Studies toward total synthesis of tautomycetin

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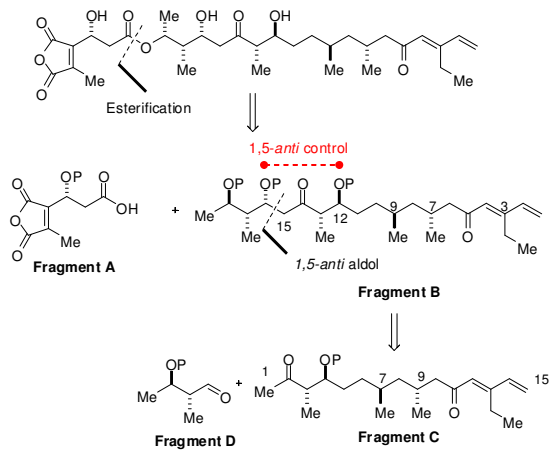
INTRODUCTION

Tautomycetin is a polyketide natural product recognized as inhibitor of serine/threonine phosphatases type I.[1] In spite of this important activity, there is no total synthesis described in the literature.[2] For this reason, we have proposed a project aiming to the total synthesis of tautomycetin. This project is carry out in two laboratories, one of those in Brazil and the other one in France.



Scheme 1: Retrosynthetic analysis

The disconnections were thought in the convergent way. The first disconnection would give us the fragments A and B, through an esterification reaction. The second disconnection affords fragments C and D, through *1,5 anti* aldol (Scheme 1).[3]

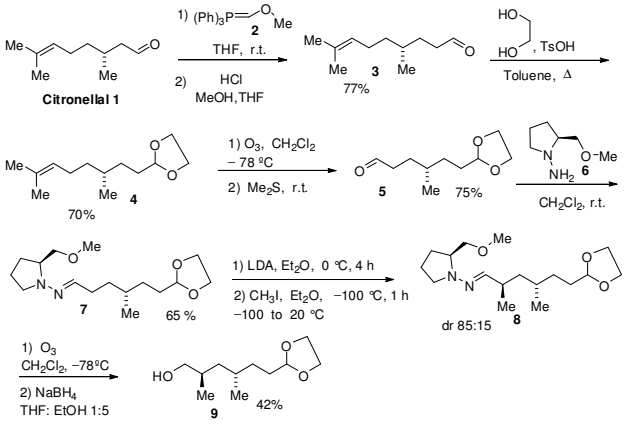
RESULTS AND DISCUSSION

In this work we describe the first results in the synthesis of fragment C.

We started with the reaction of citronellal **1** with phosphorane **2**, followed by treatment with HCl to provide aldehyde **3** in 77% yield. Aldehyde **3** was converted into ketal **4**, through condensation with ethylene glycol, using TsOH as an acid catalyst. The olefin moiety of compound **4** was cleaved through an ozonolysis reaction, providing aldehyde **5** in 75 % yield. The chiral hydrazone **7** was prepared by condensation of aldehyde **5** with chiral auxiliary SAMP **6**.

In order to prepare the 1,3-*anti* system, we tried to apply the usual Enders asymmetric alkylation conditions,[4] using THF as solvent, but compound **8** was not formed.

Nevertheless, when we changed THF by Et_2O, we obtained compound **8** in 52% yield and 85:15 diastereoisomeric ratio (Scheme 2).



Scheme 2: Results for construction of fragment C

To remove the chiral auxiliary, we used ozonolysis followed by treatment with $NaBH_4$, in order to avoid any epimerization.

CONCLUSION

We developed a synthetic pathway to obtain compound **9**, which has the *1,3-anti* system present in tautomycetin **1**. In spite of optimizations are needed, the results show the viability of this synthetic pathway to the synthesis of tautomicetin.

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