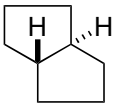
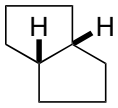
Problem Session (2) **2021.8.21 Risa Yoshinga**

Please explain the reaction mechanisms.

Topic: trans bicyclo[3.3.0]octane



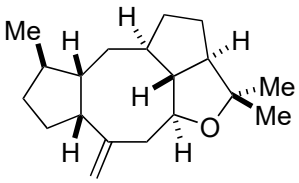
trans-fused [3.3.0]



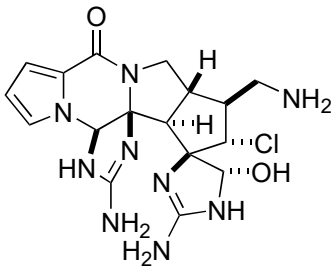
cis-fused [3.3.0]

Cal SE: Δ = ~13.0 kcal/mol
Exp SE: Δ = ~6.4 kcal/mol

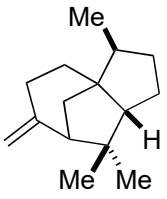
Natural products including trans bicyclo[3.3.0]octane



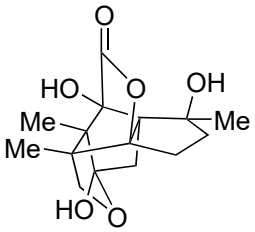
epoxydictymene



palau'amine

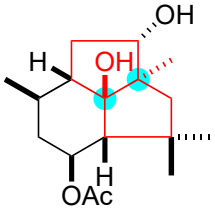


β-funebrene



illisimonin

Problem 1

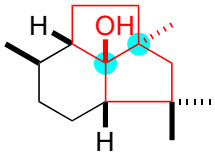


4β-Acetoxyprobotryane-9β, 15α-diol (1-2)

Isolation
R. Durán-Patro,; A. J. Colmenares,; R. Hernández-Galán,; I. G. Collado, *Tetrahedron,* **2001**, *57*, 1929.

Structural features
- Strained *trans* bicyclo[3.3.0]octane
- 7 Contifuous stereocenters: two vicinal quaternary
- No total synthesis reported

Problem 2



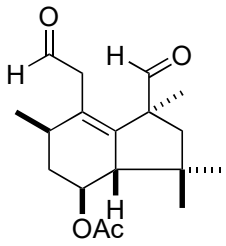
(−)-presilphiperfolan-8-ol

Isolation
Bohlmann, F.; Zdero, C.; Jakupovic, J.; Robinson, H.; King, R. M. *Phytochemistry* **1981**, *20*, 2239.

X-ray structure determination
Coates, R. M.; Ho, Z.; Klobus, M.; Wilson, S. R. *J. Am. Chem. Soc.* **1996**, *118*, 9249.

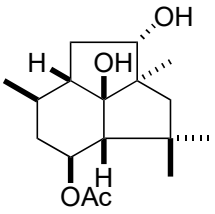
Structural features
- Strained *trans* bicyclo[3.3.0]octane
- 5 Contifuous stereocenters: two vicinal quaternary
- No total synthesis reported

problem 1



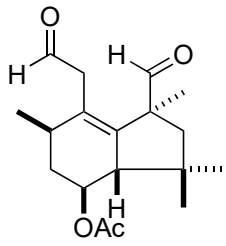
1-1

1. SmI_2 (2.0 eq), THF (0.2 M), 0 °C to 25 °C, 60%
2. 4-Acetamido-TEMPO (1.5 eq), PTSA (1.5 eq), CH_2Cl_2 (0.3 M), 0 °C, 78%
3. TESOTf (1.4 eq), Et_3N (1.5 eq), CH_2Cl_2 (0.9 M); *m*-CPBA (3.0 eq), $NaHCO_3$ (10.0 eq)
4. $LiN(TMS)_2$ (2.5 eq), THF (0.9 M);
5. Pd/C (0.07 w%), EtOAc (0.03 M), H_2 (50 bar), 64% (3 steps)
6. TBAF (4.0 eq), O_2 (balloon), THF (0.02 M), 78%
7. Red-Al (1.1 eq), CH_2Cl_2 (0.03 M), -25 °C; $Pb(OAc)_4$ (2.5 eq), EtOAc (15.5 M) 0 °C; K_2CO_3 (50.0 eq), MeOH (0.02 M)
8. BH_3/SMe_2 (3.0 eq), THF (0.03 M), 0 to 25 °C, 80%



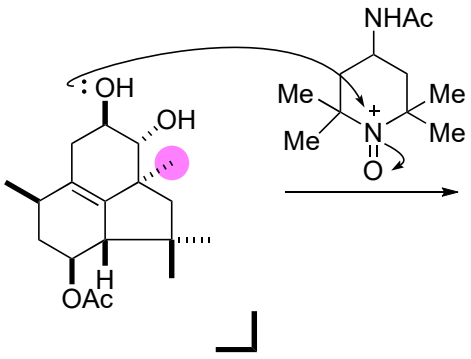
1-2

Zhang, W.; Zhou, Z. X.; Zhu, X. J.; Sun, Z. H.; Dai, W. M.; Li, C. C. *J. Am. Chem. Soc.* **2020**, *142*, 19868.



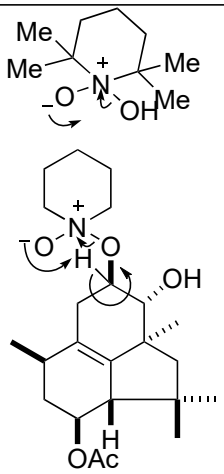
1-1

Discussion 1: stereoselectivity of SmI_2-mediated Pinacol Coupling



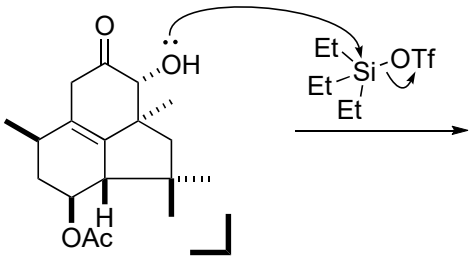
1-3

step 1



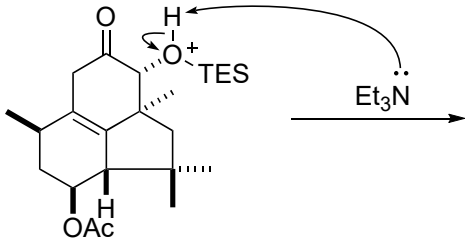
1-4

work up

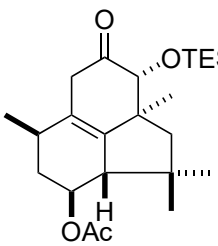


1-5

step 2

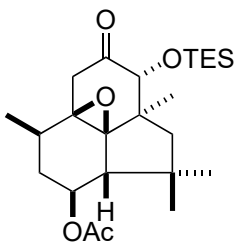


1-6



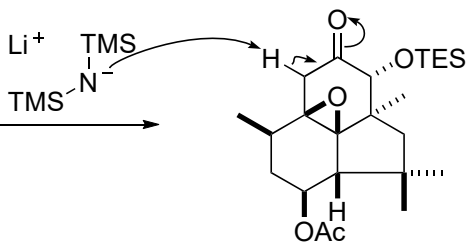
1-7

Discussion 2: stereoselectivity of Prilezhaev Epoxidation

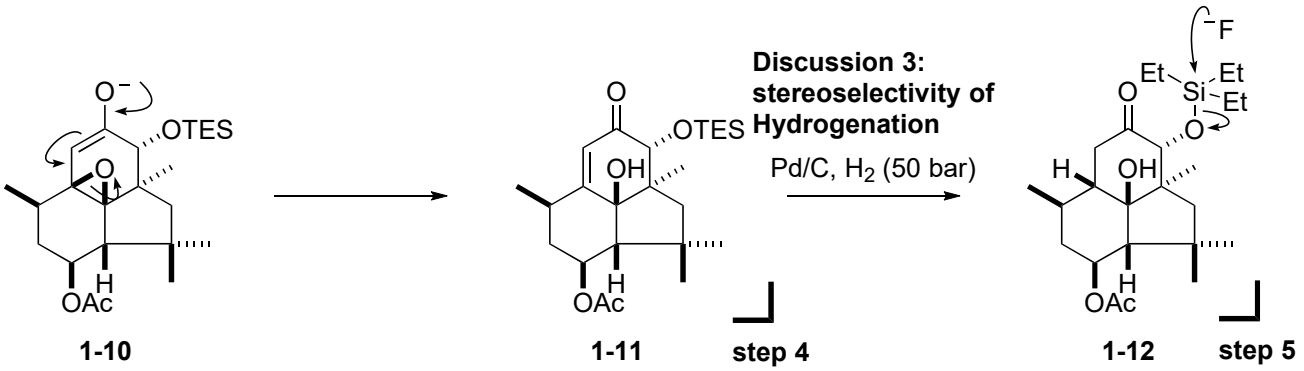


1-8

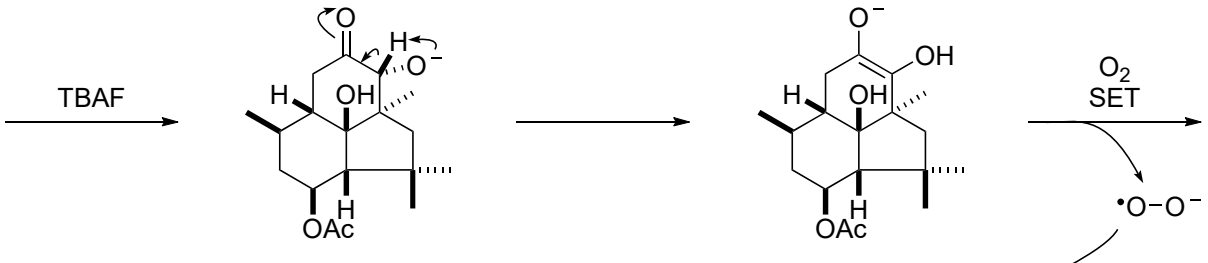
step 3



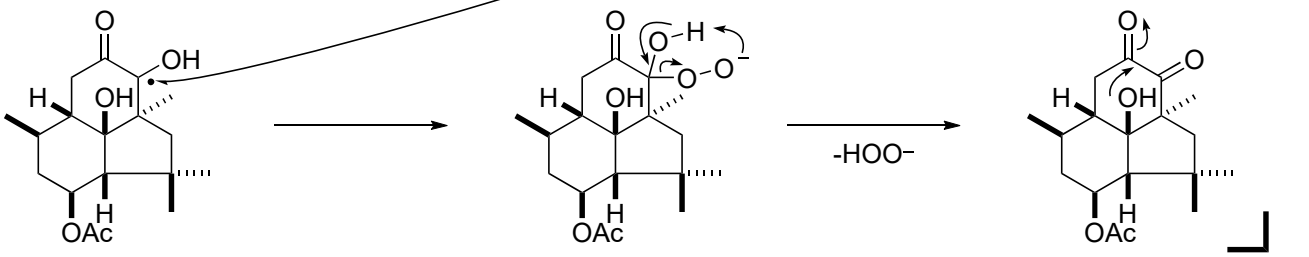
1-9



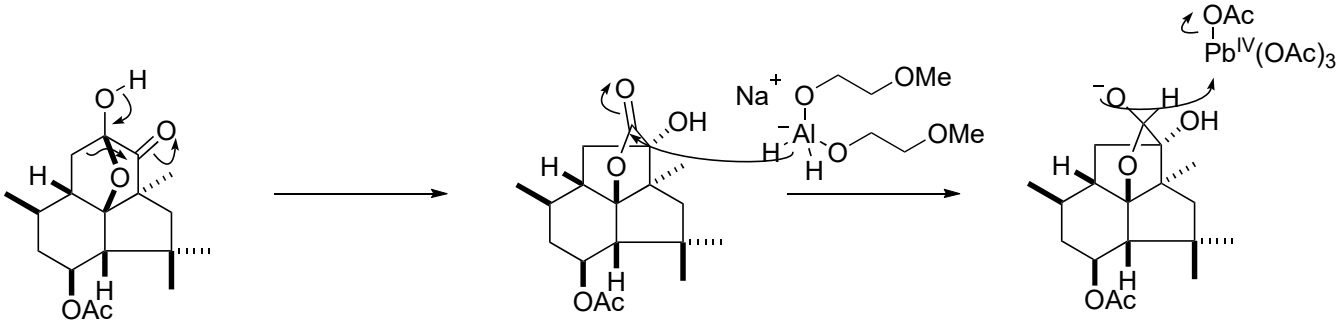
1-10 **1-11** **step 4** **1-12** **step 5**



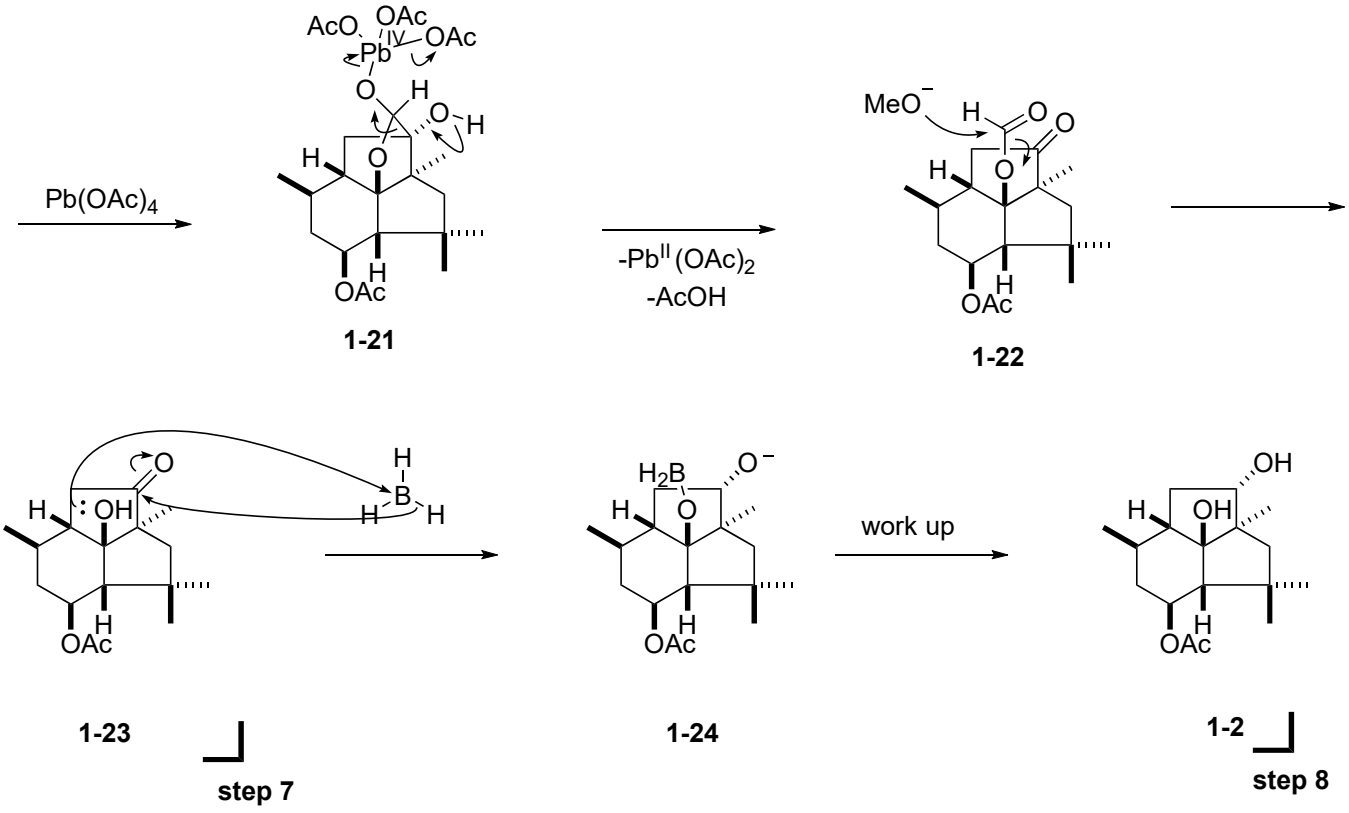
1-13 **1-14**



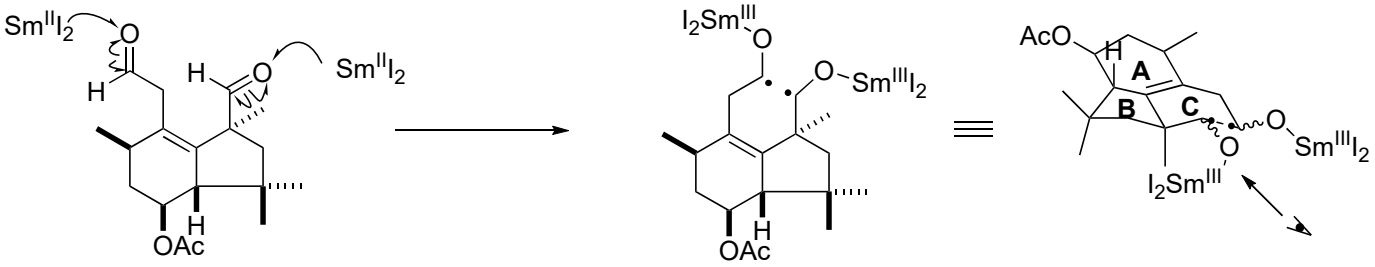
1-15 **1-16** **1-17** **step 6**



1-18 **1-19** **1-20**

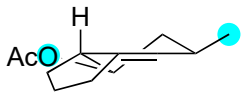

Pb(OAc)4
AcO
OAc
Pb
OAc
O
H
O
H
H
O
OAc
H
-PbII(OAc)2
-AcOH
MeO−
H
O
O
H
O
OAc
H
1-21
1-22
O
H
H
B
H
H
: OH
OAc
H
H2B
O−
H
O
OAc
H
work up
OH
H
OH
OAc
H
1-23
step 7
1-24
1-2
step 8

Discussion 1: stereoselectivity of SmI_2-mediated Pinacol Coupling



1-1 **1-25**

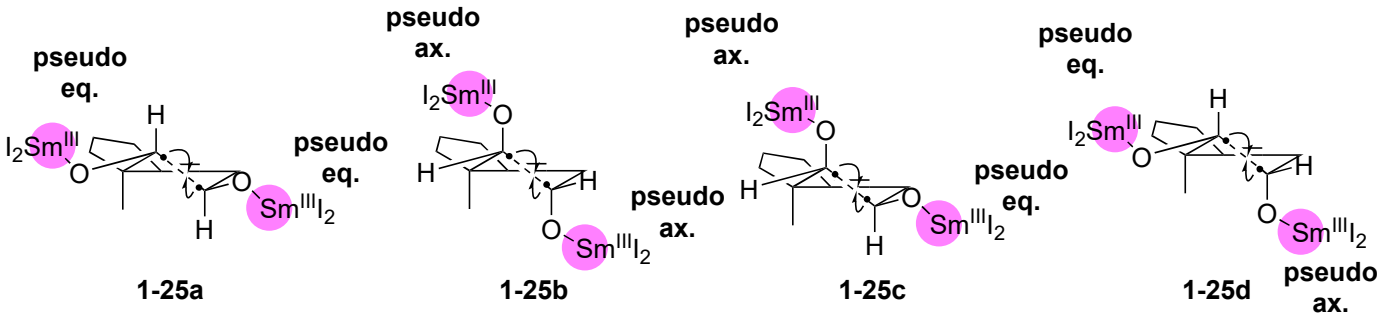
A ring



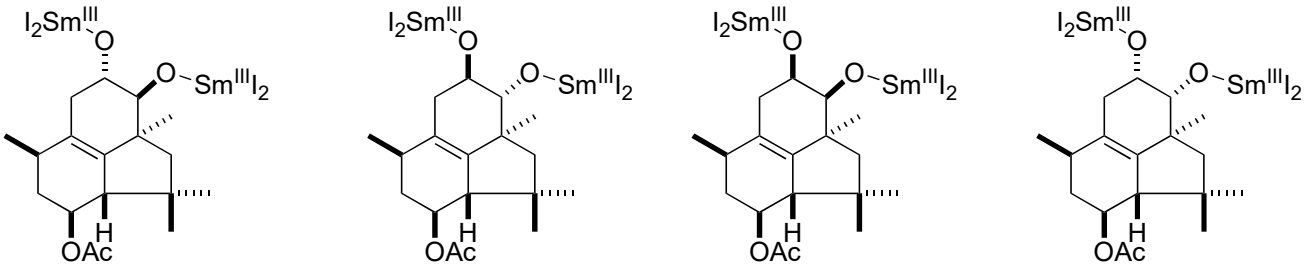
C ring

a **b** **c** **d**

pseudo eq. pseudo eq. pseudo ax. pseudo ax. pseudo ax. pseudo eq. pseudo eq. pseudo ax.

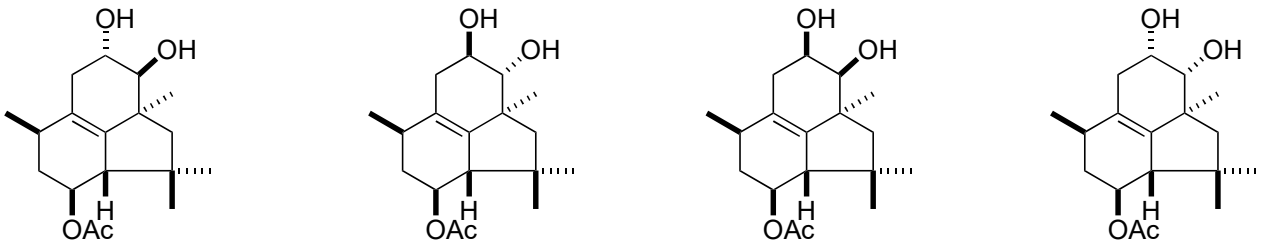


1-25a **1-25b** **1-25c** **1-25d**



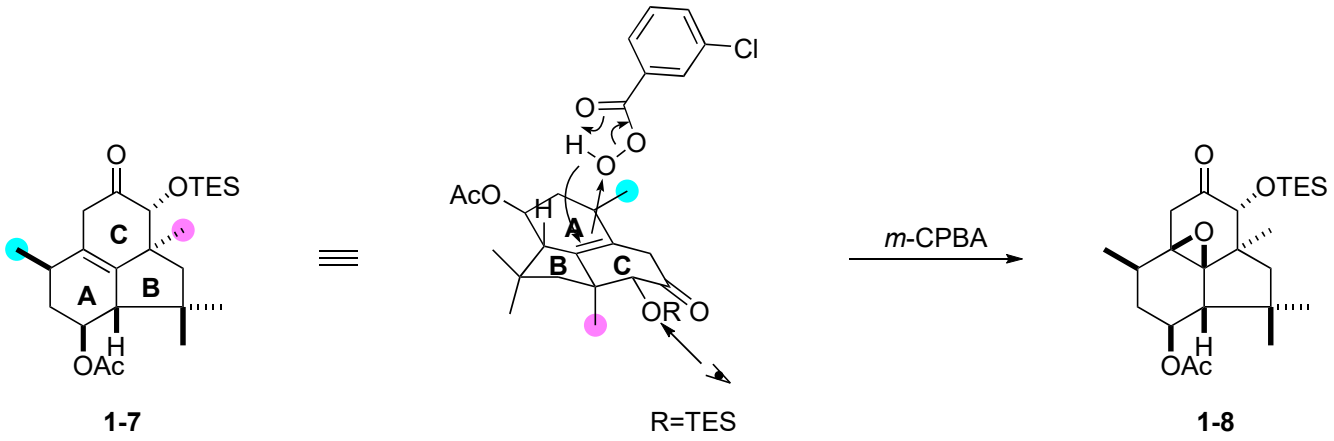
1-26a **1-26b** **1-26c** **1-26d**

work up work up work up work up



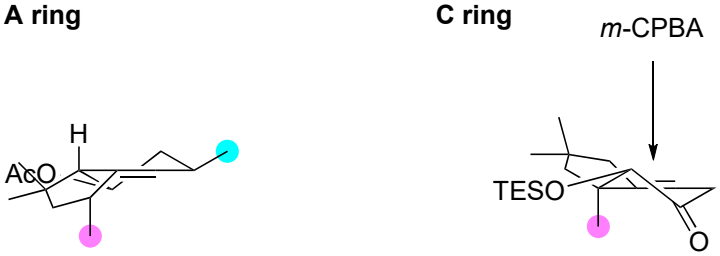
1-3a **1-3b** **1-3c** **1-3d**

Discussion 2: stereoselectivity of Prilezhaev Epoxidation

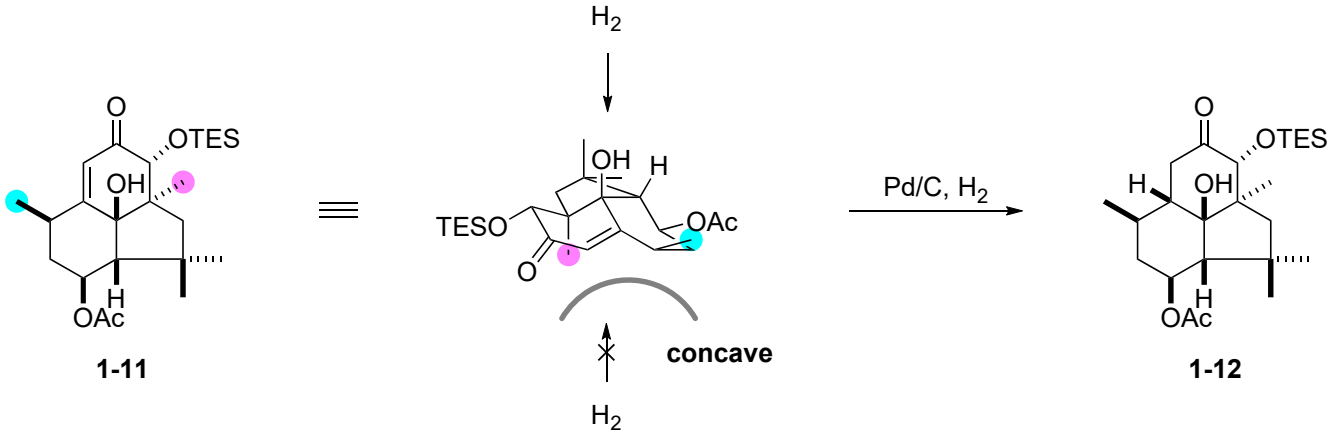


1-7 R=TES **1-8**

A ring **C ring**

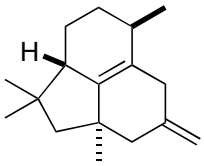


Discussion 3: stereoselectivity of Hydrogenation



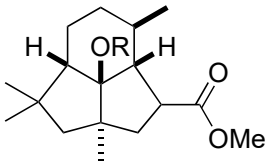
1-11 **1-12**

problem 2



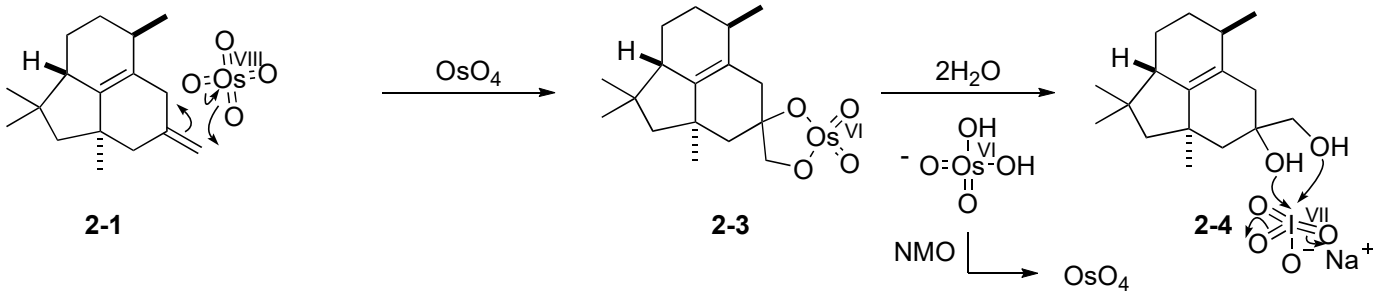
2-1

1. OsO_4 (14 mol%), NMO (4.3 eq), acetone : H_2O (3 : 3, 0.07 M), 23 °C;
   $NaIO_4$ (4.3 eq), 23 °C
2. *m*-CPBA (3.0 eq), $NaHCO_3$ (8.0 eq), CH_2Cl_2 (0.1 M), 23 °C
3. $LiN(TMS)_2$(3.0 eq), THF (0.1 M), -78 to 0 °C;
   MeOH (5.0 eq), 23 °C;
   $[Cu(PPh_3)_3H]_6$ (0.4 eq), benzene (0.2 M), 23 °C, 28% (4 steps)
4. TMSOTf (5.0 eq), Et_3N (6.0 eq), CH_2Cl_2 (0.1 M), 23 °C, quantitative
5. *p*-ABSA (20.0 eq), DBU (30.0 eq), CH_3CN (0.1 M), 23 °C, 95%
6. $h\nu$ (130 W Hg lamp), MeOH (0.04 M), Et_3N (1.4 eq), 83%

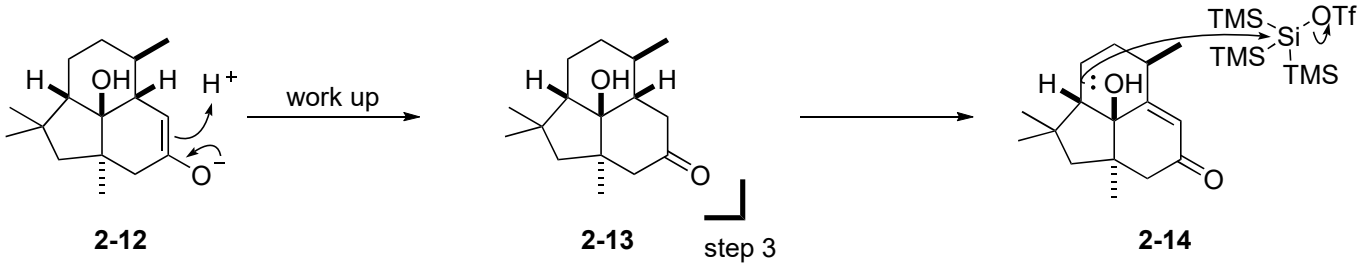


2-2

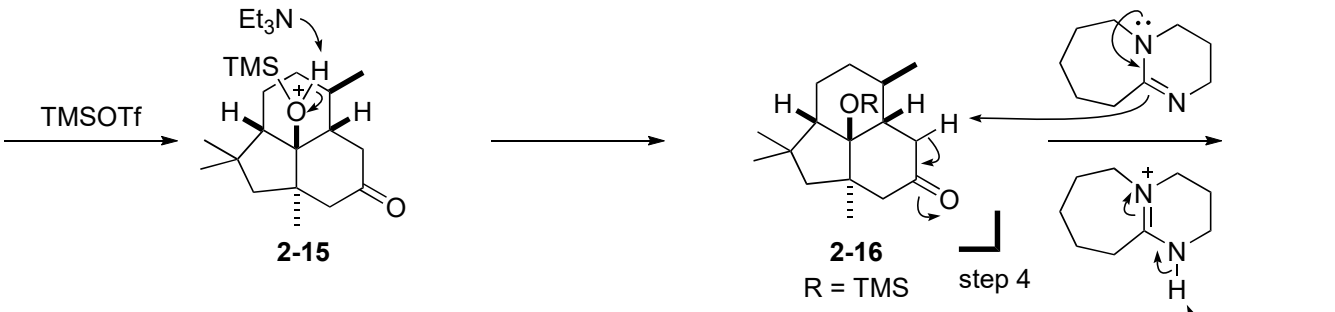
Hu, P.; Snyder, S. A. *J. Am. Chem. Soc.* **2017**, *139*, 5007.



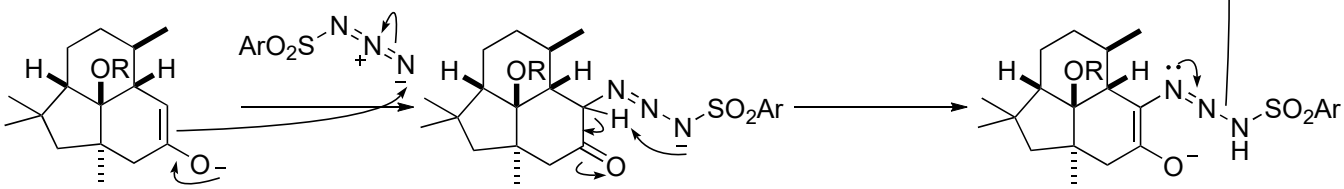
2-1 **2-3** **2-4** **2-5** **2-6** **2-7** **2-8** **2-9** **2-10** **2-11**



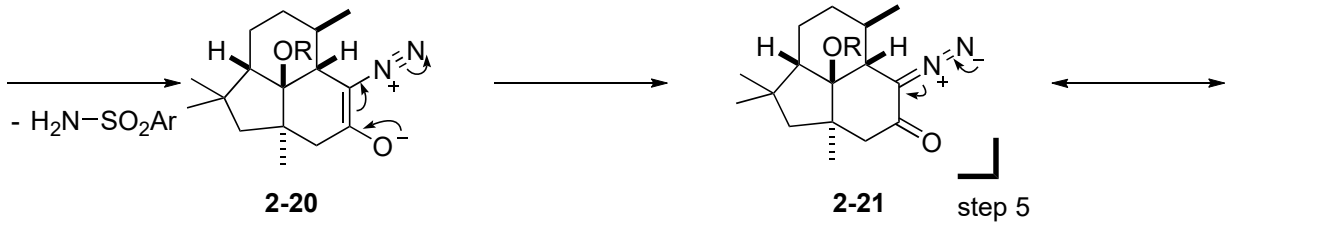
2-12 **2-13** **2-14**



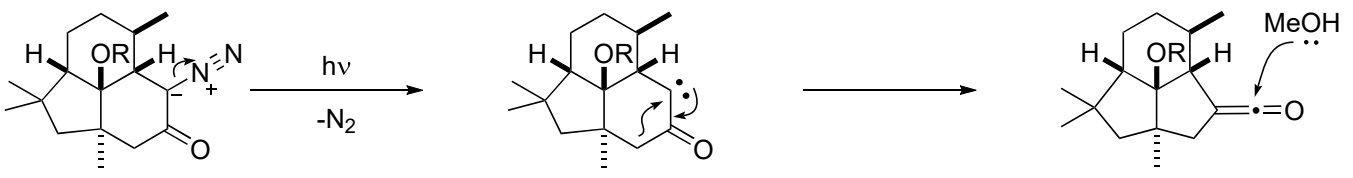
2-15 **2-16**



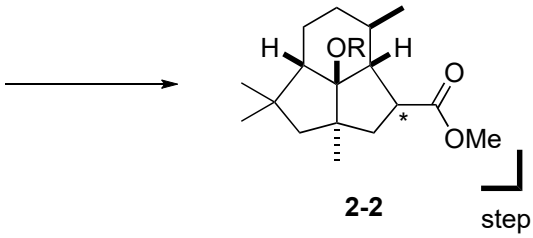
2-17 **2-18** **2-19**



2-20 **2-21**



2-22 **2-23** **2-24**

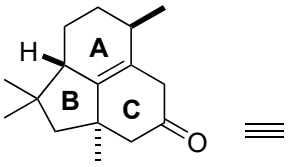


2-2

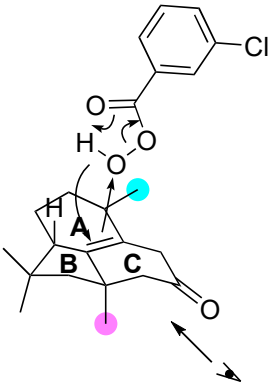
step 6

*This stereocenter installed in this reaction will disappear in the next reaction anyway. That' why it has not been revealed.

Discussion 1: stereoselectivity of Prilezhaev Epoxidation

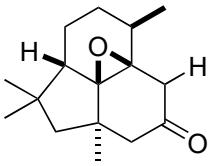


2-7



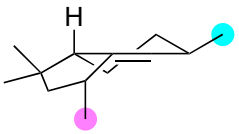
R=TES

m-CPBA



2-8

A ring



C ring

m-CPBA