



Studies Towards Asymmetric Total Synthesis of Populene D

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Keywords: Populene D, π -Allylic Complex, Total Synthesis.

INTRODUCTION

Populene D (**Figure 1**) was isolated from the trunk of *Thespesia populnea*, as optically active, however its absolute configuration has not been assigned. Some biological activity tests were carried out with this compound and amongst, the activity against cervical cancer (HeLa) must be highlighted ($IC_{50}=0.95 \mu\text{g/mL}$).¹ The synthesis of this natural product has not been reported. Herein, we show studies towards the asymmetric total synthesis of populene D, using as the key step an iodine-catalyzed Prins cyclization reaction (**Figure 1**).²

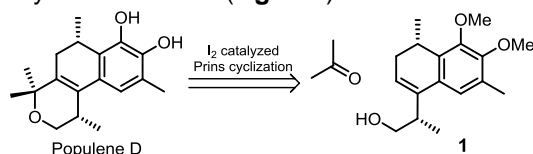
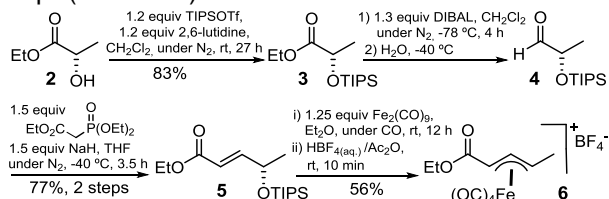


Figure 1. I_2 catalyzed Prins cyclization towards populene D.

RESULTS AND DISCUSSION

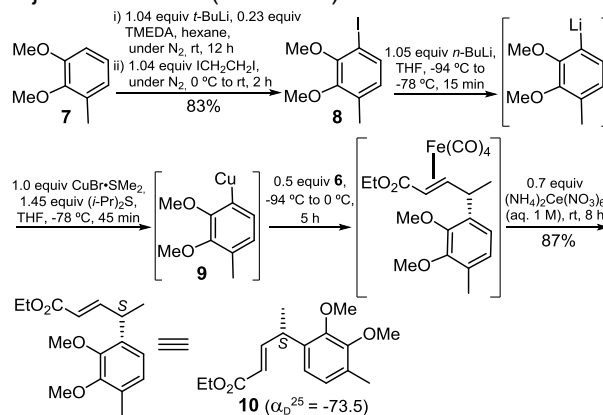
The first steps of the asymmetric total synthesis of populene D are summarized in **Scheme 1**, **Scheme 2** and **Scheme 3**. The iron complex **6** was prepared from commercial available lactic ester **2**, by protection reaction with TIPSOTf,³ followed by reduction with DIBAL,⁴ then Homer-Wadsworth-Emmons olefination (leading only to the *E*-isomer selectively),⁵ and finally, complexation reaction using diiron nonacarbonyl⁶ in 36% yield over four steps (**Scheme 1**).



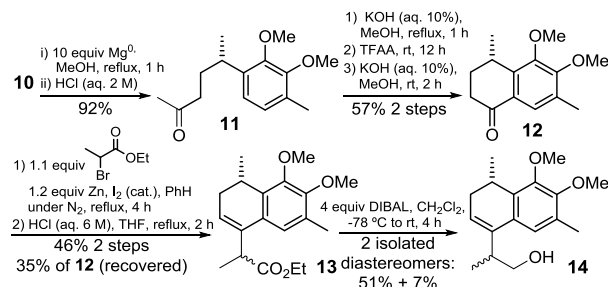
Scheme 1. Synthesis of π -allylic complex **6**.

The aryl iodide **8** was obtained by *ortho*-lithiation with *t*-BuLi followed by iodination with 1,2-diiodoethane in 83% yield. The α,β -unsaturated ester **10**, was achieved by coupling reaction between **8** and **6** via the cuprate intermediate **9**, in 87% yield and in high enantioselectivity, according to the α_D value (**Scheme 2**).⁶ The synthesis of the homoallylic alcohol **14** was then completed by a sequence of reduction with metallic magnesium in MeOH,⁶ hydrolysis with KOH, intramolecular Friedel-Crafts acylation catalyzed by TFAA,⁷ Reformatsky reaction, dehydration⁸ and reduction with

DIBAL⁹ in six steps with 12% global yield, considering the major diastereomer (**Scheme 3**).



Scheme 2. Synthesis of coupling product **10**.



Scheme 3. Synthesis of homoallylic alcohol **14**.

CONCLUSION

Twelve steps of the total synthesis of populene D have been accomplished. The longest linear sequence has eleven steps and 4% global yield, considering the major diastereomer. Two additional steps will lead to the target molecule.

ACKNOWLEDGEMENTS

FAPESP, CNPq and CAPES for financial support.

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