

Supporting Information

Optically Pure Diphenoxy Derivatives as More Flexible Probes for β -Amyloid Plaques

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1. HPLC chromatograms of key target compounds

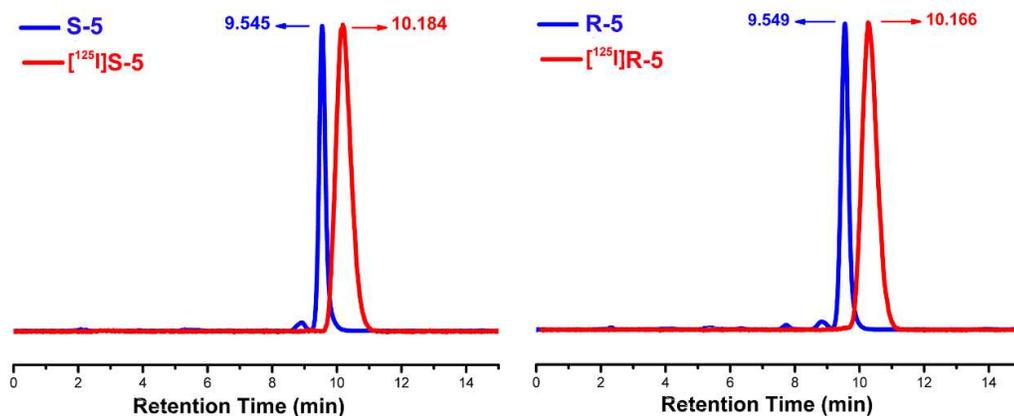


Figure S1 HPLC chromatograms of (*S*)-[¹²⁵I]**5** and (*R*)-[¹²⁵I]**5**.

Table S1 HPLC chromatograms data of (*S*)-[¹²⁵I]**5** and (*R*)-[¹²⁵I]**5**.

Compd	Flow rate (mL/min)	Mobile phase ACN %	Agela Technologies, 5 μm	Retention time (RT, min)	Purity (%)
S-5	1	70	4.6 × 250 mm	9.545	96.543
(<i>S</i>)-[¹²⁵ I] 5	1	70	4.6 × 250 mm	10.184	99.936
R-5	1	70	4.6 × 250 mm	9.549	96.319
(<i>R</i>)-[¹²⁵ I] 5	1	70	4.6 × 250 mm	10.166	98.986

2. Inhibition curves of key target compounds

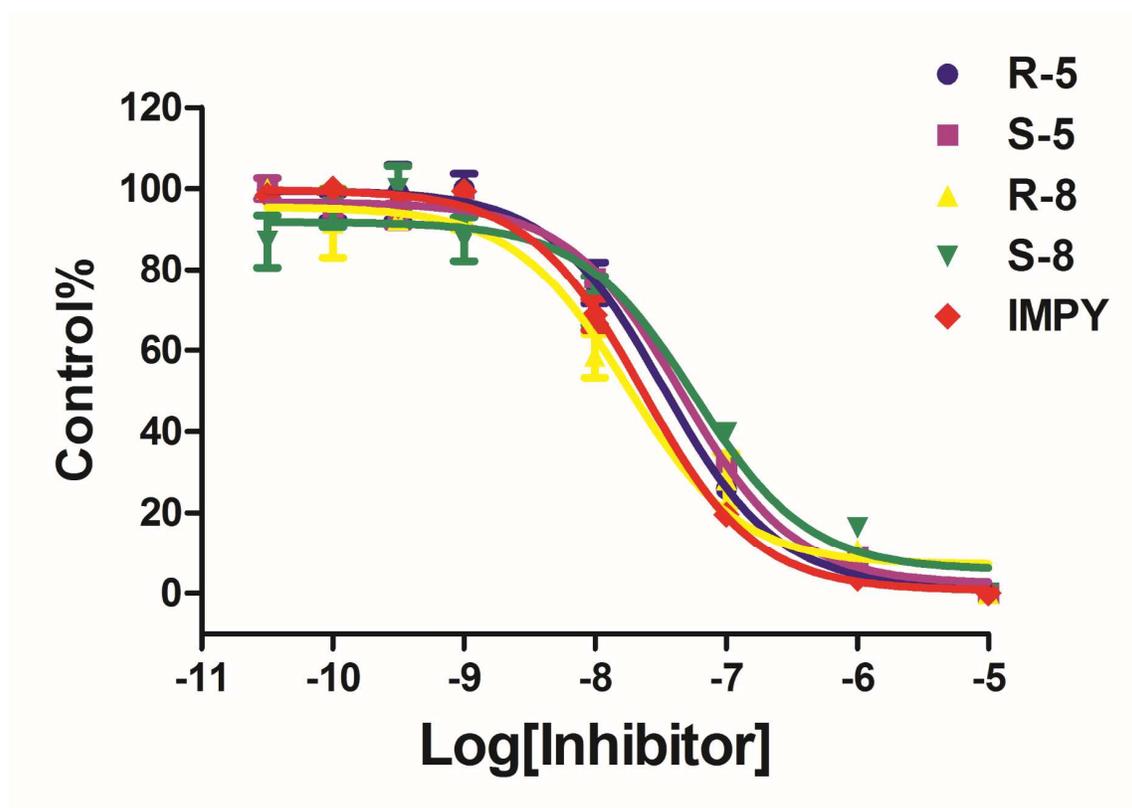


Figure S2. Inhibition curves of optically pure diphenoxy derivatives and **IMPY** for the binding of [¹²⁵I]IMPY to A β ₁₋₄₂ aggregates.

3. Biodistribution in normal ICR mice of (*S*)-[¹²⁵I]5 and (*R*)-[¹²⁵I]5

Table S2 Biodistribution in normal mice (ICR, 5 weeks, 22 – 25 g, male) after i.v. injection of (*S*)-[¹²⁵I]5 and (*R*)-[¹²⁵I]5. ^a

Organ	2 min	10 min	30 min	60 min
(<i>S</i>)-[¹²⁵ I]5 (Log <i>D</i> = 3.26 ± 0.12)				
Blood	10.86 ± 4.31	12.36 ± 4.40	10.95 ± 2.79	4.83 ± 1.71
Brain	4.37 ± 0.70	2.44 ± 0.46	0.80 ± 0.18	0.23 ± 0.04
Heart	6.47 ± 0.28	4.25 ± 1.18	1.77 ± 0.43	0.71 ± 0.18
Liver	21.96 ± 5.77	19.90 ± 1.47	6.21 ± 2.73	2.47 ± 1.20
Spleen	6.82 ± 1.86	5.01 ± 1.39	2.02 ± 0.67	0.62 ± 0.17

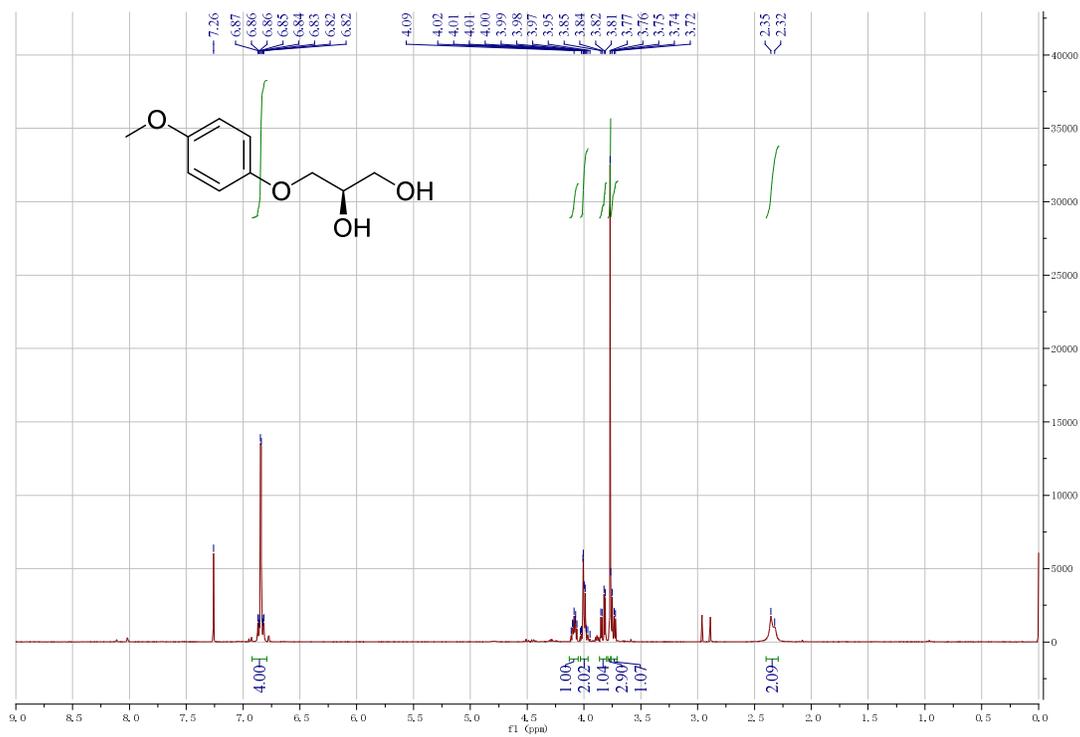
Lung	10.28 ± 5.90	6.20 ± 1.94	2.71 ± 0.89	1.91 ± 1.10
Kidney	11.41 ± 1.28	28.22 ± 1.36	11.22 ± 5.01	9.55 ± 4.32
Pancreas	11.86 ± 2.66	4.95 ± 0.25	1.99 ± 0.33	1.02 ± 0.41
Muscle	7.27 ± 2.54	3.37 ± 0.54	1.82 ± 0.91	0.57 ± 0.24
Intestine ^b	6.23 ± 1.79	13.54 ± 4.56	34.88 ± 2.10	36.70 ± 8.94
Stomach ^b	0.16 ± 0.02	0.25 ± 0.10	0.13 ± 0.02	0.16 ± 0.02
Thyroid ^b	1.05 ± 0.25	2.18 ± 1.19	2.46 ± 1.05	2.72 ± 1.58
<i>(R)</i> -[¹²⁵ I]5 (Log <i>D</i> = 2.97 ± 0.04)				
Blood	9.34 ± 2.01	7.08 ± 1.91	6.15 ± 3.44	5.60 ± 3.08
Brain	3.72 ± 0.31	1.81 ± 0.30	0.50 ± 0.14	0.21 ± 0.12
Heart	6.87 ± 0.64	3.13 ± 0.83	1.41 ± 0.57	0.69 ± 0.32
Liver	22.65 ± 2.37	16.39 ± 2.47	5.69 ± 1.69	2.23 ± 1.52
Spleen	4.79 ± 1.81	3.43 ± 2.67	0.97 ± 0.38	0.62 ± 0.16
Lung	6.73 ± 0.52	4.45 ± 1.24	2.52 ± 1.32	1.14 ± 0.57
Kidney	11.16 ± 0.85	17.87 ± 7.67	10.75 ± 1.55	3.19 ± 2.36
Pancreas	8.43 ± 0.97	3.83 ± 0.91	1.21 ± 0.36	0.97 ± 0.69
Muscle	4.83 ± 0.56	2.88 ± 0.90	1.04 ± 0.46	0.83 ± 0.68
Intestine ^b	5.32 ± 0.07	20.68 ± 7.96	40.28 ± 15.15	36.19 ± 8.43
Stomach ^b	0.17 ± 0.04	0.10 ± 0.02	0.06 ± 0.01	0.07 ± 0.01
Thyroid ^b	1.13 ± 0.27	1.42 ± 0.6	1.19 ± 0.74	0.87 ± 0.59

^a Expressed as % injected dose per gram. Average for 5 mice ± standard deviation.

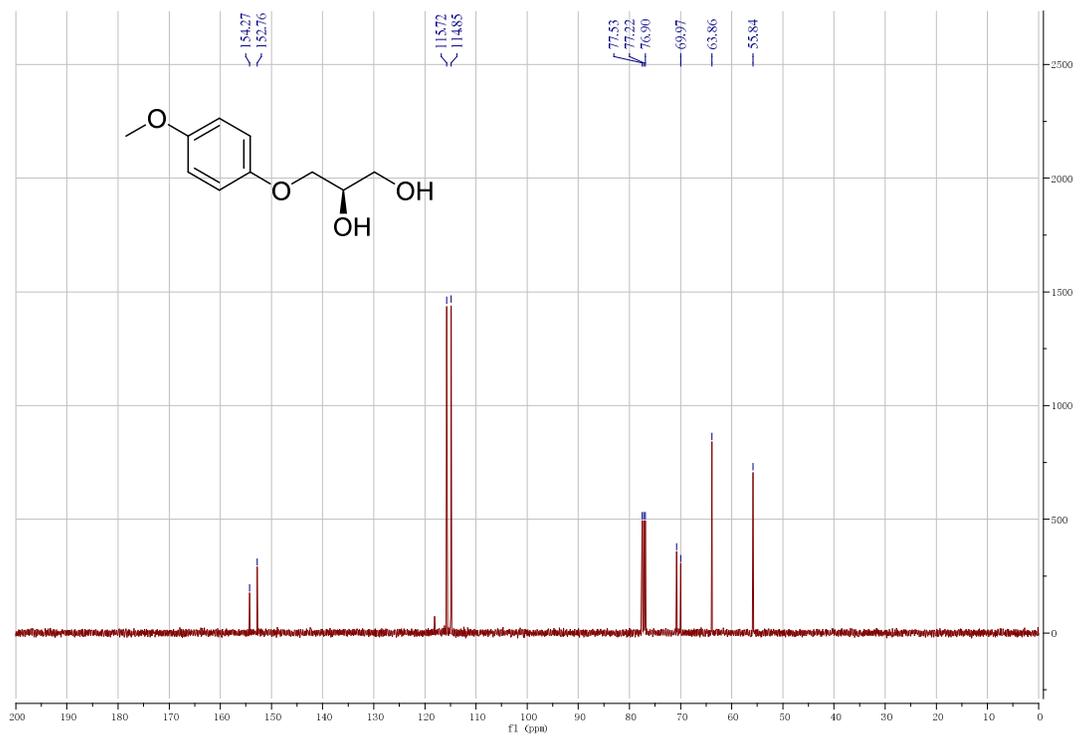
^b Expressed as % injected dose per organ.

4. ¹H-NMR, ¹³C-NMR and HRMS data of synthesized compounds

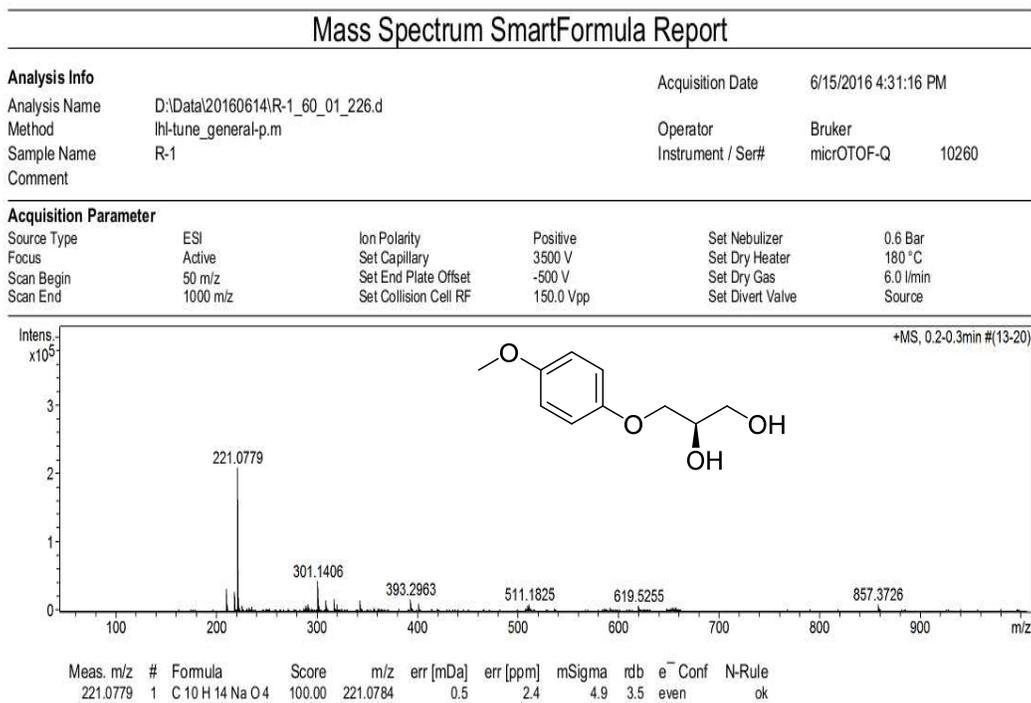
¹H-NMR for compound (*R*)-1



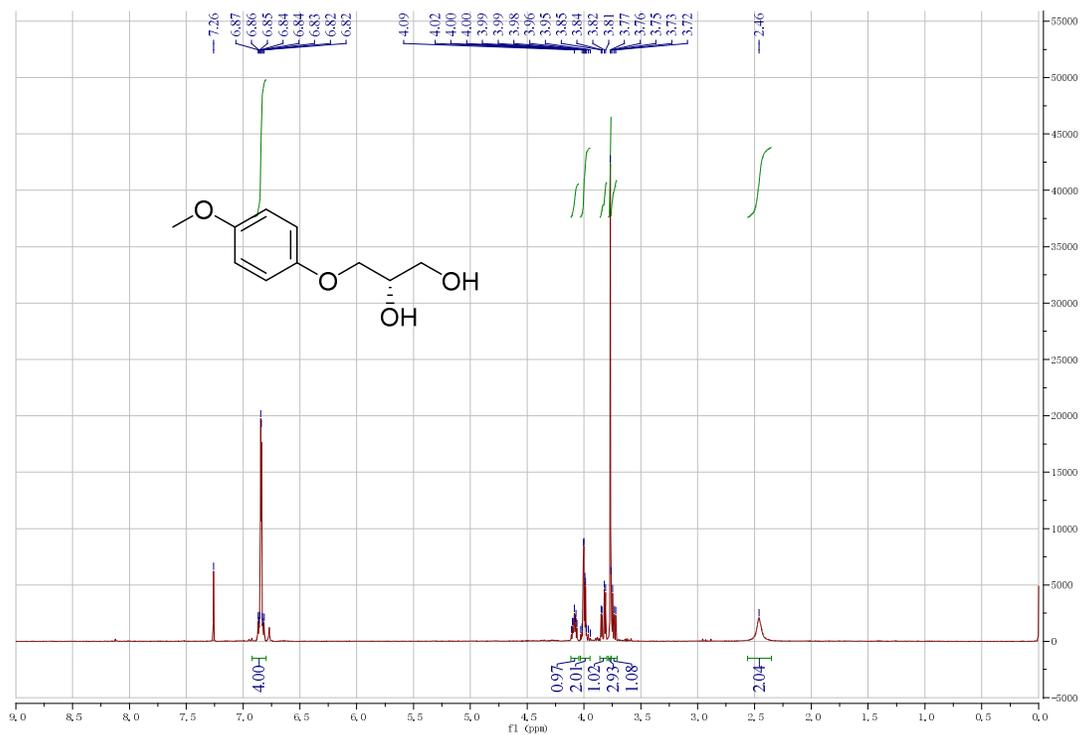
¹³C-NMR for compound (*R*)-1



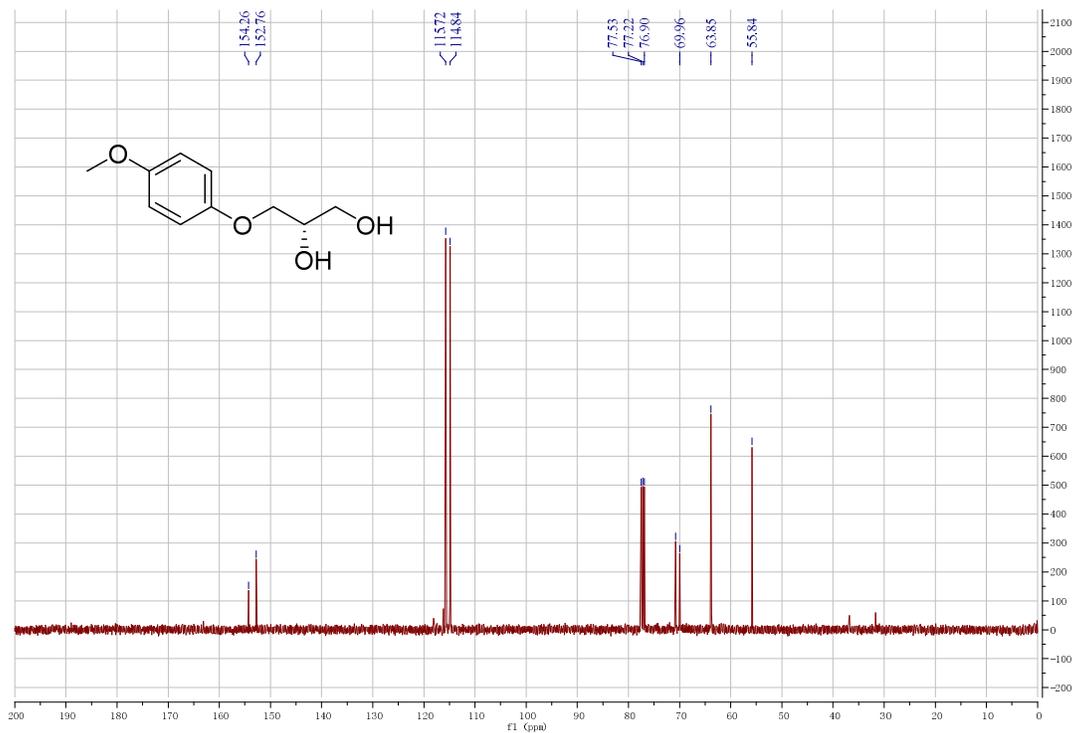
HRMS for compound (R)-1



¹H-NMR for compound (S)-1



¹³C-NMR for compound (S)-1



HRMS for compound (S)-1

Mass Spectrum SmartFormula Report

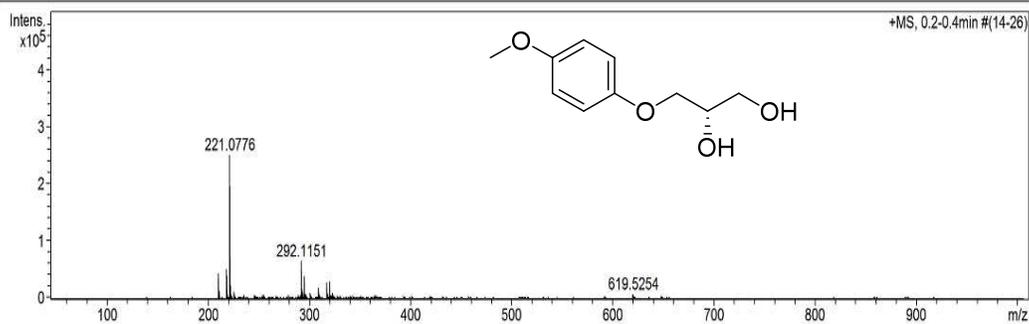
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 Instrument / Ser# micrOTOF-Q 10260

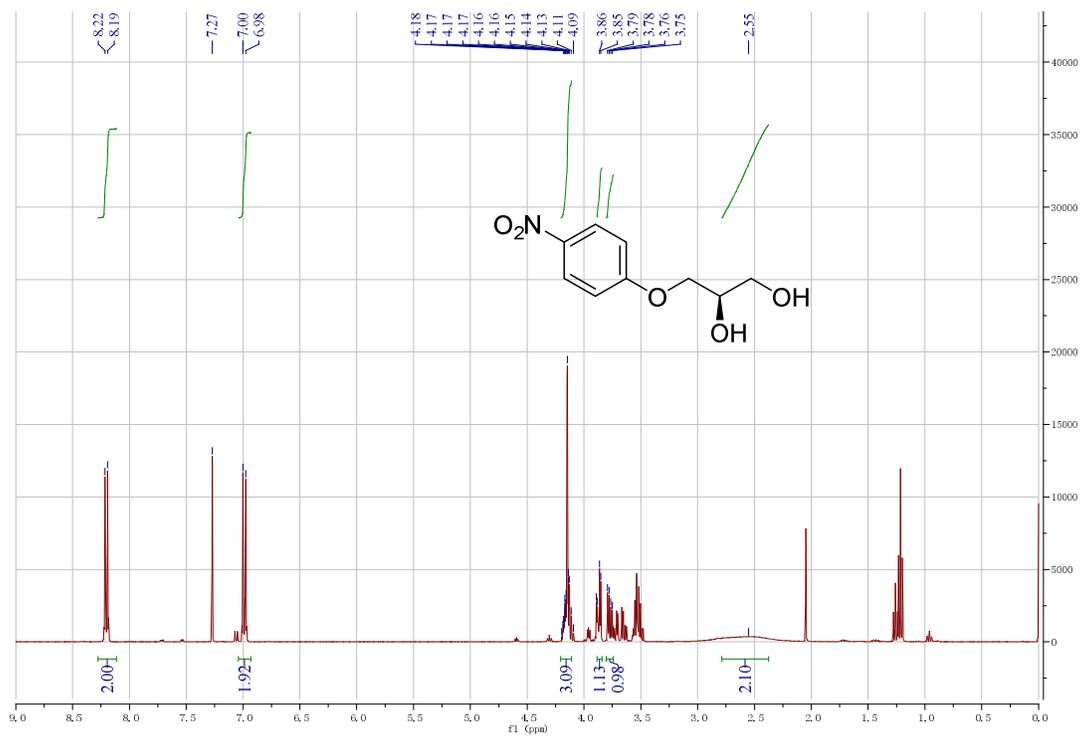
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Scan End	1000 m/z	Set Collision Cell RF	150.0 Vpp	Set Divert Valve	Source

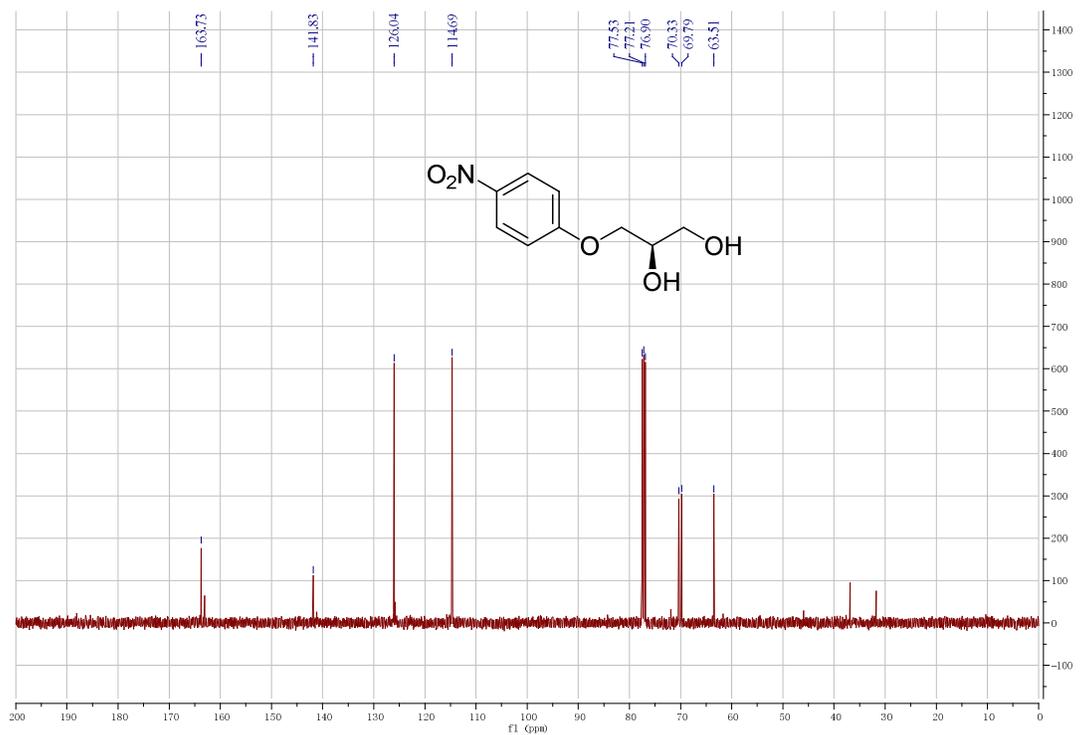


Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e ⁻ Conf	N-Rule
221.0776	1	C 10 H 14 Na O 4	100.00	221.0784	0.8	3.7	1.7	3.5	even	ok

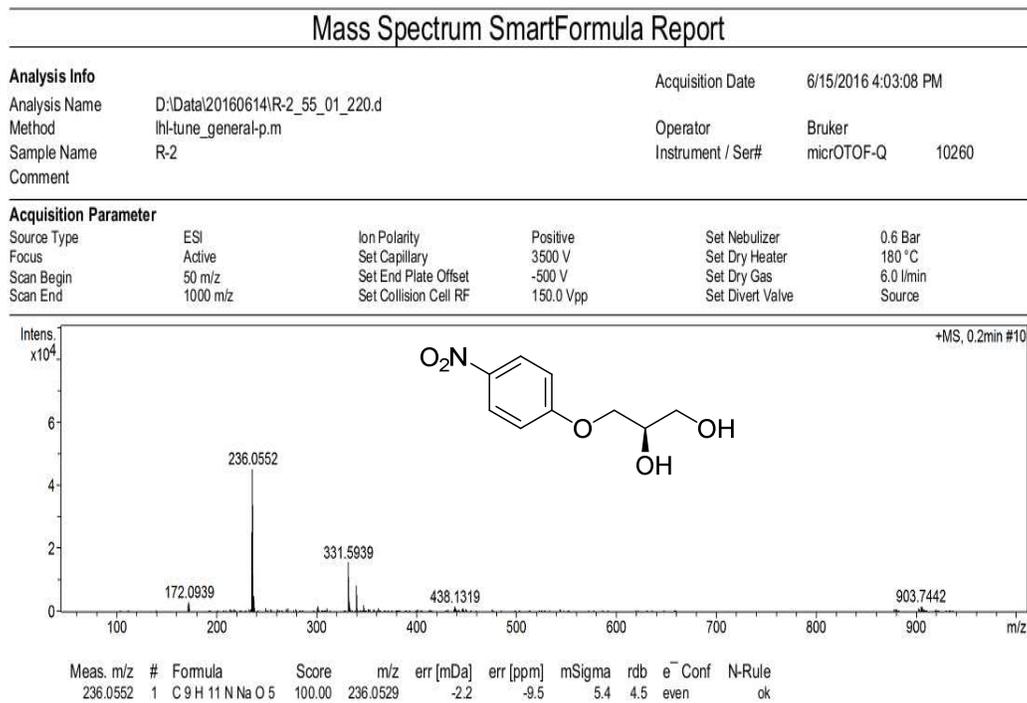
$^1\text{H-NMR}$ for compound (*R*)-2



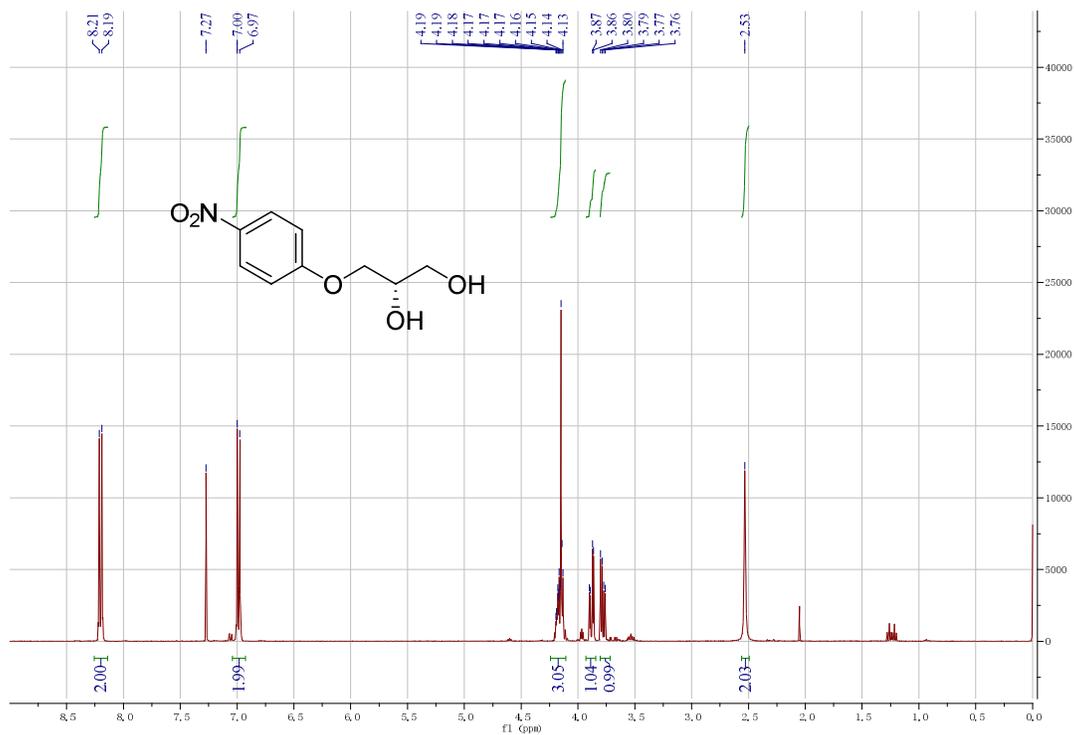
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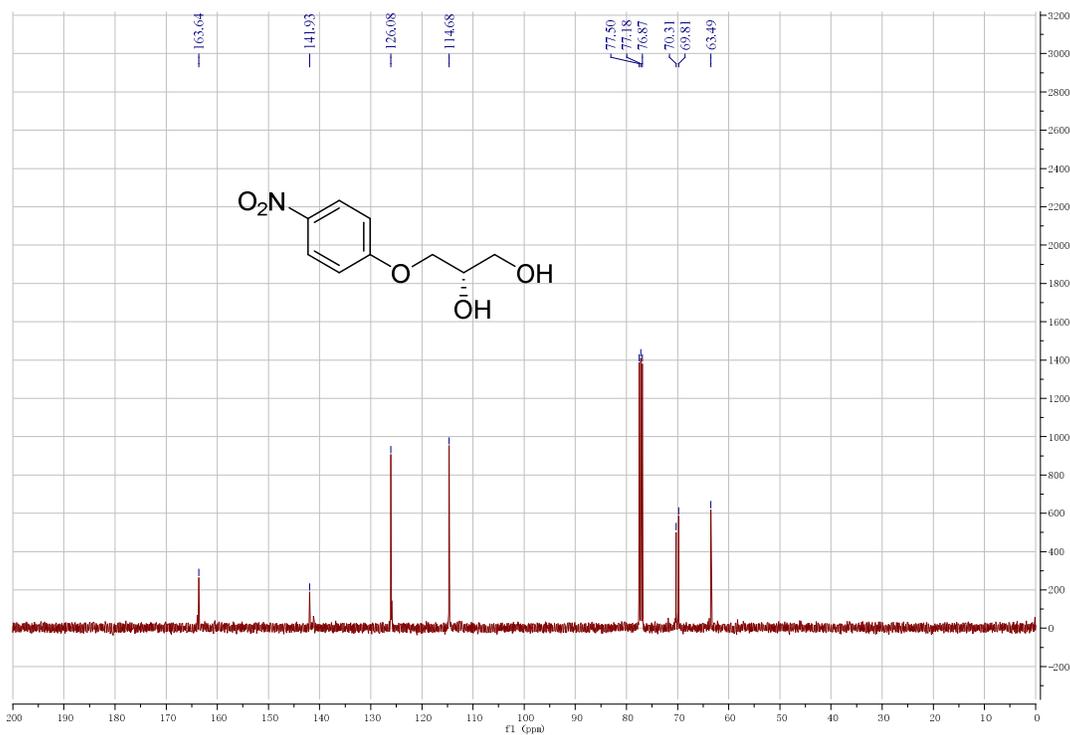
HRMS for compound (R)-2



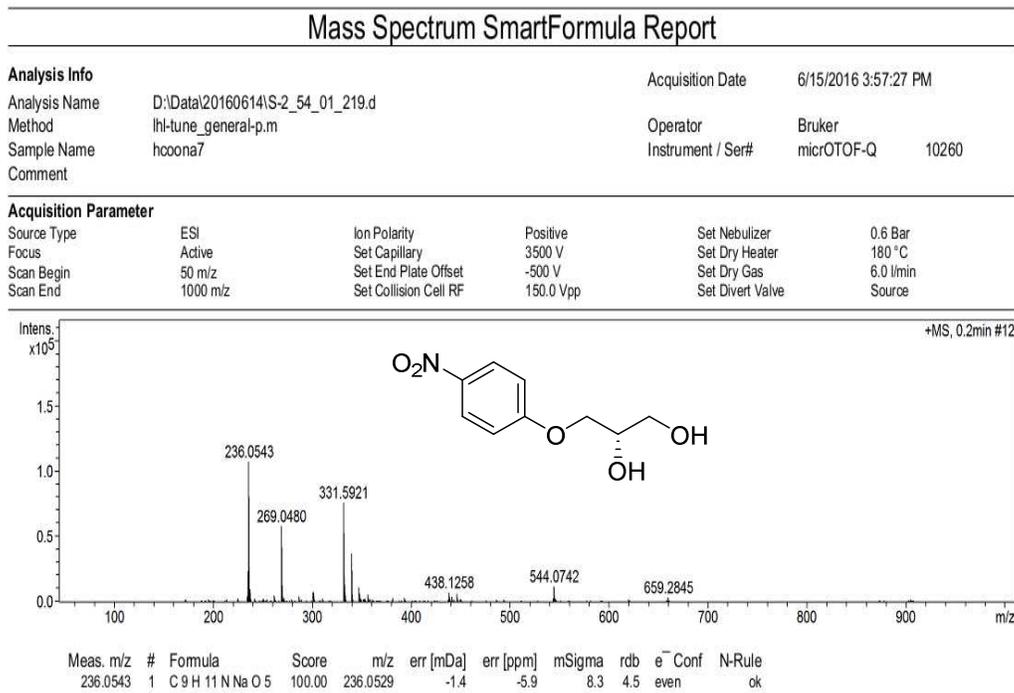
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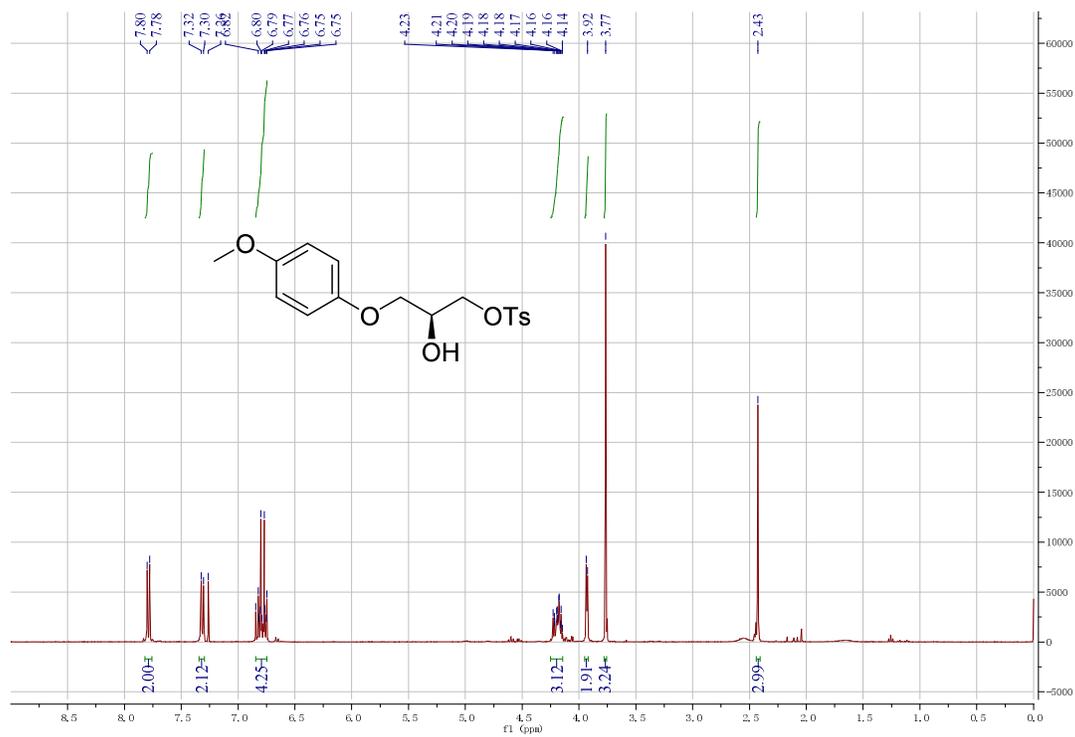
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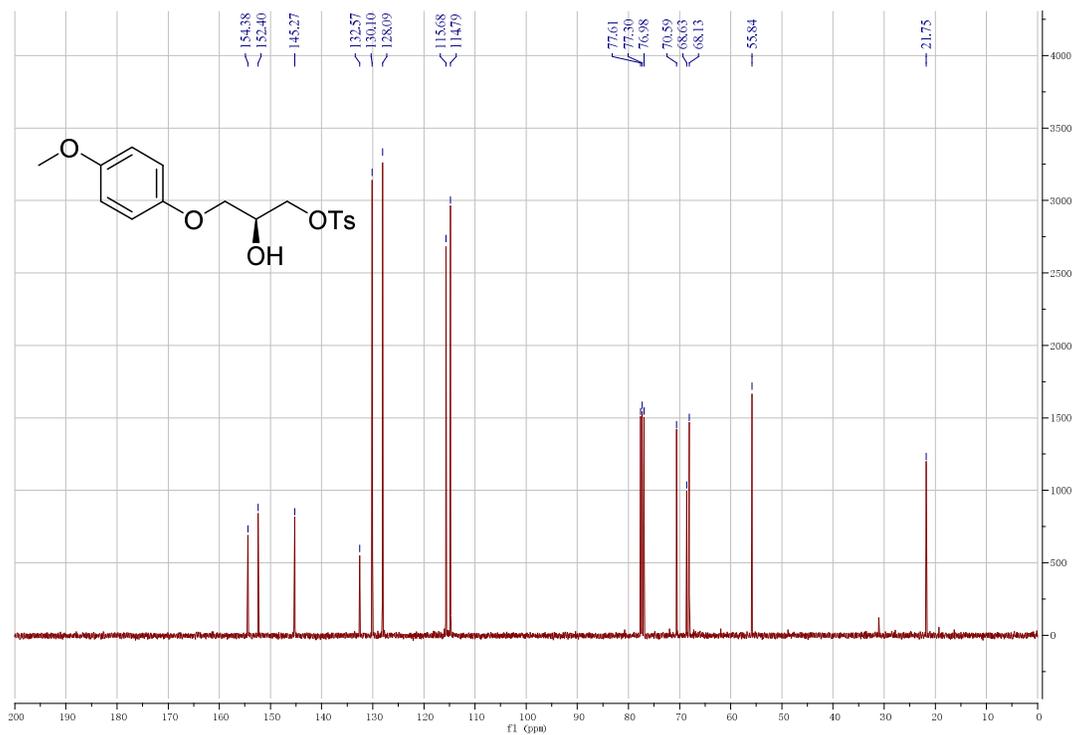
HRMS for compound (S)-2



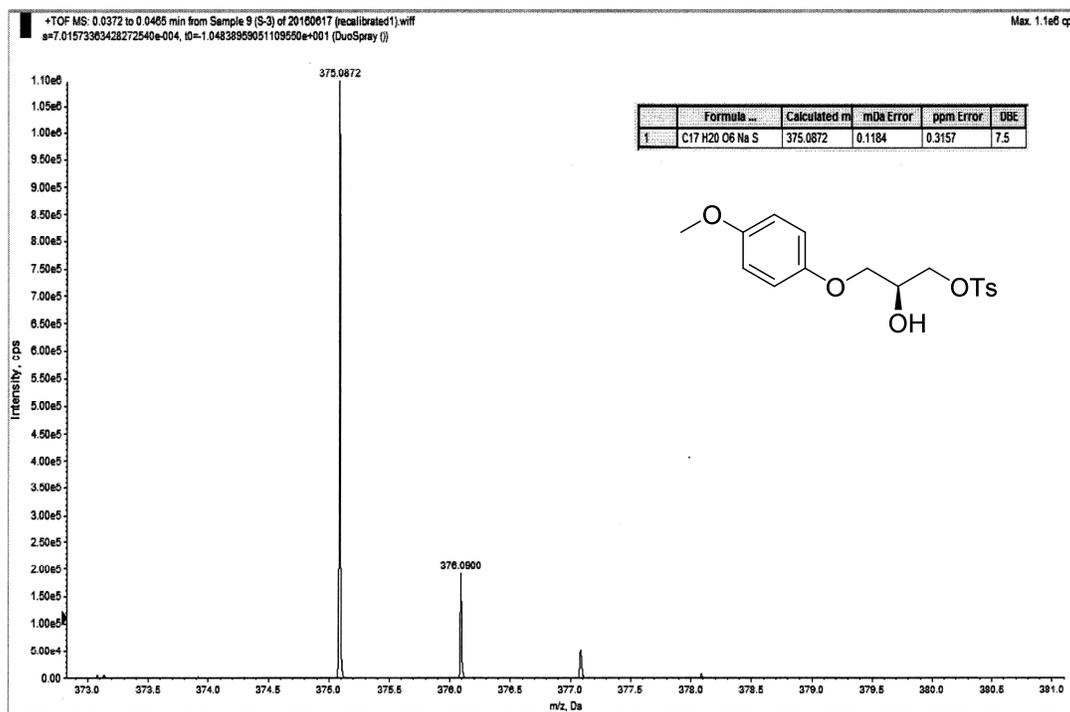
¹H-NMR for compound (S)-3



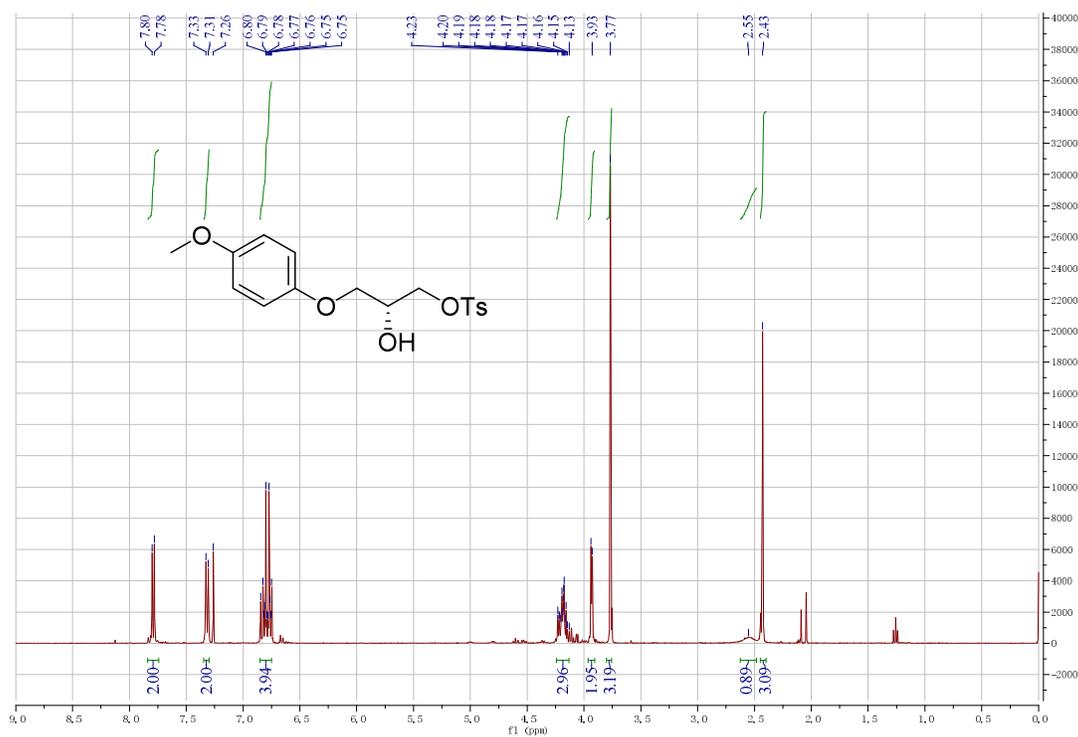
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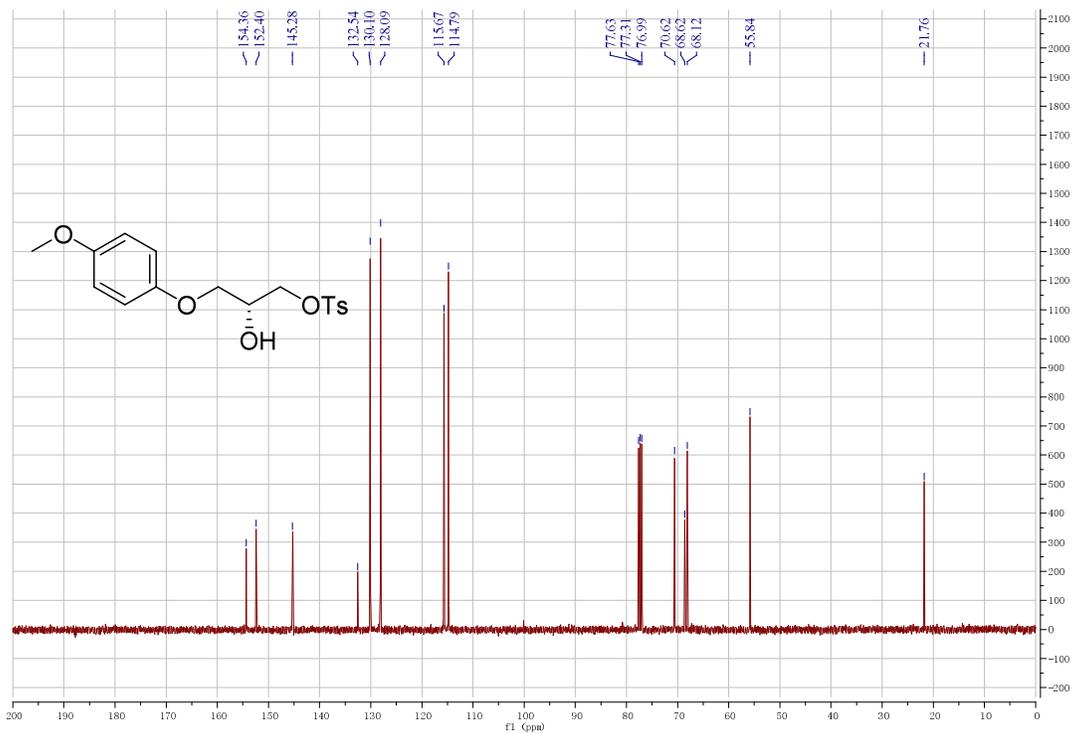
HRMS for compound (S)-3



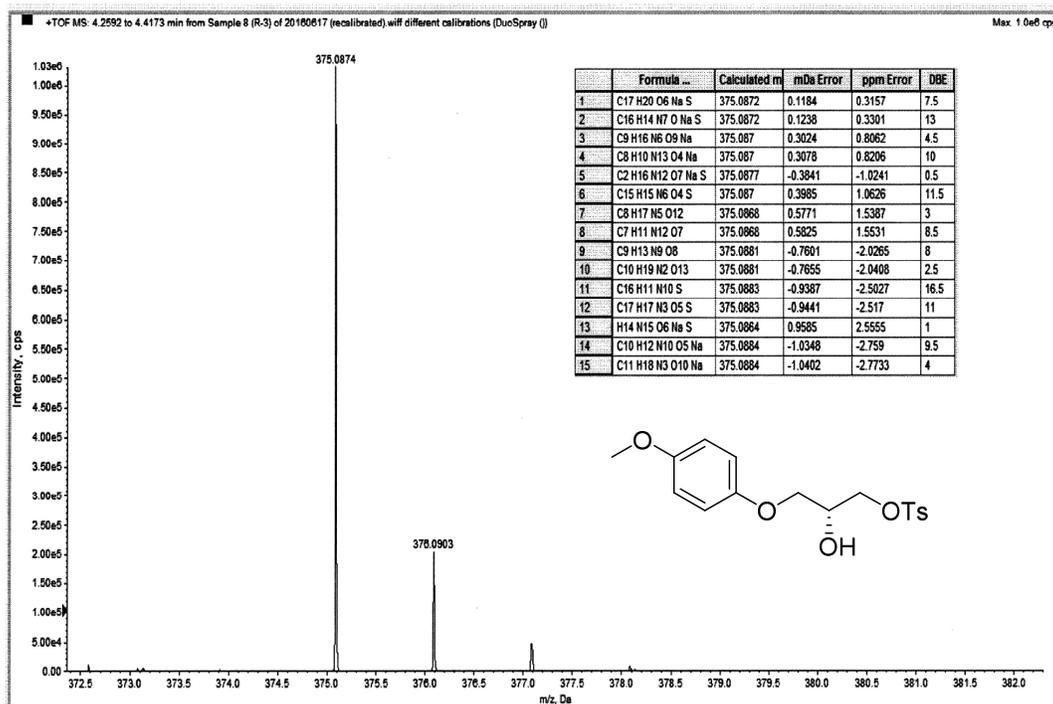
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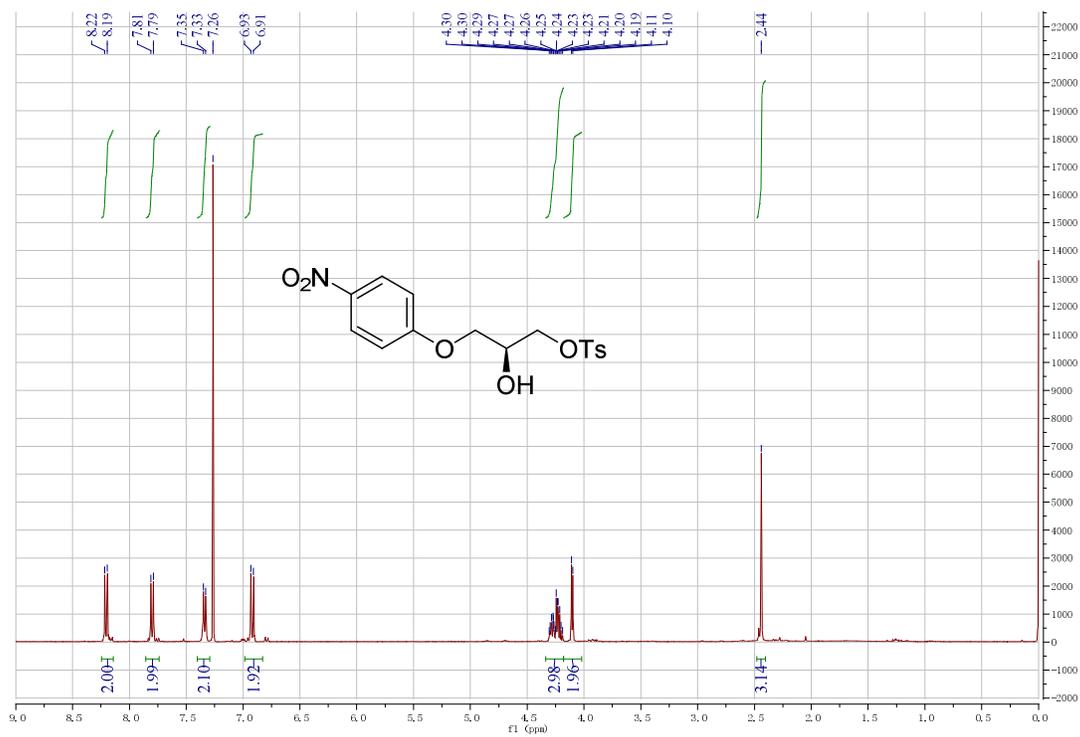
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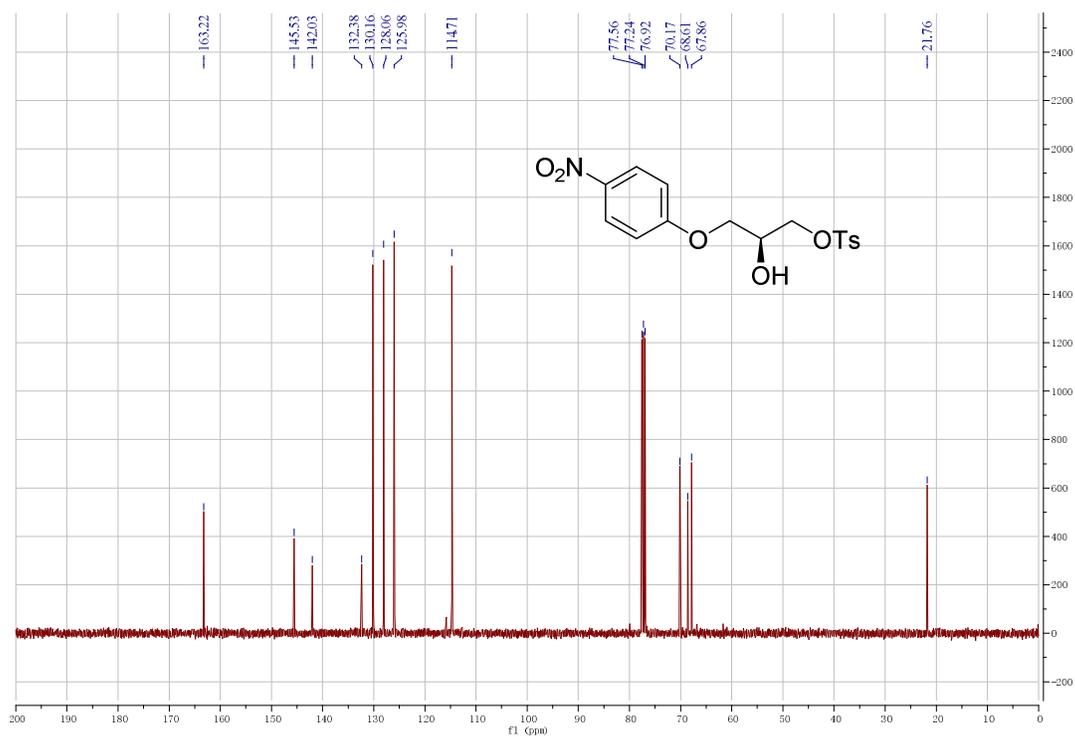
HRMS for compound (R)-3



$^1\text{H-NMR}$ for compound (*S*)-4



$^{13}\text{C-NMR}$ for compound (*S*)-4



HRMS for compound (S)-4

Mass Spectrum SmartFormula Report

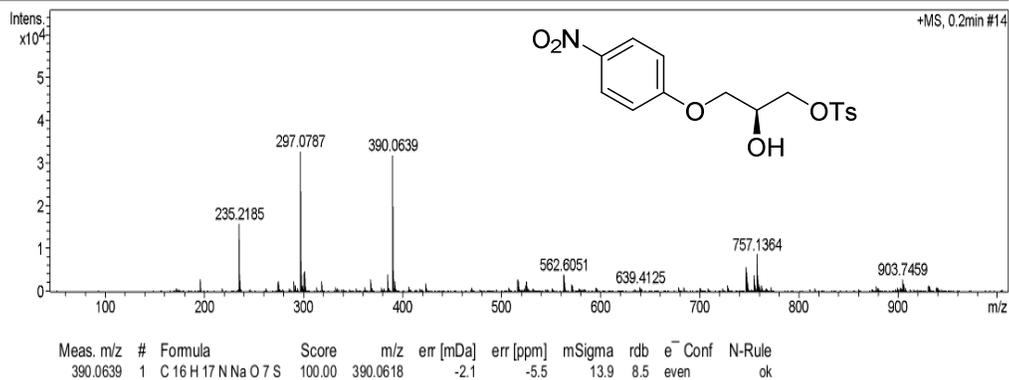
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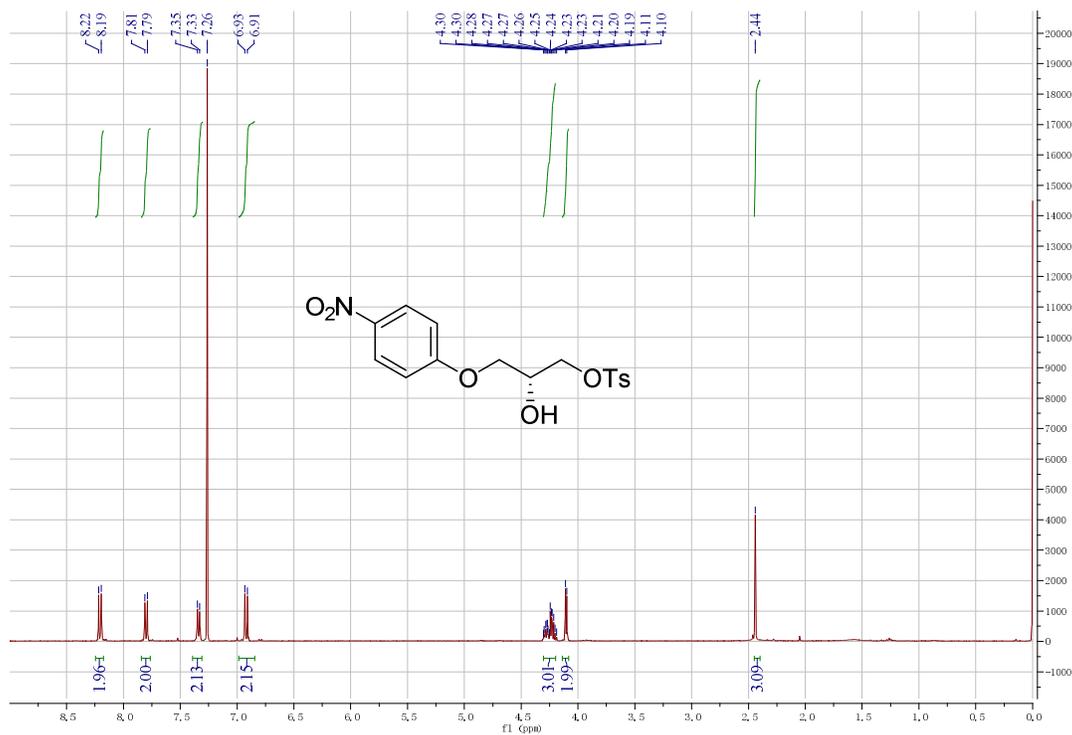
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 Instrument / Ser# micrOTOF-Q 10260

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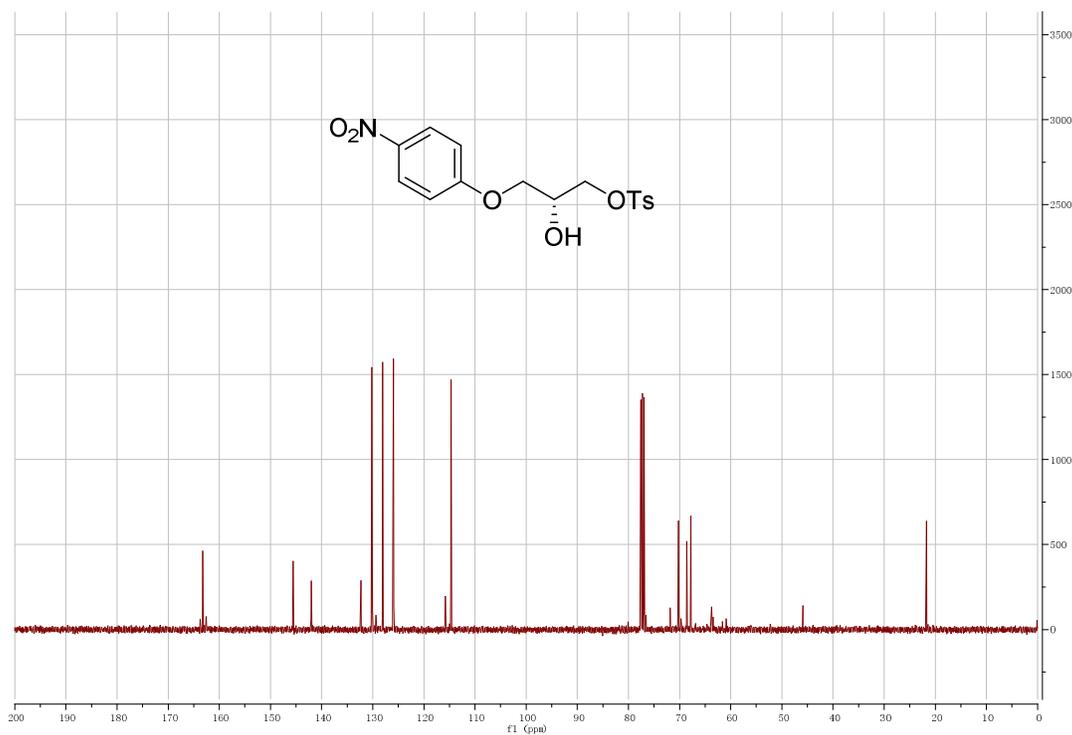
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 Scan End 1000 m/z Set Collision Cell RF 150.0 Vpp Set Divert Valve Source



¹H-NMR for compound (R)-4



¹³C-NMR for compound (R)-4



HRMS for compound (R)-4

Mass Spectrum SmartFormula Report

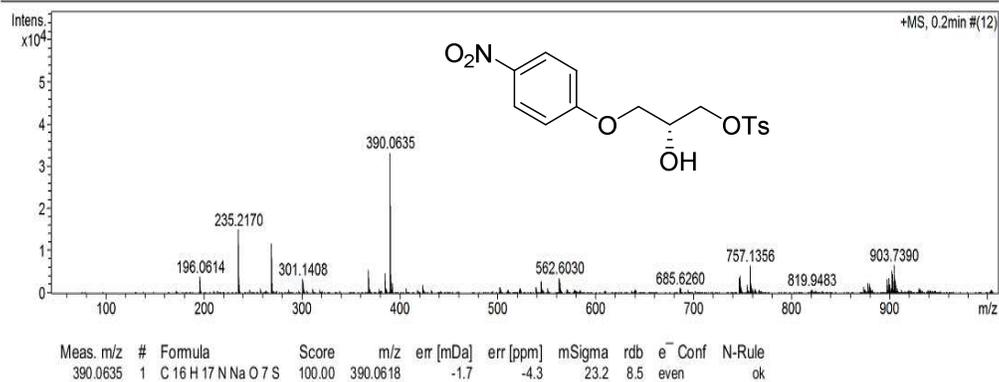
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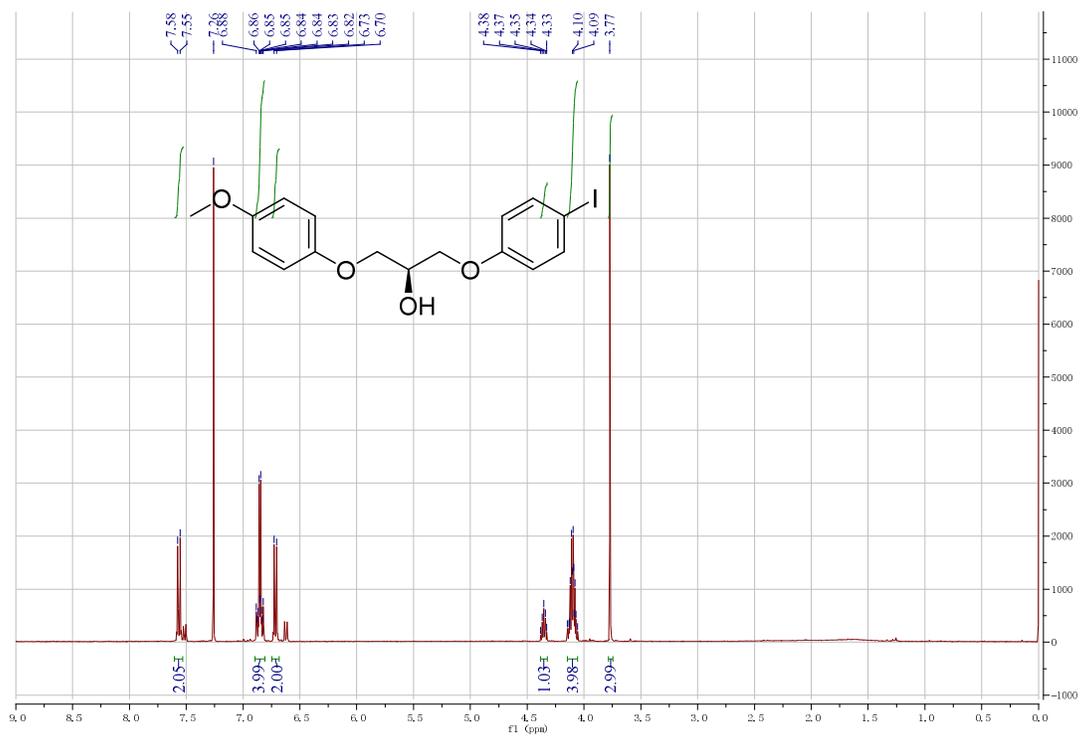
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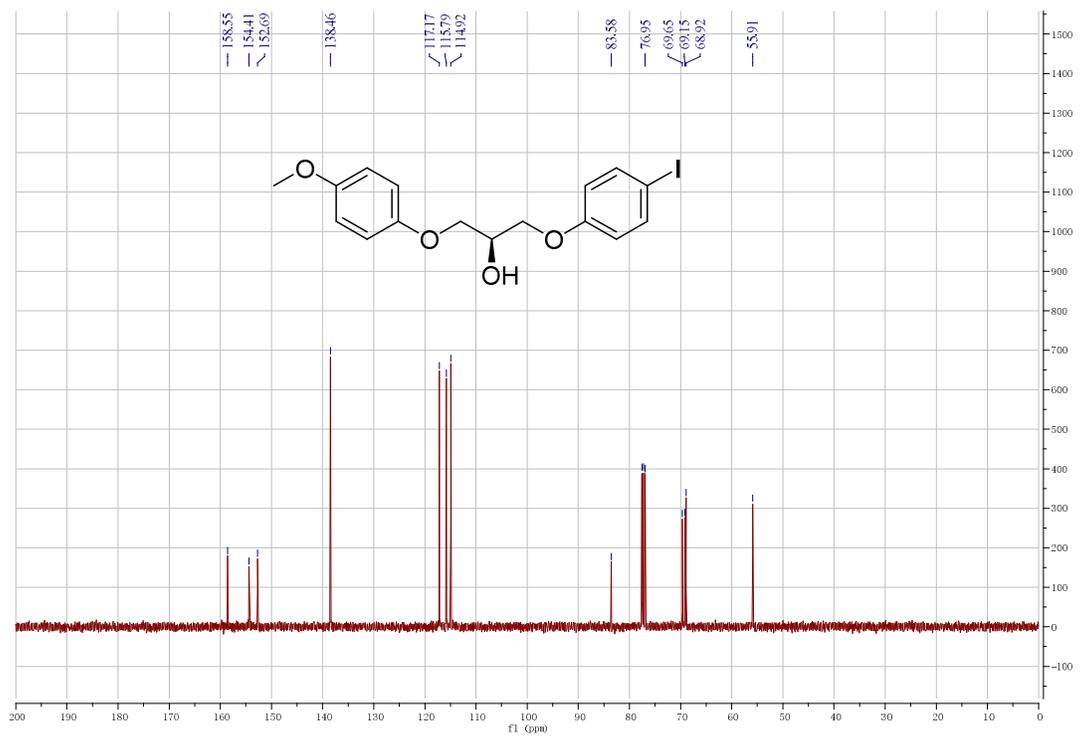
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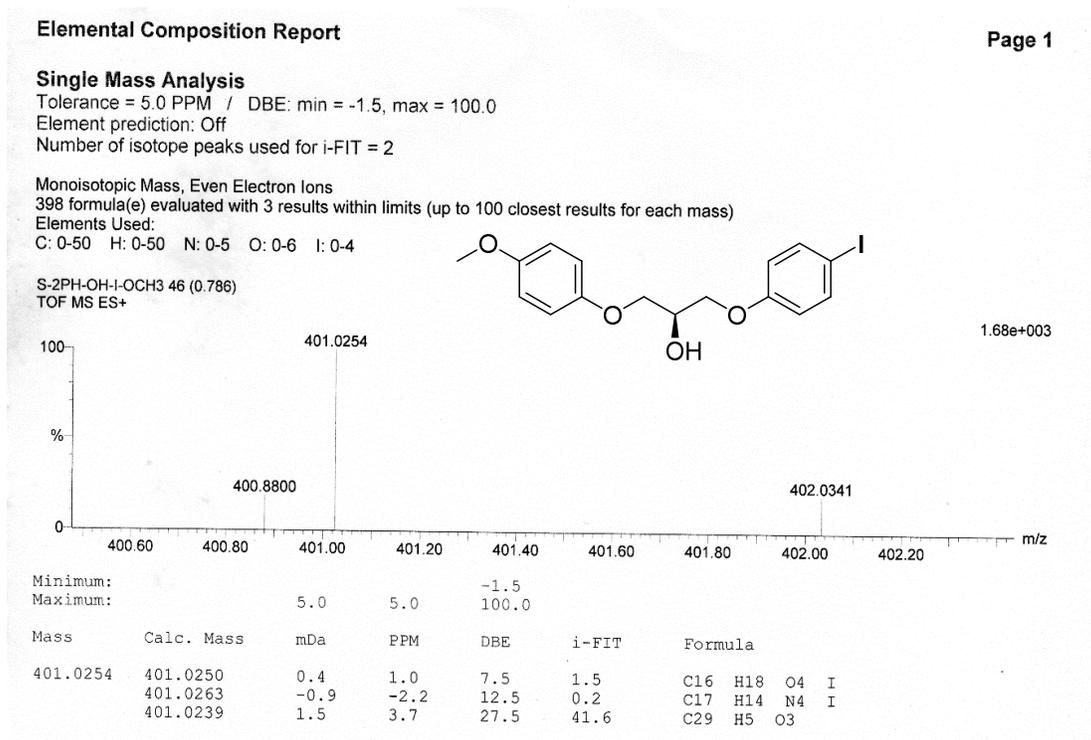
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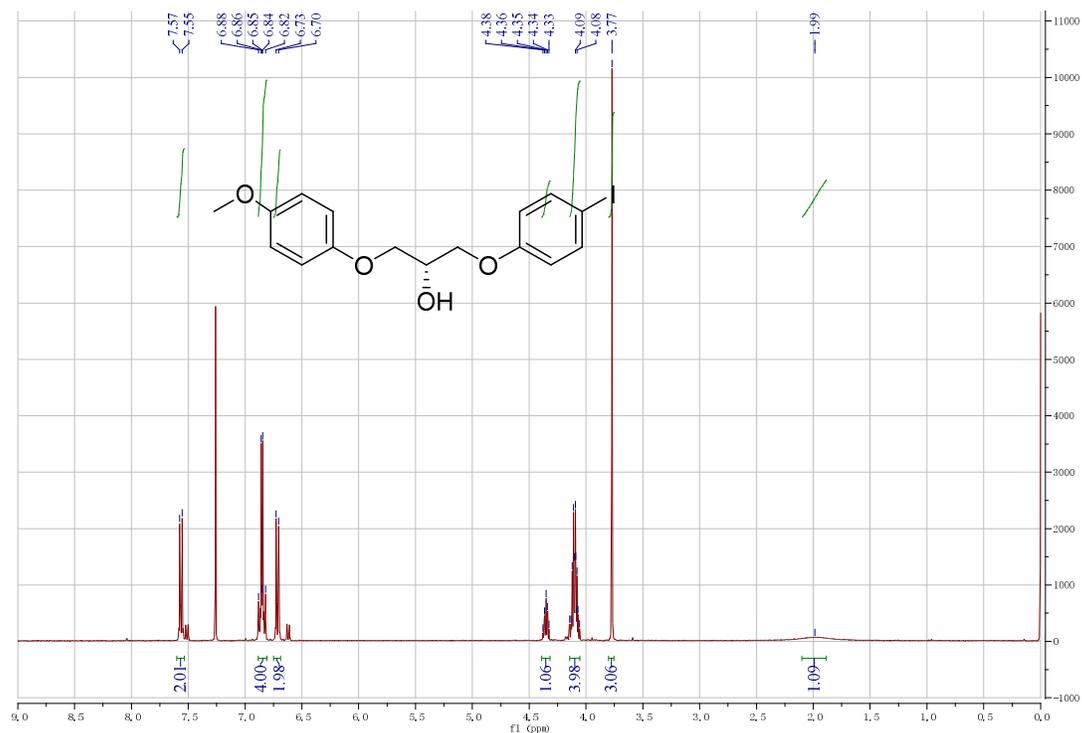
¹³C-NMR for compound (S)-5



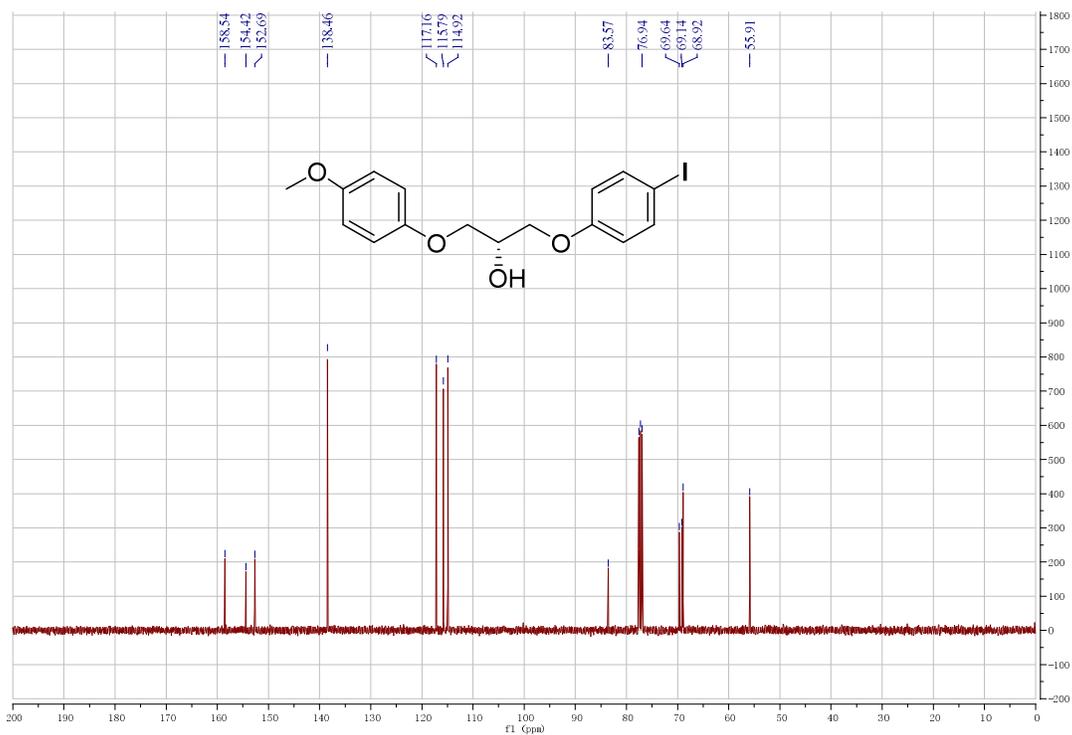
HRMS for compound (S)-5



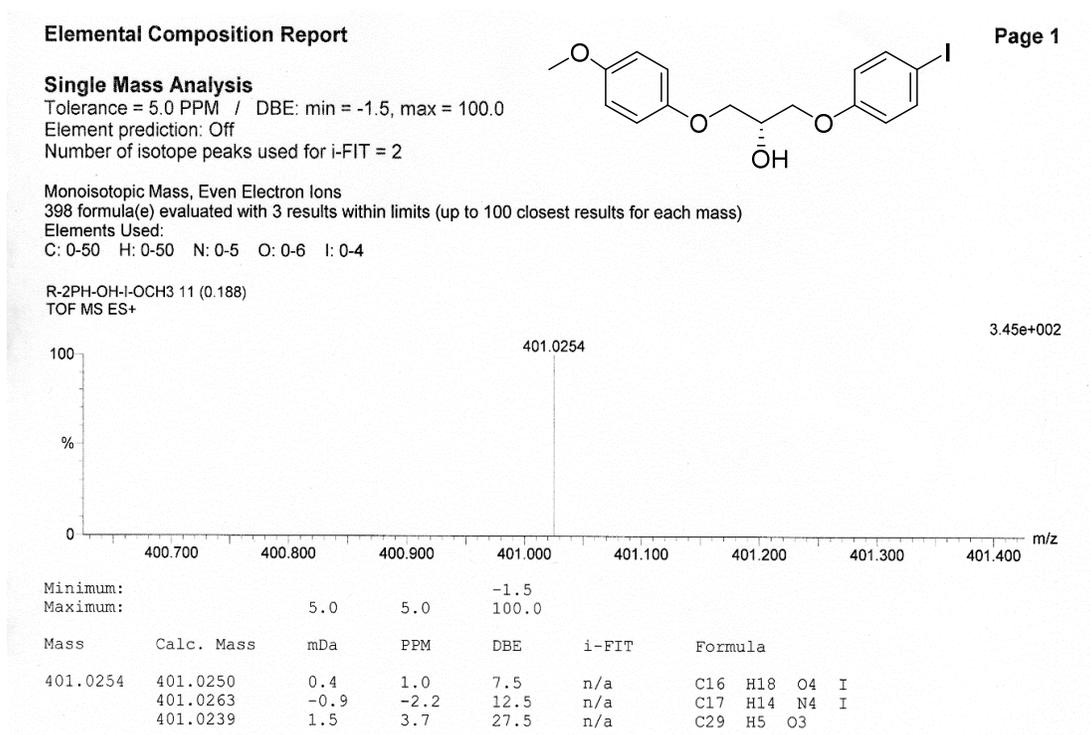
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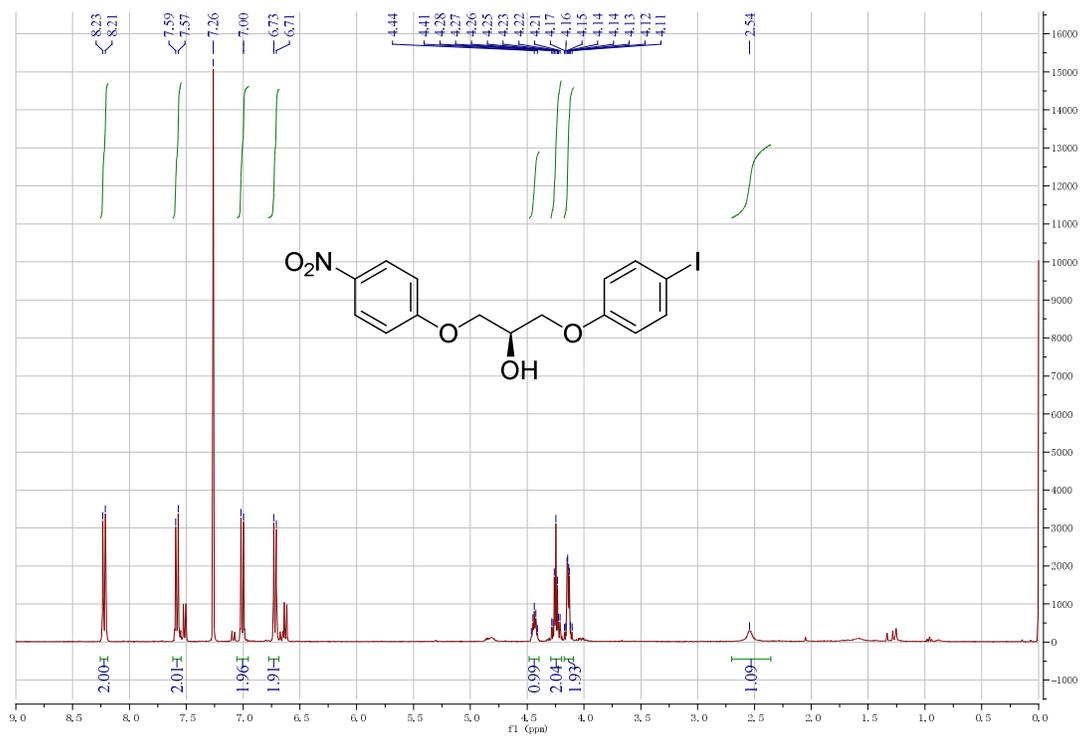
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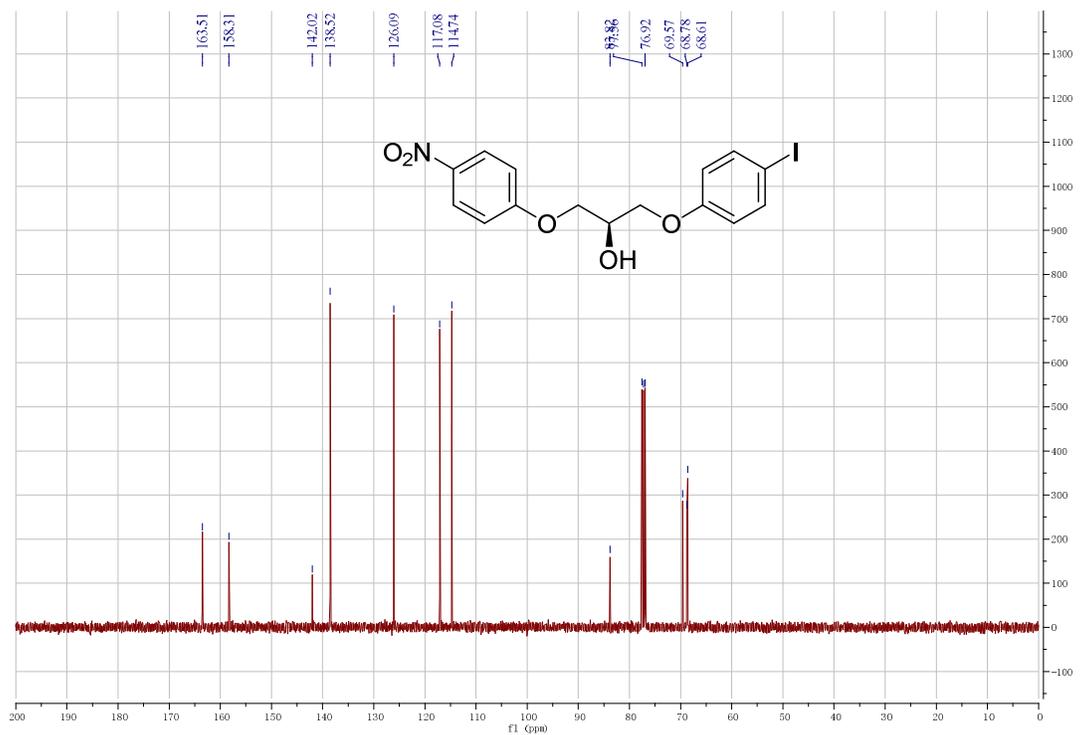
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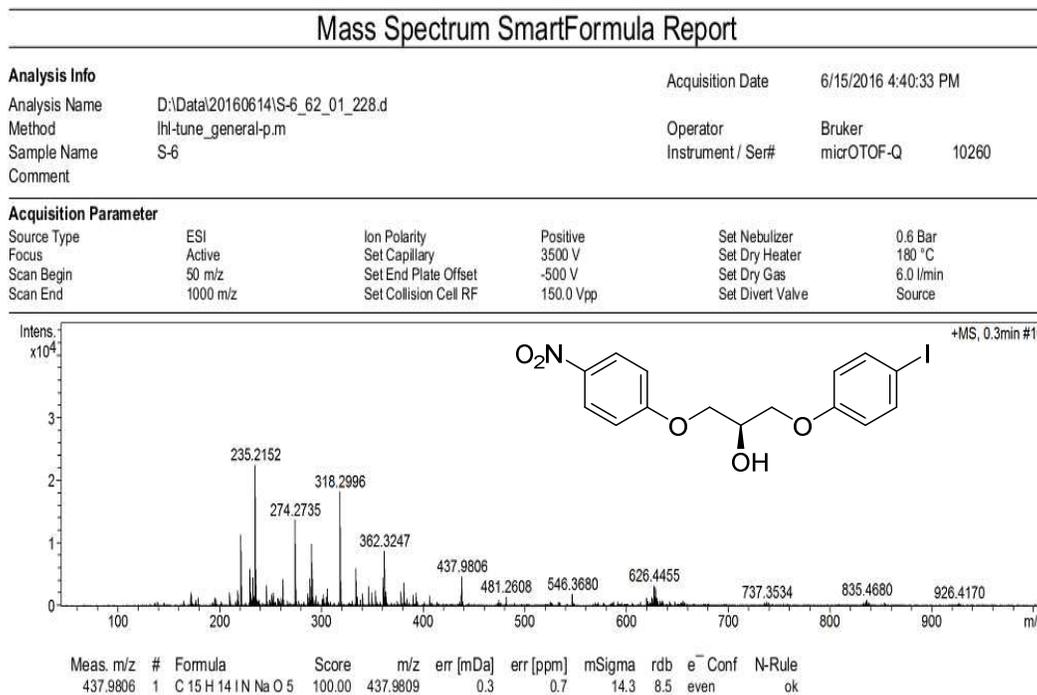
$^1\text{H-NMR}$ for compound (*S*)-6



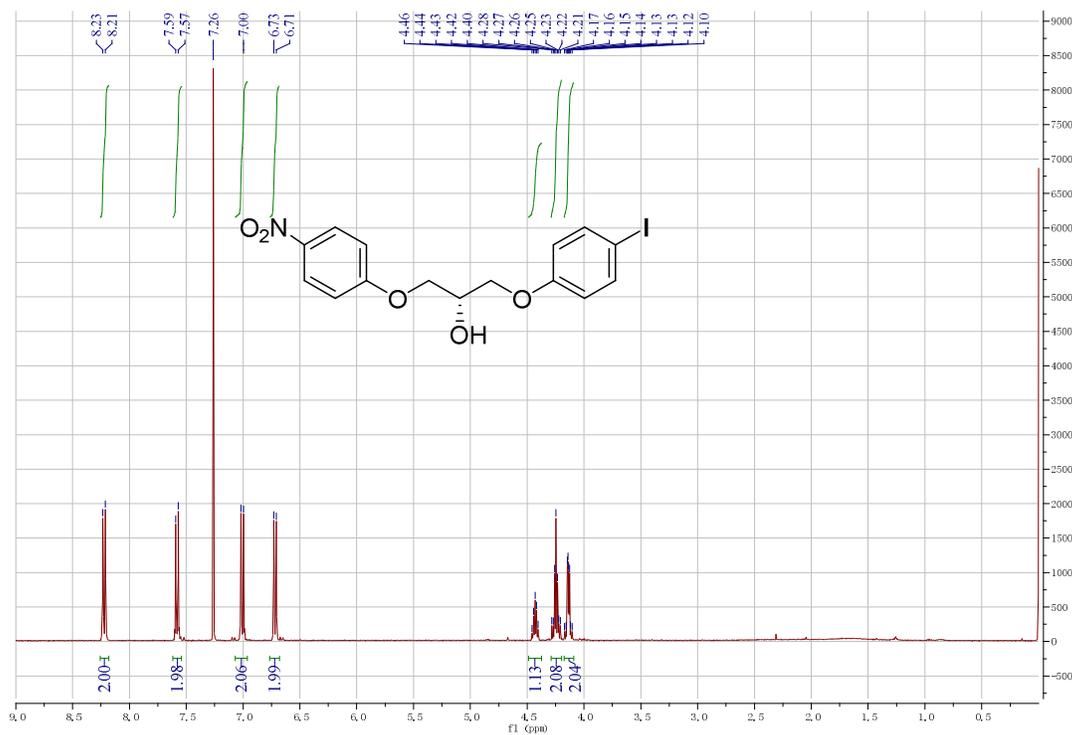
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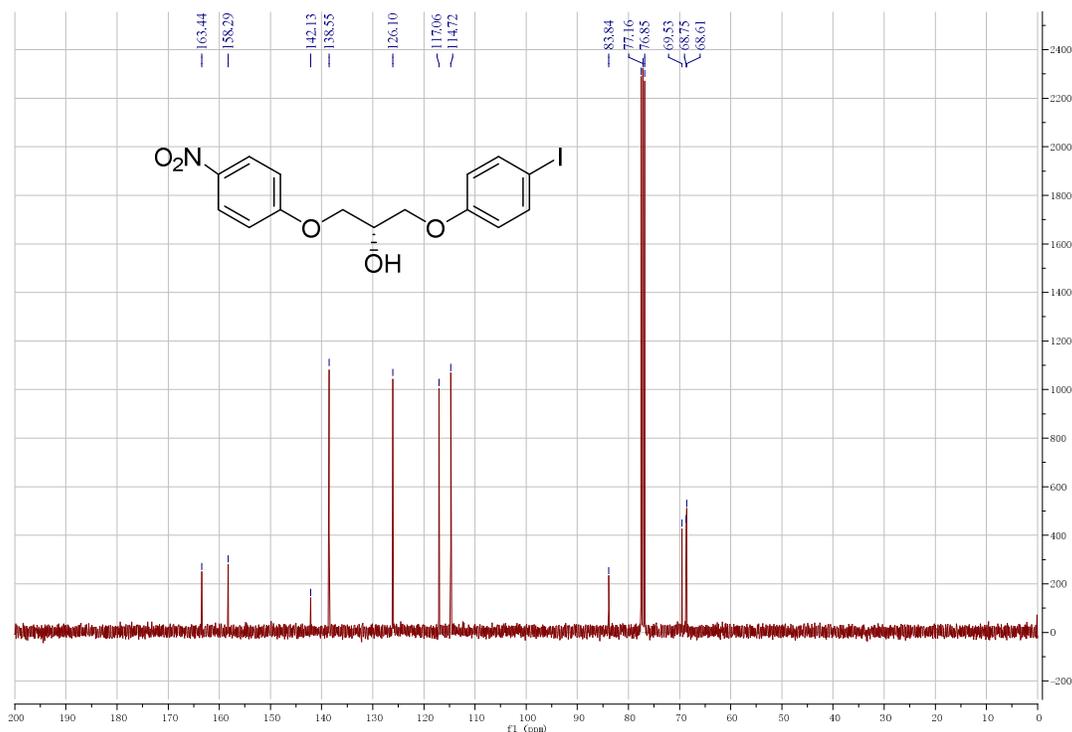
HRMS for compound (S)-6



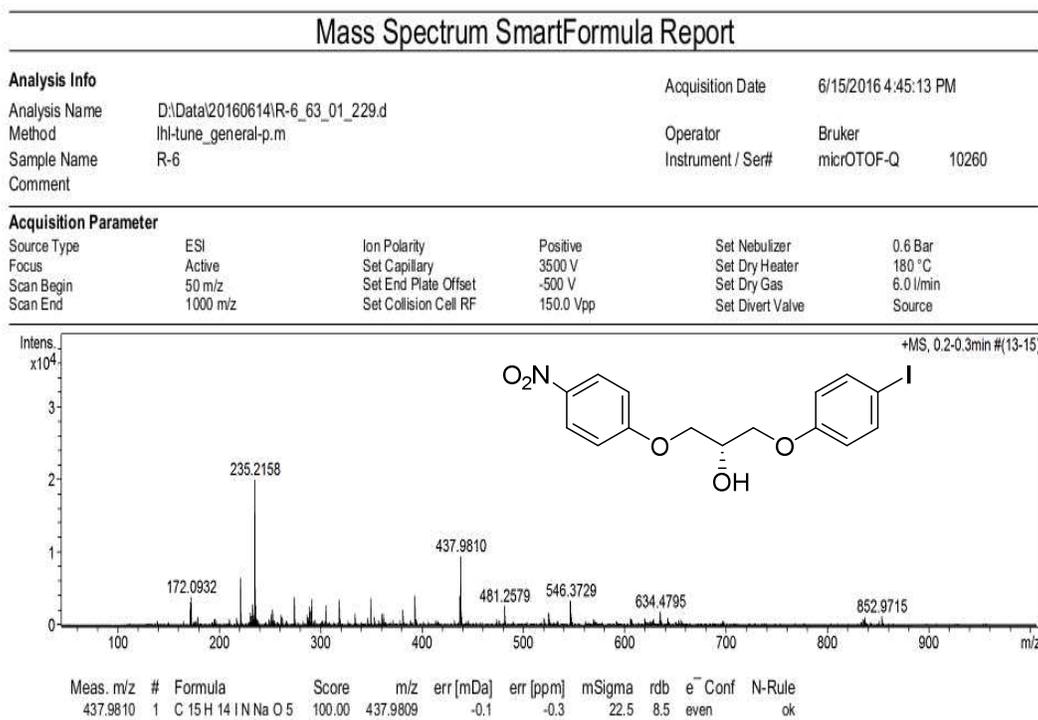
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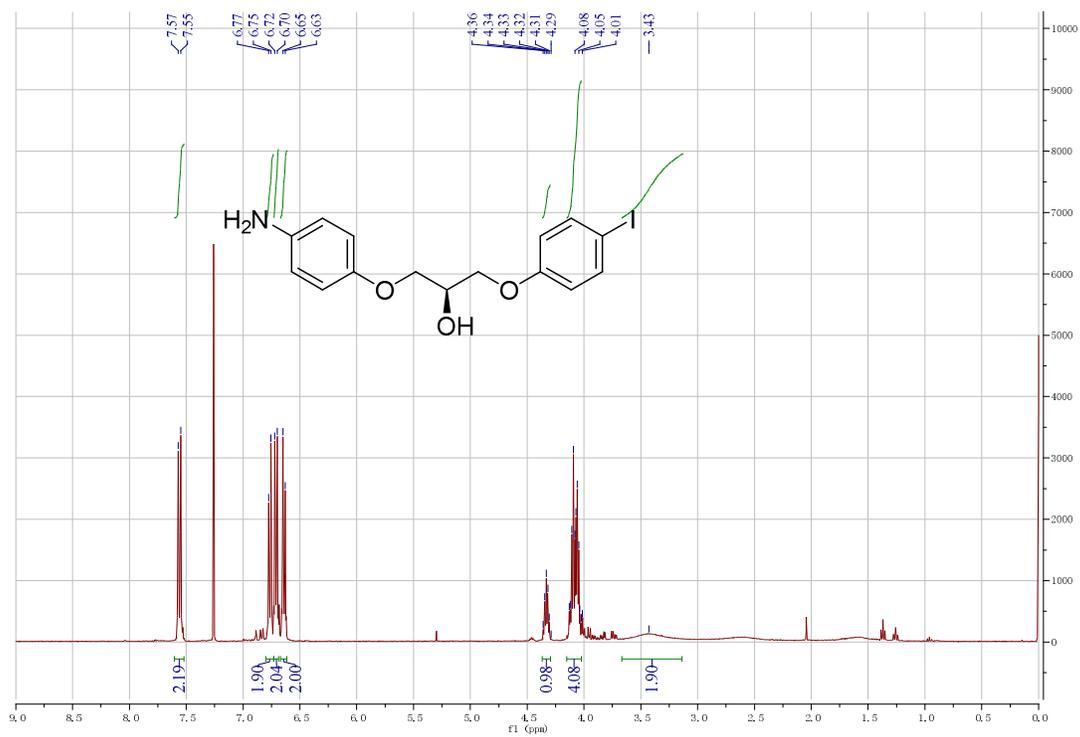
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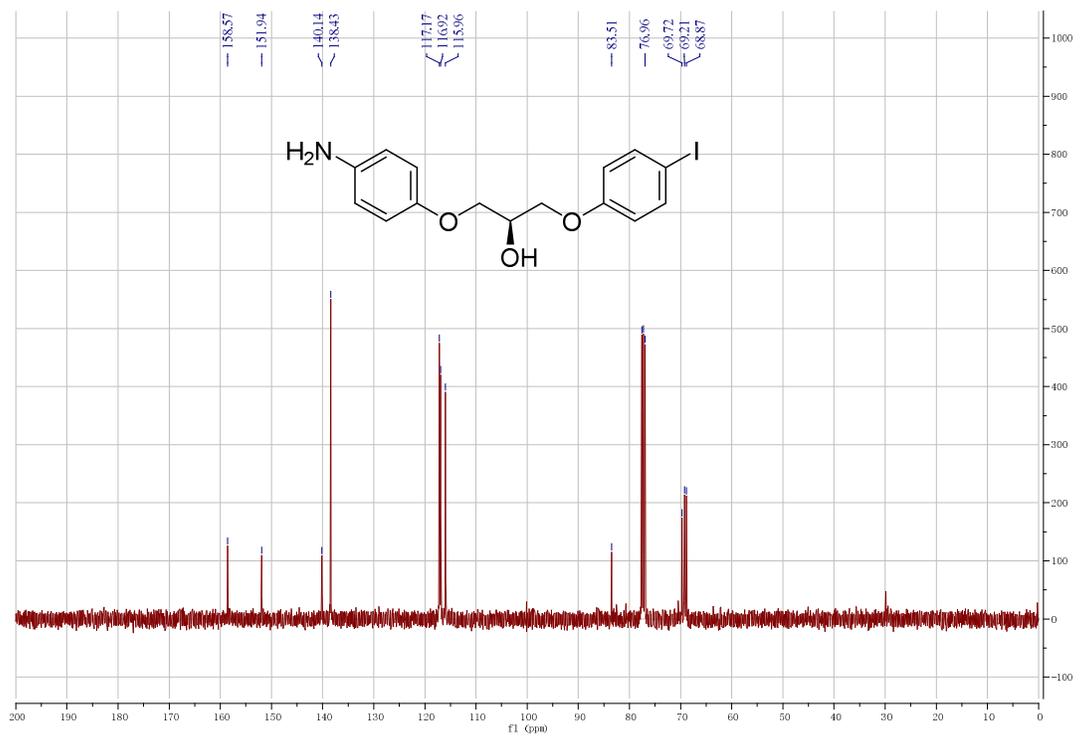
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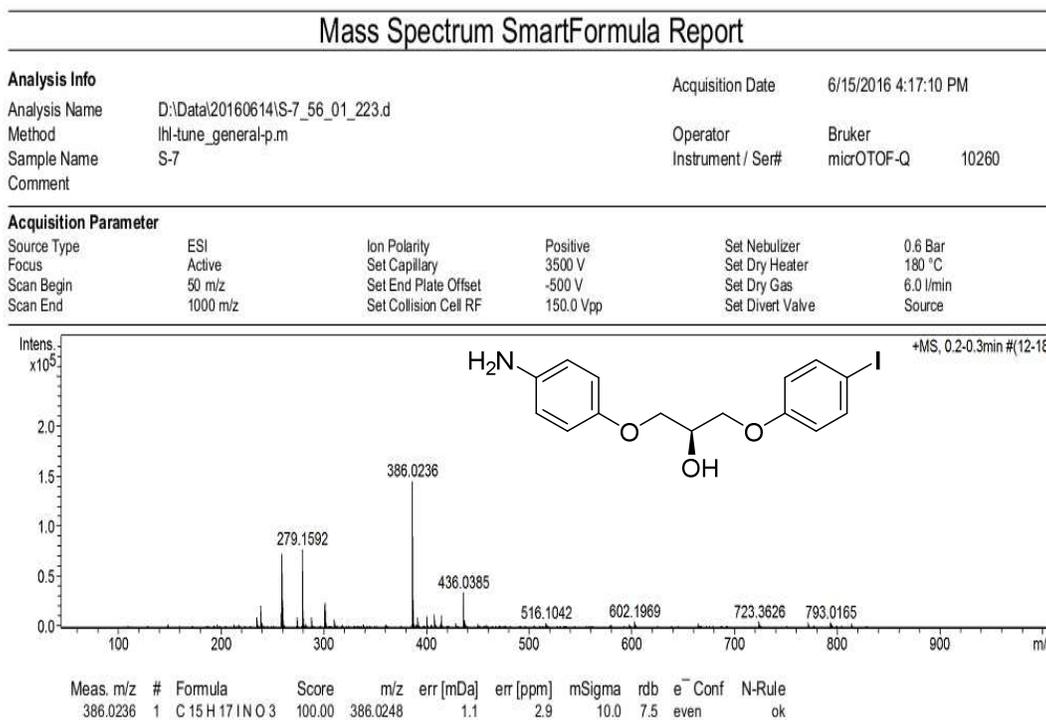
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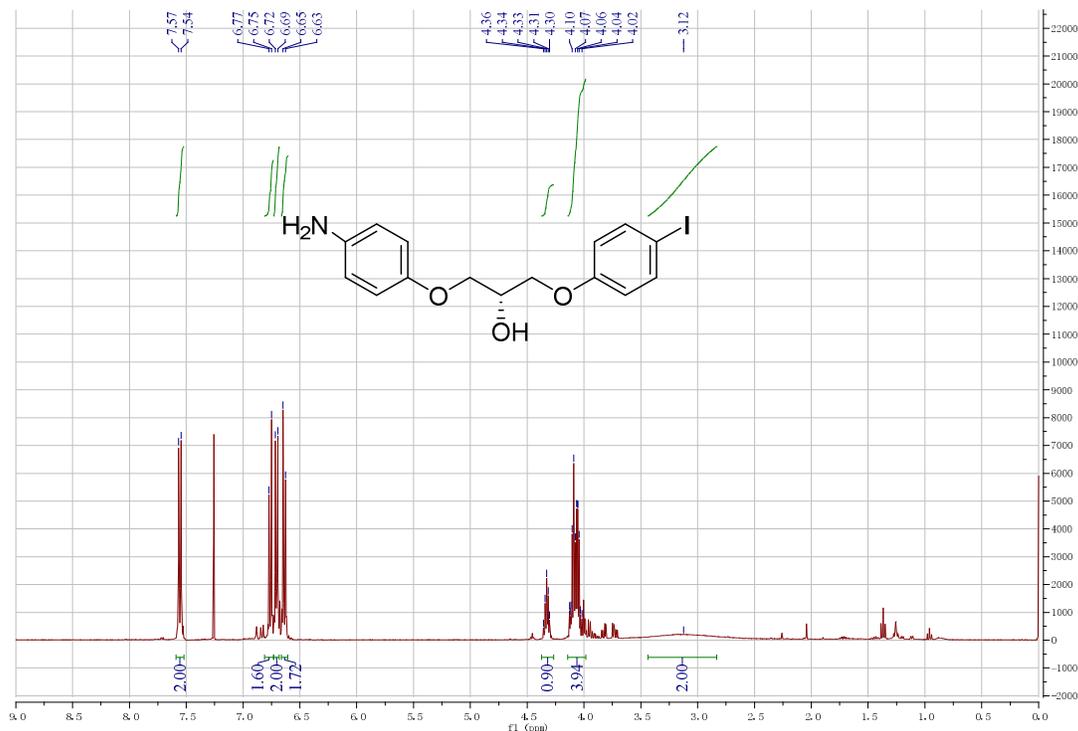
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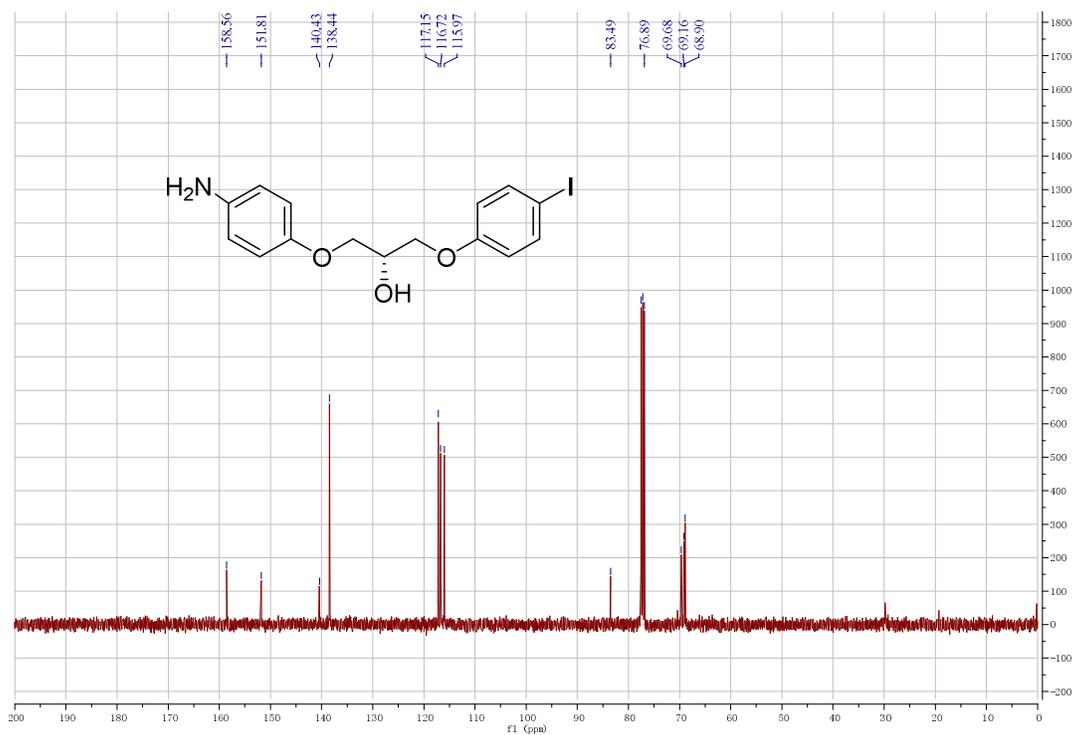
HRMS for compound (S)-7



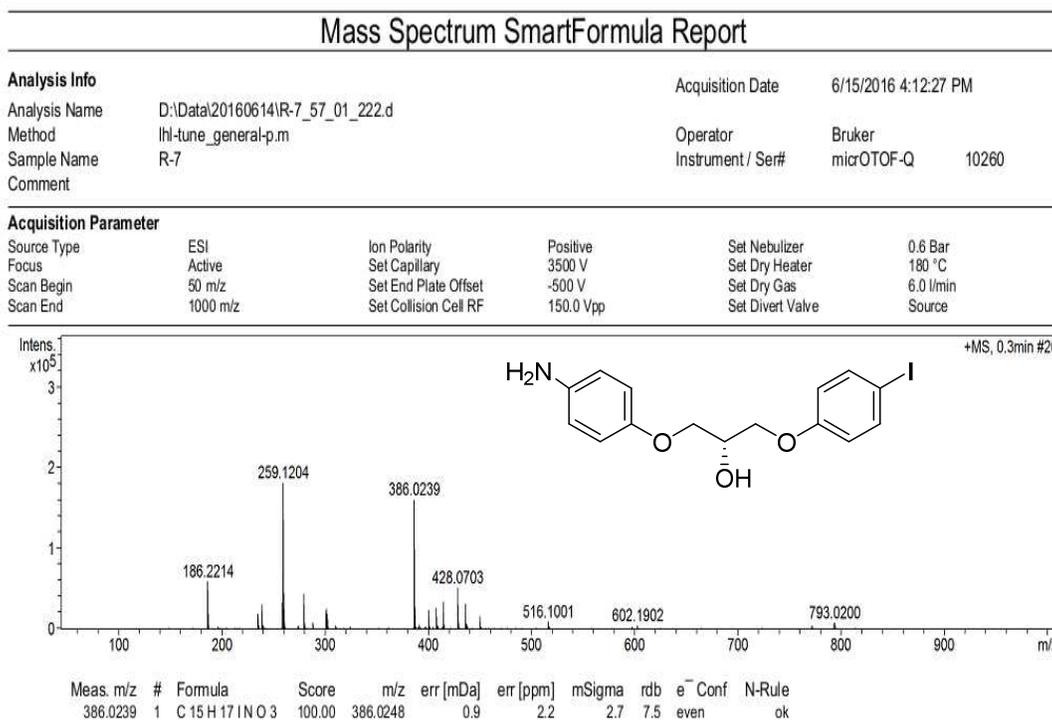
¹H-NMR for compound (R)-7



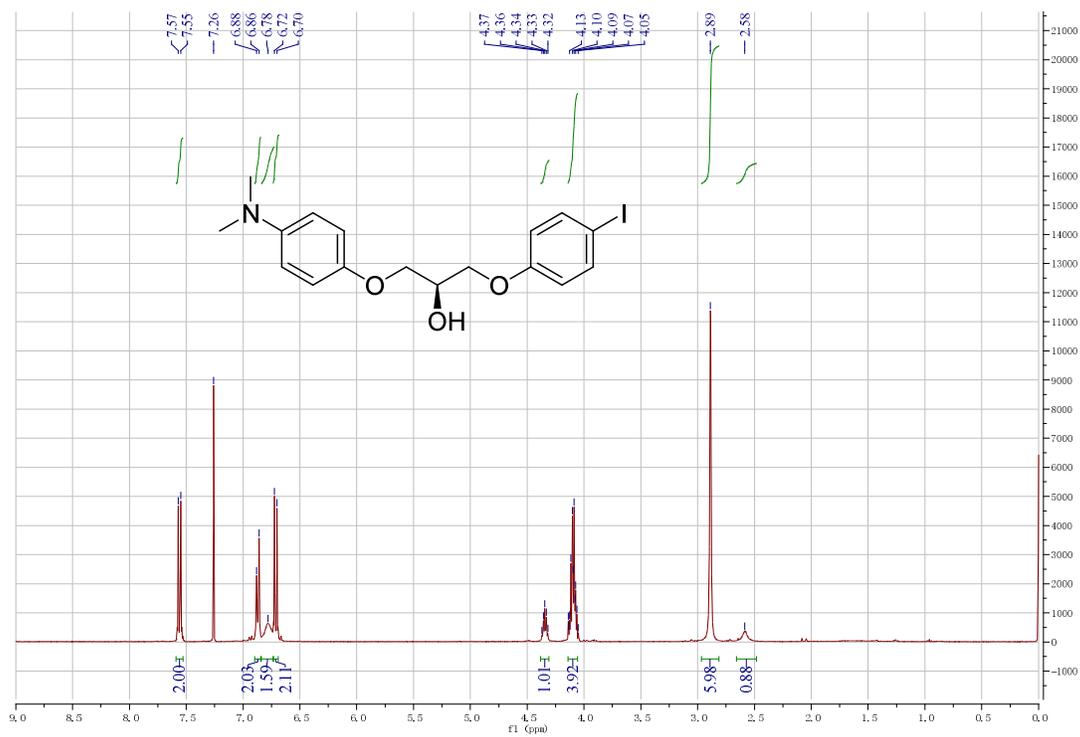
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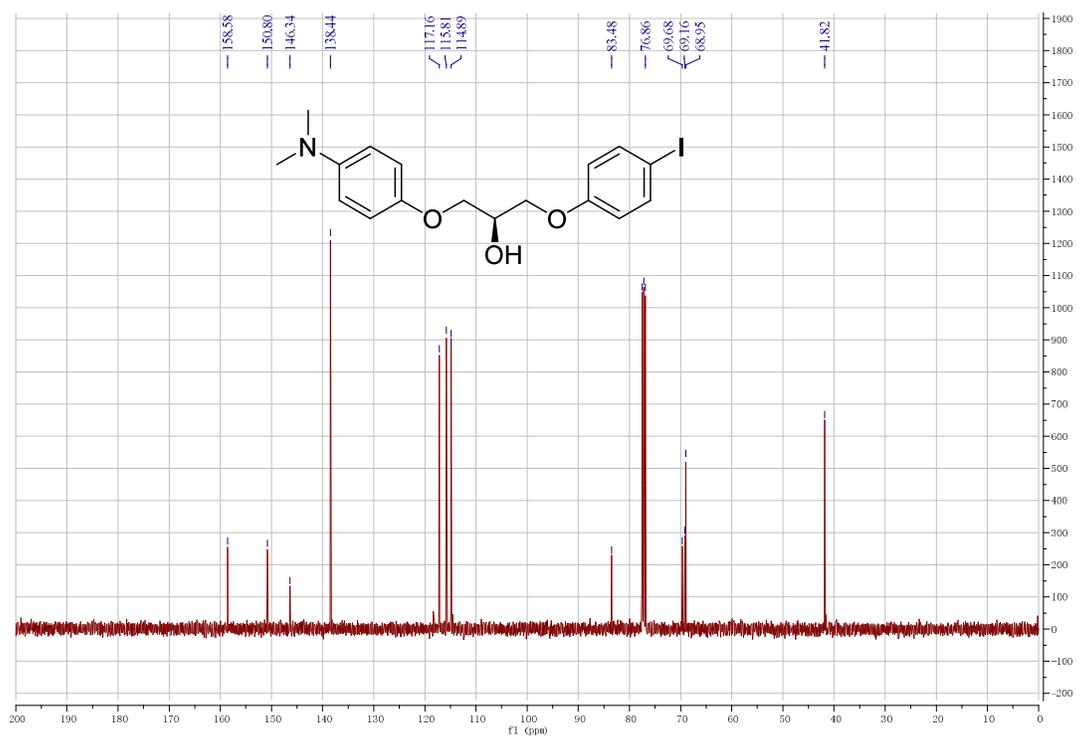
HRMS for compound (R)-7



$^1\text{H-NMR}$ for compound (*S*)-**8**



$^{13}\text{C-NMR}$ for compound (*S*)-**8**



HRMS for compound (S)-8

Elemental Composition Report

Single Mass Analysis

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 Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

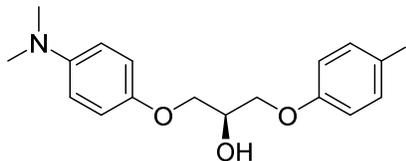
612 formula(e) evaluated with 3 results within limits (up to 100 closest results for each mass)

Elements Used:

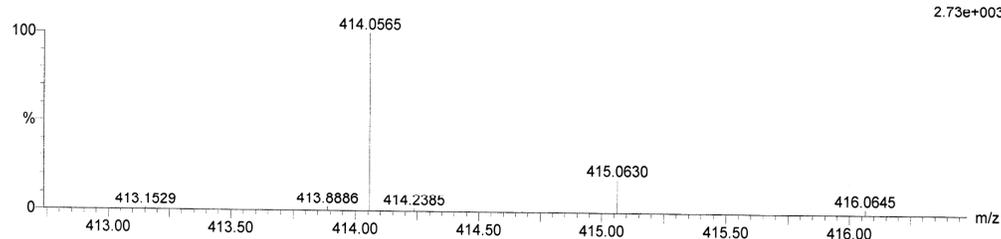
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ZPH-S-OH-NME2-I 17 (0.290)

TOF MS AP+



Page 1



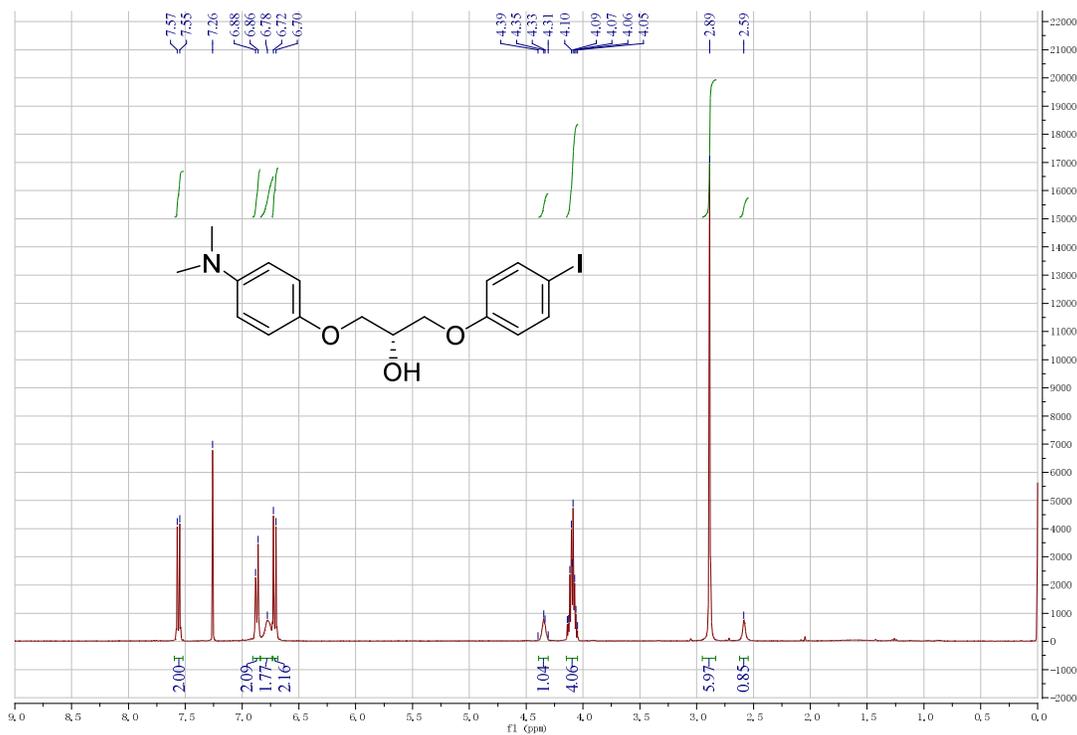
2.73e+003

Minimum:

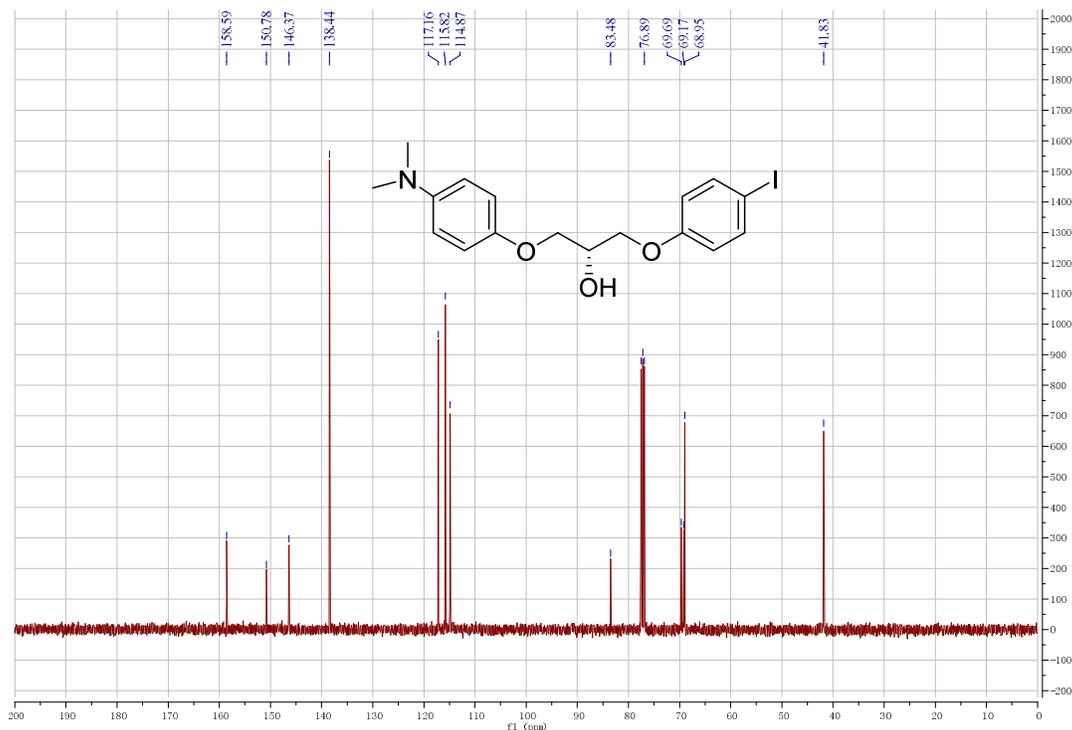
Maximum: 5.0 3.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
414.0565	414.0566	-0.1	-0.2	7.5	0.8	C17 H21 N O3 I
	414.0574	-0.9	-2.2	14.5	5.5	C18 H12 N3 O9
	414.0555	1.0	2.4	27.5	106.7	C30 H8 N O2

¹H-NMR for compound (R)-8



¹³C-NMR for compound (R)-8



HRMS for compound (R)-8

Elemental Composition Report

Single Mass Analysis

Tolerance = 3.0 PPM / DBE: min = -1.5, max = 100.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

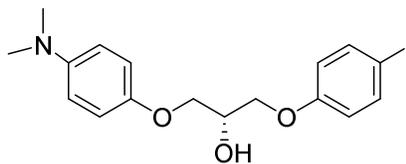
612 formula(e) evaluated with 3 results within limits (up to 100 closest results for each mass)

Elements Used:

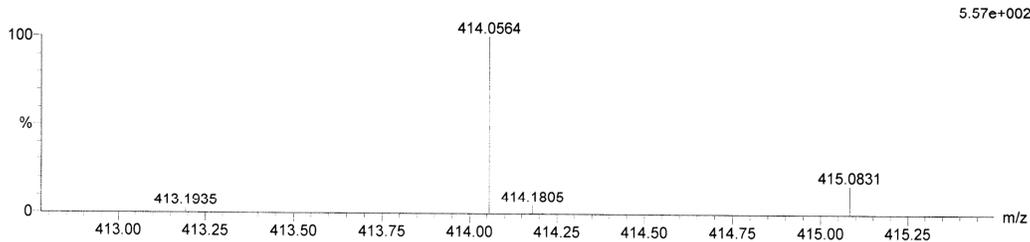
C: 0-50 H: 0-50 N: 0-5 O: 0-11 I: 0-4

2PH-R-OH-NME2-I 30 (0.513)

TOF MS AP+



Page 1



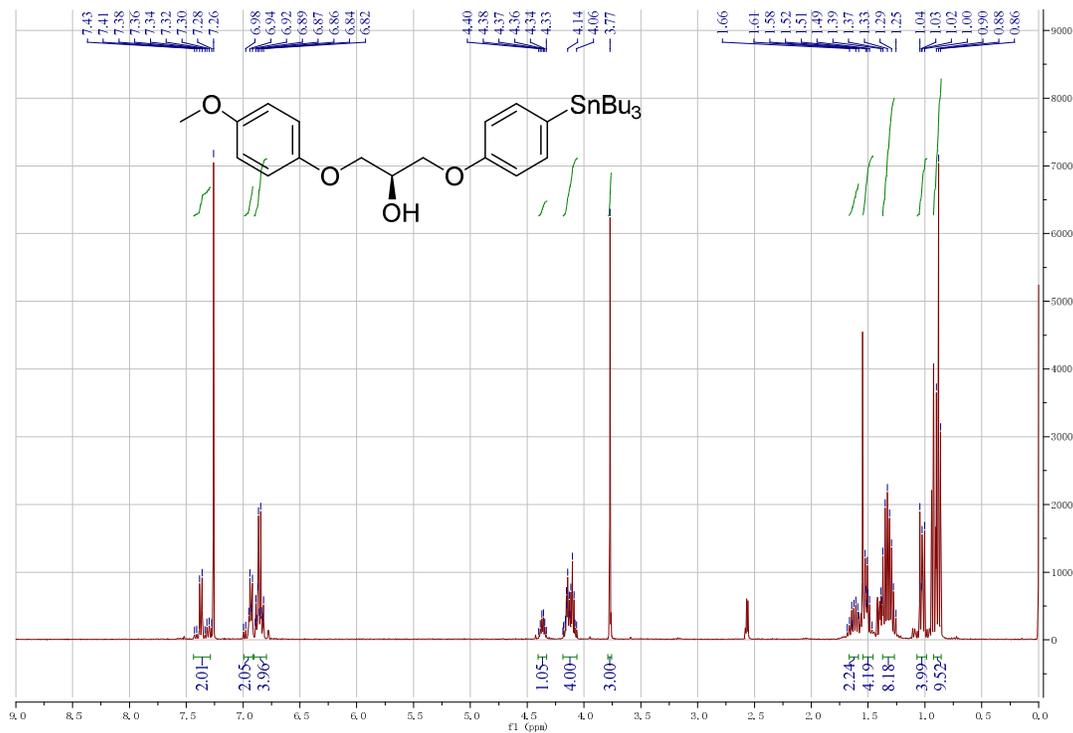
Minimum:

Maximum: 5.0 3.0 -1.5 100.0

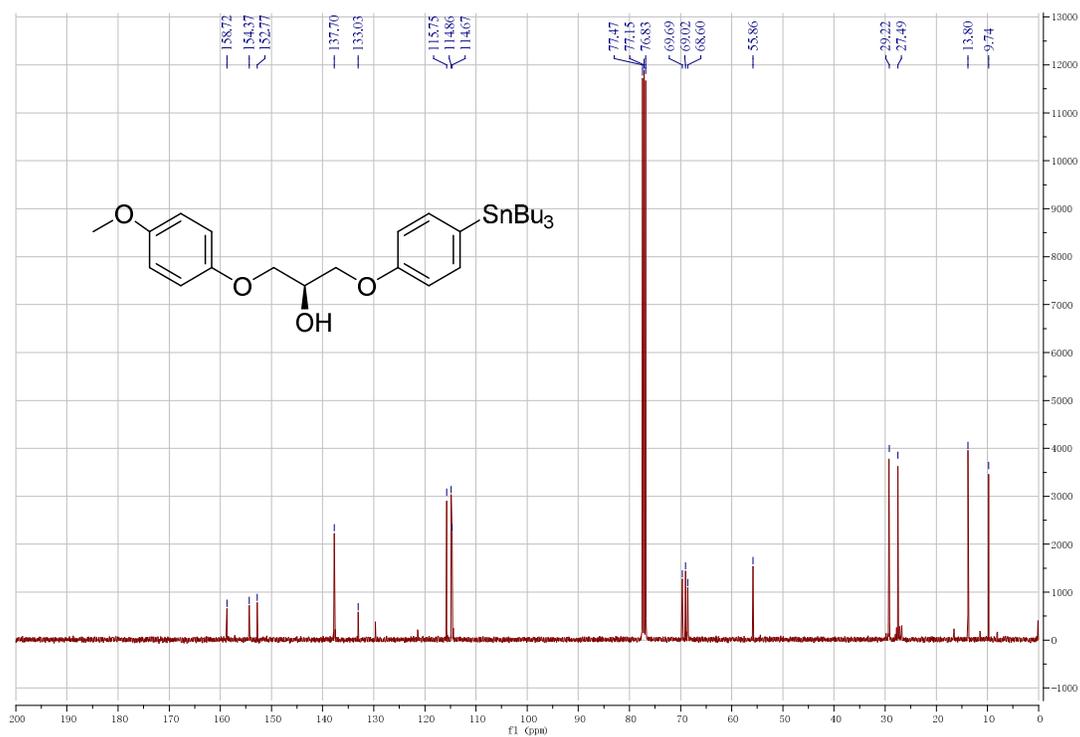
Mass Calc. Mass mDa PPM DBE i-FIT Formula

414.0564	414.0566	-0.2	-0.5	7.5	2.7	C17 H21 N O3 I ✓
	414.0555	0.9	2.2	27.5	n/a	C30 H8 N O2
	414.0574	-1.0	-2.4	14.5	n/a	C18 H12 N3 O9

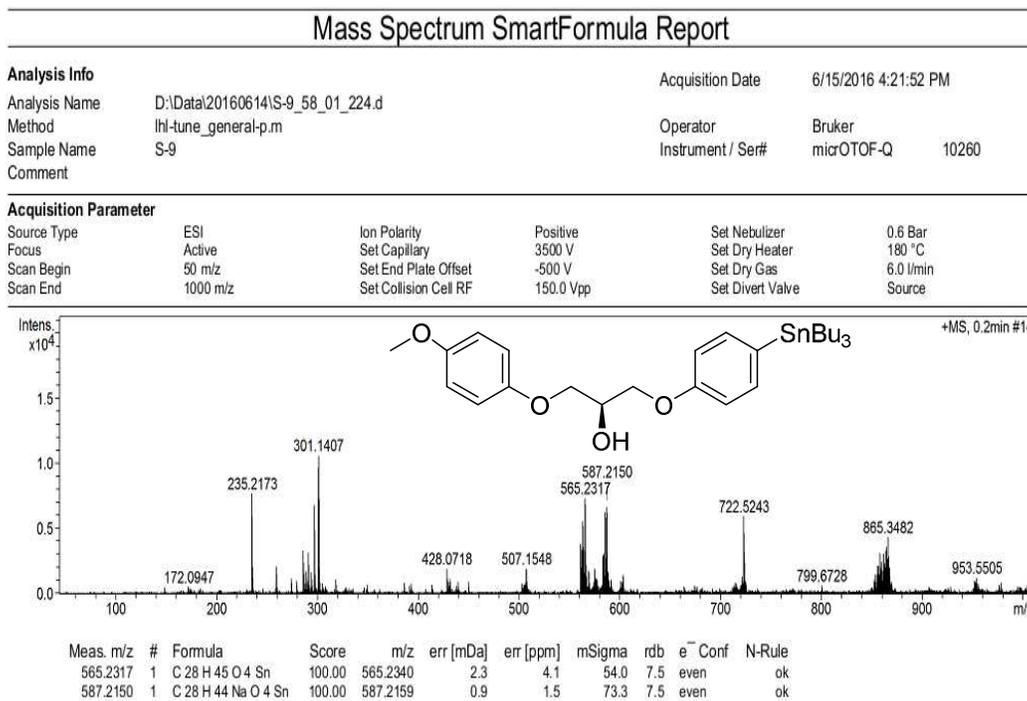
$^1\text{H-NMR}$ for compound (*S*)-**9**



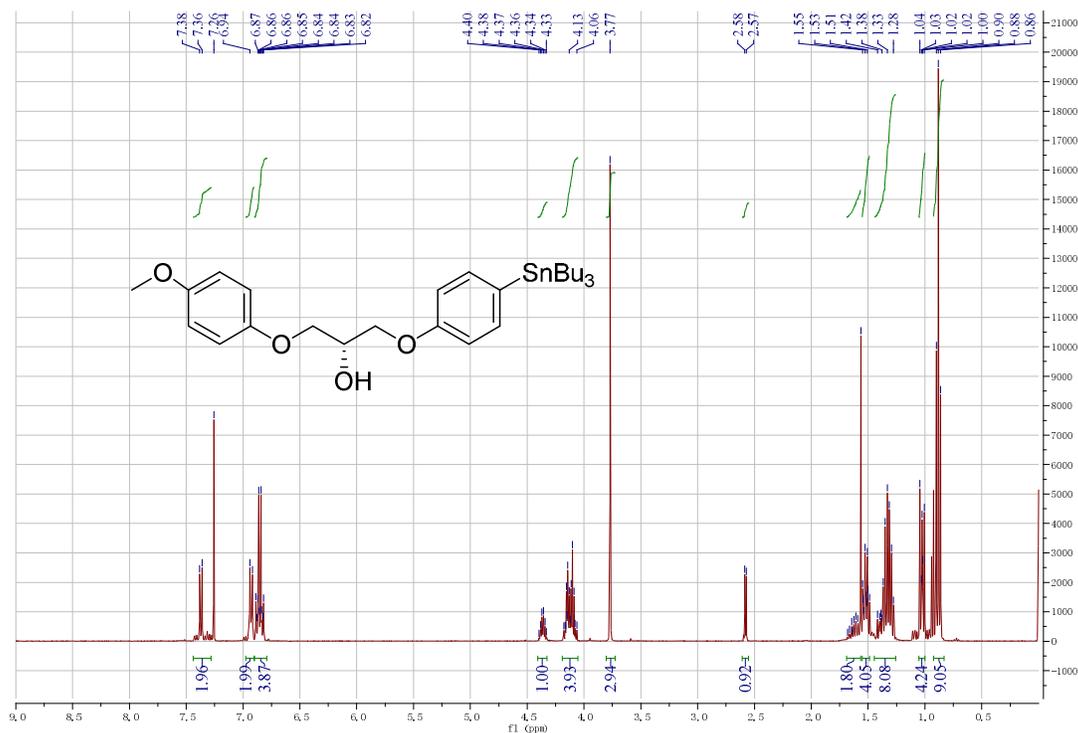
$^{13}\text{C-NMR}$ for compound (*S*)-**9**



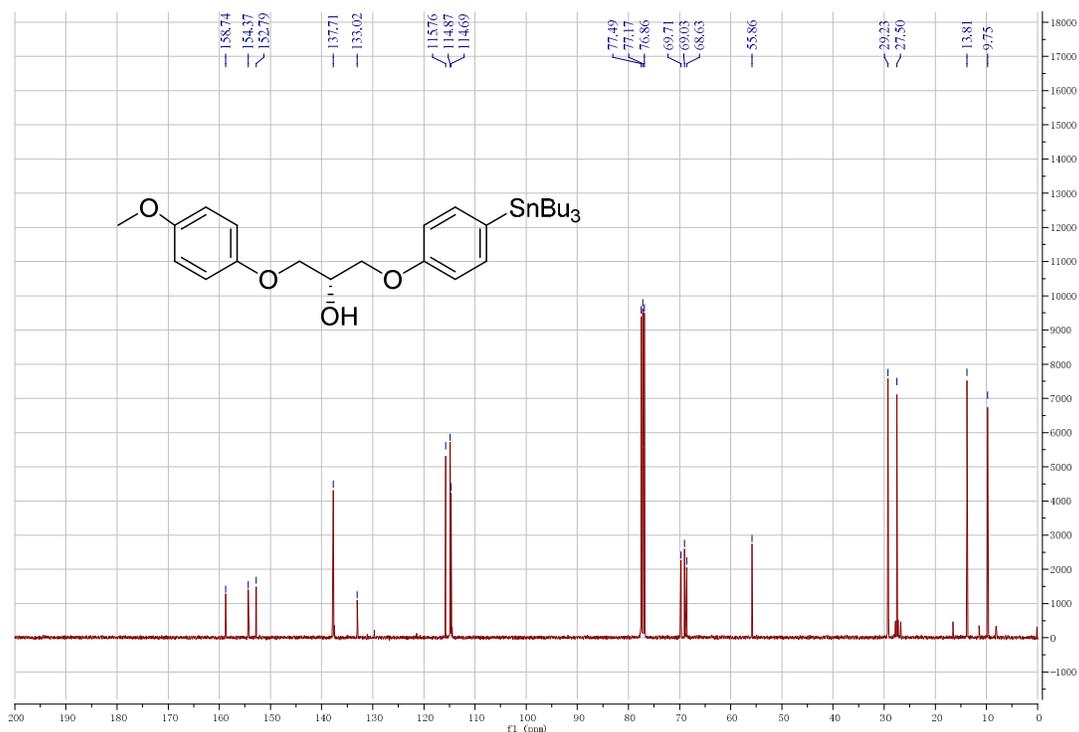
HRMS for compound (S)-9



¹H-NMR for compound (R)-9



¹³C-NMR for compound (R)-9



HRMS for compound (R)-9

Mass Spectrum SmartFormula Report

Analysis Info		Acquisition Date	
Analysis Name	D:\Data\20160614\R-9_59_01_225.d	6/15/2016 4:26:34 PM	
Method	lhl-tune_general-p.m	Operator	Bruker
Sample Name	R-9	Instrument / Ser#	micrOTOF-Q 10260
Comment			
Acquisition Parameter			
Source Type	ESI	Ion Polarity	Positive
Focus	Active	Set Capillary	3500 V
Scan Begin	50 m/z	Set End Plate Offset	-500 V
Scan End	1000 m/z	Set Collision Cell RF	150.0 Vpp
		Set Nebulizer	0.6 Bar
		Set Dry Heater	180 °C
		Set Dry Gas	6.0 l/min
		Set Divert Valve	Source

