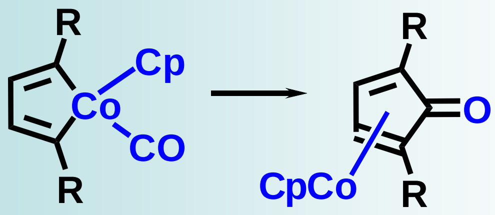
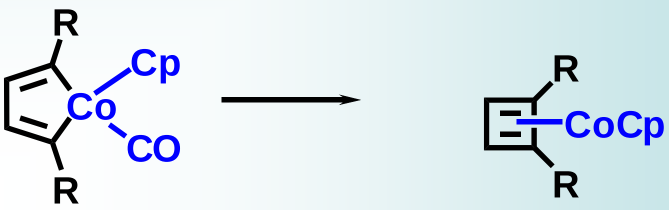
3. Interrupting the 2+2+2

-there are a number of reactions that start to follow this 2+2+2 pathway, getting to the metallacyclopentdiene or metallacyclopentene, and then go differently
-only a time to look at a couple, but there are many more in synthesis
see: *Topics in Organometallic Chemistry* 2006, *19* entire issue

The Pauson-Khand Reaction

-two of the side products from the 2+2+2 are:



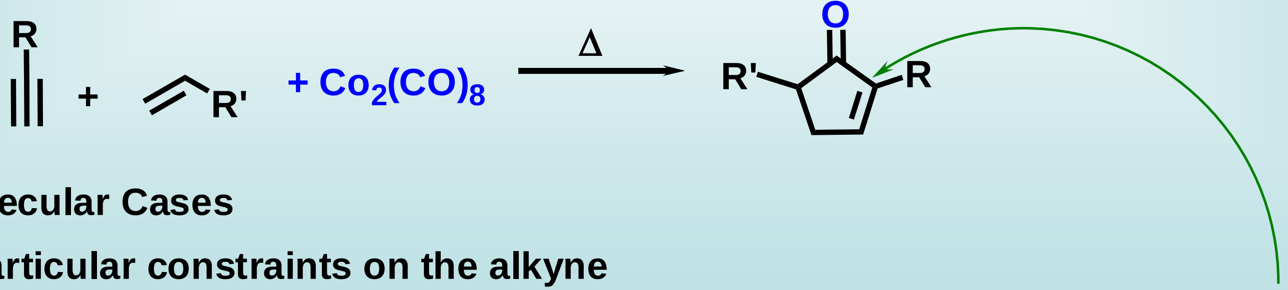


(Fe : Knolker, H.J.)

-cyclopentadienones are not very stable compounds, but if one of the C=C's is reduced, you have very useful cyclopentenones

-this type of material is often obtained by using and alkyne, and alkene, and $Co_2(CO)_6$ (or an alkyne-$Co_2(CO)_6$ complex)

i.e.,

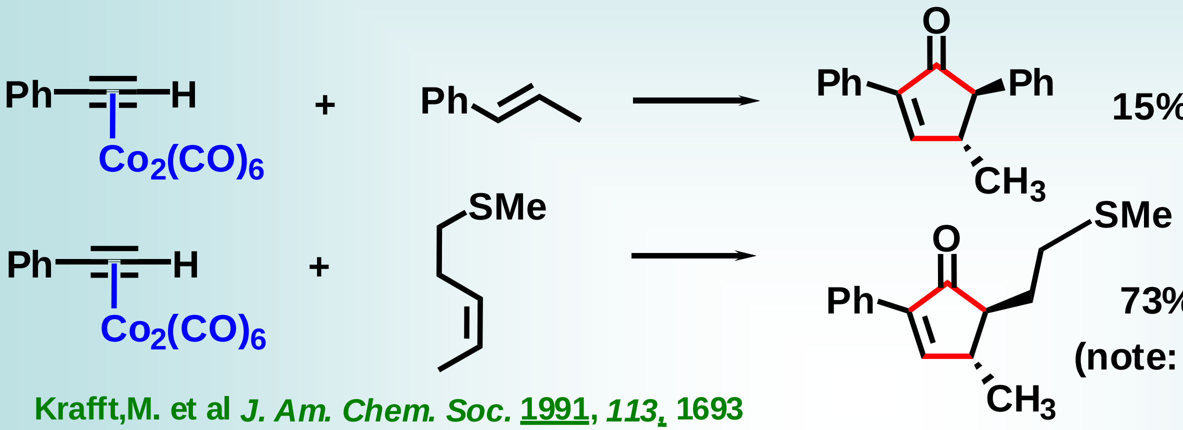


Intermolecular Cases

-no particular constraints on the alkyne
-if you have an unsymmetrical alkyne, larger groups end up next to C=O, as in

Alkene Partner

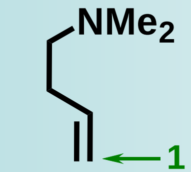
-simple alkenes don't work especially well, unless present in huge excess
(Note: this is making progress)
-strained alkenes, "non β-hydride" alkenes (bridged bicyclic akenes),
and alkenes with ligands attached (X = NR_2, SR, O?) give better yield, high regioselectivity



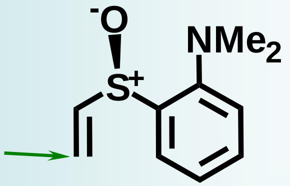
15% **ordinary alkene**

73% **coordinating substit.**
(note: trans)

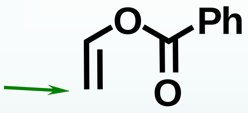
Krafft,M. et al *J. Am. Chem. Soc.* 1991, *113*, 1693



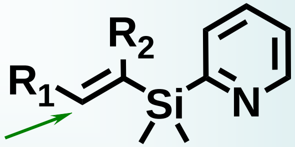
Krafft



Carretero
-also chiral

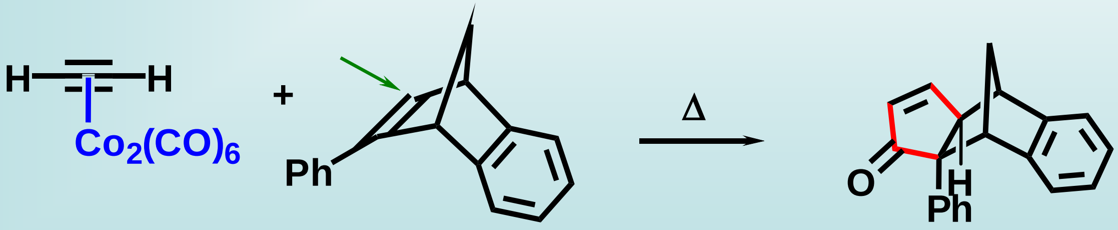


Kerr
-loses benzoate



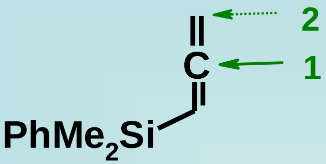
Yoshida (with $Ru_3(CO)_{12}$)
-loses Si

arrow is where
1st C-C bond
forms



bridged bicyclic alkene
(non β-hydride)

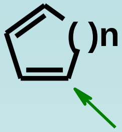
high %



Cazes (no β-H)

especially
n = small

even n = normal
with mild conditions



"no β-H"

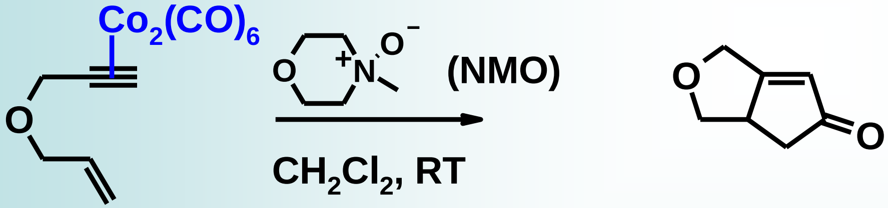
Reviews focussing on intermolecular reactions

R Gibson, S.E. et al *Angew. Chem. Int. Ed.* 2005, *44*, 3022.
R Laschat, S. *Synlett* 2005, 2547.

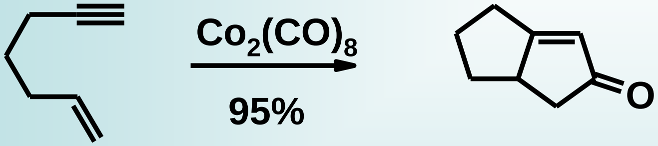
-except for sulphoxides, alkenes with EWG's rarely work

Intramolecular Cases

-reaction works much better when alkene and alkyne are in the same molecule

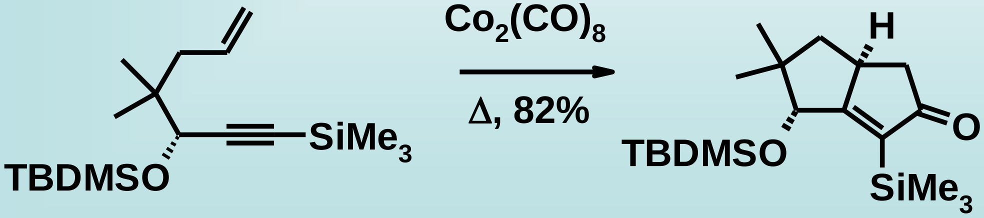


85%



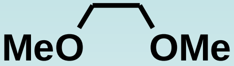
60% (old conds)

-often particularly good for all carbon bridges when there is a gem dialkyl in the bridge

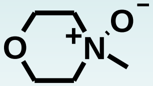


gem dimethyl or Thorpe-Ingold effect

-there are subtle stereochemical matters which are beyond this course's scope
-many recent advances have increased yields and allowed reactions under milder conditions

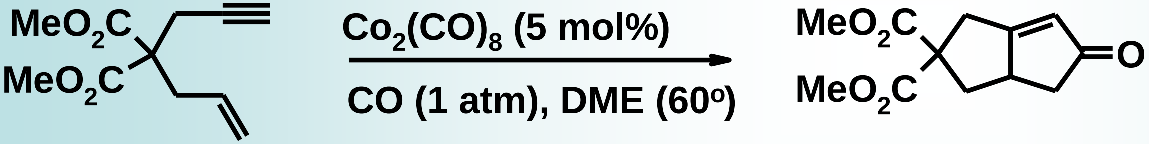
i.e., polar aprotic solvents (CH_3CN, DME 
)

-use of 1° amines ($CyNH_2$) and mercaptans (^nBuSMe) R Sugihara *Chem, Eur. J.* 2001, *7*, 1589

-photolysis
-3° amine oxides (Me_3N^+-O^-, TMANO), (NMO) 
 and room temp

Catalysis

-the new holy Grail - to use catalytic amounts of metal and CO gas (under as low a pressure as possible), or a CO substitute (some aldehydes)



$Co_2(CO)_8$ (5 mol%)

CO (1 atm), DME (60°)

83%

-other metals (other than Co) now are common, especially for catalytic chemistry; I think that Rh^I is gradually replacing Co

Rh^I	25	$[RhCl(CO)_2]_2$
Mo^o	12	$Mo(CO)_6$ -allenes(Brummond)
Ru^o	8	$Ru_3(CO)_{12}$
Ir^I	4	
Ti^{II}	7	

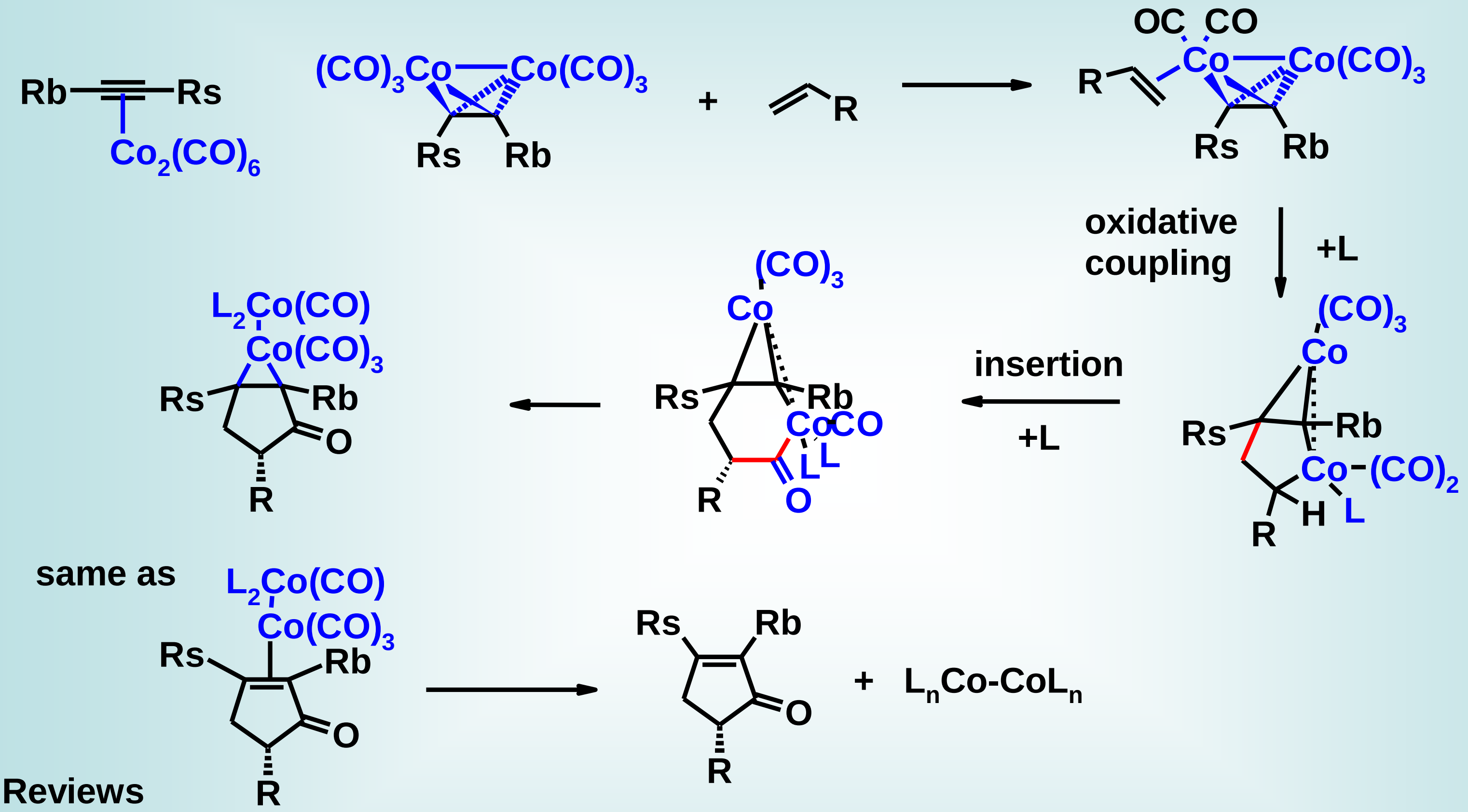
Zr^{II}	4
Fe^o, hν	4
Co nanoparticles	2
Co^I	1
W	1

Most recent reviews:

R Shibata,T. *Adv. Synth. Catal.* 2006, *348*, 2328.
R Pérez-Castells, J. *Top Organomet Chem* 2006, *19*, 207
R Strübing, D.; Beller, M. *Top Organomet Chem* 2006, *18*, 165

Mechanism of Pauson-Khand

-unnaturally complex looking, because presence of second metal, which is just 'along for the ride'



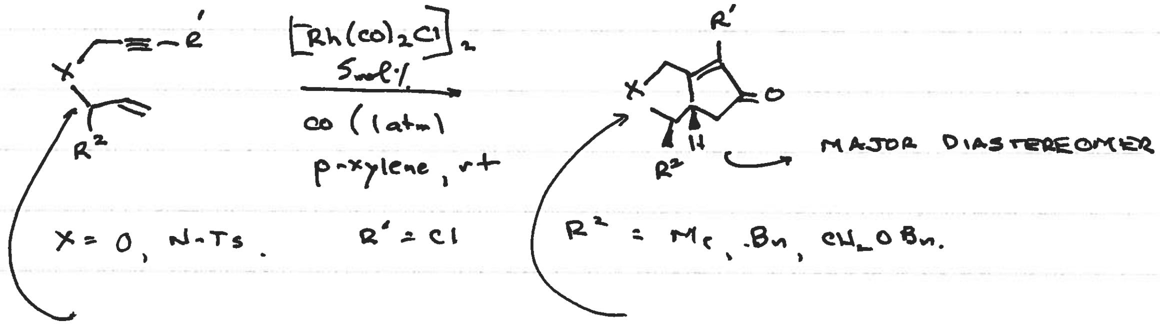
Reviews

R Chung, Y.K. et al *Synlett* 2005, 545 (Co nanoparticles)
R Krafft, M.E. *Tetrahedron* 2004, *66*, 9795. (Interrupted P.-K.)
R Alcaide, J.C.; Almendros, P. *Eur. J. Org. Chem.* 2004, 3377 (allenes)
R Perez-Castells, J. *Chem. Soc. Rev.* 2004, *33*, 32.
R Gibson, S.E. *Angew. Chem. Int. Ed. Engl.* 2003, *42*, 1800 (catalytic)
R Carretero, J.C. *Eur. J. Org. Chem.* 2002, *288*
R Carretero, J.C. *Synlett* 2001, 26.
R Brummond, K. *Tetrahedron* 2000, *56*, 3262 (allenes)
R Geis, G.; Schmalz, H.-G. *Angew. Chem. Int. Ed. Engl.* 1998, *37*, 911
R Schore, N.E. Comprehensive Organometal. Chem. II 1992, Vol 12, Ch 7.2
R Schore, N.E. *Org. React.* 1991, *40*, 1.
R Schore, N.E. *Chem. Rev.* 1988, *88*, 1081.

BURNIE, A. J.; EVANS, P. A.* TOP. ORGANOMET. CHEM. 2008, 61, 167.

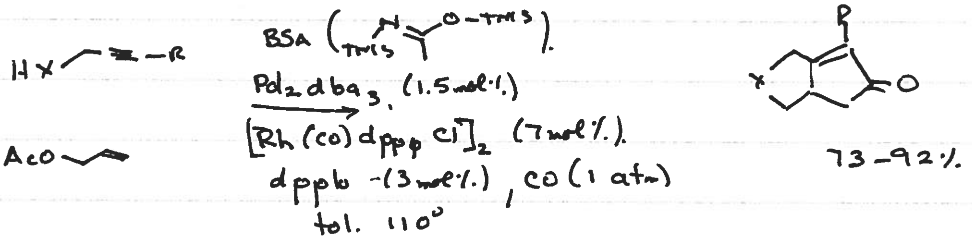
Rh(I) IS QUITE GOOD AT CATALYZING THE PAUSON-KHAND

- MUST BE IN CO ATMOSPHERE, BUT PRESSURES DO NOT NEED TO BE HIGH (1 ATM. NORMAL).
- EARLY EFFORTS ARE AT HIGH T (110°), BUT NOW OFTEN DONE AT RT



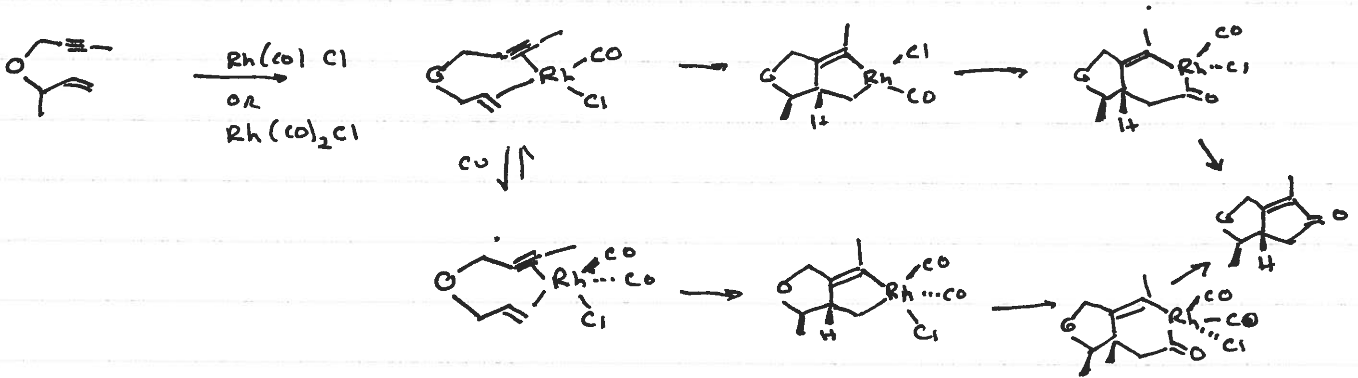
X = O, N-Ts.   R' = Cl   R^2 = Me, Bn, CH$_2$OBn.

RING CREATED IN OXIDATIVE COUPLING STEP IS ALMOST ALWAYS 5-MEMBERED



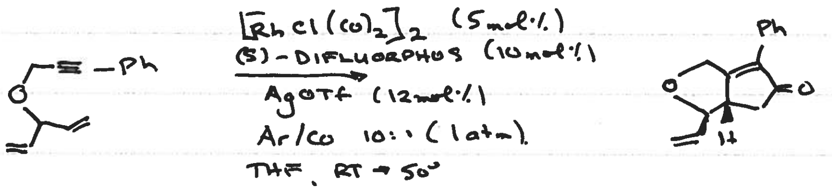
X = C(CO$_2$Et)(CO$_2$Et), NTs   R = Ph, Me, H*

MECH. AT LOW CO PRESSURE / HIGH PRESSURE



HIGHER de at HIGHER P.

THE USE OF Rh ALSO ALLOWS THE ADDITION OF CHIRAL LIGANDS, AND ULTIMATELY ENANTIOSELECTIVE PAUSON-KHANDS

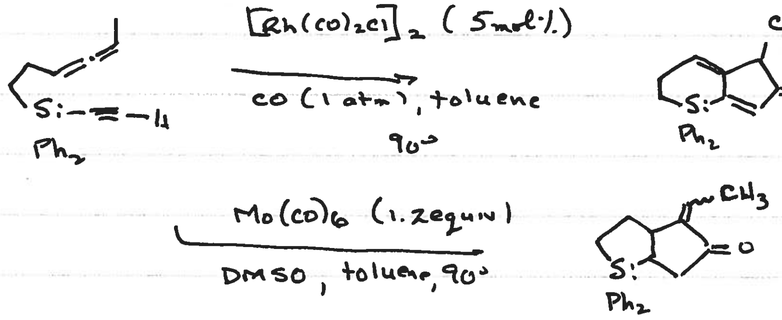


91% (93% ee)

- ALLENIC PAUSON-KHAND RXNS.

ALCADE, B.; AMENDROS, P.
EUR. J. ORG. CHEM. 2004, 3377.

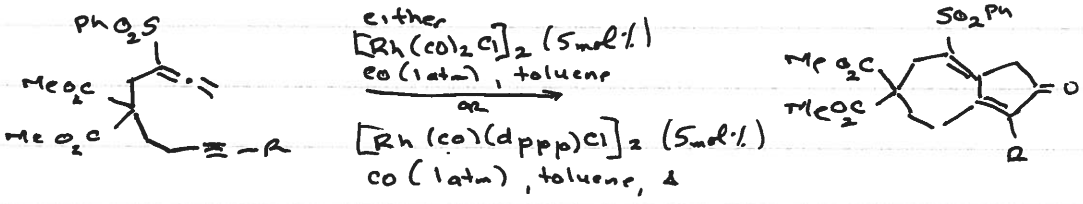
- THE PAUSON-KHAND RXN BETWEEN ALKYNES & ALLENES IS ALSO V. RELIABLE. WITH Rh(I) CATALYSIS, IT IS THE 'OUTSIDE' ALKENE THAT PARTICIPATES, EXCLUSIVELY
  - THE ALLENE MAY BE TERMINALLY UNSUBSTITUTED, OR MONOSUBSTITUTED.
- BY CONTRAST, IF ONE WANT THE 'INSIDE' ALKENE TO PARTICIPATE, ONE USES $Mo(CO)_6$, BUT IT IS STOICHIOMETRIC - $Co_2(CO)_8$ (OR THE ALKYNE-$Co_2(CO)_6$ COMPLEX) IS NOT COMPLETELY SELECTIVE



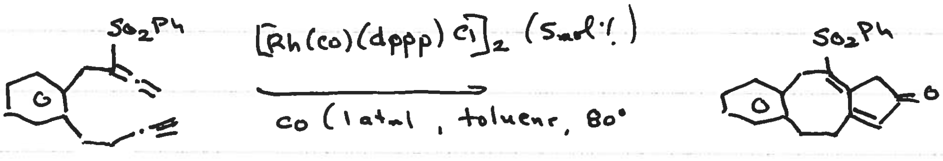
64% SQUARE PLANAR T.S. TO OXID. COUPLING

64% TRIG. BIPY T.S. TO OXID. COUPLING.

- UNLIKE THE RXN OF SIMPLE ALKENES, THE Rh^I CATALYZED ALLENIC P-K'S WILL NOW ALLOW (READILY) MEDIUM RING FORMATION, IN ADDN TO THE CYCLOPENTENONE



70-84%

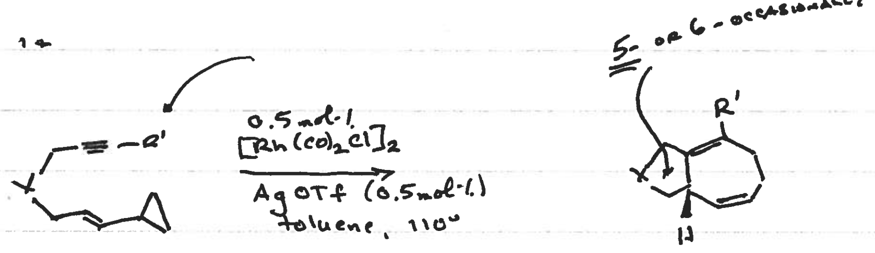


90%

YLIJOKI, K.E.O.; STRYKER, J.M
CHEM. REV. 2013, 113, 2244.

WHEN 2+2+2'S GO WRONG II. 5+2 CYCLOADDITIONS.

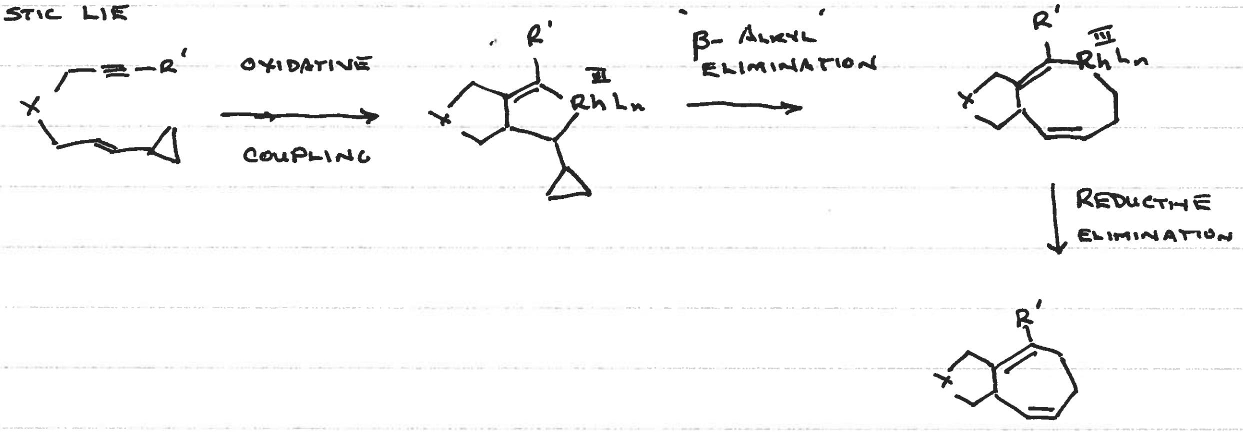
- WHEN THE ENYNE HAS AN APPENDED CYCLOPROPANE, AND XS CO IS LEFT OUT, THE RXN TAKES A RELATED, BUT DISTINCT COURSE
- WARNING - I WILL START WITH A WHITE LIE, AND EVENTUALLY CORRECT



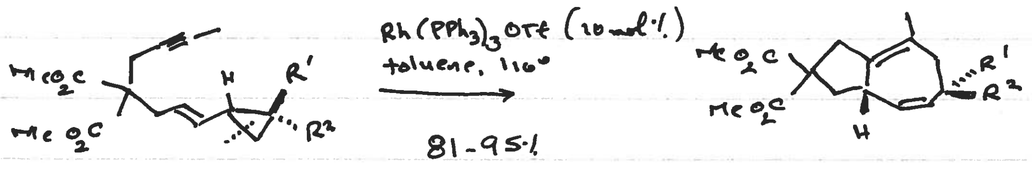
$R' = H^*$, Me, CO_2Me, TMS, Ph

* $R' = H$ NEEDS $ClRh(PPh_3)_3$

MECHANISTIC LIE



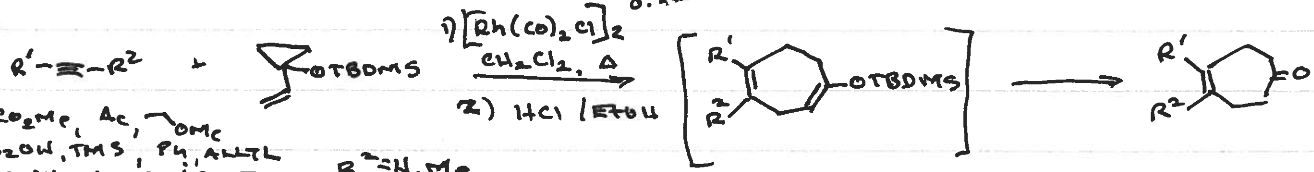
- MOSTLY 5- MEMBERED RING CASES, ALONG WITH A FEW 6- MEMBEREDED ONES
- THE CYCLOPROPANE CAN BE SUBSTITUTED - WHETHER THE MORE OR LESS SUBSTITUTED BOND OF THE CYCLOPROPANE DEPENDS ON THE SUBSTITUENT AND THE CATALYST, BUT WITH $Rh(PPh_3)_3OTf$, IT IS <u>MOSTLY</u> THE LESS SUBST. BOND



MAJOR

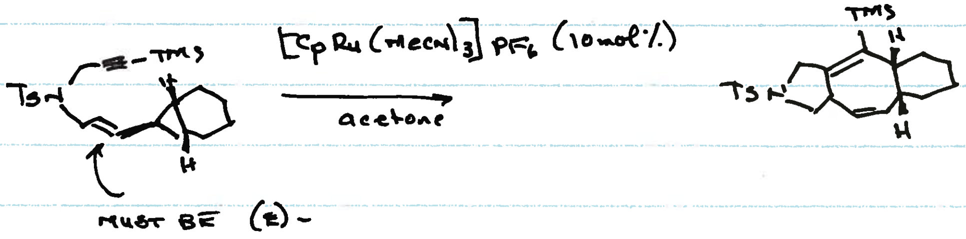
$R' = CO_2Me$ OR H
$R^2 = H$ OR CO_2Me

INTERMOLECULAR CASES DON'T WORK IN SIMPLE CASES, BUT HETEROATOM VCP'S DO GO WITH $[Rh(CO)_2Cl]_2$ MORE REACTIVE VCP AND CATALYST



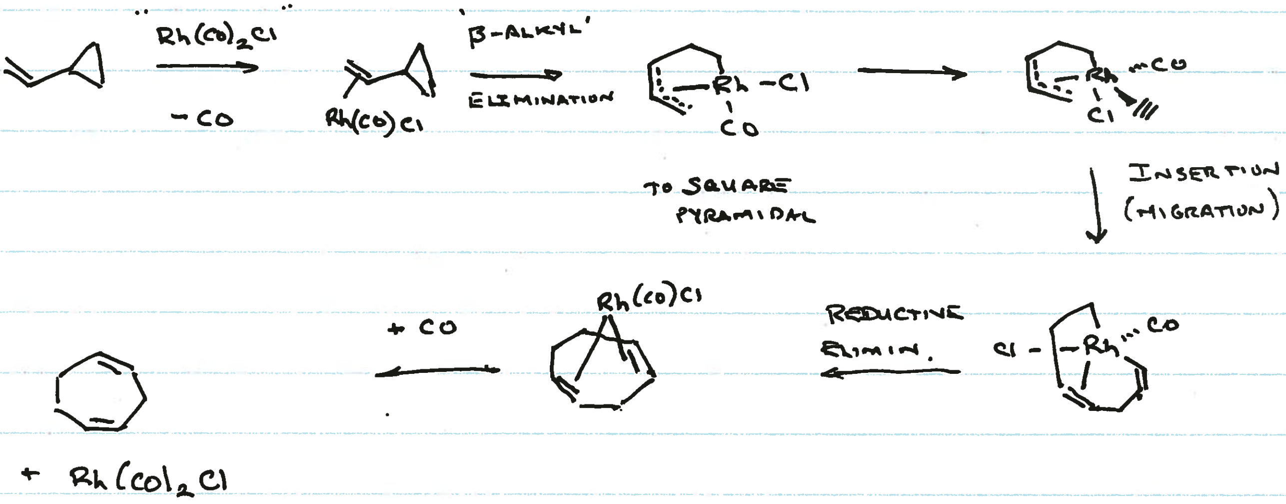
R' = CO_2Me, Ac, ~OMe
CH_2OH, TMS, Ph, ALLYL
CYCLOHEXENE, ^iPr, Et, H $R^2 = H$, Me

ALTERNATIVE - Ru^{II} USUALLY $[CpRu(MeCN)_3]^+ PF_6^-$ DOES V. CLOSELY ANALOGOUS CHEMISTRY, BUT IS LESS FULLY EXPLORED.



NOW FOR THE LIE - FOR Ru^{II}, THE MECHANISM GIVEN ON THE PREVIOUS PAGE IS LIKELY CORRECT.

FOR Rh^{I}, THE CYCLOPROPANE RING OPENING IS WAY EARLIER, BEFORE THE OXIDATIVE COUPLING STEP.



YES, ALLENES WILL PARTICIPATE, BUT SINCE C-C BOND FORMATION IS AN INSERTION AND NOT AN OXIDATIVE COUPLING, THE 'OUTSIDE'/DISTAL ALKENE RULE OF THE PAUSON-KHAND'S DOES NOT ALWAYS HOLD.