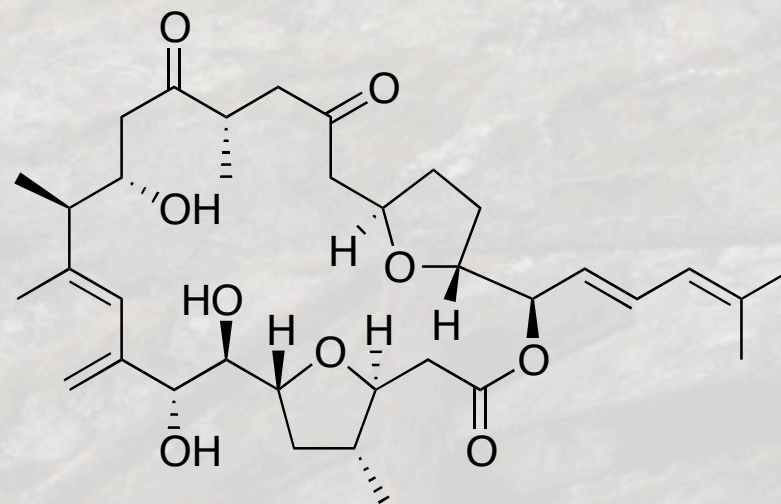
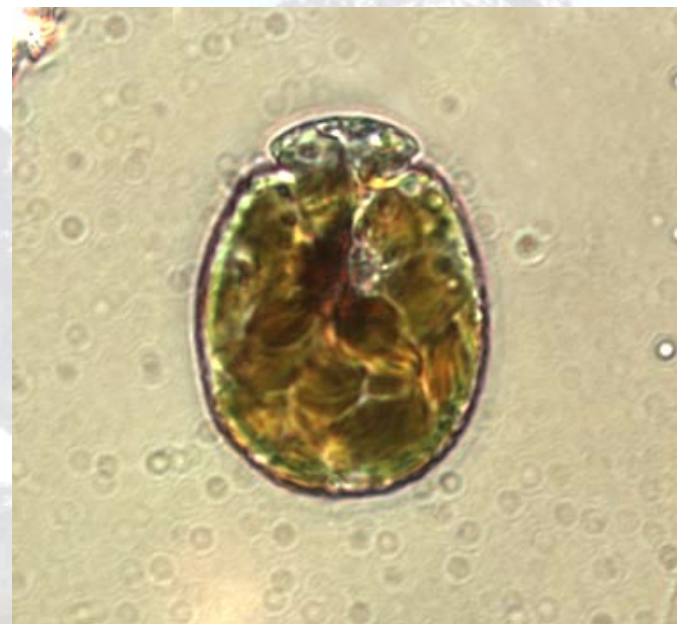




# Introduction

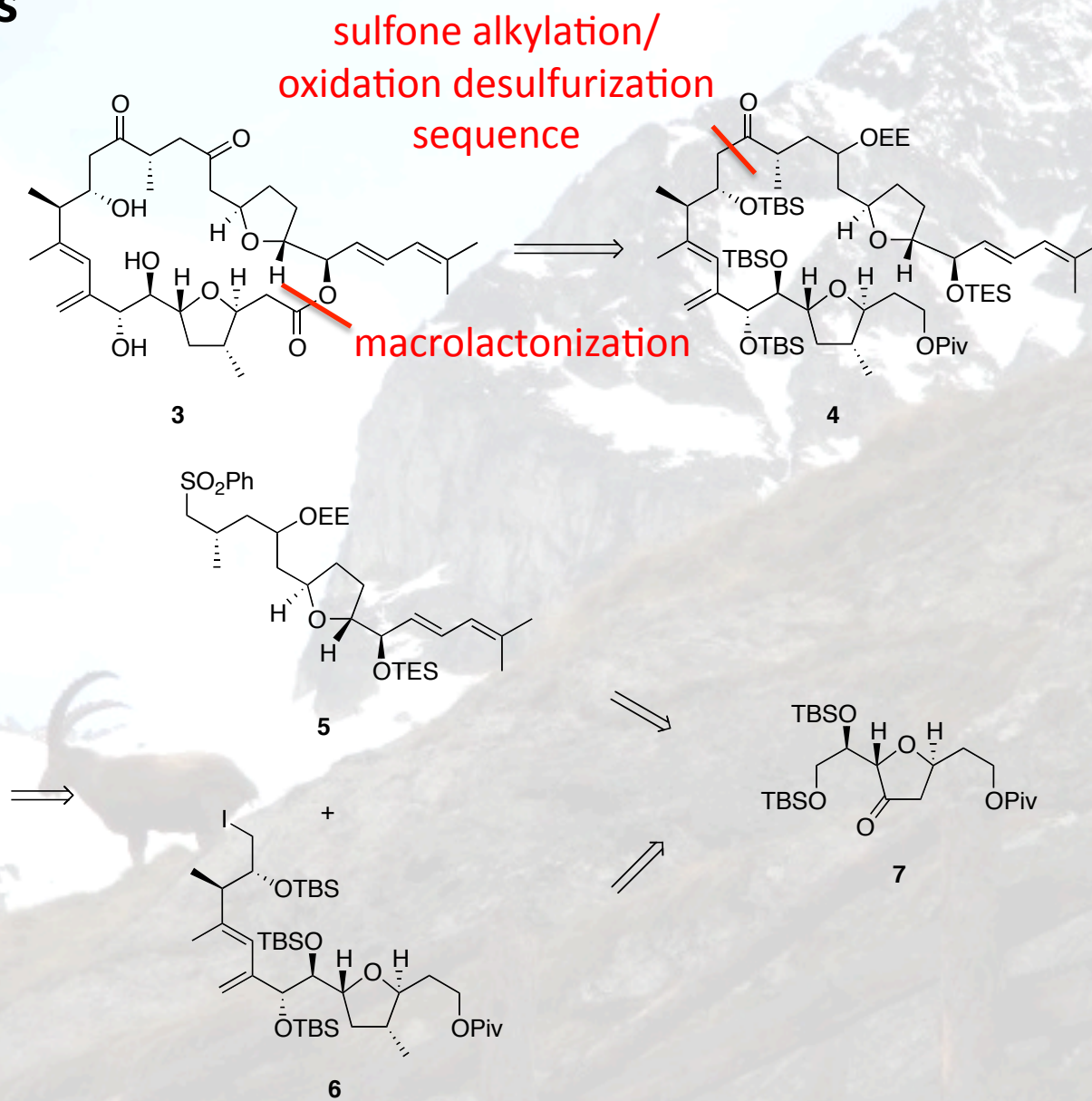
- isolated from the dinoflagellate *Amphidinium* sp in 1991
- over 30 members of this family were isolated
- cytotoxic activities
- amphidinolide F:
  - 11 stereogenic centers
  - 25-membered macrolactone
  - 2 trans-disposed tetrahydrofuran ring systems
  - 1,4-diketone motif
  - highly substituted diene moiety
- first total synthesis (confirmation of absolute and relative stereochemistry of the natural product)



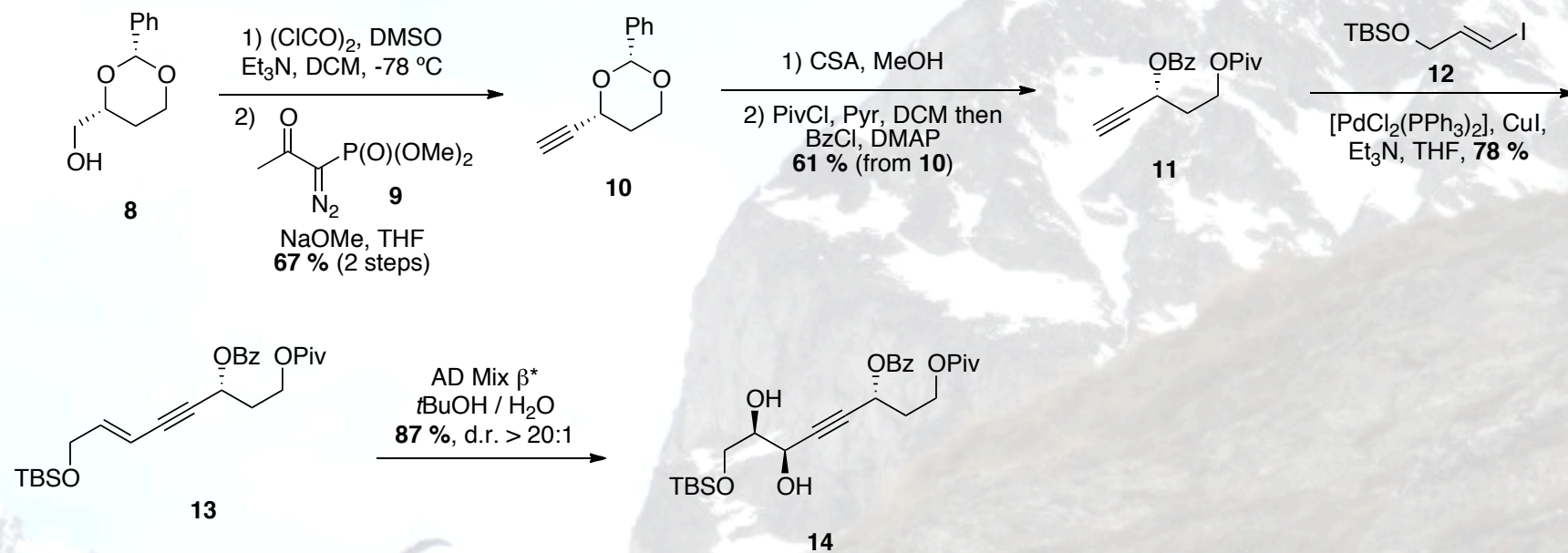
S. Mahapatra, R. G. Carter, *Angew. Chem. Int. Ed.* **2012**, *51*, 7948 – 7951.

J. Kobayashi, M. Tsuda, M. Ishibashi, H. Shigemori, T. Yamasu, H. Hirota, T. Sasaki, *J. Antibiot.* **1991**, *44*, 1259 – 1261.

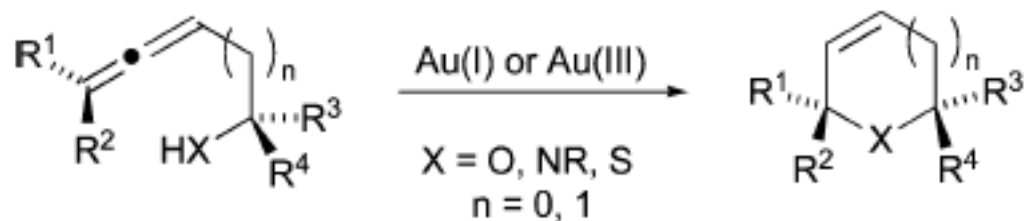
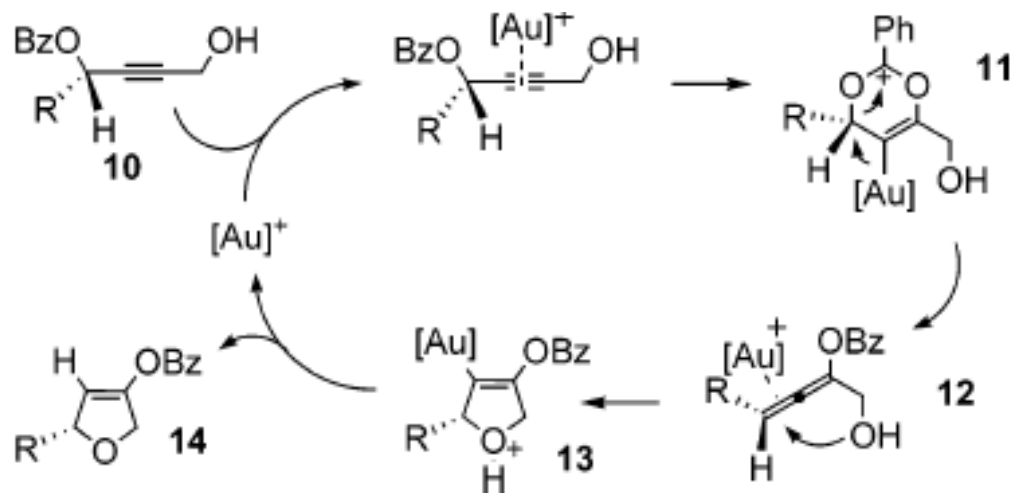
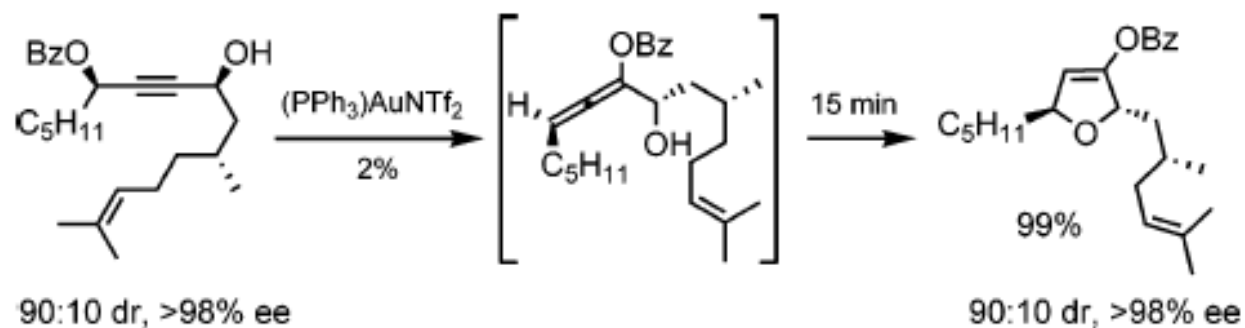
# Retrosynthesis



## Synthesis of common intermediate 7:



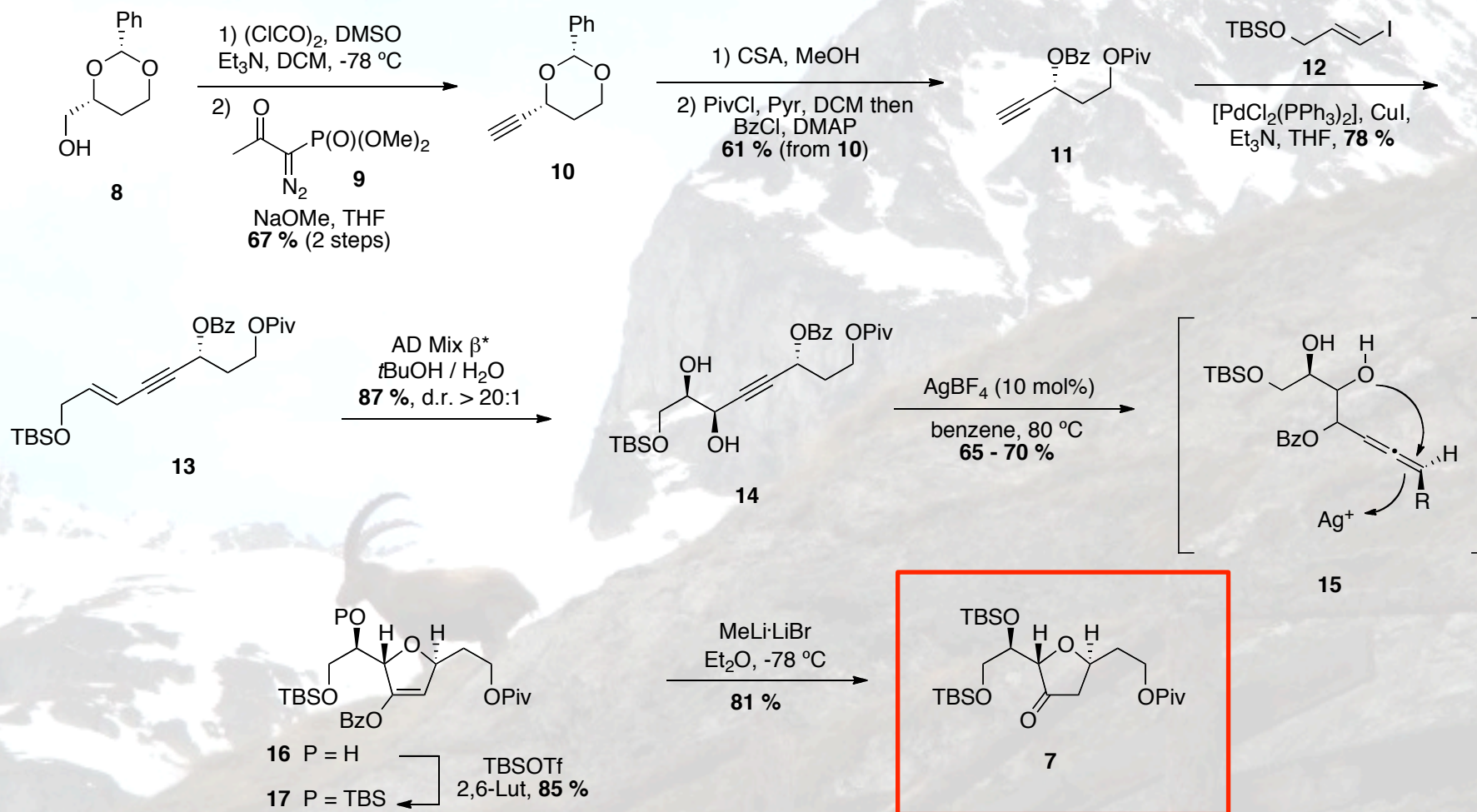
## Gold(I)-Catalyzed cyclization of allenes: Gagosz et al. and Krause et al.



A. Buzas, F. Istrate, F. Gagosz, *Org. Lett.* **2006**, *8*, 1957 – 1959.

V. Folz, N. Krause, *Org. Biomol. Chem.* **2007**, *5*, 1519 – 1521.

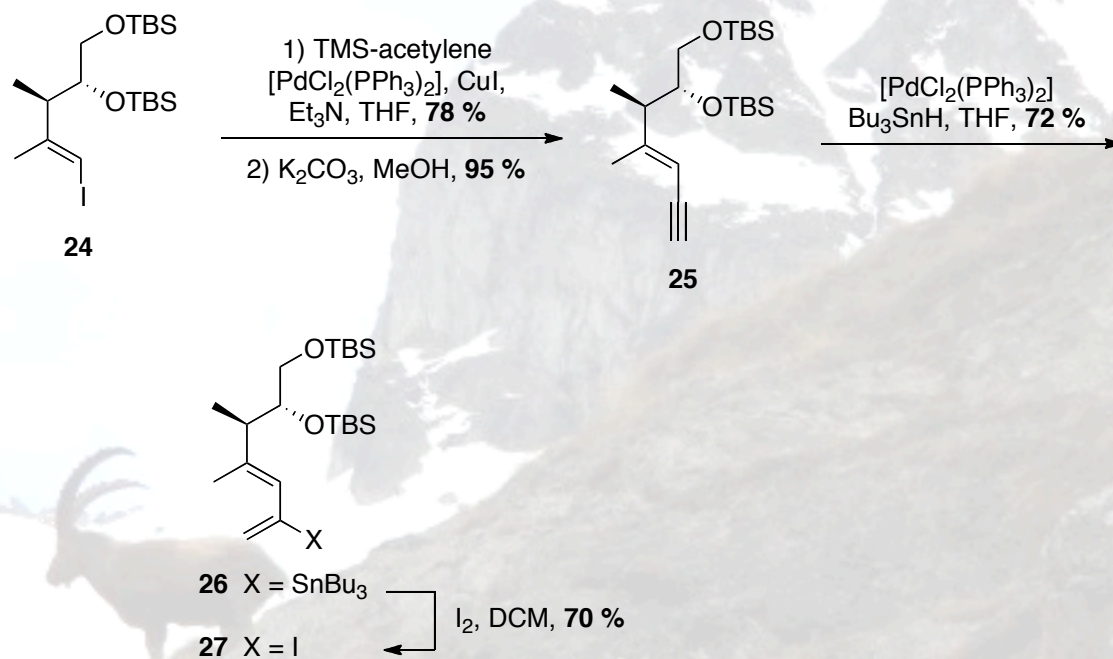
## Synthesis of common intermediate 7:



building block for trans-disposed  
furan-prcontaining natural products

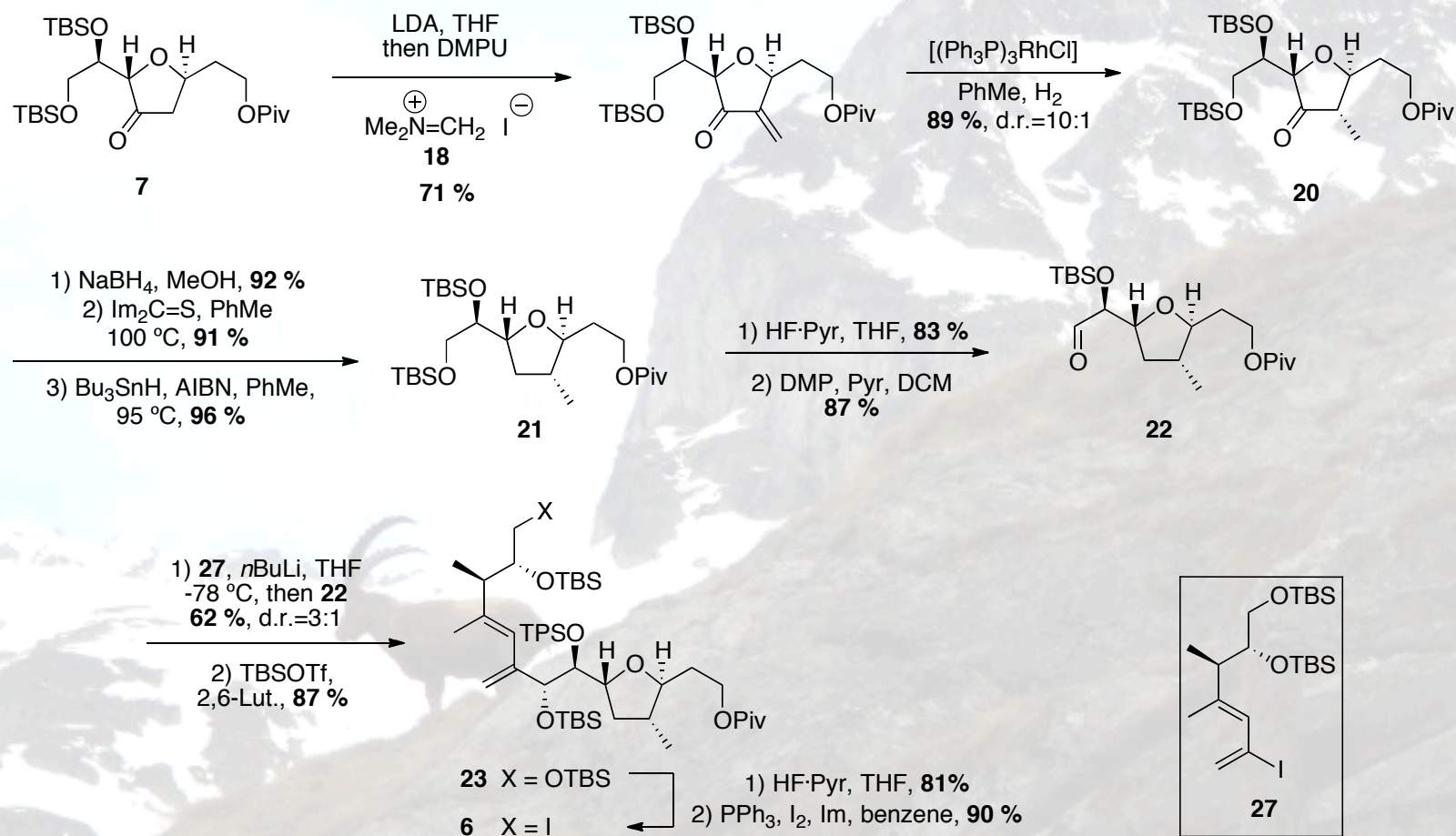


## Synthesis of 27:

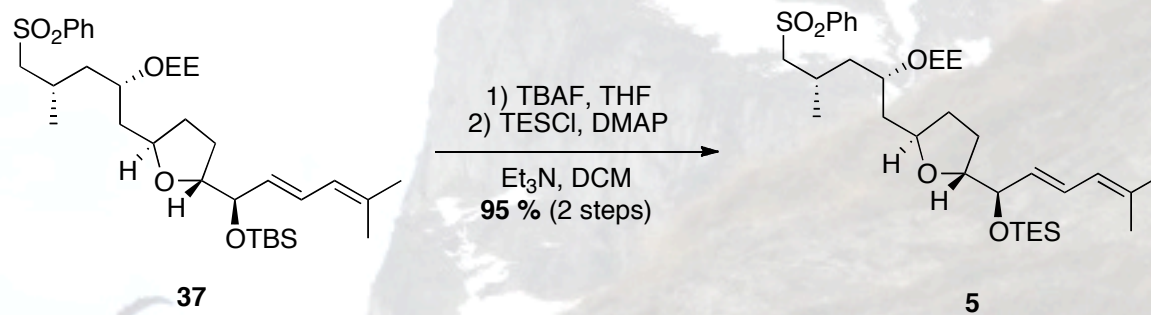




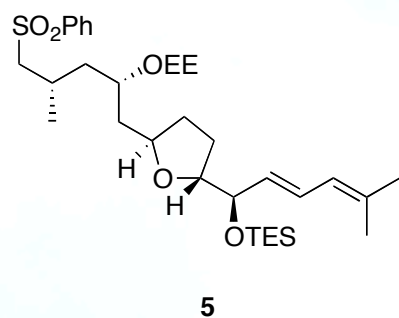
## Synthesis of subunit 6:



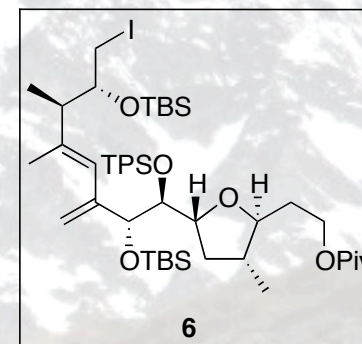
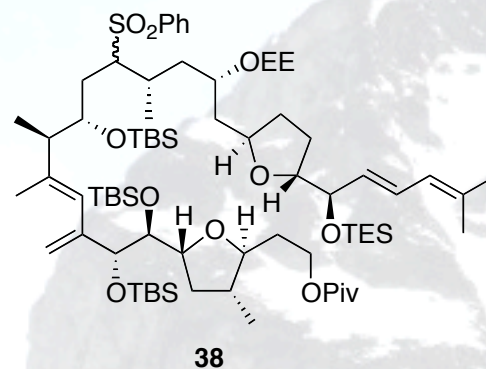




## Completion of the synthesis:

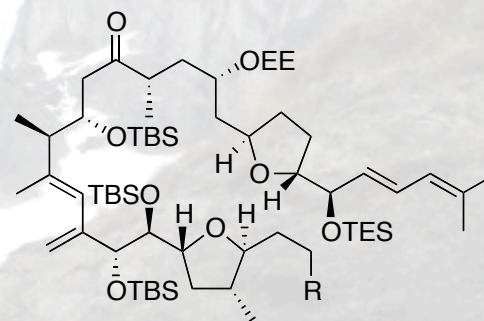


LHMDs, THF  
 HMPA then **6**  
 -10 °C to RT  
 2.5h, 74 %



LDA, DMPU, THF;  
 Davis oxaziridine  
 -50 to -35 °C

**4 + 39: 65 %**  
 (1.8:1 **4:39**)  
 (94 % brsm)



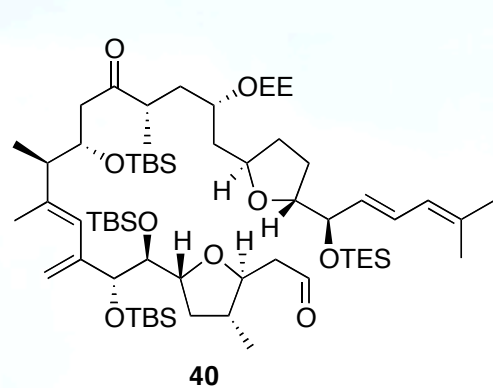
**4** R = CH<sub>2</sub>OPiv (42 %)

**39** R = CH<sub>2</sub>OH (23 %)

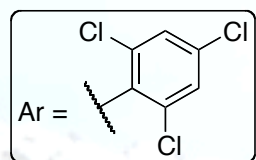
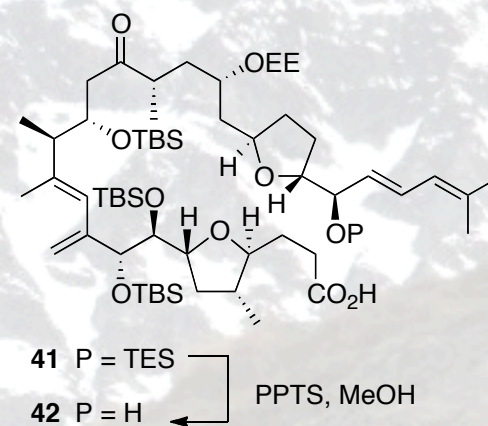
**40** R = CHO

DMSO, (ClCO)<sub>2</sub>  
 Et<sub>3</sub>N, DCM, **83 %**

1) LAH, Et<sub>2</sub>O  
 2) DMSO, (ClCO)<sub>2</sub>,  
 Et<sub>3</sub>N, DCM, **83 %** (2 steps)

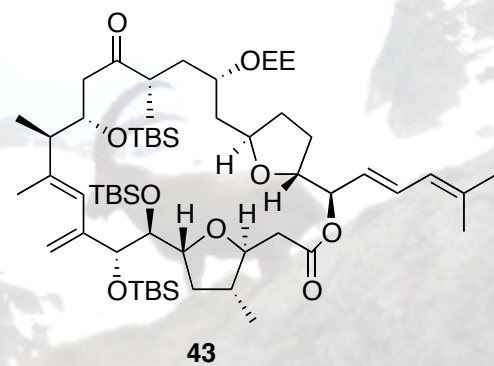


NaClO<sub>2</sub>, 2-Me-butene  
NaH<sub>2</sub>PO<sub>4</sub>·H<sub>2</sub>O  
tBuOH/H<sub>2</sub>O, **85 %**

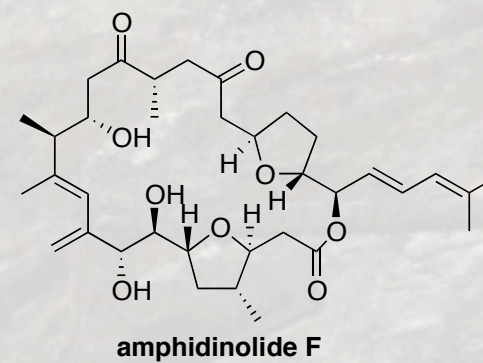


ArCOCl, Et<sub>3</sub>N  
PhMe/THF

DMAP, **65 %** (2 steps)




1) AcOH, THF/H<sub>2</sub>O  
2) DMP, Pyr, **62 %** (2 steps)  
3) Et<sub>3</sub>N·3HF, Et<sub>3</sub>N/MeCN  
7d, **56 %**



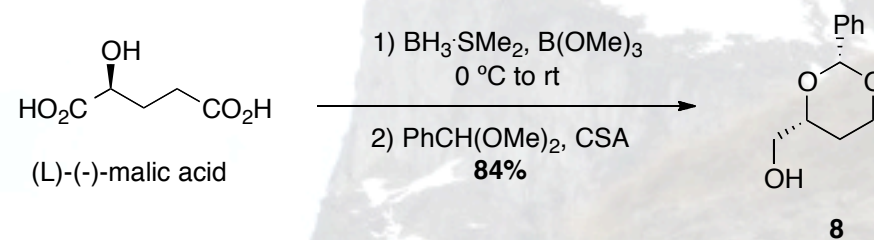
# Conclusion

- first total synthesis of amphidinolide F
- synthetic amphidinolide F matched with the reported isolation data ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR,  $[\alpha]_D$ )
- silver-catalyzed dihydrofuran formation
- regioselective hydrostannylation of an enyne
- sulfone alkylation/ desulfurization sequence

A faded background image of a mountain landscape. In the foreground, a wooden fence runs across the bottom. A goat with curved horns stands on a rocky ledge in the middle ground. In the background, a large, rugged mountain peak is covered in snow under a blue sky with light clouds.

# End

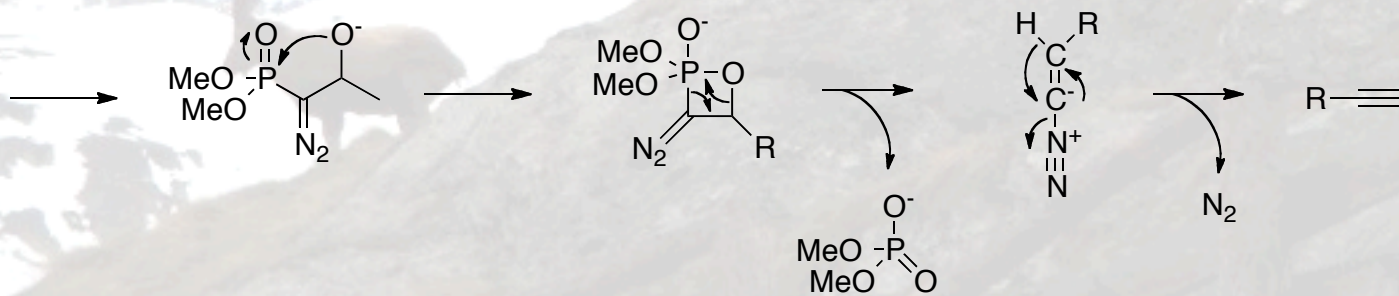
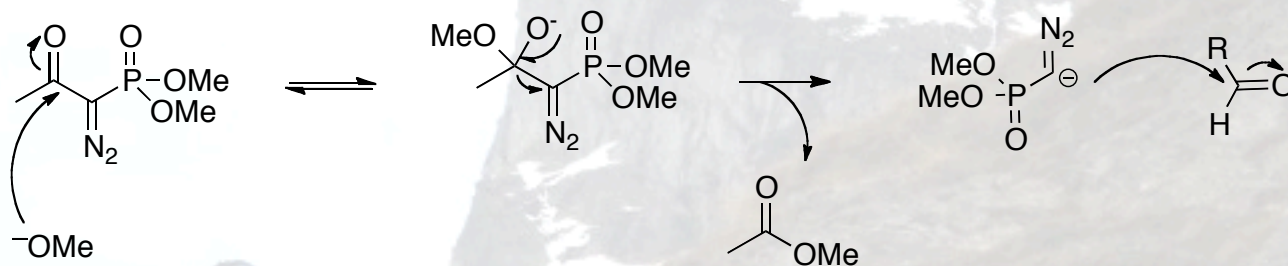
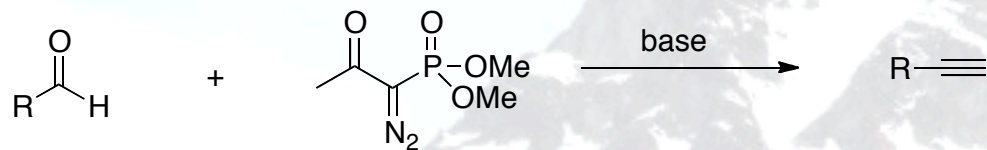
## Synthesis of starting material 8:



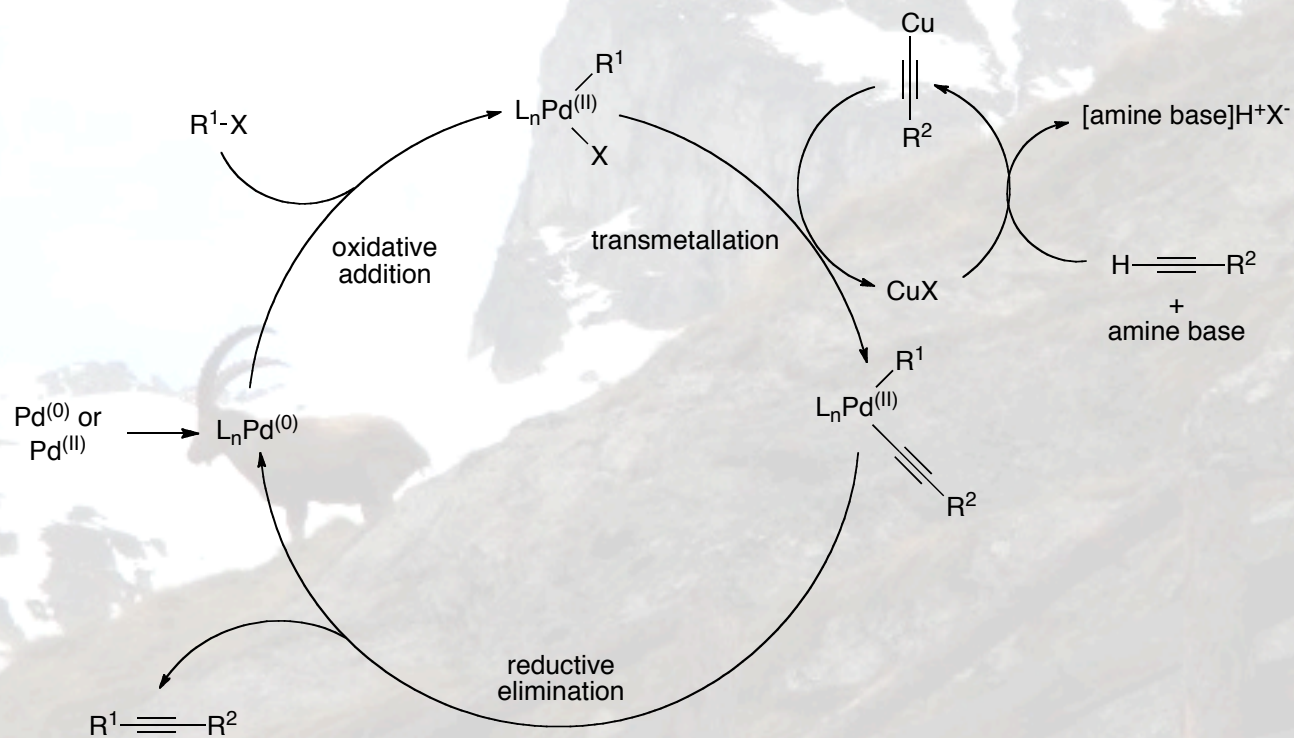
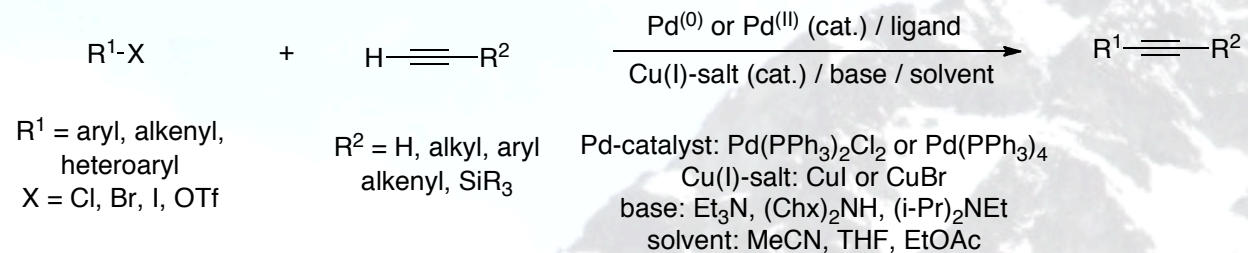
O. Flögel, M. G. O. Amombo, H.-U. Reissig, G. Zahn, I. Brüdgam, H. Hartl, *Chem Eur. J.* **2003**, *9*, 1405 – 14115.  
B. Herradon, *Tetrahedron: Asymmetry* **1991**, *2*, 191 – 194.



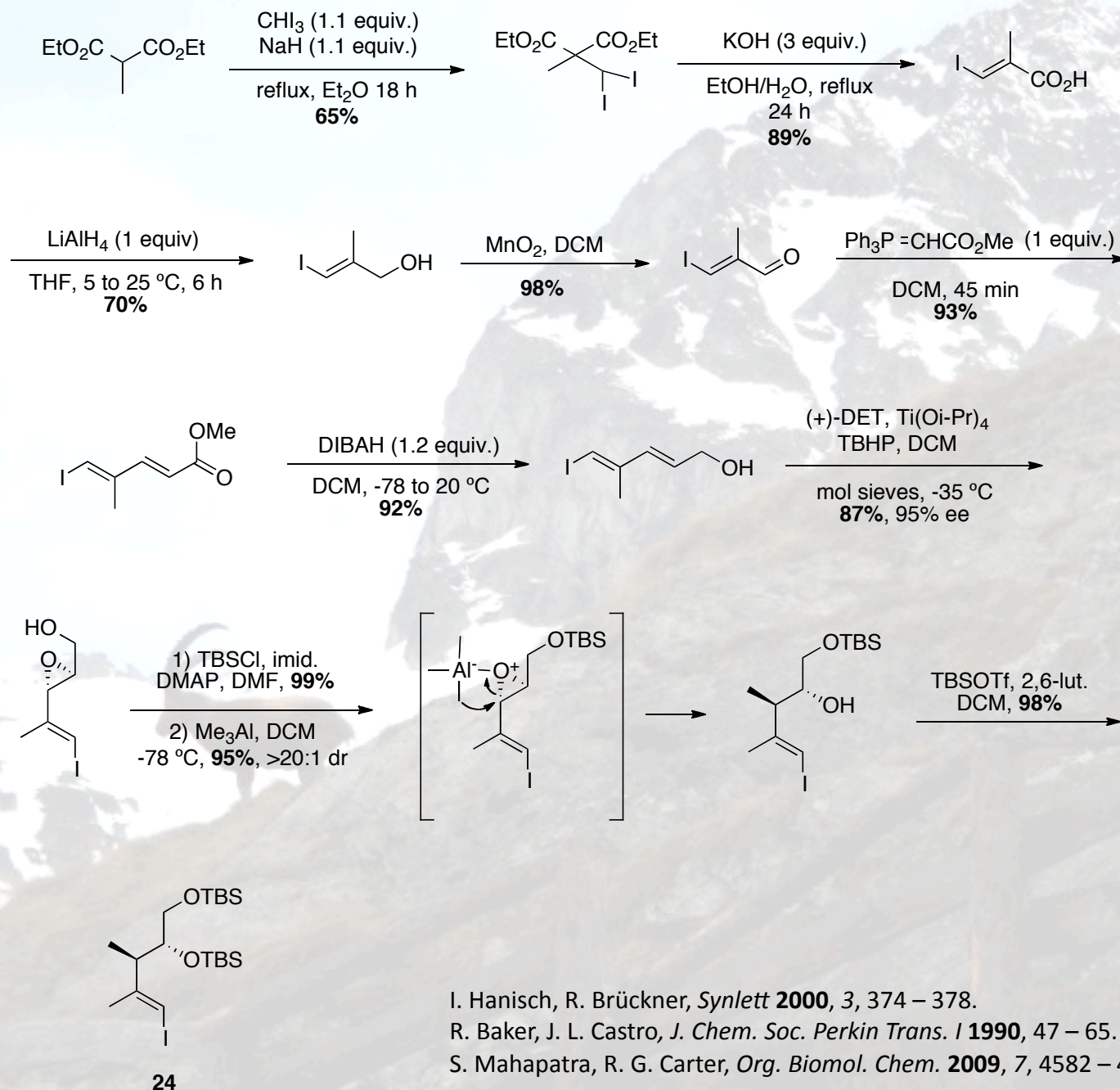
# Ohira-Bestmann reaction:



## Sonogashira cross-coupling:



## Synthesis of starting 24:

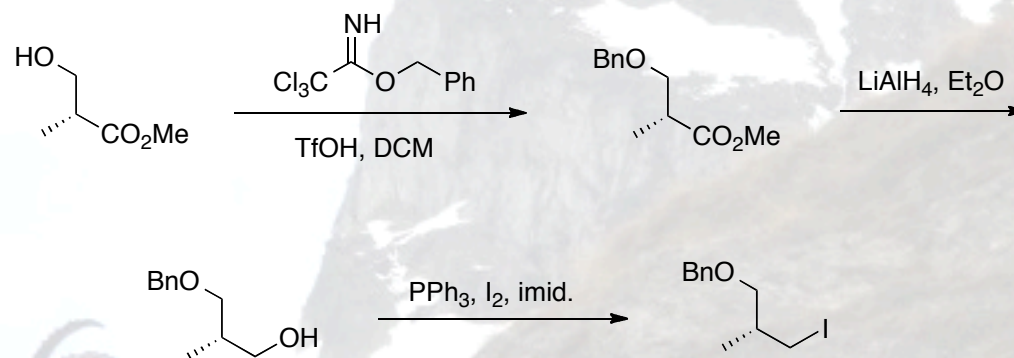


I. Hanisch, R. Brückner, *Synlett* **2000**, 3, 374 – 378.

R. Baker, J. L. Castro, *J. Chem. Soc. Perkin Trans. I* **1990**, 47 – 65.

S. Mahapatra, R. G. Carter, *Org. Biomol. Chem.* **2009**, 7, 4582 – 4585.

## Synthesis of starting 30:



B. G. Vong, S. Abraham, A. X. Xiang, E. A. Theodorakis, *Org. Lett.* **2003**, *5*, 1617 – 1620.  
J. D. White, M. Kawasaki, *J. Org. Chem.* **1992**, *57*, 5292, 5300.

## Oxidative desulfonylation with Davis oxaziridine:

