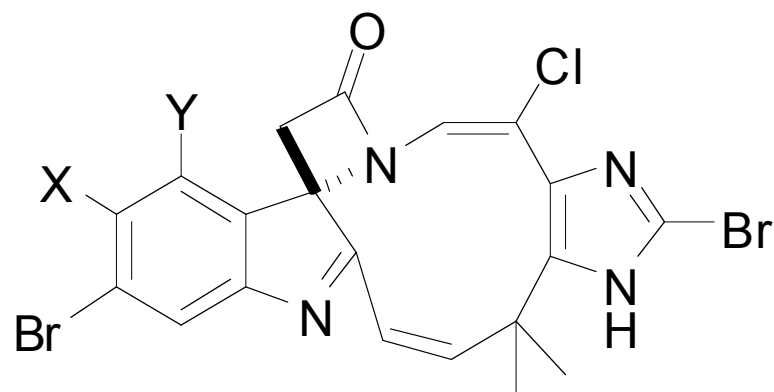


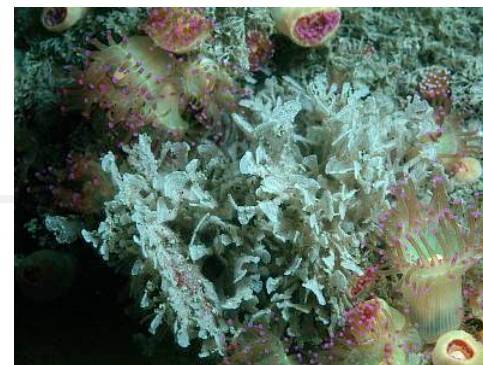


# Total Synthesis of the Chartellines



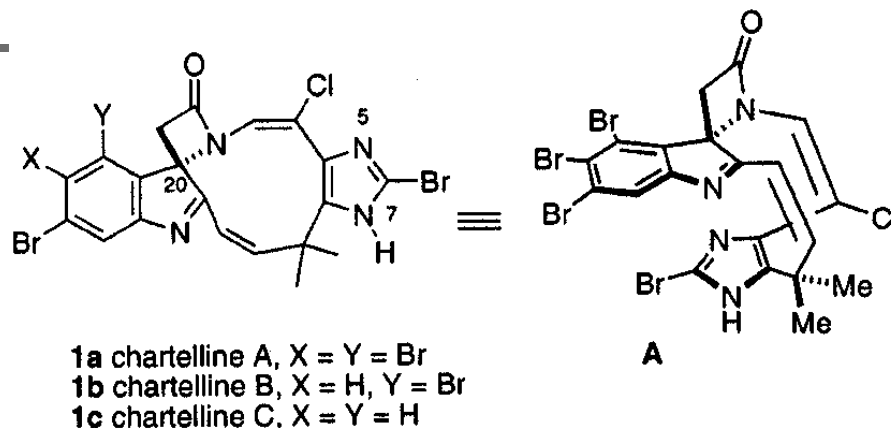
chartelline A, X = Y = Br  
chartelline B, X = H, Y = Br  
chartelline C, X = Y = H

# Background



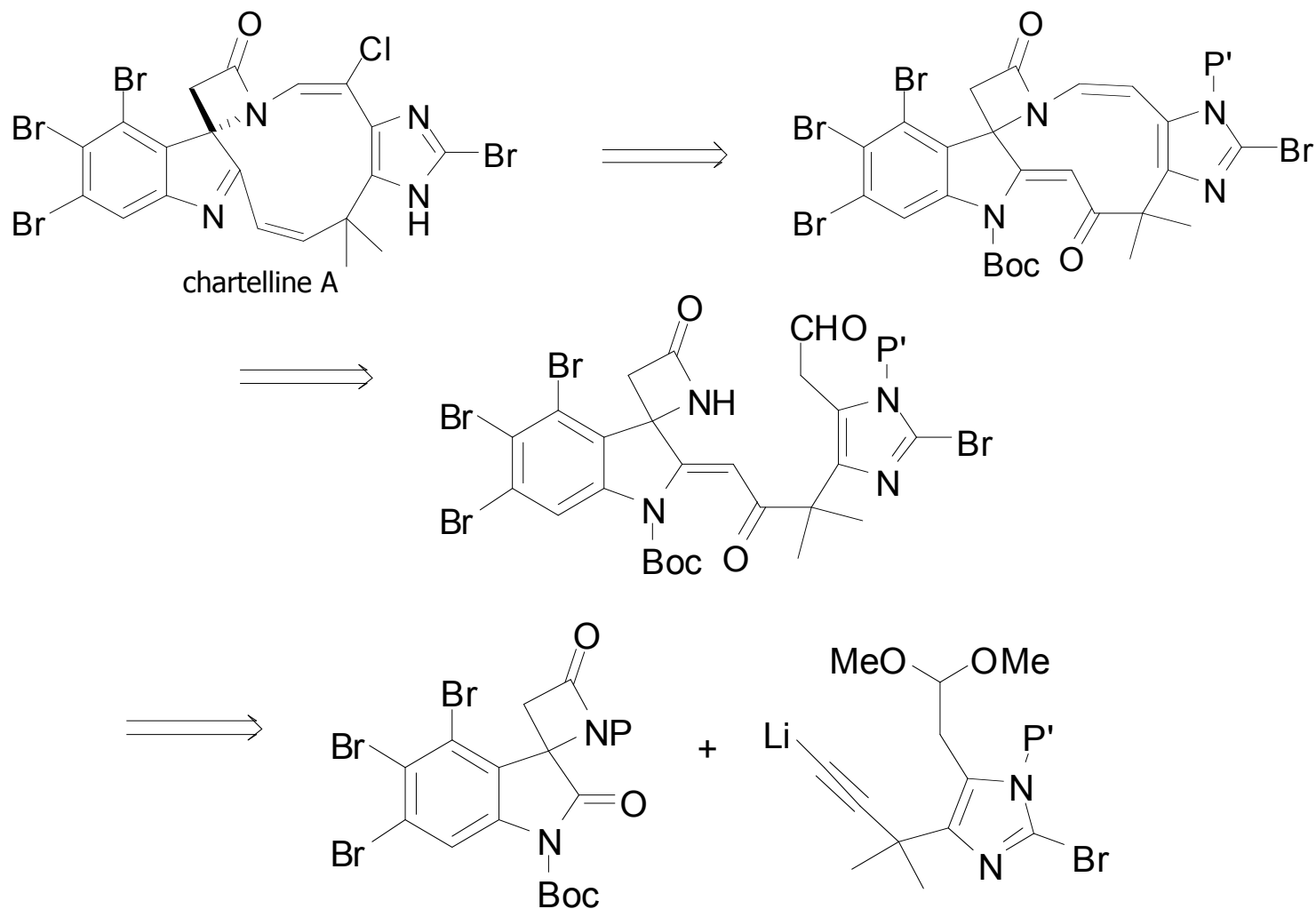
- Chartellines A, B, and C were isolated in the 1980s by Christophersen and co-workers
- Isolated from the marine bryozoan *Chartella papyracea* collected in the North Sea
- Chartelline A completely lacks any significant biological activity but remains a target of interest due to its novel and complex structure
- In 2006, the Weinreb group reported their progress toward the total synthesis of chartelline A and the Baran group reported the first total synthesis of chartelline C

# The Chartellines as Synthetic Targets

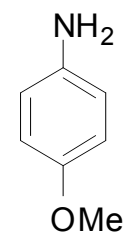
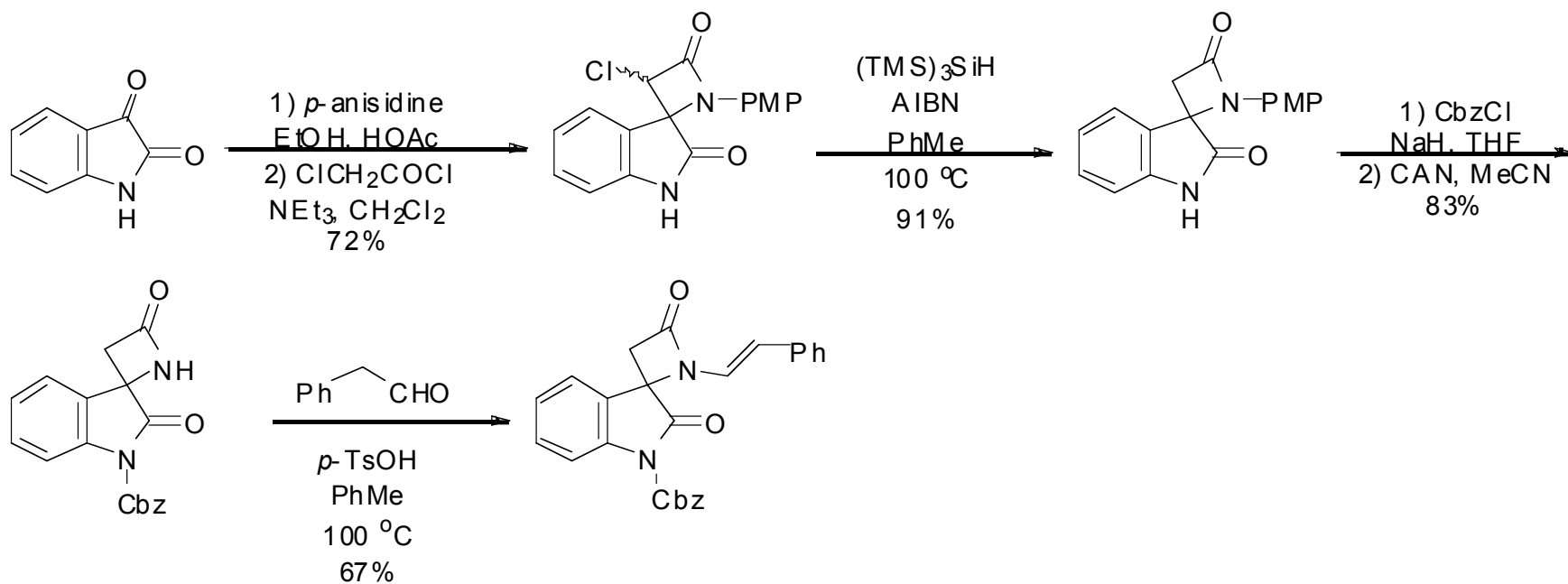
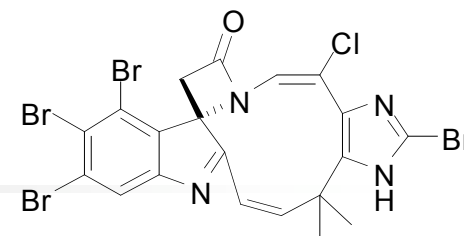


- Structure and stereochemistry of chartelline A confirmed by X-ray crystallography
- 10-membered ring adopts a rigid tube-like conformation, indicating little conjugation present between the ring systems
- Indolenine system almost perpendicular to the spiro-β-lactam ring and is close to parallel to the imidazole ring
- Dense array of sensitive functionalities: spiro-β-lactam, indolenine, chloroenamide, and 2-bromoimidazole units

# Weinreb's Retrosynthesis of Chartelline A

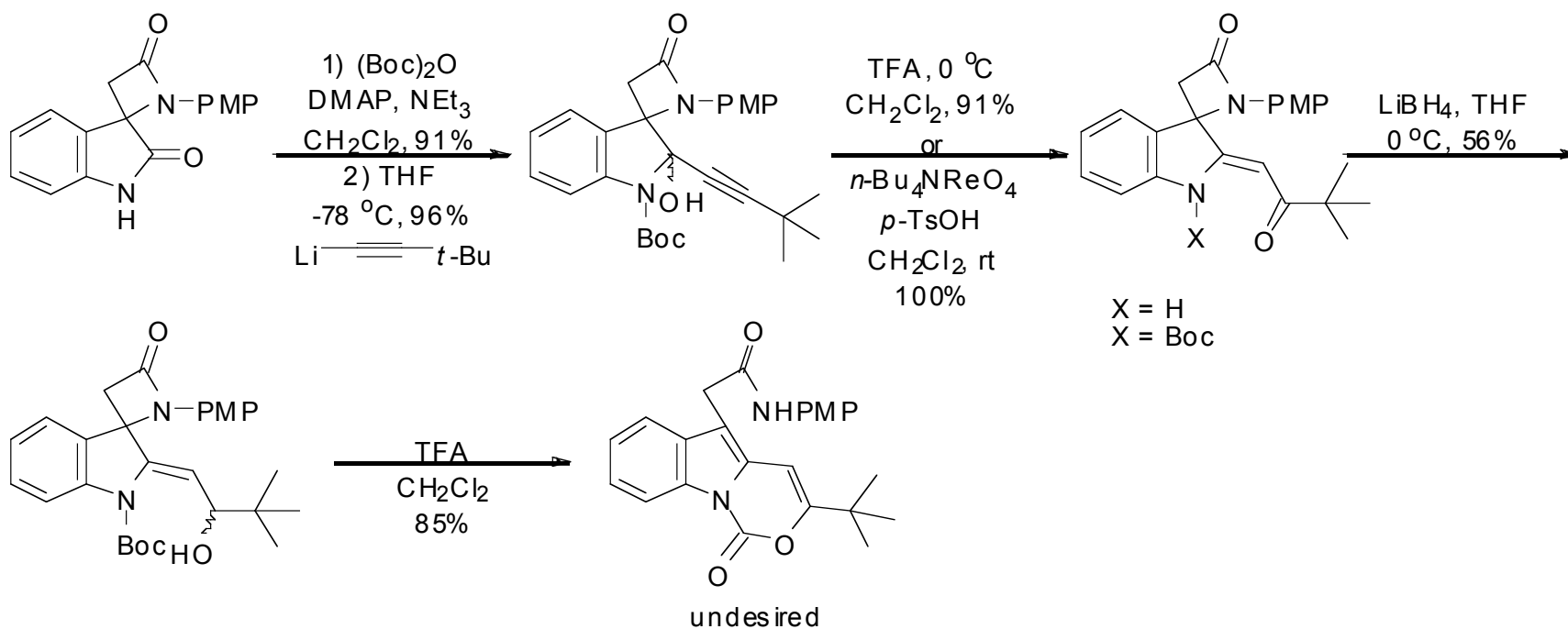
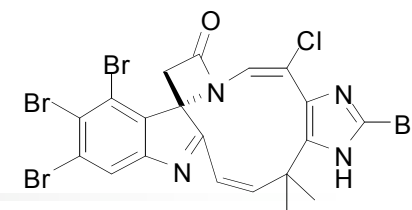


# Model Studies

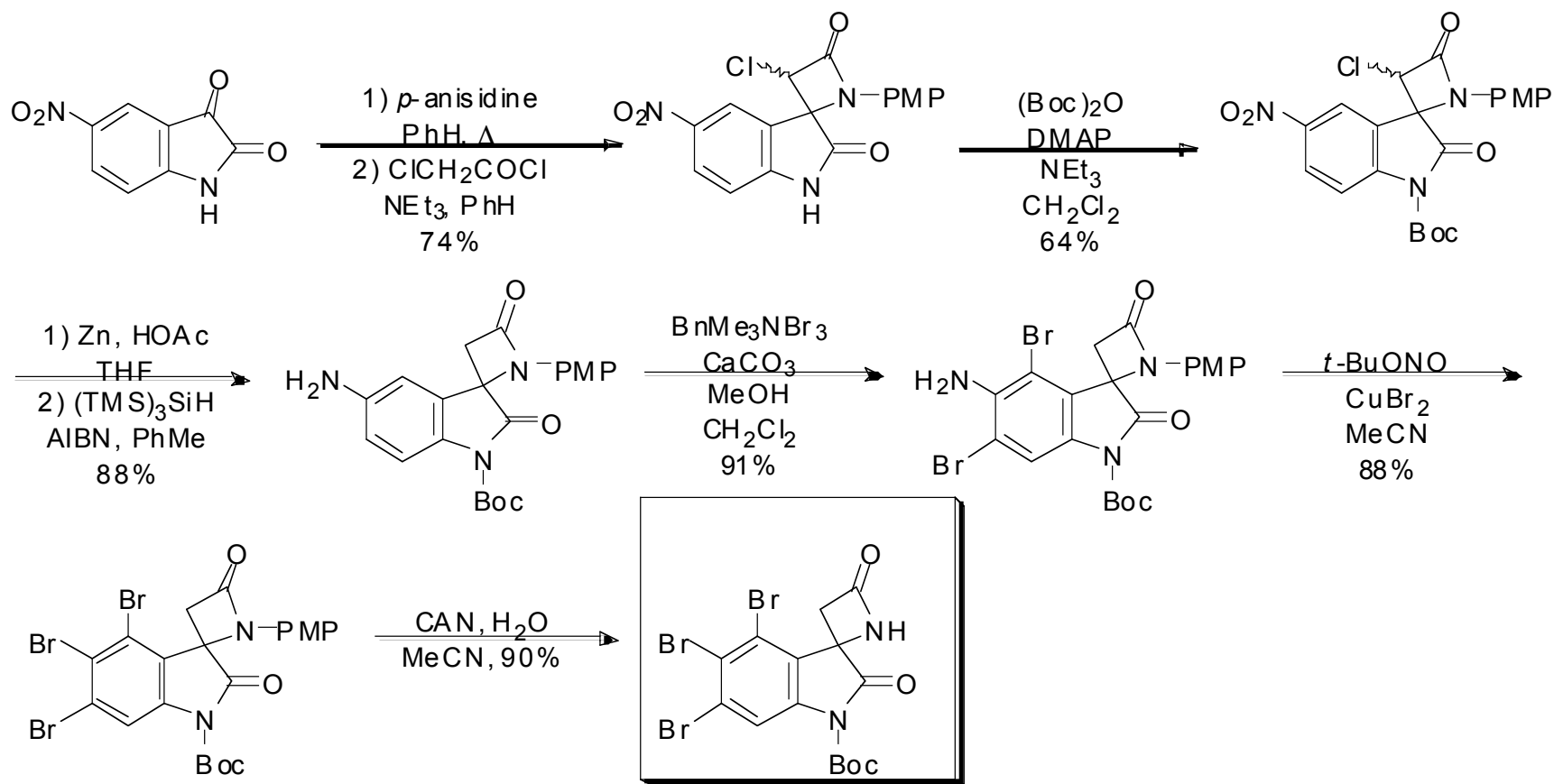


*p*-anisidine

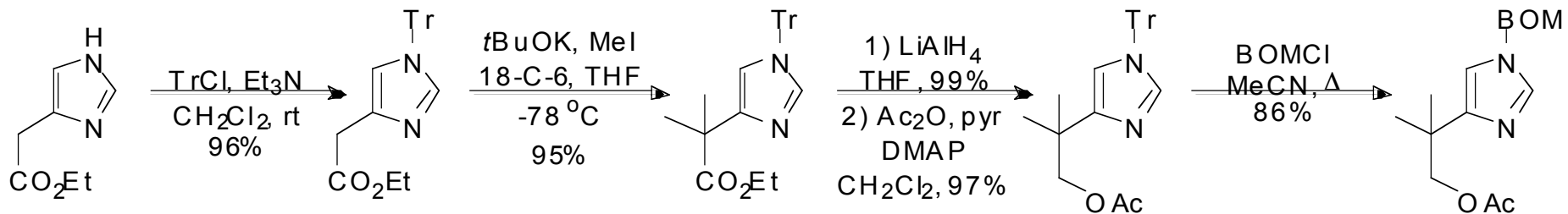
# More Model Studies



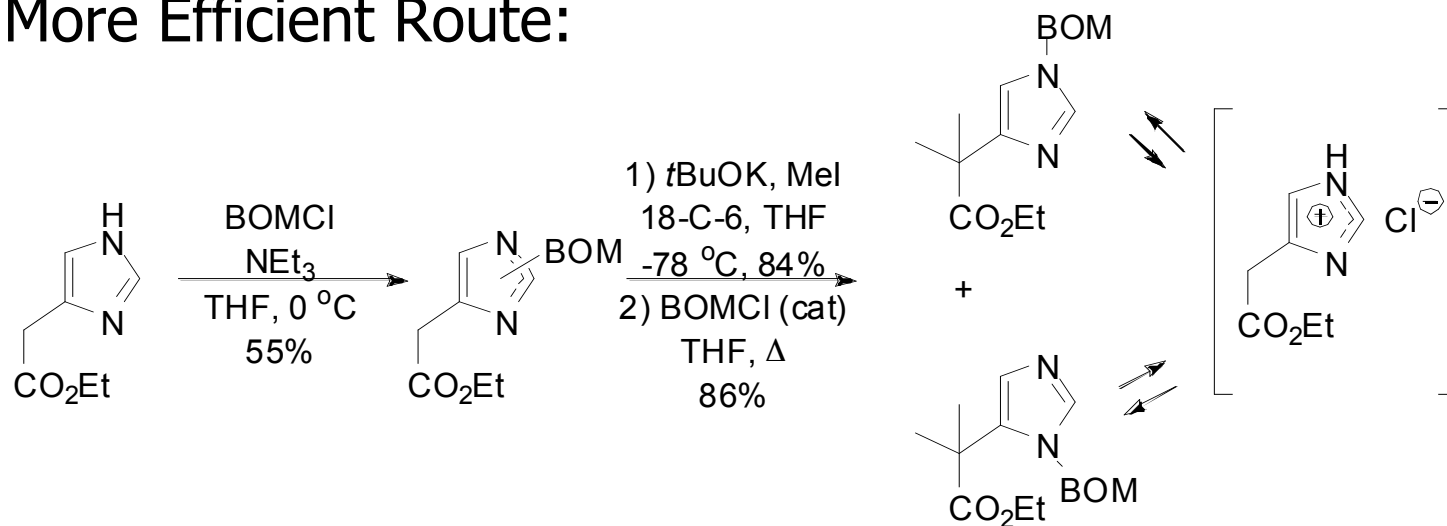
# Synthesis of Tribrominated $\beta$ -lactam Moiety



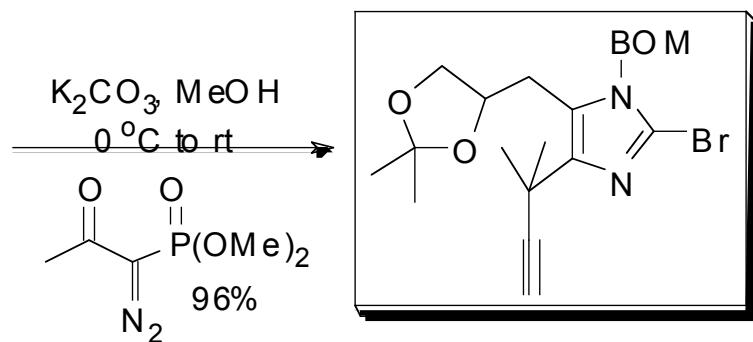
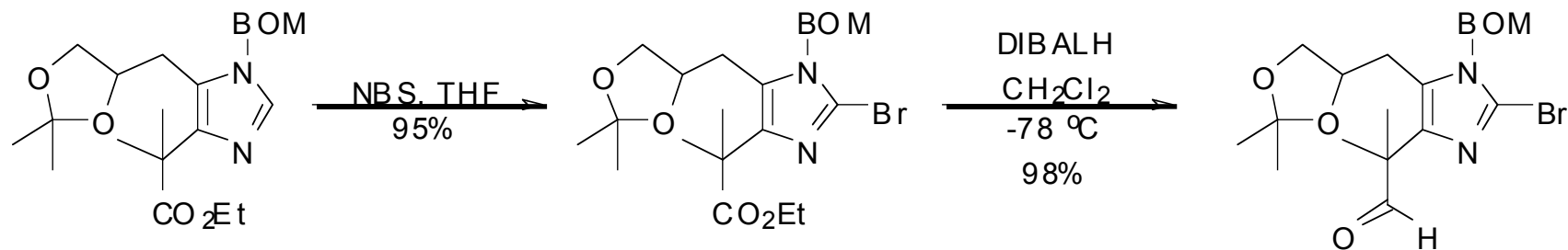
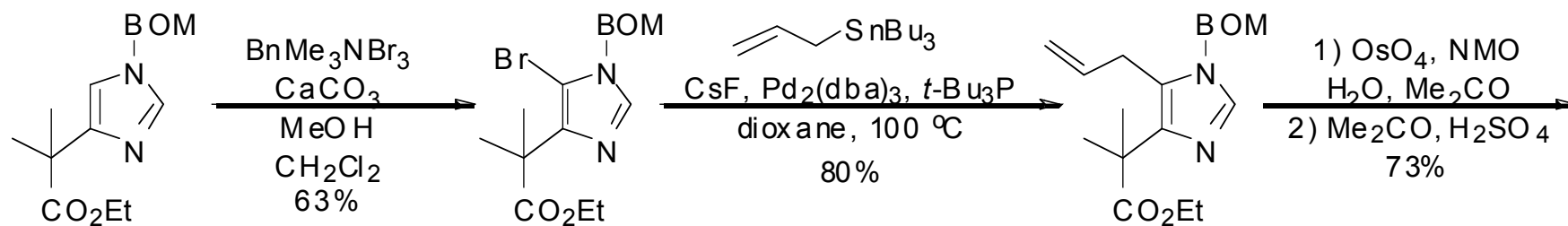
# Preparation of Imidazole Fragment



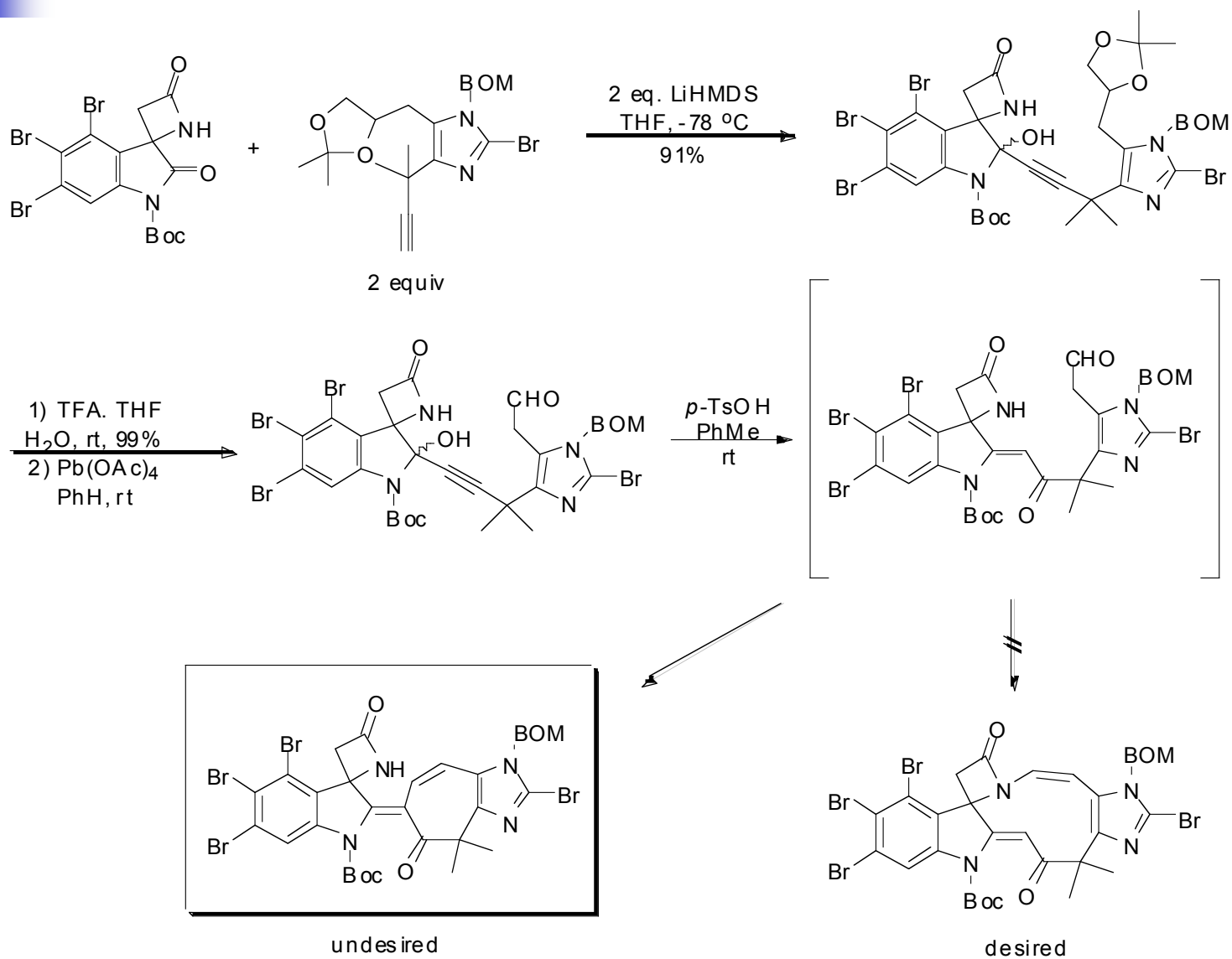
## More Efficient Route:



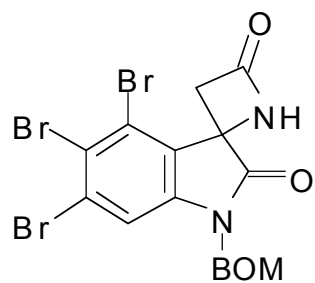
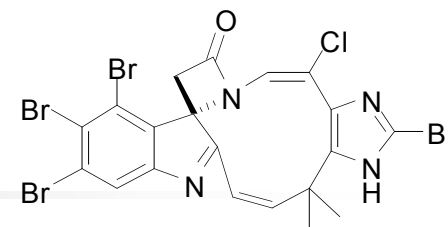
# Completion of Imidazole Fragment



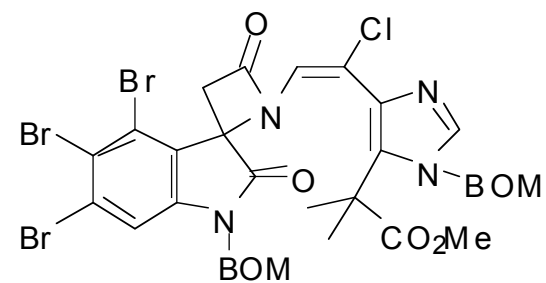
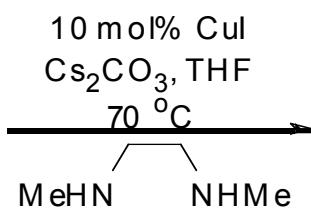
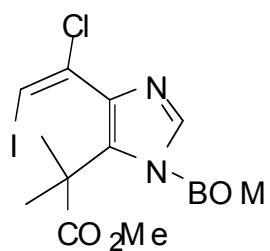
# Coupling of Fragments



# New Methodology

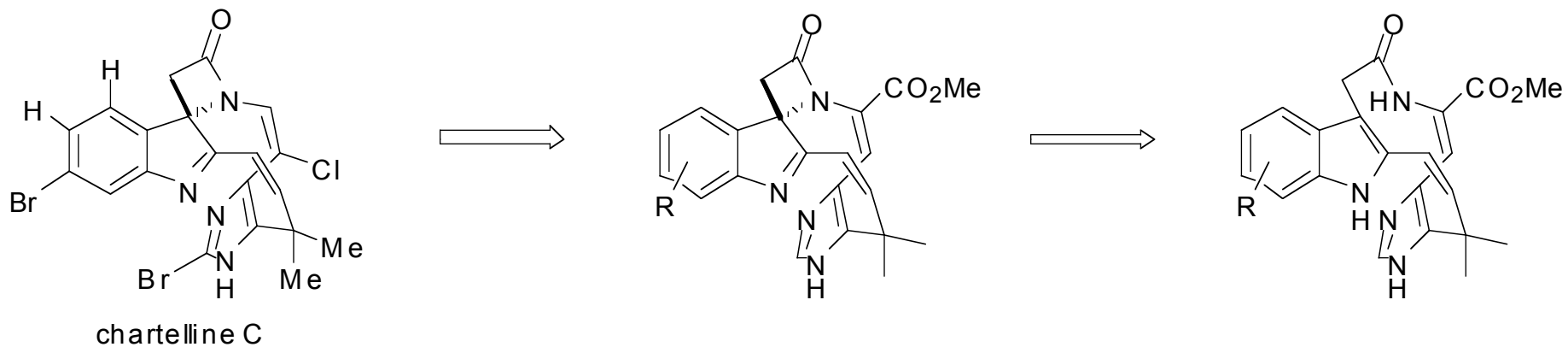


+

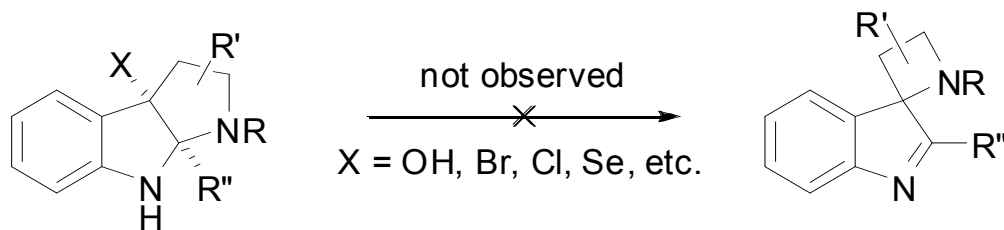


45% (67% br sm)

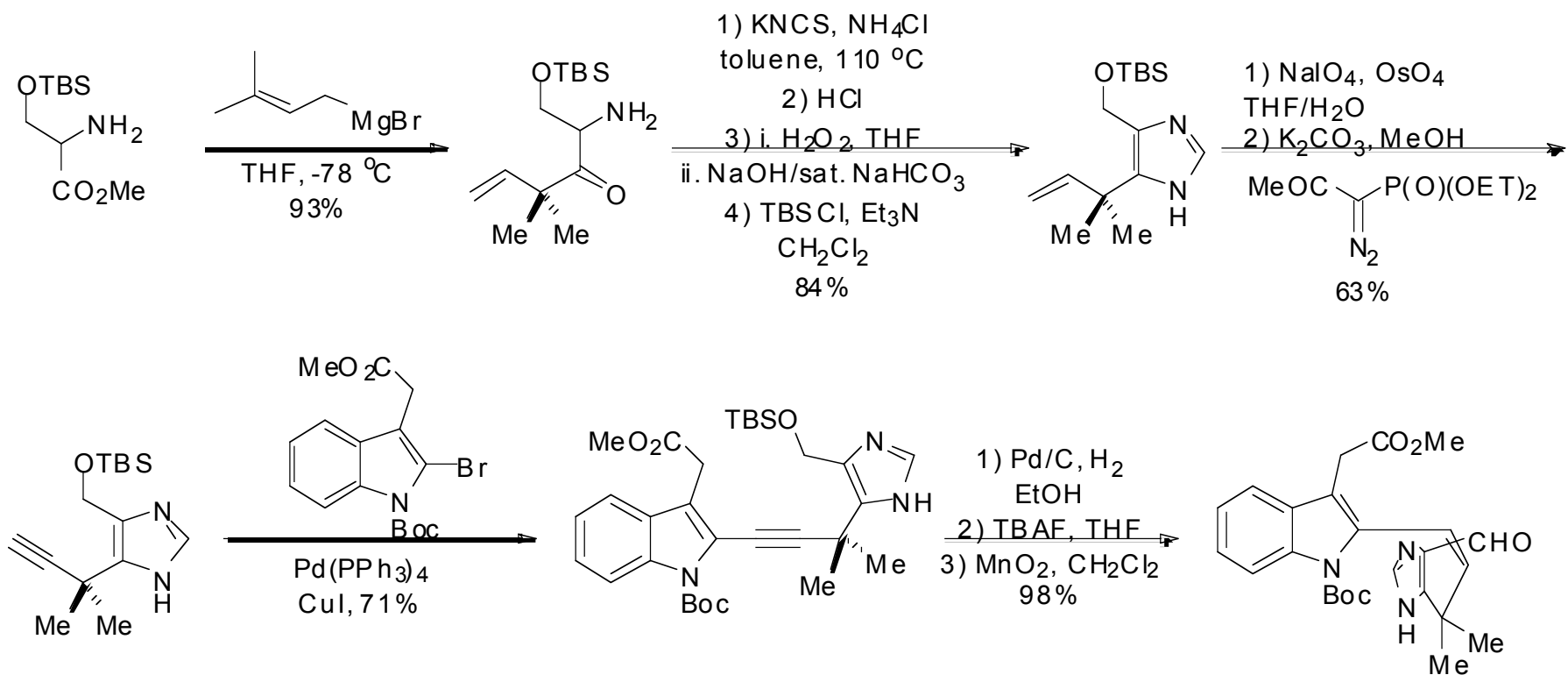
# Baran's Approach to Chartelline Carboskeleton



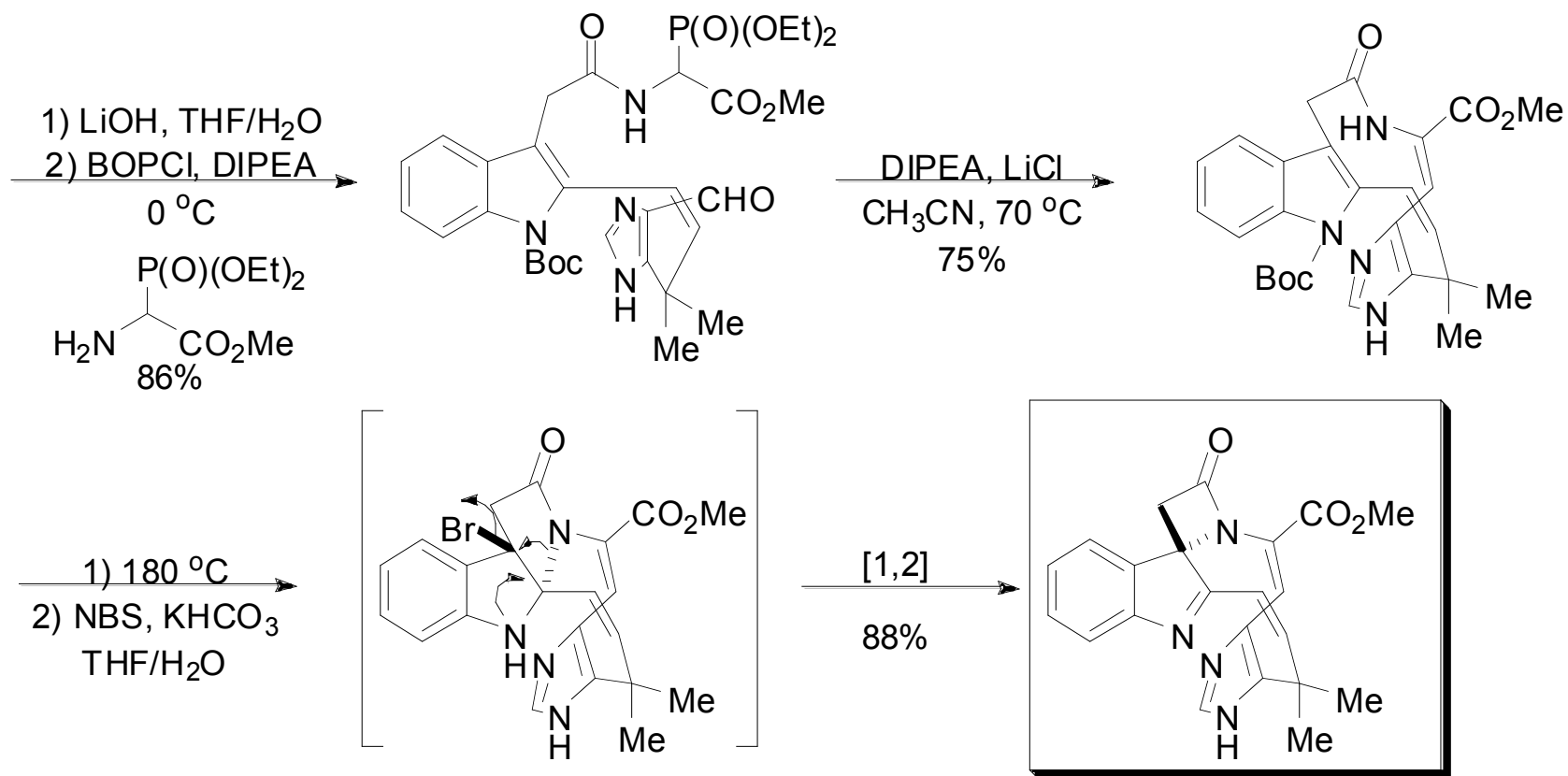
"...there are no examples for such a ring contraction of a pyrroloindoline unit and ample precedent that suggests its failure..."



# Synthesis of Chartelline Carboskeleton

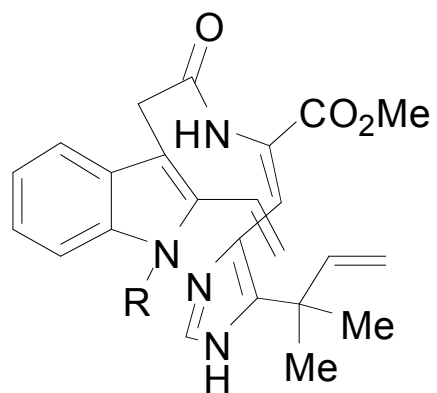


# Continued...

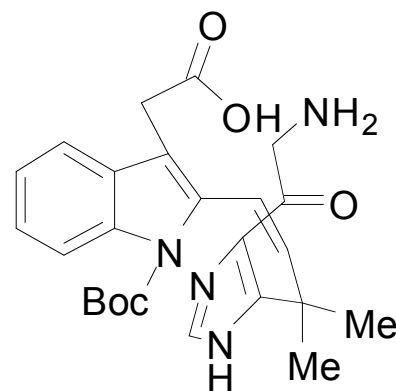


19% overall yield  
10 steps

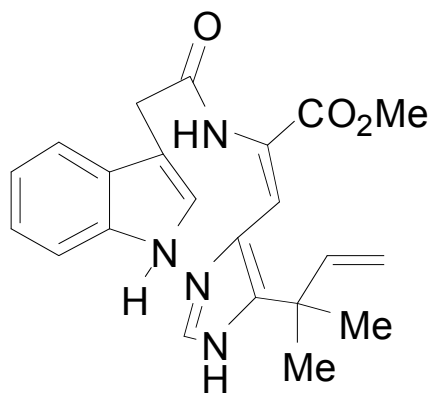
# Dead End Routes to the Chartelline Skeleton



Ring-closing metathesis

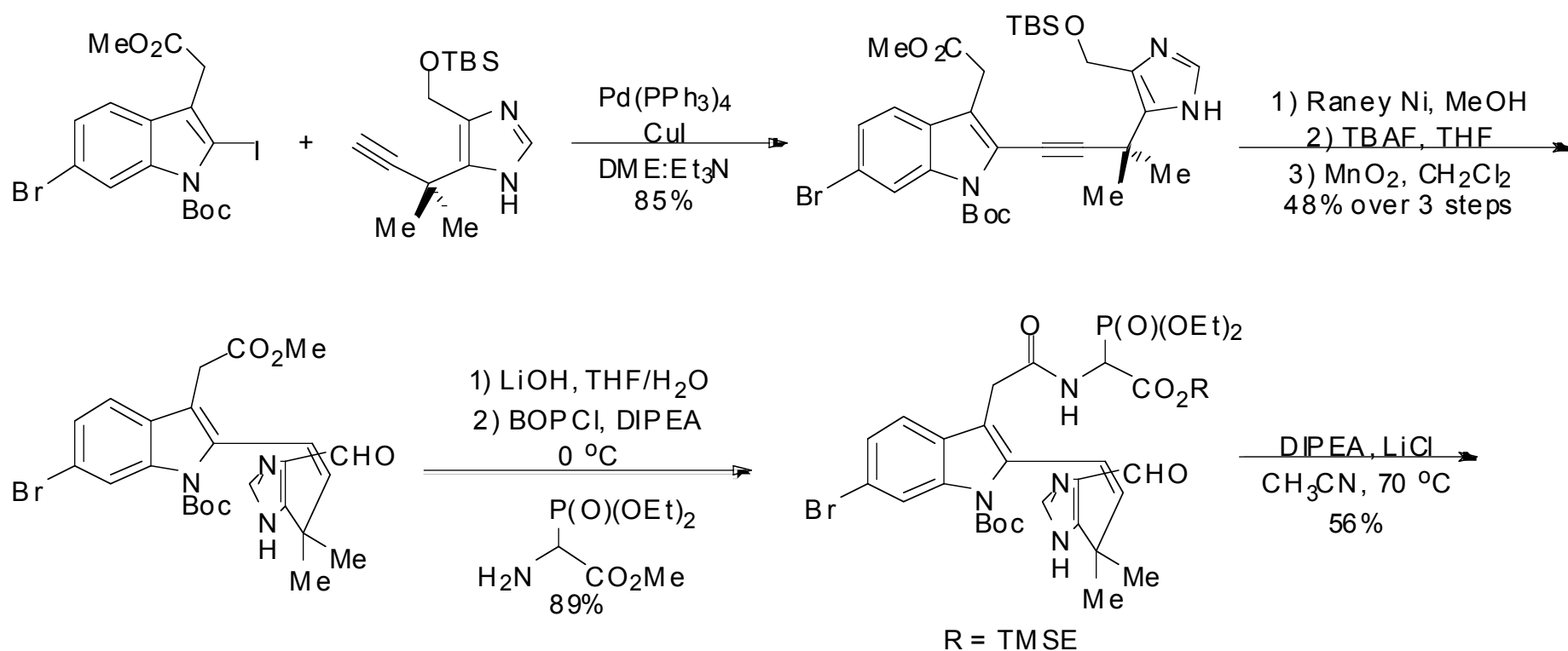


Macrolactamization



Heck-type ring closure

# Baran's Total Synthesis of Chartelline C



Baran, P.S.; Shenvi, R. A. *J. Am. Chem. Soc.* **2006**, ASAP.

# Continued...

