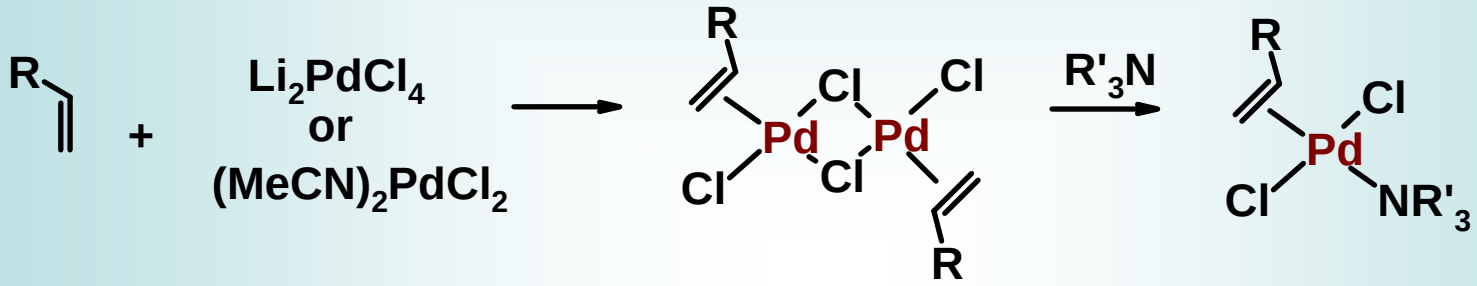
Pd^{II} Complexes of Alkenes

-probably the other major choice in alkene-TM complexes

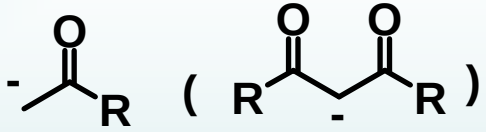
Early Chemistry

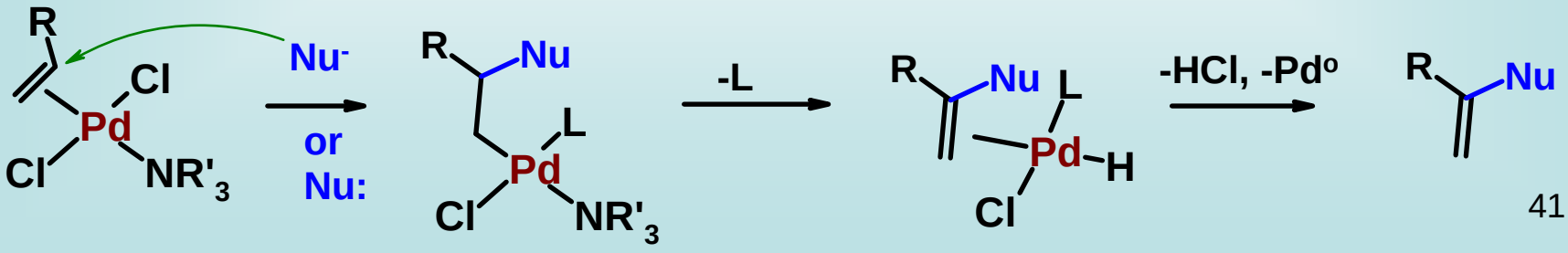
-Pd^{II} forms comlexes with alkenes; an amine ligand is usually added to break up dimer and make a more reactive species



-susceptible to attack by nucleophiles on the more substituted C

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

$Nu:/Nu^-$ = R_2NH, H_2O (ROH),  amines, water, alcohols, enolates



BUT.....This is stoichiometric in Pd, and $PdCl_2$ 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)

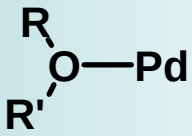
However, if one has a stoichiometric oxidant present to oxidize the Pd^o back to Pd^{II}, the could in principle be catalytic

- this can work: oxidant is most often O_2 or benzoquinone (BQ), or Cu^{II}

Earliest Successes

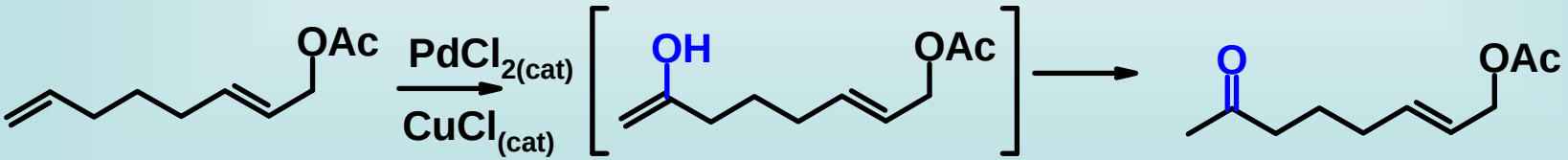
- is with oxygen based nucleophiles (H_2O, ROH)

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



and **R–O–Pd** **are not tremendously strong interactions**

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



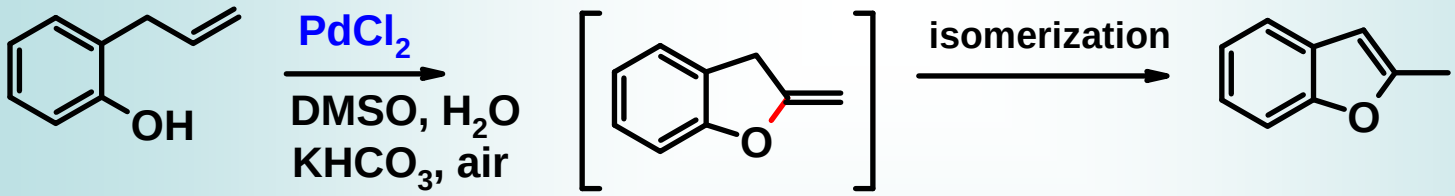
actually not true species

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

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

-$CuCl_2$ oxidizes Pd^o back to Pd^{II}; O_2 oxidizes Cu^I back to Cu^{II}

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

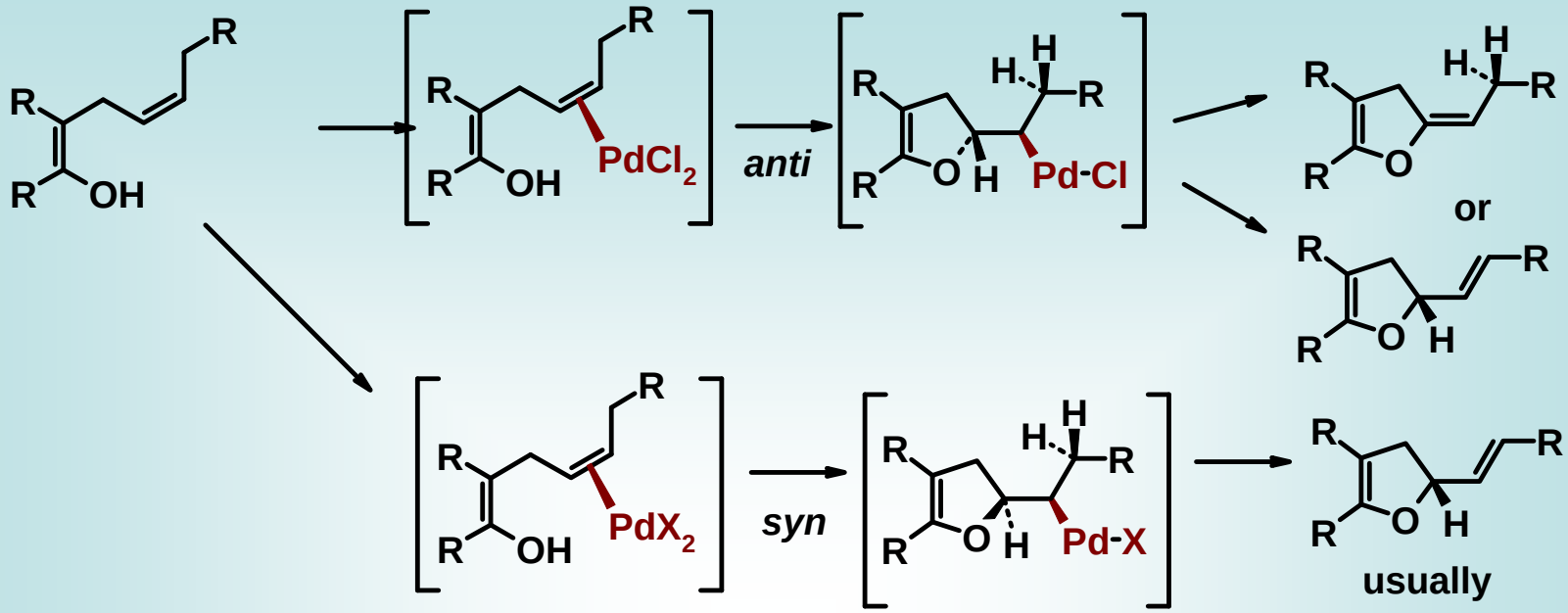


-normal tendency is to form 5- membered ring over 6- membered ring;
this tendency can be overriden in some cases

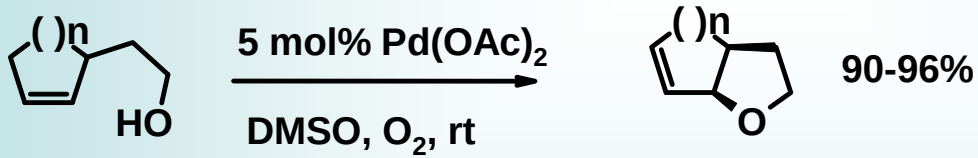
- first work was with $PdCl_2$ as the Pd^{II} source, but now it is often replaced with other Pd^{II} salts

-Reason - with Cl^- salts, attack of Nu is *anti* to Pd; whereas with $Pd(OAc)_2$, $Pd(OCOCF_2)_2$, attack is *syn* to Pd

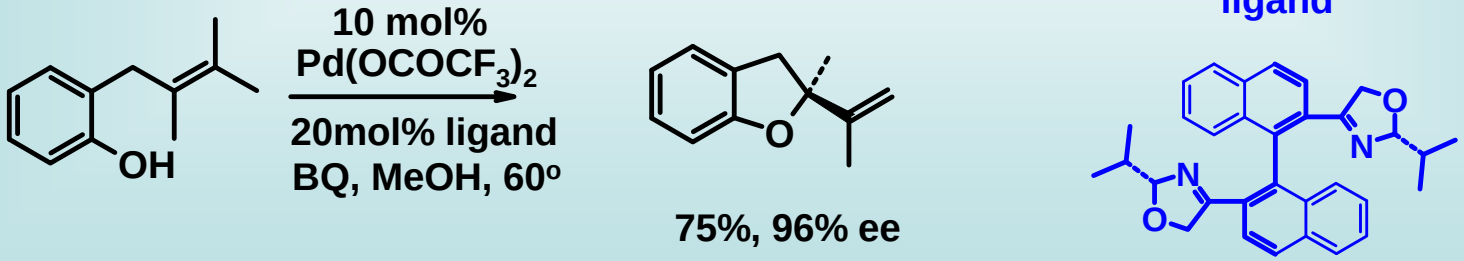
-*syn* attack allows/forces β-H elimination <u>away</u> from ring



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

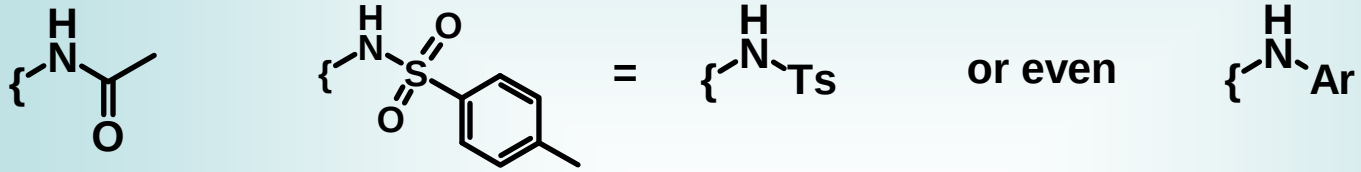


Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* 1998, *63*, 5071

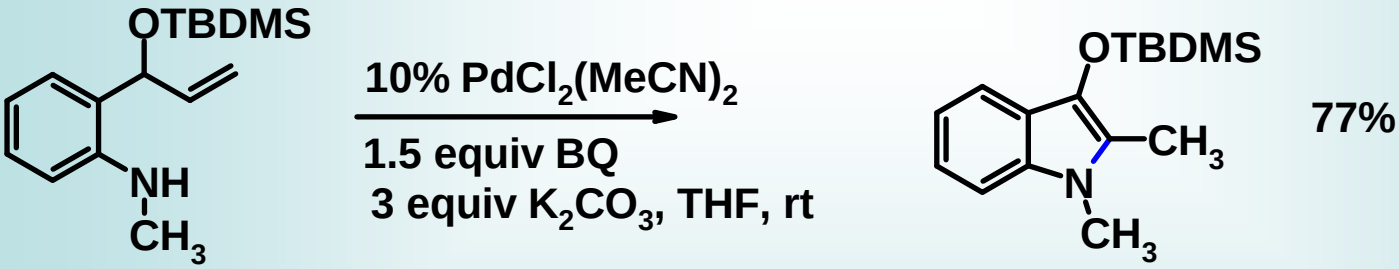
N Nucleophiles **-sometimes called aza-Wacker**

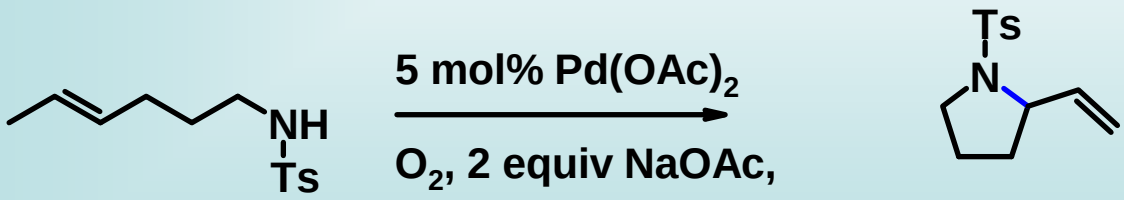
-problem with amine ligands - these are generally too basic/nucleophilic; tend to displace alkene as ligand

-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

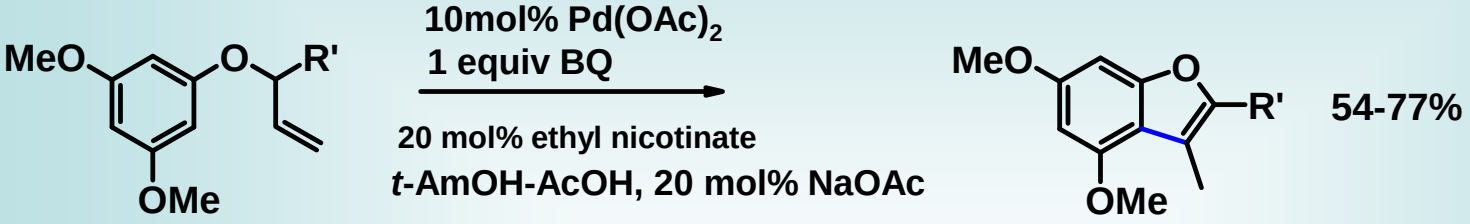


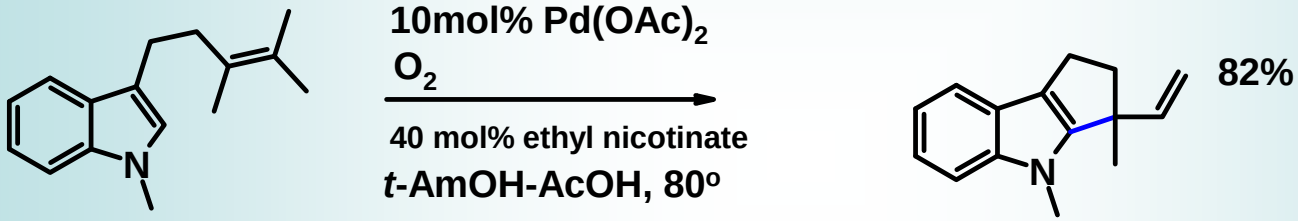


R Minatti, A.; Munoz, K. *Chem. Soc. Rev.* 2007, *36*, 1142.

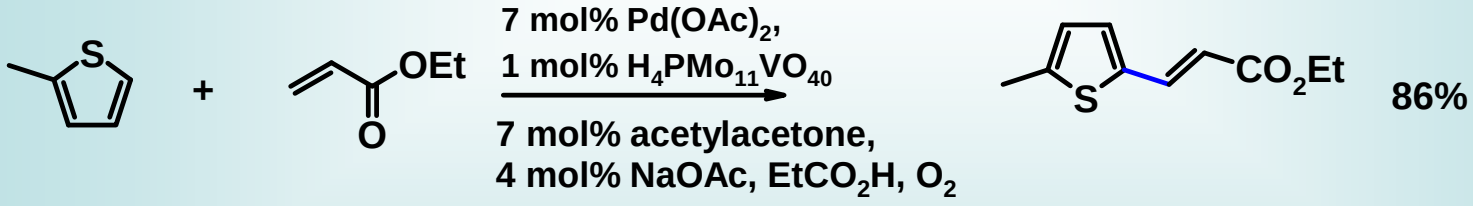
Carbon Nucleophiles

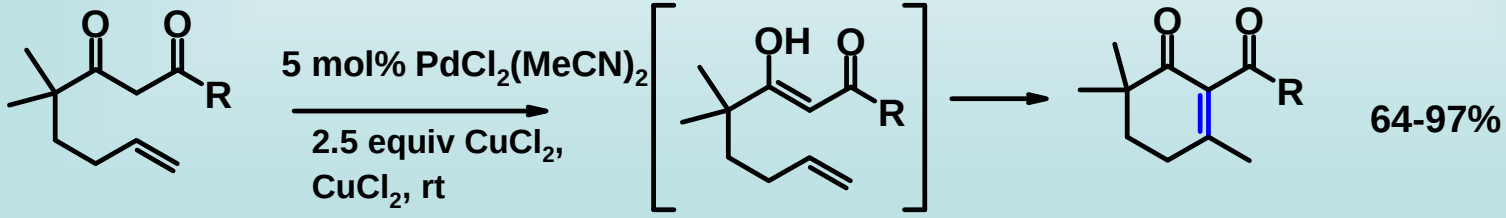
-success in these nucleophilic attack reactions has even been extended to carbon based nucleophiles such as silyl enol ethers, enolizable β-dicarbonyls, electron rich aromatics and heterocycles - there are even some intermolecular cases



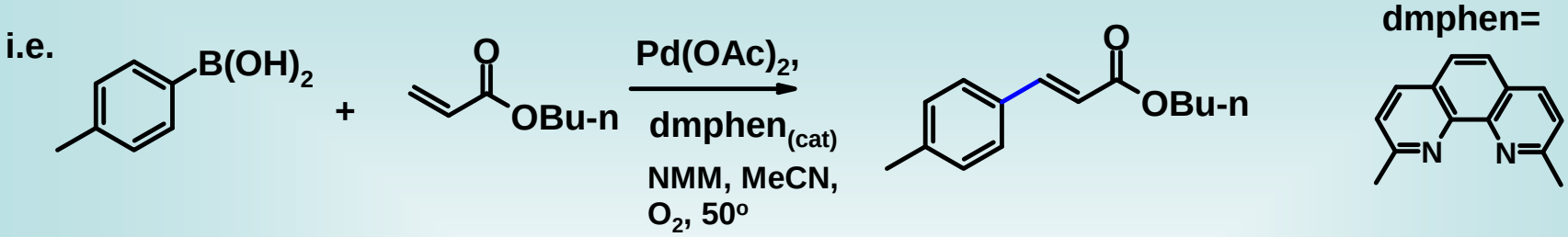


Ferreira, E. M.; Stoltz, B. M.* *J. Am. Chem. Soc.* 2003, *125*, 9578.





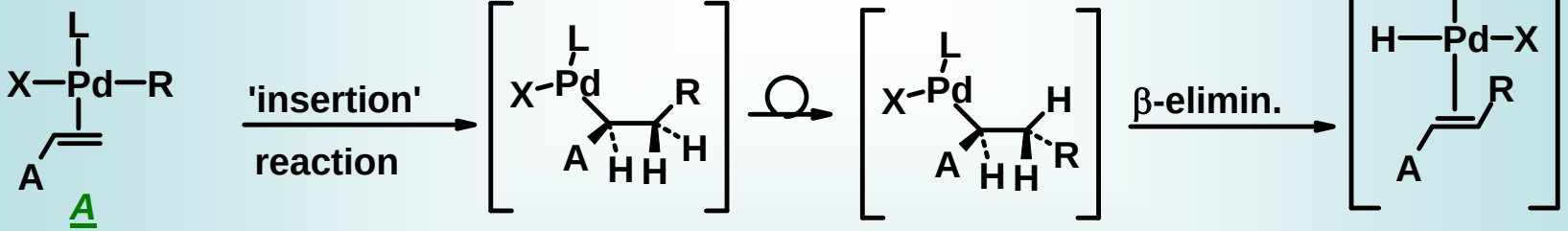
even organometallics, i.e., Ar-HgOAc (ancient history), $ArB(OH)_2$, $ArSnR'_3$



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

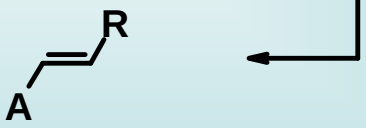
We have been hiding an important point for a bit now, though

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



A

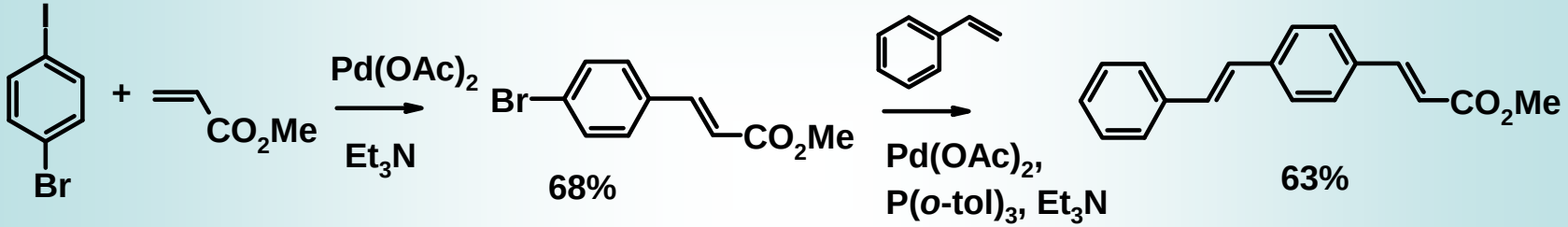
Nu bound to metal



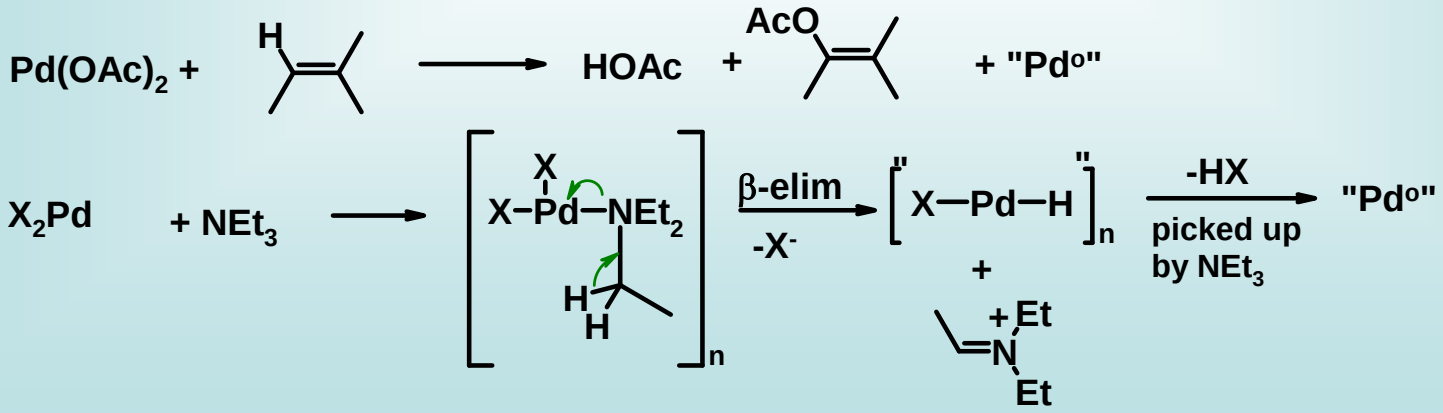
-much more common way to get at the intermediates ***A***
-by oxidative addition of Pd^o to organic halides/triflates
-called Heck reaction

Reveiws - 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. (mechansitic 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)



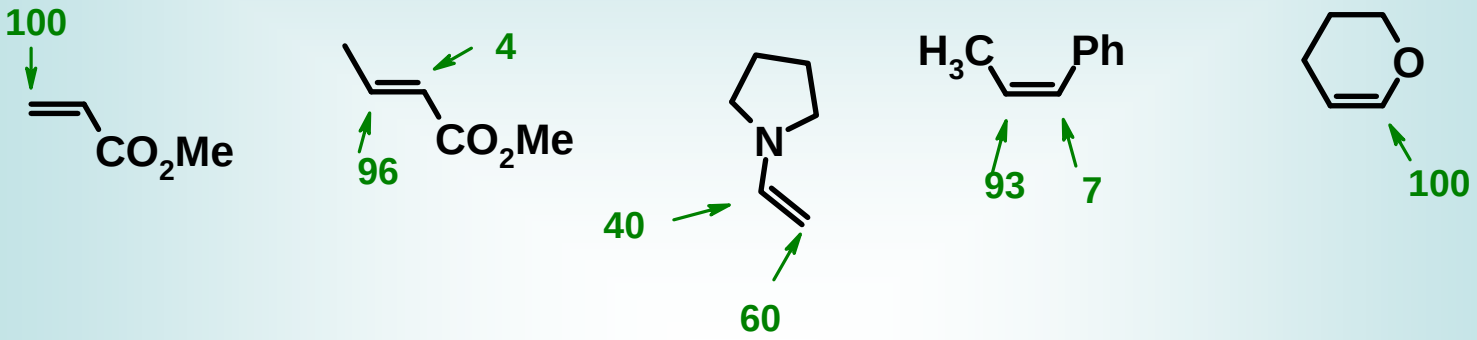
So now we need Pd^{o}, but we added Pd^{II}
Not a typo; Pd^{II} complexes often used and reduced *in situ*



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

i.e.

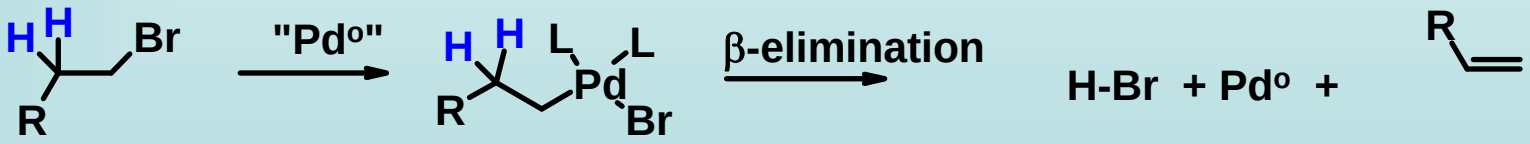


Stereochemistry

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

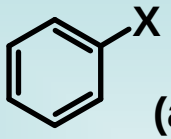
Nature of the Organic Halide

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

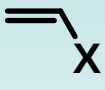


β-elimination takes place <u>before</u> any coupling can occur

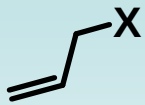
Thus



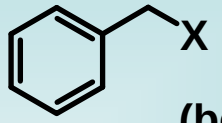
(aryl)



(vinyl)



(allyl)



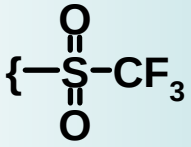
(benzyl)

Halides

-Br is most common choice

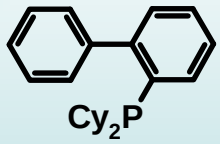
-I faster at oxidative addn, but more side rxns (sometimes better, sometimes worse)

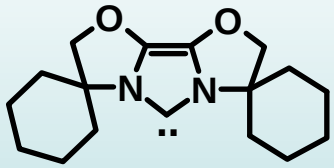
-triflates are excellent pseudohalides

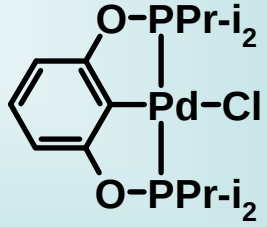


-Cl historically sluggish, but coming along nicely with new catalysts, including sterically hindered phosphines, carbenes as ligands, and ortho- metallated palladacycles

i.e., P^tBu_3



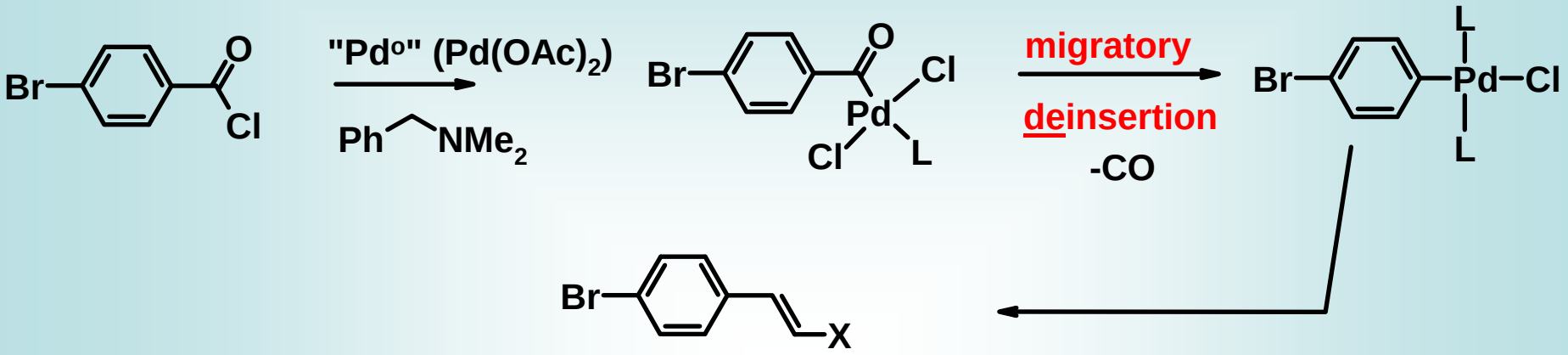




R Whitcome, N. J.; Hii, K. K.; Gibson, S. E. T*etrahedron* 2001, *57*, 7449.
R Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed. Engl.* 2002, *41*, 4176.
R Christmann, U.; Vilar, R.* *Angew. Chem. Int. Ed.* 2005, *44*, 366

A cute but increasingly irrelevant variation - acid chlorides

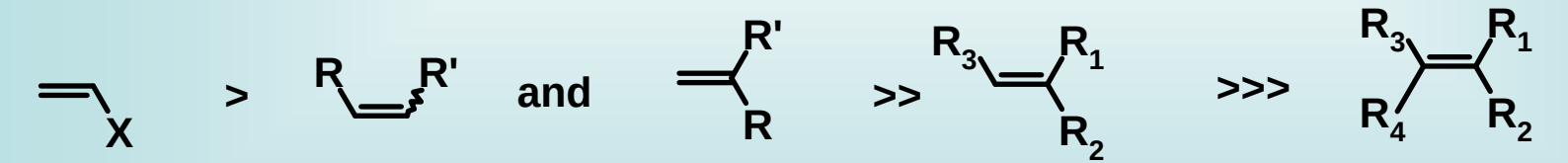
-aryl chlorides are very reactive to oxidative addition, and may be accessibe when the halides are not



-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.

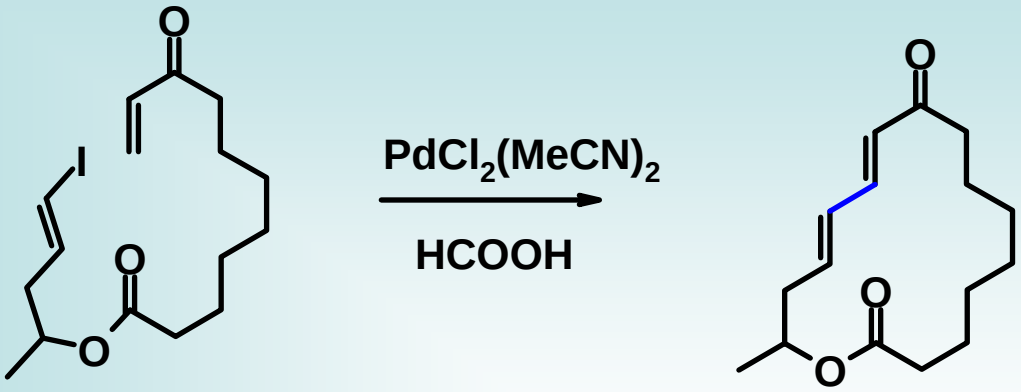
The Alkene

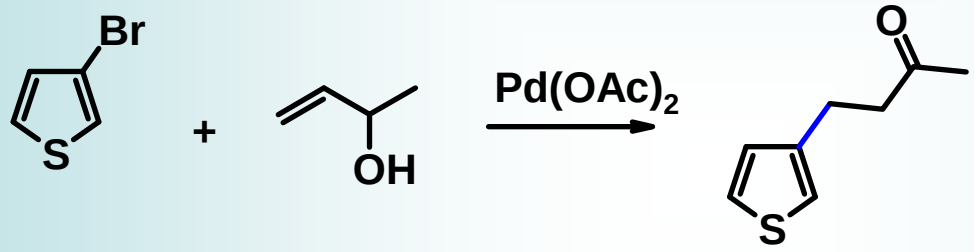


monosub **disubst.** **trisubst** **tetrasubst. -forget it**

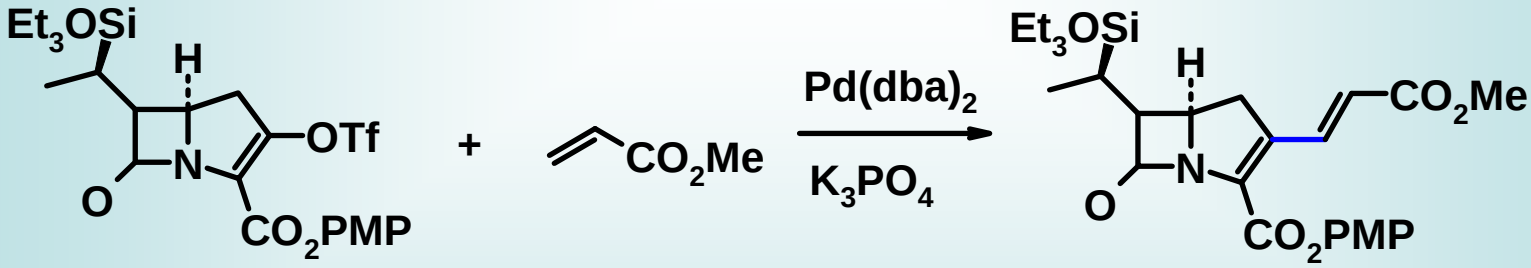
only practical ones

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

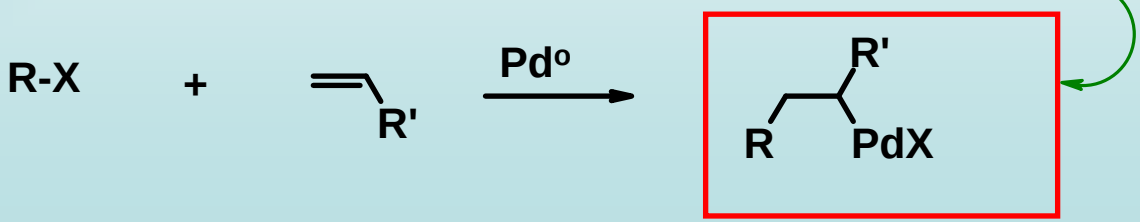




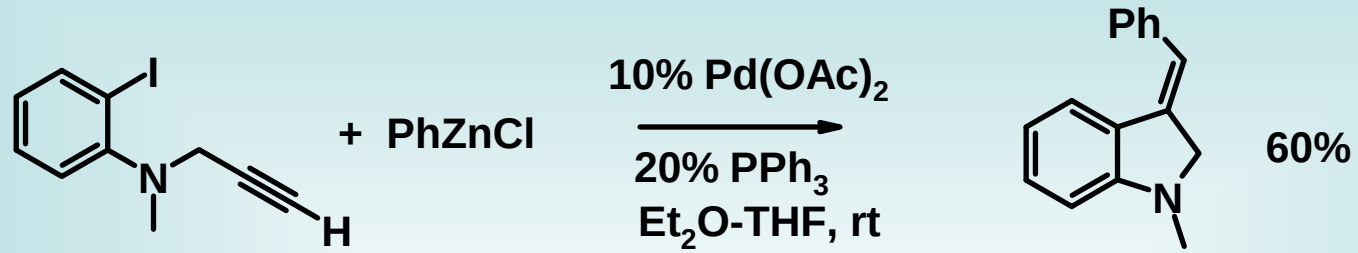
Note what happens to β-elimination process



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

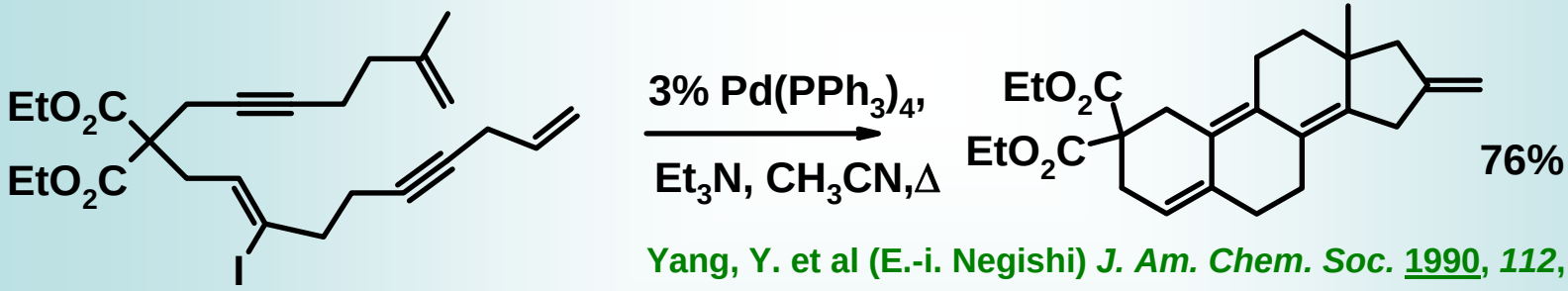


a) Trap with organometallics



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 Organopalldium 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

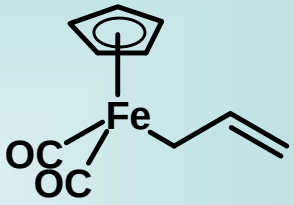
R Shibasaki, M. Soden, C. D. Kojima, A. T*etrahedron* 1997*, 53*, 7371

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

η^3- Hydrocarbon Metal Complexes

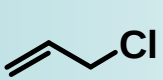
i.e.  type complexes

Note: We will discuss these here, too; even though they're η^1



Preparation of η^3-allyl Complexes

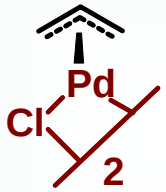
i) From olefins (alkenes) with allylic leaving groups



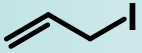
Na_2PdCl_4

$CO, H_2O, MeOH$

(Pd^o generated *in situ*)

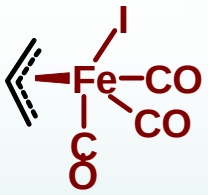


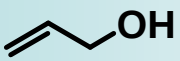
$+ CO_2$ $+2\ HCl$ $+$ $2\ NaCl$



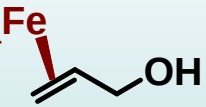
$Fe(CO)_5$ or $Fe_2(CO)_9$

Δ, -CO





$Fe_2(CO)_9$



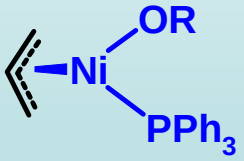
HBF_4

$Et_2O, -H_2O$

BF_4^-

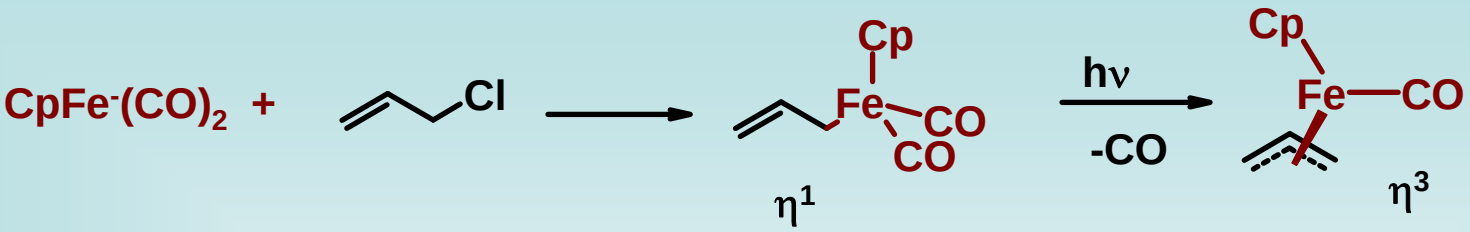
$Ni(cod)_2$

PPh_3

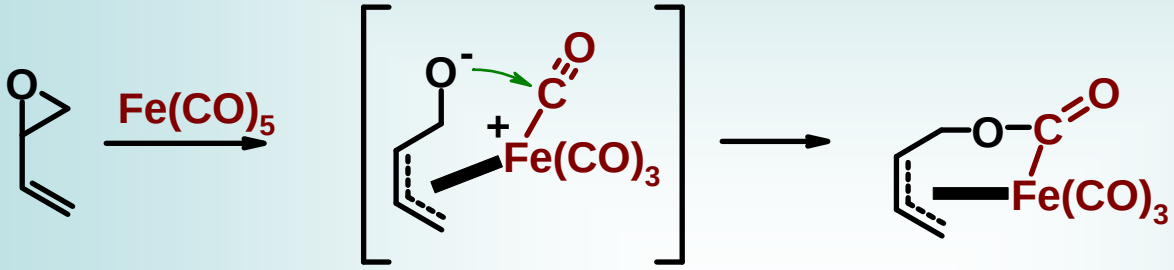


$+\ 2$

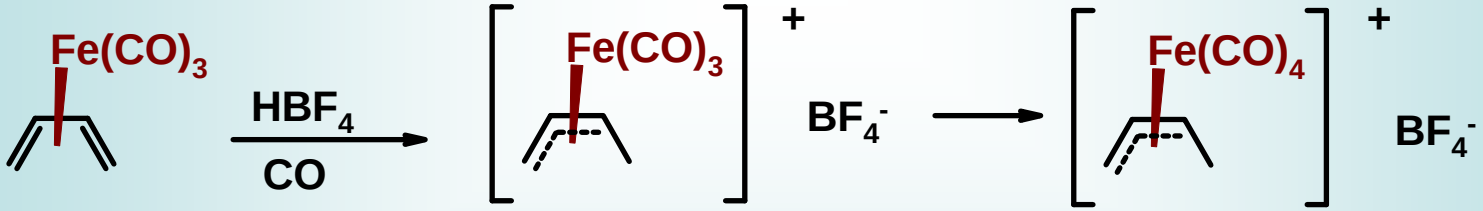
R = Ph, Ac



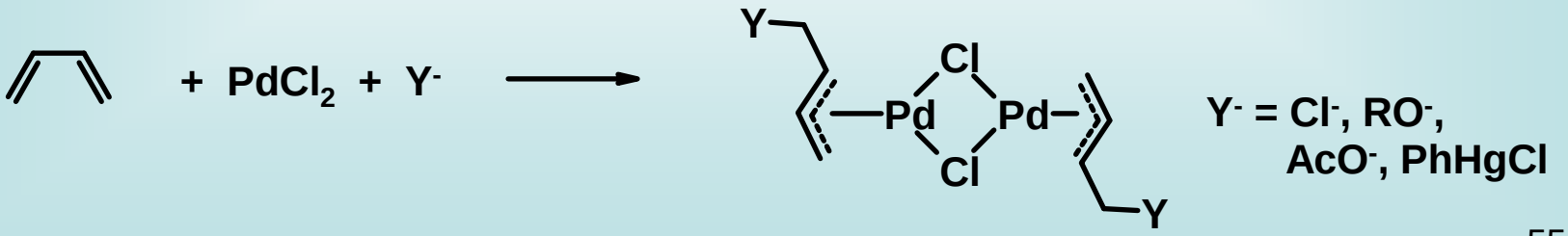
Fish, R. W. et al (Rosenblum) *J. Organomet. Chem.* 1976, *105*, 101.



ii) From Metal-Diene Complexes

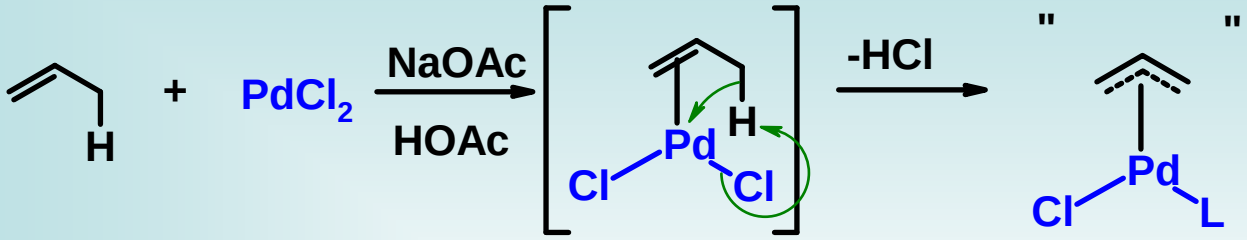


Salzer, A.*; Hafner, A. *Helv. Chem. Acta* 1983, *66*, 1774.

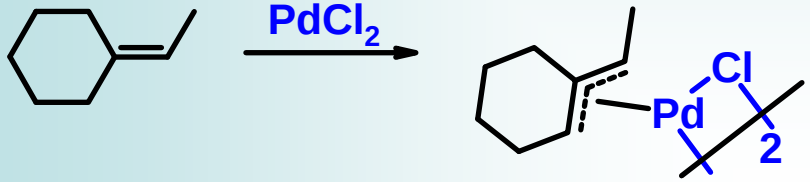


Trost, B. *Tetrahedron* 1977, *33*, 2615.

iii) Activation of allylic C-H Bonds
-most applicable for Pd complexes

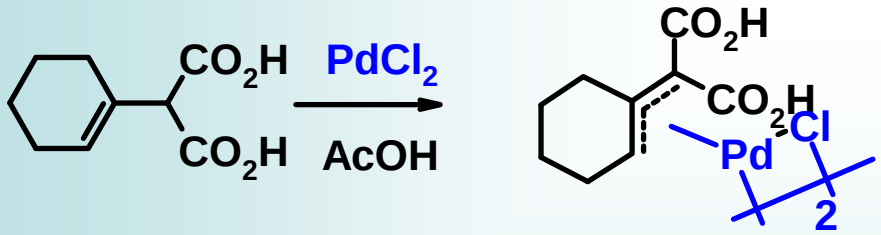


i.e.,



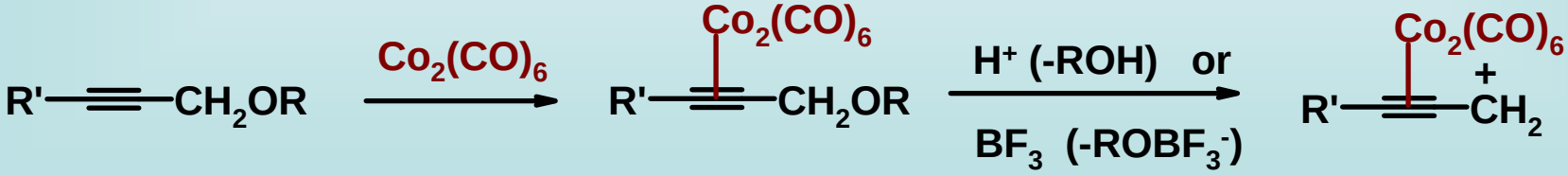
Trost, B. M. T*etrahedron Lett.* 1974, 2603.

Huttl, R. *Chem. Ber.* 1968, *101*, 252.



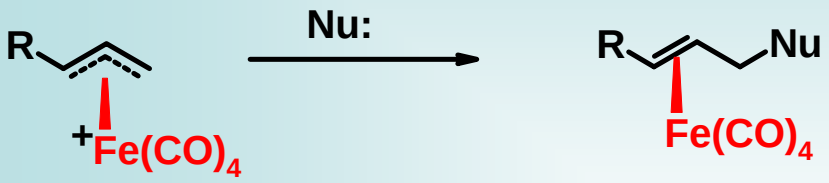
Chrisope, D. R.; Beak, P.; Saunders, W. H., *J. A. Chem. Soc.* 1988, *110*, 230

iv) Propargyl (di)Co complexes



Allyl/Propargyl η^3- Complexes as Electrophiles

a) Cationic allyl tetracarbonyl complexes



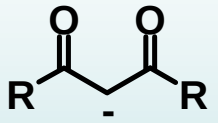
-complexes react with a pretty wide range of nucleophiles to give η^2-alkene complexes as immediate products

-these η^2-alkene complexes are not all that stable, easily decomplexed by mild oxidant

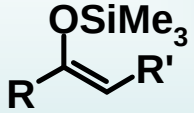
-allyl attack is presominantly at less substituted side of allyl unit (more later)

Nu: can be... R_3N (amines), Ph_3P (phosphines), R_2Cd (RMgBr), RCu(CN)ZnI

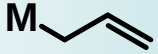
electron rich arenes, H^- (Et_3SiH),



,



,



(M = Me_3Si, Bu_3Sn, R_2B)

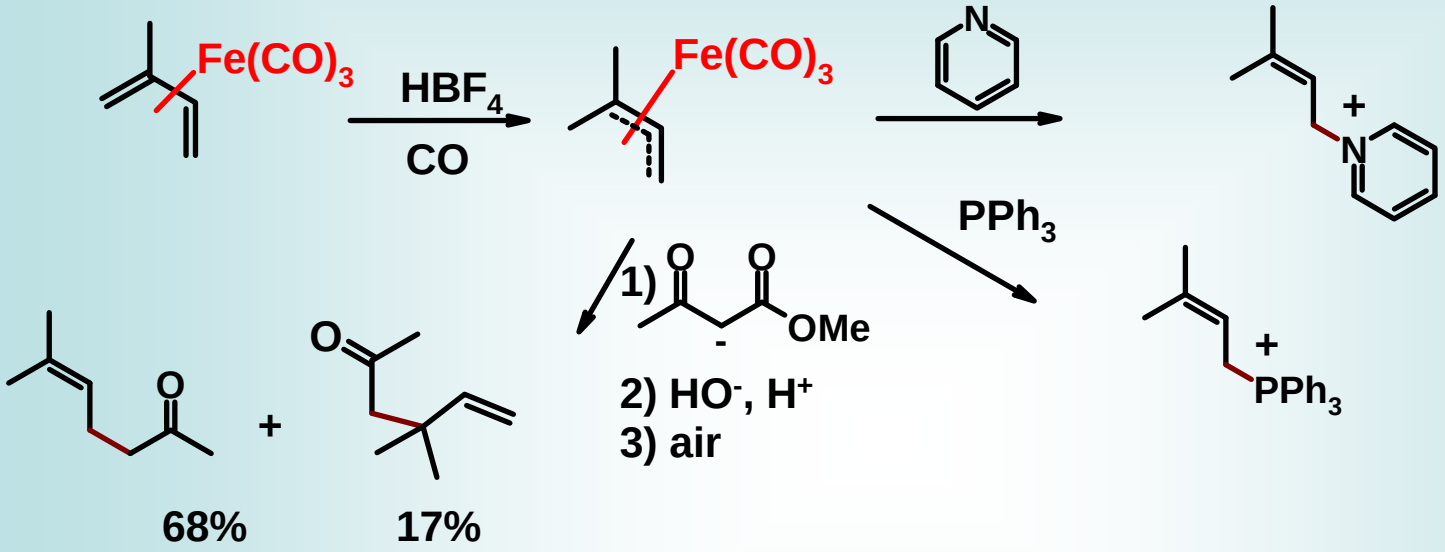
R Pearson, A. J. "Iron Compounds in Organic Synthesis", Academic Press, 1994, Ch.3

R Green, J. R.; Donaldson, W. A., in "Encyclopedia of Inorganic Chemistry", Lukehart, C. M., ed., Wiley 1994, V 4, p. 1735.

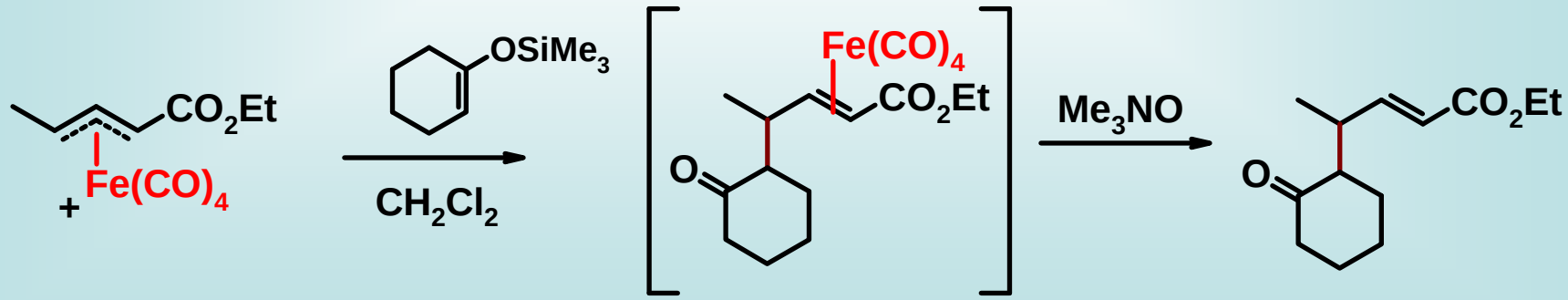
Regiochemistry

-Site of attack is normally at the less substituted <u>end</u> of the allyl unit

-C2 attack has <u>never</u> been observed



-Site of attack is <u>away</u> from electron withdrawing group



Green, J. R.*; Carroll, M. K. *Tetrahedron Lett.* <u>1991</u>, *32*, 1141.

Why care?

-allyl cations are very highly reactive; either too unstable to prepare or too reactive to be isolated or control their reactivity

-site γ-to carbonyl is normally nucleophilic; therefore this is *umpolung* reactivity

-iron allyls are geometrically stable

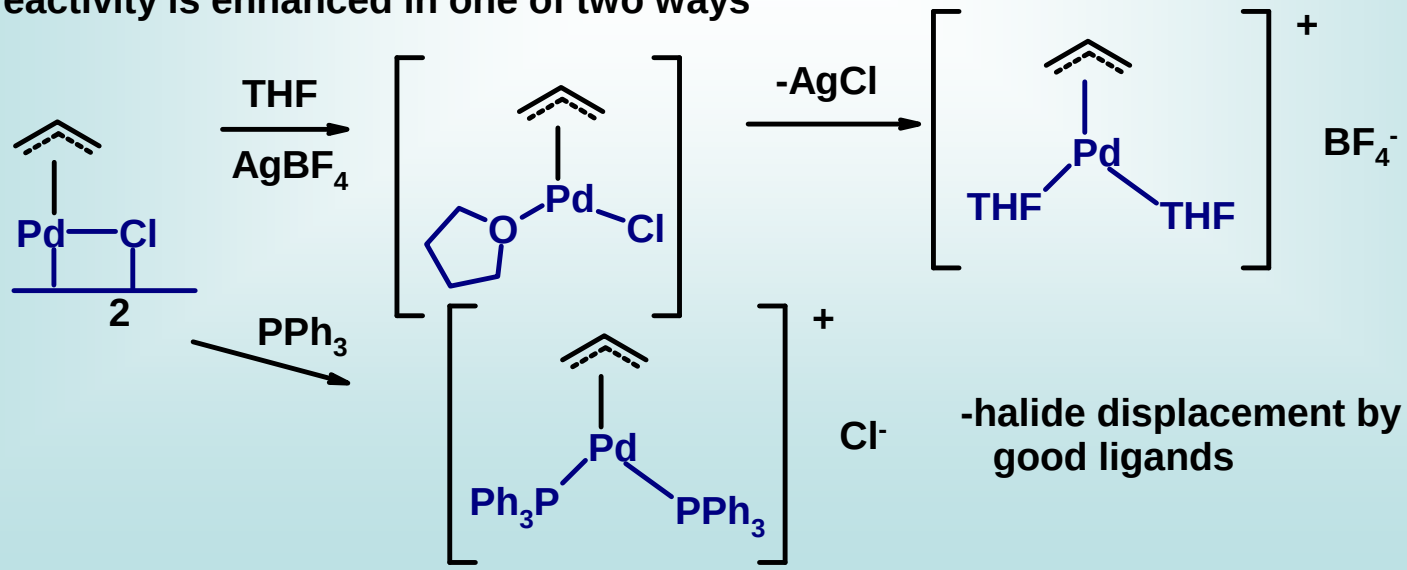
R de Koning, H.; Hiemstra, H.; Moolenar, M. J.; Speckamp, W. N. *Eur. J. Org. Chem.* 1998, 1729.
R Enders, D.; Jandeleit, B.; von Berg, S. *Synlett* 1997, 421.

b) Allylpalladium^{II} Complexes

Hegedus, p. 245 start
Tsuji, p. 116-168

-by FAR, the most widely used η^3-allylmetals
-like the Pd alkene complexes, the chloro- bridged dimers usually aren't reactive enough

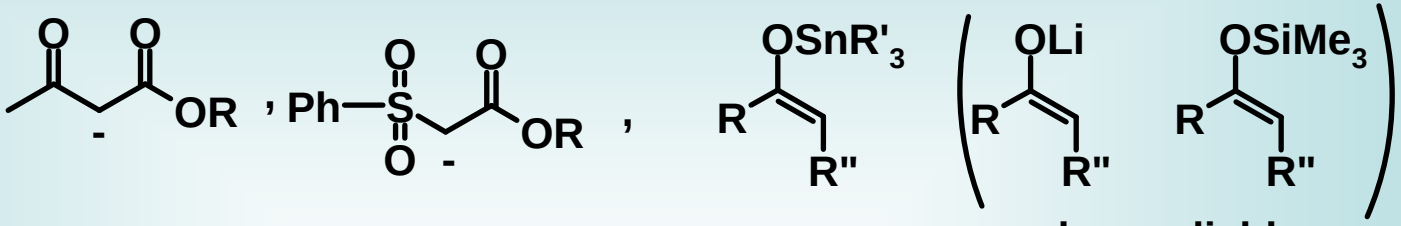
-reactivity is enhanced in one of two ways



-halide displacement by good ligands

-can also be activated by other ligands (esp. phosphines), dimethyl sulphoxide (DMSO), hexamethylphosphoric triamide (HMPA)

- once 'activated', these can undergo nucleophilic attack by several reagents

AcO^-, R_2NH, 

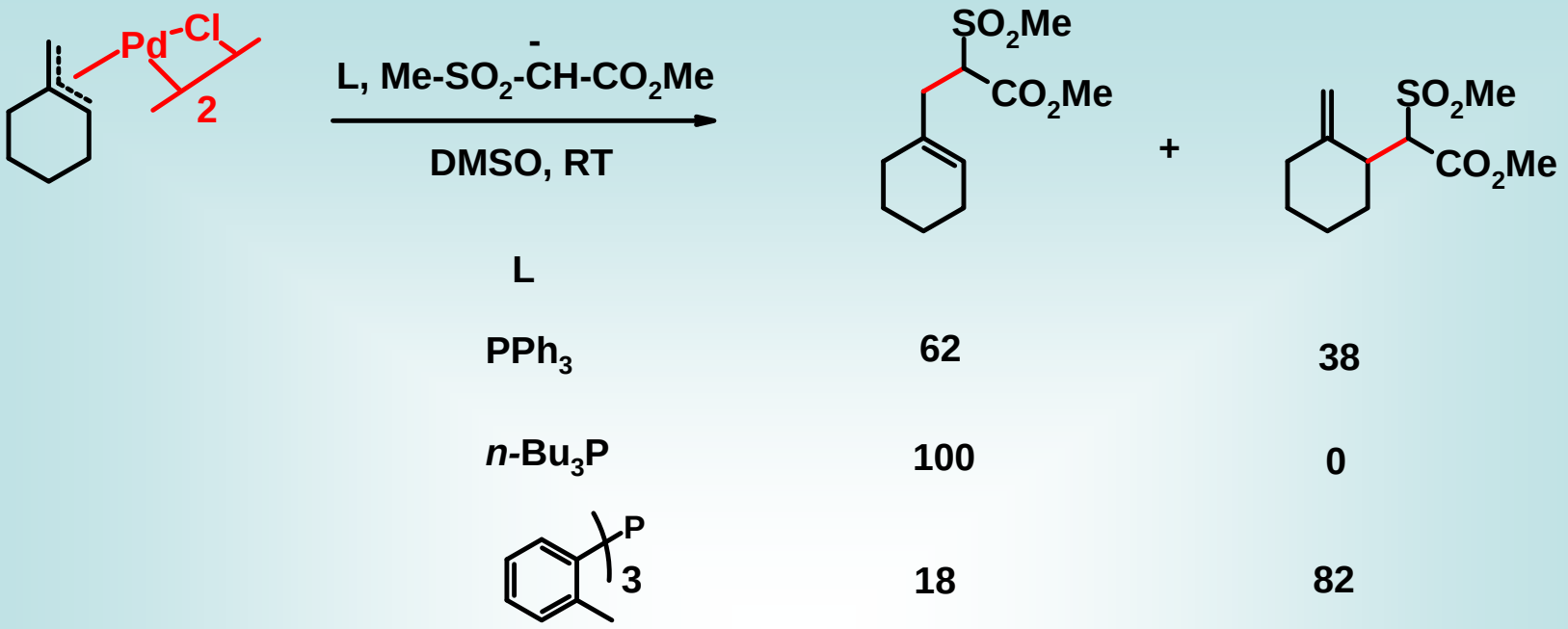
less reliable

-attack superficially similar to allylirons
-i.e., normally at the less substituted allyl terminus
-this can, however, be affected by choice of phosphine ligand

-rationale - more electron rich C-Pd bond shouold be the stronger one - this is the more substituted one
- therefore the less substituted one is more weakly held, so Nu^- attacks there

-BUT , with a bigger ligand (i.e., (*o*-tol)$_3$P), there is a steric repulsion between PdL_2 and the more substituted C - makes that bond <u>weaker</u>, more easily attacked

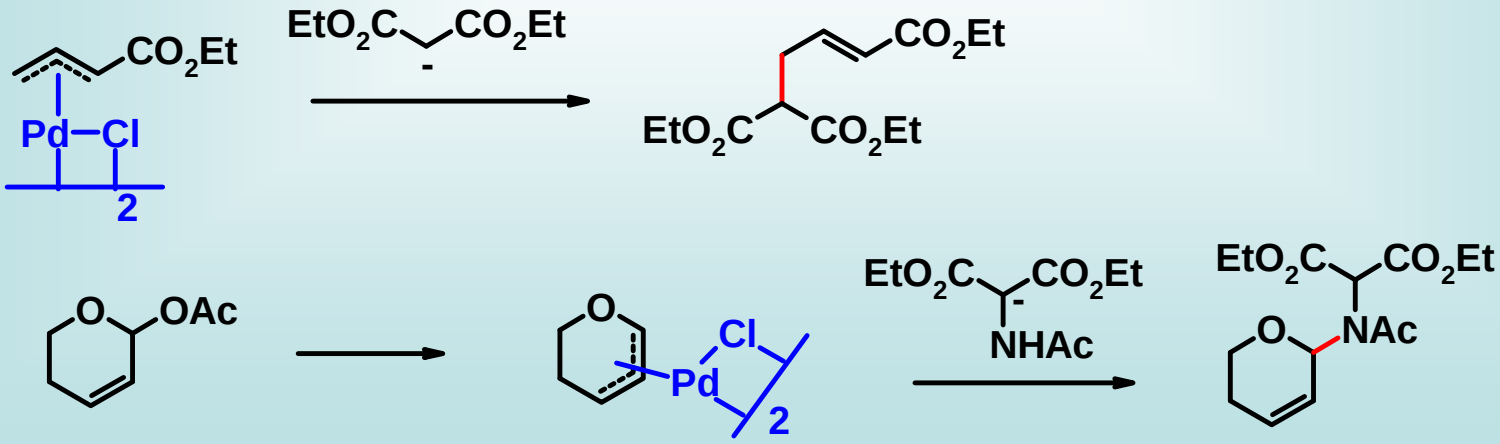
Consider.....



L		
PPh_3	62	38
n-Bu_3P	100	0
	18	82

Trost, B. M. et al *J. Am. Chem. Soc.* 1978, *100*, 3416.

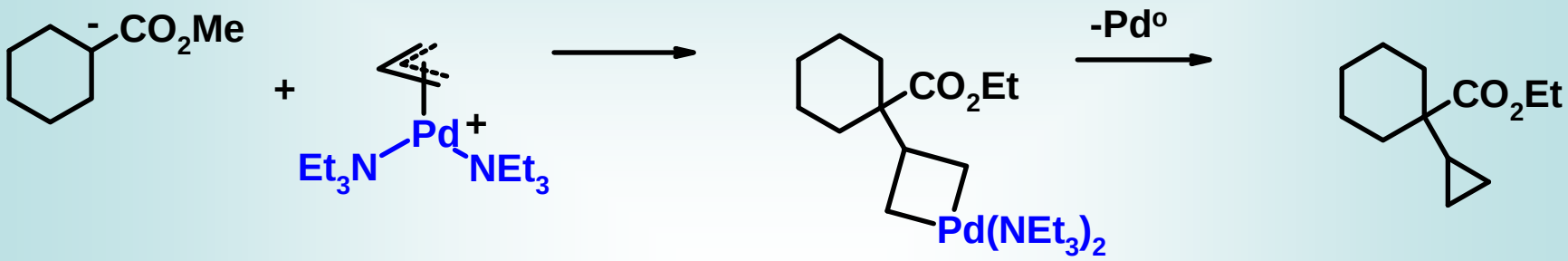
-electron withdrawing groups direct attack to the end site remote to the group
-electron donating groups direct attack to the end near the EDG



-there are rare cases of attack at the central carbon of the allyl unit - C-2 attack

-usually observed for Nu^- with high pKa's (20-30), or where the central carbon has a leaving group

-C-2 attack has very limited use in synthetic organic chemistry so far

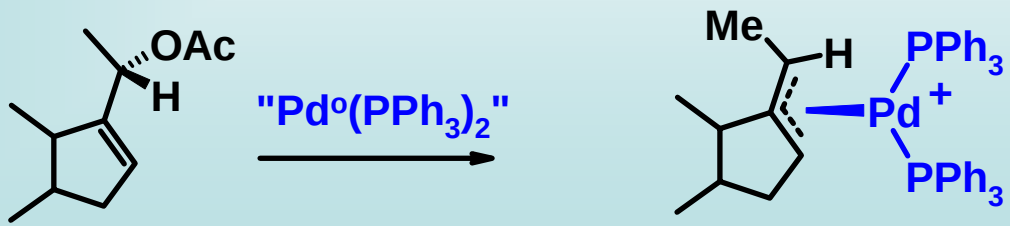


-for a good discussion and lead refs, see...

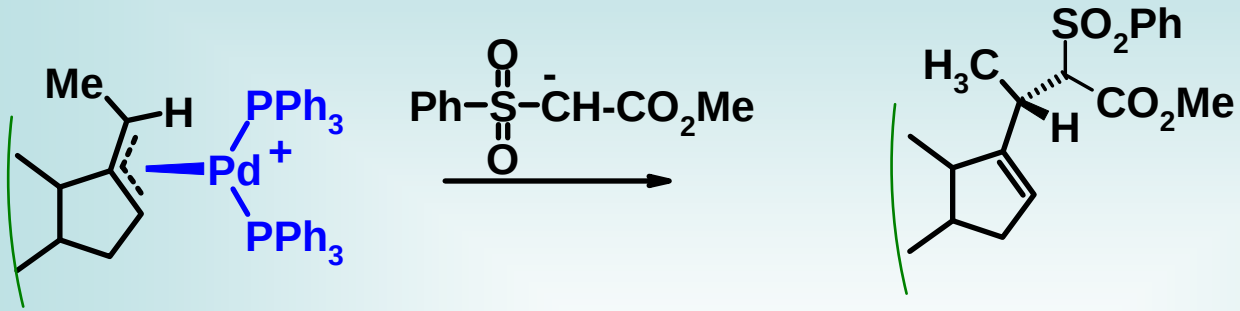
Aranyos, A., et al (Backvall, J. R.) *Organometallics* 1997, *16*, 1058.
Organ, M. et al *J. Am. Chem. Soc.* 1998, *120*, 9283.

Stereochemistry of Attack

-recall - oxidative addition to for π- allyl is on a alkyl centre, and therefore goes with inversion of configuration

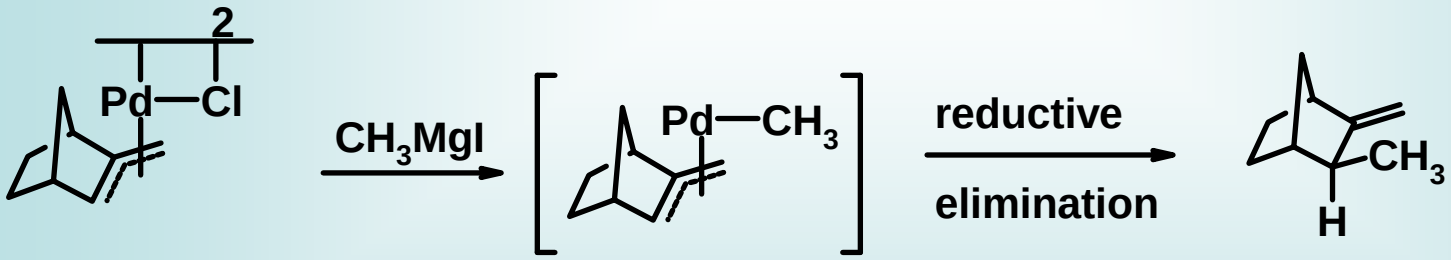


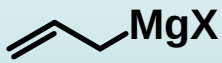
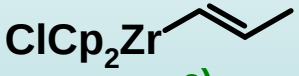
-now, nucleophilic attack on the allylpalladium normally occurs *away* from the palladium (it could be called backside attack, too), so overall there is a retention of configuration at carbon



Note: This is the normal (and ideal) situation
non-stabilized carbanions are not usually good for attack on these species;
when the do work, the mechanism is different....

- then, the initial attack step is on the metal, which is followed by reductive elimination to give retention for this step

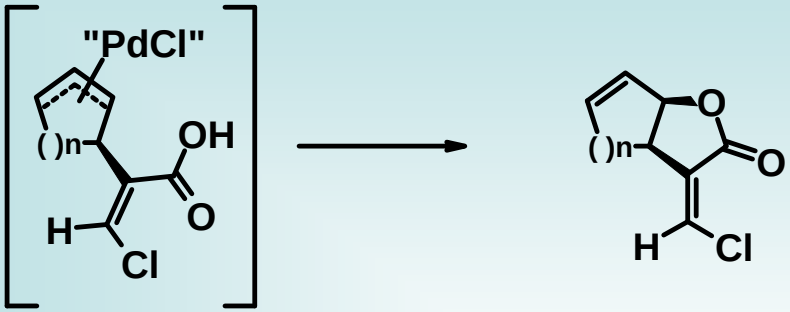


Nu⁻ = MeMgX,  a)  b) PhMgBr  c)

Tetrahedron Lett. 1979, 3221
J. Chem. Soc., Chem. Commun. 1984, 107
b) *Organometallics*, 1985, *4*, 417

J. Organomet. Chem. 1975, *102*, 359
a) J. Am. Chem. Soc. 1984, *106*, 5028.
c) J. Am. Chem. Soc. 1982, *104*, 1310 and 5028.

-Acetate/carboxylate will attack with retention under special conditions, or if forced by the constraints of the molecule

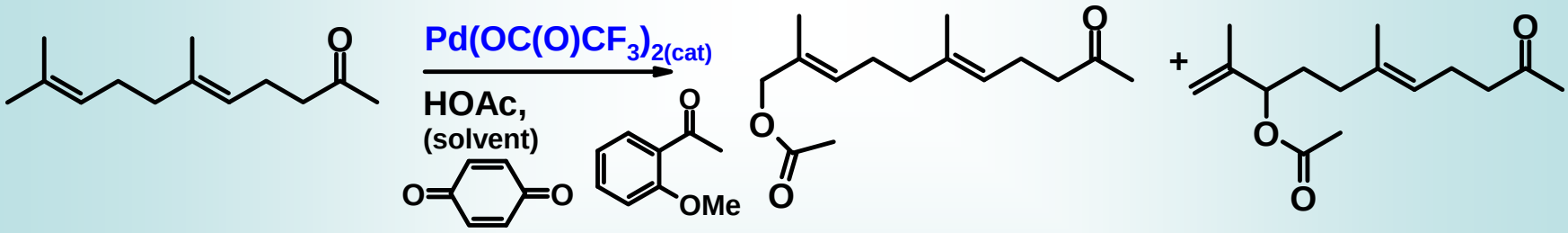


Larock, R.C. *J. Org. Chem.* 1984, *49*, 3662.

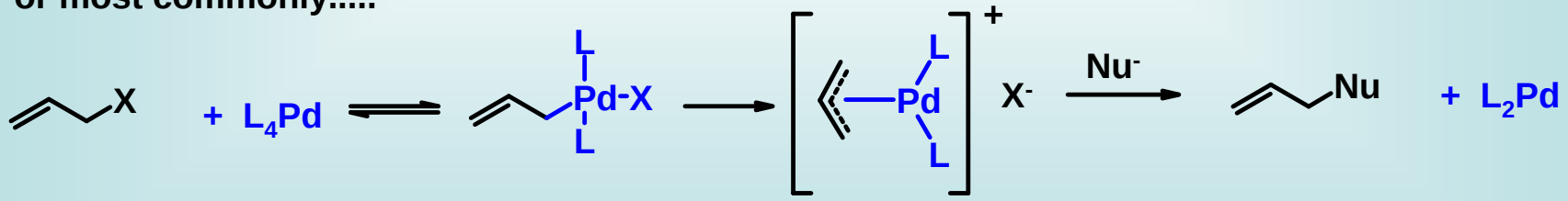
The best news is that many, many, many of these reactions can be done as catalytic reactions

for example, allylic oxidation

McMurry, J. R.; Kocovsky, P. *Tetrahedron Lett.* 1984, *25, 4187.*



or most commonly.....



X = -OAc, -OC-R, -OC-OR, -OPh, -OH, -SO2Ph, -NO2,