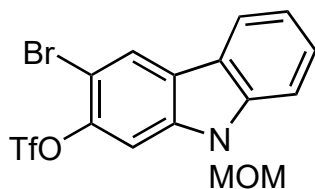


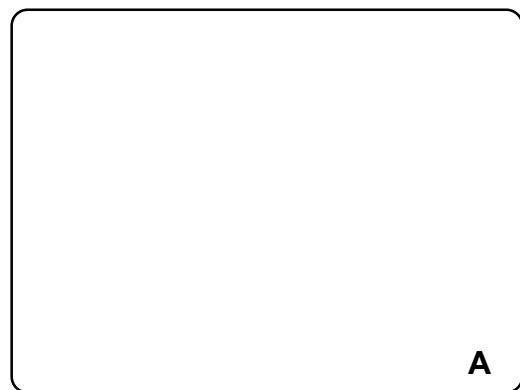
## Total Synthesis of (-)-Tubingensin B Enabled by the Strategic Use of an Aryne Cyclization

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

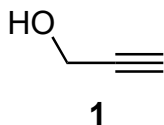
*Nat. Chem.* **2017**, *9*, 944-949



1-4



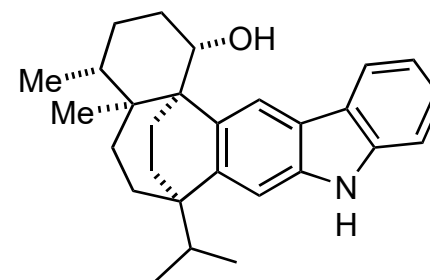
- 1) **1**, Pd(PPh<sub>3</sub>)<sub>4</sub>, NEt<sub>3</sub>, CuI, DMF
- 2) MeMgBr, CuI, THF  
*then* I<sub>2</sub>, THF
- 3) MsCl, NEt<sub>3</sub>
- 4) LiEt<sub>3</sub>BH



**1**

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

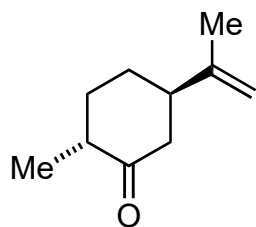
1) Please name the reaction?



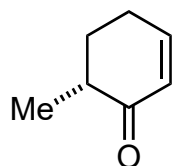
**(-)-Tubingensin B**

Key Features:

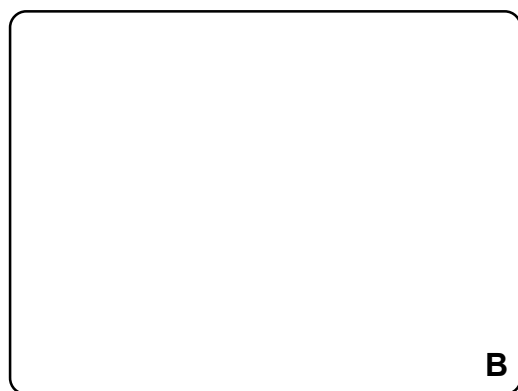
- Indole diterpenoid
- Isolated in 1989
- Cytotoxic against cervical cancer cells with an IC<sub>50</sub> of 4 mg/mL
- Antiviral activity against HSV-1 with an IC<sub>50</sub> of 9 mg/mL



5-6

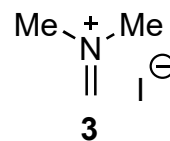
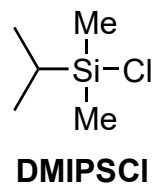
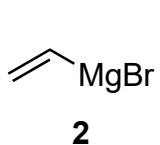


7-13



- 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,  $CH_2Cl_2$



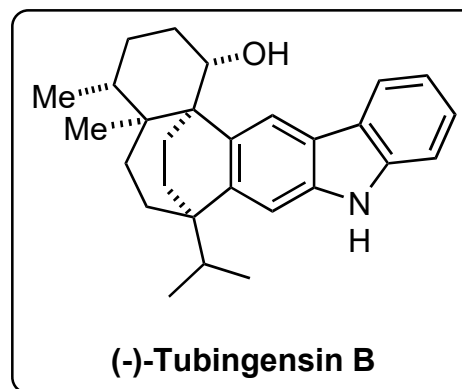
(5) *Hint: Ozonolysis with MeOH does not afford ketone/aldehyde/alcohol*

(6) Please propose a mechanism

8) Please name the reaction

11) Please name the reaction

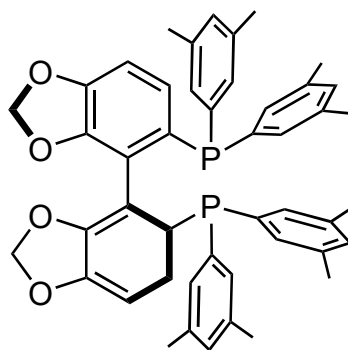
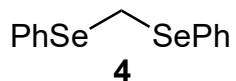
12-13) Please name the reagent **3** and the reaction. Propose a mechanism.



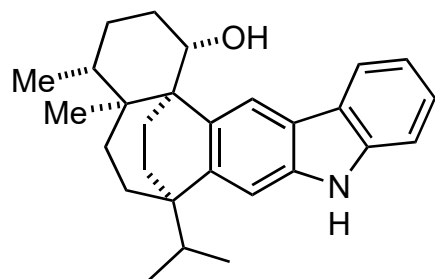


- 14) **4**, *n*-BuLi, CuCN•2LiCl, TESCl
- 15) NaNH<sub>2</sub>, *t*-BuOH, **23 °C, 1.5 h**
- 16) [Rh(OH)(cod)]<sub>2</sub>, toluene, 100 °C
- 17) Bu<sub>3</sub>SnH, AIBN
- 18) 3 N HCl, (HOCH<sub>2</sub>)<sub>2</sub>
- 19) (*S*)-Ru(OAc)<sub>2</sub>(DM-SEGPHOS)  
H<sub>2</sub> (1500 psi), KOH, *i*-PrOH

- 14) *Hint: It is not a lithiation*
- 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.

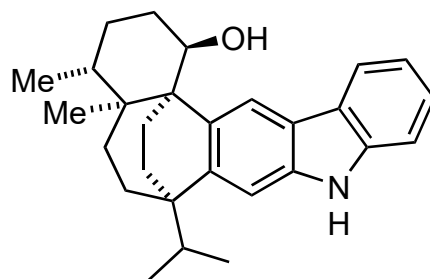


**DM-SEGPHOS**



**(-)-Tubingensin B**

1:1.3



**Epi-tubingensin B**