

## Enzymatic Kinetic Resolution of Hydroxy Oxazolines

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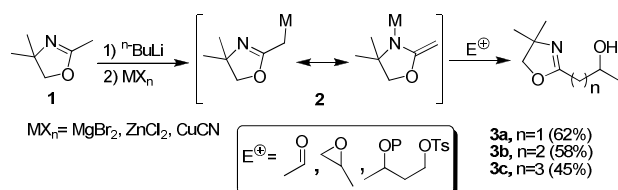
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### INTRODUCTION

Functionalized 2-oxazolines containing stereogenic centers are important precursors in organic synthesis, particularly in the syntheses of substituted lactones.<sup>1</sup> The enzymatic kinetic resolution is a tool widely used to obtain enriched enantiomerically compounds. In addition, secondary alcohols are efficiently resolved by kinetic resolution.<sup>2</sup> In the present work, we developed a synthetic route where hydroxyl 2-oxazolines were submitted to kinetic resolution. This class of compounds could be used in synthesis of bioactive chiral lactones.

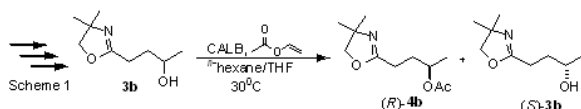
### RESULTS AND DISCUSSION

The hydroxy 2-oxazolines **3a-c** were prepared in an one pot operation. The aza-enolate **2**, generated in situ by an acid-base reaction of the oxazoline **1** and *n*-BuLi, was condensed with aldehydes, epoxides or tosylates, in presence of an appropriate metallic salt, leading to the formation of hydroxy 2-oxazolines **3a-c** in good yields. (Scheme 1).



Scheme 1. Preparation of hydroxy oxazolines

The racemic hydroxy 2-oxazoline **3b** (*n*=2) was submitted to the enzymatic kinetic resolution, using the enzyme CAL-B<sup>®</sup> (NOVOZYME-435) and a mix of 9:1 *n*-Hexane/THF as solvent (Scheme 2).



Scheme 2. Kinetic resolution of **3b**

The enantiomeric excess of acetate **4b**, was determined by GC analysis. The integration showed that the acetate **4b** has 97% of *e.e.* The a racemic mixture was previously synthesized and the enantiomers were separated using a chiral column. The absolute configuration of the **4b** was indirectly

determined by polarimetric analysis of the respective valerolactone **5**, as the (*R*) isomer. (Figure 1).

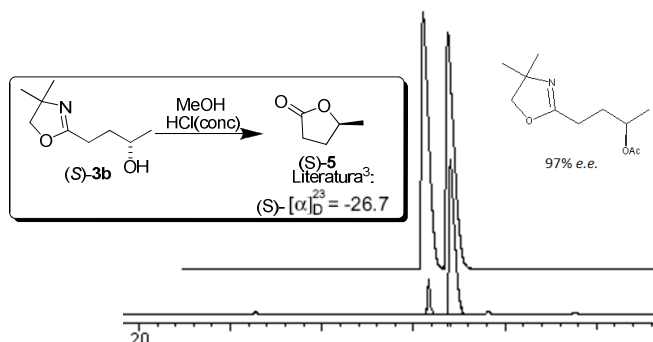


Figure 1. Chiral GC analysis of **4b**

Another application of these enantioenriched building blocks is the synthesis of compound **7** that is present in the blend of the pheromone of the carpenter bee *Xylocopa hirtissima*<sup>4</sup> (Figure 2).

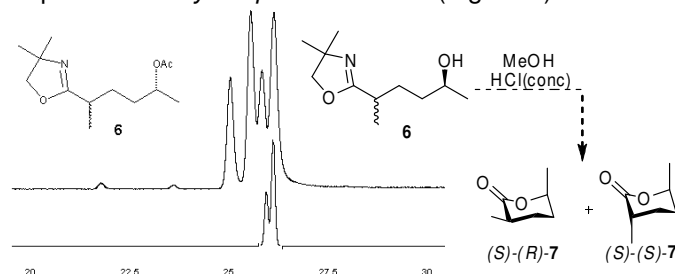


Figure 2. Chiral GC analysis of **6**

### CONCLUSION

Hydroxy 2-oxazolines were obtained in good isolated yields. Studies concerning the enzymatic resolution of these compounds gave good enantioselectivity and its application in the synthesis of biological active compounds are under investigation.

### ACKNOWLEDGEMENTS

PRONEX-CNPq; FACEPE; INCT-INAMI; CAPES.

### REFERENCES

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