Studies Towards Asymmetric Total Synthesis of Populene D

Eloisa E. Ishikawa, Luiz F. Silva, Jr.*
Instituto de Química, USP, CP 26077, CEP 05513-970 São Paulo SP, Brazil

*luizfsjr@iq.usp.br and elo.ishikawa@iq.usp.br

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 (IC50=0.95 μg/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

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 DIBAL6, then Horner-Wadsworth-Emmons olefination (leading only to the E-isomer selectively),5 and finally, complexation reaction using diiron nonacarbonyl,7 in 36% yield over four steps (Scheme 1).

The aryl iodide 8 was obtained by ortho-lithiation with t-BuLi followed by iodination with 1,2-diodoethane in 83% yield. The ω,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 αH value (Scheme 2).6 The synthesis of the homoallylic alcohol 14 was then completed through a sequence of reduction with metallic magnesium in MeOH,8 hydrolysis with KOH, intramolecular Friedel-Crafts acylation catalyzed by TFAA,9 Reformatsky reaction, dehydration10 and reduction with DIBAL9 in six steps with 12% global yield, considering the major diastereomer (Scheme 3).

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.

REFERENCES


15th Brazilian Meeting on Organic Synthesis – 15th BMOS – November 10-13, 2013 - Campos do Jordão, Brazil