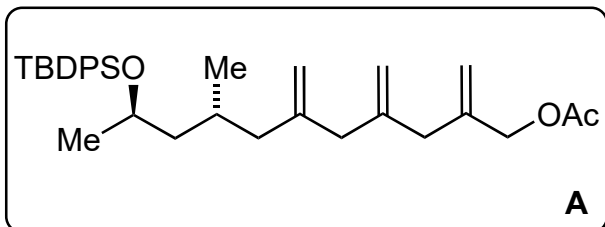


Total Synthesis of Limaol

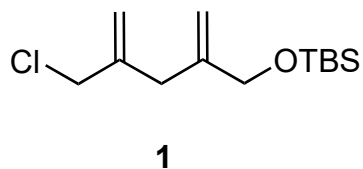
S. N. Hess, X. Mo, C. Wirtz, and A. Fürstner
J. Am. Chem. Soc. **2021**, *143*, 6, 2464–2469.



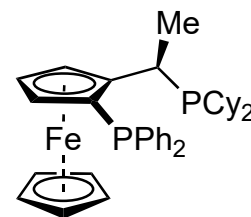
1-11



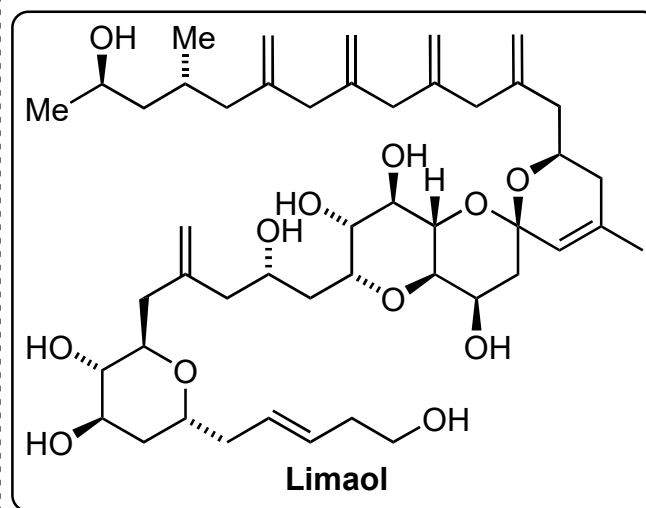
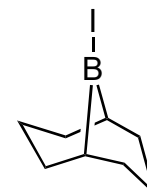
- 1) $\text{H}_2\text{C}=\text{CHMgBr}$, CuI
- 2) TBDPSCl , imidazole
- 3) Grubbs II, $\text{H}_2\text{C}=\text{CHCO}_2\text{Me}$
- 4) TMS-SEt , AlCl_3
- 5) MeMgBr , $\text{CuBr}\cdot\text{SMe}_2$,
(*S,R*)-Josiphos (2%)
- 6) Et_3SiH , Pd/C
- 7) Ohira-Bestmann reagent, K_2CO_3 ,
 MeOH
- 8) 9-I-9-BBN, *then* AcOH
- 9) Zn , LiCl , *then* **1**, $\text{Pd}(\text{PPh}_3)_4$
- 10) TBAF
- 11) Ac_2O , pyridine, DMAP

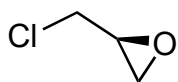


5) Structure of (*S,R*)-Josiphos?

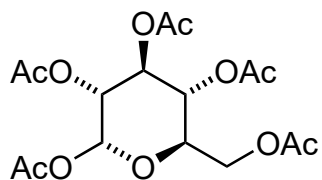
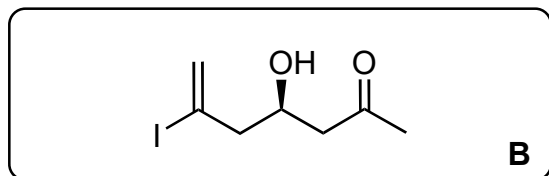


8) Structure of 9-I-9-BBN?



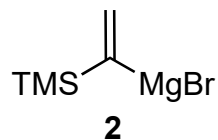


12-15



16-27

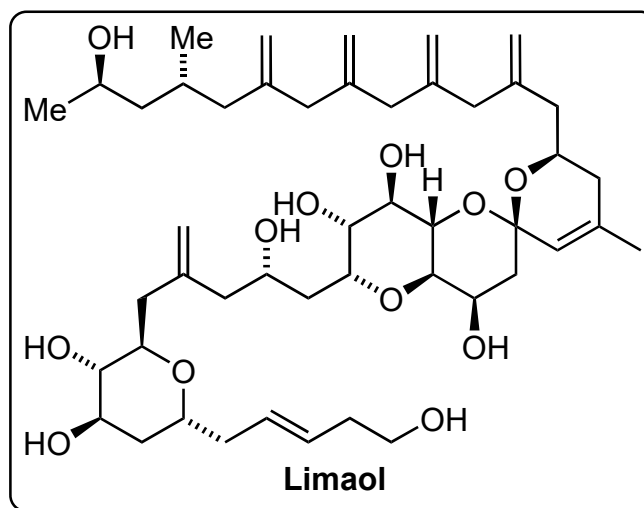
- 12) **2**, CuCN
- 13) NaOH
- 14) ICl, *then* TBAF
- 15) ethyl vinyl ether, *t*-BuLi, BF₃•OEt₂, *then* aq HCl

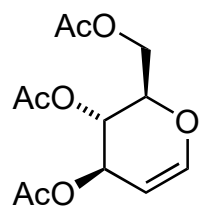
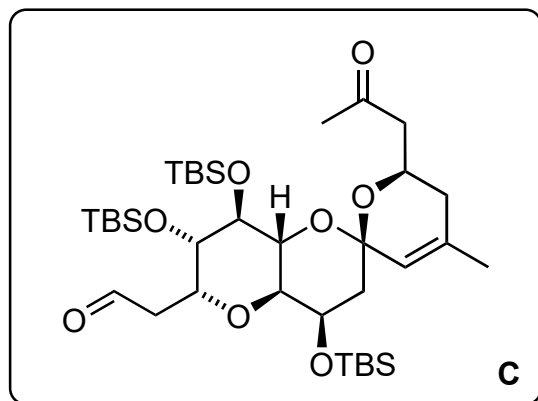


- 16) allyltrimethylsilane, BF₃•OEt₂
- 17) NaOMe
- 18) MeOC₆H₄CH(OMe)₂, *p*-TsOH
- 19) TBSOTf (2.6 equiv), 2,6-lutidine
- 20) DIBAL
- 21) (COCl)₂, DMSO, Et₃N
- 22) **3**, **4** (cat.)
- 23) TBSOTf, 2,6-lutidine
- 24) DDQ
- 25) **B**, Pd₂(dba)₃, PPh₃, Cul, HN(*i*-Pr)₂
- 26) **5** (cat), PPTS
- 27) OsO₄, NaIO₄

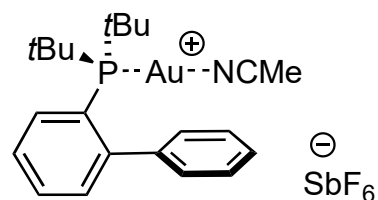
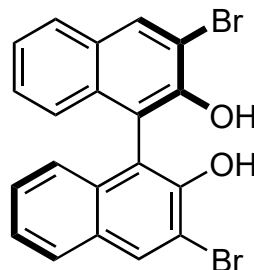
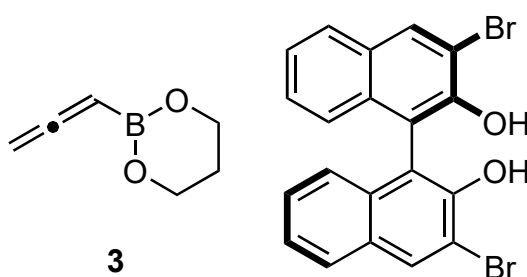
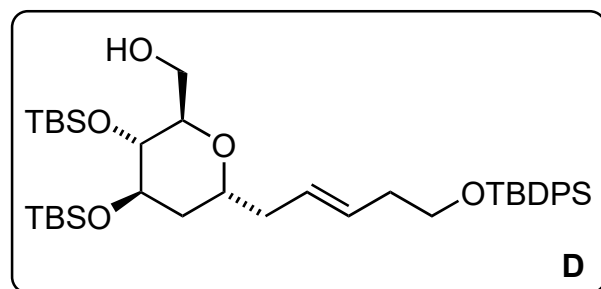
25) Name the reaction.
Sonogashira coupling

26) Hint: 2 rings are formed.

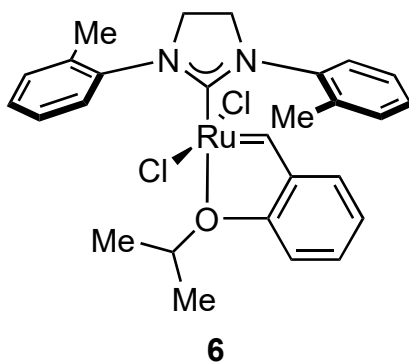




28-34

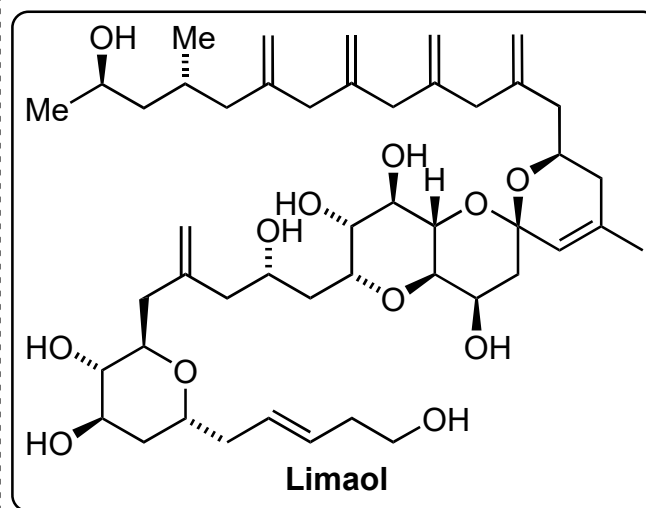
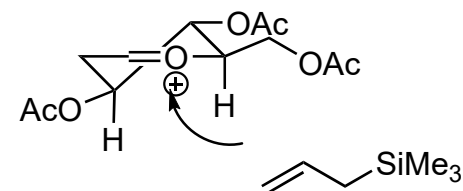


- 28) $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, NaI, MeOH
 29) TMSOTf, allyltrimethylsilane
 30) K_2CO_3 , MeOH
 31) TBSOTf (excess), 2,6-lutidine
 32) **6** (cat), 3-buten-1-ol
 33) TBDPSCI, imidazole
 34) CSA

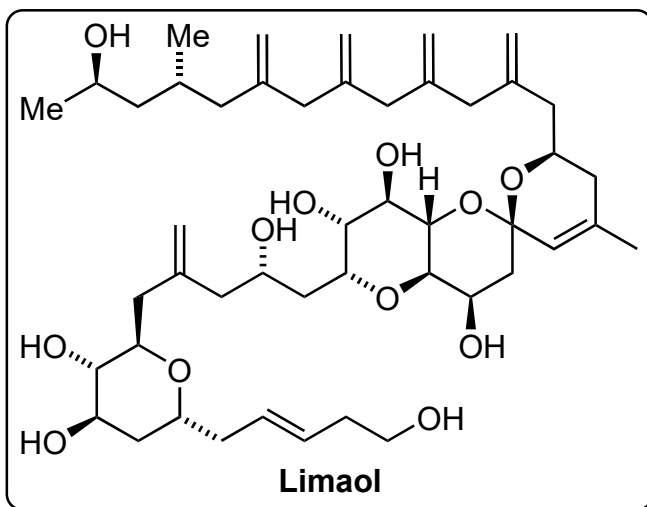


29) Draw a transition state to explain the stereochemical outcome.

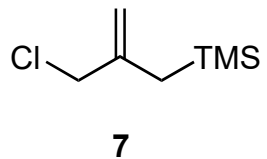
Curtin-Hammett situation:



35-45



- 35) $\text{Pb}(\text{OAc})_4$
- 36) **7**, SnCl_4
- 37) *n*-BuLi, $(\text{Bu}_3\text{Sn})_2$
- 38) $\text{MgBr}_2 \cdot \text{OEt}_2$, **C**
- 39) PPh_3 , 4-nitrobenzoic acid, DEAD
- 40) NaOH
- 41) TBSOTf, 2,6-lutidine
- 42) Ph_3CK , PhNTf_2
- 43) $(\text{Bu}_3\text{Sn})_2\text{CuCNLi}$
- 44) **A**, $\text{Pd}(\text{PPh}_3)_4$, CuTC, $[\text{Bu}_4\text{N}][\text{Ph}_2\text{P}(=\text{O})\text{O}]$
- 45) HF•pyridine



44) Name the reaction.
Stille coupling