Electronic Supplementary Information

A Concise and Sequential Synthesis of Nitroimidazooxazole based Drug, Delamanid and related compound

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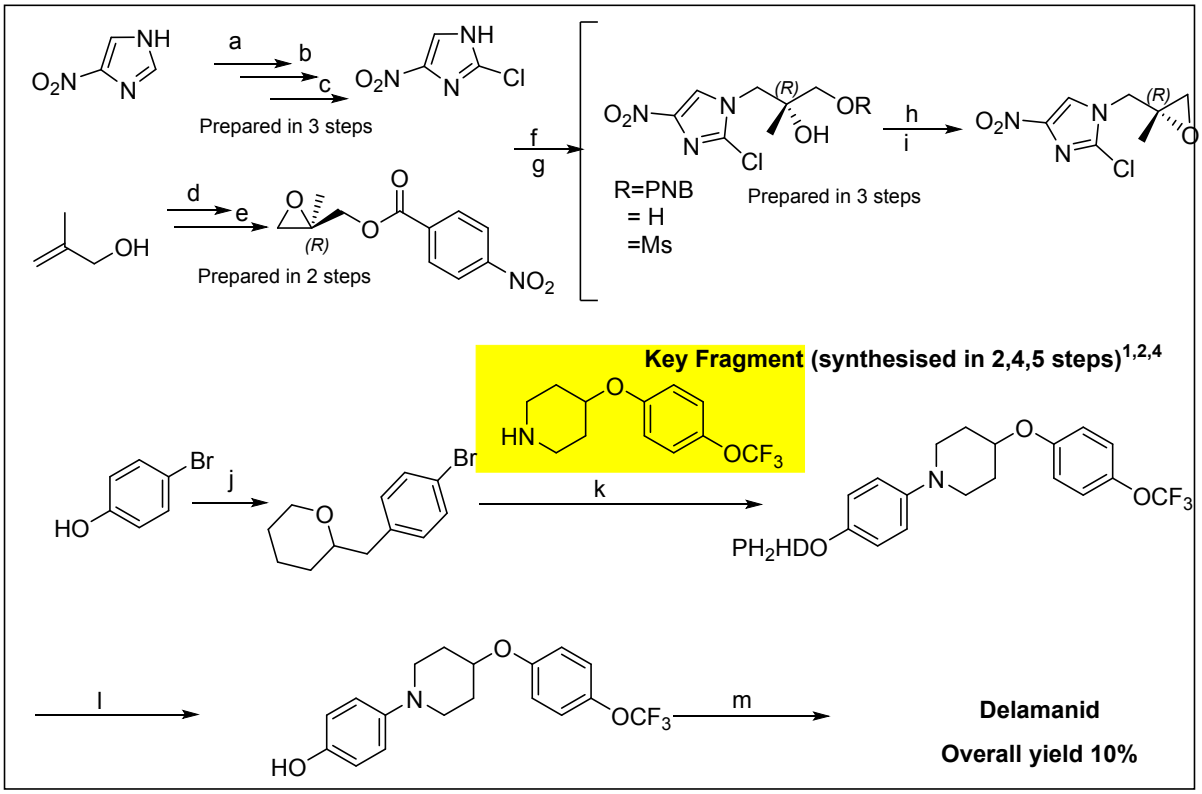
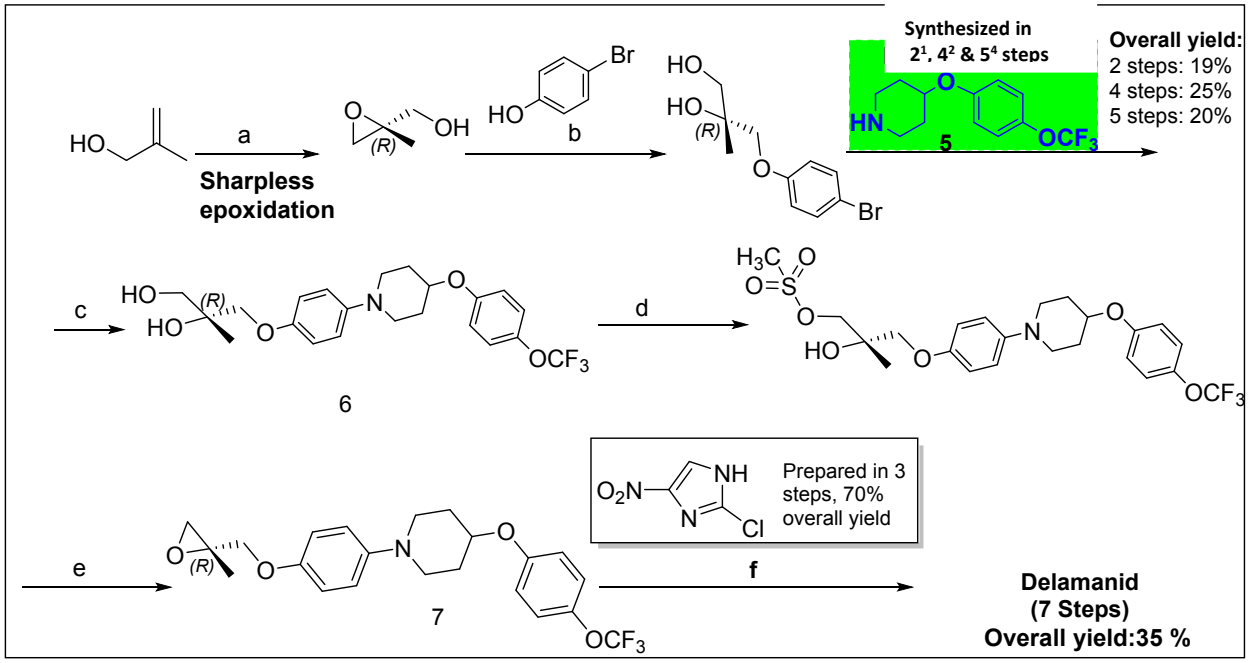
Figure S1: Synthesis of Delamanid developed by Otsuka pharmaceutical Ltd. (2004)[3]



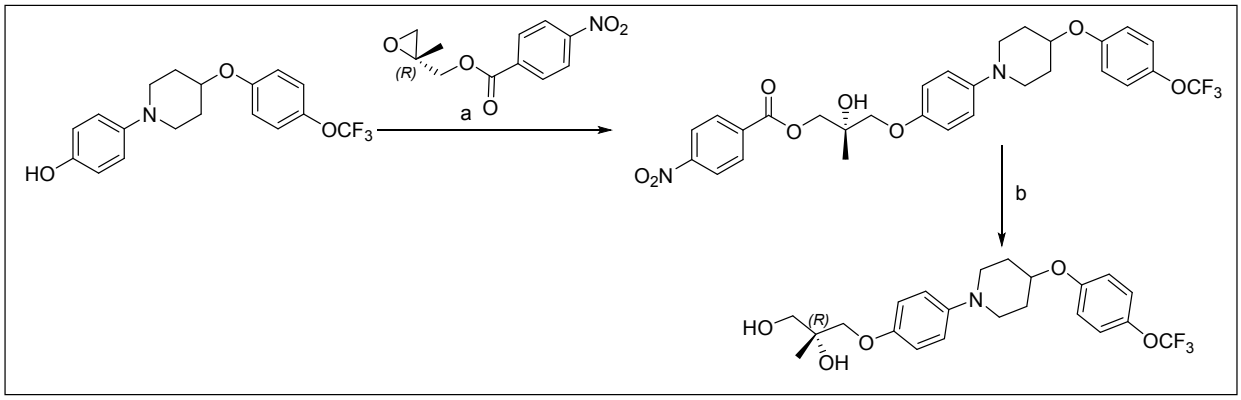
Reagent and conditions: a) HNO_3, AcOH, Ac_2O, 5 °C, 2 h, and then at rt, 12 h, 69%; b) chloro benzene, 120-125 °C, 50 h, 95%; c) Conc. HCl, 90-95 °C, 12 h, 50%; d) $Ti(OPr\text{-}i)_4$, Di-*i-Pr*- D-tartrate, CH_2Cl_2, -35°C, cumene hydroperoxide, -35°C, DCM, 1h, -20 °C, 35 hrs.; e) P-nitrobenzoyl chloride, Et_3N, DCM, rt, 80%; f) Et_3N, AcOEt, 60-65 °C, 6 h, 87%; g) K_2CO_3, MeOH, rt, 2h, 97%; h) MsCl, pyridine, <15 °C, 2 h; i) DBU, AcOEt, rt, 2 h, 75%; j) Pyridinium-p-toluenensulfonate, overnight, rt, 96%; k) $Pd(OAc)_2$, *rac*-BINAP, Cs_2CO_3, toluene, reflux, 30 min, 64%; l) pyridinium p-toluenesulfonate, EtOH, 70 °C, 24 h, 94%; m) NaH, DMF, 50 °C, 2 h, 48%. $[\alpha]_D^{25}$ -8.0 ° (***c*** 1, Chloroform).

Figure S2: Improved reported route for the synthesis of Delamanid[5]



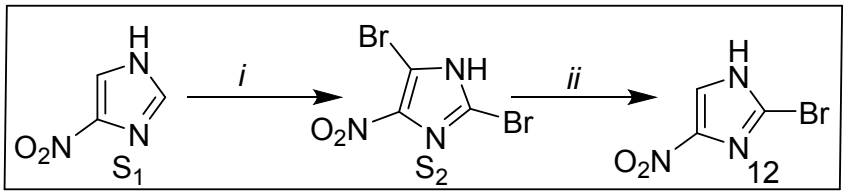
Reagent and conditions: a) $Ti(OPr\text{-}i)_4$, di-i-Pr-D-tartrate, CH_2Cl_2, -35°C, cumene hydroperoxide, -35°C, DCM, 1h, -20 °C, 35 h, 82%; b) 10% aqueous. NaOH, toluene, 55 °C, 5 h, cooled overnight, 76%; c) NaOBu-*t*, Pd_2dba_3 ,*t*-BuXPhos, toluene, 110 °C, 3 h; d) MsCl, Et_3N, DCM, <15 °C, 2 h; e) DBU, AcOEt, rt, 2 h, 77% ; f) *t*-BuOAc, NaOAc, 110 °C, 4 hrs. 73%.

Figure S3: Synthesis of key intermediate diole[5, 6]



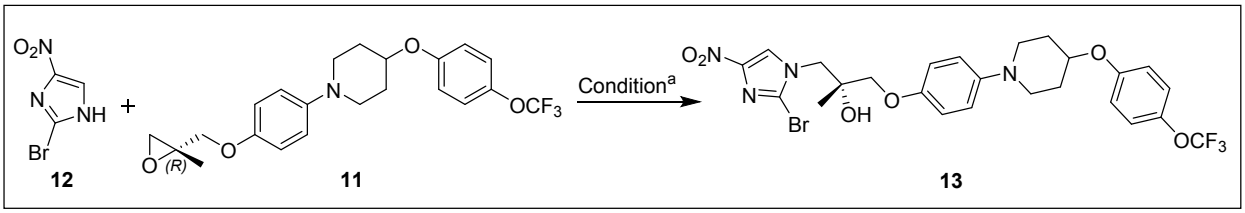
[a,b] Reagent and conditions: a) Et_3N, ethyl acetate, 60 °C, 24 h, 92%; b) K_2CO_3, MeOH, rt, 2h, 93%.

Figure S4: Synthesis of key intermediate 2-bromo-4-nitroimidazole **12**[7]



[i,ii]**Reagent and conditions:** i) compound S1 (88 mmol), bromine (211 mmol), $NaHCO_3$ (202 mmol), water (50 mL), 0 °C, 4h, 65 °C, 6 h, 88%; ii) compound S2 (85 mmol), KI (123 mmol), sodium sulfite (123 mmol), acetic acid, 120 °C, 16 h, 64%.

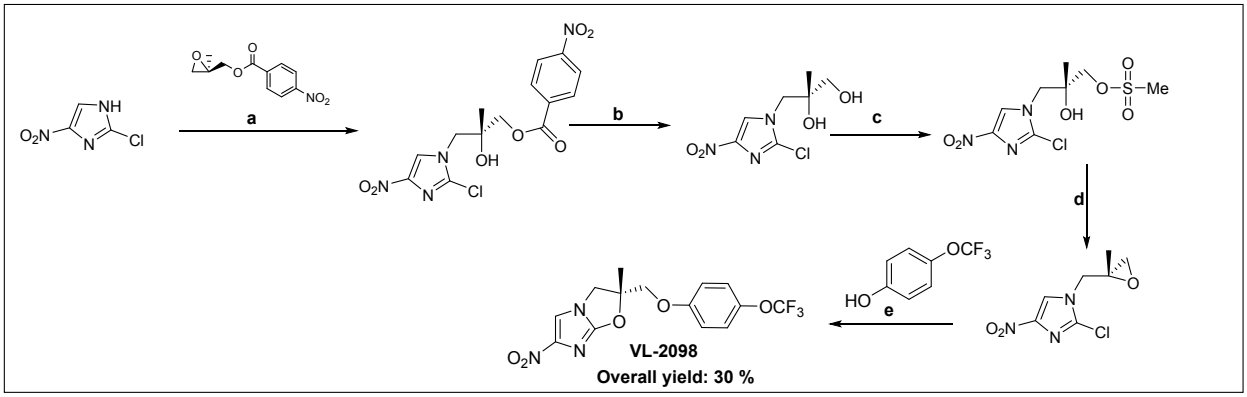
Table S1: Optimization table of coupling of 2-bromo-4-nitroimidazole **12** with compound **11**



entry	Solvent	Base	Temp. °C	% Yield
1	Ethyl acetate	Et_3N	70	NR
2	---	Et_3N	80	Trace amount
3	---	DBU	100	NR
4	DMF	Cs_2CO_3	100	Trace amount
5	---	DIPEA	115	89

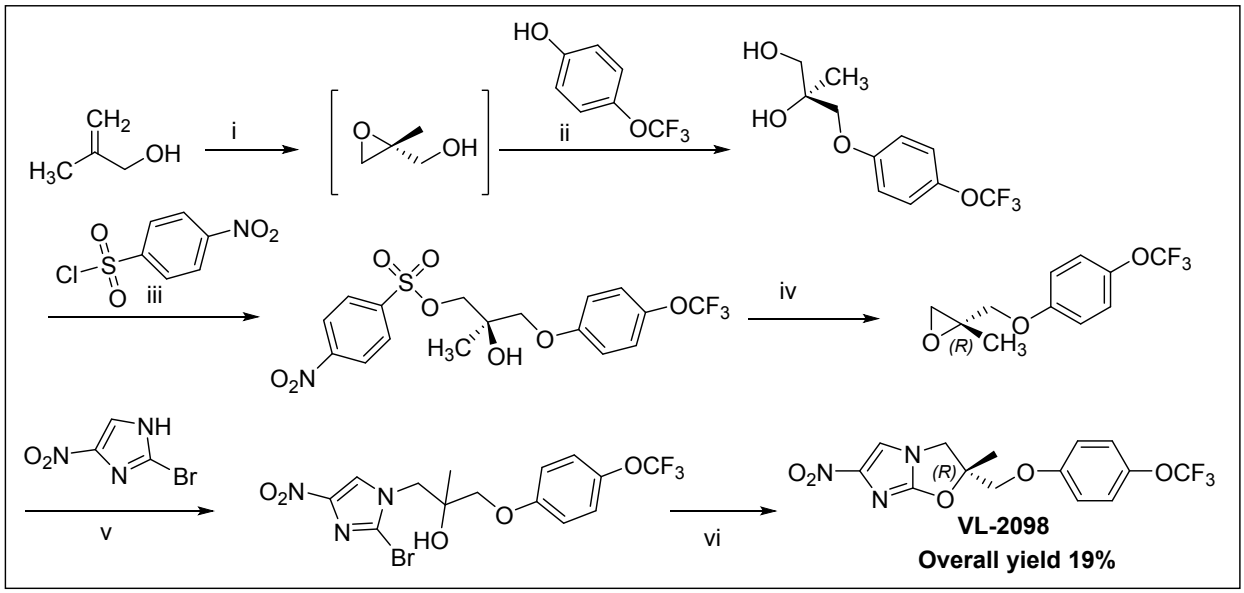
[a]**Reagent and Conditions:** compound **12** (1 mmol), compound **11** (1 mmol), DIPEA (15 mmol), 115 °C, 12 h.

Figure S5: First reported route for the synthesis of VL-2098[3, 8, 9]



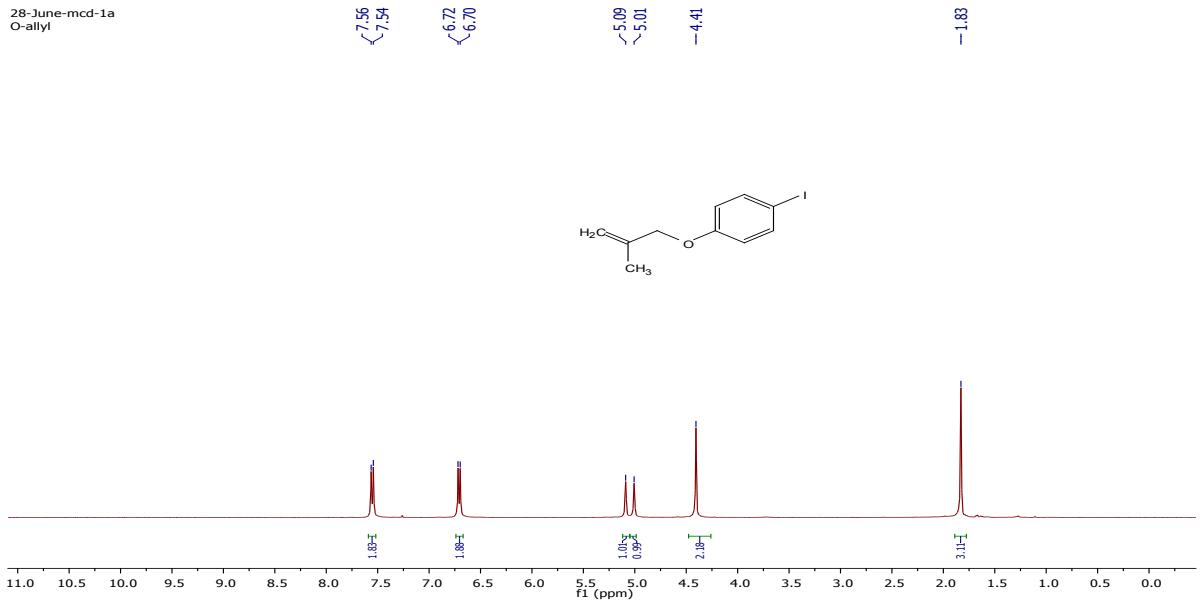
Reagent and Conditions: a) Et_3N, AcOEt, 60-65 °C, 6 h, 87%; b) K_2CO_3, MeOH, rt, 2h, 97%; c) MsCl, pyridine, <15 °C, 2 h; d) DBU, AcOEt, rt, 2 h, 75%; e) NaH, DMF, 50 °C, 2 h, 48%.

Figure S5: Scalable reported route for the synthesis of VL-2098[6]

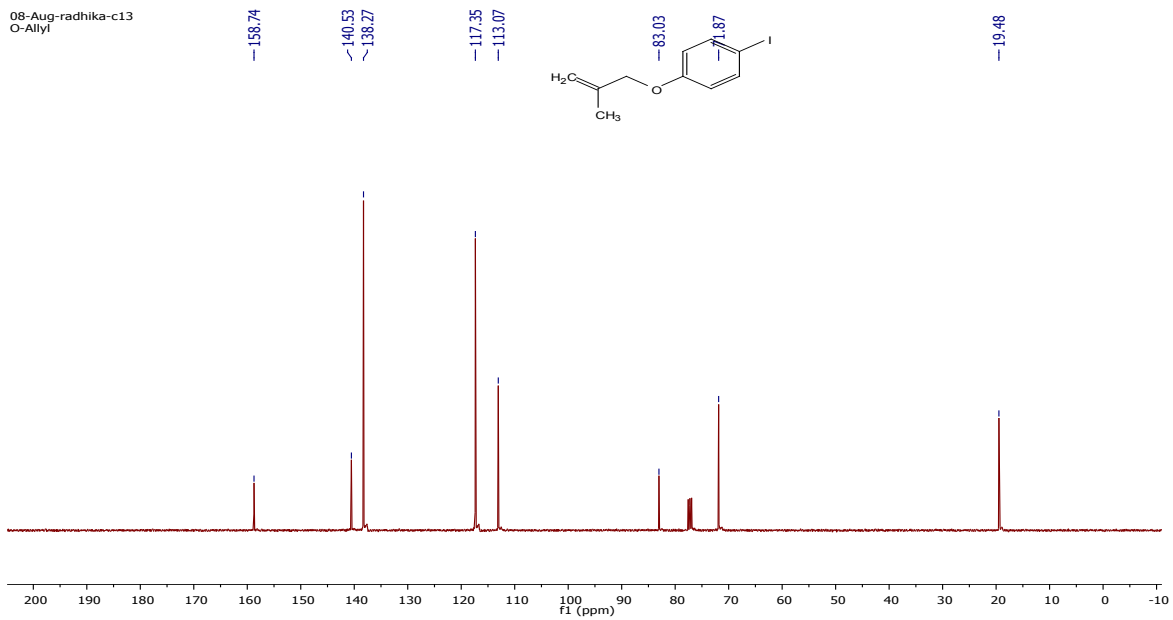


Reagent and conditions: i) $Ti(O\text{-}iPr)_4$, D(-)DIPT, TBHP, DCM, -25 °C to -30 °C,43% ii) K_2CO_3, 4-trifluromethoxyphenol, MeOH, rt-60 °C,; iii) Et_3N, 0 to -5 °C.; iv) Aqueous NaOH sol.,0 °C -15 °C, 92%; v) DIPEA, 110 °C -115 °C, 96%; vi) K_2CO_3, DMF, 90 °C, 51%.

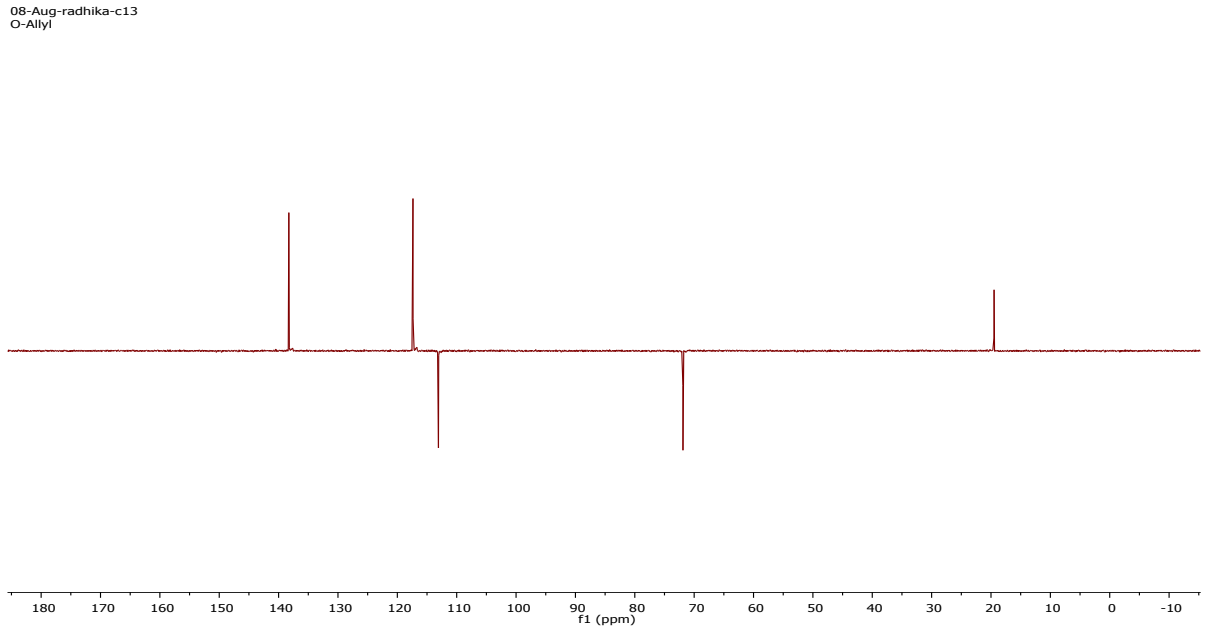
^{1}H NMR of 1-iodo-4-((2-methylallyl)oxy)benzene 3:



^{13}C NMR spectra of compound 3:



DEPT NMR spectra of compound 3:



GC-MS spectra of compound 3:

IIIM GCMS ANALYSIS REPORT

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Analyzed	: 9/25/2019 8:23:36 PM
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Sample Name	: SS
Vial #	: 61
Injection Volume	: 0.50
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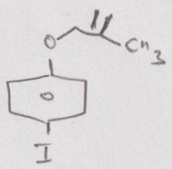
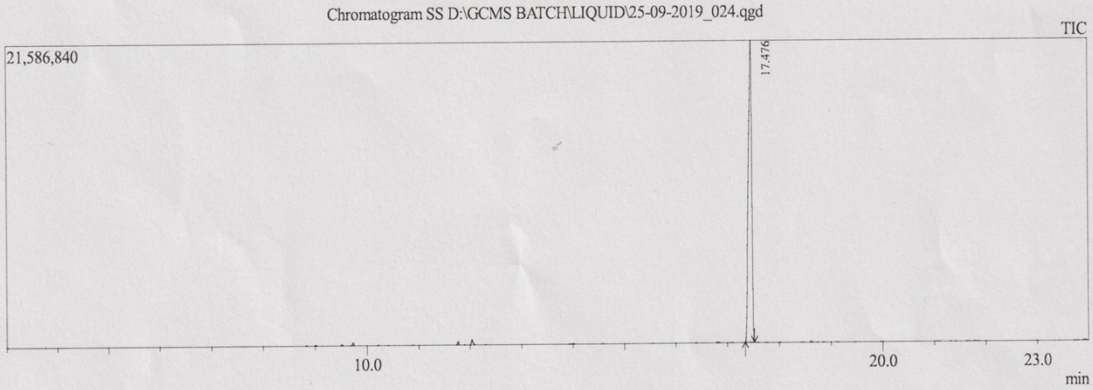
Method File	: D:\GCMS METHOD\GCMS-GENERAL.qgm
Tuning File	: D:\Tuning\Tuning_NM_F1_25092019.qgt
Modified by	: Admin
Modified	: 9/25/2019 8:47:37 PM



Chromatogram SS D:\GCMS BATCH\LIQUID\25-09-2019_024.qgd



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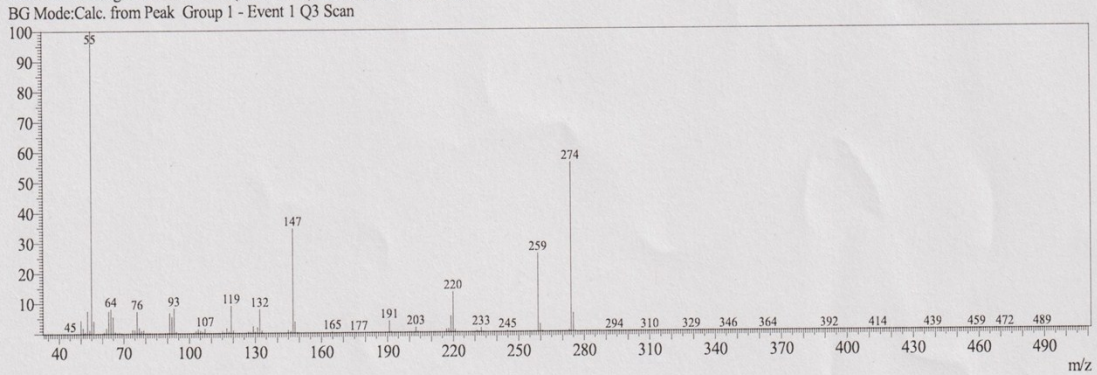
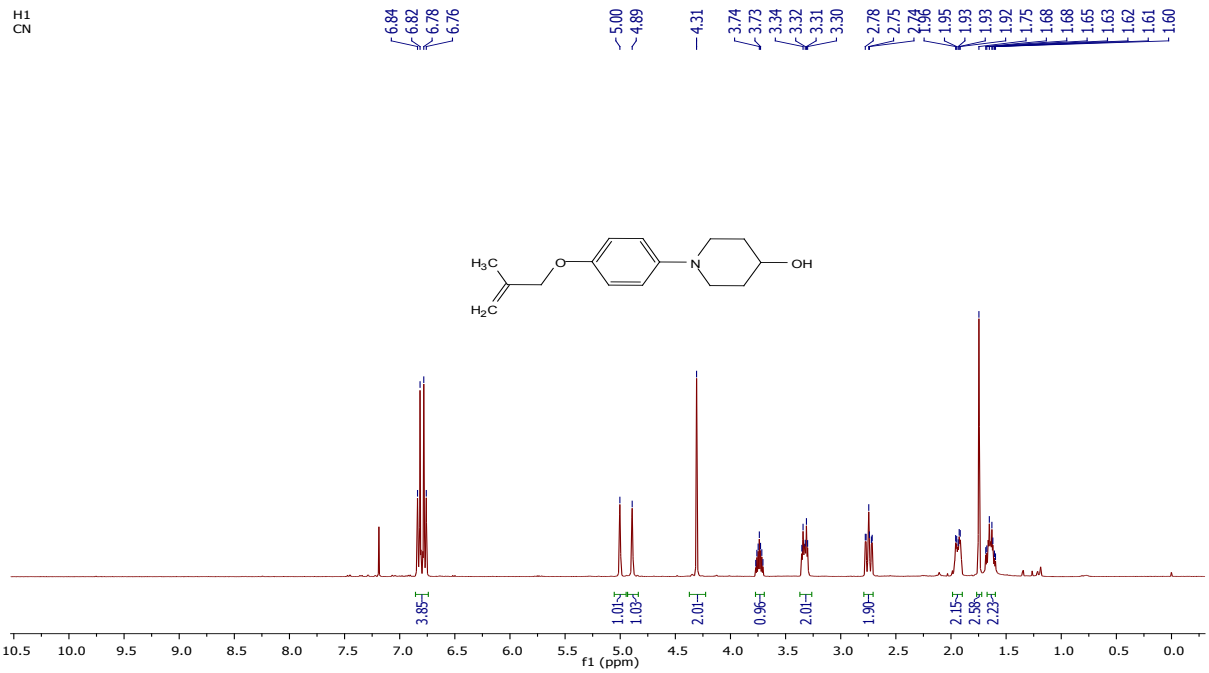
				98439225	100.00	21530310	100.00			

Spectrum

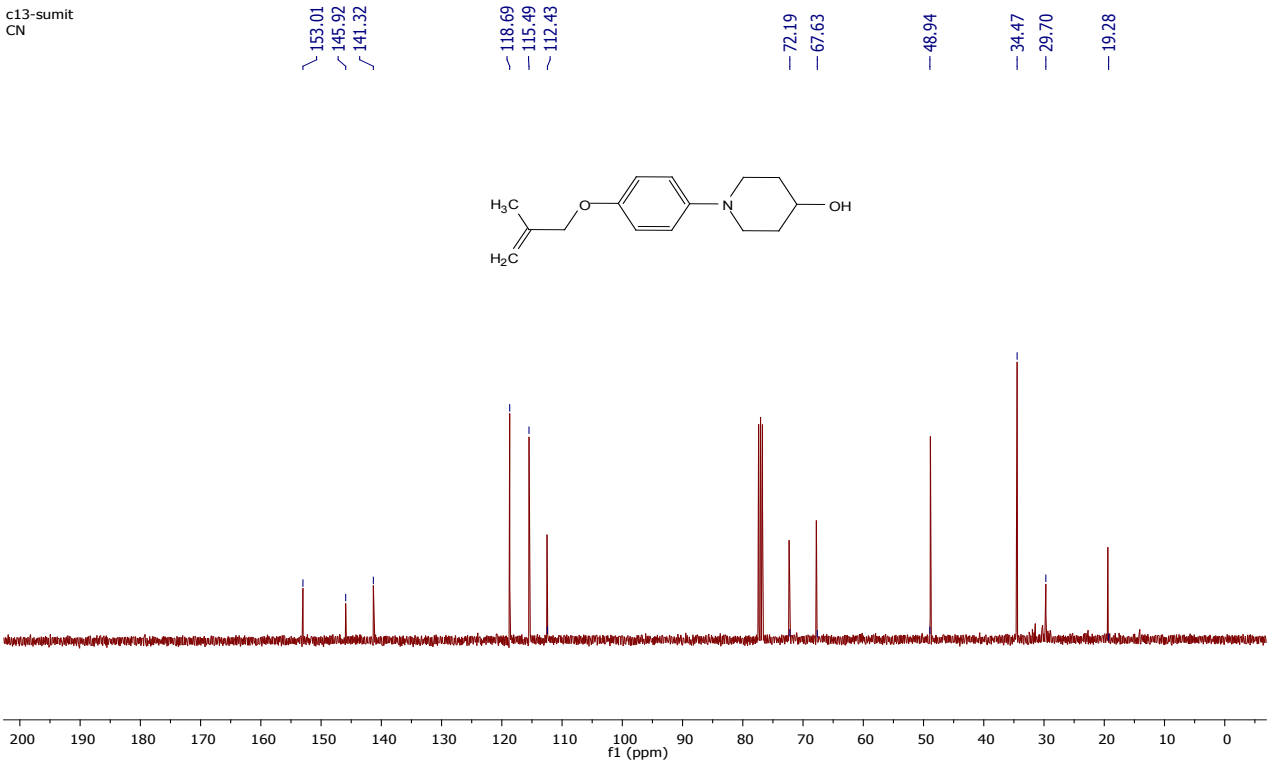
Line#:1 R.Time:17.475(Scan#:2896)
MassPeaks:353
RawMode:Averaged 17.470-17.480(2895-2897) BasePeak:55(5634423)
BG Mode:Calc. from Peak Group 1 - Event 1 Q3 Scan



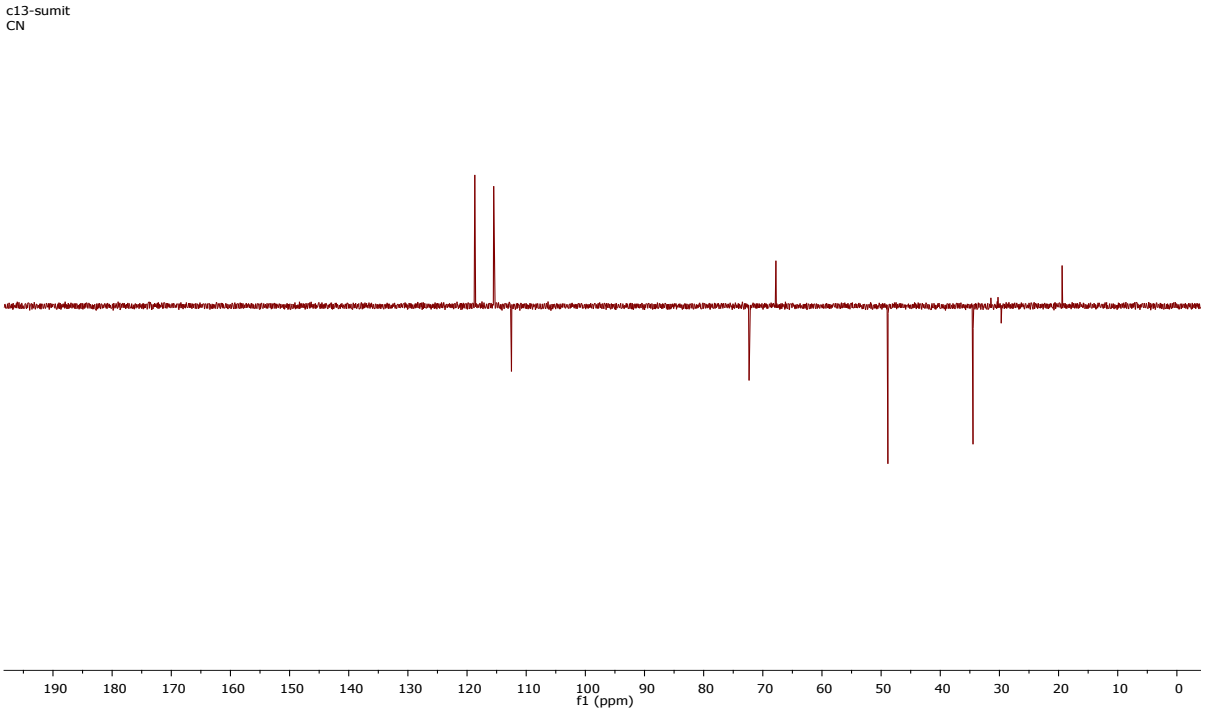
^{1}H NMR spectra of 1-(4-((2-methylallyl) oxy) phenyl) piperidin-4-ol (compound 5):



^{13}C NMR spectra of compound 5:



DEPT NMR spectra of compound 5:



HRMS spectra of compound 5:

Qualitative Compound Report

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Sample Type	Sample	**Position**	Vial 5
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Acq Method	vishal_12-01-13.m	**Acquired Time**	29-07-2019 PM 4:06:20
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**

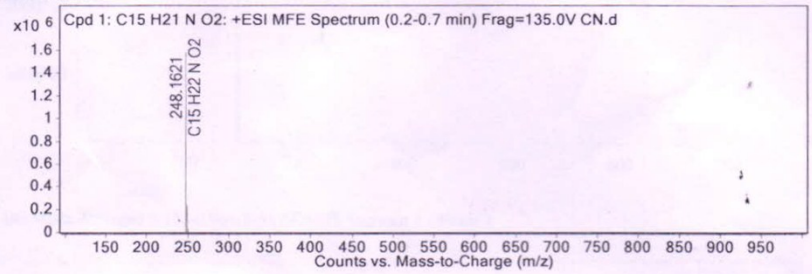
Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 1: C15 H21 N O2	0.3	247.1549	C15 H21 N O2	C15 H21 N O2	9.48	C15 H21 N O2

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C15 H21 N O2	248.1621	0.3	Find by Molecular Feature	247.1549

MFE MS Spectrum



MS Spectrum Peak List

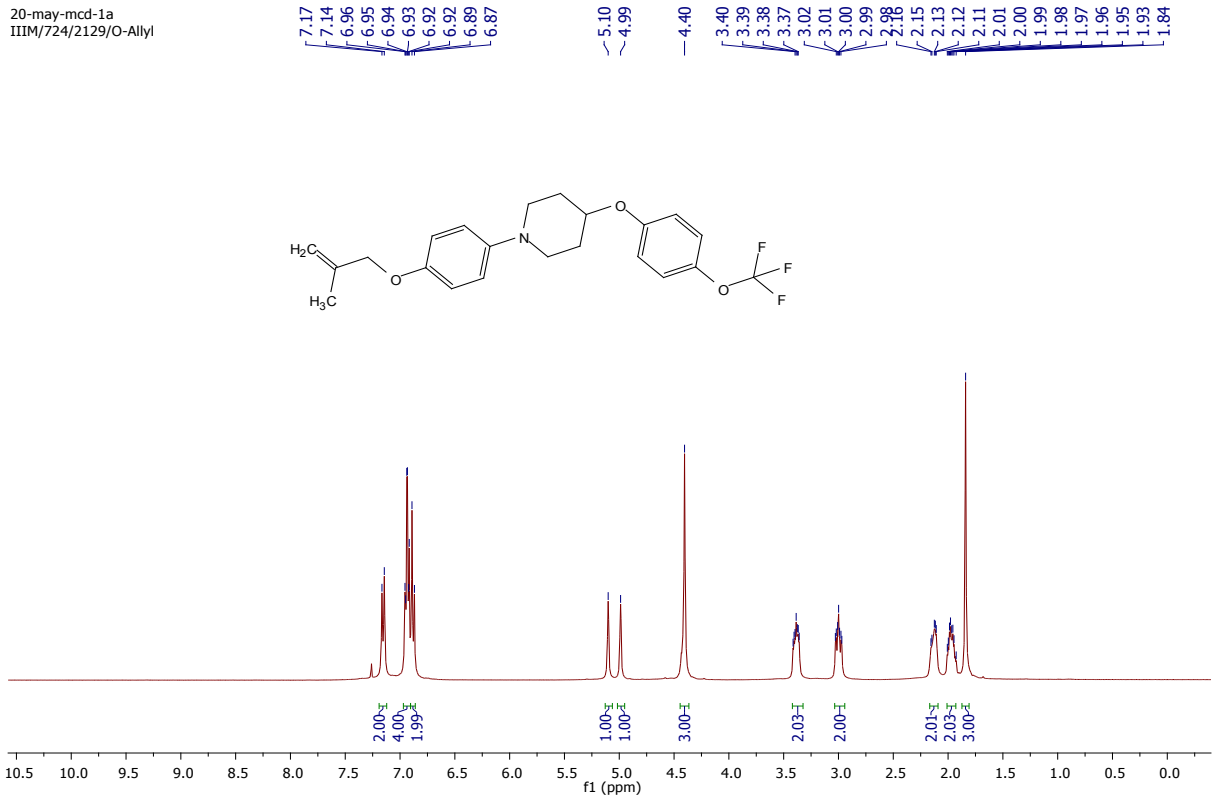
m/z	z	Abund	Formula	Ion
248.1621	1	1580674.75	C15 H22 N O2	(M+H)+
249.1656	1	236278.91	C15 H22 N O2	(M+H)+
250.1683	1	24820.82	C15 H22 N O2	(M+H)+
251.1715	1	1789.34	C15 H22 N O2	(M+H)+
252.1741	1	270.2	C15 H22 N O2	(M+H)+

Predicted Isotope Match Table

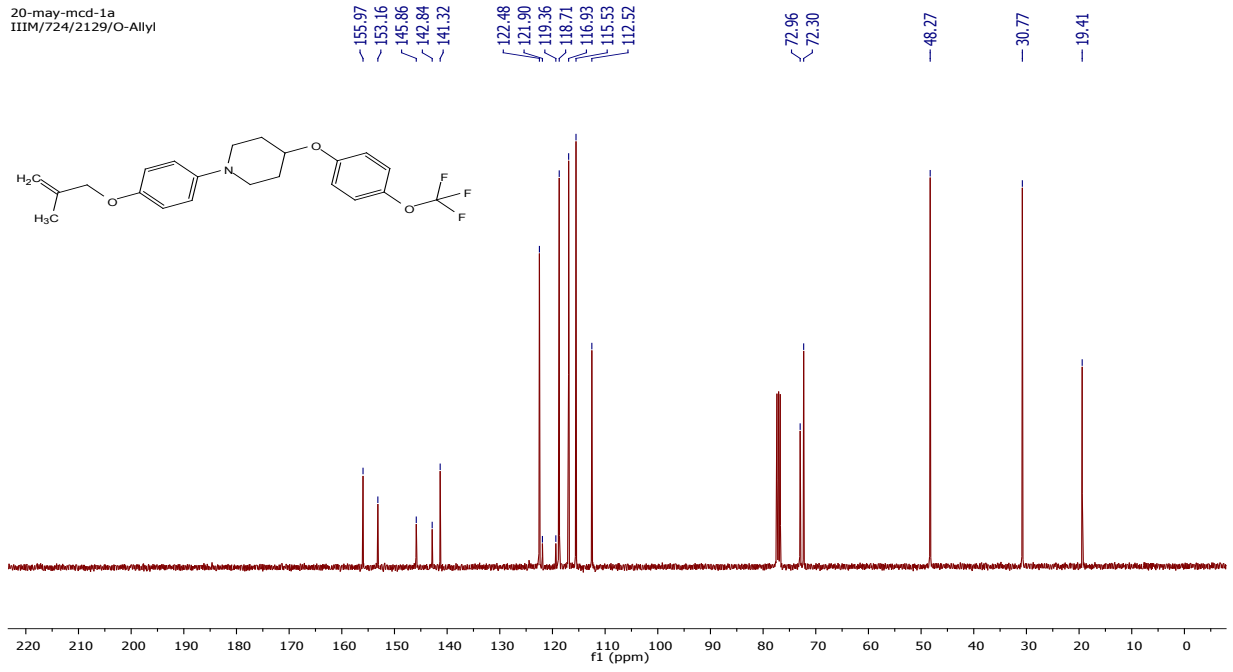
Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	248.1621	248.1645	9.56	100	100	85.73	84.16
2	249.1656	249.1678	8.72	14.95	16.92	12.81	14.24
3	250.1683	250.1705	8.98	1.57	1.75	1.35	1.48
4	251.1715	251.1731	6.6	0.11	0.14	0.1	0.11
5	252.1741	252.1758	6.56	0.02	0.01	0.01	0.01

--- End Of Report ---

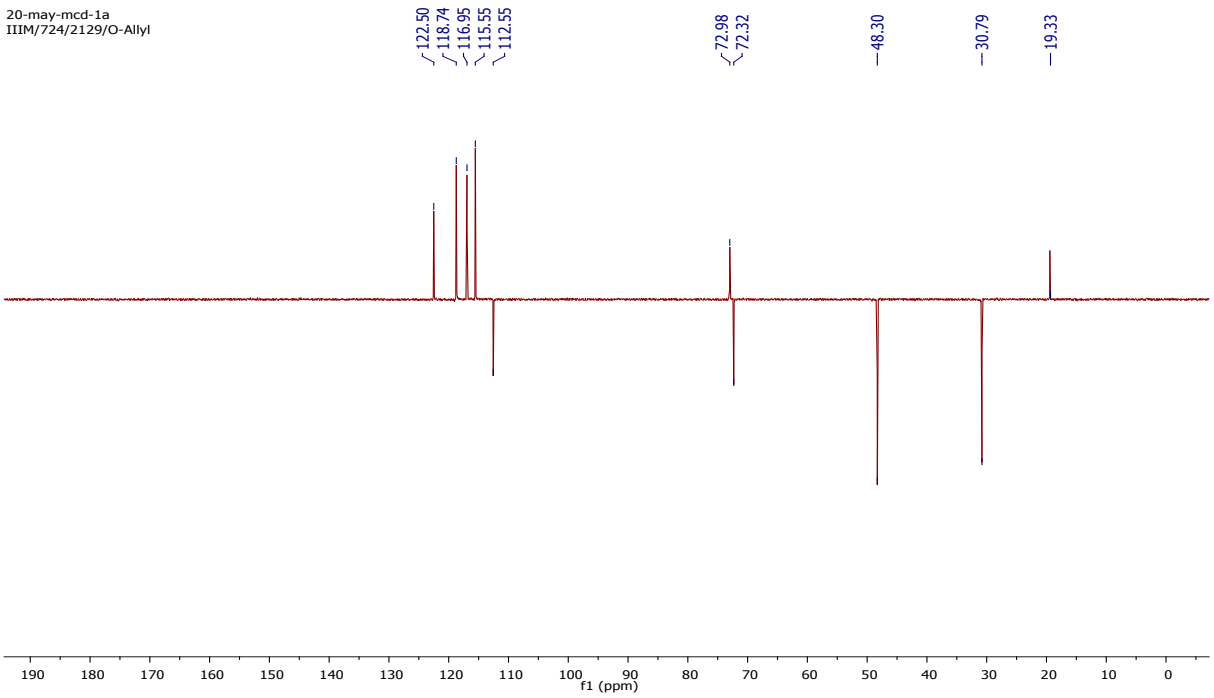
^{1}H NMR spectra of 1-(4-((2-methylallyl) oxy) phenyl)-4-(4-(trifluoromethoxy) phenoxy) piperidine 8:



^{13}C NMR spectra of compound 8:



DEPT NMR of compound 8:



HRMS spectra of compound 8:

Qualitative Compound Report

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Comment			

Sample Group		**Info.**
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Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
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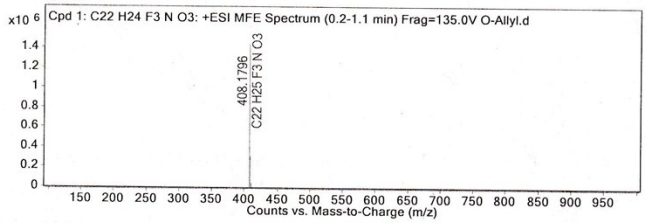
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C22 H24 F3 N O3	408.1796	0.3	Find by Molecular Feature	407.1724

MFE MS Spectrum



MS Spectrum Peak List

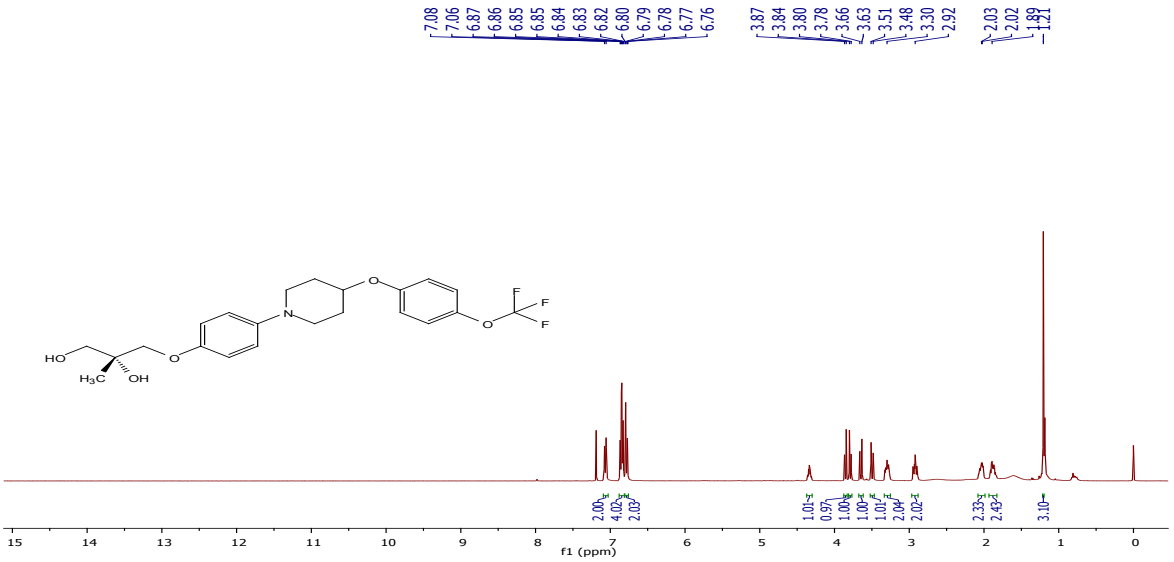
m/z	z	Abund	Formula	Ion
408.1796	1	1442303.5	C22 H25 F3 N O3	(M+H)+
409.183	1	315526.09	C22 H25 F3 N O3	(M+H)+
410.1855	1	41759.36	C22 H25 F3 N O3	(M+H)+
411.1881	1	5410.89	C22 H25 F3 N O3	(M+H)+
412.1904	1	776.41	C22 H25 F3 N O3	(M+H)+

Predicted Isotope Match Table

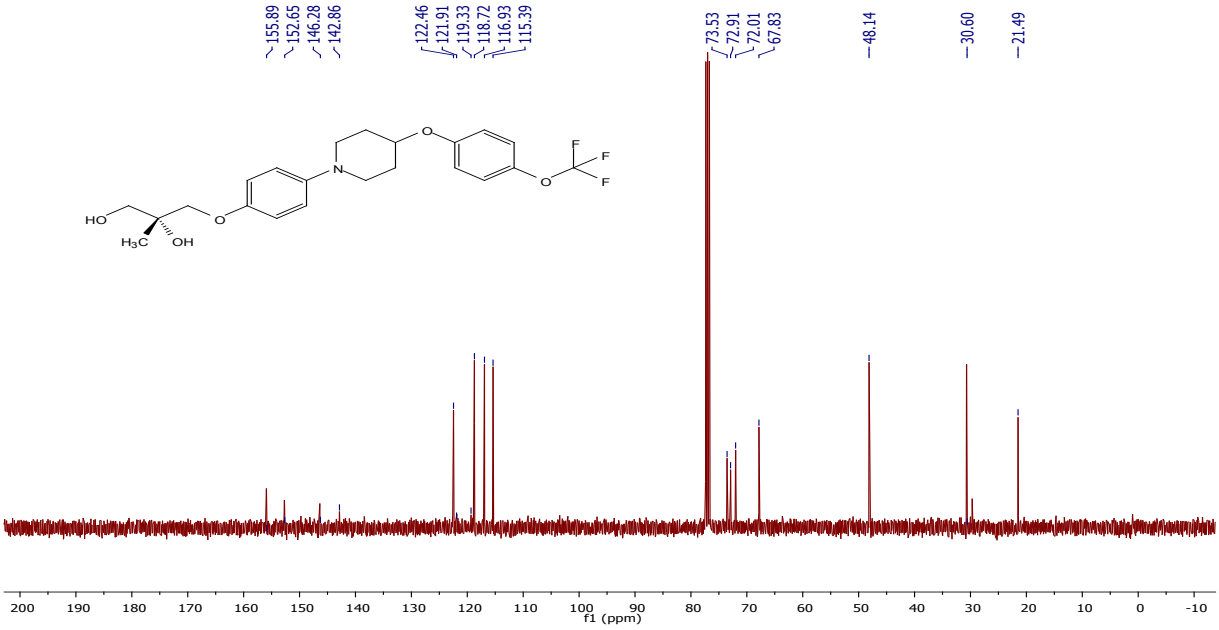
Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	408.1796	408.1781	-3.74	100	100	79.87	77.84
2	409.183	409.1814	-3.9	21.88	24.56	17.47	19.12
3	410.1855	410.1843	-2.97	2.9	3.5	2.31	2.73
4	411.1881	411.187	-2.51	0.38	0.37	0.3	0.29
5	412.1904	412.1897	-1.72	0.05	0.03	0.04	0.02

--- End Of Report ---

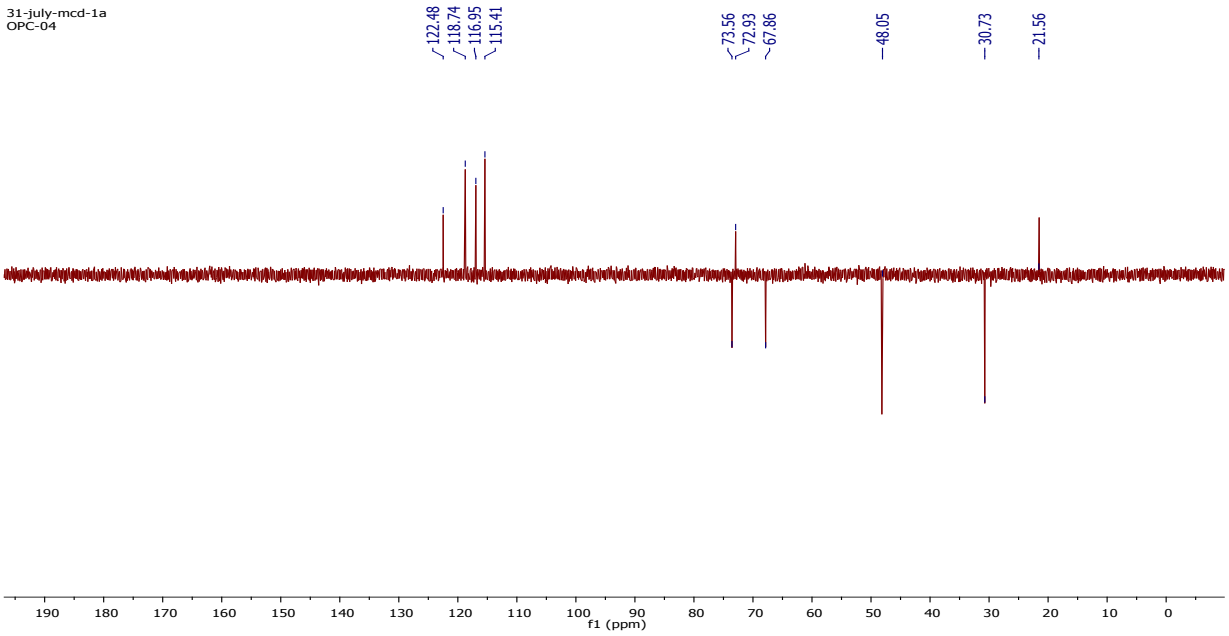
^{1}H NMR spectra of (R)-2-methyl-3-(4-(4-(4-(trifluoromethoxy)phenoxy) piperidin-1-yl)phenoxy)propane-1,2-diol R-(-)-9:



^{13}C NMR spectra of compound R-(-)-9:



DEPT NMR of compound R-(-)-9:



HRMS spectra of compound R-(-)-9:

Qualitative Compound Report

Data File	Dihydroxy.d	**Sample Name**	Dihydroxy
Sample Type	Sample	**Position**	Vial 11
Instrument Name	Instrument 1	**User Name**	
Acq Method	vishal_12-01-13.m	**Acquired Time**	28-05-2019 PM 1:22:16
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**
Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
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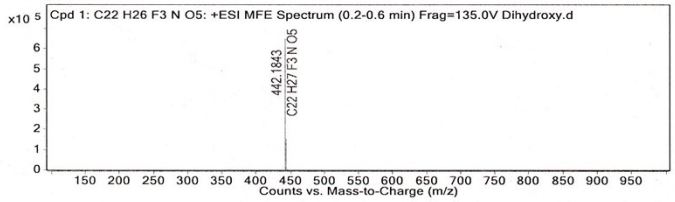
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C22 H26 F3 N O5	442.1843	0.3	Find by Molecular Feature	441.1769

MFE MS Spectrum



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
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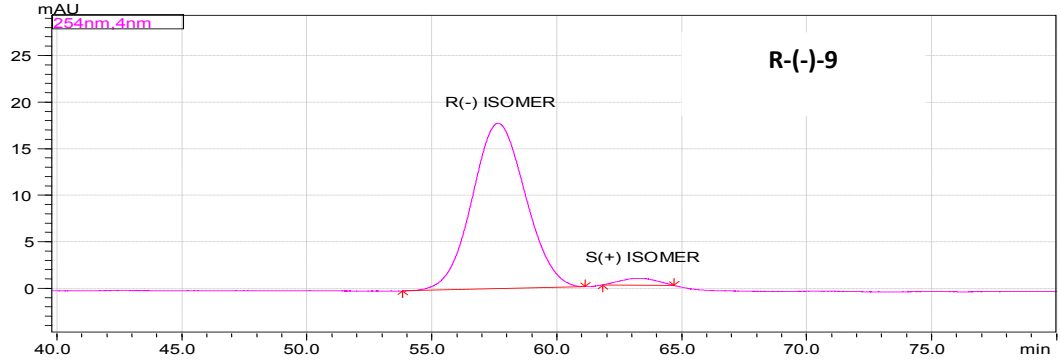
443.187	1	155680.05	C22 H27 F3 N O5	(M+H)+
444.1896	1	24169.09	C22 H27 F3 N O5	(M+H)+
445.1921	1	3636.27	C22 H27 F3 N O5	(M+H)+
446.1942	1	350.89	C22 H27 F3 N O5	(M+H)+

Predicted Isotope Match Table

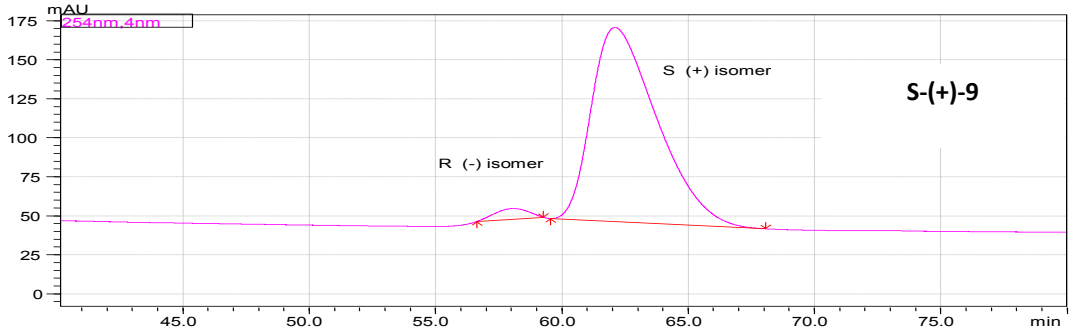
Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	442.1843	442.1836	-1.63	100	100	77.91	77.45
2	443.187	443.1869	-0.23	24	24.66	18.7	19.1
3	444.1896	444.1896	-0.12	3.73	3.94	2.9	3.05
4	445.1921	445.1922	0.31	0.56	0.47	0.44	0.37
5	446.1942	446.1948	1.34	0.05	0.05	0.04	0.04

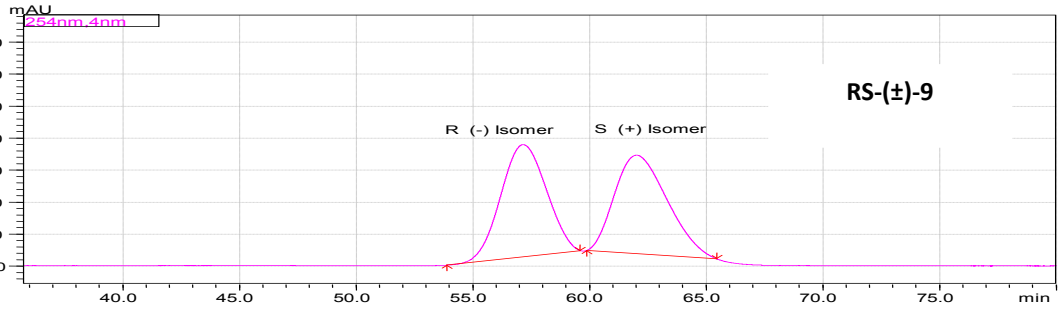
--- End Of Report ---

Chiral HPLC spectra of compound R-(-)-9, S-(+)-9, RS-(±)-9:



$$\% \text{ ee} = \left[\frac{\text{Area of A - Area of B}}{\text{Area of A + Area of B}} \right] \text{X } 100 = \left[\frac{2643863.0 - 77438.00}{2643863.0 + 77438.00} \right] \text{X } 100 = 94.31\% \text{ ee}$$





Peak	Ret. Time	Area	Height	Area%
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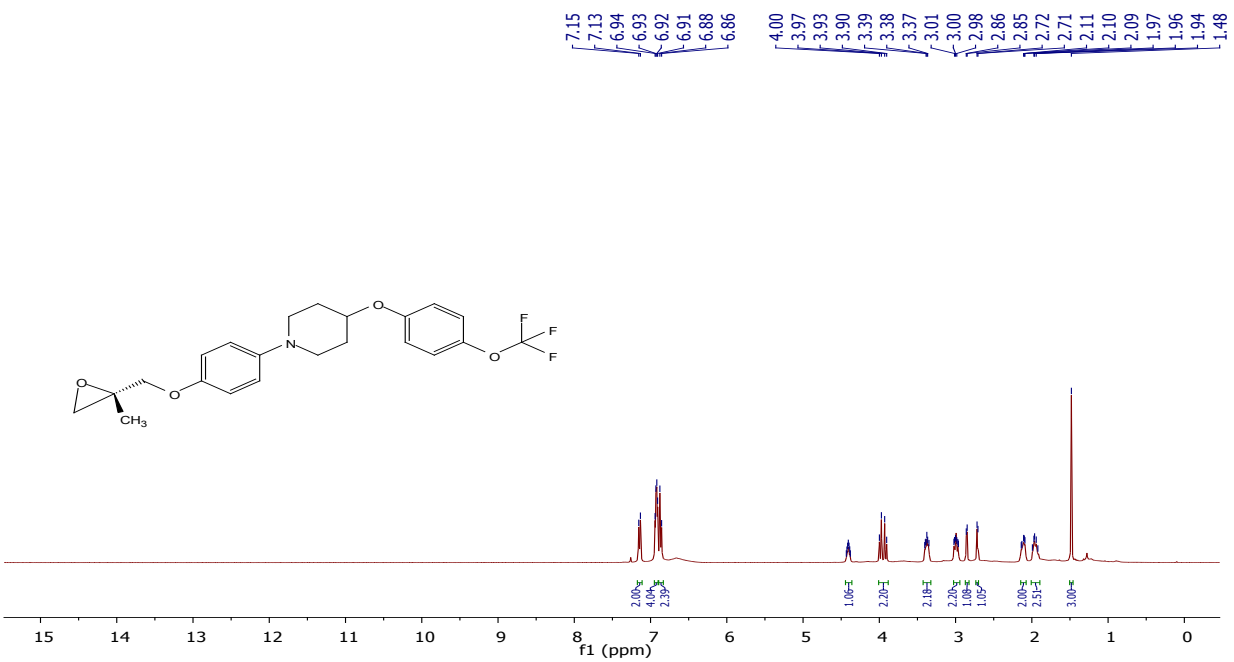
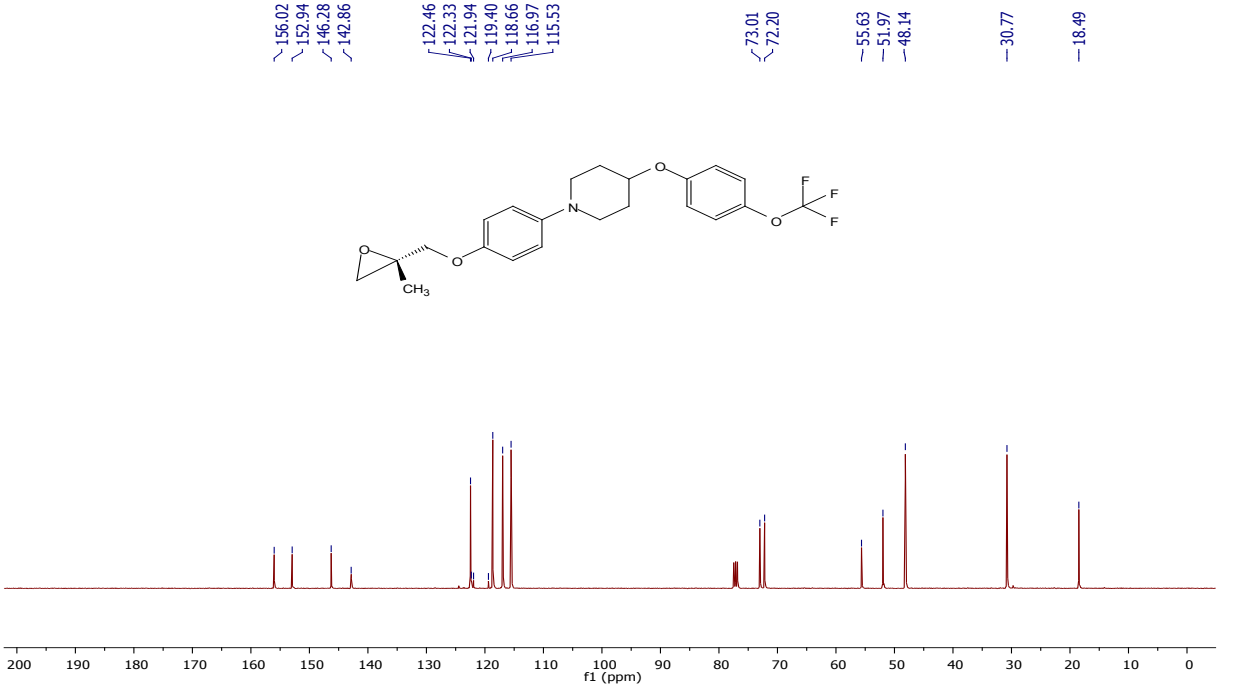
2.	62.018	5957286	34202	51.881

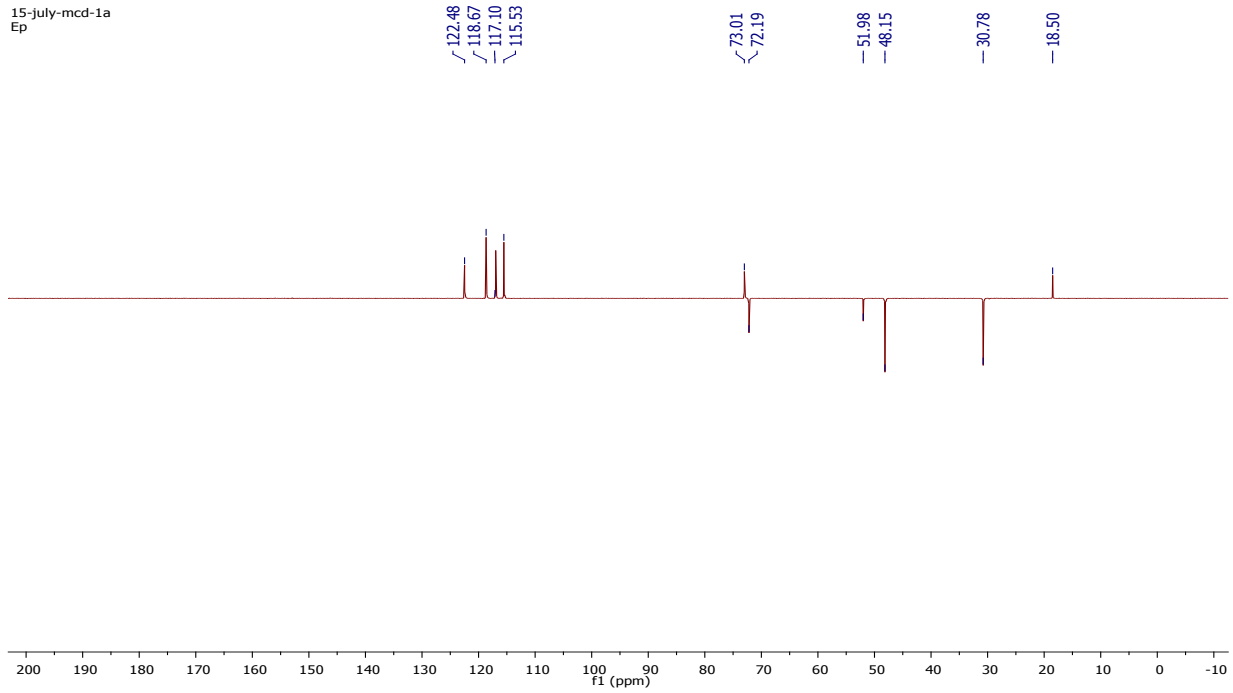
^{1}H NMR spectra of R)-1-(4-((2-methyloxiran-2-yl)methoxy)phenyl)-4-(4-trifluoromethoxy)phenoxy) 11:



^{13}C NMR spectra of R)-1-(4-((2-methyloxiran-2-yl)methoxy)phenyl)-4-(4-trifluoromethoxy)phenoxy) 11:



DEPT NMR of compound 11:



HRMS spectra of compound 11:

Qualitative Compound Report

Data File	EP.d	**Sample Name**	EP
Sample Type	Sample	**Position**	Vial 24
Instrument Name	Instrument 1	**User Name**	
Acq Method	vishal_12-01-13.m	**Acquired Time**	19-07-2019 PM 12:53:13
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

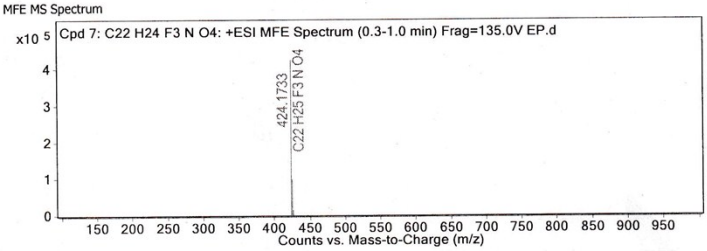
Sample Group **Info.**
Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 7: C22 H24 F3 N O4	0.4	423.1659	C22 H24 F3 N O4	C22 H24 F3 N O4	-0.38	C22 H24 F3 N O4

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 7: C22 H24 F3 N O4	424.1733	0.4	Find by Molecular Feature	423.1659

MFE MS Spectrum



MS Spectrum Peak List

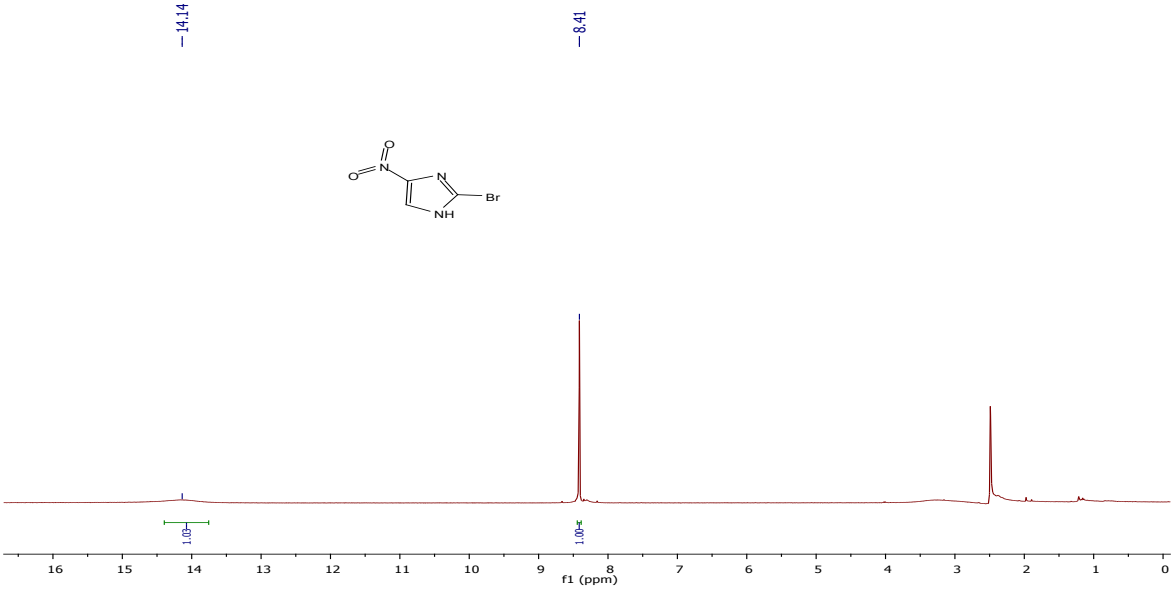
m/z	z	Abund	Formula	Ion
424.1733	1	424925.94	C22 H25 F3 N O4	(M+H)+
425.176	1	97555.55	C22 H25 F3 N O4	(M+H)+
426.1792	1	14421.54	C22 H25 F3 N O4	(M+H)+
427.181	1	2406.82	C22 H25 F3 N O4	(M+H)+

Predicted Isotope Match Table

Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	424.1733	424.173	-0.65	100	100	78.79	77.68
2	425.176	425.1763	0.75	22.96	24.6	18.09	19.11
3	426.1792	426.1791	-0.35	3.39	3.72	2.67	2.89
4	427.181	427.1818	1.89	0.57	0.42	0.45	0.33

--- End Of Report ---

^{1}H NMR spectra of 2-Bromo-4-nitro-1H-imidazole 12:



HRMS spectra of compound 12:

Qualitative Compound Report

Data File	NI-Br.d	**Sample Name**	NI-Br
Sample Type	Sample	**Position**	Vial 25
Instrument Name	Instrument 1	**User Name**	
Acq Method	vishal_12-01-13.m	**Acquired Time**	19-07-2019 PM 12:57:30
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

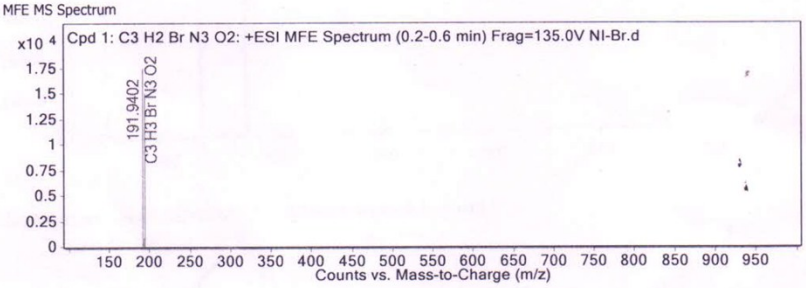
Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 1: C3 H2 Br N3 O2	0.3	190.9327	C3 H2 Br N3 O2	C3 H2 Br N3 O2	1.75	C3 H2 Br N3 O2

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C3 H2 Br N3 O2	191.9402	0.3	Find by Molecular Feature	190.9327

MFE MS Spectrum



MS Spectrum Peak List

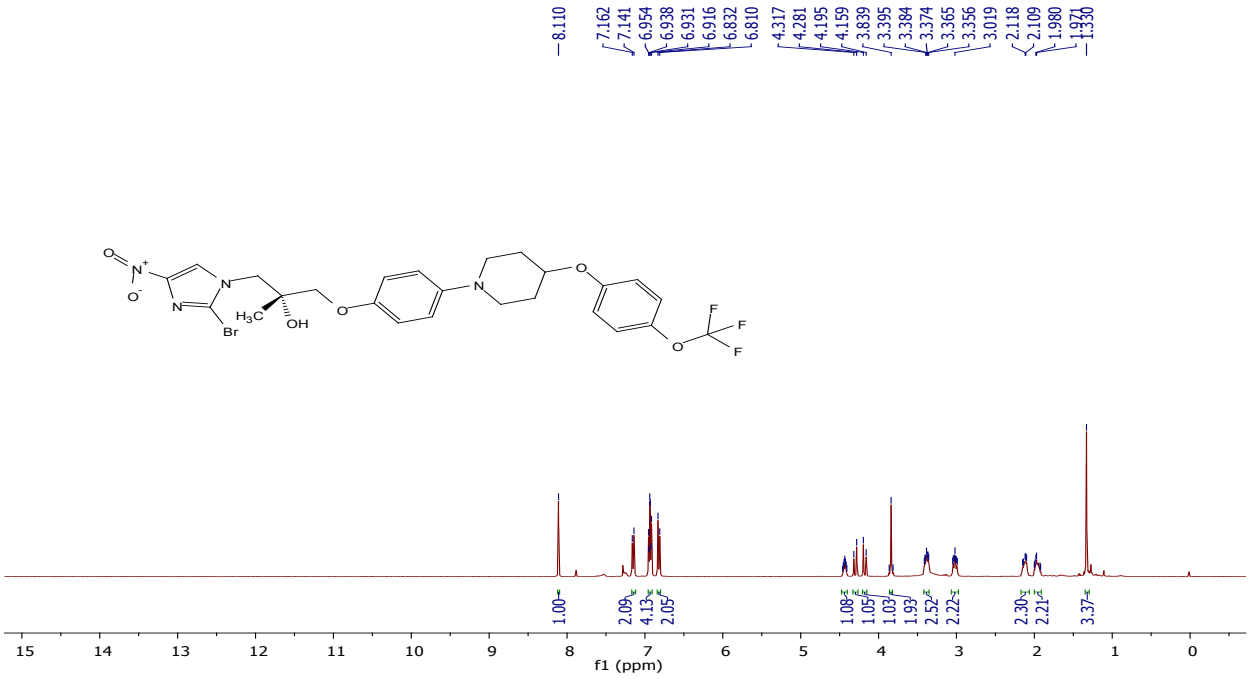
m/z	z	Abund	Formula	Ion
191.9402	1	17450.45	C3 H3 Br N3 O2	(M+H)+
192.9407	1	912.85	C3 H3 Br N3 O2	(M+H)+
193.938	1	14996.04	C3 H3 Br N3 O2	(M+H)+
194.9374	1	1018.41	C3 H3 Br N3 O2	(M+H)+

Predicted Isotope Match Table

Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	191.9402	191.9403	0.68	100	100	50.76	48.41
2	192.9407	192.9422	7.5	5.23	4.45	2.66	2.15
3	193.938	193.9383	1.75	85.93	97.77	43.62	47.33
4	194.9374	194.9401	14.18	5.84	4.35	2.96	2.11

--- End Of Report ---

^{1}H NMR spectra of 1-(2-bromo-4-nitro-1H-imidazol-1-yl)-2-methyl-3-(4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)phenoxy)propan-2-ol 13:



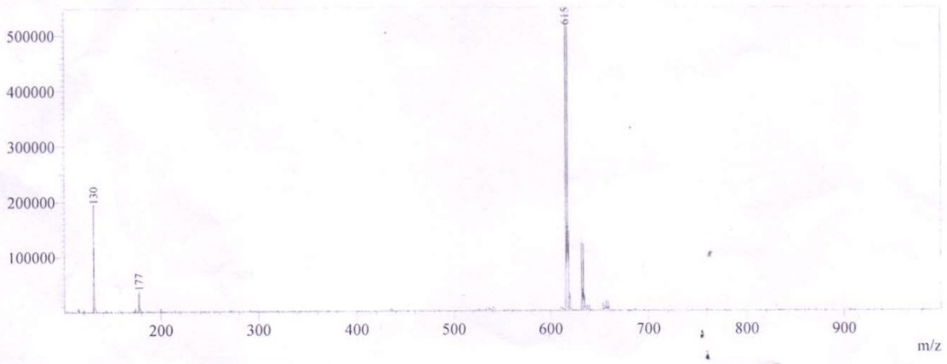
LC-MS spectra of compound 13:

Sample Information

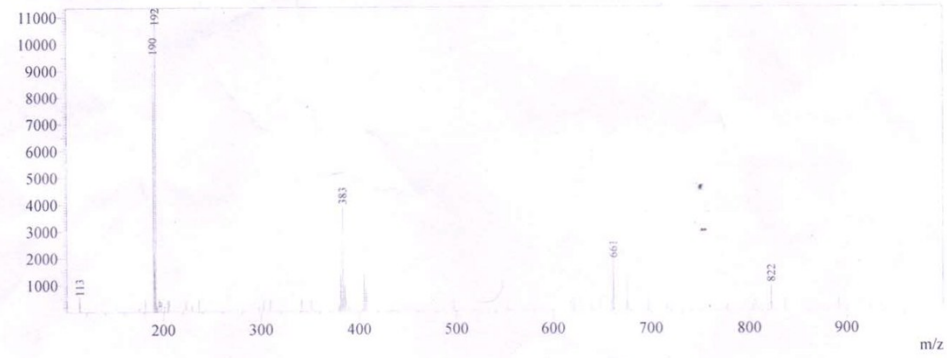
Sample Name	: SS	Sample ID	:
Tray#	: 1	Vial#	: 61
Injection Volume	: 2	Data File	: 22-7-19MS6.lcd
Method File	: MS Scan.lcm	Processed by	: System Administrator
Date Processed	: 22-07-2019 17:15:15		

MS Spectrum

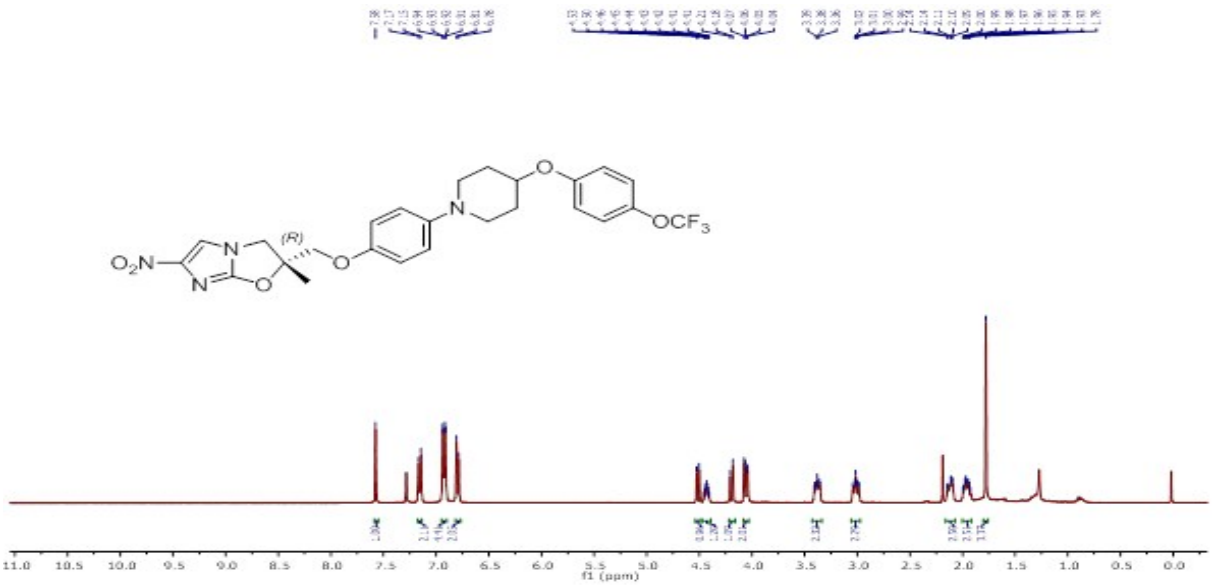
BG Mode:Averaged 0.440-0.981(27-59)$EndIf$ Segment 1 - Event 1



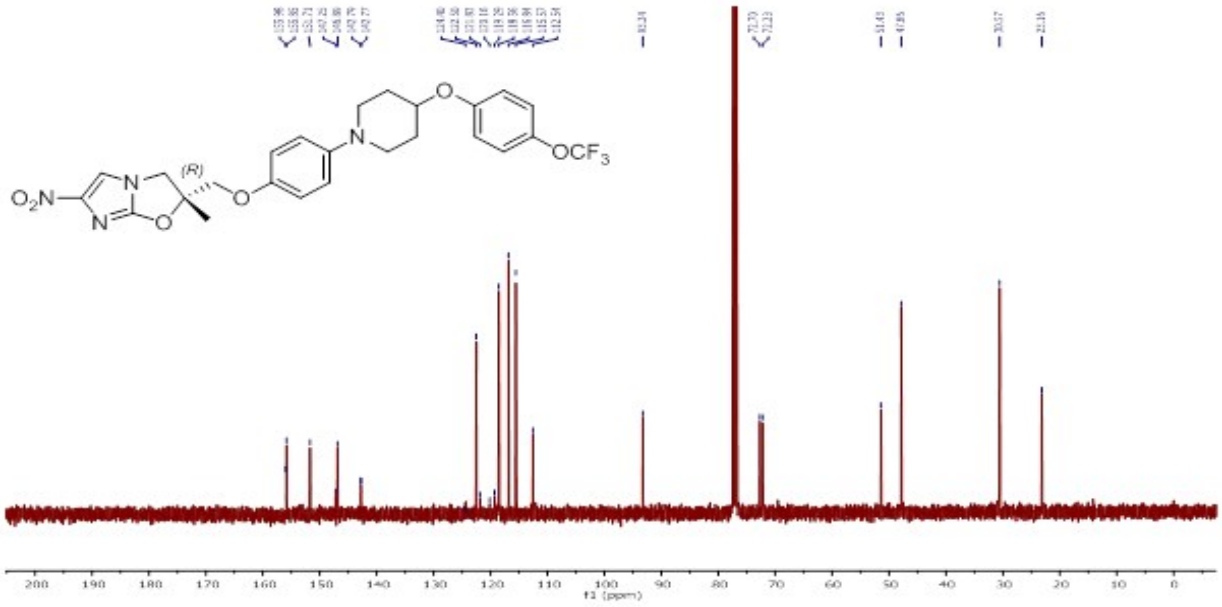
BG Mode:Averaged 0.457-0.964(28-58)$EndIf$ Segment 1 - Event 2



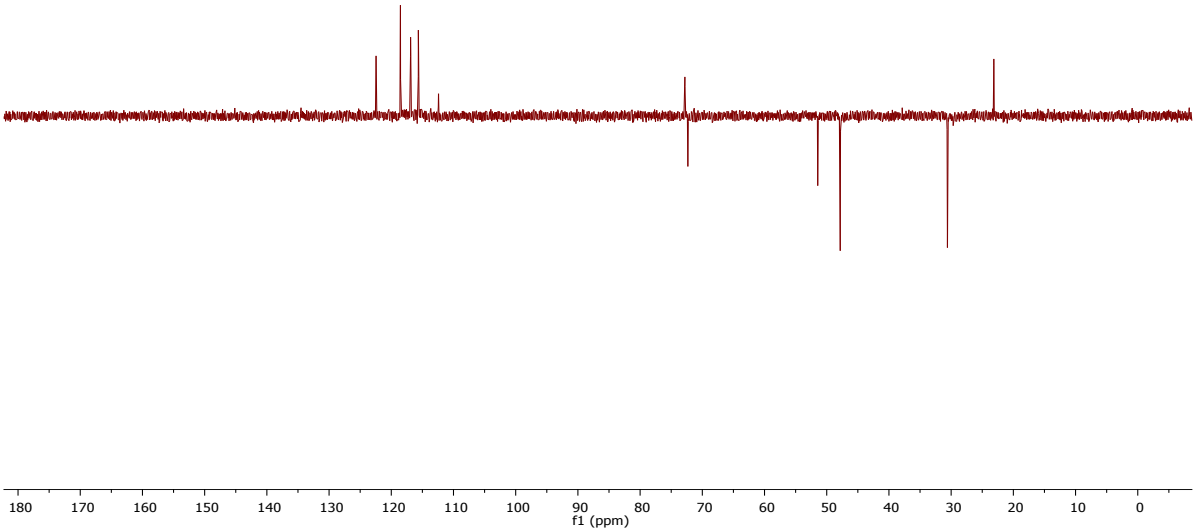
^{1}H NMR spectra of 2-methyl-6-nitro-2-((4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)phenoxy)methyl)-2,3-dihydroimidazo[2,1-b]oxazole II, Delamanid:



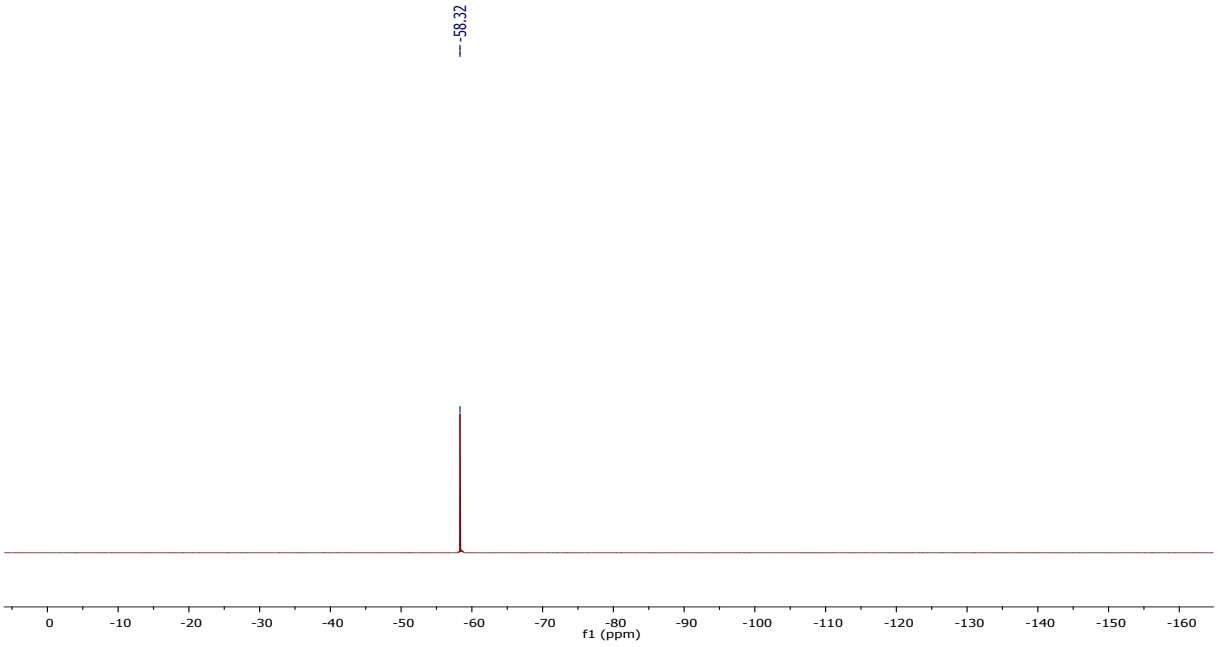
^{13}C NMR spectra of Delamanid II:



DEPT NMR of Delamanid II:



^{19}F NMR spectra of Delamanid II:



HRMS spectra of compound Delamanid II:

Qualitative Compound Report

Data File	OPC.d	**Sample Name**	OPC
Sample Type	Sample	**Position**	Vial 5
Instrument Name	Instrument 1	**User Name**	
Acq Method	vishal_12-01-13.m	**Acquired Time**	24-07-2019 PM 1:40:31
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

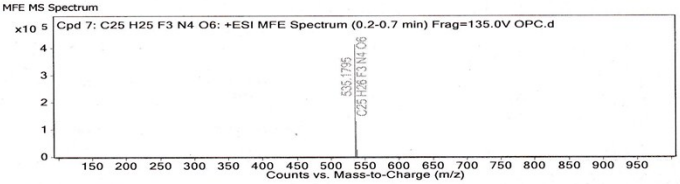
Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 7: C25 H25 F3 N4 O6	0.3	534.1712	C25 H25 F3 N4 O6	C25 H25 F3 N4 O6	2.63	C25 H25 F3 N4 O6

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 7: C25 H25 F3 N4 O6	535.1795	0.3	Find by Molecular Feature	534.1712

MFE MS Spectrum



MS Spectrum Peak List

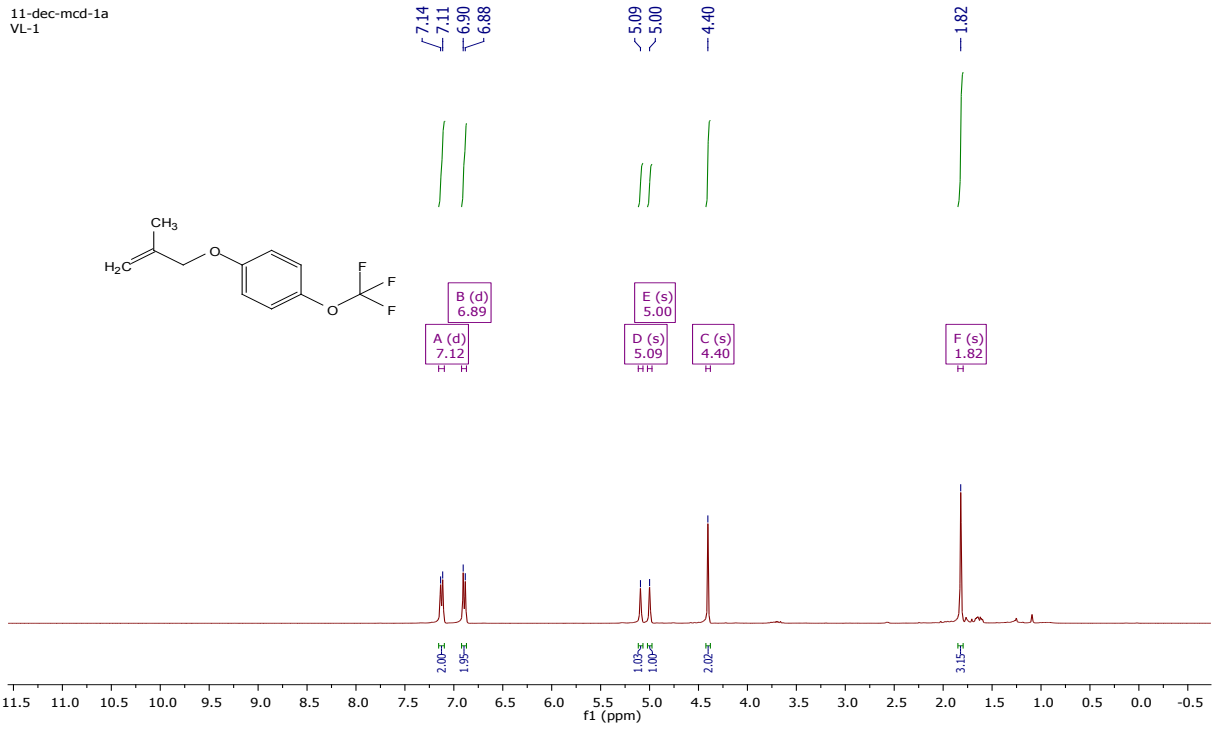
m/z	z	Abund	Formula	Ion
535.1795	1	413908.19	C25 H26 F3 N4 O6	(M+H)+
536.1802	1	129875.09	C25 H26 F3 N4 O6	(M+H)+
537.1753	1	26357.12	C25 H26 F3 N4 O6	(M+H)+

Predicted Isotope Match Table

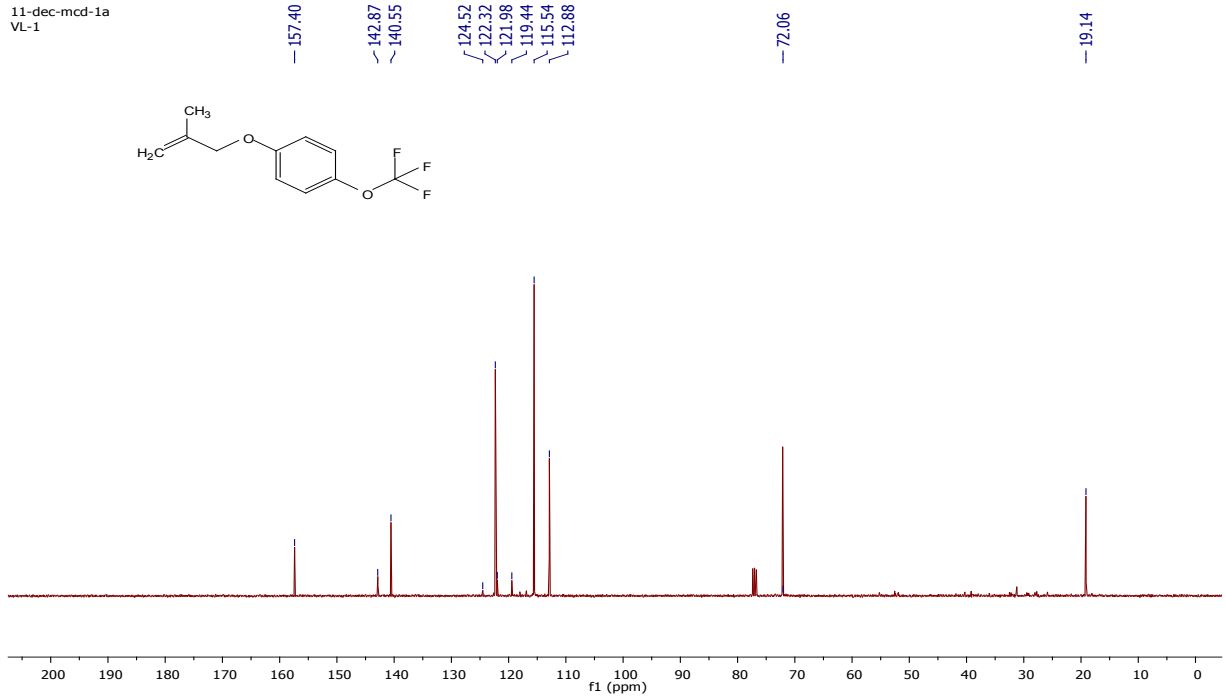
Isotope	*m/z*	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	535.1795	535.1799	0.79	100	100	72.6	74.45
2	536.1802	536.183	5.11	31.38	29.03	22.78	21.61
3	537.1753	537.1856	19.11	6.37	5.3	4.62	3.94

--- End Of Report ---

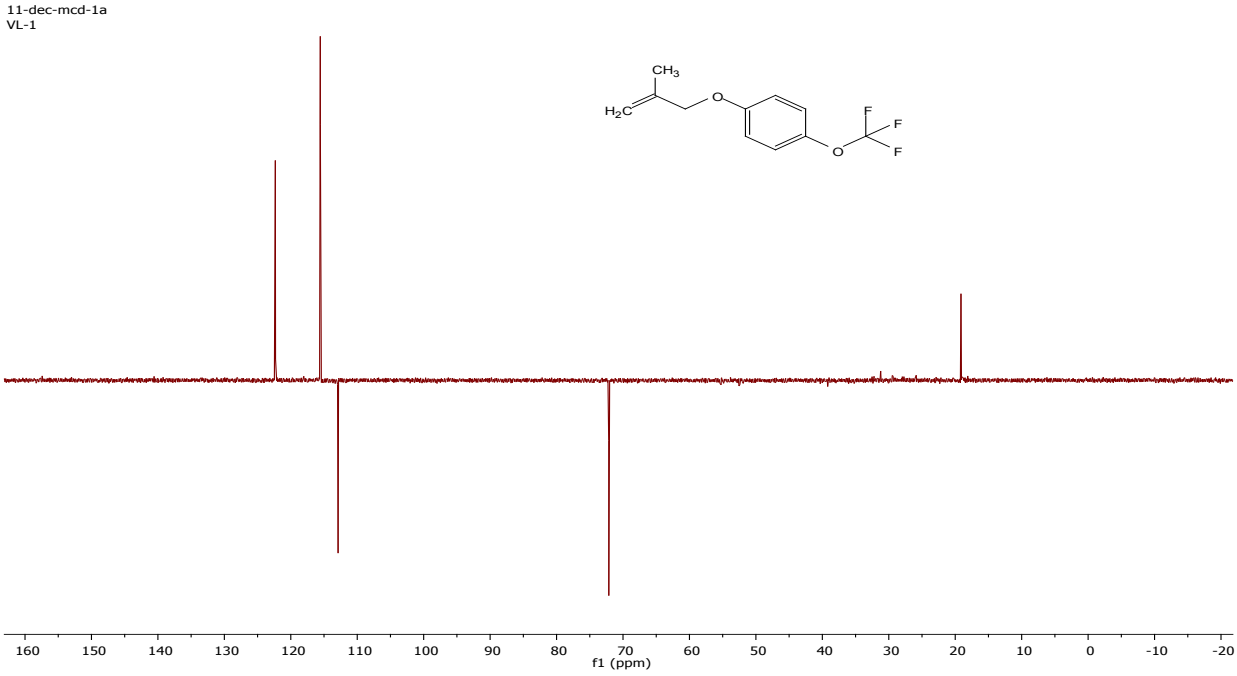
^{1}H NMR spectra of 1-((2-methylallyl)oxy)-4-(trifluoromethoxy)benzene (14):



^{13}C NMR spectra of 1-((2-methylallyl)oxy)-4-(trifluoromethoxy)benzene (14):



DEPT NMR spectra of 1-((2-methylallyl)oxy)-4-(trifluoromethoxy)benzene (14):



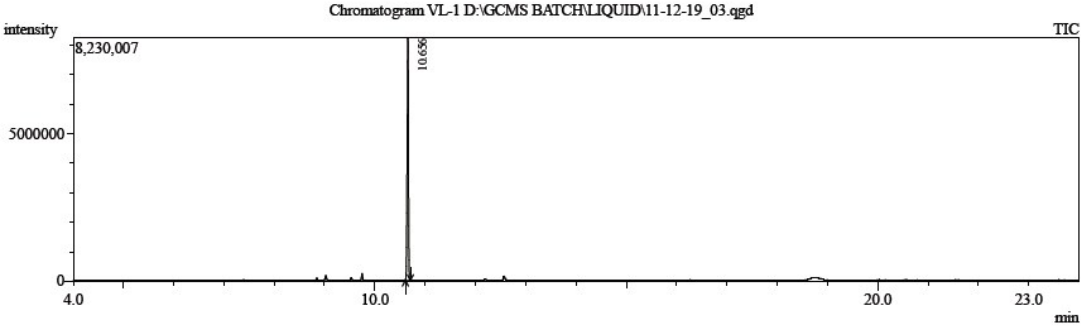
GC-MS spectra of compound 14:

IIIM GCMS ANALYSIS REPORT

Sample Information

Analyzed by	**: ADMIN**
Analyzed	**: 12/12/2019 6:29:47 PM**
Sample Type	**: Unknown**
Sample Name	**: VL-1**
Sample Amount	**: 1**
Vial #	**: 52**
Injection Volume	**: 0.20**
Data File	**: D:\GCMS BATCH\LIQUID\11-12-19_03.qgd**
Method File	**: D:\GCMS METHOD\GCMS-GENERAL.qgm**
Tuning File	**: D:\Tuning\TUNING_NM_F2_12122019.qgt**
Modified by	**: Admin**
Modified	**: 12/12/2019 6:53:47 PM**

Chromatogram VL-1 D:\GCMS BATCH\LIQUID\11-12-19_03.qgd

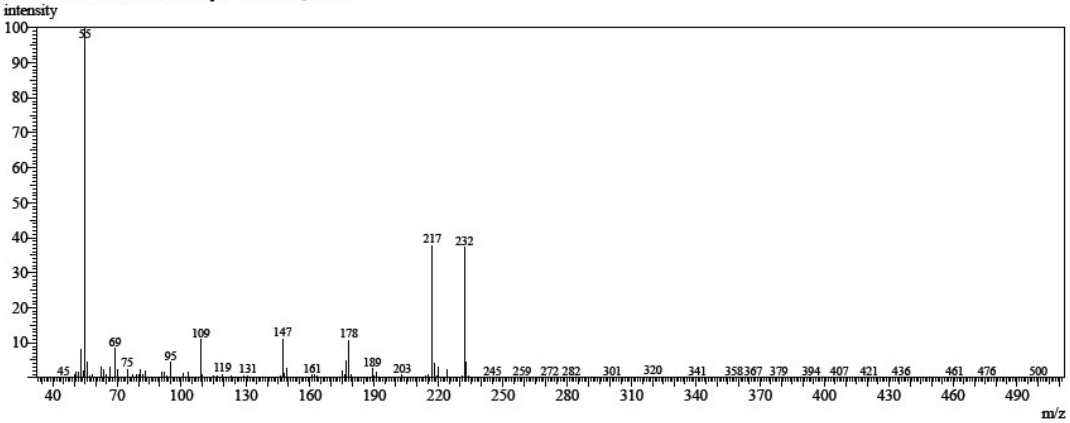


Peak Report TIC

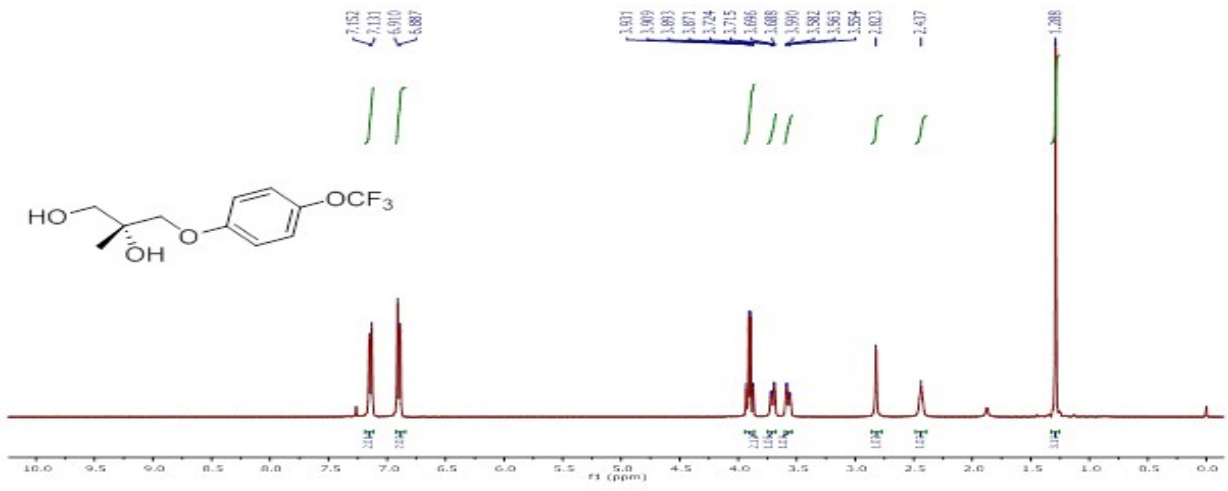
Peak#	R.Time	I.Time	F.Time	Area	A/H	Area%	Height	Name
1	10.656	10.605	10.705	14919663	1.82	100.00	8189101	(S)-(-)-1,2,4-Butanetriol, 4-pentafluoropropionate
				14919663		100.00	8189101	

Spectrum

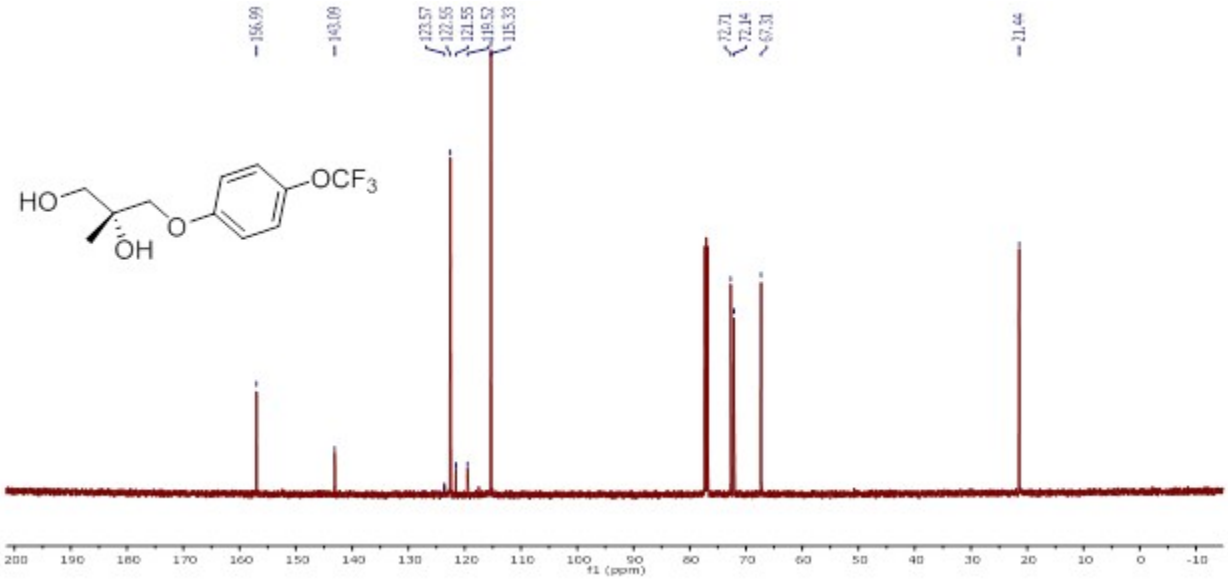
Line#:1 R.Time:10.655(Scan#:1332)
MassPeaks:341
RawMode:Averaged 10.650-10.660(1331-1333) BasePeak:55(2450883)
BG Mode:Calc. from Peak Group 1 - Event 1 Q3 Scan



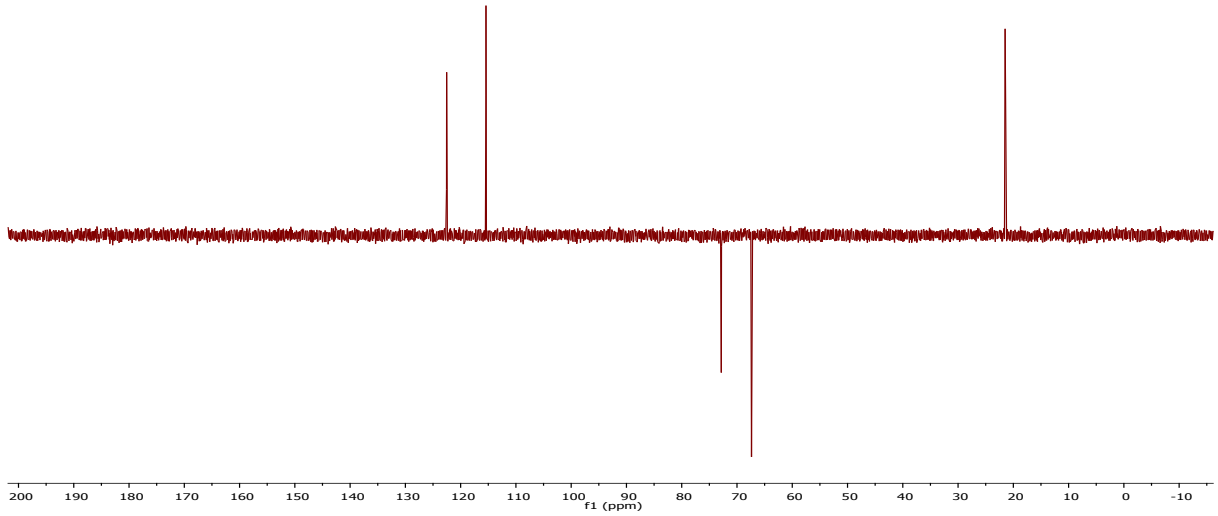
^{1}H NMR spectra of (R)-2-methyl-3-(4-(trifluoromethoxy)phenoxy)propane-1,2-diol *R*-(+)-15:



^{13}C NMR spectra of (R)-2-methyl-3-(4-(trifluoromethoxy)phenoxy)propane-1,2-diol *R*-(+)-15::

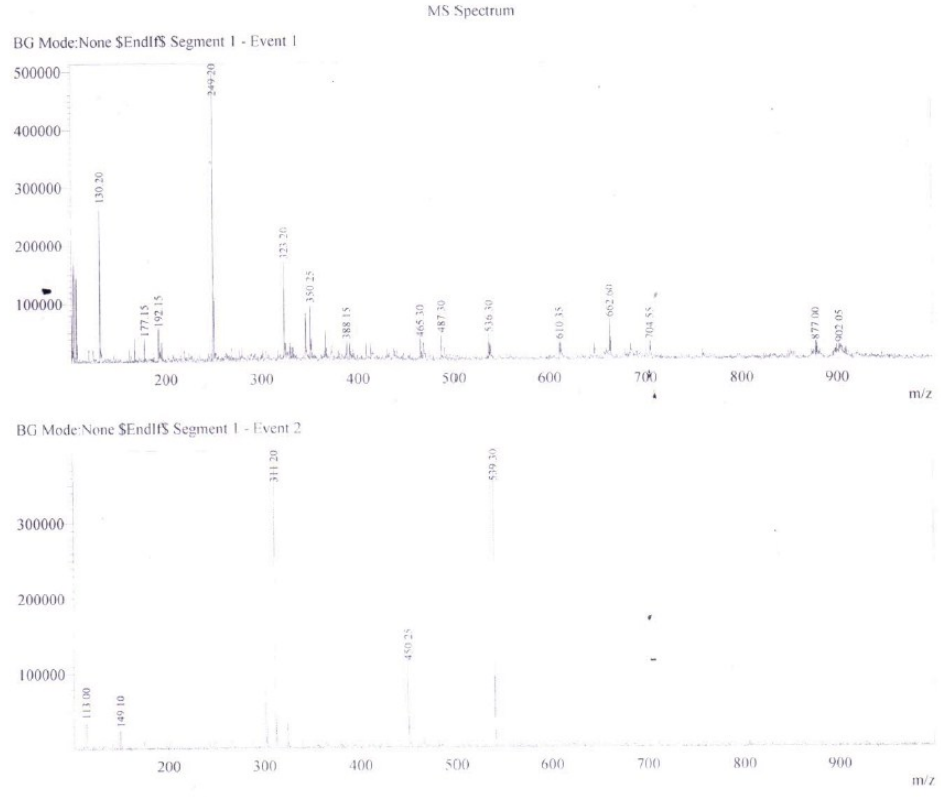


DEPT NMR spectra of (R)-2-methyl-3-(4-(trifluoromethoxy)phenoxy)propane-1,2-diol *R*-(+)-15:

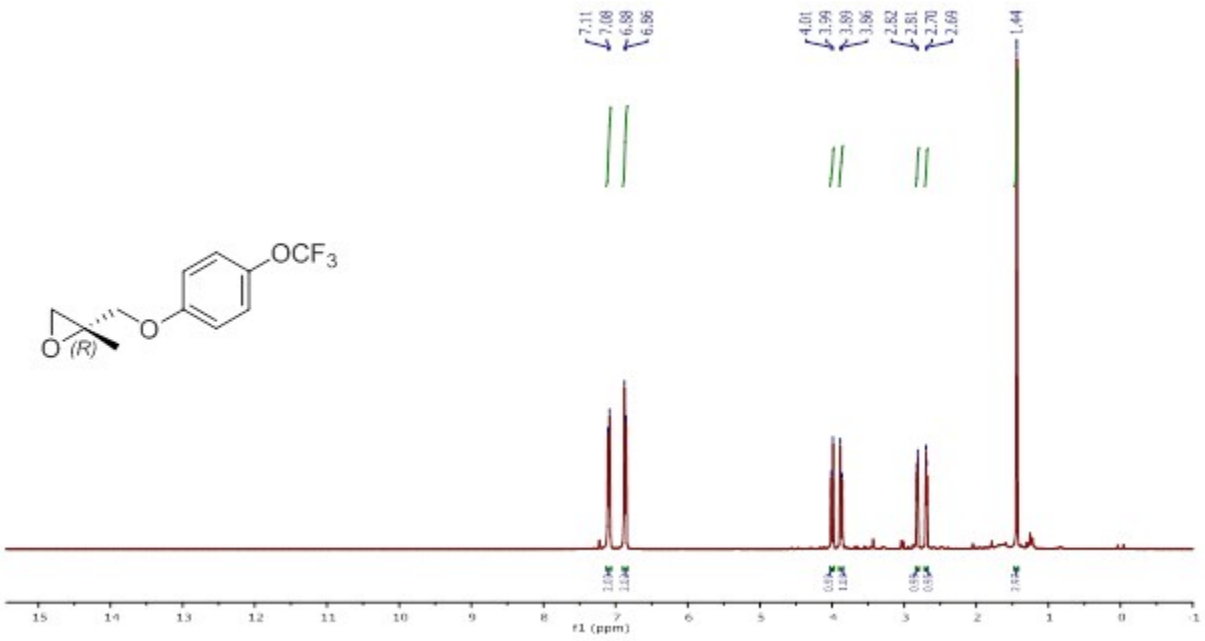


LC-MS spectra of compound *R*-(+)-15:

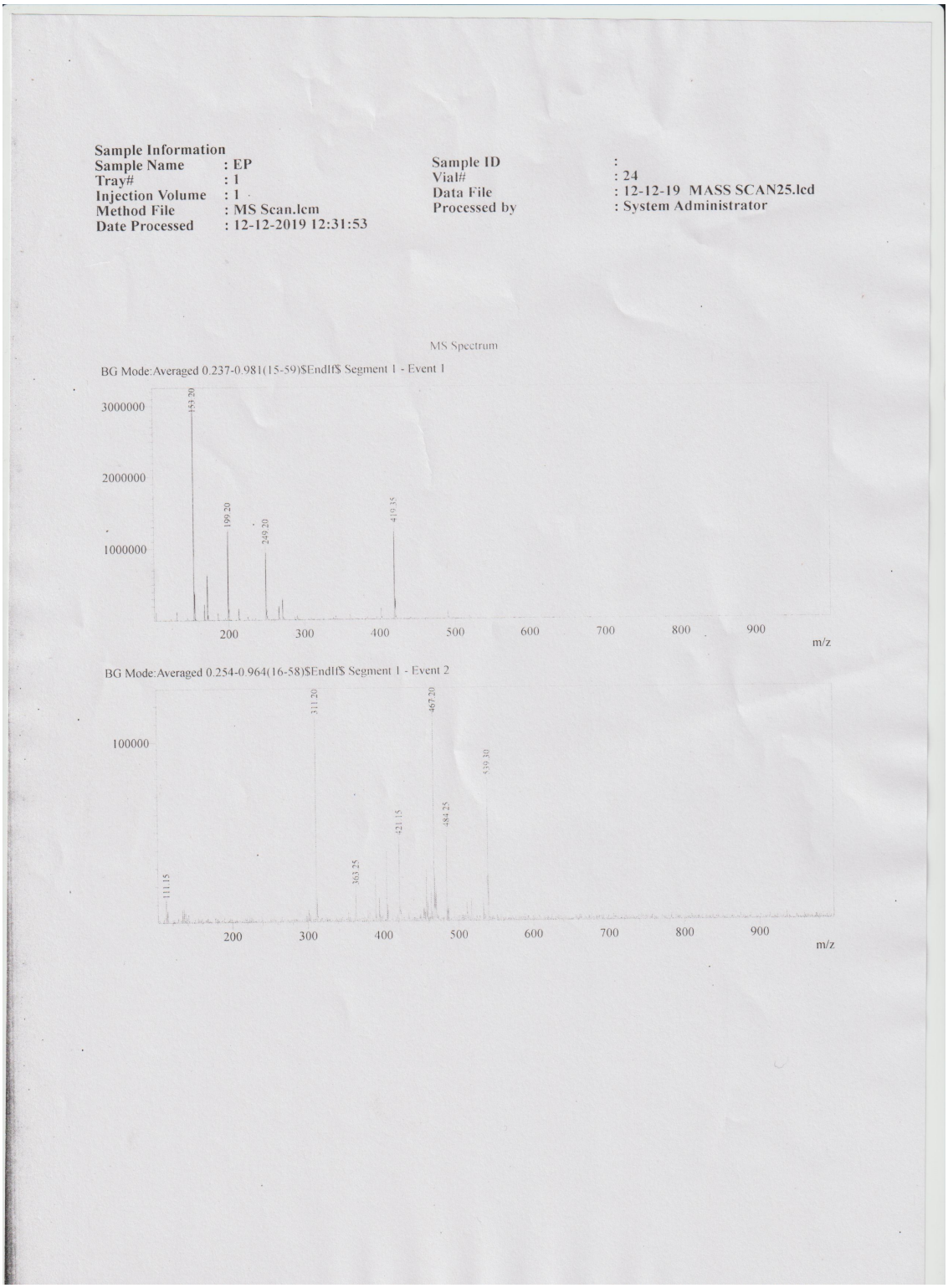
Sample Information			
Sample Name	: S1	Sample ID	:
Tray#	: 1	Vial#	: 51
Injection Volume	: 1	Data File	: 16-12-19 MASS SCAN59.lcd
Method File	: MS Scan.lcm	Processed by	: System Administrator
Date Processed	: 16-12-2019 16:07:44		



^{1}H NMR spectra of (*R*)-1-(4-((2-methyloxiran-2-yl)methoxy)phenyl)-4-(4-trifluoromethoxy)phenoxy) (17):



LC-MS spectra of compound 17:



Sample Information

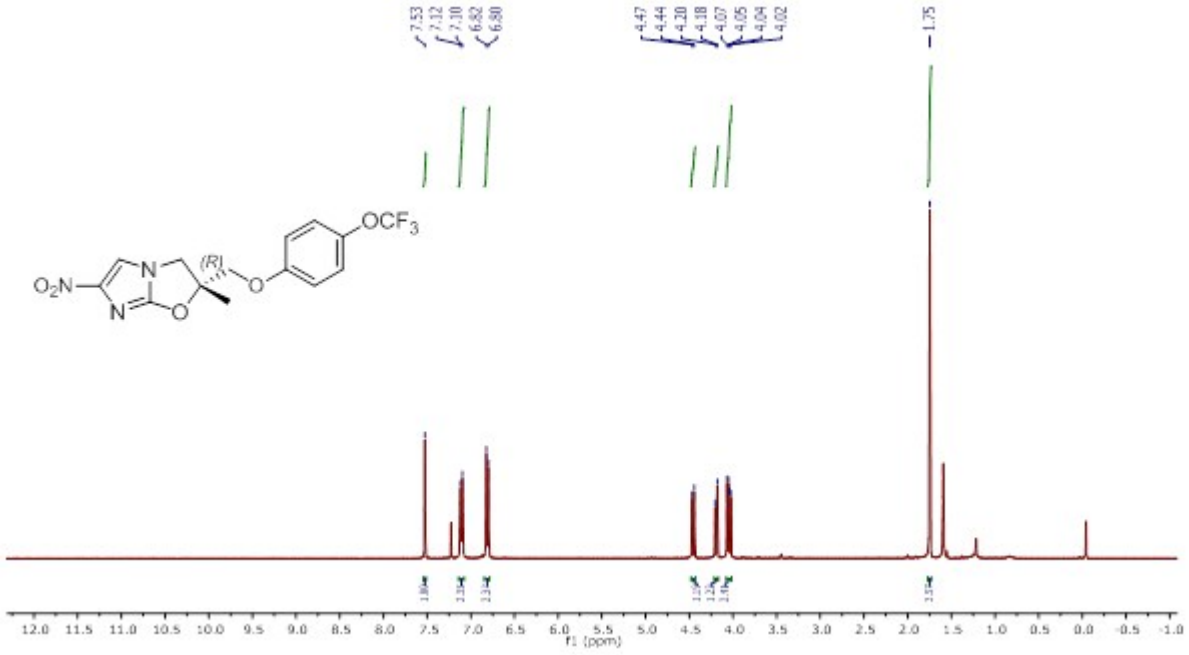
Sample Name	: EP	Sample ID	:
Tray#	: 1	Vial#	: 24
Injection Volume	: 1	Data File	: 12-12-19 MASS SCAN25.lcd
Method File	: MS Scan.lcm	Processed by	: System Administrator
Date Processed	: 12-12-2019 12:31:53		

MS Spectrum

BG Mode:Averaged 0.237-0.981(15-59)$EndIf$ Segment 1 - Event 1

BG Mode:Averaged 0.254-0.964(16-58)$EndIf$ Segment 1 - Event 2

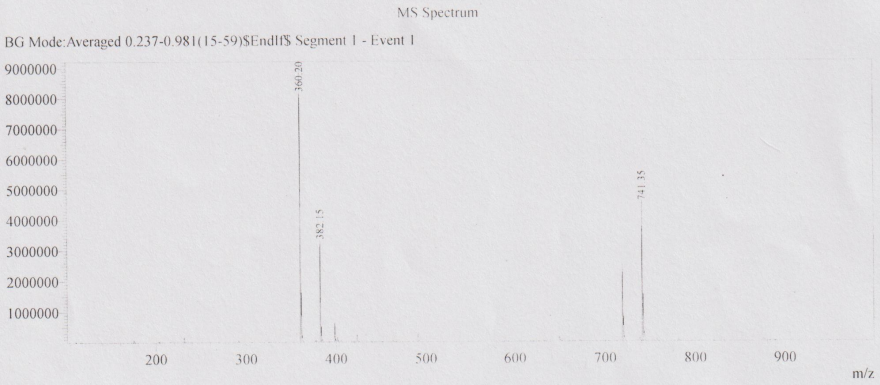
^{1}H NMR spectra of (R)-2-methyl-6-nitro-2-((4-(trifluoromethoxy)phenoxy)methyl)-2,3-dihydroimidazo[2,1-b]oxazole (VL-2098, VII):

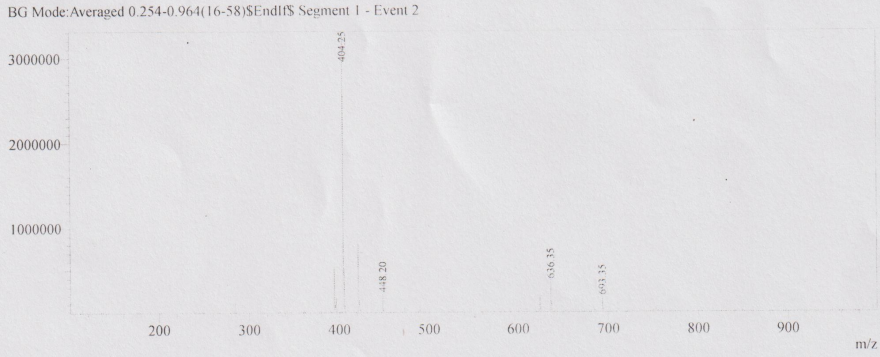


LC-MS spectra of compound VII (VL-2098):

Sample Information

Sample Name	: VL F	Sample ID	:
Tray#	: 1	Vial#	: 23
Injection Volume	: 1	Data File	: 12-12-19 MASS SCAN24.lcd
Method File	: MS Scan.lcm	Processed by	: System Administrator
Date Processed	: 12-12-2019 12:30:16		





References:

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2. Masahiro Miyake, A. A., Takahira Okado Method for producing the 1-4-(Hydroxyphenyl)-4-(4-(trifluoromethoxy)phenoxy)piperidine or salt thereof. 2018.
3. Tsubouchi Hidetsugu, S. H., Kuroda Hideaki, Itotani Motohiro, Hasegawa Takeshi, Haraguchi Yoshikazu, Kuroda Takeshi, Matsuzaki Takayuki, Tai Kuninori, Komatsu Makoto, Matsumoto Makoto, Hashizume Hiroyuki,Tomishige Tatsuo, Seike, Kawasaki Masanori, Sumida Takumi, Miyamura Shin 2,3-dihydro-6-nitroimidazo[2,1-b]oxazoles. 2004.
4. Bruhn, D. F., Scherman, M.S., Woolhiser, L.K., Madhura, D.B., Maddox, M.M., Singh, A.P., Lee, R.B., Hurdle, J.G., McNeil, M.R., Lenaerts, A.J. and Meibohm, B, Pentacyclic nitrofurans with in vivo efficacy and activity against nonreplicating Mycobacterium tuberculosis. *PloS one* **2014,** *9*, e87909.
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7. Pedada, S. R.; Satam, V. S.; Tambade, P. J.; Kandadai, S. A.; Hindupur, R. M.; Pati, H. N.; Launay, D.; Martin, D., An Improved Kilogram-scale synthesis of 2-Bromo-4-nitro-1 H-imidazole: A key building block of nitroimidazole Drugs. *Organic Process Research & Development* **2013,** *17*, 1149-1155.
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9. Sasaki, H.; Haraguchi, Y.; Itotani, M.; Kuroda, H.; Hashizume, H.; Tomishige, T.; Kawasaki, M.; Matsumoto, M.; Komatsu, M.; Tsubouchi, H., Synthesis and antituberculosis activity of a novel series of optically active 6-nitro-2, 3-dihydroimidazo [2, 1-b] oxazoles. *Journal of medicinal chemistry* **2006,** *49*, 7854-7860.