Cytochalasins

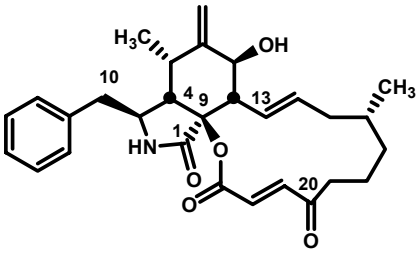
Ke Li

Group Meeting 01/18/06

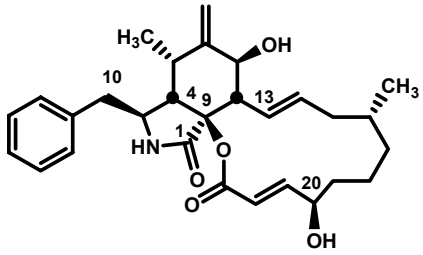
Cytochalasins

KE LI

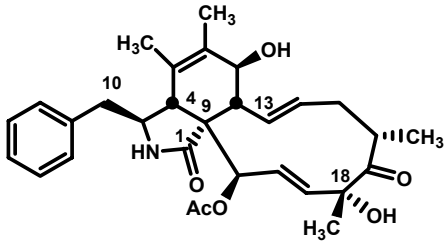
Cytochalasins (Greek *cytos*, cell; *chalasis*, relaxation) are a family of fungal metabolites with complex and diverse molecular structure and various biological activities. The common structure motif shared among different members is a rigid bicycic isoindolone core which is fused to a macrocycle. The different macrocyclic structures are believed to play an importrant role in the determination of biological activity. Most of cytochalasins are commercially available now for biological studies, which explains why there are only a few total synthesis in the field.



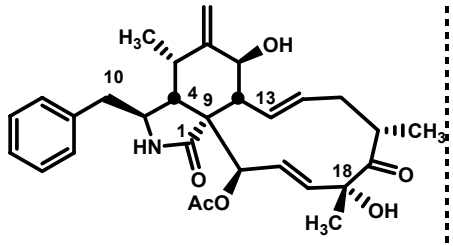
Cytochalasin A



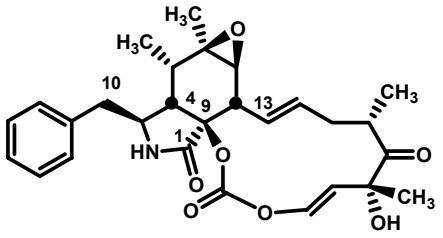
Cytochalasin B



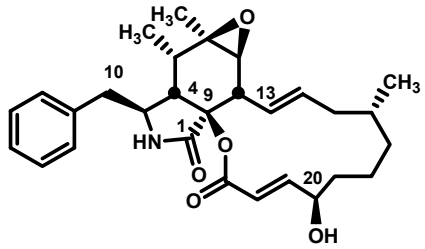
Cytochalasin C



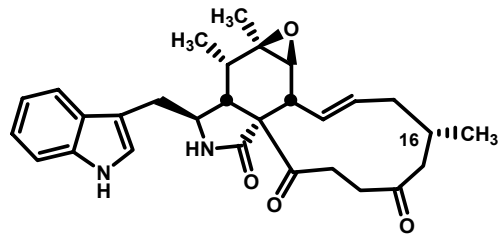
Cytochalasin D



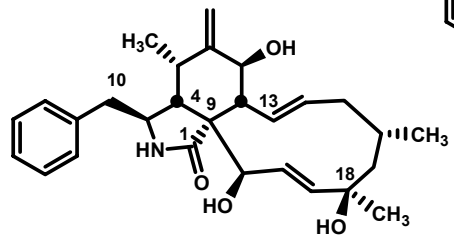
Cytochalasin E



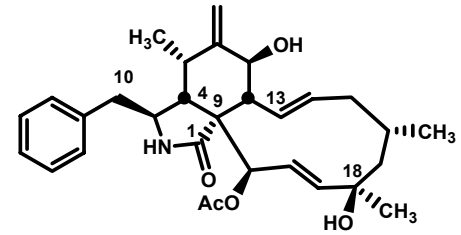
Cytochalasin F



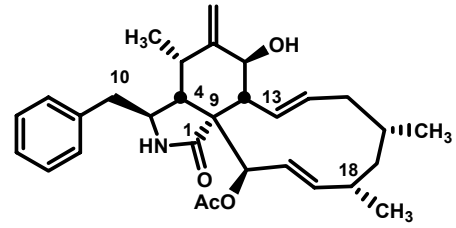
Cytochalasin G



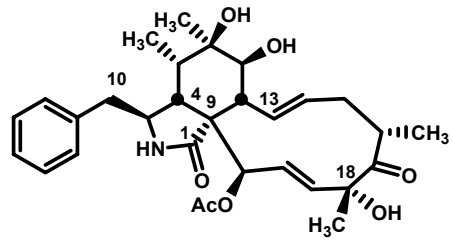
Cytochalasin J



Cytochalasin H



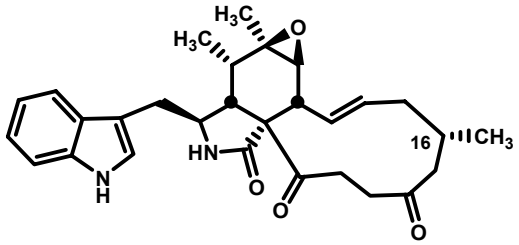
L-696,474



Cytochalasin O

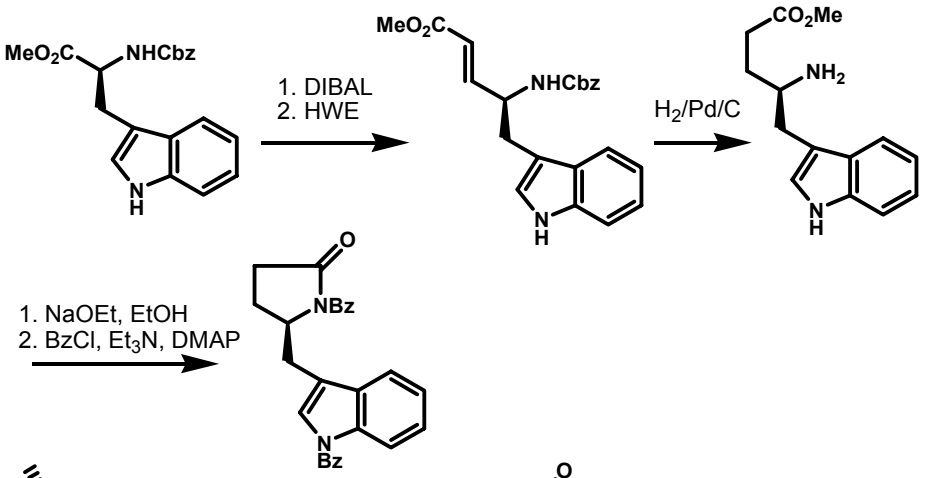
Cytochalasins

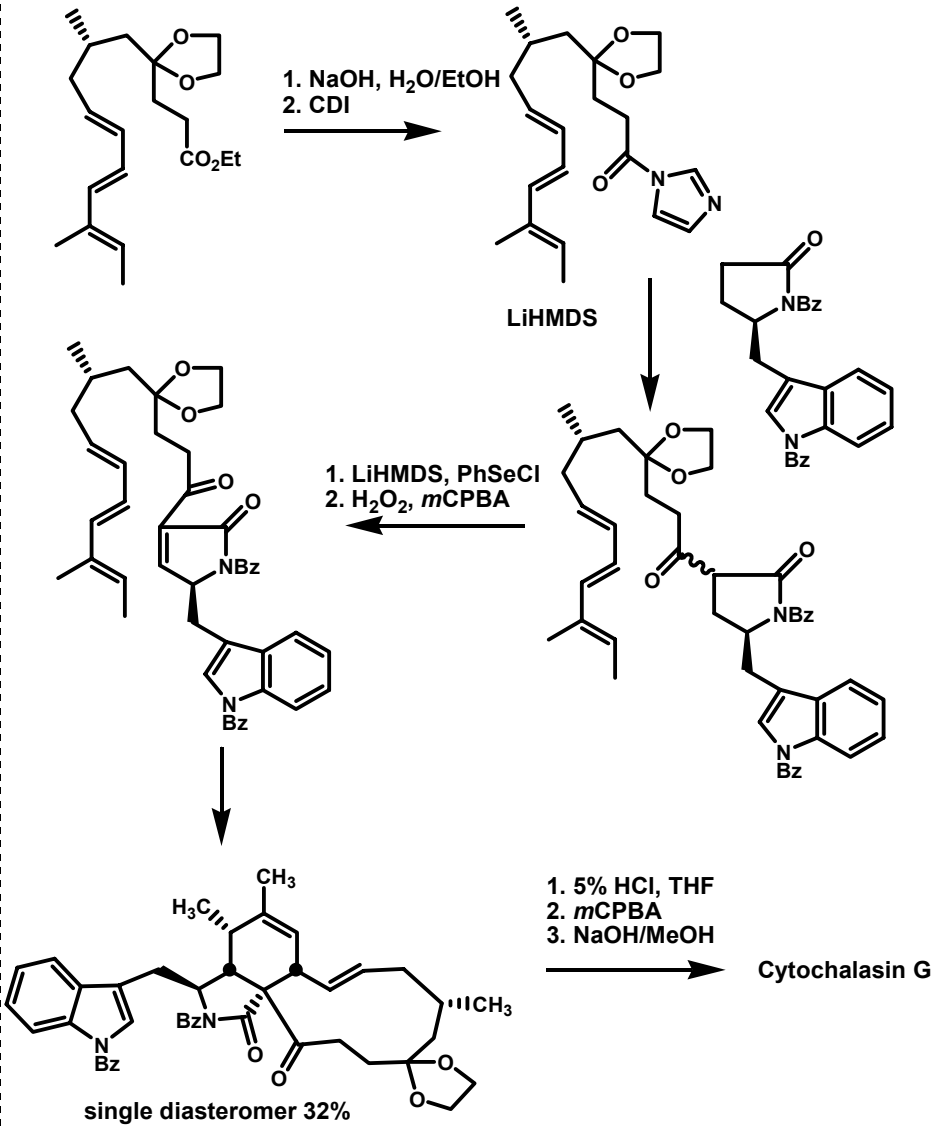
KE LI

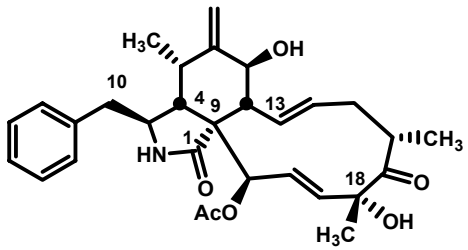


Cytochalasin G

Thomas, E.J. and coworkers *J. Chem. Soc. Chem. Comm. 1986,* 1447

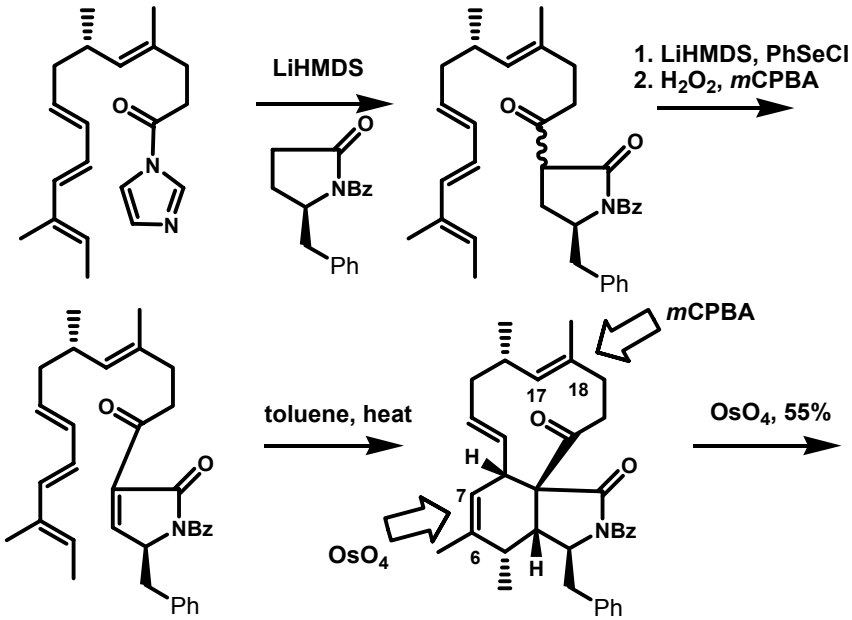


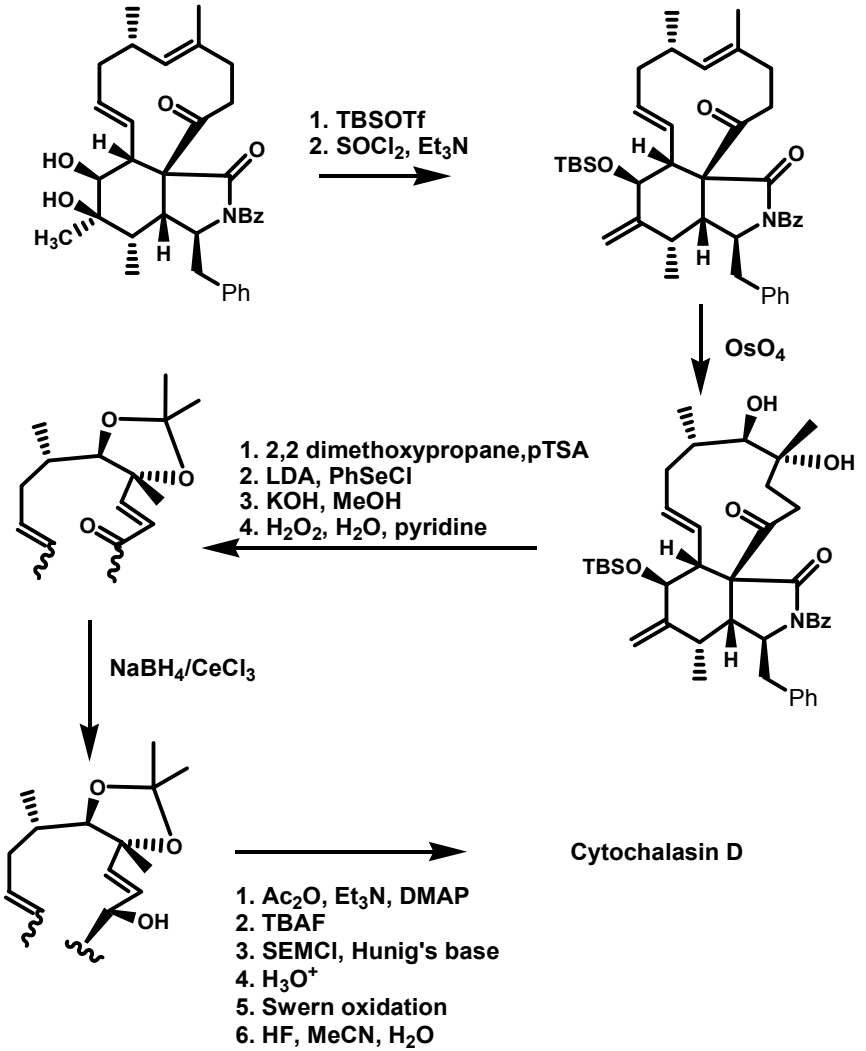


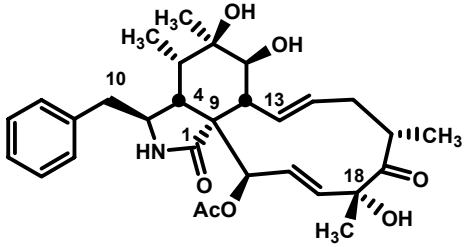


Cytochalasin D

Thomas, E.J. and coworkers *J. Chem. Soc. Chem. Comm. 1990,* 464

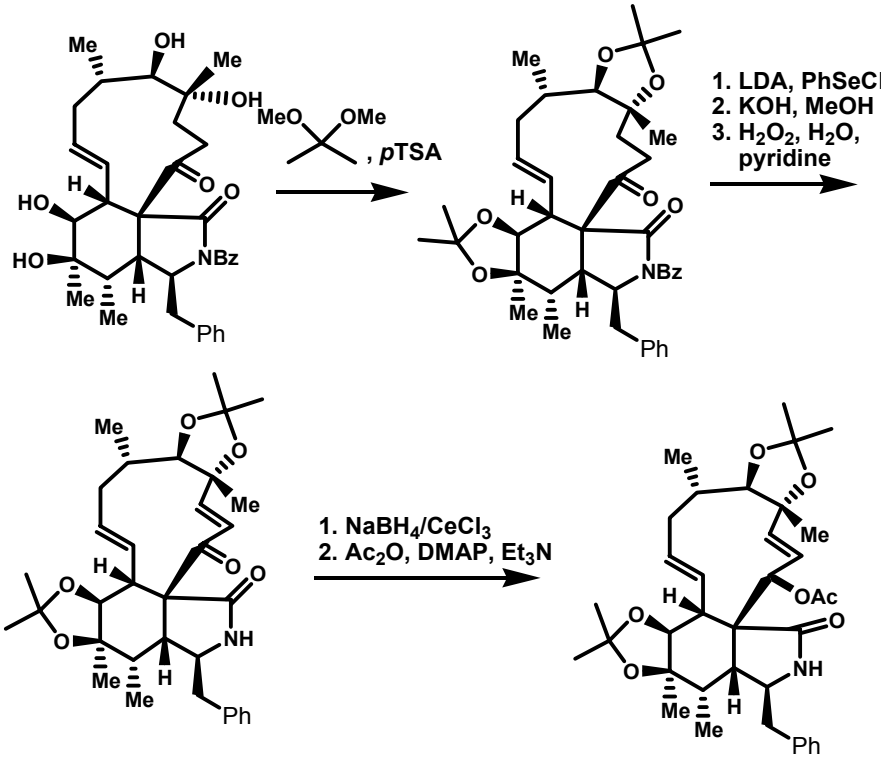


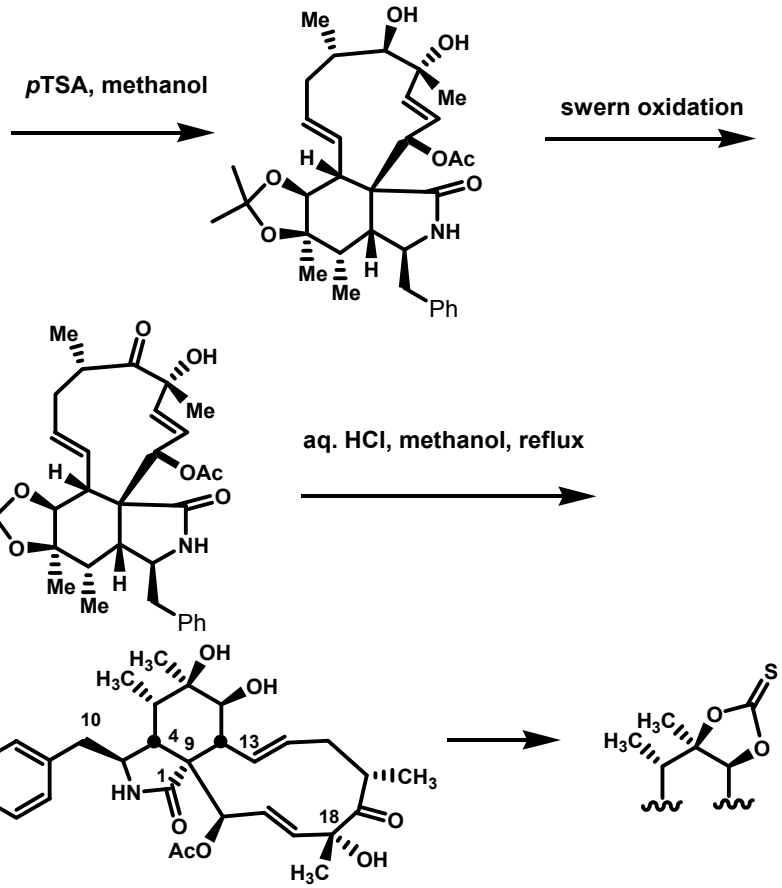




Cytochalasin O

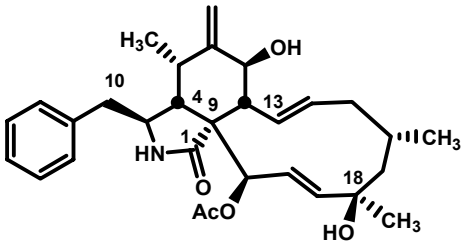
Thomas, E.J. and coworkers *J. Chem. Soc. Perkins Trans. 1, 1999, 3269*





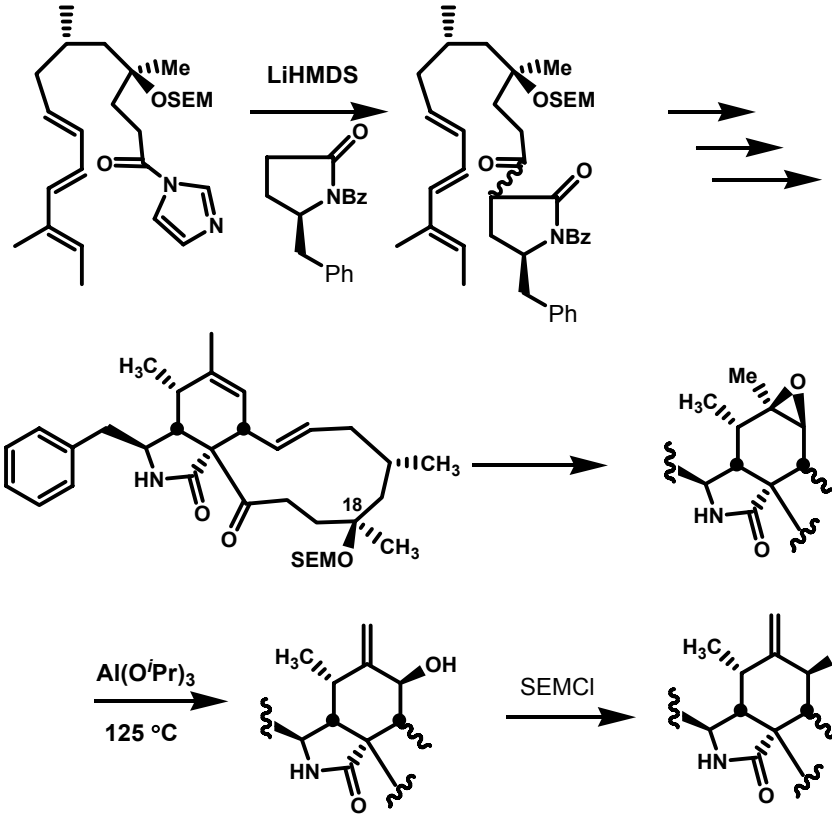
Cytochalasin O

absolute configuration was confirmed by total synthesis



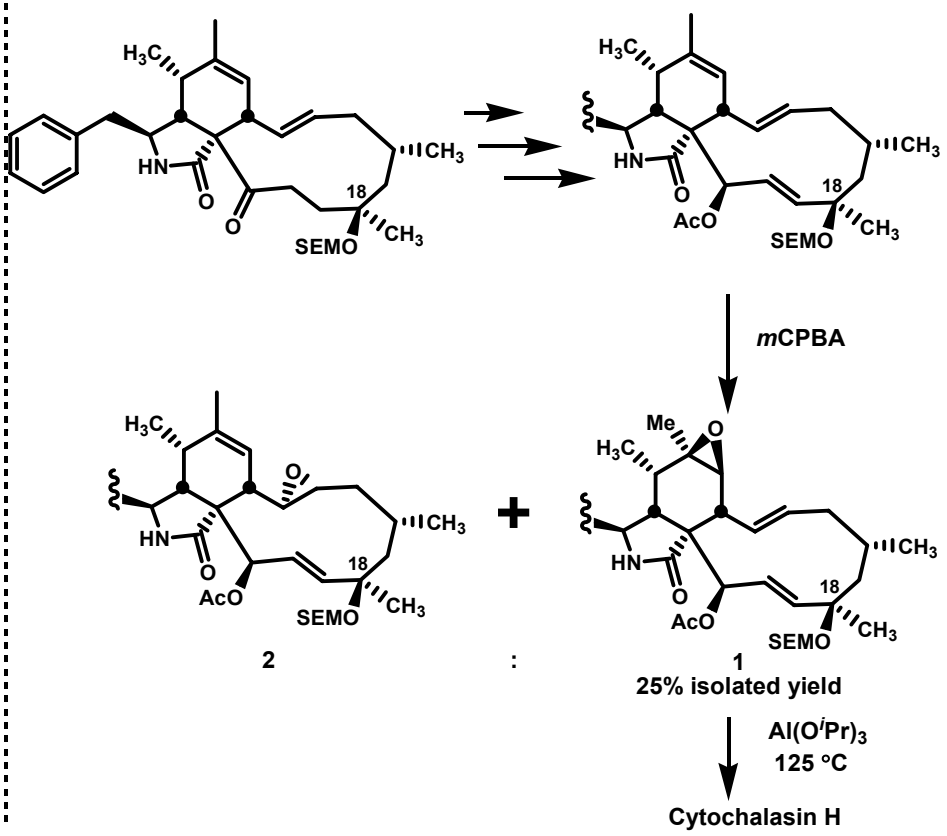
Cytochalasin H

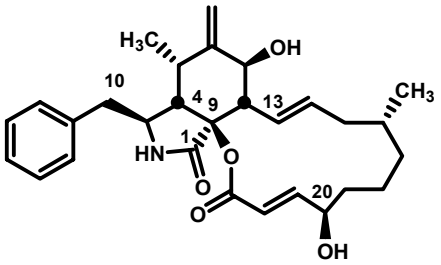
Thomas, E.J. and coworkers *J. Chem. Soc. Chem. Comm. 1986, 724, 727*



Cytochalasin H

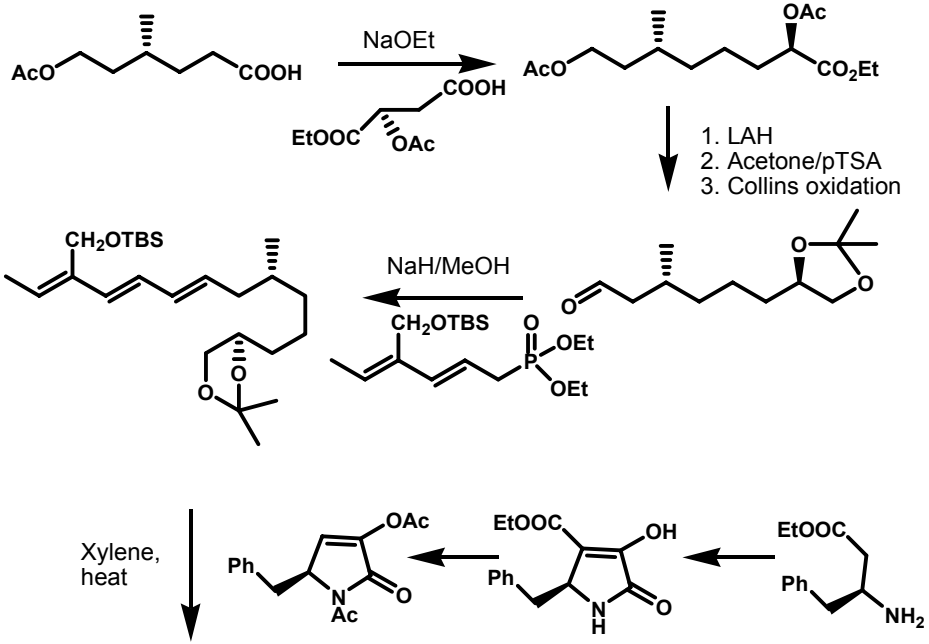
Alternative route:

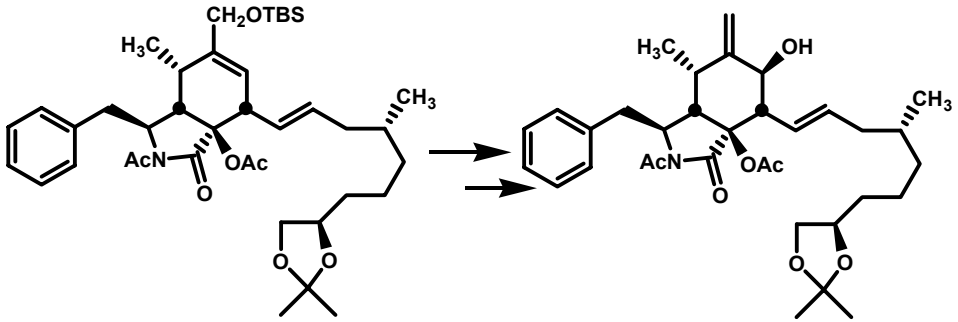




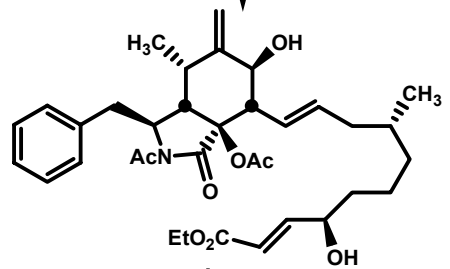
Cytochalasin B

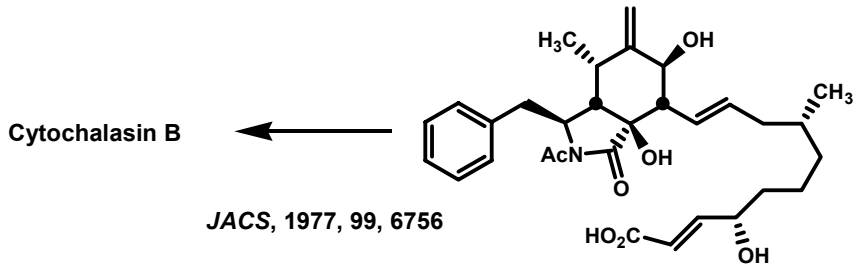
Stork, JACS, 1978, 100, 7775



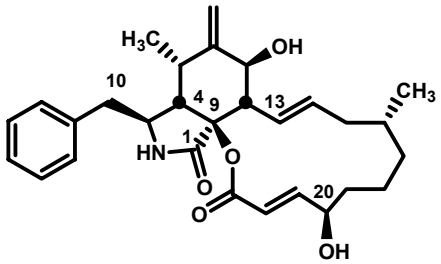


4:1 favored desired isomer



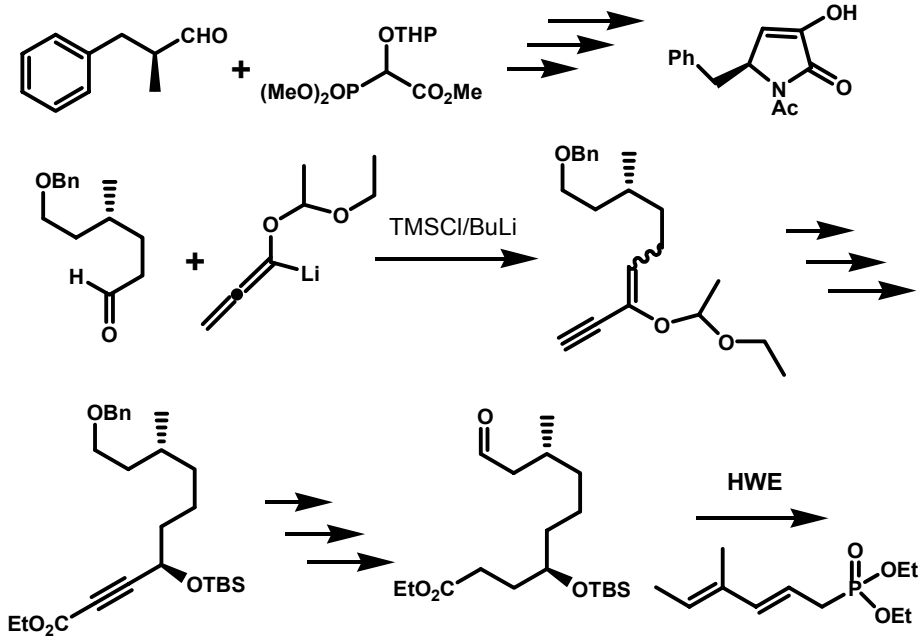


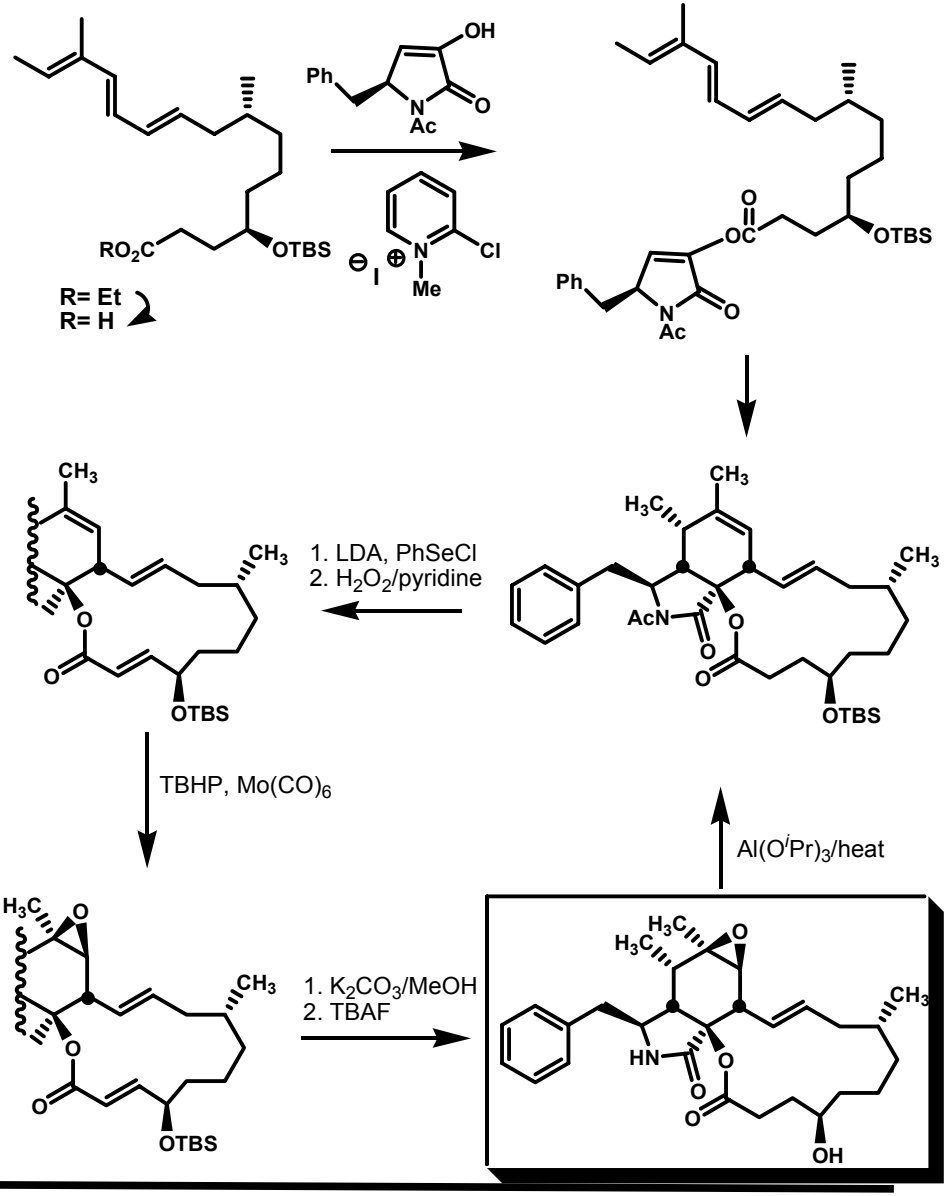
JACS, 1977, 99, 6756

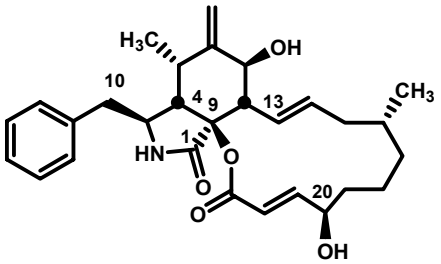


Cytochalasin B

Stork, *JACS*, 1983, 105, 5510

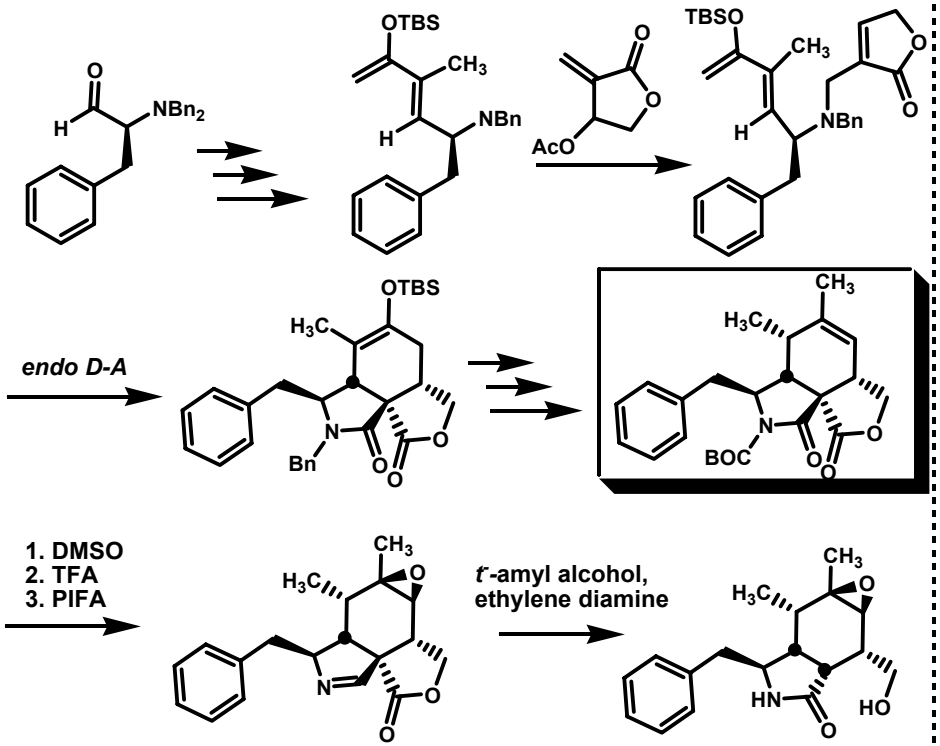


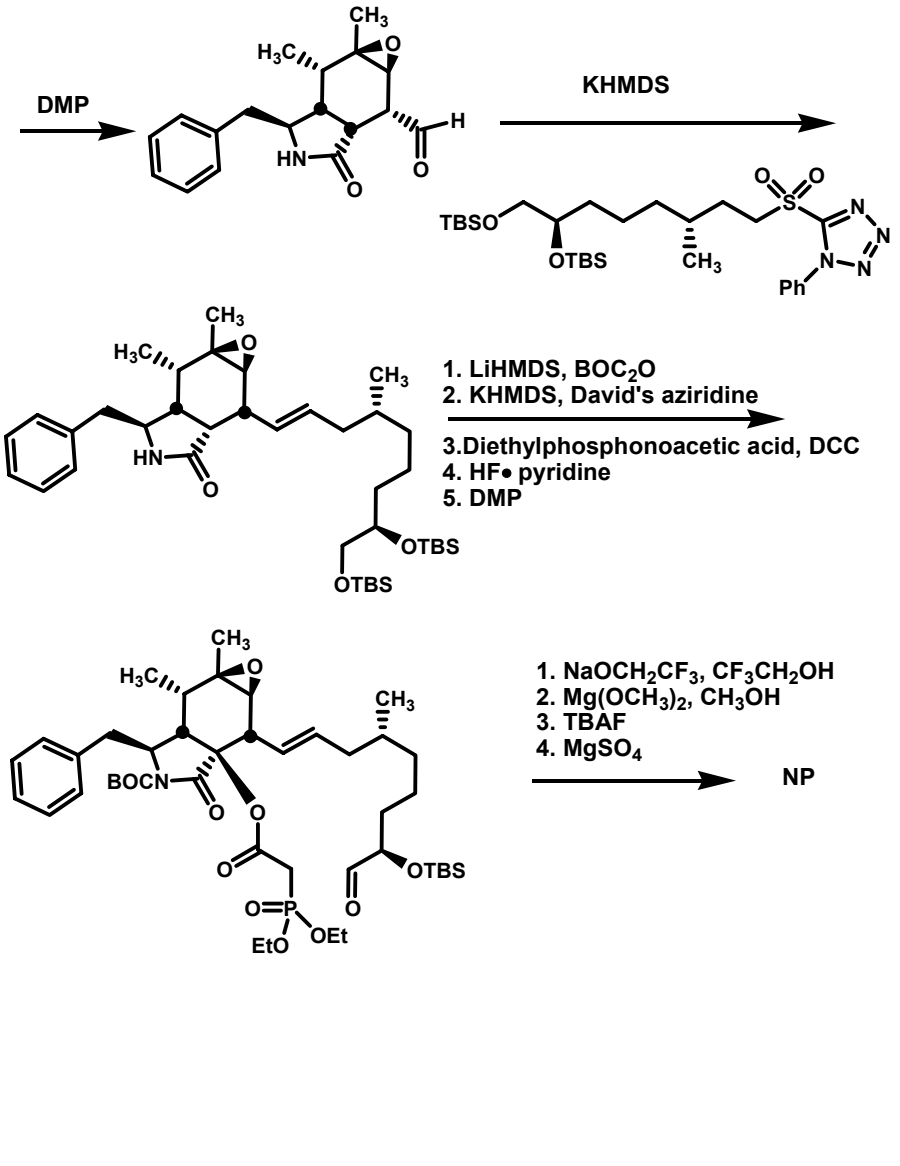


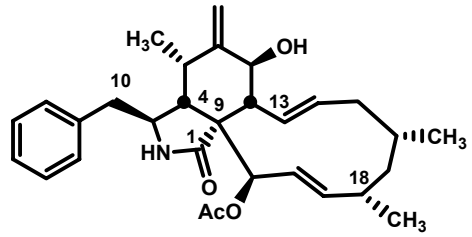


Cytochalasin B

Myers, PNAS, 2004, 101, 12048

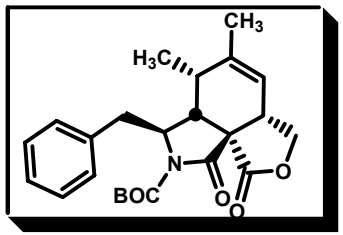


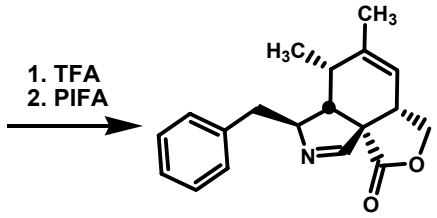




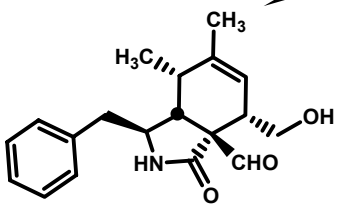
L-696,474

Myers, PNAS, 2004, 101, 12048



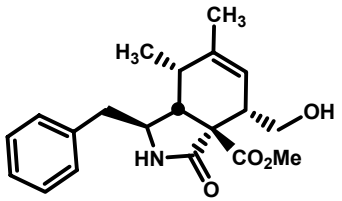


1. TFA
2. PIFA

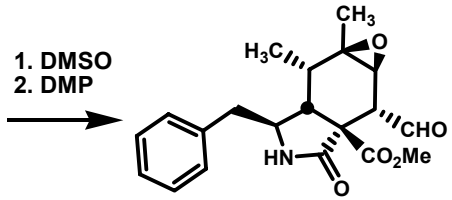


$EtCO_2Et/H_2O$

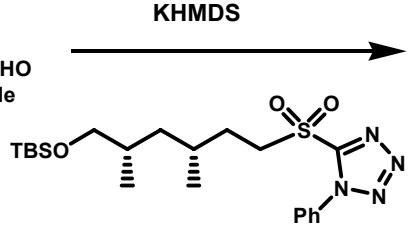
AcOH



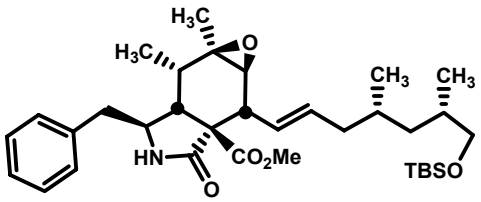
1. 1,3-diaminopropane, CF_3CH_2OH then pH 7 buffer
2. KOH, I_2, CH_3OH



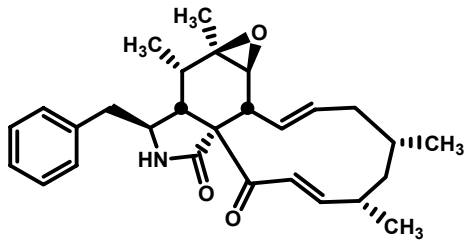
1. DMSO
2. DMP



KHMDS

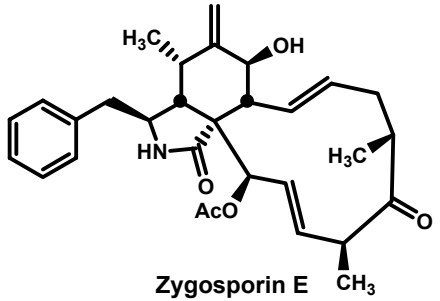


1. $(CH_3O)_2POCH_2Li$
2. TBAF
3. DMP
4. $NaOCH_2CF_3$, CF_3CH_2OH



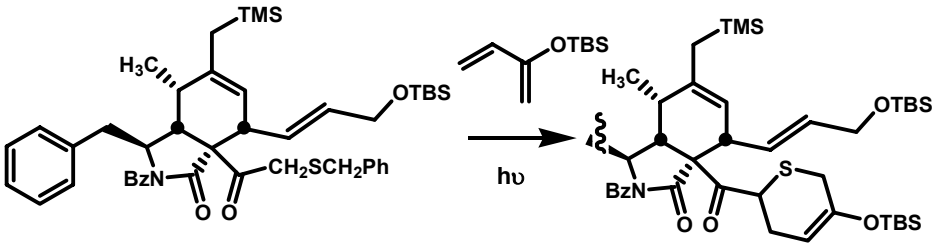
1. $CeCl_3$, $NaBH_4$
2. Ac_2O, pyridine
3. $MgSO_4$

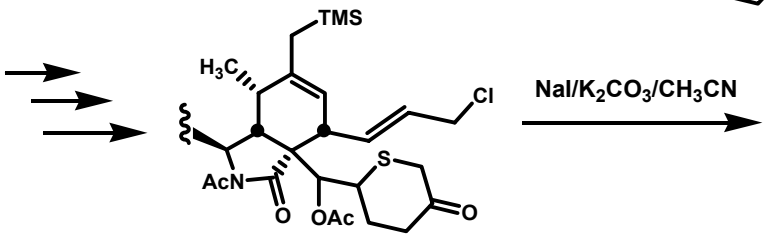
NP

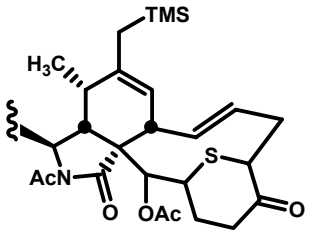


Zygosporin E

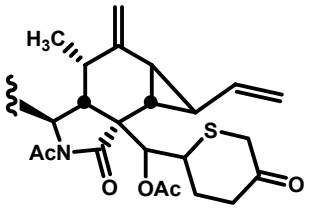
Vedejs, E. *et al*, *JACS*, 1984, *106*, 4617
JACS, 1988, *110*, 4822



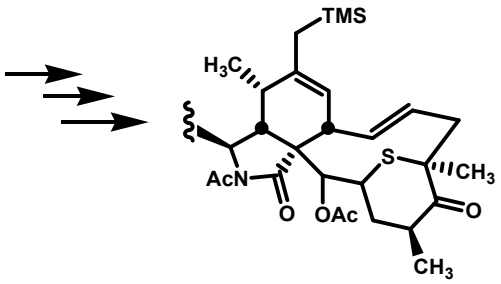


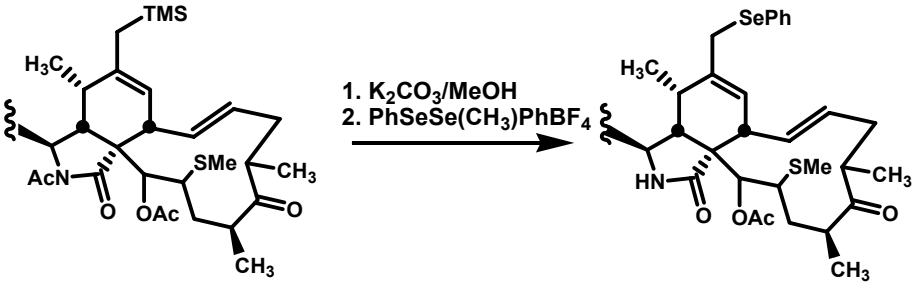


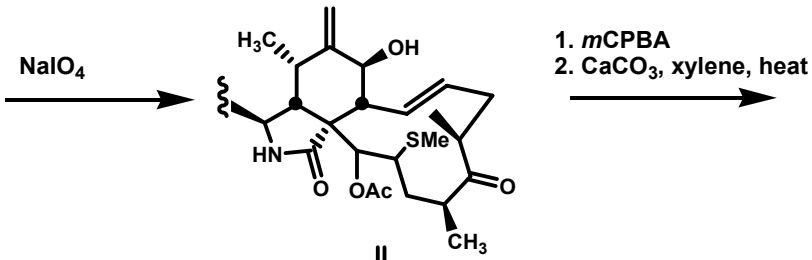
desired product 71%

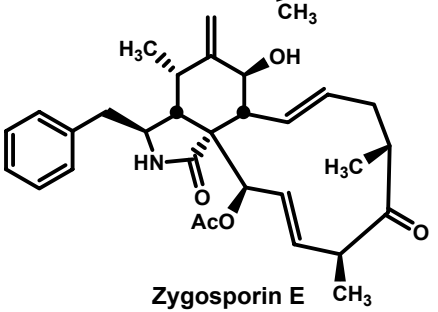


side product 9%

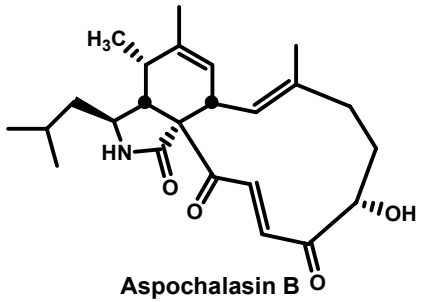


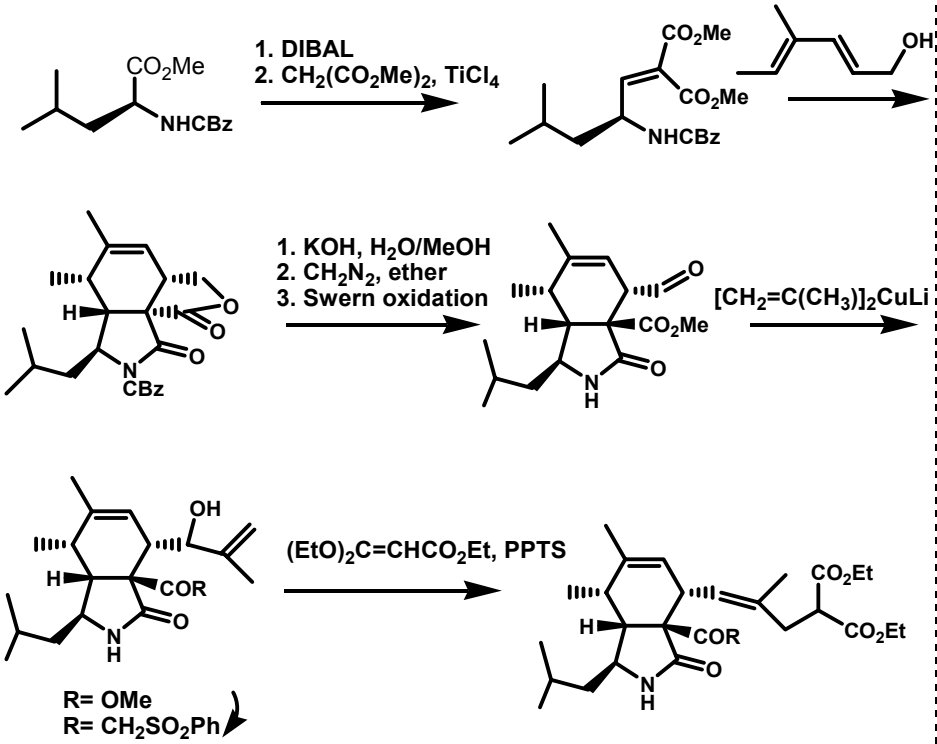
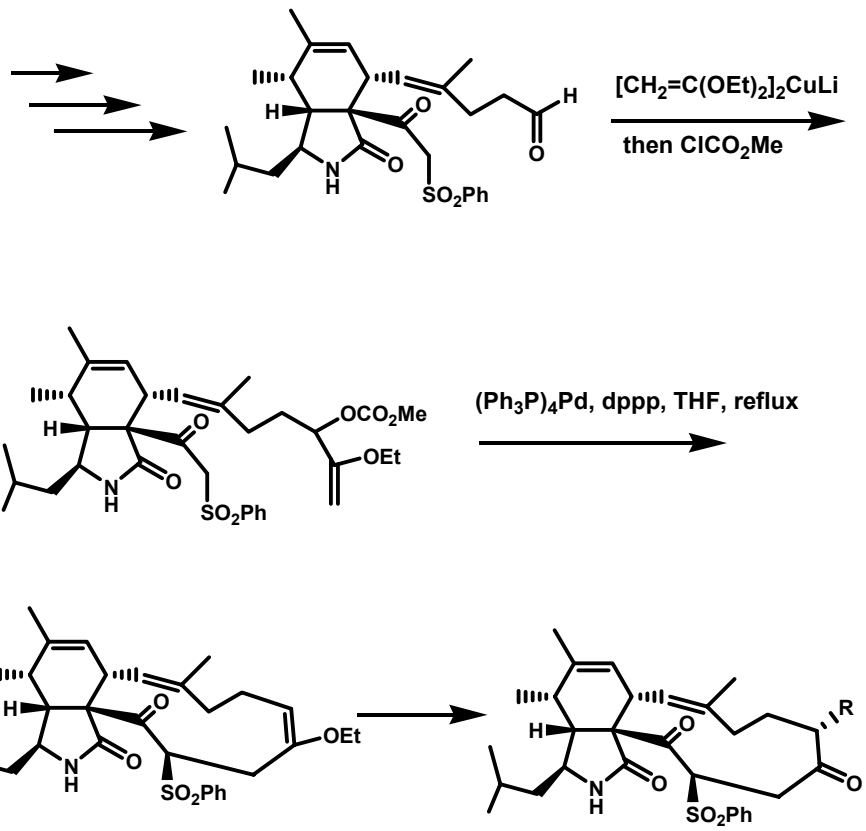






Zygosporin E



Aspochalasin B

Trost, B.M.. *et al*, *JACS*, 1989, *111*, 8281