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Asymmetric synthesis of the alkaloids from *Erythrina* family

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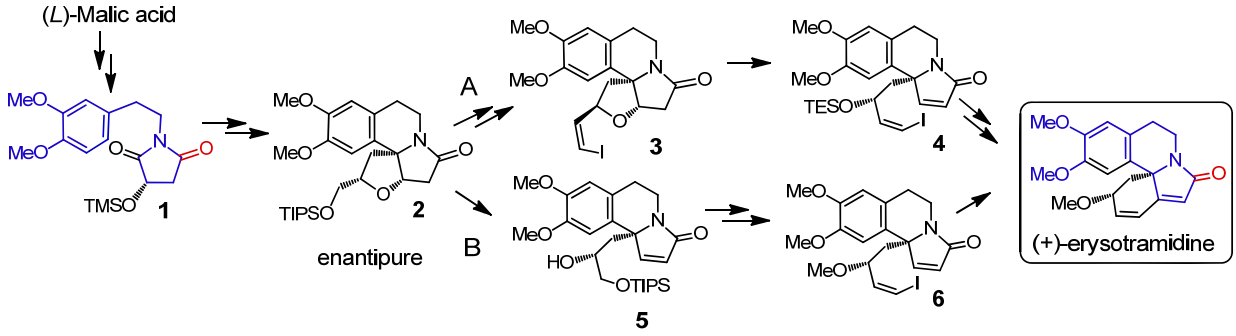
The main goal of this dissertation was to elaborate a new methodology for the synthesis of naturally occurring (+)-erysotramidine, the alkaloid with complex structure from *Erythrina* family. Compounds from this family show a strong and diverse biological activity on the central nervous system, and also exhibit anti-tumor effect.

Readily available from (*L*)-malic acid imide **1**, was converted in several steps to enantiomerically pure key derivative **2**.



Based on compound **2**, two pathways of the synthesis of (+)-erysotramidine were elaborated, which differ in order of reaction sequence. Pathway **A**: starting from **2**, *Z*-vinyl iodide **3** was prepared, and subjected to triethylsilil triflate induced retro-Michael reaction. The obtained silyl derivative **4** smoothly underwent intermolecular Heck reaction to give demethyl erysotramidine. Methylation of the hydroxyl group under standard conditions (n-Bu_4NBr, NaH, MeI,) gave the title compound.

Alternatively, **2** was treated with TMS-triflate to give alcohol **5**, which was then converted to methyl ether (Pathway **B**). Methylation of the hydroxyl group, posed some problems since the use of strong bases led back to **2** in a fast Michael addition. Other methods of alkylation, such as MeI/Ag_2O, CH_2N_2/HBF_4, or a Meerwein salt/lutidine were not effective. This problem was solved by using trimethylsilyl diazomethane in the presence of Mukaiyama acid and molecular sieves 4Å. As in the route **A**, methoxy derivative was converted to the *Z*-vinyl iodide **6** and then subjected to Heck cyclization furnishing (+)-erysotramidine.

A major problem in the synthesis of the target compound by both routes was Wittig olefination of the corresponding aldehyde. Apart from desired *Z*-vinyl iodide, in the reaction mixture ylide's side products e.g. vinyl *gem*-diodide and acetylene derivatives were always present. To minimize the formation of side products, the suspension of the phosphonium salt was added dropwise to a solution of the base, what effectively inhibited the site reactions of in situ generated ylide.

The synthesis of enantiomerically pure (+)-erysotramidine was successfully accomplished by using both routes. In each case the overall yield was approx. 10%.

A synthesis of the precursors of alkenoid-type Erythrina alkaloids by applying a reductive Heck reaction and throughout the organocopper compounds was also accomplished.