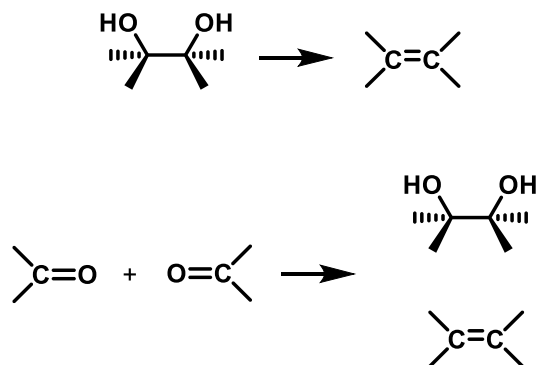


# **Organic synthesis**

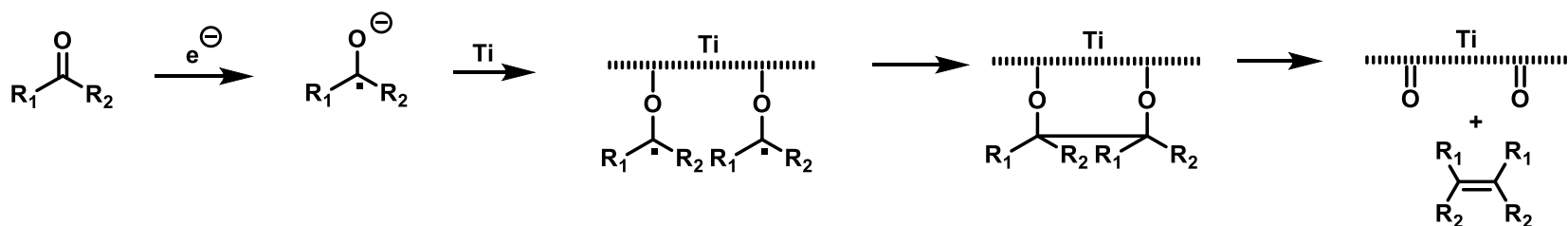
**Kamil Paruch**

***Masaryk University, Brno***

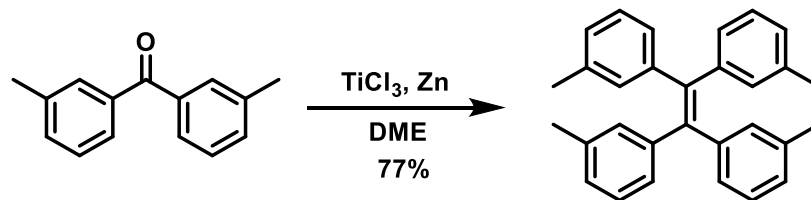
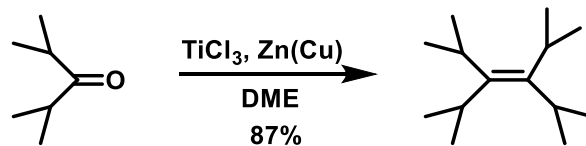


### McMurry reaction

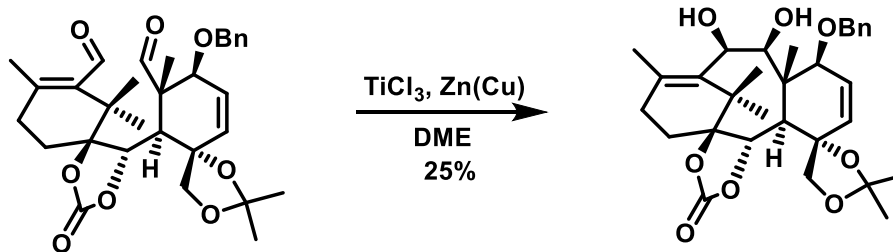
- reductive coupling of carbonyl compounds on Ti



- can be used for preparation of *sterically hindered* olefins
- reaction can be stopped in the diol phase

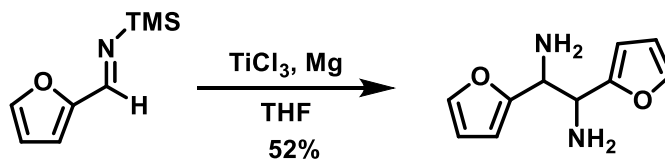


*Tetrahedron* **1986**, 42, 2111..

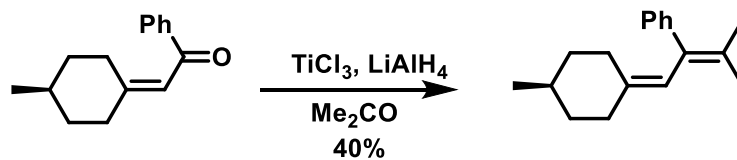


*J. Am. Chem. Soc.* **1995**, 117, 645.

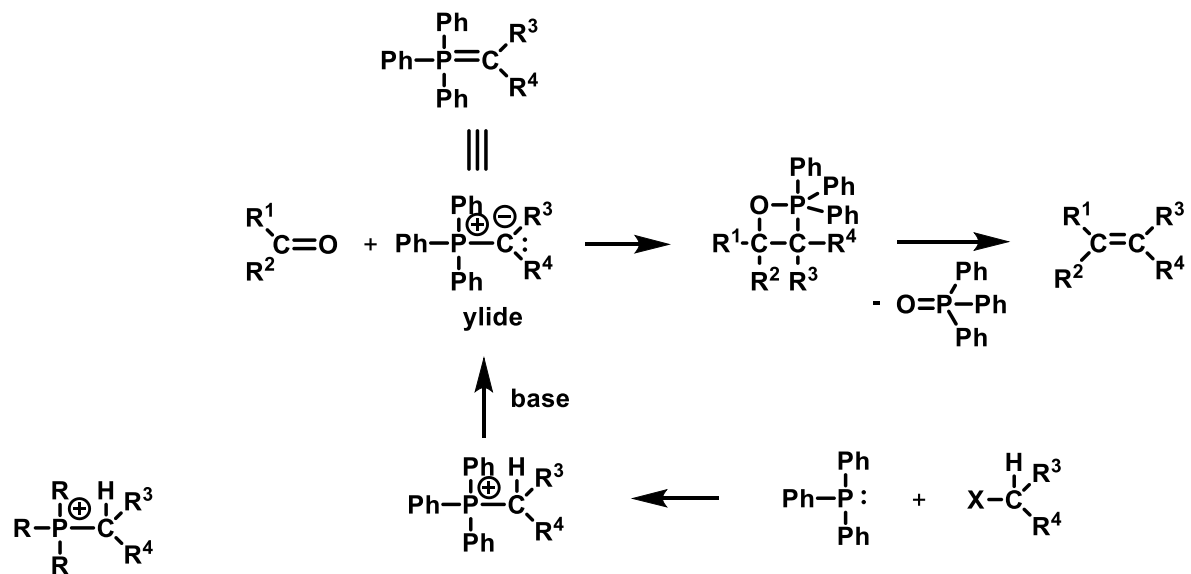
- imines can be also coupled



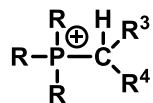
- unsymmetrical products (cross coupling): typically, one component in excess



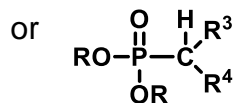
*J. Org. Chem.* **1986**, 51, 2361.



$\text{R}^3, \text{R}^4 = \text{alkyl, aryl} \longrightarrow \text{strong base (removal of H}^+) \longrightarrow \text{nonstabilized ylide} \longrightarrow \text{(Z)-alkene}$

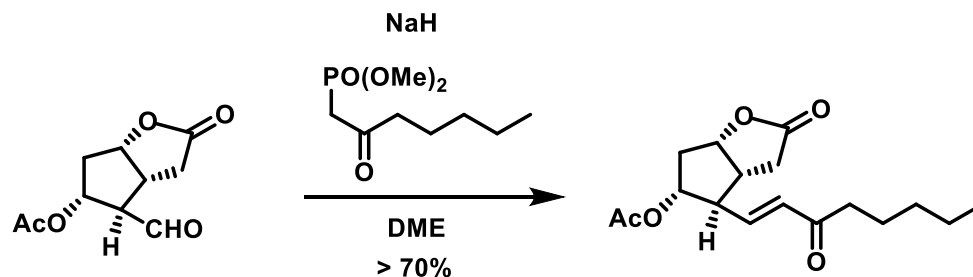


$\text{R}^3, \text{R}^4 = \text{electron acceptor} \longrightarrow \text{weaker base (removal of H}^+) \longrightarrow \text{stabilized ylide} \longrightarrow \text{(E)-alkene}$



(Horner-Wadsworth-Emmons)

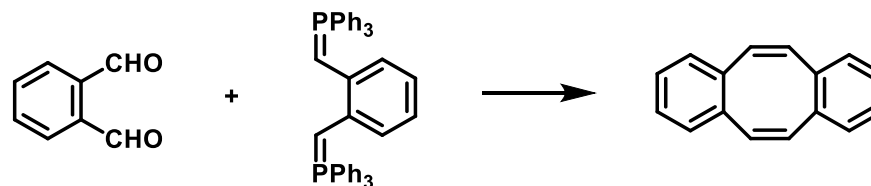
- Wittig reaction is often used in the synthesis of complex molecules



*J. Am. Chem. Soc.* **1969**, *91*, 5675.

Note: complexation with ZnCl<sub>2</sub> will remove triphenylphosphine oxide, even from polar solvents: *J. Org. Chem.* **2017**, *82*, 9931.

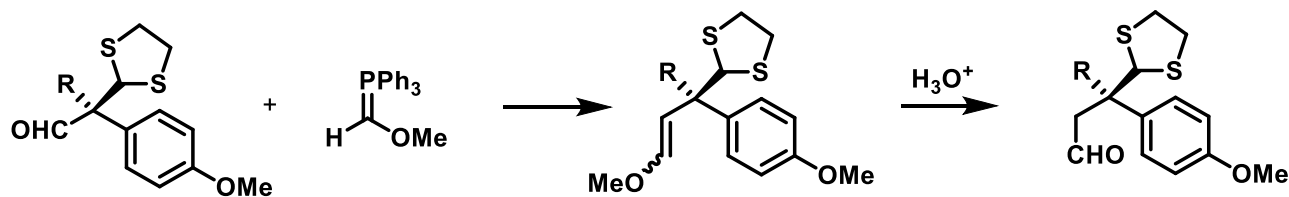
(double) Wittig reaction can be used for construction of cyclic systems



*Synthesis* **1975**, 765.

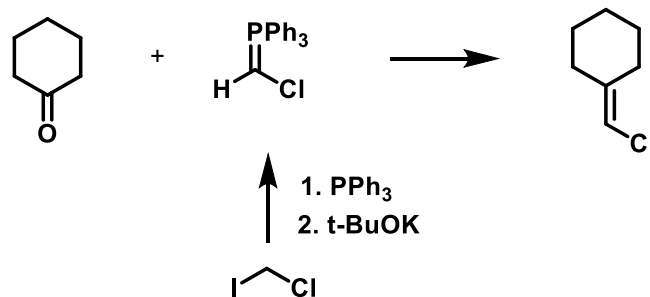
homologation of aldehydes  $\text{H}-\text{C}(\text{PPh}_3)=\text{OMe}$

e.g.



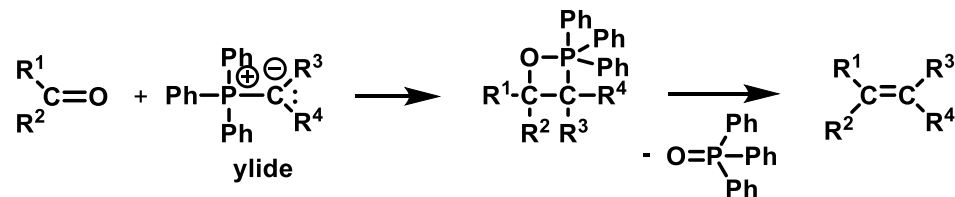
*J. Org. Chem.* **1989**, 54, 3831.

similarly: chloromethylenation

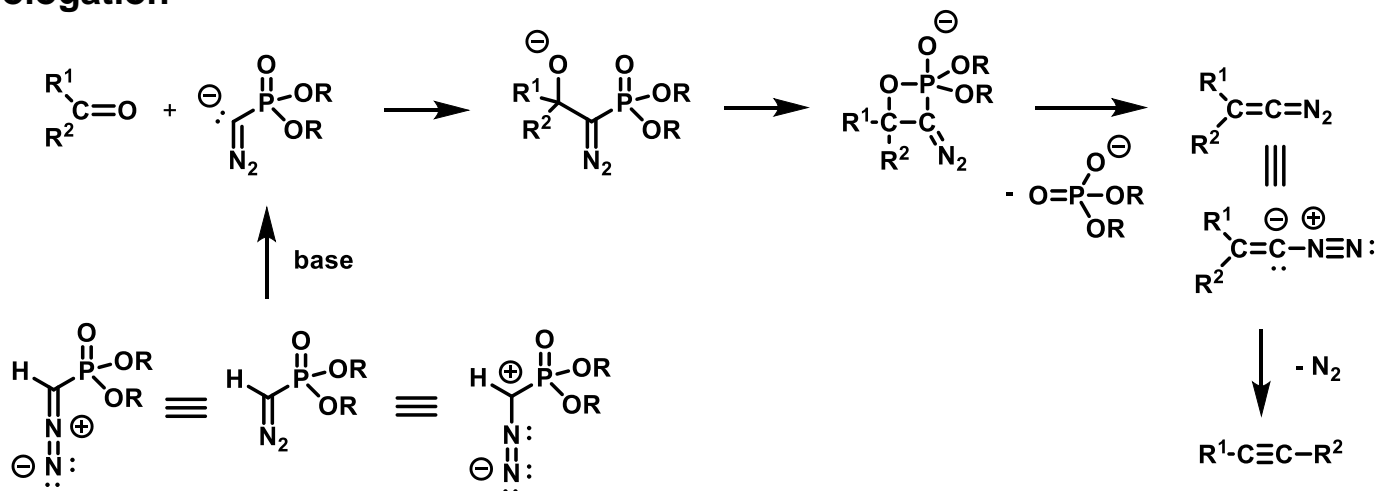


*Tetrahedron Lett.* **1980**, 21, 4021.

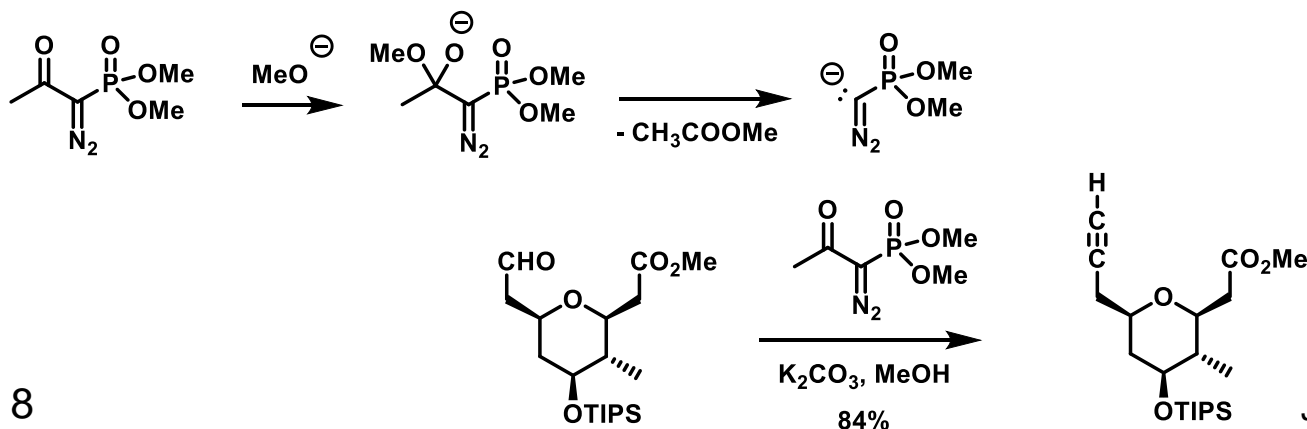
## Wittig reaction



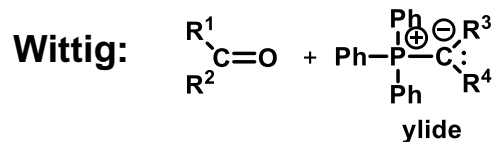
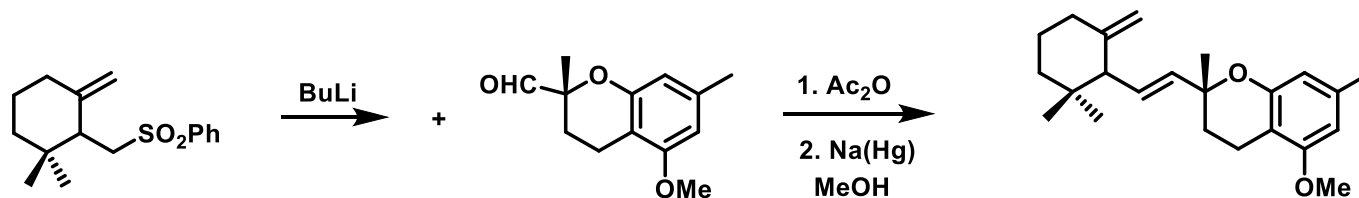
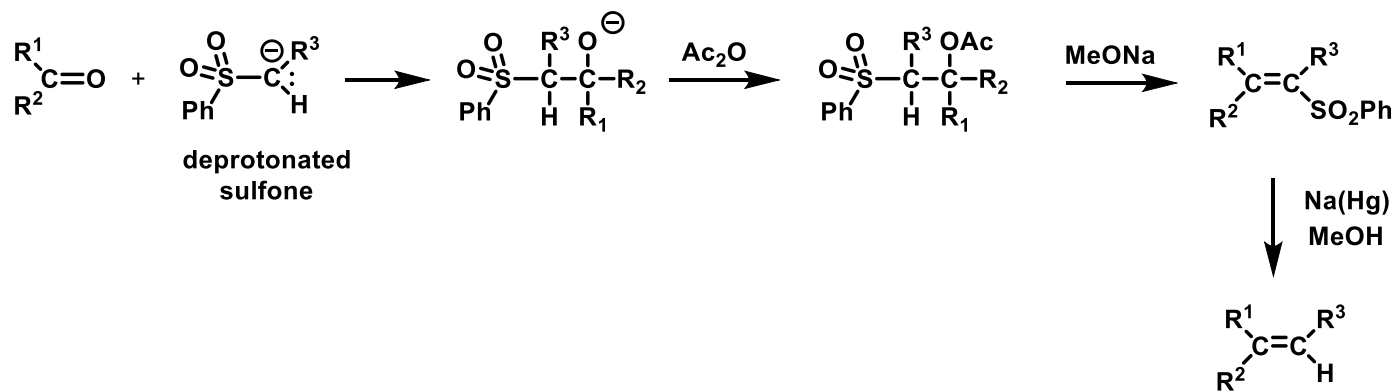
## Seyferth-Gilbert homologation



**Ohira-Bestmann alkyne synthesis:** frequently used for conversion of aldehydes to terminal alkynes



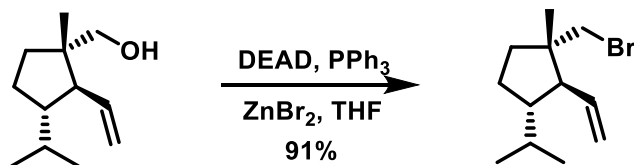
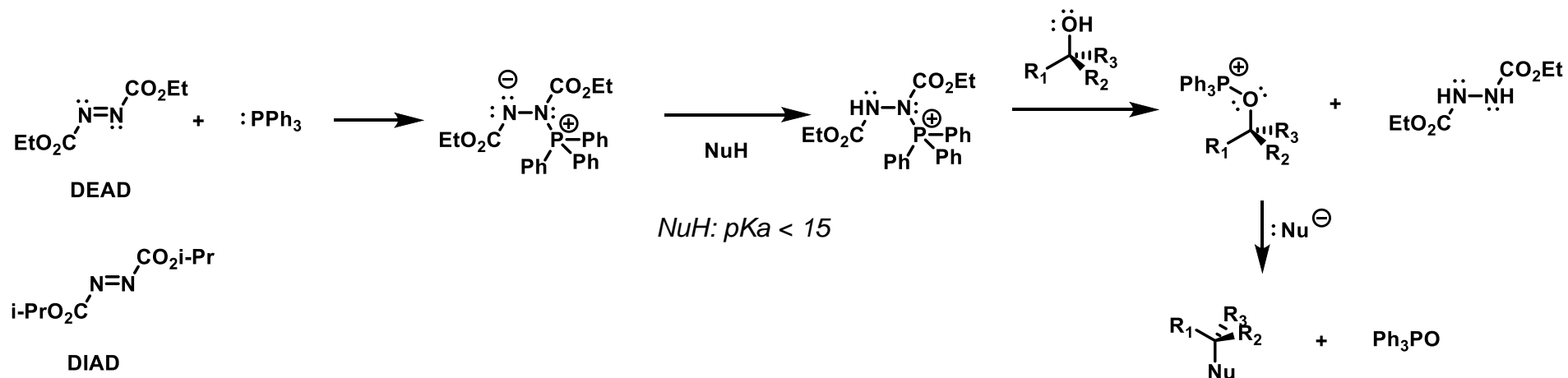


**Julia-Lythgoe:**

93% overall

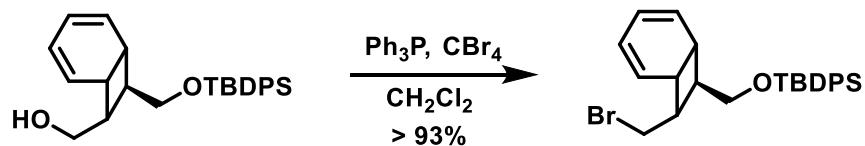
## Mitsunobu reaction

- nucleophilic substitution of OH under mild conditions
- S<sub>N</sub>2 -> inversion of configuration



*J. Org. Chem.* **1987**, 52, 2960.

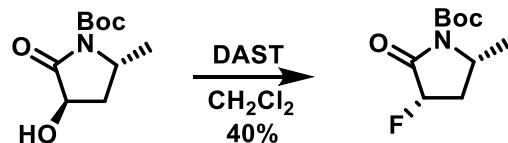
note: Ph<sub>3</sub>P + CBr<sub>4</sub> (CCl<sub>4</sub>) : OH -> Br (Cl)



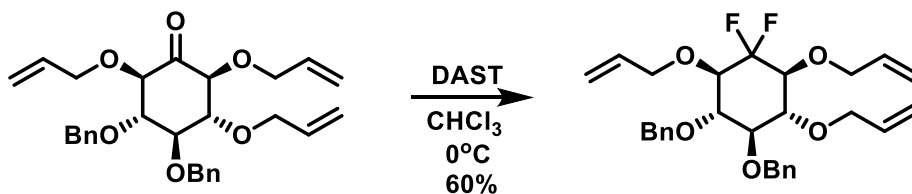
*J. Am. Chem. Soc.* **1982**, 104, 5560.

note:  $\text{Et}_2\text{NSF}_3$  (DAST) :  $\text{OH} \rightarrow \text{F}$

$\text{C}=\text{O} \rightarrow \text{CF}_2$

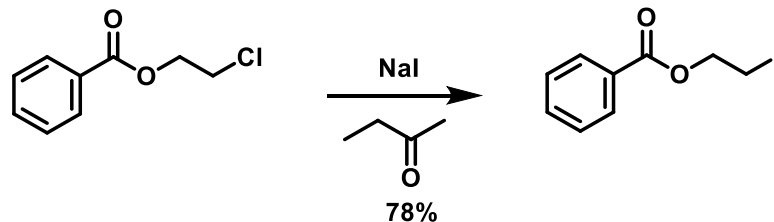


*Tetrahedron Lett.* **1992**, 33, 1509.

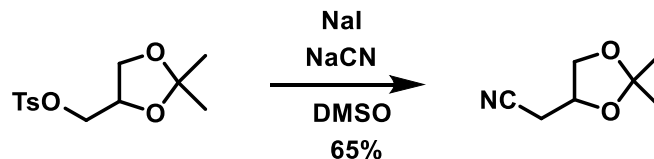


*Tetrahedron Lett.* **1988**, 29, 5217.

note:  $\text{NaI}$  :  $\text{Cl}, \text{Br}, \text{OMs}, \text{OTs} \rightarrow \text{I}$  (Finkelstein reaction)

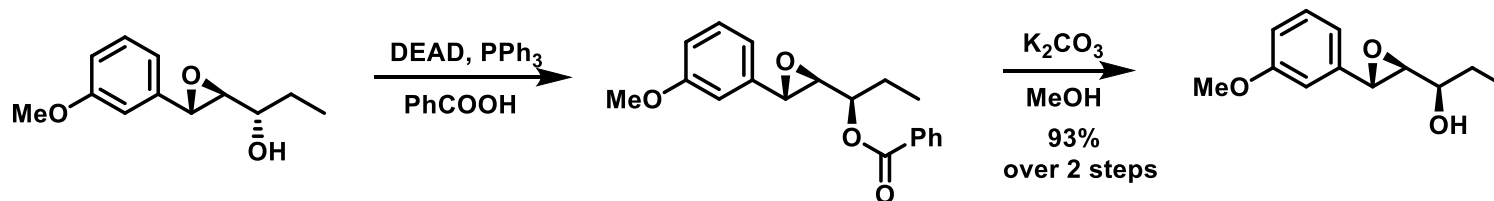


*Org. Synth., Coll. Vol.* **1963**, 4, 84.

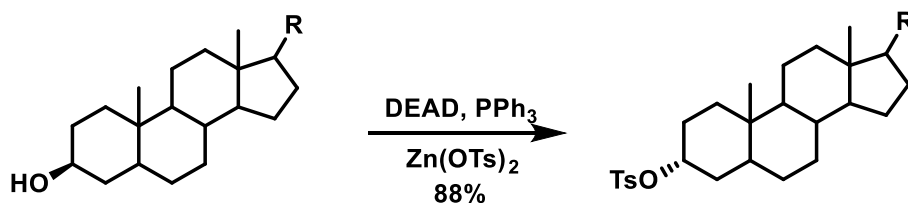


*J. Am. Chem. Soc.* **1980**, 102, 6304.

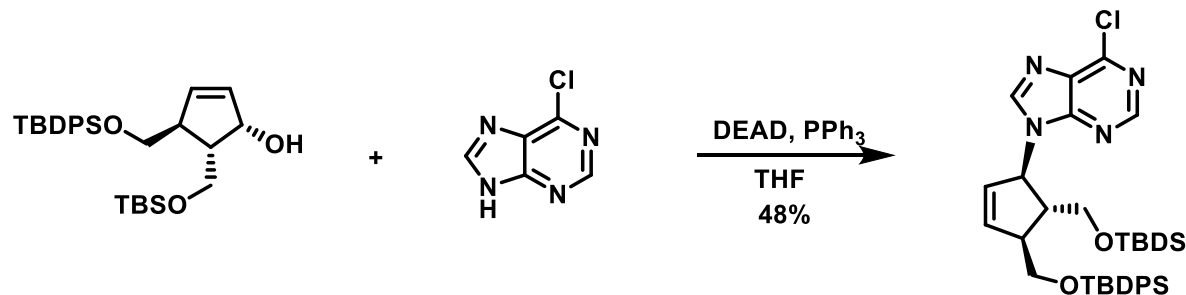
- Mitsunobu reaction: often method of choice for *inversion of configuration*
- also used for preparation of esters, lactones, amides, lactams and amines



*J. Org. Chem.* **1991**, *56*, 741.

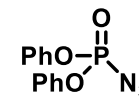


*J. Am. Chem. Soc.* **1982**, *104*, 1774.

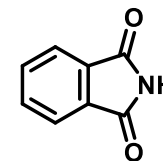


*Tetrahedron Lett.* **1992**, *33*, 3507.

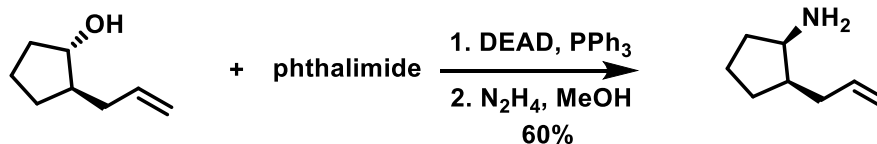
- generation of C-N bond: DPPA and phthalimide: common Nu sources of N



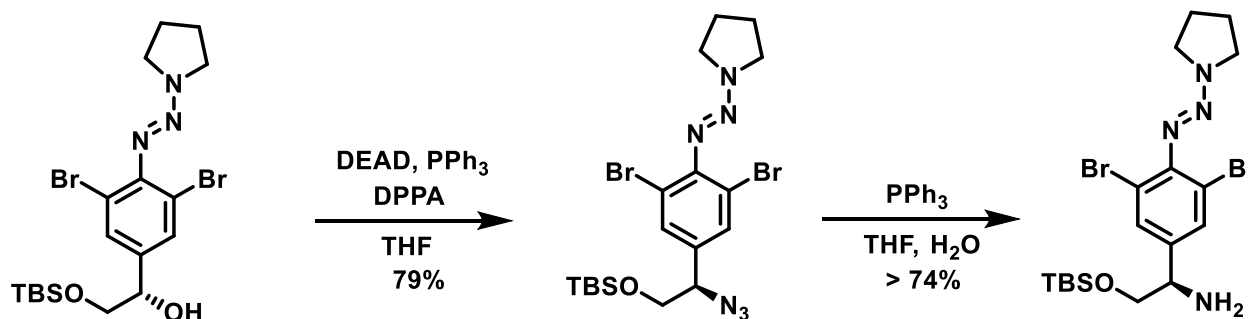
DPPA



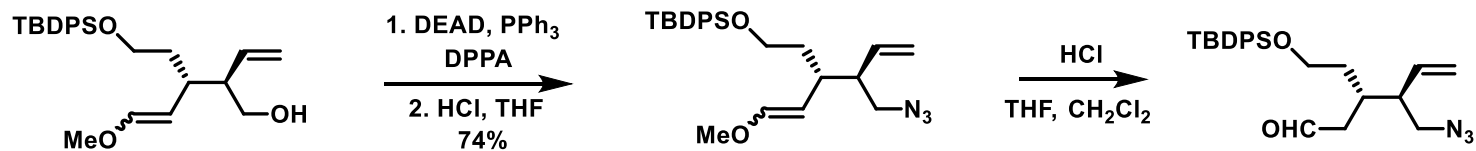
phthalimide



*Org. Synth., Coll. Vol. 7, 1990, 501.*



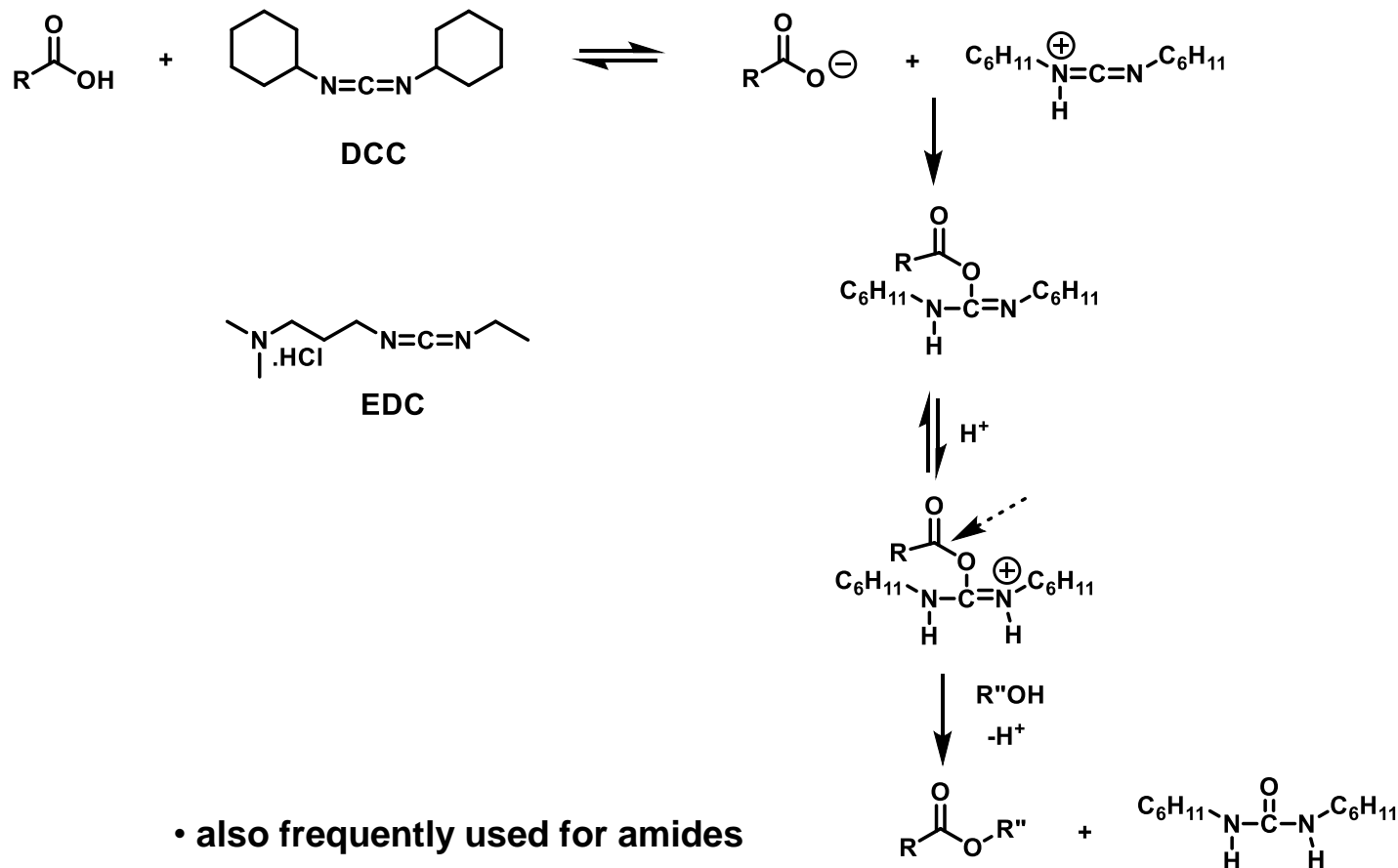
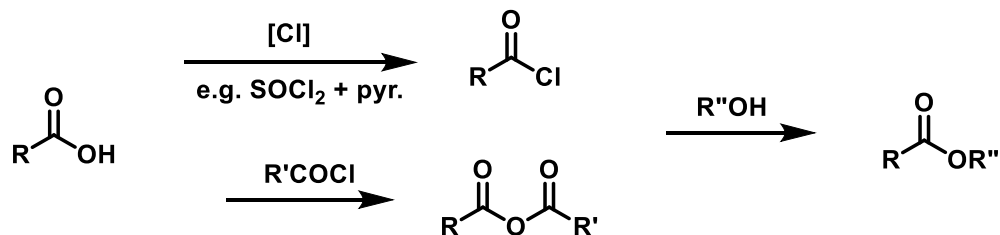
*Angew. Chem. Int. Ed. Engl. 1999, 38, 240.*

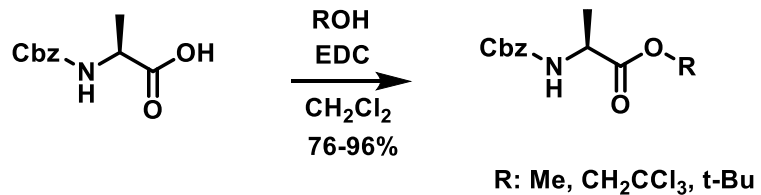


*J. Am. Chem. Soc.* **2001**, 123, 3239.

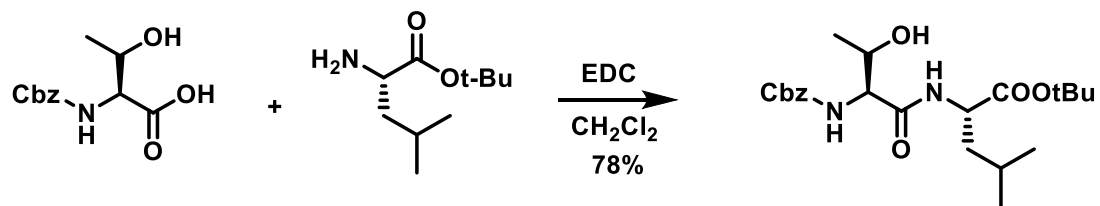


- esterification**
- conversion of carboxylic acids into derivatives with better leaving groups
  - Mitsunobu rxn





*J. Org. Chem.* **1982**, 47, 1962.



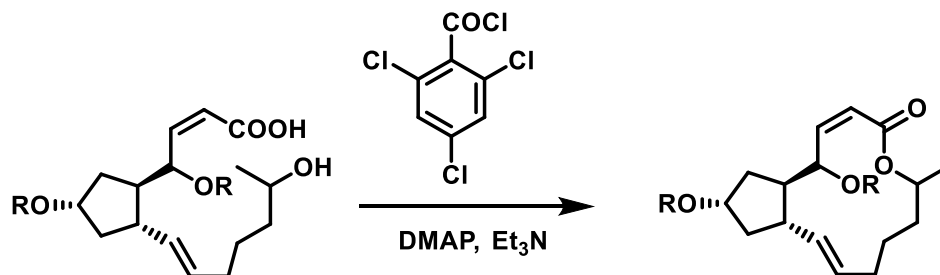
*J. Am. Chem. Soc.* **1973**, 95, 875.



## macrolactonization

- often applied in synthesis of (biologically active) macrolides

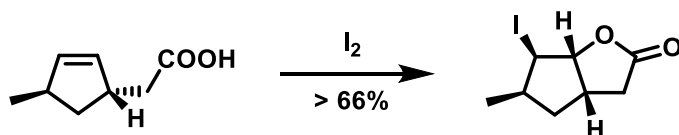
## Yamaguchi macrolactonization



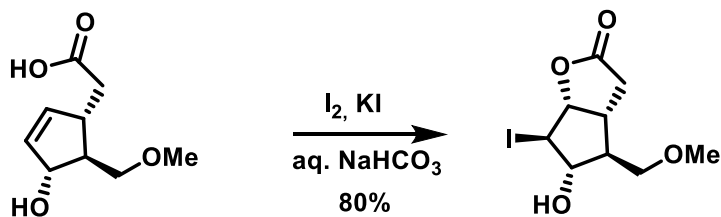
*Chem. Lett.* **1979**, 1021.

## iodolactonization

- *anti* attack on cyclic iodonium intermediate



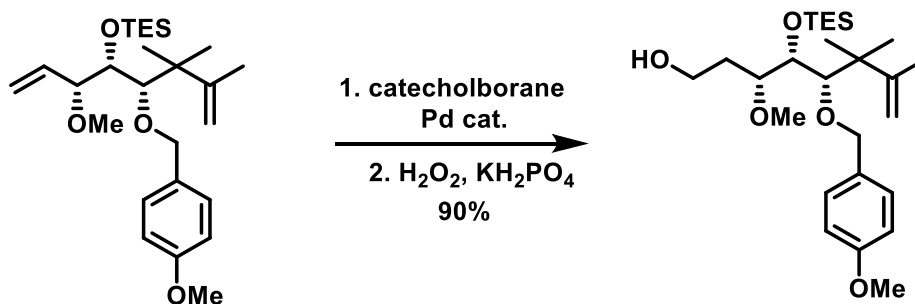
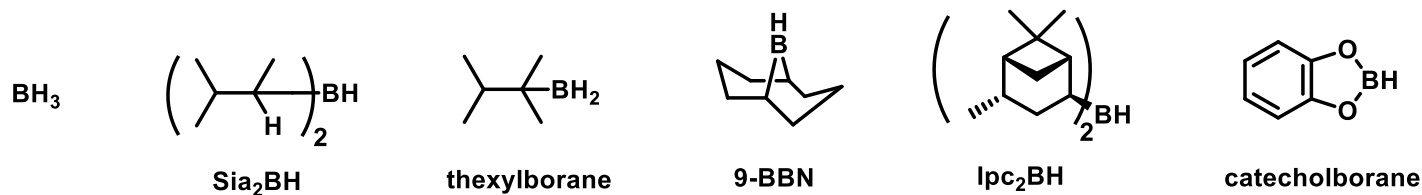
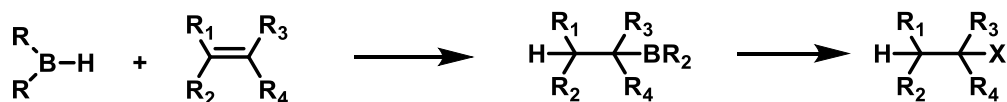
*J. Am. Chem. Soc.* **1985**, 107, 1448.



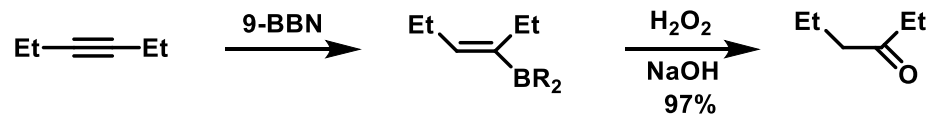
*J. Am. Chem. Soc.* **1969**, 91, 5675.

## hydroboration (and subsequent transformations)

- “anti-Markovnikov” addition on double/triple bonds
- sterically hindered boranes: high regio- and stereoselectivity
- products of hydroboration can be converted into different derivatives



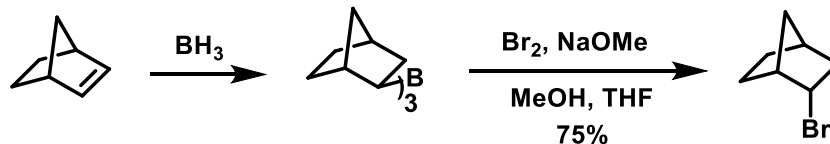
## hydroboration of alkynes



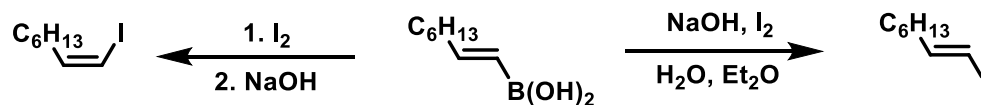
*J. Am. Chem. Soc.* **1979**, 101, 96.

terminal alkynes: *E*-alkenes

C-BR<sub>2</sub> → C-halogen

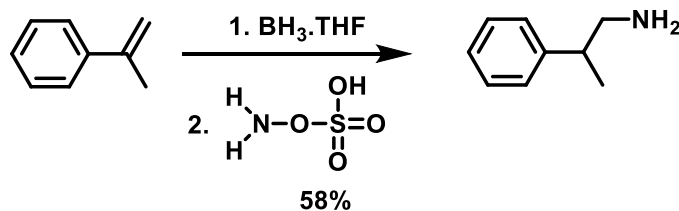


*J. Chem. Soc., Chem. Commun.* **1971**, 521.

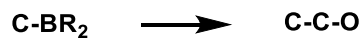


*J. Am. Chem. Soc.* **1973**, 95, 5786.

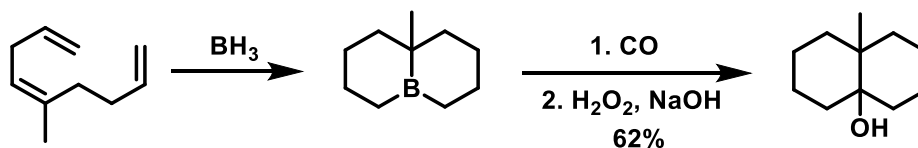
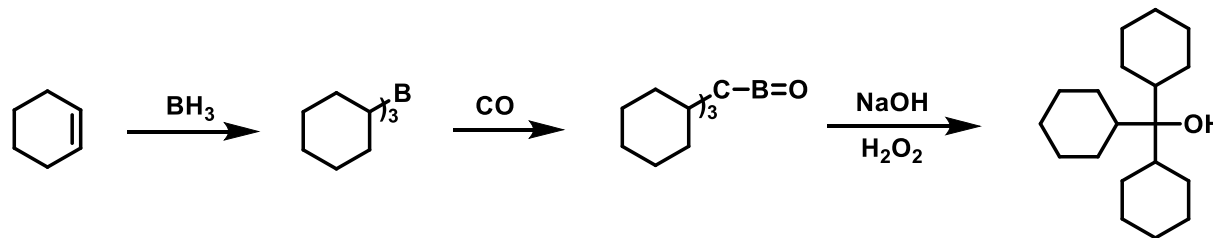
C-BR<sub>2</sub> → C-N



*J. Am. Chem. Soc.* **1964**, 86, 3565.



carbonylation of boranes

*J. Am. Chem. Soc.* **1969**, 91, 1224.