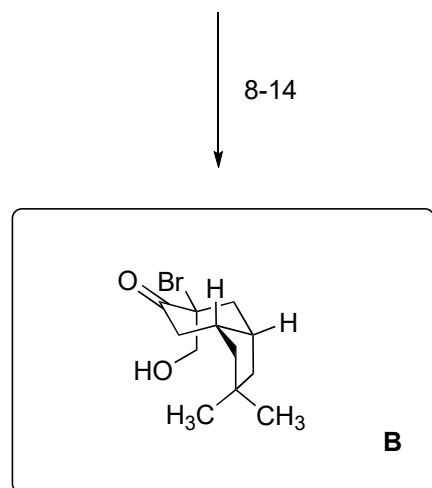
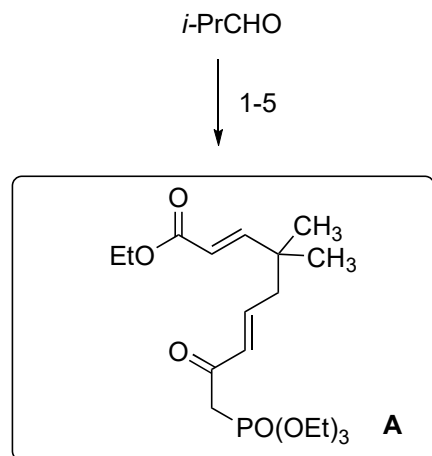
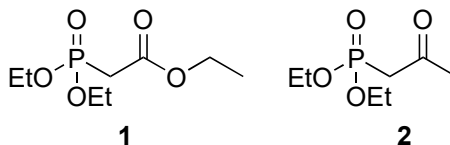


A Carbene Catalysis Strategy for the Synthesis Protoilludane Natural Products: Total Synthesis of Armillaridin and Isovelleral

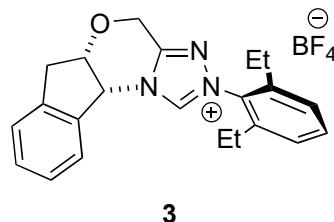
M. T. Hovey, D. T. Cohen, D. M. Walden, P. H.-Y. Cheong, K. A. Scheidt,
Angew. Chem. Int. Ed. **2017**, *56*, 9864-9867.



- 1) morpholine, *p*-TsOH
- 2) BrCH₂CHCH₂
- 3) NaH, **1**
- 4) O₃; DMS
- 5) *i*-Pr₂NEt, LiCl, **2**
- 6) CuO, I₂
- 7) P(OEt)₃



- 8) DIBAL-H
- 9) MnO₂
- 10) 5 mol% **3**, *i*-Pr₂NEt
- 11) LiAl(O*t*-Bu)₃H
- 12) H₂, Pd/C
- 13) (CH₂O)_n, Ba(OH)₂
- 14) TsNBr₂, MeCN/H₂O



Which variant of the HWE reaction represents step 5?

What is the role of LiCl?

Masamune–Roush-modified HWE reaction

LiCl coordinates to the carbonyl groups of the

ketophosphonate and makes the CH₂-group more acidic → weaker bases can be employed; ideal for base sensitive substrates

Step 7: Please name the reaction

Michaelis–Arbuzov reaction

Step 10: Please come up with a mechanism

see below

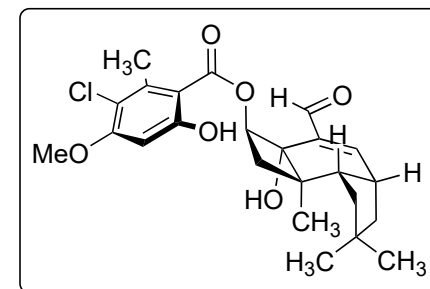
Step 11: How do you prepare the reagent? What is the difference to LAH?



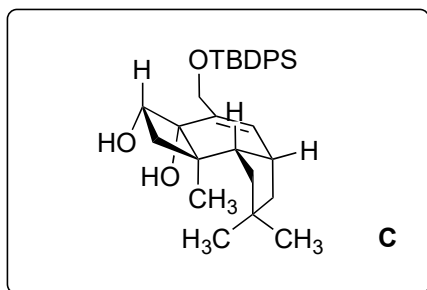
Compared to LAH this reagent is less reactive, sterically more hindered and stoichiometry can be better controlled.

Relative reactivity can be ranked as follows:

(*J. Am. Chem. Soc.* **1964**, *86*, 1079)

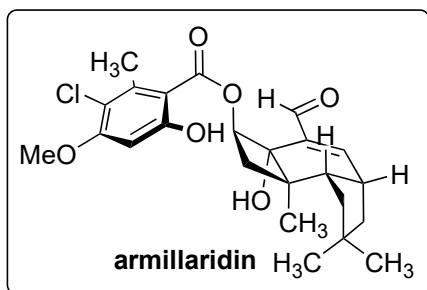


15-22

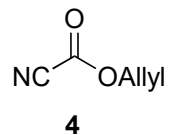


23-27 **isovelleral**

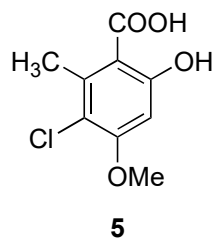
28-30



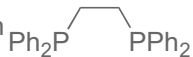
- 15) TBDPSCI, imH
- 16) Li₂CO₃, LiBr, DMF
- 17) LDA, **4**
- 18) K₂CO₃, MeI
- 19) Pd₂(dba)₃, DPPE
- 20) OsO₄, NMO
- 21) NaIO₄
- 22) VCl₃, Zn, HMPA



- | | |
|--------------------------------|-------------------------------------|
| 23) DMS, NCS, NEt ₃ | 28) DIAD, PPh ₃ , ArCOOH |
| 24) NaHB(OAc) ₃ | 29) TBAF |
| 25) EDCI, DMAP, 5 | 30) 4-NHAc-TEMPO, |
| 26) TBAF | <i>p</i> -TsOH |
| 27) 4-NHAc-TEMPO, | |
| <i>p</i> -TsOH | |

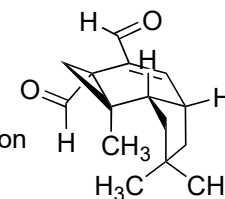
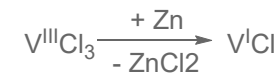


Step 19: Please name the reaction. What is DPPE? What could be the drawbacks of direct allylation?

Tsuji–Trost–Stoltz decarboxylative allylation
 DPPE = 1,2-Bis(diphenylphosphino)ethane 
 Direct allylation might be plagued by O-alkylation (in this case also oxidation to the phenol).

Step 22: Please name the reaction. What is the active Vanadium species?

Pinacol reaction



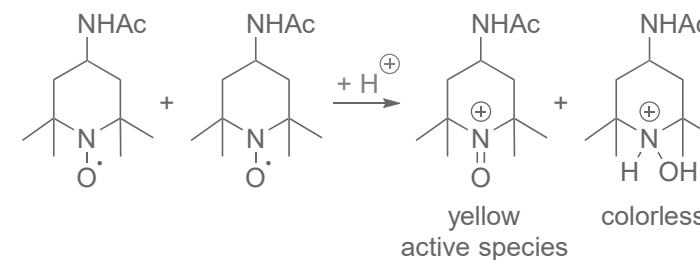
Step 23 and 28: Please name the reaction

23: Corey–Kim oxidation

28: Pinacol rearrangement

Step 27 and 30: What is the active species in this reaction? What is the advantage of 4-NHAc-TEMPO over TEMPO?

isovelleral



The reaction is colorimetric (yellow to colorless) and the hydroxyl ammonium salt is insoluble in CH₂Cl₂ and can be easily removed by filtration.

Step 10 mechanism

