

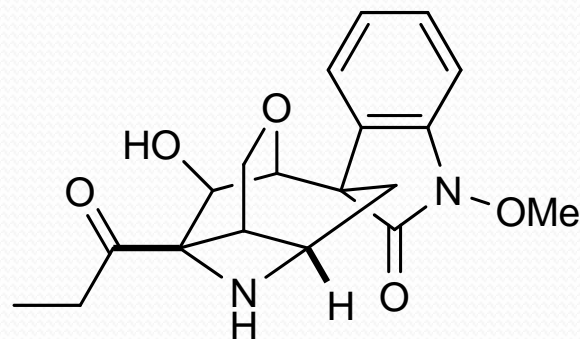
Christian Gloor
Journal Club Group Meeting
10.10.2013

Total Synthesis of (±)-Gelsemoxonine

S. Diethelm and E. M. Carreira
J. Am. Chem. Soc. 2013, 135, 8500-8503

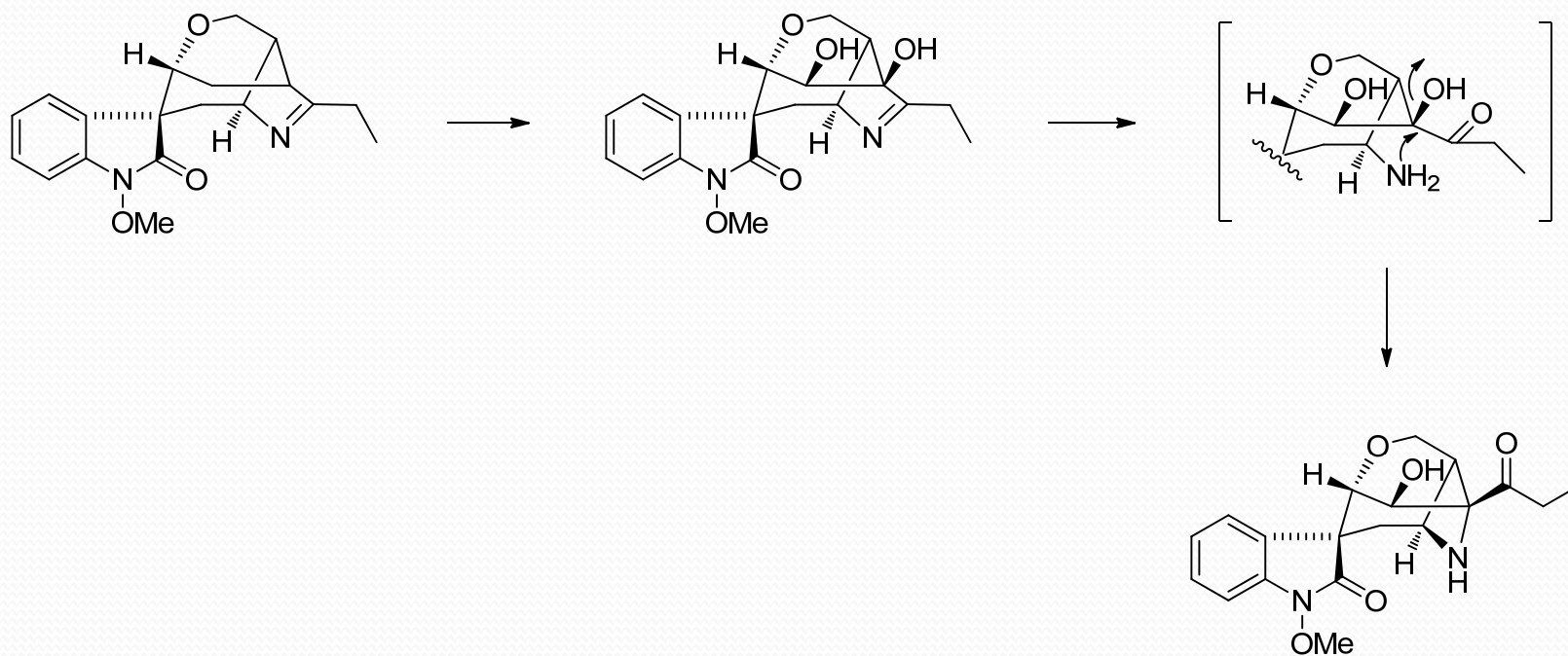
Isolation, Structure and biological activity

- Gelsemoxine was first isolated from *Gelsemium elegans* in 1991



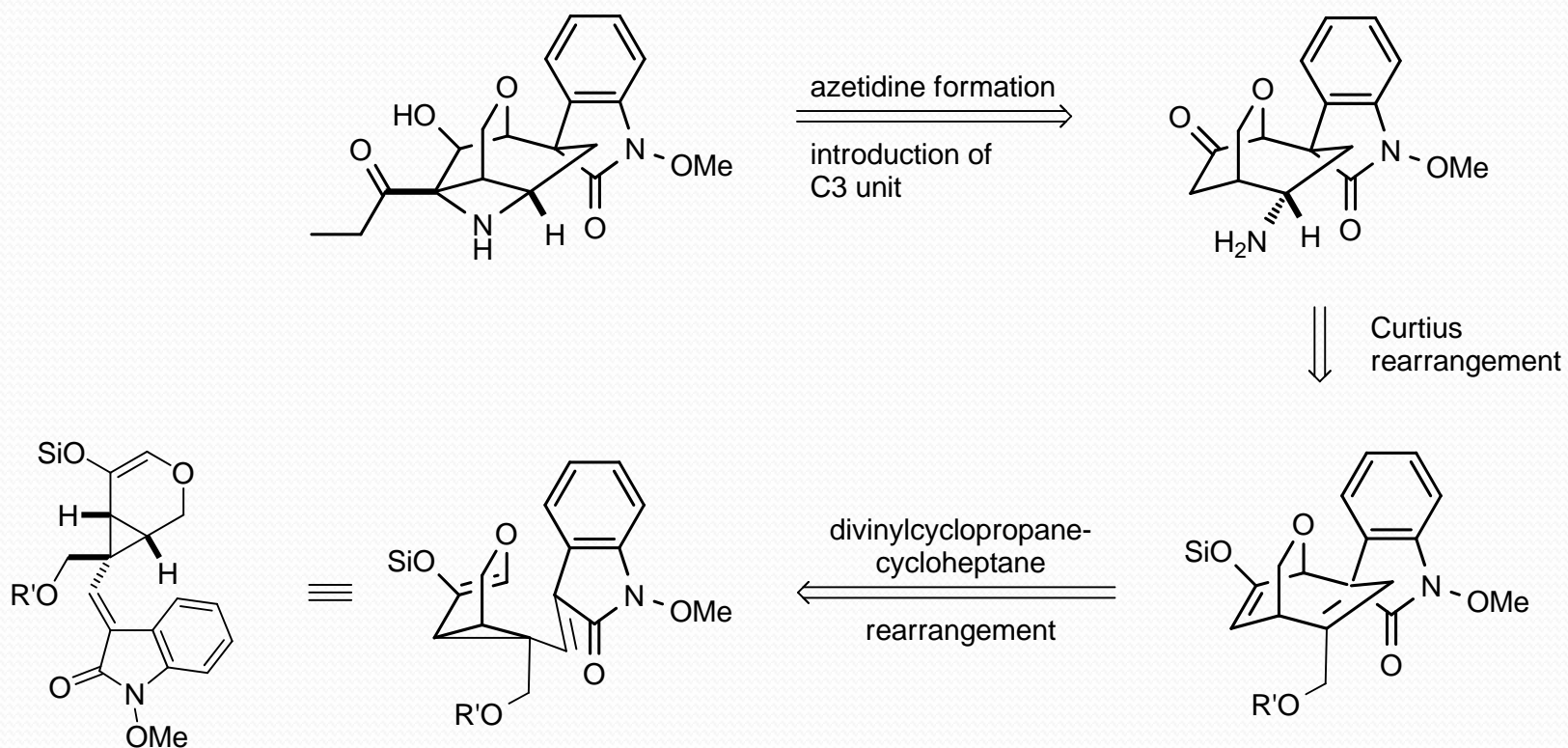
- Belongs to the family of gelsemium alkaloids
- Relatively unique azetidine moiety with a fully substituted carbon, six continuous, densely packed stereocenters, spirocenter
- *Gelsemium elegans* is used in traditional Asian medicine for over thousand years as an analgesic, antispasmodic and as a remedy for certain kinds of skin ulcers.

Biosynthesis proposal



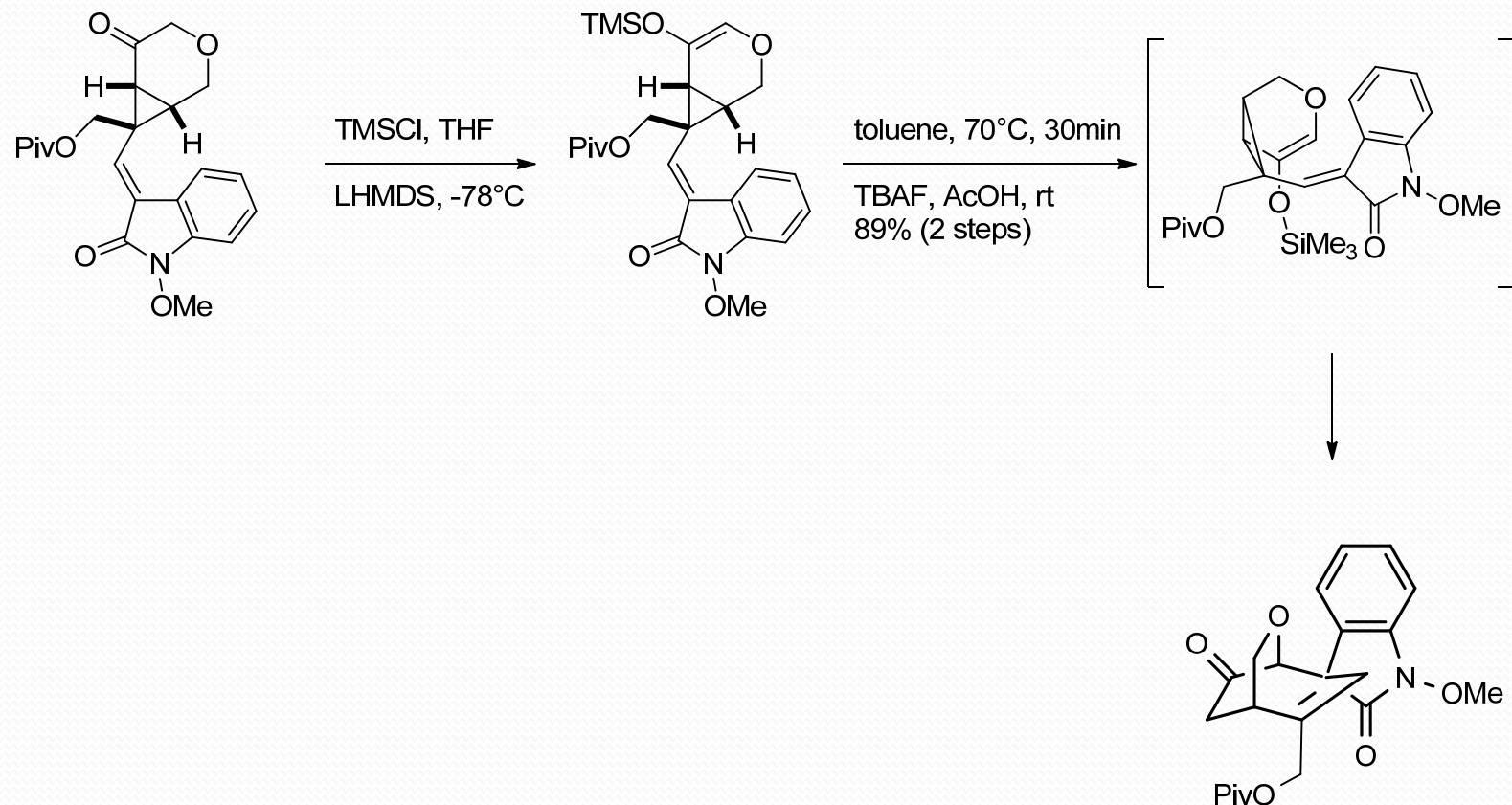
Kitajima, M.; Kogure, N.; Yamaguchi, K.; Takayama, H.; Aimi, N. *Org. Lett.* **2003**, *5*, 2075

Retrosynthetic approach of Fukuyama's group



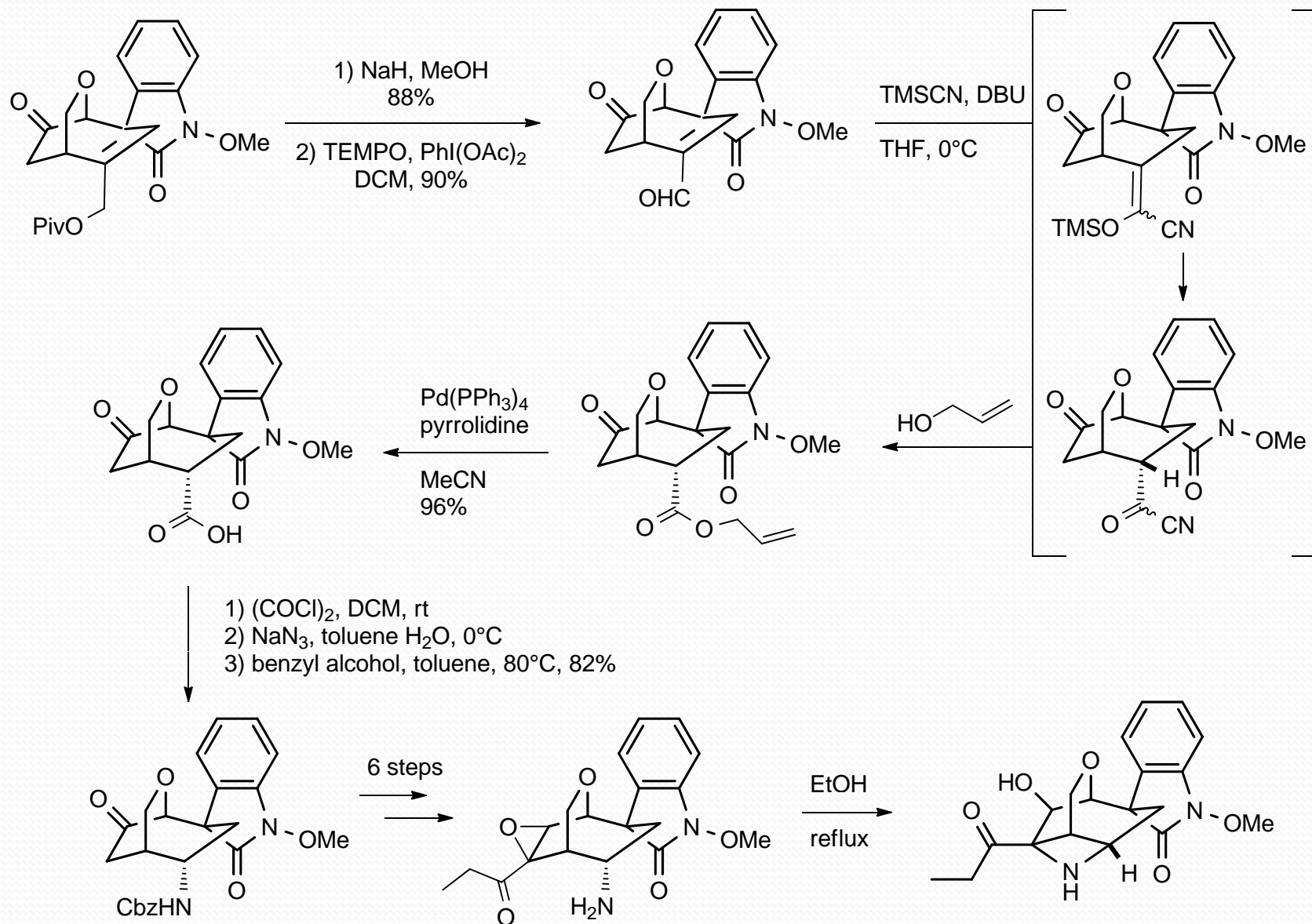
Synthesis of Fukuyama's group

Divinylcyclopropane-Cycloheptadiene Rearrangement

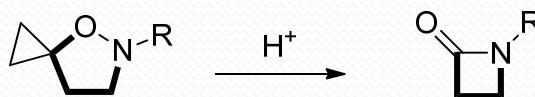
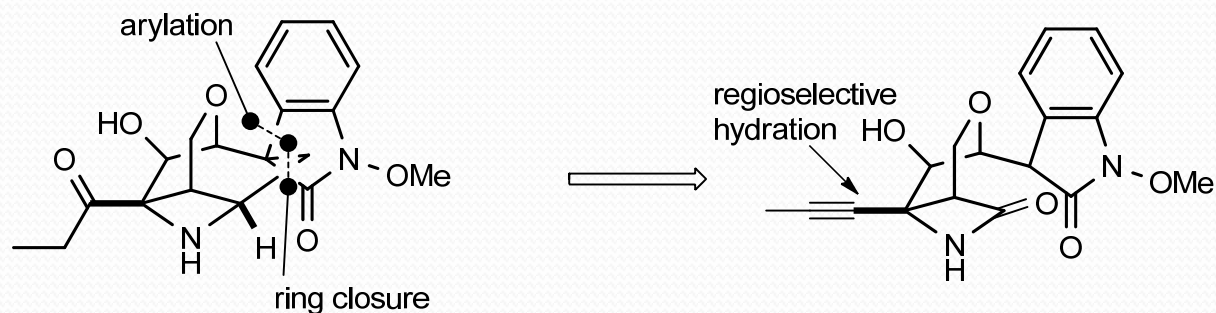


Shimokawa, J.; Harada, T.; Yokoshima, S.; Fukuyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 17634

Synthesis of Fukuyama's group

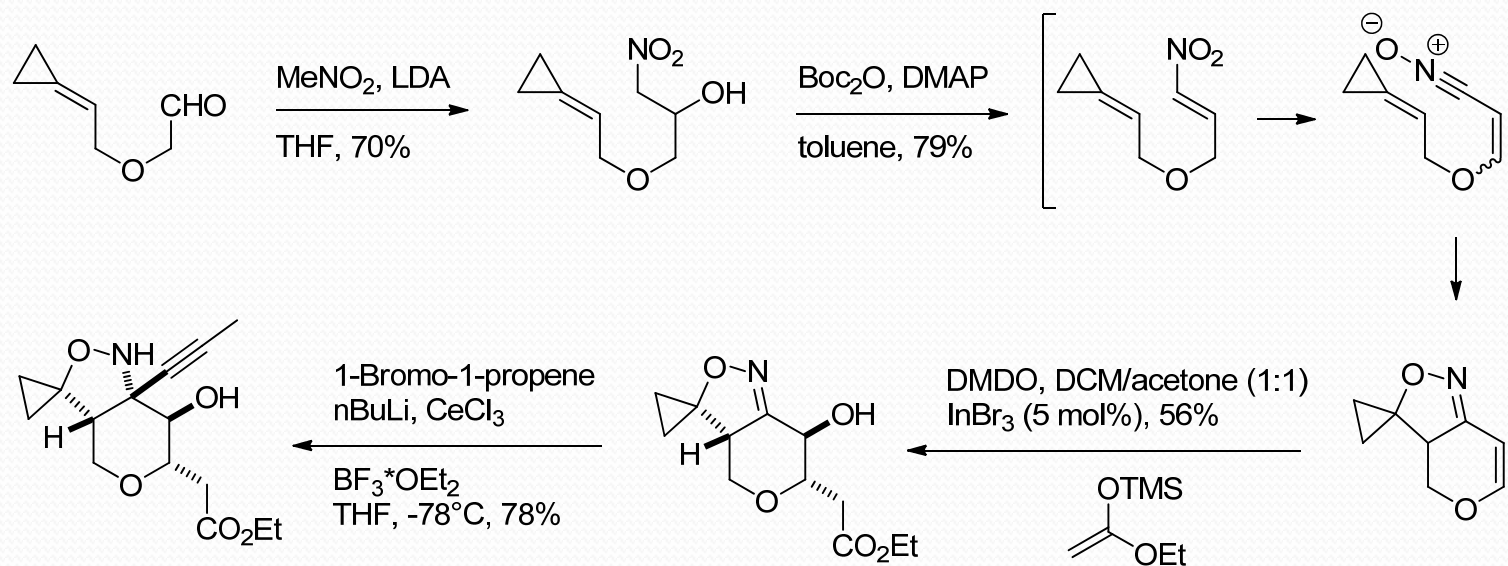


Retrosynthetic approach of Carreira's group

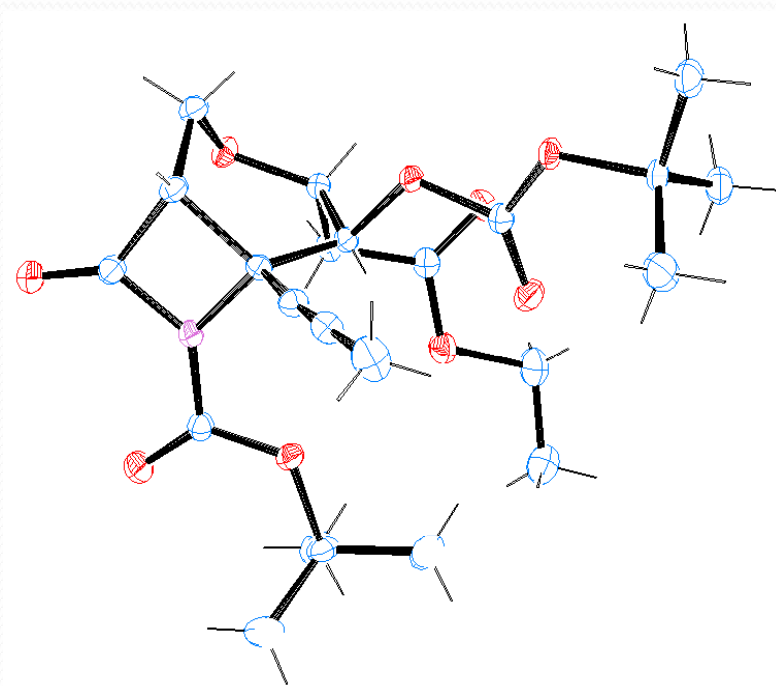
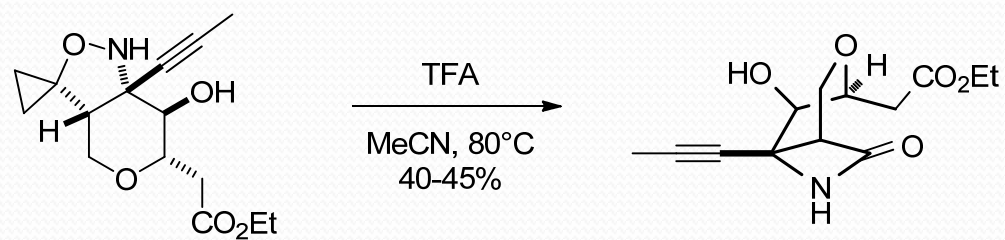


Diethelm, S.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 8500
Brandi, A. et al. *J. Am. Chem. Soc.* **2000**, *122*, 8075

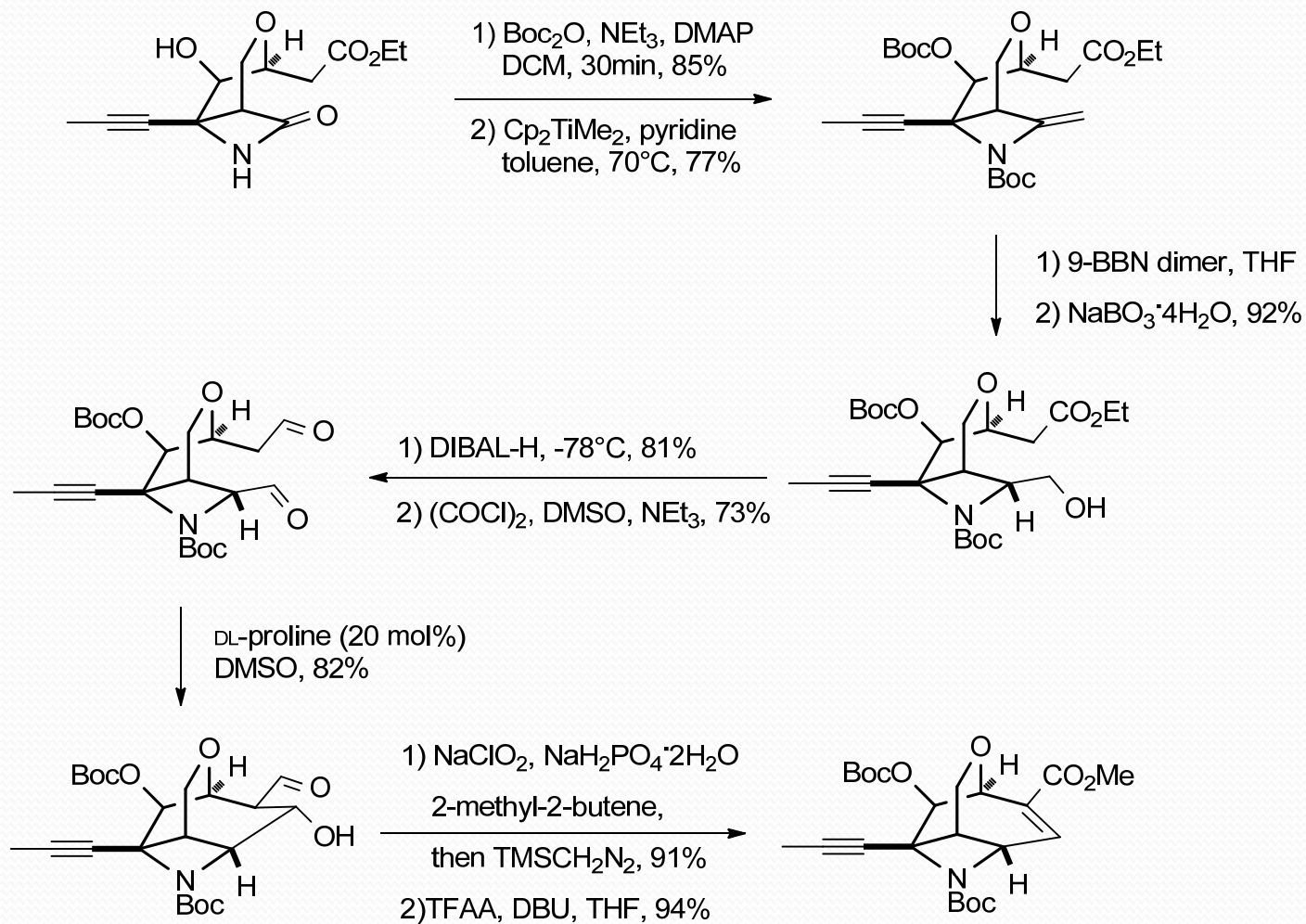
Synthesis of Carreira's group



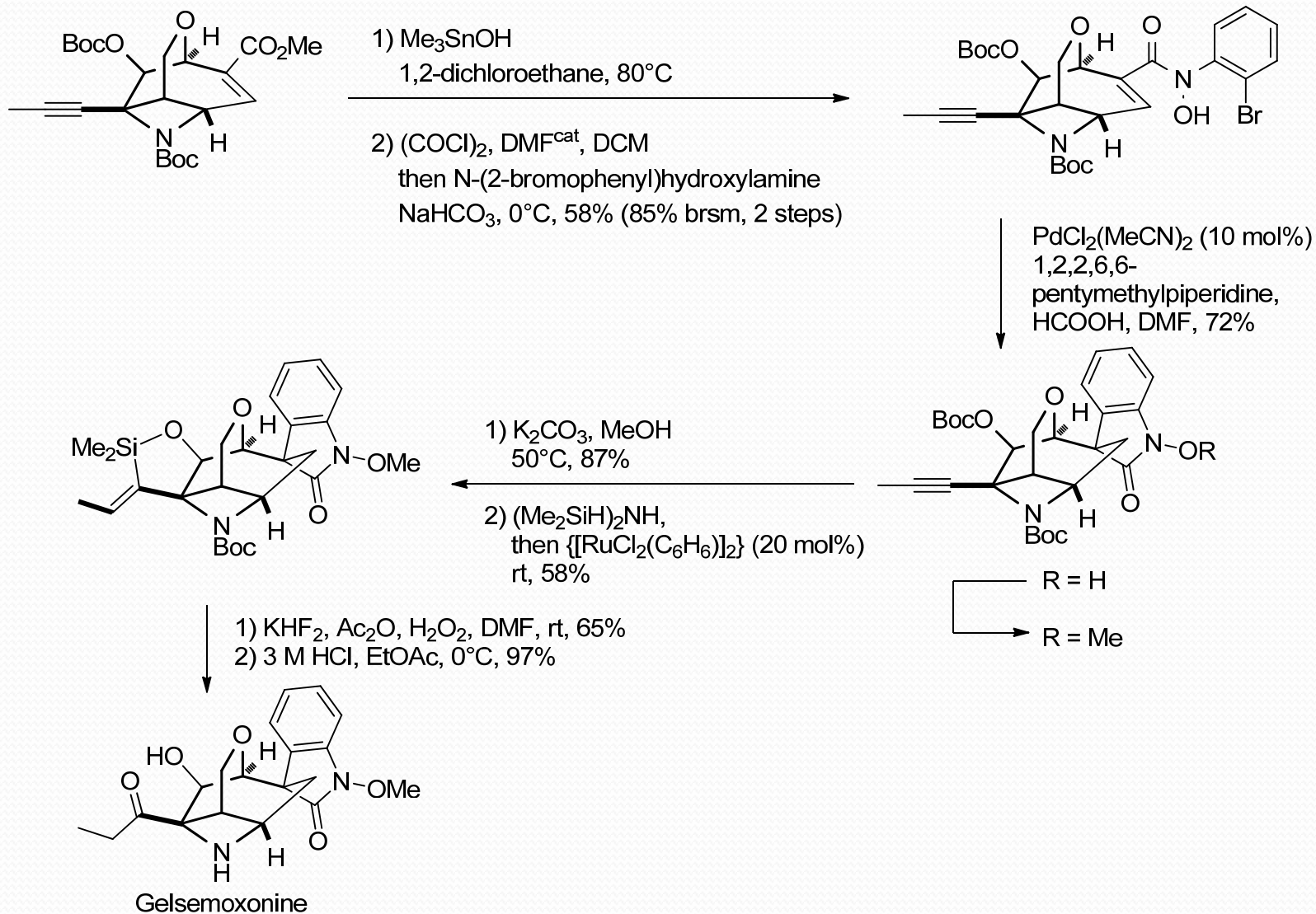
Synthesis of Carreira's group



Synthesis of Carreira's group



Synthesis of Carreira's group



Conclusion

- total synthesis was achieved with 21 linear steps and an overall yield of 14%
- A ring contraction was used to build up the azetidine
- A diastereoselective reductive Heck cyclization was applied for the construction of the oxindol ring
- The ethyl ketone was generated with a directed hydrosilylation of a tripple bond



Thank you for your attention

Ring contraction – New Synthesis of β -Lactams

