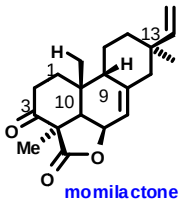
Avec le soutien de :

POSTDOCTORAL POSITION AVAILABLE IN ORGANIC SYNTHESIS FROM UNIVERSITY OF STRASBOURG

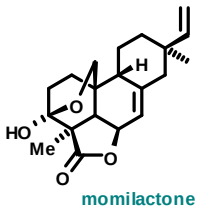
Total synthesis of momilactones A and B (MOMI-SynTot)

Context and project summary

Plants that are attacked by pathogenic microorganisms respond with a variety of defense reactions. One such reaction is the production of phytoalexins and the most active rice phytoallexin was determined as momilactone B. Momilactone A was also found in all culture solutions, but seems to be less active. These allelochemicals initially known as antibiotics are considered now as useful compounds in chemoprevention or therapy of different cancers (colon, breast, blood cells) and recently in the **frame of cancer stem cells inhibition**.



momilactone A



momilactone B

No total synthesis of these important diterpenoids has been described so far. Just the synthesis of the racemic form of momilactone A has been described by Deslongchamps a few years ago.

Therefore different goals are pursued in this first total synthesis i) Access to intermediates in order to target the pharmacophoric core. ii) Development of a diastereoselective Diels-Alder reaction **using new enantiopure sulfinylquinones as dienophiles** iii) **an unprecedented transition metal-catalyzed intramolecular cyclization** stereoselectively forming a quaternary stereogenic center**.** iv) **the preparation of analogues** which are not available by

chemical modifications of the natural products for medicinal chemistry purpose and a better understanding of their anticancer activity. The biological activity of these intermediates (precursors) will be evaluated by biologists in the frame of European networks: COST action CM 1407 with the aim of developing innovative multi-targeted cancer therapies and COST action CA 15135. In collaboration with NAMEDIC (Namur Medicines and Drug Innovation Centre, http://www.namedic.be), modern technologies such high pressure within flow chemical setups, microwave chemistry and mecanochemistry will be examined in the course of this total synthesis.

Candidate profile

The purpose of this post-doctoral project will be to actively contribute to the first total synthesis of momilactones A and B in collaboration with a PhD student based at the laboratory of organic synthesis, university of Namur, Belgium (https: //directory.unamur.be/staff/slanners). The candidate will be firstly involved in the development of the transition metal-catalyzed intramolecular cyclization stereoselectively forming the quaternary stereogenic center which is a structural feature of pimirane diterpenes with a lack of a general strategy for its construction. In this context, we are inviting applications from **highly motivated organic chemists** with a strong background in organic chemistry, transition metal catalysis and structural analyses (NMR, MS). Skills and experience in flow chemistry or mecanochemistry would be an advantage but are not a pre-requisite.

The post-doc will start in 2017, for a period of 18 months. The contract will be signed with ICFRC (International Center for Frontier Research in Chemistry) and the university of Strasbourg.

The net salary will be around 2 300€/month.

Application / Submission

Please send a CV, a motivation letter and two recommendation letters to Gilles Hanquet **ghanquet@unistra.fr** and Sabine Choppin **sabine.choppin@unistra.fr**

Deadline for submission of applications: 2016, December 31th

The successful candidate will be hosted in the laboratory of synthesis and catalysis directed by Pr. F. Colobert (www.syncat.org) ECPM Strasbourg, France

(Laboratoire de Chimie Moléculaire (UMR 7509) Website : http: //ecpm.unistra.fr/recherche/laboratoire-de-chimie-moleculaire-umr-7509/