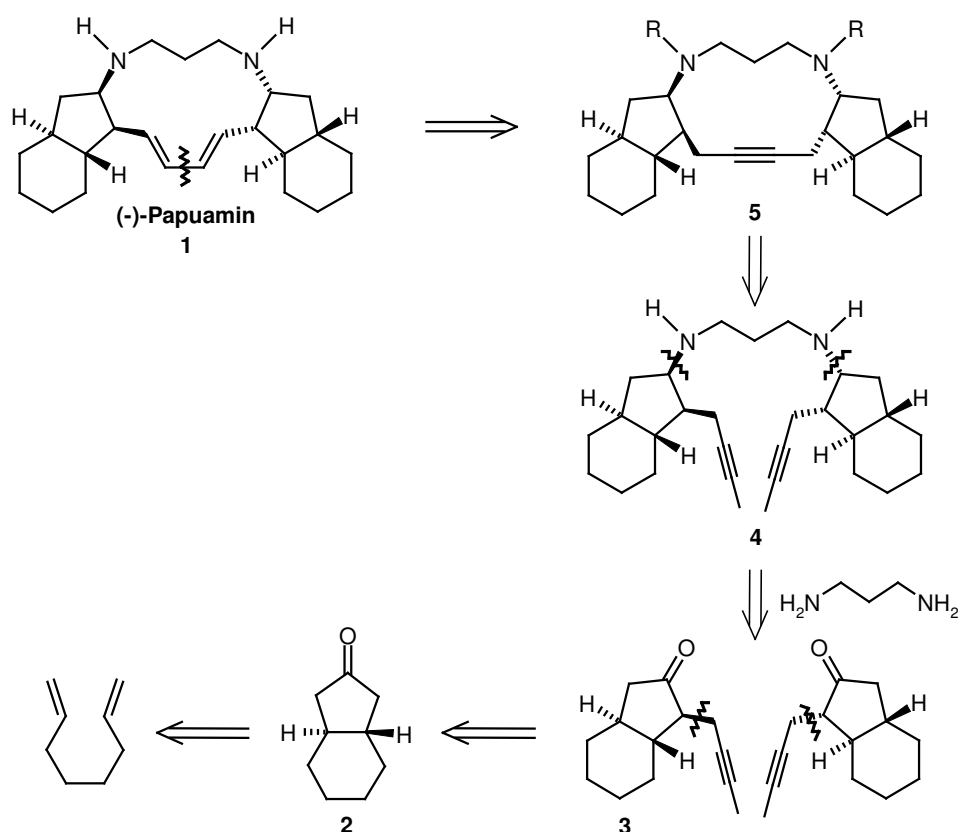


## Towards the Total Synthesis of (-)-Papuamine

(-)-Papuamine (**1**) is a  $C_2$ -symmetric, pentacyclic alkaloid isolated from the marine sponge *haliclona* sp..<sup>[1,2]</sup> It was found to inhibit the growth of different types of fungi such as *Candida albicans*, *Bacillus subtilis*, *Staphylococcus aureus* or *Trichophyton mentagrophytes* and is therefore among the most promising new fungicides.<sup>[3]</sup> Because of its interesting structure and its biological activity, we choose this natural compound as a synthesis target.

The starting point in our synthetic approach is 1,7-octadiene, which is transformed to *trans*-perhydroindan-2-one (**2**) in an one-pot cyclozirconation-carbonylation sequence.<sup>[4]</sup> Formation of the SAMP-hydrazone<sup>[5]</sup> followed by alkylation leads to a separable mixture of diastereoisomers **3**. The synthesis continues with a double reductive amination and protection of the secondary amine groups. One of the key steps in our synthesis is the ring closing alkyne methathesis (RCAM)<sup>[6]</sup> of **4**, which gives access to macrocycle **5** in good yields. A base-catalysed isomerisation of the triple bond<sup>[7]</sup> to the desired *E,E*-diene (or other two step procedures to the diene) and deprotection of the amine groups should complete the synthesis to (-)-Papuamine (**1**). These last steps are presently under investigation.



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