

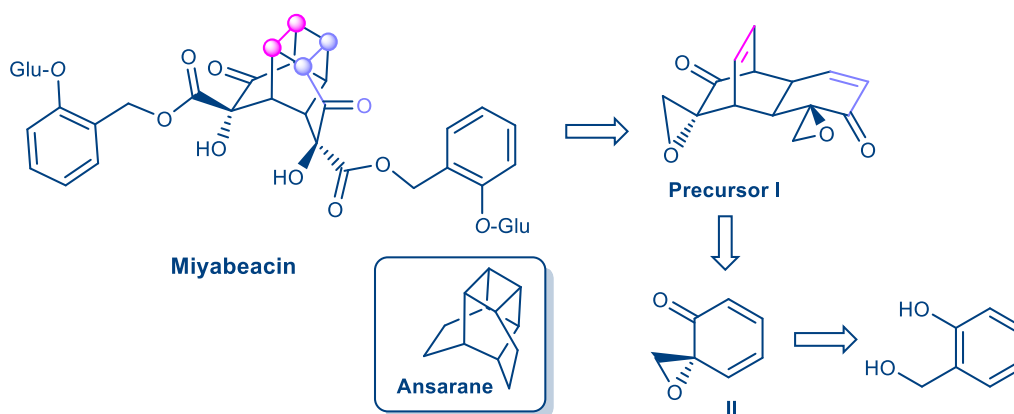
Ph-D Proposal 2023 – ED Chimie 206

Total synthesis of Miyabeacin – Synthèse totale de la Miyabéacine

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Context: Willows divided into 1500 different species are an important source of bioactive compounds, including of course, salicylic acid and its derivatives. Recently, Miyabeacin was isolated from *Salix miyabeana*. This molecule can be considered as a salicinoid dimer with a rare ansarane subunit.^[1] Its biological properties have been evaluated and it appears active against various cancers of breast and oesophagus.

Project: Due its properties and the presence of the non-usual ansarane skeleton, this molecule represents a target of choice in total synthesis. The formation of the two four-membered rings could be achieved by an intramolecular [2+2] cycloaddition from enone I. This precursor will be easily reached by taking advantage of a Diels-Alder reaction between two identical fragments II.^[2] The opening of the two oxirane entities of the cycloadduct should provide an access to a tetrol derivative. After oxidation, the resulting diacid will possess the core structure of the target molecule. Post-fonctionnalisations (esterifications, amidations, ...) will be conducted to reach I and to create a library of analogues that can be further tested thanks to the internal Chimiotek of the research unit. The same precursor I will be implicated into new tandem processes including radical cyclization to reach original polycyclic structures.

Candidate profile: The candidate should have a strong background in organic chemistry (M2 degree) and characterisation methods (NMR) and a high level of dynamism and enthusiasm. No experience in photochemistry and radical chemistry are required.

[1] J. L. Ward et al. 2] *Scientific reports* **2020**, *10* : 6477.

[2] M. Bergner, D. C. Duquette, L. Chio, B. M. Stoltz *Org. Lett.* **2015**, *17*, 3008-3010.