PEOPLE

MARIE CURIE ACTIONS

Intra-European Fellowships (IEF)

Call: FP7-PEOPLE-2009-IEF

Asymmetric Organocatalysed Diels-Alder/Fragmentation Cascades

"ASODAFCA"

Asymmetric Organocatalysed Diels-Alder/Fragmentation Cascades

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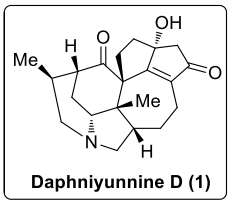
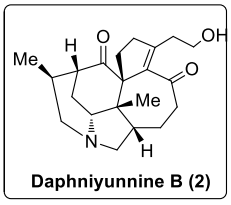
1: WORK PROGRESS AND ACHIEVEMENTS DURING THE PERIOD:

INTRODUCTION

Our proposal is based on the development of the intramolecular Diels-Alder reaction of 2-amino-furan derivatives (IMDAF) as powerful tool for the quick synthesis of complex polycyclic compounds related to the Daphnyphillum family, in particular Daphniyunnine D. This molecule, first isolated in 2006 from Daphniphyllum yunnanense,[1] presents an interesting anti-cancer activity (IC50 0.6μg.mL-1 against A-549 cell lines) and has never been synthesised.

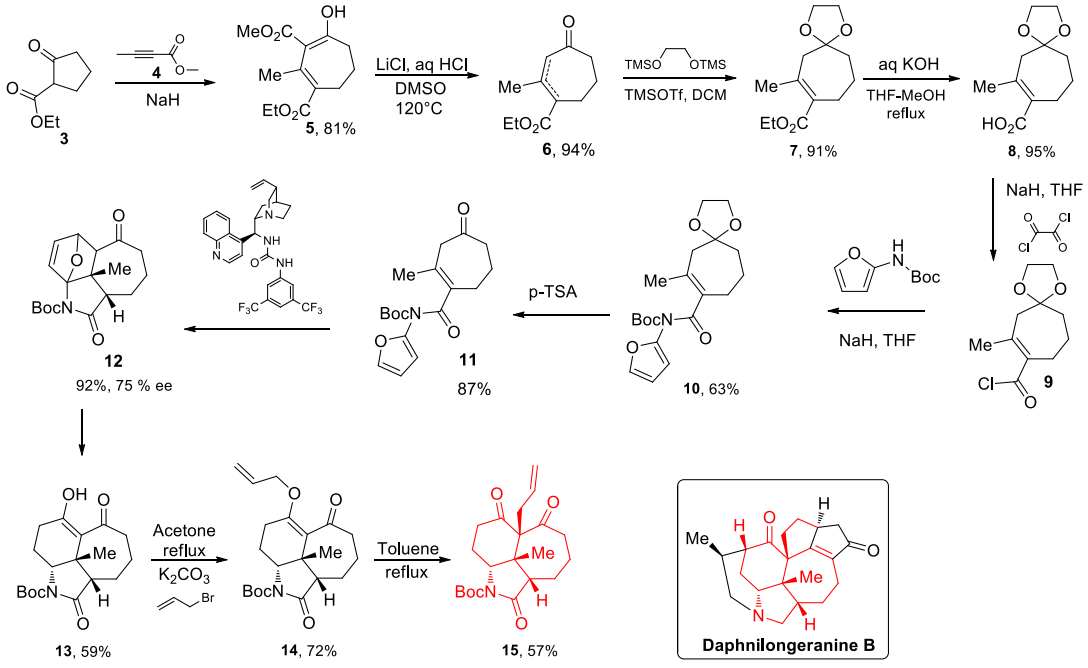




RESULTS

Intramolecular Furan-Diels Alder route to the core of Daphniyunnine D

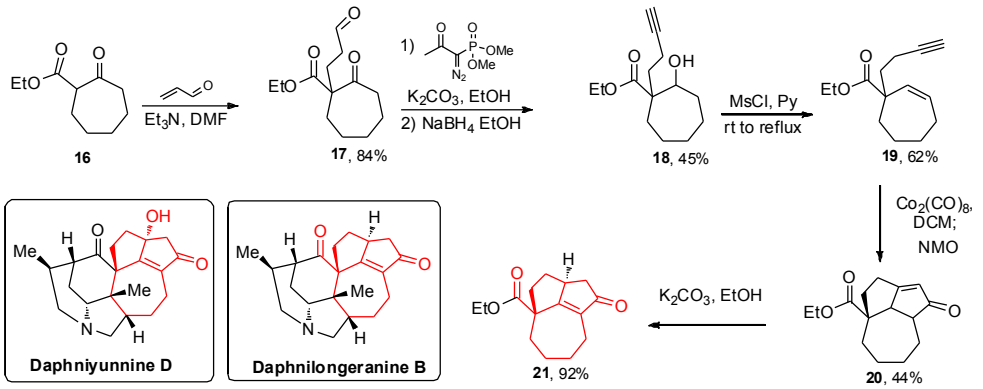
An enantioselective route to the functionalized core of daphniyunnine D has been developed using a newly developed enantioselective intramolecular Diels Alder of tethered furans as proposed in ASODAFCA. The synthetic synthetic sequence is currently being investigated in the Dixon laboratories in order to achieve the first total synthesis of this natural product..



[1] Zhang, H.; Yang, S.-P.; Fan, C.-Q.; Ding, J.; Yue, J.-M. *J. Nat. Prod.* **2006**, *69*, 553–557.

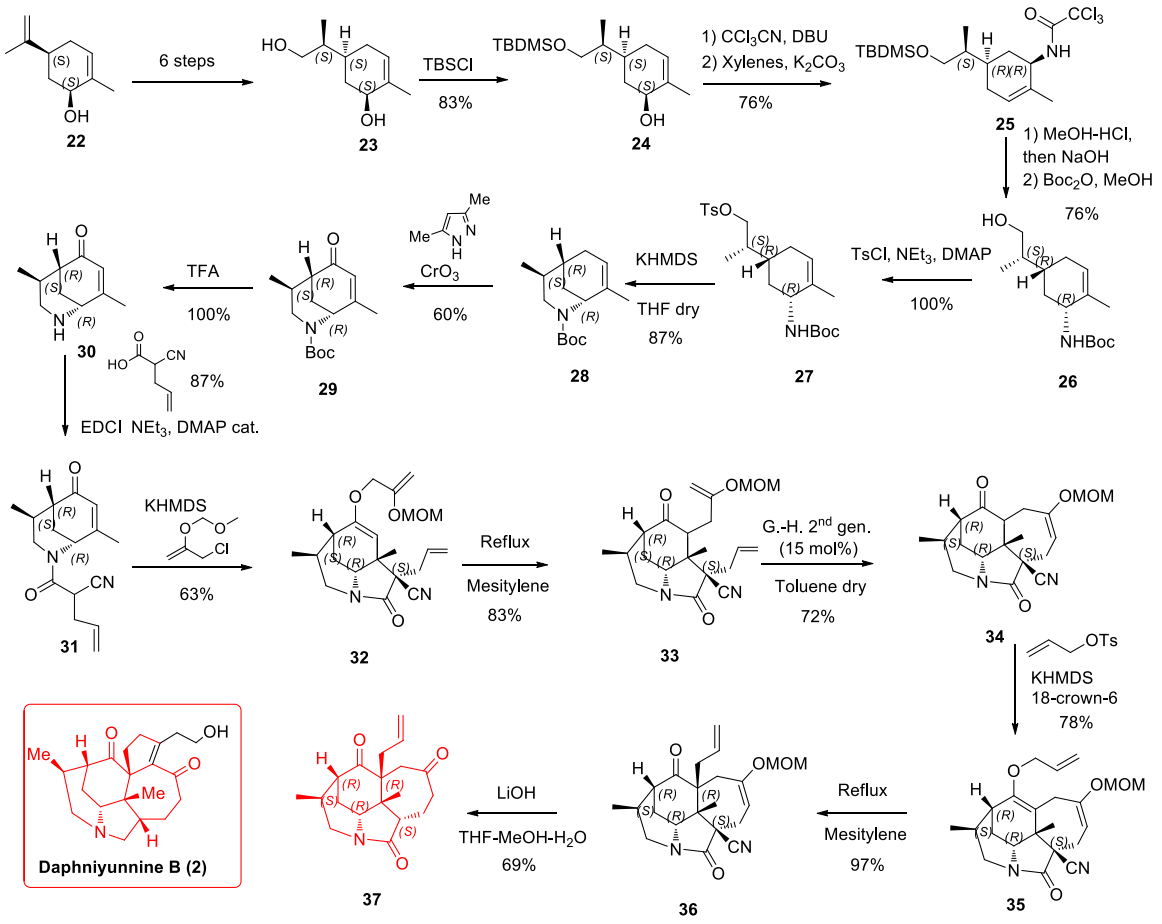
Pauson-Khand approach to the 7-5-5 ring system of Daphnyiunnine D and Daphnilongeranine B

The construction of the 7-5-5 ring system Daphnyiunnine D and Daphnilongeranine B (highlighted part in Scheme 2) has been successfully achieved using a Pauson-Khand approach (Scheme 2). The route has been published in Organic Letters (see attached list of publicationsand will be used as an end-game for the sequence proposed in Scheme 1.



Michael addition-RCM route to the functionalized tetracyclic core of Daphniyunnine B

An enantioselective route for the enantioselective total synthesis of Daphniyunnine B has been developed starting from cheap, commercially available (S)-carvone. In the most advanced intermediate 4 of the 5 ring systems have been established and ALL the stereocenters present in the final product have been installed. We anticipate the completion of the total synthesis in the Dixon laboratories in a short period of time. The racemic route based on a similar approach has been already published in Organic Letters (see attached list of publications).



2) Summary of the progress of the research training

2-1) Research Skills and techniques:

NMR techniques, GC, HPLC, *etc.*, and the determination of enantiomeric excess using a variety of methods.

2-2) Communication skills:

Results, progress and the work plan for the near future have been discussed on a weekly basis, and the presentation of results to the group have been made every week following the group's usual timetable. Weekly group meetings offered the opportunity for in-depth discussions involving all post-doctoral and post-graduate workers. In addition, weekly one-to-one meetings with Prof. Dixon have been often used to discuss progress, strategy and the direction of the research.