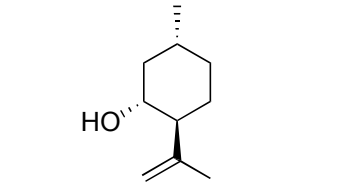
Total Synthesis of 4-Desmethyl-3α-hydroxy-15-rippertene

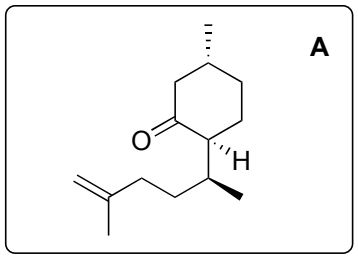
Henning, R., Metz, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 1157–1159



Isopulegol

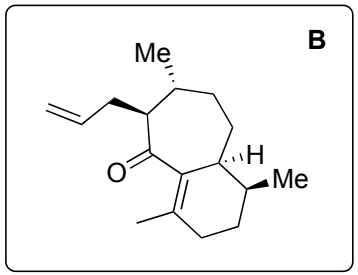
1-4

1) TMSCl, imidazole, DMAP
2) Et_2BH, Et_2O
3) Et_2Zn, CuCN•2LiBr, methallyl bromide
   HCl wash
4) PCC, DCM



5-9

5) $TMSCHN_2$, Me_3Al, DCM, then 1M HCl
6) $K_2OsO_2(OH)_4$ (cat.), $NaIO_4$, pyridine
7) *t*-BuOK, *t*-BuOH, THF, 65 ºC
8) LiHMDS, then allyl iodide

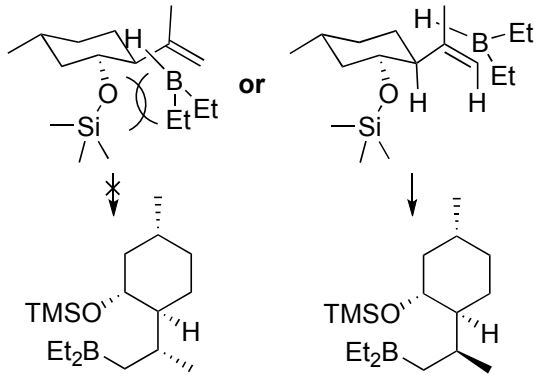


9-13

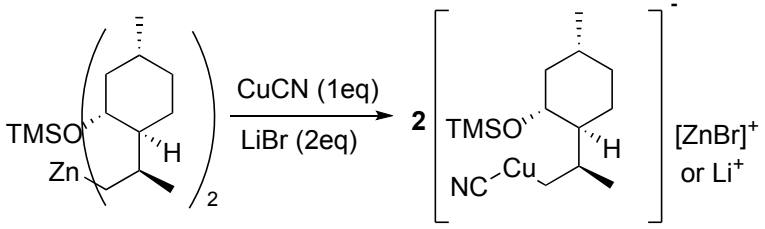
9) $PdCl_2$, p-benzoquinone, DMA/H_2O
10) *t*-BuOK, *t*-BuOH, THF, MW, 40 ºC
11) $LiAlH_4$, Et_2O, –78 ºC
12) Propargyl bromide, TBAI, aq. KOH
13) *t*-BuOK, *t*-BuOH, THF, MW, 150ºC

Explain the stereochemical outcome in step 2

Conformation of the molecule to avoid allylic strain favours attack from opposite face to OTMS

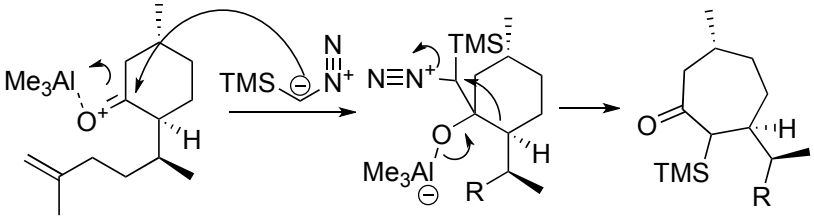


What is the reactive species in step 3?

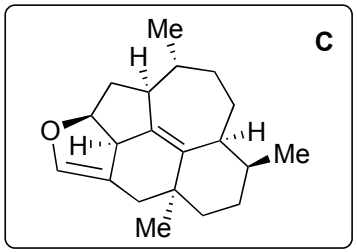


J. Org. Chem. 1988,53, 2390-2392

Mechanism of 5. What is the role of $AlMe_3$?

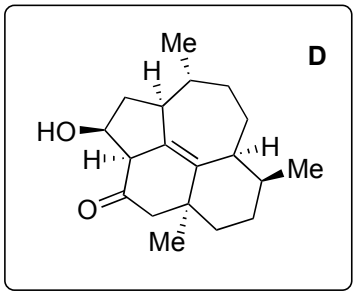


$AlMe_3$ acts as a Lewis acid. Avoids epoxide formation. Enhances reaction speed
Migration of the other alkane side happened in proportion 1 to 0.88. (favoured the desired product)



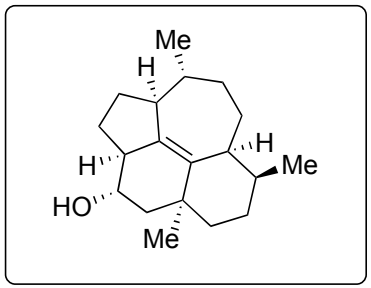
14-18

14) TsOH, THF, H_2O
15) TPAP (cat.), NMO, 4A molsieves
16) LiHMDS, THF, –78 °C, then MoOPH
17) 50% aq. KOH, THF
18) $LiAlH_4$
19) $NaIO_4$, THF, H_2O



19-23

20) $Me_4NBH(OAc)_3$, AcOH, MeCN/THF
21) MOMCl, DIPEA, TBAI, –40°C
22) *n*-BuLi, THF, then CS_2, then MeI
23) Bu_3SnH, AIBN, PhMe, reflux
24) 6N HCl, THF



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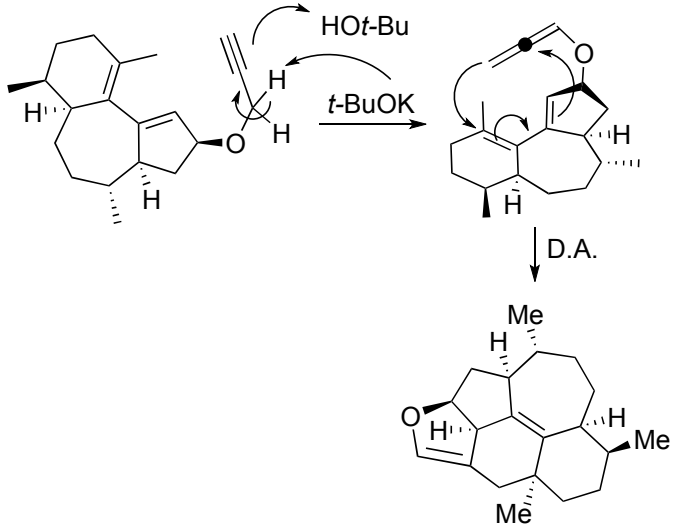
Name the reaction in step 9

Wacker oxidation

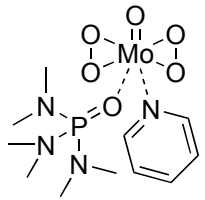
Provide a mechanism for step 13



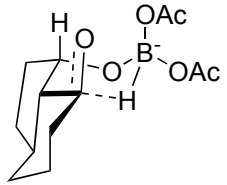
Name the reaction in step 15

Ley-Griffith Oxidation

Structure of MoOPH? Hint: Molibdenum (VI)



Explain the stereochemical outcome in step 20



Lowest 1,3 diaxial repulsion
Chair-like transition state