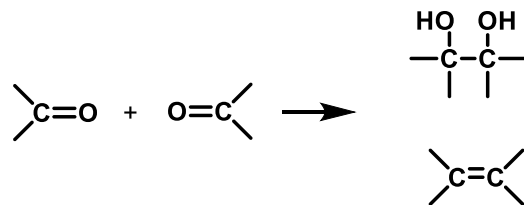
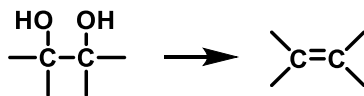


Organic synthesis

Kamil Paruch

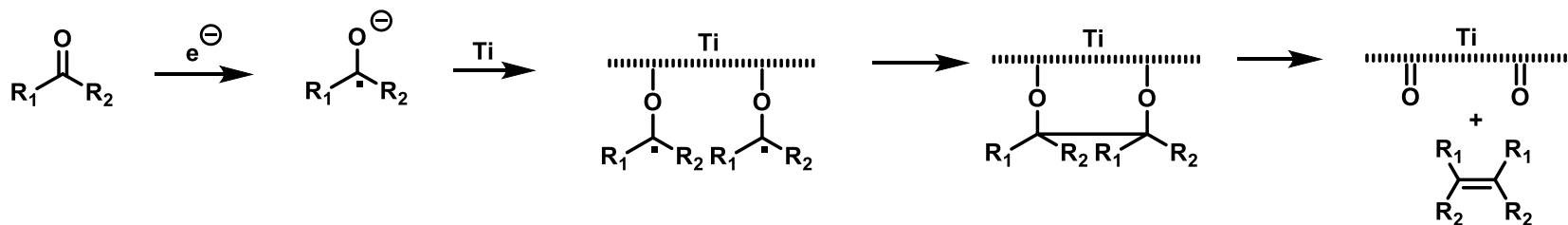
Masaryk University, Brno

reduction

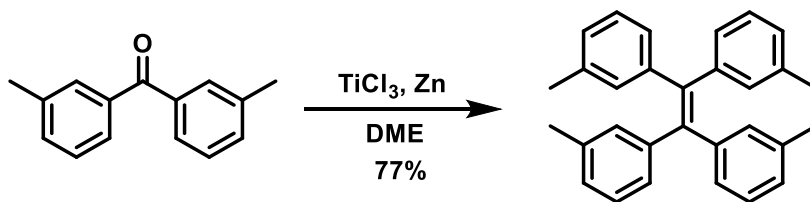
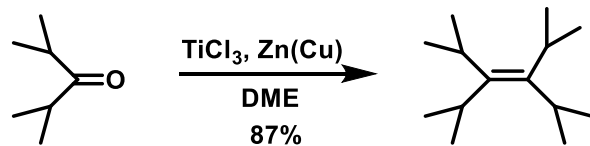


McMurry reaction

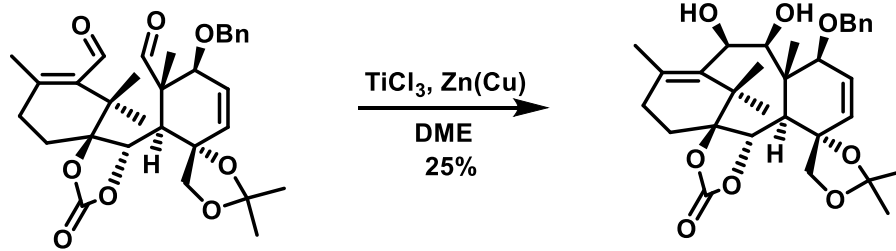
- reductive coupling of carbonyl compounds on Ti



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

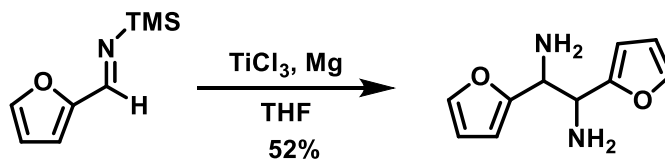


Tetrahedron **1986**, 42, 2111..

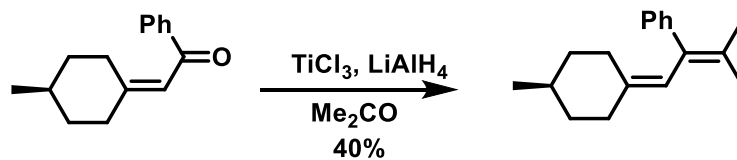


J. Am. Chem. Soc. **1995**, 117, 645.

- imines can be also coupled

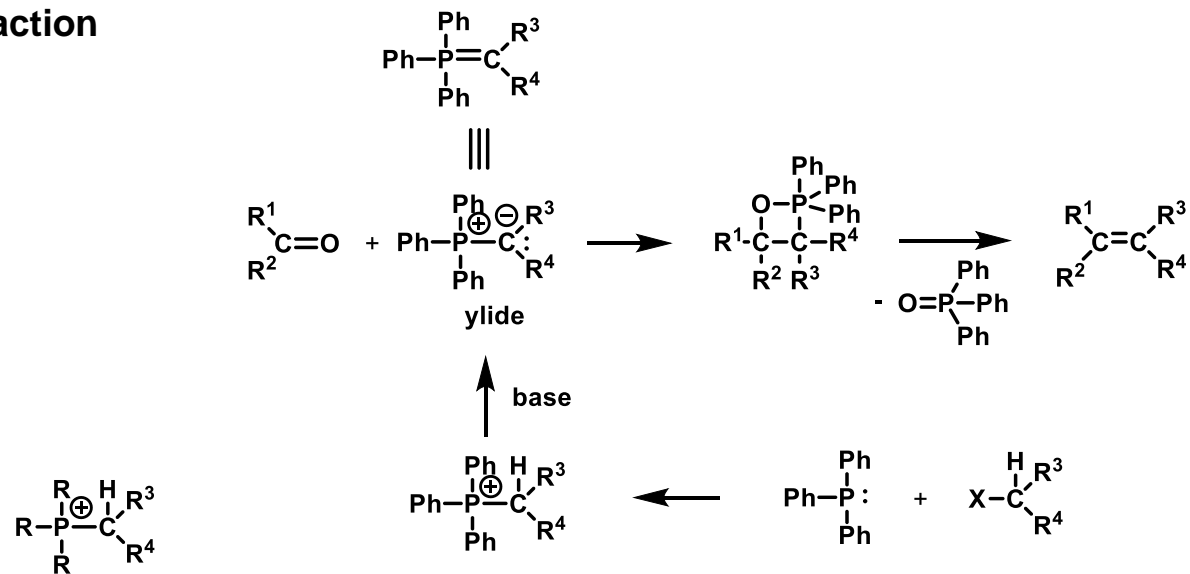


- unsymmetrical products (cross coupling): typically, one component in excess

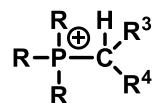


J. Org. Chem. **1986**, 51, 2361.

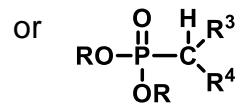
Wittig reaction



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

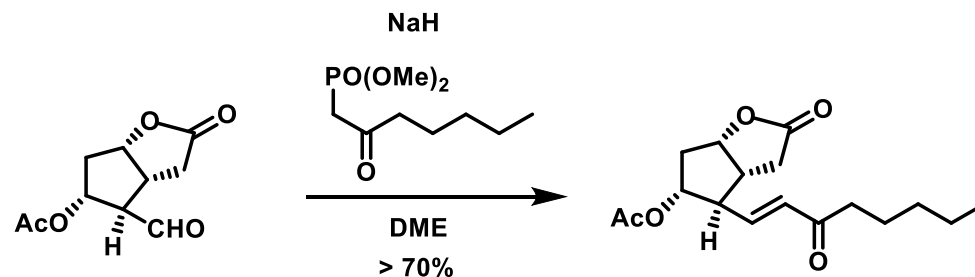


$\text{R}^3, \text{R}^4 = \text{electron acceptor} \longrightarrow \text{weaker base (removal of H}^+) \longrightarrow \text{stabilized ylide} \longrightarrow \text{(E)-alkene}$



(Horner-Wadsworth-Emmons)

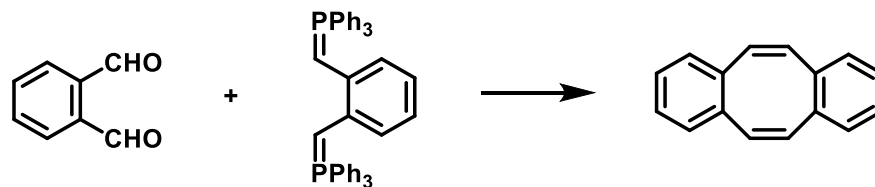
Wittig reaction is often used in the synthesis of complex molecules



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

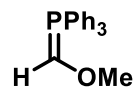
Note: complexation with ZnCl₂ will remove triphenylphosphine oxide, even from polar solvents: *J. Org. Chem.* **2017**, *82*, 9931.

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

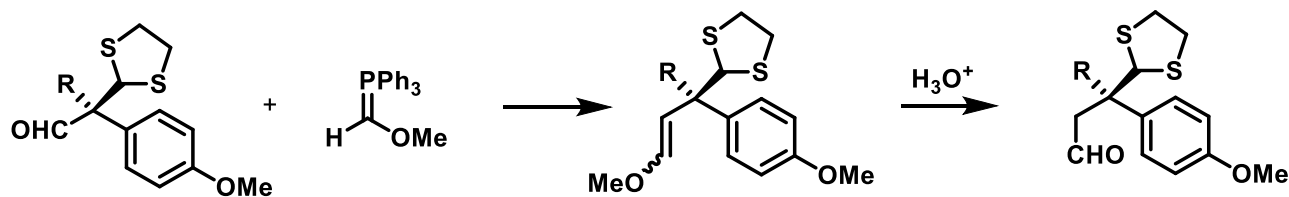


Synthesis **1975**, 765.

homologation of aldehydes

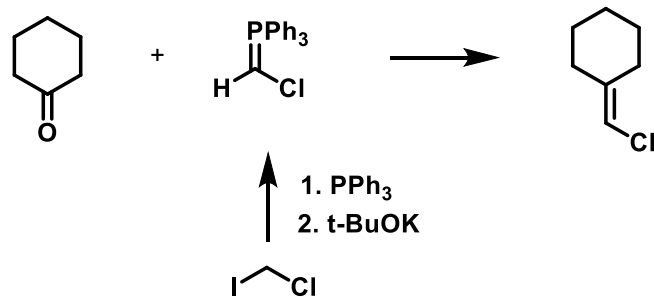


e.g.



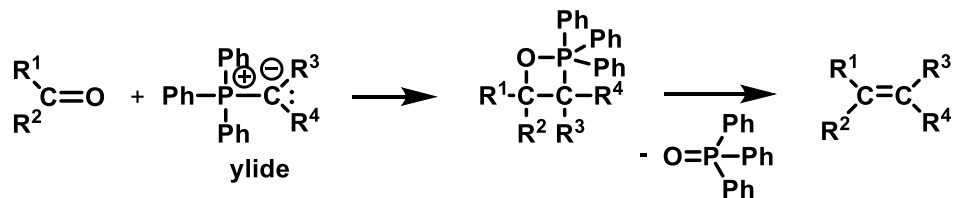
J. Org. Chem. **1989**, 54, 3831.

similarly: chloromethylenation

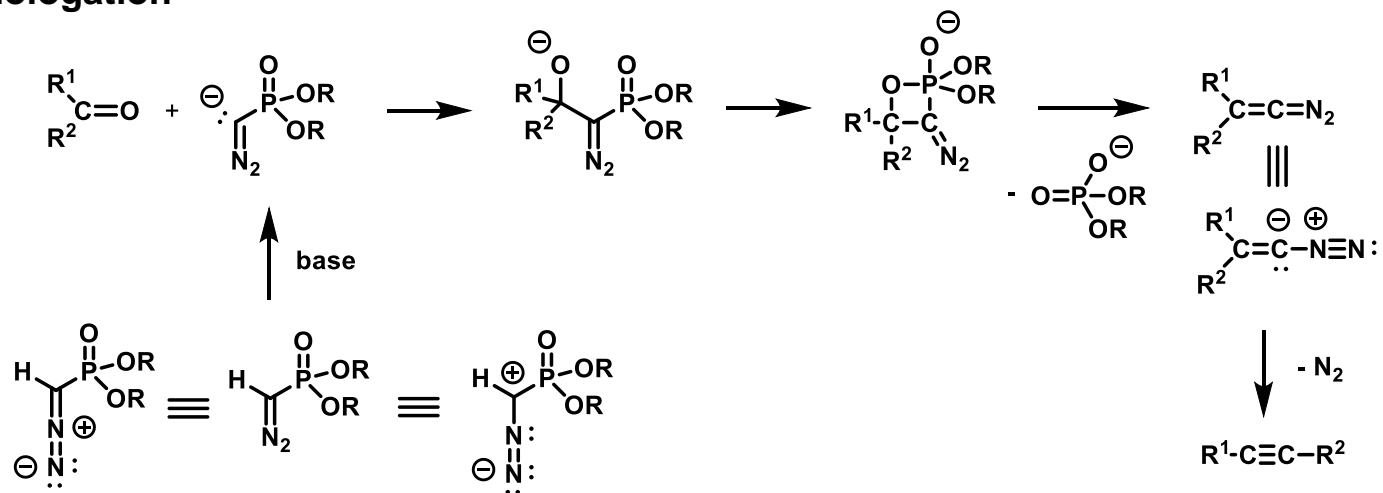


Tetrahedron Lett. **1980**, 21, 4021.

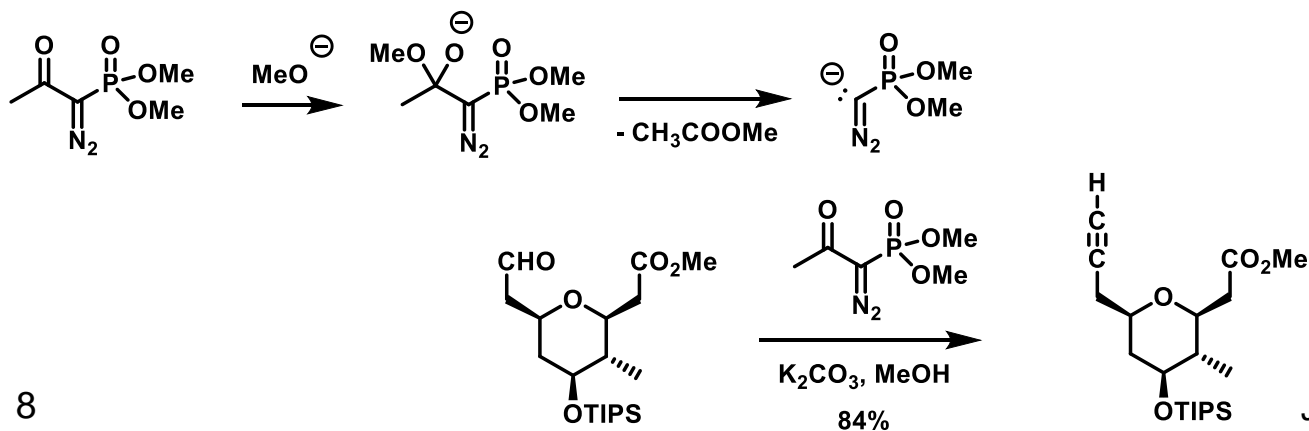
Wittig reaction



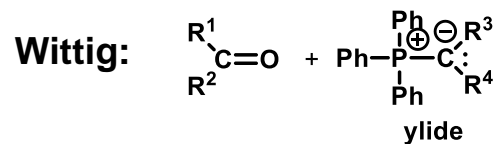
Seyferth-Gilbert homologation



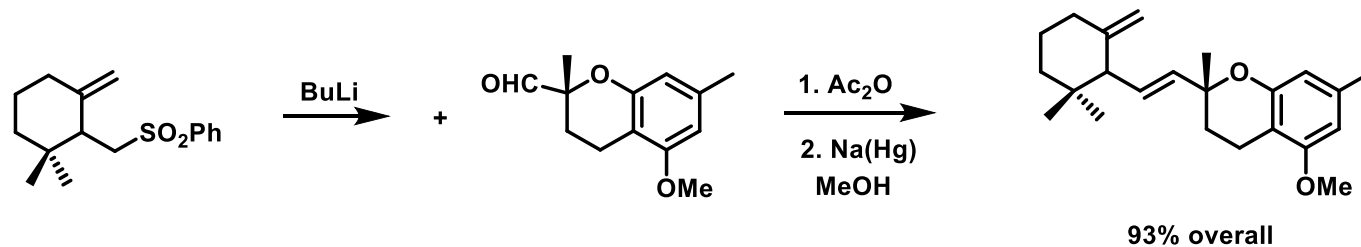
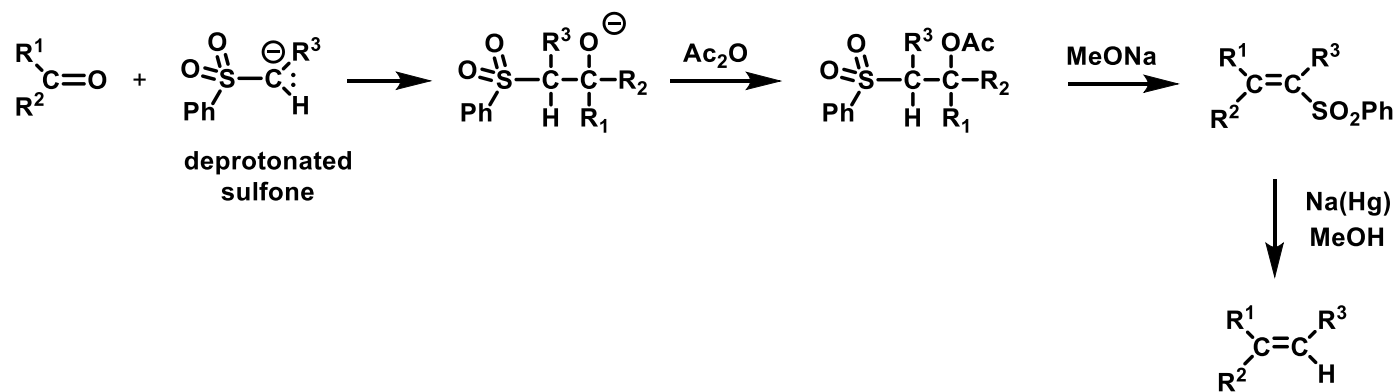
Ohira-Bestmann alkylation: frequently used for conversion of aldehydes to terminal alkynes



Julia-Lythgoe olefination



Julia-Lythgoe:

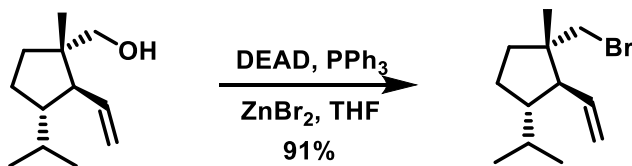
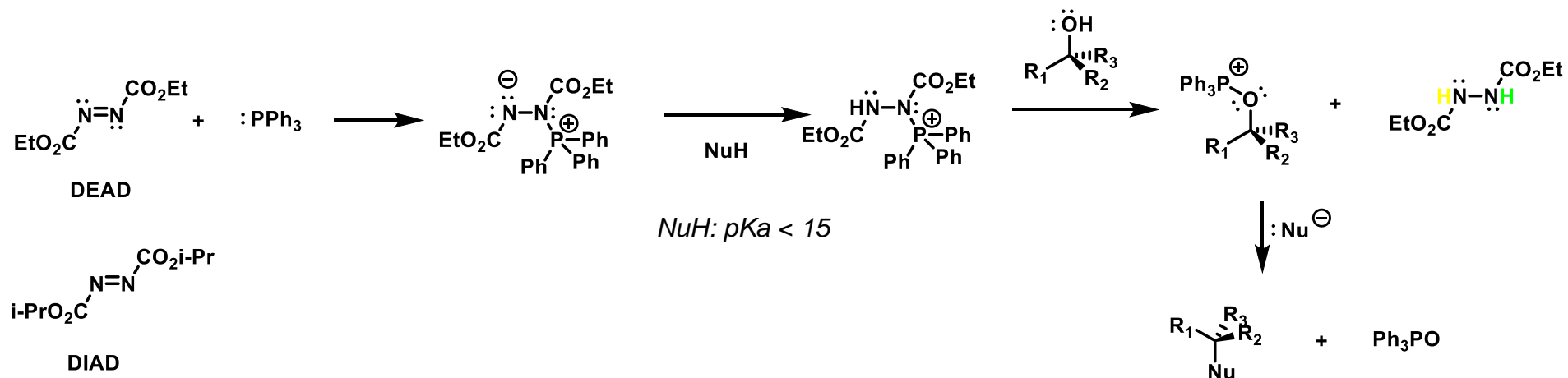


Angew. Chem. Int. Ed. **2003**, *42*, 3943.

conversions of functional groups

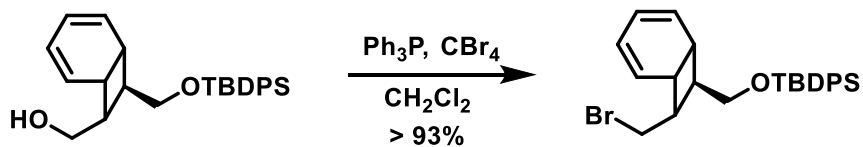
Mitsunobu reaction

- nucleophilic substitution of OH under mild conditions
- S_N2 -> inversion of configuration



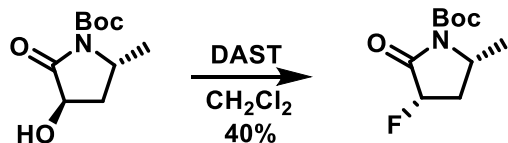
J. Org. Chem. **1987**, 52, 2960.

note: Ph₃P + CBr₄ (CCl₄) : OH -> Br (Cl)

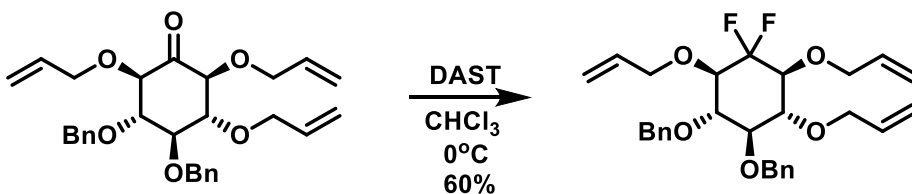


J. Am. Chem. Soc. **1982**, 104, 5560.

note: Et_2NSF_3 (DAST) : $\text{OH} \rightarrow \text{F}$
 $\text{C}=\text{O} \rightarrow \text{CF}_2$

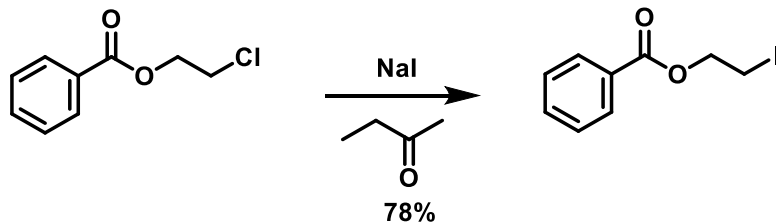


Tetrahedron Lett. **1992**, 33, 1509.

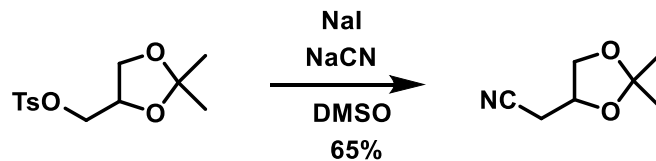


Tetrahedron Lett. **1988**, 29, 5217.

note: NaI : Cl , Br , OMs , OTs \rightarrow I (Finkelstein reaction)

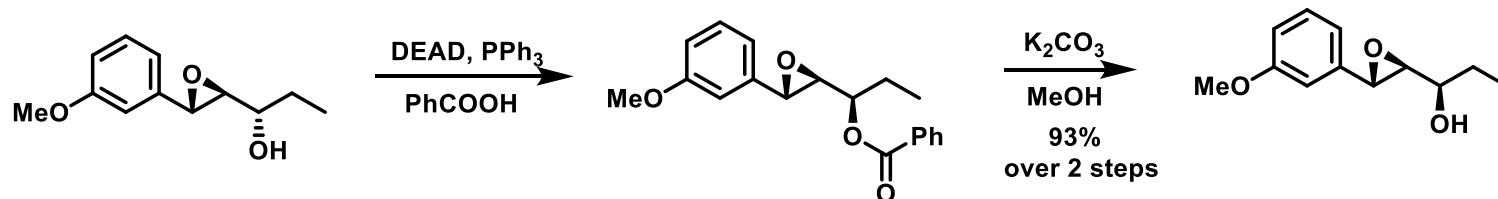


Org. Synth., Coll. Vol. **1963**, 4, 84.

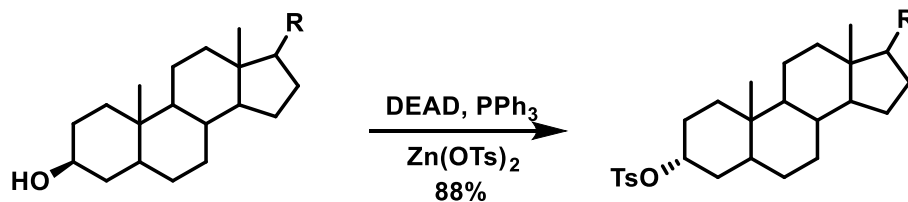


J. Am. Chem. Soc. **1980**, 102, 6304.

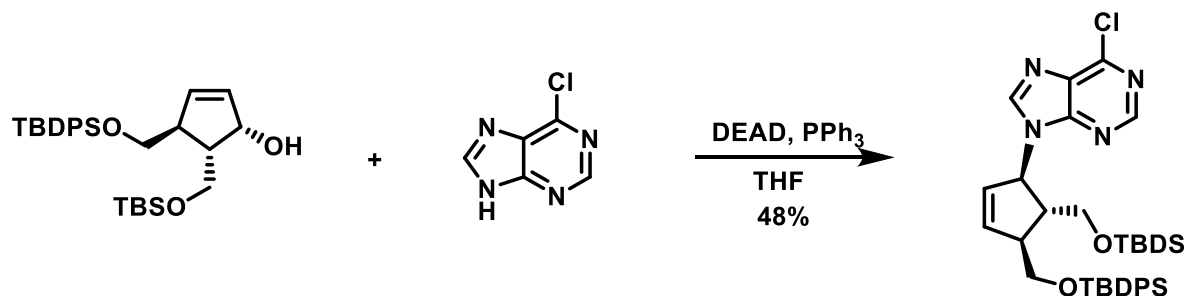
- Mitsunobu reaction: often method of choice for *inversion of configuration*
- also used for preparation of esters, lactones, amides, lactams and amines



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

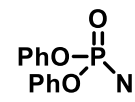


J. Am. Chem. Soc. **1982**, *104*, 1774.

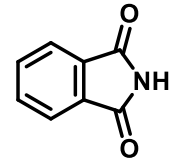


Tetrahedron Lett. **1992**, *33*, 3507.

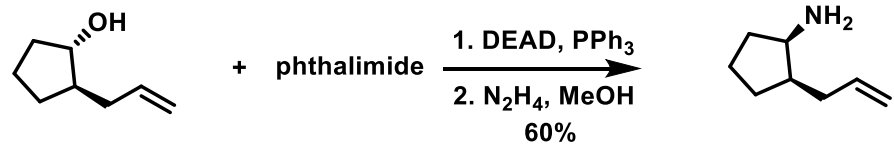
- generation of C-N bond: DPPA and phthalimide: common Nu sources of N



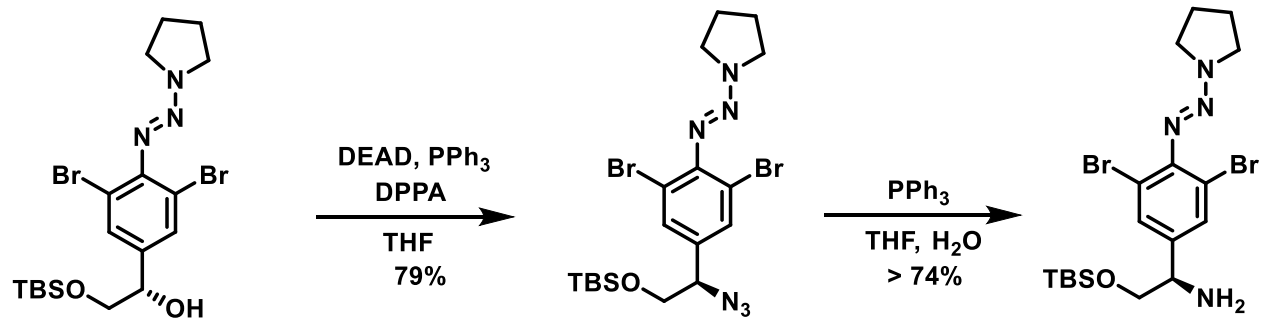
DPPA



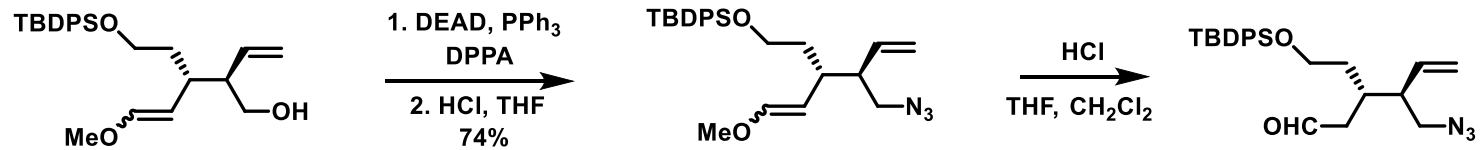
phthalimide



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



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

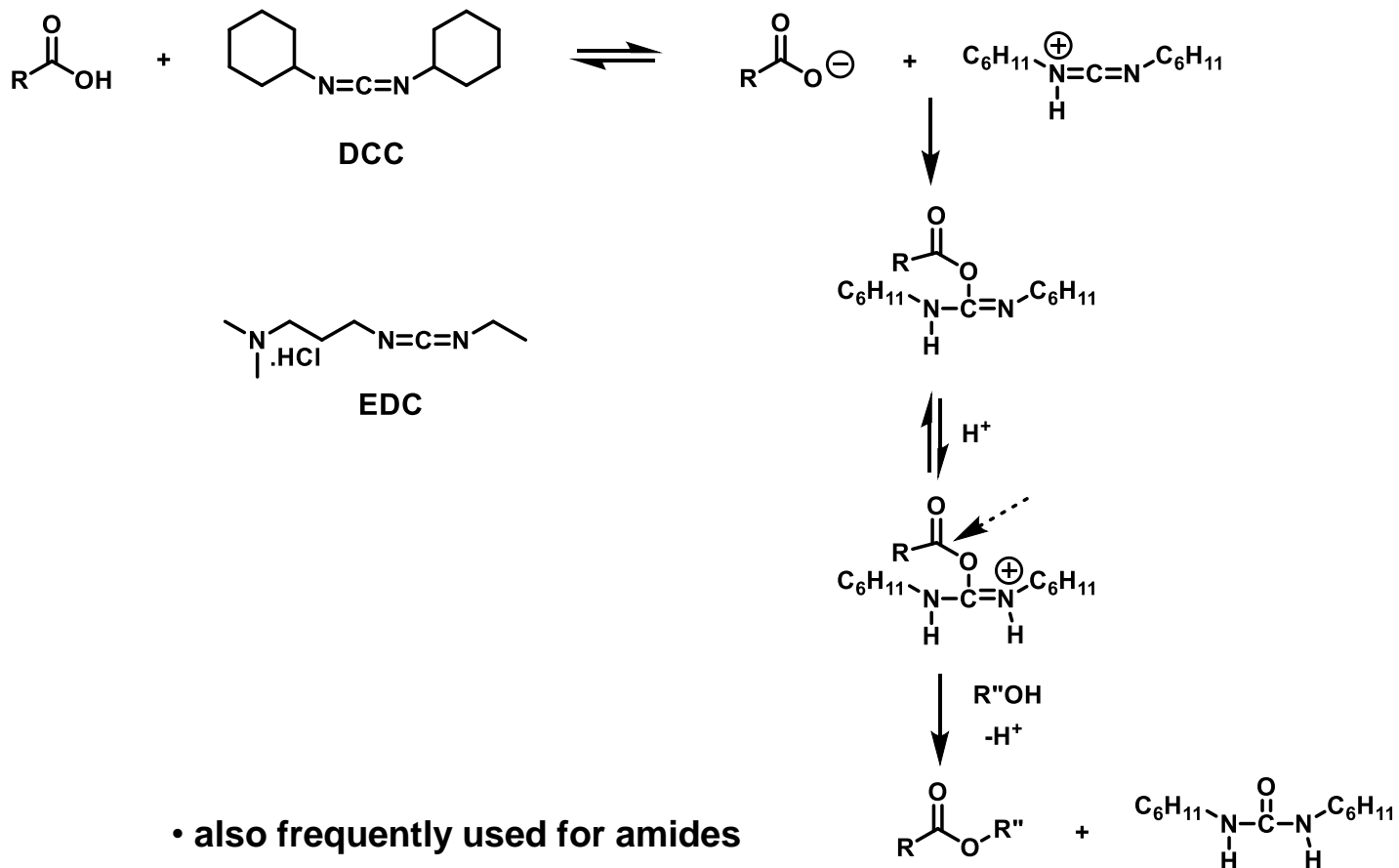
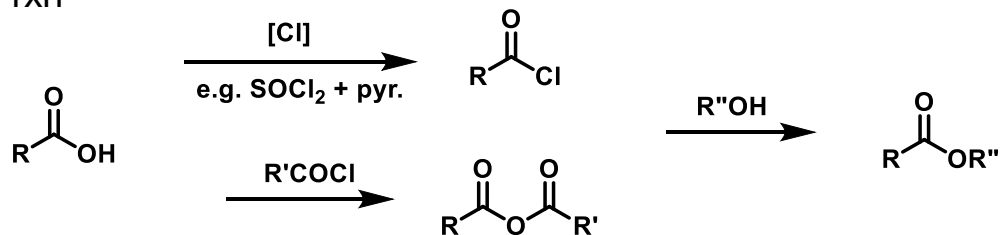


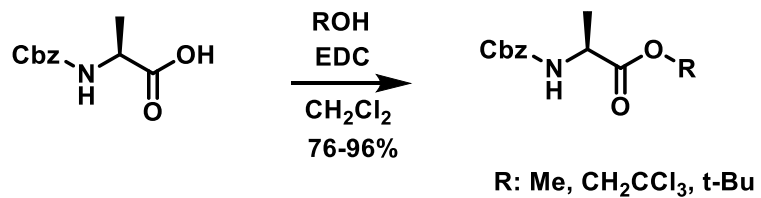
J. Am. Chem. Soc. **2001**, 123, 3239.

esterification

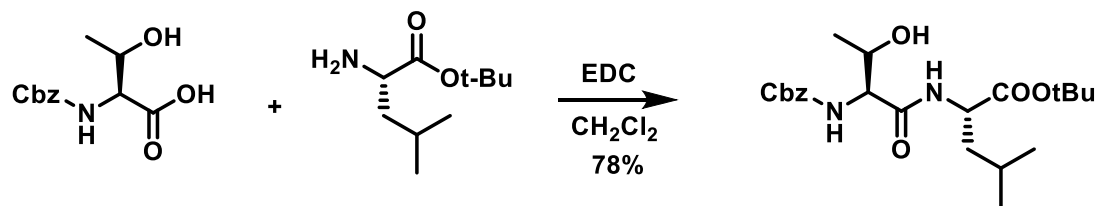
- conversion of carboxylic acids into derivatives with better leaving groups

- Mitsunobu rxn





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

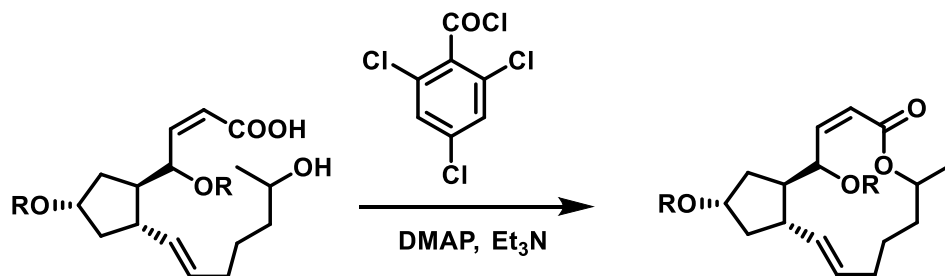


J. Am. Chem. Soc. **1973**, 95, 875.

macrolactonization

- often applied in synthesis of (biologically active) macrolides

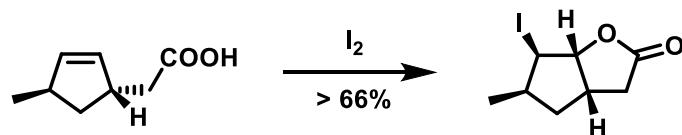
Yamaguchi macrolactonization



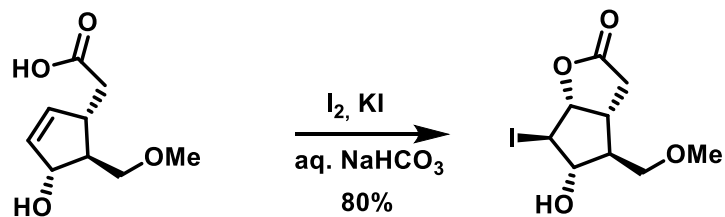
Chem. Lett. **1979**, 1021.

iodolactonization

- *anti* attack on cyclic iodonium intermediate



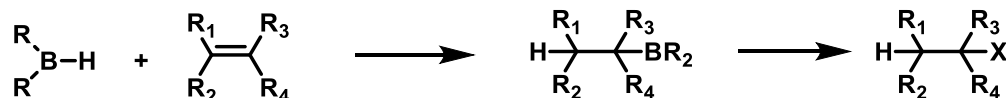
J. Am. Chem. Soc. **1985**, 107, 1448.



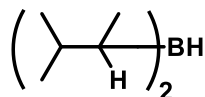
J. Am. Chem. Soc. **1969**, 91, 5675.

hydroboration (and subsequent transformations)

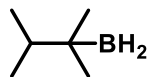
- “anti-Markovnikov” addition on double/triple bonds
- sterically hindered boranes: high regio- and stereoselectivity
- products of hydroboration can be converted into different derivatives



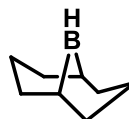
BH_3



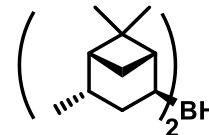
Sia₂BH



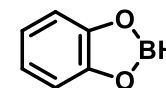
thexylborane



9-BBN



Ipc₂BH

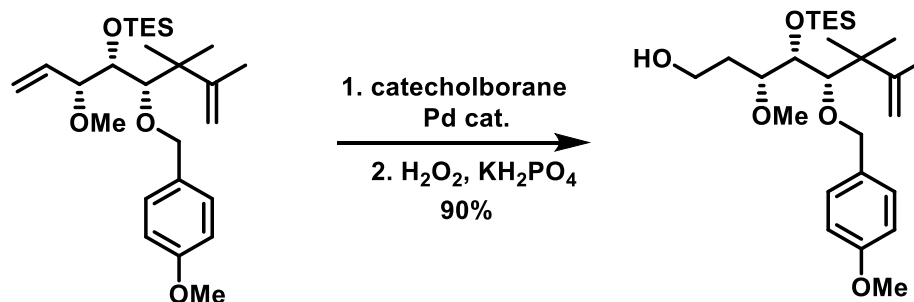


catecholborane

C-BR₂

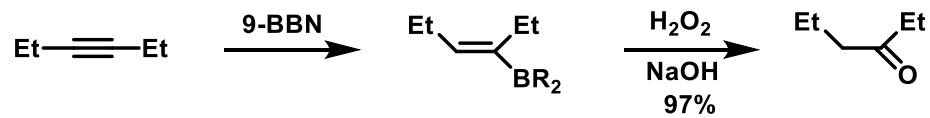


C-O



J. Am. Chem. Soc. **1992**, *114*, 6671.

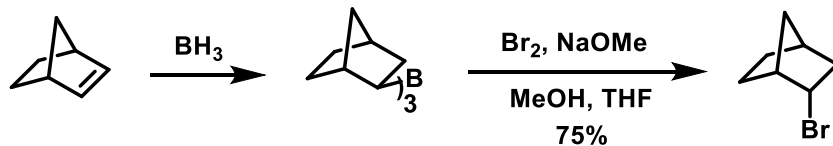
hydroboration of alkynes



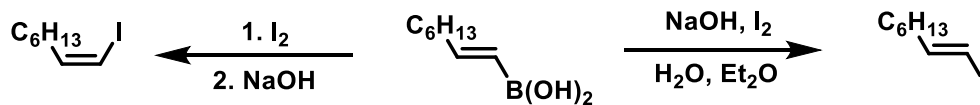
J. Am. Chem. Soc. **1979**, 101, 96.

terminal alkynes: *E*-alkenes

C-BR₂ → C-halogen

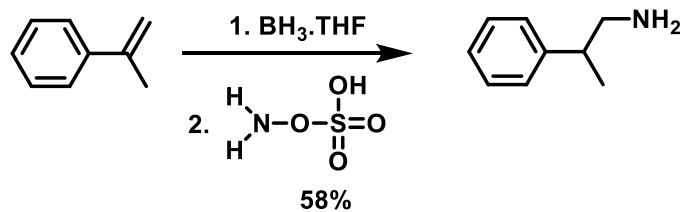


J. Chem. Soc., Chem. Commun. **1971**, 521.

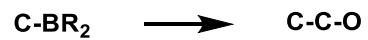


J. Am. Chem. Soc. **1973**, 95, 5786.

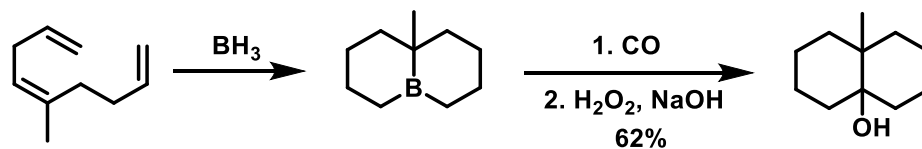
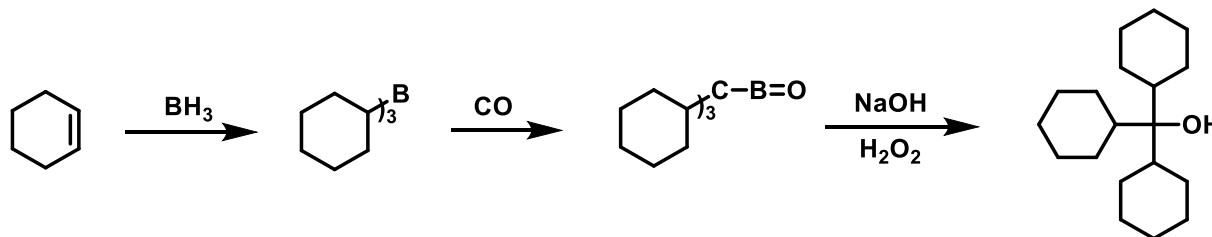
C-BR₂ → C-N



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



carbonylation of boranes



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