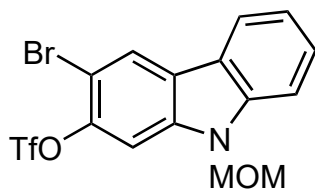


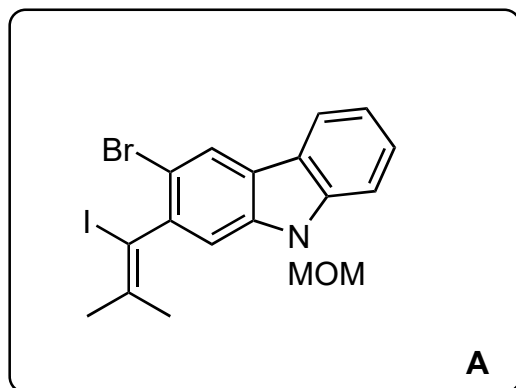
Total Synthesis of (-)-Tubingensin B Enabled by the Strategic Use of an Aryne Cyclization

Corseello, M. A.; Kim, J.; Garg, N. K.

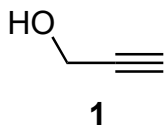
Nat. Chem. **2017**, *9*, 944-949



1-4



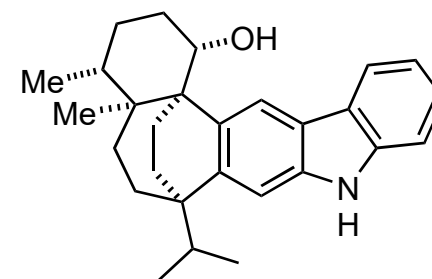
- 1) **1**, Pd(PPh₃)₄, NEt₃, CuI, DMF
- 2) MeMgBr, CuI, THF
then I₂, THF
- 3) MsCl, NEt₃
- 4) LiEt₃BH



Q. What is the name of the heterocyclic framework? How would you make the starting material?

- *Carbazole*
- *Bromination of commercially available hydroxycarbazole, Tt₂O protection of OH and then N-MOM protection*

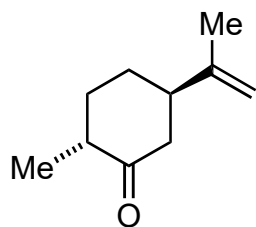
1) Please name of the reaction?
Sonogashira coupling



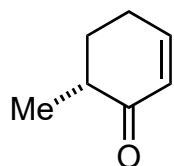
(-)-Tubingensin B

Key Features:

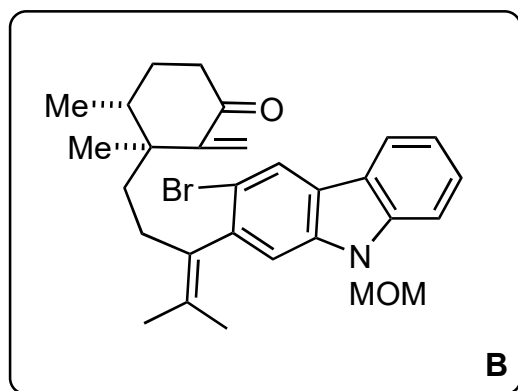
- Indole diterpenoid
- Isolated in 1989
- Cytotoxic against cervical cancer cells with an IC₅₀ of 4 mg/mL
- Antiviral activity against HSV-1 with an IC₅₀ of 9 mg/mL



5-6

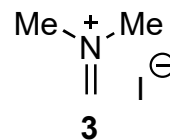
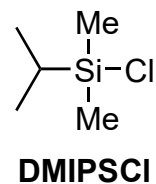
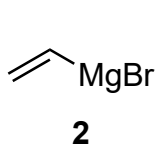


7-13

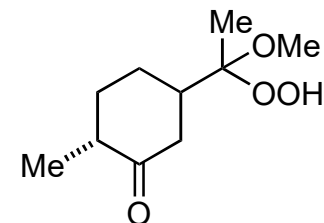


- 5) O_3 , MeOH
 6) $Cu(OAc)_2 \cdot H_2O$, $FeSO_4 \cdot 7H_2O$

- 7) MeLi•LiBr, Et_2O
 8) PCC, CH_2Cl_2
 9) **2**, CuI, THF
 then HMPA, DMIPSCI
 10) 9-BBN, THF
 11) **A**, $Pd_2(dba)_3$, $AsPh_3$, K_3PO_4 , DMF, 23 °C
 12) **3**, 18-Crown-6, KF, THF
 13) *m*-CPBA, CH_2Cl_2

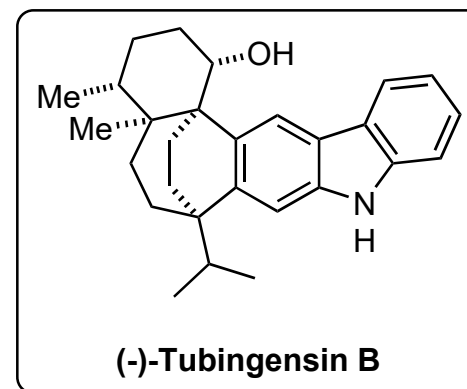


(5) *Hint: Ozonolysis with MeOH does not afford ketone/aldehyde/alcohol*



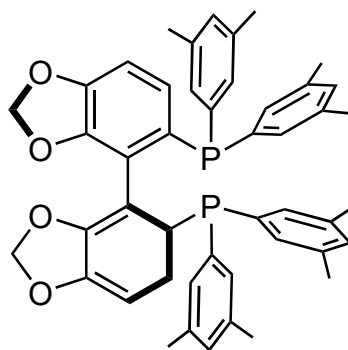
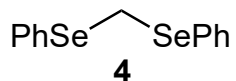
(6) Please propose a mechanism
See below
 8) Please name the reaction.
Babler-Dauben oxidation

11) Please name the reaction
Suzuki-Miyaura coupling
 12-13) Please name the reagent **3** and the reaction. Propose a mechanism.
Eschenmoser's reagent and Eschenmoser's methenylation





- 14) **4**, *n*-BuLi, CuCN•2LiCl, TESCI
- 15) NaNH₂, *t*-BuOH, **23 °C, 1.5 h**
- 16) [Rh(OH)(cod)]₂, toluene, 100 °C
- 17) Bu₃SnH, AIBN
- 18) 3 N HCl, (HOCH₂)₂
- 19) (*S*)-Ru(OAc)₂(DM-SEGPHOS)
H₂ (1500 psi), KOH, *i*-PrOH

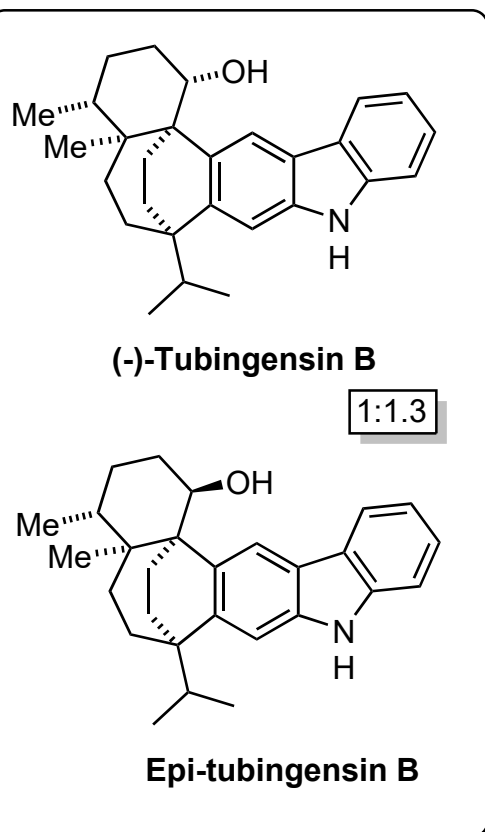
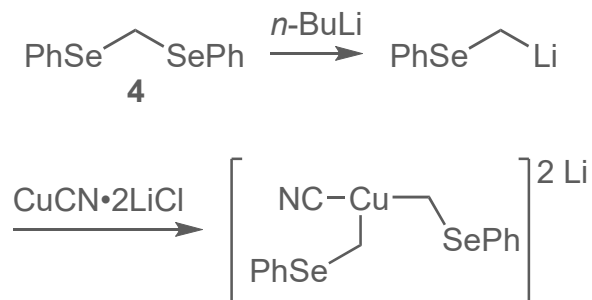


DM-SEGPHOS

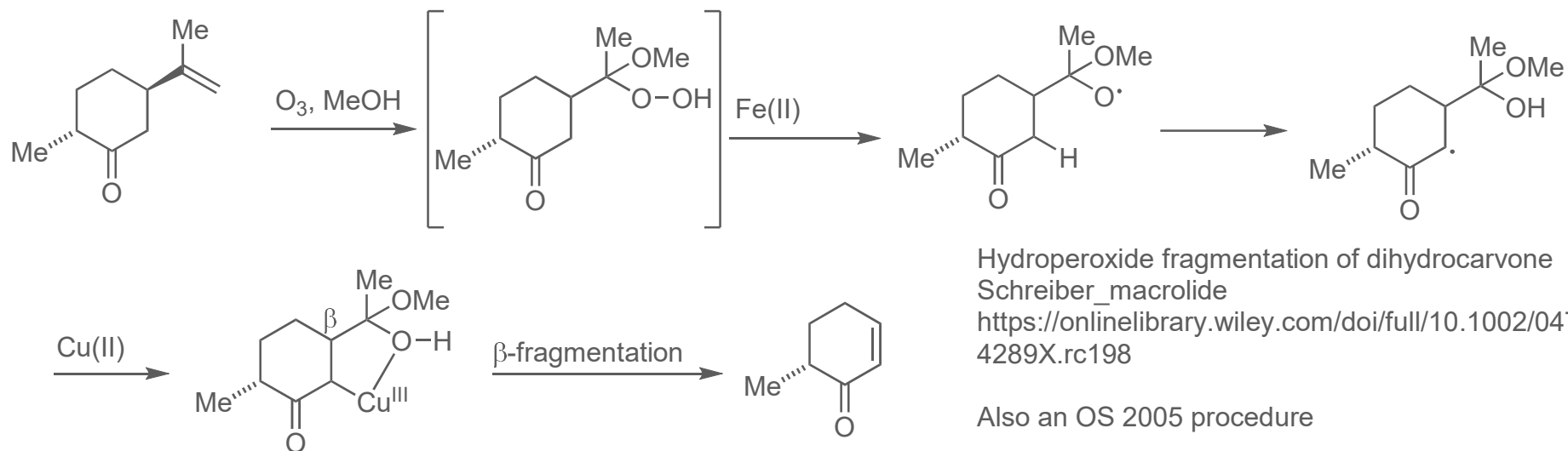
- 14) *Hint: It is not a lithiation
It is a lithium-selenide exchange*
- 15) Please provide a mechanism. Is this step concerted/stepwise according to Woodward-Hoffmann rule?
- 16) *Hint: C-C activation.*

- 19) Please name the hydrogenation condition.
Noyori's hydrogenation condition

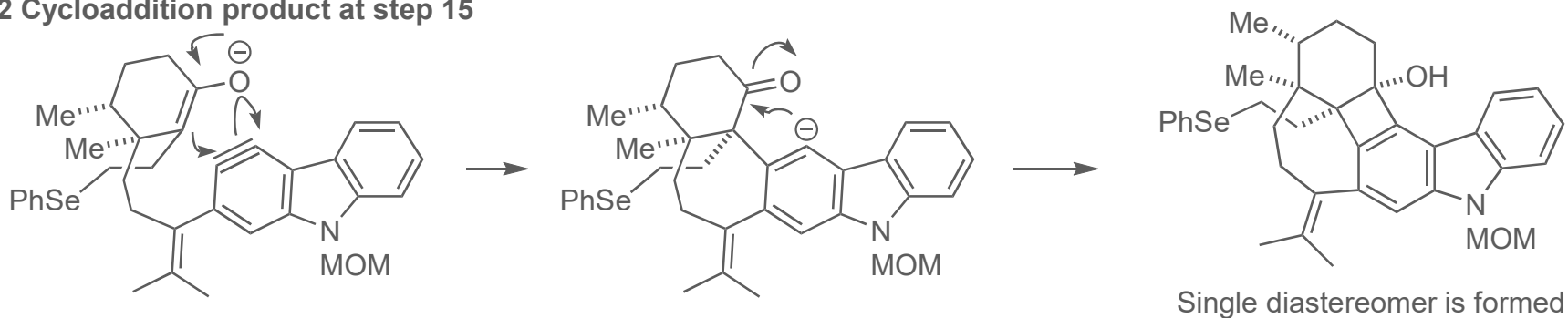
Step 14 mechanism:



Mechanism of Step 5 and 6:



2+2 Cycloaddition product at step 15



Rh-catalyzed C-C cleavage

