

Christian Gloor  
Topic Review  
26.02.2014

# The chemistry of Albert Padwa

## Application in Alkaloid Synthesis

# Overview

- Albert Padwa
- 1,3-Dipolar Cycloaddition Chemistry
- Pummerer Induced Processes
- Michael addition/dipolar cycloaddition cascade of bis(phenylsulfonyl)diene
- Intramolecular Diels-Alder Reaction of 2-Amidofurans

# Albert Padwa

- Born in New York City
- B.A. Columbia University
- Ph.D. Columbia University
- Post Doc University of Wisconsin
- Assistant Professor Ohio State University (1963)
- Associate Professor SUNY Buffalo (1967-1969)
- Professor SUNY Buffalo (1969-1979)
- William Patterson Timmie Professor of Chemistry at Emory University (since 1979)



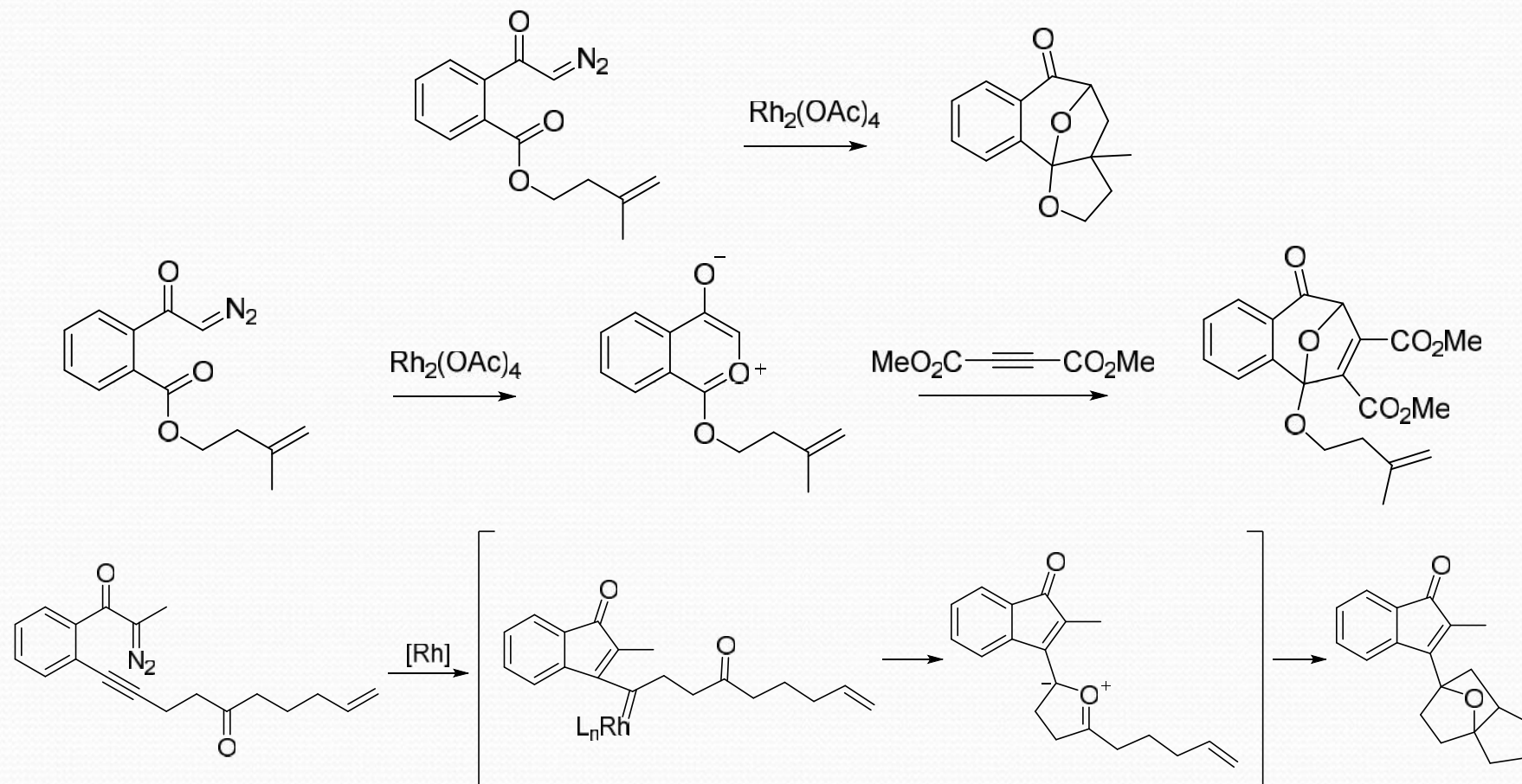
EMORY  
UNIVERSITY

<http://euch6f.chem.emory.edu/padwa.html>

<http://www.emory.edu/>

Padwa, A.; Cheng, B.; Zou Y. *Aust. J. Chem.* **2014**, *67*, 343

# 1,3-Dipolar Cycloaddition Chemistry



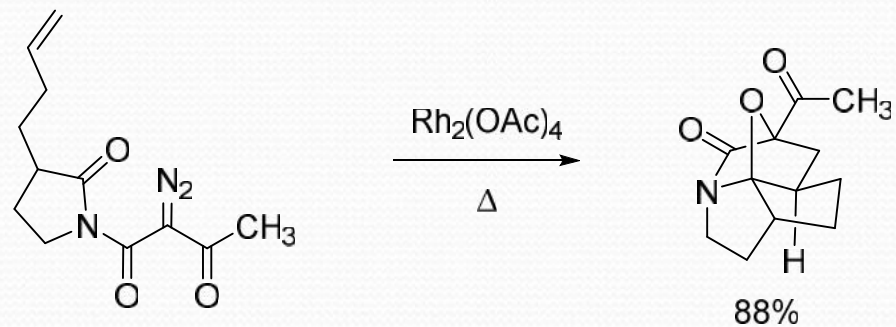
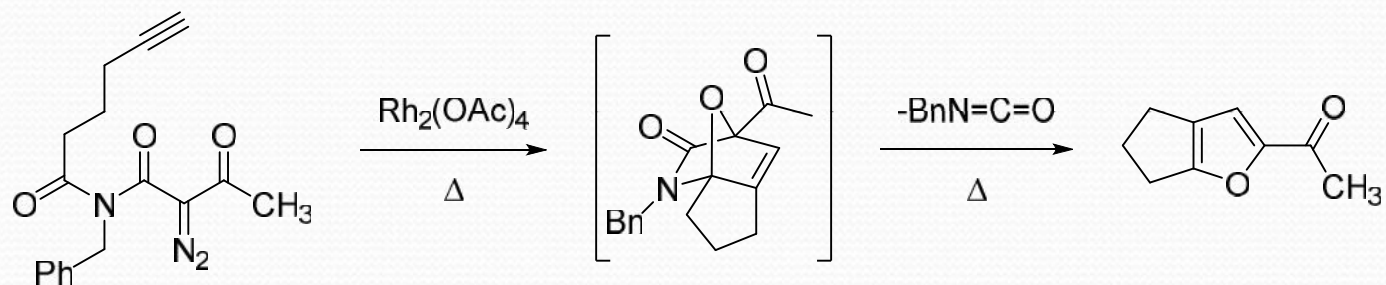
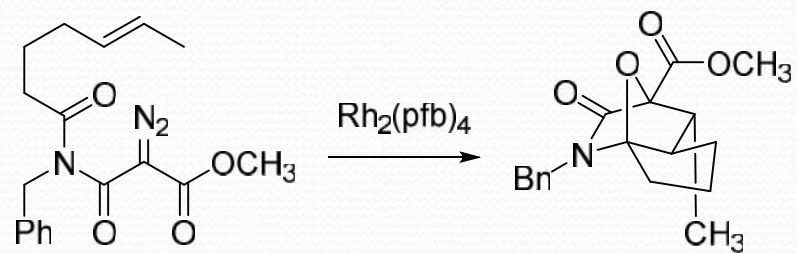
Padwa, A.; Carter, S.P.; Nimmesgern, H. *J. Org. Chem.* **1986**, *51*, 1157-1158

Padwa, A.; Carter, S.P.; Nimmesgern, H.; Stull, P.D. *J. Am. Chem. Soc.* **1988**, *110*, 2894-2900

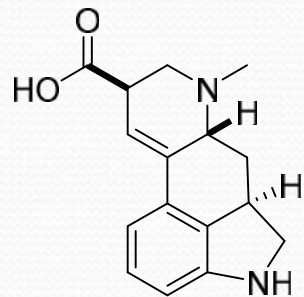
Padwa, A.; Fryxell, G.E.; Zhi, L. *J. Org. Chem.* **1988**, *53*, 2877-2878

Padwa, A.; Kassir, J.M.; Semones, M.A.; Weingarten, M.D. *J. Org. Chem.* **1995**, *60*, 53-62

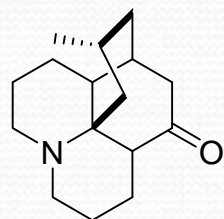
# 1,3-Dipolar Cycloaddition Chemistry



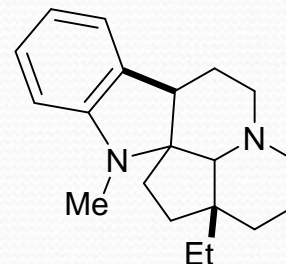
# Application of the 1-3-dipolar cycloaddition



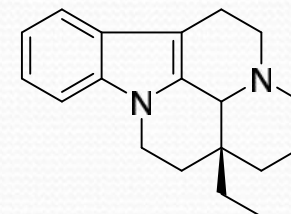
lyseric acid



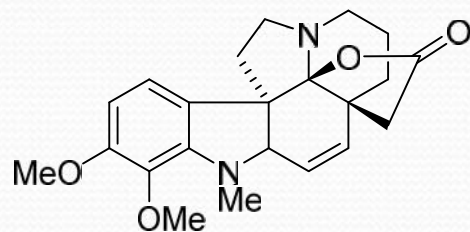
lycopodine



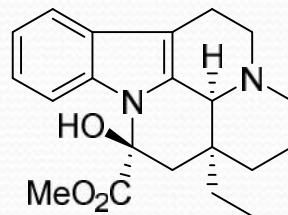
Vallesamidine



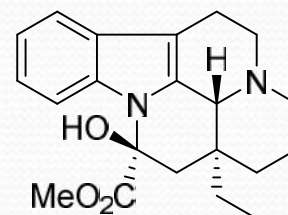
*epi*-16,17-dihydroeburnamenine



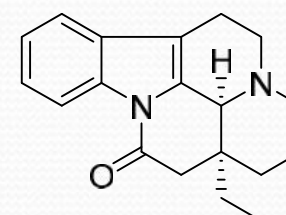
Aspidophytine



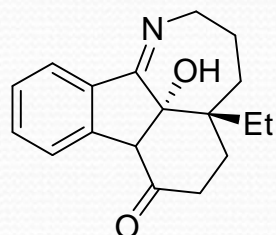
vincamine



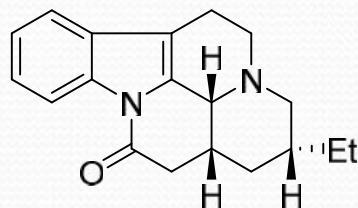
3*H*-epivincamine



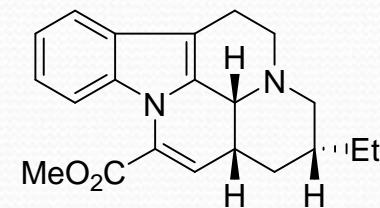
eburnamonine



mersicarpine

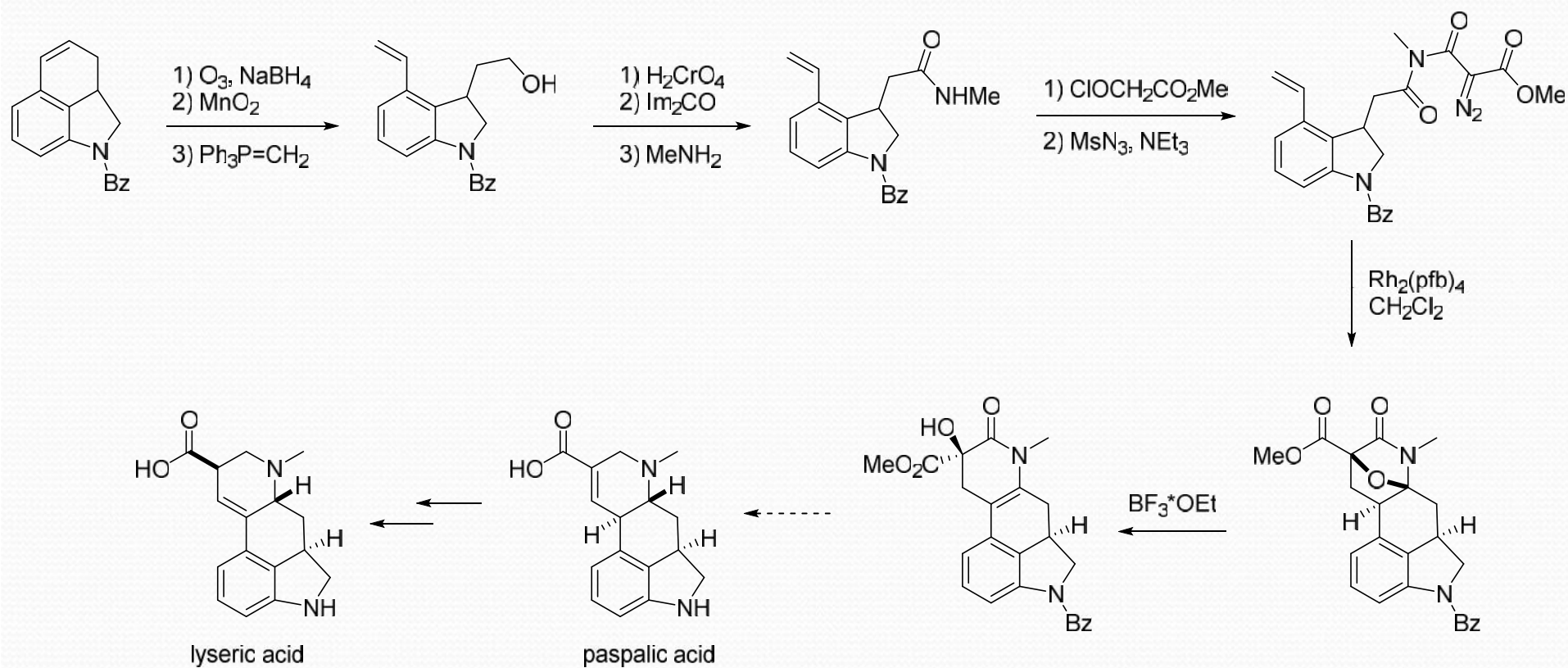


tacamonine



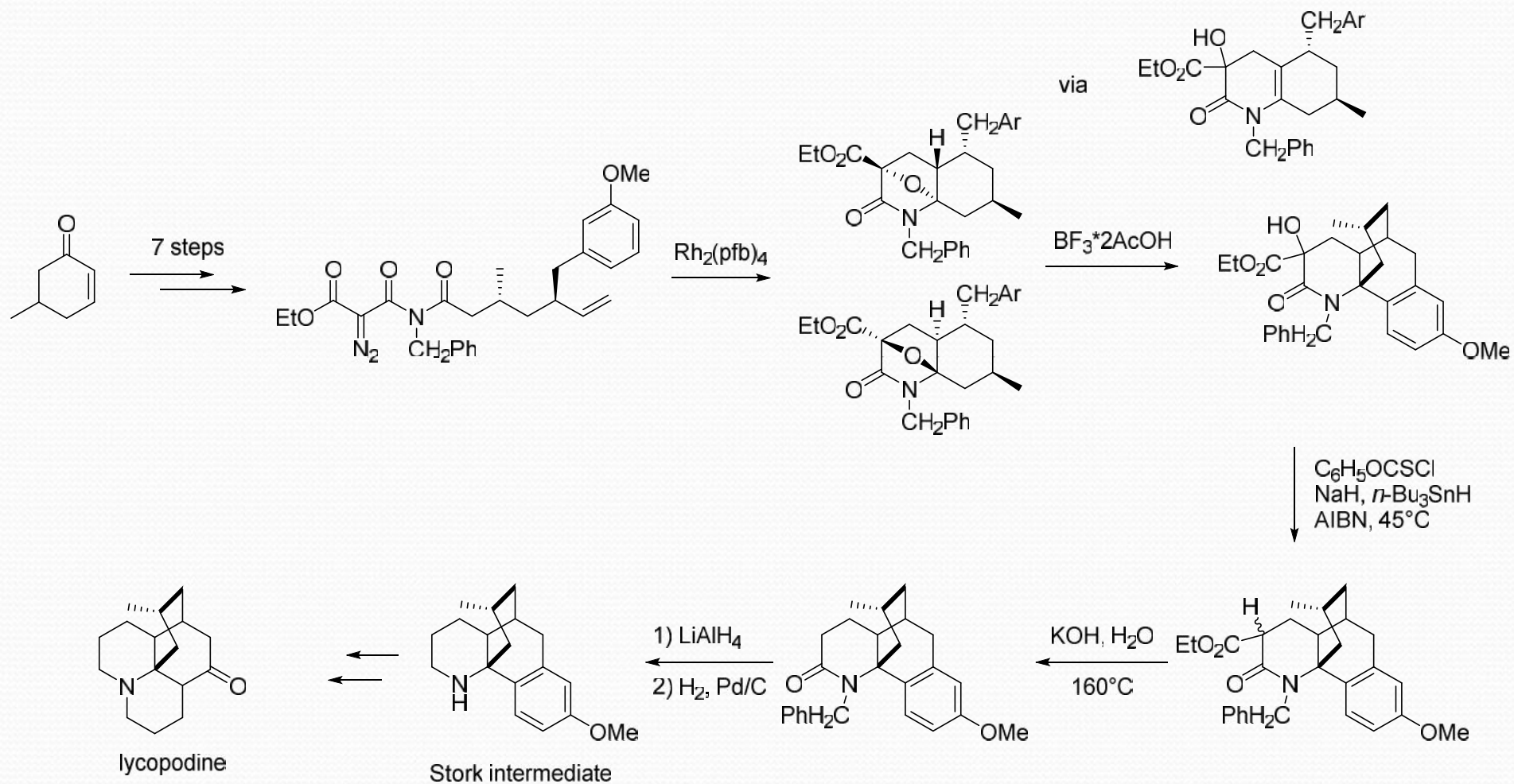
apotacamine

# Towards lyseric acid



Marino Jr., J.P.; Osterhout, M.H.; Padwa, A. *J. Org. Chem.* **1995**, *60*, 2704-2713

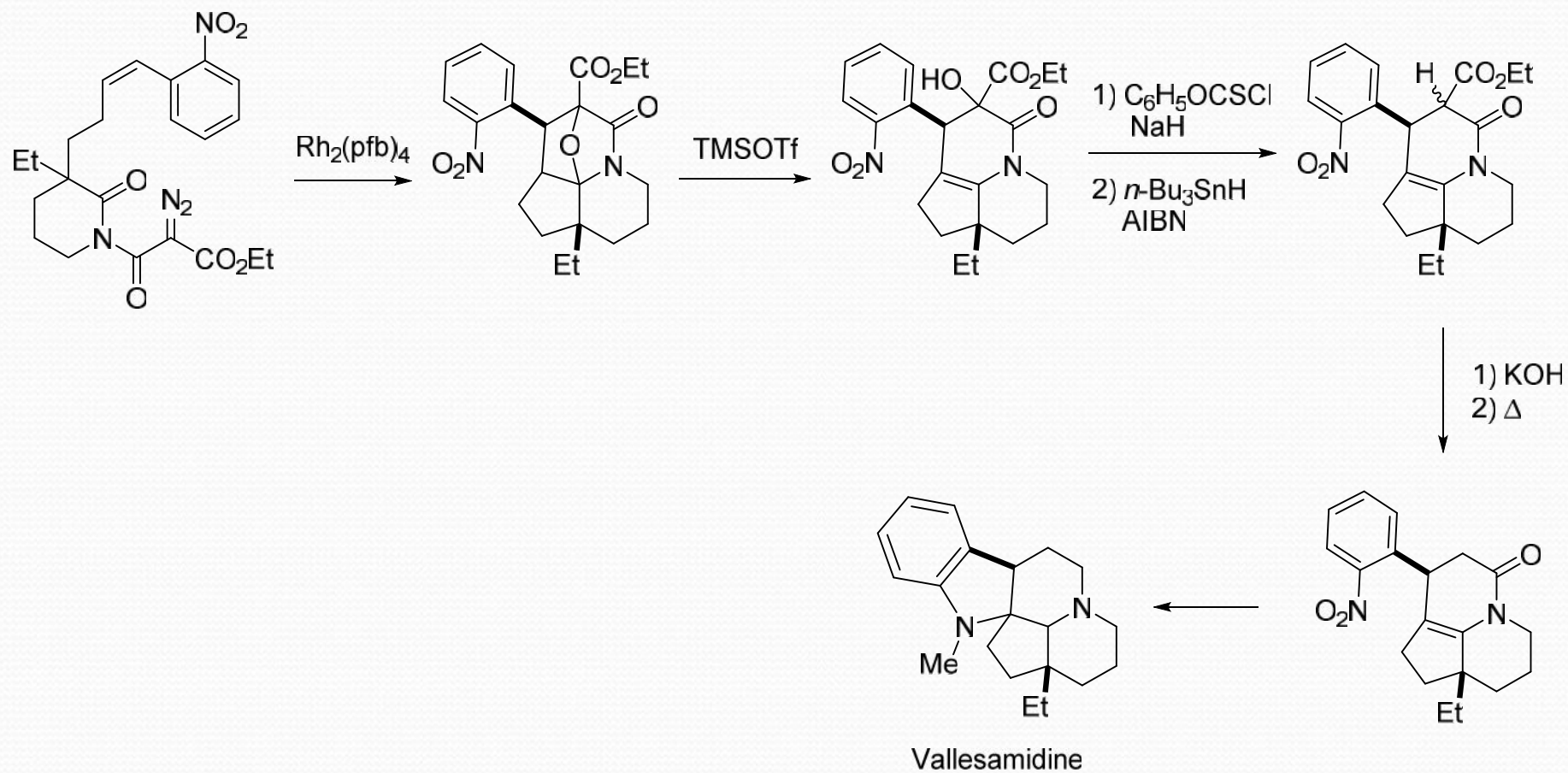
# Formal synthesis of lycopodine



Padwa, A.; Brodney, M.A.; Marino Jr., J.P.; Sheehan, S.M. *J. Org. Chem.* **1997**, *62*, 78-87

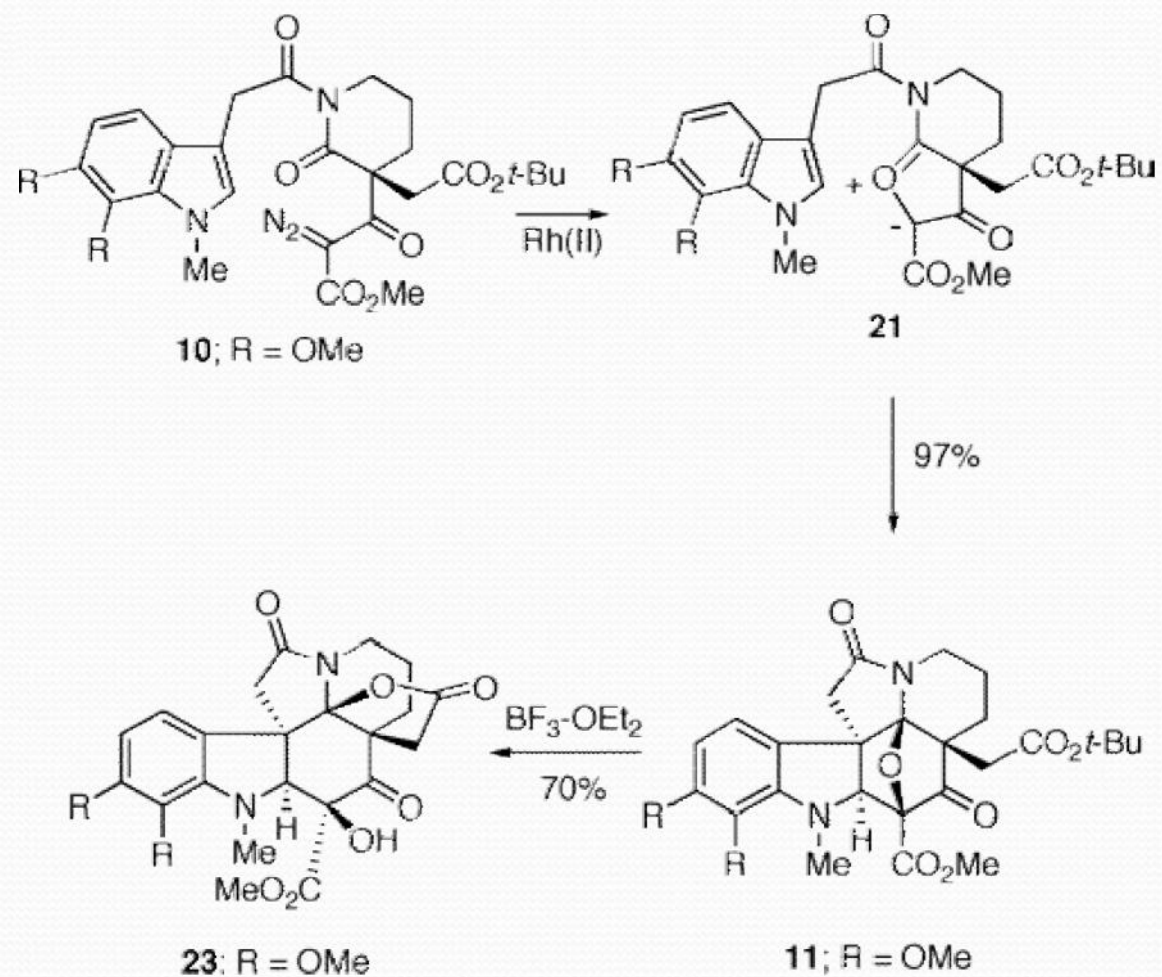


# Total synthesis of Vallesamidine

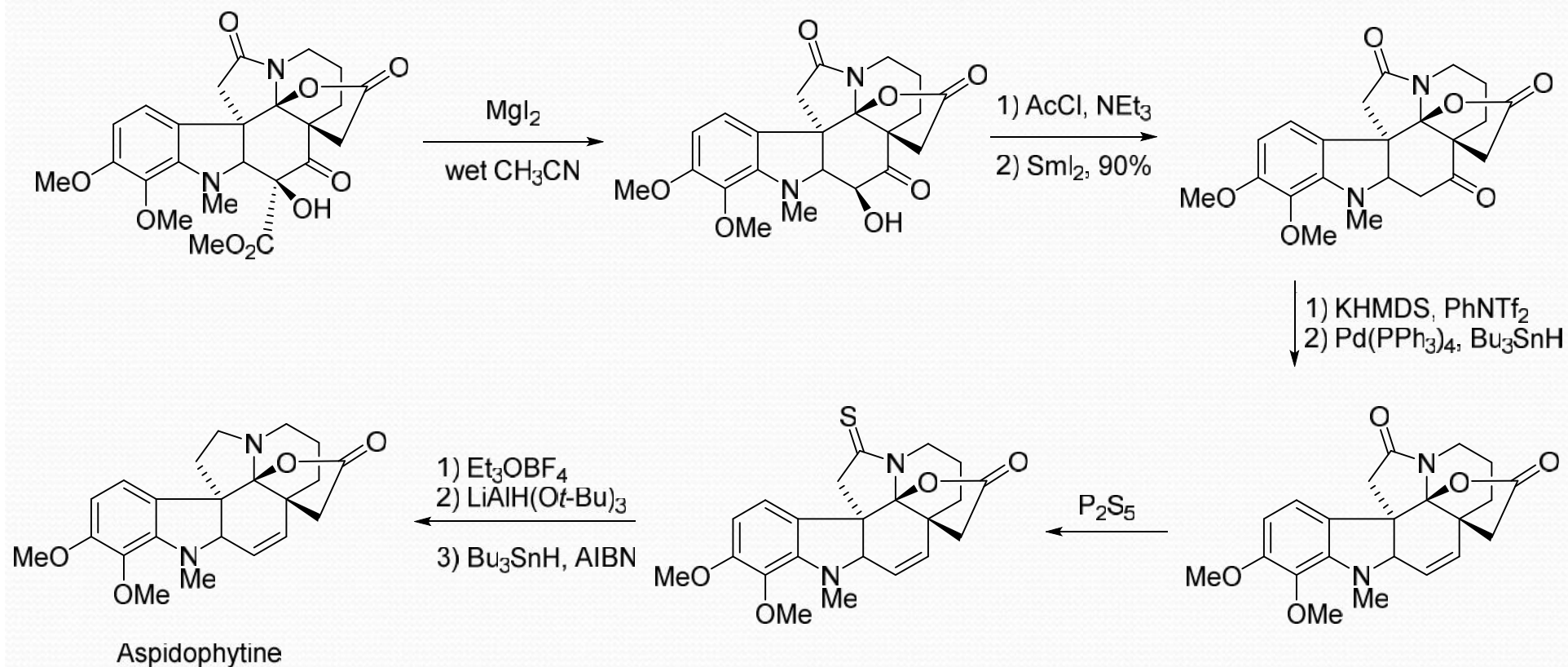


Padwa, A.; Harring, S.R.; Semones, M.A. *J. Org. Chem.* **1998**, *63*, 44-54

# Total synthesis of Aspidophytine

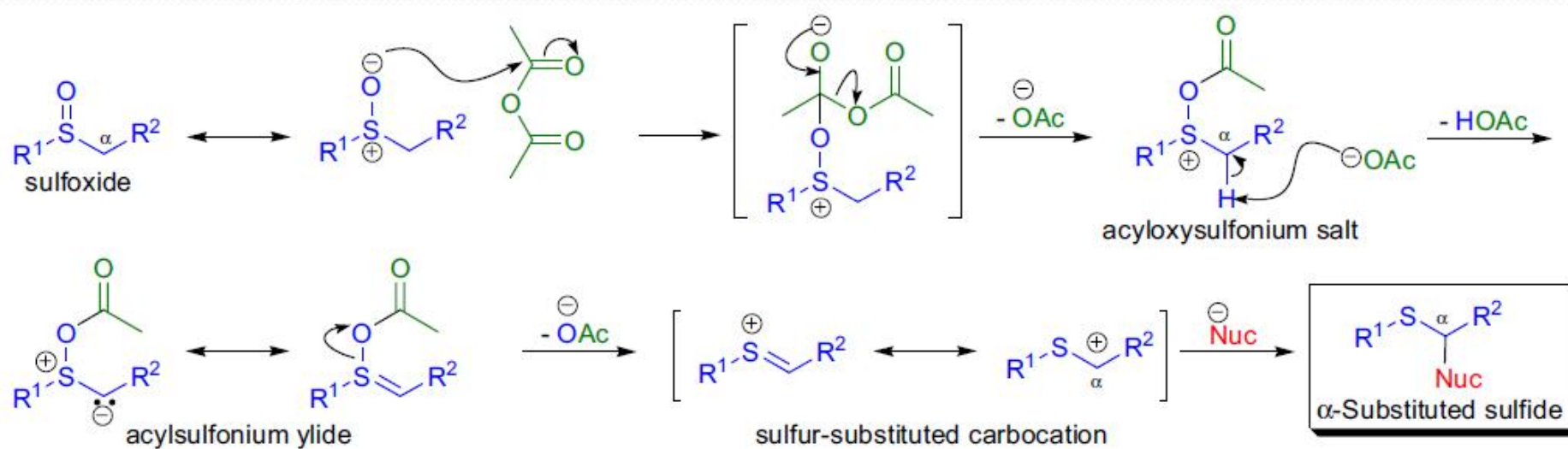


# Total synthesis of Aspidophytine

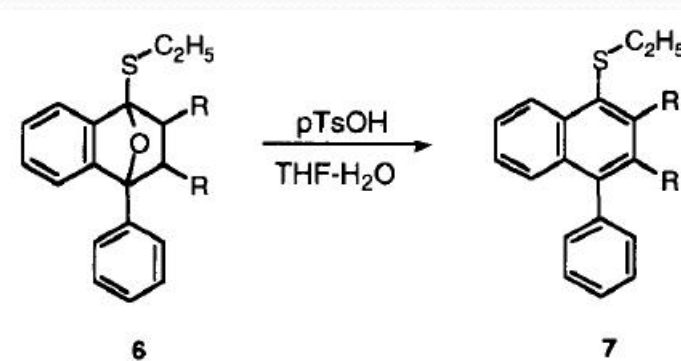
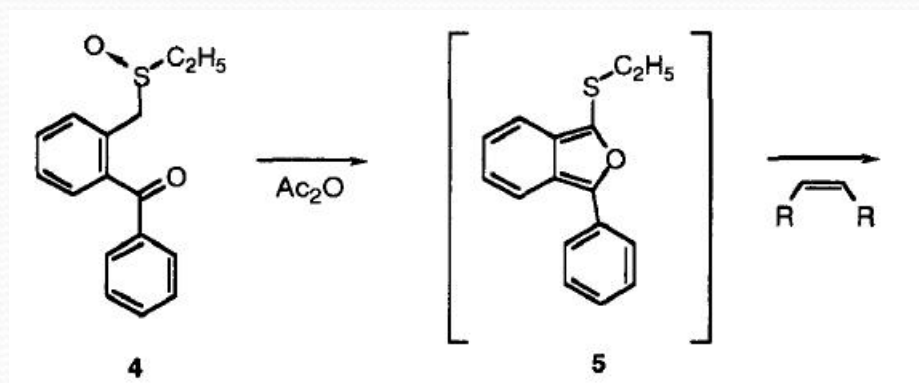


# Pummerer Rearrangement

- Synthesis of  $\alpha$ -substituted sulfides from sulfoxides via sulfonium ylide

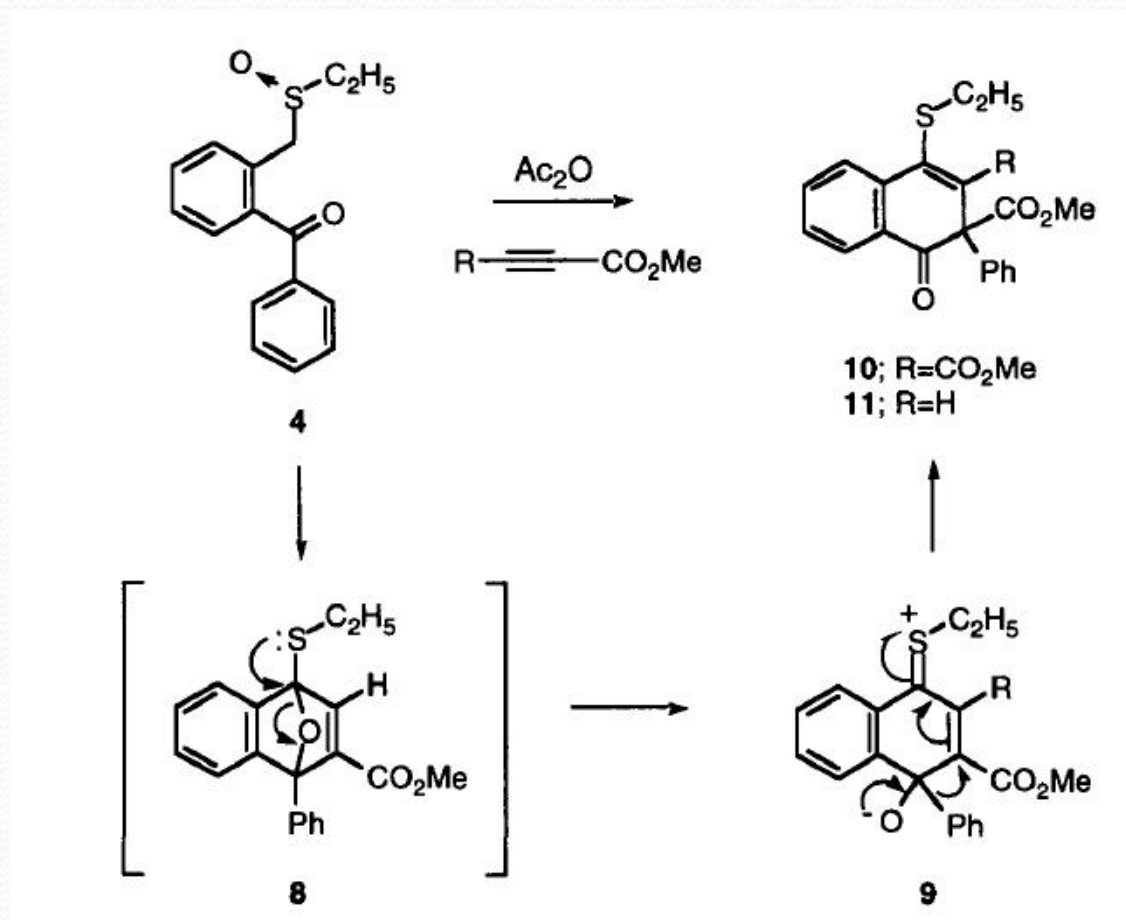


# Synthesis of $\alpha$ -thio substituted naphthalene derivatives

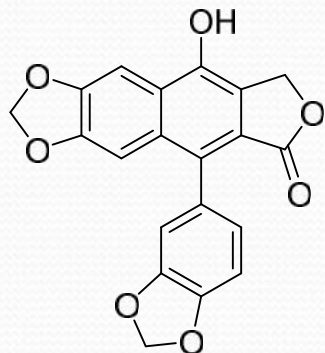


**6a** (maleic anhydride); 87% (1.7:1)  
**6b** (N-phenyl maleimide); 73% (10:1)  
**6c** (*trans*-1,2-bis(phenylsulfonyl)ethylene); 69% (1:1)  
**7d** (cyclohexene); 6%

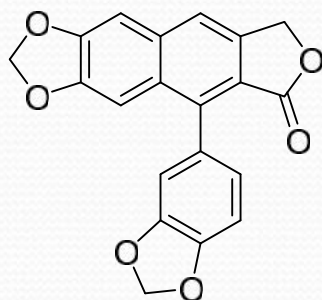
# Synthesis of $\alpha$ -thio substituted naphthalene derivatives



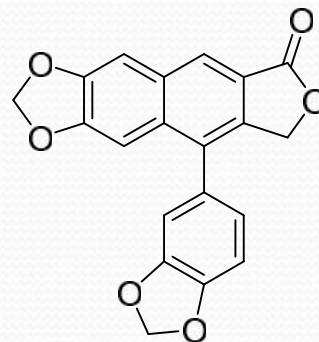
# Application of Pummerer Induced Processes



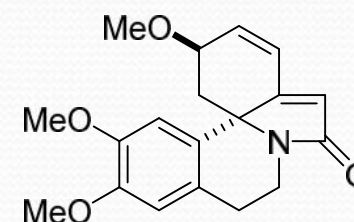
Taiwanin E



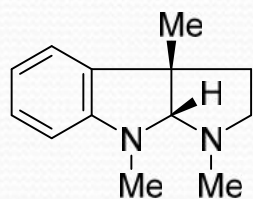
Taiwanin C



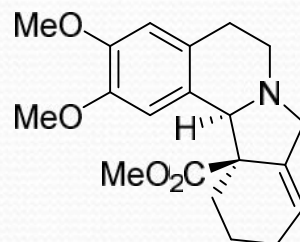
Justicidin E



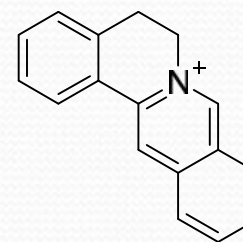
Erysotramidine



Desoxyeseroline

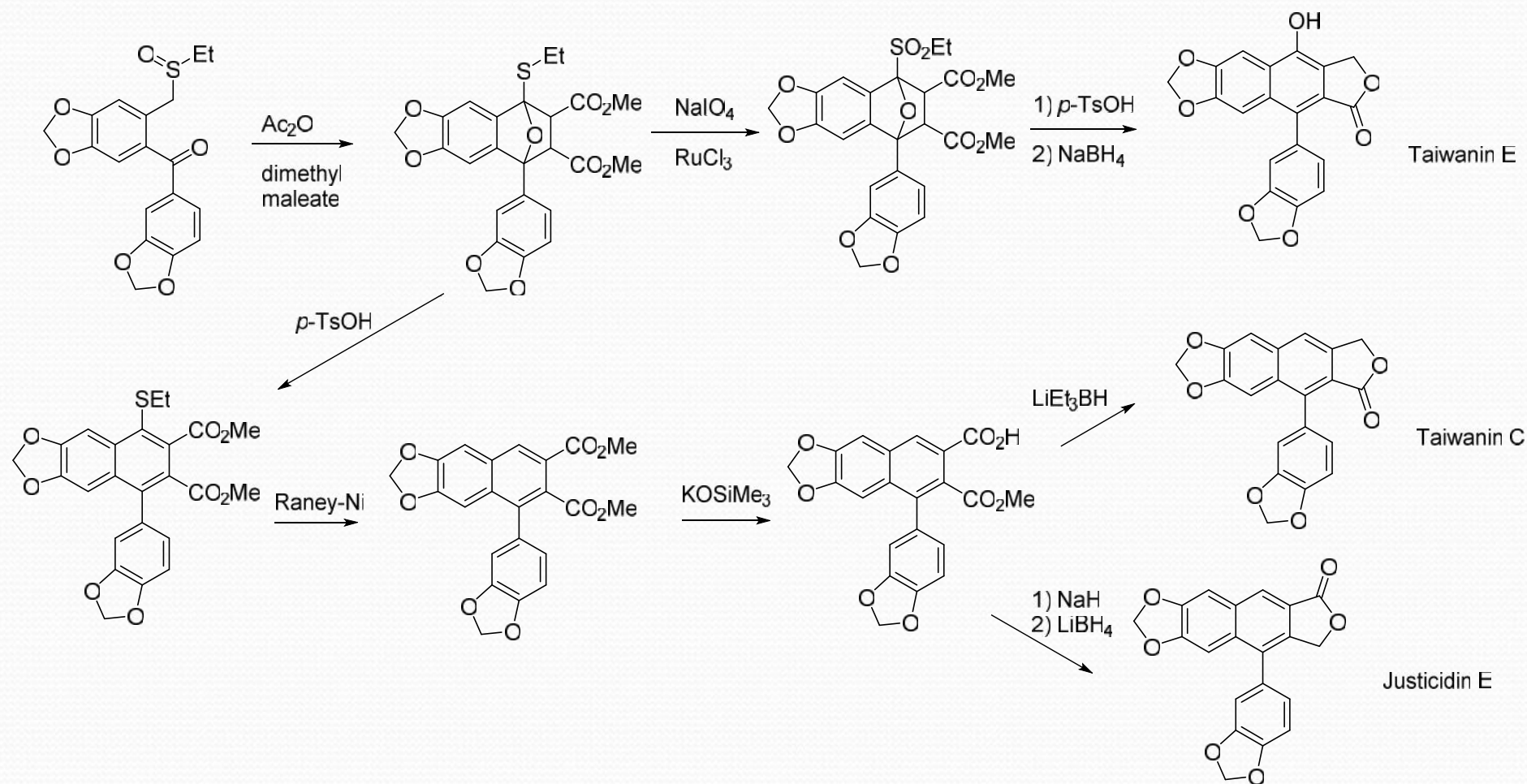


Jamtine



Core skeleton of  
protoberberine alkaloids

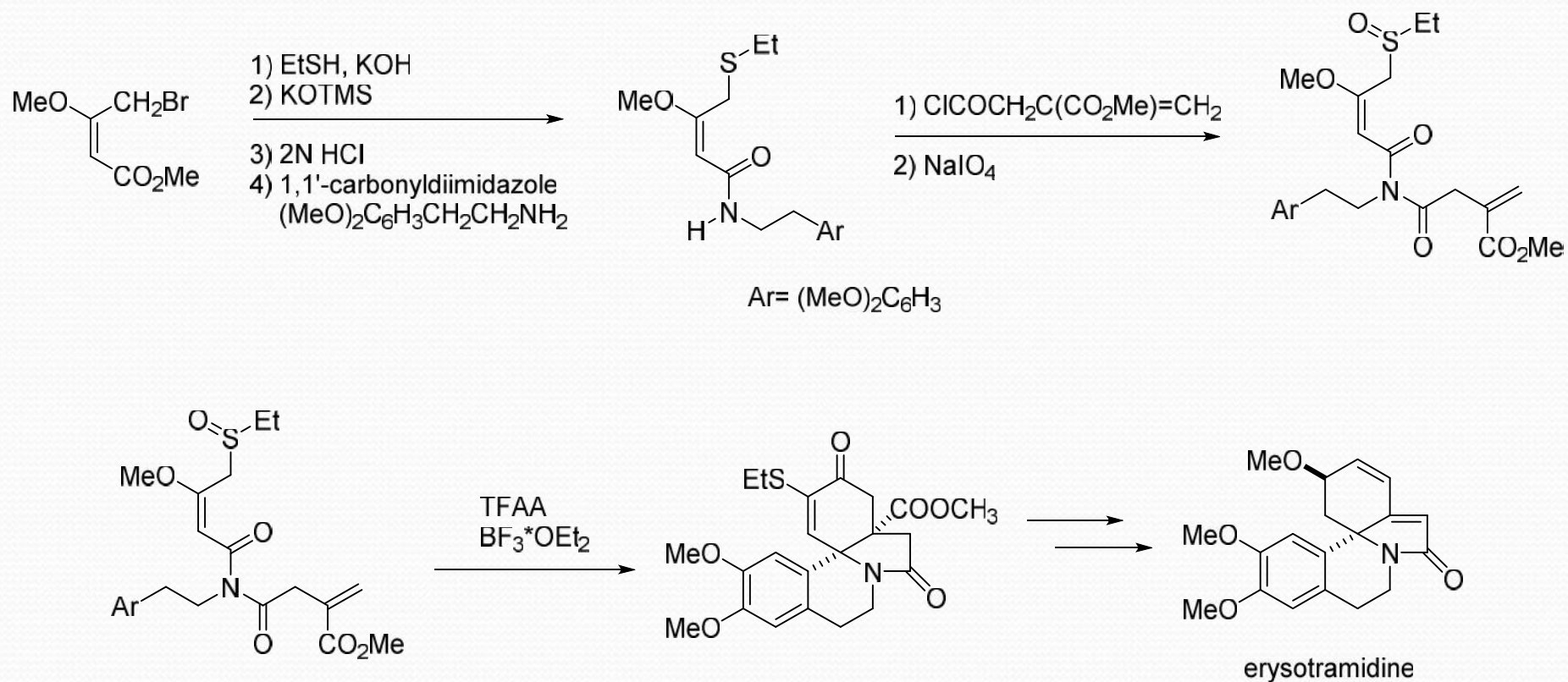
# Tandem Pummerer-Diels-Alder reaction sequence



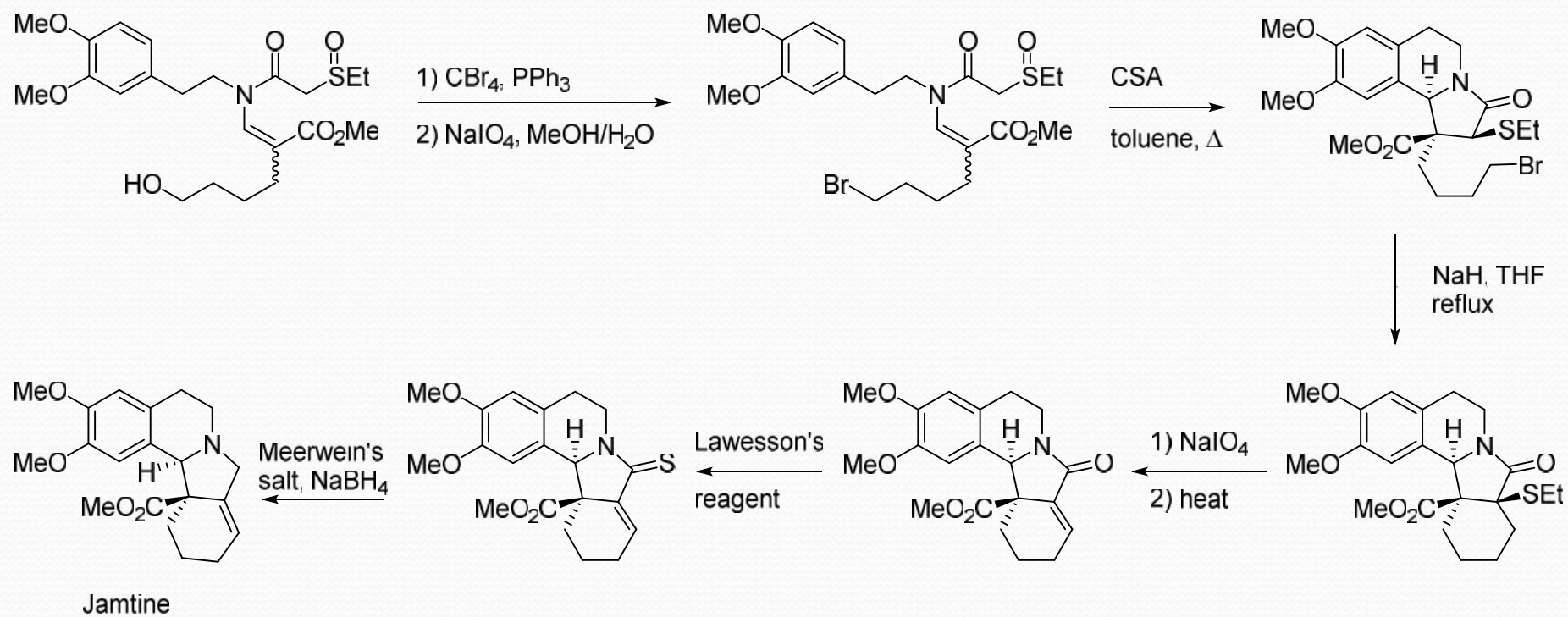
Padwa, A.; Cochran, J.E.; Kappe, C.O. *J. Org. Chem.* **1996**, *61*, 3706-3714



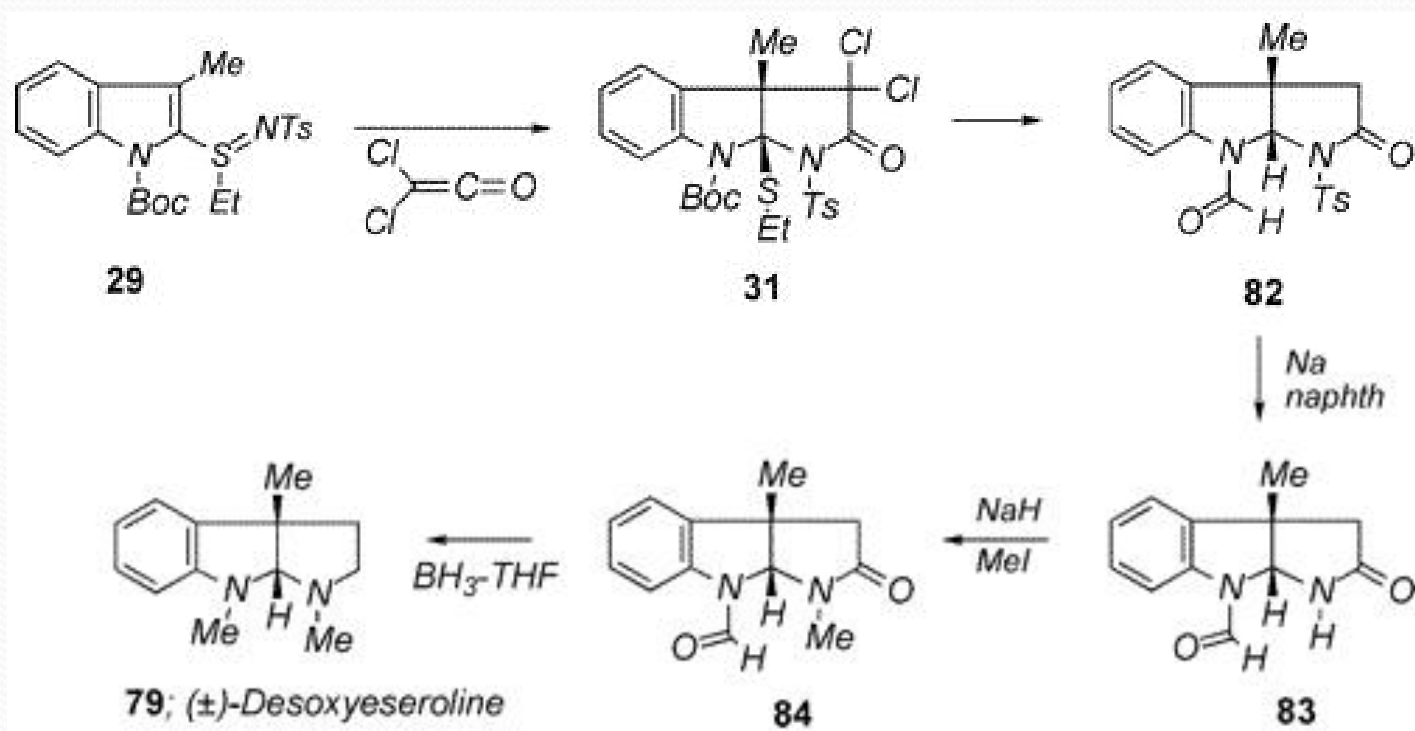
# Total synthesis of Erysotramidine



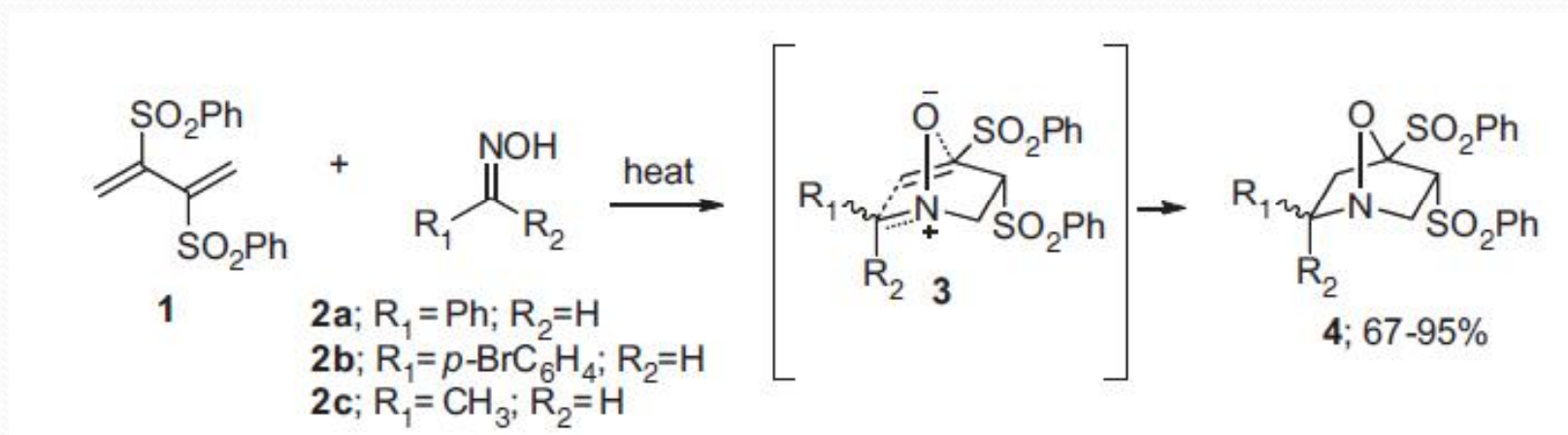
# Total synthesis of (±)-Jamtine



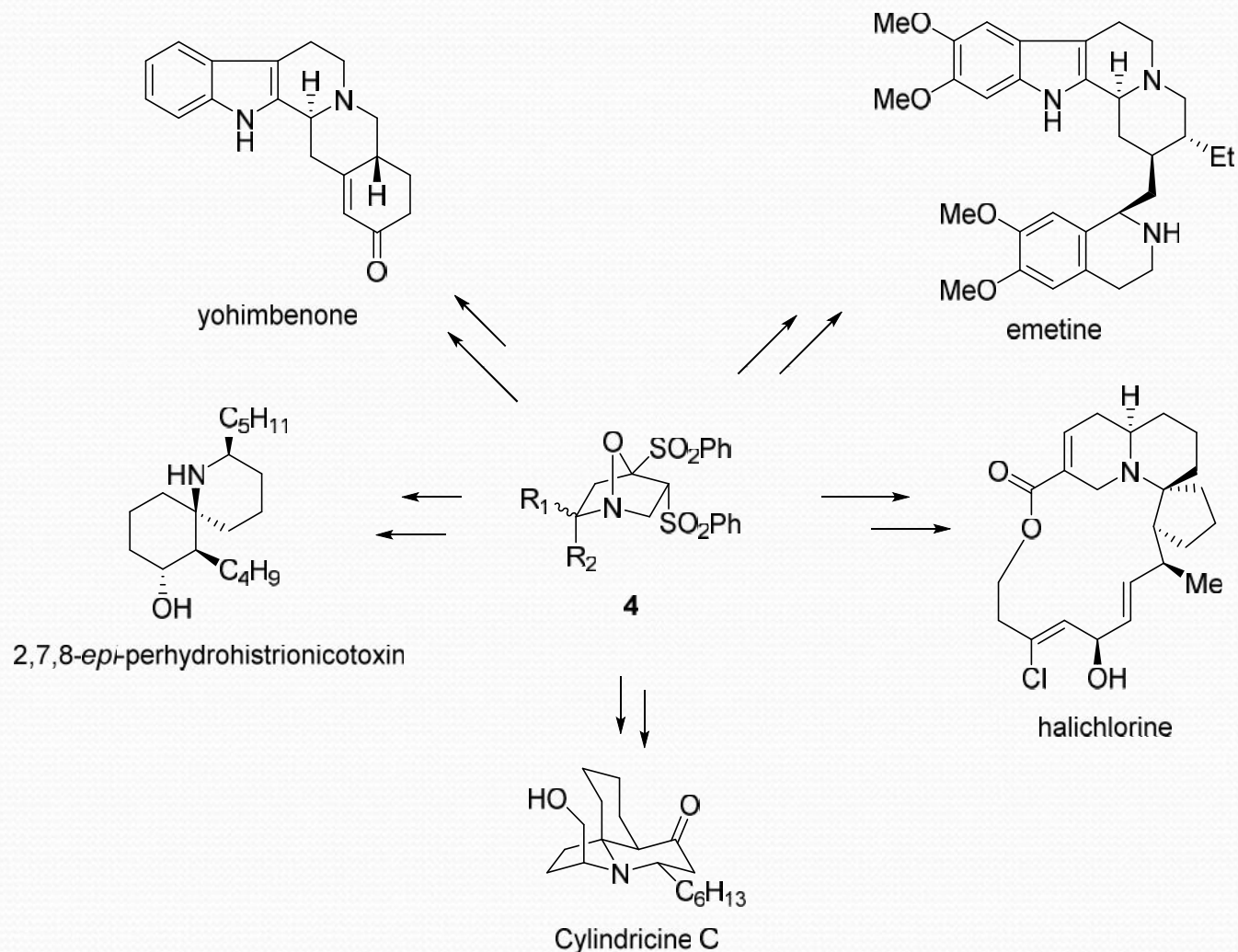
# Synthesis of (±)-Desoxyeseroline



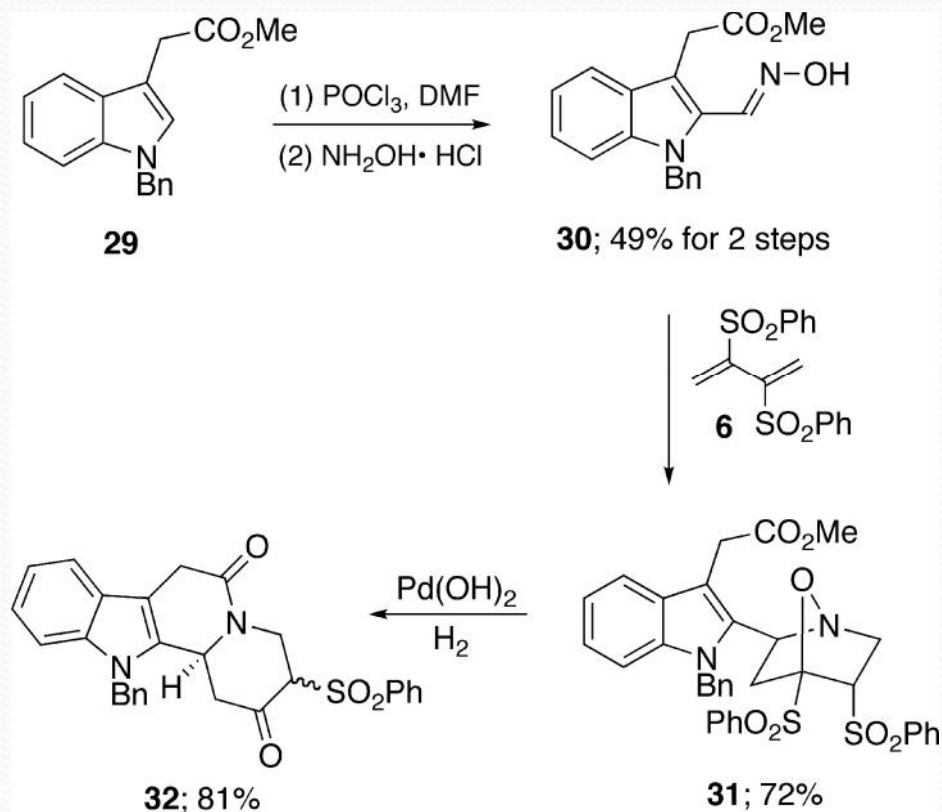
# Michael addition/dipolar cycloaddition cascade of bis(phenylsulfonyl)diene



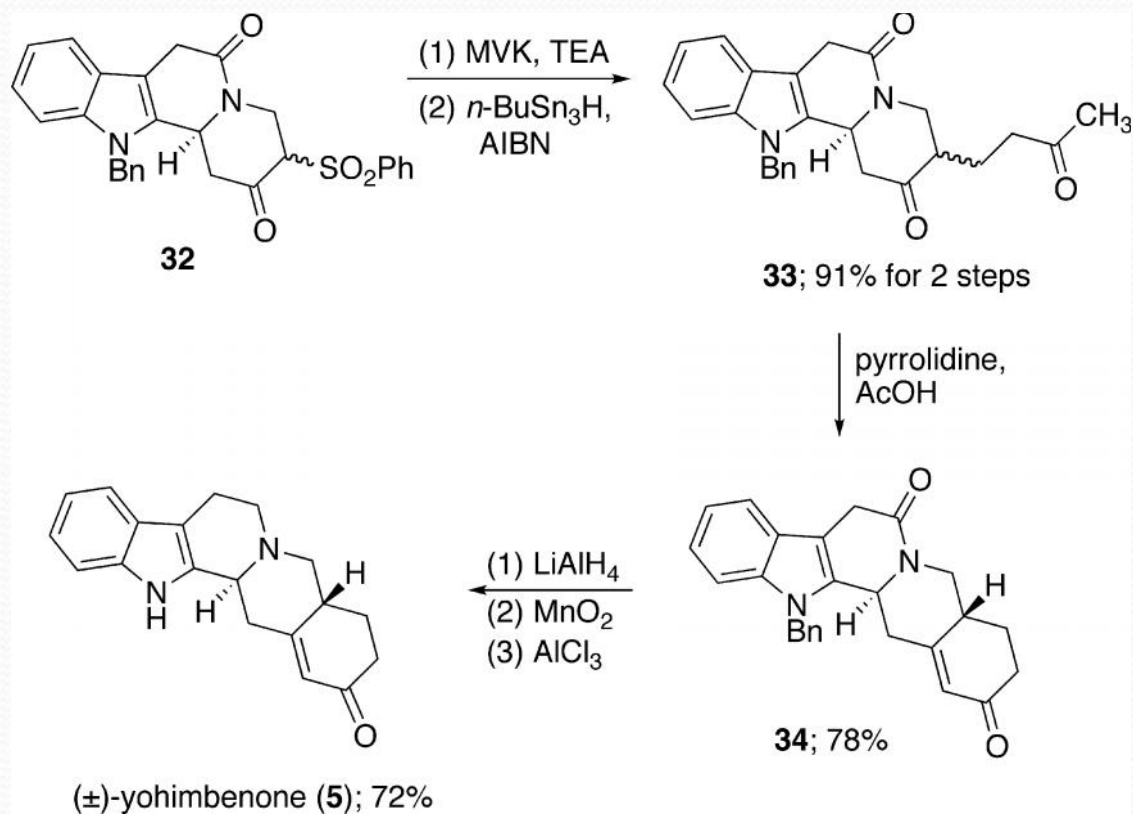
# Michael addition/dipolar cycloaddition cascade of bis(phenylsulfonyl)diene



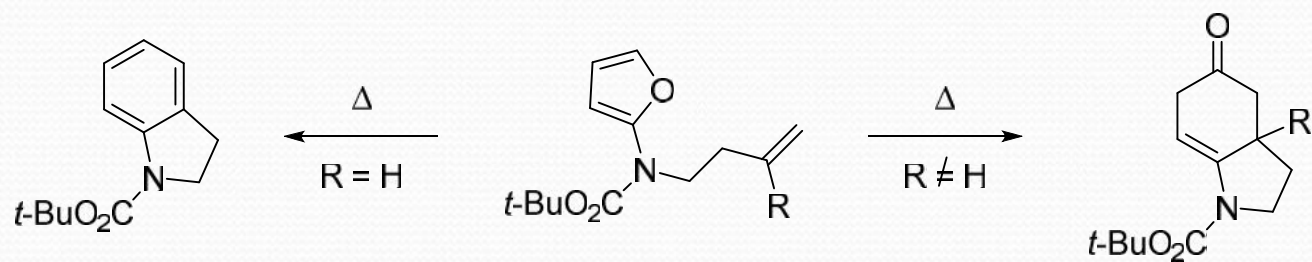
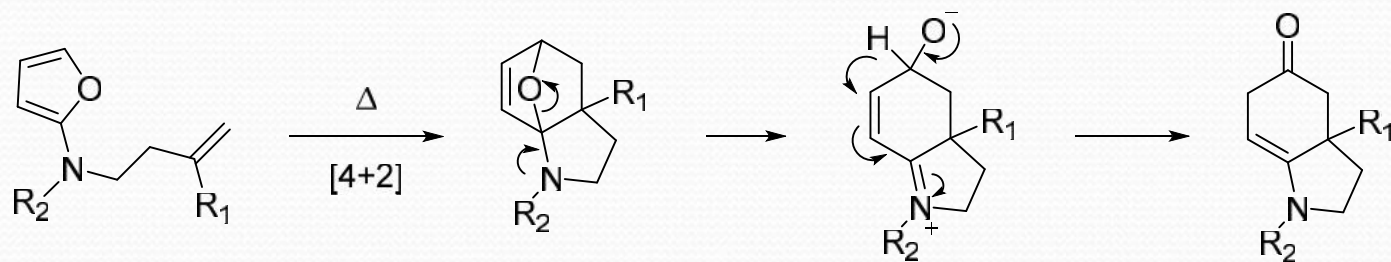
# Total synthesis of (±)-yohimbenone



# Total synthesis of (±)-yohimbenone

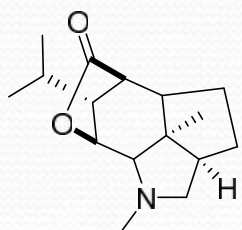


# Intramolecular Diels-Alder Reaction of 2-Amidofurans

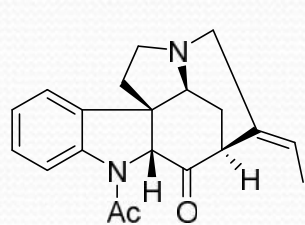




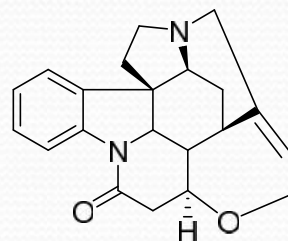
# Application of the Intramolecular Diels-Alder Reaction of 2-Amidofurans



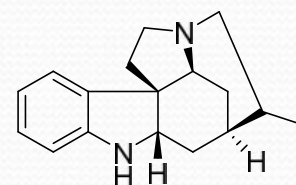
dendrobine



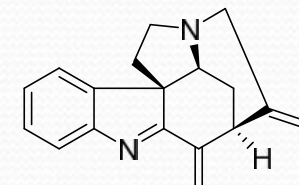
strychnopivotine



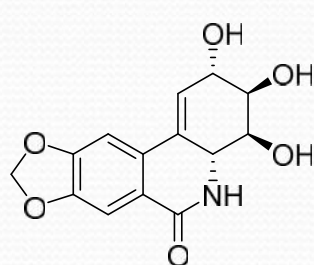
strychnine



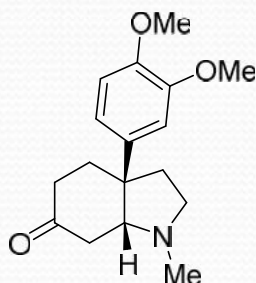
Tubifolidine



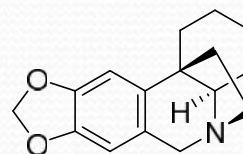
Valparicine



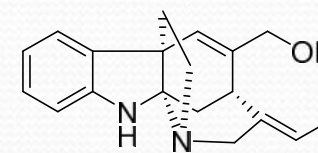
Lycoricidine



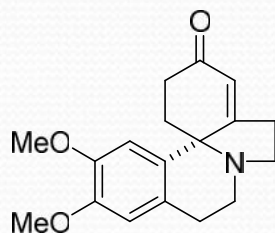
mesembrine



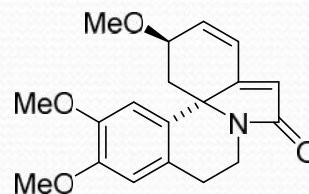
crinane



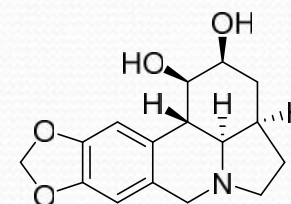
minfiensine



3-Demethoxyerythratidinone

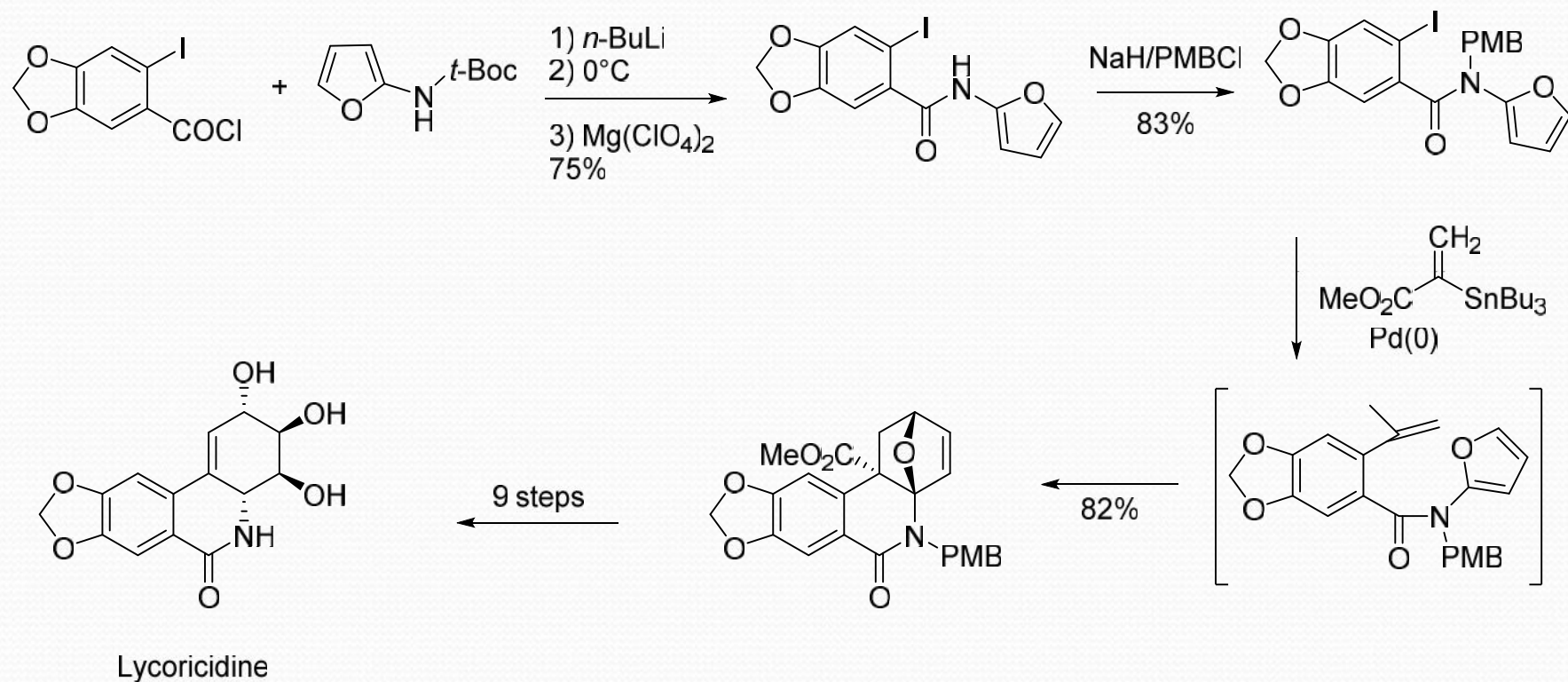


Erysotramidine

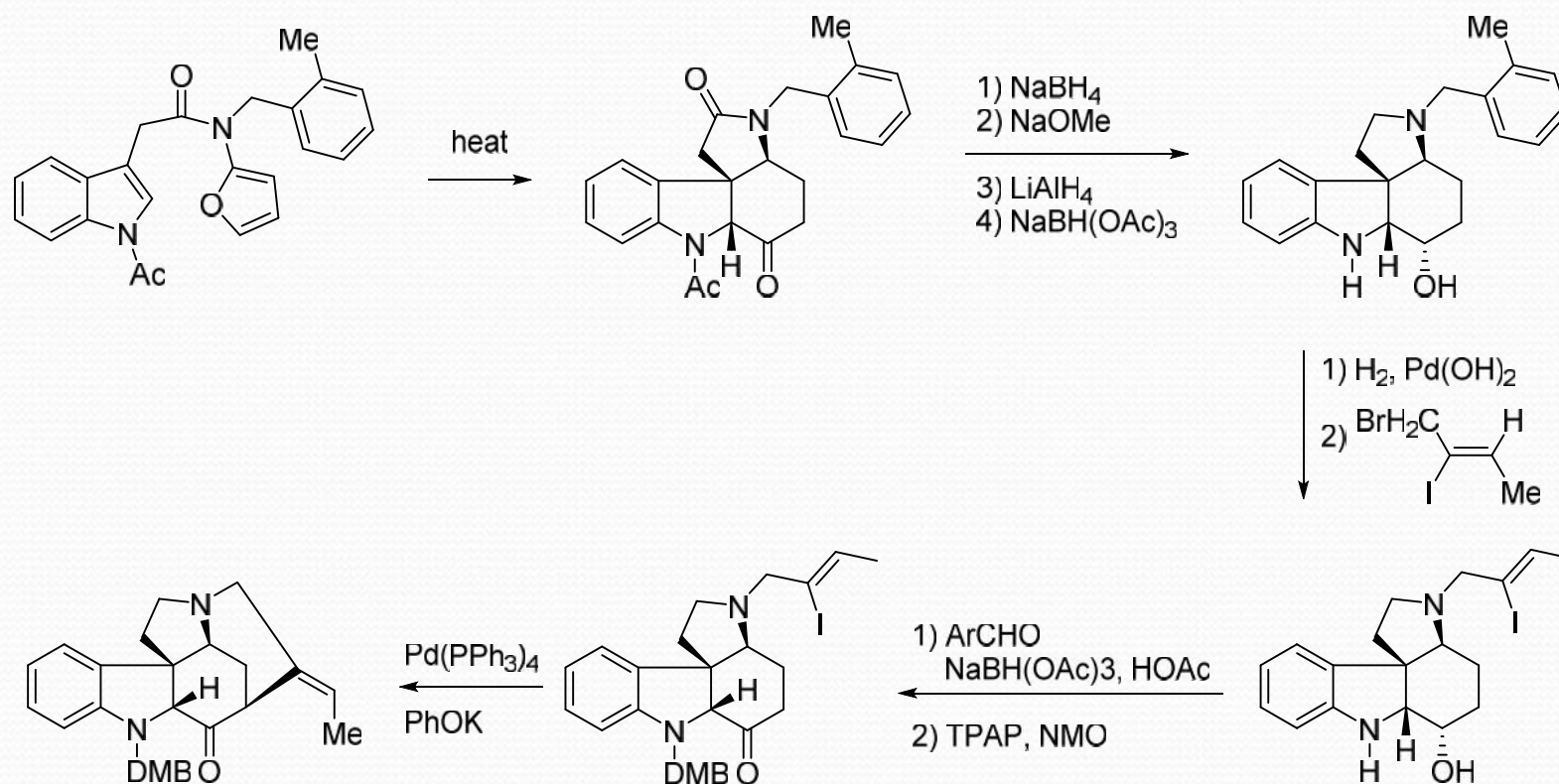


*epi*-zephyranthine

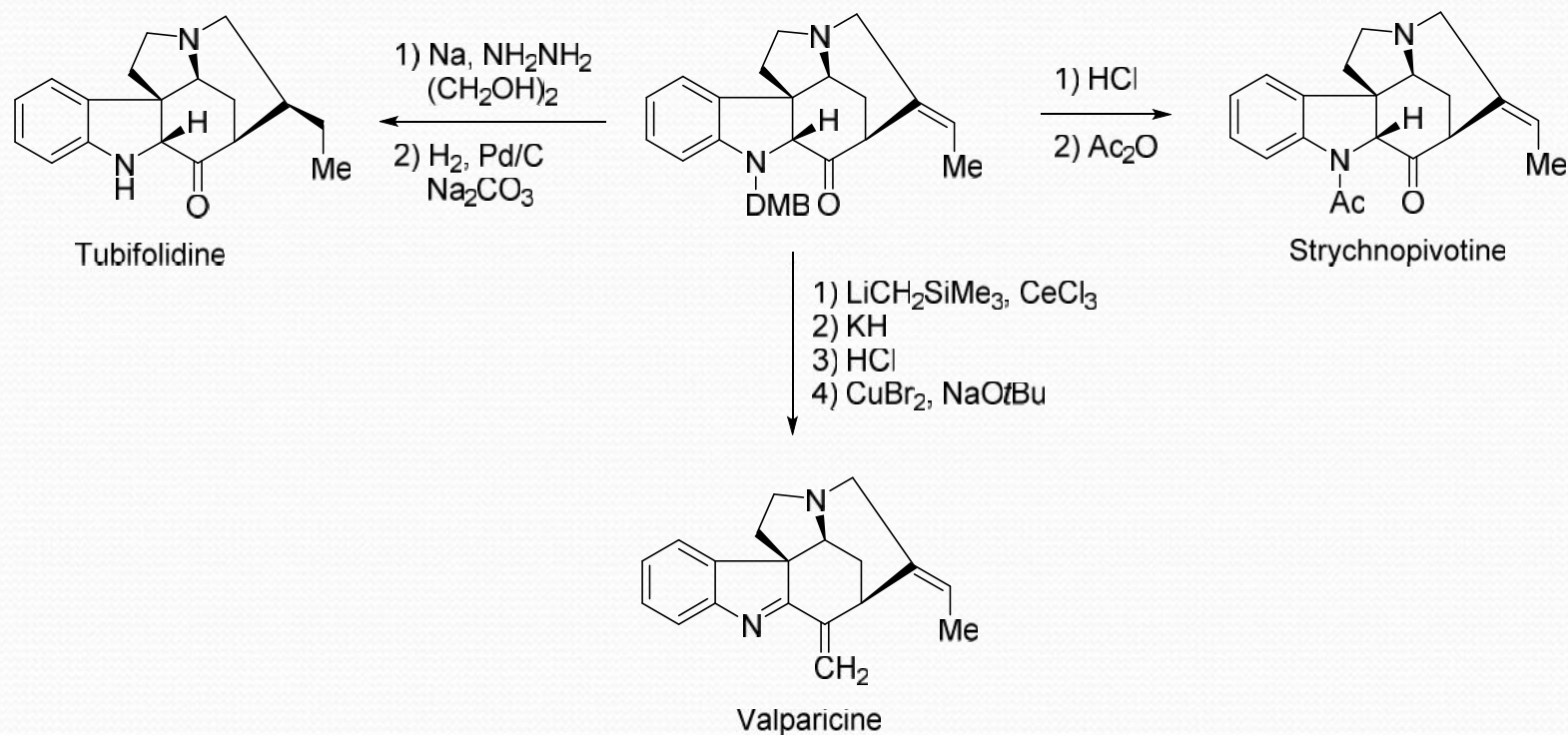
# Total Synthesis of (±)-Lycoricidine



# General synthetic entry to the *Strychnos* alkaloid family



# General synthetic entry to the *Strychnos* alkaloid family



# Conclusion

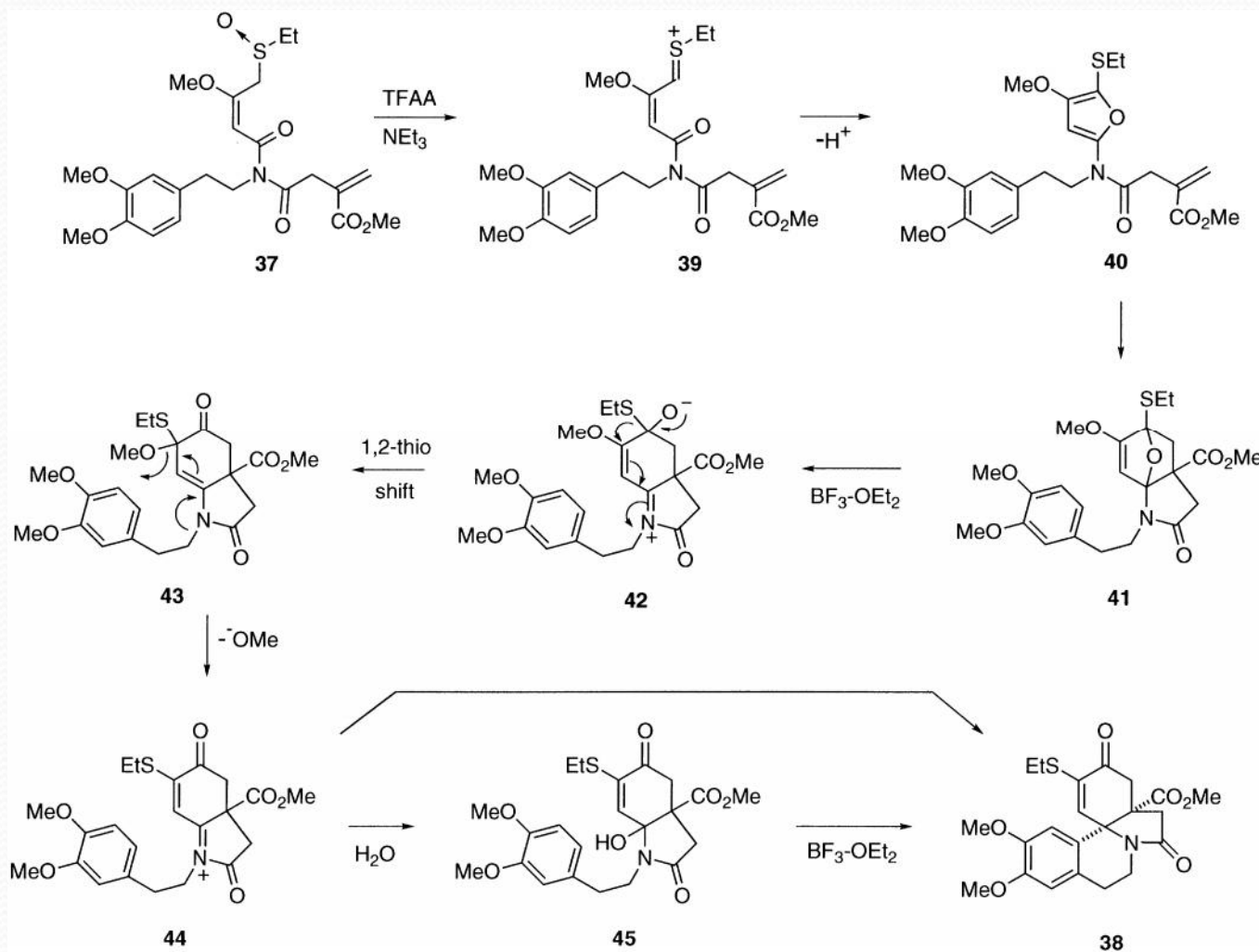
- different cascade reactions were developed and applied in different total synthesis
- over 850 publications since 1963 were produced in the laboratory of Albert Padwa



Thank you for your attention



# Pummerer Induced Processes



Padwa, A., Hennig, R., Kappe, C.O.; Reger, T.S. *J. Org. Chem.* **1998**, *63*, 1144-1155



# Synthesis of (±)-Desoxyeseroline

