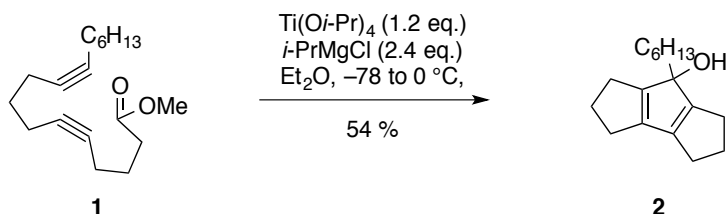


Problem Session (6)

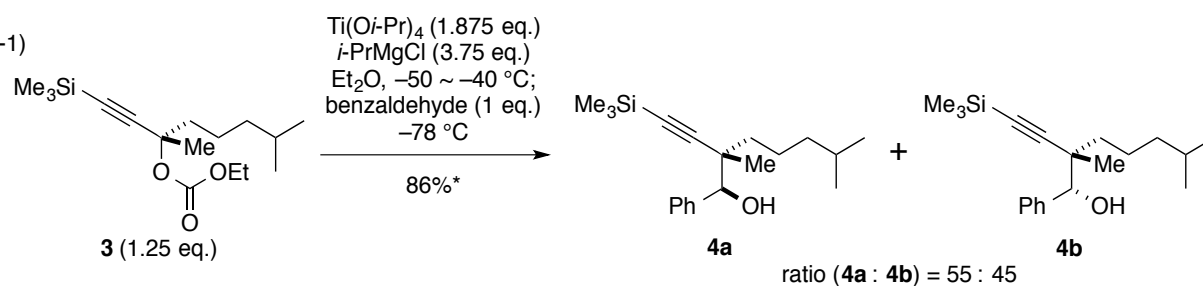
2016. 4. 9 Shunichiroh Katoh

Please fill in the blanks and provide the reaction mechanisms.

(1)

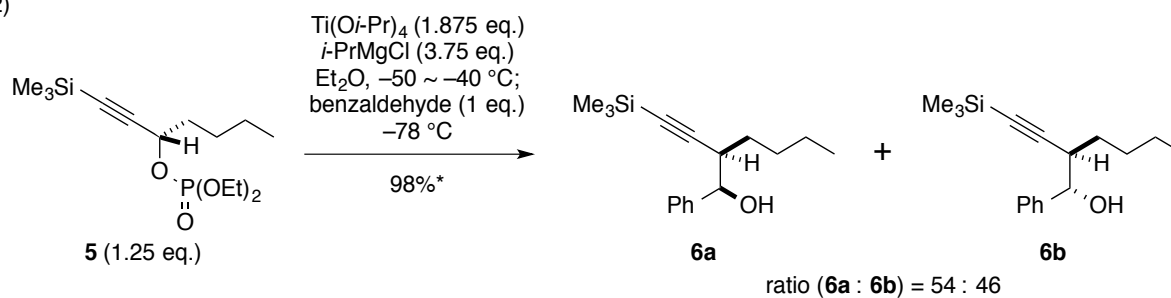


(2-1)



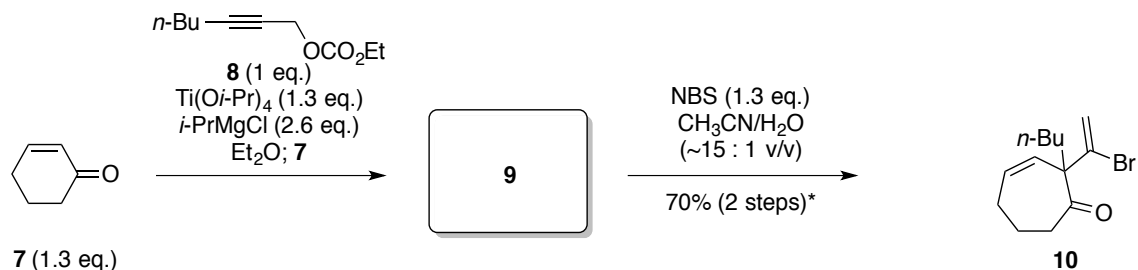
* Based on benzaldehyde

(2-2)



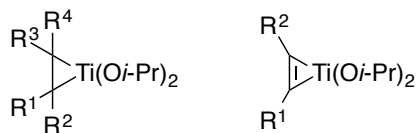
* Based on benzaldehyde

(3)

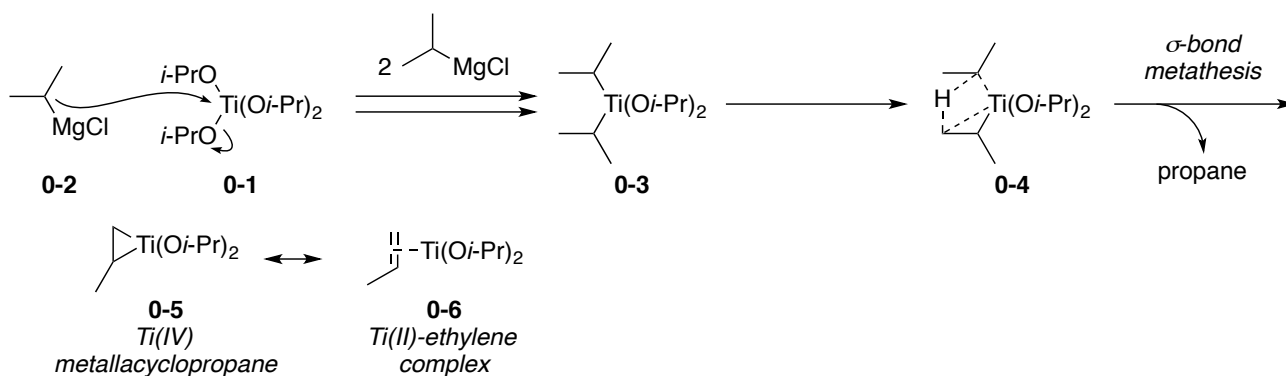


* Based on **8**

Main Topic : Reactions around titanacyclopropanes and titanacycloprenes



0. Introduction

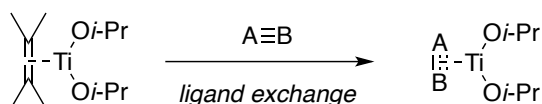
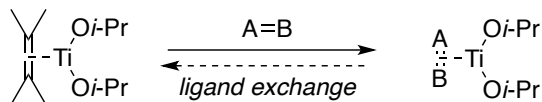


First report:

Kulinkovich, O. G. et al *Zh. Org. Khim.* **1989**, 25, 2244; *Russ. J. Org. Chem.* **1989**, 25, 2027. (Kulinkovich reaction)

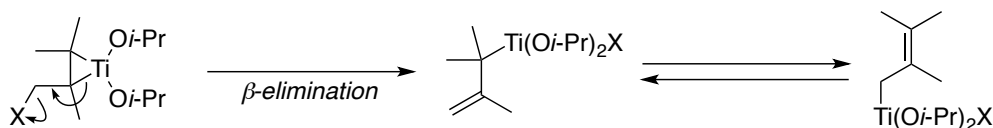
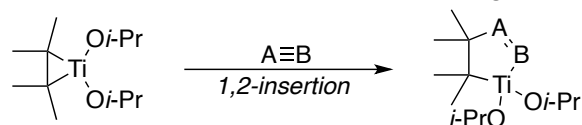
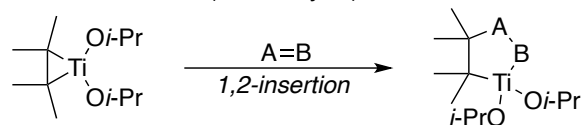
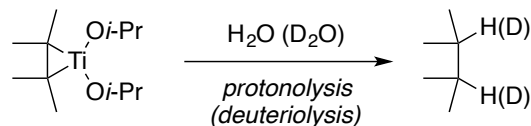
0.1. Reactivity

Ligand-like reactions

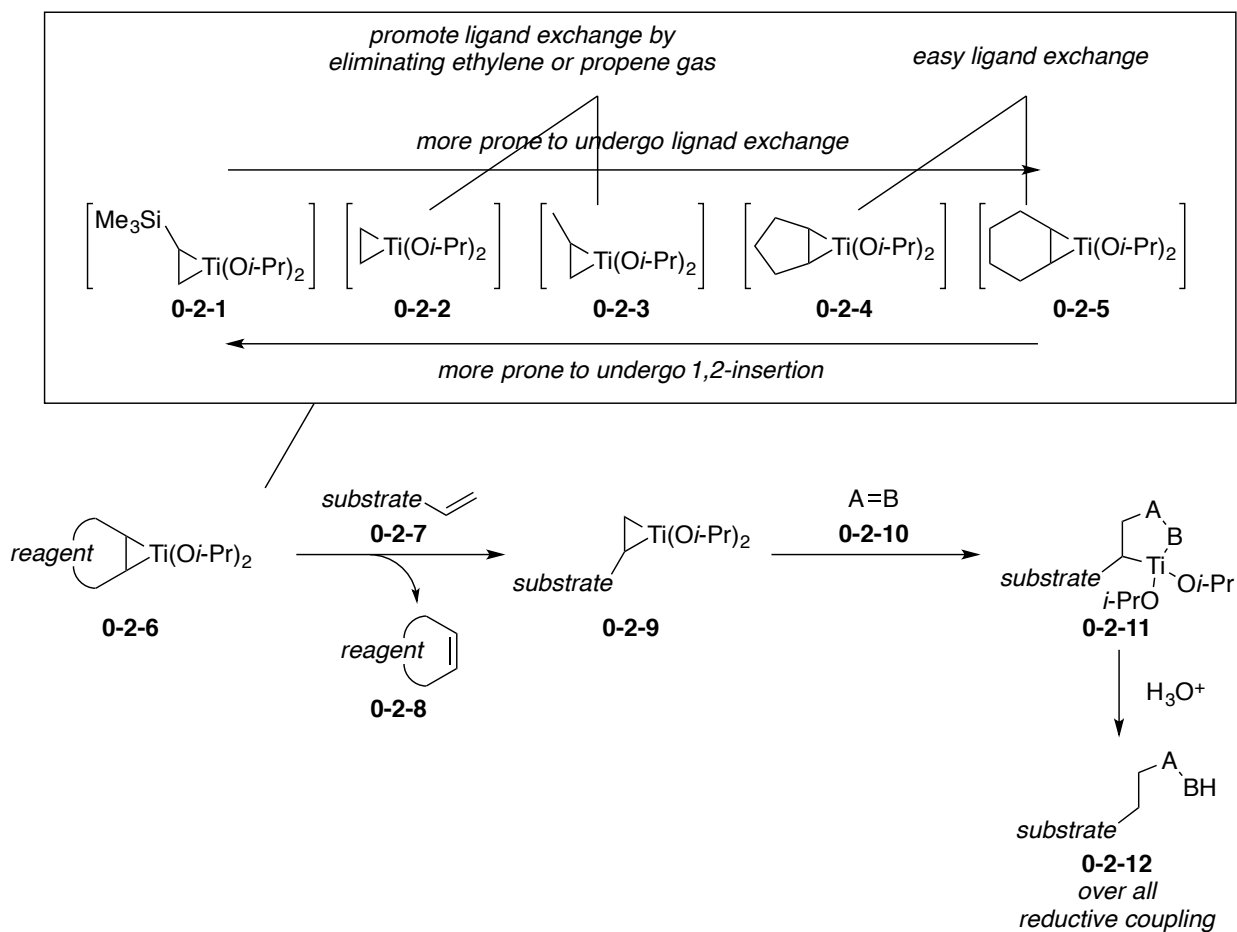


irreversible (Problem 1 ~ 3)

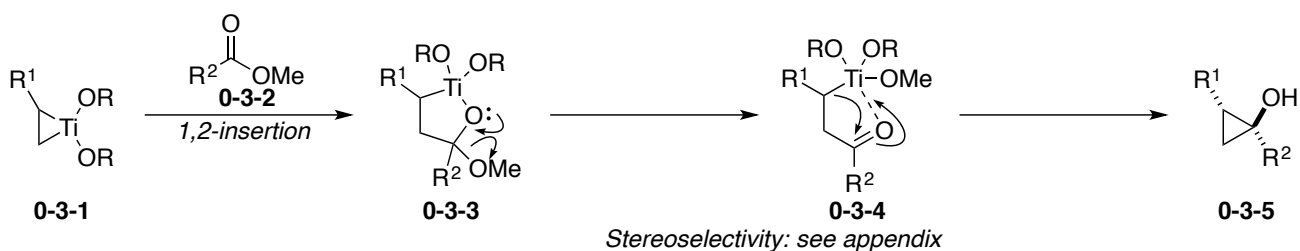
1,2-dianion-like reactions



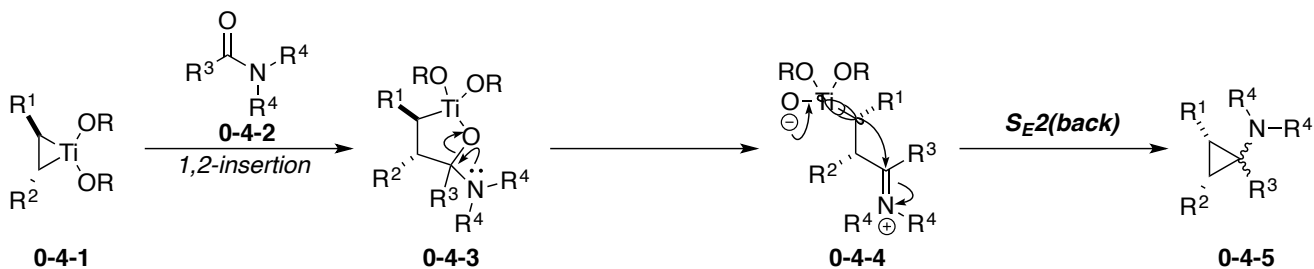
0.2. First step: introduction of substrate onto the titanium center and C-C bond formation



0.3. Kulinkovich reaction: alkene + ester \rightarrow cyclopropyl alcohol



0.4. Kulinkovich-de Meijere reaction: alkene + amide \rightarrow cyclopropyl amine

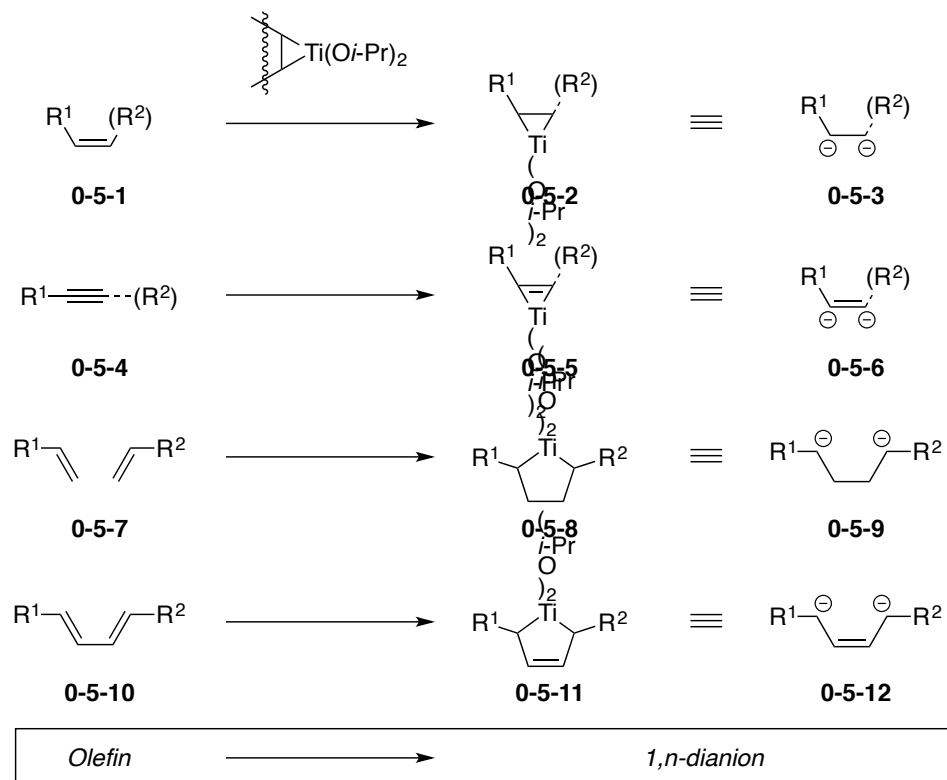


Detailed mechanism: see appendix

See also:

Casey, C. P.; Strotman, N. A. *J. Am. Chem. Soc.* **2004**, *126*, 1699.

0.5. Short summary



Advantage:

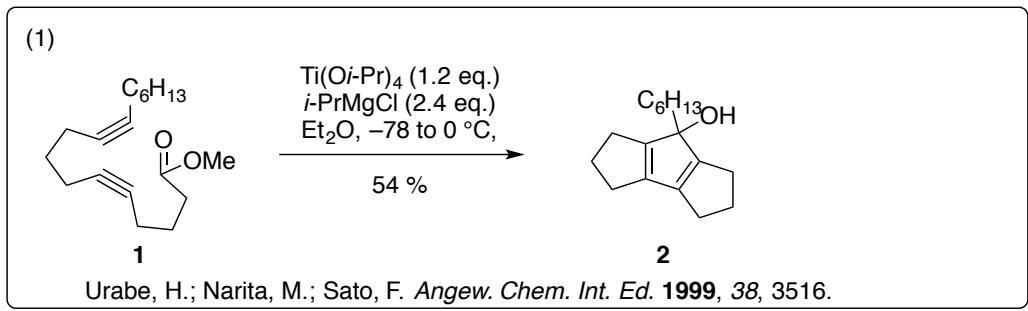
- Non-toxic
- Inexpensive
- Free hydroxy groups tolerate

Disadvantage:

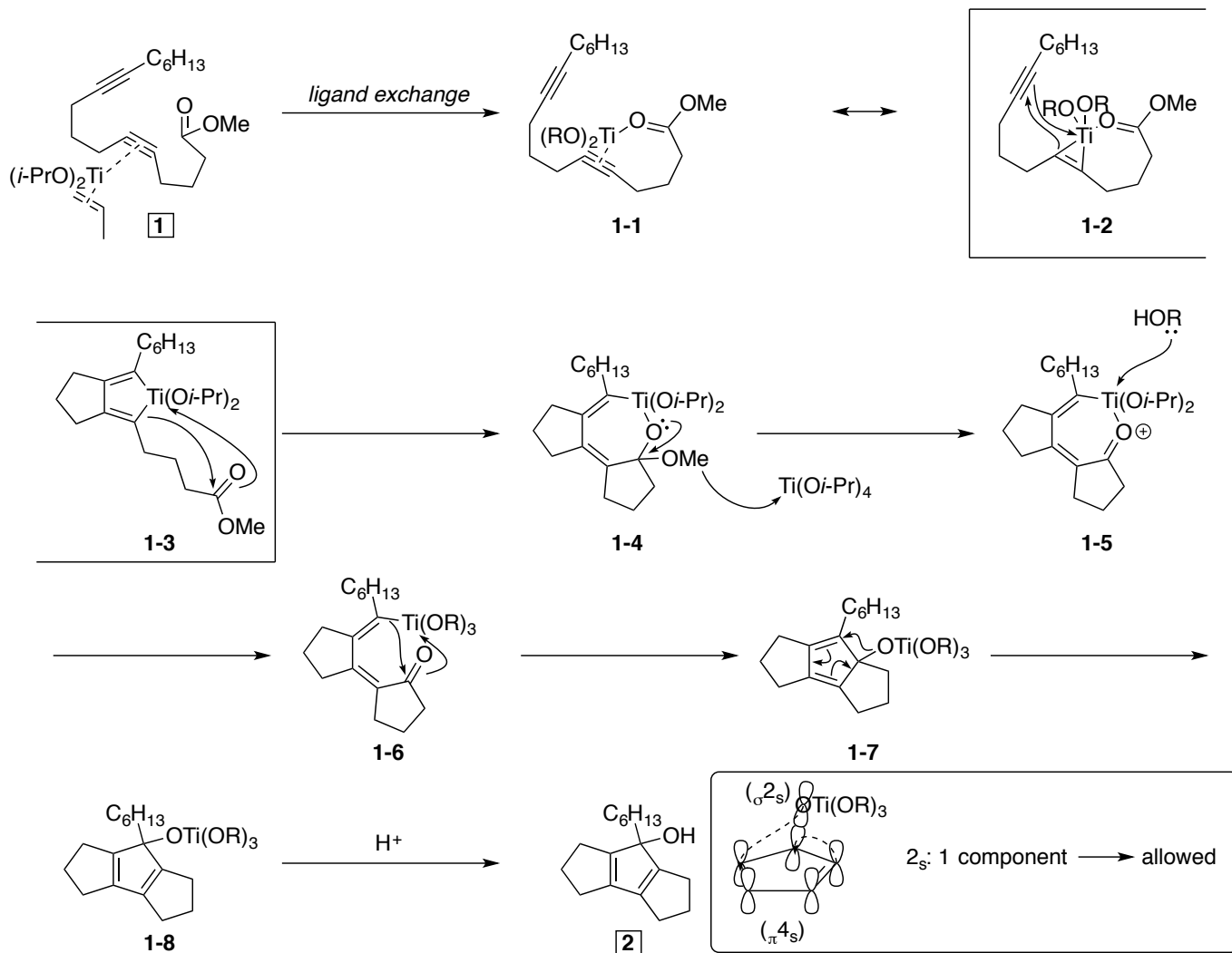
- Sensitive to steric hinderance
- Usually needs more than 1 equivalent of titanium(IV)

Recent reviews:

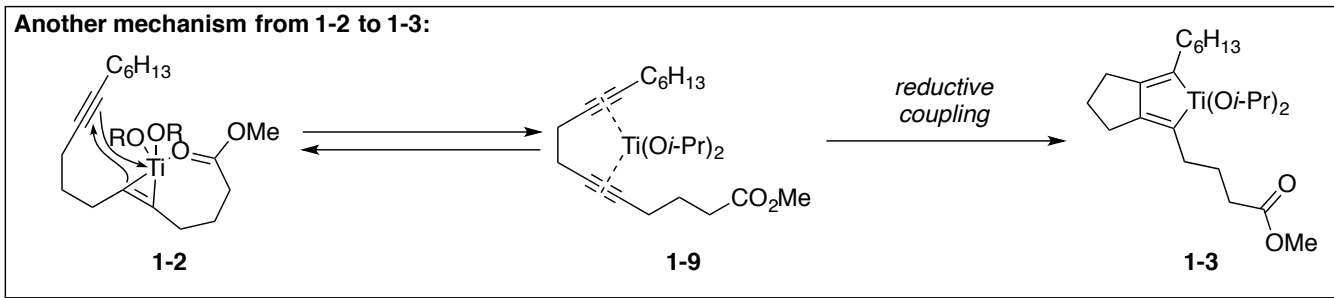
Wolan, A.; Six, Y. *Tetrahedron* **2010**, *66*, 15; *Tetrahedron* **2010**, *66*, 3097.

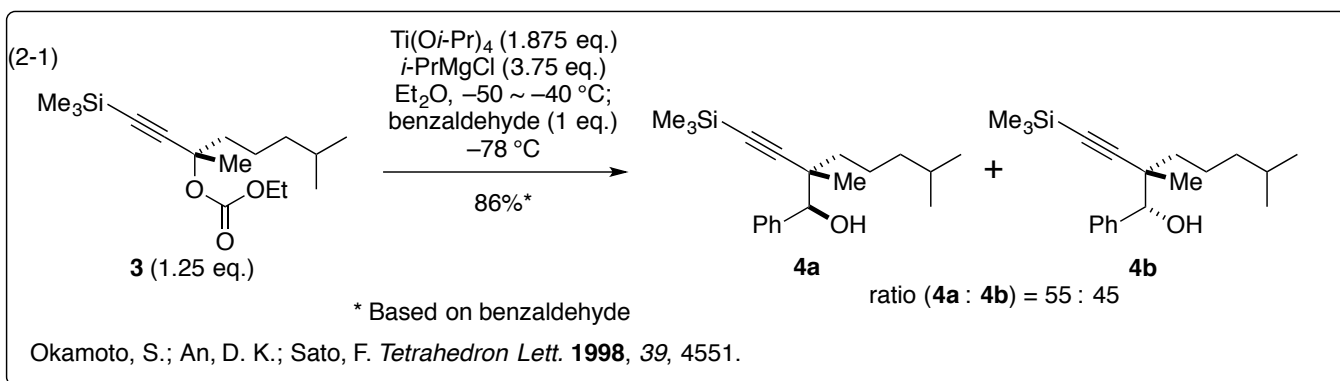


1. Answer

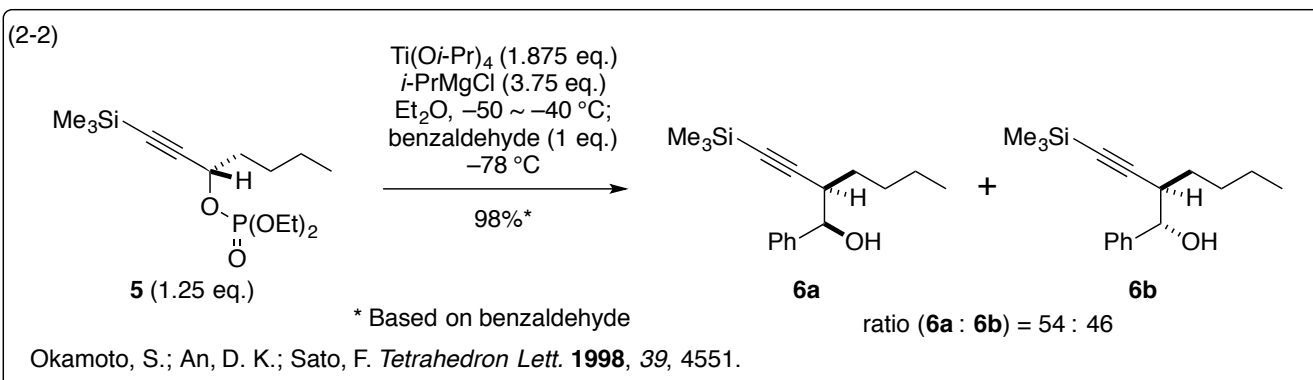
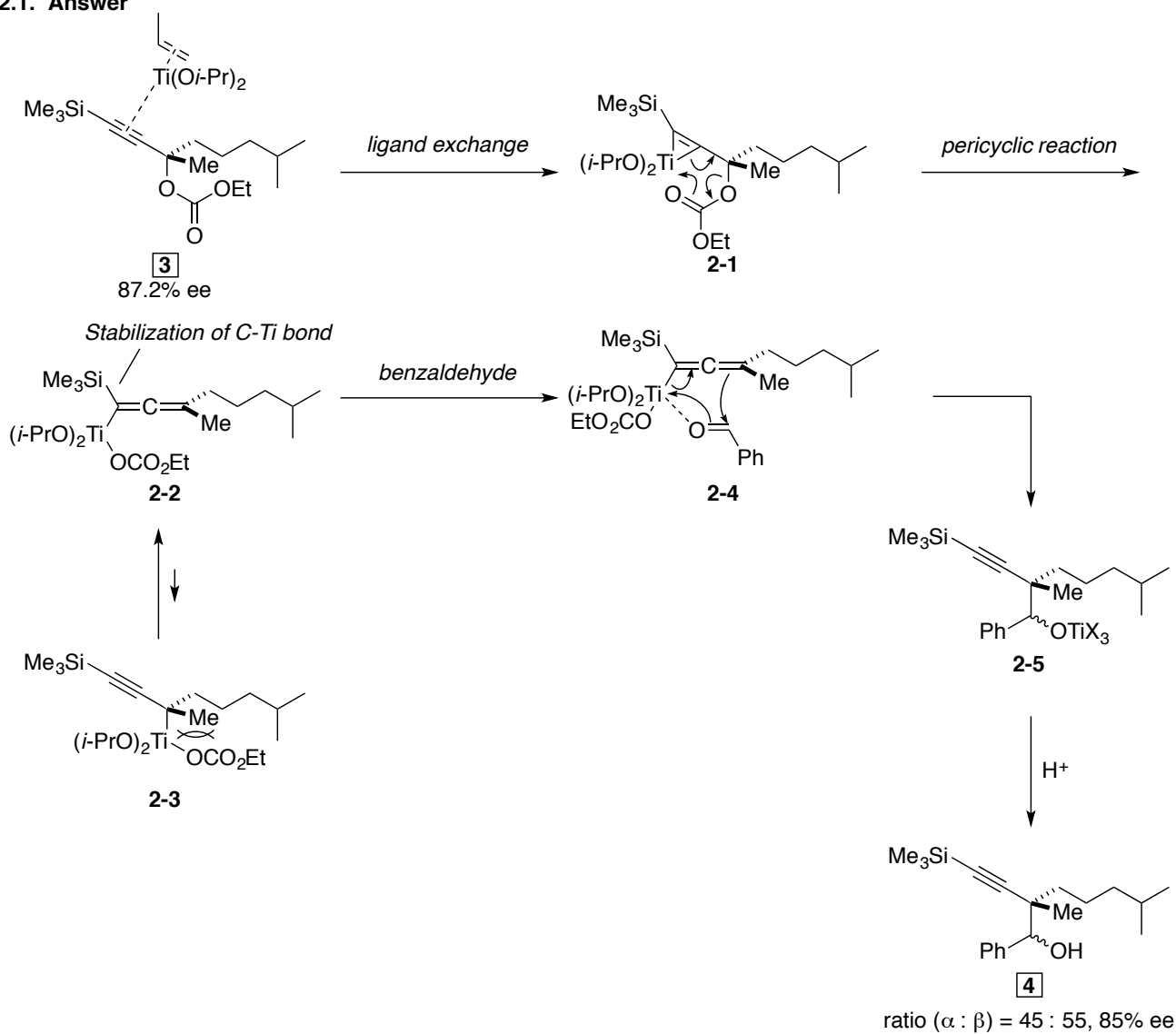


Another mechanism from 1-2 to 1-3:

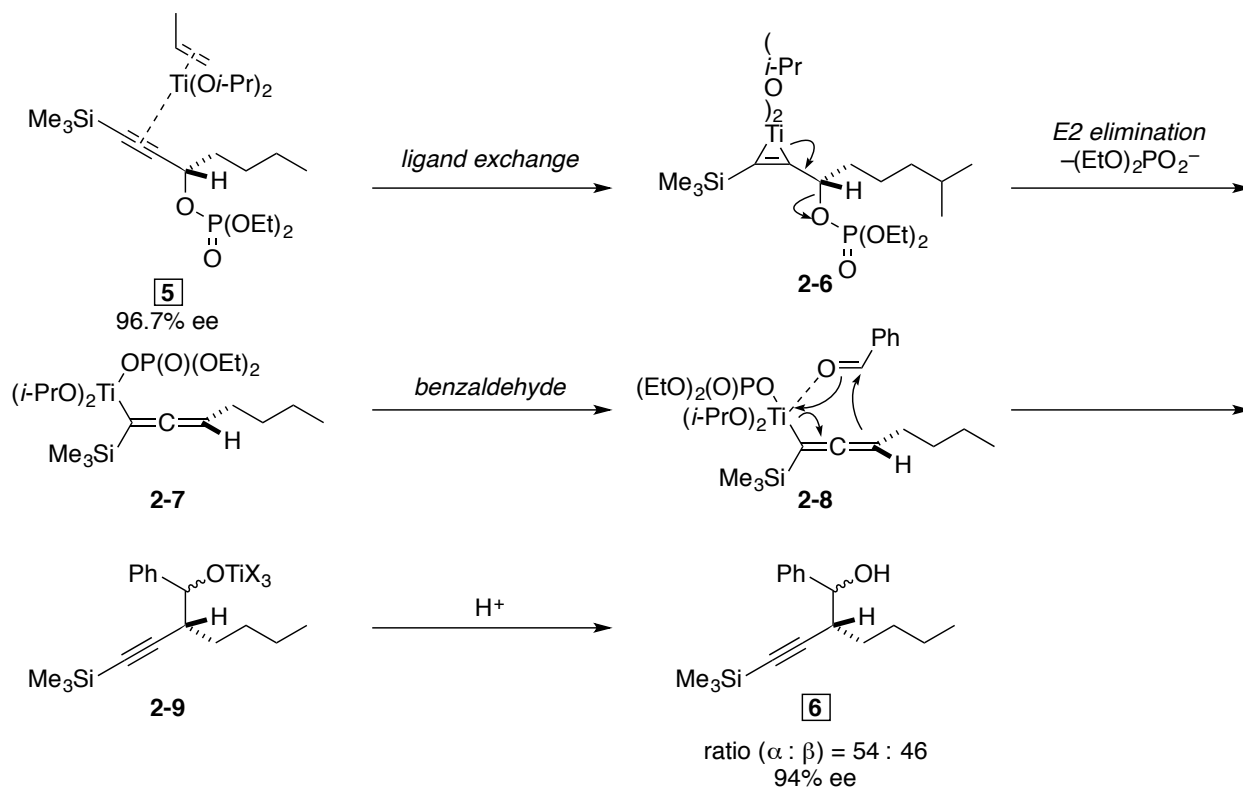




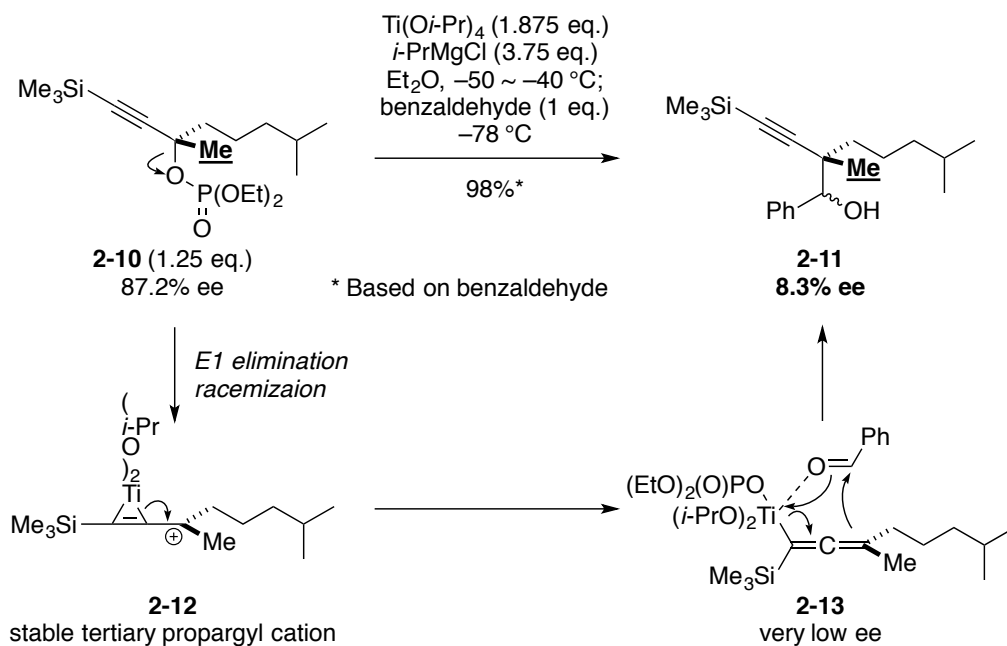
2.1. Answer



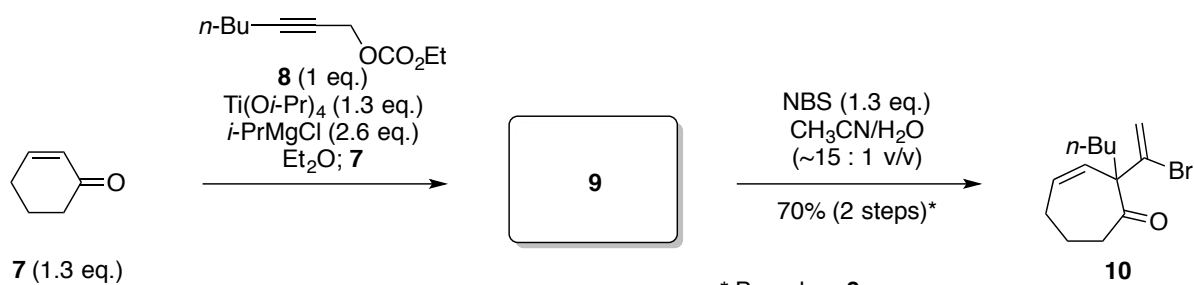
2.2. Answer



2.3. Another example



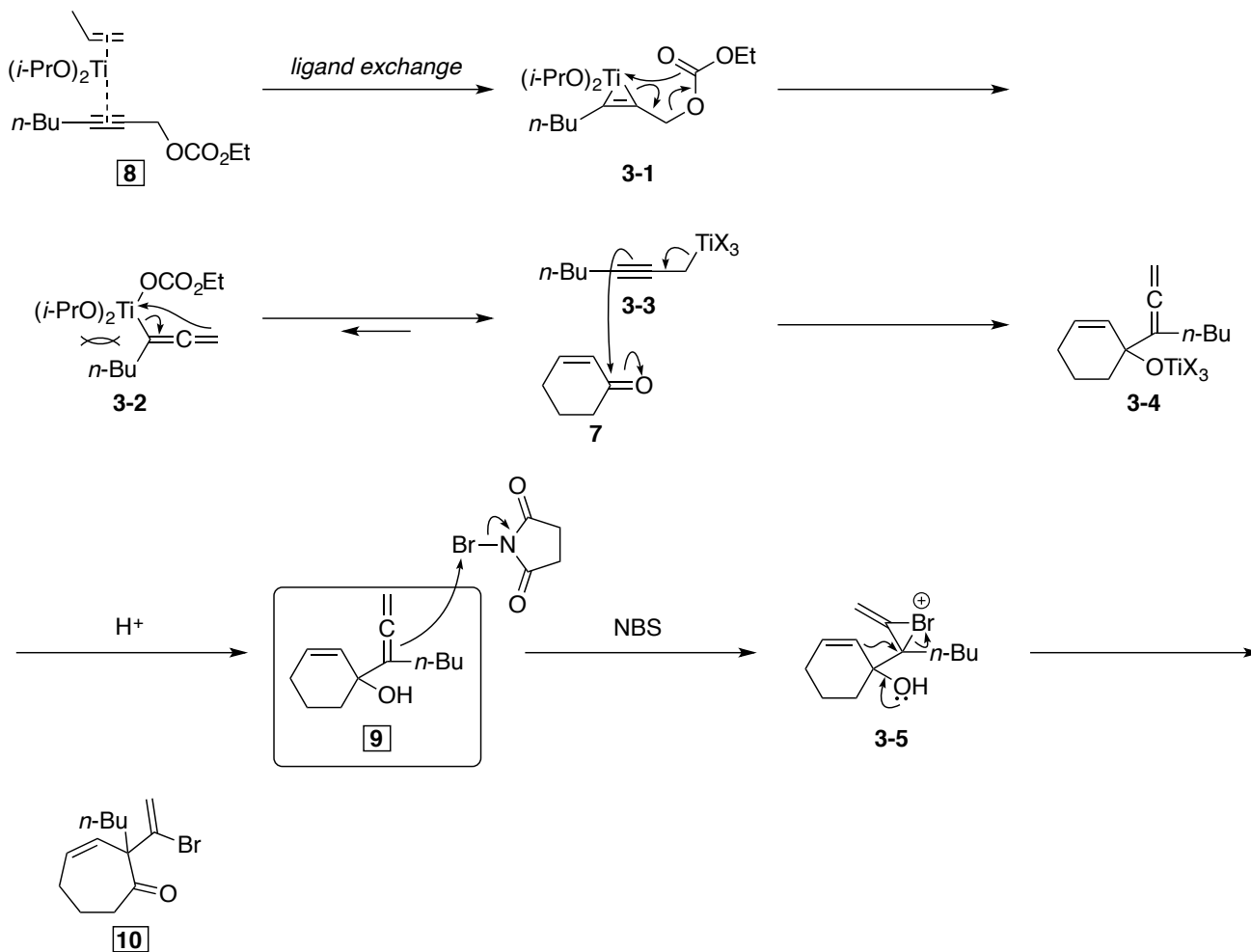
(3)



* Based on 8

He, J.-Q.; Shibata, D.; Ohno, C.; Okamoto, S. *Tetrahedron Lett.* 2008, 49, 6724.

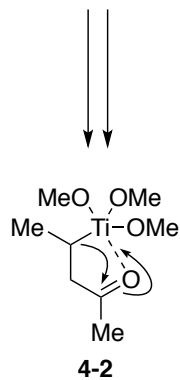
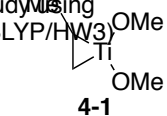
3. Answer



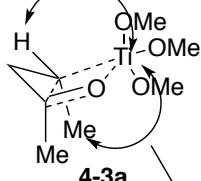
Appendix

4.1. Stereoselectivity of Klinkovich reaction (Computational study)

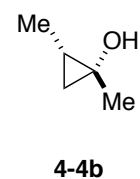
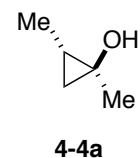
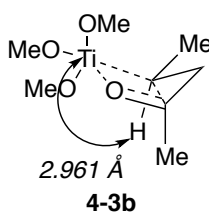
Meising
B3LYP/HW3



higher agostic effect
2.440 Å

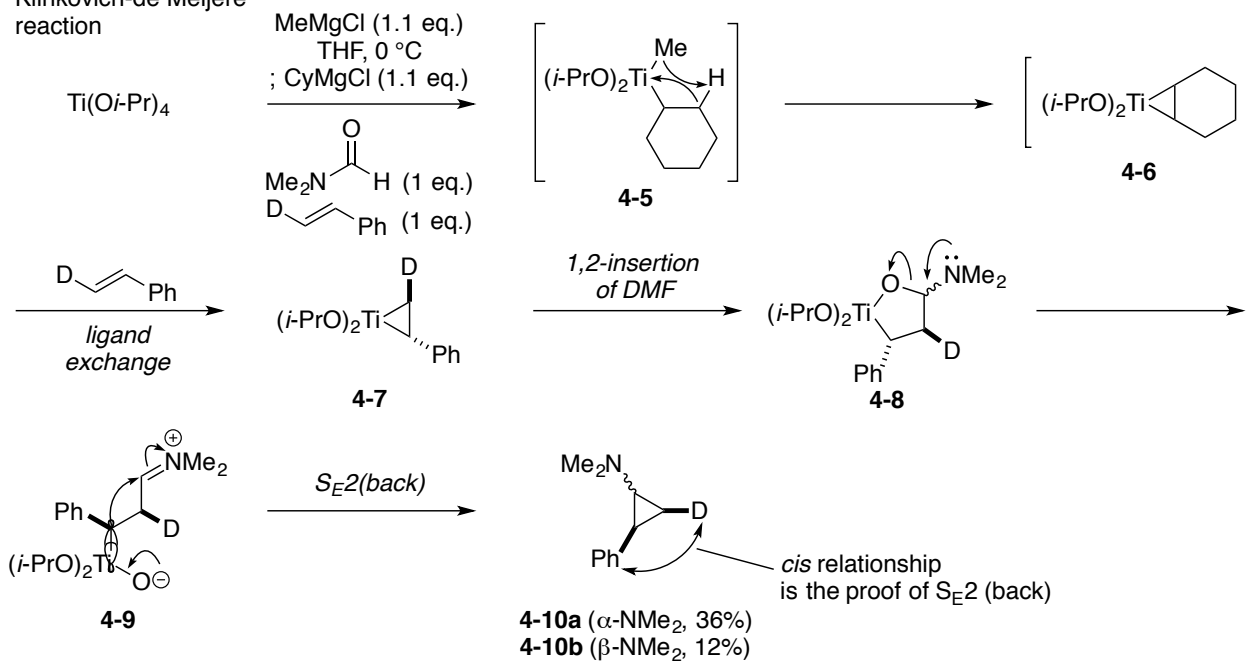


The distance between Me and Ti is said to be a little bit longer



Wu, Y.-D.; Yu, Z.-X. *J. Am. Chem. Soc.* **2001**, *123*, 5777.

4.2. Proof of S_E2 (back) mechanism of Klinkovich-de Meijere reaction



Casey, C. P.; Strotman, N. A. *J. Am. Chem. Soc.* **2004**, *126*, 1699.