

PEOPLE  
MARIE CURIE ACTIONS

**Intra-European Fellowships (IEF)**

**Call: FP7-PEOPLE-2009-IEF**

**Direct Enantioselective N-Acyl Iminium Cyclisation Cascades  
“DIRENICC”**

# Direct Enantioselective N-Acyl Iminium Cyclisation Cascades

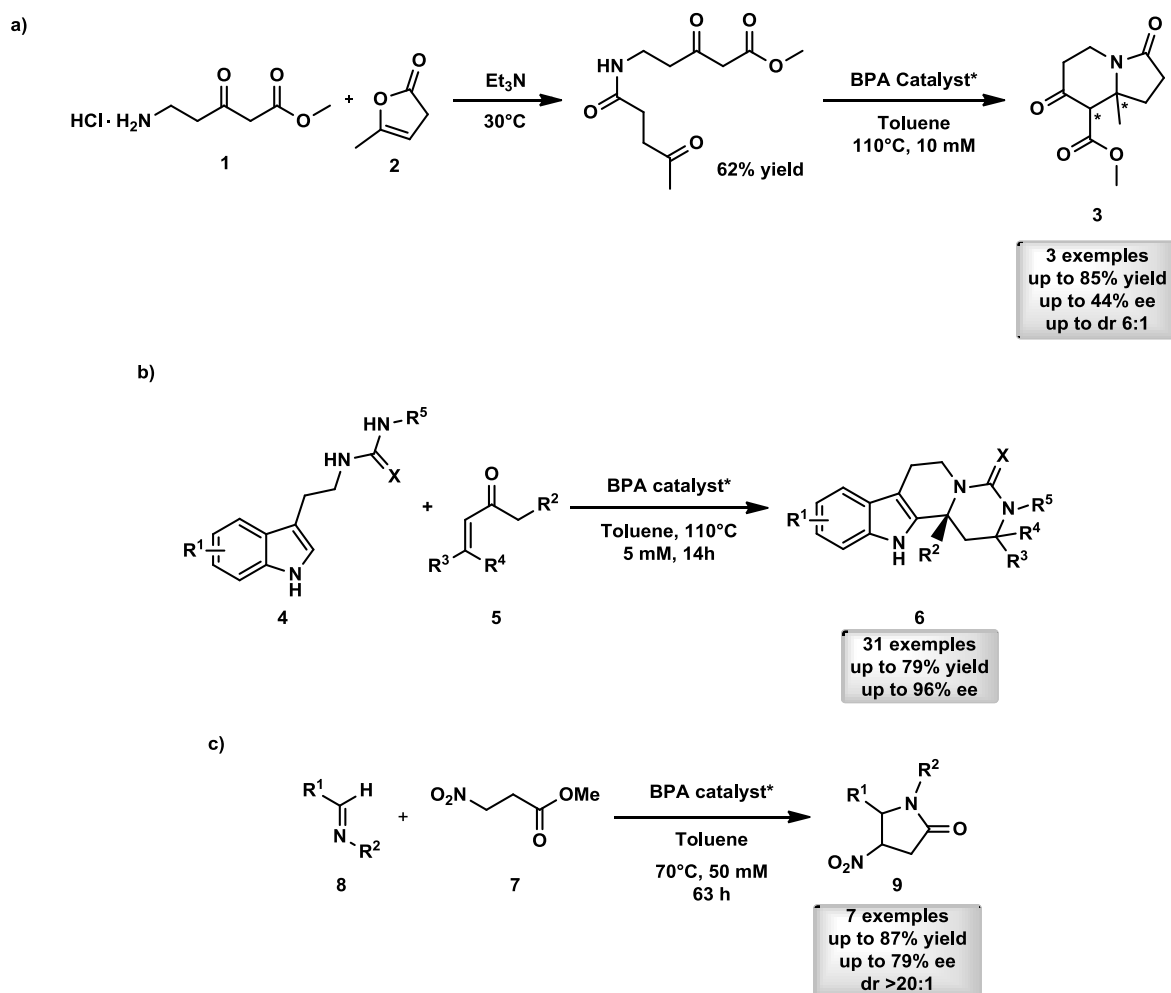
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## 1: PUBLISHABLE SUMMARY

The main objectives of the project were to develop new highly enantioselective powerful methodologies, such as asymmetric Bronsted acid catalysed cyclisation cascades in order to access to complex heterocyclic core structures.

During the fellowship we successfully developed three new cyclisation cascades catalysed by chiral Bronsted Binol phosphoric acids. These methodologies allowed us to access to a large variety of complex azacyclic compounds as summarised in scheme 1.



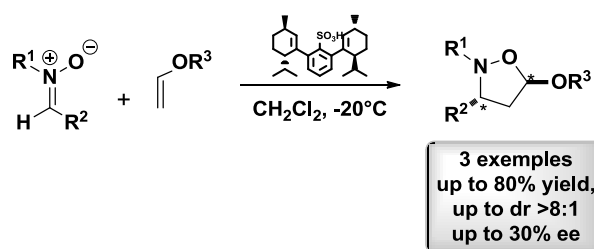
Scheme 1

Starting from an amine bearing a  $\beta$ -ketoester **1** and a lactone **2**, we were able to synthesise new tetracyclic compounds **3** via a N-acyl iminium cyclisation cascade with good yield and moderate enantioselectivity (scheme 1, a)).

Using a similar methodology but starting from a tryptamine urea derivative **4** and a vinyl ketone **5** we successfully prepared a range of azabicycles **6** in good yield and excellent enantioselectivity, *via* an enantioselective Michael addition, iminium cyclization cascade (scheme 1 b)). This work has been submitted for publication to *Angewandte Chemie International Edition*.

In addition, we developed the first asymmetric nitro-Mannich / lactamisation cascade, starting from nitroester **7** and an imine **8** with moderate to good yields and enantioselectivities (scheme 1, c)).

Furthermore, we synthesised some new chiral phosphoric acid derivatives and evaluated their efficiency in a range of asymmetric transformations. The best results were obtained for the cyclisation of nitrones (scheme 2).



**Scheme 2**

This work will be submitted for publication to *Tetrahedron Asymmetry* at the beginning of 2012.