

Total Synthesis of Sandresolide B and Amphilectolide

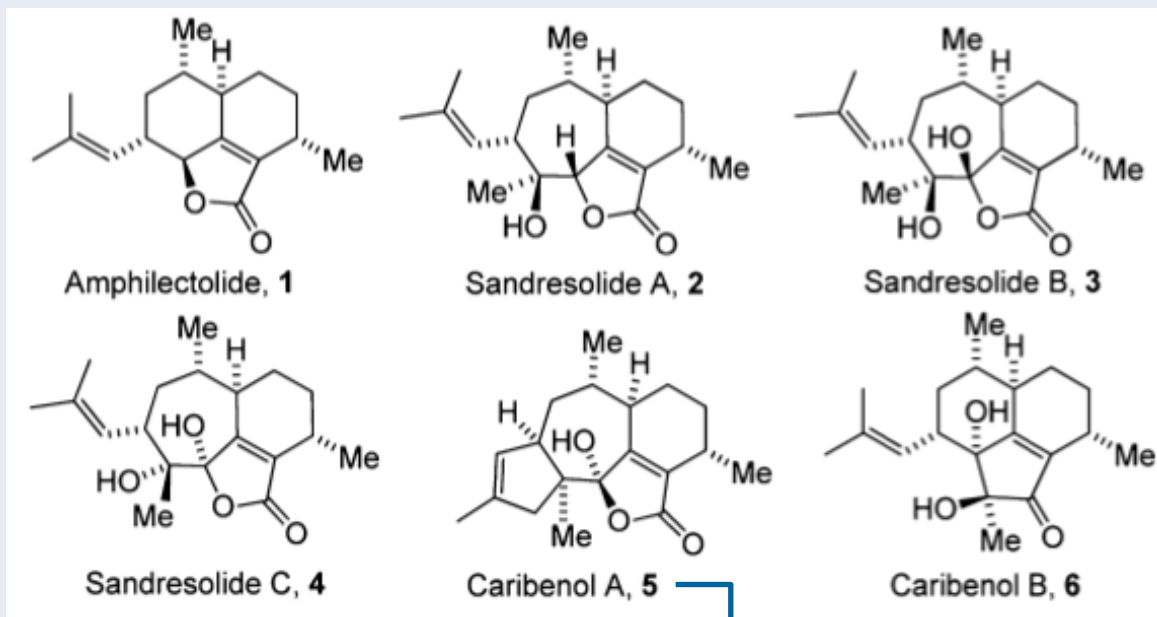
Ingrid T. Chen, Irina Baitinger, Lucas
Schreyer, and Dirk Trauner*

University of Munich, Germany

Organic
LETTERS

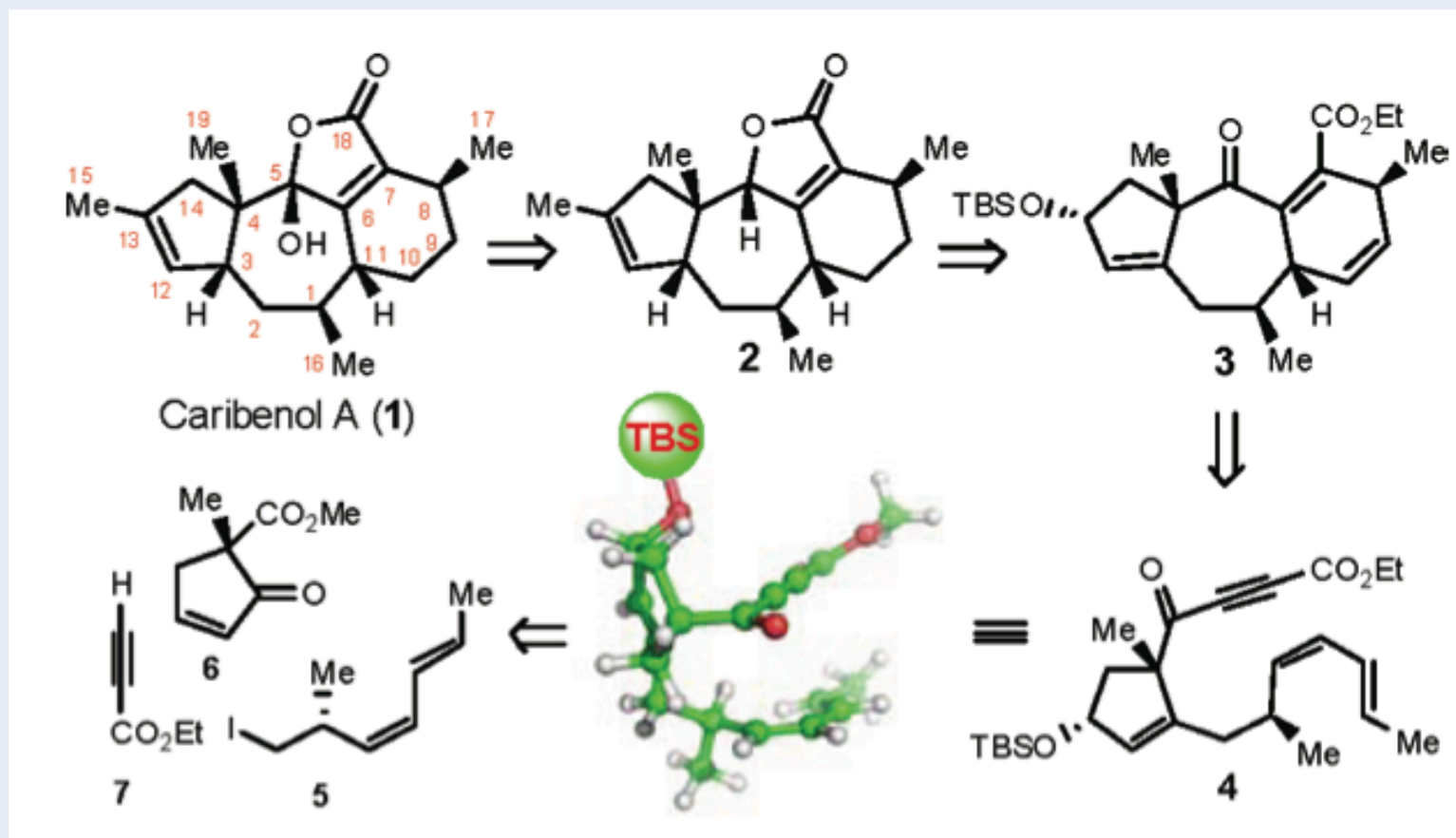
Org Lett **2014**, 16, 166–169.
[dx.doi.org/10.1021/ol403156r](https://doi.org/10.1021/ol403156r)

- Since the 1980's more than **40 marine metabolites** have been isolated from ***Pseudopterogorgia elisabethae***, a caribbean octocoral
- **1 – 6** isolated from coral from deep-sea expedition near **Sand Andrés island, Columbia**, by Rodríguez and coworker.
- **Biological activity** against inflammation, tuberculosis, cancer, and antiplasmodial activity



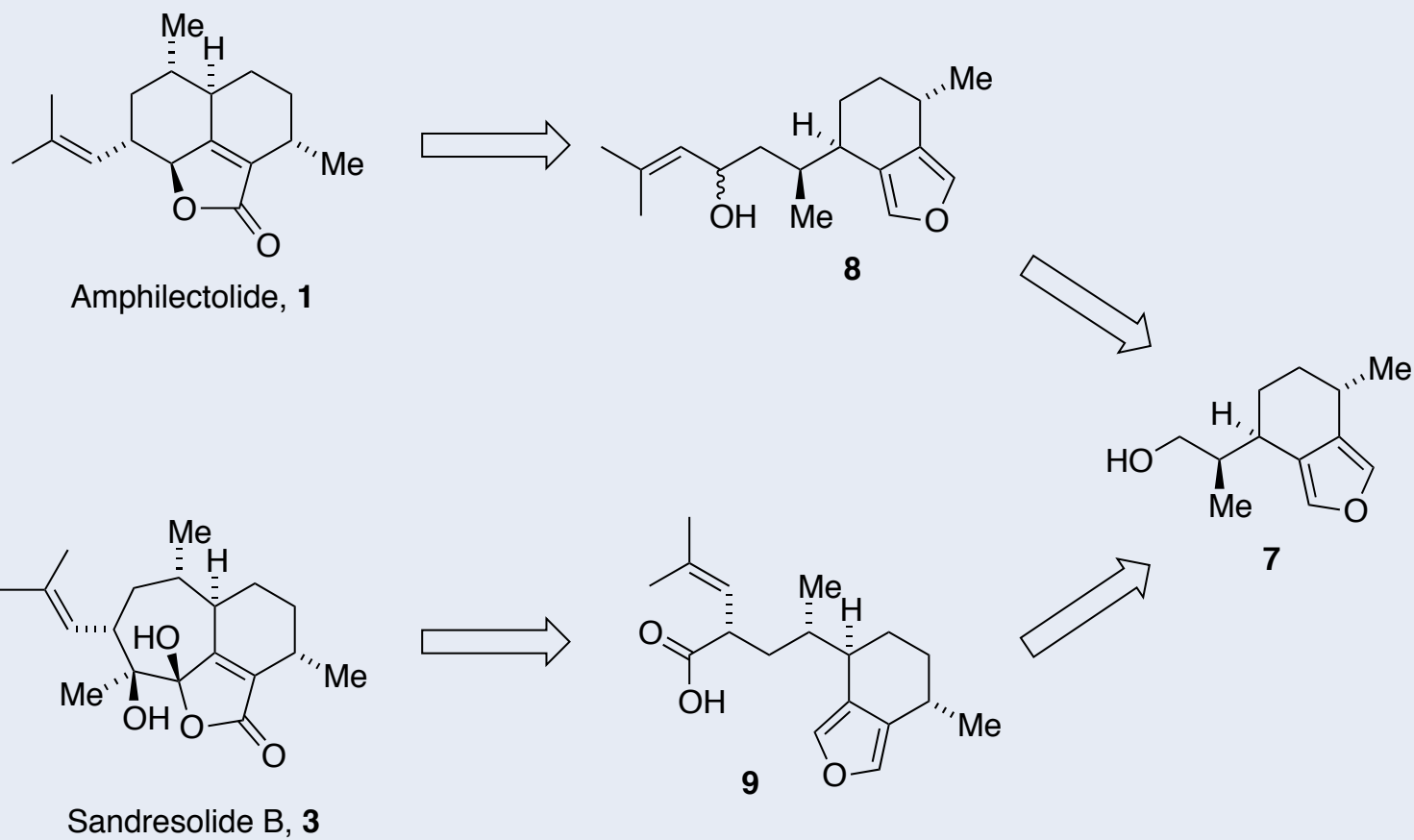
Yang et al. *JACS* **2010**, 132, 13608.

Asymmetric Total Synthesis of Caribanol A

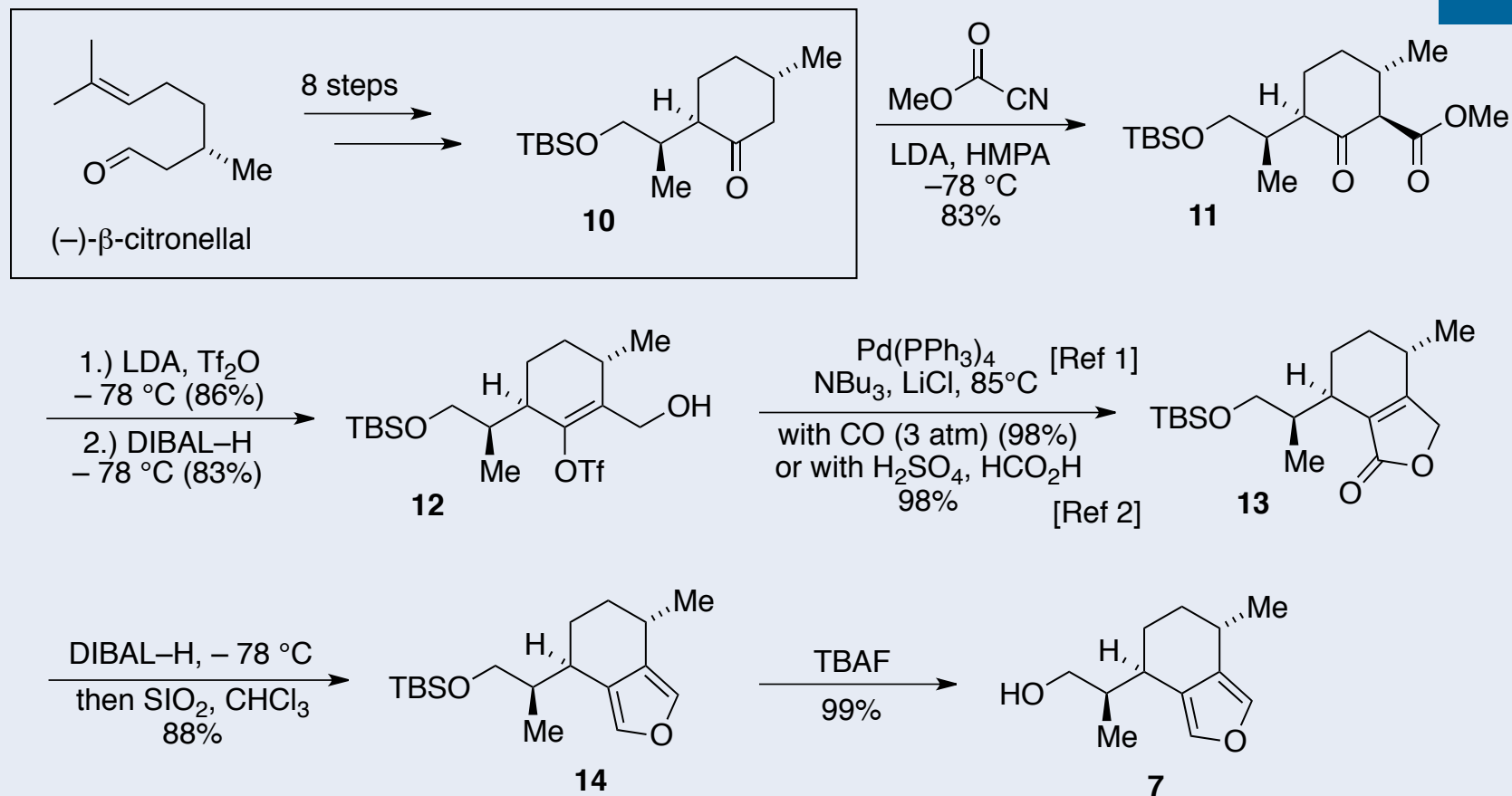


Liu, L.-Z.; Han, J.-C.; Yue, G.-Z.; Li, C.-C.; Yang, Z. *J. Am. Chem. Soc.* **2010**, *132*, 13608–13609.

Retrosynthetic Analysis



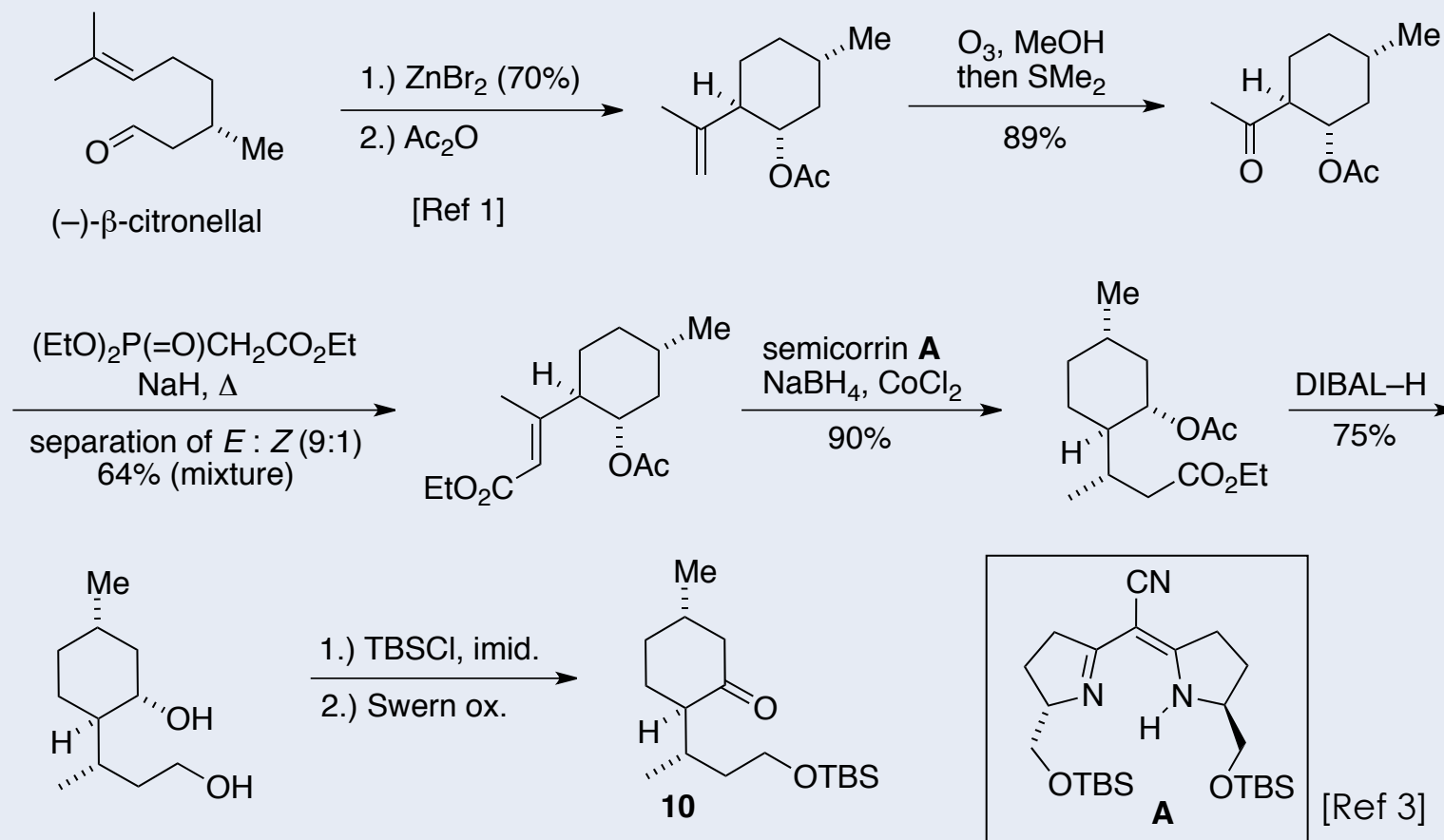
Preparation of Key Furan Building Block 7



¹ Crisp, G. T.; Meyer, A. G. *J. Org. Chem.* **1992**, *57*, 6972–6975.

² Brancour, C.; Fukuyama, T.; Mukai, Y.; Skrydstrup, T.; Ryu, I. *Org Lett* **2013**, *15*, 2794–2797.

Synthesis of Compound **10**²

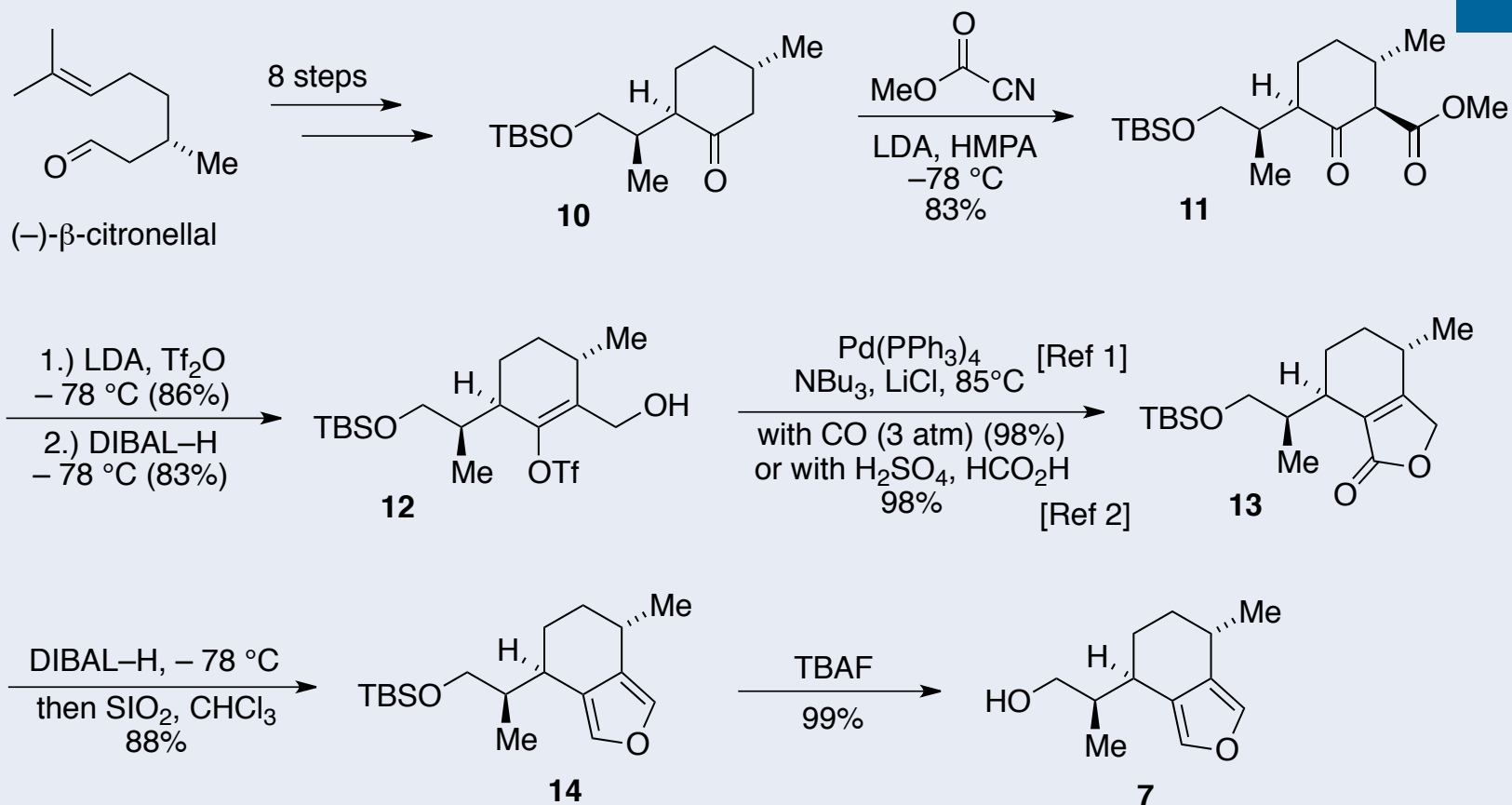


¹ Nakatani, Y.; Kawashima, K. *Synthesis* **1978**, 1978, 147–148.

² Kocienski, P. J.; Pontiroli, A.; Qun, L.. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2356–2366.

³ Pfaltz, A. *Acc. Chem. Res.* **1993**, 26, 339–345.

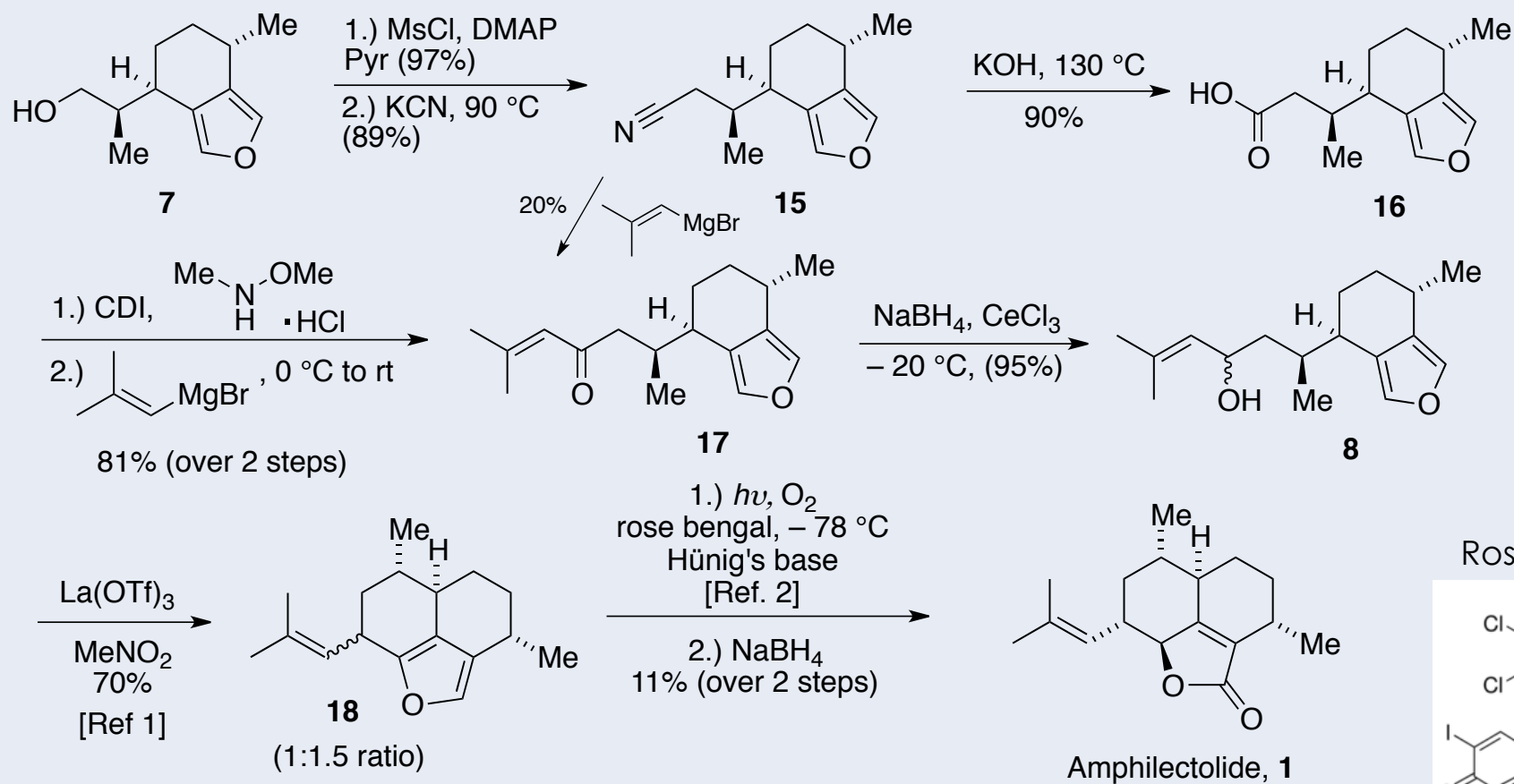
Preparation of Key Furan Building Block 7



¹ Crisp, G. T.; Meyer, A. G. *J. Org. Chem.* **1992**, *57*, 6972–6975.

² Brancour, C.; Fukuyama, T.; Mukai, Y.; Skrydstrup, T.; Ryu, I. *Org Lett* **2013**, *15*, 2794–2797.

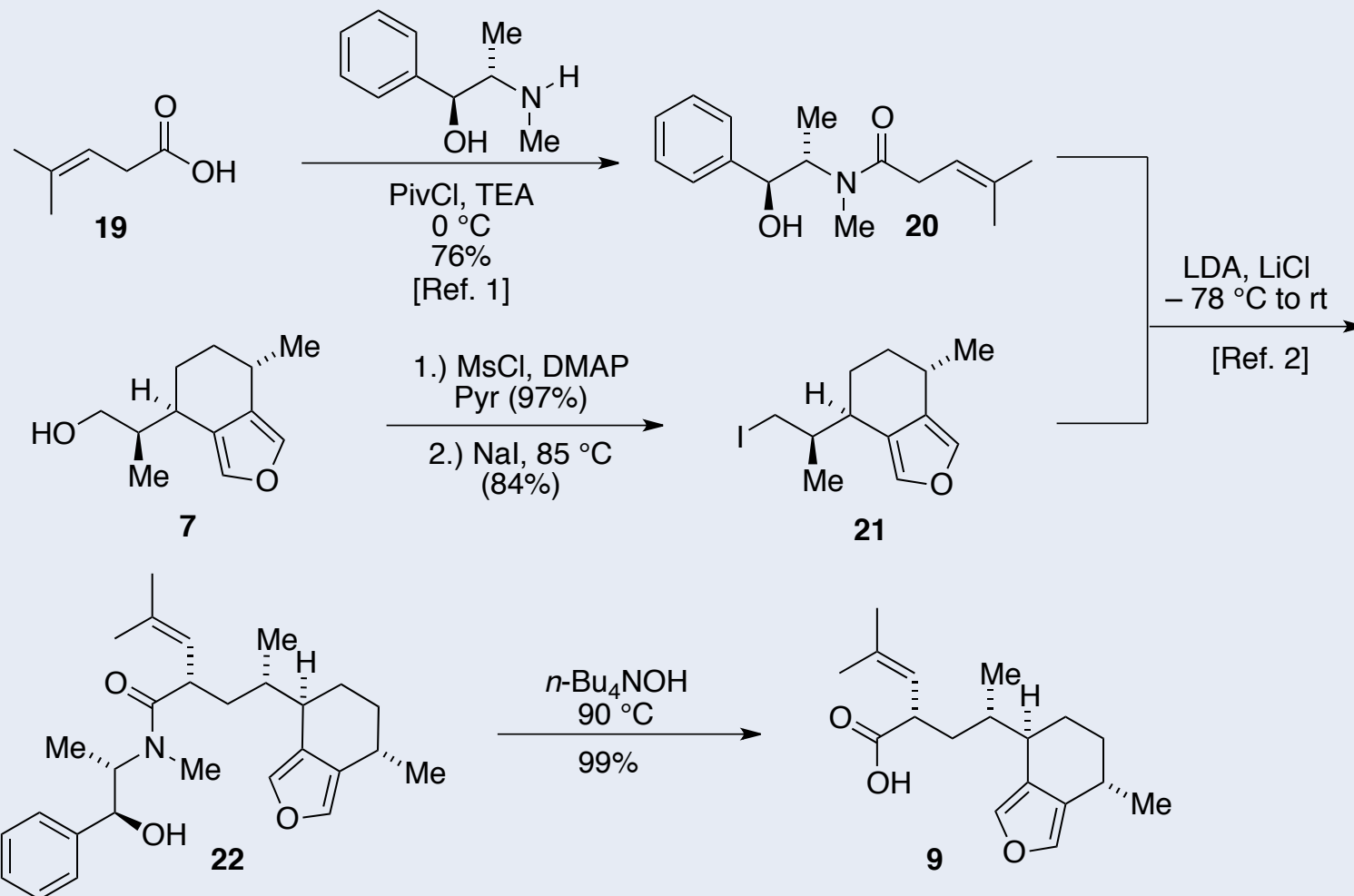
Total Synthesis of Amphilectolide, 1



¹ Noji, M.; Ohno, T.; Fuji, K.; Futaba, N.; Tajima, H.; Ishii, K. *J. Org. Chem.* **2003**, *68*, 9340–9347.

² Kernan, M. R.; Faulkner, D. J. *J. Org. Chem.* **1988**, *53*, 2773–2776.

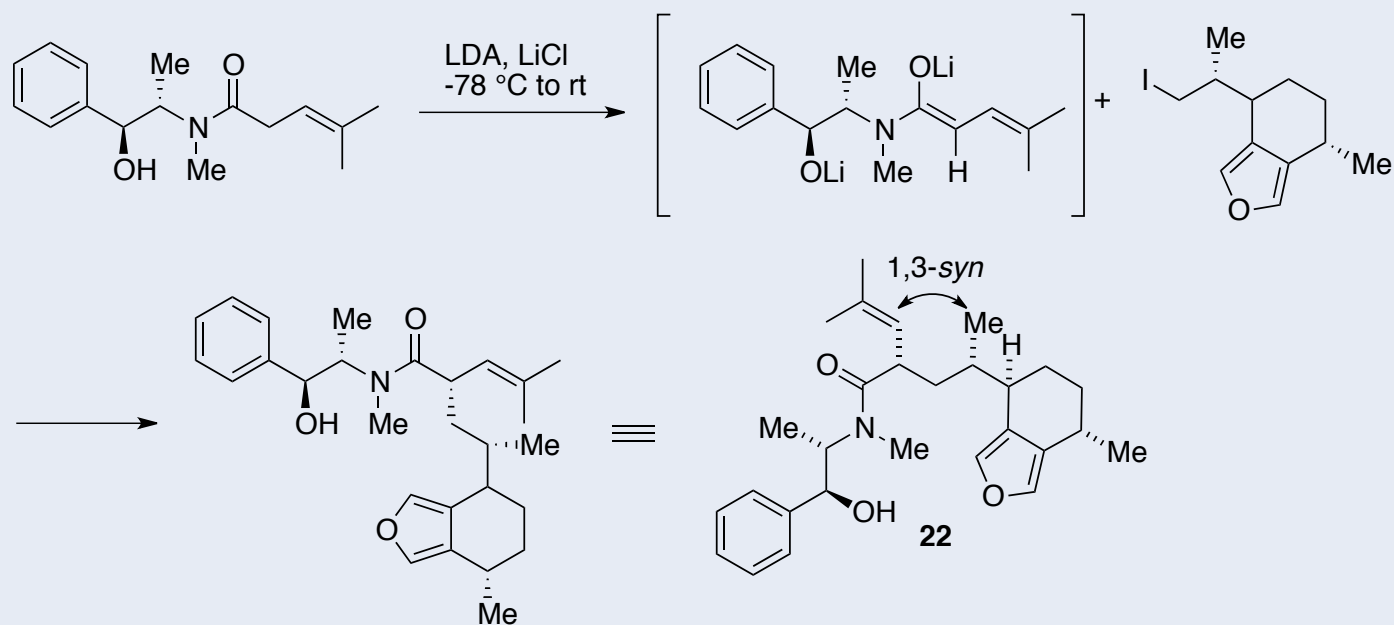
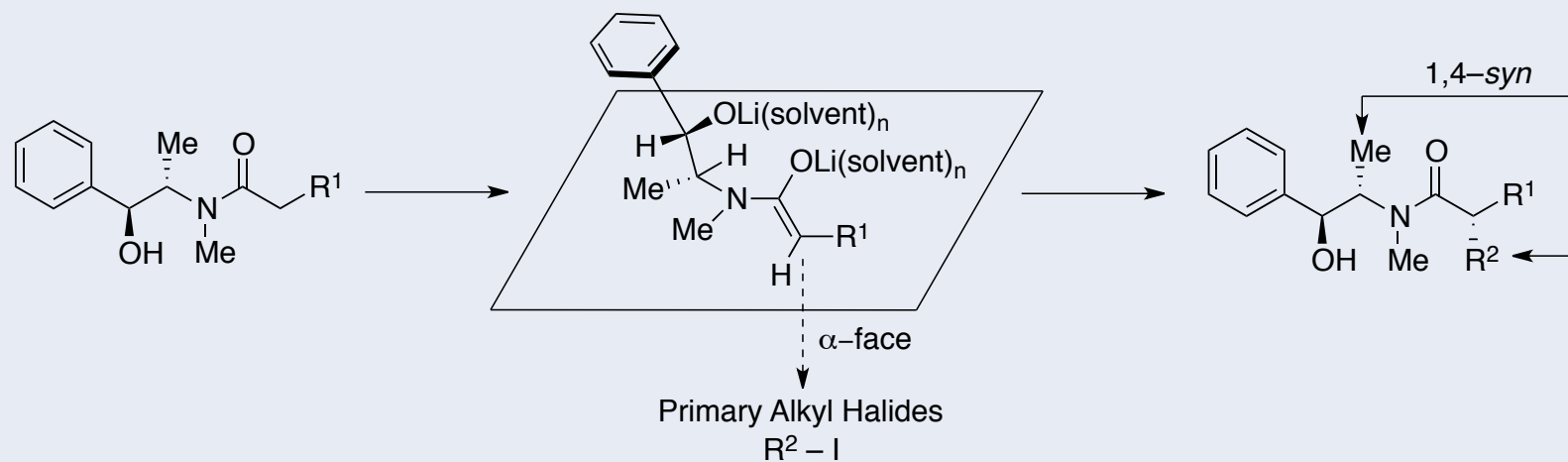
Myers Alkylation to Access Ring-Closure Precursor **9**



¹ Myers, A. G.; Yang, B. H.; Chen, H.; Gleason, J. L. *J. Am. Chem. Soc.* **1994**, *116*, 9361–9362.

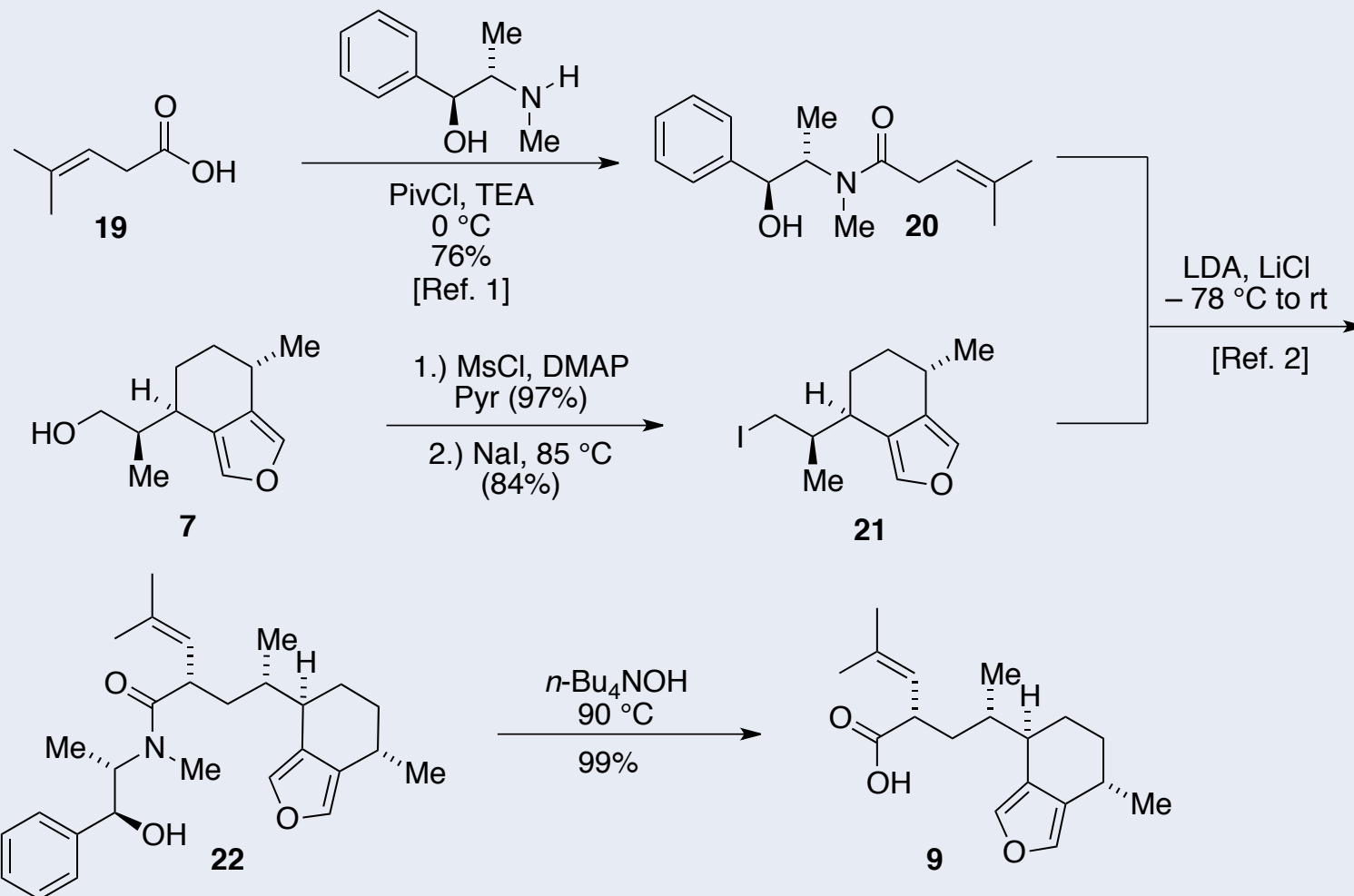
² Myers, A. G. *et al.* *J. Am. Chem. Soc.* **1997**, *119*, 6496–6511.

Myers Alkylation



Myers, A. G. et al. *J. Am. Chem. Soc.* **1997**, *119*, 6496–6511.

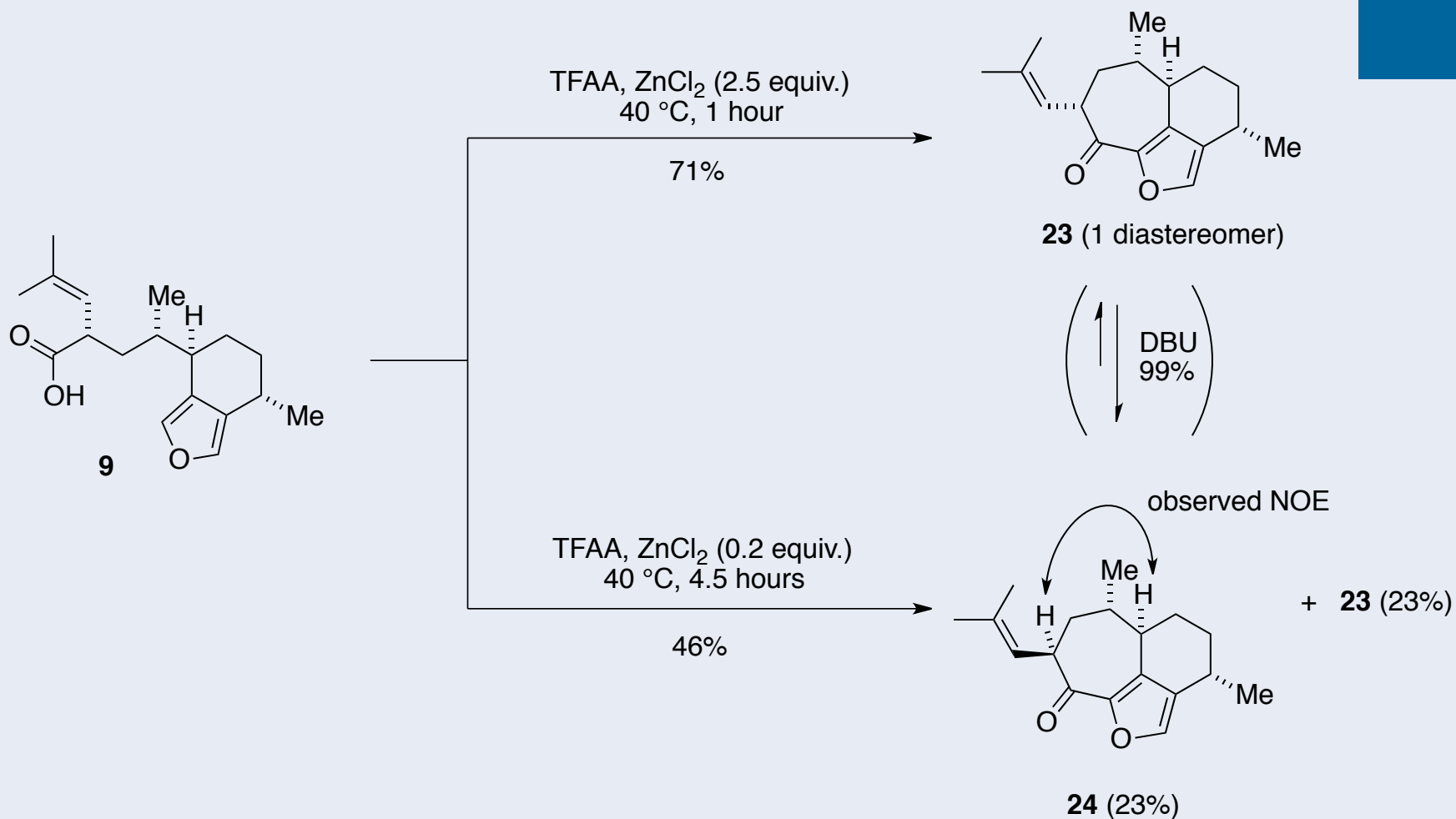
Myers Alkylation to Access Ring-Closure Precursor **9**



¹ Myers, A. G.; Yang, B. H.; Chen, H.; Gleason, J. L. *J. Am. Chem. Soc.* **1994**, *116*, 9361–9362.

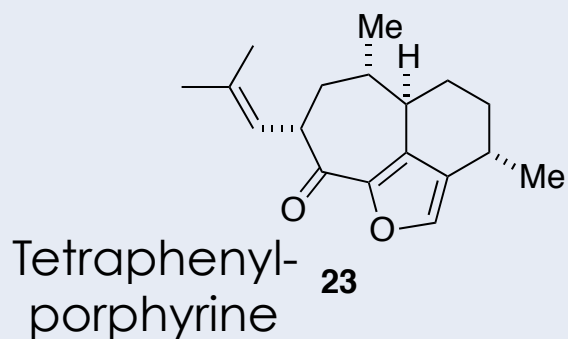
² Myers, A. G. *et al.* *J. Am. Chem. Soc.* **1997**, *119*, 6496–6511.

Ring Closure and NOE Correlation to Characterize **24**



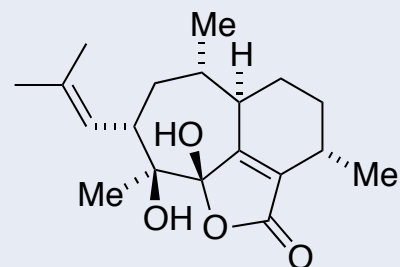
→ **24** thermodynamic product, **6.7 kcal/mol** more stable than **23** (kinetic product) (10'000 step Monte Carlo search, solvent-free OPLS algorithm)

Completion of Sandresolide B, 3

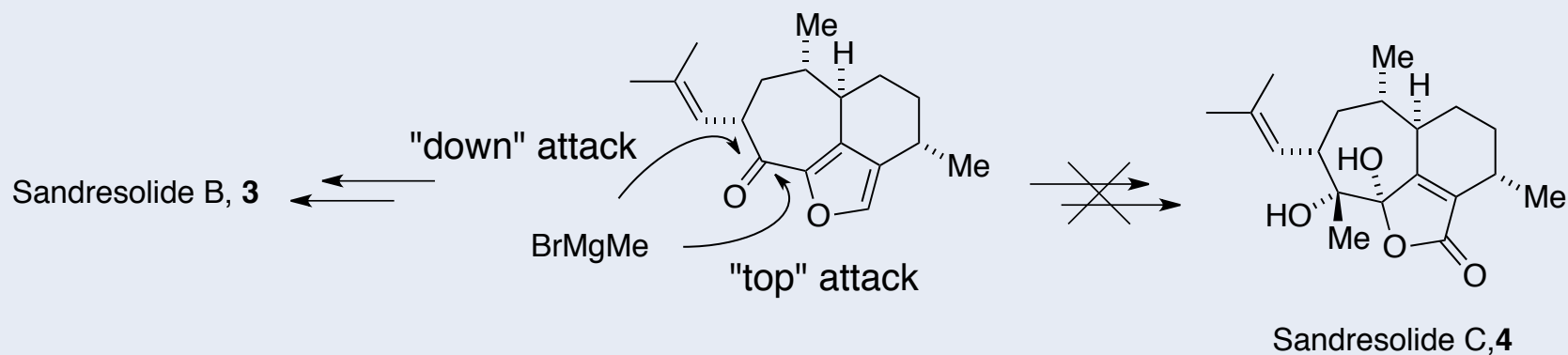
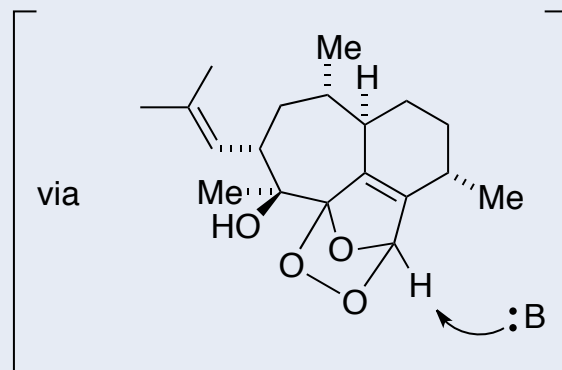
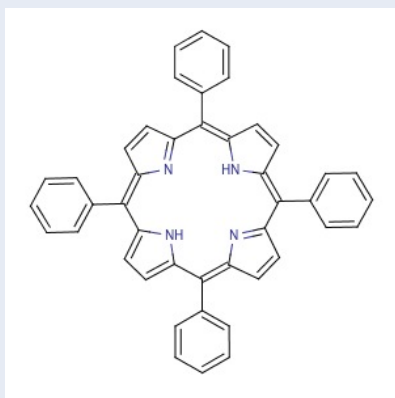


1.) MeMgBr, -78 °C

2.) $h\nu$, O₂, TPP
-78 °C then DBU
51% (over 2 steps)



Sandresolide B, 3



Conclusion

- Scalable route to furan building block **7**
- First total synthesis of amphilectolide, **1**, and sandresolide B, **3**
- Intramolecular Friedel-Craft alkylation for **1** and acylation for **3** to build third ring
- Use of two different sensitizer for photooxygenations (rose bengal and tetraphenylporphyrine)
- The use of building block **7** for the synthesis of other alkaloids of same source (*Pseudopterogorgia elisabethae*) is under active investigation