

Sujet de stage de Master 2

Laboratoire : Département de Chimie Moléculaire

Directeur : Didier Boturyn

Intitulé de l'équipe : SeRCO

Responsable : Jean-François Poisson

Nom et Qualité du Responsable du Stage : Sébastien Carret (Mcf)

HDR oui

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Parcours de Master 2 : Organic Synthesis (SOIPA)

Titre du sujet : THIOIMIDATES chemistry : synthesis of (-)cephalotaxine and alcaloid derivatives

Objectifs visés du stage :

Development of an enantiopure access to the Harringtonine alkaloids family.

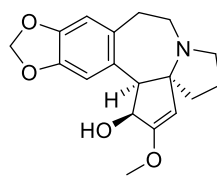
Intérêts pédagogiques et compétences visées :

Reactions under anhydrous conditions. Multistep synthesis. Purification and characterization/analytical techniques. Bibliographic research.

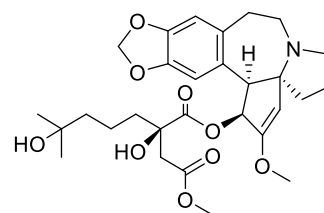
Résumé :

For the past years, chemists have been interested in Homoharringtonine, a natural cephalotaxine ester, a potent antileukemic compound used therapeutically, especially for leukemias resistant against tyrosine kinase inhibitors. These alkaloids of the harringtonine family are extracted from Cephalotaxus, evergreen trees from southern China characterised by an extremely slow growth and currently in extinction. Their synthetic preparation thus becomes essential for clinical studies.

Recently, our team has achieved the total synthesis of (+)-Kirkine which is an alkaloid from the Lycorine family, thanks to the preparation of an uncommon sulfinylthioimidate intermediate. The objective of this internship is to explore the reactivity panel of this new intermediate and develop a concise synthesis of (-)-cephalotaxine to avoid extraction.



(-)-cephalotaxine



(-)-homoharringtonine
 $Cl_{50} = 0.017 \mu\text{M}$ (P388)

Approches & matériels utilisés:

The student will use most of the techniques in organic synthesis (inert atmosphere, low temperature, small quantity reaction), as well as numerous analytical methods to determine the structures of the compounds obtained (NMR, supercritical CO₂ HPLC, UHPLC-MS, Mass). The student will develop flow reaction conditions.

Domaines de compétences souhaitées du candidat:

Good level in organic chemistry, experience in separation techniques and analysis methods; use of bibliographic databases.

Dates du stage : January – June 2023