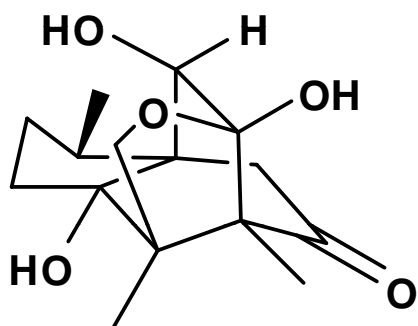
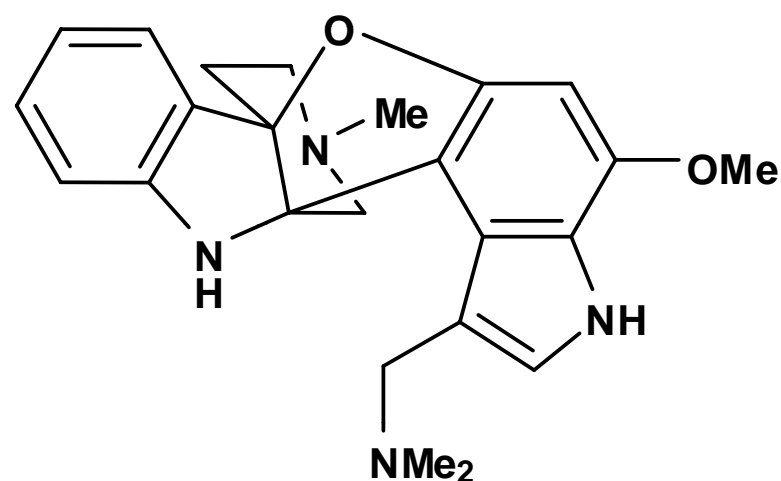


# Recent Highlights from the Danishefsky Laboratory



**11-O-Debenzoyltashironin**



**Phalarine**

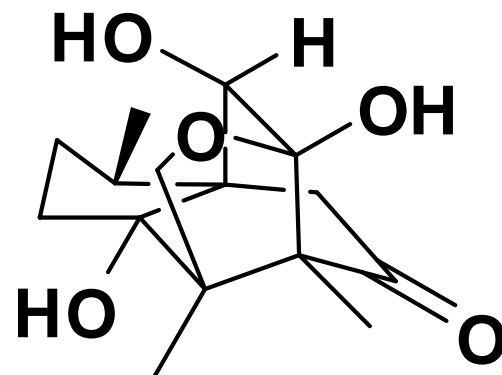
Anne-Marie Dechert

November 7, 2007

# 11-0-Debenzoyltashironin

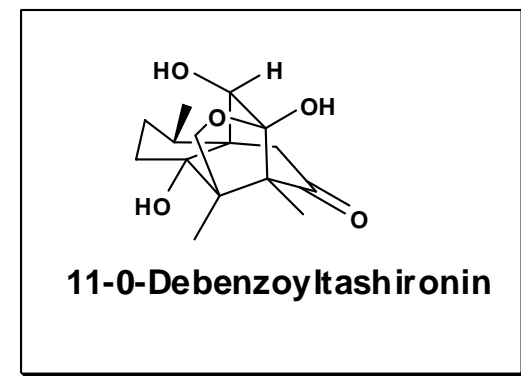
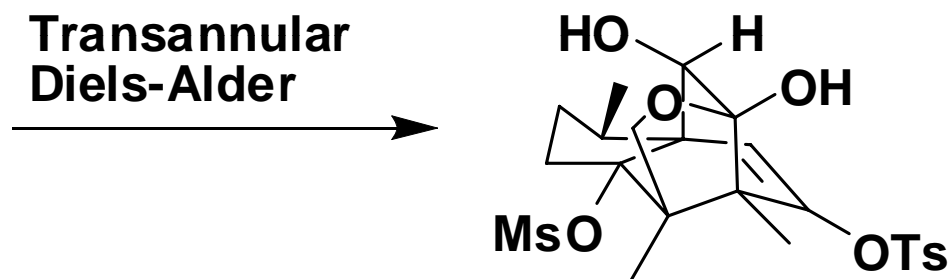
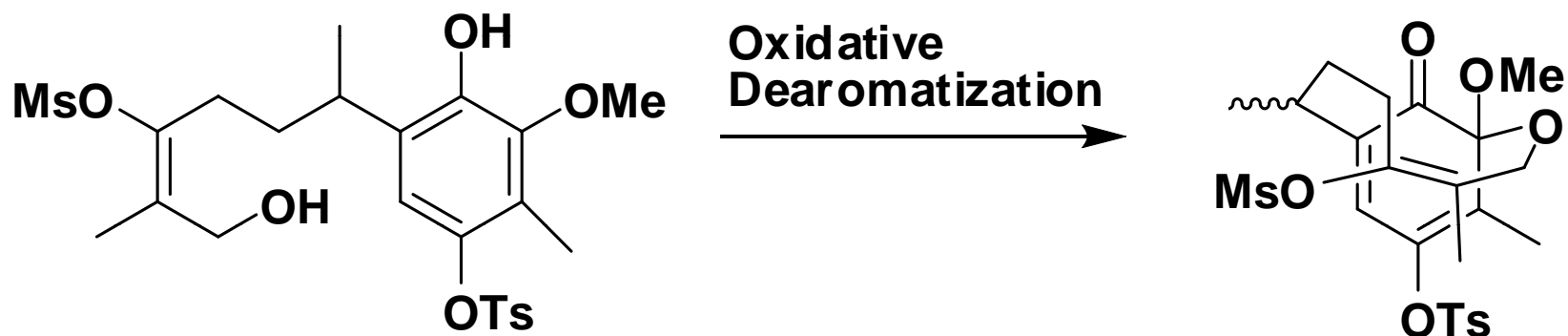
## Background and Structural Features

- Isolated from the pericaps of *Illicium merrillianum*
- Shown to induce neurite outgrowth in fetal rat cortical neurons at low concentrations
- 7 contiguous stereocenters, 3 all carbon quarternary centers

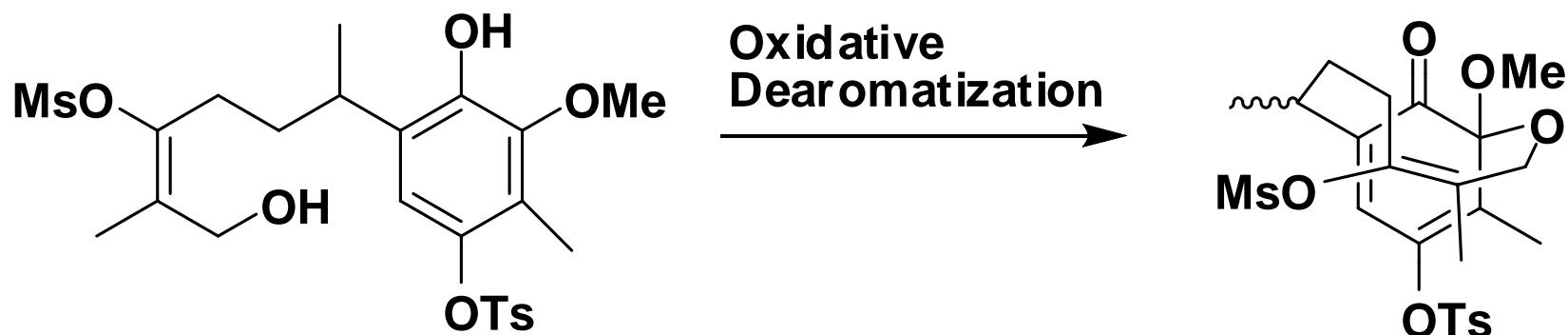


**11-0-Debenzoyltashironin**

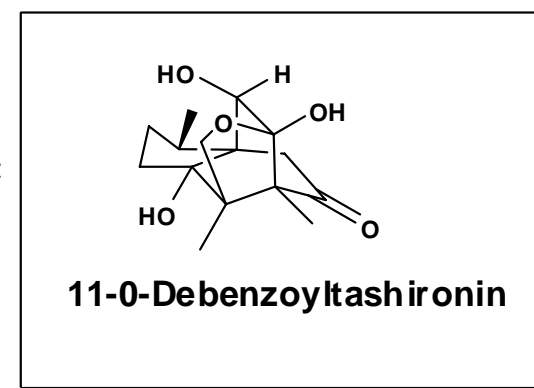
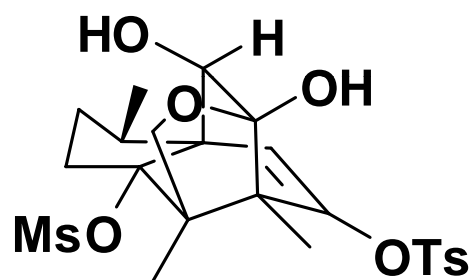
# Synthetic Strategy



# Synthetic Strategy

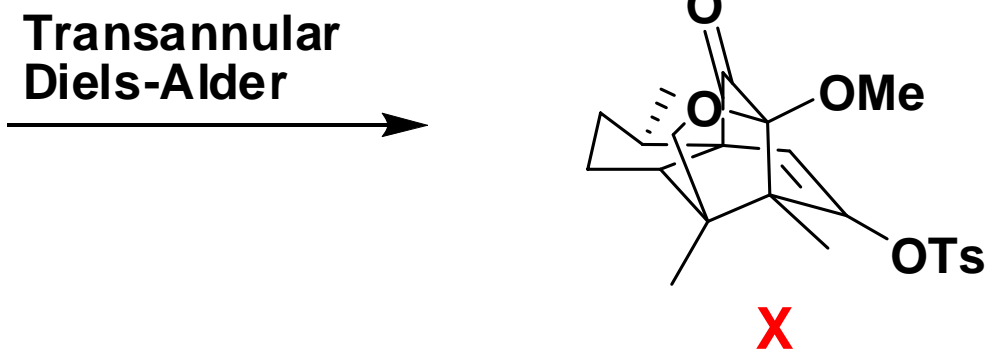
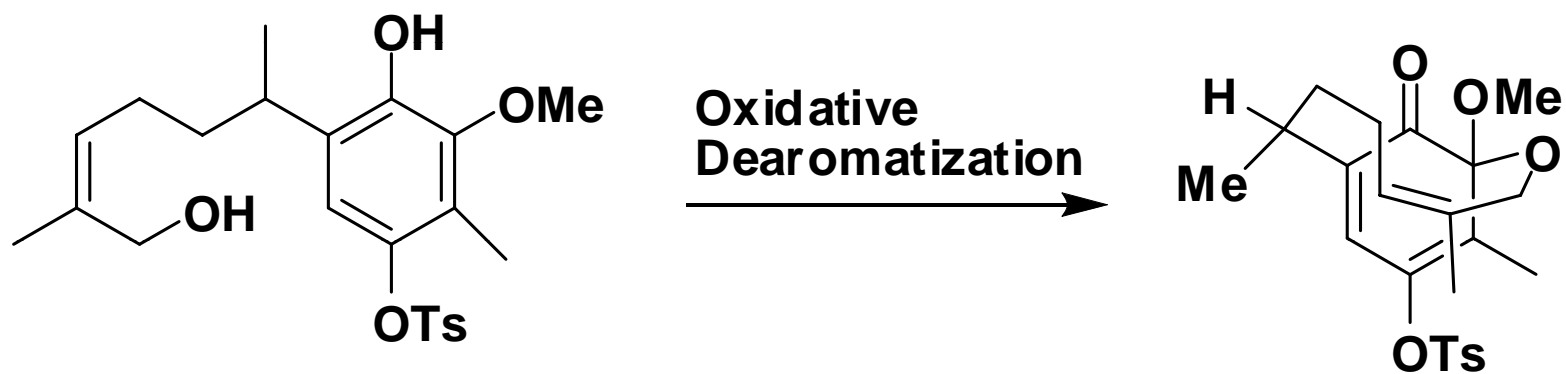


Transannular  
Diels-Alder  
~~X~~

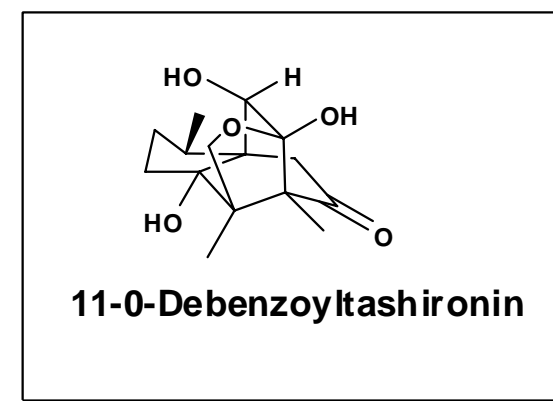


Believed that the cyclization didn't occur because of the electronic and steric constraints that the mesyl enol ether imposed.

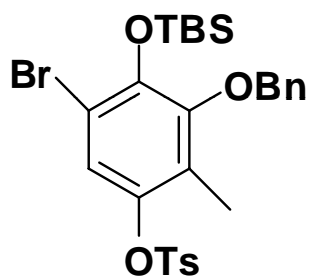
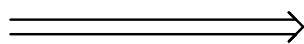
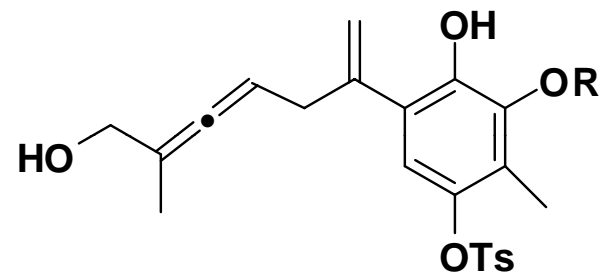
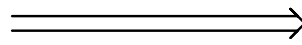
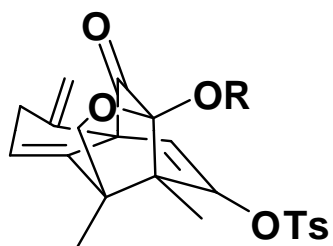
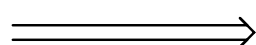
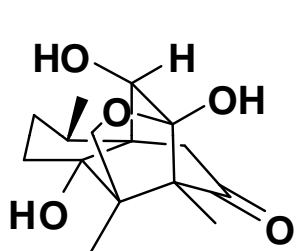
# Synthetic Strategy



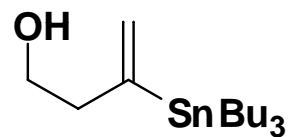
Wrong epimer!



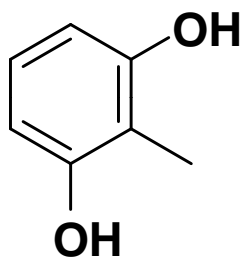
# Synthetic Strategy



+



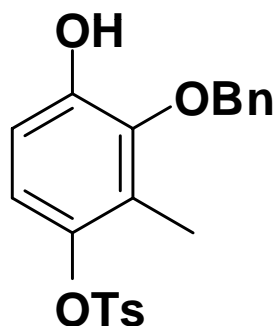
# Synthesis of the Aryl Bromide



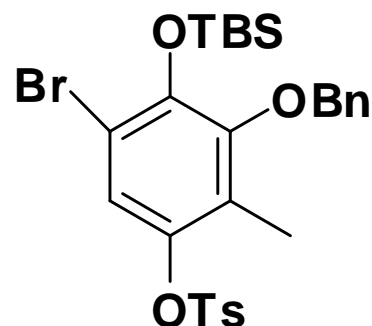
1.  $\text{Zn}(\text{CN})_2$ ,  $\text{HCl}$  (99 %)
2.  $\text{TsCl}$  (57 %)
3.  $\text{BnBr}$ ,  $\text{K}_2\text{CO}_3$ , TBAI (97 %)

1. *m*CPBA
2. TEA

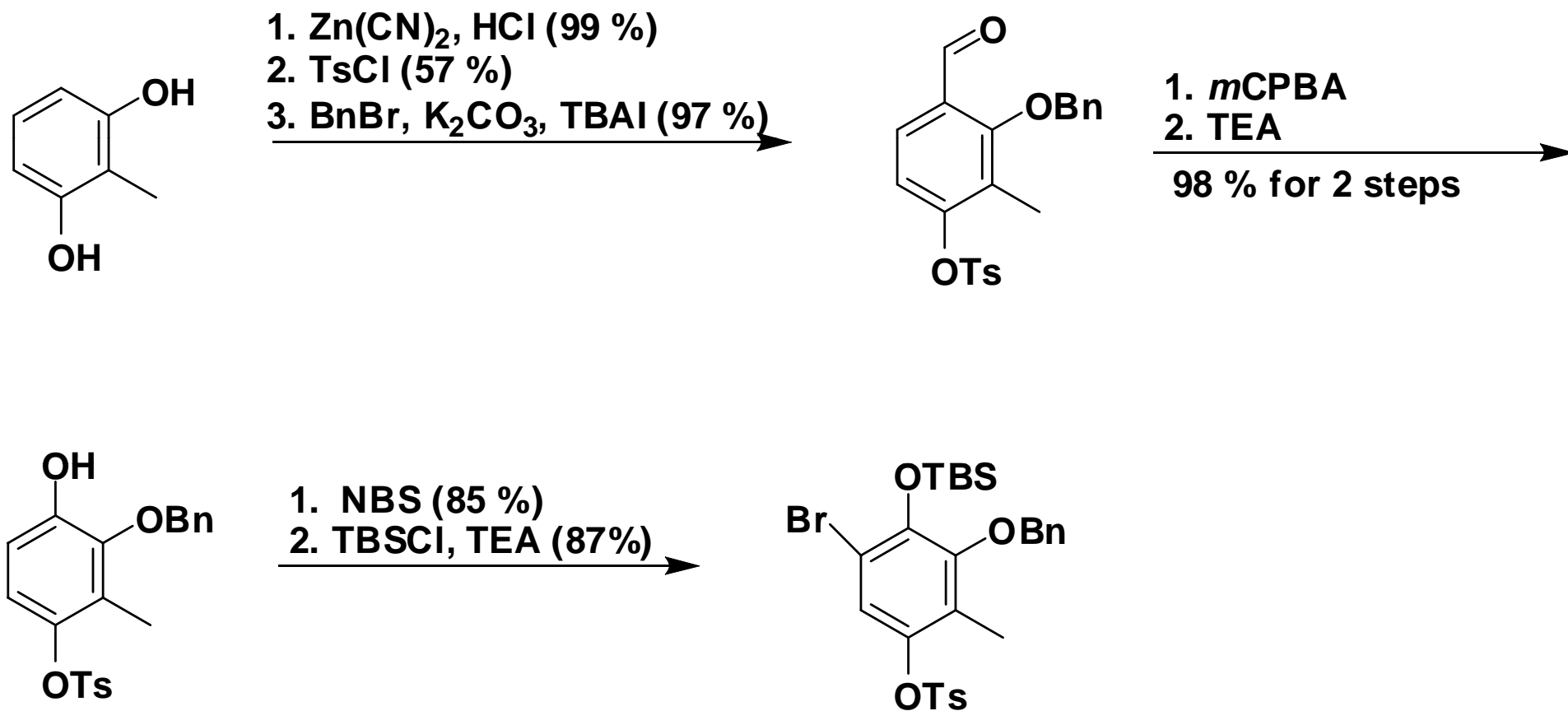
98 % for 2 steps



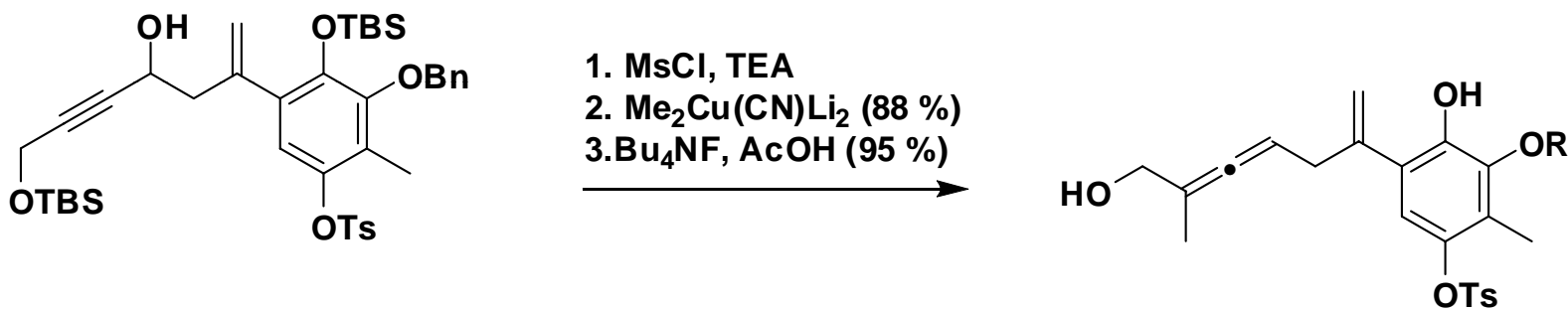
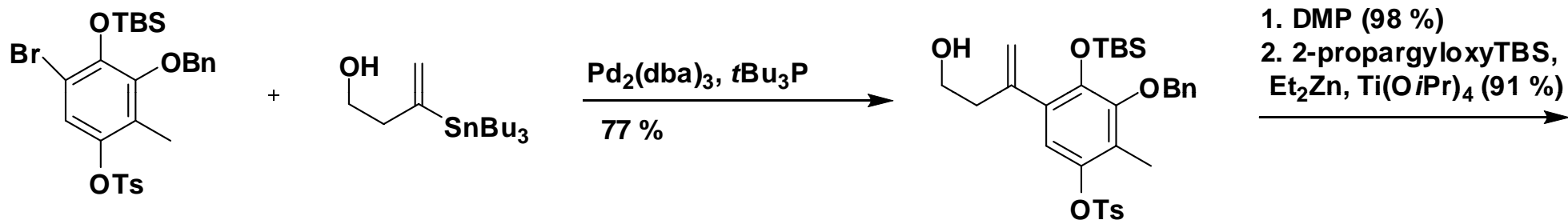
1. NBS (85 %)
2. TBSCl, TEA (87%)



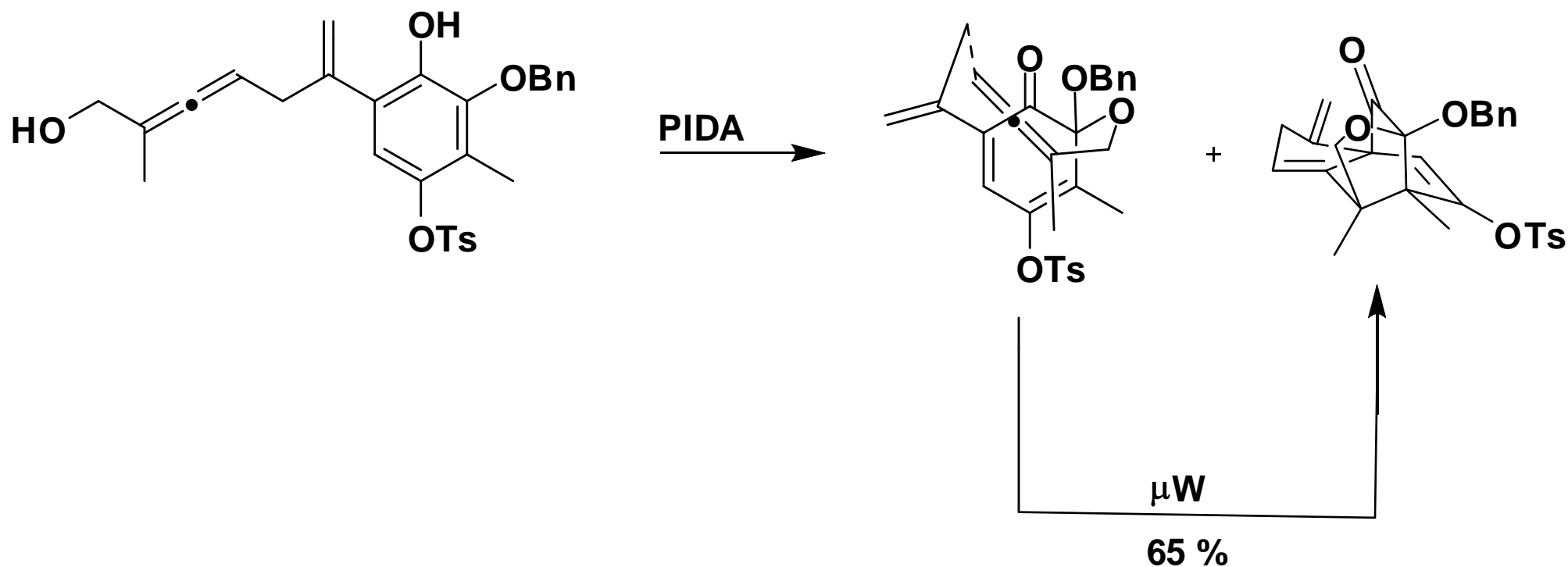
# Synthesis of the Aryl Bromide



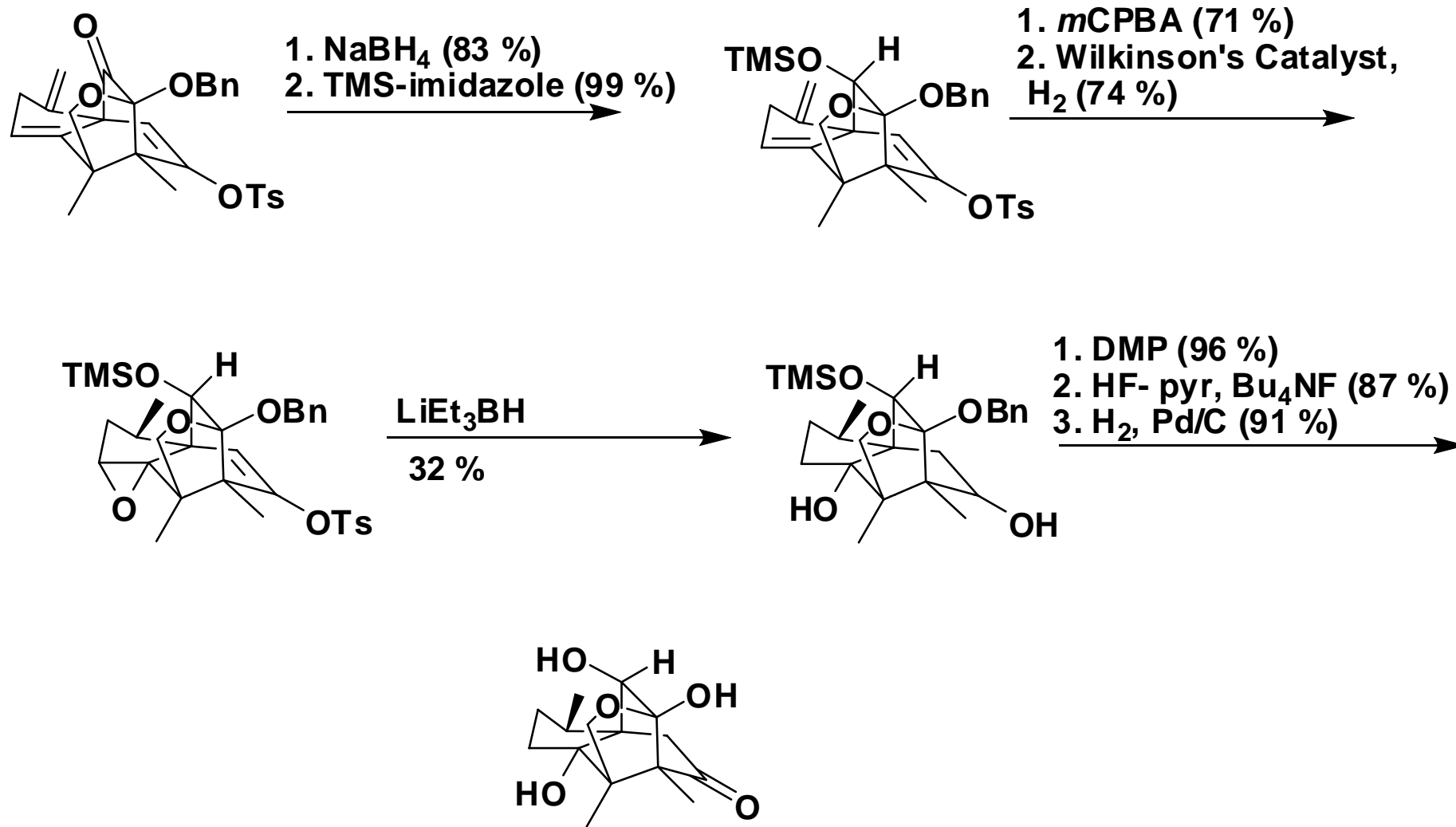
# Synthesis of the Oxidative Dearomatization Precursor



# Oxidative Dearomatization, Transannular Diels-Alder

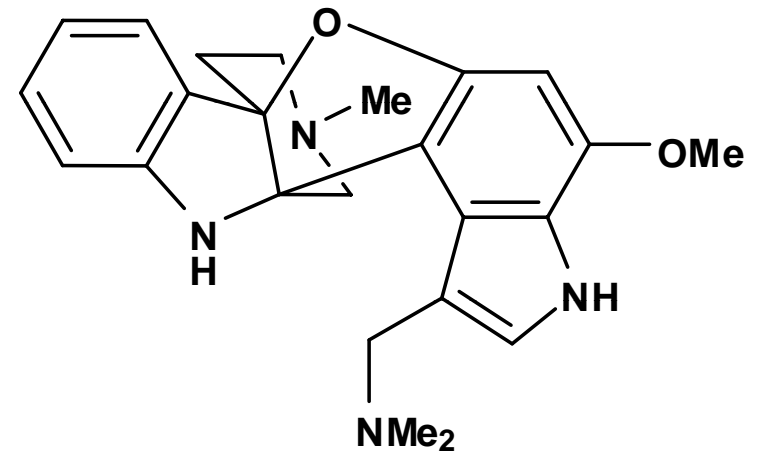


# End Game



# Phalarine

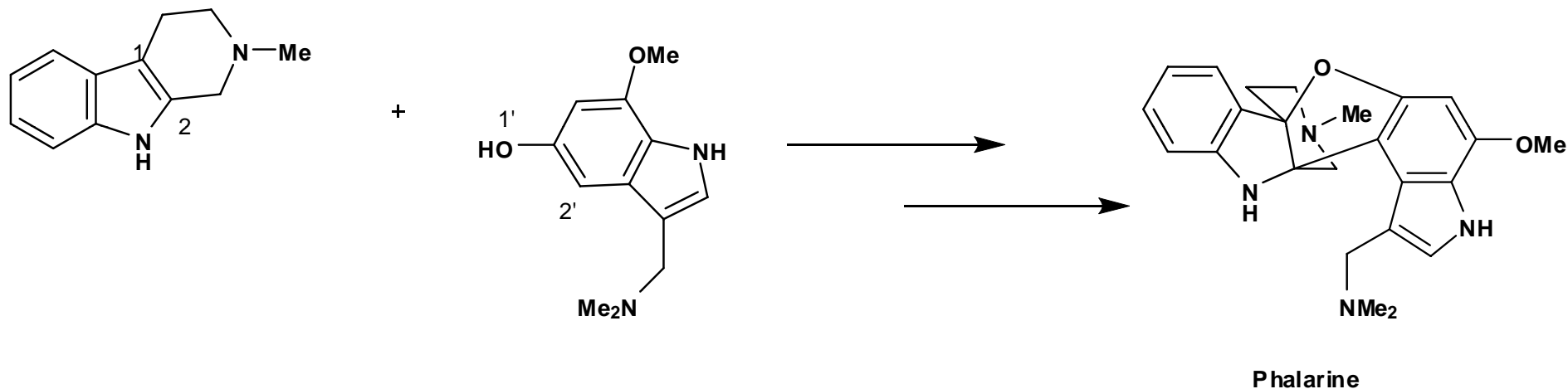
- Isolated from the *phalris coerulescens*, characterized in 1999
- Furanobisindole alkaloid
- First synthesis reported by Danishefsky



**Phalarine**

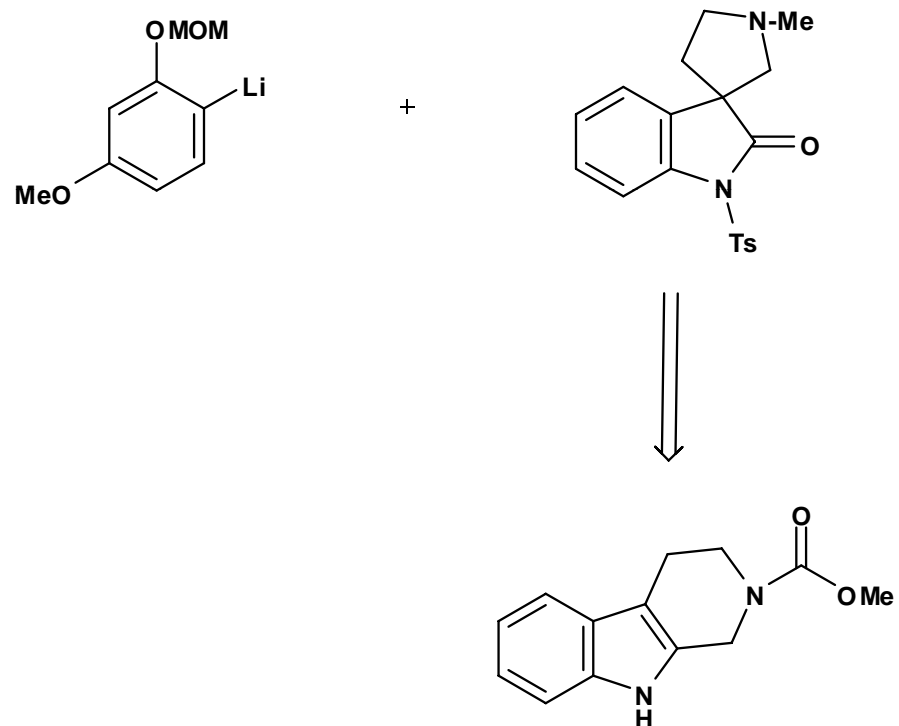
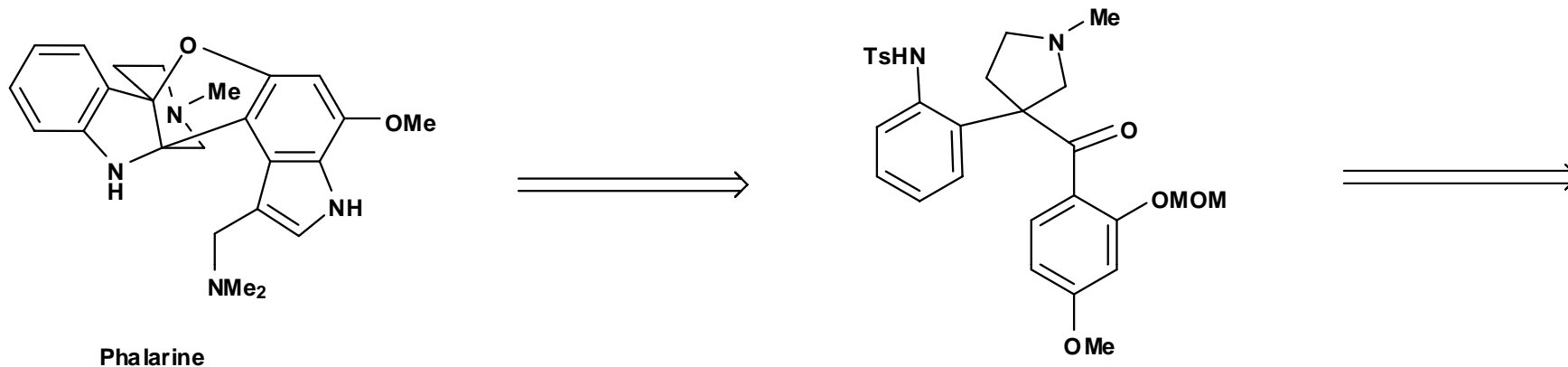


# Synthetic Strategy

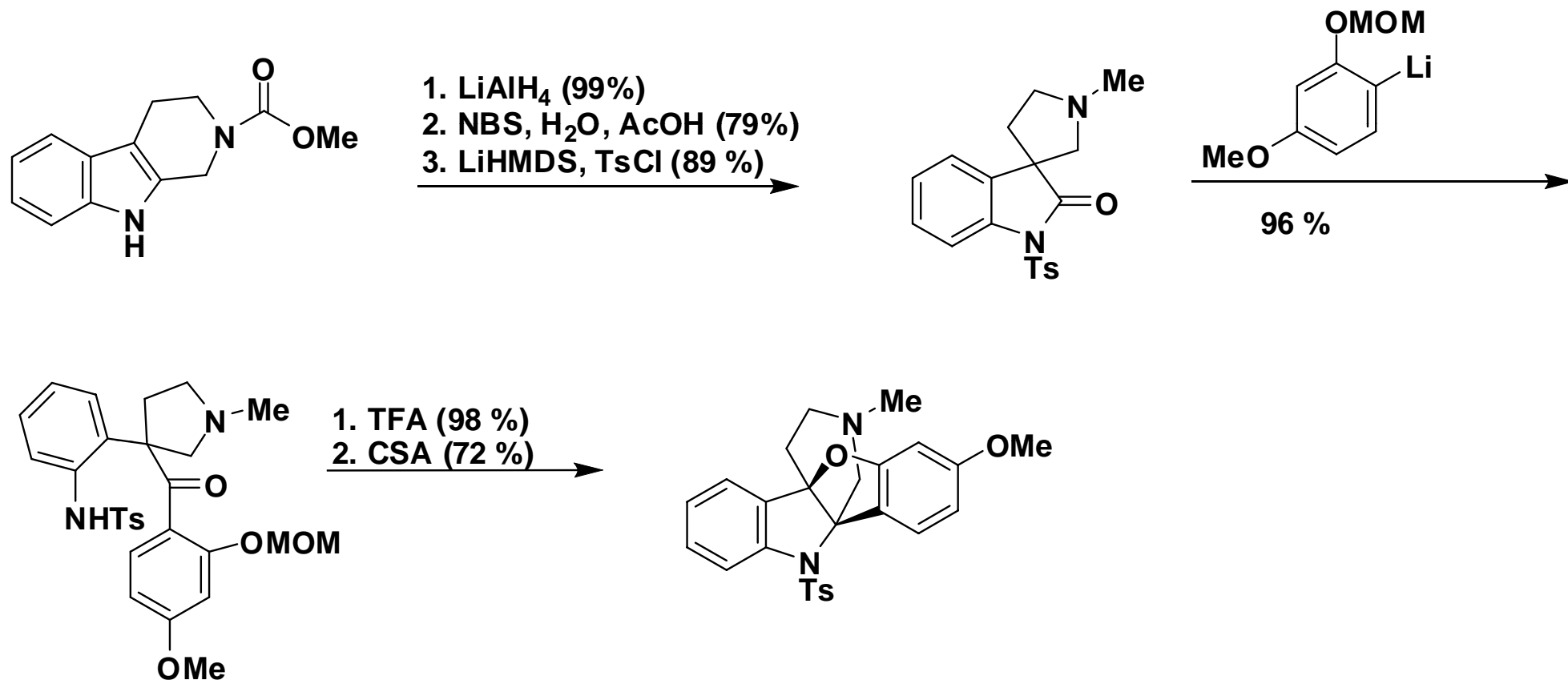


The model system gave the opposite of what was desired!

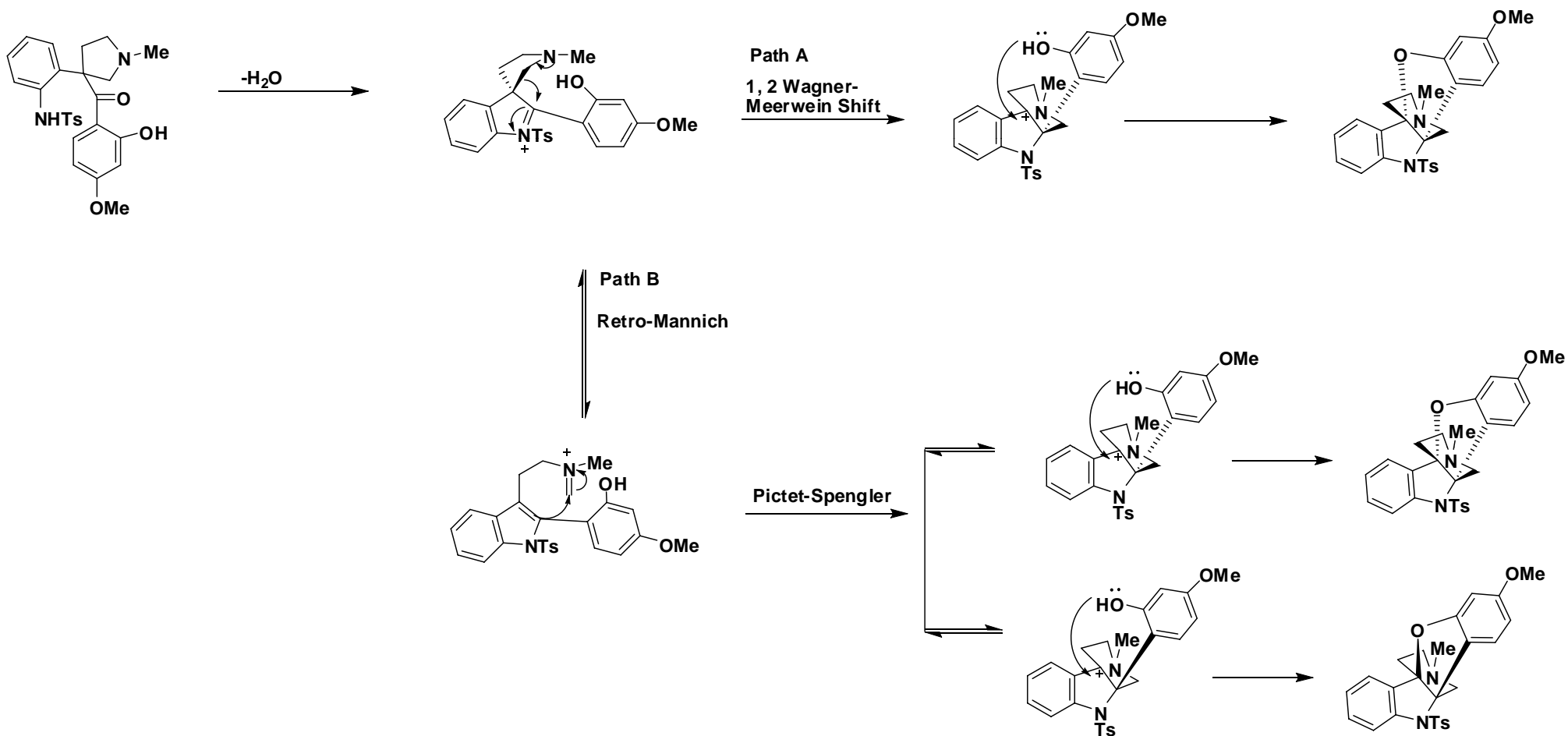
# Retrosynthesis



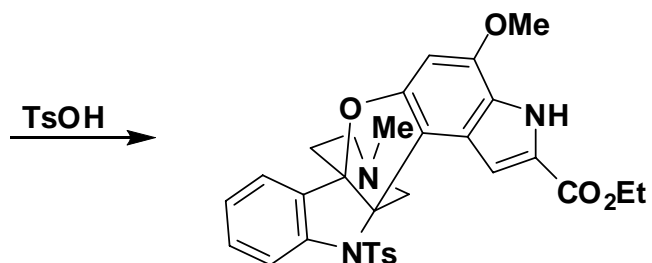
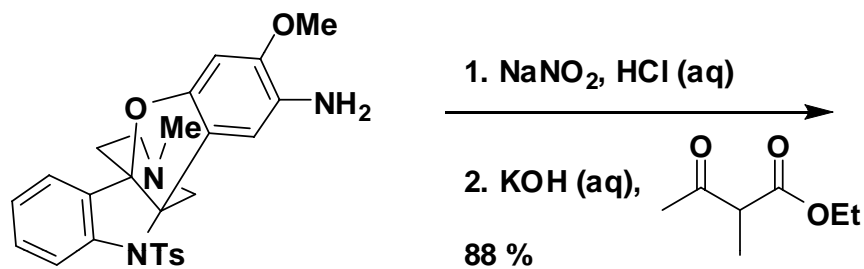
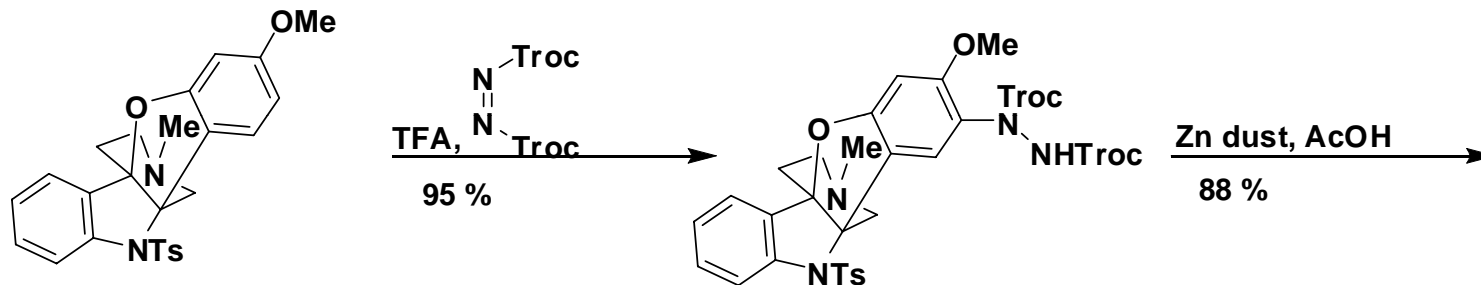
# Azaspiroindolenine synthesis



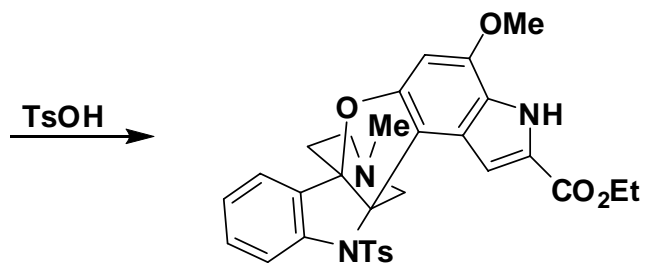
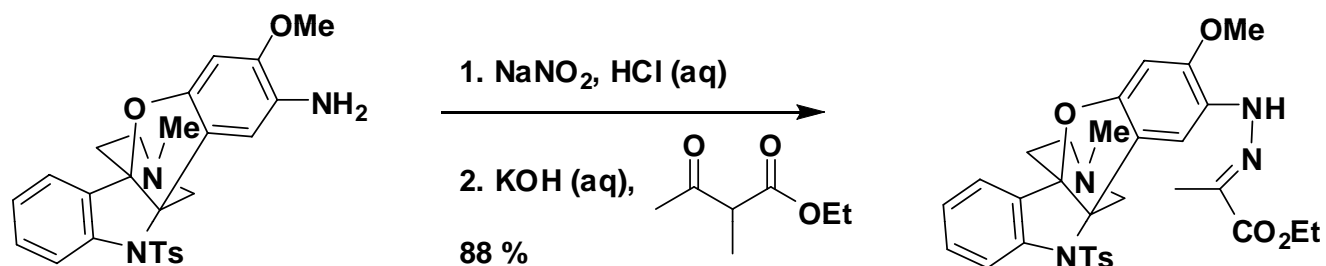
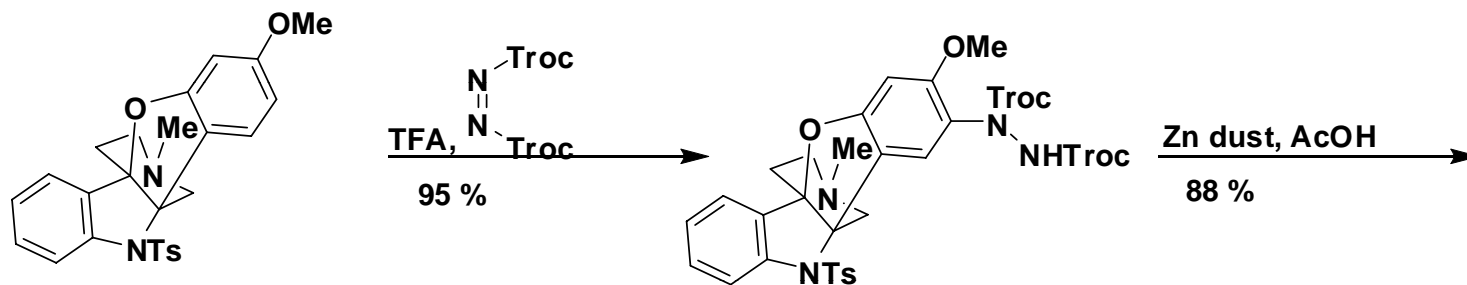
# Two Mechanistic Possibilities



# Attempted Completion

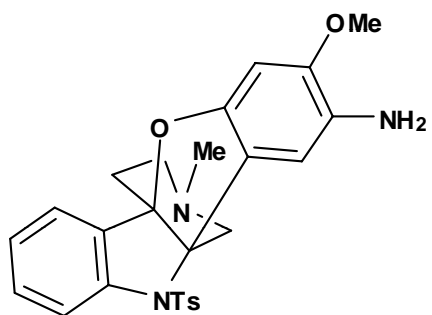


# Attempted Completion



< 5% desired product

# End Game

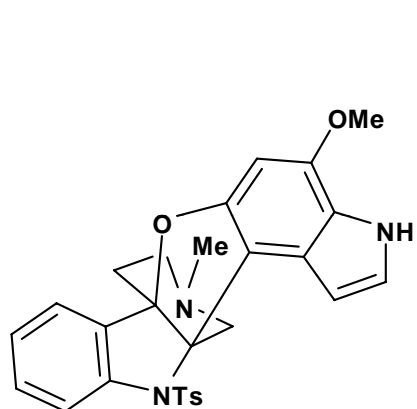


a. MeSCH<sub>2</sub>CO<sub>2</sub>Et, SO<sub>2</sub>Cl<sub>2</sub>  
b. proton sponge  
c. Et<sub>3</sub>N, AcOH

66 %

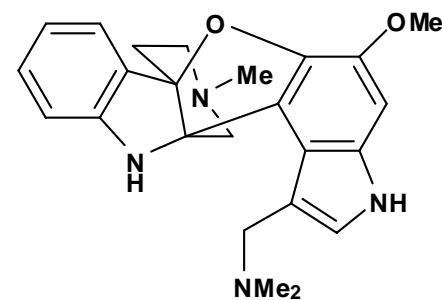
1. BH<sub>3</sub>  
2. R<sub>4</sub>Ni

(90 % over 2 steps)



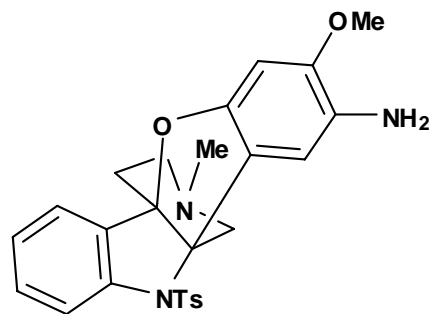
1.  $\begin{array}{c} \text{Cl} \\ | \\ \text{Me}-\text{N}^+-\text{Me} \\ || \\ \text{N} \end{array}$ , AcOH (74 %)

2. Na(Hg), Na<sub>2</sub>HPO<sub>4</sub> (90 %)



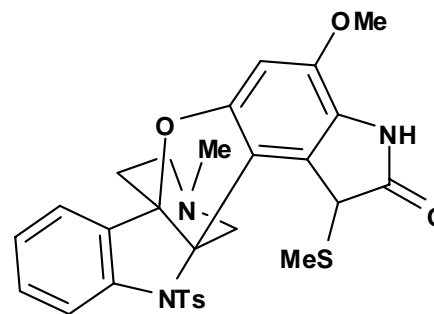
Phalarine

# End Game



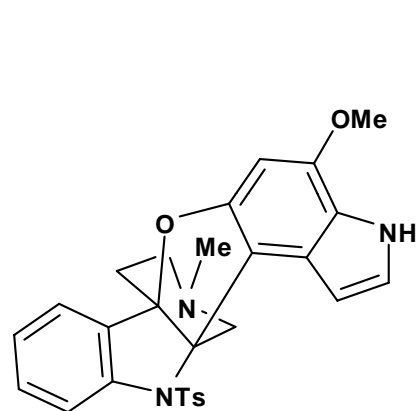
a. MeSCH<sub>2</sub>CO<sub>2</sub>Et, SO<sub>2</sub>Cl<sub>2</sub>  
b. proton sponge  
c. Et<sub>3</sub>N, AcOH

66 %



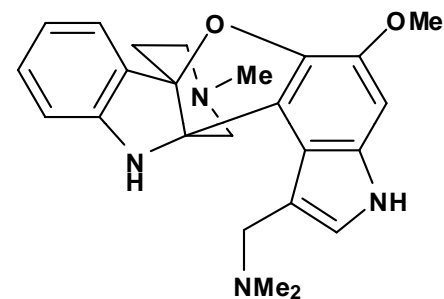
1. BH<sub>3</sub>  
2. R<sub>4</sub>Ni

(90 % over 2 steps)



1.  $\begin{array}{c} \text{Cl} \\ | \\ \text{Me}-\text{N}^+-\text{Me} \\ || \\ \text{N} \end{array}$ , AcOH (74 %)

2. Na(Hg), Na<sub>2</sub>HPO<sub>4</sub> (90 %)



Phalarine