Asymmetric Total Synthesis of (–)- and (+)-Strychnine and the Wieland–Gumlich Aldehyde

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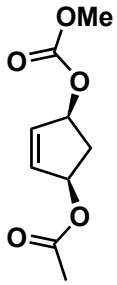
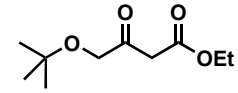
How do you make this enantiopure?





NaH, 1% $Pd_2(dba)_3$
15% PPh_3, THF

2 diastereomers

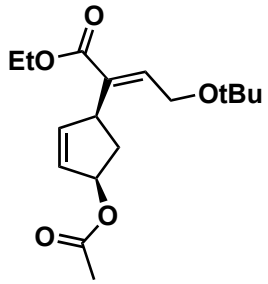
$NaCNBH_3$

$TiCl_4$, THF

+

DCC, CuCl

PhH, 80 °C



E-configuration formed via syn elimination
Knowing this helps to predict products in previous step

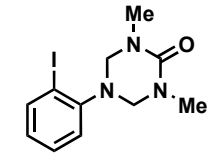
1. DIBAL, DCM
   –78 °C
2. TIPSCl, TMG
   NMP, –10 °C
3. CrO_3, H_2SO_4
   acetone/H_2O
   –5 °C

i.

ii. $PhNTf_2$
THF
–78 to 0 °C

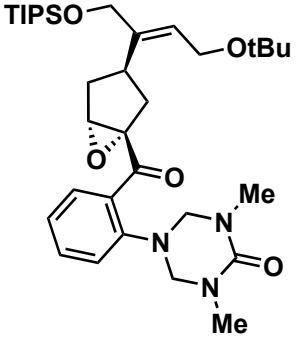
$(Me_3Sn)_2$,
$Pd(PPh_3)_4$

LiCl, THF
60 °C



CO (3.5 atm)
$Pd_2(dba)_3$, Ph_3As
LiCl, NMP
70 °C

???

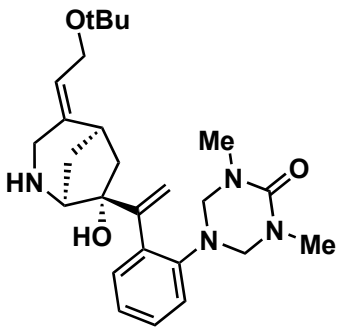


1. $Ph_3{=}CH_2$
2. TBAF

3. MsCl, DIPEA
4. LiCl
5. CF_3CONH_2
   NaH

1. NaH, PhH
   100 °C

2. KOH, EtOH
   H_2O, 60 °C



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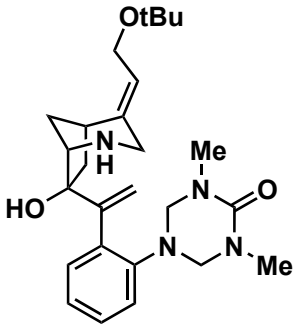

paraformaldehyde
Na_2SO_4

MeCN, 80 °C

Draw a mechanism!
What is the retron and synthon for this famous reaction

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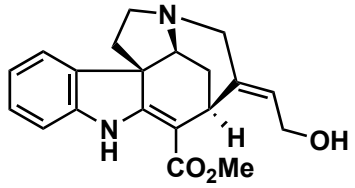
Try to draw the product with the atoms in the same locations as above on the right, just with new bonds drawn.

Try to draw the product in the way that strychnine is typically drawn.

What named reagent is best for this kind of reaction?

1a. LDA
1b. ???????
THF, –78 °C

2. HCl, MeOH

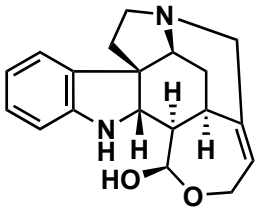


Zn, H_2SO_4

$MeOH/H_2O$
reflux

1. NaOMe, MeOH
   RT

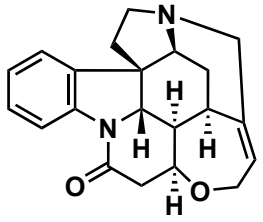
2. DIBAL, DCM
   –78 °C



Wieland–Gumlich aldehyde

HO_2C CO_2H

Ac_2O, NaOAc
HOAc, 110 °C



(–)-strychnine