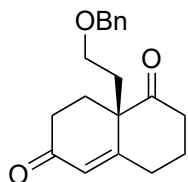
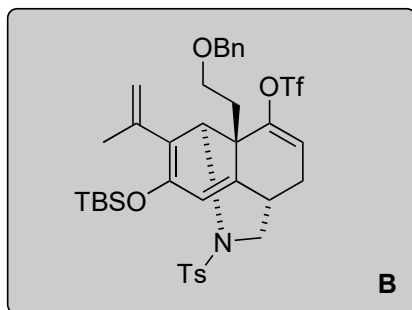


Total Synthesis of Dapholdamine B and Dapholdamine B Lactone

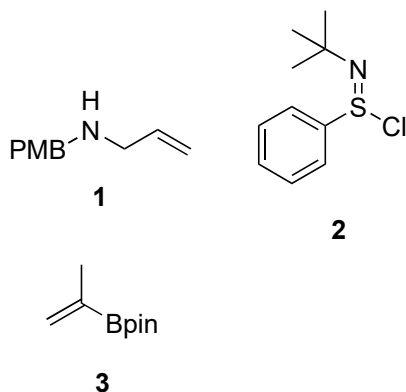
L.-D. Guo, J. Hou, W. Tu, Y. Zhang, Y. Zhang, L. Chen, J. Xu, *J. Am. Chem. Soc.* **2019** *141*, 11613–11720.



1 - 9



- 1) $\text{CH}(\text{OMe})_3$, PTSA then **1**, HCHO
- 2) $\text{Pd}(\text{PPh}_3)_4$, 1,3-dimethylbarbituric acid, $\text{Pd}(\text{PPh}_3)_4$, then NaHCO_3 , TsCl
- 3) ZnMe_2 , LiBr, $\text{Ni}(\text{acac})_2$
- 4) LHMDs, -78°C , then **2**
- 5) H_2O_2 , NaOH
- 6) LiBr, CH_3CN , MW, 120°C
- 7) XPhos Pd G2, **3**, K_3PO_4
- 8) CAN
- 9) KHMDS, TBSCl, -78°C then KHMDS, PhNTf_2 , 0°C



- 1) Name the reaction.

vinyllogous Mannich reaction

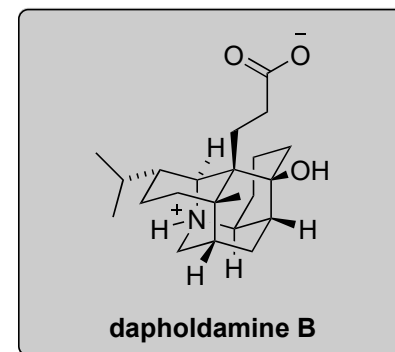
- 1) *Hint: start with forming a dienol.*

- 4) Draw a mechanism for the dehydrogenation.

See below

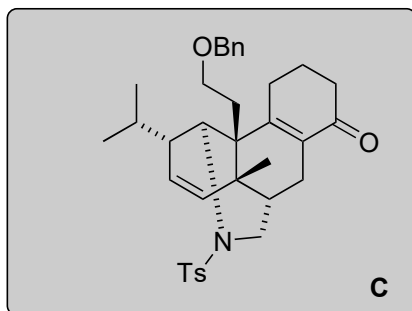
- 6) *Hint: a vinyl bromide is formed.*

- 9) *Hint: cyclization. Two heteroatoms are triflated.*

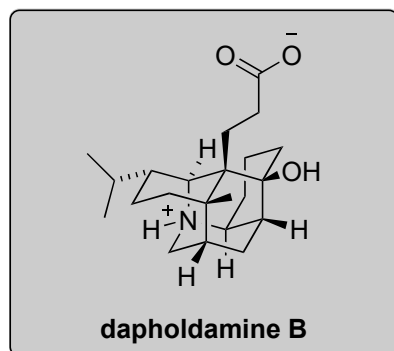


B

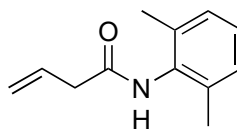
10 – 14



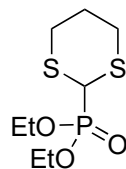
15 - 20



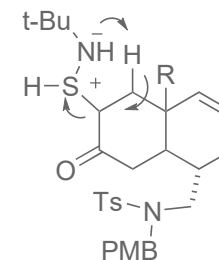
- 10) Crabtree's catalyst, H₂, then TBAF, HOAc
- 11) NaBH₄
- 12) SOCl₂, pyridine
- 13) **4**, 9-BBN then Pd₂(dba)₃•CHCl₃, AsPh₃, K₃PO₄
- 14) Tf₂O, 2-F-Pyr. then 2 N HCl



- 15) Pd/C, H₂ (80 bar)
- 16) TEMPO, PIDA then NaClO₂, NaH₂PO₄, then 2 N HCl
- 17) BH₃•THF then H₂O₂, NaOH aq.
- 18) Na-Naph, -78°C
- 19) PPh₃, CBr₄, DMAP, TEA
- 20) NaH, **5** then 2 N HCl then NaOH aq.



Proposed key intermediate of Step 4 mechanism:



14) *Hint: cyclization. Start with creating an activated amine. The product is an α,β -unsaturated ketone.*

15) *Hint: 1 deprotection and 2 hydrogenations. The remaining π bond is critical for step 16.*

16) *Hint: cyclization. Start with a selective oxidation.*

17) *Hint: the lactone is also reduced to the corresponding alcohol.*

18) *Hint: deprotection.*