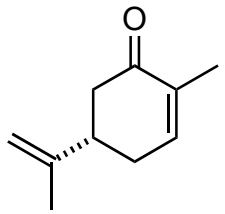
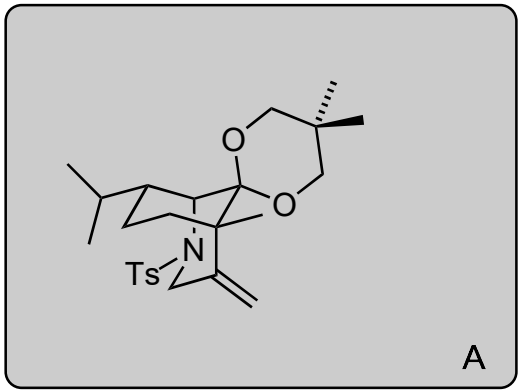
Total Synthesis of (of (−)-Daphnezomines A and B

Xu, G.; Wu, J.; Li, L.; Lu, Y.; Li, C.*

J. Am. Chem. Soc. 2020, *142*, 15240-15245.

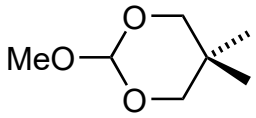


1-5

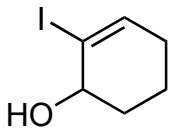


6-10

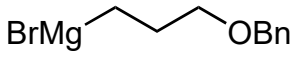
1) H_2, Rh/Alumina
then TIPSOTf, Et_3N
2) Se, Chloramine-T
3) allyl bromide, NaH
4) $Pd(OAc)_2$, O_2
5) **1**, *p*-TsOH



1



2



3

6) 9-BBN, *then* **2**, $Pd(dppf)Cl_2$
aq. NaOH, $AsPh_3$
7) TFA, *then* aq. NaOH
8) $LaCl_3$•2LiCl, **3**
9) Na, naphthalene
then Boc_2O, Et_3N, *then* DMP
10) Burgess reagent

What is the name of the starting material?
(S)-(+)-carvone

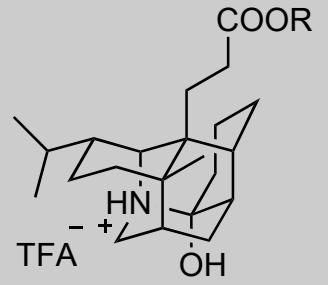
Step 2: Name the reagent and propose a mechanhism
- Sharpless aminating reagent

Step 4: Propose a mechanism
hint: another ring forms
- an oxo-π-allylpalladium species is formed as intermediate, which inserts into the alkene followed by a β-H elimination. Good way construct a,b-unsaturated cyclic ketones

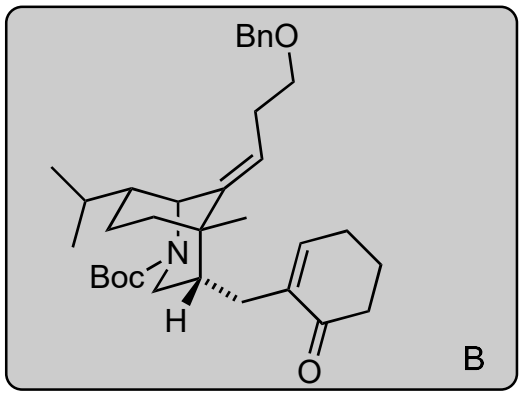
Step 6: Name of the reaction?
- B-alkyl Suzuki-Miyaura coupling

Step 8: Name of this salt?
- Knochel salt

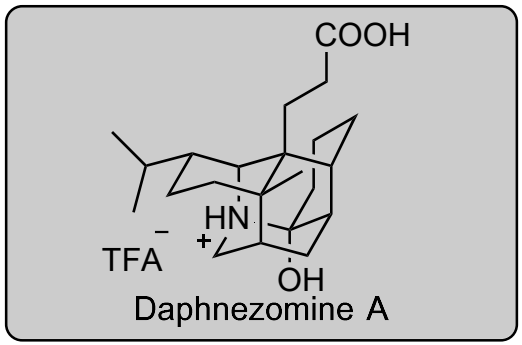
Step 10: Structure of Burgess reagent?



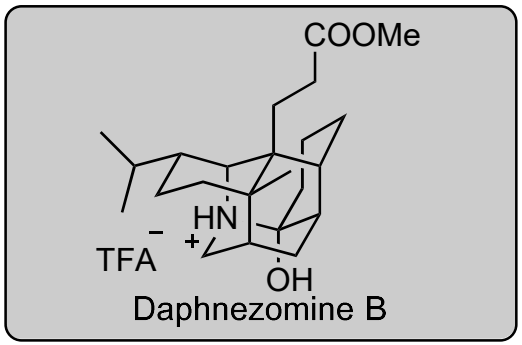
Daphnezomine A (R = H)
Daphnezomine B (R = Me)

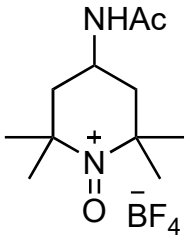


11-14

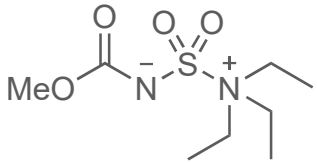


$TMSCHN_2$





4



Burgess reagent

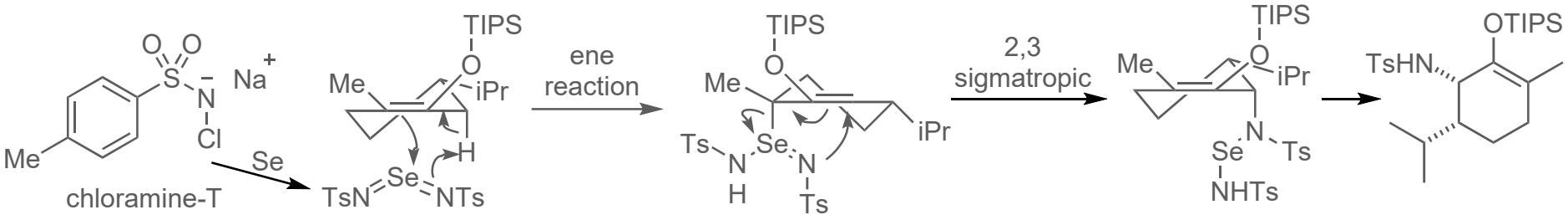
11) **4**
12) $TMSCHN_2$, *then* TFA
13) $Fe(acac)_3$, $Ph(i\text{-}PrO)SiH_2$
14) TFA

Step 11: Name of reagent **4**?
- Bobbitt's salt

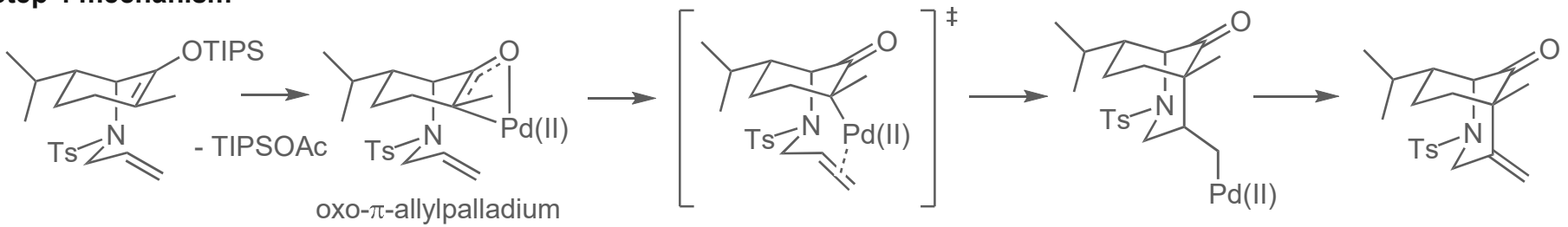
Step 13: How would you classify this reaction according to Baldwin's rule? What could be a potential competing side reaction?
Provide a mechanism
- 6-endo-trig cyclization
- enone reduction by resulting Fe-H
- HAT-mediated radical conjugate addition followed 1,5-proton transfer from ammonium ion. Presence of ammonium ion is necessary.

Step 14: *hint - epimerization*

Step 2 Mechanism:
Sharpless aminating reagentg (modified by Magnus)

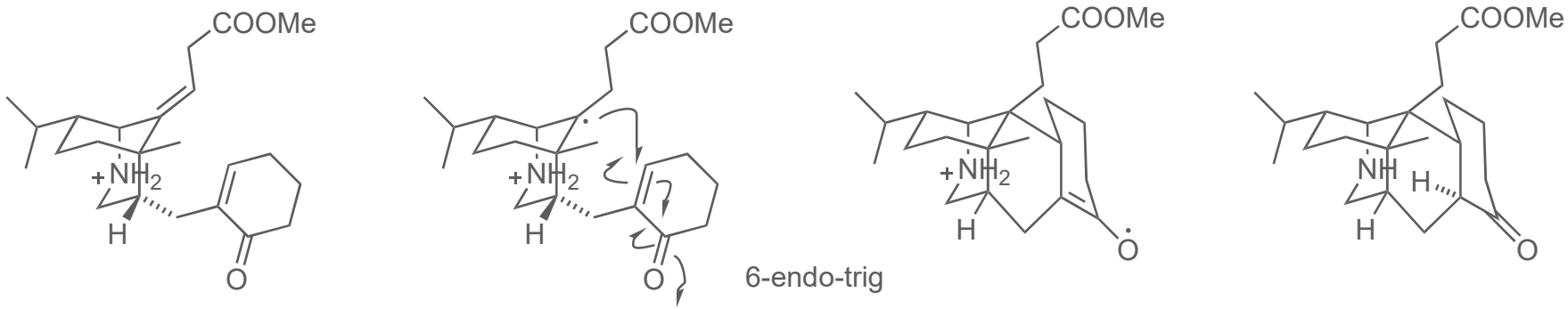


Step 4 mechanism



Step 13 mechanism

$(acac)_2Fe-H$



Competing pathway could be Fe-H insertion into enone; desired position is sterically crowded and electronically richer than enone