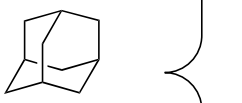
Problem Session (3) 2019/09/07 Yun-wei Xue

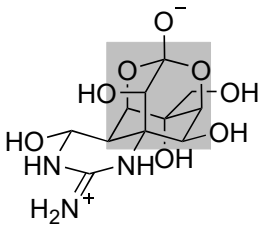
Topic: Adamantane-type natural products

0. Introduction

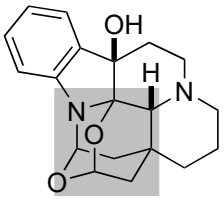
0.1 Structures



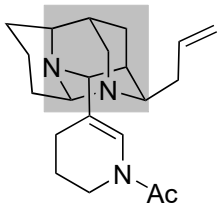
adamantane core structure



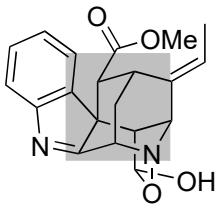
0-1
Tetrodotoxin
dioxa-adamantane



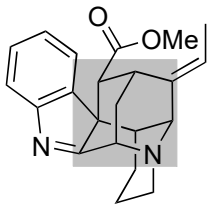
2-2
Terengganensine A
oxa, aza-adamtane
(problem 2)



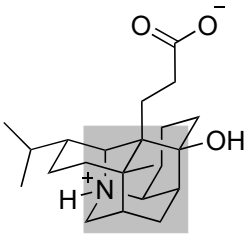
0-2
Panacosmine
diaza-adamtane



0-3
Nareline
aza-adamantane



0-4
Scholarisine H
aza-adamantane



0-5
Dapholdhamine B
aza-adamantane
(problem 1)

0.2 Total syntheses

0-1 Tetrodotoxin: Kishi, Y. *et al. J. Am. Chem. Soc.* **1972**, 94, 9219.
Ohyabu, N.; Nishikawa, T.; Isobe, M. *J. Am. Chem. Soc.* **2003**, 125, 8798.
Sato, K. *et al. J. Org. Chem.* **2005**, 70, 7496.
Bois, J. D. *et al. J. Am. Chem. Soc.* **2003**, 125, 11510.
Fukuyama, T. *et al. Angew. Chem., Int. Ed.* **2017**, 56, 1549.

2-2 Terengganensine A: Zhu, J. *et al. Angew. Chem., Int. Ed.* **2016**, 55, 6556. (problem 2)

aza-adamantane type

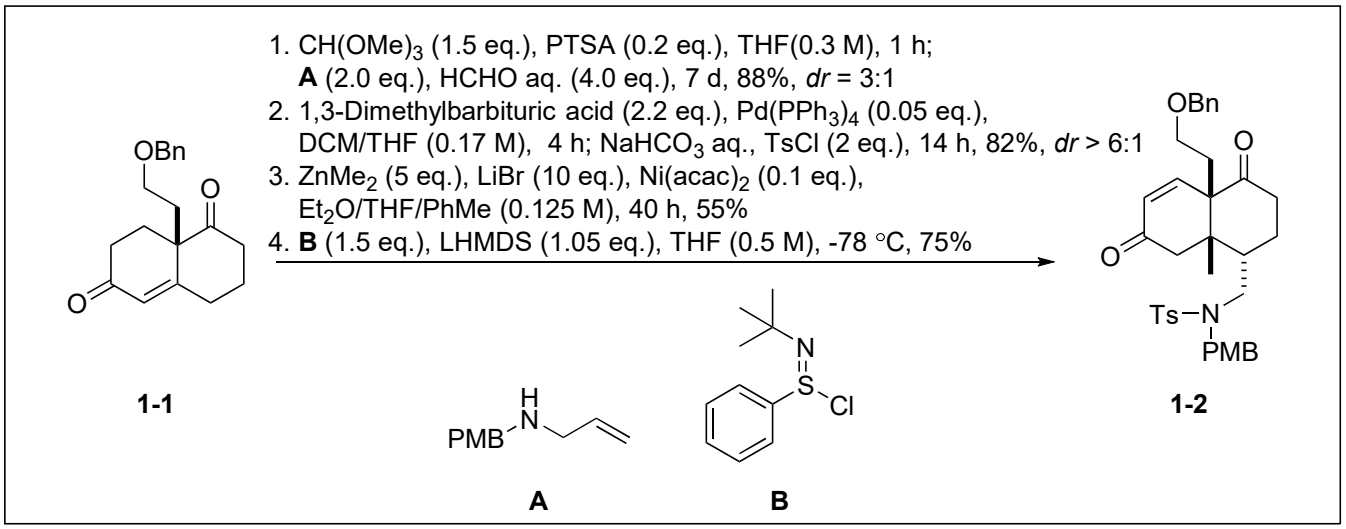
0-2 Panacosmine: no total synthesis reported

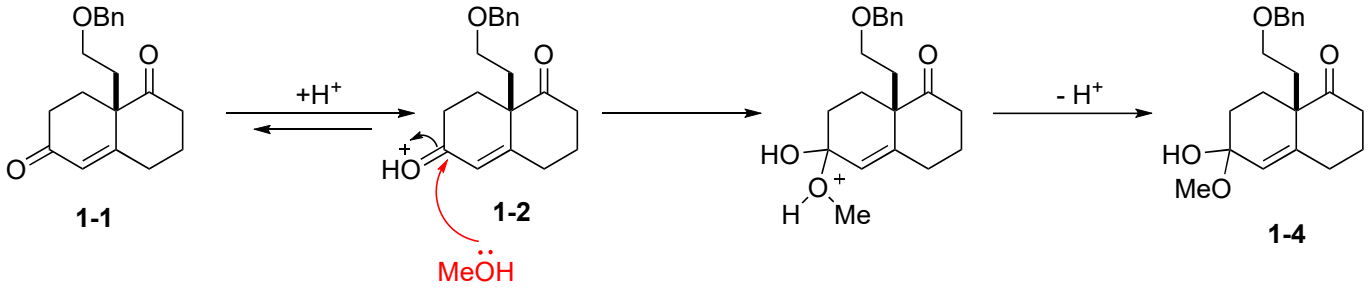
0-3 Nareline: no total synthesis reported

0-4 Scholarisine H: no total synthesis reported

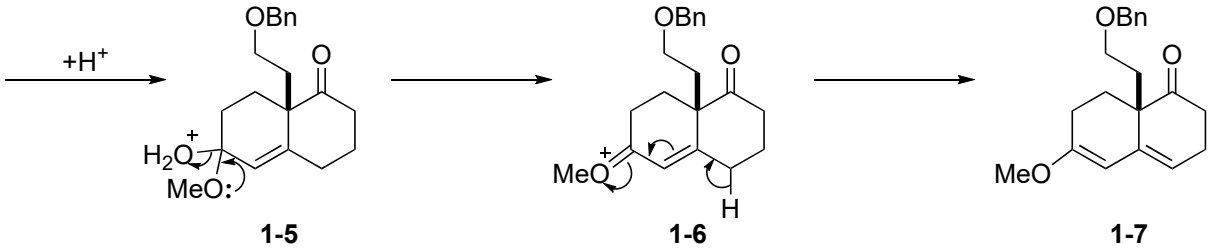
0-5 Dapholdhamine B: Xu, J. *et al. J. Am. Chem. Soc.* **2019**, 141, 11713. (problem 1)

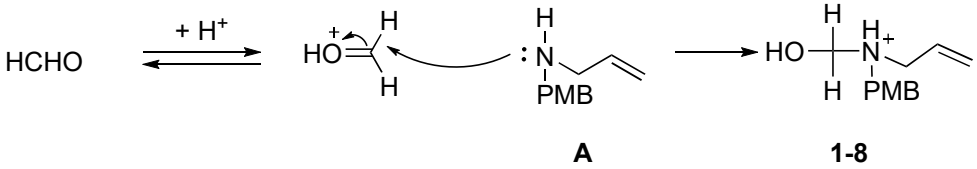
1-1. Reaction and mechanism

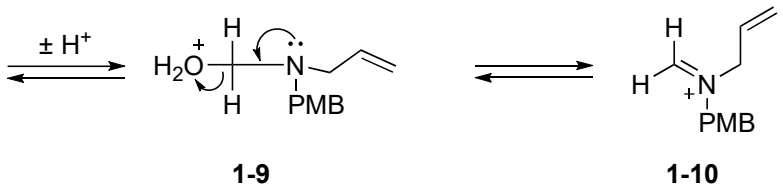


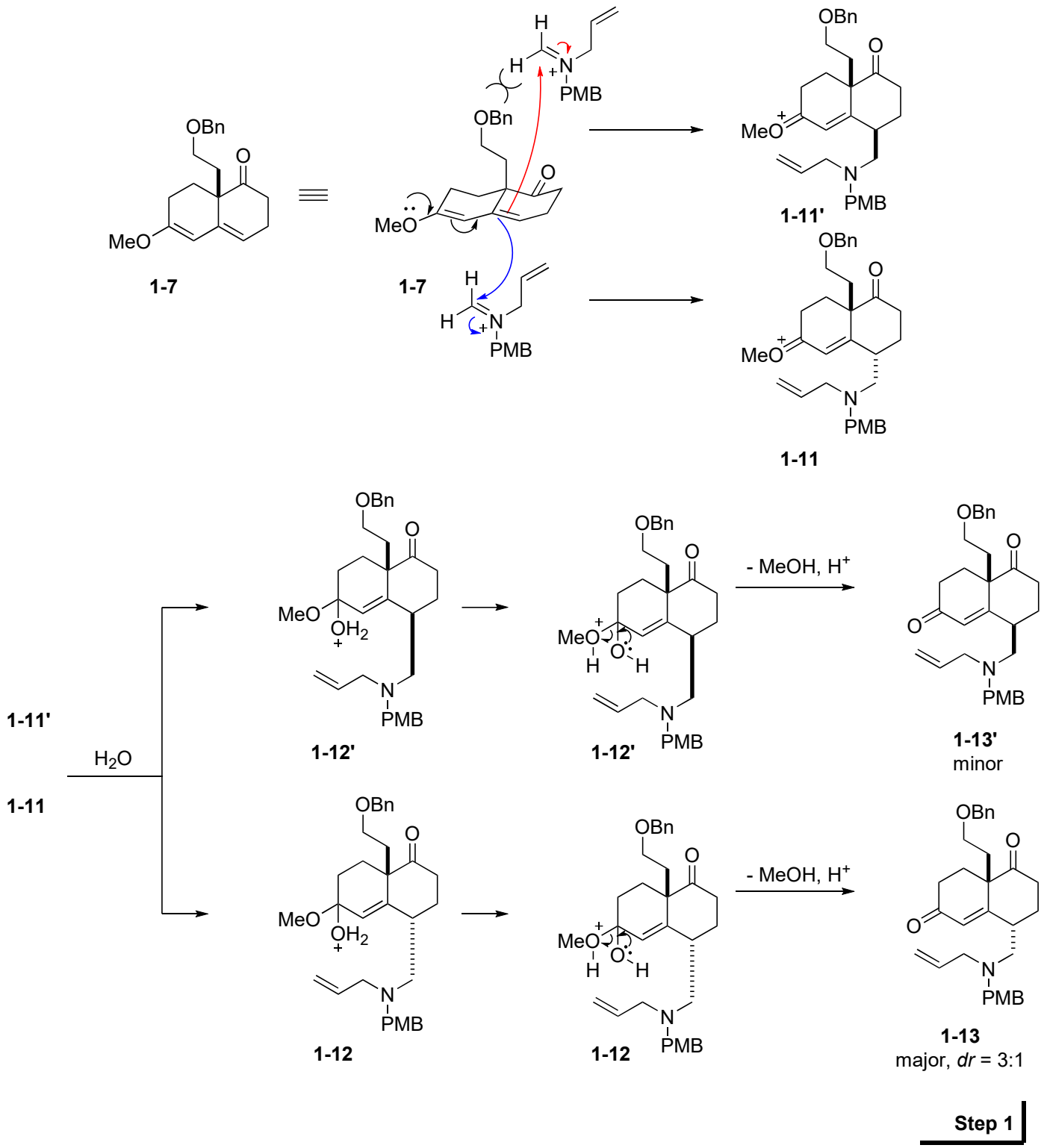


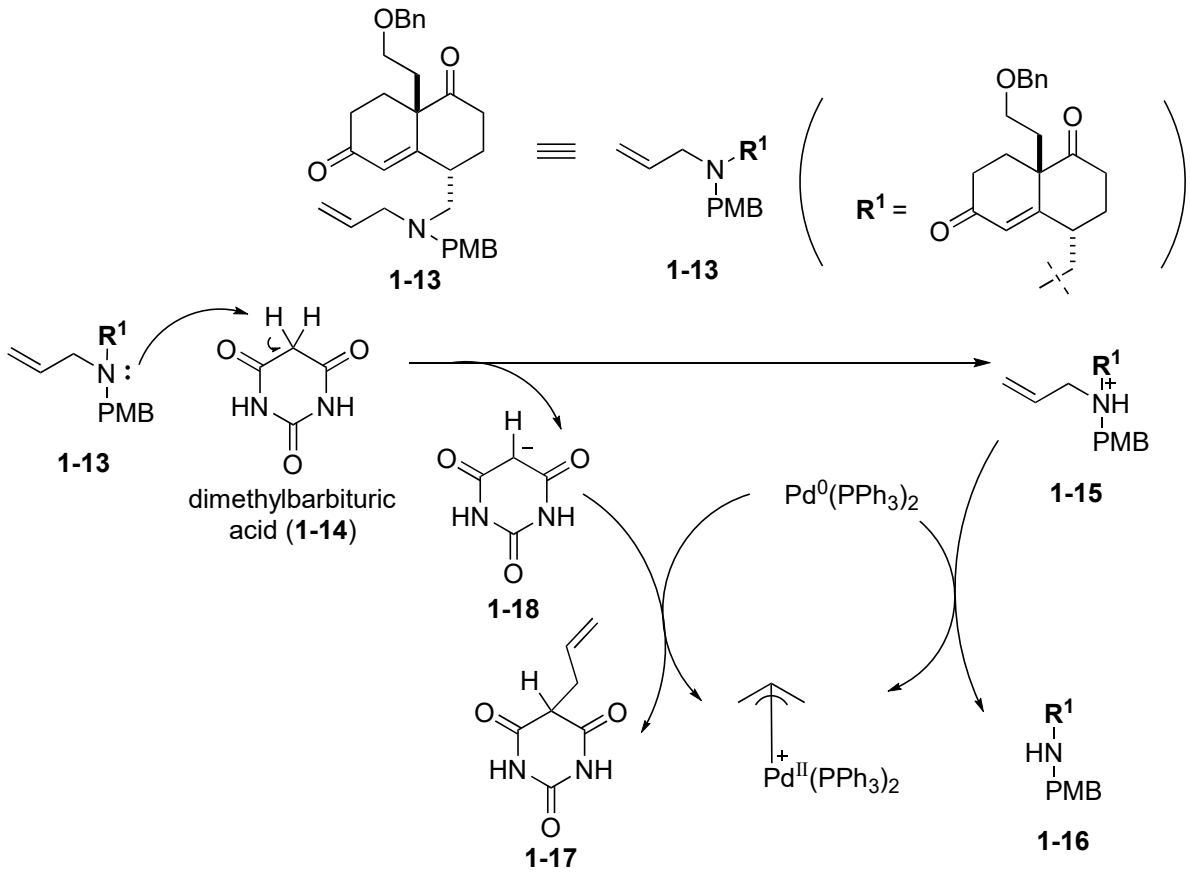
*$CH(OMe)_3$ as water scavanger.

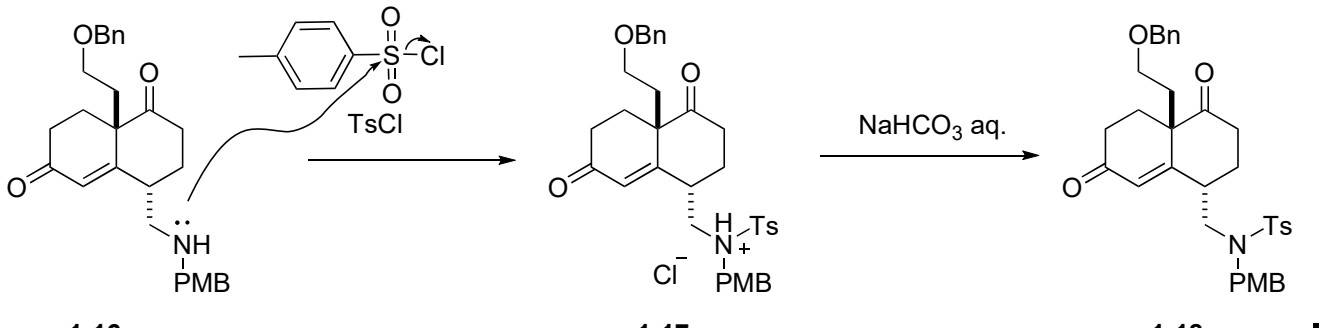


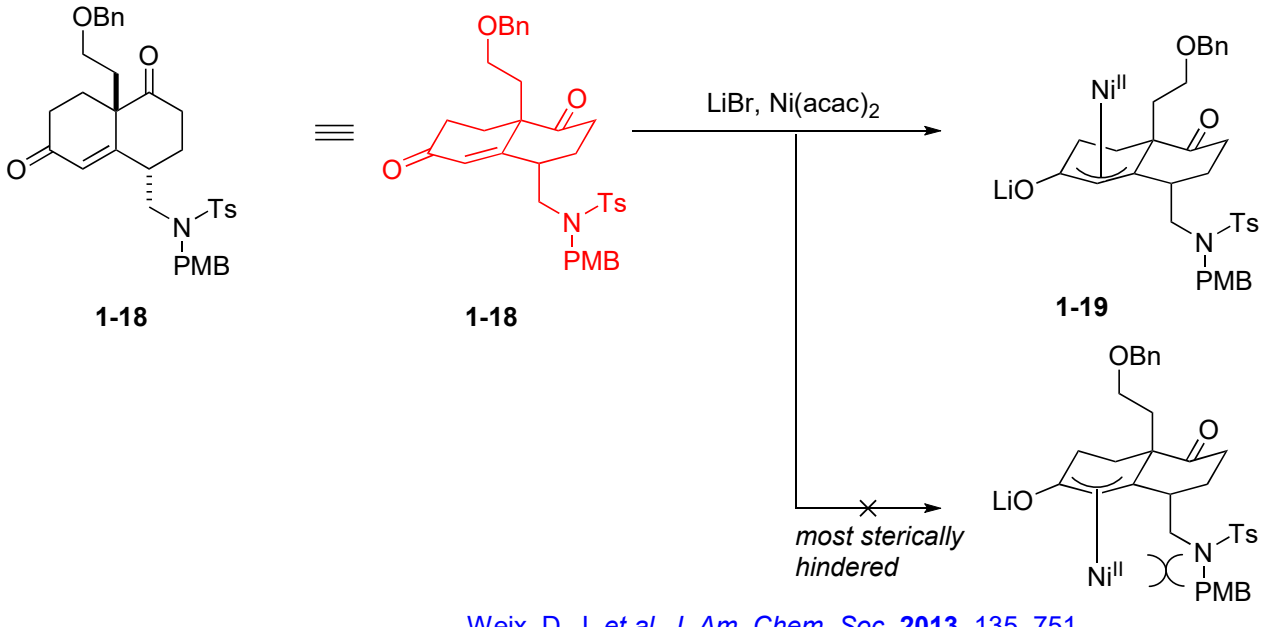




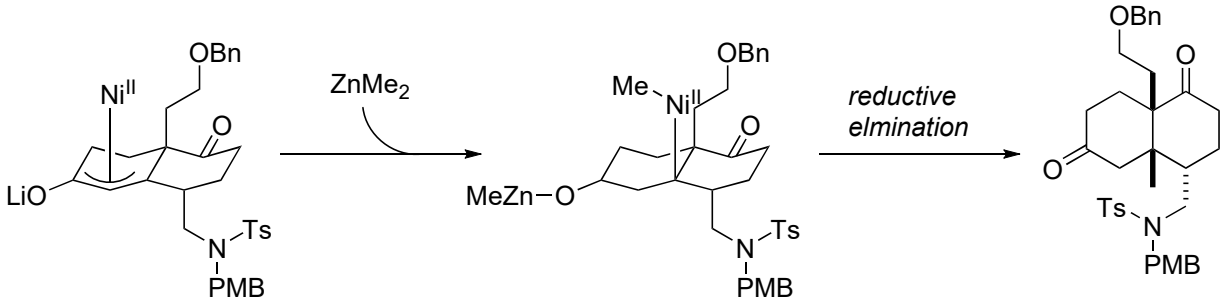

OBn
O
MeO
1-7
H
N
PMB
1-11'
1-11
H2O
OH2
1-12'
1-12
- MeOH, H+
1-13'
minor
1-13
major, dr = 3:1
Step 1







Weix, D. J. *et al. J. Am. Chem. Soc.* **2013**, 135, 751.

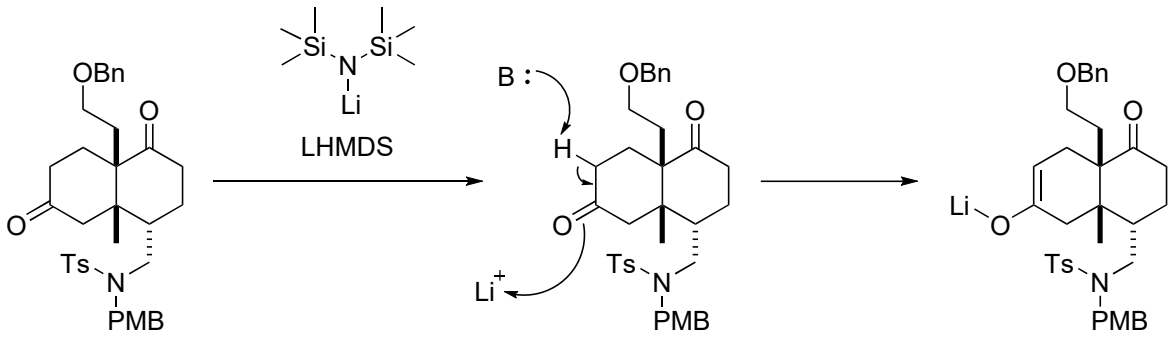


1-19 **1-20** **1-21**

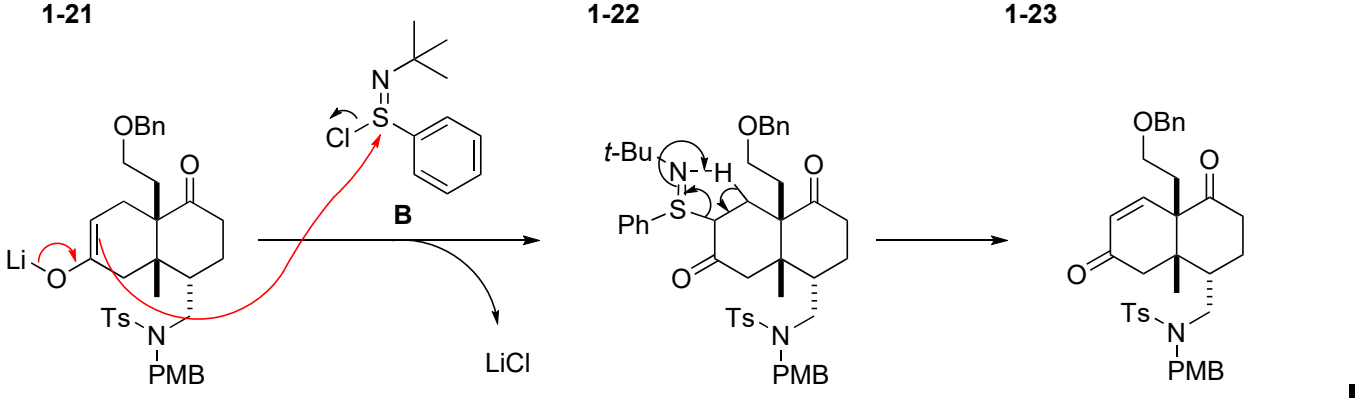
Kimura, M. *et al. Org. Lett.* **2011**, 13, 3552.

40 h, 55%
as single diastereomer

Step 3



1-21 **1-22** **1-23**

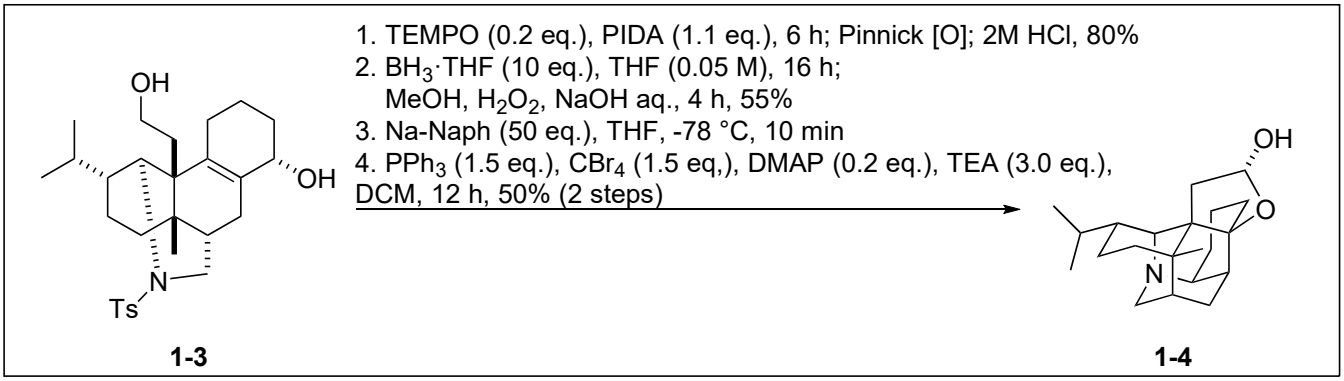


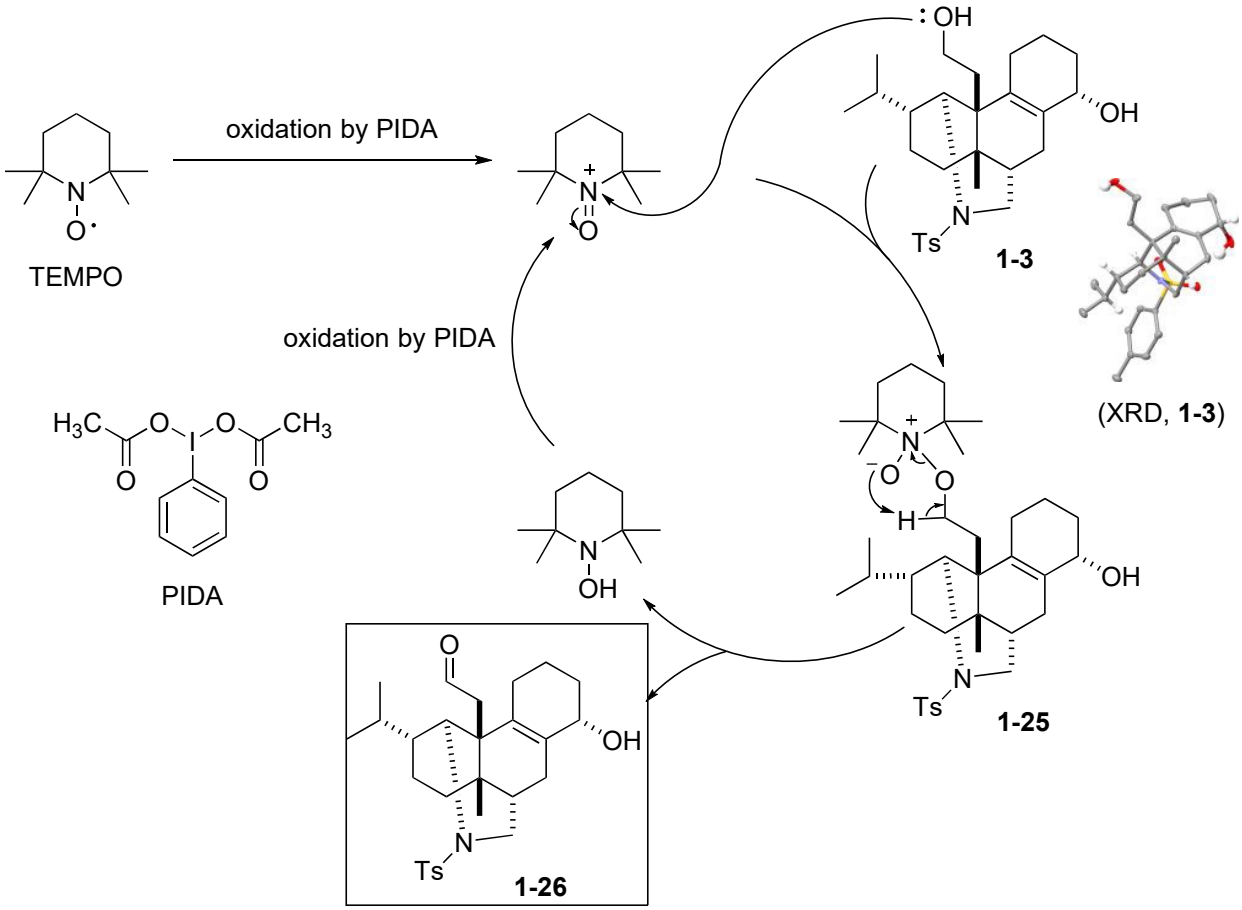
1-23 **1-24** **1-2**

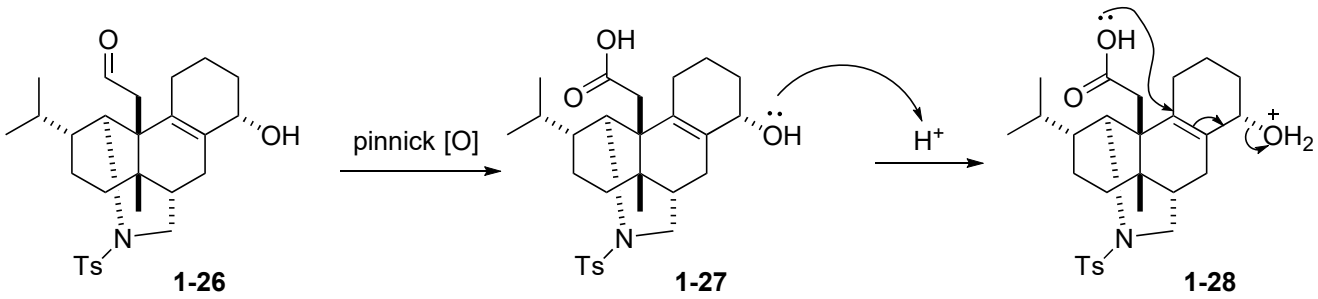
Step 4

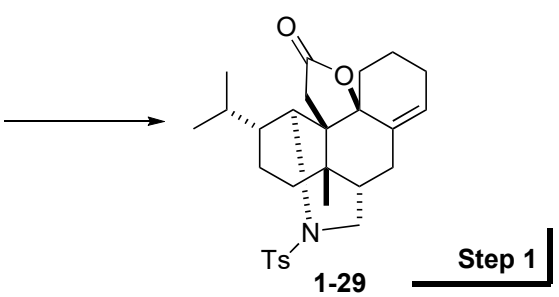
*Rather than a seven-membered ring,
this mechanism is more reasonable.

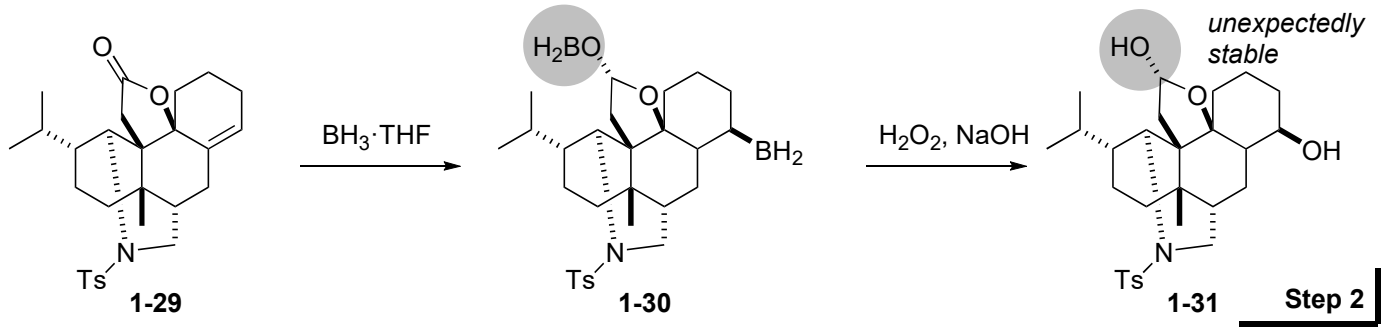
1-2. Reaction and mechanism

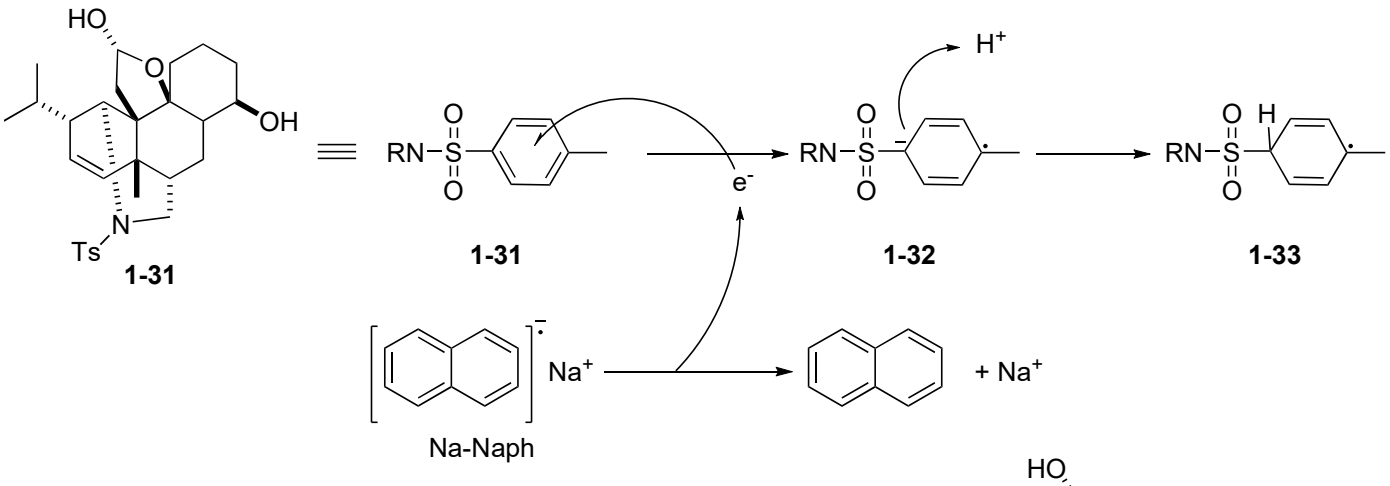


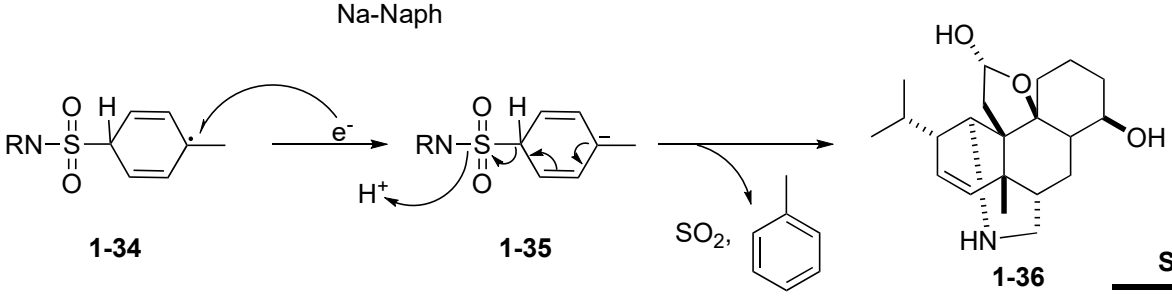


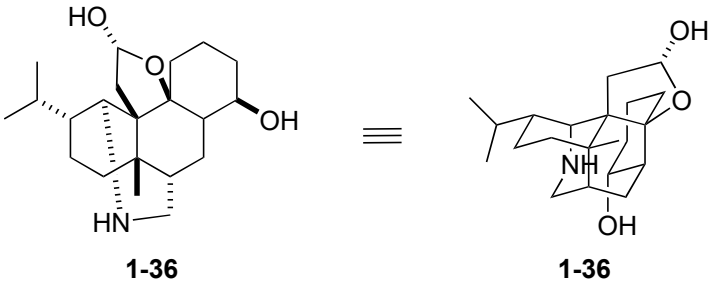


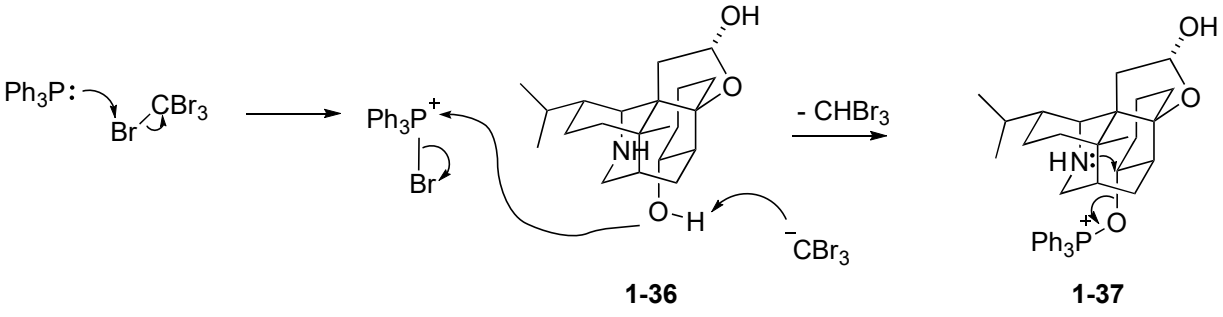


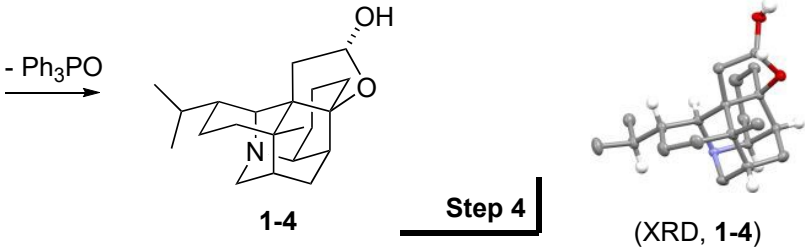

BH3·THF
H2O2, NaOH
unexpectedly stable
1-29
1-30
1-31
Step 2


1-31
1-31
1-32
1-33
Na-Naph

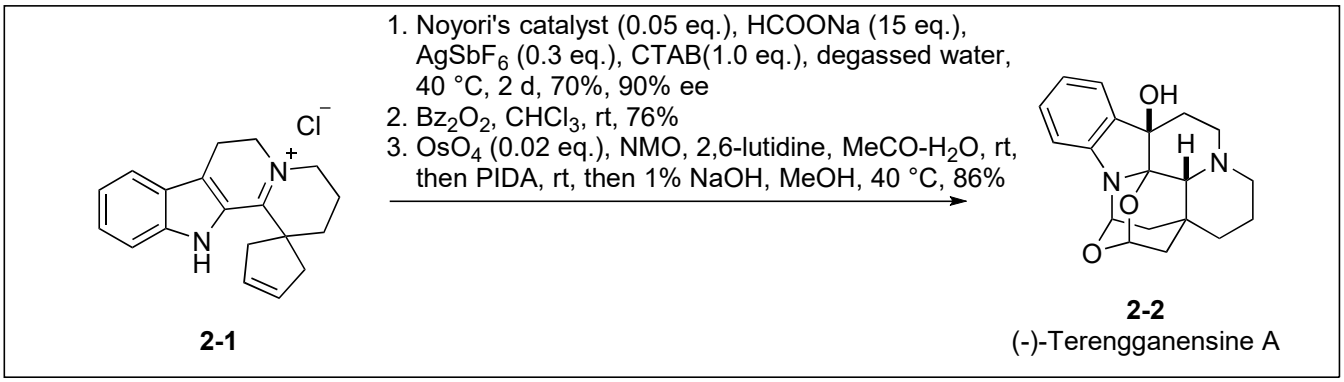

1-34
1-35
SO2,
1-36
Step 3

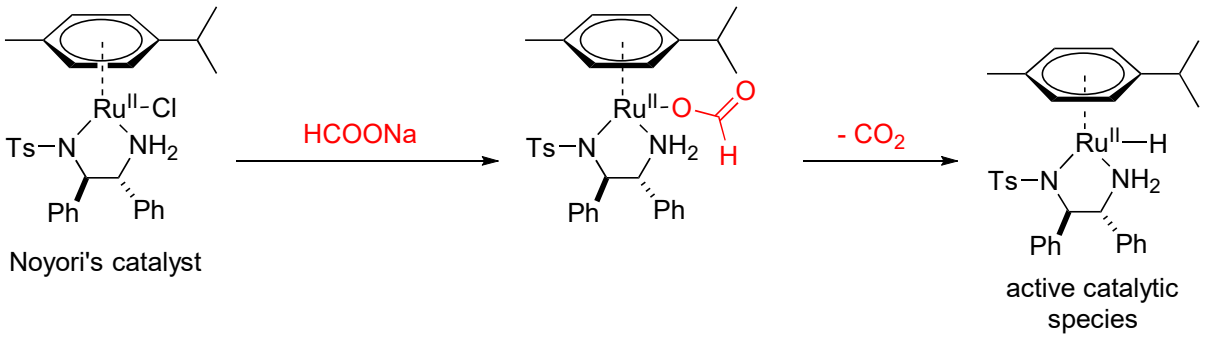

1-36
1-36

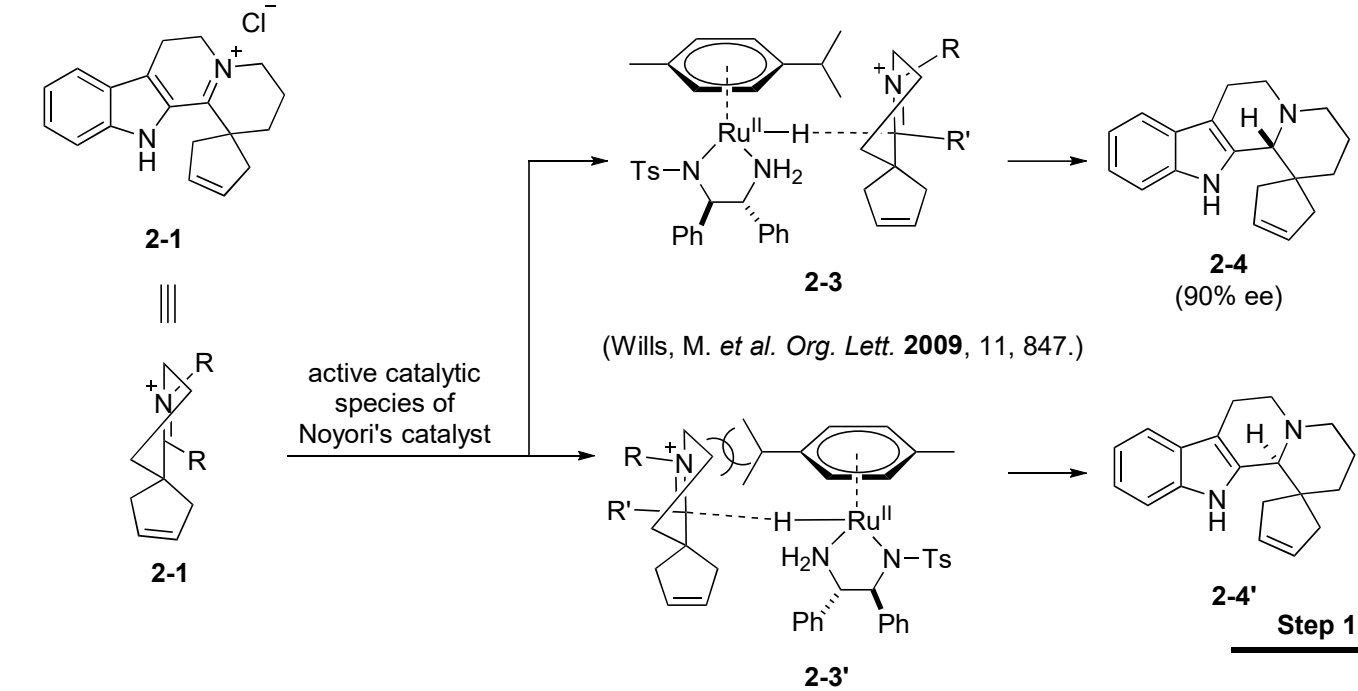

Ph3P:
CBr3
Br
Ph3P+
Br
- CHBr3
CBr3
1-36
1-37

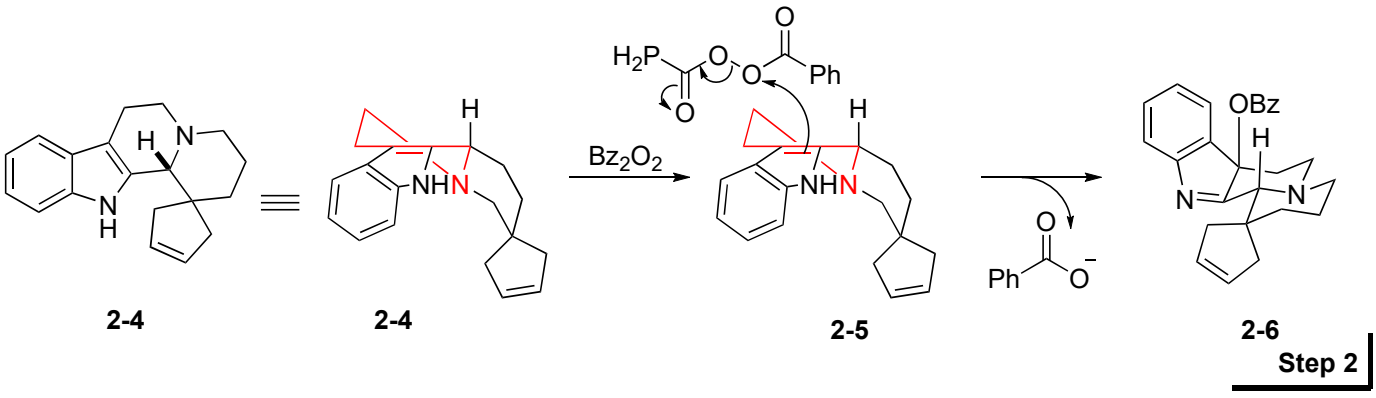

- Ph3PO
1-4
Step 4
(XRD, 1-4)

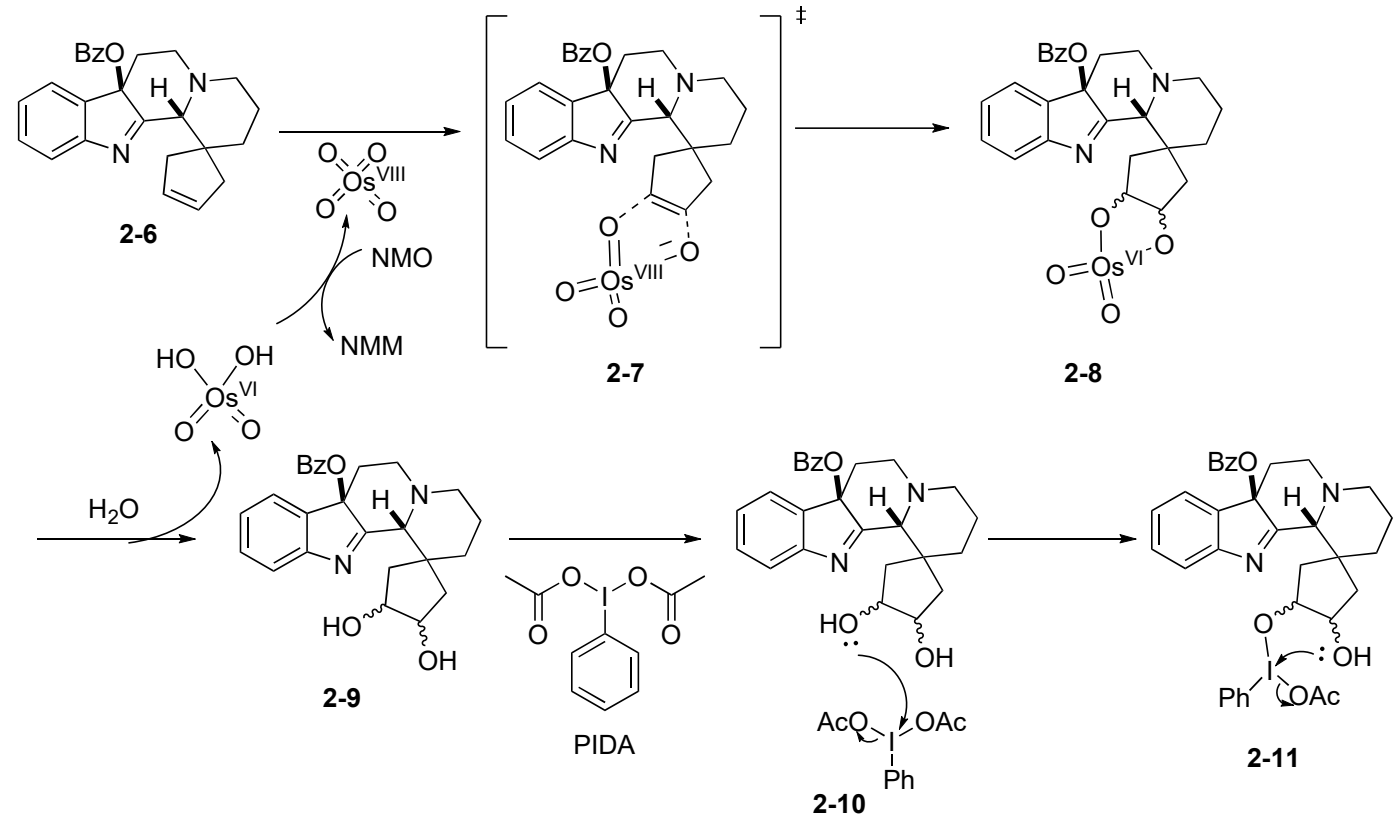
2-1. Reaction and mechanism

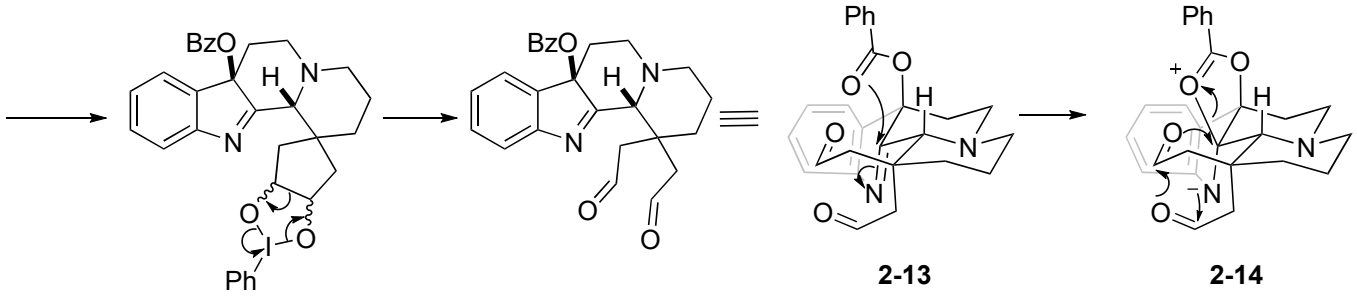


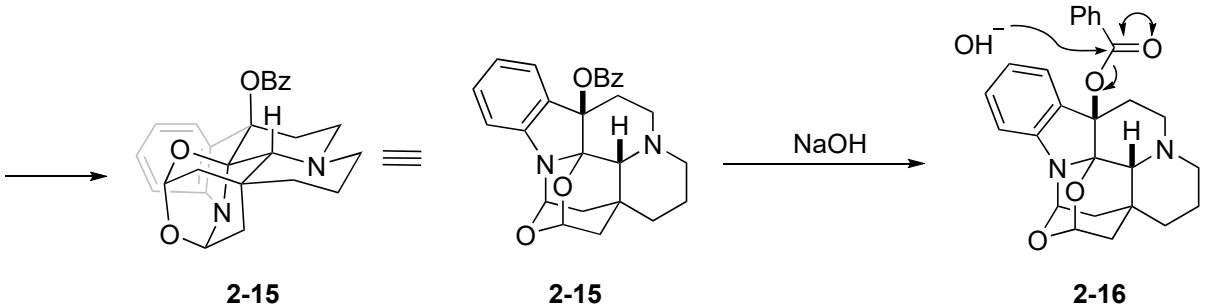


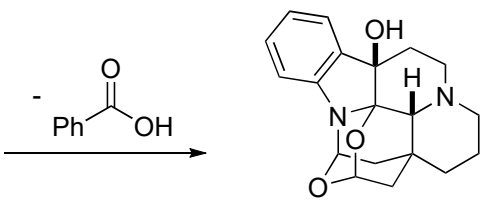












2-2
(-)-Terengganensine A

Step 3