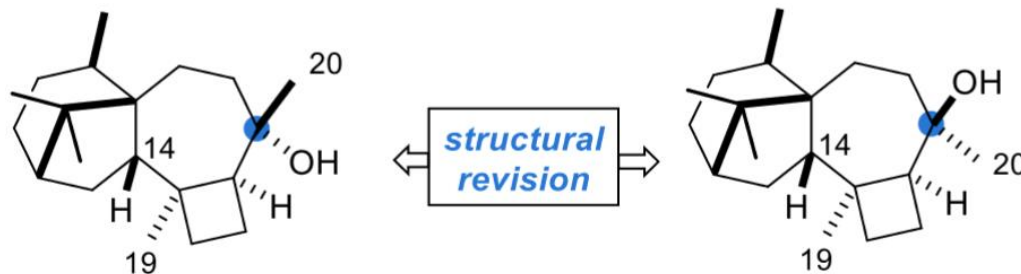


# Total Synthesis and Structural Revision of a Harziane Diterpenoid

Moritz Hönig and Erick M. Carreira  
Angew. Chem. Int. Ed. 10.1002/anie.201912982



Harziane diterpenoid  
(revised structure)



Harziane diterpenoid  
(nominal structure)



# Erick M. Carreira

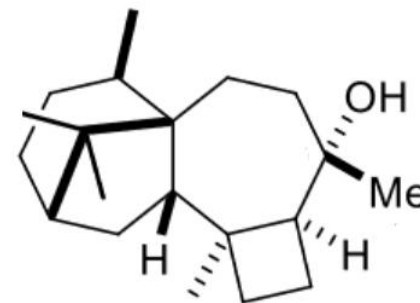


- PhD at Harvard University, 1990 (David A. Evans)
- PostDoc at Caltech, 1992 (Peter Dervan)
- Assistant Professor to full Professor at Caltech 1992-1997
- Full Professor at ETH Zurich since 1998

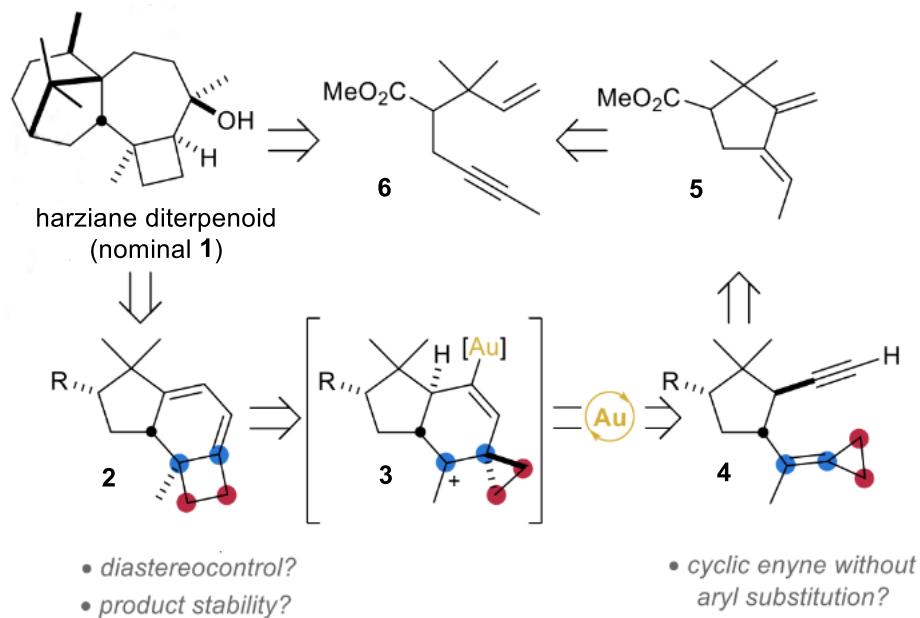
**Research:** asymmetric synthesis of biologically active, stereochemically complex, natural products

# Harziane Diterpenoids

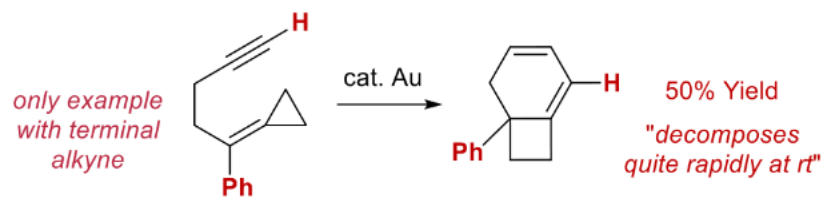
- Secondary metabolites – isolated from *Trichoderma* fungi
- 8/10 isolated members contain the unique 6–5–7–4 carbon skeleton
- Antifungal and cytotoxic activity
- No reported synthetic studies



# Retrosynthesis

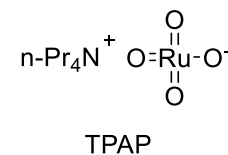
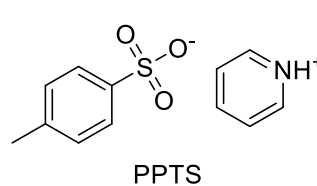
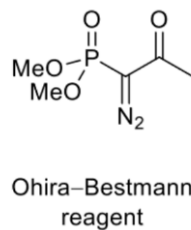
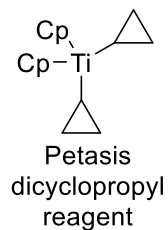
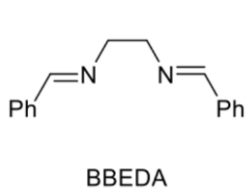
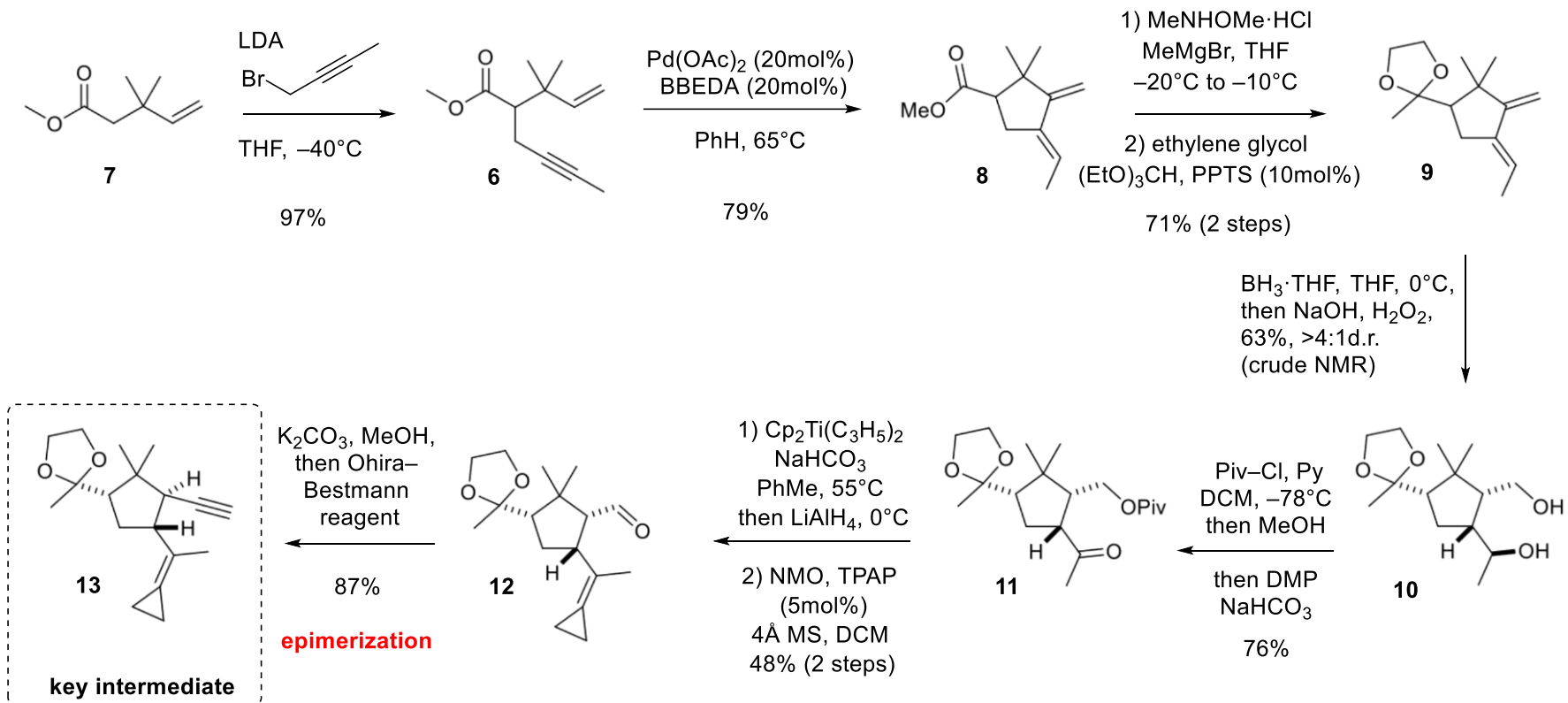


## Previous work by Gagne:

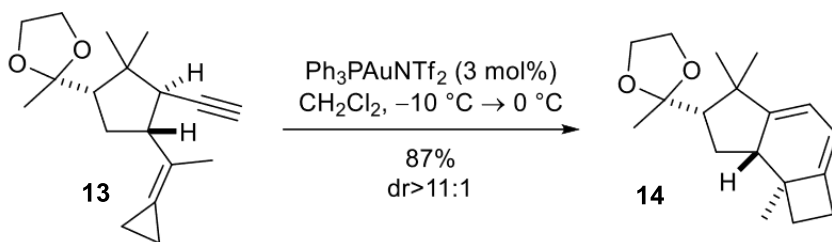


Org. Lett. 2014, 16, 2272-2275

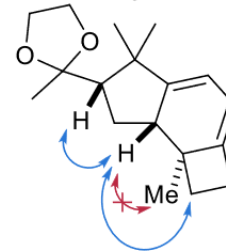
# Synthesis of the key intermediate



# Au-catalyzed cycloisomerization

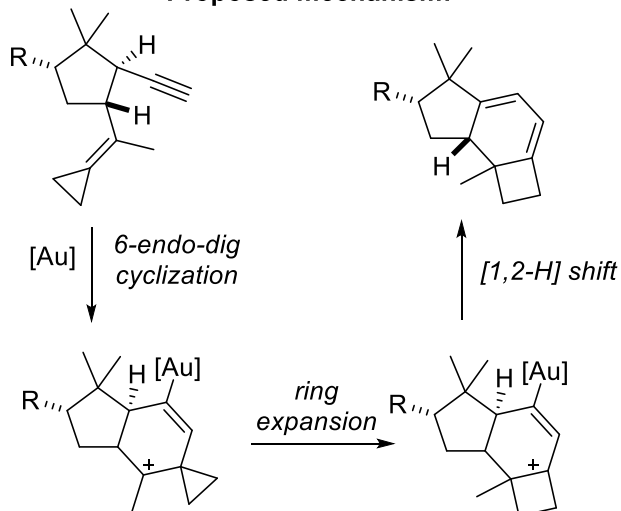


NOE analysis:



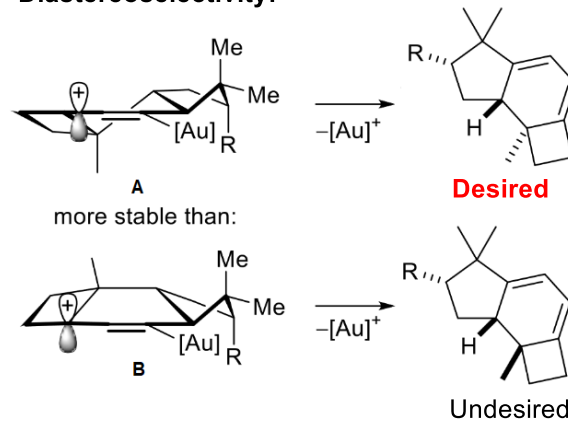
NOE observed  
no NOE observed

Proposed mechanism:

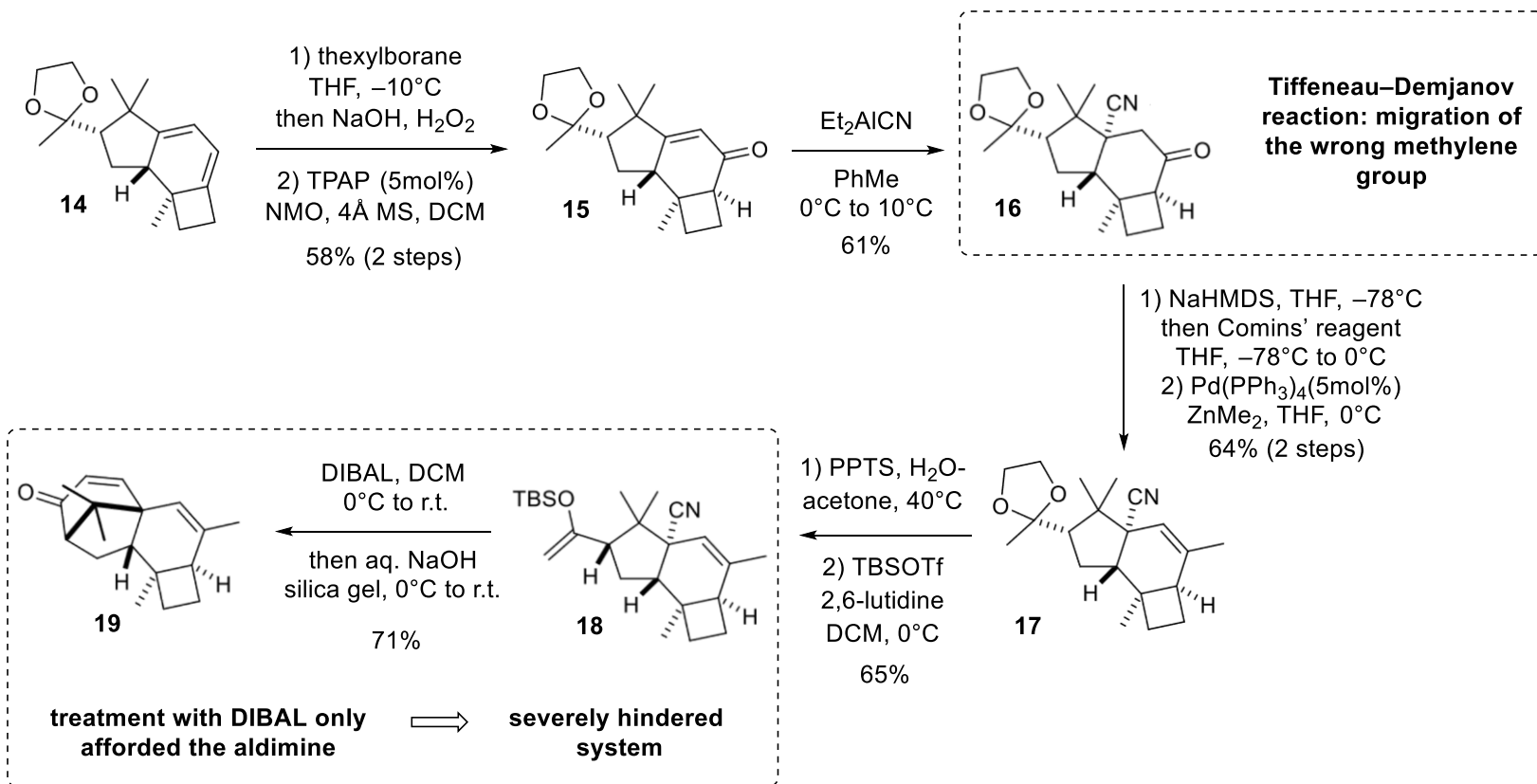


Org. Lett. **2014**, 16, 2272-2275

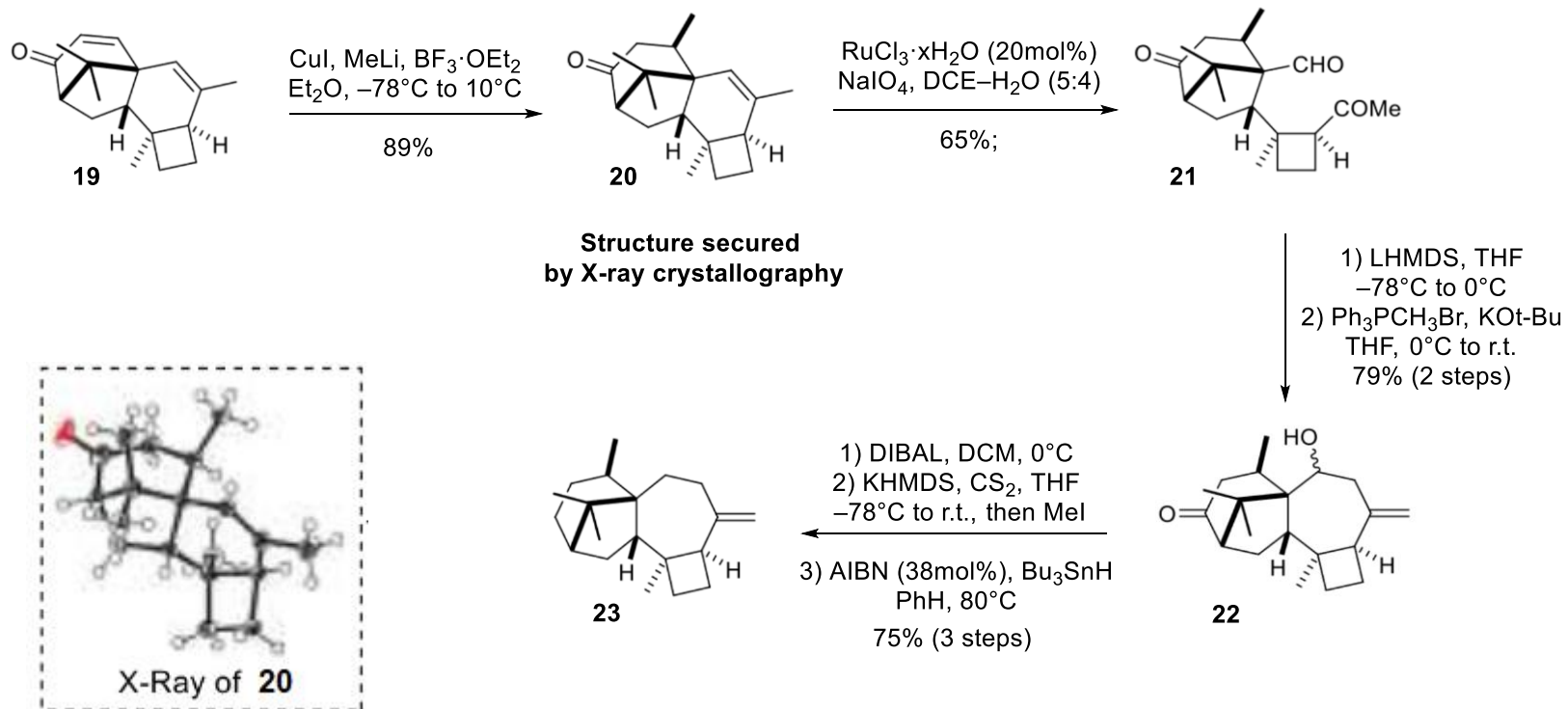
Diastereoselectivity:



# Introduction of bicyclo[3.2.1]octane ring

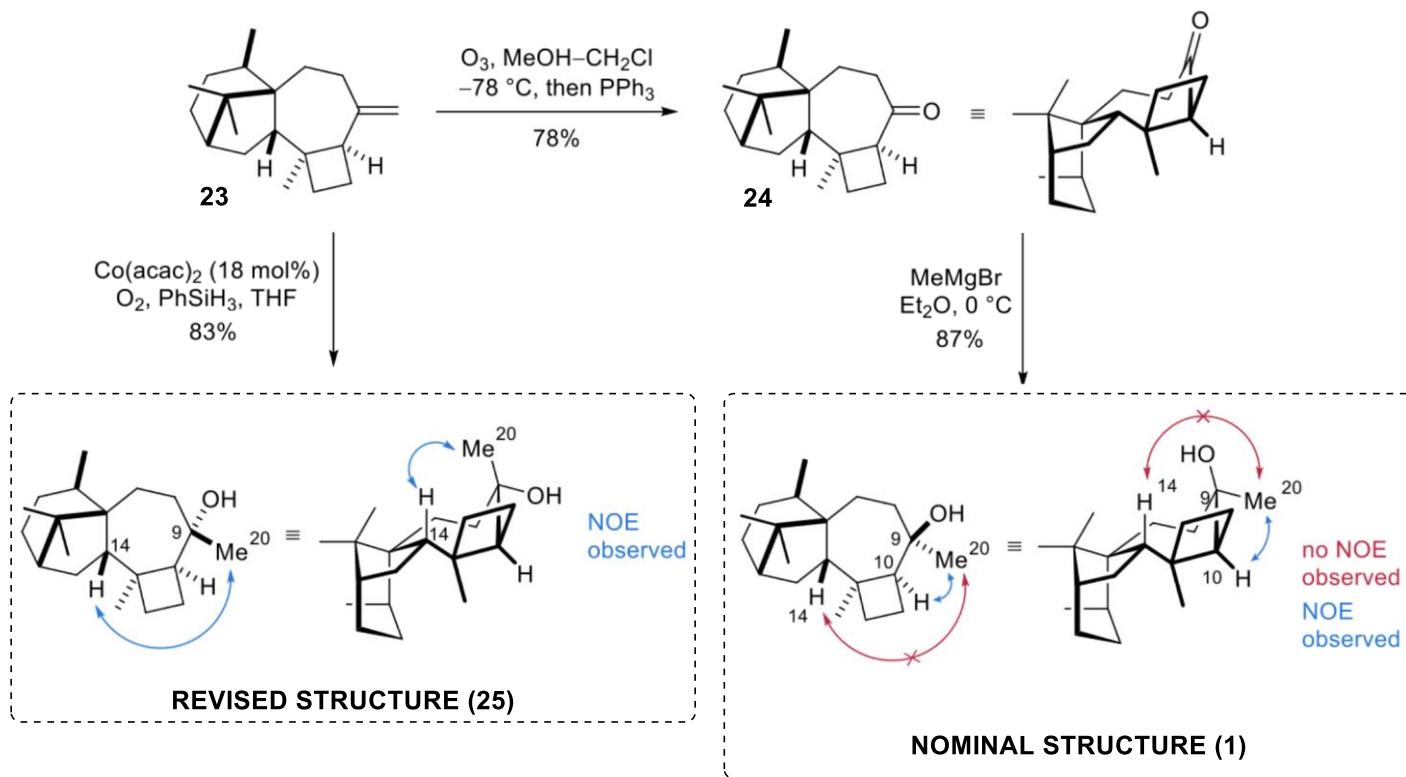


# Key ring expansion





# End game and stereochemical revision



# To sum up:

- First total synthesis of nominal harziane diterpenoid **1**
- Reassignment of configuration of the natural product
- Key step - enyne cycloisomerization leading to a key quaternary stereocenter within a cyclobutane

