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Asymmetric Synthesis and Biological Study of Suberosanes

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Abstract : Suberosanes are a small group of marine natural sesquiterpenes discovered since 1996 by Boyd, Sheu and Qi from three gorgonians. Their skeleton was previously found in quadranes produced by the terrestrial fungus Aspergillus terreus. Up to date, eleven suberosanes are described from which (-)-suberosanone and (-)-suberosenol A are reaching the picomolar cytotoxicity level on human solid tumors cell lines. Due to their impressive cytotoxic properties and their limited availability, we undertook an asymmetric synthesis of the most active members of this family in order to get insight into their absolute configurations and their biological properties. The challenge of their synthesis is the regio- and stereoselective elaboration of the compact bridged tricyclic skeleton with up to five all adjacent asymmetric centers, including a central quaternary carbon one. Our strategy is based on an aza-ene-synthesis key step which is regio-and stereo-controlled by the choice of a chiral amine enantiomer. it approach is concise and flexible, the enantiopur ABC tricyclic intermediate that have been synthesized being the common precursor of suberosanes.

Keywords : suberosanes, asymmetric synthesis, sesquiterpenes, quadranes
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