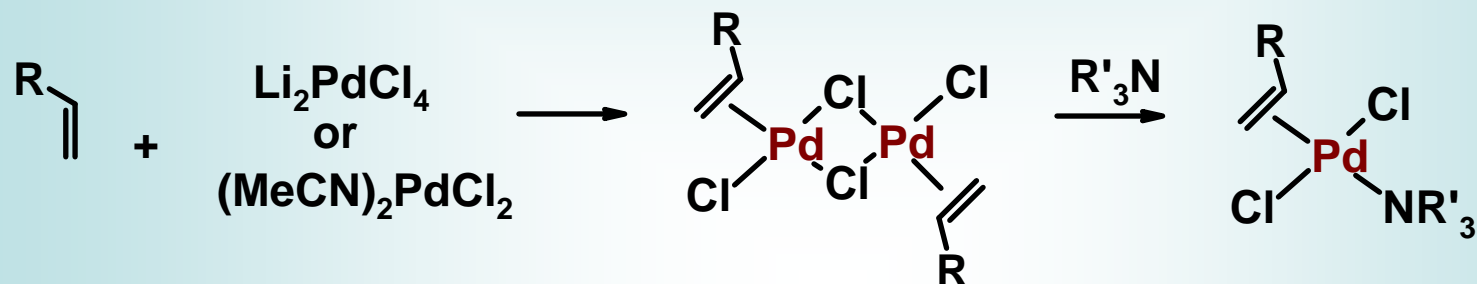


Pd^{II} Complexes of Alkenes

-probably the other major choice in alkene-TM complexes

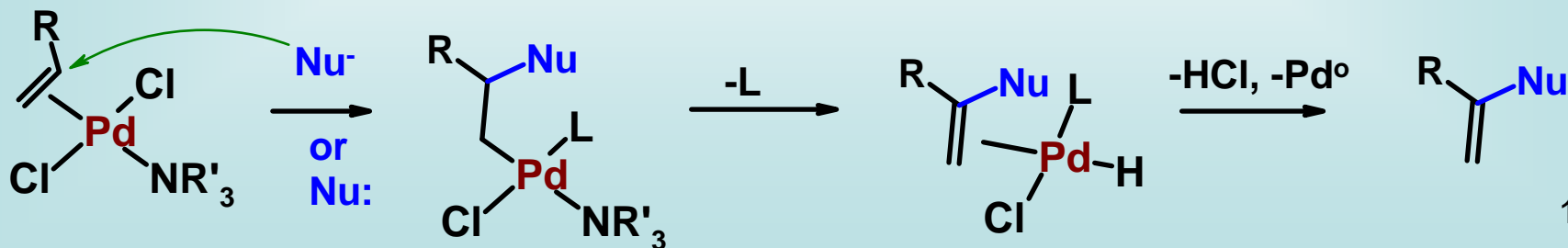
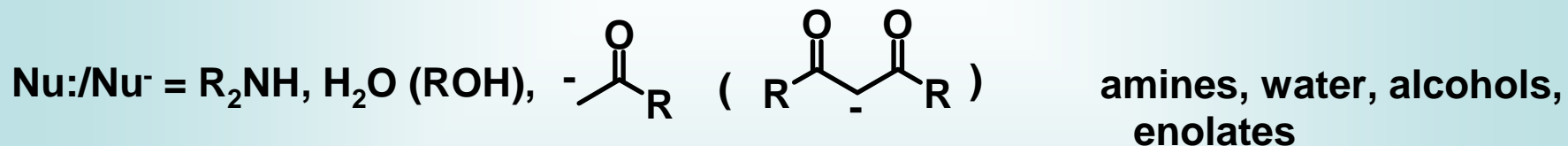
Early Chemistry

-Pd^{II} forms complexes with alkenes; an amine ligand is usually added to break up dimer and make a more reactive species



-susceptible to attack by nucleophiles on the more substituted C

-can sometimes reduce Pd off at low T, but mostly get β-H elimination



BUT.....This is stoichiometric in Pd, and PdCl₂ 1g, \$102; 25g, \$1155

see, R Hegedus p.188-201

R Handbook of Organopalladium Chemistry for Organic Synthesis V2, Ch V3

Holton, R.A. J. Am. Chem. Soc. 1985, 107, 2127 (chelating amines/sulphides)

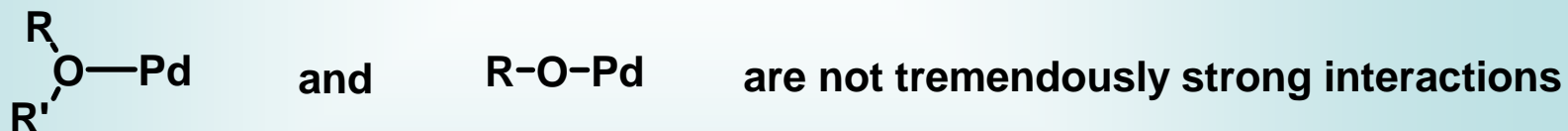
However, if one has a stoichiometric oxidant present to oxidize the Pd⁰ back to Pd^{II}, the could in principle be catalytic

- this can work: oxidant is most often O₂ or benzoquinone (BQ), or Cu^{II}

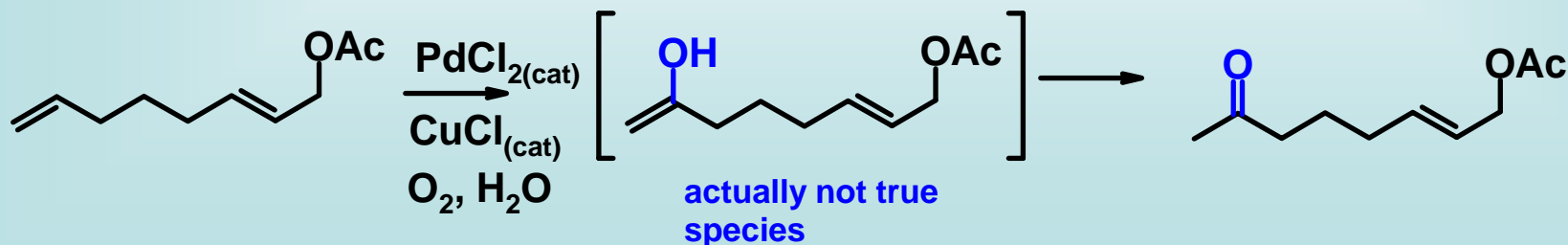
Earliest Successes

- is with oxygen based nucleophiles (H₂O, ROH)

-perhaps because oxygen nucleophiles don't displace the alkene ligand



-traditional version, with water as nucleophile, is called the Wacker process

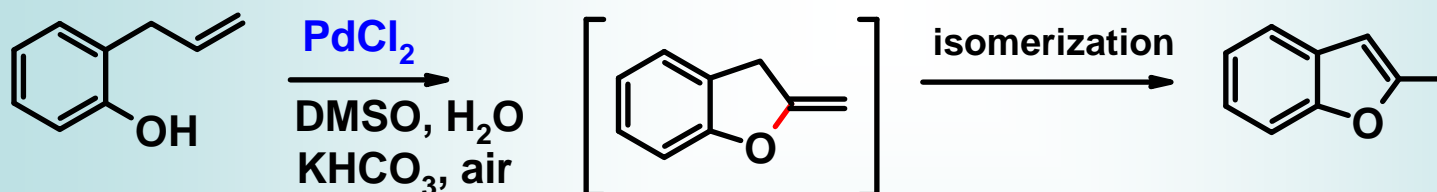


-reaction is selective for terminal alkenes; in fact intermolecular reactions for internal alkenes work poorly in most cases (*except* strong EWG substituted ones)

-Markovnikov addition - Nu: attacks most substituted side of the alkene normally
-this can be overridden by coordinating groups within the substrate

-CuCl₂ oxidizes Pd⁰ back to Pd^{II}; O₂ oxidizes Cu^I back to Cu^{II}

Alcohols and phenols can do this type of chemistry too, usually as an intramolecular addition

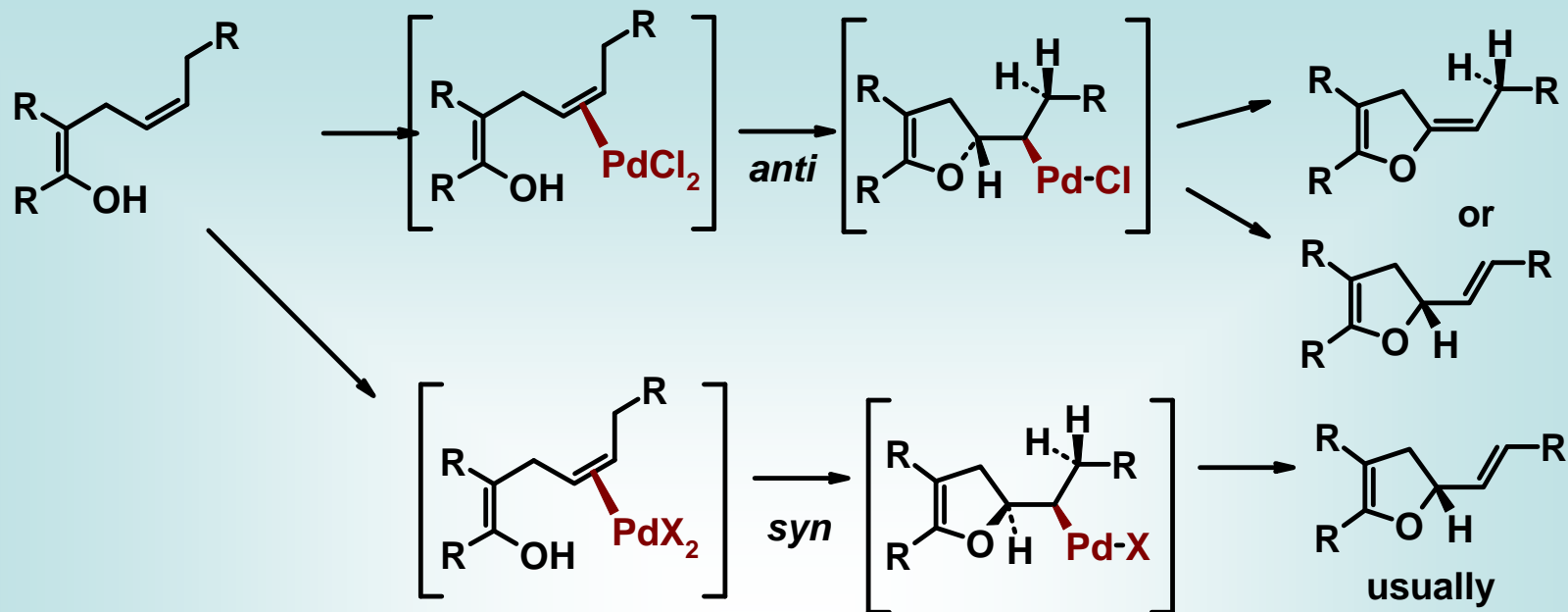


-normal tendency is to form 5- membered ring over 6- membered ring;
this tendency can be overridden in some cases

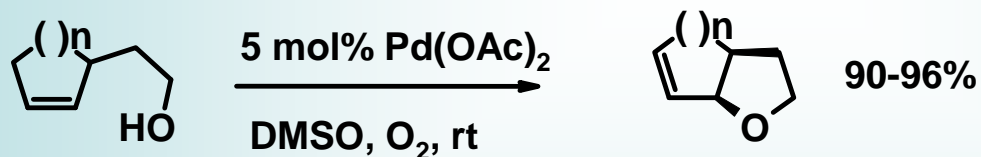
- first work was with PdCl₂ as the Pd^{II} source, but now it is often replaced with other Pd^{II} salts

-Reason - with Cl⁻ salts, attack of Nu is *anti* to Pd; whereas with Pd(OAc)₂, Pd(OCOCF₃)₂, attack is *syn* to Pd

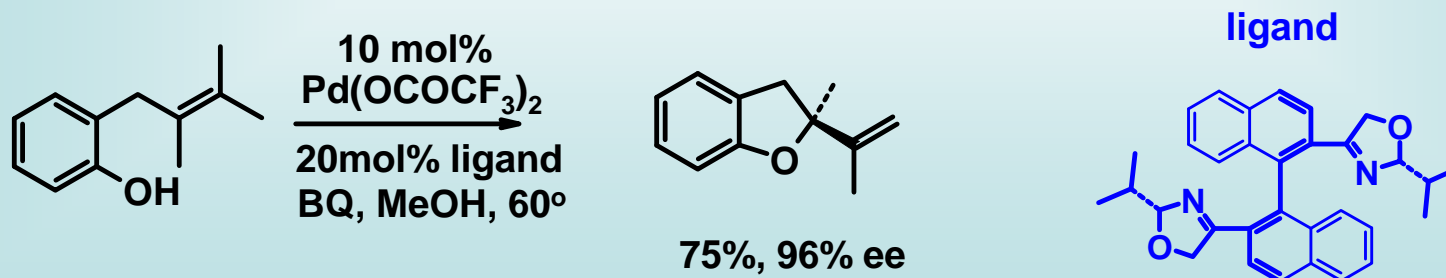
-*syn* attack allows/forces β-H elimination away from ring



Hayashi, T.; Yamasaki, K.; Mimura, M.; Uozumi, Y. *J. Am. Chem. Soc.* **2004**, *126*, 3036.



-this even allows asymmetric synthesis at the newly formed chiral centre



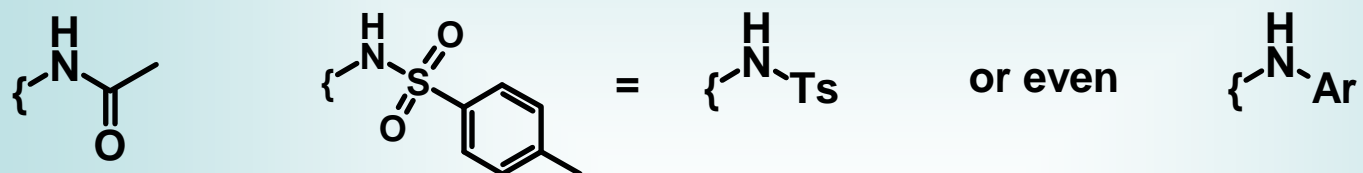
Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 5071

N Nucleophiles

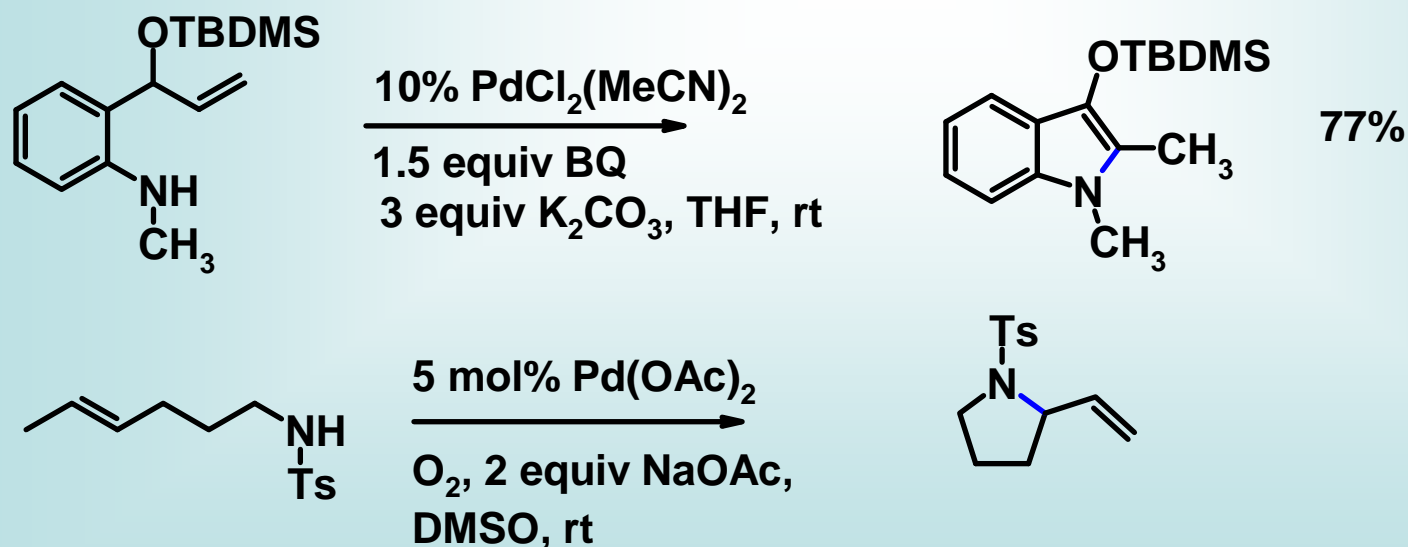
-sometimes called aza-Wacker

-problem with amine ligands - these are generally too basic/nucleophilic; tend to displace alkene as ligand

-as a result, in the vast majority of successful cases, the lone pair on N is deactivated

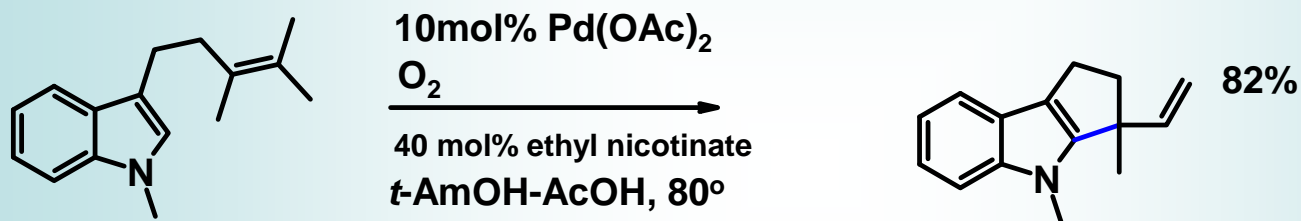
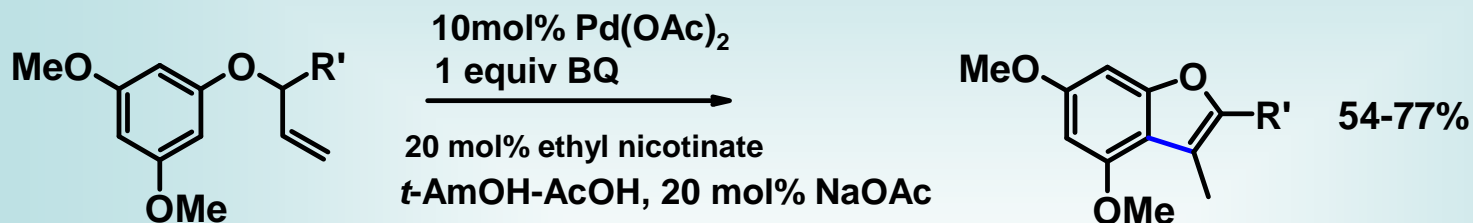


- with this restriction, this has become an increasingly important way of making heterocycles; especially possible for indole type systems

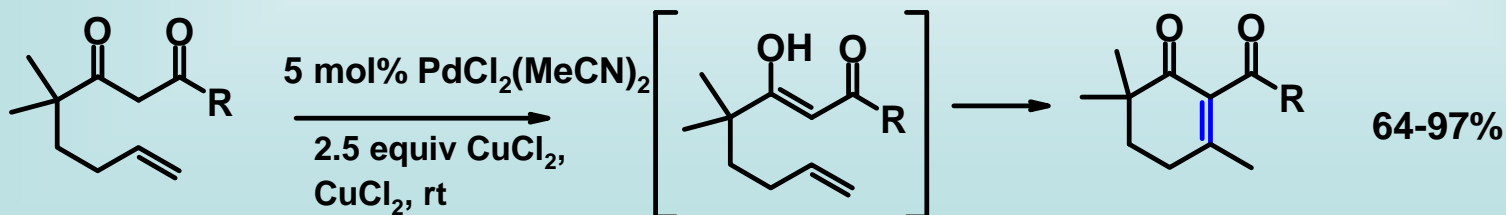
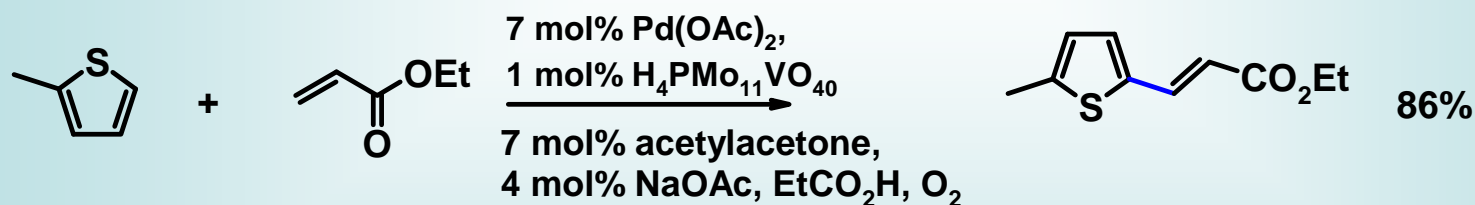


Carbon Nucleophiles

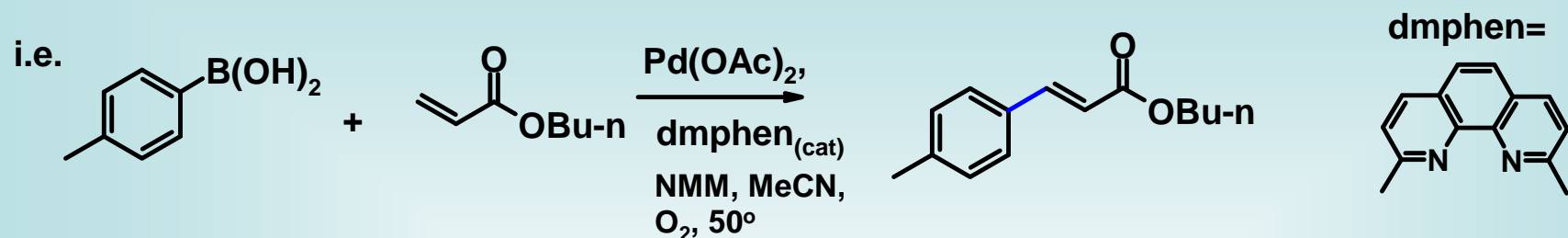
-success in these nucleophilic attack reactions has even been extended to carbon based nucleophiles such as silyl enol ethers, enolizable β -dicarbonyls, electron rich aromatics and heterocycles - there are even some intermolecular cases



Ferreira, E. M.; Stoltz, B. M.* *J. Am. Chem. Soc.* **2003**, *125*, 9578.



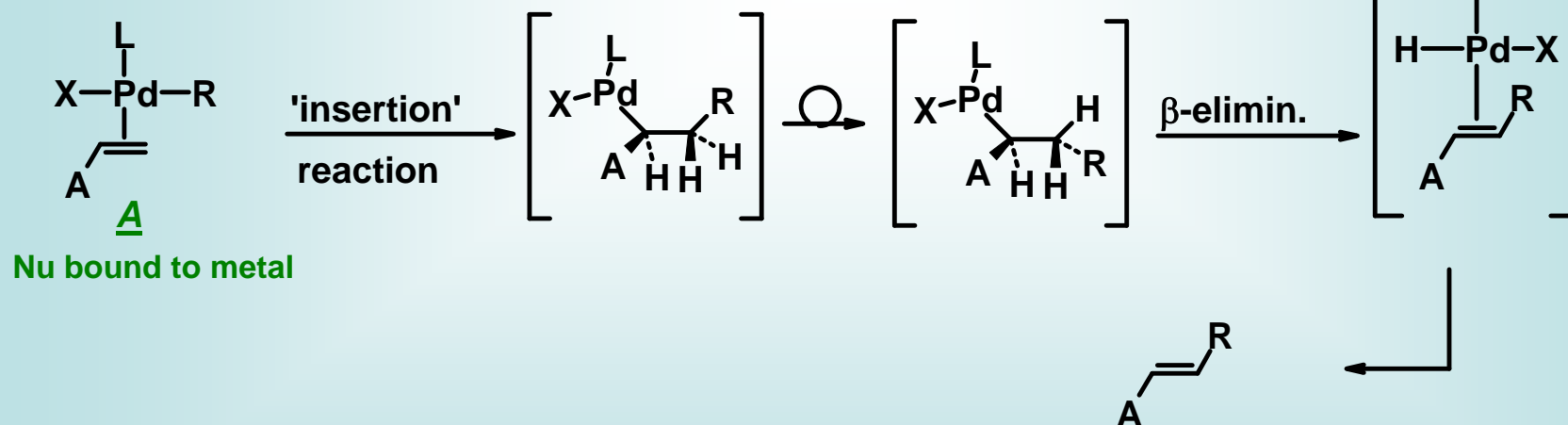
even organometallics, i.e., Ar-HgOAc (ancient history), ArB(OH)_2 , ArSnR'_3



exhaustive review [R](#) Becalli, E. M.; Broggini, G.; Martinelli, M.; Sottocomola, S. *Chem. Rev.* **2007**, *107*, 5318.

We have been hiding an important point for a bit now, though

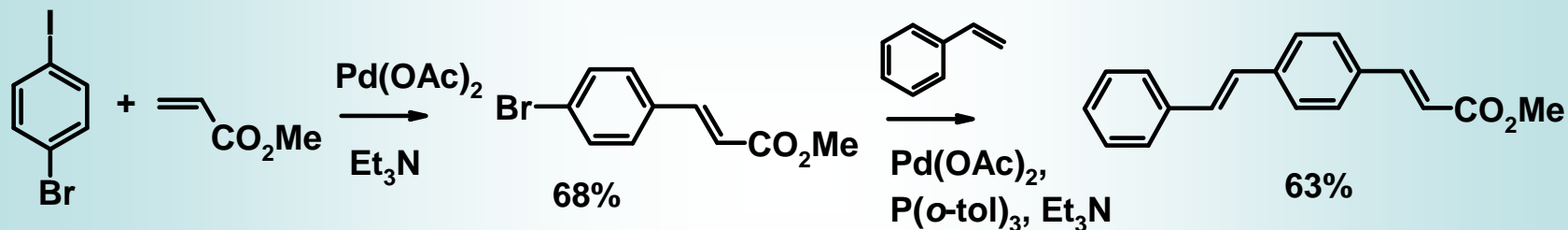
Some of these (the organometallics, *syn* attack cases) are probably going through a different intermediate than has been presented



- much more common way to get at the intermediates A
- by oxidative addition of Pd^0 to organic halides/triflates
- called Heck reaction

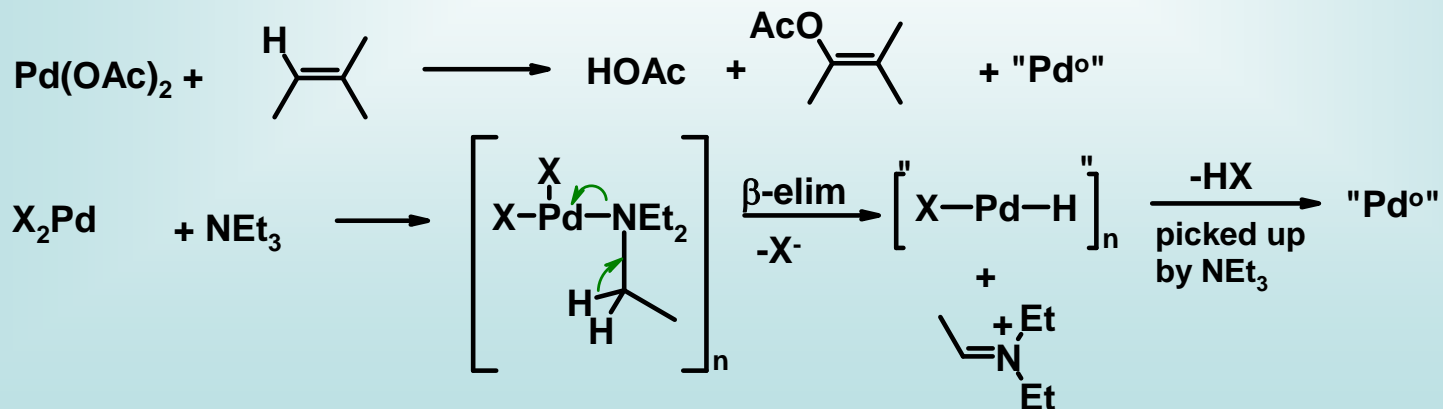
Reveiwrs - many

- R Heck, R.F. *Org. React.* **1982**, *27*, 345; *Acc. Chem. Res.* **1979**, *12*, 146.
R Larock, *Adv. Met-Org. Chem.* **1994**, *3*, 97.
R Jefery, T. *Adv. Met. Org. Chem.* **1996**, *5*, ch.4.
R Crisp, G. T. *Chem. Soc. rev.* **1998**, *27*, 427. (mechanistic detail)
R Knowles, J. P.; Whiting, A. *Org. Biomol. Chem.* **2007**, *5*, 31 mechanistic detail
R De Vries, J. G. *Dalt. Trans.* **2006**, 421 (mechanistic discussion)
R Ionso, F.; Beletskaya, I. P.; Yus, M.. *Tetrahedron* **2005**, *61*, 11771.
R Miyaura, N. *Adv. Synth. Catal.* **2004**, *346*, 1522.
R Jutand, A. *Pure Appl. Chem.* **2004**, *76*, 565 (mechanistic detail)
R Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945 (asymmetric synthesis)
R Link, J. T. *Org. React.* **2002**, *60* 157 (intramolecular rxns)



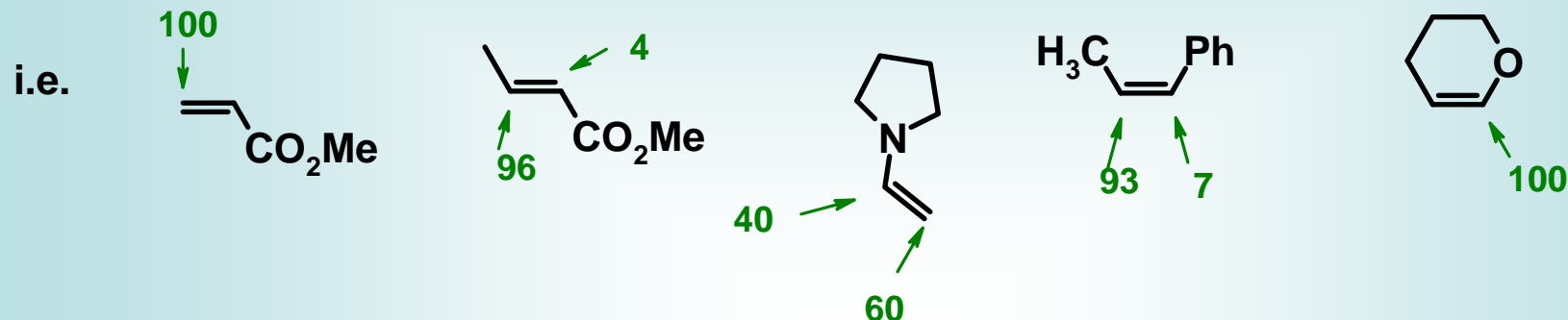
So now we need Pd⁰, but we added Pd^{II}

Not a typo; Pd^{II} complexes often used and reduced *in situ*



Regiochemistry

- somewhat different than intermolecular cases
- some tendency to go away from EWG's and towards EDG's, but sterics now (apparently) dominates
- Nu: goes 'towards' the less substituted site



Stereochemistry

- resulting alkene is usually the most thermodynamically stable one, meaning *trans*,all else being equal

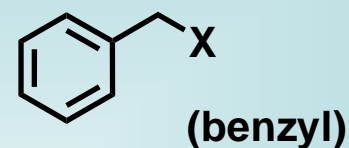
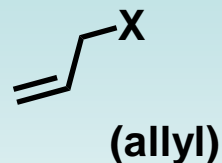
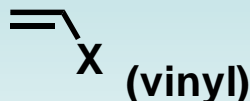
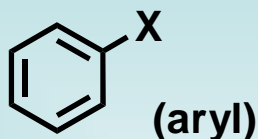
Nature of the Organic Halide

R-X (usually) can't have β -hydrogens on an sp^3 carbon atom, because of β -elimination



β -elimination takes place before any coupling can occur

Thus

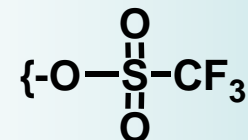


Halides

-Br is most common choice

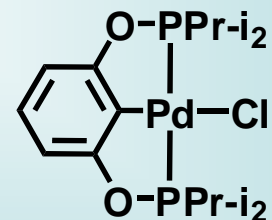
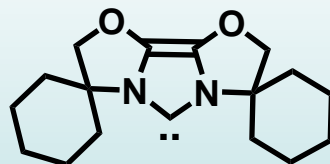
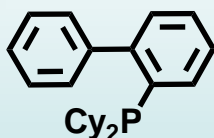
-I faster at oxidative addn, but more side rxns
(sometimes better, sometimes worse)

-triflates are excellent pseudohalides



-Cl historically sluggish, but coming along nicely with new catalysts,
including sterically hindered phosphines, carbenes as ligands, and
ortho- metallated palladacycles

i.e., P^tBu_3



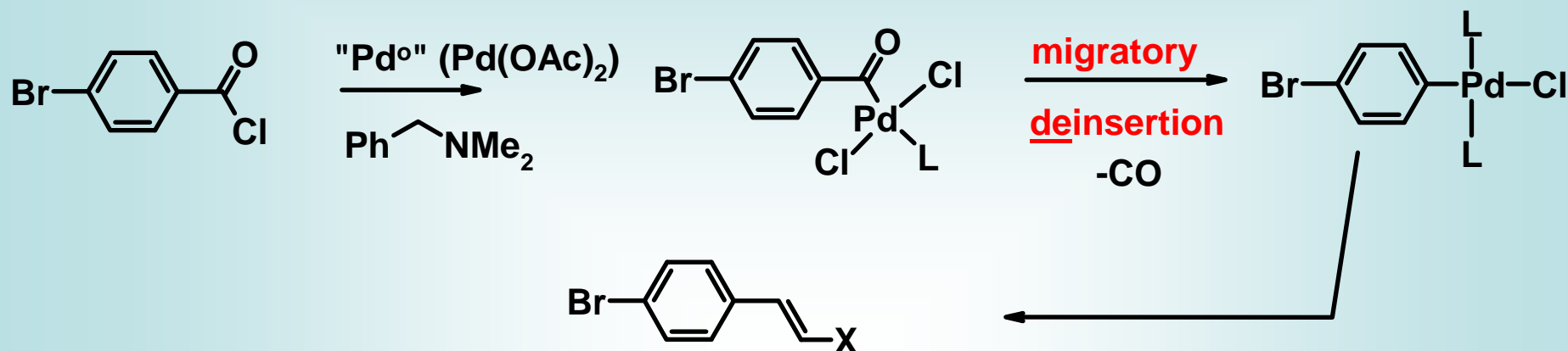
® Whitcome, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, 57, 7449.

® Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed. Engl.* **2002**, 41, 4176.

® Christmann, U.; Vilar, R.* *Angew. Chem. Int. Ed.* **2005**, 44, 366

A cute but increasingly irrelevant variation - acid chlorides

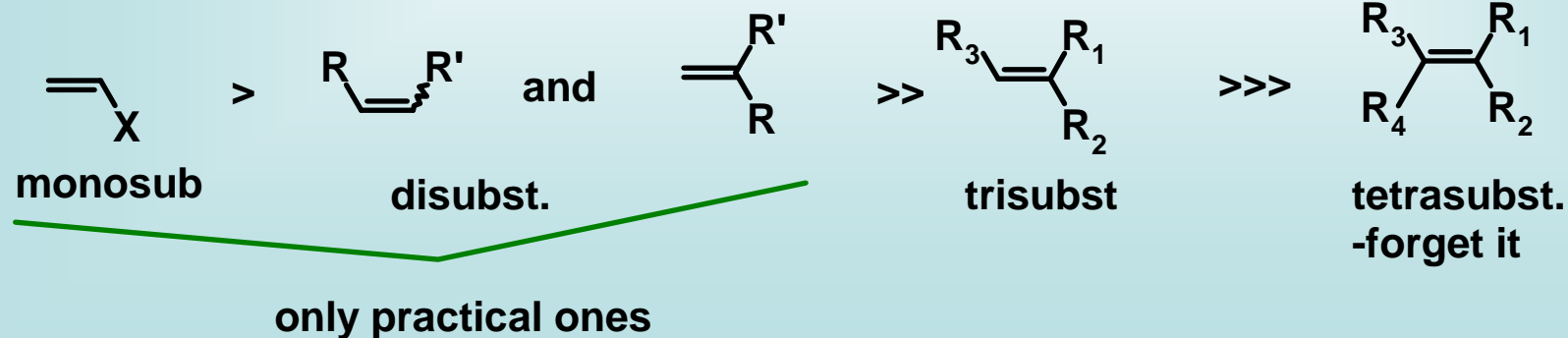
-aryl chlorides are very reactive to oxidative addition, and may be accessible when the halides are not



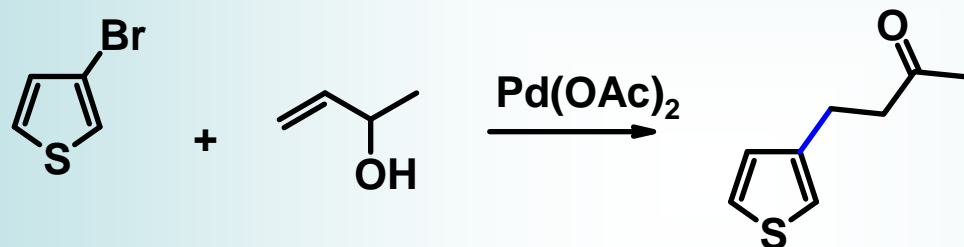
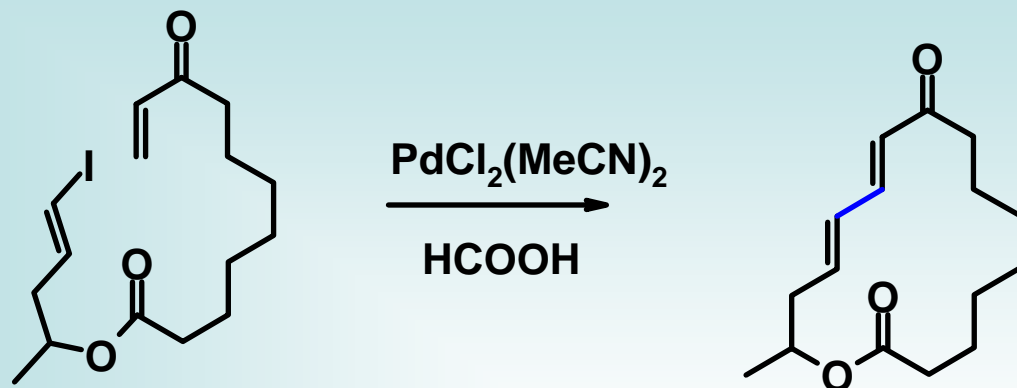
-can occur under very mild conds, in some cases - being made obsolete by improvements to aryl chloride Heck reactions

Spenser, A. *J. Organomet. Chem.* **1983**, 247, 113; **1984**, 265, 273.
 Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287.
Tetrahedron Lett. **1985**, 26 2667.

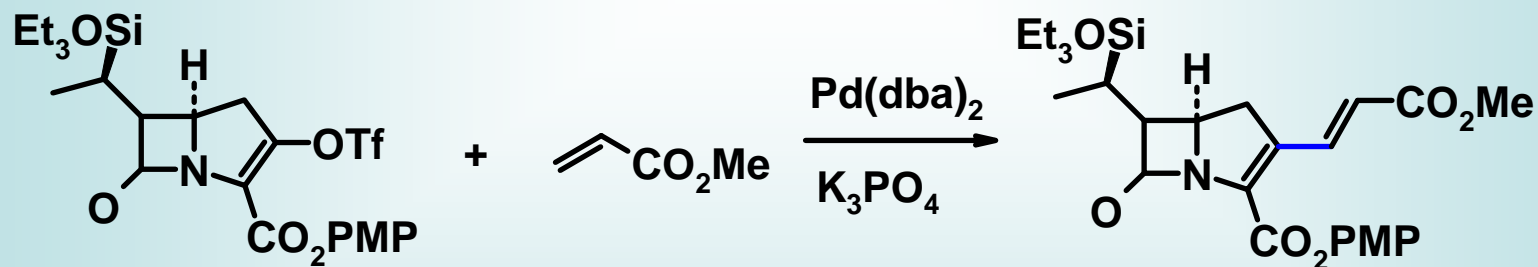
The Alkene



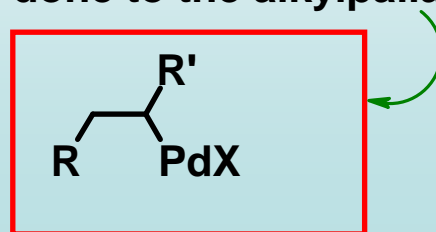
- ligands generally stabilize palladium intermediates, but aren't always added
- inorganic base is often used (instead of amine) to consume H-X



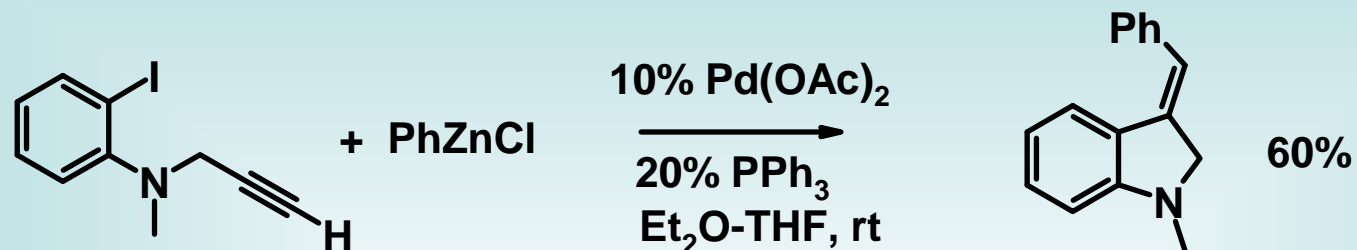
Note what happens to β -elimination process



In some cases, other things can be done to the alkylpalladium

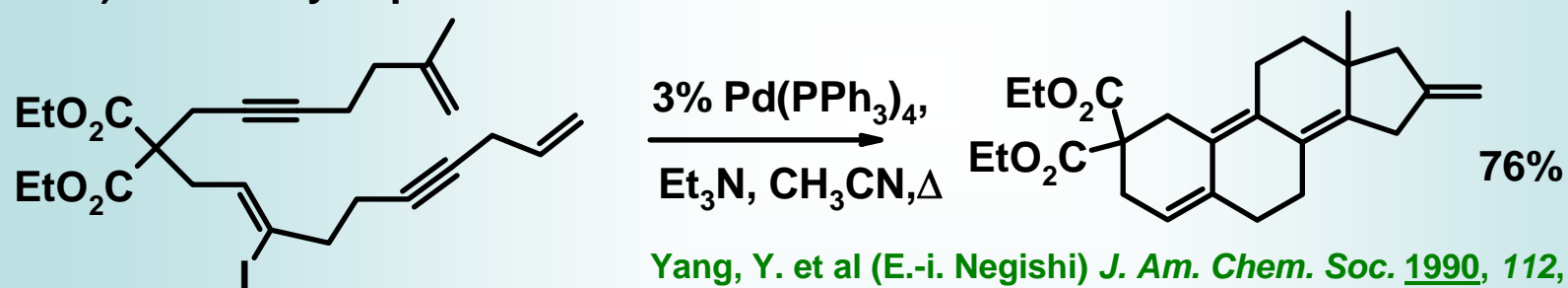


a) Trap with organometallics



Grigg, R. et al *Tetrahedron Lett.* 1990, 31, 6573 & refs therein

b) Further cyclopalladation



Yang, Y. et al (E.-i. Negishi) *J. Am. Chem. Soc.* 1990, 112, 8590.

For still more reviews, see...

R Handbook of Organopalladium Chemistry for Organic Synthesis V1, Ch IV 2.4-2.6

R Naso, F.; Marchese, G., in The Chemistry of Halides, Pseudo Halides, and Azides; Patai, S; Rappoport, Z. eds Ch. 26, Wiley 1983,

R Green, J. R. in The Chemistry of Halides, Pseudo Halides, and Azides, Supplement D2, Ch 25, Wiley 1995

R Shibasaki, M. Soden, C. D. Kojima, A. *Tetrahedron* 1997, 53, 7371

R Balme, G. Bouyssi, D.; Lomberget, T. Monteiri, N. *Synthesis* 2003, 2115