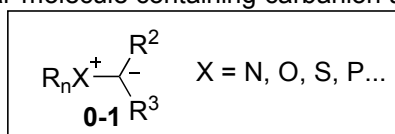


Problem Session Answer -Chemistry around Onium Ylide-

2015.10.9 Yuki Matsui

Introduction

(0-1) Onium ylide is neutral [1,2]-dipolar molecule containing carbanion attached to a heteroatom (N, O, S, P...).

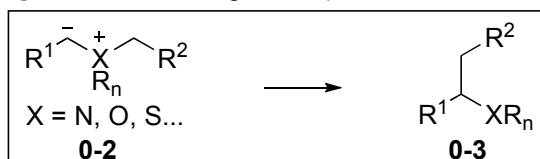


(0-2) Generation of onium ylides

1. Alkylation and deprotonation of amine, ether, sulfide or phosphine
2. Trapping carbenoid by amine, ether, sulfide or phosphine

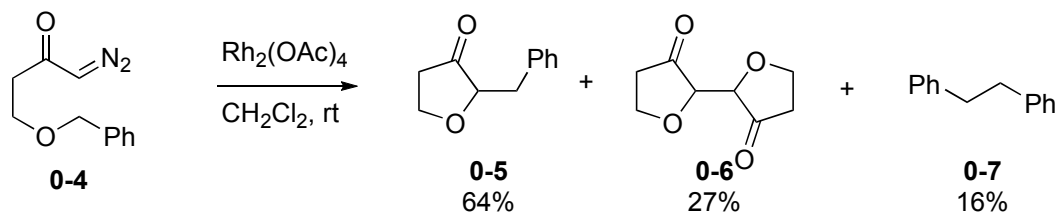
(0-2) Reactivity of onium ylides

(0-2-1) [1,2]-rearrangement ("[1,2]-Stevens rearrangement") → problem 1 and 2

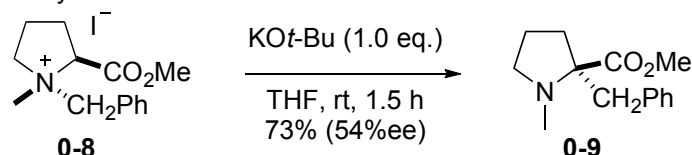


Mechanism

1. symmetry-forbidden → stepwise pathway
2. Homodimerization product was generated.

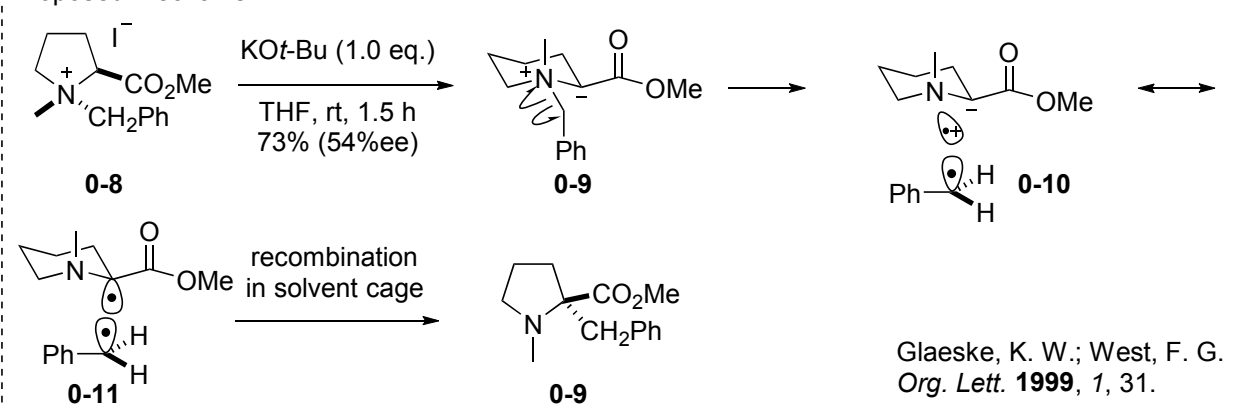


3. N to C chirality transfer was observed.

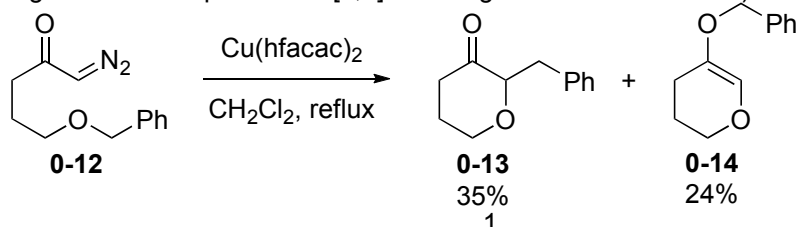


→ A rapid homolysis/recombination in solvent cage would occur.

Proposed mechanism



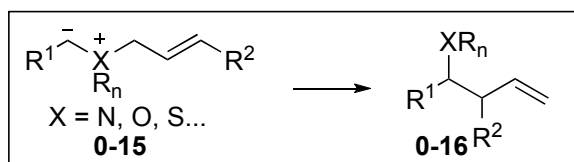
([1,4]-rearrangement is competed with [1,2]-rearrangement in some case.)



West, F. G.; Naidu, B. N.;
Tester, R. W.
J. Org. Chem. **1994**, 59, 6892.

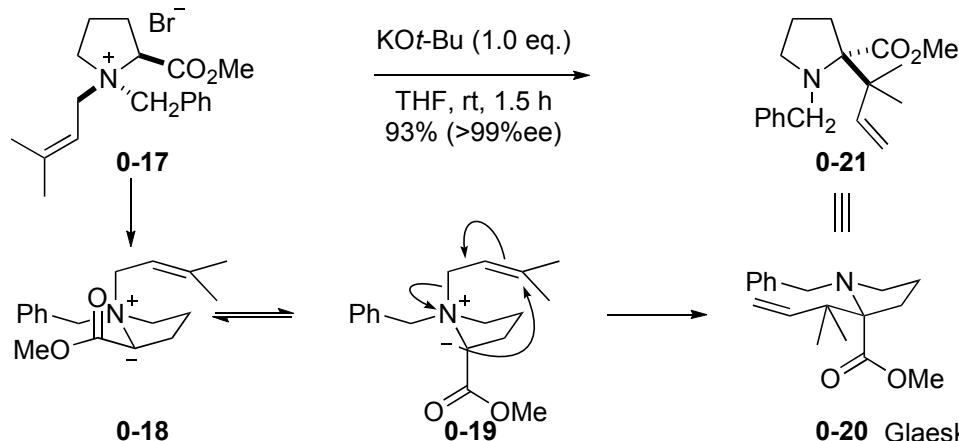
(0-2-2) [2,3]-rearrangement ("[2,3]-Stevens rearrangement" and "Sommelet-Hauser rearrangement")

→ problem 1 and 2



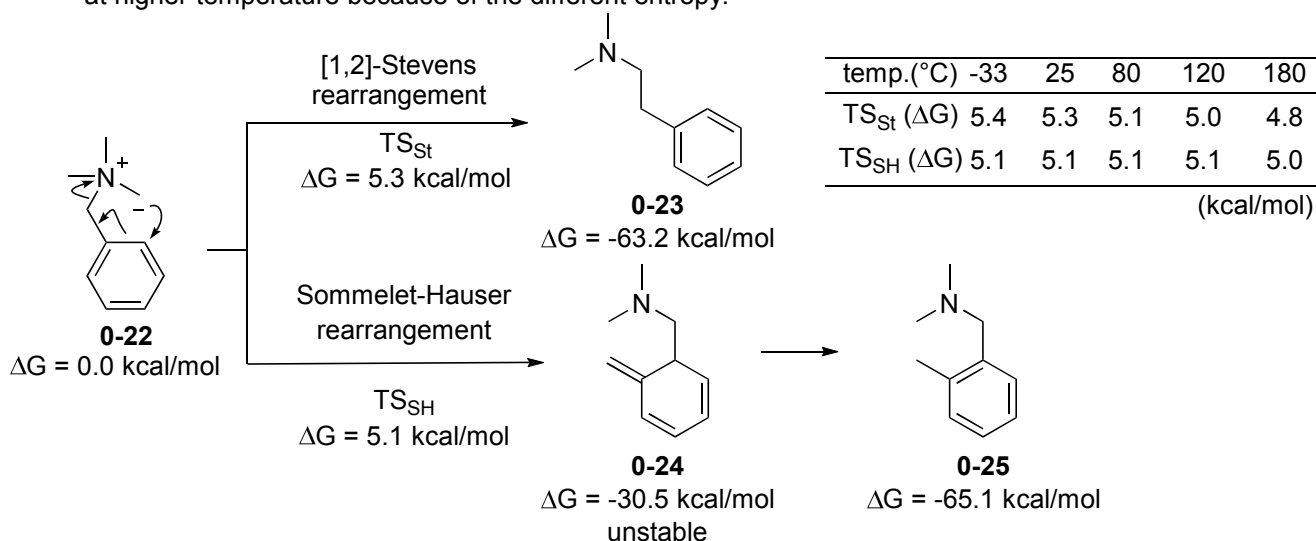
• mechanism

1. symmetry-allowed concerted process
2. Perfect level of N to C chirality transfer was observed.
3. [2,3]-Stevens-rearrangement is usually more favored than [1,2]-Stevens rearrangement probably due to lower energy of transition state.



• Sommelet-Hauser rearrangement

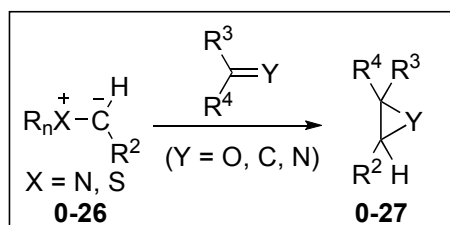
1. Sommelet-Hauser rearrangement is often competed with [1,2]-Stevens rearrangement.
2. Computational study suggests:
 - i) The intermediate of Sommelet-Hauser rearrangement **0-24** is more unstable than the product of [1,2]-Stevens rearrangement **0-23**.
When the ylide is very stable and the rearrangement is reversible, [1,2]-Stevens rearrangement is favored.
 - ii) Sommelet-Hauser rearrangement is favored at lower temperatures and the Stevens rearrangement at higher temperature because of the different entropy.



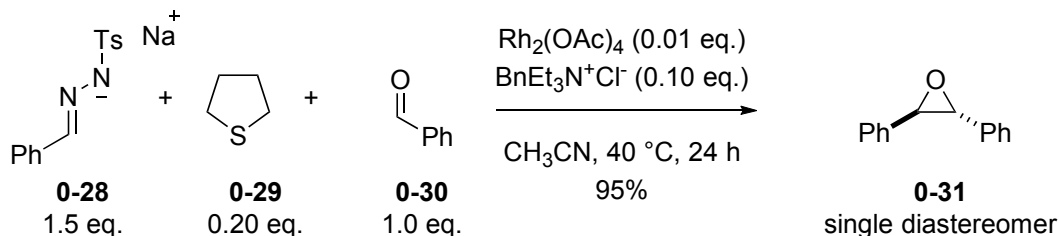
calculation method: M05-2X 6-311+G(3df, 2p) in gas phase

Ghigo, G.; Cagnina, S.; Maranzana, A.; Tonachini, G. *J. Org. Chem.* **2010**, 75, 3608.

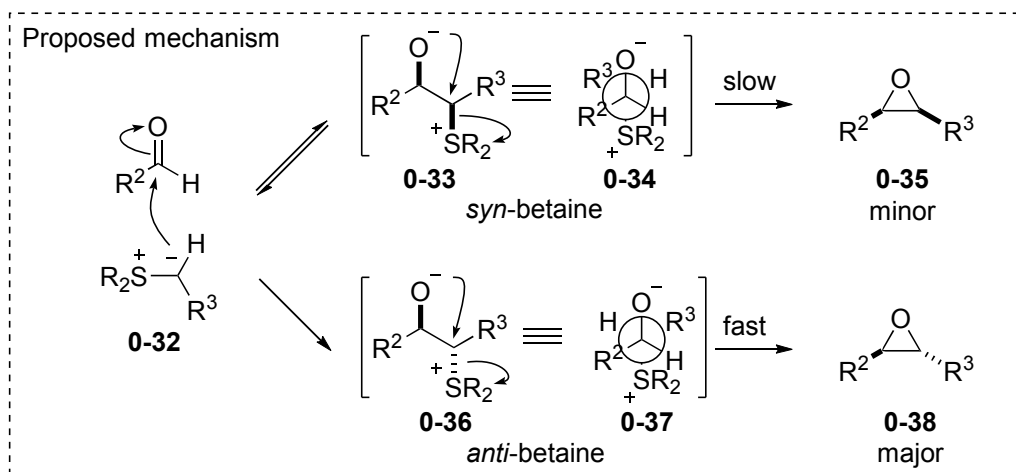
(0-2-3) Nucleophilic addition and subsequent cyclization to a three-membered ring (epoxide, cyclopropane, aziridine) ("Corey-Chaykovsky epoxidation and cyclopropanation") → problem 4



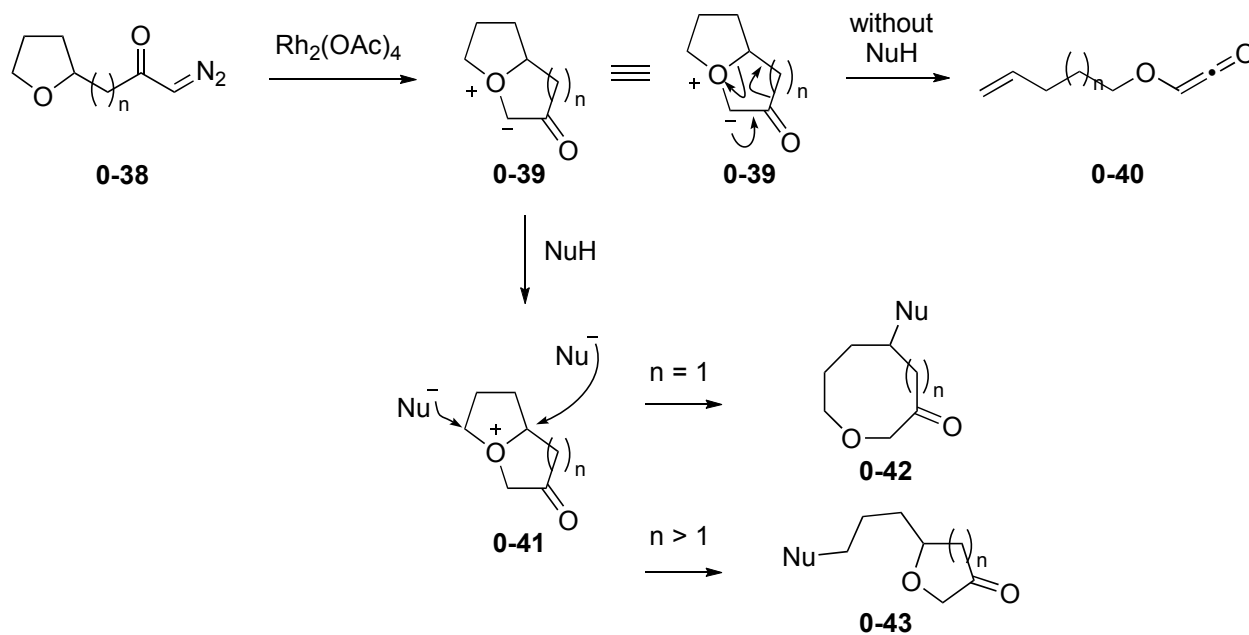
• mechanism



Aggawal, V. K. et. al. *J. Am. Chem. Soc.* **2003**, 125, 10926.



(0-2-4) α , β -fragmentation \longrightarrow problem 3



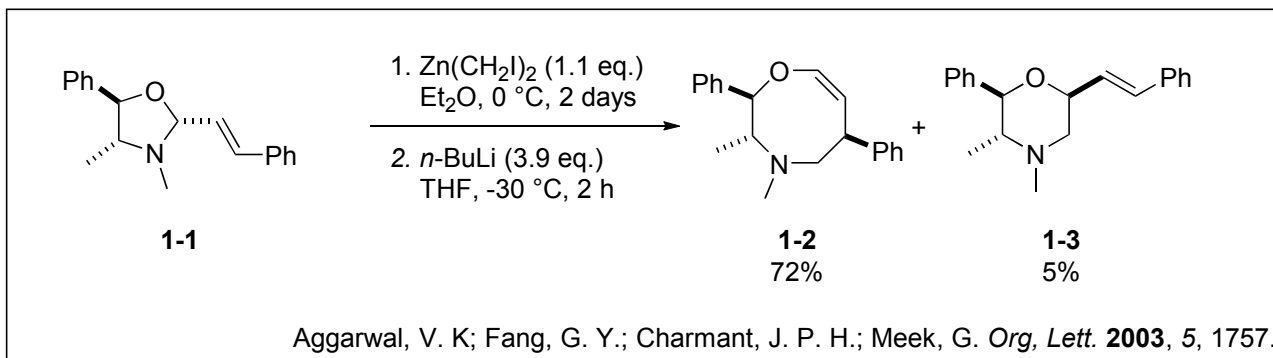
Oku, A.; Mori, T.; Sawada, Y. *J. Syn. Org. Chem. Jpn.* **2000**, 58, 934.

(0-2-5) Synthetic application

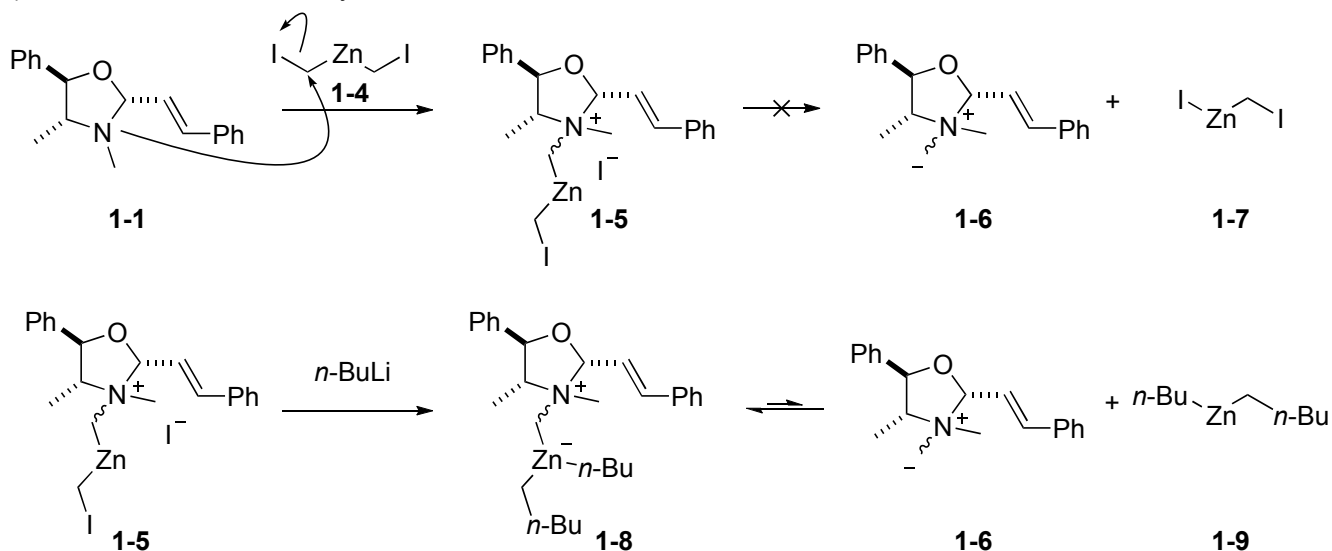
Please see reviews: Murphy, G. K.; Stewart, C.; West, F. G. *Tetrahedron*, **2013**, 69, 2667.

Vanecko, J. A.; Wan, H.; West, F. G. *Tetrahedron*, **2006**, 62, 1043.

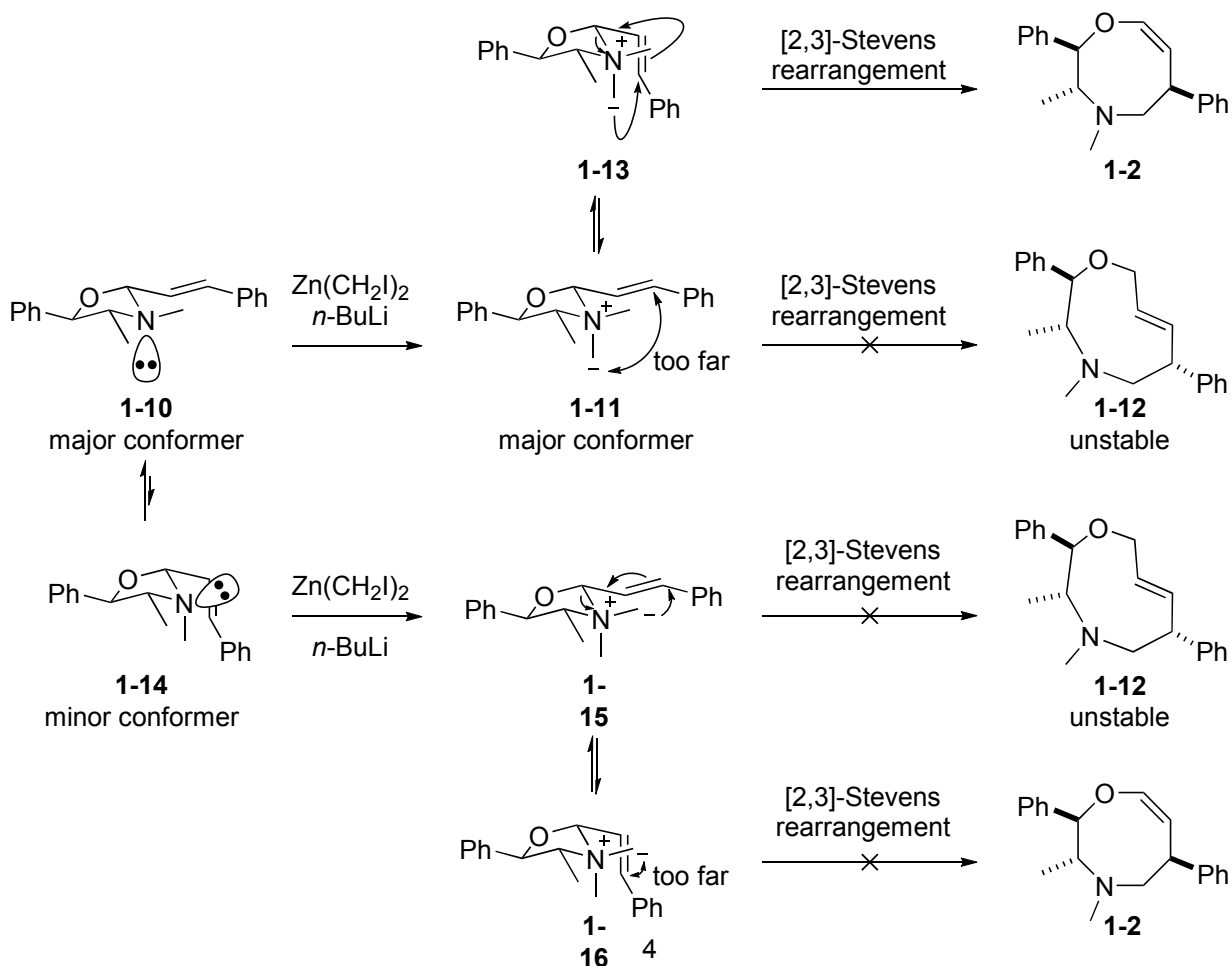
Problem1



(1-1) Generation of ammonium ylide 1-6

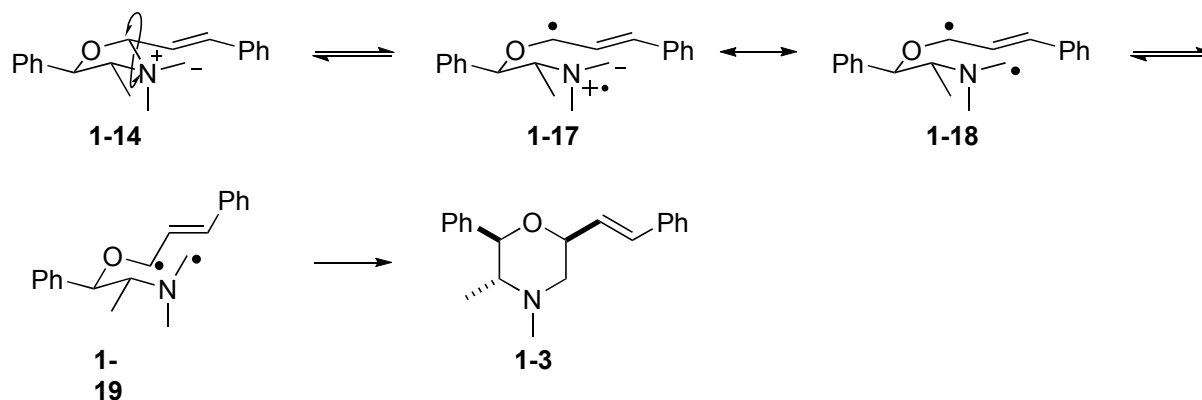


(1-2) Generation of major product 1-2

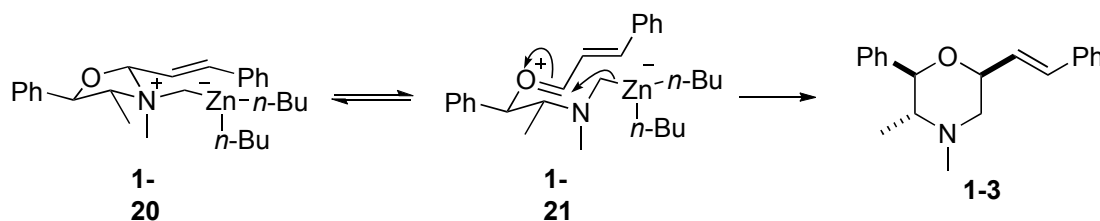


(1-3) Generation of minor product

(1-3-1) Radical pathway

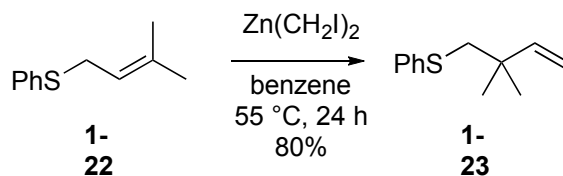


(1-3-1) Polar pathway



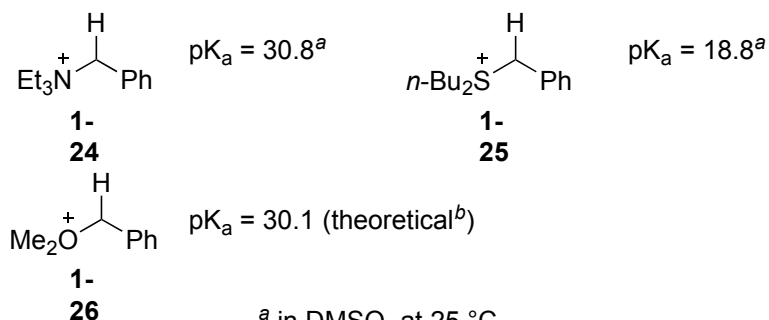
(1-4) Ammonium ylide compared to sulfonium ylide

(1-4-1) Zinc-complexed sulfonium ylide readily participate in [2,3]-Stevens rearrangement



Kozarych, Z.; Cohen, T. *Tetrahedron Lett.* **1982**, 23, 3019.

(1-4-2) pKa of sulfonium ylide and ammonium ylide

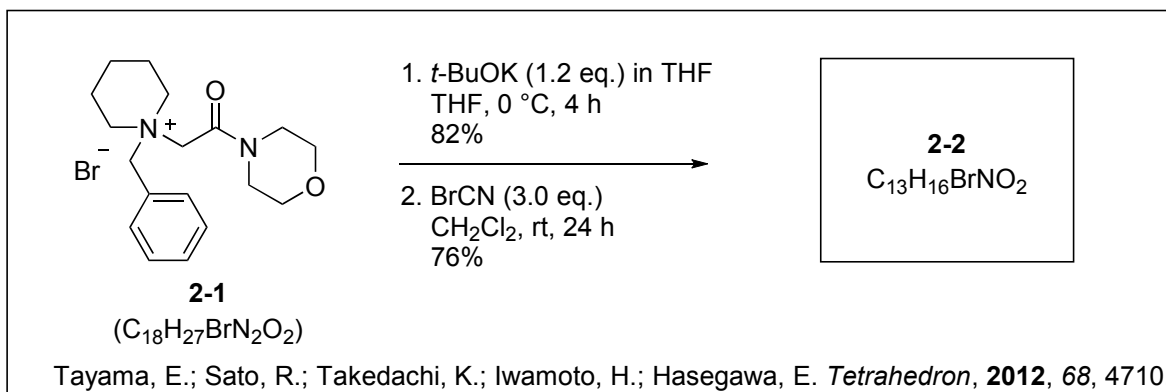


^a in DMSO, at 25 °C

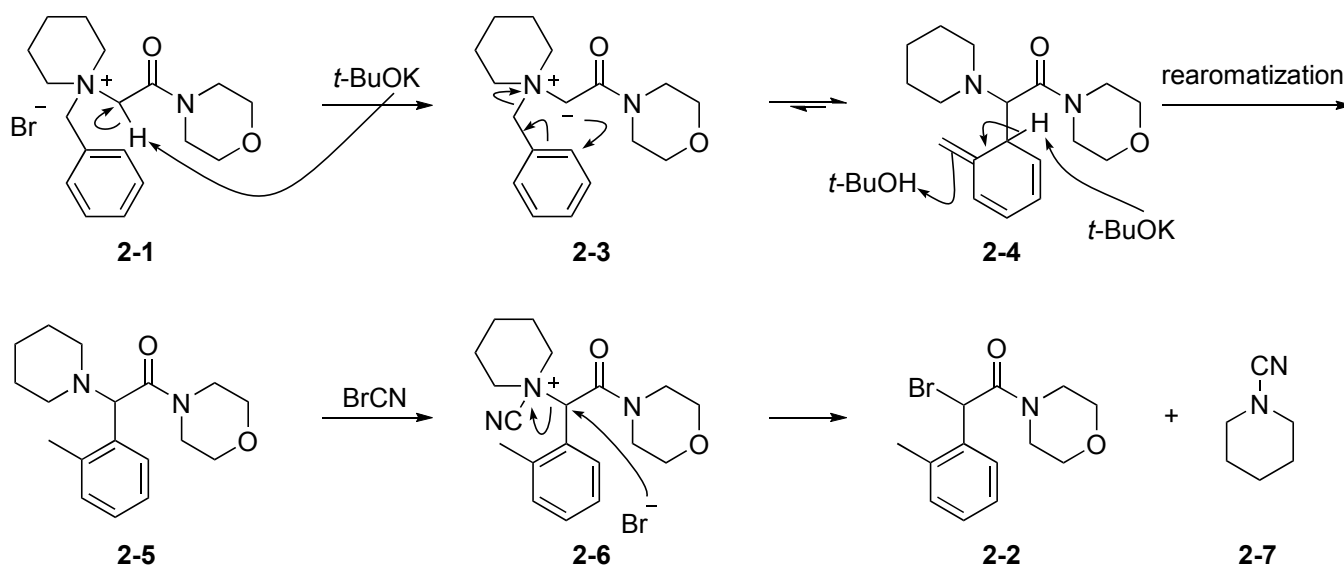
^b calculation method: ONIOM/G3B3//HF//CPCM/Bondi(1.20)

Fu, Y.; Wang, H.-J.; Chong, S.-S.; Guo, Q.-X.; Liu, Lei. *J. Org. Chem.* **2009**, 74, 810.

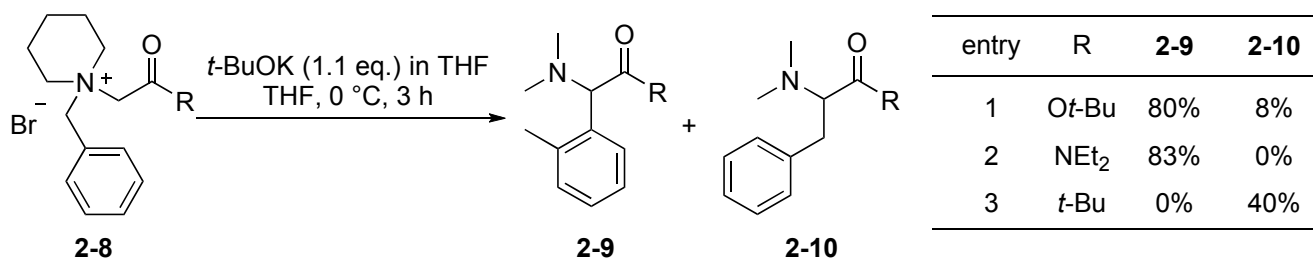
Problem 2



(2-1) Proposed mechanism

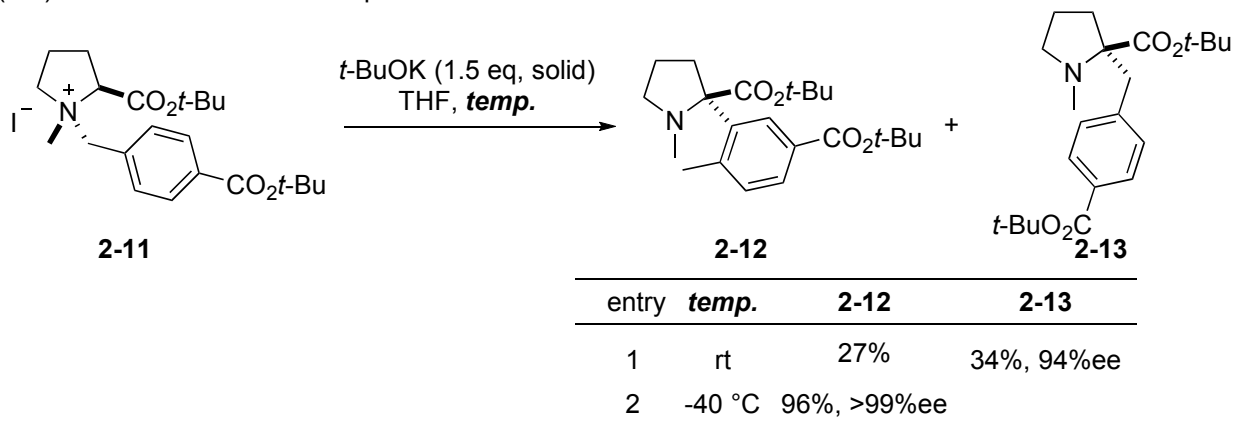


(2-2) The effect of carbonyl group attached to carbanion



Tayama, E.; Takedachi, K.; Iwamoto, H.; Hasegawa, E. *Tetrahedron*, **2010**, *66*, 9389.

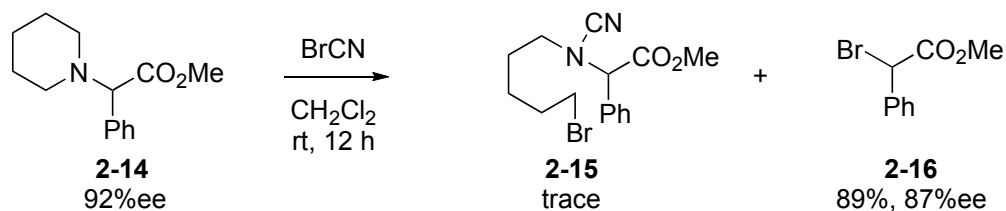
(2-3) The effect of reaction temperature



Tayama, E.; Kimura, H. *Angew. Chem. Int. Ed.* **2007**, *46*, 8869.

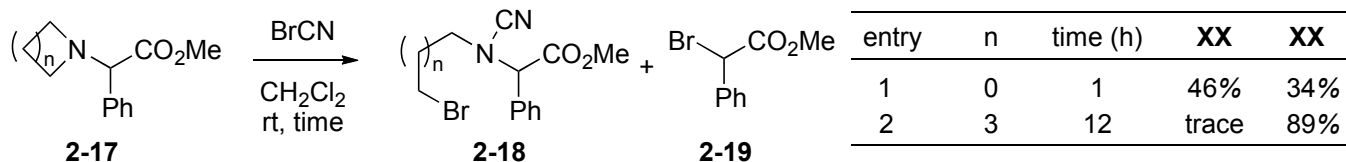
(2-4) Regioselectivity of α -substitution with cyanogen bromide

(2-4-1) α -Substitution with cyanogen bromide is S_N2 reaction.

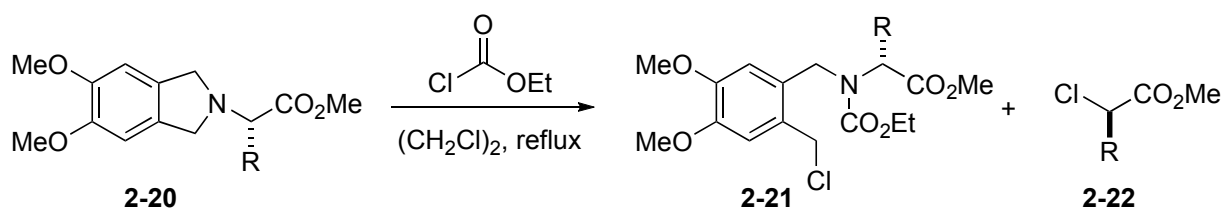


Tayama, E. *Chem. Rec.* **2015**, 15, 789.

(2-4-2) The effect of *N*, *N*-substituents

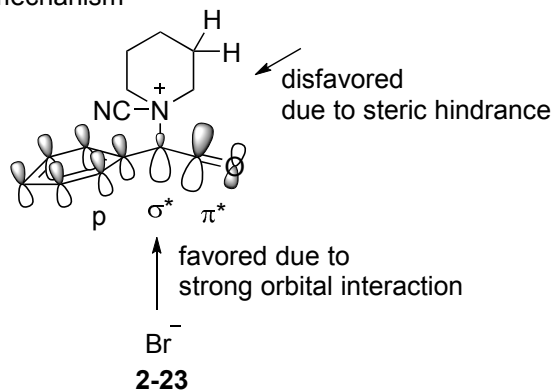


(2-4-3) The effect of α -substituents

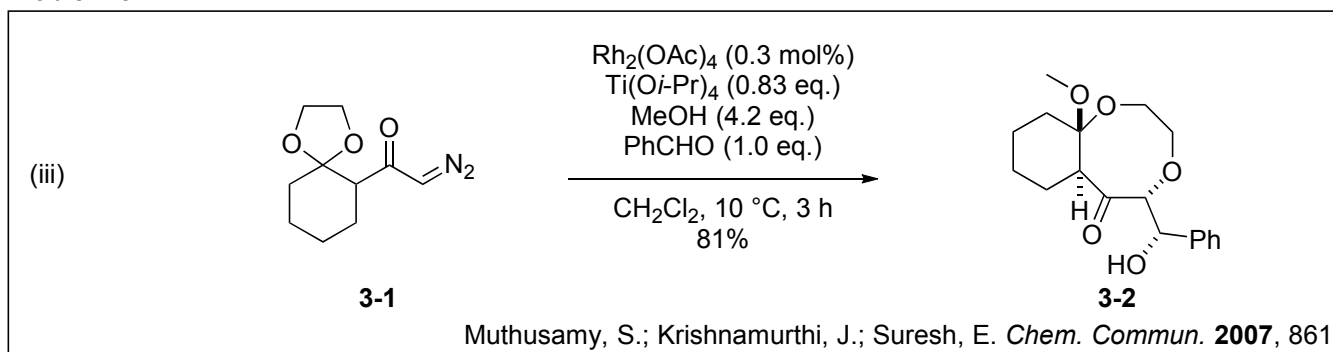


entry	R	2-21	2-22
1	CH ₂ Ph	88%	0%
2	Ph	30%	34%

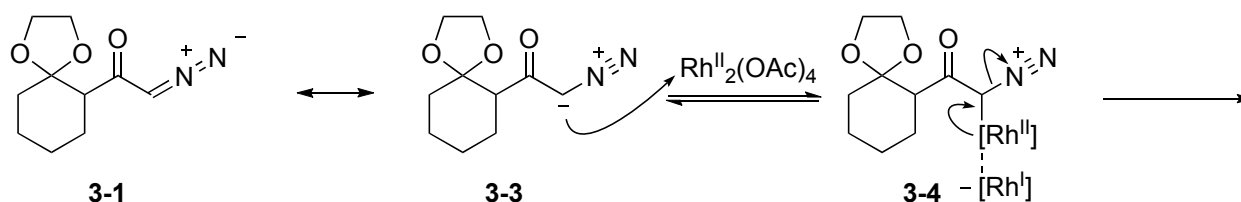
(2-4-3) Proposed mechanism

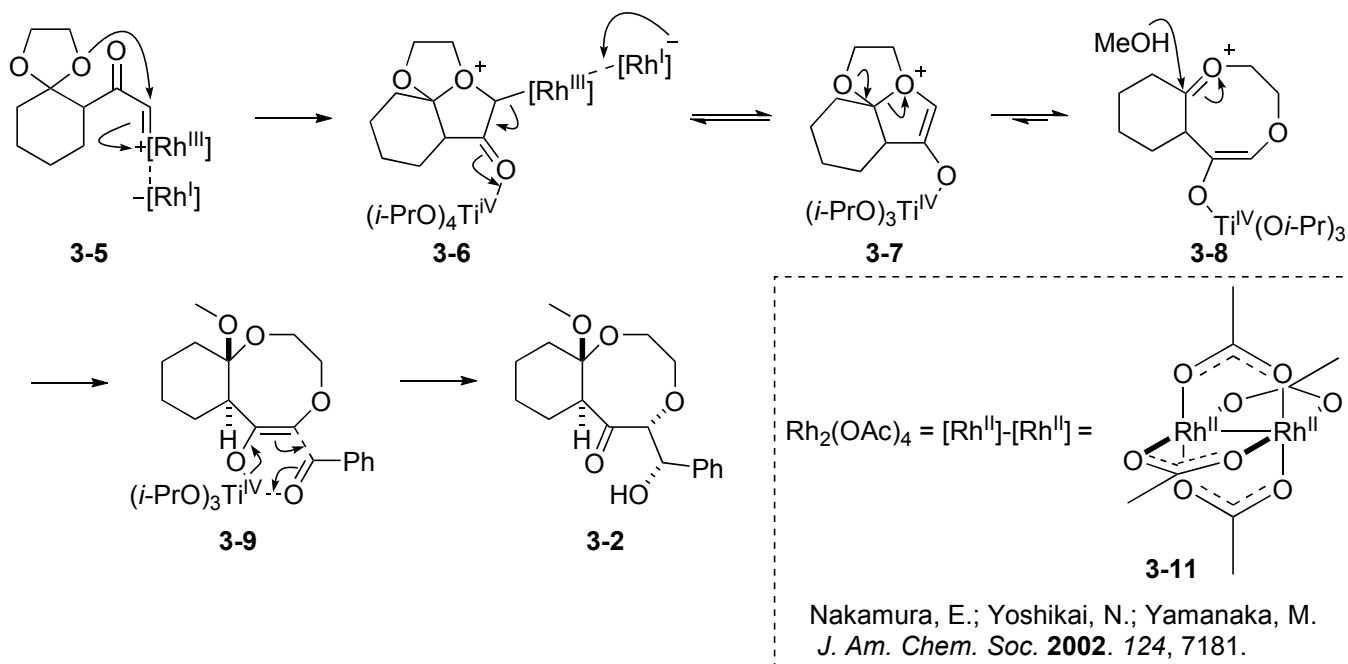


Problem 3

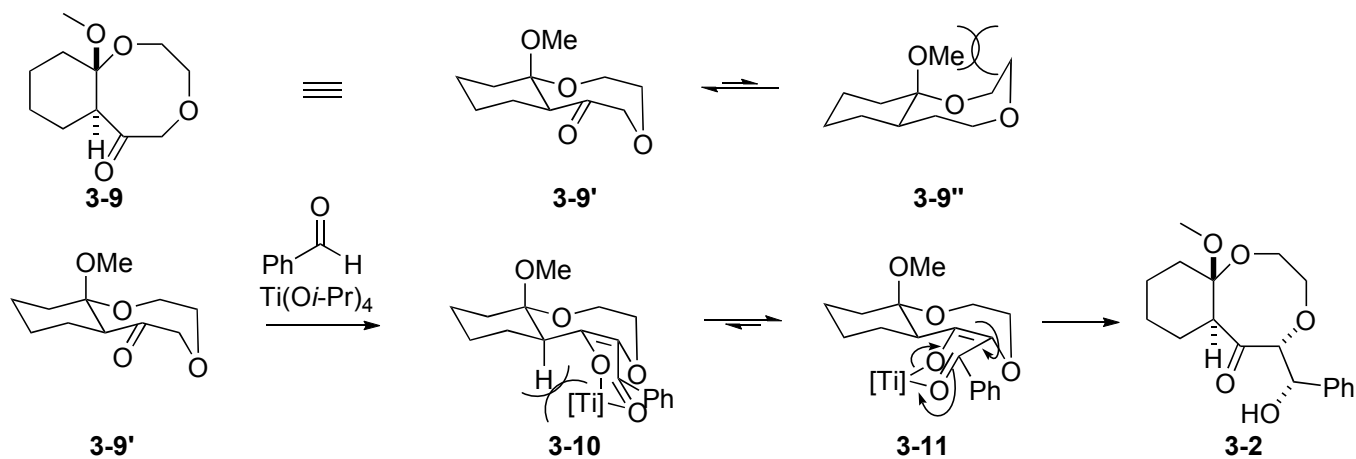


(3-1) Proposed mechanism

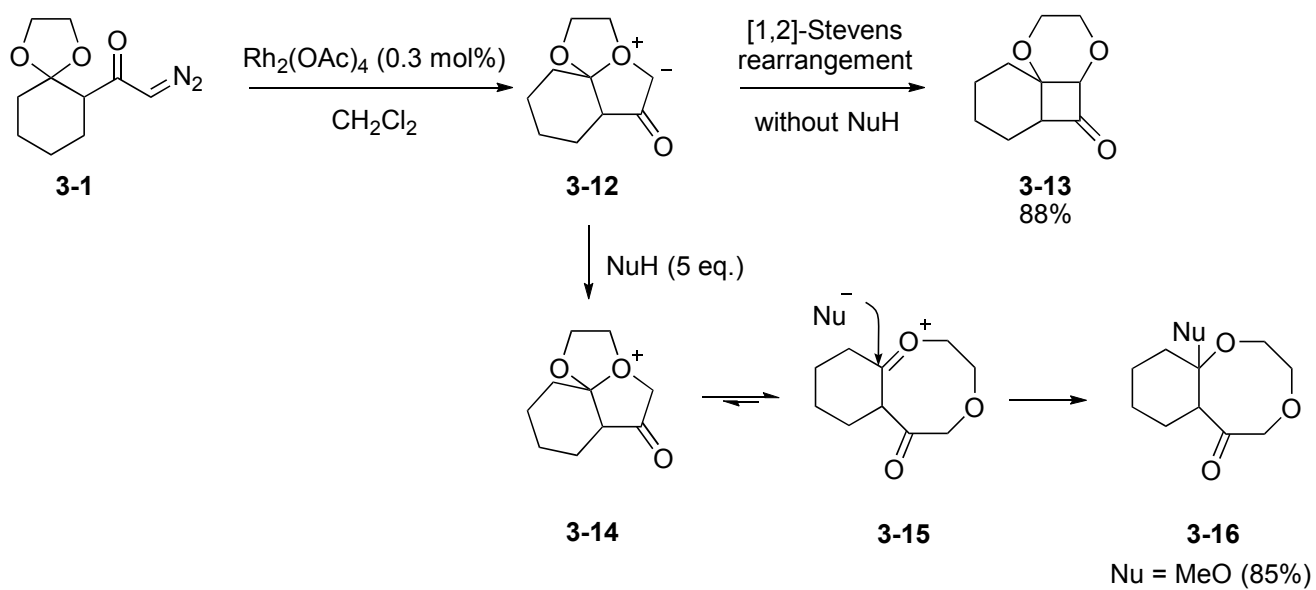




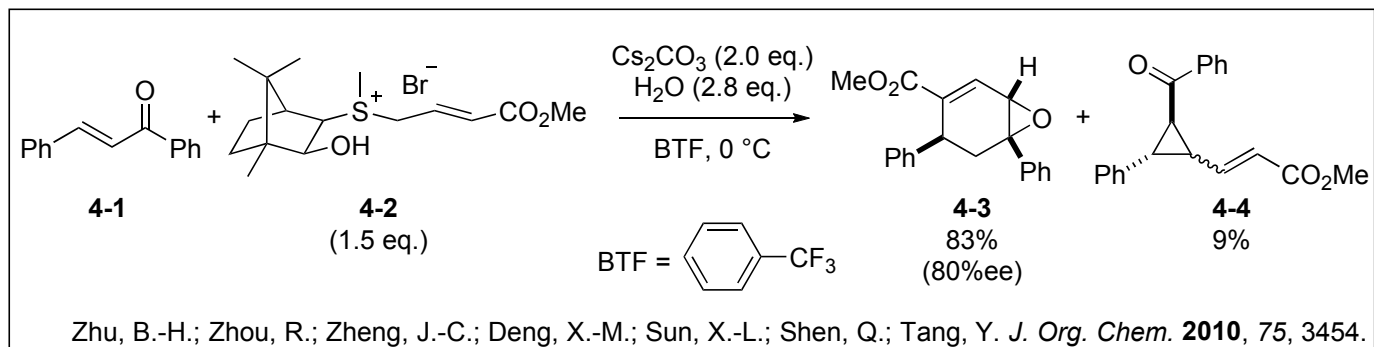
(3-2) Stereoselectivity in aldol reaction



(3-3) Control experiments without electrophile and/or nucleophile

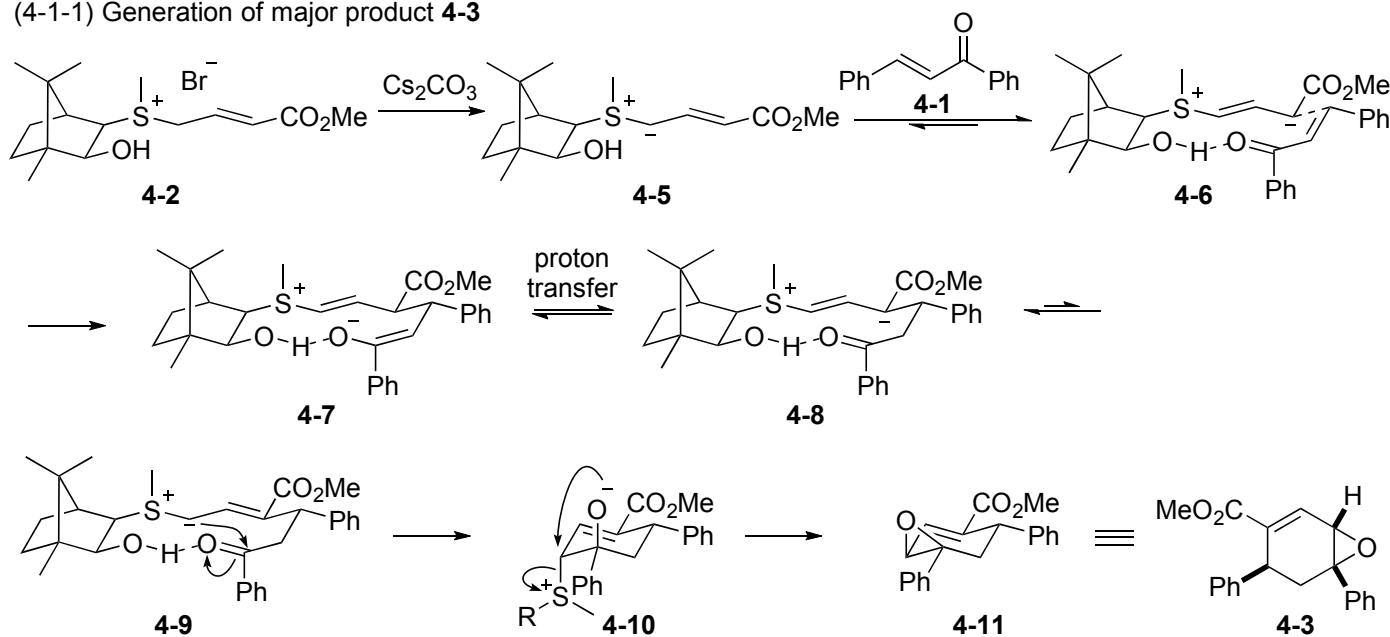


Problem 4

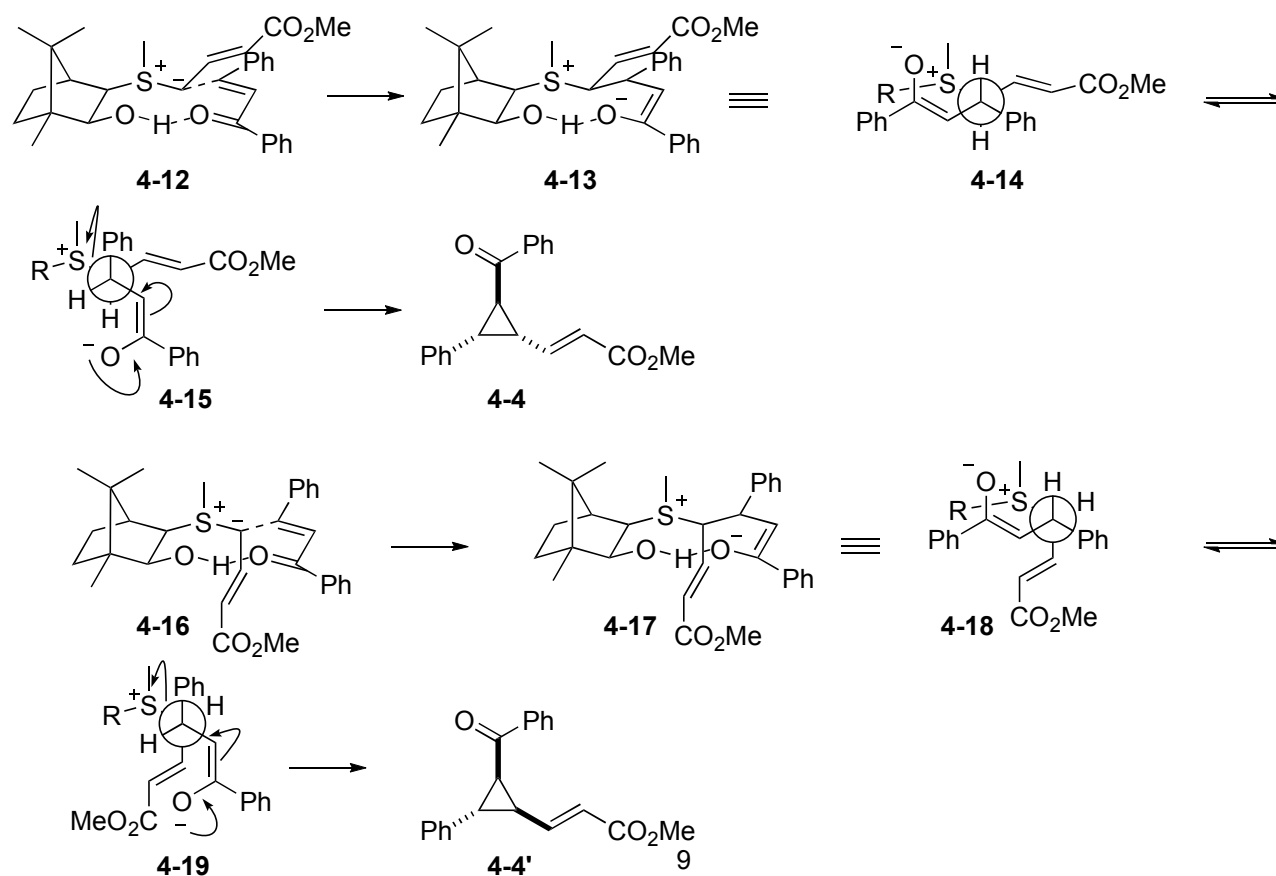


(4-1) Proposed mechanism

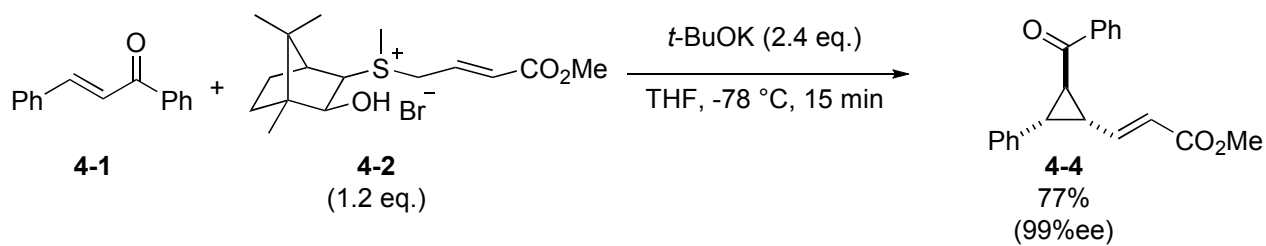
(4-1-1) Generation of major product 4-3



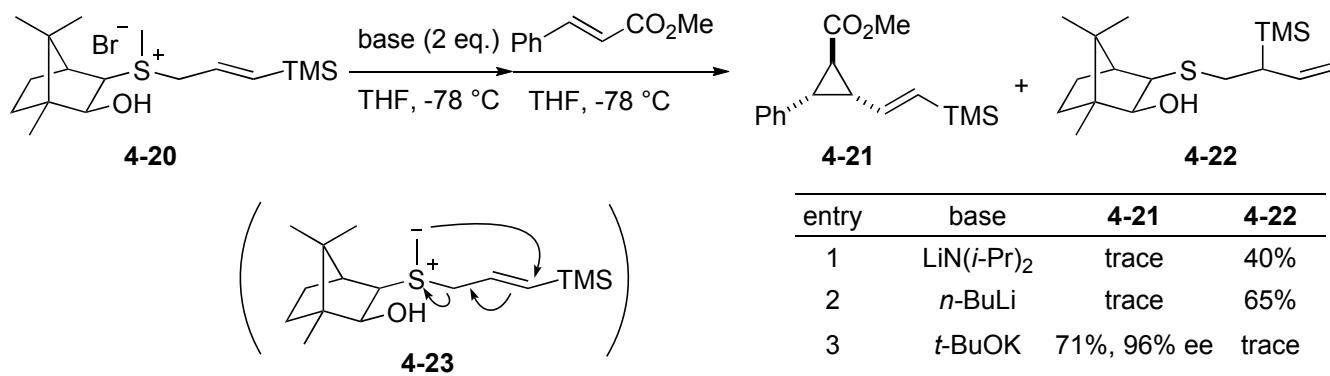
(4-1-2) Generation of minor product 4-4 and 4-4'



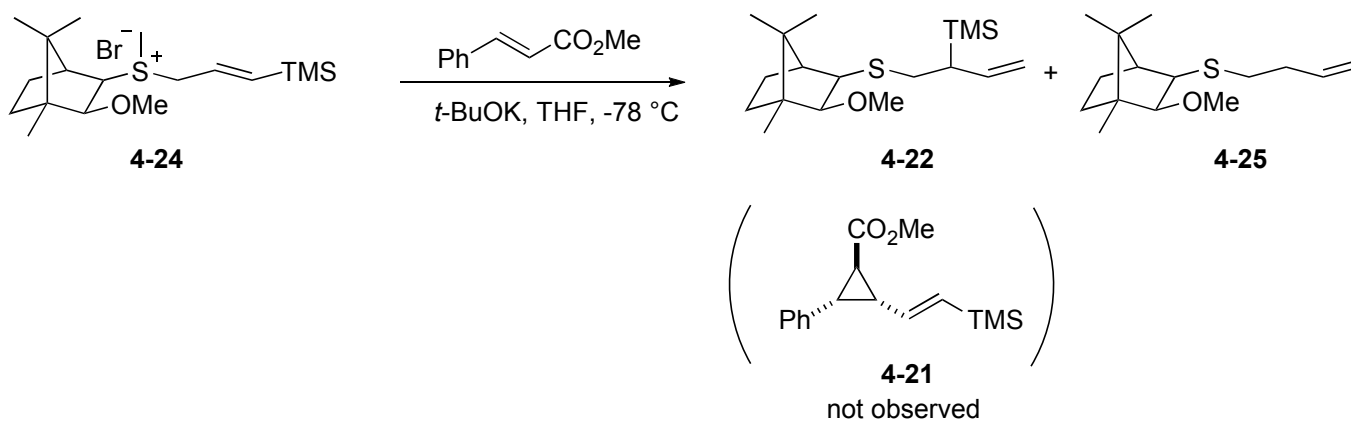
(4-2) **4-4** is the kinetic product.



(4-3) Regioselectivity of deprotonation is critical.



(4-4) Hydroxy group is essential.



Deng, X.-M.; Cai, P.; Ye, S.; Sun, X.-L.; Liao, W.-W.; Li, K.; Tang, Y.; Wu, Y.-D.; Dai, L.-X. *J. Am. Chem. Soc.* **2006**, *128*, 9730.