Products and Potential Drugs

Synthesis of Natural

SYNFACT the waster

Synthesis of (–)-β-Caryophyllene

NaBH₄ 1. DEAD, PPh3, THF, r.t. AcOH, -10 °C 2. TMS-Im, TBAF (10 mol%) 86%. dr = 15:1 ŌН THF. r.t. ÓTMS 61% В С from Haios-Parrish **D** (10 mol%) BH₃·SMe₂ THF, 0 °C ОH 1. Et₃N·3HF, THF, r.t. NaH DMF TsCl, py, r.t. r.t. to 0 °C 46% from C ÓН **ÓTMS** G F Е Grob fragmentation I, $Ph_3C^+ClO_4^-$ (10 mol%), CH_2Cl_2 , -78 °C then DIBAL, -78 °C; then Et₃N·3HF, r.t. THF, r.t. t-BuOK *i*-PrOH−*t*-BuOH 0 °C 79% . 60% (–)-β-caryophyllene 11 steps, 12% from **A**

Significance: The synthesis of β -caryophyllene and coraxenolide A by Larionov and Corey is distinctive because it is a rare example of the use of planar chirality in natural product synthesis. Both enantiomers of (2Z,6E)-6-methylcyclonona-2,6-dienone (**H**) were prepared and used as chiral precursors for the synthesis of the (–)- β -caryophyllene and coraxeniolide A.

Comment: The absence of stereoselectivity in the reduction of **C** with NaBH₄ was overcome by using the CBS reduction. Planar chiral **H** was obtained as a single enantiomer that is stable against racemization at room temperature owing to restricted C–C bond rotation in the 9-membered ring. By contrast, cyclononene racemizes in a few minutes at room temperature.

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 Synfacts 2008, 8, 0783-0783
 Published online: 23.07.2008

 DOI: 10.1055/s-2008-1077896; Reg-No.: K07708SF

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