

# Classics in Tetrahedron Letters

Jeremy Richter

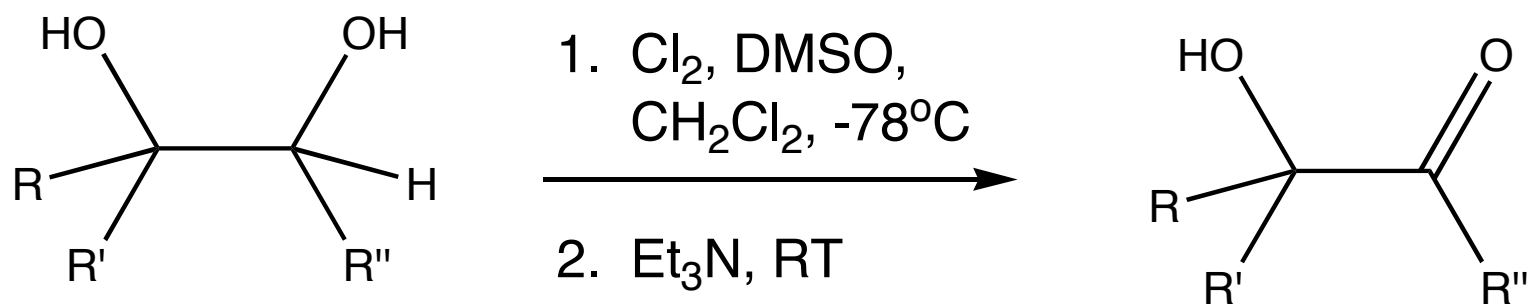
Baran Group Meeting: 9/24/03

# The Plan

- Methodology
- Protecting Groups
- Natural Products
- Syntheses

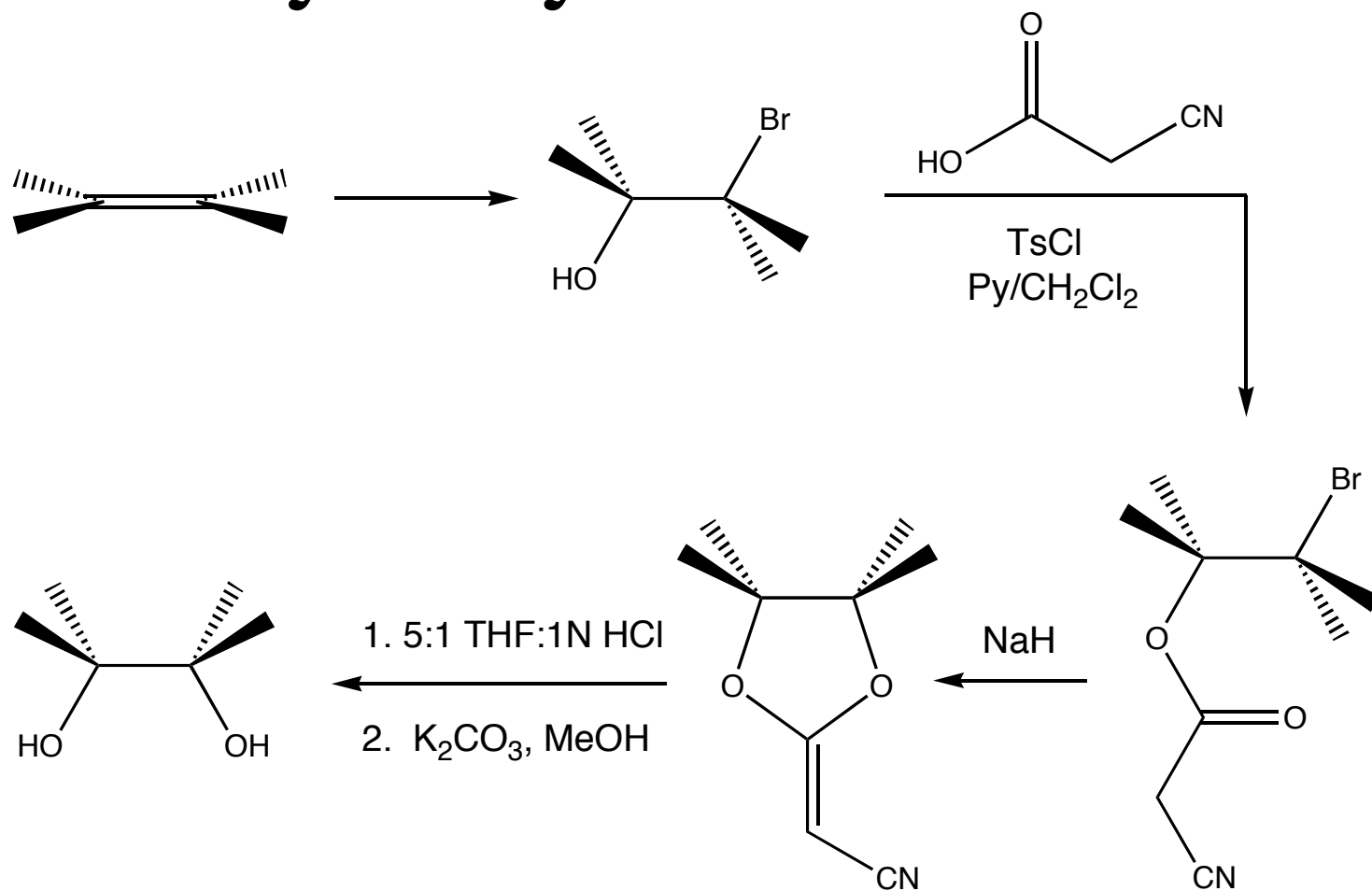
# Methodology

# Oxidation of Vicinal Diols



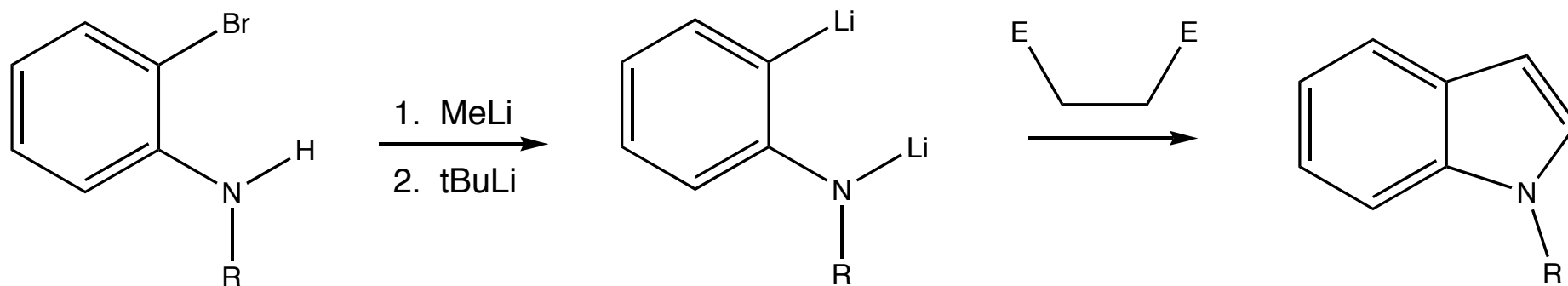
Can selectively oxidize the secondary alcohol in the presence of the tertiary alcohol without cleavage.

# cis-Hydroxylation of alkenes



Allows selectivity during bromohydrin formation

# Indole Synthesis



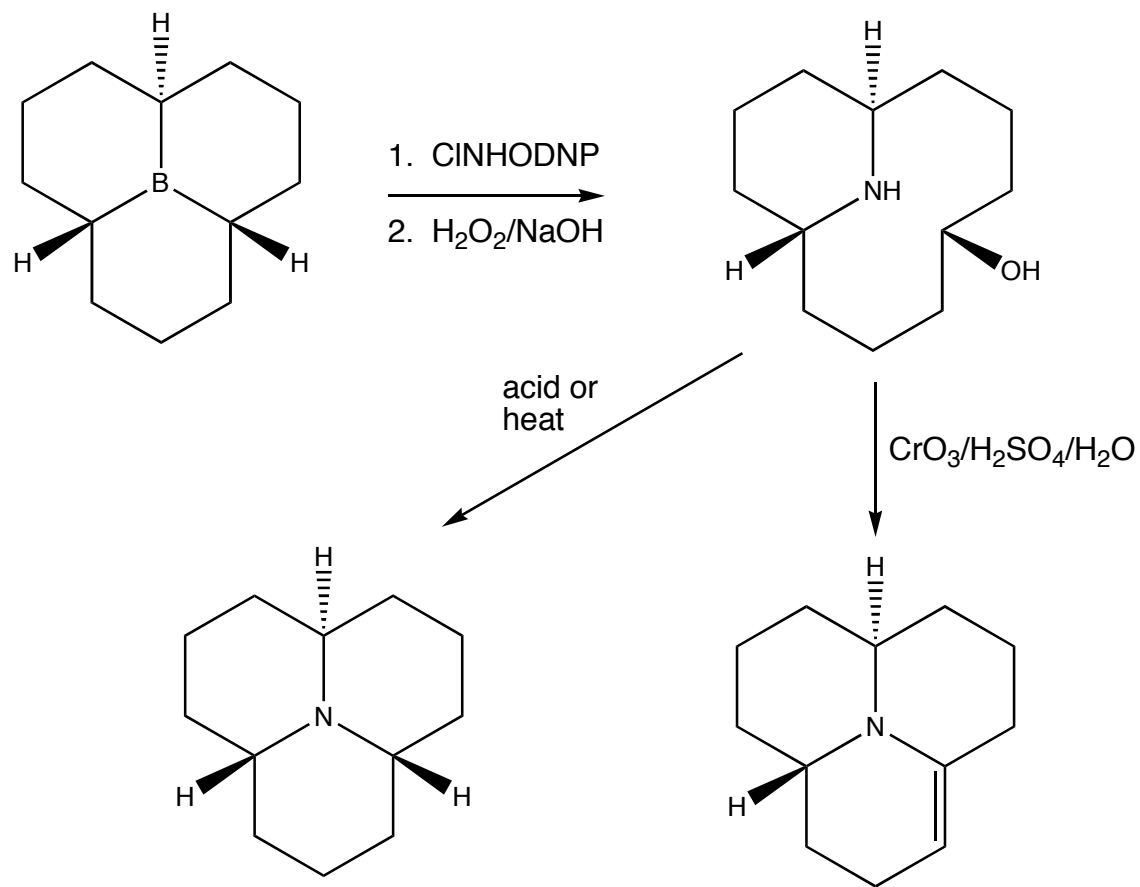
Biselectrophiles used:  $\alpha$ -chloroketones,  $\alpha,\beta$ -epoxyketone (Li enolate), and enediones

Also used 5-substituted anilines

R is a general protecting group: best results with BOC

Yields: 50-90%

# An Interesting Reaction:



Mueller. 1976, 2925

Mueller. 1979, 1991

# Alcohol Oxidations

Collins Reagent<sup>1</sup>

PCC<sup>2</sup>

PDC<sup>3</sup>

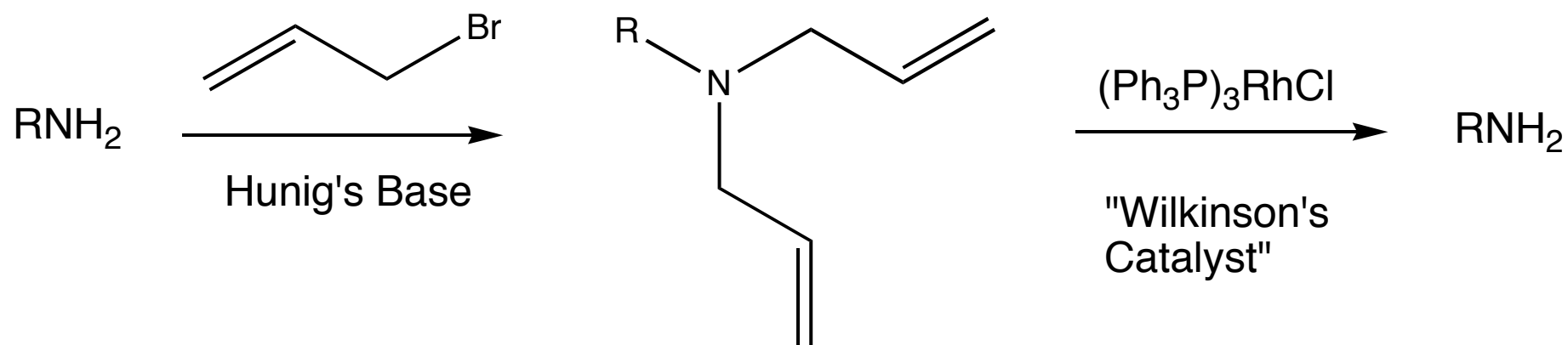
Collins. **1968**, 3363

Corey. **1975**, 2647

Corey. **1979**, 399

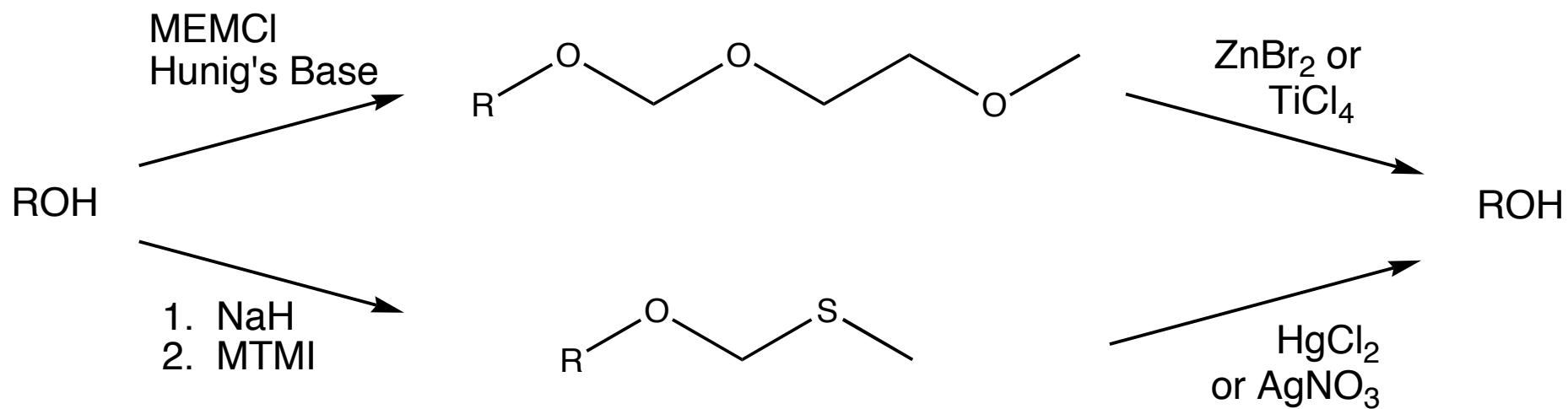
# Protecting Groups

# N,N-Diallyl



Acid/Base Stable and Nucleophile Inert

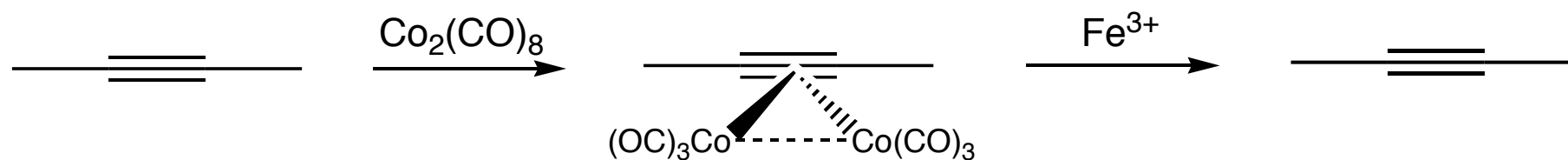
# MEM<sup>1</sup> and MTM<sup>2</sup>



<sup>1</sup>Corey. **1976**, 809

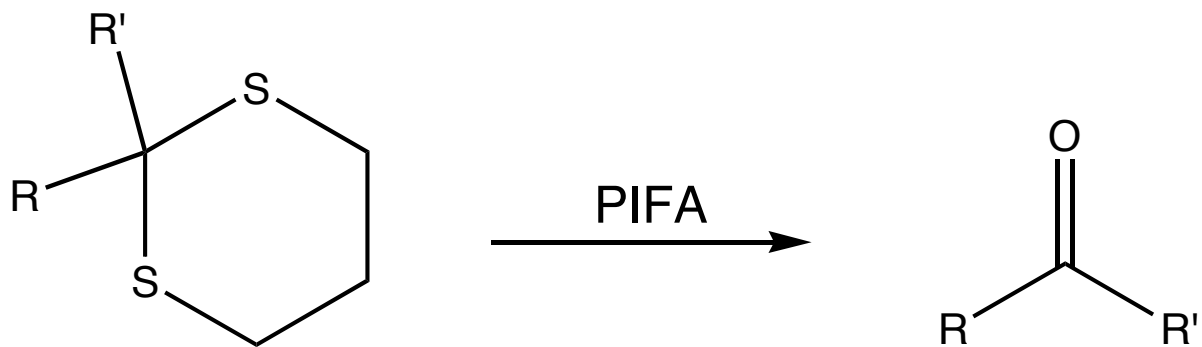
<sup>2</sup>Corey. **1975**, 3269

# Protection for Alkynes



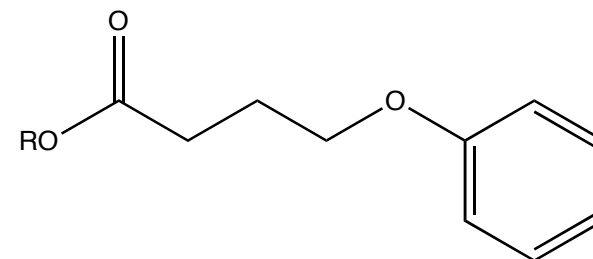
Alkyne now protected from reagents which can affect alkenes or alkynes.

# Not New, But Improved: Thioacetals



Improved method of removal which is selective for thioacetals.

# BOB<sup>1</sup>



## Protection:

1. Fisher Esterification
2. Mitsunobo Esterification
3. Jacobsen Asymmetric Epoxide Opening with Carboxylic acids, catalyzed with Co(salen)<sup>2</sup>

## Deprotection:

1. Hydrogenolysis/lactonization:  
H<sub>2</sub>, Pd/C then KOtBu

## Protecting Capability:

1. Assumed similar to other esters
2. Can remove in presence of other esters

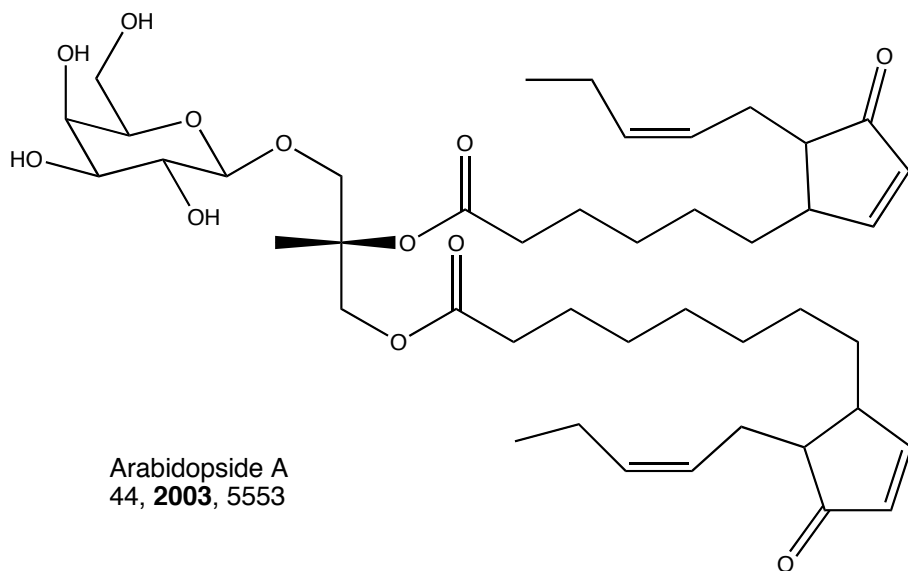
<sup>1</sup>Ganem. **2000**, 9523

<sup>2</sup>Jacobsen. **1997**, 773

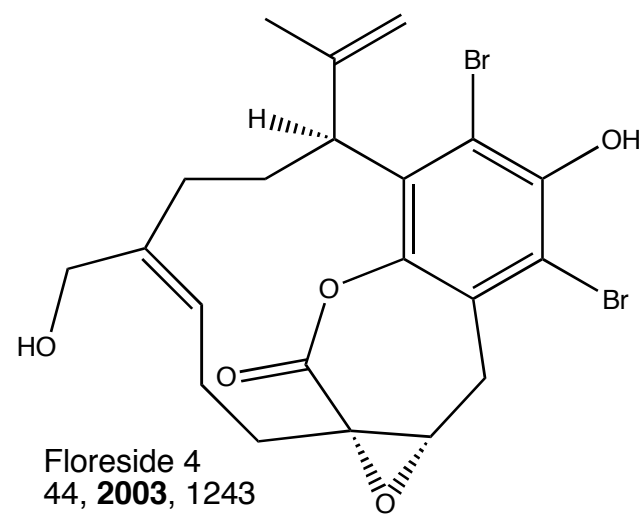
Natural Products  
Reported in  
Tetrahedron Letters



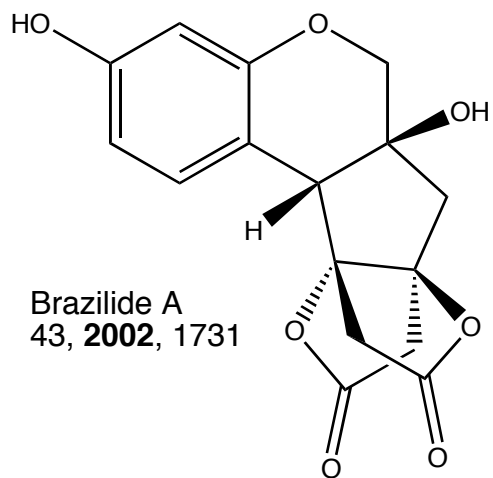
# Natural Products



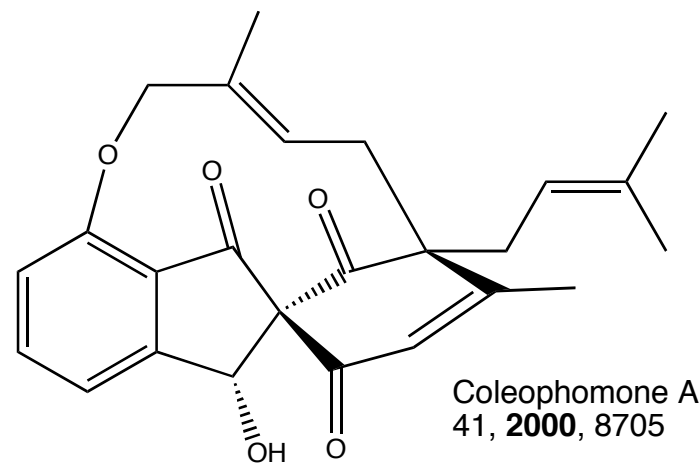
Arabidopside A  
44, 2003, 5553



Floreside 4  
44, 2003, 1243



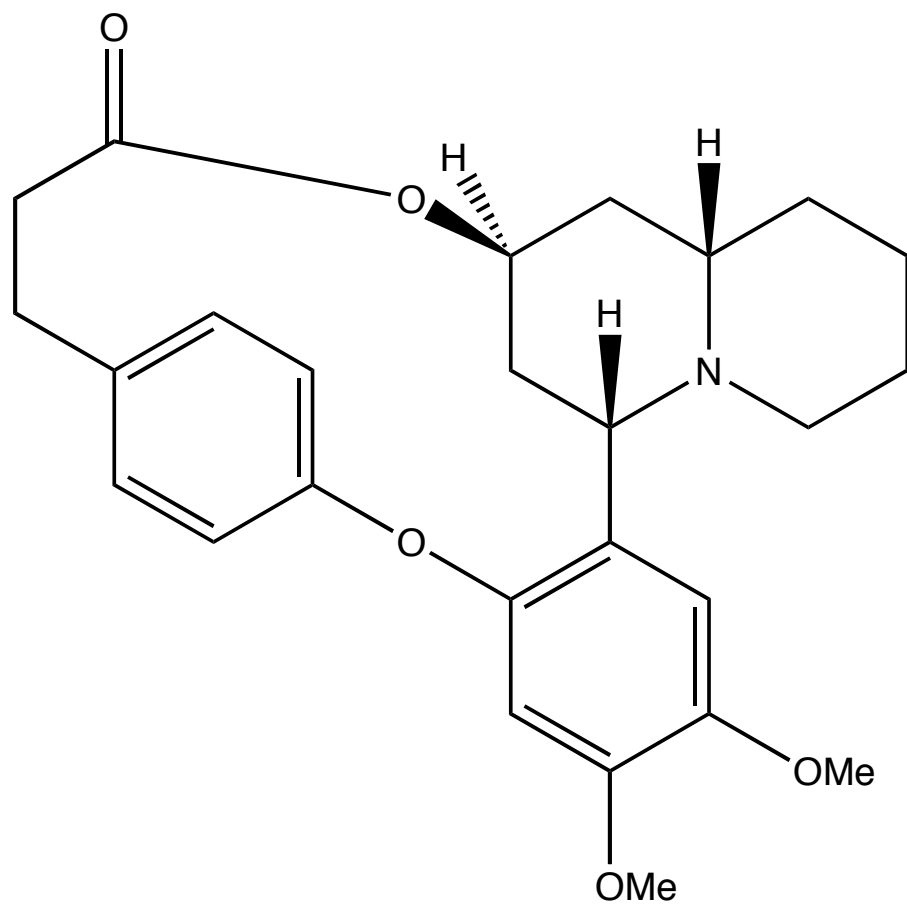
Brazilide A  
43, 2002, 1731



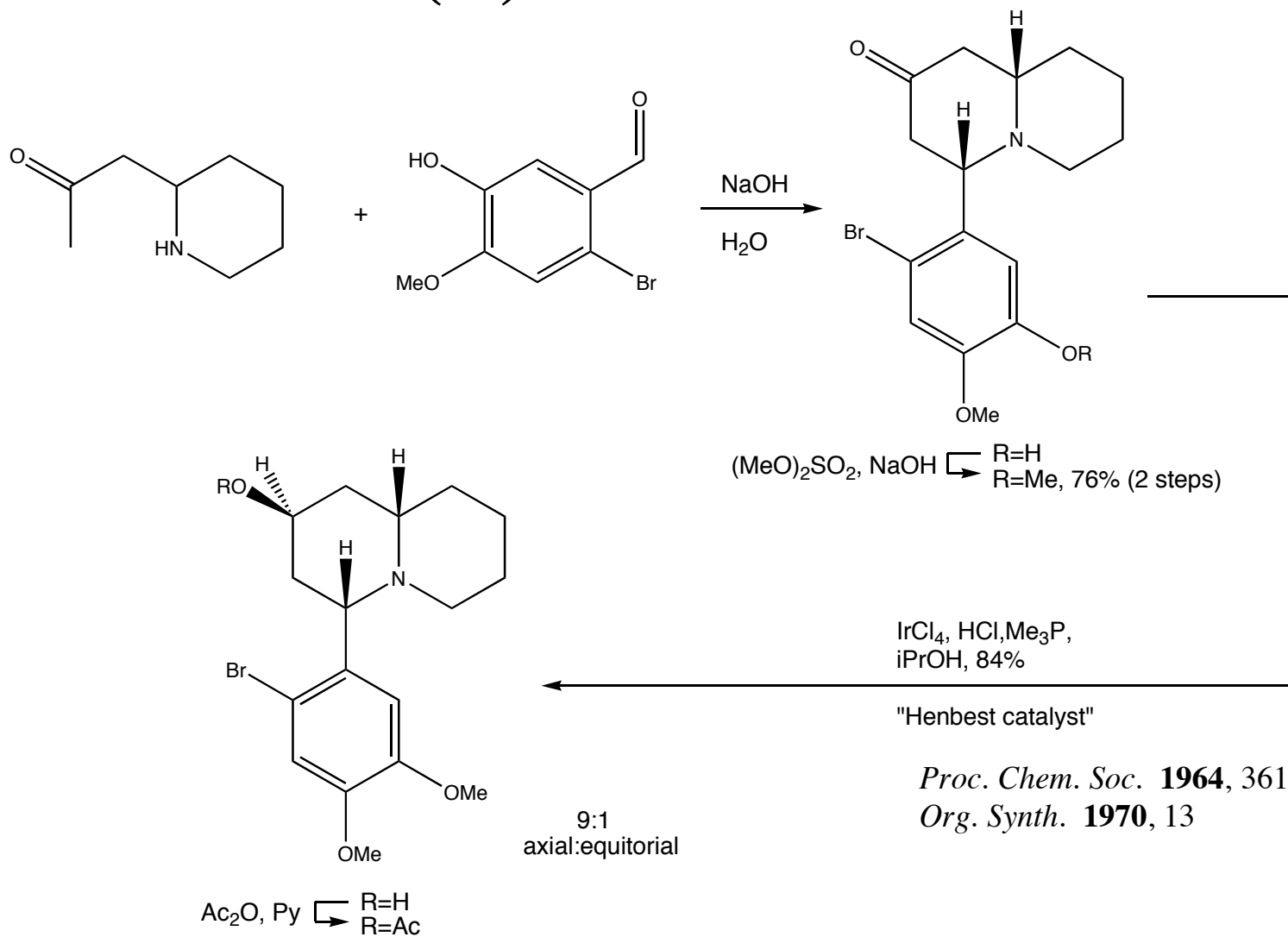
Coleophomone A  
41, 2000, 8705

# Syntheses

# (±)-Decaline



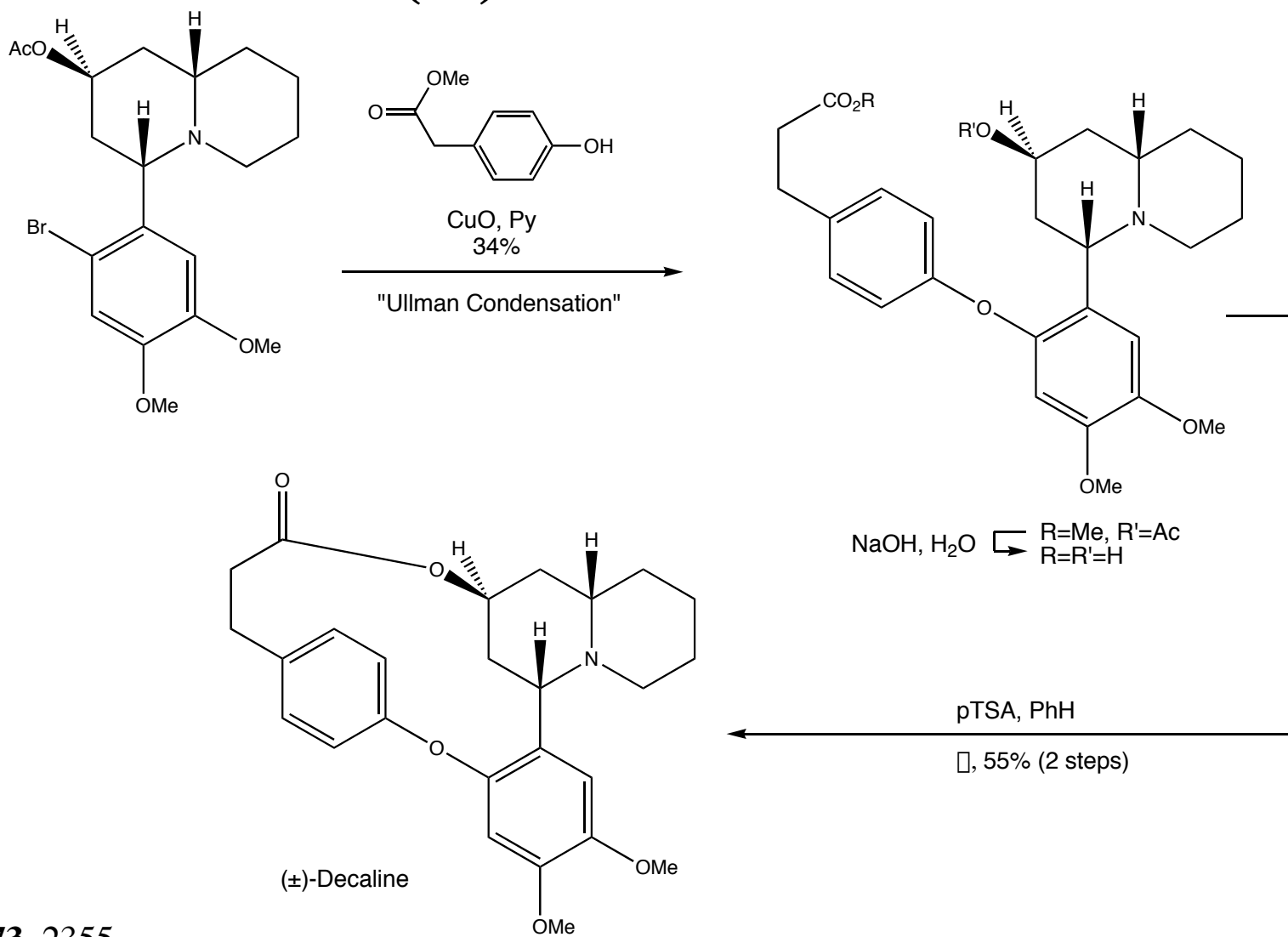
# (±)-Decaline



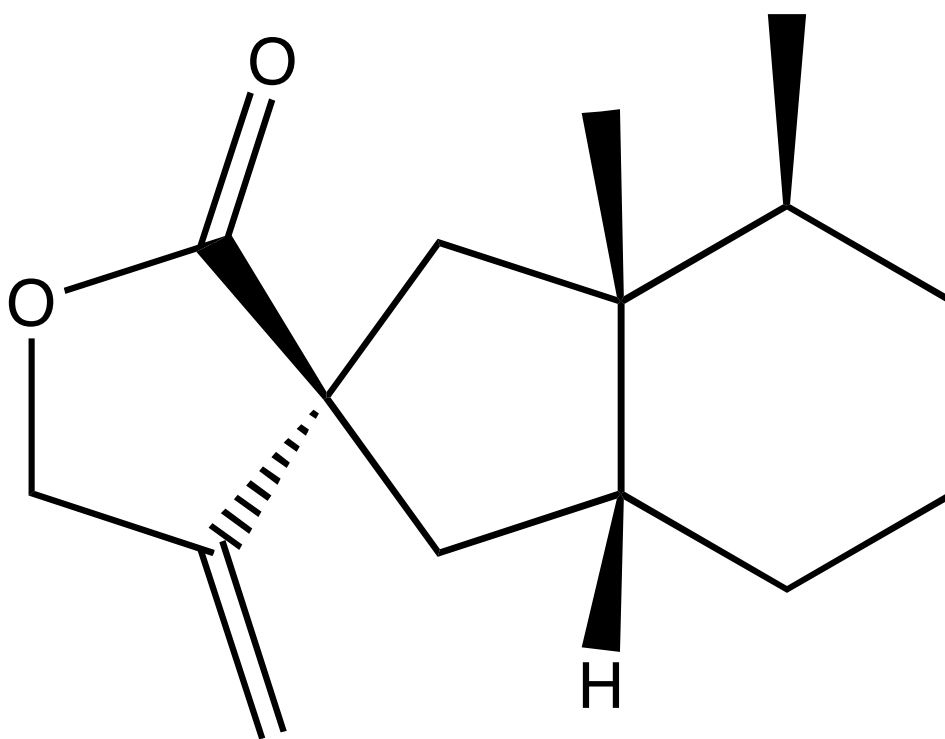
Arata. 1973, 2355

*Proc. Chem. Soc.* 1964, 361  
*Org. Synth.* 1970, 13

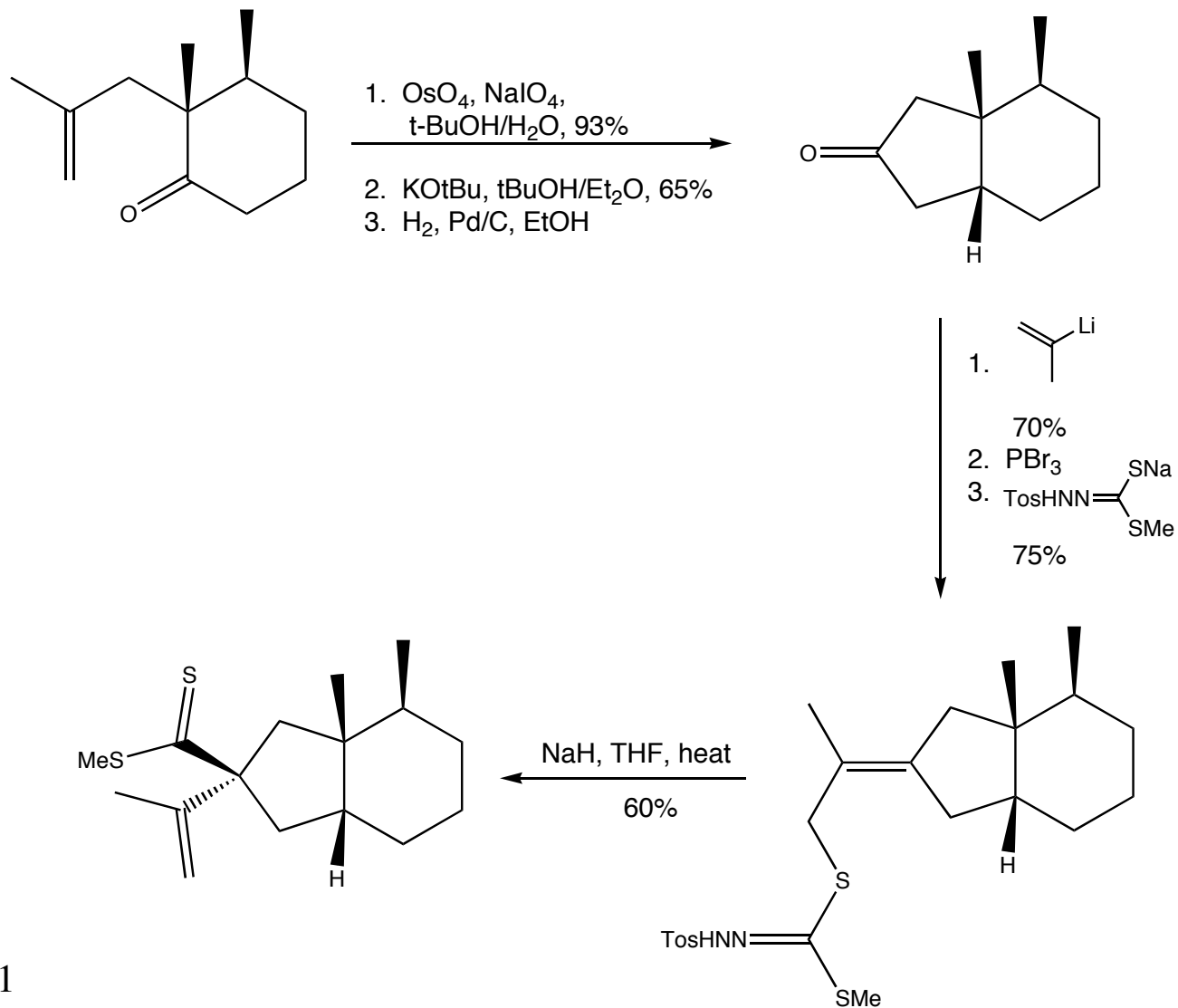
# (±)-Decaline



# (±)-Bakkenolide A

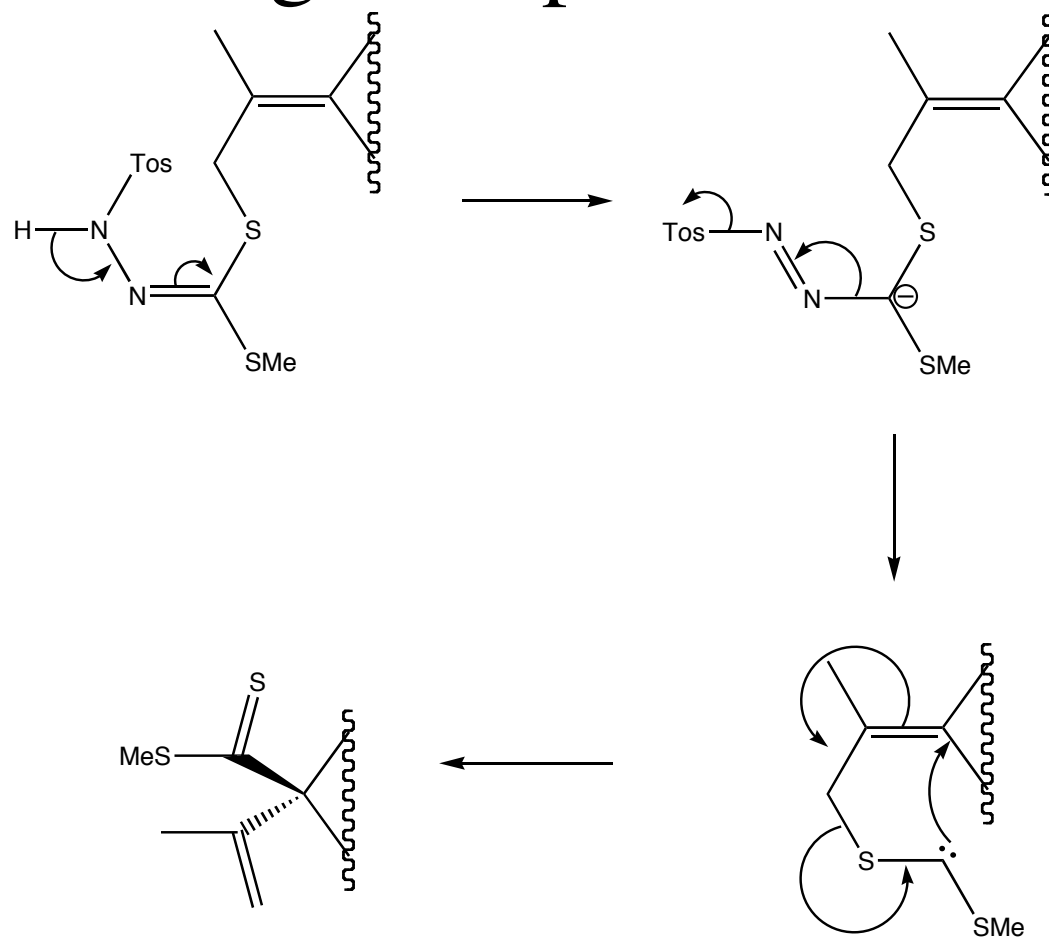


# (±)-Bakkenolide A

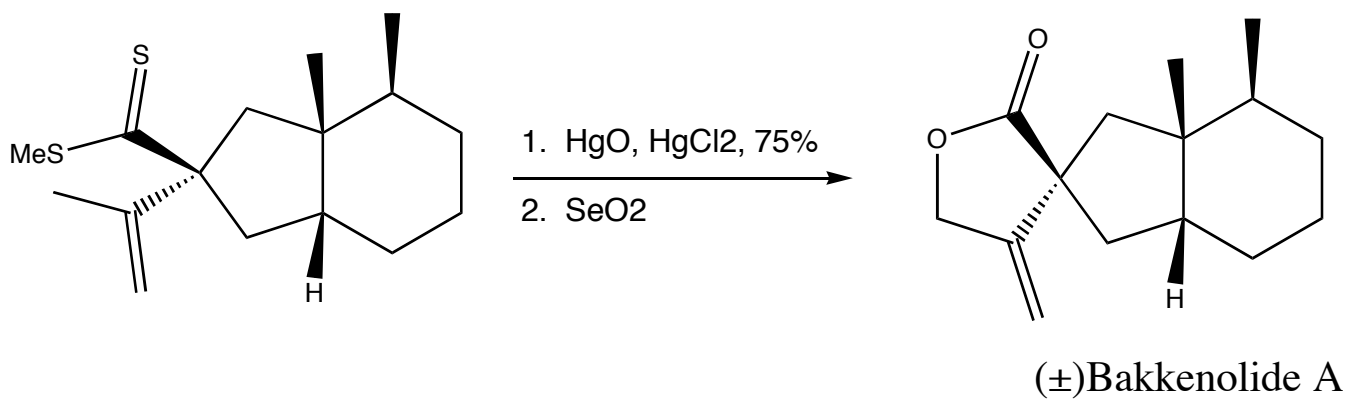


# (±)-Bakkenolide A

## Sigmatropic RAR

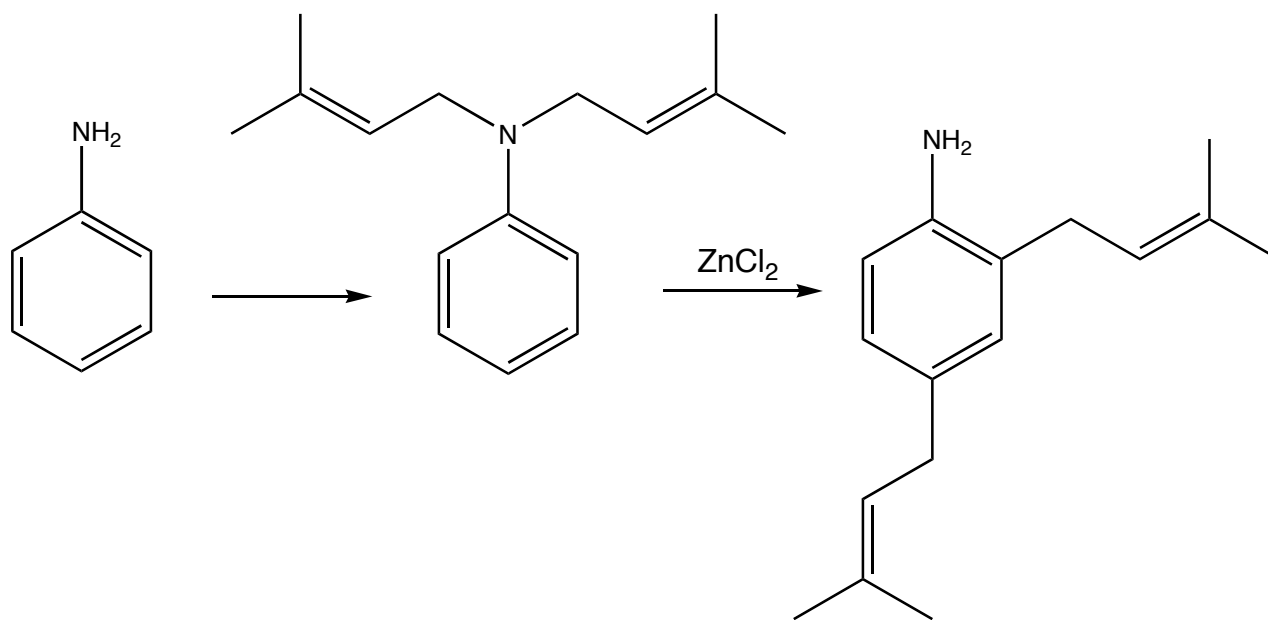


# (±)-Bakkenolide A

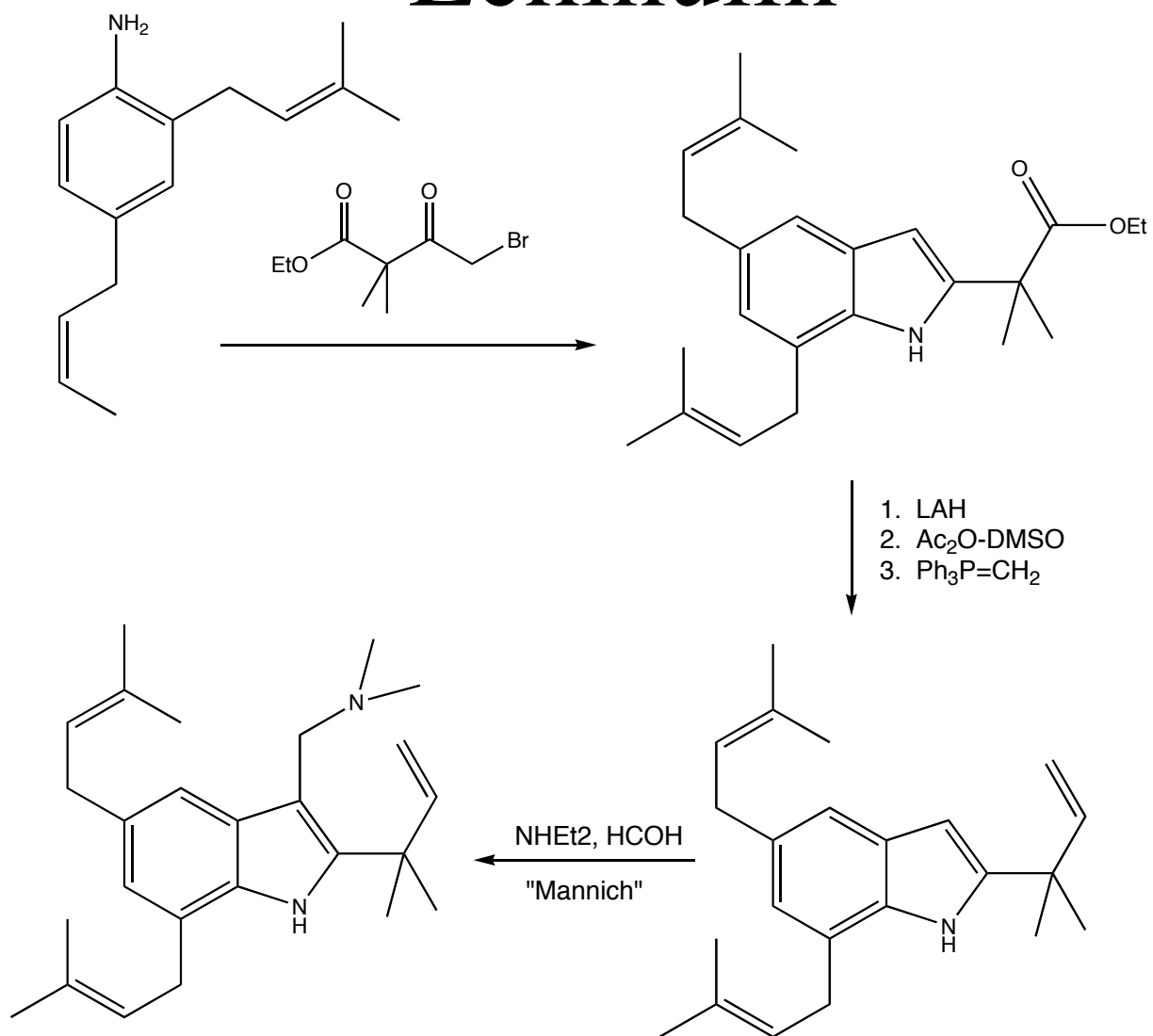




# Echinulin

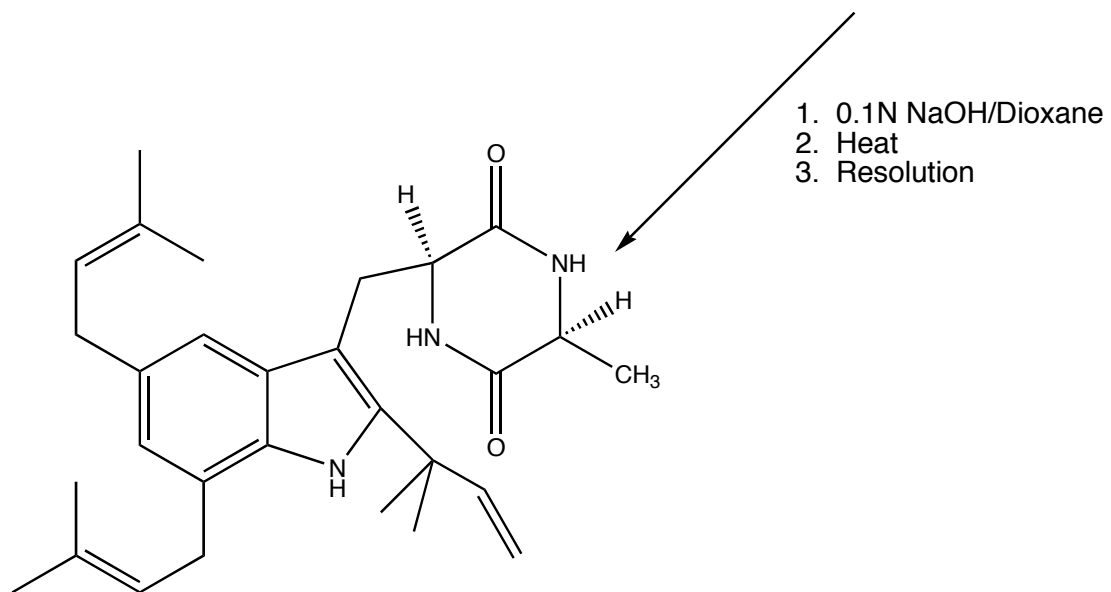
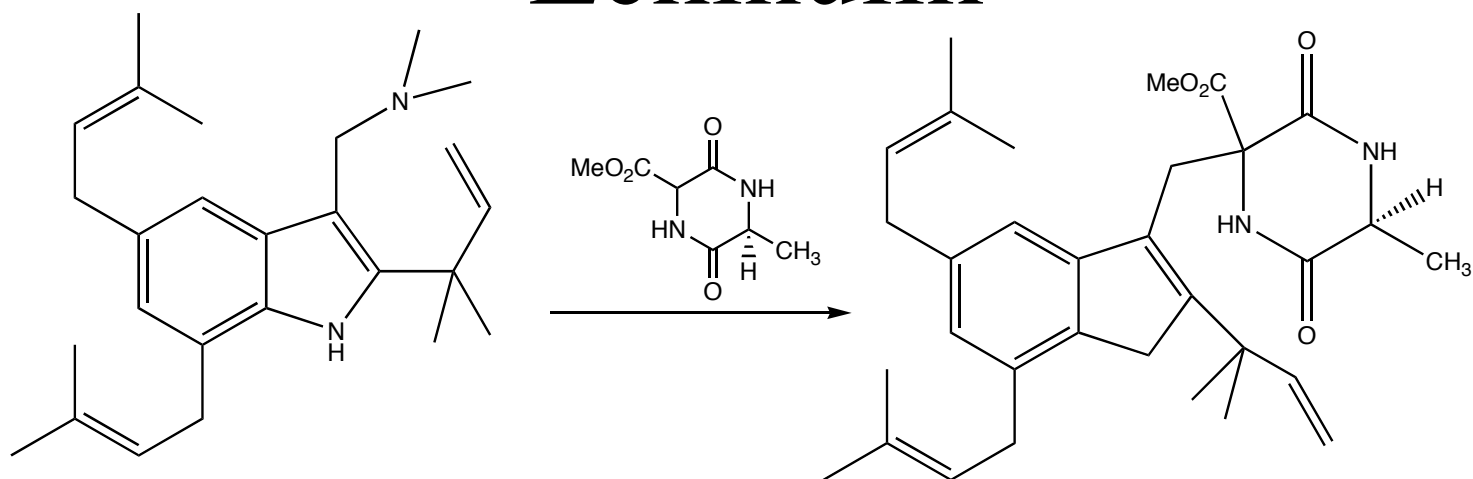


# Echinulin

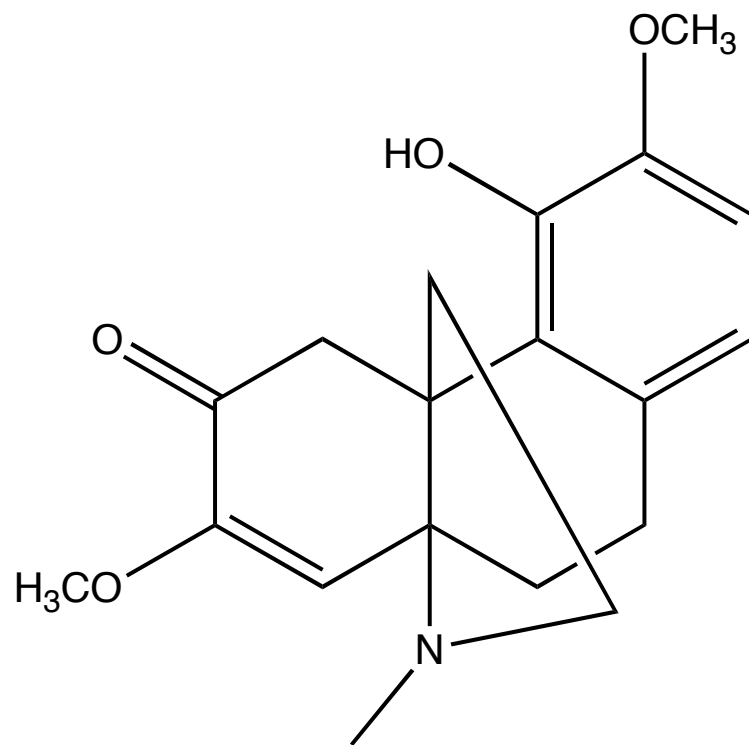


Kishi. 1971, 4665

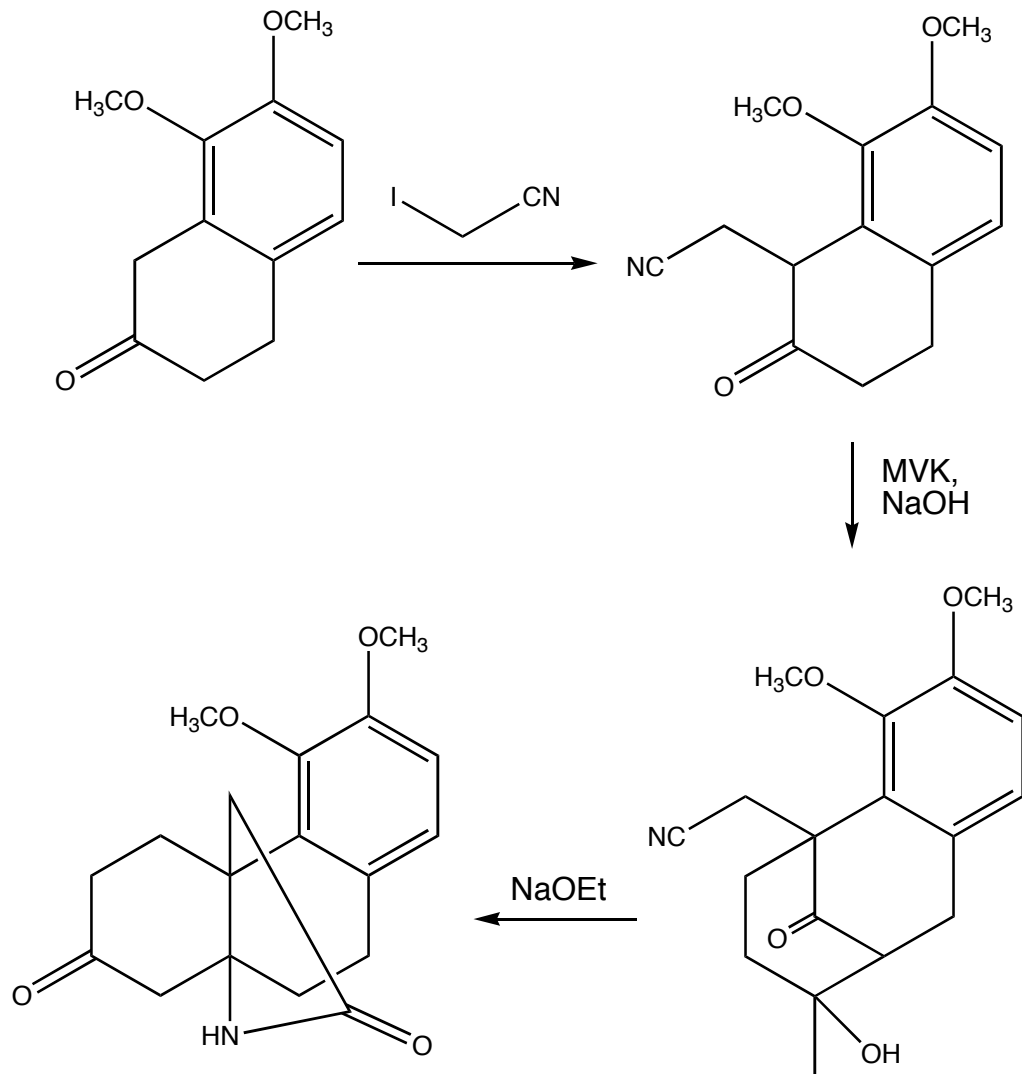
# Echinulin



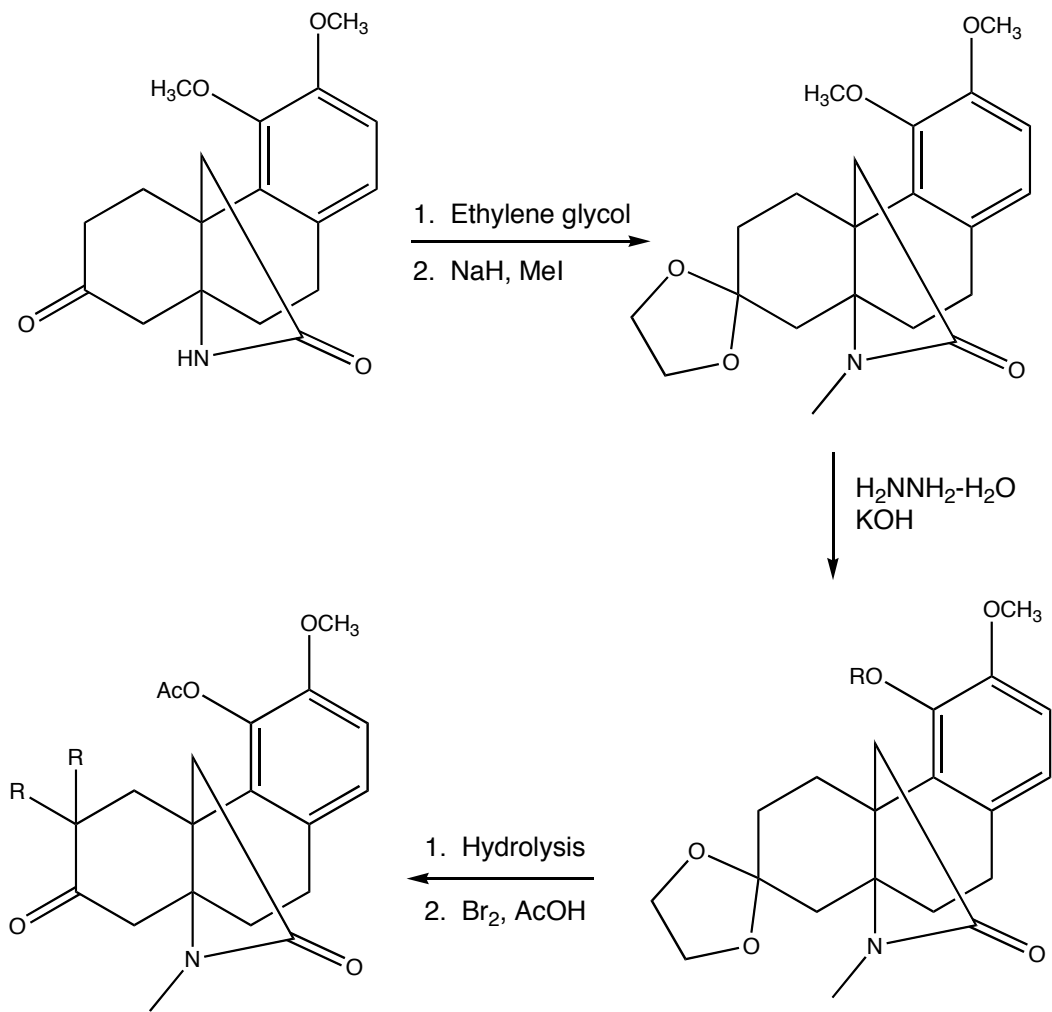
# dl-Cepharamine



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# dl-Cepharamine

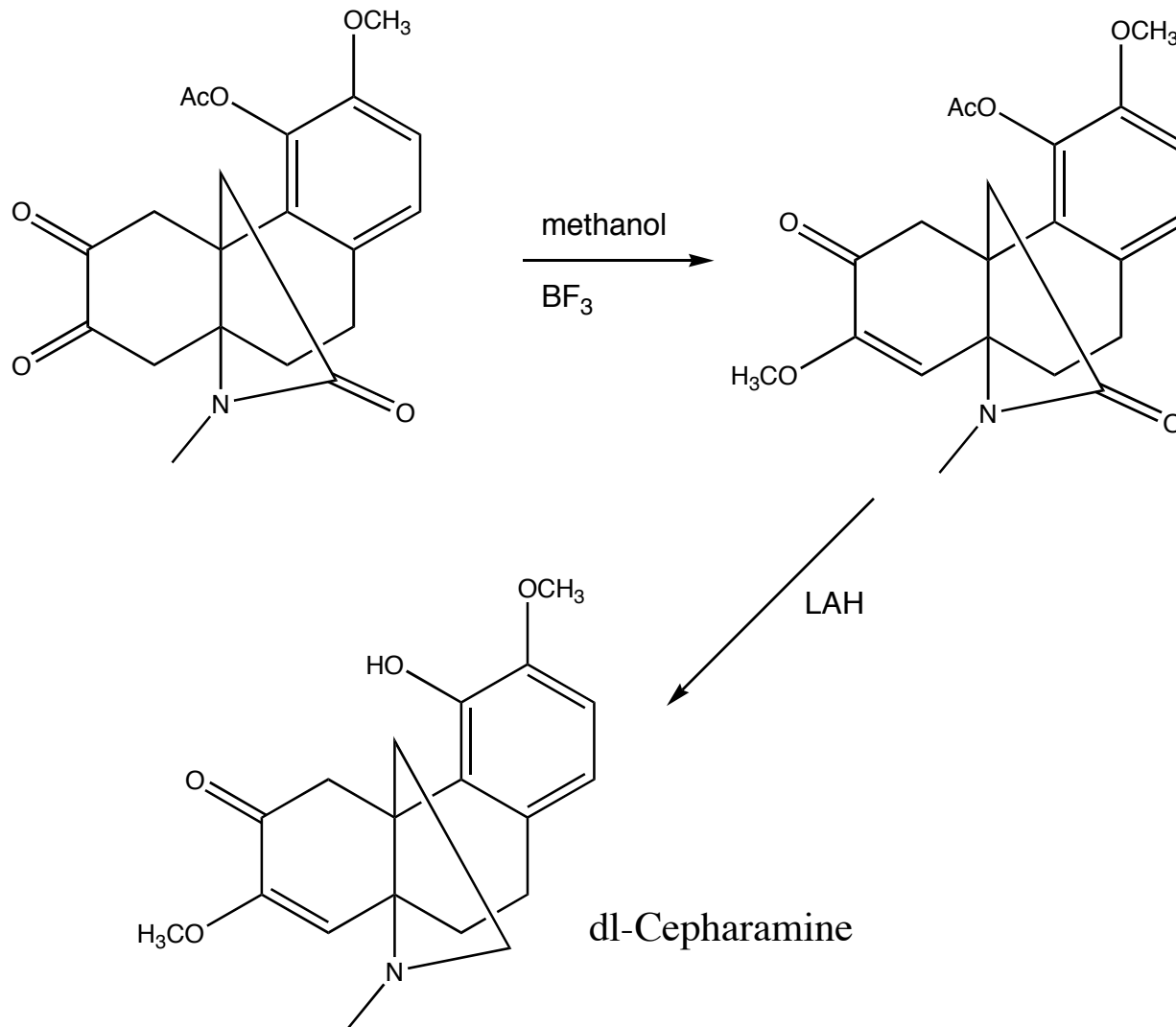


Kitano. 1969, 1611

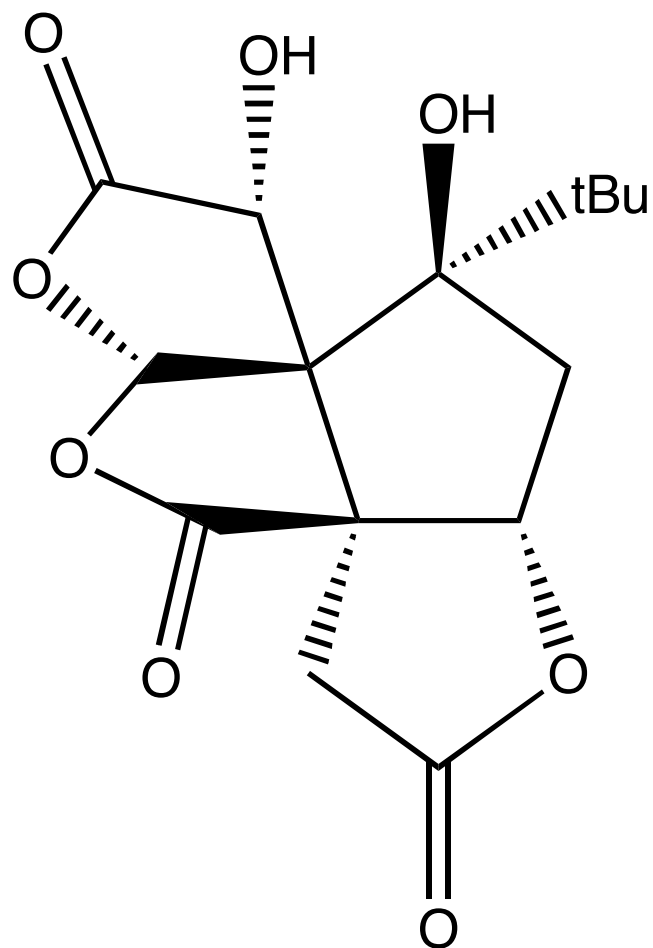
Freshly Fused  
NaOAc in HOAc  $\begin{cases} \text{R}=\text{Br} \\ \text{R}=\text{O} \end{cases}$

$\begin{cases} \text{R}=\text{H} \\ \text{R}=\text{Ac} \end{cases}$

# dl-Cepharamine

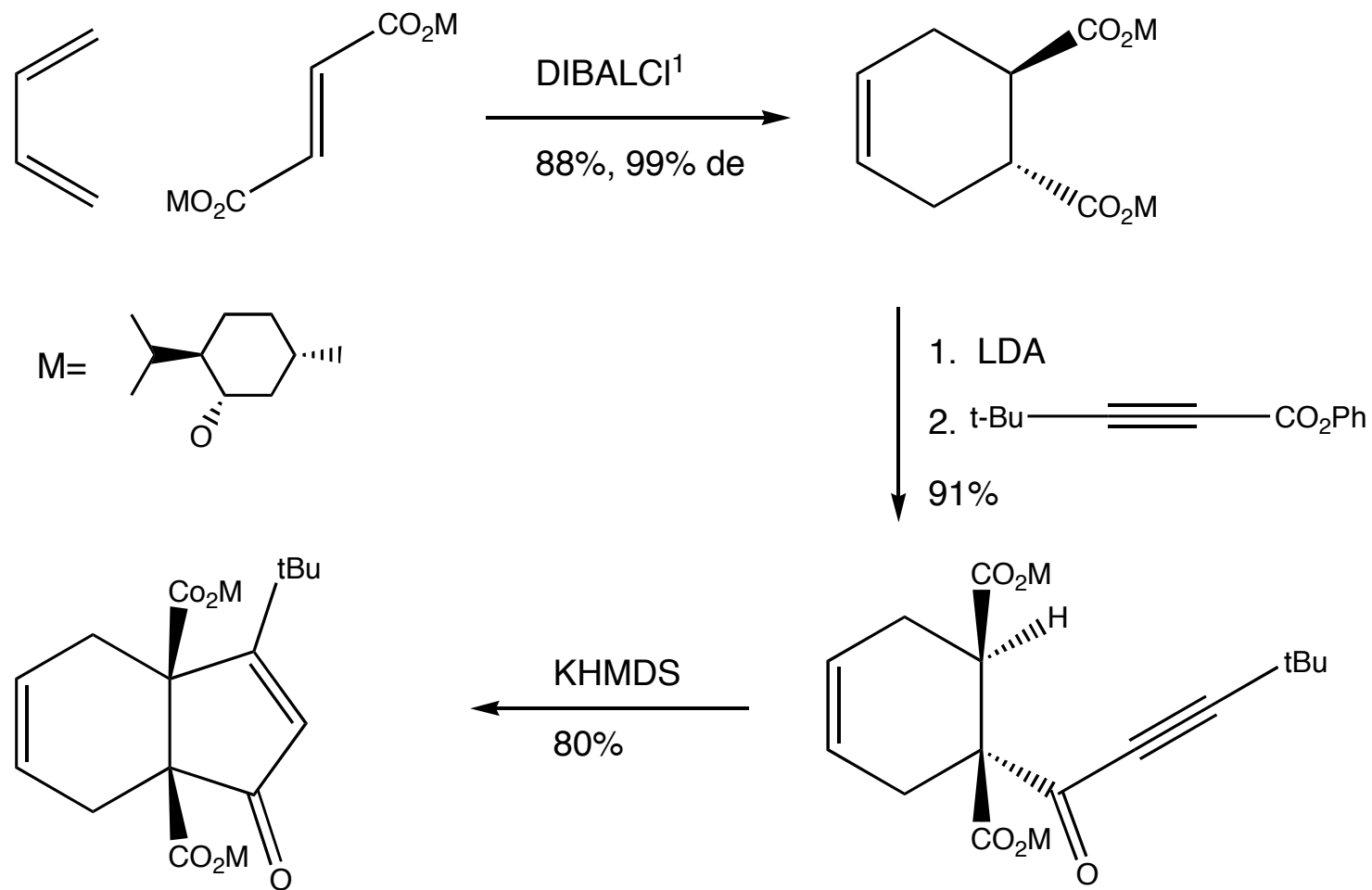


# (-)-Bilobalide

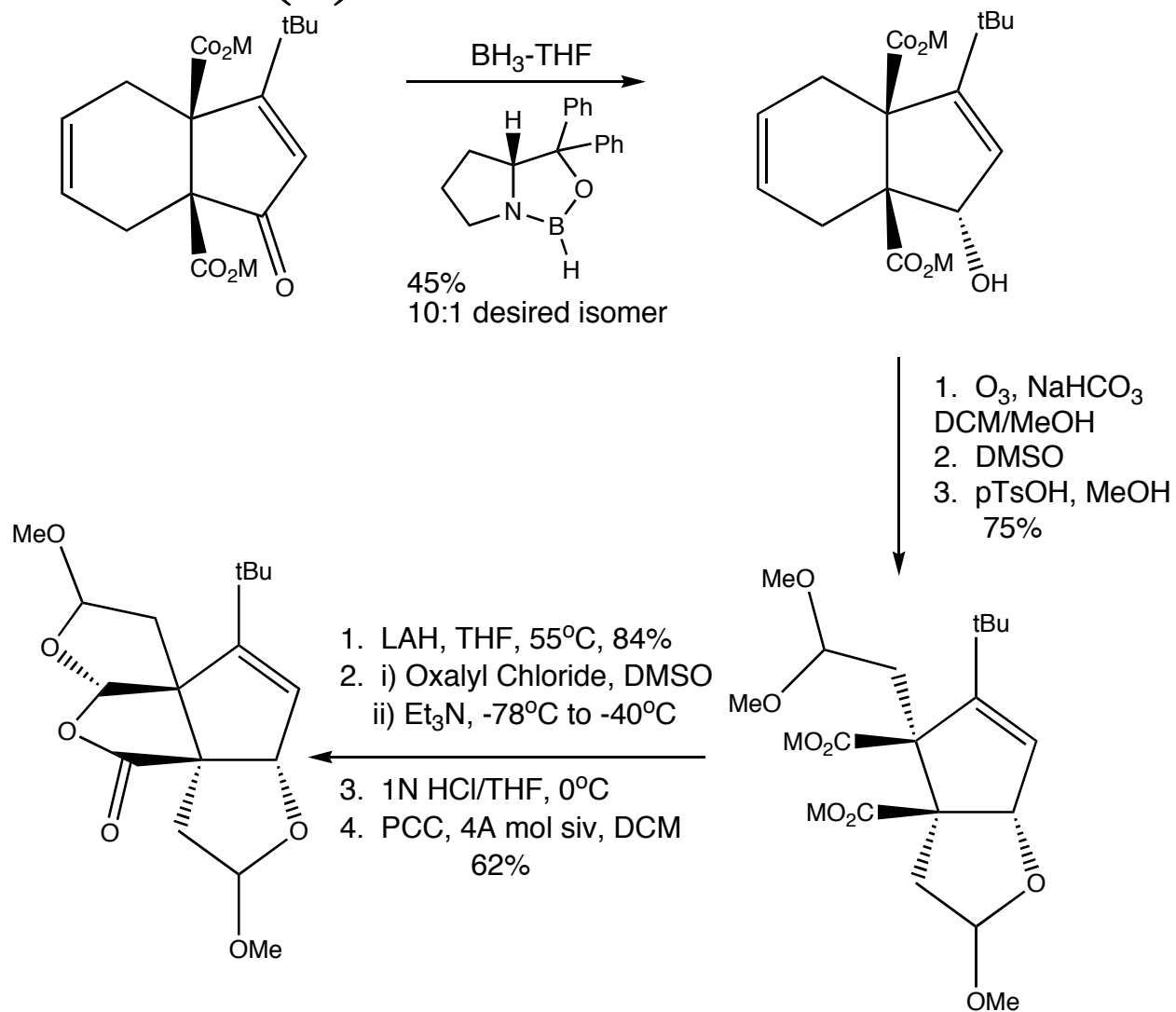


Corey. **1988**, 3423. Racemic synthesis originally presented in *J. Am. Chem. Soc.* **1987**, 7534

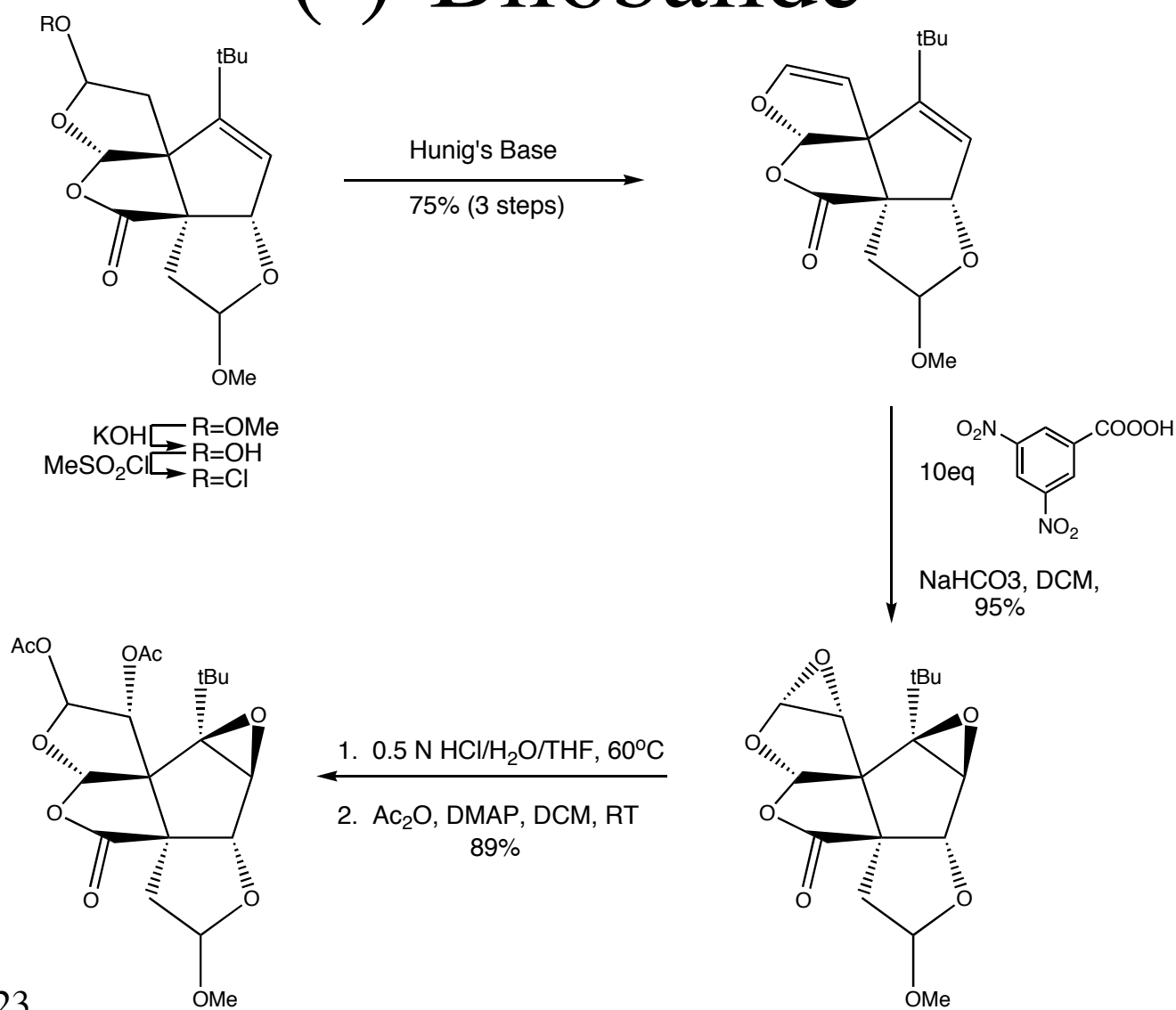
# (-)-Bilobalide



# (-)-Bilobalide

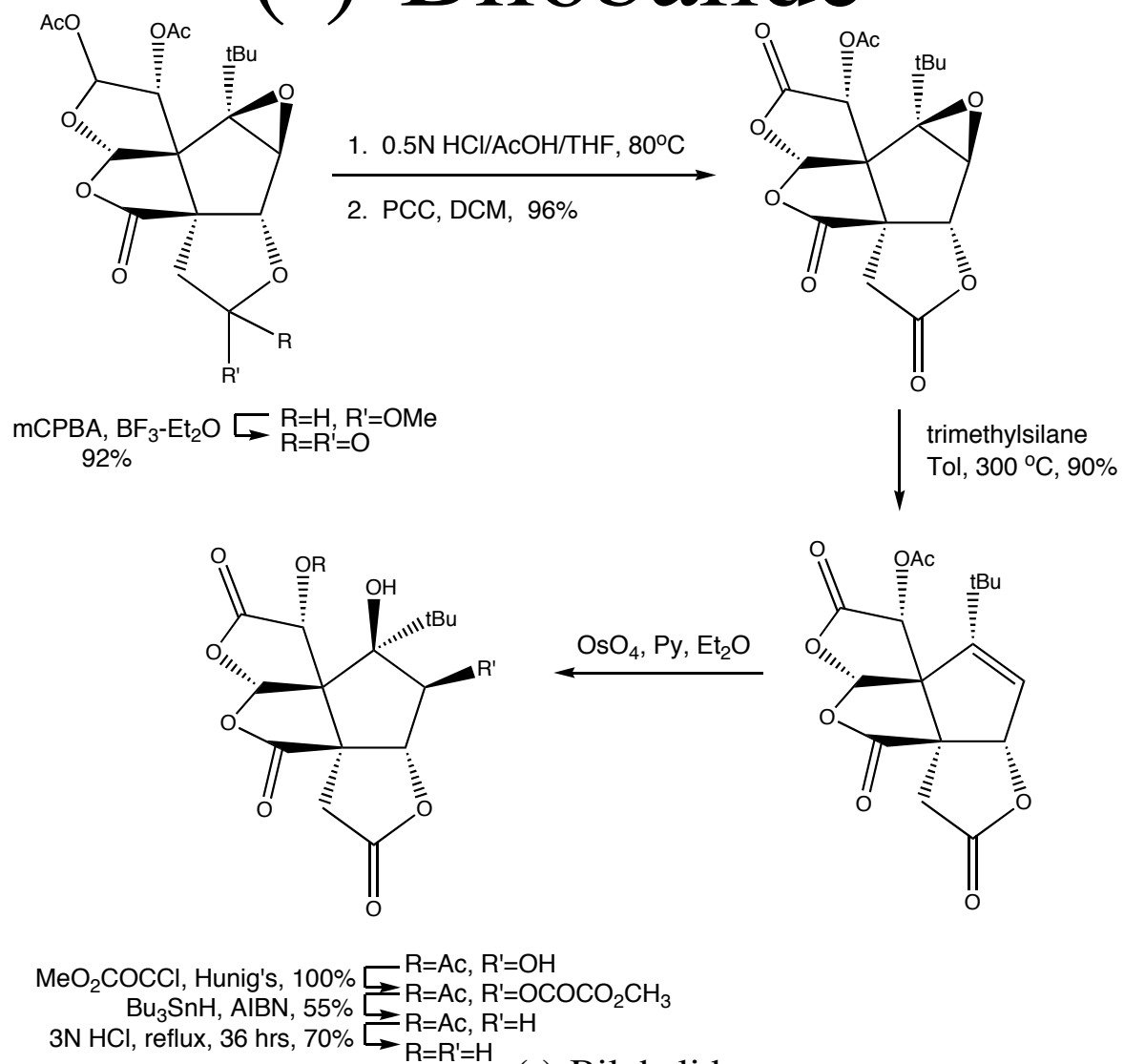


# (-)-Bilobalide



Corey. 1988, 3423.

# (-)-Bilobalide



(-)-Bilobalide

Corey. 1988, 3423.

# Conclusions