SUPPLEMENTARY INFORMATION

1.1. Reagents and chemicals

Reference standards of gemfibrozil, ofloxacin and ibuprofen were obtained from Sigma-Aldrich (Steinheim, Germany). Irbesartan, rac N-desmethyl venlafaxine, D,L-O-desmethyl venlafaxine, 1-hydroxy ibuprofen, rac α-hydroxy ibuprofen and rac 2-hydroxy ibuprofen were purchased from Toronto Research Chemicals (North York, Canada). Venlafaxine hydrochloride was obtained from LGC Promochem (London, UK). Individual stock solutions of 500 mg/L were prepared in HPLC-grade methanol (MeOH) (50 mg/L for ofloxacin).

HPLC-grade MeOH, acetonitrile (ACN), sodium hydroxide (NaOH, 99%) and formic acid (FA, 98-100%) were acquired from Scharlau (Barcelona, Spain). A Milli-Q ultra-pure water system from Millipore (Bedford, MA, USA) was used to obtain the HPLC-grade water. Leucine enkephalin, used as lock mass (*m/z* 556.2771 and *m/z* 554.2615 in positive and negative ion modes, respectively) was purchased from Sigma-Aldrich.

Solid-phase extraction (SPE) cartridges (Oasis-HLB; 3 mL, 60 mg) were purchased from Waters (Milford, MA, USA).

The compounds investigated (with their IUPAC names) were the following:

- Gemfibrozil: (5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid)
- Ofloxacin: (7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo[7.3.1.0^{5,13}]trideca-5(13),6,8,11-tetraene-11-carboxylic acid)
- Ibuprofen: ((+-)-2-(P-Isobutylphenyl)propionic acid)
- Irbesartan: (2-butyl-3-({4-[2-(2H-1,2,3,4-tetrazol-5-yl)phenyl]phenyl}methyl)-1,3-diazaspiro[4.4]non-1-en-4-one),
- Venlafaxine: (1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexan-1-ol)

Table 1SI. Stock solutions used for the preparation of mineral media.

Mineral stock solution	contents
1	8.5 g/L potassium dihydrogen orthophosphate (KH_2PO_4) 21.75 g/L dipotassium hydrogen orthophosphate (K_2HPO_4) 33.40 g/L disodium hydrogen orthophosphate dehydrate ($Na_2HPO_4 \cdot 2H_2O$) 0.5 g/L ammonium chloride (NH_4Cl)
2	27.50 g/L calcium chloride, anhydrous ($CaCl_2$)
3	22.50 g/L magnesium sulphate heptahydrate ($MgSO_4 \cdot 7H_2O$)
4	0.25 g/L iron (III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$)

1.2. Instrumentation

LC-ESI-QTOF MS

The mobile phases used were (A) H_2O and (B) MeOH, both containing 0.01% (v/v) FA. The percentage of organic modifier (B) was changed linearly as follows: 0 min, 10%; 9 min, 90%; 11 min, 90%; 11.1 min, 10%; 14 min, 10%. The column and sample temperatures were kept at 40°C and 5ºC, respectively. The injection volume was 50 µL. Nitrogen (Praxair, Valencia, Spain) was used as both drying gas and nebulising gas. The gas flow rate was set at 1000 L/h. The resolution of the TOF mass spectrometer was ~ 20,000 at full width half maximum (FWHM) at *m/z* 556. MS data were acquired over an *m/z* range of 50–1200, using a scan time of 0.3 s. The MCP detector potential was set to 3450 V. Capillary voltages of 0.7 kV and -1.7 kV were used in positive and negative ionization modes, respectively. A cone voltage of 25 V was applied. The collision gas was argon (99.995%, Praxair). The interface temperature was set to 650 ºC and the source temperature to 130 ºC. For MS^E experiments, two simultaneous acquisition functions were created: the low-energy (LE) function, with a collision energy of 4 eV, and the high energy (HE) function, with a collision energy ramp ranging from 15 to 40 eV. The same cone voltage (25 V) and collision energy ramp were used for additional MS/MS experiments, when necessary.

Calibration of the mass-axis from *m/z* 50 to 1200 was conducted daily with a 1:1 mixture of 0.05M NaOH:/5% (v/v) HCOOH, diluted (1:25) with water/ACN (20:80 v/v).

For automated accurate mass measurement, leucine enkephalin (2 mg/L) in ACN/water (50/50) at 0.1% HCOOH was used as lockmass and pumped at 20 μL/min through the lock-spray needle. The leucine enkephalin $[M+H]^+$ ion (*m/z* 556.2771) and its fragment ion (*m/z* 278.1141) were used in positive ionization mode for recalibrating the mass axis and to ensure a robust accurate mass measurement over time. In the negative, the selected ions were $[M-H]^-$ ion (*m/z* 554.2615) and its fragment ion (*m/z* 236.1035).

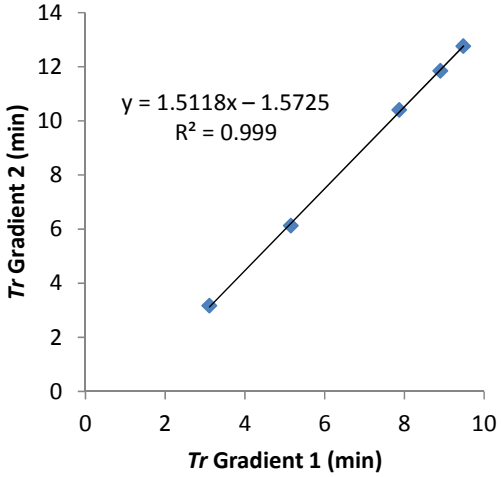
1.3. Retrospective analysis. Retention time re-calculation

It is important to appoint that in the retrospective analysis, the surface and wastewater samples had been analyzed in a previous study of Hernández et al. (2011) with different chromatography conditions, as shown in the table below.

Hence, in order to obtain comparable retention times (Tr), a gradient re-calculation was performed. For this purpose, the retention times of the five parent pharmaceuticals were measured in both gradient-conditions, ***Gradient 1*** (degradation experiments) and ***Gradient 2*** (Hernandez et al. (2011)) (See Figure below). After performing a *Tr* graphical representation, a lineal equation was obtained ($y = 1.5118x - 1.5725$) where the correlation coefficient (r) was higher than 0.99. Finally, the equation was applied for obtaining the predicted retention time of TPs and metabolites in the gradient 2.

Gradient	Analytical column	Mobile phase	Percentage of organic modifier (B)	Flow rate
Gradient 1	Acquity UPLC BEH C18 (100x2.1 mm, 1.7 µm,Waters)	A: H_2O B: MeOH, both 0.01% (v/v) FA	0 min, 10%; 9 min, 90% 11 min, 90% 11.1 min, 10%; 14 min, 10%.	0.3 mL/min.
Gradient 2			0 min, 10%; 14 min,90%; 16 min, 90%; 16.01 min, 10% 18 min, 10%.	

	Tr gradient 1 (min)	*Tr* gradient 2 (min)
Ibuprofen	8.9	11.9
Gemfibrozil	9.5	12.8
Ofloxacin	3.1	3.2
Venlafaxine	5.2	6.1
Irbesartan	7.9	10.4



Therefore:

(Tr 2,Unknown) = 1.5118 (*Tr 1,Known*) – 1.5725

Using this equation, the retention times in the gradient 2 were calculated:

Compounds	*Tr* gradient 1 (min)	*Tr* gradient 2 (min)
Irbesartan	7.6	9.9
ISW1a	6.6	8.4
ISW1b	7.3	9.5
ISW2	7.3	9.5
IB3a	6.8	8.7
IB3b	7.1	9.2
IB4	6.4	8.1
IB5	6.6	8.4
IB6	6.3	8.0
Valsartan	7.9	10.4
Venlafaxine	5.2	6.3
VB1a	3.8	4.2
VB1b	5.2	6.3
VB2	5.1	6.1
VB3a	2.7	2.5
VB3b	3.1	3.1
VB4	3.9	4.3
V1	4.1	4.6
V2	4.0	4.5
Ofloxacin	3.1	3.1
OB1	3.8	4.2
Ibuprofen	9.0	12.0
IbSW1	6.6	8.4
IbSW2a	6.5	8.3
IbSW2b	8.1	10.7
IbSW2c	8.7	11.6
IbB3	6.2	7.8
IbB4	7.1	9.2
Ib1	6.9	8.9
Gemfibrozil	9.5	12.8
GSWB1	8.4	12.8

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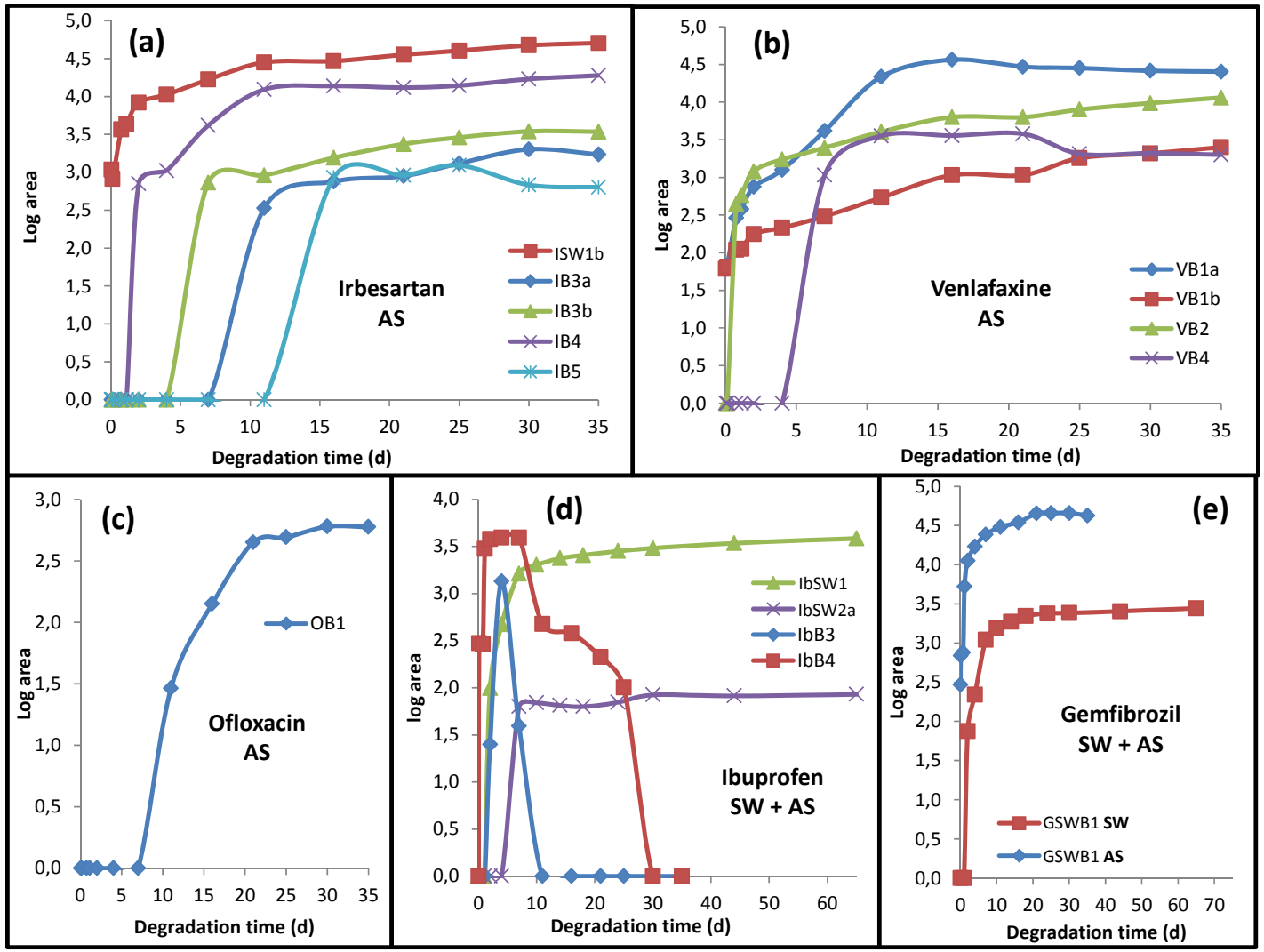


Figure 1SI. SemiLog-linear plot of formation of the main pharmaceutical TPs in: (a) irbesartan biotransformation in AS, (b) venlafaxine in AS, (c) ofloxacin in AS, (d) ibuprofen biotransformation in SW and in AS and (e) gemfibrozil in SW and in AS.

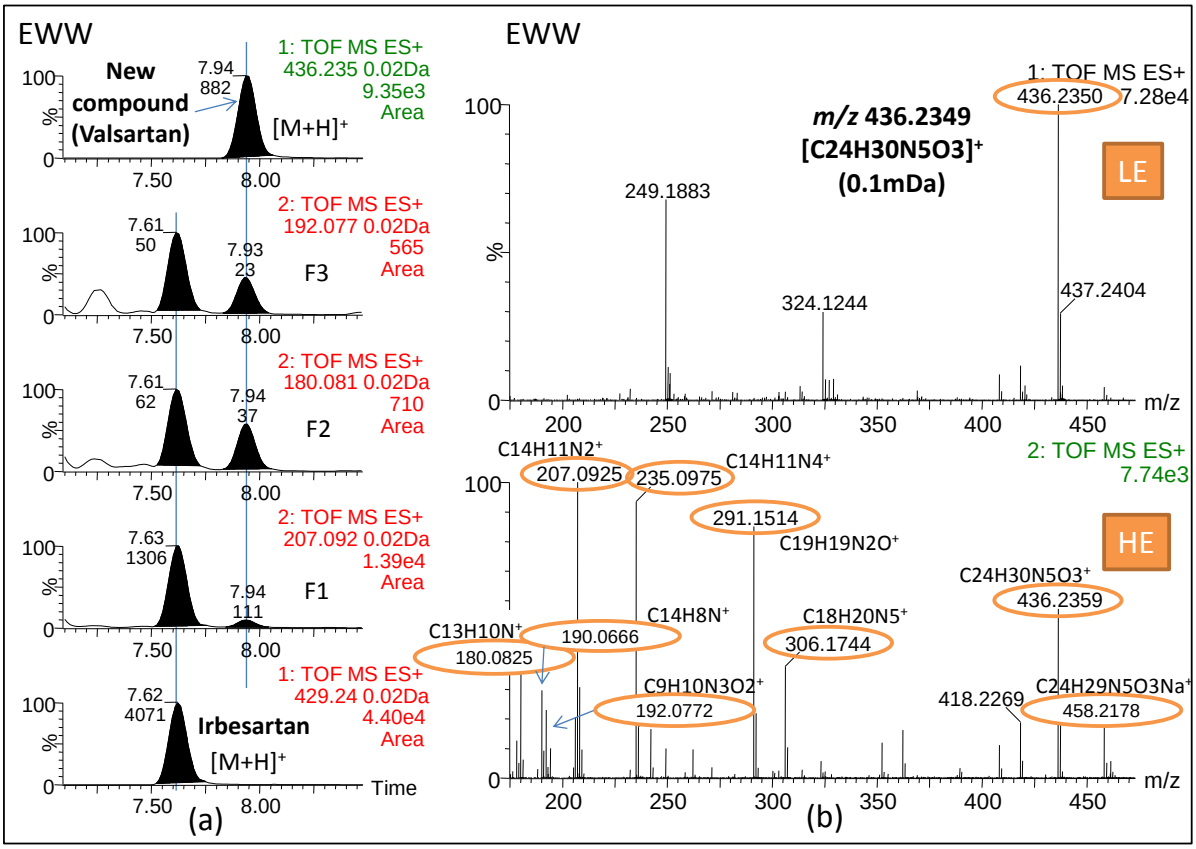


Figure 2SI. Detection of valsartan after applying the common fragmentation pathway strategy. (a) nw-XICs for $[M+H]^+$ of irbesartan and valsartan in LE, and three common fragment ions in HE. (b) LE and HE spectra of valsartan.

1.4. Proposed chemical structures and MS spectra for some TPs:

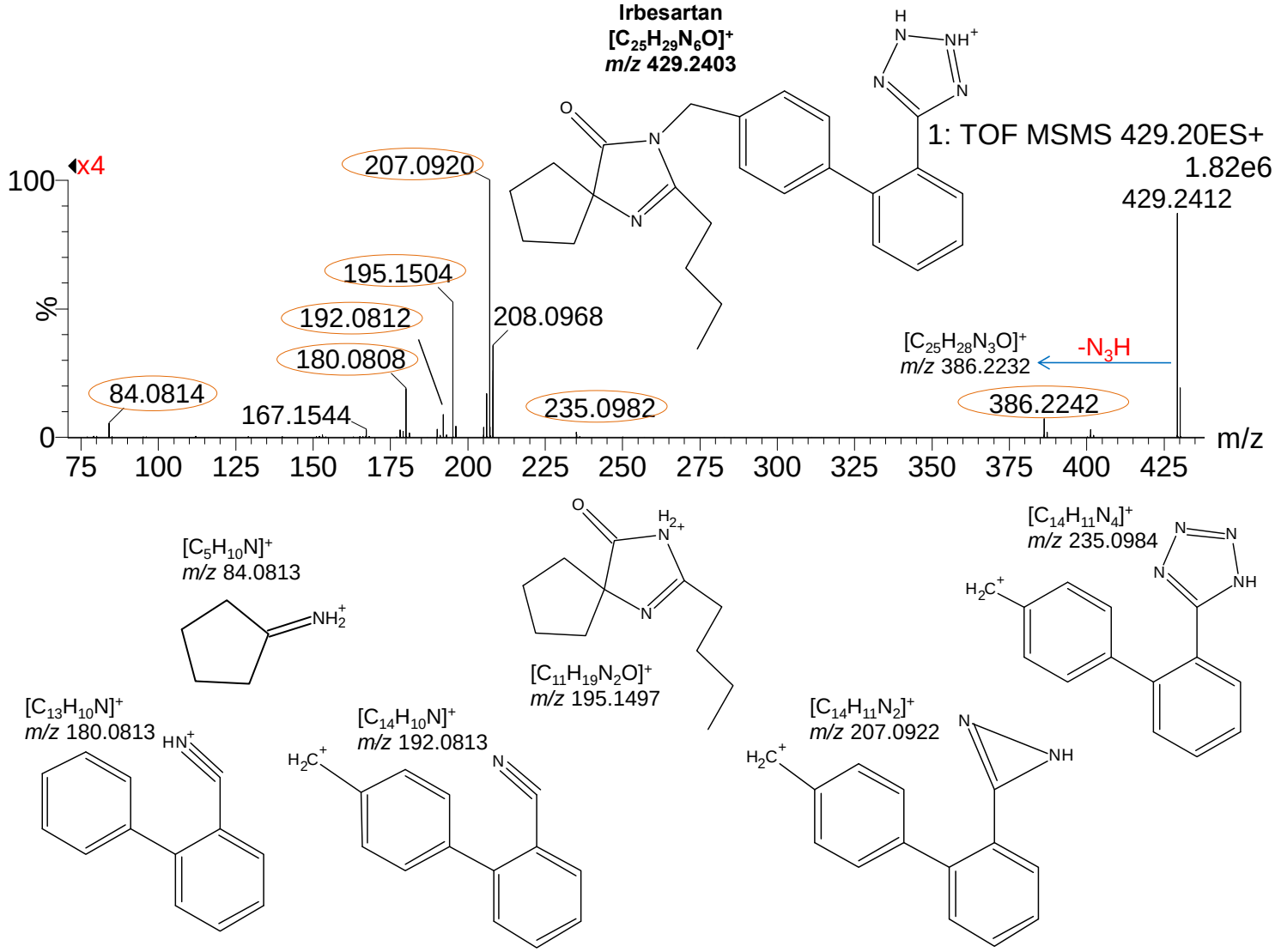
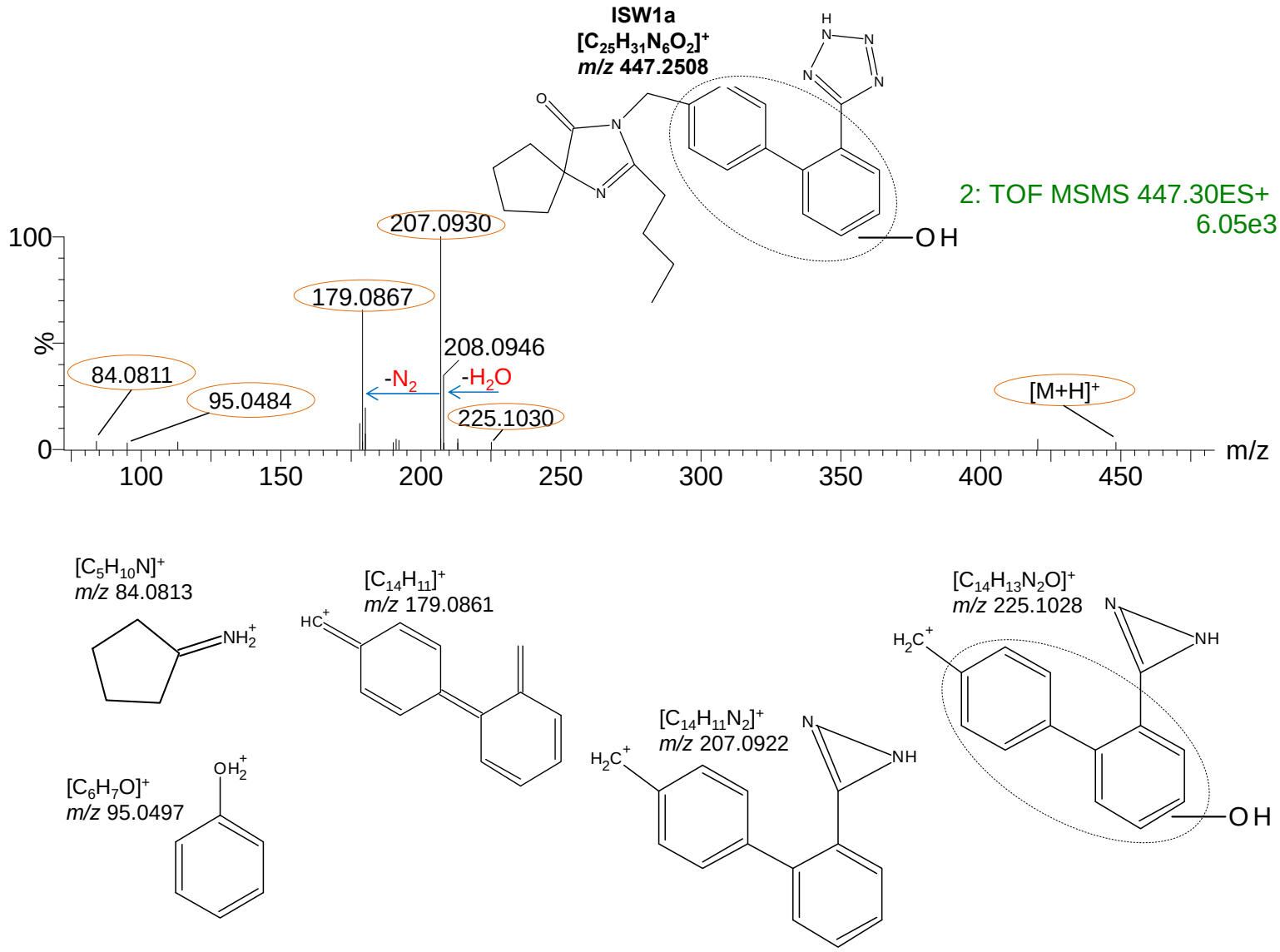


Figure 3SI. Fragmentation pathway of irbesartan.



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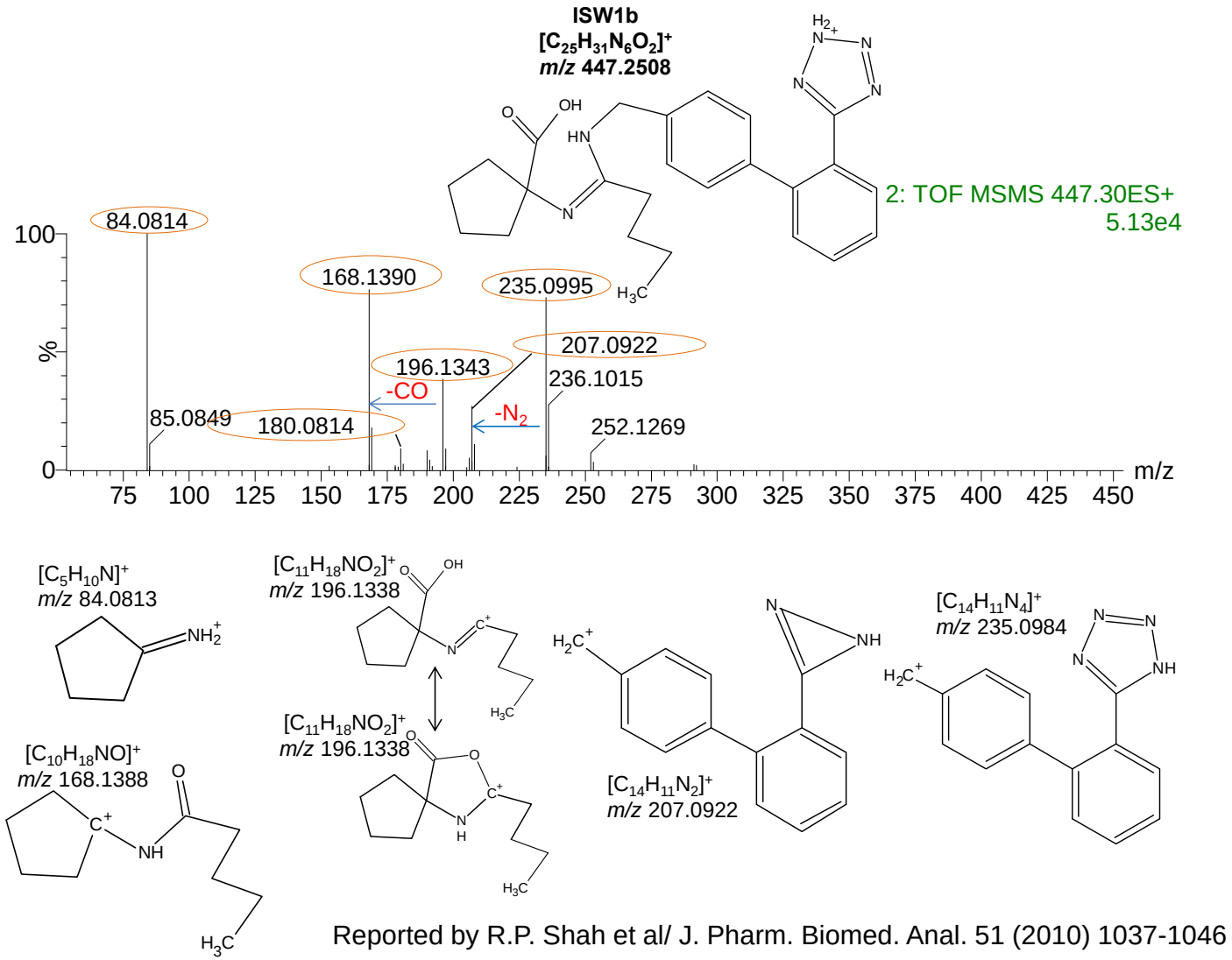
91 **Figure 4SI.** Elucidation of ISW1a.



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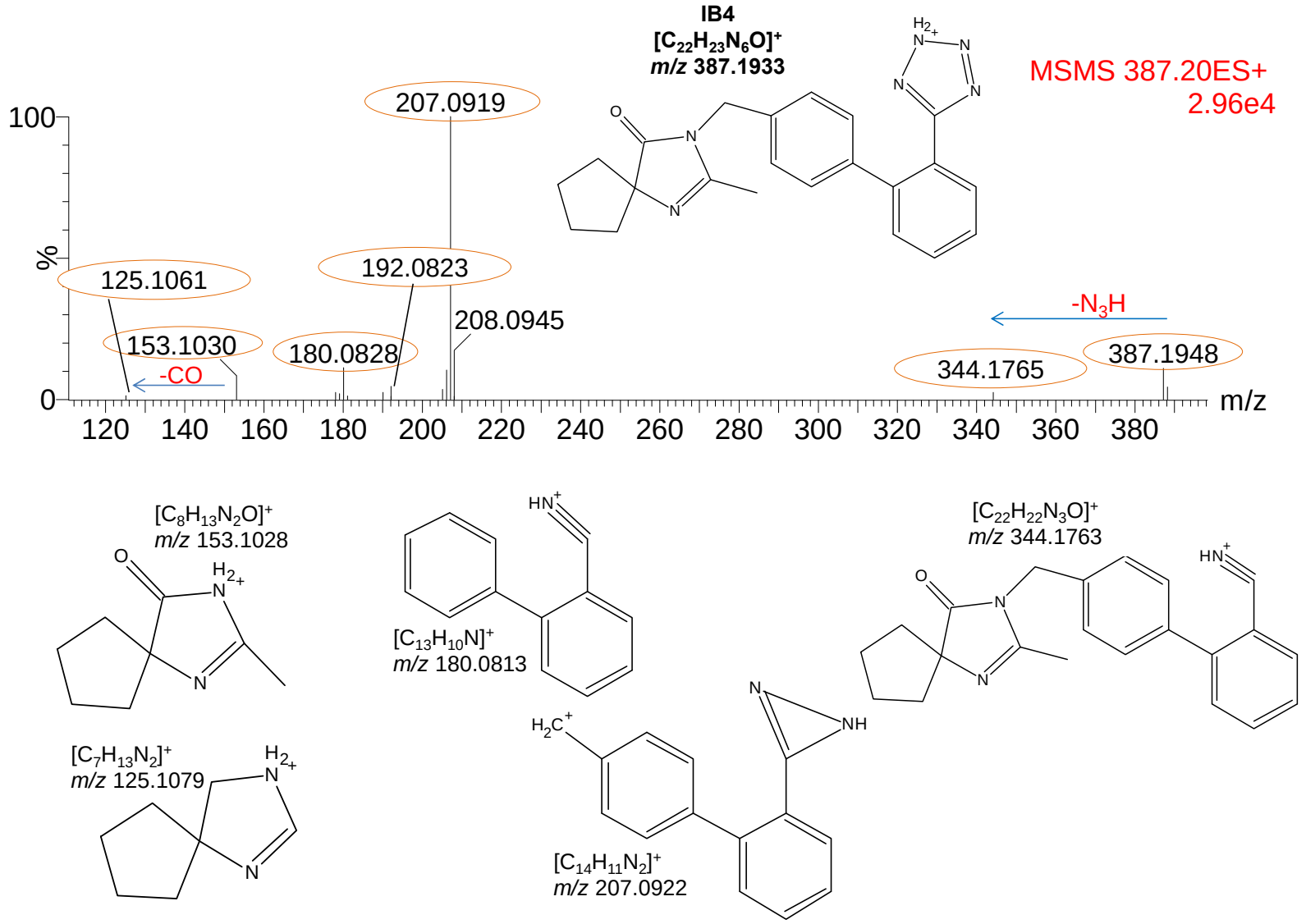
93 **Figure 5SI.** Elucidation of ISW1b.



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95 **Figure 6SI.** Elucidation of IB4.

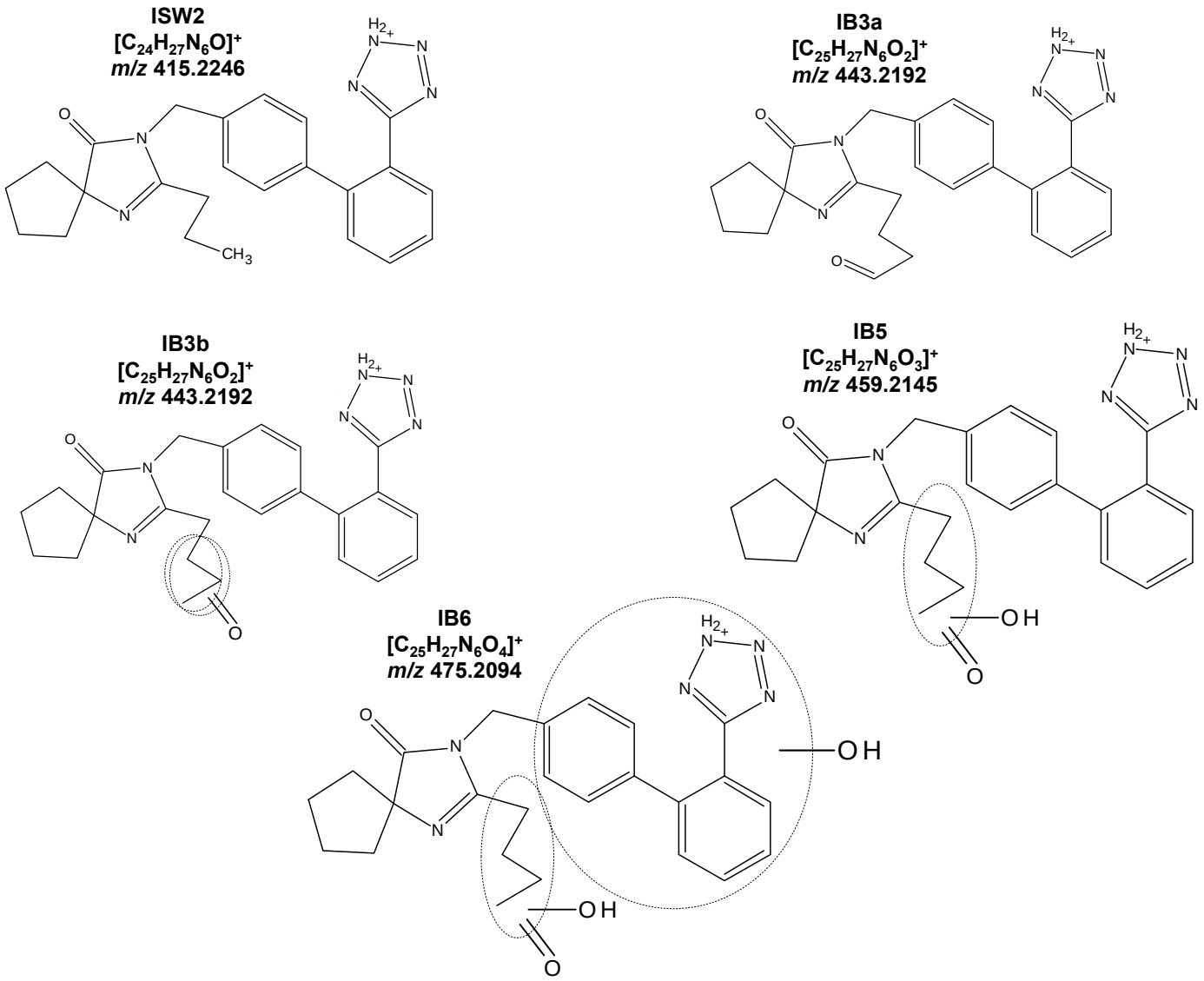
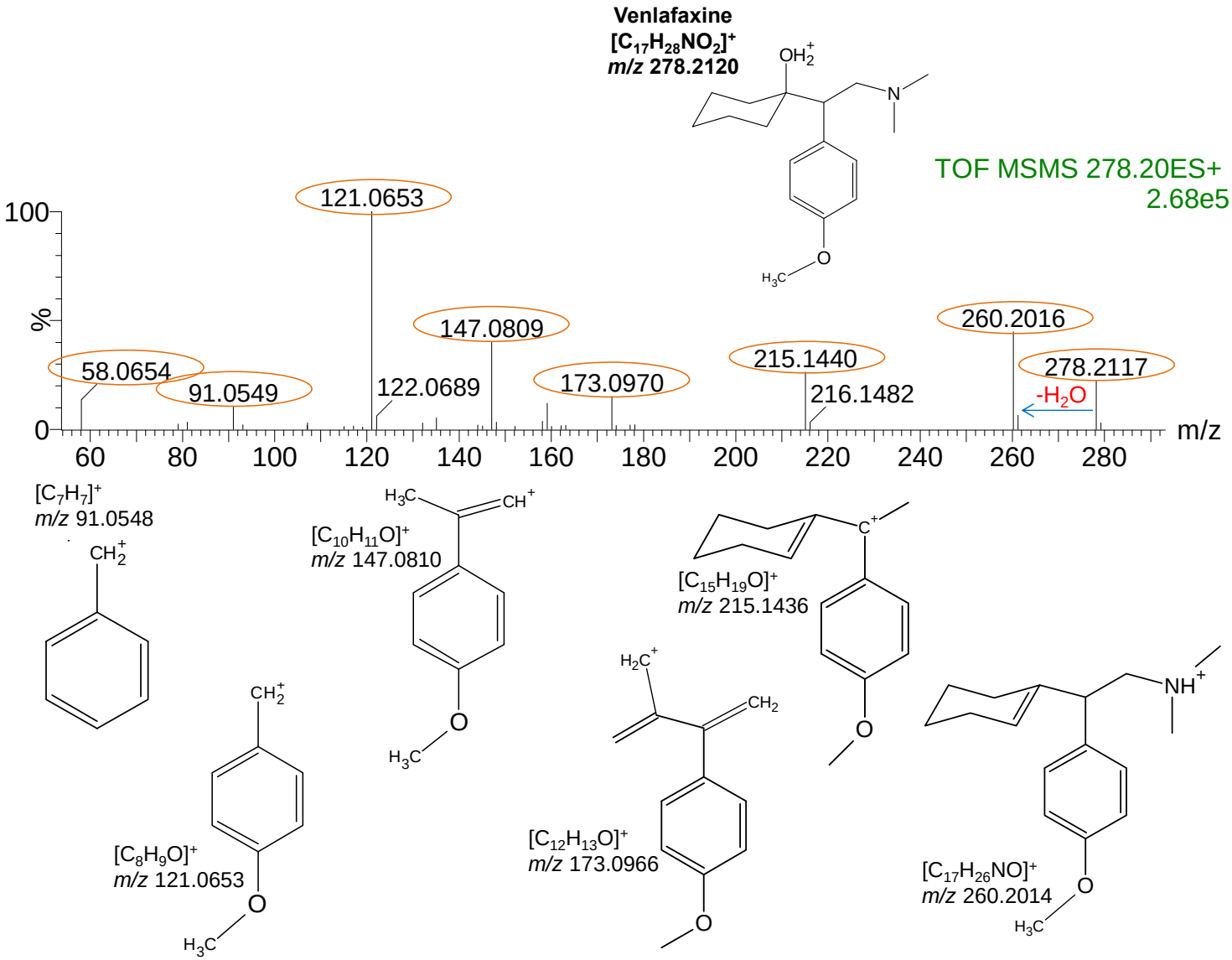


Figure 7SI. Elucidation of ISW2, IB3a, IB3b, IB5 and IB6.



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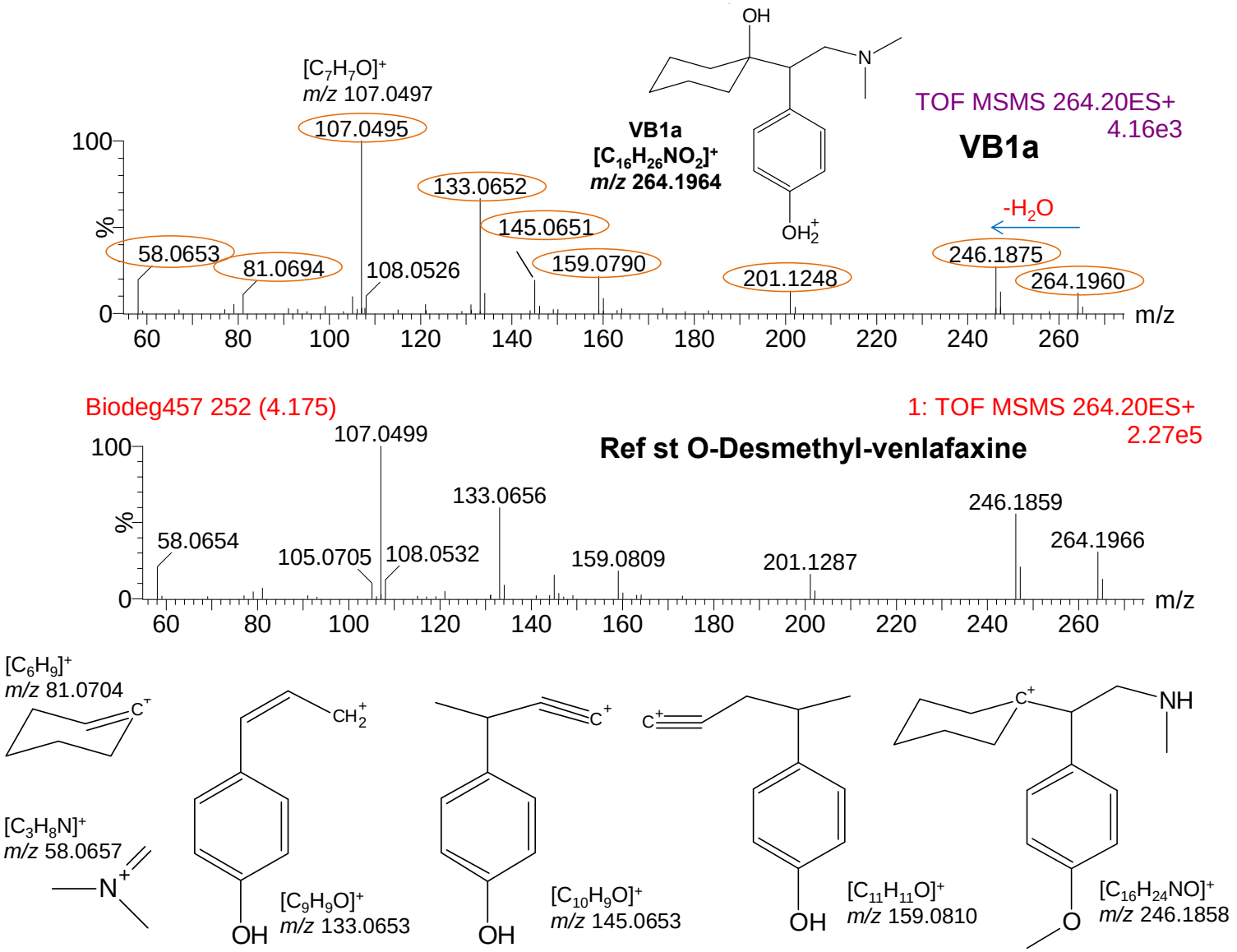
99 **Figure 8SI.** Fragmentation pathway of venlafaxine.



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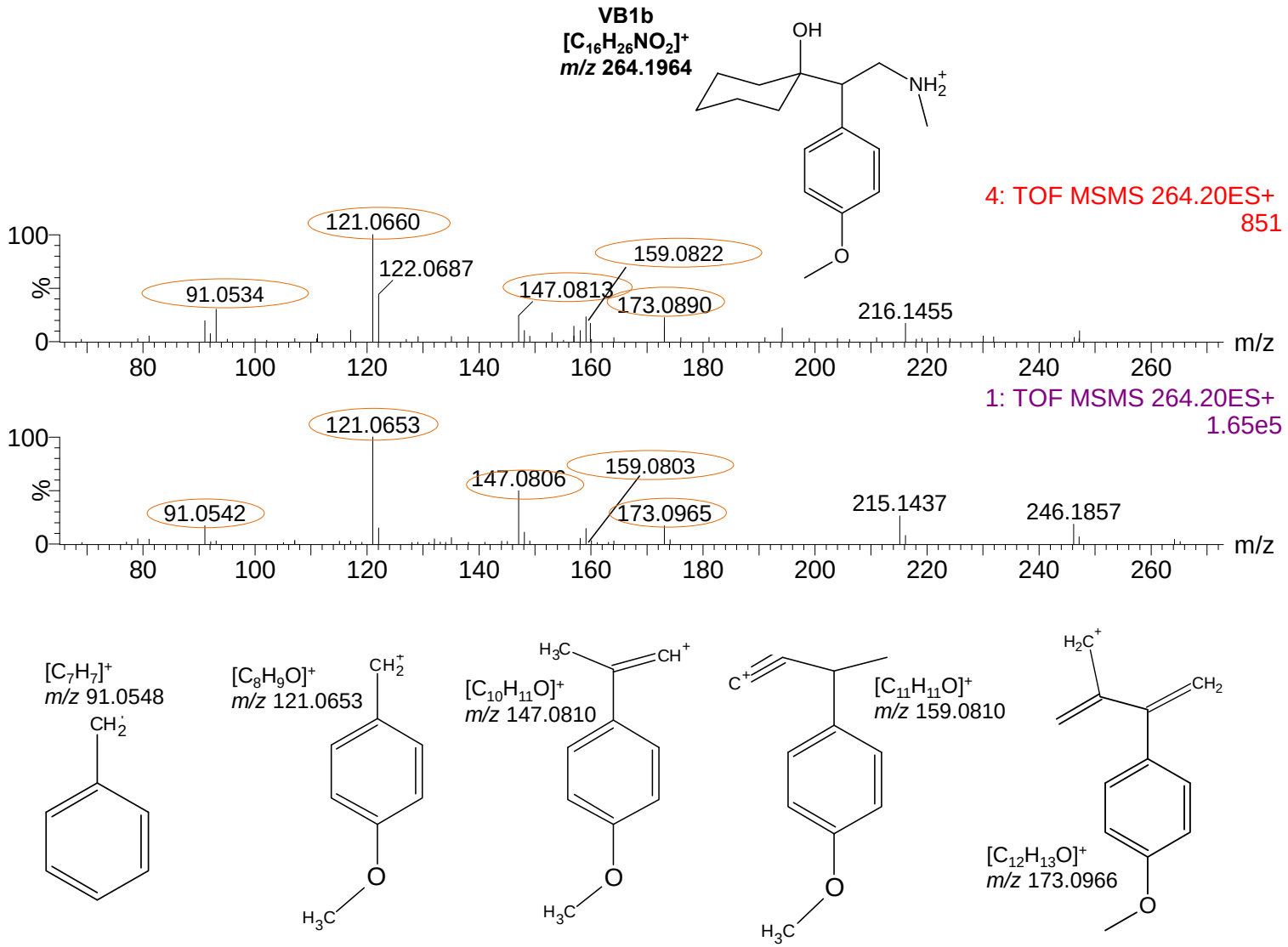
101 **Figure 9SI.** Elucidation of VB1a.



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103 **Figure 10SI.** Elucidation of VB1b.

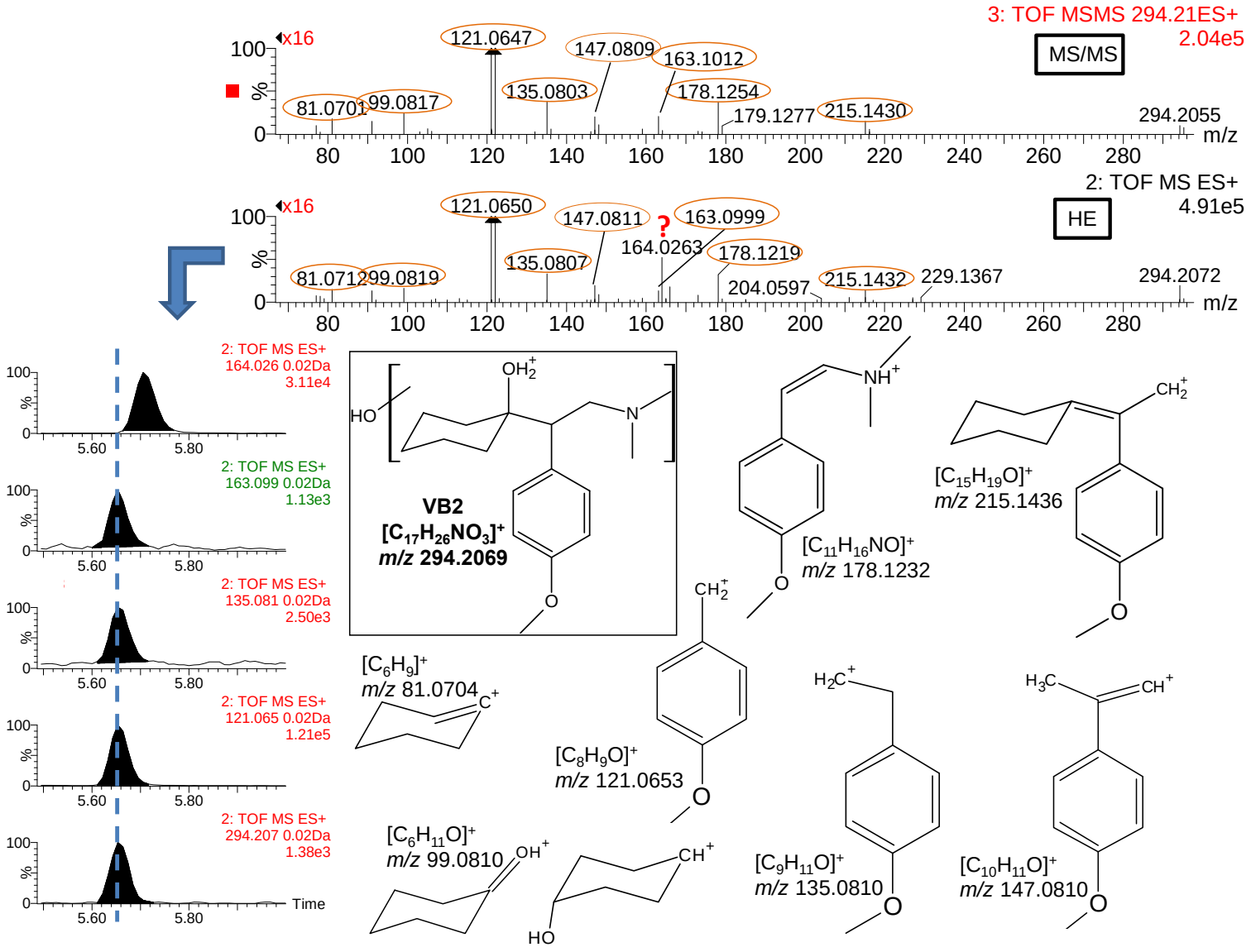
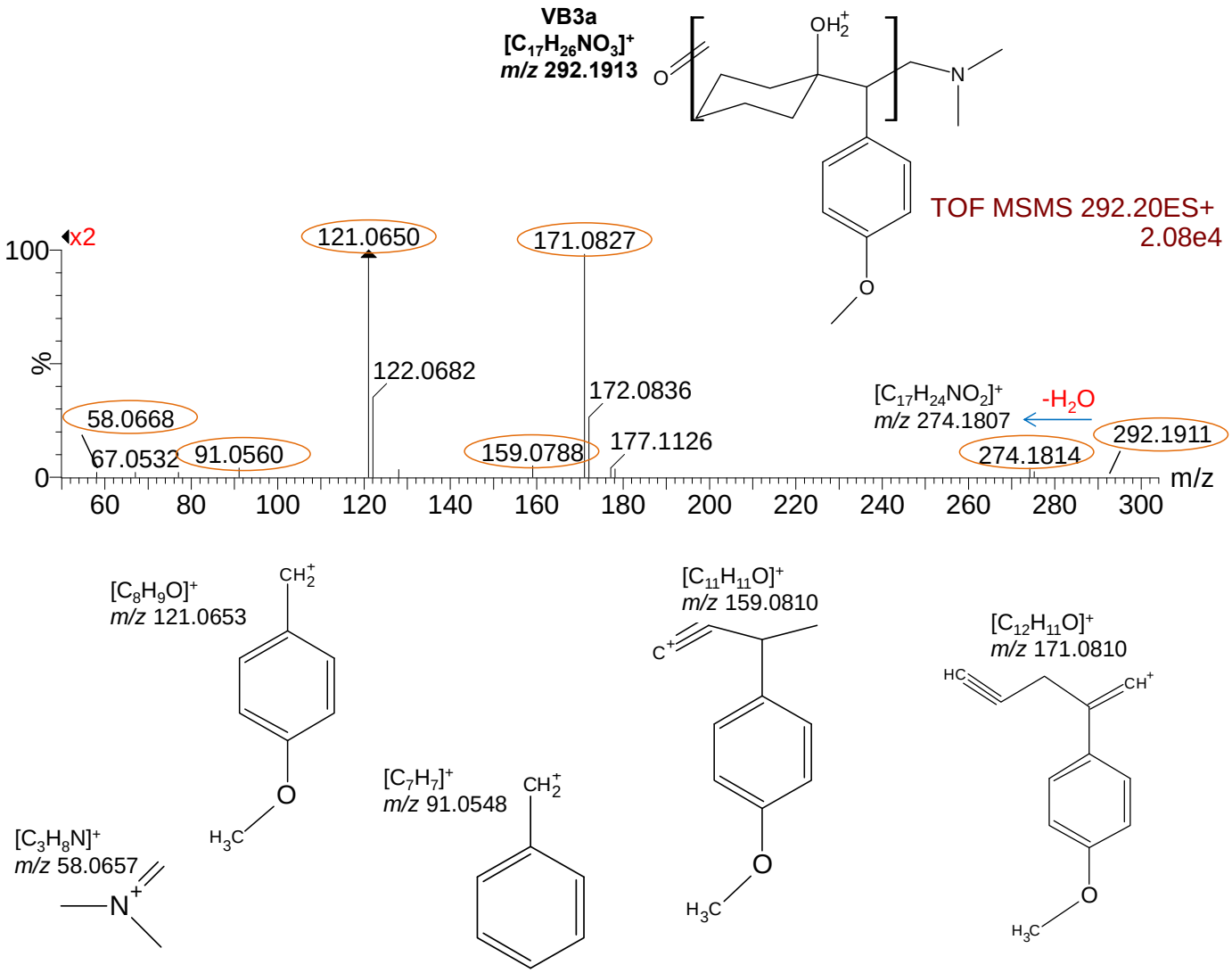


Figure 11SI. Elucidation of VB2.



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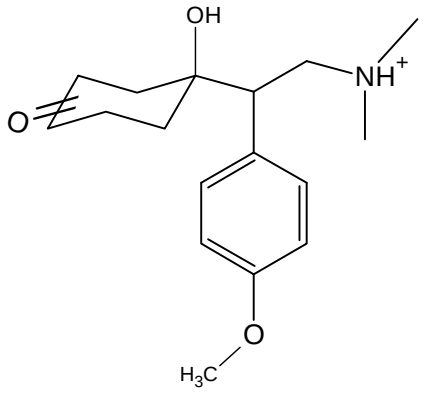
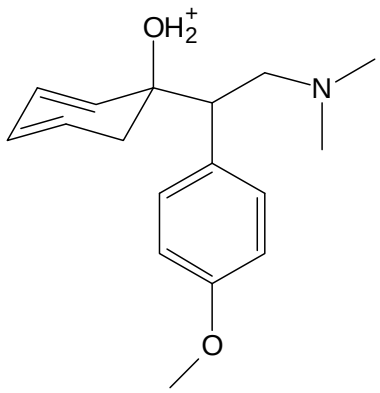
107 **Figure 12SI.** Elucidation of VB3a.

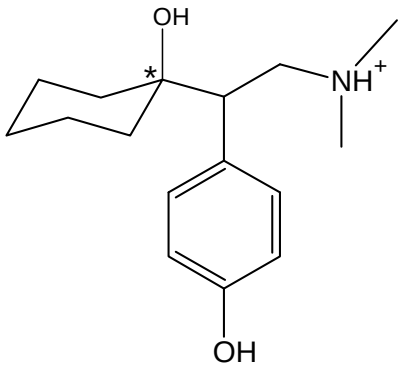
VB3b
$[C_{17}H_{26}NO_3]^+$
***m/z* 292.1913**



VB4
$[C_{17}H_{24}NO_2]^+$
***m/z* 274.1807**



V1
$[C_{16}H_{26}NO_2]^+$
***m/z* 264.1964**



V2
$[C_{17}H_{24}NO]^+$
***m/z* 258.1853**

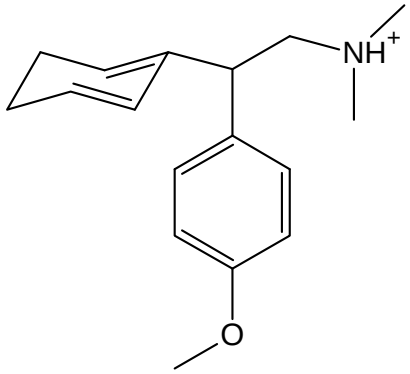


Figure 13SI. Elucidation of VB3b, VB4, V1 and V2.

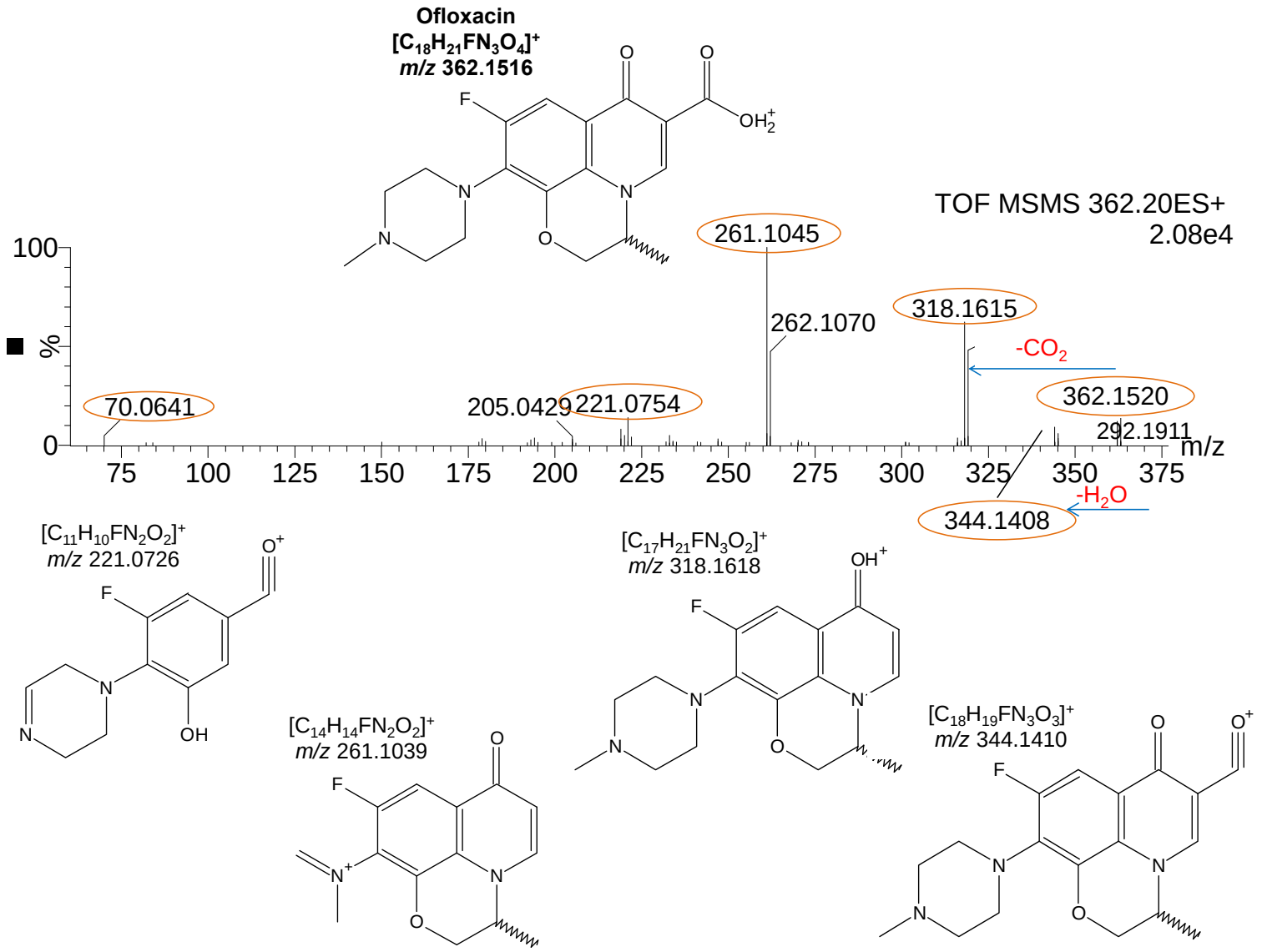
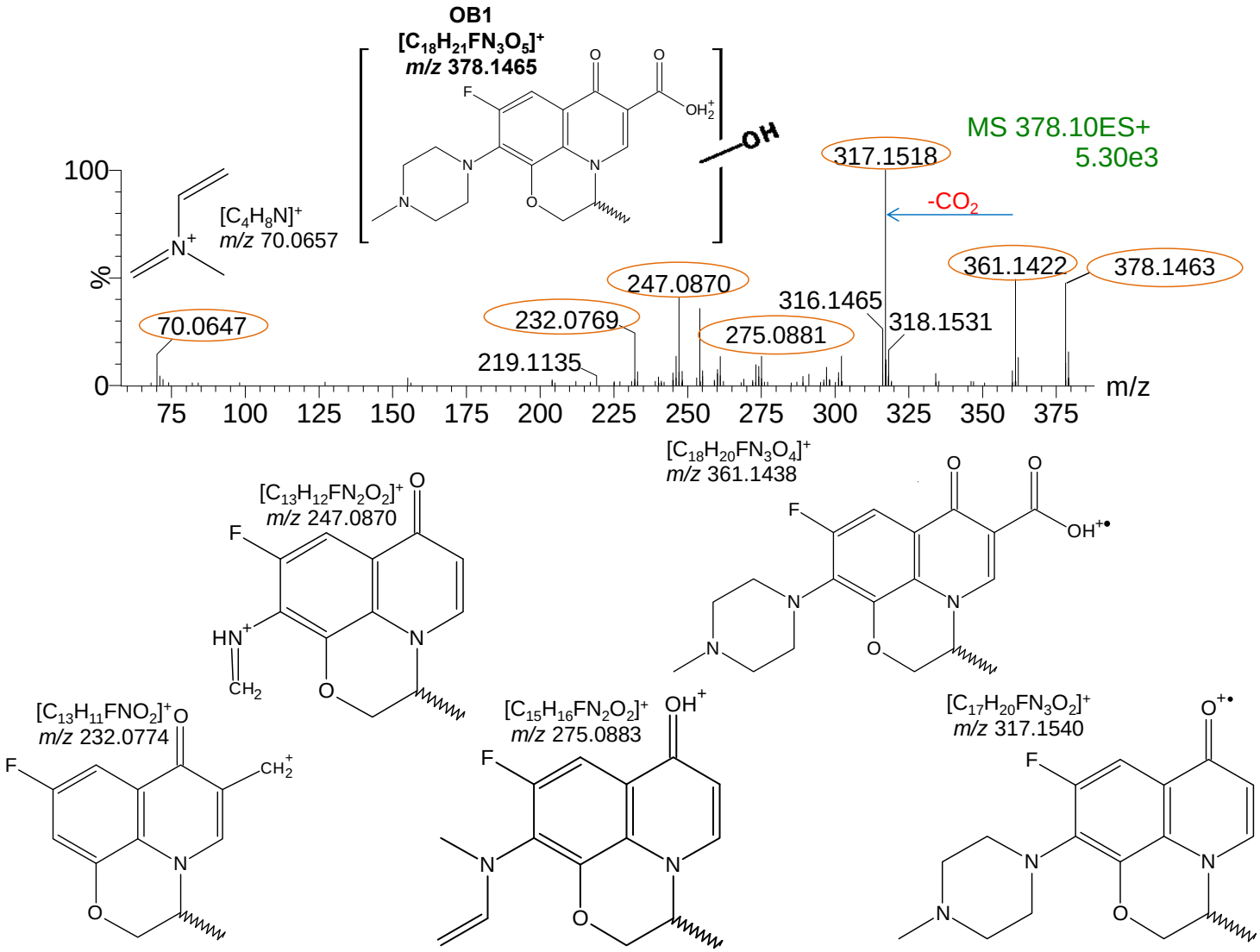


Figure 14SI. Fragmentation pathway of ofloxacin.



112

113 **Figure 15SI.** Elucidation of OB1.

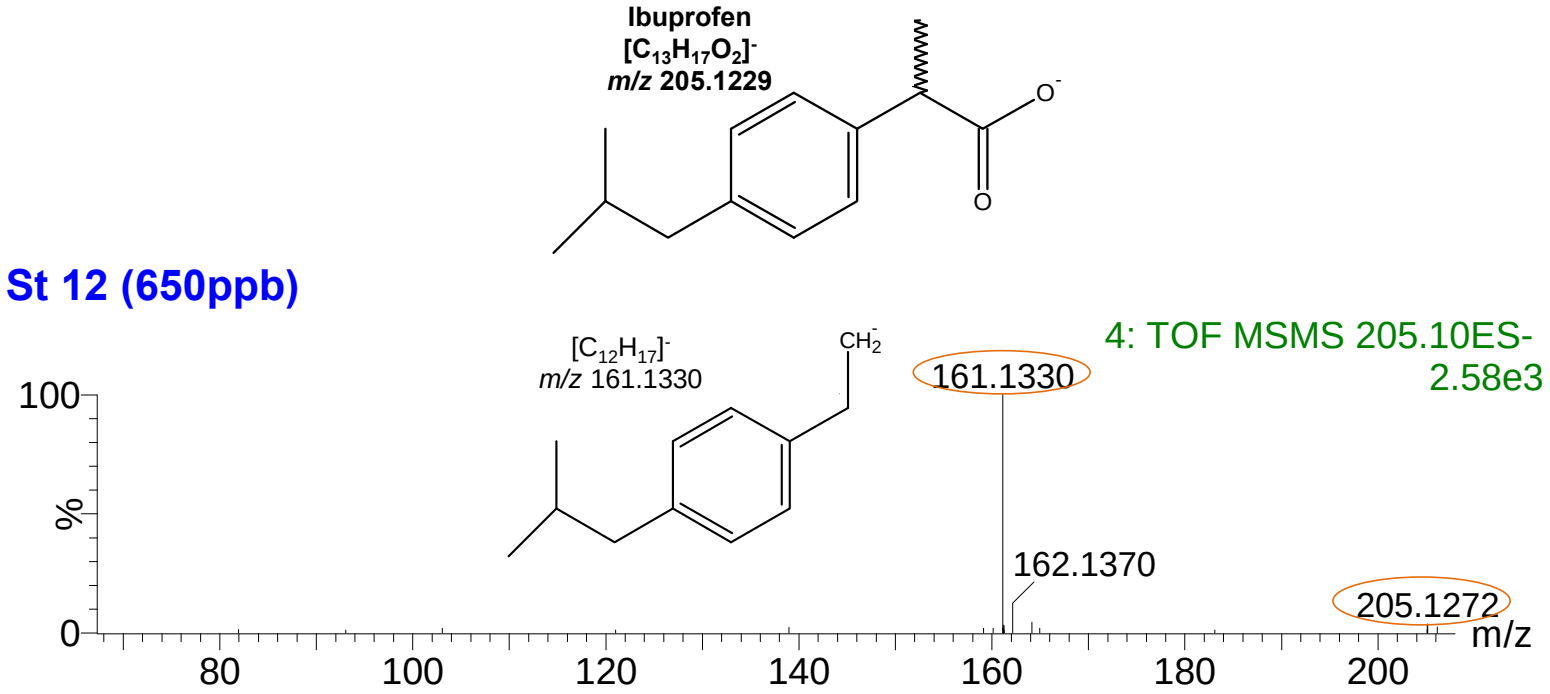


Figure 16SI. Fragmentation pathway of ibuprofen.

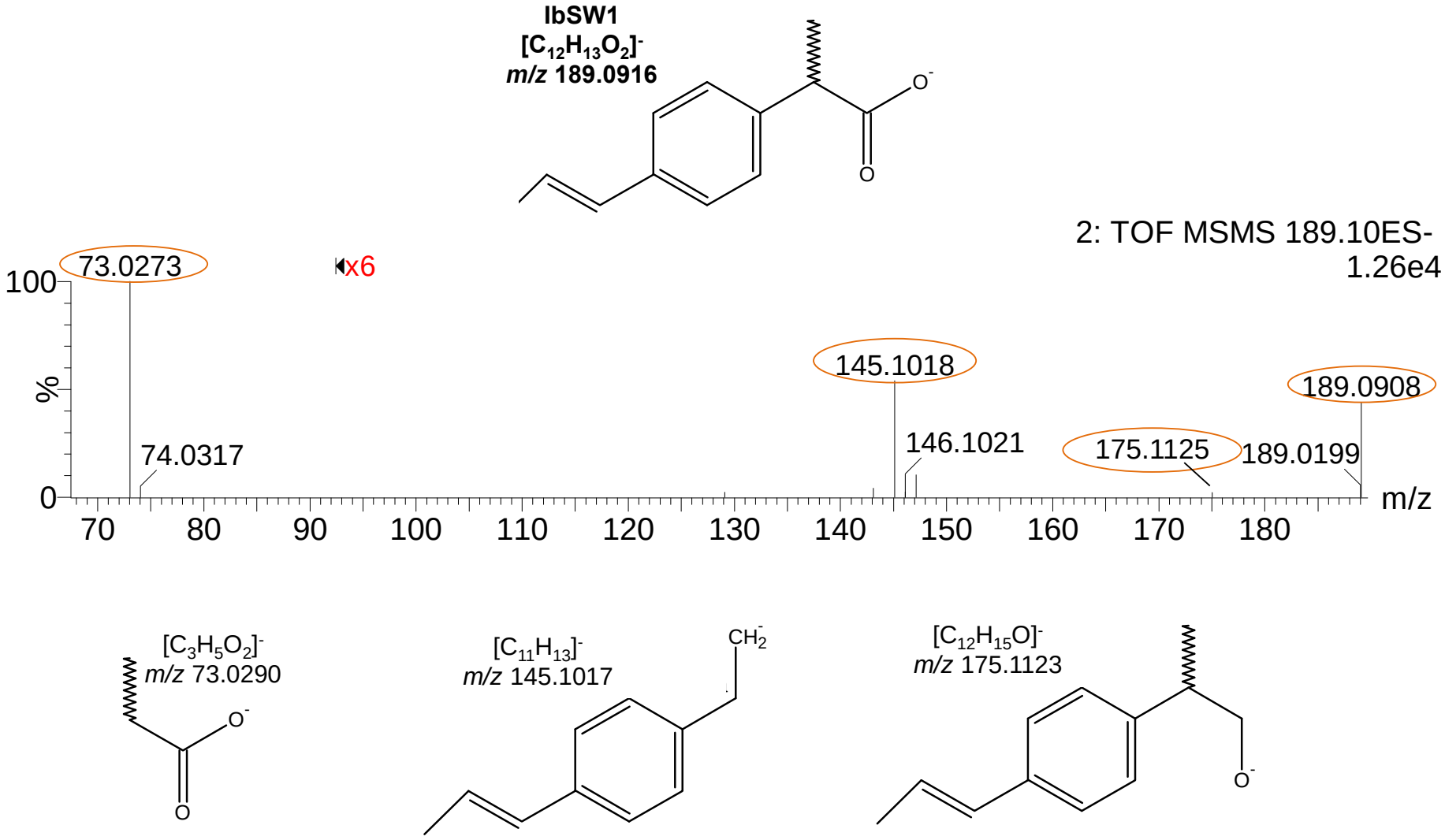
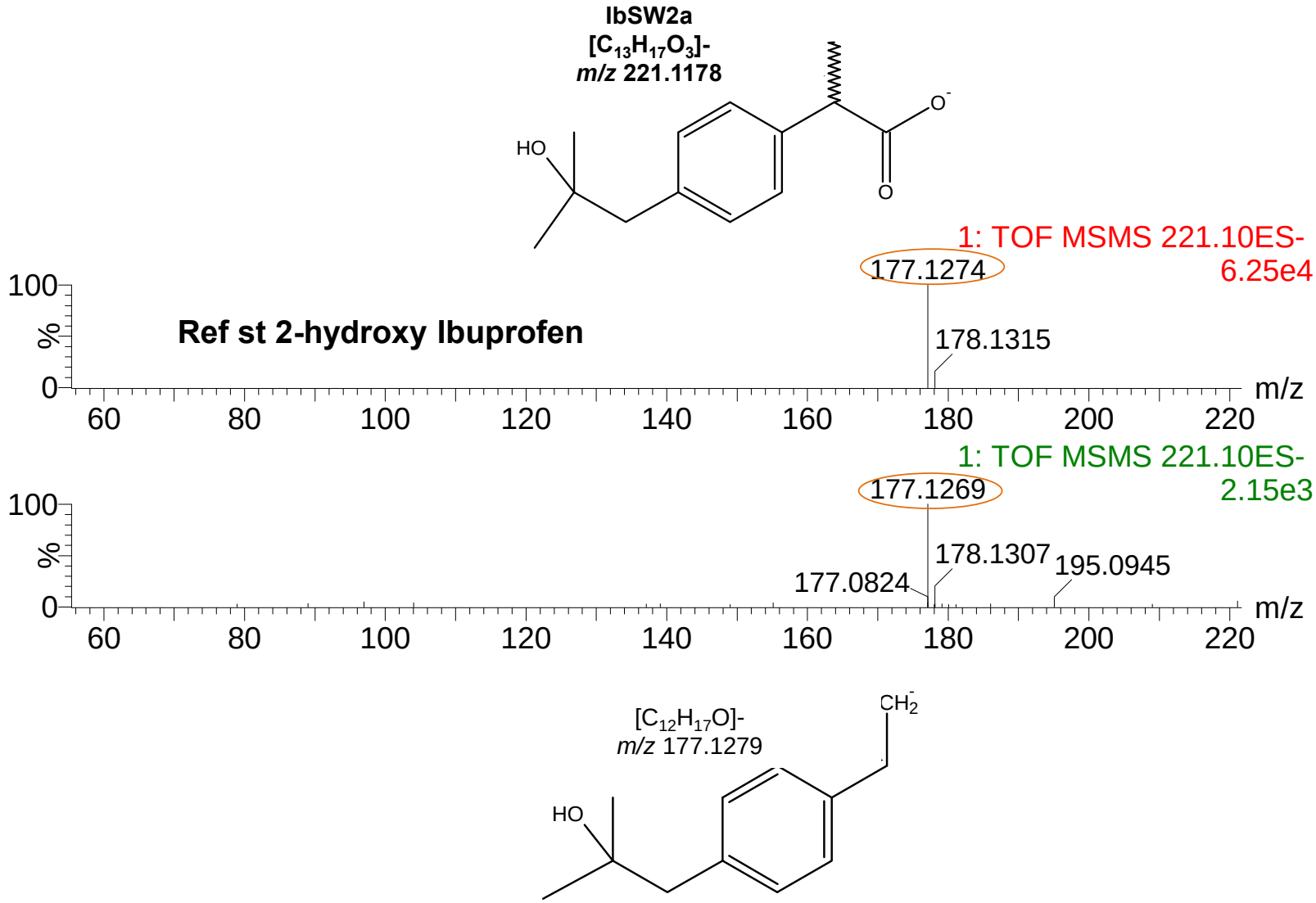


Figure 17SI. Elucidation of IbSW1.



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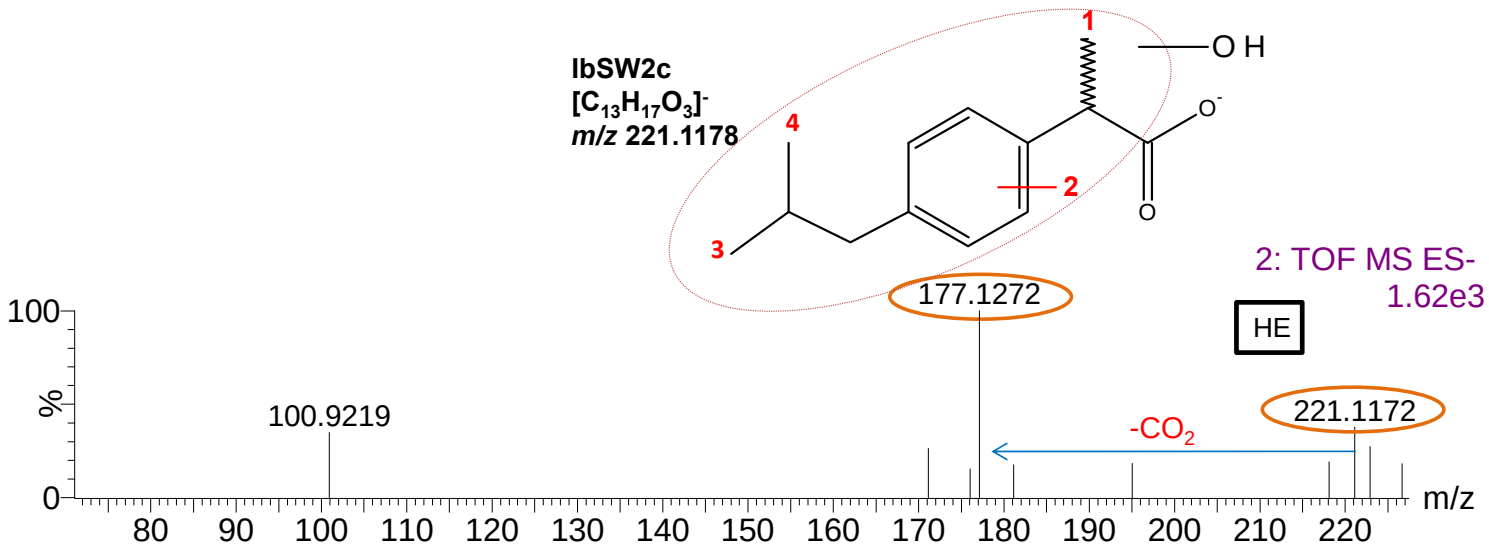
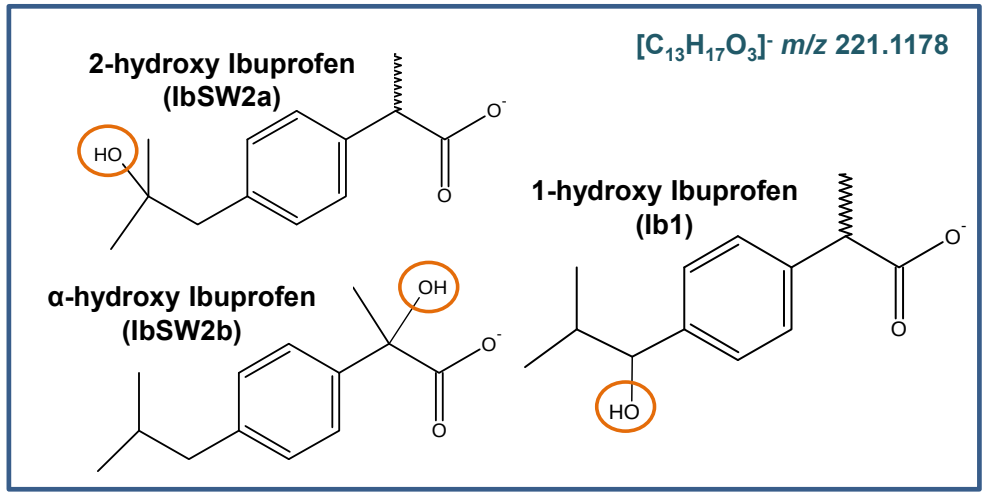
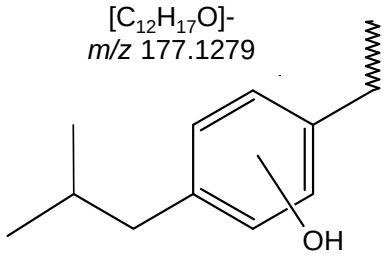
120 **Figure 18SI.** Elucidation of IbSW2a.



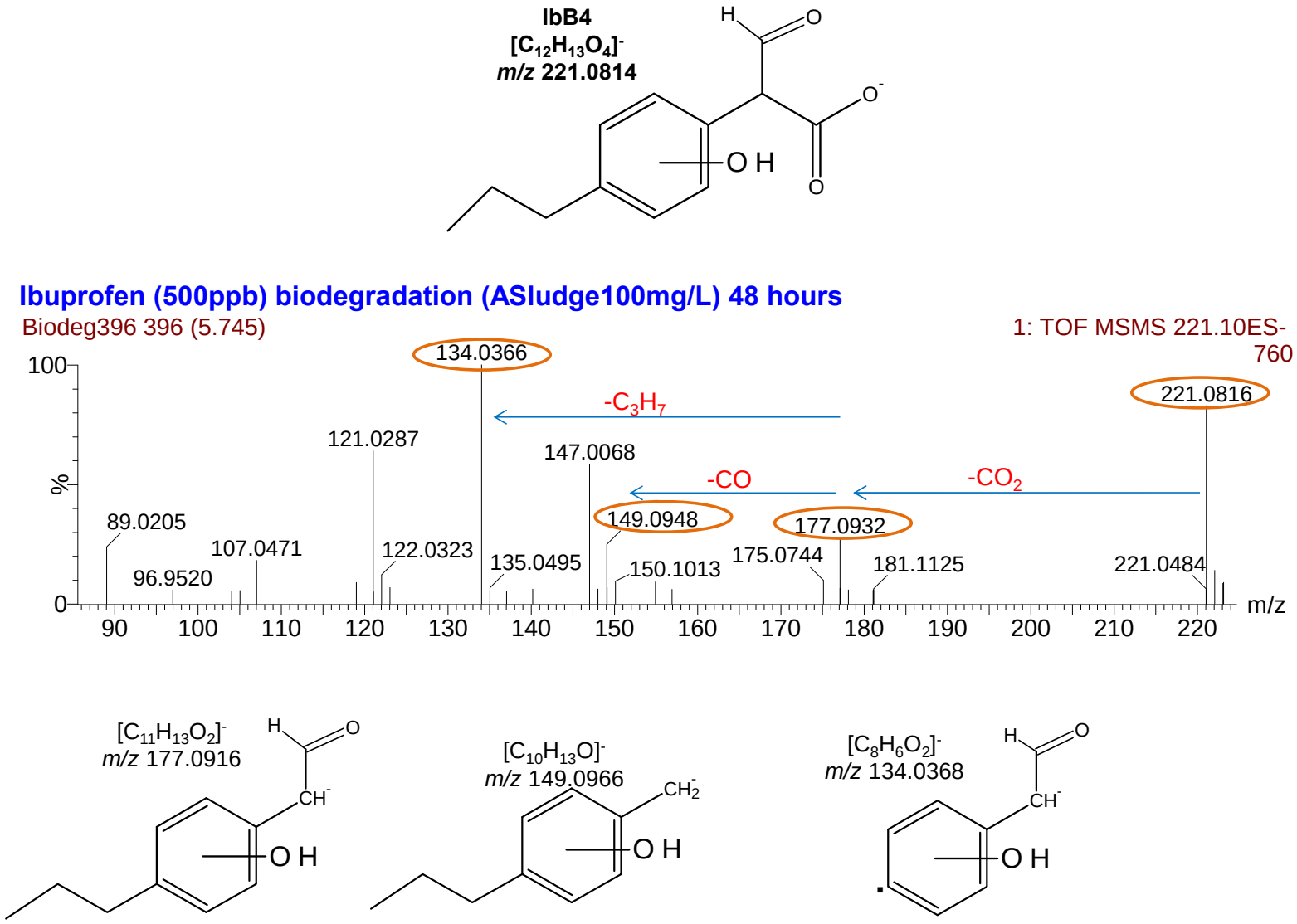
Reference standards for:





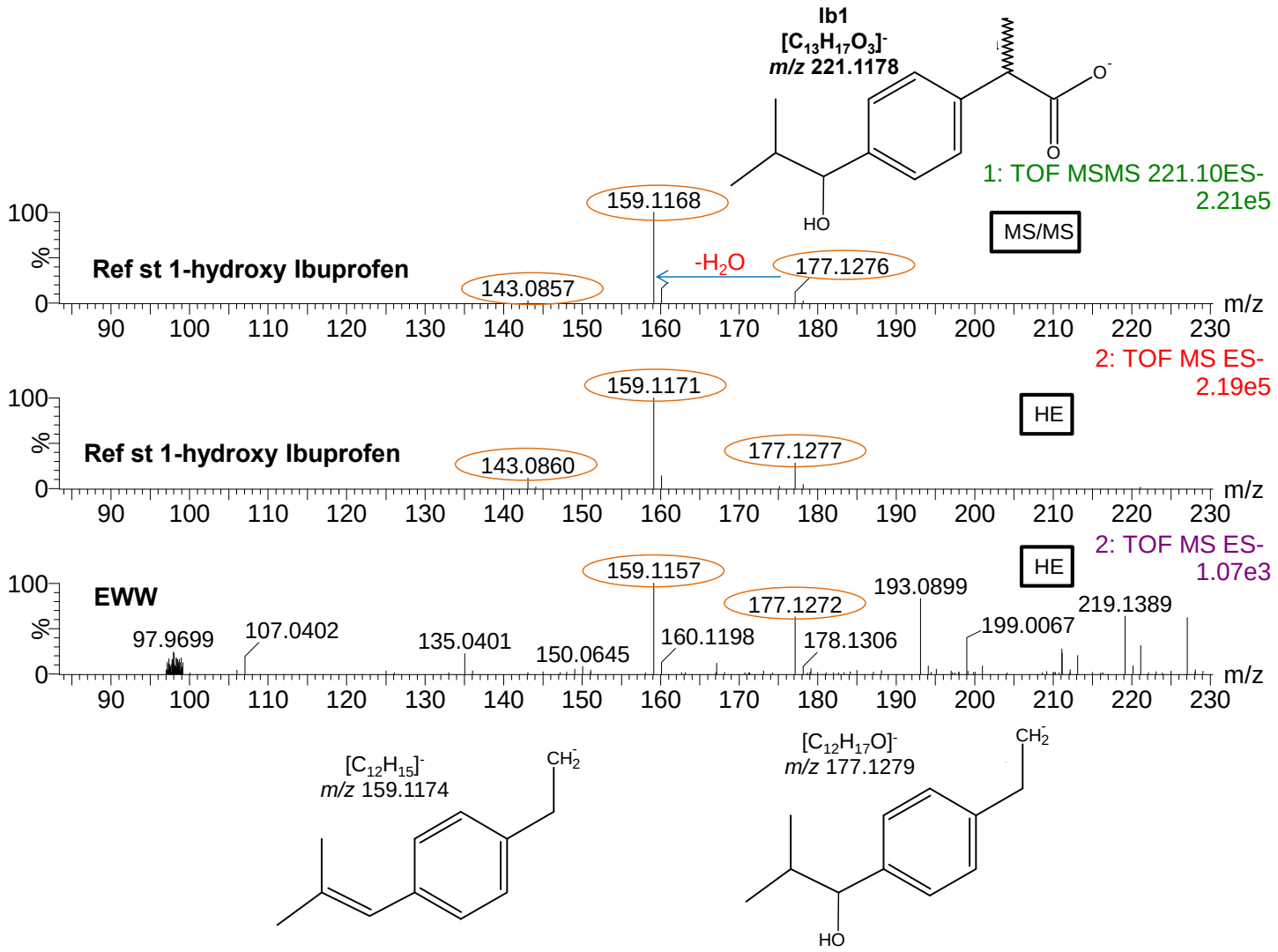
*1, 2, 3 and 4: possible hydroxylation sites

Figure 19SI. Elucidation of IbSW2c.



124

125 **Figure 20SI.** Elucidation of IbB4.



126

127 **Figure 21SI.** Elucidation of Ib1.

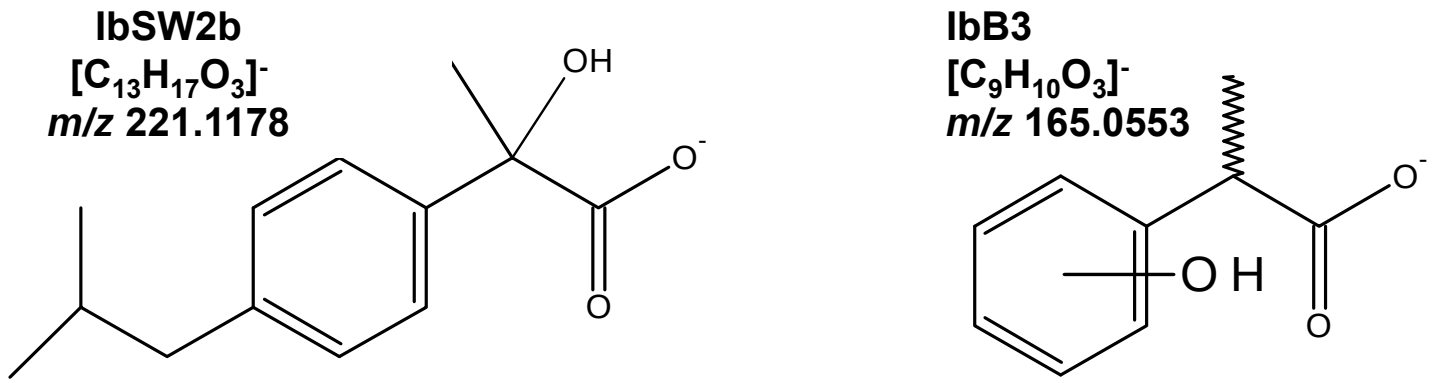
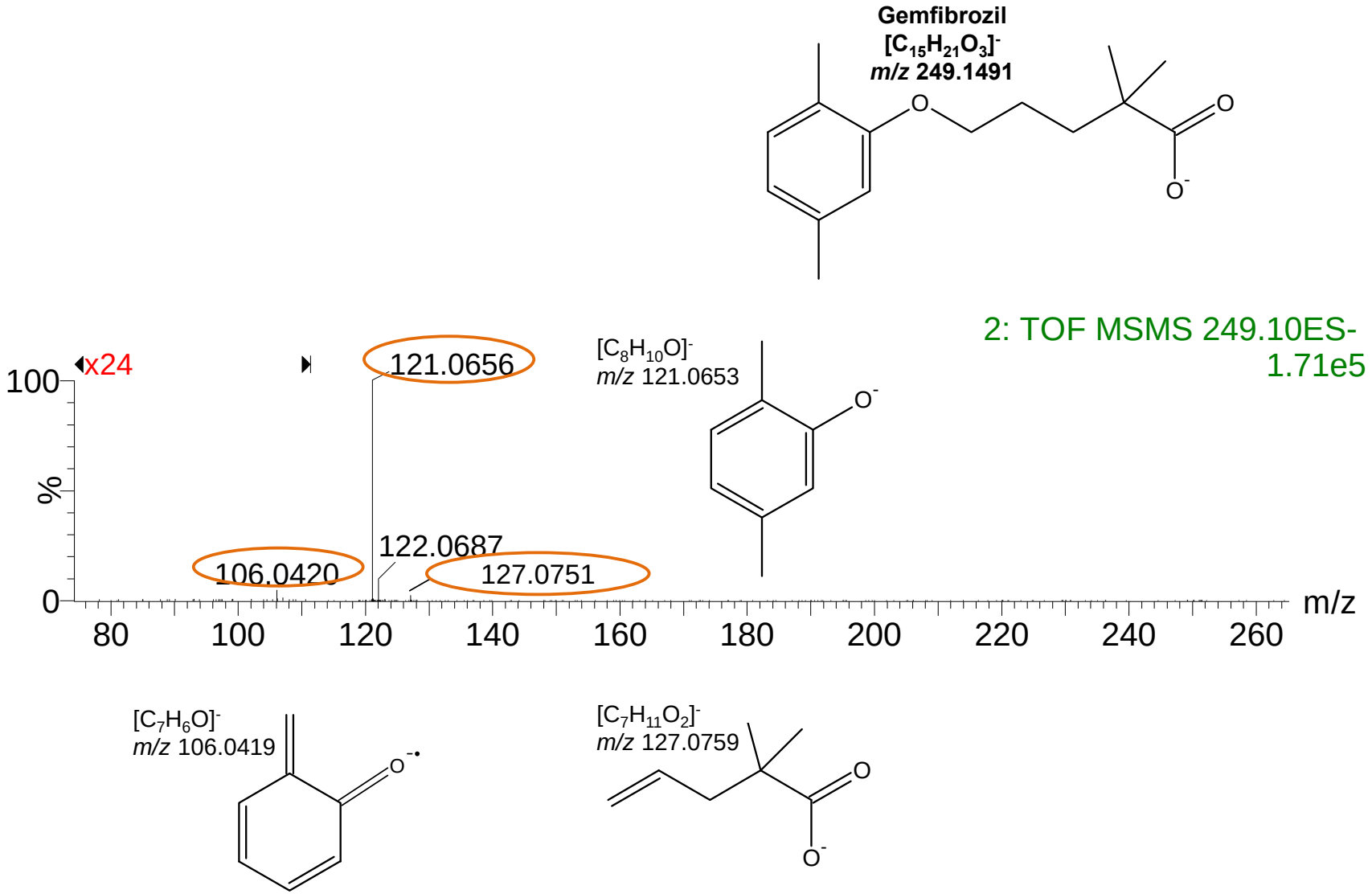


Figure 22SI. Elucidation of IbSW2b and IbB3.



143

144 **Figure 23SI.** Fragmentation pathway of gemfibrozil**.**

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