Synthesis of Streptolydigin, a Potent Bacterial RNA Polymerase Inhibitor

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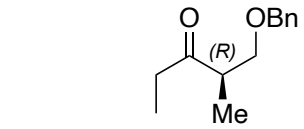


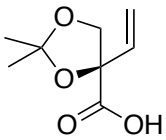
1 – 3

A

4 – 7

B

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



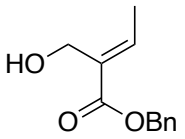
1

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

1) Please explain the selectivity.

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?

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



X

8 – 10

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

C

11 – 16

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

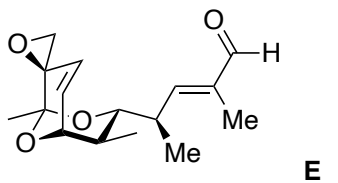
What is the structure of LDBB?

Hint: Step 16 is a selective monodepotection.

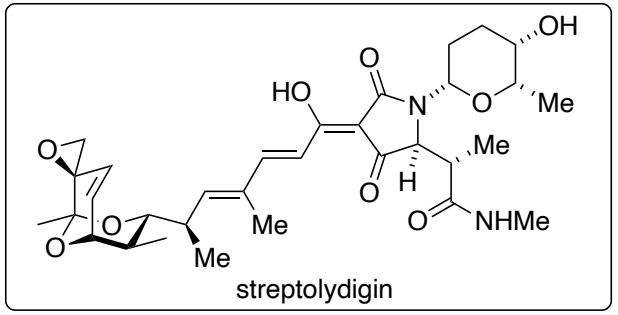
D

17 – 19

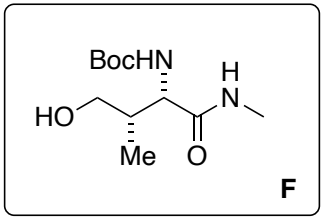
17) Tf_2O, pyridine, DBU
18) TBAF
19) DMP



E



streptolydigin



F

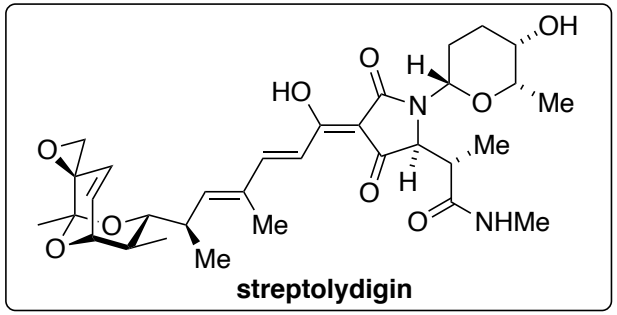
20, 21

G

22, 23

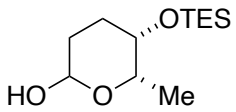
H

24



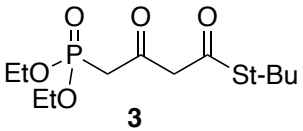
streptolydigin

20) TEMPO, PIDA
21) TFA, basic alumina



2

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



3

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

How would you prepare **F**?
Name at least one alternative method to synthesize α-amino acids.

Hint: A cyclization takes place

Key step: Please provide a mechanism.