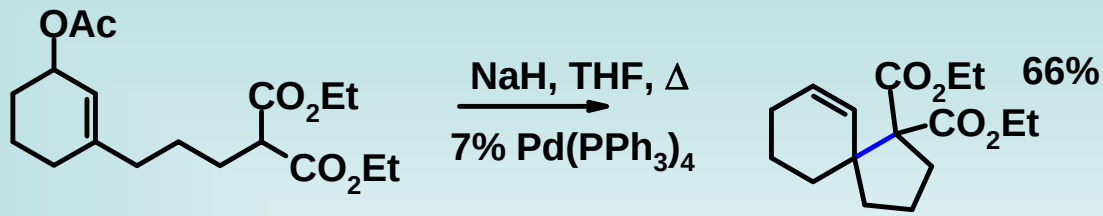
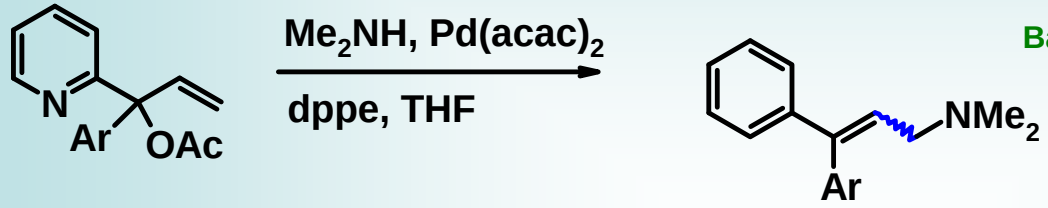
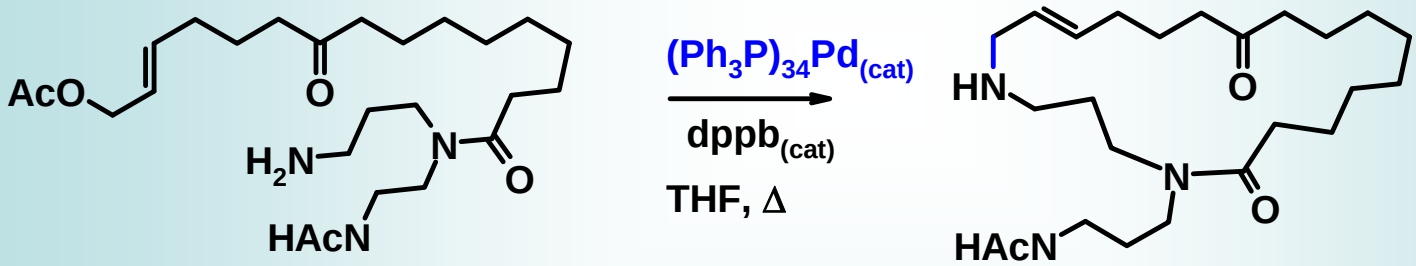
so.....



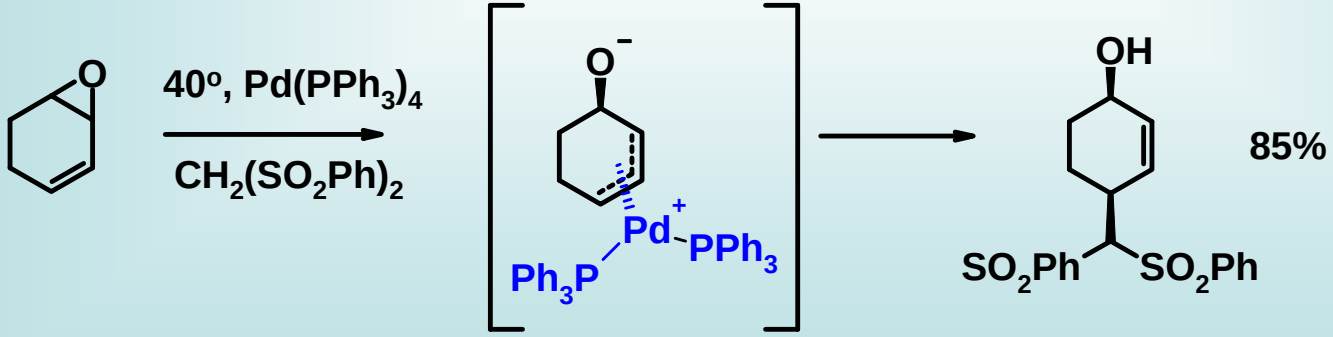
Godleski, S. A.;Valpey, R. S. *J. Org. Chem.* 1982, *47*, 381.



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



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



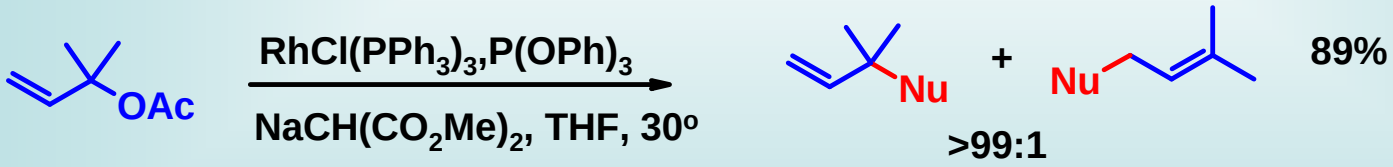
Notes on that last one: 1) Allylic substituent, CHR-OH is electron withdrawing and sterically blocking 'proximal' attack - therefore, attack is on remote (distal) end of allyl unit

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)



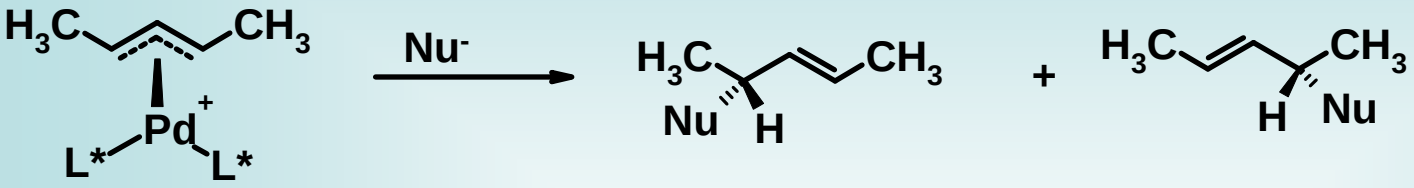
R Leahy, D. K.; Evans, P. A. Modern Rh-Catalyzed Organic Reactions, Ch. 10

-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

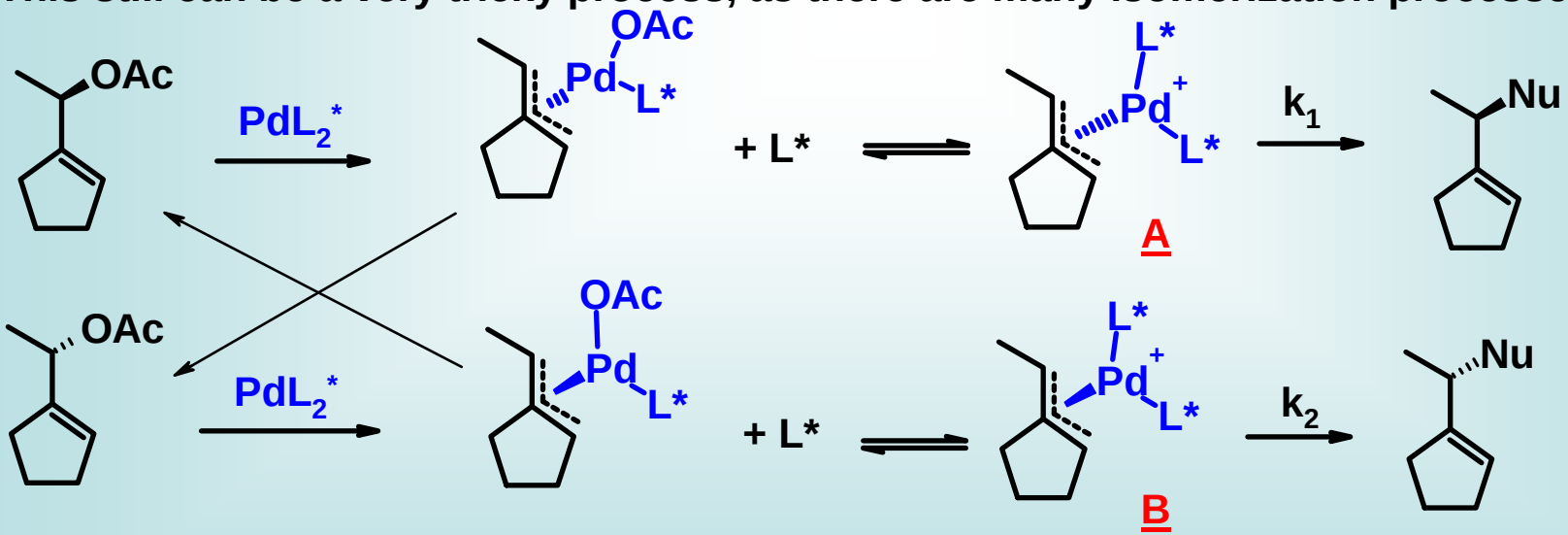
Most recent reviews

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.

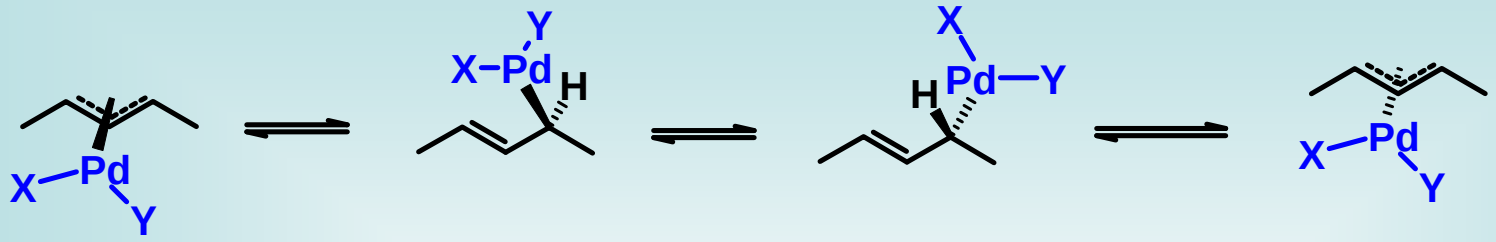
This still can be a very tricky process, as there are many isomerization processes possible



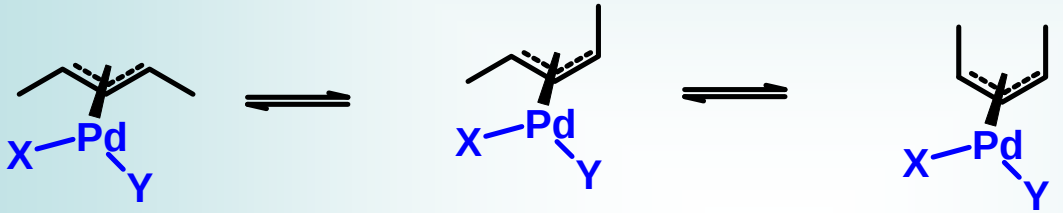
1) Under normal reaction conditions (high phosphine to Pd ratios), nucleophilic displacement is slow relative to π-allyl interconversion

-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

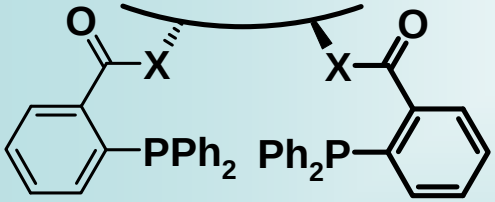


-same process can also result in *anti* / *syn*- isomerization of allyl Pd's



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

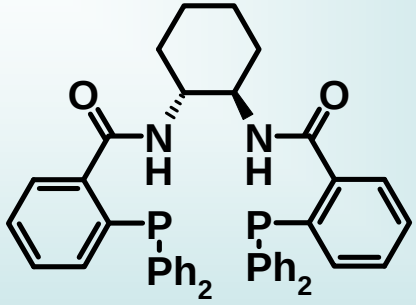
Nevertheless, there has been considerable success in this enantioselective transformation, especially using .....



DPPBA ligands

where

is a symmetrical diol diamine

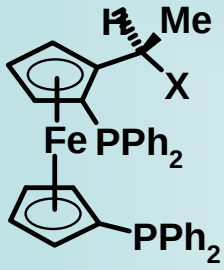


most common

see Trost reviews listed on last page

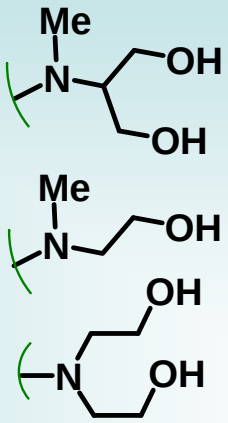
R Trost. B. M.; Van Vranken, D. L. *Chem. Rev.* 1996, *96*, 395.

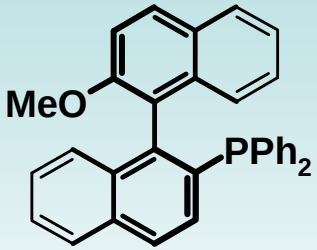
Other successful ligands



BPPF-X

X =

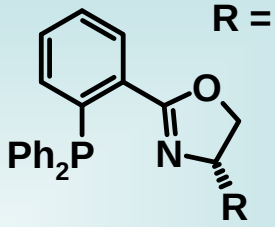


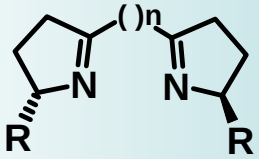


MOP (Monophosphine ligands)

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

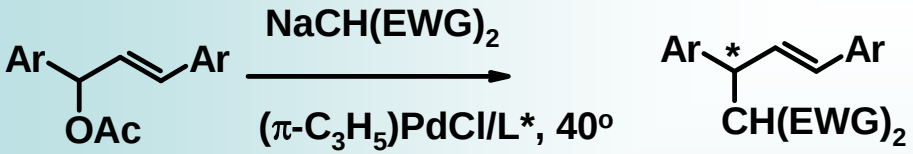
R = ^{i}Pr, ^{t}Bu





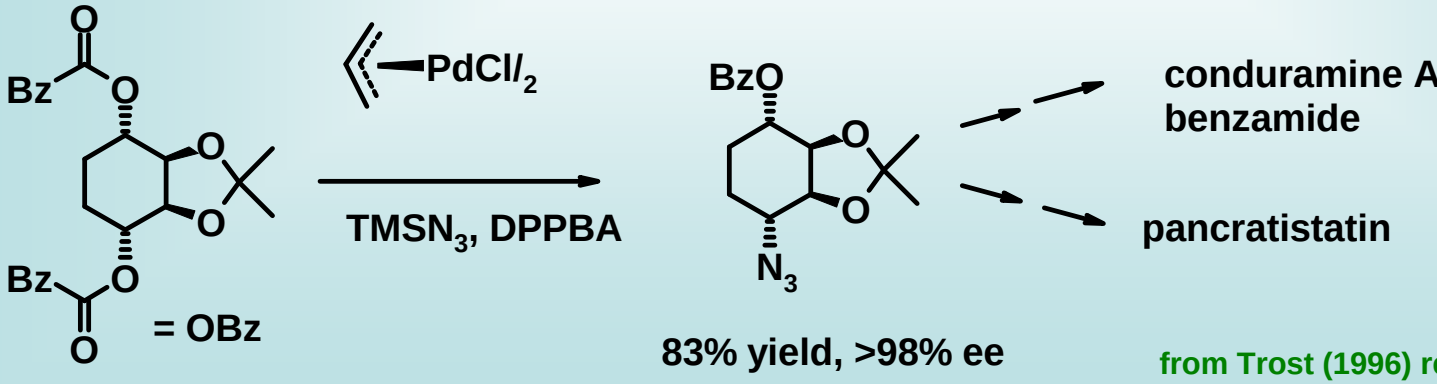
BOX (Bis-oxazoline ligands)

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.

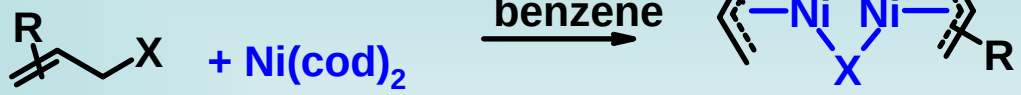


83% yield, >98% ee

from Trost (1996) review

π-Allylnickel Halides

Preparation



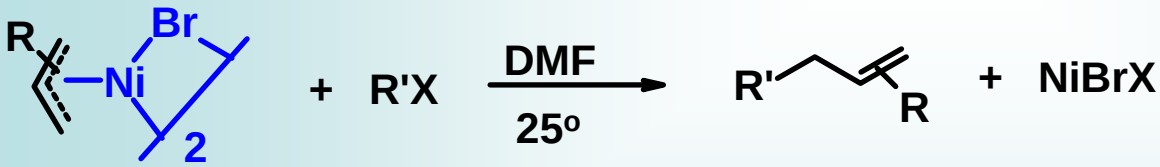
Hegedus, p.278

X = Br usually

or $Ni(CO)_4$

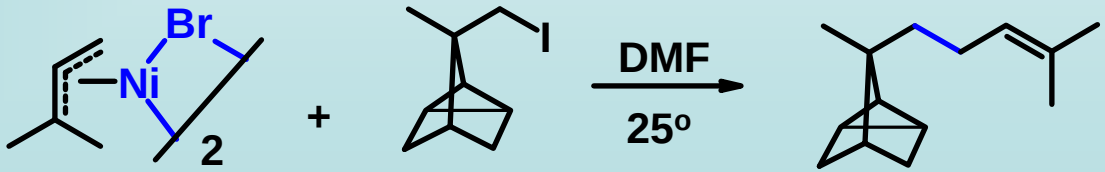
-These are isostructural, isoelectronic with the corresponding allylpalladium compounds
-Reactivity can be different, however

These can behave as if they are <u>nucleophiles</u> themselves, and will allylate organic halides (X = Br, usually)



-ketones and aldehydes are often tolerated (i.e., they survive this rxn at RT)
-esters are tolerated well

Regiochemistry - reaction occurs at less substituted allyl terminus



α-santelene

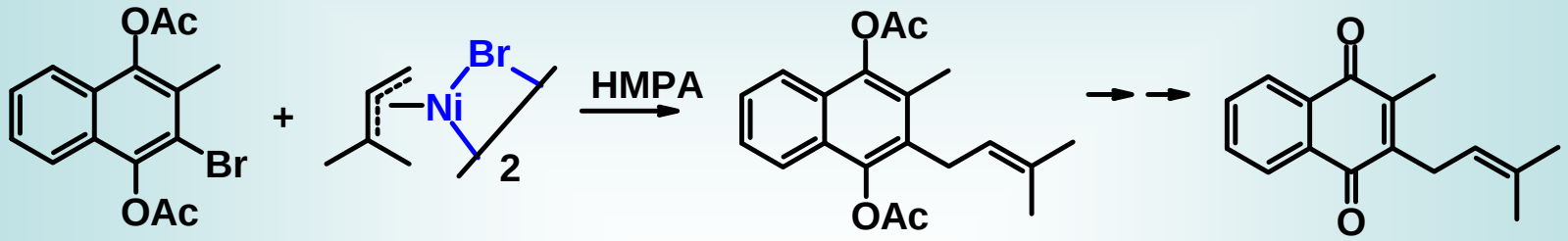
So who cares?

Look carefully at the above; the centre that's being attacked is neopentyl (i.e., $R_3C\text{-}CH_2\text{-}X$)

-neopentyl centres are normally forbidden for nuceophilic (S_N2) substitution

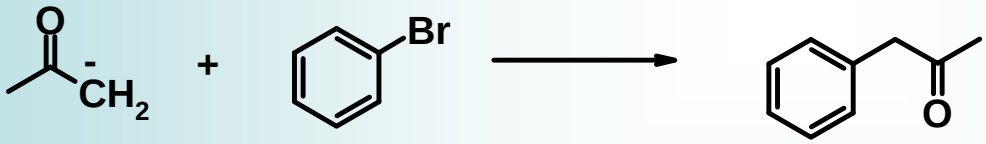
-works just fine here

-Generally true - rxn works well in cases where S_N2 is impossible (i.e., aryl halides)



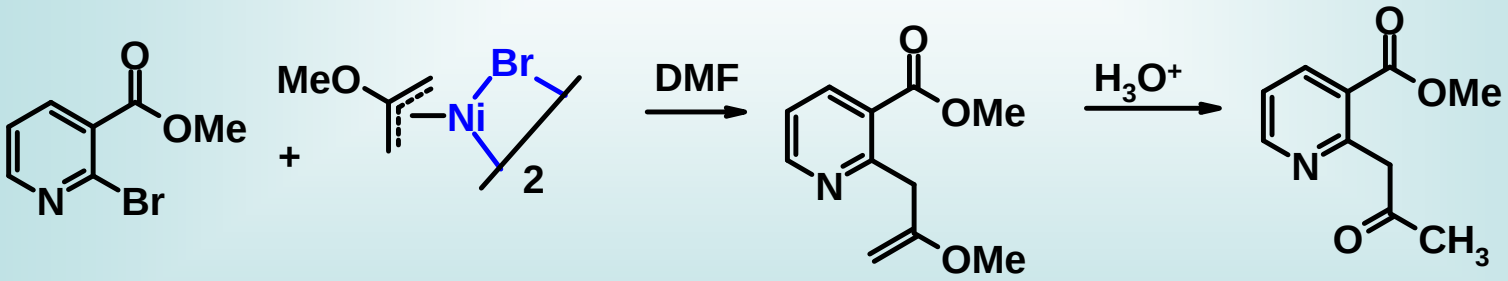
vitamin K analogue

and if you want to do...



-this is very tough directly

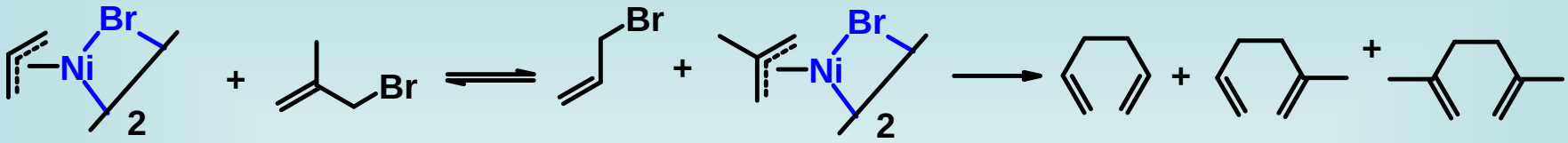
But..



Hegedus, L. S.; Stiverson, R. K. *J. Am. Chem. Soc.* 1974, *96*, 3250.
Hegedus, L. S. et al *J. Org. Chem.* 1977, *42*, 1329.

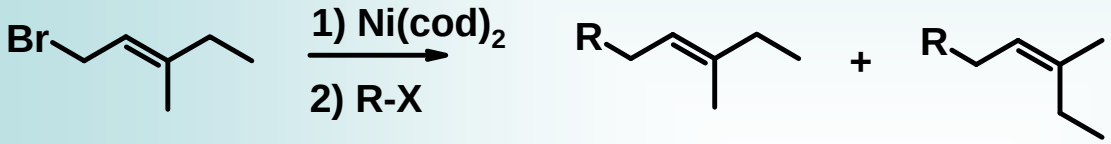
Works with aryl, vinyl, 1°, 2°, 3° alkyl bromides and iodides

However, allyl halides 'scramble'

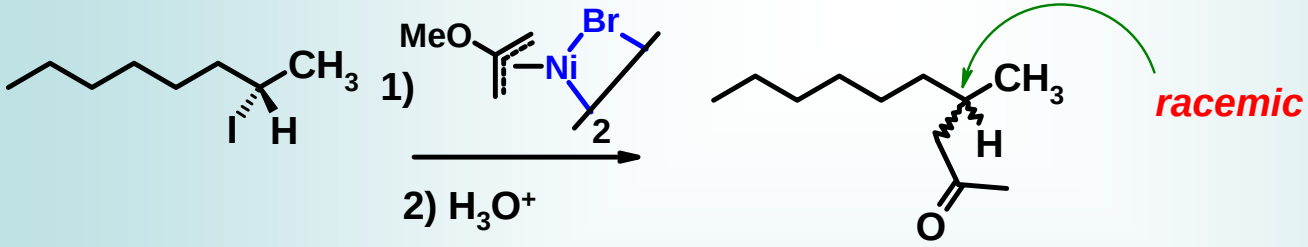


Other points

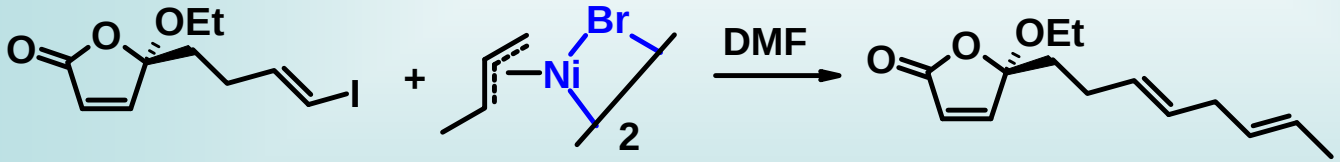
-like allylPd's the allyl fragment loses its stereochemical integrity



-chiral (and enantiomerically pure) 2° alkyl halides *racemize*



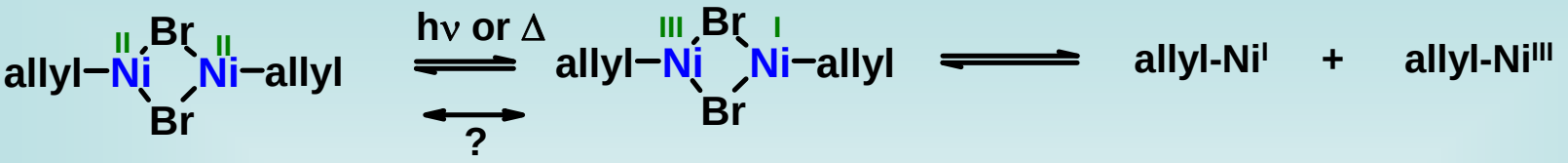
-while vinyl (alkenyl) halides retain their stereochemical integrity



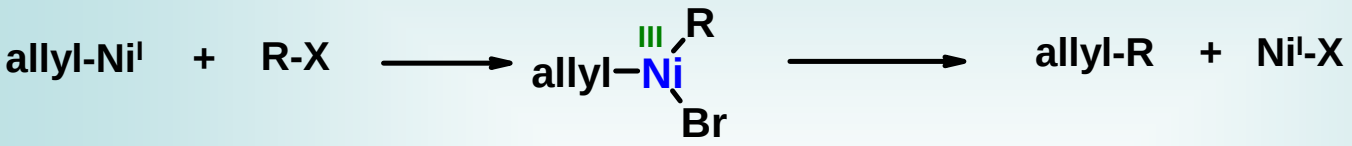
Hegedus believes that this is all due to the interventional of Ni^{I} and Ni^{III} as well as Ni^{II}

Hegedus, L. S.; Thompson, D.H.P. *J. Am. Chem. Soc.* 1985, *107*, 5663.

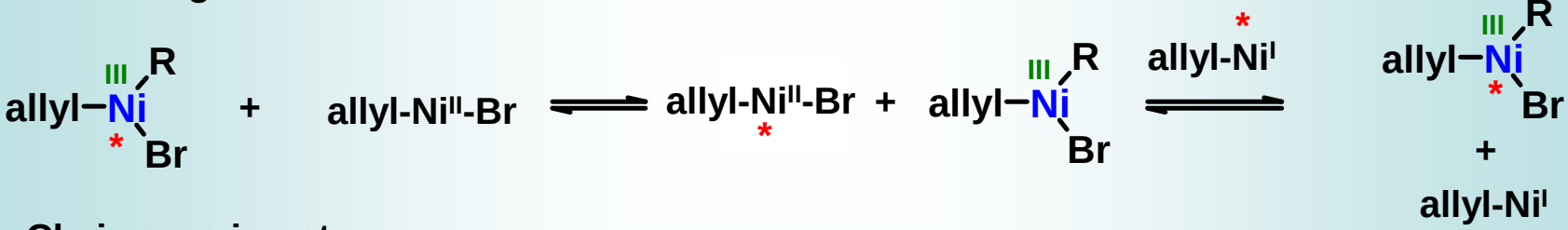
Initiation



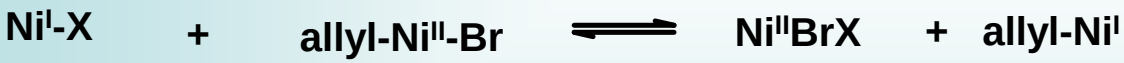
Oxidative addition/reductive elimination



Scarmbling of R



Chain carrying step



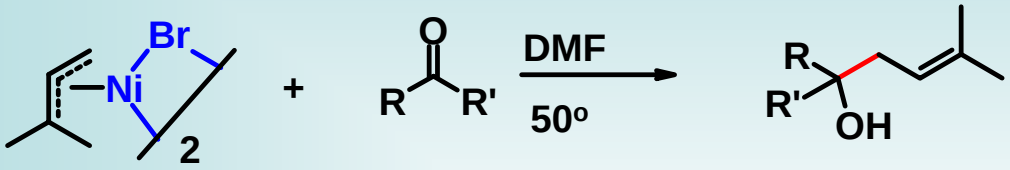
Scrambling of R goes with <u>inversion</u>, i.e., S_N2 like - therefore occurs with alkyls, but <u>not</u> alkenyls

The rest is like you expect - for alkyls, oxidative addition is with inversion, reductive elimination with retention
- for alkenyls, oxidative addition with retention, reductive elimination with retention

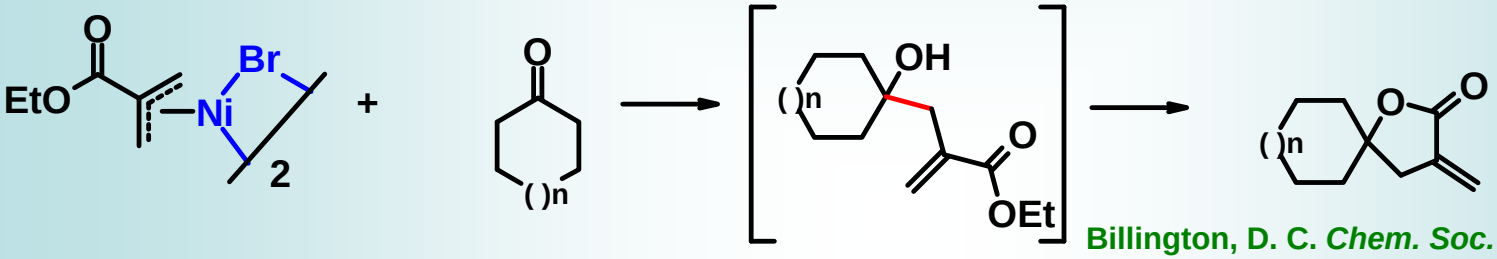
Other electrophiles

-although organic halides react preferentially, these allylnickel species will react with aldehydes and the more reactive ketones at ca. 50°C

-ordinary acyclic aliphatic and α,β-unsaturated ketones only react sluggishly

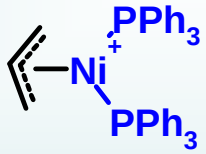


-example of use in spirocyclic α-methylene-γ-butyrolactones



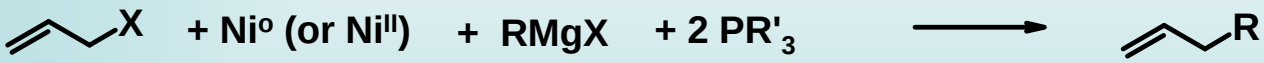
Billington, D. C. *Chem. Soc. Rev.* 1985, *14*, 93.

π-Allylnickels as Electrophiles

With two phosphine ligands 

does pretty much the same chemistry as α π-allylpalladium complexes

-what's unusual? - successful coupling of Grignard reagents, i.e.,

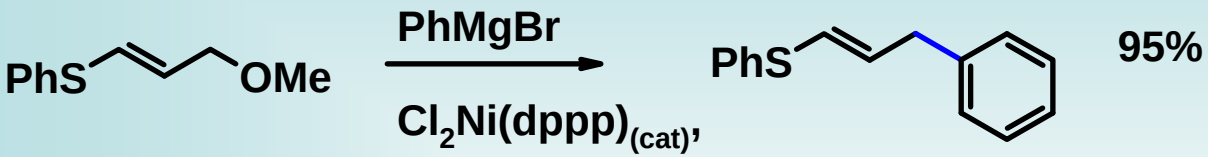


-large variety of X, including -Br, -Cl, -Oalkyl, -OAr, -$OSiR_3$, -OH, -OTHP, -SR

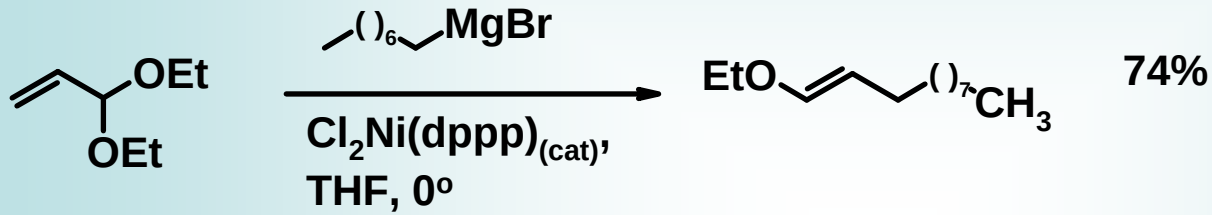
-the R of RMgX is suprising....R = Ar, or ***2° or 1° alkyl***

-β-hydride elimination is apparently a lesser problem in alkyl-Ni

β-elimination step for R = alkyls is often slow enough that one can get reasonable amounts of C-C bond formation



Sugimura, H.; Takei, H.
Chem. Lett. 1984, 351



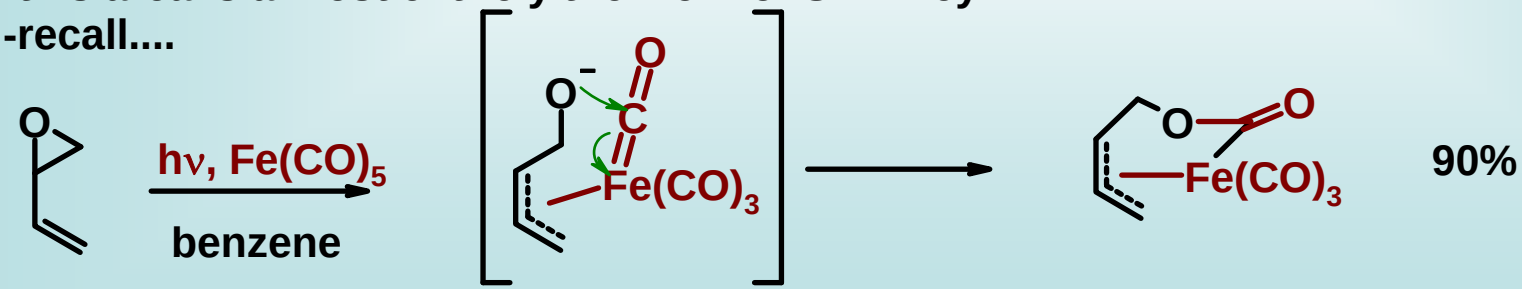
for work with chiral phosphine ligands, see:

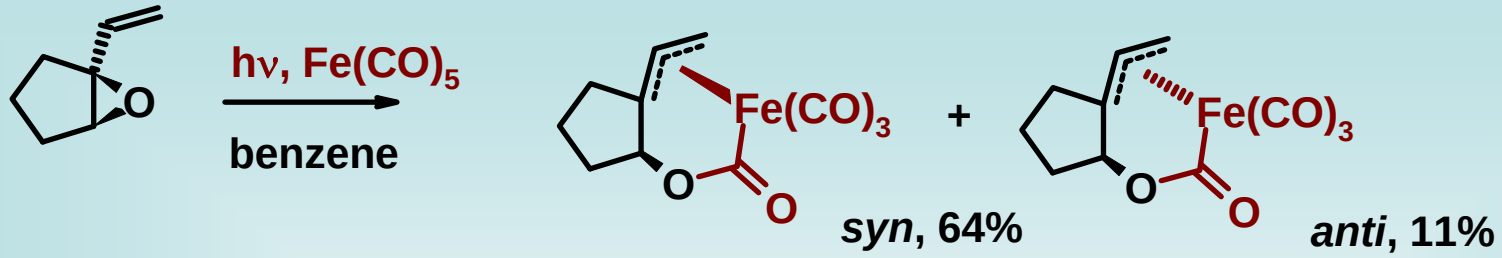
Hayashi, T., et al *J. Organomet. Chem.* 1985, *285*, 259.
Cansiglio, G., et al *Tetrahedron* 1986, *42*, 2043.

-Work in this area has slowed drastically since the mid 1980's

π-Allyliron Tetracarbonyl Lactone Complexes

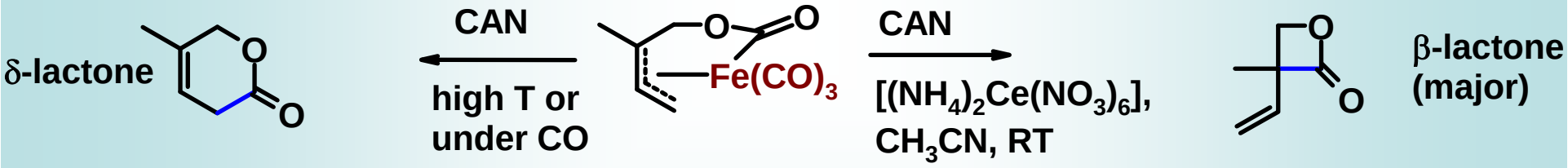
-this area is almost entirely the work of S. V. Ley
-recall....



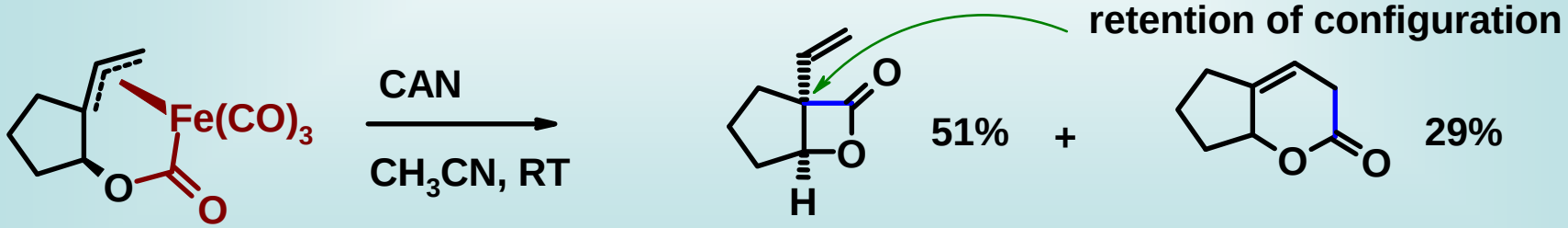


-Note: Photochemical conditions usually give retention (completely) - in above case, one can actually separate the diastereomers chromatographically

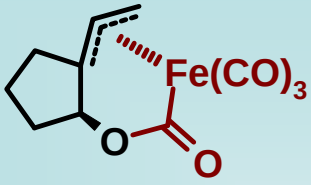
-when one attempts the typical oxidative metallation, it causes *reductive elimination* and therefore C-C bond formation - with two possible outcomes



Note: The stereochemical nature of the reductive elimination step is *retention*

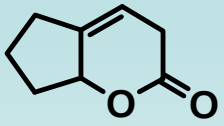


while, conversely



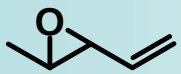
CAN

CH_3CN, RT



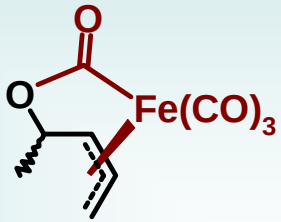
likely because the *trans* fused β-lactone would be impossibly strained

Examples of the use of this in the synthesis of δ-lactones



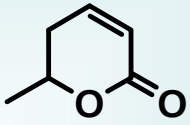
$Fe_2(CO)_9$

THF

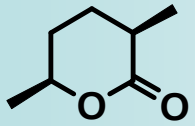


195°, 60 atm CO

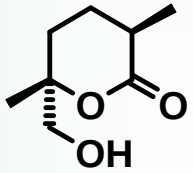
benzene, 73%



parasorbic acid lactone (racemic) -naturally occurring lactone from *sorbus acucupara*



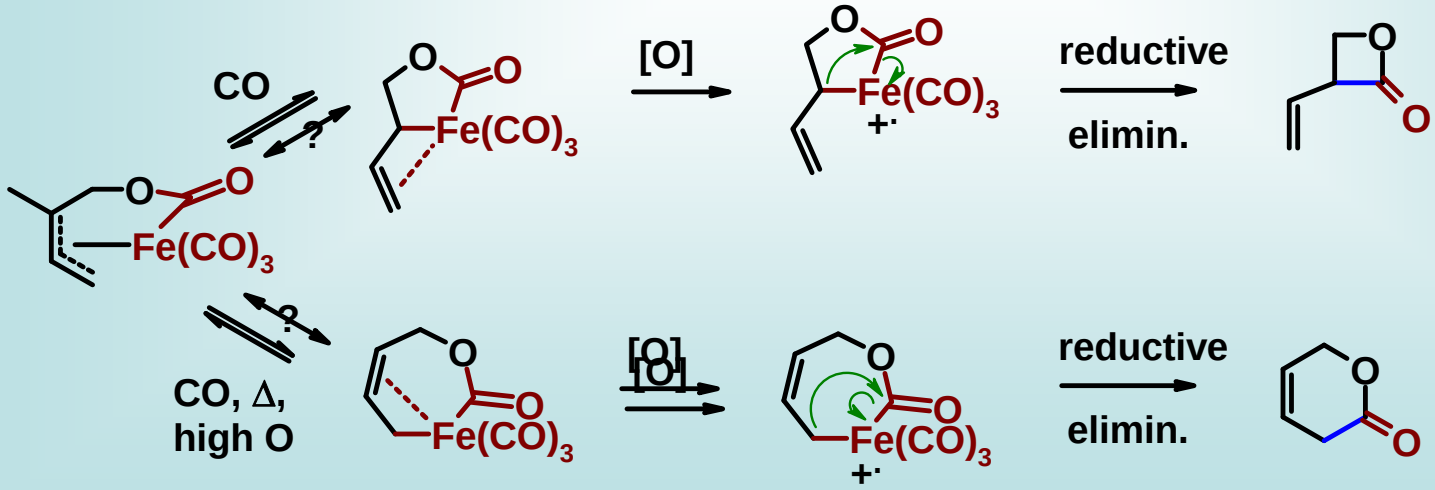
carpenter bee pheromone



malyngolide

Ley, S.V. et al *J. Organomet. Chem.* 1985, *285*, C17.

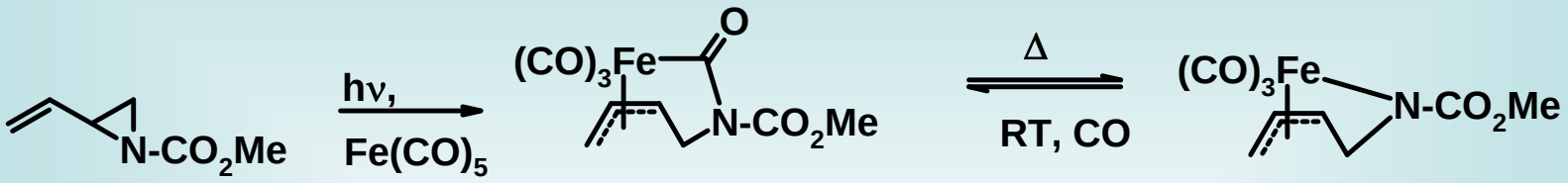
The two routes to C-C brond formation



π-Allyltricarbonyl Lactam Complexes

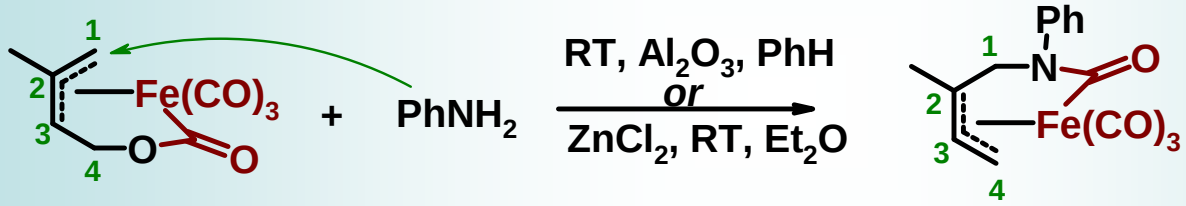
-these have had a larger impact than the corresponding lactone complexes

Preparation - less common

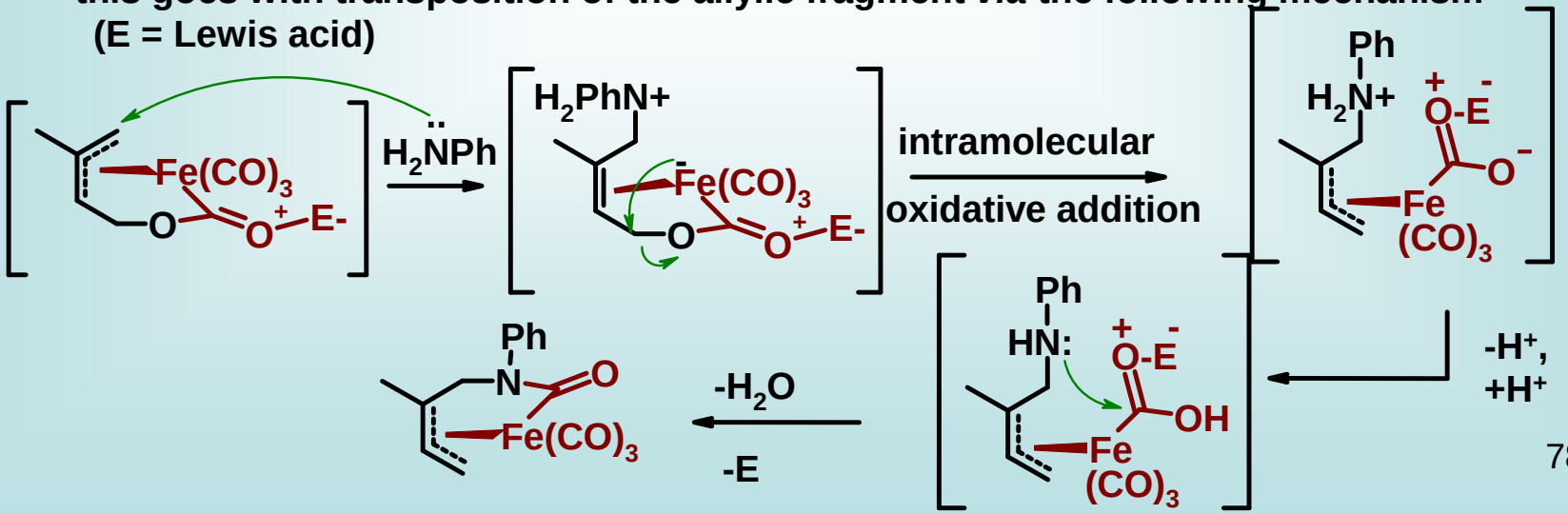


-but, vinyl aziridines aren't all that readily accessible, so....

-can be made more readily from the lactone complexes, through Lewis acid mediated substitution



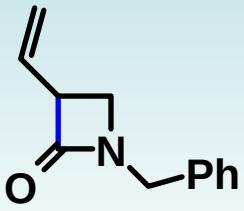
-this goes with transposition of the allylic fragment *via* the following mechanism (E = Lewis acid)



-when these compounds are oxidized, the reductive elimination is more highly selective for the β-lactam

-30° - RT

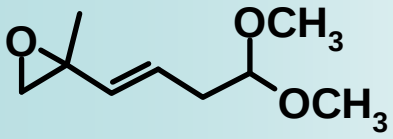
CAN, EtOH, 72%



β-lactam
(azetidinone)

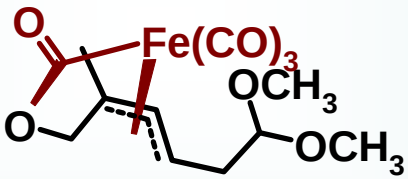
-these 3-alkenyl-2-azetidinones are not so readily accessible for other methods

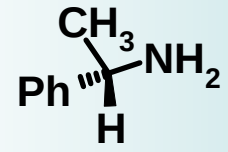
-example of synthetic use (+)-thienamycin



hν, Fe(CO)5

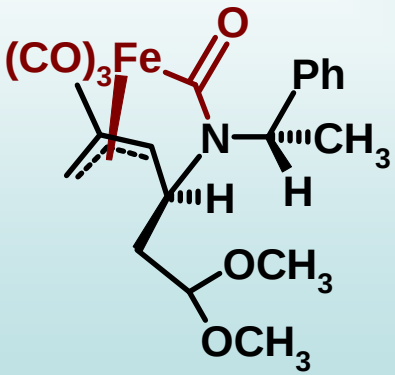
benzene, RT



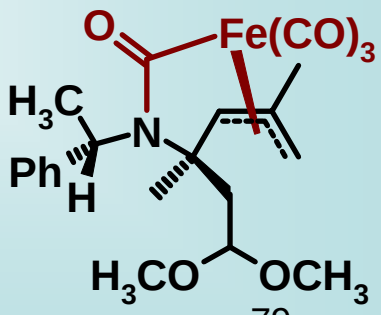


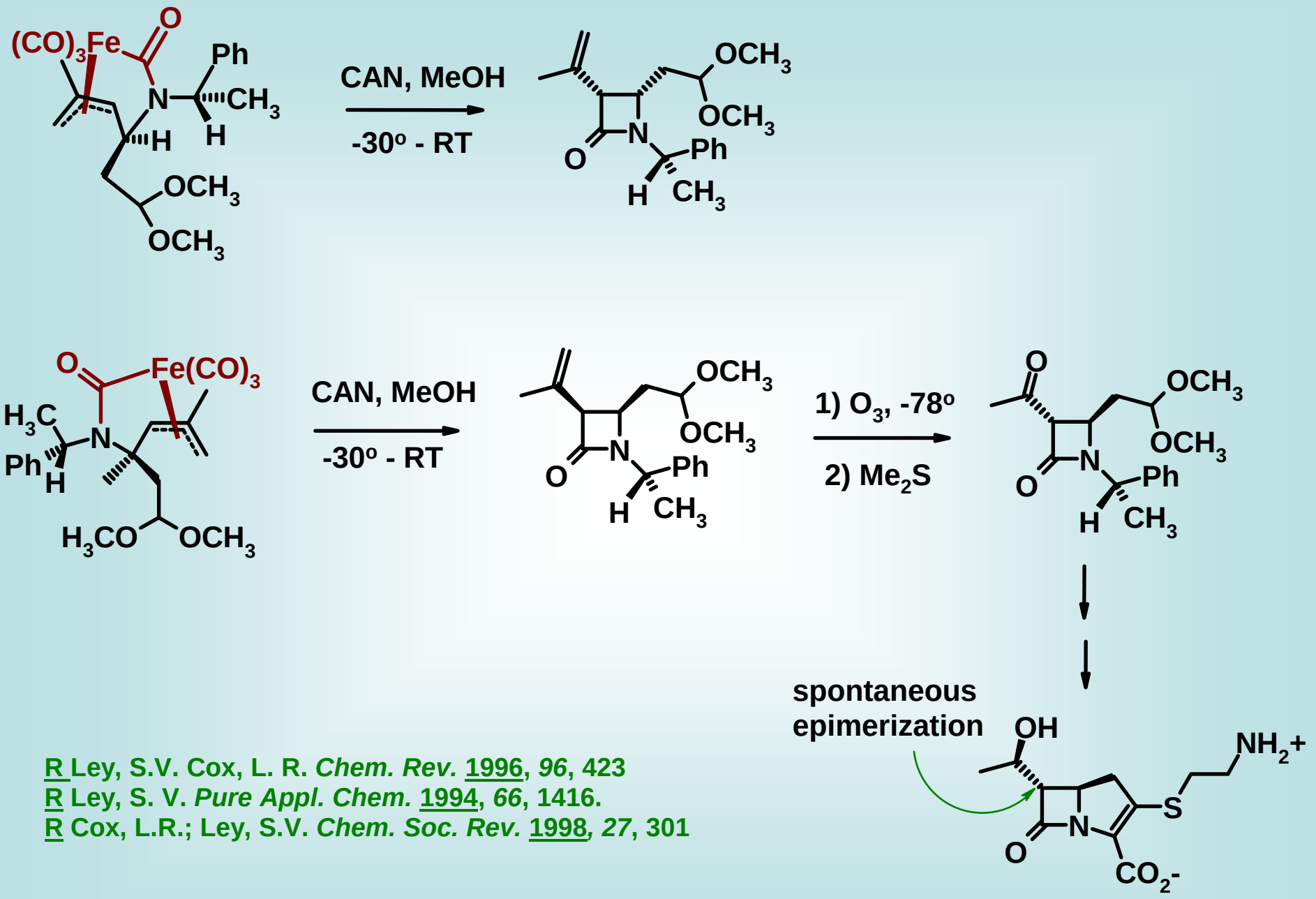
ZnCl2-TMEDA,
Et2O/THF

-can separate the two diastereomers chromatographically



+





R Ley, S.V. Cox, L. R. *Chem. Rev.* 1996, *96*, 423
R Ley, S. V. *Pure Appl. Chem.* 1994, *66*, 1416.
R Cox, L.R.; Ley, S.V. *Chem. Soc. Rev.* 1998, *27*, 301

(+)-thienamycin