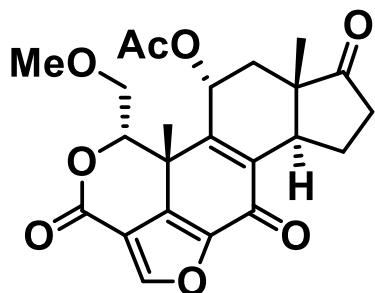
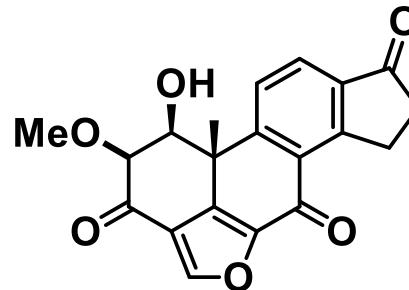


Total Synthesis of Wortmannin and Viridin



(+)-Wortmannin



(-)-Viridin

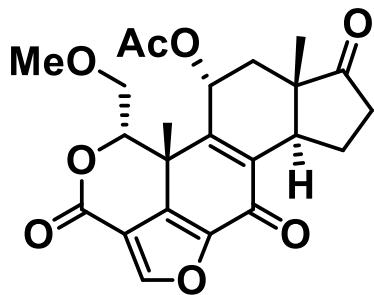
Chideraa Nwachukwu

Roberts group

Synthesis Club

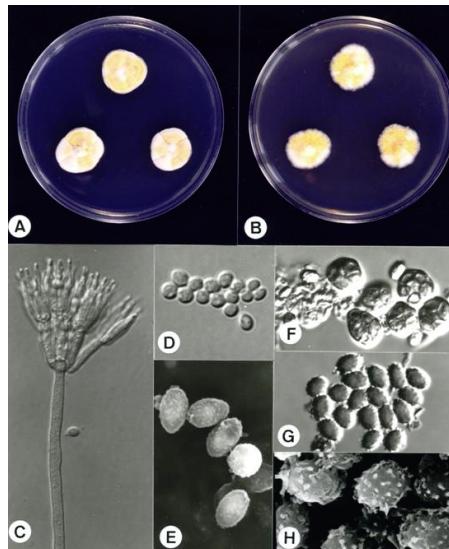
27 February 2019

Wortmannin



(+)-Wortmannin

- ❖ Antifungal and anti-inflammatory antibiotics
- ❖ Phosphoinositide 3-kinases (PI3Ks) inhibitor with $IC_{50} = 5\text{nM}$

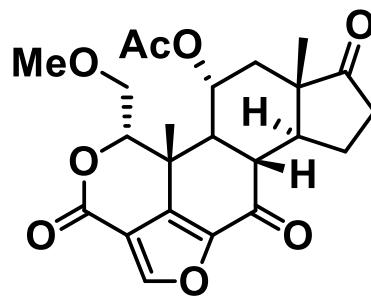


- ❖ Isolated from culture filtrates of *Penicillium* and *Myrothecium* species in 1972

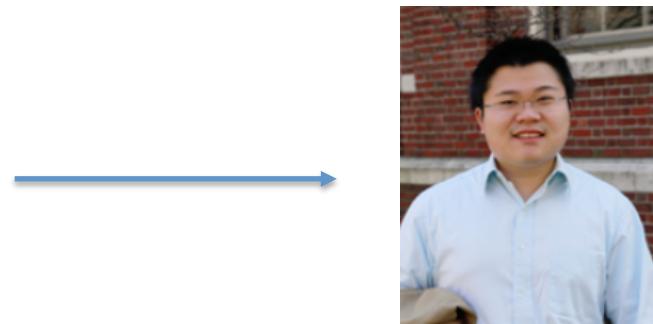
Wortmannin



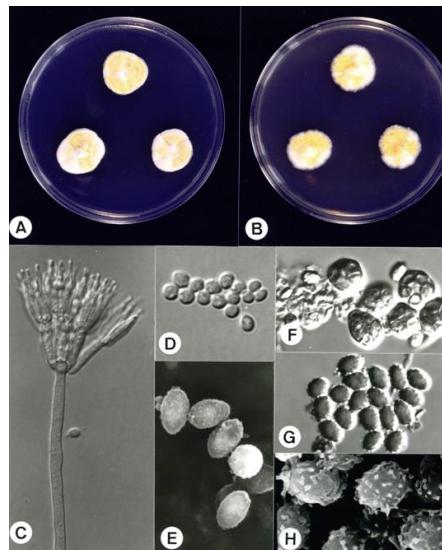
Shibasaki completed
the first total synthesis
in 1996



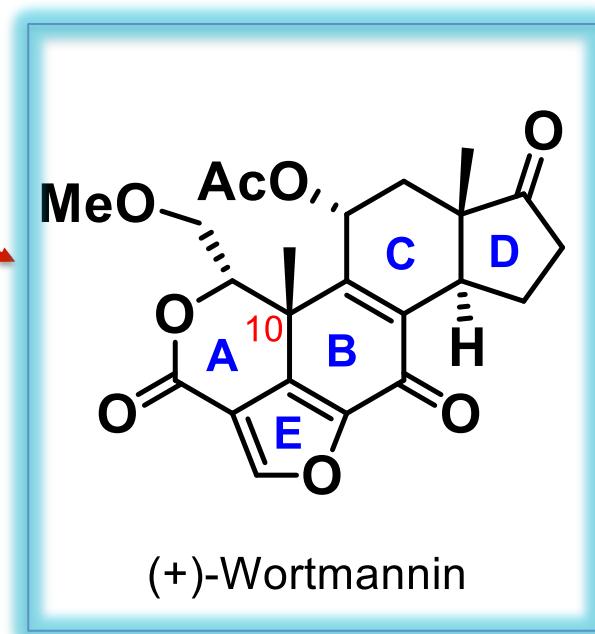
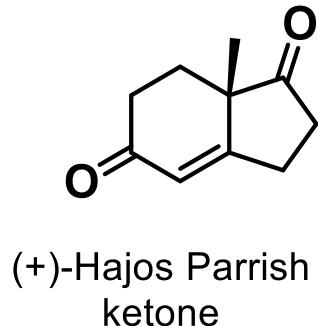
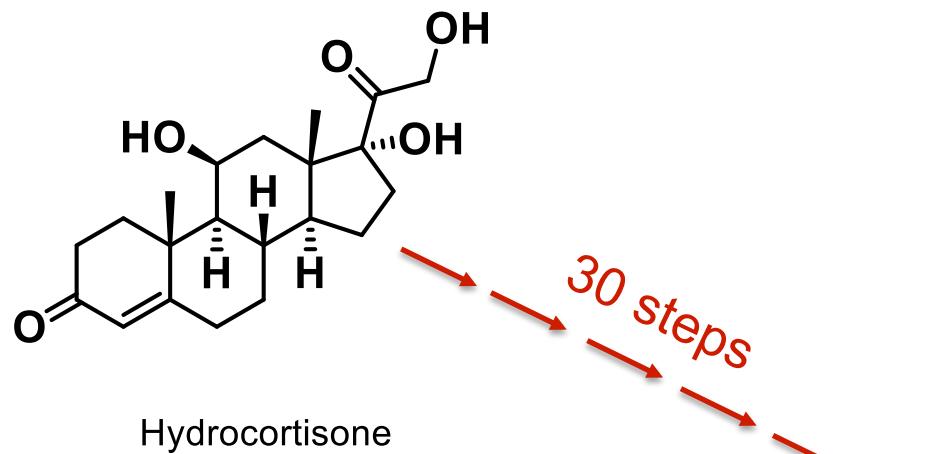
(+)-Wortmannin



Most recent total synthesis by Luo
in 2017



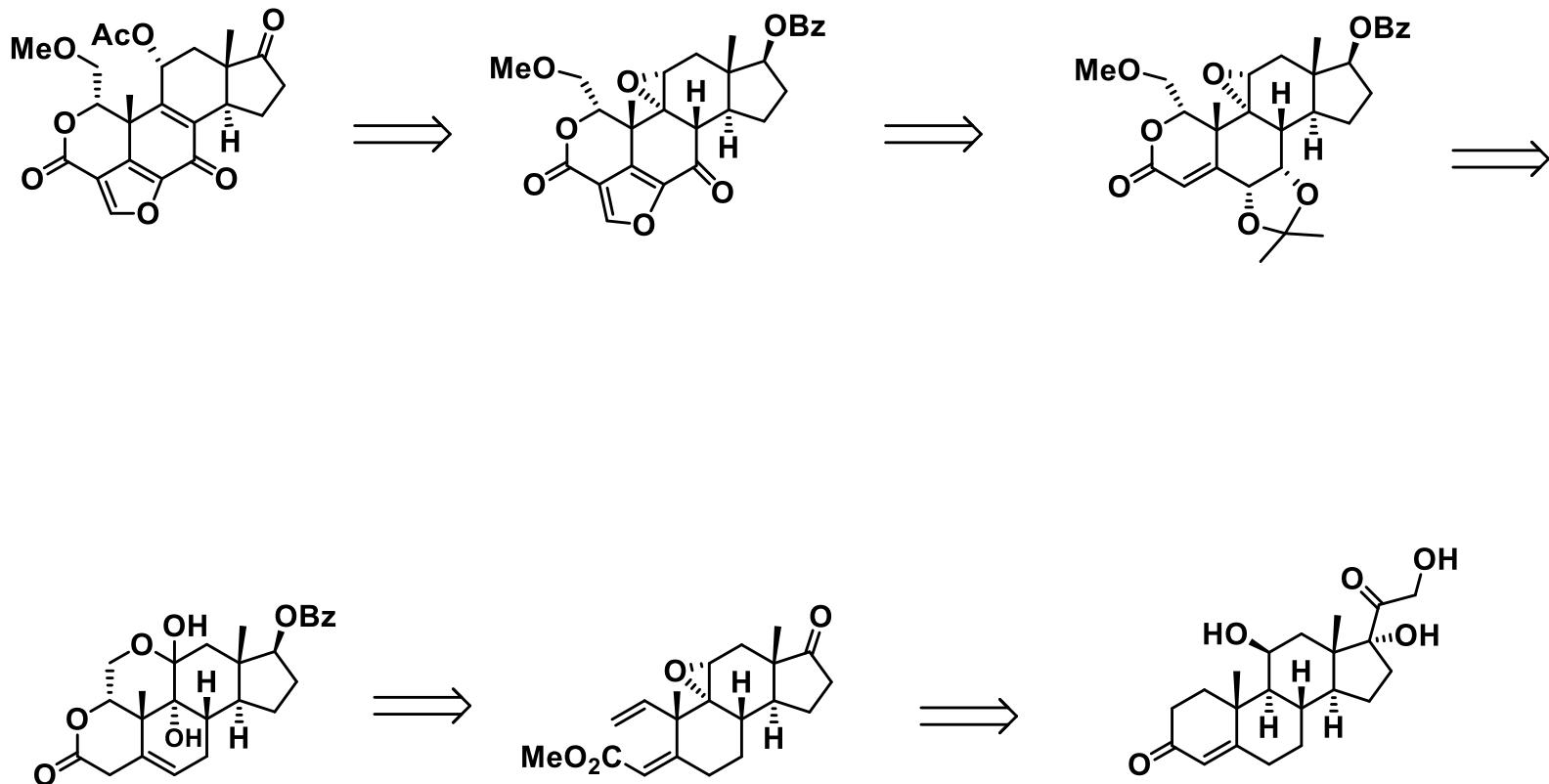
Wortmannin



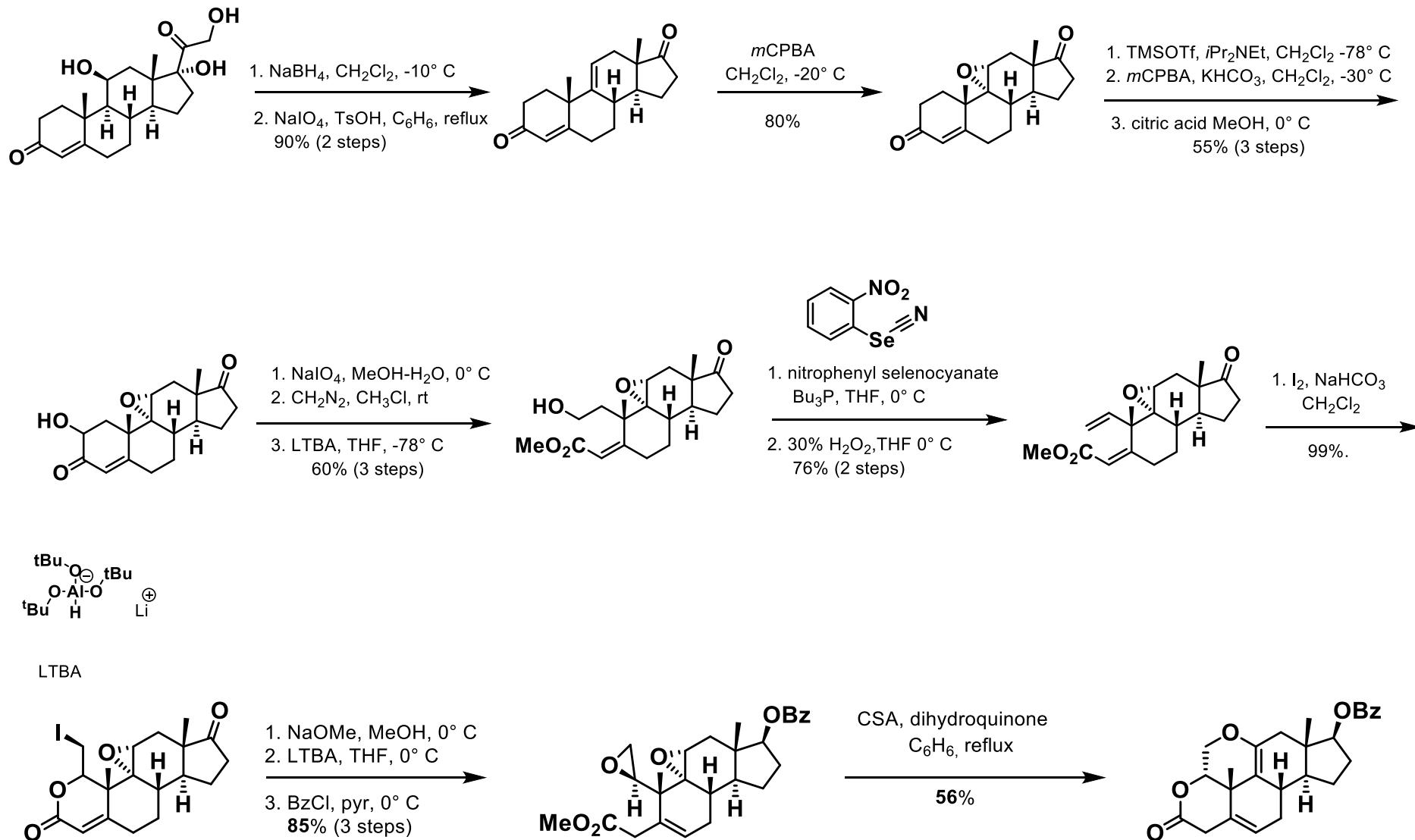
Guo, Y.; Quan, T.; Luo, T. *J. Am. Chem. Soc.* **2017**, 139, 6815–6818

Sato, S.; Nakada, M.; Shibasaki, M. *Tetrahedron Lett.* **1996**, 37, 6141–6144.

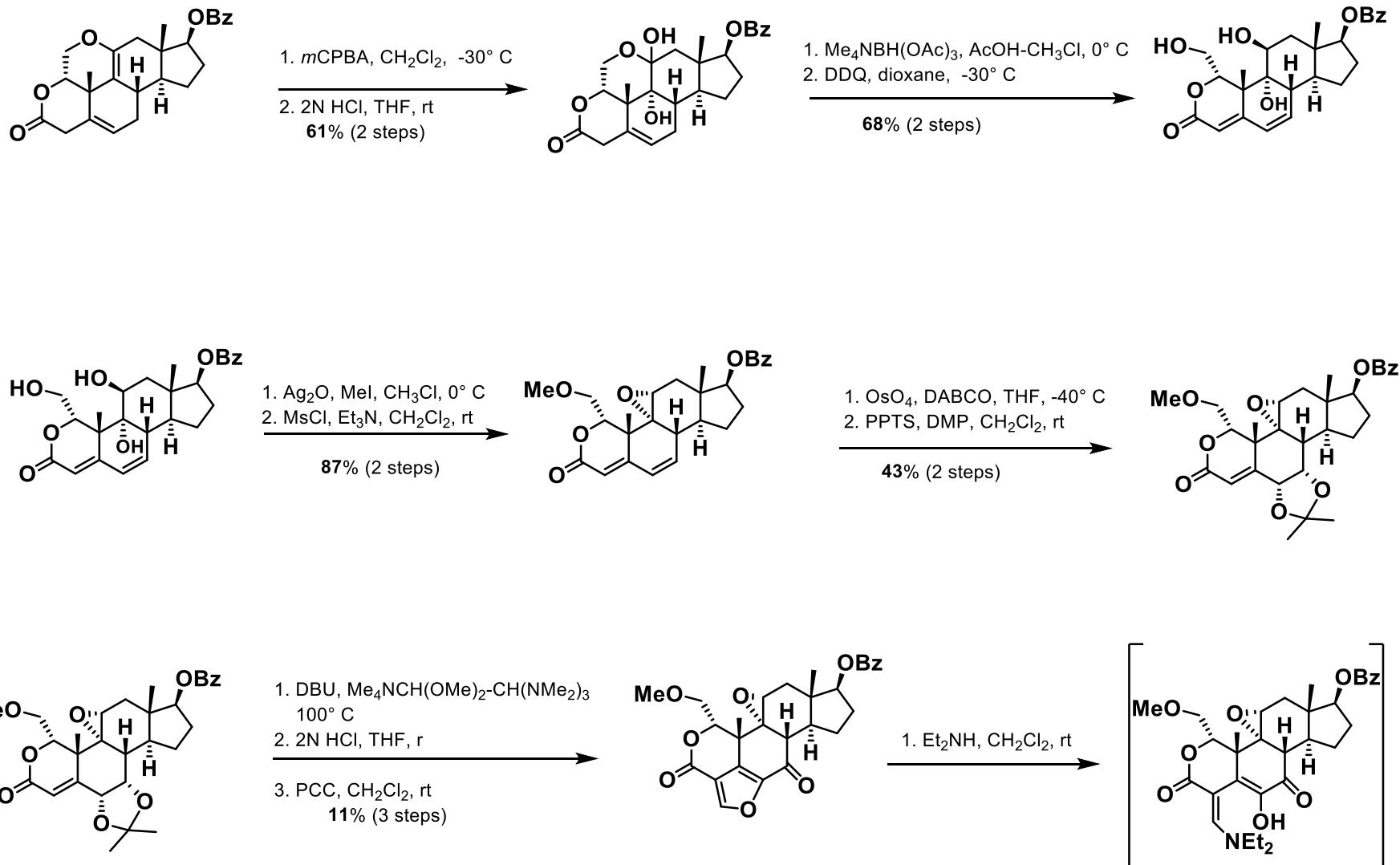
Synthesis by Shibasaki



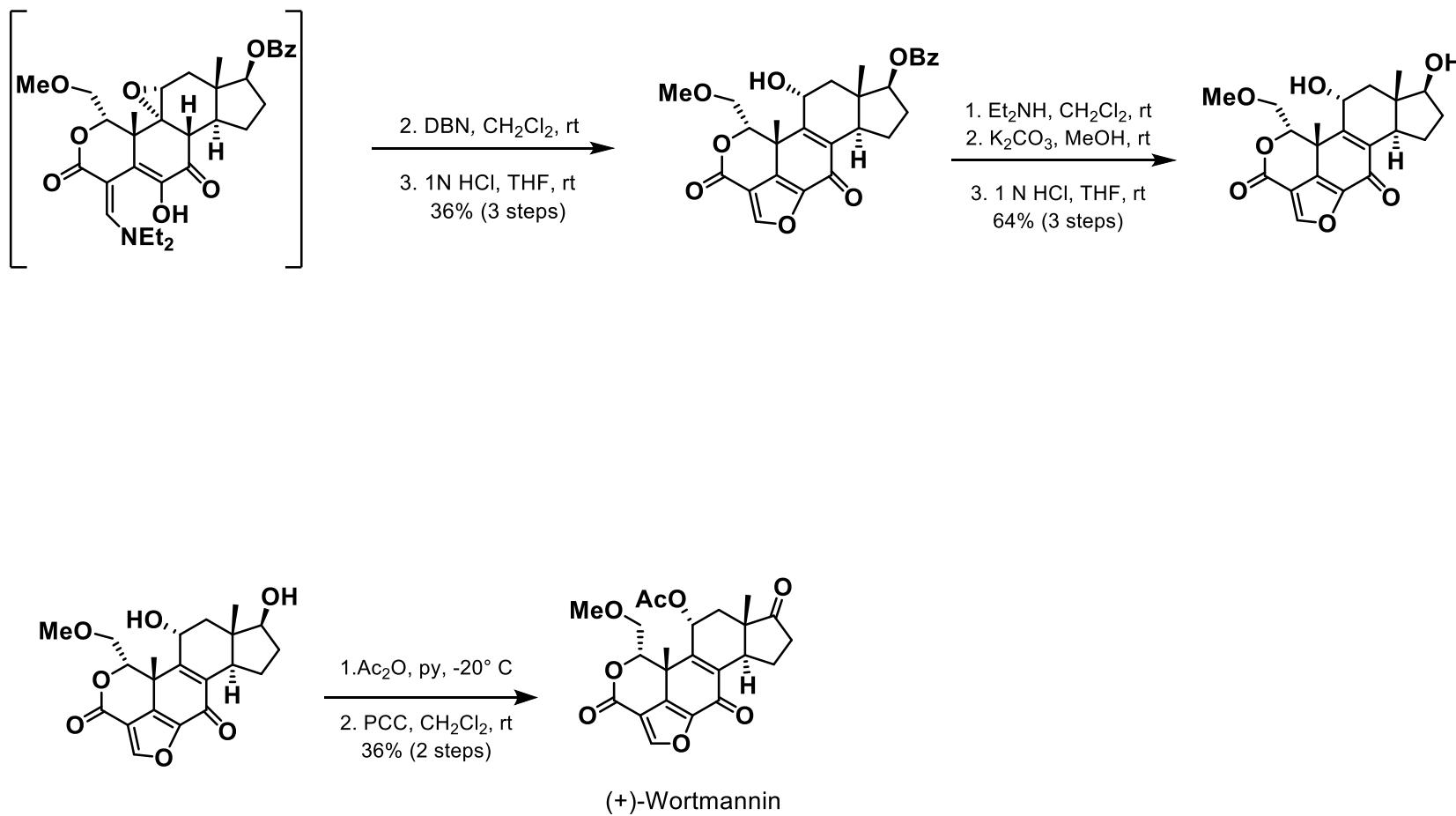
Synthesis by Shibasaki



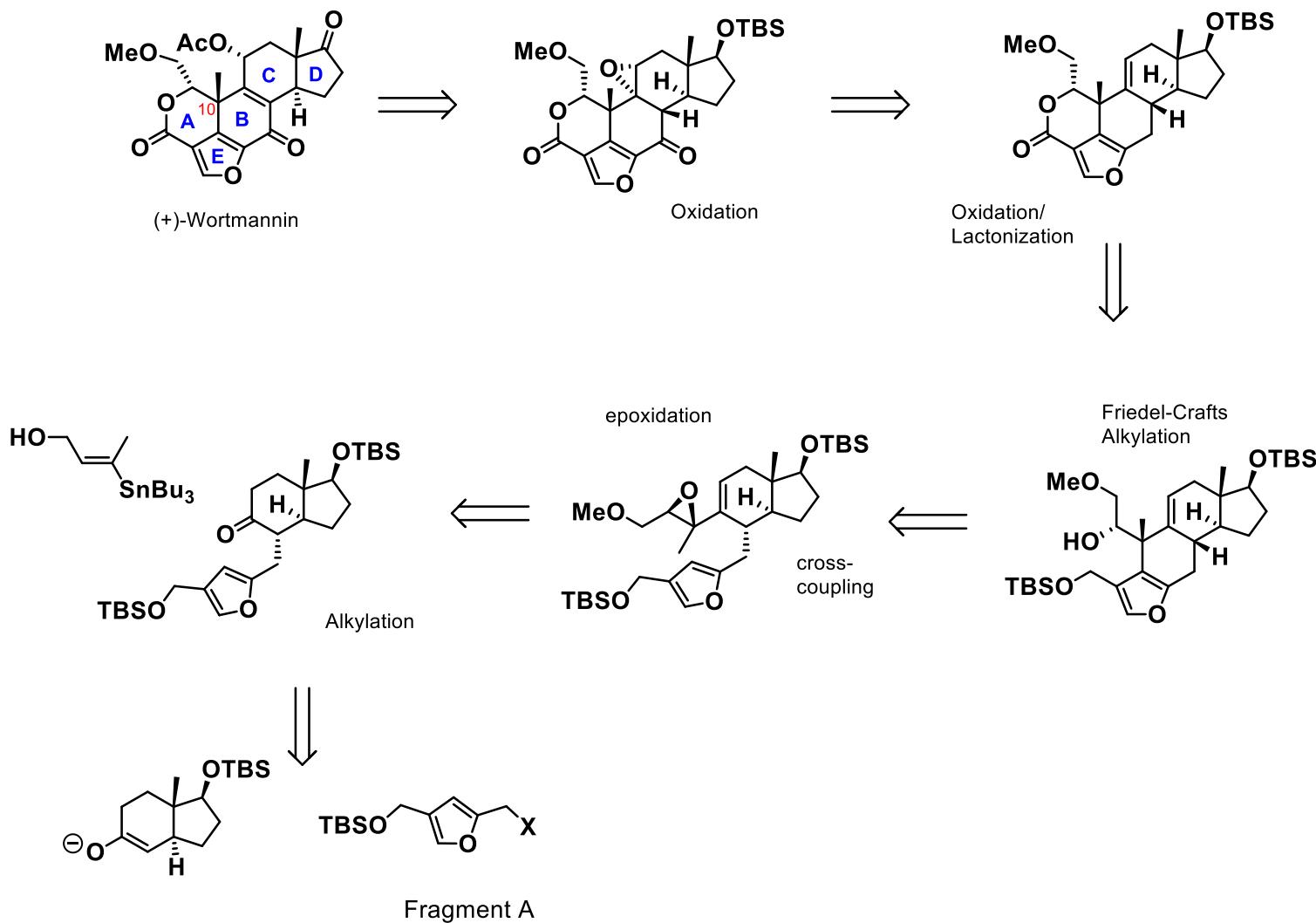
Synthesis by Shibasaki



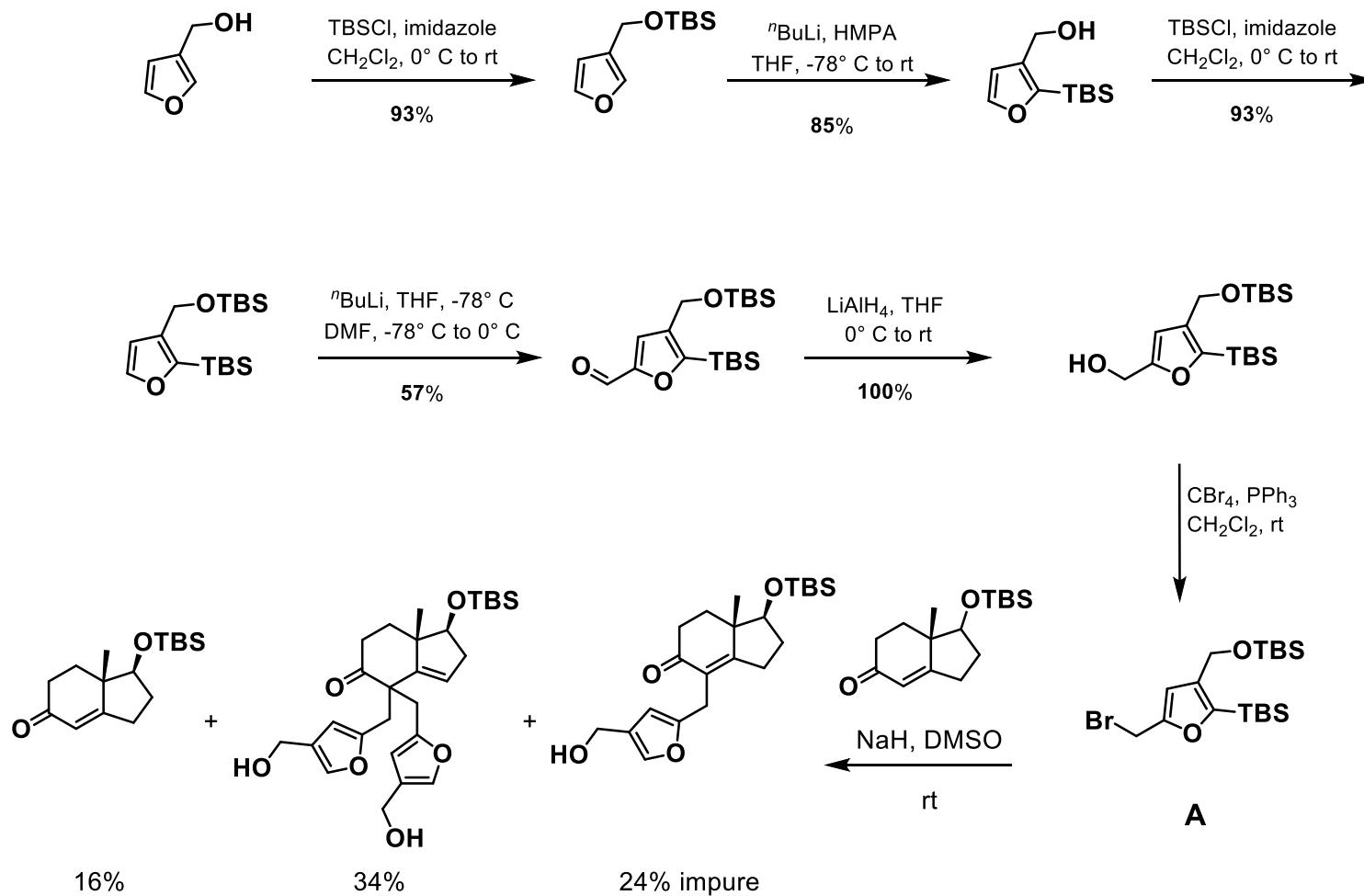
Synthesis by Shibasaki



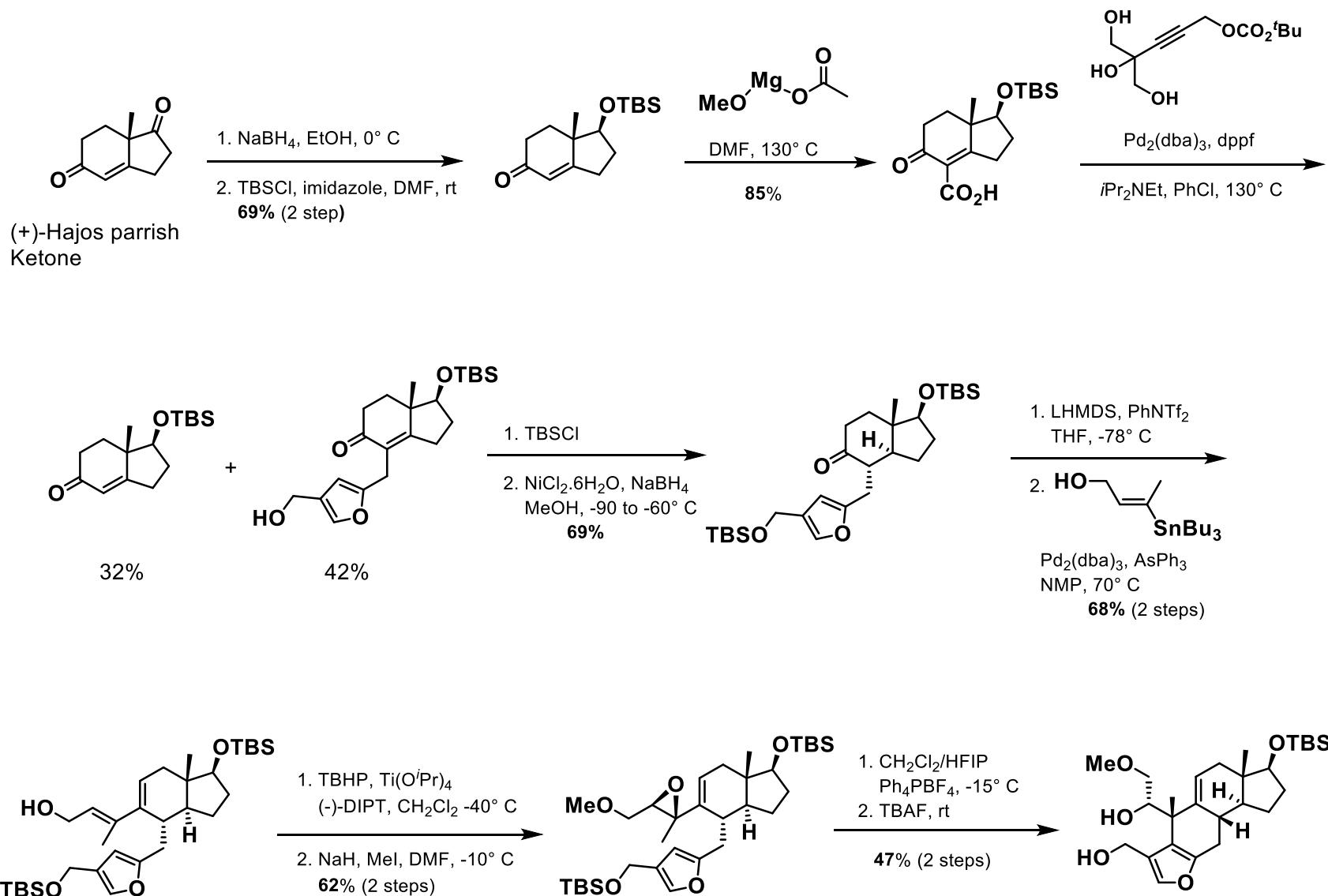
Synthesis by Luo



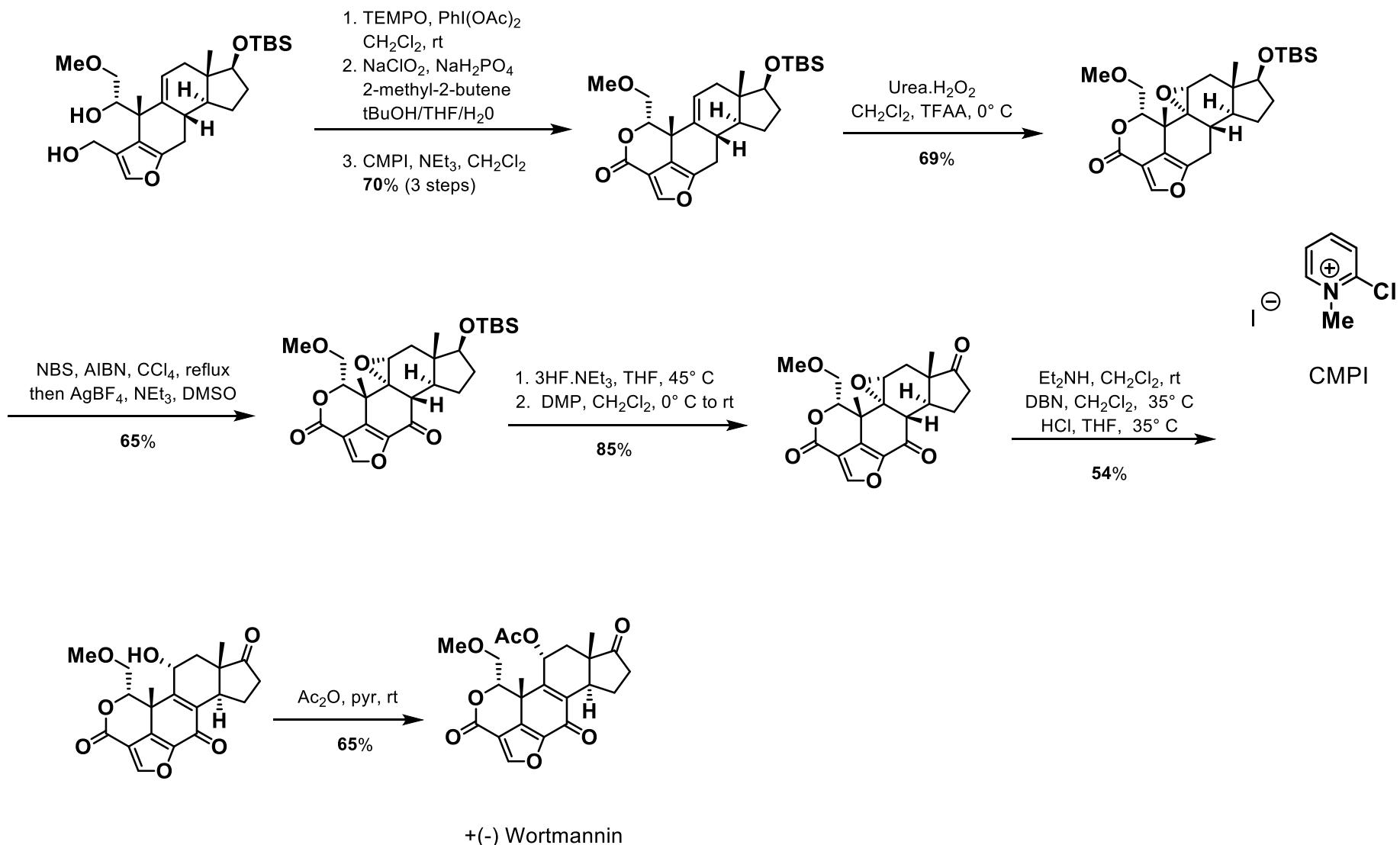
Synthesis of Fragment A



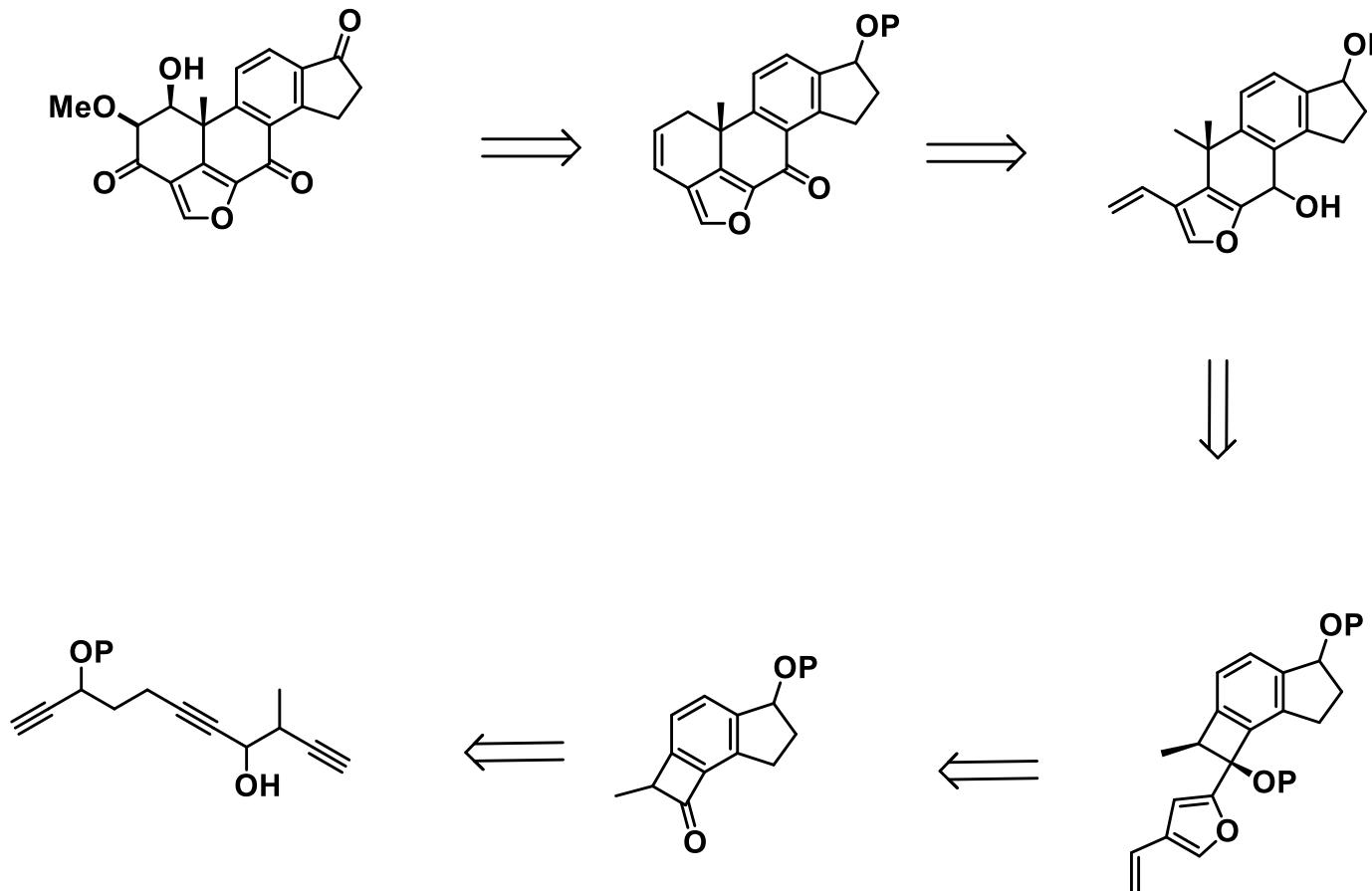
Synthesis by Luo



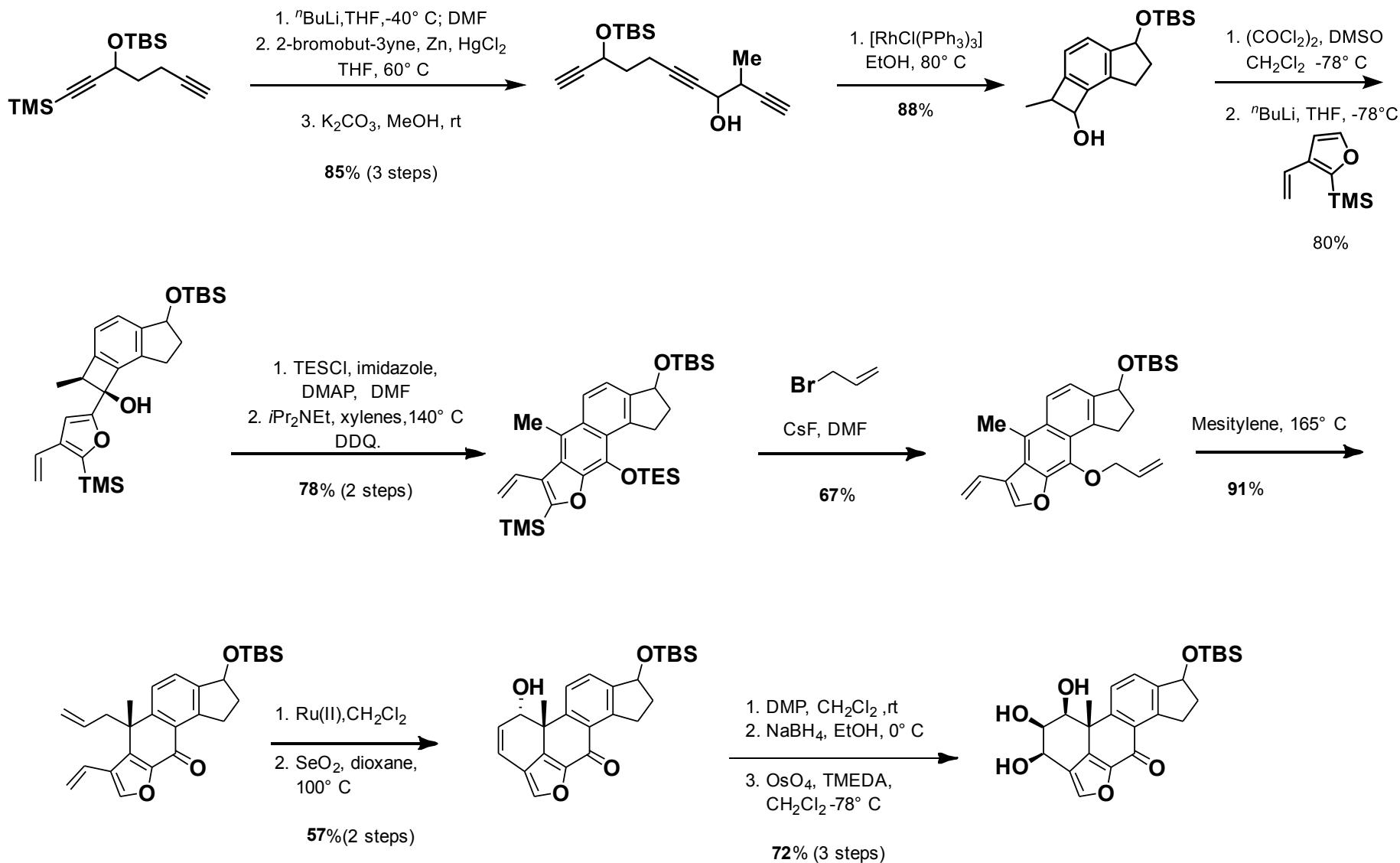
Synthesis by Luo



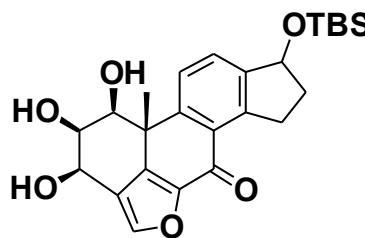
Retrosynthesis of Viridin



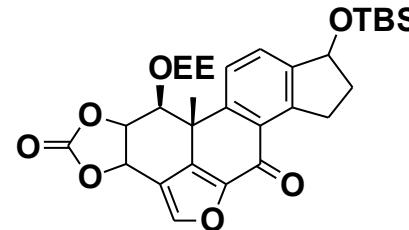
Synthesis of Viridin



Synthesis of Viridin

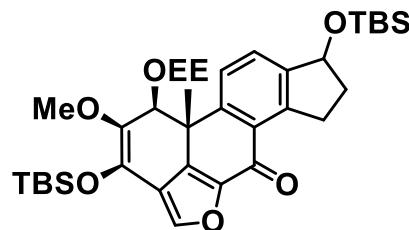


1. triphosgene, pyr, CH₂Cl₂, rt
2. PPTS, ethyl vinyl ether
CH₂Cl₂, rt
87% (2 steps)



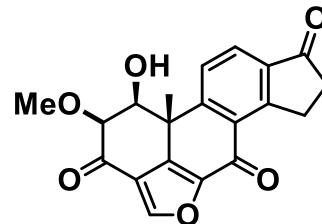
1.LiOH, THF/H₂O, pyr, CH₂Cl₂
2. TBSOTf, 2,6-lutidine
CH₂Cl₂, -78° C

3.NaHMDS, toluene, -78° C
MeOTf
70% (3 steps)



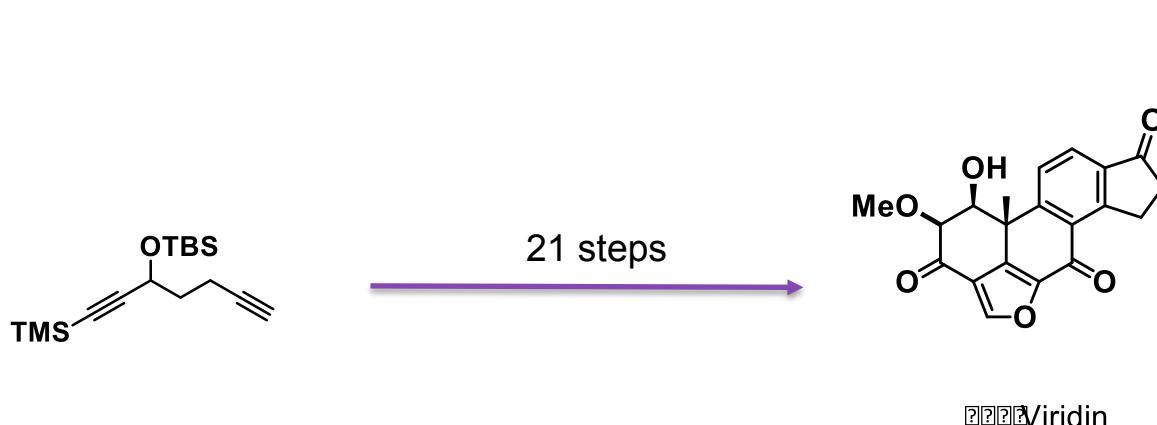
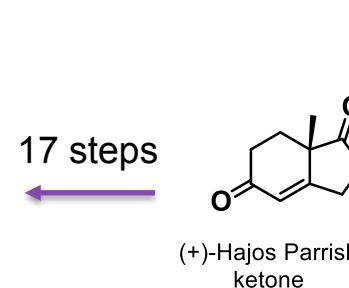
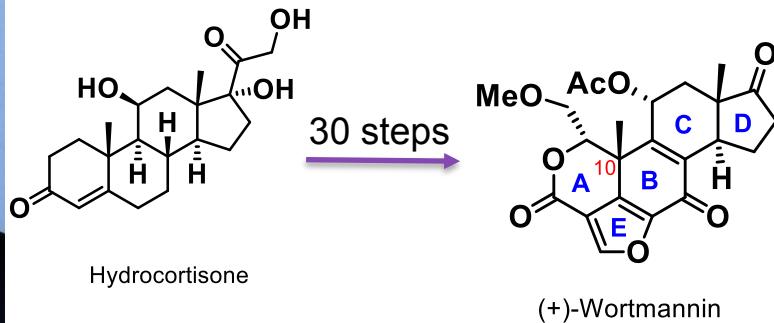
1. *n*Bu₄NF, THF, rt
2. DMP, CH₂Cl₂, rt

3. PPTS, MeOH, rt
82% (3 steps)



Viridin

Summary



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Anderson, E. A.; Alexanian, E. J.; Sorenson, E. J. *Angew.Chem.Int.Ed.* **2004**, 43,1998–2001