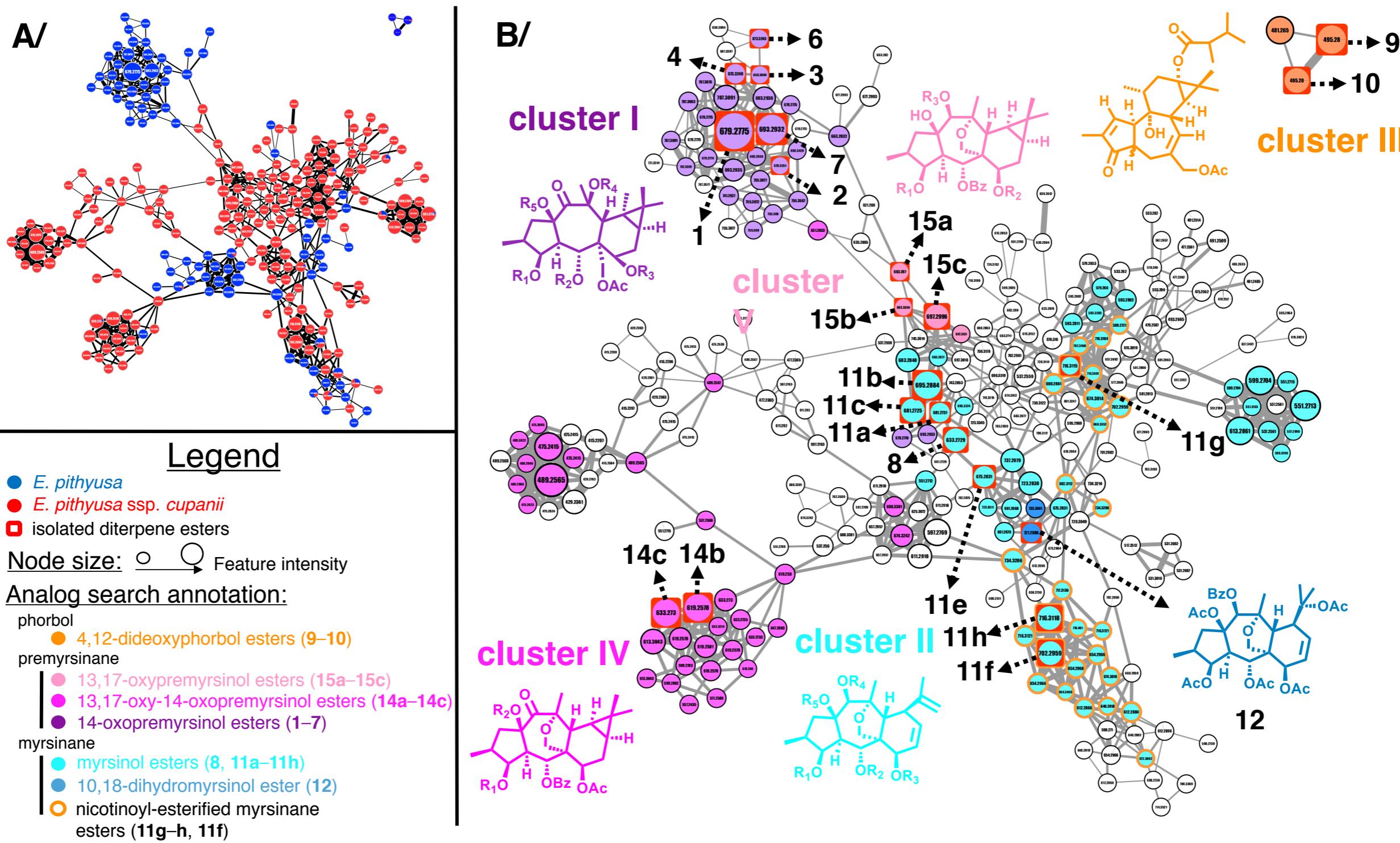


# Investigation of Premyrsinane and Myrsinane Esters in Euphorbia cupanii and Euphorbia pithyusa with MS2LDA and Combinatorial Molecular Network Annotation Propagation

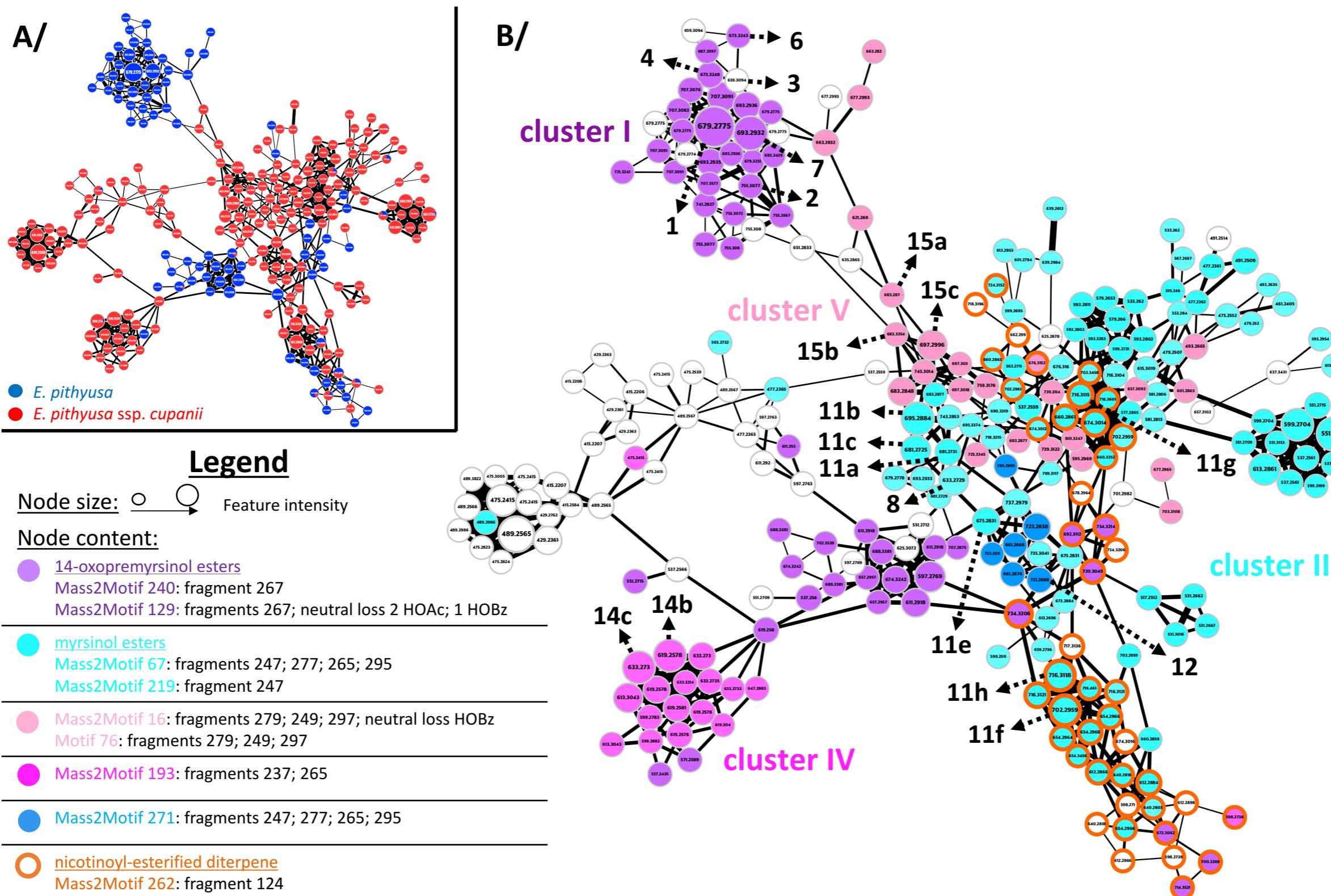
Manuscript figures in high-definition

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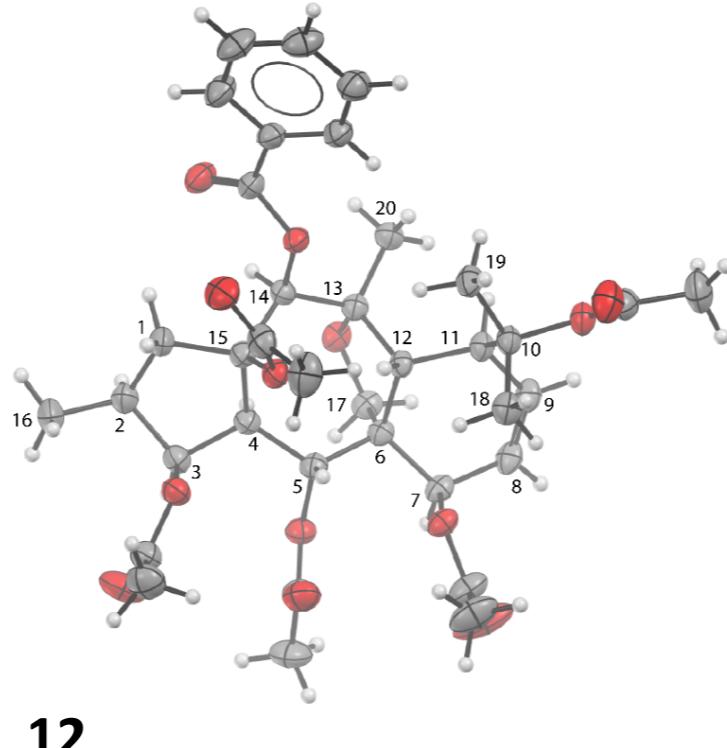
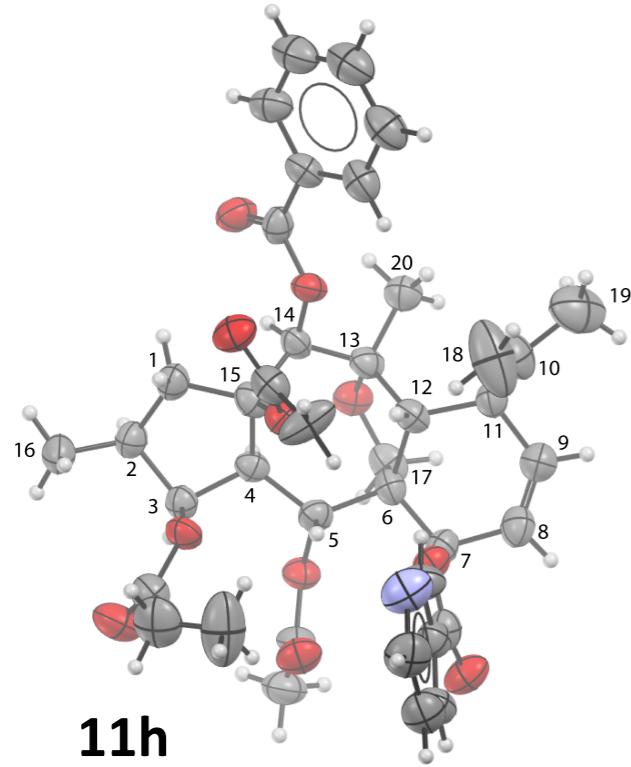
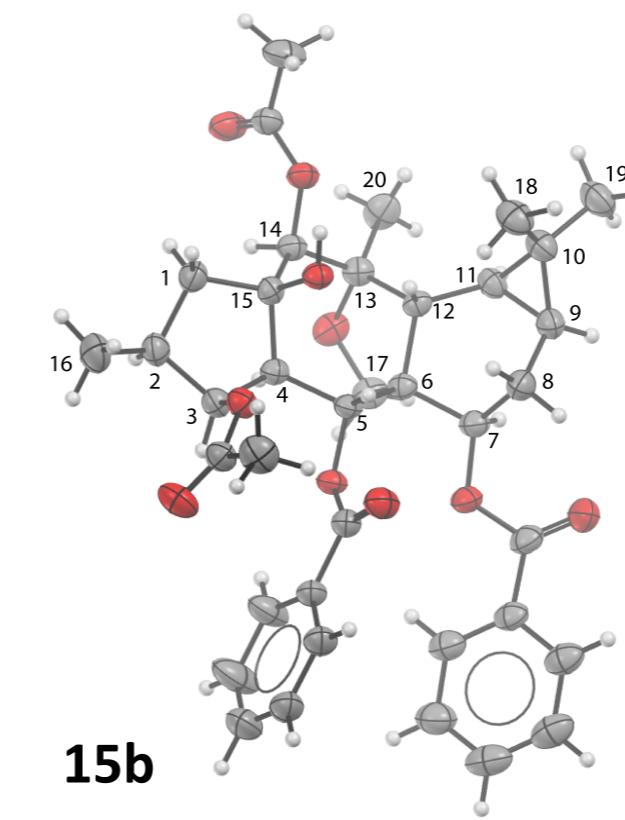
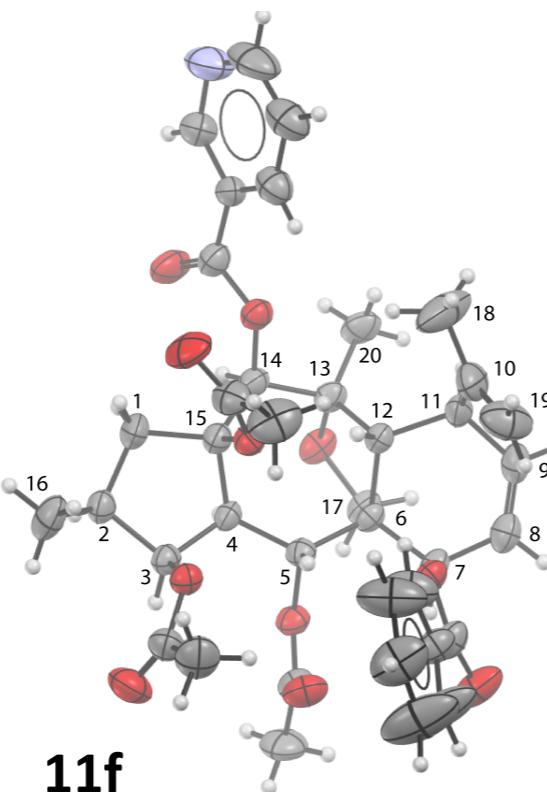
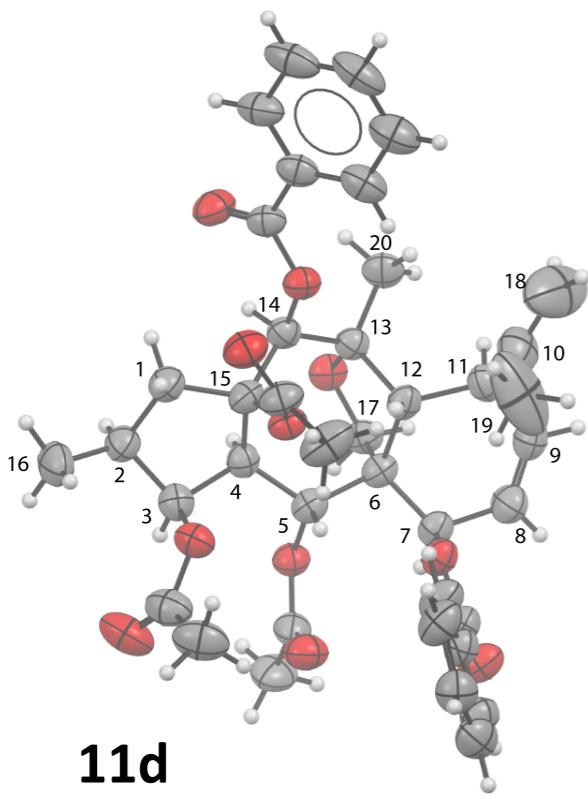
**Figure 1.** Euphorbia diterpene esters and tigliane molecular networks from extracts of two species. (A) Diterpene ester comparison between *E. pithyusa* (blue) and *E. cupanii* (red). (B) Analogue search and reference compound annotations with the previously isolated compounds (1–10) from *E. pithyusa* and the MN-guided isolated compounds from *E. cupanii* (11a–h, 12, 14b–c, and 15a–c) and their clustering (I–V).



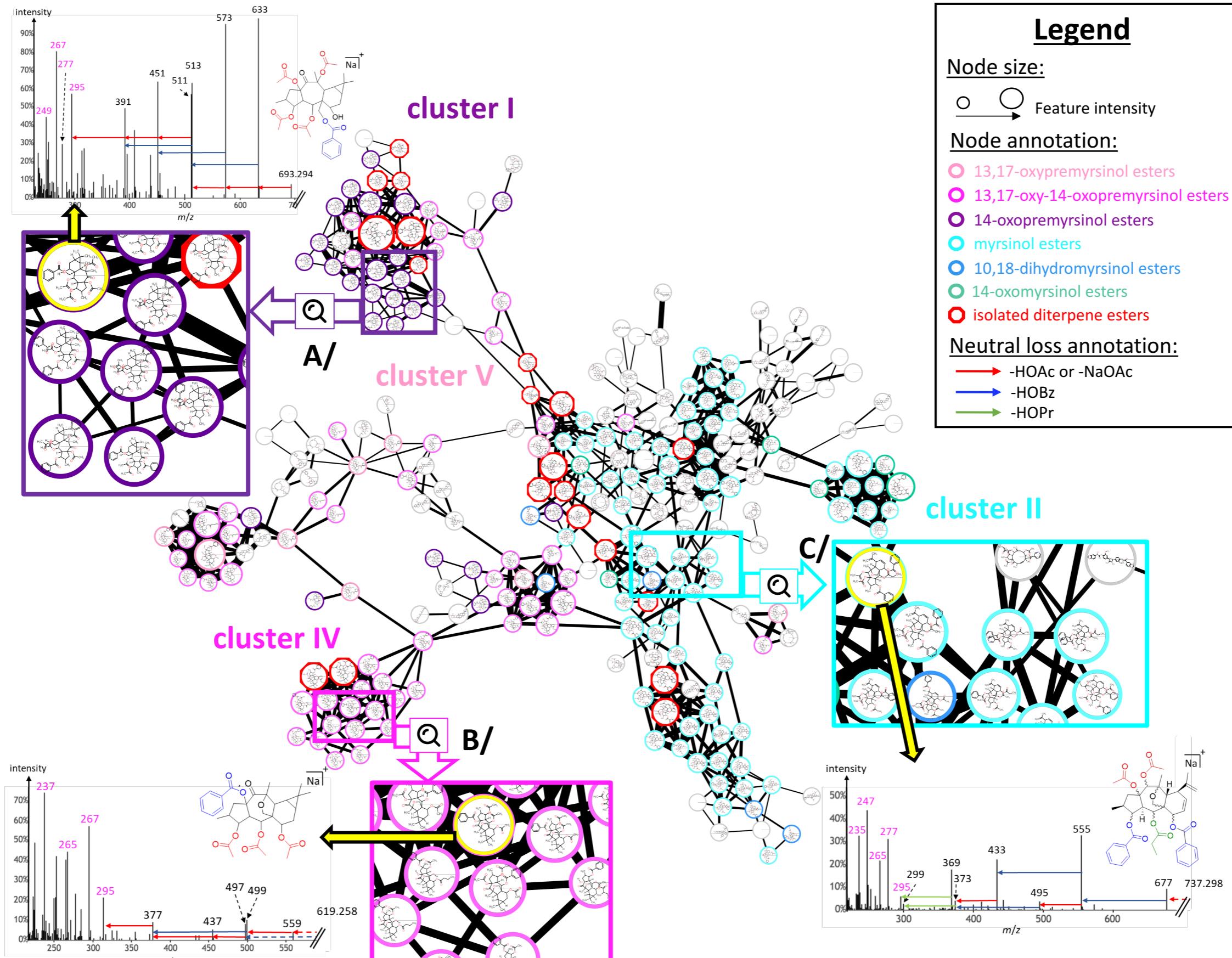
**Figure 2.** Figure 2. Euphorbia diterpene esters network from the extract of two species. (A) Diterpene ester comparison between *E. pithyusa* (blue) and *E. cupanii* (red). (B) Mass2Motifs annotation and their associated fragment ion(s) and neutral loss(es), generated with the MS2LDA Web app and visualized in Cytoscape.



**Figure 4.** ORTEP views of the X-ray structures of compounds 11d, 11f, 11h, 12, and 15b.



**Figure 6.** Diterpene ester molecular networks from *E. pithyusa* and *E. cupanii* samples, annotated with combinatorial network annotation propagation (C-NAP), using a combinatorial structure database (CSDB) of premyrsinane and myrsinane esters. The annotated spectra for the first rank structure (TOP1) proposed by C-NAP are presented for three nodes (boxes 6A–6C and Figures S19–S21, Supporting Information).



**Figure 7.** First rank (TOP1) structure annotation obtained with different scores (MetFrag, Fusion, Consensus, and Hybrid Fusion Consensus) with both NAP and C-NAP.

