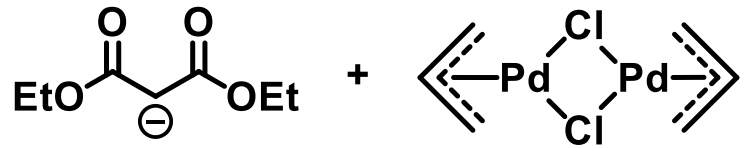
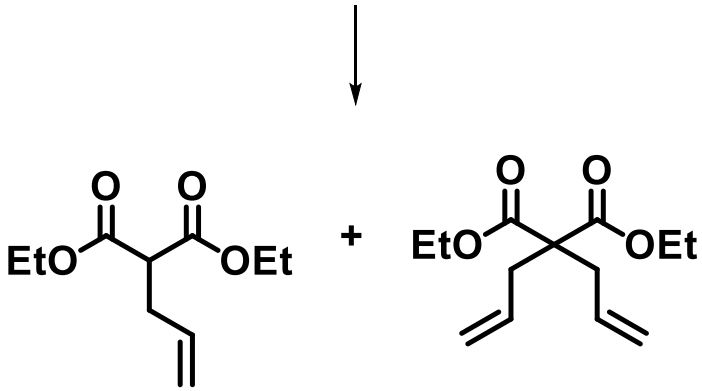
Tsuji-Trost Reaction

➢ Early report on stoichiometric Tsuji-Trost reaction

- **Stoichiometric reaction**



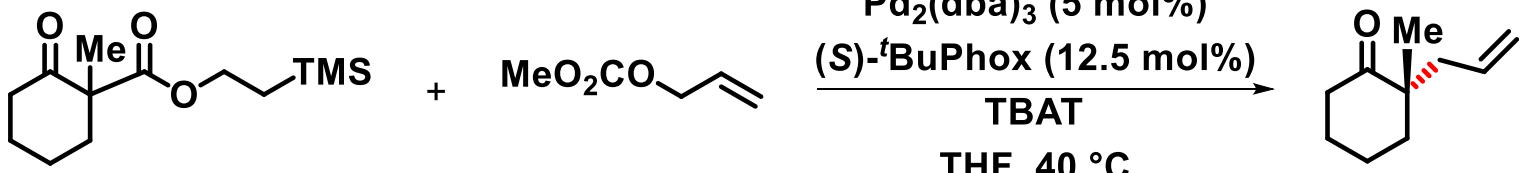


Tetrahedron Lett. **1965**, *49*, 4387

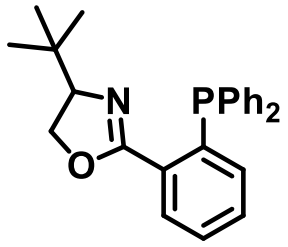
Tsuji-Trost Reaction

➢ Catalytic Tsuji-Trost reaction

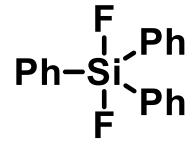
➢ Selected examples



81%
ee 86%

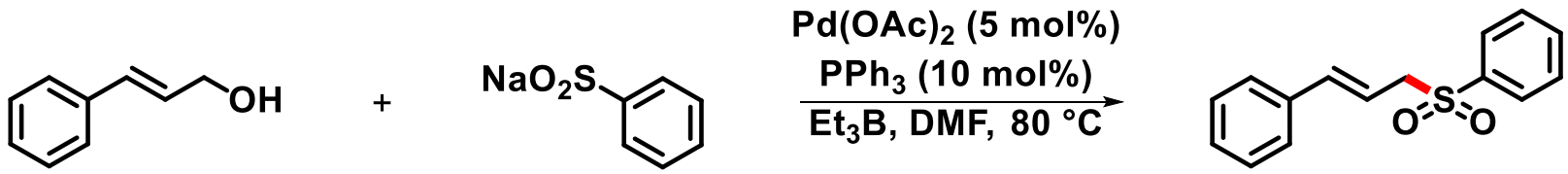


(*S*)-^{t}BuPhox



TBAT
tetrabutylammonium difluorotriphenylsilicate

Org. Lett. **2014**, *16*, 2314



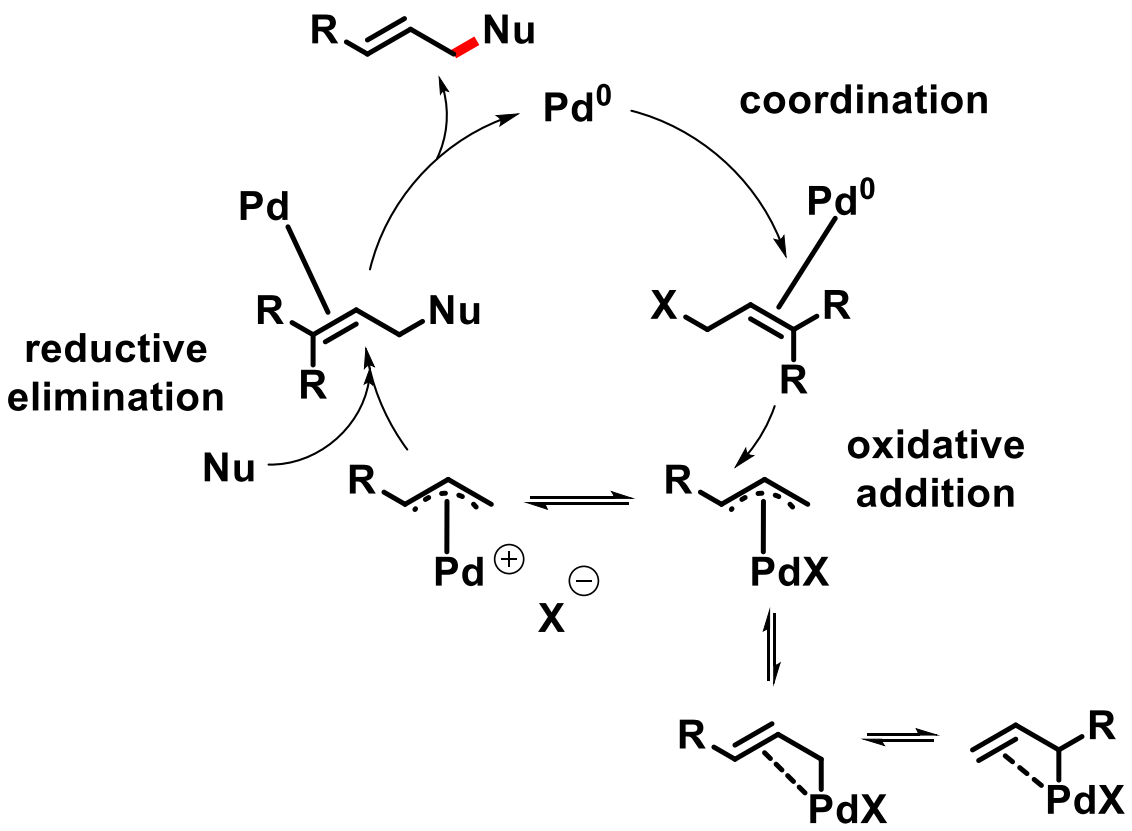
94%

J. Org. Chem. **2005**, *70*, 6506

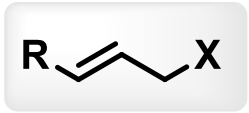
Tsuji-Trost Reaction

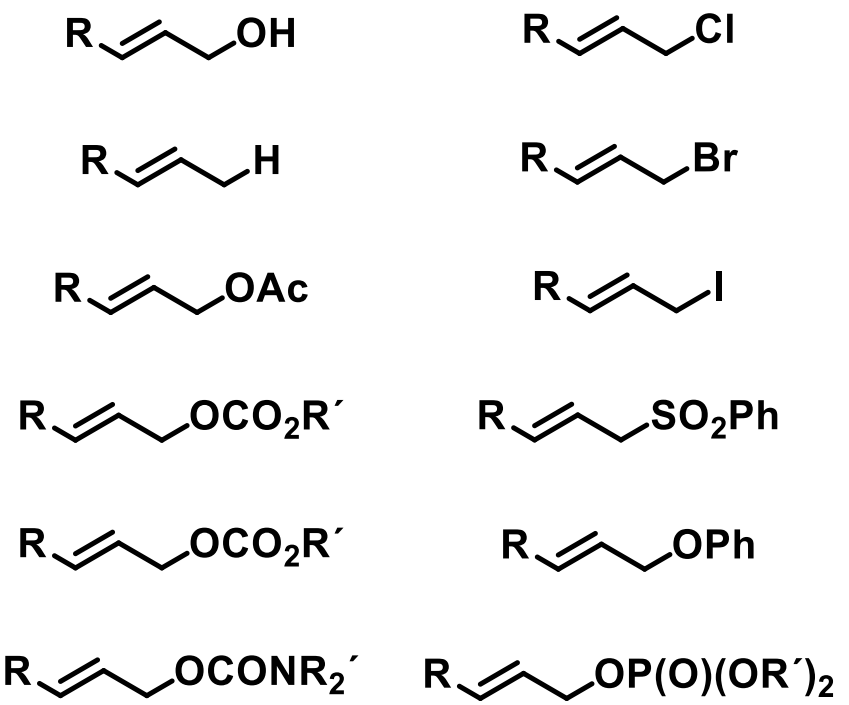
➢ Catalytic Tsuji-Trost reaction

- Simplified mechanism



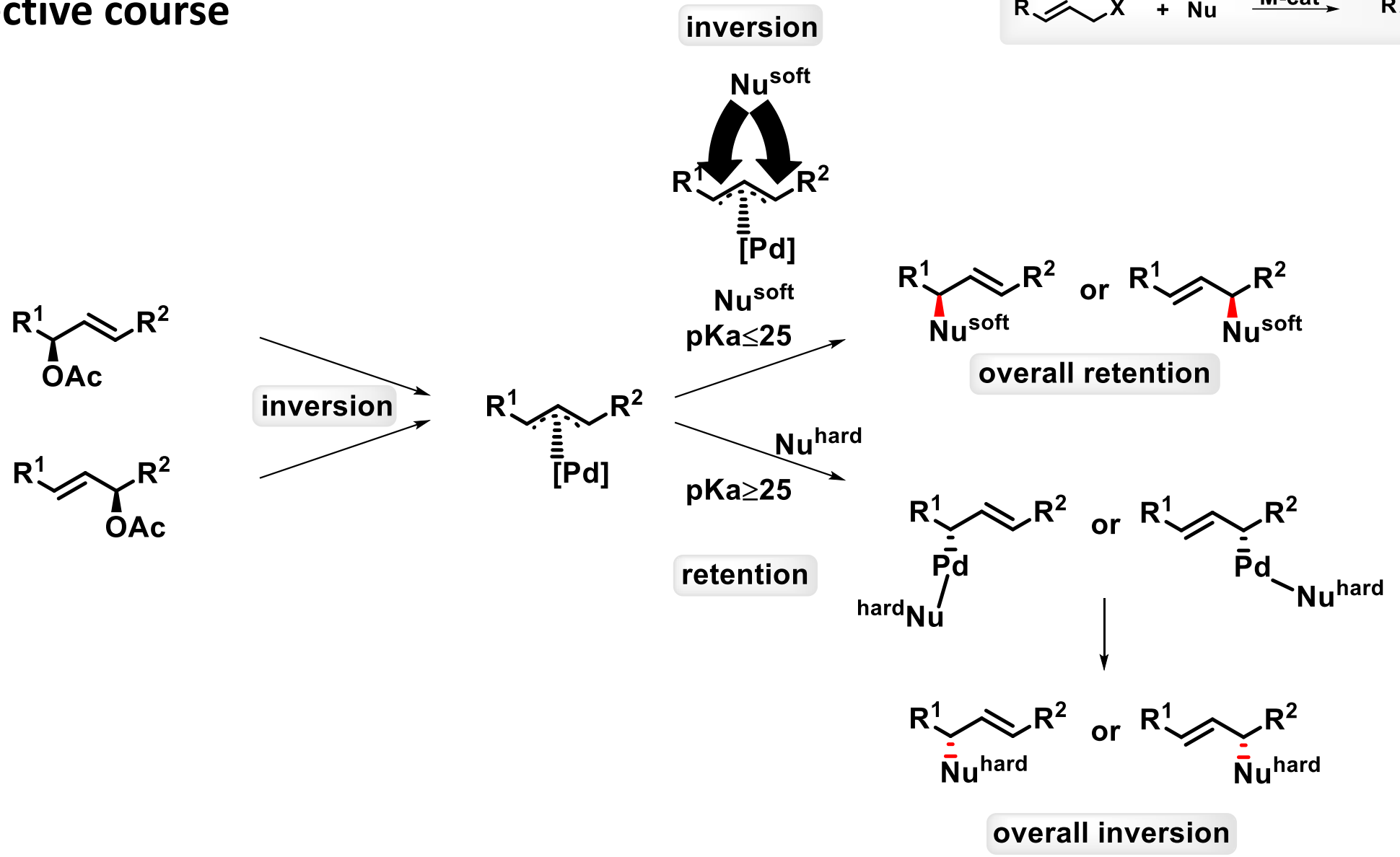
- Substrate scope





Tsuji-Trost Reaction

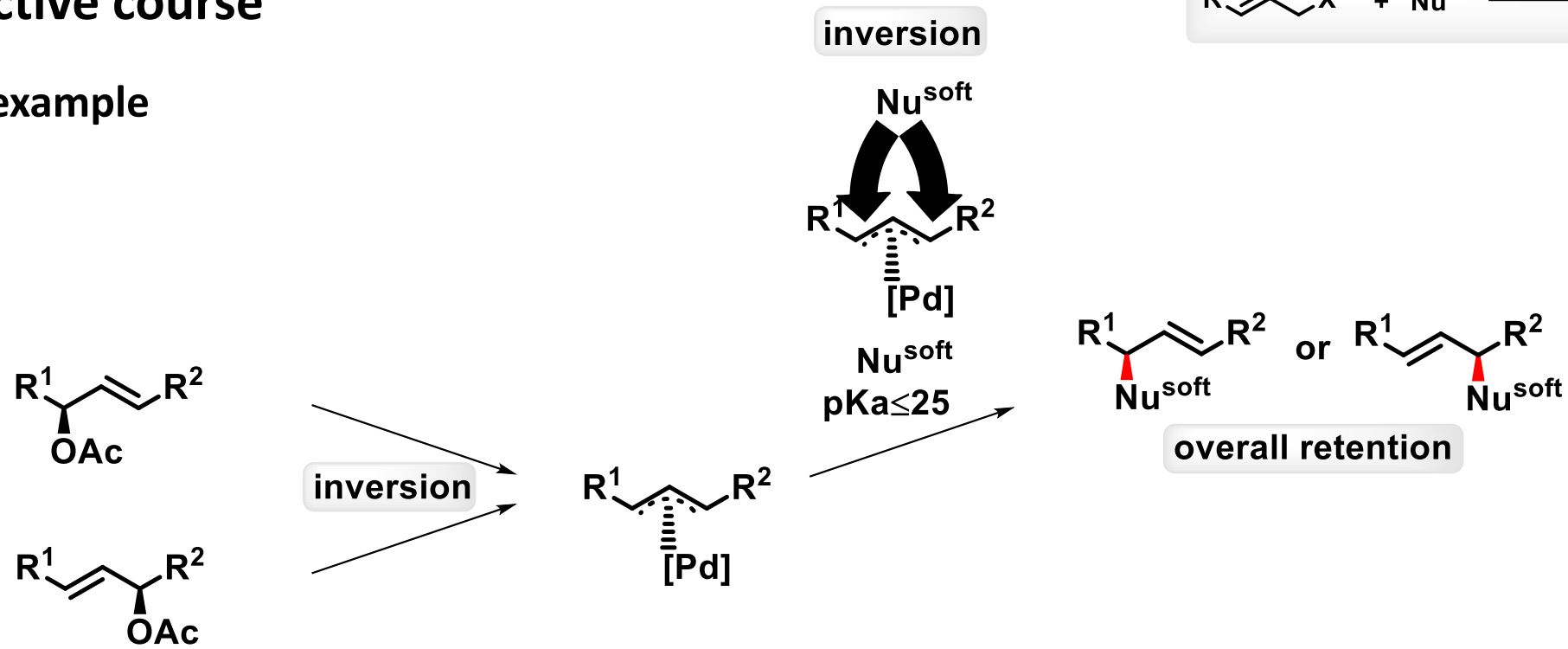
➢ Stereoselective course

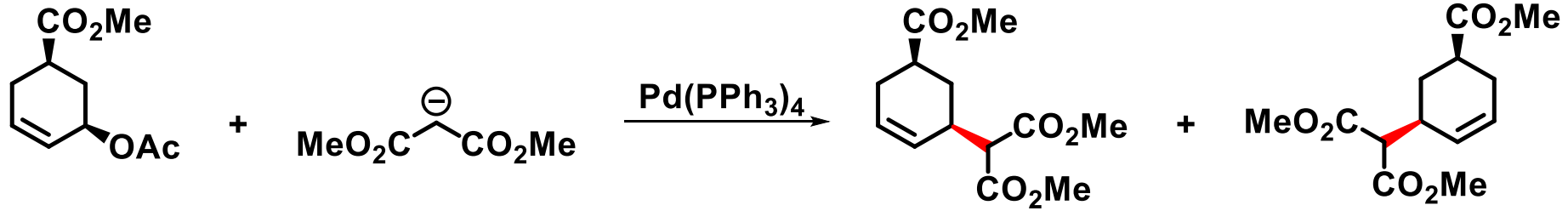


Tsuji-Trost Reaction

➢ Stereoselective course

- **Selected example**



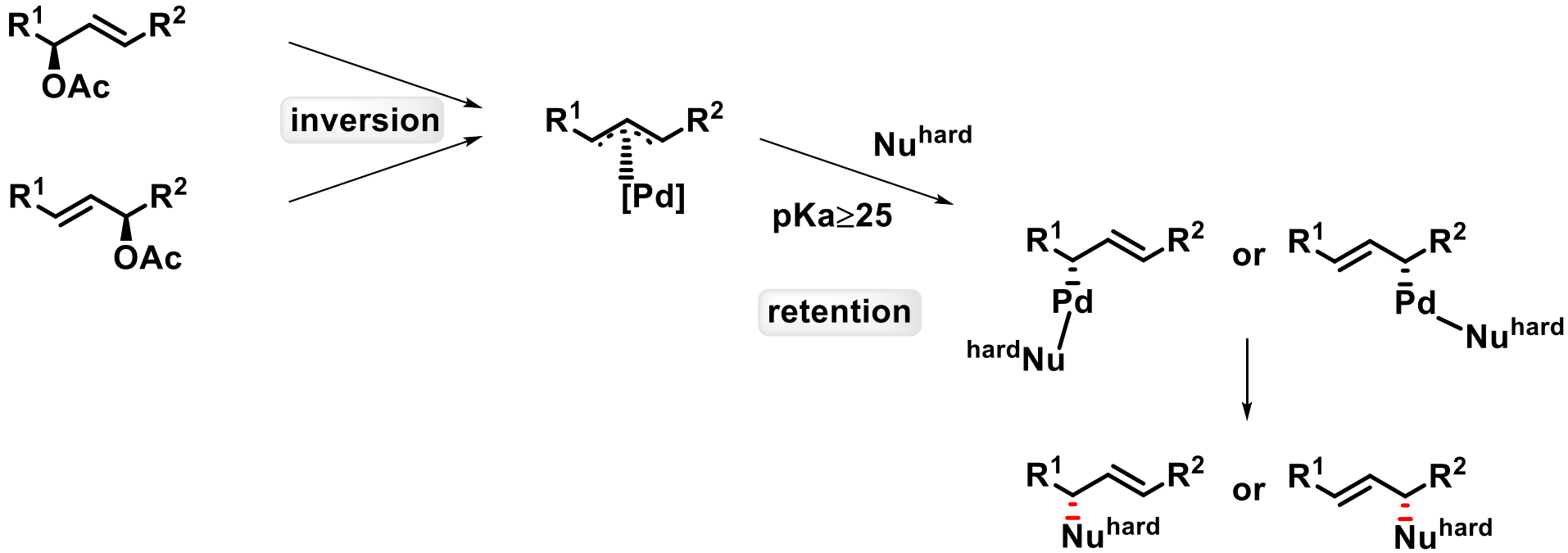


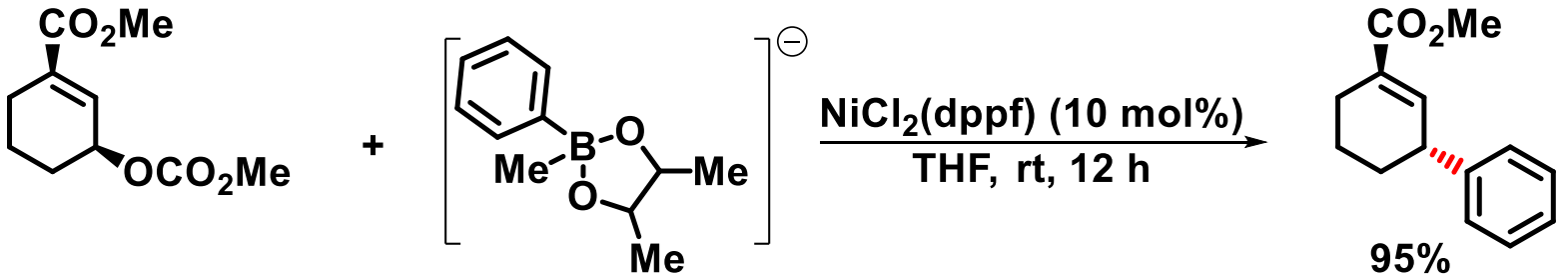
J. Am. Chem. Soc. **1980**, *102*, 4730

Tsuji-Trost Reaction

➢ Stereoselective course

- **Selected example**



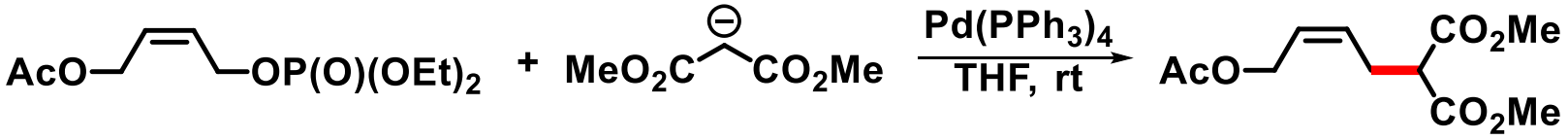


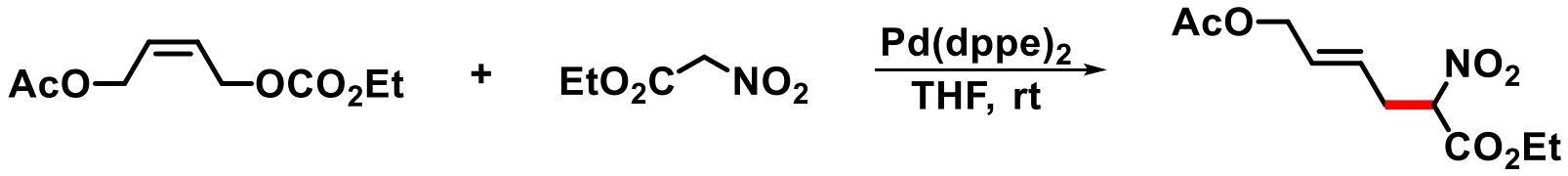
J. Org. Chem. **1996**, *61*, 5391

Tsuji-Trost Reaction

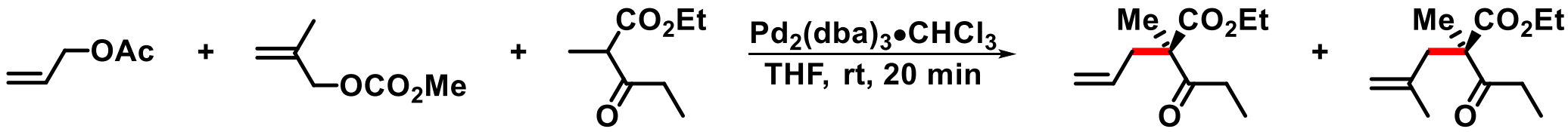
➢ Scope of the Tsuji-Trost reaction

- **The relative reactivity of carbonates, phosphates and acetates**
  - **allyl carbonate > allyl phosphate > allyl acetate**





- **Can be controlled by ligand choice**



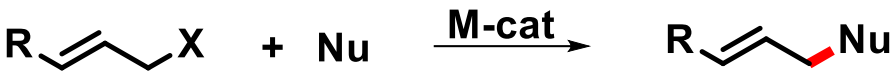
L = PPh_3 16:84

L = $P(OEt)_3$ 3:97

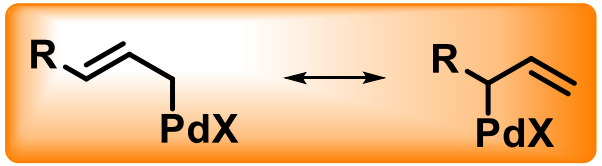
Tetrahedron Lett. **1982**, *23*, 5549; *J. Org. Chem.* **1985**, *50*, 1523; *Tetrahedron Lett.* **1984**, *25*, 3579

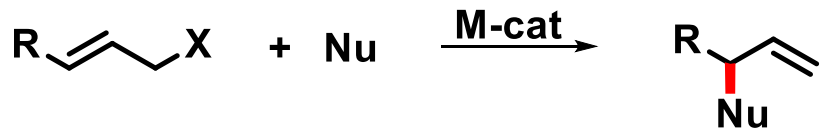
Tsuji-Trost Reaction

➢ Regioselectivity of the Tsuji-Trost reaction



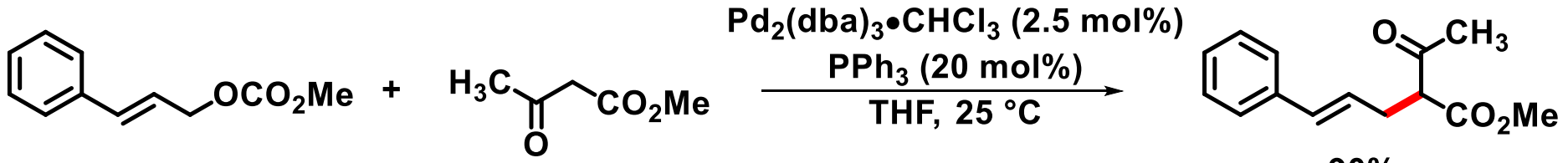
typical for Ni and Pd





typical for Mo, W, Ru, Rh, Ir

- **Palladium-catalyzed reaction with C-nucleophiles**

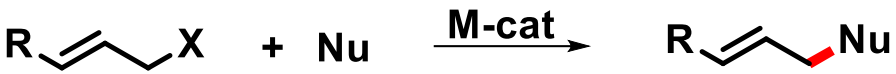


90%

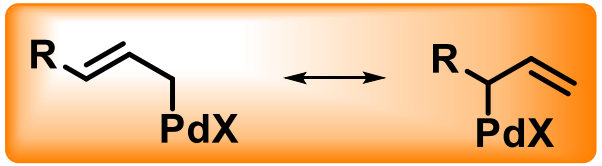
J. Org. Chem. **1985, *50***, 1523

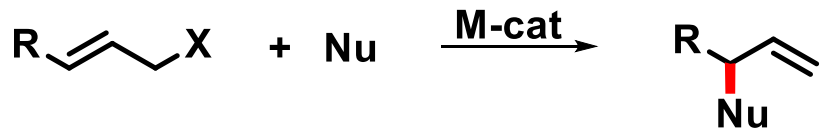
Tsuji-Trost Reaction

➢ Regioselectivity of the Tsuji-Trost reaction



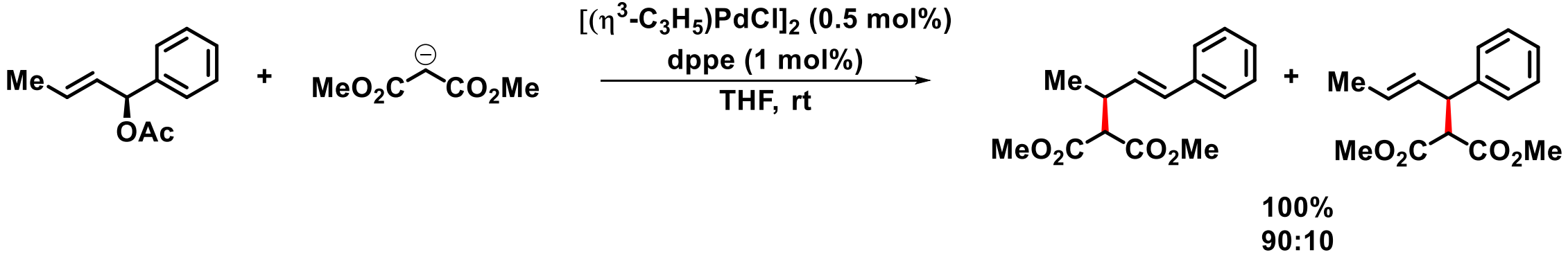
typical for Ni and Pd





typical for Mo, W, Ru, Rh, Ir

- **Palladium-catalyzed reaction with C-nucleophiles**

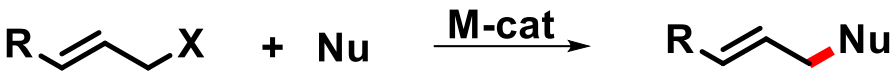


100%
90:10

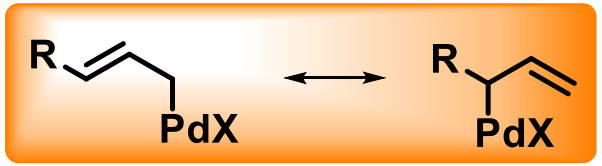
J. Org. Chem. **1986**, *51*, 723; *J. Chem. Soc. , Chem. Commun.* **1984**, 648

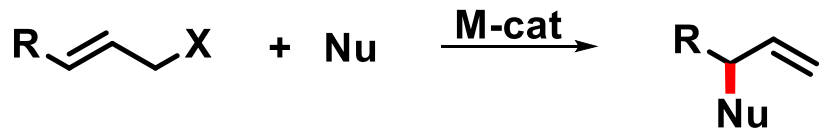
Tsuji-Trost Reaction

➢ Regioselectivity of the Tsuji-Trost reaction



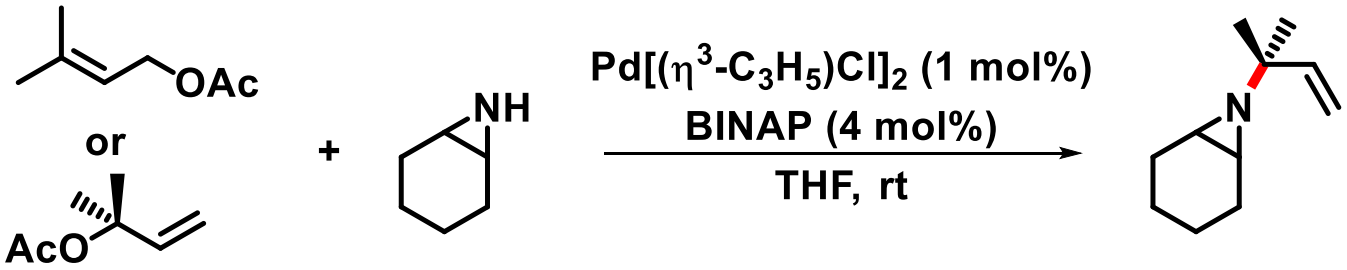
typical for Ni and Pd





typical for Mo, W, Ru, Rh, Ir

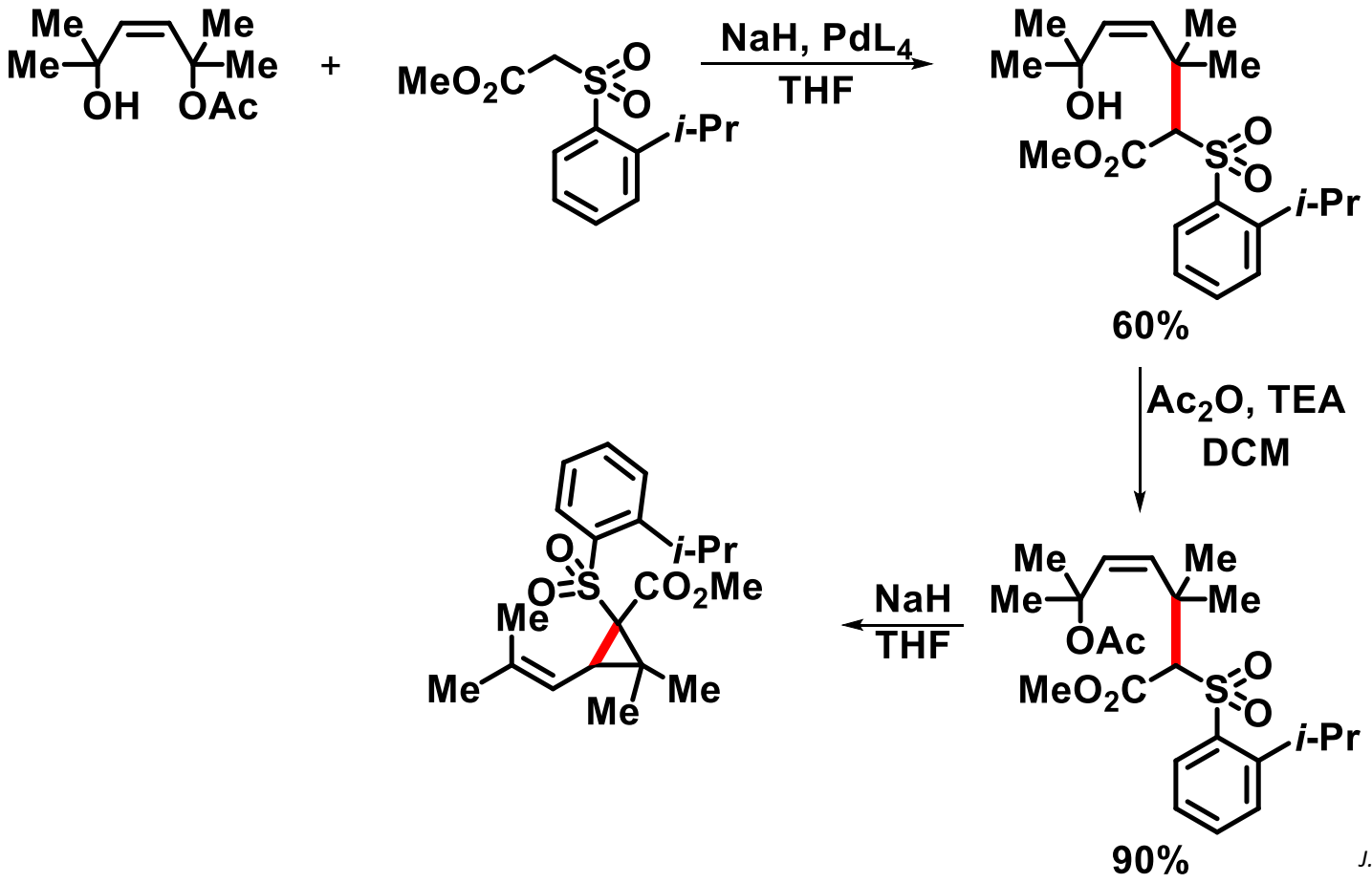
- **Palladium-catalyzed reaction with O and N-nucleophiles**



J. Am. Chem. Soc. **2004**, *126*, 5086; *J. Am. Chem. Soc.* **2005**, *127*, 17516; *Angew. Chem. Int. Ed.* **2007**, *46*, 7259

Tsuji-Trost Reaction

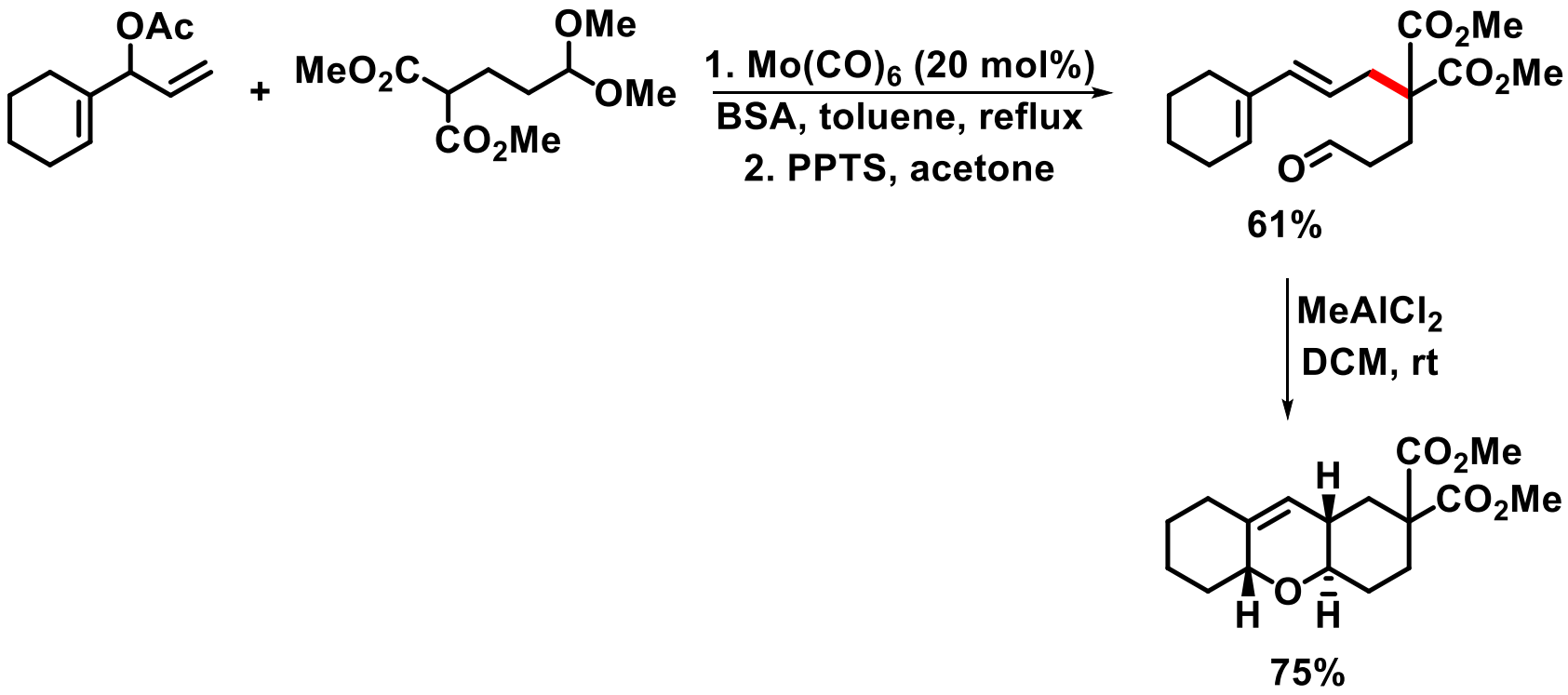
➢ Selected examples



J. Org. Chem. **1983**, *46*, 2414

Tsuji-Trost Reaction

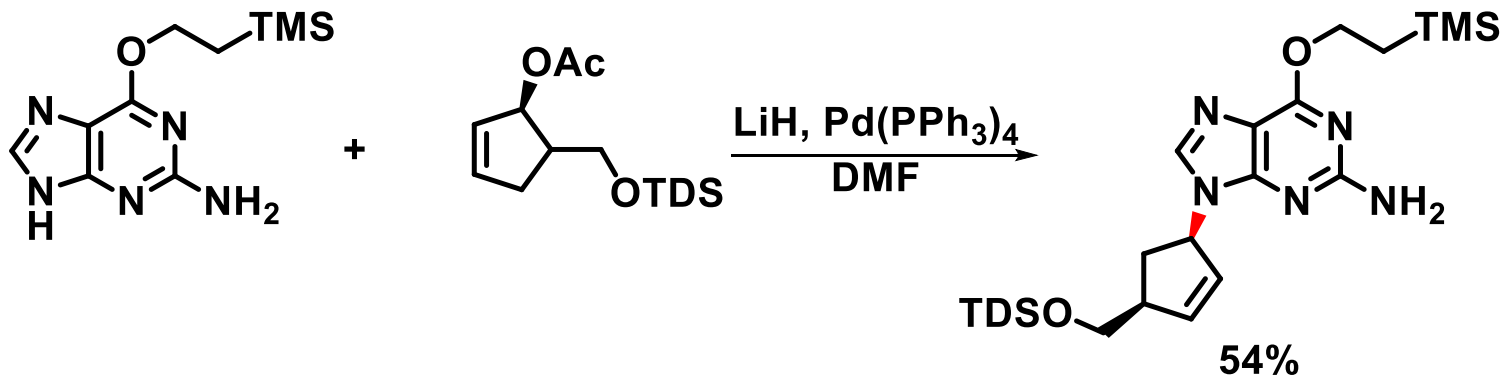
➢ Selected examples



J. Am. Chem. Soc. **1984**, 106, *7641*

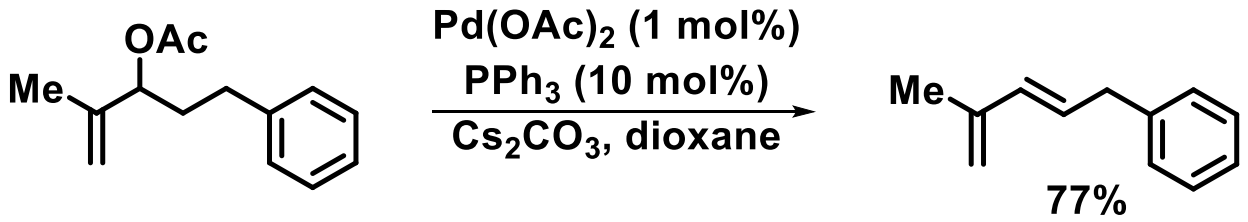
Tsuji-Trost Reaction

➢ Selected examples



Tetrahedron Lett. **1992**, *33*, 1085

- **Nucleophile-free conditions**

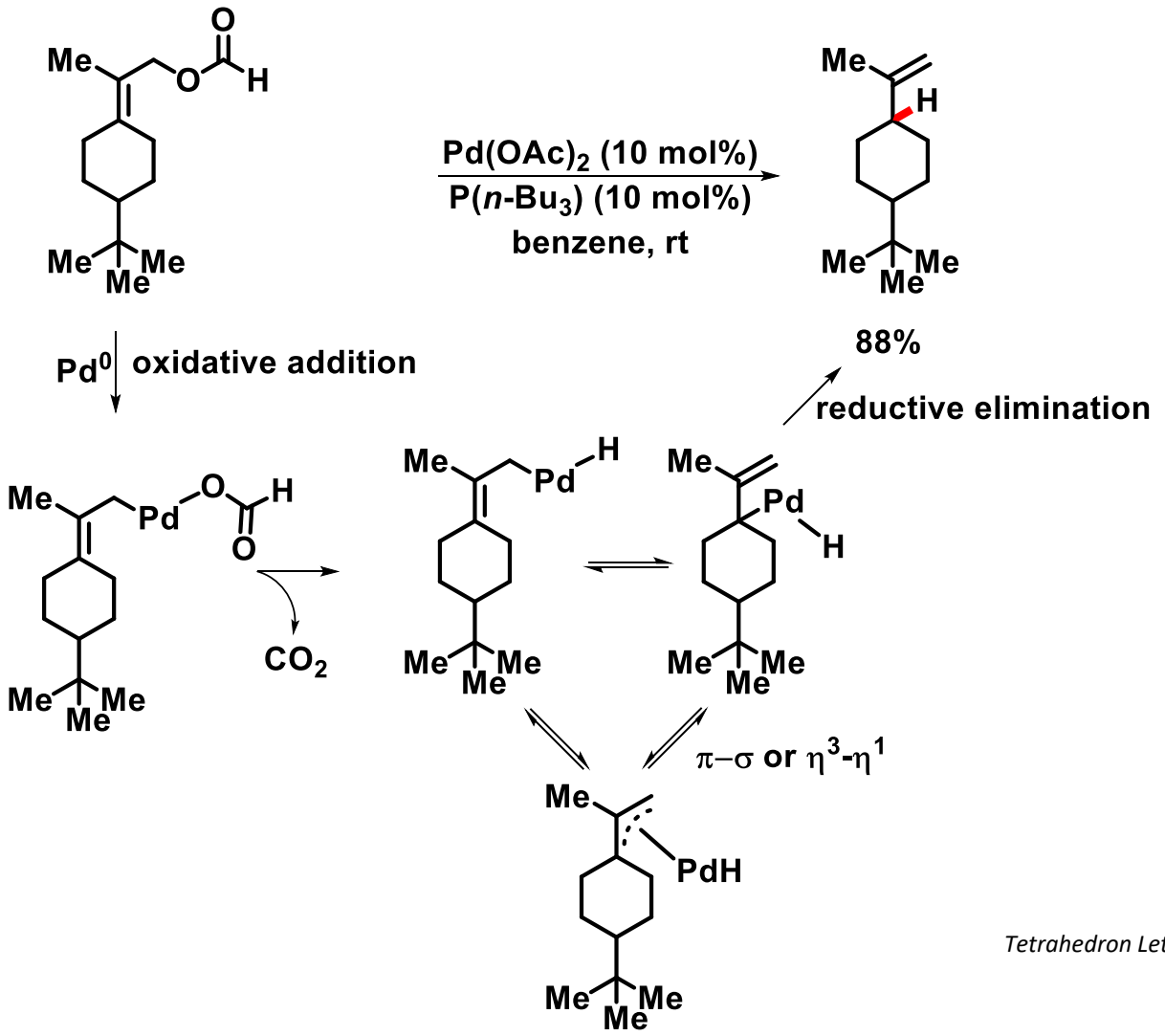


J. Org. Chem. **1988**, *53*, 4886

Tsuji-Trost Reaction

➢ Selected examples

- **Hydride as a nucleophile**



Tetrahedron Lett. **1992**, *33*, 2987

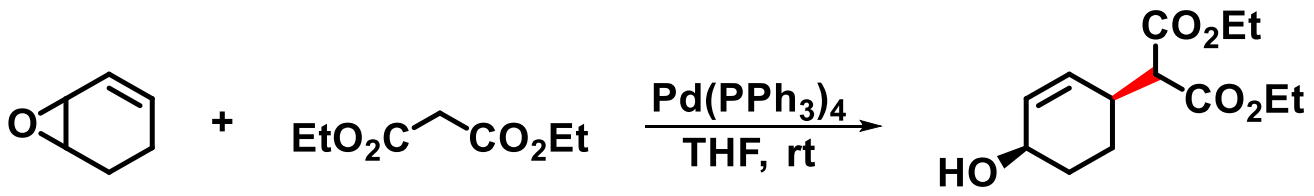
Tsuji-Trost Reaction

➢ Selected examples

- **Epoxides are good electrophiles**

84%, *E*:*Z* = 96:4

Tetrahedron Lett. **1981**, *22*, 2575

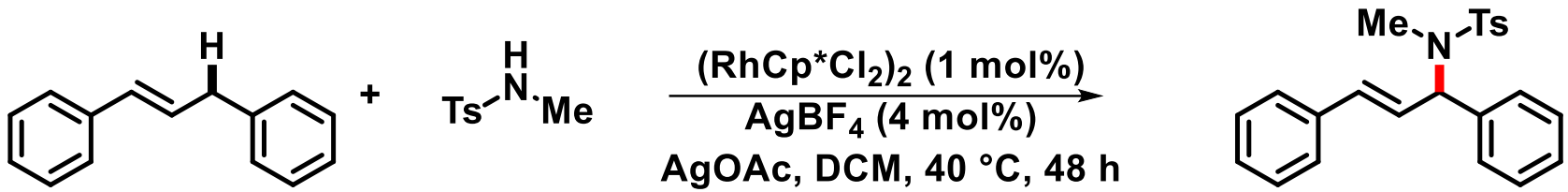


J. Am. Chem. Soc. **1981**, *103*, 5969

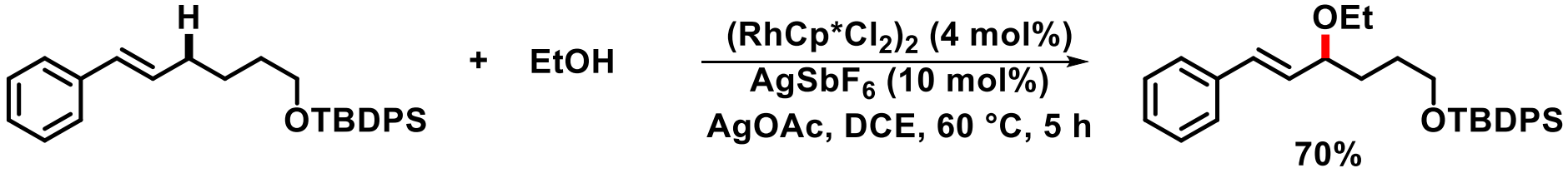
Tsuji-Trost Reaction

➢ Selected examples

- **Rhodium catalyzed C–H functionalization**



Angew. Chem. Int. Ed. **2017**, *56*, 13666

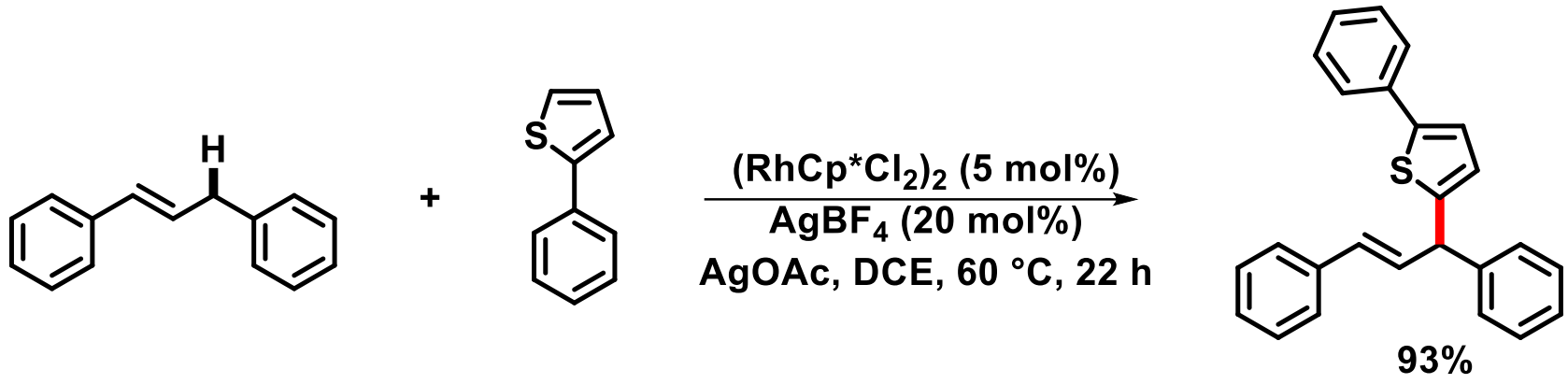


Angew. Chem. Int. Ed. **2018**, *57*, 14911

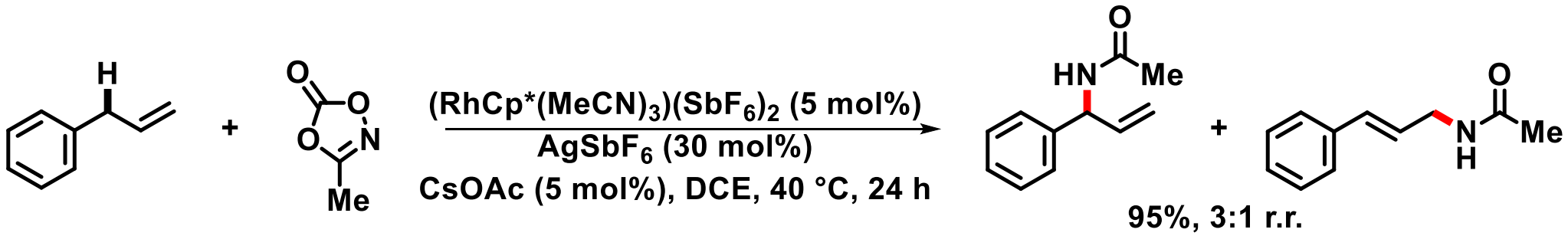
Tsuji-Trost Reaction

➢ Selected examples

- **Rhodium catalyzed C–H functionalization**



Angew. Chem. Int. Ed. **2018**, *57*, 15248



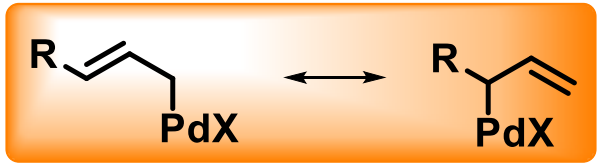
ACS Catal. **2019**, *9*, 5474

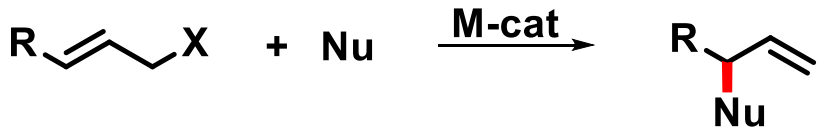
Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

- **Regioselectivity**

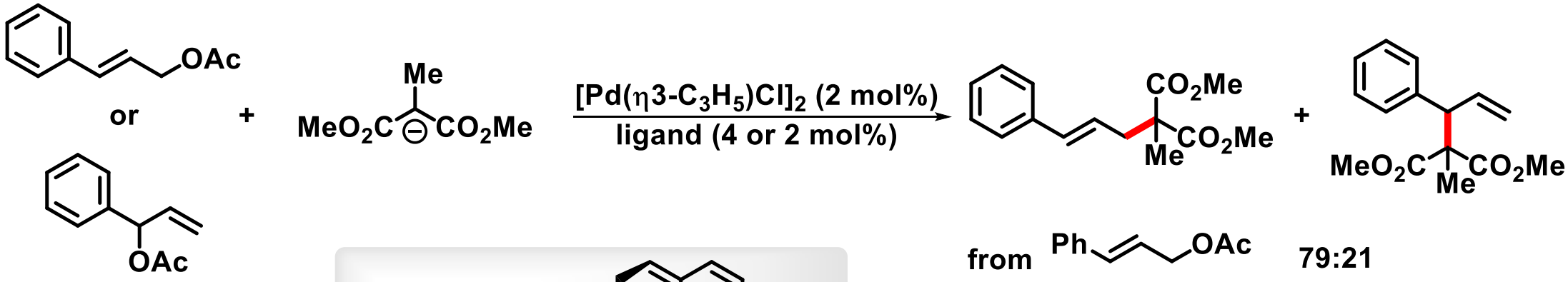
typical for Ni and Pd



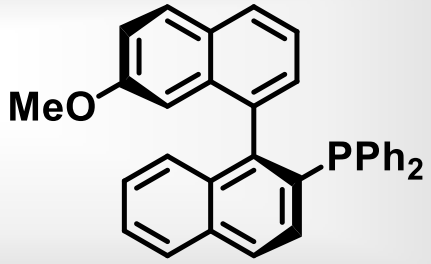


typical for Mo, W, Ru, Rh, Ir

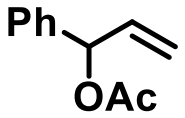
- **Regiochemical „memory effect“**



ligand =



from 79:21

from  23:77

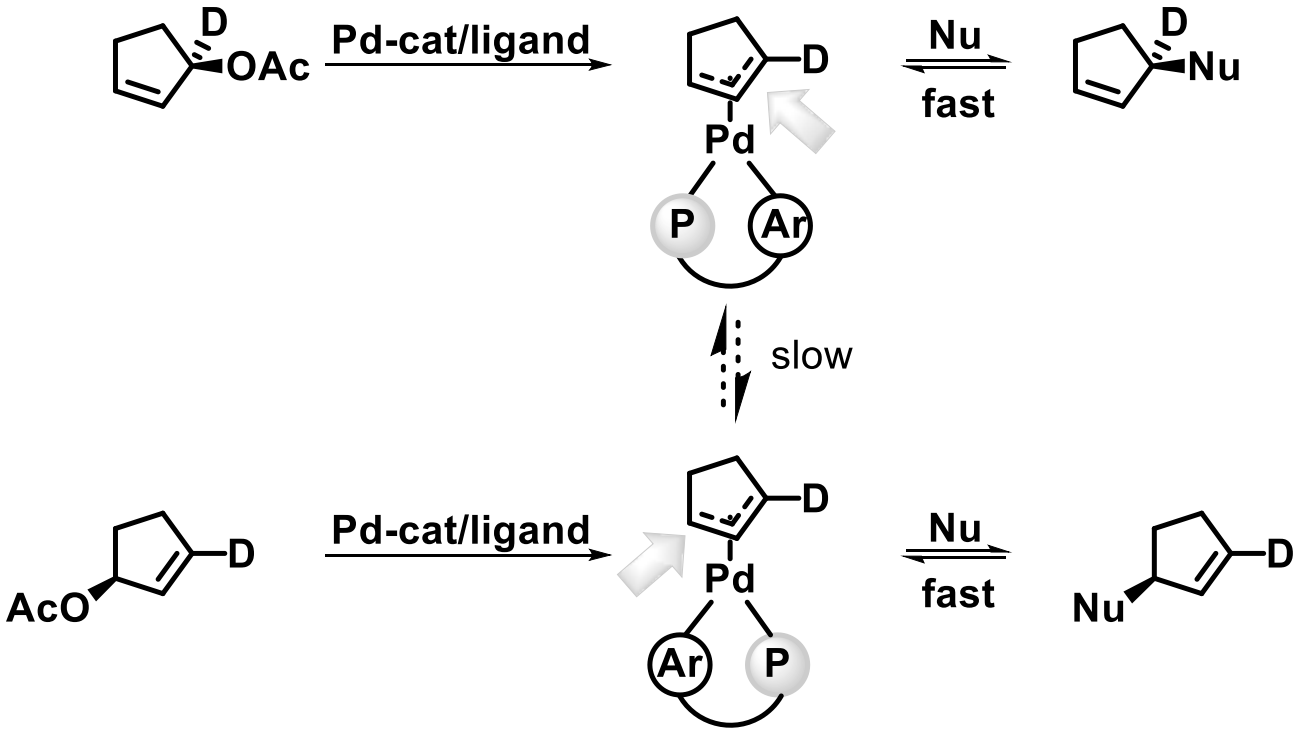
J. Am. Chem. Soc. **1998**, *120*, 1681

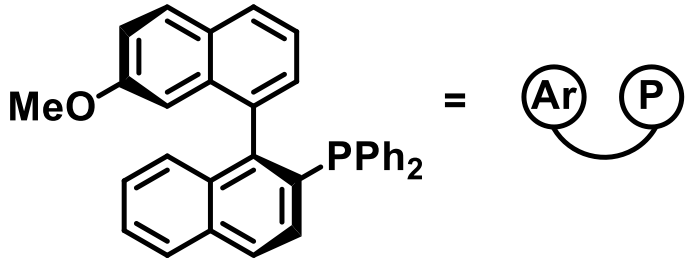
Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

- **Regioselectivity**

○ Regiochemical „memory effect“ – Explanation



ligand = 

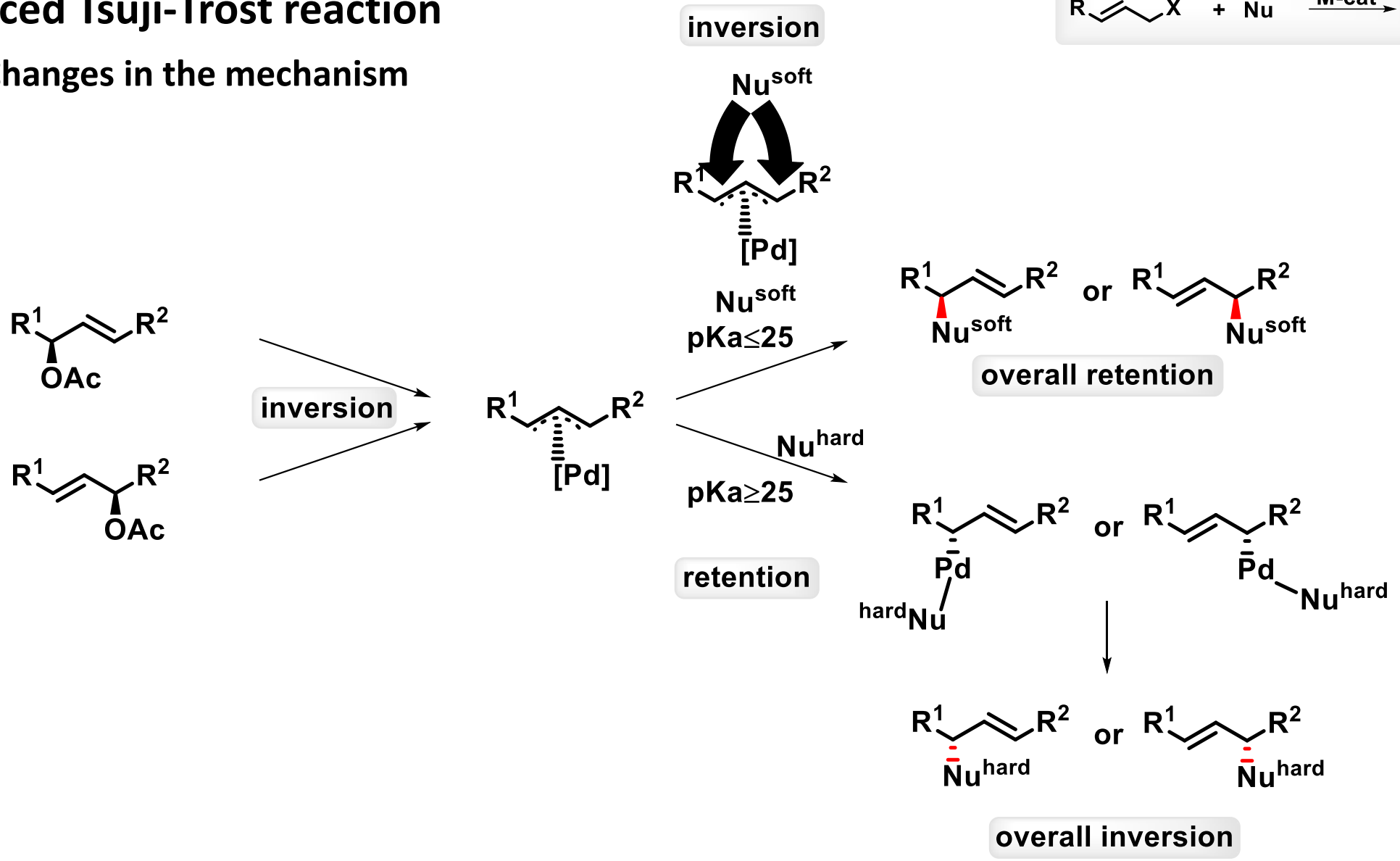
=

J. Am. Chem. Soc. **1998**, *120*, 1681

Tsuji-Trost Reaction

Advanced Tsuji-Trost reaction

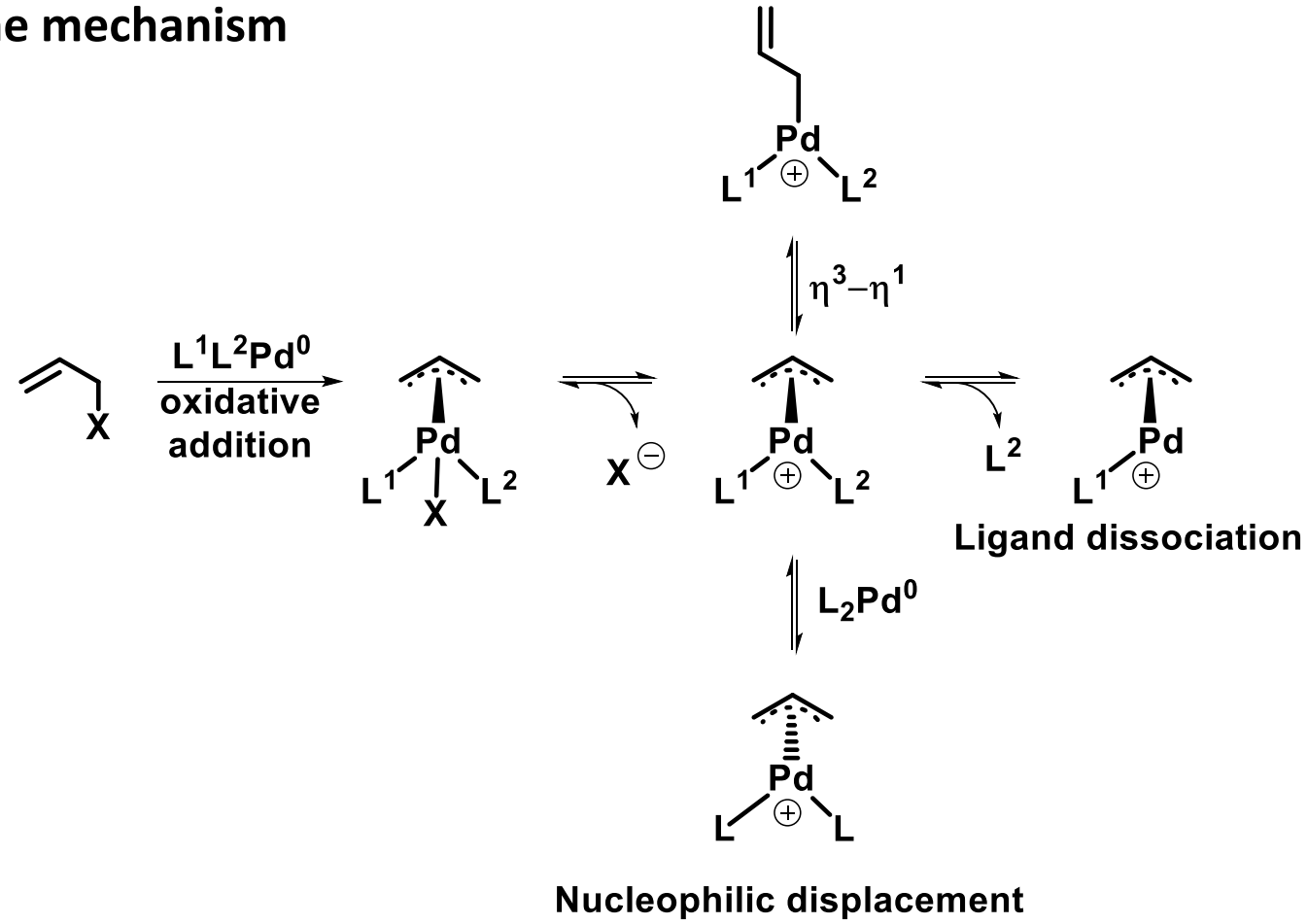
- Changes in the mechanism



Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

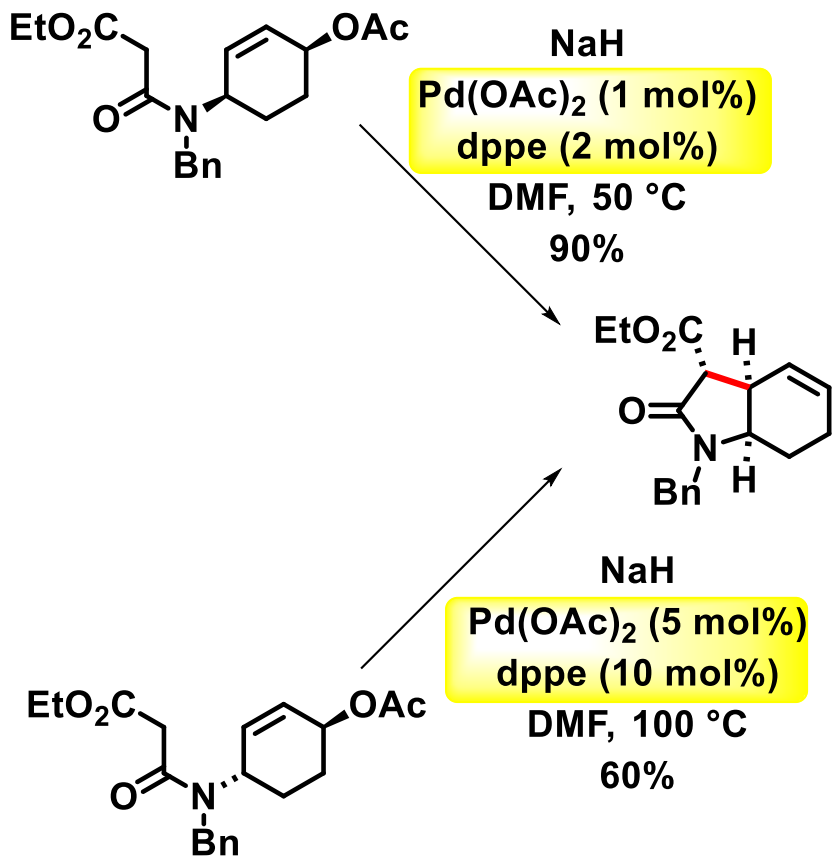
- **Changes in the mechanism**

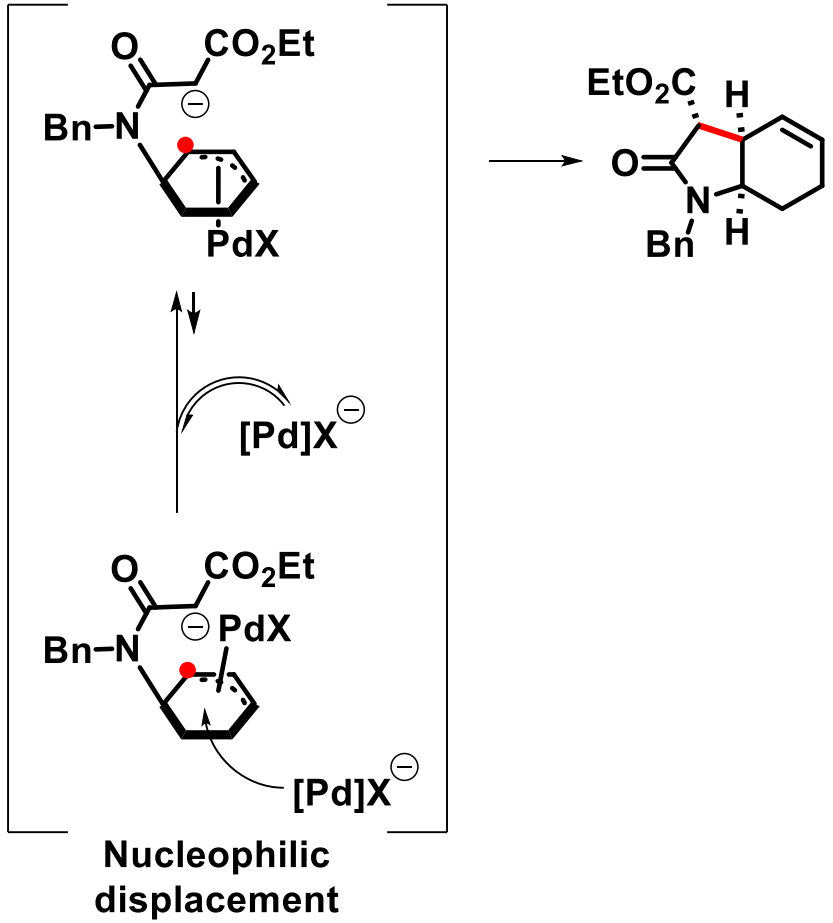


Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

- **Changes in the mechanism**



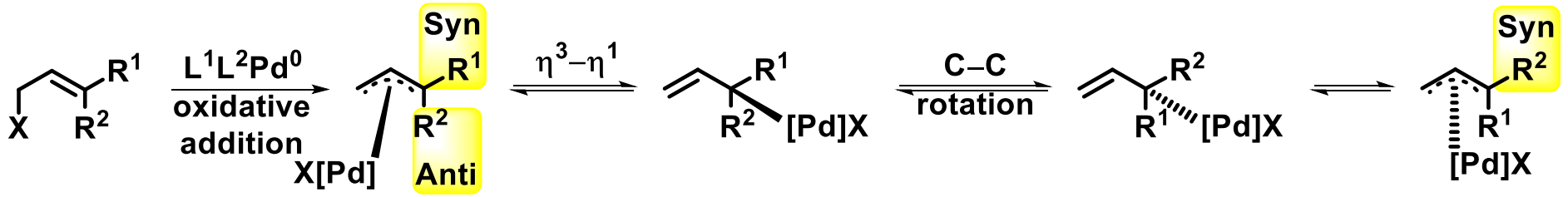


Eur. J. Org. Chem. **2004**, 2840

Tsuji-Trost Reaction

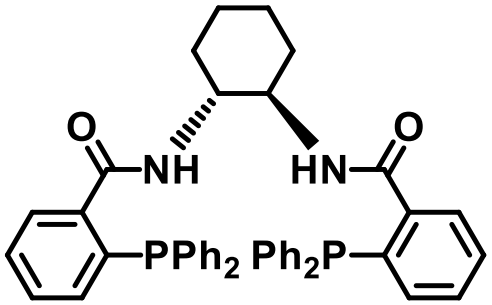
➢ Enantioselective Tsuji-Trost reaction

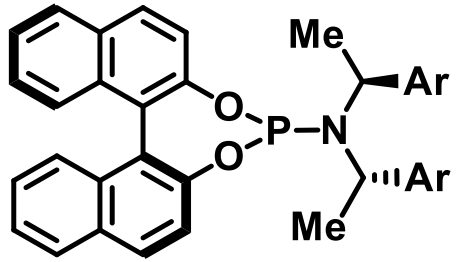
- Syn-anti Exchange and enantioselective Tsuji-Trost reaction

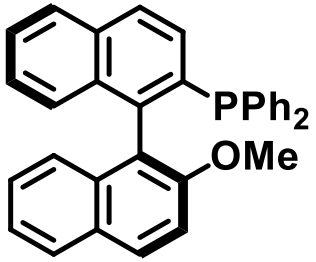


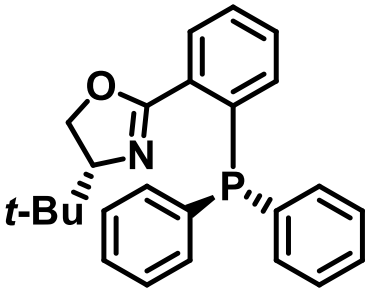
  - Oxidative addition is enantiodiscriminating step – Syn-Anti Exchange is undesirable
  - Nucleophili attack is enantiodiscriminating step – Syn-Anti Exchange is desirable

○ Typical ligands for enantioselective Tsuji-Trost reaction





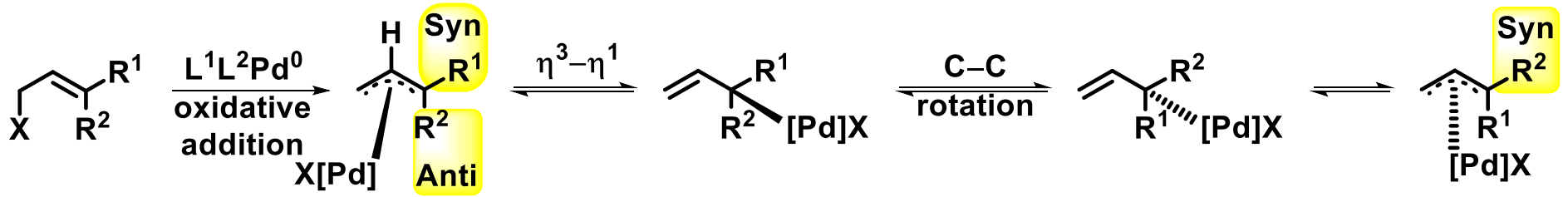




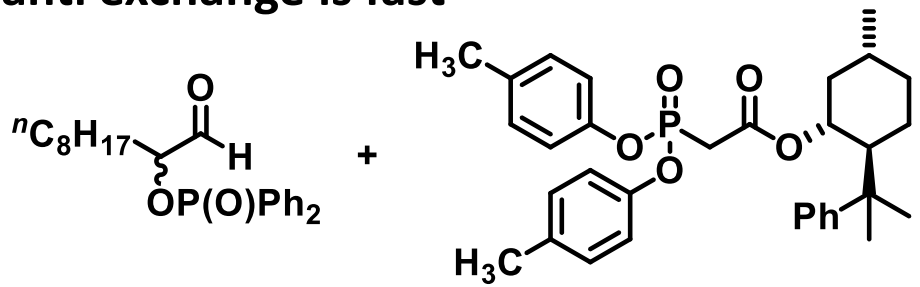
Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

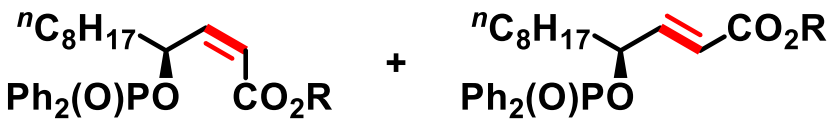
- **Syn-anti exchange and enantioselective Tsuji-Trost reaction**



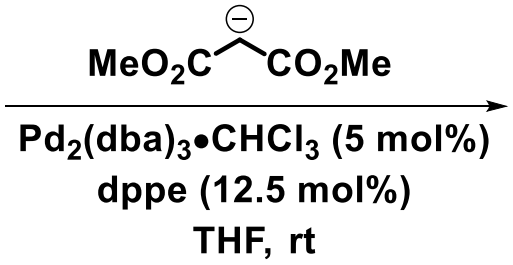
- **Syn-anti exchange is fast**

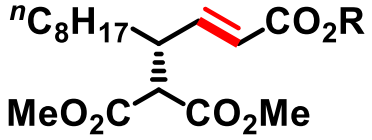


KHMDS
THF, -78 °C



E/*Z* = 46:54





77%

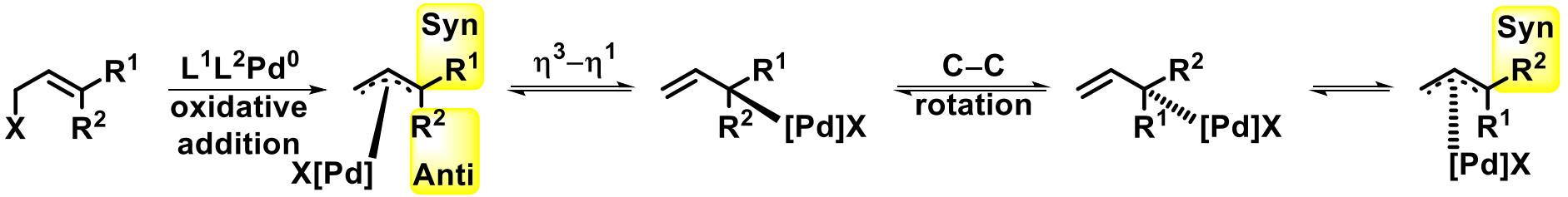
Only E alkene!!

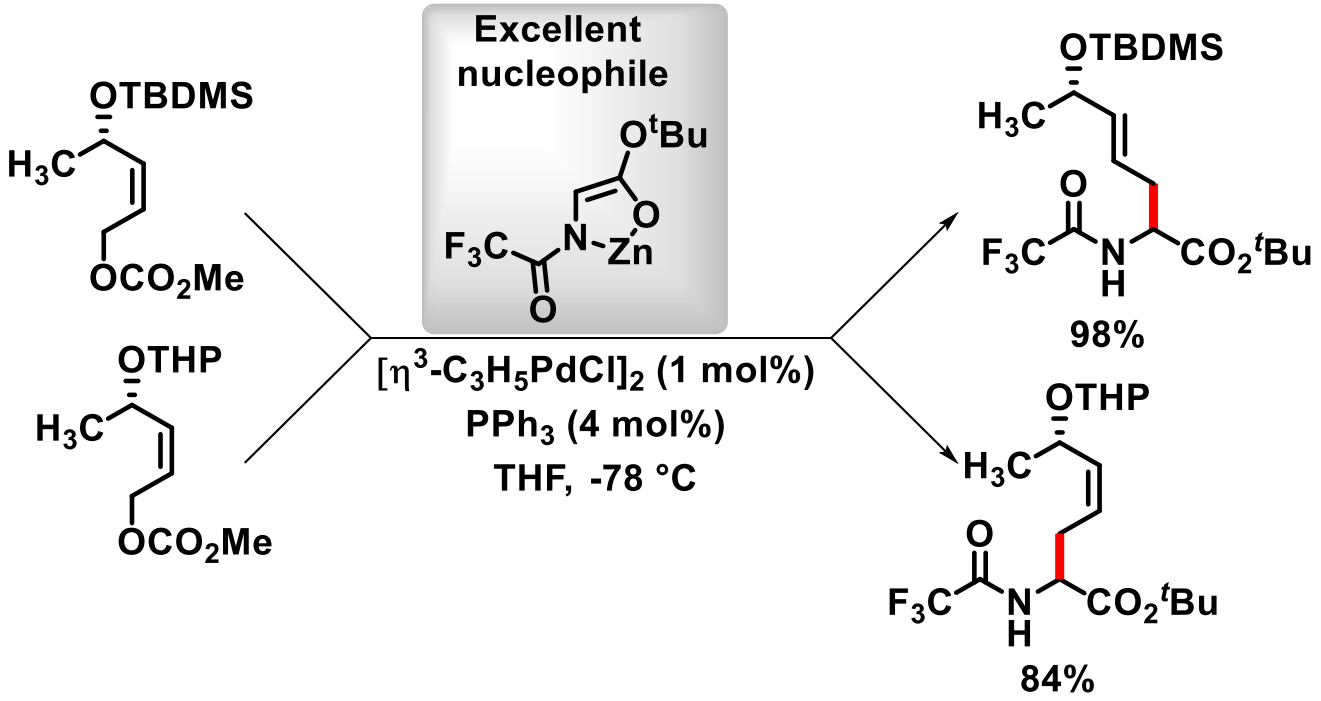
J. Am. Chem. Soc. **2001**, *123*, 9738

Tsuji-Trost Reaction

➢ Advanced Tsuji-Trost reaction

- **Syn-anti exchange and enantioselective Tsuji-Trost reaction**





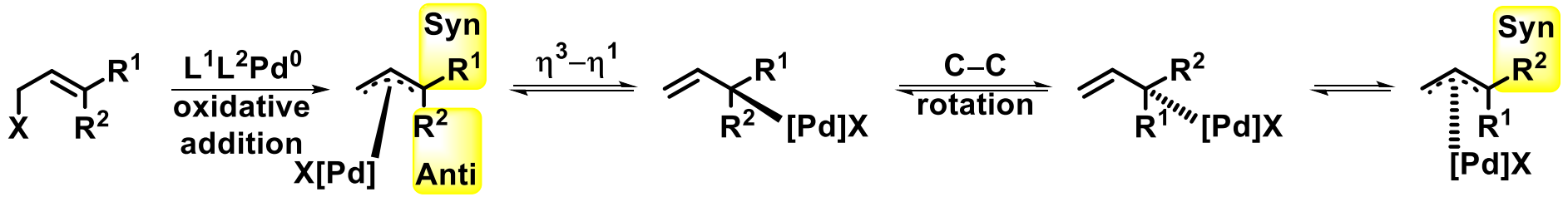
J. Org. Chem. **2006**, *71*, 8950

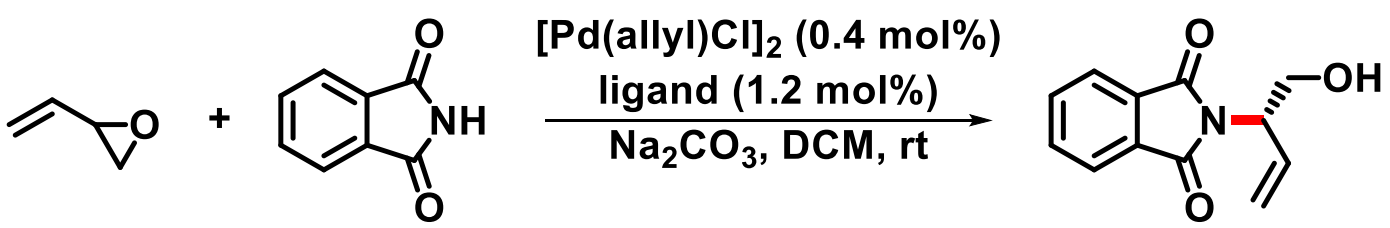
Slow Syn-Anti exchange, fast nucleophilic atack

Tsuji-Trost Reaction

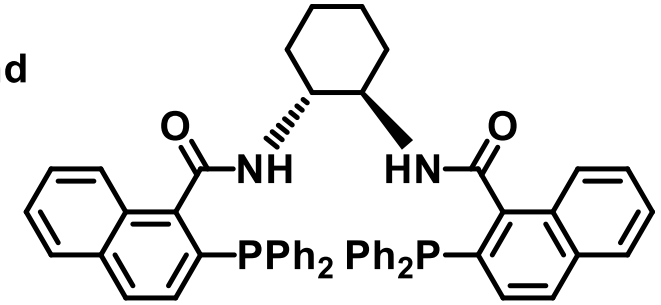
➢ Enantioselective Tsuji-Trost reaction

- **Syn-anti Exchange and enantioselective Tsuji-Trost reaction**





ligand

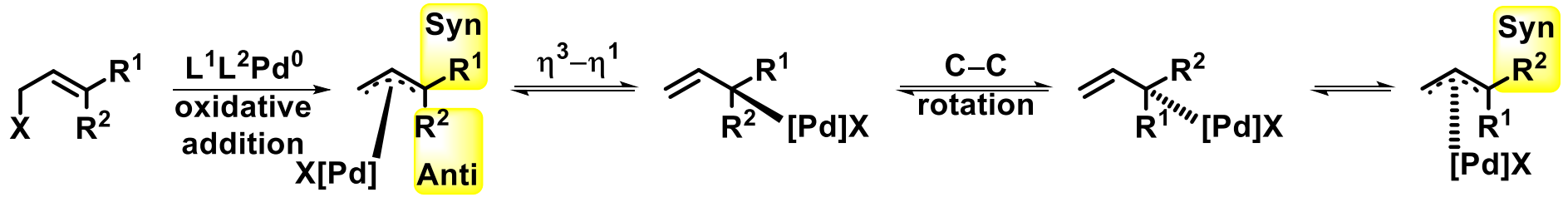


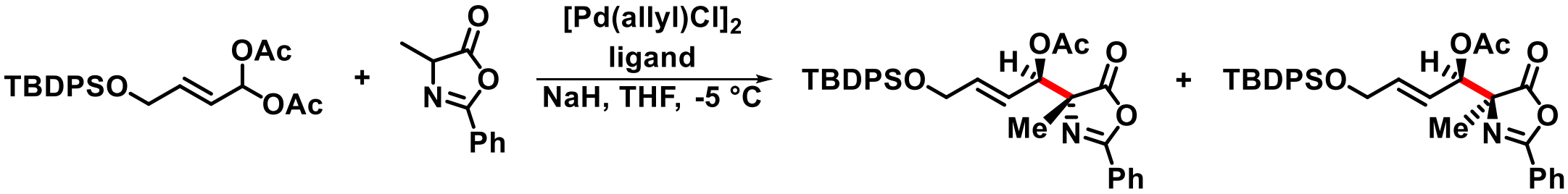
Angew. Chem. Int. Ed. **2003**, 42, 5987

Tsuji-Trost Reaction

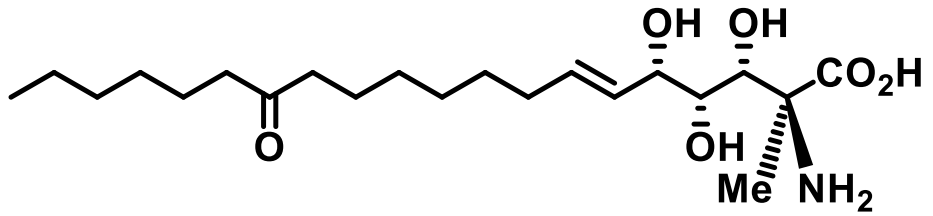
➢ Enantioselective Tsuji-Trost reaction

- **Syn-anti Exchange and enantioselective Tsuji-Trost reaction**



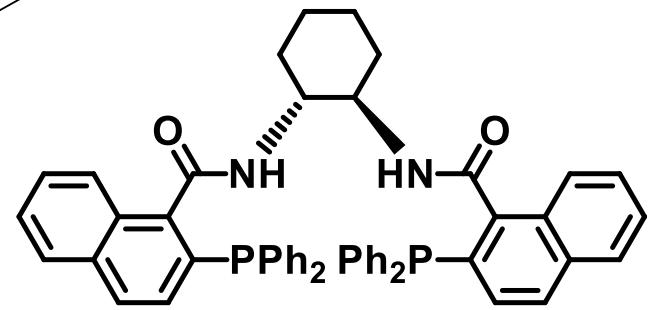


1:10.5
89% ee



Sphingofungin F

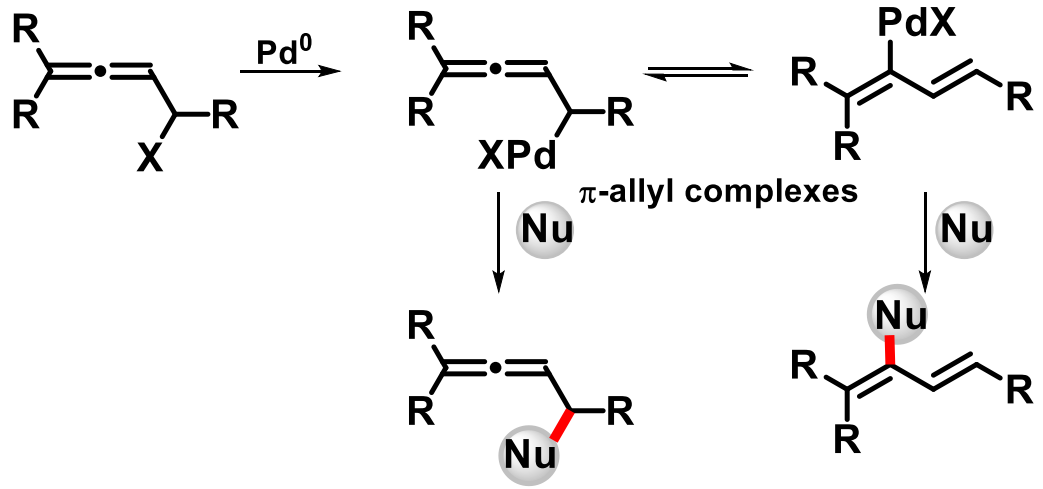
ligand

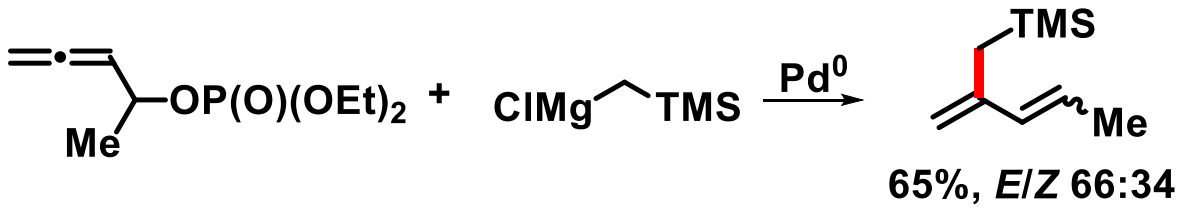


J. Am. Chem. Soc. **1998**, 120, 6818; *J. Am. Chem. Soc.* **2001**, *123*, 12191

Tsuji-Trost Reaction

➢ Allenes as a source for π–allyl intermediates



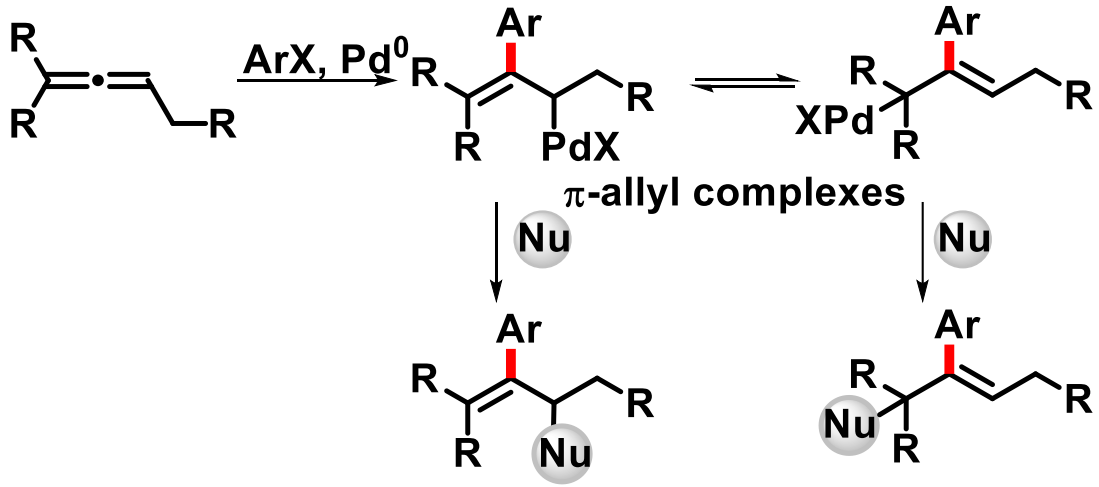


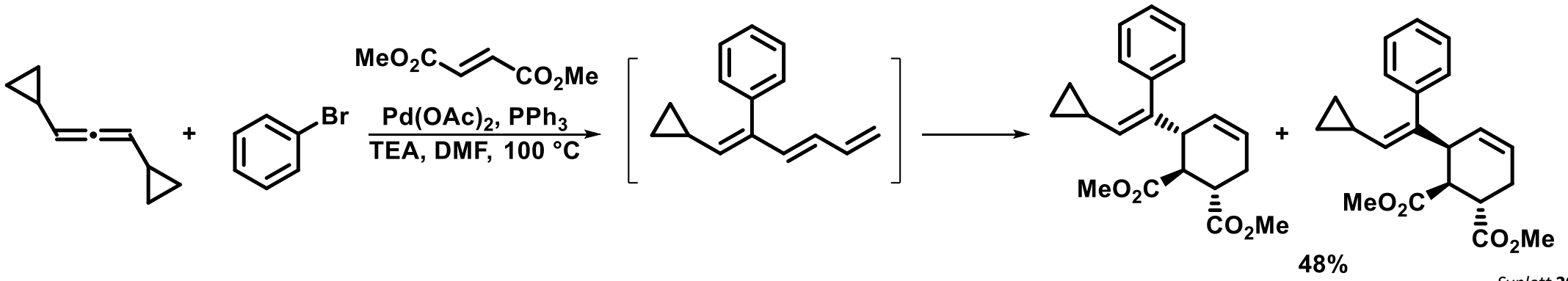
65%, *E*/*Z* 66:34

Tetrahedron **1987**, *43*, 3441

Tsuji-Trost Reaction

➢ Allenes as a source for π–allyl intermediates

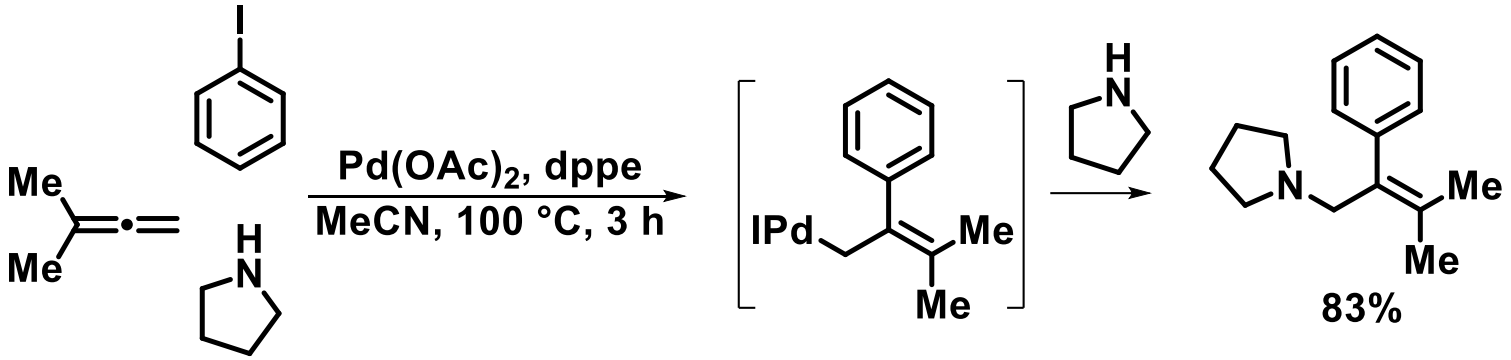




Synlett **2003**, 195

Tsuji-Trost Reaction

➢ Allenes as a source for π–allyl intermediates



Adv. Synth. Cat. **2001**, *343*, 255