Synthesis of Natural Products and Potential Drugs

## Key words

caryophyllene
planar chirality
CBS reduction
Grob fragmentation


Corey-Bakshi-Shibata reduction


F




E


THF, r.t.
61\%


都


B


J 84\%
 $86 \%, \mathrm{dr}=15: 1$

A
from Hajos-Parrish reaction

I, $\mathrm{Ph}_{3} \mathrm{C}^{+} \mathrm{ClO}_{4}^{-}(10 \mathrm{~mol} \%), \mathrm{CH}_{2} \mathrm{Cl}_{2},-78^{\circ} \mathrm{C}$
then DIBAL, $-78^{\circ} \mathrm{C}$; then $\mathrm{Et}_{3} \mathrm{~N} \cdot 3 \mathrm{HF}$, r.t.


Significance: The synthesis of $\beta$-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-2,6dienone $(\mathbf{H})$ were prepared and used as chiral precursors for the synthesis of the (-)- $\beta$-caryophyllene and coraxeniolide A .

Comment: The absence of stereoselectivity in the reduction of $\mathbf{C}$ with $\mathrm{NaBH}_{4}$ was overcome by using the CBS reduction. Planar chiral $\mathbf{H}$ 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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[^0]:    synfacts Contributors: Philip Kocienski, Arndt W. Schmidt
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