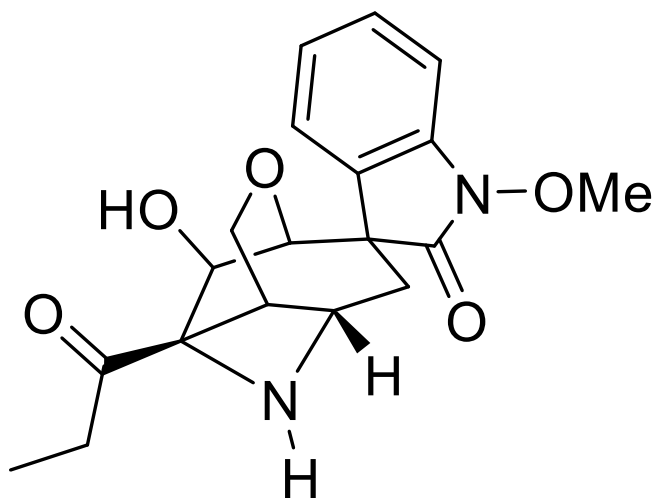


# Total Synthesis of Gelsemoxonine through a Spirocyclopropane Isoxazolidine Ring Contraction<sup>1</sup>

Stefan Diethelm and Erick Carreira



Gelsemoxonine

Presented by Grace Hubbell

CEM 850

March 3<sup>rd</sup>, 2018

# Gelsemoxonine Background

Plants of the *Gelsemium* species endemic to China and Japan have long been used in traditional Asian medicine for their **antispasmodic** and **analgesic** activities.<sup>2</sup>

Several alkaloids in this family have also demonstrated **antitumor** and **anti-inflammatory** activities.<sup>3</sup>

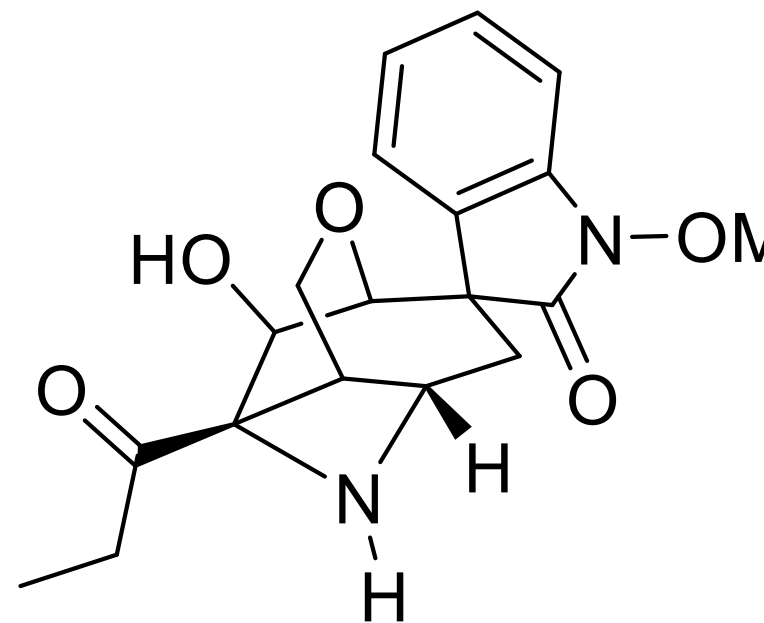
*Gelsemium* alkaloid obtained from the plant *Gelsemium elegans*.<sup>4</sup>

Contains a unique azetidine ring which adds synthetic challenge.

Uchiyama, M.; Arai, Y.; Takayama, H.; Aimi, N. *Proc. Japan Acad., Ser. B* **1998**, *74*, 159.

Uchiyama, M.; Nakamura, T.; Kogure, N.; Ogawa, M.; Mitsuno, Y.; Ono, K.; Yano, S.; Aimi, N.; Takayama, H. *J. Nat. Prod.* **2006**, *69*, 715.

Uchiyama, M.; Cordell, G.A.; Ni, C.-Z.; Clardy, J. *Phytochemistry* **1991** *30*, 1311.

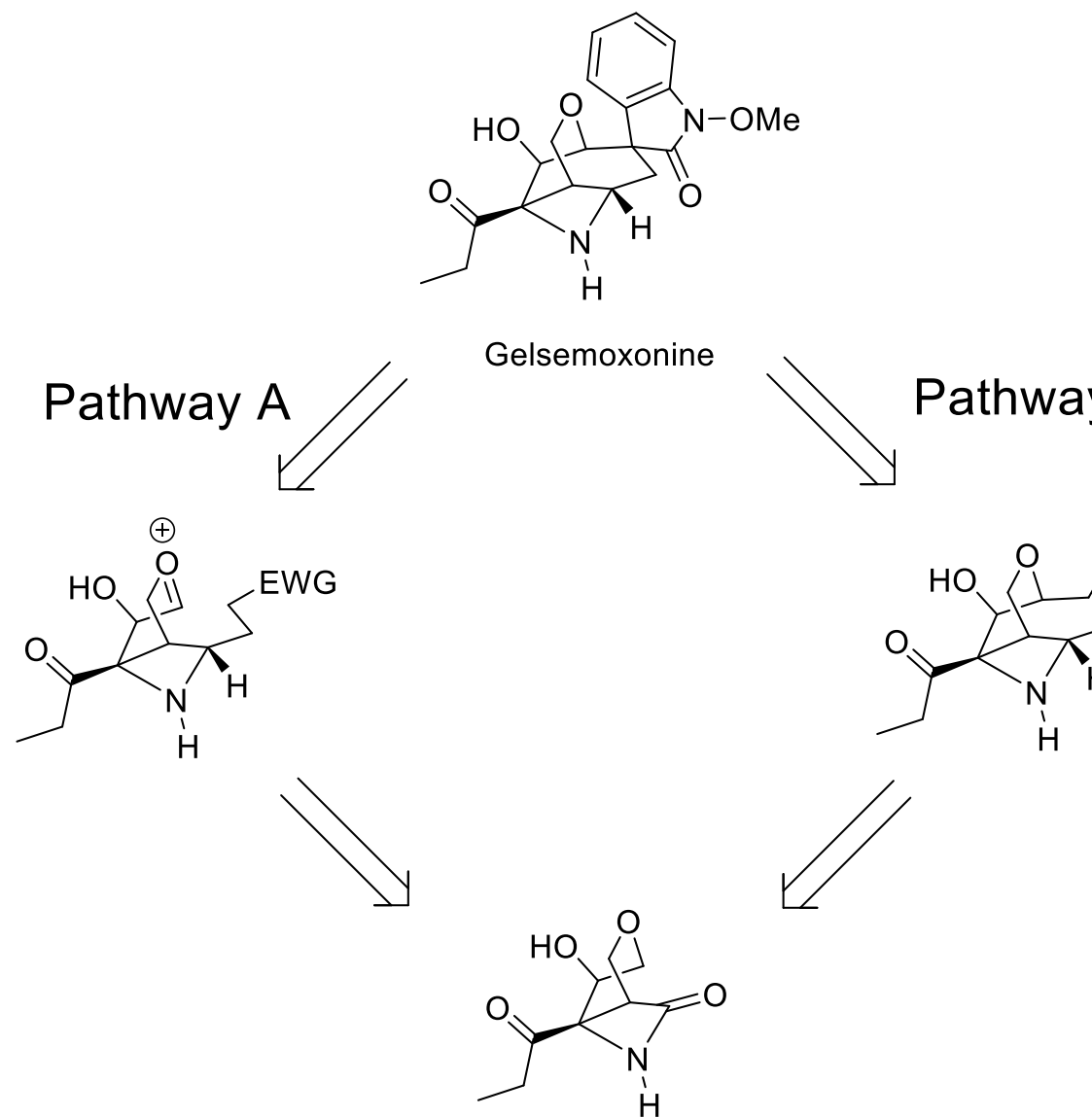


Gelsemoxonine

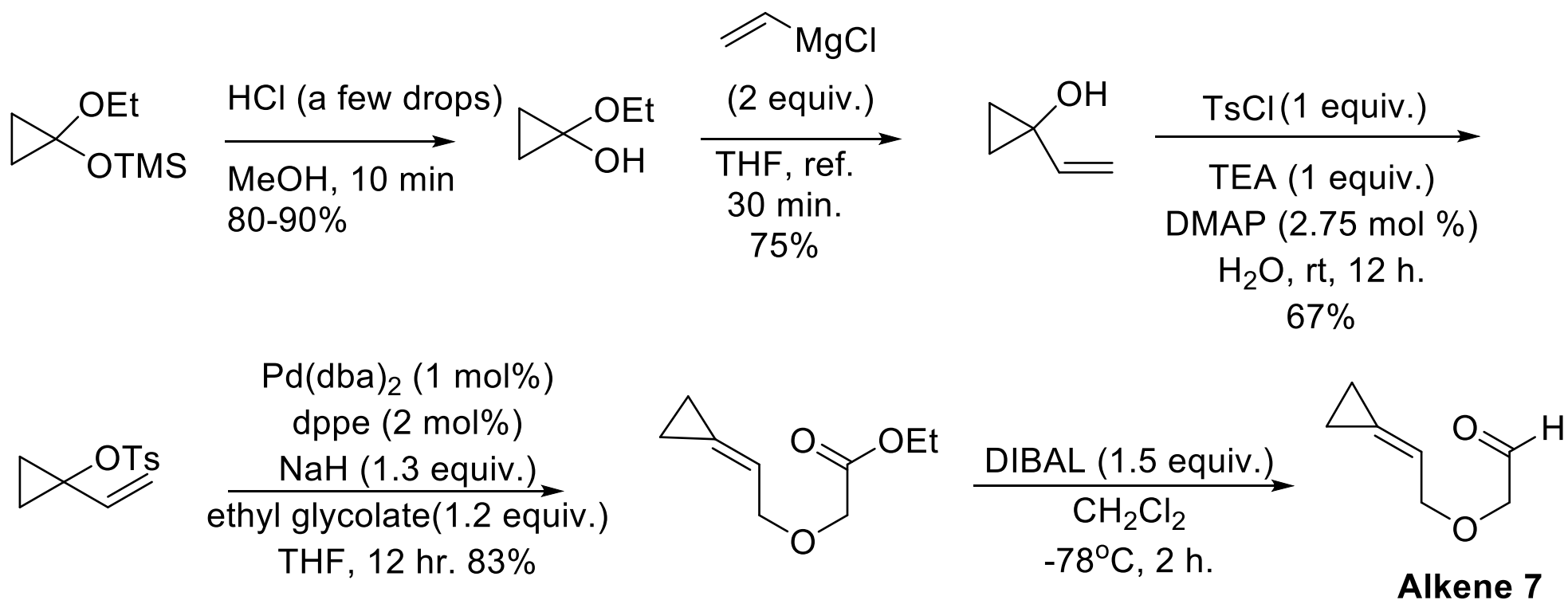
# Retrosynthetic Analysis

Two main pathways were explored as retrosynthetic pathways. Pathway B was eventually chosen to obtain the natural product.

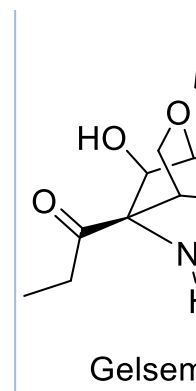
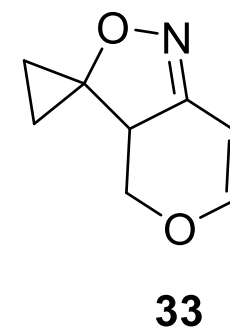
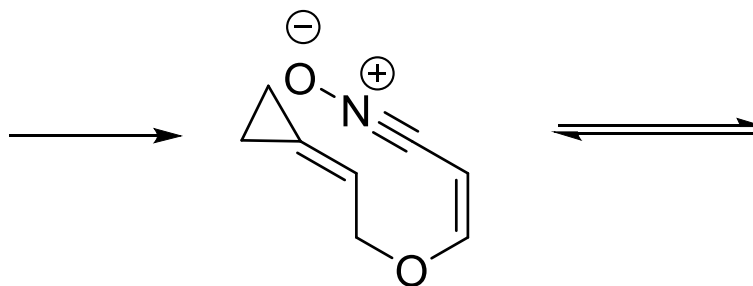
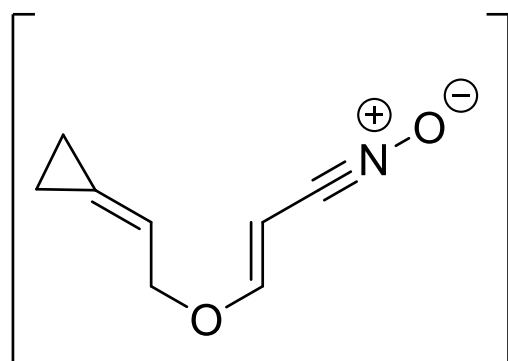
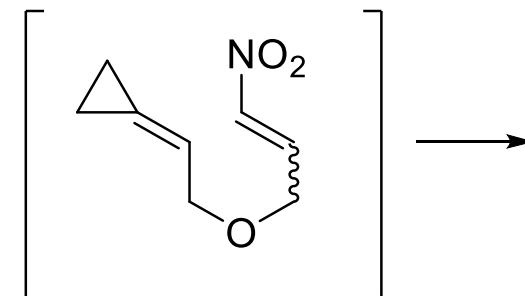
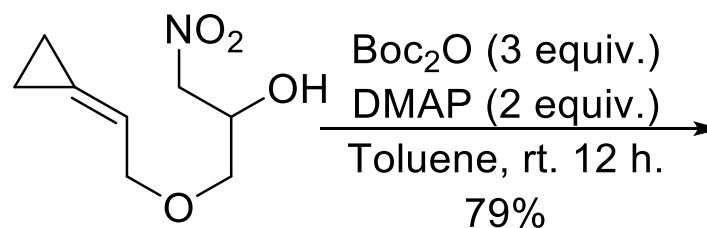
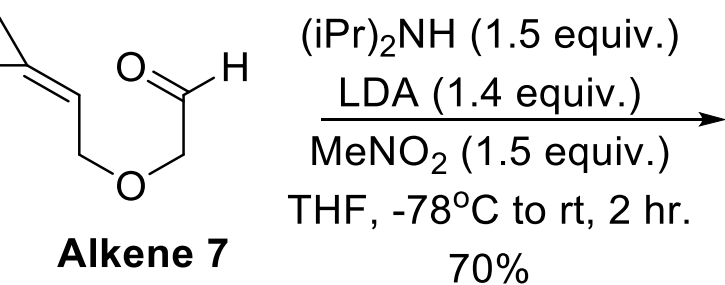
The reaction of a cyclopropane isoxazolidine ring to a  $\beta$ -lactam is key to the retrosynthesis of the azetidone ring.



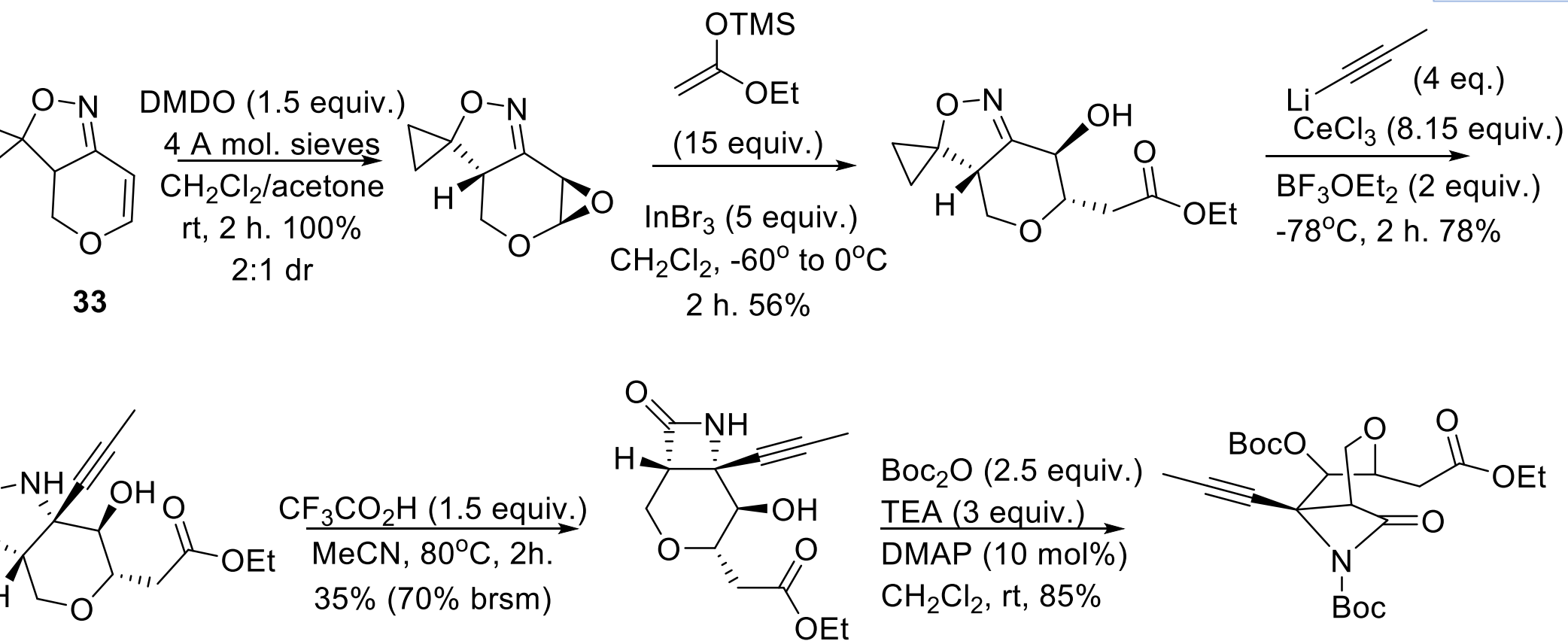
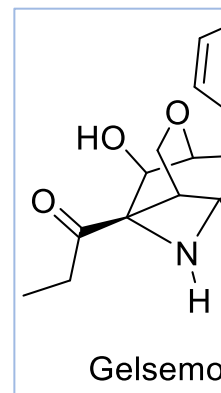
# Synthesis of Aldehyde 7



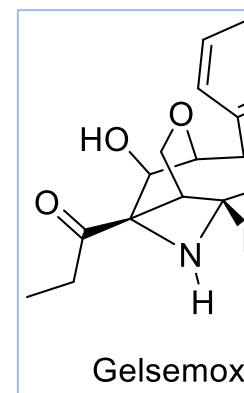
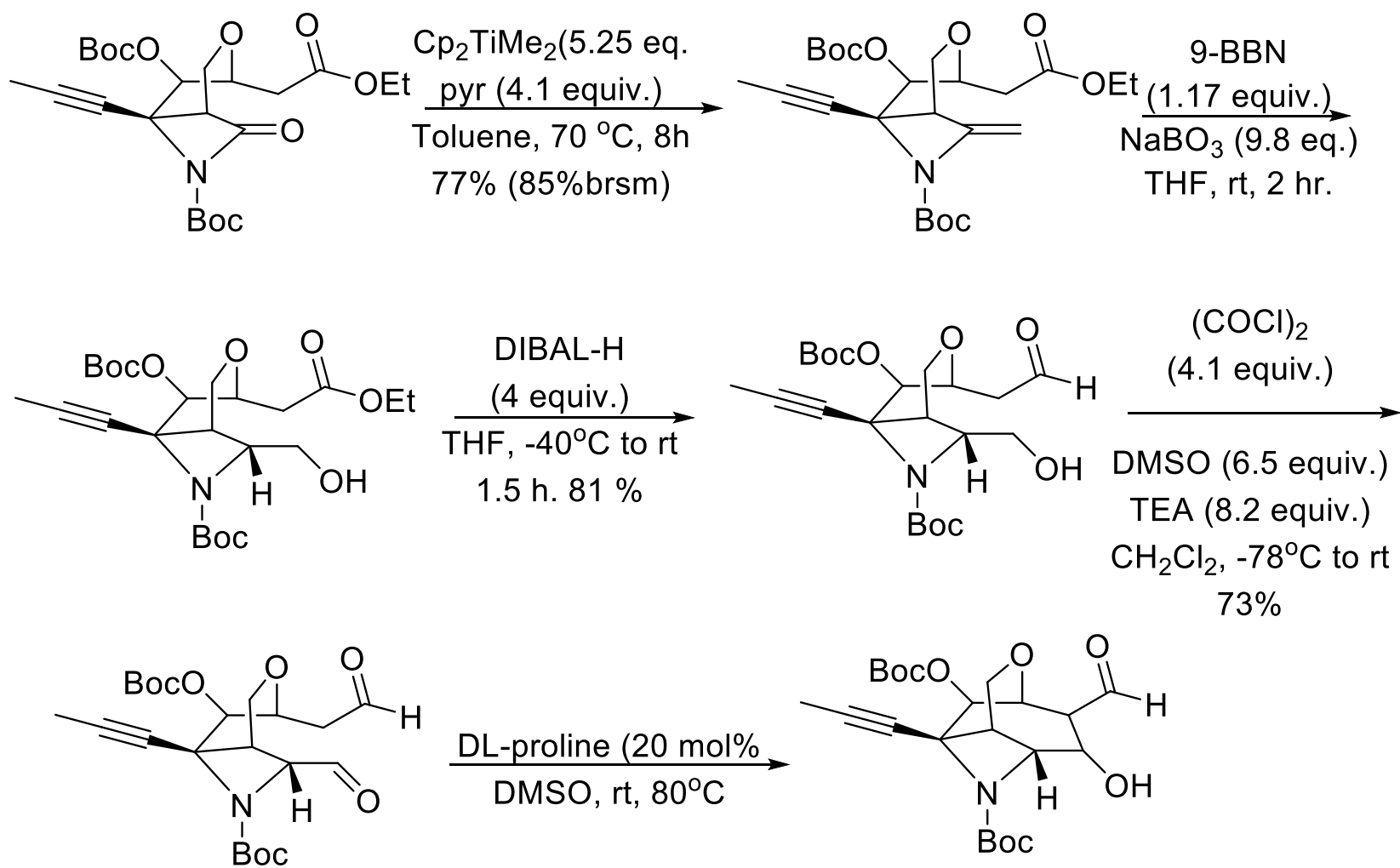
# Synthesis and Oxidation of Enol Ether 33



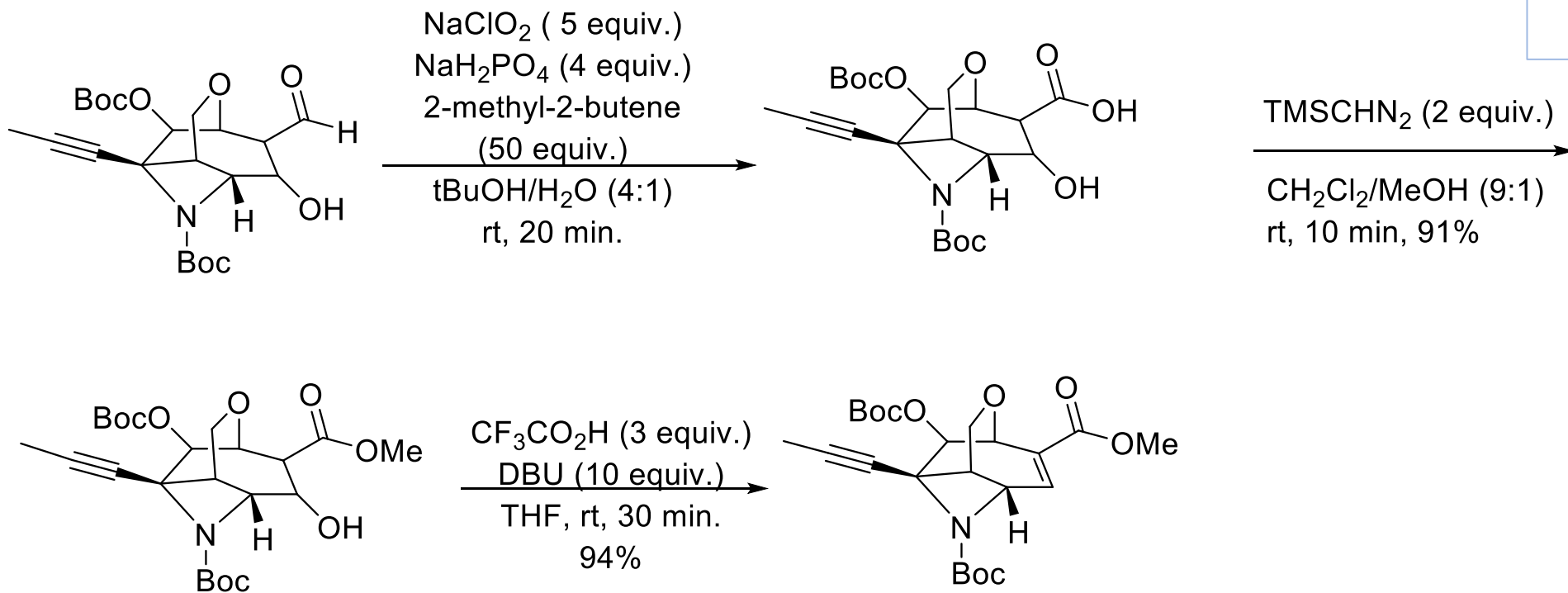
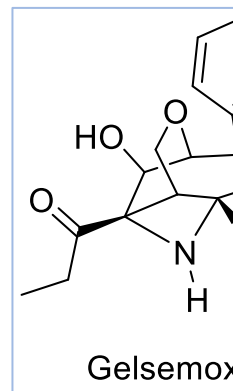
# actam Synthesis Via Cyclopropane azoline Ring Contraction



# Membered Ring Formation

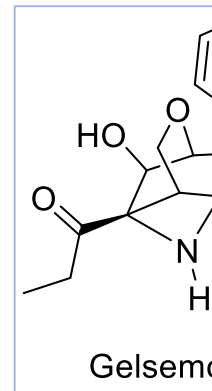
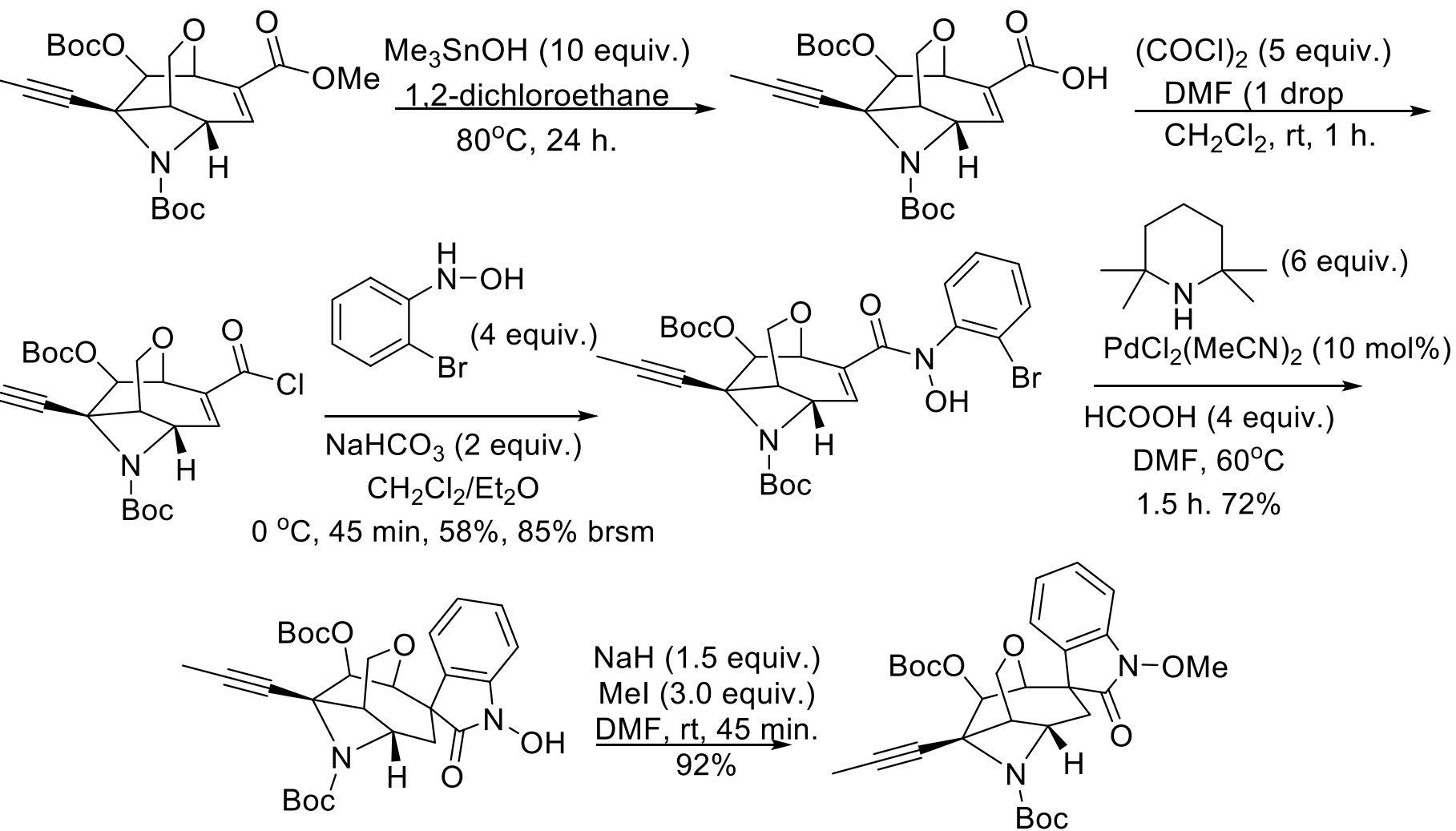


# Synthesis of $\alpha,\beta$ -unsaturated ester 62

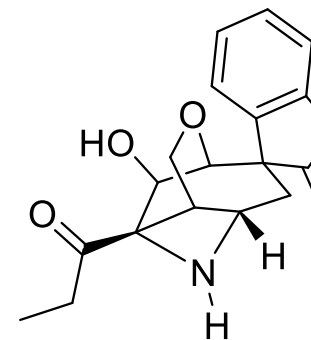
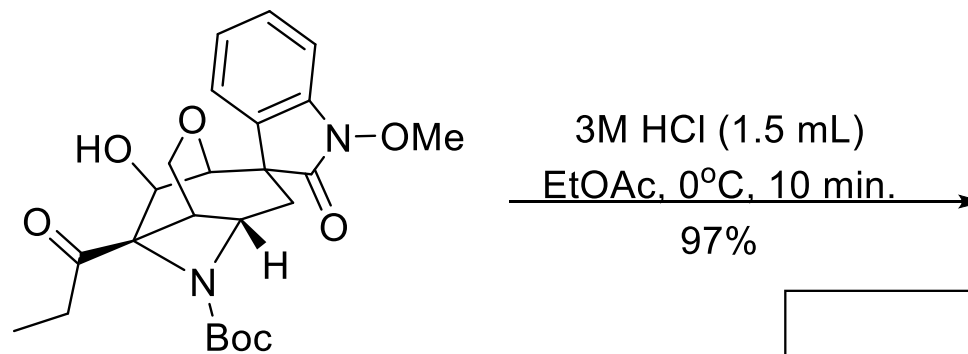
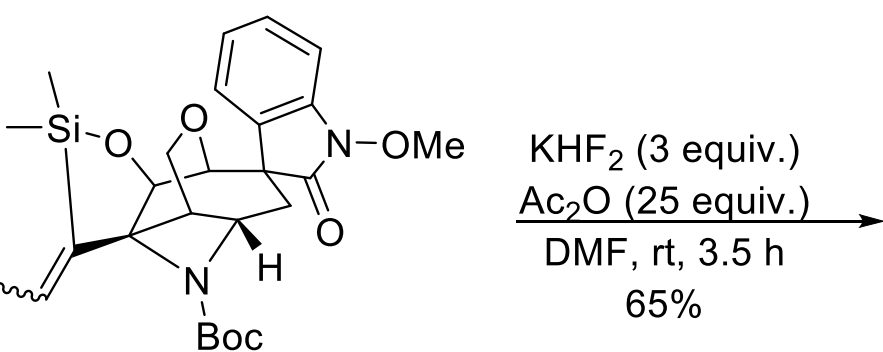
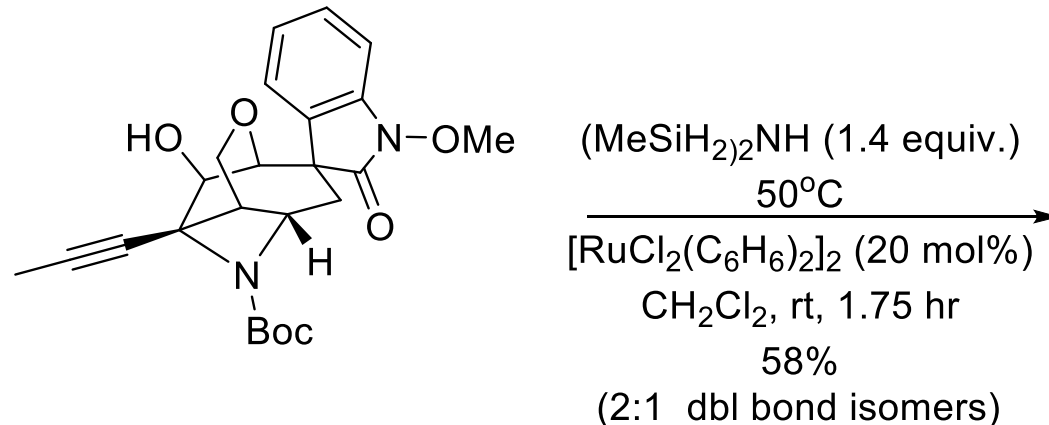
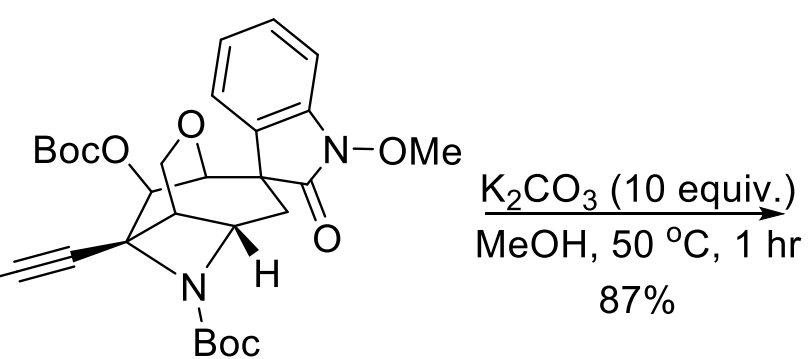




# Synthesis of Oxindole via Heck Cyclization



# One Formation and Final Steps



Gelsemoxoniol

Thank you!