Total Synthesis of the Protein Phosphatase 2A Inhibitor Lactodehydrothyrsiferol

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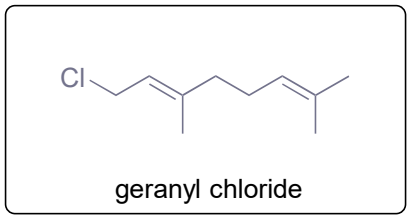
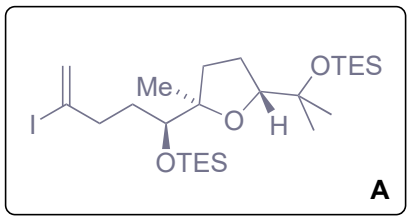
Angew. Chem. Int. Ed. **2011**, *50*, 5178–5181

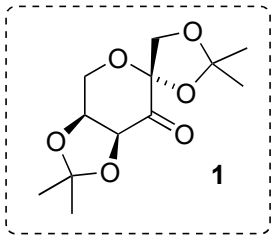


geranyl chloride

1) *n*-BuLi, TMS ; then TBAF
2) AD-mix-β, $CH_3SO_2NH_2$
3) **1**, Oxone, K_2CO_3, Bu_4NHSO_4; then py·CSA
4) TESCl, DMAP, imidazole
5) Et_3SiH, $[CpRu(NCCH_3)_3]PF_6$; then I_2, 2,6-lutidine

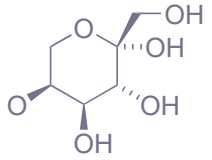


A



Shi-catalyst

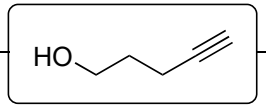
1) acetone, H_2SO_4
2) RuO_2, $NaIO_4$



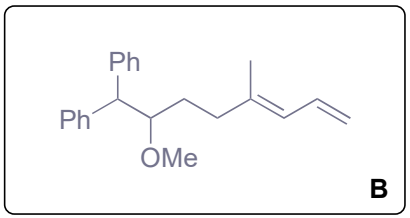
L-Fructose

How would you synthesize **1**? name?

Ref.: *J. Org. Chem.* **2005**, *70*, 10143-10146

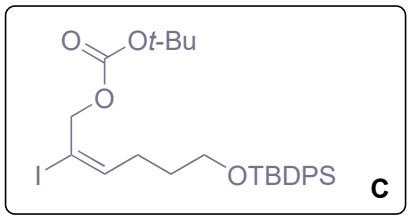


6) Me_3Al, Cp_2ZrCl_2; then I_2
7) H_2C=CHMgBr, $Pd(PPh_3)_4$
8) $(COCl)_2$, DMSO, Et_3N
9) Ph_2CH_2, *n*-BuLi
10) NaH; then MeI



B

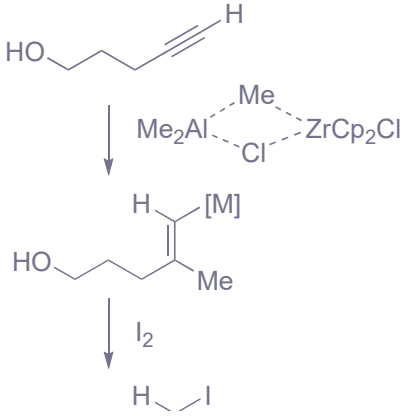
11) TBDPSCl, imidazole
12) *n*-BuLi; then $(CH_2O)_n$
13) Bu_3SnH, $Pd(PPh_3)_4$; then I_2
14) Boc_2O, *N*-methylimidazole



C

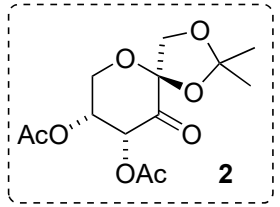
6) Regioselectivity?

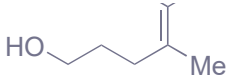
Ref.: *J. Am. Chem. Soc.* **1981**, *103*, 4985–4987

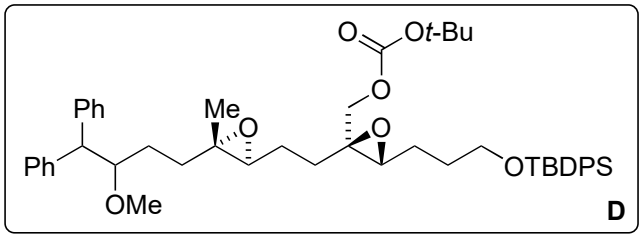


B

15) 9-BBN; then **C**, Pd(P*t*-Bu$_3$)$_2$, K$_3$PO$_4$
16) Oxone, **1**, K$_2$CO$_3$, Bu$_4$NHSO$_4$; then **2**

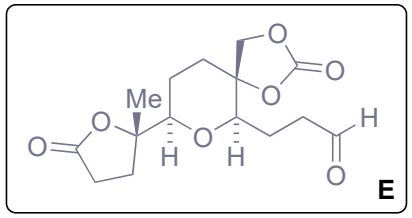




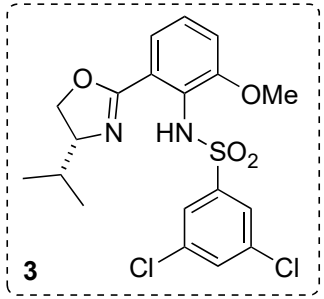


17) hν, *N*-methylquinolinium hexafluorophosphate, O_2, $Na_2S_2O_3$, NaOAc
18) *m*-CPBA, Sc(OTf)$_3$
19) IBX, DMSO

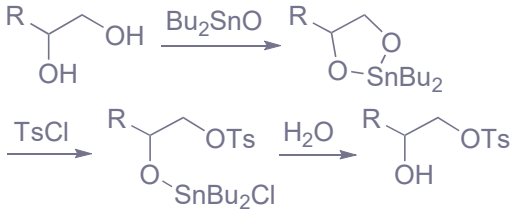
17) Mechanism?
18) Mechanism?
see below

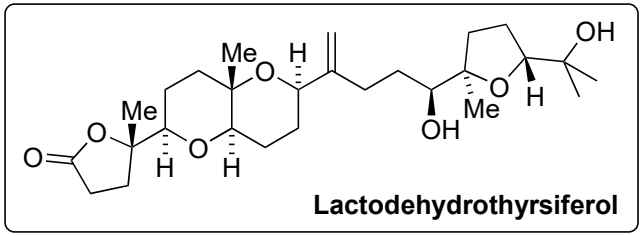


20) $CrCl_2$, $NiCl_2$·DMP, **3**, **A**, proton sponge Mn, Cp_2ZrCl_2, LiCl
21) K_2CO_3, MeOH
22) TsCl, Et_3N, Bu_2SnO
23) $NaBH_4$, HMPA, 50 °C
24) Me_3P=CHCN
25) TBAF



22) Role of Bu_2SnO?
Org. Lett. **1999**, *1*, 447–450

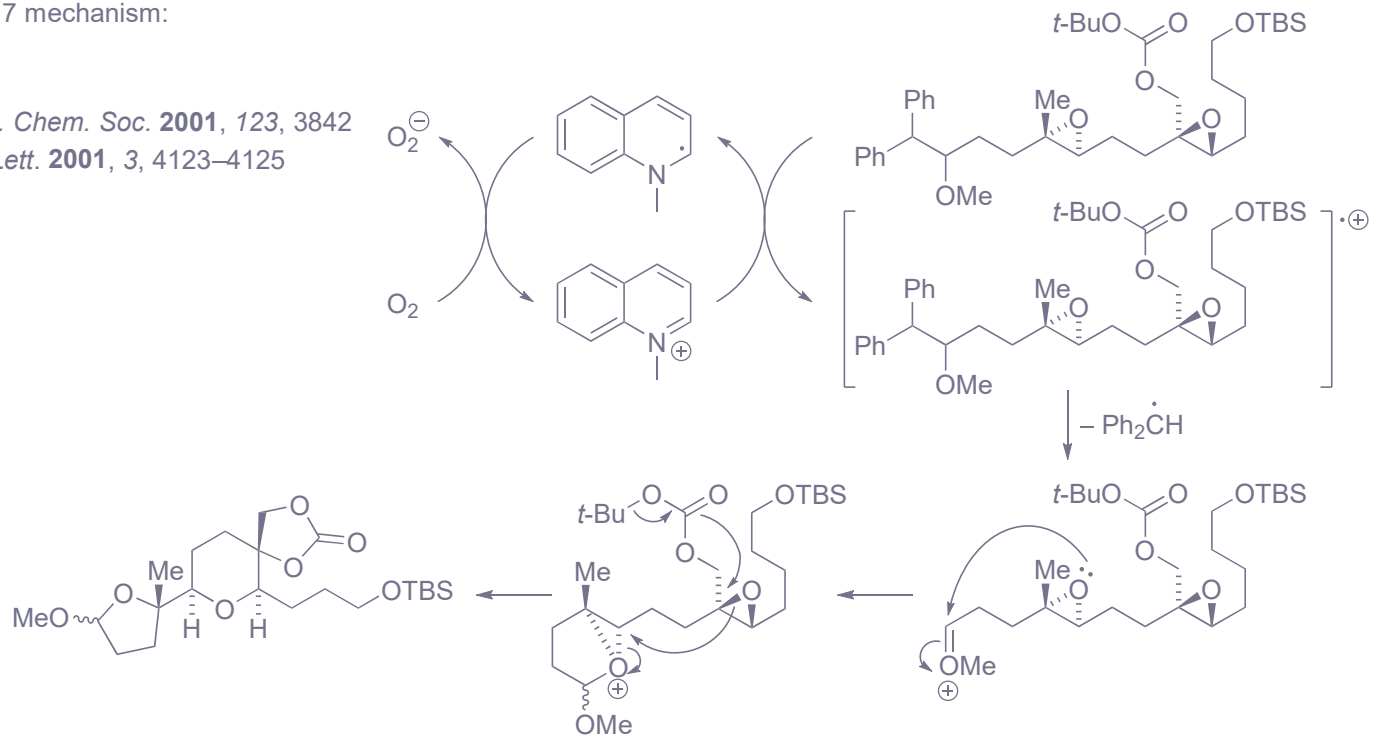




step 17 mechanism:

see

J. Am. Chem. Soc. **2001**, *123*, 3842
Org. Lett. **2001**, *3*, 4123–4125



step 18 mechanism:

see *Tetrahedron Lett.* **1978**, *19*, 419.