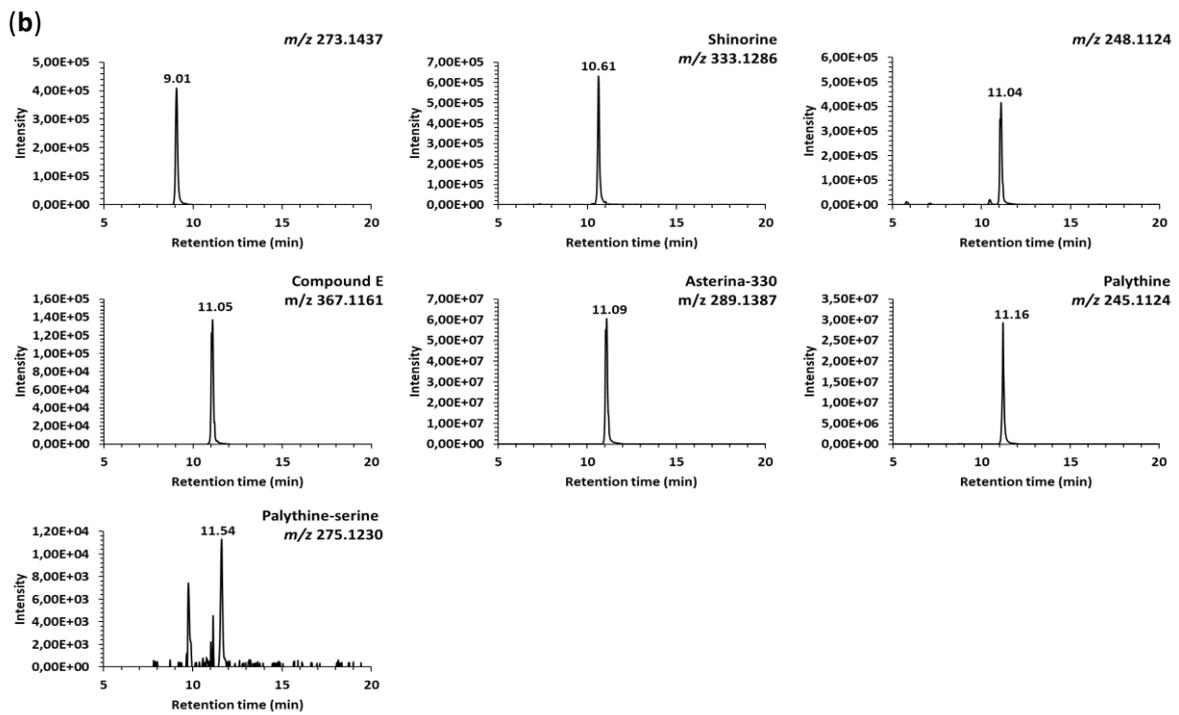
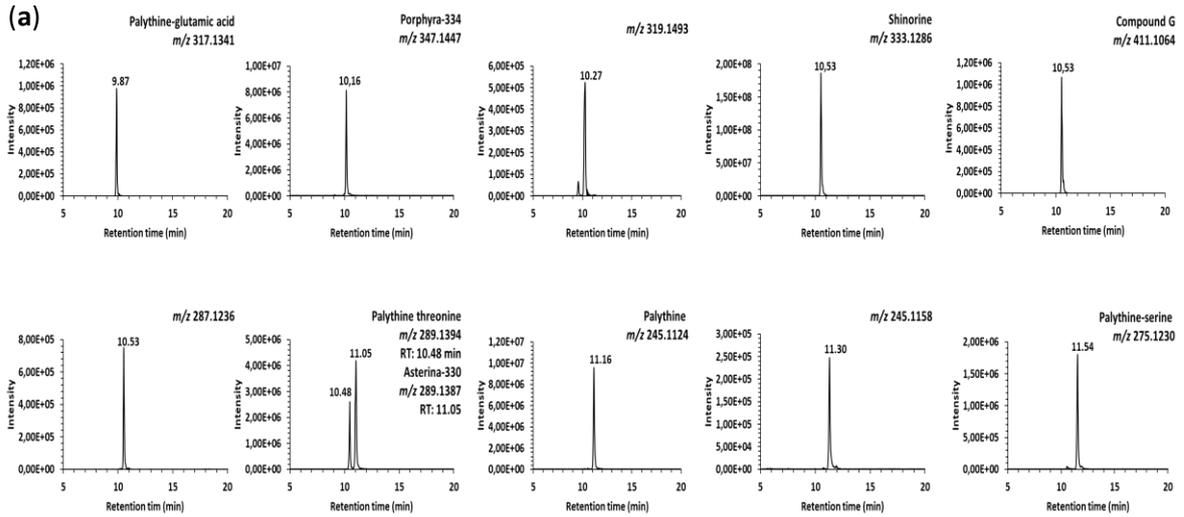
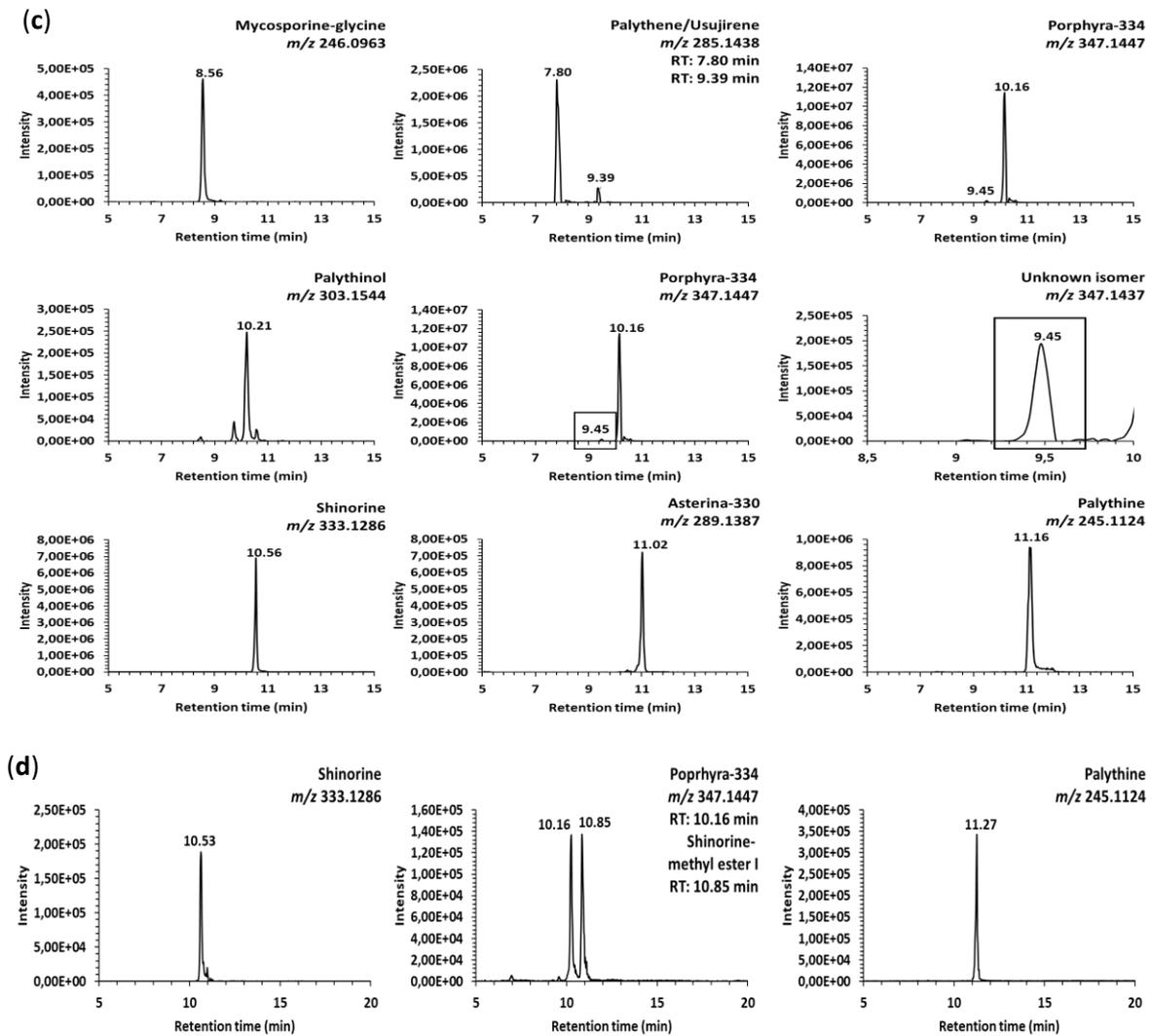
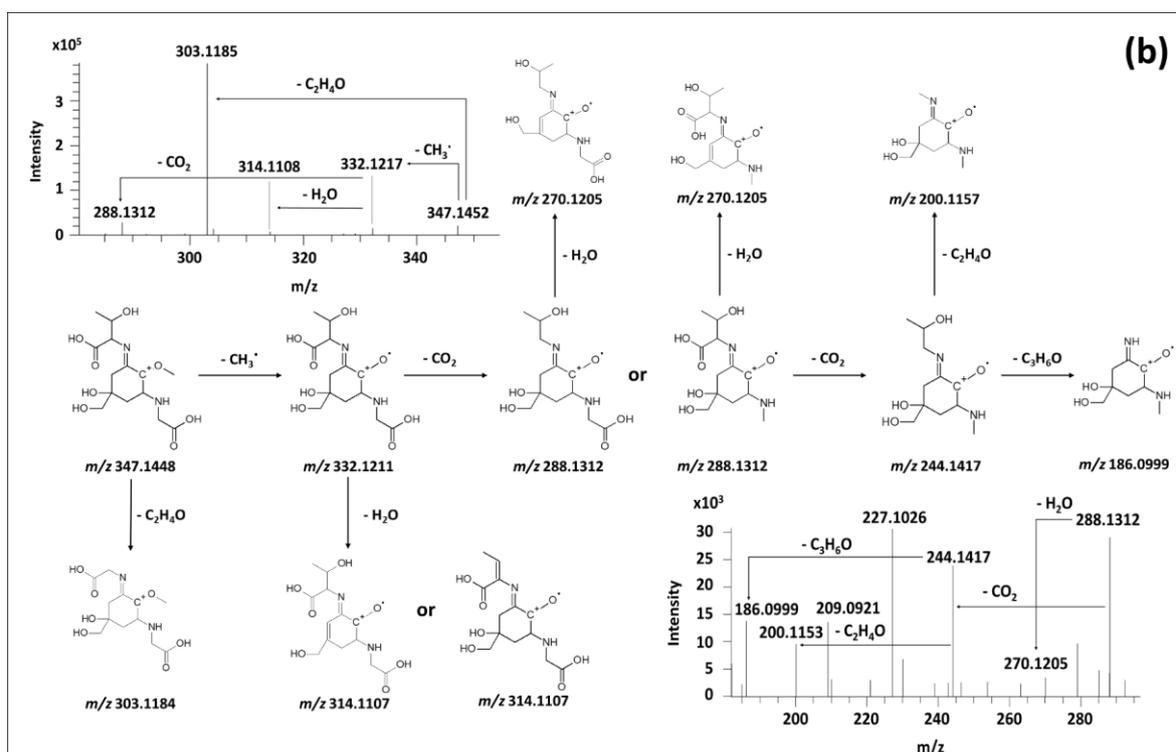
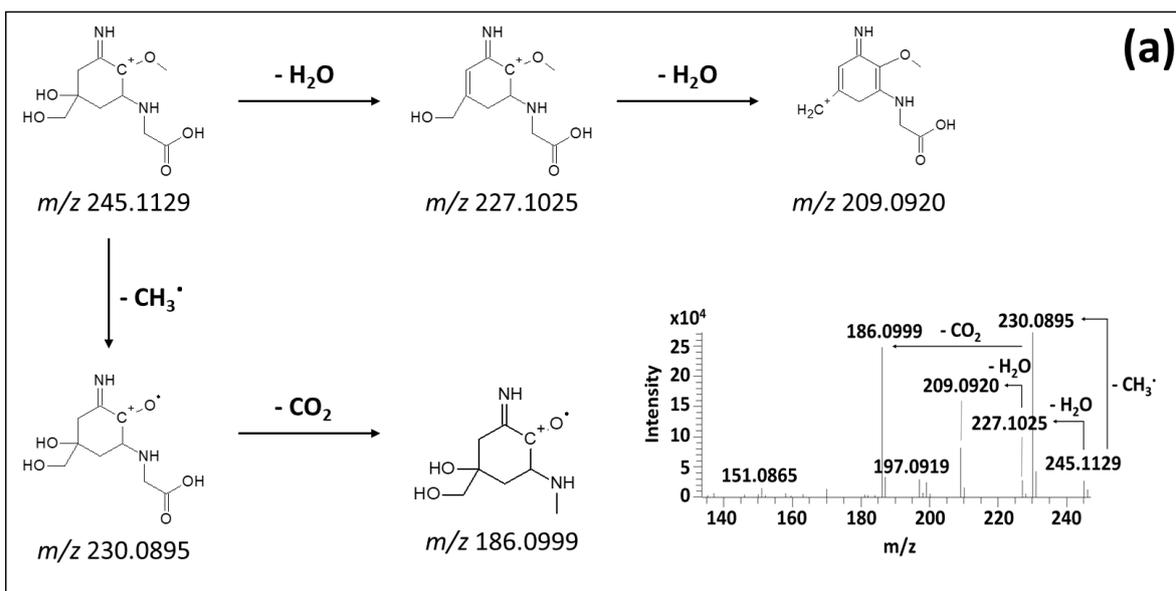


**Figure 1.** (a) MS method developed for targeted screening approach of MAAs. A Top3 MS<sup>2</sup> analysis was carried out to make the inventory of MAAs in the model algal extract *Gymnogongrus devoniensis*. Full MS Orbitrap (OT) settings: resolution 140000, mass range 150-500 m/z, dynamic exclusion 5 sec and intensity threshold 2e4. MS<sup>2</sup> scans settings: HCD50 resolution 60000, stepped collision energy 20, isolation width 2 m/z. For every detected mass, a FISH score was calculated to estimate the percentage of fragment ions generated in-silico matching with the collected spectral data. (b) Flowchart of the Targeted Screening Approach of MAAs using an Orbitrap MS based on the Top3 MS<sup>2</sup> analysis. Targeted workflow designed on Compound Discoverer™ to detect MAAs in the model algae matching with those listed in an in-house database. Description of the role of the following nodes: Find Expected Compounds. Research of compounds in the compound ion list provided by one or more Generate Expected Compounds nodes. Generate Expected Compounds. Generation of a list of m/z values for the expected compounds to find in the sample. The list includes the parent compound and its possible transformation products. Group Expected Compounds. Combination of chromatographic peaks on the basis of their chemical formula and retention times. FISH Scoring. Calculation of a score for compounds detected by the Find Expected Compounds node and annotation of the fragmentation spectra for these compounds.

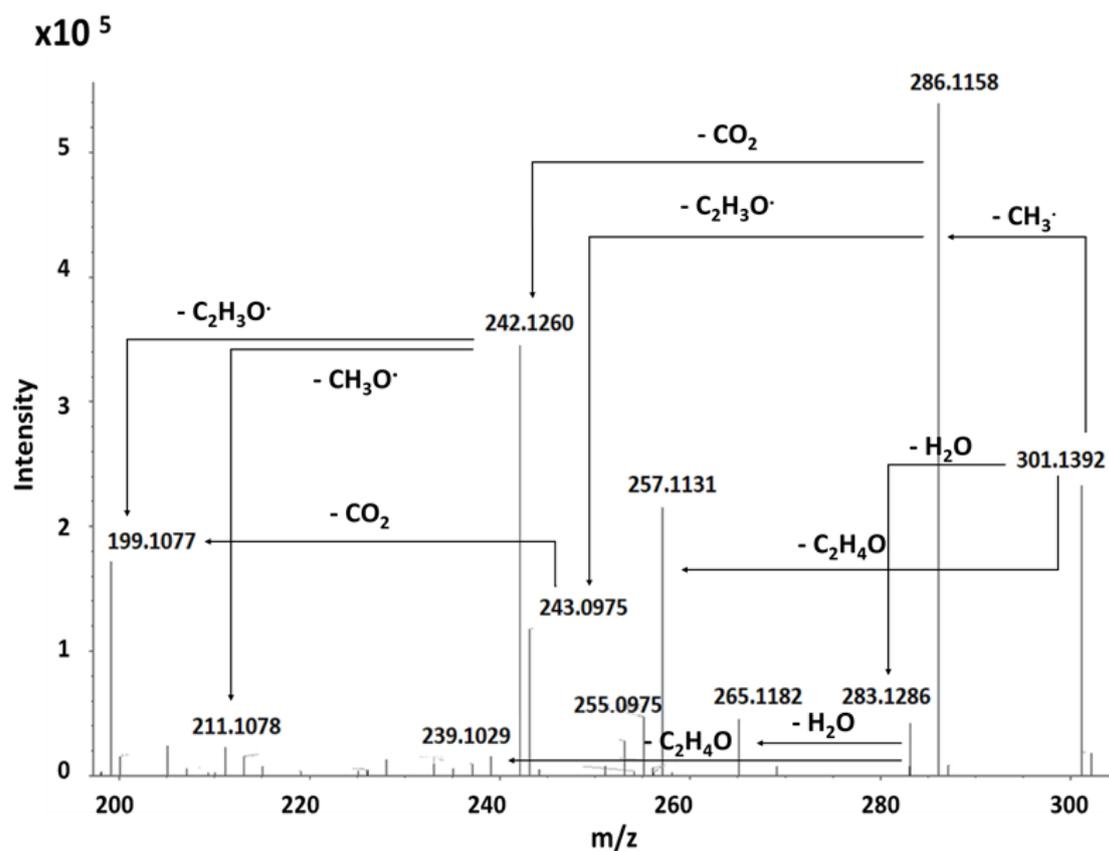




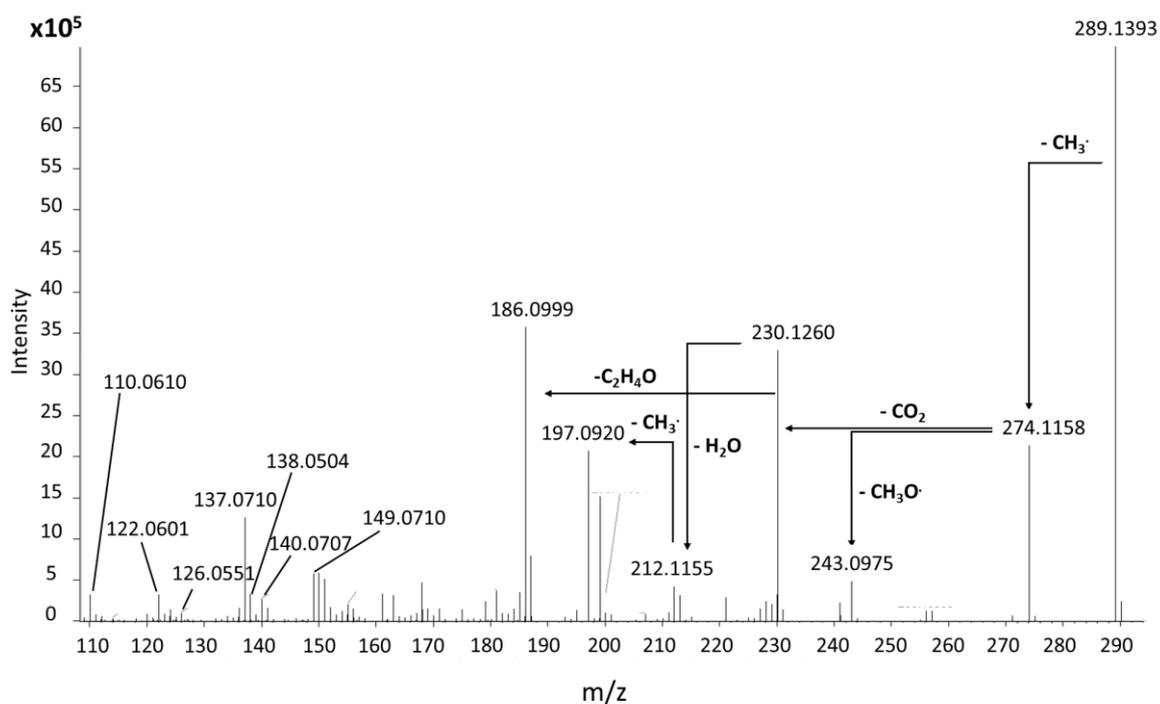
**Figure 2.** XIC of MAAs (3ppm) in *Porphyra rosengurtii* (a), *Gelidium sesquipedale* (b), *Halopithys incurva* (c) and *Cystoseira tamariscifolia* (d) separated on the Zic-chilic column. Note that in *Cystoseira tamariscifolia* extract, the XIC of  $m/z$  347.1447 displays two peaks among which the Porphyra-334 (RT : 10.16 min). The latter could correspond to the shinorine-methyl ester (RT : 10.85 min) with a FISH coverage of 73% calculated in targeted screening analysis. However, as the number of characteristic fragment ions was estimated at three, the MAA was not reported in Table 8, section 4.



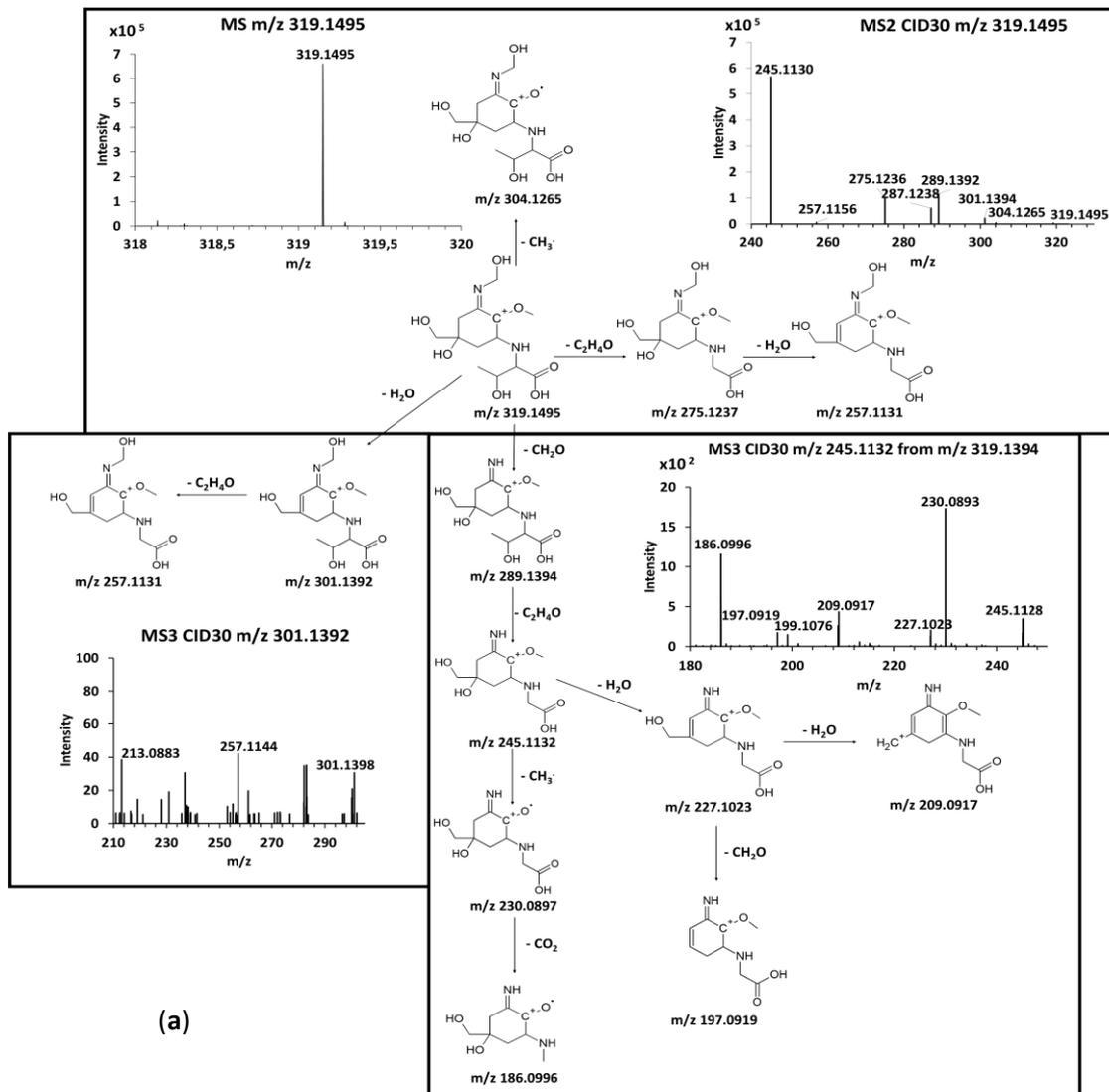
**Figure 3.** Fragmentation pathways of palythine (a) and porphyra-334 (b) obtained from their CID30 MS<sup>2</sup> spectrum.

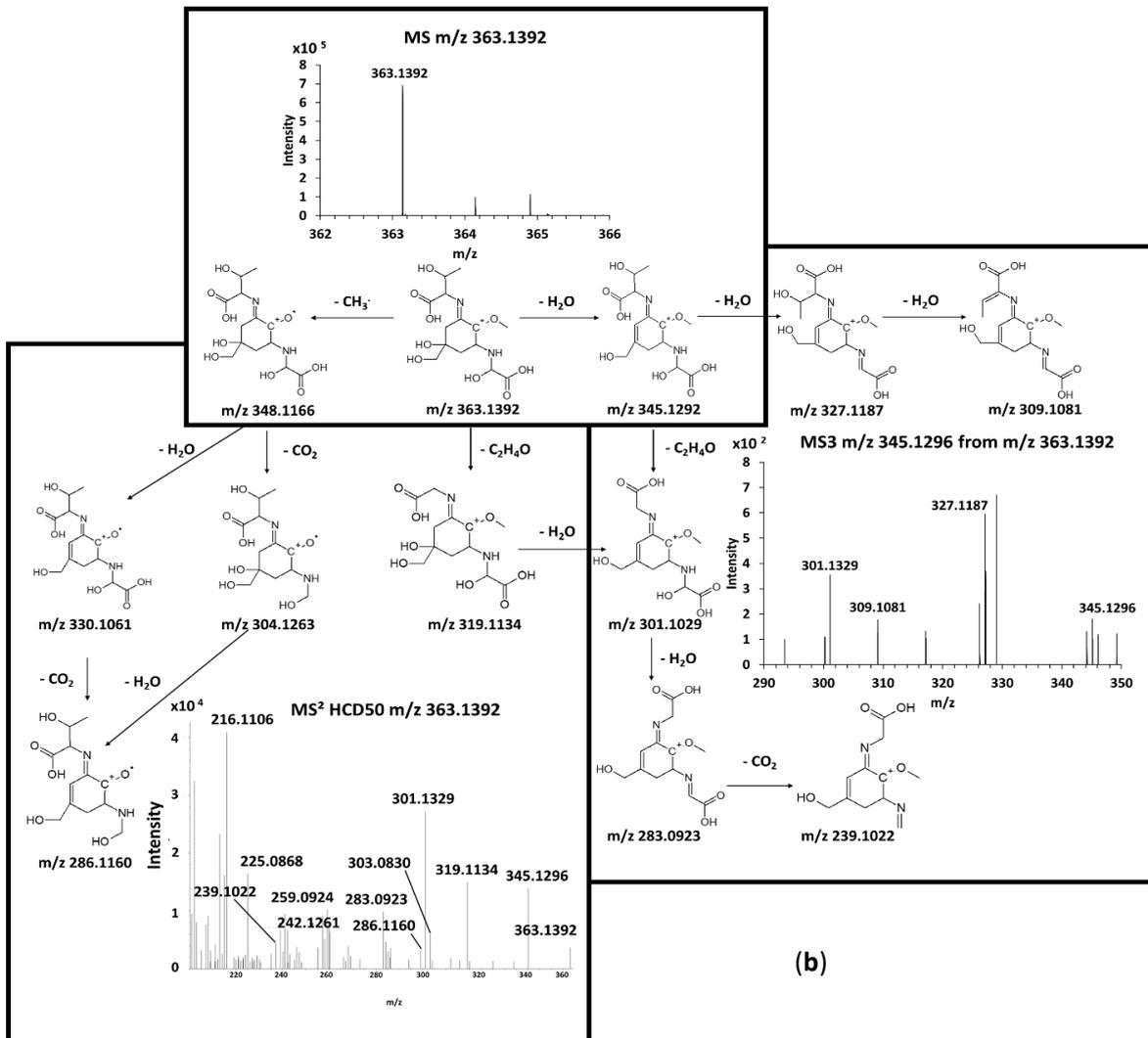


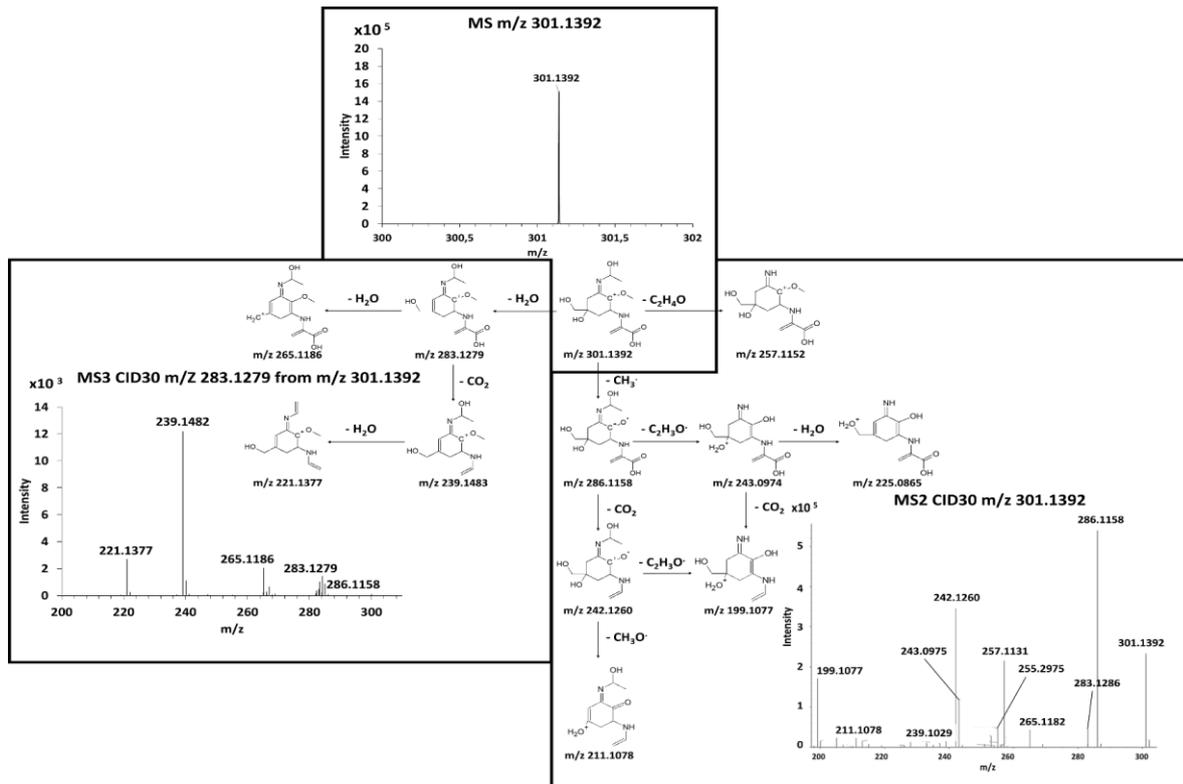
**Figure 4.** CID30 MS<sup>2</sup> spectrum of m/z 301.1392. Characteristic neutral and radical losses were annotated between the fragment ions affected on the spectrum.



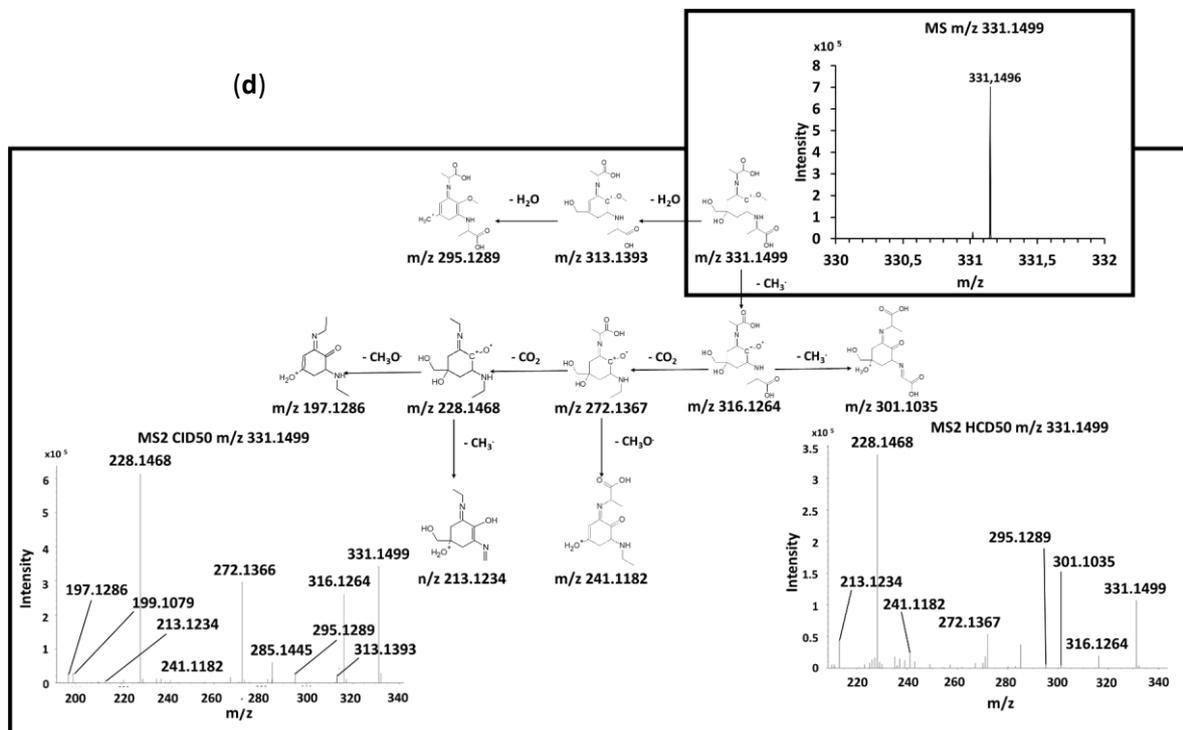
**Figure 5.** MS<sup>2</sup> spectrum of asterina-330 (m/z 289.1394) obtained in targeted screening analysis with a stepped collision energy at HCD50 +/- 20.



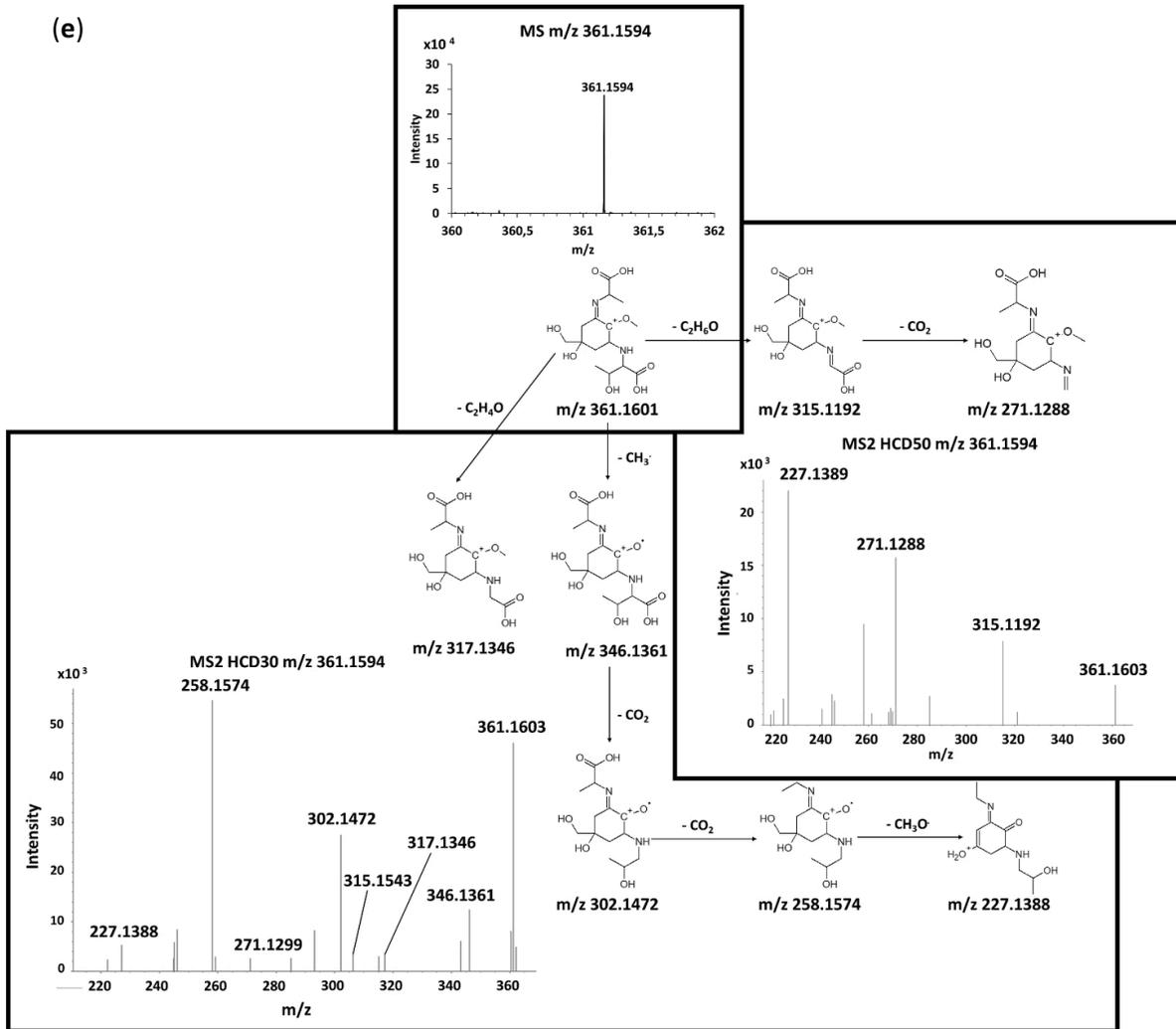


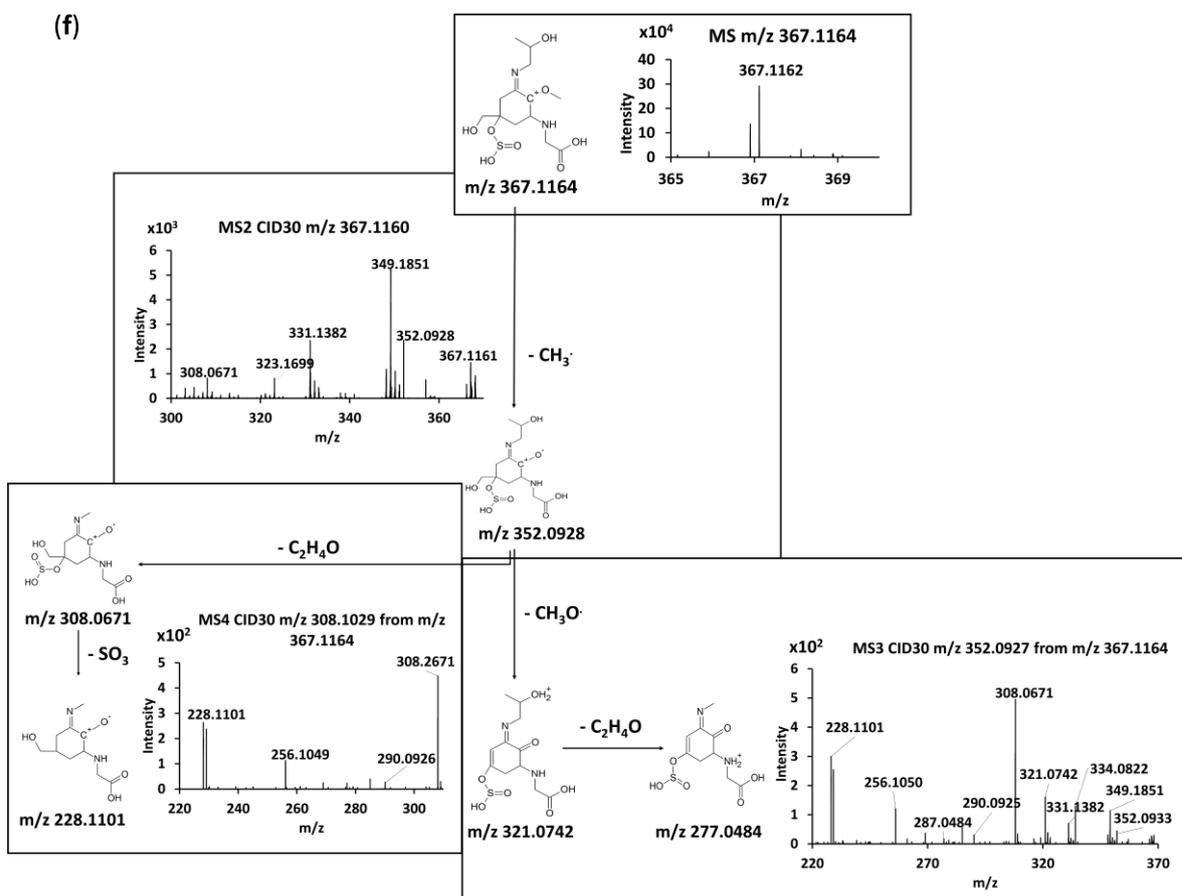


(d)



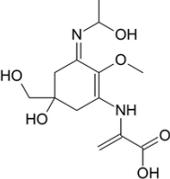
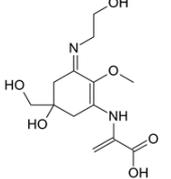
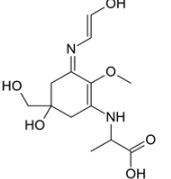
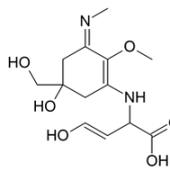
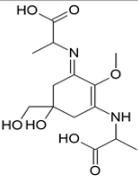
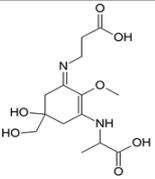
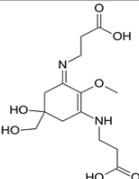
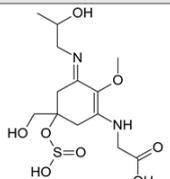
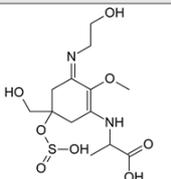
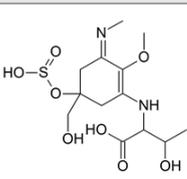
(e)





**Figure 6.** (a–f). Structural elucidation of six candidate-MAAs using ddMS<sup>2</sup> spectra obtained in untargeted analysis and their multistage fragmentation after fraction collection.

**Table 1.** Multiple structural predictions of three candidate-MAAs among the set of seven candidate-MAAs elucidated.

Compound A			
2-(((3Z)-5-hydroxy-3-((1-hydroxyethyl)imino)-5-(hydroxymethyl)-2-methoxycyclohex-1-en-1-yl)amino)prop-2-enoic acid	2-(((3Z)-5-hydroxy-3-((2-hydroxyethyl)imino)-5-(hydroxymethyl)-2-methoxycyclohex-1-en-1-yl)amino)prop-2-enoic acid	2-(((3Z)-5-hydroxy-3-((E)-2-hydroxyethylimino)-5-(hydroxymethyl)-2-methoxycyclohex-1-en-1-yl)amino)propanoic acid	(3E)-4-hydroxy-2-(((3Z)-5-hydroxy-5-(hydroxymethyl)-2-methoxy-3-(methylimino)cyclohex-1-en-1-yl)amino)but-3-enoic acid
			
FISH Score: 62%	FISH Score: 60%	FISH Score: 57%	FISH Score: 60%
Monoisotopic mass: 300.1321 Da [M+H] <sup>+</sup> m/z: 301.1392			
Compound C			
2-((E)-3-((1-carboxyethyl)amino)-5-hydroxy-5-(hydroxymethyl)-2-methoxycyclohex-2-en-1-ylidene)amino)propanoic acid	2-(((3Z)-3-((2-carboxyethyl)imino)-5-hydroxy-5-(hydroxymethyl)-2-methoxycyclohex-1-en-1-yl)amino)propanoic acid	3-((Z)-3-((2-carboxyethyl)amino)-5-hydroxy-5-(hydroxymethyl)-2-methoxycyclohex-2-en-1-ylidene)amino)propanoic acid	
			
FISH Score: 59%	FISH Score: 57%	FISH Score: 58%	
Monoisotopic mass: 330.1427 Da [M+H] <sup>+</sup> m/z: 331.1499			
Compound F			
(((3E)-5-(hydroxymethyl)-3-((2-hydroxypropyl)imino)-2-methoxy-5-(sulfinooxycyclohex-1-en-1-yl)amino)acetic acid	2-(((3Z)-3-((2-hydroxyethyl)imino)-5-(hydroxymethyl)-2-methoxy-5-(sulfinooxycyclohex-1-en-1-yl)amino)propanoic acid	3-hydroxy-2-(((3Z)-5-(hydroxymethyl)-2-methoxy-3-(methylimino)-5-(sulfinooxycyclohex-1-en-1-yl)amino)butanoic acid	
			
FISH Score: 60%	FISH Score: 59%	FISH Score: 50%	
Monoisotopic mass: 366.1096 Da [M+H] <sup>+</sup> m/z: 367.1169			