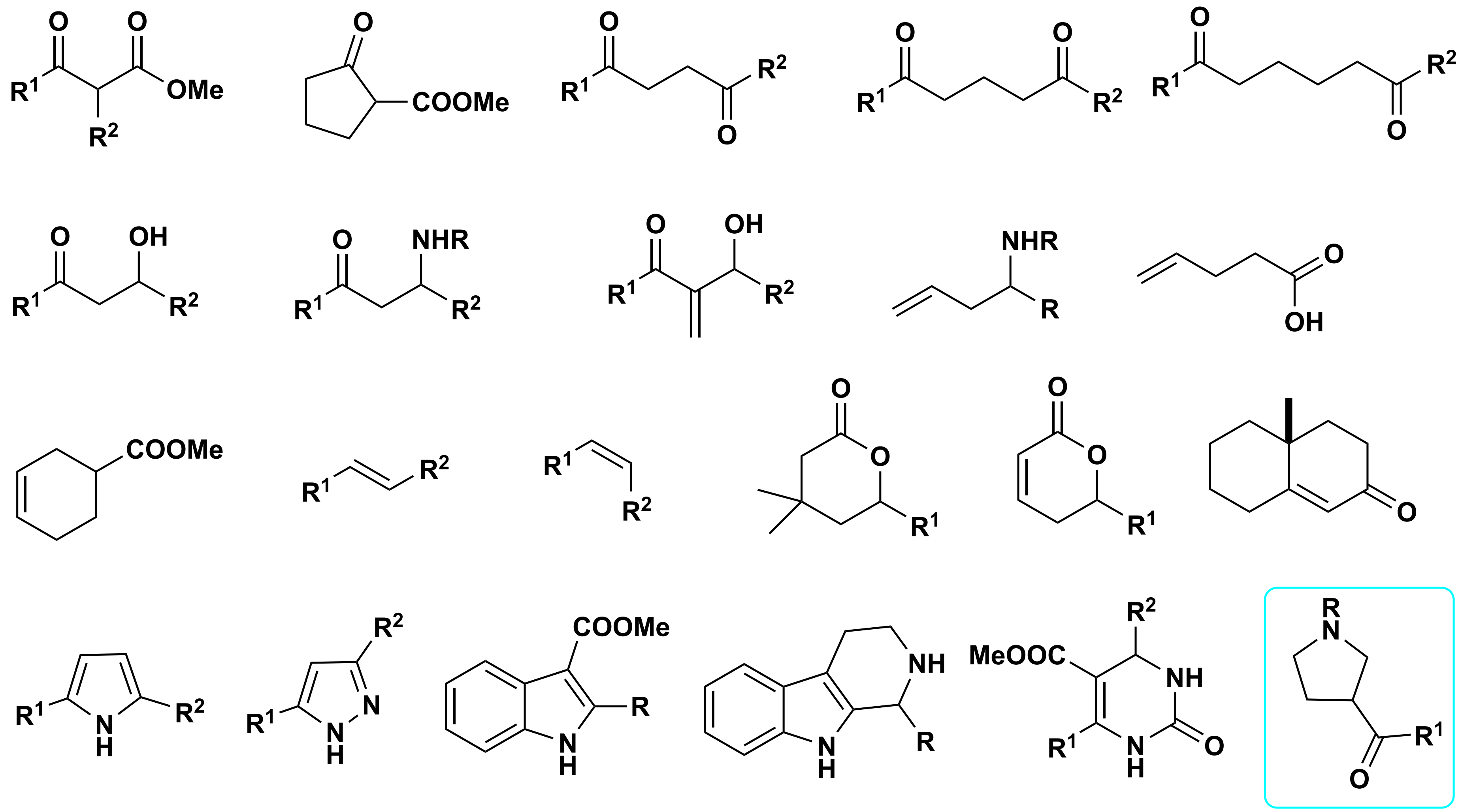
Pattern Recognition

Pattern recognition seeks to discover an exploitable substructural motif around which to organize the thought process and then the synthesis.

The most fascinating cases arise when the target itself must actually be modified leading to a more complex compound before a staple pattern is revealed

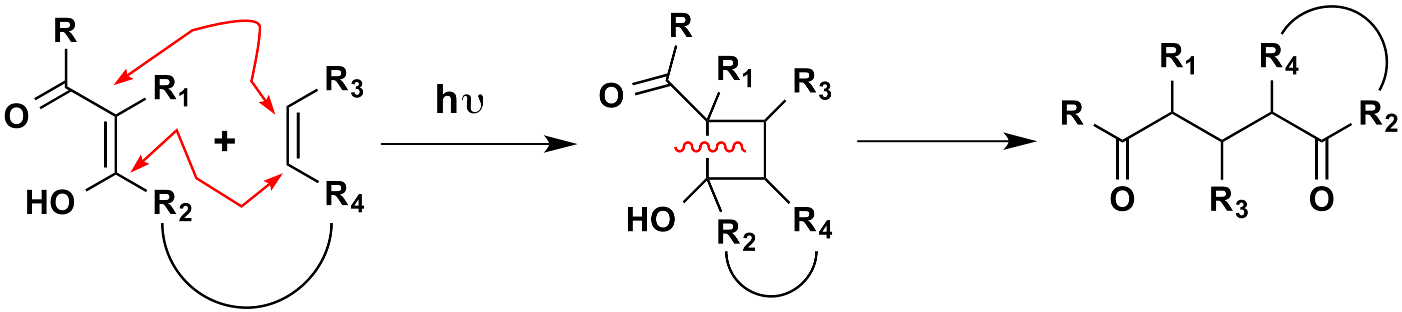
R. M. Wilson, S. J. Danishefsky, *J. Org. Chem*. **2007**, *72*, 4293-4305.

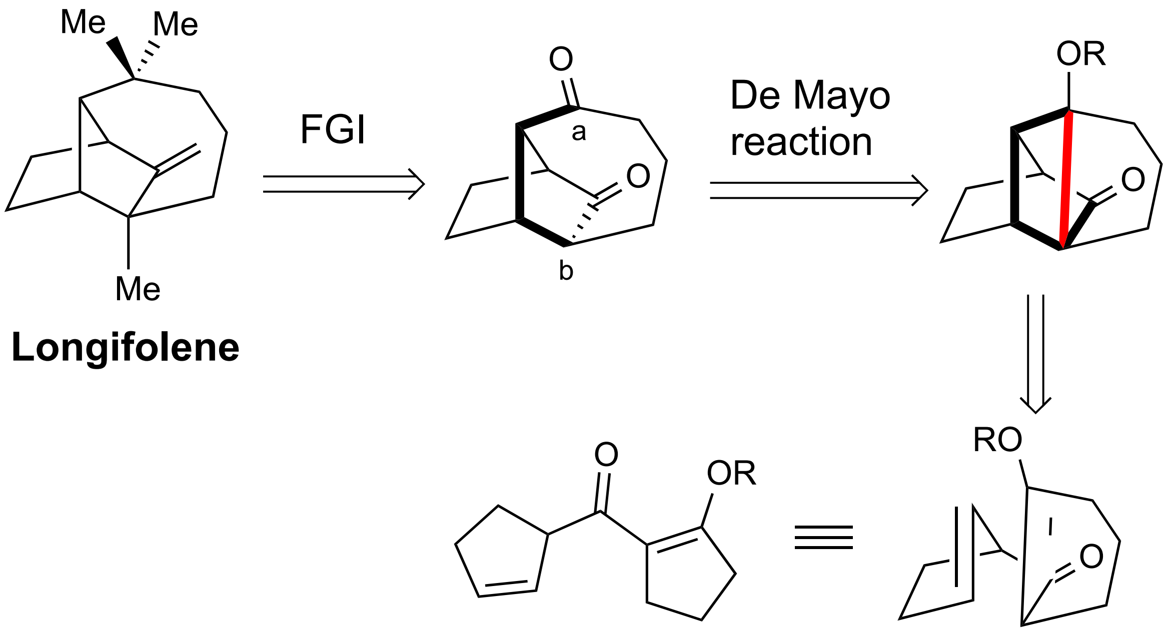
Pattern Recognition: Simple exemples



Oppolzer's Synthesis of Longifolene

De Mayo reaction

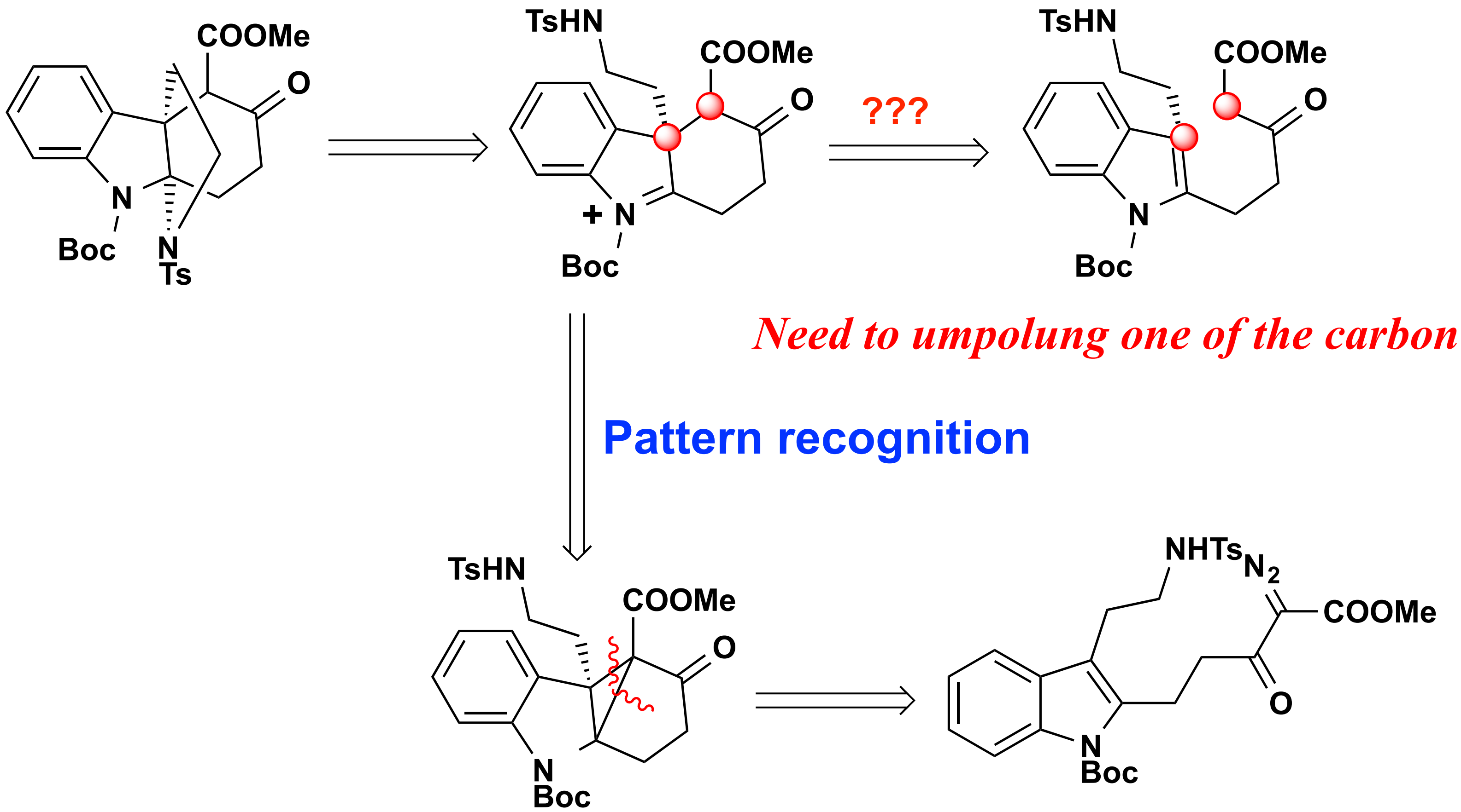




Longifolene

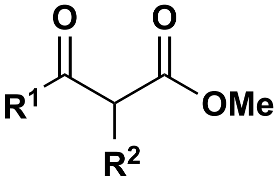
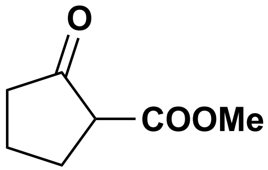
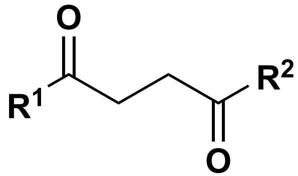
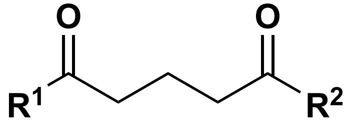
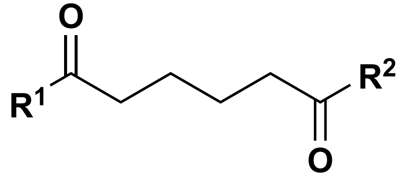
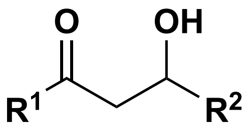
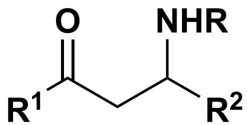
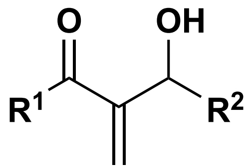
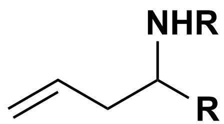
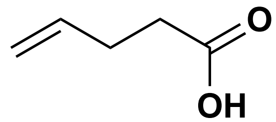
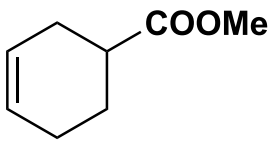
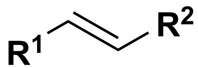
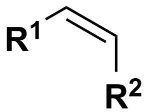
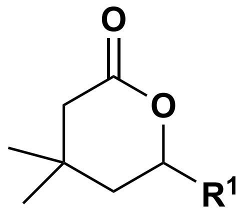
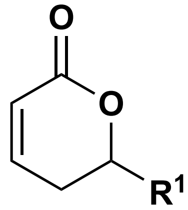
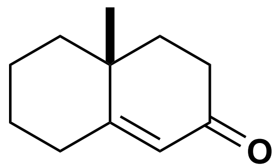
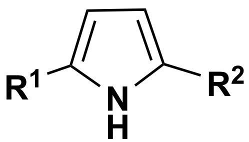
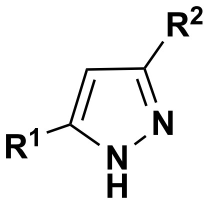
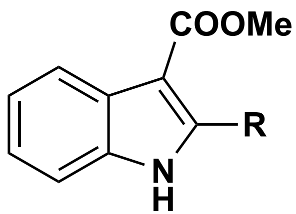
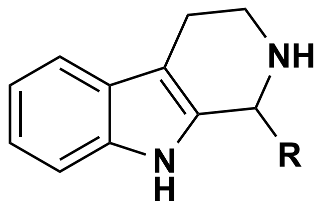
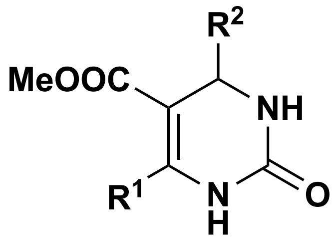
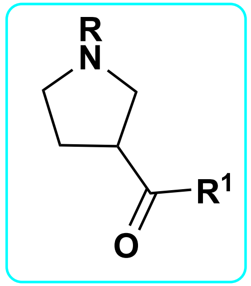
P. de Mayo, *Acc. Chem. Res.*, **1971**, *4*, 41;
W. Oppolzer, *Acc. Chem. Res.*, **1982, *15***, 135

Qin's Synthesis of Minfiensine

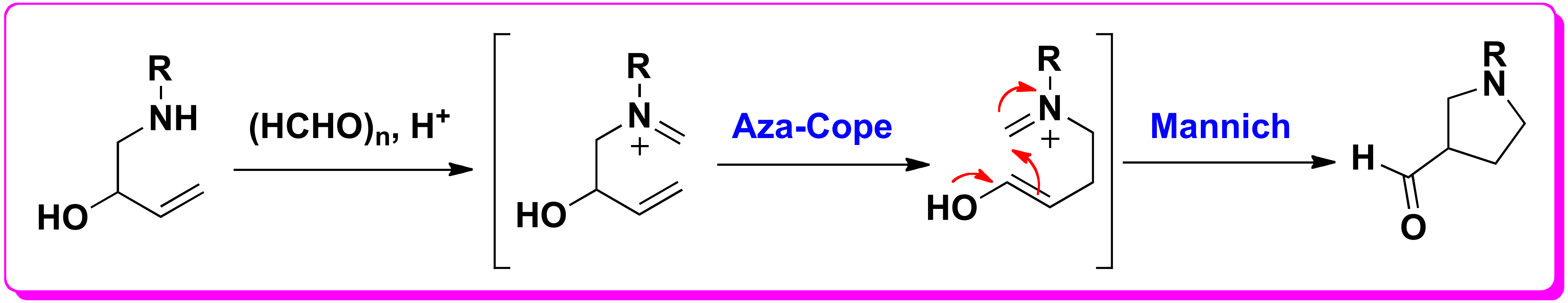


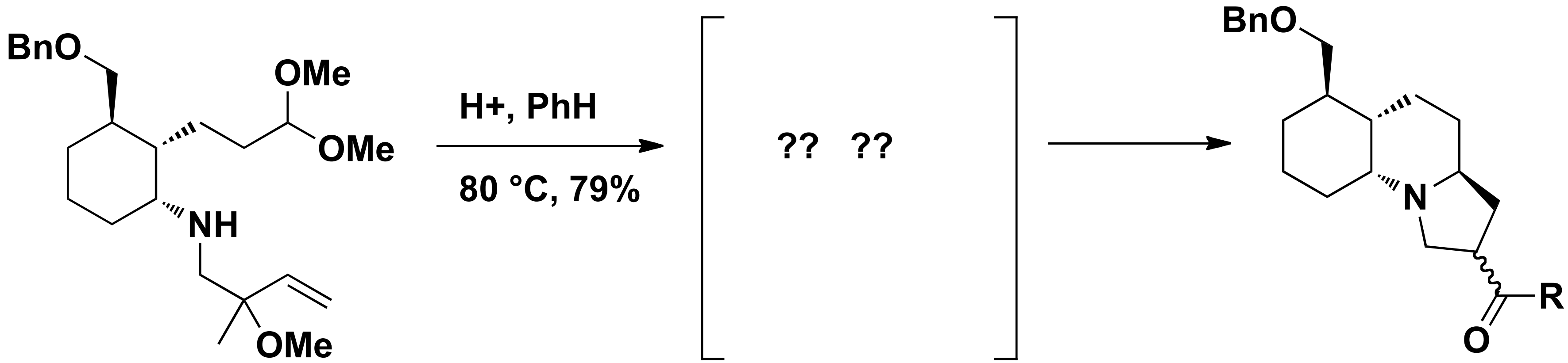
L. Shen, M. Zhang, Y. Wu, Y. Qin, *Angew. Chem. Int. Ed*. **2008**, *47*, 3618-3621.

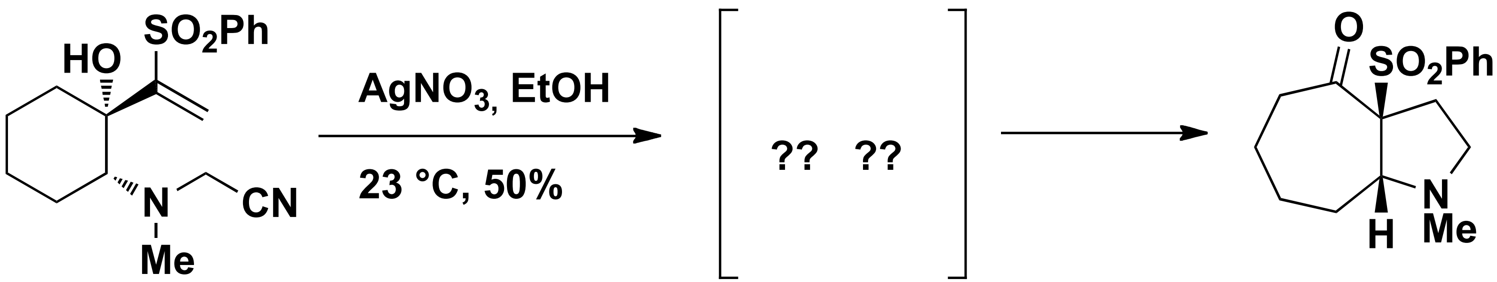
Pattern Recognition: Simple exemples

Basic of Aza-Cope/Mannich

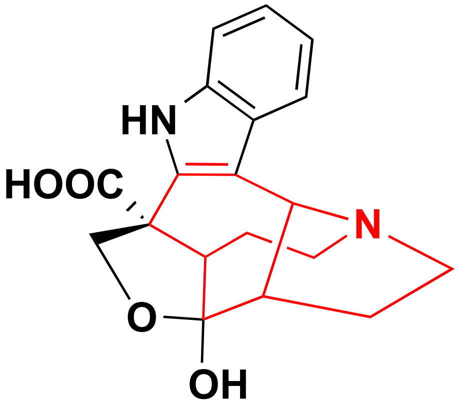




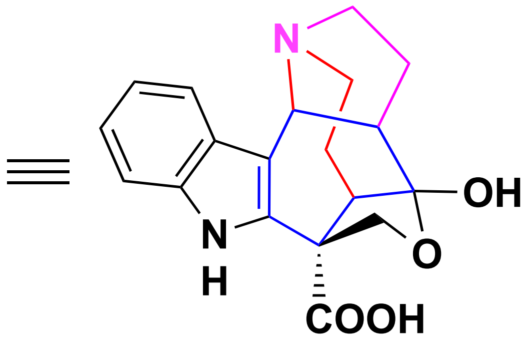


Key Motif: 3-Acyl proline!!!

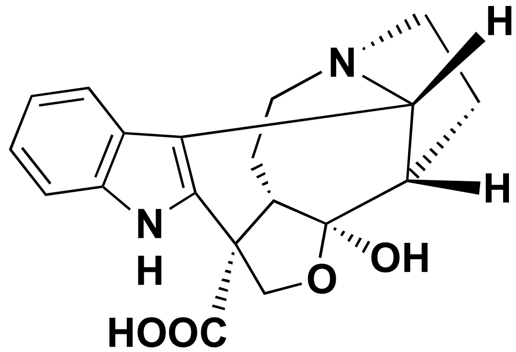
Actinophyllic acid



Actinophyllic acid



Drawing in the isolation paper

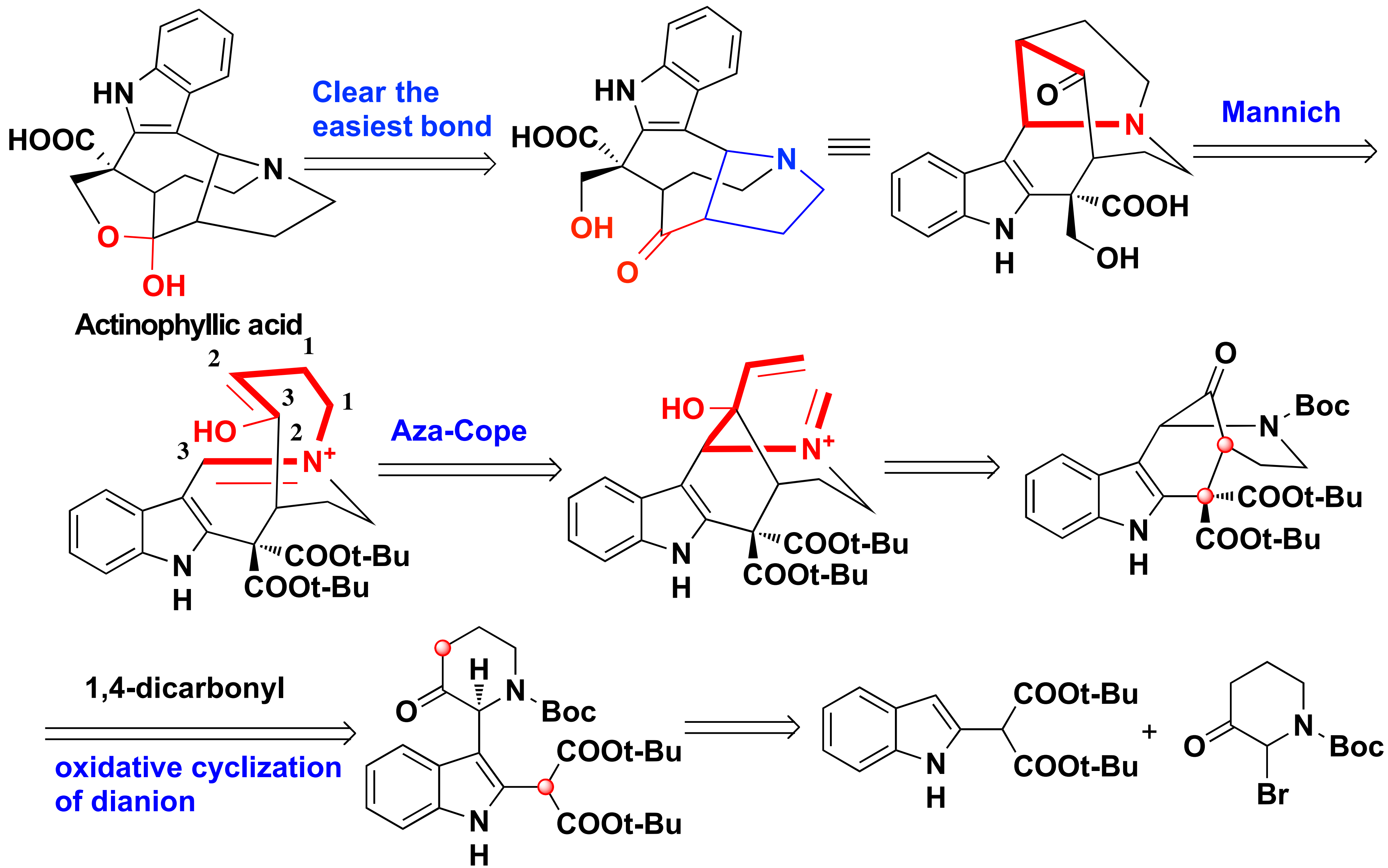


Isolated From *Alstonia actinophylla in 2005*

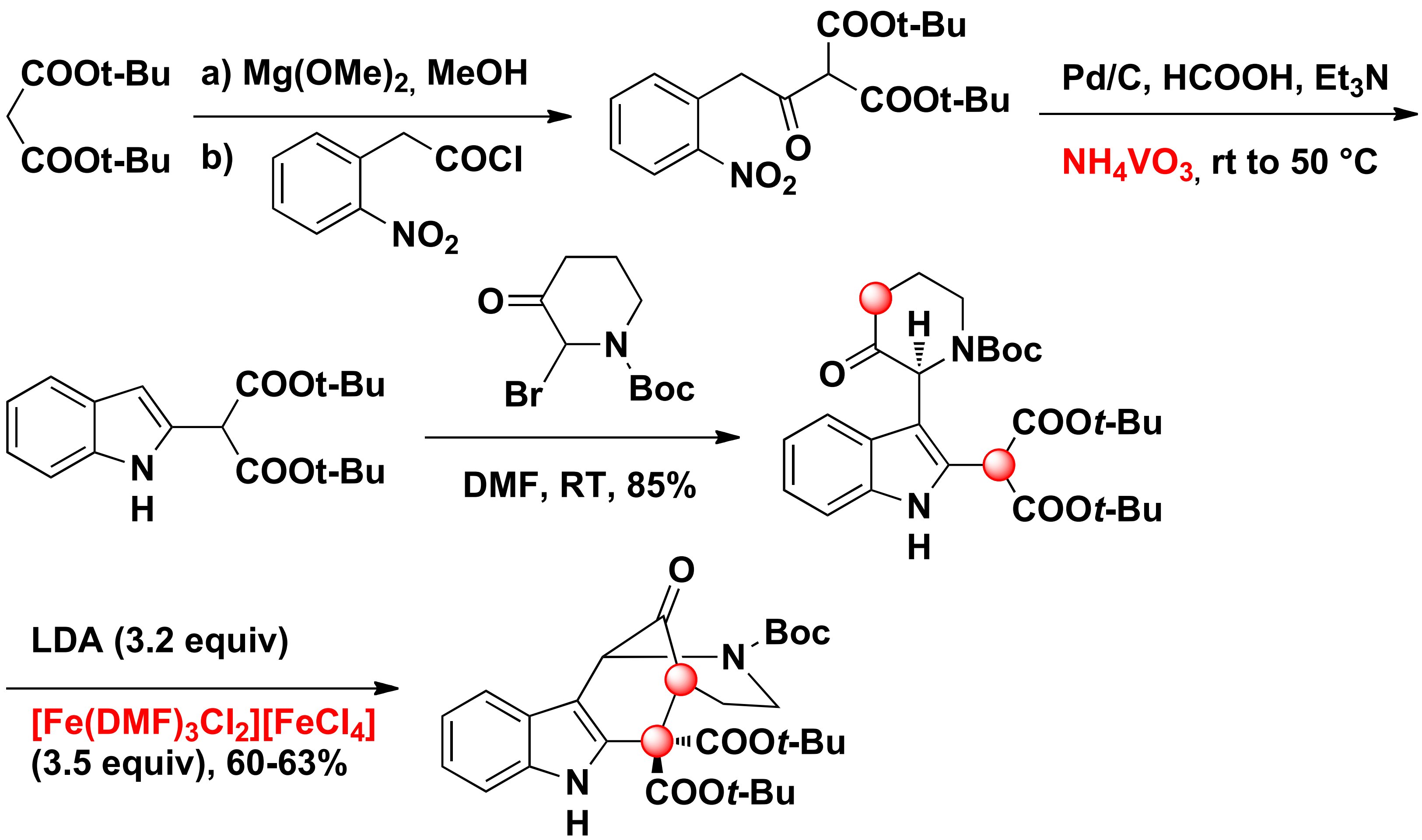
a potent inhibitor in the coupled enzyme assay TAFIa/hippuricase (IC50) 0.84 μM).

A. R. Carroll, E. Hyde, J. Smith, R. J. Quinn, G. Guymer, P. I. Foster, *J. Org. Chem.* **2005**, *70*, 1096–1099.

Overman's Synthesis of Actinophyllic acid



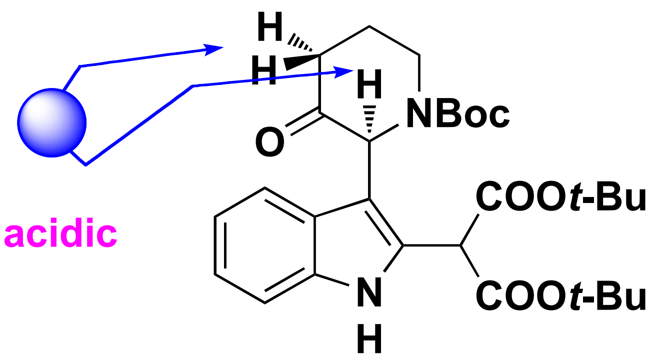
Key Oxidative dienolate cyclization

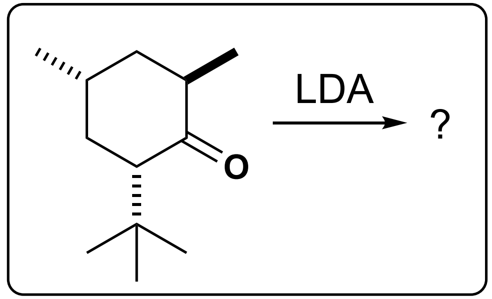


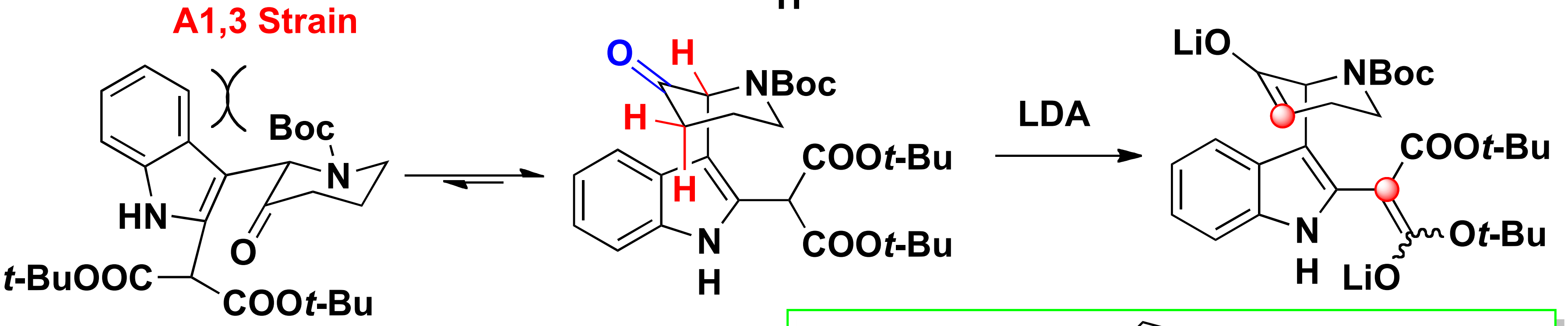
NH_4VO_3: promote the complete reduction of nitro to aniline
$[Fe(DMF)_3Cl_2][FeCl_4]$: easily prepared by dissolving $FeCl_3$ in DMF,
Diffferent bases and oxidants were tested, LDA and $[Fe(DMF)_3Cl_2][FeCl_4]$ turned out to be the best combination.

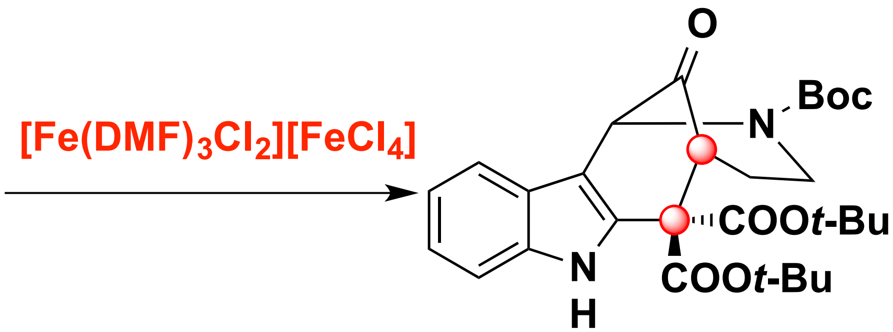
Key Oxidative Dienolate Cyclization—Regioselectivity

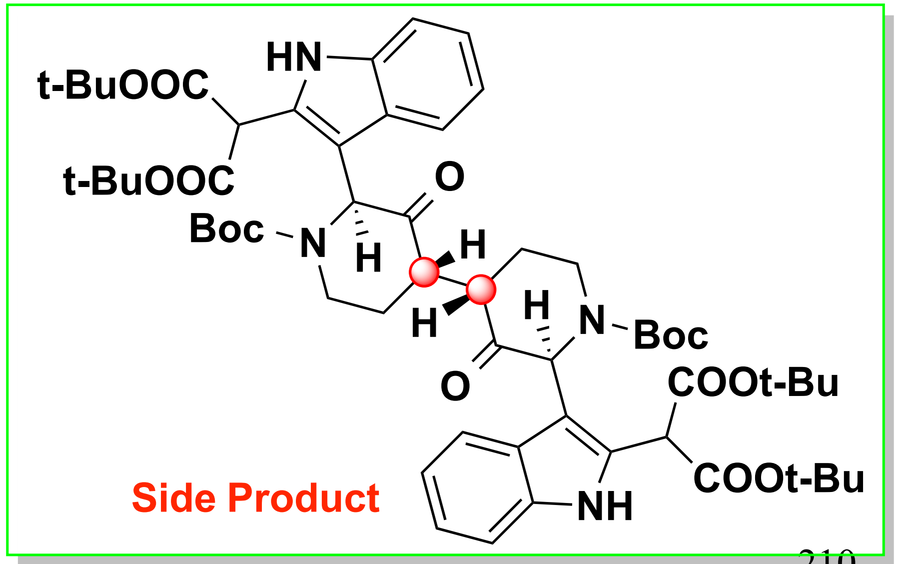
Which protons are more acidic





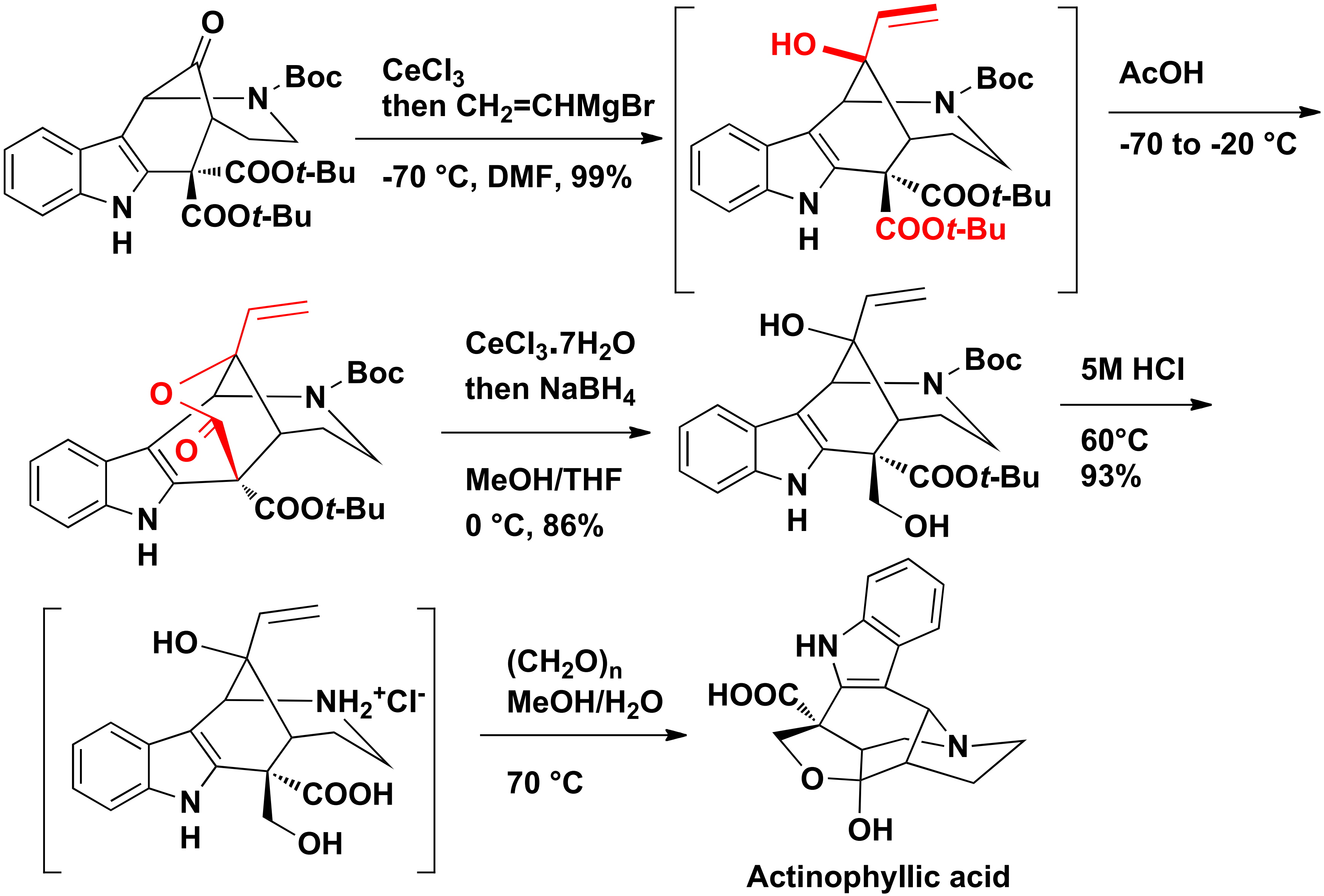






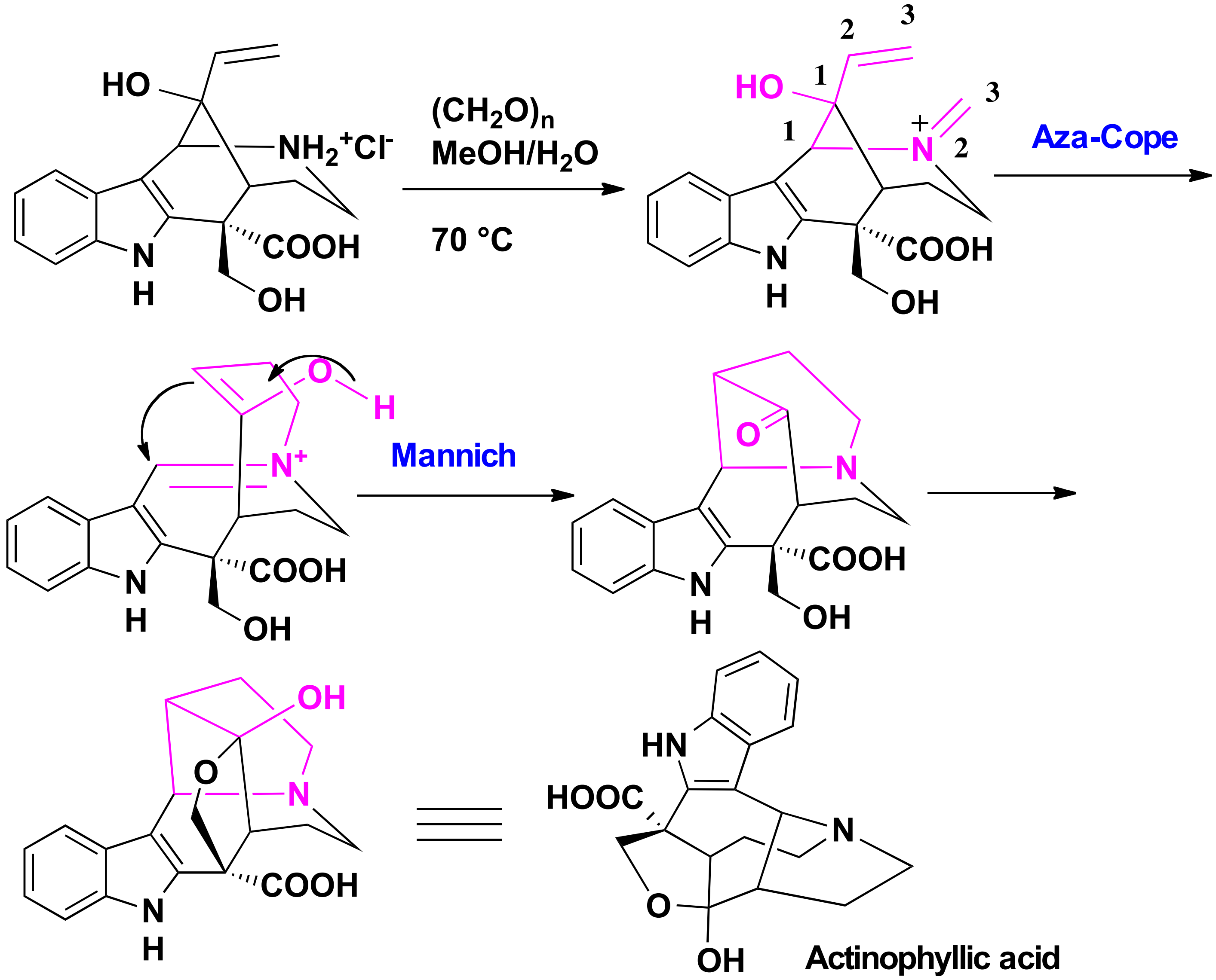
Side Product:
decreased as concentration of rxn mixture increased, Unusual !!!

Overman's Synthesis of Actinophyllic acid: Endgame



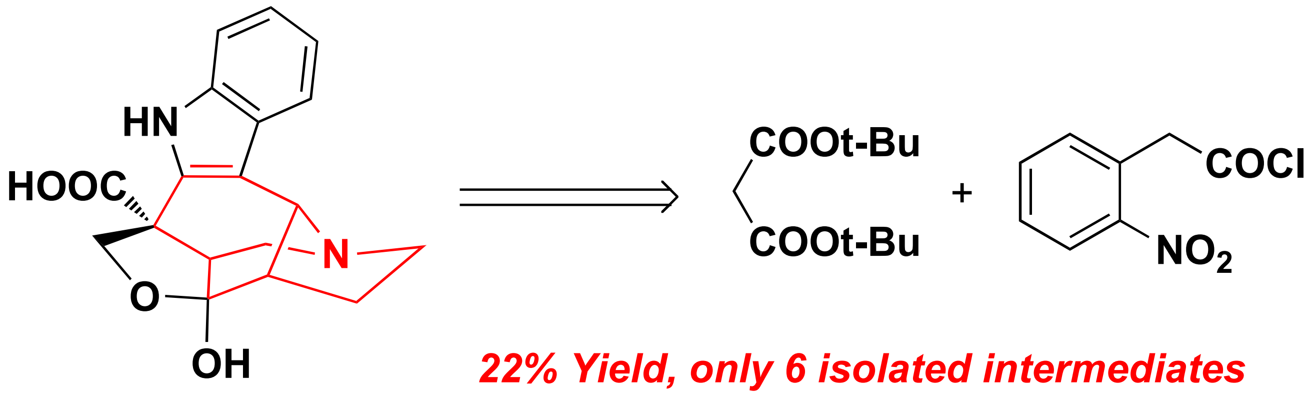
C. L. Martin, L. E. Overman, J. M. Rohde, *J. Am. Chem. Soc.* **2010**, *132*, 4894-4906.

Aza-Cope/Mannich: Pathway



C. L. Martin, L. E. Overman, J. M. Rohde, *J. Am. Chem. Soc.* **2010**, *132*, 4894-4906.

Actinophyllic acid: Summary



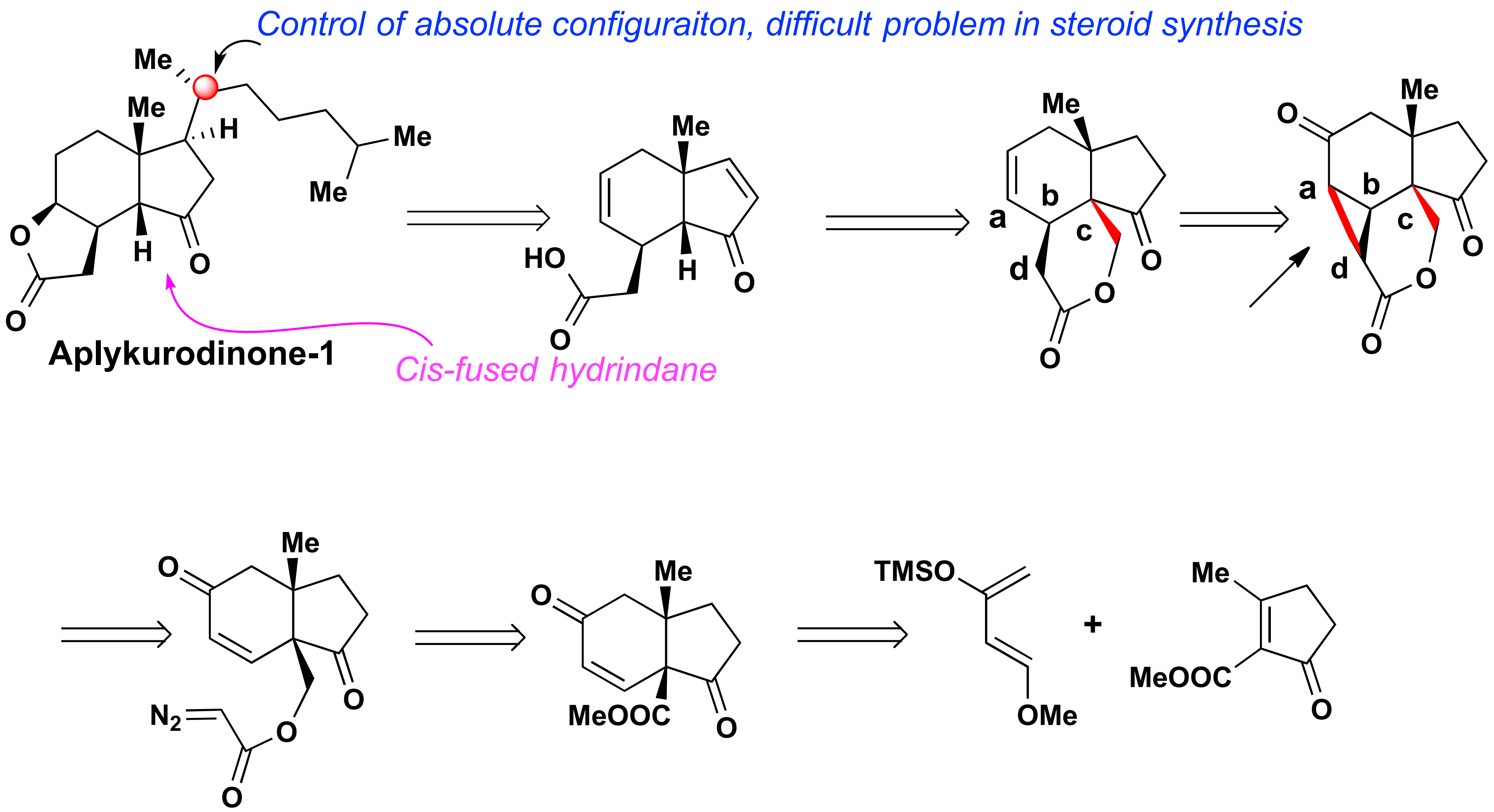
22% Yield, only 6 isolated intermediates

Key steps:

a) Intramolecular oxidative cyclization of dienolate
b) Domino Aza-Cope/Mannich sequence
c) Conformation Analysis

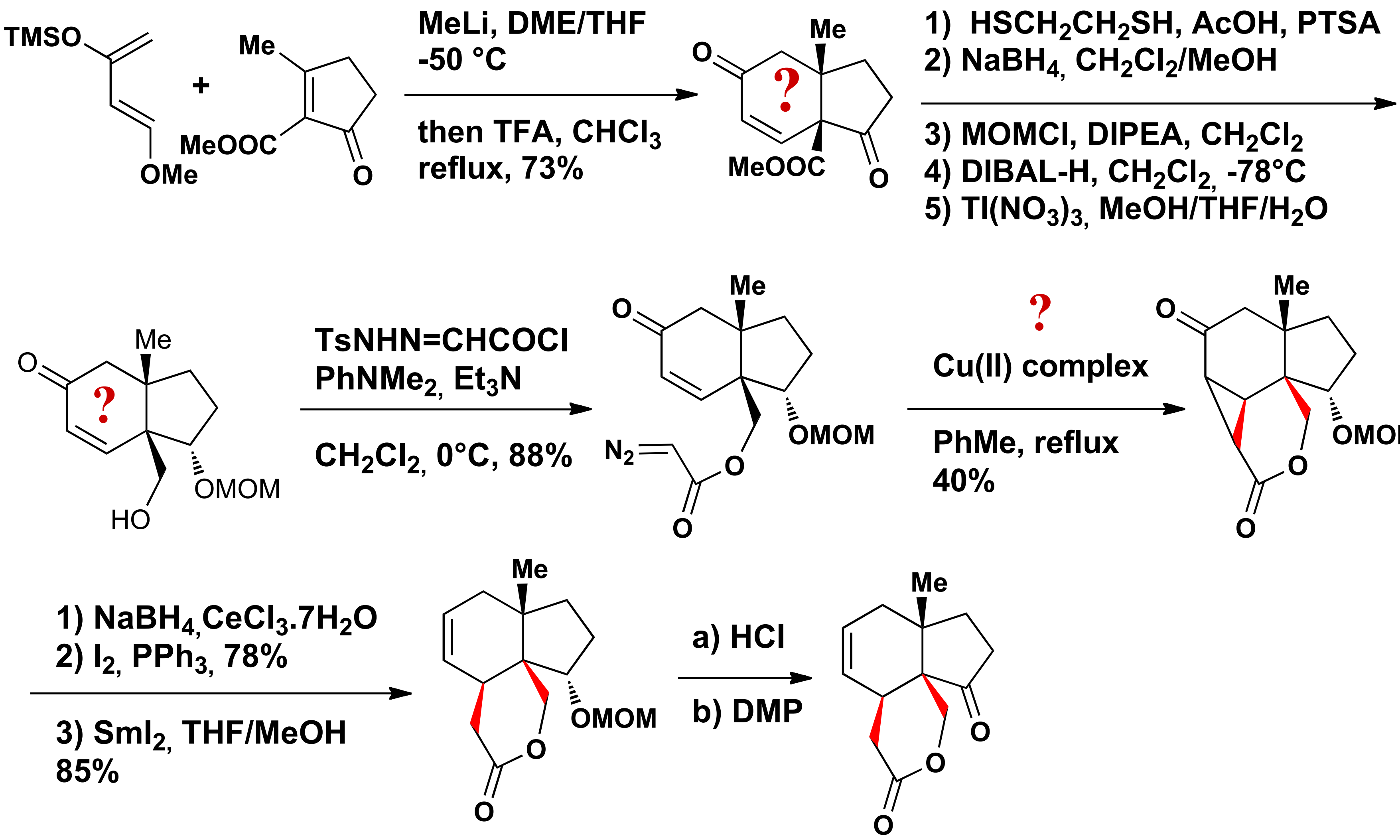
C. L. Martin, L. E. Overman, J. M. Rohde, *J. Am. Chem. Soc*. **2010**, *132*, 4894-4906.

Danishefsky's Retro Synthesis of Aplykurodinone



Y. Zhang, S. J. Danishefsky, *J. Am. Chem. Soc.* **2010**, *132*, 9567-9569.

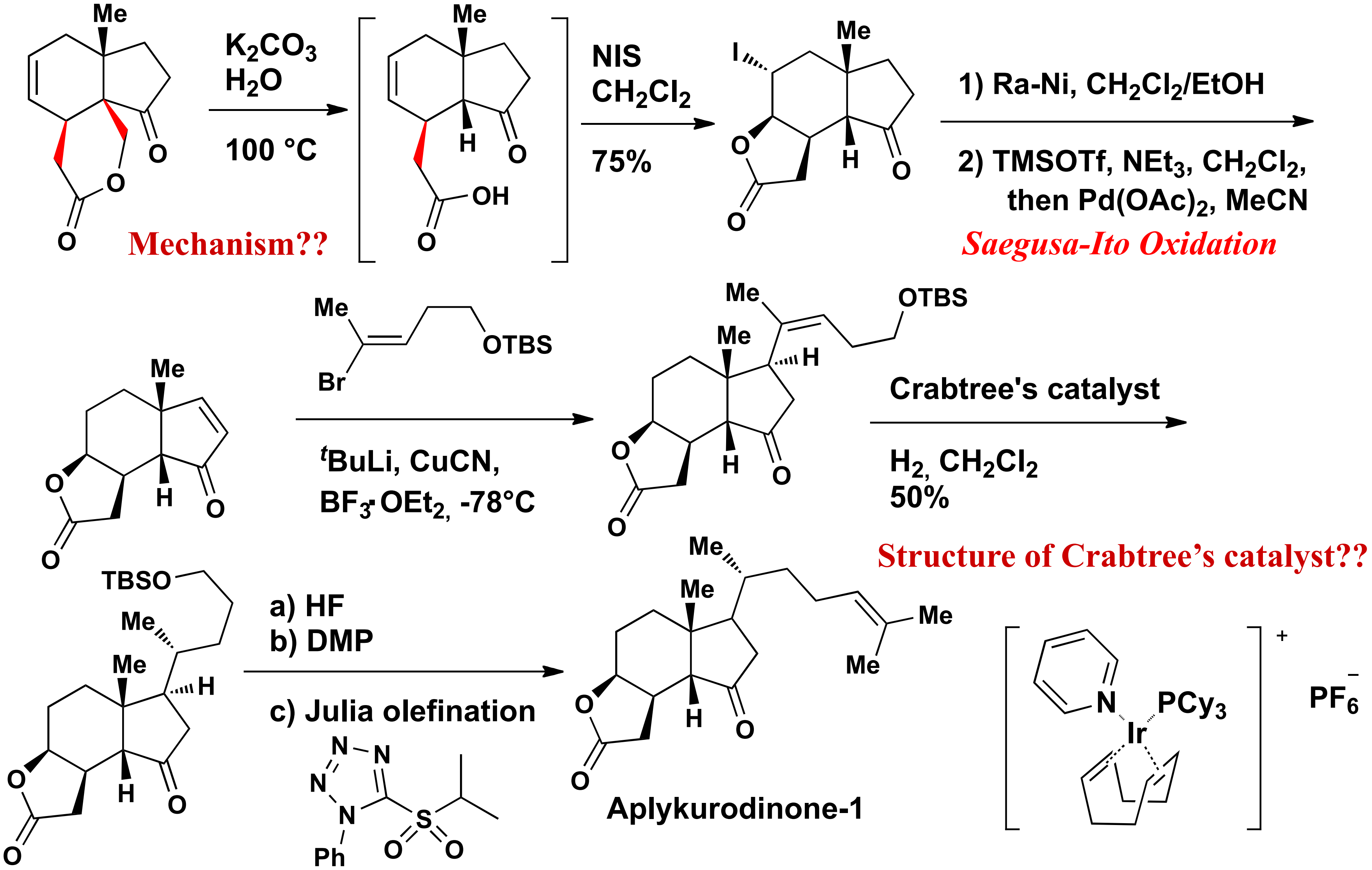
Danishefsky's Synthesis-1



Structure of intermediate

Appel reaction
Mitsunobu reaction

Traceless Stereochemical guidance



Julia olefination; Julia-Kocienski olefination

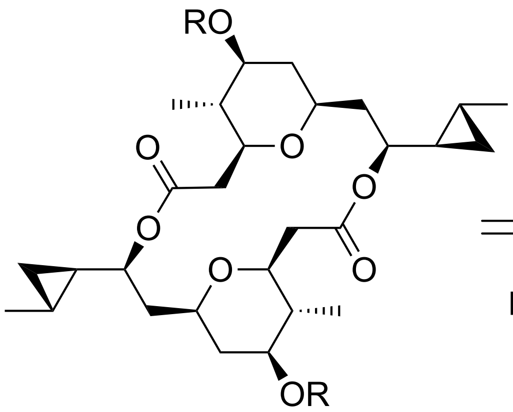
Y. Zhang, S. J. Danishefsky, *J. Am. Chem. Soc*. **2010**, *132*, 9567-9569.

Summary of Danishefsky's Synthesis of Aplykurodinone

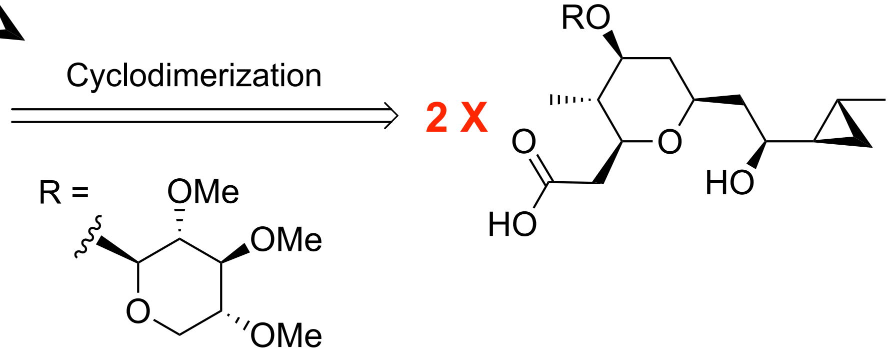
1) Diels-Alder reaction under basic conditions
2) Intramolecular cyclopropanation
3) Retro-aldol
4) Iodolactonization
5) 1,4-Addition of cuprate to enone
6) Julia reaction, Julia-Kocienski Reaction

Symmetry in Natural Products

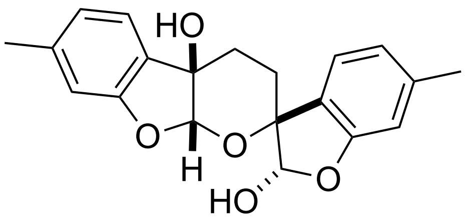
Obvisous symmetry

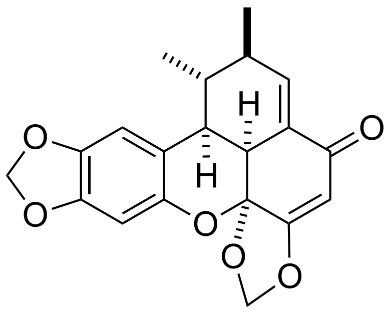


Clavosolide A



Hidden symmetry:





Propose reasonable synthetic routes for the above two natural products by exploiting the hidden symmetry of the targets.