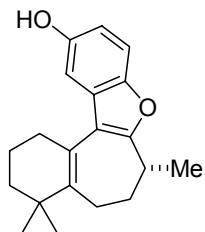


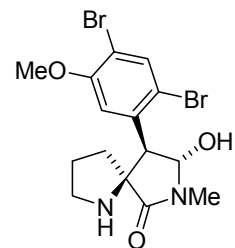
# Total Syntheses Completed by the Trauner Group

Robert Moreau  
Supergroup Meeting  
15 September 2004

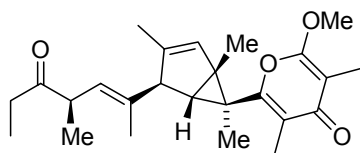
# Completed Total Syntheses



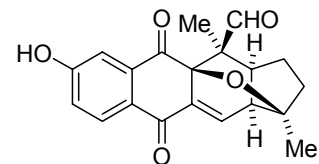
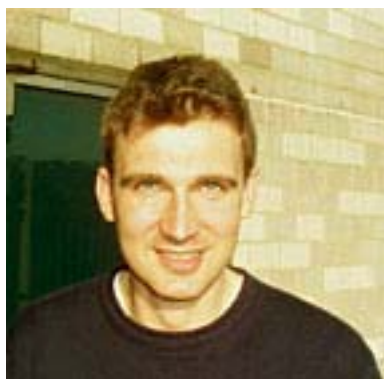
frondosin B



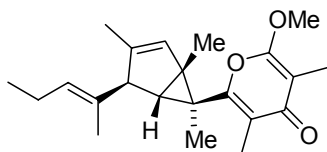
amathaspiramide F



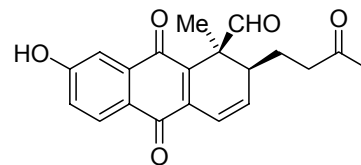
crispatene



pinnatal

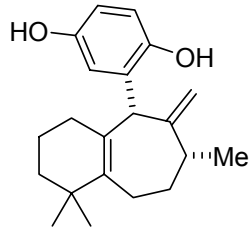


photodeoxytridachione

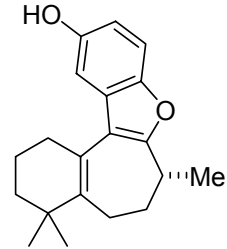


sterekunthal A

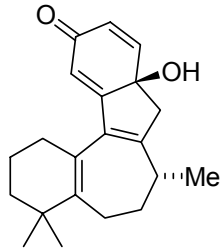
# Frondosins



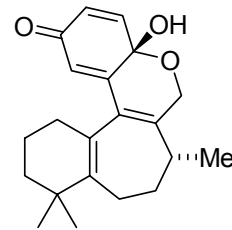
frondosin A



frondosin B



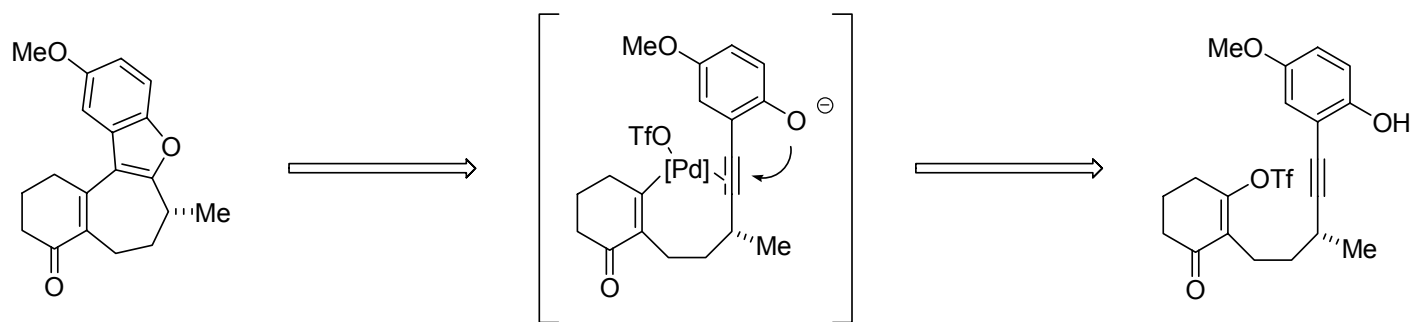
frondosin C



frondosin D

- marine terpenoids from the sponge *Dysidea frondosa*
- inhibit interleukin-8 binding in the low micromolar range and could, therefore, be used to prevent rheumatoid arthritis and psoriasis
- also have been shown to exhibit HIV-inhibitory properties

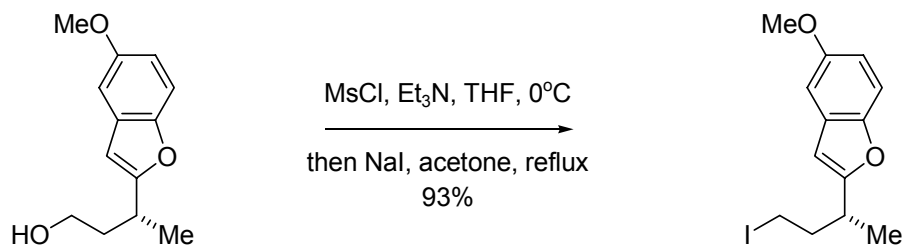
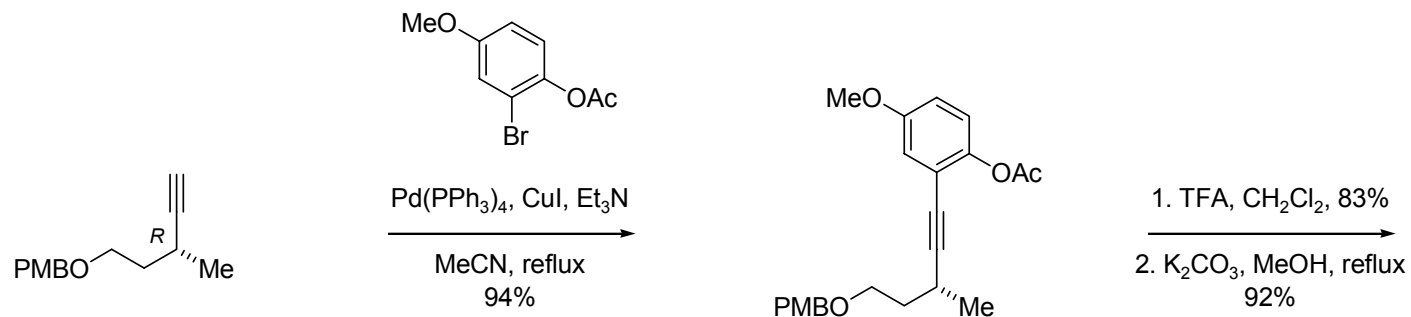
# Frondosin B Retrosynthesis



- desired a one-step bicyclization via the first intramolecular Arcadi-Cacchi reaction

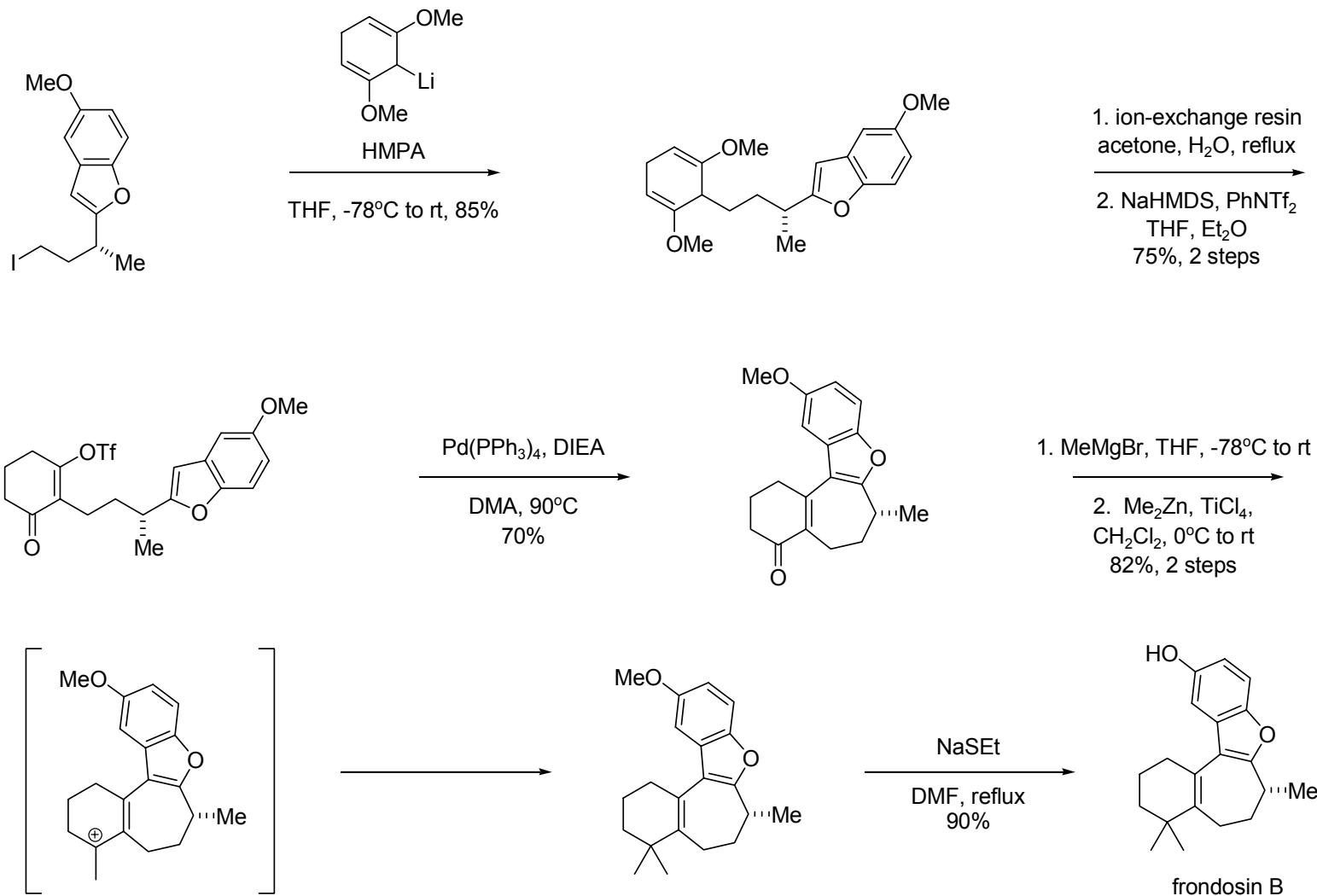
C.C. Hughes, D. Trauner. *Angew. Chem. IE.* **2002**, 1569.

# Synthesis of Benzofuran Alkyl Iodide

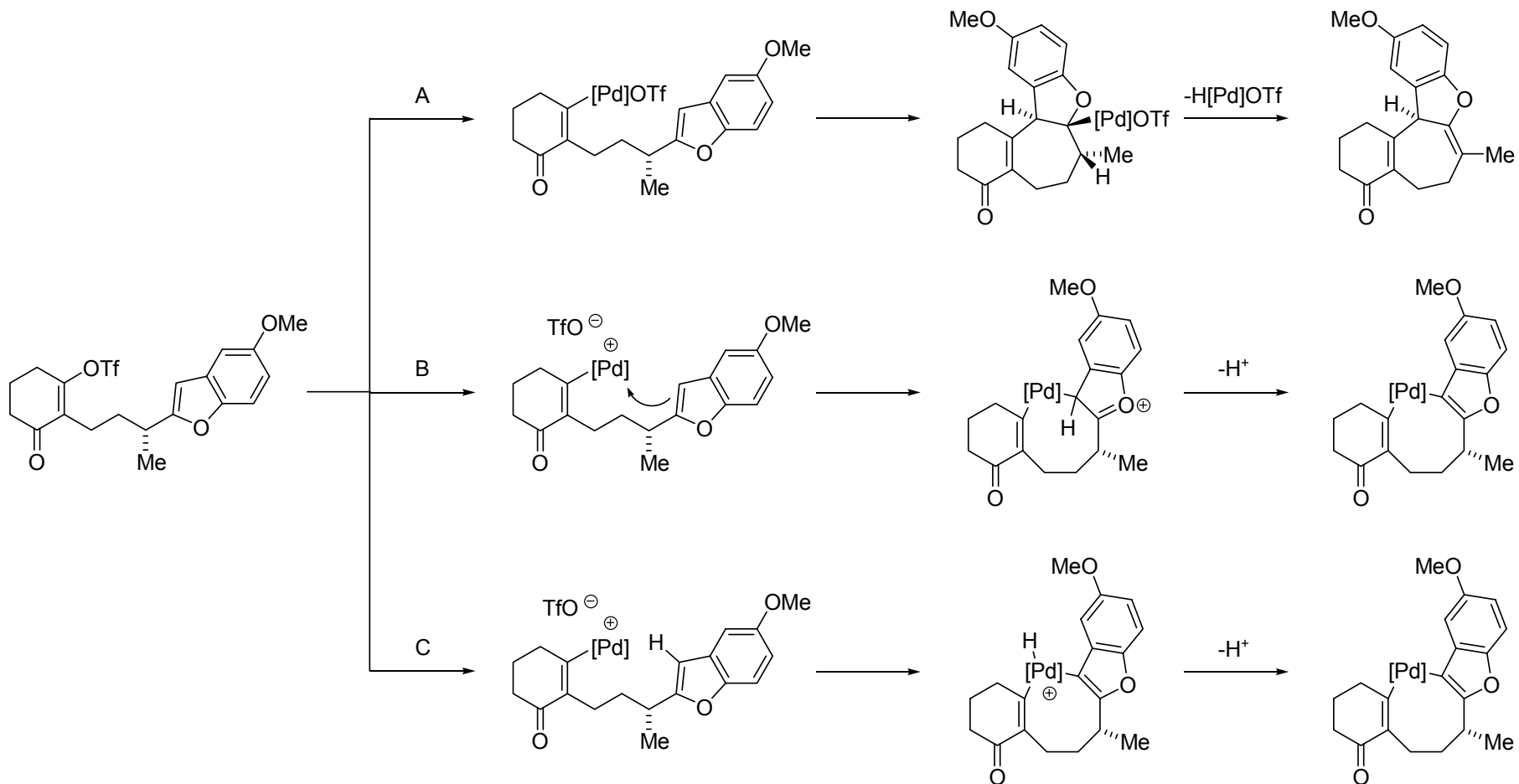


Alkyne starting material preparation: A. Murai, T. Oka. *Tetrahedron* **1998**, 54, 1.

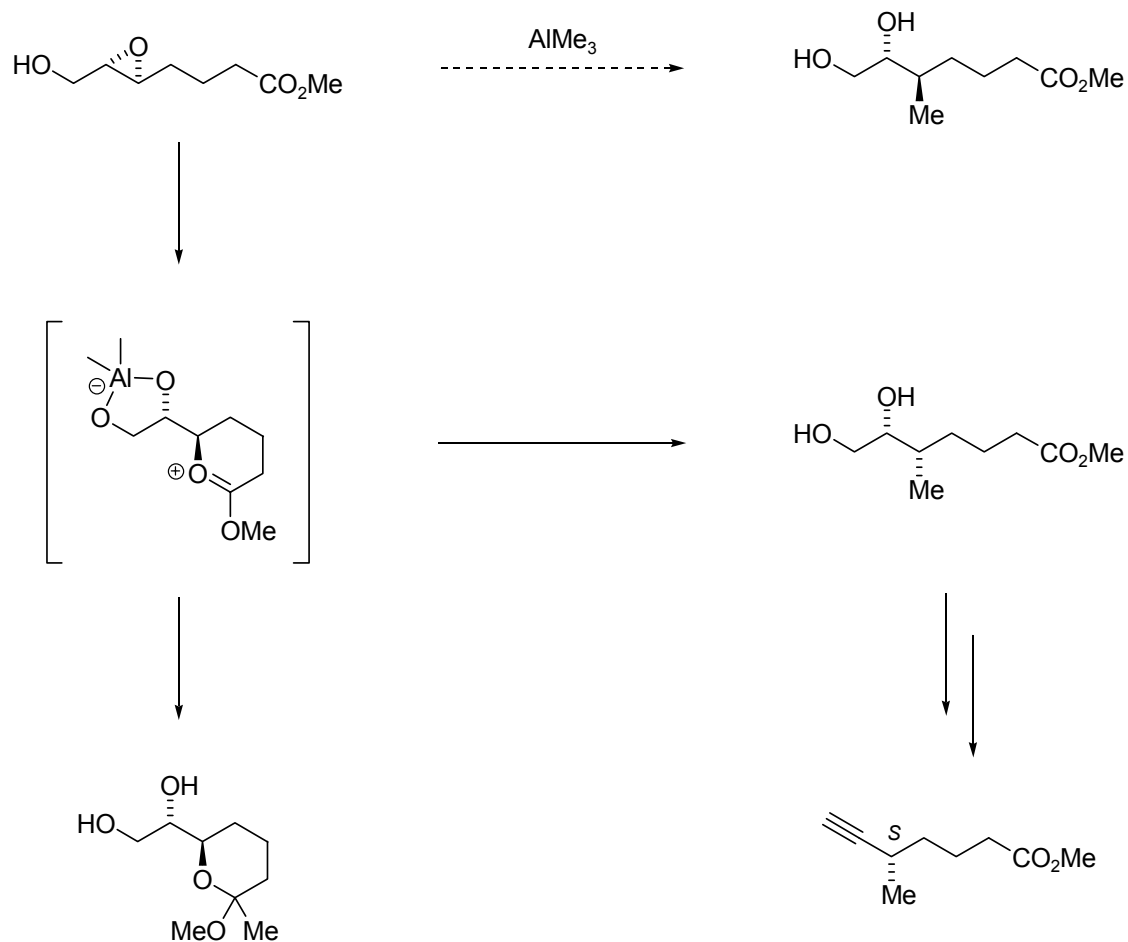
# Completion of the Synthesis



# Mechanistic Insights



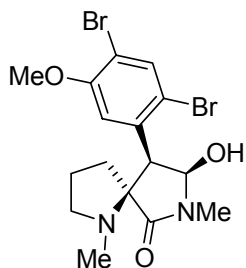
# Danishefsky's Alkyne



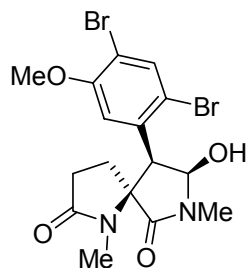
S.J. Danishefsky, M. Inoue, M.W. Carson, A.J. Frontier. *JACS*, **2001**, 1878.



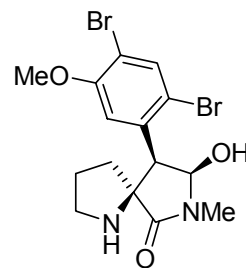
# Amathaspiramides



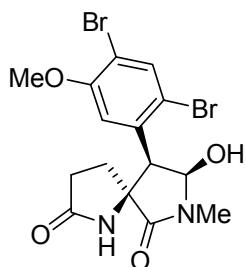
amathaspiramide A



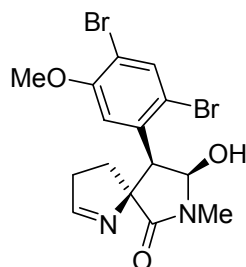
amathaspiramide B



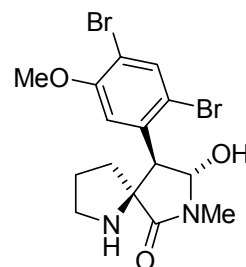
amathaspiramide C



amathaspiramide D



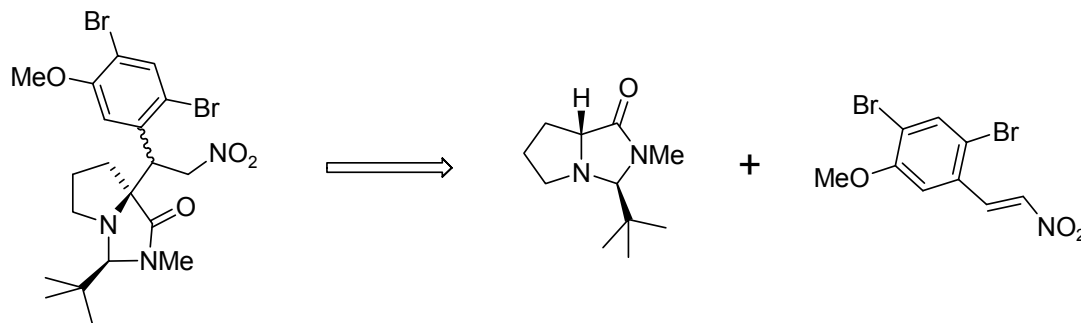
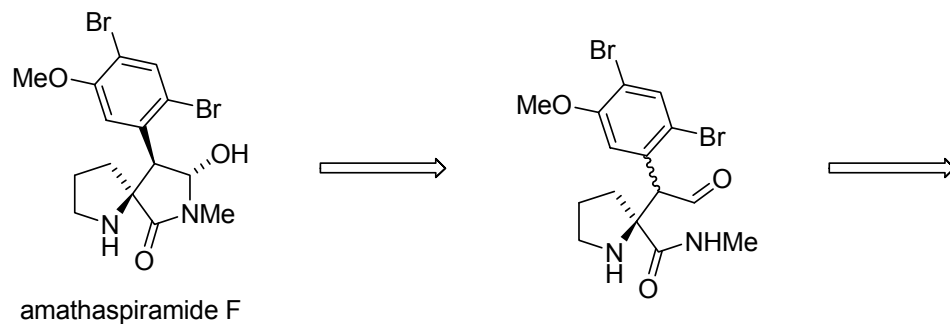
amathaspiramide E



amathaspiramide F

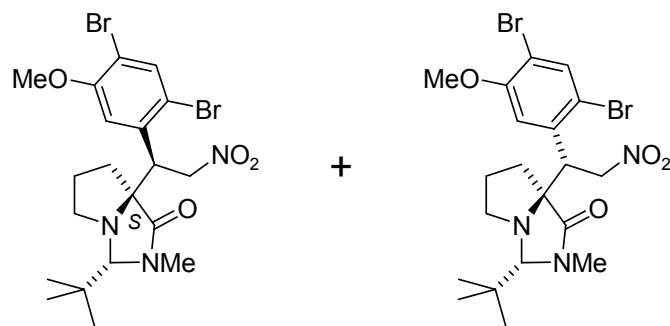
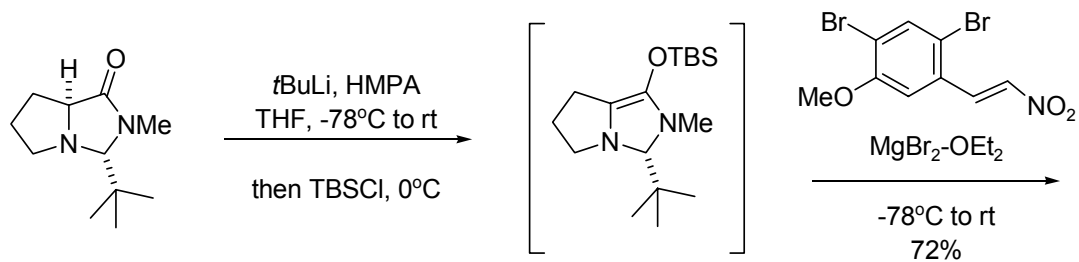
- marine alkaloids isolated from a New Zealand collection of the bryozoan *Amathia wilsoni*
- novel spirobicyclic core of pyrrolidine and pyrrolidinone rings
- several are moderately cytotoxic or show antiviral and antibiotic properties

# (-)-Amathaspiramide F Retrosynthesis



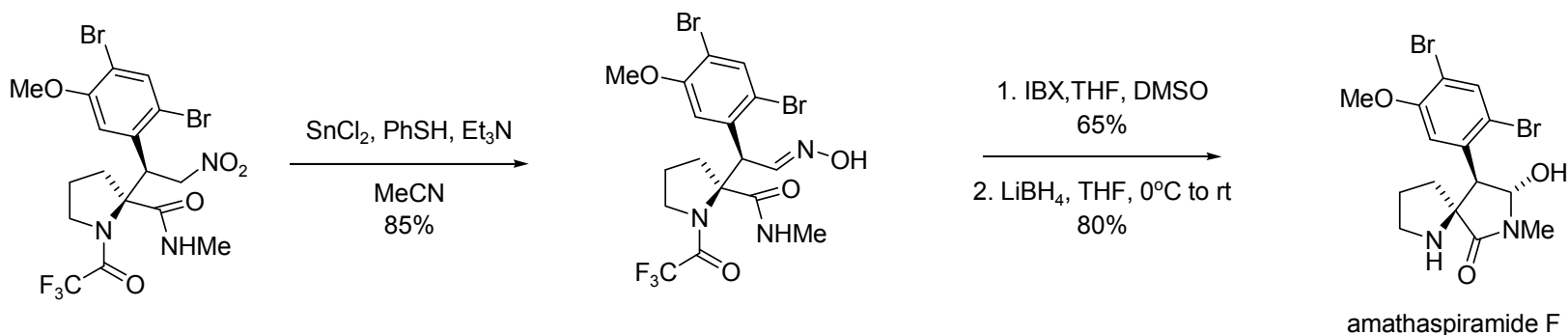
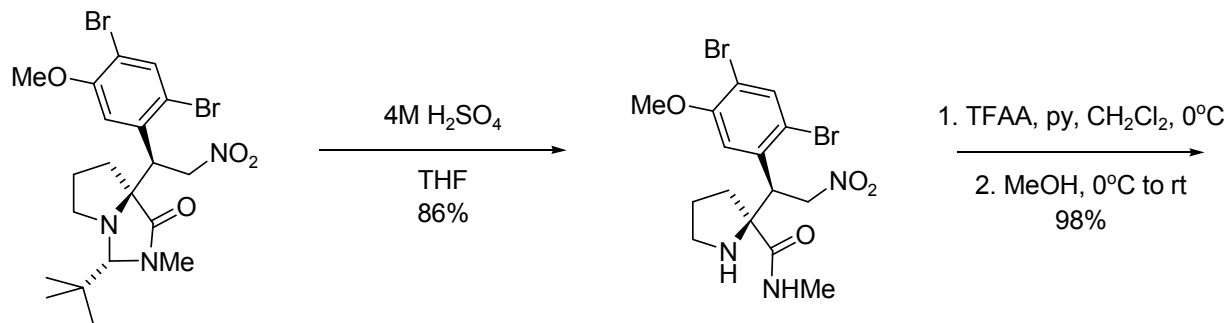
C.C. Hughes, D. Trauner. *Angew. Chem. IE.* **2002**, 4556.

# Proline Alkylation

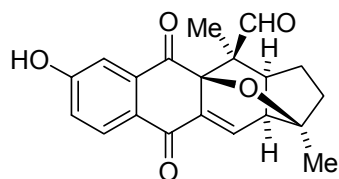


10:1

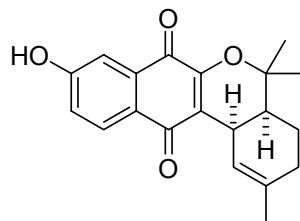
# Completion of the Synthesis



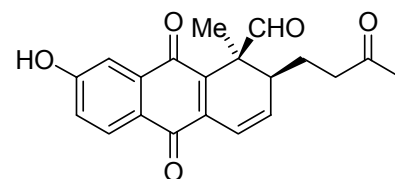
# Biomimetic Synthesis of Pinnatal and Sterekunthal



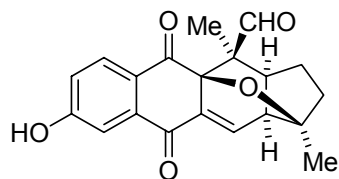
pinnatal



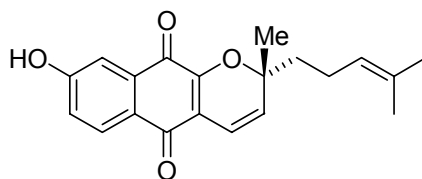
pyranokunthone A



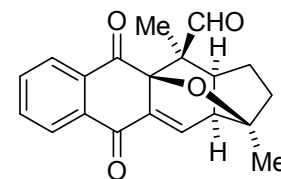
sterekunthal A



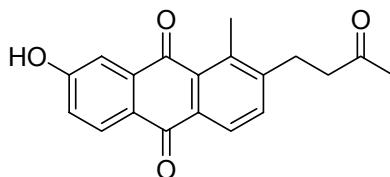
isopinnatal



pyranokunthone B



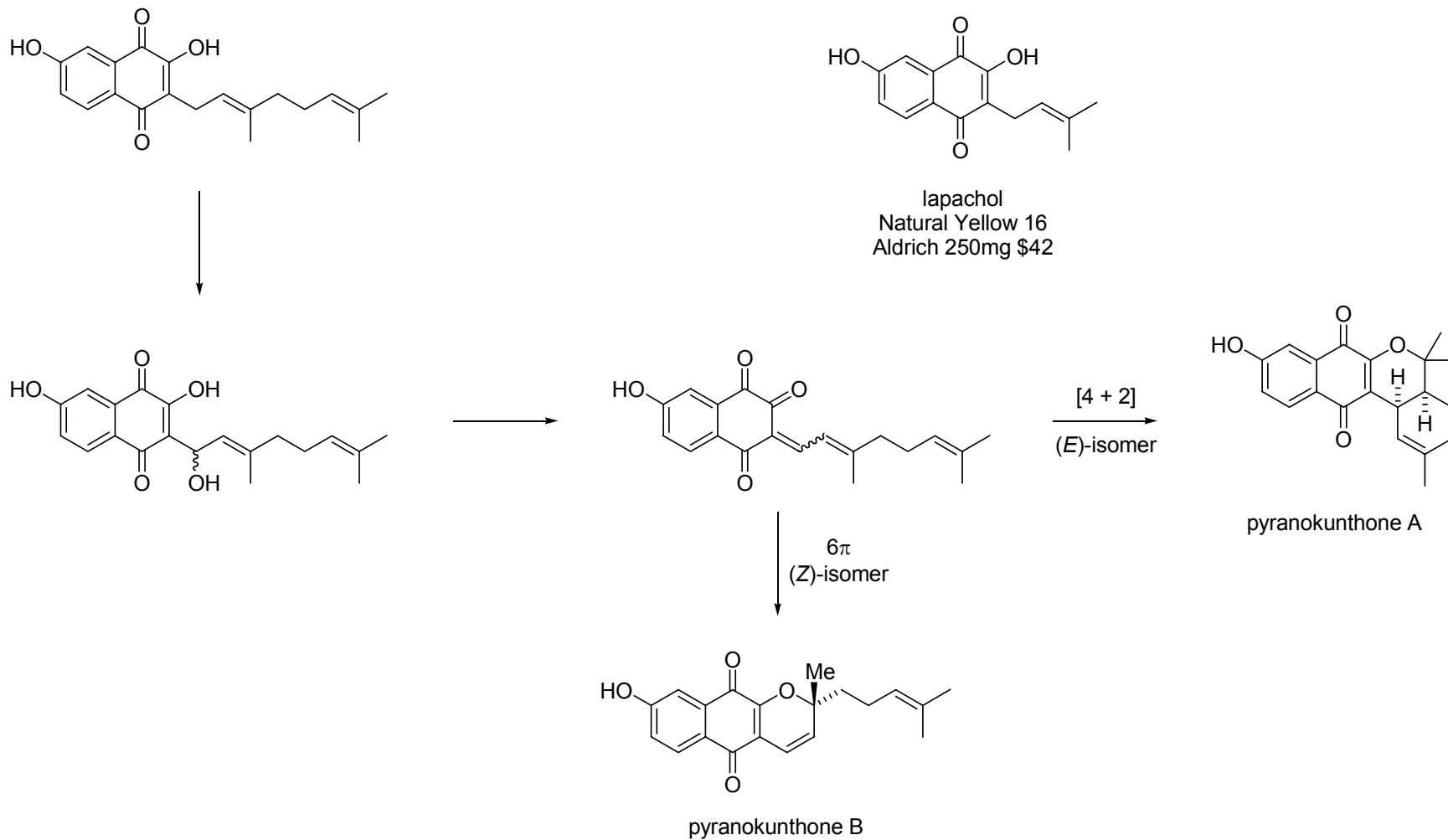
sterekunthal B



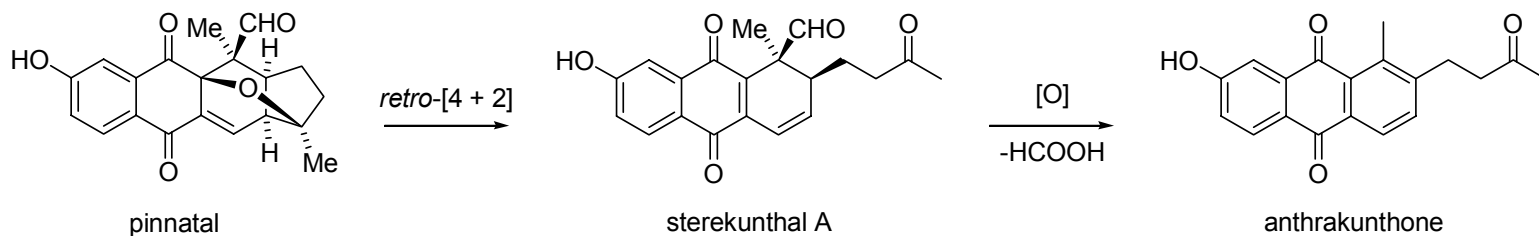
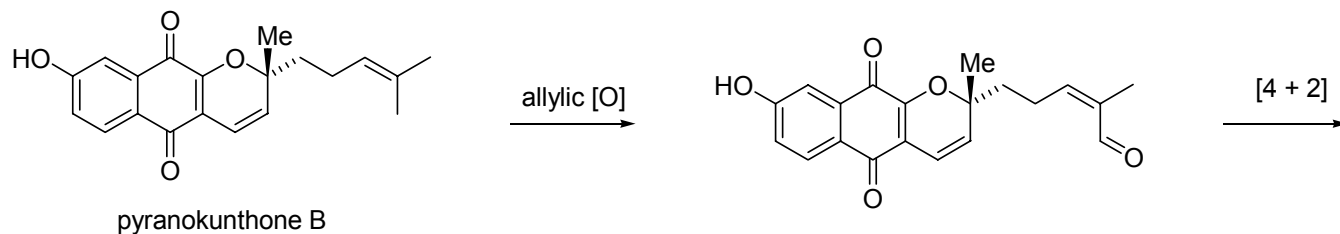
anthrakunthone

- Isolated from the *Bignoniaceae* plant family
- Lead compounds for antimalarial drugs

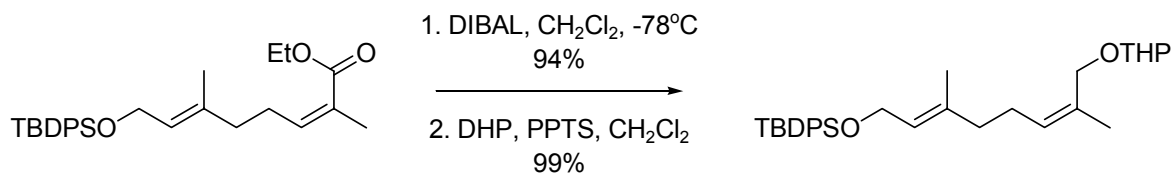
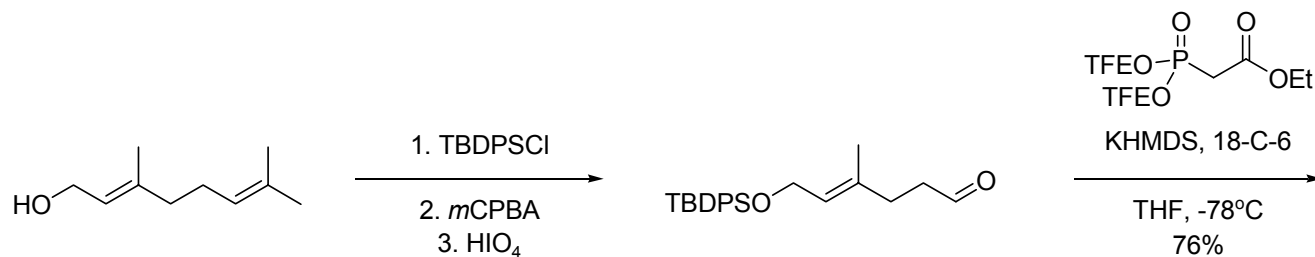
# Biosynthetic Hypothesis



# Biosynthetic Hypothesis, cont.

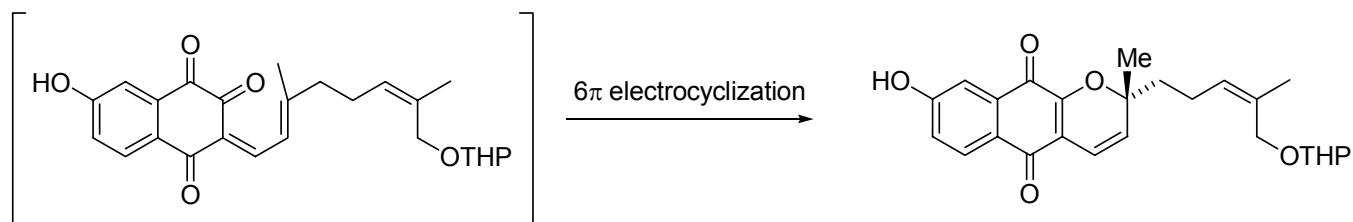
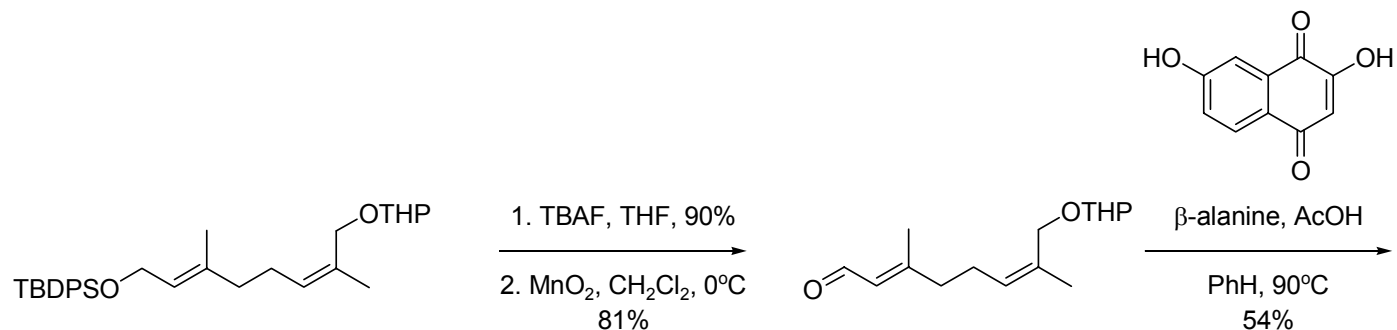


# Differentiated Diol Synthesis

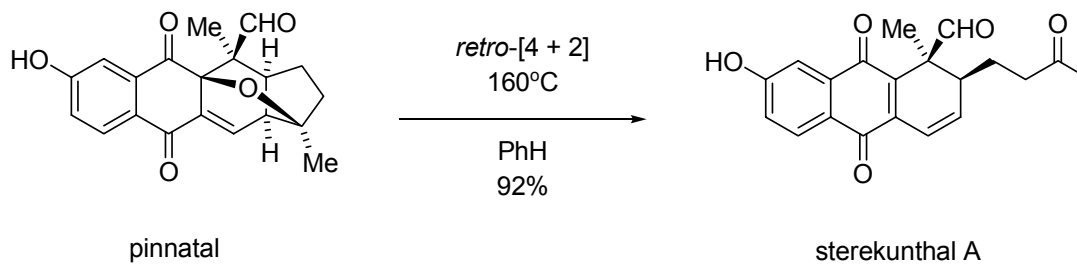
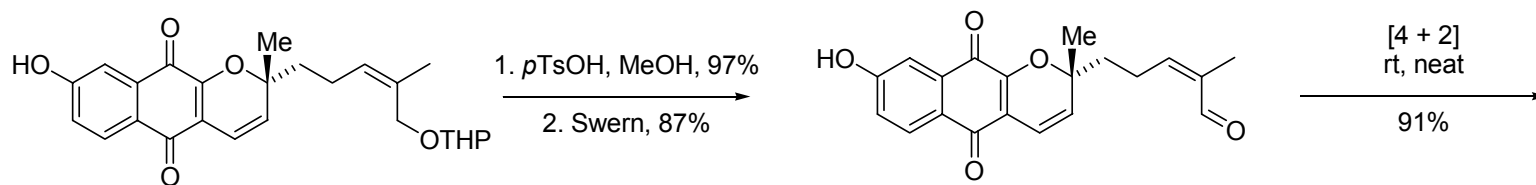




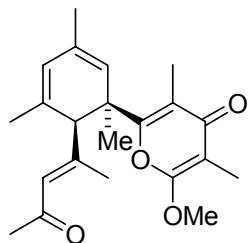
# Advancement of the Synthesis



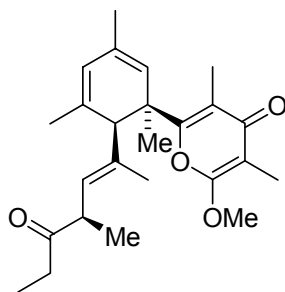
# Completion of Synthesis



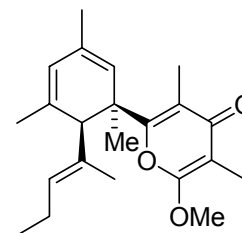
# Molluscan Polypropionates



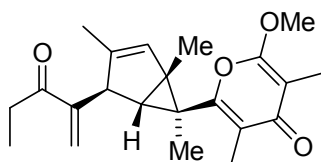
tridachiapyrone A



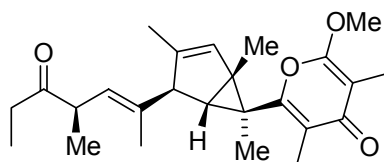
tridachiapyrone I



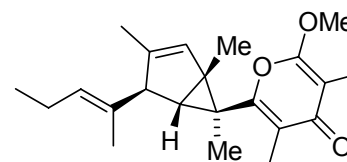
9,10-deoxytridachione



tridachiapyrone E



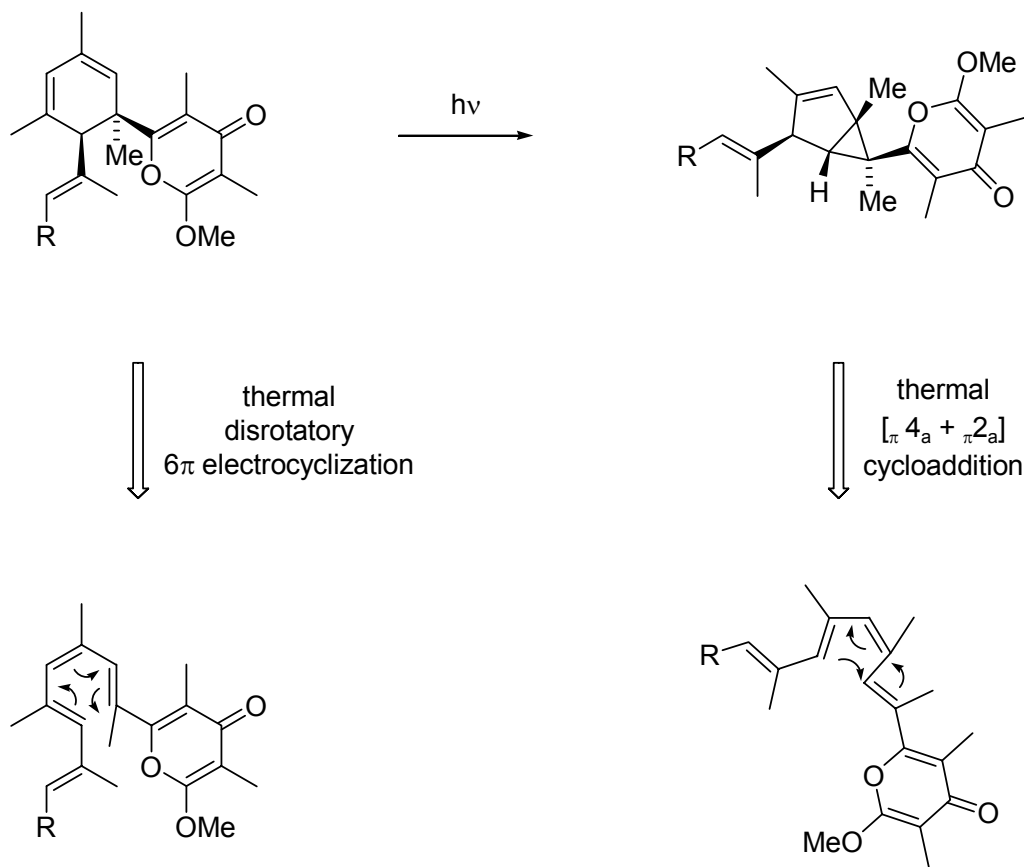
crispatene



photodeoxytridachione

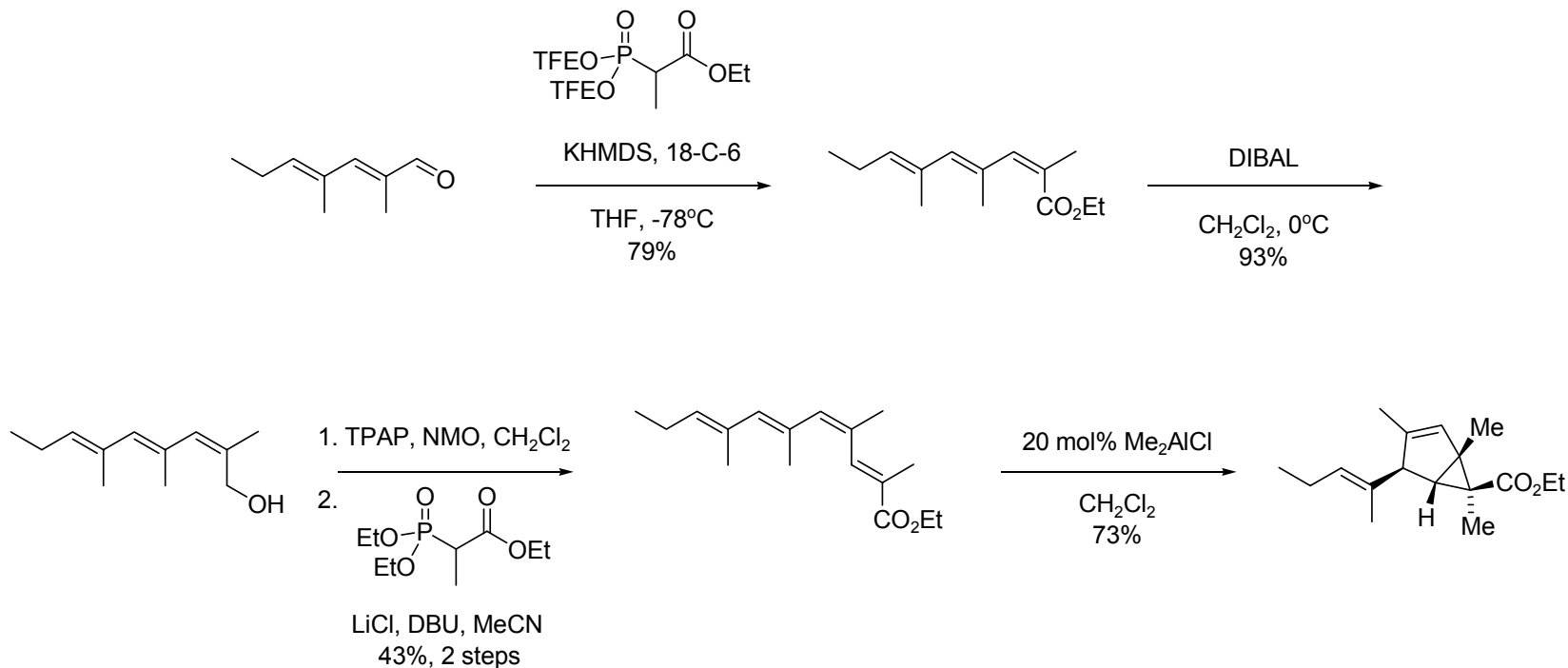
- feature an  $\alpha$ -methoxy- $\gamma$ -pyrone moiety and are proposed to act as a natural sunscreen due to their UV-light-absorbent properties
- two categories: those featuring a cyclohexadiene core and others with a bicyclo[3.1.0]hexene core
- (-)-crispatene isolated from the mollusc *Elysia crispata* in 1981 by Ireland

# Interrelationship



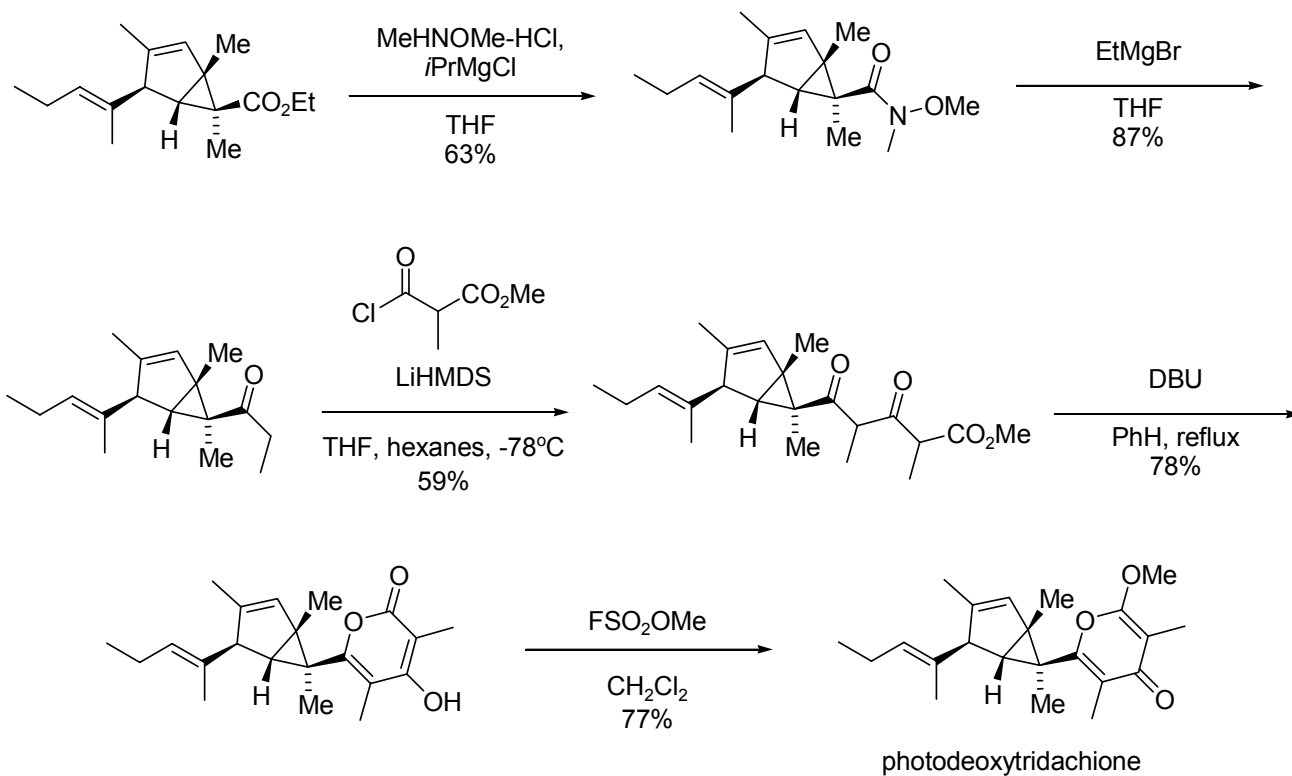
- in 1979, Ireland and Scheuer found that the cyclohexadiene core can be photochemically converted to the bicyclo[3.1.0]hexene core in vivo and in vitro
- this suggests that both compounds are directly derived from a common acyclic precursor

# Photodeoxytridachione Core Synthesis

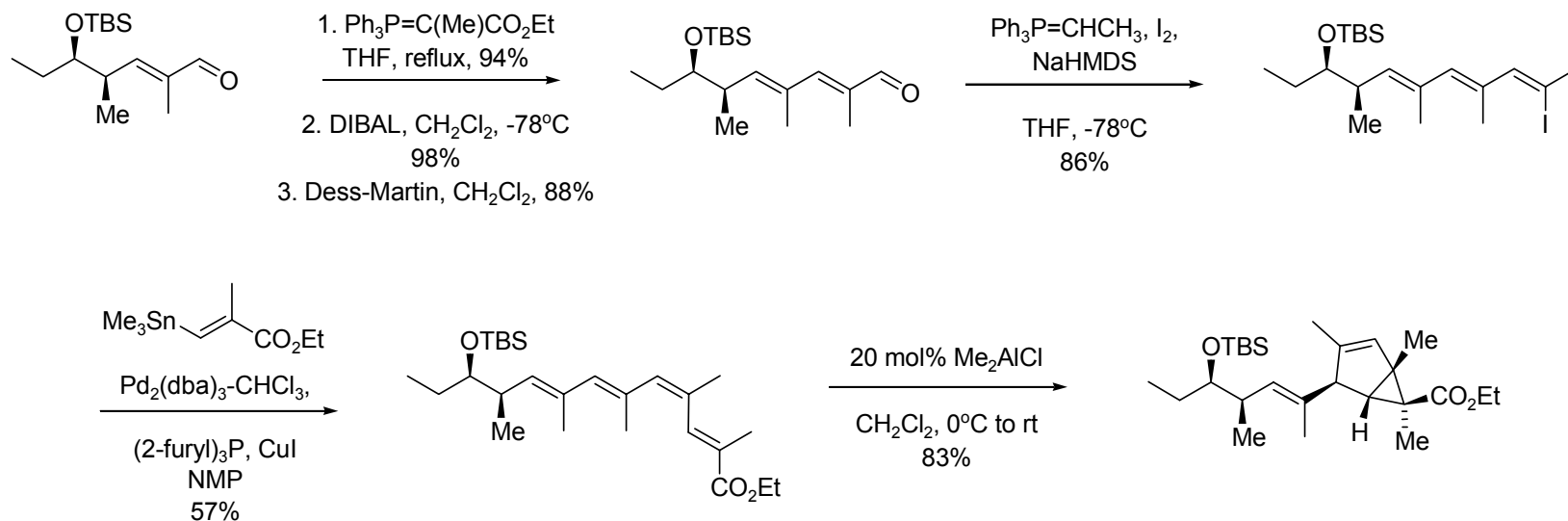


- A.K. Miller, D. Trauner. *Angew. Chem. IE.* **2003**, 549.

# Completion of the Synthesis

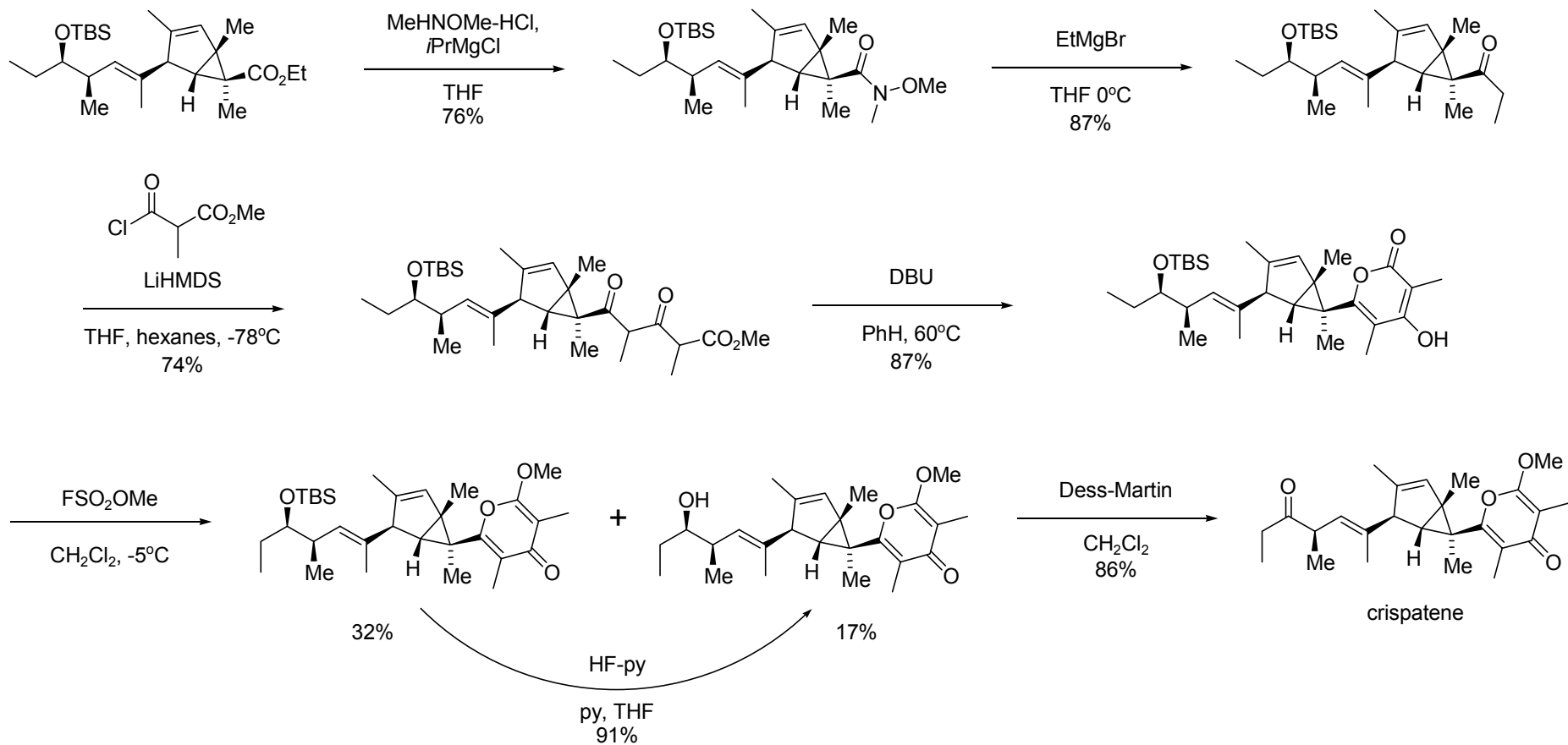


# (-)-Crispatene Core Synthesis



- A.K. Miller, D.H. Byun, C.M. Beaudry, D. Trauner. *PNAS*. **2004**, 12019.

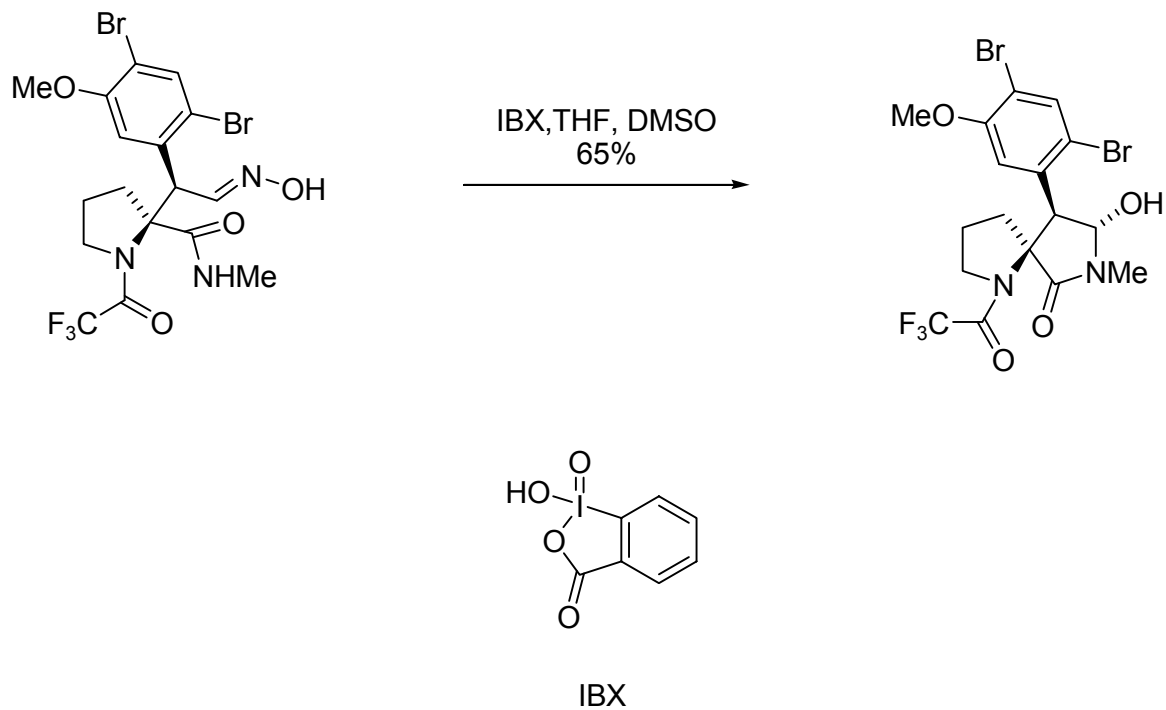
# Completion of the Synthesis





# Problem 1

During the total synthesis of amathspiramide F, the Trauner group oxidatively cleaved an oxime with IBX to close the pyrrolidinone ring. Please provide a mechanism for this transformation.



Method: D.S. Bose, P. Srinivas. *Synlett*, **1998**, 977.

# Problem 2

Please explain why, under Lewis acid catalysis,  $6\pi$  electrocyclicization is effectively outcompeted by the  $[\pi 4_a + \pi 2_a]$  cycloaddition to give the bicyclo[3.1.0]hexene moiety seen below.

