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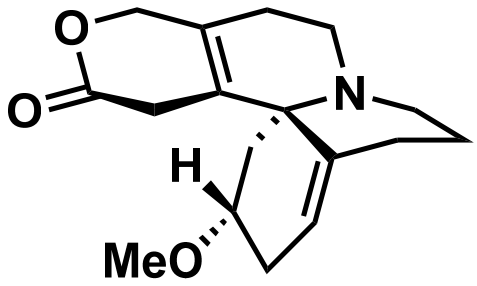
Enantioselective Total Synthesis of (+)-Dihydro-β-erythroidine

Sebastian Clementson,[†,‡] Mikkel Jessing,[‡] Henrik Pedersen,[§] Paulo Vital,*[,‡] and Jesper L. Kristensen*[,†]

[†]Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen, Denmark

[‡]Molecular Discovery and Innovation, H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark

[§]Compound Management and Analytical Chemistry, H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark

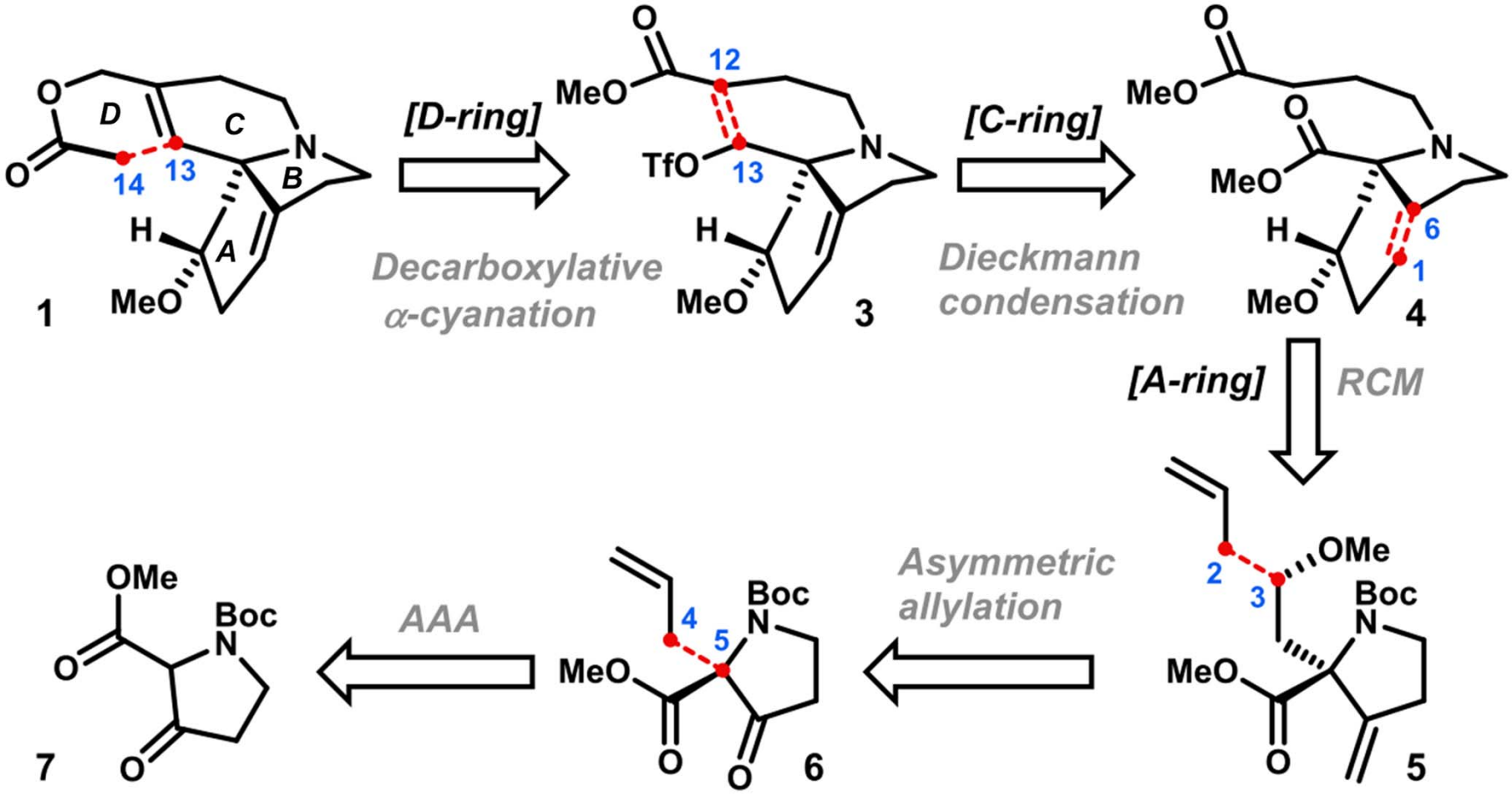


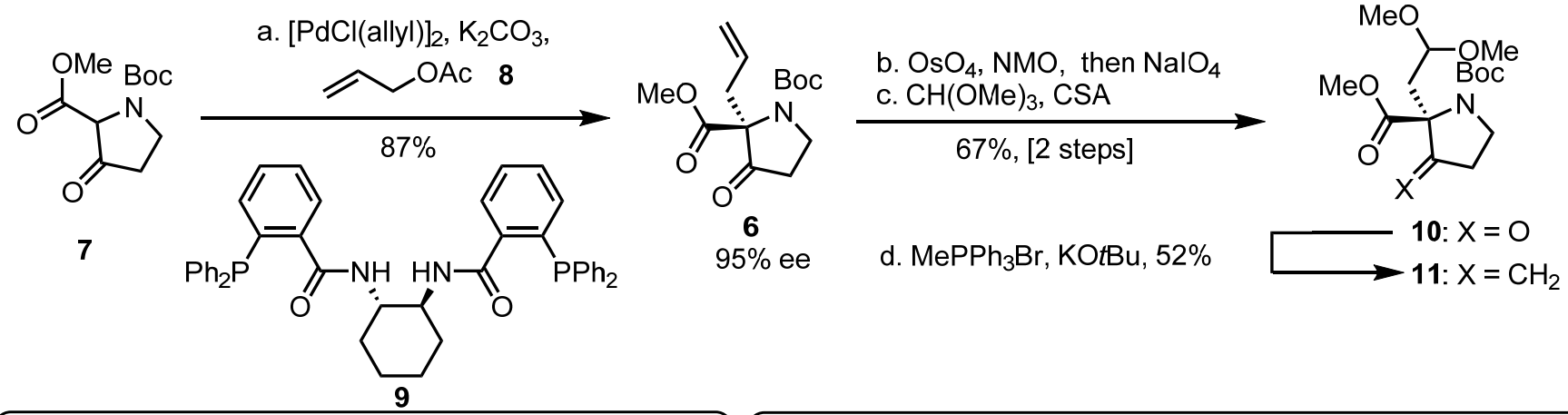
(+)-Dihydro-β–erythroidine
(+)-DHβE

- Found in the seeds of the Erythrina americana family of Mexican coral plants
- One of the most potent nicotine acetylcholine receptor (nAChR) antagonists ($IC_{50}(\alpha_4\beta_2)$: 0.11 μM)
- Antidepressant-like activities in preclinical assays
- Muscle relaxant in the treatment of Parkinson's disease
- α-tertiary amine and tetracyclic spiroamine

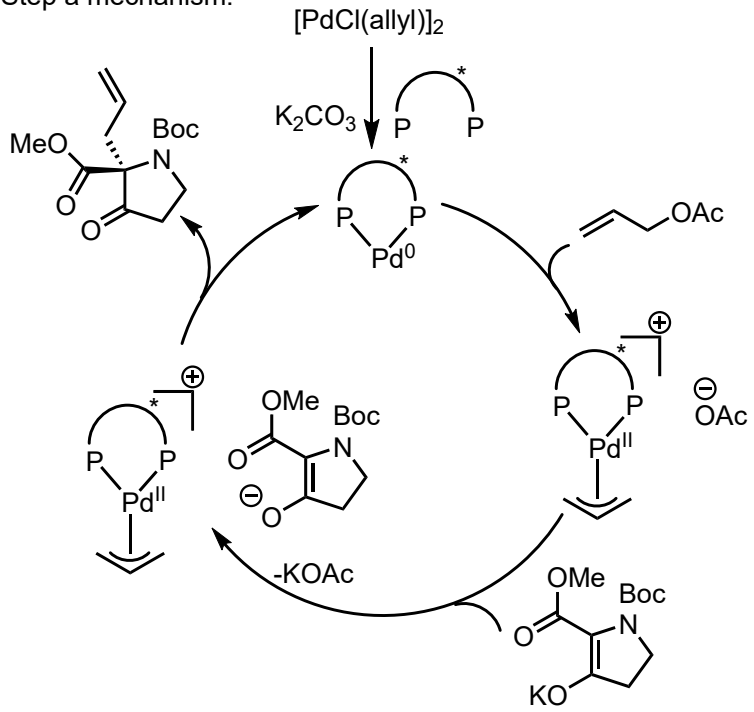
Ziyong Wang
Liu Research Group
Total synthesis presentation
6/25/2019

Retrosynthetic analysis

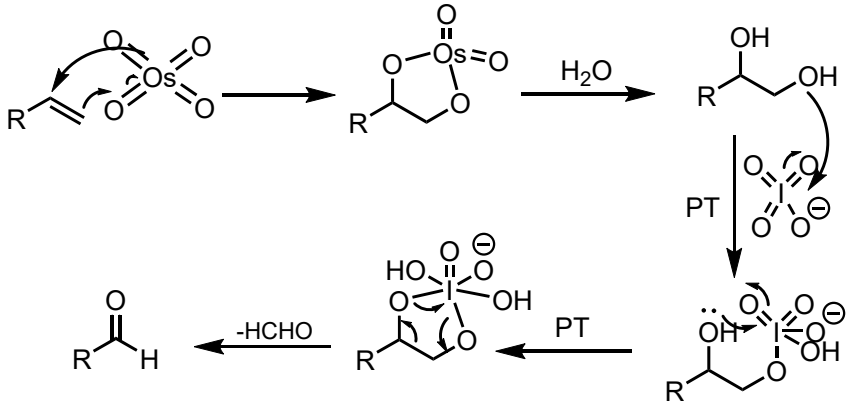




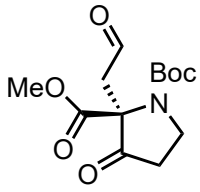
Step a mechanism:

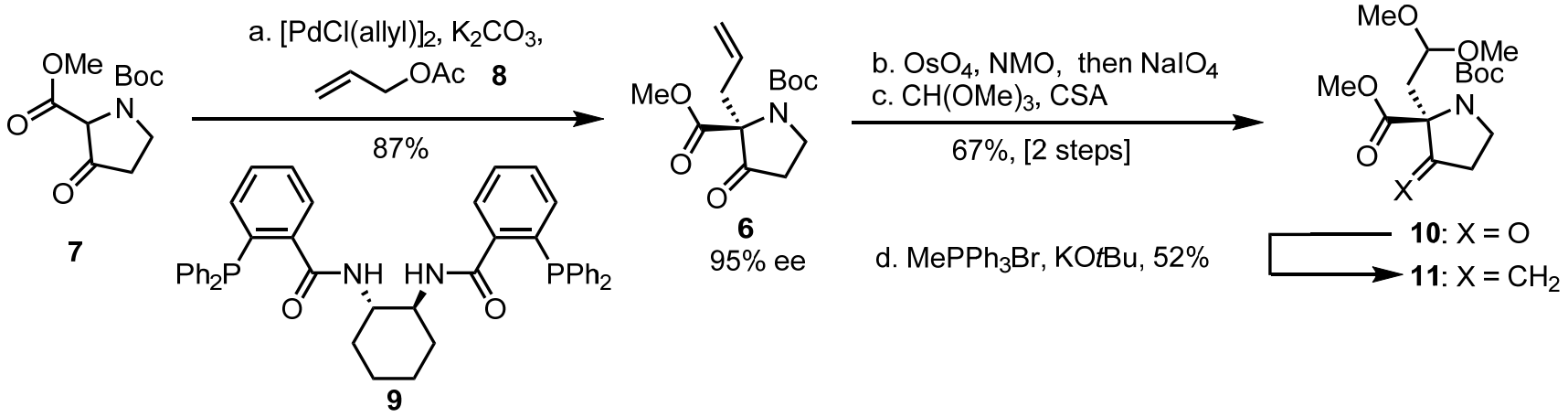


Step b mechanism:

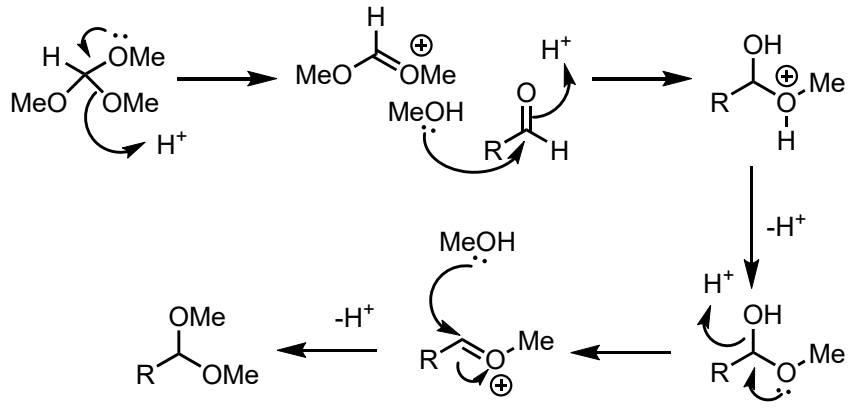


intermediate after step b:

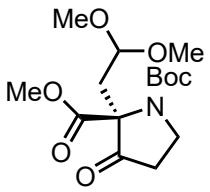




Step c mechanism:



intermediate after step c:



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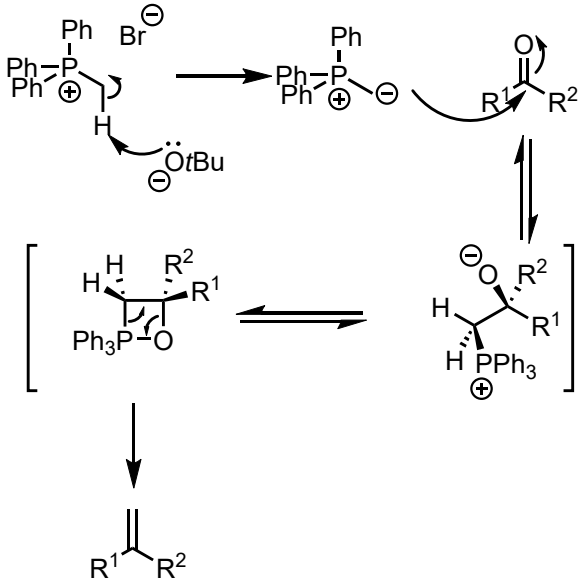
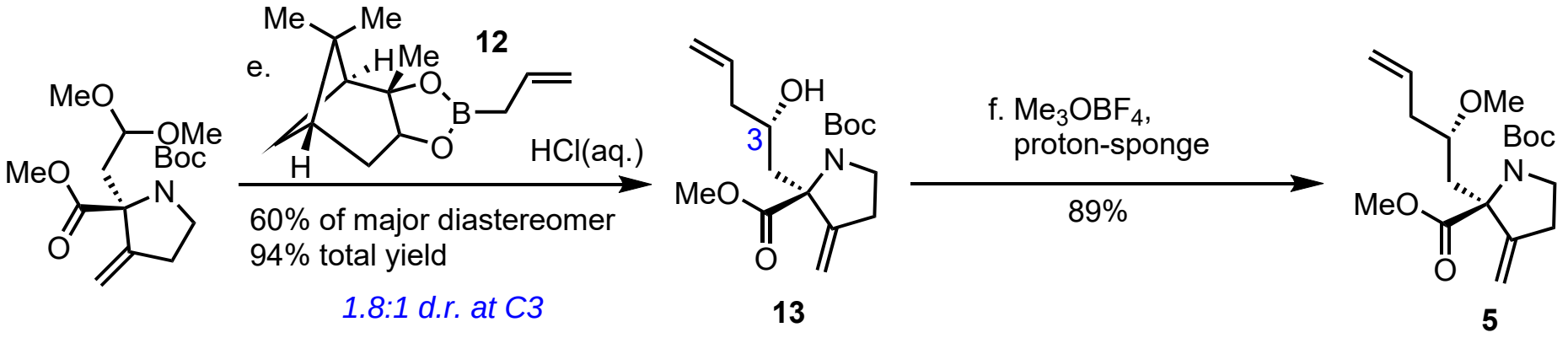
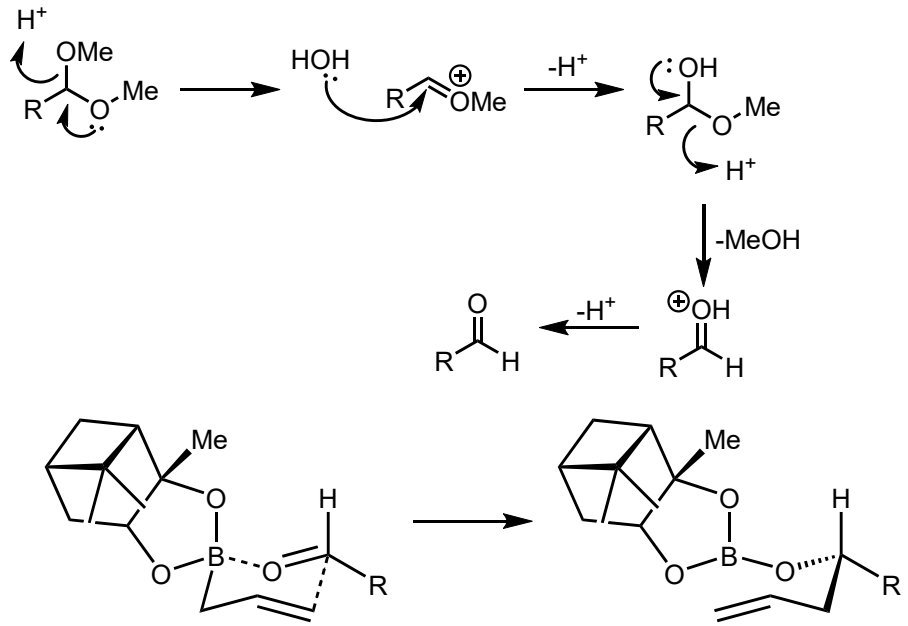
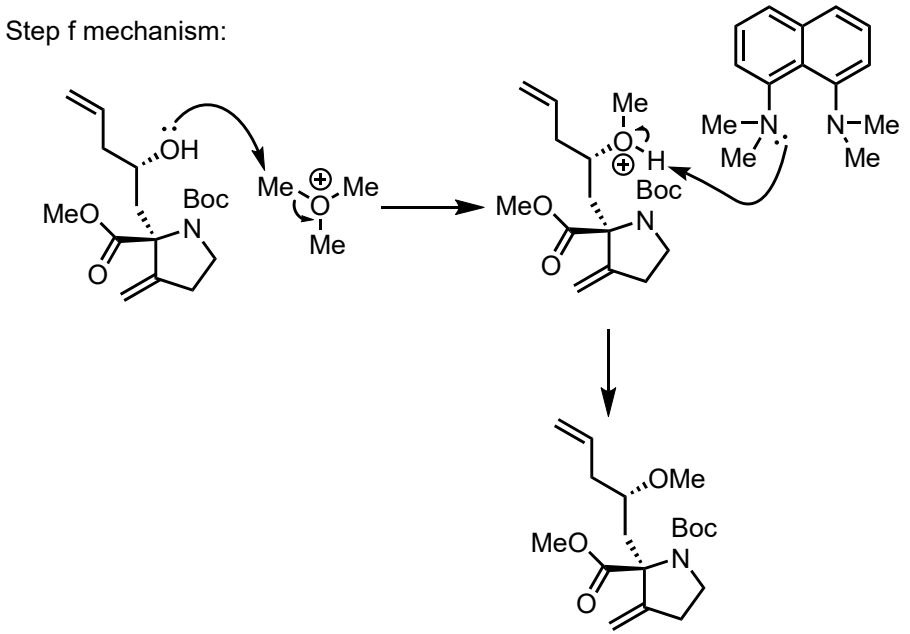


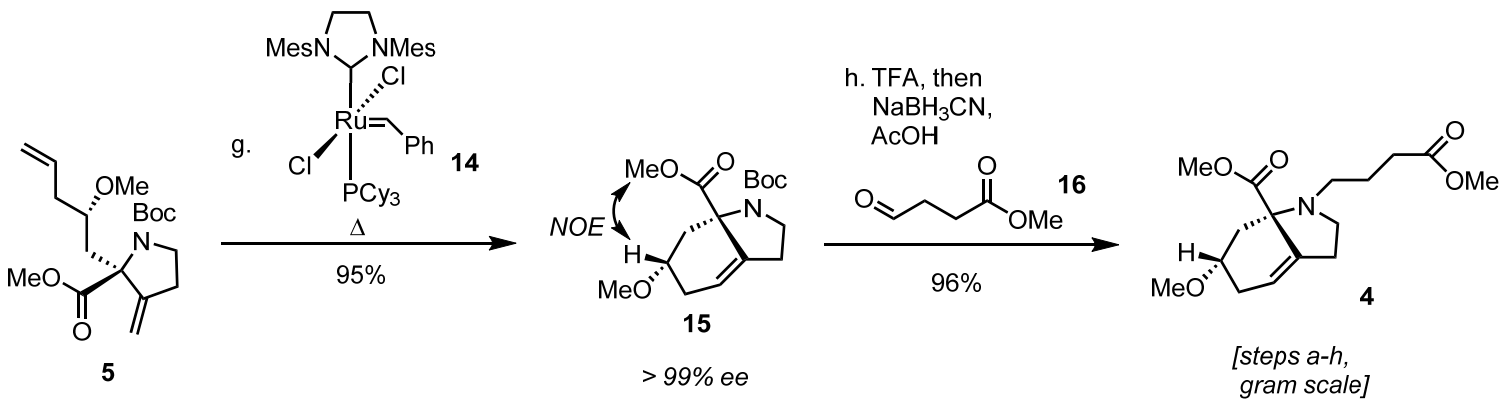


Step e mechanism:

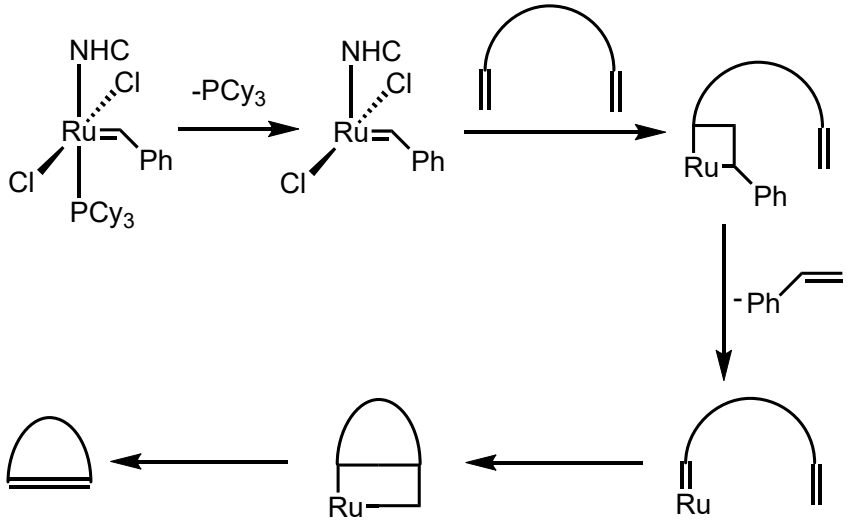


Step f mechanism:

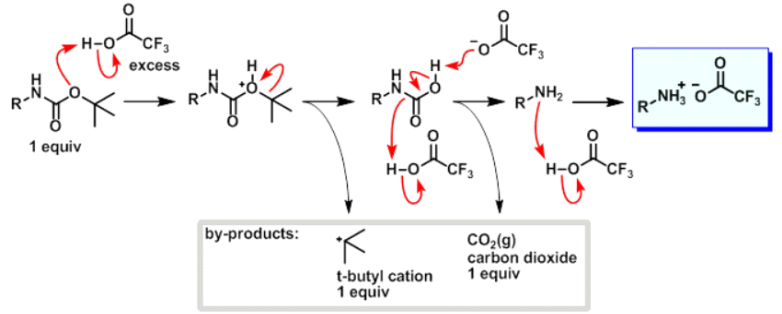




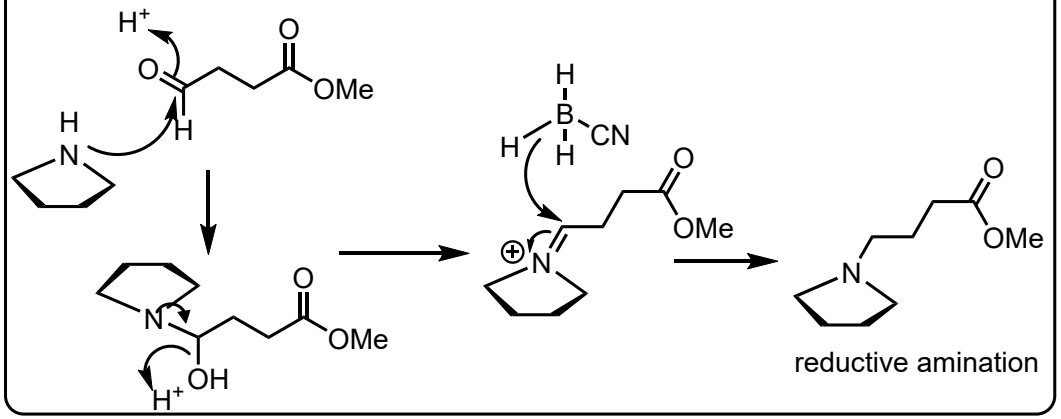
Step g mechanism:



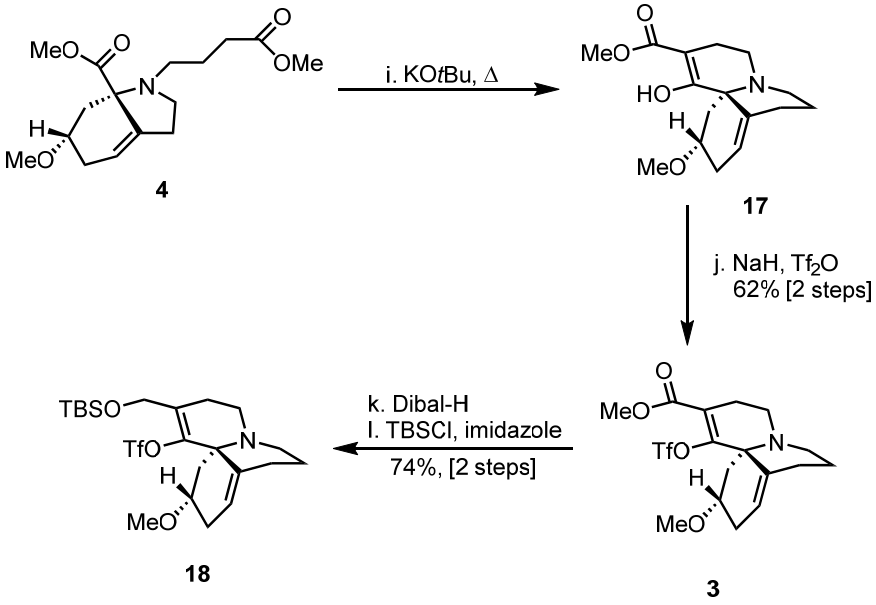
Step h mechanism:



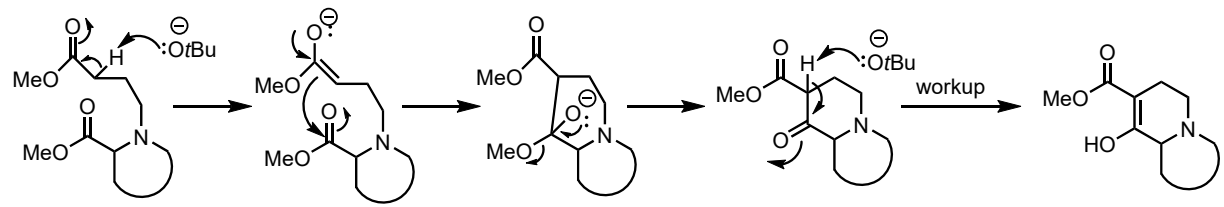
Boc deprotection:



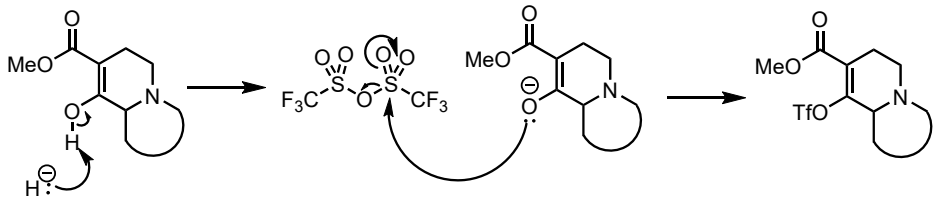
reductive amination



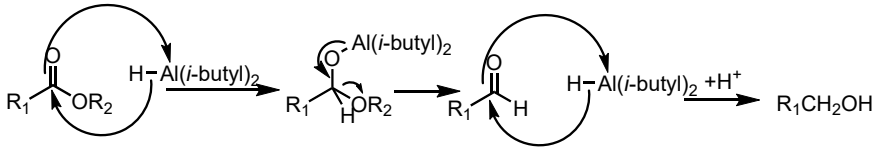
Step i mechanism:



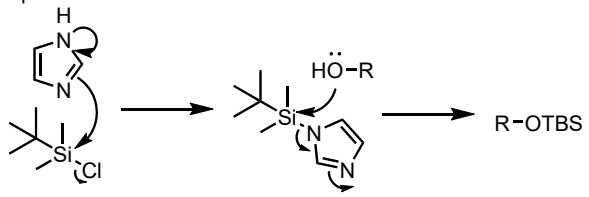
Step j mechanism:

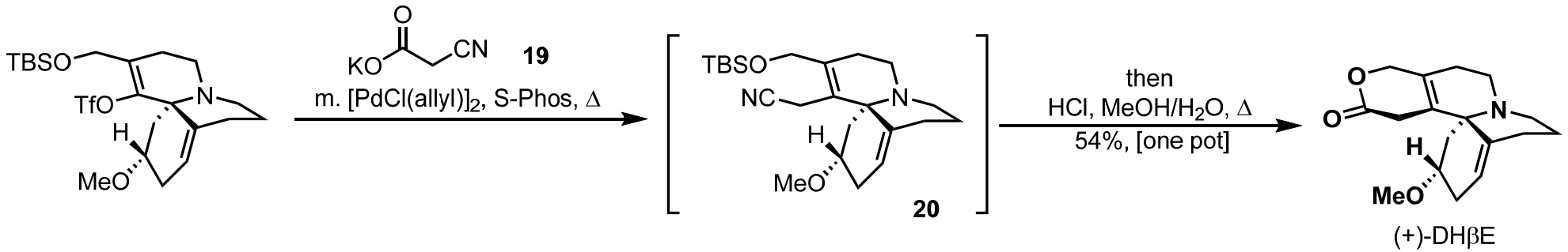


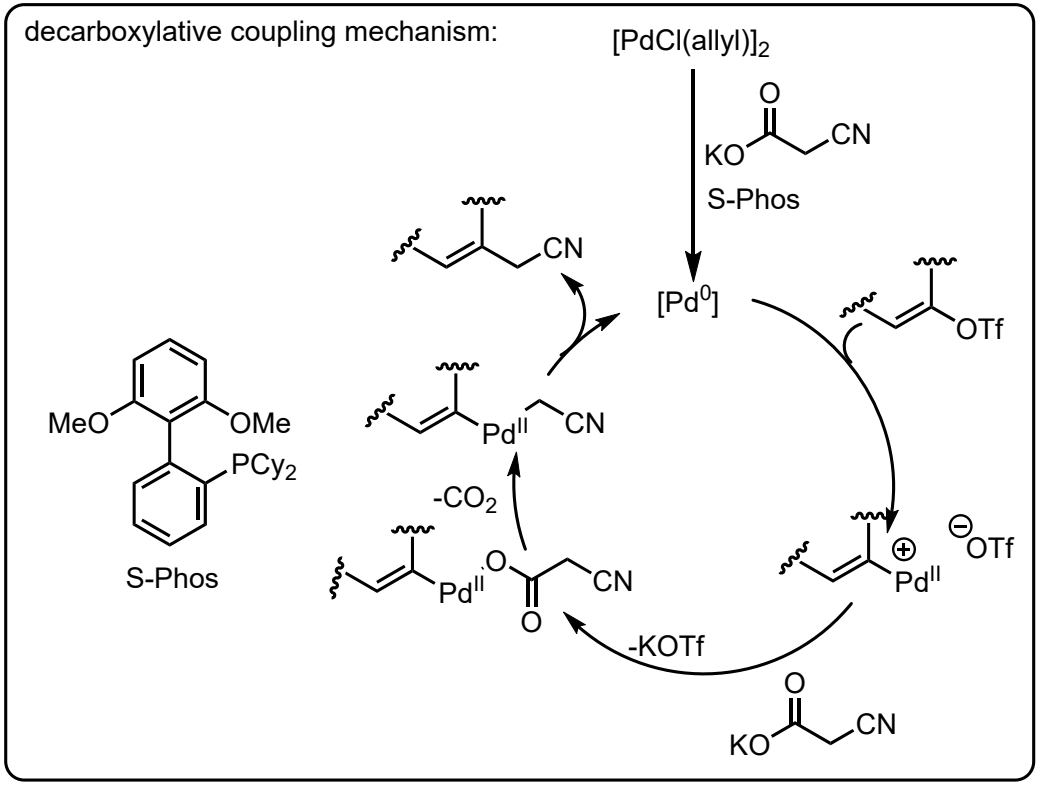
step k mechanism:

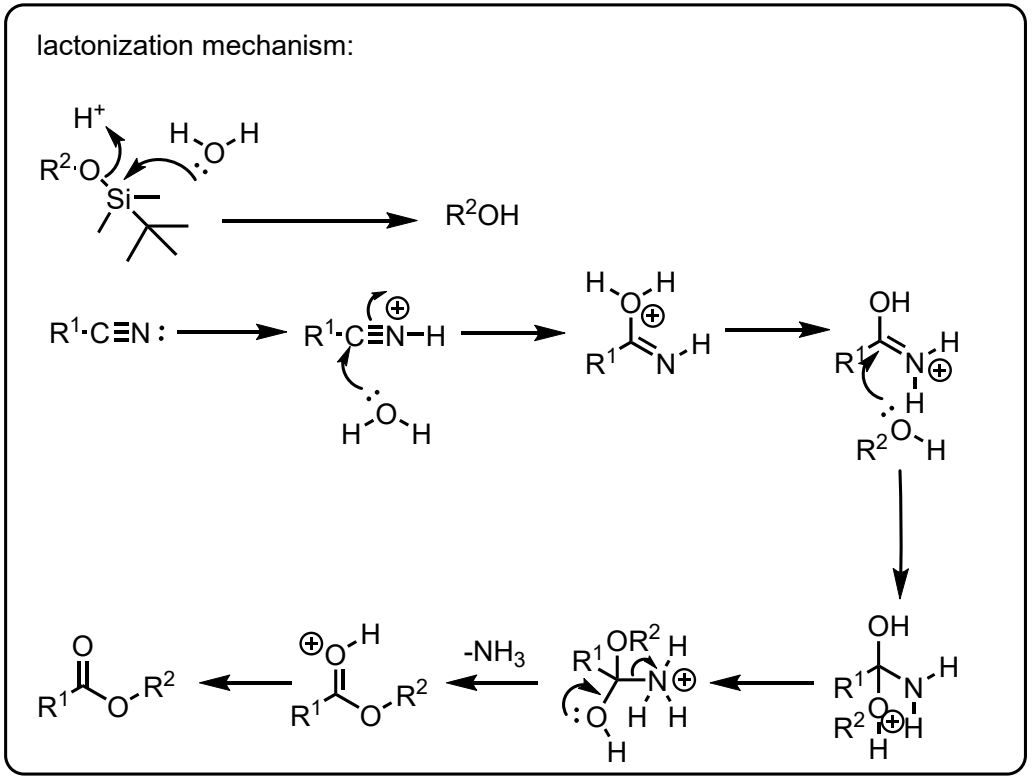


step l mechanism:




TBSO
TfO
H
MeO
N
KO
CN
19
m. [PdCl(allyl)]2, S-Phos, Δ
TBSO
NC
H
MeO
20
then
HCl, MeOH/H2O, Δ
54%, [one pot]
O
O
N
H
MeO
(+)-DHβE


decarboxylative coupling mechanism:
[PdCl(allyl)]2
KO
CN
S-Phos
[Pd0]
CN
OTf
MeO
OMe
PCy2
S-Phos
PdII
CN
-CO2
PdII
O
CN
O
PdII
OTf
-KOTf
KO
CN


lactonization mechanism:
H+
R2O
Si
H
O
H
R2OH
R1C≡N:
R1
C
N
H
O
H
H
O
H
R1
N
H
OH
R1
N
H
H
R2
O
H
OH
R1
N
H
R2
O
H
H
R1
OR2
H
N
O
H
H
H
-NH3
O
H
R1
O
R2
R1
O
R2
O
R1
O
R2