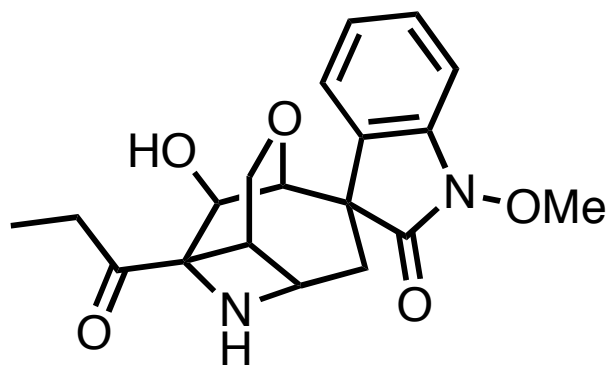


Total Synthesis of Gelsemoxonine

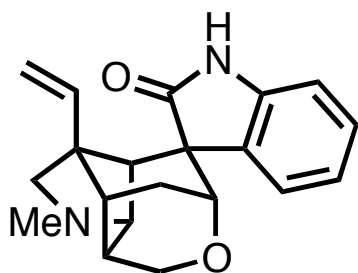
Jun Shimokawa, Takaaki Harada,
Satoshi Yokoshima, and Tohru Fukuyama*



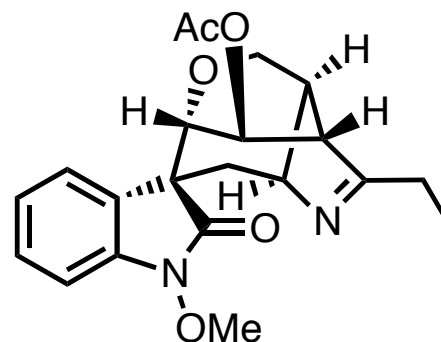
Brandon Parks
Wipf Group Current Literature
November 12, 2011

Gelsemium Alkaloids

- ❖ Isolated from *Gelsemium elegans*
- ❖ Large family of alkaloids broken into 5 subgroups:
 - Sarpagine, koumine, humantenine, gelsedine, and gelsemine
- ❖ Several pharmacological effects have been reported
 - Analgesic, anti-inflammatory, and anti-tumor activities



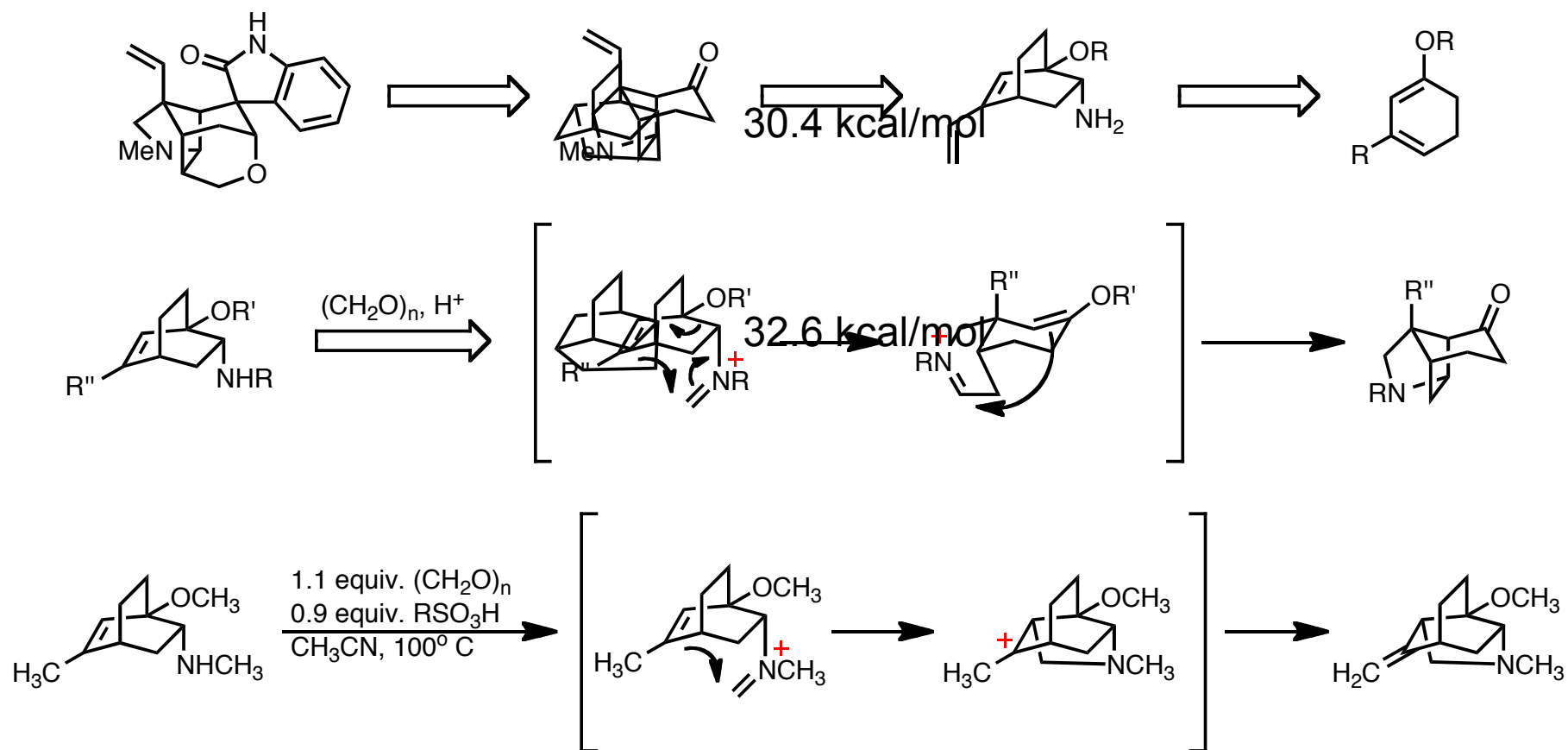
Gelsemine



14-Acetoxygelsenicine

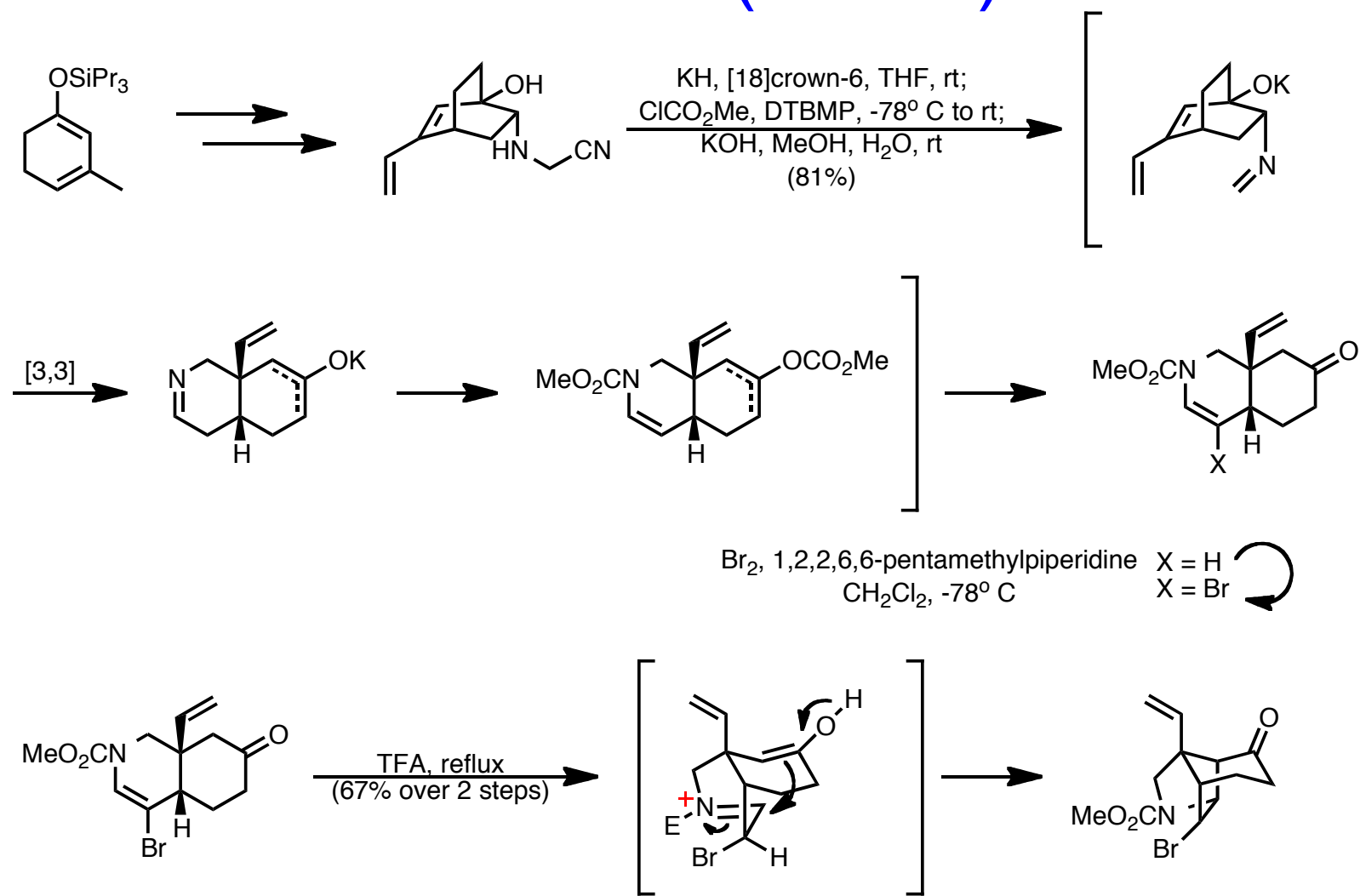
Takayama, H.; et.al. *J. Nat. Prod.*, **2006**, 69, 715-718
Zhang, L.; Lin, J.; Wu, Z. *J. Chin. Med. Mat.*, **2003**, 26, 451-453.

Construction of the Gelsemine Core – Overman (Part 1)



Earley, W.G.; Meier, G.P.; Jacobsen, E.J.; Oh, T.; Overman, L.E., *Tet. Lett.*, **1988**, 29, 3781-3784

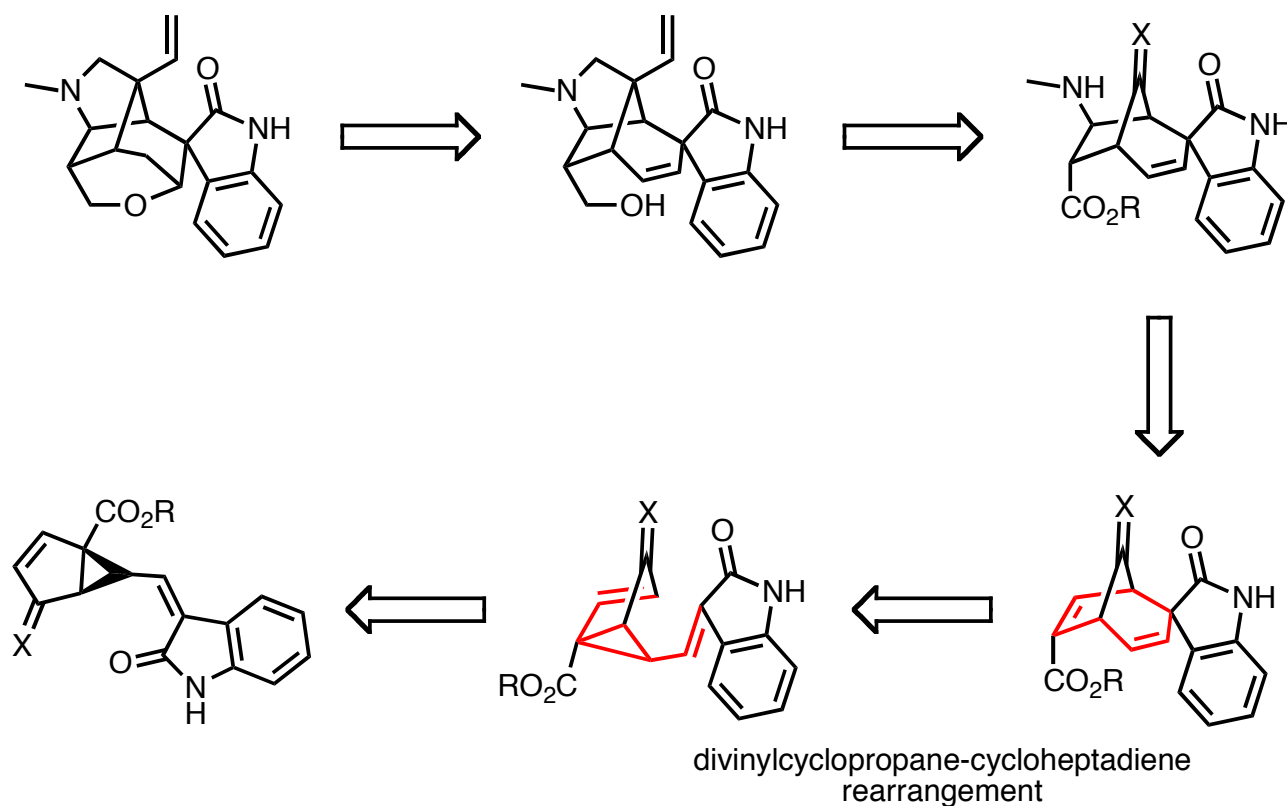
Construction of the Gelsemine Core – Overman (Part 2)



Earley, W.G.; Meier, G.P.; Jacobsen, E.J.; Oh, T.; Overman, L.E., *Tet. Lett.*, **1988**, 29, 3781-3784.

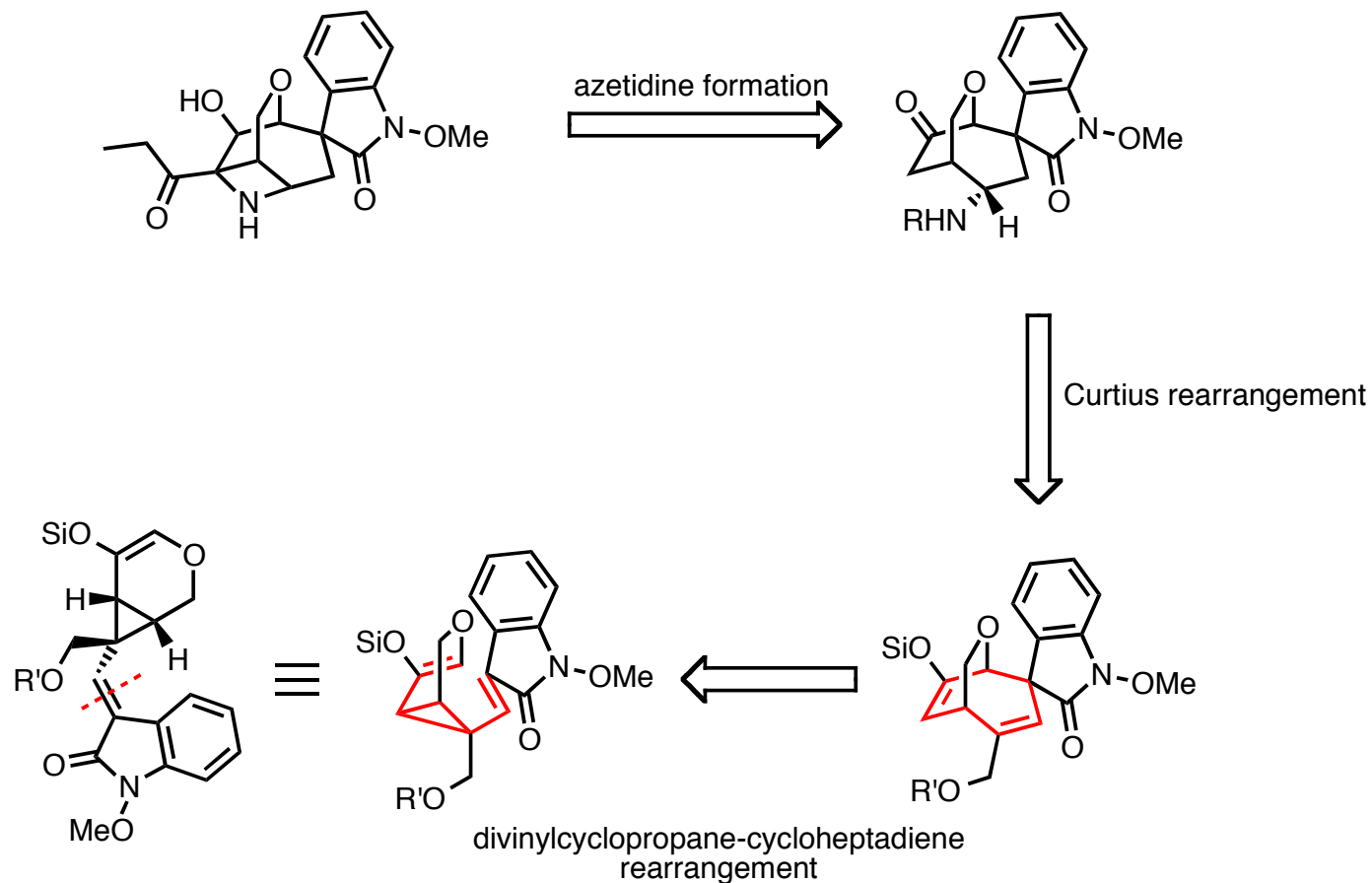
Madin, A.; O'Donnell, C.J.; Oh, T.; Old, D.W.; Overman, L.E.; Sharp, M.J. *Angew. Chem. Int. Ed.*, **1999**, 38, 2934-2936.

Construction of the Gelsemine Core – Fukuyama



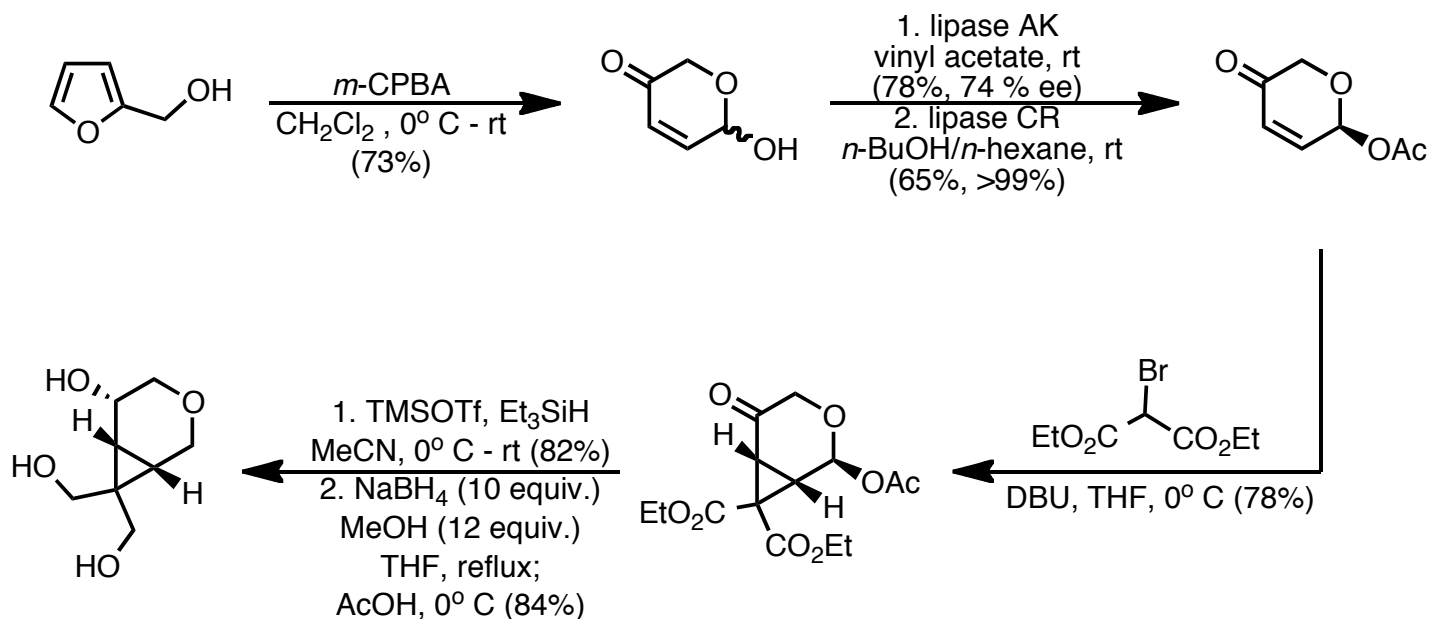
Fukuyama, T.; Liu, G., *Pure & Appl. Chem.*, **1997**, *69*, 501-505.

Gelsemoxonine Retrosynthetic Analysis

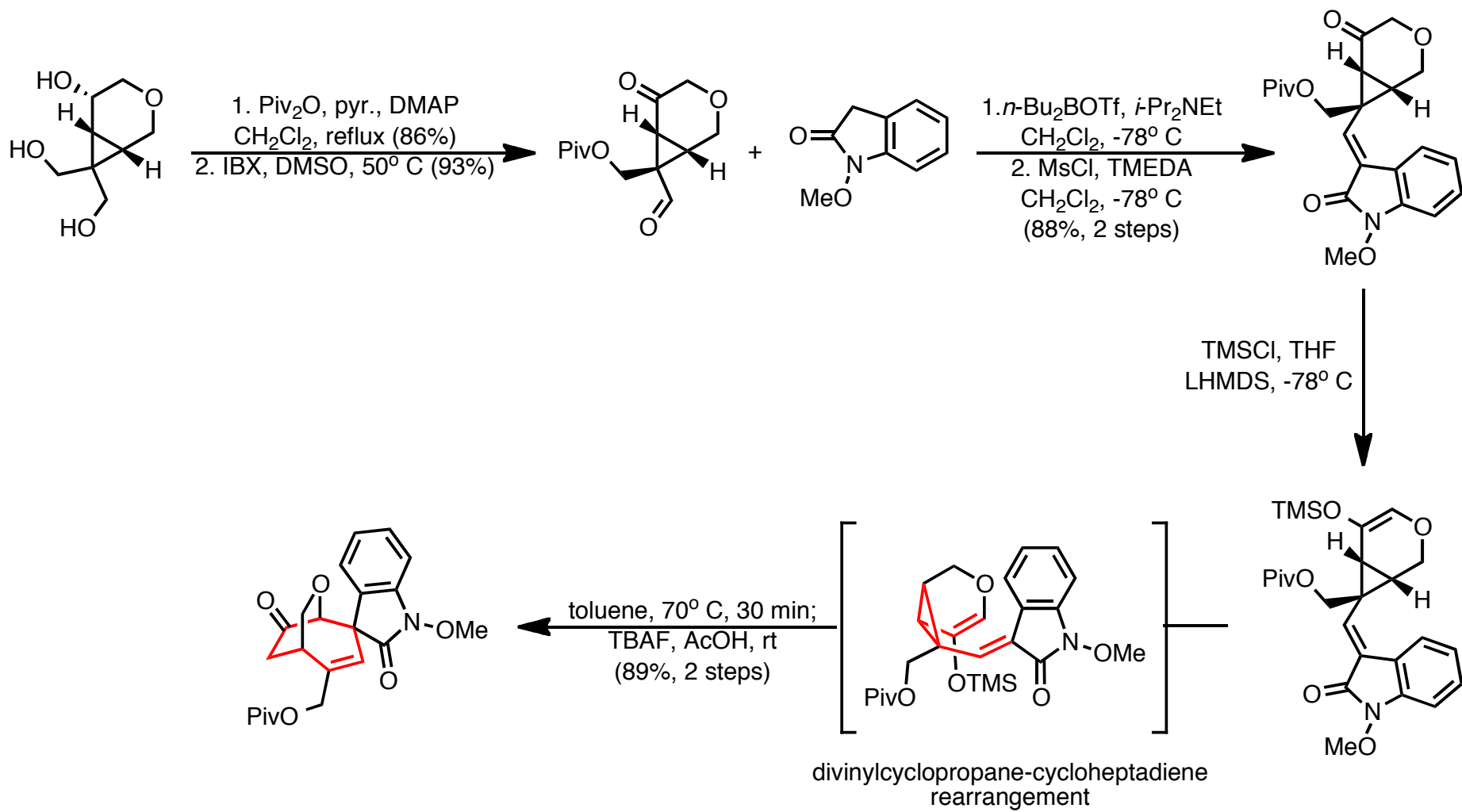


Shimokawa, J.; Harada, T.; Yokoshima, S.; Fukuyama, T., *J. Am. Chem. Soc.*, **2011**, 133, 17634-17637.

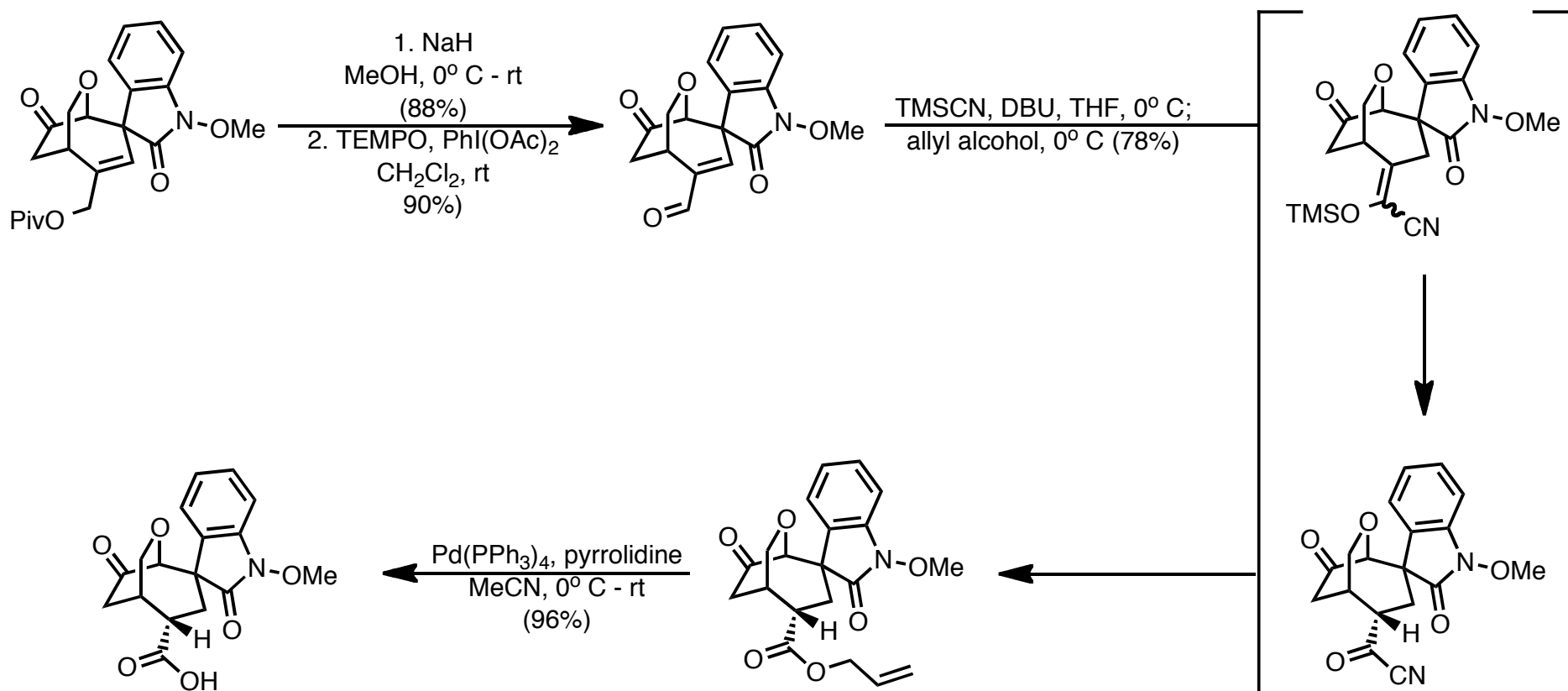
Synthesis of Key Cyclopropane Intermediate



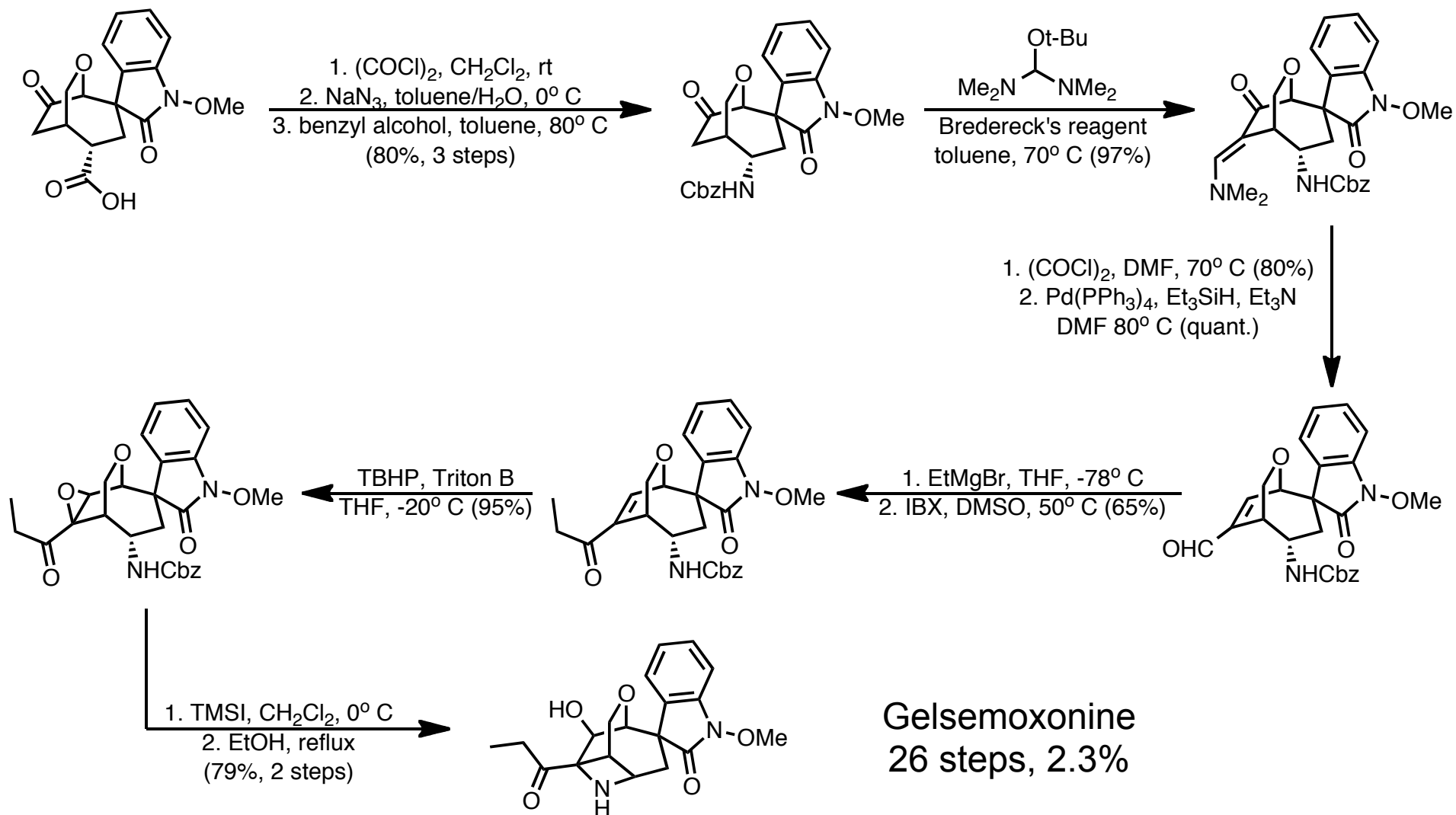
Synthesis of Divinylcyclopropane



Installation of Key Stereochemistry



End Game Synthesis



Conclusions

- ❖ First total synthesis of gelsemoxonine in 26 steps with an overall yield of 2.3%
- ❖ Spiro indolinone quaternary center installed utilizing a divinylcyclopropane-cycloheptadiene rearrangement
- ❖ Key stereochemistry established via a TMSCN-DBU isomerization