Synthesis of Streptolydigin, a Potent Bacterial RNA Polymerase Inhibitor
Sergey V. Pronin and Sergey A. Kozmin

1) TiCl$_4$, Ti(Oi-Pr)$_4$, DIPEA, (E)-crotonaldehyde
2) SmI$_2$, MeCHO, THF
3) K$_2$CO$_3$, MeOH, H$_2$O

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

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?

Evans Tishchenko reduction

Alternative *anti*-reduction: *Evans–Saksena reduction*
conditions: Me$_4$NBH(OAc)$_3$

*Narasaka–Prasad reduction*
conditions: Bu$_2$BOMe, NaBH$_4$

Attack according to Fuerst–Plattner rule
8) MeNHOMe • HCl, i-PrMgCl
9) MeLi
10) p-TsOH

11) LiDBB
12) DMP
13) Ph₃PC(Me)CO₂Et, PhMe, Δ
14) DIBAL-H
15) TIPS-Cl, imidazole, DMAP
16) LiAlH₄

17) Tf₂O, pyridine, DBU
18) TBAF
19) DMP

How could you access 1 from X?

1) AD-mix β, MeSO₂NH₂
2) Me₂C(OMe)₂, PPTS
3) Tf₂O, py, then DBU
4) KOH, MeOH

60% over 4 steps

What is the structure of LiDBB?

Freeman's reagent

Hint: Step 16 is a selective monodeprotection

streptolydigin
How would you prepare $\mathbf{F}$ from a common chiral building block? 

*see below*

Hint: In step 20 a cyclization takes place

Name at least one alternative method to synthesize $\alpha$-amino acids.
- Strecker reaction, asymmetric variants available
- Schöllkopf method
- Sharpless aminohydroxylation

**Key step:** please provide a mechanism
Mechanism of step 24

In this case, OBn could coordinate to Ti(IV)

Step 1, explanation for the observed selectivity:

general model for α-chiral ketones

unfavored

favored

Mechanism of step 24

Dieckmann cyclization + imide opening

Horner–Wadsworth–Emmons olefination

Synthesis of F:

1) LAH
2) NBS, PPh₃
3) Mg, (CH₂Br)₂, then CO₂

BnO⁻ Me

(R)-Roche ester

PivCl, NE₃

then TrisylN₃

H₂, Pd/C

Boc₂O

F

streptolydigin