Electronic Supplementary Information

Enantio-pure synthesis of dihydrobenzo[1,4]-oxazine-3-carboxylic acids and approach to benzoxazinyl oxazolidinones

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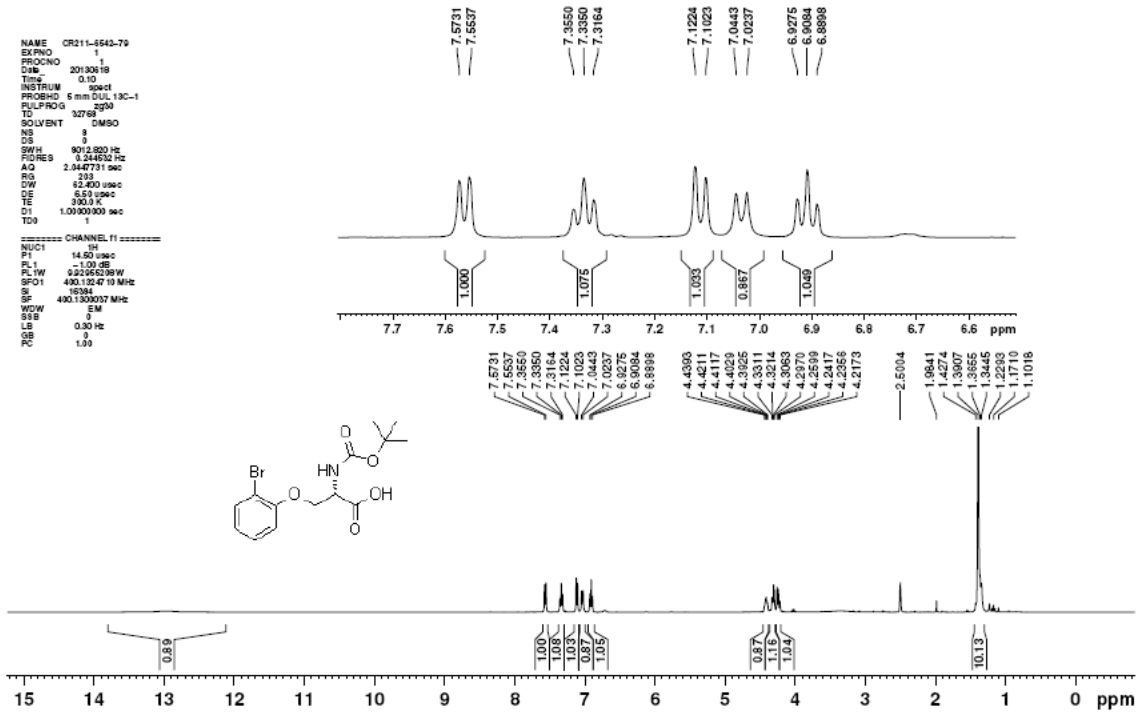
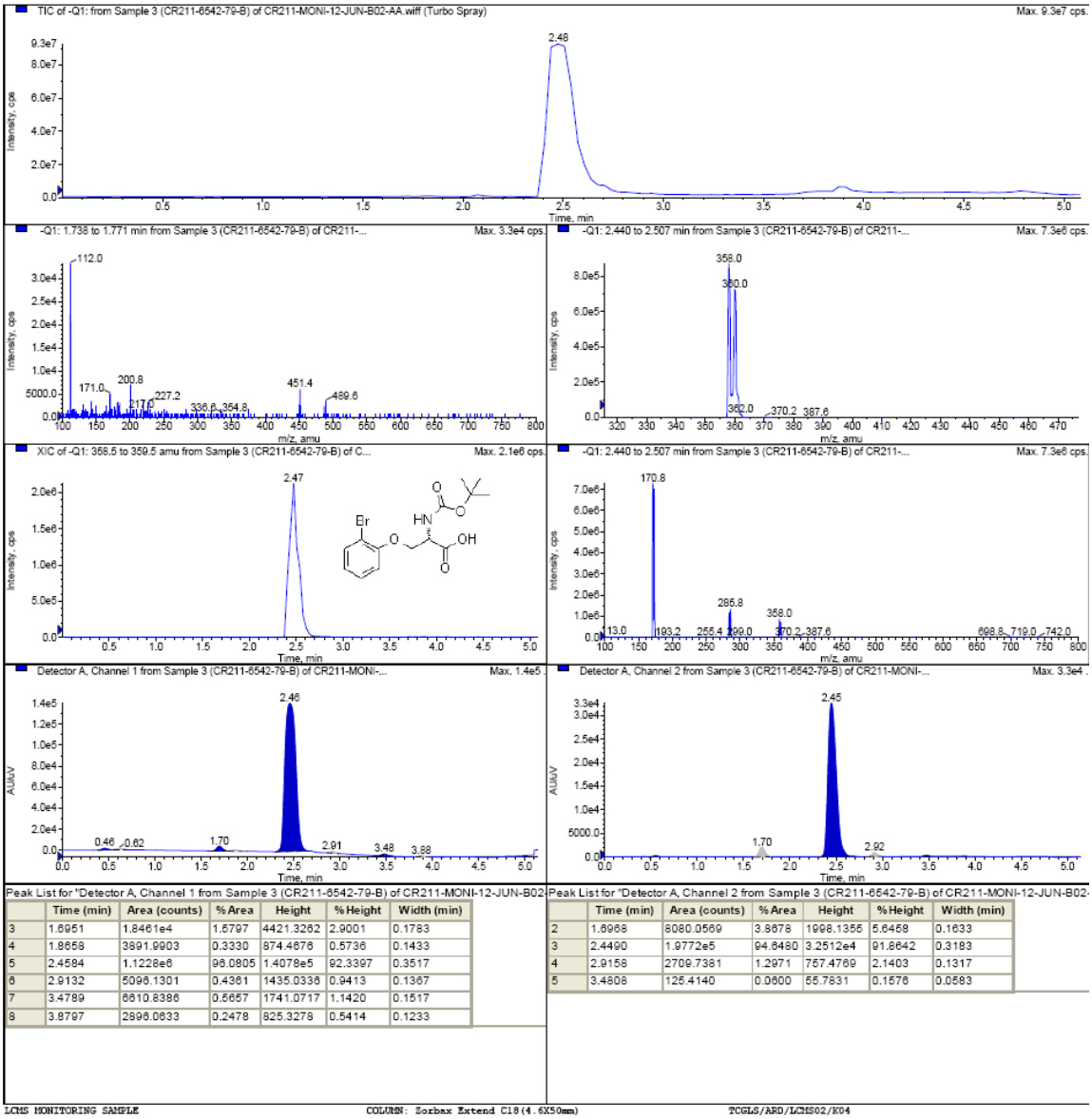
Contents

NMR Spectra, LC-MS and HPLC Chromatogram



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3a



Peak List for "Detector A, Channel 1 from Sample 3 (CR211-6542-79-B) of CR211-MONI-12-JUN-B02-

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
3	1.6951	1.8461e4	1.5797	4421.3262	2.9001	0.1783
4	1.8658	3891.9903	0.3330	874.4676	0.5736	0.1433
5	2.4584	1.1228e6	96.0805	1.4078e5	92.3397	0.3517
6	2.9132	5096.1301	0.4361	1435.0336	0.9413	0.1367
7	3.4789	6610.8386	0.5657	1741.0717	1.1420	0.1517
8	3.8797	2896.0633	0.2478	825.3278	0.5414	0.1233

Peak List for "Detector A, Channel 2 from Sample 3 (CR211-6542-79-B) of CR211-MONI-12-JUN-B02-

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
2	1.6968	6080.0569	3.8678	1998.1355	5.6458	0.1633
3	2.4490	1.9772e5	94.6480	3.2512e4	91.8642	0.3183
4	2.9158	2709.7381	1.2971	757.4769	2.1403	0.1317
5	3.4808	125.4140	0.0600	55.7831	0.1576	0.0583

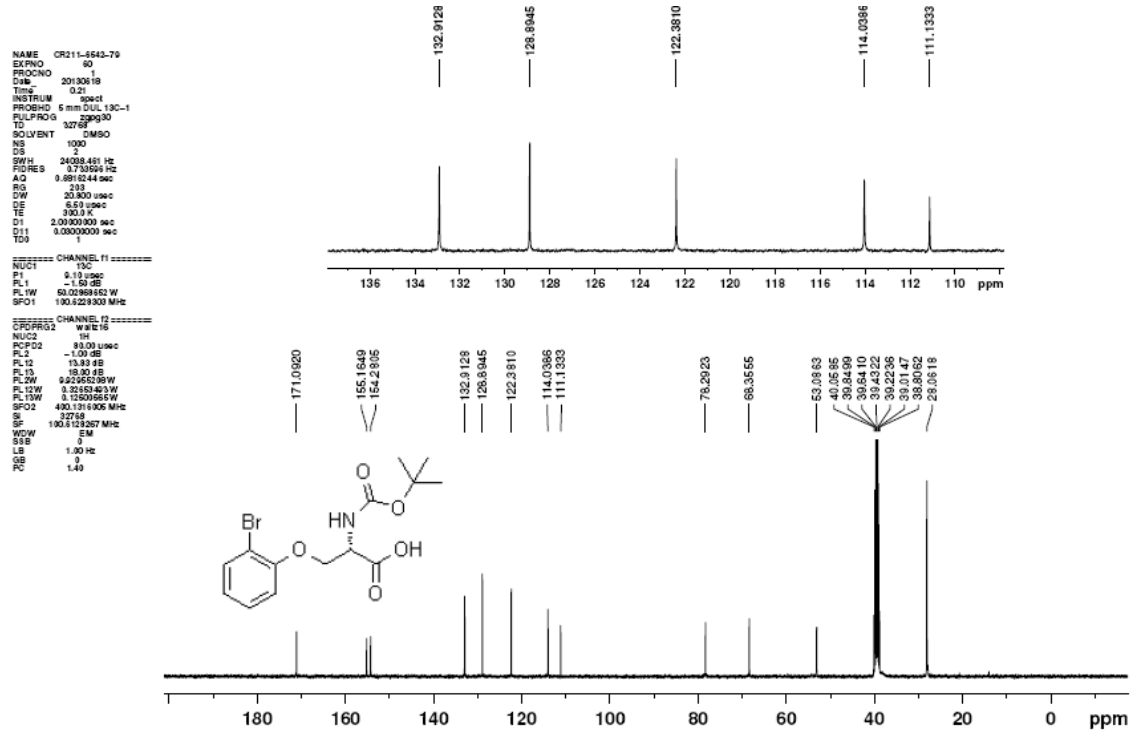
LCMS MONITORING SAMPLE COLUMN: Zorbax Extend C18(4.6X50mm) TCGLS/ARD/LCMS02/K04

Channel 1 at wavelength 220 nm,
Channel 2 at wavelength 260 nm

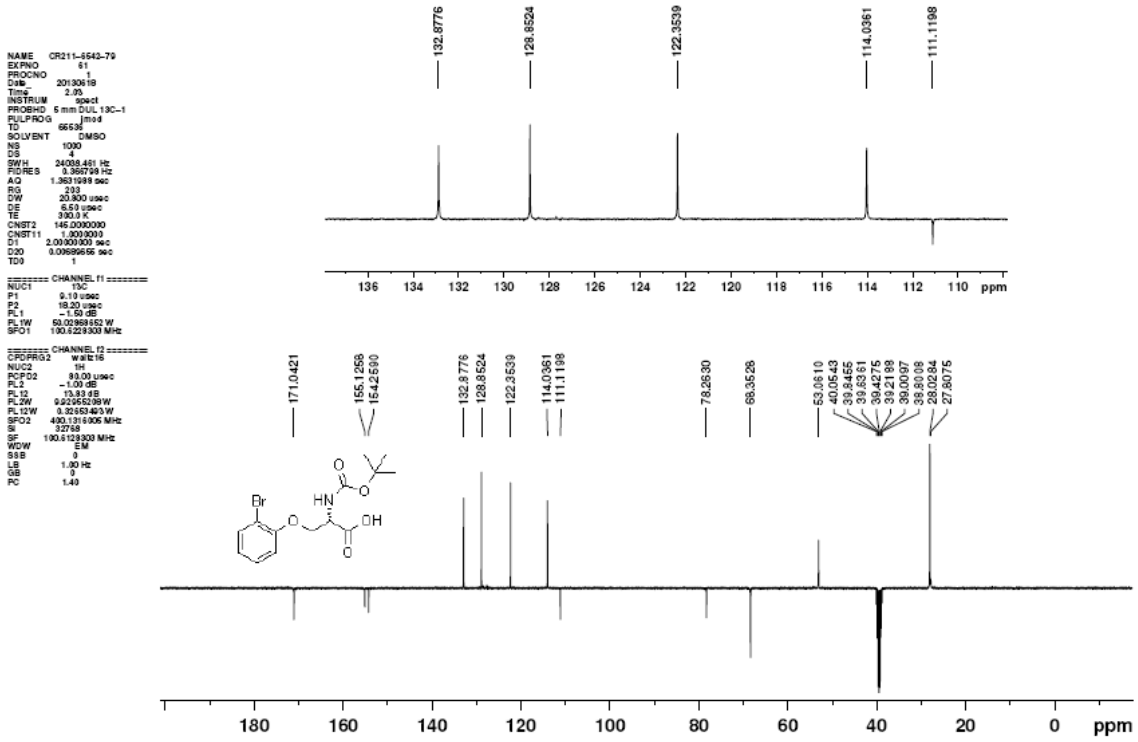
NH4OAc:ACN

Analysed by

LCMS spectrum of compound 3a



^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 3a



APT NMR spectrum (100MHz, DMSO-d_6) of compound 3a

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Injection Date   : 1/8/2015     2:44:23 PM      Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\JAN-2015\080115 2015-01-08 09-48-05->
Analysis Method  : C:\CHEM32\1\METHODS\A1.M
Last Changed     : Wed, 7. Jan. 2015,  06:20:38 pm

Sample ID:CR211-8259-67(D1+L1)

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                          ->
                                                Ref :KD/08.01.15/370
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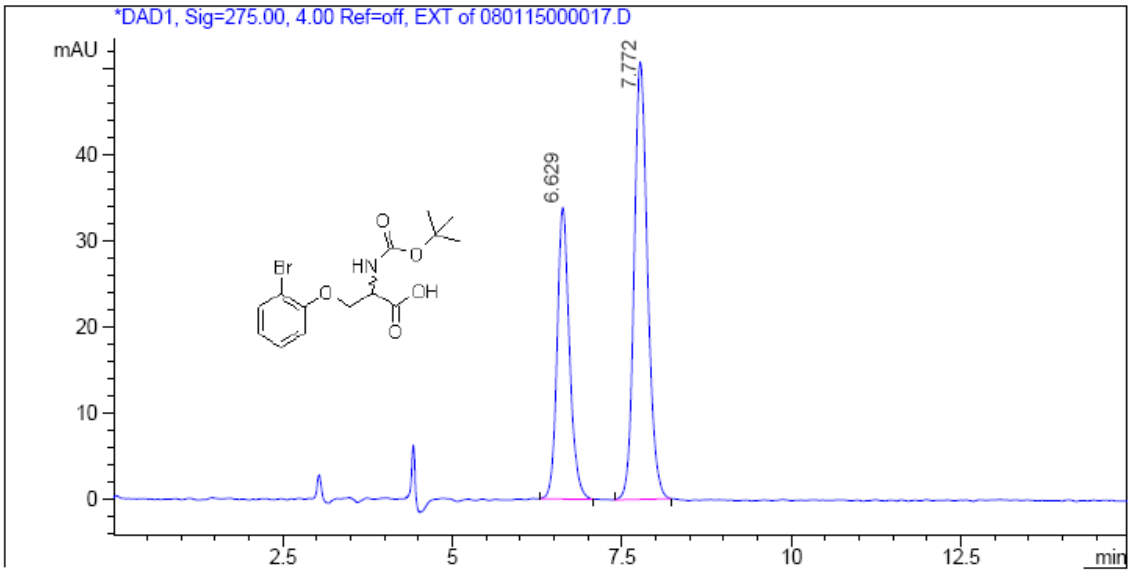


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```
Signal  1: DAD1, Sig=275.00, 4.00 Ref=off, EXT
```

Peak #	RT [min]	Area	Area %
1	6.63	429.50	38.00
2	7.77	700.67	62.00

Chiral HPLC of a mixture of D- and L-isomer of compound 3a prepared by external mixing (not racemic mixture)

```
                                                Location   :     Vial 39
Acq Operator     : KONDABABU                    Inj. No.   :          1
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Analysis Method  : C:\CHEM32\1\METHODS\A1.M
Last Changed     : Wed, 7. Jan. 2015,  06:20:38 pm

Sample ID:CR211-8259-67L1

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                        ->
                                                Ref :KD/08.01.15/371
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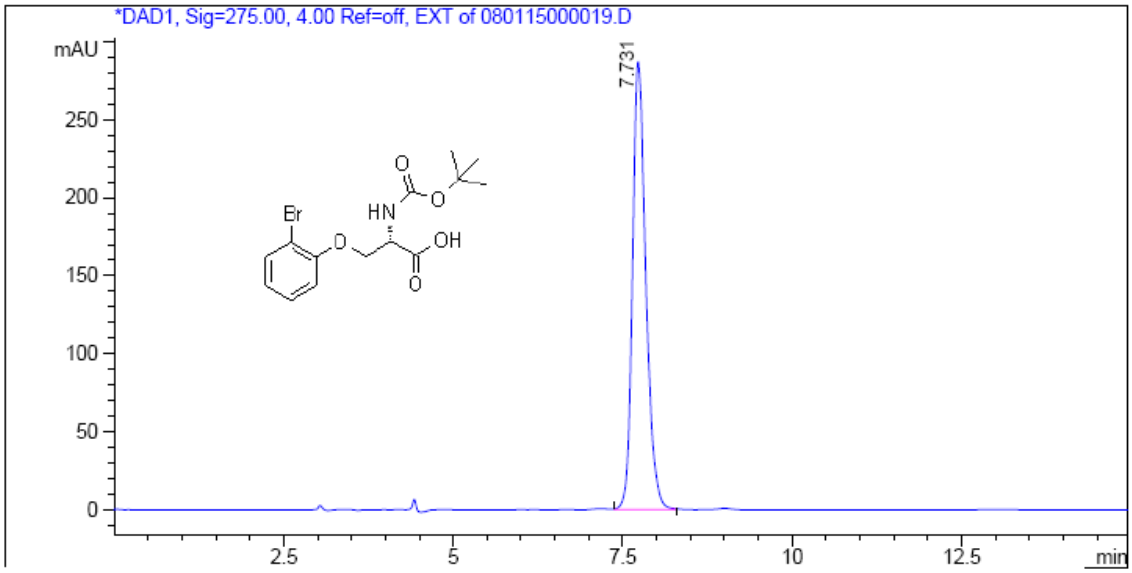


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Signal  1: DAD1, Sig=275.00, 4.00 Ref=off, EXT

|Peak|   RT      |   Area    |  Area %  |
| #  |  [min]    |-----------|----------|
|----|-----------|           |          |
|   1|      7.73|   3937.79|    100.00|
---------------------------------------
```

Chiral HPLC of L-isomer of compound 3a

```
                                                Location   :     Vial 38
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 1/8/2015     3:00:35 PM      Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\JAN-2015\080115 2015-01-08 09-48-05->
Analysis Method  : C:\CHEM32\1\METHODS\A1.M
Last Changed     : Wed, 7. Jan. 2015,  06:20:38 pm

Sample ID:CR211-8259-67D1

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                          ->
                                                Ref :KD/08.01.15/372
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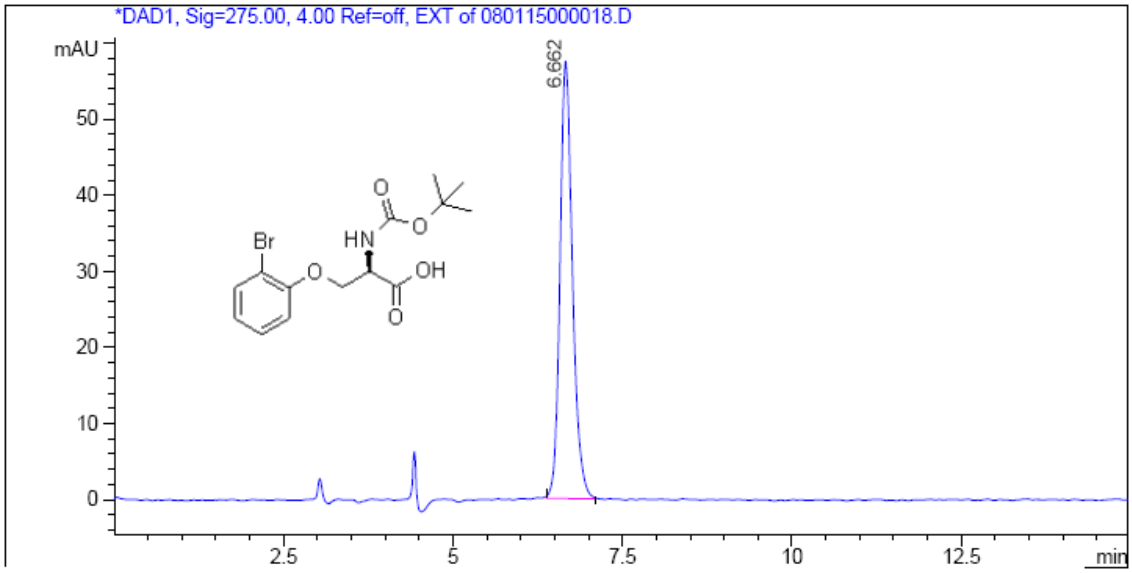


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==========================================================================


Signal  1: DAD1, Sig=275.00, 4.00 Ref=off, EXT

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      6.66|    735.45|    100.00|
```
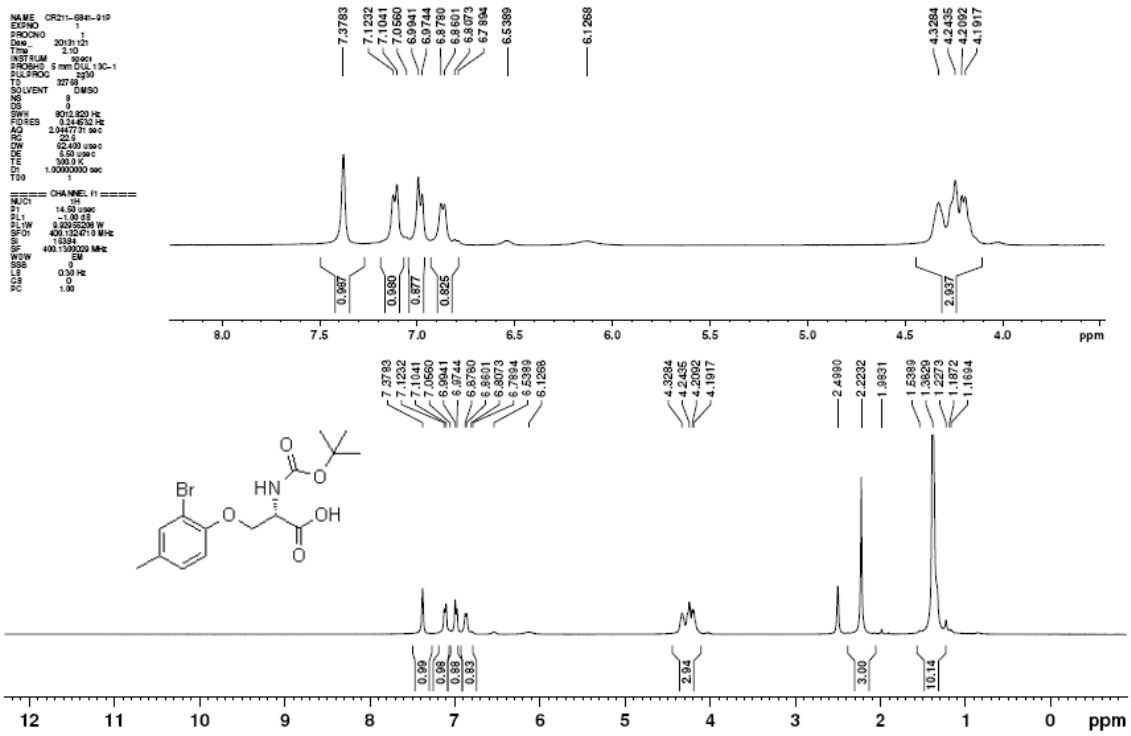
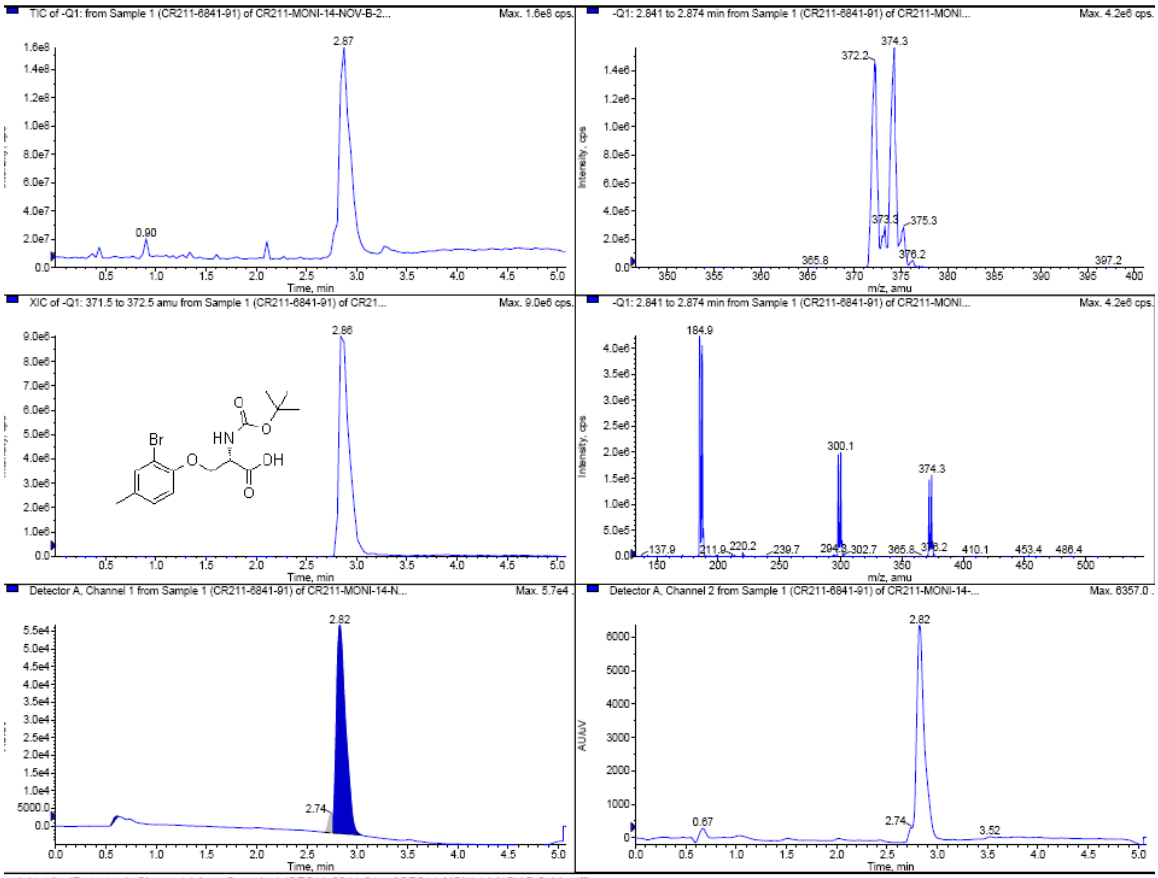

Chiral HPLC of D-isomer of compound 3a



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3b



eak List for "Detector A, Channel 1 from Sample 1 (CR211-6841-91) of CR211-MONI-14-NOV-B-2-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
	0.6081	2049.3342	0.5259	478.1325	0.7420	0.0733	Base to Base
	2.7416	1.4054e4	3.6064	5178.6177	8.0367	0.0817	Valley
	2.8250	3.7359e5	95.8677	5.8781e4	91.2213	0.2850	Valley

CMS MONITORING SAMPLE

*COLUMN- X-BRIDGE
ACN:NH4OAc

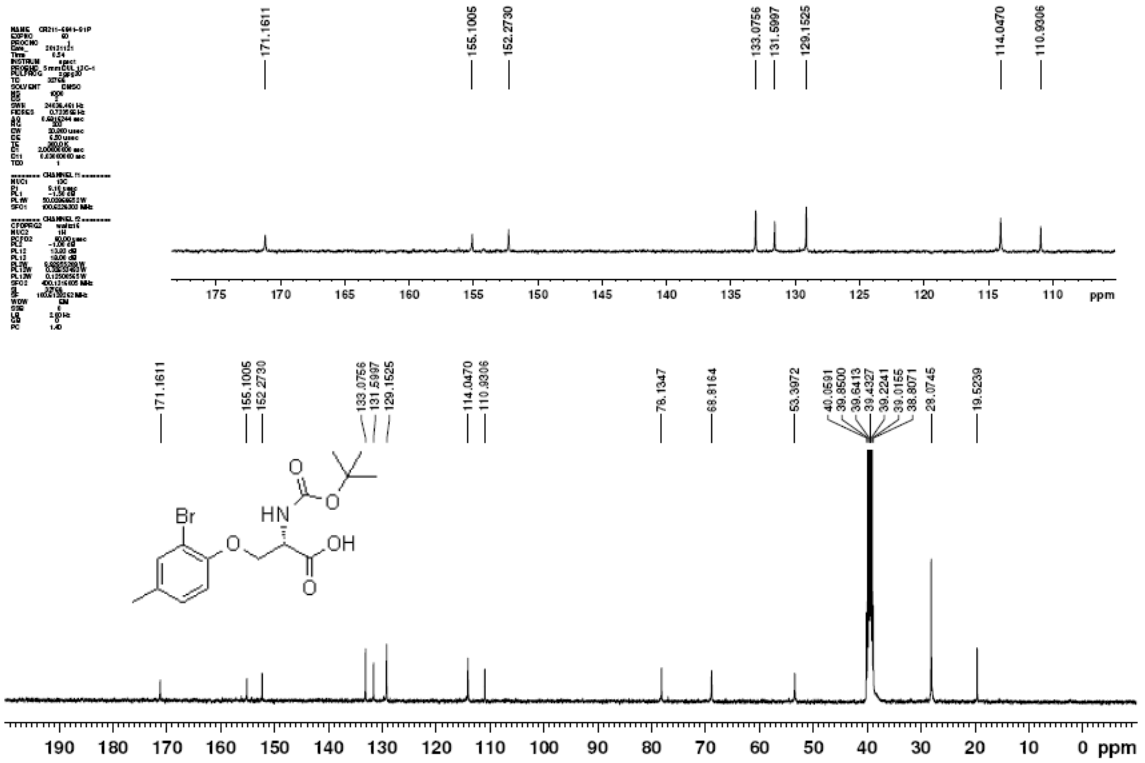
TCGLS/ARD/LCMS03/K05

annel 1 at wavelength 220 nm
annel 2 at wavelength 260 nm

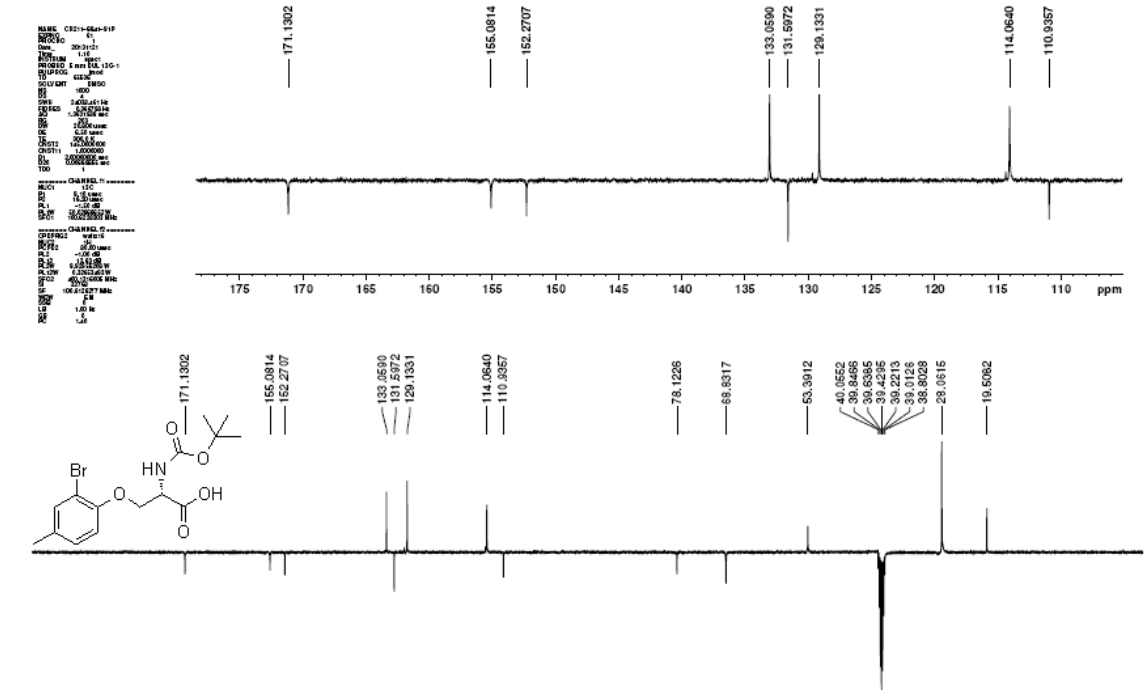
Anlalysed By

Checked By

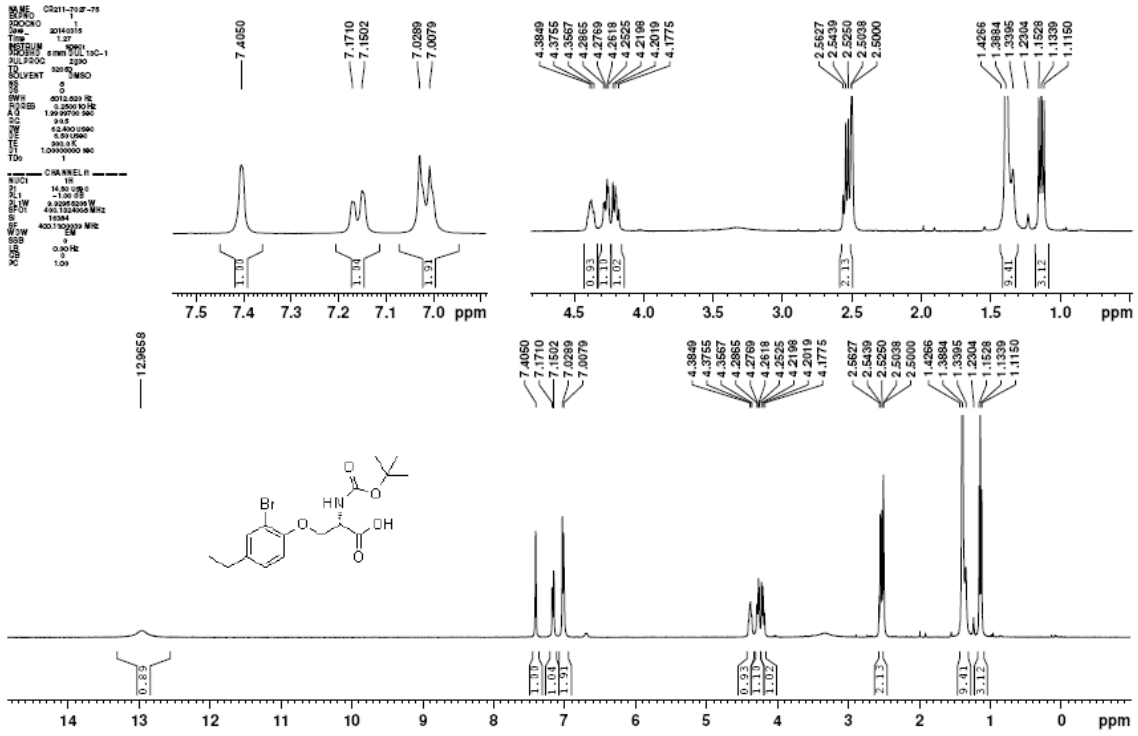
LCMS spectrum of compound 3b



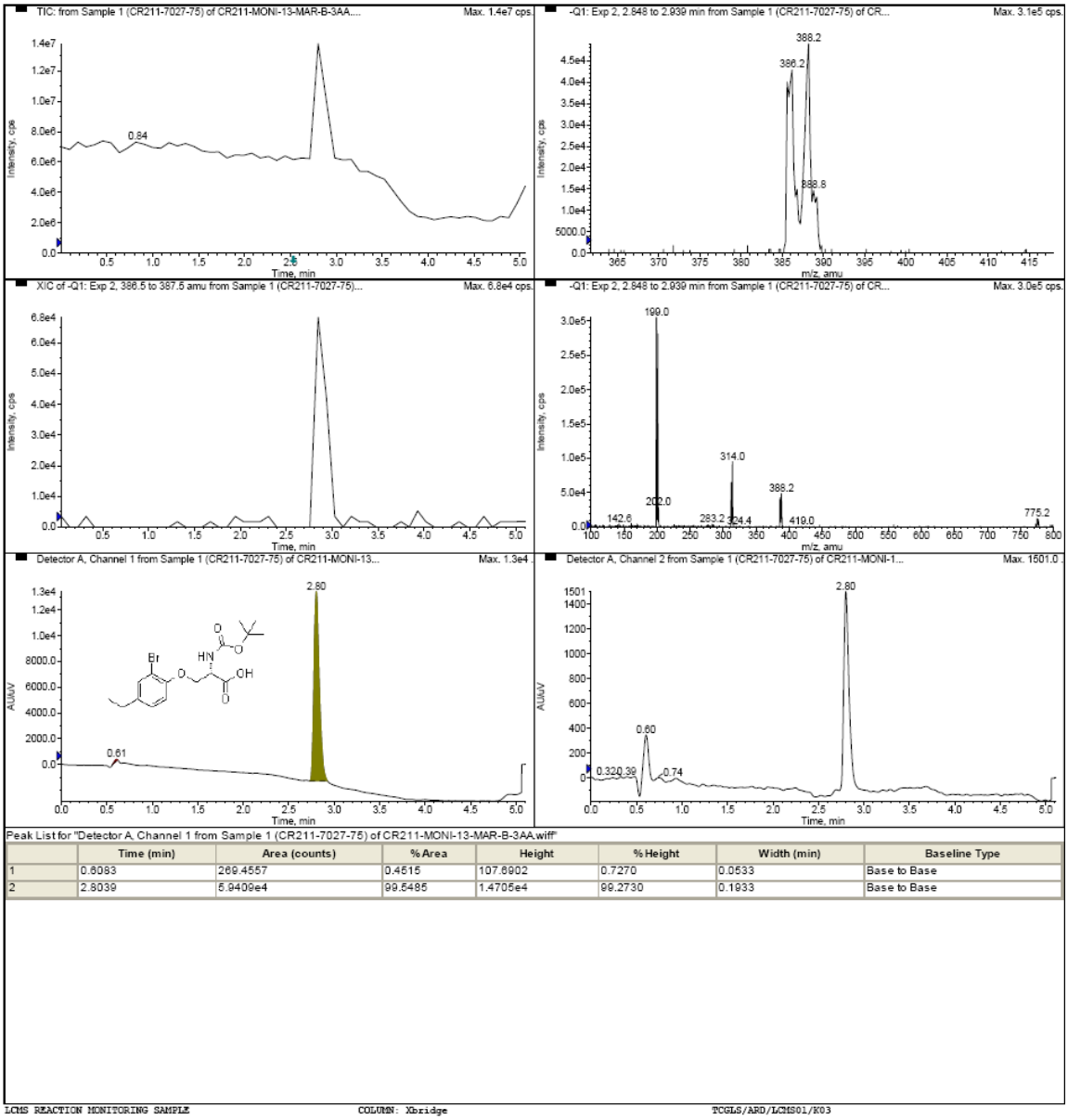
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3b



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3b



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3c



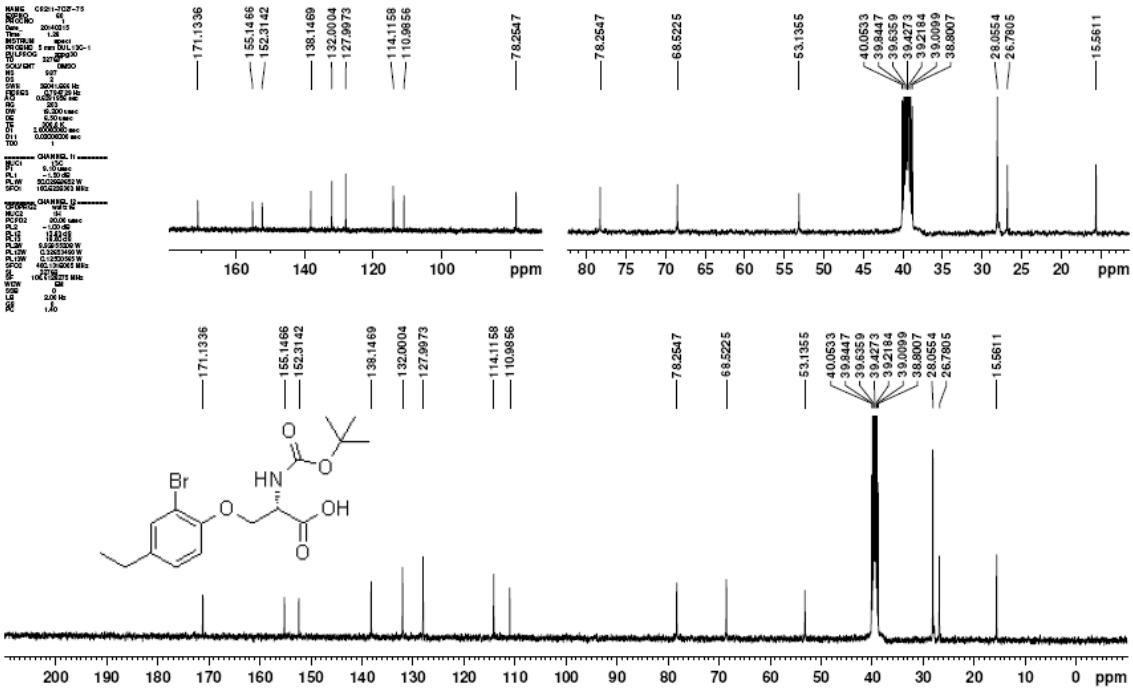
Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7027-75) of CR211-MONI-13-MAR-B-3AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.6083	269.4557	0.4515	107.6902	0.7270	0.0533	Base to Base
2	2.8039	5.9409e4	99.5485	1.4705e4	99.2730	0.1933	Base to Base

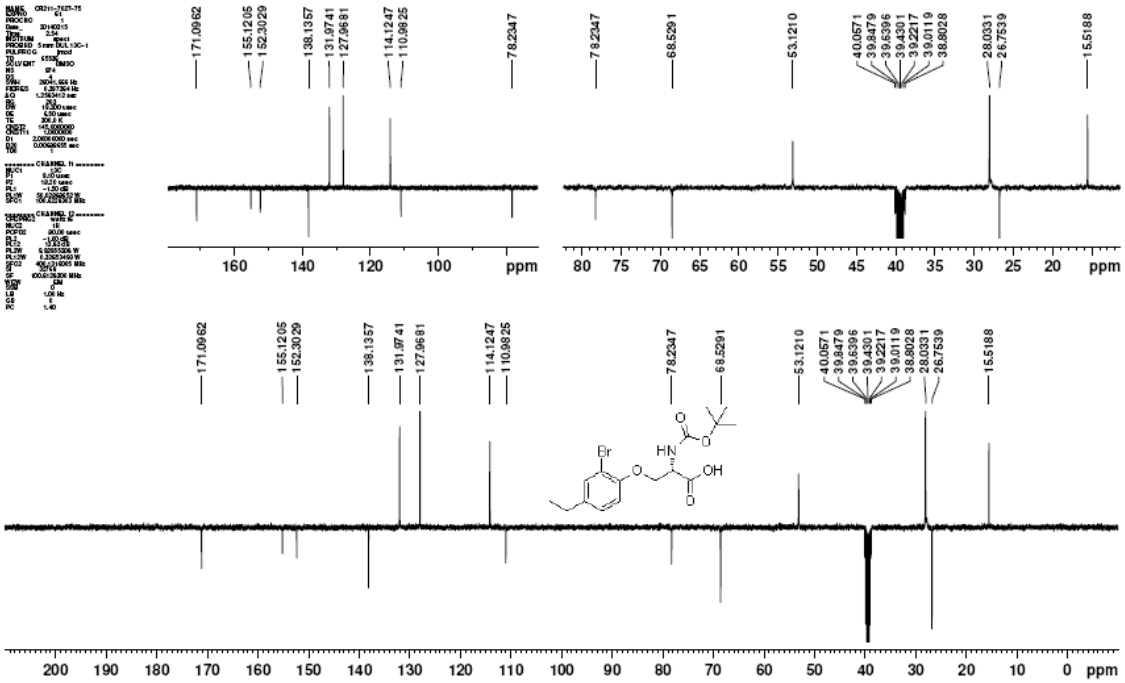
LCMS REACTION MONITORING SAMPLE COLUMN: Xbridge TCGLS/ARD/LCMS01/K03

Channel 1 at wavelength 220 nm, NH4OAc:ACN Analysed by
Channel 2 at wavelength 260 nm

LCMS spectrum of compound 3c



^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3c



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3c

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Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
Last Changed     : Wed, 31. Dec. 2014, 11:42:13 am
                   (modified after loading)
Sample ID : CR211-7027-75(D+L)

Column Name : Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Flow Rate : 1.0ml/min
Mobile Phase : Hexane/ETOH/TFA : 90/10/0.1
Solubility : MeOH                                                          ->
                                                      Ref :KD/31.12.14/1668
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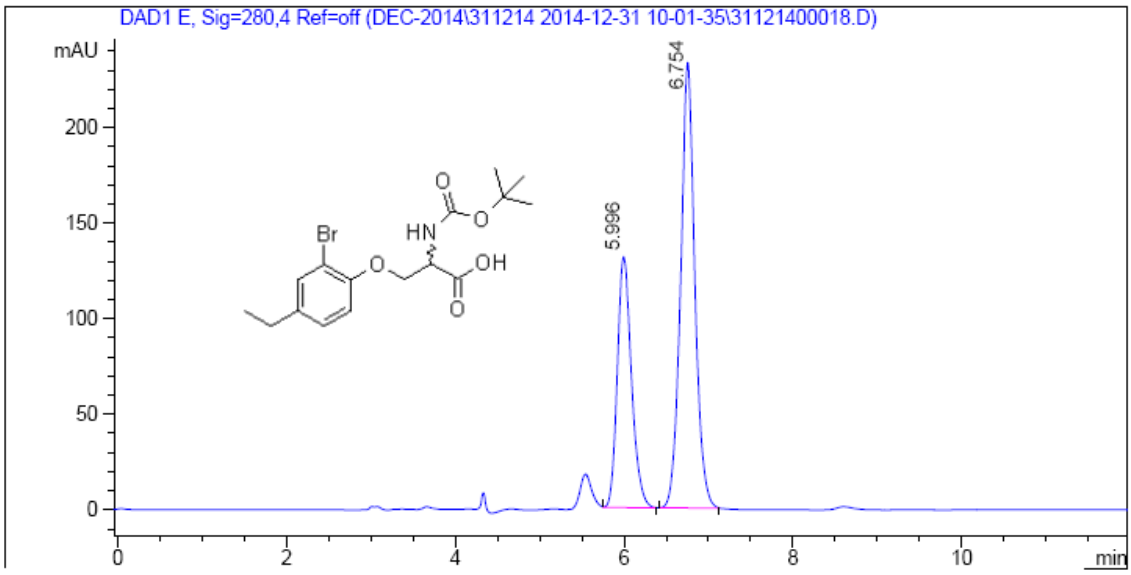


```
Signal  1: DAD1 E, Sig=280,4 Ref=off

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      6.00|   1525.69|     35.89|
|   2|      6.75|   2724.89|     64.11|
---------------------------------------
```

Chiral HPLC of a mixture of D- and L-isomer of compound 3c prepared by external mixing (not racemic mixture)

```
                                                Location   :      Vial 9
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/31/2014   5:00:06 PM      Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
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                   (modified after loading)
Sample ID : CR211-7027-75L

Column Name : Chioralpak IA(250x4.6mm)5µ
ARD/K/7804
Flow Rate : 1.0ml/min
Mobile Phase : Hexane/ETOH/TFA : 90/10/0.1
Solubility : MeOH                                                       ->
                                                Ref :KD/31.12.14/1671
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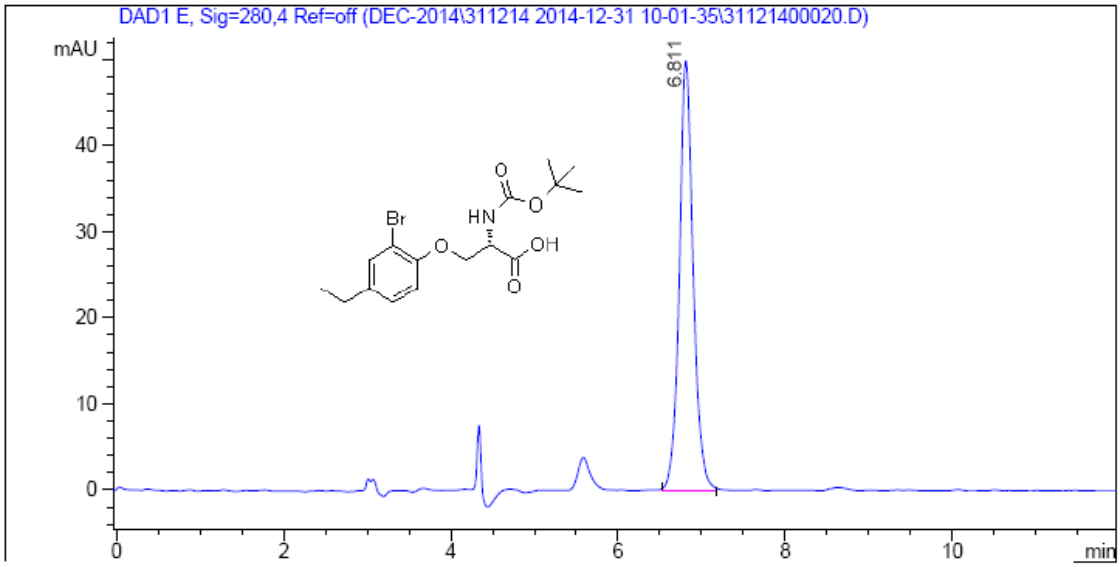


```
Signal  1: DAD1 E, Sig=280,4 Ref=off

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      6.81|    573.96|    100.00|
---------------------------------------
```

Chiral HPLC of L-isomer of compound 3c

```
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Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/31/2014   4:47:00 PM      Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
Last Changed     : Wed, 31. Dec. 2014, 11:42:13 am
                   (modified after loading)
Sample ID : CR211-7027-75D

Column Name : Chioralpak IA(250x4.6mm)5µ
ARD/K/7804
Flow Rate : 1.0ml/min
Mobile Phase : Hexane/ETOH/TFA : 90/10/0.1
Solubility : MeOH                                                    ->
                                                Ref :KD/31.12.14/1670
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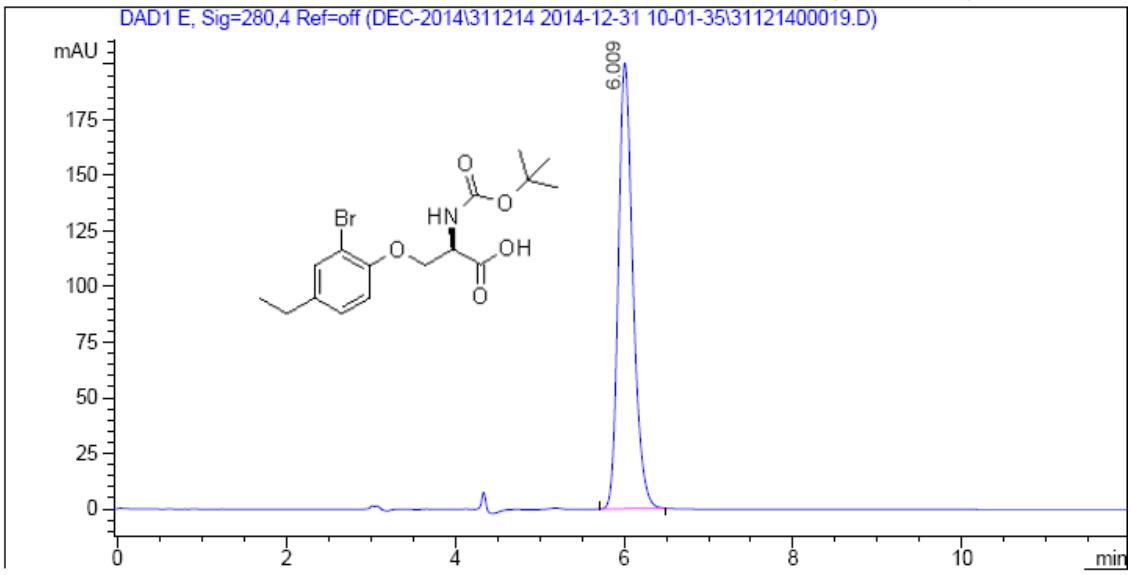
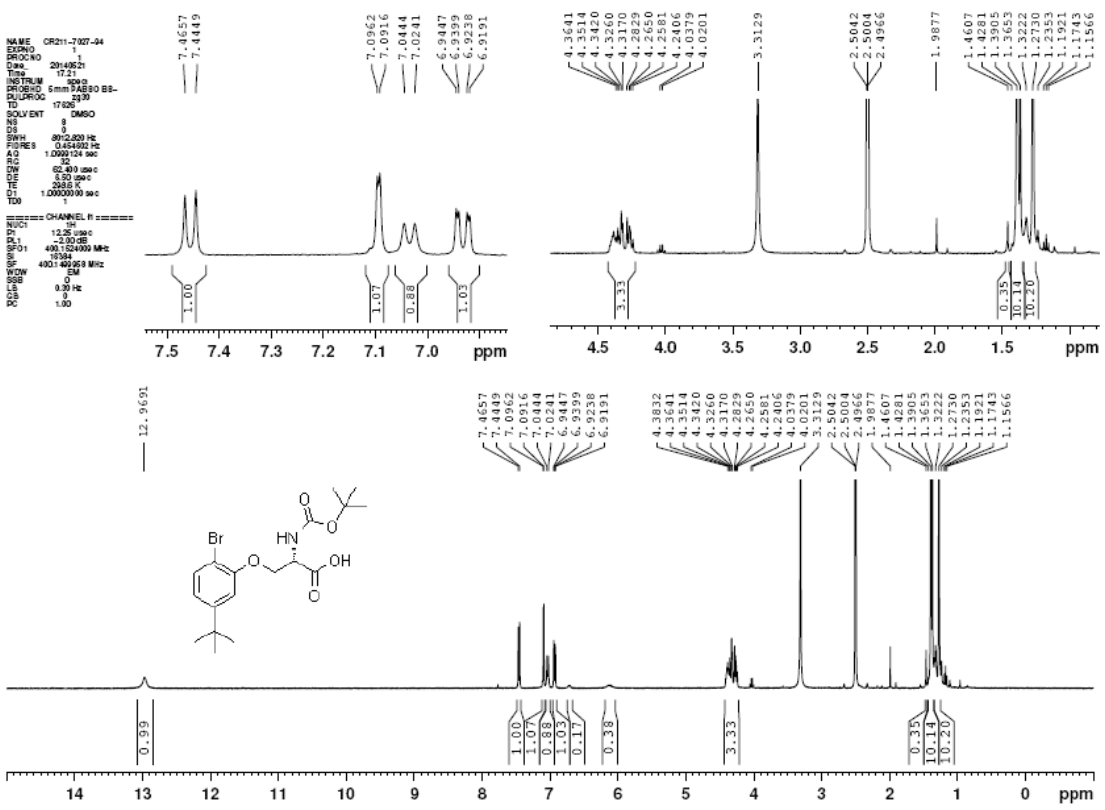


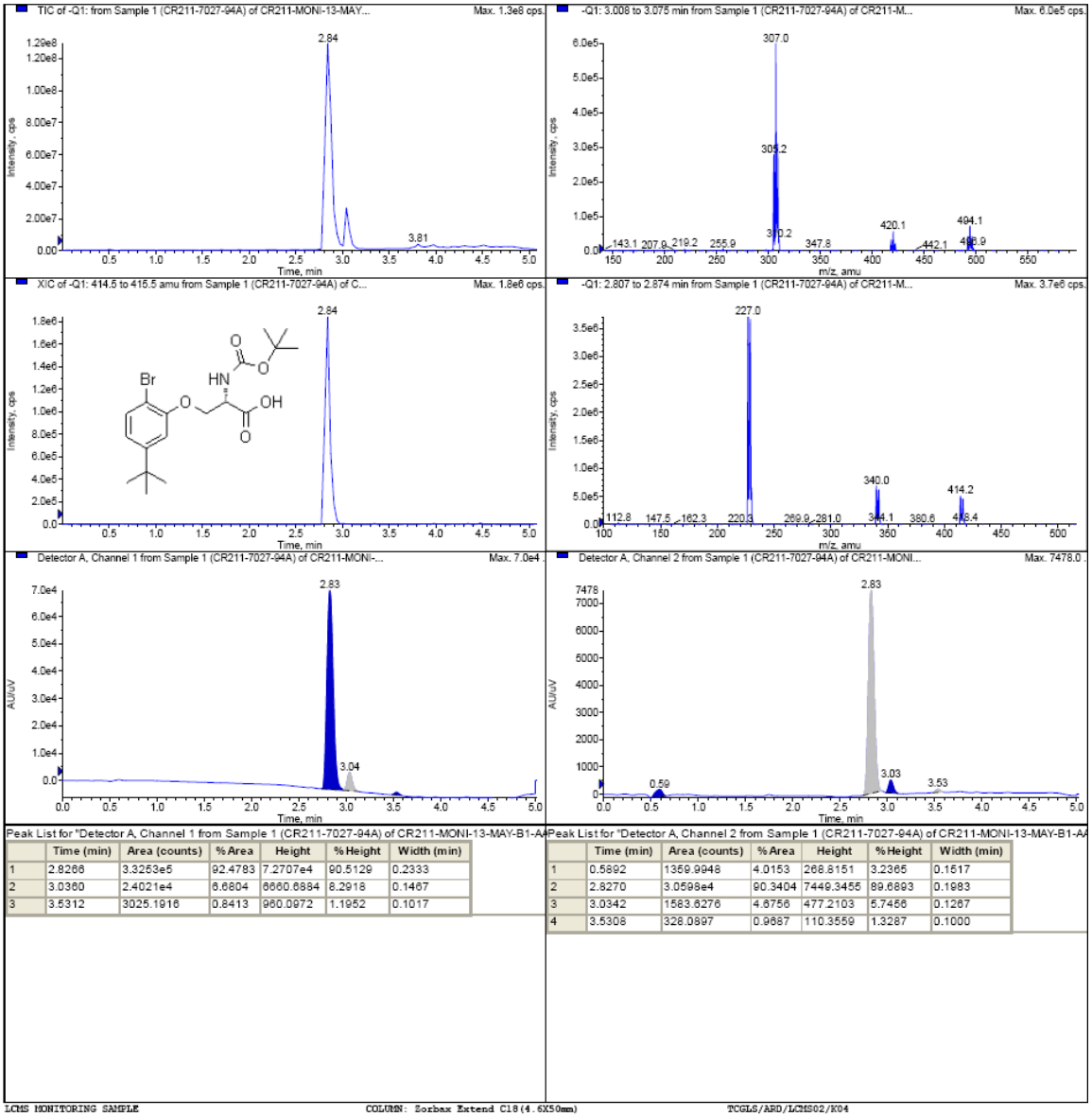

```
Signal  1: DAD1 E, Sig=280,4 Ref=off

|Peak|   RT      |   Area    |  Area %   |
| #  |  [min]    |-----------|-----------|
|----|-----------|           |           |
|   1|      6.01|   2404.71|    100.00|
```

Chiral HPLC of D-isomer of compound 3c



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3d



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7027-94A) of CR211-MONI-13-MAY-B1-AA

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	2.8266	3.3253e5	92.4783	7.2707e4	90.5129	0.2333
2	3.0360	2.4021e4	6.6804	6660.6884	8.2918	0.1467
3	3.5312	3025.1916	0.8413	960.0972	1.1952	0.1017

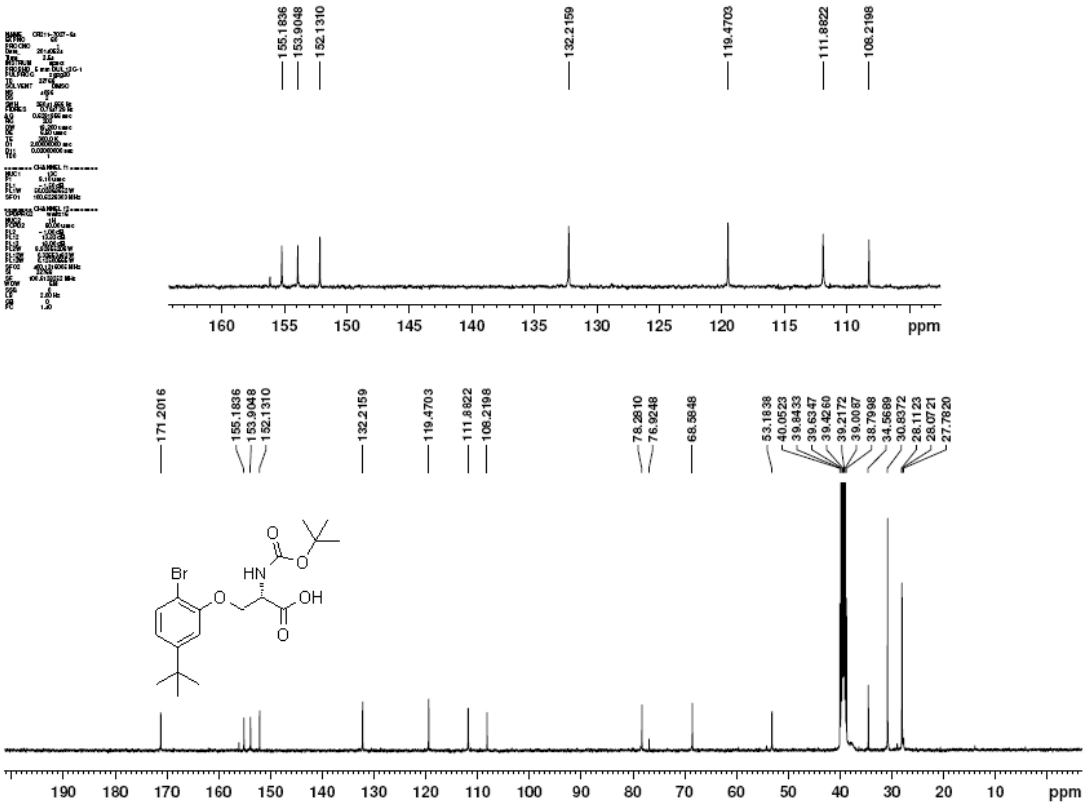
Peak List for "Detector A, Channel 2 from Sample 1 (CR211-7027-94A) of CR211-MONI-13-MAY-B1-AA

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.5892	1359.9948	4.0153	268.8151	3.2365	0.1517
2	2.8270	3.0598e4	90.3404	7449.3456	89.6893	0.1983
3	3.0342	1583.8276	4.6756	477.2103	5.7456	0.1267
4	3.5308	328.0897	0.9687	110.3559	1.3287	0.1000

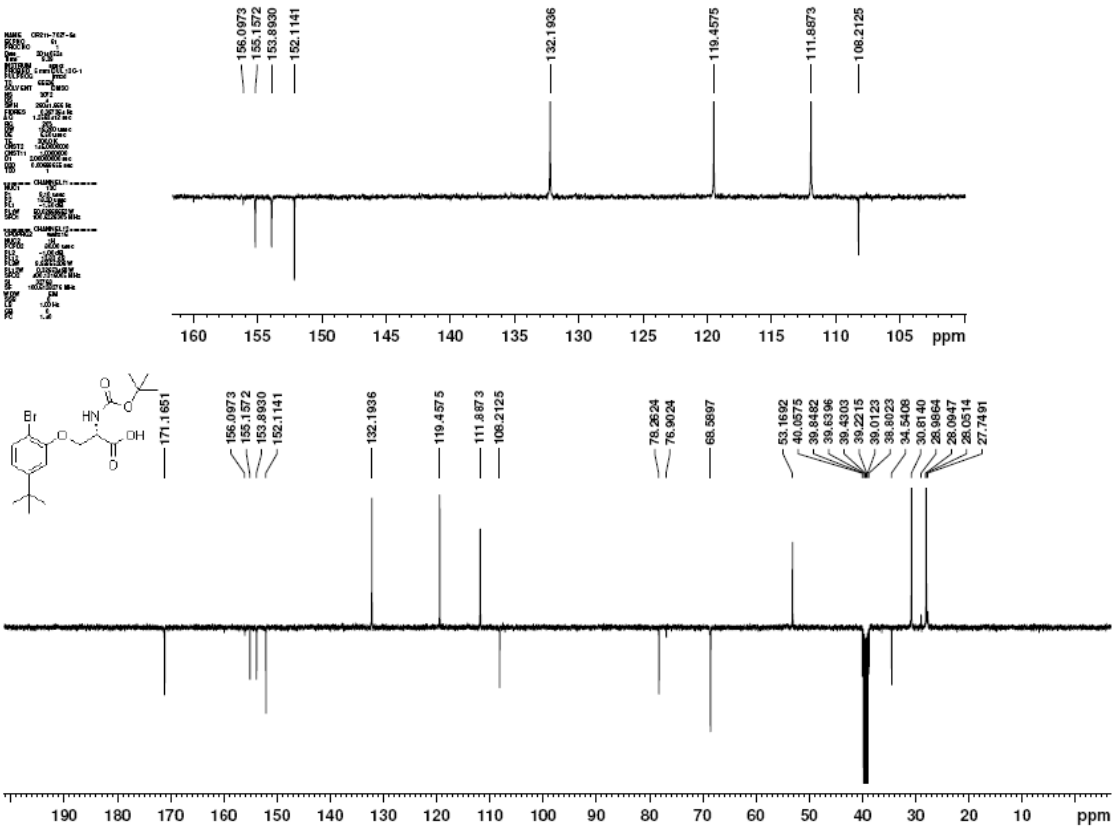
LCMS MONITORING SAMPLE COLUMN: Sorbax Extend C18(4.6X50mm) TCGLS/ARD/LCMS02/K04

Channel 1 at wavelength 220 nm, NH4OAc:ACN Analysed by
Channel 2 at wavelength 260 nm

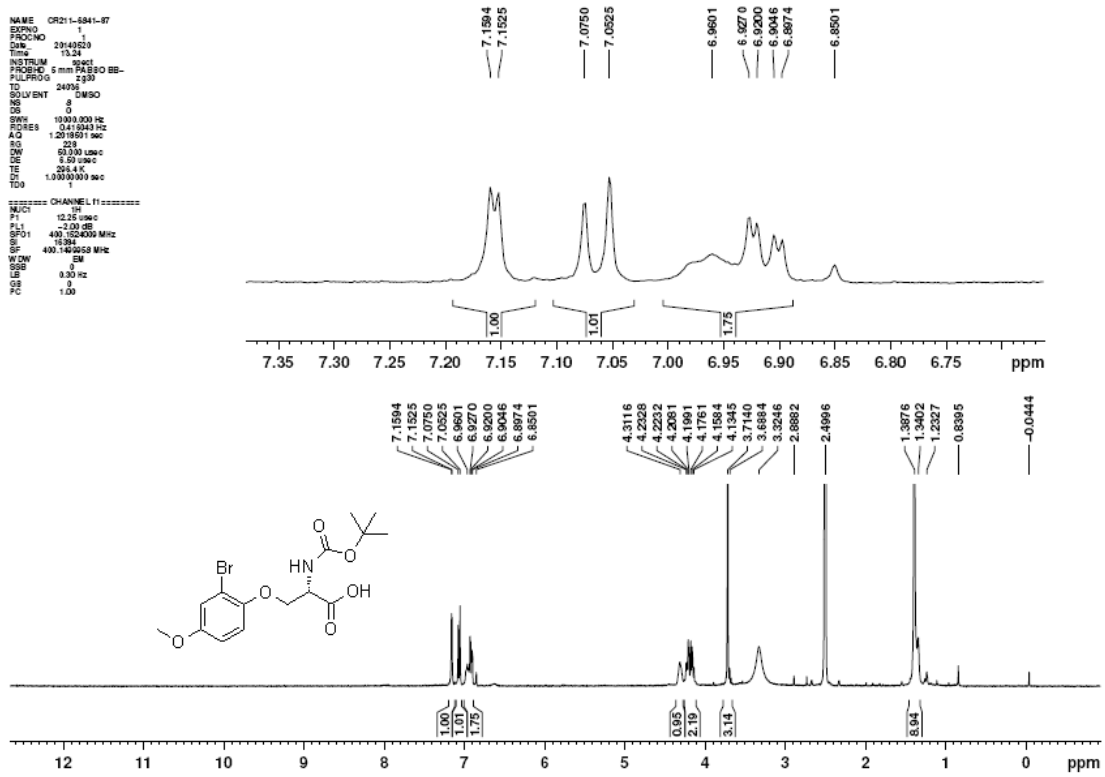
LCMS spectrum of compound 3d



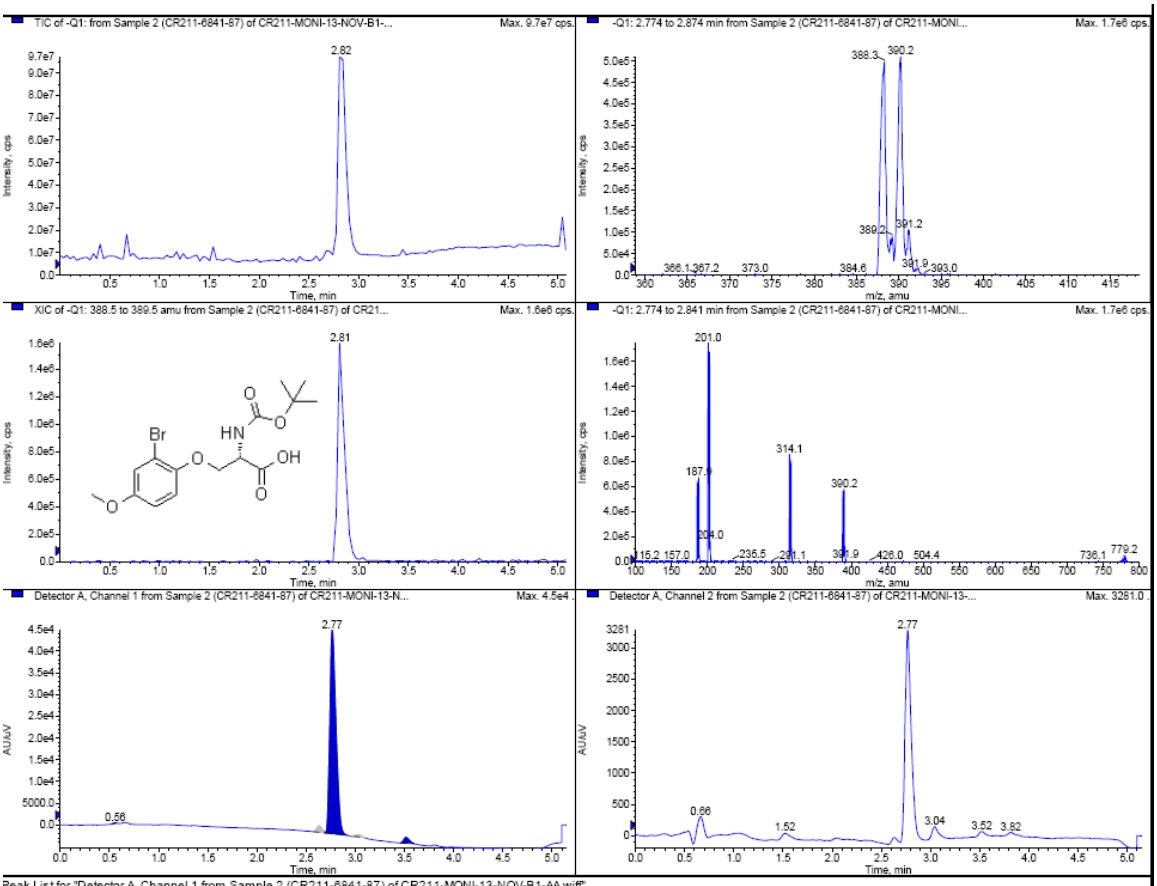
^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 3d



APT NMR spectrum (100MHz, DMSO-d_6) of compound 3d



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3e



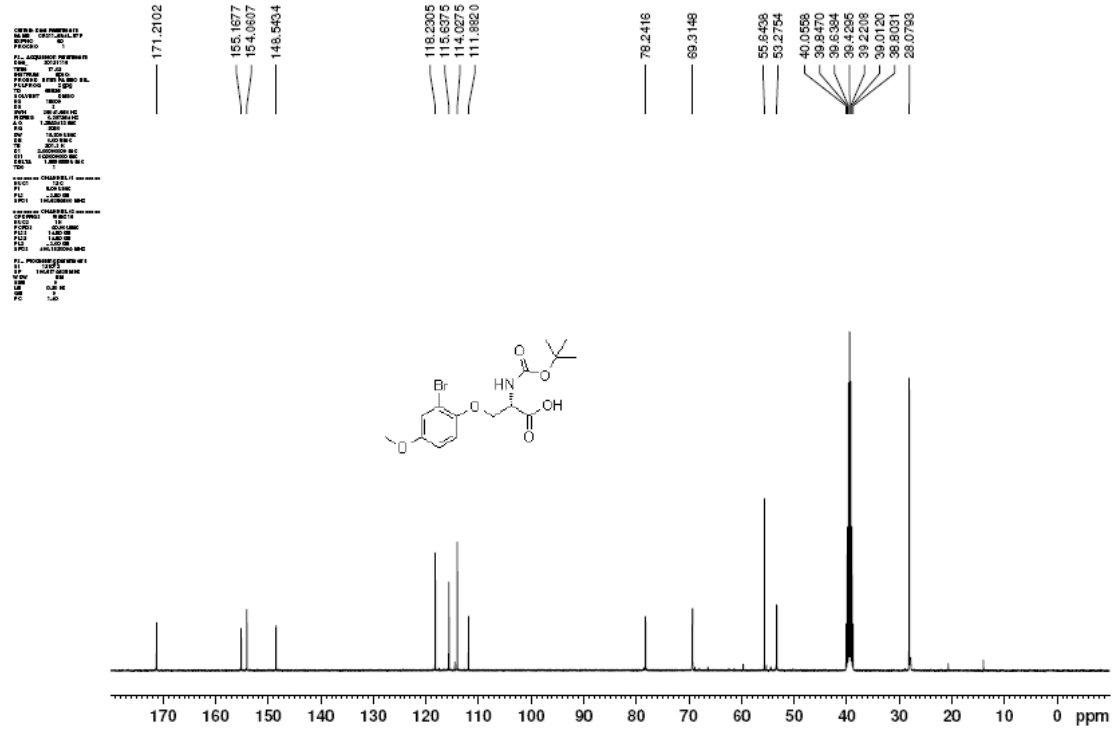
Peak List for "Detector A, Channel 1 from Sample 2 (CR211-6841-87) of CR211-MONI-13-NOV-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5600	160.5282	0.0748	94.4020	0.1883	0.0433	Base to Base
2	2.6329	5102.4594	2.3767	1426.7554	2.8455	0.1183	Valley
3	2.7655	2.0260e5	94.3706	4.6809e4	93.3554	0.2217	Valley
4	3.0314	1657.9832	0.7723	464.7623	0.9269	0.1083	Base to Base
5	3.5183	5164.8458	2.4057	1345.7459	2.6839	0.1400	Base to Base

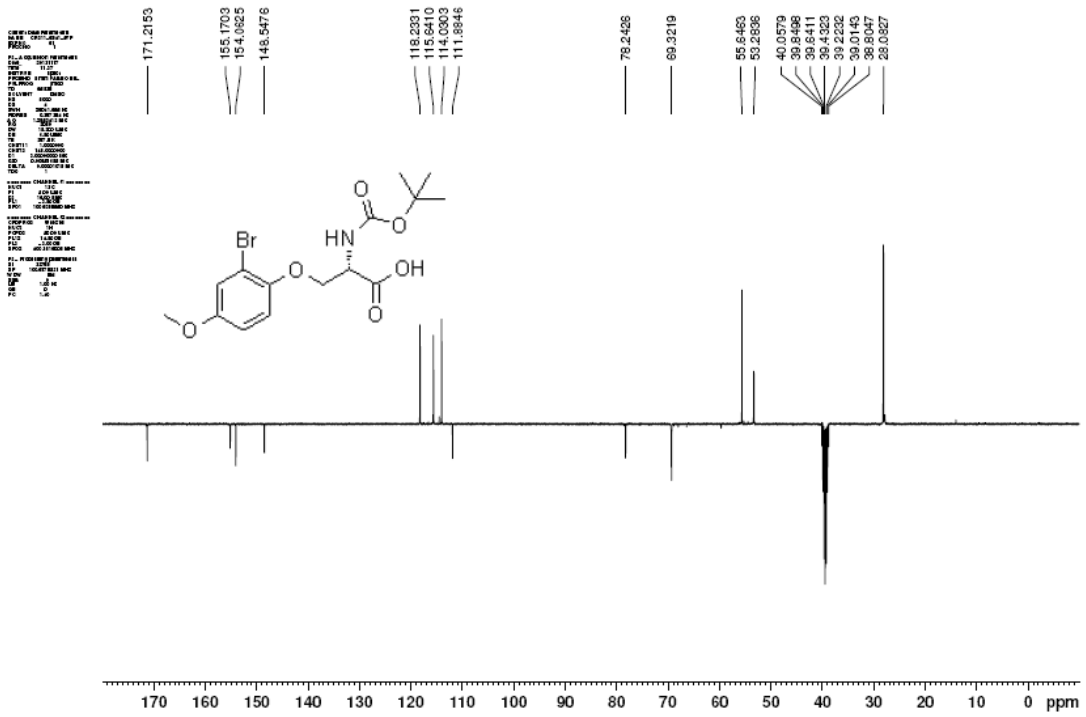
LCMS MONITORING SAMPLE
*COLUMN- X-BRIDGE
ACN:NH4OAc
TCGLS/ARD/LCMS03/K05

Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm
Anlalysed By
Checked By

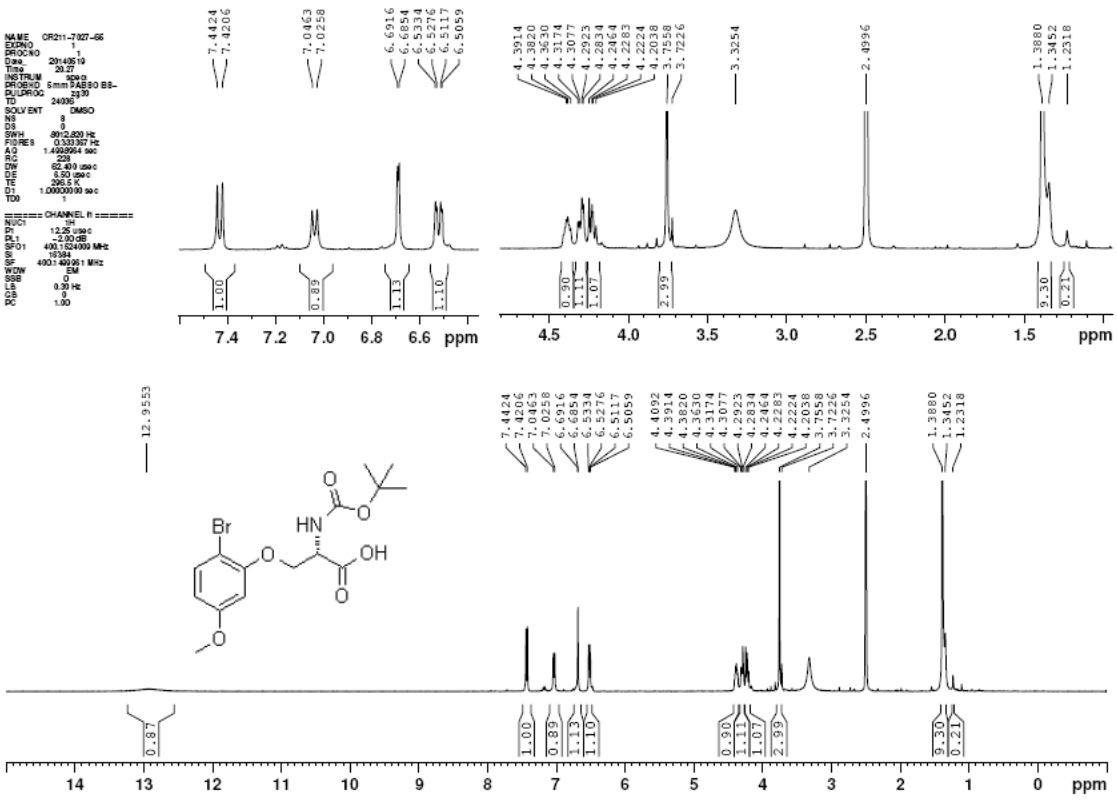
LCMS spectrum of compound 3e



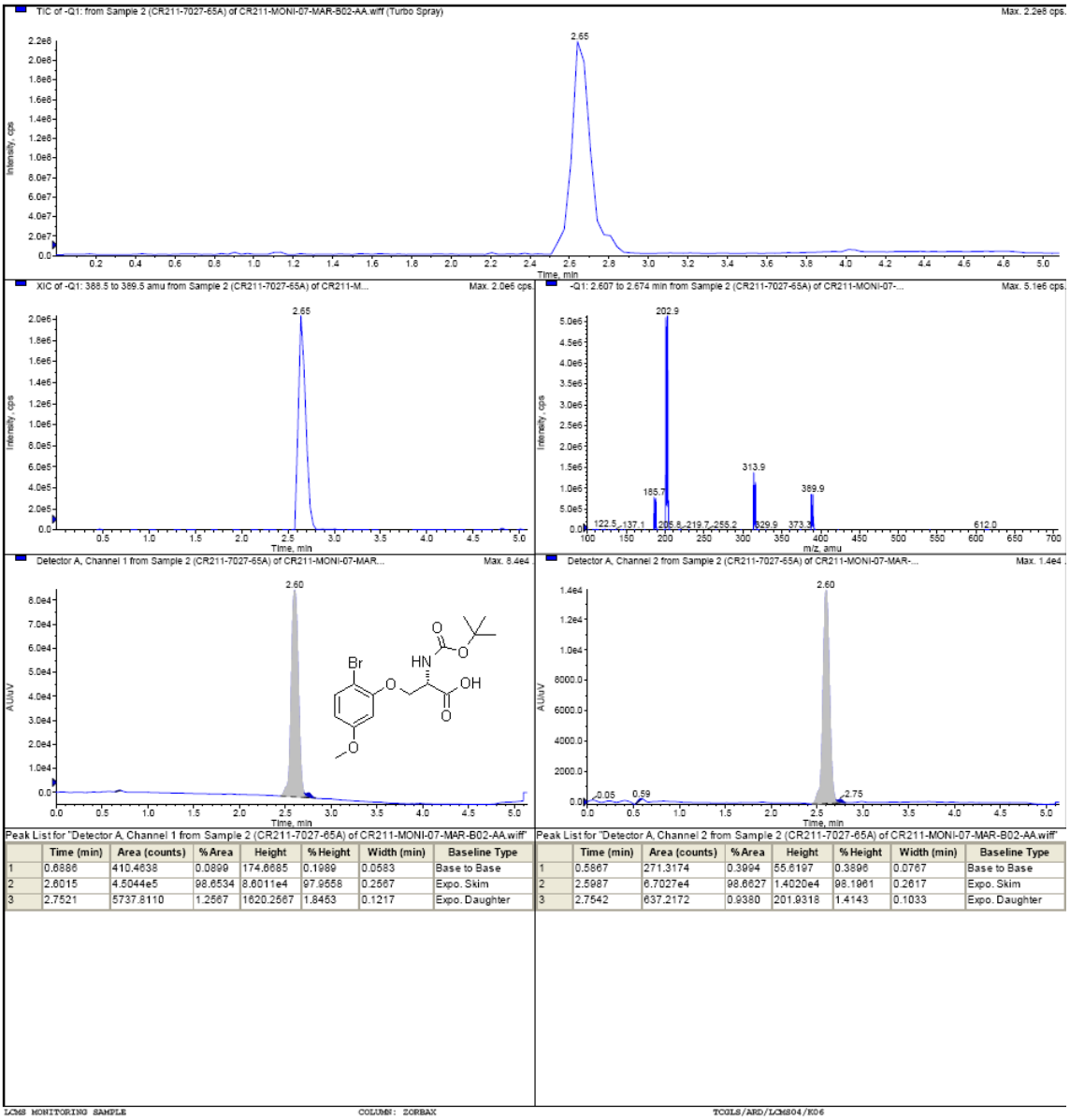
^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 3e



APT NMR spectrum (100MHz, DMSO-d_6) of compound 3e



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3f



Peak List for "Detector A, Channel 1 from Sample 2 (CR211-7027-65A) of CR211-MONI-07-MAR-B02-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.6886	410.4638	0.0899	174.6685	0.1989	0.0583	Base to Base
2	2.6015	4.5044e5	98.6534	8.6011e4	97.9558	0.2567	Expo. Skim
3	2.7521	5737.8110	1.2567	1620.2567	1.8453	0.1217	Expo. Daughter

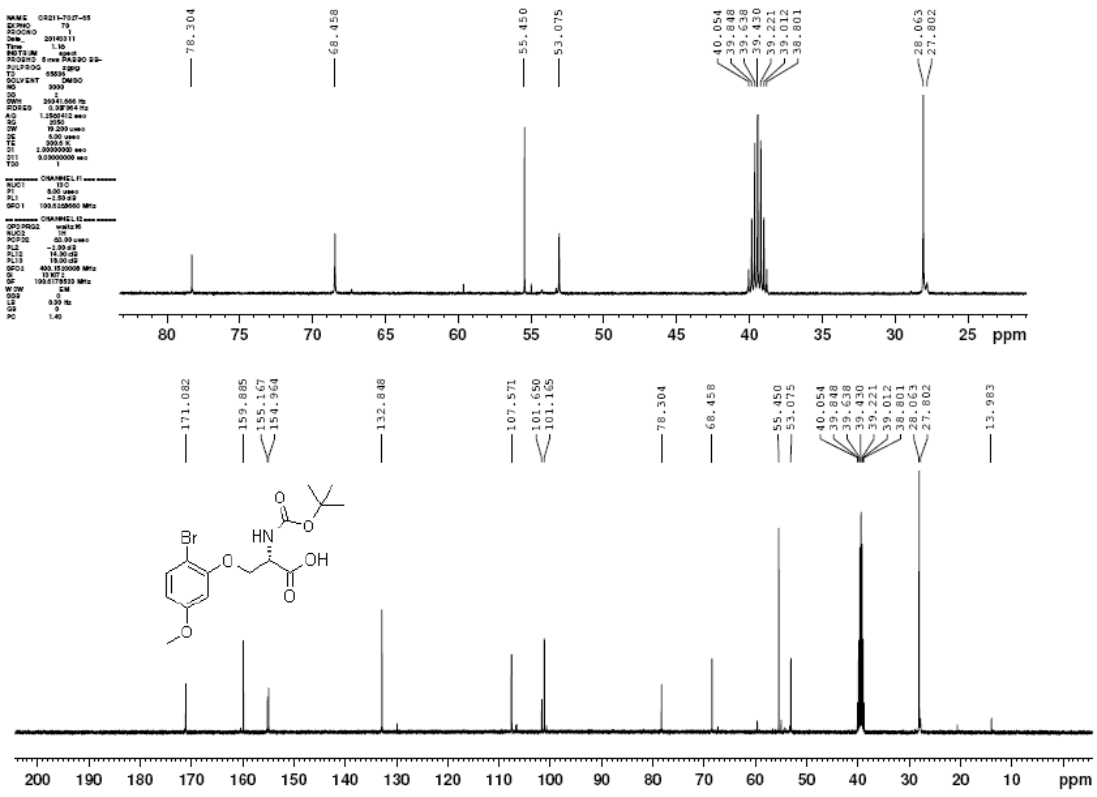
Peak List for "Detector A, Channel 2 from Sample 2 (CR211-7027-65A) of CR211-MONI-07-MAR-B02-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5867	271.3174	0.3994	55.6197	0.3896	0.0767	Base to Base
2	2.5987	6.7027e4	98.6627	1.4020e4	98.1961	0.2617	Expo. Skim
3	2.7542	637.2172	0.9380	201.9318	1.4143	0.1033	Expo. Daughter

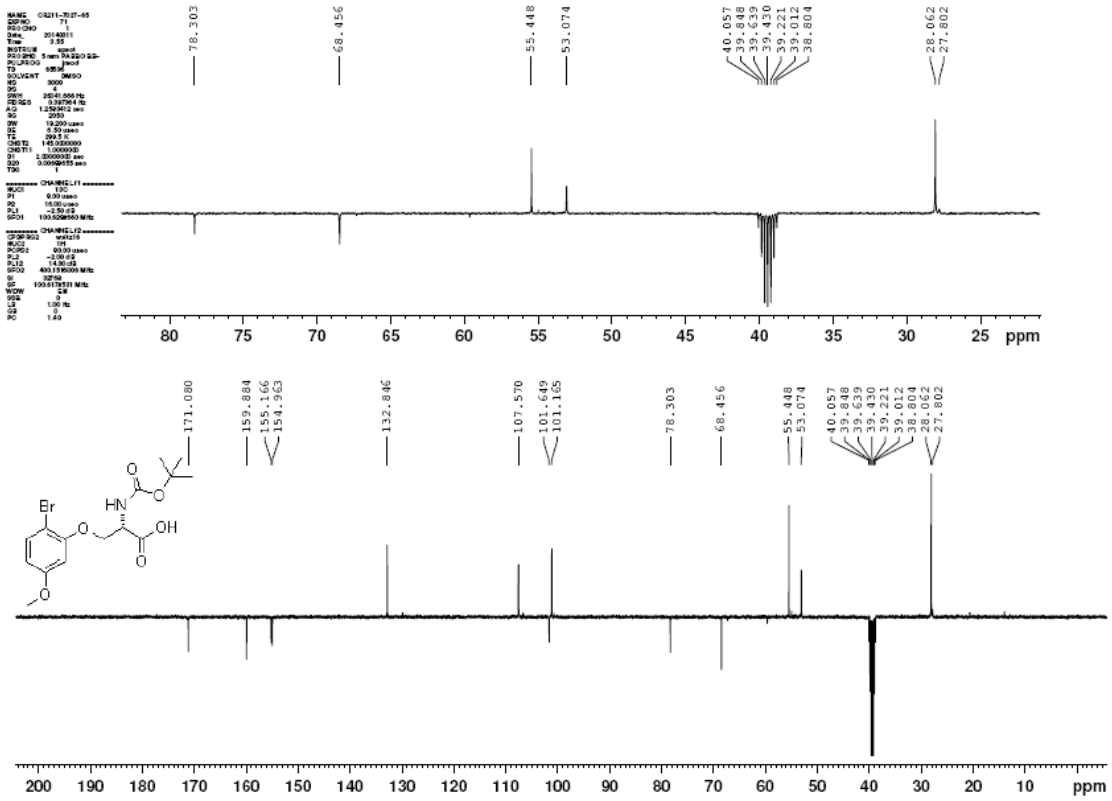
LCMS MONITORING SAMPLE COLUMN: ZORBAX TCGLS/ARD/LCMS04/K06

Channel 1 at wavelength 220 nm, Channel 2 at wavelength 260 nm NH4OAc:ACN Analyzed by

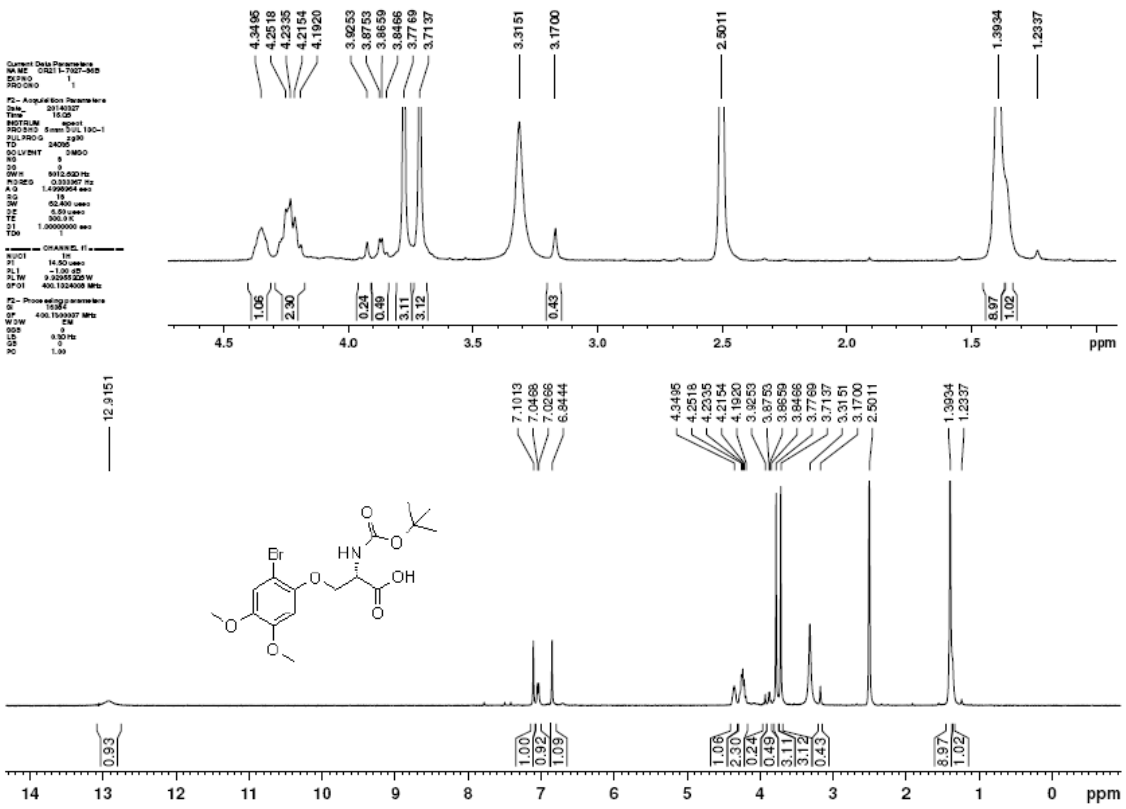
LCMS spectrum of compound 3f



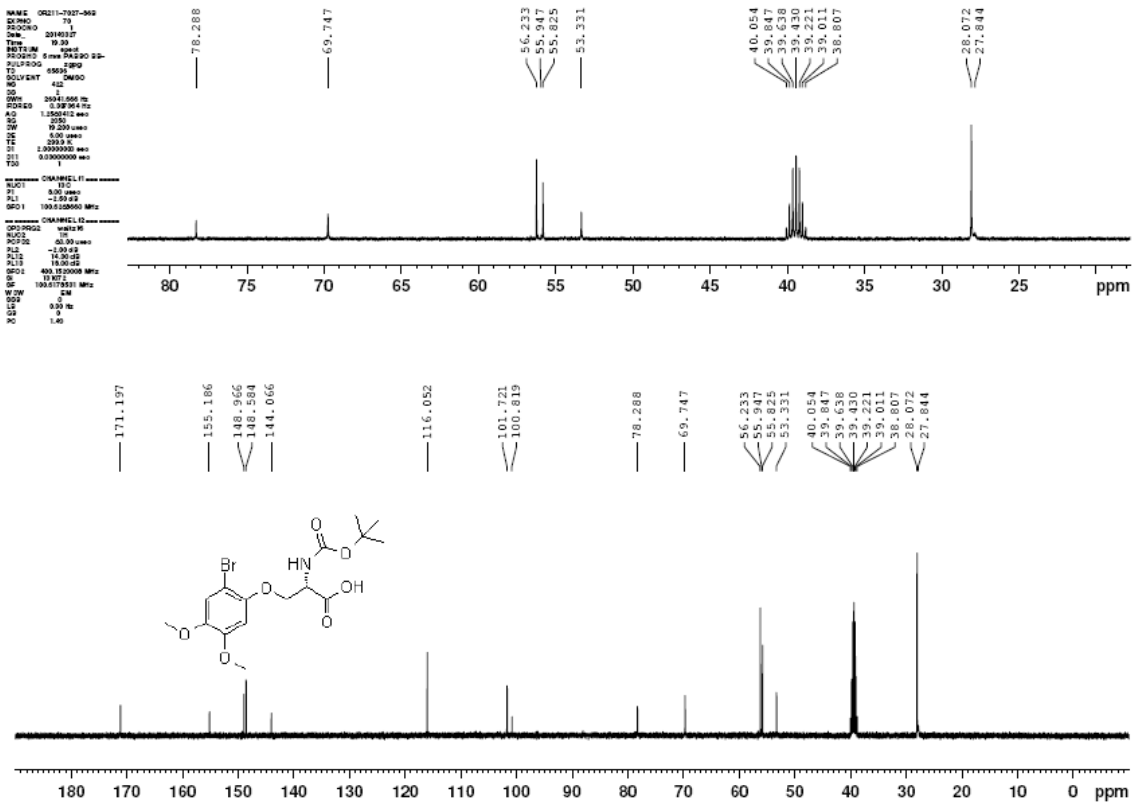
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3f



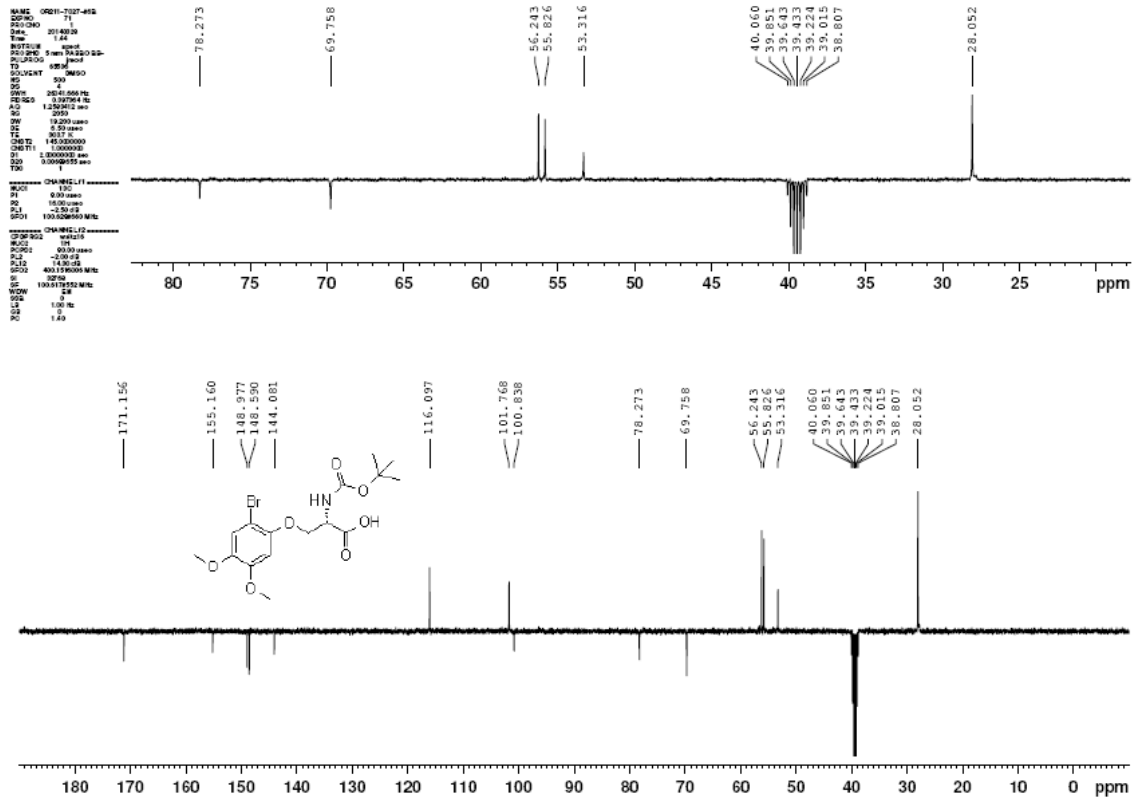
APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3f



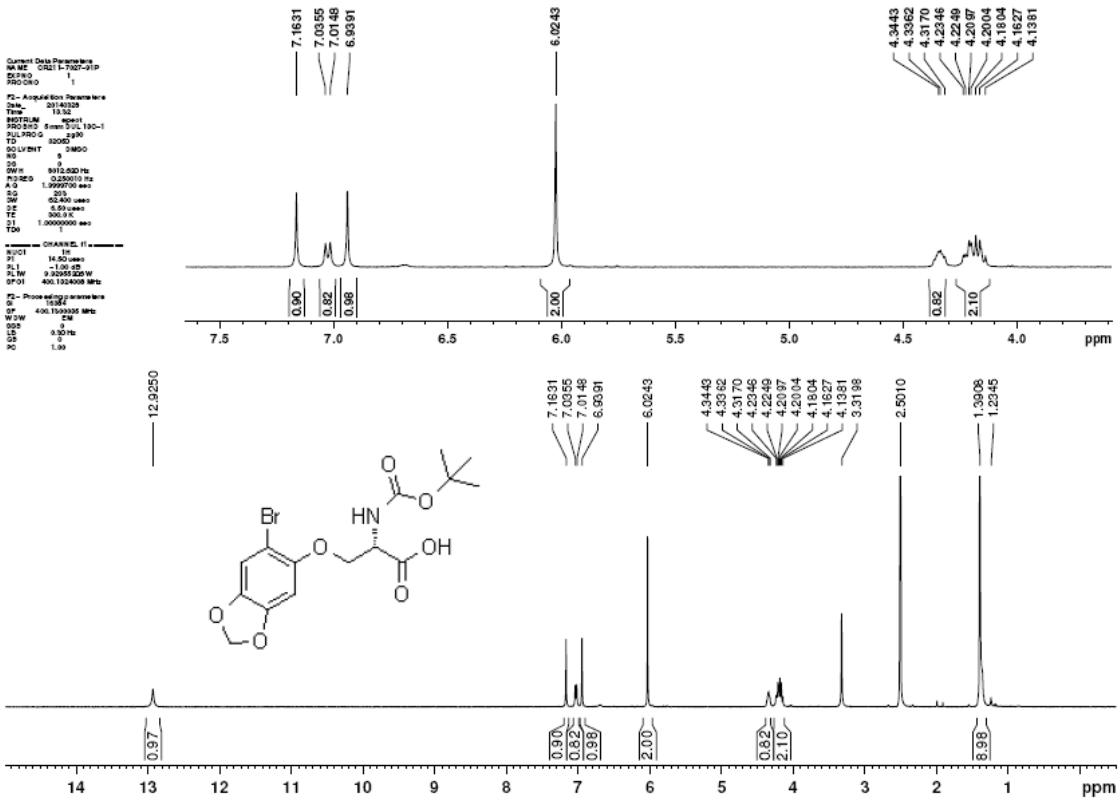
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3g



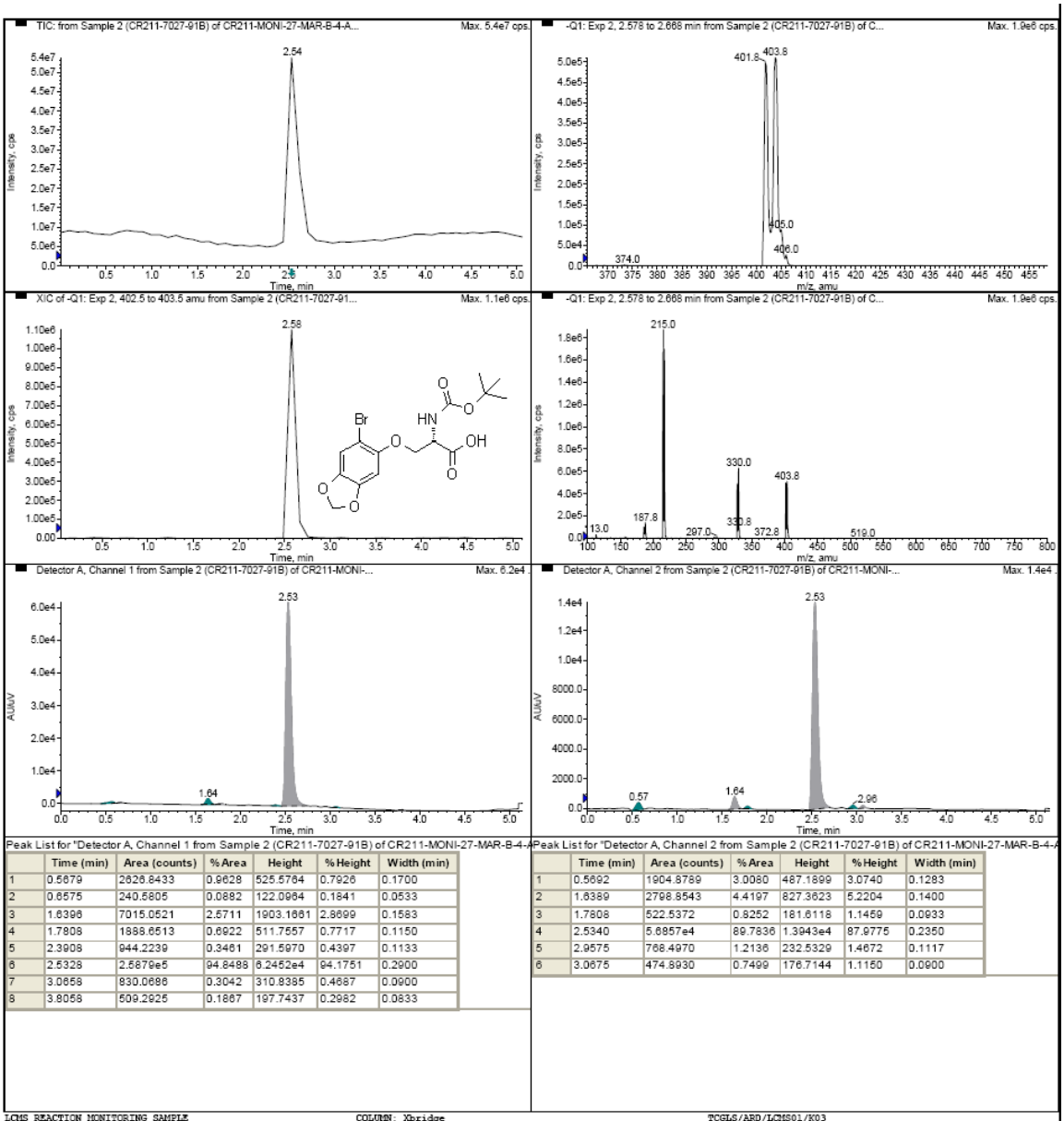
^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 3g



APT NMR spectrum (100MHz, DMSO-d_6) of compound 3g



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3h



Peak List for "Detector A, Channel 1 from Sample 2 (CR211-7027-91B) of CR211-MONI-27-MAR-B-4-A

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.5679	2626.8433	0.9628	525.5764	0.7926	0.1700
2	0.6575	240.5805	0.0882	122.0964	0.1841	0.0533
3	1.6396	7015.0521	2.5711	1903.1661	2.8699	0.1583
4	1.7808	1888.6513	0.6922	511.7557	0.7717	0.1150
5	2.3908	944.2239	0.3461	291.5970	0.4397	0.1133
6	2.5328	2.5879e5	94.8488	6.2452e4	94.1751	0.2900
7	3.0658	830.0686	0.3042	310.8385	0.4687	0.0900
8	3.8058	509.2925	0.1867	197.7437	0.2982	0.0833

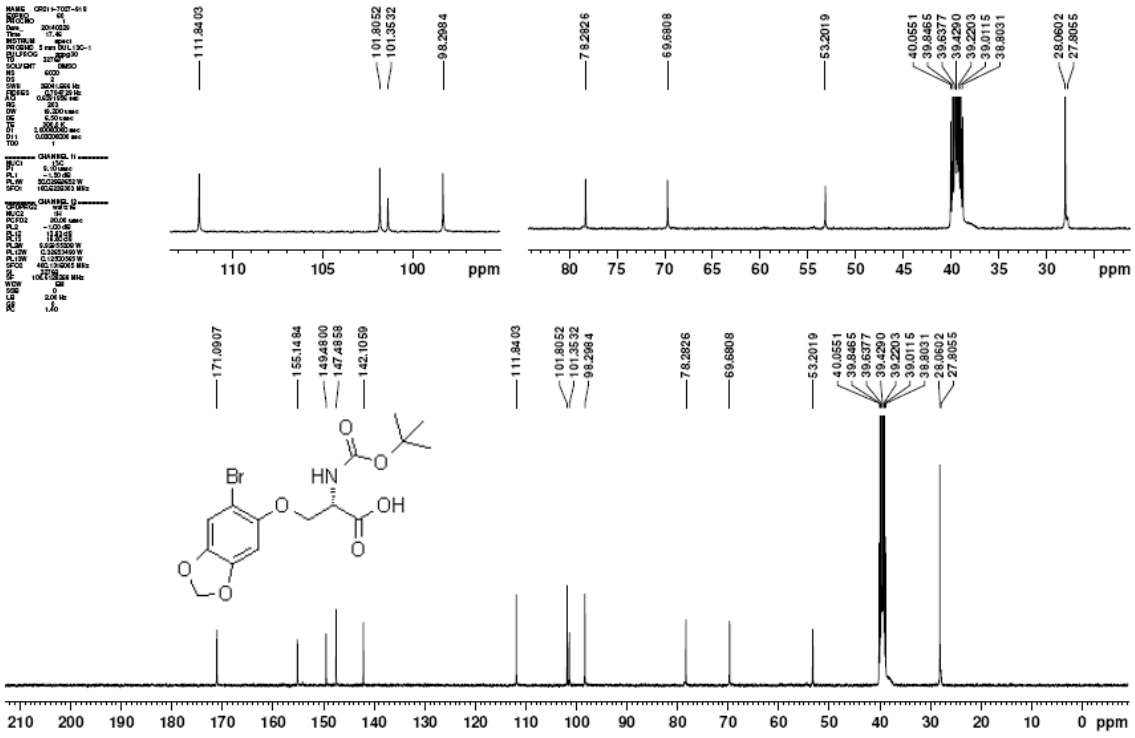
Peak List for "Detector A, Channel 2 from Sample 2 (CR211-7027-91B) of CR211-MONI-27-MAR-B-4-A

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.5692	1904.8789	3.0080	487.1899	3.0740	0.1283
2	1.6389	2798.8543	4.4197	827.3623	5.2204	0.1400
3	1.7808	522.5372	0.8252	181.6118	1.1459	0.0933
4	2.5340	5.6857e4	89.7836	1.3943e4	87.9775	0.2350
5	2.9575	768.4970	1.2136	232.5329	1.4672	0.1117
6	3.0675	474.8930	0.7499	176.7144	1.1150	0.0900

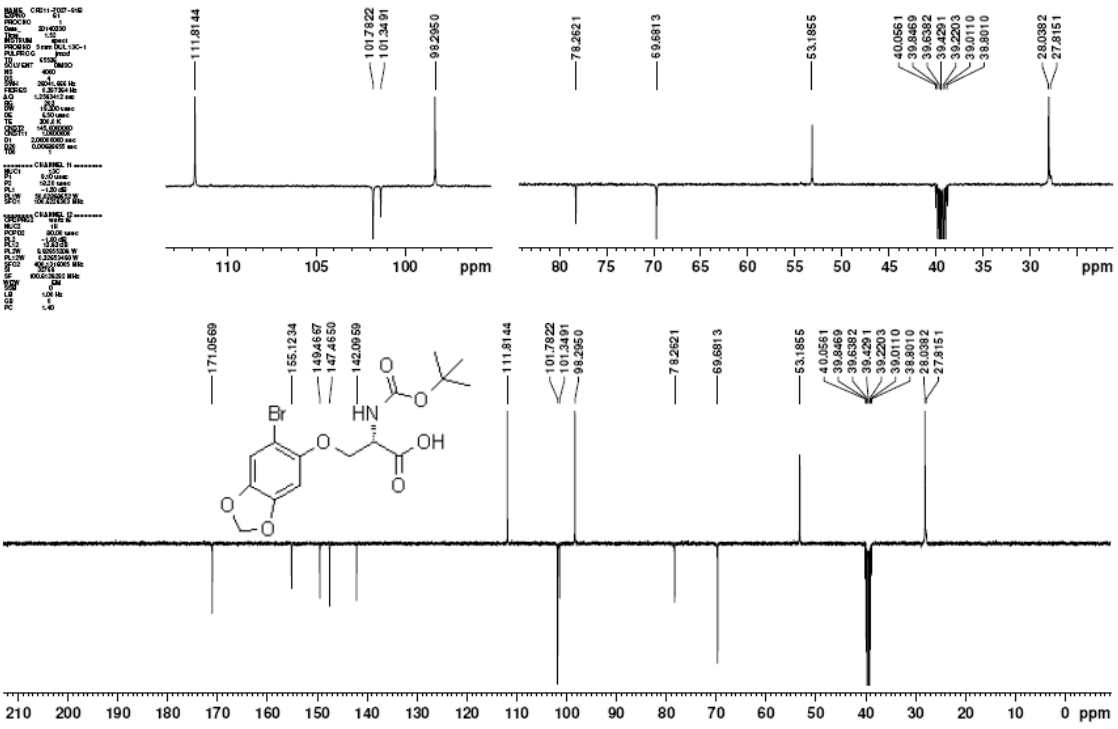
LCMS REACTION MONITORING SAMPLE COLUMN: Xbridge TCGLS/ARD/LCMS01/K03

Channel 1 at wavelength 220 nm, NH4OAc:ACN Analysed by
Channel 2 at wavelength 260 nm

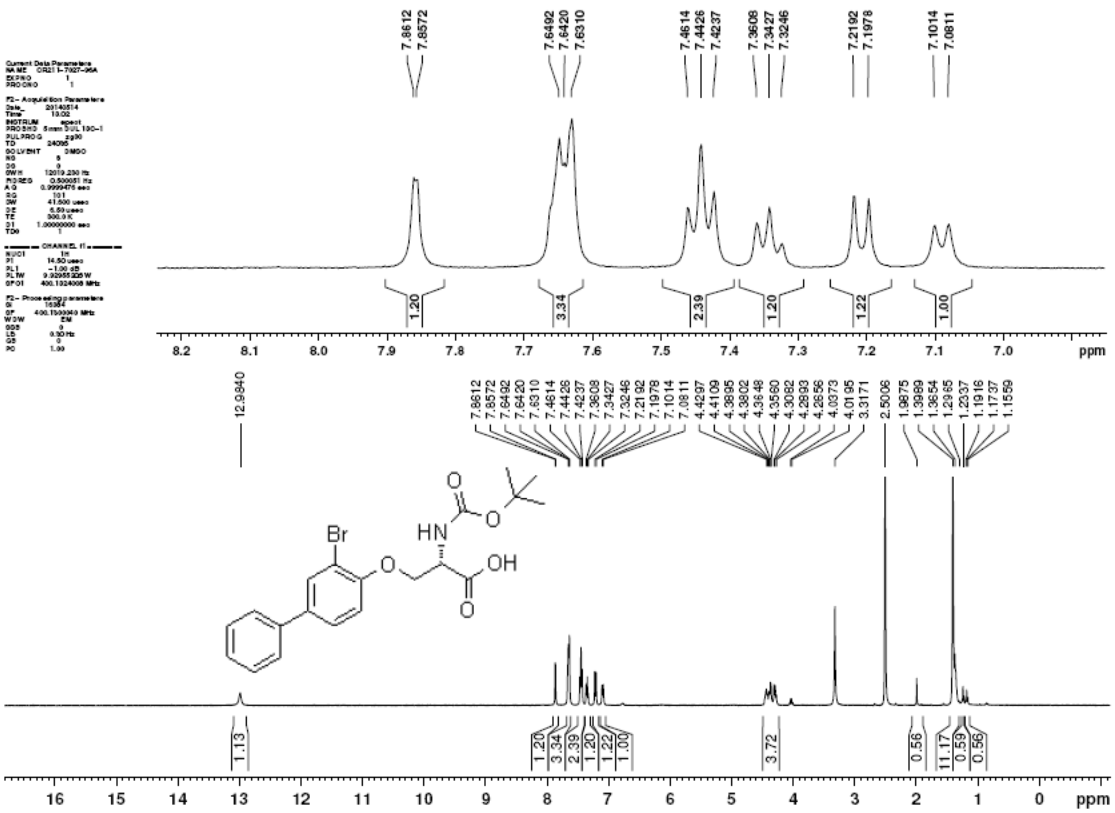
LCMS spectrum of compound 3h



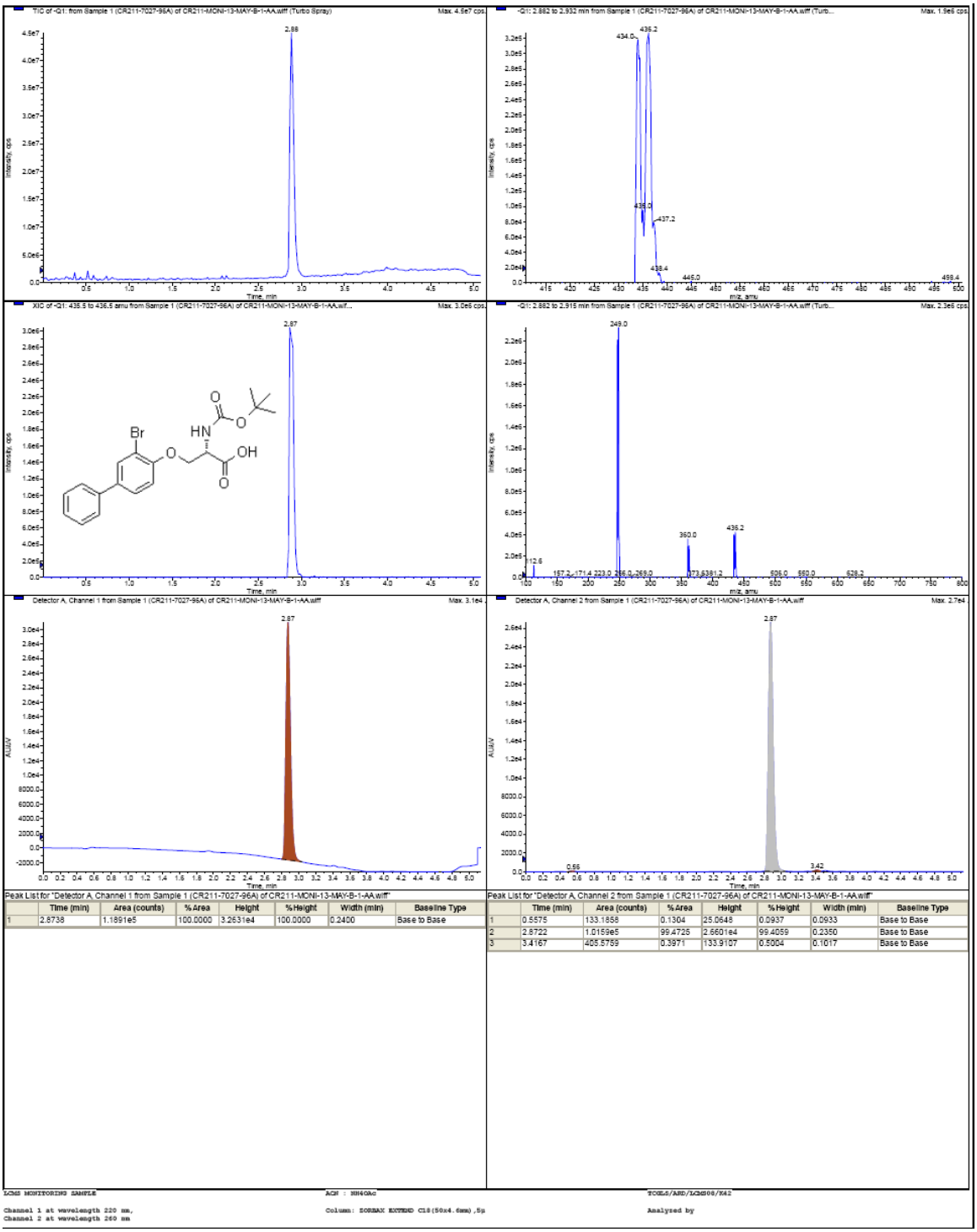
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3h



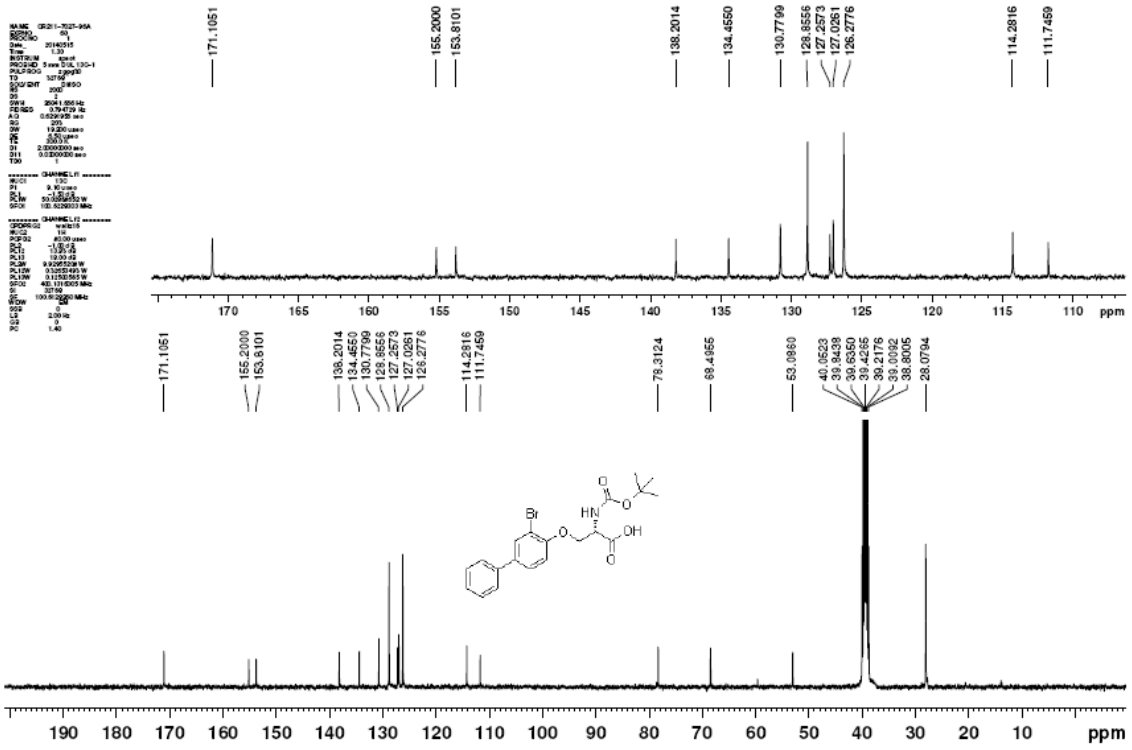
APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3h



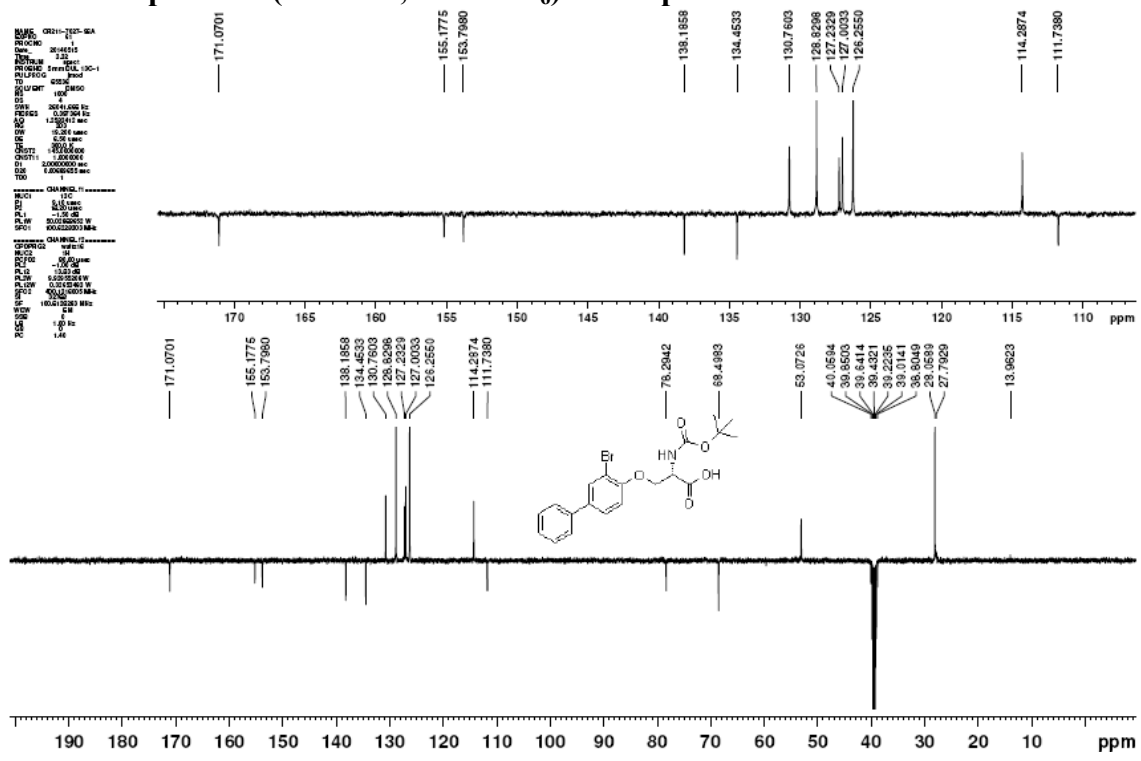
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3i



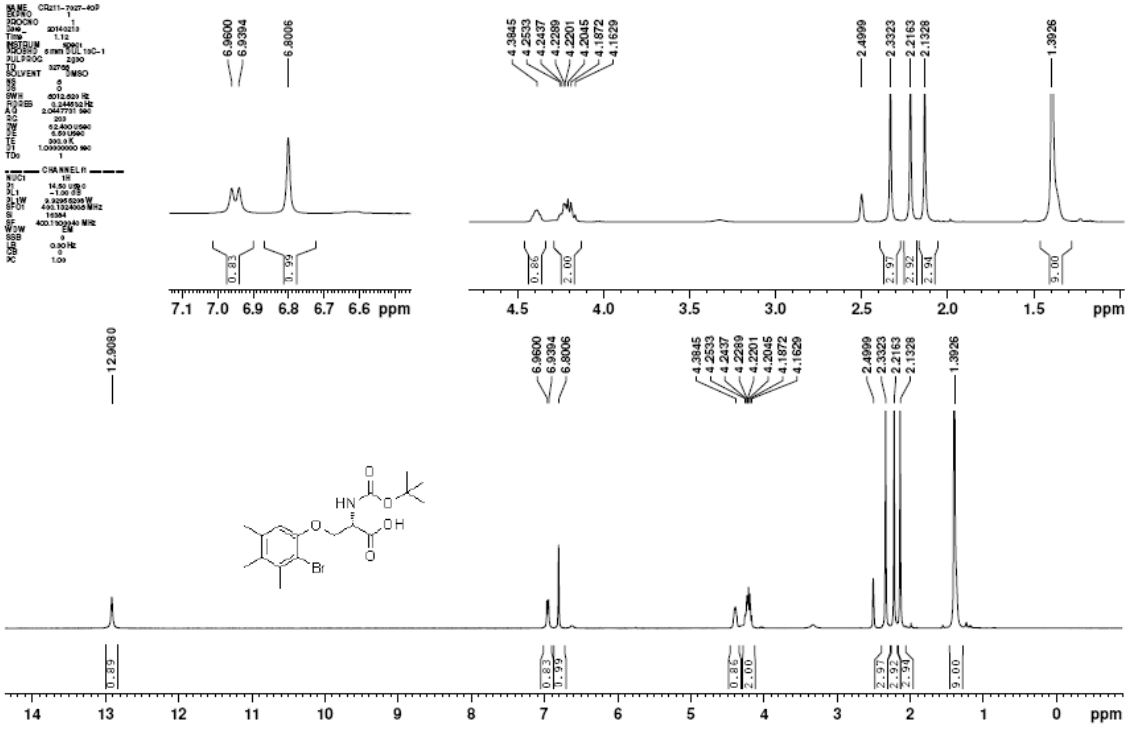
LCMS spectrum of compound 3i



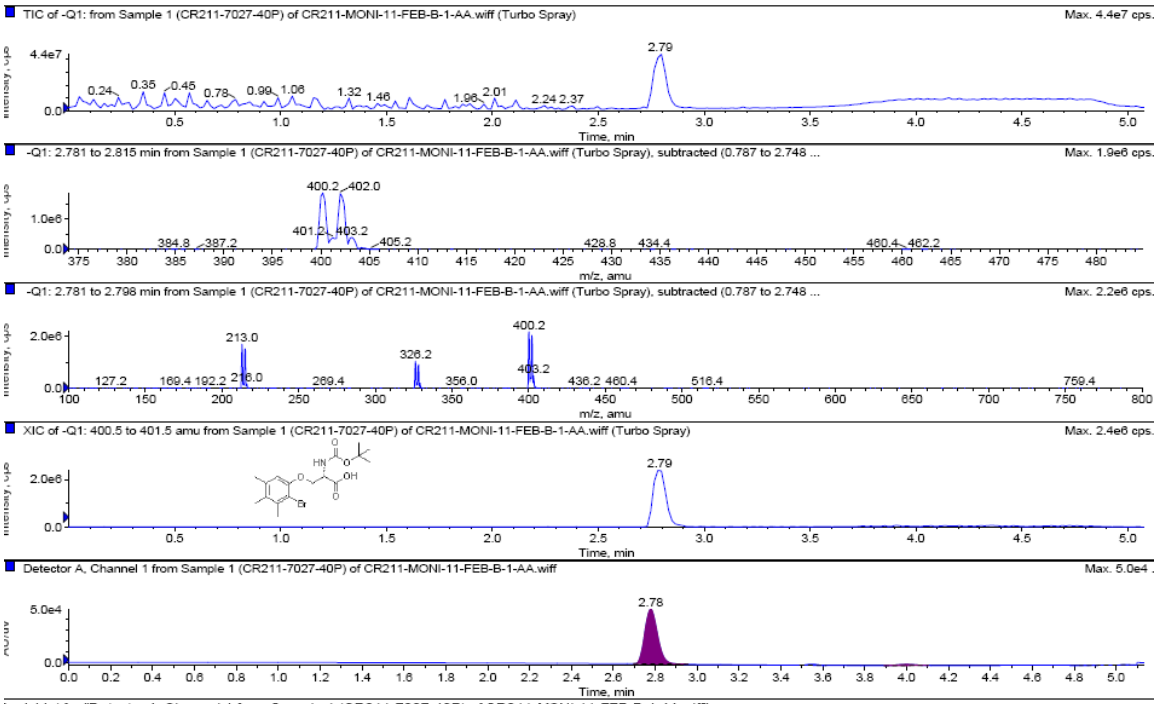
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3i



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3i



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3j

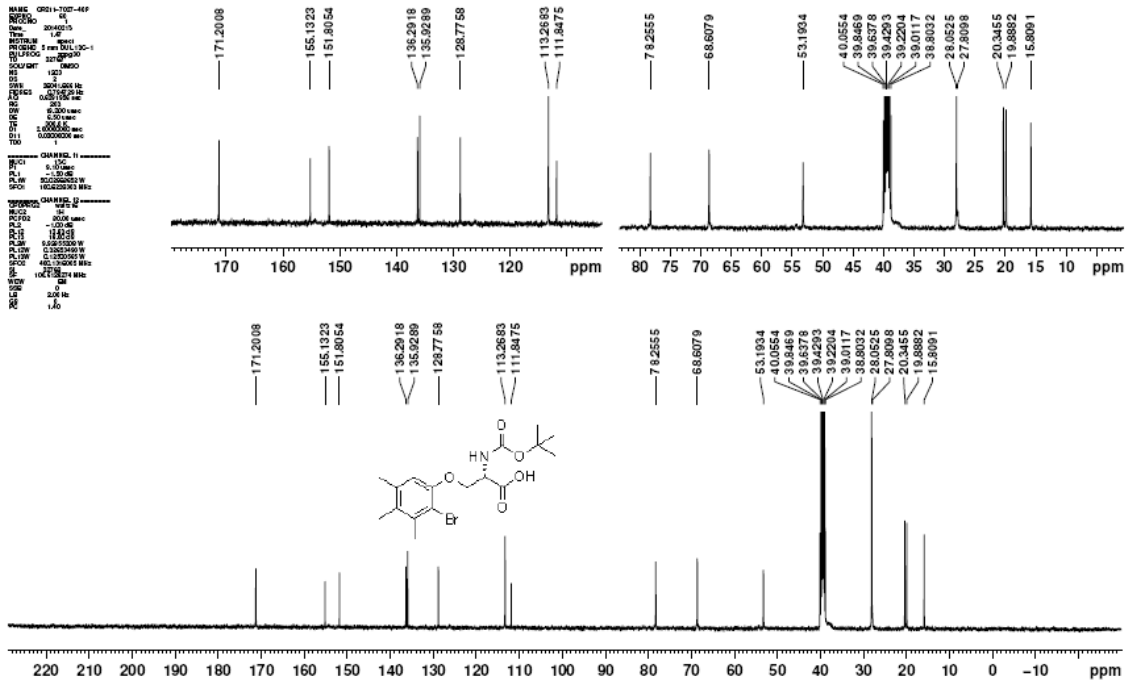


Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7027-40P) of CR211-MONI-11-FEB-B-1-AA.wiff"

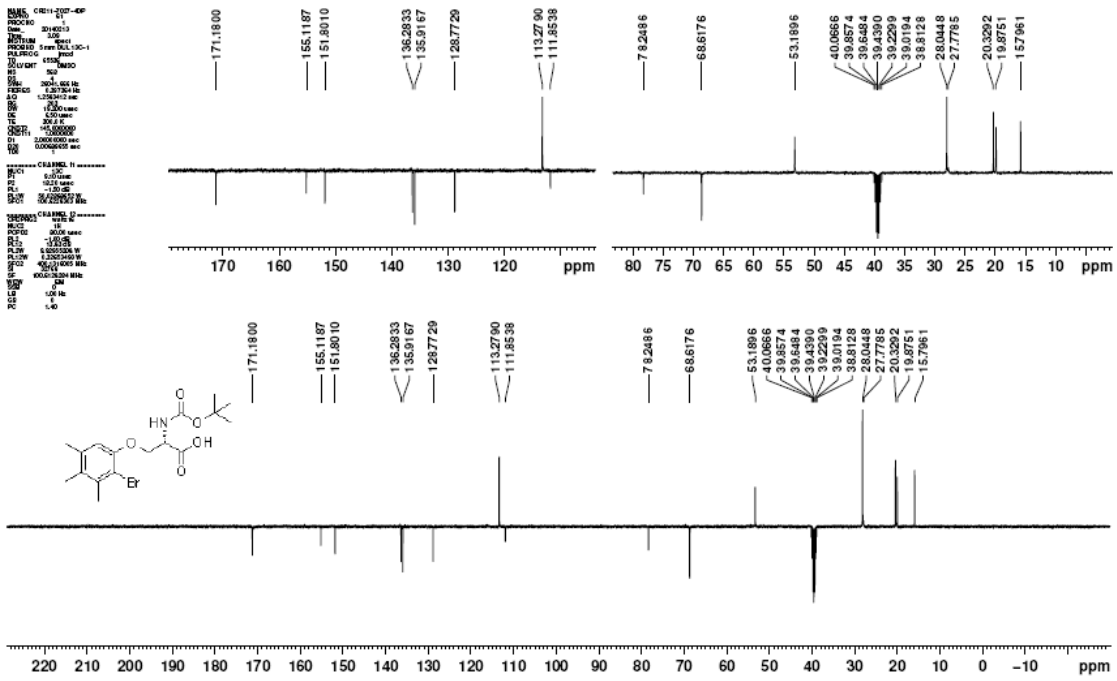
	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.7784	2.1387e5	94.9729	5.0898e4	96.1457	0.2600	Base to Base
2	3.5468	2941.3560	1.3062	867.7189	1.6391	0.1267	Base to Base
3	3.9997	7157.5663	3.1785	1172.6588	2.2152	0.2100	Base to Base
4	5.0650	1221.6333	0.5425	0.0000	0.0000	0.2433	Base to Base

CMS MONITORING SAMPLE
Column: ZORBAX
Analyzed by
NH4OAc:ACN
TCGLS/ARD/LCMS08/K42
Checked by :

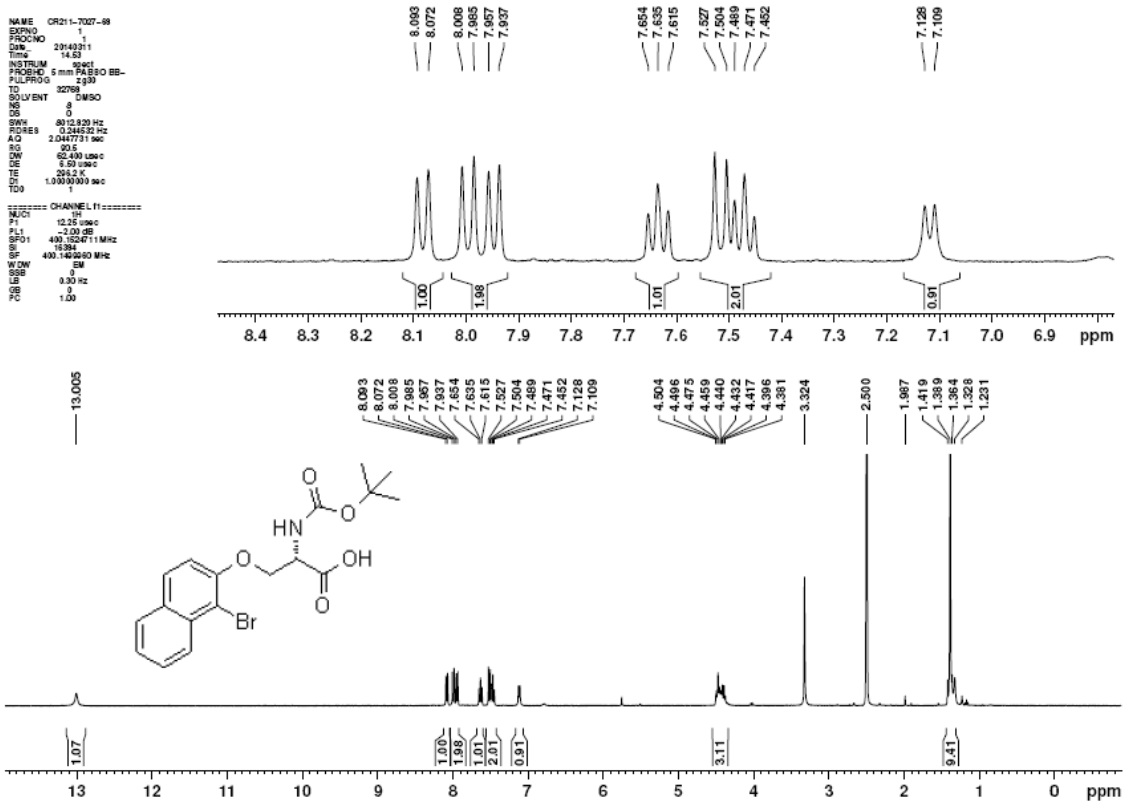
LCMS spectrum of compound 3j



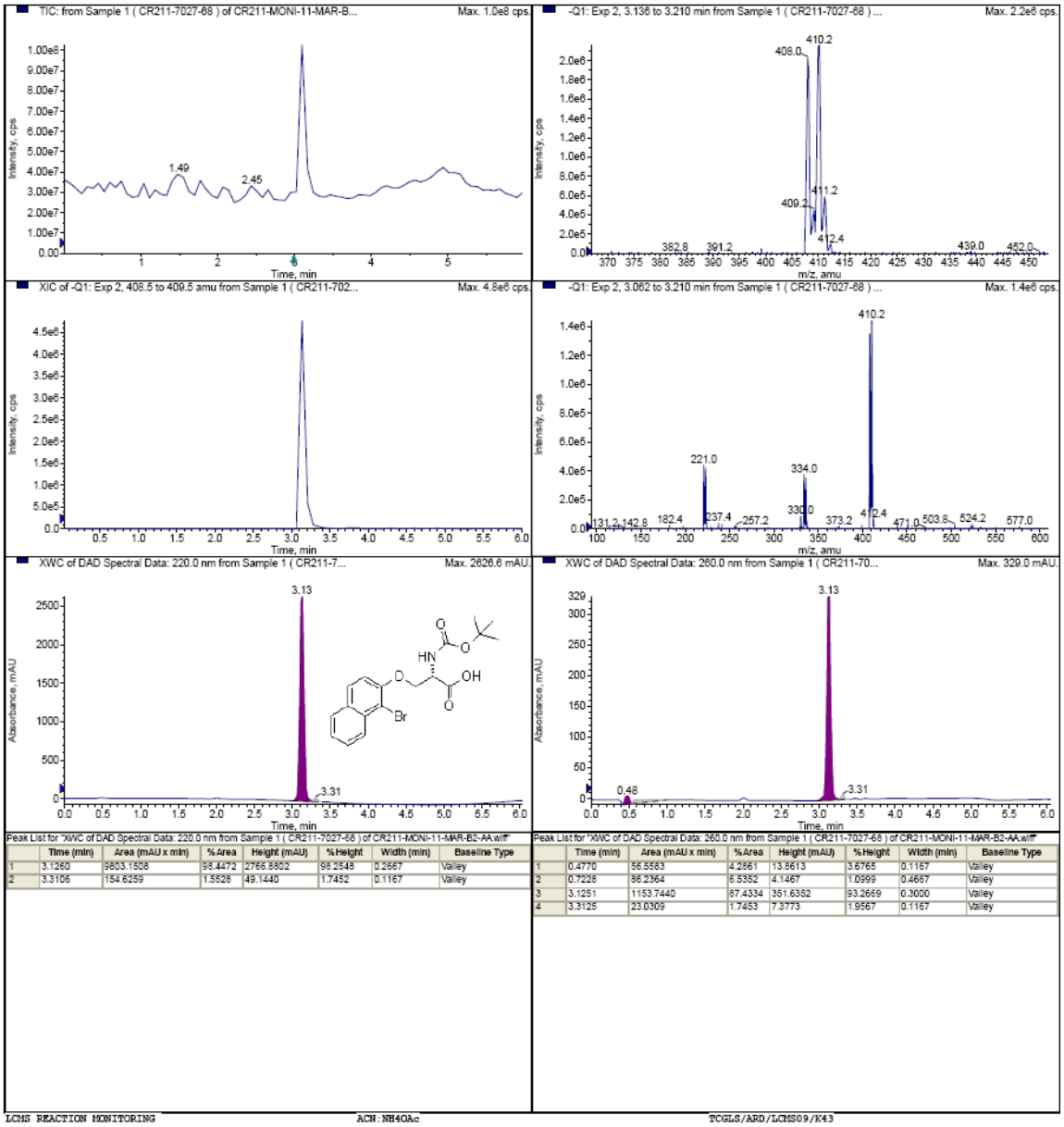
^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 3j



APT NMR spectrum (100MHz, DMSO-d_6) of compound 3j



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 3k



Peak List for "XWC of DAD Spectral Data: 220.0 nm from Sample 1 (CR211-7027-68) of CR211-MONI-11-MAR-B2-AA.wiff"

	Time (min)	Area (mAU x min)	% Area	Height (mAU)	% Height	Width (min)	Baseline Type
1	3.1260	9803.1508	98.4472	2766.8802	98.2548	0.2667	Valley
2	3.3106	154.6259	1.5528	49.1440	1.7452	0.1167	Valley

Peak List for "XWC of DAD Spectral Data: 260.0 nm from Sample 1 (CR211-7027-68) of CR211-MONI-11-MAR-B2-AA.wiff"

	Time (min)	Area (mAU x min)	% Area	Height (mAU)	% Height	Width (min)	Baseline Type
1	0.4770	56.5583	4.2861	13.8613	3.6765	0.1167	Valley
2	0.7228	86.2364	6.5352	4.1467	1.0999	0.4667	Valley
3	3.1251	1153.7440	87.4334	351.6352	93.2669	0.3000	Valley
4	3.3125	23.0309	1.7453	7.3773	1.9567	0.1167	Valley

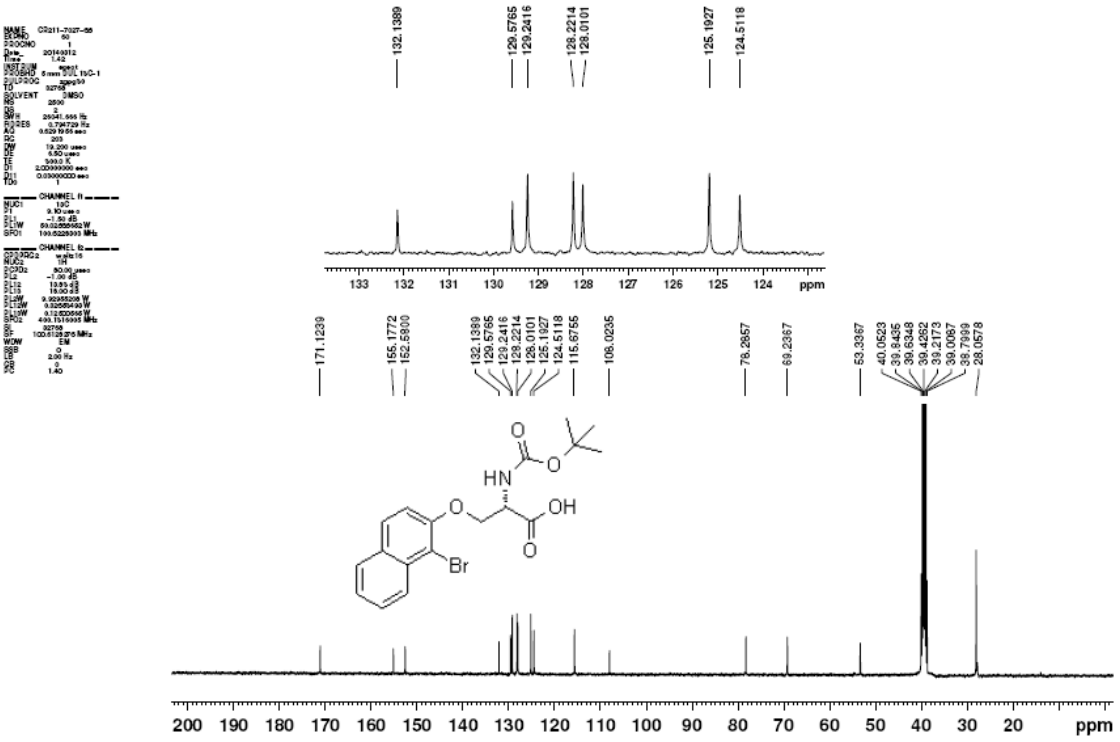
LCMS REACTION MONITORING ACN:NH4OAc TCGLS/ARD/LCMS09/K43

Channel 1 at wavelength 220 nm,
Channel 2 at wavelength 260 nm

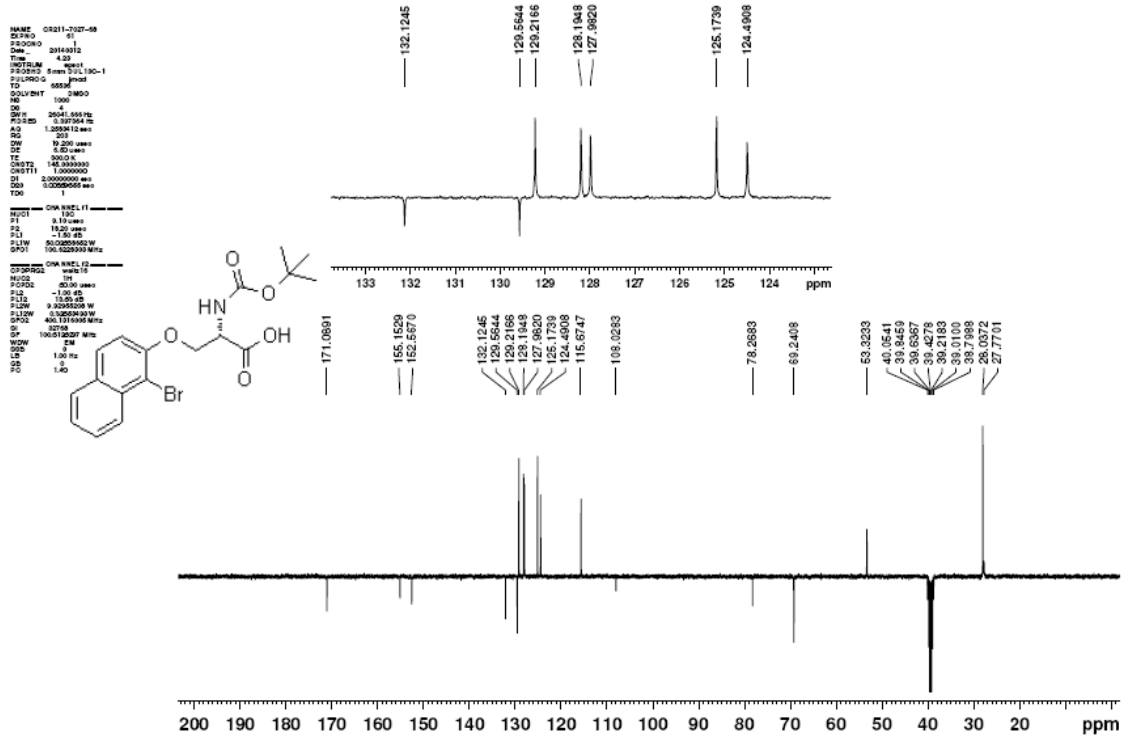
Column : SORBAX C18

Analyzed by

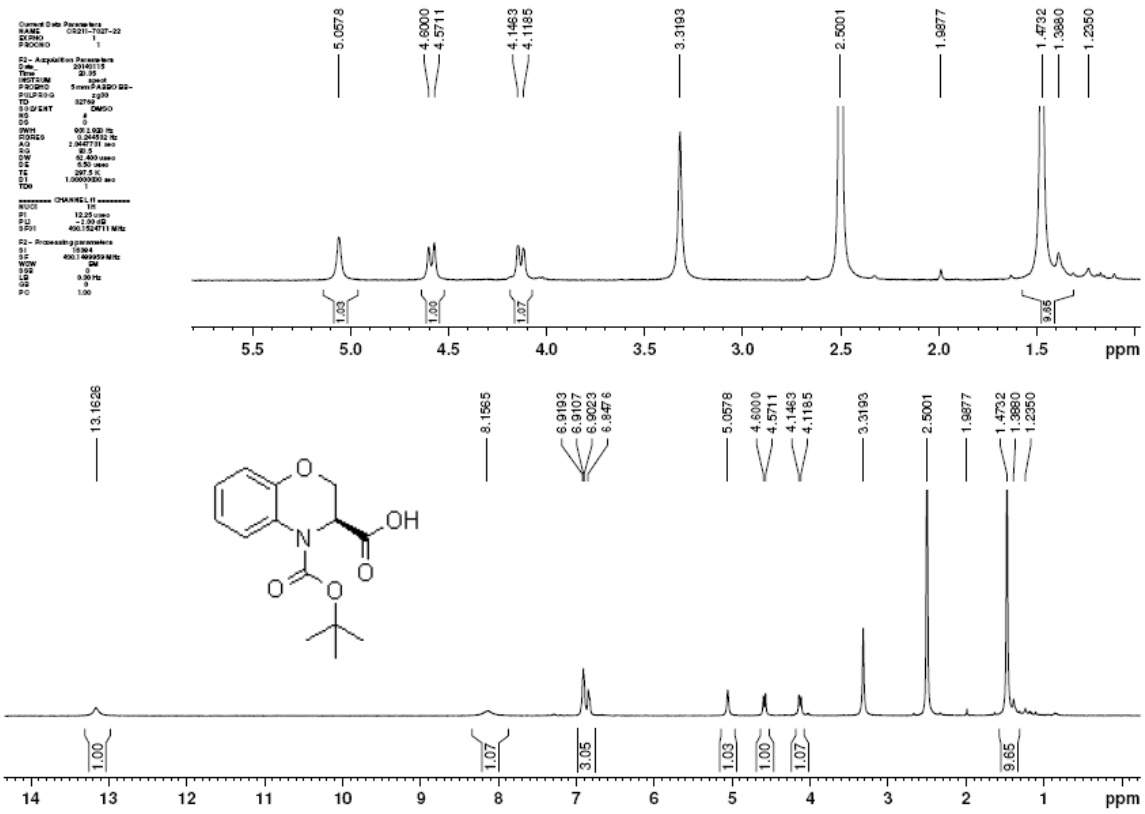
LCMS spectrum of compound 3k



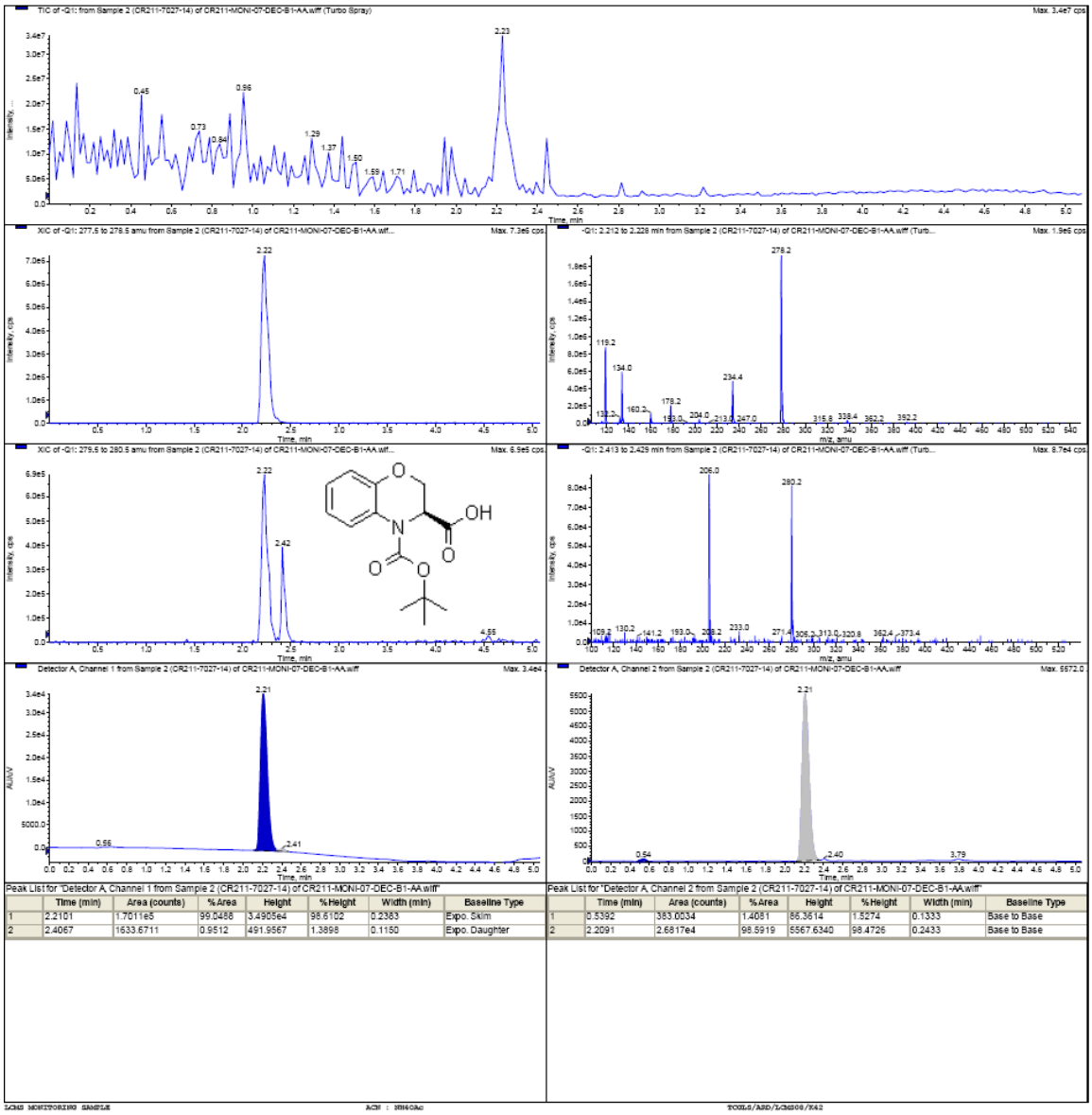
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 3k



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 3k



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4a



Peak List for "Detector A, Channel 1 from Sample 2 (CR211-7027-14) of CR211-MONI-07-DEC-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.2101	1.7011e5	99.0488	3.4905e4	98.6102	0.2383	Expo. Skim
2	2.4067	1633.6711	0.9512	491.9567	1.3898	0.1150	Expo. Daughter

Peak List for "Detector A, Channel 2 from Sample 2 (CR211-7027-14) of CR211-MONI-07-DEC-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5392	383.0034	1.4081	86.3614	1.5274	0.1333	Base to Base
2	2.2091	2.6817e4	98.5919	5567.6340	98.4726	0.2433	Base to Base

LCMS MONITORING SAMPLE ACN : NH4OAc TOOLS/ABD/LCMS06/K42

Channel 1 at wavelength 220 nm,
Channel 2 at wavelength 260 nm

Column: SORBAX EXTEND C18(50x4.6mm),5µ

Analysed by

LCMS spectrum of compound 4a

```
Analysis Method : C:\CHEM32\1\DATA\2014\JAN-14\140114D 2014-01-14 12-47-->
Last Changed    : Tue, 24. Dec. 2013, 00:26:54 pm

Acq. Method     : C:\CHEM32\1\DATA\2014\JAN-14\160114A 2014-01-16 09-36-
                  29\TCGLSKL.M

                                                  Ref: MVP/16.01.14/840
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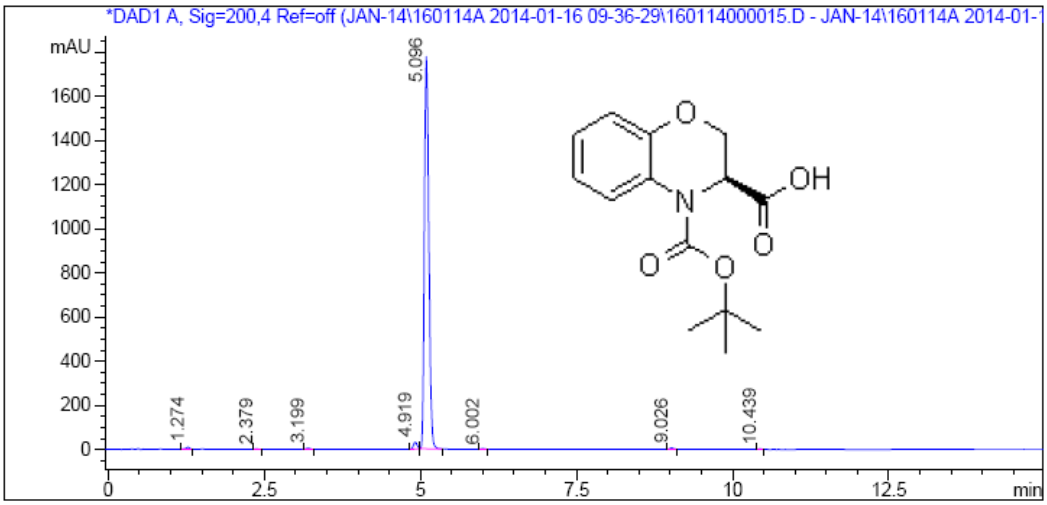


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================================================================================

Signal  1:DAD1 A, Sig=200,4 Ref=off
|Peak|   RT    |   Area    | Area % |
| #  |  [min]  |           |        |
|----|---------|-----------|--------|
|   1|     1.27|      43.92|    0.48|
|   2|     2.38|       8.95|    0.10|
|   3|     3.20|      25.19|    0.28|
|   4|     4.92|     126.88|    1.40|
|   5|     5.10|    8834.74|   97.17|
|   6|     6.00|      14.52|    0.16|
|   7|     9.03|      28.36|    0.31|
|   8|    10.44|       9.83|    0.11|
-----------------------------------
```
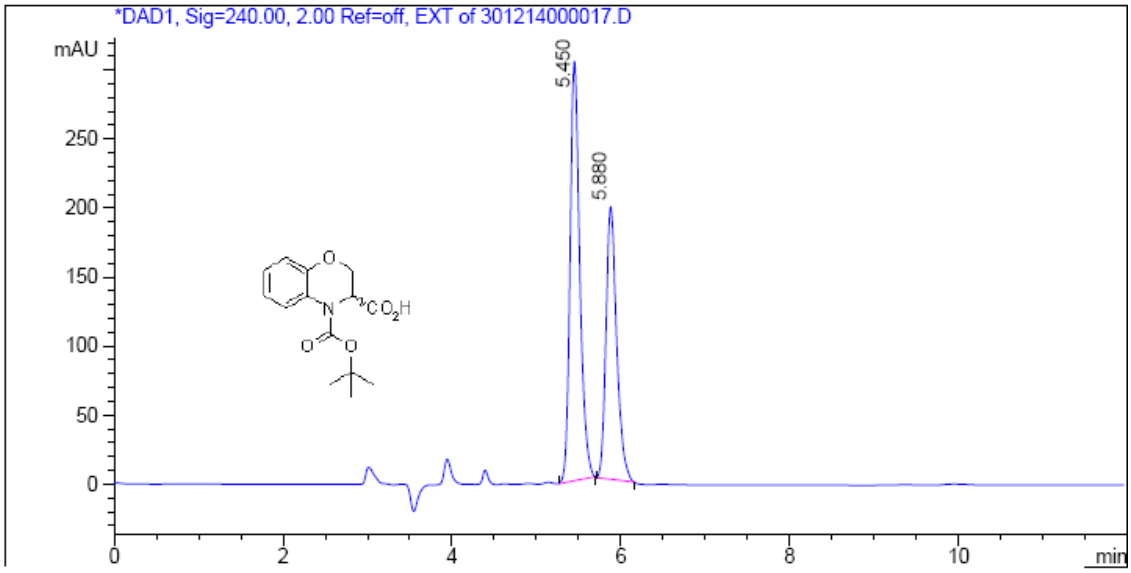

HPLC purity of compound 4a

```
                                                Location   :     Vial 77
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/30/2014   4:45:45 PM      Inj. Vol.  :        2 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\301214 2014-12-30 09-49-44->
Analysis Method  : C:\CHEM32\1\METHODS\A-1.M
Last Changed     : Tue, 30. Dec. 2014, 04:46:47 pm
                   (modified after loading)
Samole ID CR211-7027-84(D+L)

Column Name : Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solubility:MEOH                                                        ->
                                                Ref :KD/30.12.14/1578
```

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```

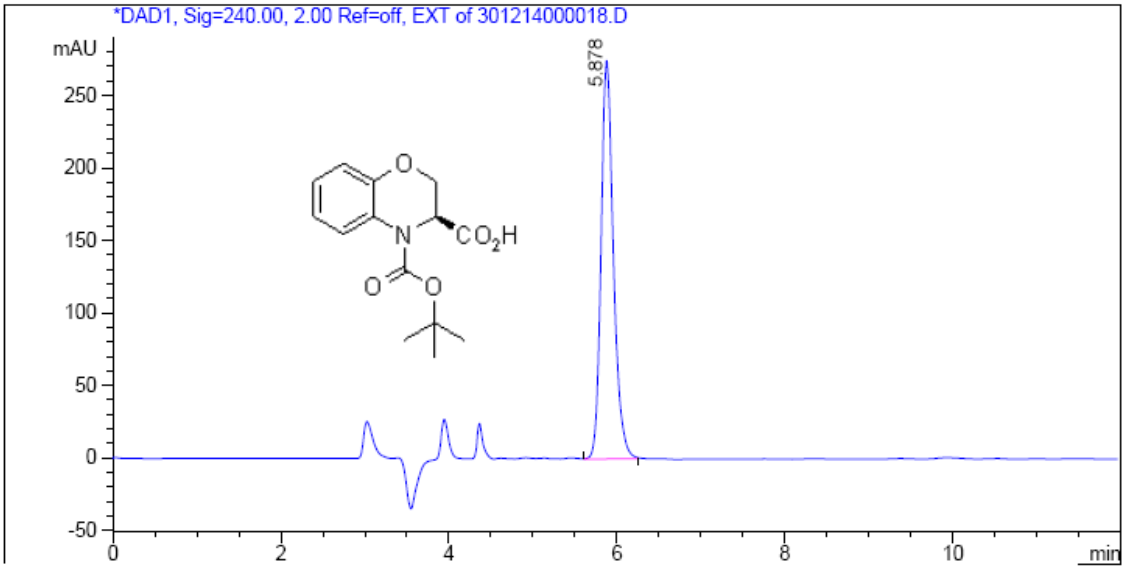
Signal 1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

Peak #	RT [min]	Area	Area %
1	5.45	2421.20	58.26
2	5.88	1734.52	41.74

Chiral HPLC of a mixture of D- and L-isomer of compound 4a prepared by external mixing (not racemic mixture)

```
                                                  Location   :      Vial 78
Acq Operator     : KONDABABU                      Inj. No.   :           1
Injection Date   : 12/30/2014   4:59:44 PM        Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\301214 2014-12-30 09-49-44->
Analysis Method  : C:\CHEM32\1\METHODS\A-1.M
Last Changed     : Tue, 30. Dec. 2014, 04:46:47 pm
                   (modified after loading)
Samole ID CR211-7027-84L

Column Name : Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solubility:MEOH                                                          ->
                                                  Ref :KD/30.12.14/1579
```




```
================================================================================


Signal  1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      5.88|   2817.12|    100.00|
---------------------------------------
```

Chiral HPLC of L-isomer of compound 4a

```
                                                Location   :     Vial 79
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/30/2014   4:31:43 PM      Inj. Vol.  :        2 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\301214 2014-12-30 09-49-44->
Analysis Method  : C:\CHEM32\1\METHODS\A-1.M
Last Changed     : Tue, 30. Dec. 2014, 04:46:47 pm
                   (modified after loading)
Samole ID CR211-7027-84D

Column Name : Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phase:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solubility:MEOH                                                        ->
                                                Ref :KD/30.12.14/1580
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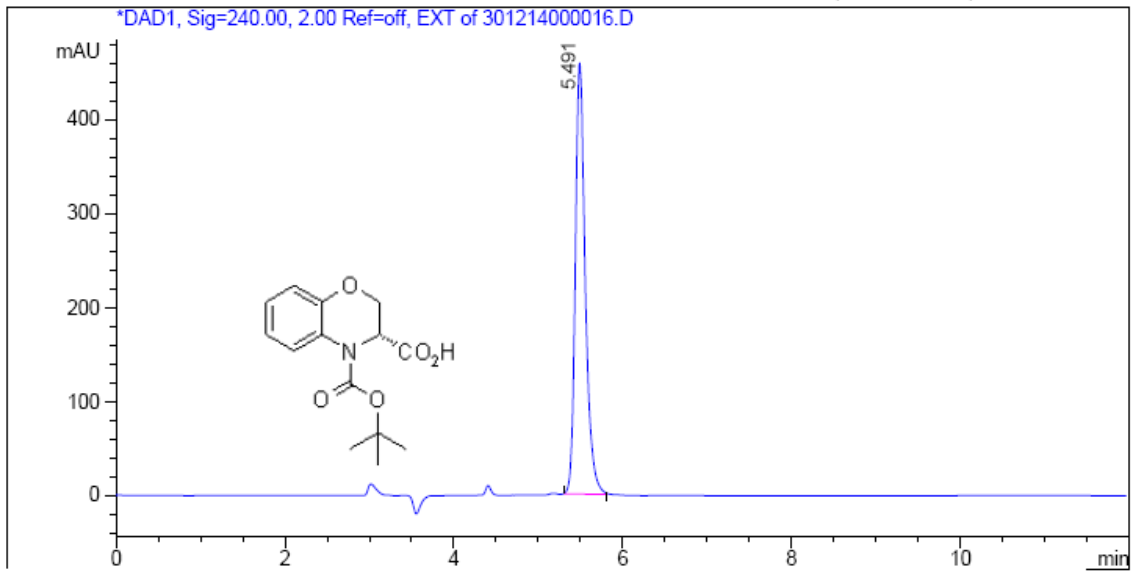


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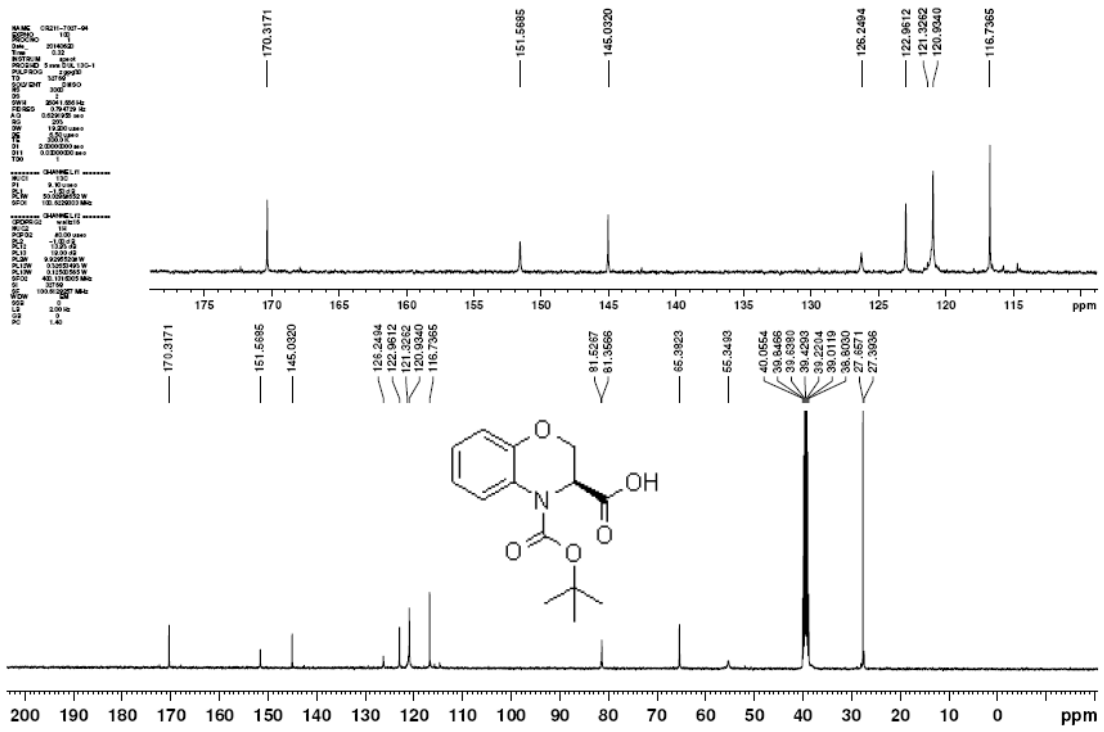
==========================================================================

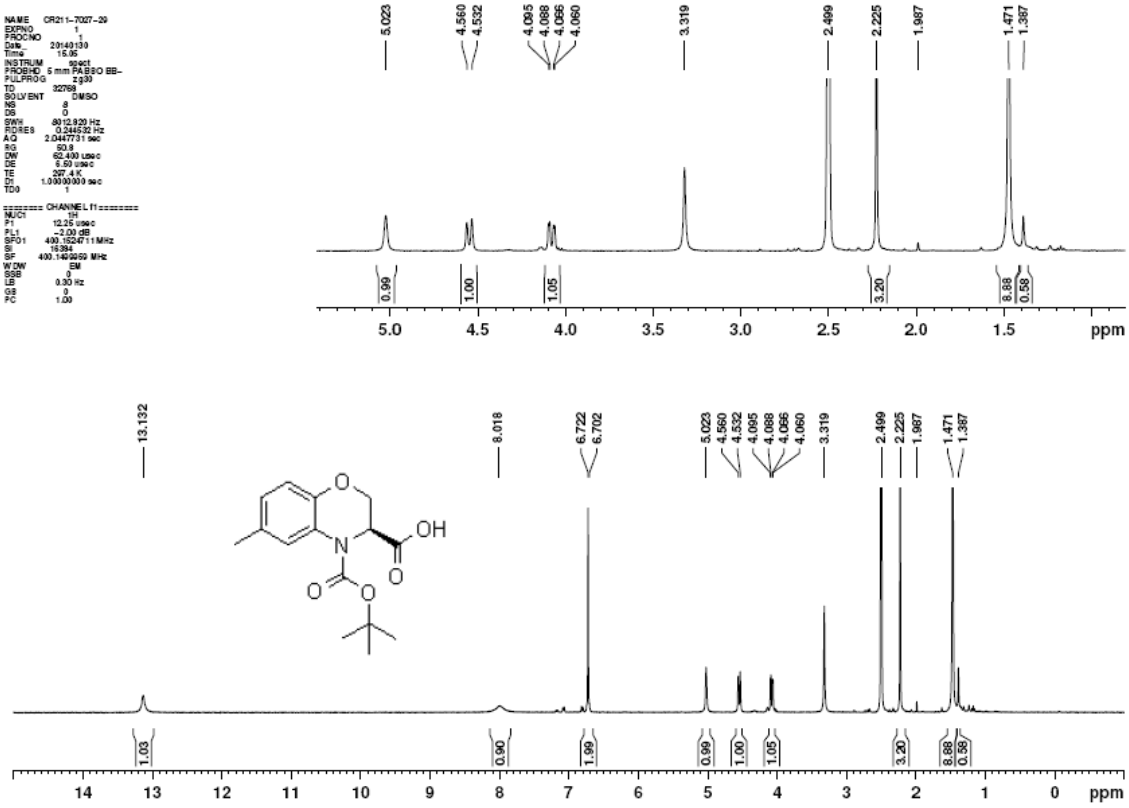
Signal  1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      5.49|   3759.34|    100.00|
---------------------------------------
```

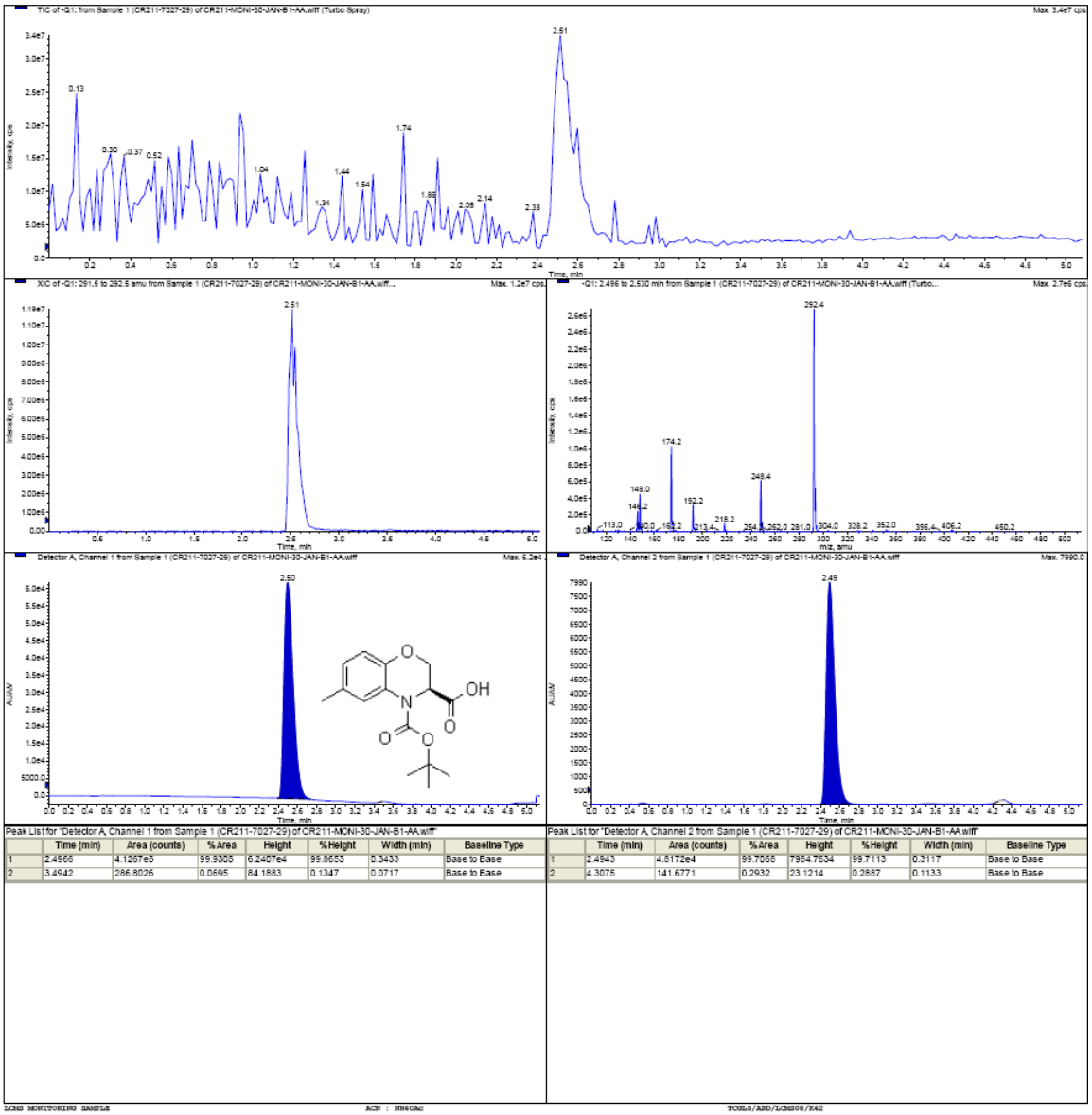
Chiral HPLC of D-isomer of compound 4a



^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 4a



^{1}H NMR spectrum (400MHz, DMSO-d$_6$) of compound 4b



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7027-29) of CR211-MONI-30-JAN-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.4966	4.1267e5	99.9305	6.2407e4	99.8653	0.3433	Base to Base
2	3.4942	286.8026	0.0695	84.1883	0.1347	0.0717	Base to Base

Peak List for "Detector A, Channel 2 from Sample 1 (CR211-7027-29) of CR211-MONI-30-JAN-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.4943	4.8172e4	99.7068	7984.7634	99.7113	0.3117	Base to Base
2	4.3075	141.6771	0.2932	23.1214	0.2887	0.1133	Base to Base

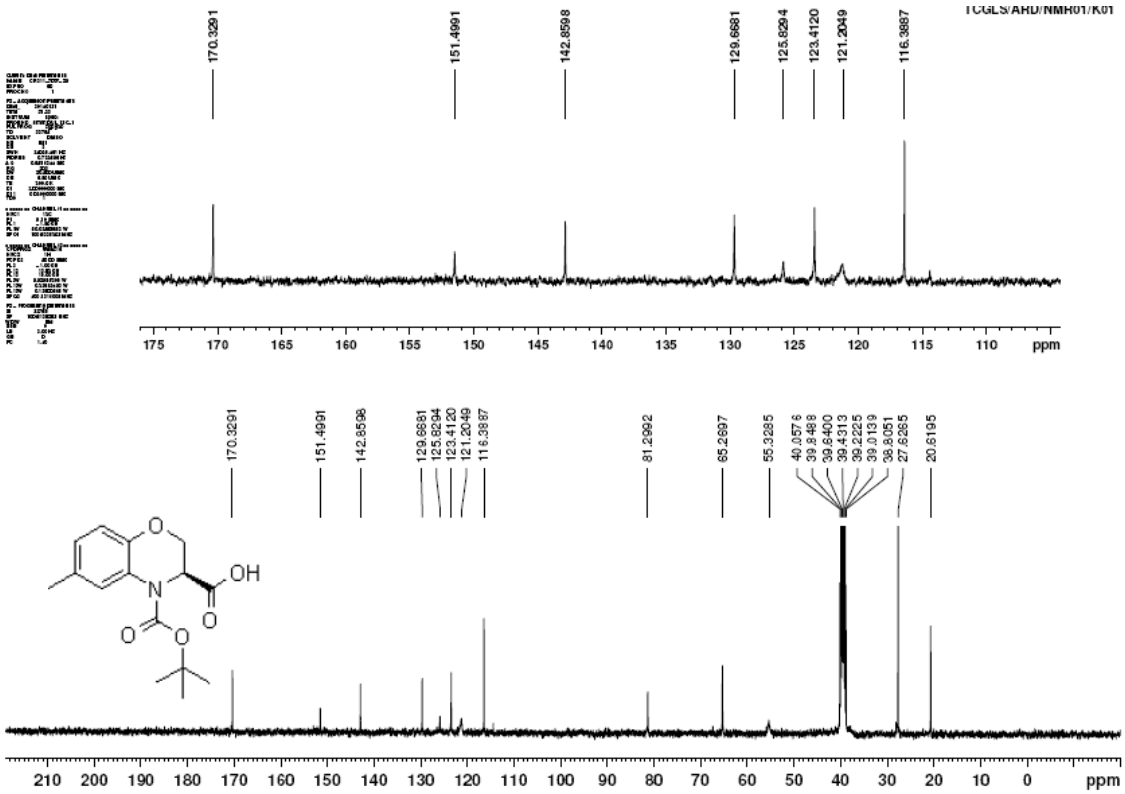
LCMS MONITORING SAMPLE ACN : NH4OAc TOOLS/ASD/LCMS08/K42

Channel 1 at wavelength 220 nm,
Channel 2 at wavelength 260 nm

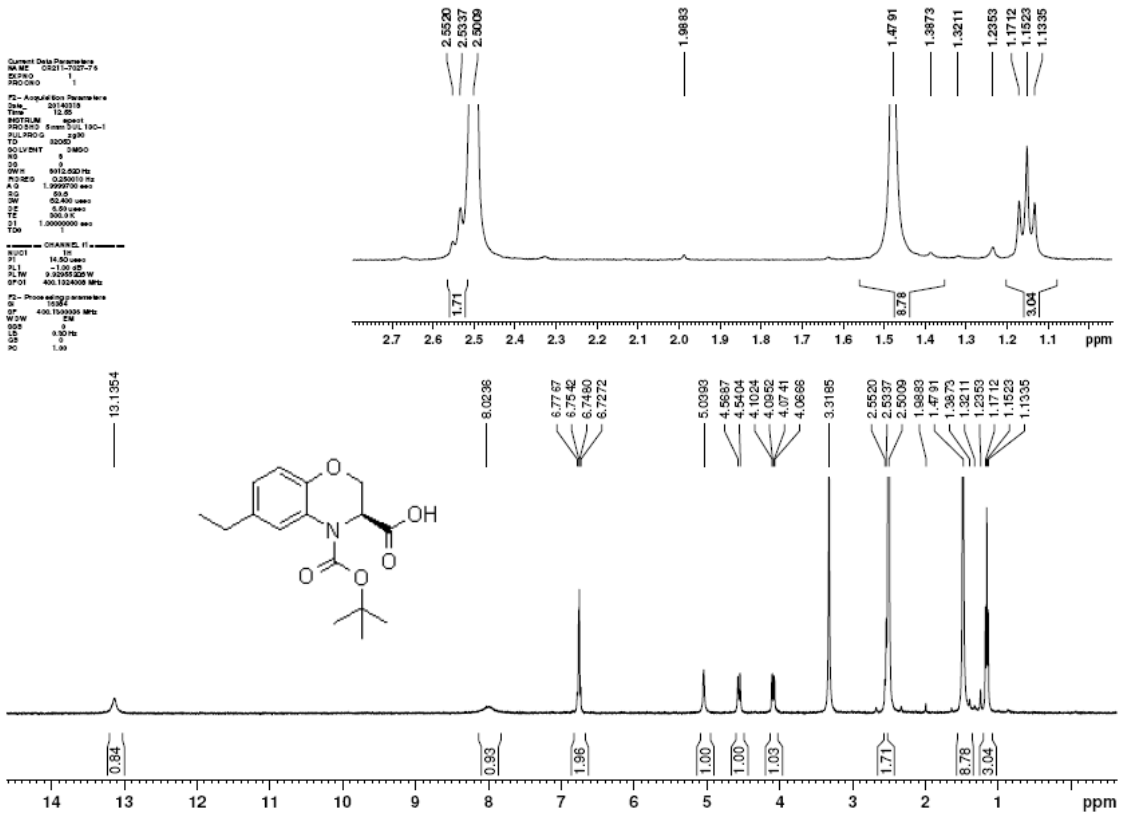
Column: ZORBAX EXTEND C18(50x4.6mm),5µ

Analysed by

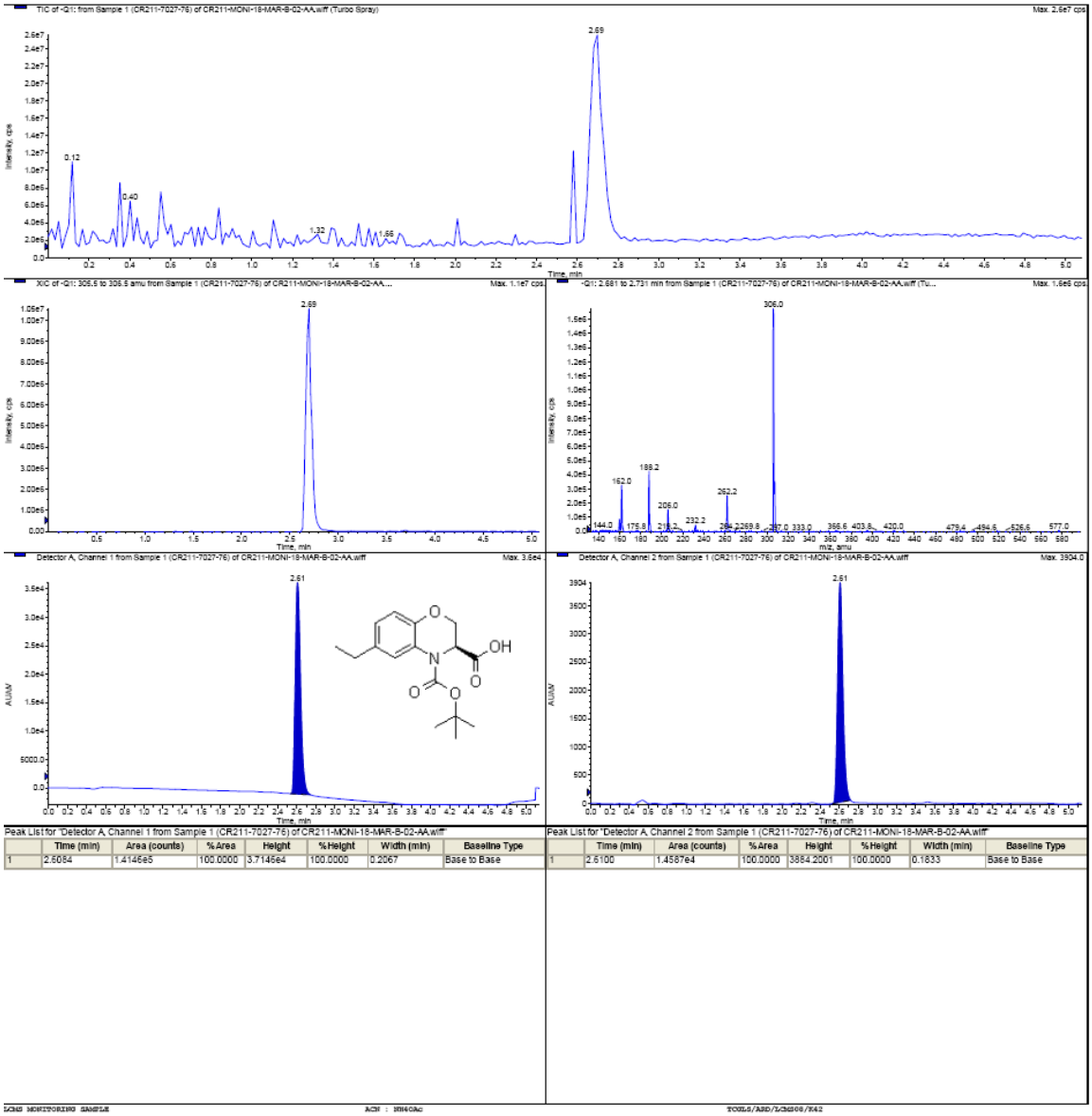
LCMS spectrum of compound 4b



^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 4b



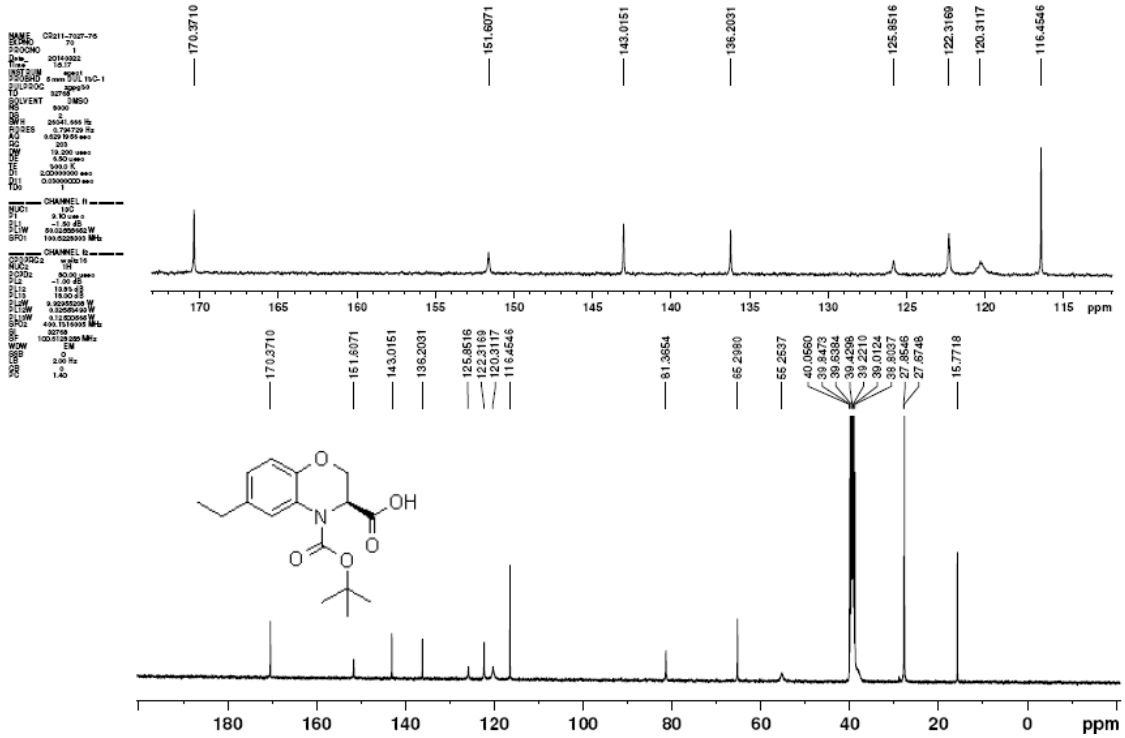
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4c



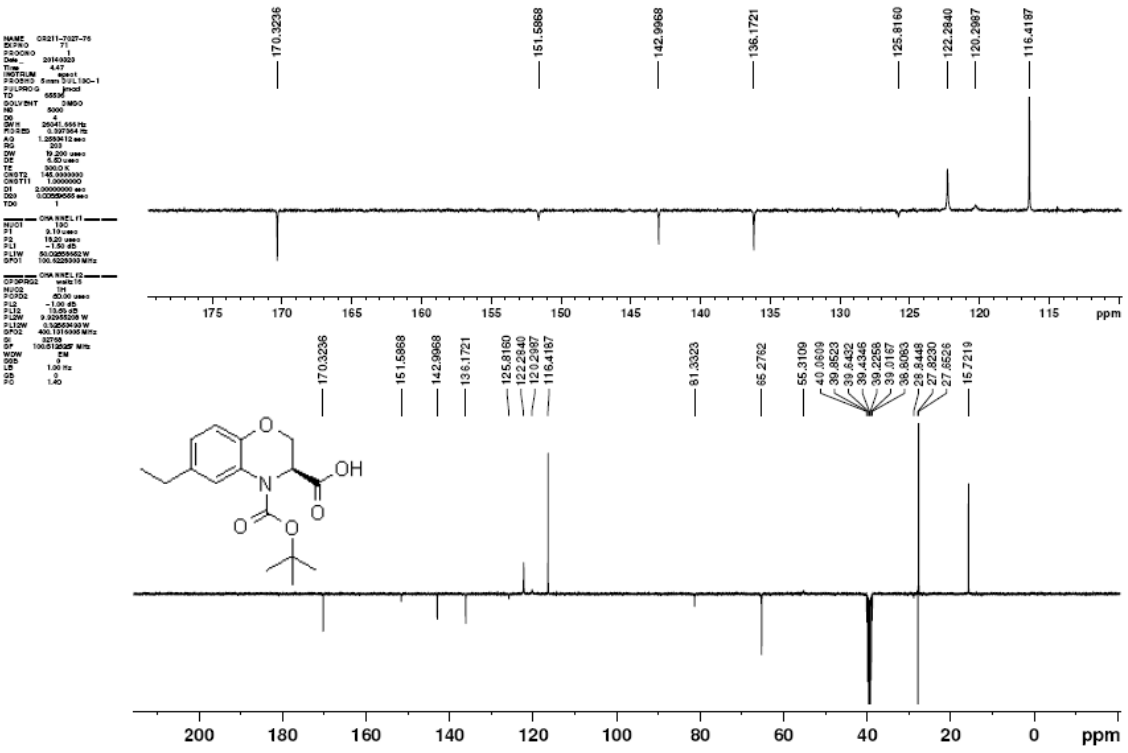
	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.6084	1.4146e5	100.0000	3.7146e4	100.0000	0.2067	Base to Base

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.6100	1.4587e4	100.0000	3884.2001	100.0000	0.1633	Base to Base

LCMS spectrum of compound 4c



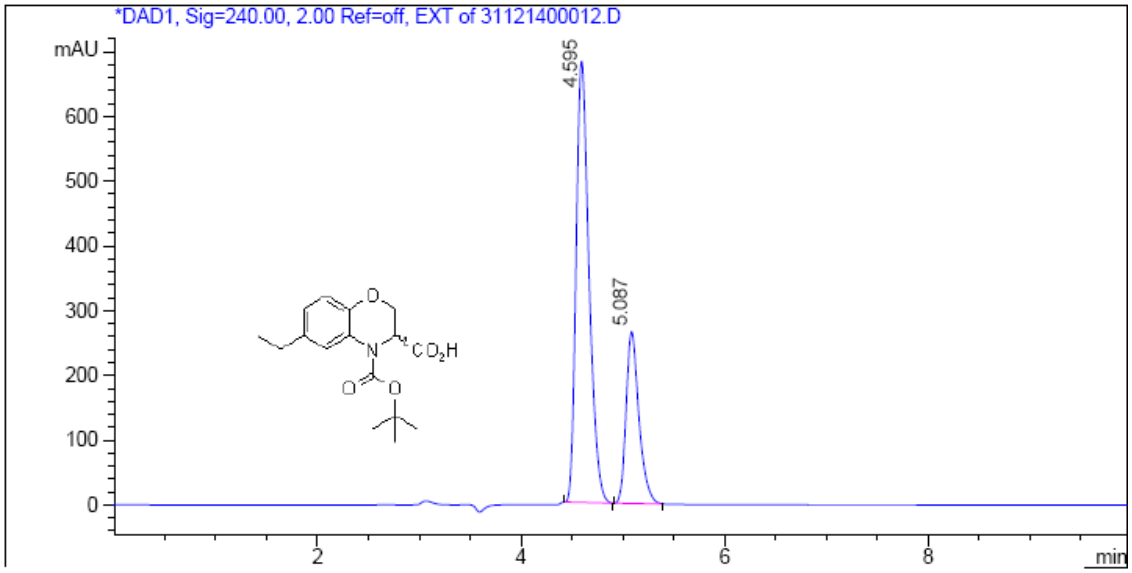
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 4c



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 4c

```
                                                Location   :     Vial 16
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/31/2014   2:49:30 PM      Inj. Vol.  :        2 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
Last Changed     : Wed, 31. Dec. 2014, 11:42:13 am
                   (modified after loading)
Sample ID:CR211-8259-96(D+L)

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phaes:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                          ->
                                                Ref :KD/31.12.14/1663
```




```
================================================================================


Signal  1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      4.60|   5991.55|     72.08|
|   2|      5.09|   2320.53|     27.92|
---------------------------------------
```

Chiral HPLC of a mixture of D- and L-isomer of compound 4a prepared by external mixing (not racemic mixture)

```
                                                Location   :     Vial 17
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/31/2014   2:27:12 PM      Inj. Vol.  :        2 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
Last Changed     : Wed, 31. Dec. 2014, 11:42:13 am
                   (modified after loading)
Sample ID:CR211-8259-96L

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phaes:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                          ->
                                                Ref :KD/31.12.14/1664
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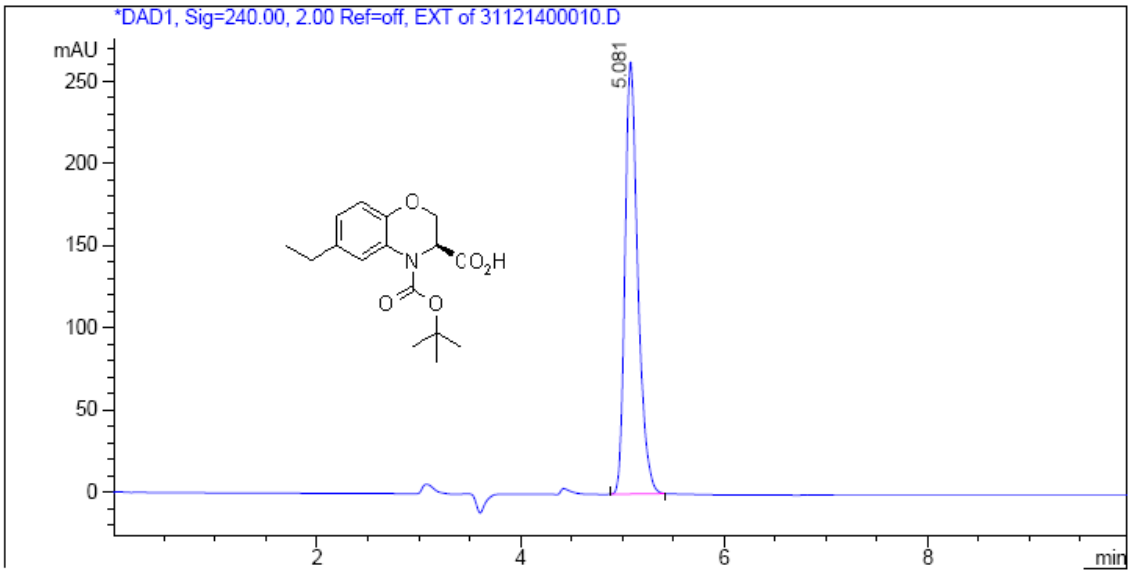


```
================================================================================


Signal  1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

|Peak|   RT      |   Area    |  Area %  |
| #  |  [min]    |-----------|----------|
|----|-----------|           |          |
|   1|      5.08|   2311.14|    100.00|
```

Chiral HPLC of L-isomer of compound 4c

```
                                                Location   :     Vial 18
Acq Operator     : KONDABABU                    Inj. No.   :          1
Injection Date   : 12/31/2014   2:38:21 PM      Inj. Vol.  :        2 µl
Acq. Method      : C:\Chem32\1\DATA\DEC-2014\311214 2014-12-31 10-01-35->
Analysis Method  : C:\CHEM32\1\METHODS\B2.M
Last Changed     : Wed, 31. Dec. 2014, 11:42:13 am
                   (modified after loading)
Sample ID:CR211-8259-96D

Column Name:Chiralpak IA(250x4.6mm)5µ
ARD/K/7804
Mobile Phaes:Hexane/EtOH/TFA:90/10/0.1
Flow Rate:1.0 ml/min
Solublity:MeOH                                                          ->
                                                Ref :KD/31.12.14/1665
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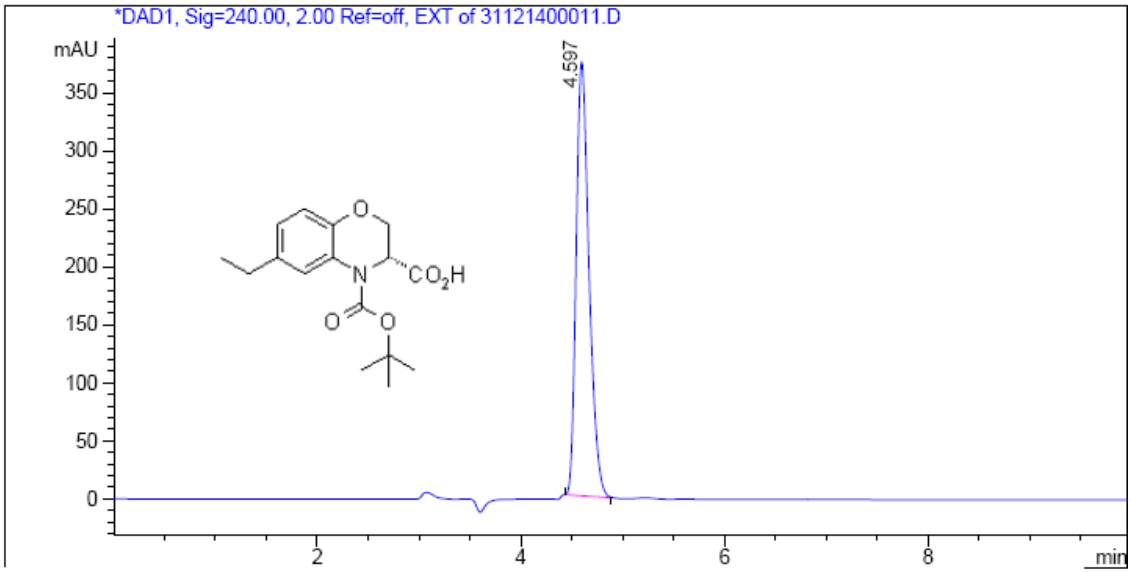
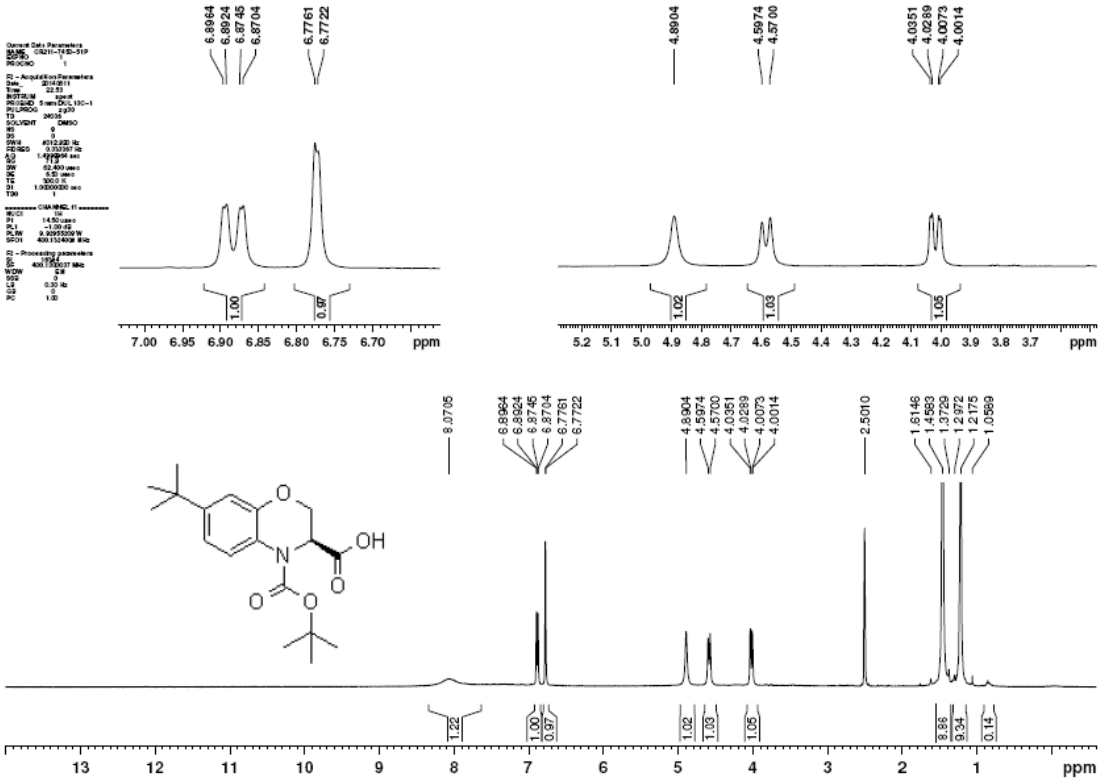



```
================================================================================

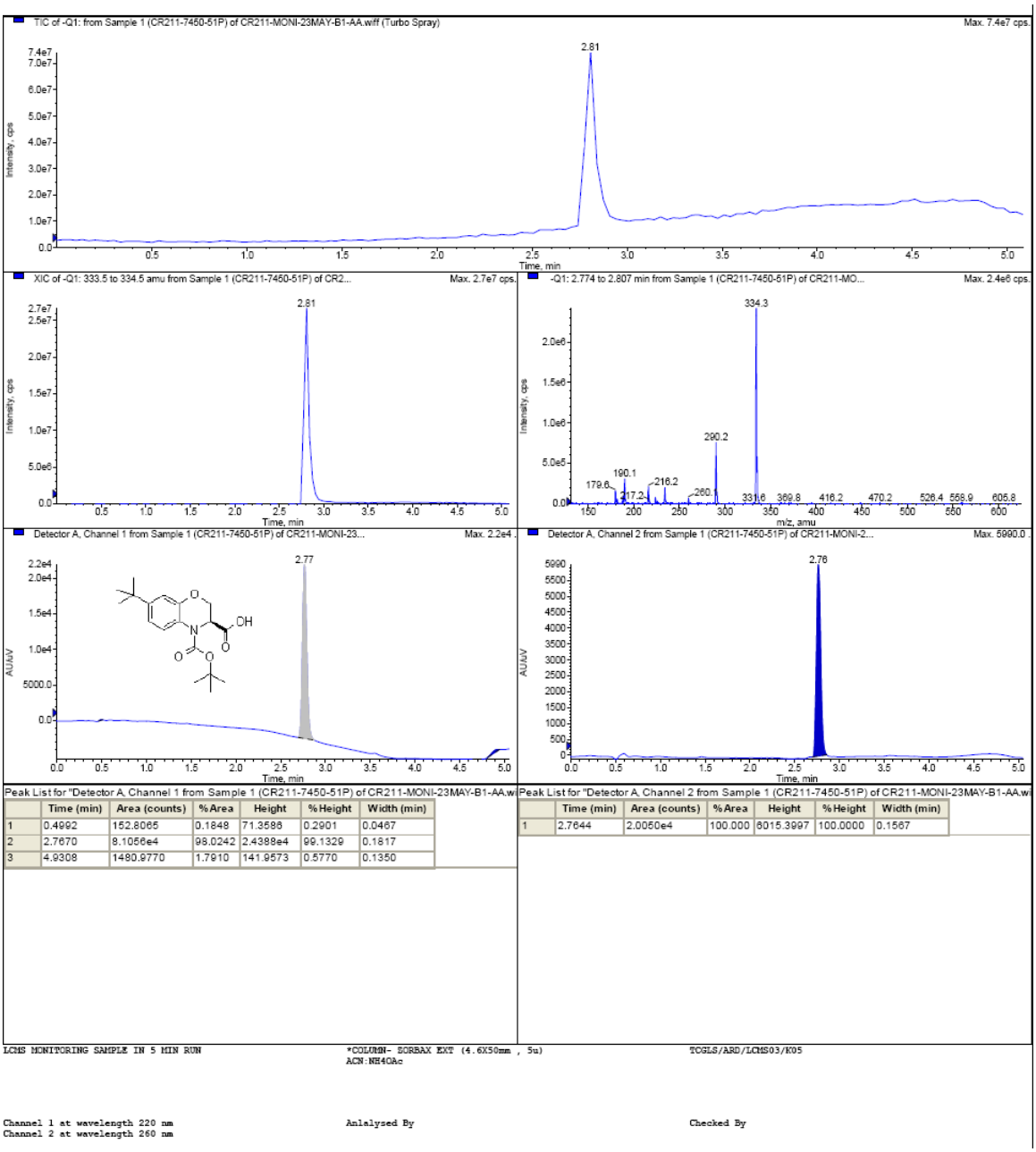

Signal  1: DAD1, Sig=240.00, 2.00 Ref=off, EXT

|Peak|   RT     |   Area    |  Area %   |
| #  |  [min]   |-----------|-----------|
|----|----------|           |           |
|   1|      4.60|   3280.72|    100.00|
---------------------------------------
```

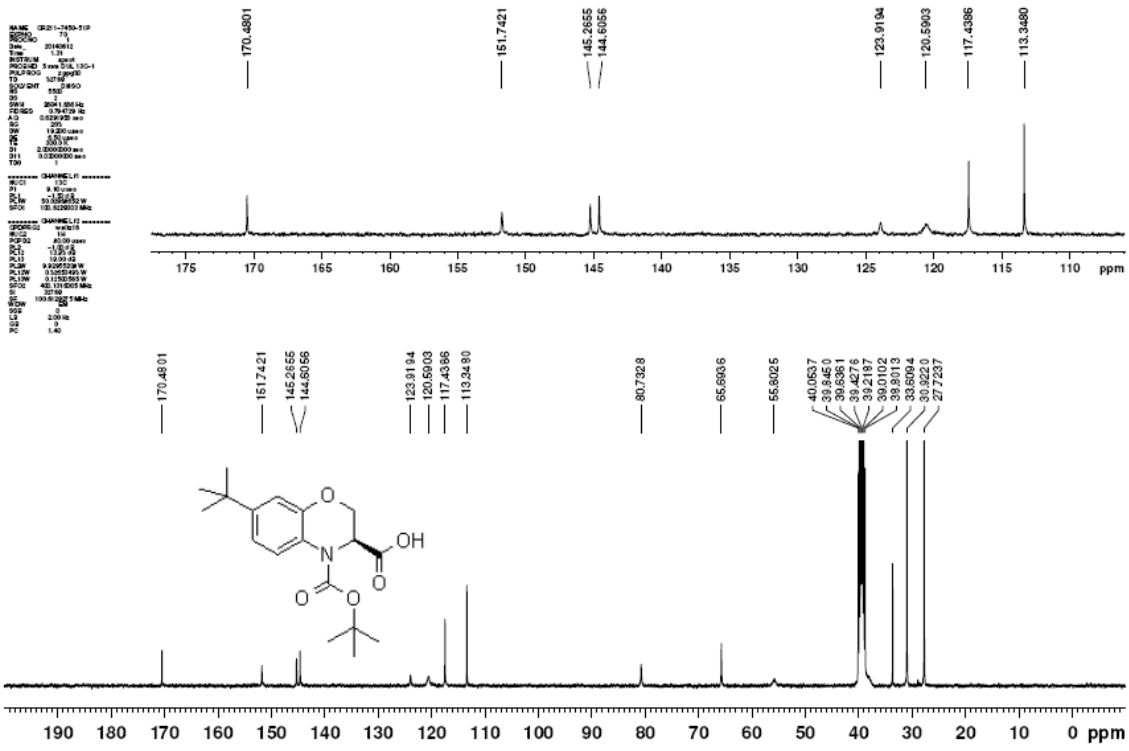
Chiral HPLC of D-isomer of compound 4c



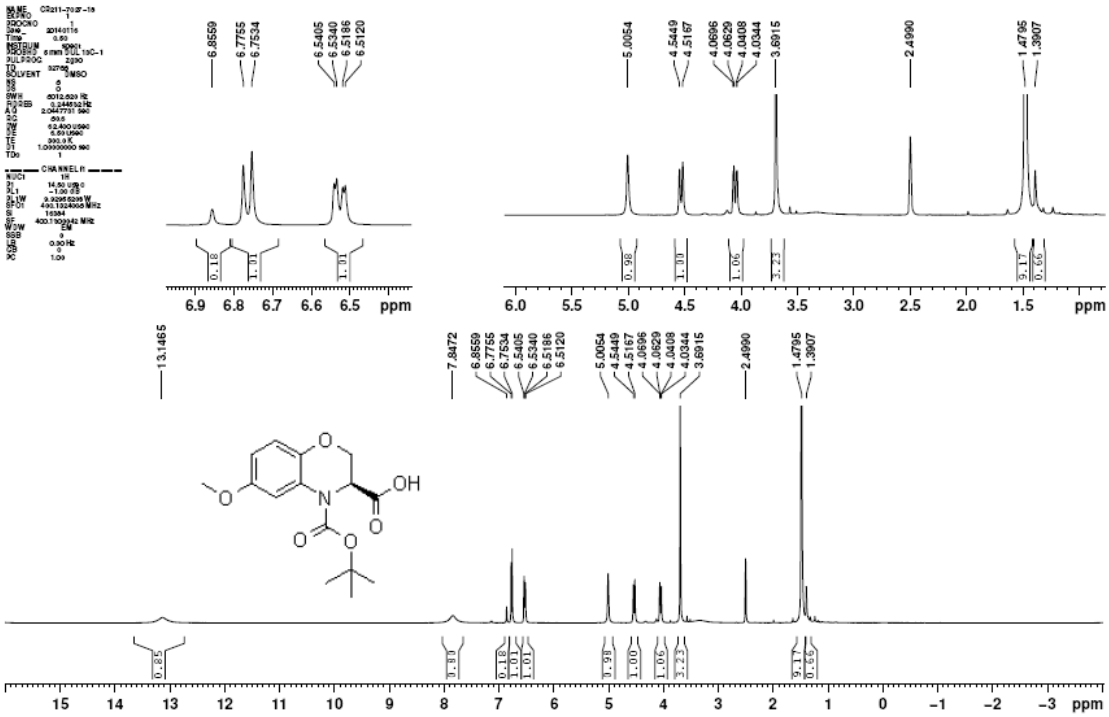
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4d



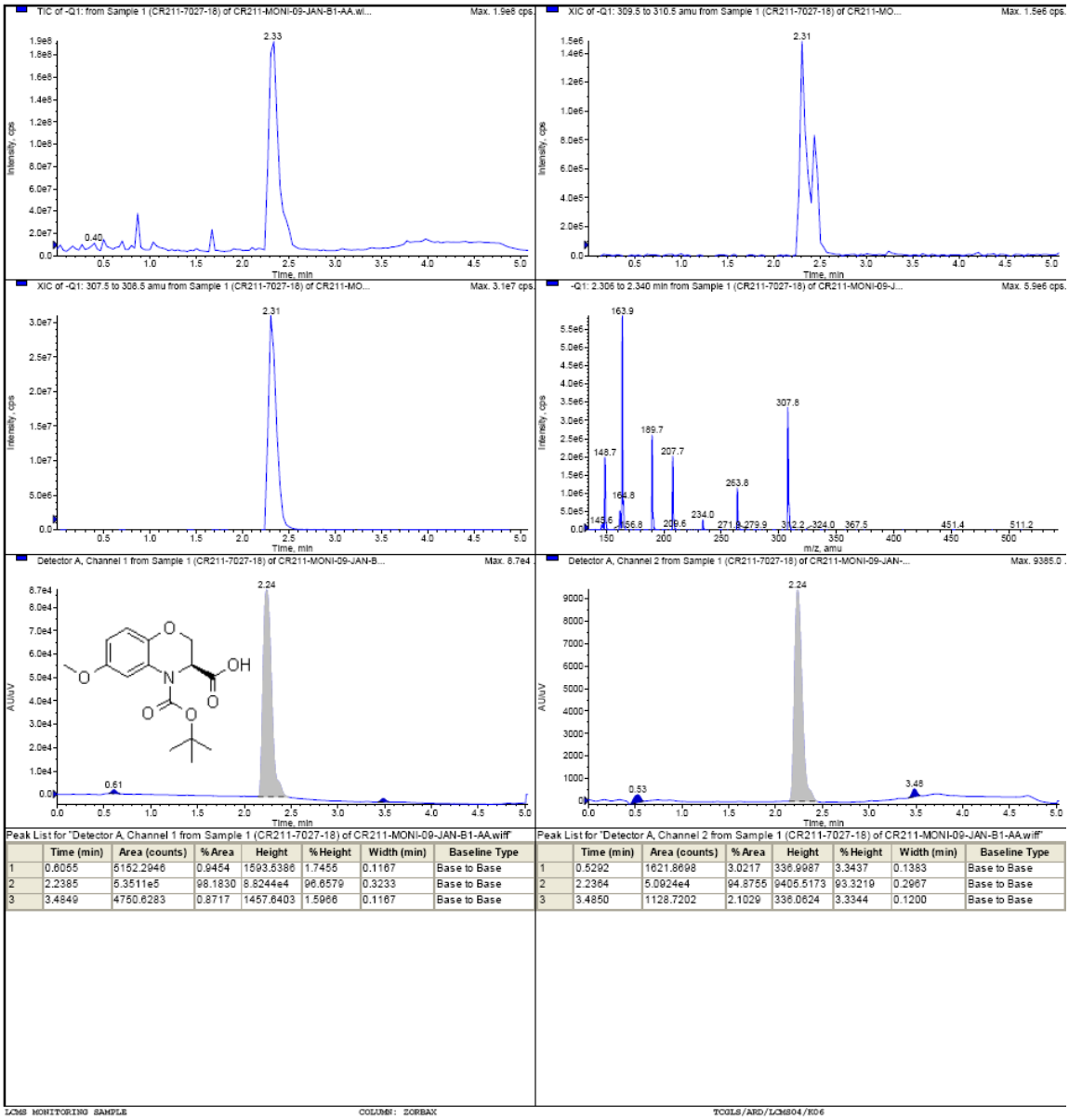
LCMS spectrum of compound 4d



^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 4d



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4e



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7027-18) of CR211-MONI-09-JAN-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.6065	5152.2946	0.9454	1593.5386	1.7455	0.1167	Base to Base
2	2.2385	5.3511e5	98.1830	8.8244e4	96.6579	0.3233	Base to Base
3	3.4849	4750.6283	0.8717	1457.6403	1.5966	0.1167	Base to Base

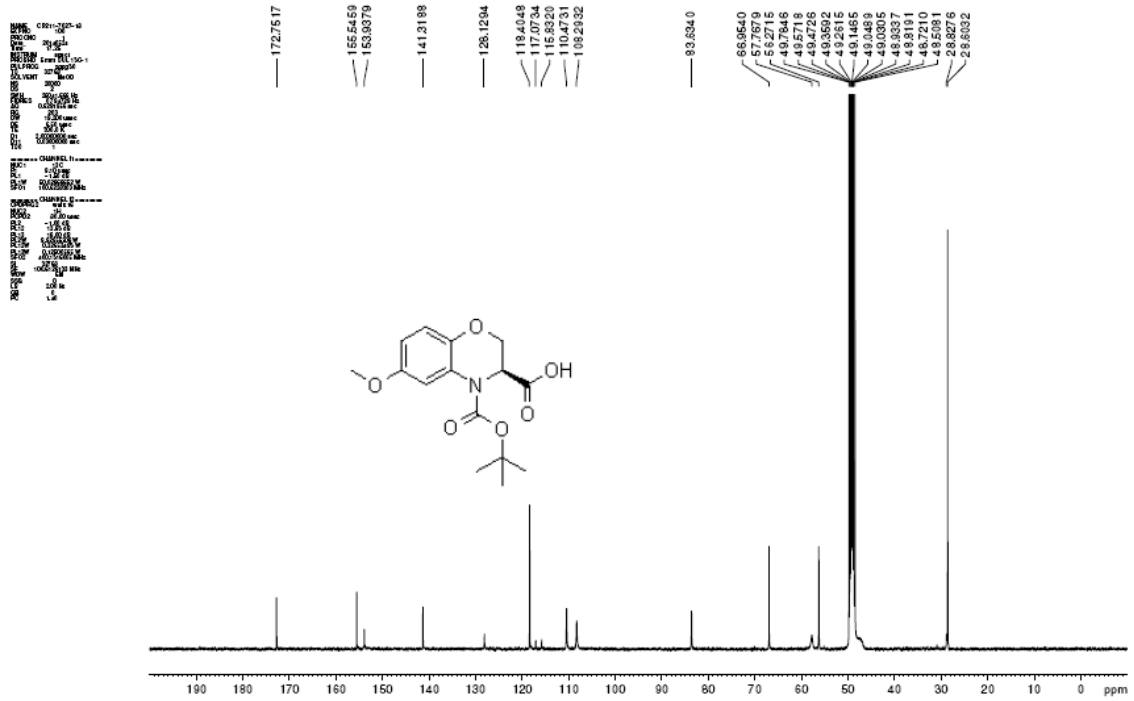
Peak List for "Detector A, Channel 2 from Sample 1 (CR211-7027-18) of CR211-MONI-09-JAN-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5292	1621.8698	3.0217	336.9987	3.3437	0.1383	Base to Base
2	2.2364	5.0924e4	94.8755	9405.5173	93.3219	0.2967	Base to Base
3	3.4850	1128.7202	2.1029	336.0624	3.3344	0.1200	Base to Base

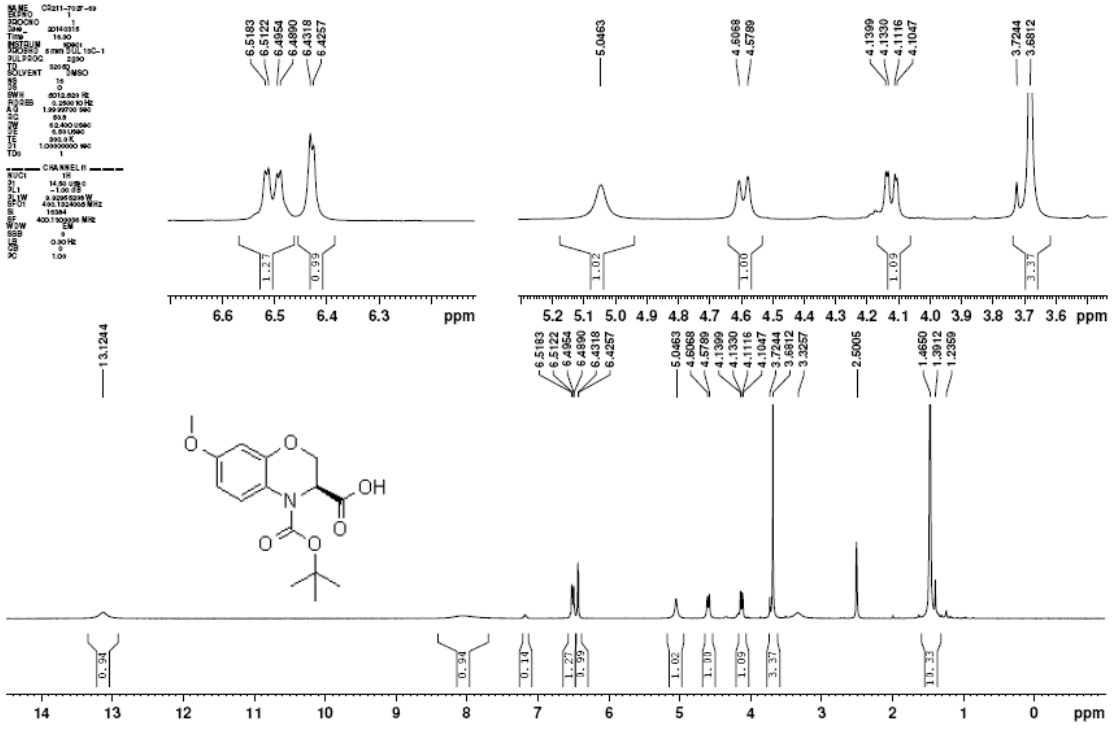
LCMS MONITORING SAMPLE COLUMN: ZORBAX TCOLS/ARD/LCMS04/KD6

Channel 1 at wavelength 220 nm, Channel 2 at wavelength 260 nm NH4OAc:ACN Analyzed by

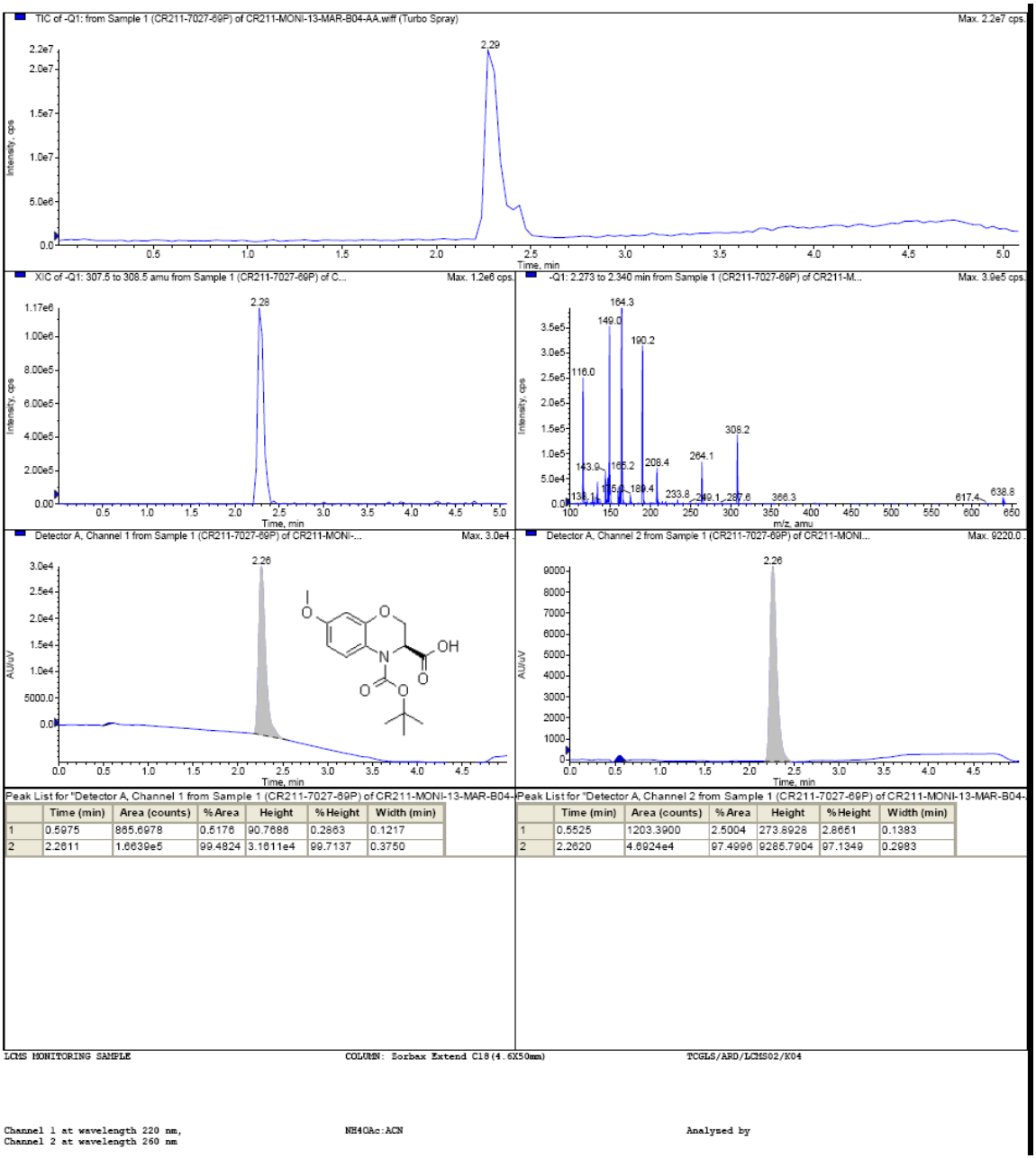
LCMS spectrum of compound 4e



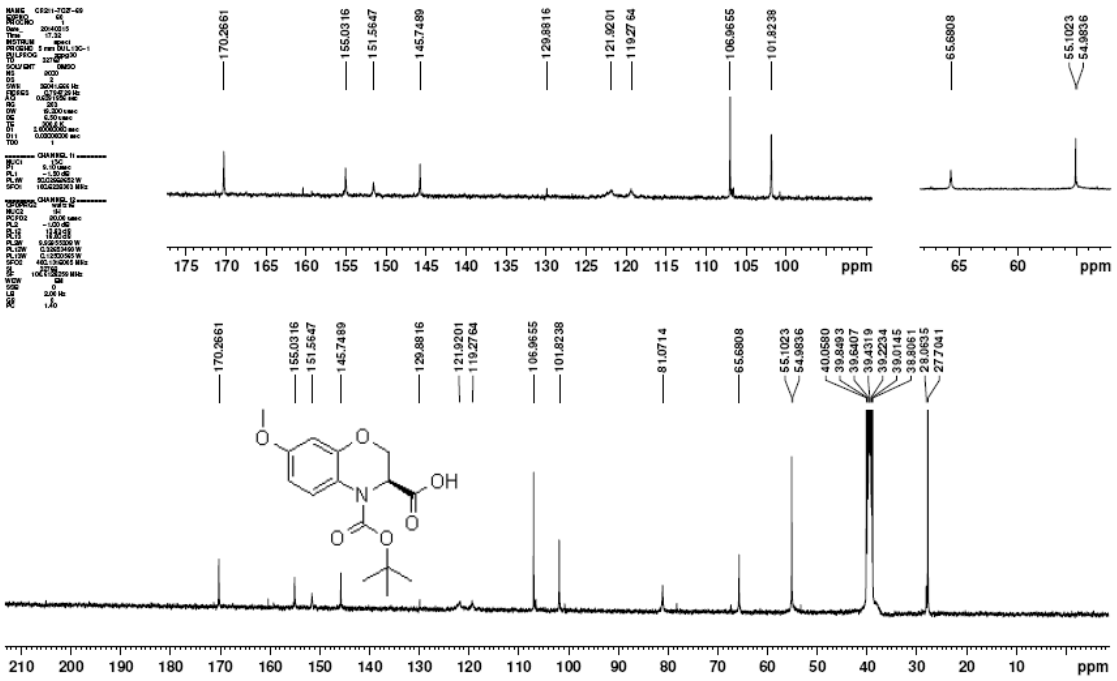
^{13}C NMR spectrum (100MHz, MeOD) of compound 4e



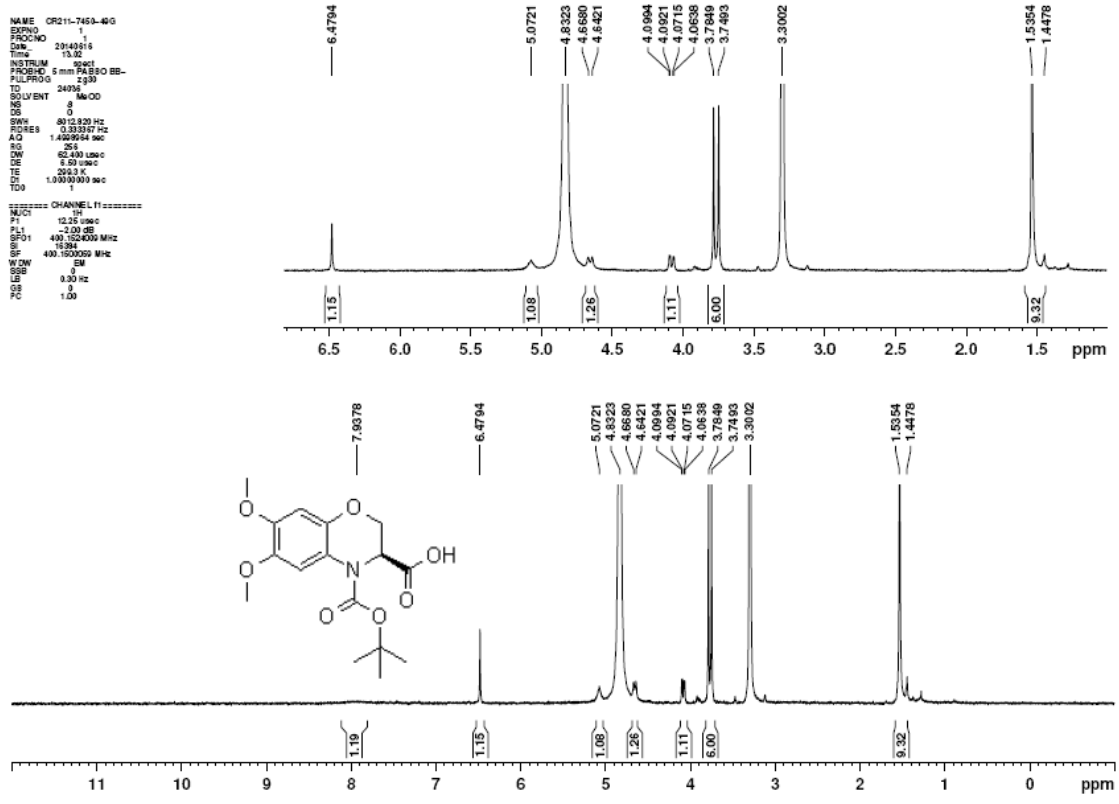
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4f



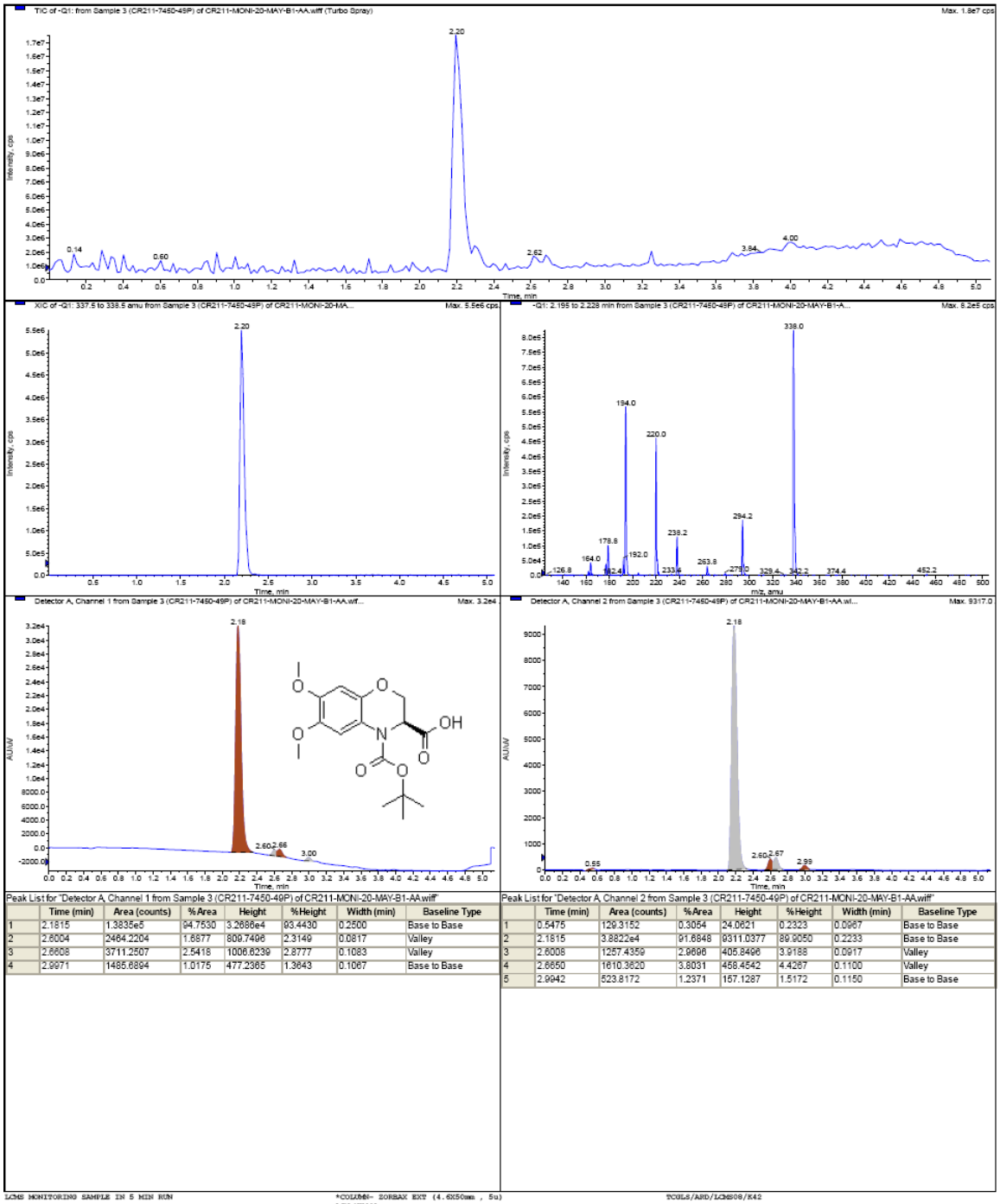
LCMS spectrum of compound 4f



^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 4f



^{1}H NMR spectrum (400MHz, MeOD) of compound 4g



Peak List for "Detector A, Channel 1 from Sample 3 (CR211-7450-49P) of CR211-MONI-20-MAY-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	2.1815	1.3835e5	94.7530	3.2686e4	93.4430	0.2500	Base to Base
2	2.6004	2464.2204	1.6877	809.7496	2.3149	0.0817	Valley
3	2.6608	3711.2507	2.5418	1006.6239	2.8777	0.1083	Valley
4	2.9971	1485.6894	1.0175	477.2365	1.3643	0.1067	Base to Base

Peak List for "Detector A, Channel 2 from Sample 3 (CR211-7450-49P) of CR211-MONI-20-MAY-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5475	129.3152	0.3054	24.0621	0.2323	0.0967	Base to Base
2	2.1815	3.8822e4	91.6848	9311.0377	89.9050	0.2233	Base to Base
3	2.6008	1257.4359	2.9696	405.8496	3.9188	0.0917	Valley
4	2.6650	1610.3620	3.8031	458.4542	4.4267	0.1100	Valley
5	2.9942	523.8172	1.2371	157.1287	1.5172	0.1150	Base to Base

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN:- ZORBAX EXT (4.6X50mm , 5u)
ACN:NH4OAc

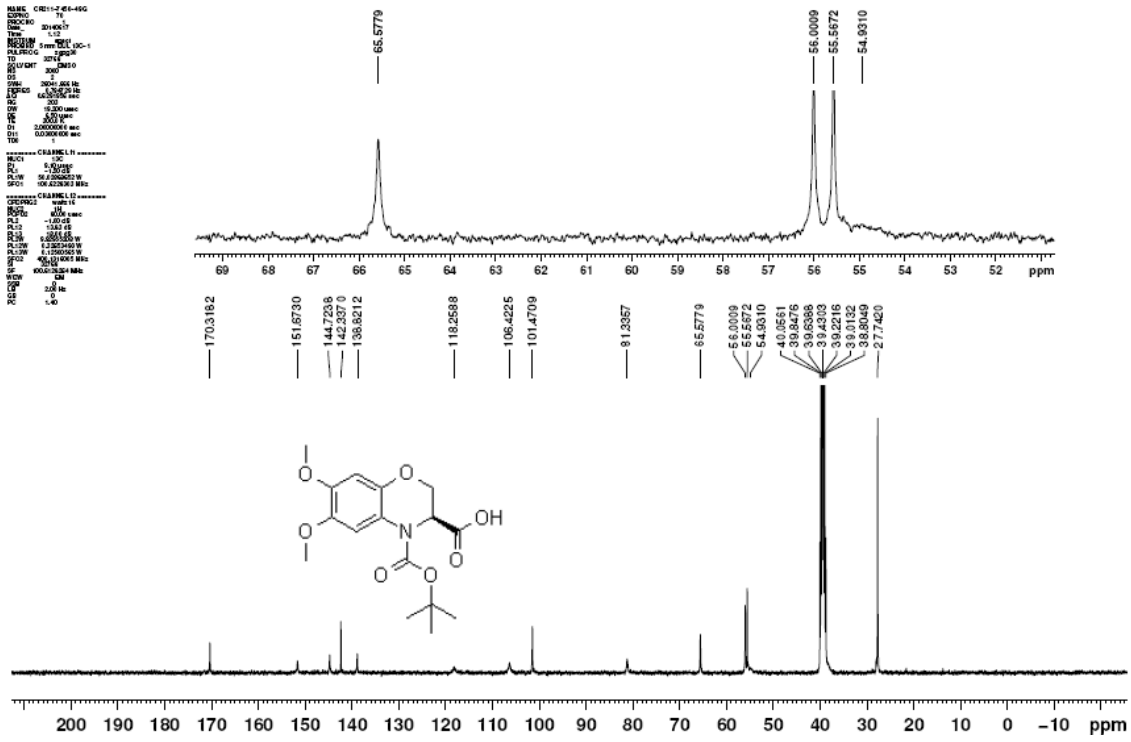
TCGLS/ARD/LCMS08/K42

Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

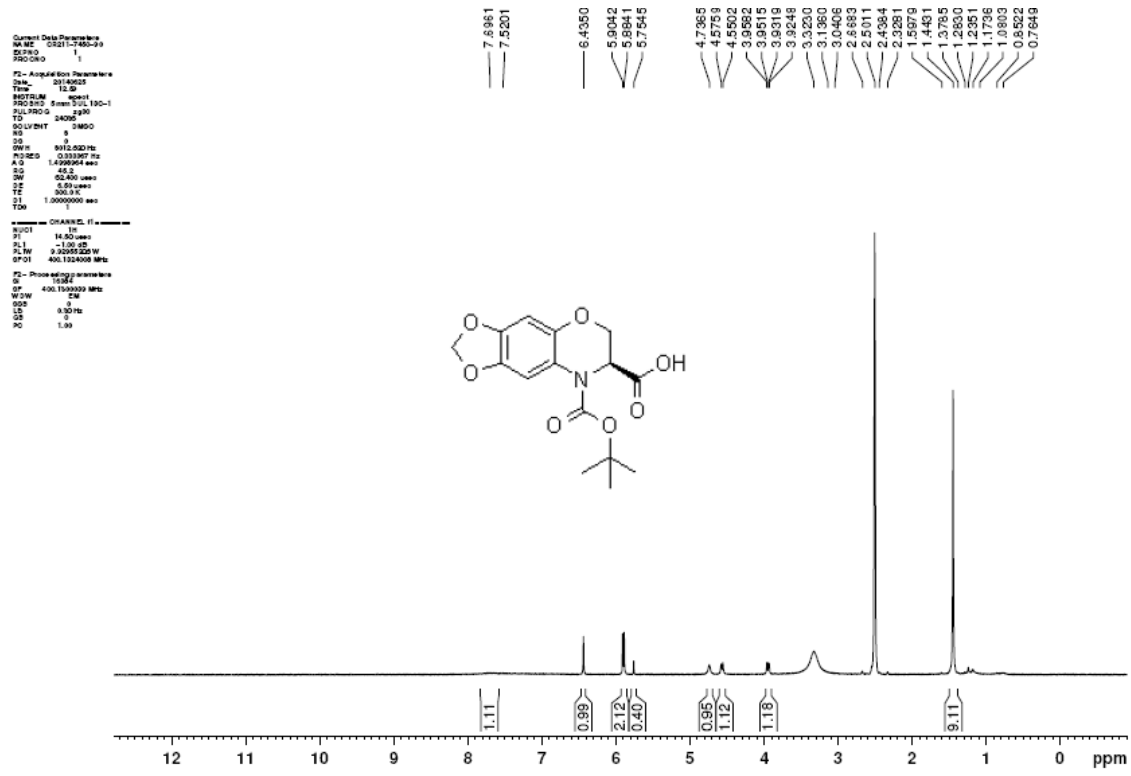
Analysed By

Checked By

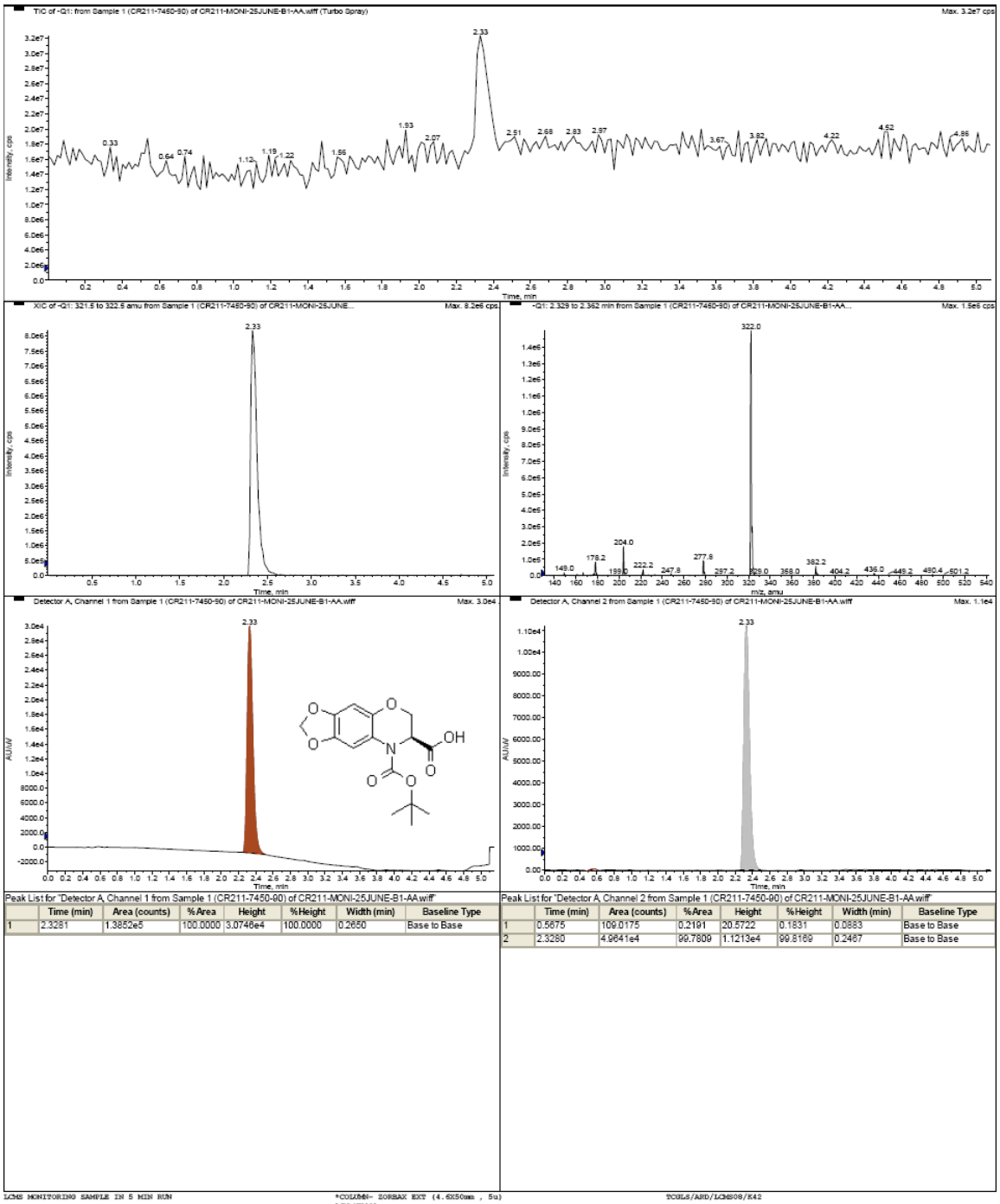
LCMS spectrum of compound 4g



^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 4g



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4h



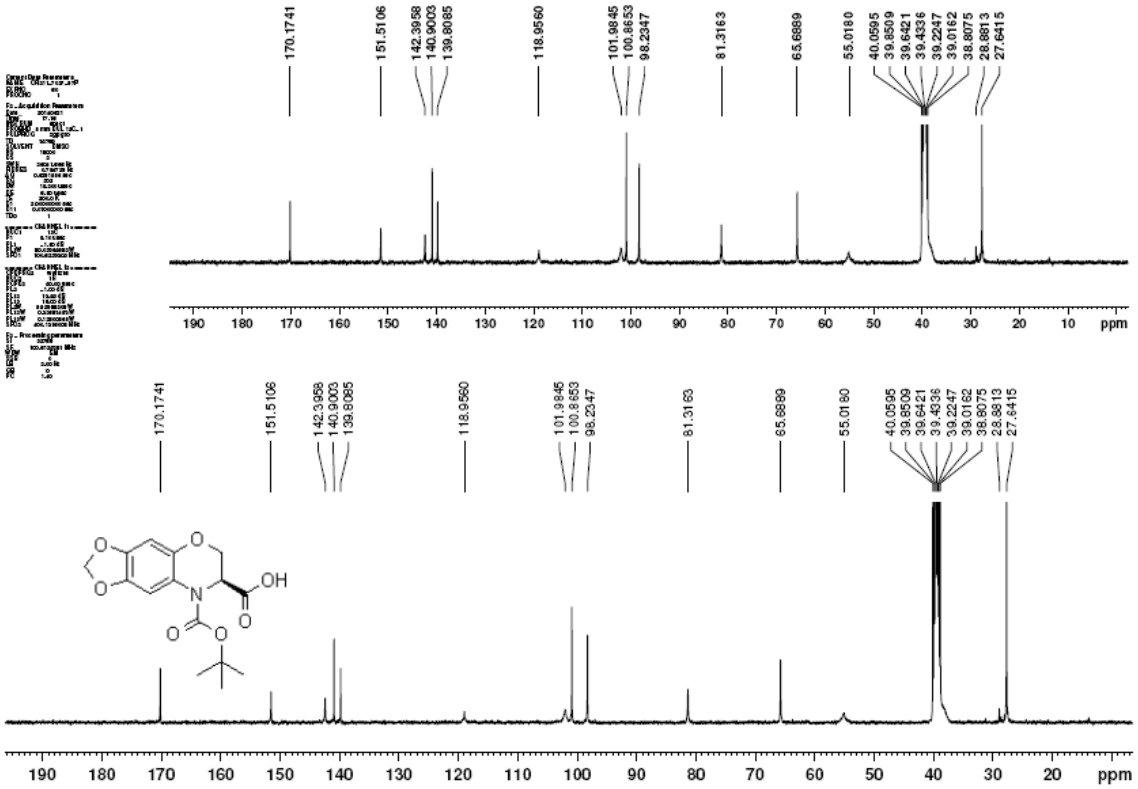
Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7450-90) of CR211-MONI-25JUNE-B1-AA.wiff"

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
1	2.3281	1.3852e5	100.0000	3.0746e4	100.0000	0.2650	Base to Base

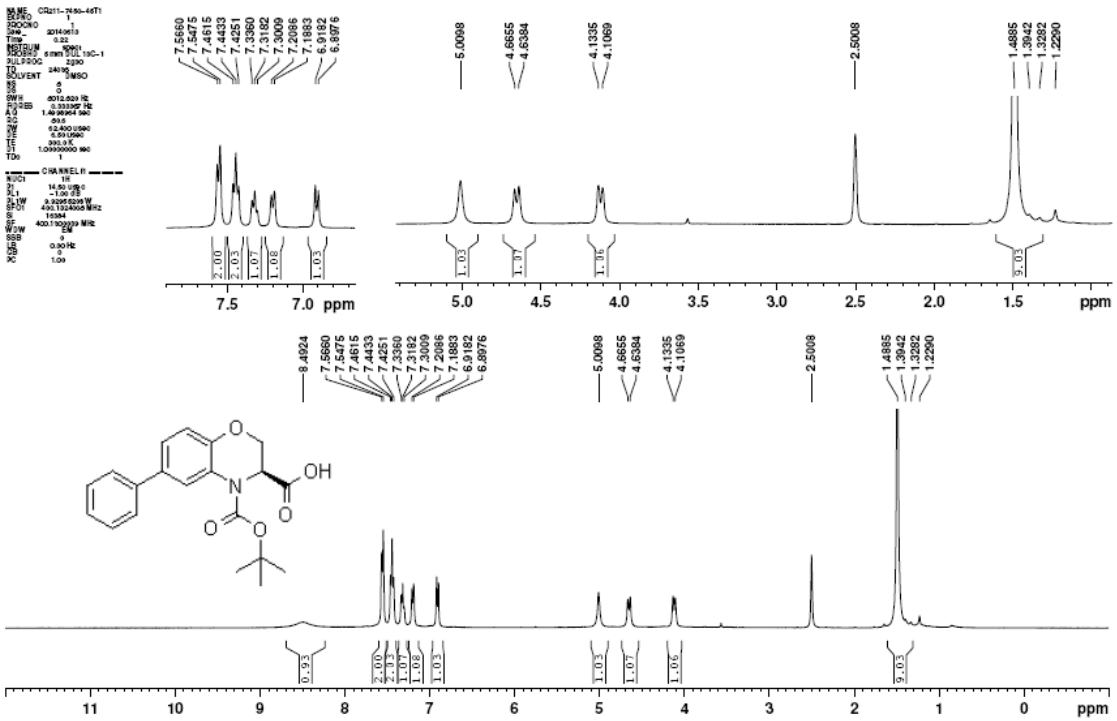
Peak List for "Detector A, Channel 2 from Sample 1 (CR211-7450-90) of CR211-MONI-25JUNE-B1-AA.wiff"

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
1	0.5675	109.0175	0.2191	20.5722	0.1831	0.0883	Base to Base
2	2.3280	4.9641e4	99.7809	1.1213e4	99.8169	0.2467	Base to Base

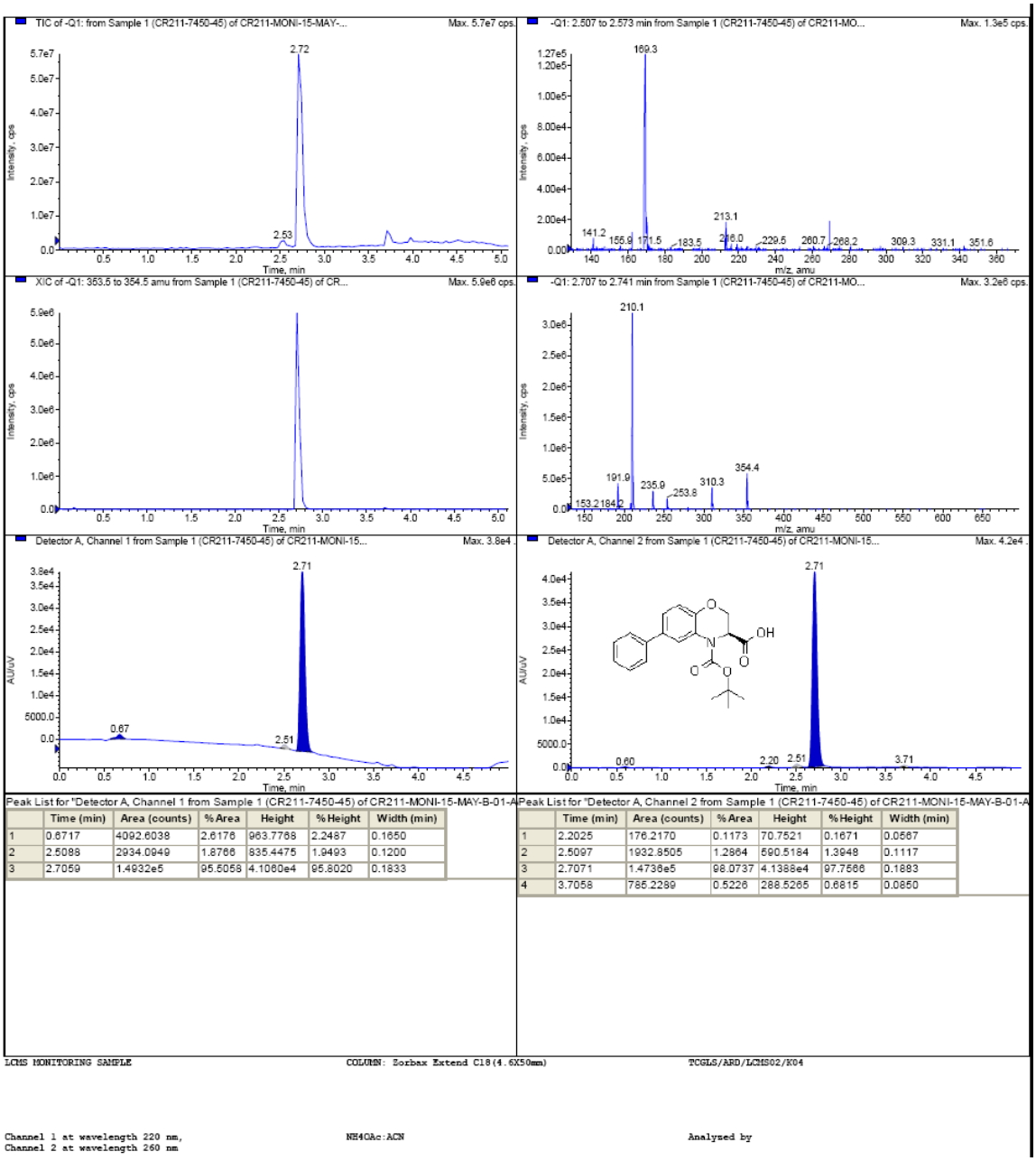
LCMS spectrum of compound 4h



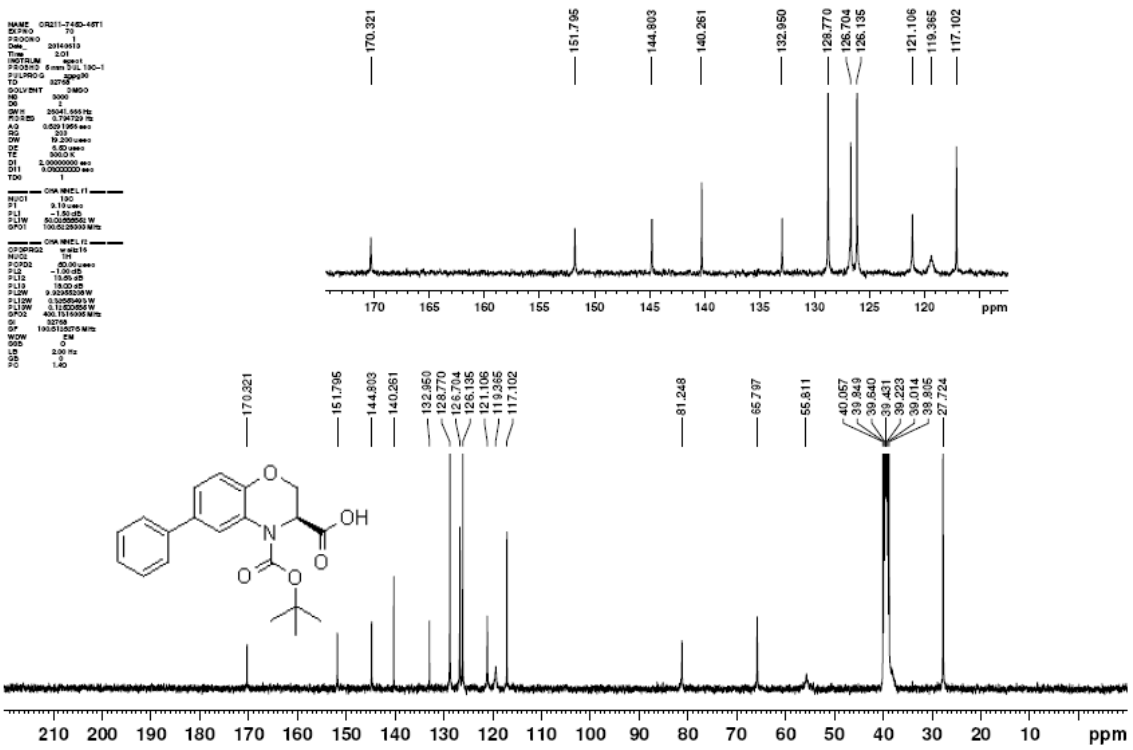
^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 4h



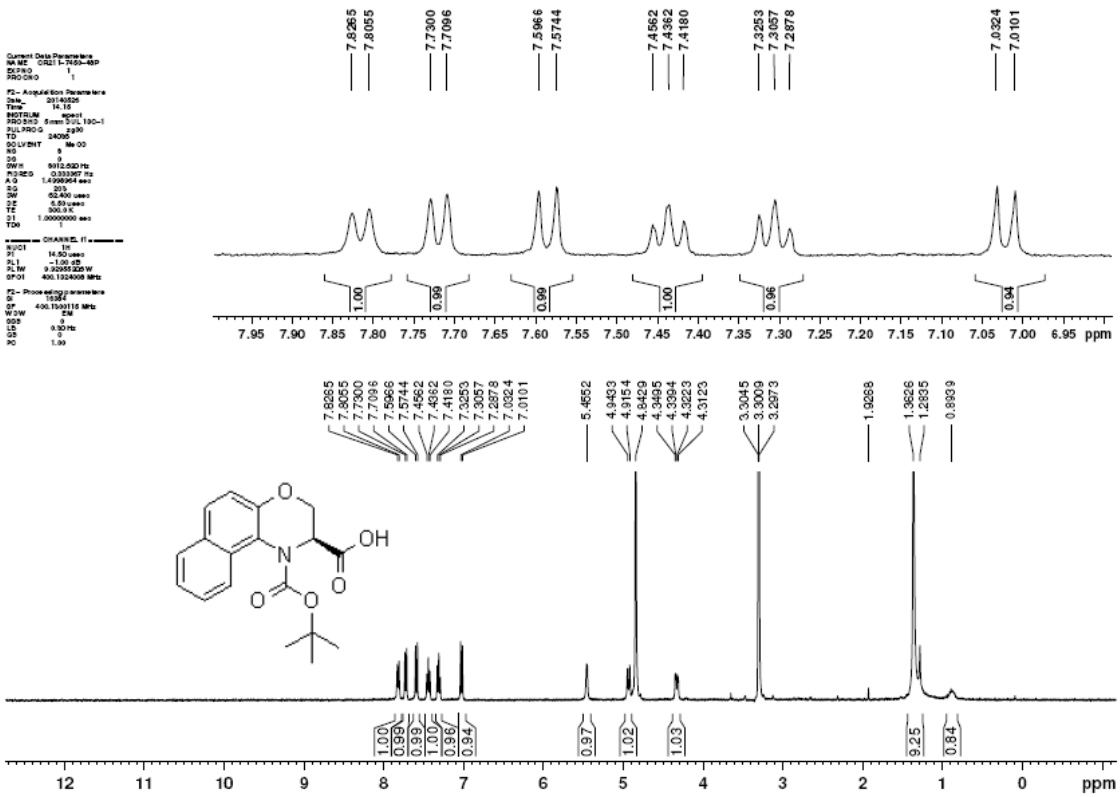
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 4i



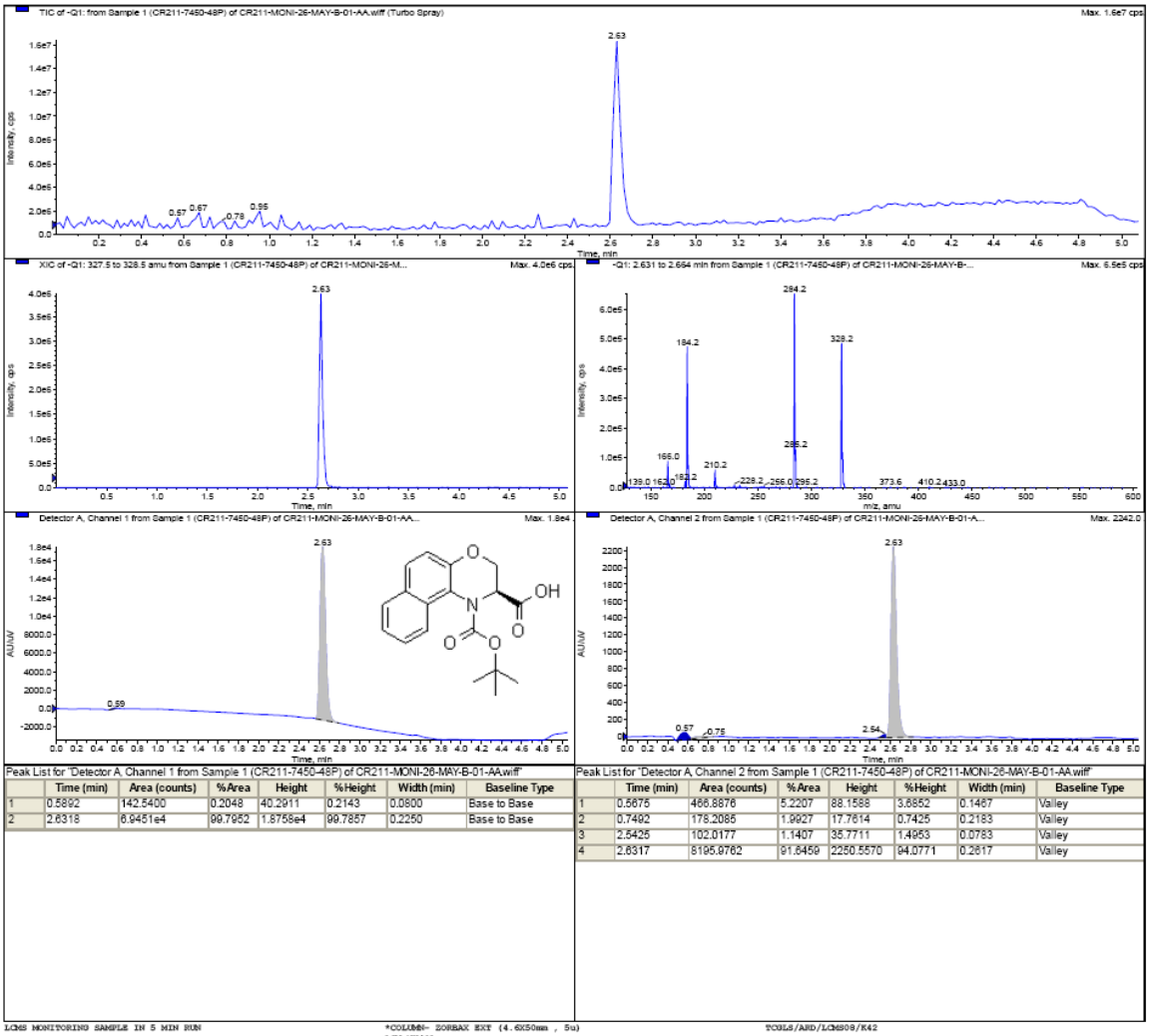
LCMS spectrum of compound 4i



^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 4i



^{1}H NMR spectrum (400MHz, MeOD) of compound 4k



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-7450-48P) of CR211-MONI-26-MAY-B-01-AA.wiff"

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
1	0.5892	142.5400	0.2048	40.2911	0.2143	0.0600	Base to Base
2	2.6318	6.9451e4	99.7952	1.8758e4	99.7857	0.2250	Base to Base

Peak List for "Detector A, Channel 2 from Sample 1 (CR211-7450-48P) of CR211-MONI-26-MAY-B-01-AA.wiff"

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
1	0.5675	466.8876	5.2207	88.1588	3.6852	0.1467	Valley
2	0.7492	178.2085	1.9927	17.7614	0.7425	0.2183	Valley
3	2.5425	102.0177	1.1407	35.7711	1.4953	0.0783	Valley
4	2.6317	8195.9762	91.6459	2250.5570	94.0771	0.2617	Valley

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN:- ZORBAX EXT (4.6X50mm , 5u)
ACN:NH4OAc

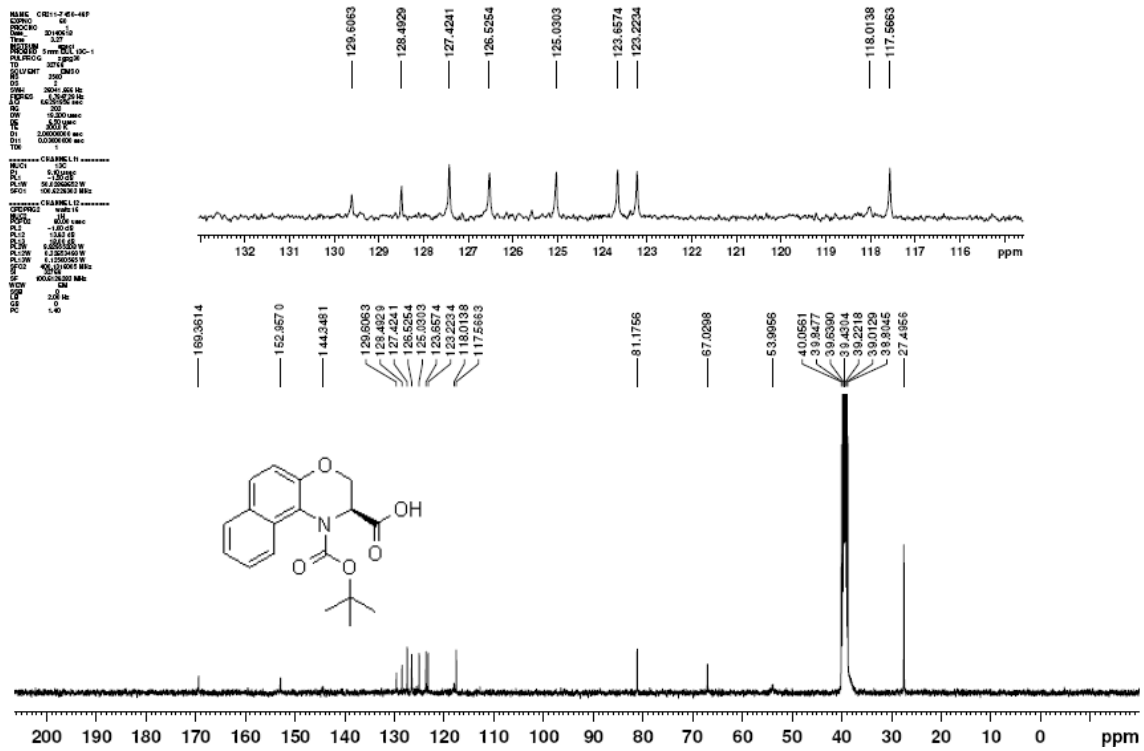
TOOLS/AMD/LCMS09/K42

Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

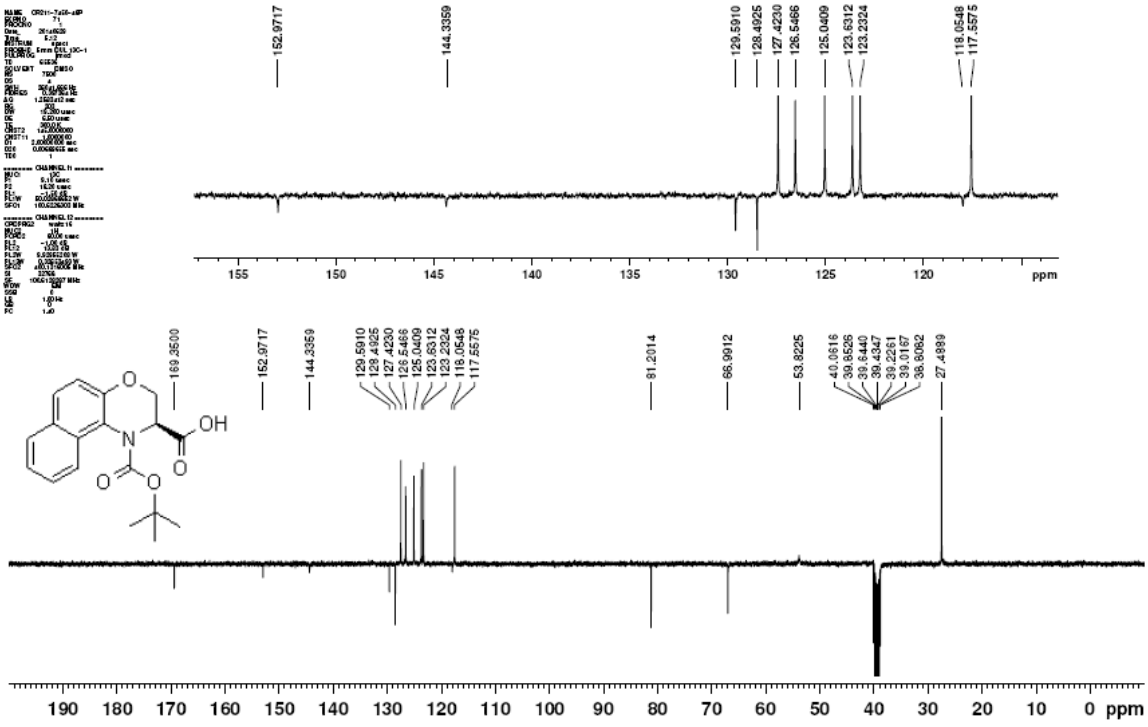
Analysed By

Checked By

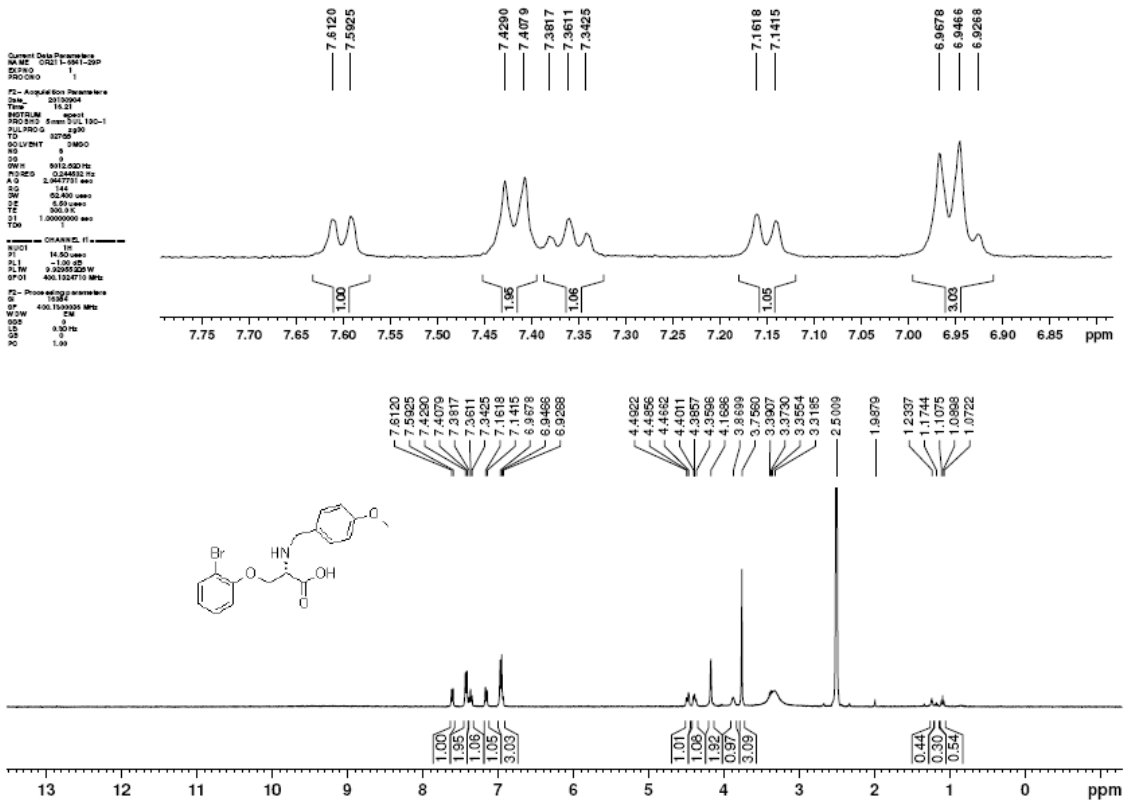
LCMS spectrum of compound 4k



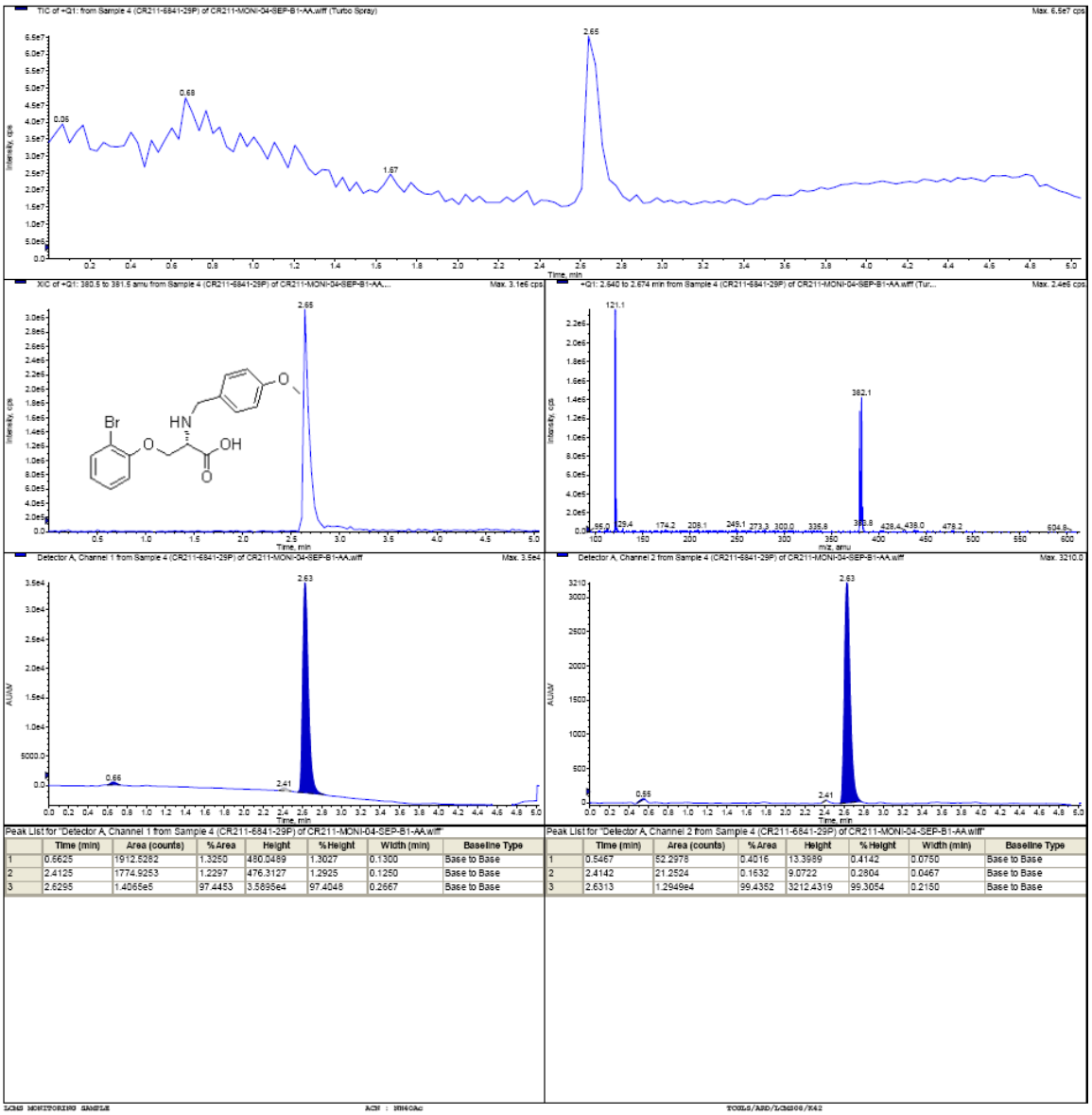
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 4k



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 4k



^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 10a



Peak List for "Detector A, Channel 1 from Sample 4 (CR211-6841-29P) of CR211-MONI-04-SEP-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.6625	1912.5282	1.3250	480.0489	1.3027	0.1300	Base to Base
2	2.4125	1774.9253	1.2297	476.3127	1.2925	0.1250	Base to Base
3	2.6295	1.4065e5	97.4453	3.5895e4	97.4048	0.2667	Base to Base

Peak List for "Detector A, Channel 2 from Sample 4 (CR211-6841-29P) of CR211-MONI-04-SEP-B1-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.5467	52.2978	0.4516	13.3989	0.4142	0.0750	Base to Base
2	2.4142	21.2524	0.1632	9.0722	0.2804	0.0467	Base to Base
3	2.6313	1.2949e4	99.4352	3212.4319	99.3054	0.2150	Base to Base

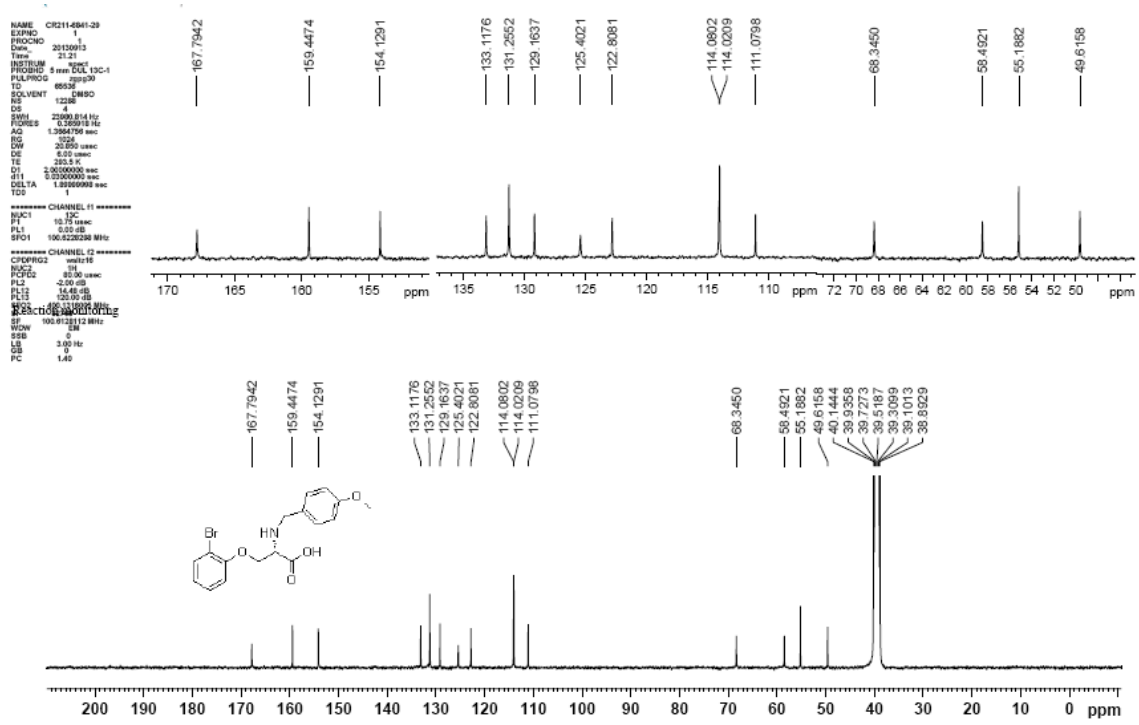
LCMS MONITORING SAMPLE ACN : NH4OAc TOOLS/ABD/LCMS08/K42

Channel 1 at wavelength 220 nm.
Channel 2 at wavelength 260 nm

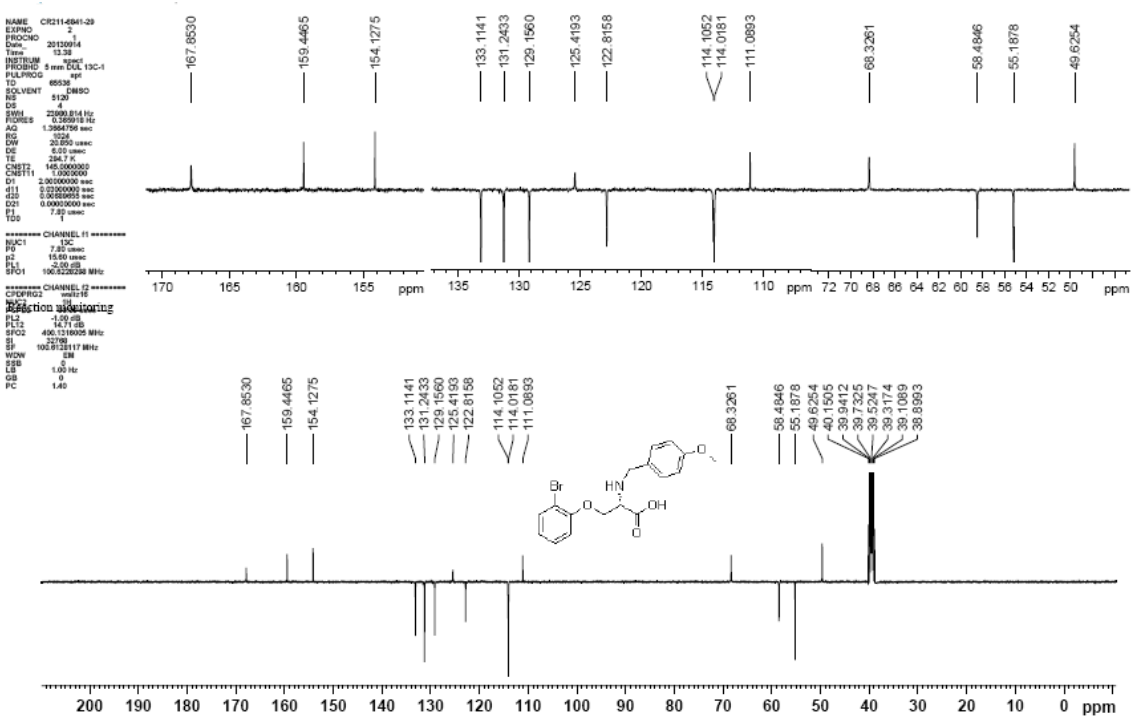
Column: ECOSMAX EXTEND C18(50x4.6mm),5µ

Analyzed by

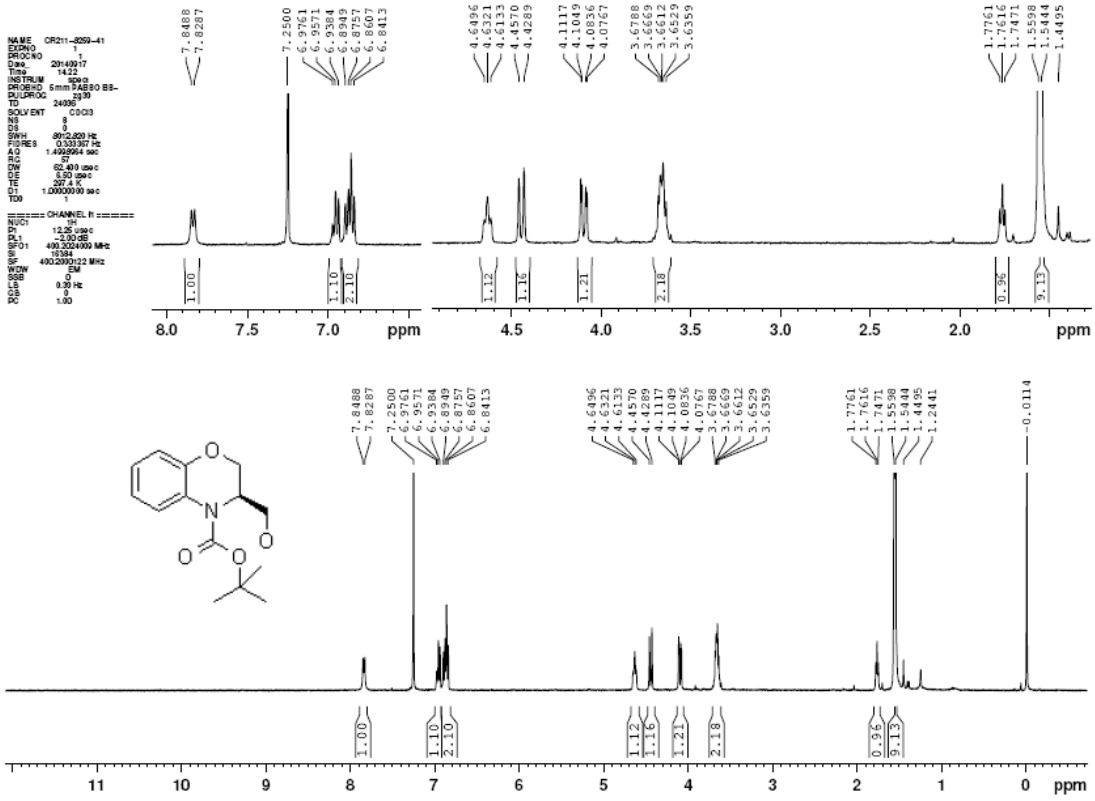
LCMS spectrum of compound 10a



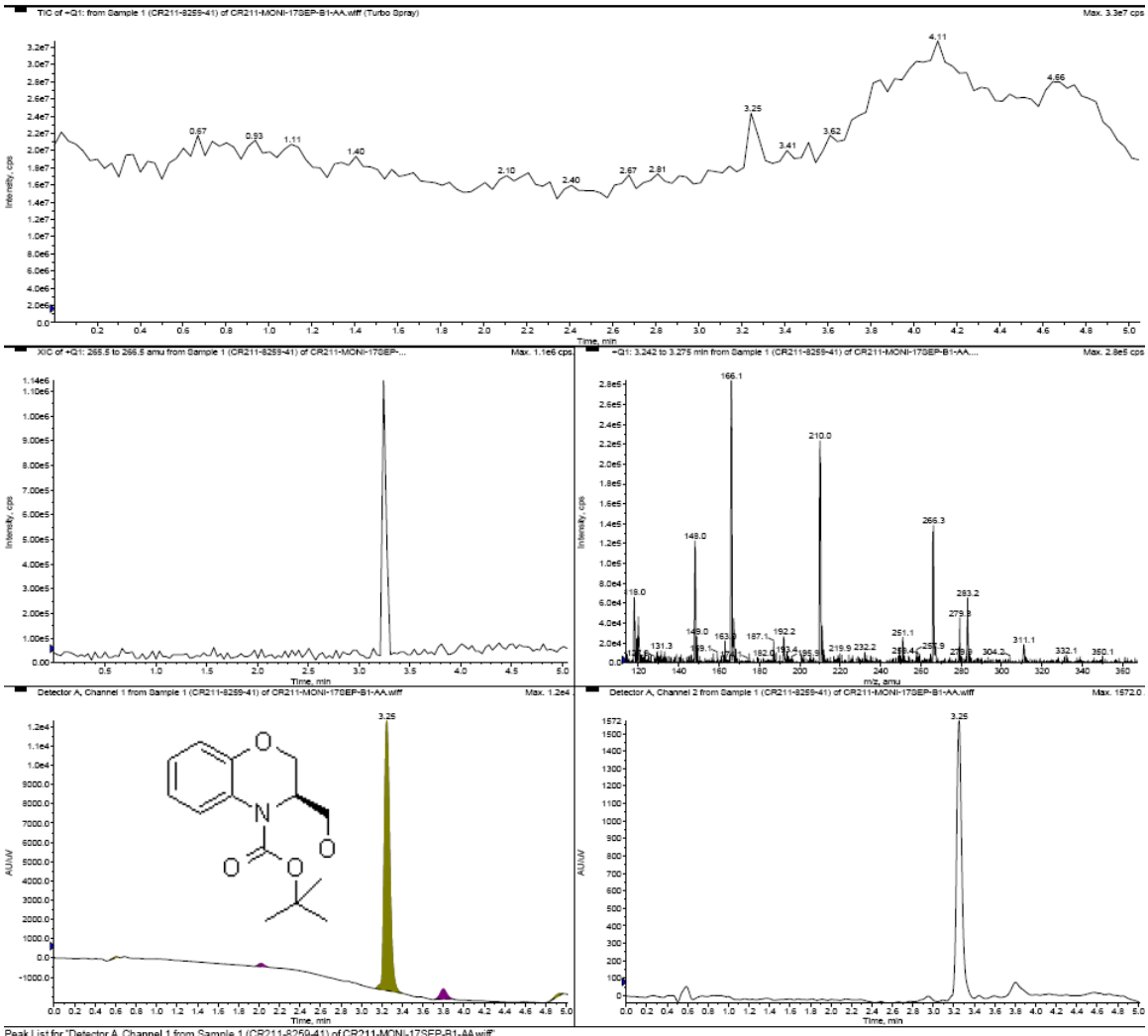
^{13}C NMR spectrum (100MHz, DMSO-d$_6$) of compound 10a



APT NMR spectrum (100MHz, DMSO-d$_6$) of compound 10a



-^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 12a



Peak List for 'Detector A, Channel 1 from Sample 1 (CR211-8259-41) of CR211-MONI-17SEP-B1-AA.wiff'

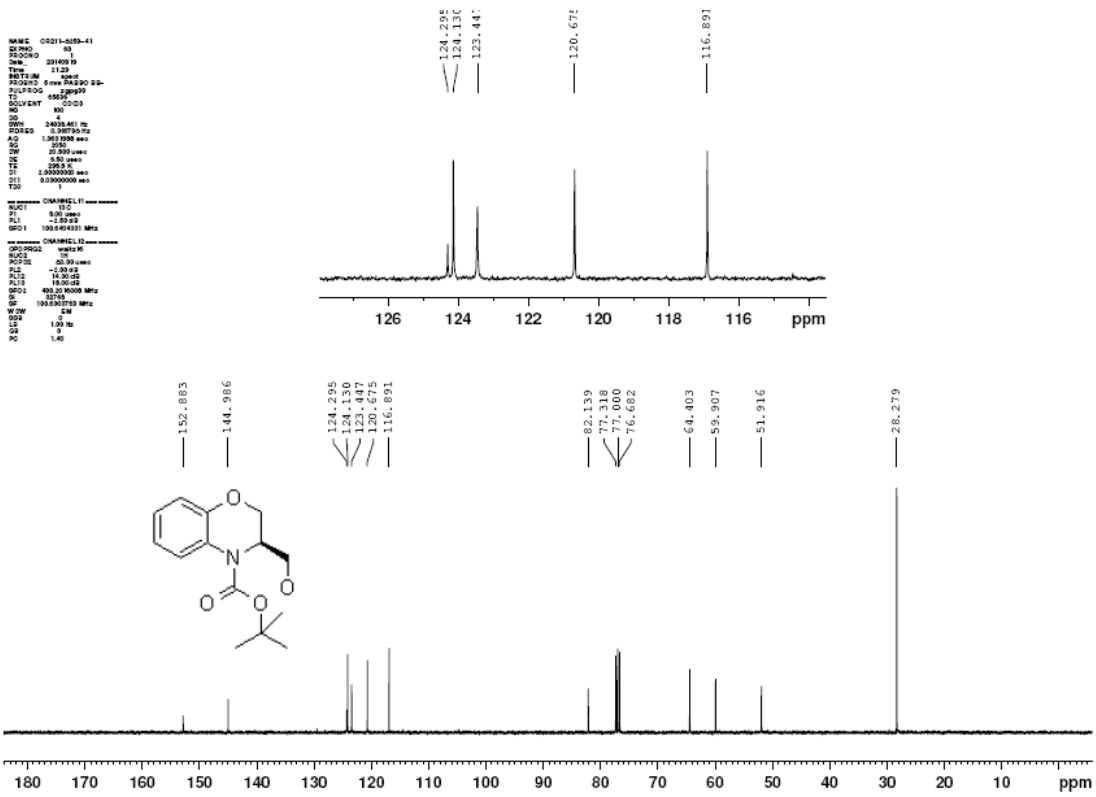
	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
1	0.6067	117.1511	0.2172	36.8027	0.2491	0.0767	Base to Base
2	2.0200	543.3418	1.0072	153.7812	1.0411	0.1133	Base to Base
3	3.2475	5.0610e4	93.8146	1.3993e4	94.7309	0.2633	Base to Base
4	3.8008	2237.3023	4.1472	521.6326	3.5313	0.1683	Base to Base
5	4.9458	439.0097	0.8138	66.1110	0.4476	0.1233	Base to Base

LCMS MONITORING SAMPLE IN 5 MIN RUN | *COLUMN- ZORBAX EXT (4.6X50mm , 5u) ACN:NH4OAc | TCGLS/ASD/LCMS08/K42

Channel 1 at wavelength 220 nm | Analysed By | Checked By

Channel 2 at wavelength 260 nm

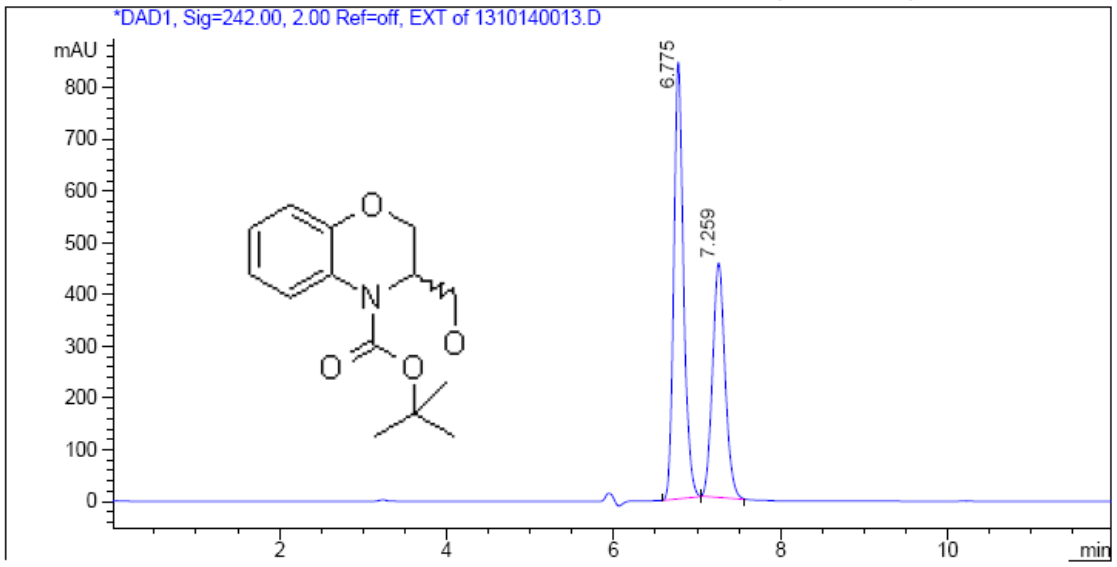
LCMS spectrum of compound 12a



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 12a

```
Sample Name      : CR211-8259-41-RECEMIC                    Seq Line->   13
                                                  Location   :     Vial 73
Acq Operator     : KONDABABU                      Inj. No.   :        1
Injection Date   : 10/13/2014                     Inj. Vol.  :      1 µl
Acq. Method      : C:\Chem32\1\DATA\OCT-2014\131014 2014-10-13 11-13-36->
Analysis Method  : C:\CHEM32\1\METHODS\100-ETOH.M
Last Changed     : Mon, 13. Oct. 2014, 02:16:16 pm
                   (modified after loading)
Samole ID :CR211-8259-41-RECEMIC

Column Name : Chiralpak AD-H(250x4.6mm)5µ
ARD/K/7842
Mobile Phase:EtOH:100
Flow Rate:0.5 ml/min
Solubility:MeOH                                                          ->
                                                  Ref : KD/13.10.14/409
```




```
================================================================================


Signal  1: DAD1, Sig=242.00, 2.00 Ref=off, EXT

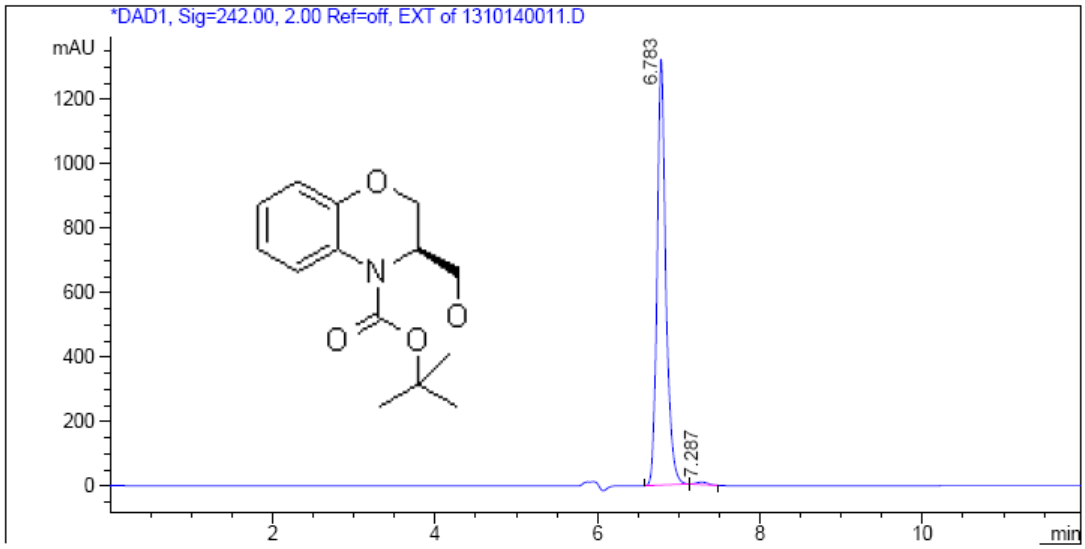
|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      6.78|   6839.40|     59.14|
|   2|      7.26|   4725.63|     40.86|
---------------------------------------

--------------------------------------------------------------------------------
```

Chiral HPLC of a mixture of D- and L-isomer of the compound 12a, prepared by external mixing (not racemic mixture)

```
Sample Name     : CR211-8259-41L                          Seq Line->   11
                                                  Location   :     Vial 74
Acq Operator    : KONDABABU                       Inj. No.   :        1
Injection Date  : 10/13/2014                      Inj. Vol.  :      2 µl
Acq. Method     : C:\Chem32\1\DATA\OCT-2014\131014 2014-10-13 11-13-36->
Analysis Method : C:\CHEM32\1\METHODS\100-ETOH.M
Last Changed    : Mon, 13. Oct. 2014, 02:16:16 pm
                  (modified after loading)
Samole ID :CR211-8259-41L

Column Name : Chiralpak AD-H(250x4.6mm)5µ
ARD/K/7842
Mobile Phase:EtOH:100
Flow Rate:0.5 ml/min
Solubility:MeOH                                                        ->
                                          Ref : KD/13.10.14/410
```




```
================================================================================


Signal  1: DAD1, Sig=242.00, 2.00 Ref=off, EXT

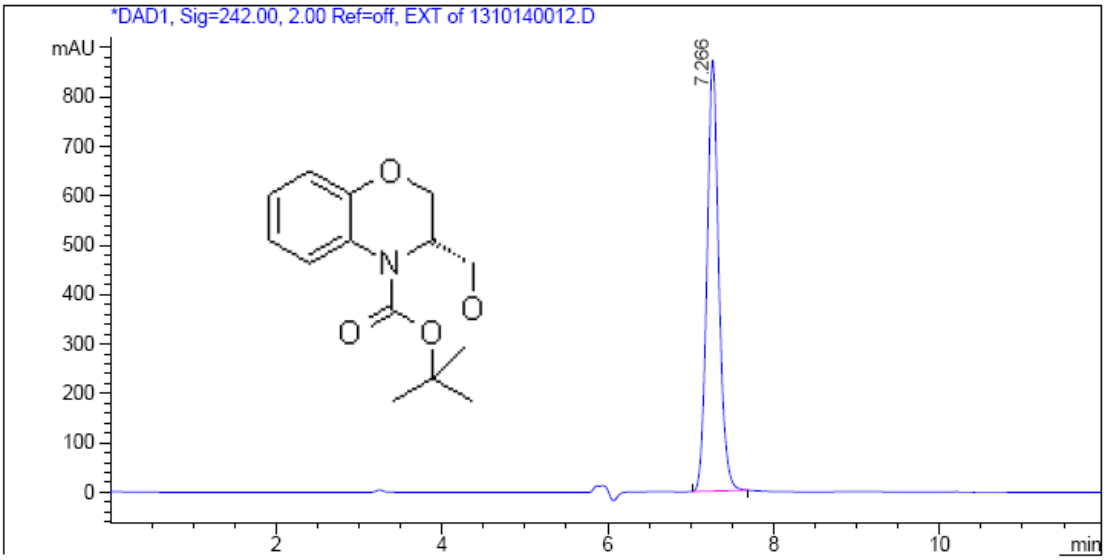
|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|      6.78|   9899.81|     99.23|
|   2|      7.29|     77.16|      0.77|
---------------------------------------

================================================================================
```

Chiral HPLC of *L*-isomer 12a

```
Sample Name      : CR211-8259-41D                          Seq Line->   12
                                                  Location   :     Vial 75
Acq Operator     : KONDABABU                      Inj. No.   :        1
Injection Date   : 10/13/2014                     Inj. Vol.  :      2 µl
Acq. Method      : C:\Chem32\1\DATA\OCT-2014\131014 2014-10-13 11-13-36->
Analysis Method  : C:\CHEM32\1\METHODS\100-ETOH.M
Last Changed     : Mon, 13. Oct. 2014, 02:16:16 pm
                   (modified after loading)
Samole ID :CR211-8259-41D

Column Name : Chiralpak AD-H(250x4.6mm)5µ
ARD/K/7842
Mobile Phase:EtOH:100
Flow Rate:0.5 ml/min
Solubility:MeOH                                                          ->
                                                  Ref : KD/13.10.14/411
```



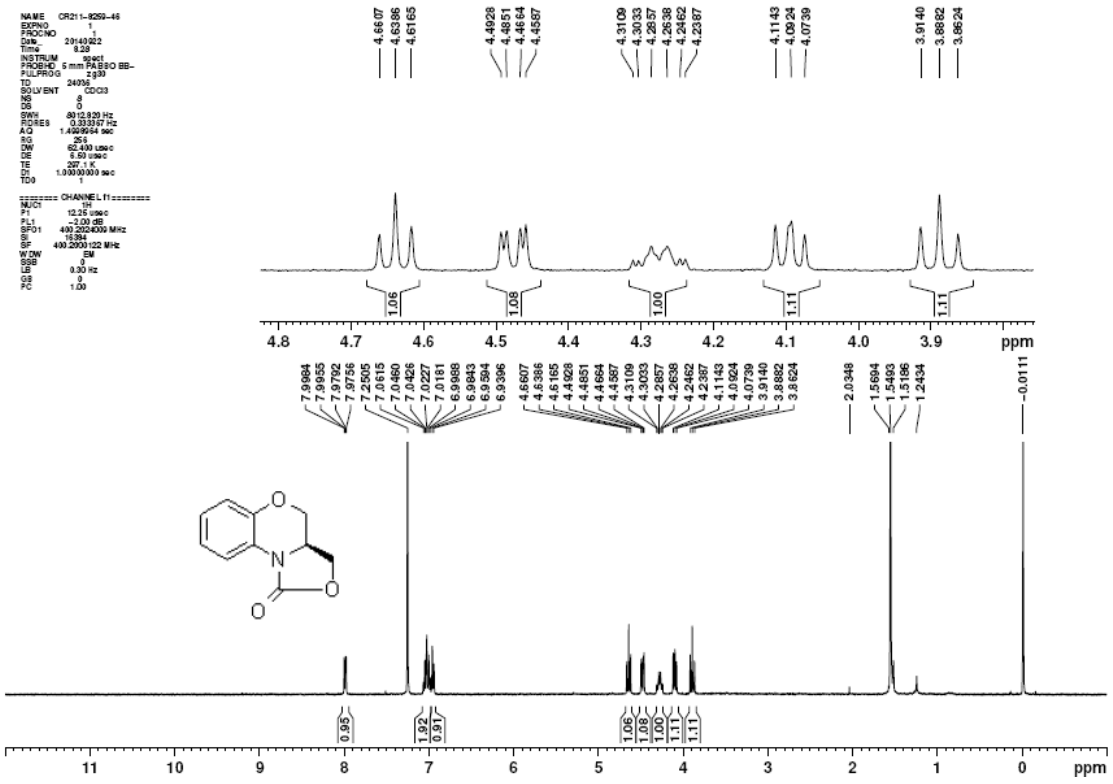

```
================================================================================


Signal  1: DAD1, Sig=242.00, 2.00 Ref=off, EXT

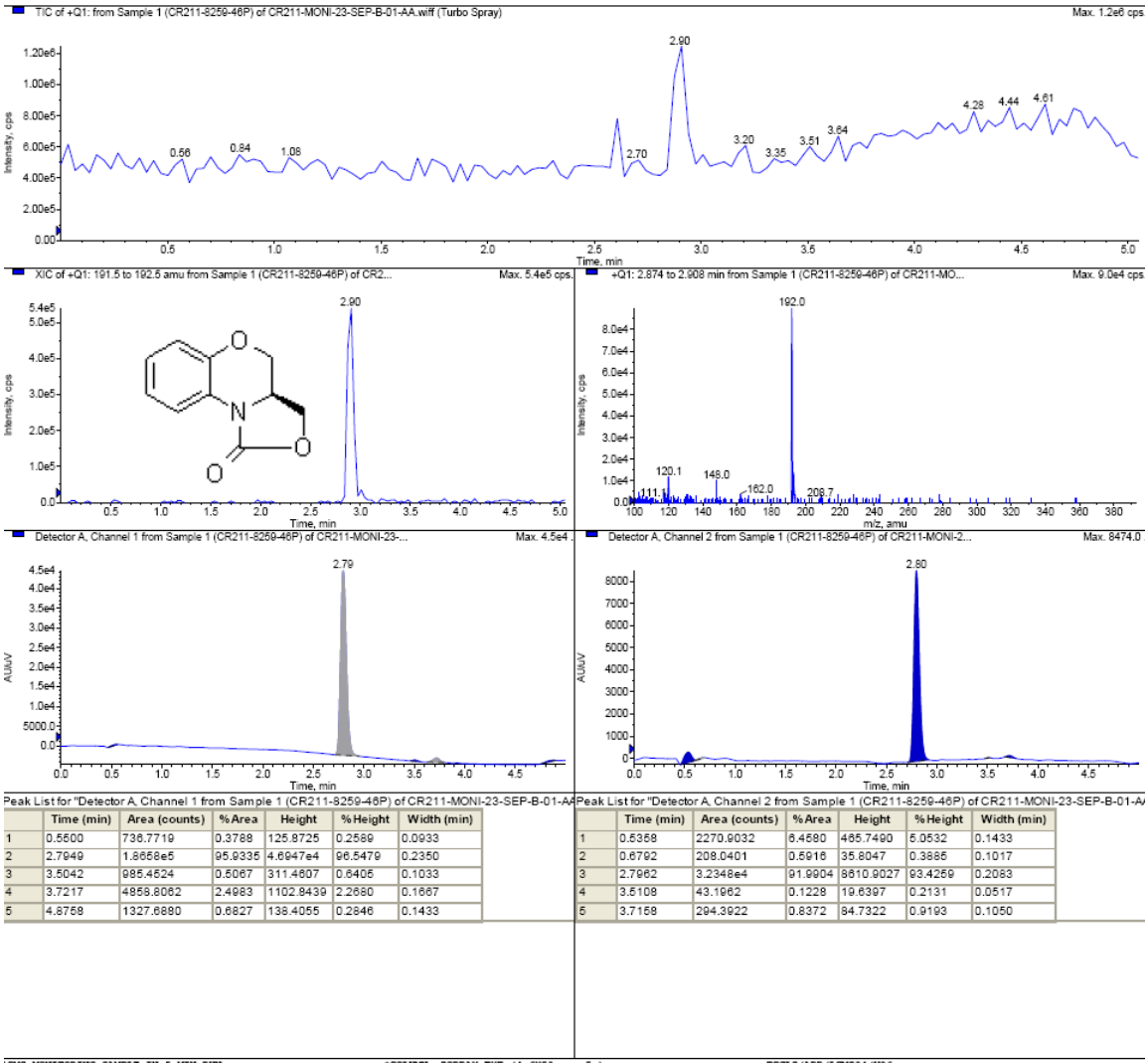
|Peak|   RT      |   Area    |  Area %  |
| #  |  [min]    |-----------|----------|
|----|-----------|           |          |
|   1|      7.27|   8639.68|    100.00|
---------------------------------------

================================================================================
```

Chiral HPLC of *D*-isomer 12a



^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 13a



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-8259-46P) of CR211-MONI-23-SEP-B-01-AA

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)
1	0.5600	736.7719	0.3788	125.8725	0.2589	0.0933
2	2.7949	1.8658e5	95.9335	4.6947e4	96.5479	0.2350
3	3.5042	985.4524	0.5067	311.4607	0.6406	0.1033
4	3.7217	4858.8062	2.4983	1102.8439	2.2680	0.1667
5	4.8758	1327.6880	0.6827	138.4055	0.2846	0.1433

Peak List for "Detector A, Channel 2 from Sample 1 (CR211-8259-46P) of CR211-MONI-23-SEP-B-01-AA

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)
1	0.5358	2270.9032	6.4580	465.7490	5.0532	0.1433
2	0.6792	208.0401	0.5916	35.8047	0.3885	0.1017
3	2.7962	3.2348e4	91.9904	8610.9027	93.4259	0.2083
4	3.5108	43.1962	0.1228	19.6397	0.2131	0.0517
5	3.7158	294.3922	0.8372	84.7322	0.9193	0.1050

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN- SORBAX EXT (4.6X50mm , 5u)
ACN:NH4OAc

TCGLS/ARD/LCMS04/K06

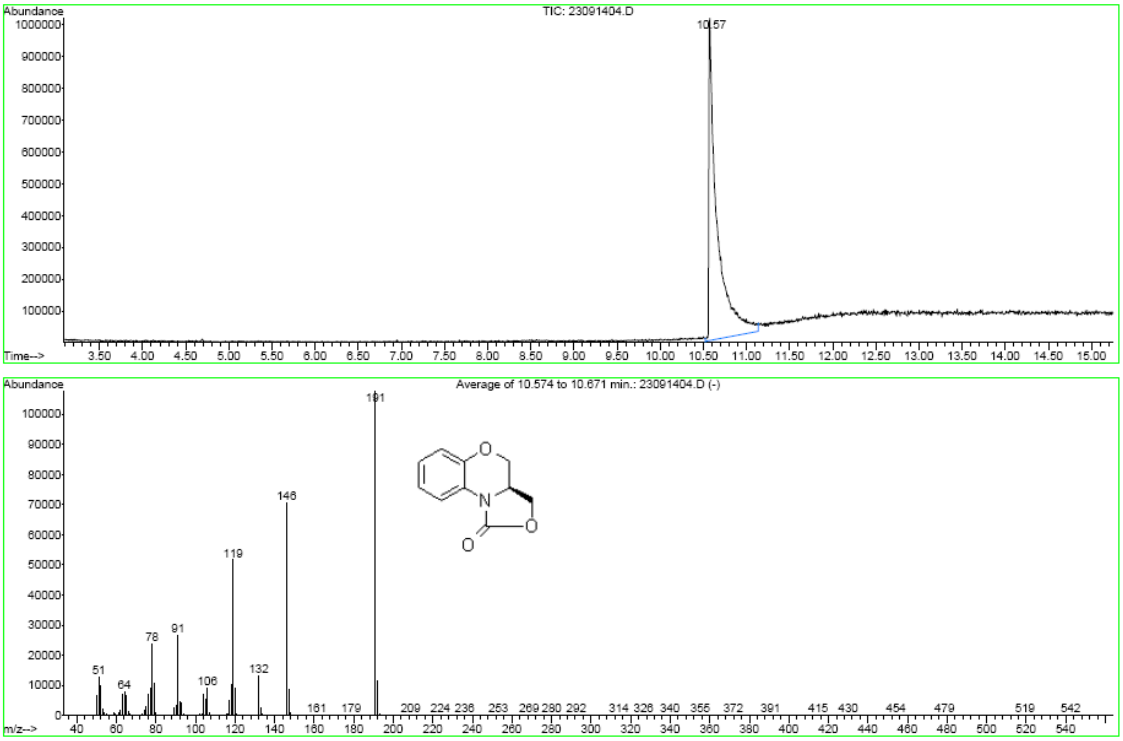
Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

Anlalysed By

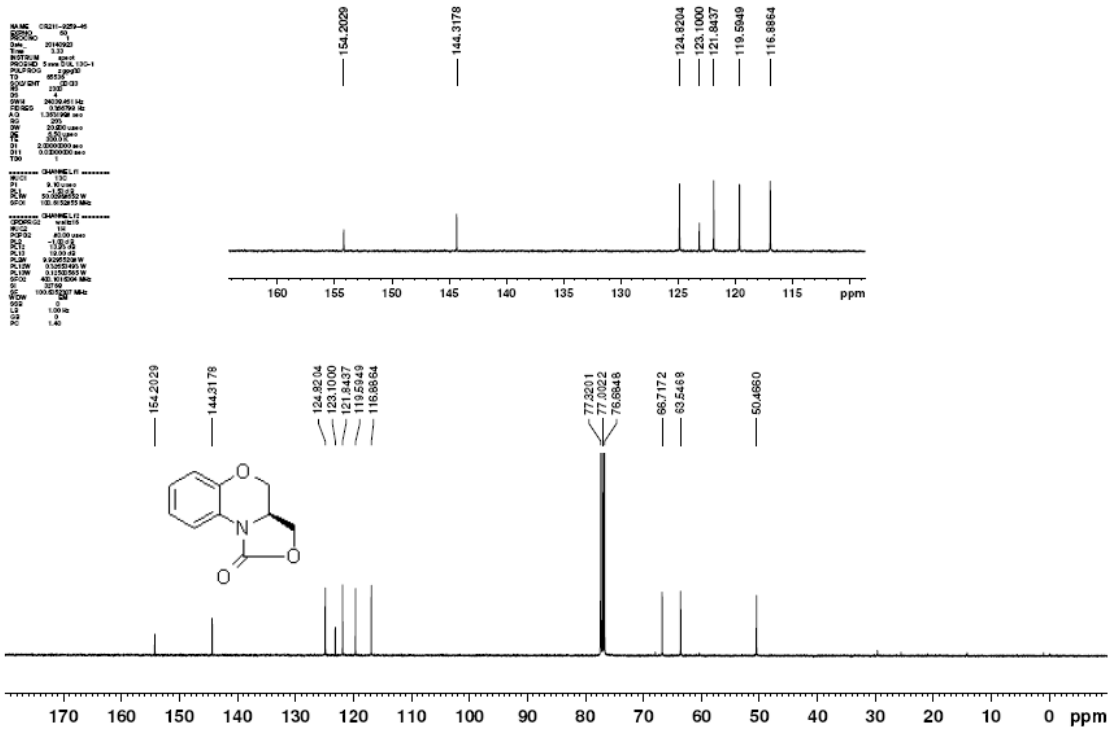
Checked By

LCMS spectrum of compound 13a

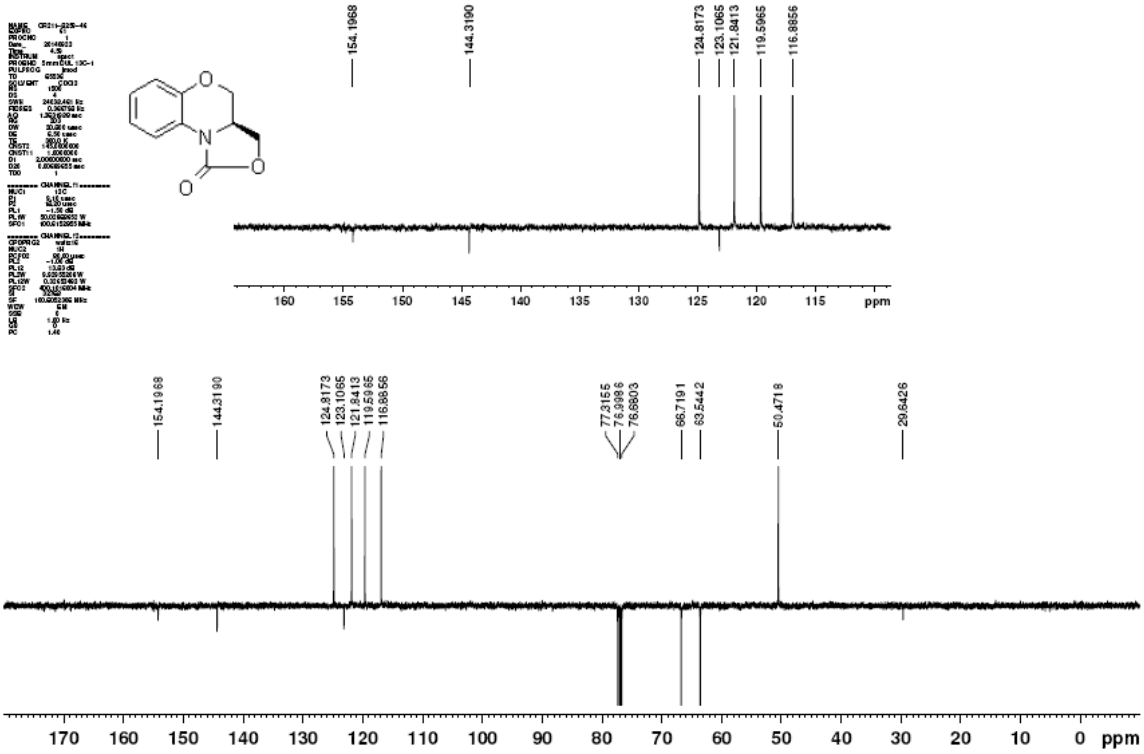
```
File       : C:\MSDCHEM\1\DATA\SEPT--14B\23091404.D
Operator   :
Acquired   : 23 Sep 2014  12:24     using AcqMethod TCG50
Instrument :    Instrumen
Sample Name: CR211-8259-46P
Misc Info  :
Vial Number: 2
```



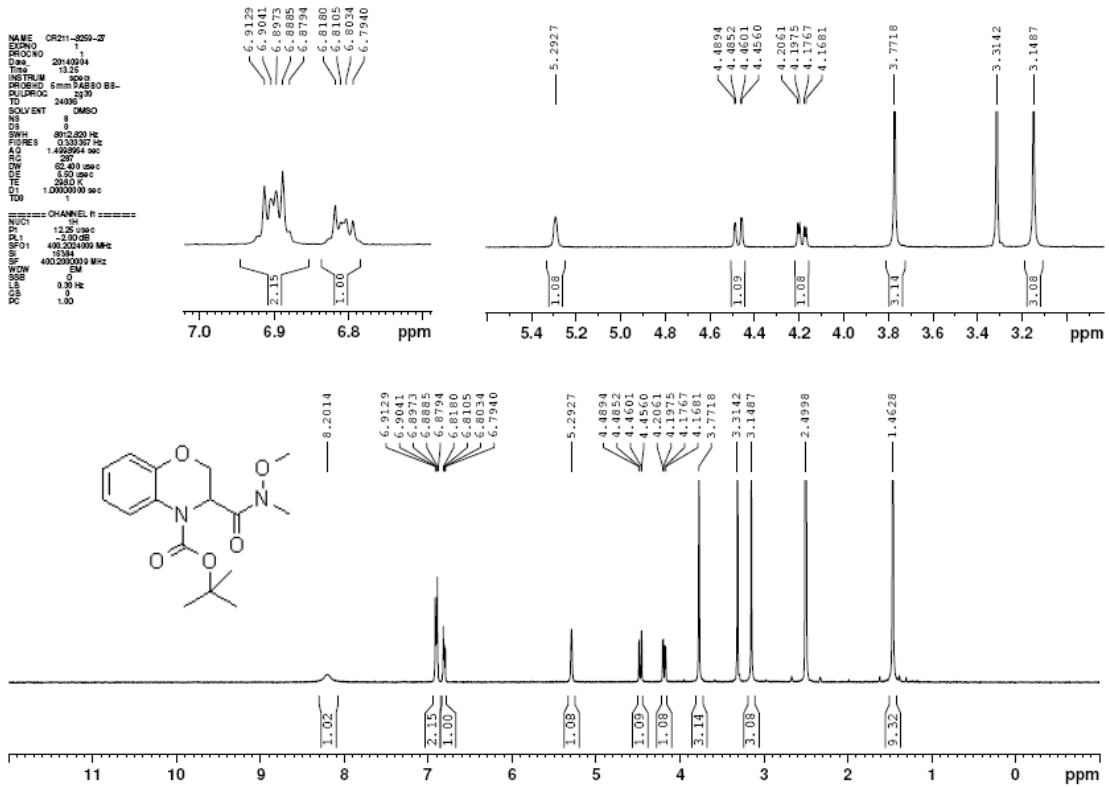
GCMS of Compound 13a



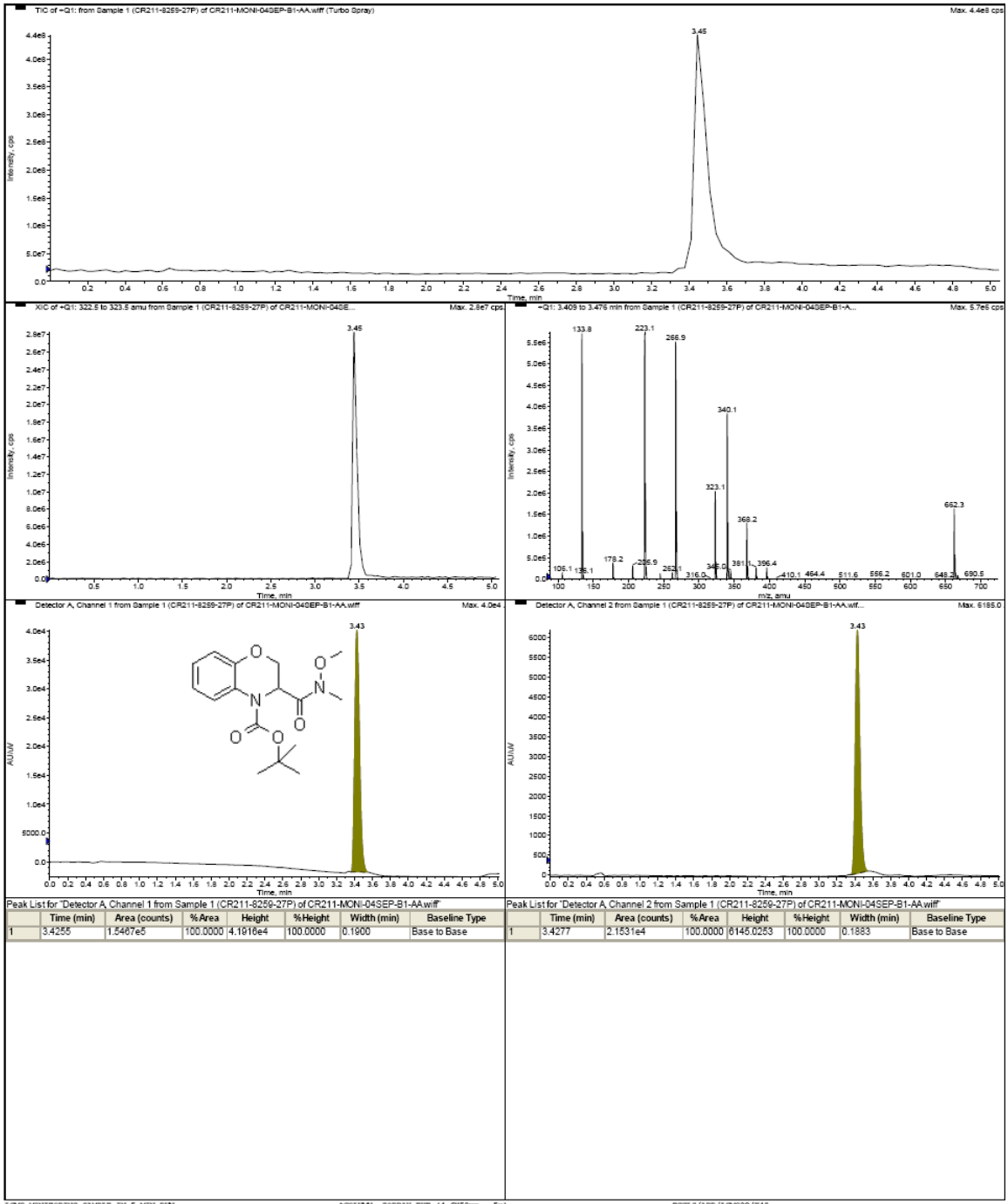
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 13a



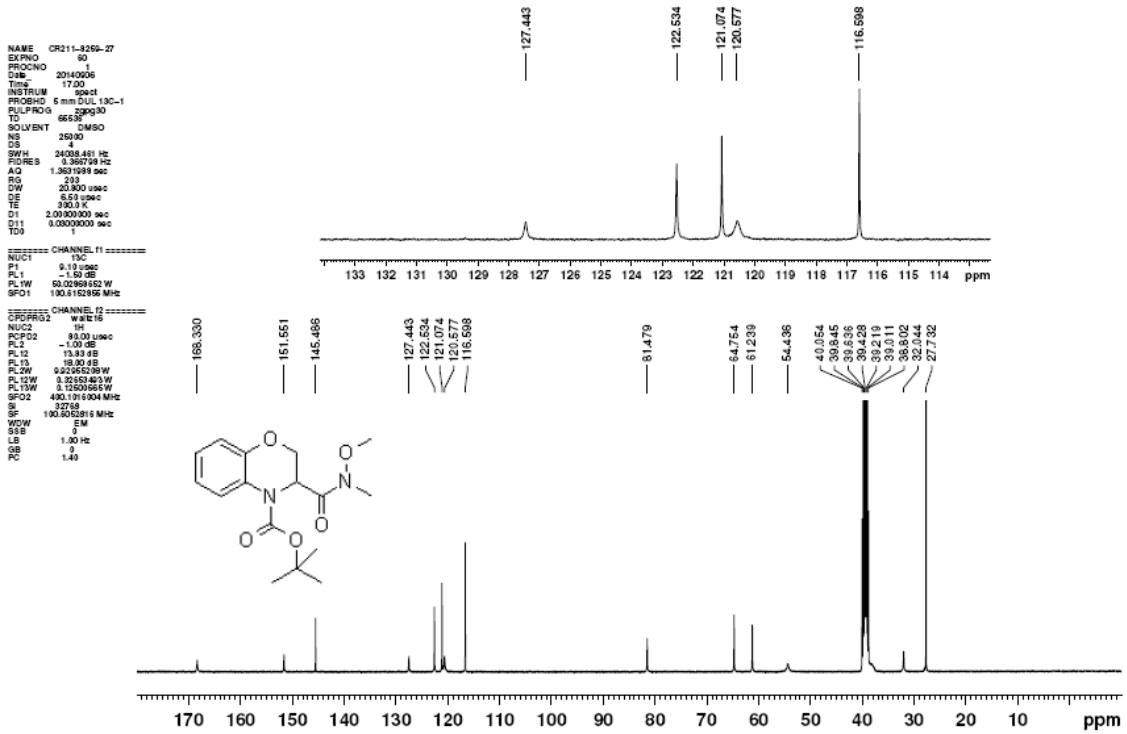
APT NMR spectrum (100MHz, $CDCl_3$) of compound 13a



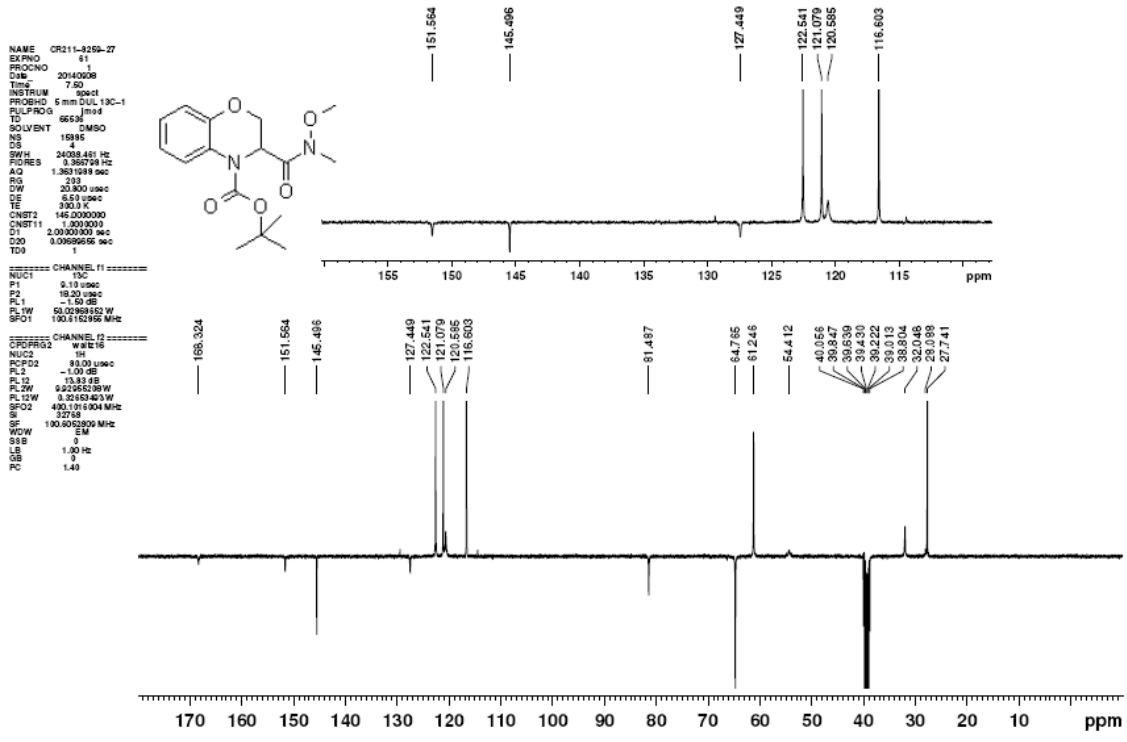
^{1}H NMR spectrum (400MHz, DMSO-d_6) of compound 14a



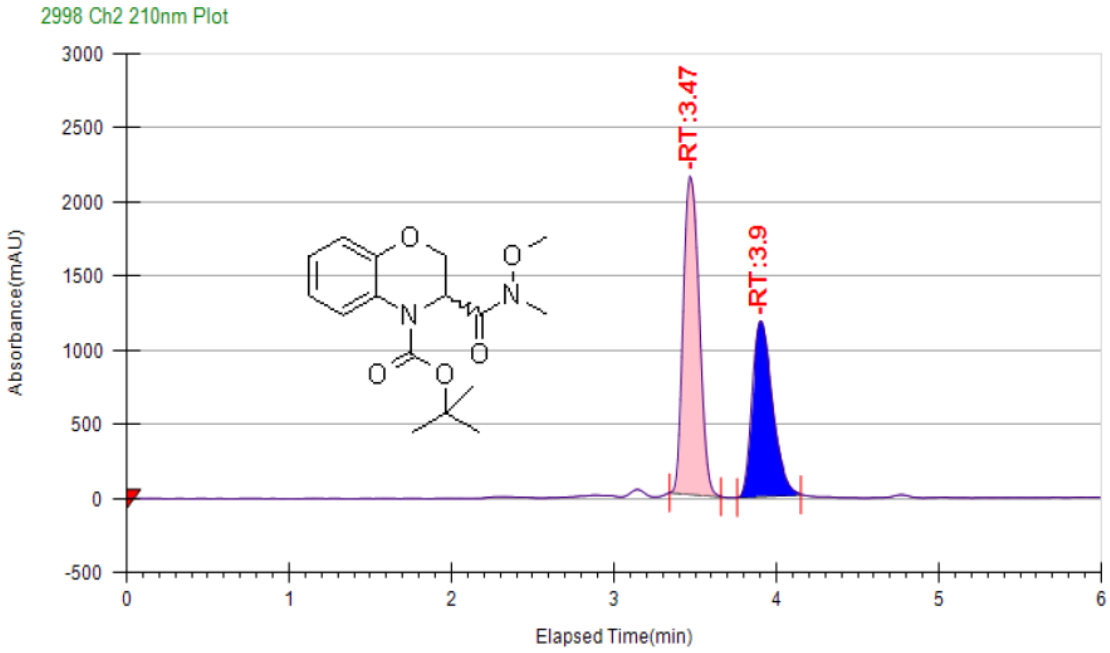
LCMS spectrum of compound 14a



^{13}C NMR spectrum (100MHz, DMSO-d_6) of compound 14a



APT NMR spectrum (100MHz, DMSO-d_6) of compound 14a



General Information

Log Author	Log Date	Report By	Report Date	Notes
Waters	10/13/2014 10:52:58 AM	Default User	10/13/2014	

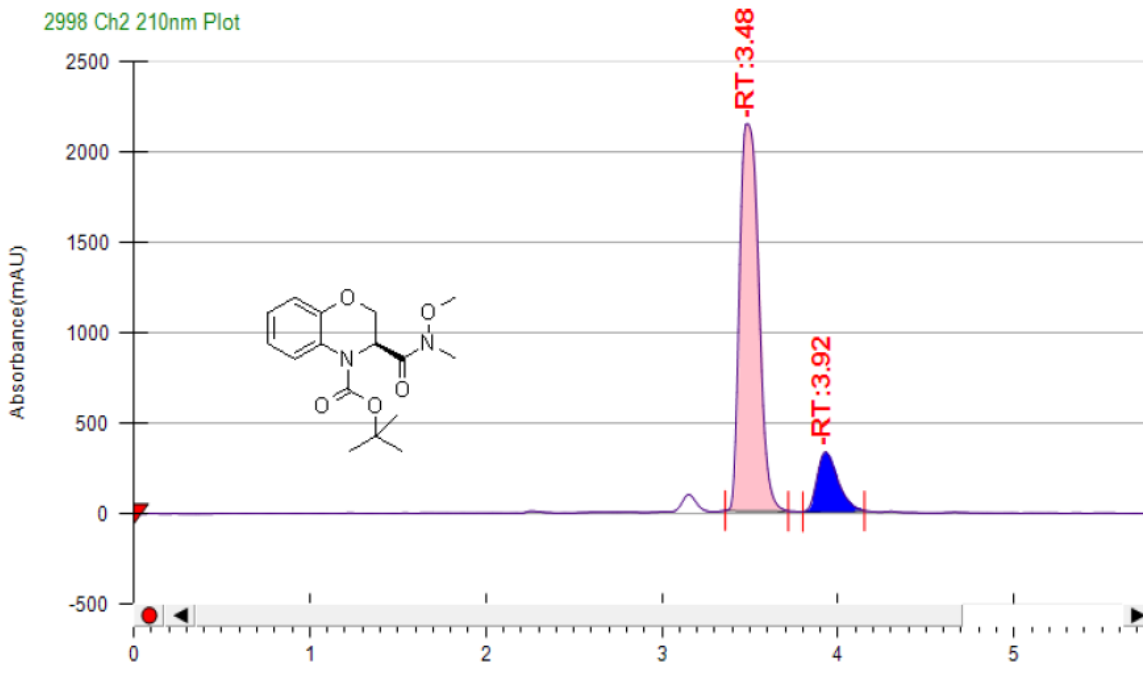
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-35	10	MEOH	IE	CR211-8259-28(D+L)	14B	35	2	35	120

Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	58.5066	14287.5978	3.47 min	2147.3801	0
2	41.4934	10132.8952	3.9 min	1185.3585	0

Chiral HPLC of a mixture of D- and L-isomer of compound 14a prepared by external mixing (not racemic mixture)



General Information

Log Author	Log Date	Report By	Report Date	Notes
Waters	10/13/2014 11:12:24 AM	Default User	10/13/2014	

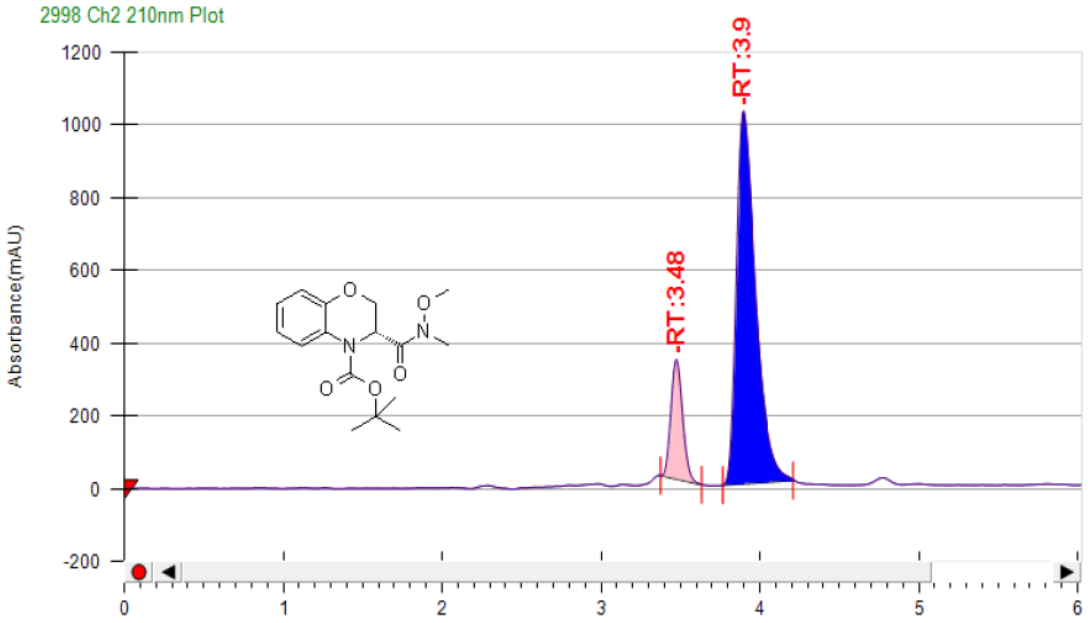
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-35	10	MEOH	IE	CR211-8259-28L	15D	35	2	35	120

Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	85.6812	15834.2896	3.48 min	2139.2609	0
2	14.3188	2646.1799	3.92 min	328.4731	0

Chiral HPLC of L-isomer 14a



General Information

Log Author	Log Date	Report By	Report Date	Notes
Waters	10/13/2014 11:02:41 AM	Default User	10/13/2014	

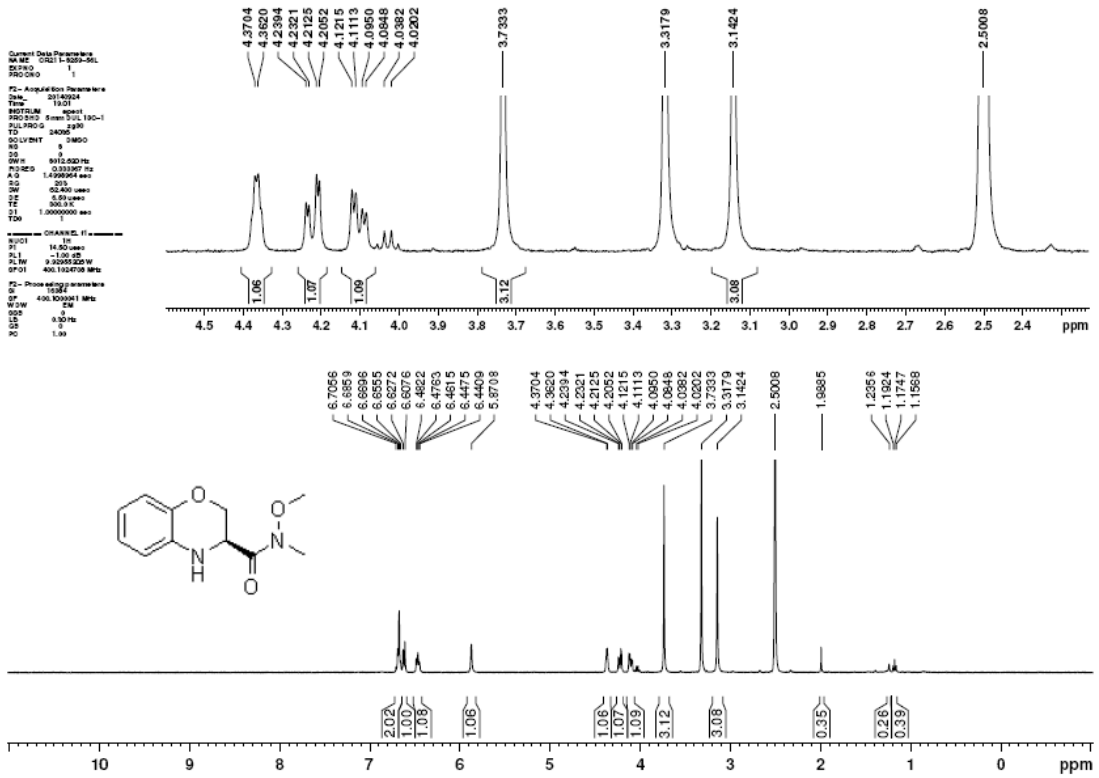
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-35	10	MEOH	IE	CR211-8259-28D	14D	35	2	35	120

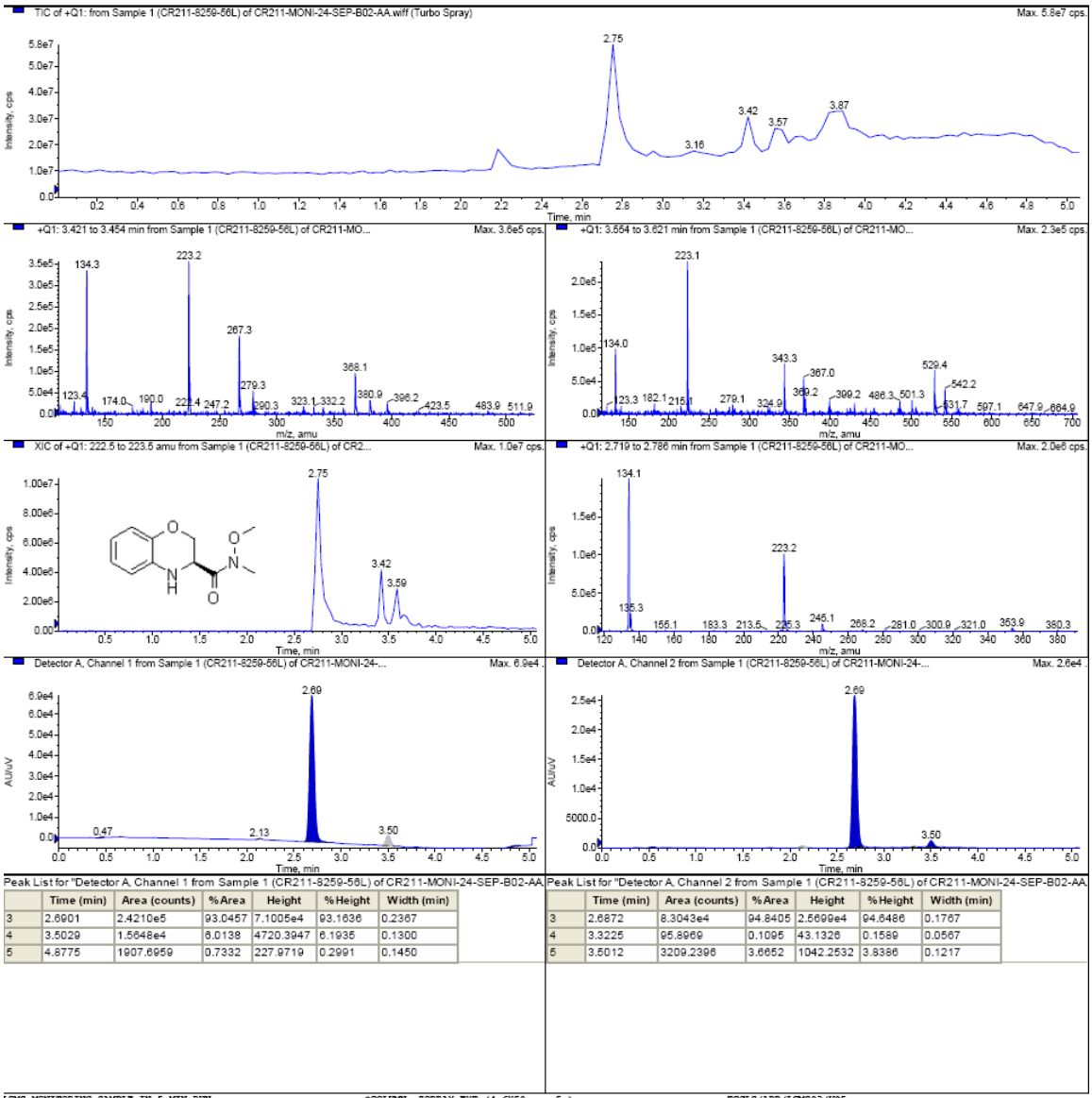
Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	16.1967	1632.3176	3.48 min	329.2397	0
2	83.8033	8445.7415	3.9 min	1025.4338	0

Chiral HPLC of D-isomer 14a



-^{1}H NMR spectrum (400MHz, DMSO d_6) of compound 18a



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-8259-56L) of CR211-MONI-24-SEP-B02-AA.

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)
3	2.6901	2.4210e5	93.0457	7.1005e4	93.1636	0.2367
4	3.5029	1.5648e4	6.0138	4720.3947	6.1935	0.1300
5	4.8775	1907.6959	0.7332	227.9719	0.2991	0.1450

Peak List for "Detector A, Channel 2 from Sample 1 (CR211-8259-56L) of CR211-MONI-24-SEP-B02-AA.

	Time (min)	Area (counts)	%Area	Height	%Height	Width (min)
3	2.6872	8.3043e4	94.8405	2.5699e4	94.6486	0.1767
4	3.3225	95.8969	0.1095	43.1326	0.1589	0.0567
5	3.5012	3209.2396	3.6652	1042.2532	3.8386	0.1217

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN- SORBAX EXT (4.6X50mm , 5u)
ACN:NH4OAc

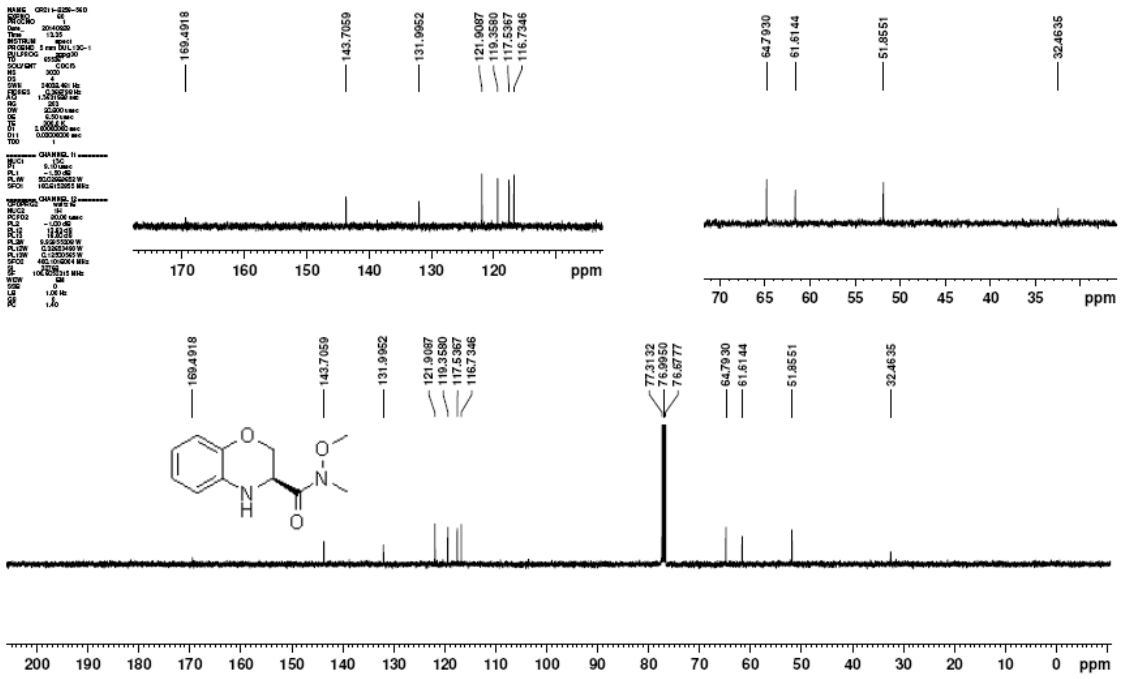
TCGLS/ARD/LCMS03/K05

Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

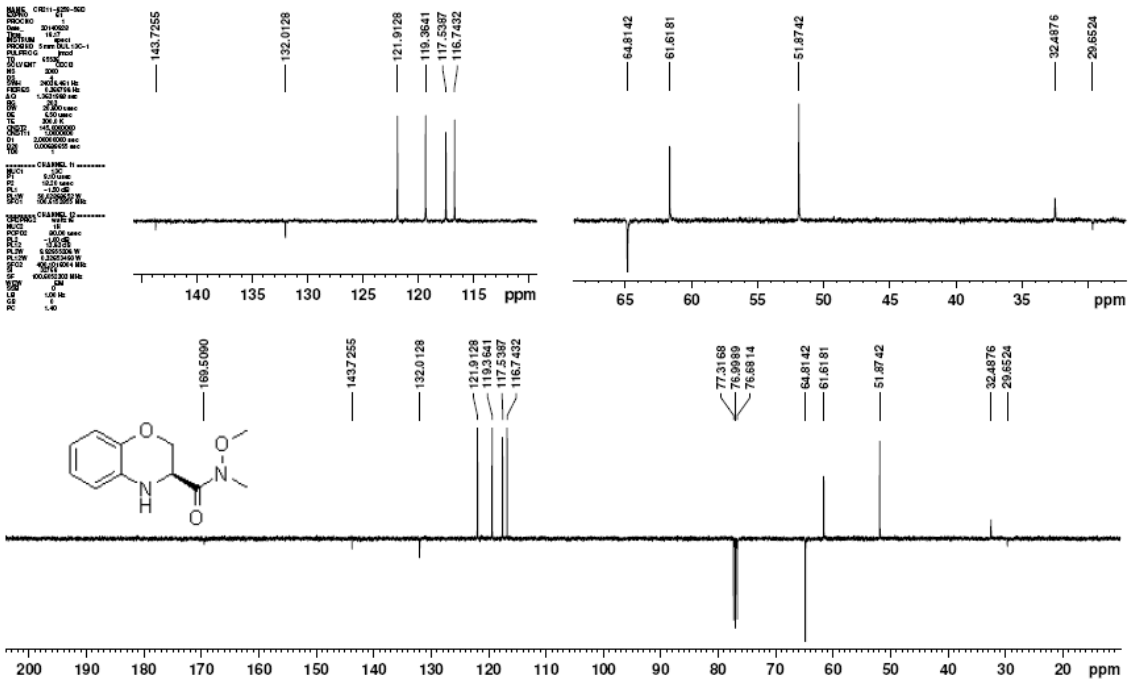
Analysed By

Checked By

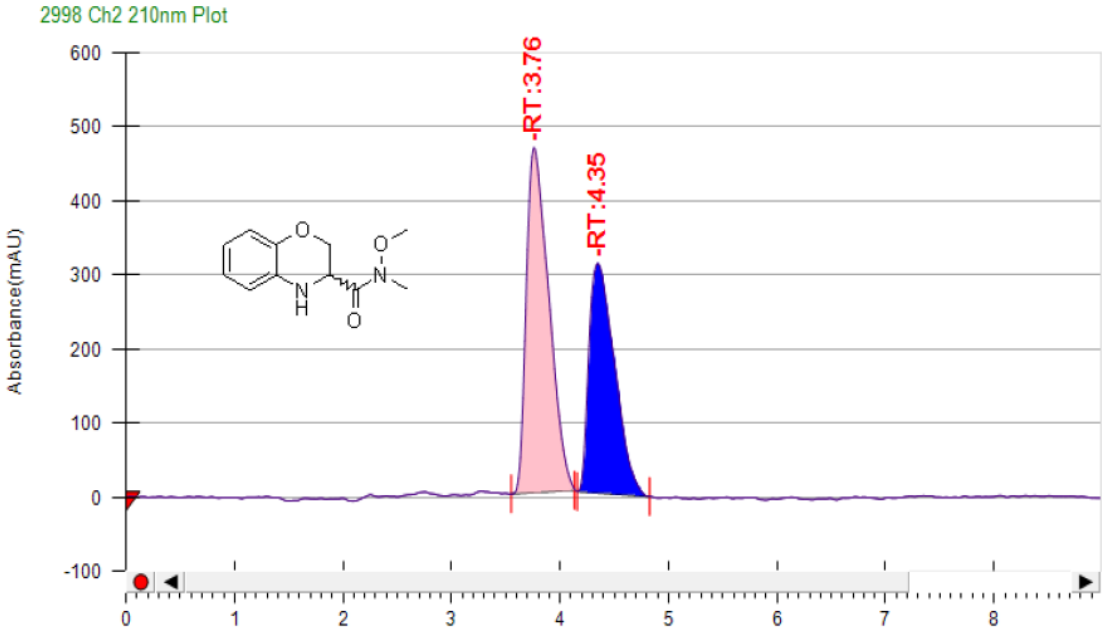
LCMS spectrum of compound 18a



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 18a



APT NMR spectrum (100MHz, $CDCl_3$) of compound 18a



General Information

Log Author	Log Date	Report By	Report Date	Notes
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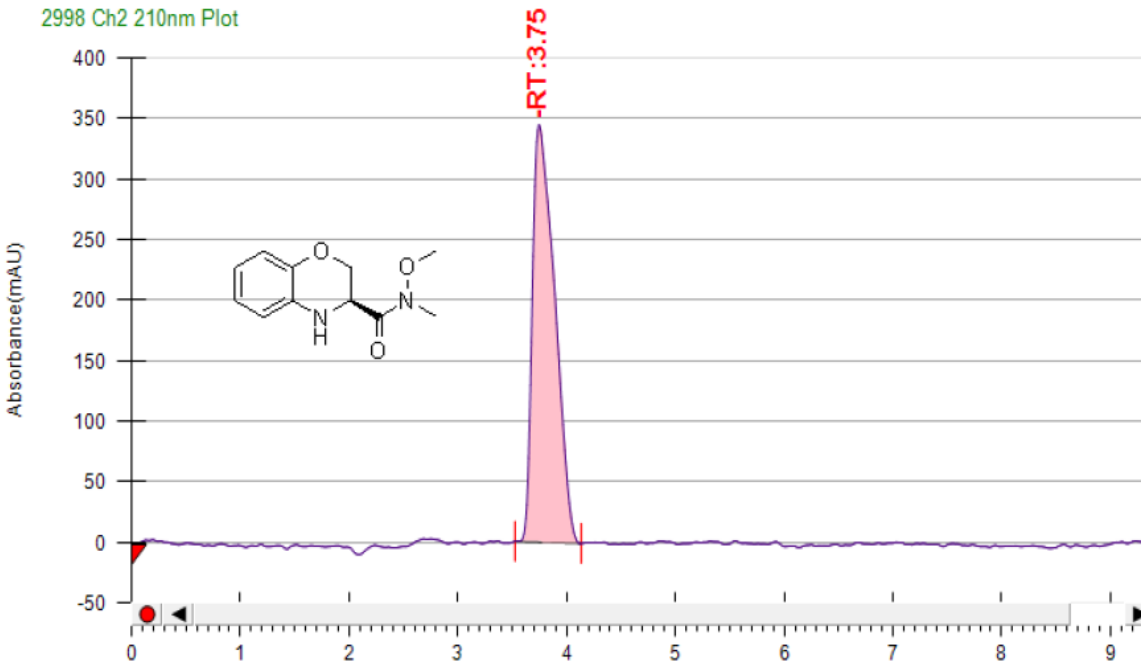
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-25	10	MEOH	CELLULOSE-1	CR211-8259-70-RAC	12C	35.2	2	25	80

Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	56.8055	6612.1758	3.76 min	465.6584	0
2	43.1945	5027.8524	4.35 min	309.8057	0

Chiral HPLC of manual mixture of (D+L) isomers 18a



General Information

Log Author	Log Date	Report By	Report Date	Notes
Waters	10/8/2014 5:11:14 PM	Default User	10/8/2014	

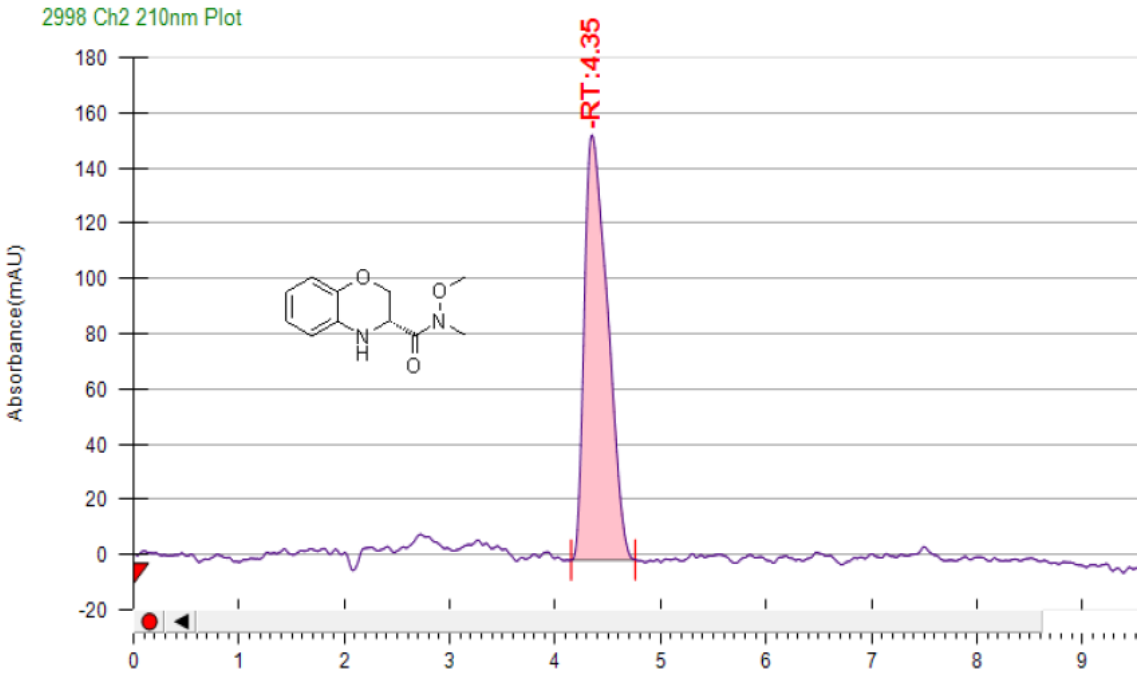
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-25	10	MEOH	CELLULOSE-1	CR211-8259-70L	14C	35.1	2	25	80

Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	100	4831.0649	3.75 min	344.2187	3749

Chiral HPLC of L-isomer 18a



General Information

Log Author	Log Date	Report By	Report Date	Notes
Waters	10/8/2014 4:58:32 PM	Default User	10/8/2014	

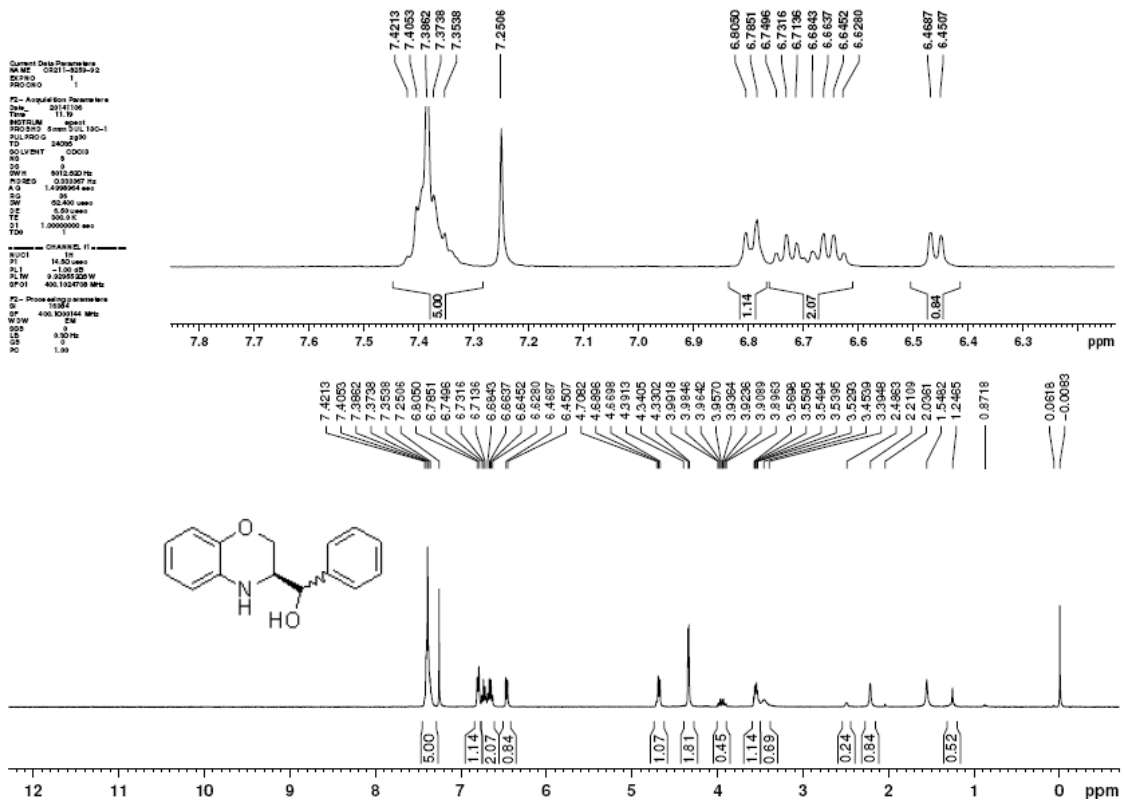
Run Information

Instrument Method	Inj. Vol.	Solvent	Column	Sample	Well Location	Temp.	Flow	% Modifier	Pressure
M-2-25	10	MEOH	CELLULOSE-1	CR211-8259-70D	13C	34.8	2	25	80

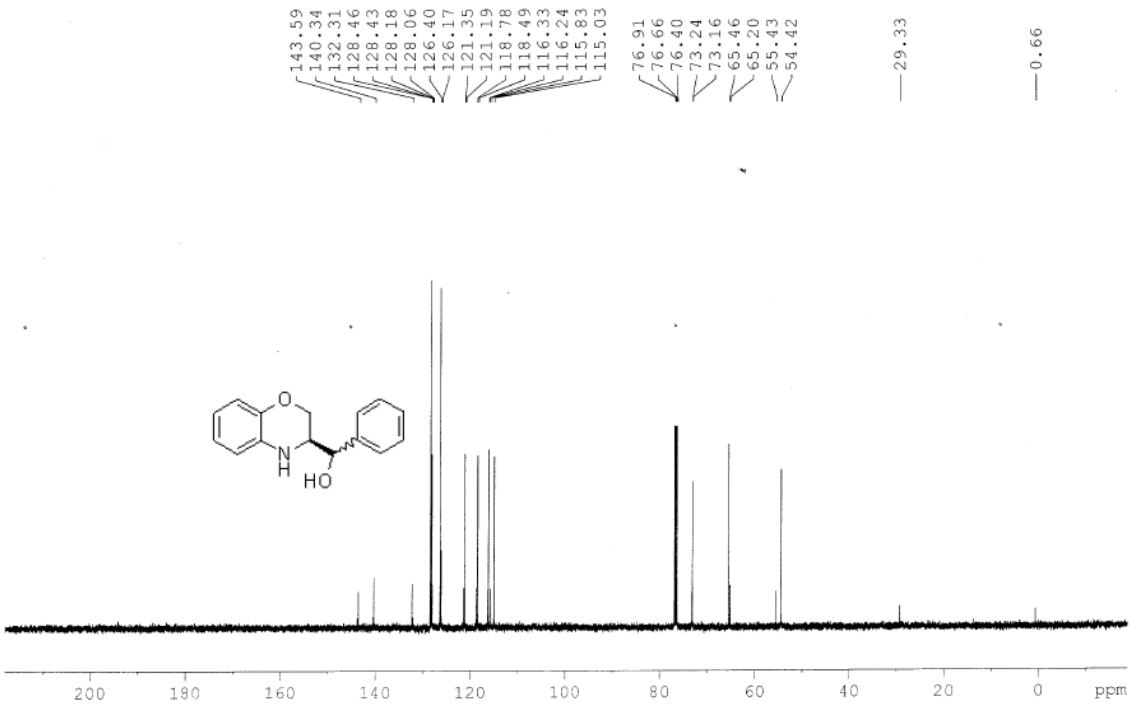
Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	100	2324.0992	4.35 min	153.8755	0

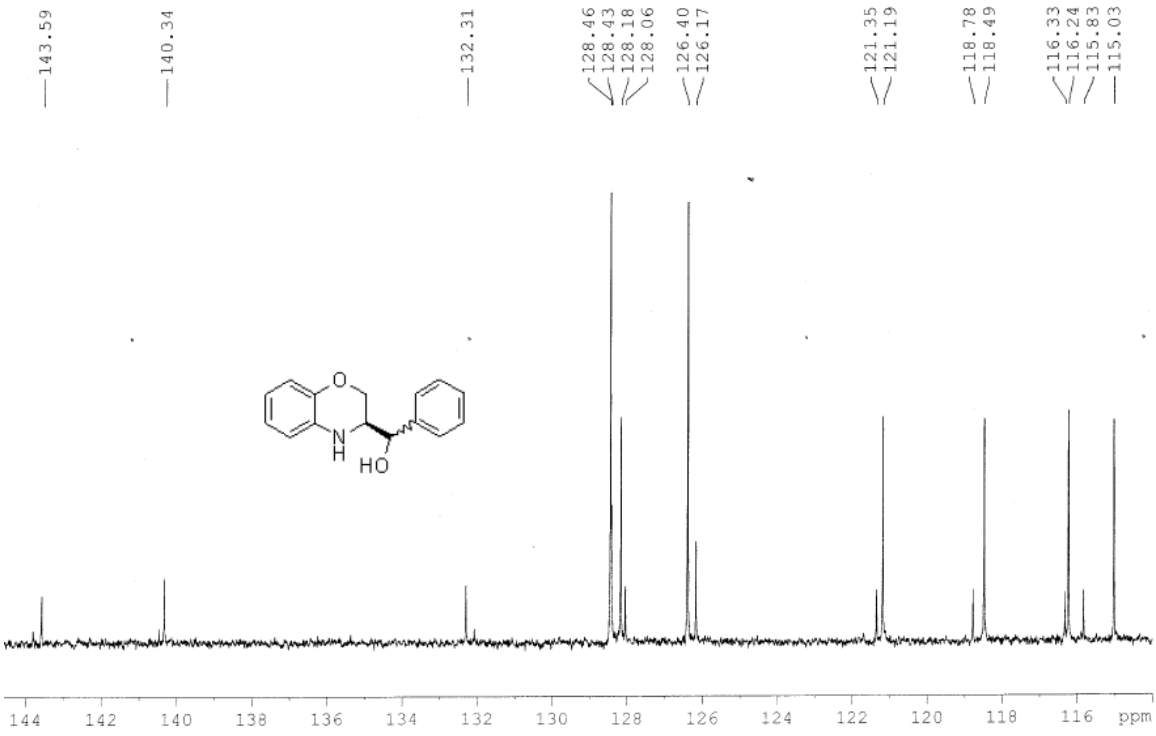
Chiral HPLC of D-isomer 18a



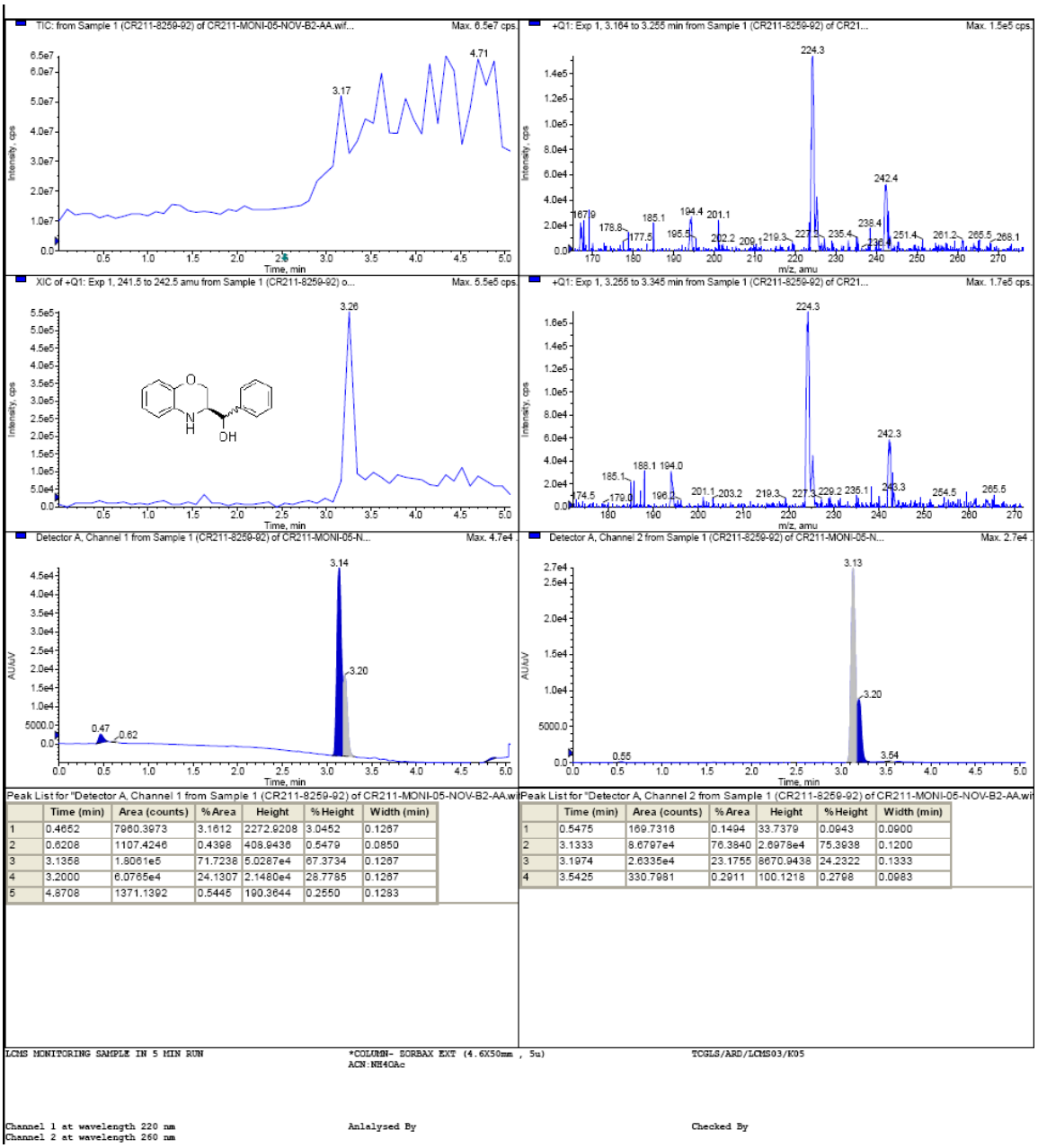
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 20a



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 20a



Expansion of ^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 20a



	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.4652	7960.3973	3.1612	2272.9208	3.0452	0.1267
2	0.6208	1107.4246	0.4398	408.9436	0.5479	0.0850
3	3.1358	1.8061e5	71.7238	5.0287e4	67.3734	0.1267
4	3.2000	6.0765e4	24.1307	2.1480e4	28.7785	0.1267
5	4.8708	1371.1392	0.5445	190.3644	0.2550	0.1283

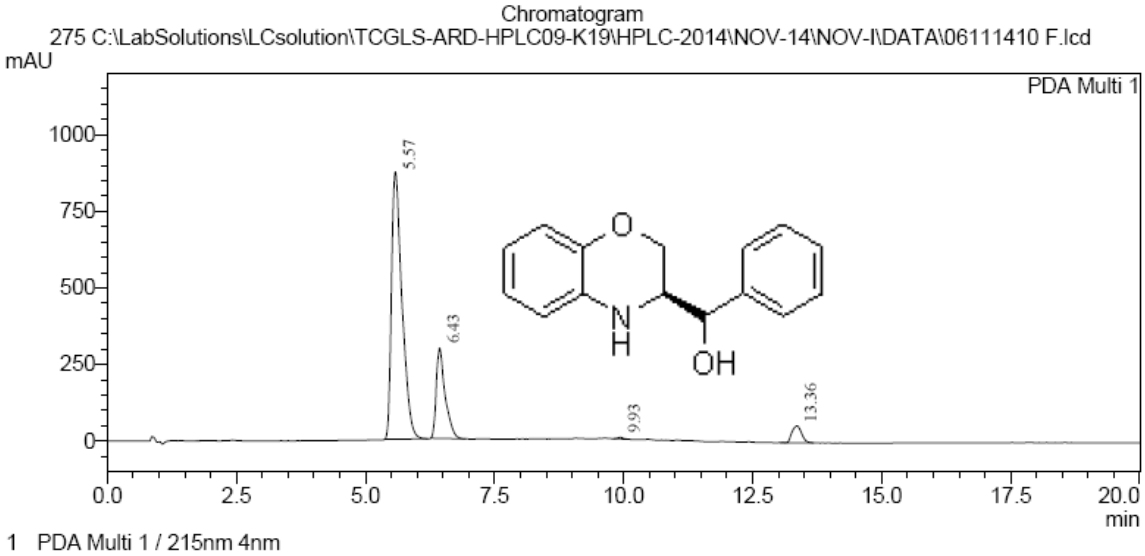
	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.5475	169.7316	0.1494	33.7379	0.0943	0.0900
2	3.1333	8.6797e4	76.3840	2.6978e4	75.3938	0.1200
3	3.1974	2.6335e4	23.1755	8670.9438	24.2322	0.1333
4	3.5425	330.7981	0.2911	100.1218	0.2798	0.0983

LCMS spectrum of compound 20a

C:\LabSolutions\LCsolution\TCGLS-ARD-HPLC09-K19\HPLC-2014\NOV-14\NOV-I\DATA\06111410 F.lcd

Method File Name	: NPR150-AA_50_1.lcm	Sample Name	: CR211-8259-92
Data File Name	: 06111410 F.lcd	Tray#	: 1
Acquired by	: Sushovan Ghatak	Vail #	: 13
Data Acquired	: 11/6/2014 2:36:33 PM	Inj Volume	: 2 uL
Data Processed	: 11/6/2014 3:32:54 PM	Column	: GEMINI NX C-18 (100x4.6mm)5u
Ref.No	: SG/06.11.14/275	Mobile phase-A	: ACN
		Mobile phase-C	: 10mM NH4OAC in water
		Diluent	: ACN

<Chromatogram>



1 PDA Multi 1 / 215nm 4nm

PeakTable

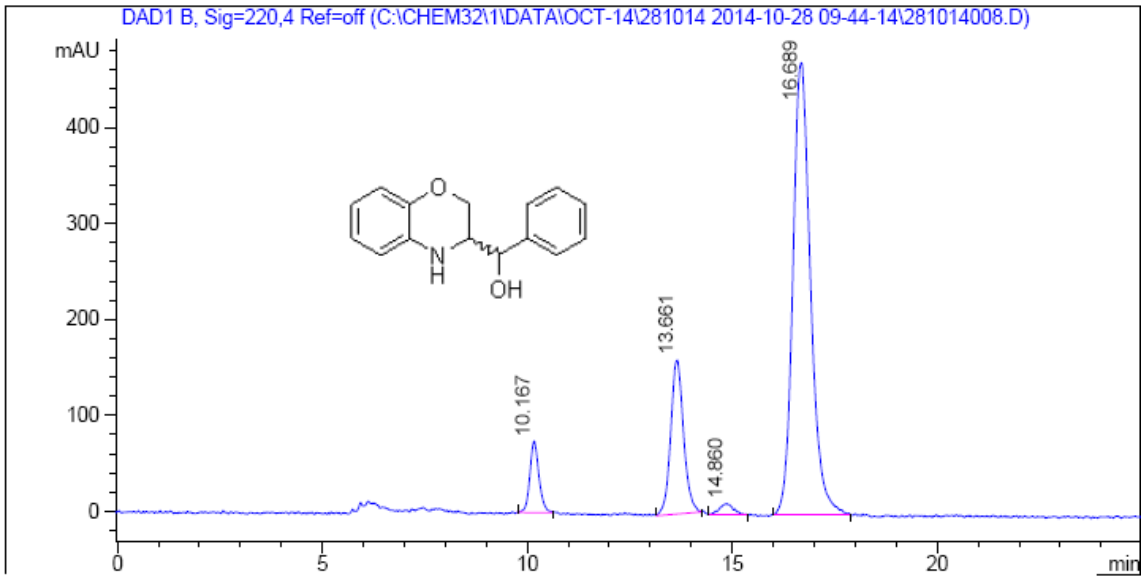
PDA Ch1 215nm 4nm

Peak#	Ret. Time	Area	Area %
1	5.57	12373636	74.26
2	6.43	3543196	21.26
3	9.93	39181	0.24
4	13.36	706740	4.24
Total		16662753	100.00

HPLC Purity of compound 20a

```
                                                        Seq Line->    8
                                                Location   :     Vial 27
Acq Operator     : KONDABABU                    Inj. No.   :          1
  Injection Date: 10/28/2014                    Inj. Vol.  :        5 µl
Acq. Method      : C:\Chem32\1\DATA\OCT-14\281014 2014-10-28 09-44-14\C.M
Analysis Method : C:\CHEM32\1\METHODS\100-ETOH.M
Last Changed     : Tue, 28. Oct. 2014, 01:51:05 pm
                   (modified after loading)
Sample ID :CR211-8259-85-Racemic

Column name:YMC Amylose-C(4.6x250mm) 5µ ,
ARD/K/7787
Mobile Phase : EtOH:100
Flow rate : 0.5 ml/min ,
Slubility : MeOH                                                    ->
                                                Ref : KD/28.10.14/1138
```



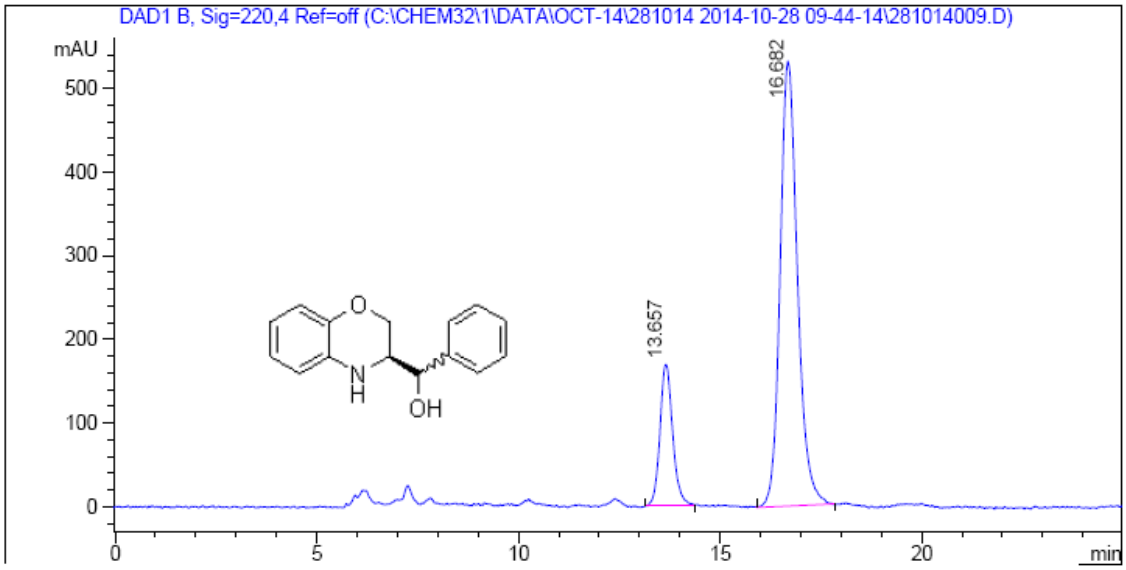

```
Signal  1: DAD1 B, Sig=220,4 Ref=off

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|     10.17|   1153.65|      6.05|
|   2|     13.66|   3497.58|     18.35|
|   3|     14.86|    278.25|      1.46|
|   4|     16.69|  14127.36|     74.13|
---------------------------------------
```

Chiral HPLC of epimeric mixture of (D+L) isomers of 20a

```
                                                    Location   :      Vial 28
Acq Operator     : KONDABABU                        Inj. No.   :           1
  Injection Date: 10/28/2014                        Inj. Vol.  :         5 µl
Acq. Method      : C:\Chem32\1\DATA\OCT-14\281014 2014-10-28 09-44-14\C.M
Analysis Method  : C:\CHEM32\1\METHODS\100-ETOH.M
Last Changed     : Tue, 28. Oct. 2014, 01:51:05 pm
                   (modified after loading)
Sample ID :CR211-8259-85L

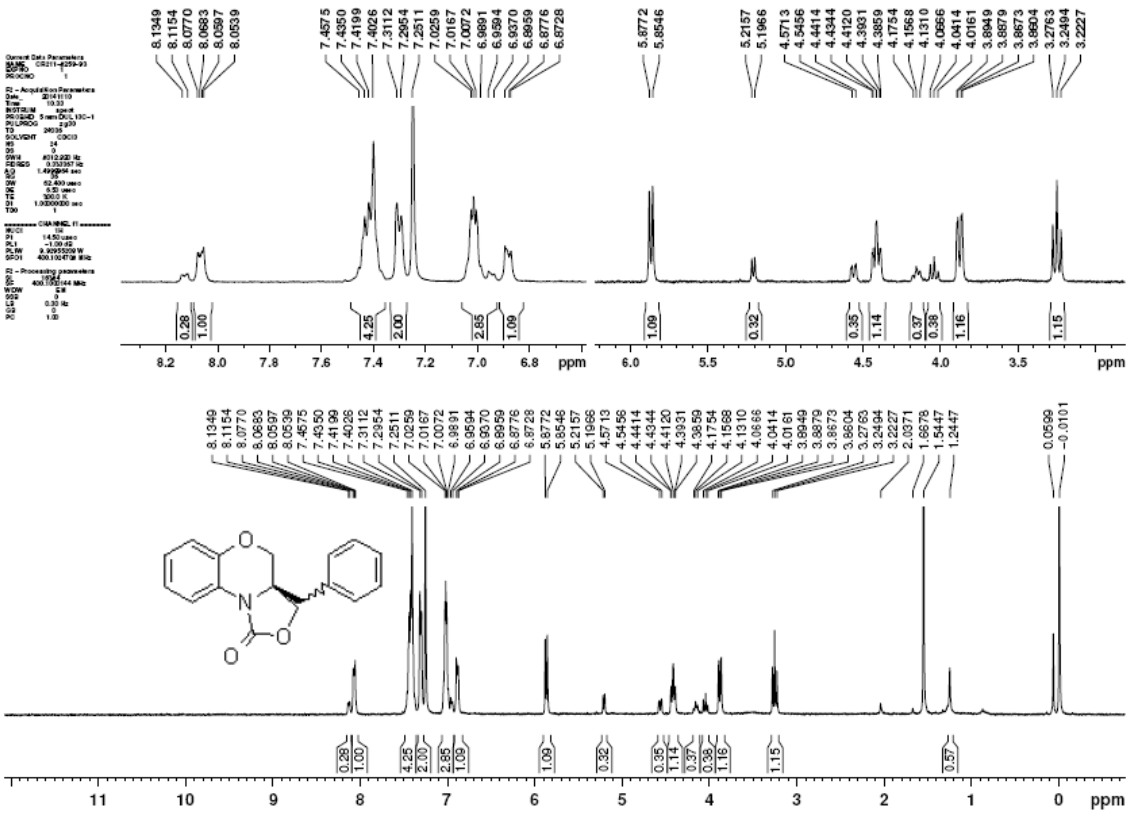
Column name:YMC Amylose-C(4.6x250mm) 5µ ,
ARD/K/7787
Mobile Phase : EtOH:100
Flow rate : 0.5 ml/min ,
Slubility : MeOH                                                          ->
                                                    Ref : KD/28.10.14/1139
```



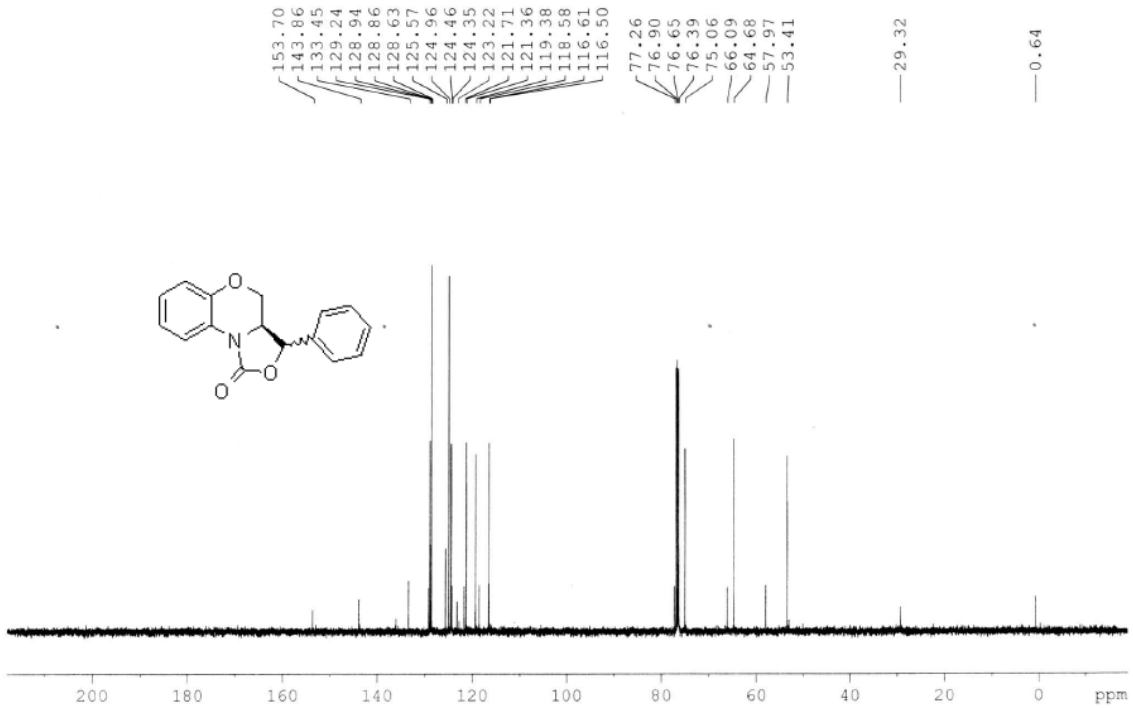

```
Signal  1: DAD1 B, Sig=220,4 Ref=off

|Peak|   RT     |   Area    |  Area %  |
| #  |  [min]   |-----------|----------|
|----|----------|           |          |
|   1|     13.66|   3671.87|     18.79|
|   2|     16.68|  15871.83|     81.21|
---------------------------------------
```

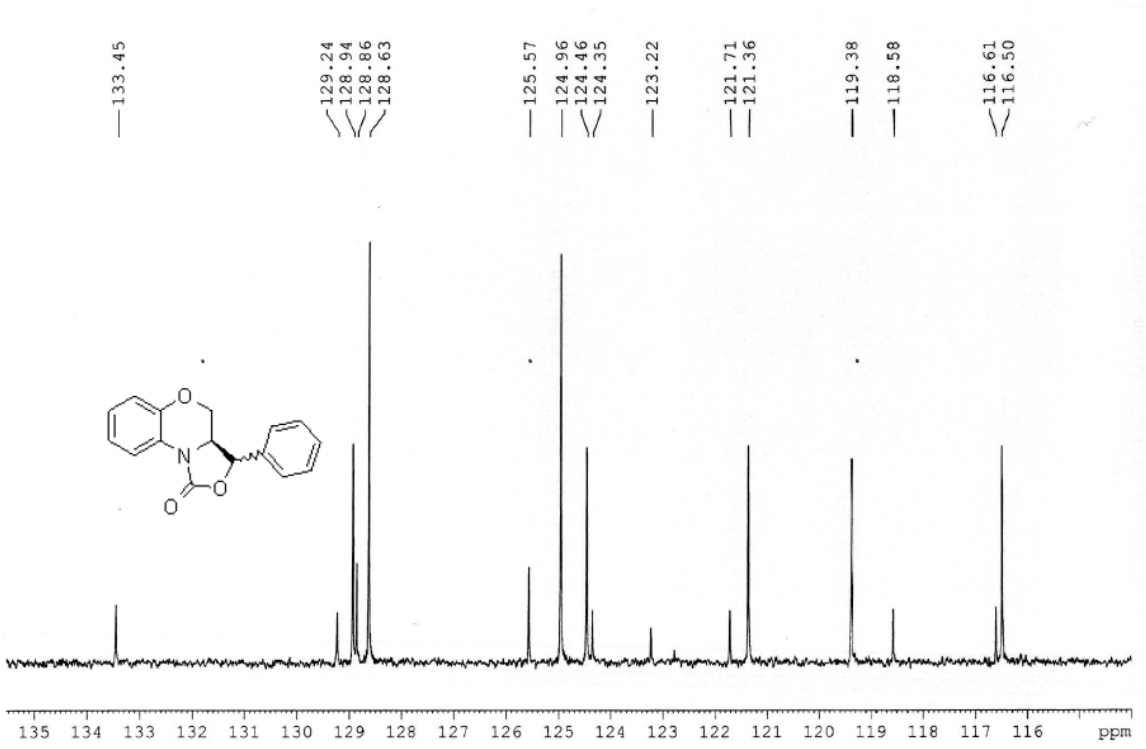
Chiral HPLC of L-isomer 20a



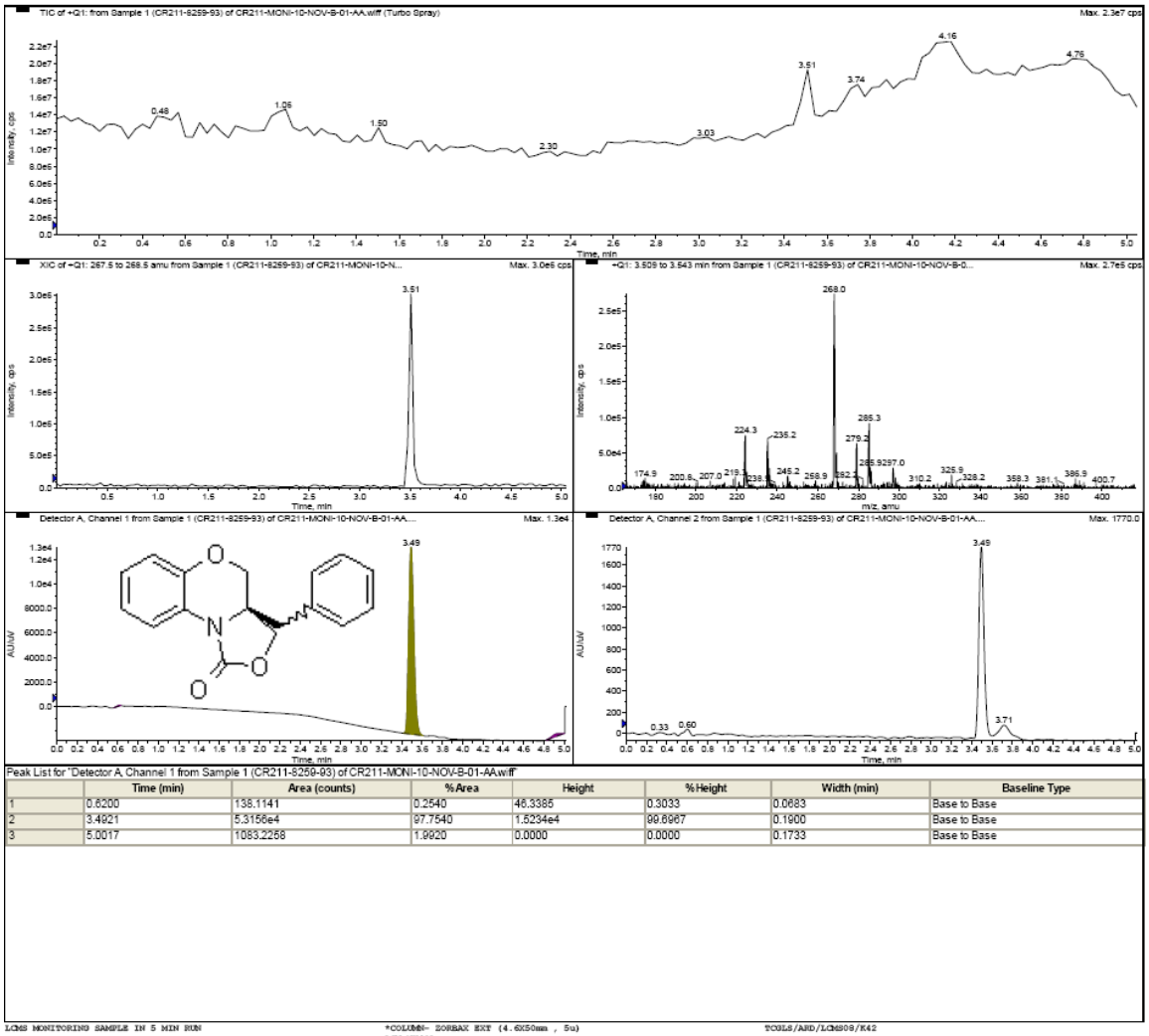
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 21a



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 21a



Expansion of ^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 21a



Peak List for "Detector A, Channel 1 from Sample 1 (CR211-8259-93) of CR211-MONI-10-NOV-B-01-AA.wiff"

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)	Baseline Type
1	0.6200	138.1141	0.2540	46.3385	0.3033	0.0683	Base to Base
2	3.4921	5.3156e4	97.7540	1.5234e4	99.6967	0.1900	Base to Base
3	5.0017	1083.2258	1.9920	0.0000	0.0000	0.1733	Base to Base

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN- ZORBAX EXT (4.6X50mm , 5u)
ACN:NH4OAc

TCGLS/ARD/LCMS09/K42

Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

Analysed By

Checked By

LCMS spectrum of compound 21a

```
Column Name:Poroshell 120 EC-C-18 (100*4.6 mm)2.7µ,Dilu
ent:MEOH
Mobile Phase-A1:0.05%TFA in WATER,-B1:ACN,Flow:1.0mL/mi                    ->
Injection Date  : Mon, 10. Nov. 2014 11:45:46   Location   :    Vial 82
Sample Name     : CR211-8259-93                       Inj. No.->        1
Acq Operator    : PRIYA                          Inj. Vol.  :       12 µl

Analysis Method : C:\CHEM32\1\METHODS\POLAR.M
Last Changed    : Mon, 10. Nov. 2014, 10:34:28 am
                  (modified after loading)

Acq. Method     : C:\CHEM32\1\DATA\2014\NOV-14\101114A 2014-11-10 09-30-
                  05\POLAR.M
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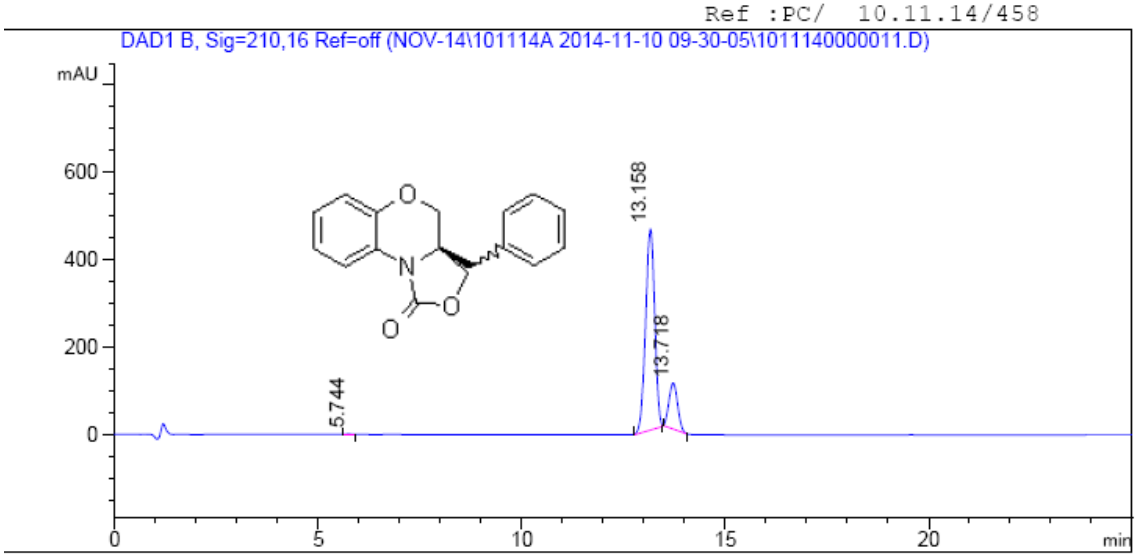
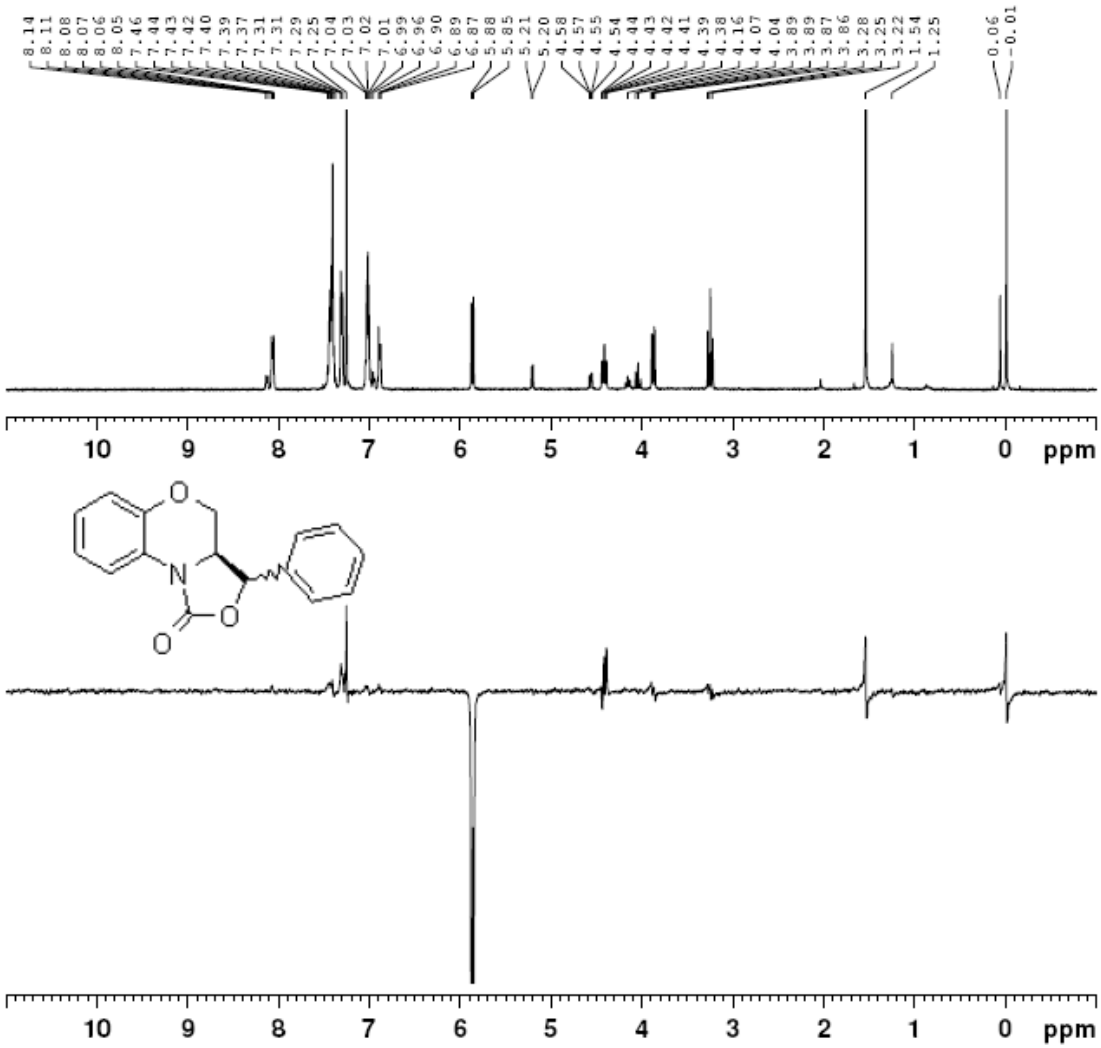
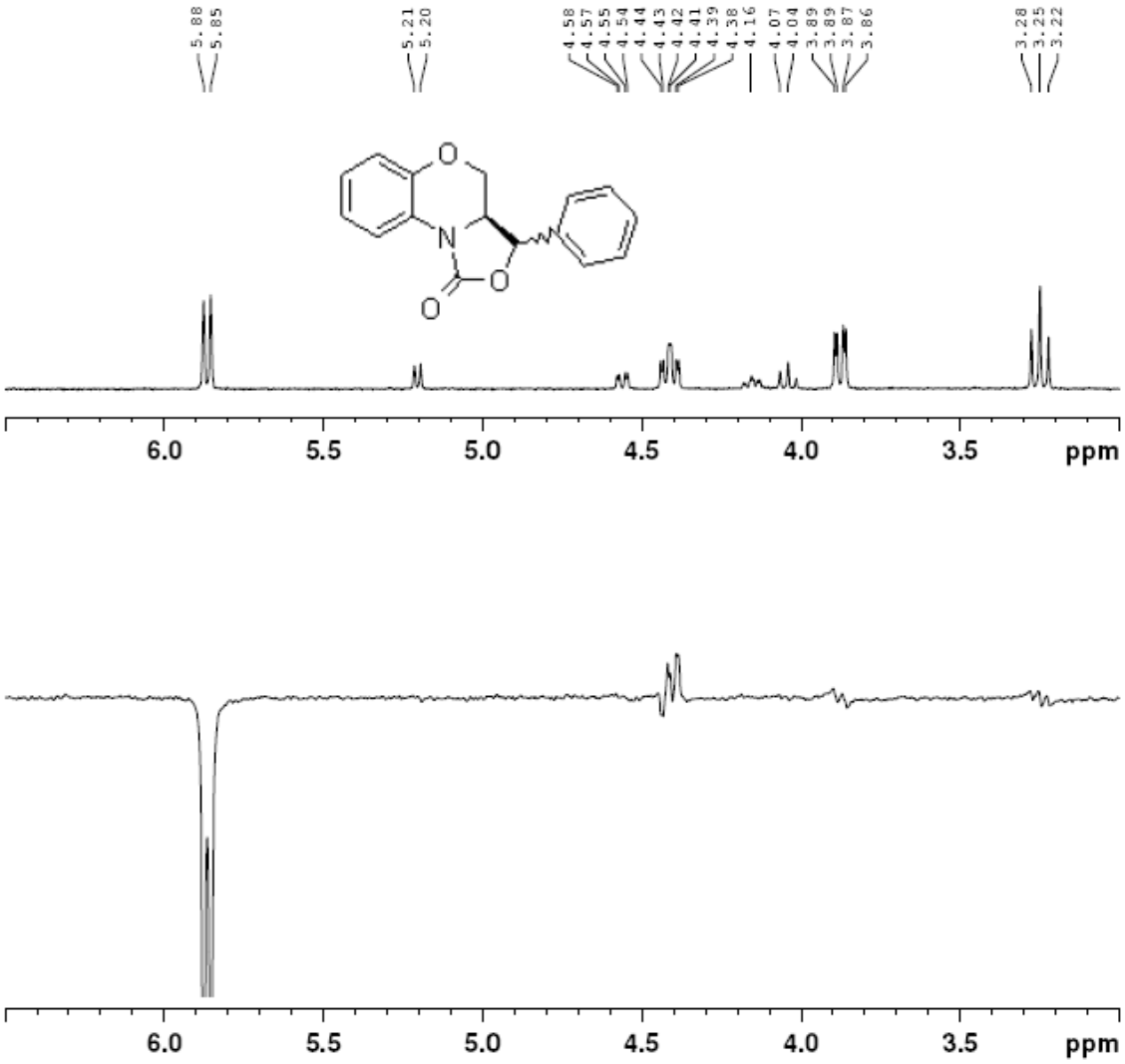



```
================================================================================

================================================================================
Signal  1 :DAD1 B, Sig=210,16 Ref=off

|Peak|   RT    |   Area    | Area % |
| #  |  [min]  |           |        |
|----|---------|-----------|--------|
|   1|     5.74|       8.48|    0.10|
|   2|    13.16|    7209.08|   82.14|
|   3|    13.72|    1558.91|   17.76|
-----------------------------------
================================================================================
                         *** End of Report ***
```

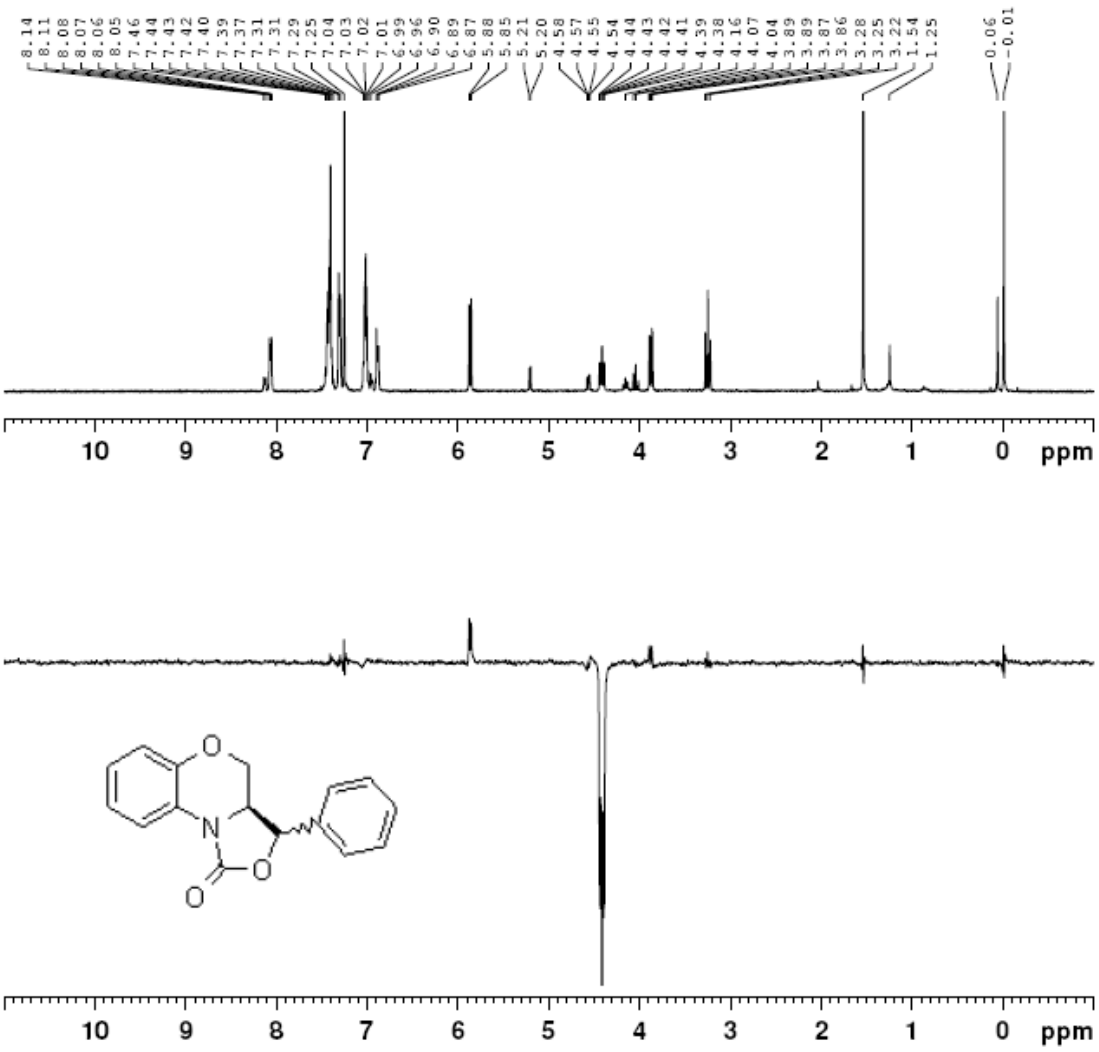
HPLC Purity of compound 21a



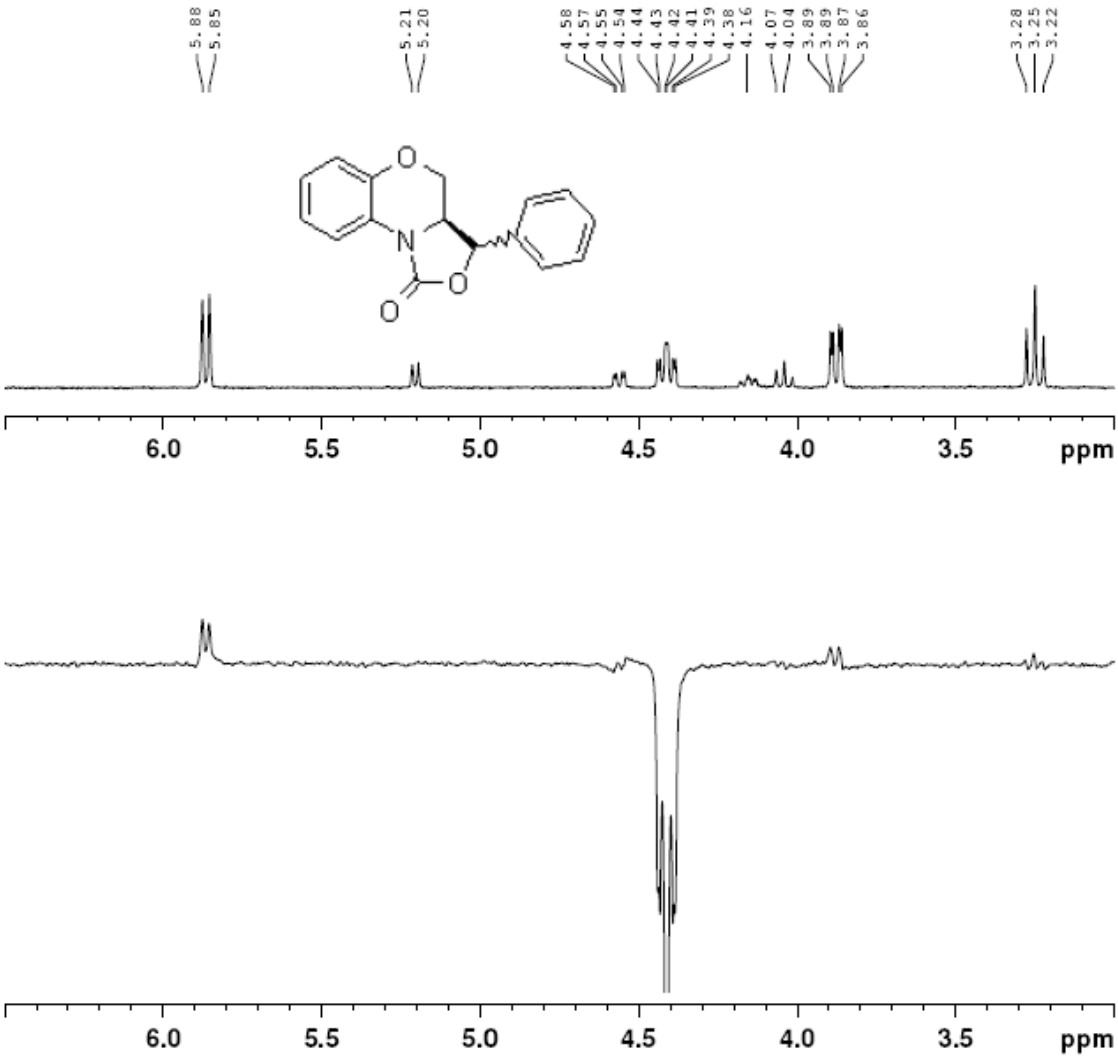
NOE1 of compound 21a



Expansion of NOE1 of compound 21a



NOE 2 of compound 21a



Expansion of NOE 2 of compound 21a