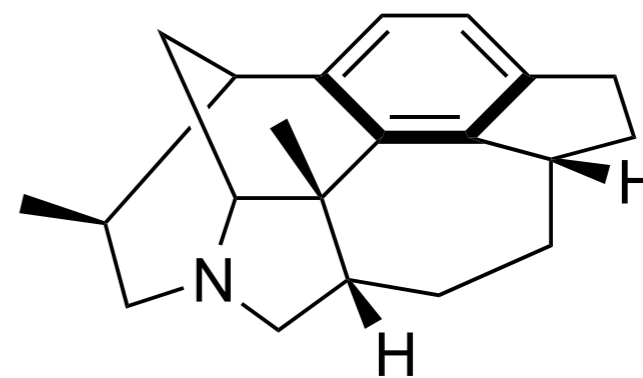


Total synthesis of the *Daphniphyllum* alkaloid: daphenylline

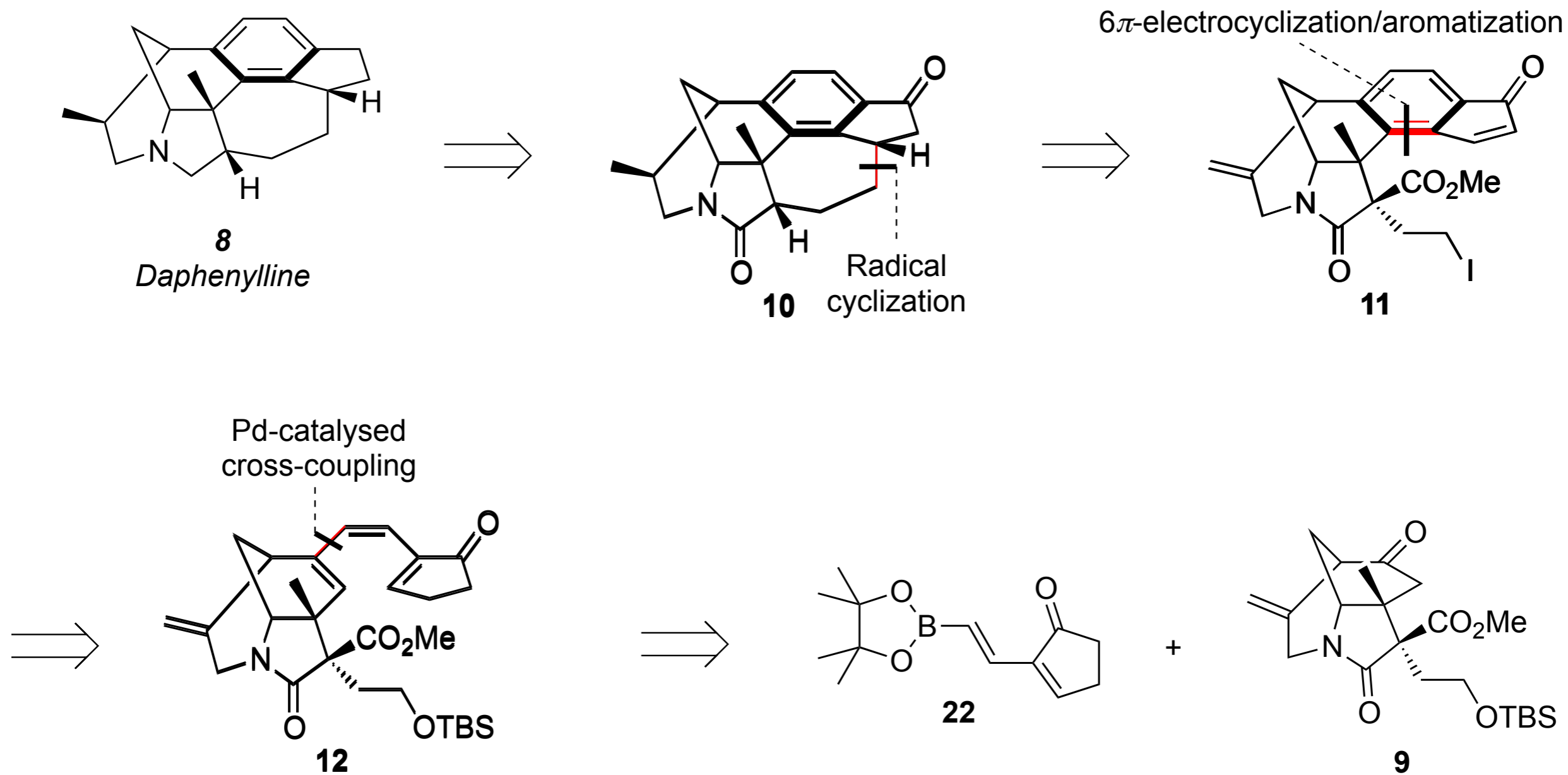
Lu, Z.; Li, Y.; Deng, J.; Li, A. *Nature Chem.* **2013**, 5, 679–684
doi:10.1038/nchem.1694

Introduction

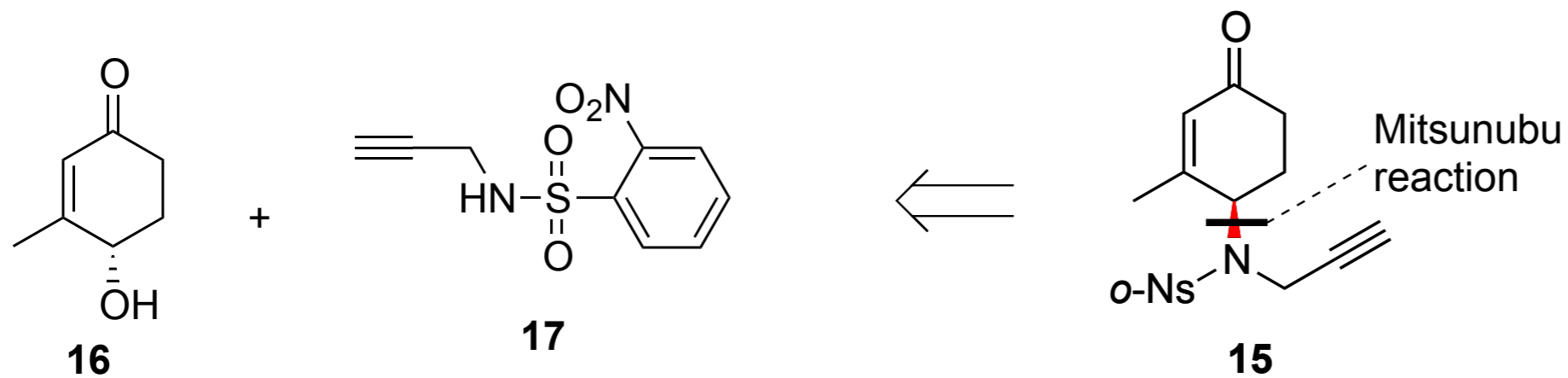
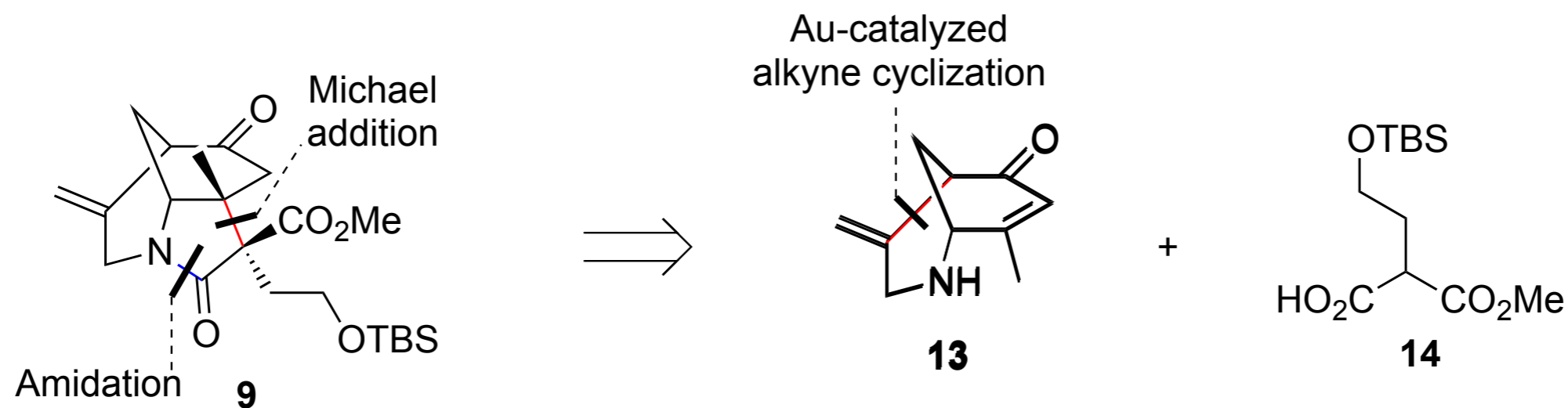
- Isolated from the fruits of *D. longeracemosum* (Hao, 2009)
- 6 stereogenic centers
- 6 cycles with 1 bridge 6,1,5-tricyclic motif

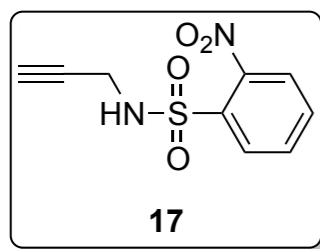


Retrosynthesis

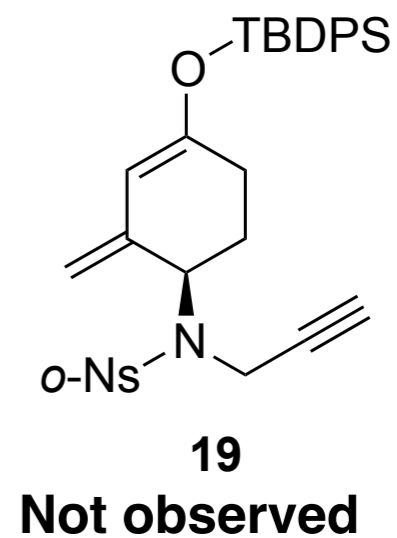
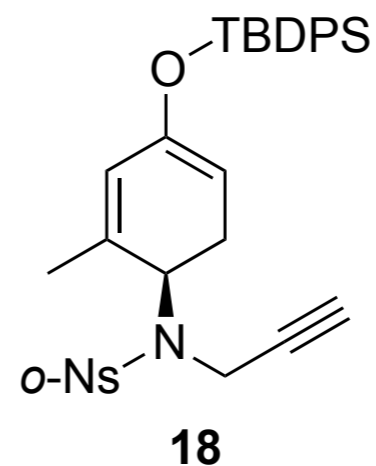
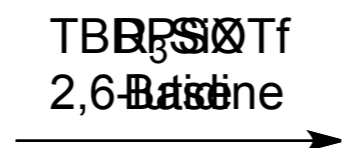
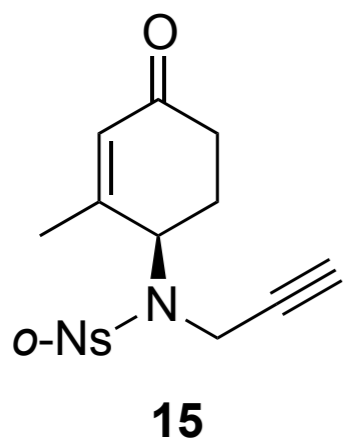
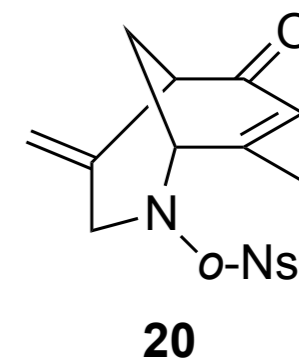
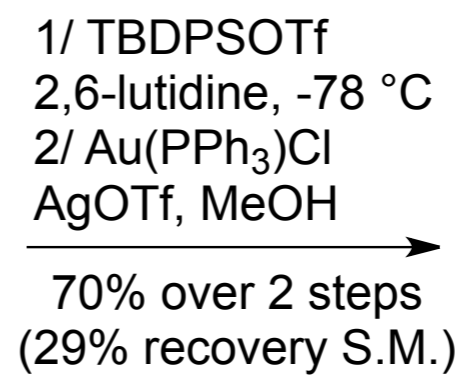
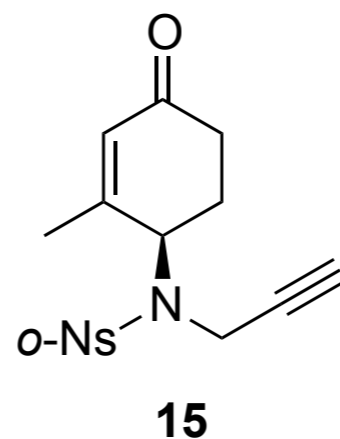
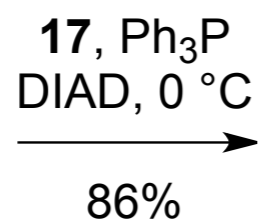
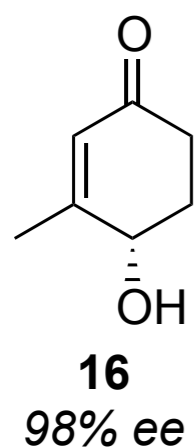


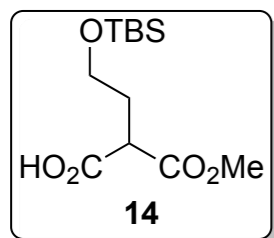
Retrosynthesis



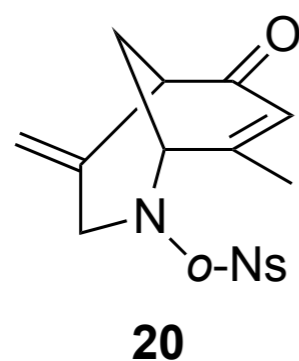
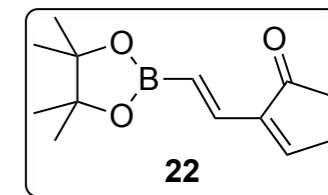


Synthesis of fragment 20





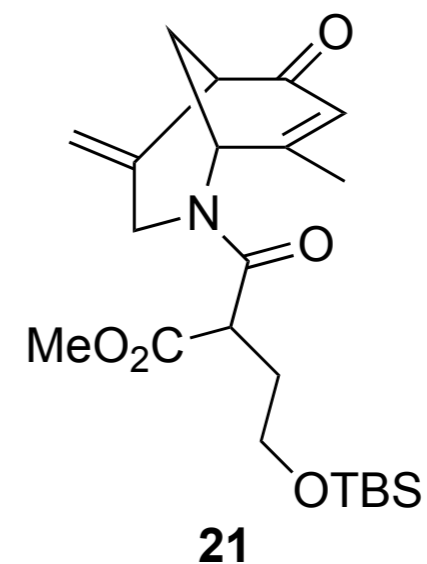
Synthesis of fragment 23



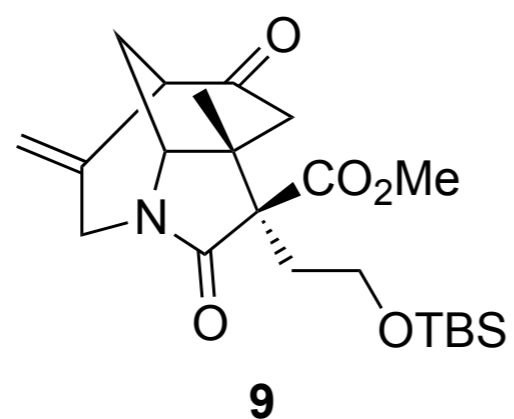
1/ K_2CO_3
p-thiocresol

2/ **14**, *t*-BuOH
EDC·HCl, Et_3N

72% (over 2 steps)



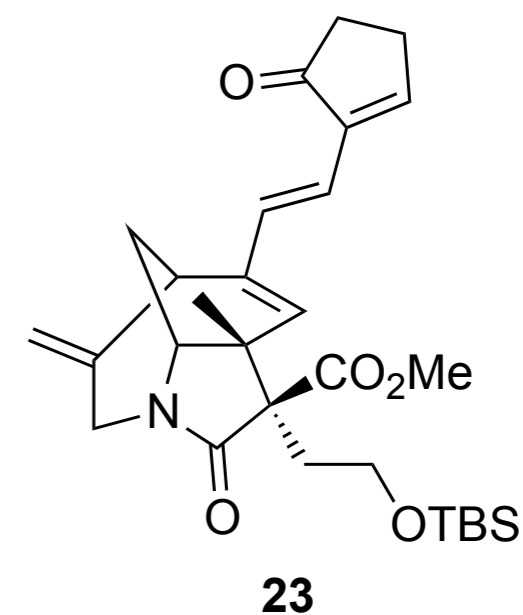
K_2CO_3 , 100 °C
86%



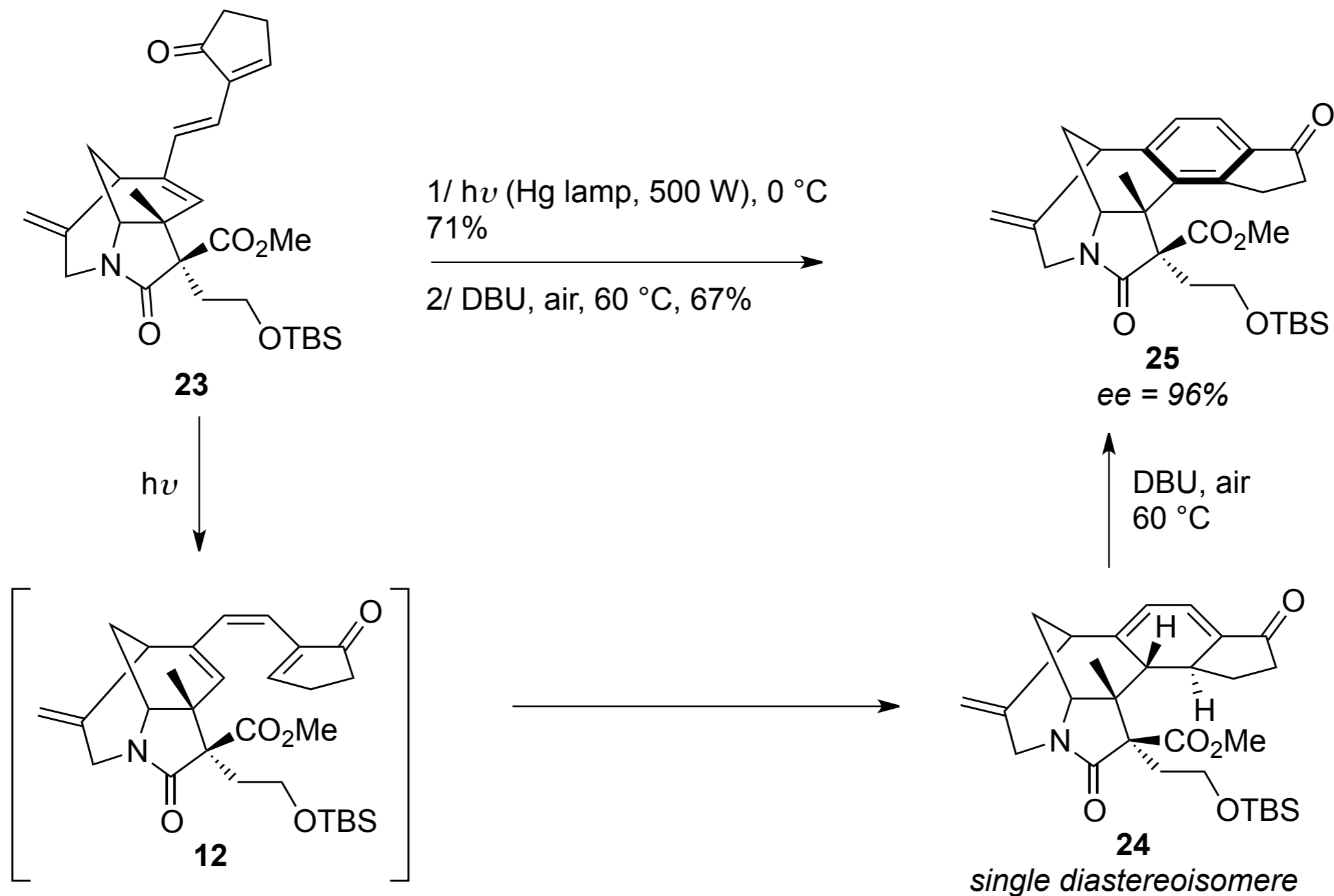
1/ KHMDS, $PhNTf_2$
-78 °C

2/ **22**, $Pd(PPh_3)_4$ cat.
 K_2CO_3 , 60 °C

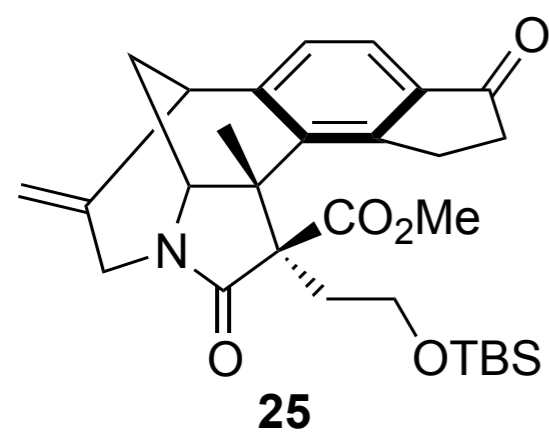
73% (over 2 steps)



Synthesis of fragment 25

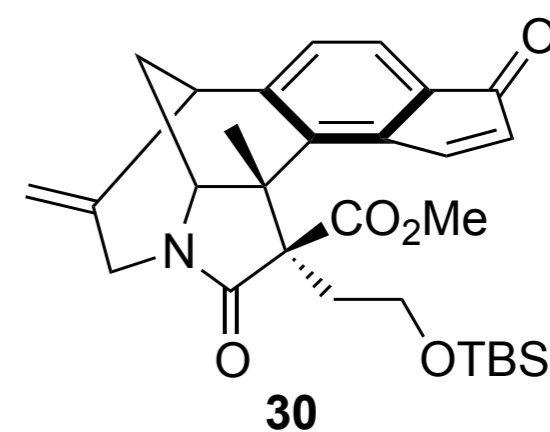


Synthesis of fragment 31



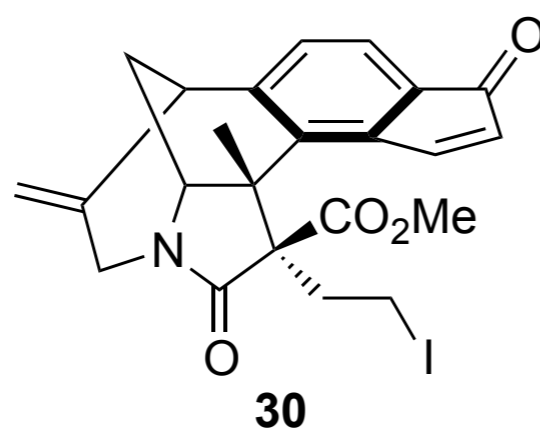
1/ TMSOTf, Et₃N, -78 °C
2/ Pd(OAc)₂

81%
(over 2 steps)



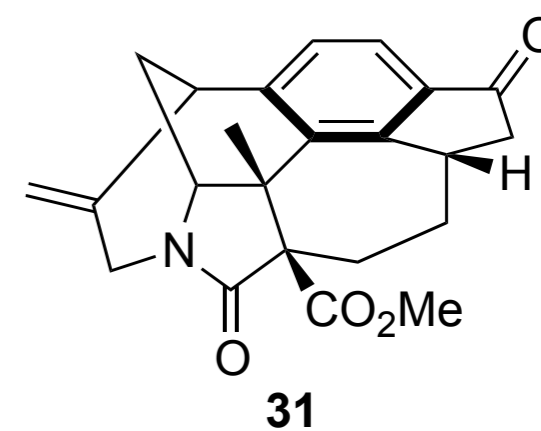
1/ HF·Py, 0 °C
2/ I₂, PPh₃, imidazole

93%
(over 2 steps)

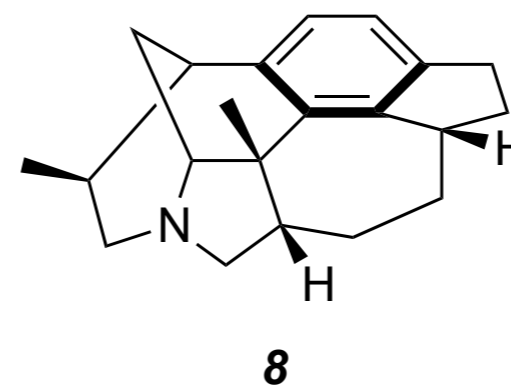
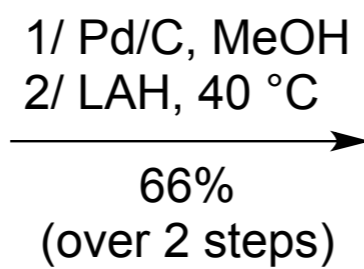
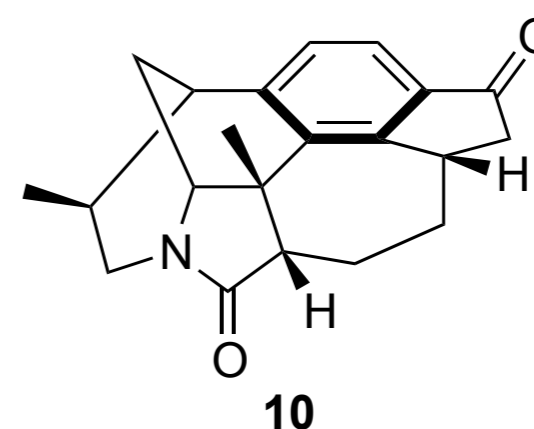
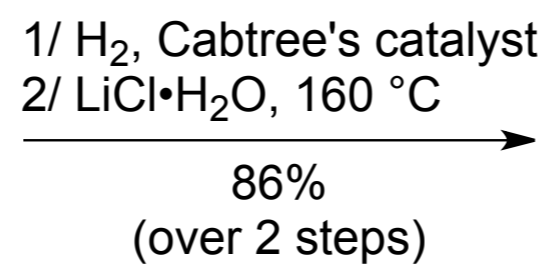
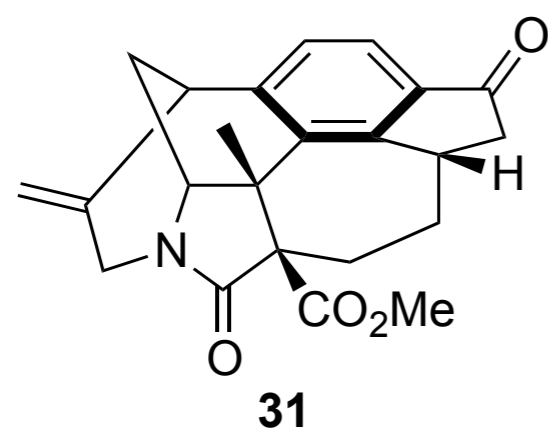
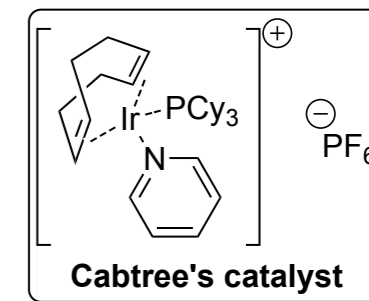


(TMS)₃SiH, AIBN, 75°C

98%



End of the Synthesis



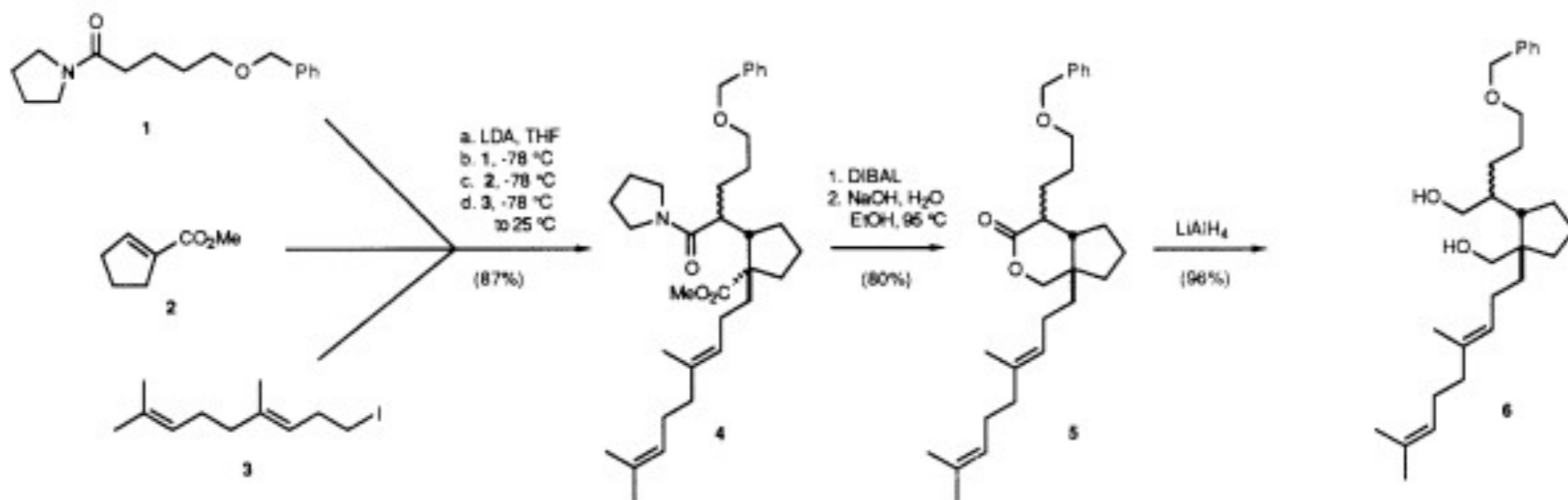
Daphenylline

Conclusion

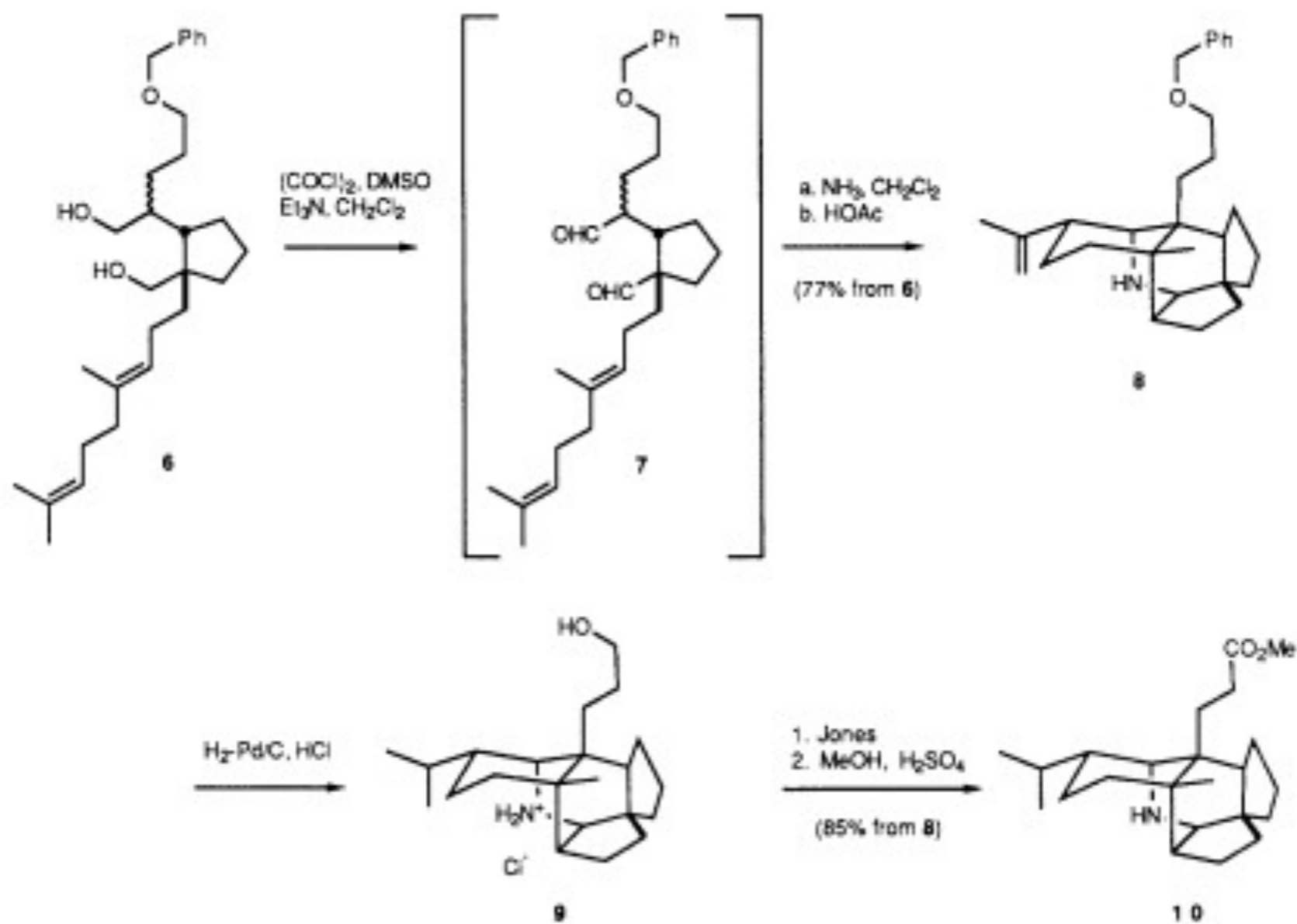
- 19 linear steps : overall Yield = 5%
- 3 key-steps :
 - gold-catalyzed cyclization
 - photoinduced isomerization/electrocyclization cascade
 - *7-exo-trig* radical cyclization

Thank you
for your attention

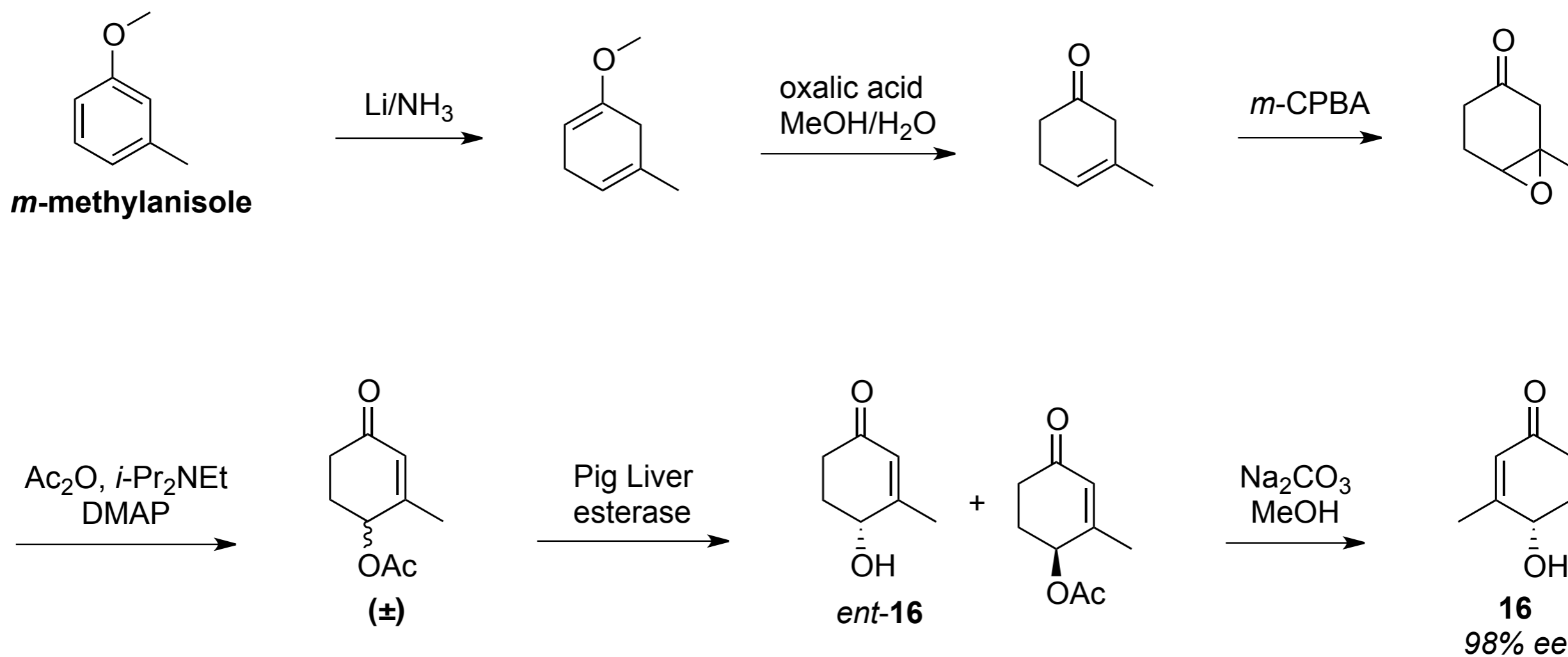
Synthesis of Methyl Homosecodaphniphyllate



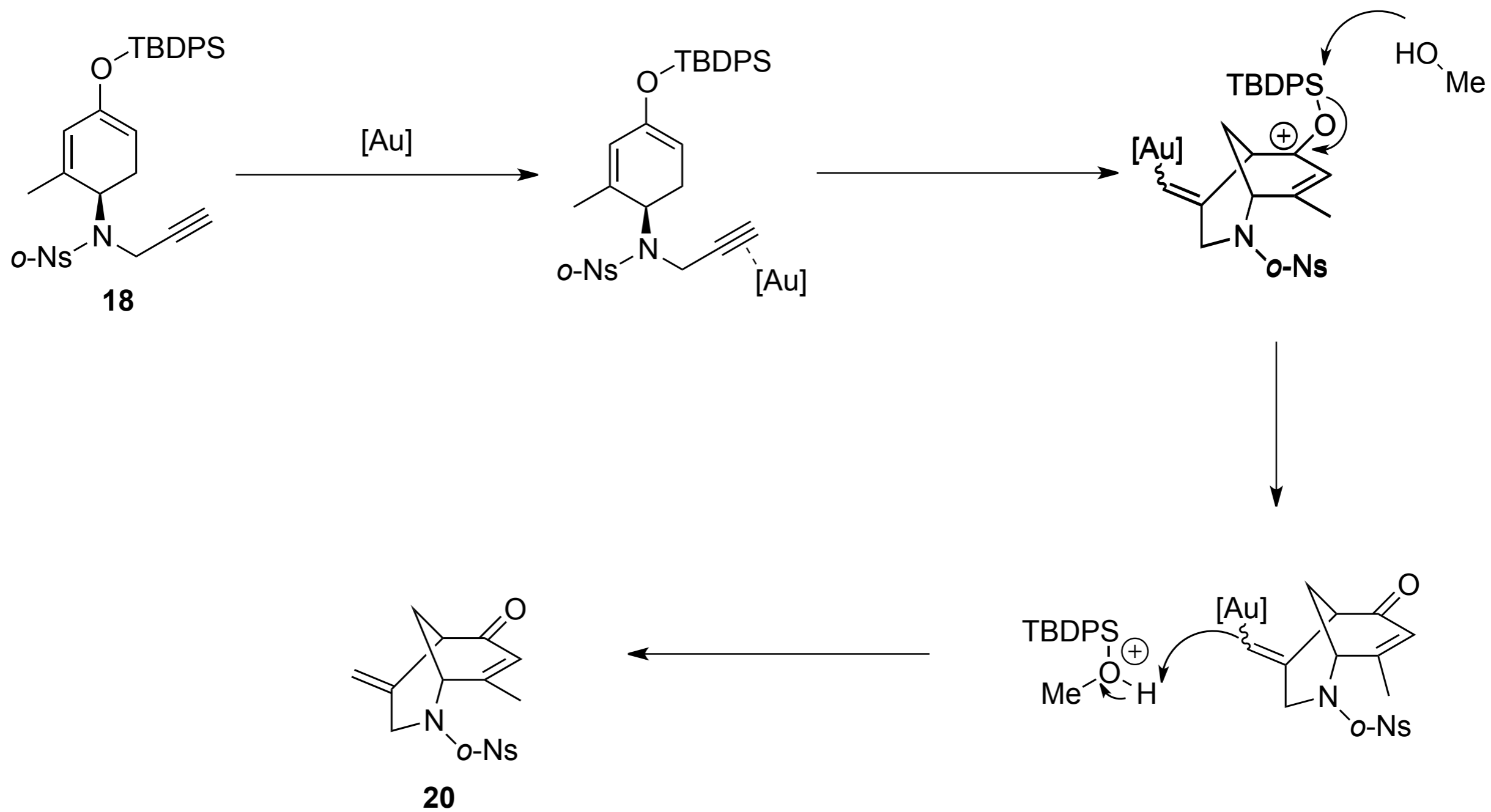
Synthesis of Methyl Homosecodaphniphyllate



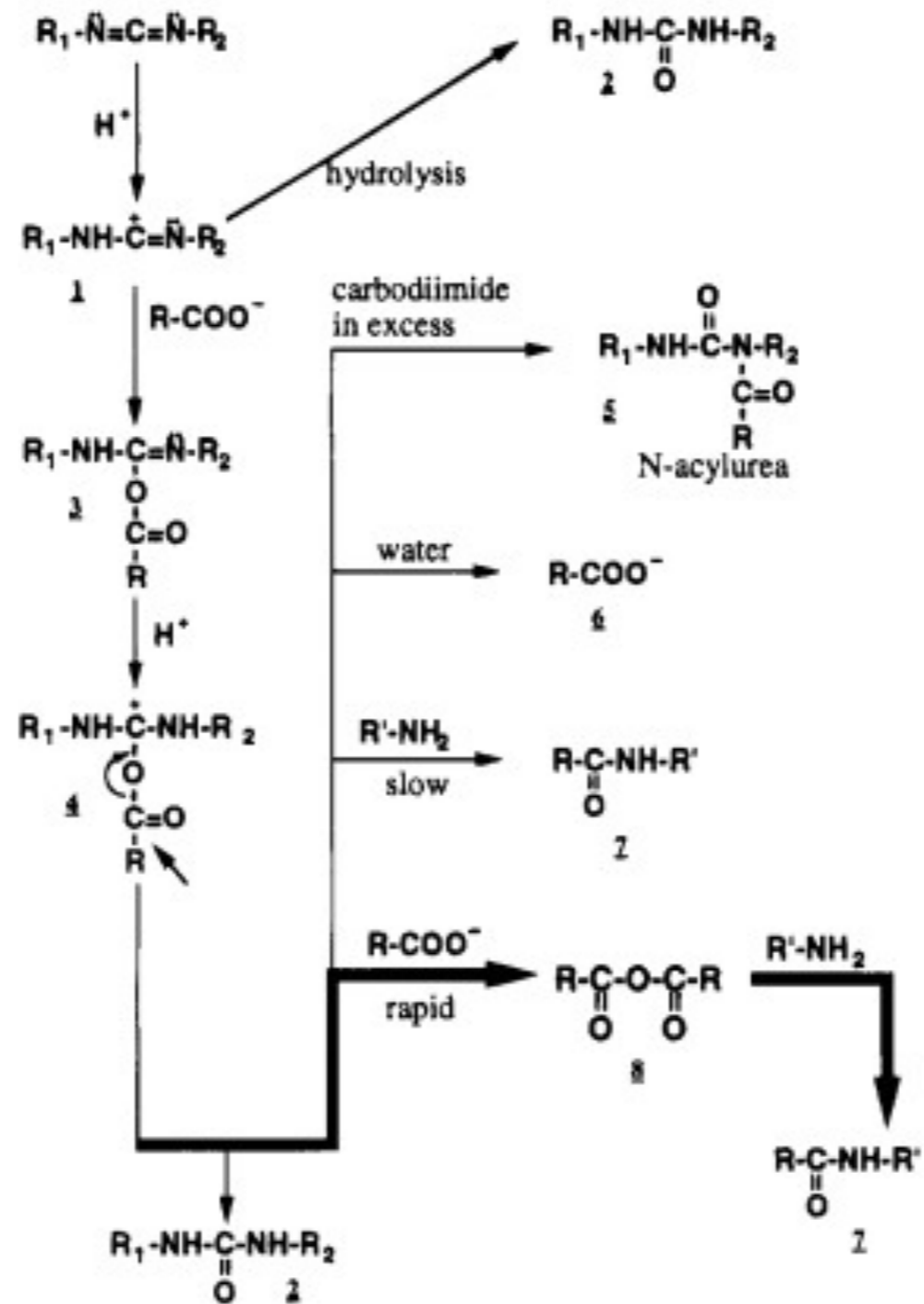
Synthesis of 16



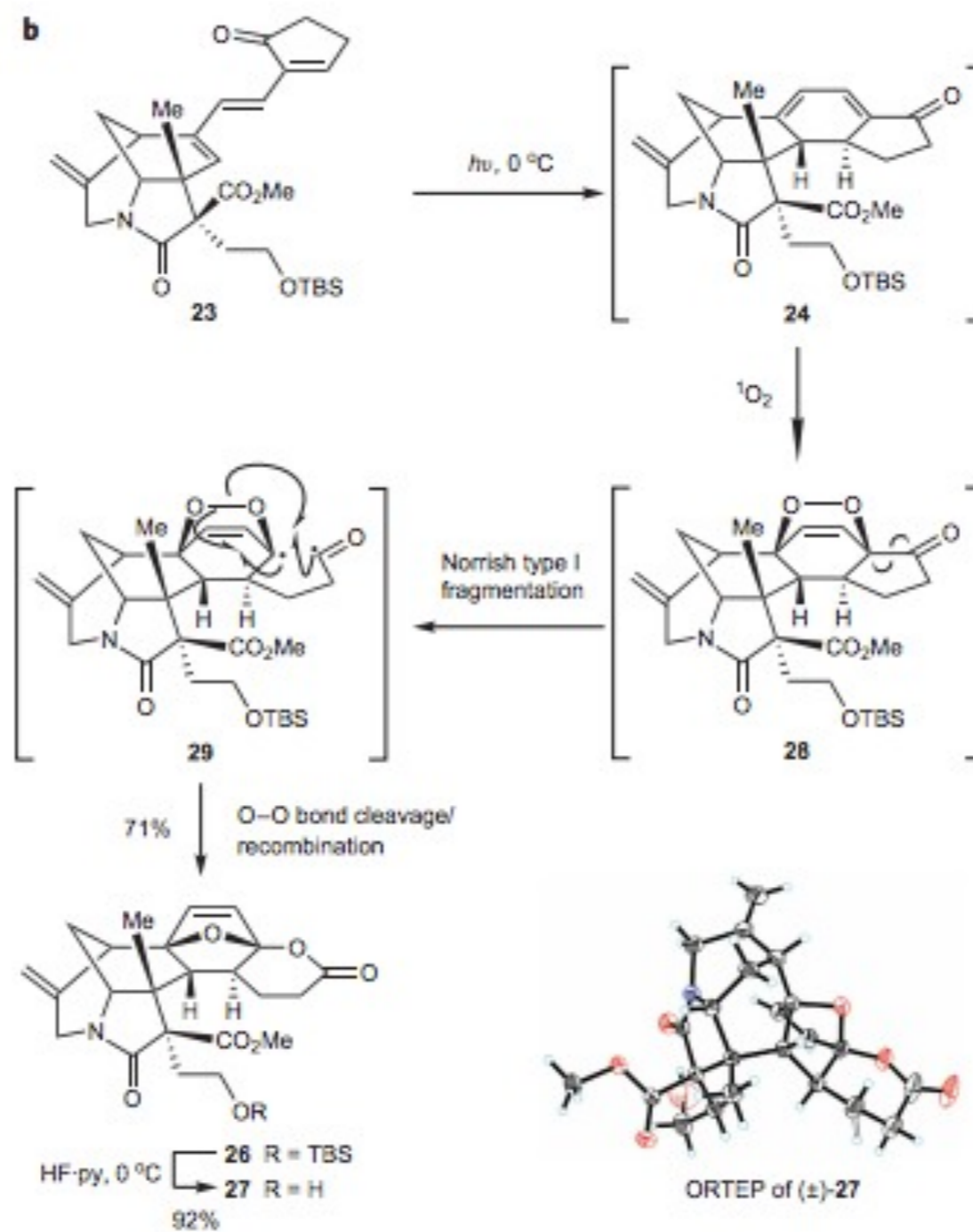
Synthesis of fragment 20 (Mechanism)



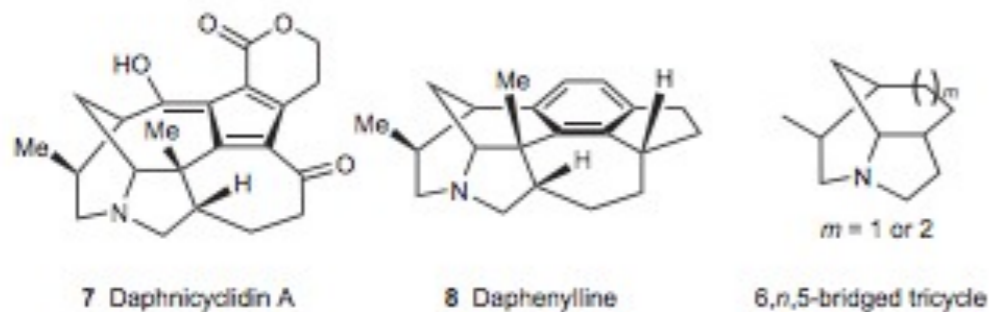
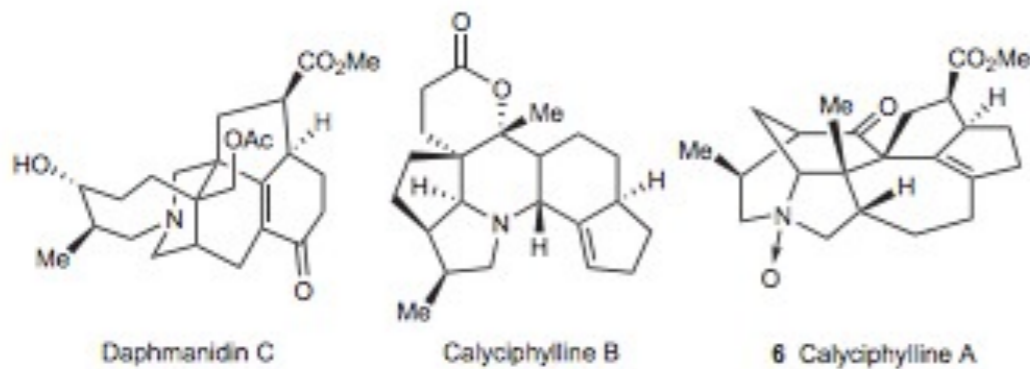
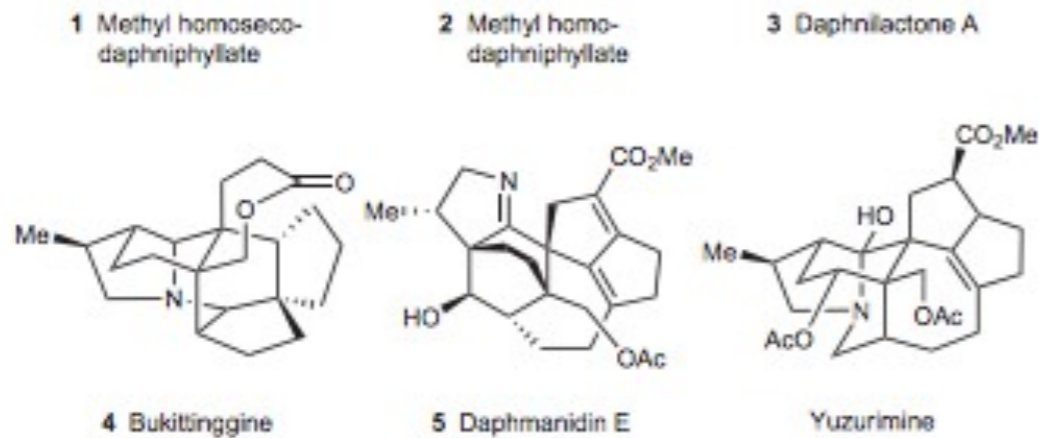
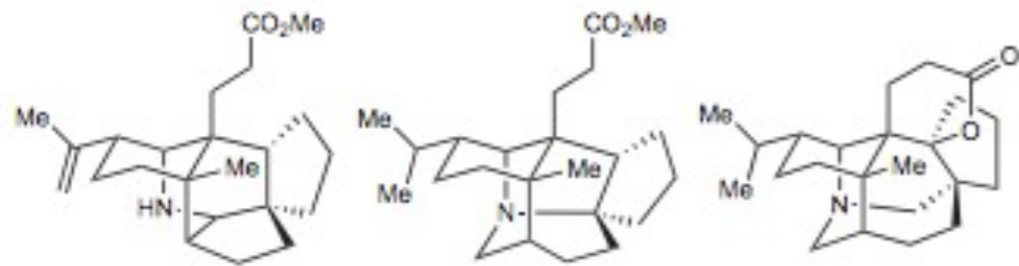
Amidation



Without DBU



Introduction



- Isolated from Daphniphyllum (Asian Plants)
- More of 250 alkaloids
- 20 subfamilies
- Daphnicyclidin A : anticancer