

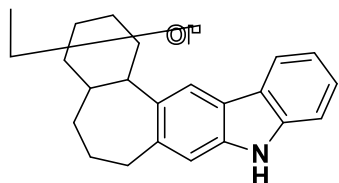
Total synthesis of (-)-tubingensin B enabled by the strategic use of an aryne cyclization

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*

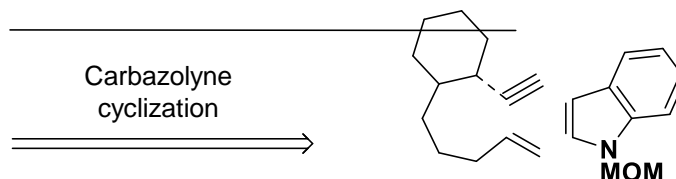
and *vitro* an

Retrosynthesis

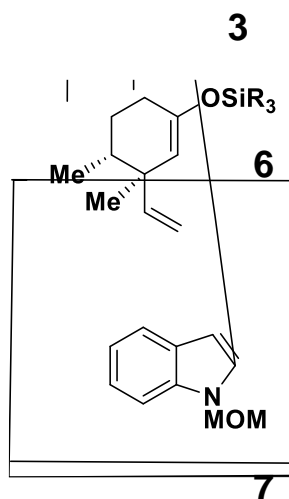


Radical cyclization
and functional group
manipulations

Tubingensin B (1)



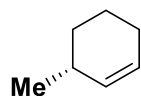
Carbazolyne
cyclization



Fragment
coupling

4

5



SI-1

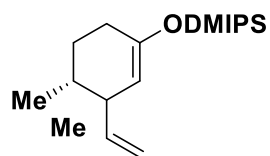
i. vinylMgBr, CuI
THF, -78 °C
ii. HMPA, *i*-PrMe₂SiCl
-78 to 23 °C
(quantitative yield)

(-)-11

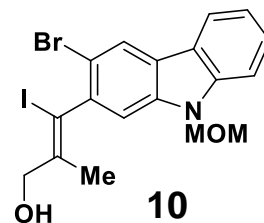
9

(i) MeMgBr, CuI
THF, -78 to 23 °C

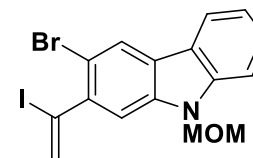
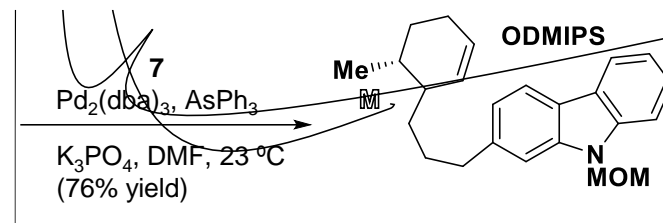
(ii) I₂, THF
-78 to 23 °C
(71% yield)

**(-)-11**

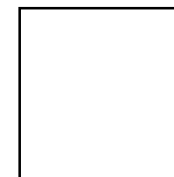
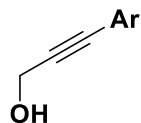
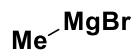
9-BBN
THF
-78 to 50 °C

**10**

1. MsCl, Et₃N
CH₂Cl₂, 0 to 23 °C
2. LiEt₃BH,
-78 to 23 °C
(81% yield, 2 steps)

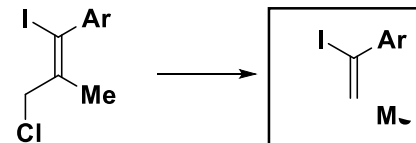
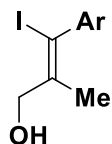
**7****13**

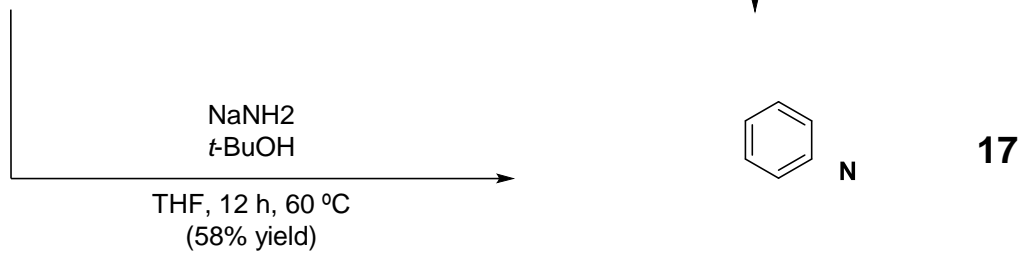
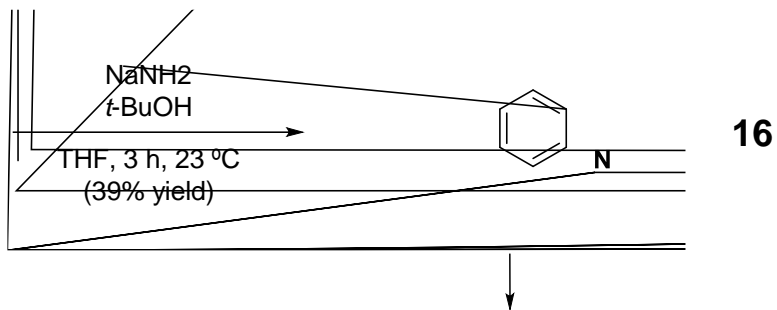
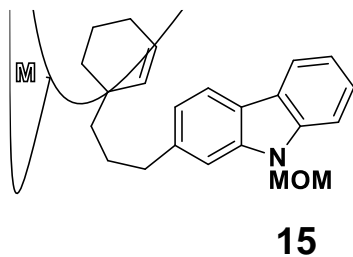
Carbometallation/Iodination



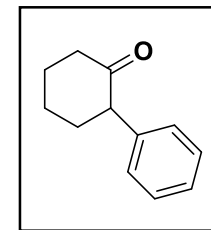
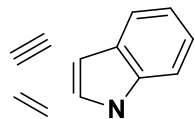
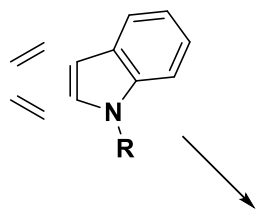
Two-step Deoxygenation protocol

Me

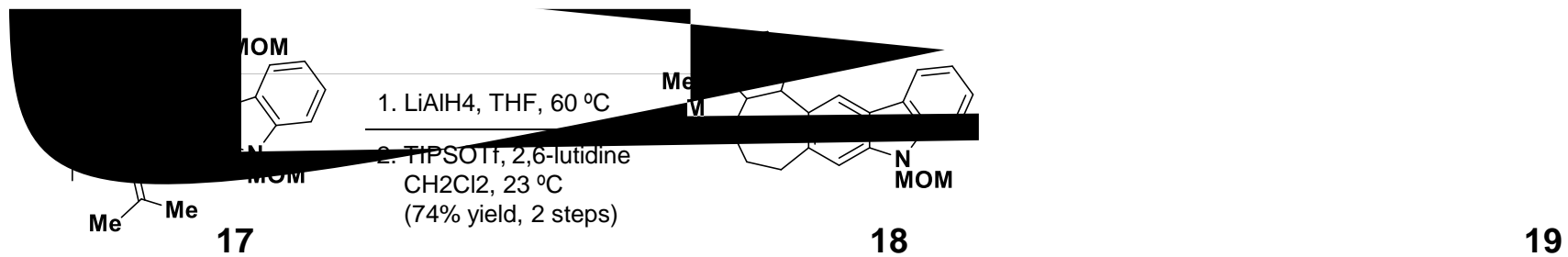




Carbazolyne (heteroaryne) cyclization

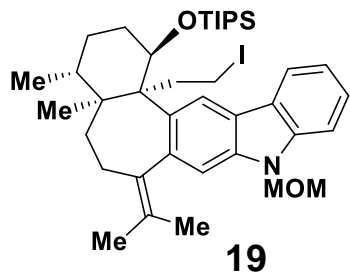


17



Reduction and silyl protection



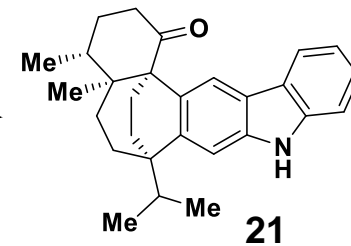


Bu₃SnH, AIBN

Toluene, 110 °C
(89% yield)

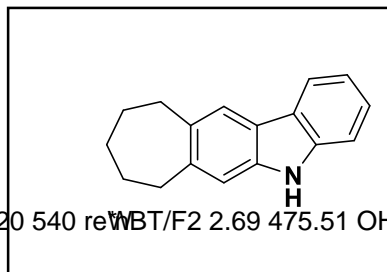
20

1. TBAF, THF 60 °C
2. DMP, NaHCO₃, CH₂Cl₂
3. 3 N HCl, (HOCH₂)₂
THF, 55 °C
(46% yield, 3 steps)



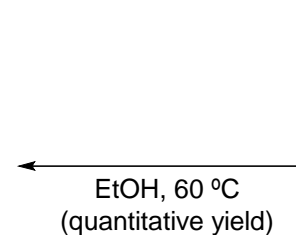
1 : 4

(qu27/P 4MCID 29>BDC 77.28 8220 540 reWB/F2 2.69 475.51 OH

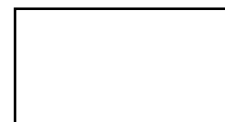
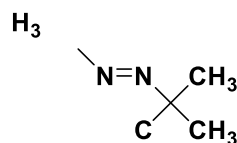


(-)-Tubingensin B (**1**)

Epi-tubingensin B (epi-**1**)

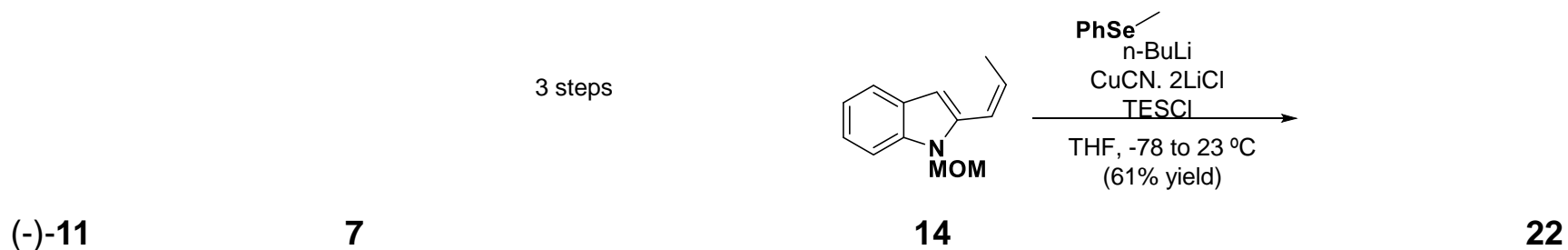


Radical cascade



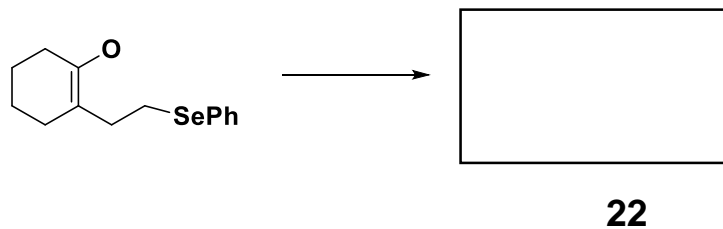
20

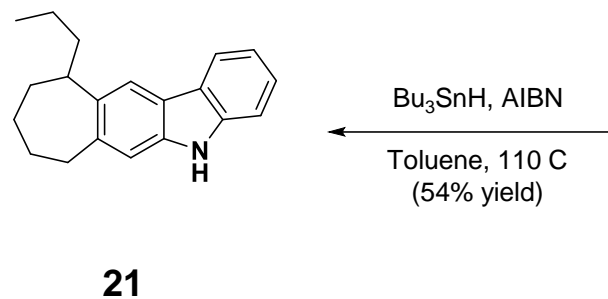
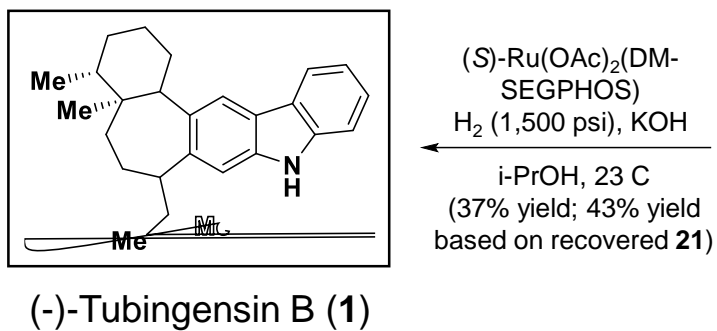
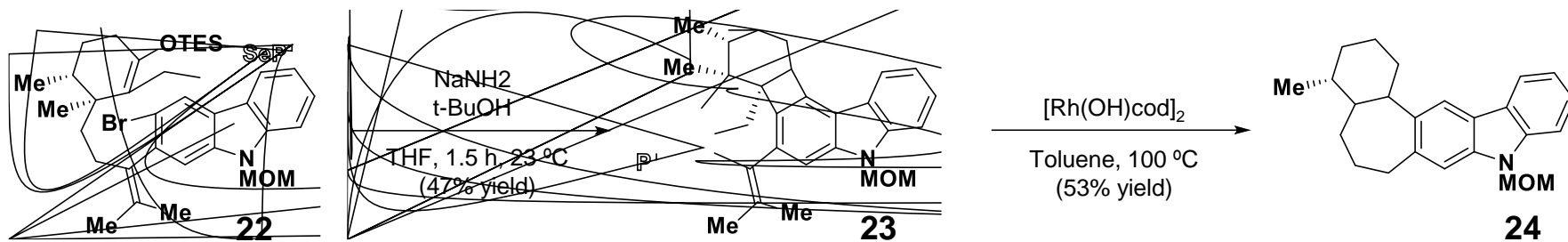
Alternative route in order to provide better product yield, utilizing phenyl-Selenium



Phenyl-Selenium addition and silyl trapping

PhSe-





Murakami's Rhodium-catalyzed ring opening

