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

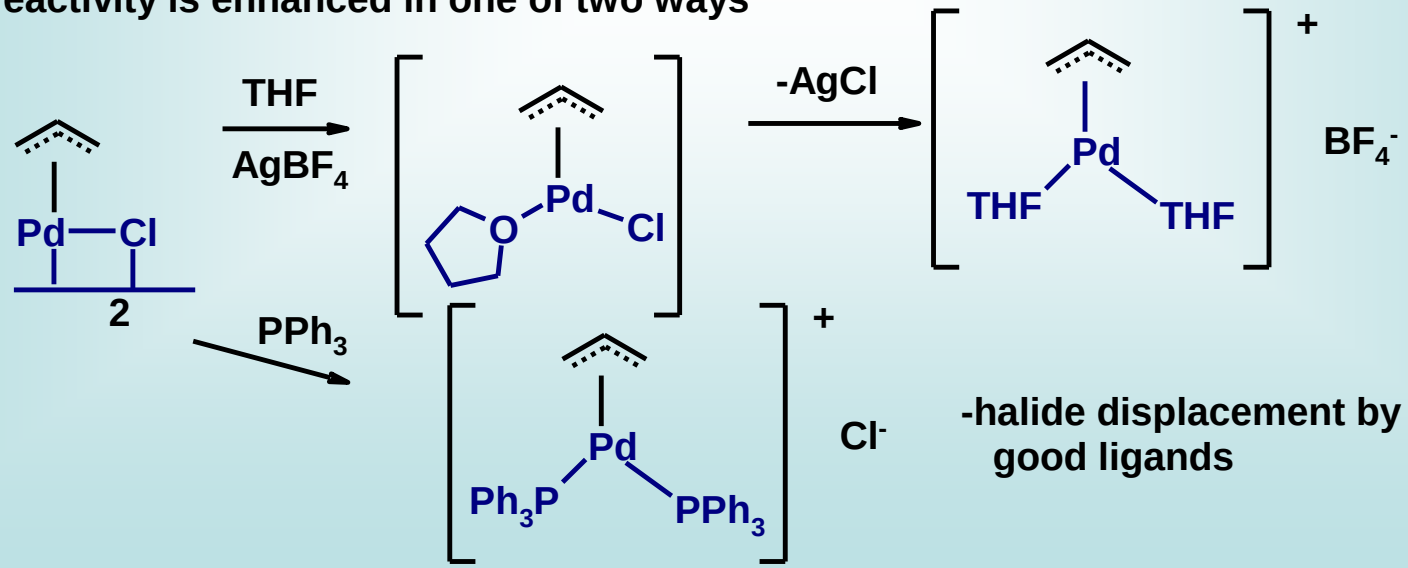
R de Koning, H.; Hiemstra, H.; Moolenar, M. J.; Speckamp, W. N. *Eur. J. Org. Chem.* 1998, 1729.
R Enders, D.; Jandeleit, B.; von Berg, S. *Synlett* 1997, 421.

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

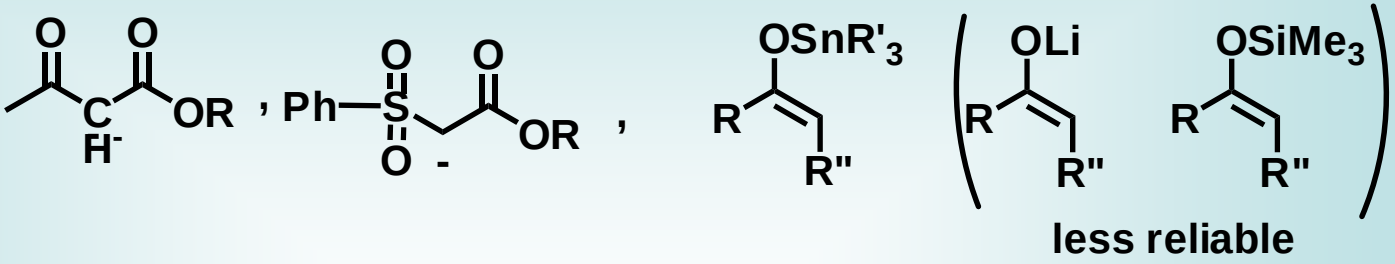
-reactivity is enhanced in one of two ways



-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, 

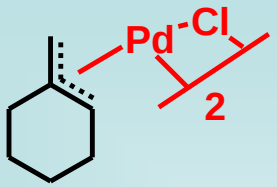
less reliable

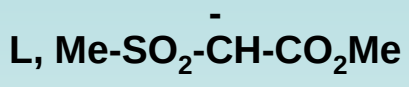
-attack superficially similar to allylirons
-i.e., normally at the less substituted allyl terminus
-this can, however, be affected by choice of phosphine ligand

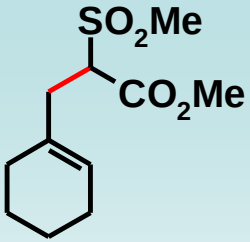
-rationale - more electron rich C-Pd bond should be the stronger one - this is the more substituted one
- therefore the less substituted one is more weakly held, so Nu^- attacks there

-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

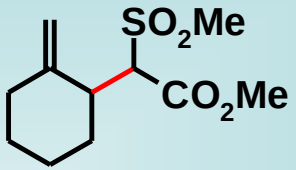
Consider.....

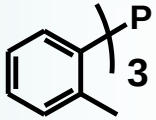






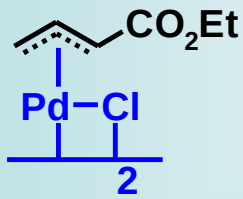
+

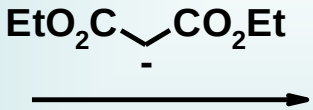


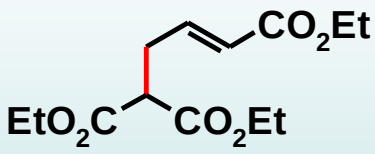
L		
PPh_3	62	38
n-Bu_3P	100	0
	18	82

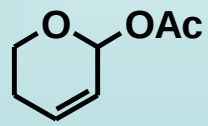
Trost, B. M. et al *J. Am. Chem. Soc.* 1978, *100*, *3416.*

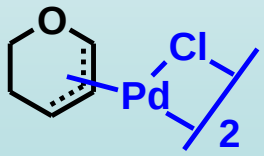
-electron withdrawing groups direct attack to the end site remote to the group
-electron donating groups direct attack to the end near the EDG

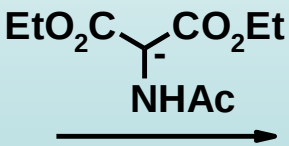


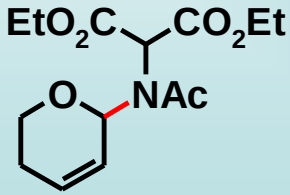








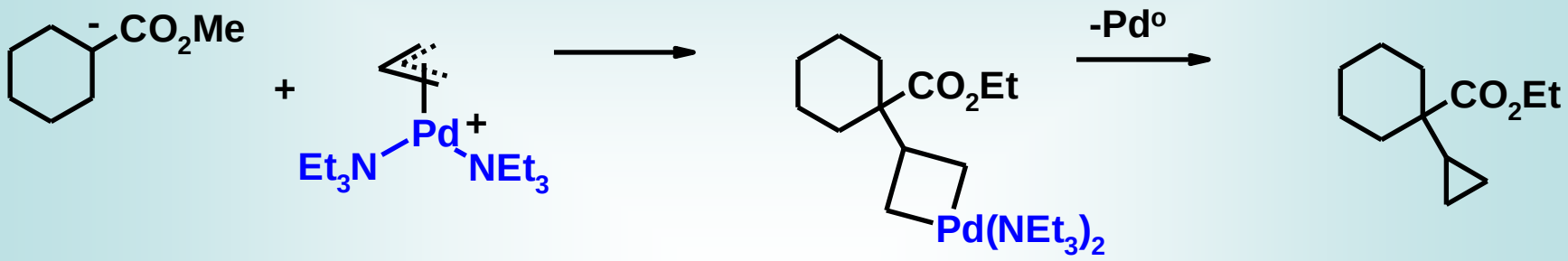




-there are rare cases of attack at the central carbon of the allyl unit - C-2 attack

-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

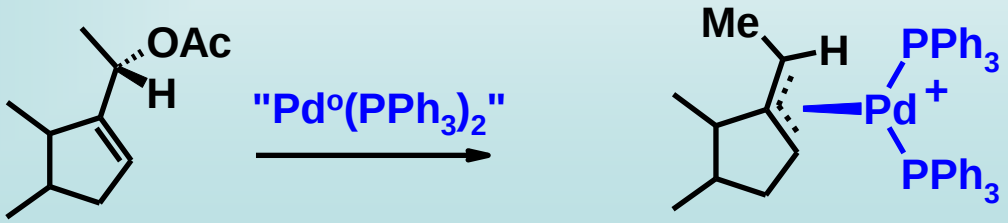


-for a good discussion and lead refs, see...

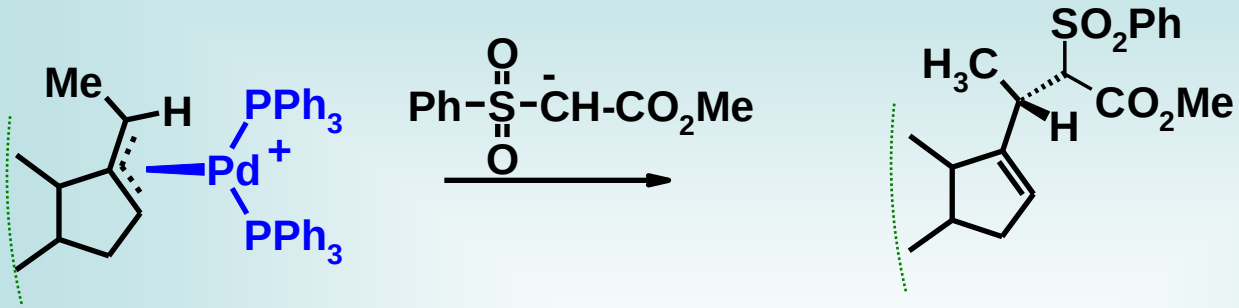
Aranyos, A., et al (Backvall, J. R.) *Organometallics* 1997, *16*, 1058.
Organ, M. et al *J. Am. Chem. Soc.* 1998, *120*, 9283.

Stereochemistry of Attack

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

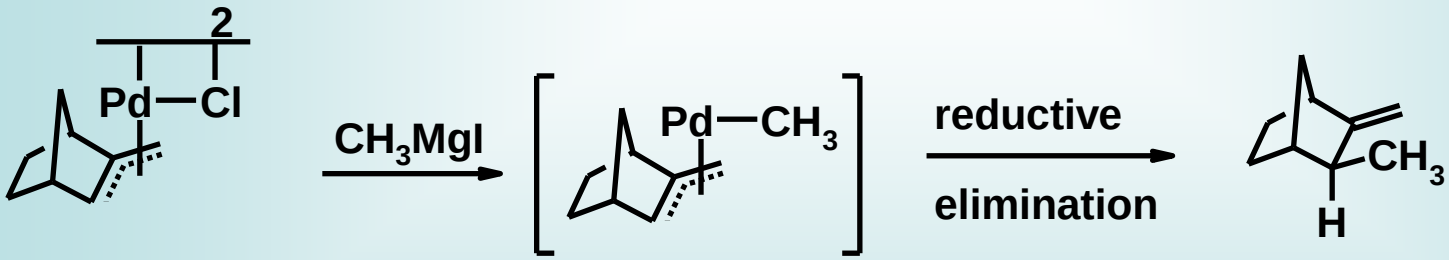


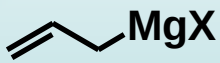
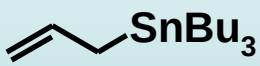
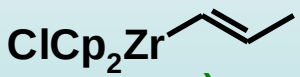
-now, nucleophilic attack on the allylpalladium normally occurs *away* from the palladium (it could be called backside attack, too), so overall there is a retention of configuration at carbon



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

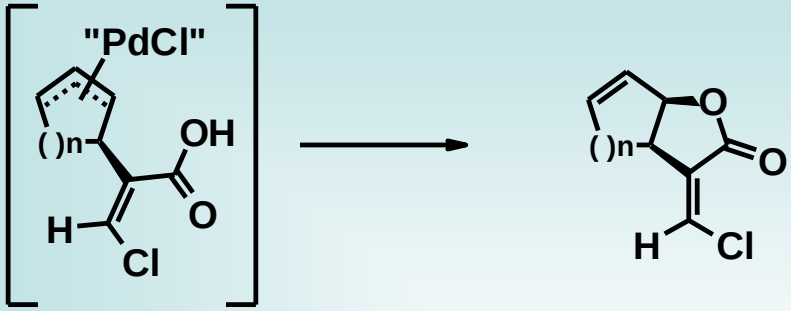


Nu⁻ = MeMgX,  a)  b) PhMgBr  c)

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

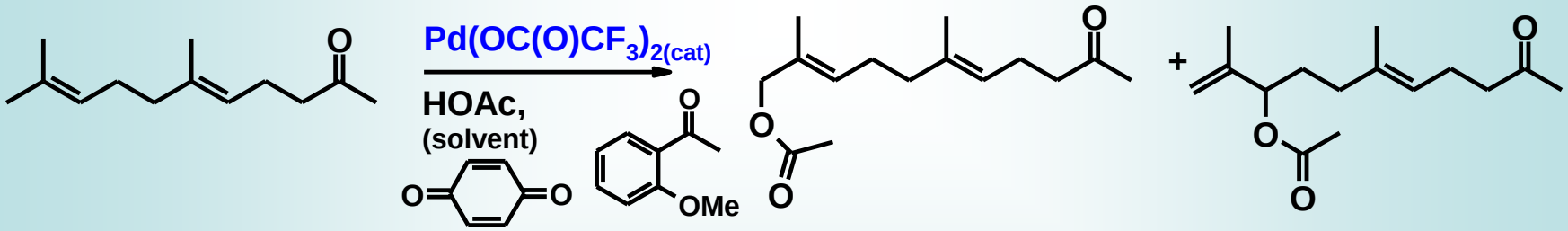


Larock, R.C. *J. Org. Chem.* 1984, *49*, 3662.

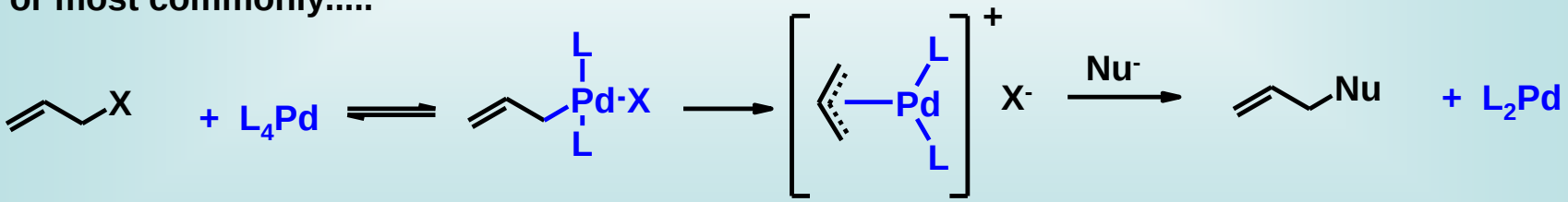
The best news is that many, many, many of these reactions can be done as catalytic reactions

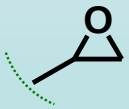
for example, allylic oxidation

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

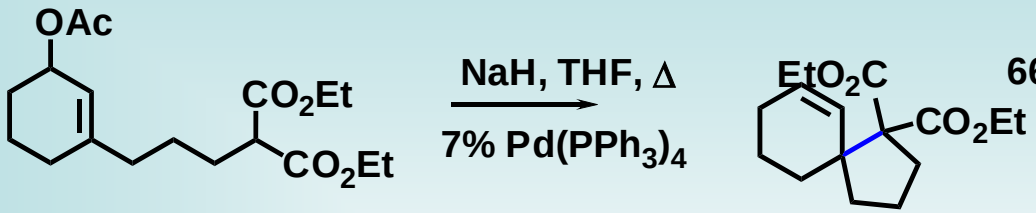


or most commonly.....

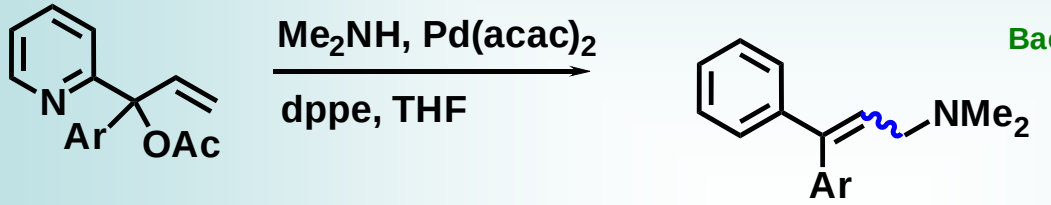


X = -OAc, -OC-R, -OC-OR, -OPh, -OH, -SO_2Ph, -NO_2, 

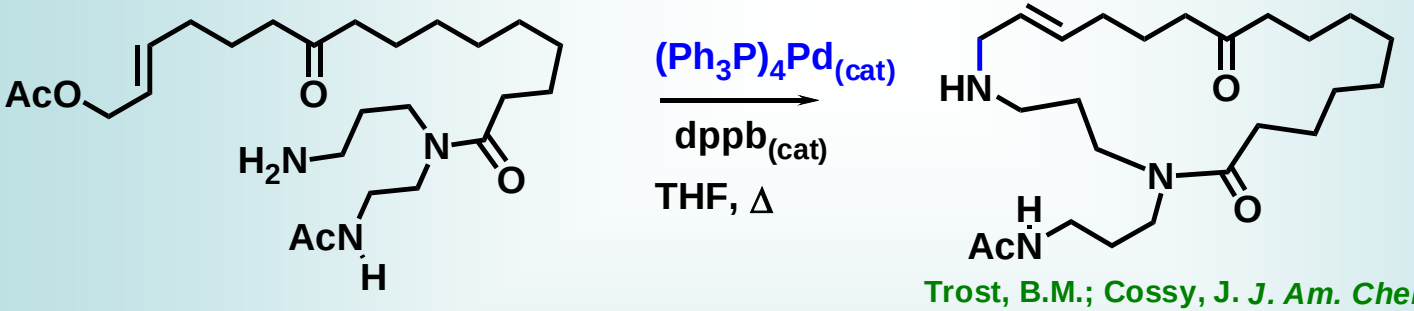
so……



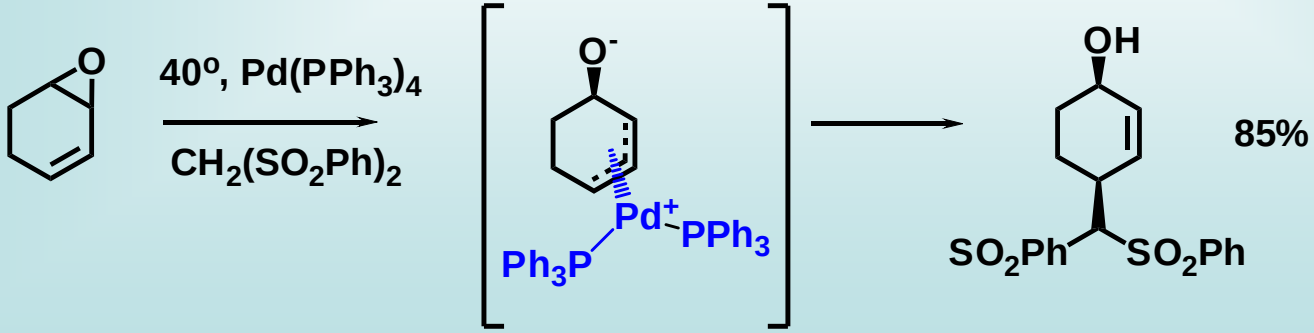
Godleski, S. A.;Valpey, R. S. *J. Org. Chem.* 1982, *47*, 381.



Backvall, J. R. *J. Org. Chem.* 1981, *46*, 3479.



Trost, B.M.; Cossy, J. *J. Am. Chem. Soc.* 1982, *104*, 6881.



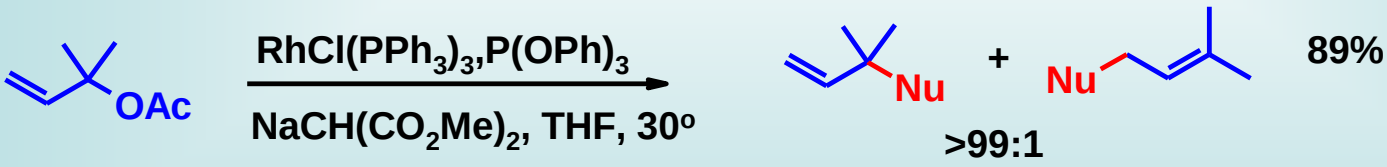
Notes on that last one: 1) Allylic substituent, CHR-OH is electron withdrawing and sterically blocking 'proximal' attack - therefore, attack is on remote (distal) end of allyl unit

2) Oxidative addition goes with inversion
Nucleophilic attack is from backside of Pd allyl = inversion
so overall retention

Question: How about the other possible regiochemical outcome, i.e., attack at more substituted end?

If you instead use Co group catalysts, particularly Rh^{I} and Ir^{I}, and use less donating ligands (phosphites, esp. $P(OPh)_3$), it is clear that allyl more 'electrophilic', so location of '+' resonance for more critical - attack on more substituted end.

R Takeuchi, R. *Synlett* 2002, 1954 (Ir)



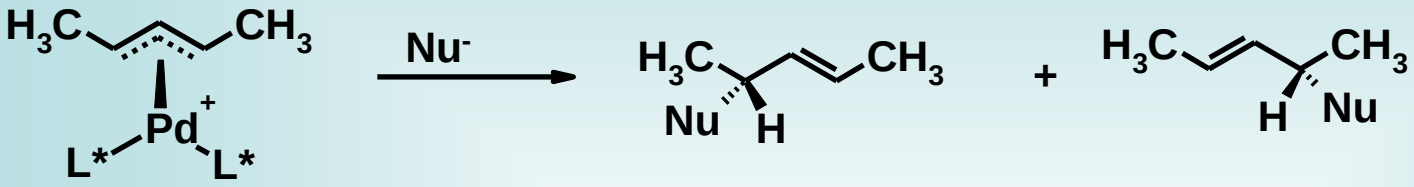
R Leahy, D. K.; Evans, P. A. Modern Rh-Catalyzed Organic Reactions, Ch. 10

-Other metal systems such as Ir^{III}, Mo^{II} can do similar substitutions

R Krska, S. W. et al (+Trost, B. M.); Pure Appl. Chem. 2004, 76, 625.(Mo)

Enantioselectivity

-most of the work has been done on allyls with symmetrical substitution patterns, using a chiral ligand



$Nu^- = {}^-CH(CO_2Et)_2$ especially

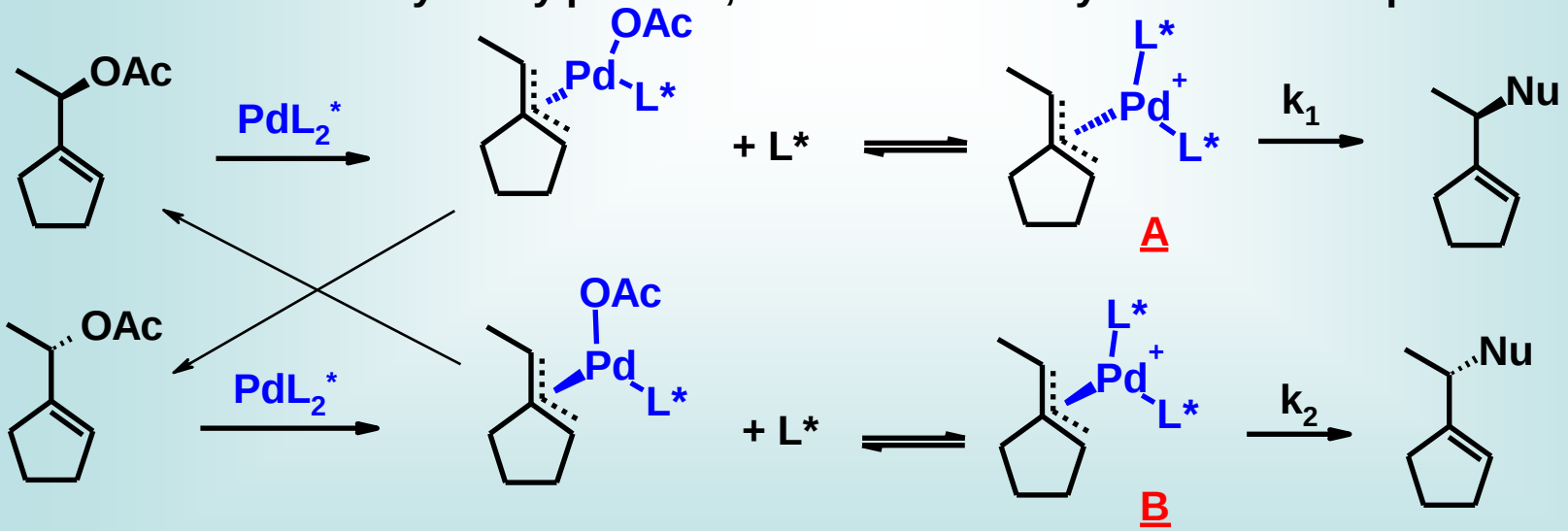
Most recent reviews

R Trost, B. M. *J. Org. Chem.* 2004, *69*, 5813.

R Trost, B. M. *Chem. Rev.* 2003, *103*, 2921.

R Graening, T.; Schmalz, H.-G. *Angew. Chem. Int. Ed.* 2003, *42*, 2580.

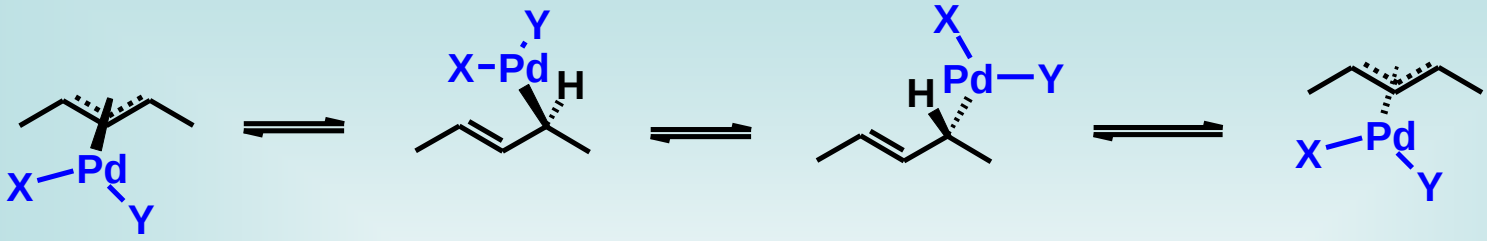
This still can be a very tricky process, as there are many isomerization processes possible



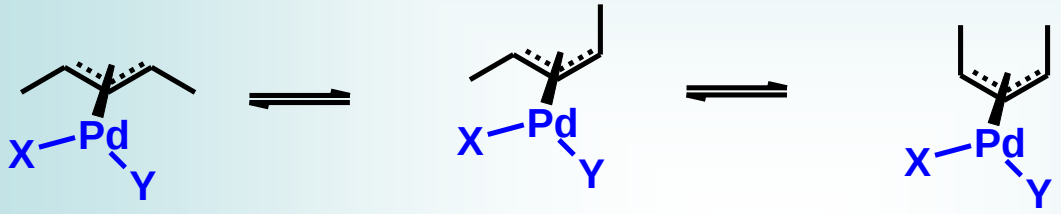
1) Under normal reaction conditions (high phosphine to Pd ratios), nucleophilic displacement is slow relative to π-allyl interconversion

-therefore, the product can depend of stabilities of A and B

2) Acyclic systems can racemize by an η^3 - η^1 - η^3 mechanism

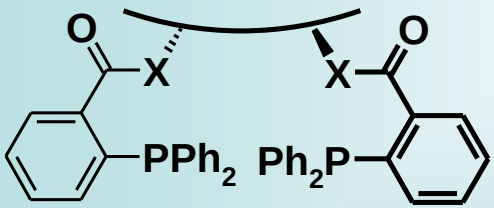


-same process can also result in *anti* / *syn*- isomerization of allyl Pd's



syn,syn- ***syn,anti-*** ***anti,anti-***

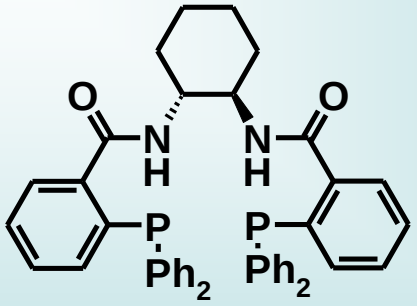
Nevertheless, there has been considerable success in this enantioselective transformation, especially using .....



DPPBA ligands

where

is a symmetrical diol diamine

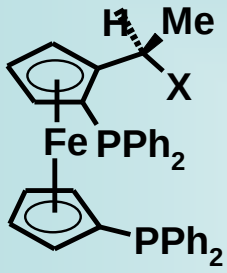


most common

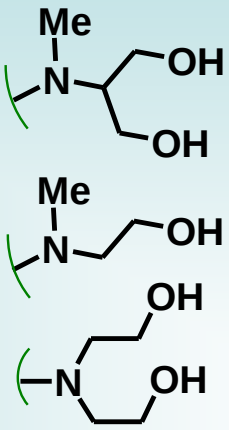
see Trost reviews listed on last page

R Trost. B. M.; Van Vranken, D. L. *Chem. Rev.* 1996, *96*, 395.

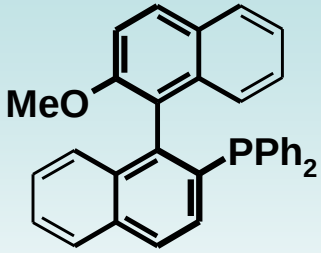
Other successful ligands



X =



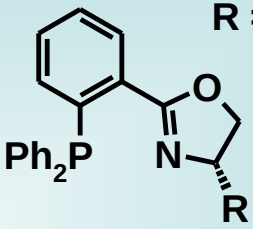
BPPF-X

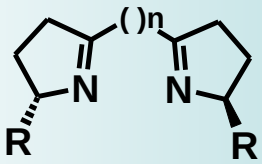


MOP (Monophosphine ligands)

R Hayashi, T. *J. Organomet. Chem.* 1999, *576*, 195.

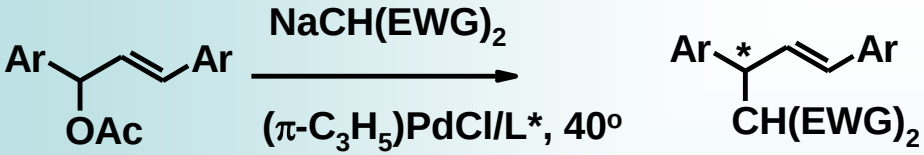
R = ^{i}Pr, ^{t}Bu





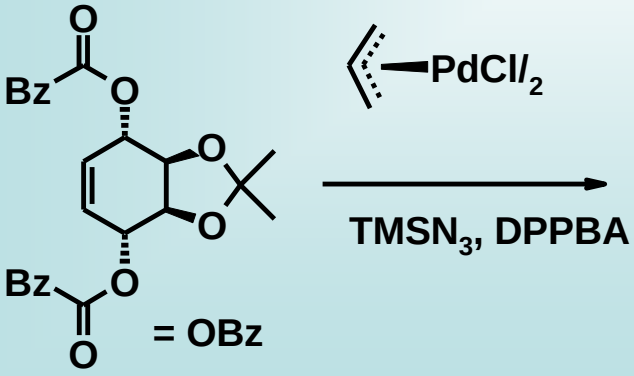
BOX (Bis-oxazoline ligands)

R Pfaltz, A. *Acc. Chem. Res.* 1993, *26*, 339.

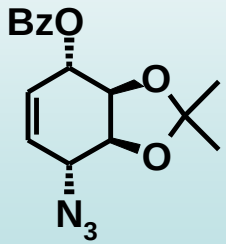


up to 96% ee with (R)- or (S)- BPPFX

Hayashi, T. et al *Tetrahedron Lett.* 1986, *27*, 191.



$TMSN_3$, DPPBA

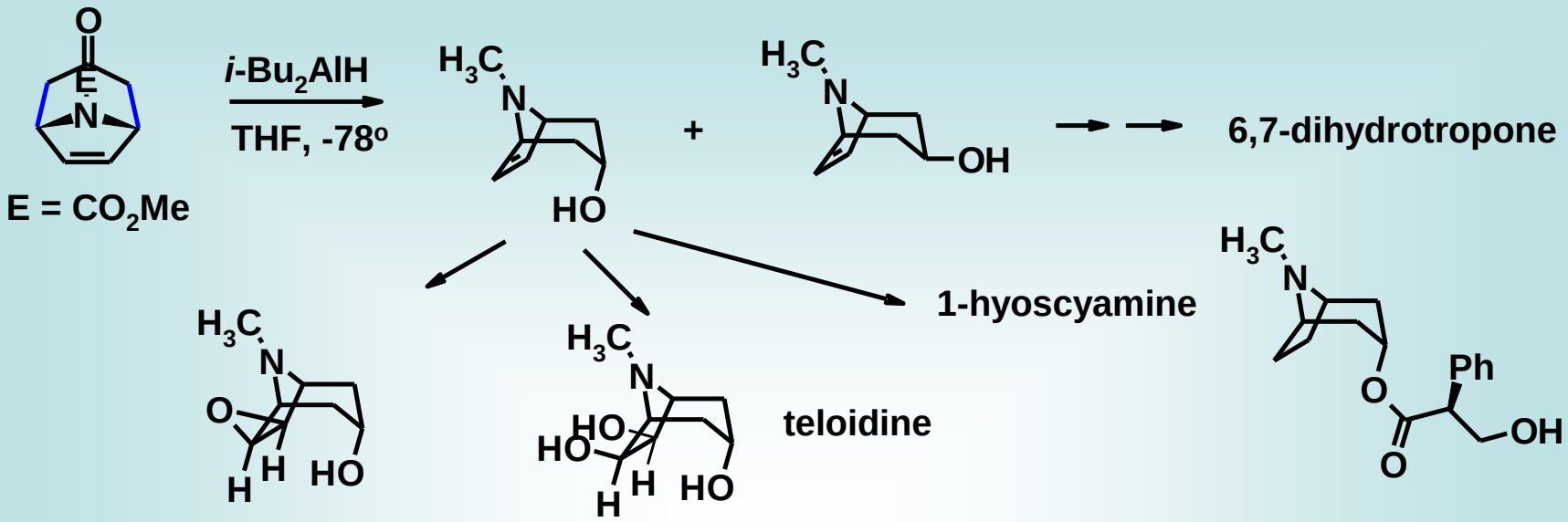


conduramine A-1
benzamide

pancratistatin

83% yield, >98% ee

from Trost (1996) review



many other natural product syntheses

for reviews, see

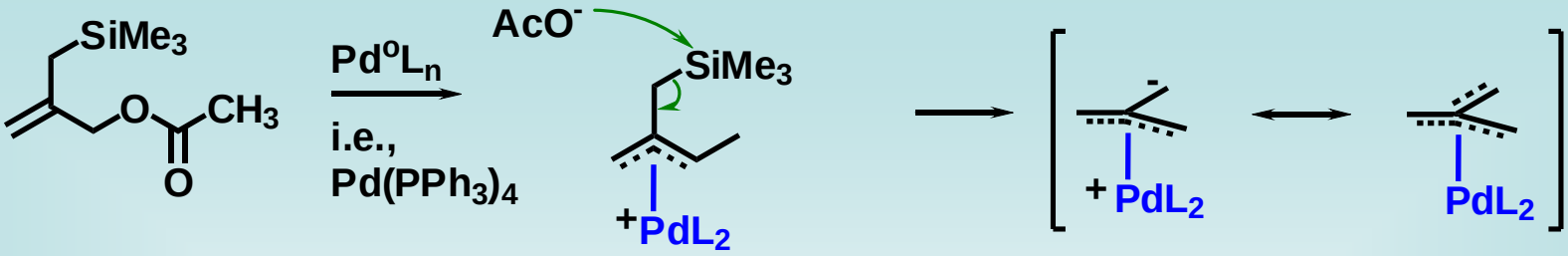
R Noyori, R. *Acc. Chem. Res.* 1979, *12*, 61.
R Noyori, R. *Org. React.* 1983, *29*, 162.
R Mann, J. *Tetrahedron* 1986, *42*, 4611.
part of R Rigby, J. H. Pigge, F. C. *Org. React*. 1997, *51*, 351
R Harmata, M. *Tetrahedron* 1997, *53*, 6235

η^4- Complexes

η^4-Trimethylenemethane Complexes

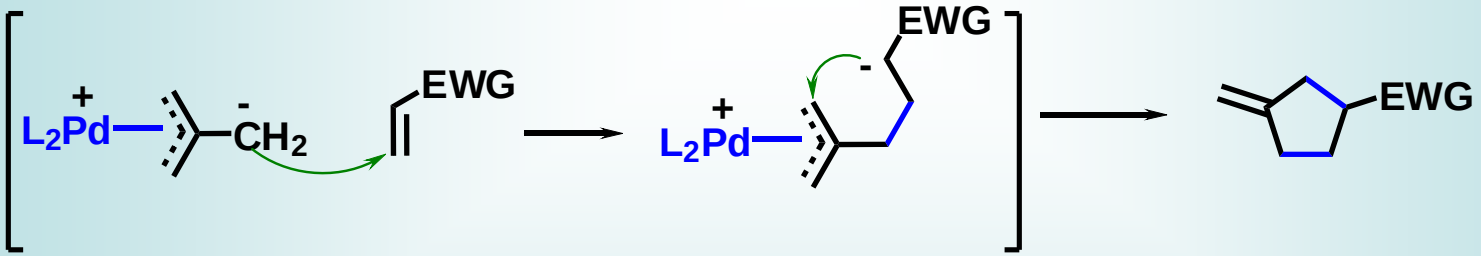
-predominantly used with palladium, due to use of metal in catalytic amounts
-iron also known and used some, but it is stoichiometric

-consider the following substrate that looks like a precursor to an η^3-allylpalladium



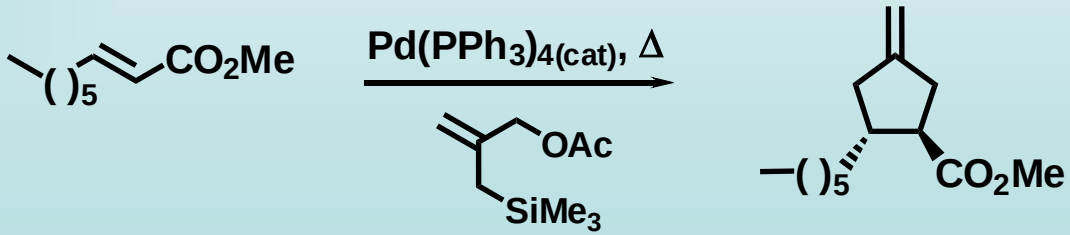
- in these cases, the Pd is coordinated to all 4 carbon atoms
- this is a <u>trimethylenemethane</u> complex
-excellent reagent for 3+2 cycloaddition reactions

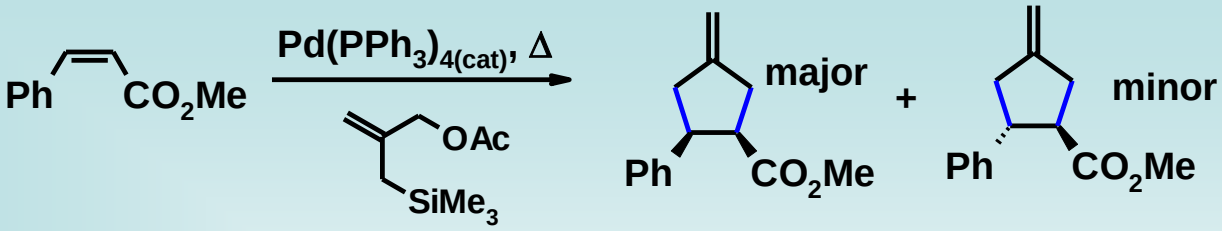
-mechanism



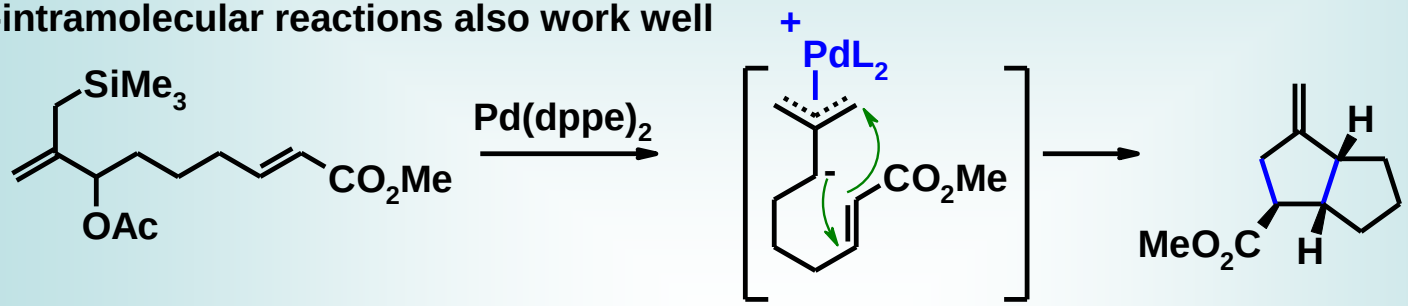
-stereochemical considerations

-about alkene - get mostly retention of configuration, but not <u>perfectly</u> so



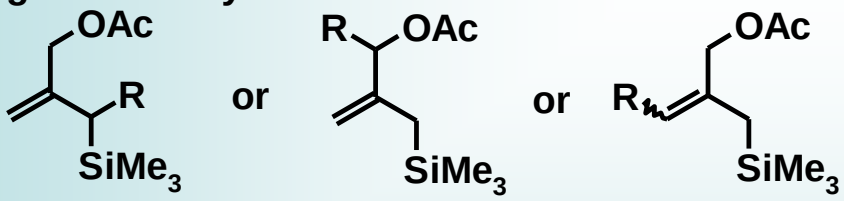


-intramolecular reactions also work well



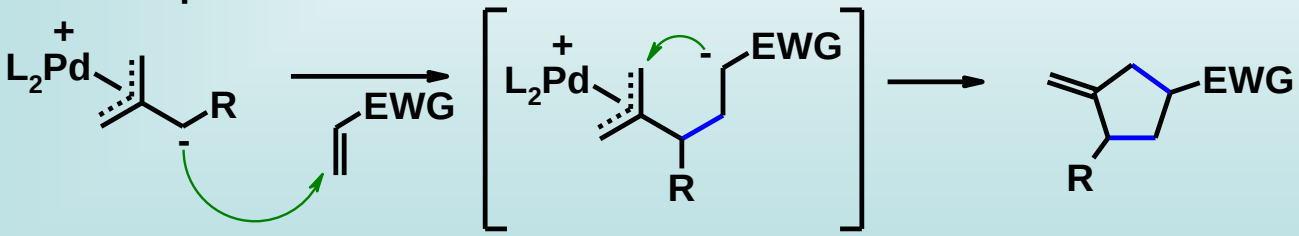
-other aspects of the stereochemistry (i.e., diastereoselectivity) have been well established, but are beyond the course's scope

Regiochemistry



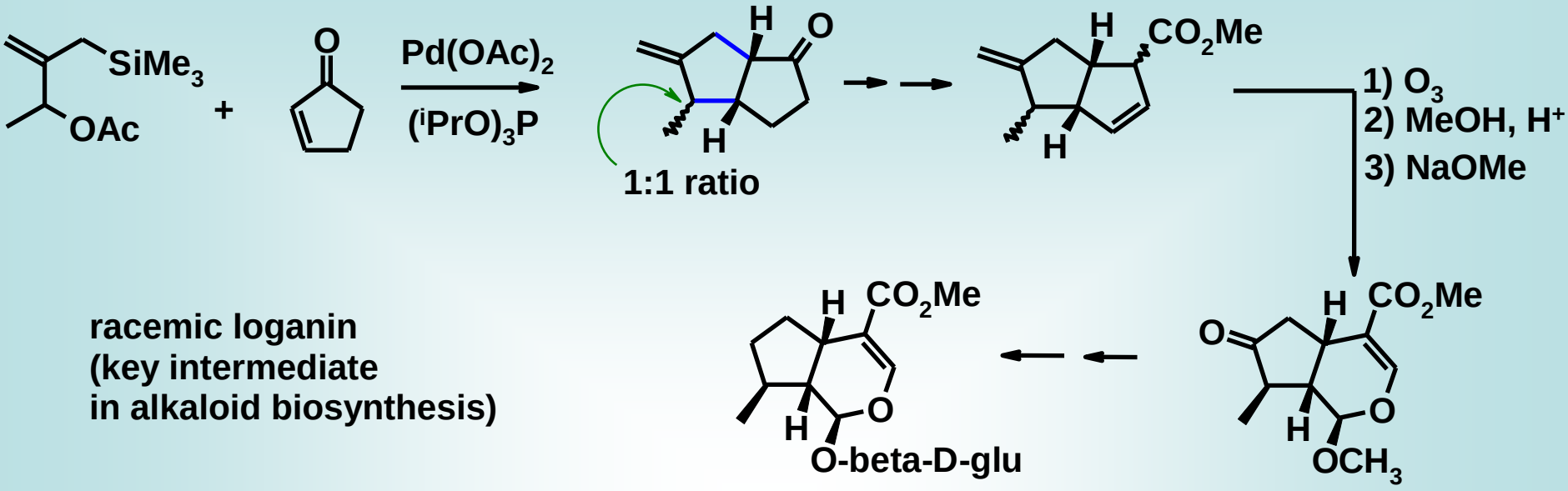
R = alkyl
electron withdrawing
electron donating

-regardless, it doesn't matter (much),
-the produc is as if.....



-no *real* mechanistic explanation for this result

-example of use in synthesis - loganin



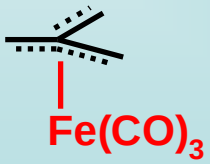
-there is *some* work on reacting TMM-Pd complexes with C=O and C=N-EWG in the presence of R_3Sn-X co-catalysts

-see Trost, B. M. et al J. Am. Chem. Soc. 1990, 112, 408.
Trost, B. M. et al J. Am. Chem. Soc. 1993, 115, 6636.

For reviews in the area see:

Trost R *Angew. Chem. Int. Ed. Engl.* 1986, *25*, 1.
R *Pure Appl. Chem.* 1988, *60*, 1615.
R 'Comprehensive Organic Synthesis' V. 5, p. 271 (1991)
R *Org. React.* 2002, *61*, 1.

Iron tricarbonyl - trimethylenemethane complexes also known



see Donaldson, W.A. *J. Org. Chem.* 1995, *60*, 1611.
Frank-Neumann, M. *Tetrahedron: Asymm.* 1996, *7*, 3193.
R Green, J. R.; Donaldson, W.A. 'Encyclopedia of Inorganic Chemistry, Vol. 4, 1994