

Synthesis, characterization and *in vitro* evaluation of novel enantiomerically-pure sulphonamide antimalarials

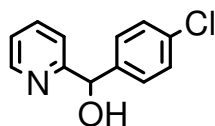
Sebastian Anusha^{1§}, Ameya Sinha^{2§}, Babu Rajeev C.P¹, Trang TT Chu², Jessin Mathai³, Huang Ximei⁴, Julian E Fuchs^{5,6}, NanjundaSwamy Shivanaju, Andreas Bender⁷, Peter Rainer Preiser⁴, Kanchugarakoppal S. Rangappa⁸, Basappa^{1*}, Rajesh Chandramohanadas^{2*}

Supplementary Information

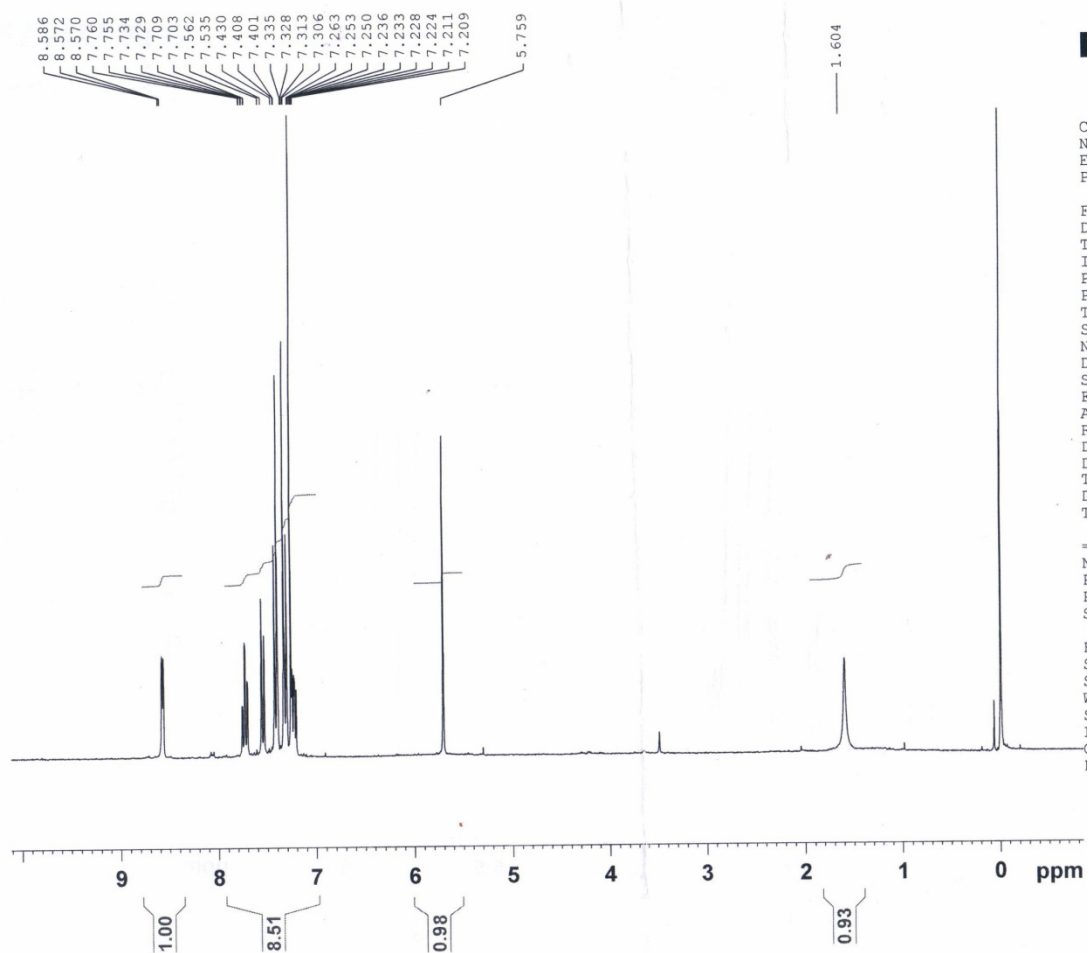
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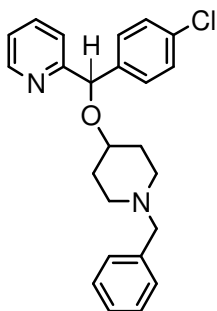
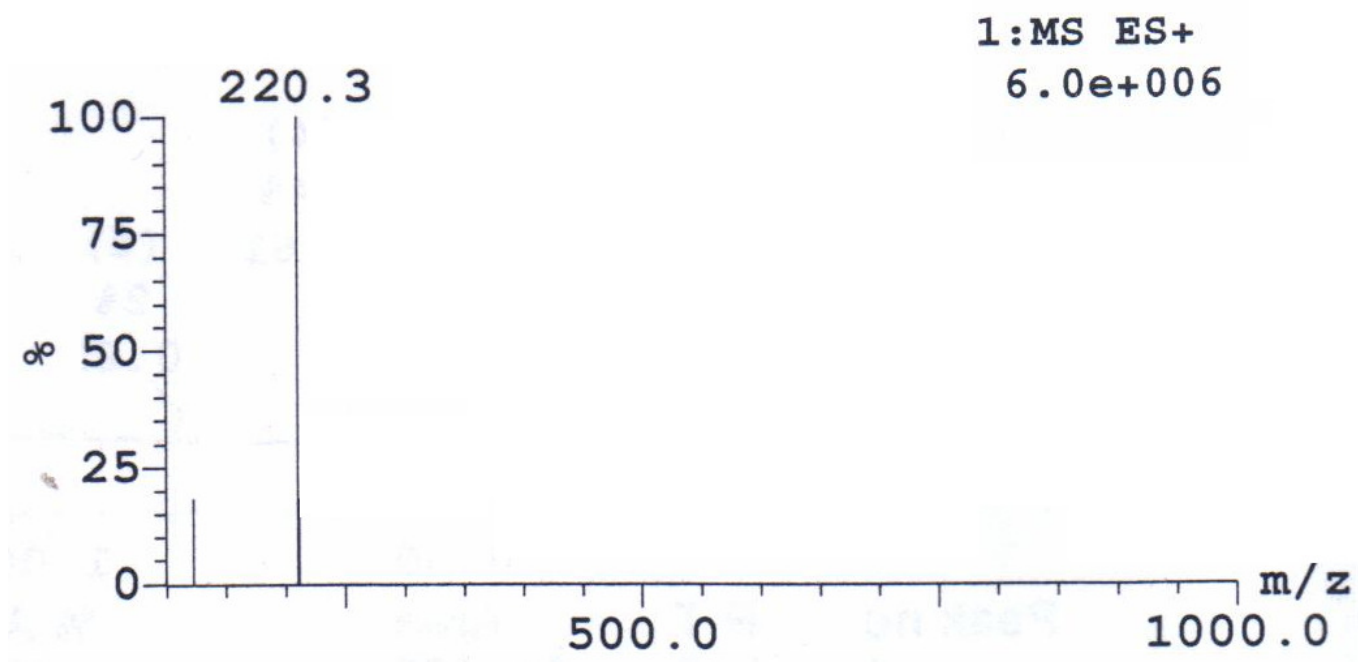
Spectral characterisation of compound 1.....	SI-01
Spectral characterisation of compound 3.....	SI-02
Spectral characterisation of compound 4.....	SI-03
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Spectral characterisation of compound 6p.....	SI-21
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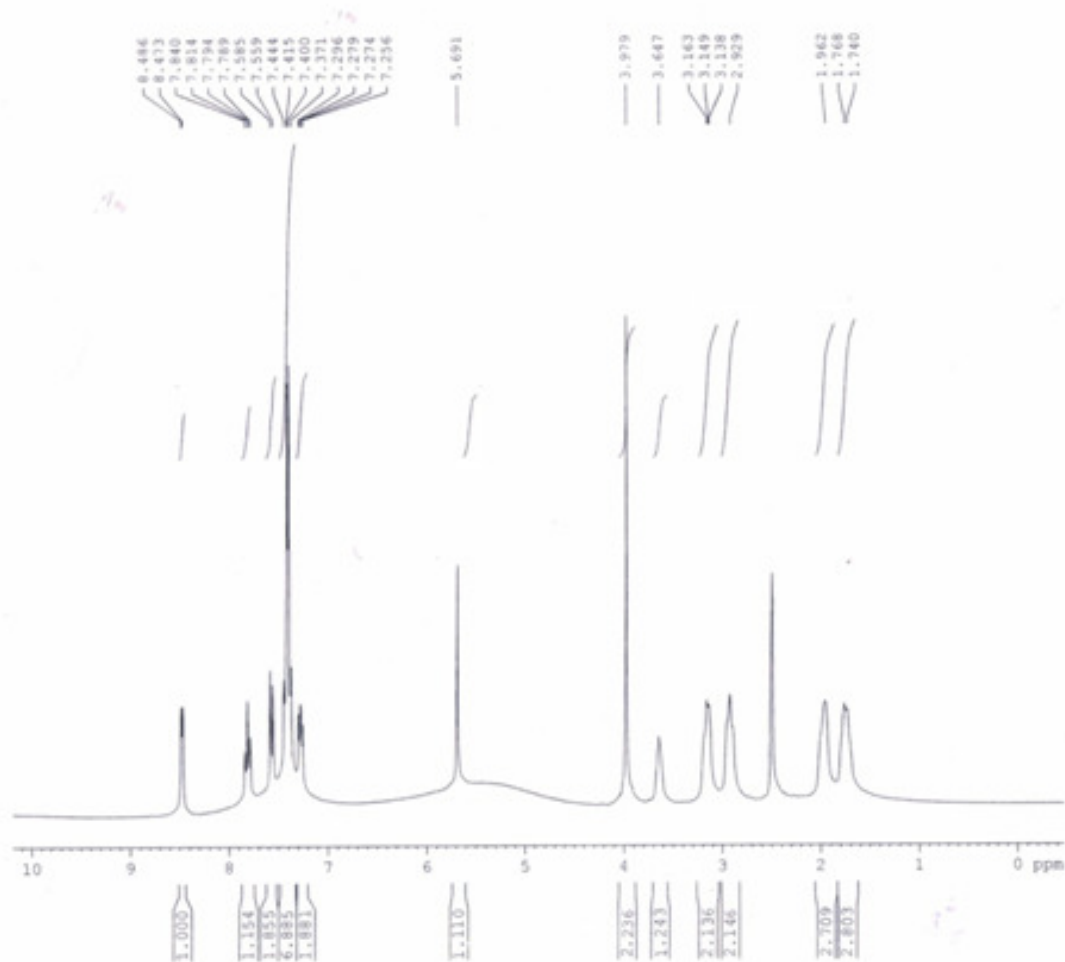


(4-chlorophenyl)methyl(pyridine-2-yl)methanol (1): Yield (6g, 86%) ¹H-NMR (300 MHz, CDCl₃) 8.58 (d, 1H), 8.57-7.20(m, 7H), 5.75 (s, 1H), 1.60(s, 1H); LCMS (MM:ES+APCI) 220.3(M+H)⁺ ; C₁₂H₁₀ClNO: C, 65.61; H, 4.59; N, 6.38; Found: C, 65.78; H, 4.69; N, 6.32;



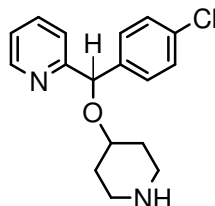
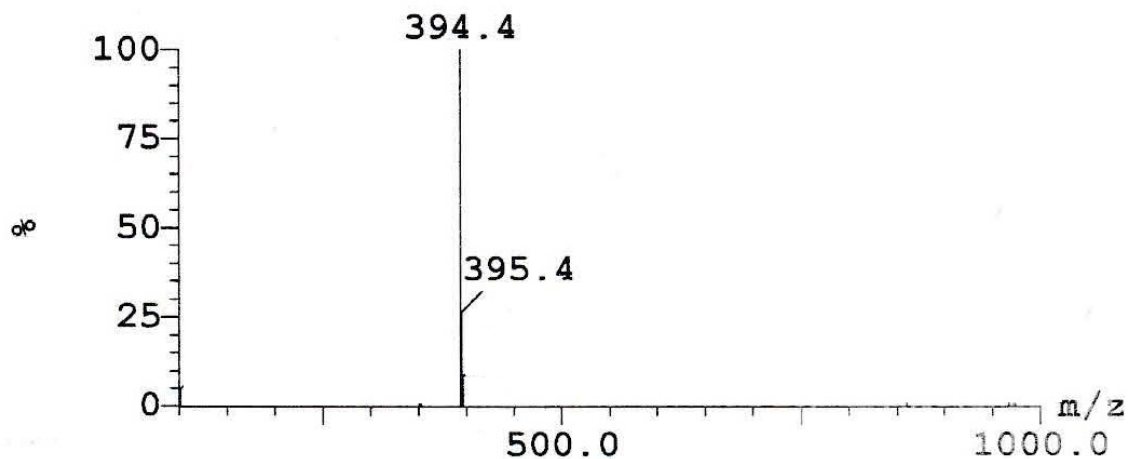


2-((1-benzylpiperidin-4-yloxy)(4-chlorophenyl)methyl)pyridine (3): Yield (8.1g, 90.8%).% ¹H-NMR (300 MHz, CDCl₃) 8.48-7.25 (m, 13H), 5.69(s, 1H), 3.97 (s, 2H), 3.64(m, 1H), 3.14(m, 2H), 2.92(m, 2H), 1.96(m, 2H), 1.74(m, 2H); LCMS (MM:ES+APCI) 394.4(M+H)⁺ ; Anal.Calcd for C₂₄H₂₅ClN₂O : C 73.36; H 6.41; N 7.13; Found: C, 73.26; H, 6.45; N, 7.16;

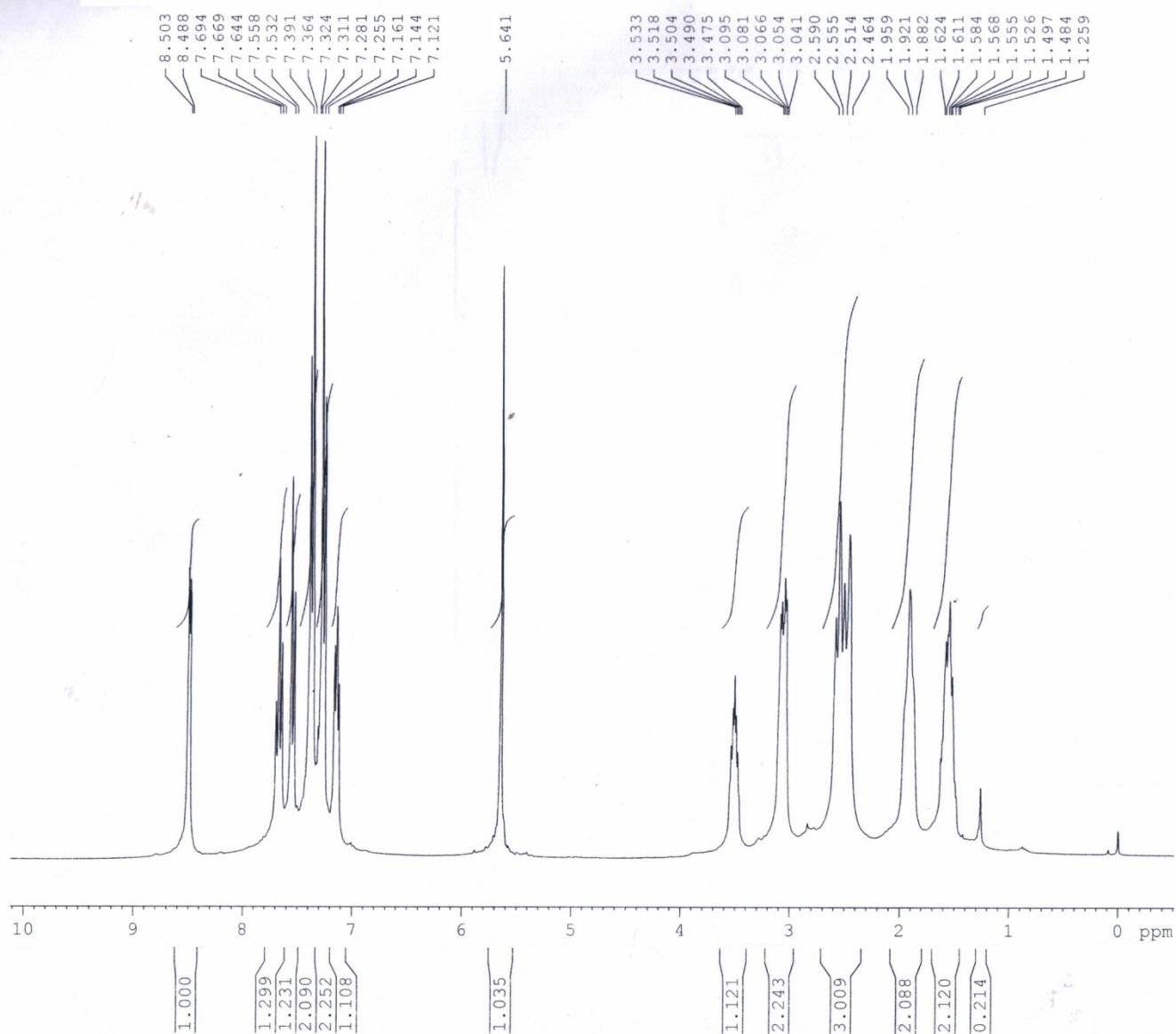


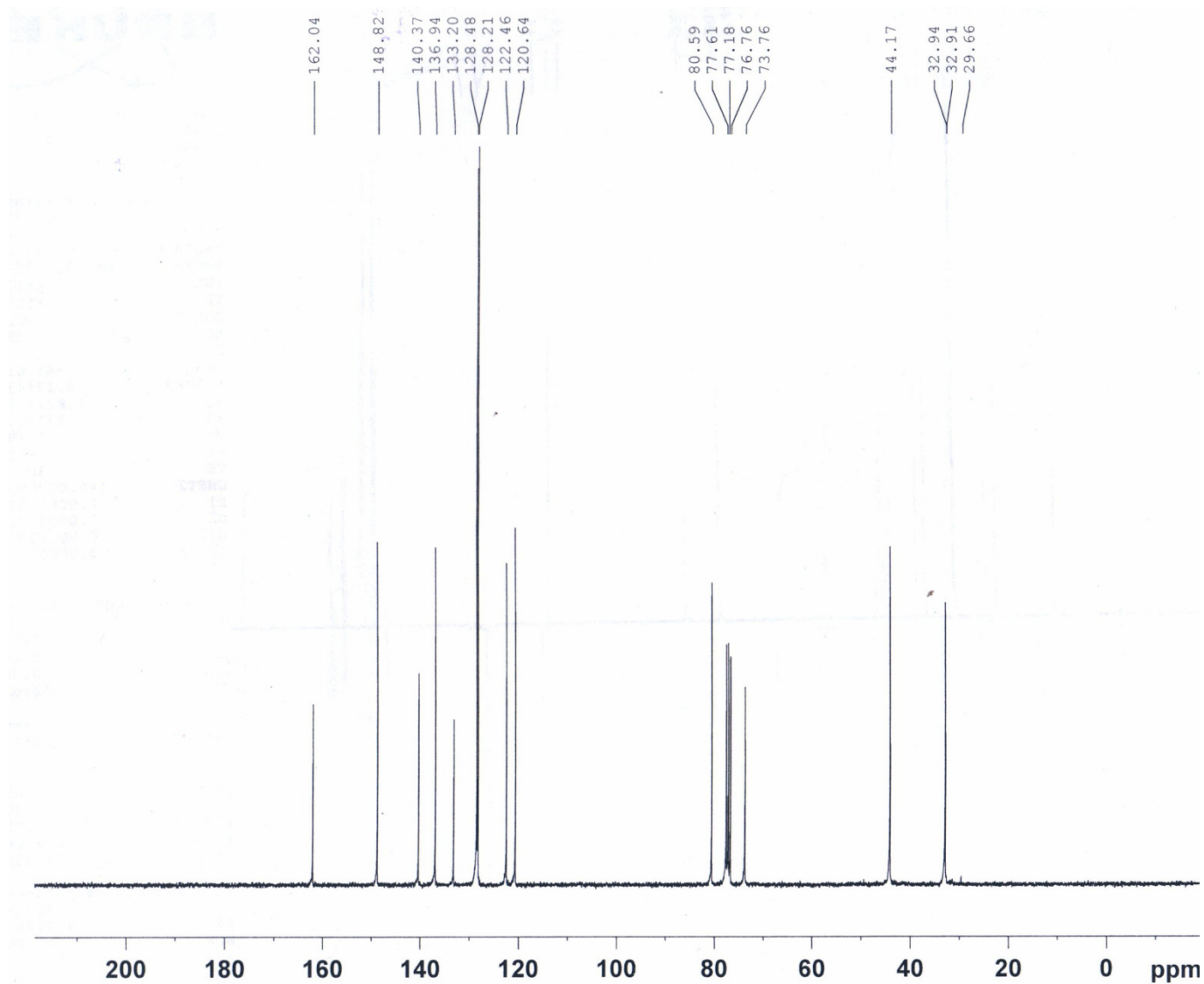
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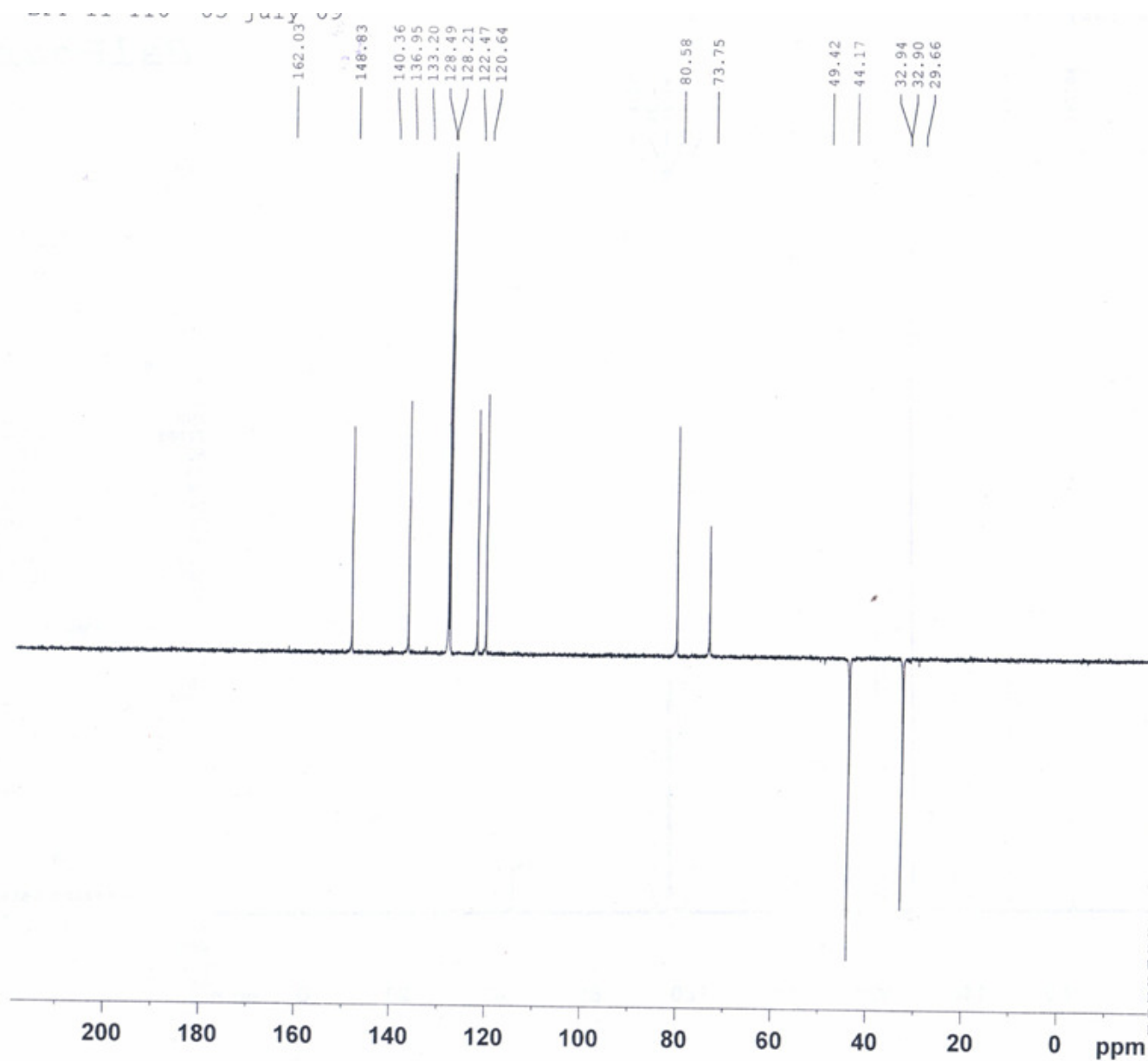
1:MS ES+
 4.1e+007



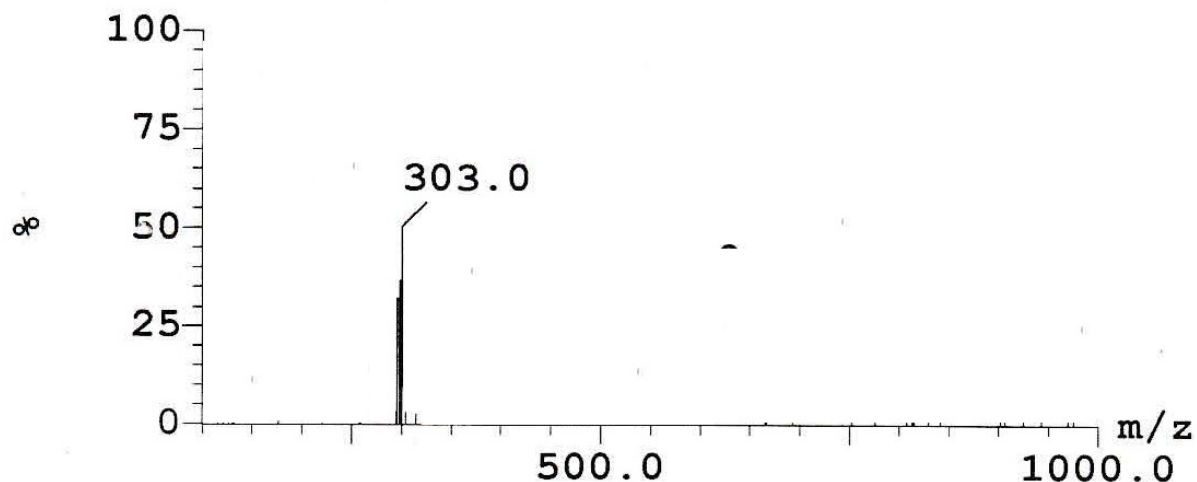
2-((4-chlorophenyl)(piperidin-4-yloxy)methyl)pyridine (4) : Yield (7.6 g, 94.5%).% 1H-NMR (300 MHz, CDCl₃) 8.50-7.12 (m, 8H), 5.64(s, 1H), 3.53 (m,1H), 3.09(m, 2H), 2.59-2.46(m,3H,-CH₂,-NH) 1.9(m, 2H), 1.6(m, 2H); 13C-NMR (75 MHz, CDCl₃) 162.04, 148.82, 140.37, 136.94, 133.20, 128.48, 128.21, 122.46, 120.64, 80.59, 73.76, 44.17, 32.94, 32.91, 29.66 ; DEPT attached; LCMS (MM:ES+APCI) 303(M+H)⁺; Chiral HPLC (%ee) 49.91:50.09



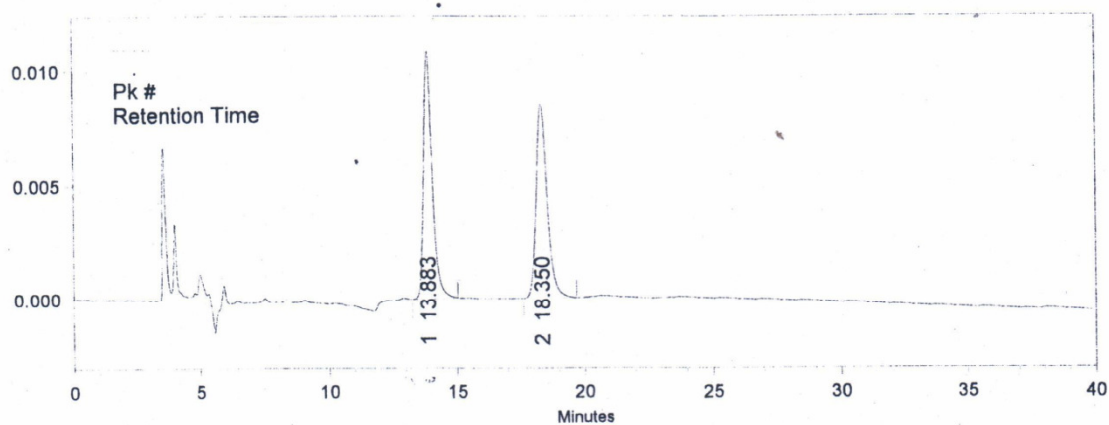




Peak ID Time
 3 1.73
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 9.1e+004

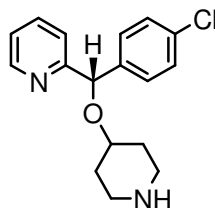


Description: Mobile Phase :n-Hexane:IPA:EDA(90:10:0.1) Flow:1.0ml/min
 Detector:220 nm column:CHI-004
 Spl Prepn:20mg in 10ml with diluent(n-Hexane:Ethanol:DEA(50:50:0.1))



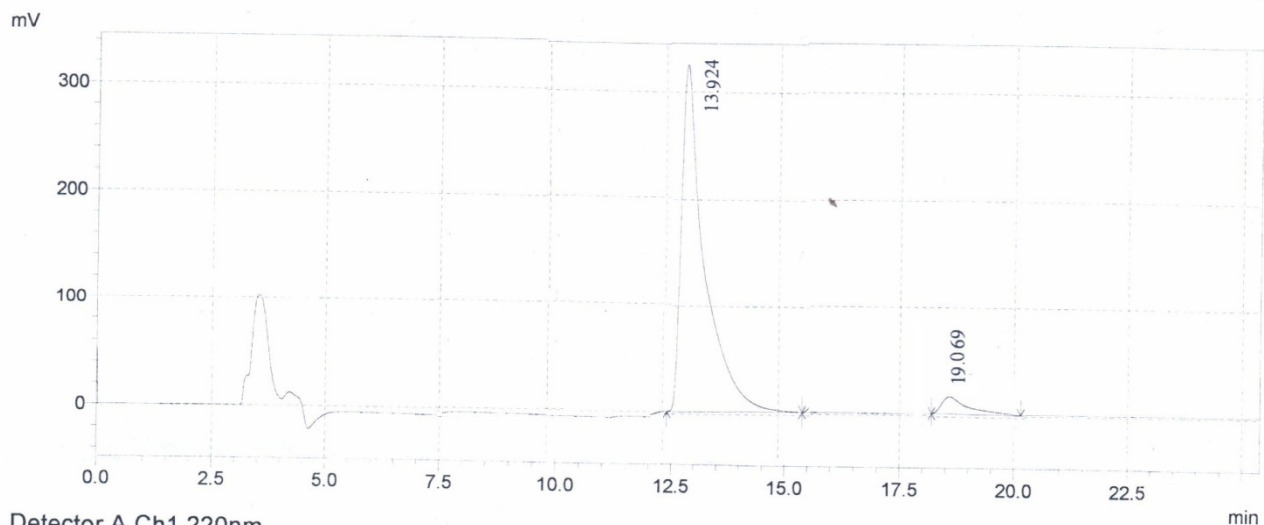
Detector A (260nm)

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Totals		511005	100.00



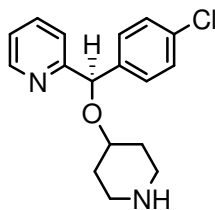
(R)-(+)-2-((4-chlorophenyl)(piperidin-4-yloxy)methyl)pyridine (4a) : Yield (3.79g, 94.5%).
 Anal.Calcd for C₁₇H₁₉ClN₂O : C 67.43; H 6.32; N 9.25; Found: C, 67.49; H, 6.28; N, 9.29; Chiral
 HPLC (%ee) 98.4; [α]_D= +11(C 0.05, MeOH);

Description: Mobile Phase :n-Hexane:IPA;EDA(90:10:0.1) Flow:1.0ml/min
 Detector:220 nm column:CHI-004
 Spl Prepn:20mg in 10ml with diluent(n-Hexane:Ethanol:DEA(50:50:0.1))



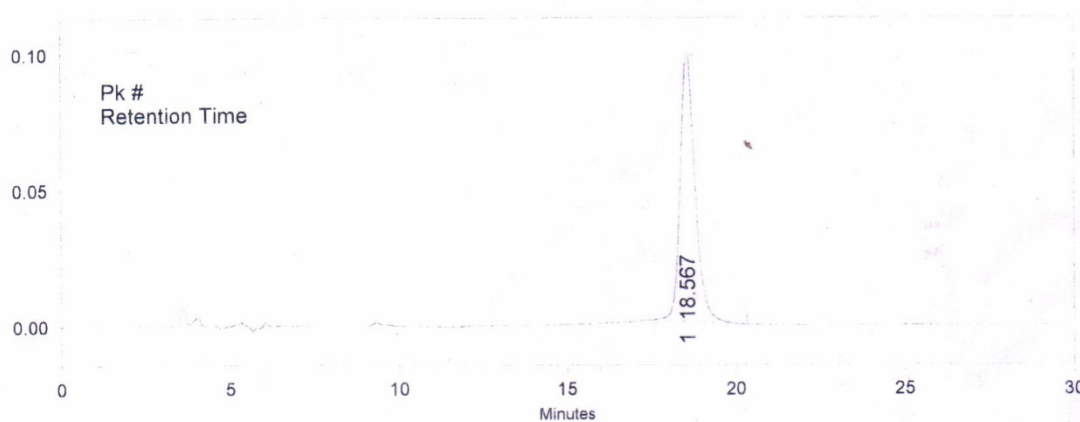
Detector A Ch1 220nm

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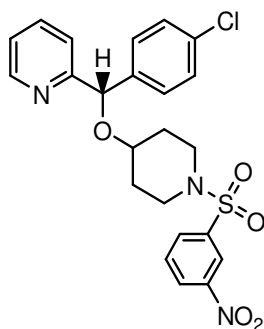
(S)-(-)-2-((4-chlorophenyl)(piperidin-4-yloxy)methyl)pyridine (4b) : Yield (3.85g, 95.5%) ;
 Anal.Calcd for C₁₇H₁₉ClN₂O : C 67.43; H 6.32; N 9.25; Found: C, 67.38; H, 6.37; N, 9.24; Chiral
 HPLC (%ee) 100; [α]_D= -11 (C 0.05, MeOH);

Sample Description: Mobile Phase(Hexane:IPA:EDA) 90:10:0.1
 Flow rate:1.0ml/min Detector:220nm Column:CHI-004

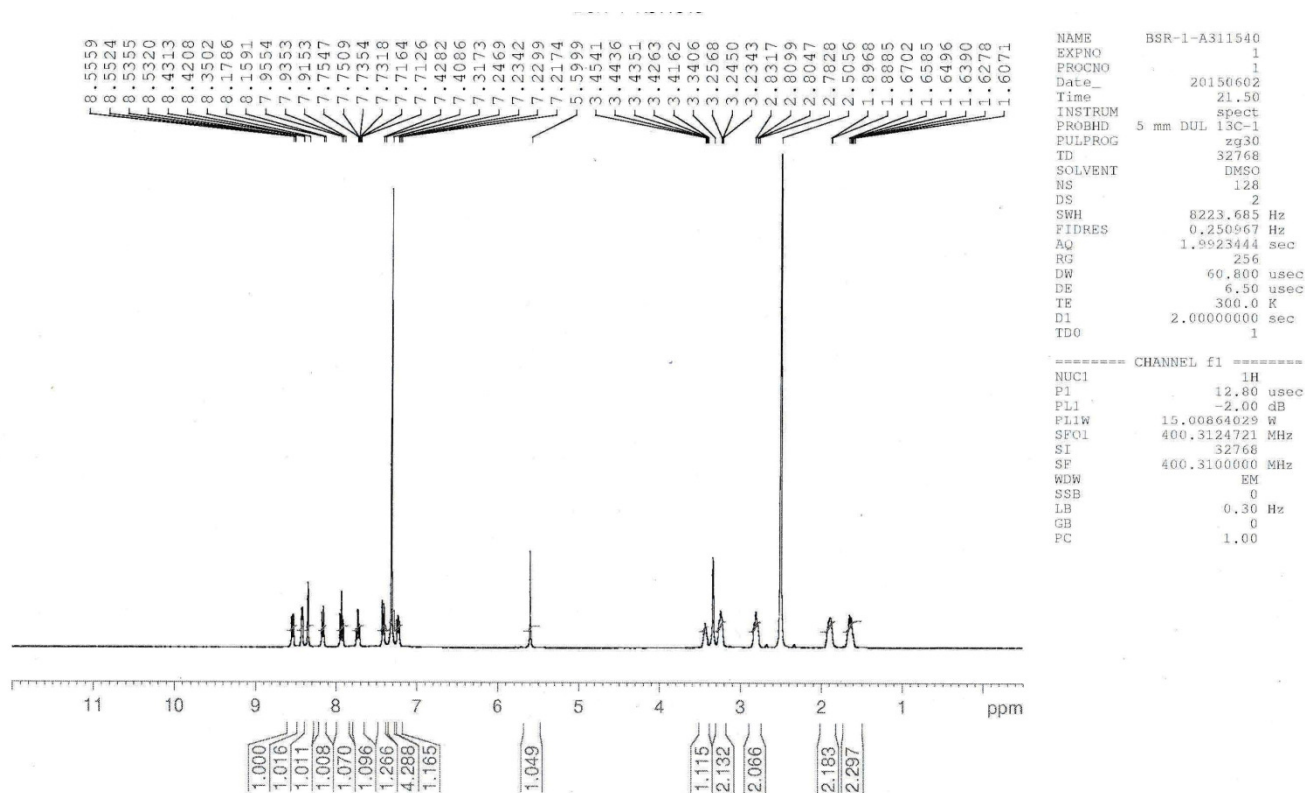


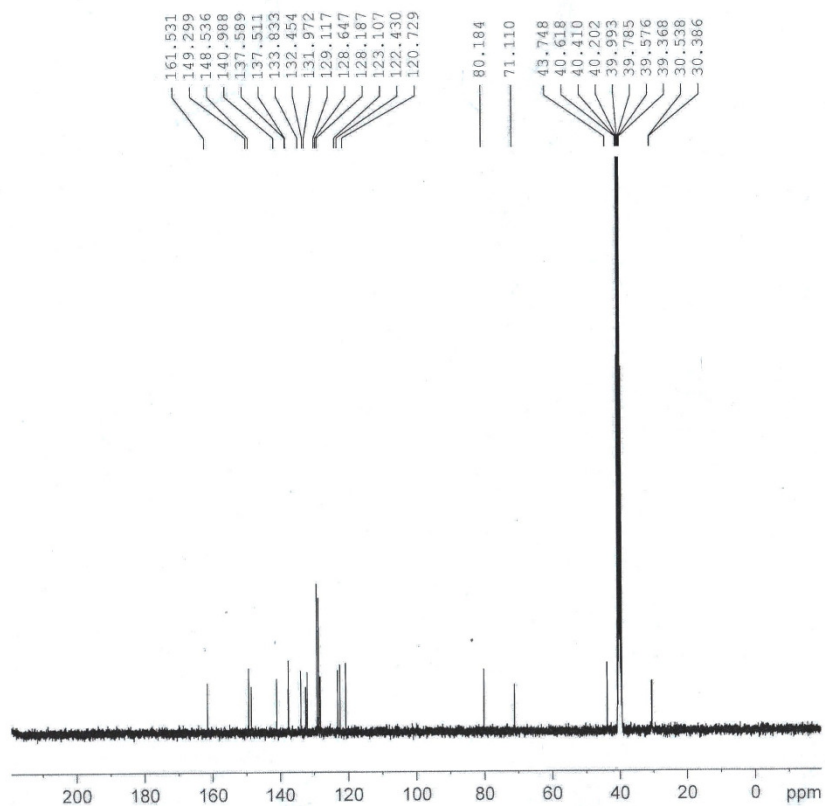
Detector A (220nm)

Pk #	Retention Time	Area	Area Percent
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Totals		2968663	100.00



(R)-2-((4-chlorophenyl)((1-((3-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6a): Yield (270mg, 84.3%); Tan colored solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.55- 8.53(d,J=8.0Hz,1H), 8.43- 8.42(d, J=4.0Hz,1H), 8.35 (s,1H), 8.17- 8.15 (d,J=8.0Hz,1H), 7.95- 7.91(t,J=8.0Hz,1H),7.75-7.71(m,1H), 7.42- 7.40(d,J=8.0Hz,1H),7.31-7.21(m, 5H), 5.59(s, 1H), 3.45-3.41(m, 1H), 3.25-3.23(m, 2H), 2.83- 2.78(m, 2H) 1.89- 1.88 (m, 2H) 1.67- 1.60 (m, 2H); ¹³C-NMR (DMSO-d₆);161.53, 149.29, 148.53, 140.98, 137.58, 137.51, 133.83, 132.45, 131.97, 129.11, 128.64, 128.18, 123.10, 122.43, 120.72, 80.18, 71.11, 43.74, 30.53, 30.38; HRMS Calcd 510.086; Found: 510.086(M+Na⁺); Anal.Calcd for C₂₃H₂₂ClN₃O₅S : C 56.61; H 4.54; N 8.67; Found: C, 56.63; H, 4.57; N, 8.65; Chiral HPLC (%ee) 99.9





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 PROCNO 1

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 SOLVENT DMSO
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 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
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 DE 6.00 usec
 TE 296.9 K
 D1 2.00000000 sec
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 DELTA 1.89999998 sec
 TDO 1

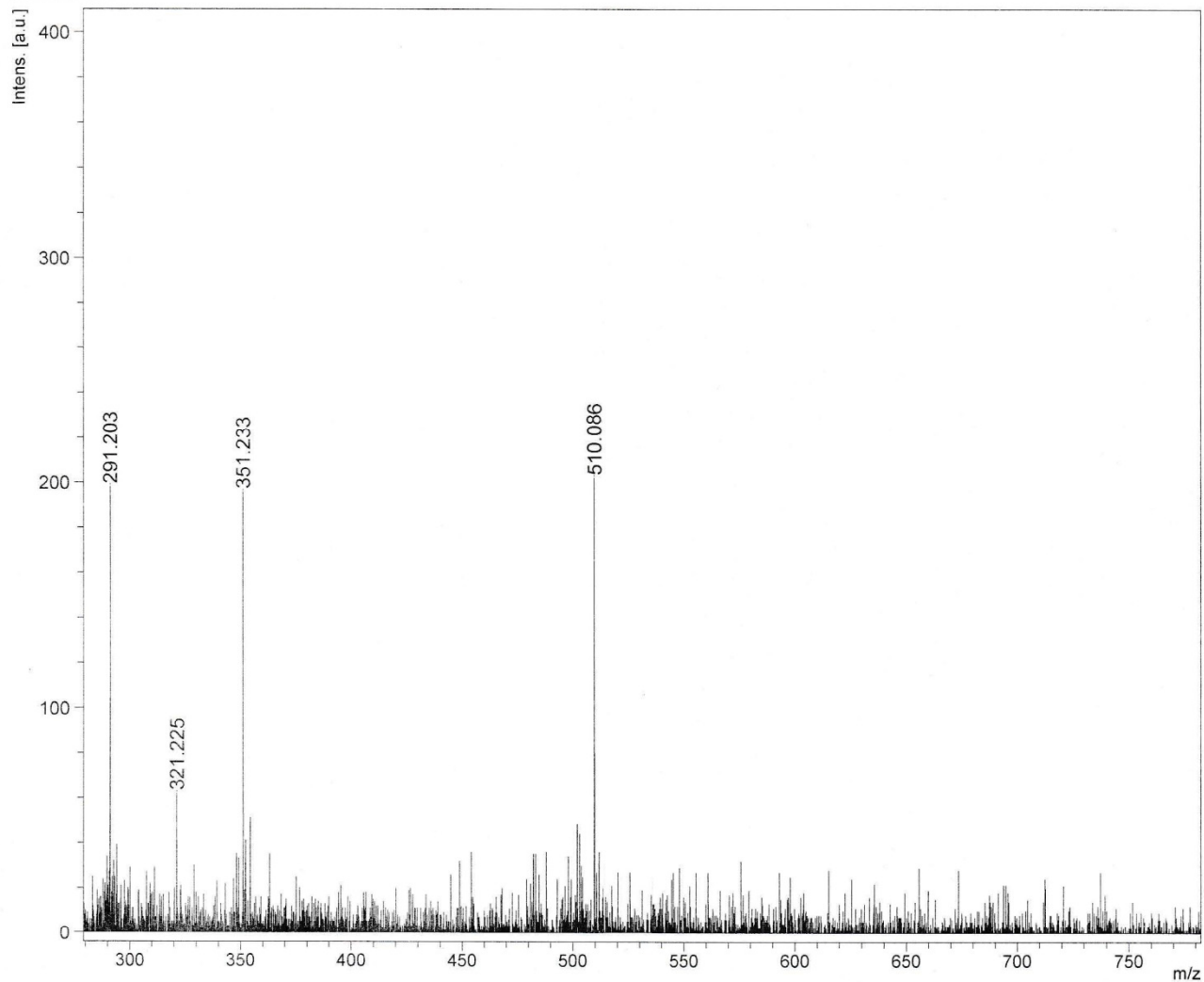
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 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
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 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Comment 1

Comment 2

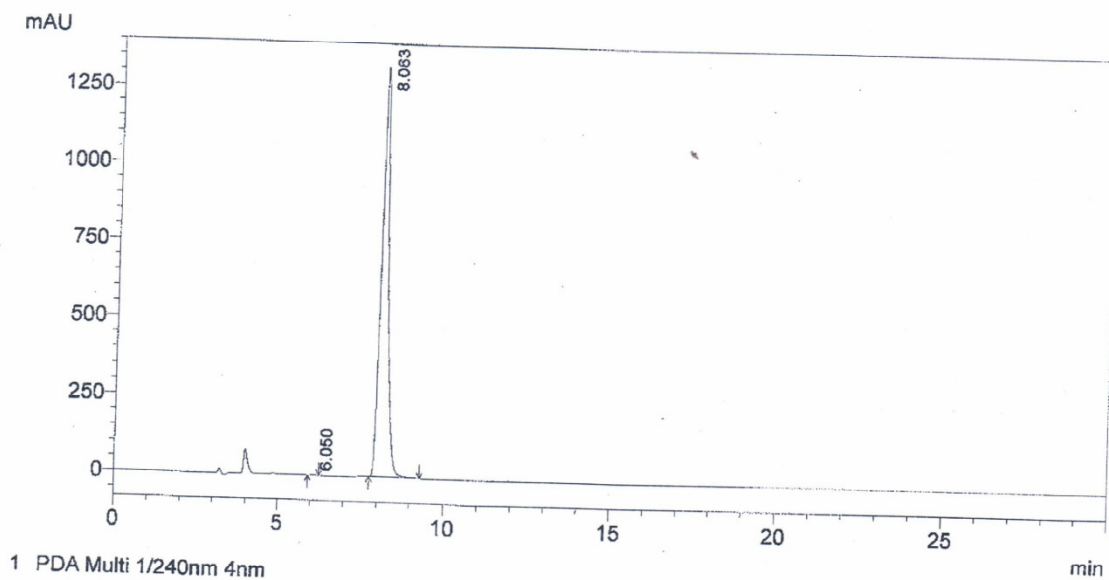


Acquisition Parameter

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Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

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Sample ID :
Data File Name : BSR-1
Method File Name : 8020TFAHEXET

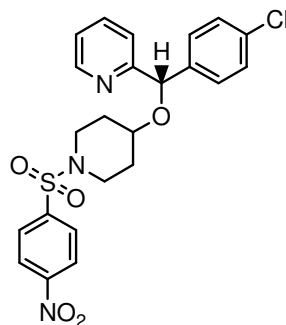
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FLOW: 1.0ml/min



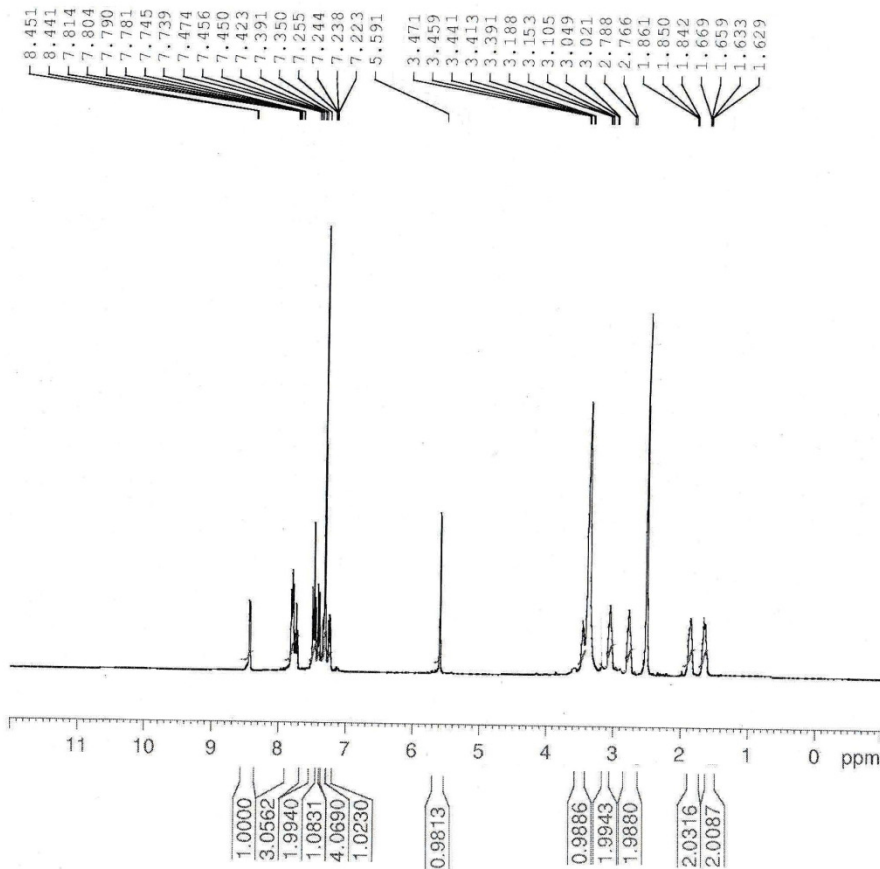
PDA Ch1 240nm 4nm

PeakTable

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Total		20683135	100.000



(R)-2-((4-chlorophenyl)((1-((4-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6b): Yield (287mg, 89.6%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-*d*₆) 8.45- 8.44(d,J=4Hz,1H), 7.81- 7.73(m,3H), 7.45- 7.35 (m,7H), 7.25- 7.22(d,J=8.0Hz,1H), 5.59(s, 1H), 3.47- 3.39(m, 1H), 3.04- 3.02(m, 2H), 2.78- 2.76(m, 2H), 1.86- 1.84 (m, 2H), 1.66- 1.62 (m, 2H); ¹³C-NMR (DMSO-*d*₆);161.67, 149.11, 148.63, 140.38, 137.58, 137.45, 133.13, 132.45, 132.09, 129.11, 128.64, 128.13, 123.39, 122.43, 120.12, 80.09, 71.01, 43.74, 30.50, 30.22; HRMS Calcd 510.086; Found: 510.086(M+Na⁺); Anal.Calcd for C₂₃H₂₂ClN₃O₅S : C 56.61; H 4.54; N 8.67; Found: C, 56.64; H, 4.53; N, 8.64; [α]_D= -37.6(C 0.01, MeOH);

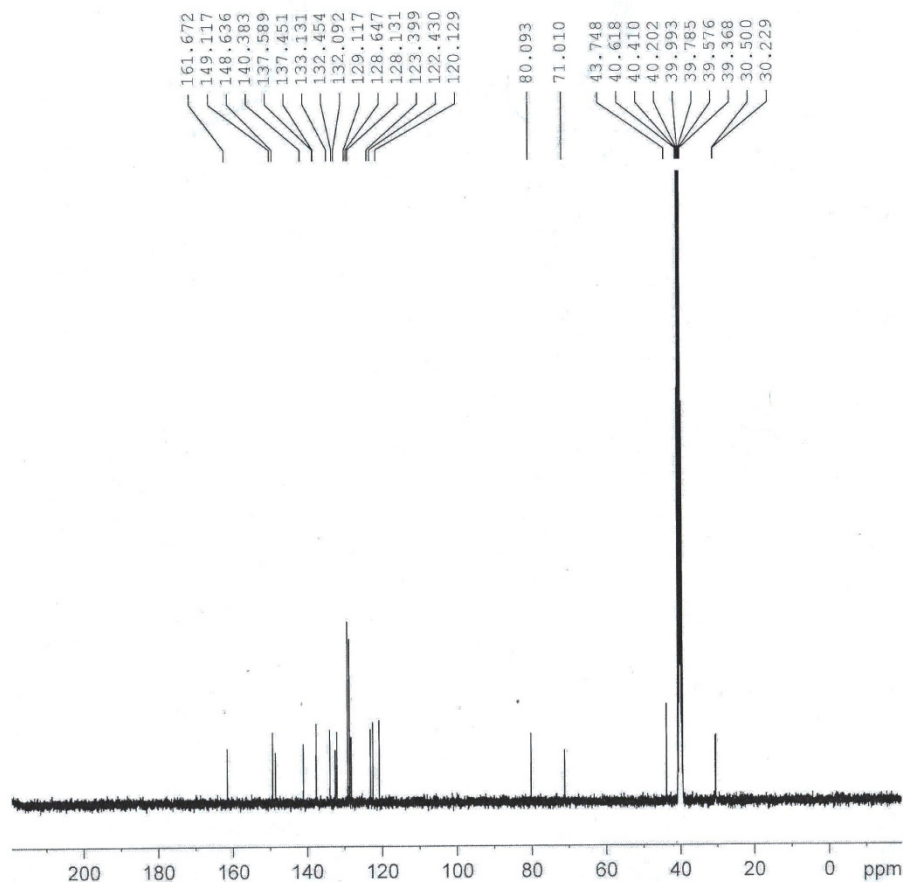


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 SOLVENT DMSO
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 FIDRES 0.250967 Hz
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 RG 144
 DW 60.800 usec
 DE 6.00 usec
 TE 295.8 K
 D1 2.00000000 sec
 TD0 1

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F2 - Processing parameters
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 SF 400.3730000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
NAME bsr2
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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SOLVENT DMSO
NS 2500
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FIDRES 0.733596 Hz
AQ 0.6816244 sec
RG 28.5
DW 20.800 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

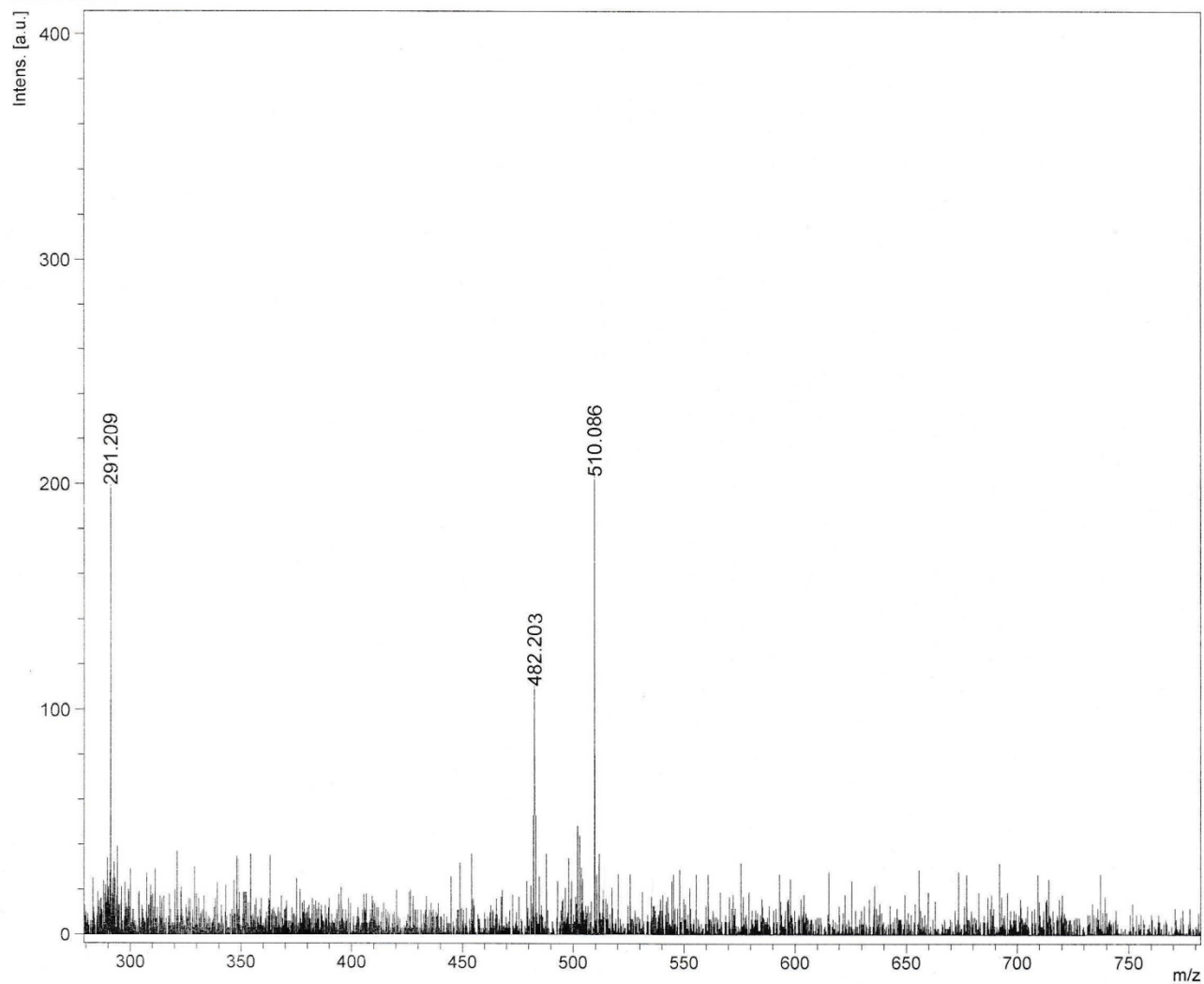
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SFO1 100.6839383 MHz

===== CHANNEL f2 =====
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NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 13.30 dB
PL13 15.50 dB
SFO2 400.3746015 MHz

F2 - Processing parameters
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

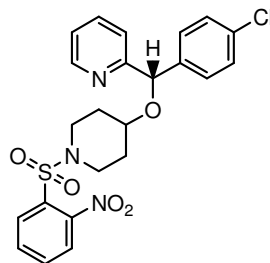
Comment 1

Comment 2

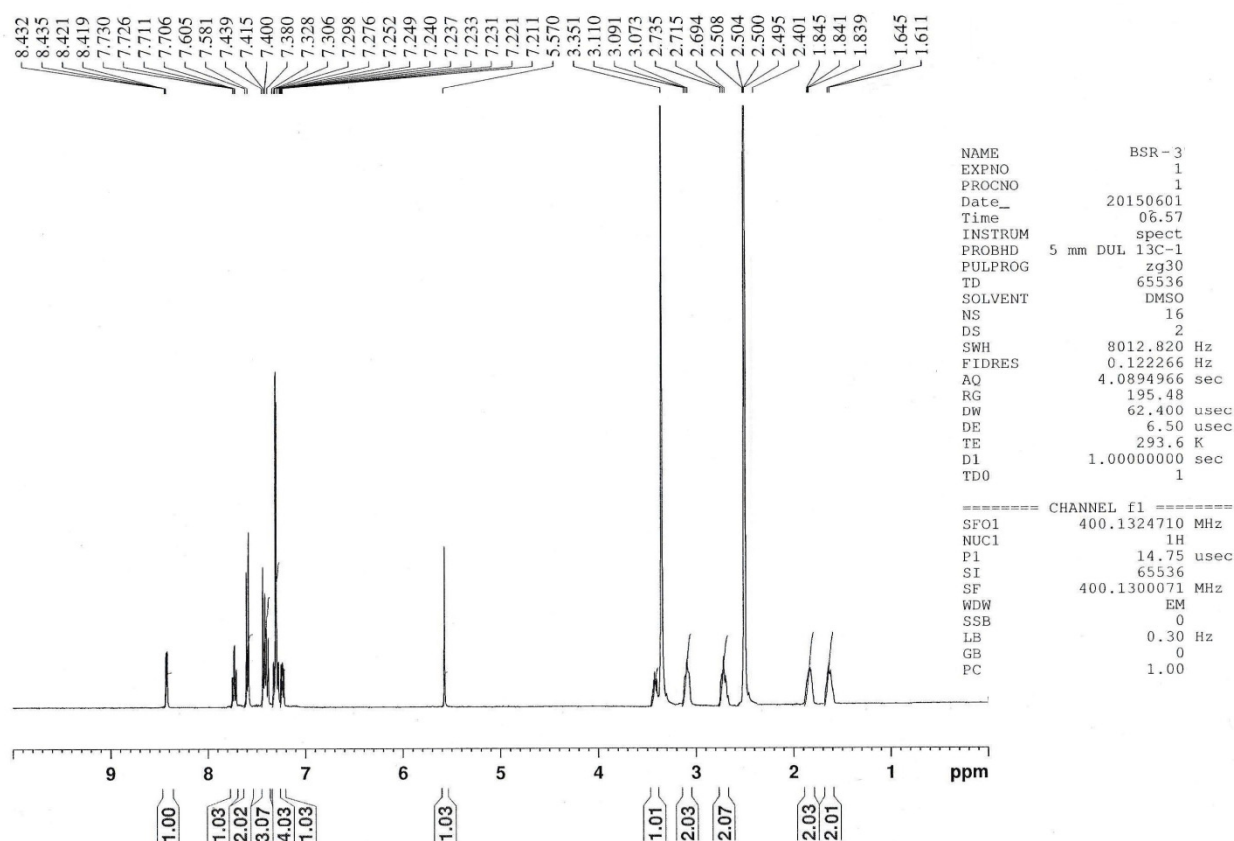


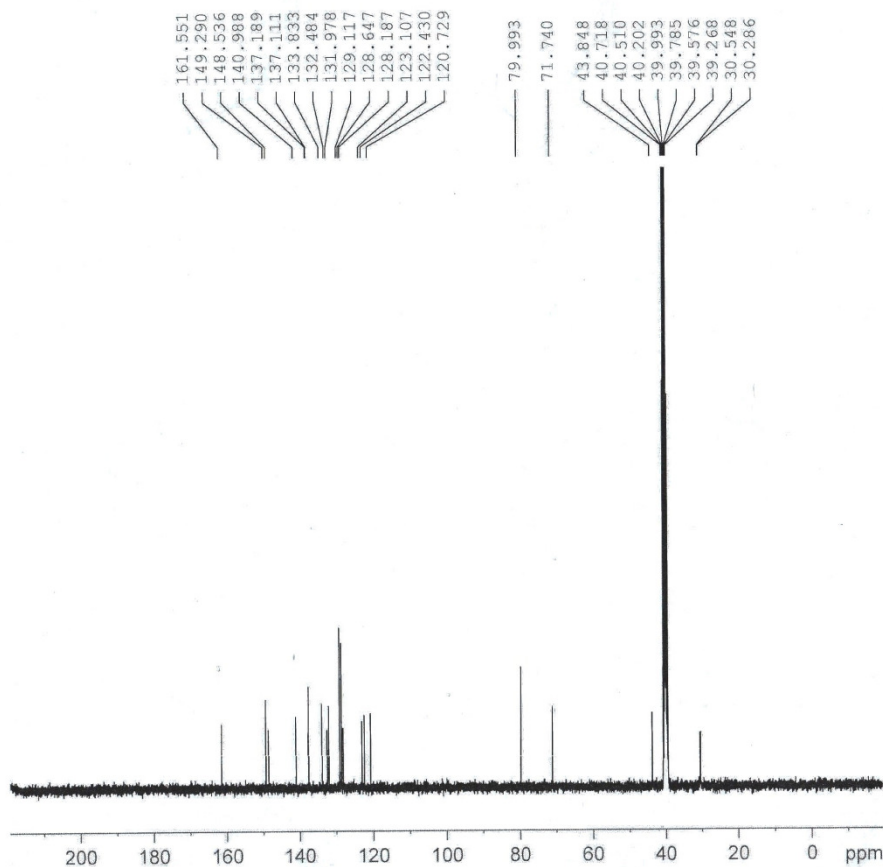
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Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	



(R)-2-((4-chlorophenyl)((1-((2-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6c): Yield (267mg, 83.4%); Tan coloured solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.43- 8.41(d, $J=8\text{Hz}$, 1H), 7.73- 7.70(m, 1H), 7.60- 7.58 (d, $J=8.0\text{Hz}$, 2H), 7.43- 7.32(m, 3H), 7.30- 7.21 (m, 5H), 5.57(s, 1H), 3.35(m, 1H), 3.11- 3.07(m, 2H), 2.73- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.64- 1.61 (m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6); 161.55, 149.29, 148.53, 140.98, 137.18, 137.11, 133.83, 132.48, 131.97, 129.11, 128.64, 128.18, 123.10, 122.43, 120.72, 79.99, 71.74, 43.84, 30.54, 30.28; HRMS Calcd 510.086; Found: 510.086($\text{M}+\text{Na}^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{22}\text{ClN}_3\text{O}_5\text{S}$: C 56.61; H 4.54; N 8.67; Found: C, 56.64; H, 4.55; N, 8.69; Chiral HPLC (%ee) 96.0





Current Data Parameters
NAME bsr3
EXPNO 5
PROCNO 2

F2 - Acquisition Parameters
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Time 06.31
INSTRUM spect
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PULPROG zgpg30
TD 32768
SOLVENT DMSO
NS 2500
DS 2
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 0.6816244 sec
RG 28.5
DW 20.800 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TDO 1

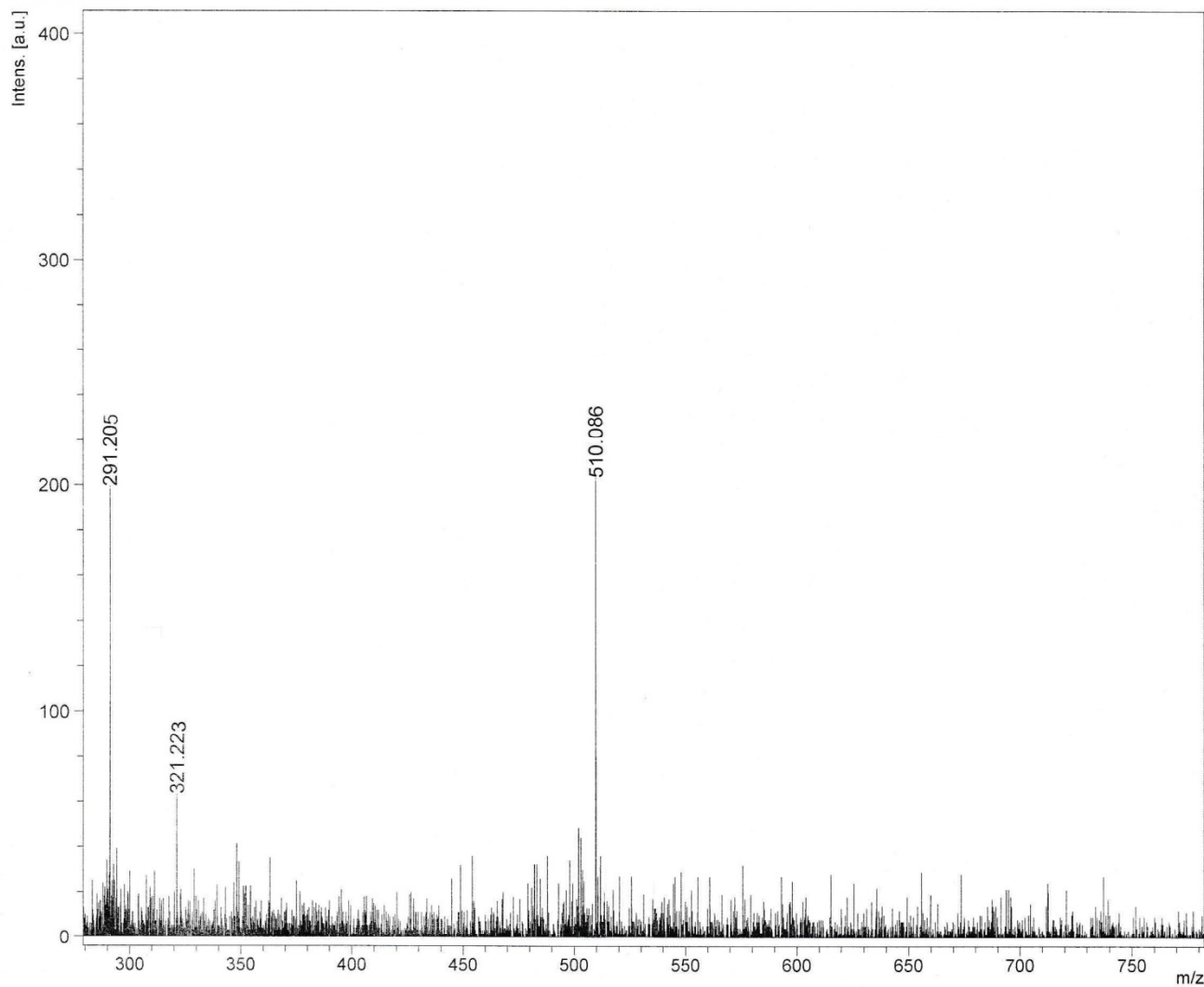
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P1 8.15 usec
PL1 -2.00 dB
SFO1 100.6839383 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 13.30 dB
PL13 15.50 dB
SFO2 400.3746015 MHz

F2 - Processing parameters
SI 32768
SF 100.6738710 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Comment 1

Comment 2

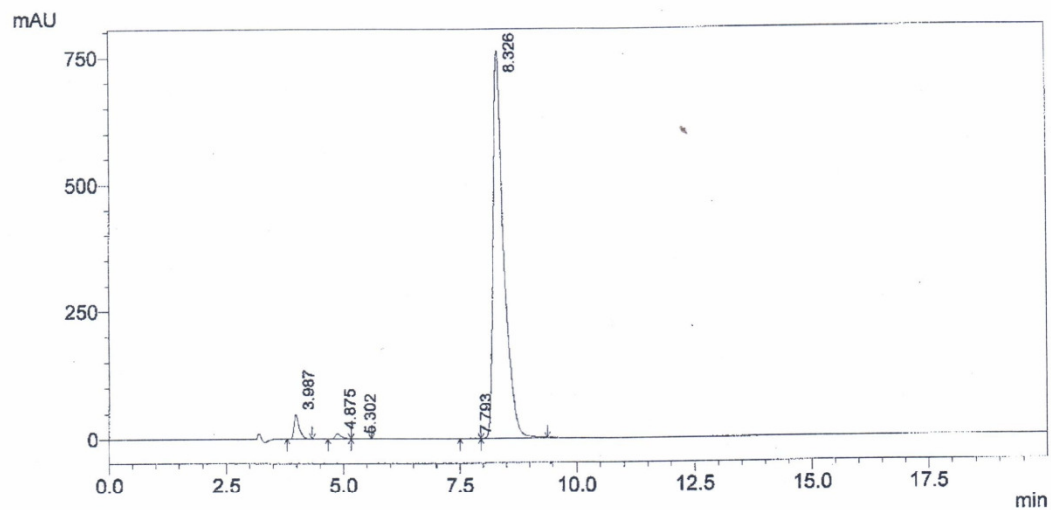


Acquisition Parameter

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Calibration reference list used	

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Method File Name : 2080TFAHEXET

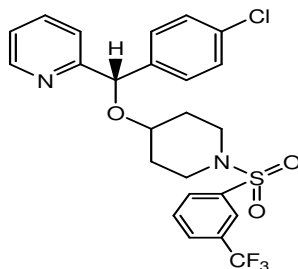
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FLOW: 1.0ml/min



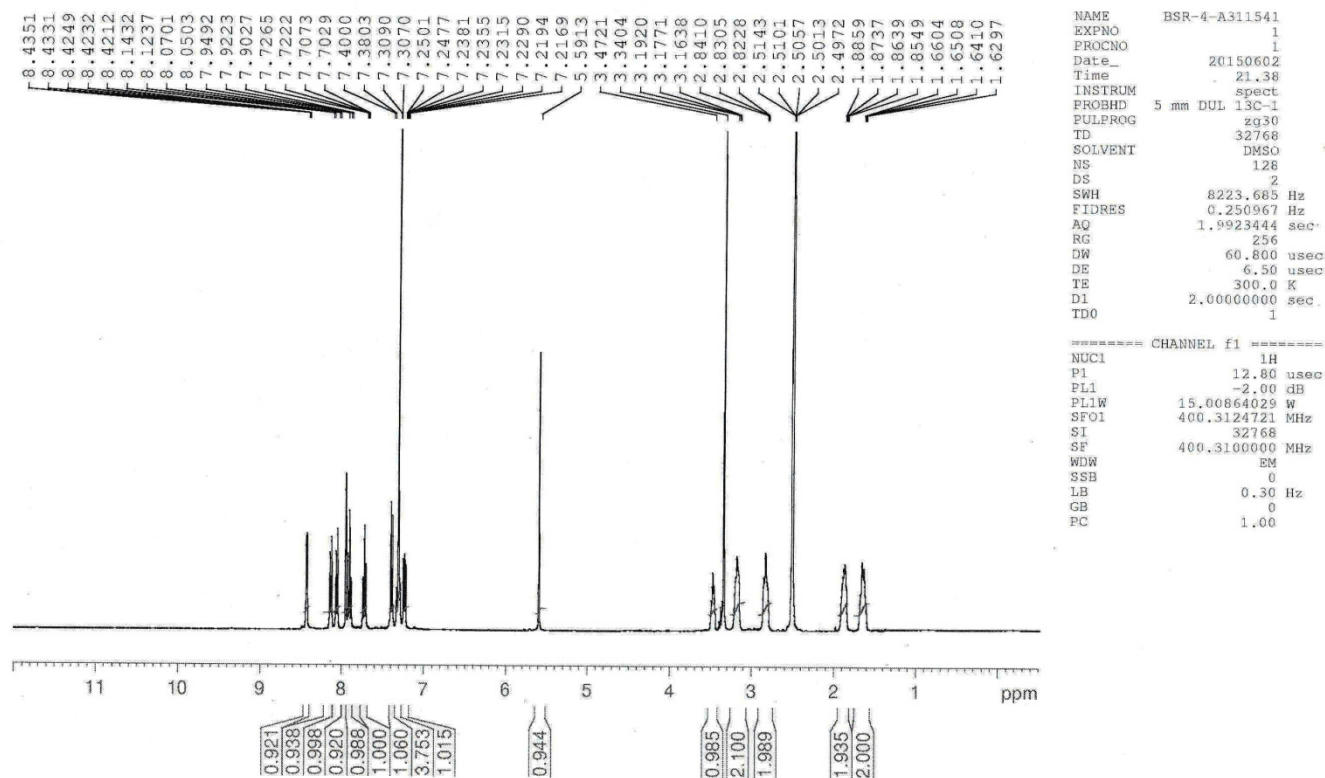
1 PDA Multi 1/240nm 4nm

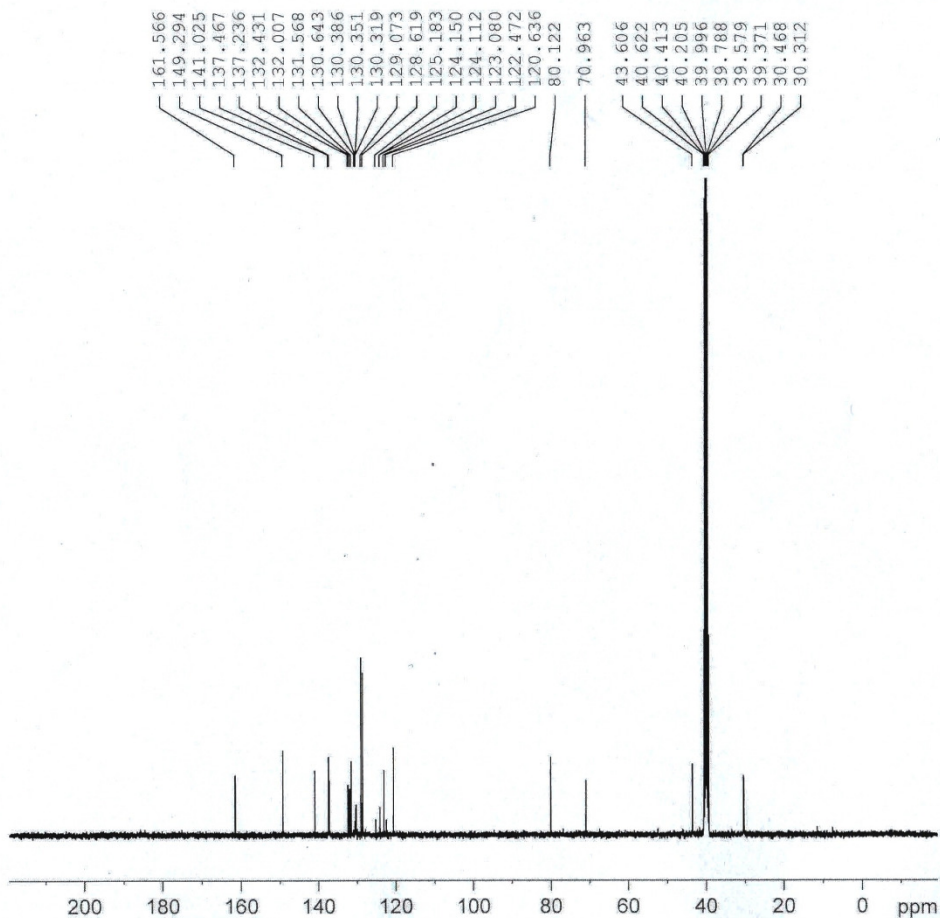
PeakTable

PDA Ch1 240nm 4nm			
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3	5.302	10506	0.085
4	7.793	15967	0.129
5	8.326	11915030	96.045
Total		12405620	100.000



(R)-2-((4-chlorophenyl)((1-((3-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6d):
 Yield (290mg, 86.5%); Off-white solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.43- 8.42(d, $J=4\text{Hz}$, 1H), 8.14- 8.12(d, $J=8.0\text{Hz}$, 1H), 8.07- 8.05(d, $J=8.0\text{Hz}$, 1H), 7.94- 7.90(m, 2H), 7.72- 7.70 (m, 1H), 7.40- 7.38(d, $J=8\text{Hz}$, 1H), 7.30- 7.21(m, 5H), 5.59(s, 1H), 3.47(m, 1H), 3.19- 3.16(m, 2H), 2.84- 2.82(m, 2H), 1.88- 1.86 (m, 2H), 1.64- 1.62 (m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6); 161.56, 149.29, 141.02, 137.46, 137.23, 132.43, 132.00, 131.56, 130.64, 130.38, 130.35, 130.31, 129.07, 128.61, 125.18, 124.15, 124.11, 123.08, 122.47, 120.63, 80.12, 70.96, 43.60, 30.46, 30.31; HRMS Calcd 511.107; Found: 511.1067(M+H)
 Anal. Calcd for $\text{C}_{24}\text{H}_{22}\text{ClFN}_3\text{O}_3\text{S}$: C 56.42; H 4.34; N 5.48; Found: C, 56.39; H, 4.37; N, 5.47; $[\alpha]_D = -39.7$ (C 0.01, MeOH);





Current Data Parameters
 NAME bsr4-A311541
 EXPNO 2
 PROCNO 1

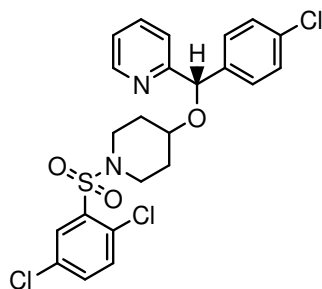
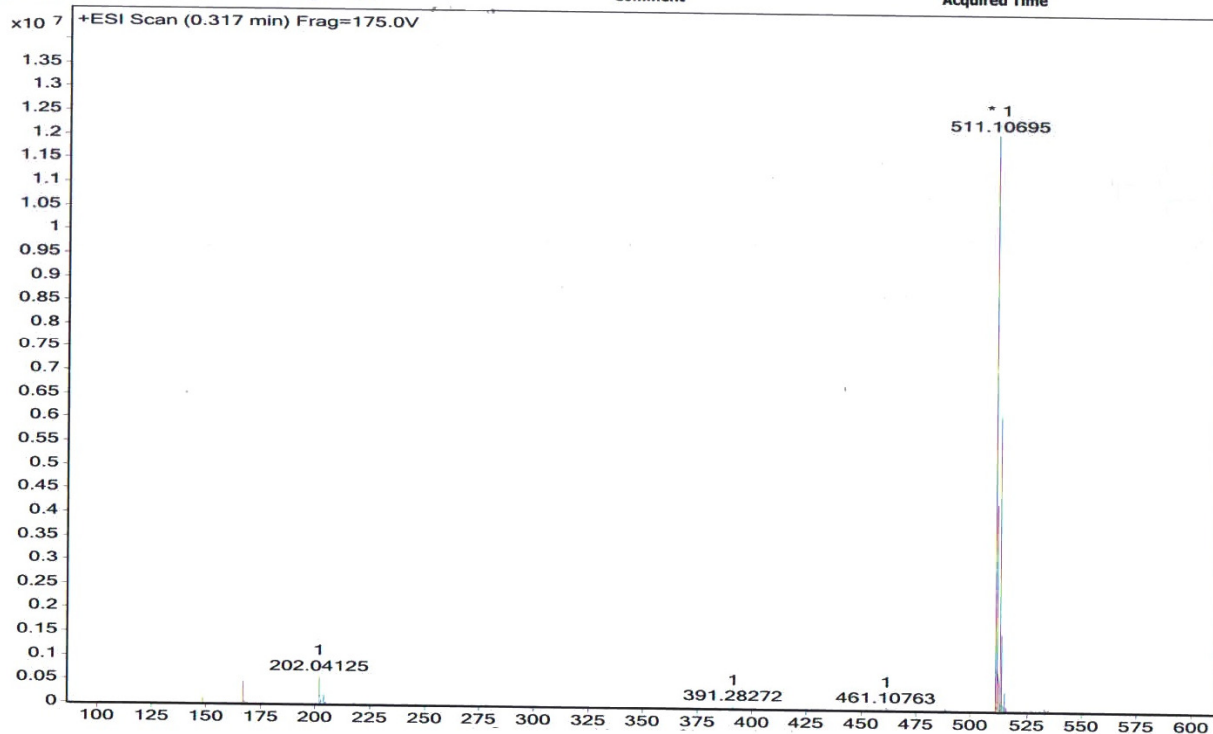
F2 - Acquisition Parameters
 Date_ 20150604
 Time 23.32
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 2500
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 32
 DW 20.800 usec
 DE 6.00 usec
 TE 296.9 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TDO 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

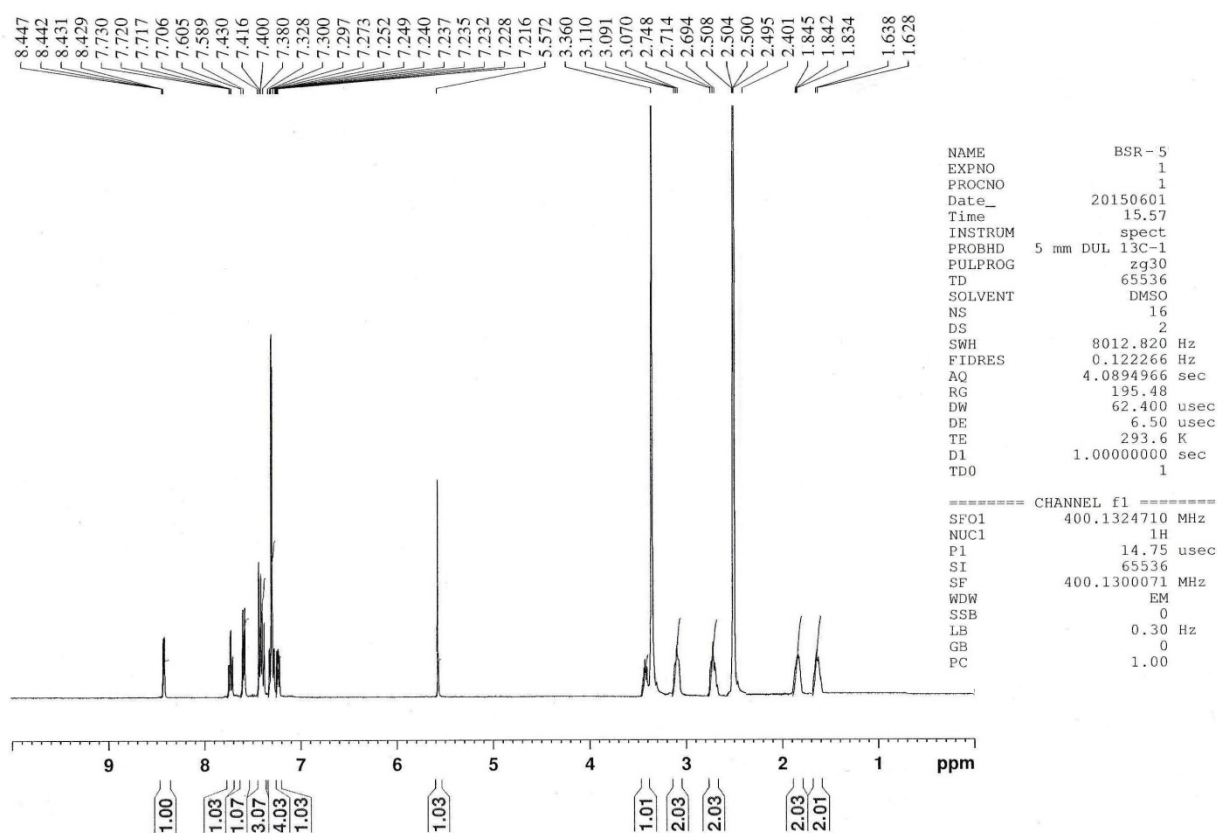
===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

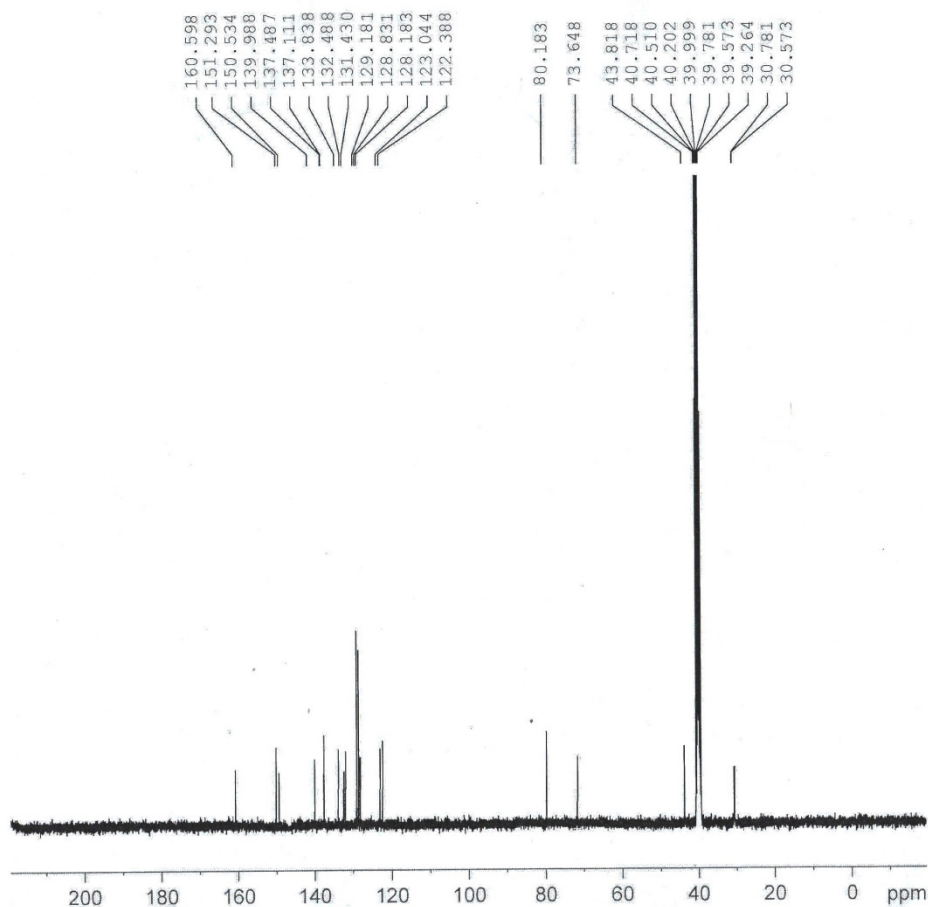
F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



(R)-2-((4-chlorophenyl)((1-((2,5-dichlorophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6e):
Yield (296mg, 88.3%); Brown low melting solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.44- 8.42(d, J=8.0Hz, 1H), 7.73- 7.70(m, 1H), 7.60- 7.58 (d, J=8.0Hz, 1H), 7.43- 7.32(m, 3H), 7.30- 7.21 (m, 5H), 5.57(s, 1H), 3.36(m, 1H), 3.11- 3.07(m, 2H), 2.74- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.63- 1.62 (m, 2H); ¹³C-NMR (DMSO-d₆); 160.59, 151.29, 150.53, 139.96, 137.48, 137.11, 133.83, 132.48, 131.43, 129.18, 128.83, 128.19, 123.04, 122.38, 80.18, 73.64, 43.81, 30.78, 30.57; HRMS Calcd 511.0417; Found: 511.0411(M+H); Anal. Calcd for C₂₃H₂₁Cl₃N₂O₃S : C 53.97; H 4.14; N 5.47; Found: C, 53.94 ; H, 4.19; N, 5.50; Chiral HPLC (%ee) 98.7;





Current Data Parameters
NAME bsr5
EXPNO 5
PROCNO 2

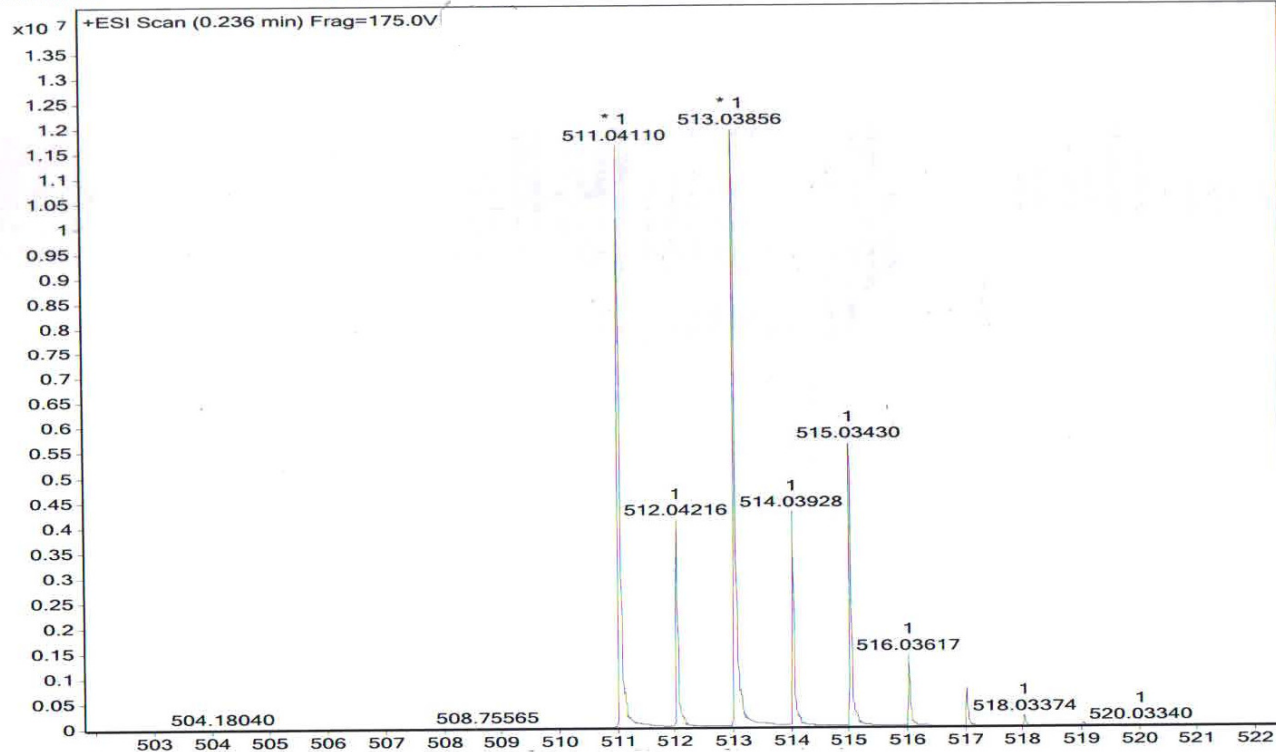
F2 - Acquisition Parameters
Date_ 20150604
Time_ 06.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32768
SOLVENT DMSO
NS 2500
DS 2
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 0.6816244 sec
RG 28.5
DW 20.800 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 8.15 usec
PL1 -2.00 dB
SFO1 100.6839383 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 13.30 dB
PL13 15.50 dB
SFO2 400.3746015 MHz

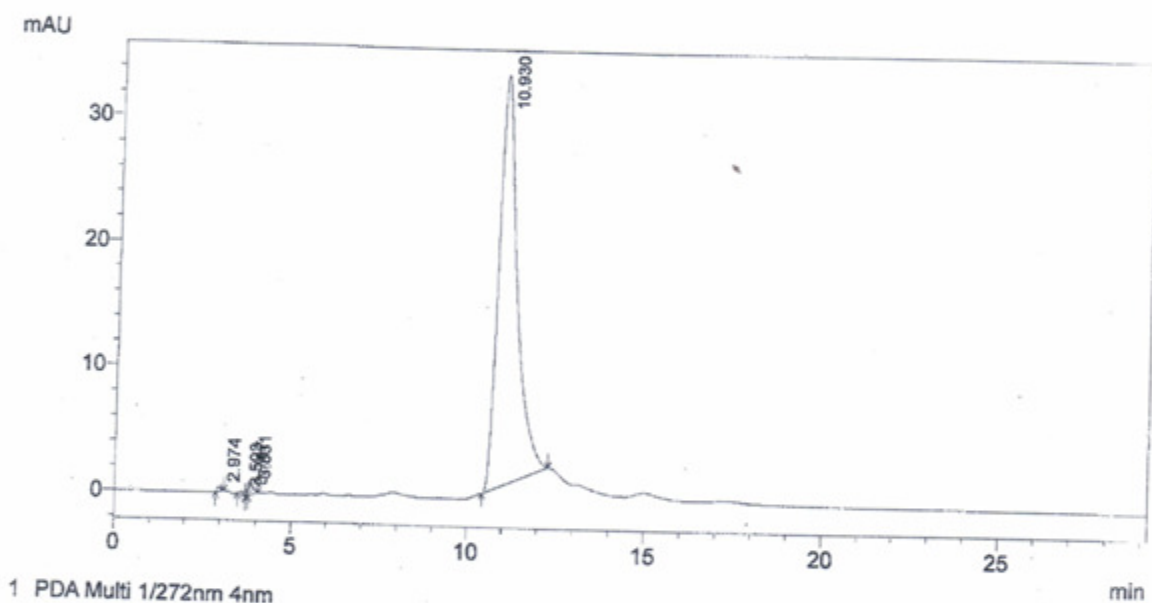
F2 - Processing parameters
SI 32768
SF 100.6738710 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



Sample Name : BSR-5
 Sample ID :
 Data File Name : BSR-5
 Method File Name : 2080TFAHEXET

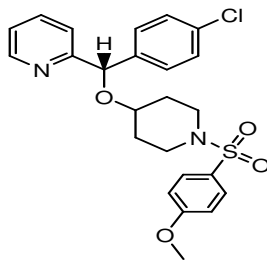
Method information : Column: CHIRAL PAK IA (250x4.6)mm 5mic
 Mobile Phase: 'A': 0.1% TFA IN HEXANE:ETHANOL (20:80)
 FLOW: 1.0ml/min



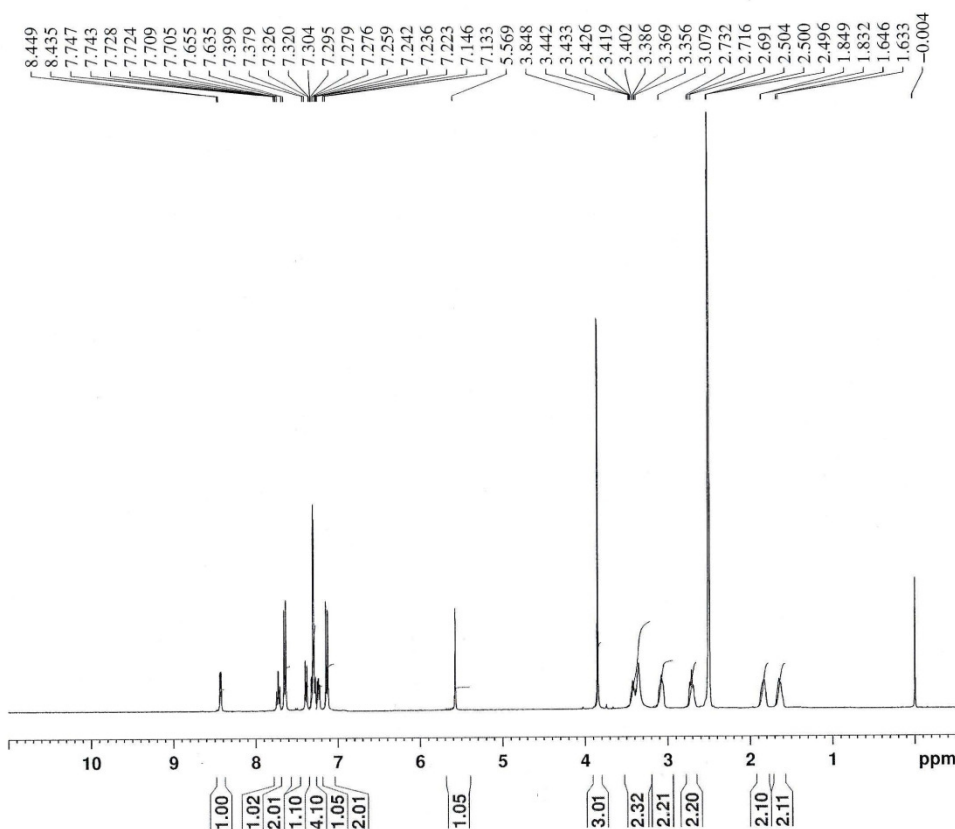
1 PDA Multi 1/272nm 4nm

PeakTable

Peak#	Ret. Time	Area	Area %
1	2.974	3016	0.251
2	3.593	2560	0.213
3	3.747	1322	0.110
4	3.831	7519	0.626
5	10.930	1186140	98.799
Total		1200558	100.000



(R)-2-((4-chlorophenyl)((1-((4-methoxyphenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6f): Yield (260mg, 83.8%); Off-white solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.44- 8.43 (d, $J=4\text{Hz}$, 1H), 7.74- 7.70(m, 1H), 7.65- 7.63 (d, $J=8.0\text{Hz}$, 2H), 7.39- 7.37(d, $J=8.0\text{Hz}$, 1H), 7.32- 7.22 (m, 5H), 7.14- 7.12(d, $J=8.0\text{Hz}$, 1H), 5.56(s, 1H), 3.84 (s, 3H), 3.44(m, 1H), 3.07(m, 2H), 2.73- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.64- 1.62 (m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6); 162.96, 161.06, 148.99, 141.00, 137.40, 132.41, 130.05, 129.09, 128.61, 126.90, 123.17, 120.72, 115.00, 79.88, 71.16, 55.99, 43.52, 30.42, 30.21; HRMS Calcd 495.112; Found: 495.112 ($\text{M}+\text{Na}^+$); Anal. Calcd for $\text{C}_{24}\text{H}_{25}\text{ClN}_2\text{O}_4\text{S}$: C 60.94; H 5.33; N 5.92; Found: C, 60.98; H, 5.31; N, 5.96; $[\alpha]_D = -40.5$ (C 0.01, MeOH);

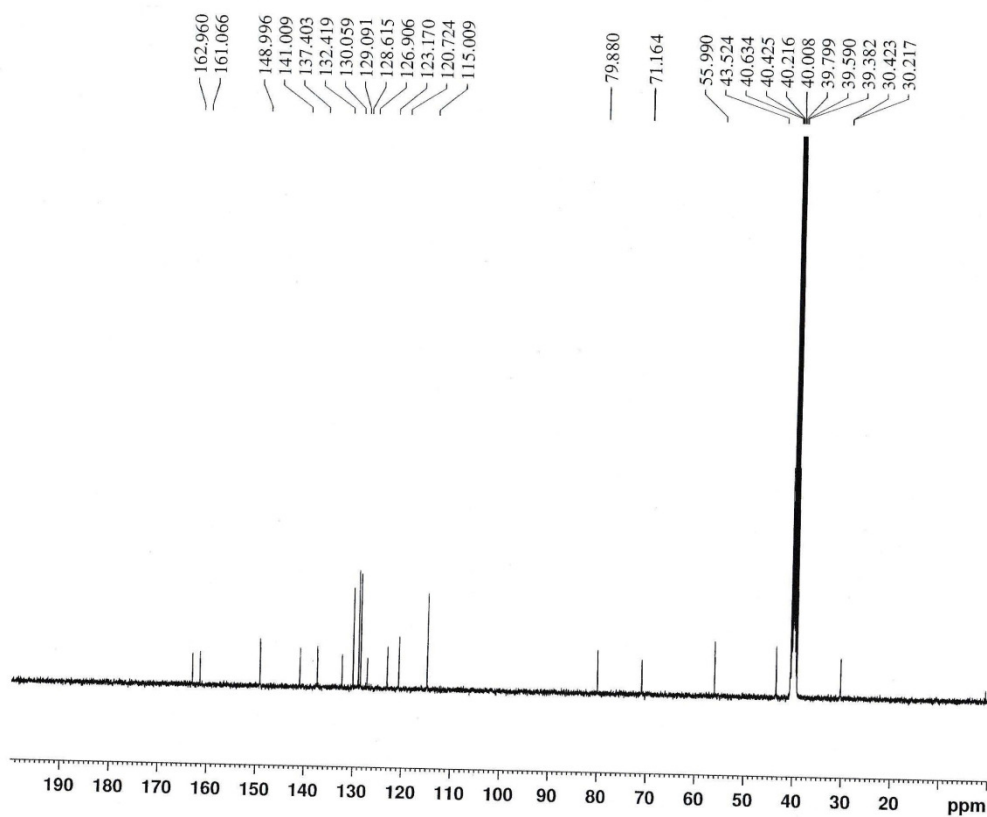


```

NAME          ARV15000116
EXPNO         1
PROCNO        1
Date_         20150526
Time          12.12
INSTRUM       spect
PROBHD        5 mm DUL 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            16
DS            2
SWH           8012.820 Hz
FIDRES        0.122266 Hz
AQ            4.0894966 sec
RG            195.48
DW            62.400 usec
DE            6.50 usec
TE            294.6 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
SF01          400.1324710 MHz
NUC1          1H
P1            14.75 usec
SI            65536
SF            400.1300071 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00

```

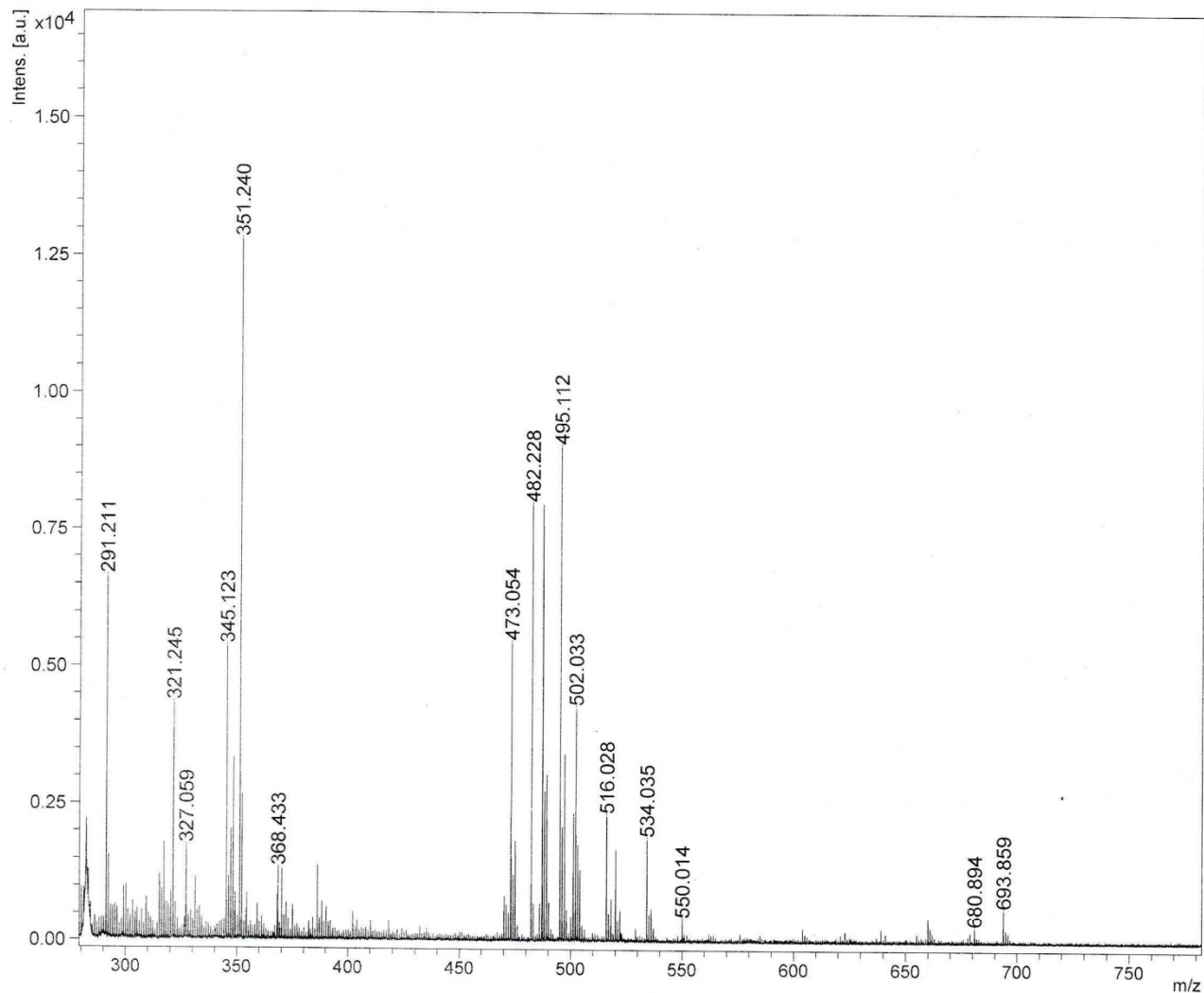


NAME ARV15000116-13C
EXPNO 1
PROCNO 1
Date_ 20150527
Time 0.11
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 2048
DS 4
SWH 28409.092 Hz
FIDRES 0.433488 Hz
AQ 1.1534836 sec
RG 195.48
DW 17.600 use
DE 6.50 use
TE 297.6 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 100.6228293 MHz
NUC1 13C
P1 9.10 use
SI 32768
SF 100.6127685 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

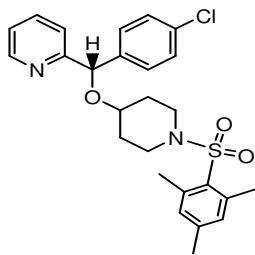
Comment 1

Comment 2

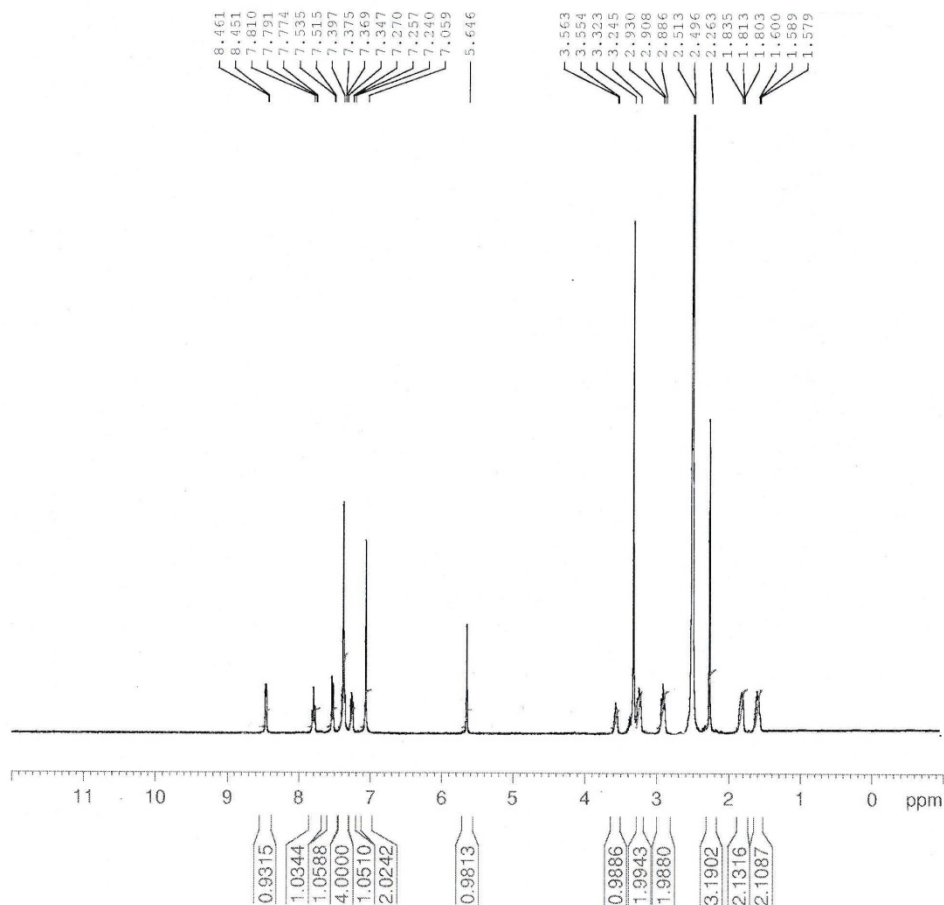


Acquisition Parameter

Date of acquisition	2015-06-16T11:17:01.734+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	



(R)-2-((4-chlorophenyl)((1-(mesitylsulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6g): Yield (280mg, 88%); White solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.46- 8.45(d, $J=4\text{Hz}$, 1H), 7.81- 7.77(m, 1H), 7.53- 7.51 (d, $J=8.0\text{Hz}$, 1H), 7.39- 7.34(m, 4H), 7.27- 7.24 (m, 1H), 7.05 (s, 2H), 5.64(s, 1H), 3.56(m, 1H), 3.32(s, 6H), 3.24(m, 2H), 2.93- 2.88(m, 2H), 2.26 (s, 3H), 1.83- 1.80 (m, 2H), 1.60- 1.57 (m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6) 161.71, 149.32, 142.85, 141.17, 140.03, 137.60, 132.45, 132.31, 132.14, 129.16, 128.70, 120.80, 80.34, 71.79, 41.63, 30.68, 30.59, 22.76, 20.90; HRMS Calcd 507.148; Found: 507.148 ($\text{M}+\text{Na}^+$); Anal. Calcd for $\text{C}_{26}\text{H}_{29}\text{ClN}_2\text{O}_3\text{S}$: C 64.38; H 6.03; N 5.78; Found: C, 64.41; H, 6.01; N, 5.79; Chiral HPLC (%ee) 96.2;

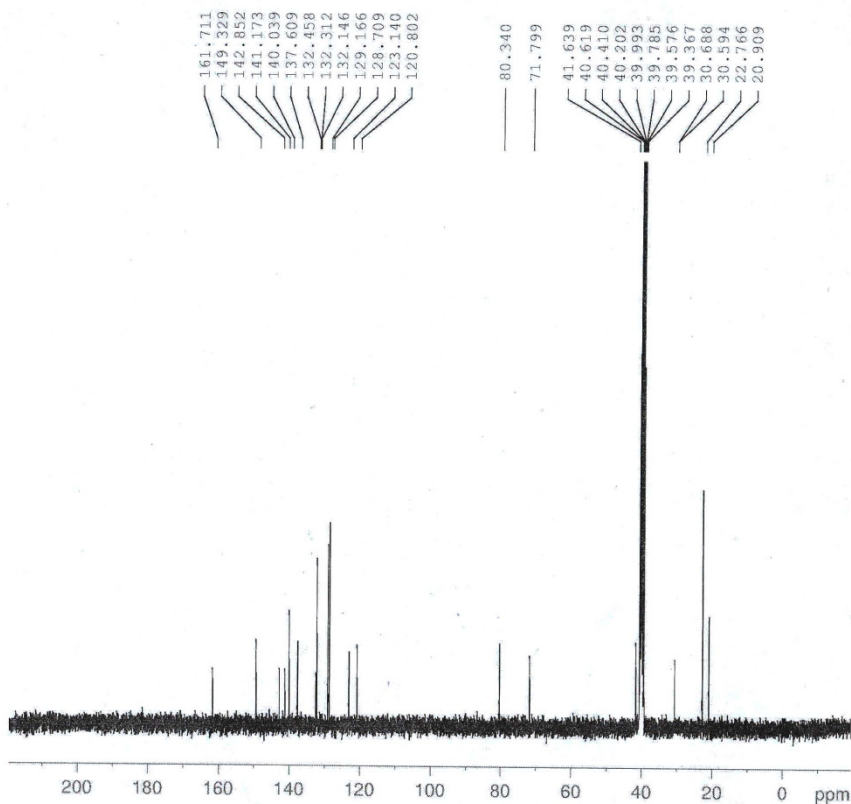


Current Data Parameters
 NAME A330923
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150623
 Time 10.28
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zg30
 TD 32768
 SOLVENT DMSO
 NS 8
 DS 2
 SWH 8389.262 Hz
 FIDRES 0.256020 Hz
 AQ 1.9530228 sec
 RG 406.4
 DW 59.600 usec
 DE 6.00 usec
 TE 297.3 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 13.20 usec
 PL1 -3.00 dB
 SFO1 400.2338023 MHz

F2 - Processing parameters
 SI 32768
 SF 400.2300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



```

Current Data Parameters
NAME      A330923
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20150624
Time      2.39
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         32768
SOLVENT   DMSO
NS         1024
DS         2
SWH        24038.461 Hz
FIDRES     0.733596 Hz
AQ         0.6816244 sec
RG         32
DW         20.800 usec
DE         5.00 usec
TE         296.7 K
D1         2.00000000 sec
d11        0.03000000 sec
DELTA     1.89999998 sec
TDO        1

===== CHANNEL f1 =====
NUC1       13C
P1         8.15 usec
PL1        -2.00 dB
SFO1       100.6839383 MHz

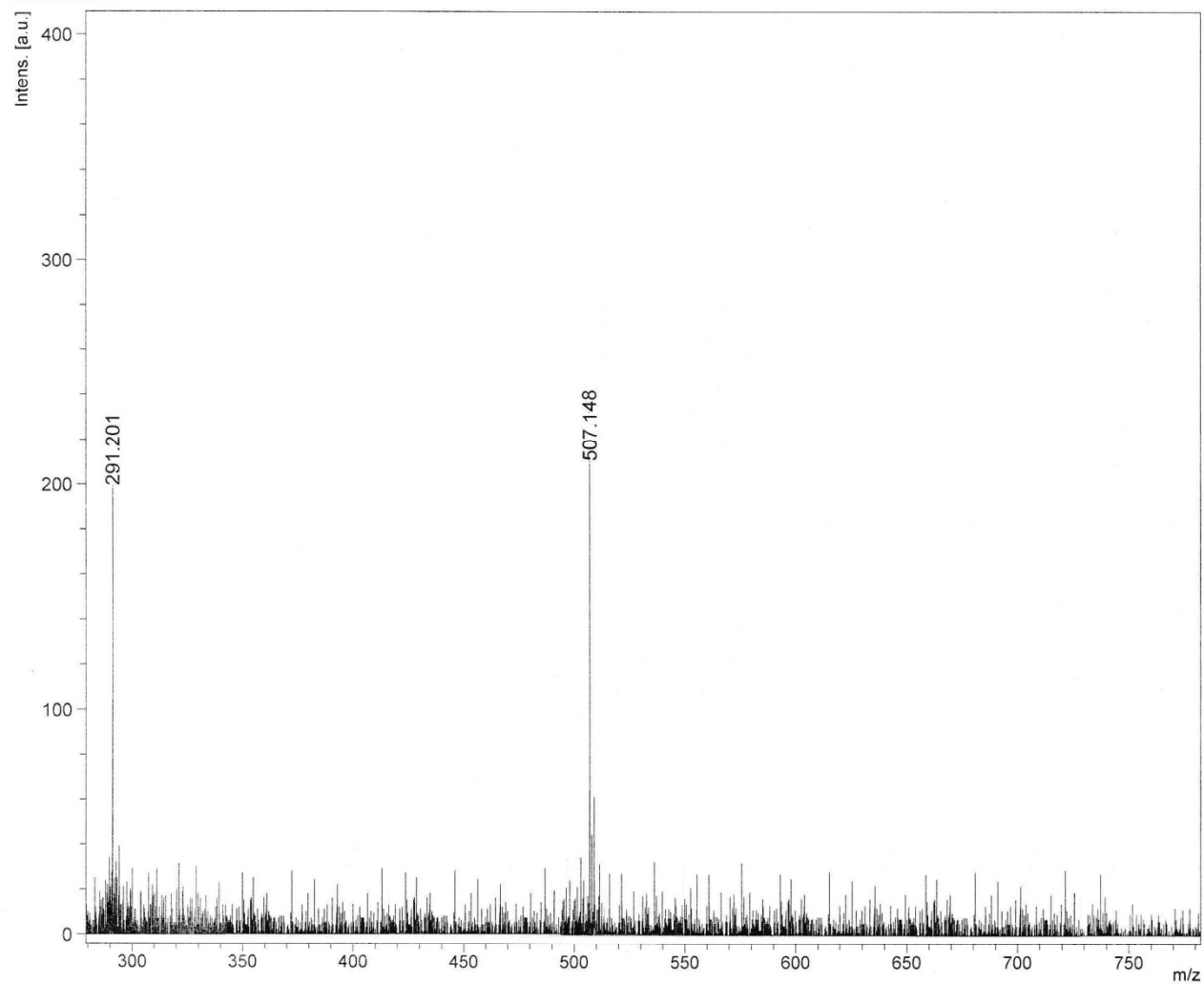
===== CHANNEL f2 =====
CPDPRG2    waltz16
NUC2       1H
PCPD2      80.00 usec
PL2        -2.00 dB
PL12       13.30 dB
PL13       15.50 dB
SFO2       400.3746015 MHz

F2 - Processing parameters
SI         32768
SF         100.6738710 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40

```

Comment 1

Comment 2

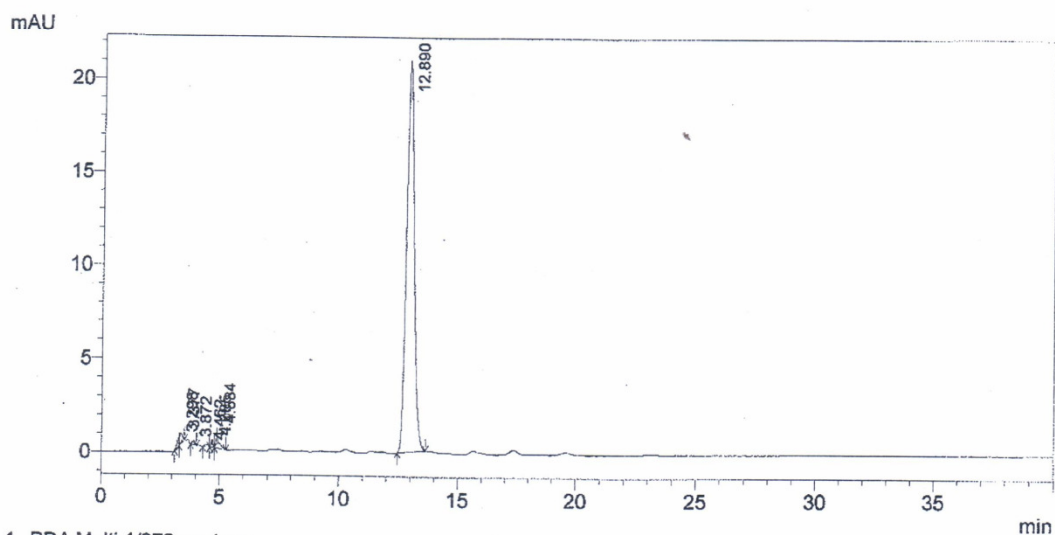


Acquisition Parameter

Date of acquisition	2015-06-16T11:15:20.921+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name :BSR-7
 Sample ID :
 Data File Name :BSR-7
 Method File Name :2080TFAHEXET

Method information:Column:CHIRAL PAK IA(250x4.6)mm 5mic
 Mobile Phase'A':0.1%TFA IN HEXANE:ETHANOL(20:80)
 FLOW:1.0ml/min

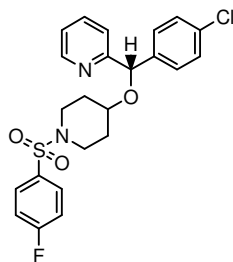


1 PDA Multi 1/272nm 4nm

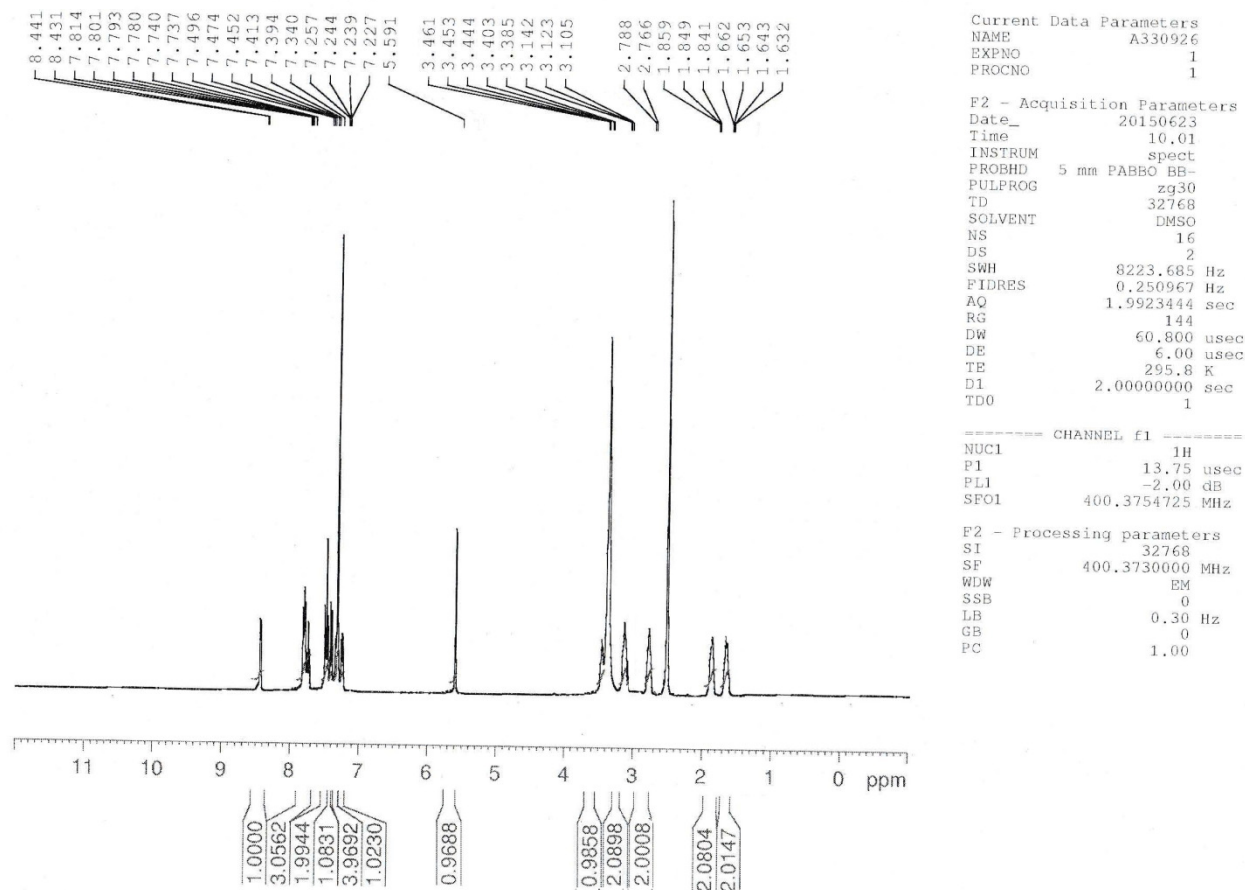
PeakTable

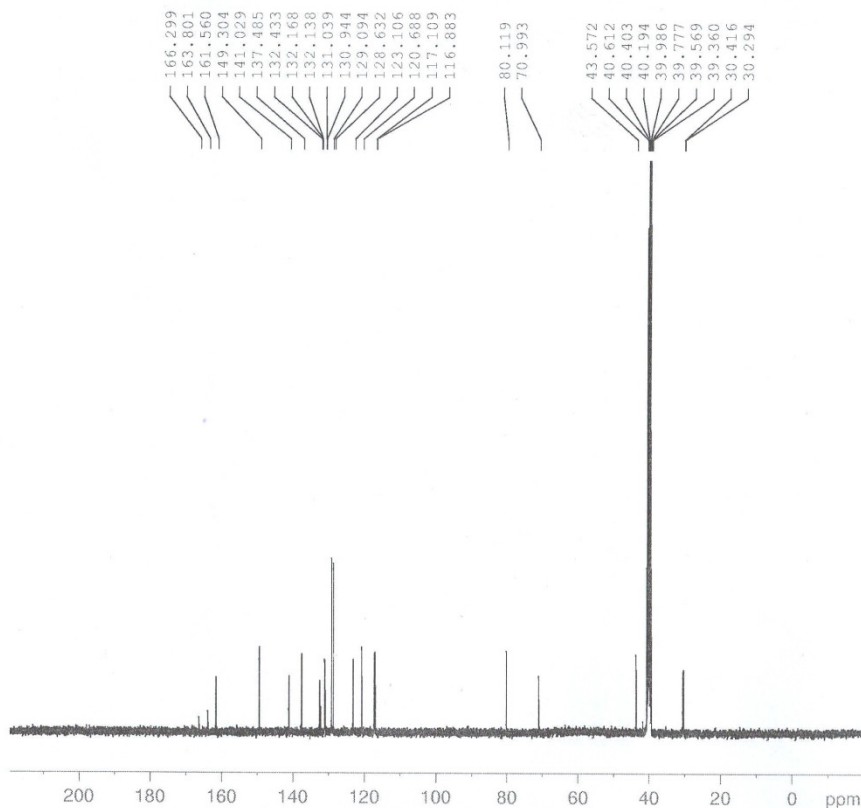
PDA Ch1 272nm 4nm

Peak#	Ret. Time	Area	Area %
1	3.298	2812	0.553
2	3.377	4583	0.902
3	3.872	1134	0.223
4	4.462	1089	0.214
5	4.685	2209	0.435
6	4.884	7083	1.394
7	12.890	489284	96.279
Total		508194	100.000



(R)-2-((4-chlorophenyl)((1-((4-fluorophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6h): Yield (268mg, 88.7%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.44- 8.43(d,J=4Hz,1H), 7.81- 7.73(m,3H), 7.49- 7.22 (m, 8H), 5.59(s, 1H), 3.46(m, 1H), 3.14- 3.10(m, 2H), 2.78- 2.76(m, 2H), 1.85- 1.84 (m, 2H) 1.66 1.63(m, 2H); ¹³C-NMR (DMSO-d₆) 166.29, 163.80, 161.56, 149.30, 141.02, 137.48, 132.43, 132.16, 132.13, 131.03, 130.94, 129.09, 128.63, 123.10, 120.68, 117.10, 116.88, 80.11, 70.99, 43.57, 30.41, 30.29; HRMS Calcd 483.092; Found: 483.092 (M+Na⁺); Anal.Calcd for C₂₃H₂₂ClFN₂O₃S : C 59.93; H 4.81; N 6.08; Found: C, 59.89; H, 4.77; N, 6.12; Chiral HPLC (%ee) 97.2;





Current Data Parameters
 NAME A330926
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150624
 Time 1.47
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 1024
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 36
 DW 20.800 usec
 DE 6.00 usec
 TE 296.7 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TD0 1

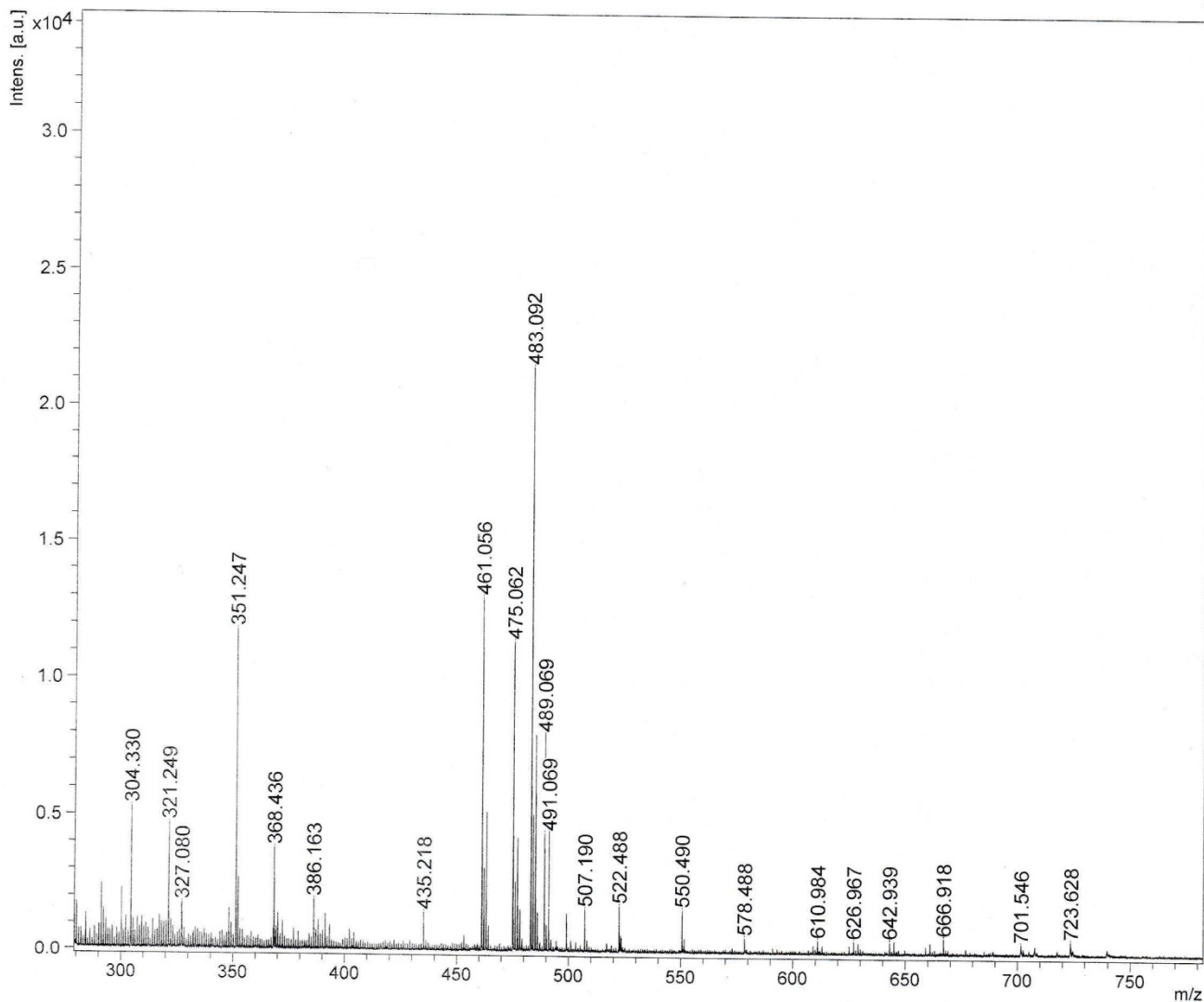
===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 60.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Comment 1

Comment 2

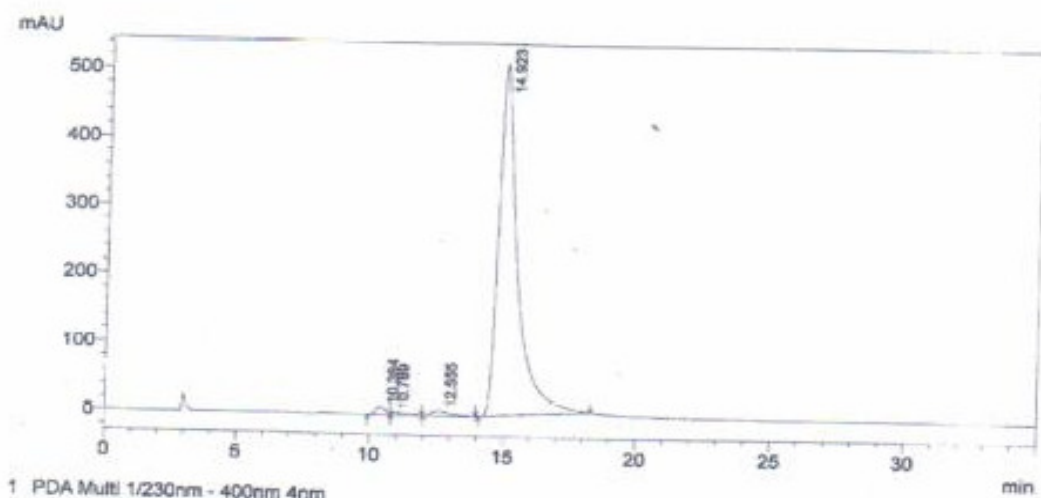


Acquisition Parameter

Date of acquisition	2015-06-16T11:16:43.171+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name : BSR-8
 Sample ID :
 Data File Name : BSR-8
 Method File Name : 2080TFAHEXET

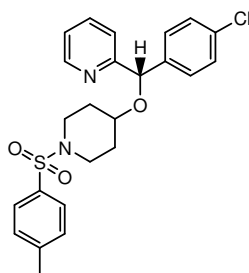
Method Information Column: CHIRAL PAK 1A (250x4.6)mm 5mic
 Mobile Phase 'A': 0.1%TFA IN HEXANE:ETHANOL(20:80)
 FLOW: 1.0ml/min



PDA Ch1 230nm - 400nm 4nm

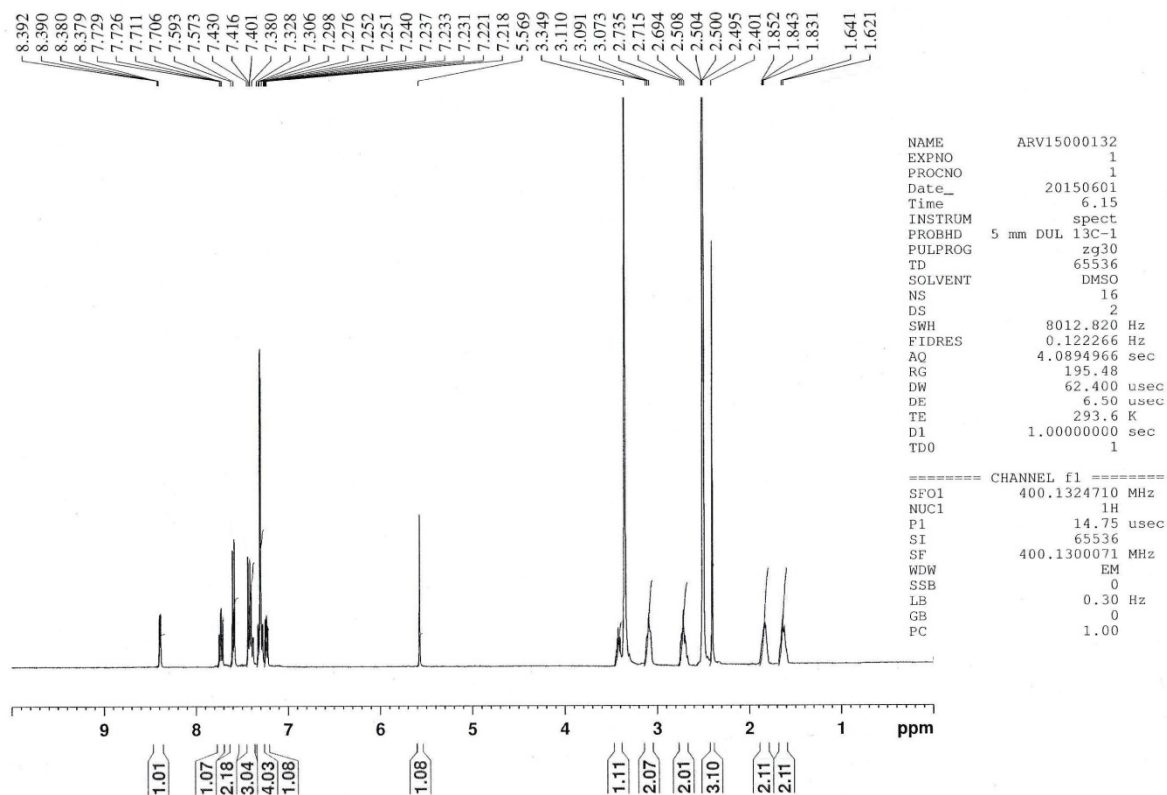
Peak#	Ret. Time	Area	Area %
1	10.384	300707	1.121
2	10.789	137043	0.511
3	12.555	311919	1.163
4	14.923	26070958	97.205
Total		26820886	100.000

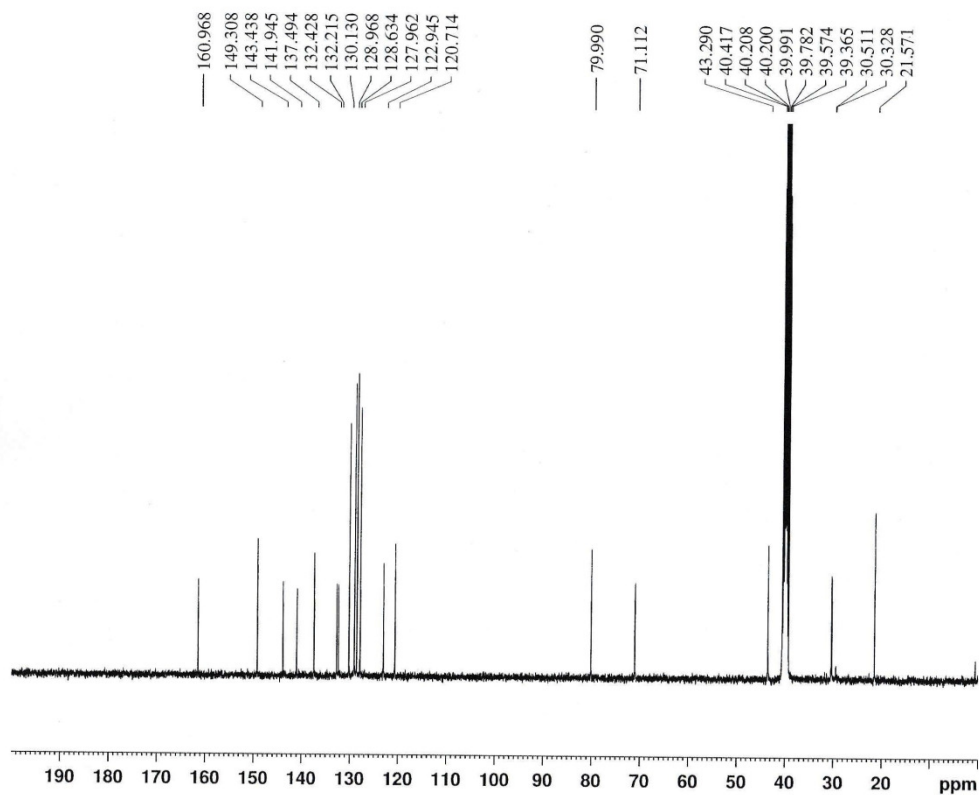
PeakTable



(R)-2-((4-chlorophenyl)((1-tosylpiperidin-4-yl)oxy)methyl)pyridine (6i): Yield (254mg, 84.3%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.39- 8.37(d,J=8Hz,1H), 7.72- 7.70(m,1H), 7.59- 7.57

(d,J=8.0Hz, 2H), 7.43- 7.38(m, 3H),7.32- 7.21 (m, 5H), 5.56(s, 1H), 3.34(m, 1H), 3.11- 3.07(m, 2H), 2.73- 2.69(m, 2H), 2.40(s,3H), 1.85- 1.83(m, 2H), 1.64- 1.62 (m, 2H); ¹³C-NMR (DMSO-d₆)160.96, 149.30, 143.43, 141.94, 137.49, 132.42, 132.21, 130.13, 128.96, 128.63, 127.96, 122.94, 120.71, 79.99, 71.11, 43.29, 30.51, 30.32, 21.57; HRMS Calcd 479.117; Found: 479.117 (M+Na⁺); Anal.Calcd for C₂₄H₂₅ClN₂O₃S : C 63.08; H 5.51; N 6.13; Found: C, 63.06; H, 5.48; N, 6.14; Chiral HPLC (%ee) 99;





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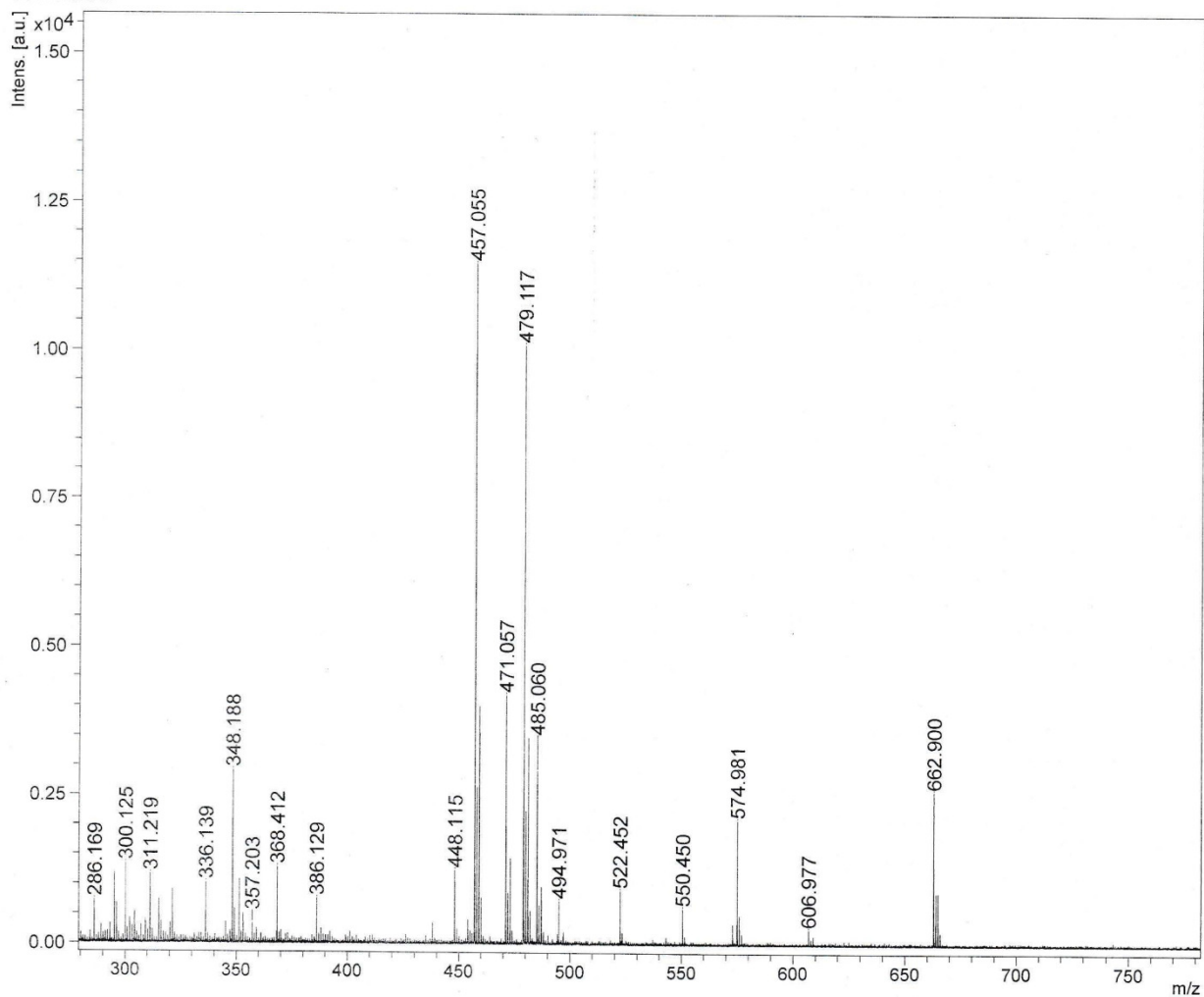
NAME      ARV15000132-13C
EXPNO     1
PROCNO    1
Date_     . 20150531
Time      1.05
INSTRUM   spect
PROBHD    5 mm DUL 13C-1
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         5000
DS         4
SWH        28409.092 Hz
FIDRES     0.433488 Hz
AQ         1.1534836 sec
RG         195.48
DW         17.600 use
DE         6.50 use
TE         294.9 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      100.6228293 MHz
NUC1       13C
P1         9.10 use
SI         32768
SF         100.6127685 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40

```

Comment 1

Comment 2

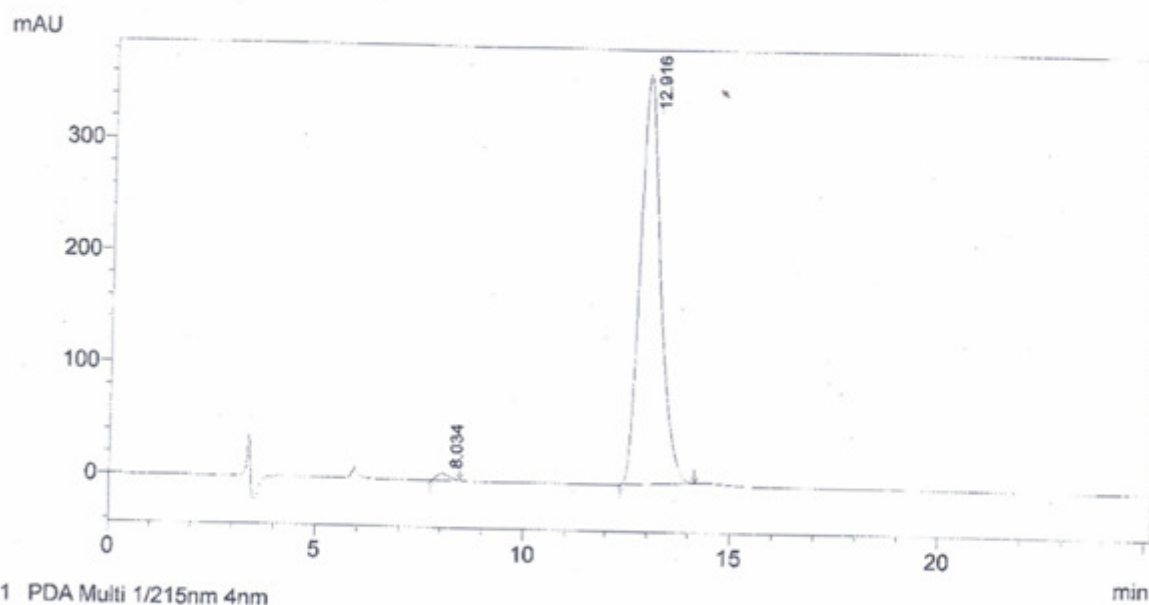


Acquisition Parameter

Date of acquisition	2015-06-16T11:16:12.984+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name : BSR-9
Sample ID :
Data File Name : BSR-9
Method File Name : 5050TFA HEXET

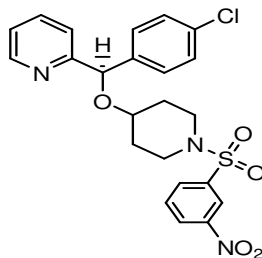
Method information: Column: CHIRAL PAK IC (250x4.6)mm 5mic
Mobile Phase 'A': 0.1% TFA IN HEXANE:ETHANOL (50:50)
Flow: 1.0ml/min



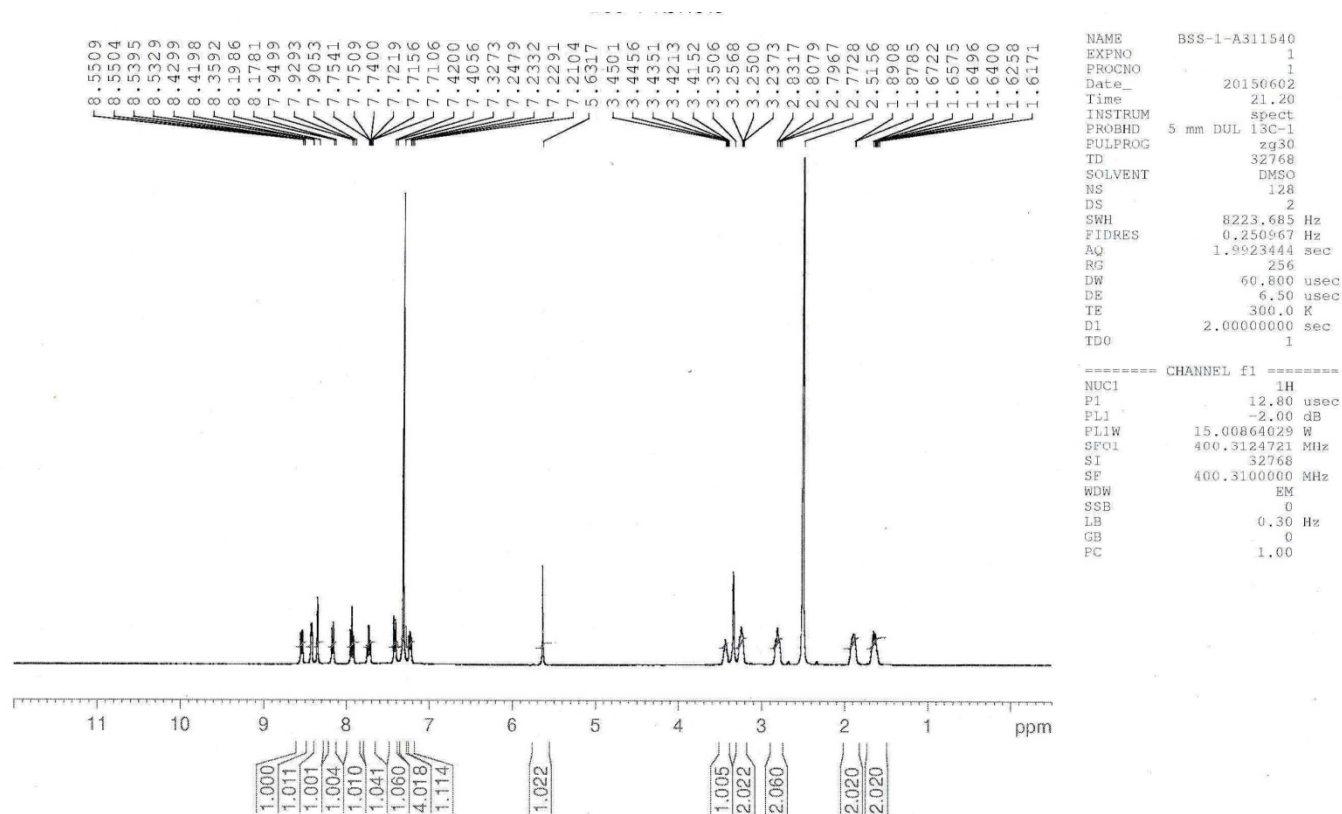
PDA Ch1 215nm 4nm

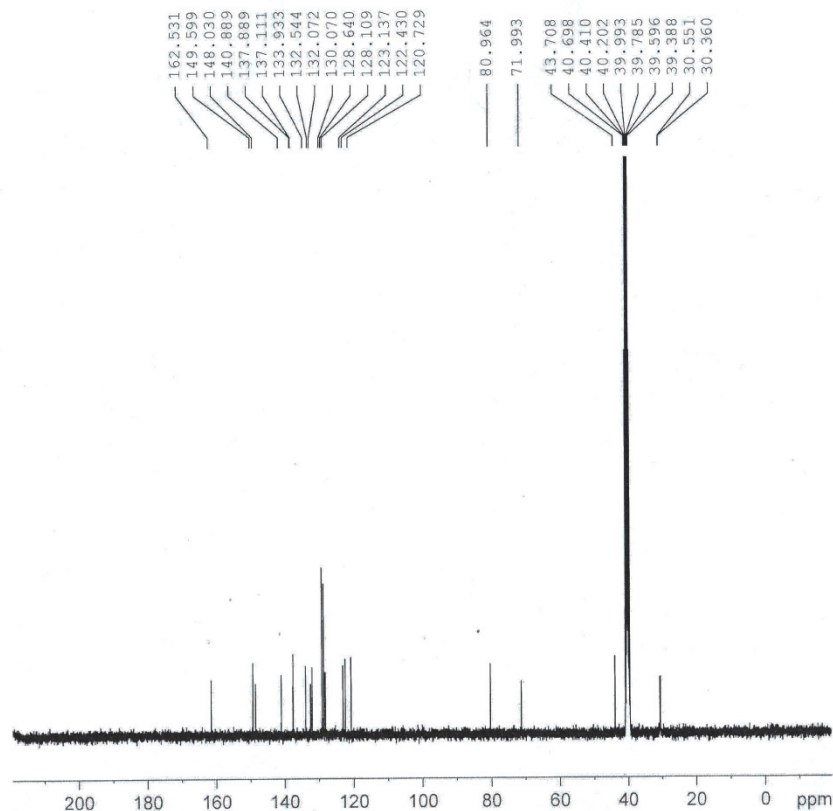
PeakTable

Peak#	Ret. Time	Area	Area %
1	8.034	121117	0.963
2	12.916	12455887	99.037
Total		12577005	100.000



(S)-2-((4-chlorophenyl)((1-((3-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6j): Yield (265mg, 82%); Tan colored solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.55- 8.53 (d,J=8.0Hz,1H), 8.42- 8.41(d, J=4.0Hz,1H), 8.35 (s,1H), 8.19- 8.17 (d,J=8.0Hz,1H), 7.94- 7.90(t,J=8.0Hz,1H),7.75-7.71(m,1H), 7.42-7.40(d,J=8.0Hz,1H),7.32-7.21(m, 5H), 5.63(s, 1H), 3.45-3.41(m, 1H), 3.25-3.23(m, 2H), 2.83- 2.77(m, 2H) 1.89- 1.87 (m, 2H) 1.67- 1.61 (m, 2H); ¹³C-NMR (DMSO-d₆);162.53, 149.59, 148.03, 140.88, 137.88, 137.11, 133.93, 132.54, 132.07, 130.07, 128.64, 128.10, 123.13, 122.43, 120.72, 80.96, 71.99, 43.70, 30.55, 30.36; HRMS Calcd 510.086; Found: 510.086(M+Na⁺); Anal.Calcd for C₂₃H₂₂ClN₃O₅S : C 56.61; H 4.54; N 8.67; Found: C, 56.58; H, 4.57; N, 8.67; Chiral HPLC (%ee) 97.2





```

Current Data Parameters
NAME      bssl-A311540
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20150604
Time      21.50
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         32768
SOLVENT   DMSO
NS         2500
DS         2
SWH        24038.461 Hz
FIDRES     0.733596 Hz
AQ         0.6816244 sec
RG         28.5
DW         20.800 usec
DE         6.00 usec
TE         296.9 K
D1         2.00000000 sec
d11        0.03000000 sec
DELTA     1.89999998 sec
TD0        1

===== CHANNEL f1 =====
NUC1       13C
P1         8.15 usec
PL1        -2.00 dB
SFO1       100.6839383 MHz

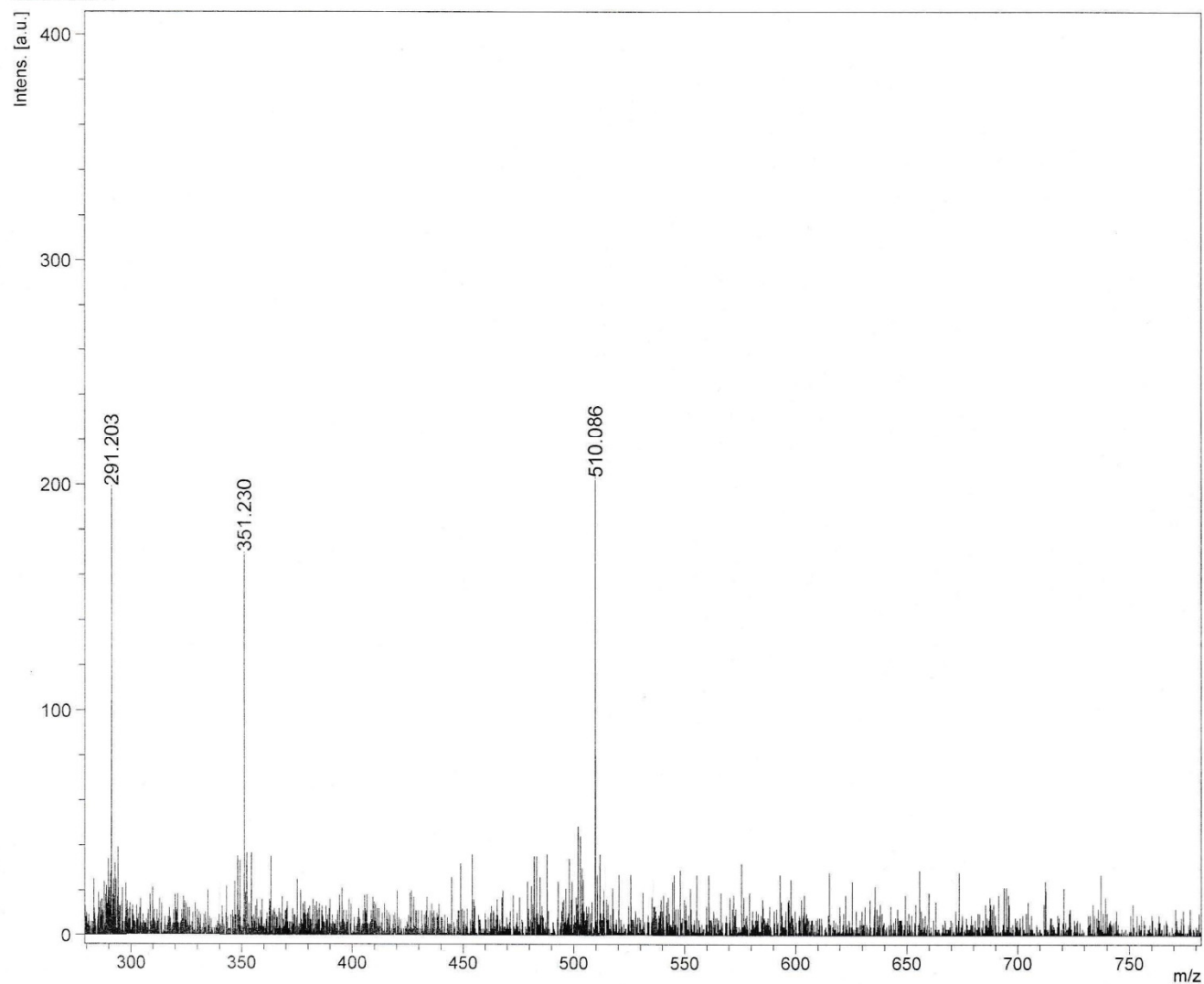
===== CHANNEL f2 =====
CPDPRG2    waltz16
NUC2       1H
PCPD2      80.00 usec
PL2        -2.00 dB
PL12       13.30 dB
PL13       15.50 dB
SFO2       400.3746015 MHz

F2 - Processing parameters
SI         32768
SF         100.6738710 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40

```

Comment 1

Comment 2

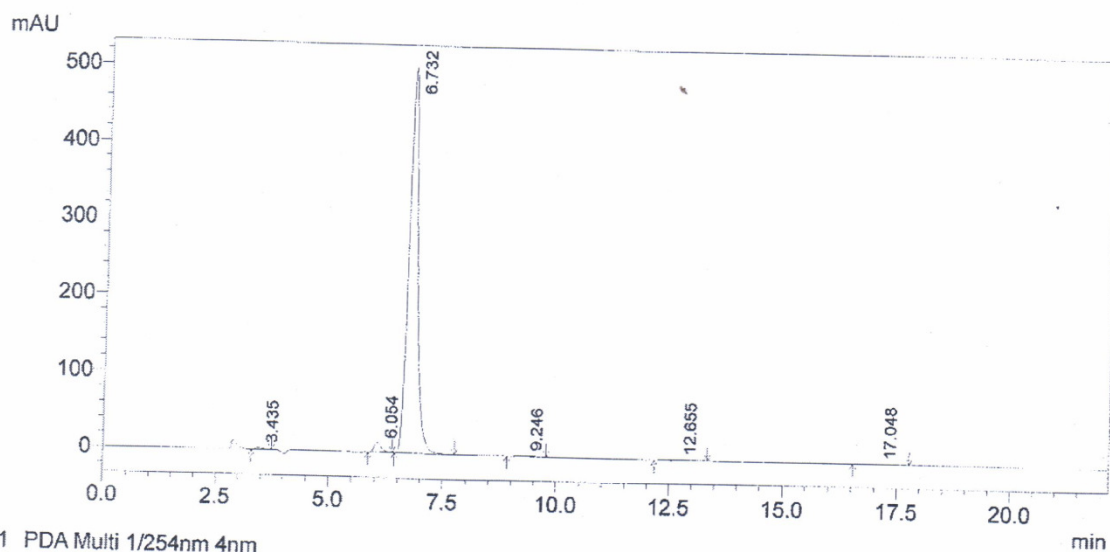


Acquisition Parameter

Date of acquisition	2015-06-16T11:05:30 921+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name : BSS-1
 Sample ID :
 Data File Name : BSS-1
 Method File Name : 7030TFAHXXET

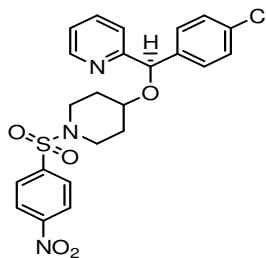
Method information: Column: CHIRAL PAK IC(250x4.6)mm 5mic
 Mobile Phase 'A': 0.1%TFA IN HEXANE:ETHANOL(7030)
 Flow: 1.0ml/min



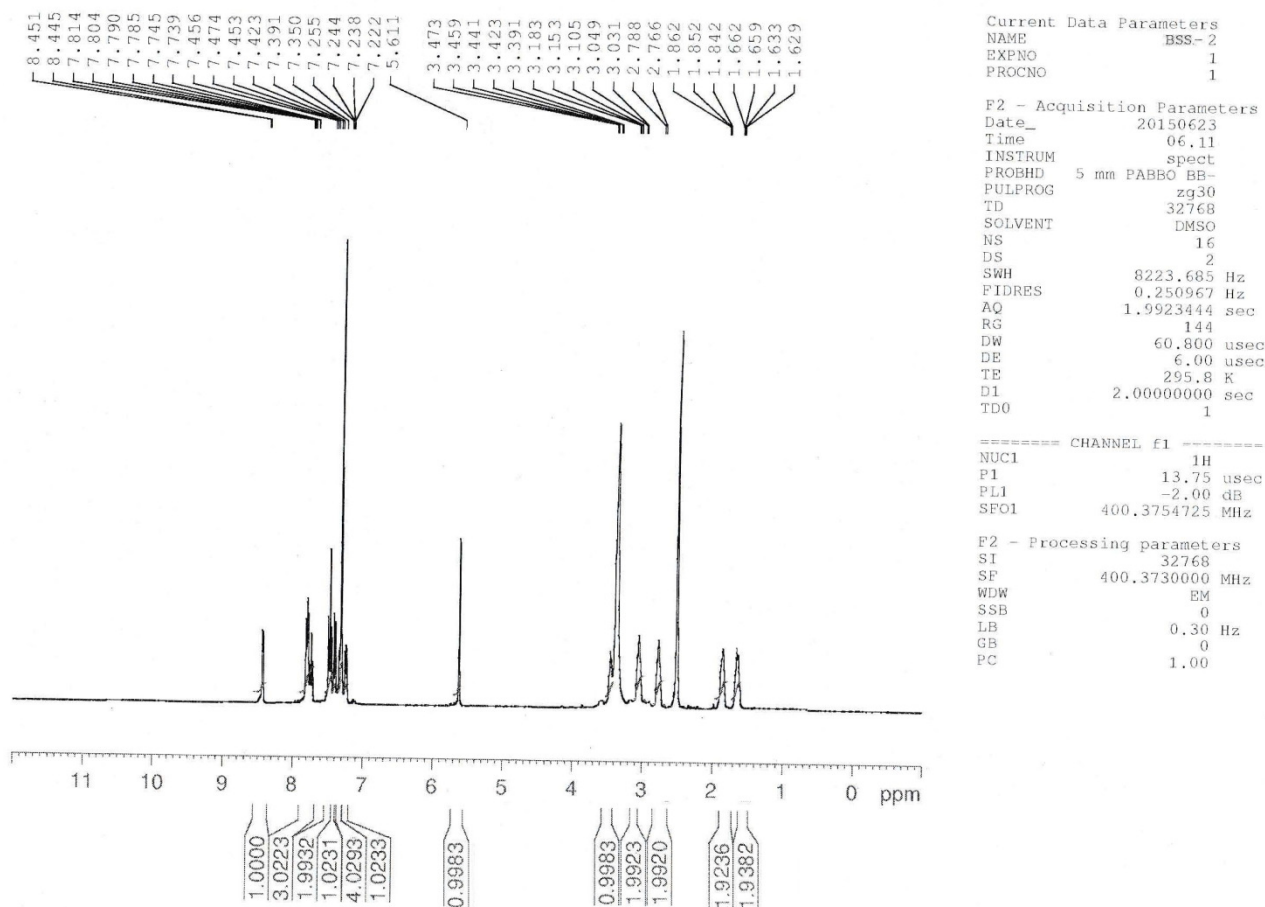
1 PDA Multi 1/254nm 4nm

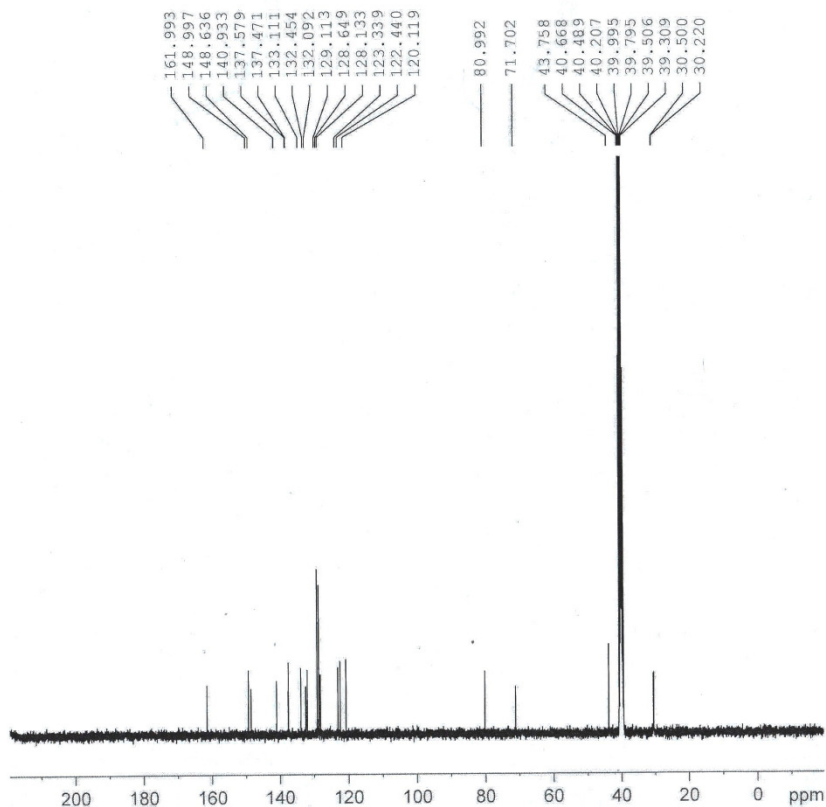
PeakTable

Peak#	Ret. Time	Area	Area %
1	3.435	23822	0.324
2	6.054	134780	1.832
3	6.732	7152513	97.237
4	9.246	21532	0.293
5	12.655	12621	0.172
6	17.048	10521	0.143
Total		7355789	100.000



(S)-2-((4-chlorophenyl)((1-((4-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6k): Yield (283mg, 88%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.45- 8.44(d,J=4Hz,1H), 7.81- 7.73(m,3H), 7.45- 7.35 (m,7H), 7.25- 7.22(d,J=8.0Hz,1H), 5.61(s, 1H), 3.47- 3.39(m, 1H), 3.04- 3.03(m, 2H), 2.78- 2.76(m, 2H), 1.86- 1.84 (m, 2H), 1.66- 1.62 (m, 2H); ¹³C-NMR (DMSO-d₆);161.99, 148.99, 148.63, 140.93, 137.57, 137.47, 133.11, 132.45, 132.09, 129.11, 128.64, 128.13, 123.33, 122.44, 120.11, 80.99, 71.70, 43.75, 30.50, 30.22; HRMS Calcd 510.086; Found: 510.086(M+Na⁺); Anal.Calcd for C₂₃H₂₂ClN₃O₅S : C 56.61; H 4.54; N 8.67; Found: C, 56.68; H, 4.53; N, 8.69; [α]_D= +37.6(C 0.01, MeOH);





Current Data Parameters
NAME bss2
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date 20150604
Time 15.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32768
SOLVENT DMSO
NS 2500
DS 2
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 0.6816244 sec
RG 28.5
DW 20.800 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TDO 1

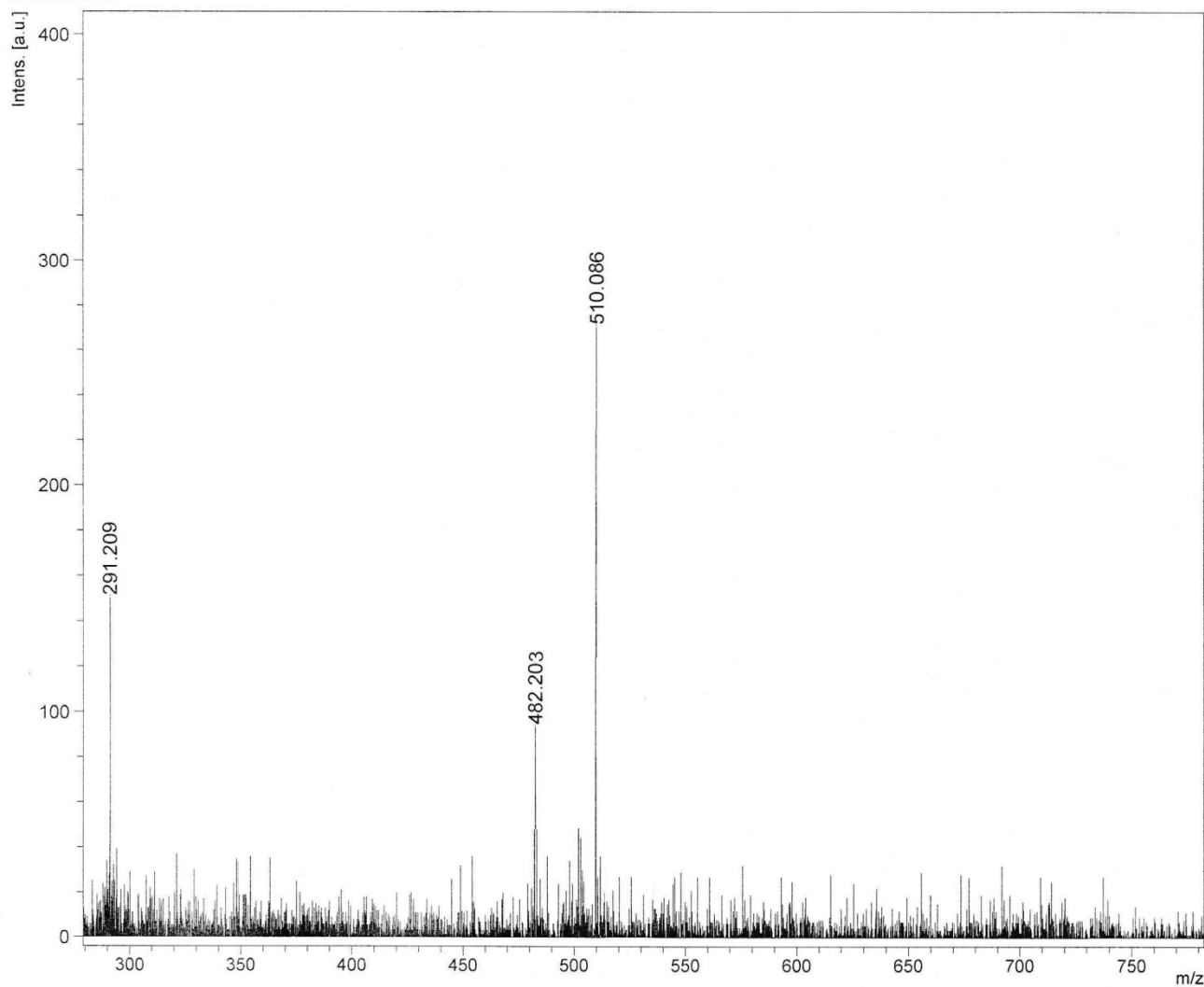
===== CHANNEL f1 =====
NUC1 13C
P1 8.15 usec
PL1 -2.00 dB
SFO1 100.6839383 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 13.30 dB
PL13 15.50 dB
SFO2 400.3746015 MHz

F2 - Processing parameters
SI 32768
SF 100.6738710 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

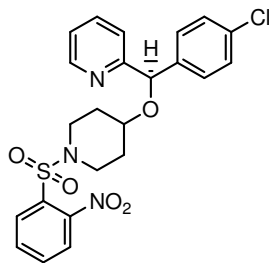
Comment 1

Comment 2

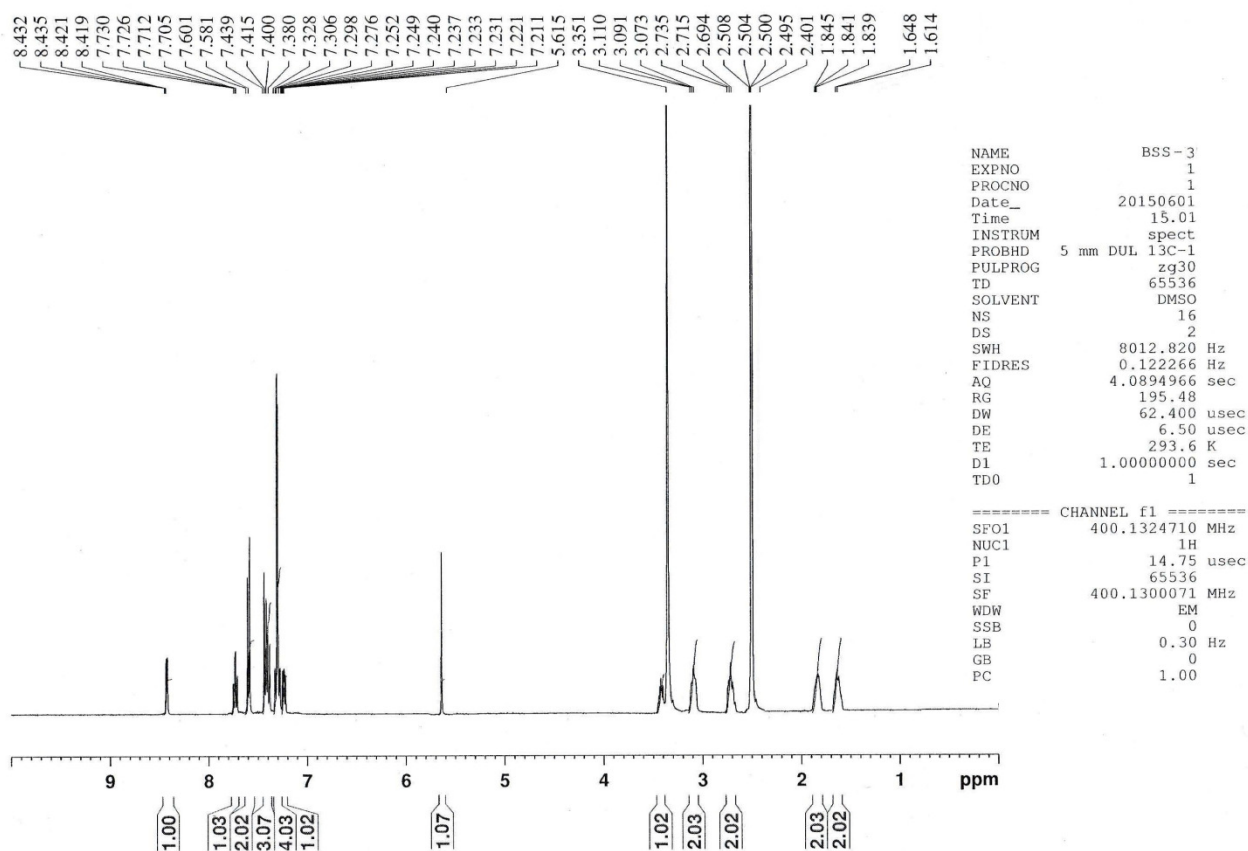


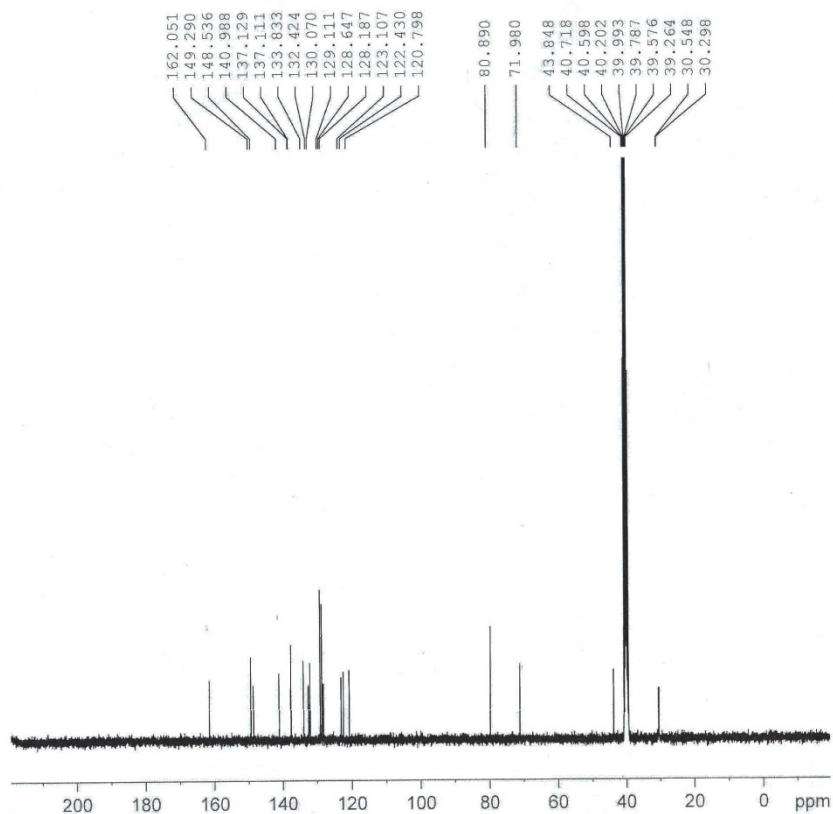
Acquisition Parameter

Date of acquisition	2015-06-16T10:17:50.921+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	



(S)-2-((4-chlorophenyl)((1-((2-nitrophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6l): Yield (273mg, 85%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.43- 8.41(d,J=8Hz,1H), 7.73- 7.70(m,1H), 7.60- 7.58 (d,J=8.0Hz, 2H), 7.43- 7.32(m, 3H),7.30- 7.21 (m, 5H), 5.61(s, 1H), 3.35(m, 1H), 3.11- 3.07(m, 2H), 2.73- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.64- 1.61 (m, 2H); ¹³C-NMR (DMSO-d₆);162.05, 149.29, 148.53, 140.98, 137.12, 137.11, 133.83, 132.42, 130.07, 129.11, 128.64, 128.18, 123.10, 122.43, 120.79, 80.89, 71.98, 43.84, 30.54, 30.29; HRMS Calcd 510.086; Found: 510.086(M+Na⁺); Anal.Calcd for C₂₃H₂₂ClN₃O₅S : C 56.61; H 4.54; N 8.67; Found: C, 56.56; H, 4.59; N, 8.71; Chiral HPLC (%ee) 97.6;





Current Data Parameters
 NAME bss3
 EXPNO 5
 PROCNO 2

F2 - Acquisition Parameters
 Date 20150604
 Time 06.40
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 2500
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 28.5
 DW 20.800 usec
 DE 6.00 usec
 TE 296.9 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TDO 1

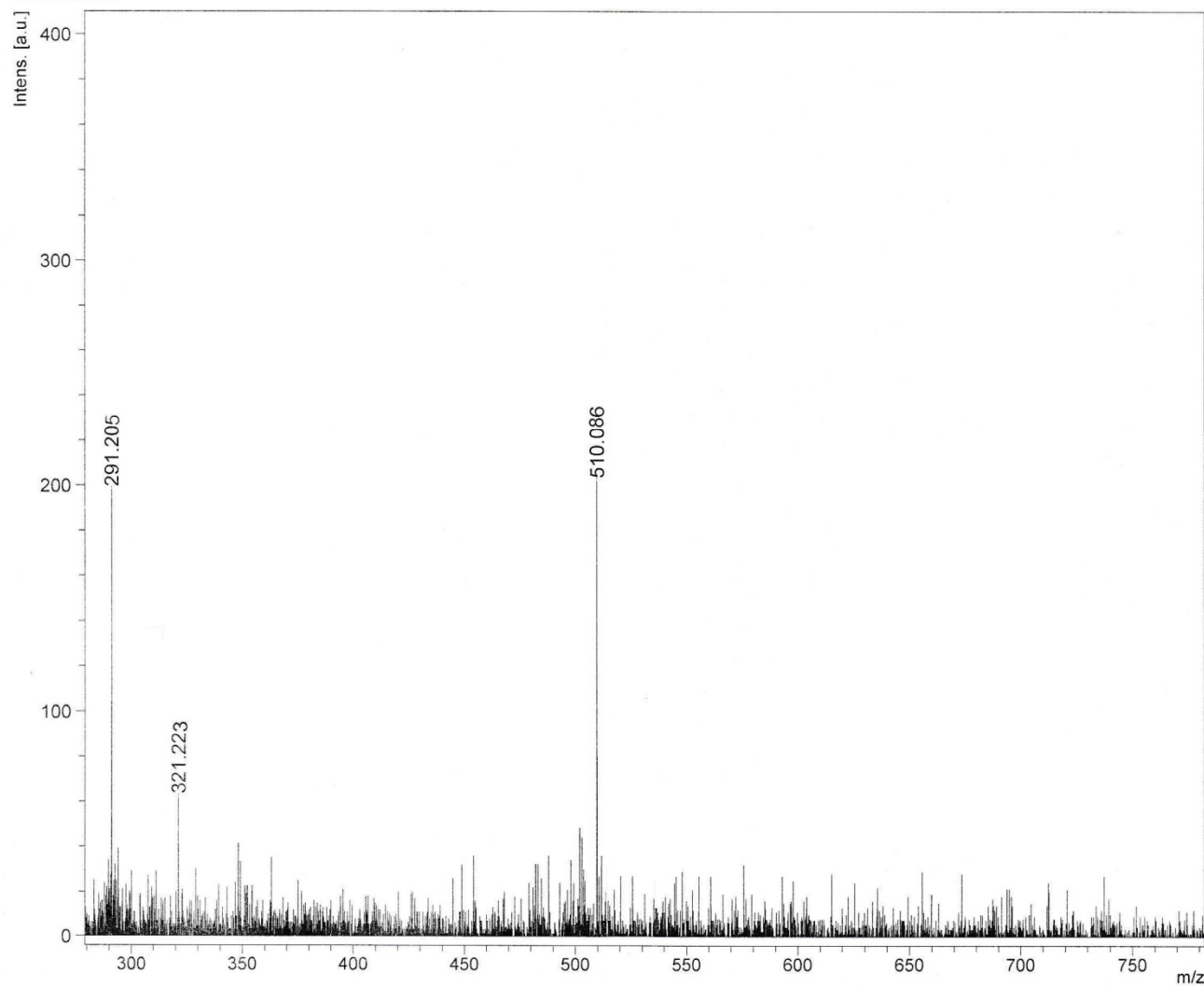
===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Comment 1

Comment 2

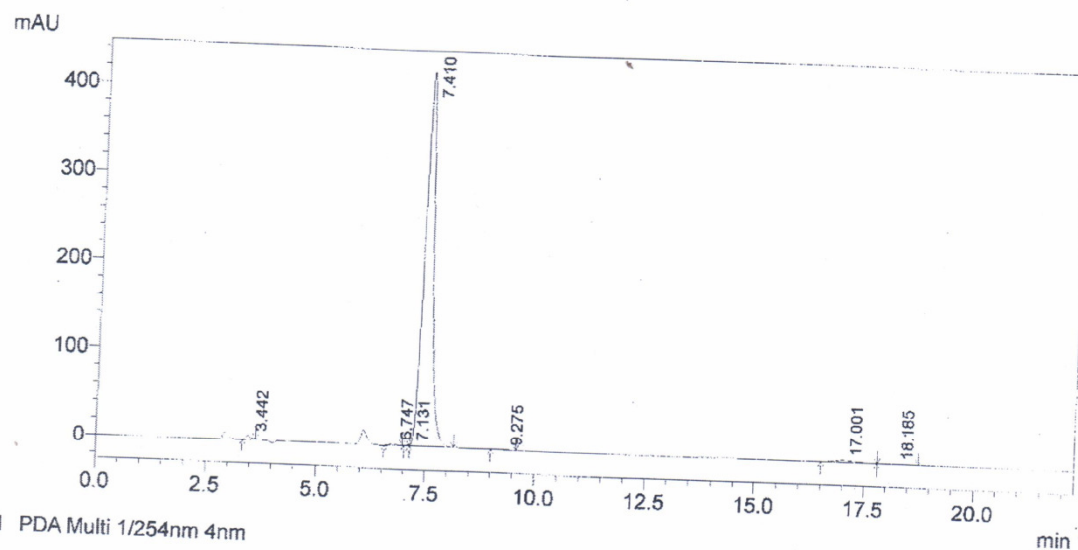


Acquisition Parameter

Date of acquisition	2015-06-16T15:05:30.921+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name : BSS-3
 Sample ID :
 Data File Name : BSS-3
 Method File Name : 7030TFAHEXET

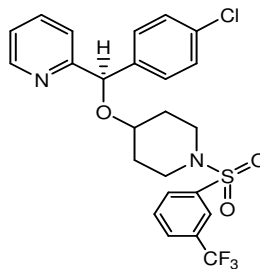
Method information : Column: CHIRAL PAK IC (250x4.6)mm 5mic
 Mobile Phase 'A': 0.1%TFA IN HEXANE:ETHANOL (70:30)
 Flow: 1.0ml/min



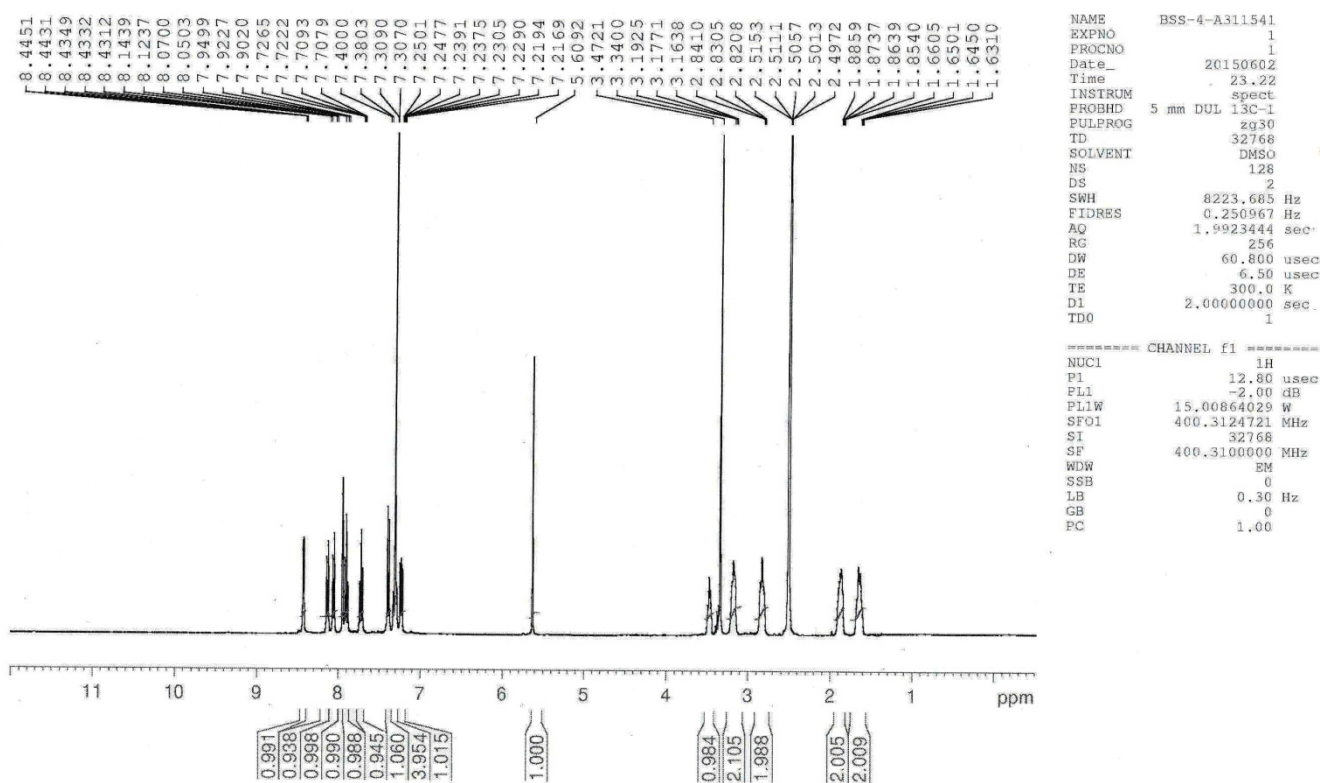
1 PDA Multi 1/254nm 4nm

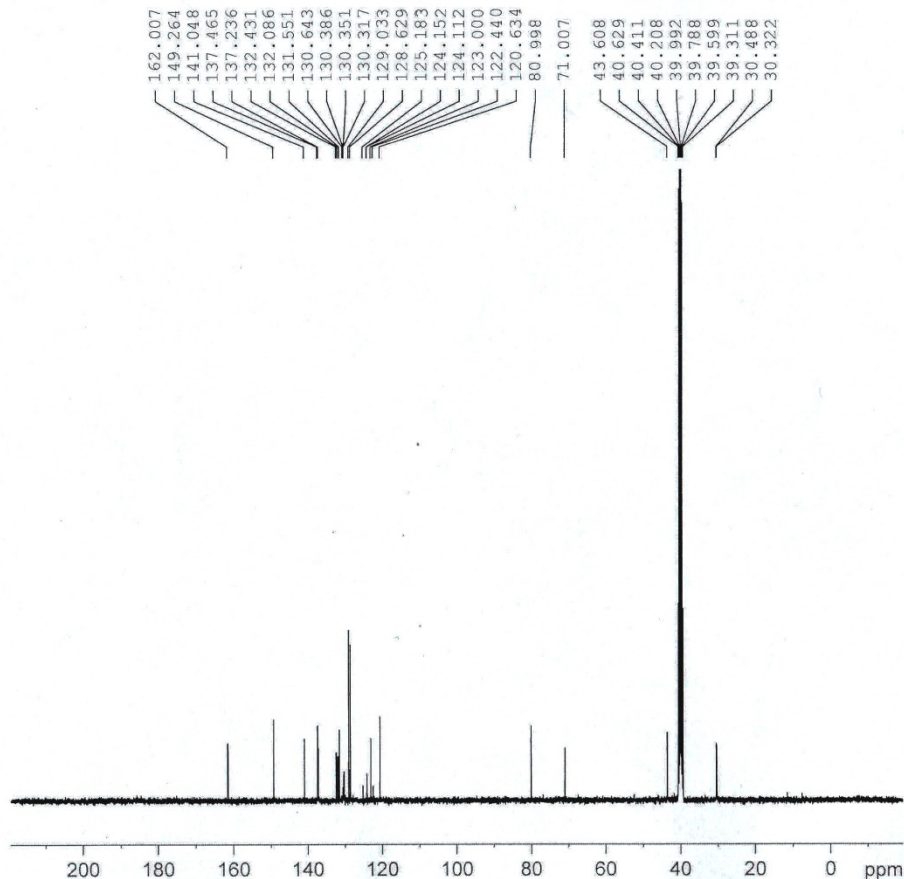
PeakTable

Peak#	Ret. Time	Area	Area %
1	3.442	31464	0.491
2	6.747	20743	0.323
3	7.131	5832	0.091
4	7.410	6261080	97.624
5	9.275	3344	0.052
6	17.001	82553	1.287
7	18.185	8473	0.132
Total		6413489	100.000



(S)-2-((4-chlorophenyl)((1-((3-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6m): Yield (288mg, 86%); Off-white solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.44- 8.43(d, J=4Hz,1H), 8.14- 8.12(d, J=8.0Hz, 1H), 8.07- 8.05(d, J=8.0Hz, 1H), 7.94- 7.90(m, 2H), 7.72- 7.70 (m, 1H), 7.40- 7.38(d, J=8.0Hz,1H), 7.30- 7.21(m,5H), 5.60(s, 1H), 3.47(m, 1H), 3.19- 3.16(m, 2H), 2.84- 2.82(m, 2H), 1.88- 1.86 (m, 2H), 1.66- 1.63 (m, 2H); ¹³C-NMR (DMSO-d₆); 162.00, 149.26, 141.04, 137.46, 137.23, 132.43, 132.08, 131.55, 130.64, 130.38, 130.35, 130.31, 129.03, 128.62, 125.18, 124.15, 124.11, 123.00, 122.44, 120.63, 80.99, 71.00, 43.60, 30.48, 30.32; ; HRMS Calcd 511.107; Found: 511.1067(M+H) ; Anal.Calcd for C₂₄H₂₂ClFN₃O₃S : C 56.42; H 4.34; N 5.48; Found: C, 56.47; H, 4.33; N, 5.52; [α]_D= +39.7(C 0.01, MeOH);





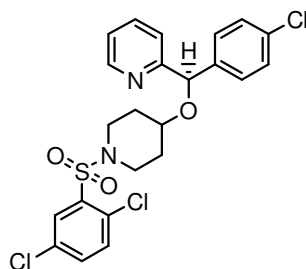
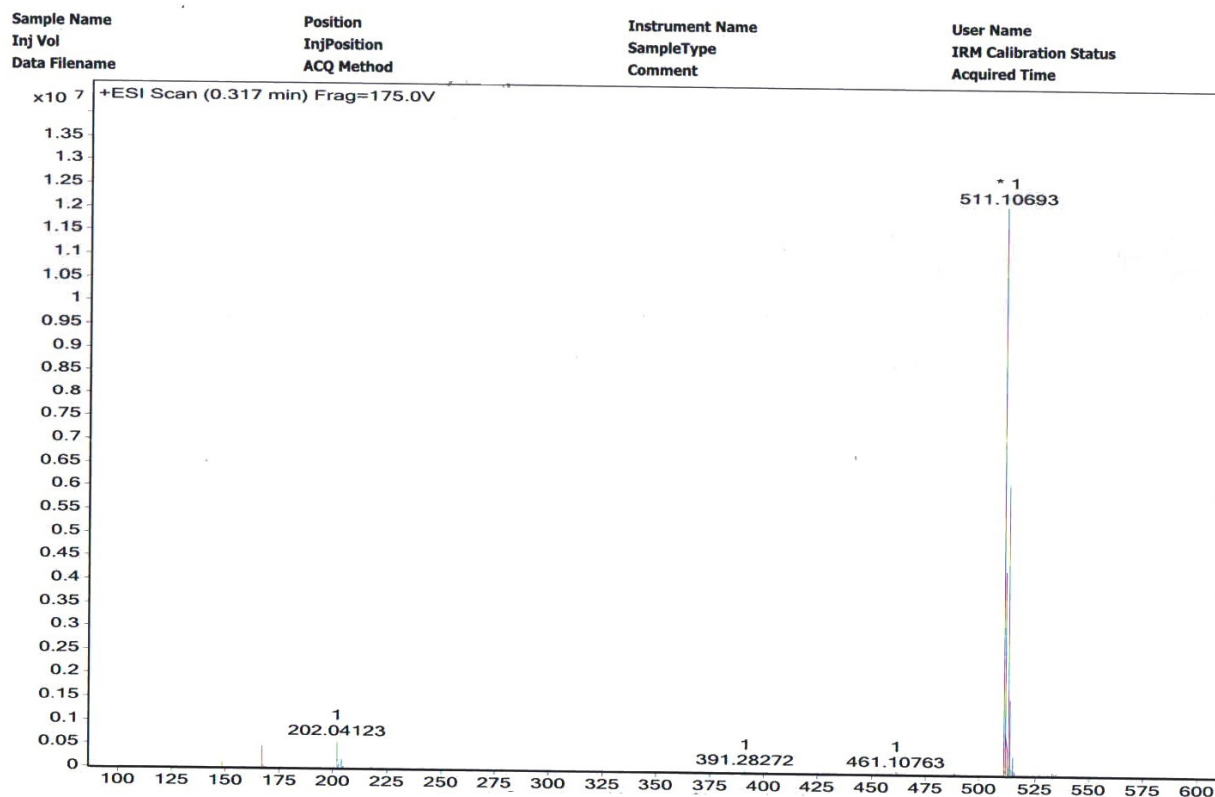
Current Data Parameters
 NAME bss4-A311541
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date 20150604
 Time 03.27
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 2500
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 32
 DW 20.800 usec
 DE 6.00 usec
 TE 296.9 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999999 sec
 TD0 1

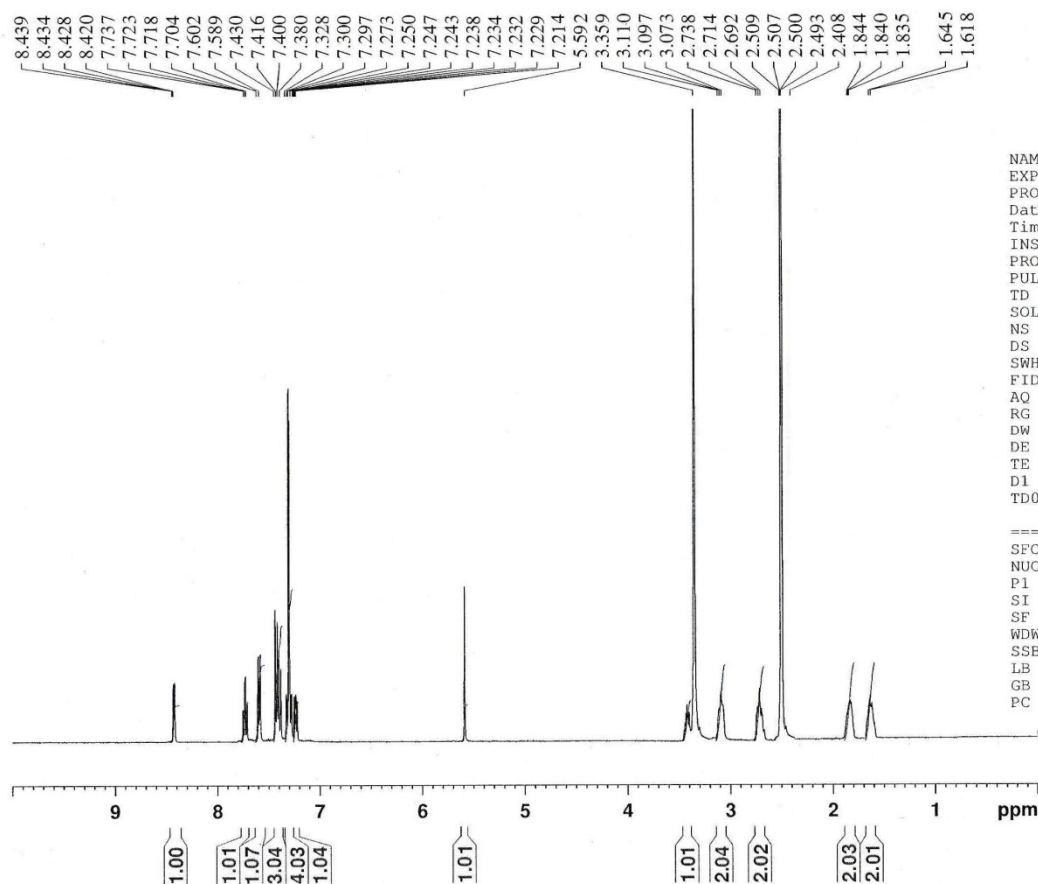
===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



(S)-2-((4-chlorophenyl)((1-((2,5-dichlorophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6n): Yield (291mg, 87%); Brown low melting solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.43- 8.42(d, J=8.0Hz,1H), 7.73- 7.70(m,1H), 7.60- 7.58 (d, J=8.0Hz, 1H), 7.43- 7.32(m, 3H),7.30- 7.21 (m, 5H), 5.59(s, 1H), 3.35(m, 1H), 3.11- 3.07(m, 2H), 2.73- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.64- 1.61 (m, 2H); ¹³C-NMR (DMSO-d₆);160.99, 151.99, 150.93, 139.98, 137.48, 137.11, 133.83, 132.48, 131.43, 129.18, 128.83, 128.11, 123.01, 122.33, 80.99, 73.98, 43.81, 30.78, 30.91; HRMS Calcd 511.0417; Found: 511.0411(M+H); Anal.Calcd for C₂₃H₂₁Cl₃N₂O₃S : C 53.97; H 4.14; N 5.47; Found: C,53.93 ; H, 4.16; N, 5.56; Chiral HPLC (%ee) 98;

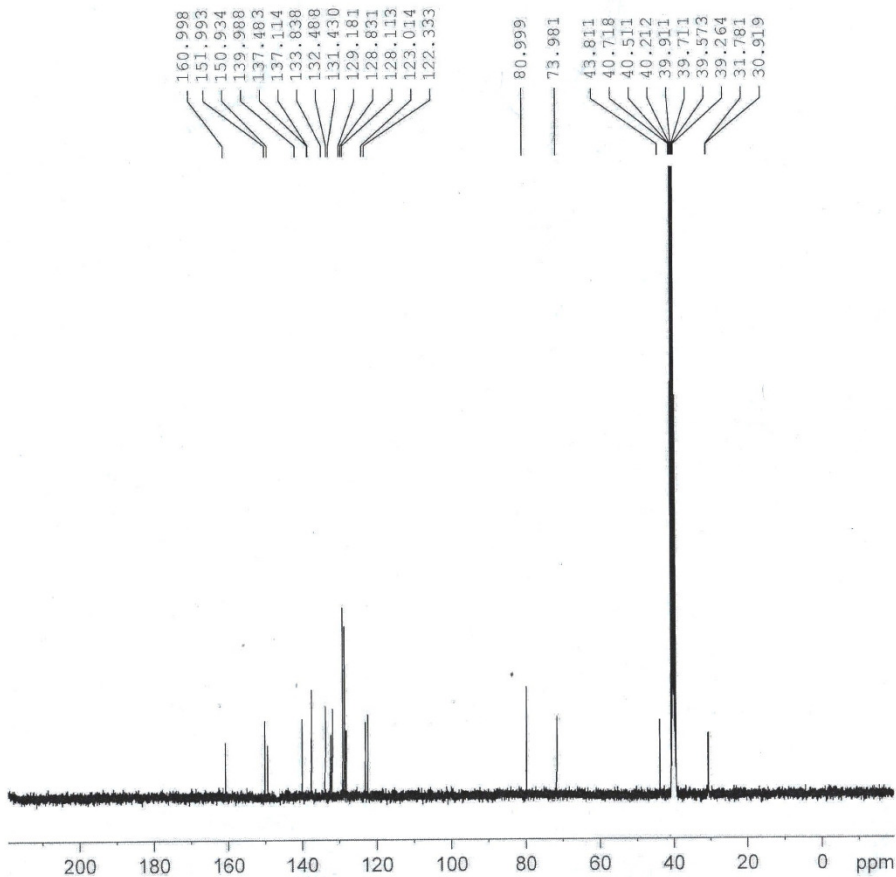


```

NAME          BSS-5
EXPNO         1
PROCNO        1
Date_         20150601
Time          15.20
INSTRUM       spect
PROBHD        5 mm DUL 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            16
DS            2
SWH           8012.820 Hz
FIDRES        0.122266 Hz
AQ            4.0894966 sec
RG            195.48
DW            62.400 usec
DE            6.50 usec
TE            293.6 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          400.1324710 MHz
NUC1           1H
P1            14.75 usec
SI            65536
SF            400.1300071 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00

```



Current Data Parameters
 NAME bss5
 EXPNO 5
 PROCNO 2

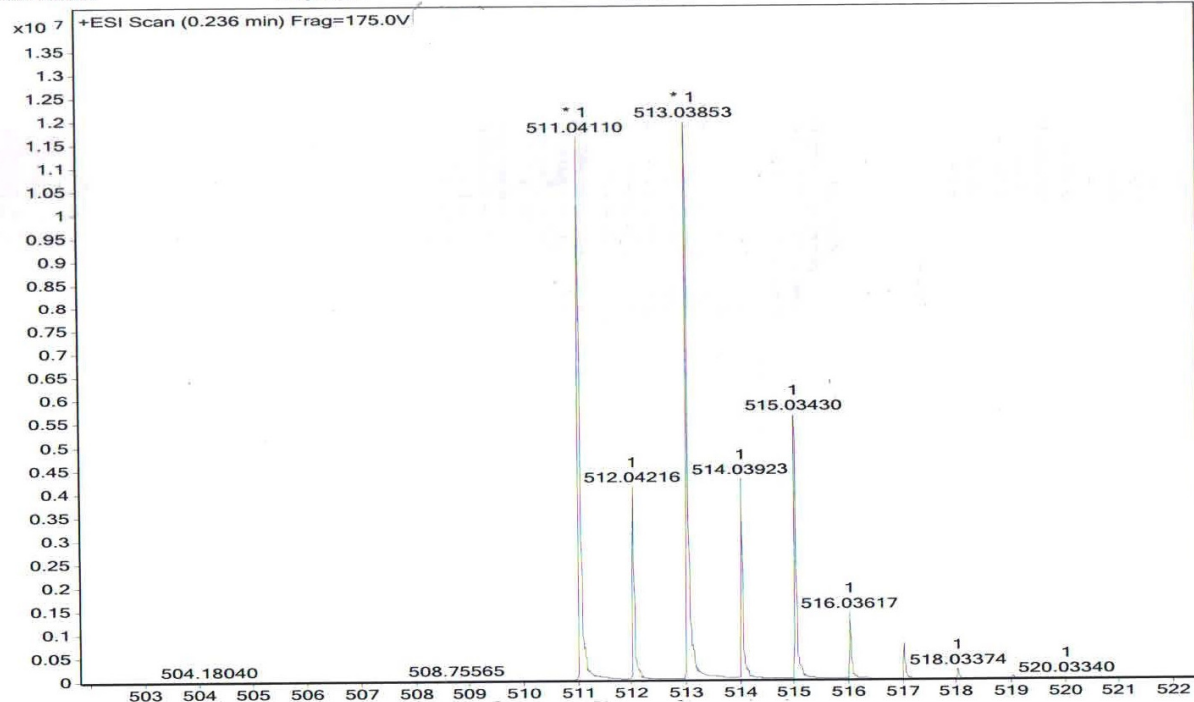
F2 - Acquisition Parameters
 Date_ 20150604
 Time_ 00.25
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 2500
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 28.5
 DW 20.800 usec
 DE 6.00 usec
 TE 296.9 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TDO 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

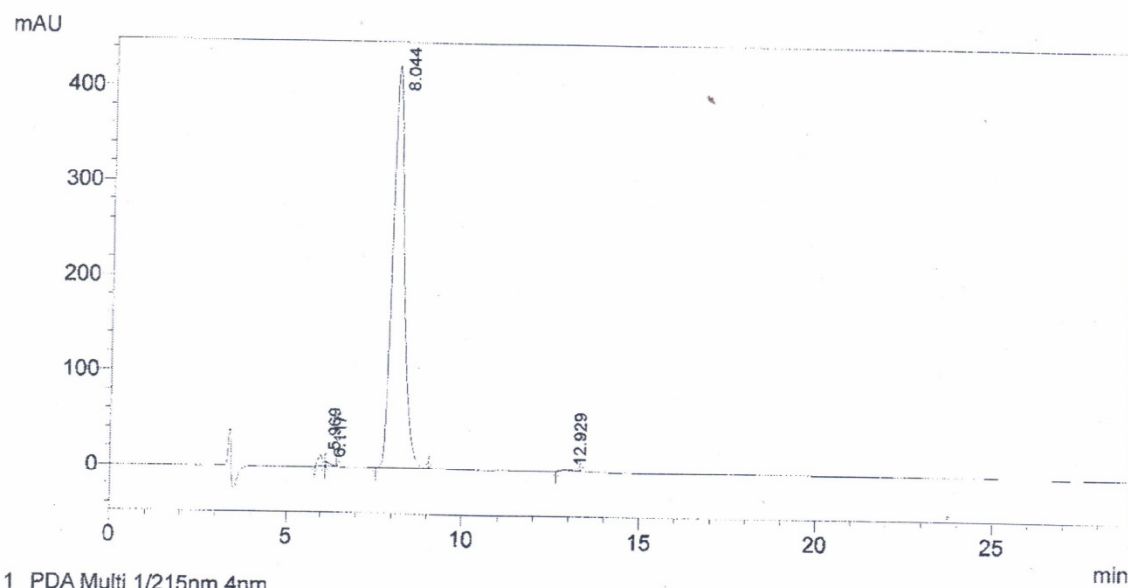
F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



Sample Name : BSS-5
 Sample ID :
 Data File Name : BSS-5
 Method File Name : 5050TFAHEXET

Method information : Column: CHIRAL PAK IC(250x4.6)mm 5mic
 Mobile Phase: 0.1%TFA IN HEXANE:ETHANOL(50:50)
 Flow: 1.0ml/min

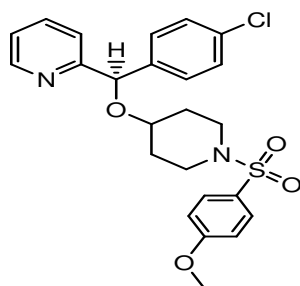


1 PDA Multi 1/215nm 4nm

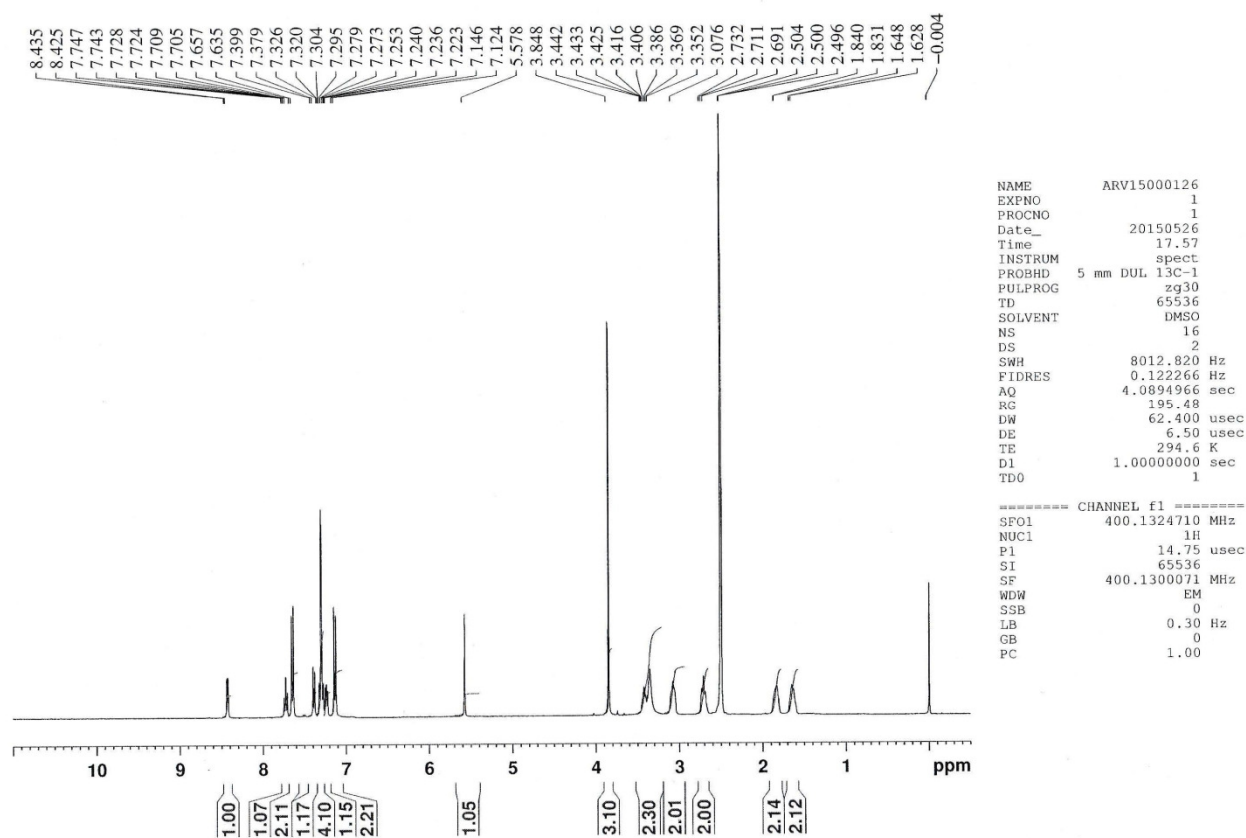
PeakTable

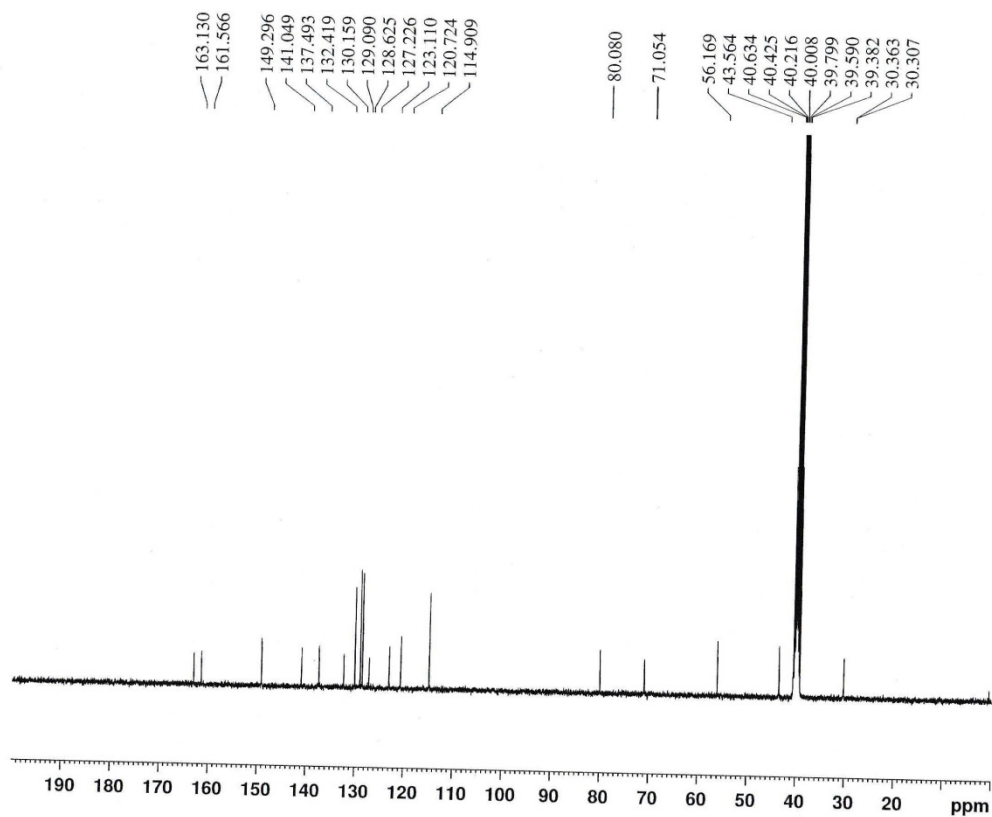
PDA Ch1 215nm 4nm

Peak#	Ret. Time	Area	Area %
1	5.969	121594	1.204
2	6.117	37066	0.367
3	8.044	9902501	98.040
4	12.929	39304	0.389
Total		10100465	100.000



(S)-2-((4-chlorophenyl)((1-((4-methoxyphenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6o):
Yield (266mg, 86%); Off-white solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.43- 8.42 (d,J=4Hz,1H), 7.74- 7.70(m,1H), 7.65- 7.63 (d,J=8.0Hz, 2H), 7.39- 7.37(d, J=8.0Hz, 1H),7.32- 7.22 (m, 5H), 7.14- 7.12(d, J=8.0Hz, 1H),5.57(s, 1H), 3.84 (s,3H), 3.44(m, 1H), 3.07(m, 2H), 2.73- 2.69(m, 2H), 1.84- 1.83 (m, 2H), 1.64- 1.62 (m, 2H); ¹³C-NMR (DMSO-d₆);163.13, 161.56, 149.29, 141.04, 137.49, 132.41, 130.15, 129.09, 128.62, 127.22, 123.11, 120.72, 114.90, 80.08, 71.05, 56.16, 43.56, 30.36, 30.30; HRMS Calcd 495.112; Found: 495.112(M+Na⁺); Anal.Calcd for C₂₄H₂₅ClN₂O₄S : C 60.94; H 5.33; N 5.92; Found: C, 60.91; H, 5.37; N, 5.95; [α]_D= +40.5(C 0.01, MeOH);



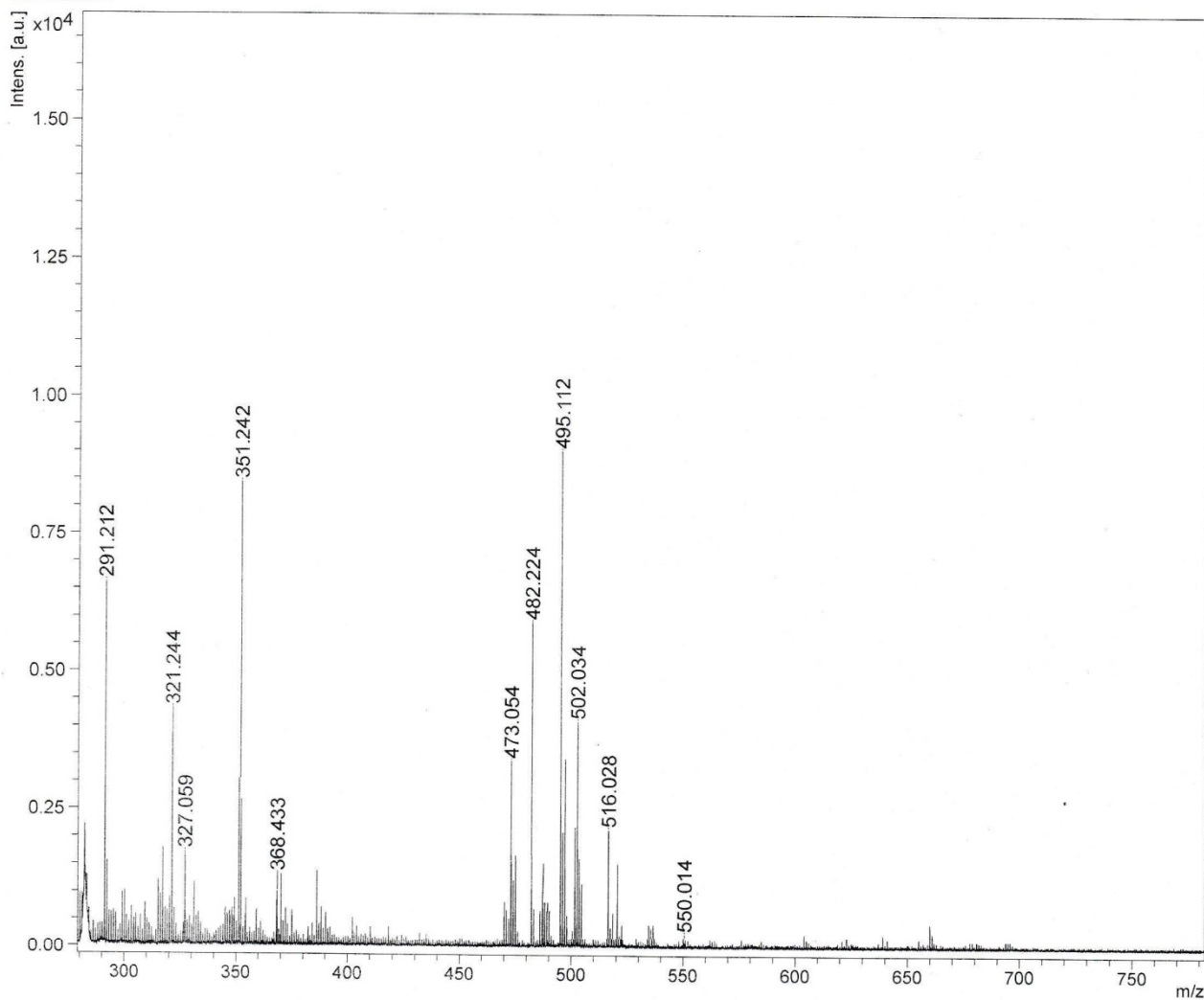


NAME ARV15000126-13C
 EXPNO 1
 PROCNO 1
 Date_ 20150527
 Time 0.11
 INSTRUM spect
 PROBHD 5 mm DUL 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 2048
 DS 4
 SWH 28409.092 Hz
 FIDRES 0.433488 Hz
 AQ 1.1534836 sec
 RG 195.48
 DW 17.600 use
 DE 6.50 use
 TE 297.6 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

===== CHANNEL f1 =====
 SFO1 100.6228293 MHz
 NUC1 13C
 P1 9.10 use
 SI 32768
 SF 100.6127685 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

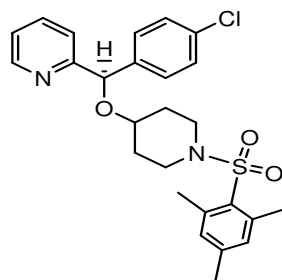
Comment 1

Comment 2

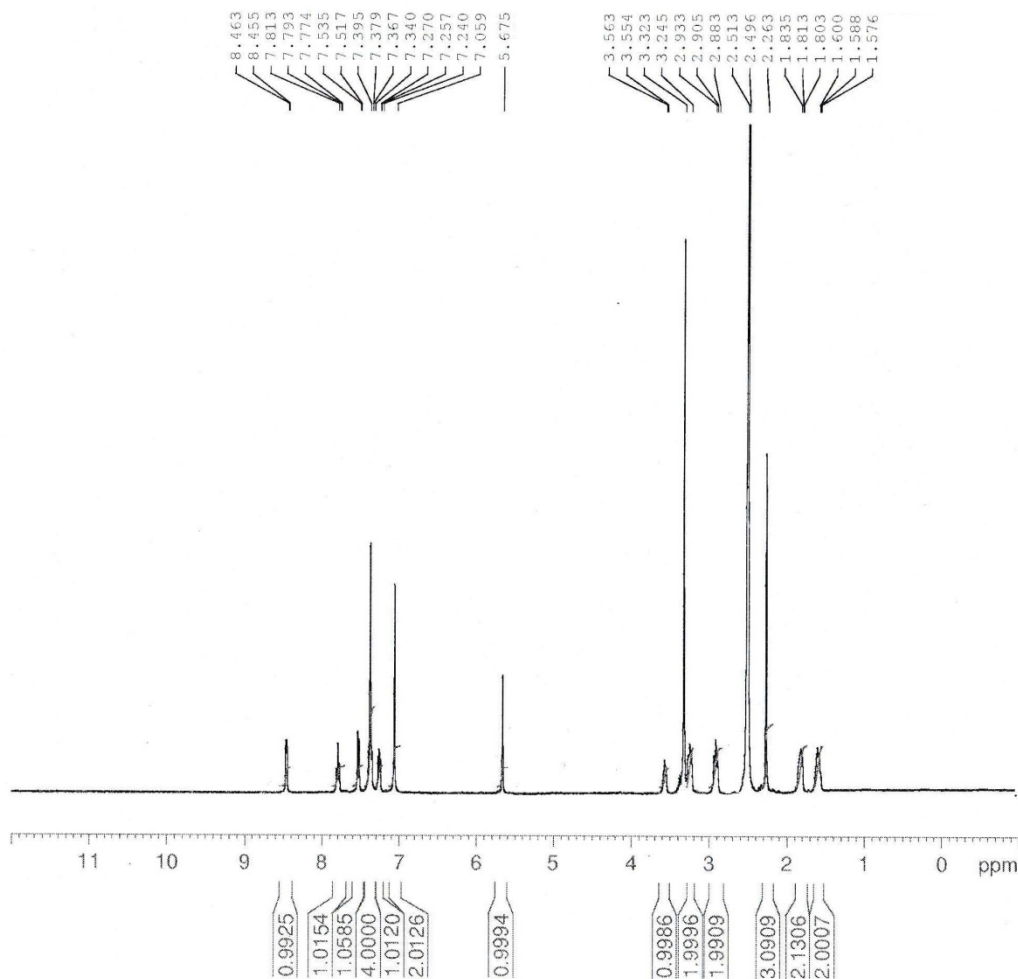


Acquisition Parameter

Date of acquisition	2015-06-16T11:05:15.734+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	



(S)-2-((4-chlorophenyl)((1-(mesitylsulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6p) : Yield (281mg, 88.5%); White solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.46- 8.45(d,J=4Hz,1H), 7.81- 7.77(m,1H), 7.53- 7.51 (d,J=8.0Hz, 1H), 7.39- 7.34(m, 4H),7.27- 7.24 (m, 1H),7.05 (s, 2H), 5.67(s, 1H), 3.56(m, 1H), 3.32(s, 6H),3.24(m, 2H), 2.93- 2.88(m, 2H), 2.26 (s,3H), 1.83- 1.80 (m, 2H), 1.60- 1.57 (m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6) 160.03, 149.85, 142.14, 141.17, 140.03, 137.17, 132.45, 132.31, 132.16, 129.16, 128.60, 120.80, 80.99, 71.99, 41.63, 30.62, 30.53, 22.75, 20.96; HRMS Calcd 507.148; Found: 507.148 ($\text{M}+\text{Na}^+$); Anal.Calcd for $\text{C}_{26}\text{H}_{29}\text{ClN}_2\text{O}_3\text{S}$: C 64.38; H 6.03; N 5.78; Found: C, 64.42; H, 5.99; N, 5.81; Chiral HPLC (%ee) 97.1;

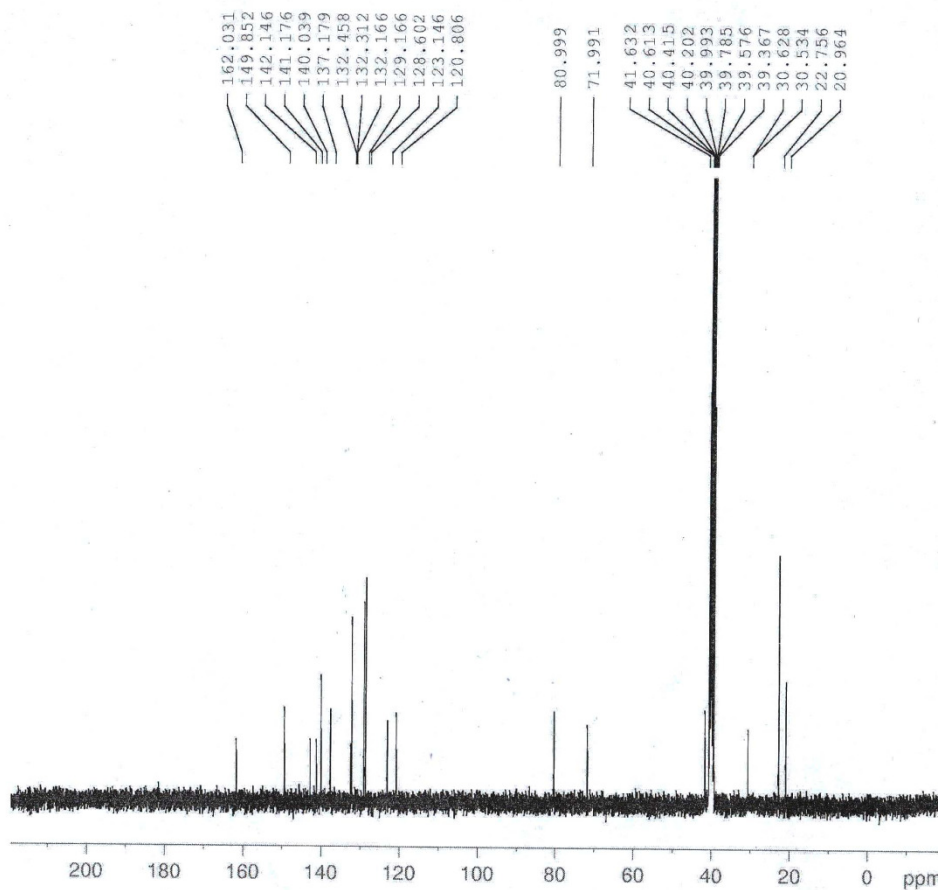


Current Data Parameters
NAME A330922
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150623
Time 12.20
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 8
DS 2
SWH 8389.262 Hz
FIDRES 0.256020 Hz
AQ 1.9530228 sec
RG 406.4
DW 59.600 usec
DE 6.00 usec
TE 297.3 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 13.20 usec
PL1 -3.00 dB
SFO1 400.2338023 MHz

F2 - Processing parameters
SI 32768
SF 400.2300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Current Data Parameters
 NAME A330922
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150624
 Time 10.39
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 1024
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 32
 DW 20.800 usec
 DE 6.00 usec
 TE 296.7 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TD0 1

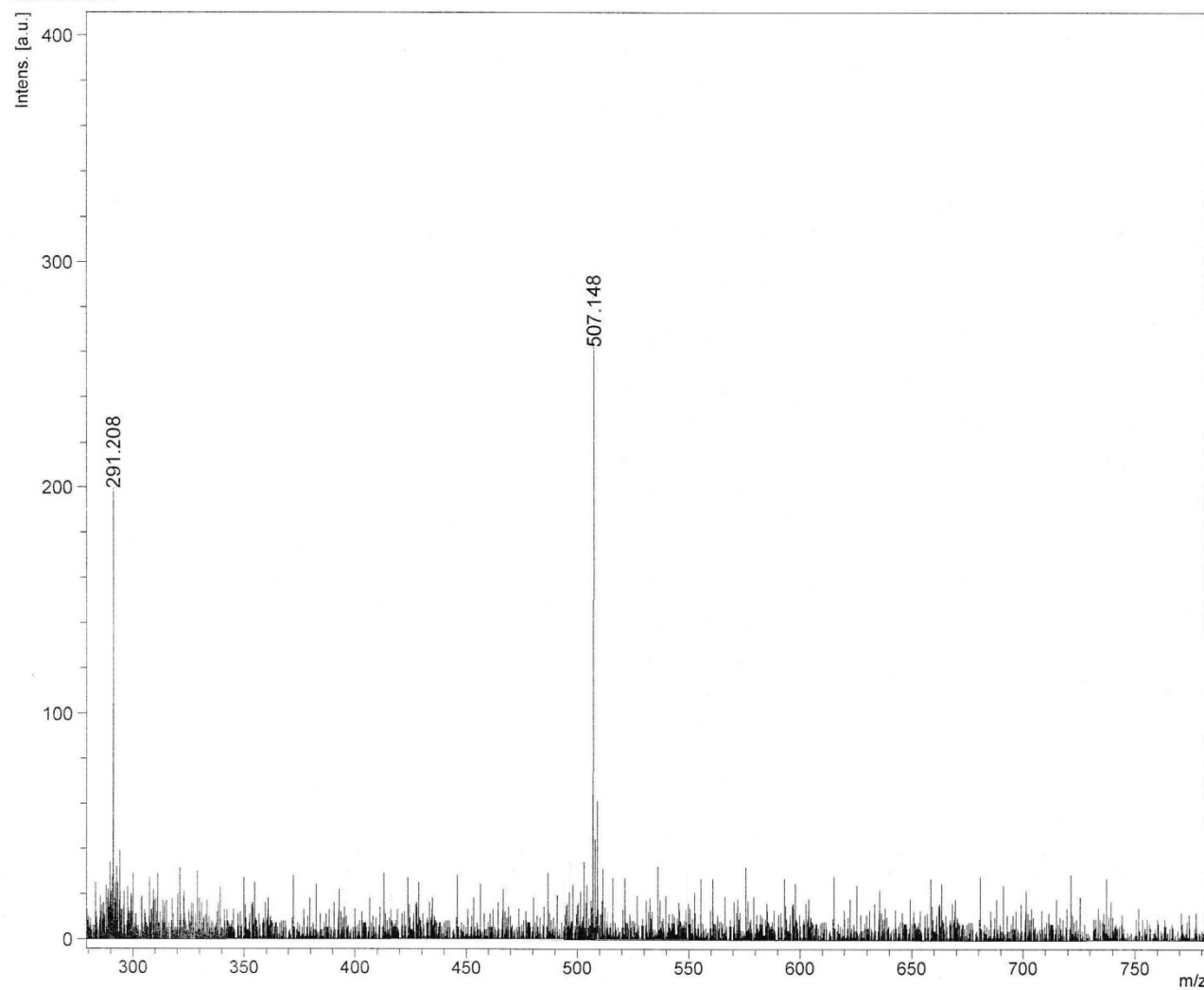
===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Comment 1

Comment 2

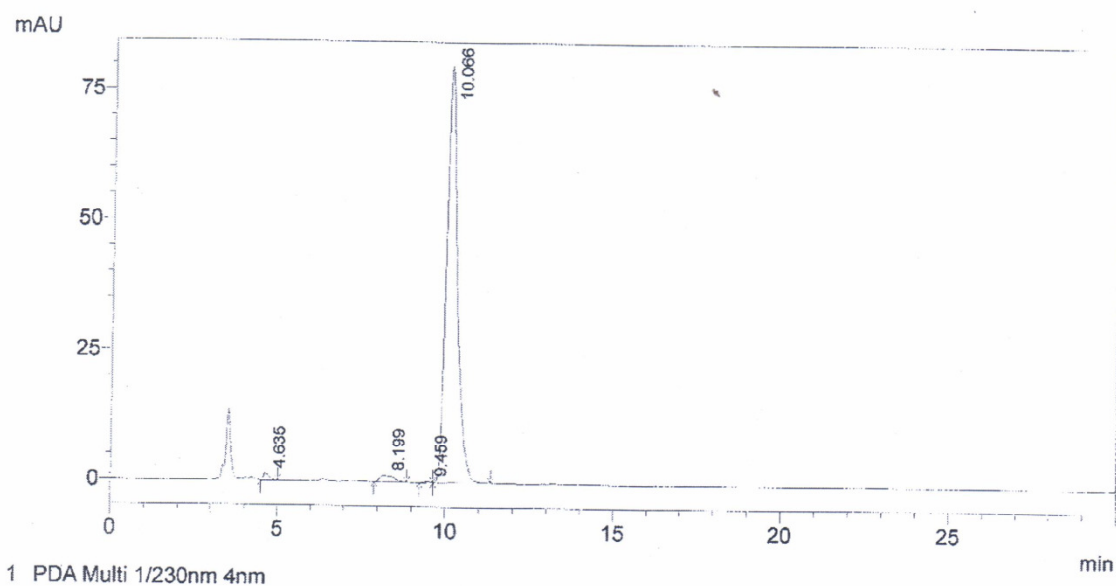


Acquisition Parameter

Date of acquisition	2015-06-16T11:30:20.921+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name : BSS-7
Sample ID :
Data File Name : BSS-7
Method File Name : 5050TFAHEXET

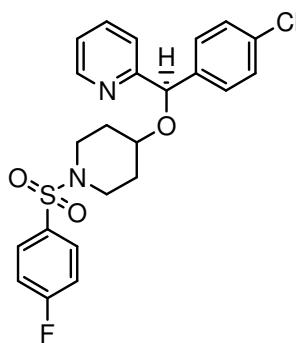
Method information : Column: CHIRAL PAK IC (250x4.6)mm 5mic
Mobile Phase 'A': 0.1% TFA IN HEXANE:ETHANOL (50:50)
Flow: 1.0ml/min



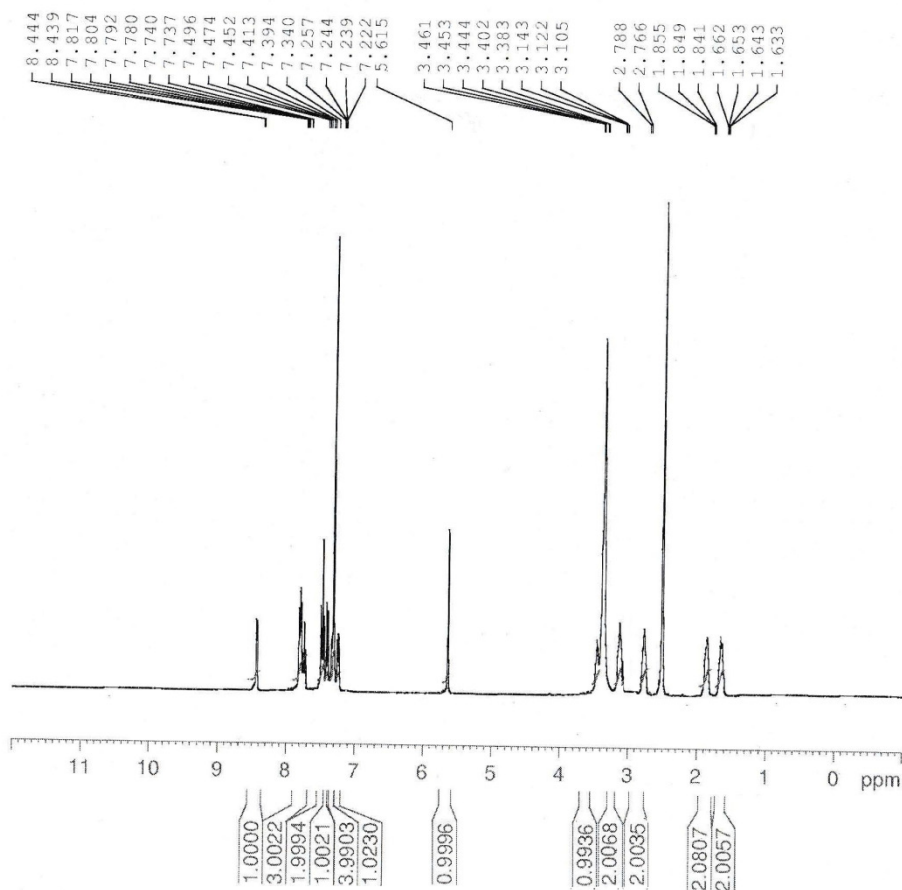
PeakTable

PDA Ch1 230nm 4nm

Peak#	Ret. Time	Area	Area %
1	4.635	14694	0.792
2	8.199	34798	1.876
3	9.459	3668	0.198
4	10.066	1801333	97.133
Total		1854493	100.000



(S)-2-((4-chlorophenyl)((1-((4-fluorophenyl)sulfonyl)piperidin-4-yl)oxy)methyl)pyridine (6q): Yield (259mg, 86%); Tan coloured solid; $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) 8.44- 8.43(d, $J=4\text{Hz}$, 1H), 7.81- 7.73(m, 3H), 7.49- 7.22 (m, 8H), 5.61(s, 1H), 3.46(m, 1H), 3.14- 3.10(m, 2H), 2.78- 2.76(m, 2H), 1.85- 1.84 (m, 2H), 1.66- 1.63(m, 2H); $^{13}\text{C-NMR}$ (DMSO-d_6) 166.39, 163.83, 161.54, 149.34, 141.01, 137.48, 132.43, 132.16, 132.13, 131.03, 130.94, 129.04, 128.61, 123.10, 120.48, 117.40, 116.18, 80.94, 71.03, 43.57, 30.46, 30.31; HRMS Calcd 483.092; Found: 483.092 ($\text{M}+\text{Na}^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{22}\text{ClFN}_2\text{O}_3\text{S}$: C 59.93; H 4.81; N 6.08; Found: C, 59.85; H, 4.87; N, 6.11; Chiral HPLC (%ee) 98.9;

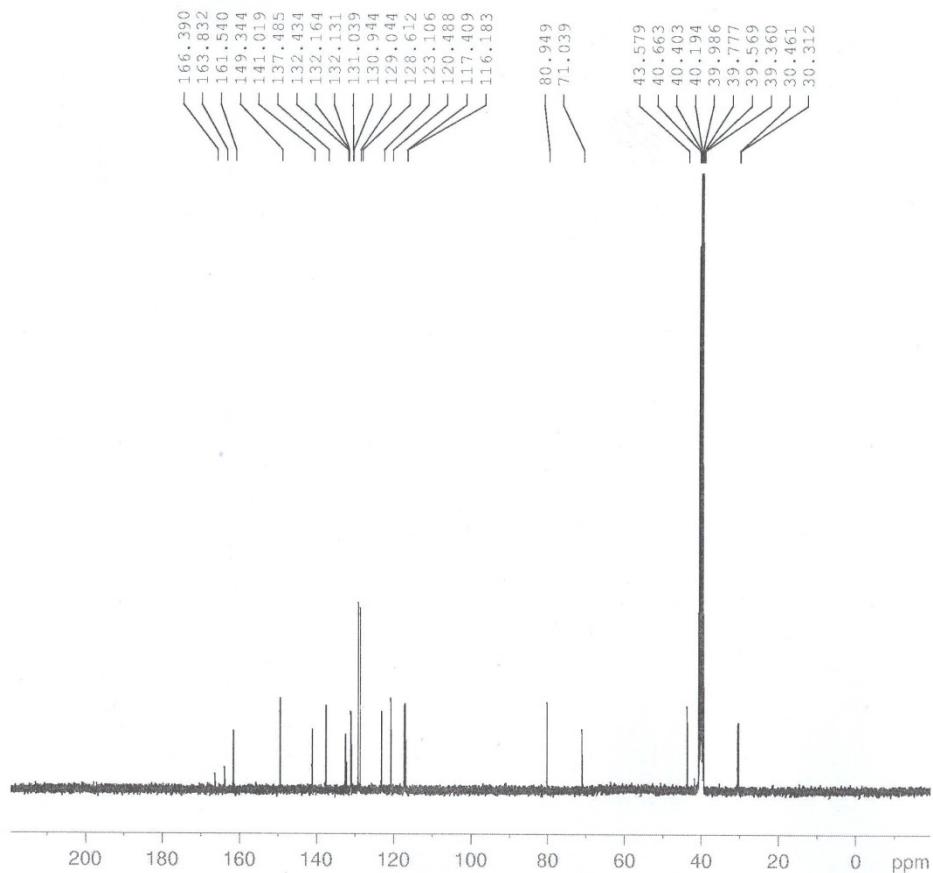


Current Data Parameters
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 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150623
 Time 12.21
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zg30
 TD 32768
 SOLVENT DMSO
 NS 16
 DS 2
 SWH 8223.685 Hz
 FIDRES 0.250967 Hz
 AQ 1.9923444 sec
 RG 144
 DW 60.800 usec
 DE 6.00 usec
 TE 295.8 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 13.75 usec
 PL1 -2.00 dB
 SFO1 400.3754725 MHz

F2 - Processing parameters
 SI 32768
 SF 400.3730000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
 NAME A330966
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150624
 Time 6.30
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpg30
 TD 32768
 SOLVENT DMSO
 NS 1024
 DS 2
 SWH 24038.461 Hz
 FIDRES 0.733596 Hz
 AQ 0.6816244 sec
 RG 36
 DW 20.800 usec
 DE 6.00 usec
 TE 296.7 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TD0 1

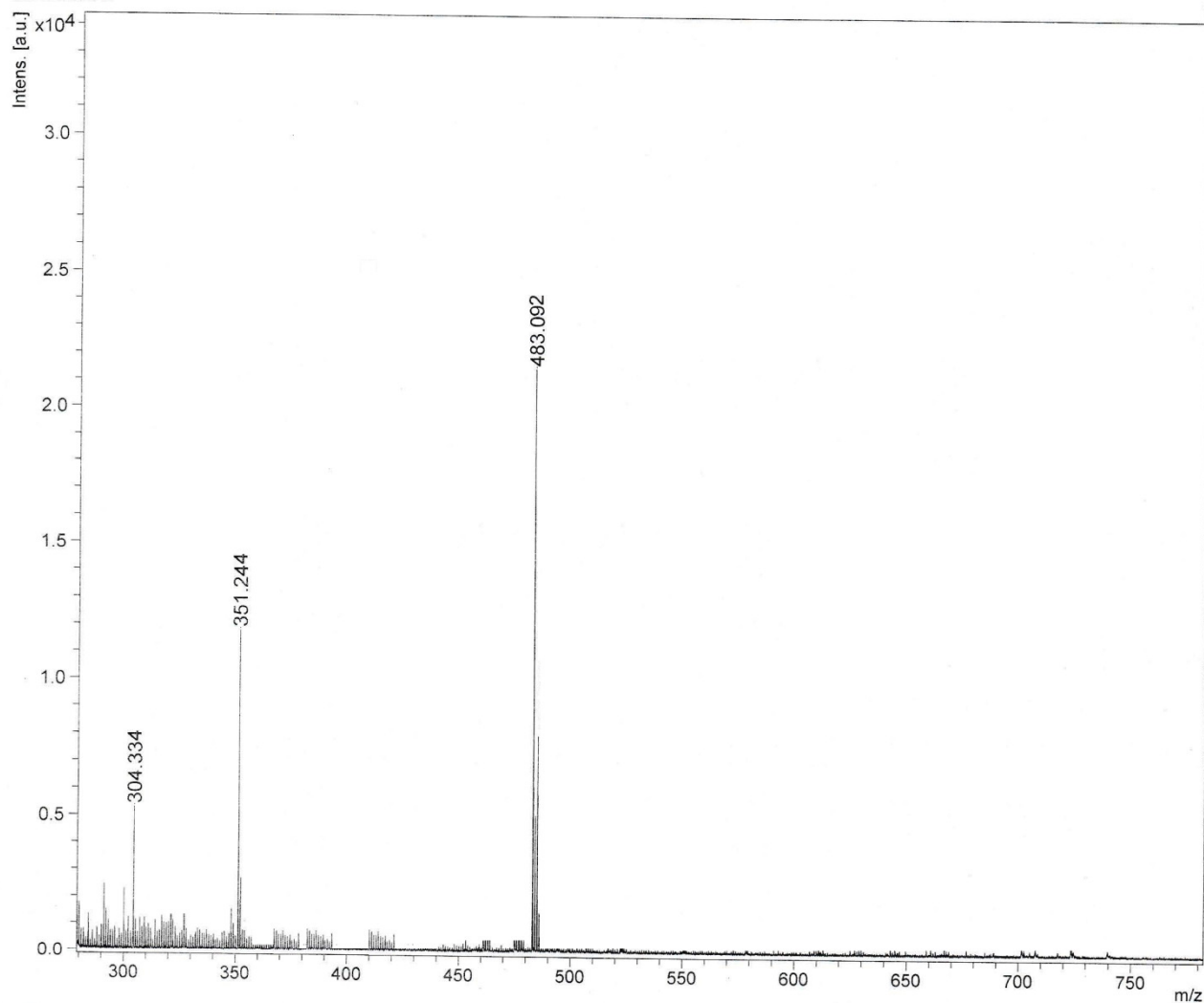
===== CHANNEL f1 =====
 NUC1 13C
 P1 8.15 usec
 PL1 -2.00 dB
 SFO1 100.6839383 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 13.30 dB
 PL13 15.50 dB
 SFO2 400.3746015 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6738710 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Comment 1

Comment 2

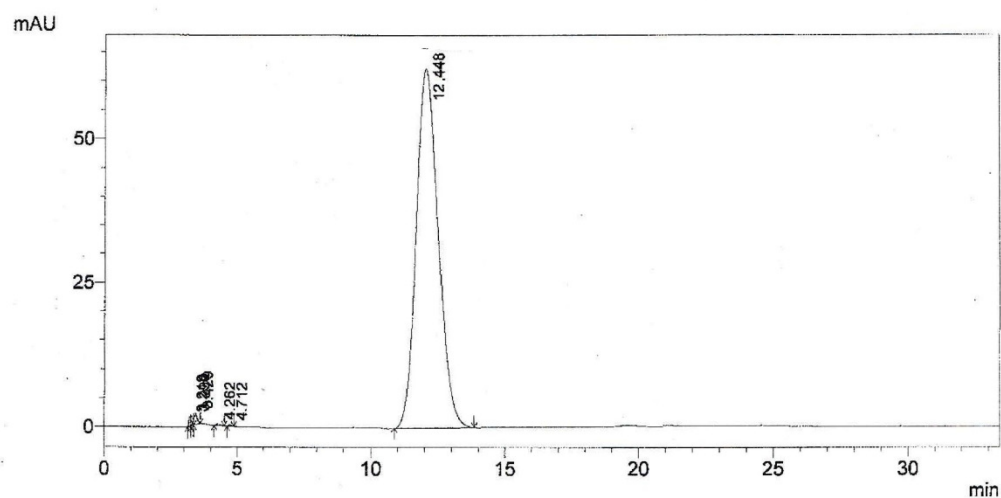


Acquisition Parameter

Date of acquisition	2015-06-16T11:16:16.171+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name :BSS-8
Sample ID :
Data File Name :BSS-8
Method File Name :2080TFAHEXET

Method information :Column:CHIRAL PAK IA(250x4.6)mm 5mic
Mobile Phase'A':0.1%TFA IN HEXANE:ETHANOL(20:80)
FLOW:1.0ml/min

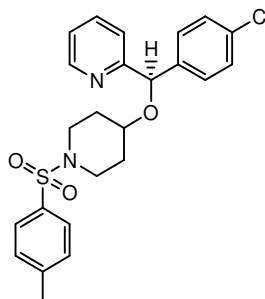


1 PDA Multi 1/272nm 4nm

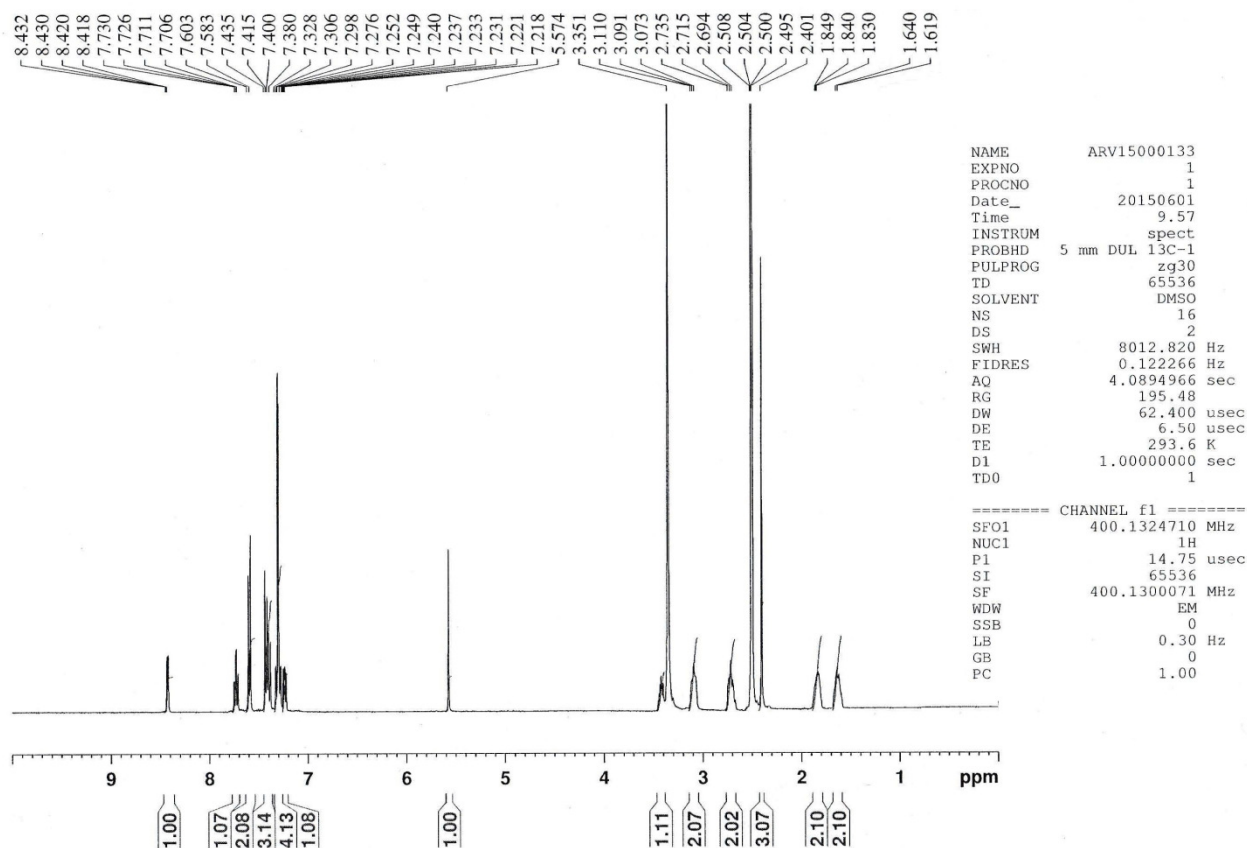
PeakTable

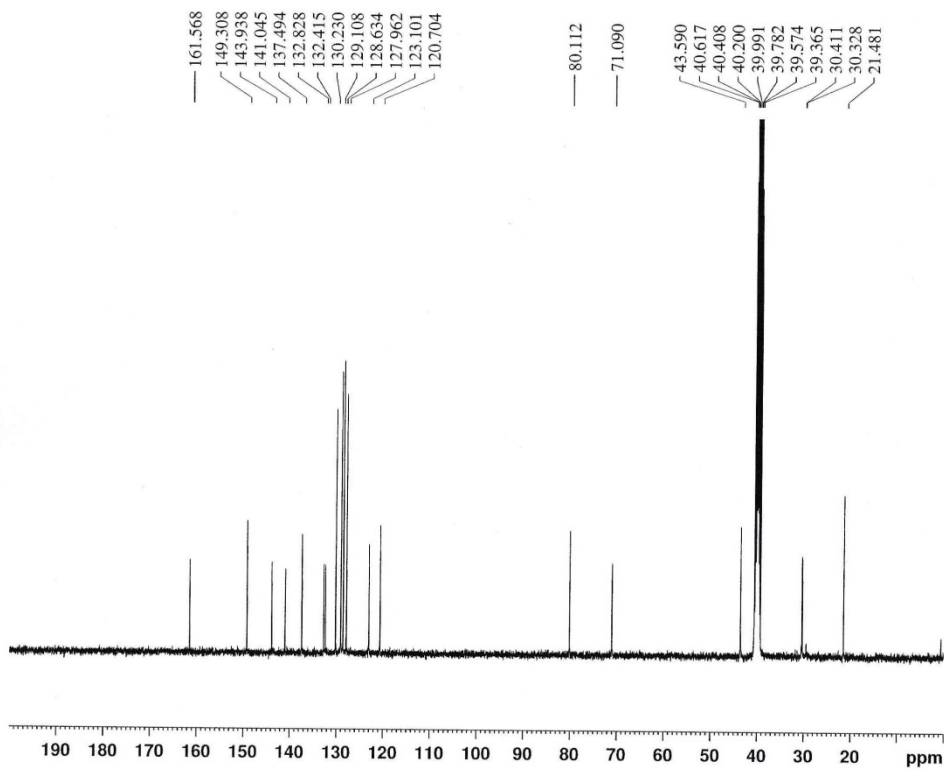
PDA Ch1 272nm 4nm

Peak#	Ret. Time	Area	Area %
1	3.218	8391	0.232
2	3.299	9448	0.261
3	3.429	14155	0.392
4	4.262	2836	0.078
5	4.712	1750	0.048
6	12.448	3577012	98.988
Total		3613591	100.000



(S)-2-((4-chlorophenyl)((1-tosylpiperidin-4-yl)oxy)methyl)pyridine (6r): Yield (263mg, 87.3%); Tan coloured solid; ¹H-NMR (400 MHz, DMSO-d₆) 8.43- 8.41(d,J=8Hz,1H), 7.73- 7.70(m,1H), 7.60- 7.58 (d,J=8.0Hz, 2H), 7.43- 7.38(m, 3H),7.32- 7.21 (m, 5H), 5.57(s, 1H), 3.35(m, 1H), 3.11- 3.07(m, 2H), 2.73- 2.69(m, 2H), 2.40(s,3H), 1.84- 1.83(m, 2H), 1.64- 1.61 (m, 2H); ¹³C-NMR (DMSO-d₆)161.56, 149.30, 143.93, 141.04, 137.49, 132.82, 132.41, 130.23, 129.10, 128.63, 127.96, 123.10, 120.70, 80.11, 71.09, 43.29, 30.41, 30.32, 21.48; HRMS Calcd 479.117; Found: 479.117(M+Na⁺); Anal.Calcd for C₂₄H₂₅ClN₂O₃S : C 63.08; H 5.51; N 6.13; Found: C, 63.11; H, 5.55; N, 6.09; Chiral HPLC (%ee) 97.5;





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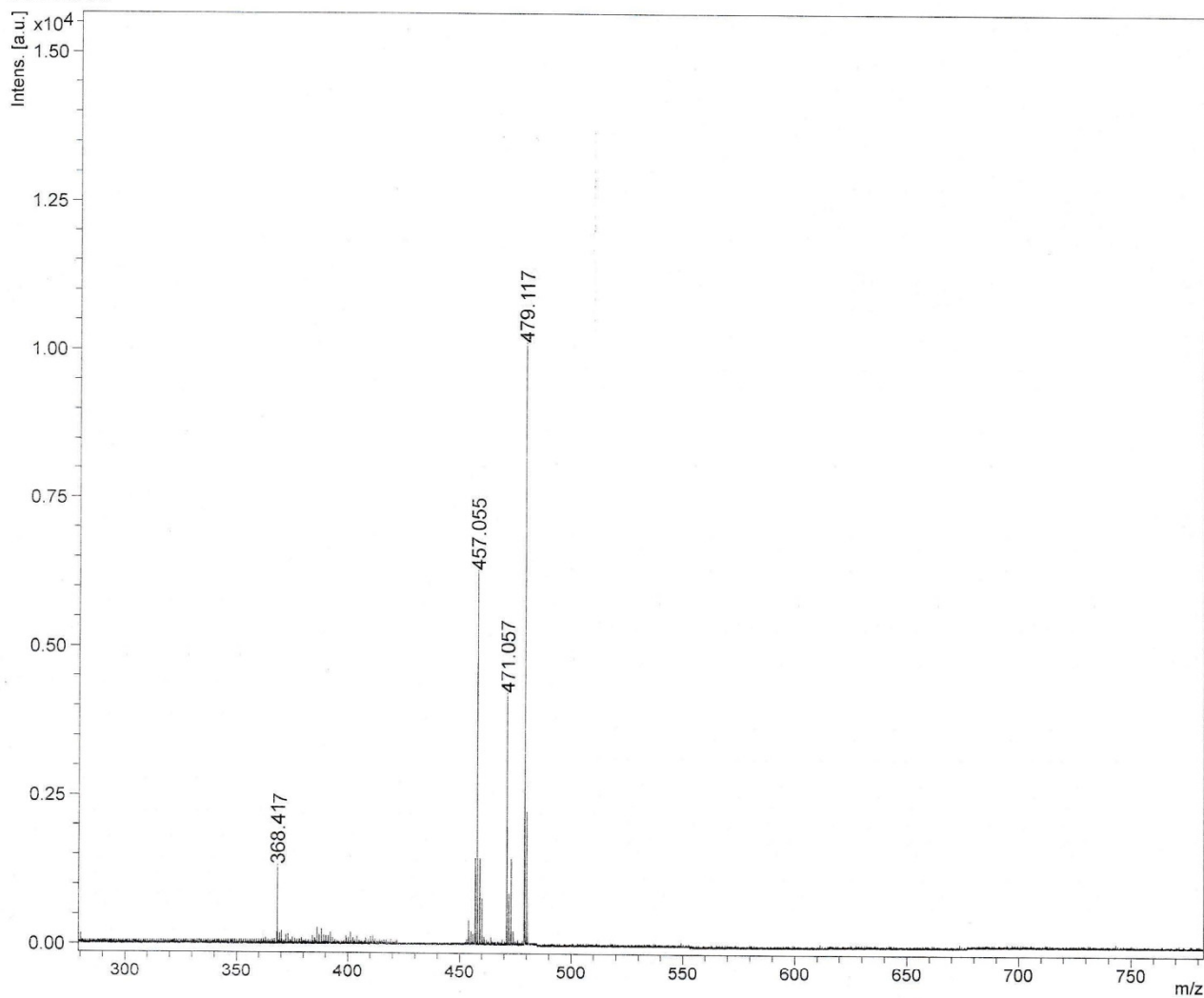
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EXPNO     1
PROCNO    1
Date_     . 20150531
Time      4.10
INSTRUM   spect
PROBHD    5 mm DUL 13C-1
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         5000
DS         4
SWH        28409.092 Hz
FIDRES     0.433488 Hz
AQ         1.1534836 sec
RG         195.48
DW         17.600 use
DE         6.50 use
TE         294.9 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      100.6228293 MHz
NUC1       13C
P1         9.10 use
SI         32768
SF         100.6127685 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40

```

Comment 1

Comment 2

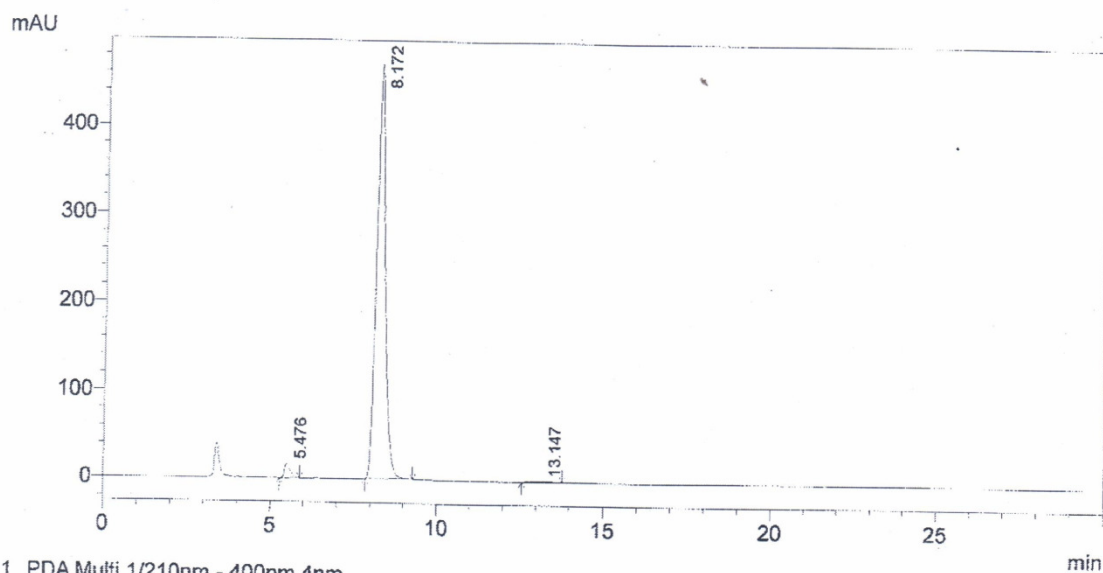


Acquisition Parameter

Date of acquisition	2015-06-16T11:00:12.984+05:30
Acquisition method name	D:\Methods\flexControlMethods\RP_PepMix.par
Acquisition operation mode	Reflector
Voltage polarity	POS
Number of shots	200
Name of spectrum used for calibration	
Calibration reference list used	

Sample Name :BSS-9
Sample ID :
Data File Name :BSS-9
Method File Name :5050TFAHEXET

Method information:Column:CHIRAL PAK IC(250x4.6)mm 5mic
Mobile Phase'A':0.1%TFA IN HEXANE:ETHANOL (50:50)
Flow:1.0ml/min

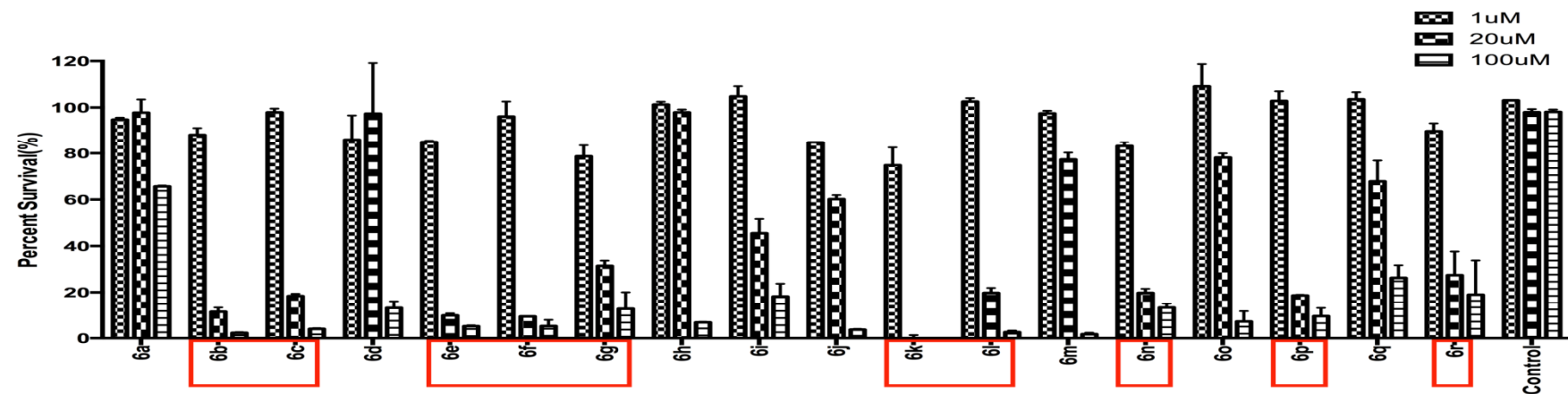


1 PDA Multi 1/210nm - 400nm 4nm

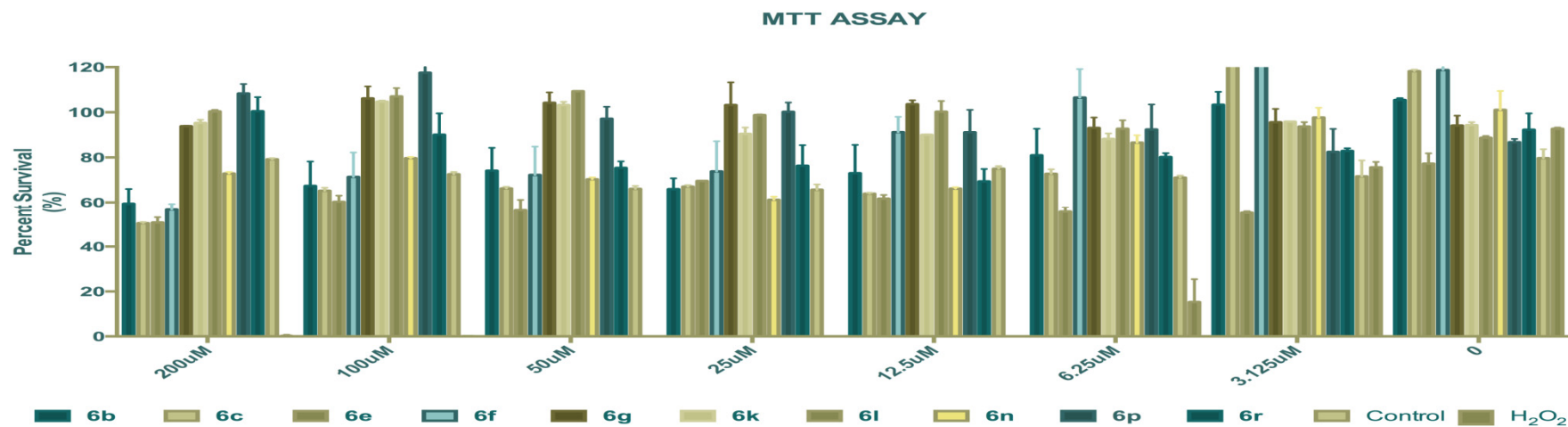
PeakTable

PDA Ch1 210nm - 400nm 4nm			
Peak#	Ret. Time	Area	Area %
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2	8.172	8690456	97.554
3	13.147	21315	0.239
Total		8908368	100.000

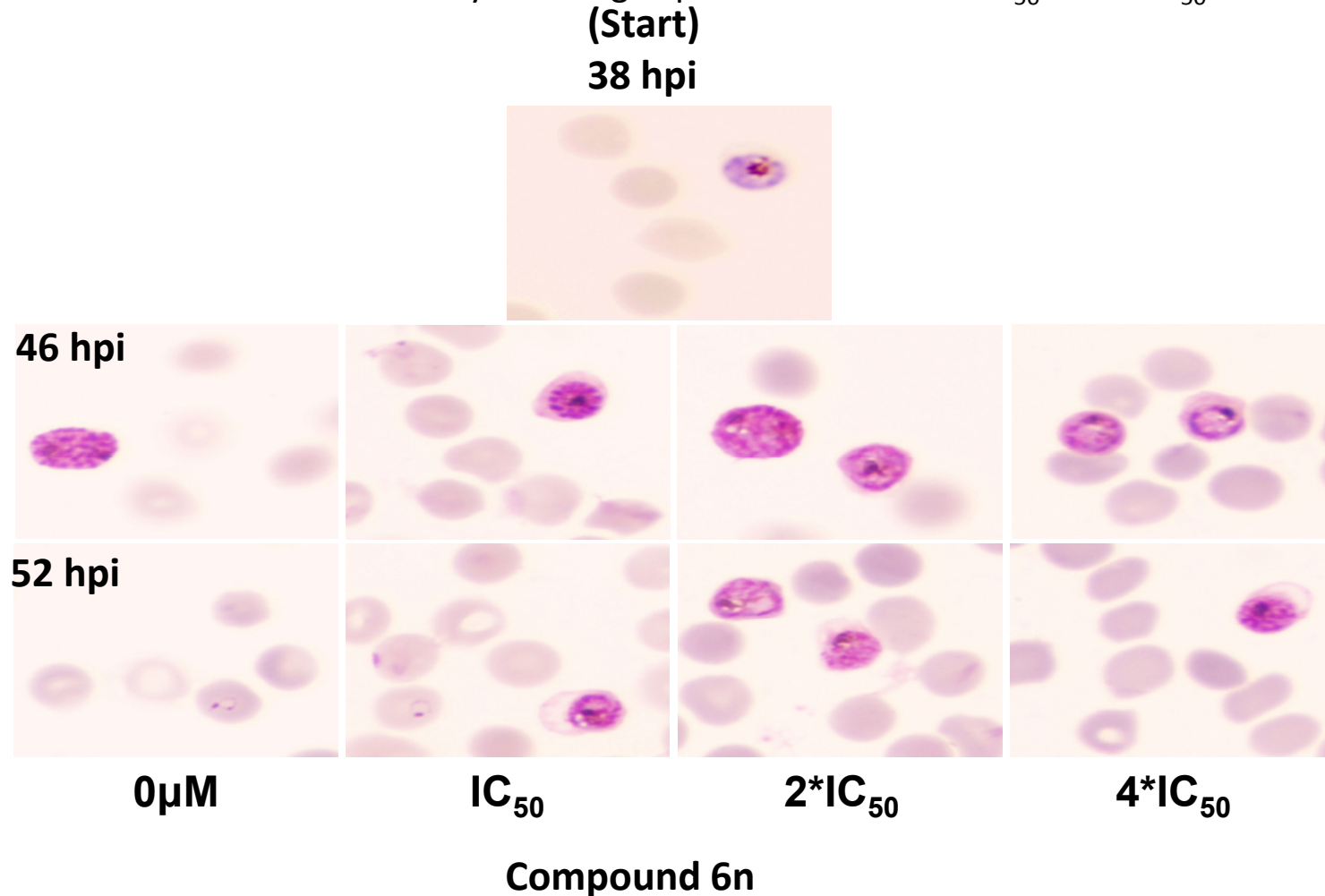
Supplemental Figure S2: Inhibitory activity of title compounds against *P. falciparum*



Supplemental Figure S3: Cytotoxicity studies of anti-malarial compounds against MDCK cells



Supplemental Figure S4: Microscopic images of Giemsa-stained parasites treated with 6n at 38hpi, 46hpi and 52 hpi at varying concentrations. DMSO-treated parasites developed normally into multinucleated schizonts (46hpi), egressed and invaded to form new ring-stage parasites (52hpi). Parasites treated with 6n failed to mature ultimately resulting in parasite death at $2 \times \text{IC}_{50}$ and $4 \times \text{IC}_{50}$ concentrations.



Supplementary Figure S5: *In vivo* efficacy of the most effective compound 6n on *P. yoelii* infected BALB/c mice model.

