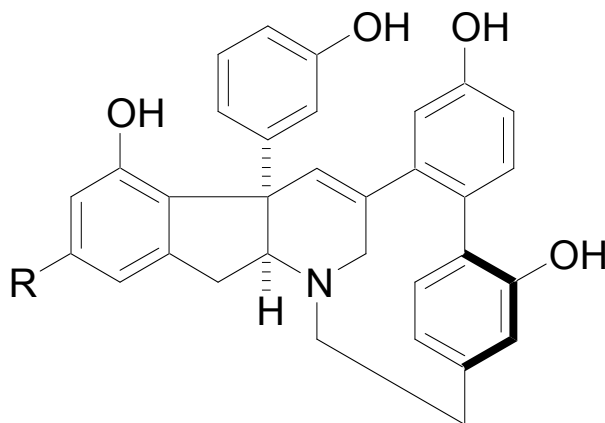


# Haouamine A and B

JME 4/26/06

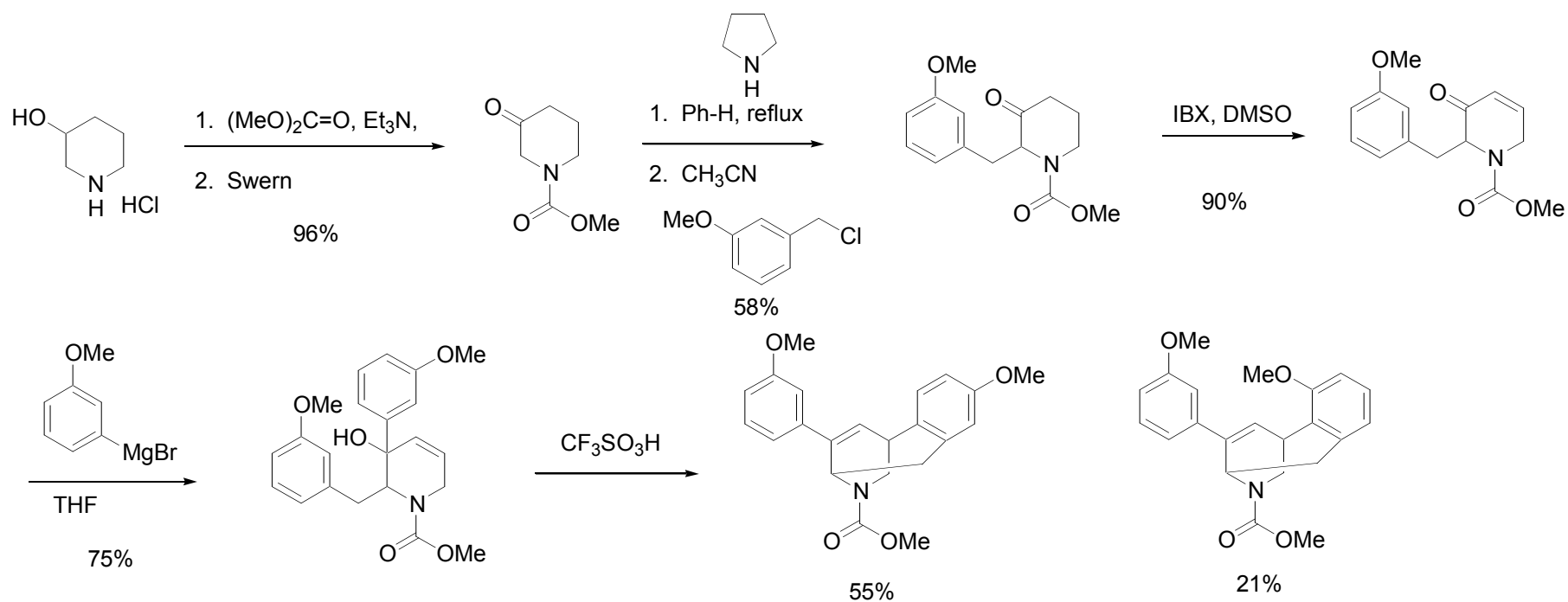
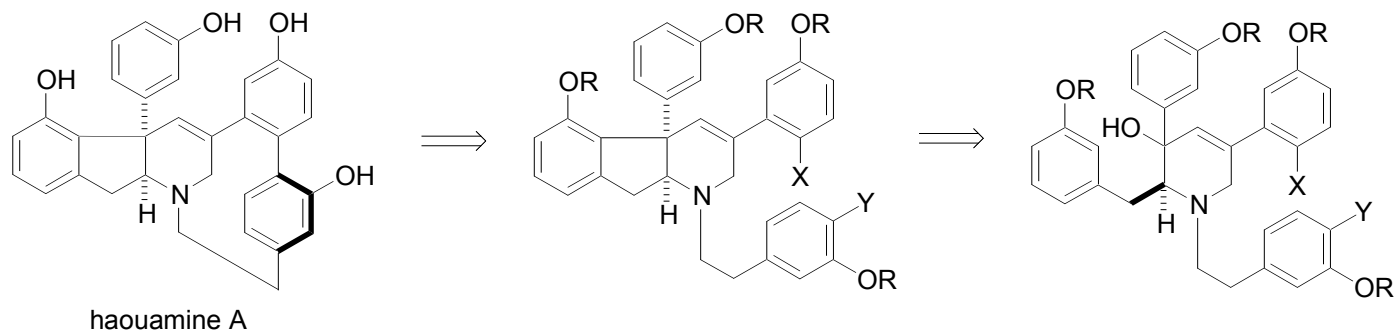


haouamine A    R = H  
haouamine B    R = OH

- Isolated from the ascidian *Aplidium haouarianum* in 2003 off the southern coast of Spain
- Haouamine A is potent and selective for cytotoxic activity against the HT-29 cell line ( $IC_{50} = 0.1 \mu\text{g/mL}$  )
- Haouamine B showed cytotoxicity against the MS-1 cell line ( $IC_{50} = 5 \mu\text{g/mL}$  )
- Structure determined by X-ray crystallographic data
- Contains an indeno-tetrahydropyridine moiety, a strained aza-paracyclophane moiety, a diaryl quaternary center, and an *anti*-Bredt double bond
- Synthetic efforts by Rawal, Trauner, Baran, Wipf, and Weinreb

Garrido, L.; Zubia, E.; Ortega, M. J.; Salva, J. J. *J. Org. Chem.* **2003**, *68*, 293.

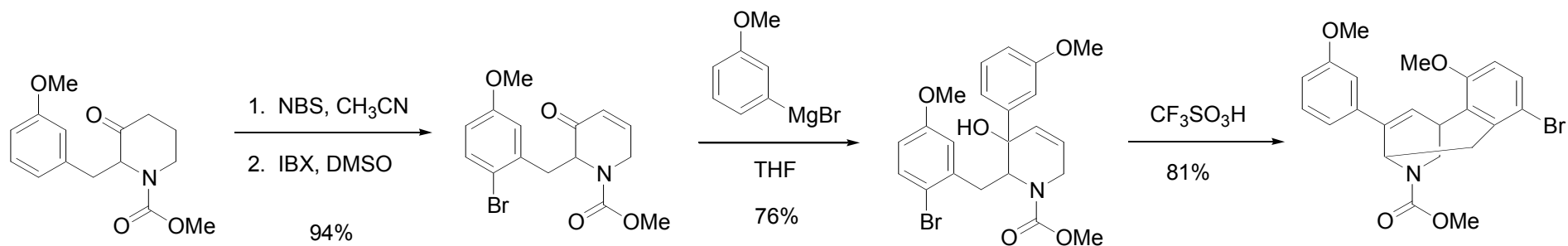
# Rawal's Approach



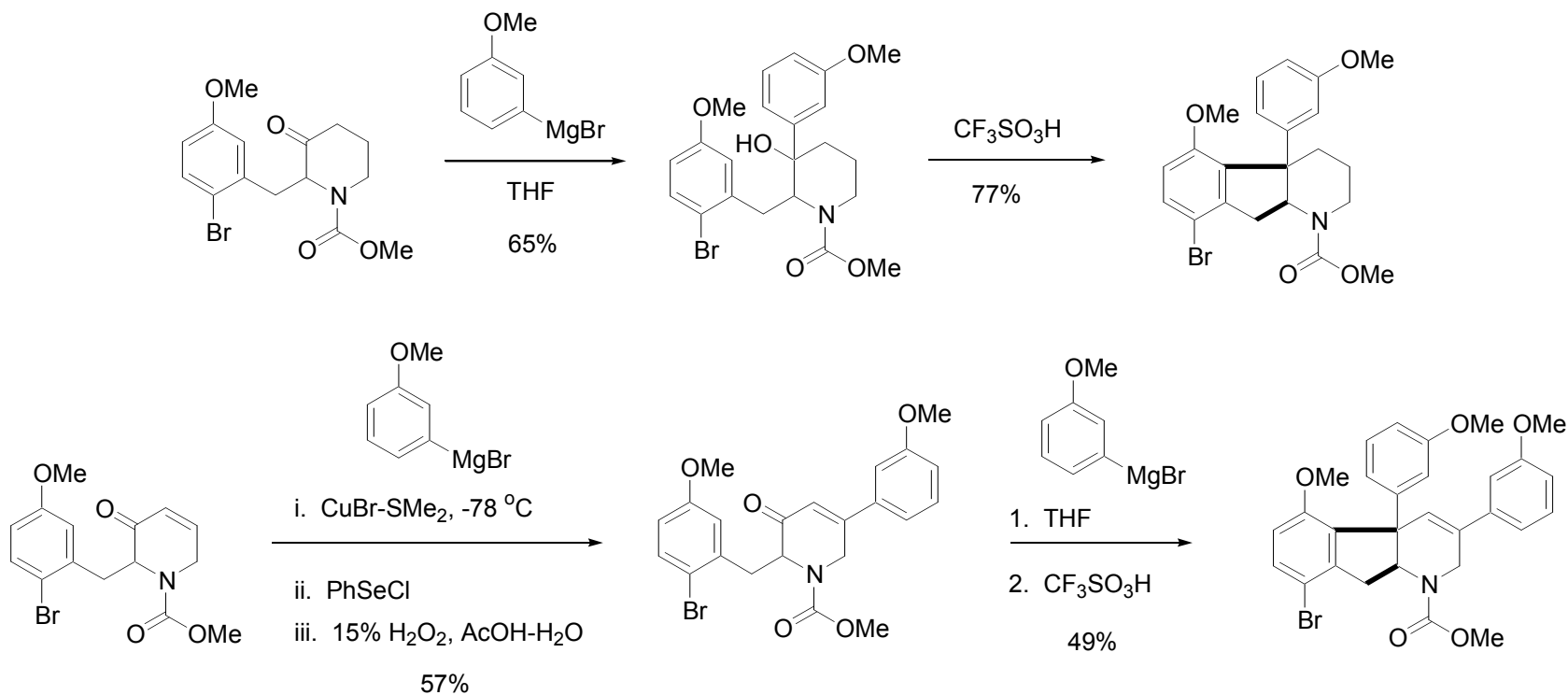
Smith, N. D.; Hayashida, J.; Rawal, V. H. *Org. Lett.* **2005**, *7*, 4309.

# Rawal's Approach (Cont.)

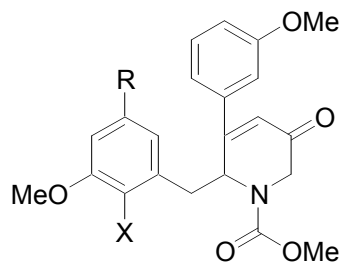
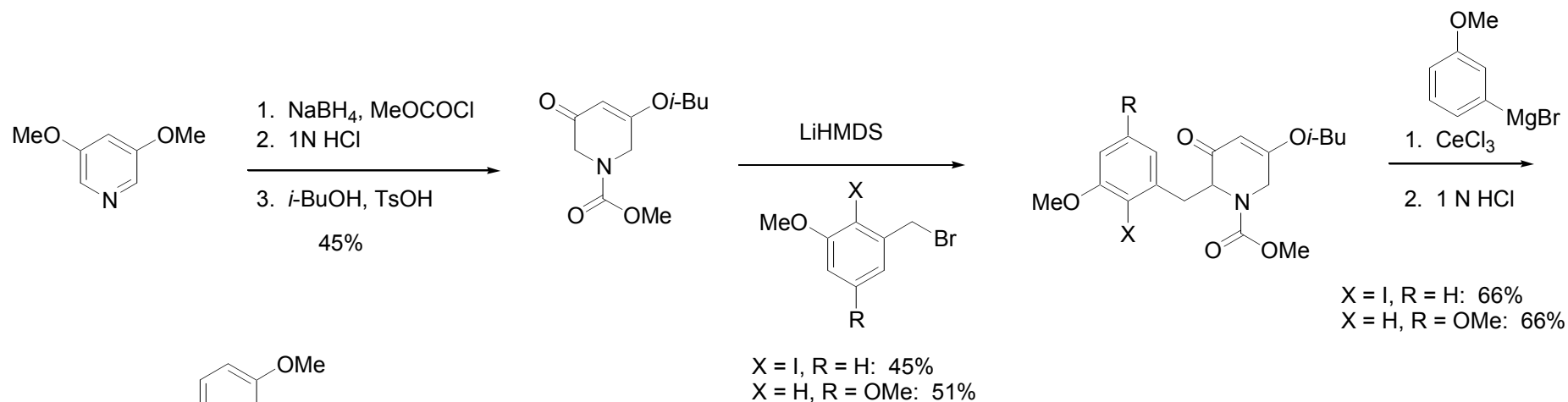
## Para-Blocking Group



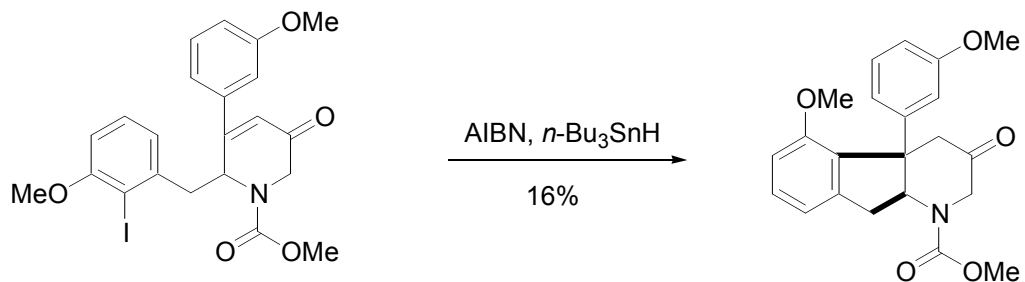
## Saturated Model



# Trauner's Approach



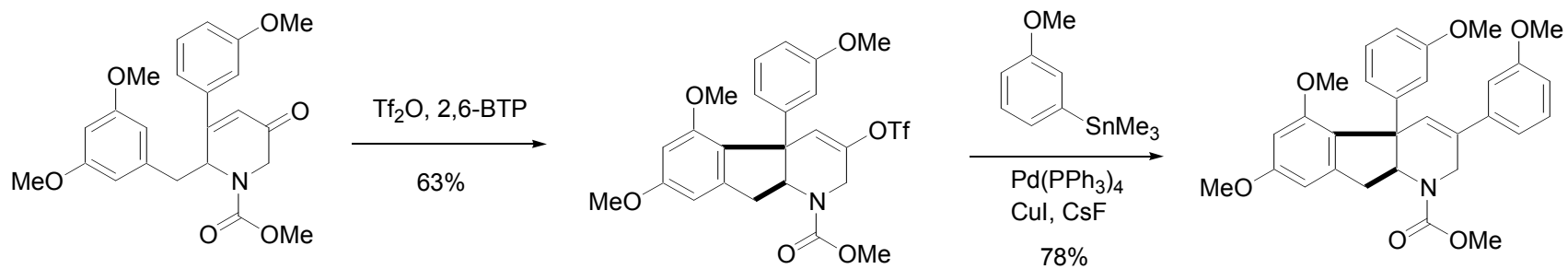
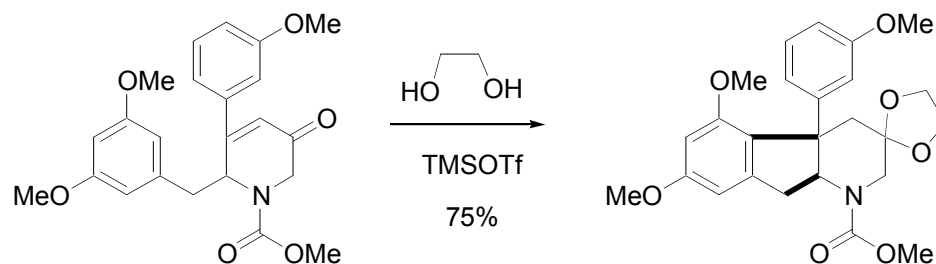
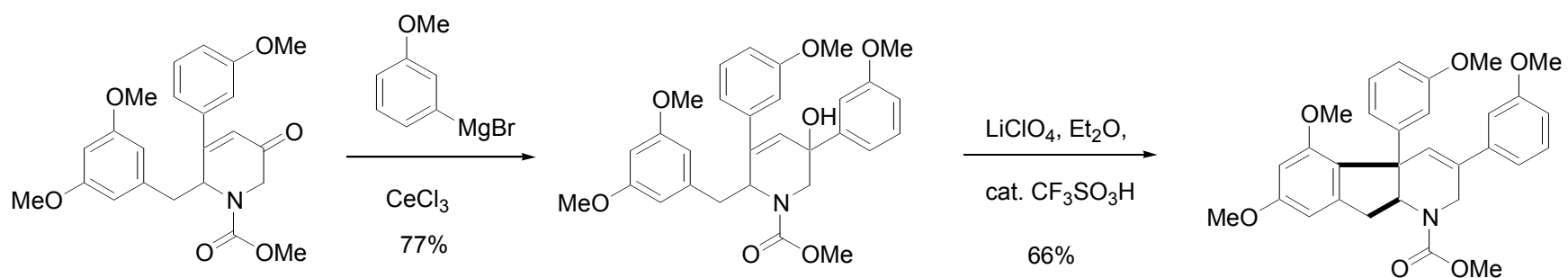
## Radical cyclization



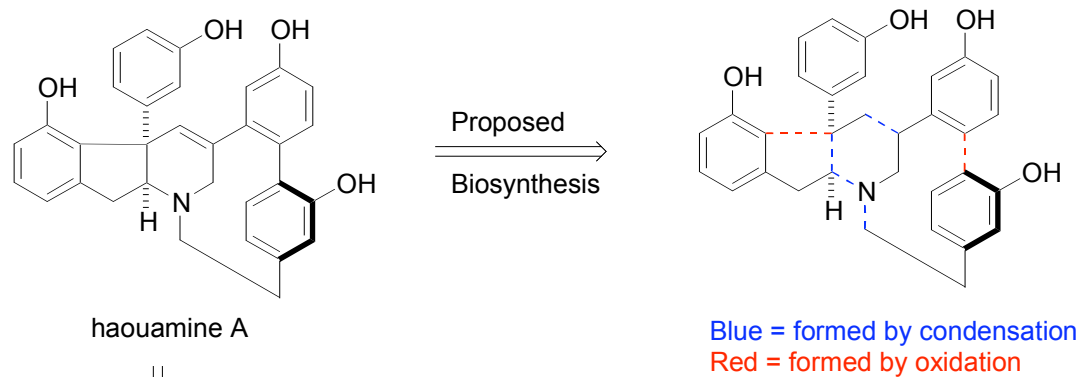
Grundl, M. A.; Trauner, D. *Org. Lett.* **2006**, *8*, 23.

# Trauner's Approach (Cont.)

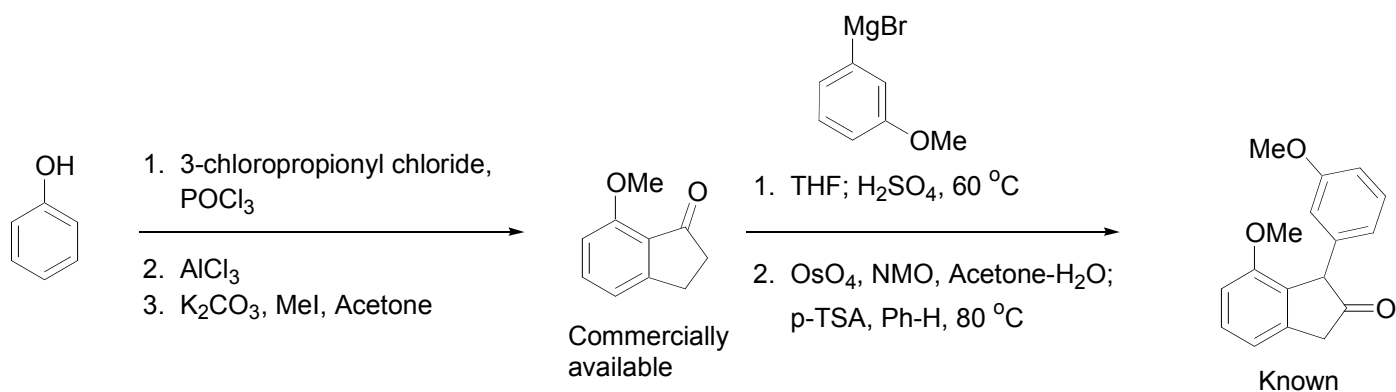
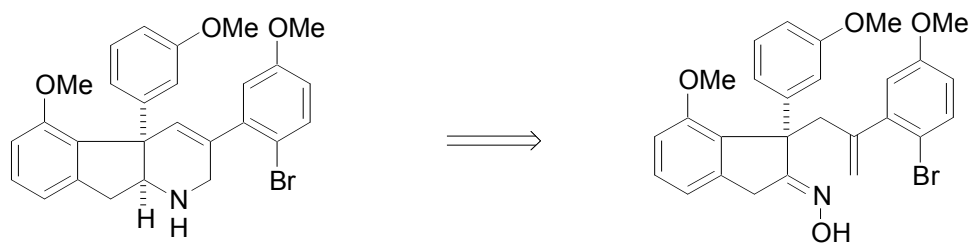
## Friedel-Crafts



# Baran's Total Synthesis

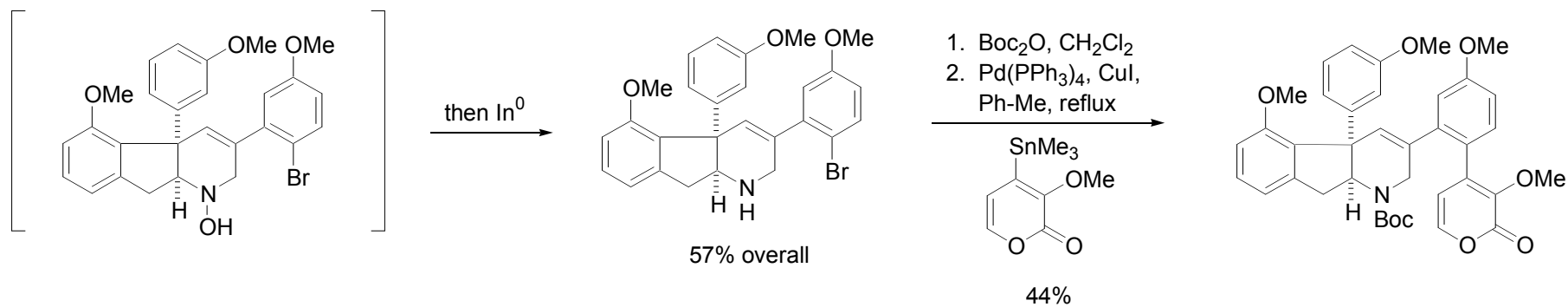
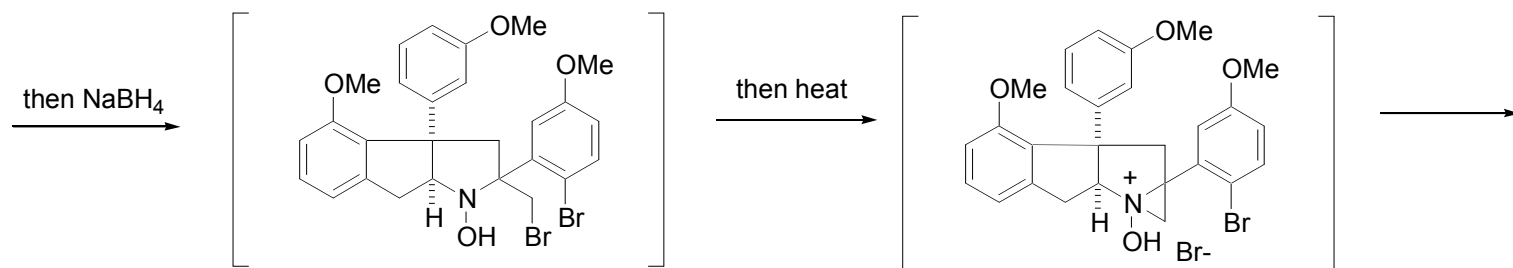
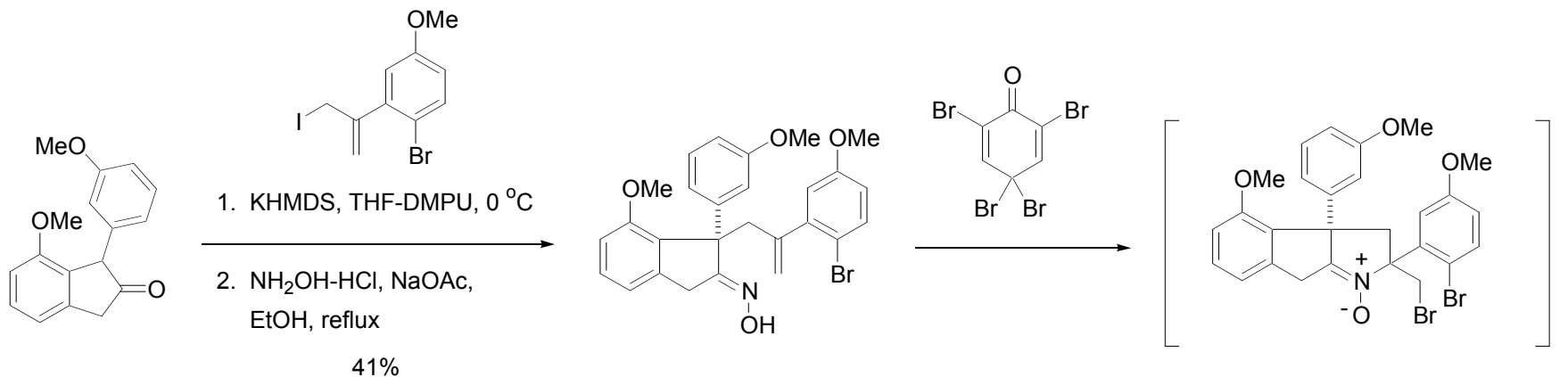


haouamine A

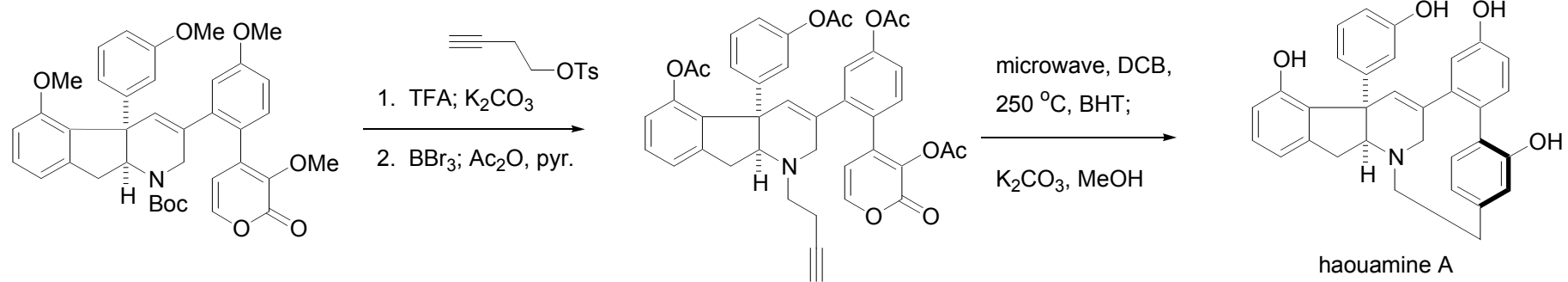


Baran, P. S.; Burns, N. Z. *J. Am. Chem. Soc.* **2006**, *128*, 3908.

# Baran's Total Synthesis (Cont.)

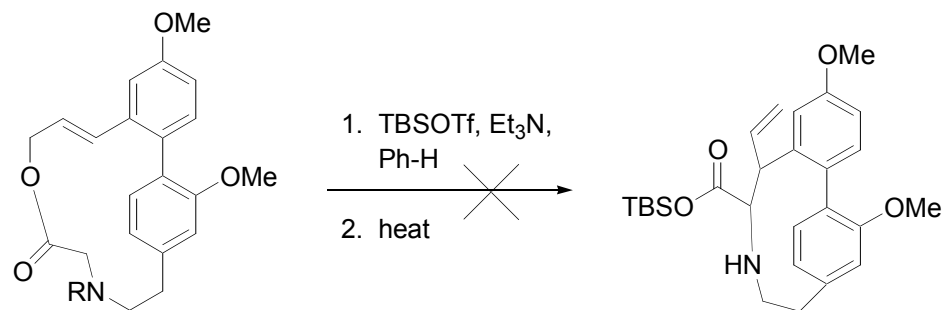
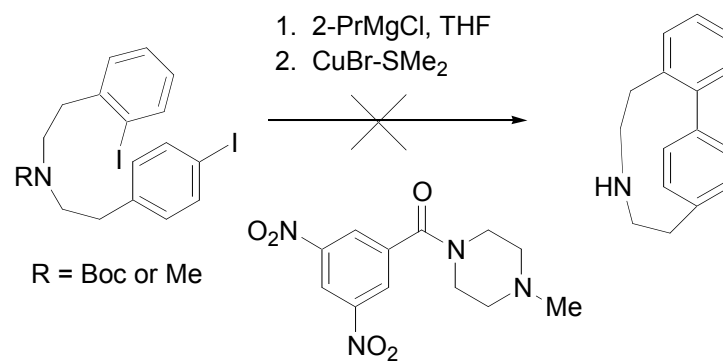
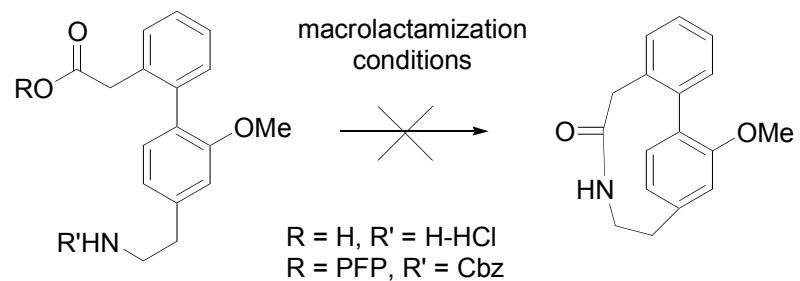


# Baran's Total Synthesis (Cont.)



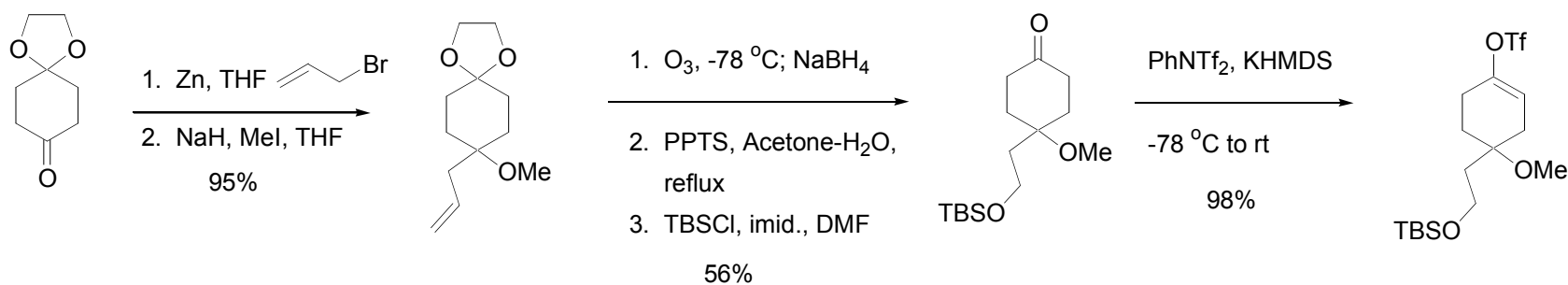
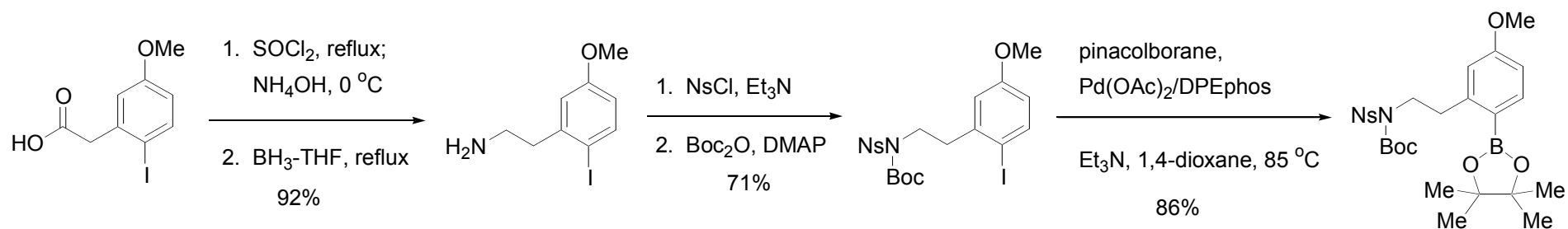
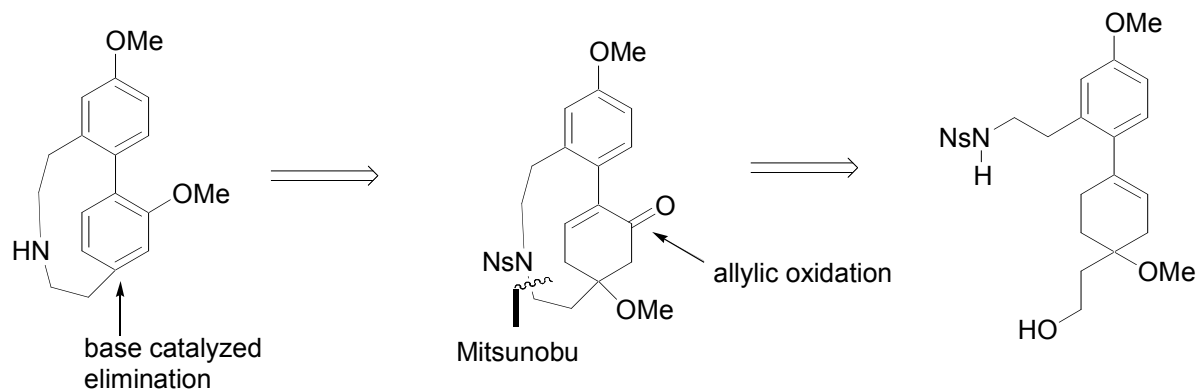
# Wipf's Approach to the Paracyclophane Core

What didn't work?

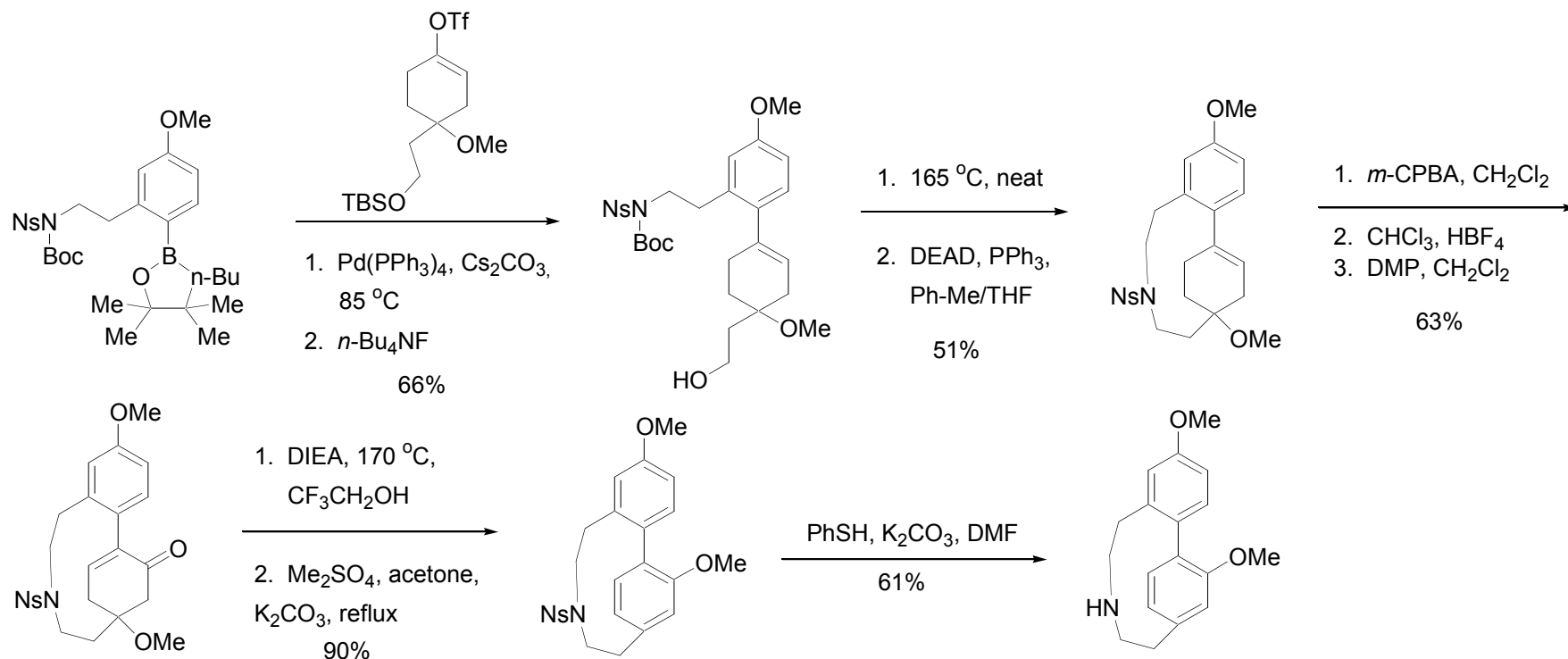


Wipf, P.; Furegati, M. *Org. Lett.* **2006**, *8*, ASAP.

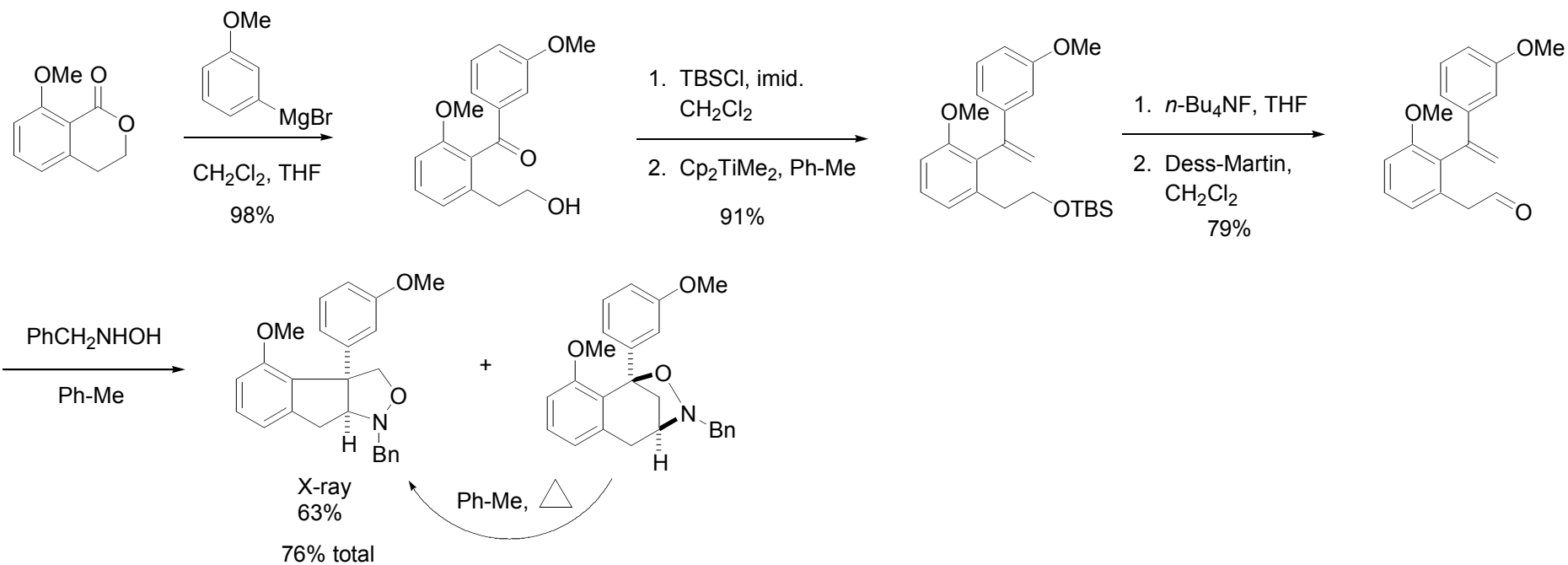
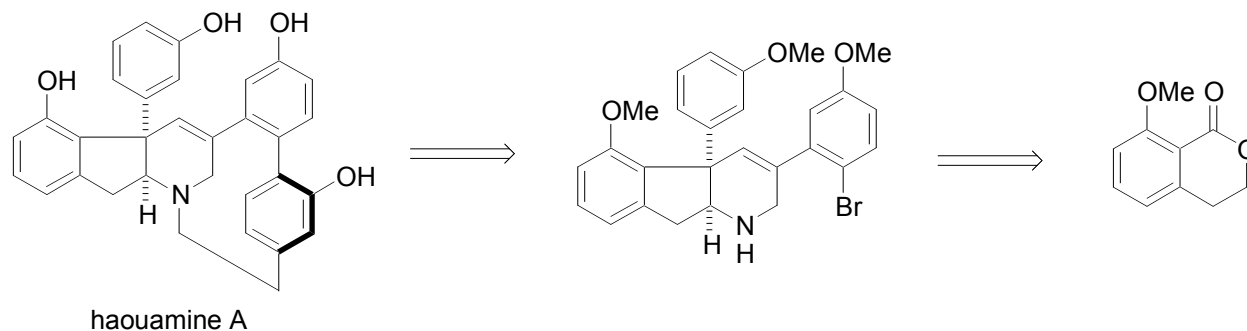
# Wipf's Approach (Cont.)



# Wipf's Approach (Cont.)



# Hot Off the Presses, Weinreb's Approach



Jeong, J. H.; Weinreb, S. M. *Org. Lett.* **2006**, *8*, ASAP

# Weinreb's Formal Synthesis

