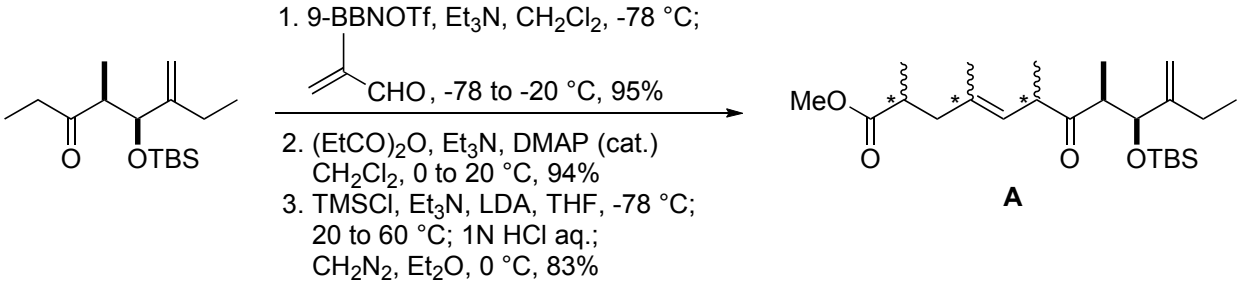
Problem Session (4)

Masaki Koshimizu 2014. 11. 28

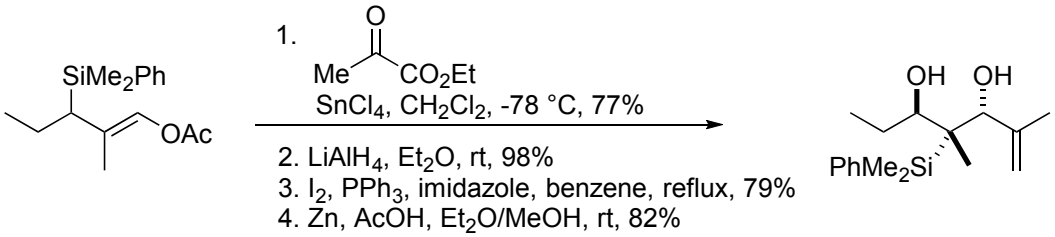
Please provide correct stereochemistry in compound A (Epimerization didn't occur.)

1.



Please provide reaction mechanism of the following schemes

2.



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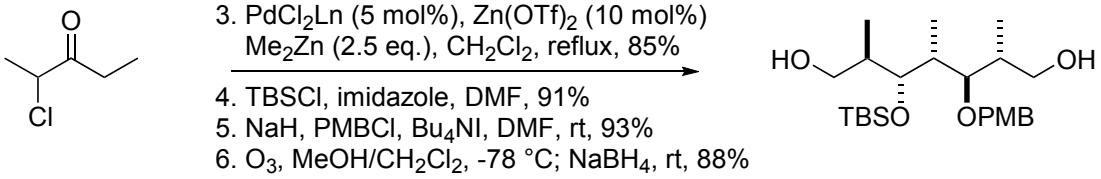

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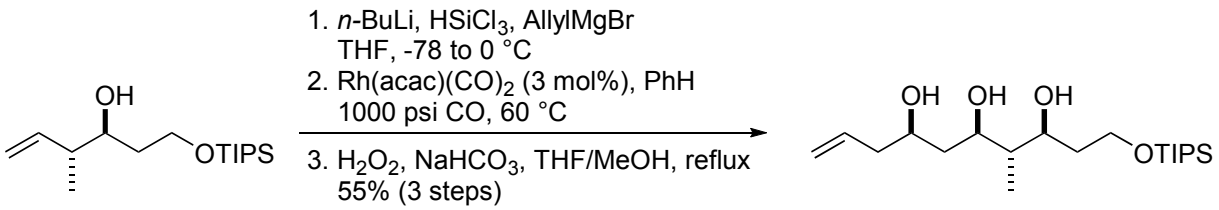
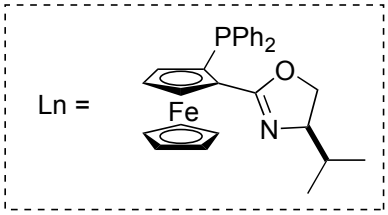
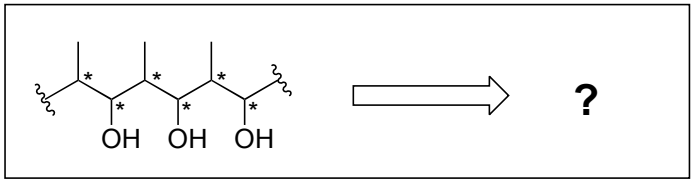




Problem Session (4): Answer

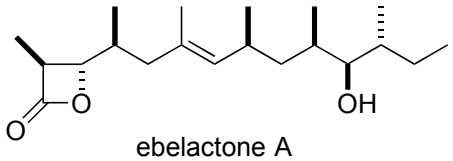
2015. 11. 28 Masaki Koshimizu

Stereoselective Construction of Skipped Polyol and Polymethyl Structural Motif

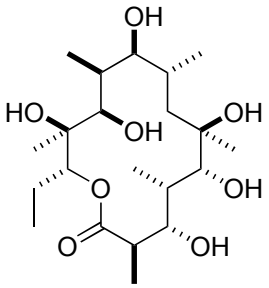


Introduction

Polyketide Structure



ebelactone A
(problem **1**)

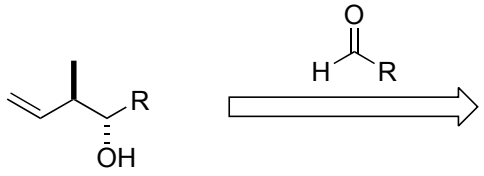


(9*S*)-dihydroerythronolide A
(problem **2**)

Synthetic Approach

Conventional method (problem 1)

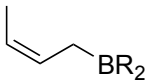
0-1. Crotylation (大学院講義　有機化学II p52-53)



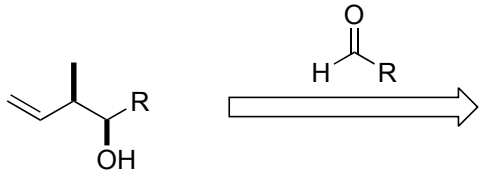
transition state

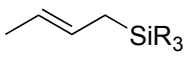
cyclic (problem 4)

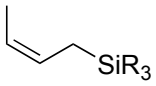
0-1 anti



cyclic



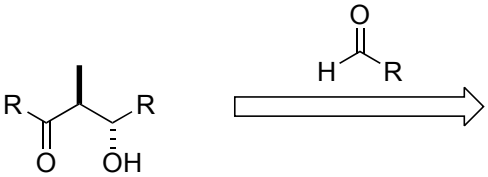


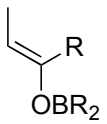


acyclic

0-2 syn

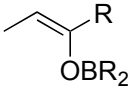
0-2-1. Aldol reaction (大学院講義　有機化学II p45-51)



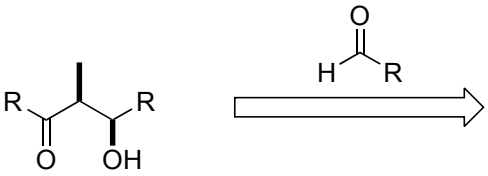


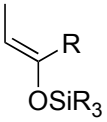
cyclic

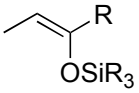
0-3 anti



cyclic (problem 1 ,2 reactions)





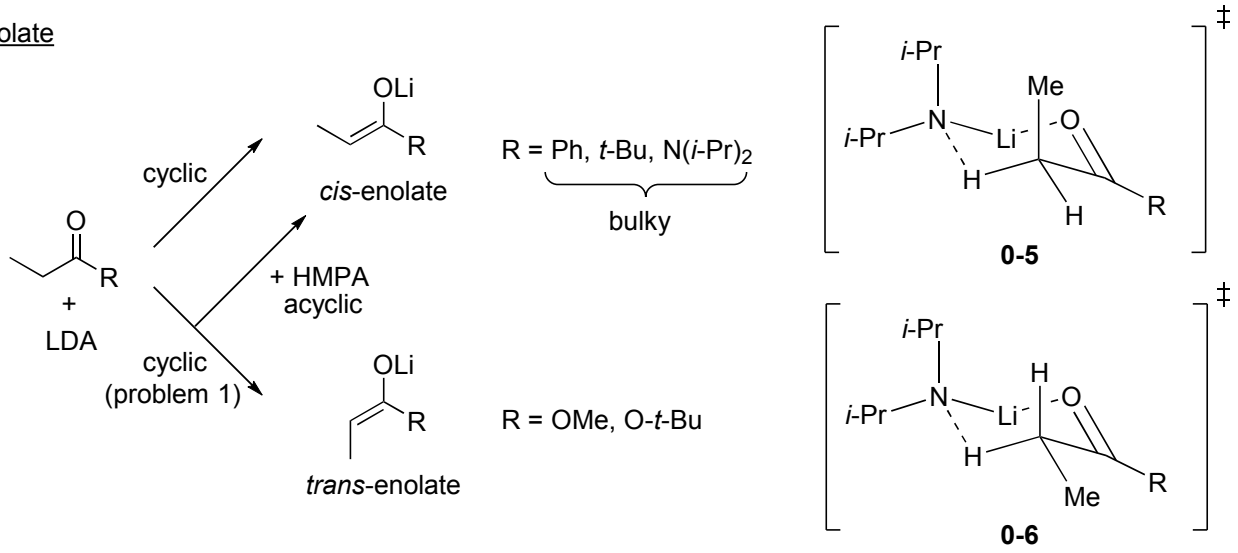


acyclic

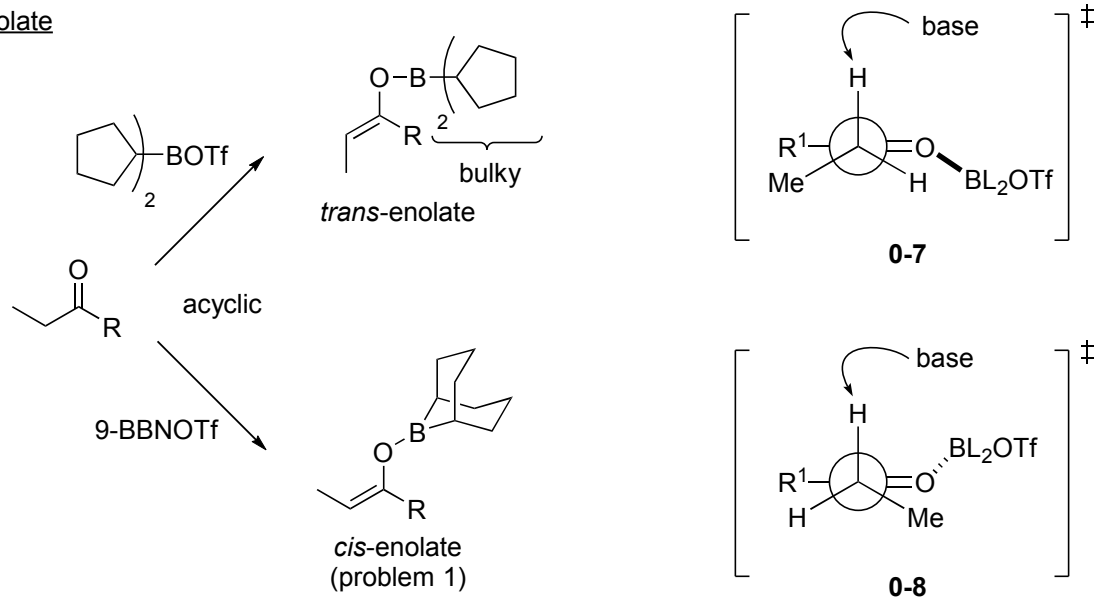
0-4 syn

0-2-2. Stereoslective enol formation（大学院講義　有機化学II p45-51）

Li-enolate



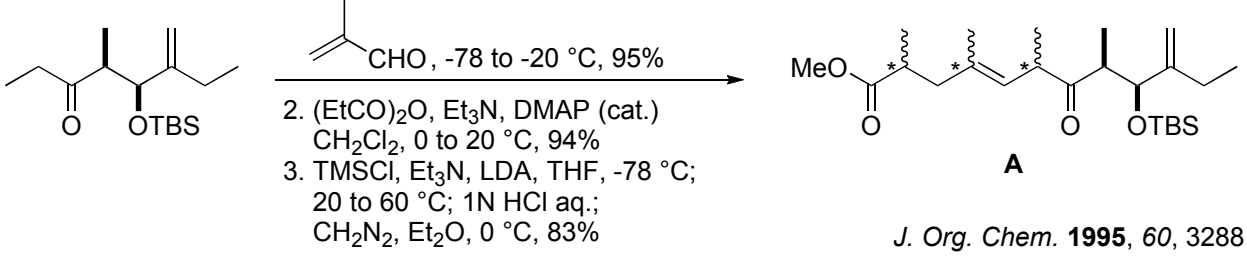
B-enolate



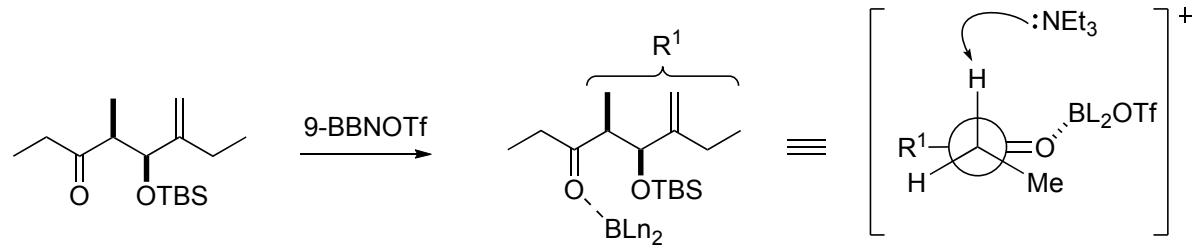
Unconventional method
Non-aldol approach (problem **2**, **3**, **4**)

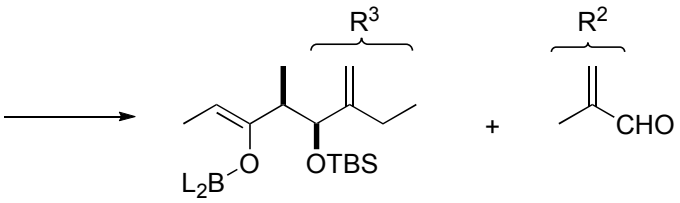
Answer

1.

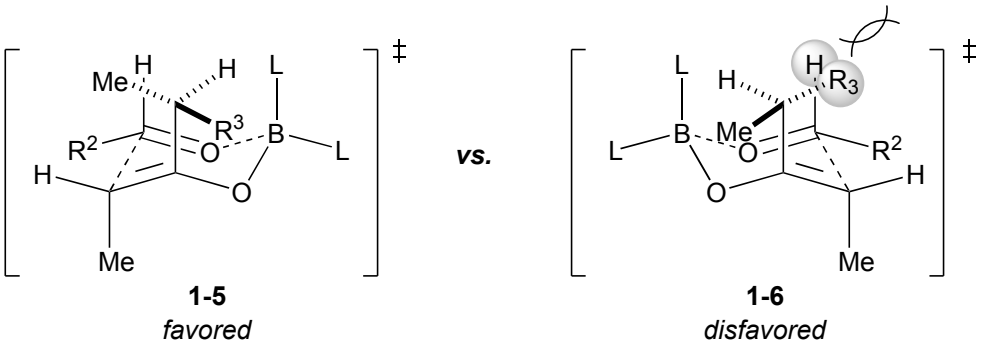


J. Org. Chem. **1995**, *60*, 3288.

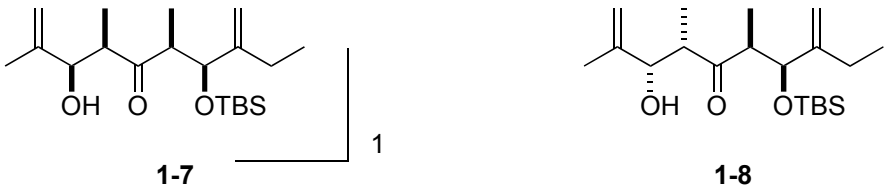


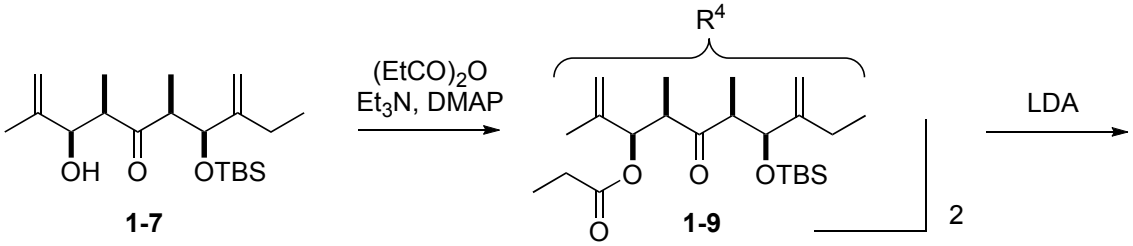


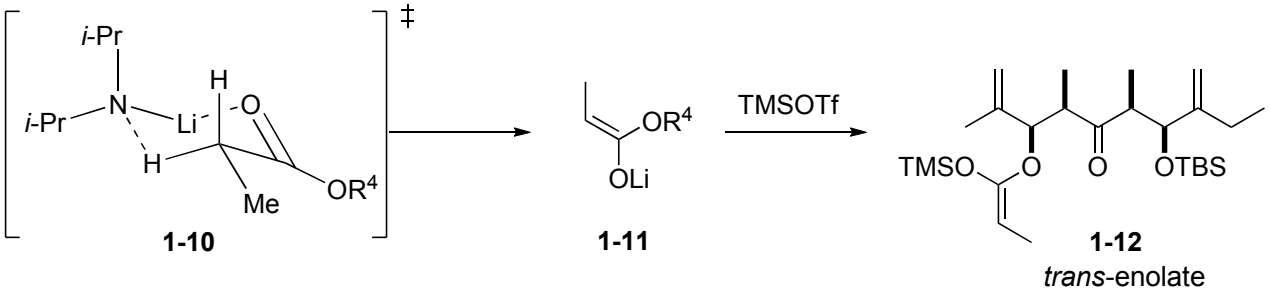
Substrate-controled aldol reaction of chiral ethyl ketone

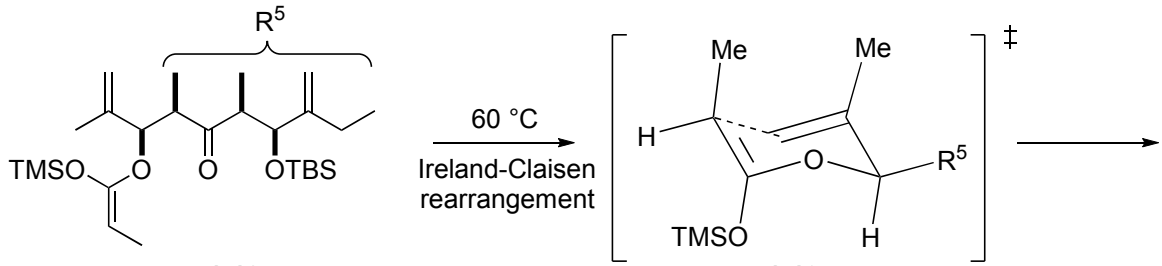


syn-selective aldol reaction

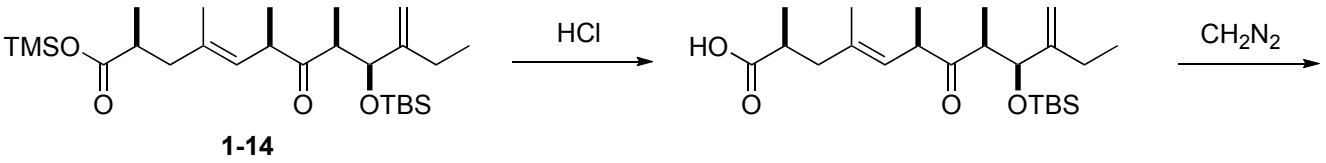




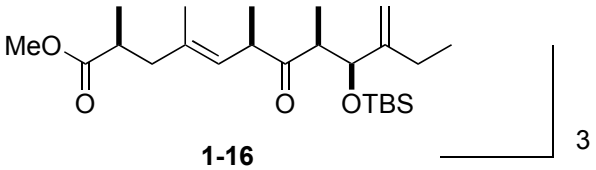




1-12 **1-13**



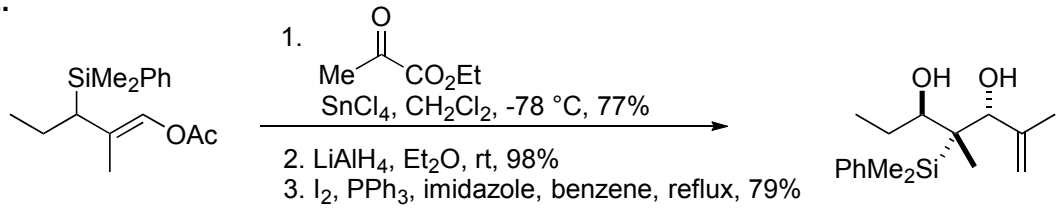
1-14



1-16
compound **A**

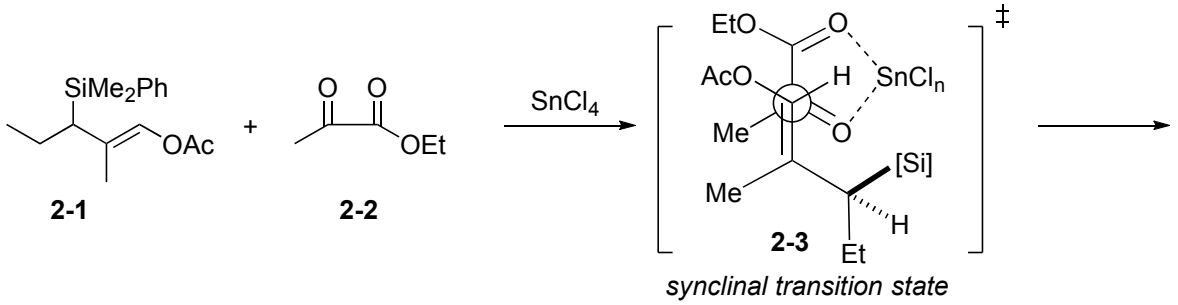
3

2.



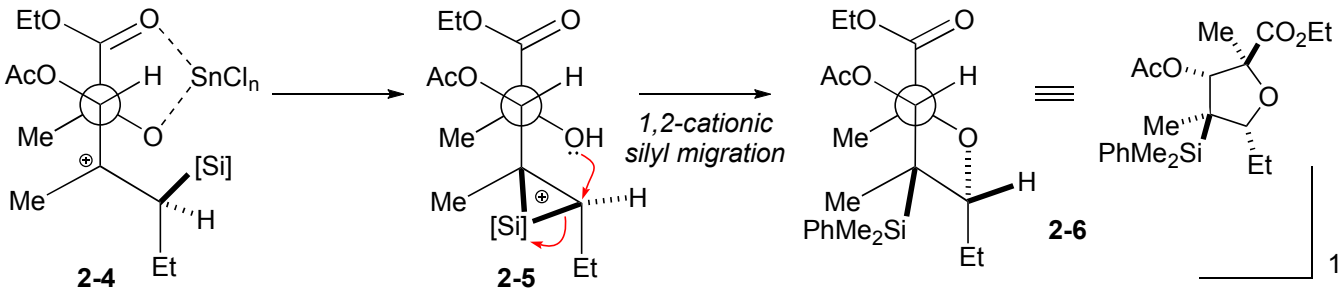
J. Am. Chem. Soc. **2003**, *125*, 6018.

formal [3+2] cycloaddition



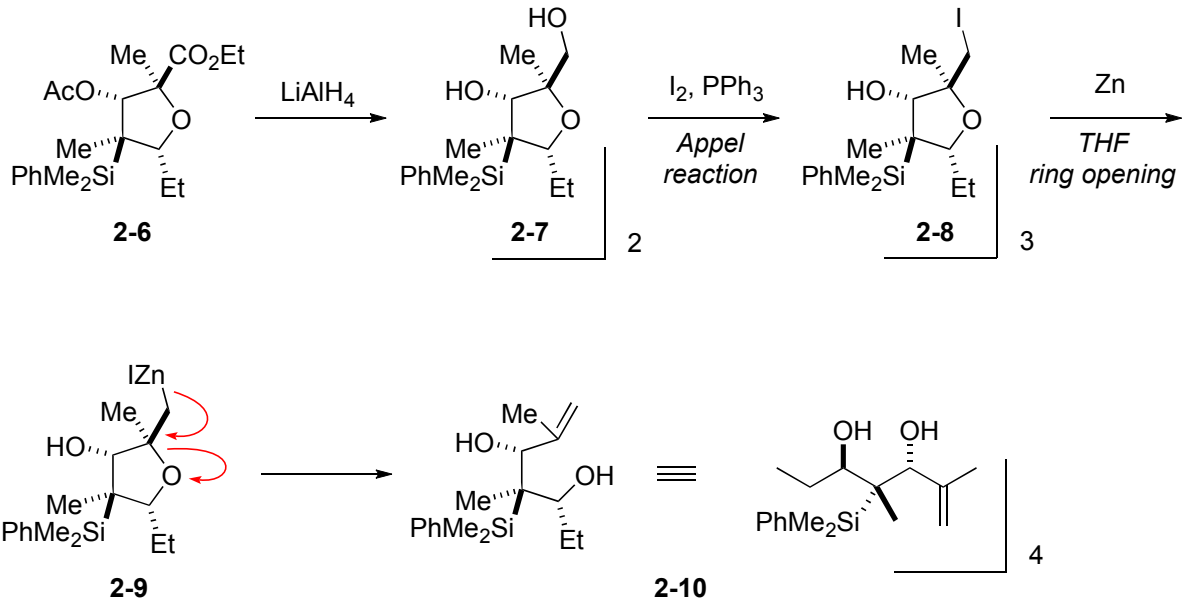
2-1 **2-2** **2-3**

synclinal transition state

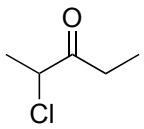


2-4 **2-5** **2-6**

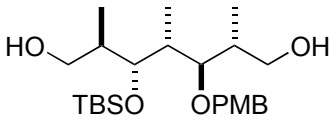
1



3.

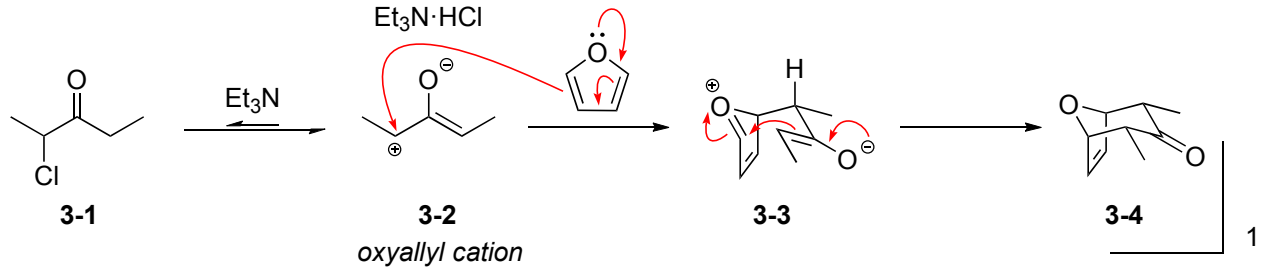


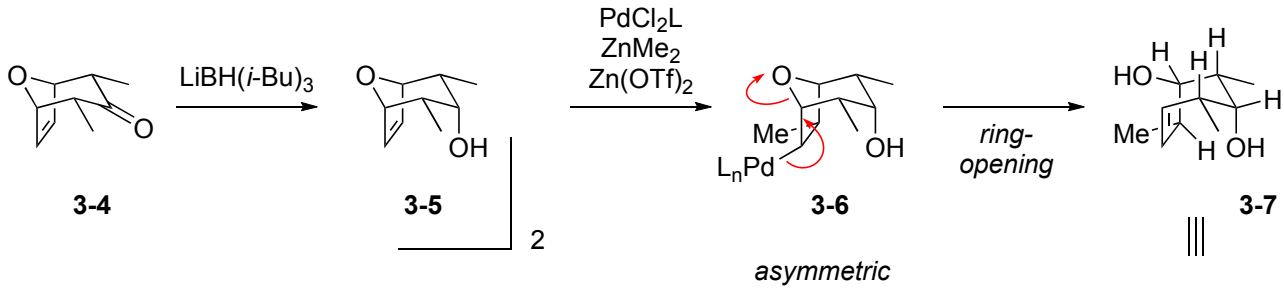
1. furan, Et_3N/H_2O, rt, 45%
2. $LiBH(i\text{-}Bu)_3$, THF, -78 °C to rt, 90%
3. $PdCl_2L$ (5 mol%), $Zn(OTf)_2$ (10 mol%) Me_2Zn (2.5 eq.), $(CH_2Cl)_2$, reflux, 85%
4. TBSCl, imidazole, DMF, 91%
5. NaH, PMBCl, Bu_4NI, DMF, rt, 93%
6. O_3, $MeOH/CH_2Cl_2$, -78 °C; $NaBH_4$, rt, 88%

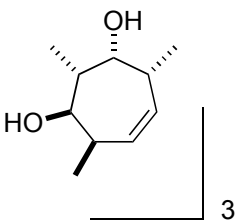


Org. Lett. **2002**, *4*, 1879.

formal [4+3] cycloaddition

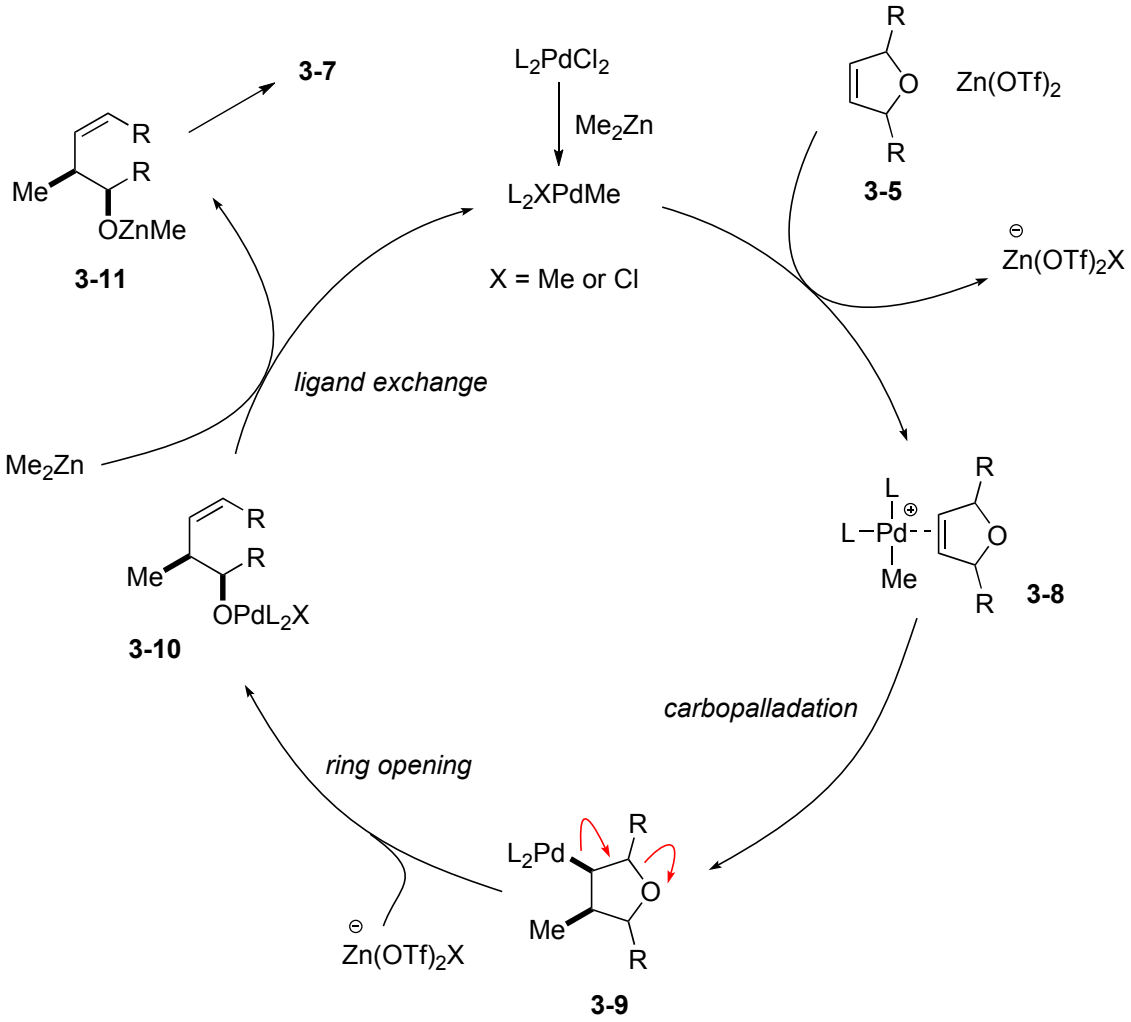


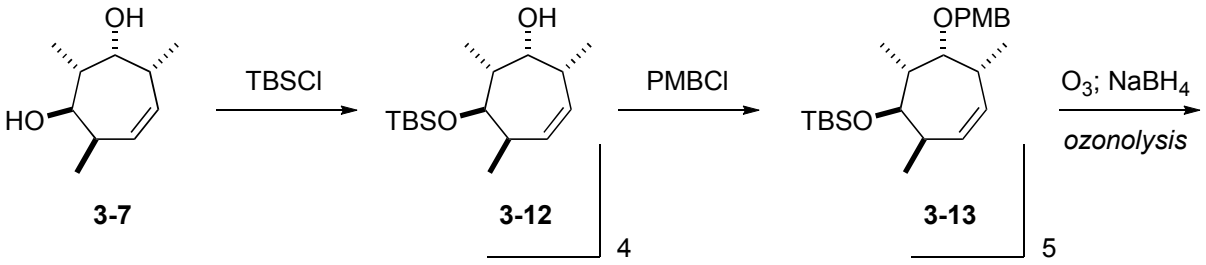


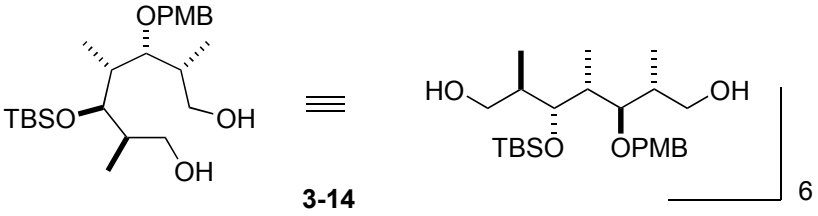


3

<catalytic cycle>

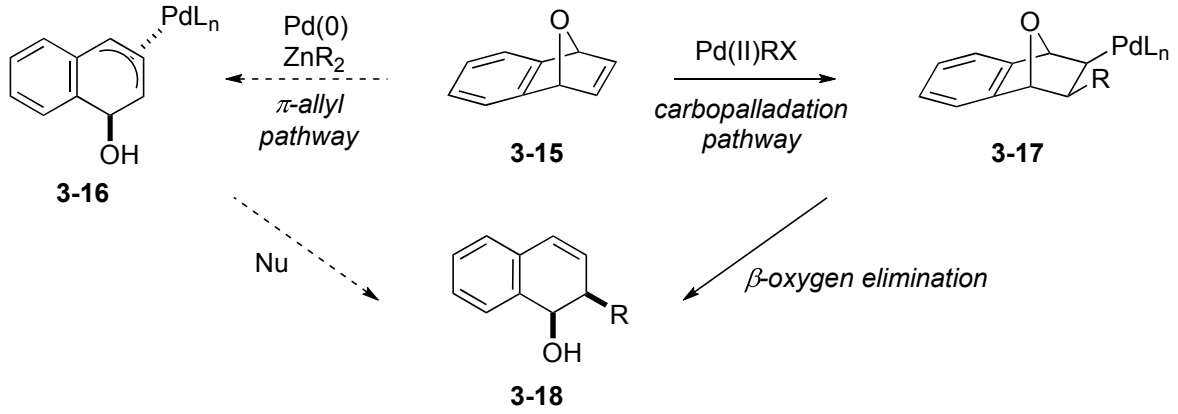






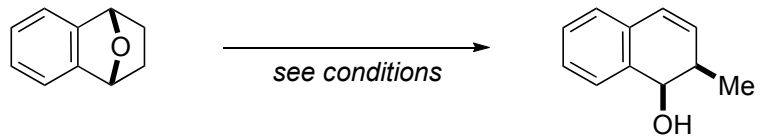
<Support for carbopalladation pathway> *J. Am. Chem. Soc.* **2001**, *123*, 6834.

π-allyl pathway vs. carbopalladation pathway



3-16 **3-15** **3-17** **3-18**

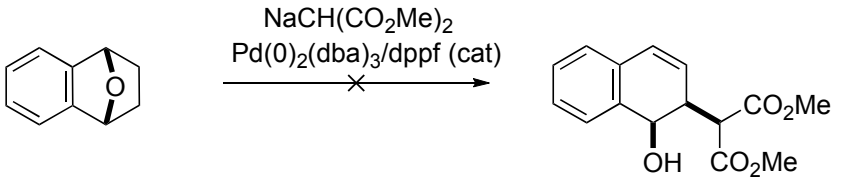
Reactions of oxabenzonorbornadiene with Pd(0)



3-19 **3-20**

$Pd(0)_2(dba)_3$/dppf (cat), $ZnMe_2$, 24 h — very low conversion

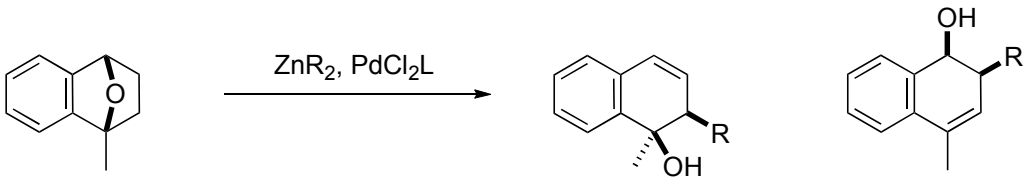
$Pd(II)Cl_2(dppf)_2$ (cat), $ZnMe_2$, 12 h — complete



3-19 **3-21** not detected

Tsuji-Trost Reaction didn't occur.

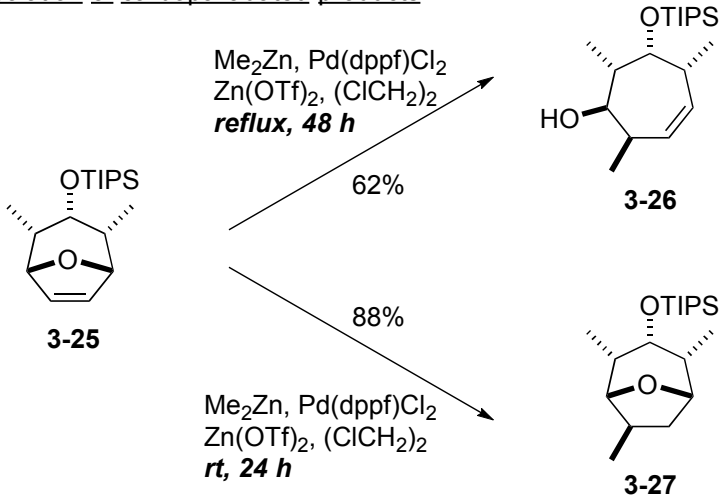
Reactions with unsymmetrical substrate



3-22 **3-23** **3-24** not detected

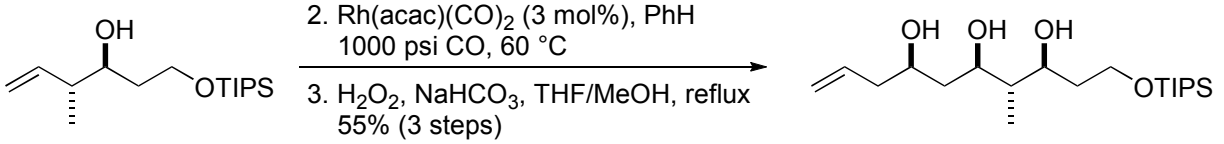
If lewis acid promoted reaction was taking place, ionization at the tertiary center would be expect to generate **3-24**.

Isolation of carbopalladated products

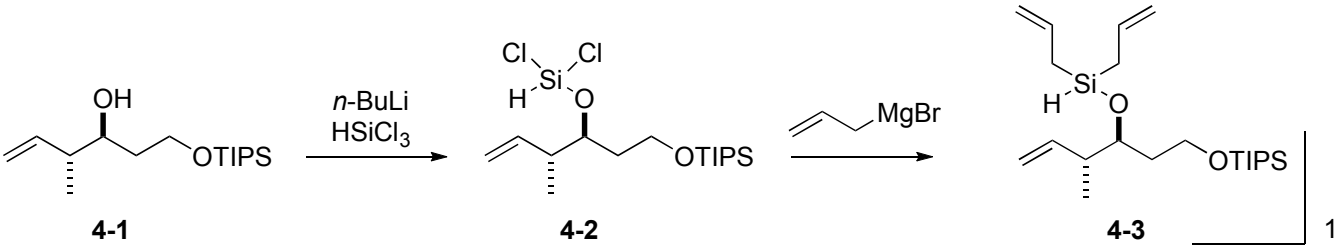


3-25 **3-26** **3-27**

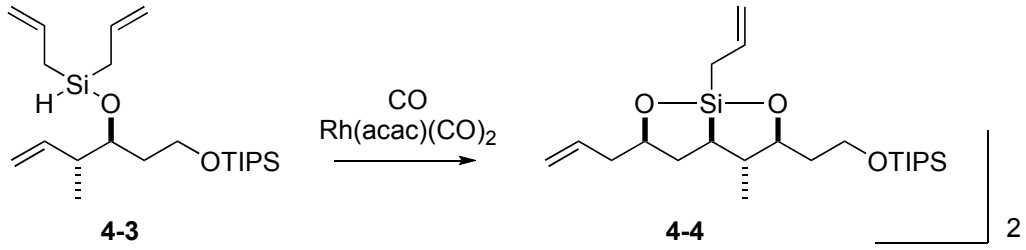
4.



J. Am. Chem. Soc. **2001**, *123*, 341.

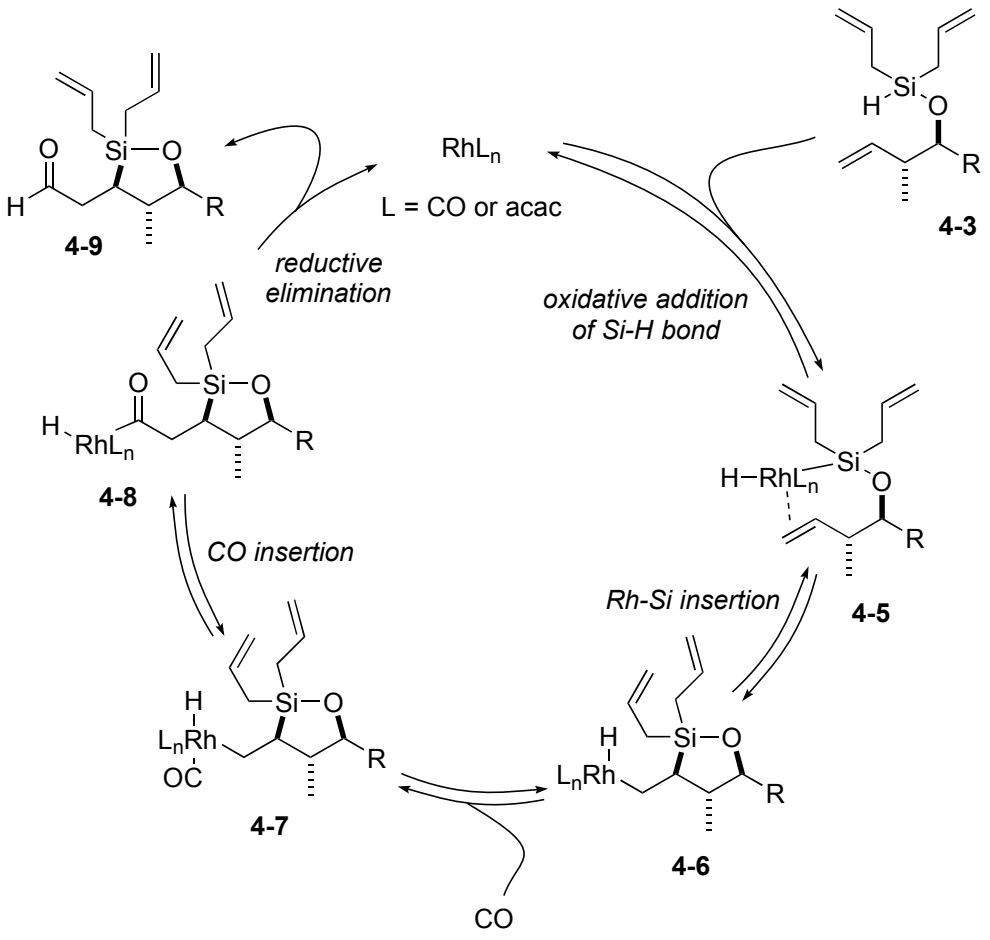


4-1 **4-2** **4-3**

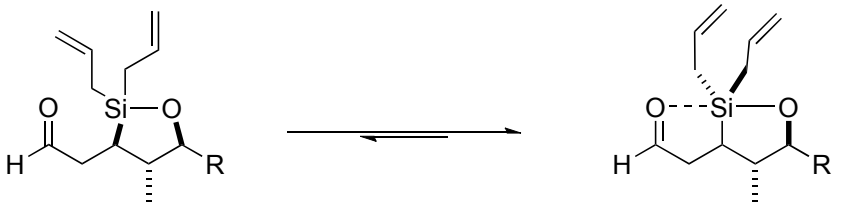


4-3 **4-4**

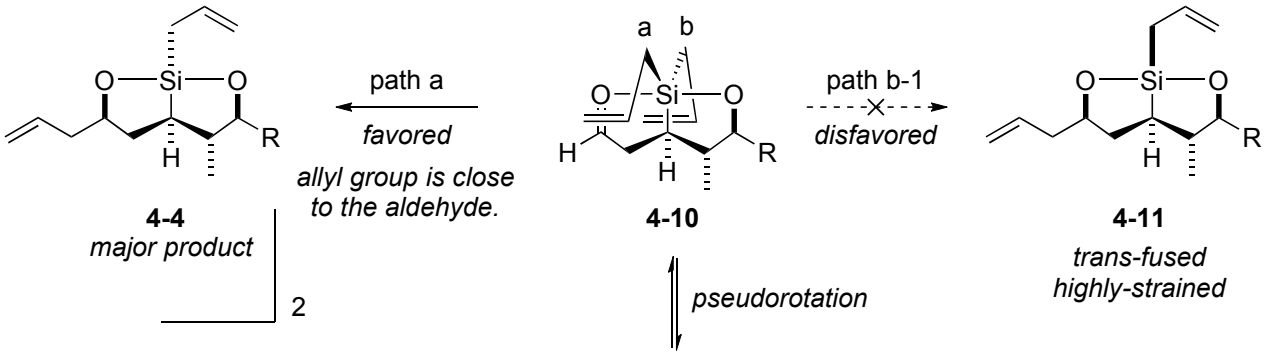
Silylformylation of olefin



Allyl group transfar



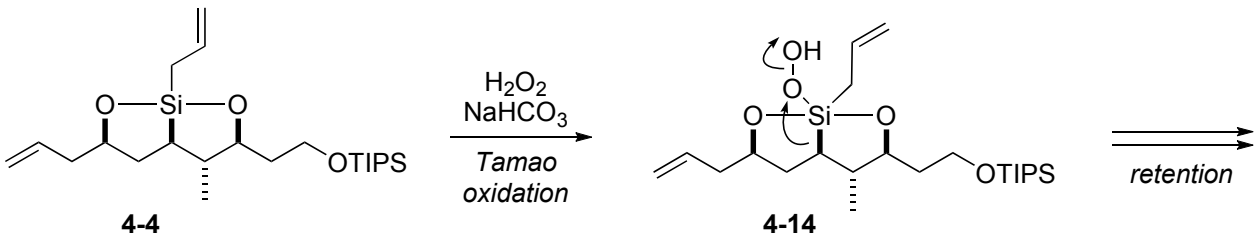
4-9 **4-10**
trigonal-bipyramidal



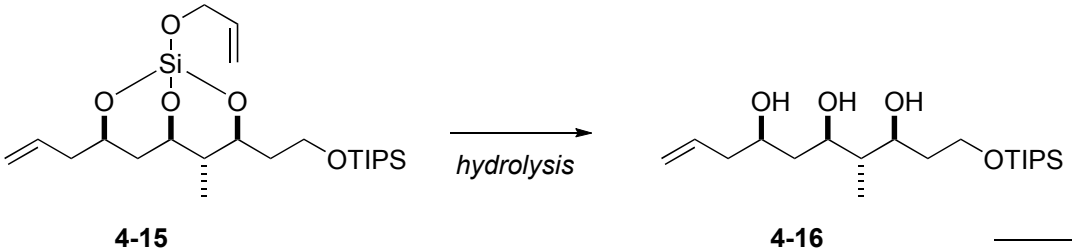
4-4
major product

4-10 **4-11**
trans-fused highly-strained

4-12 **4-13**
minor product

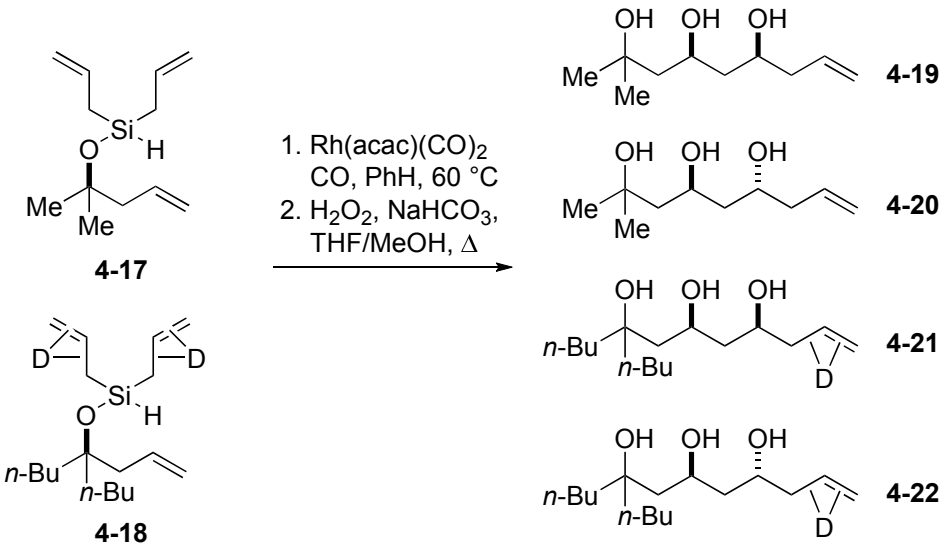


4-4 **4-14**



4-15 **4-16**

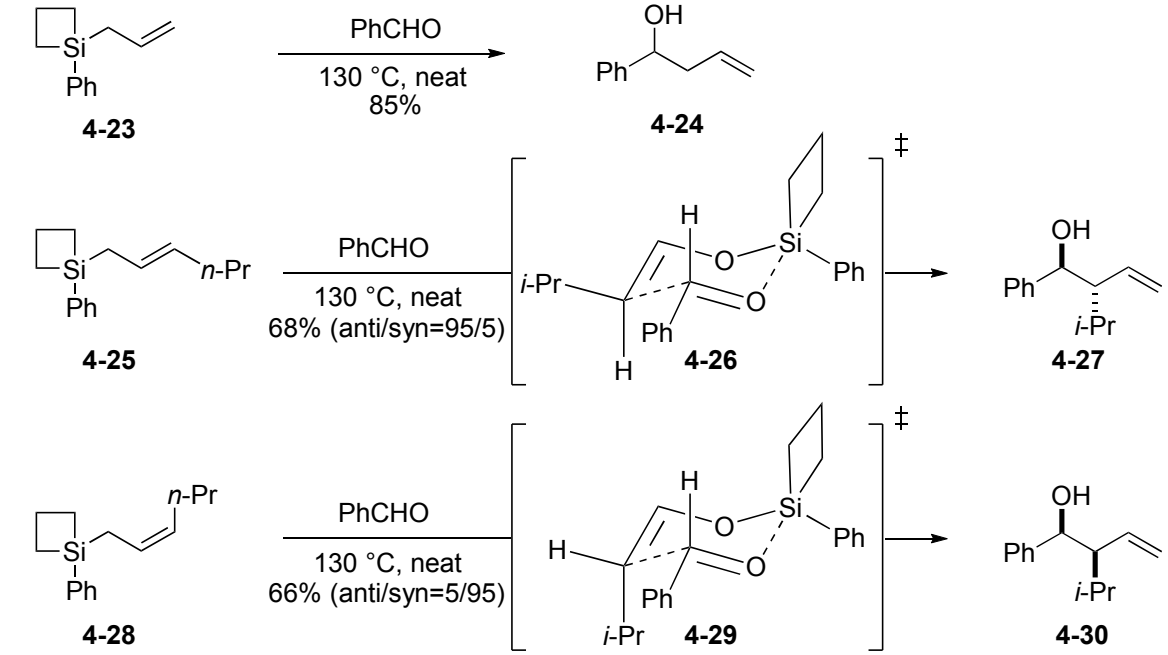
<Crossover experiment> *J. Am. Chem. Soc.* **2000**, *122*, 8587.



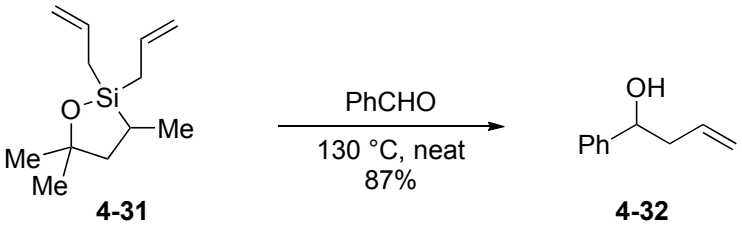
The results indicated intramolecular allyl group transfar.

<Uncatalyzed allyl addition>

allylsilacyclobutane (C-Si-C = ~80°) *J. Org. Chem.* **1994**, *59*, 7152.



oxasilacyclopentane (O-Si-C = ~95°)



Strain release Lewis acidity