

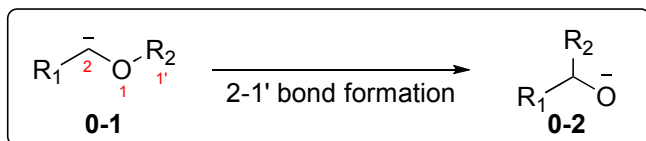
Problem Session (5) Answer -Wittig Rearrangement-

2015.6.27 Shun Yoshioka

Introduction

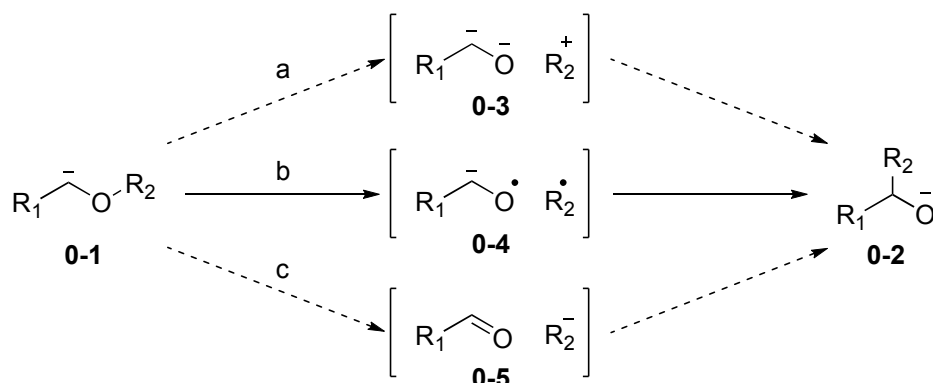
(O-1) defined as O- to C-bond rearrangement of α -ethereal carbanion (α -metalated ether)

(O-2) [1,2]-rearrangement



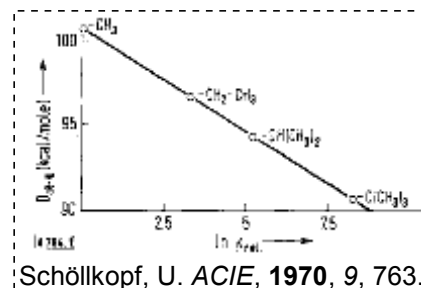
• reaction mechanism

- symmetry forbidden for thermal condition \rightarrow *not* concerted pathway (see Katoh, S. PS, 2015/5/9)
- stepwise (dissociation-recombination) pathways

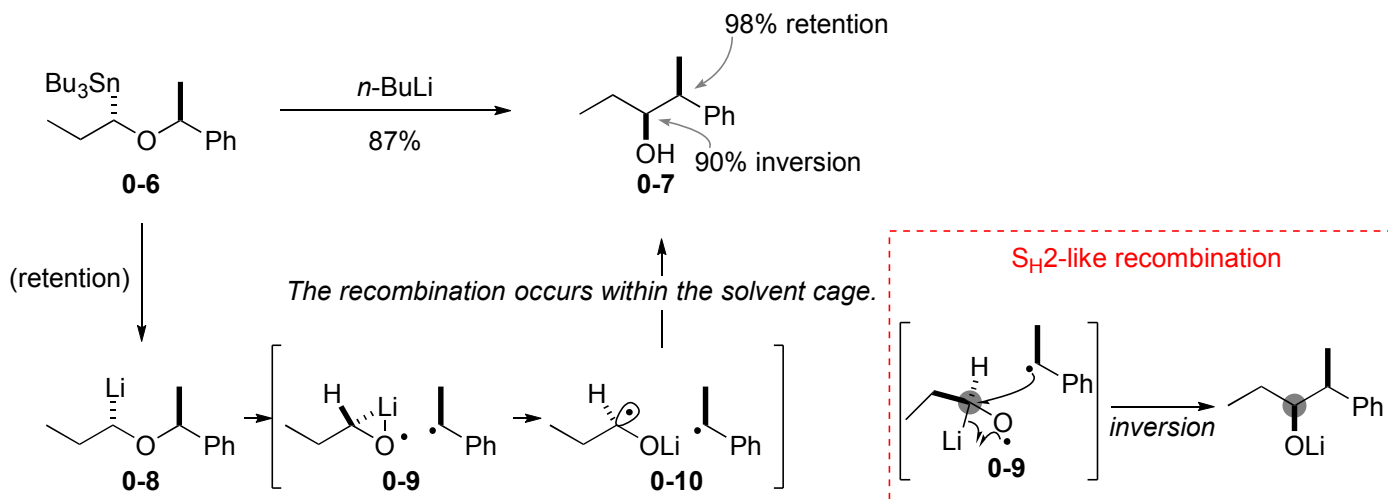


migratory aptitude of R_2 is methyl < *prim*-alkyl < *sec*-alkyl < *tert*-alkyl
 \rightarrow **pathway b** (radical anion + radical) is accepted.

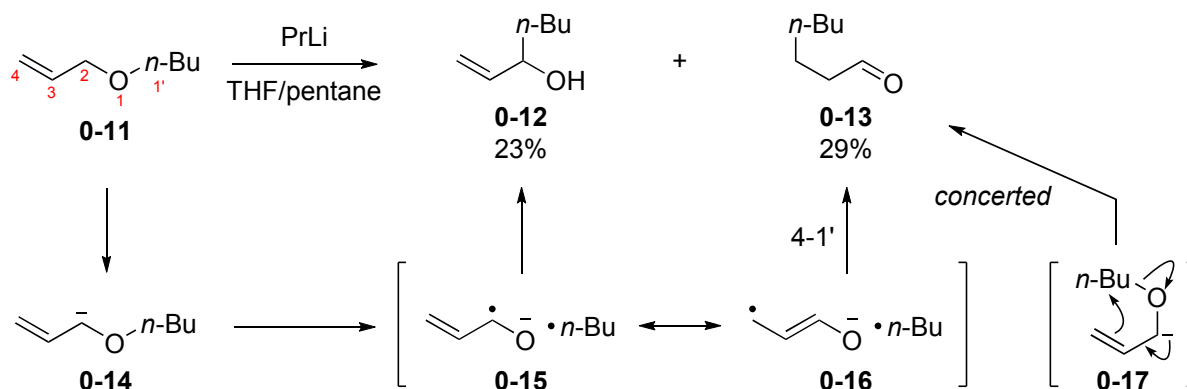
theoretical study, see: Tonachini, P. et al. *JOC* **1998**, *63*, 9756.



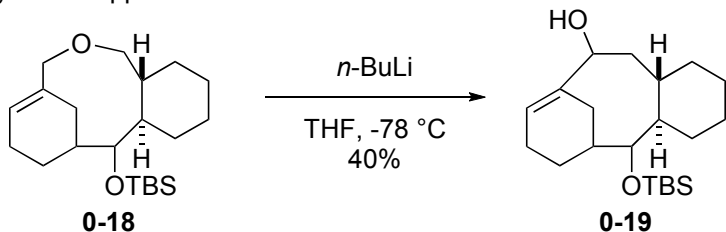
• stereochemical course of the reaction / geminate radical pair or free radicals



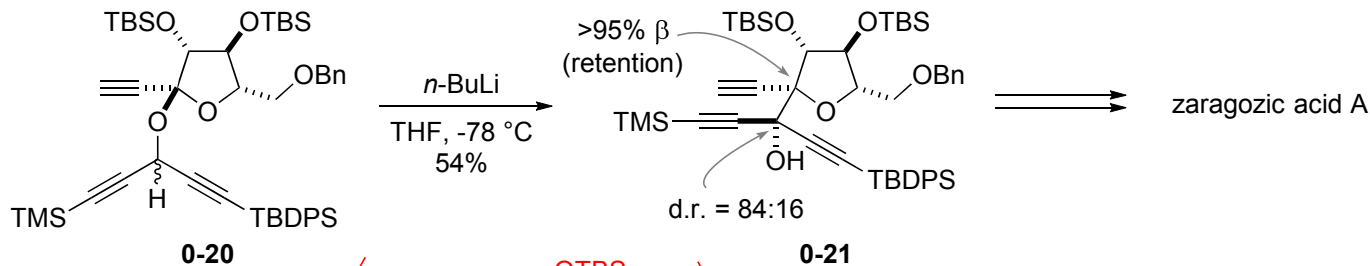
• [1,4]-rearrangement (side reaction)



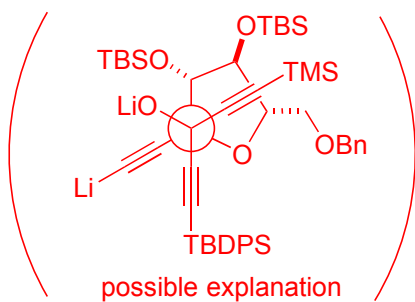
- synthetic application



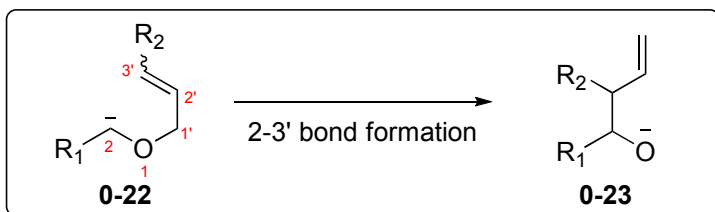
Yadav, J. S. et. al. *TL* **1991**, 32, 2629.



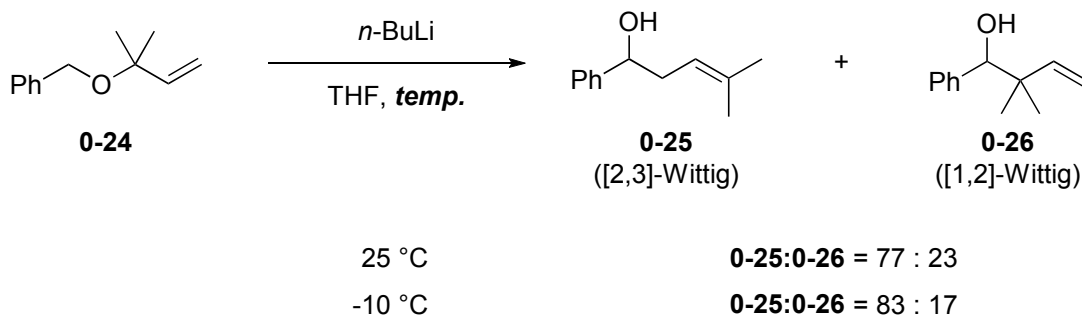
Tomooka, K. et. al. *ACIE* **2000**, 39, 4502.



(0-3) [2,3]-rearrangement

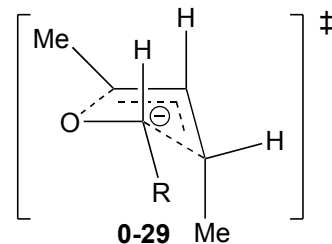
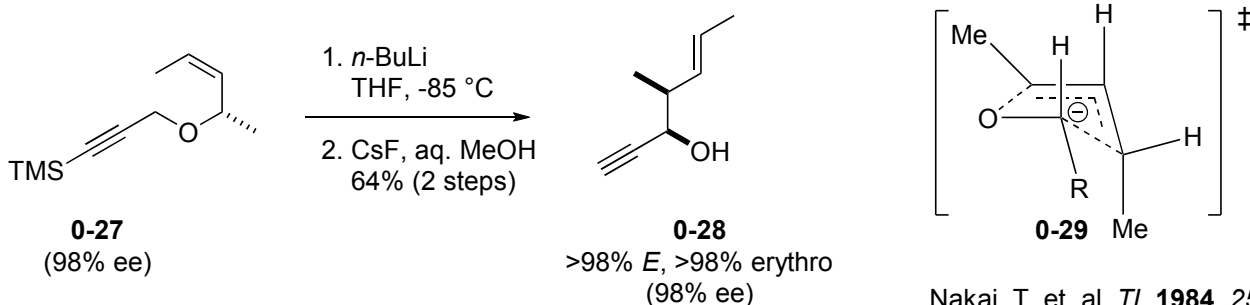


- symmetry allowed for thermal condition \rightarrow concerted pathway (sigmatropic rearrangement)
- competition with [1,2]-rearrangement



The entropic factor may be reduced at lower temperature. Baldwin, J. E. et. al. *TL* **1970**, 353.

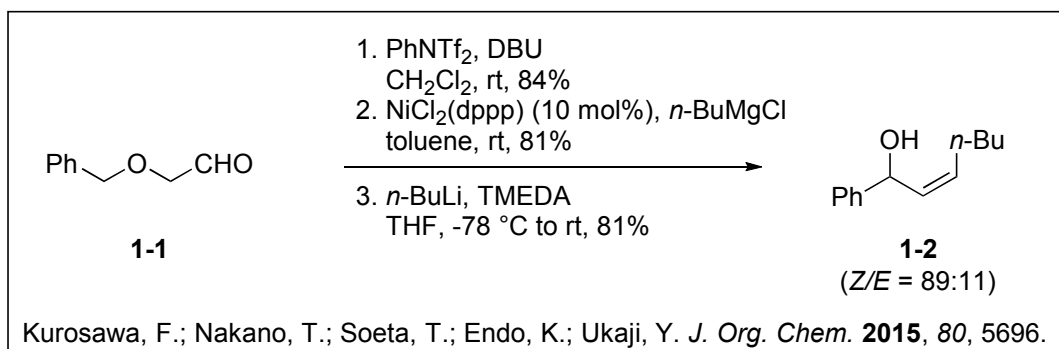
- chiral transfer



Nakai, T. et. al. *TL* **1984**, 25, 565.

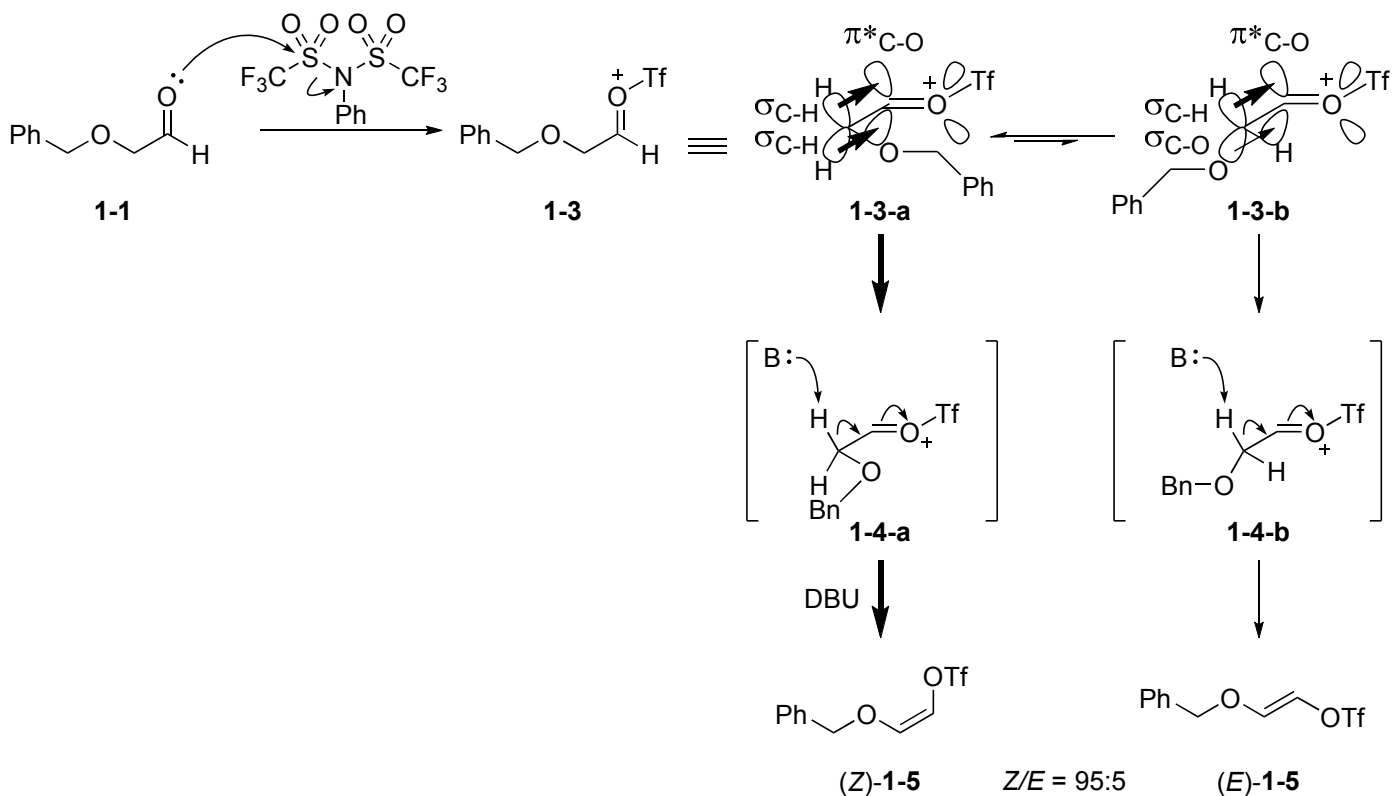
- wide application to natural product syntheses

Problem 1

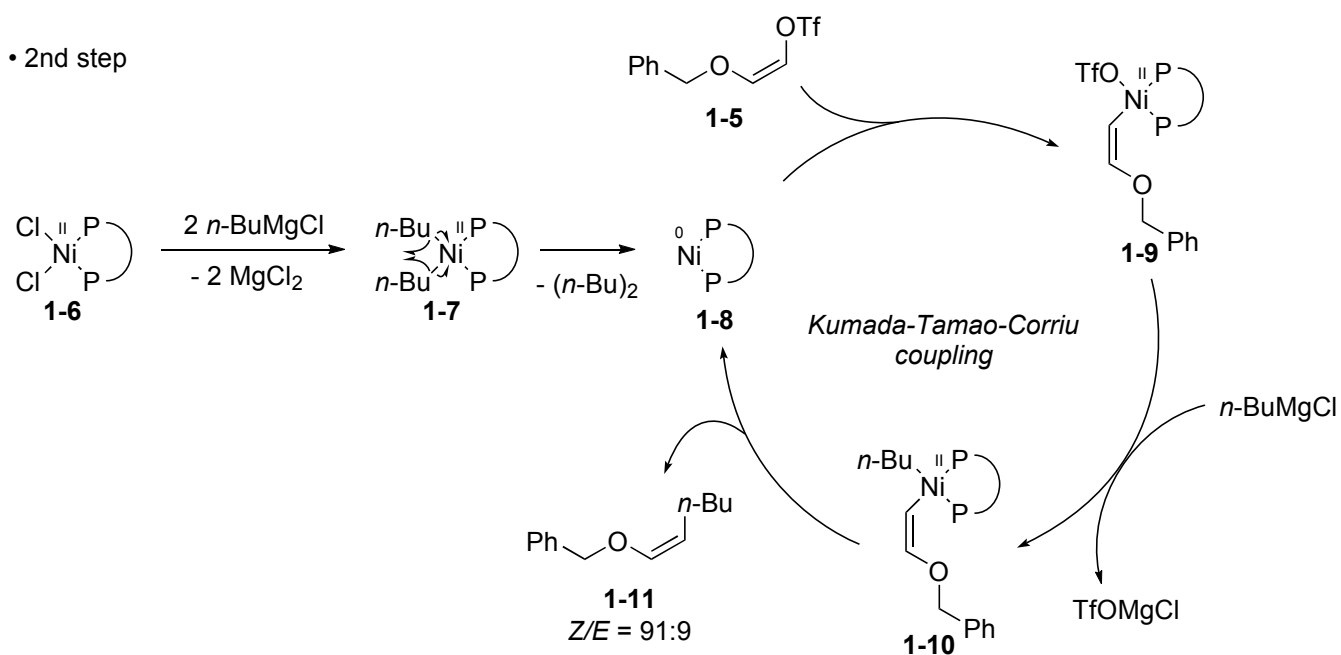


1-1. proposed reaction mechanisms

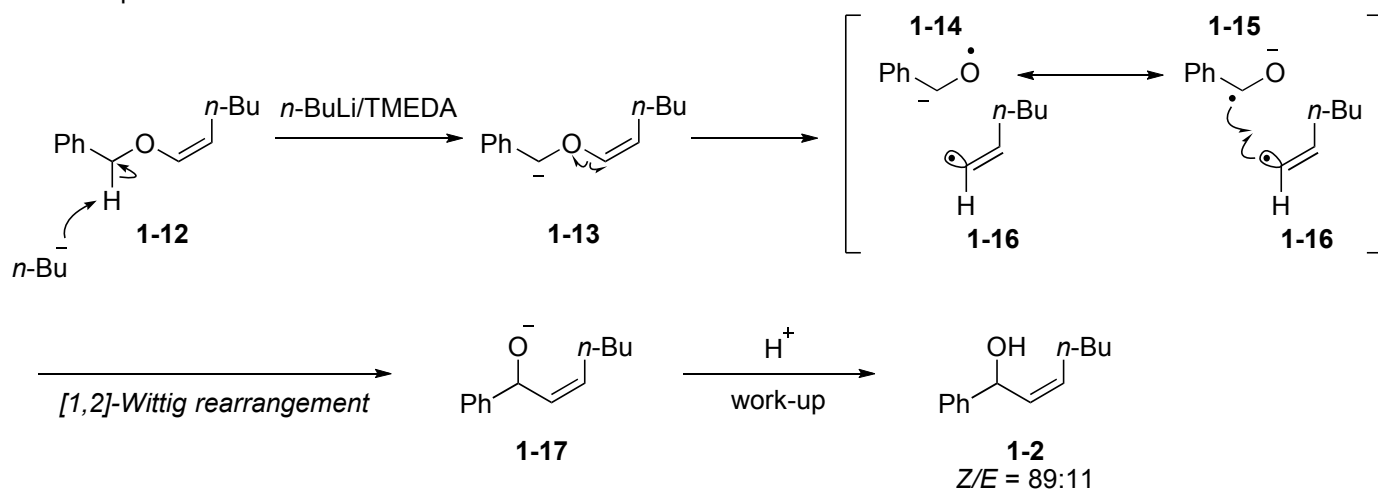
• 1st step



• 2nd step

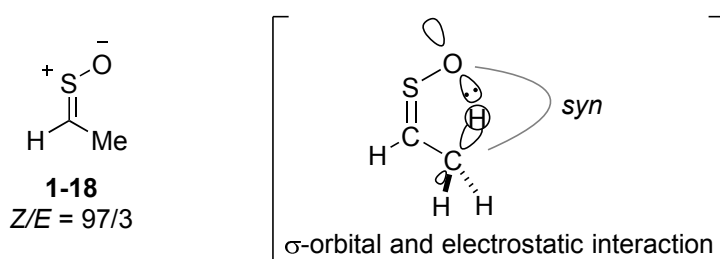


• 3rd step



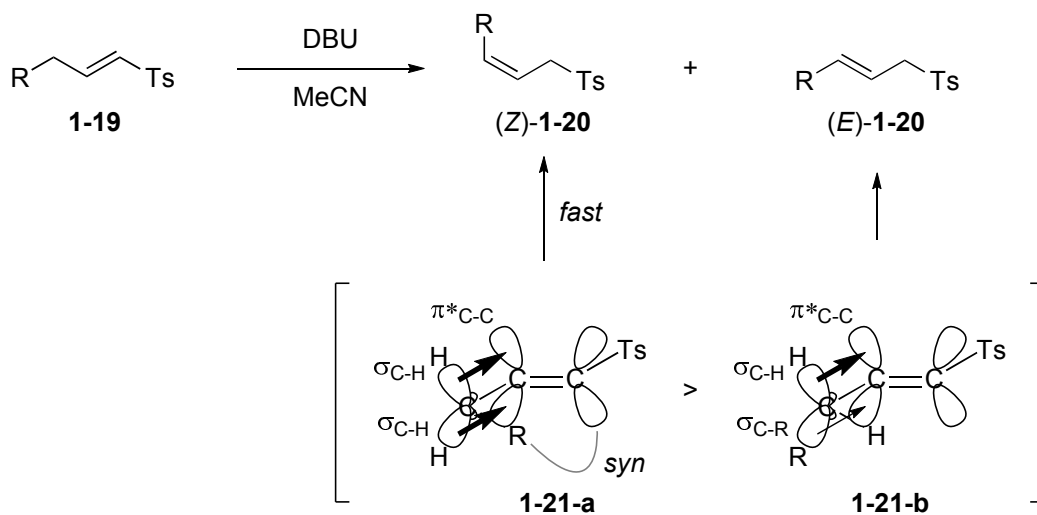
1-2. discussion

- *syn*-effect (preference of *syn*-conformation overcoming steric hindrance)
- stereochemistry of S-oxide



Block, E. et. al. *TL* **1981**, 22, 29.

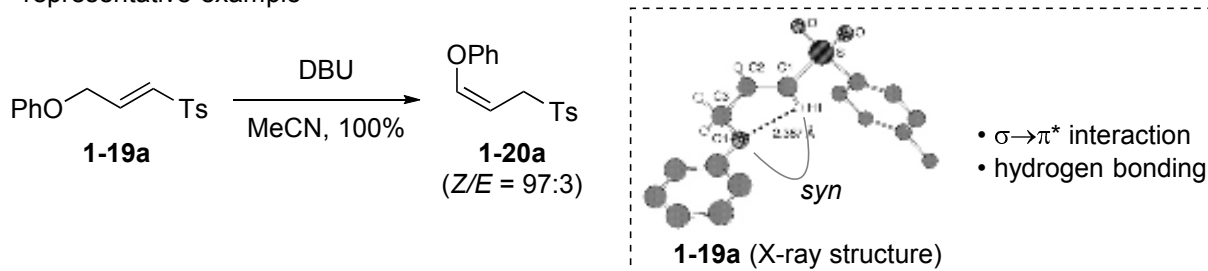
- double bond migration



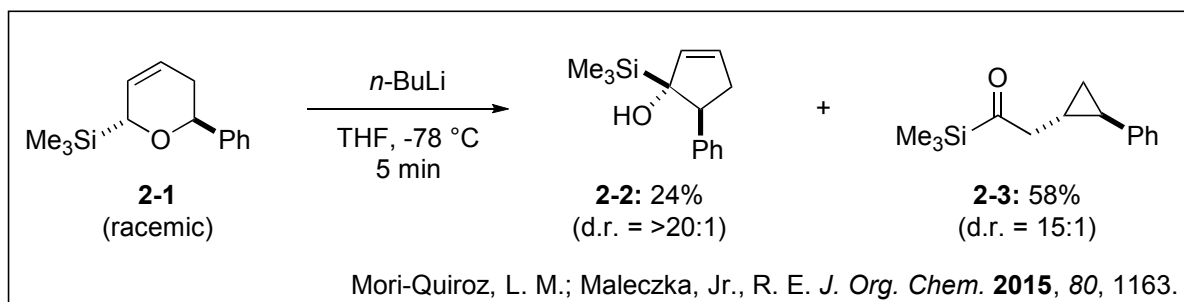
<relative degree of "syn-effect">

EtO \approx ArO > Cl \geq Br > Me > MeS \geq RCH₂ > *i*-Pr \gg *t*-Bu, Ph

<representative example>

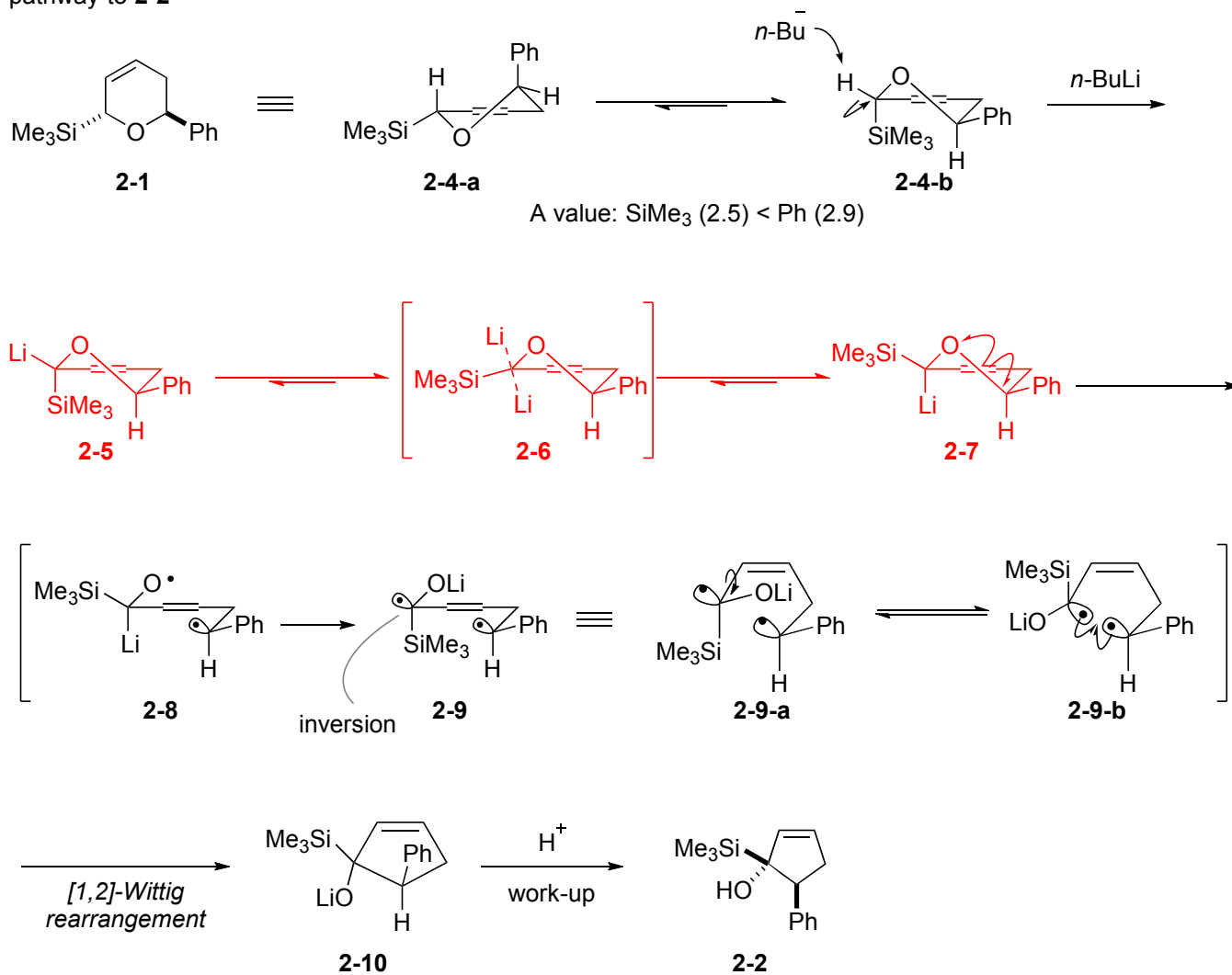


Problem 2

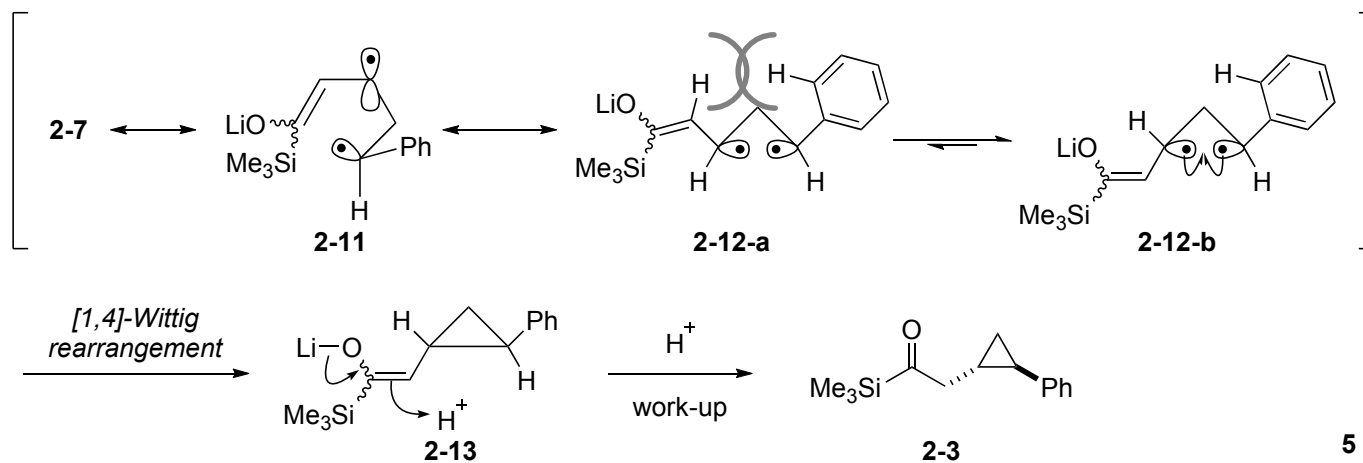


2-1. proposed reaction mechanisms

• pathway to **2-2**

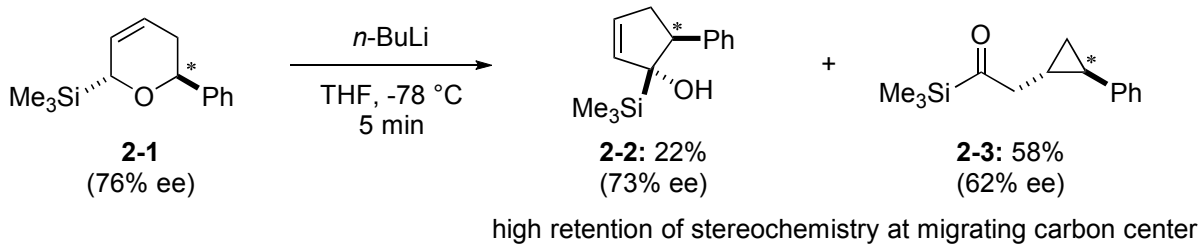


• pathway to **2-3**

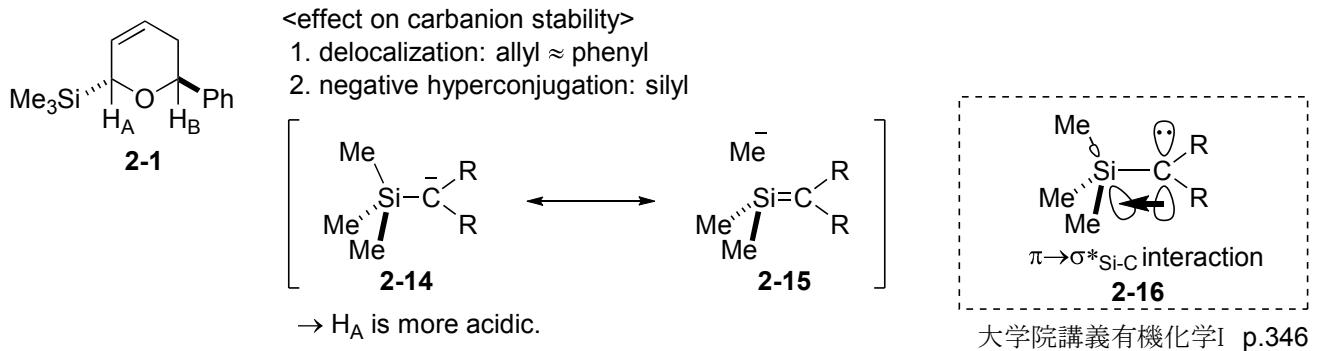


2-2. discussion

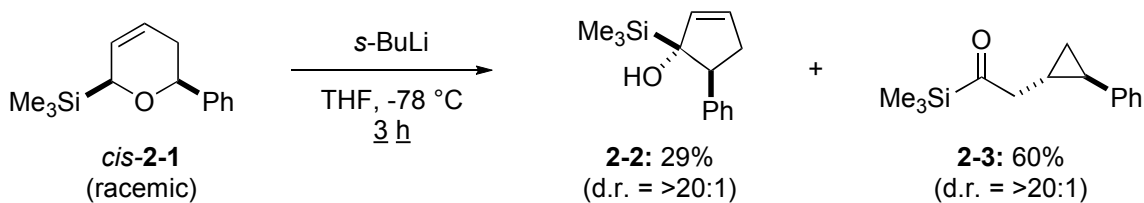
- stereochemical course of the reaction



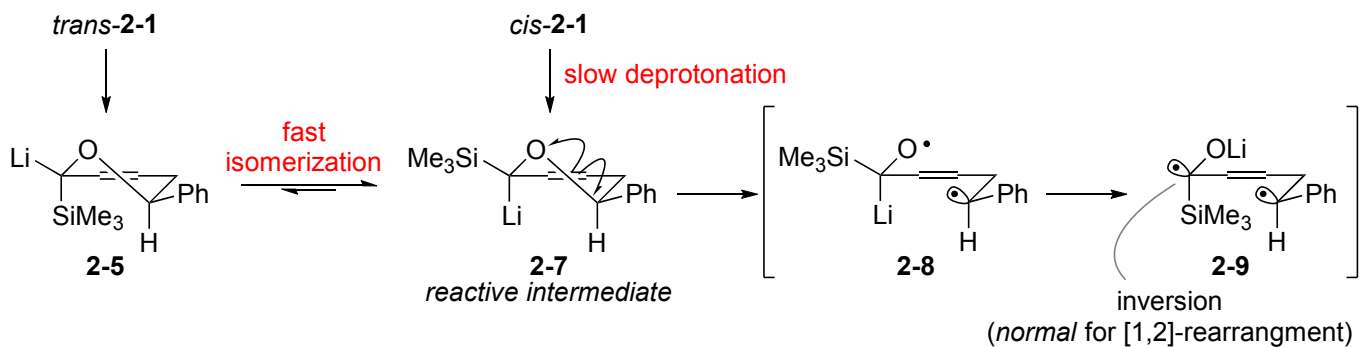
- regioselectivity of deprotonation



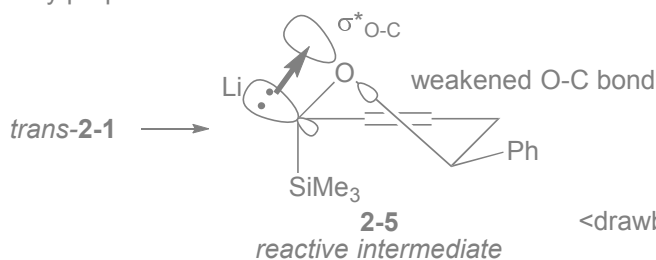
- Which is common (reactive) intermediate?



1. full stereoconvergence → existence of common intermediate
2. 2-2 is the diastereomer which has larger torsional strain (TMS and Ph are *cis*-relationship).
→ The reactions pass through common intermediate before generating biradical species.
3. author's proposal

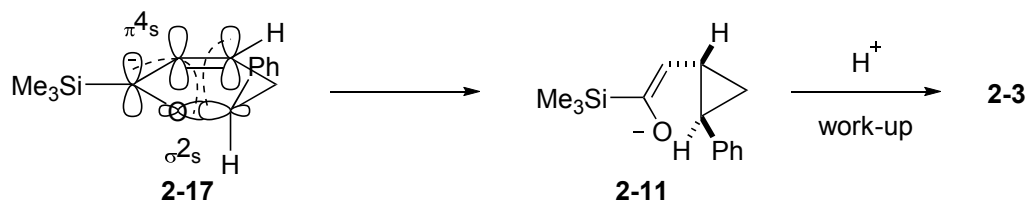


4. my proposal

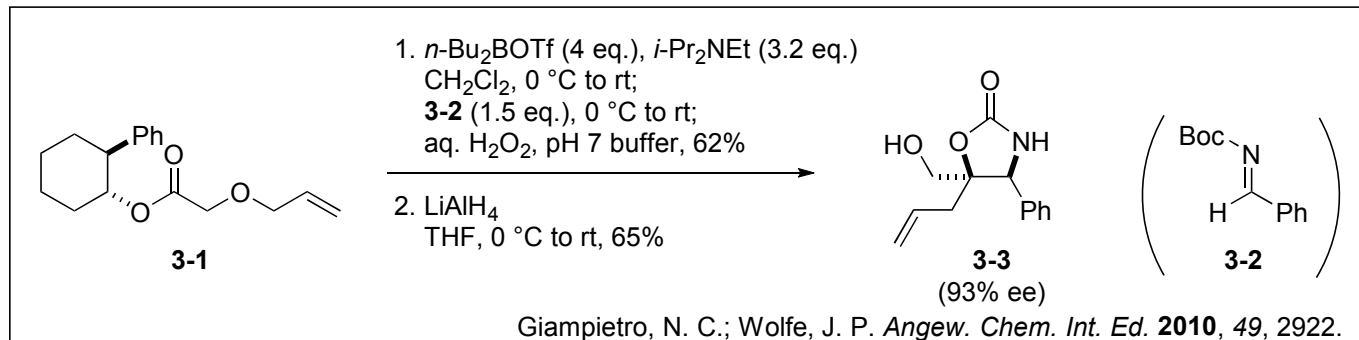


<drawback> The unusual retention mechanism is considered.

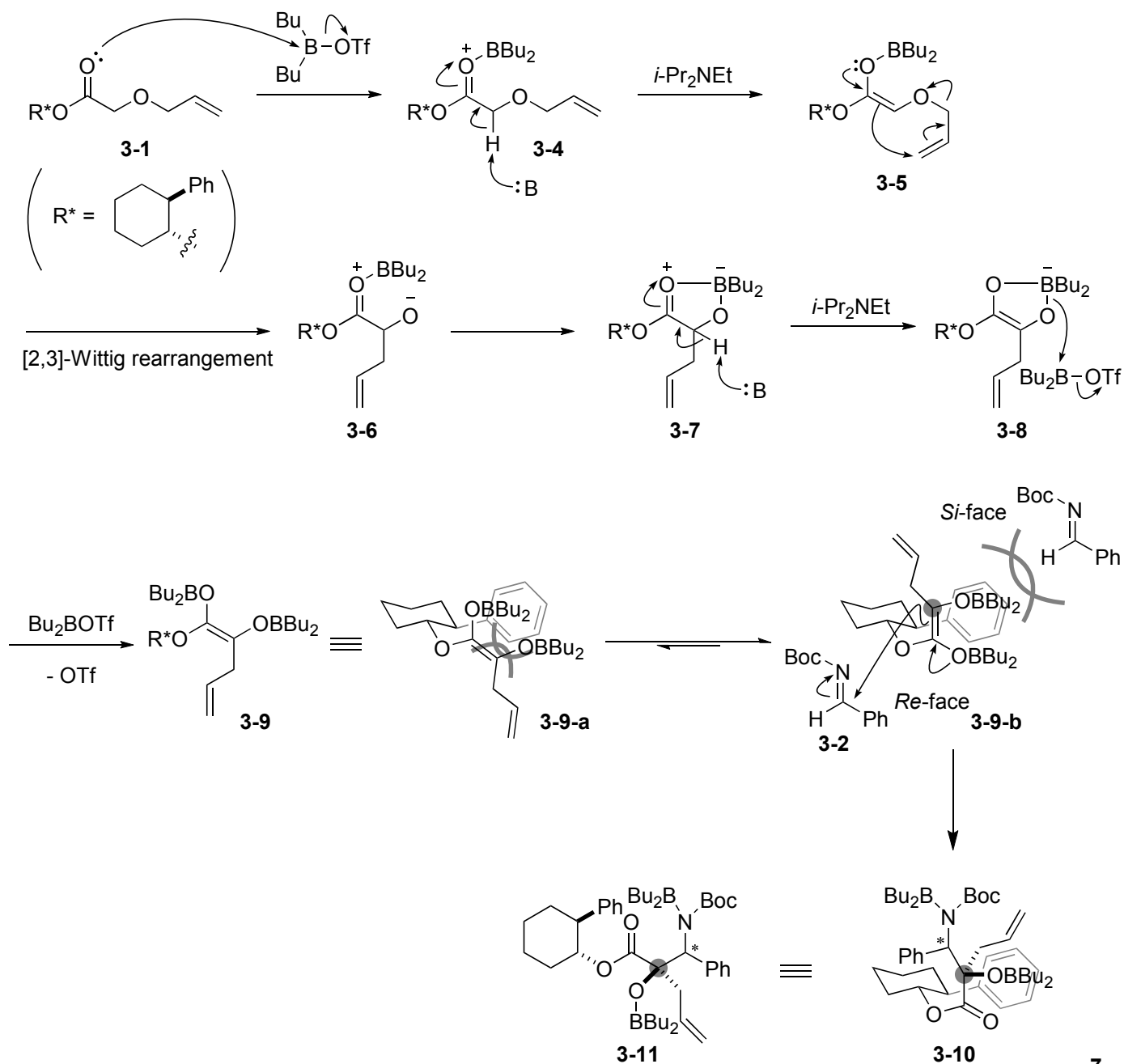
- concerted mechanism of [1,4]-rearrangement



Problem 3

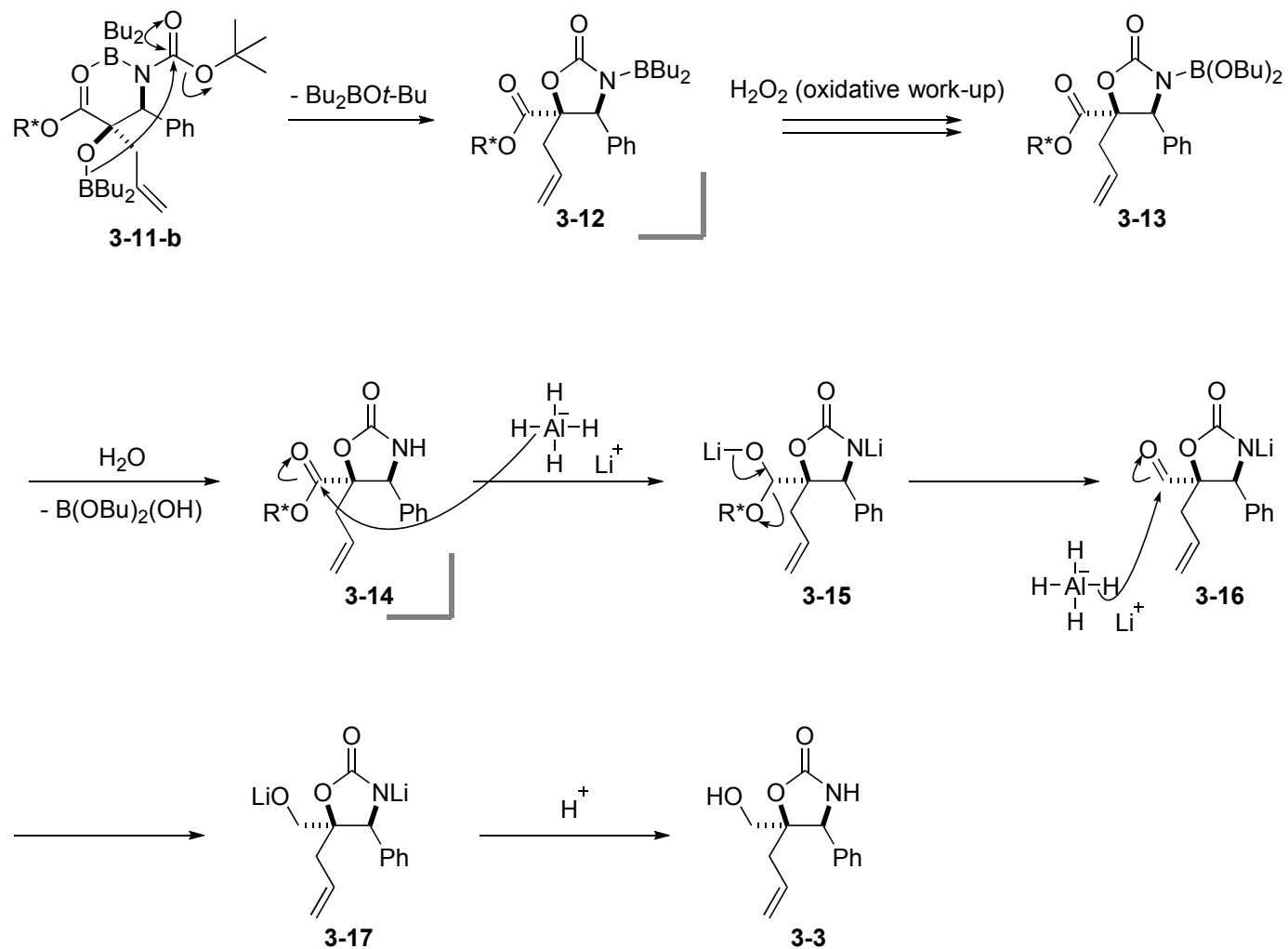
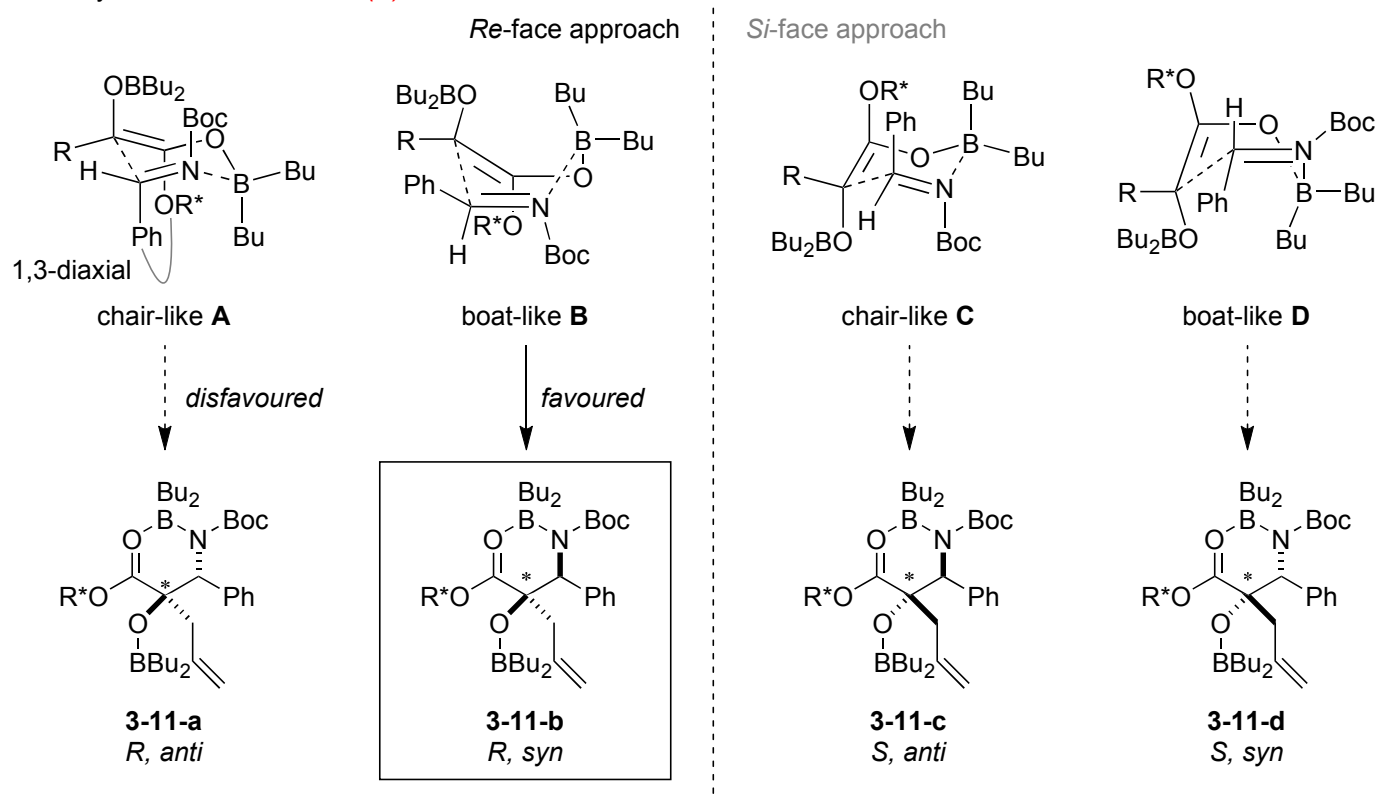


3-1. proposed reaction mechanisms



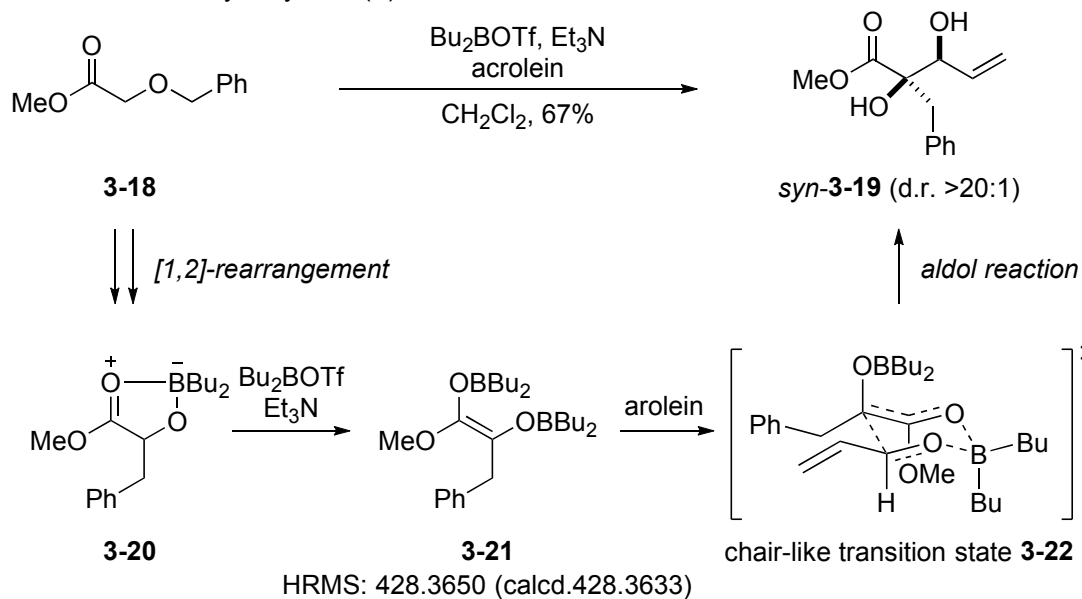
diastereoselectivity of Mannich-type reaction

R = allyl, No isomerization of (*E*)-imine is considered.



3-2. discussion

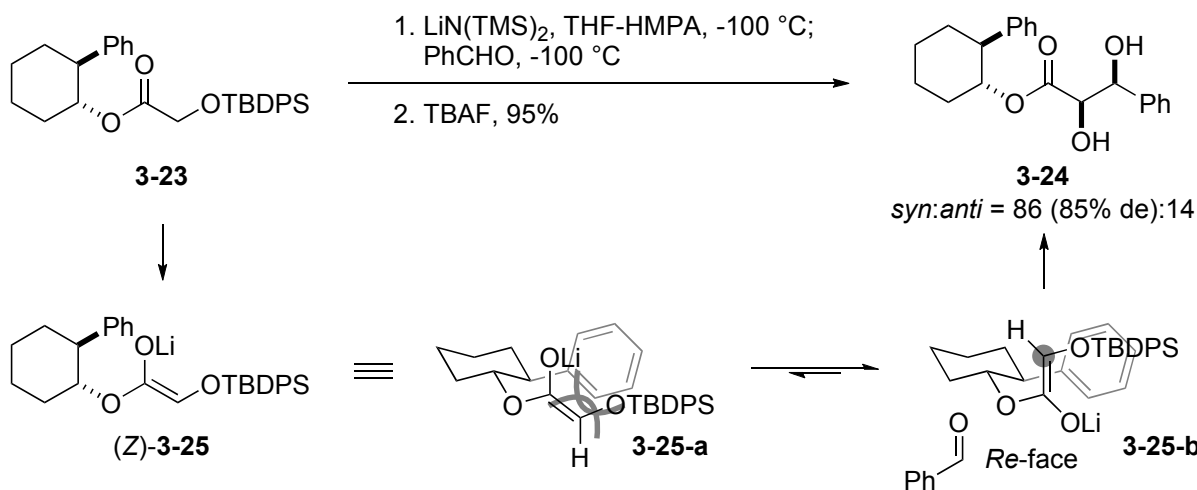
- consideration of doubly borylated (Z)-enolate



Wolfe, J. P. et. al. *OL* **2006**, *8*, 4661.

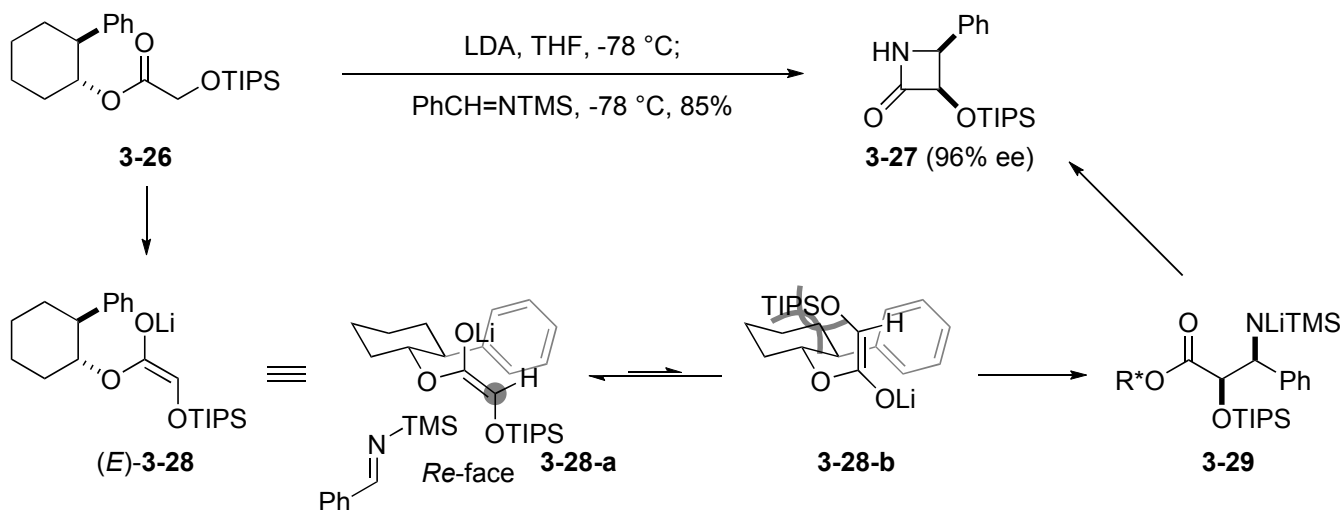
- *trans*-2-phenylcyclohexanol as a chiral auxiliary

- aldol reaction of (Z)-enolate



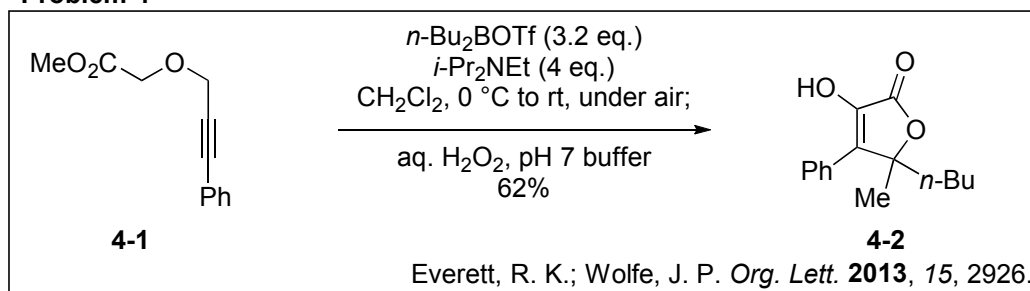
Yamamoto, H. et. al. *JOC* **1993**, *58*, 5301.

- Mannich-type reaction of (E)-enolate

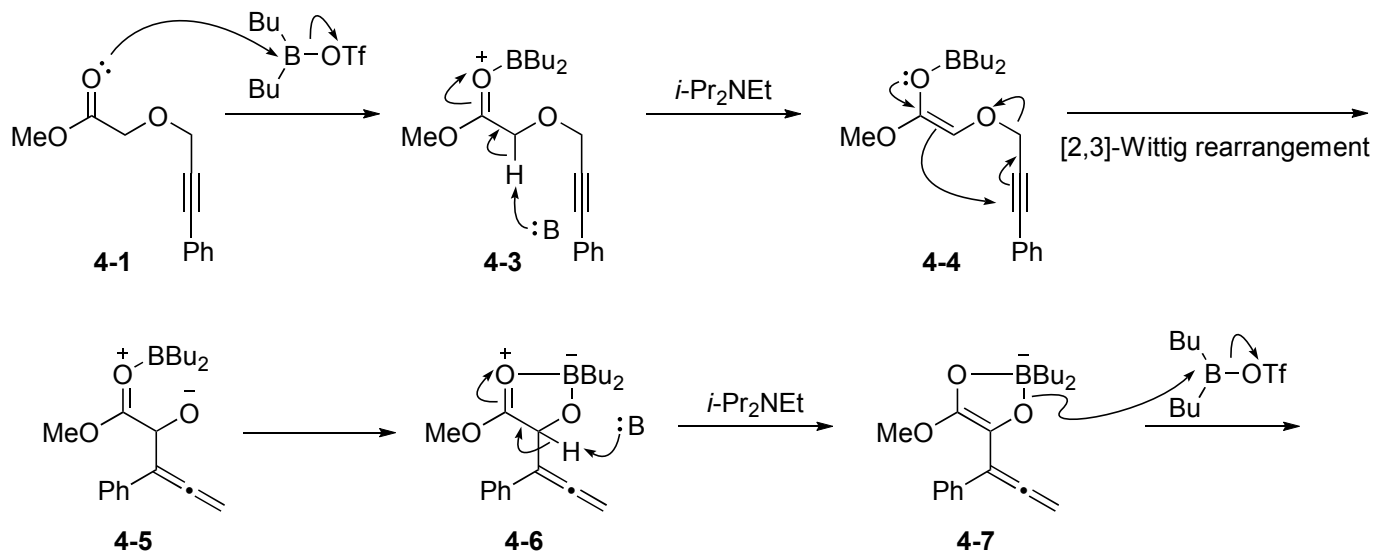


Ojima, I. et. al. *Tetrahedron* **1992**, *48*, 6985.

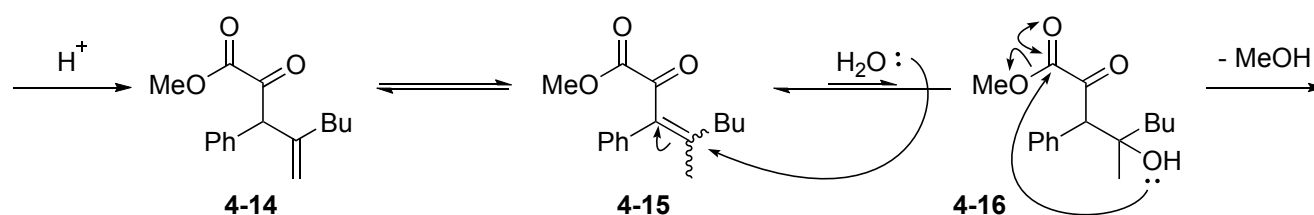
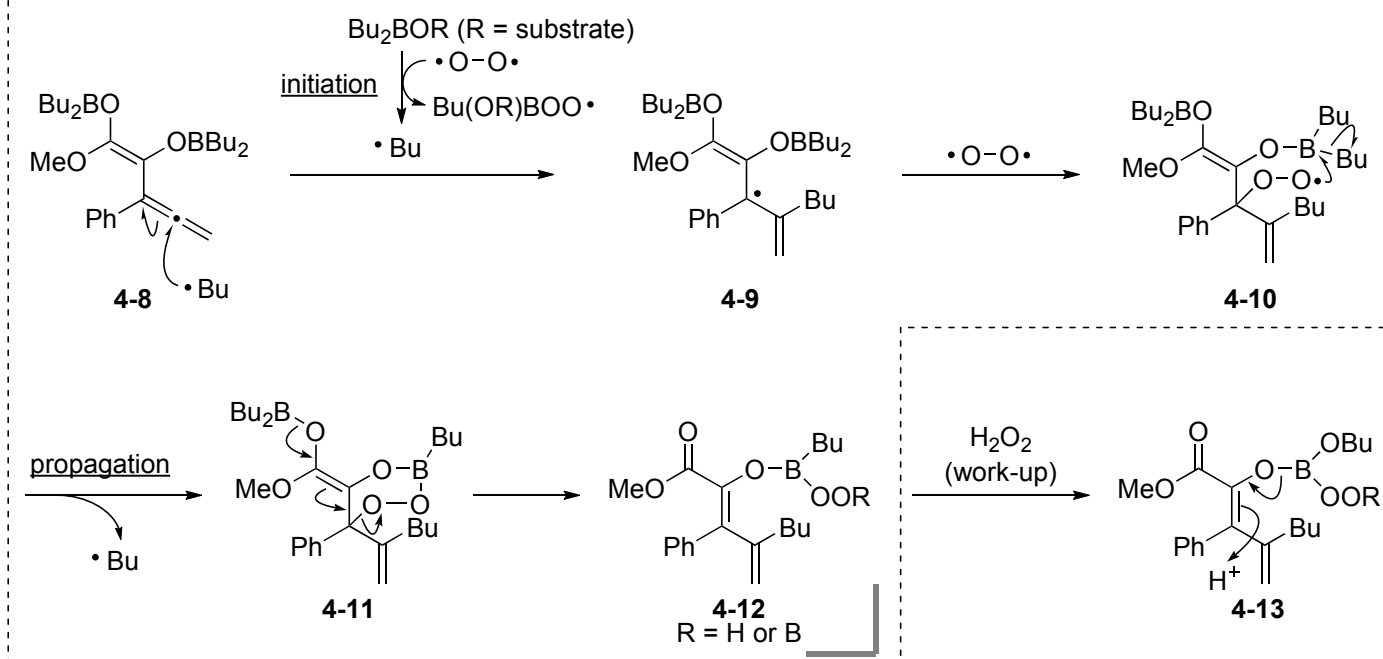
Problem 4

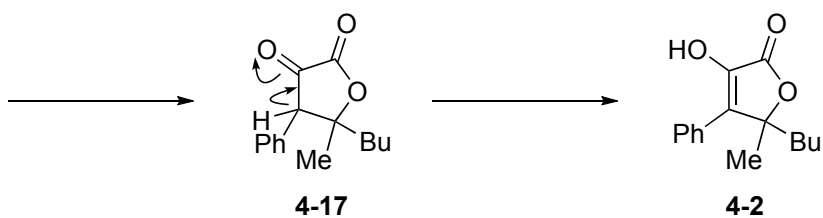


4-1. proposed reaction mechanisms

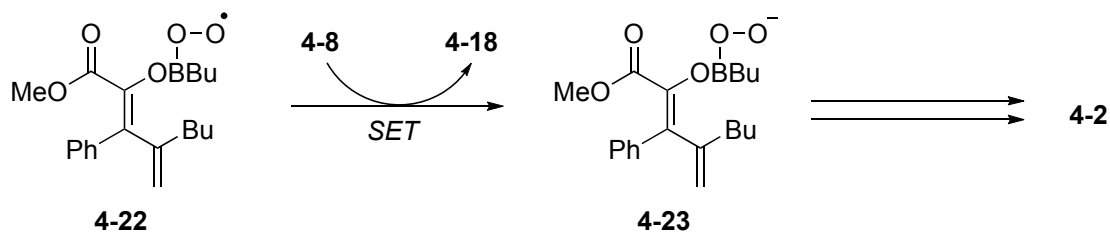
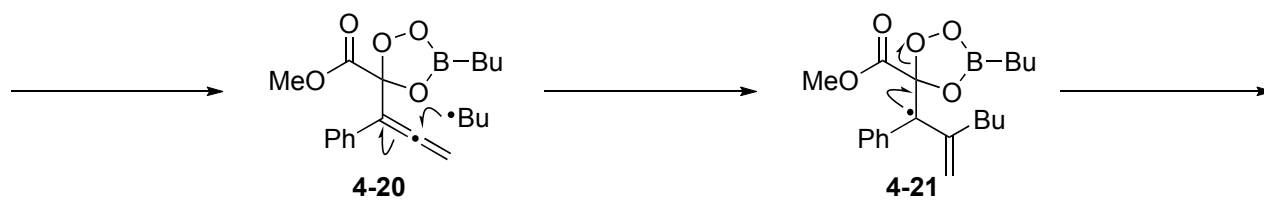
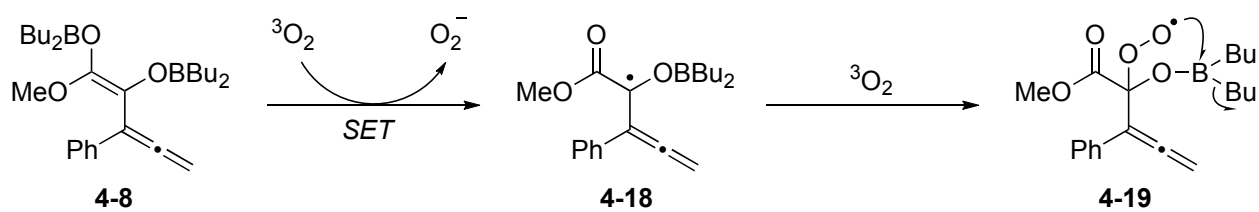


mechanism A (author's proposal)



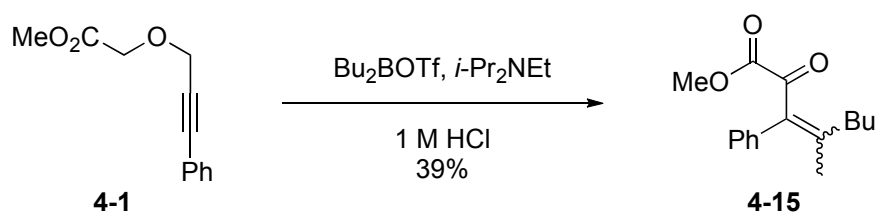


mechanism B (Prof. Inoue's proposal)



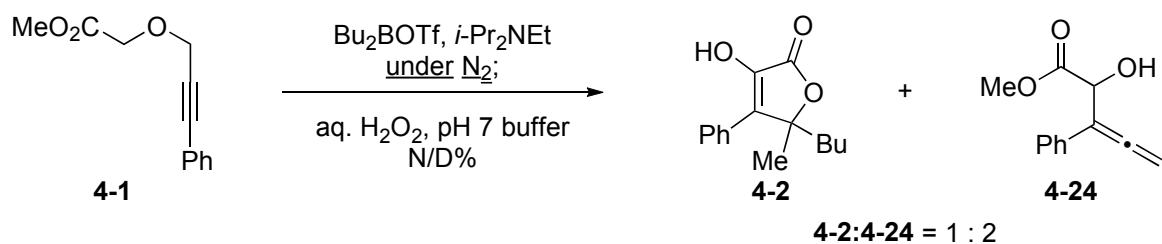
4-2. discussion

- acidic work-up

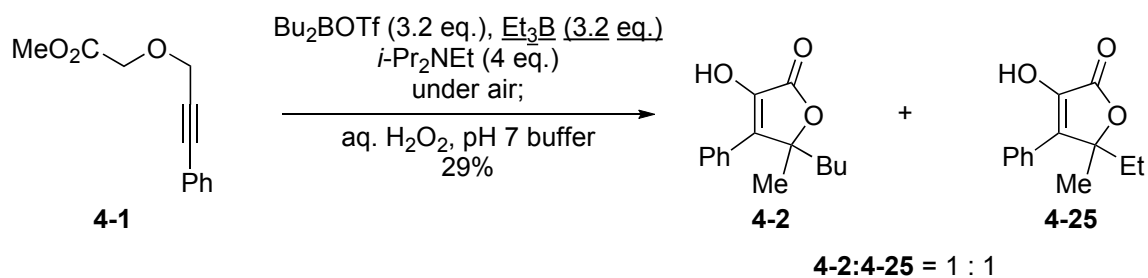


H_2O_2 did not work in oxidation process of the substrate.

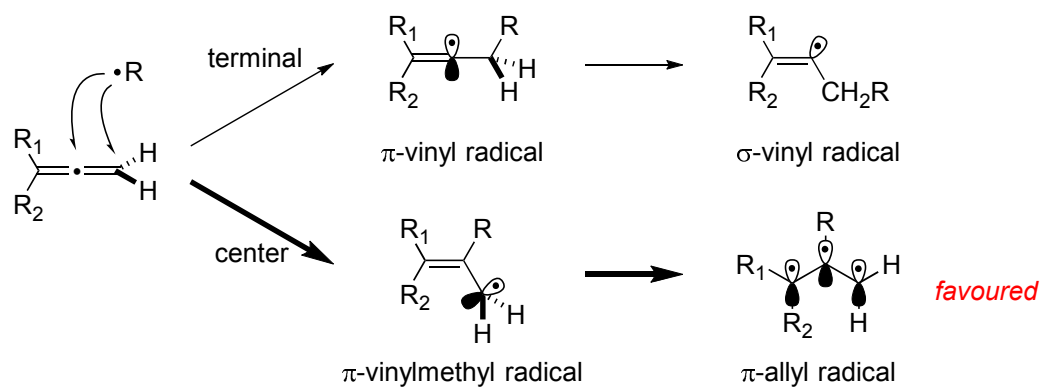
- allene intermediate / radical pathway



- reaction in the presence of triethylborane



- alkyl radical addition to allene



The radical addition generally proceeds at **center carbon** except for non-substituted allene.