Total Synthesis and Anti-Cancer Activity of All Known Communesin Alkaloids and Related Derivatives

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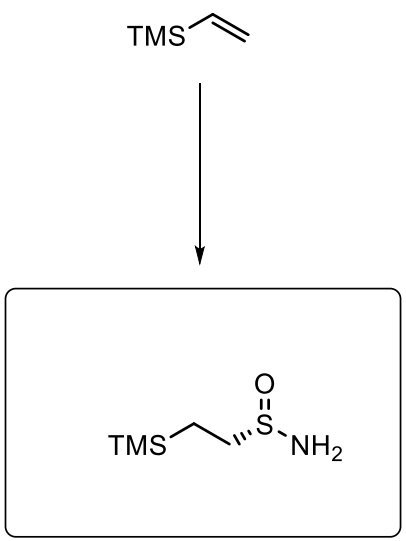
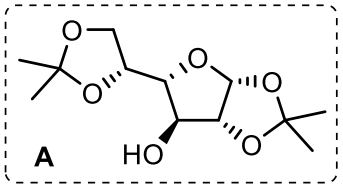
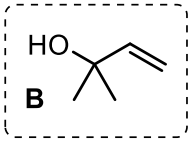
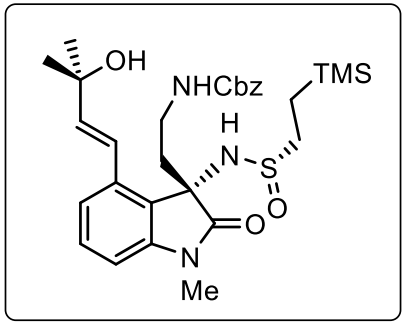


1) AIBN, tBuSH, Δ
2) $NaIO_4$, MeOH
3) sulfuryl chloride, Et_2O
4) **A**, DIPEA, PhMe, CH_2Cl_2
5) LiHMDS, THF
then silica gel, MeOH



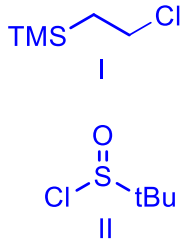
6) 4-bromo-1-methylisatin, $Ti(OEt)_4$, CH_2Cl_2
7) allylmagnesium bromide, $MgBr_2$, CH_2Cl_2
8) O_3, MeOH, *then* $NaBH_4$
9) *o*-NsNHCbz, DIAD, PPh_3, THF, *then* PhSH, Cs_2CO_3
10) **B**, $Pd(OAc)_2$, Ag_2CO_3, DMF-H_2O



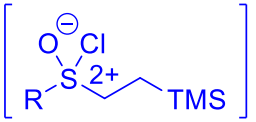


Step 3: Let's discuss the mechanism!

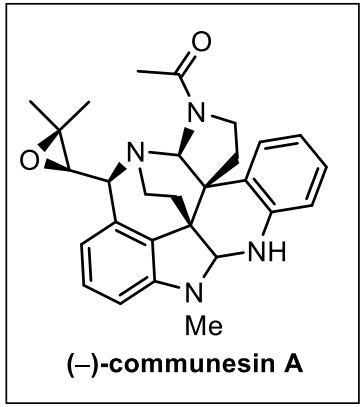
The original Paper describes a high solvent dependecy and observed the formation of I and II in CH_2Cl_2
(an abnormal Pummerer reaction might be possible)
"Eur. J. Org. Chem. 2001, 1643-1654"
suggests a chloro-sulfoxonium ion intermediate



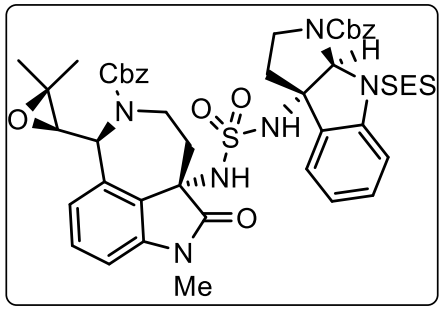
*Step 4: What is **A** derived from?*
-> D-glucose

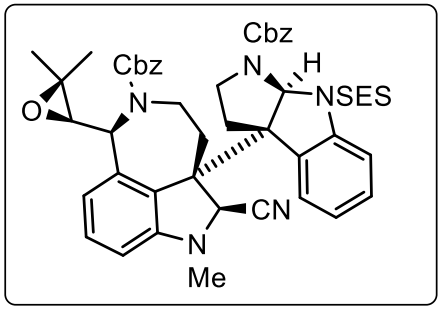


Step 8: What is reduced by $NaBH_4$? -> the ozonide intermediate!
Step 9 & 10: Name the Reactions
-> Mitsunobi Reaction, Mizoroki-Heck



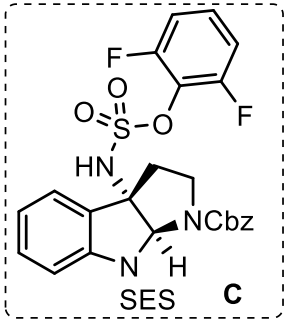
(–)-communesin A



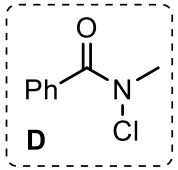


(–)-communesin A

11) $Ca(OTf)_2$, MeCN
12) 1,1,1-trifluoroacetone, H_2O_2, K_2CO_3, EDTA, MeCN-H_2O
13) TASF, H_2O, DMF
14) **C**, DMAP, THF

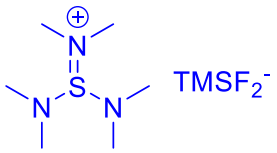


15) $LiBH_4$, MeOH, THF
16) TMSCN, H_2O, HFIP
17) **D**, PS-BEMP, MeOH
18) hν (350 nm)

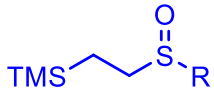


19) $Pd(OH)_2$/C, H_2,EtOH
20) tBuOLi, EtOH
21) PPTS, Ac_2O, EtOH
22) TASF, DMF

Step 13: Structure of TASF?

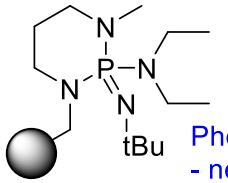


Step 14: What Protecting Group is SES? Advantages?



deprotection via F^-
(= non-acidic,non-reducing)

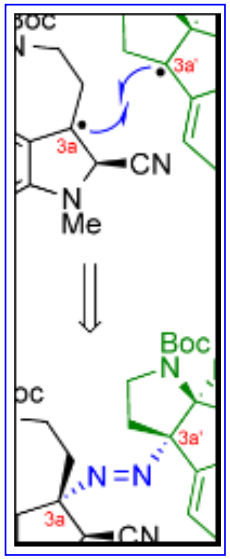
Step 17: PS-BEMP =



What compound class does BEMP belong to and what properties is this class known for?

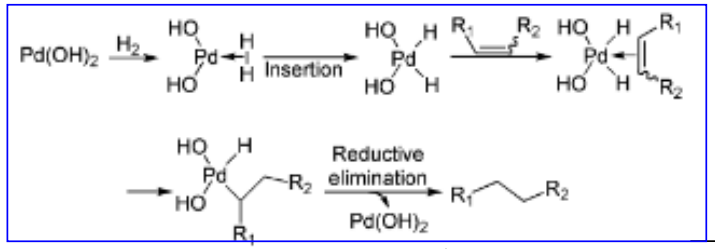
Phosphazene
- neutral superbase (2000x more basic than DBU, pKa of related Schwesinger Base = 43)
- weak nucleophile (more sterically hindered than DBU)
- conjugate acid is inert and non-hydrogen-bonding

Step 18: Mechanism?

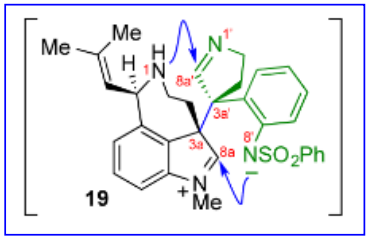


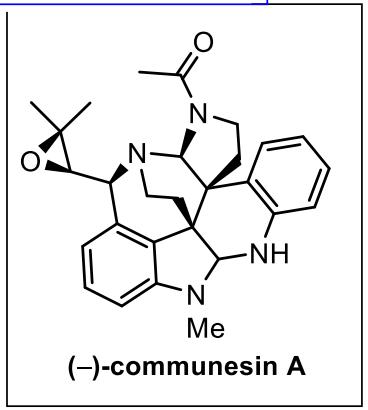
Step 19: Name of Reagent? Principal Mechanism?

Pearlman Catalyst



Step 20: Mechanism?





(–)-communesin A