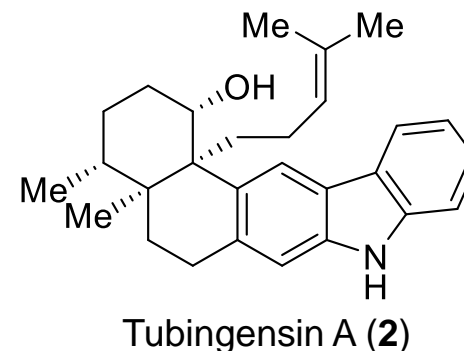
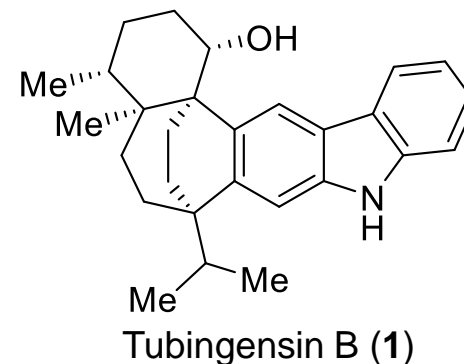


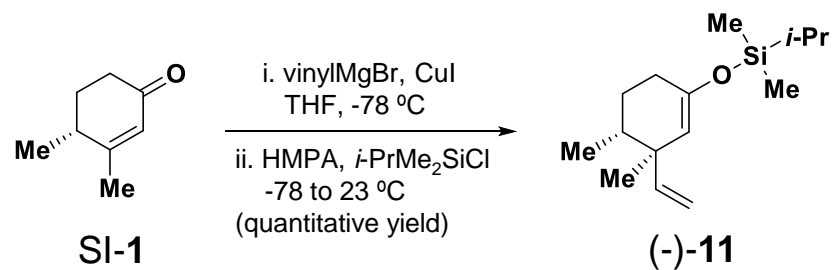
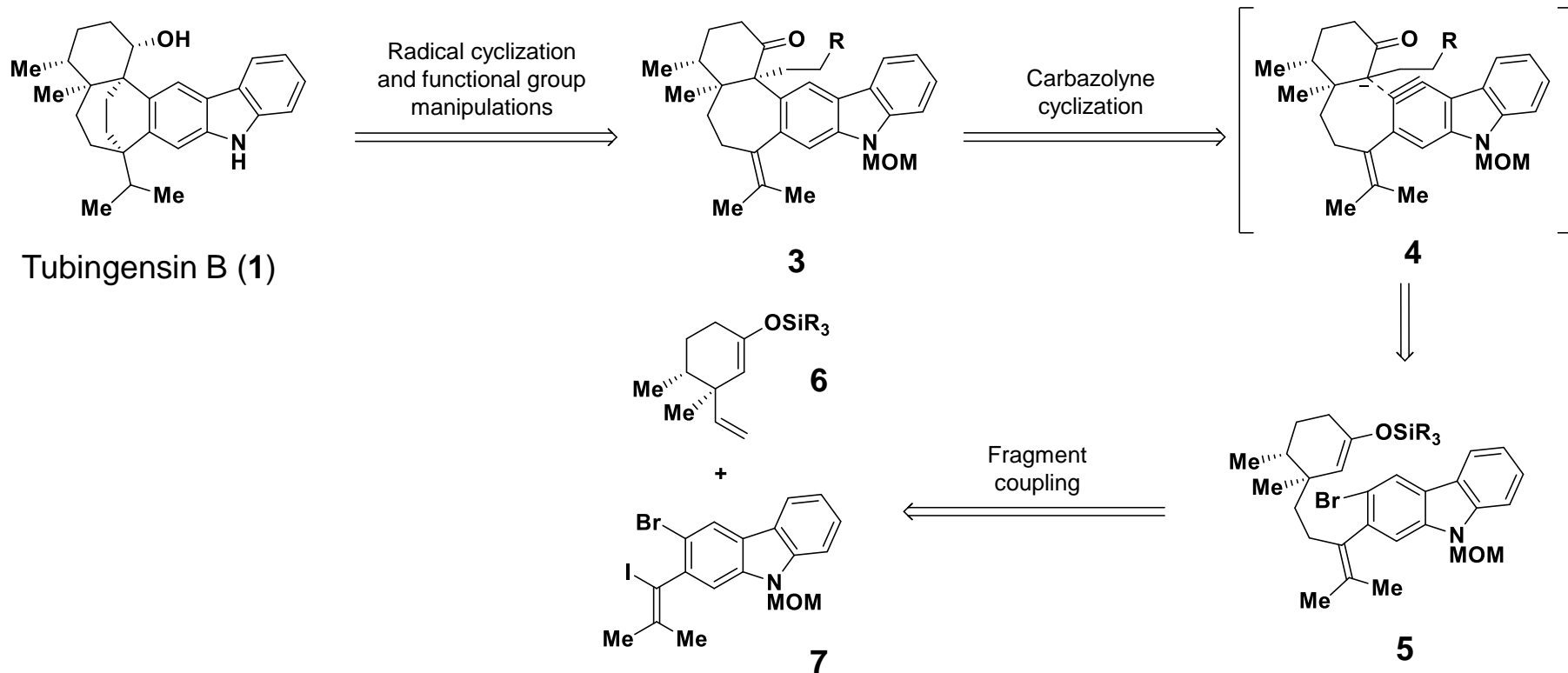
Total synthesis of (-)-tubingensin B enabled by the strategic use of an aryne cyclization

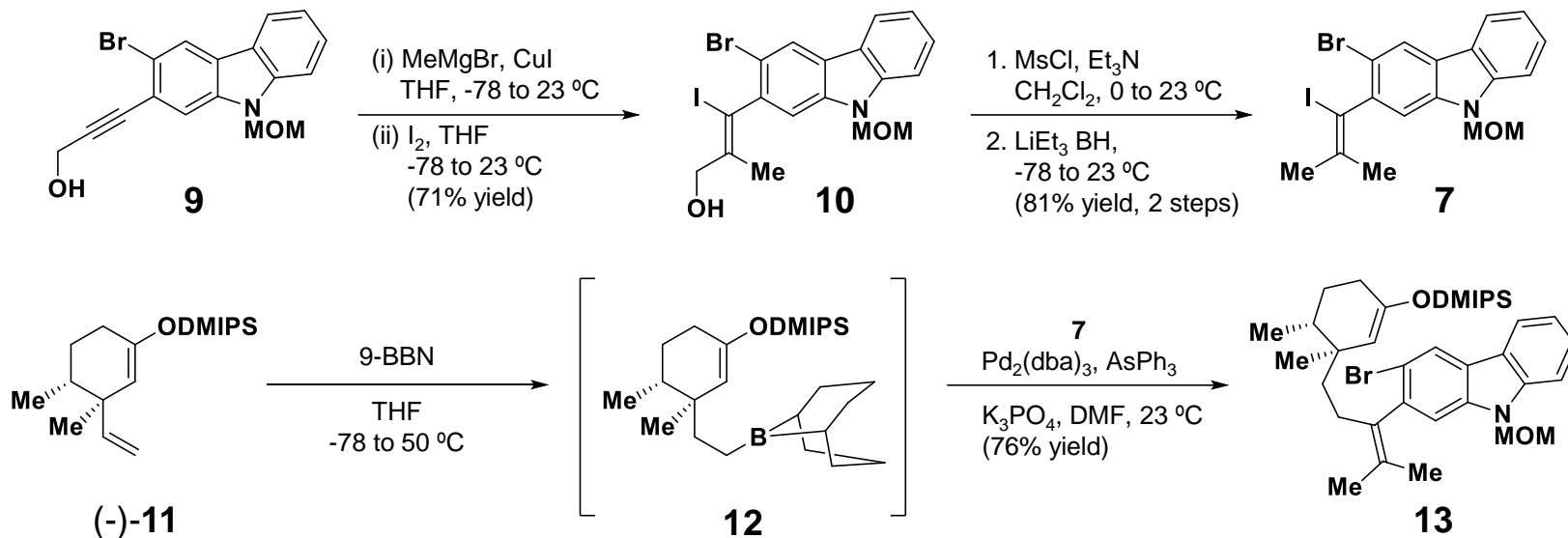
Michael A. Corsello, Junyong Kim, and Neil K. Garg
Nat. Chem. **2017**, 9, 944 - 949.

- An indole diterpenoid isolated from the fungus *Aspergillus tubingensis* in 1989.
- Exhibits activity against crop pests, cytotoxicity against cervical cancer cells, and *in vitro* antiviral activity against herpes simplex virus type 1 (HSV-1).
- The molecule contains a carbazole unit which at first seems deceptively simple, but is in the presence of two adjacent sp^2 - sp^3 C-C bond linkages.
- Bicyclo[3.2.2]nonane core fused to the carbazole, and a densely functionalized six-membered ring.
- The natural product possesses five stereogenic centers, four of which are contiguous, three are quaternary, and two vicinal quaternary.
- Garg group previously synthesized Tubingensin A, and adapted that procedure to synthesize Tubingensin B.
- Key reactions are a late-stage radical cyclization, as well as an carbazolyne (aryne) cyclization followed by a Rh-catalyzed fragmentation.

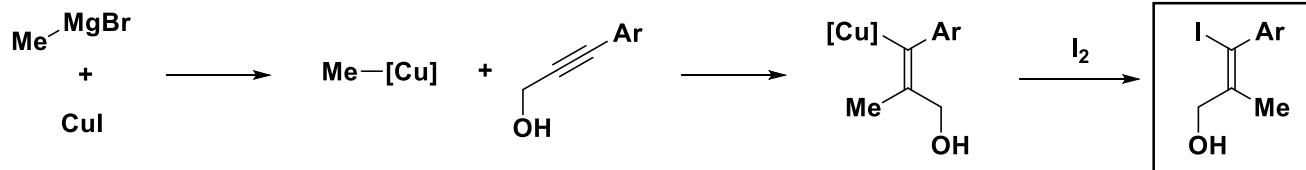


Retrosynthesis

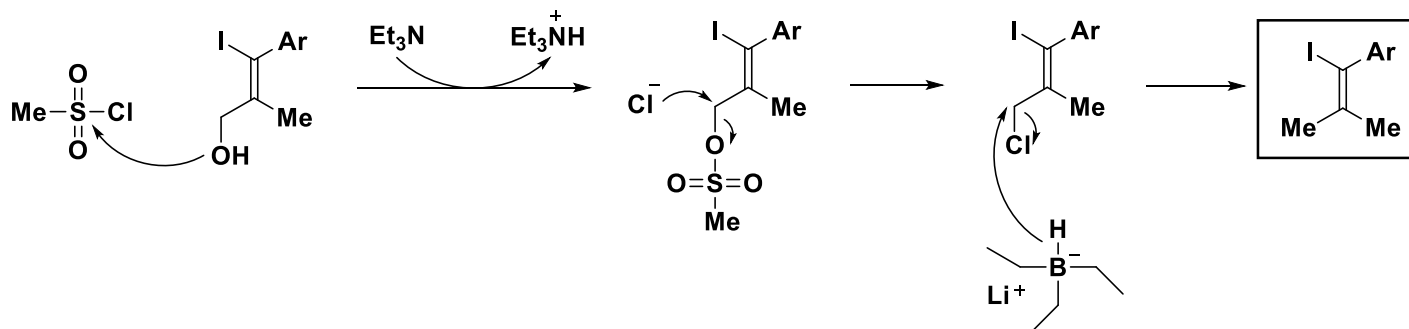


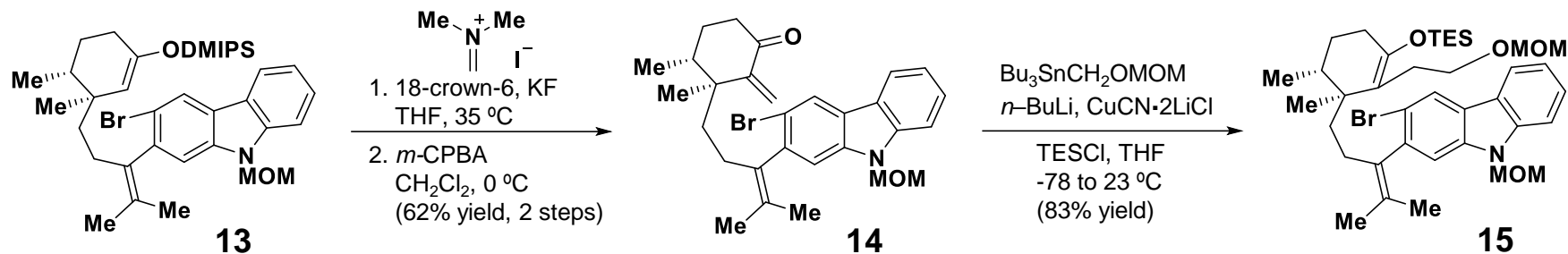


Carbometallation/Iodination

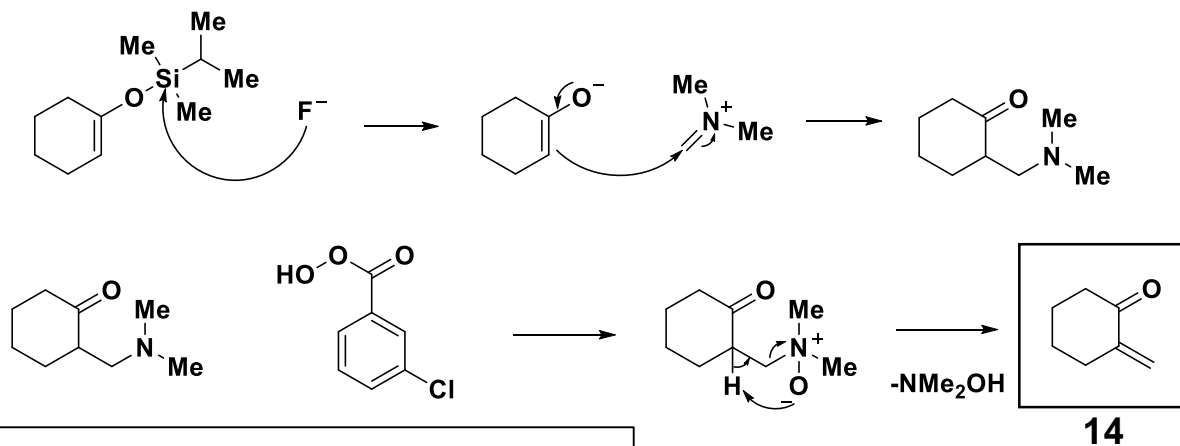


Two-step Deoxygenation protocol

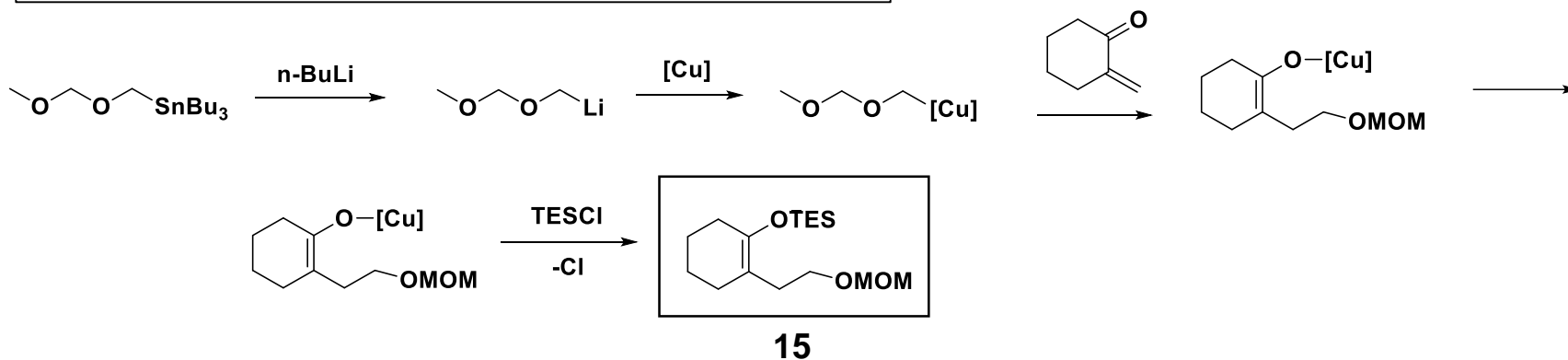


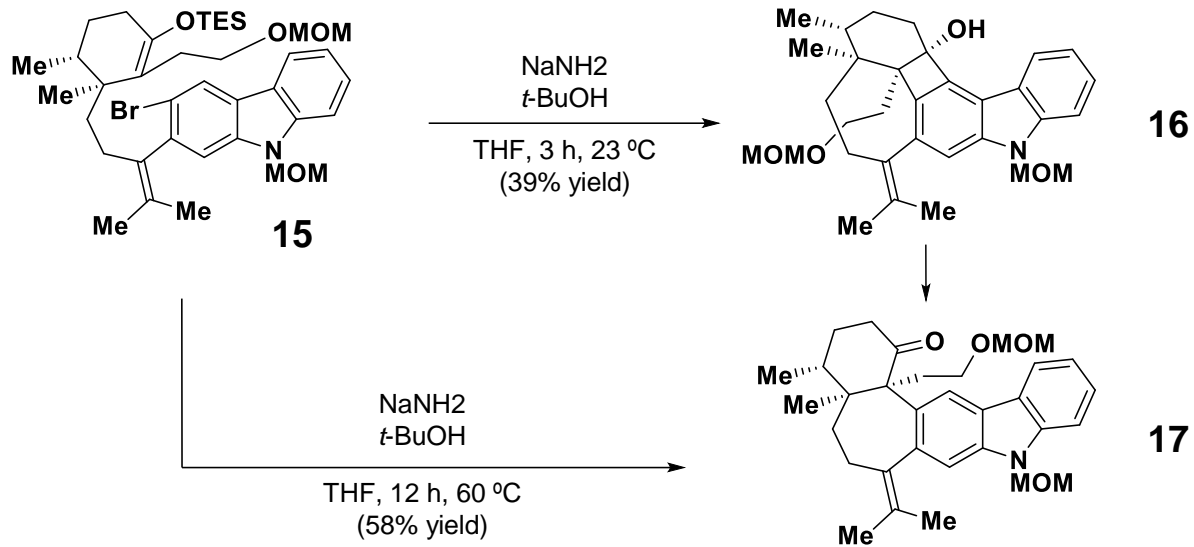


Eschenmoser methenylation

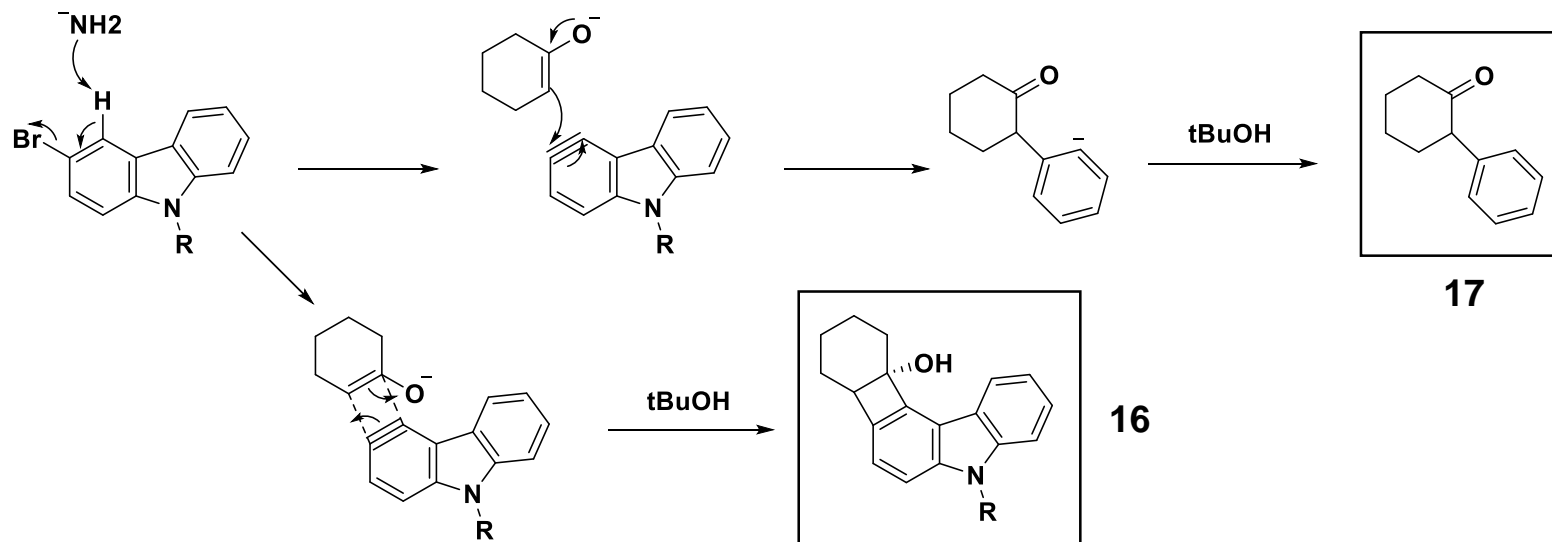


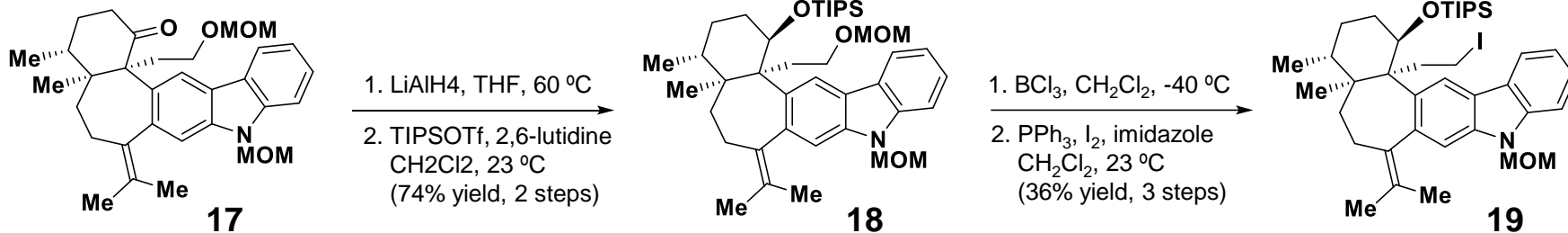
Conjugate addition with *in situ* prepared cuprate



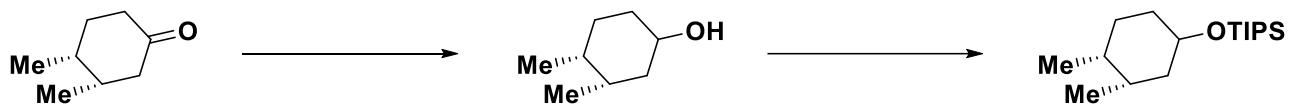


Carbazolyne (heteroaryne) cyclization

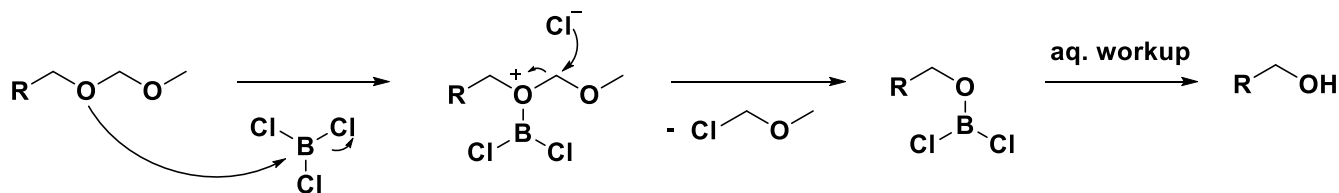




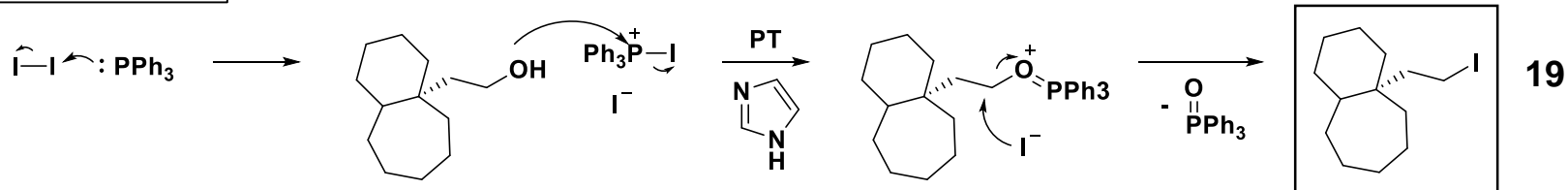
Reduction and silyl protection

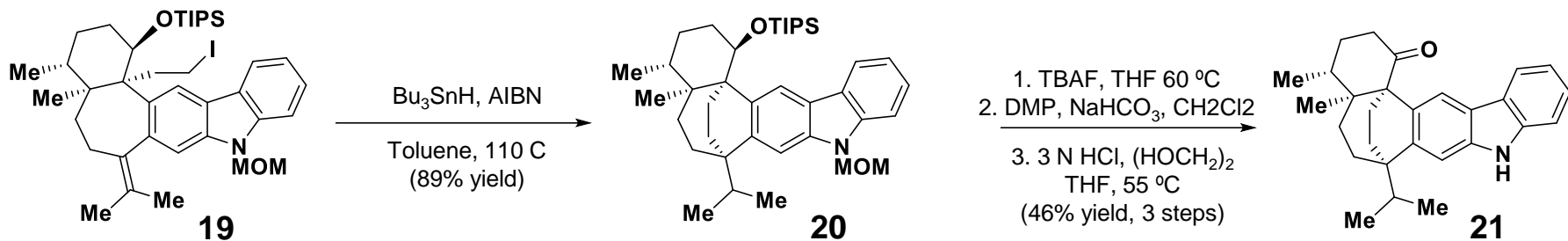


MOMO deprotection with BCl_3

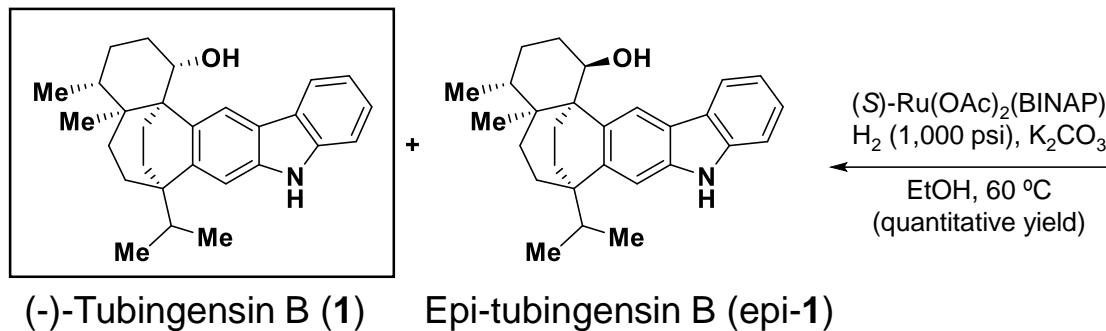


Appel Reaction

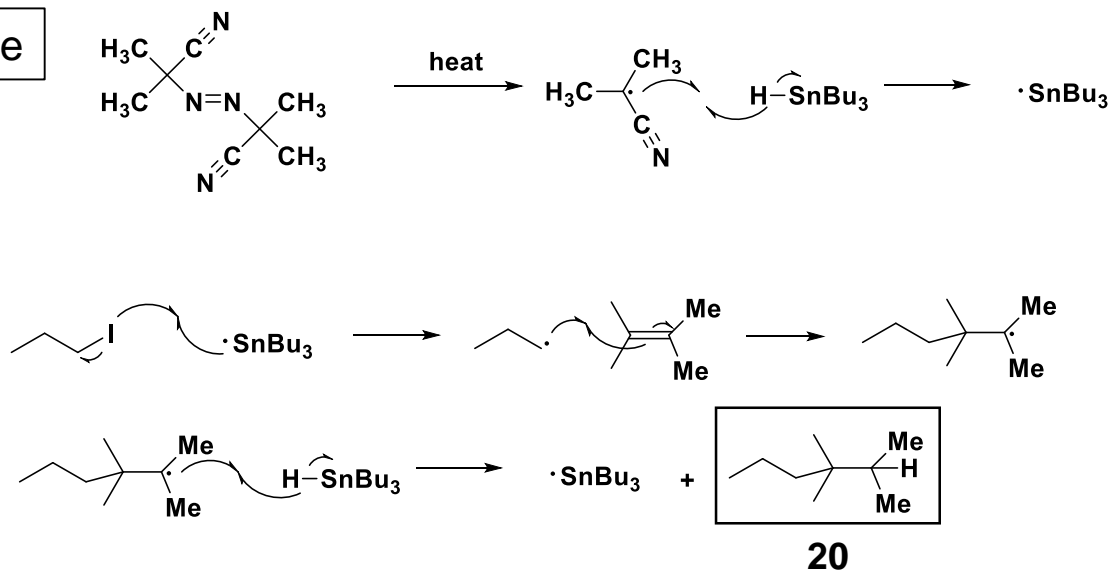




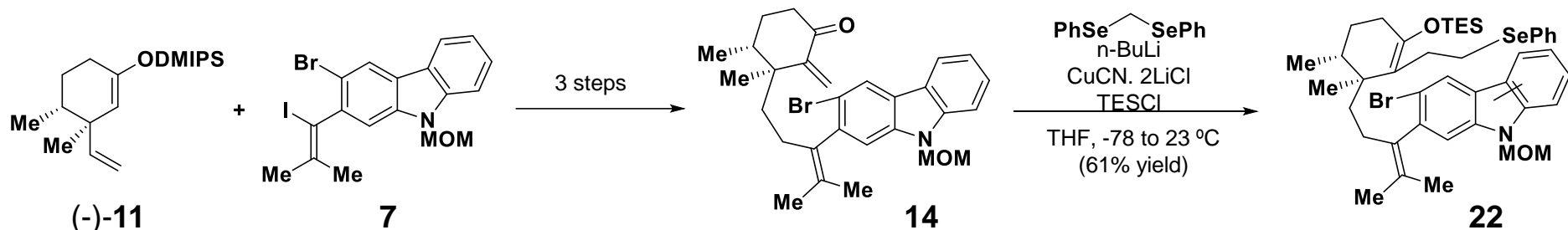
1 : 4



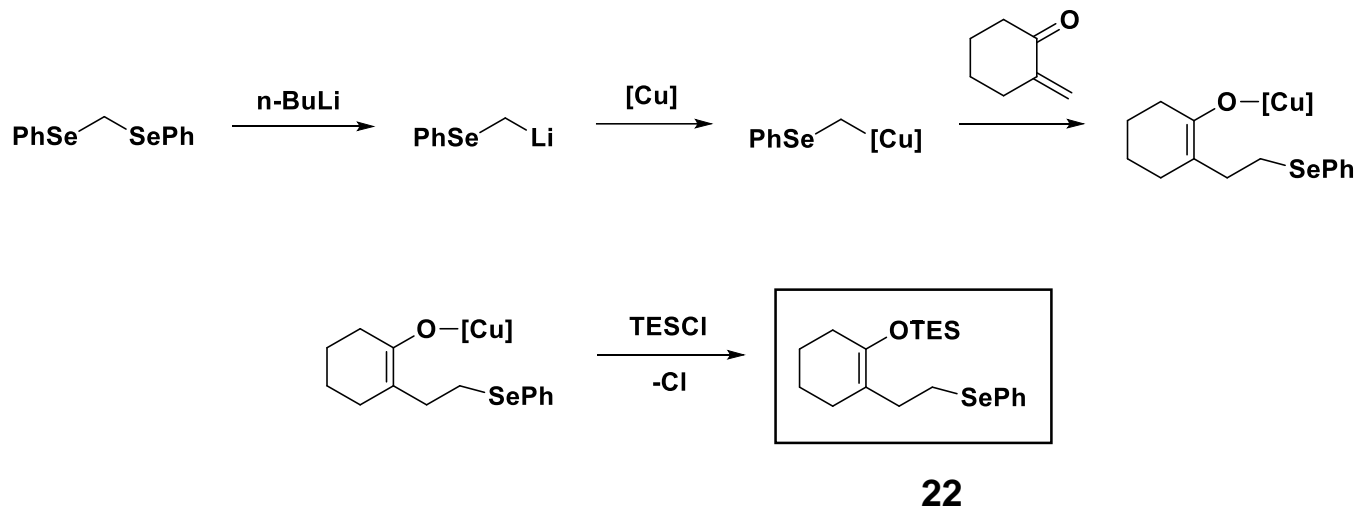
Radical cascade

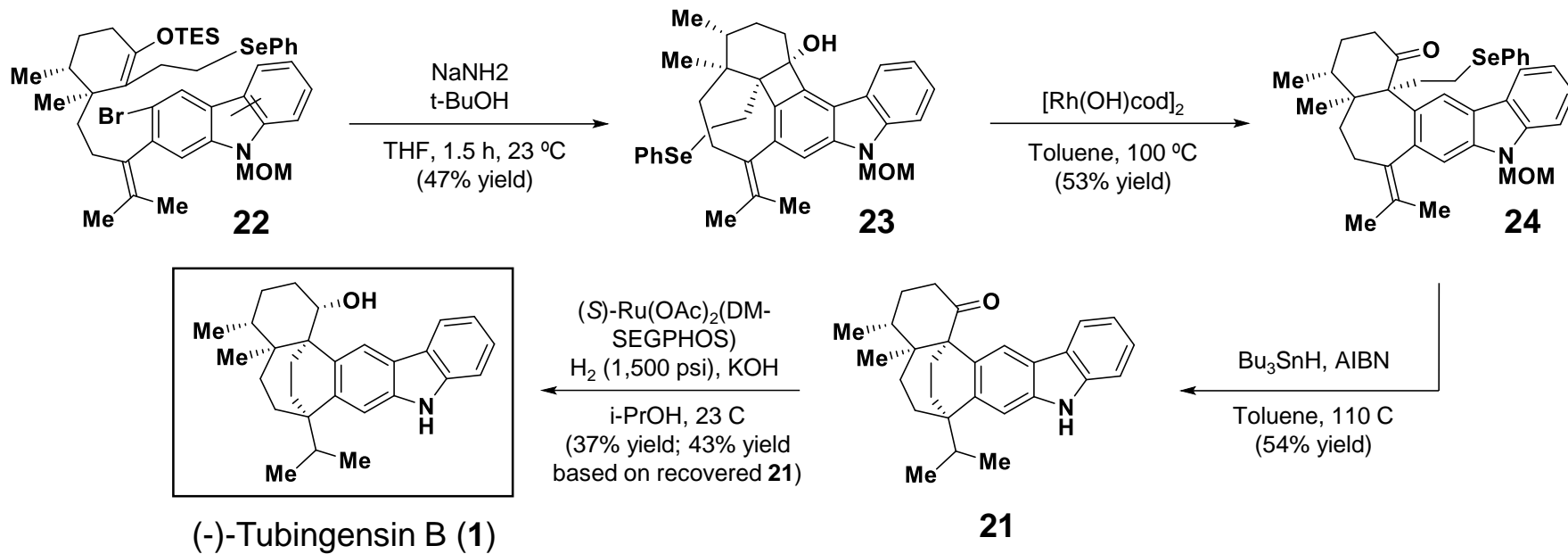


Alternative route in order to provide better product yield, utilizing phenyl-Selenium



Phenyl-Selenium addition and silyl trapping





Murakami's Rhodium-catalyzed ring opening

