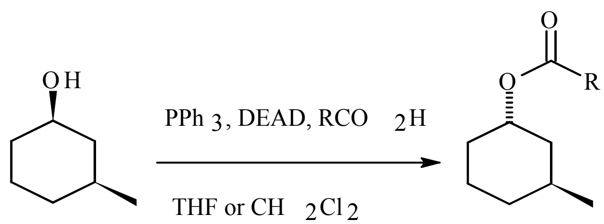
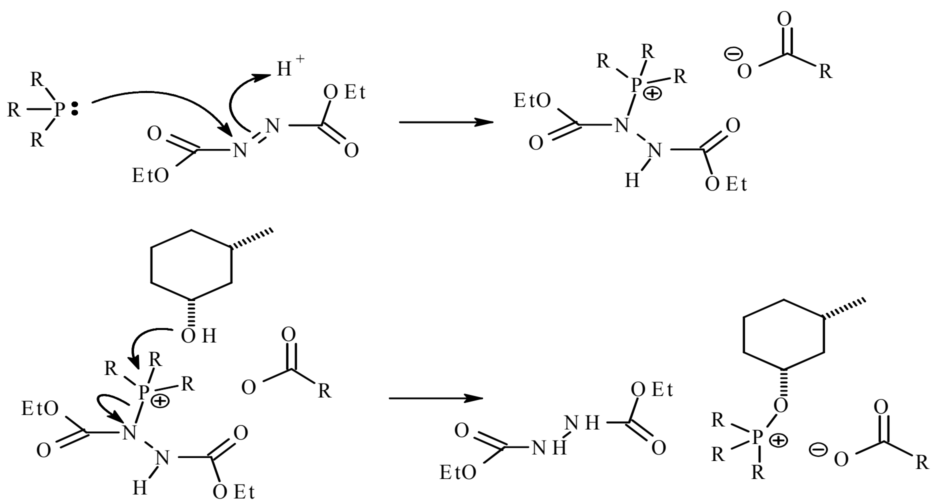
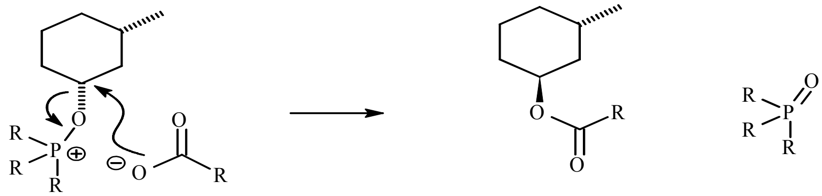
Chem 535-Synthetic Organic Chemistry

Corrections.

1. Like protecting groups, the procedures described below are to be avoided if they can be avoided.
   1.1. They add steps to the synthesis; one of the aims of good synthetic practice is to minimize the amount of steps in a synthesis.
2. **Carbinol Inversion**.
   2.1. **General Scheme**:
      2.1.1. 

   2.2. note inversion of carbinol
   2.3. **Mechanism**:



      2.3.1. 

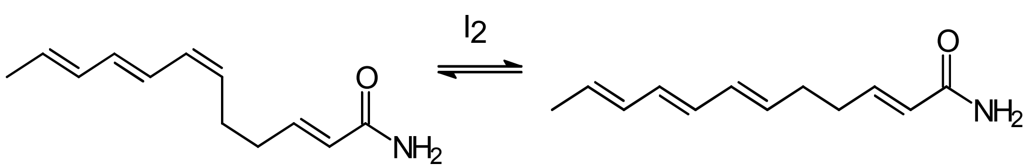
   2.4. Notes:

2.4.1. The reaction is driven by the strength of the P=O bond.
2.4.2. The acidity of nucleophile's conjugate base should be lower than 15, other nucs besides carboxylates are used.
2.4.3. Reaction fails with tertiary alcohols.

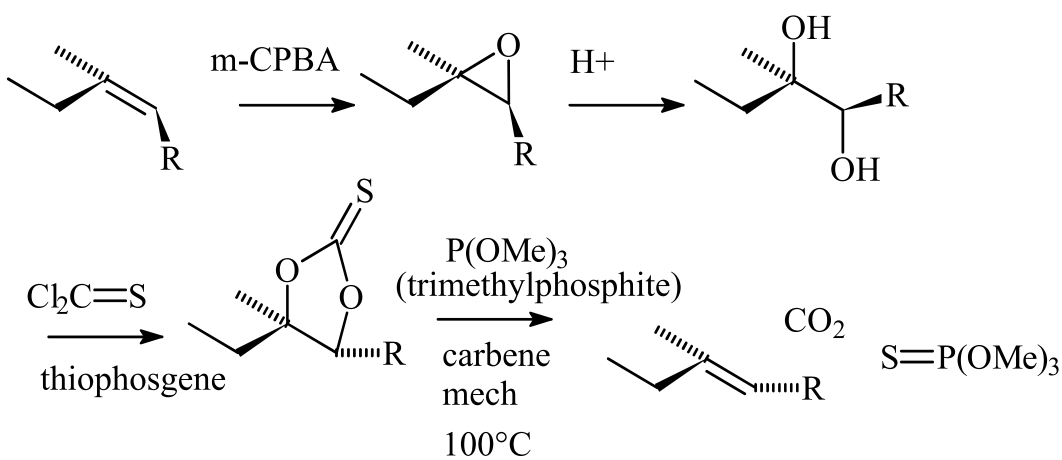
2.5. **References**:
2.5.1. Hughs, D. L. *Org. Reacts.* **1992**, *42*, 335. (review)
2.5.2. Mitsunobu, O. *Syn* **1981**, 1. (review)

3. **Olefin inversion**.
3.1. **References**:
3.1.1. Review: *Tetrahedron* **1980**, *36*, 557.

4. I_2 has been used to invert alkenes
4.1. The method is mild, but many functional groups will not suffer the oxidizing conditions.
4.2. Product is the thermodynamic alkene.
4.3.



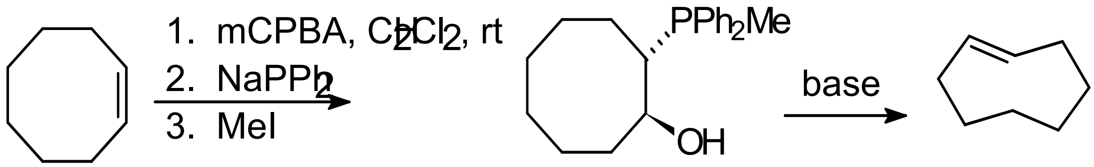
5. If you can't find a way to selectively make the right olefin in the presence of existing functionality make the wrong one and invert it



5.1. Reference: Corey, E.J.; Winter, R.A. *J. Am. Chem. Soc.* **1965**, *87*, 935.

5.1.1. Belongs to the general class of reactions called extrusion reactions.

5.1.2. Do you think you can draw a mechanism?

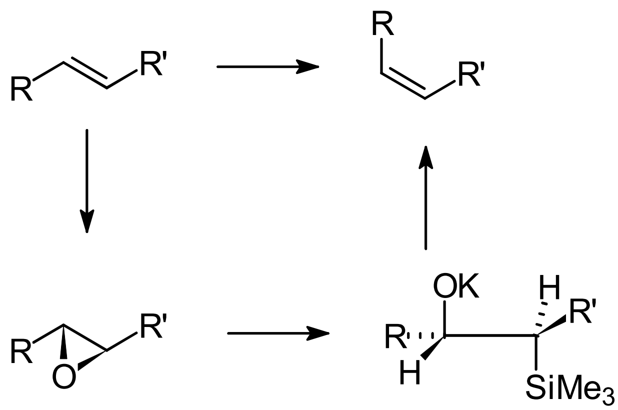


6.

6.1. Vedejs, E.; Snoble, K.A.; Fuchs, P.L. *J. Org. Chem.* **1973**, *38*, 1178.

6.2. A general way to invert alkenes.

6.3. What is wrong with the eight-membered ring with a *trans*-double bond?



7.

7.1. oxidation *m*-CPBA, CH_2Cl_2, rt

7.2. Me_3SiK, syn elimination

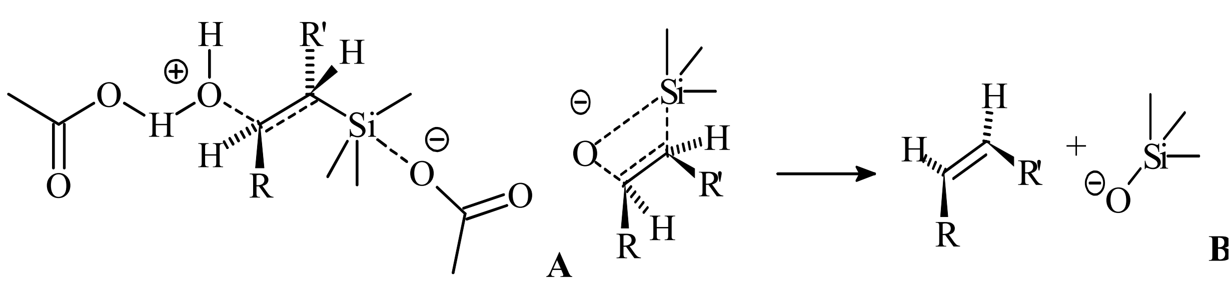
8. Manipulation of β-hydroxy silane elimination

8.1. Reetz, M.T.; Plachky, M. *Synthesis*, **1976**, 199.

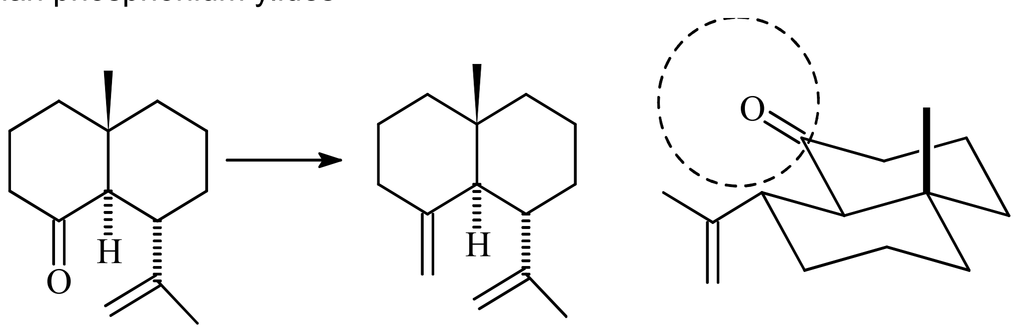
8.2. Dervan, P.B.; Shippey, M.A. *J. Am. Chem. Soc.* **1976**, *98*, 1265.

8.3. If you quench the silylalcohol before it eliminates and treat the material to HOAc/NaOAc, there is enough push-pull electronic effect to make the material eliminate through an antiperiplanar transition state (**A below**).

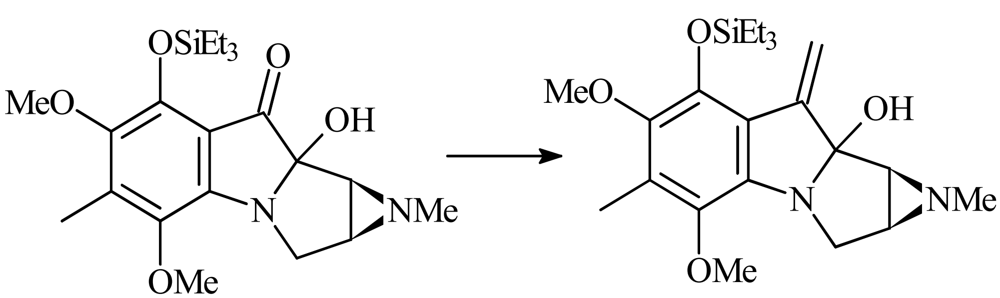
8.4. Under basic conditions the olefin selective inverts. (**B below**)



9. **More about Peterson-type reagents**:
   9.1. is another path to the above chemistry that I presented as an olefin inversion protocol
   9.2. "Peterson reagent" usually refers to α-silylanions
   9.3. R_3Si-CR'R''
10. Differences between Wittig ylides and the Peterson reagents
   10.1. Peterson reagents are more basic
      10.1.1. ylide pKa ~ 20
      10.1.2. Peterson reagent ~ 38
   10.2. Peterson reagents apparently are less sterically demanding and more reactive than phosphonium ylides



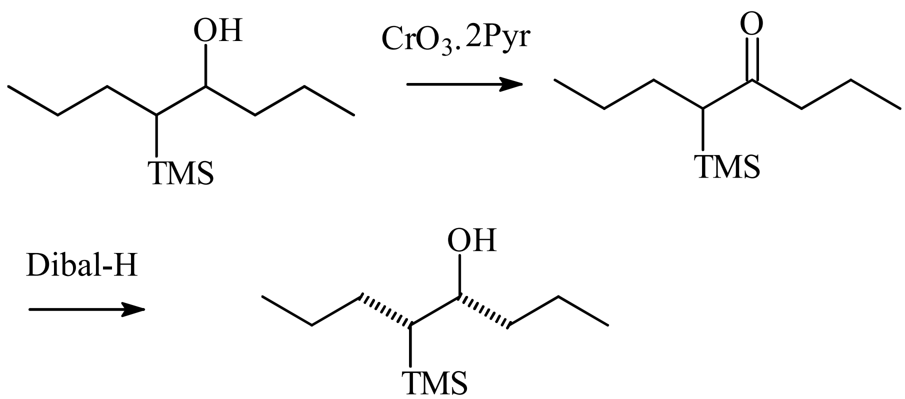
   10.3.
      10.3.1. The Peterson reagent methylenates this enone where triphenylphosoniummethylide failed.

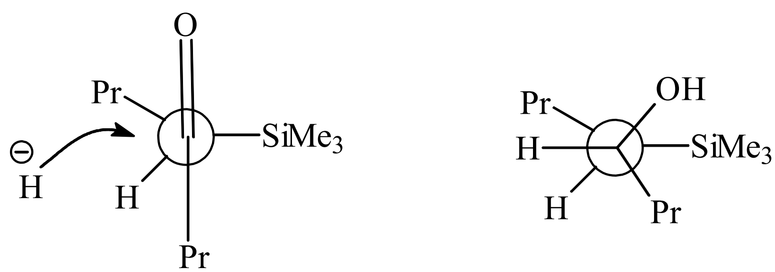


   10.4.
      10.4.1. Versatility in Peterson reaction approach to olefinations.
      10.4.2. For reviews of Peterson olefination see: a. Chan, T.H. *Acc. Chem. Res*. **1977**, *10*, 442 b. Magnus, P. *Aldricha. Chem. Acta*. **1980**, *13*, 43.
11. The stereoselectivity of elimination reactions of β-hydroxysilanes is determined by acidic versus basic conditions.
   11.1. Base: KH, NaH, HOtBu (polar organic solvent)
      11.1.1. HOtBu because MH is really a bad base, HOtBu is a proton shuttle catalyst

11.2. Acid: BF_3OEt_2 or CH_3CO_2H / CH_3CO_2Na

11.2.1. There is just enough push-pull effect in the later to perform the elimination stereospecifically.





Felkin-Ahn

11.2.2. *Comprehensive Organic Synthesis* vol 8 page 3 Trost, B. and Fleming, I. eds.

12. Since reduction and nucleophilic additions to these α-keto silanes are diastereoselective anti or syn elimination of the O-SiMe₃ can be used to stereoselectively synthesize substituted alkenes.