Title: **Synthesis of the precursors for the preparation of β-methyl indolines and Lorcaserin using asymmetric catalysis**

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Nowadays, in pharmaceutical industry the increasing demand of efficient synthesis of chiral amines with biological properties, for example β-methyl indolines or Lorcaserin, led scientist to develop different strategies. All the pathways used until now were based on racemic resolution or the use of chiral auxiliaries. Interestingly, none of them was based on catalytic asymmetric synthesis.

Several precedents reported that one of the best applications of iridium-catalyst was the hydrogenation of unfunctionalised alkenes. Because of that, a few years ago, our group developed iridium-MaxPHOX family, which showed a wide range of applications.

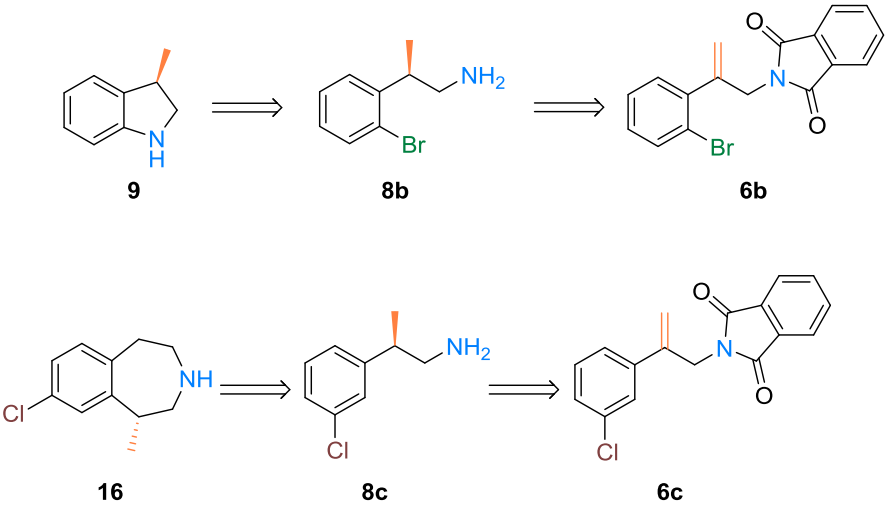
It was found that Ir-MaxPHOX complexes have showed outstanding selectivity in the hydrogenation of cyclic enamides, alkyl imines, aryl imines, allyl tosyl amines and allyl phthalimides with up 96% e.e.

With all this in mind, we designed two different ways for the preparation of the precursors of the synthesis of indolines and Lorcaserin.

The first strategy was a three-step pathway, involving a Wittig reaction to obtain (**2**), followed by an alpha-bromination of the alkene (**5**) and finally doing a S_N2 reaction to achieve (**6**). However, its biggest drawback was that involved lachrymator compounds and for that reason the gram-scale synthesis was restricted.

Consequently, we developed another pathway, which was performed in six steps avoiding lachrymator molecules. We started with an oxidation of commercial ketones using hypervalent iodine compound to obtain (**3**) with very good yields. In the next step, an acidic hydrolysis was performed to get molecule (**10**). Afterwards, the allyl alcohol was protected with TBSCl to perform a Wittig reaction and finally we deprotected the alcohol with standard conditions and performed a Mitsunobu reaction.

Once we obtained the precursors (**6**) for both ways, we could perform the iridium catalysed hydrogenation, which led us the products **7a**, **7b** and **7c** with very good yields and astonishing e.e. After that, we deprotected phthalimide groups to obtain products **8b** and **8c**. Finally, for indolines **9**, we tried a one-pot cyclization reaction without results and for **8c** we could obtain molecule **13**, which had already been used in the synthesis of Lorcaserin **16**.



Scheme: Retrosynthetic schemes for the preparation of β-methyl indolines (up) and Lorcaserin (down) planed in our TFG

Keywords: Chiral amines, total synthesis, asymmetric catalysis.