Since time is limited we will talk about some specific chemistries of Ru (group 8), Rh, and Ir (group 9)

Electronegativity: Fe(1.83), Ru(2.20); Os(2.20)
Co(1.88), Rh(2.28); Ir (2.20)
Note: Electronegativity of H is 2.2 and C is 2.55

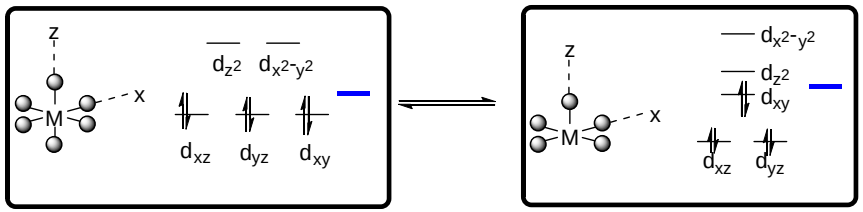
Group 8: 97% of crystal structures are of 18e- compounds. +2 oxidation state + six 2e- ligands = 18e-.

Most common oxidation states.

Fe: +2>+3>0
Ru: +2>+3>>+4
Os: +2>+4>+3

+2 oxidation state = d^6 = octahedral

Note: Since they are 18e- complexes, most Ru catalysts will require ligand dissociation to form active catalyst species.



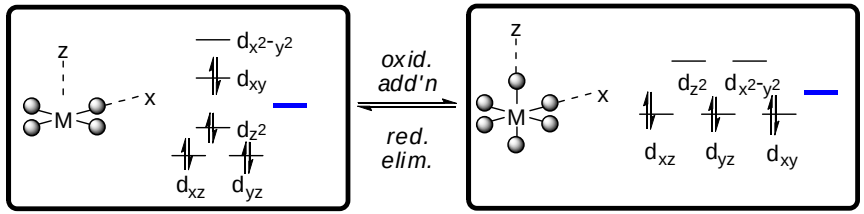
Ru(II) d^6 Ru(II) d^6

Group 9: +3 oxidation state is very common (d^6), but other oxidation states become prevalent.

Co: +2>+3>+1
Rh: +1>+3
Ir: +3>+1

Note: Rh and Ir have potential for clean 2e- oxidation/reduction processes…that's one reason they are efficient catalysts for many reactions.

d^8 metals are often excellent catalysts because they
A) have open coordination sites by virtue of sq. planar geometry.
B) can form ca. equally stable d^6 octahedral complexes upon oxidative addition.



Rh(I), Ir(I) - d^8 Rh(III), Ir(III) - d^6

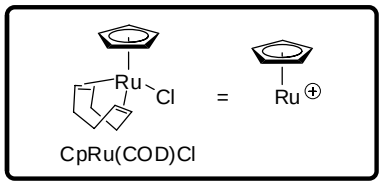
Ruthenium:

There are far too many ruthenium-catalyzed reactions to address directly in this course. Noyori Hydrogenation and Olefin Metathesis are the most common.

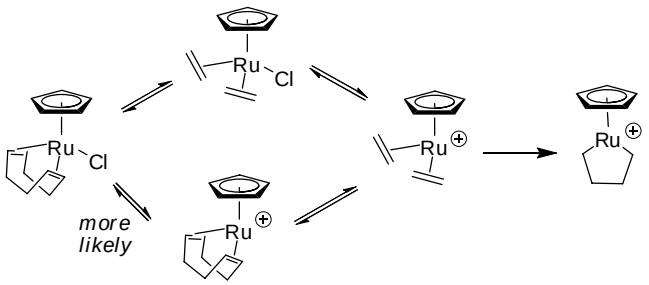
Non-metathesis C-C bond forming reactions. Nice reviews see: Trost, B. M. *CR* **2001** 2067; *ACIE* **2005** 6630. Murahashi, S. *CR* **1998** 2599.

Metallacyclopentanes and pentenes via reductive cyclization:

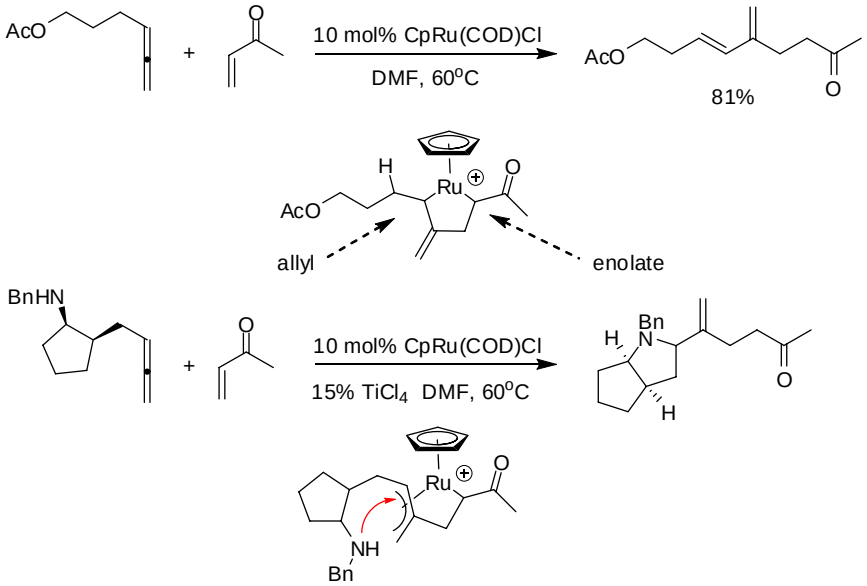
Because CpRu(COD)Cl has an ionizable chloride and a labile COD ligand, Trost equates it to the idealized cationic CpRu.



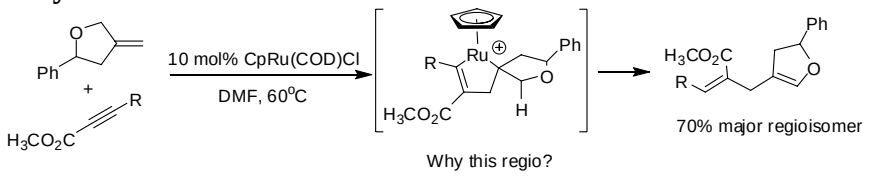
CpRu(COD)Cl



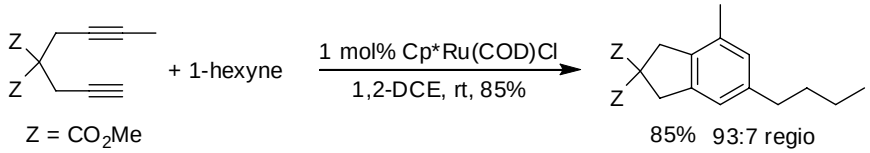
General Strategy: Reductive coupling of alkenes/alkynes then utilizing the resulting metallacycle.



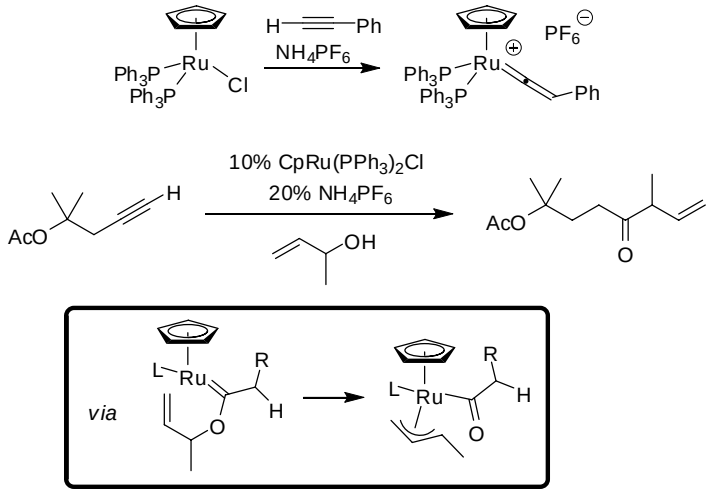
Alkyne-olefin



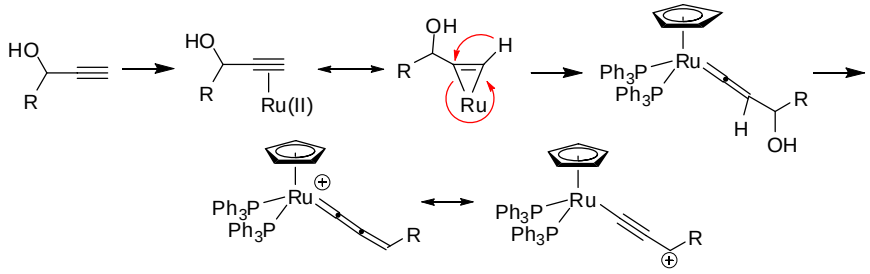
Alkyne-alkyne



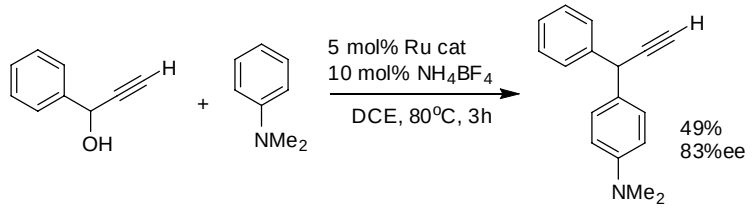
Vinylidene chemistry

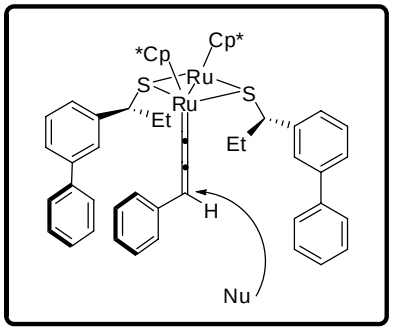


Allenylidenes:

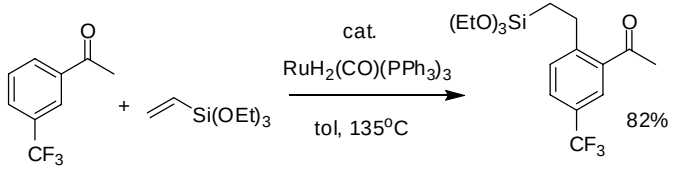


Asymmetric Arylation *ACIE* **2007**, 6488.

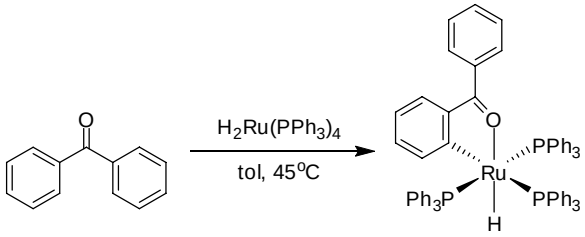




C-H activation. Murai, S.: One of the very first catalytic C-H activation/functionalization reactions. *Nature* **1993** 529; *BCS Jpn* **1995** 62.

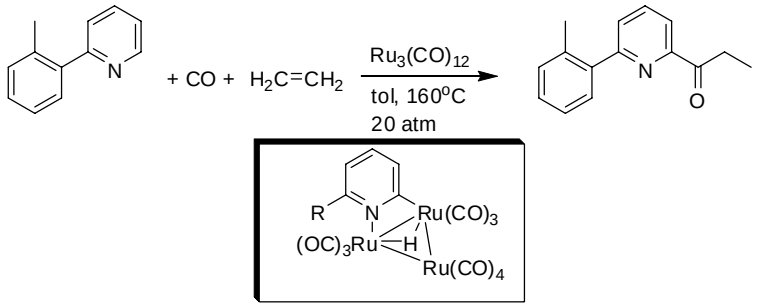


Note: The C-H activation was known: Halpern, J. *J. Organomet. Chem.* **1987** 155; *Pure Appl. Chem.* **1987** 173.



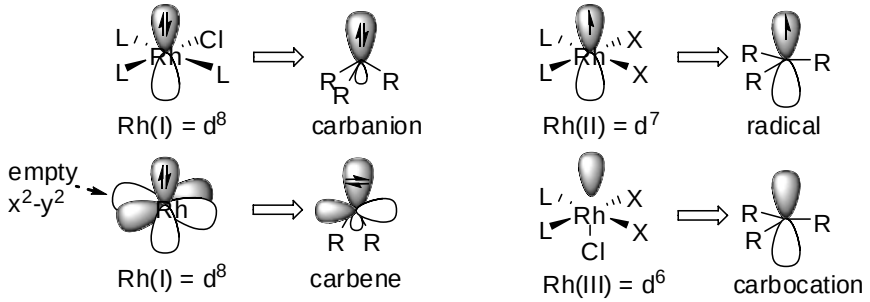
The activation was thought to be kinetically directed to the ortho positions, however Alan Goldman has shown that C-H activation of the meta- and para-hydrogens is faster, but ortho is thermodynamically favored due to chelation. *JACS* **2004** 13192.

$Ru_3(CO)_{12}$ clusters selectively activate C-H bonds α-to heteroatoms.



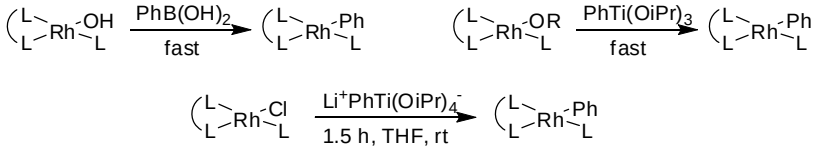
Rhodium

Isolobal Analogies: Halpern, J. *C&E News* **1966**, Oct 31, 68.



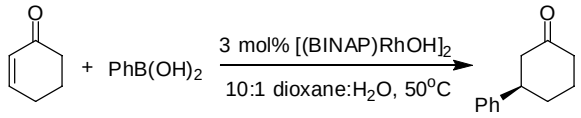
Conjugate Addition/Reduction of Enones.

Transmetallation of boronic acids to Rh(I) is facile. See Hartwig, J. F. *JACS* **2007** 1876.

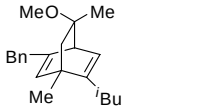


Note: Transmetallation occurs directly with Rh(I) precursors.
Conjugate additions of boronic acids and aryltitanium reagents. Hayashi, T.; Feringa, B.; Carreira, E….

Asymmetric additions:

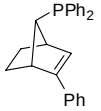


Brief Survey of Ligands:

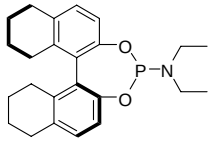


Carriera, E. *JACS* **2005** 10850
good for cinnamaldehydes
electron rich and
electron poor ArB(OH)$_2$

Hayashi, T. *JACS* **2003** 11509
good for enones, bulky acrylates
electron rich and poor ArB(OH)$_2$



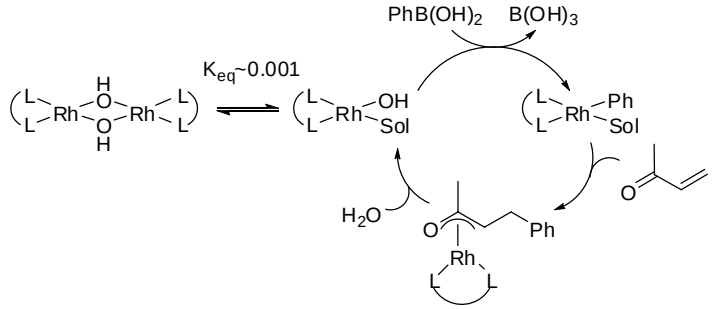
Hayashi, T. *JACS* **2007** 2130
good for enones, maleimides
electron rich and poor ArB(OH)$_2$



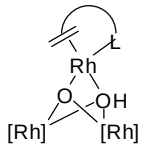
Feringa, B. L. *JOC* **2003** 9481
good for cyclic enones and acrylates
electron rich ArB(OH)$_2$

Hayashi has done beautiful mechanistic work on the conjugate addition of boronic acids and titanates. See: B: *JACS* **2007** 2130; *JACS* **2006** 3904; Ti: *PNAS* **2004**, 5445.

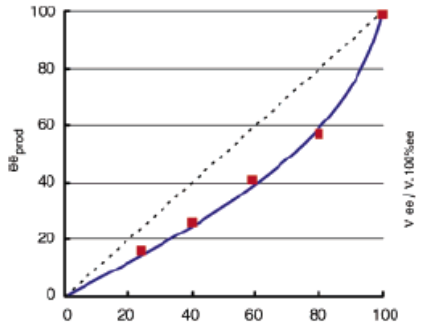
Summary of the mechanism. (Transmetallation, Carborhodation, Hydrolysis)



Note: Catalyst is a dimer, so rate = k[Rh]$^{0.5}$[PhB(OH)$_2$]^1[MVK]^0
Rate-limiting formation of Rh-Ph complex.
Rhodium trimers (with phosphine-alkene chelating ligands) are more reactive than the dimers: Hayashi, T.; *JACS* **2007**, 2130.



ee of product has a nonlinear dependence on the ee of the ligand.

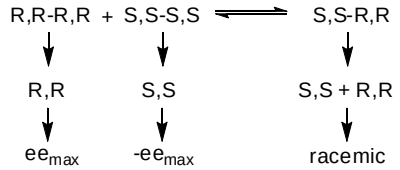


From Hayashi, T. *JACS* **2006** 3904. Phosphine-alkene complexes also show nonlinear effects.

Nonlinear effects on ee often result when dimeric catalyst species exist.

Imagine that your ligand is 80% ee. 90% of the ligand is R,R and 10% is S,S.

You will have the possibility for homochiral dimers R,R-R,R and S,S-S,S as well as heterochiral dimers R,R-S,S.

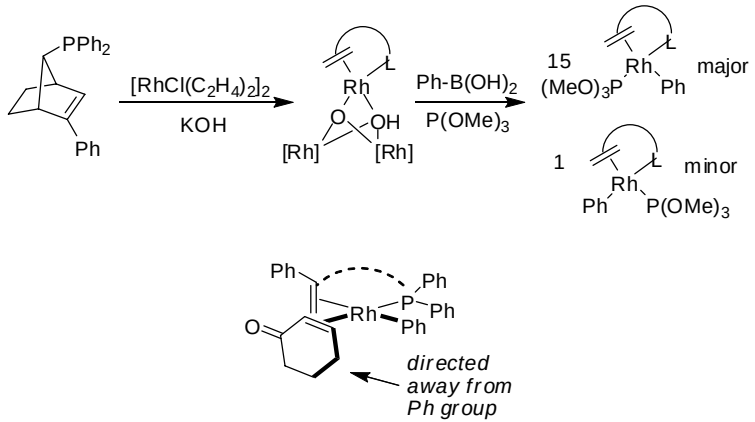


Consider: If the heterochiral dimer is very stable, then essentially all of the minor (S,S) enantiomer is tied up in an unreactive state and the ee_{obs}>ee_{Lig}. This is **asymmetric amplification**.

Much Worse: If the homochiral dimers are much more stable then the heterochiral dimer is more reactive and will produce more racemic product.

Origin of enantioselectivity (of course varies with ligand).

Note: transmetalation preferentially occurs trans to the weaker donor ligand. The consequence is that substrate (or external ligand) binds *trans* to phosphine (L).

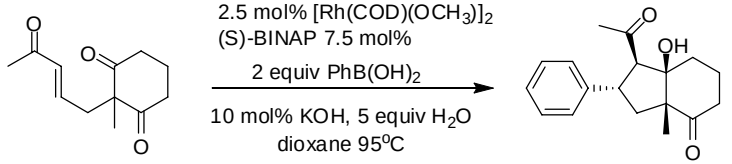


Why this geometry? Strong donors are *trans* to good π-acceptors.

Note: The conjugate addition creates a rhodium enolate intermediate. Gilbert Stork pioneered the use of enones as latent enolates.

Reductive Aldol. Conjugate reduction-aldol cascade work well for either hydride or alkyl additions.

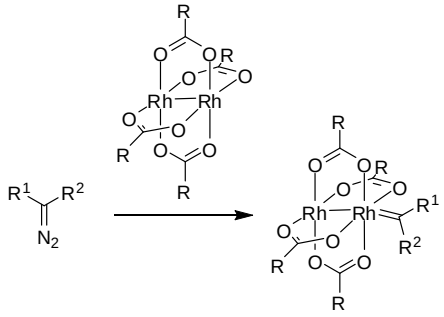
Desymmetrization by conjugate addition-aldol. Krische, M. J. *PNAS* **2004** 5421; *JACS* **2003** 1111.



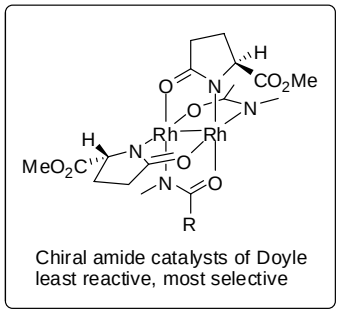
97%, >99:1 dr, 90% ee

Rh-carbene chemistry. Good reviews. Davies, H. M. L. *Chem. Rev*. **2003** 2861. Doyle, M. P. *Chem. Rev*. **1998** 911.

Carbenoid transfer catalyst: Want a metal that has an open coordination site, is a good σ-acceptor (binds carbene) and does not backbond well (electrophilic carbene). Electron withdrawing ligands also help. Bulky ligands may also favor C-H insertion.

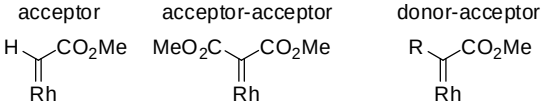


R = CH_3 less reactive, more selective
R = CF_3 more reactive, less selective



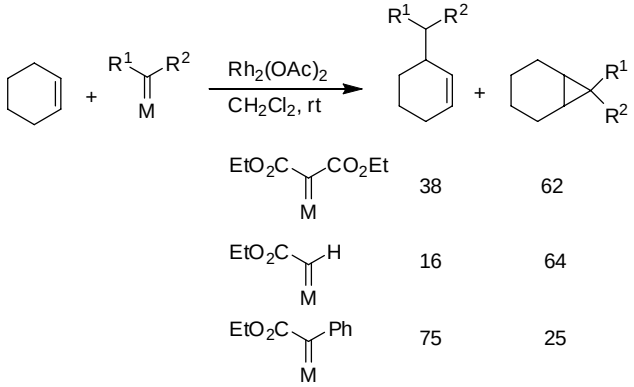
Chiral amide catalysts of Doyle
least reactive, most selective

Carbenoid classes:

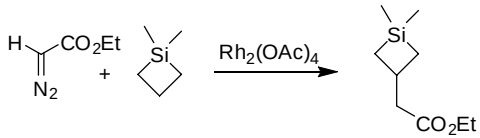


R = Ph, vinyl, alkynyl

Cyclopropanation vs. C-H insertion.

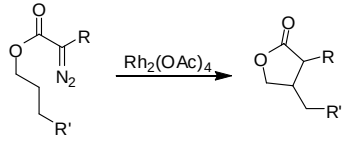


Note: The more electrophilic the carbene, the greater tendency to undergo cyclopropanation.

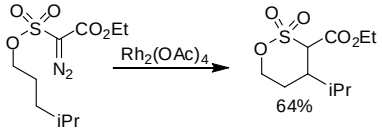


Si stabilizes β-cations and α-anions. This expt shows that there is + charge buildup on the carbon undergoing C-H insertion. C-H insertion α-to donor heteroatoms is also favored and 3°>2°>1°>Me

Intramolecular C-H insertions.

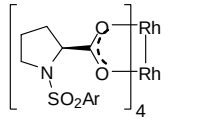


Taber, D. *JACS* **1986,** 7686.



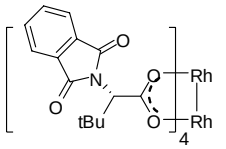
Novikov, A. V. *OL* **2007,** 61. Du Bois, J. *OL* **2007,** 4363.

Some catalysts for asymmetric carbenoid reactions.

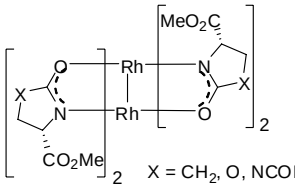


Ar = *p*-$(C_{12}H_{25})C_6H_4$

Rh_2(S-DOSHP)$_4$

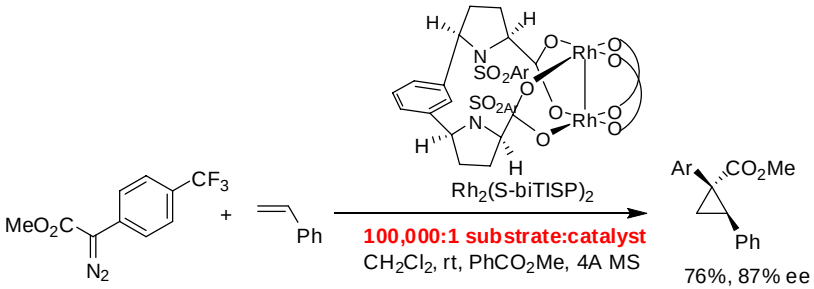


Hashimoto, *TL* **1990** 5173; *OL* **2002,** 3887



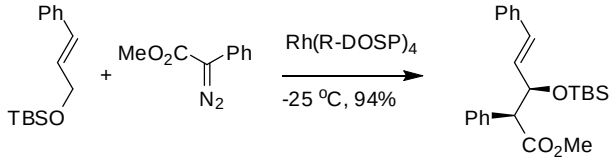
Doyle, M. P. in Ojima *Catalytic Asymmetric Synthesis*; CH5

An example of asymmetric cyclopropanation. Davies, H. M. L. *OL* **2003** 1403.



Note: bidentate acetate ligand + $PhCO_2Me$ additive lead to long catalyst lifetime. The benzoate probably binds to, and stablizes the unstaturated Rh-catalyst, preventing decomposition.

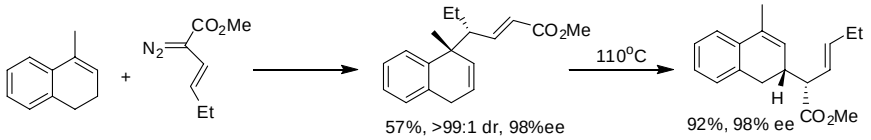
An example of asymmetric C-H insertion from Davies, H. *Org. Biomol. Chem*. **2005** 4176.



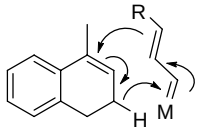
> 97:3 dr, 88% ee

Note: Donor-acceptor carbenes are exceptional at intermolecular C-H insertion. Also, insertion next to heteroatoms is facile.

C-H activation-Cope-retroCope

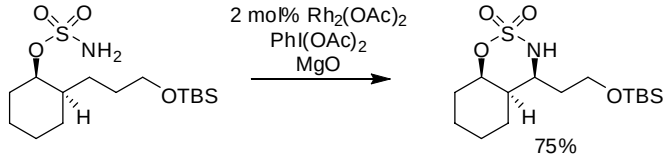


Note: The first product cannot be formed by direct C-H insertion followed by Cope rearrangement (it is thermodynamically less stable than the "direct C-H insertion product").

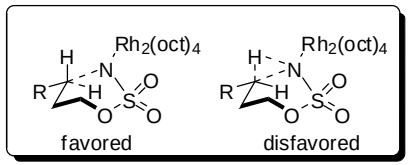


Amination by nitrene insertion: Du Bois, J. Modern Rhodium-Catalyzed Organic Reactions 2005, 379-416.

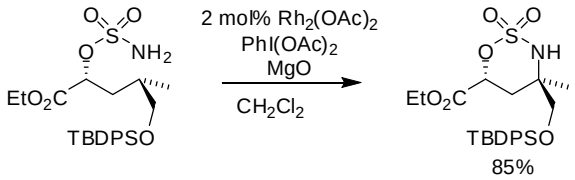
Stereoselective Intramolecular: Du Bois, J. *JACS* **2001** 6935.



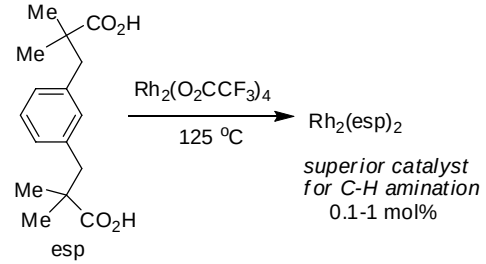
Model for stereoselectivity. *OL* **2003** 4823.



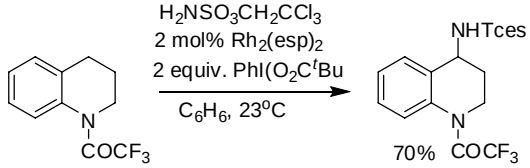
Stereospecificity. Du Bois, J. *JACS* **2002**, 12950.



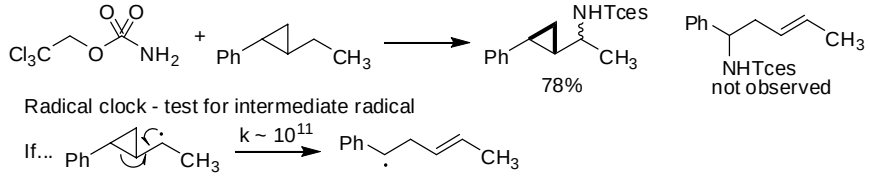
Better catalyst: *JACS* **2004** 15378.



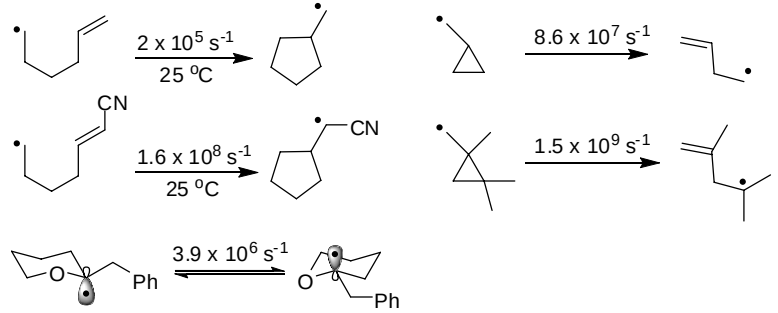
esp-catalyst allows intermolecular amination with the alkane as the limiting reagent. *JACS* **2007** 562.



Note: Iminoiodinanes are likely precursors to metal nitrenes.



Other radical clocks.



Hammett analysis:

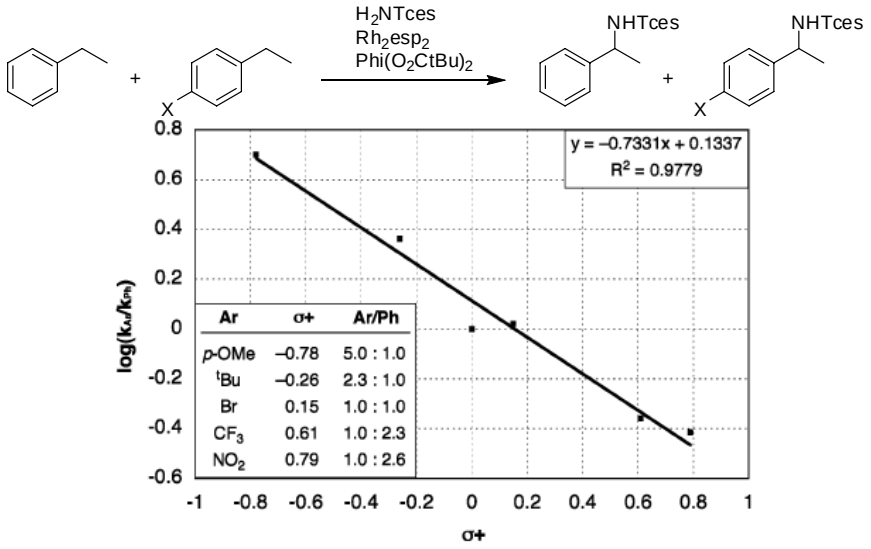
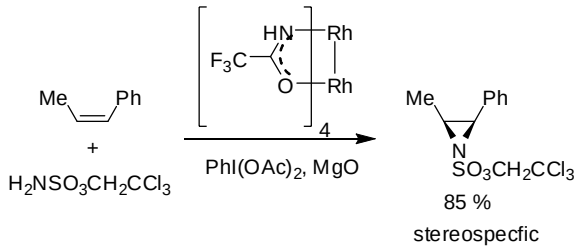


Figure 6. Hammett analysis through competition experiments with *p*-substituted ethylbenzene substrates.

Blatently stolen from : DuBois, J. *JACS* **2007** 562.

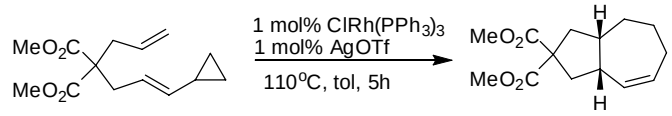
Aziridination. Intramolecular with electron deficient Rh-catalyst. *JACS* **2002**, 13672



Note: The aminating reagent cannot undergo intramolecular C-H insertion.

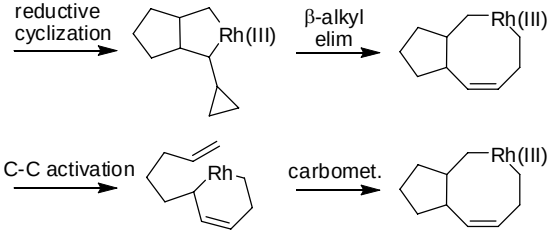
Carbocyclizations.

[5+2] Wender, P. A. *JACS* **1998** 1940. Intermolecular [5+2] *JACS* **1998** 10976.



Note: $[Rh(CO)_2Cl]$ is a superior catalyst and (arene)Rh(I) complexes are even better. *ACIE* **2002** 4550.

Mechanistic possibilities.

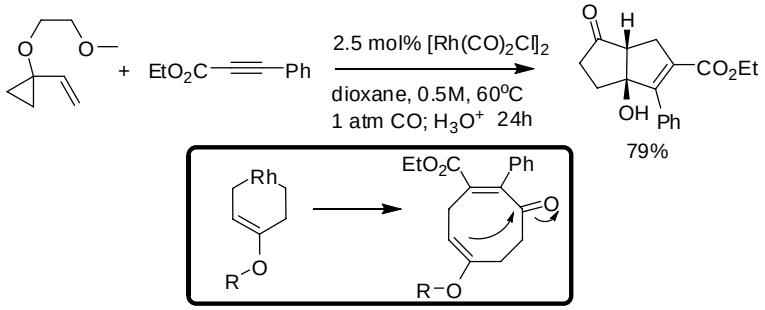


Observation: reaction of vinylcyclopropane with Rh(CO)2Cl produces an intermediate. Reaction of this intermediate with alkyne produces product.

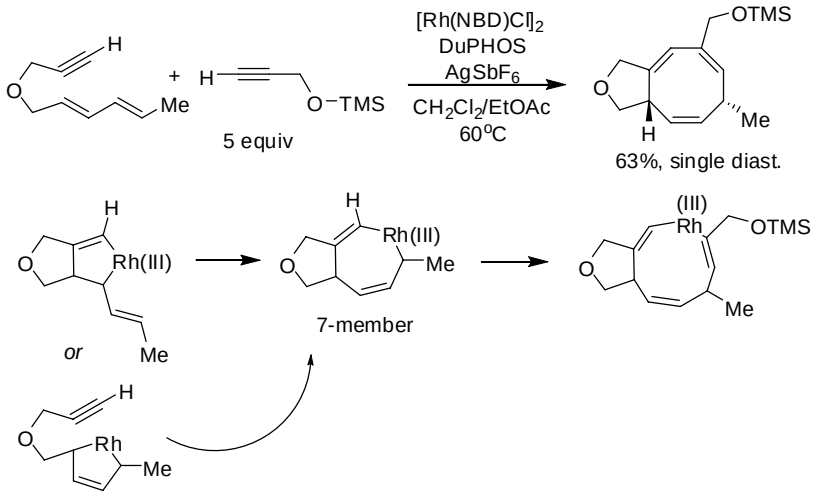
Calculations also support C-C activation-carbometalation-reductive elim. path. Migratory insertion is predicted to be rate-limiting. Houk and Wender *JACS* **2004** 9154.

Many variations, the simplest being…

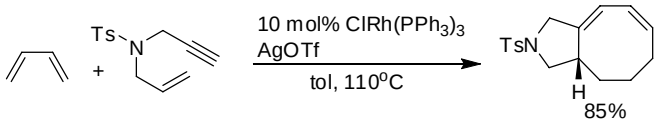
[5+2+1] Wender *JACS* **2002** 2876.



[4+2+2] Gilbertson, S. *JACS* **2002** 8784.

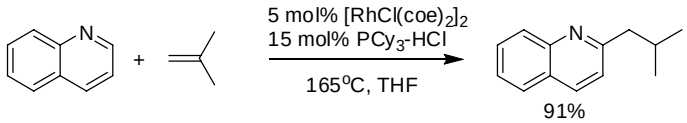


Also, Evans, P. A. *JACS* **2002** 8782.

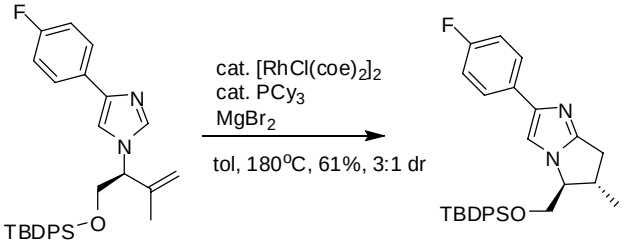


Note: Run under an atmosphere of butadiene.

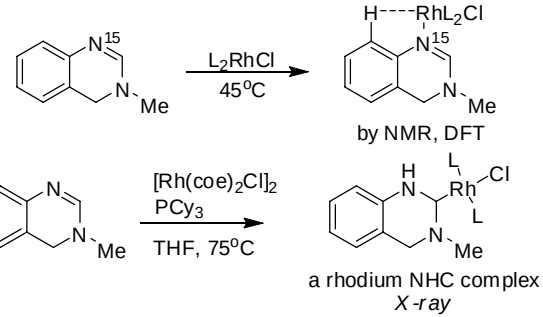
C-H activation Bergman, R. G.; Ellman, J. *JACS* **2007** 5332



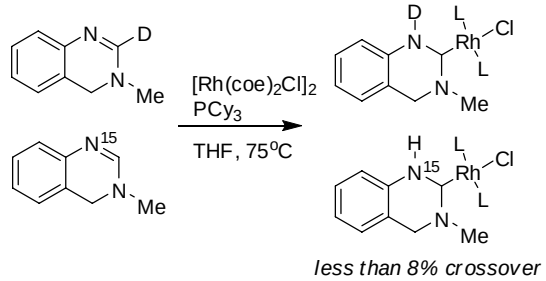
JACS **2007** 490.



Mechanism: Bergman, Ellman, *JACS* **2006** 2452.



Note: an NHC complex undergoes addition to alkenes, so they might not be such innocent ligands after all.



Reaction is intramolecular.

Summary of mechanism.