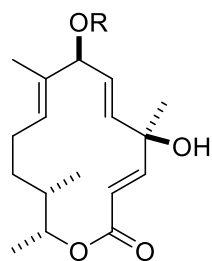


Selective Formation of a Trisubstituted Alkene Motif by *trans*-Hydrostannation/Stille Coupling: Application to the Total Synthesis and Late-Stage Modification of 5,6-Dihydrocineromycin B

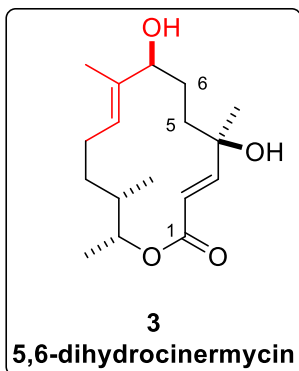
Stephan M. Rummelt, Johannes Preindl, Heiko Sommer, and Alois Fürstner
Max-Planck-Institut für Kohlenforschung 45470 Mülheim/Ruhr (Germany)
Angew. Chem. Int. Ed. **2015**, *54*, 6241–6245 DOI: 10.1002/anie.201501608

Presented by Hyelee Lee, Liu Research Group, Boston College

I. Introduction



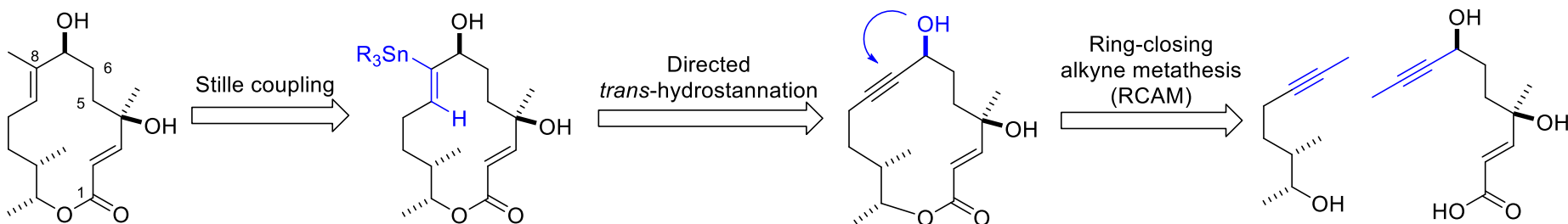
1 R= Me
2 R= H



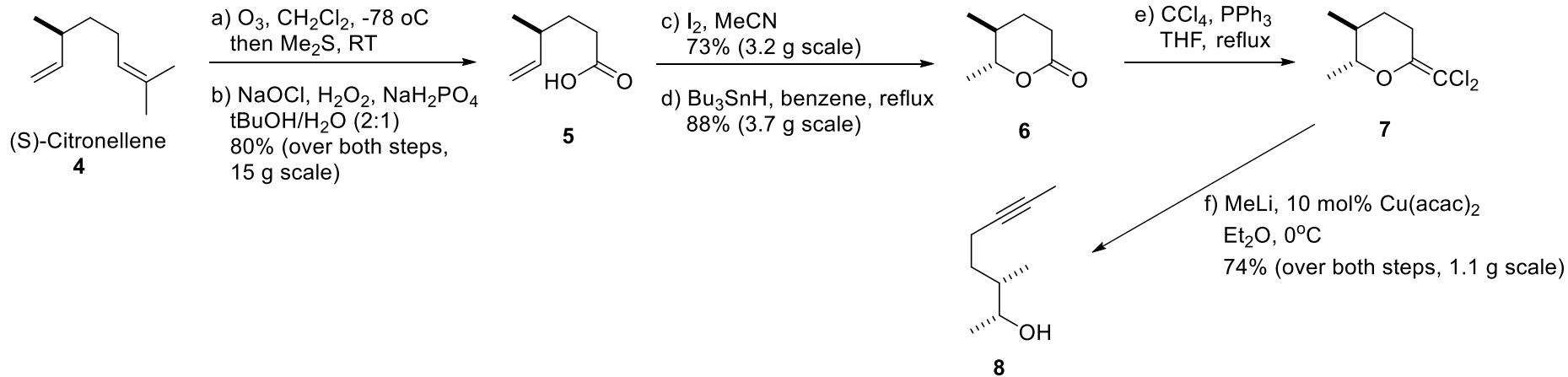
3
5,6-dihydrocineromycin

- Compound **1** was reported as an inhibitor of methicillin-resistant *Staphylococcus aureus* (MRSA) with a potency similar to that of vancomycin.
- Compound **3** (5,6-dihydrocineromycin) lacking the double allylic moiety around C7-OR substituent makes it chemically more robust.
- Total synthesis of compound **3** was previously reported in 2001, 2009, 2012^[1].
- E*-configured 2-methyl-but-2-en-1-ol subunit is prominently found in natural products
- Late-stage modification by diverted total synthesis is described.

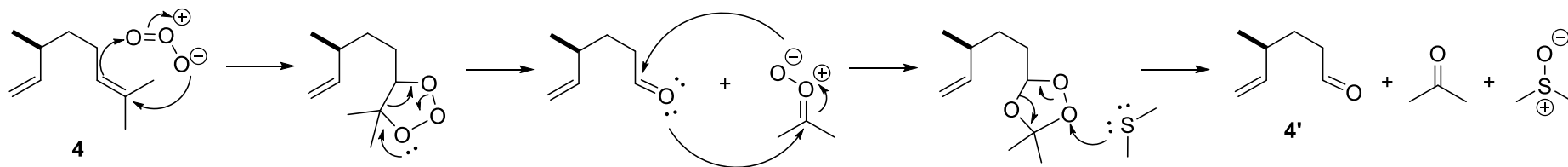
II. Retrosynthesis



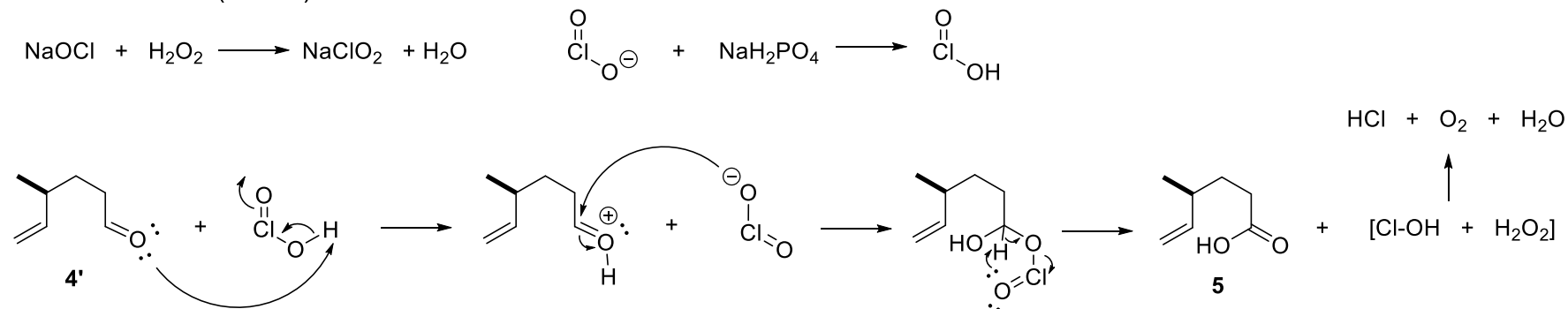
[1] a) Tietze, L. F.; Vçlkel, L. *Angew. Chem. Int. Ed.* **2001**, *40*, 901–902. b) Li, G.; Yang, X.; Zhai, H. *J. Org. Chem.* **2009**, *74*, 1356–1359. c) Reddy, G. V.; Kumar, R. S. C.; Siva, B.; Babu, K. S.; Rao, J. M. *Synlett* **2012**, 2677–2681.



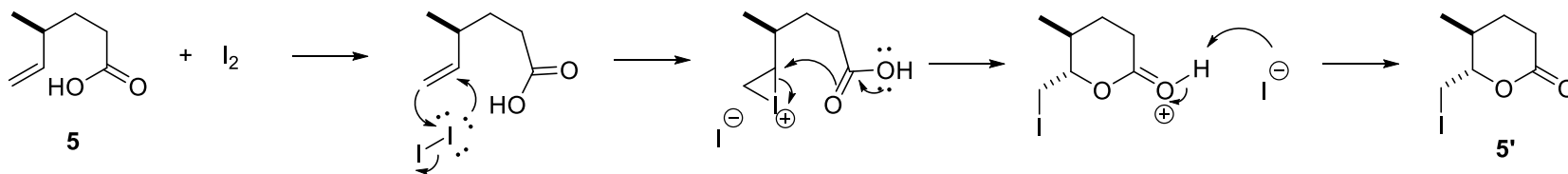
Ozonolysis (4 to 4')



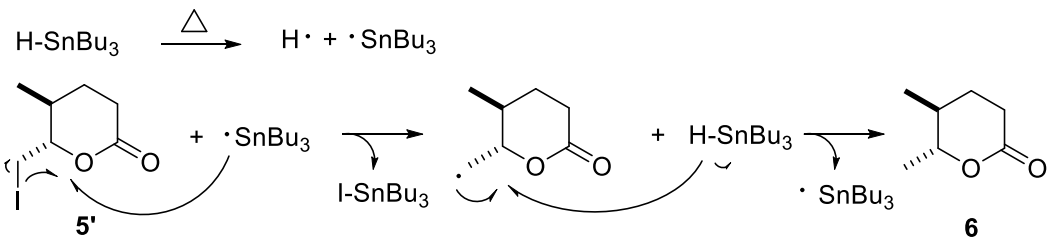
Pinnick oxidation (4' to 5)



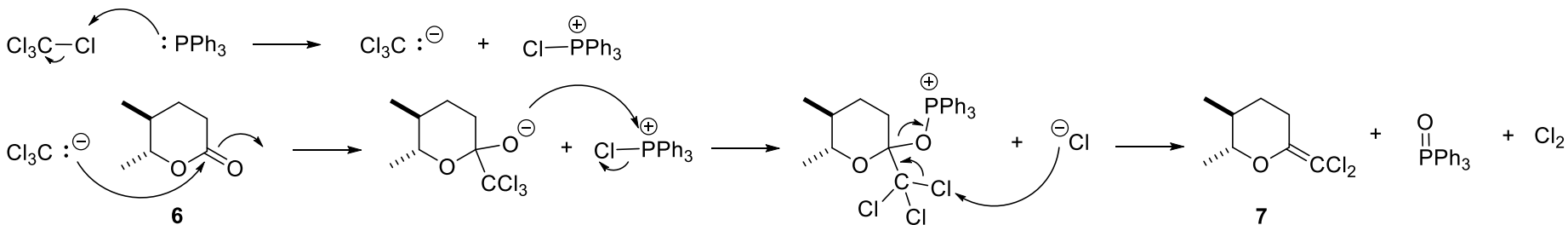
Iodolactonization (5 to 5')



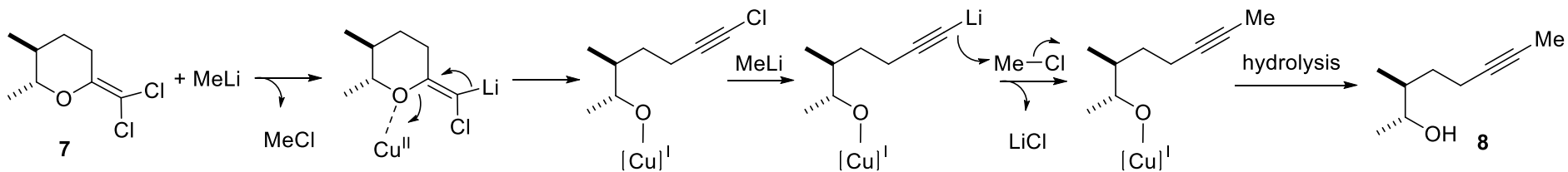
Reduction of C-I bond (5' to 6)

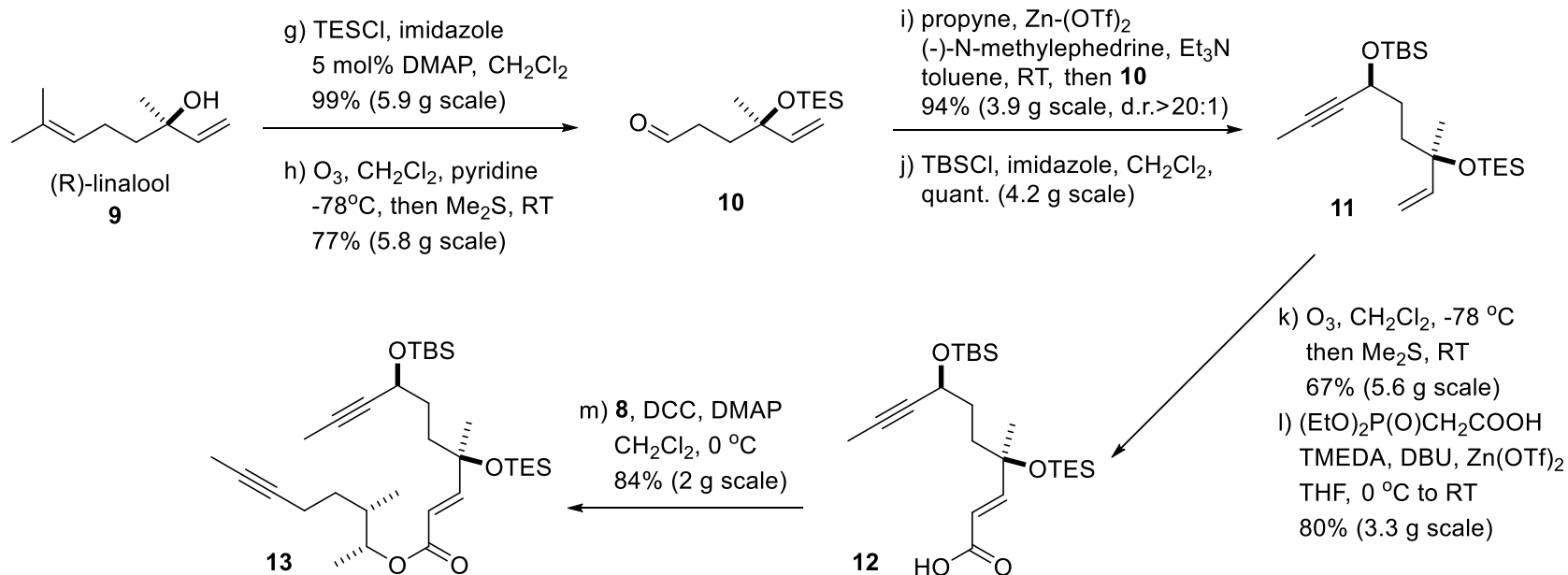


6 to 7

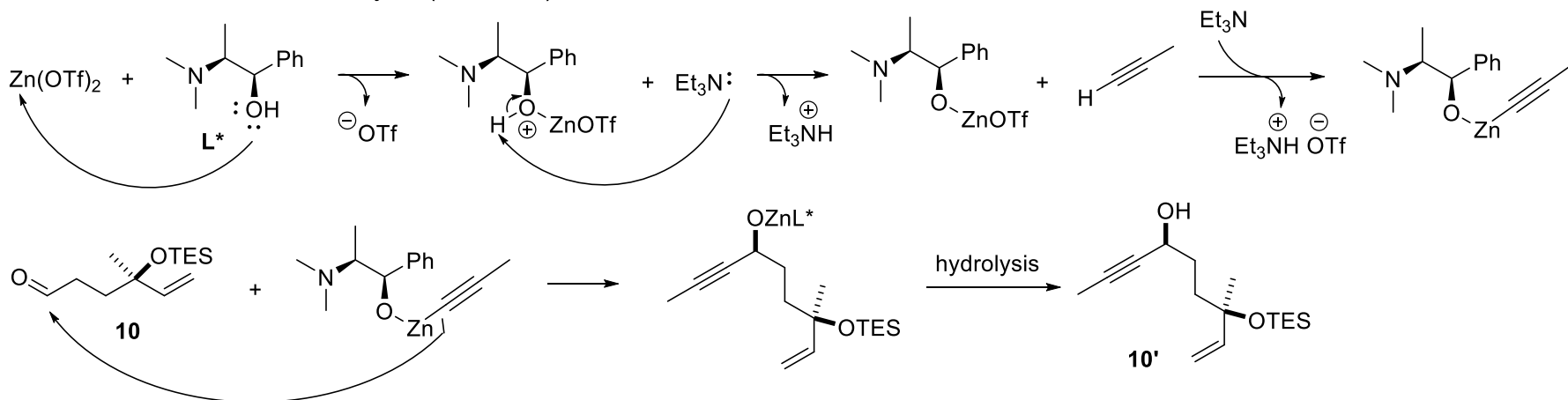


Reductive alkylation (7 to 8)

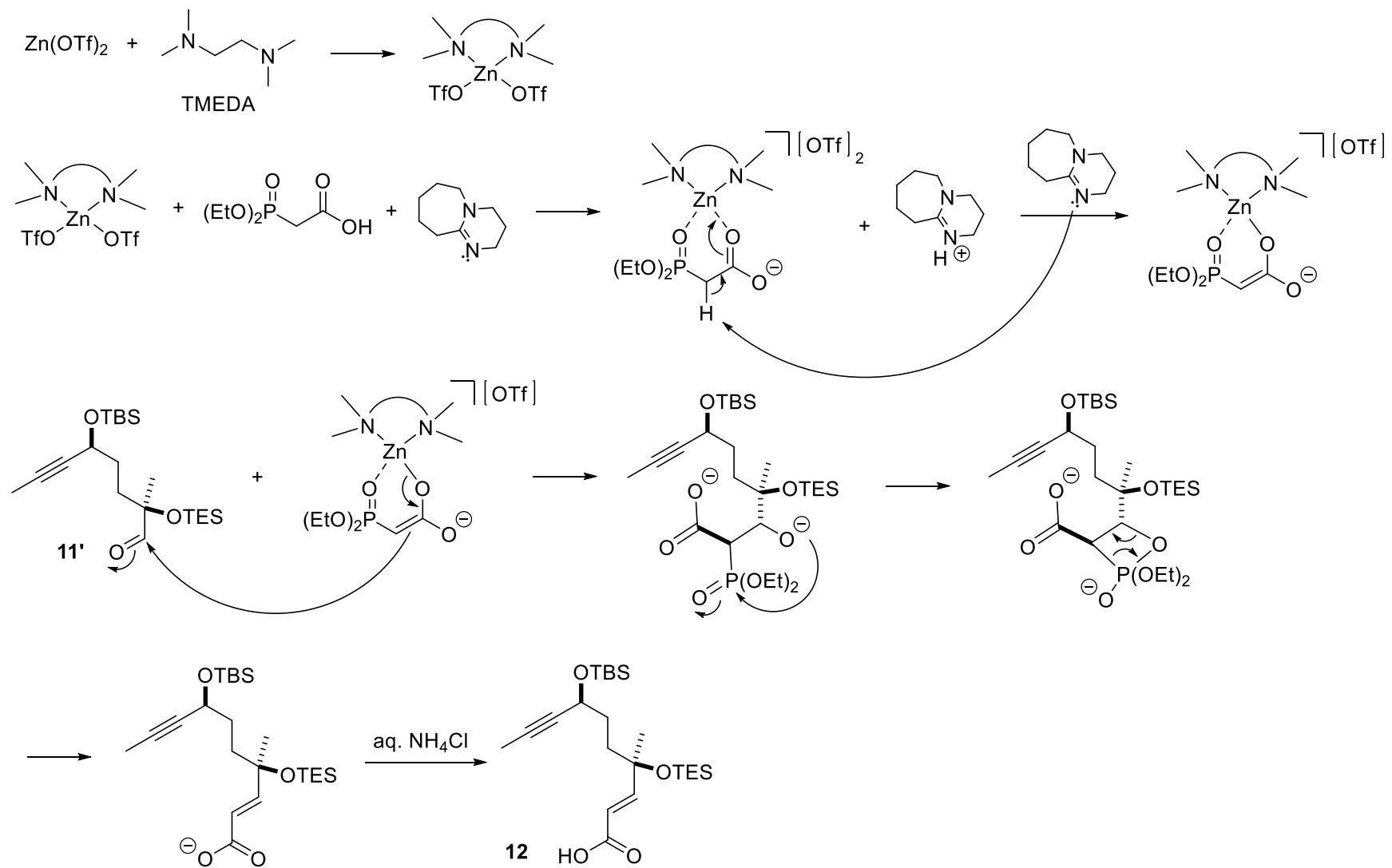




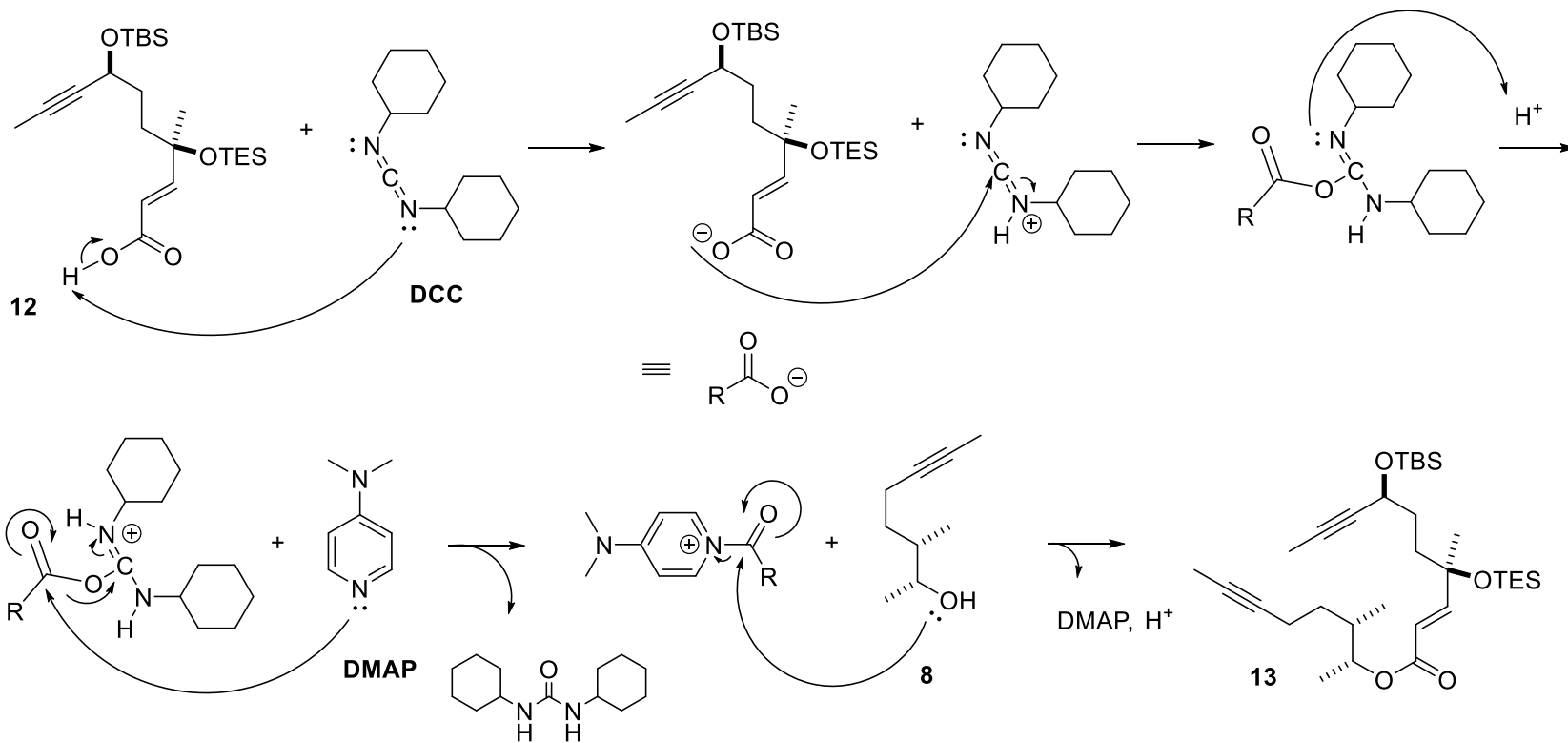
Enantioselective addition of alkyne (**10** to **10'**)^[2]

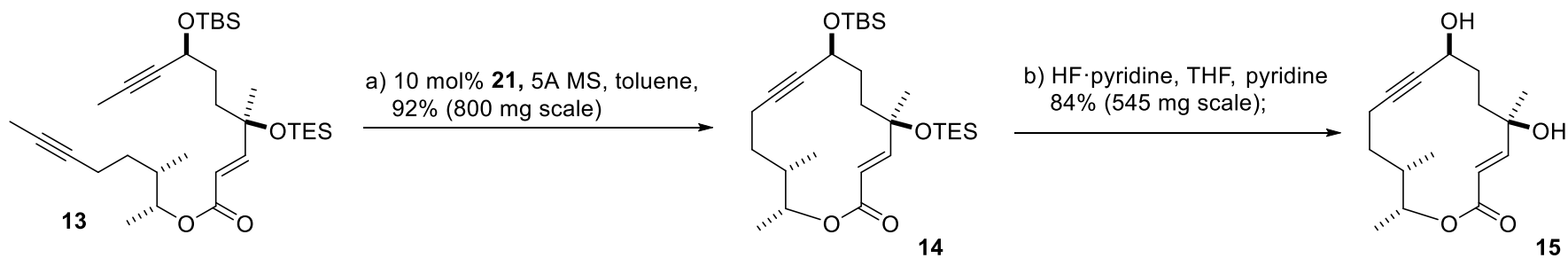


Zinc-promoted Horner-Wadsworth-Emmons olefination (**11'** to **12**)^[3]

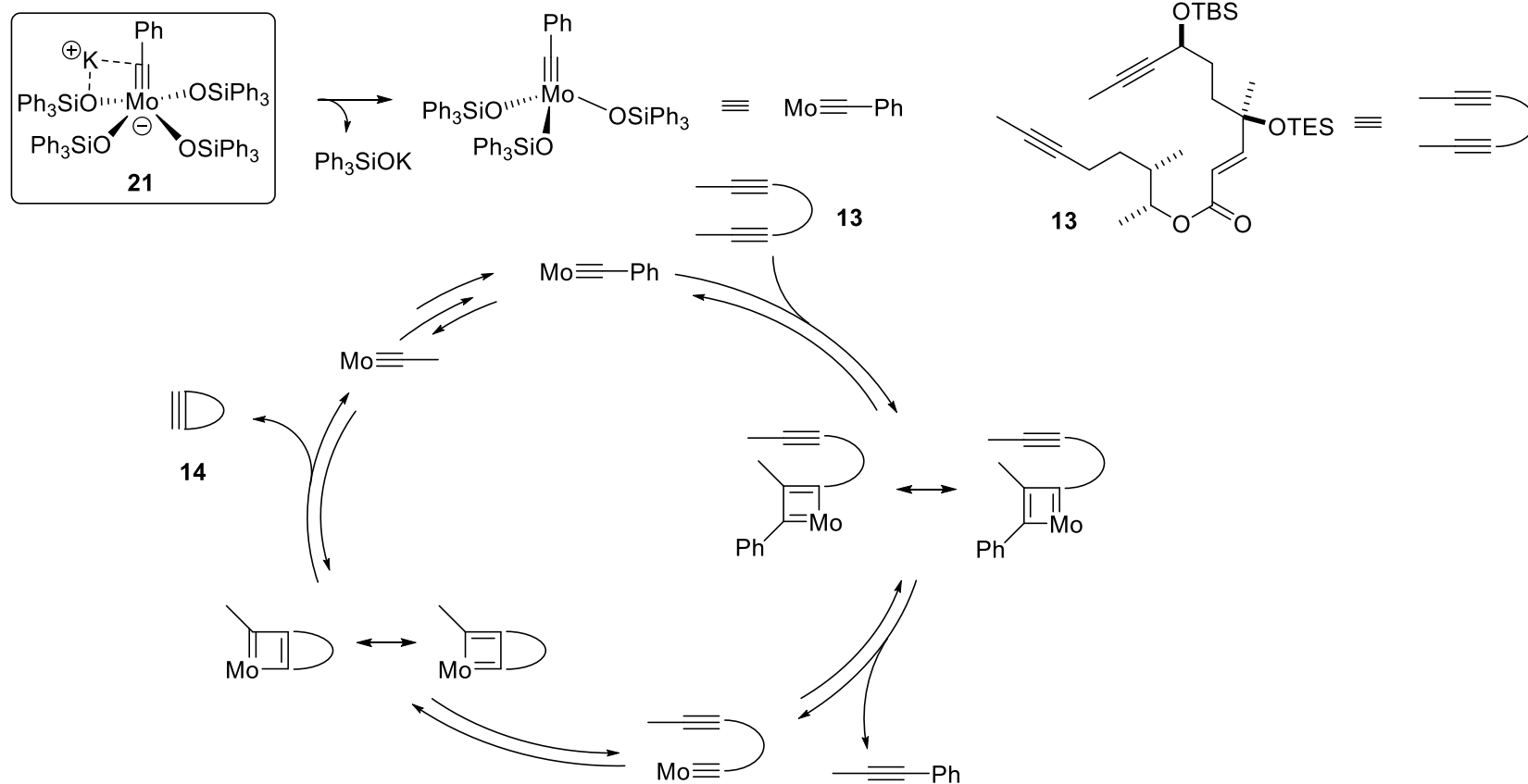


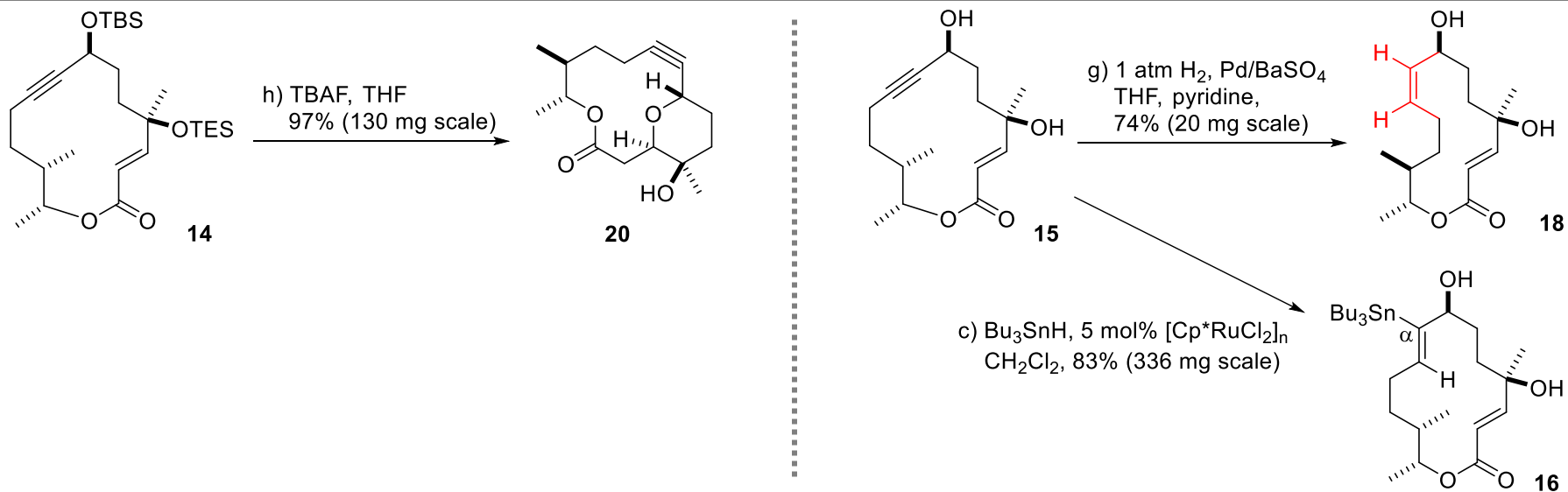
Steglich esterification (**12** to **13**)



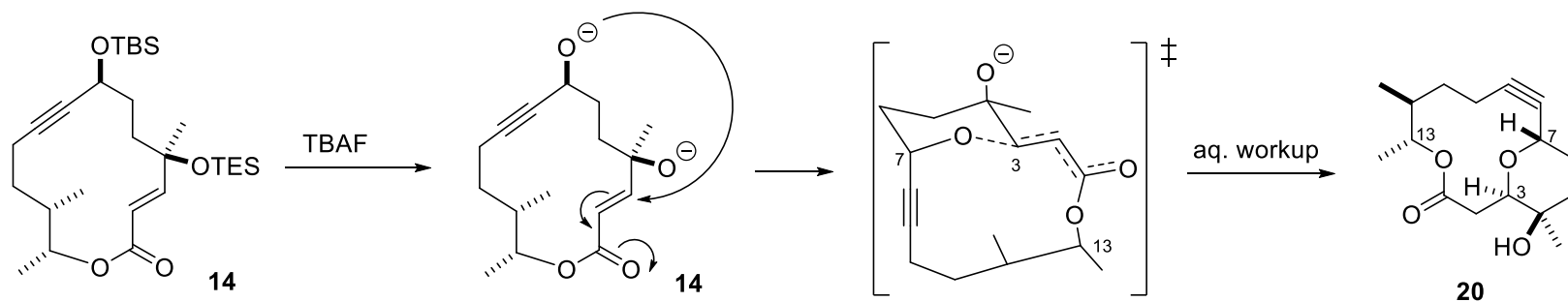


Ring-Closing Alkyne Metathesis (**13** to **14**)^[4]



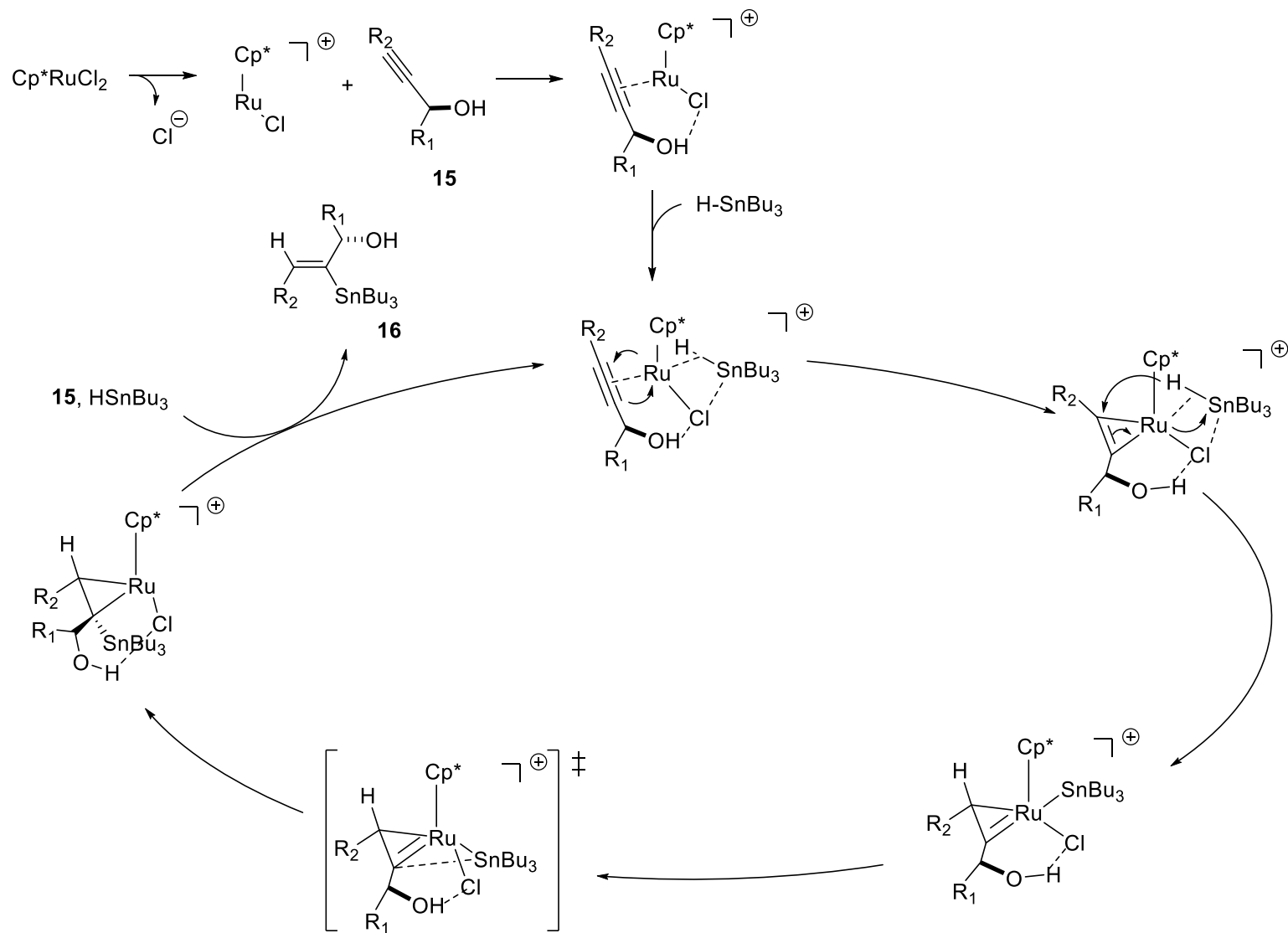


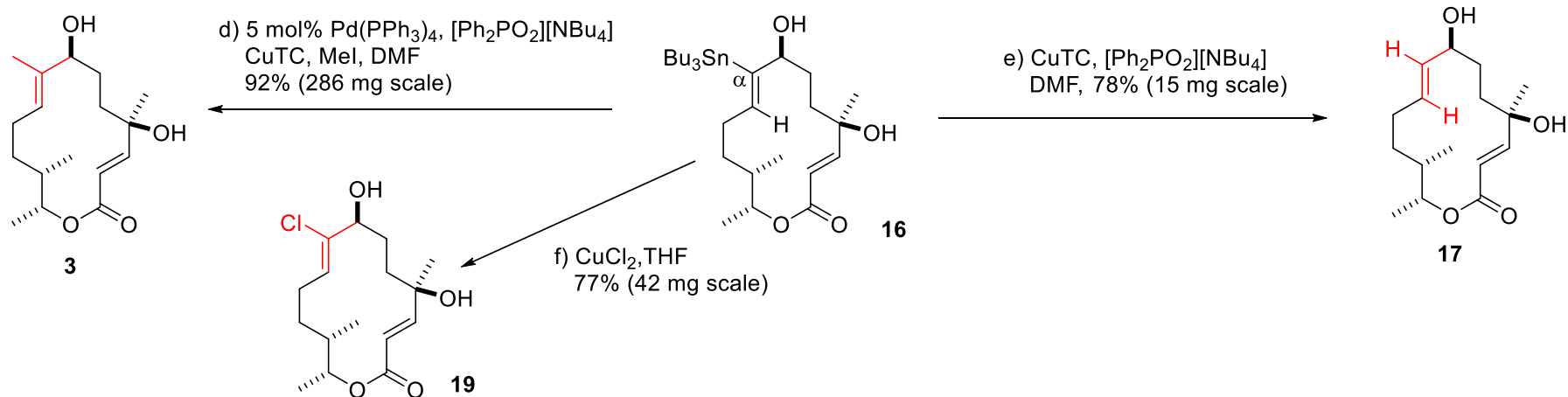
Transannular oxa-Michael reaction (**14** to **20**)



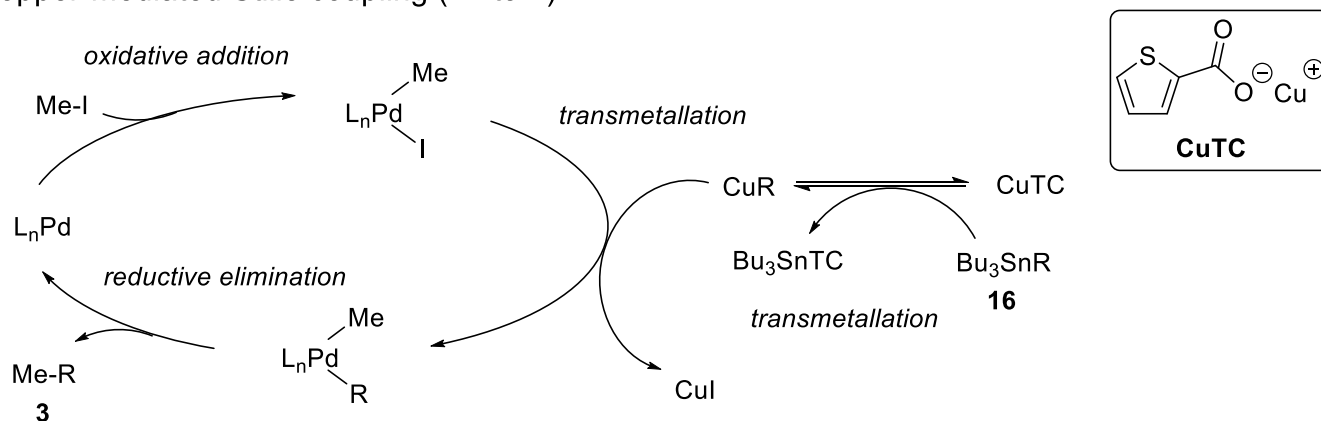
based on the crystal structure

Directed *trans*-hydrostannation (**15** to **16**)^[5]

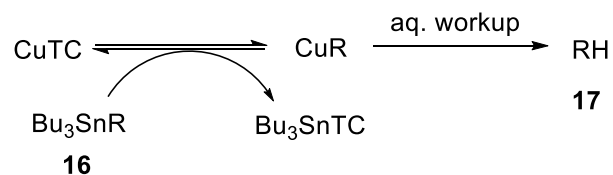




Copper-mediated Stille coupling (**16** to **3**)^[6]



16 to **17**



16 to **19**

