.2 ppm)



HPLC 10h

Area Percent Report

Page 1 of 2 Data File: C:\HPLC

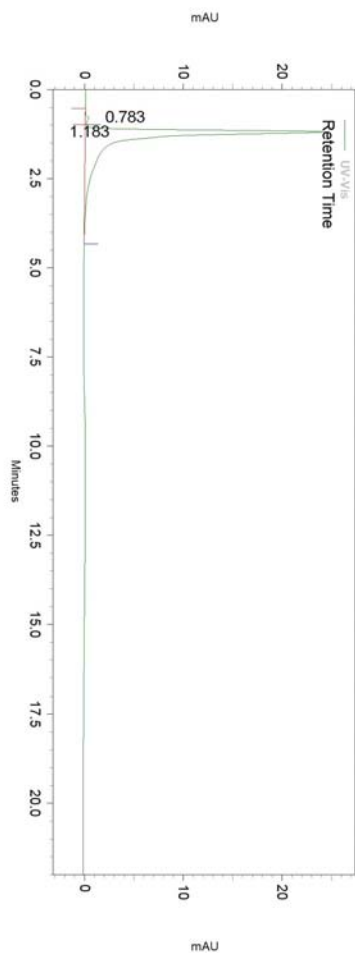
data\Roberta\RPMT744a\System11-27-2007 6-08-22 PM.dat
Acquired: 11/27/2007 6:09:02 PM

Printed: 11/27/2007 6:33:42 PM

Analyst: System
Sample ID: RPMT744a

Vial: N/A

Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.783	3580	1.013	BV
	1.183	349753	98.987	VB
Totals		353333	100.000	

Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\MeOH90CH3CN10fr1.5-21min.met
Sequence: C:\HPLC\data\Dan\abc.seq
Software Version: Version 3.1.7

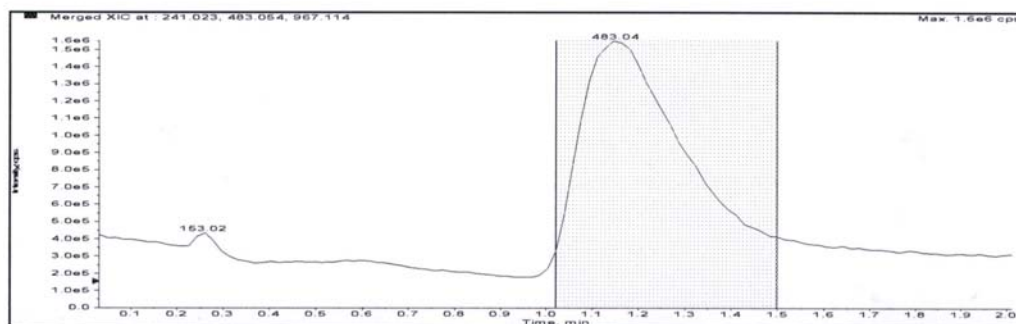
HRMS 10h

Empirical Formula Confirmation Report

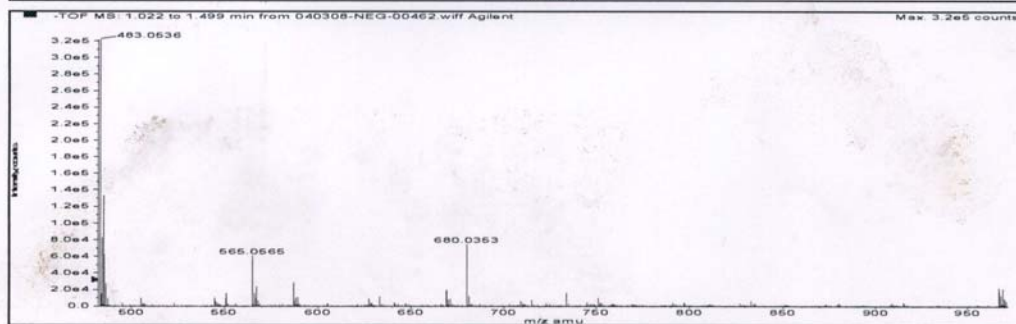
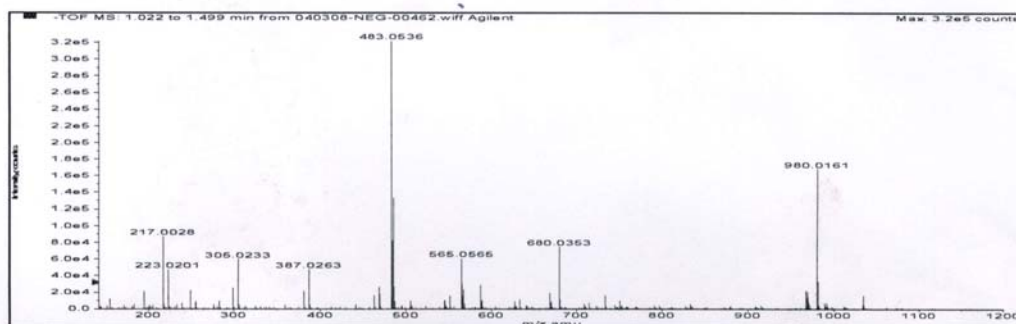
Page 1 of 1

Sample Name: YL1-170-2 Sample Location: P1-E-04 Sample Id: YL1-170-2 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00462.wiff Acq Time: March 04 2008, 02:58:32 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

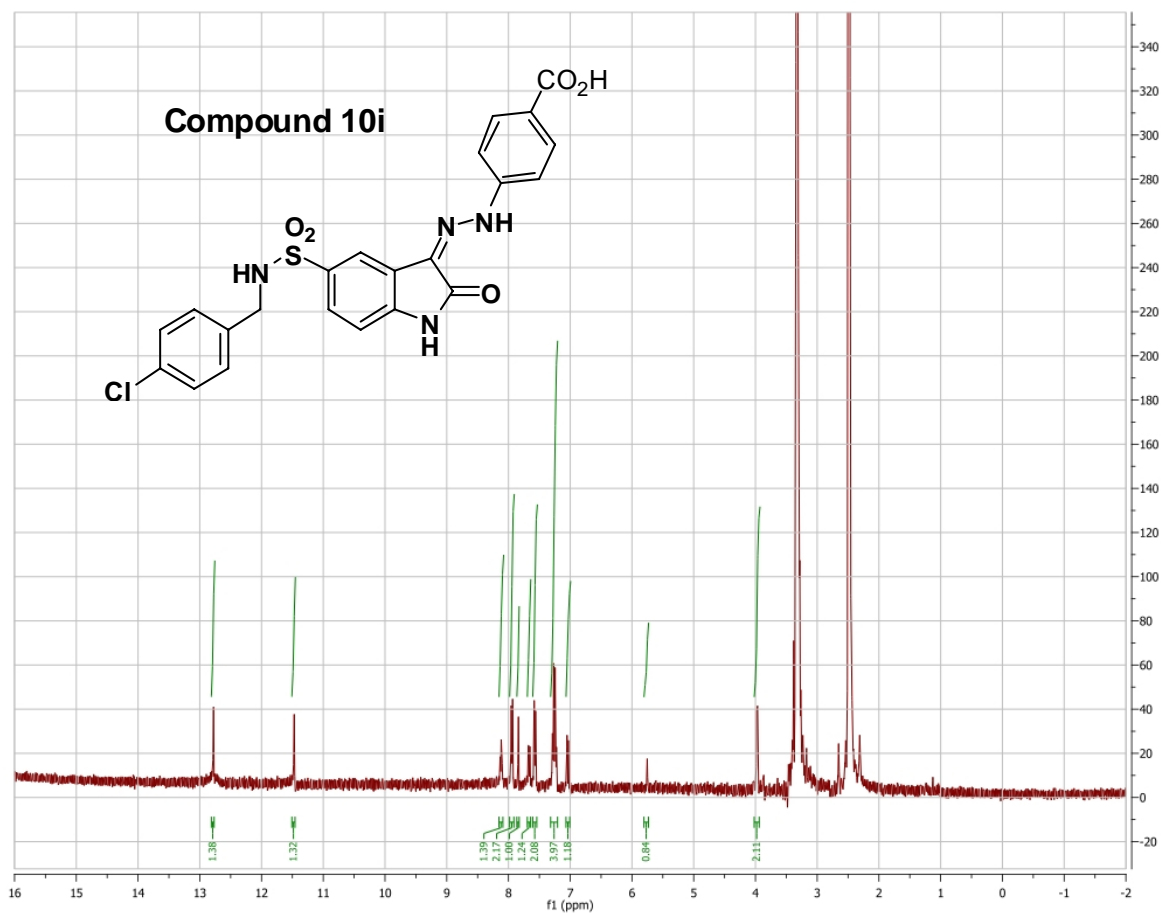


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17CIN4O5S	--	484.06082	1.15	2.01392 E7	--

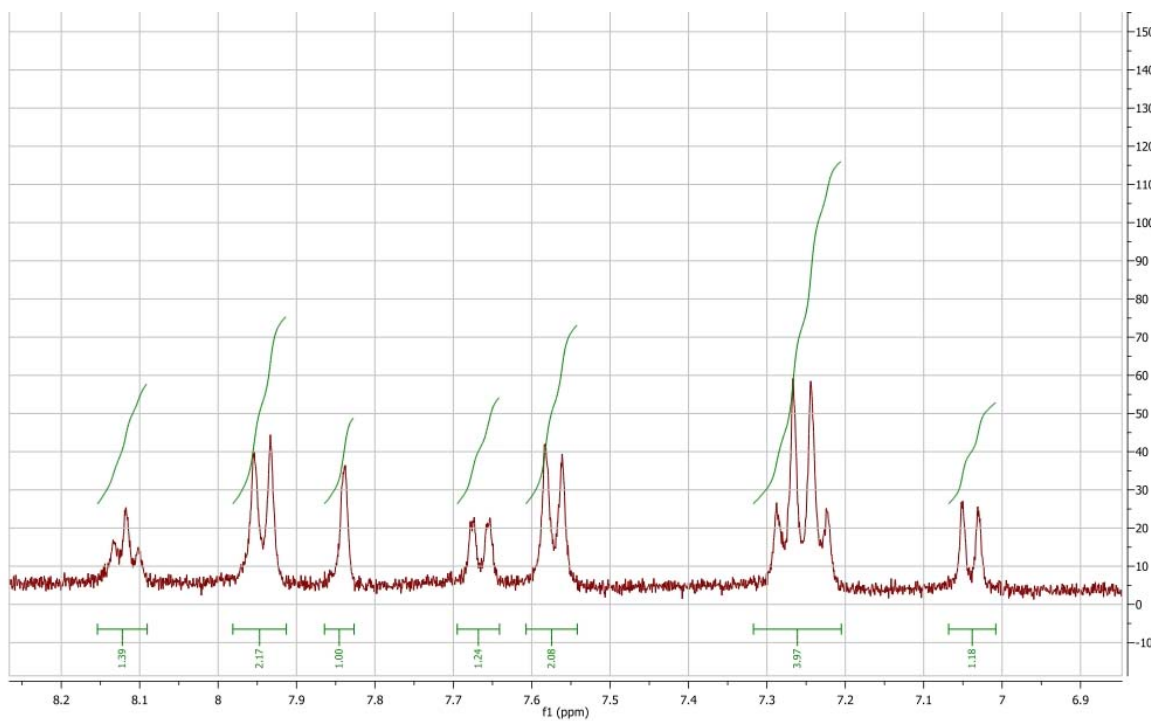
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	349261.54	483.05354	483.05360	0.05352	0.11	--
[2M-H]-	22423.29	967.11436	967.11369	-0.66943	-0.69	--

Tuesday, March 04, 2008

15:00:44 PM



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 10i (δ 6.9 – 8.2 ppm)



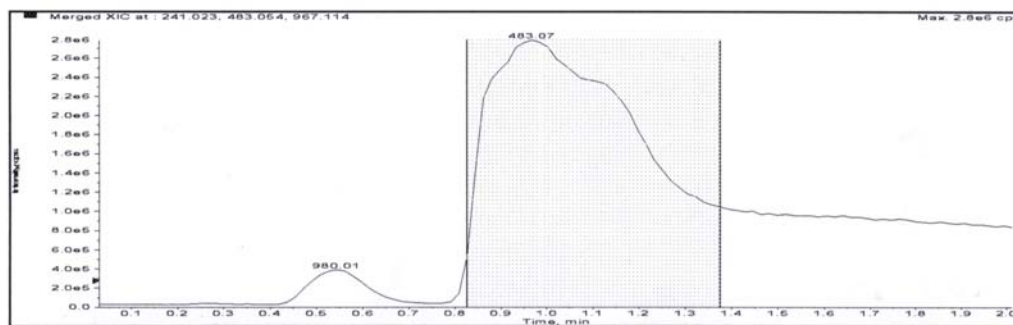
HRMS of 10i

Empirical Formula Confirmation Report

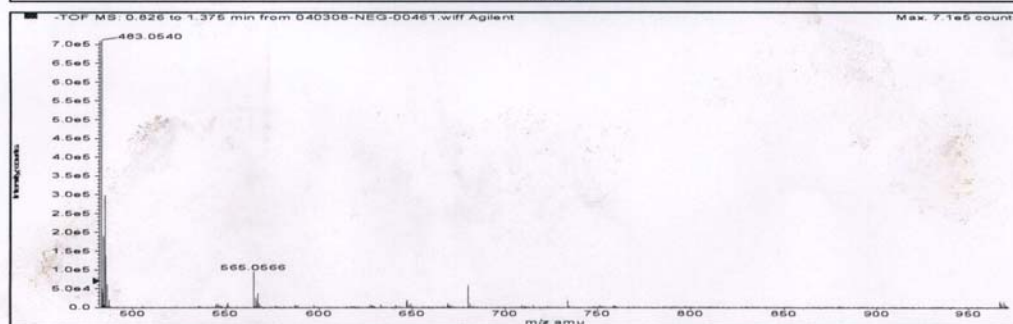
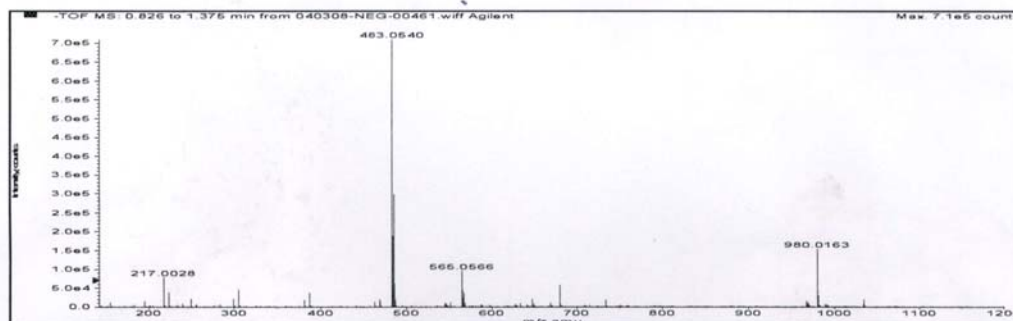
Page 1 of 1

Sample Name: YL1-170-1 Sample Location: P1-E-03 Sample Id: YL1-170-1 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00461.wiff Acq Time: March 04 2008, 02:55:32 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

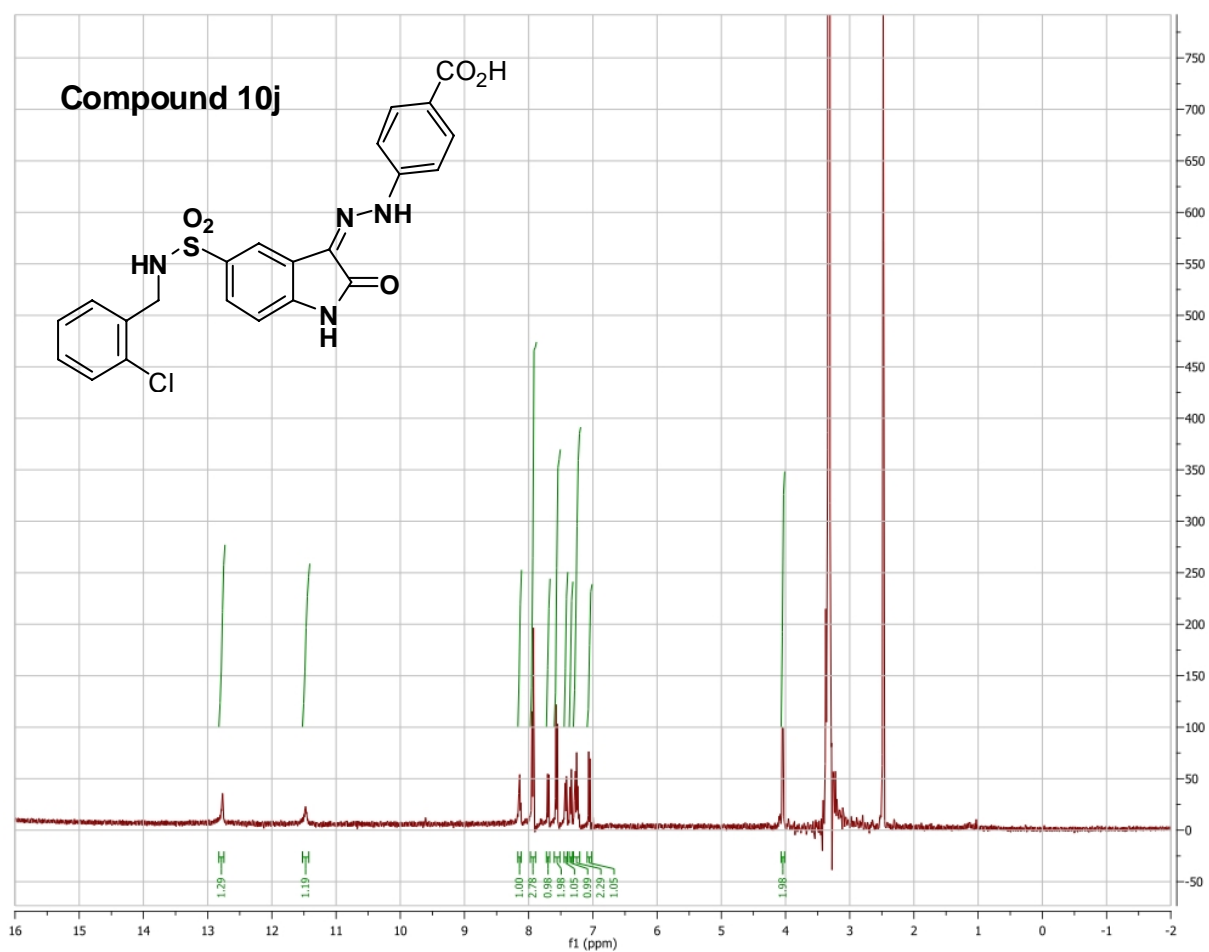


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17ClN4O5S	--	484.06082	0.97	5.43854 E7	--

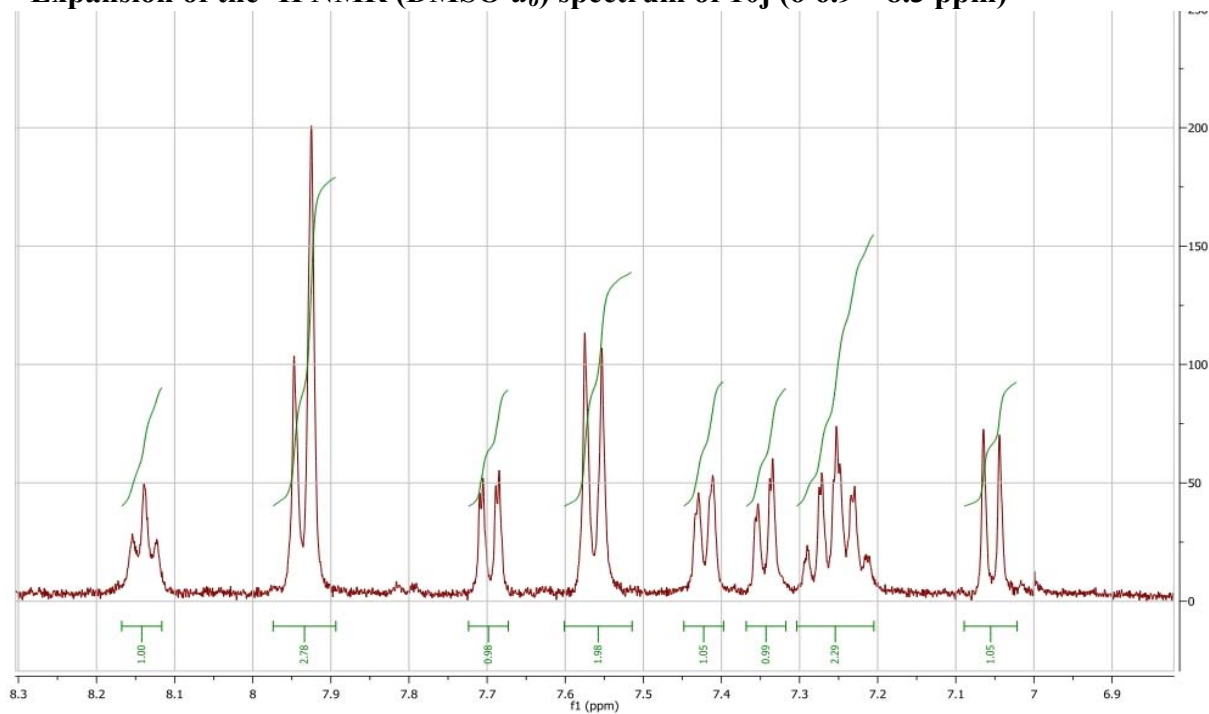
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	763172.58	483.05354	483.05402	0.48099	1.00	--
[2M-H]-	15788.34	967.11436	967.11382	-0.54284	-0.56	--

Tuesday, March 04, 2008

14:57:44 PM



Expansion of the ¹H NMR (DMSO-*d*₆) spectrum of 10j (δ 6.9 – 8.3 ppm)

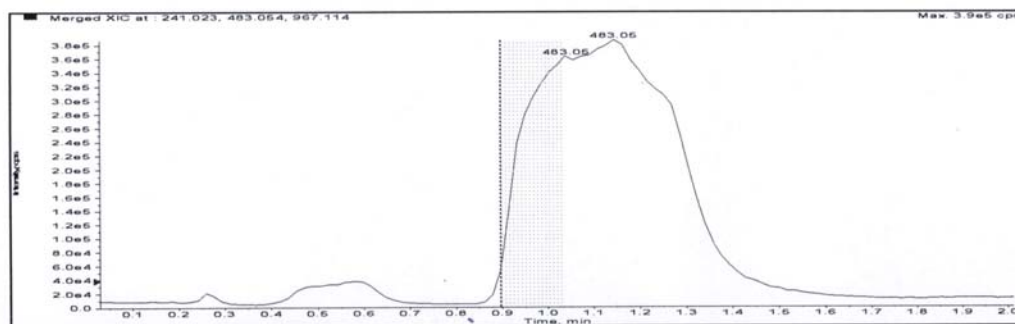


HRMS 10j

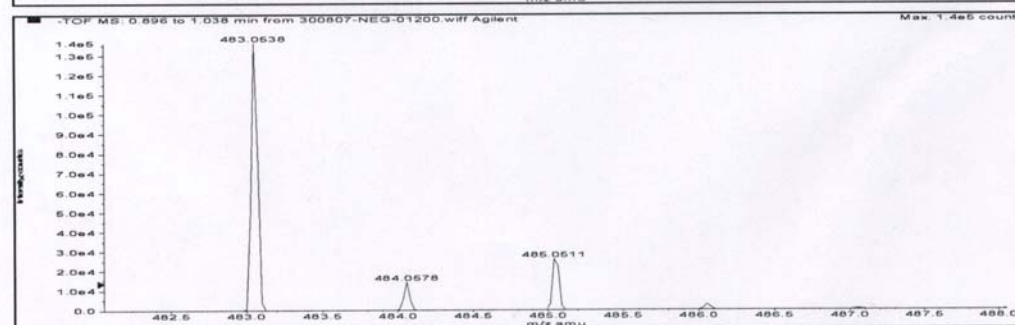
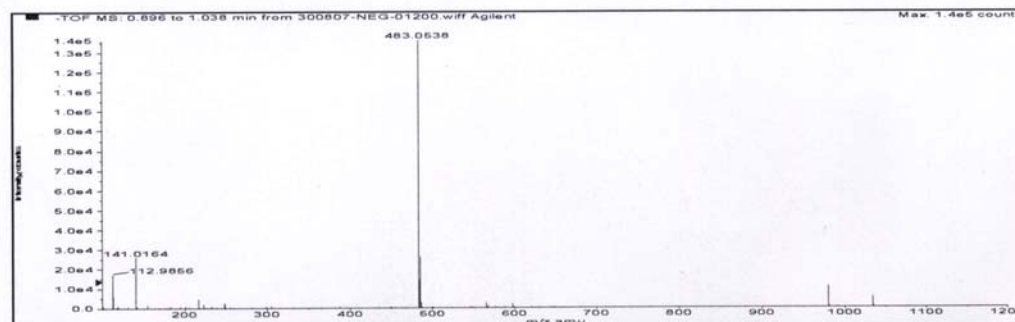
Empirical Formula Confirmation Report

Page 1 of 1

Sample Name: YL1-173-3 Sample Location: P1-A-07 Sample Id: YL1-173-3 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\08-07\Data\300807-NEG-01200.wiff Acq Time: August 30 2007, 09:51:08 AM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANMefc.xml

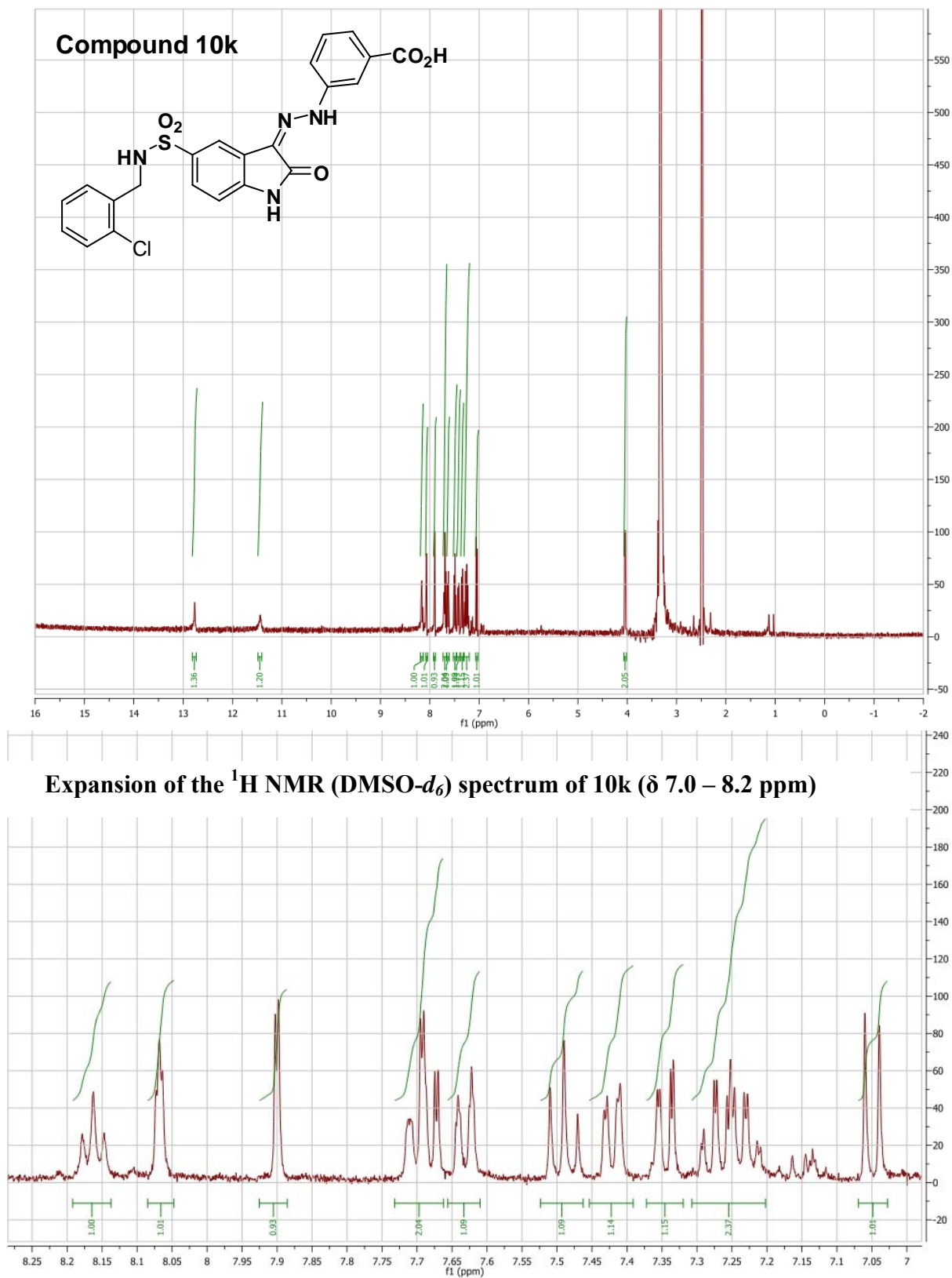


Merged XIC, Period# : 1 Experiment# : 1



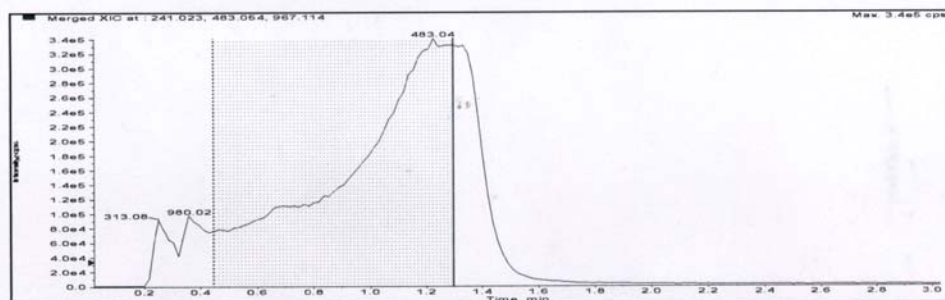
Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17CIN4O5S	--	484.06082	1.04	2.67366 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	137020.08	483.05354	483.05376	0.22260	0.46	--

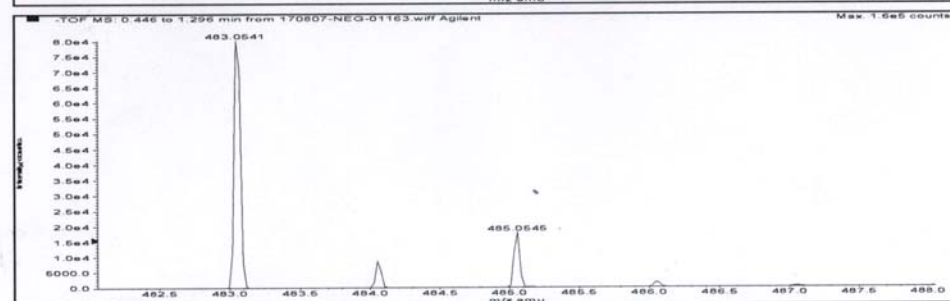
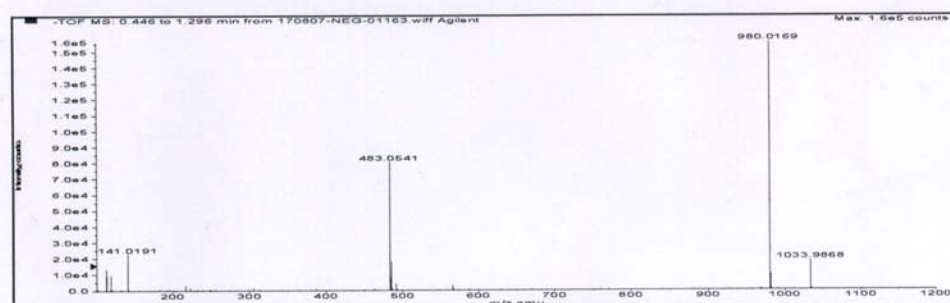


HRMS of 10k

Sample Name: YL1-173-4 Sample Location: P1-C-06 Sample Id: YL1-173-4 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\08-07\Data\170807-NEG-01163.wiff Acq Time: August 17 2007, 04:15:47 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml



Merged XIC, Period# : 1 Experiment# : 1

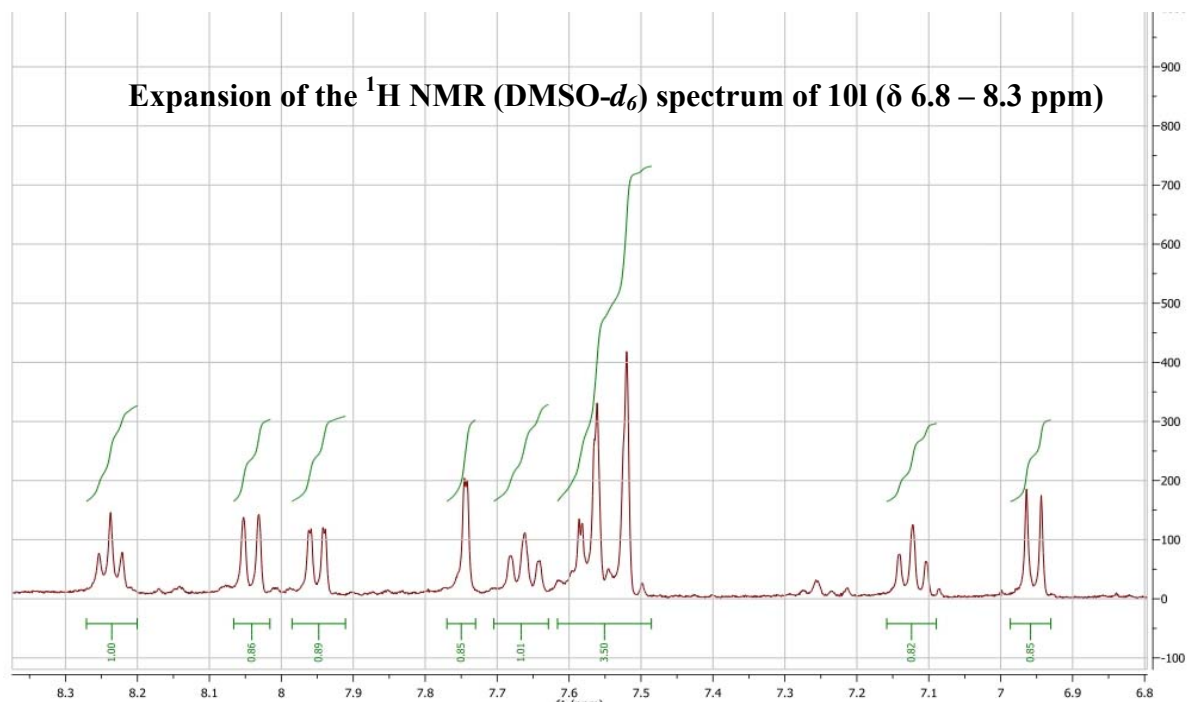
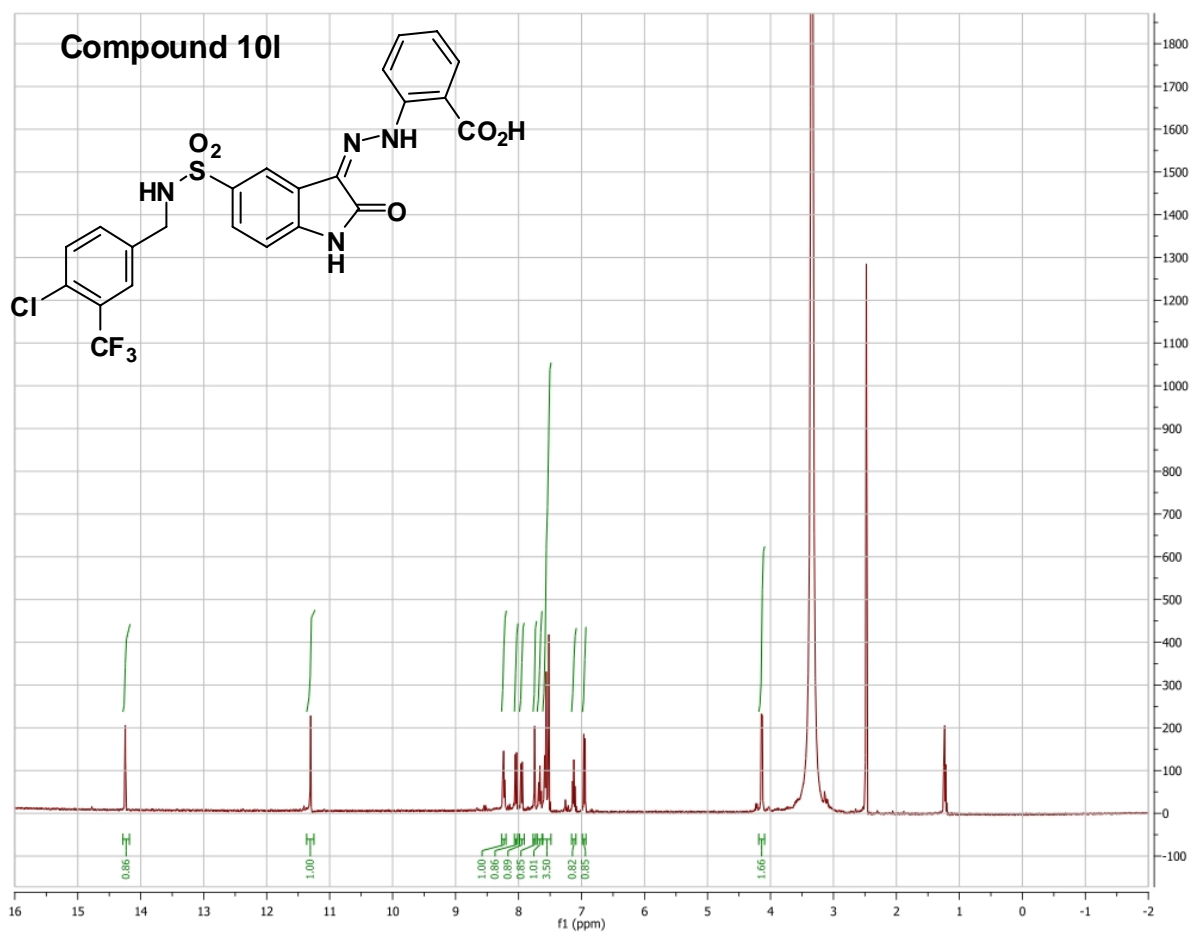


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17CIN4O5S	--	484.06082	1.23	1.50413 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	85713.38	483.05354	483.05406	0.51764	1.07	--

Friday, August 17, 2007

16:19:00 PM

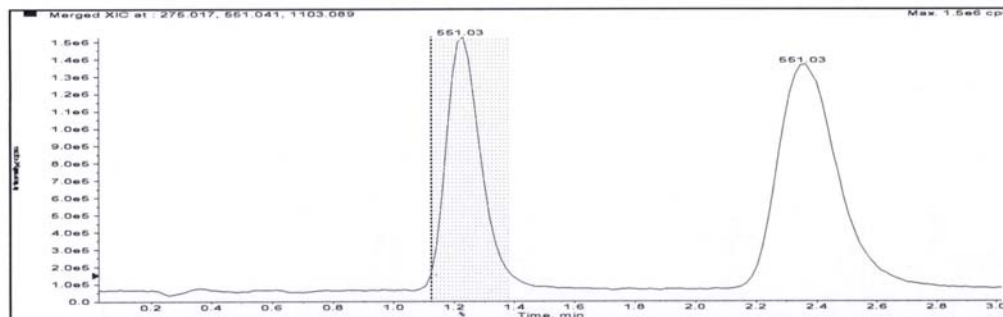


HRMS 101

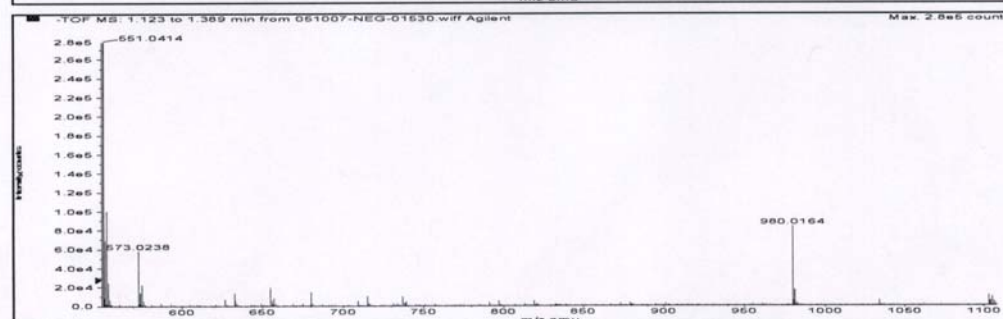
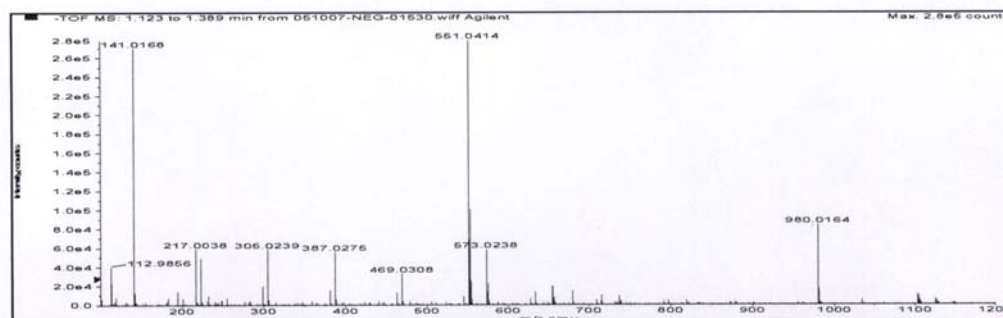
Empirical Formula Confirmation Report

Page 1 of 1

Sample Name: YL2-008-3 Sample Location: P1-A-02 Sample Id: YL2-008-3 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\10-07\Data\051007-NEG-01530.wiff Acq Time: October 05 2007, 09:43:19 AM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml

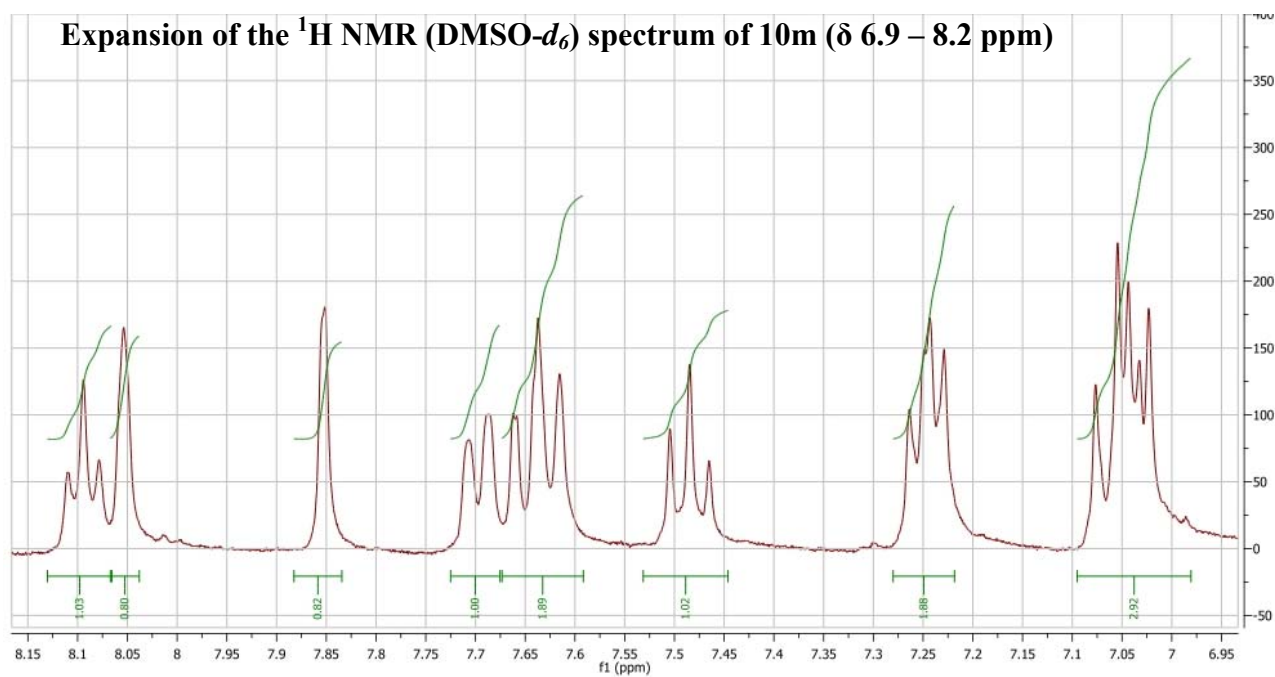
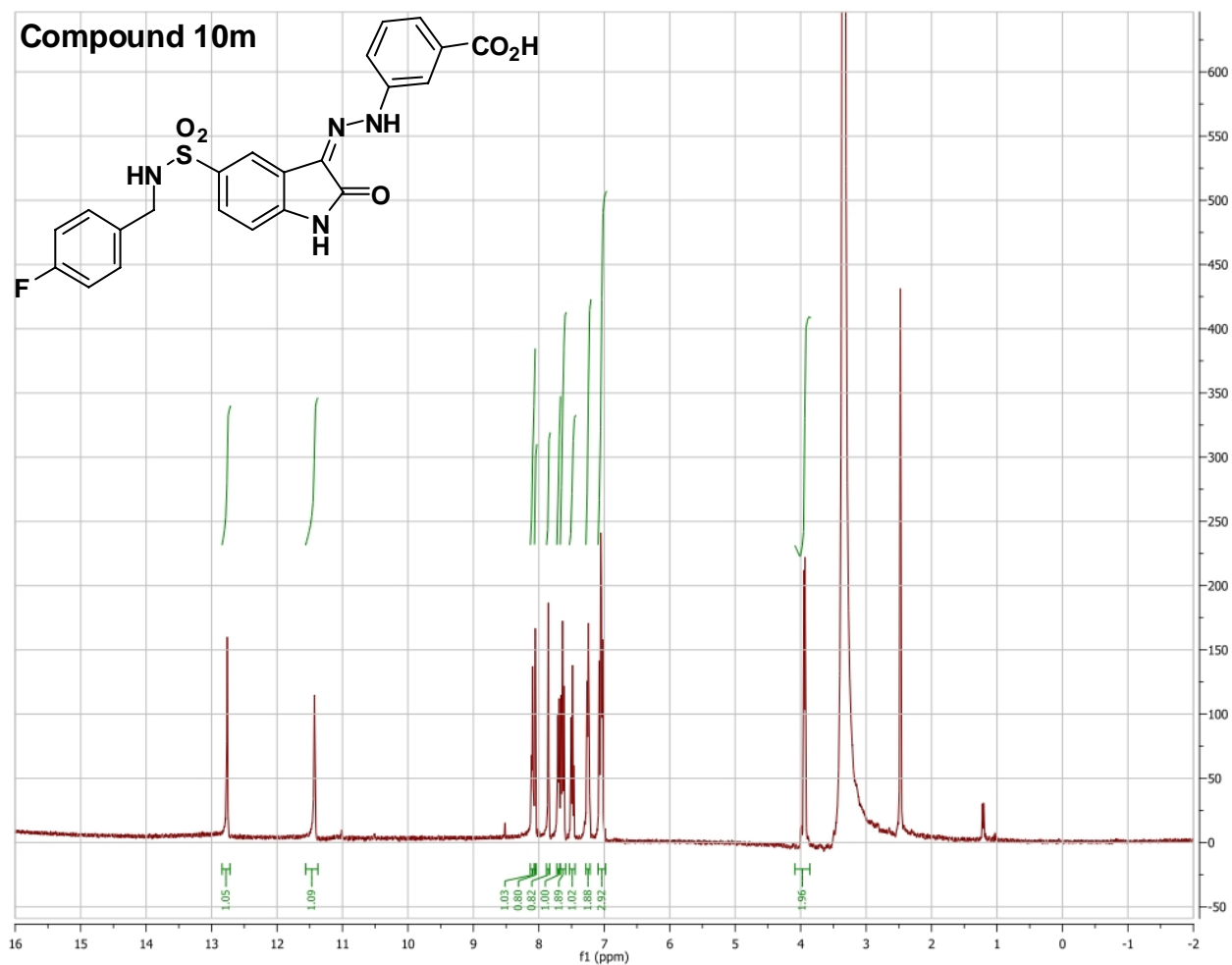


Merged XIC, Period# : 1 Experiment# : 1



Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C23H16ClF3N4O5S	--	552.04820	1.22	1.16791 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	292933.00	551.04093	551.04141	0.48694	0.88	--
[2M-H]-	10834.40	1103.08913	1103.08750	-1.63381	-1.48	--



HPLC 10m

Area Percent Report

data\Yunting\YL2-011-2\System10-16-2007 4-37-18 PM.dat
Acquired: 10/16/2007 4:37:53 PM

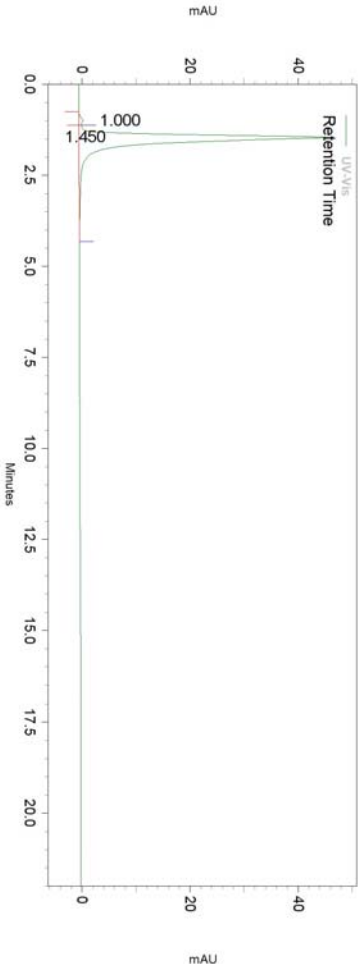
Page 1 of 2 Data File: C:\HPLC

Printed: 10/16/2007 5:00:13 PM

Analyst: System
Sample ID: YL2-011-2

Vial: N/A

Injection Volume: 0



UV-Vis Results

Name	Retention Time	Area	Area Percent	Integration Codes
	1.000	7985	1.189	BV
	1.450	663469	98.811	VB

Totals		671454	100.000	
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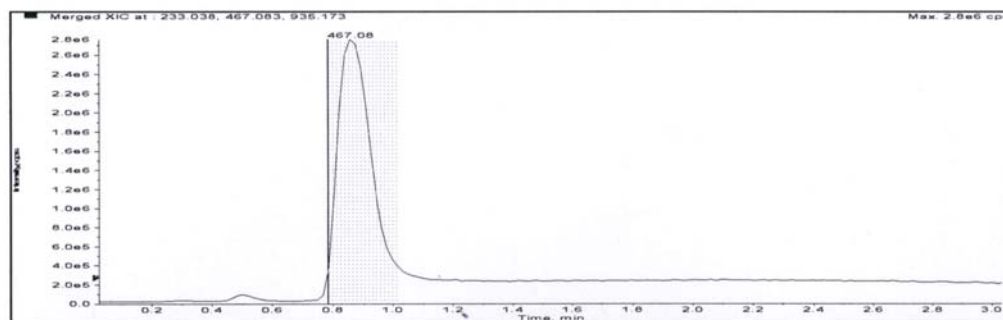
Instrument Name: HPLC
Acquisition Method: C:\EZStart\Projects\Default\Method\McOH90CH3CN10fr1.0-21min.met
Sequence: C:\HPLC\data\Dan\abc.seq
Software Version: Version 3.1.7

HRMS 10m

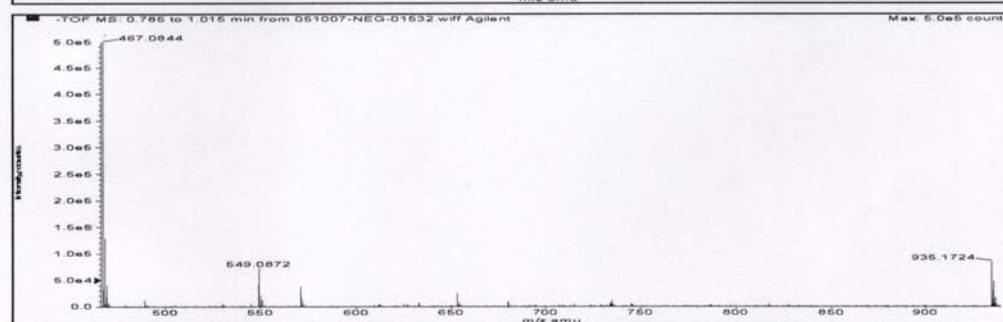
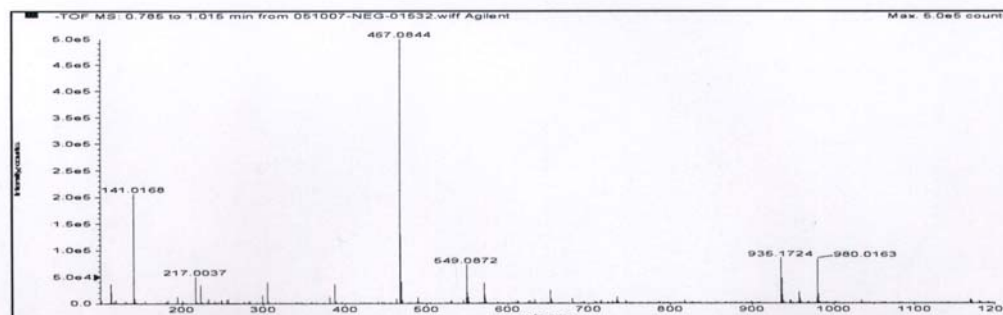
Empirical Formula Confirmation Report

Page 1 of 1

Sample Name: YL2-011-2 Sample Location: P1-A-04 Sample Id: YL2-011-2 Operator: EasyAccess
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Method: D:\TOF_Data\damethods\EASY ACCESS2.AN\mefc.xml

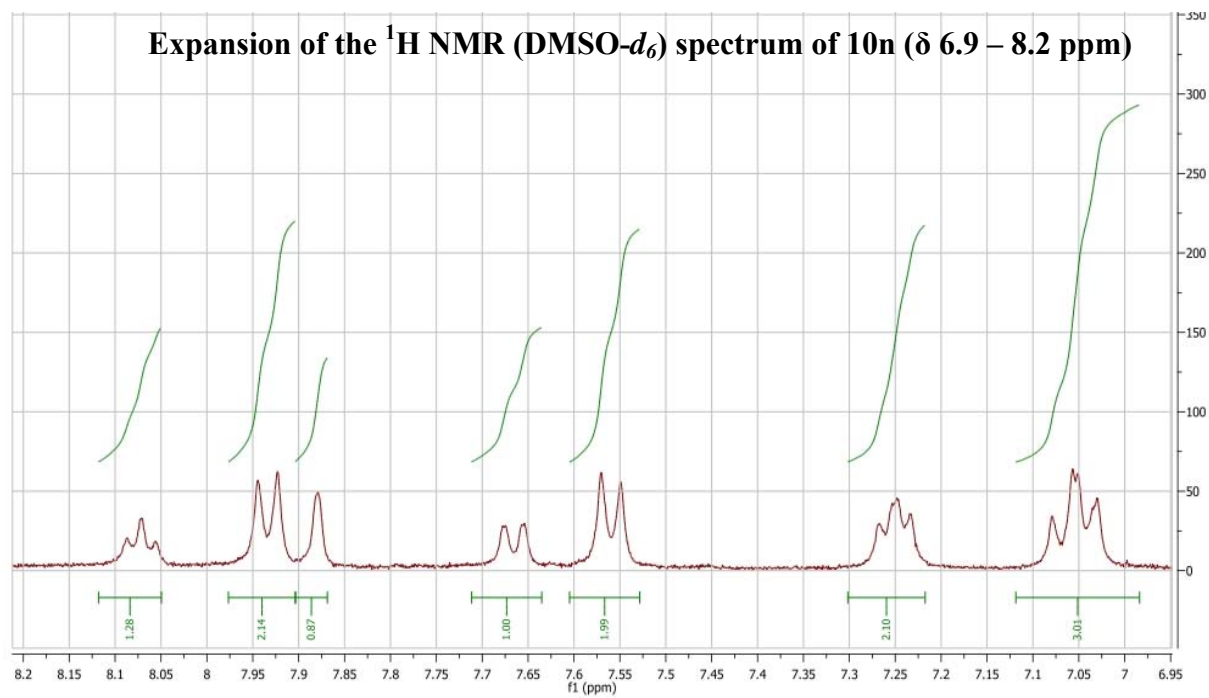
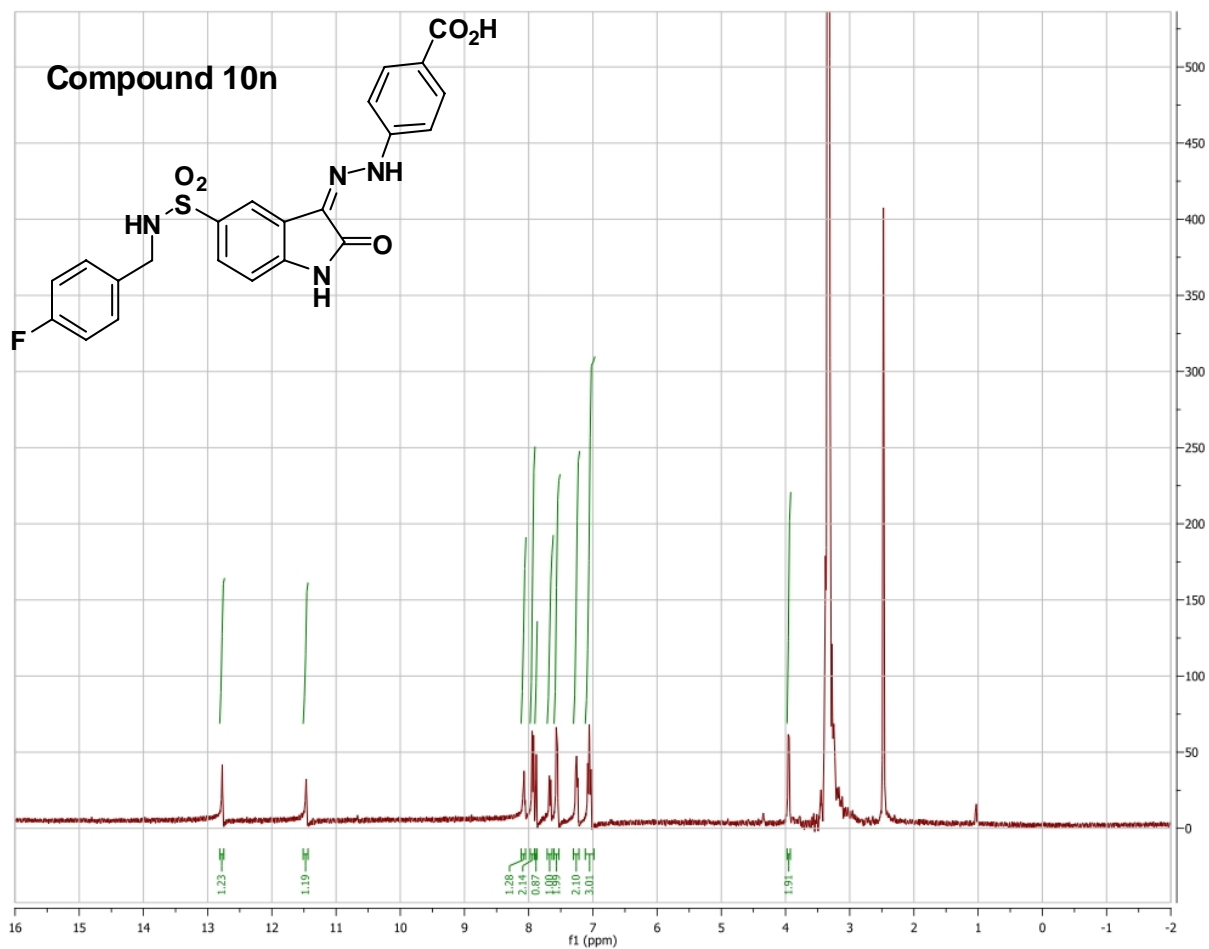


Merged XIC, Period#: 1 Experiment#: 1



Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17FN4O5S	--	468.09037	0.86	2.27549 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	518389.03	467.08309	467.08437	1.27969	2.74	--
[2M-H]-	86810.82	935.17346	935.17241	-1.04910	-1.12	--



HPLC 10n

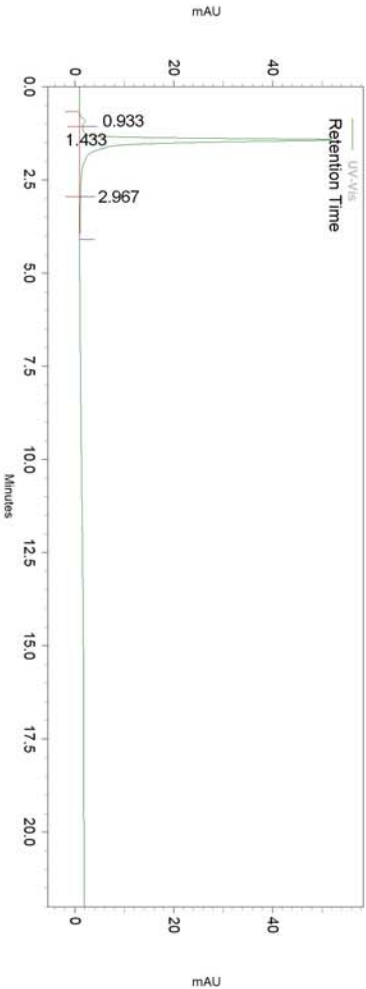
Area Percent Report

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Page 1 of 2 Data File: C:\HPLC

Printed: 10/16/2007 4:11:55 PM

Analyst: System
Sample ID: YL2-011-1 Vial: N/A Injection Volume: 0



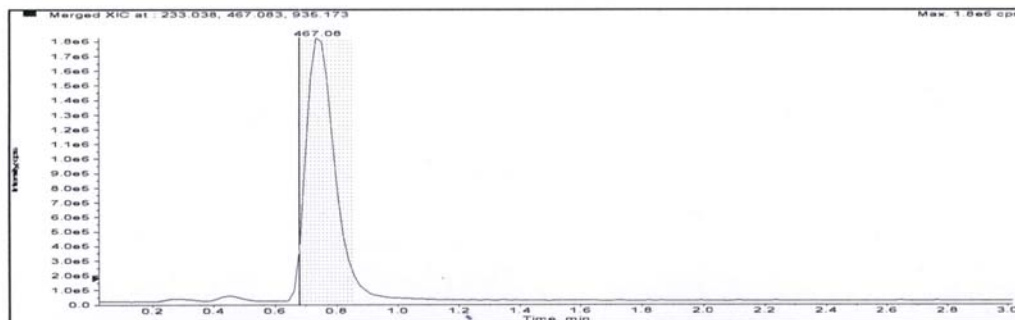
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Name	Retention Time	Area	Area Percent	Integration Codes
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	1.433	481586	96.566	VV
	2.967	4122	0.827	VB
Totals				
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HRMS 10n

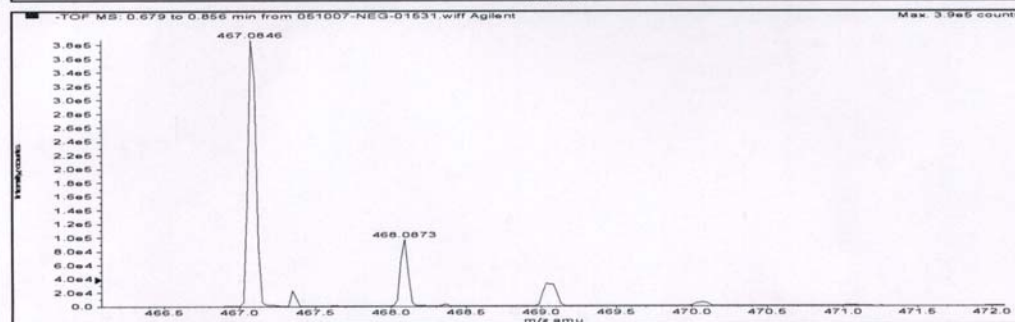
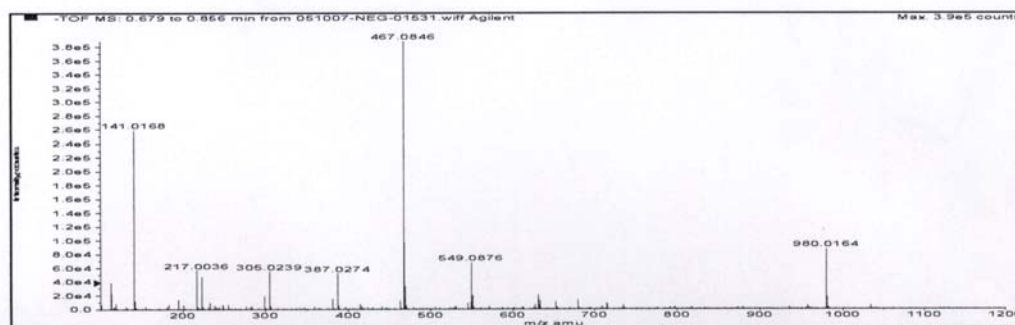
Empirical Formula Confirmation Report

Page 1 of 1

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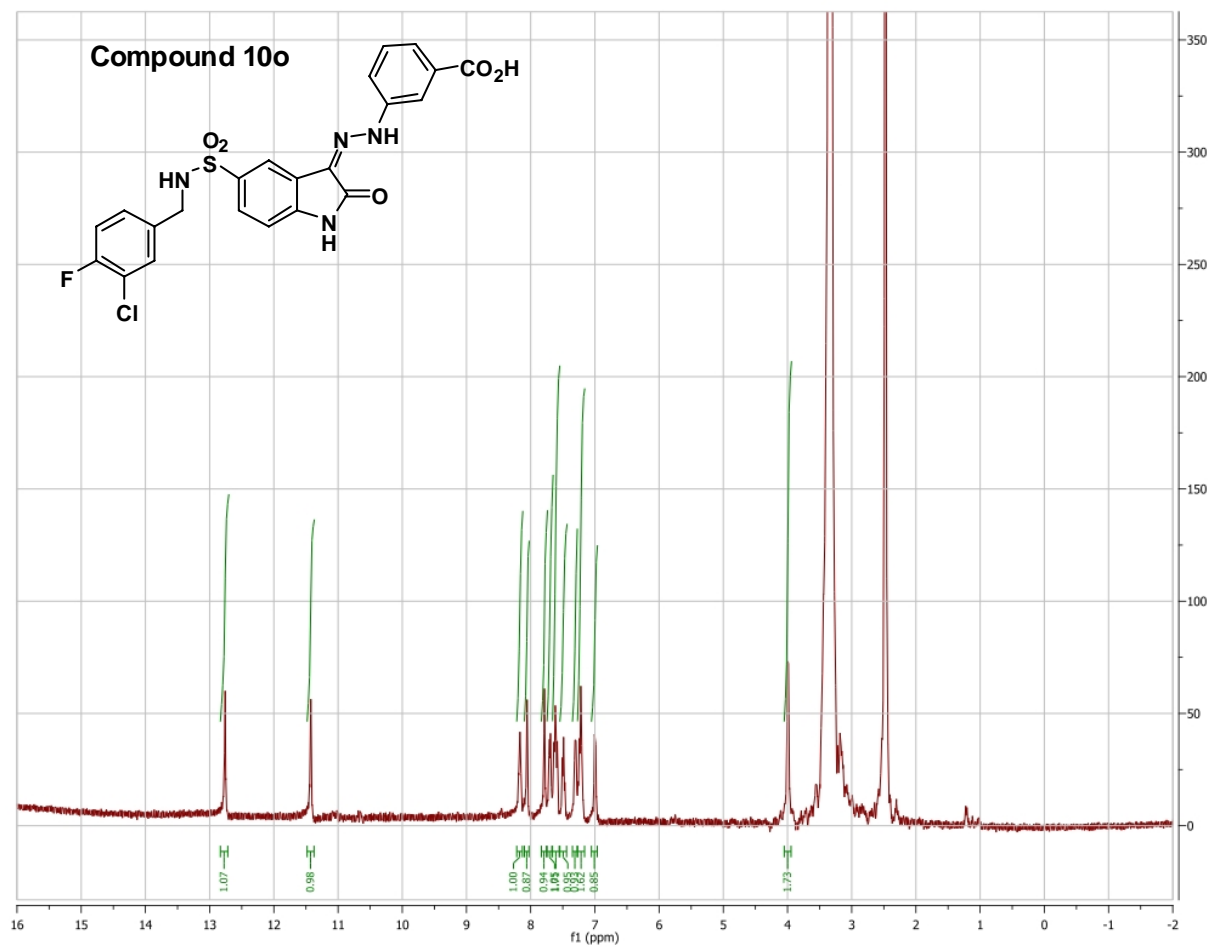


Merged XIC, Period# : 1 Experiment# : 1

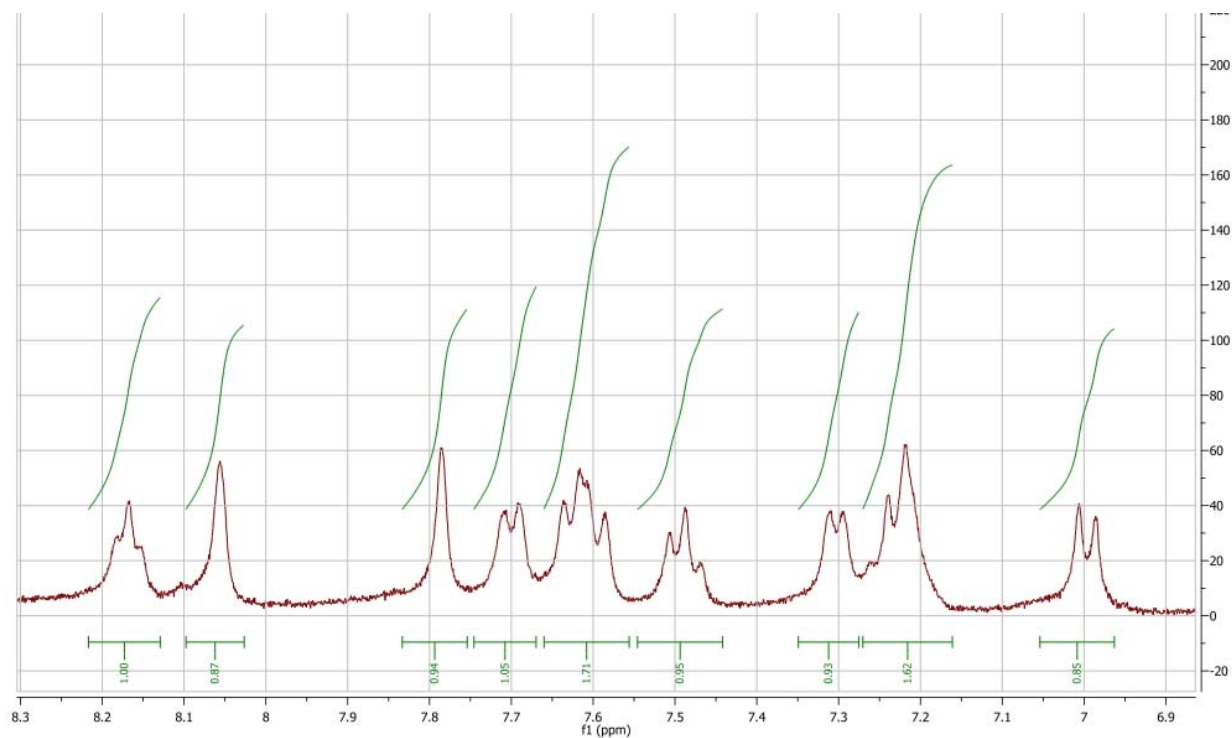


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H17FN4O5S	--	468.09037	0.74	1.16284 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	401403.69	467.08309	467.08458	1.49158	3.19	--



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 10o (δ 6.9 – 8.3 ppm)

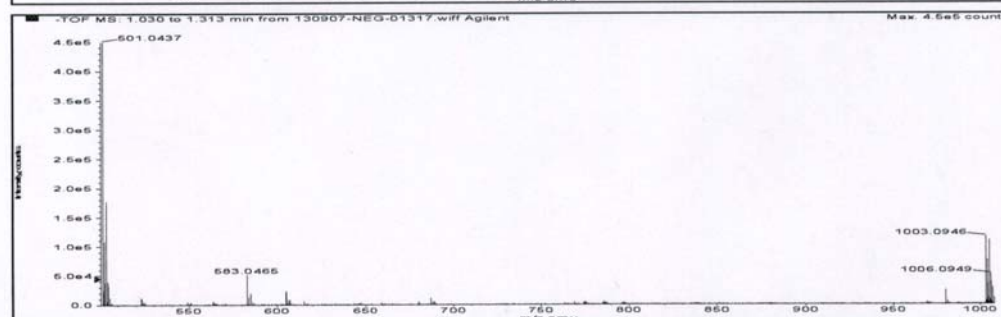
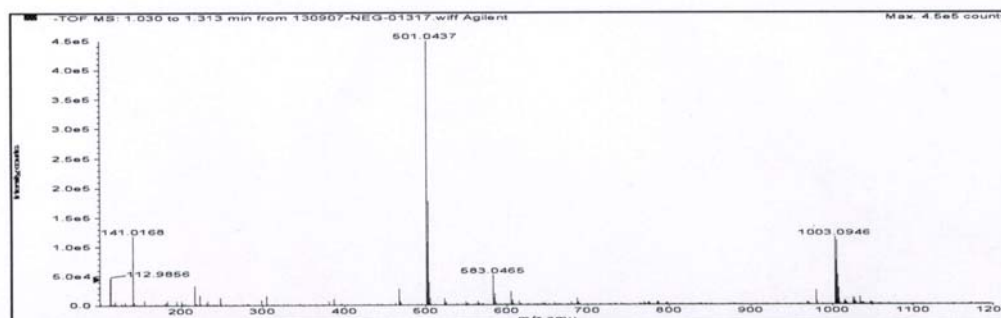
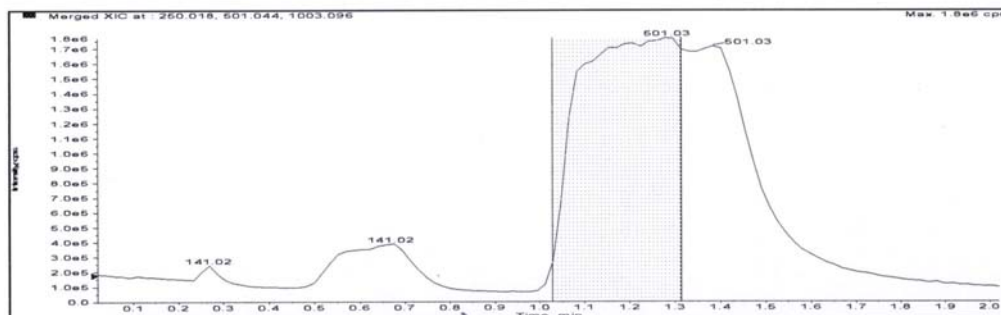


HRMS 100

Empirical Formula Confirmation Report

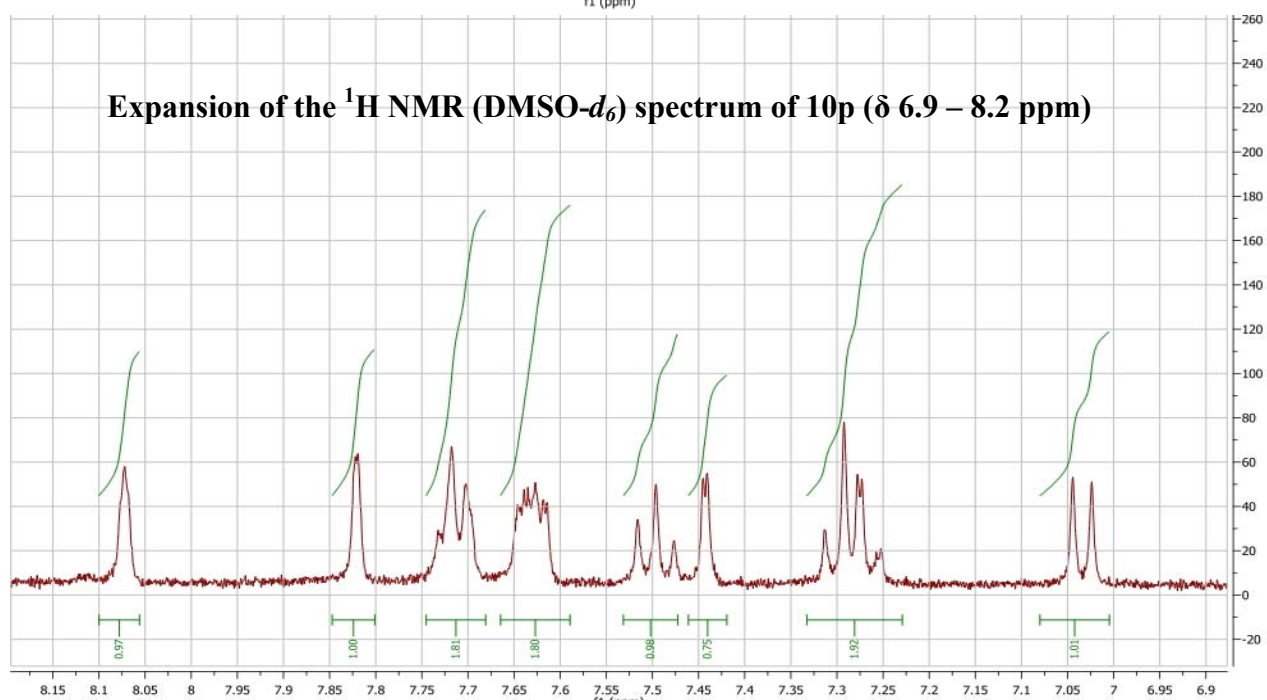
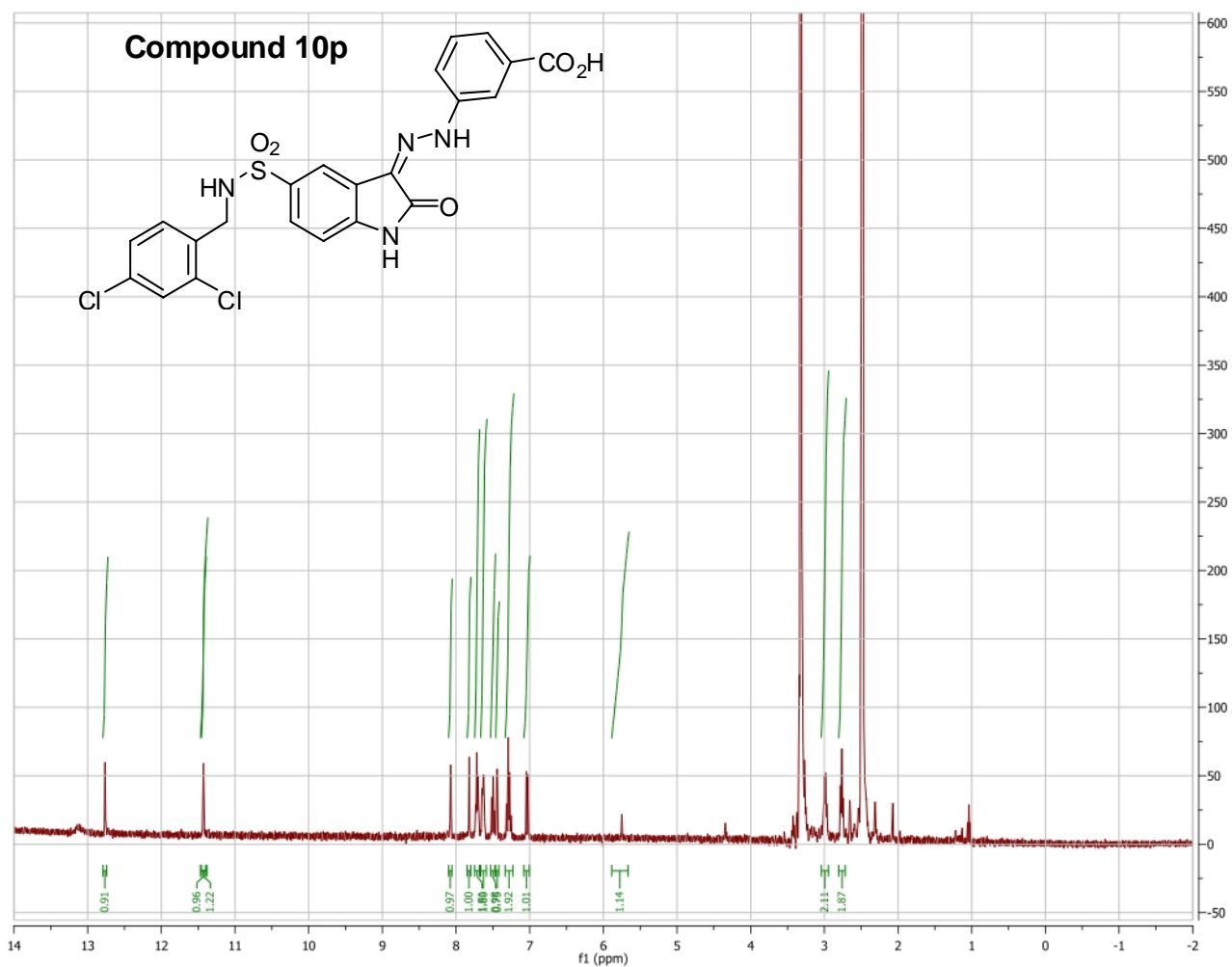
Page 1 of 1

Sample Name: YL2-005-2 Sample Location: P1-A-06 Sample Id: YL2-005-2 Operator: EasyAccess
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Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml



Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C22H16ClFN4O5S	--	502.05140	1.28	2.66757 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	484092.05	501.04412	501.04369	-0.42702	-0.85	--
[2M-H]-	123767.98	1003.09552	1003.09459	-0.92370	-0.92	--



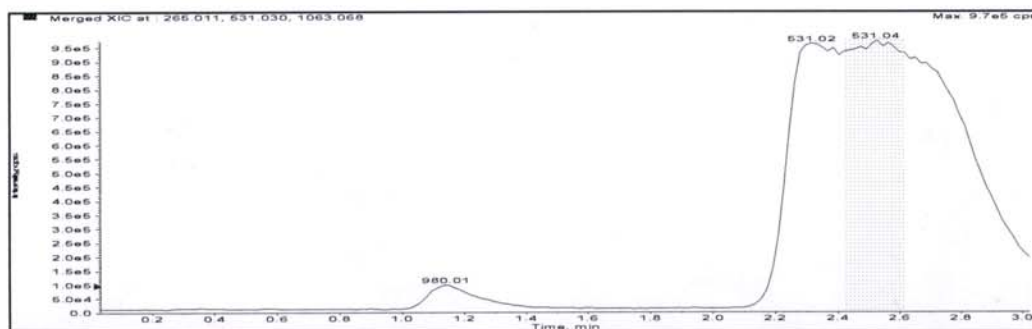
HRMS 10p

Empirical Formula Confirmation Report

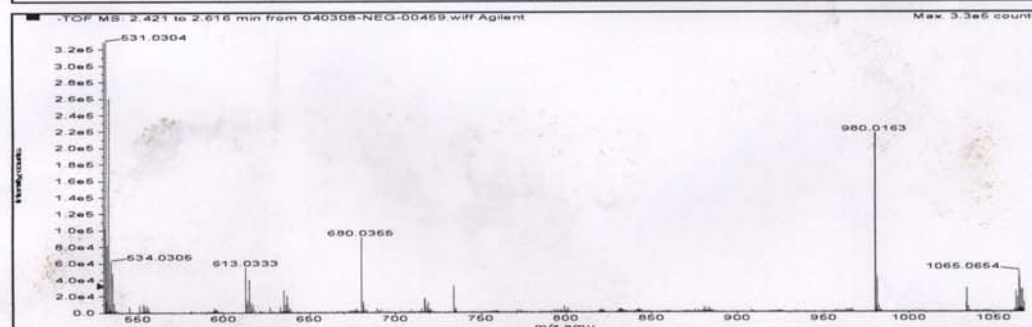
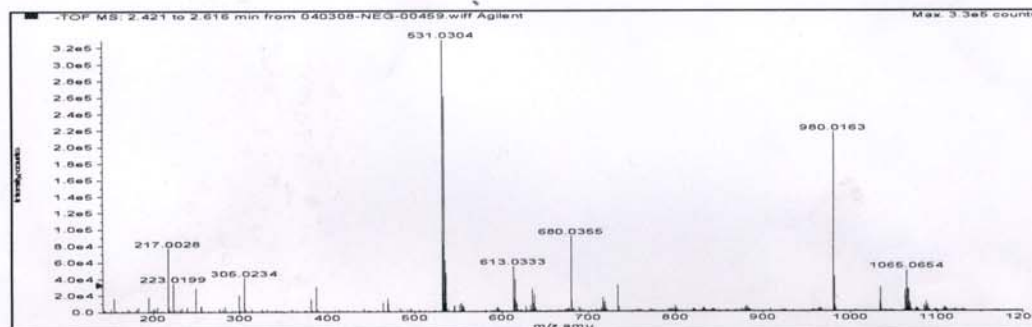
Page 1 of 1

Sample Name: YL1-164 Sample Location: P1-E-01 Sample ID: YL1-164 Operator: EasyAccess
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One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

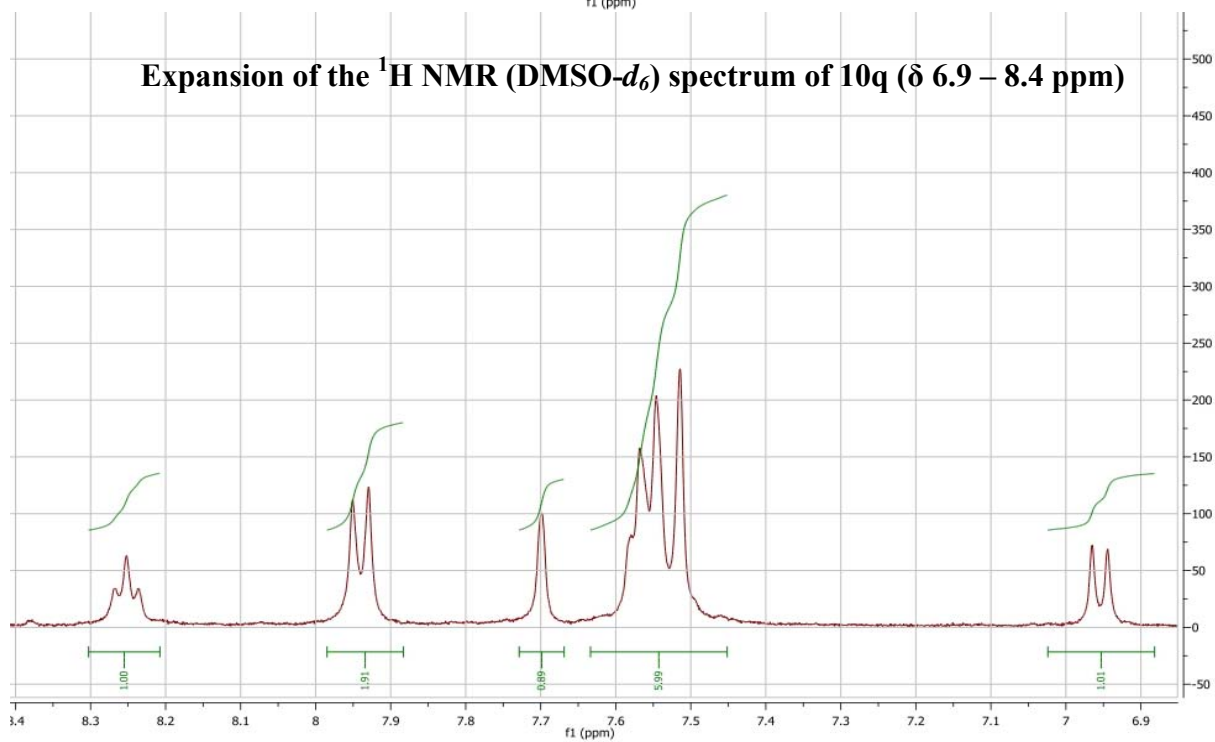
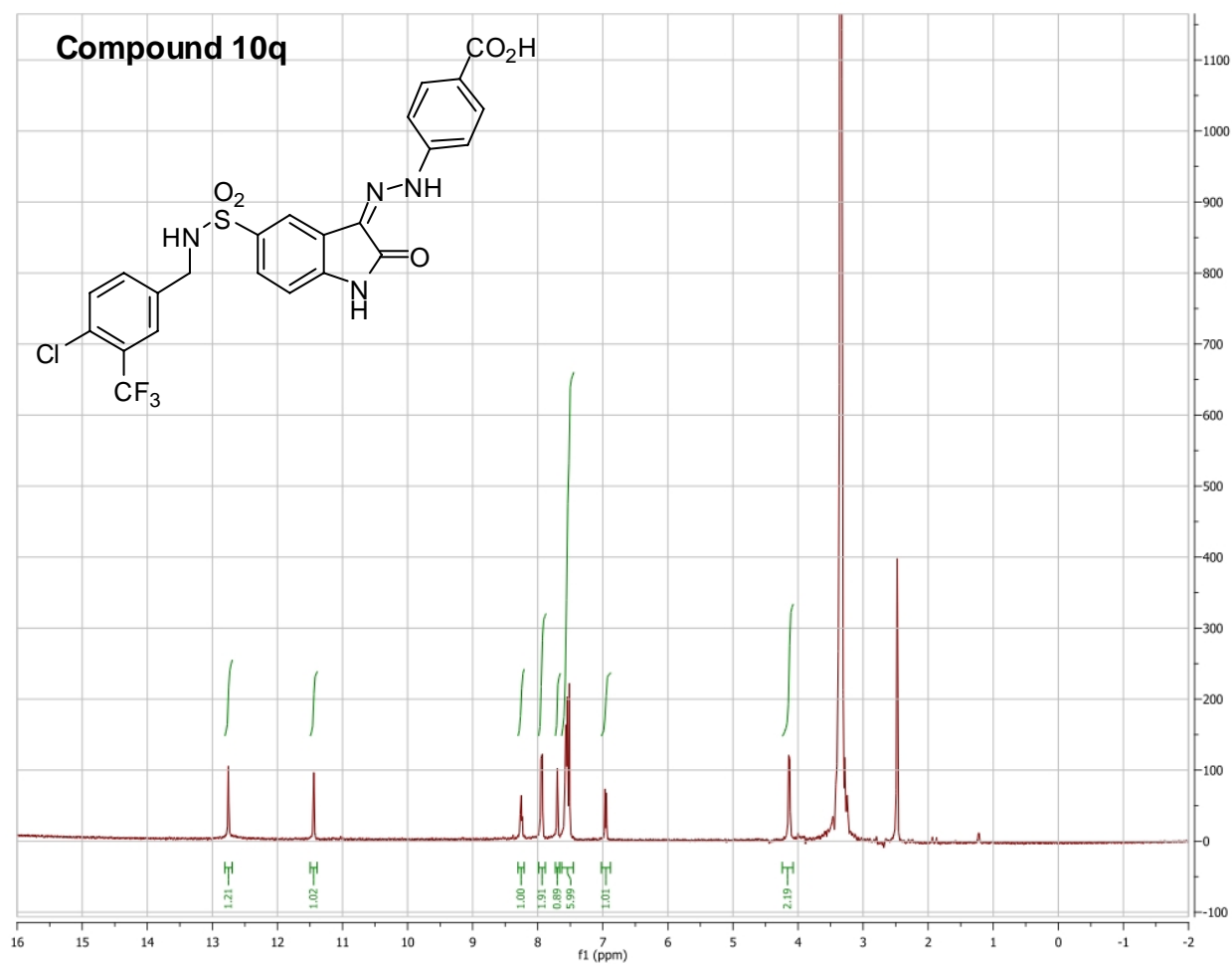


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C23H18Cl2N4O5S	--	532.03750	2.52	3.38104 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	354811.37	531.03022	531.03038	0.15894	0.30	--
[2M-H]-	26601.81	1063.06772	1063.06609	-1.62414	-1.53	--

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14:49:00 PM

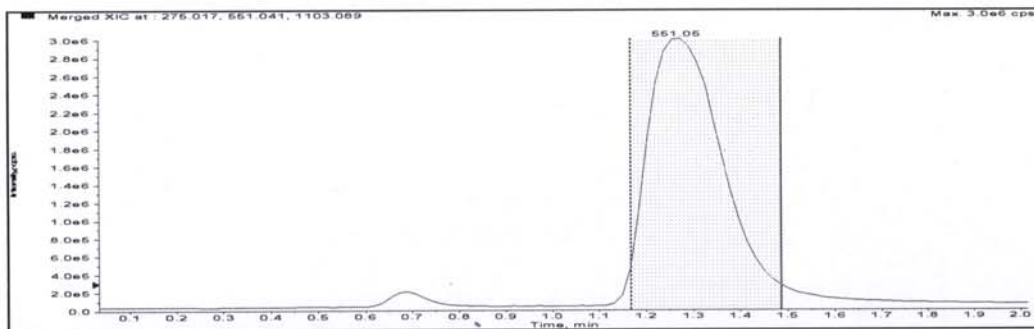


HRMS 10q

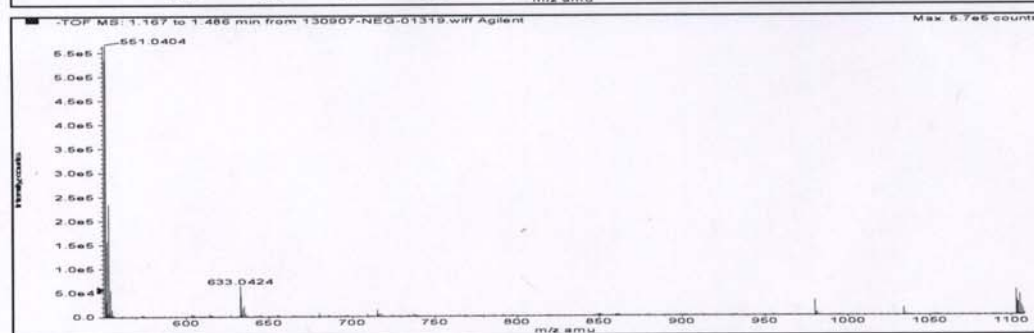
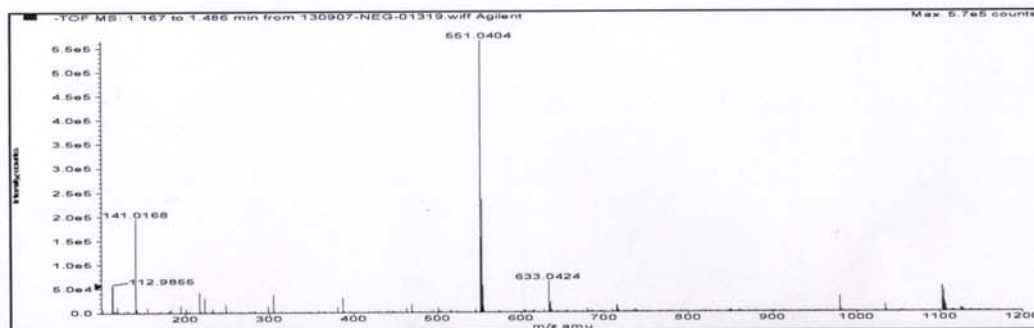
Empirical Formula Confirmation Report

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Sample Name: YL2-008-1 Sample Location: P1-A-08 Sample Id: YL2-008-1 Operator: EasyAccess
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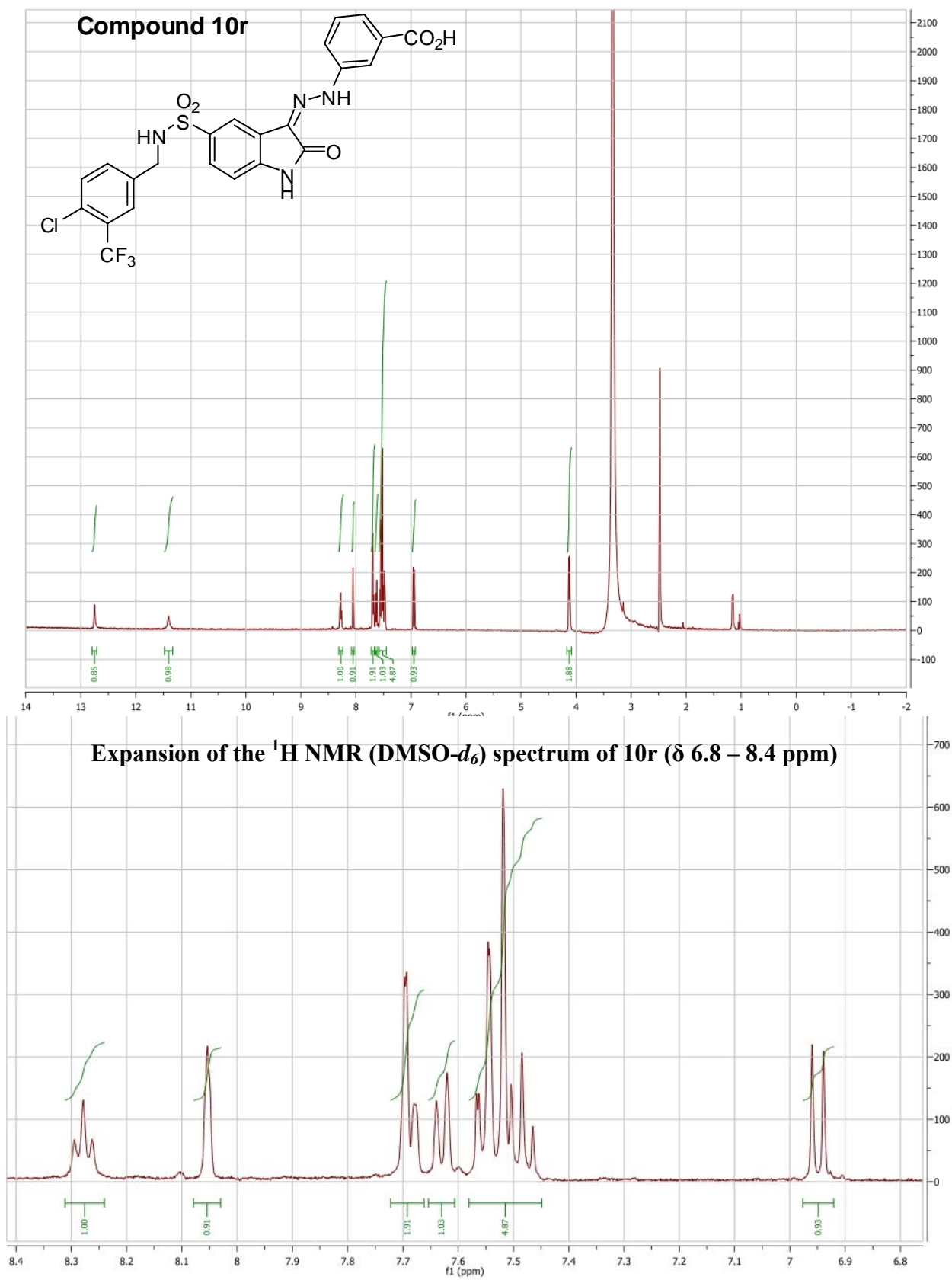


Merged XIC, Period#: 1 Experiment#: 1



Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C23H16ClF3N4O5S	--	552.04820	1.27	3.23246 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	598517.13	551.04093	551.04040	-0.52870	-0.96	--
[2M-H]-	53284.80	1103.08913	1103.08760	-1.52897	-1.39	--

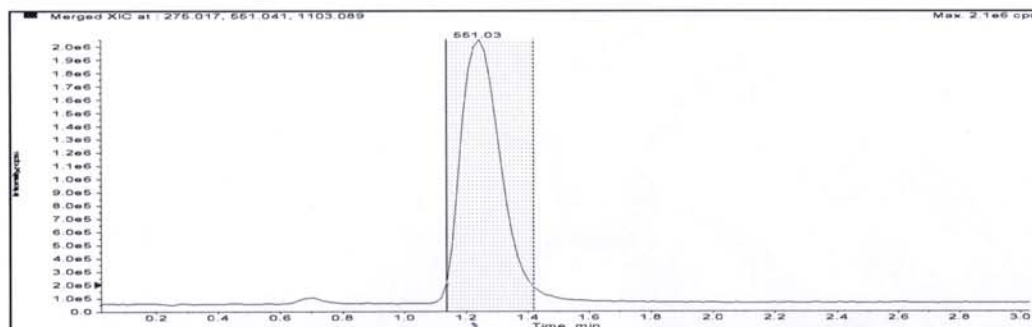


HRMS 10r

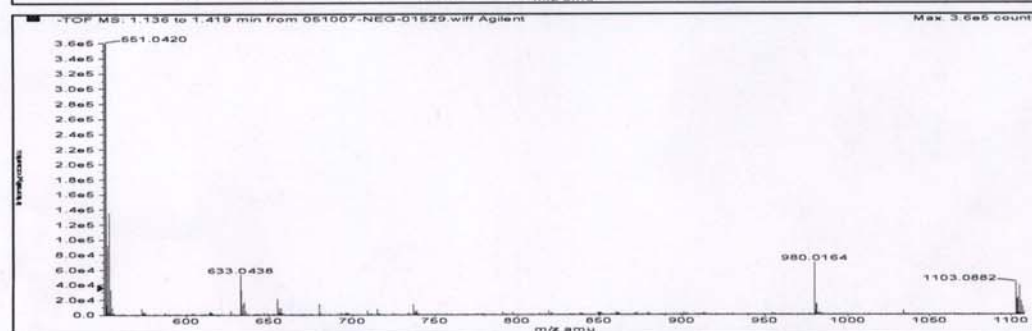
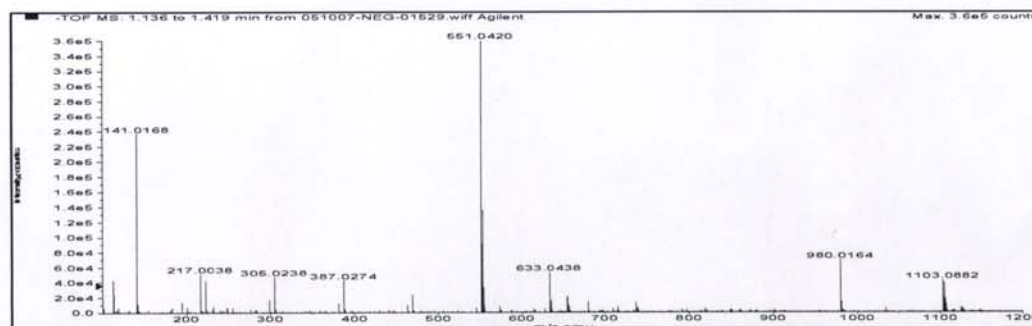
Empirical Formula Confirmation Report

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Sample Name: YL2-008-2 Sample Location: P1-A-01 Sample Id: YL2-008-2 Operator: EasyAccess
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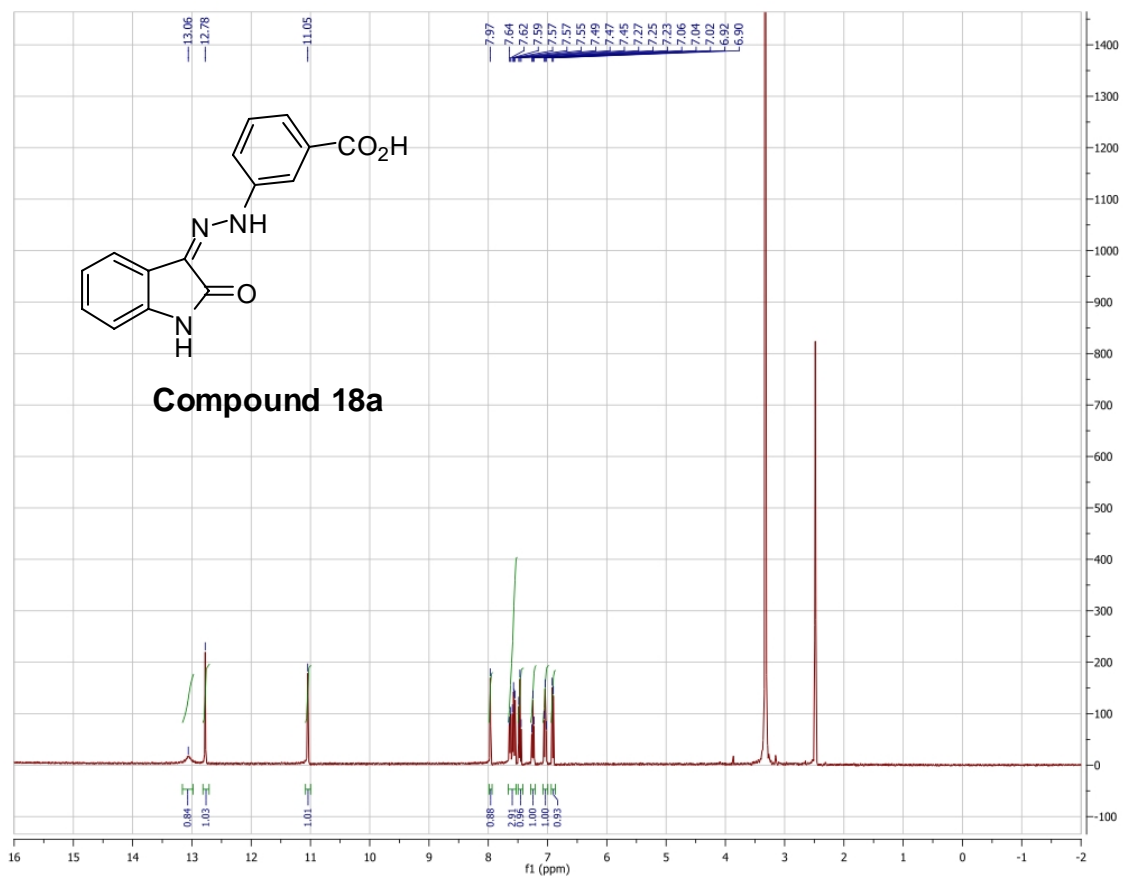


Merged XIC, Period# : 1 Experiment# : 1

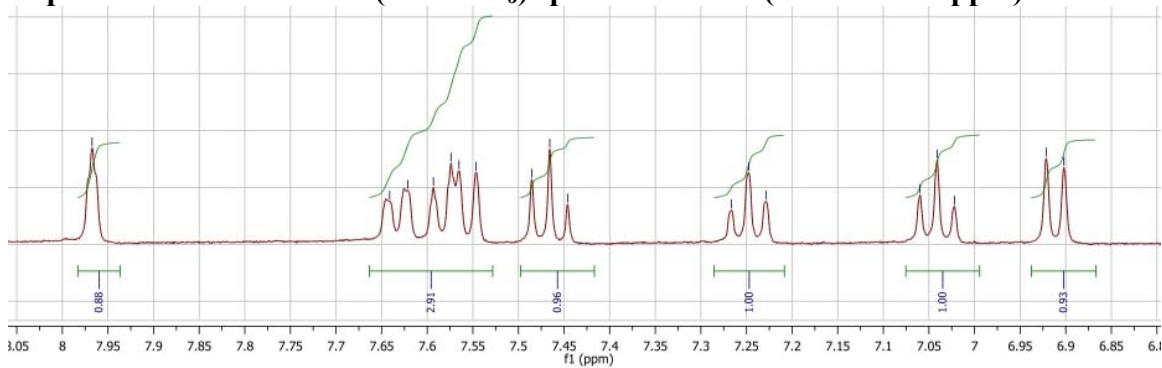


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C23H16ClF3N4O5S	--	552.04820	1.24	1.79072 E7	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	379744.59	551.04093	551.04199	1.05953	1.92	--
[2M-H]-	42931.11	1103.08913	1103.08822	-0.90894	-0.82	--



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 18a (δ 6.85 – 8.05 ppm)



HRMS 18a

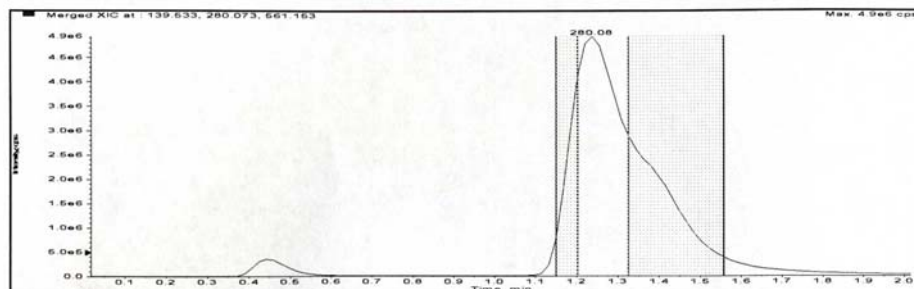
Empirical Formula Confirmation Report

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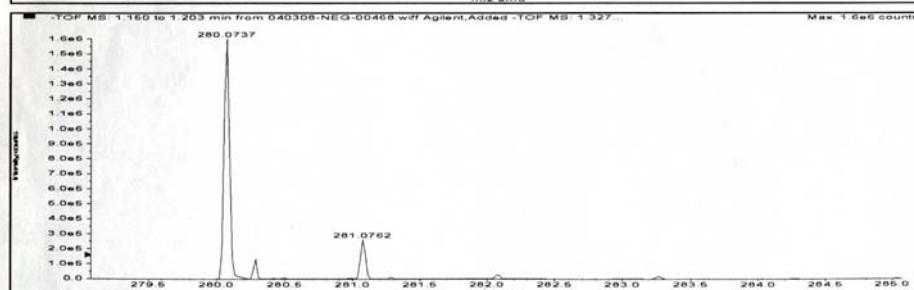
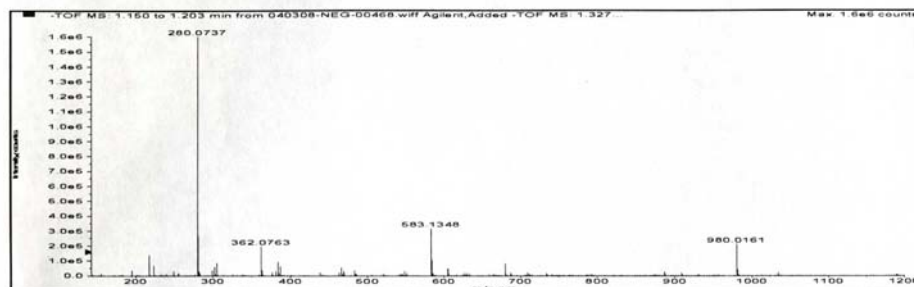
Compound 15a

Sample Name: RPM720-15a Sample Location: P1-F-01 Sample Id: RPM720-15a Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00468.wiff Acq Time: March 04 2008, 03:16:32 PM
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One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1

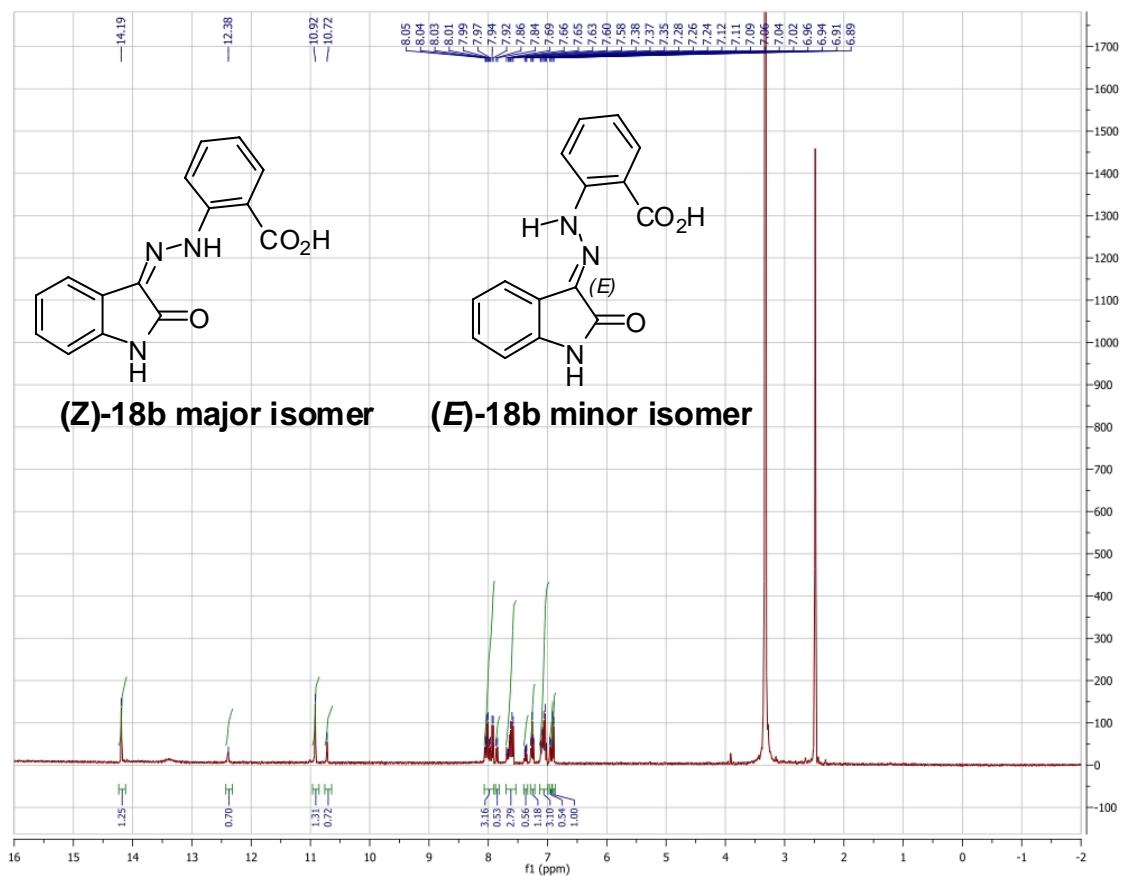


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C15H11N3O3	--	281.08004	1.24	5.99959 E7	--

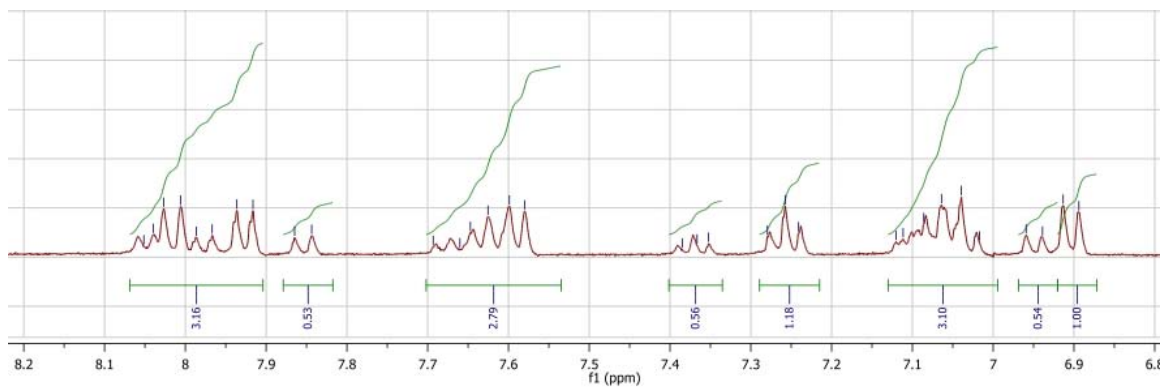
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	1612220.70	280.07276	280.07366	0.89710	3.20	--

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15:18:46 PM



Expansion of the ^1H NMR ($\text{DMSO-}d_6$) spectrum of (*E*) and (*Z*)-18b (δ 6.80 – 8.2 ppm)



HRMS (E) and (Z)-18b

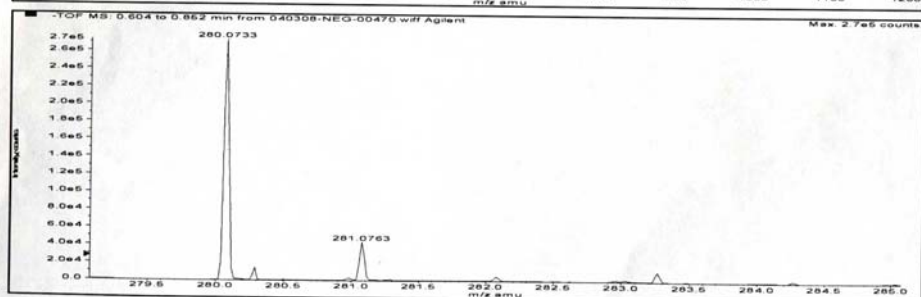
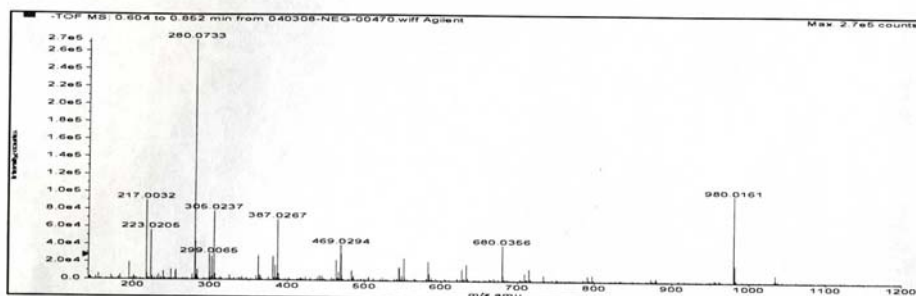
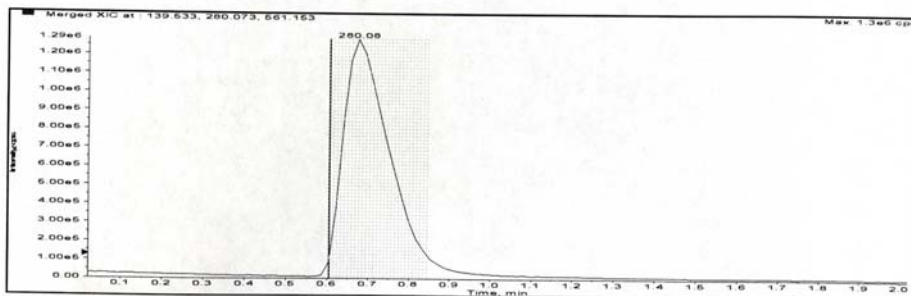
Empirical Formula Confirmation Report

Compound 15b

Page 1 of 1

Sample Name: RPM718-15b Sample Location: P1-F-03 Sample Id: RPM718-15b Operator: EasyAccess
Data File Name: D:\PE_Sciex\Data\Projects\chemist\03-08\Data\040308-NEG-00470.wiff Acq Time: March 04 2008, 03:22:29 PM
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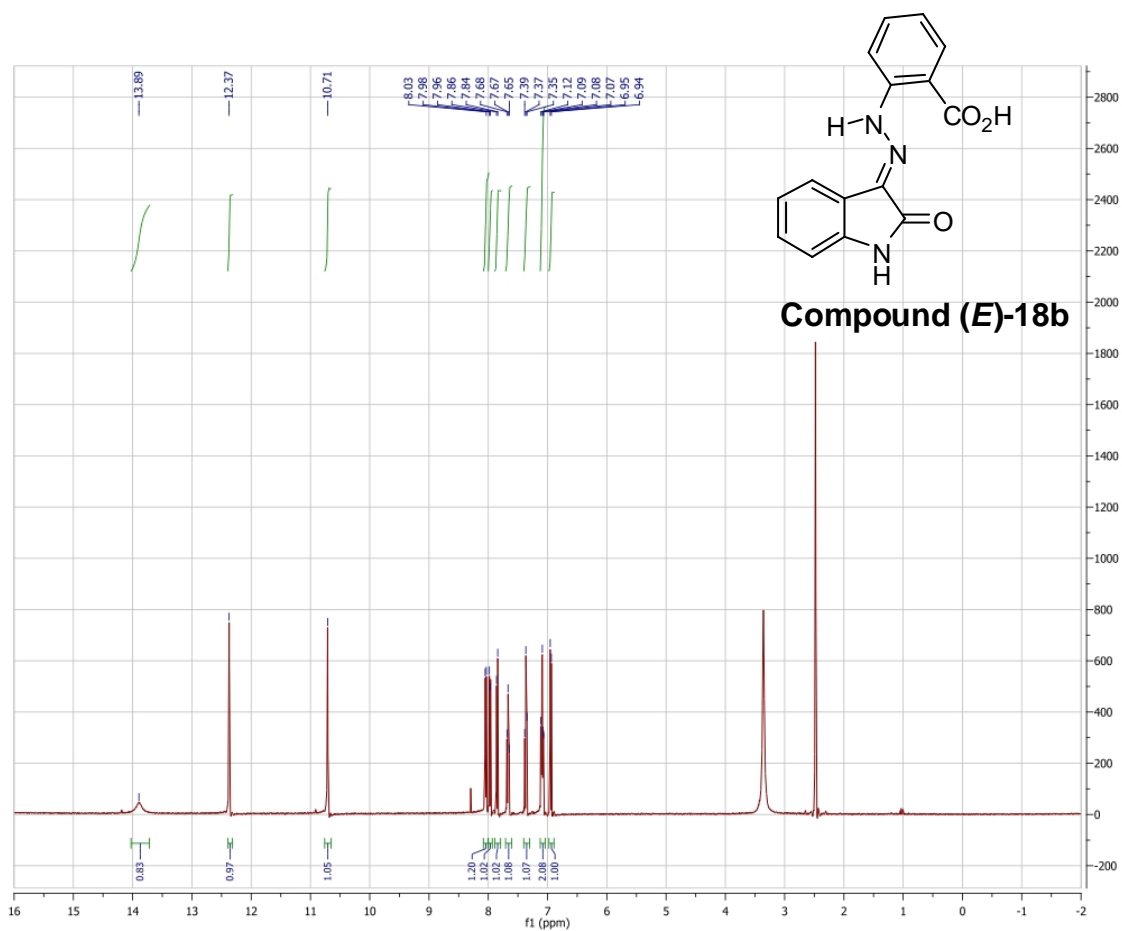


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C15H11N3O3	--	281.08004	0.68	9.96981 E6	--

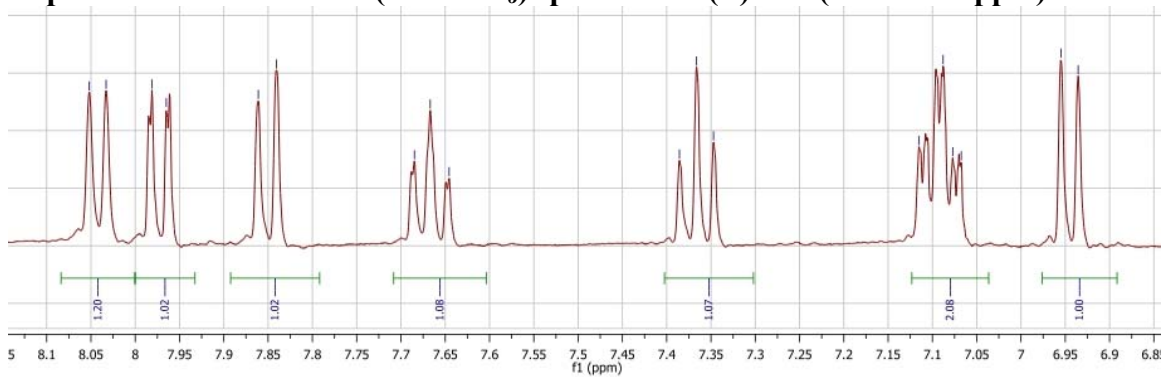
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	275203.28	280.07276	280.07329	0.52316	1.87	--

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15:24:40 PM



Expansion of the ^1H NMR ($\text{DMSO}-d_6$) spectrum of (E)-18b (δ 6.8 – 8.1 ppm)



HRMS (E)-18b

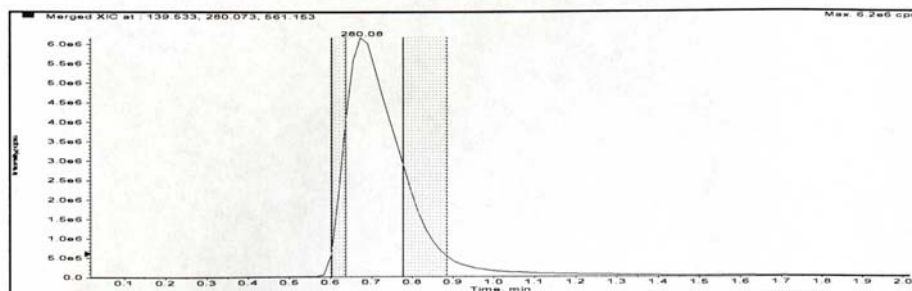
Empirical Formula Confirmation Report

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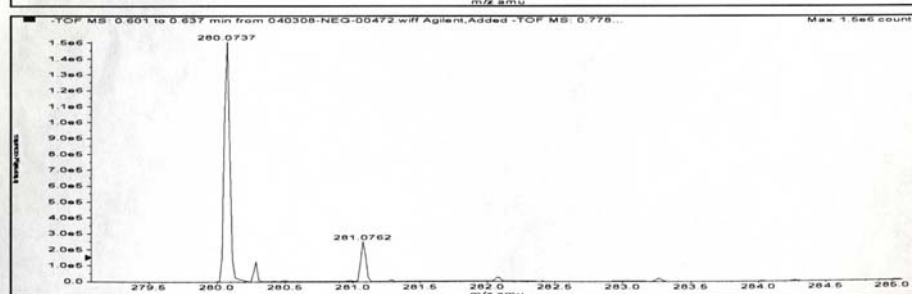
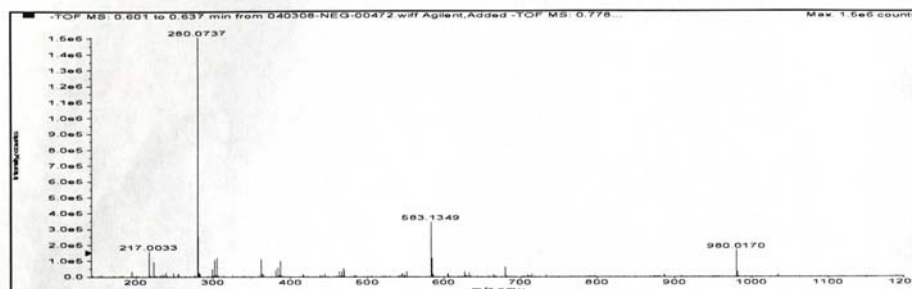
Compound 15c

Sample Name: RPM719-15c Sample Location: P1-F-05 Sample Id: RPM719-15c Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist\03-08\Data\040308-NEG-00472.wiff Acq Time: March 04 2008, 03:28:24 PM
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One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period#: 1 Experiment#: 1

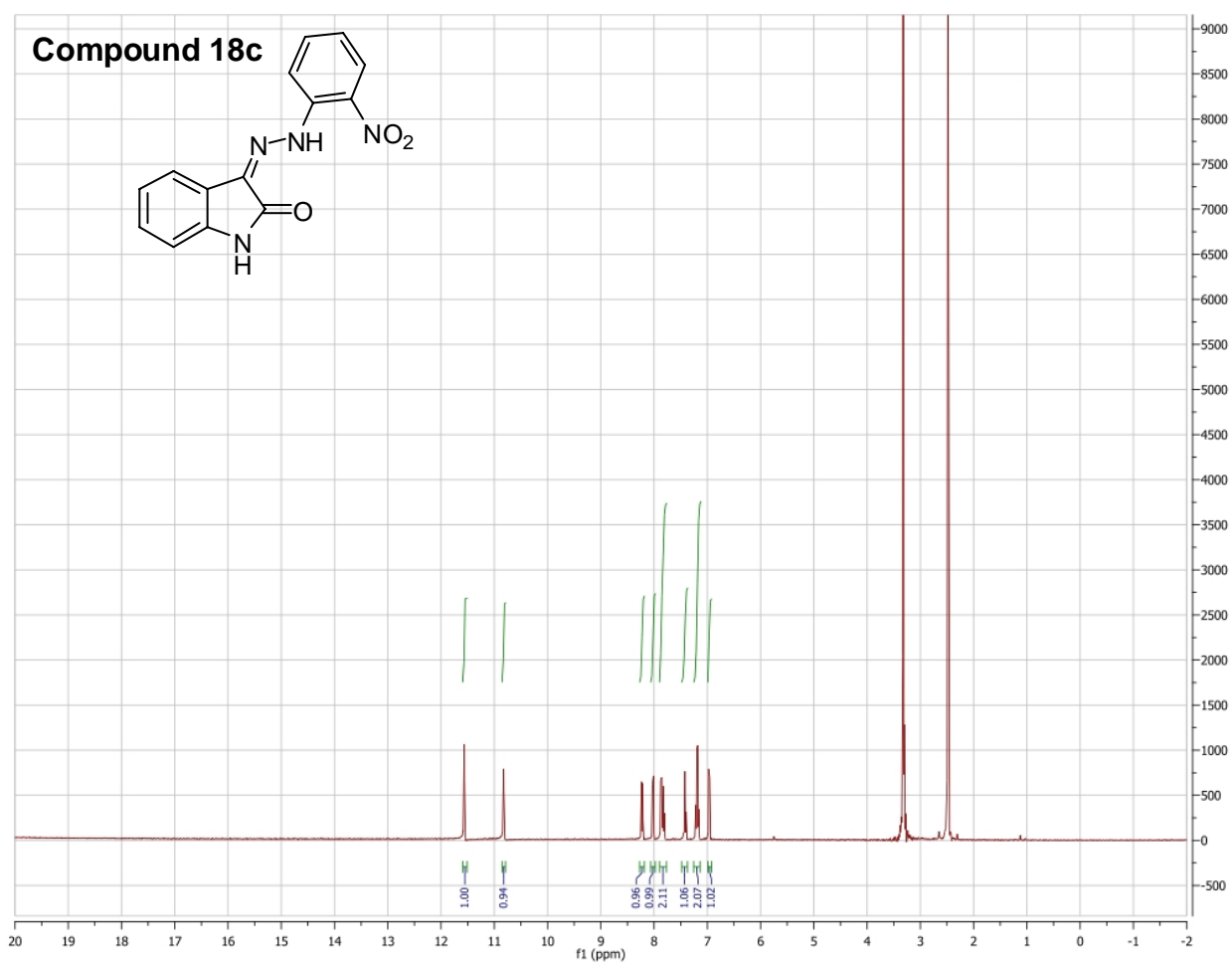


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C15H11N3O3	--	281.08004	0.68	5.61528 E7	--

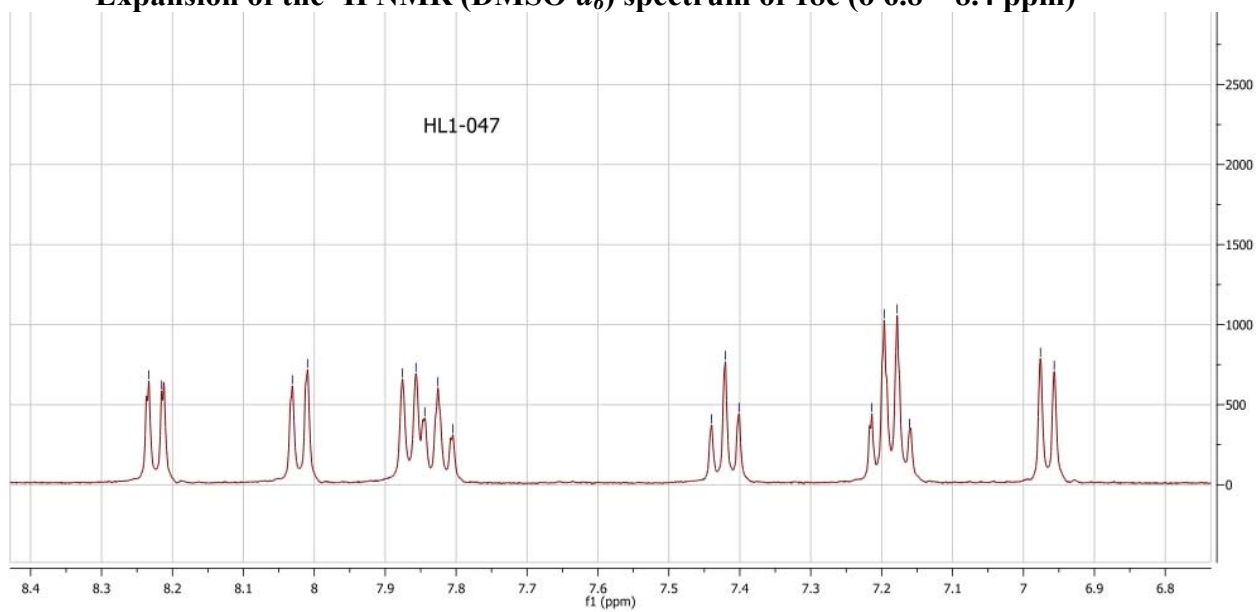
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	1516453.47	280.07276	280.07368	0.91435	3.26	--

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15:30:37 PM



Expansion of the ^1H NMR ($\text{DMSO}-d_6$) spectrum of 18c (δ 6.8 – 8.4 ppm)

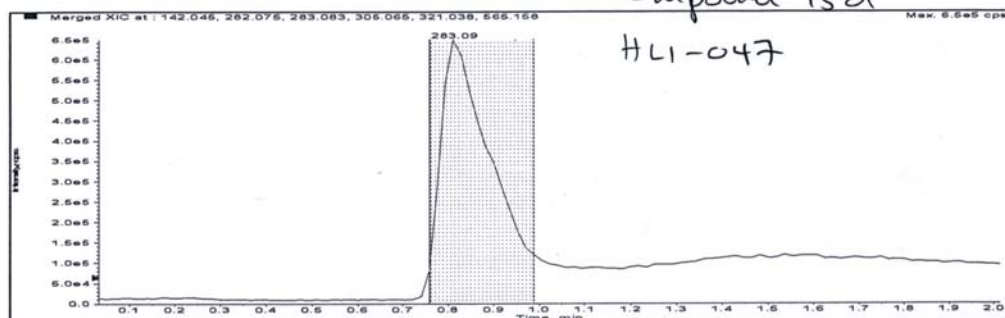


HRMS 18c

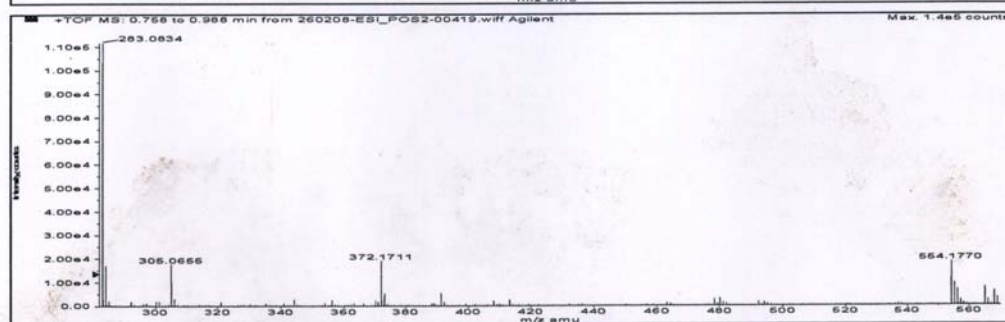
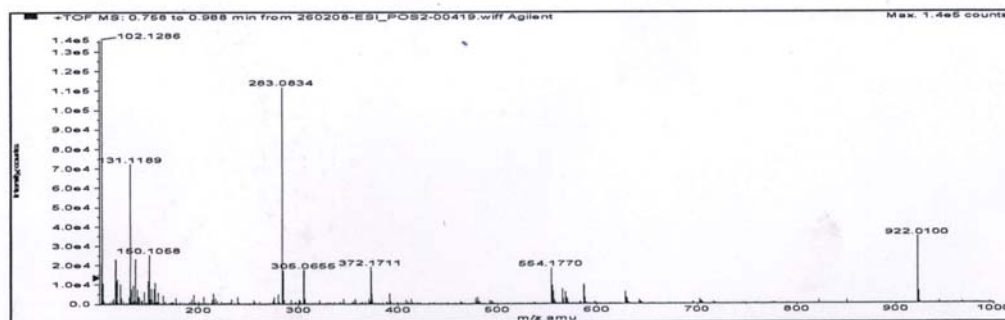
Empirical Formula Confirmation Report

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Sample Name: HL1-047 Sample Location: P1-F-04 Sample ID: HL1-047 Operator: EasyAccess
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Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml



Merged XIC, Period# : 1 Experiment# : 1

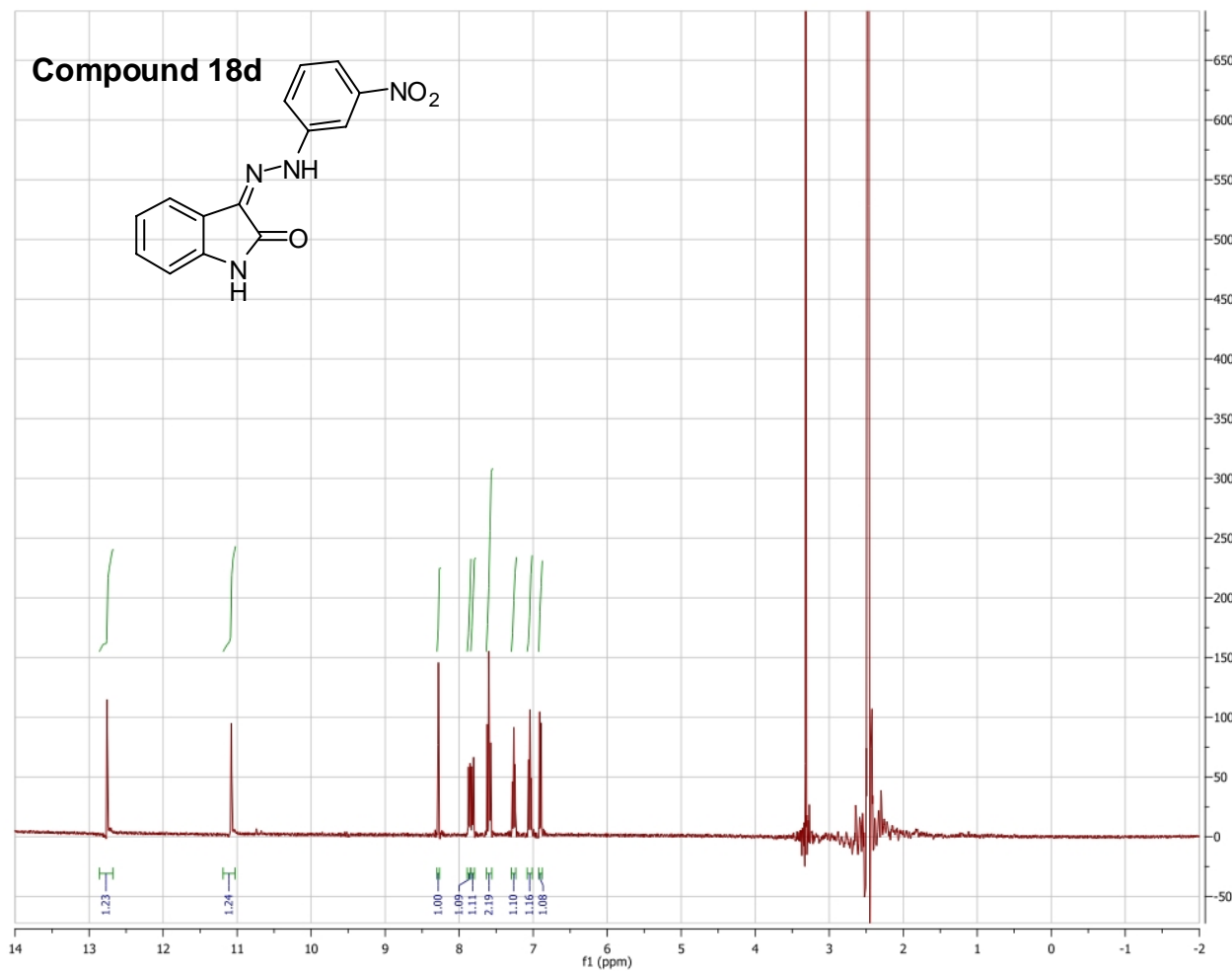


Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C14H10N4O3	--	282.07529	0.82	4.79804 E6	--

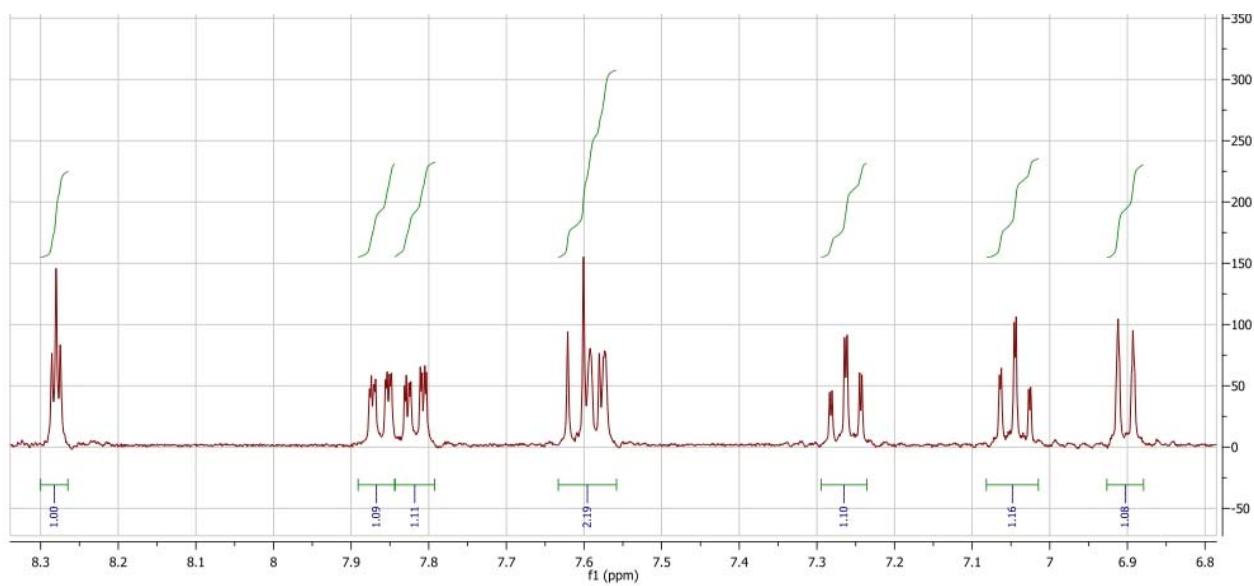
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M+H] ⁺	118777.78	283.08257	283.08339	0.82447	2.91	--
[M+Na] ⁺	19002.25	305.06451	305.06553	1.02053	3.35	--
[M+K] ⁺	1849.26	321.03845	321.03889	0.44339	1.38	--
[2M+H] ⁺	7703.38	565.15786	565.15836	0.50136	0.89	--

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16:34:50 PM



Expansion of the ^1H NMR (DMSO- d_6) spectrum of 18d (δ 6.8 – 8.3 ppm)

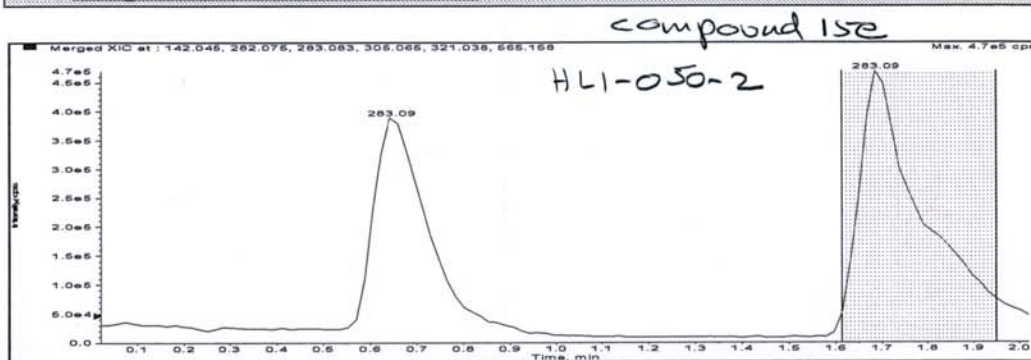


HRMS 18d

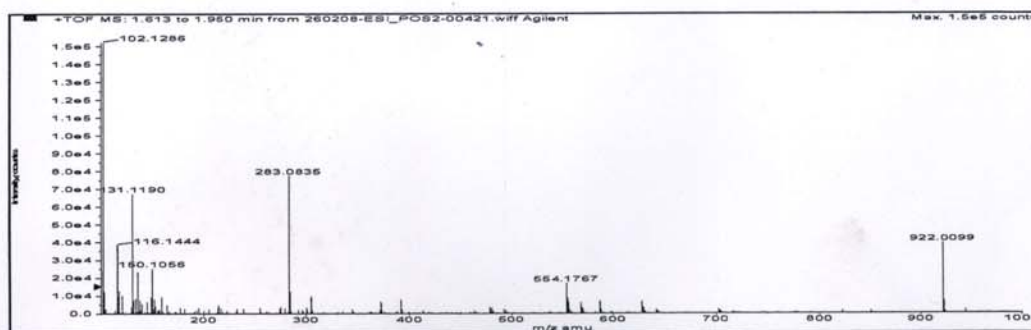
Empirical Formula Confirmation Report

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Sample Name: HL1-050-2 Sample Location: P1-F-06 Sample Id: HL1-050-2 Operator: EasyAccess
Data File Name: D:\PE Sciex Data\Projects\chemist02-08\Data\260208-ESI_POS2-00421.wiff Acq Time: February 26 2008, 04:46:29 PM
Method: D:\TOF_Data\damethods\EASY ACCESS2.ANM\efc.xml



Merged XIC, Period#: 1 Experiment#: 1



Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C14H10N4O3	--	282.07529	1.69	4.11749 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M+H] ⁺	82311.47	283.08257	283.08349	0.92122	3.25	--
[M+Na] ⁺	10235.98	305.06451	305.06544	0.92416	3.03	--

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16:48:44 PM

Computer Docking. Computer docking was performed with the X-ray crystal structure of human Shp2 (PDB identification code: 2SHP)¹ and human Shp1 (PDB identification code: 1FPR)² using the GLIDE v4.0 (Grid-Based Ligand Docking with Energetics, from Schrödinger, L.L.C.) program.^{3,4} The N-SH2 domain of Shp2, which blocks the catalytic site, was removed from the 3D structure prior to the computer docking analysis. The optimal binding geometry for each model was obtained from the GLIDE docking which relies upon Monte Carlo sampling techniques coupled with energy minimization.

References

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