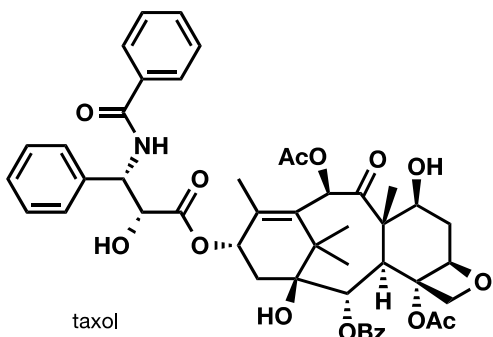




Sebastian Krüger  
Gaich-Group Seminar  
03.02.14

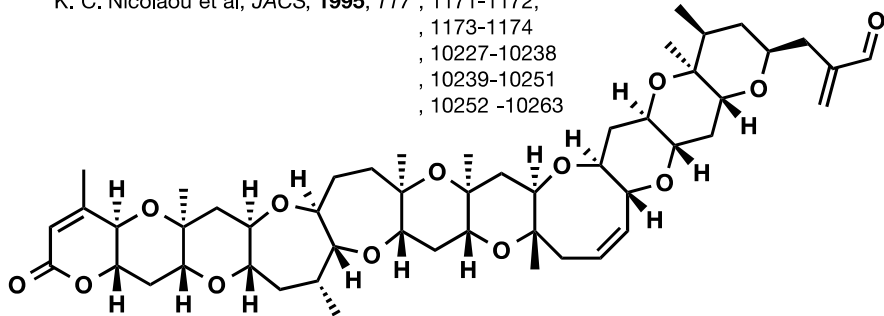
# Sytheses

## Nicolaou

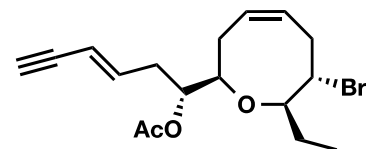
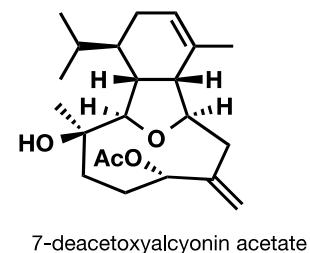
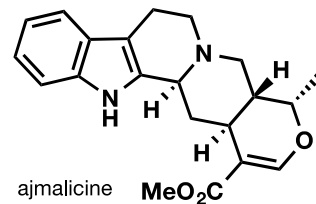
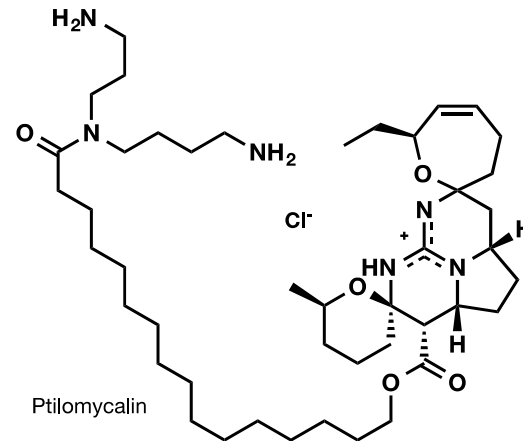


brevetoxin B, not covered

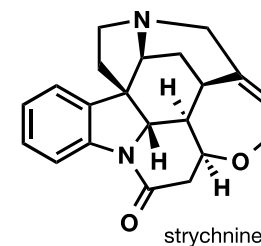
K. C. Nicolaou et al, *JACS*, **1995**, *117*, 1171-1172,  
, 1173-1174  
, 10227-10238  
, 10239-10251  
, 10252 -10263



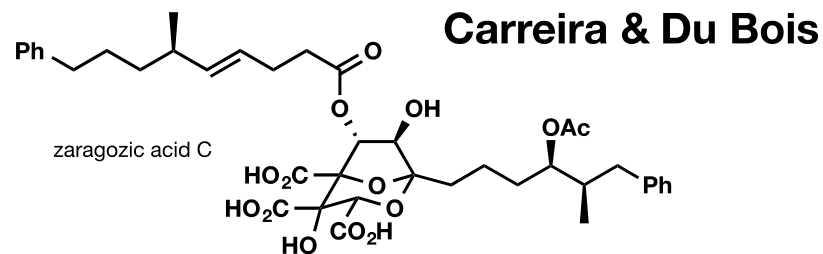
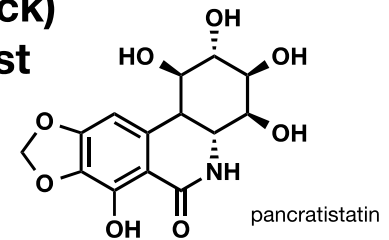
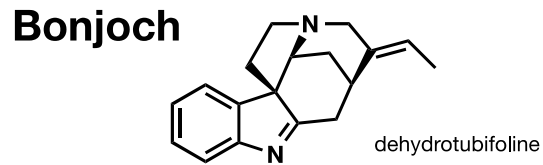
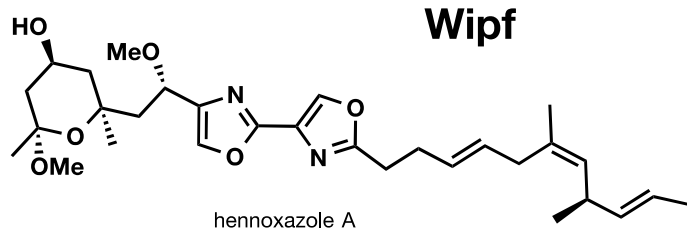
## Overman



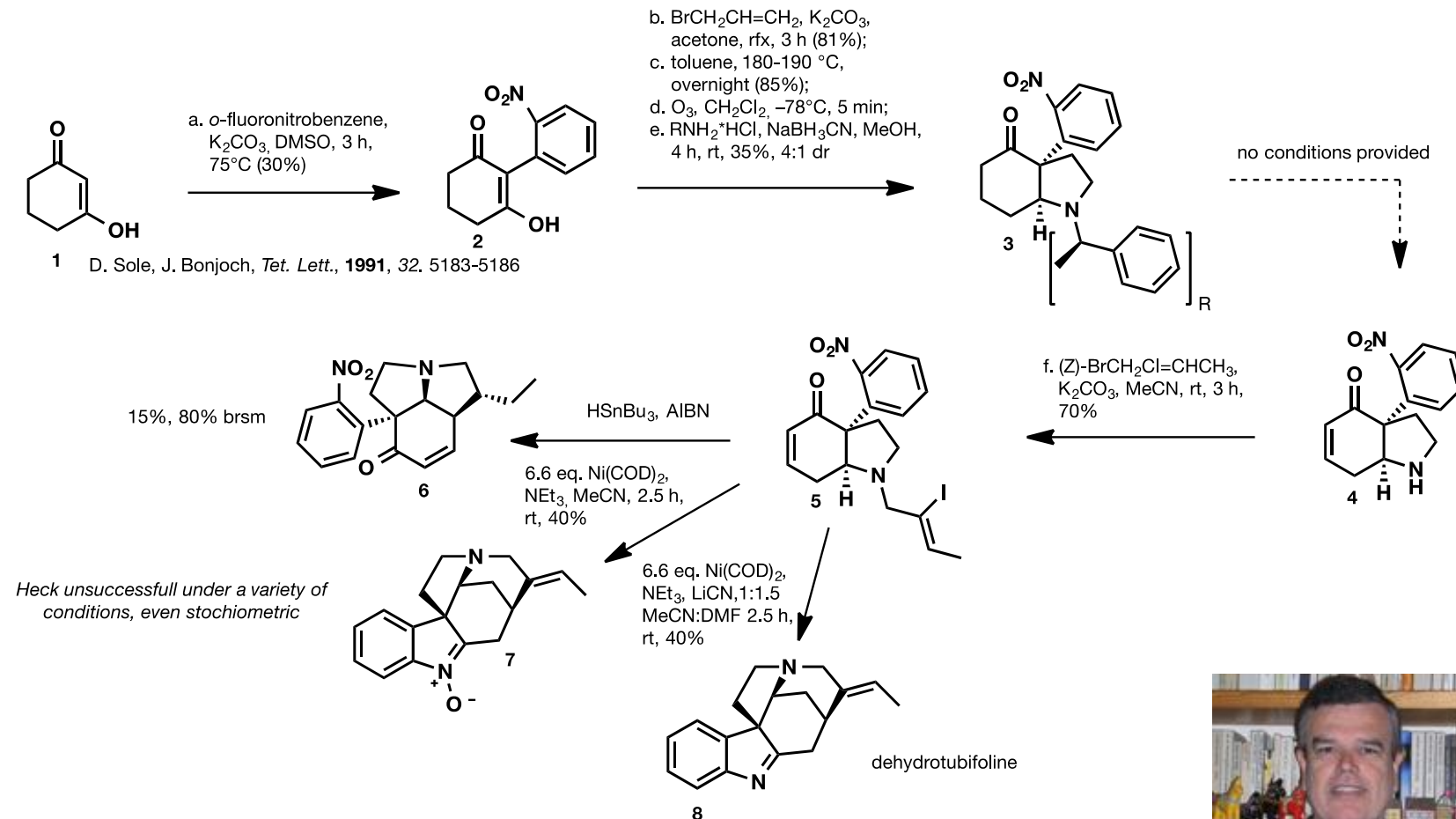
M. Bratz, W. H. Bullock,  
L. E. Overman, T. Takemoto,  
*JACS*, **1995**, *117*, 5958-5966



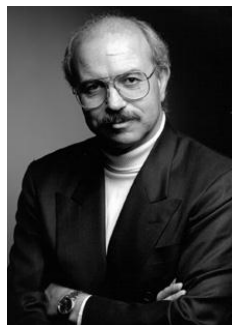
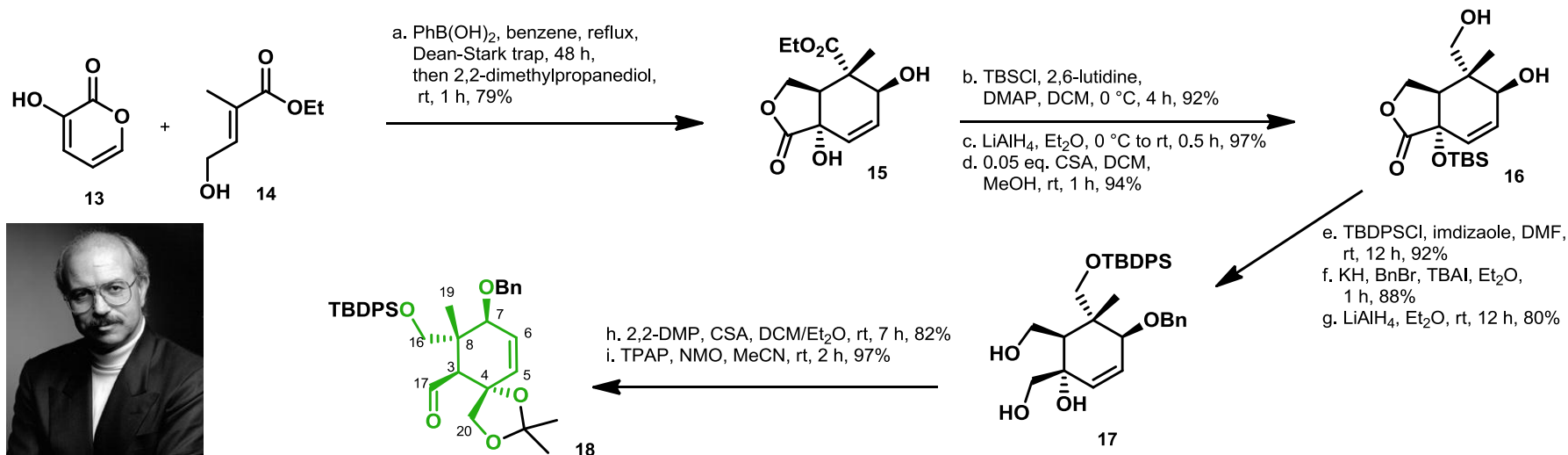
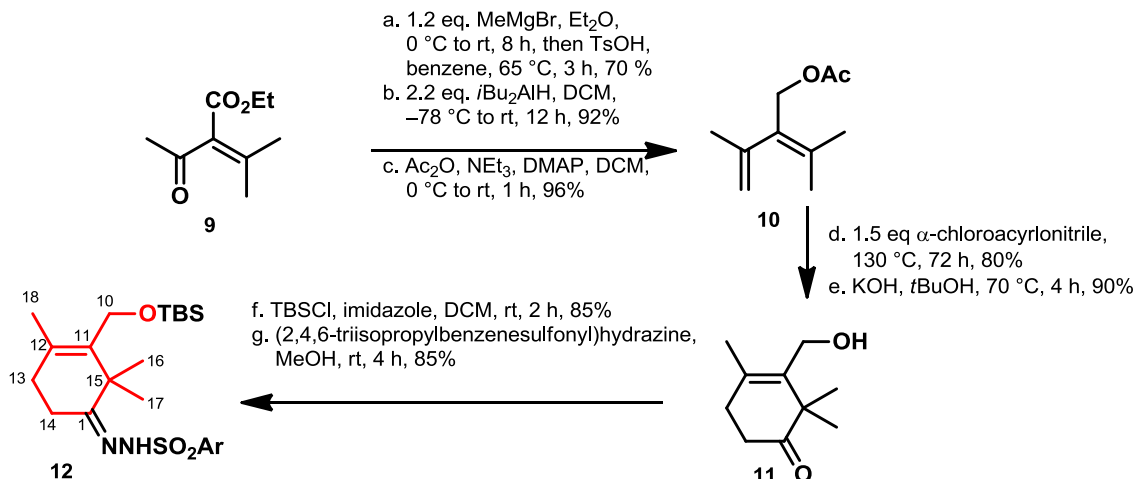
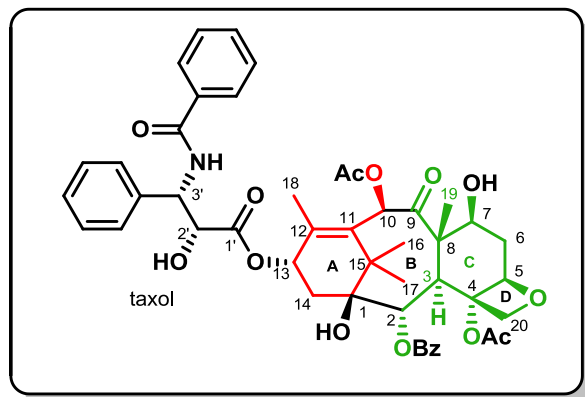
# Sytheses



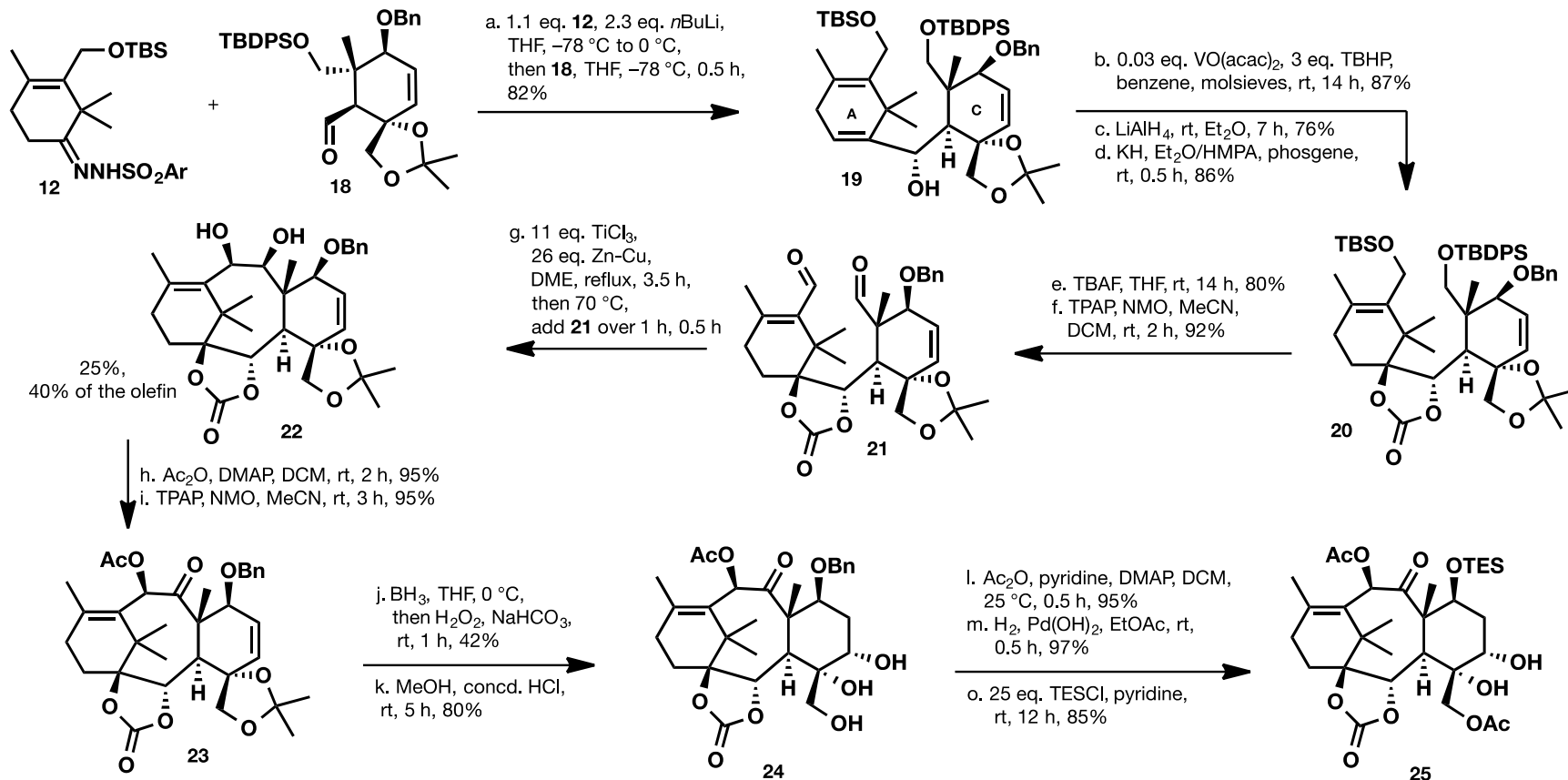
# Dehydrotubifoline - Bonjoch



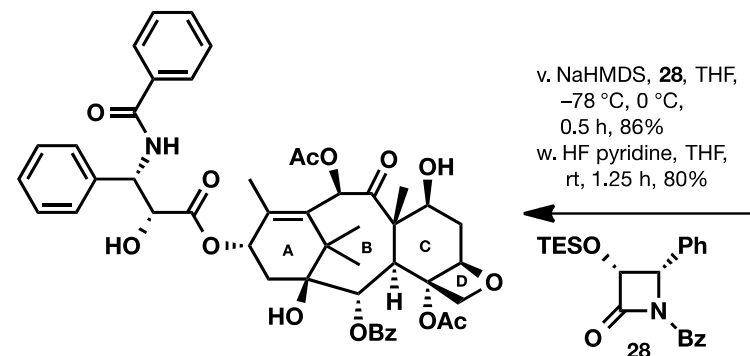
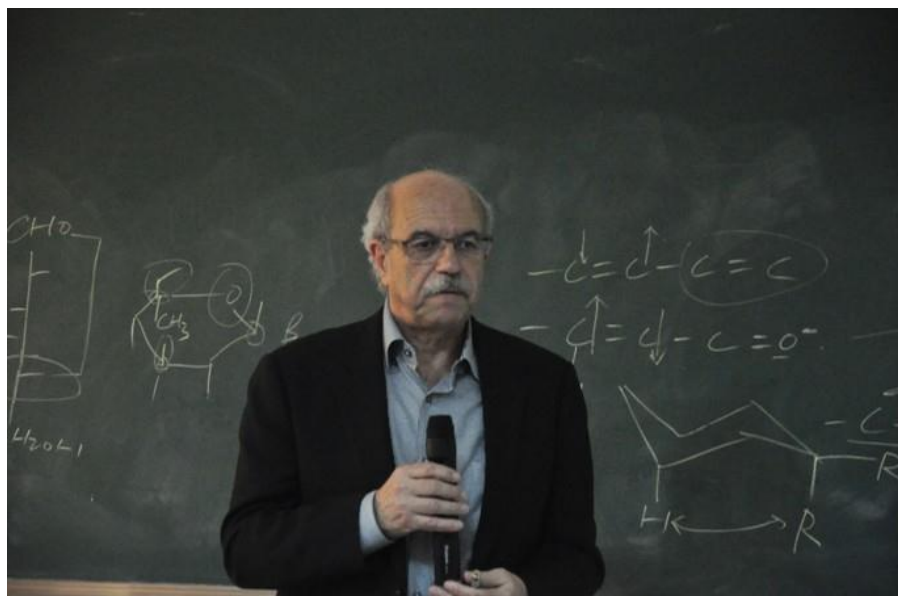
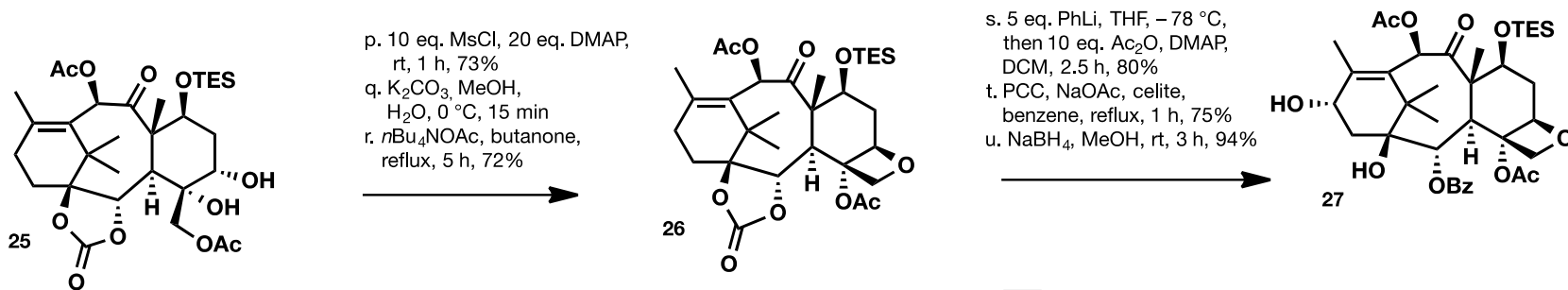
# Taxol - Nicolaou



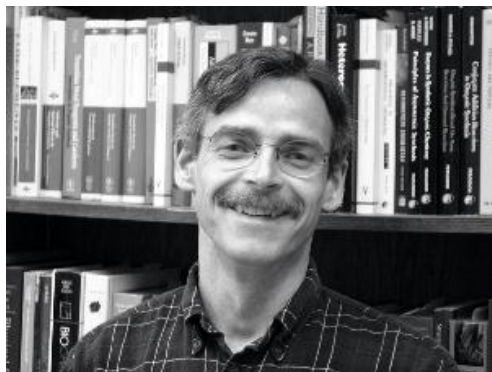
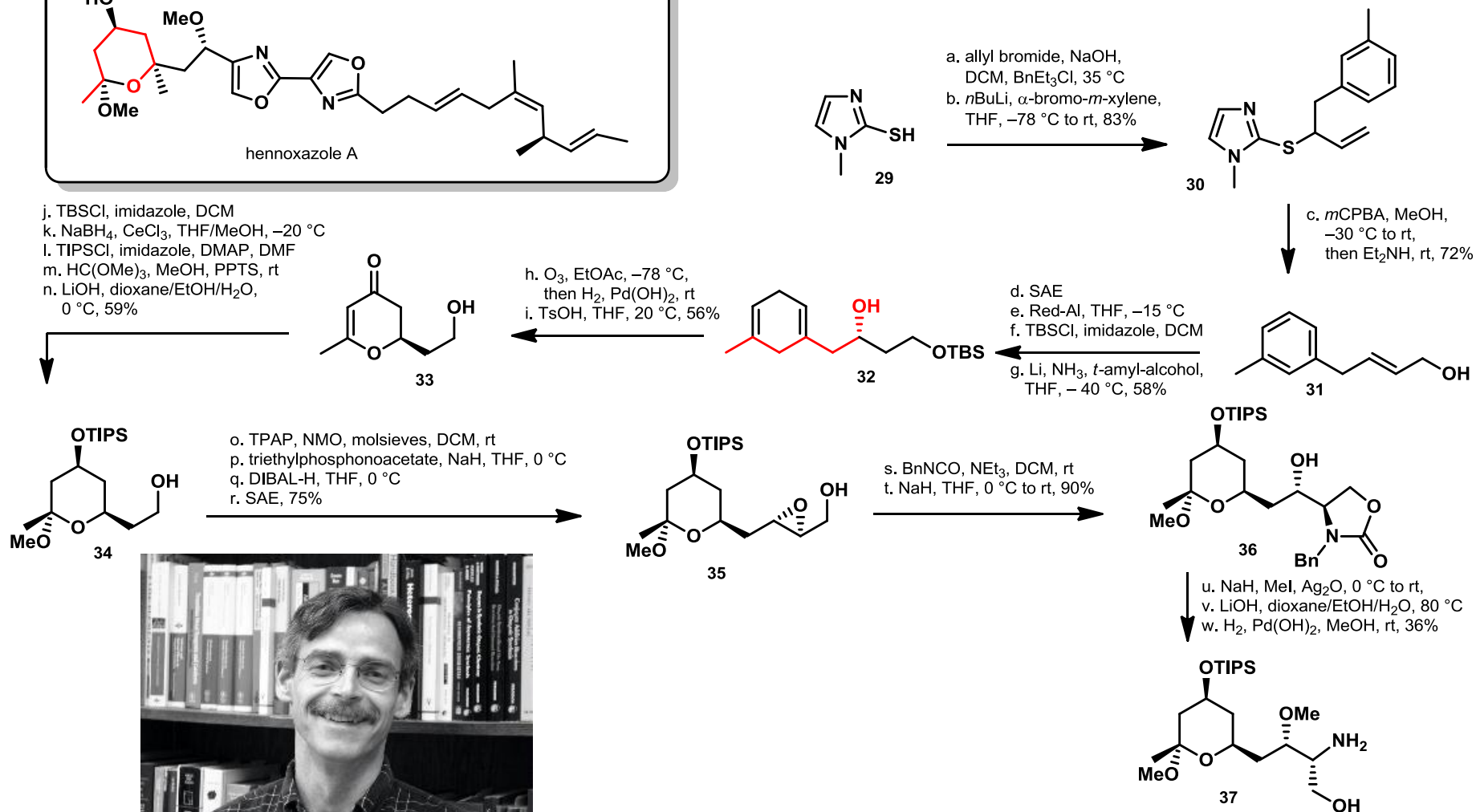
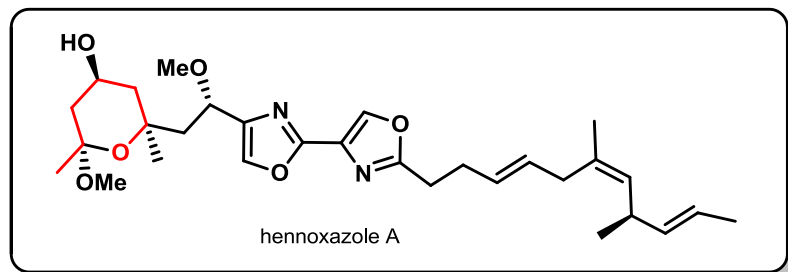
# Taxol - Nicolaou



# Taxol - Nicolaou

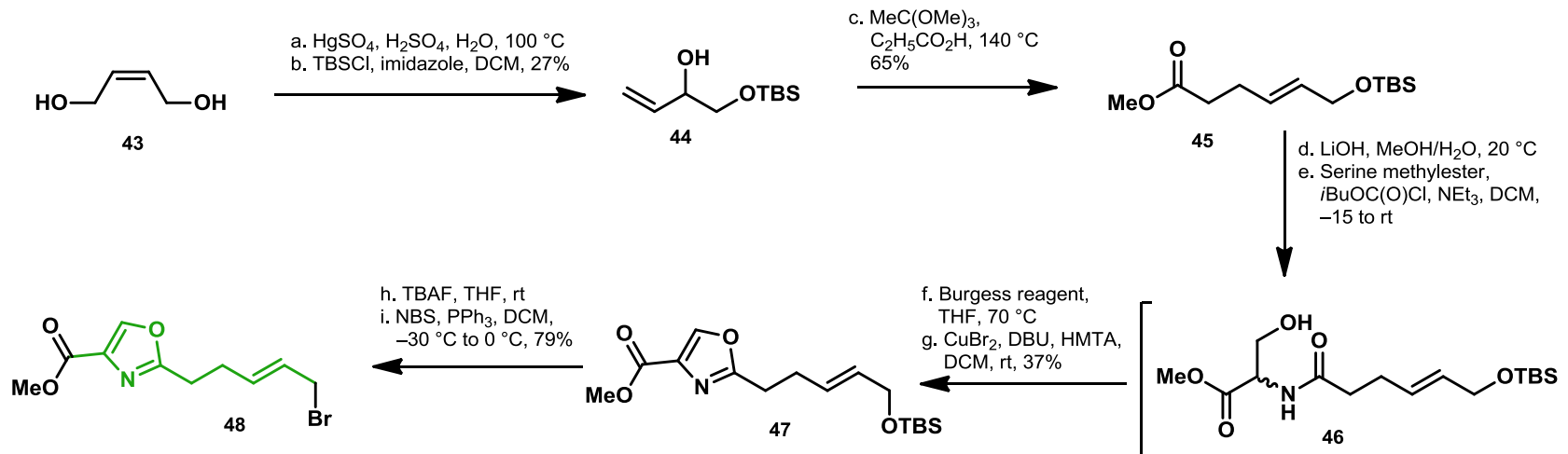
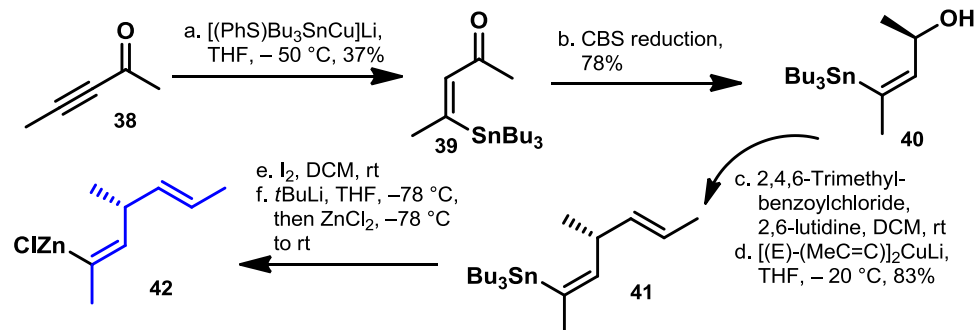
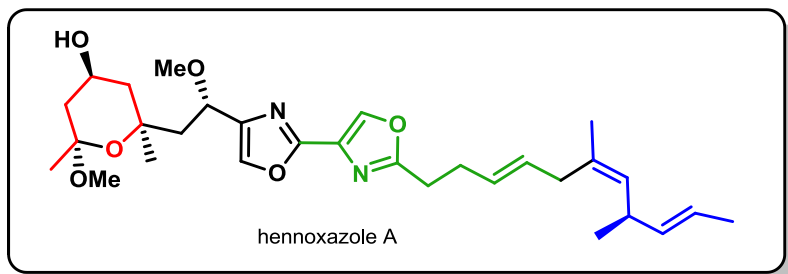


# Hennoxazole A- Wipf

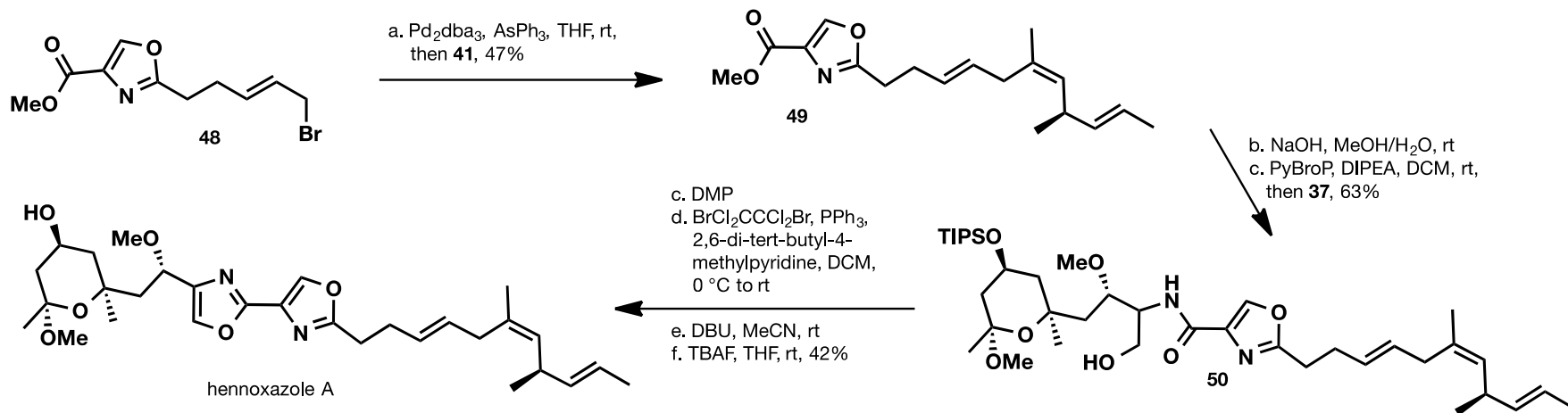




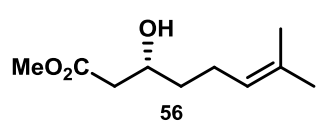
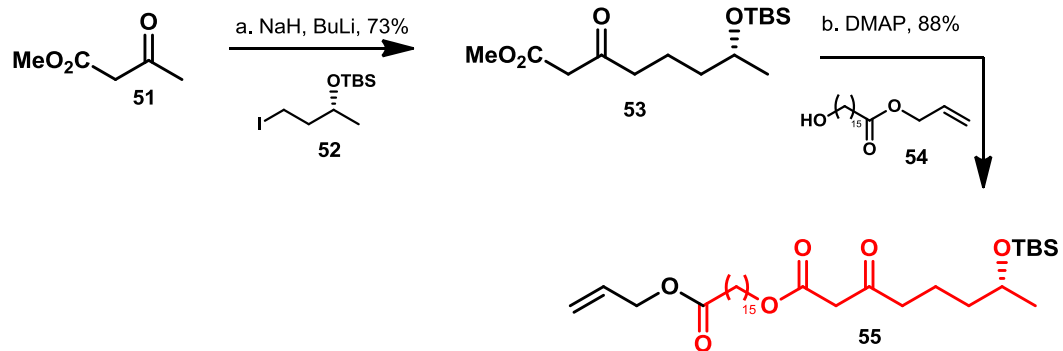
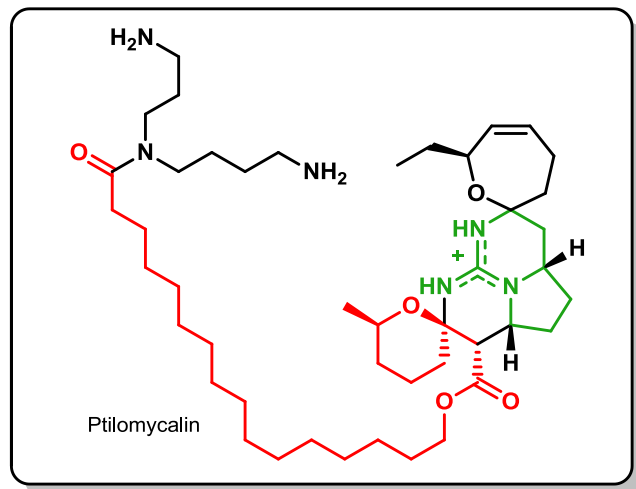
# Hennoxazole A- Wipf



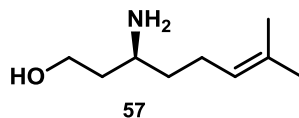
# Hennoxazole A- Wipf



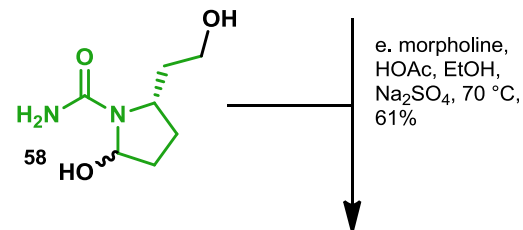
# Ptilomycalin - Overman



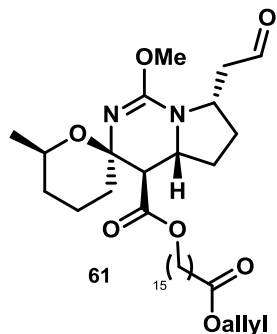
a.  $\text{HN}_3$ ,  $\text{PPh}_3$ , DEAD  
b.  $\text{LiAlH}_4$ , 72%



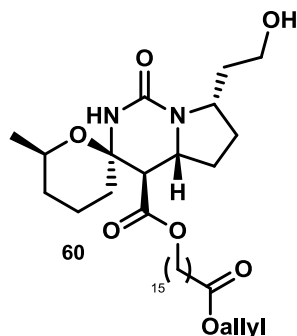
c.  $\text{KOCN}$ ,  $\text{HCl}$ , 70 °C  
d.  $\text{O}_3$ ,  $\text{MeOH}$ , -78 °C, 61%



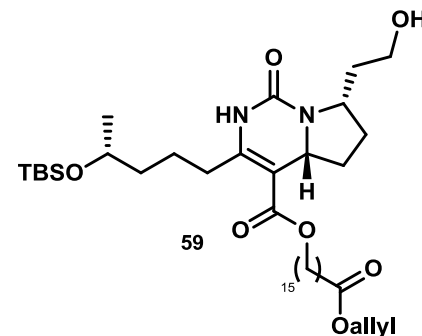
e. morpholine, HOAc, EtOH,  $\text{Na}_2\text{SO}_4$ , 70 °C, 61%



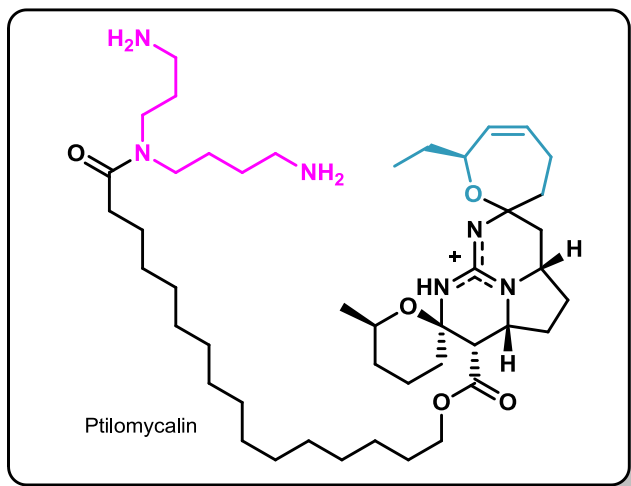
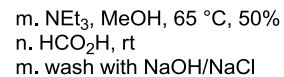
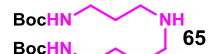
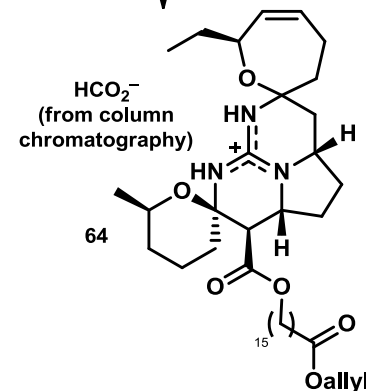
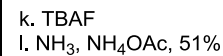
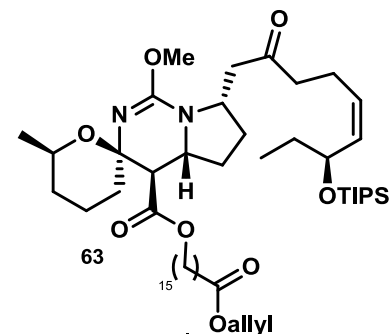
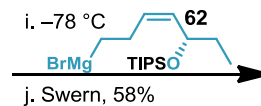
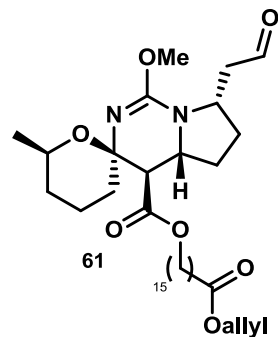
g. Swern  
h.  $\text{MeOTf}$ ,  $\text{NEt}_3$ , rt, 67%



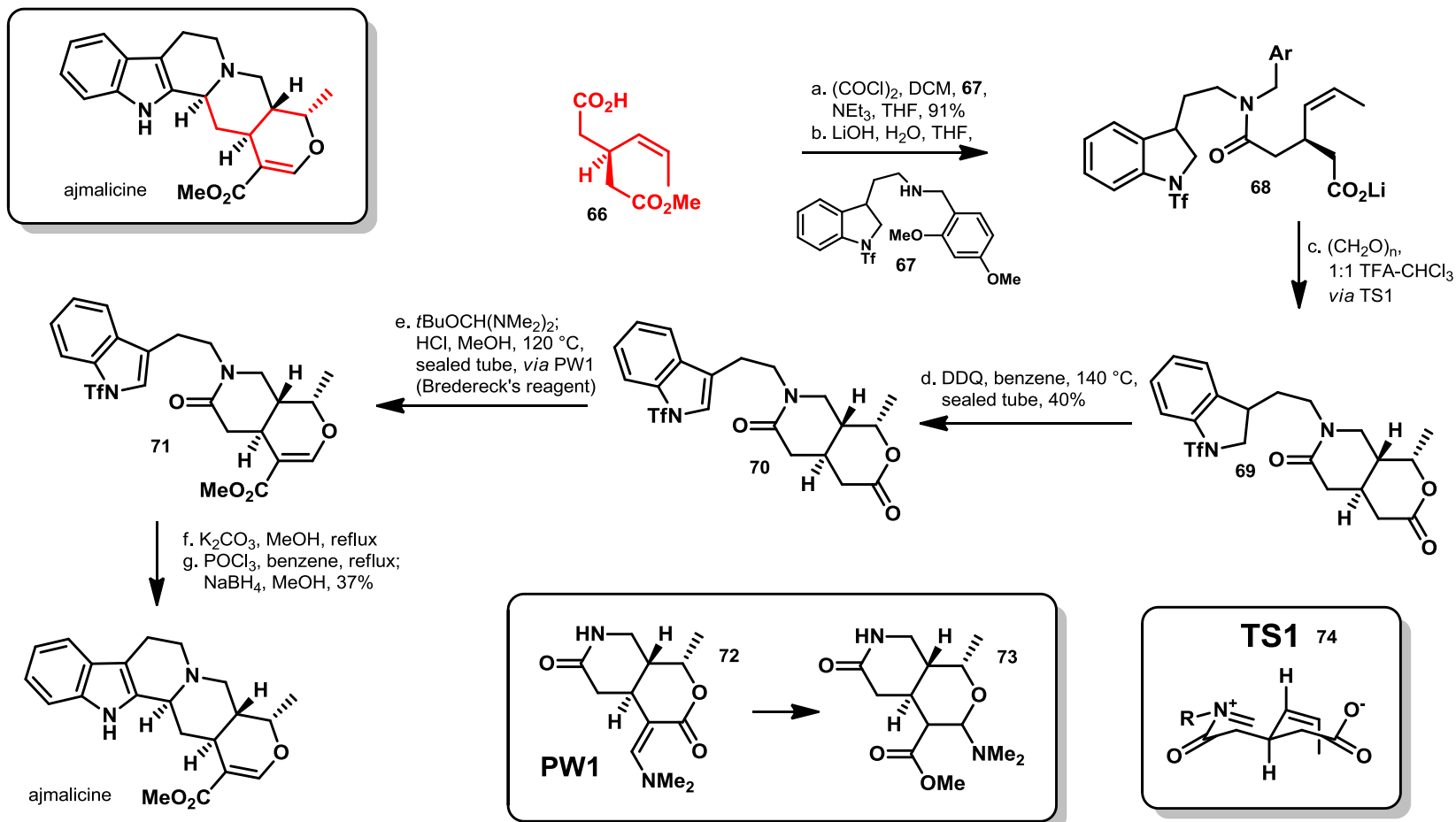
e. PPTS,  $\text{MeOH}$ , 50 °C  
f. TsOH,  $\text{CHCl}_3$ , rt, 96%



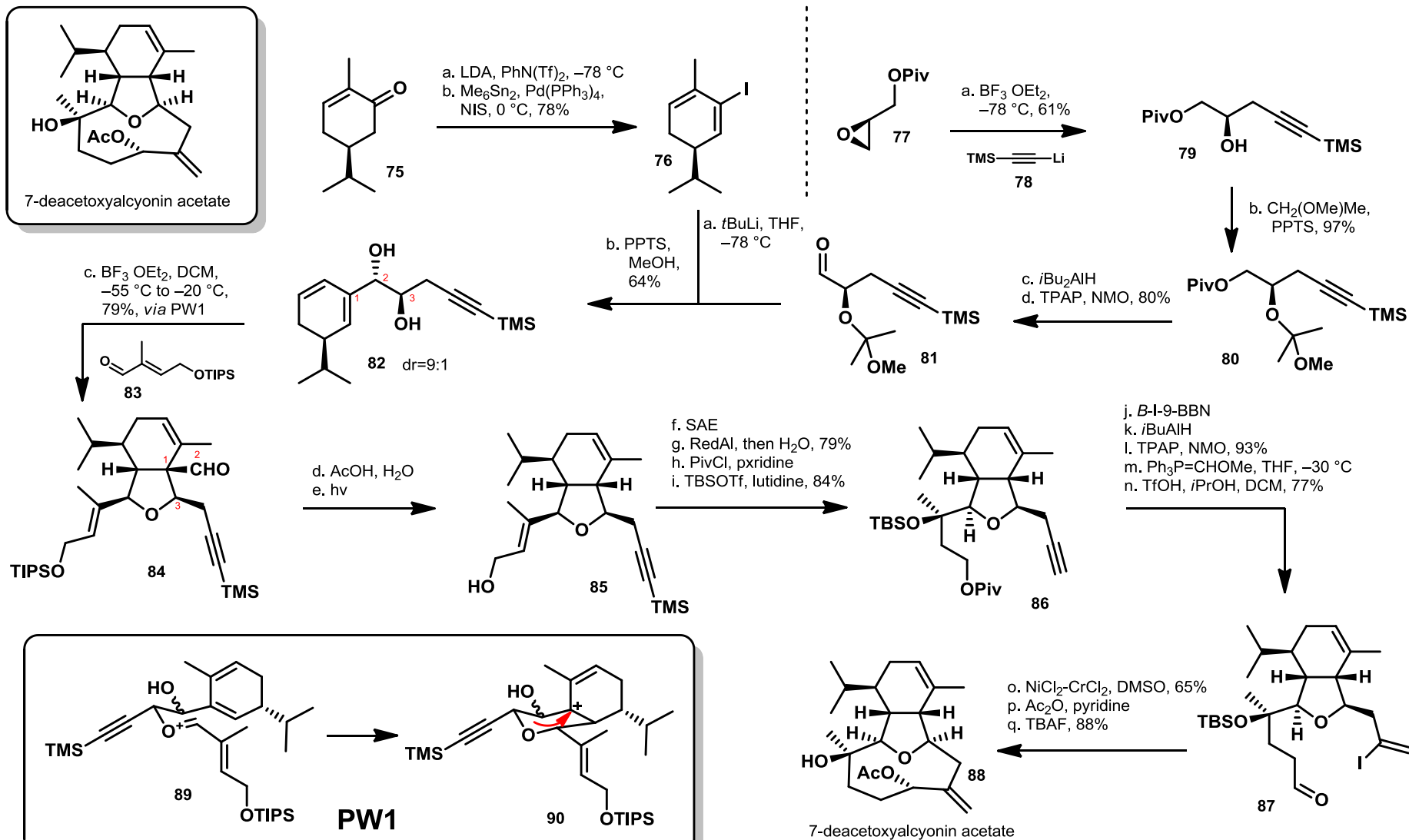
# Ptilomycalin - Overman



# Ajmalicine - Overman

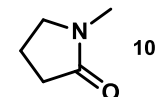
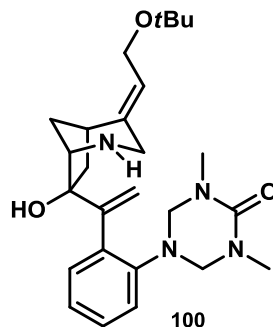
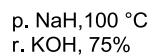
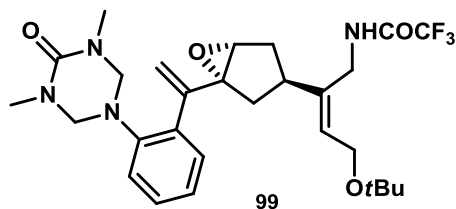
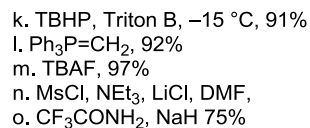
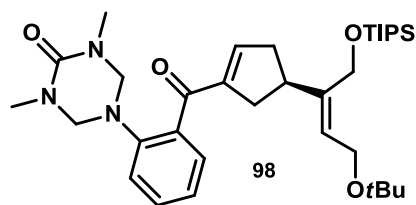
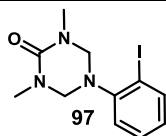
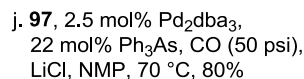
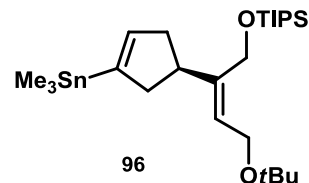
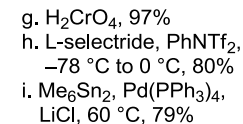
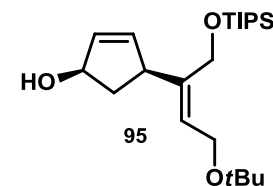
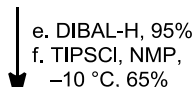
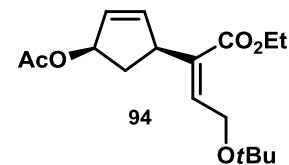
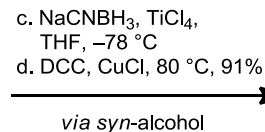
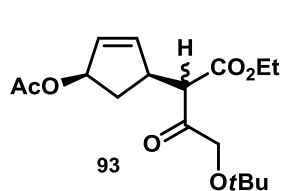
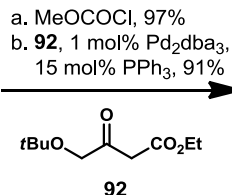
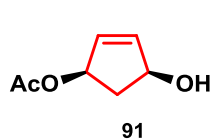
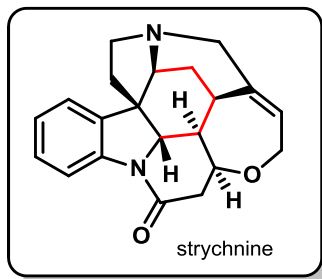


# 7-Deacetoxyalcyonin acetate - Overman



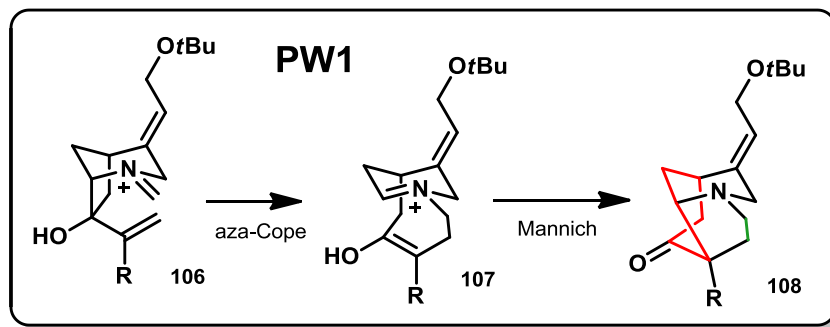
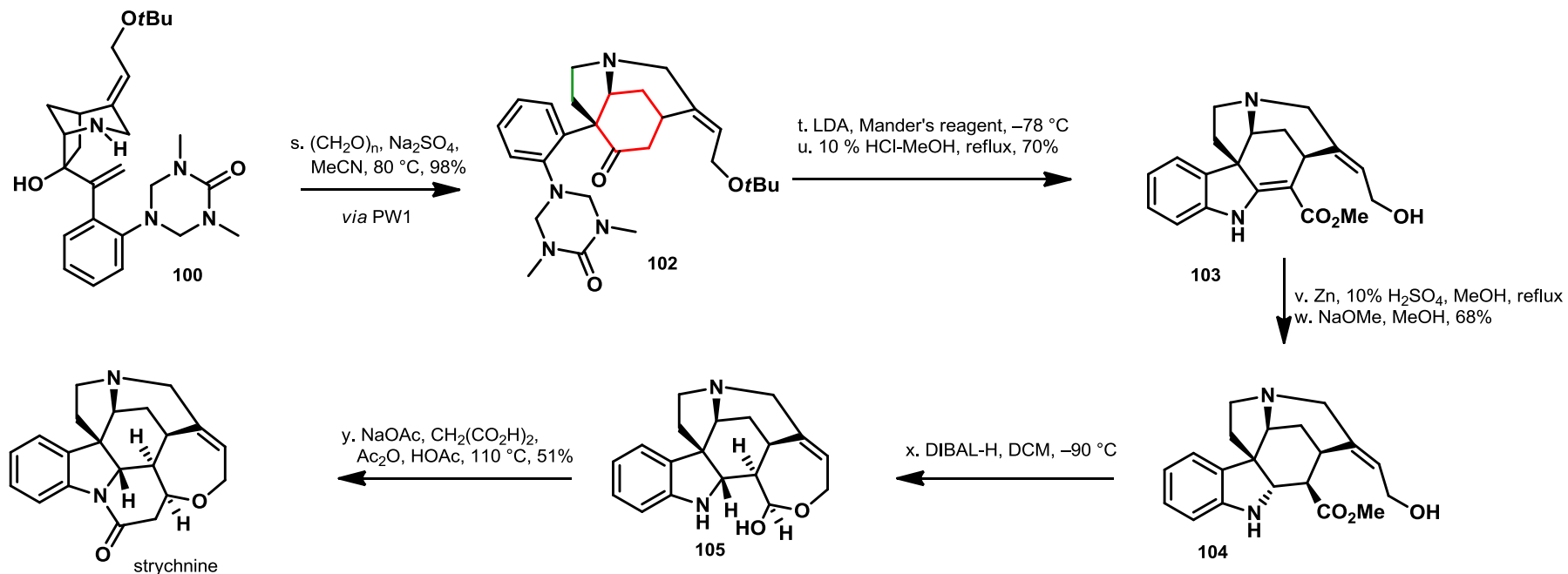
D. W. C. MacMillan, L. E. Overman, *JACS*, 1995, 117, 10391-10392

# Strychnine - Overman



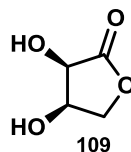
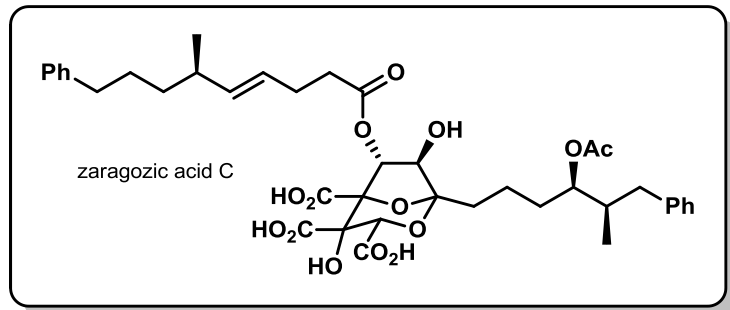
NMP=N-methyl-2-pyrrolidinone

# Strychnine - Overman

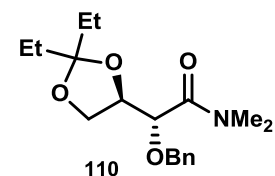




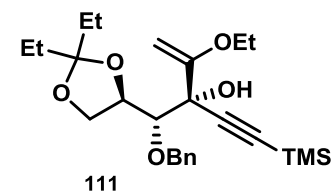
# Zaragozic Acid C – Carreira & Du Bois



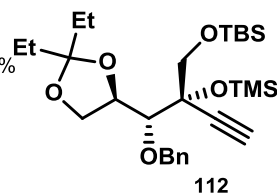
a. Me<sub>2</sub>NH, MeOH, 0 °C, 97%  
b. (MeO)<sub>2</sub>CEt<sub>2</sub>, cat. TsOH, 90%  
c. NaH, BnBr, THF, 96%



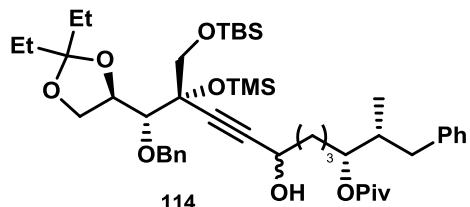
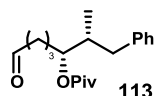
d. (ethoxyvinyl)Li, THF, -78 °C  
e. TMSCCMgBr, THF, -78 °C, 84%



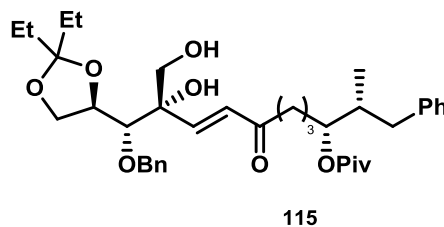
f. O<sub>3</sub>, DCM/ EtOH, -78 °C, 84%  
g. NaBH<sub>4</sub>, MeOH  
h. K<sub>2</sub>CO<sub>3</sub>, MeOH, 78%  
i. TBSCl, NEt<sub>3</sub>, then TMSCl, NEt<sub>3</sub>, DCM, 88%



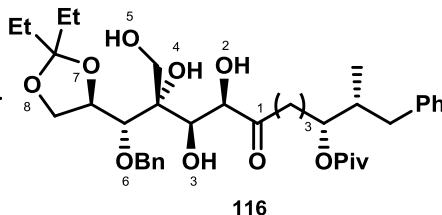
j. *n*BuLi, THF, -45 °C, then 113, LiBr, THF, 93%



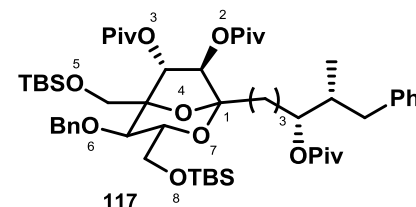
k. DMP, DCM, 93%  
l. [Cr(OAc)<sub>2</sub>, H<sub>2</sub>O]<sub>2</sub>, THF/H<sub>2</sub>O, 60%  
m. TBAF, THF, 93%



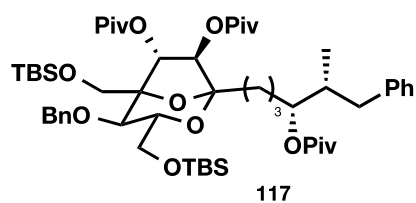
n. OsO<sub>4</sub>, NMO, Sharpless ligand, 95%, 1.7:1 desired/undesired



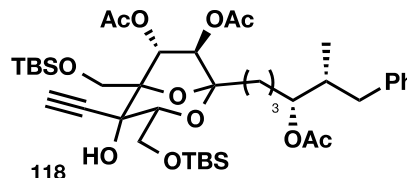
o. 0.5% HCl in MeOH, 86%  
p. TBSCl, DMAP, NEt<sub>3</sub>, DCM, 74%  
q. *t*BuCOCl, DMAP, DCE, 97%



# Zaragozic Acid C – Carreira & Du Bois

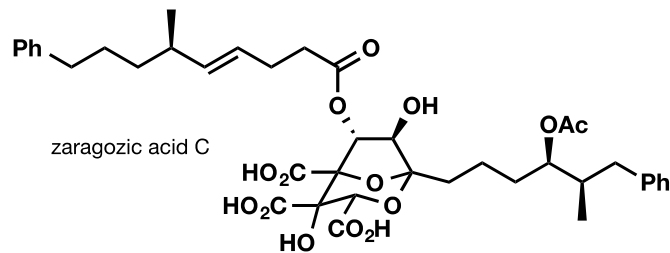


r. Pd(OH)<sub>2</sub>/C, Pd/CaCO<sub>3</sub>, H<sub>2</sub>, EtOH, 99%  
 s. Swern ox., 96%  
 t. TMSOCl, Et<sub>2</sub>O/NEt<sub>3</sub>,  
 up to 90% and 6.1:1 ratio  
 u. AgNO<sub>3</sub>, 2,6-lutidine, 90%  
 v. DIBAL-H, DCM/toluene, 84%  
 w. Ac<sub>2</sub>O, DMAP, DCM, 94%

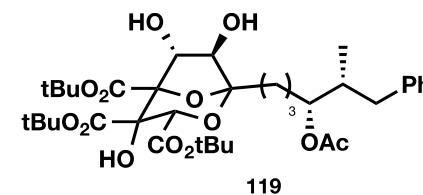
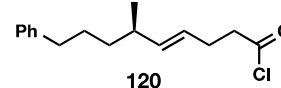


x. H<sub>2</sub>, Pd/C, pyridine  
 y. HF pyr, THF/pyridine, 64%  
 z. DMP, DCM/pyridine, 93%  
 aa. O<sub>3</sub>, DCM/MeOH, -78 °C  
 ab. Pinnick ox.

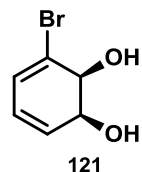
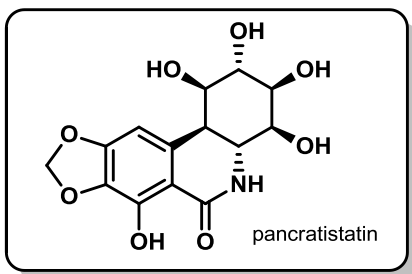
ac. N,N'-diisopropyl-O-  
*tert*-butylurea,  
 DCM, 72%  
 ad. K<sub>2</sub>CO<sub>3</sub>, MeOH, 90%



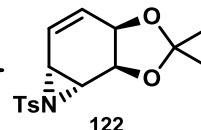
ae. (Boc<sub>2</sub>)O, 4-pyrrolidinopyridine, DCM, 82%  
 af. **120**, DCC, DMAP, 78%  
 ag. TFA, DCM, 100%



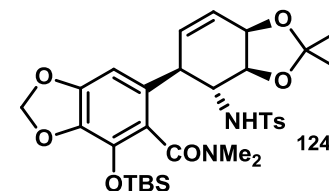
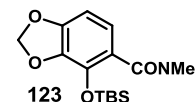
# Pancratistatin - Hudlicky



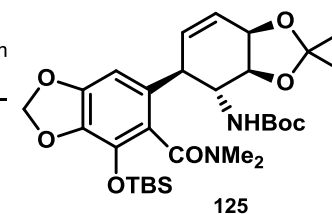
a. 2,2-DMP, TsOH, DCM  
b. PhINTs, Cu(acac)<sub>2</sub>, MeCN  
c. Bu<sub>3</sub>SnH, AIBN, THF, 78%



d. I. 123, BuLi, TMEDA, THF, -90 °C  
II. CuCN, -90 °C to -20 °C  
III. add 122, -78 °C to rt, 75%

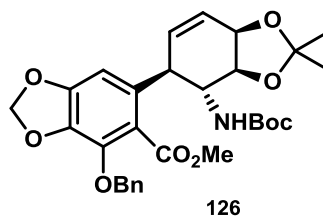


e. I. BuLi, THF  
II. (Boc)<sub>2</sub>O, 68%  
f. Na/anthracene, DME, -78 °C, 82%

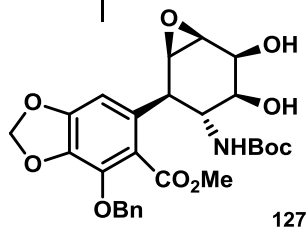


g. TBAF, THF, 93%  
h. sodium bis(methoxyethoxy)aluminum hydride, morpholine, 72%

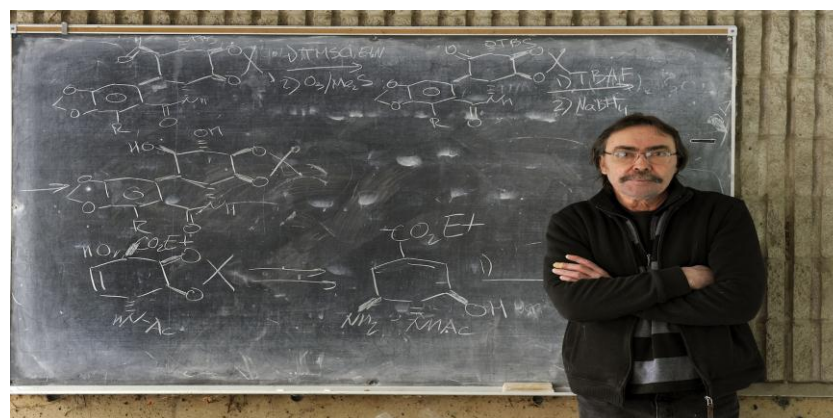
i. BnBr, K<sub>2</sub>CO<sub>3</sub>, DMF, 83%  
j. Pinnick ox.  
k. CH<sub>2</sub>N<sub>2</sub>, 98%



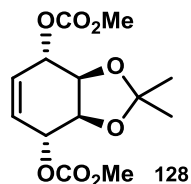
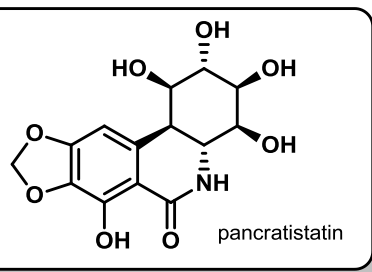
l. HOAc, H<sub>2</sub>O, 60 °C, 73%  
m. TBHP, VO(acac)<sub>2</sub>, benzene, 60 °C, 53%



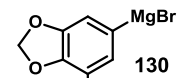
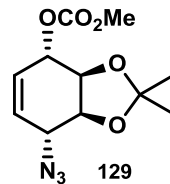
n. H<sub>2</sub>O, BzONa, 51%  
p. H<sub>2</sub>, Pd(OH)<sub>2</sub>/C, EtOAc, quant.



# Pancratistatin - Trost

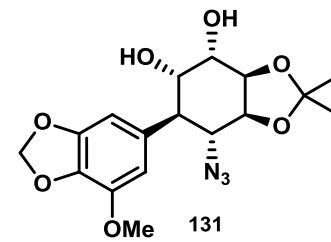


a. 0.5 mol%  $(C_3H_7PdCl)_2$ ,  
0.75 mol% STD-ligand,  
TMSN<sub>3</sub>, DCM, rt, 82%

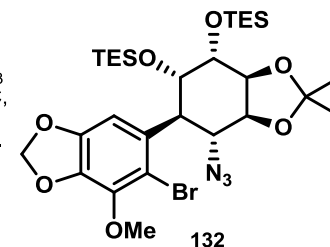


b. CuCN, THF,  
ether, 0 °C

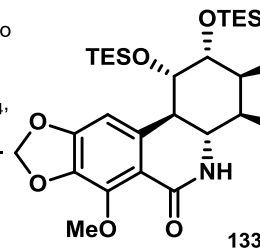
c. OsO<sub>4</sub>, NMO,  
DCM, rt, 62%



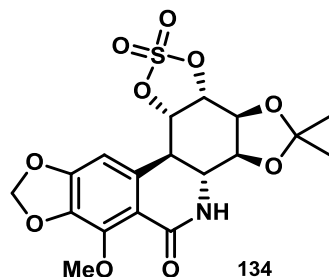
d. TESOTf, 2,6-lutidine,  
DCM, quant  
e. NBS, DMF, 75%



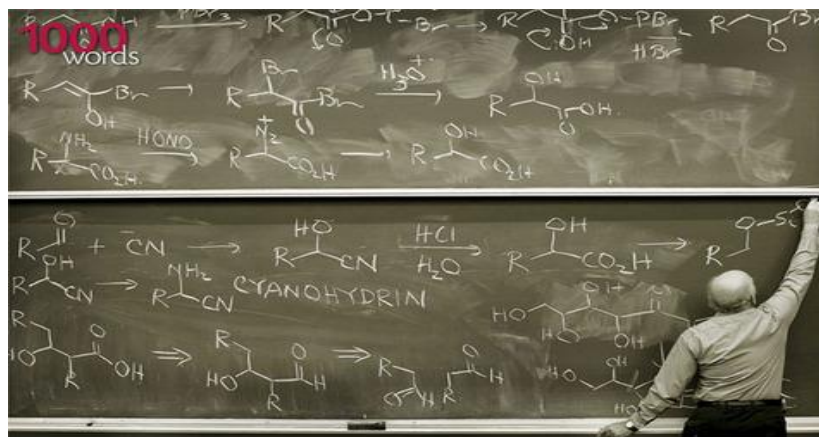
f. I. PMe<sub>3</sub>, THF, H<sub>2</sub>O  
II. COCl<sub>2</sub>, THF, NEt<sub>3</sub>  
g. tBuLi, ether, -78 °C,  
65%



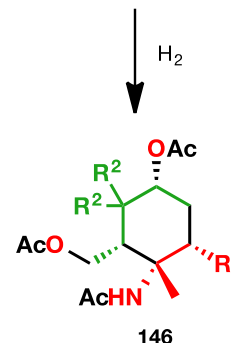
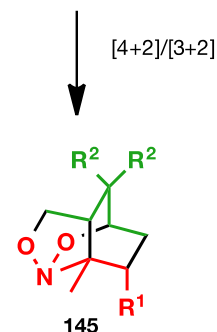
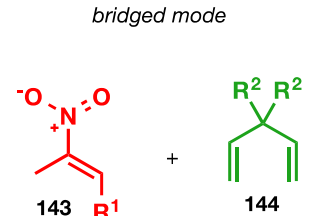
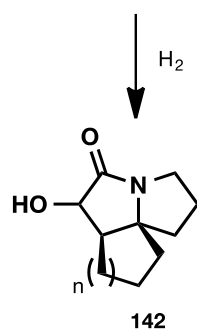
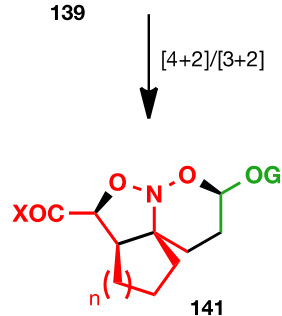
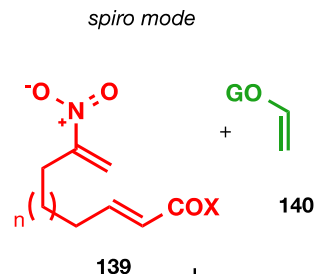
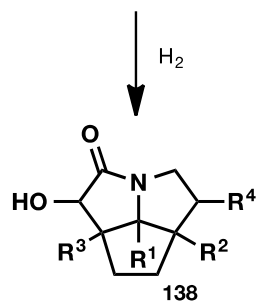
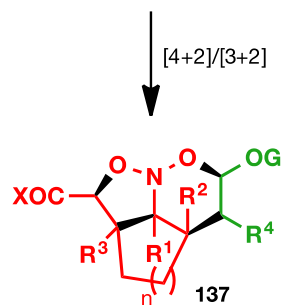
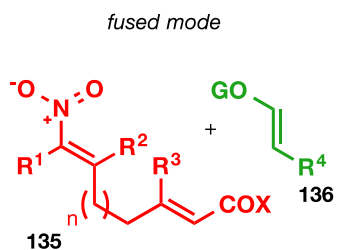
h. TBAF, THF, -78 °C to  
0 °C  
i. I. SOCl<sub>2</sub>, NEt<sub>3</sub>  
II. RuCl<sub>3</sub>, NaIO<sub>4</sub>, CCl<sub>4</sub>,  
MeCN, H<sub>2</sub>O, 72%



j. PhCO<sub>2</sub>Cs, DMF, then THF,  
H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub> workup, 85%  
k. I. MeOH, K<sub>2</sub>CO<sub>3</sub>, rt  
II. LiI, DMF, 80 °C, 85%



# [4+2] / Intra [3+2] Cy.add. - Denmark

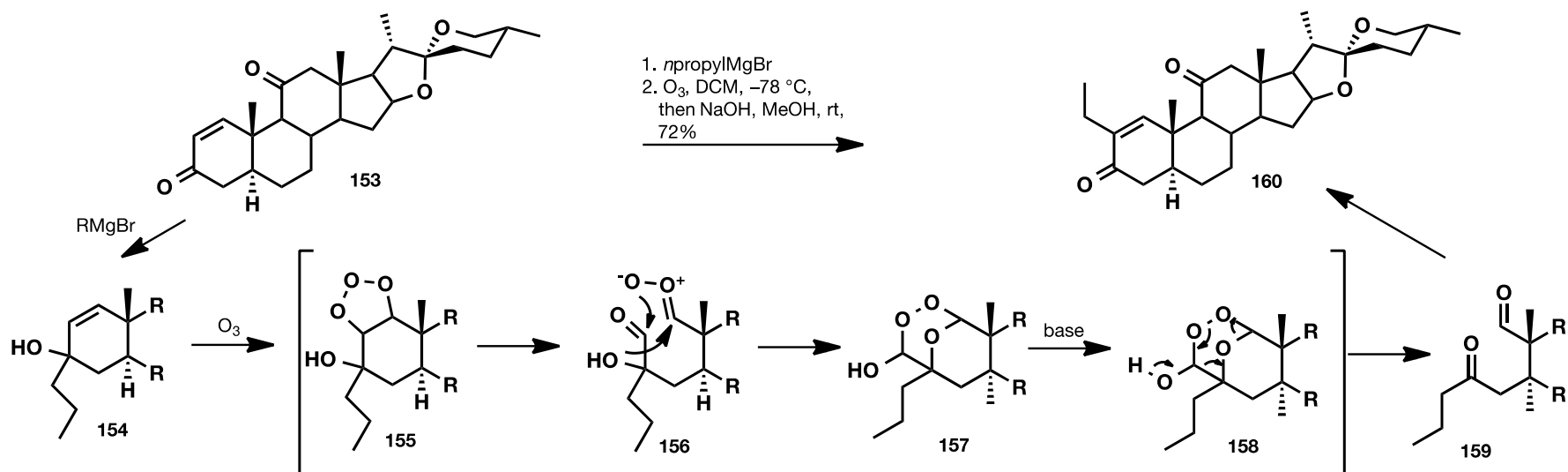
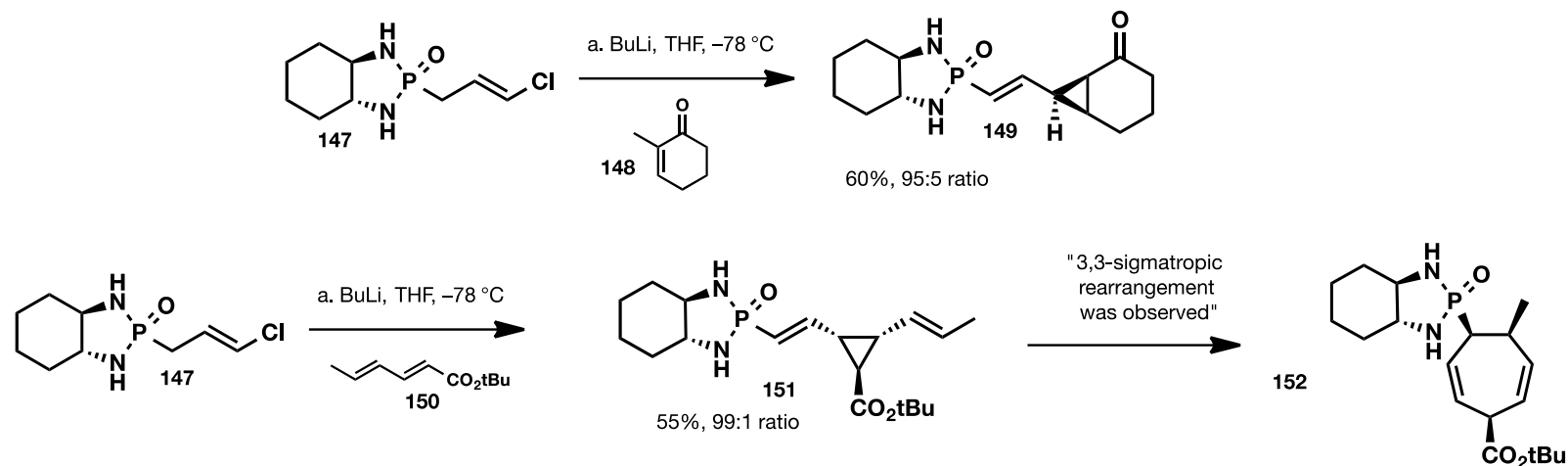


SnCl<sub>4</sub>, DCM, -15 °C, 55-91%  
then toluene, 110 °C, 79-100%

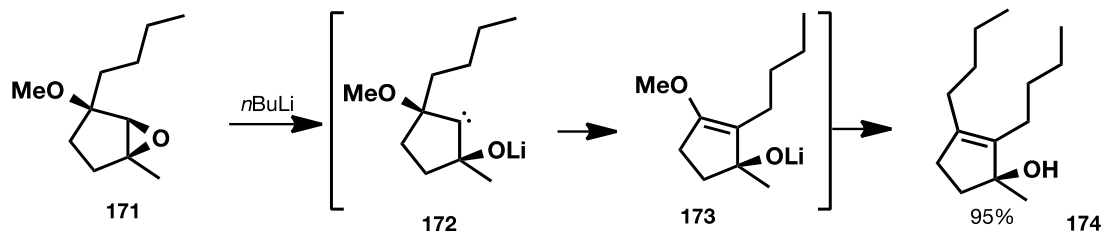
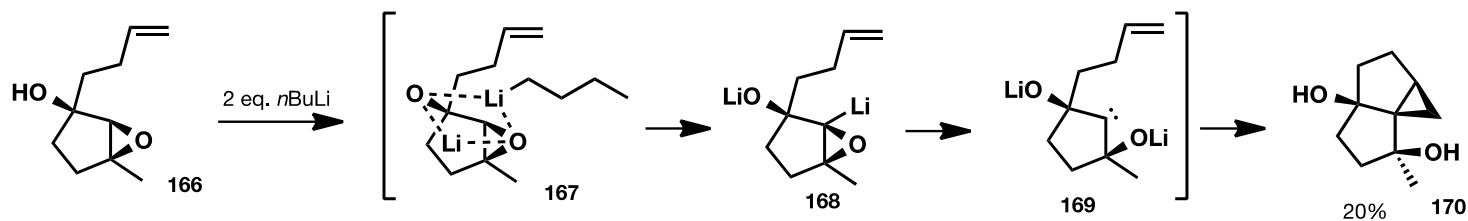
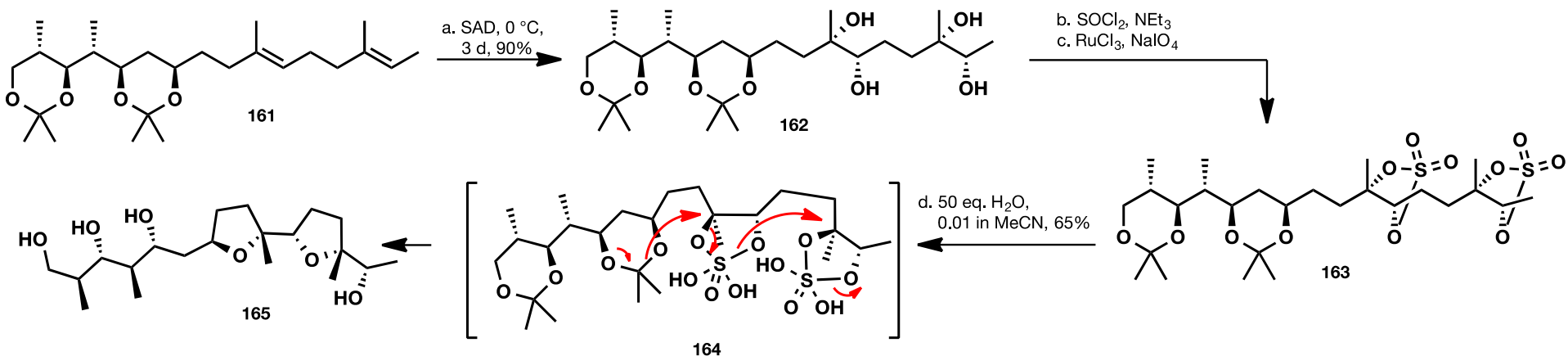
1. H<sub>2</sub>, Ra-Ni, MeOH, rt  
2. Ac<sub>2</sub>O, pyridine, 59-78%

R<sup>1</sup> can be Ph or aliphatic chains  
R<sup>2</sup> can be Me or 2 x H  
enantioselective example given

# More methodology



# More methodology



Top: T. Beauchamps, J. P. Powers, S. D. Rychnovsky, *JACS*, **1995**, *117*, 12873-12874 Bottom: E. Doris, L. Dechoux, C. Mioskowski, *JACS*, **1995**, *117*, 12700-12704

# Last slide

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**Questions?**