Synthesis of Streptolydigin, a Potent Bacterial RNA Polymerase Inhibitor

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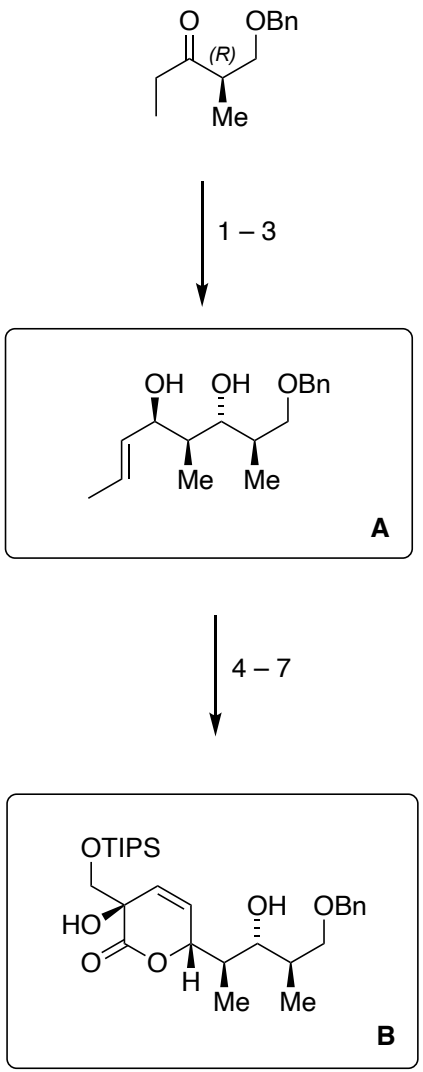
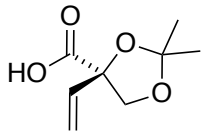


1) $TiCl_4$, $Ti(O\textit{i}\text{-}Pr)_4$, DIPEA,
(*E*)-crotonaldehyde
2) SmI_2, MeCHO, THF
3) K_2CO_3, MeOH, H_2O

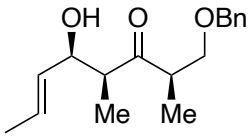
4) DCC, DMAP, **1**
5) 4 M HCl, THF
6) TIPSCl (1 equiv.), imidazole, DMAP
7) HG-II



1

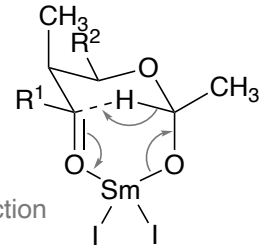
1) Please explain the selectivity. see below.

2) What is the name of this reaction? Explain the selectivity with a model. Do you know alternative reaction conditions resulting in the same selectivity? How could you obtain the opposite selectivity?

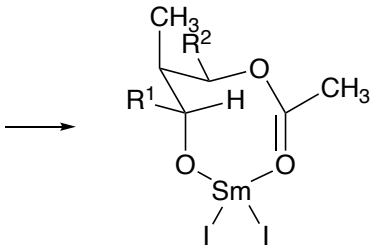


SmI_2, MeCHO

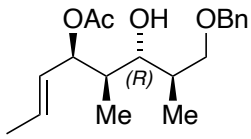
Evans Tishchenko reduction



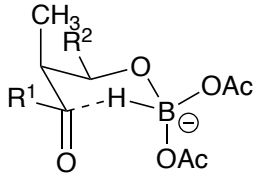
anti



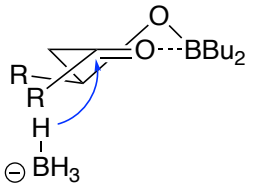
H_3O^+



Alternative *anti*-reduction:
Evans–Saksena reduction
conditions: $Me_4NBH(OAc)_3$

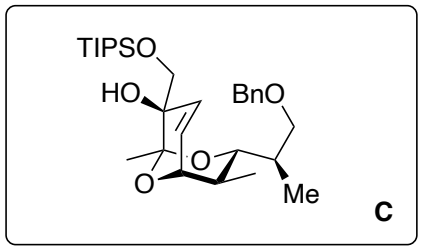


syn-1,3-diol selectivity:
Narasaka–Prasad reduction
conditions: Bu_2BOMe, $NaBH_4$

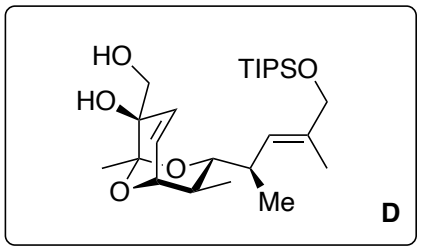


Attack according to Fuerst–Plattner rule

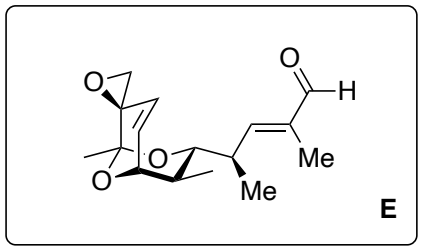
8 – 10



11 – 16



17 – 19

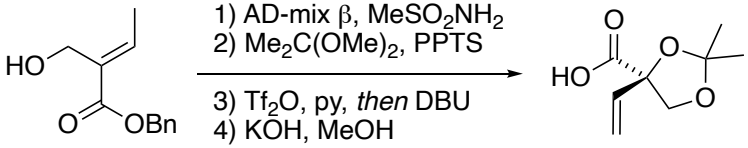


8) MeNHOMe • HCl, *i*-PrMgCl
9) MeLi
10) *p*-TsOH

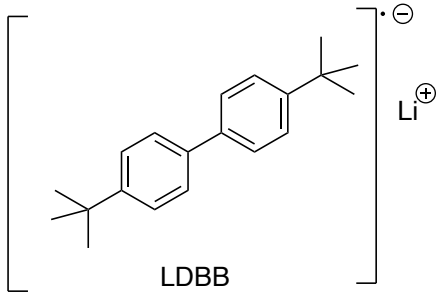
11) LiDBB
12) DMP
13) $Ph_3PC(Me)CO_2Et$, PhMe, Δ
14) DIBAL-H
15) TIPS-Cl, imidazole, DMAP
16) $LiAlH_4$

17) Tf_2O, pyridine, DBU
18) TBAF
19) DMP

How could you access **1** fom **X**?

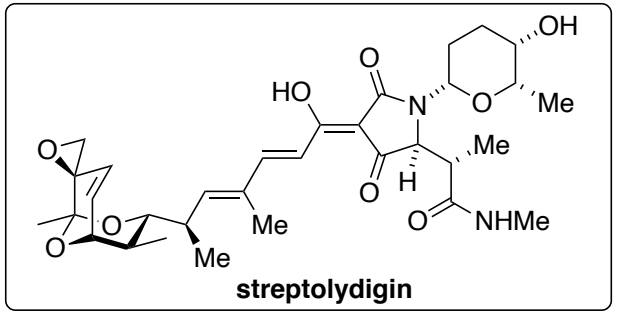


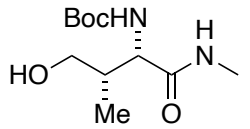
What is the structure of LiDBB?



Freeman's reagent

Hint: Step 16 is a selective monodeprotection





F

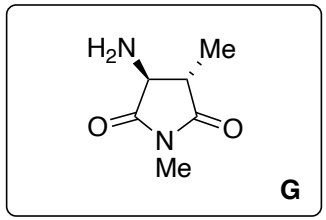
How would you prepare **F** from a common chiral building block?

see below

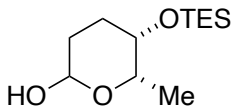
20, 21

20) TEMPO, PIDA
21) TFA, basic alumina

Hint: In step 20 a cyclization takes place



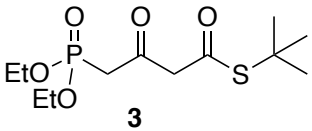
G



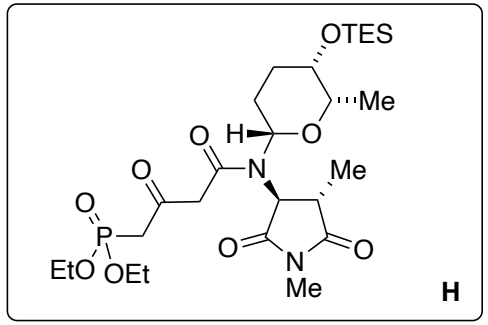
2

22, 23

22) **2**, MeOH
23) **3**, CF_3CO_2Ag, 5Å MS



3



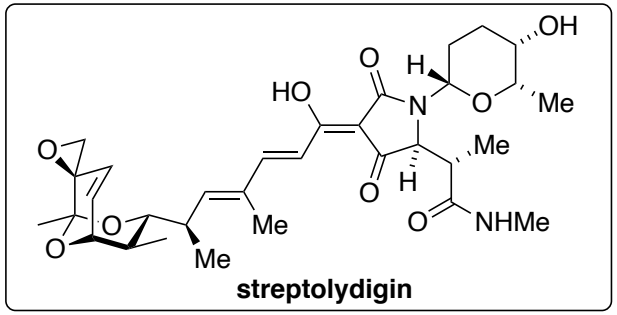
H

Name at least one alternative method to synthesize α-amino acids.
Strecker reaction, asymmetric vaiants available
Schöllkopf method
Sharpless aminohydroxylation
…

24

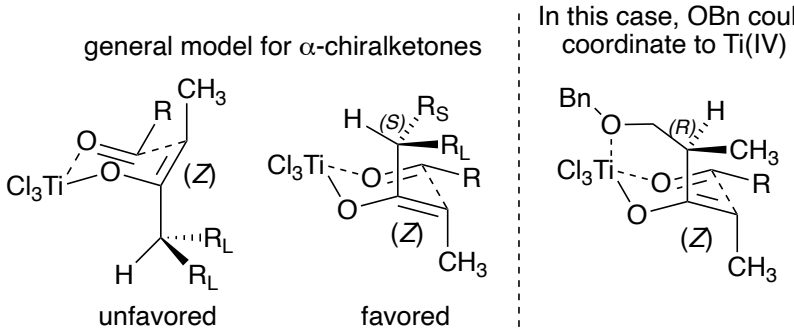
24) *t*-BuOK, THF, *then* **E**, *then* aq. HCl

Key step: please provide a mechanism

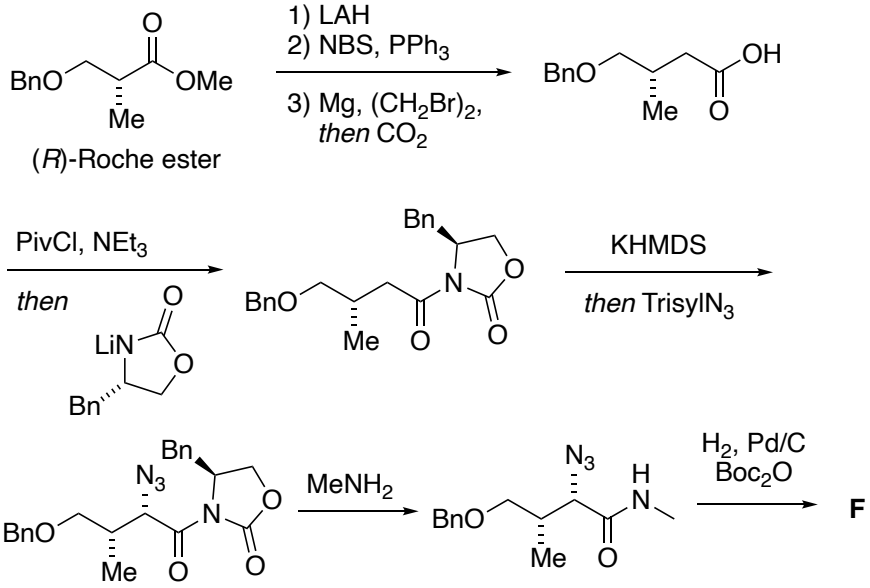


streptolydigin

Step 1, explanation for the observed selectivity:



Synthesis of F:



Mechanism of step 24