

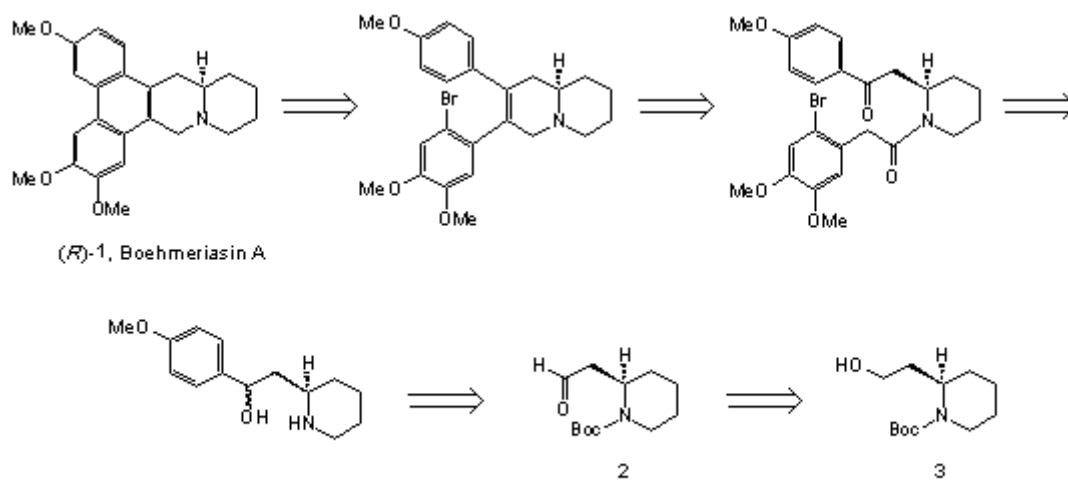
## WORK PLAN

Angiogenesis is a fundamental process in reproduction and wound healing. Under these conditions, neovascularization is tightly regulated. Unregulated angiogenesis may lead to several angiogenic diseases (rheumatoid arthritis, diabetic retinopathy, juvenile hemangiomas) and is thought to be indispensable for solid tumor growth and metastasis.

The phenanthroizidines alkaloids are natural products with a pentacyclic skeleton, a phenantrene ring fused to a saturated N-heterocycle generally an indolizidines or quinolizidines. This family includes close to 70 structurally related models that exhibit interesting biological properties, especially profound cytotoxic activity, and have shown to provide other medicinal benefits including mitotic, antileukemic, antibacterial and antibiotic activities. As a consequence of their promising biological profile, coupled with their low natural abundance and unusual architecture, the phenanthrolizidine alkaloids have engendered an impressive number of synthetic studies for the purpose of fundamental research and drug development.

In this STSM, I am suggesting the synthesis of Boehmeriasin A (1) and the future biological evaluation of its antiangiogenic activity. The synthesis will start from the conversion of the ethanpiperidine **3** to the corresponding aldehyde **2** which acts as nucleophile acceptor with the appropriate Grignard reagent (Scheme 1). The synthetic scheme will take into consideration also intramolecular crotonic condensation and radical cyclization mediated by AIBN and  $\text{Bu}_3\text{SnH}$ . After the completion of the batch synthesis I will try to apply the synthetic scheme using Flow Chemistry in order to avoid all the disadvantages of the batch synthesis.

Furthermore, I will have the possibility to learn the use of the particular instrument which is used in Flow Chemistry and can be provided by Professor .....at the University of .....and also to learn the new technology of Flow Chemistry.



**Scheme 1.** Retrosynthetic analysis of Boehmeriasin A (**1**).