Total Synthesis of Limaol

S. N. Hess, X. Mo, C. Wirtz, and A. Fürstner

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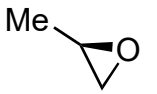

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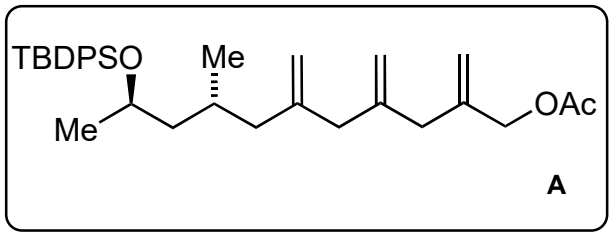
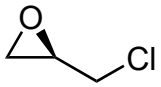
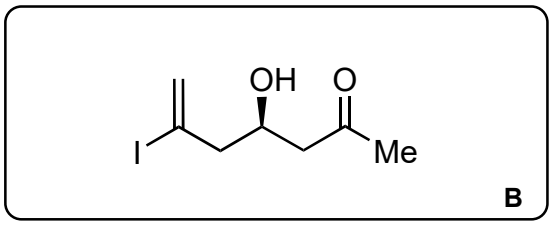
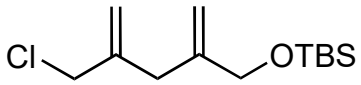




12–15

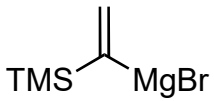


1) $H_2C{=}CHMgBr$, CuI
2) TBDPSCl, imidazole
3) Grubbs II, $H_2C{=}CHCO_2Me$
4) TMS–SEt, $AlCl_3$
5) MeMgBr, $CuBr{\bullet}SMe_2$, (*S*,*R*)-Josiphos (2%)
6) Et_3SiH, Pd/C
7) Ohira-Bestmann reagent, K_2CO_3, MeOH
8) 9-I-9-BBN, *then* AcOH
9) Zn, LiCl, *then* **1**, $Pd(PPh_3)_4$
10) TBAF
11) Ac_2O, pyr, DMAP



1

12) **2**, CuCN
13) NaOH
14) ICl, *then* TBAF
15) *t*BuLi, *then* ethyl vinyl ether, $BF_3{\bullet}OEt_2$, *then* aq HCl



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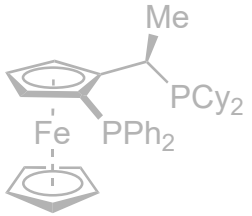
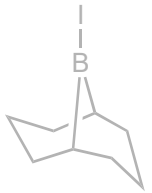
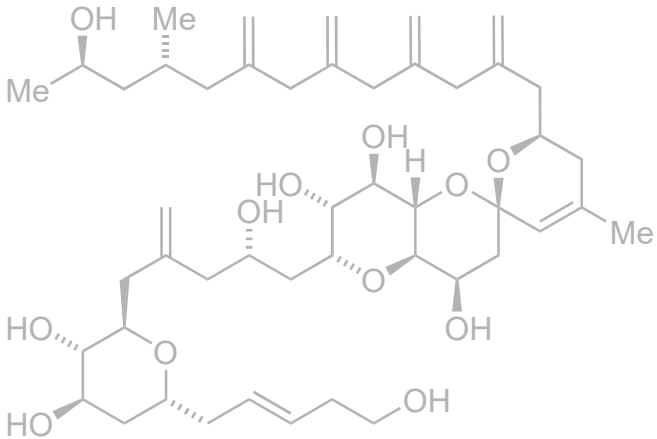
5) Structure (*S*,*R*)-Josiphos?

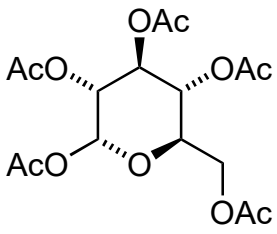


8) Structure 9-I-9-BBN?

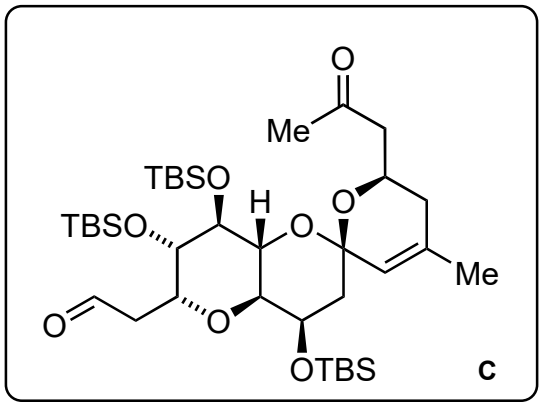




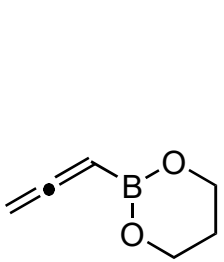
Limaol



16–27



16) allyltrimethylsilane, $BF_3{\bullet}OEt_2$
17) NaOMe
18) $MeOC_6H_4CH(OMe)_2$, *p*TsOH
19) TBSOTf (2.6 eqiuv), 2,6-lutidine
20) DIBAL
21) $(COCl)_2$, DMSO, Et_3N
22) **3**, **4** (cat.)
23) TBSOTf, 2,6-lutidine
24) DDQ
25) **B**, $Pd_2(dba)_3$, PPh_3, CuI, $HN(iPr)_2$
26) **5** (cat), PPTS
27) OsO_4, $NaIO_4$



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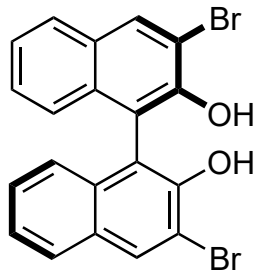

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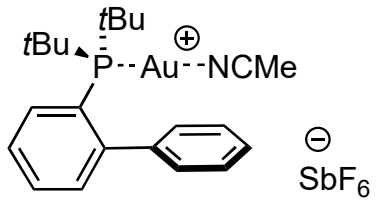

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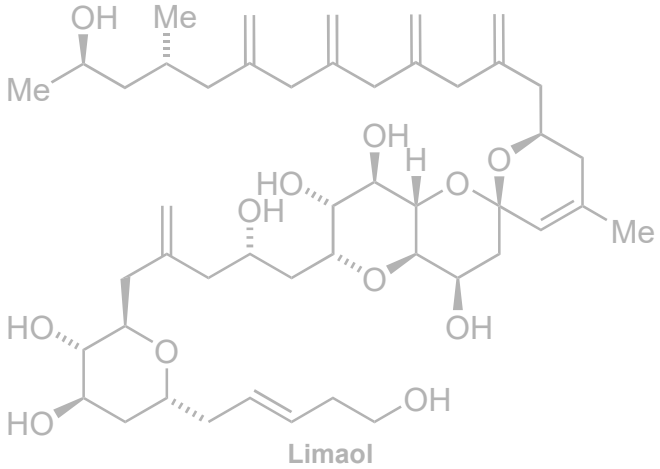
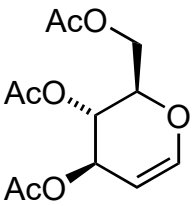
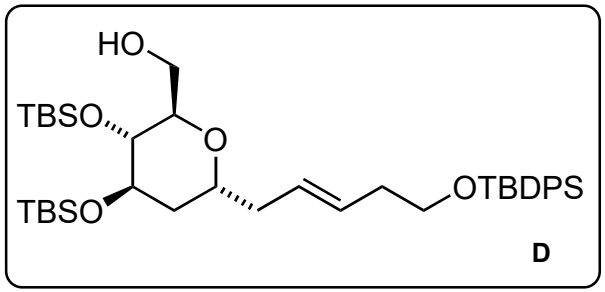
25) Name the reaction
Sonogashira coupling
26) Hint: 2 rings are formed



Limaol



28–34



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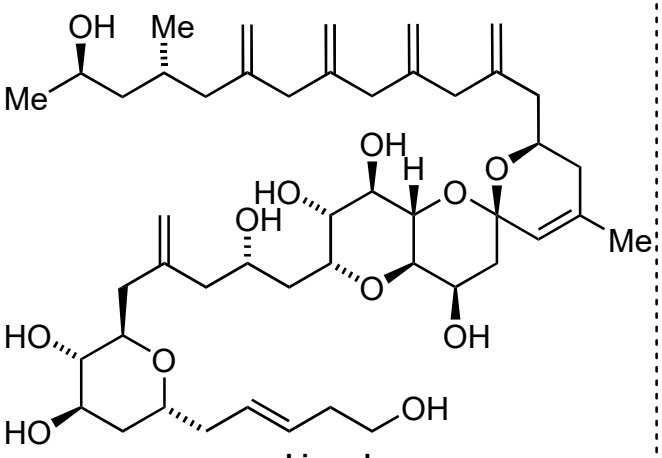
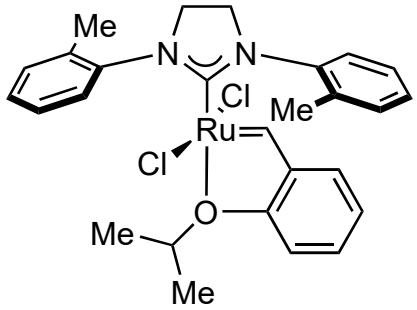


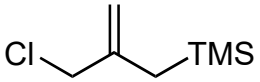
Limaol

28) $CeCl_3 \cdot 7H_2O$, NaI
29) TMSOTf, allyltrimethylsilane
30) K_2CO_3
31) TBSOTf (excess), 2,6-lutidine
32) **6** (cat), 3-buten-1-ol
33) TBDPSCl, imidazole
34) CSA



6

35) $Pb(OAc)_4$
36) **7**, $SnCl_4$
37) *n*BuLi, $(Bu_3Sn)_2$
38) $MgBr_2 \cdot OEt_2$, **C**
39) PPh_3, 4-nitrobenzoic acid, DEAD
40) NaOH
41) TBSOTf, 2,6-lutidine
42) Ph_3CK, $PhNTf_2$
43) $(Bu_3Sn)_2CuCNLi$
44) **A**, $Pd(PPh_3)_4$, CuTC, $[Bu_4N][Ph_2P(=O)O]$
45) HF•pyridine



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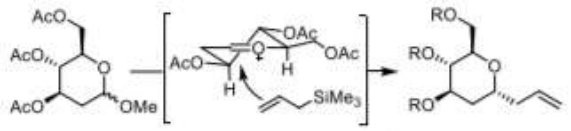
29) Draw a transition state to explain the stereochemical outcome

Curtin-Hammett situation:



44) Name the reaction

Stille coupling