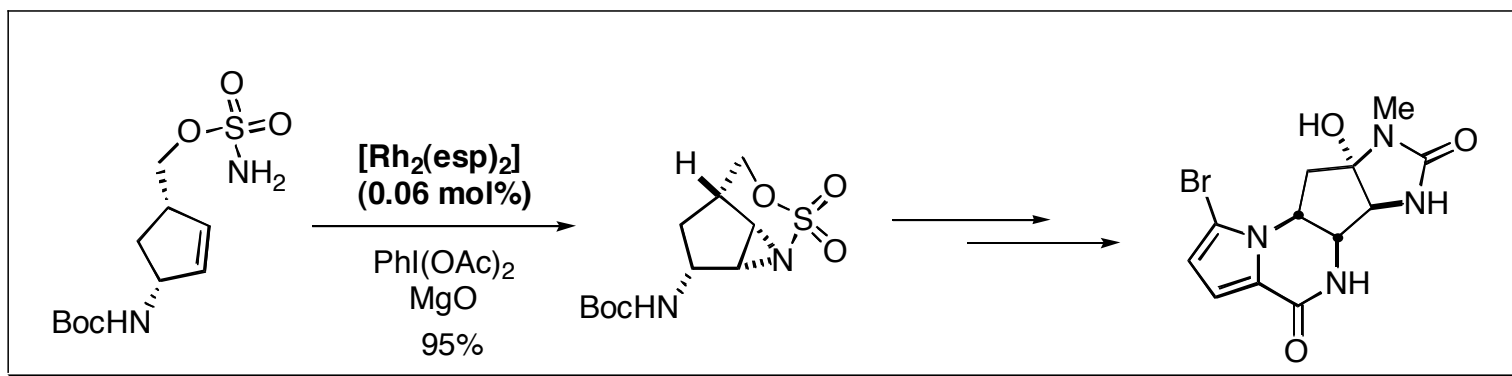


A Stereoselective Synthesis of the Bromopyrrole Natural Product (-)-Agelastatin A

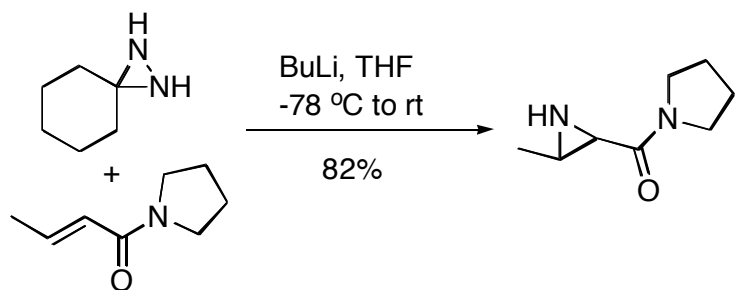
Paul M. When and J. Du Bois, *Angew. Chem. Int. Ed.* **2009**, *48*, 3802-3805.



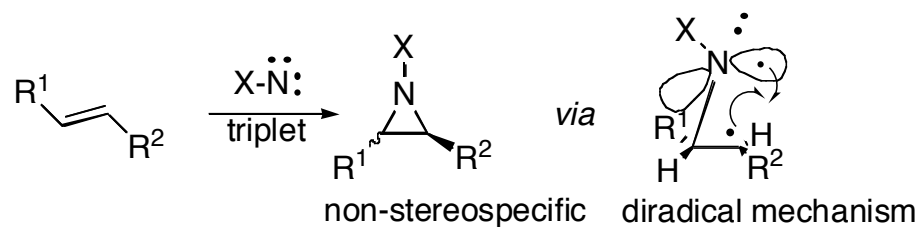
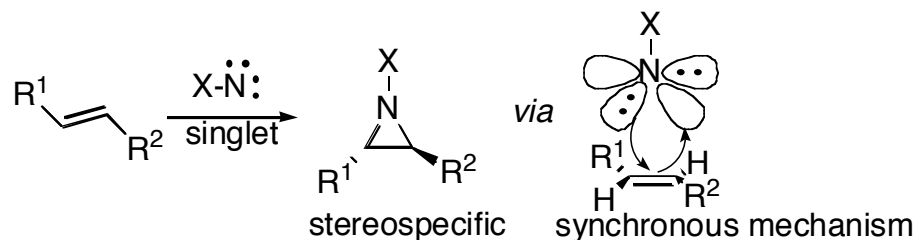
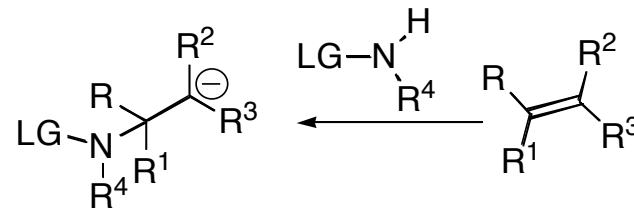
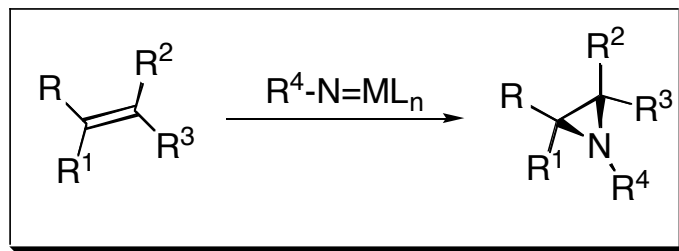
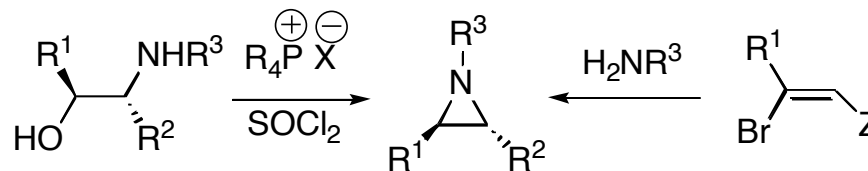
Melissa Sprachman

Current Literature: May 23, 2009

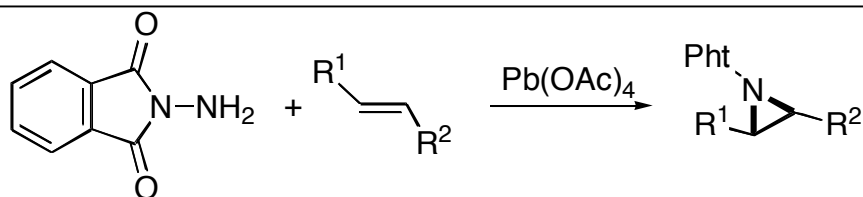
Aziridines: General Methods



Tetrahedron Lett. **1999**, *40*, 5207-5210.



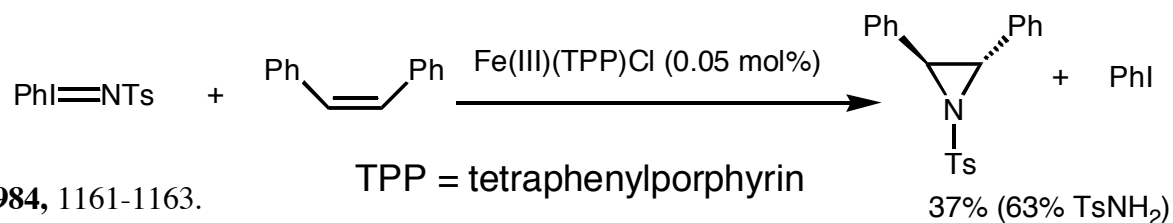
Aziridines and Epoxides in Organic Synthesis; Yudin, A. K. ed.; Wiley-VCH:Weinheim, 2006.



J. Chem. Soc. (C), **1970**, 576-582.

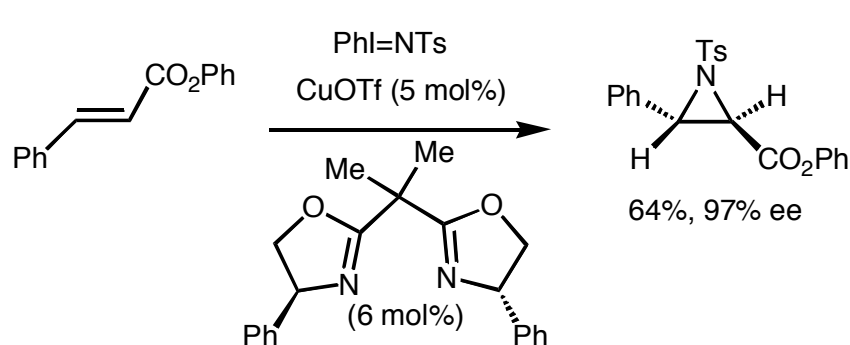
Synthesis of Aziridines via Metal-Catalyzed Nitrene Addition

Aziridation Using TsN=IPh:

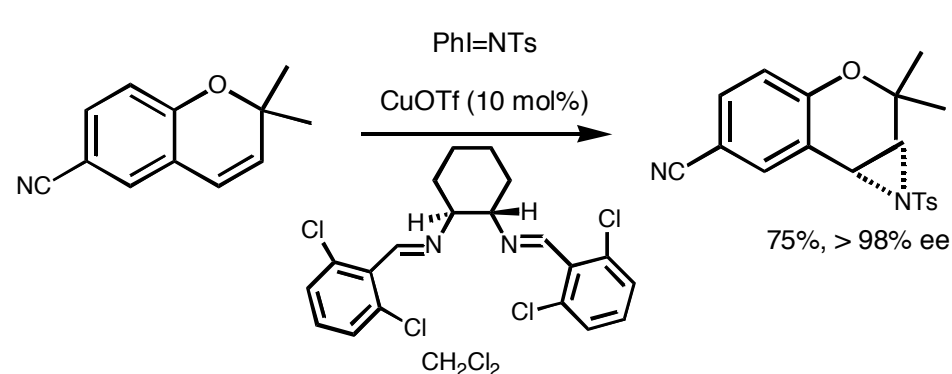


J. Chem. Soc., Chem. Commun. **1984**, 1161-1163.

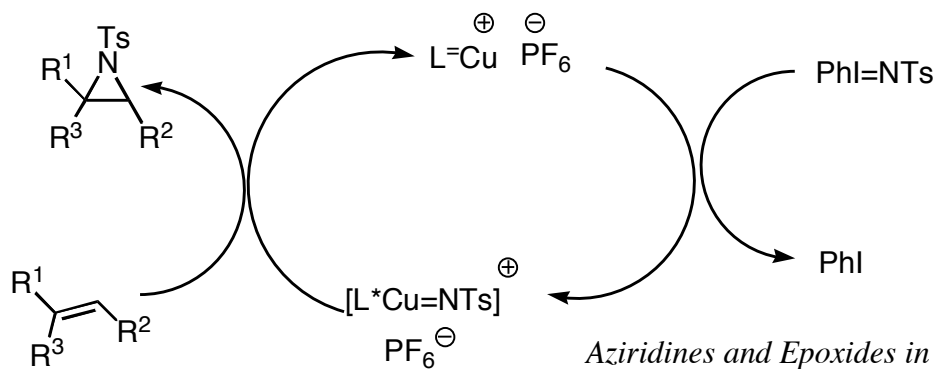
Evans and Jacobsen: Enantioselective aziridination using chiral Cu catalysts:



J. Am. Chem. Soc. **1993**, 115, 5328-5329.

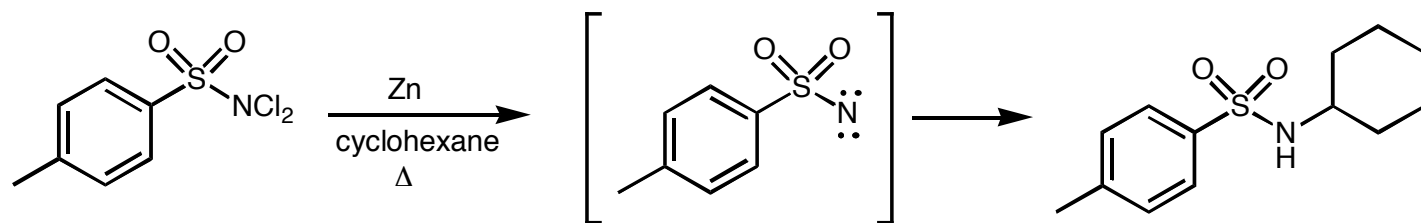


J. Am. Chem. Soc. **1993**, 115, 5326-5327.

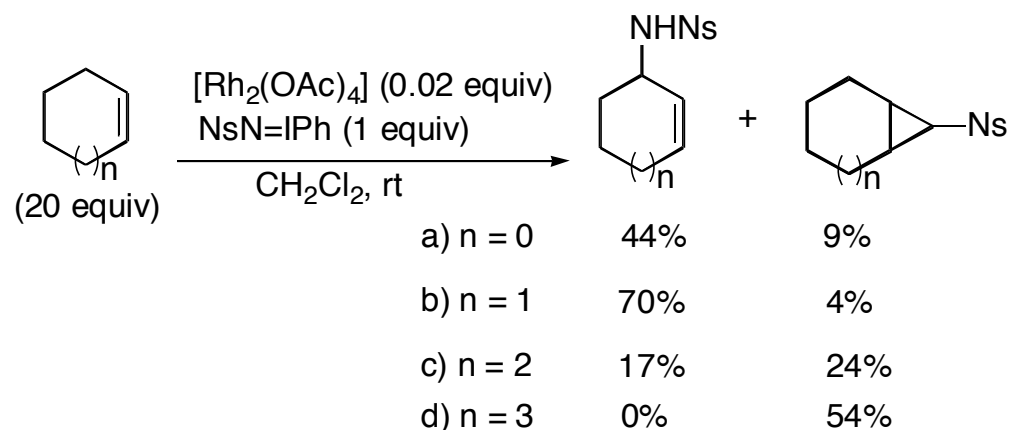


Aziridines and Epoxides in Organic Synthesis; Yudin, A. K. ed.; Wiley-VCH:Weinheim, 2006.

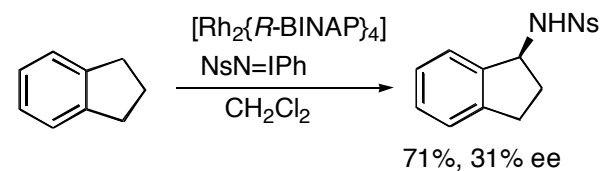
Rh-catalyzed Aziridination was developed in tandem with C-H amination



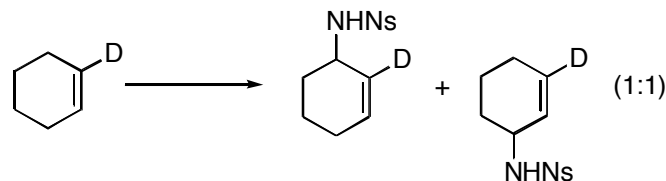
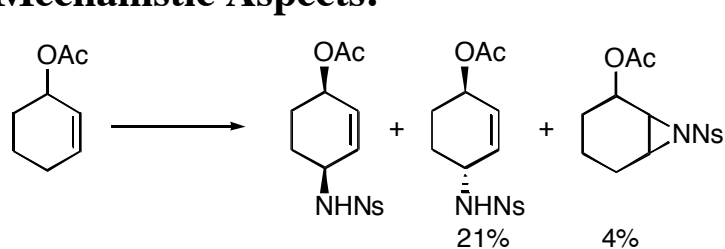
Tetrahedron Lett. **1968**, 5349-5352.



Preliminary hope for enantioselective insertion:



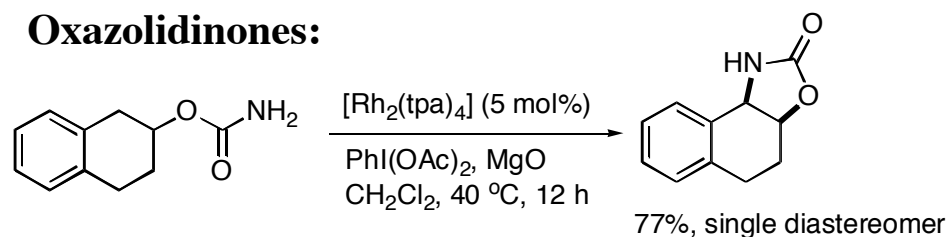
Mechanistic Aspects:



Helvetica Chim. Acta, **1997**, 80, 1087-1105.

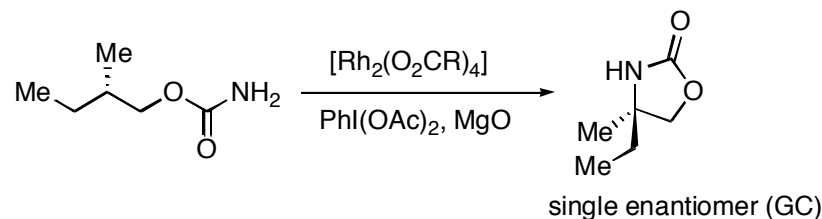
Du Bois Group Contributions: Early Developments and Mechanistic Considerations

Conversion of Carbamates to Oxazolidinones:

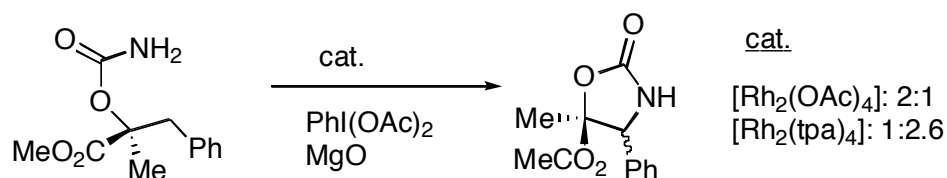


tpa = triphenylacetate

Evidence for direct insertion:

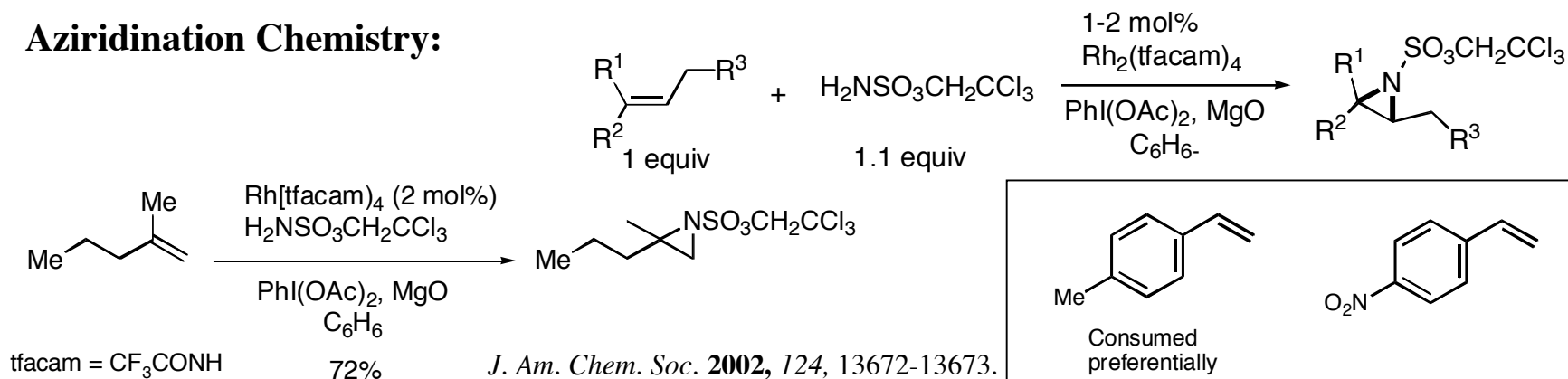


Evidence for a metallo-nitrene:



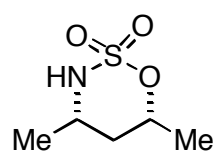
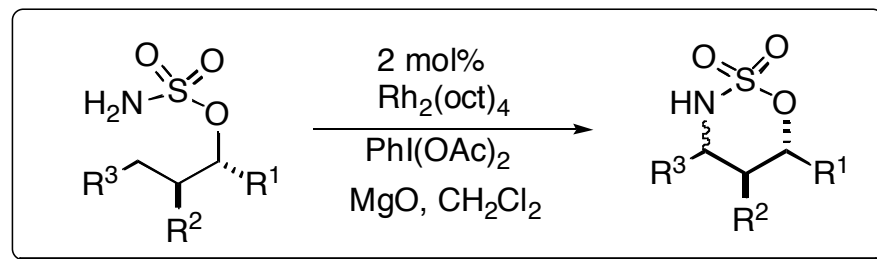
Angew. Chem. Int. Ed. **2001**, *40*, 598-560.

Aziridination Chemistry:

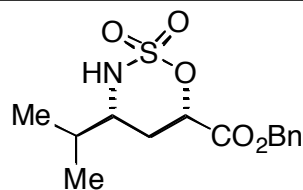


For related work using Cu and PhIO, see *J. Am. Chem. Soc.* **2001**, *123*, 7707-7708 and *Org. Lett.*, **2002**, *4*, 2481-3..

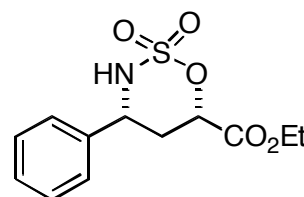
Rh-Catalyzed Amination Reactions of Chiral Sulfamates



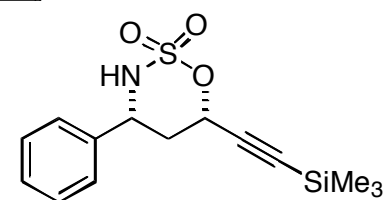
88%, 3:1 dr



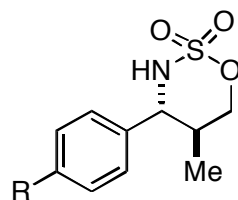
55%, 8:1 dr



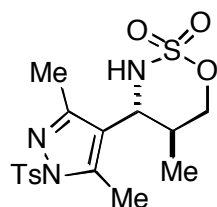
91%, 15:1 dr



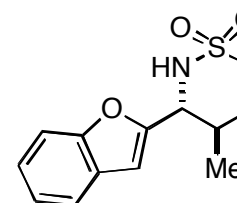
62%, 20:1 dr



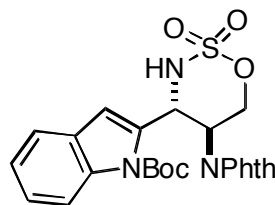
R = CF₃, 70%, 20:1 dr
R = OMe, 85%, 20:1 dr



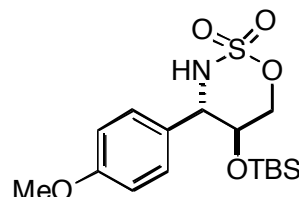
84%, 20:1 dr



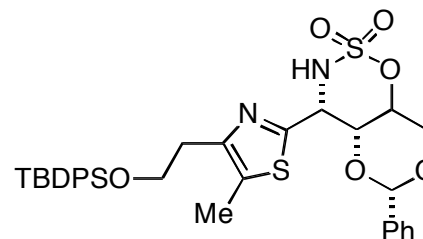
65%, 20:1 dr



85%, 12:1 dr



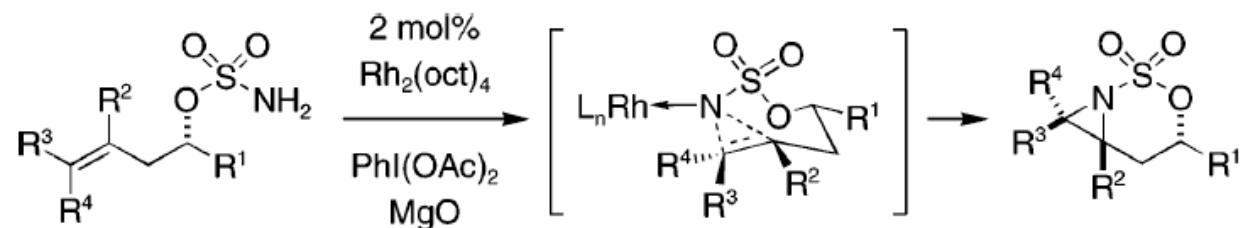
77%, 10:1 dr



92%, 20:1 dr

Org. Lett. **2003**, *5*, 4823-4826.

Aziridination Chemistry

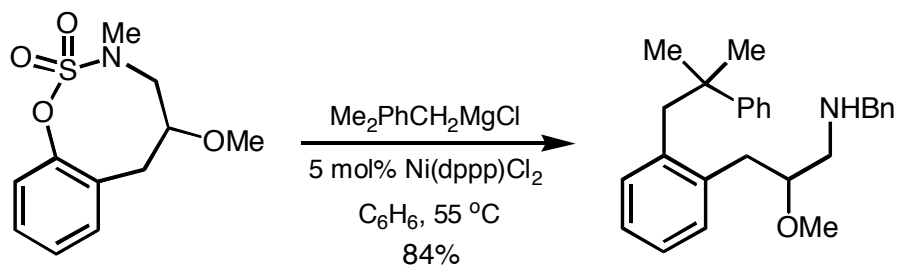
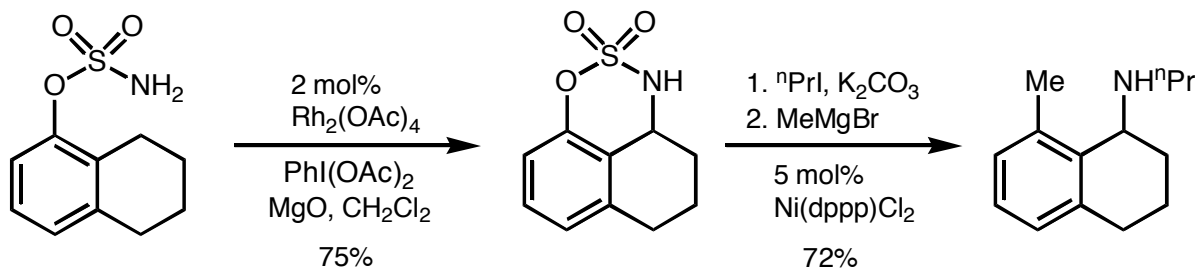


entry	substrate	major product	selectivity ^a	yield ^b
1			4:1	84
2			4:1	92
3			2.5:1	88
4			10:1	84

Org. Lett. **2003**, *5*, 4823-4826.

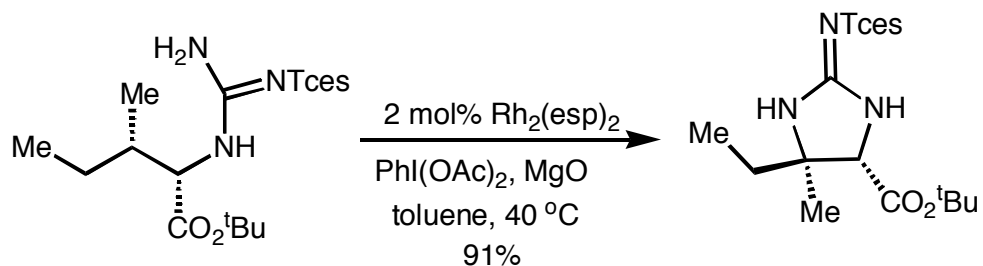
Extensions of Rh-Catalyzed Amination Reactions

Ni-catalyzed cross-coupling of cyclic sulfamates:

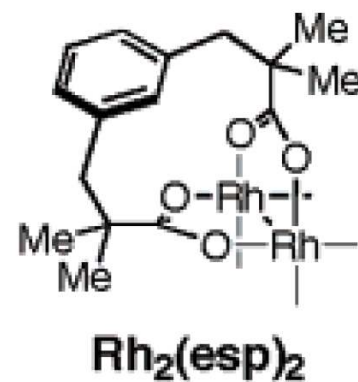


Org. Lett. **2005**, 7, 4685-4688.

Oxidative Cyclization of Urea and Guanidine Derivatives:

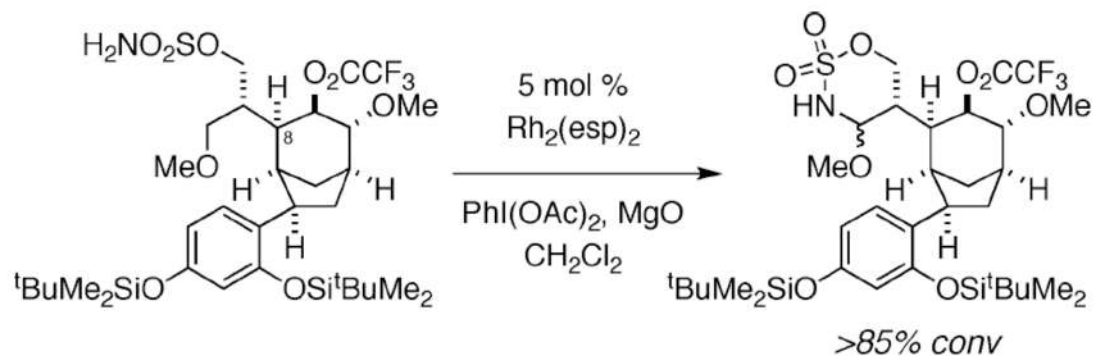
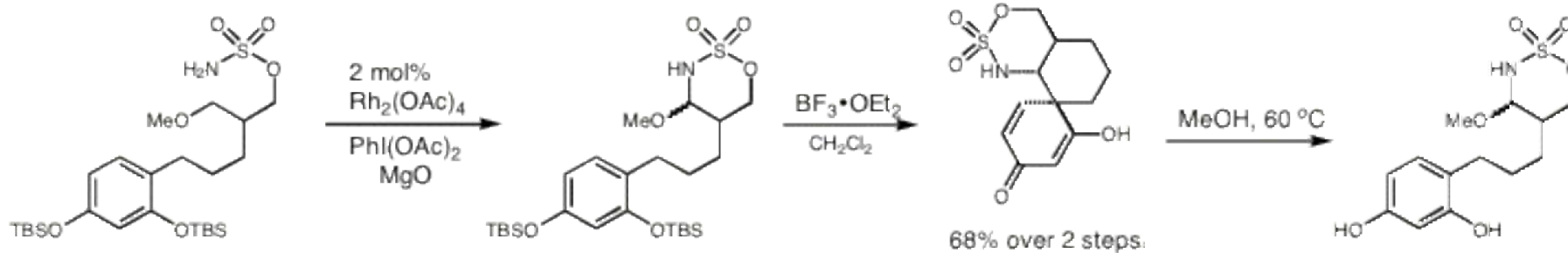
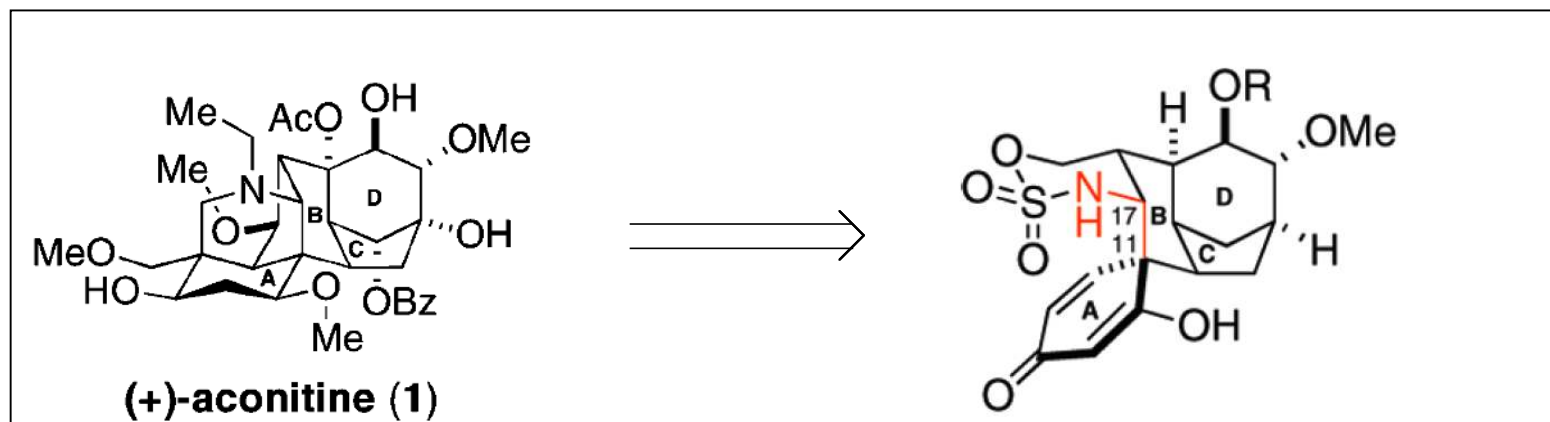


Org. Lett. **2006**, 8, 1073-1076.



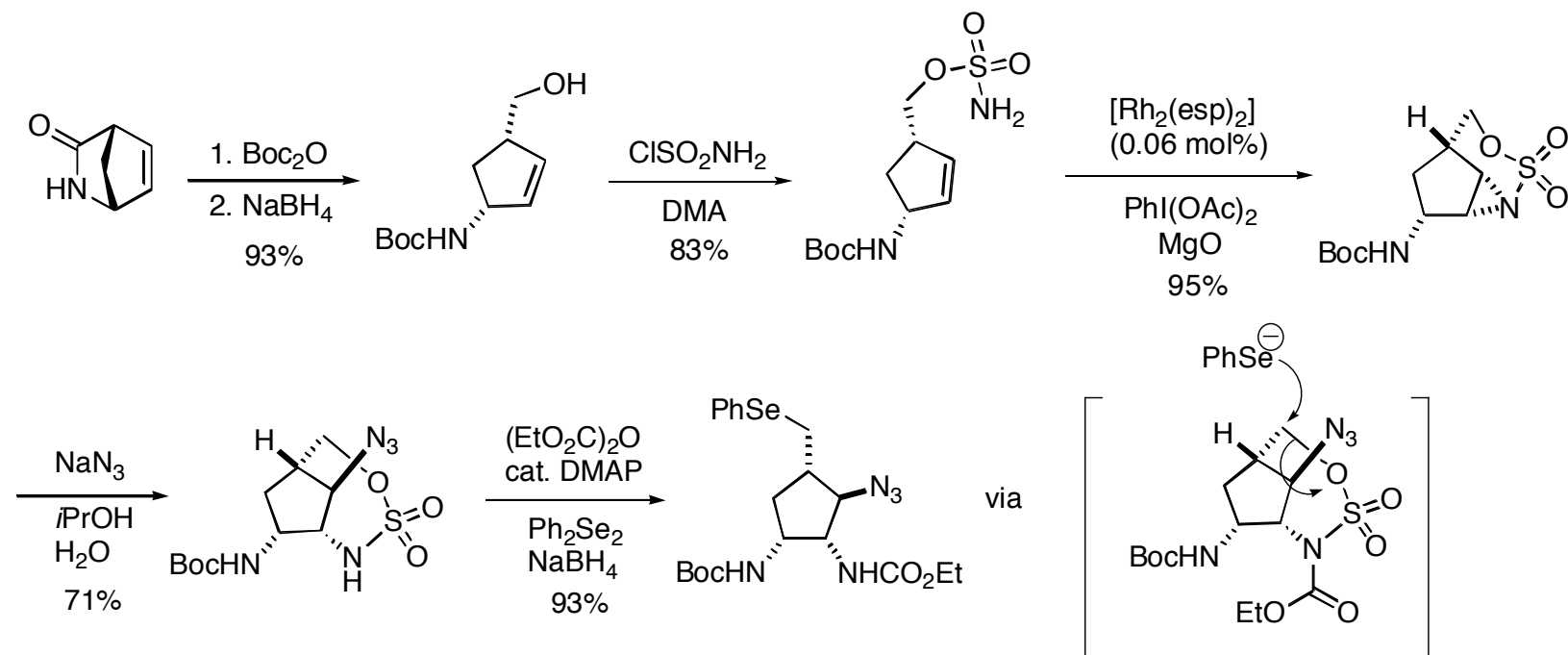
$\text{Rh}_2(\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,3-benzenedipropionate) $_2$

C-H Amination as an Application in Complex Molecule Synthesis

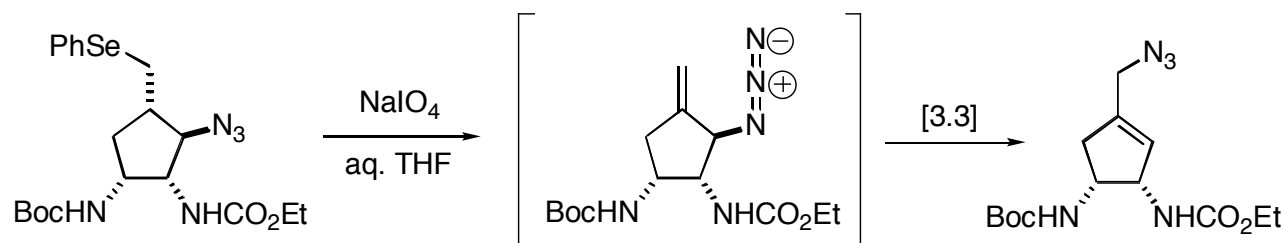


Org. Lett. **2007**, *9*, 5465-5468.

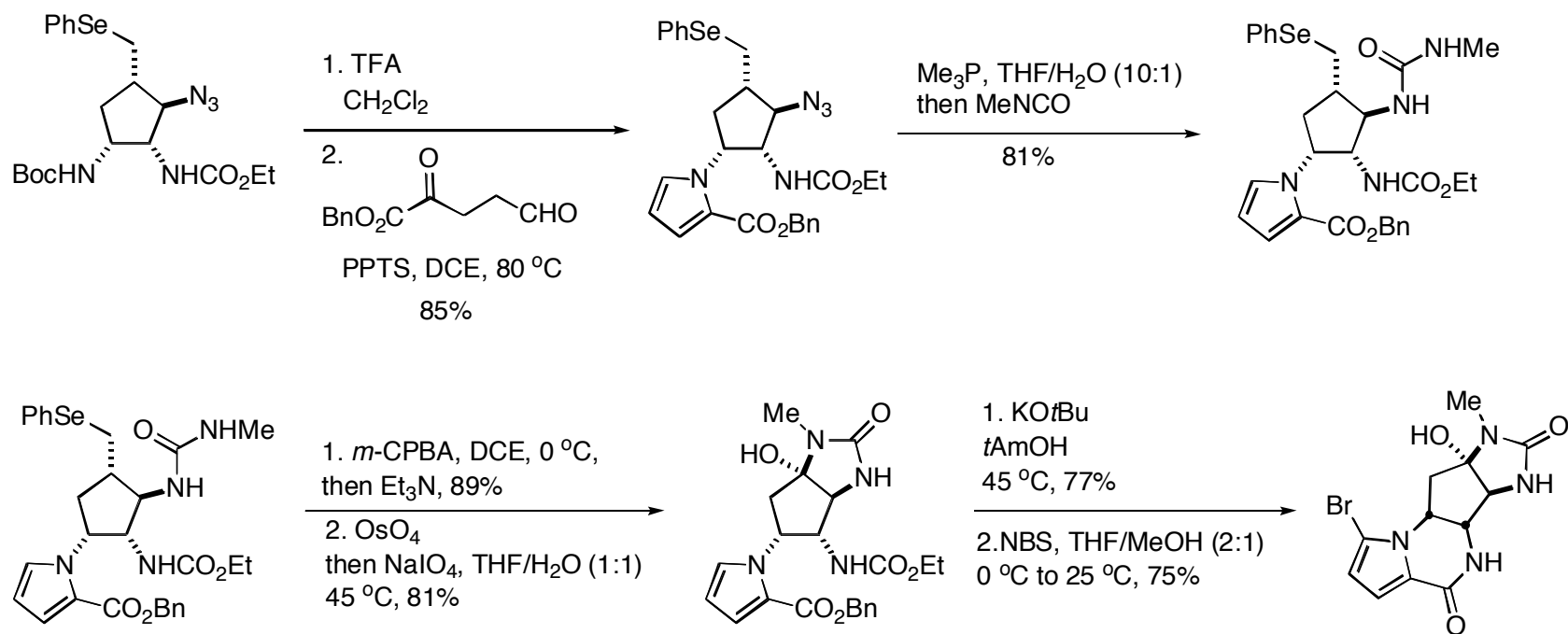
Synthesis of (-)-Agelastatin A



Problem with installation of the exocyclic olefin at this stage:

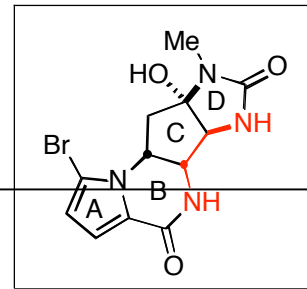


Synthesis of (-)-Agelastatin A

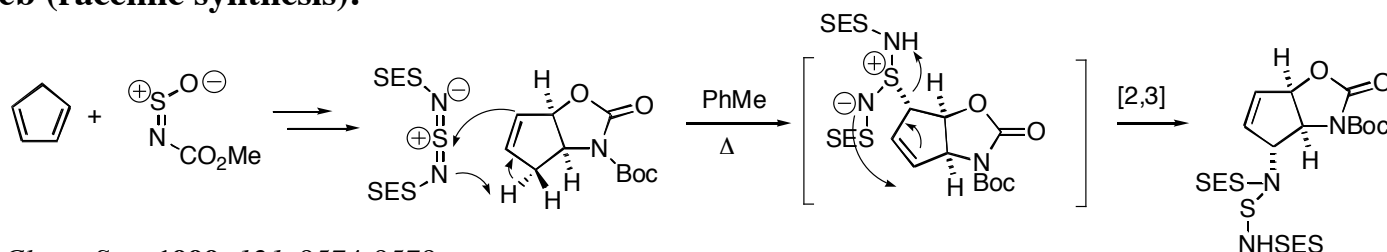


11 Steps, 15% overall yield (200 mg of natural product synthesized)

Other Routes to (-)-Agelastin A: A Comparison

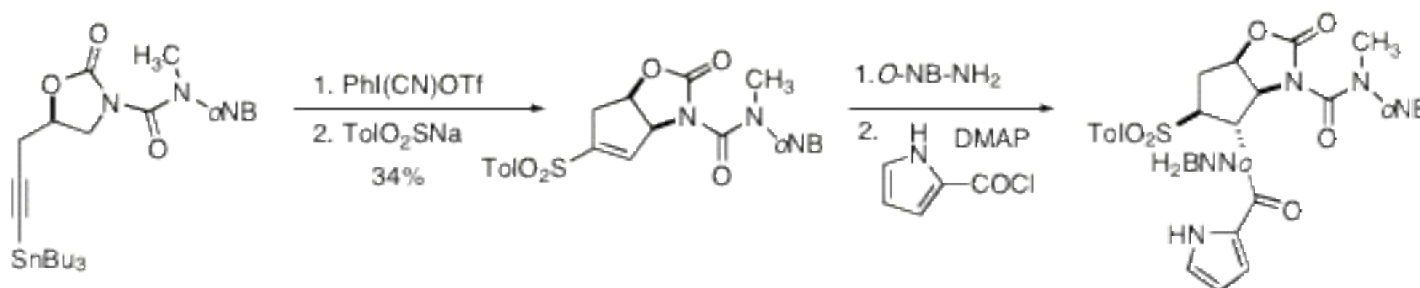


Weinreb (racemic synthesis):



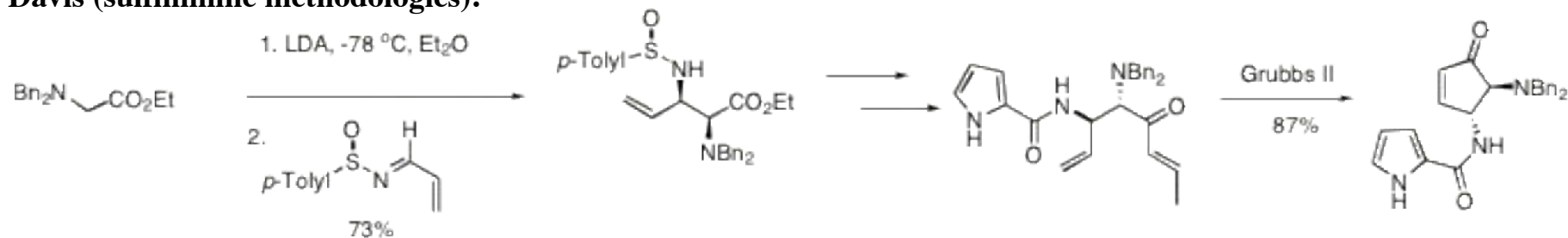
J. Am. Chem. Soc. **1999**, *121*, 9574-9579.

Feldman (via alkynylidonium salts):

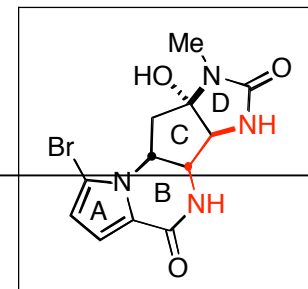


J. Org. Chem. **2002**, *67*, 7096-7109.

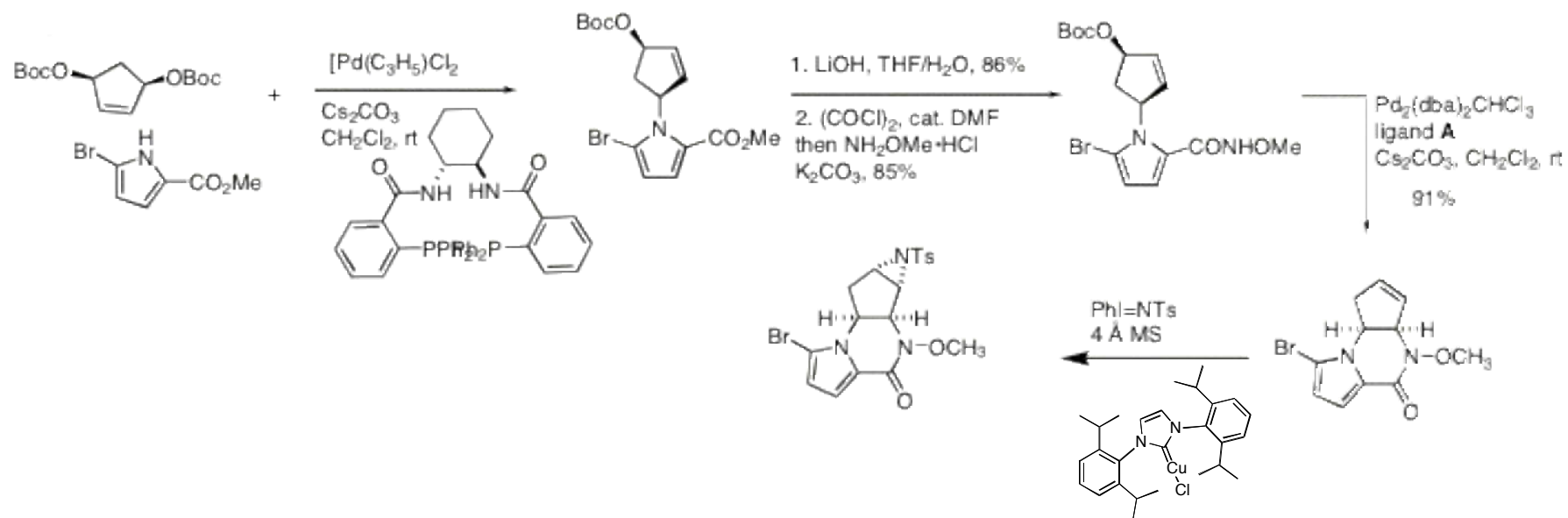
Davis (sulfinimine methodologies):



Other Routes to (-)-Agelastin A: A Comparison



Trost (Pd-catalyzed asymmetric allylic alkylation):



J. Am. Chem. Soc. **2006**, *128*, 6054-6055.

Summary and Outlook

-Rh-catalyzed selective C-H amination and olefin aziridination methods have been developed as useful tools for synthesis.

-Du Bois and co-workers have demonstrated the utility of their aziridination methodology through installation of a critical chiral C-N bond in the synthesis of (-)-Agelastatin A.