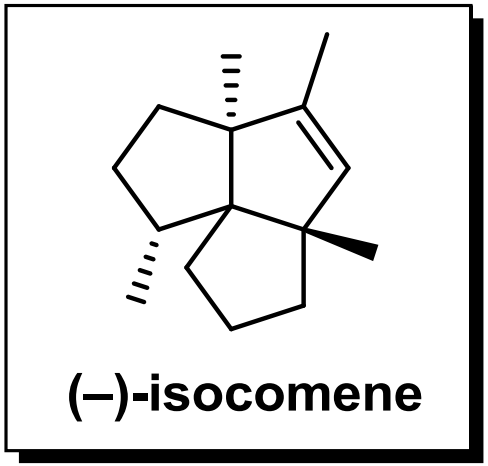
Total Synthesis of (±)-Isocomene and Related Studies



Michael C. Pirrung

J. Am. Chem. Soc. **1981**, *103*, 82-87.

Presented by Derek Ahneman

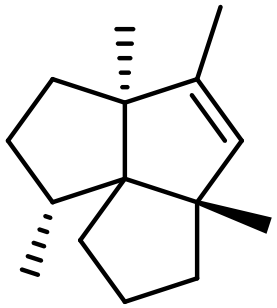
Michael C. Pirrung, Ph.D.

- Born in Cincinnati, 1955
- B.A. from University of Texas, Austin after 2.5 yrs, 1975
- Ph.D. from University of California, Berkeley, with Clayton Heathcock after less than 4 yrs, 1980
- NSF Postdoctoral Fellow at Columbia University with Gilbert Stork, 1980-81
- Assistant Professor at Stanford University, 1981-89
- Associate Professor at Duke University, 1989-94
- Professor of Chemistry at Duke University, 1994-2004
- Professor of Chemistry at University of California, Riverside, 2004-present
- Research focuses on chemical biology, synthesis, and nucleic acids

Isocomene

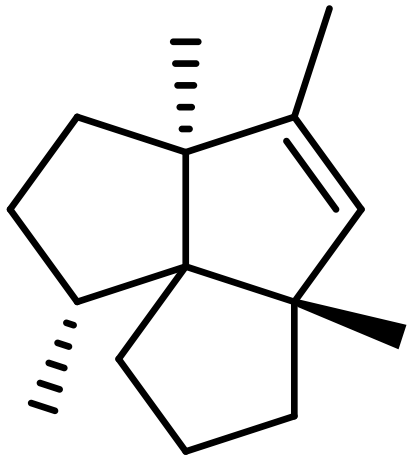
- First isolated from the Rayless Goldenrod (*Isocoma wrightii*)
- Sesquiterpene – consists of three isoprene units
- Backbone consists of three fused cyclopentane rings
- Contains three contiguous quaternary chiral centers
- No heteroatoms

Rayless Goldenrod

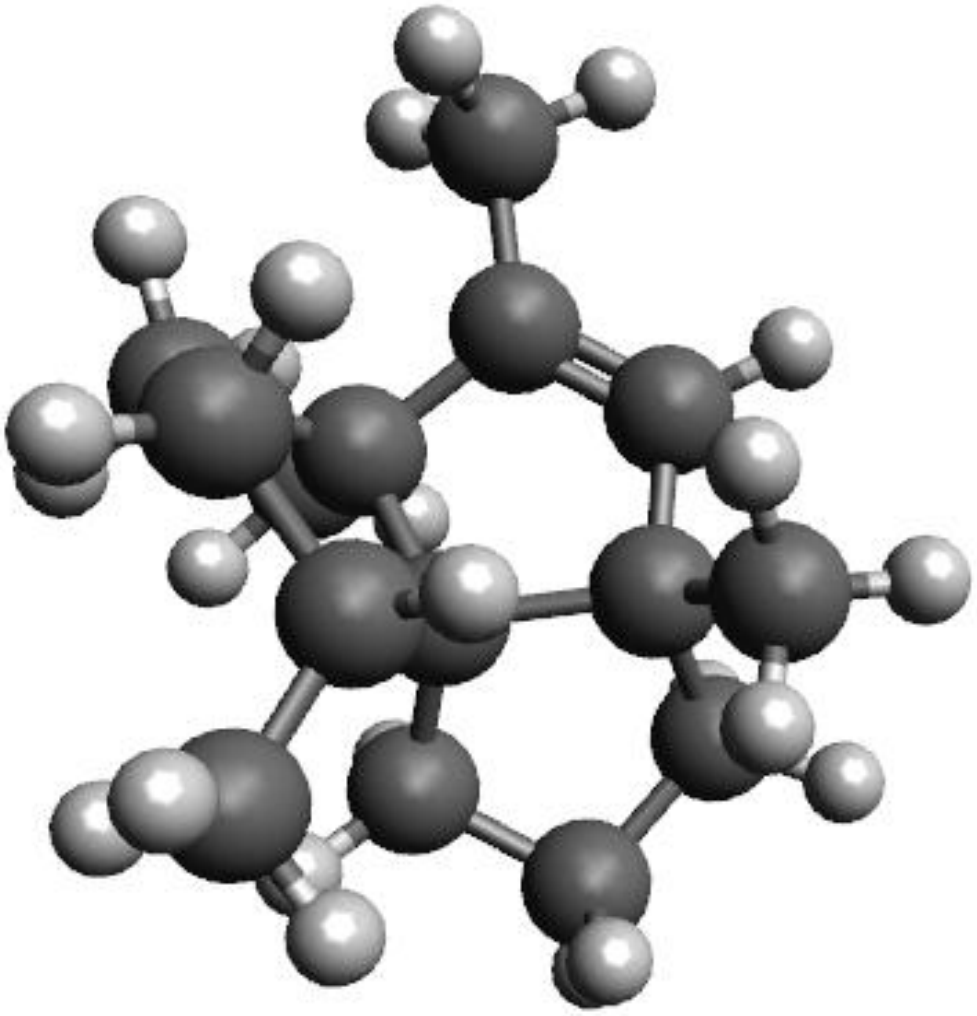


(–)-isocomene

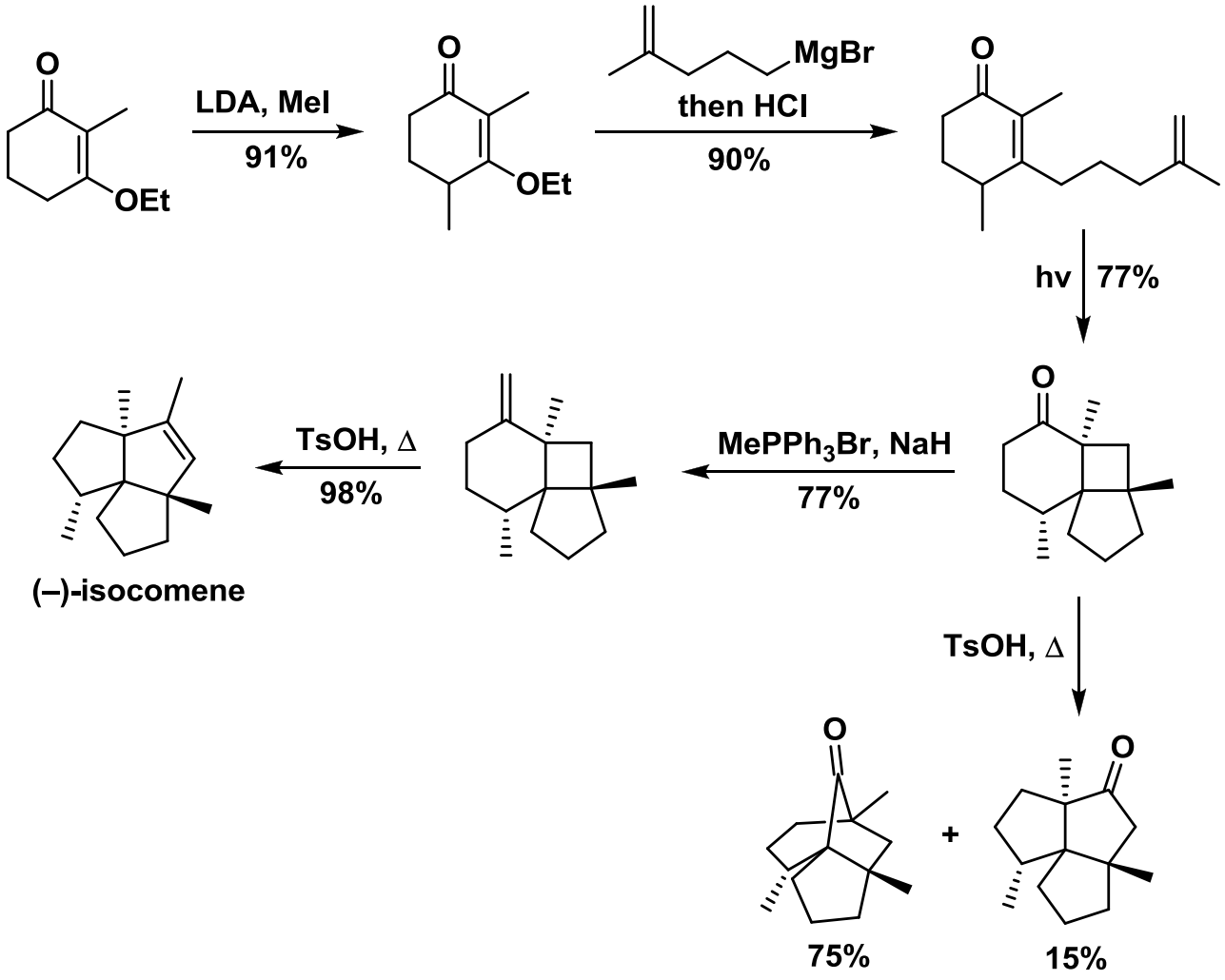
Topology of Isocomene



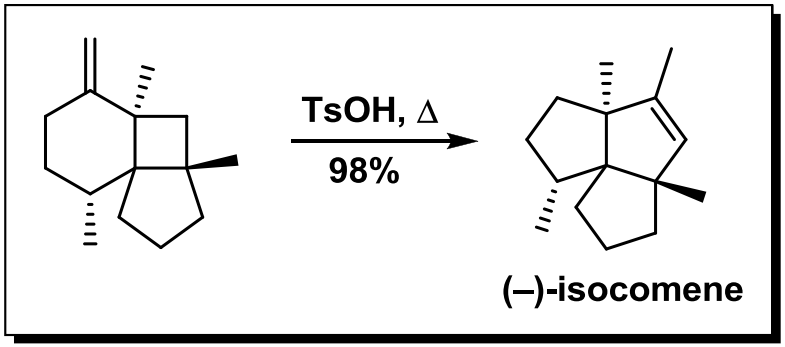
(–)-isocomene

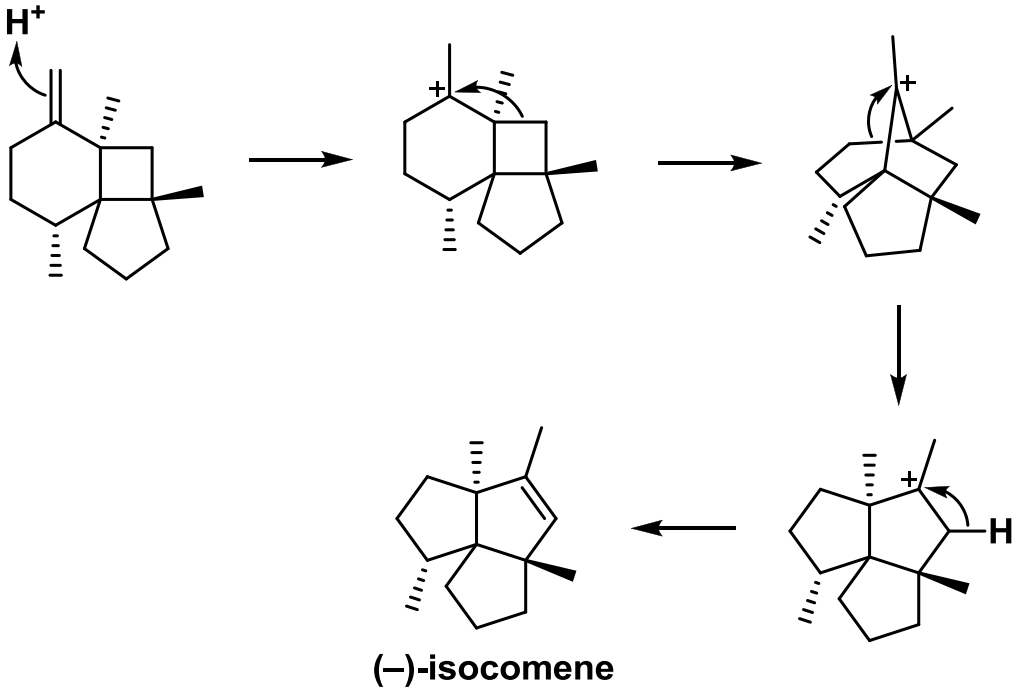


Synthesis of Isocomene

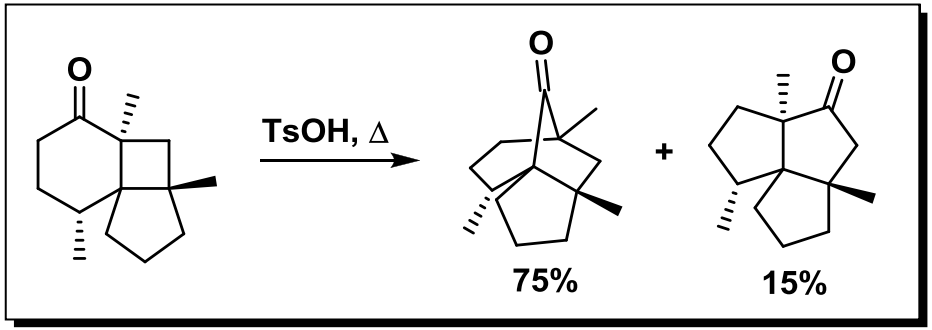


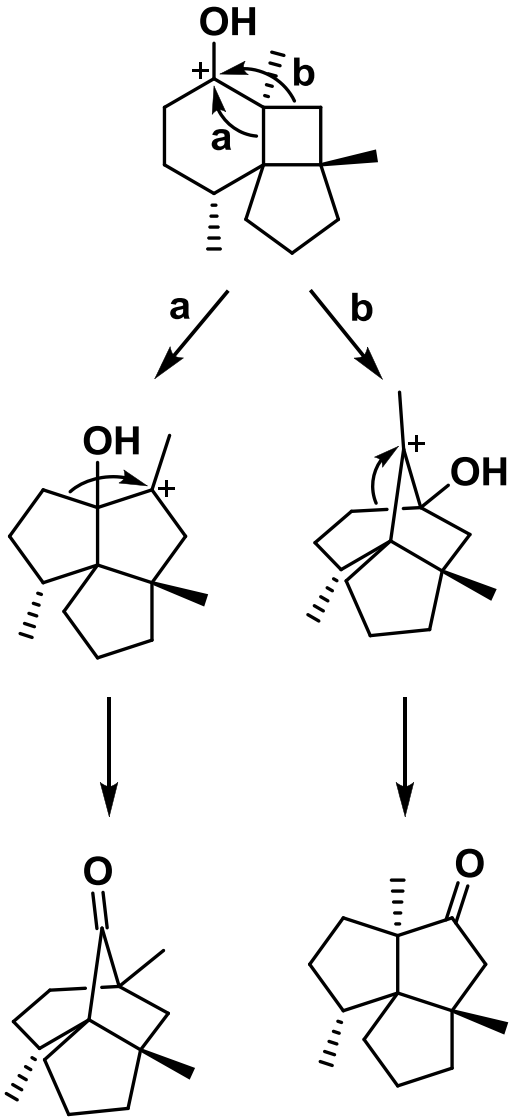
Rearrangement Mechanism



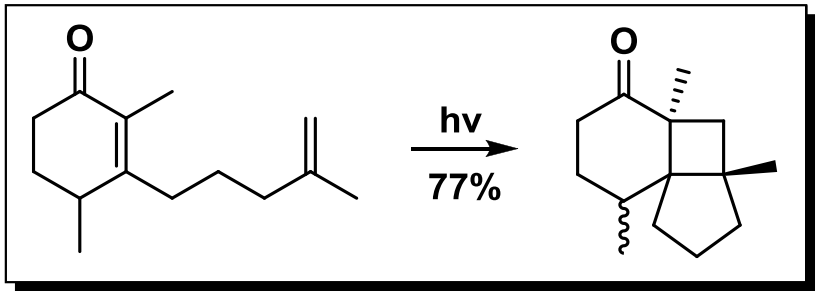


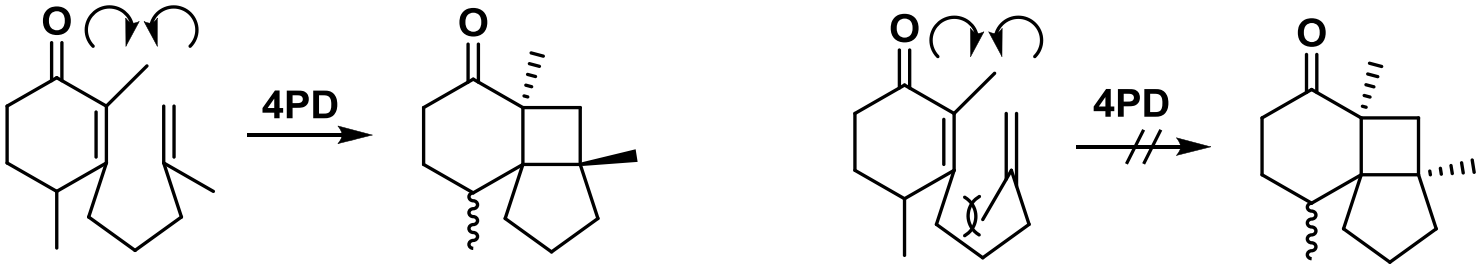
Competing Rearrangement Pathways

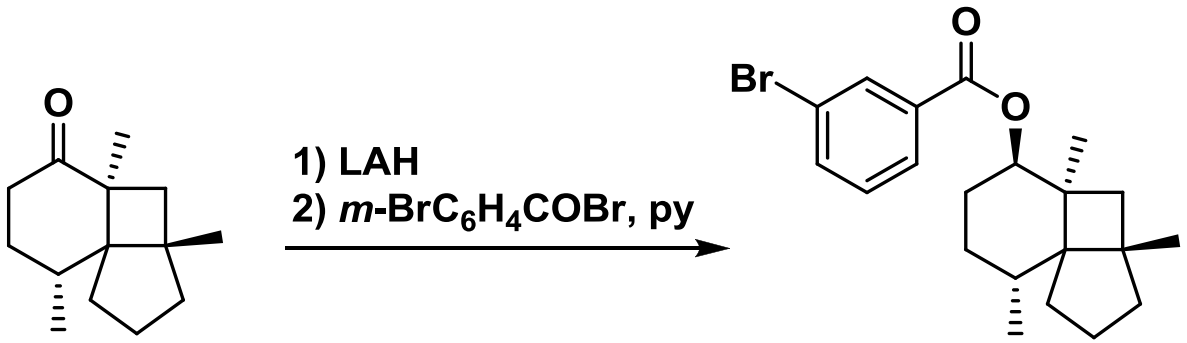




Intramolecular [2+2] Cycloaddition







analyzed by
X-ray crystallography

Conclusion

- Isocomene was synthesized in 34% yield over 7 steps
- Potential applications to the synthesis of other natural products
- Demonstrates utility of cyclobutyl carbinyl cation rearrangements