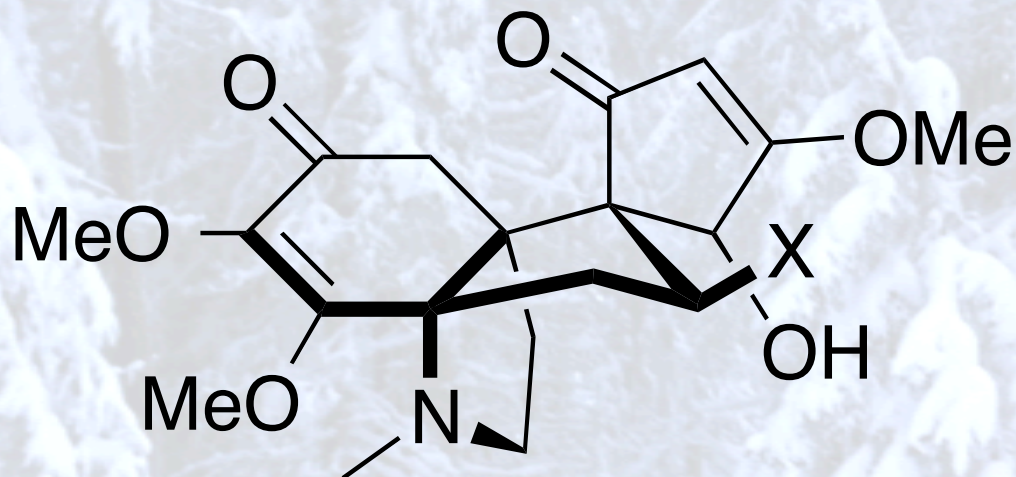
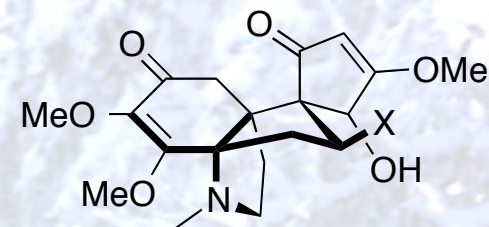


# Total Synthesis of (-)-Acutumine and (-)-Dechloroacutumine

S. M. King, N. A. Calandra, S. B. Herzon, *Angew. Chem. Int. Ed.* **2013**, *52*, 3642-3645.



X = Cl, (-)-acutumine (**1**)  
X = H, (-)-dechloroacutumine (**2**)

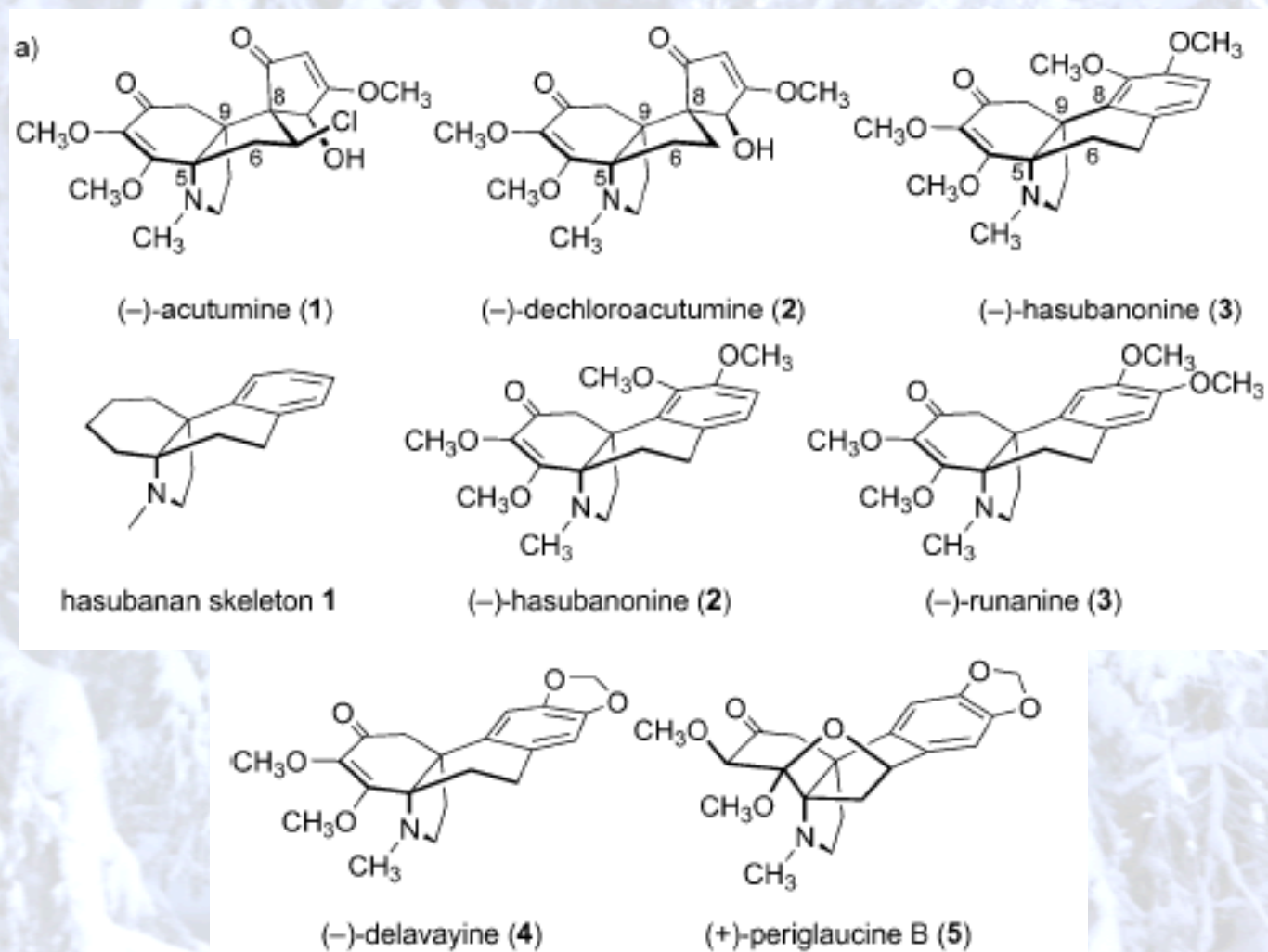


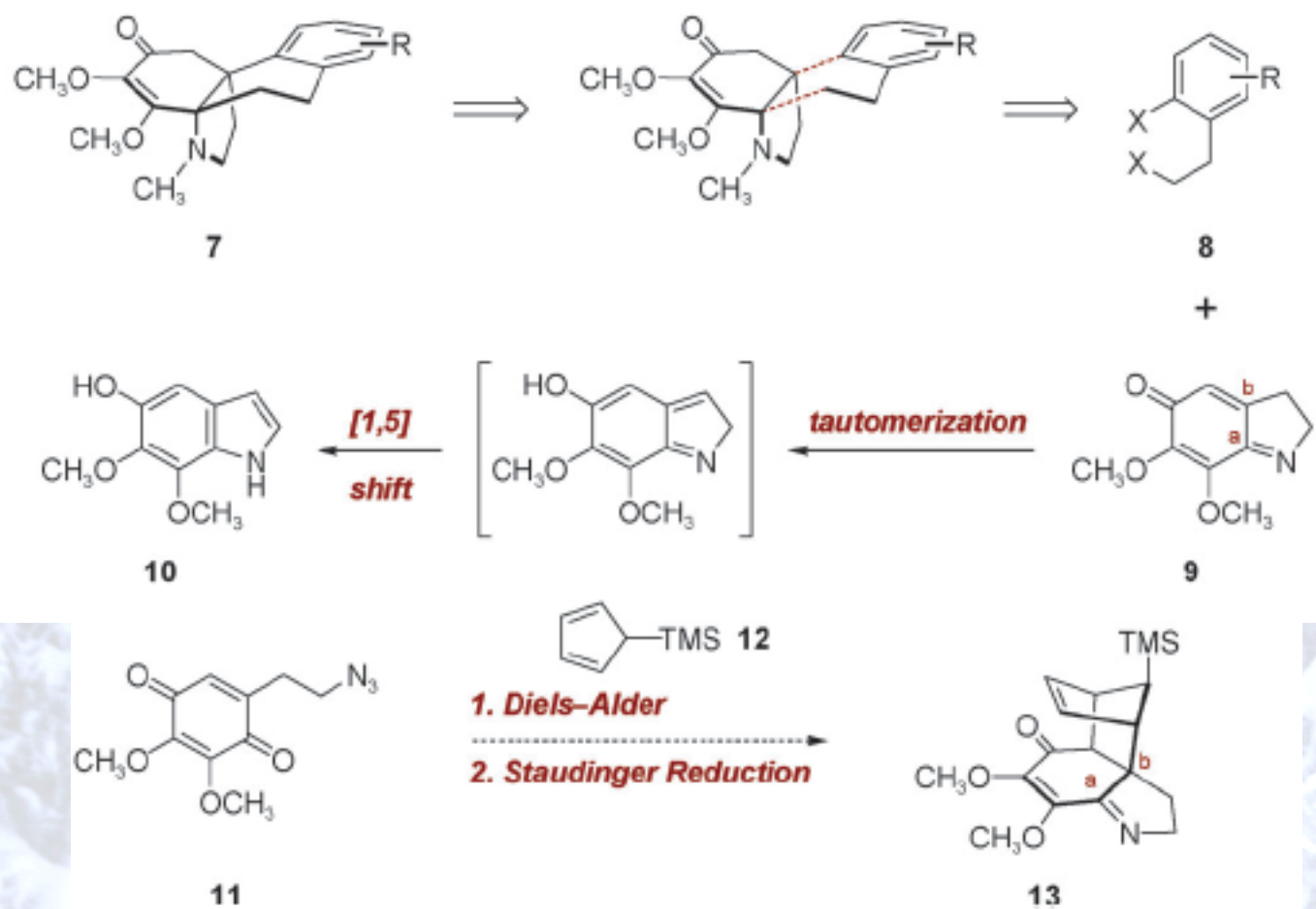
X = Cl, (-)-acutumine (1)  
 X = H, (-)-dechloroacutumine (2)

- (-)-acutumine isolated from the roots of *Sinomenium acutum* (tree in Asia)
  - inhibition of human T-cell proliferation
- (-)-dechloroacutumine was isolated from a chlorinedeficient culture of *Menispermum dauricum* (shrub in Asia and America)
- stereogenic, heavily oxidized spirocyclopentenone rings
- dense array of heteroatom-containing functional groups
- secondary alkyl chloride functional group in **1**



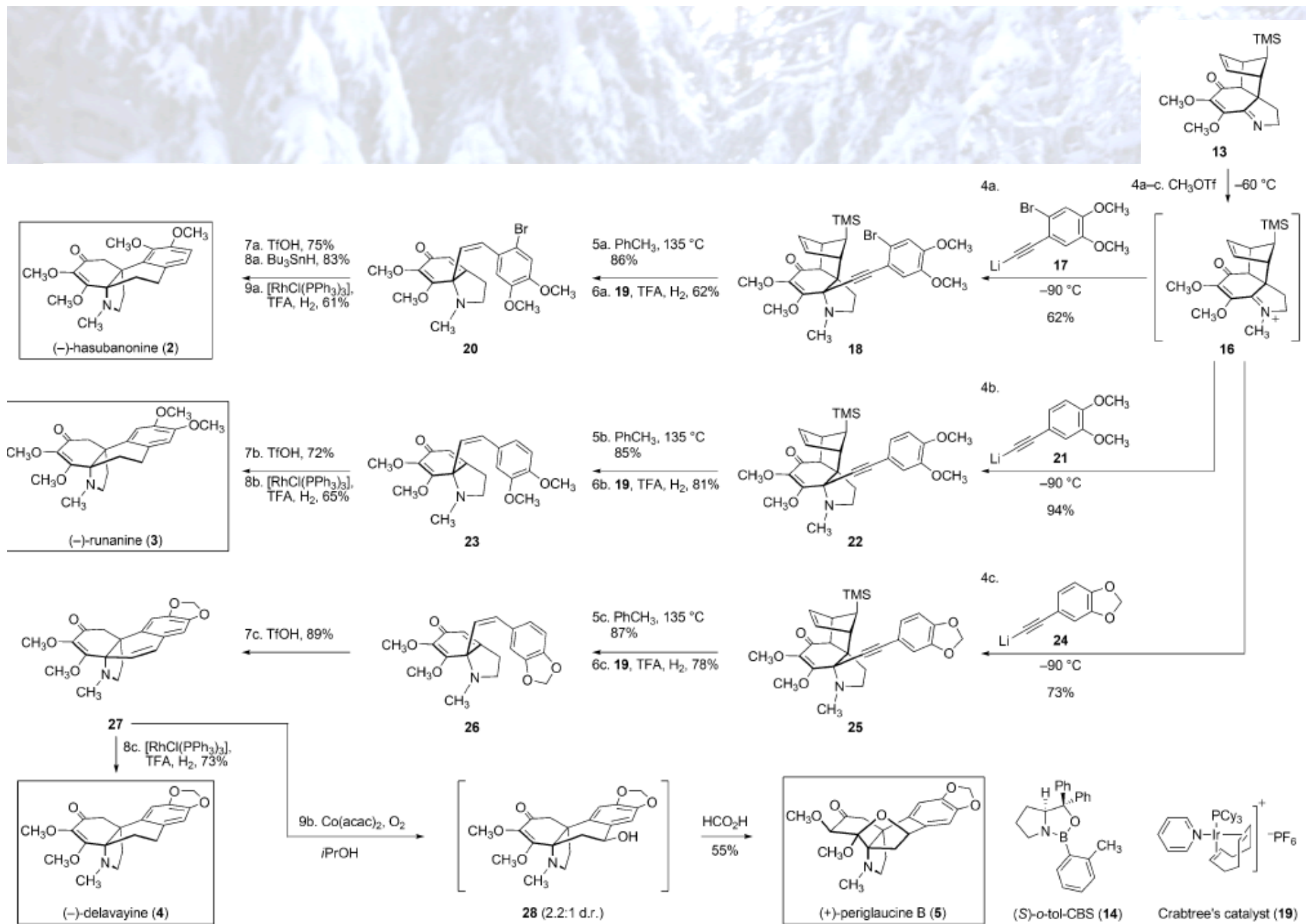
## Simple and general strategy to synthesize hasubanan alkaloids:

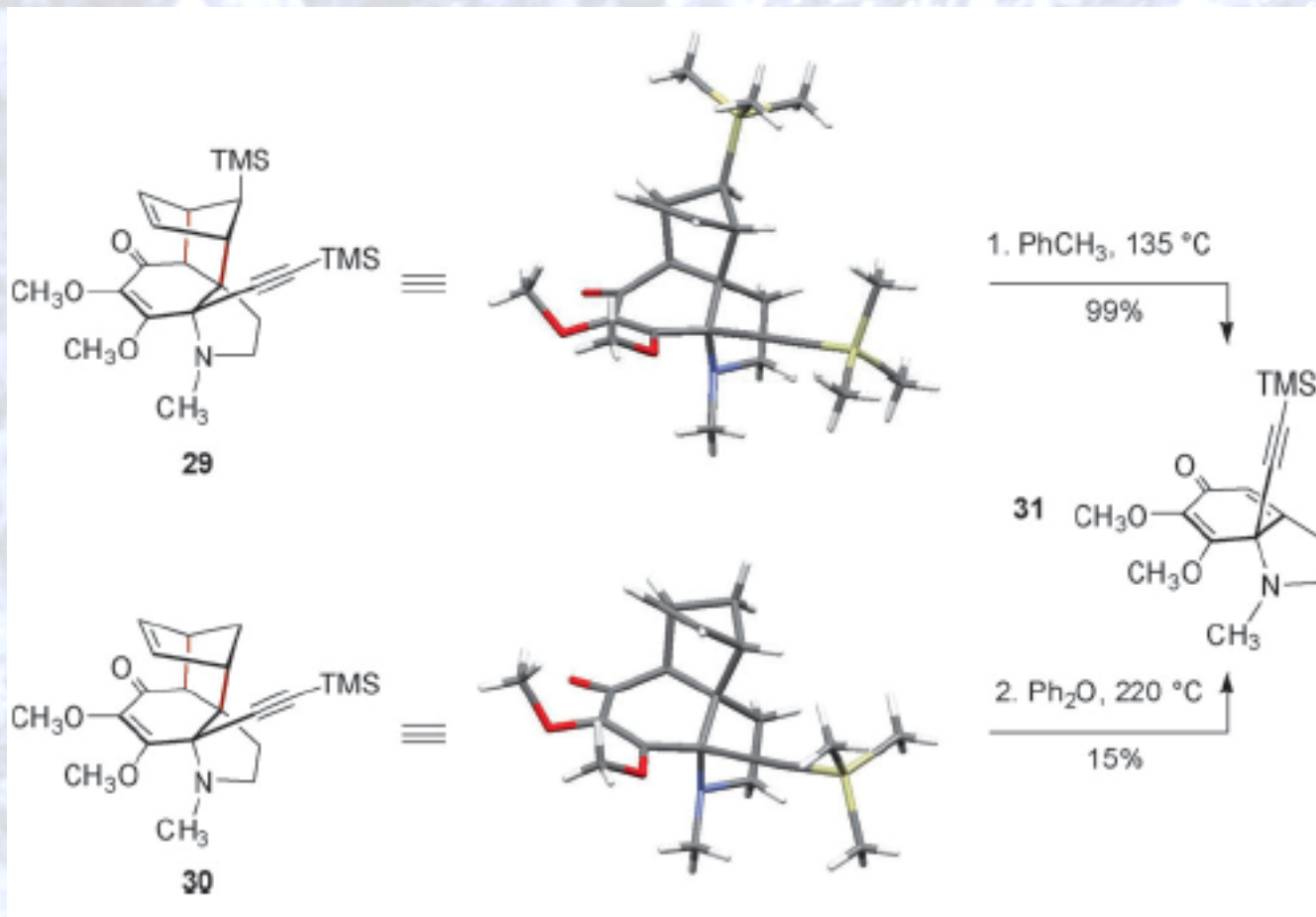




### TMS-cyclopentadiene:

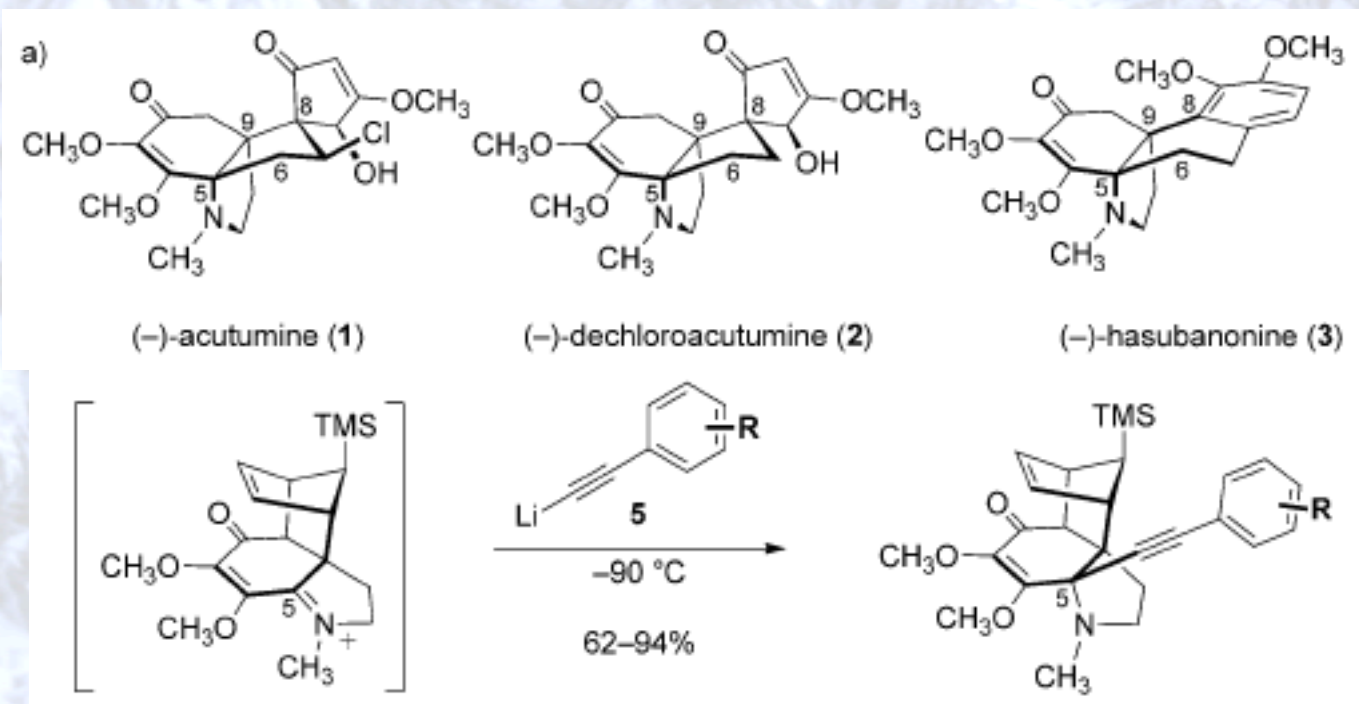
- stabilizing the azaquinone **9**
- stereochemistry control





### Explanation:

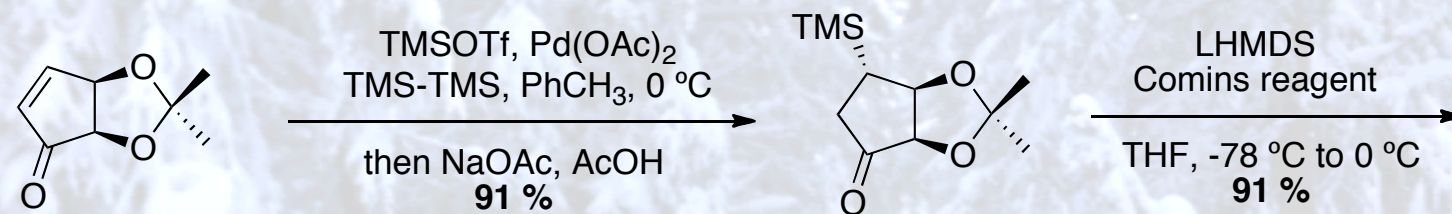
faster retro-cycloaddition reactions attributed to donation of electron density from the C-Si bonding orbital to the antibonding orbitals of the C-C  $\sigma$  bonds that are breaking in the reaction transition state



**Difference:**

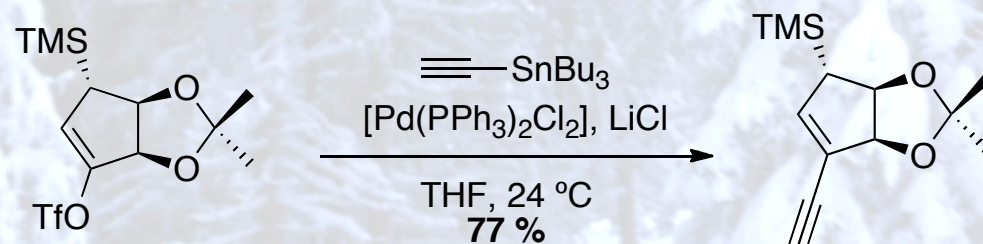
- stereoselective construction of C8-C9 bonds
- other suitable precursor to the stereogenic, highly oxidized spirocyclopentenone ring

## Synthesis of enyne **10**:



**7**  
five steps  
from D-ribose

**8**

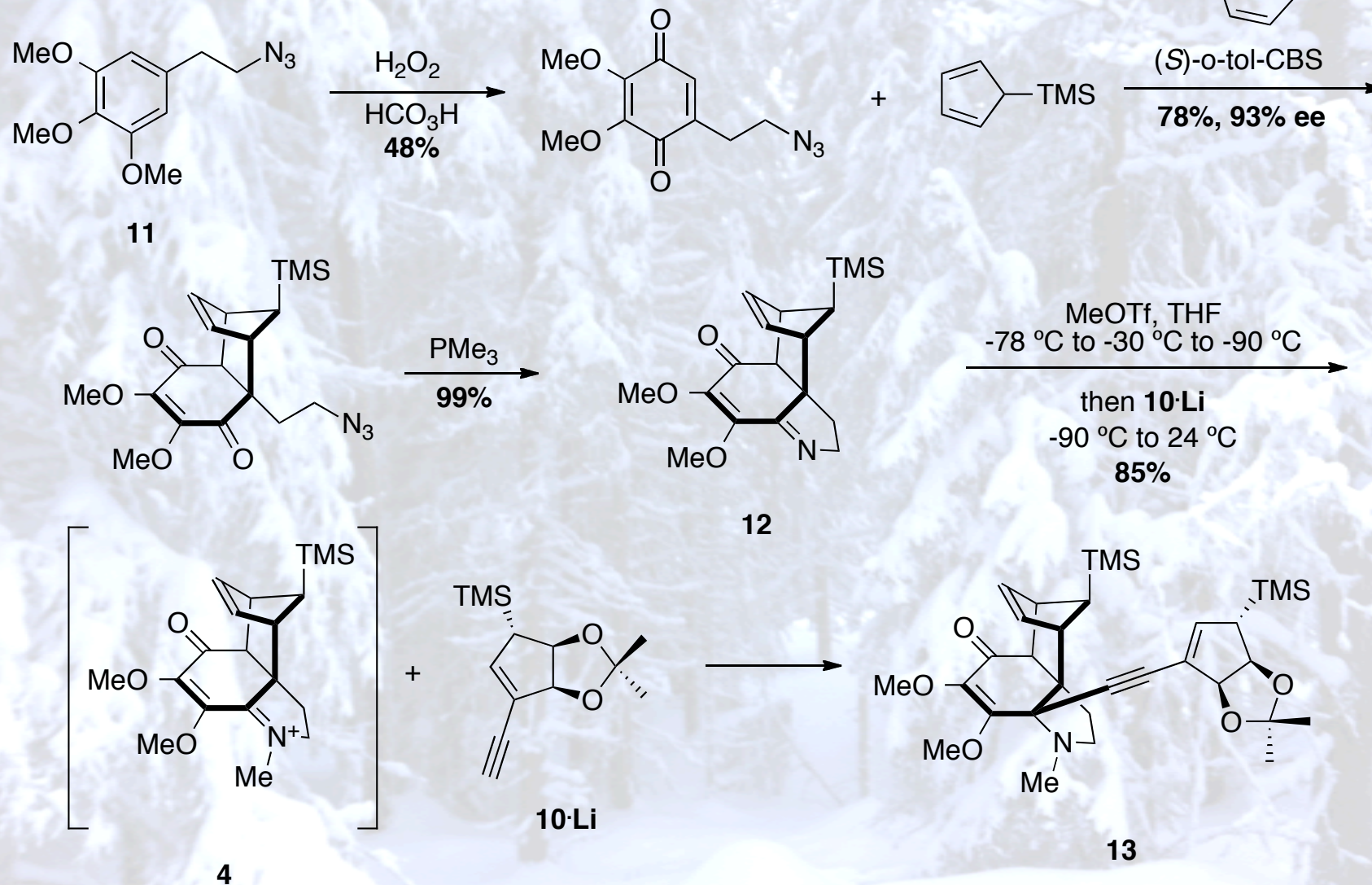


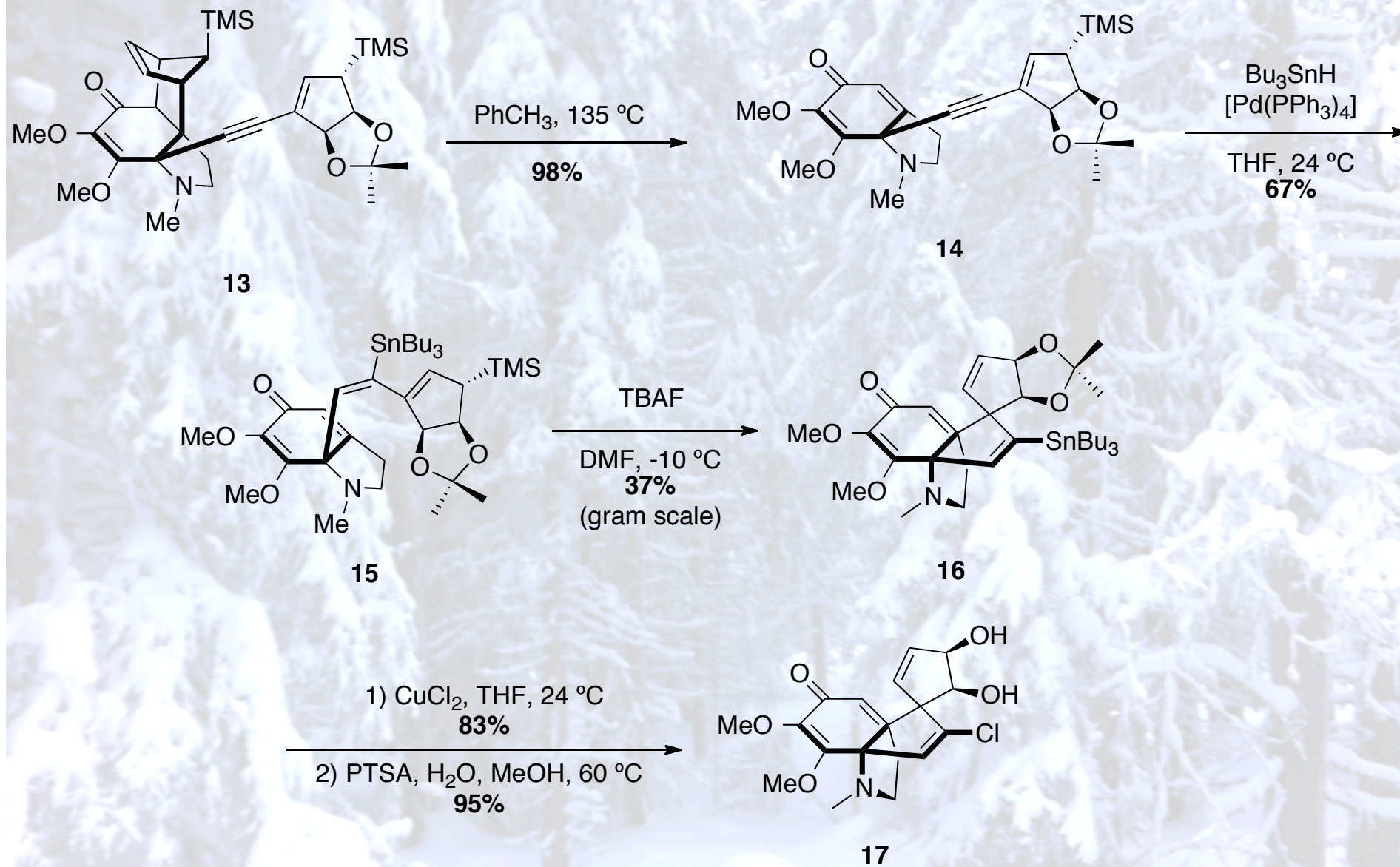
**9**

**10**

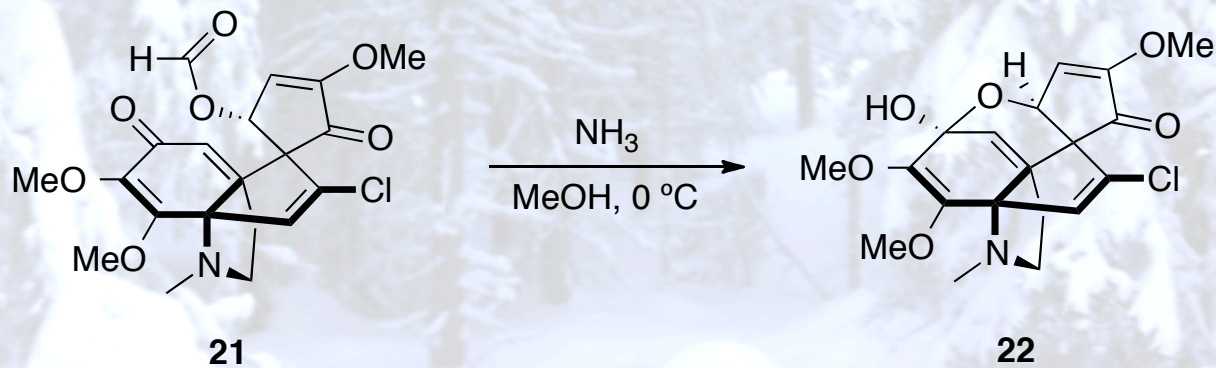
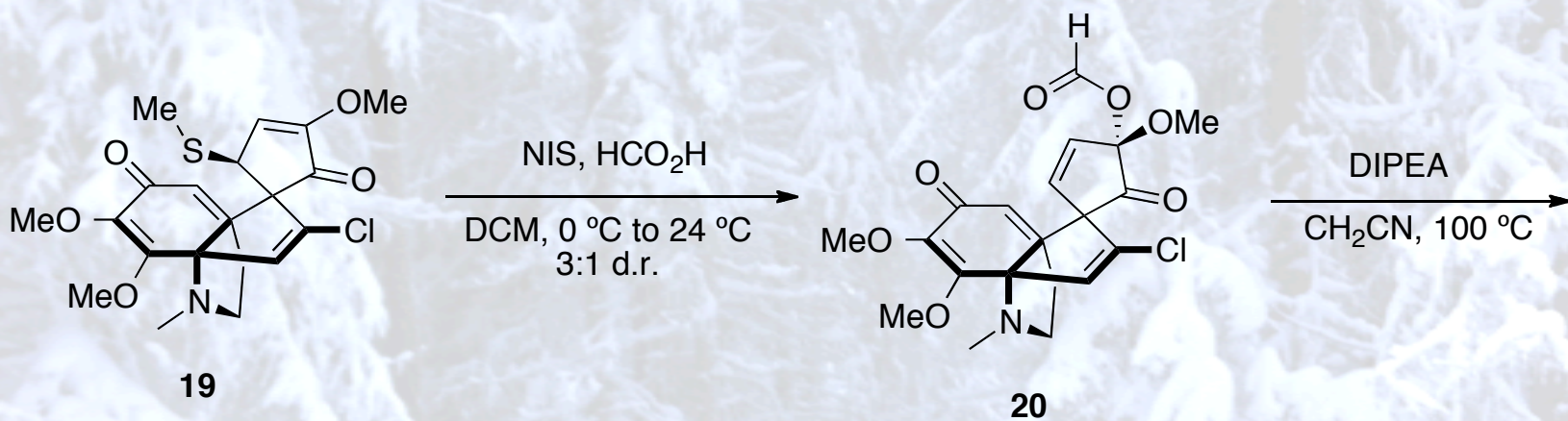
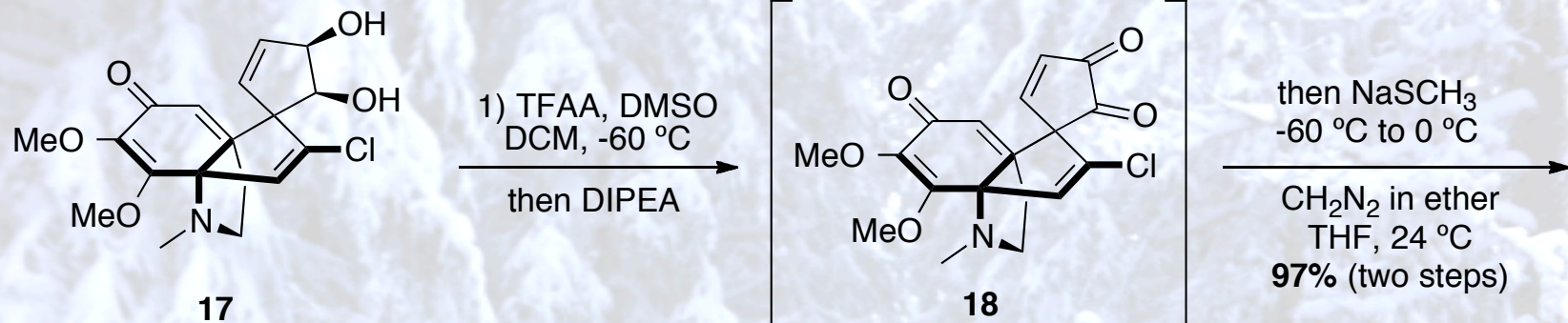


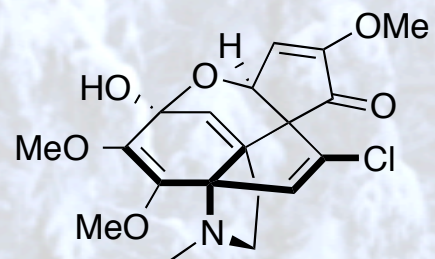
## Synthesis of diol **17**:





Completion of the syntheses:

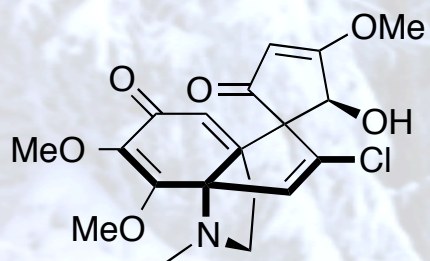




**22**

1) DMP, DCM, 24 °C

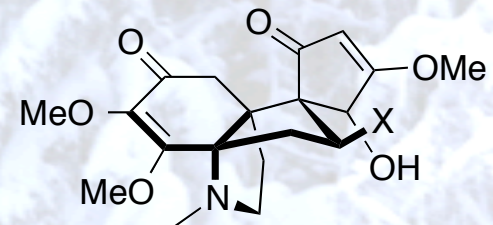
2) NaBH<sub>4</sub>, EtOH, 0 °C  
**28%** (five steps)



**23** dehydroacutumine

1) [Rh(nbd)(dppb)]BF<sub>4</sub>  
 H<sub>2</sub> (300 psi), DCE, 24 °C  
**17%** (for **1**)

2) H<sub>2</sub>, Pd/C  
**60%** (for **2**)



X = Cl, (-)-acutumine (**1**)  
 X = H, (-)-dechloroacutumine (**2**)

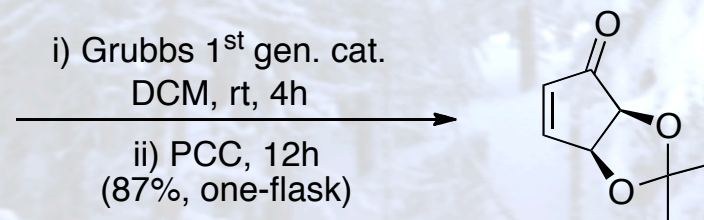
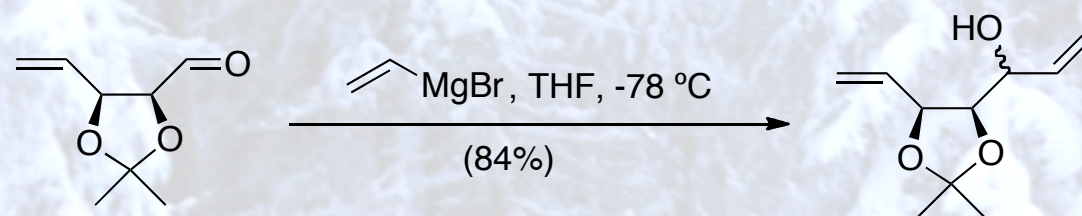
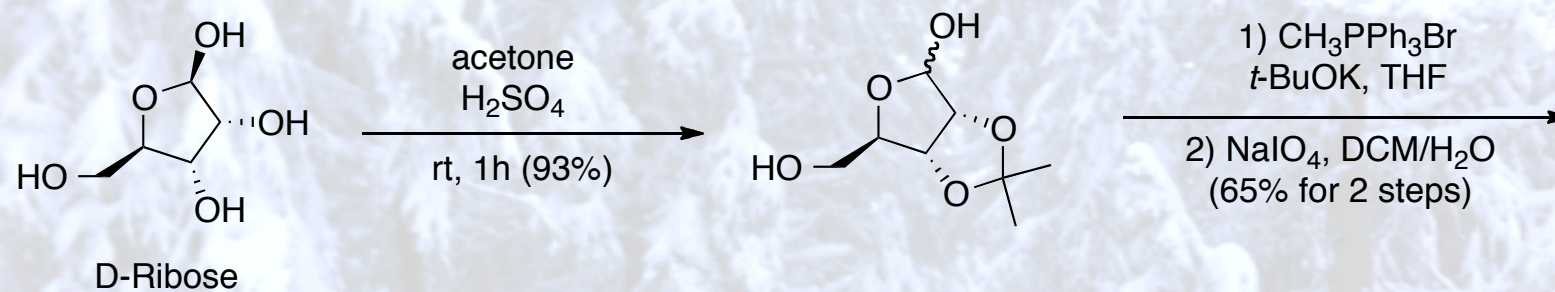
## Conclusion:

- strategic application of TMS-cyclopentadiene as stabilization and stereocontrolled element
- stereo- and regioselective hydrostannylation
- Hosomi-Sakurai cyclization to form two contiguous quaternary centers
- allylic formate rearrangement to establish the oxygenation pattern of the spirocyclopentenone rings
- selective hydrogantion



**END**

## Synthesis of starting compound 7:



## Synthesis of starting compound **11**:

