

## Total Synthesis of Limaol

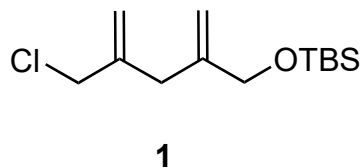
S. N. Hess, X. Mo, C. Wirtz, and A. Fürstner  
*J. Am. Chem. Soc.* **2021**, *143*, 6, 2464–2469.



1-11

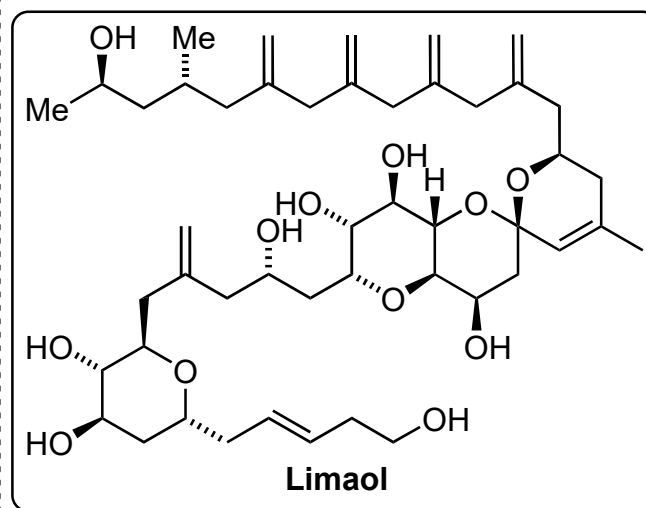


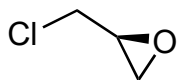
- 1)  $\text{H}_2\text{C}=\text{CHMgBr}$ ,  $\text{CuI}$
- 2)  $\text{TBDPSCI}$ , imidazole
- 3) Grubbs II,  $\text{H}_2\text{C}=\text{CHCO}_2\text{Me}$
- 4)  $\text{TMS-SEt}$ ,  $\text{AlCl}_3$
- 5)  $\text{MeMgBr}$ ,  $\text{CuBr}\cdot\text{SMe}_2$ ,  
(*S,R*)-Josiphos (2%)
- 6)  $\text{Et}_3\text{SiH}$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



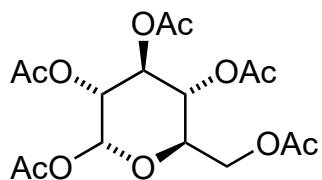
5) Structure of (*S,R*)-Josiphos?

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





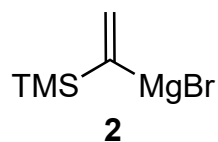
12-15



16-27



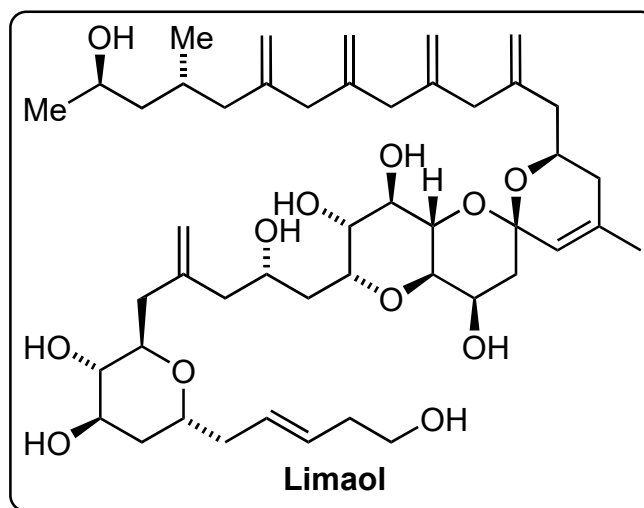
- 12) **2**, CuCN
- 13) NaOH
- 14) ICl, *then* TBAF
- 15) ethyl vinyl ether, *t*-BuLi, BF<sub>3</sub>•OEt<sub>2</sub>, *then* aq HCl

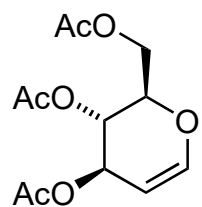
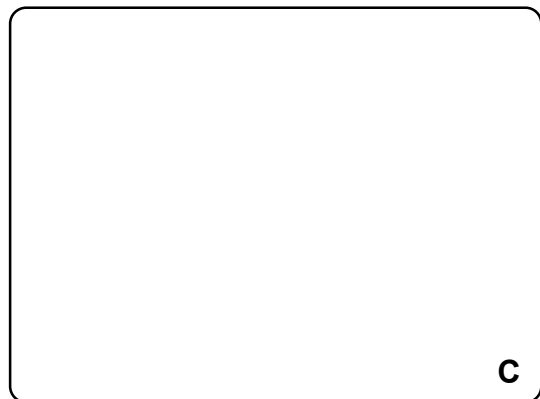


- 16) allyltrimethylsilane, BF<sub>3</sub>•OEt<sub>2</sub>
- 17) NaOMe
- 18) MeOC<sub>6</sub>H<sub>4</sub>CH(OMe)<sub>2</sub>, *p*-TsOH
- 19) TBSOTf (2.6 equiv), 2,6-lutidine
- 20) DIBAL
- 21) (COCl)<sub>2</sub>, DMSO, Et<sub>3</sub>N
- 22) **3**, **4** (cat.)
- 23) TBSOTf, 2,6-lutidine
- 24) DDQ
- 25) **B**, Pd<sub>2</sub>(dba)<sub>3</sub>, PPh<sub>3</sub>, Cul, HN(*i*-Pr)<sub>2</sub>
- 26) **5** (cat), PPTS
- 27) OsO<sub>4</sub>, NaIO<sub>4</sub>

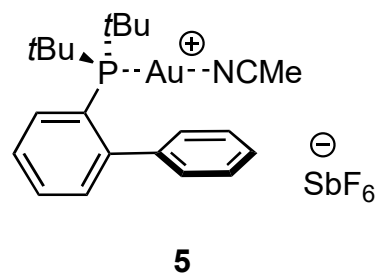
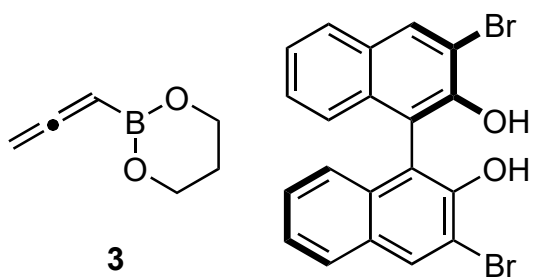
25) Name the reaction.

26) Hint: 2 rings are formed.

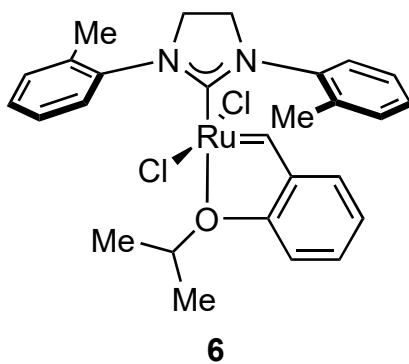




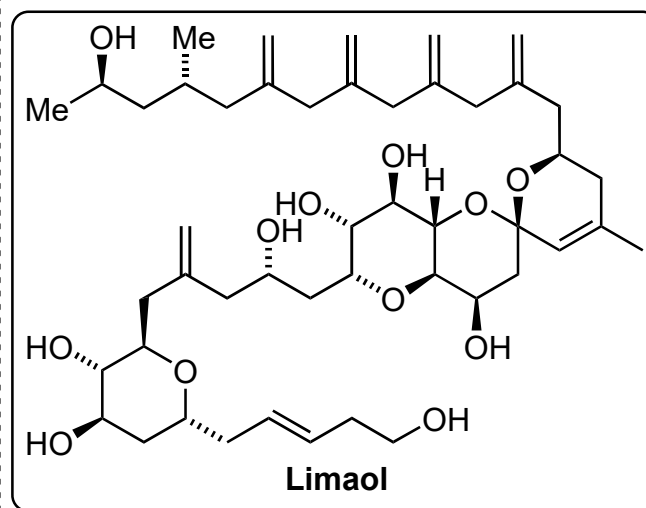
28-34



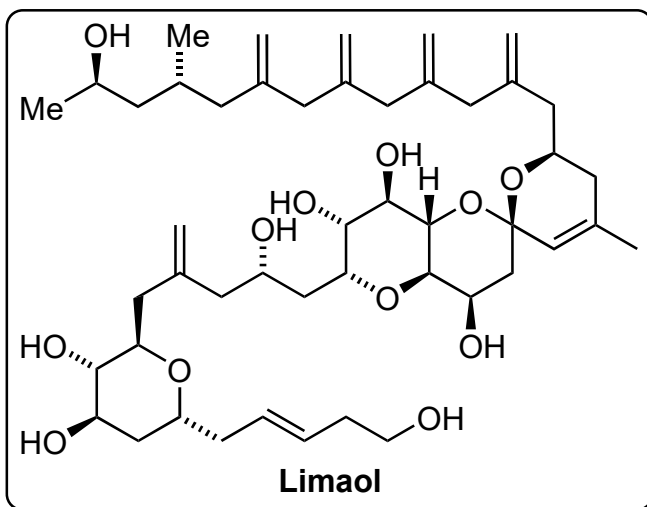
- 28)  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ , NaI, MeOH  
 29) TMSOTf, allyltrimethylsilane  
 30)  $\text{K}_2\text{CO}_3$ , MeOH  
 31) TBSOTf (excess), 2,6-lutidine  
 32) **6** (cat), 3-buten-1-ol  
 33) TBDPSCI, imidazole  
 34) CSA



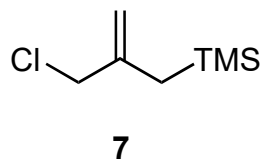
29) Draw a transition state to explain the stereochemical outcome.



35-45



- 35)  $\text{Pb}(\text{OAc})_4$
- 36) **7**,  $\text{SnCl}_4$
- 37) *n*-BuLi,  $(\text{Bu}_3\text{Sn})_2$
- 38)  $\text{MgBr}_2 \cdot \text{OEt}_2$ , **C**
- 39)  $\text{PPh}_3$ , 4-nitrobenzoic acid, DEAD
- 40) NaOH
- 41) TBSOTf, 2,6-lutidine
- 42)  $\text{Ph}_3\text{CK}$ ,  $\text{PhNTf}_2$
- 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.