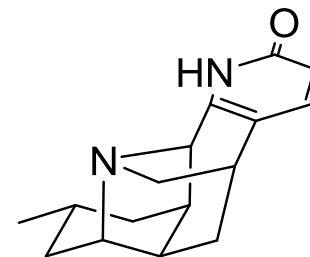
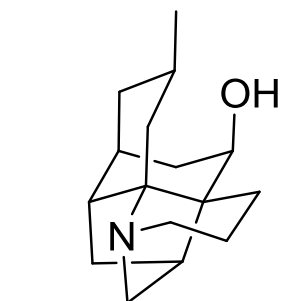
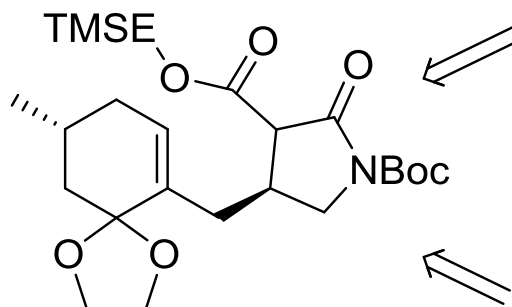
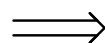
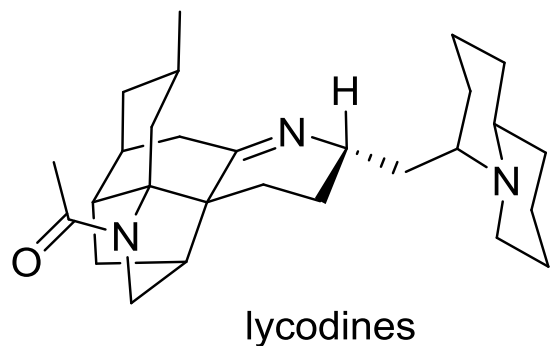


A Unified Approach to *Lycopodium* Alkaloids

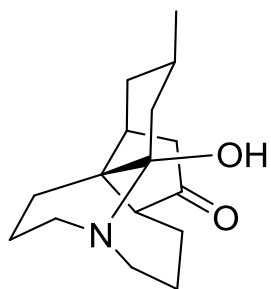


Lee, A. S.; Liao, B. B.; Shair, M. D.
J. Am. Chem. Soc. **2014**, *136*, 13442-13452.

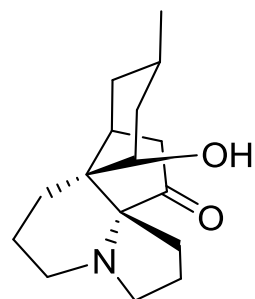
John Milligan
Current Literature

Wipf Group Meeting- October 11, 2014

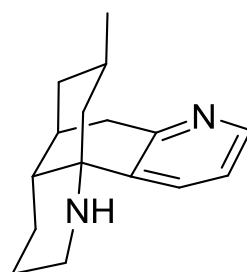
Lycopodium Alkaloids



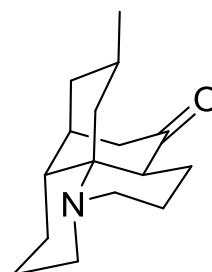
fawcettimine



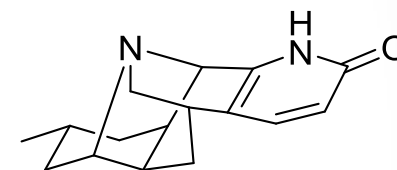
serrantinine



lycodine

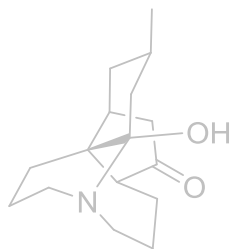


lycopodine

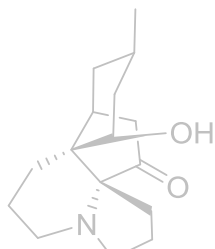


miscellaneous

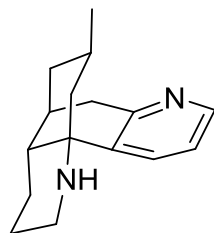
Biological Activity



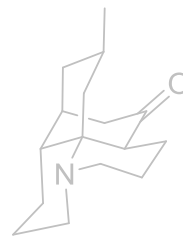
fawcettimine



serrantinine



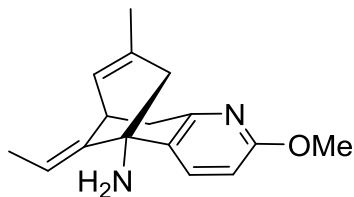
lycodine



lycopodine

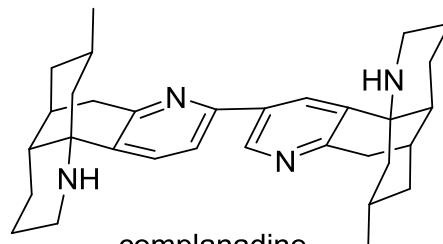


miscellaneous



huperzine A

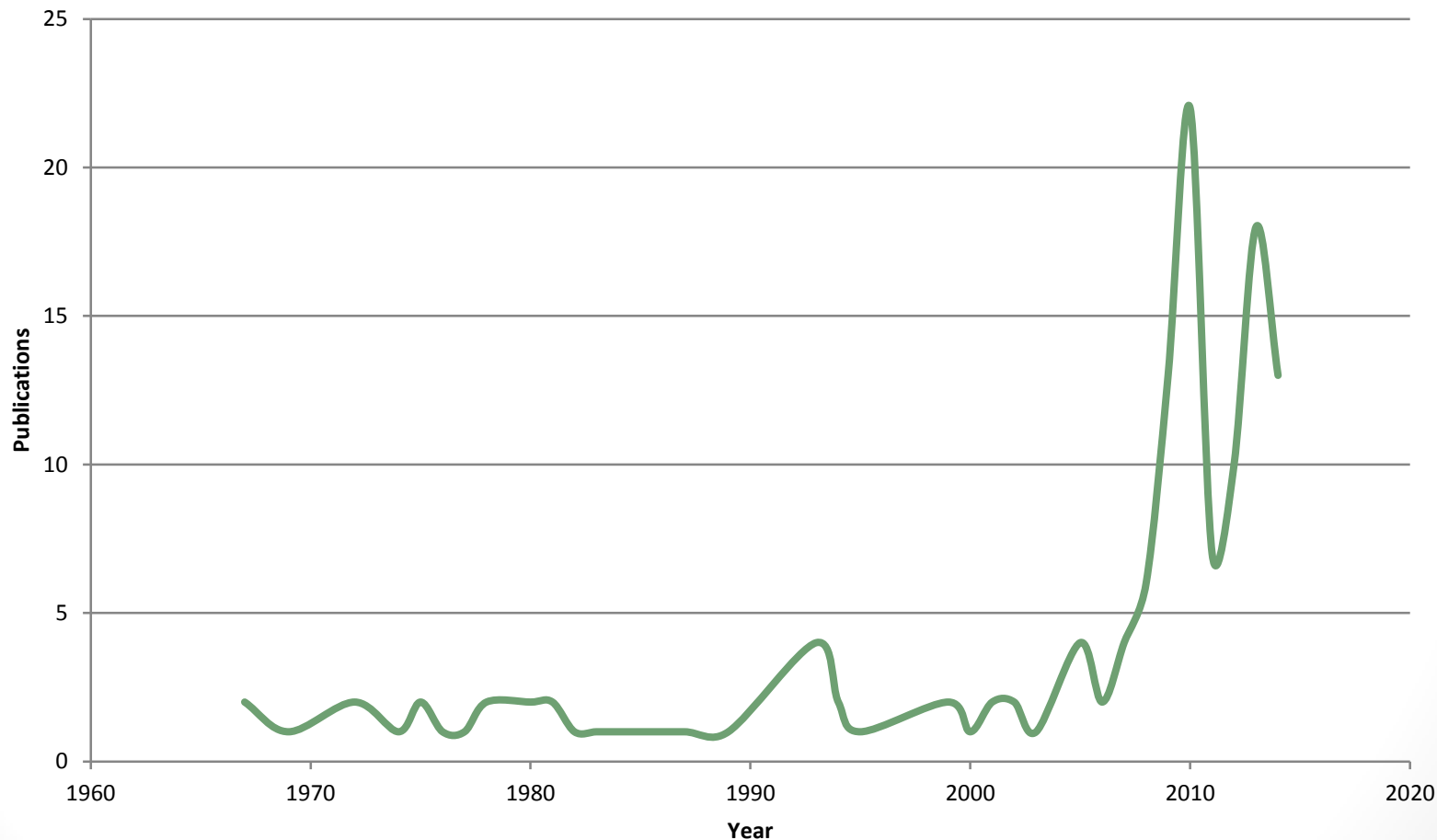
acetylcholine esterase
IC₅₀: 82 nmol



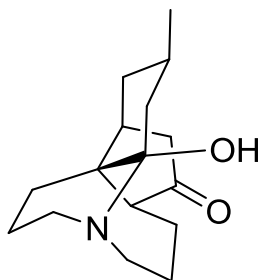
complanadine

promotes secretion
of neurotrophic factors

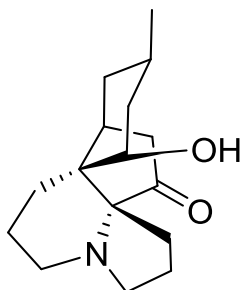
Total synthesis of *Lycopodium* alkaloids



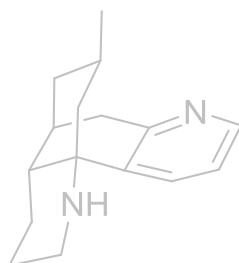
Multi-type “unified strategies”



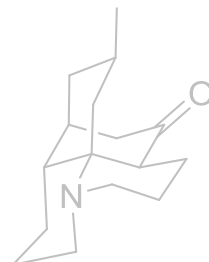
fawcettimine



serrantinine



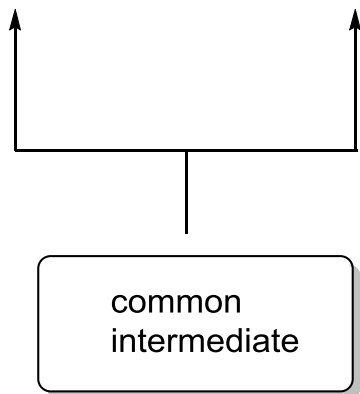
lycodine



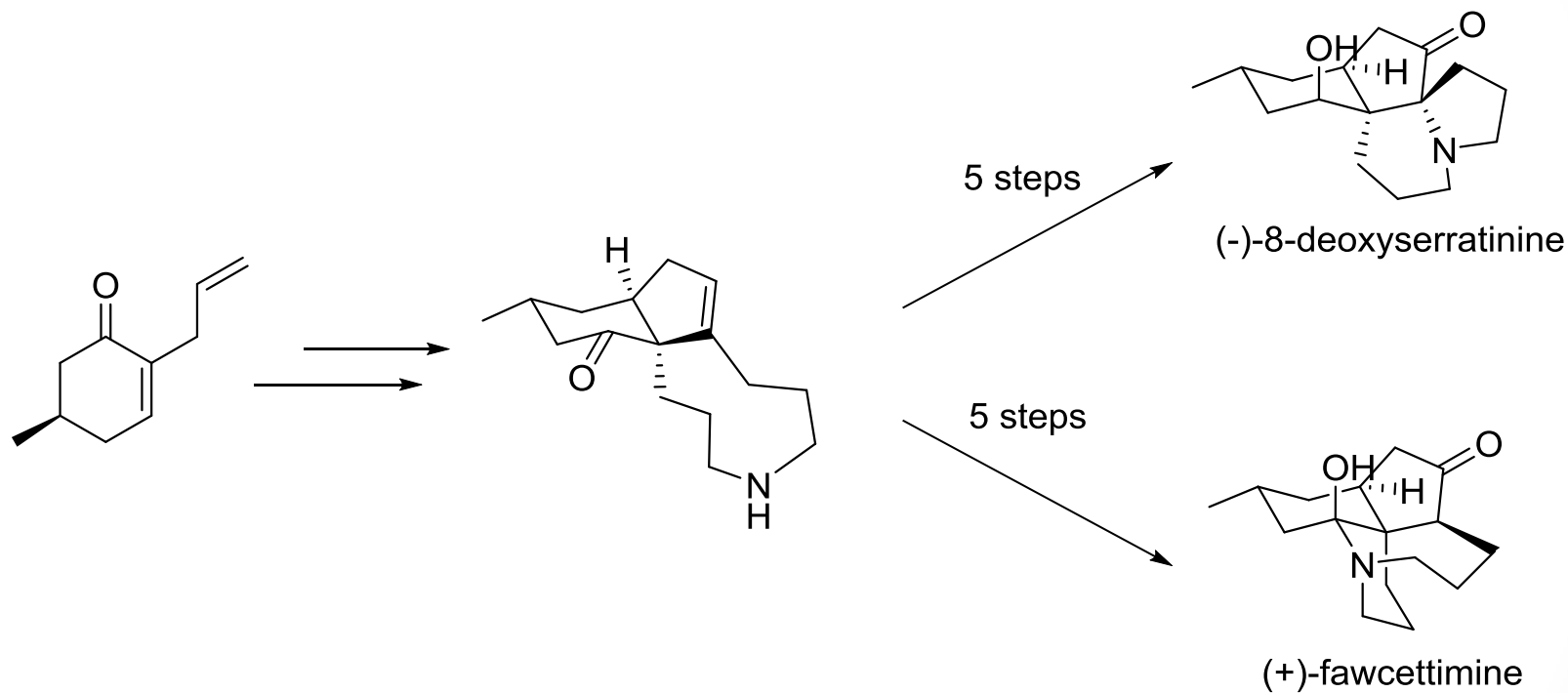
lycopodine



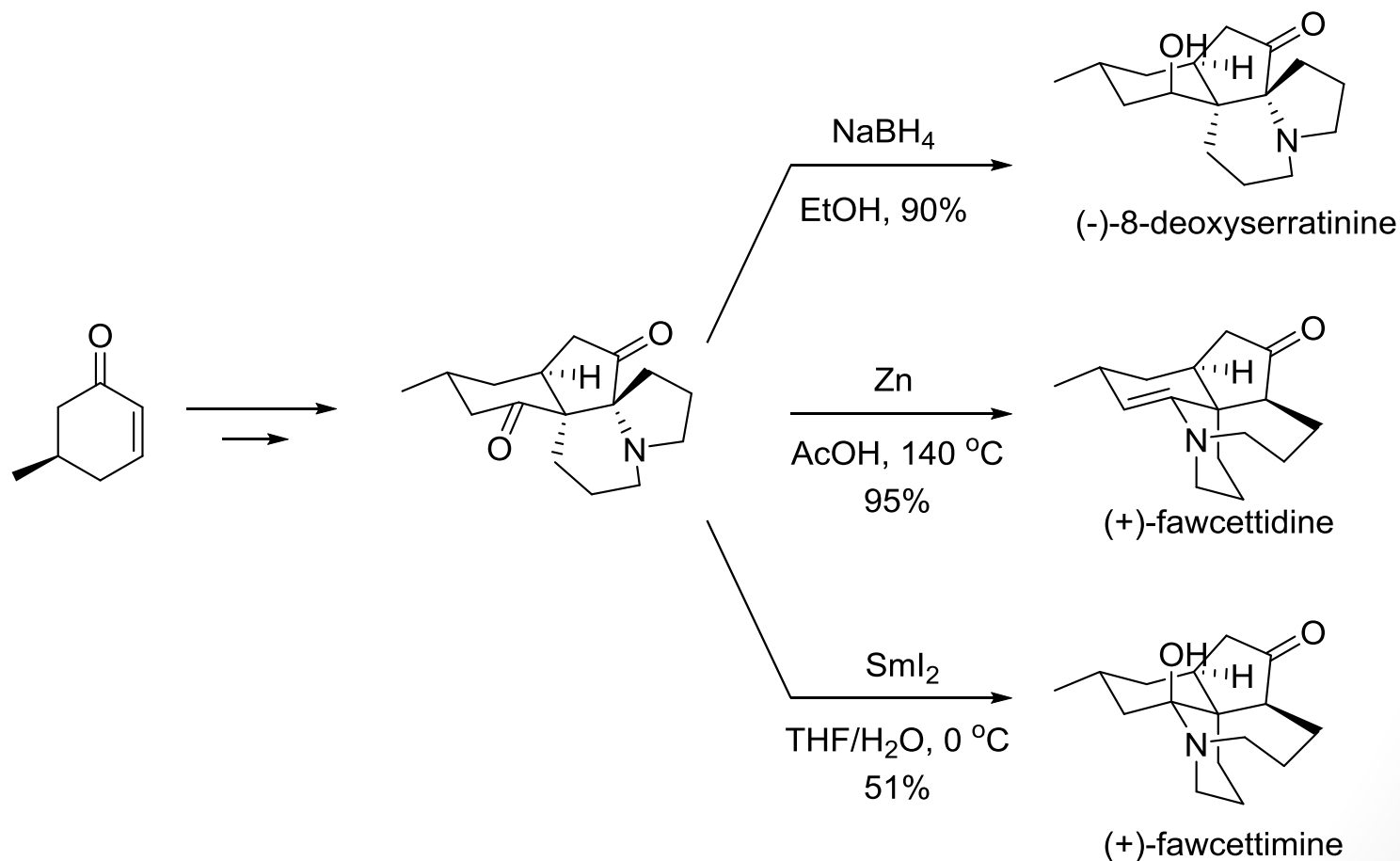
miscellaneous



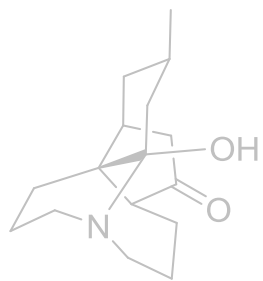
Multi-type “unified strategies”



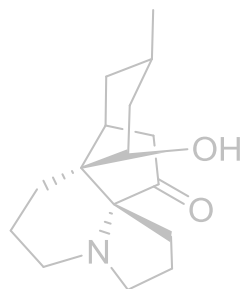
Multi-type “unified strategies”



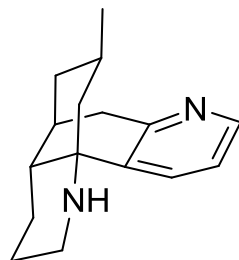
A diverse unified strategy?



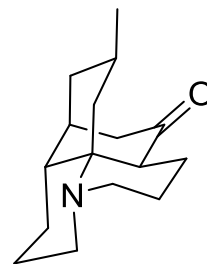
fawcettimine



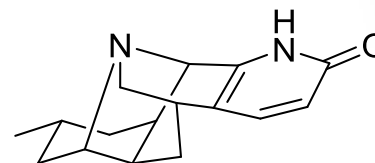
serrantinine



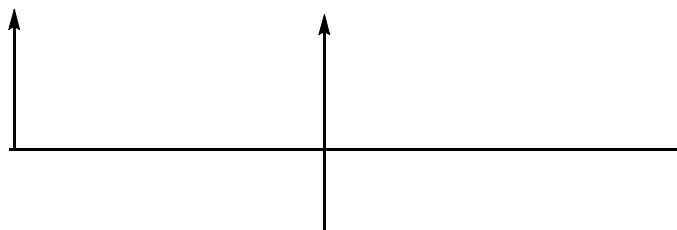
lycodine



lycopodine



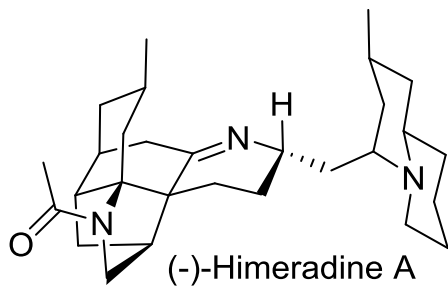
miscellaneous



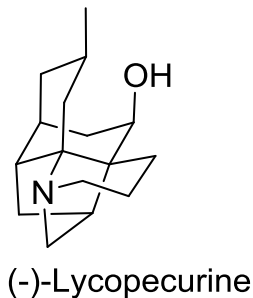
common
intermediate

A diverse unified strategy?

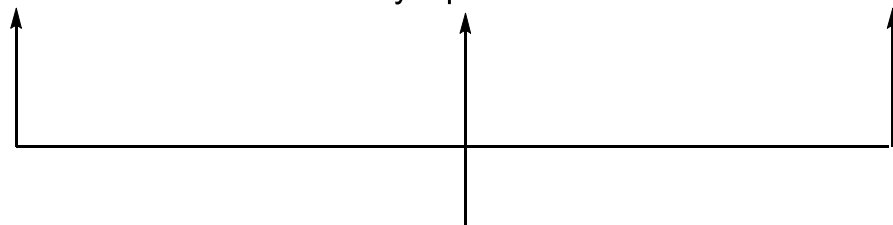
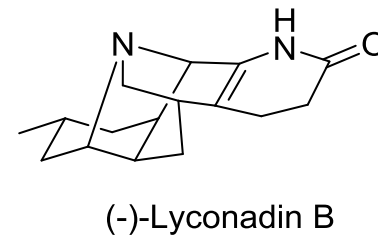
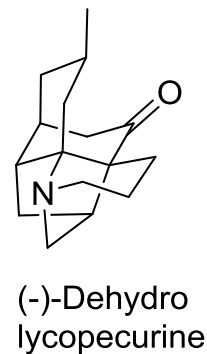
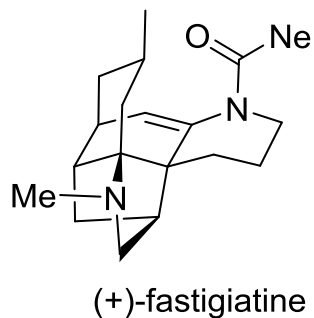
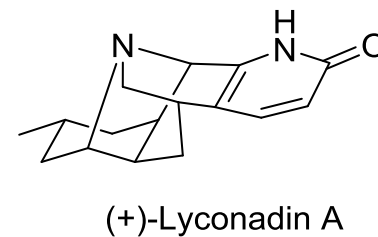
lycodine



lycopodine



miscellaneous

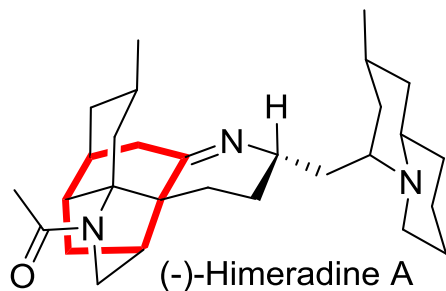


common
intermediate

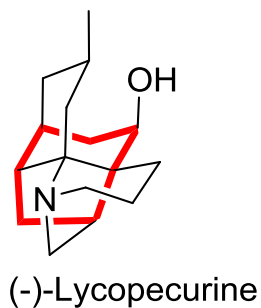
Page 9 of 34

A diverse unified strategy?

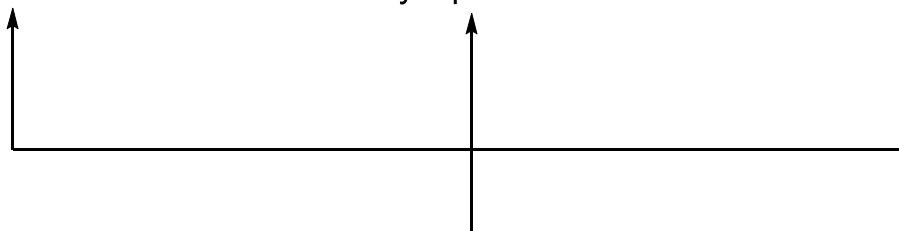
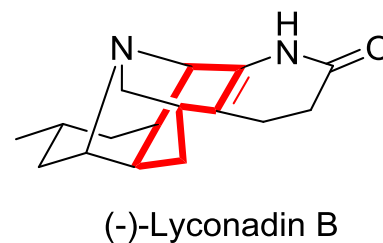
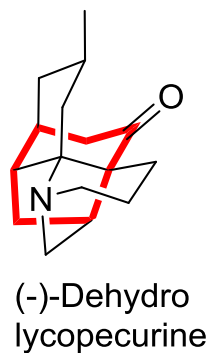
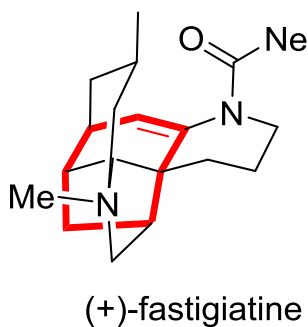
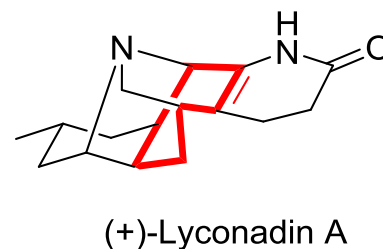
lycodine



lycopodine

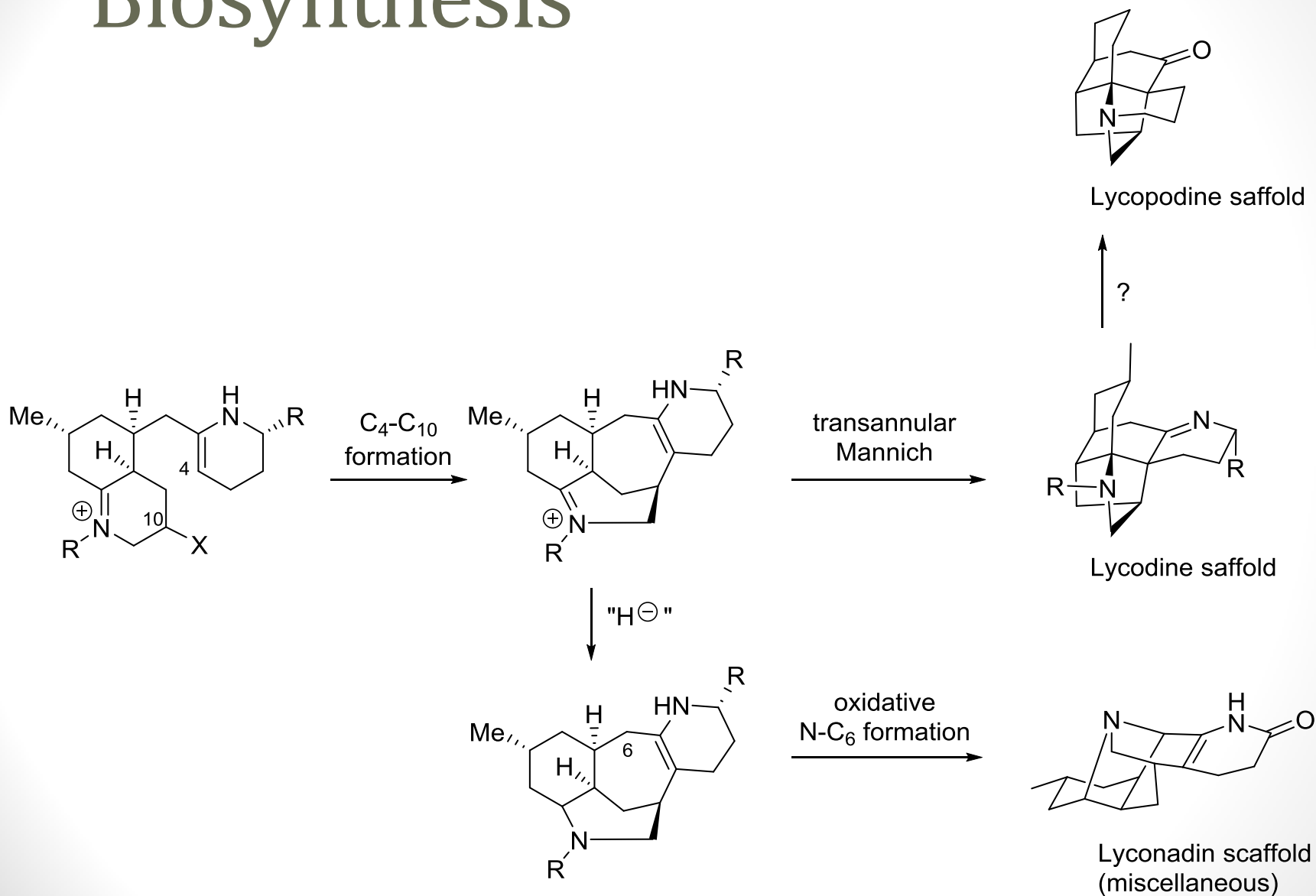


miscellaneous

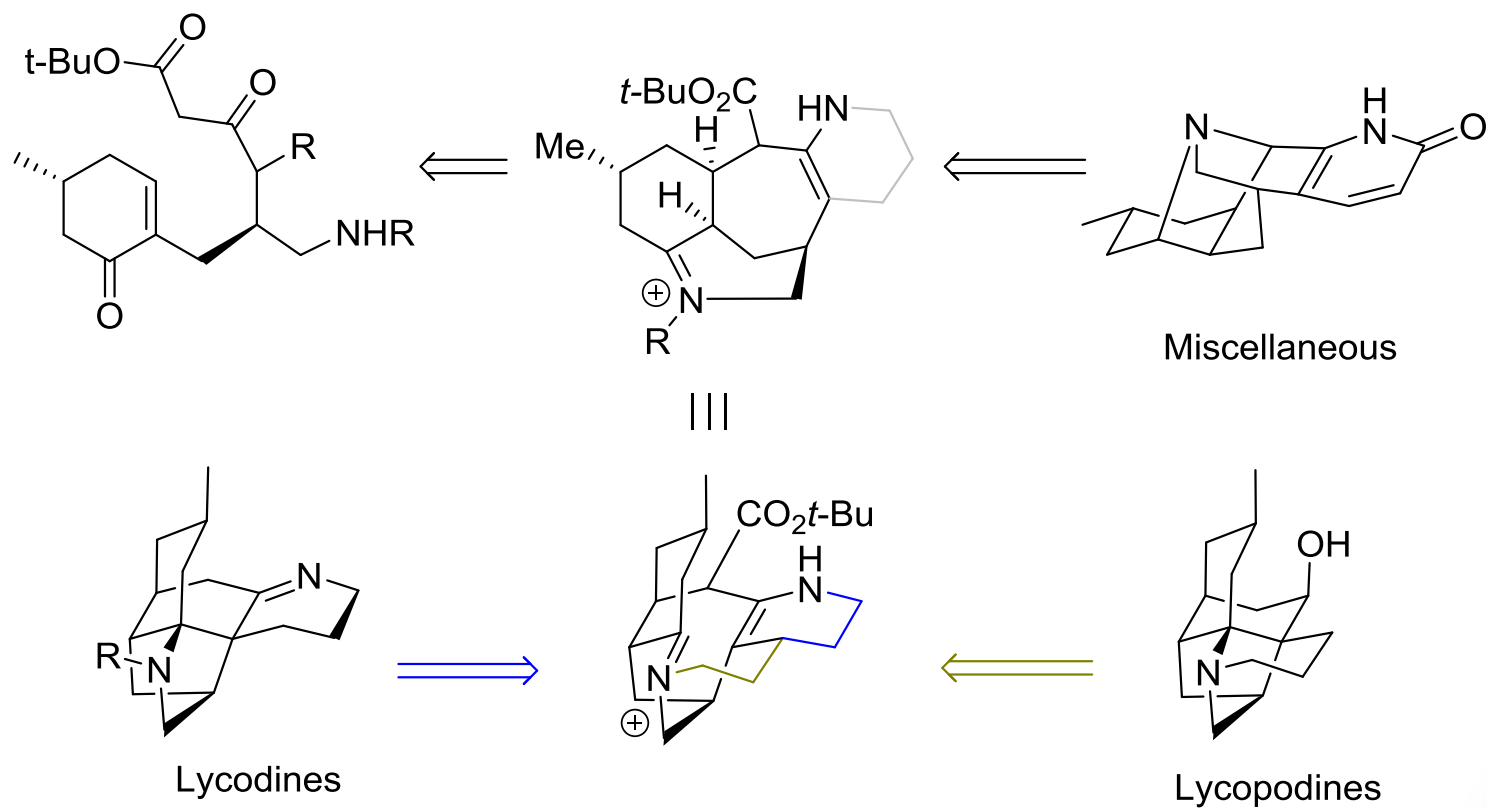


common
intermediate

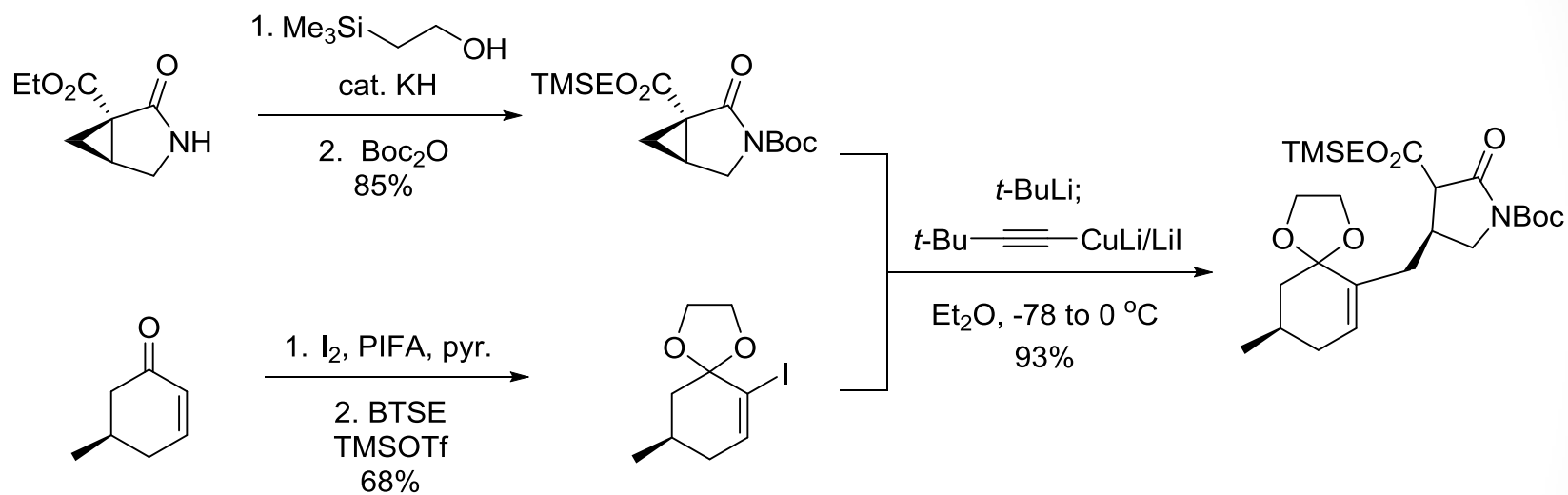
Biosynthesis



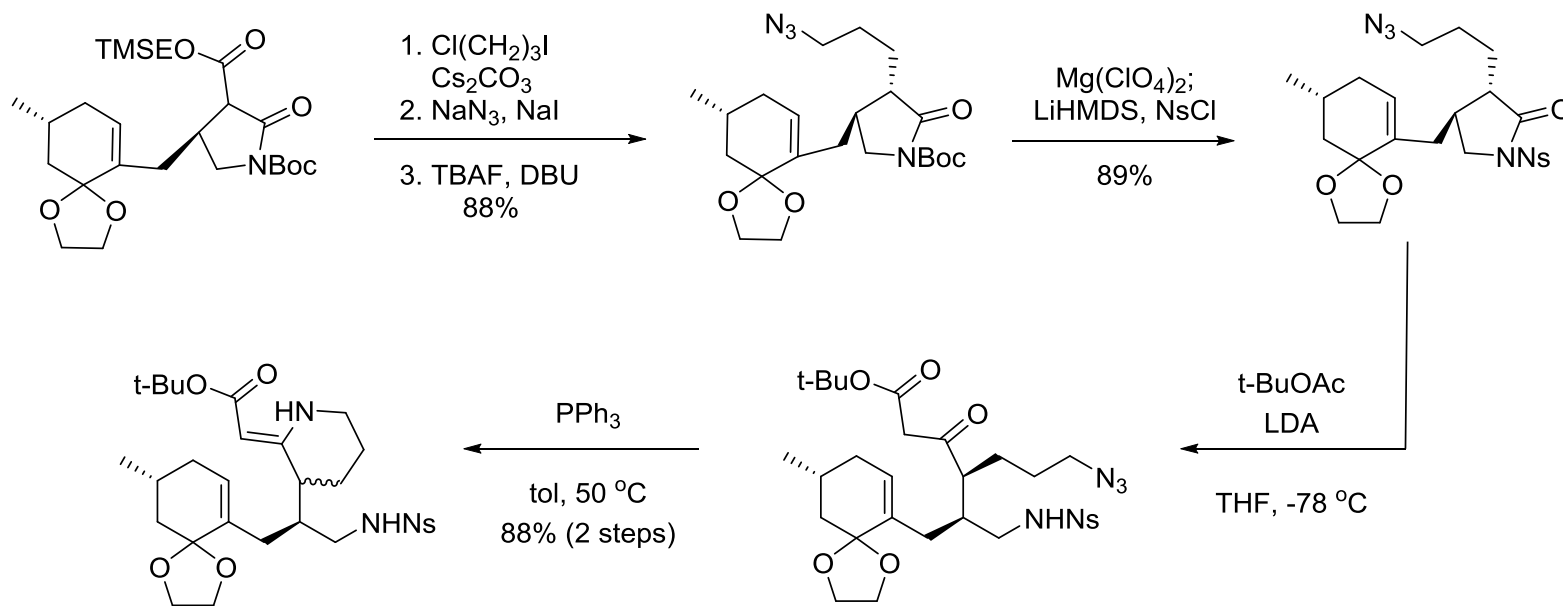
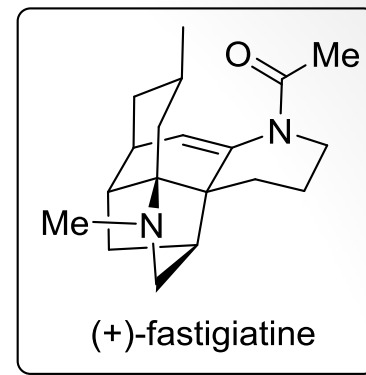
Biomimetic retrosynthesis



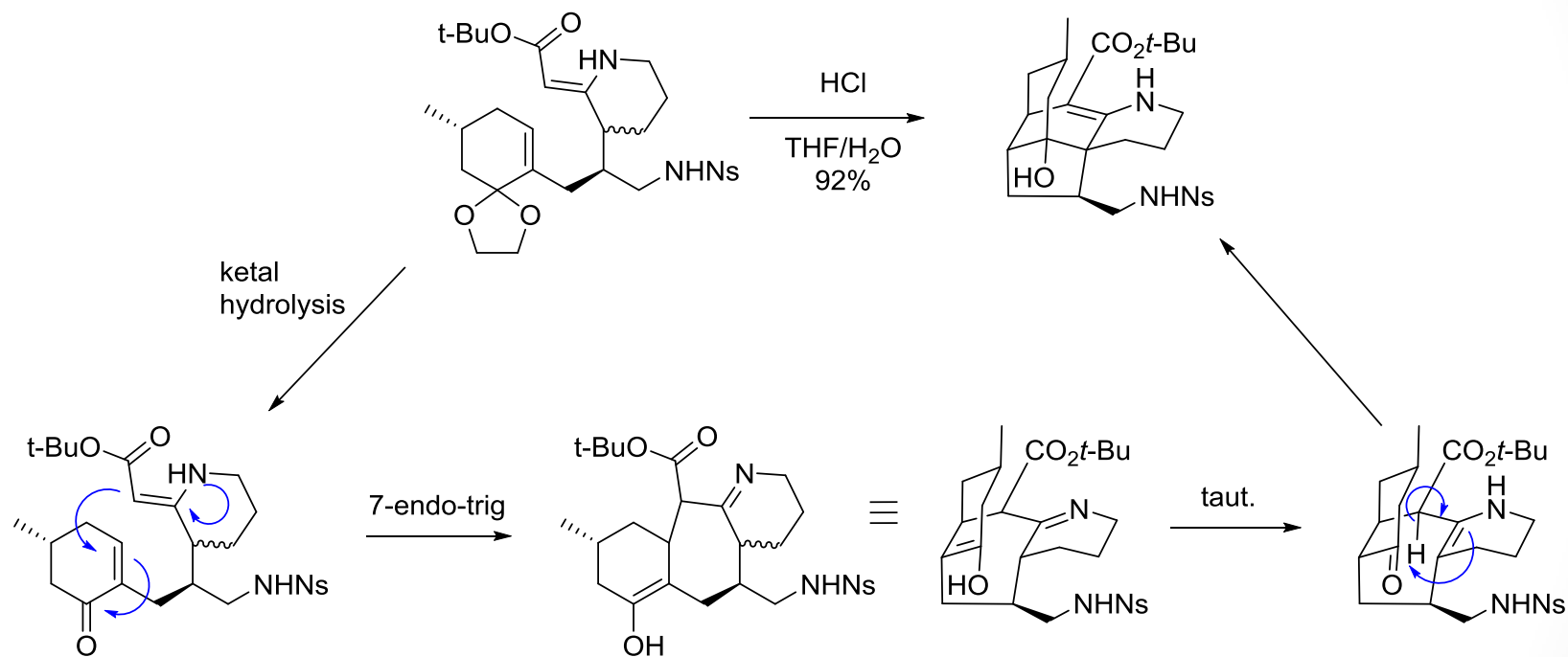
Common intermediate



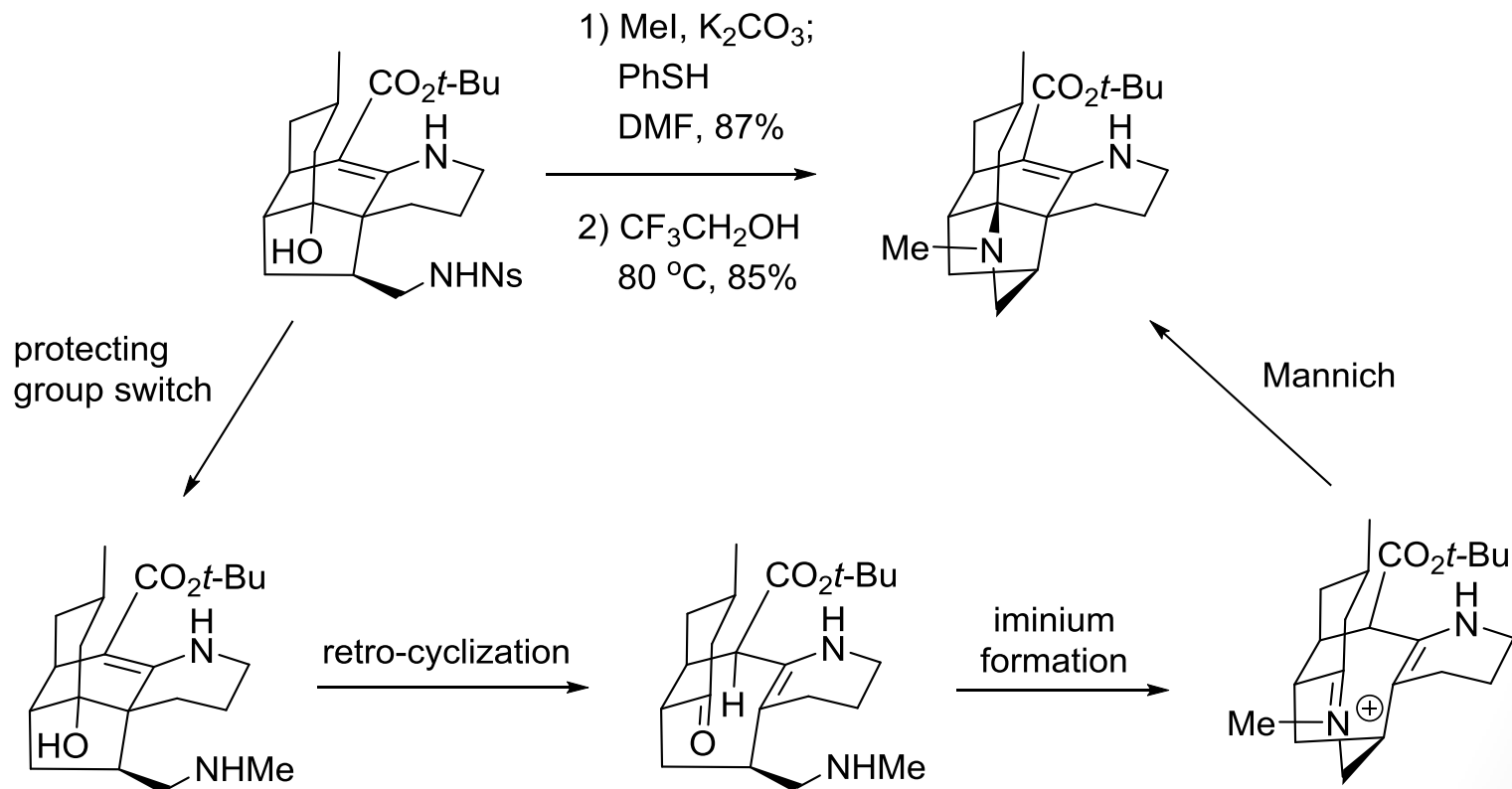
(+)-Fastigiatine



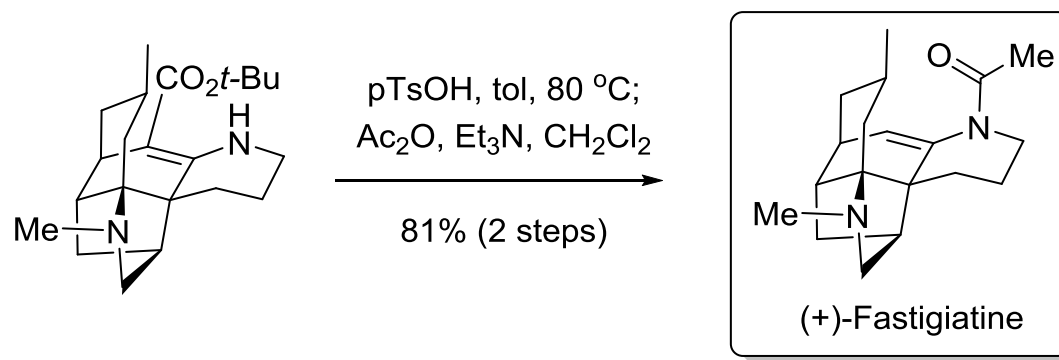
(+)-Fastigiatine



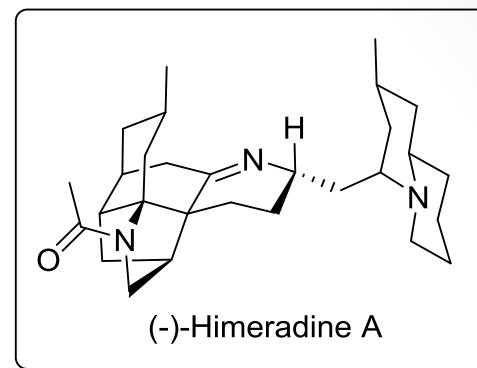
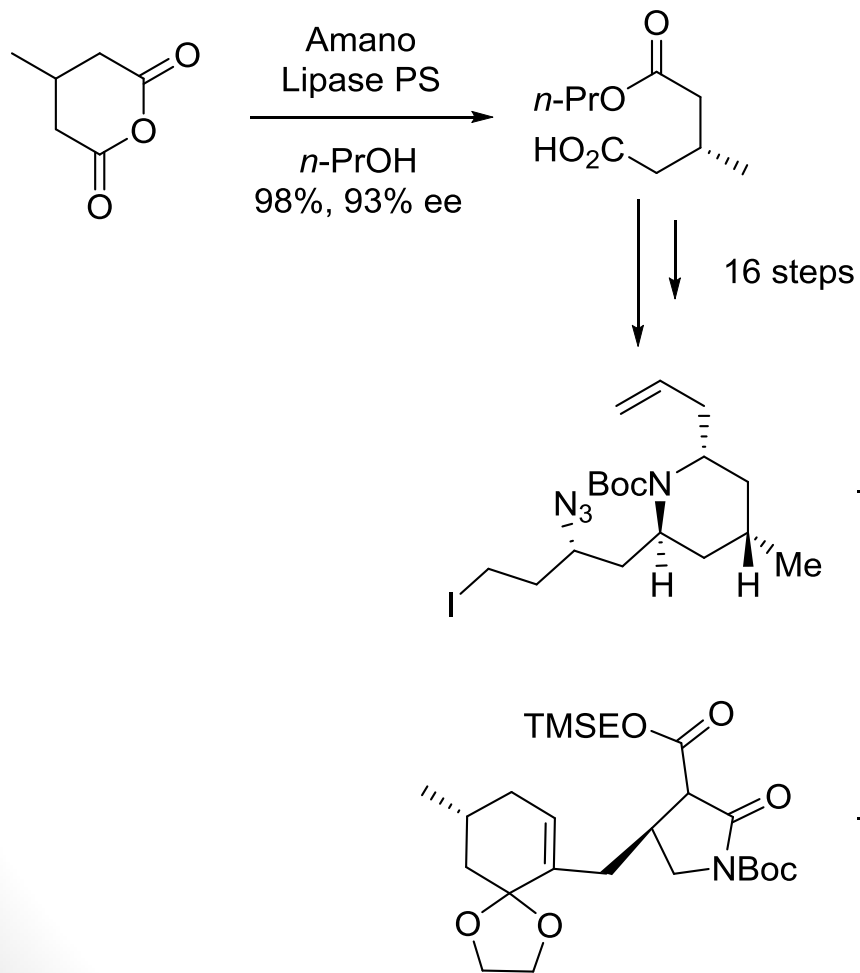
(+)-Fastigiatine



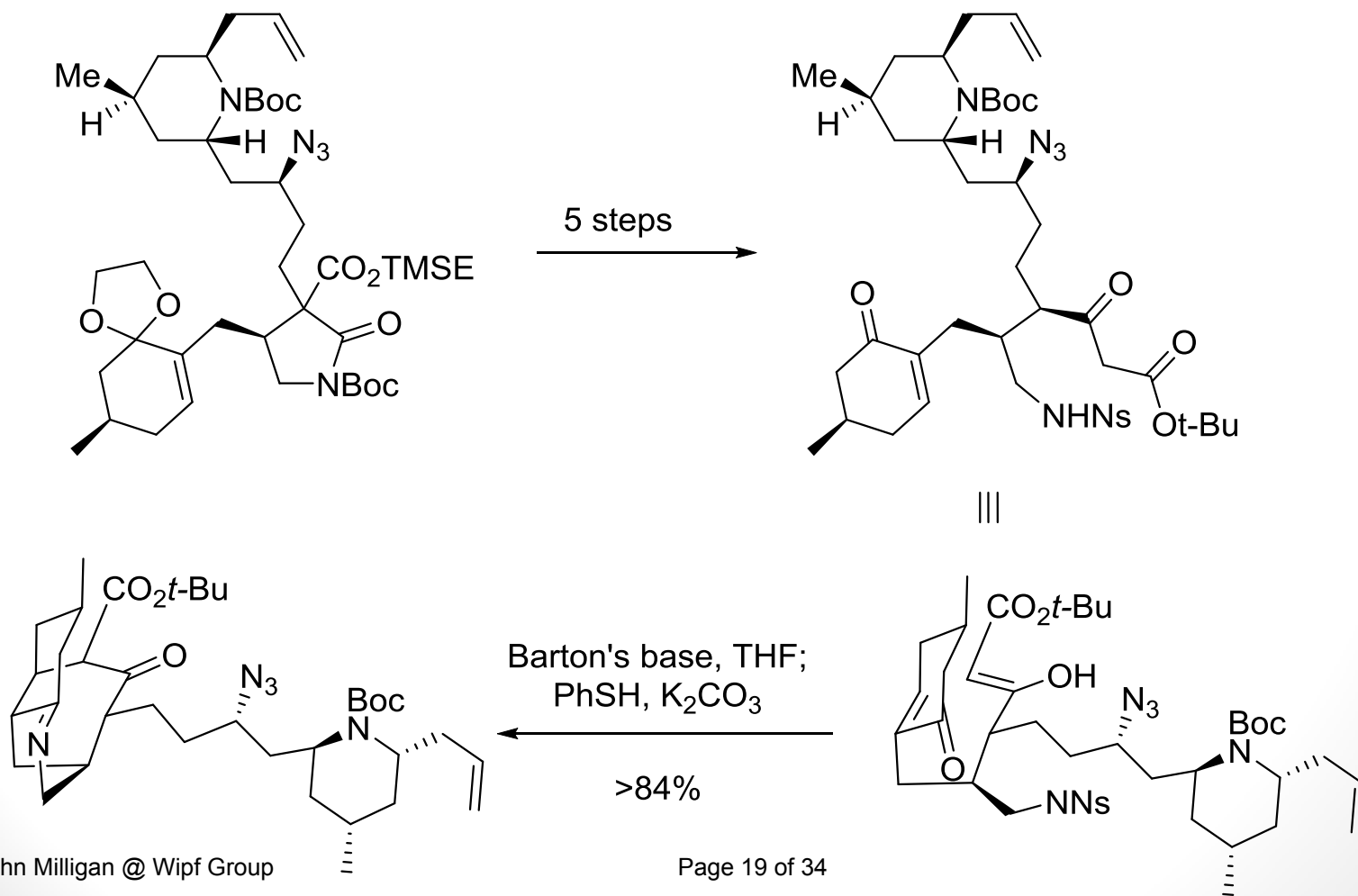
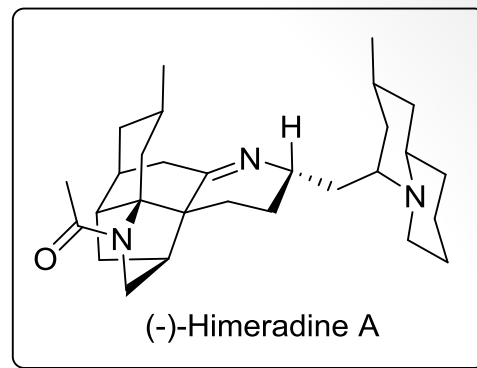
(+)-Fastigiatine



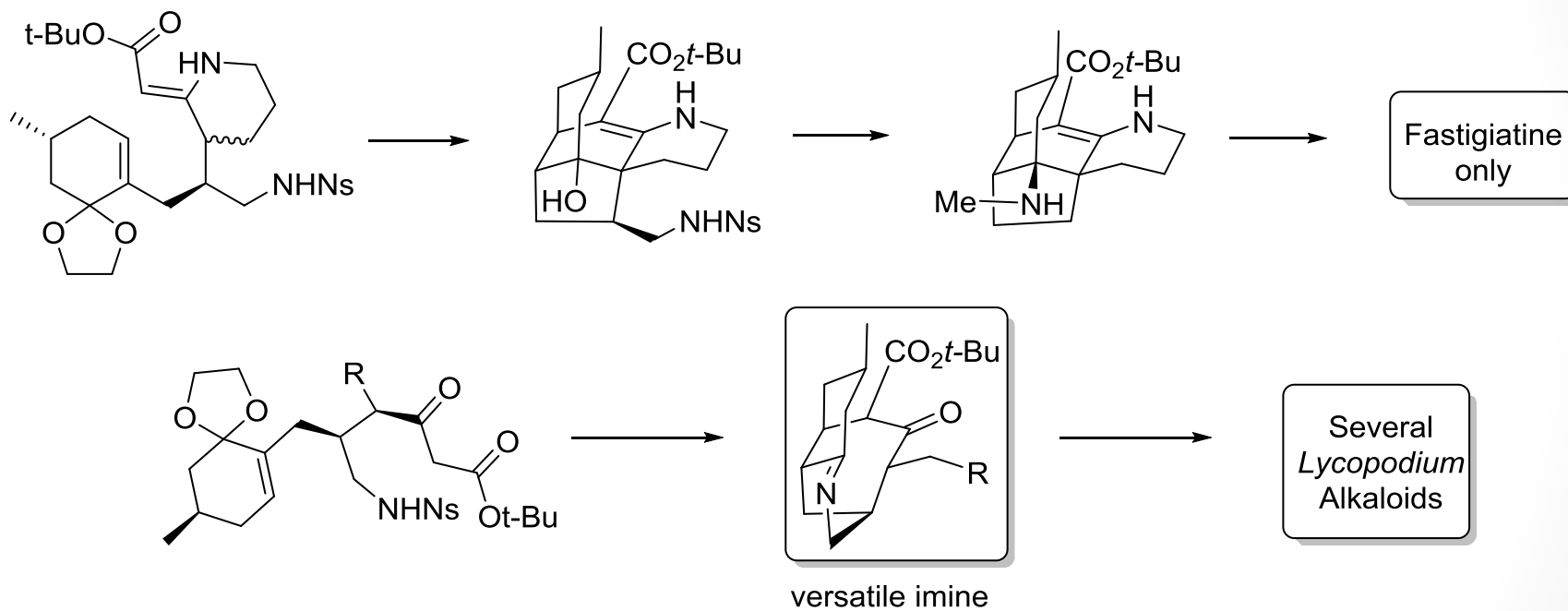
(-)-Himeradine A



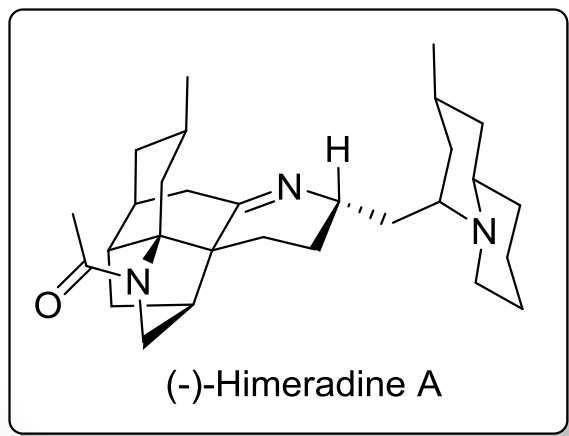
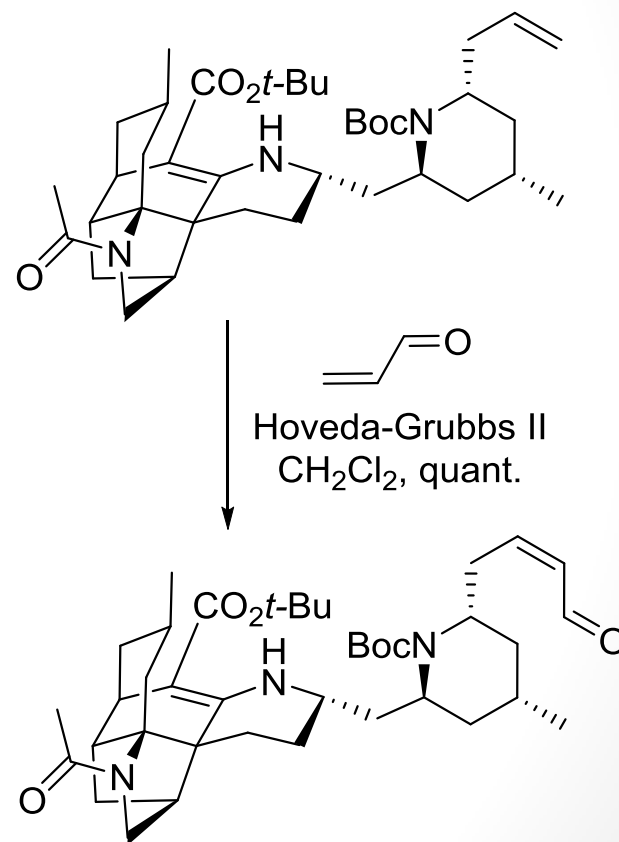
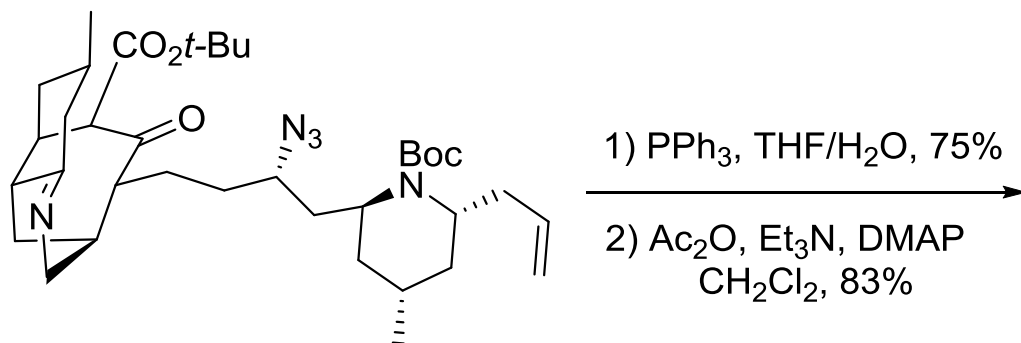
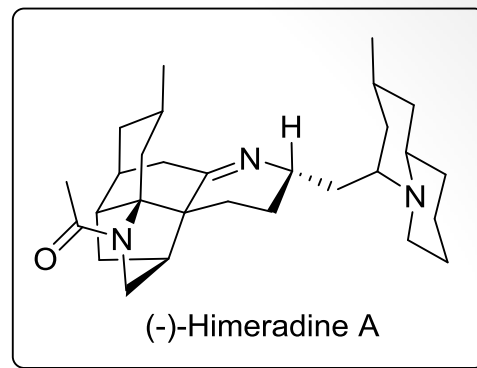
(-)-Himeradine A



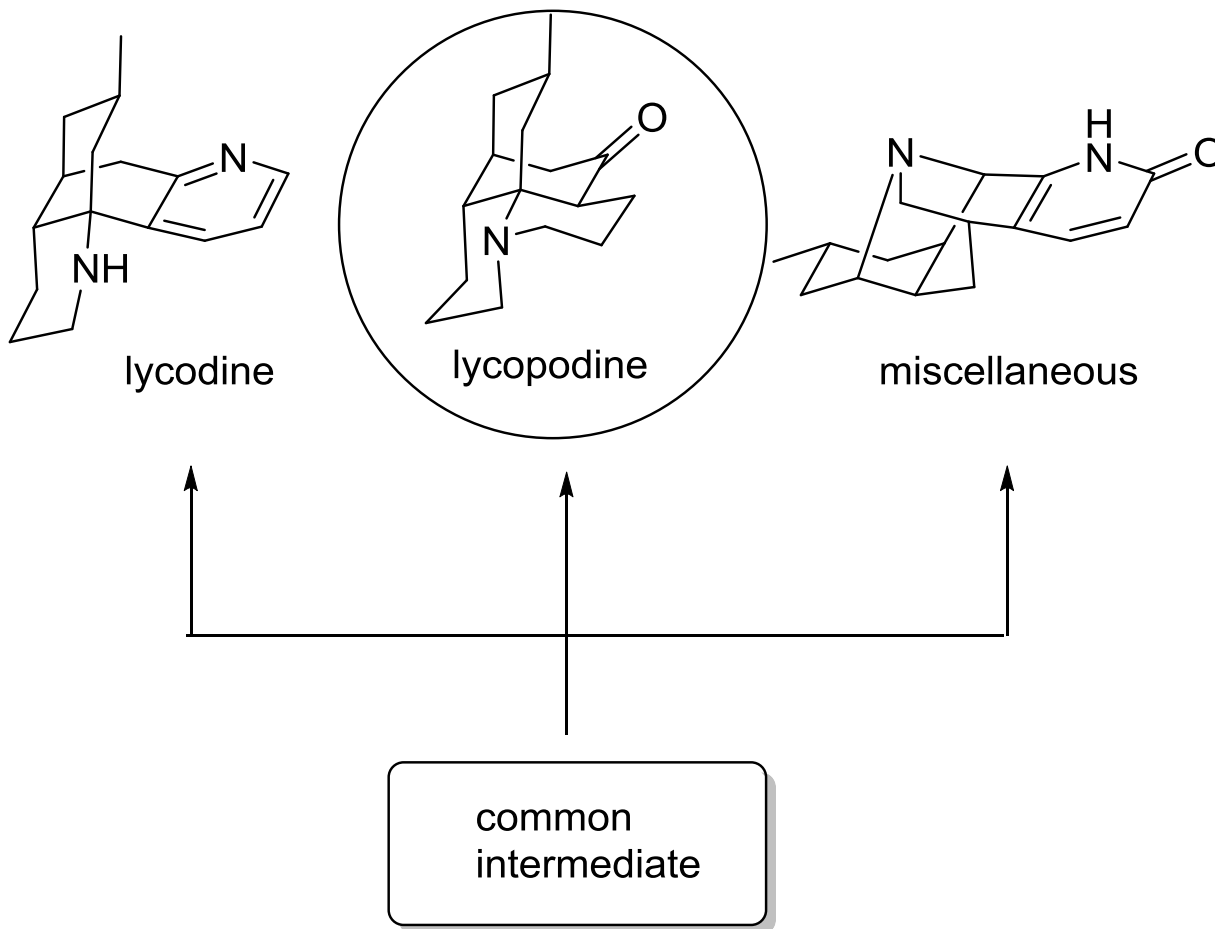
Comparison



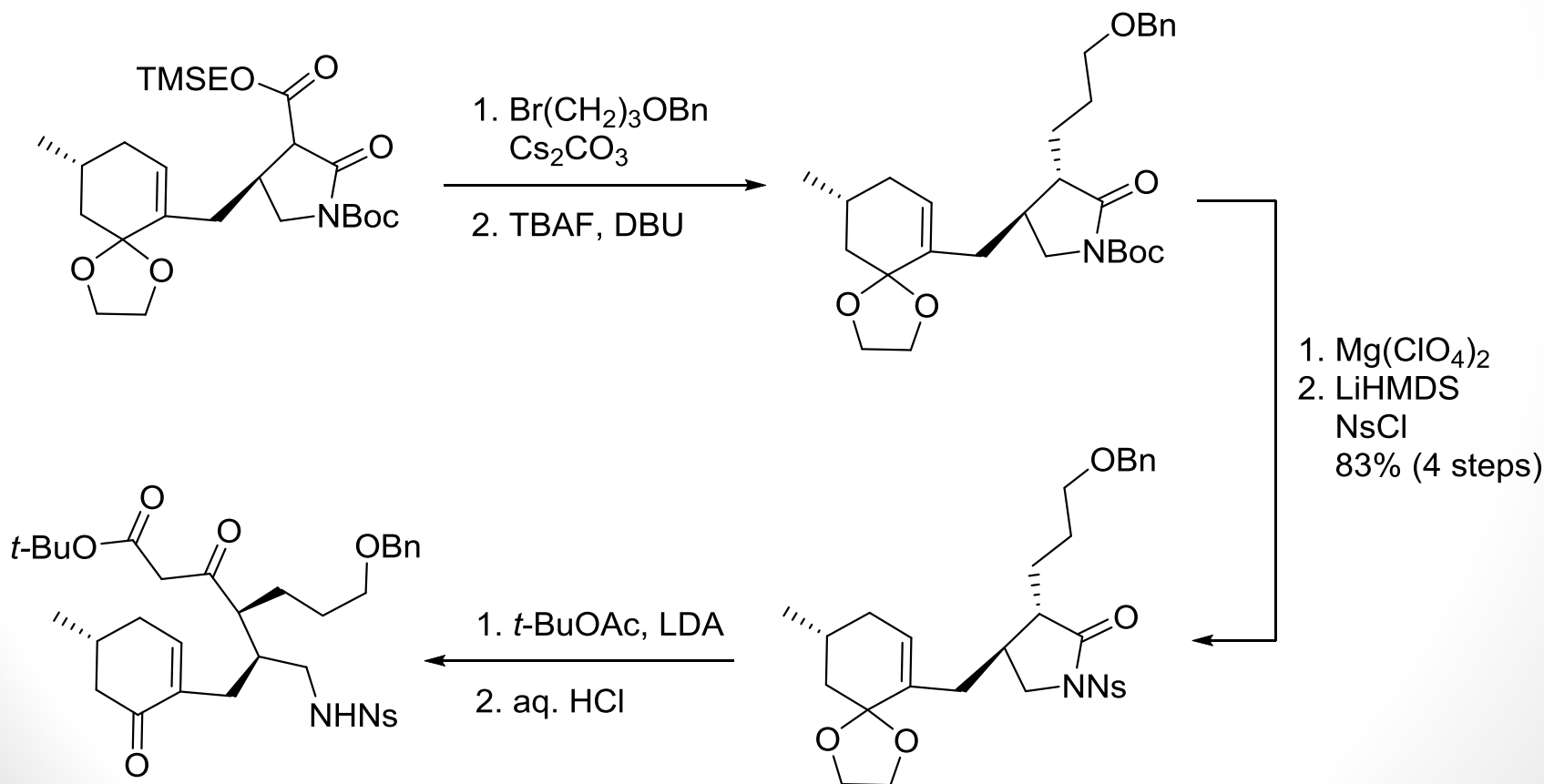
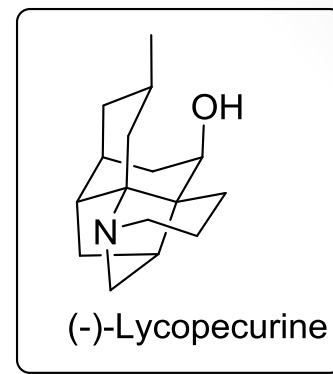
(-)-Himeradine A



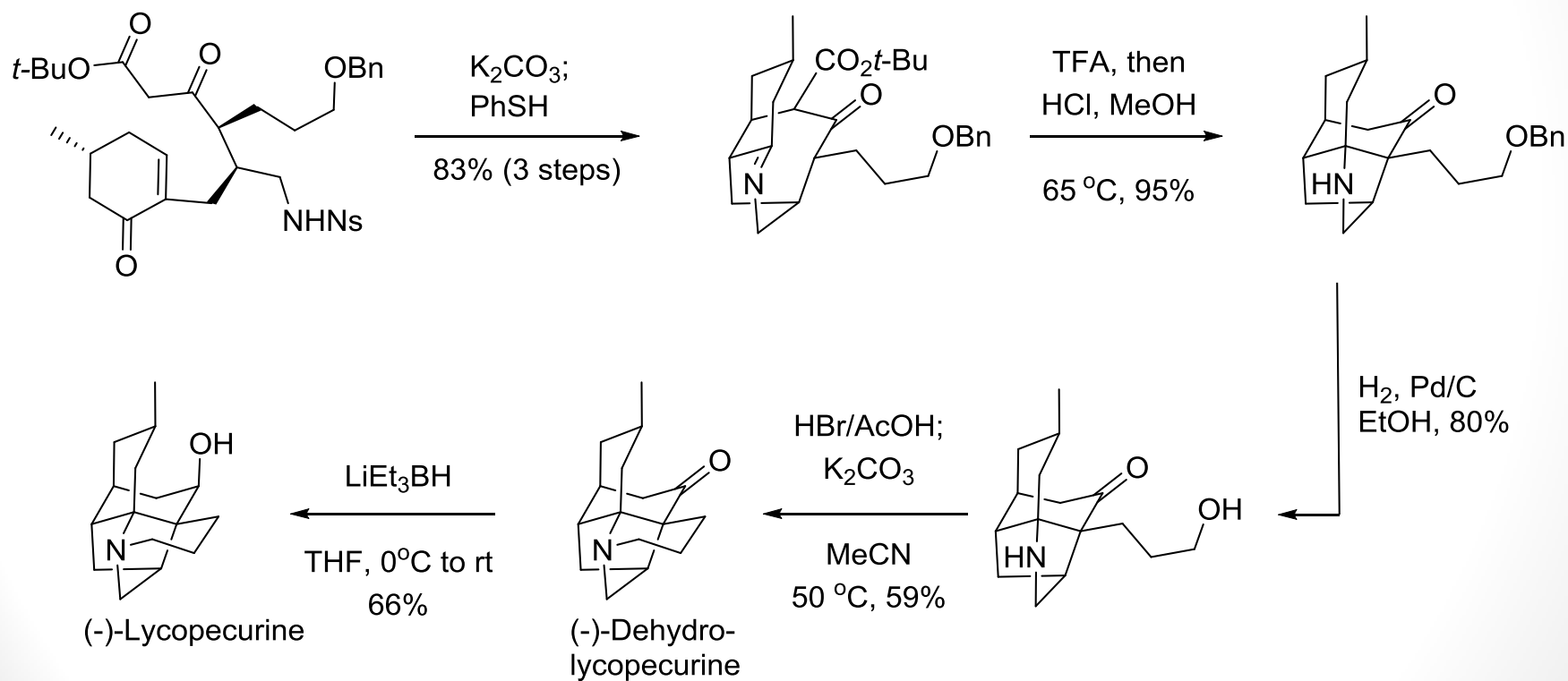
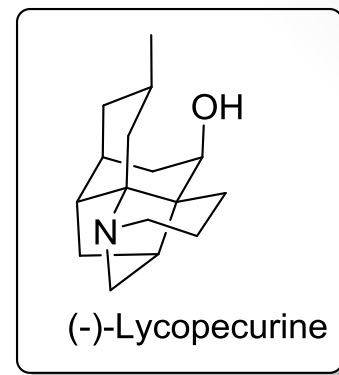
6 steps

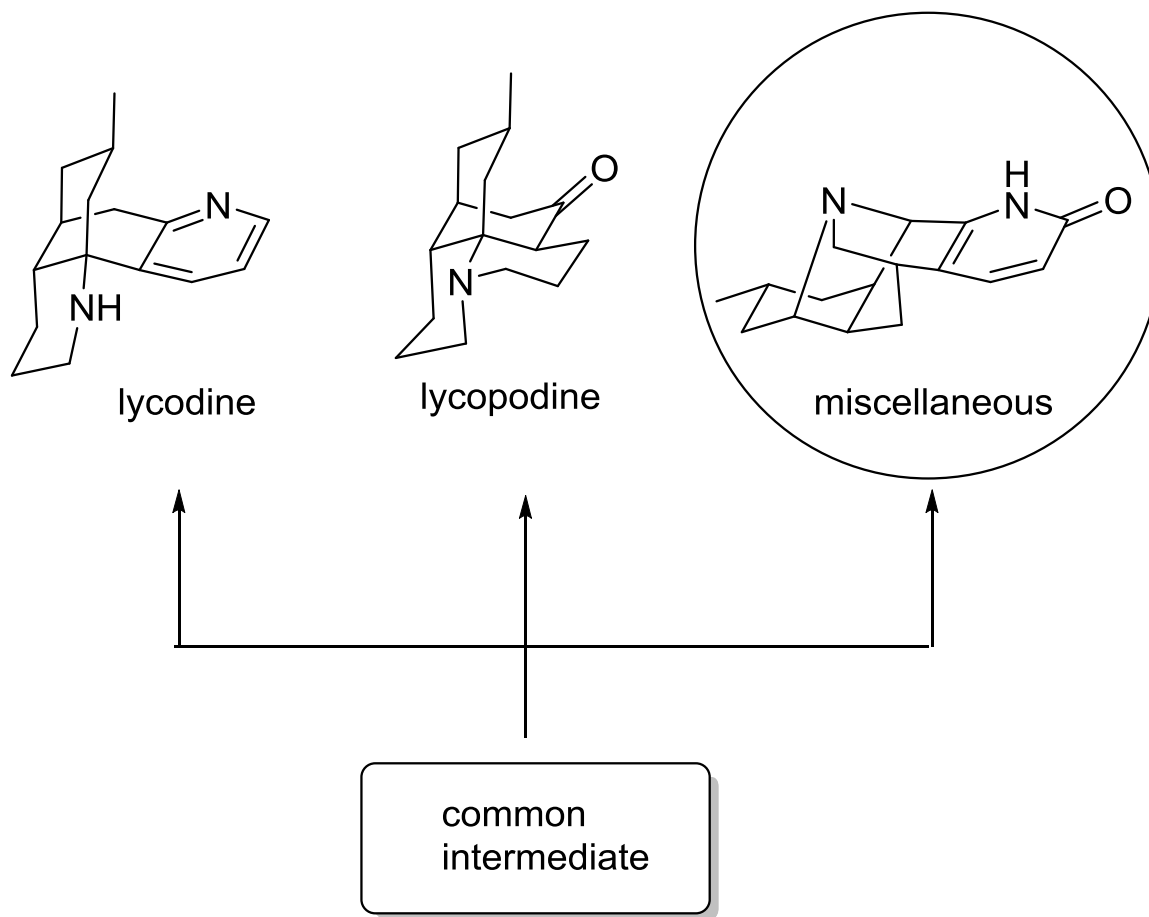


(-)-Lycopecurine

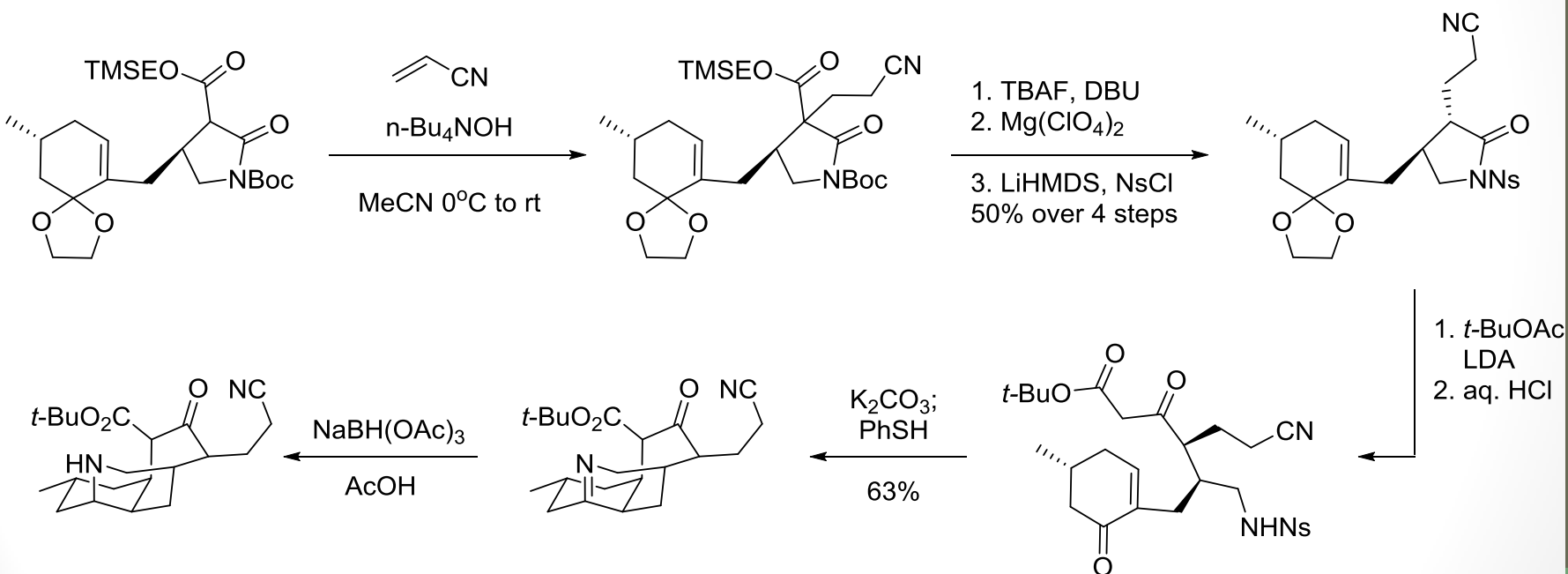
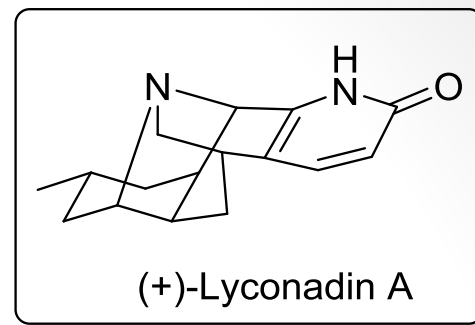


(-)-Lyclopecurine

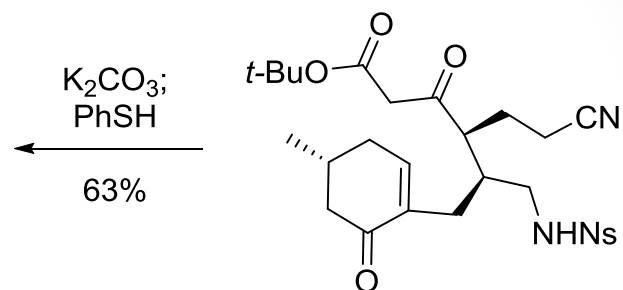
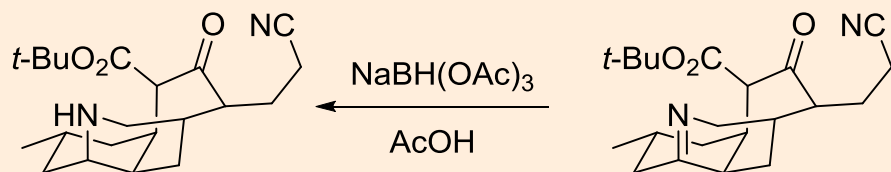




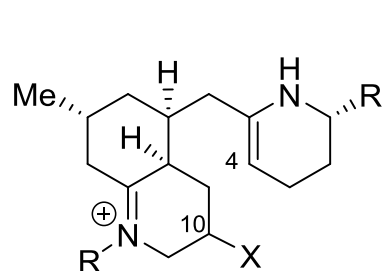
Lyconadin A



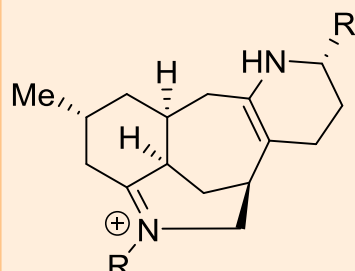
Lyconadin A



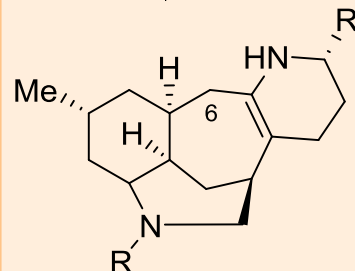
Biosynthesis:



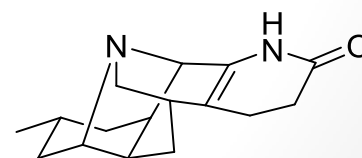
$\text{C}_4\text{-C}_{10}$
 formation



"H[⊖]"

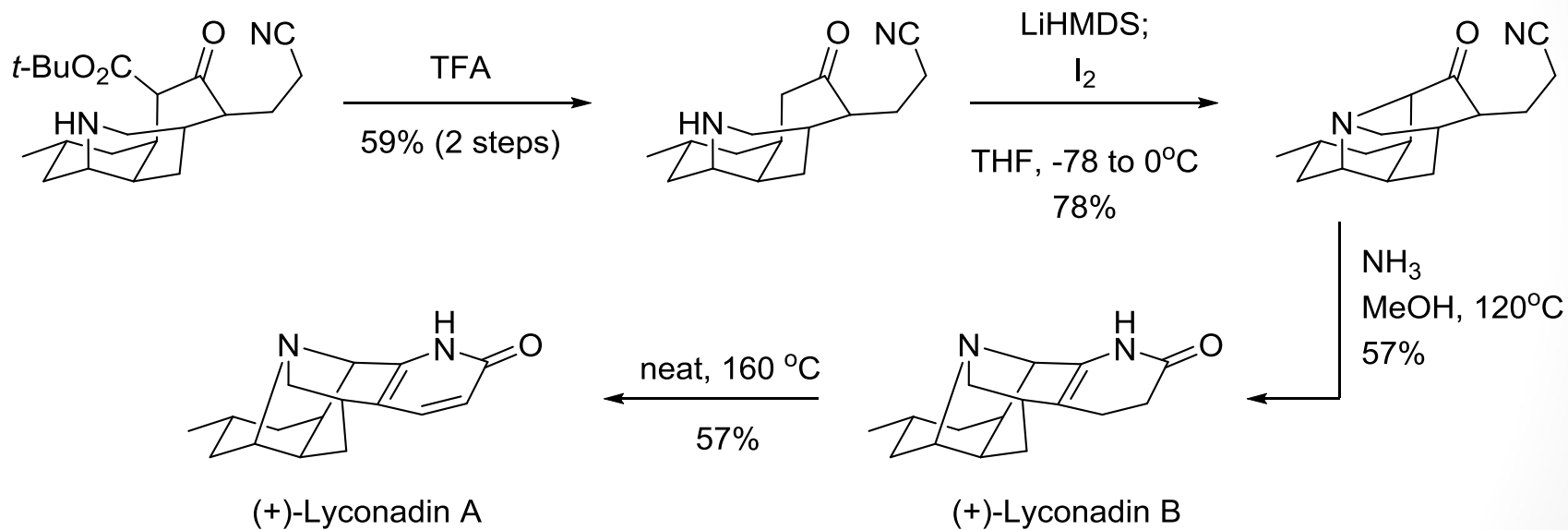
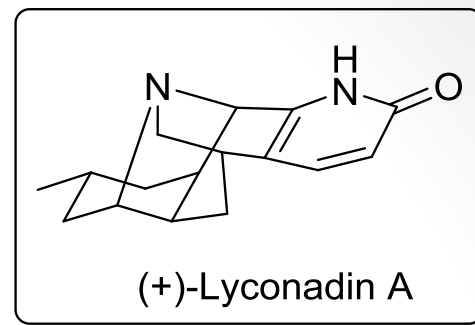


oxidative
N-C₆ formation

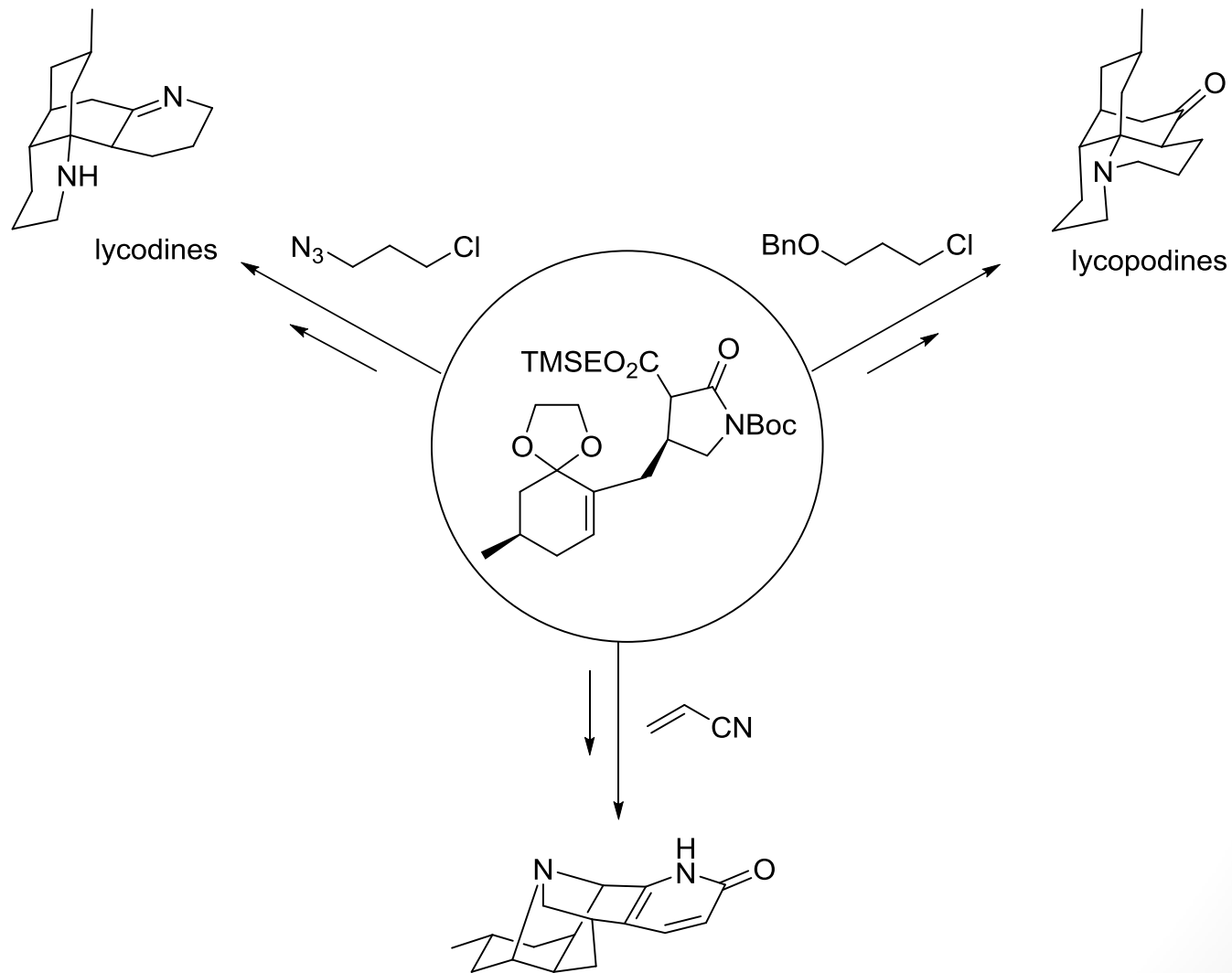


Lyconadin scaffold
(miscellaneous)

Lyconadin A

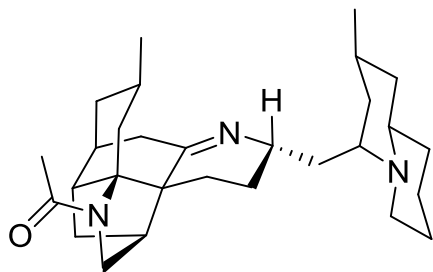


Summary



Summary

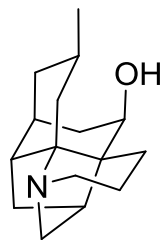
lycodine



(-)-Himeradine A

First synthesis
31 steps, ca. 2%

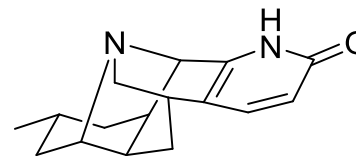
lycopodine



(-)-Lycopodine

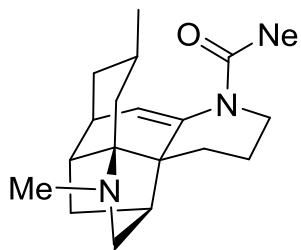
First synthesis
12 steps, 21%

miscellaneous



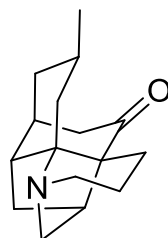
(+)-Lyconadin A

12 steps, 4%



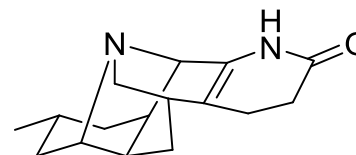
(+)-fastigiatine

First synthesis
13 steps, ca. 30%



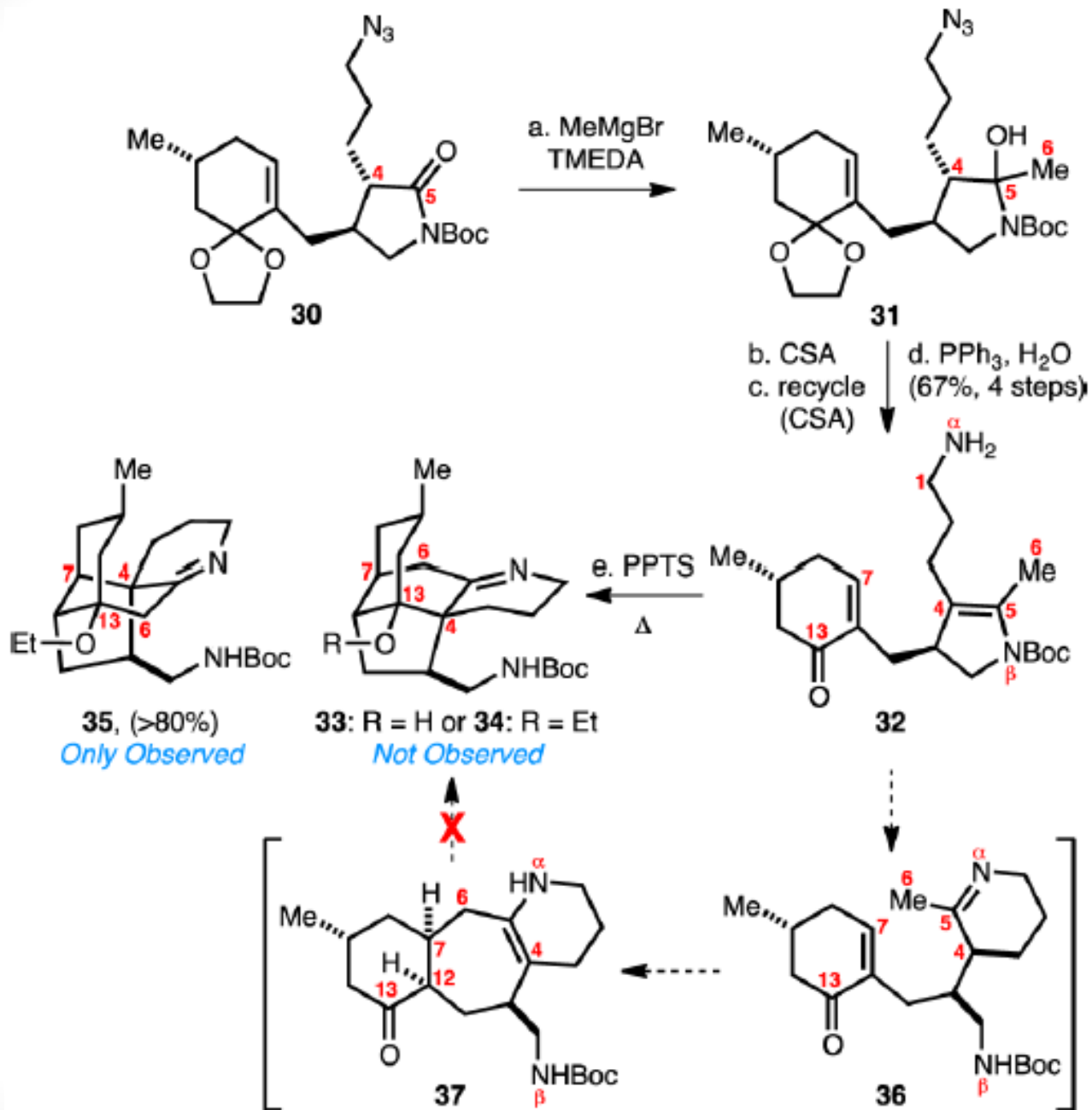
(-)-Dehydro
lycoperine

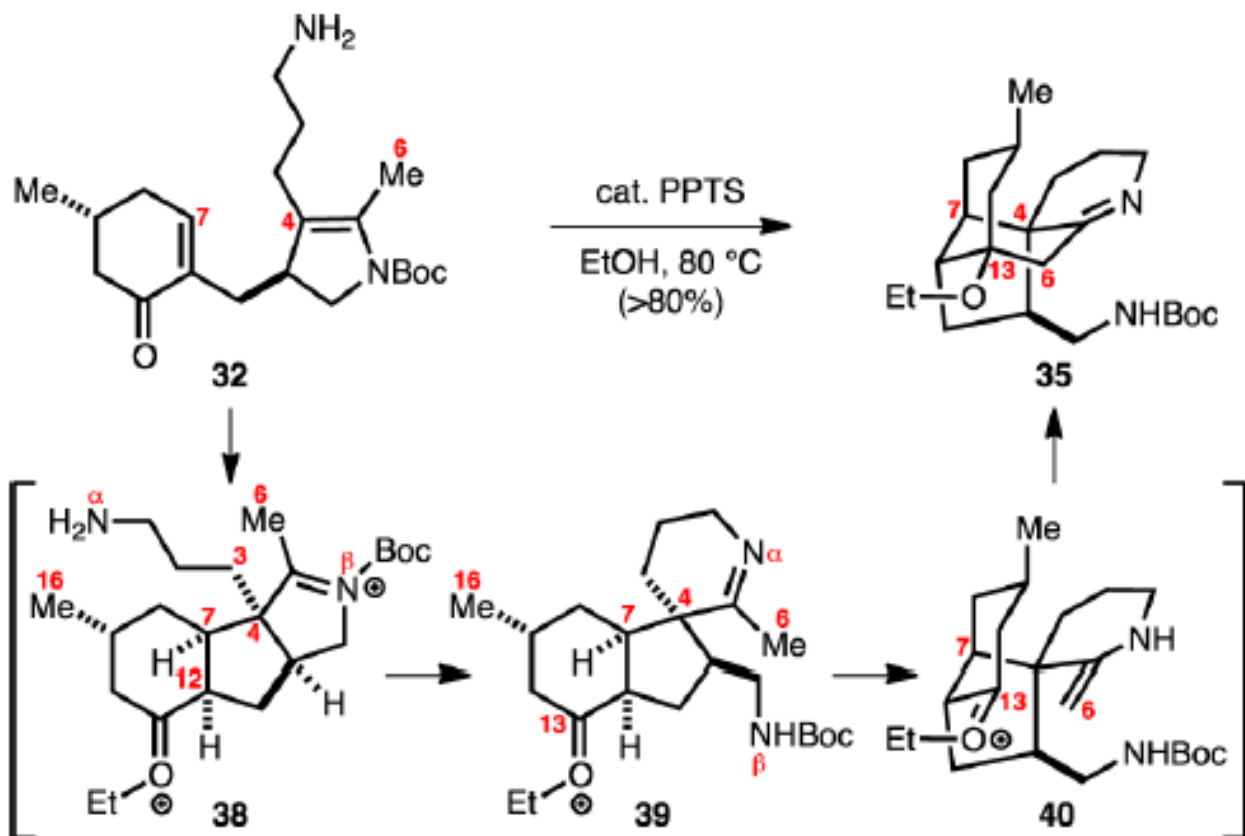
First synthesis
11 steps, 31%



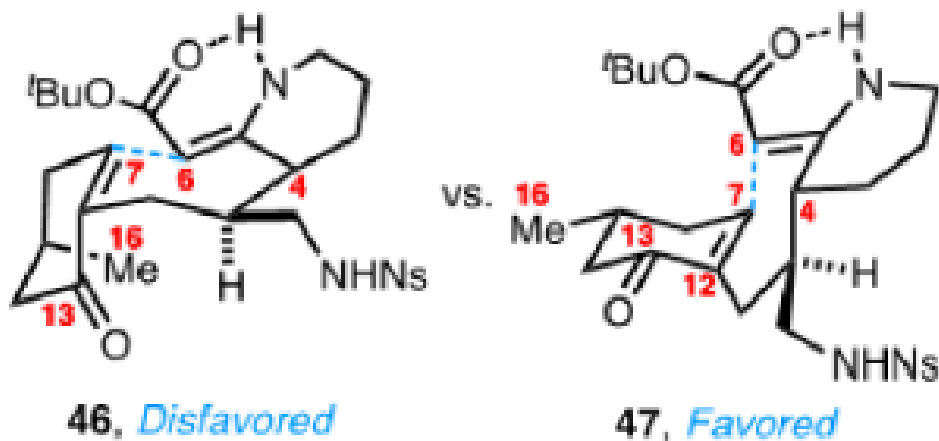
(-)-Lyconadin B

11 steps, 8%





Diastereoselectivity



Sarpong's oxidative C-N formation

