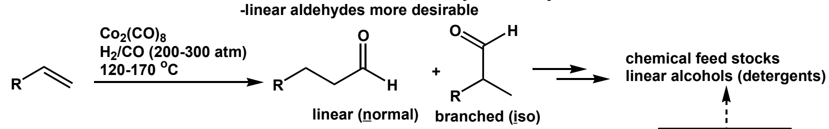
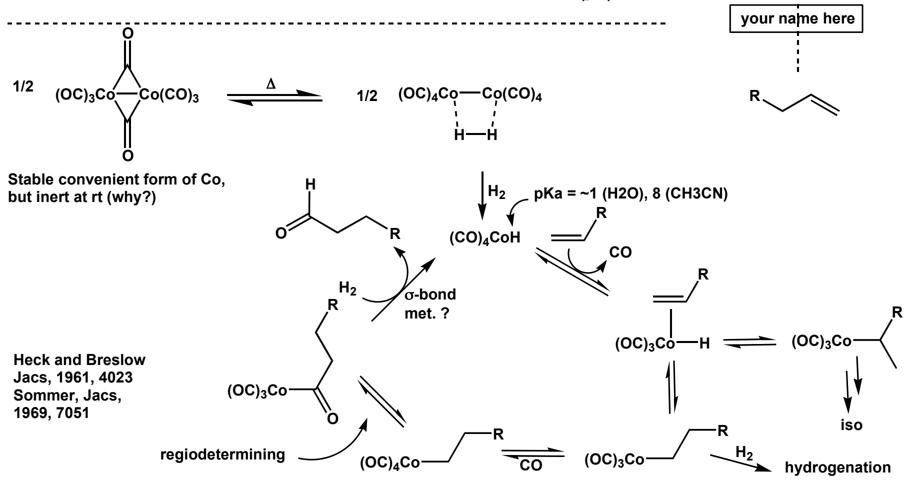
The Oxo process

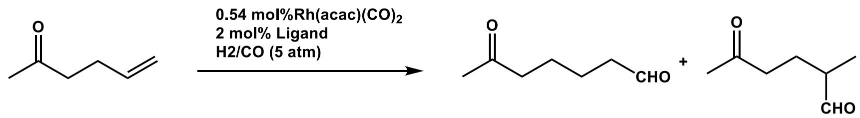
- developed in 1938 by Otto Roelen
- Principle method for hydroformylation of terminal alkenes industrially
- more that 4 million tons aldehyde annually
- linear aldehydes more desirable

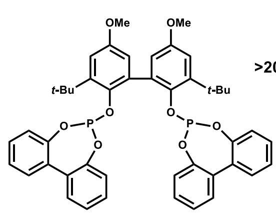


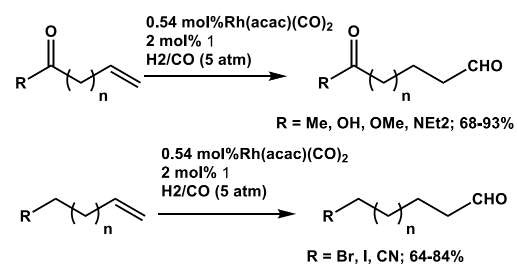


Activity for hydroformylation: Rh>>Co>>Ir, Ru>Os>Pt>Pd>Fe>Ni
but $Rh(acac)(CO)_2$ = $25/mmol; $Co_2(CO)_8$ = $0.16/mmol (strem prices)

Regioselectivity with Rh catalysts:



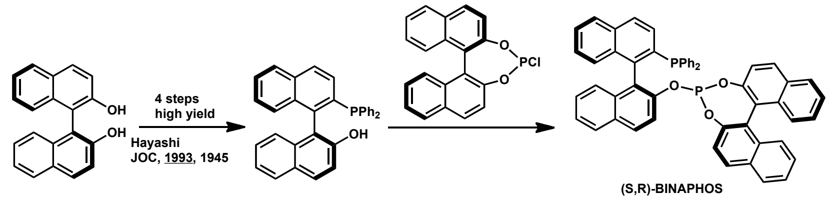
ligand	n:i
PPh_3	2.4:1
$P(OPh)_3$	3:1
 1	>20:1

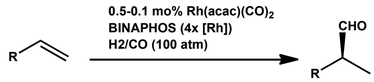


Ligand 1 described in a patent by Billig (Union Carbide) in 1988.
Buchwald reported substrate scope.

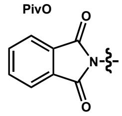
Buchwald, JACS, 1993, 2066

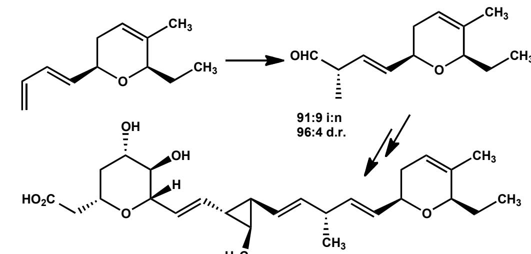
Asymmetric Hydroformylation: under-developed



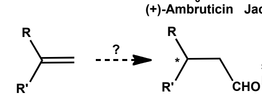


n:i selectivity "beyond the discussion here"
Nozaki, JACS, 1997, 4413

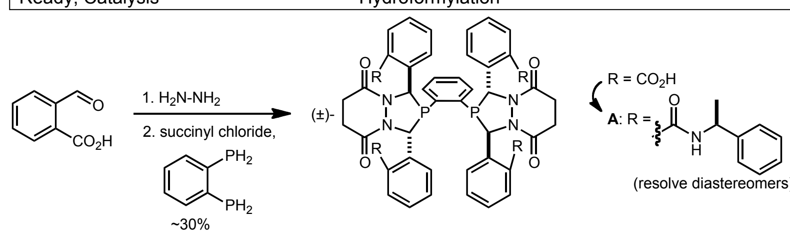
R	% ee	i:n
Ph	92	88:12
4-OMe-Ph	88	87:13
4-ClPh	93	87:13
4-CF_3-Ph	93	96:4
PivO	93	88:12
	85	89:11

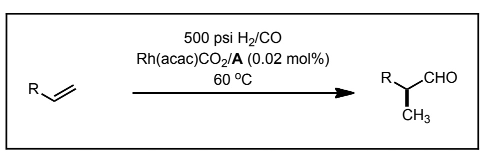


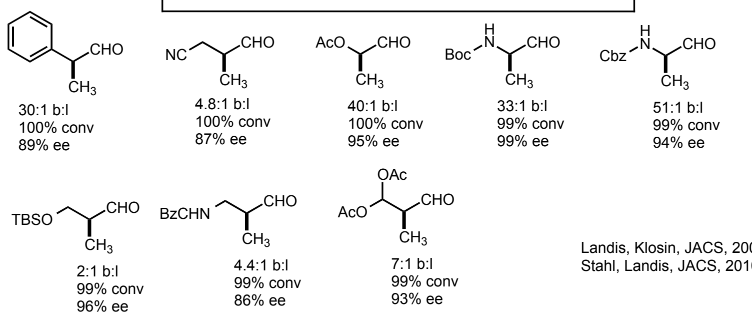
Jacobsen, JACS, 2001, 10772



see Breit, Eur. JOC, 1998, 1123,
Buchwald, JACS, 2011, 19080

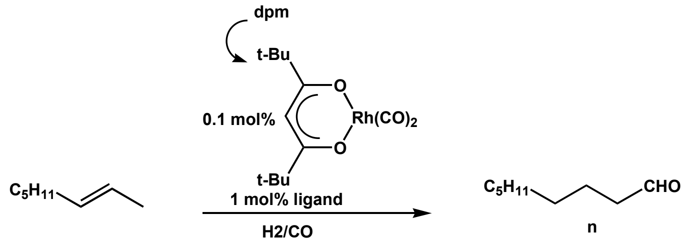




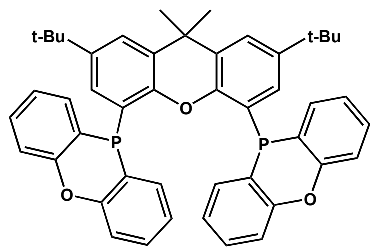


Landis, Klosin, JACS, 2005, 5040
Stahl, Landis, JACS, 2010, 14027

Ready; Catalysis Hydroformylation-4



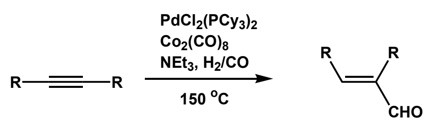
Mixture of branched isomers
i

ligand	n:i
PPh3	0.9:1
	9.2:1

Can you explain how and why??
van Leeuwen, ACIEE, 1999, 336

Ready; Catalysis Hydroformylation

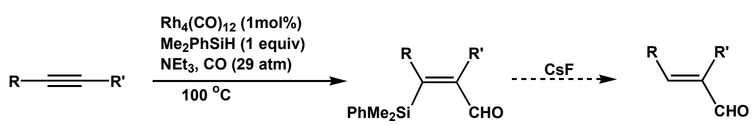
Alkyne hydroformylation/silylformylation: Unsolved, but would be nice



Role of Co is not clear. Many other metal carbonyls accelerate rxn. Cocatalyst could help carbonyl insertion. However, rate dependent on H2 pressure, suggesting hydrogenolysis may be rate determining.

Hidai, JACS, 1997, 6448

R = alkyl, 88-95%
R = Ph, 53% (much stilbene)
R = Ph, 77% (w/o Cobalt)
R = Ph, Me, 85%, 3:2 regio (w/o Cobalt)



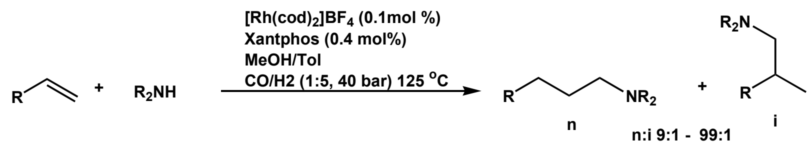
R = Me, Pr, Ph, cHex, allyl
R' = H, Me, Ph, CO2M2

yields mostly >70%
Often poor E/Z

Matsuda, JACS, 1989, 2332

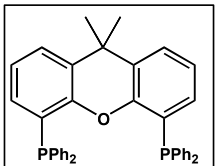
Ready; Catalysis Hydroformylation

Tandem hydroformylation/reductive amination or hydroaminomethylation

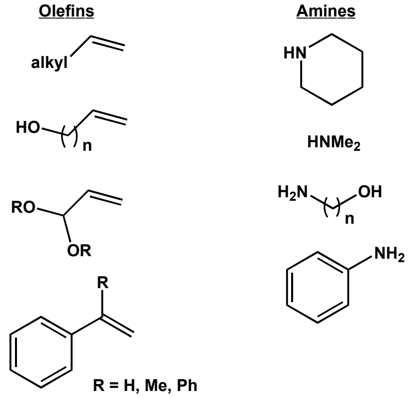


n:i 9:1 - 99:1
y: most >90%

Beller
JACS, 2003, 10311



Xantphos ($17/g Aldrich)

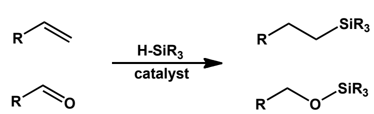


R = H, Me, Ph

Ready; Catalysis Hydrosilylation

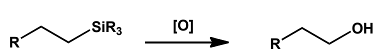
Hydrosilylation

What:



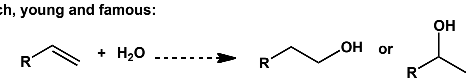
catalyst usually = Pt, Rh, Pd, Ir

why:



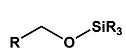
or as adhesives, surfactants
(major applications industrially)

To retire rich, young and famous:



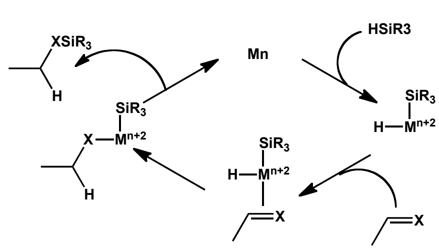
H-OH	120
C=C	60
O-C	-90
C-H	-100

ΔH ~ -10 kcal/mol



= protected alcohol

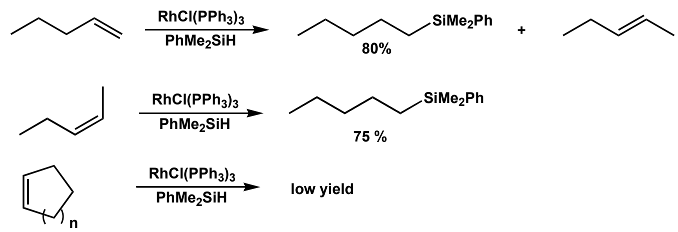
How:

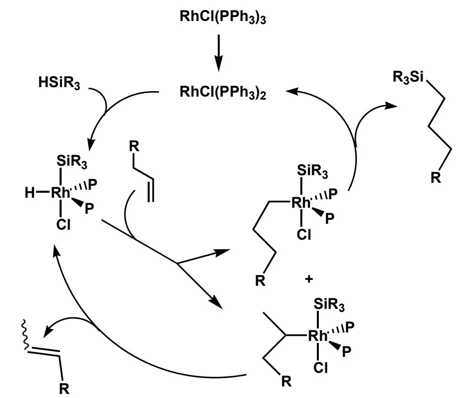


Note in some cases X-Si bond formation precedes H-C bond formation

Ready; Catalysis — Hydrosilylation

Rhodium [Rh(I) - Rh(III)]

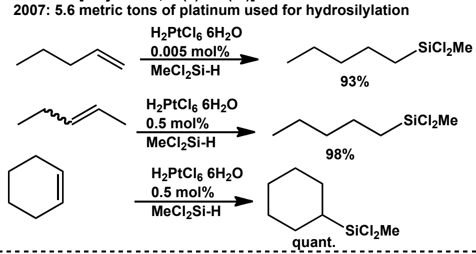




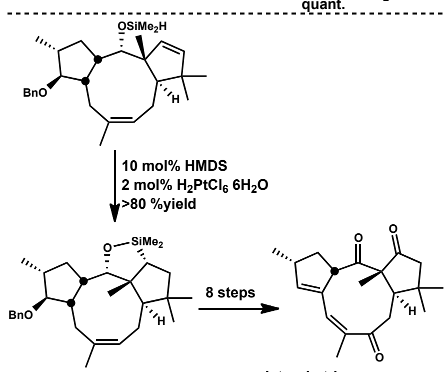
Chalk JOMC, 1970 (21) 207

Ready; Catalysis — Hydrosilylation

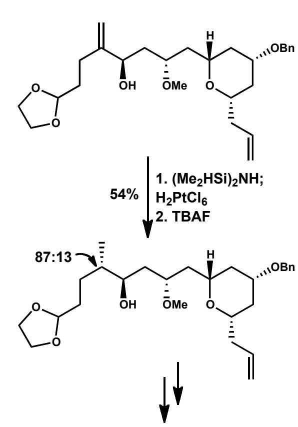
Platinum [very active, Pt(II) - Pt(IV)]
2007: 5.6 metric tons of platinum used for hydrosilylation



Has been suggested that Pt colloids are the real catalyst. These are suspensions of fine particles 10-1000 A radius. These solutions appear homogeneous and are able to pass through filters.



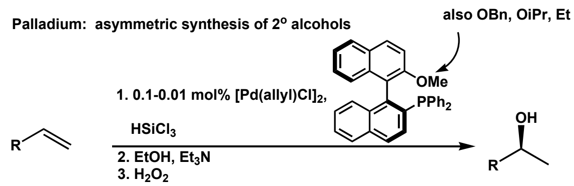
Jatrophatrione
Paquette, JACS, 2002, 6542



Leucascandrolide A
Kozmin, OL, 2001, 755

Ready; Catalysis Hydrosilylation

Palladium: asymmetric synthesis of 2° alcohols

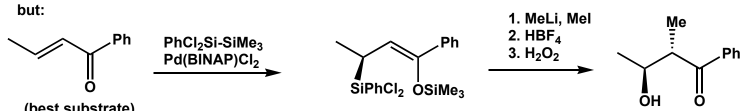


	yield	%ee	i:n
R = n-alkyl	60's	95-97	5:1 - 20:1
R = cHex	45	96	3:1

Hayashi, JACS, 1991, 9887

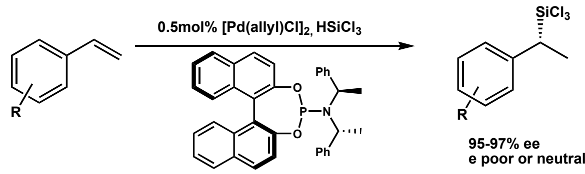
Note: they propose MOP accelerates R.E.; Insertion is rate determining, so get kinetic product
Note: w/ BINAP (and other chelating phosphines) no reaction, propose inert 16e s.p. complex:

but:



(best substrate) 54%, 85% ee 70%

Hayashi, Ito
Tetrahedron, 1994, 335

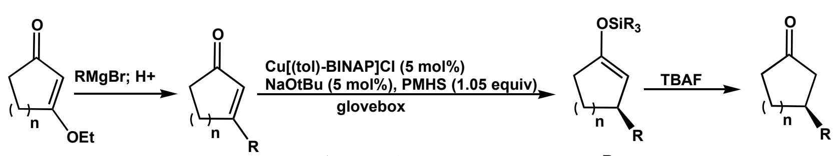


95-97% ee
e poor or neutral aromatic

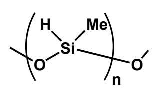
Johannsen
JACS, 2002, 4558

Ready; Catalysis Hydrosilylation

Cu: an alternative to conjugate addn.
for early work with [$(Ph_3P)CuH]_6$ 'strykers reagent' see stryker, jacs, 1989, 8818



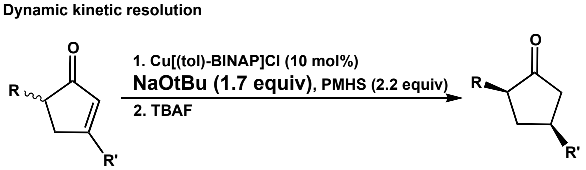
PMHS = polymethylhydrosiloxane
cheap, safe

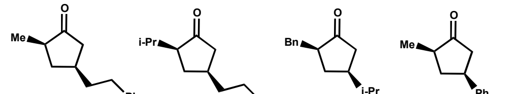


mw = 3200-1700

R	n	y	ee
n-alkyl	1	~80	94-98
iPr	1	88	94
Bu	2	82	87
-$(CH_2)_2$Ph	3	82	96

Dynamic kinetic resolution

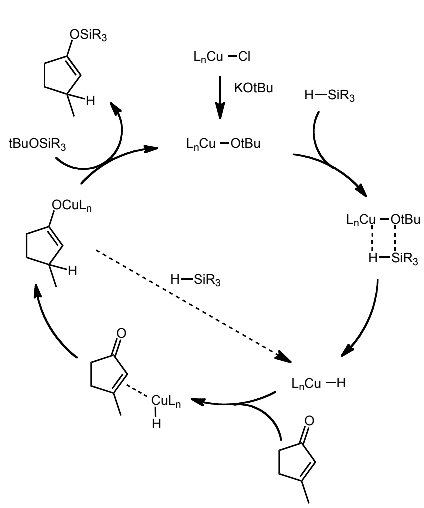


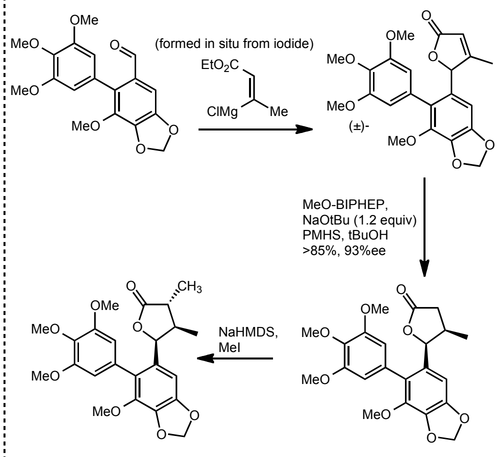


91% ee	93% ee	93% ee	91% ee
91:9 cis:trans	93:7 cis:trans	92:8 cis:trans	97:3 cis:trans
89% yield	94% yield	95% yield	90% yield

Buchwald Jacs, 2000, 6797; 2002, 2892

Cu-Catalyzed Hydrosilylation: Mechanism and Application

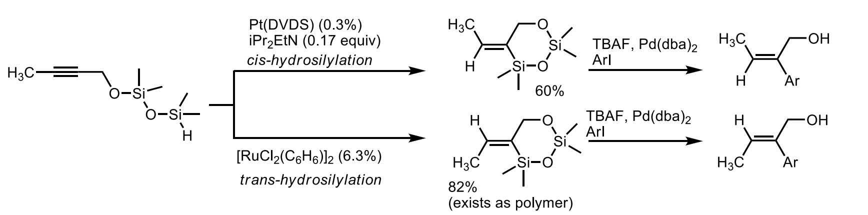




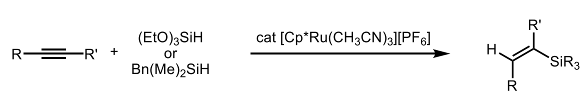
Buchwald, ACIE, 2005, 6177

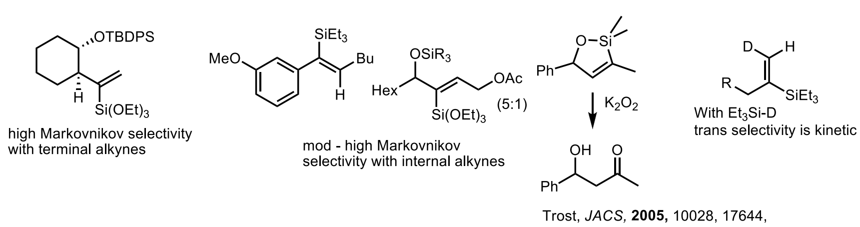
Ready; Catalysis Hydrosilylation

Alkyne Hydrosilylation



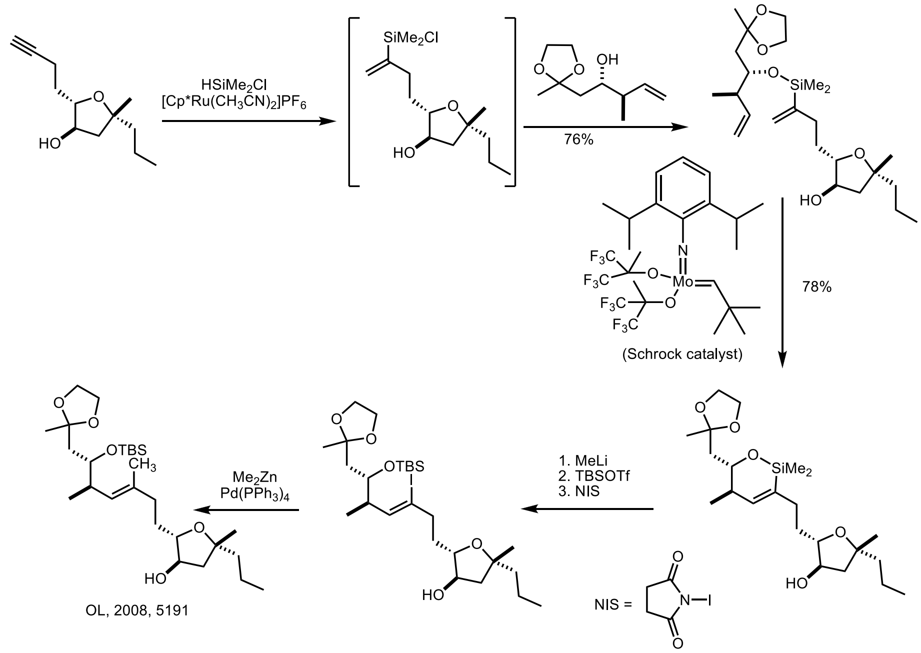
Denmark, *OL*, **2003**, 1119





Trost, *JACS*, **2005,** 10028, 17644,

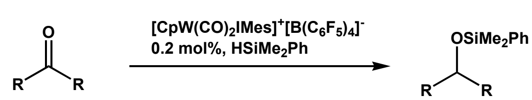
Ready; Catalysis Hydrosilylation



OL, 2008, 5191

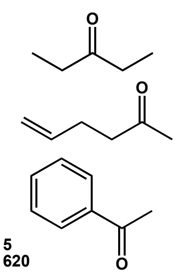
Ready; Catalysis Hydrosilylation

Ketone Hydrosilylation: a remarkable catalyst

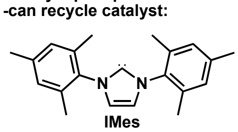


y ~90

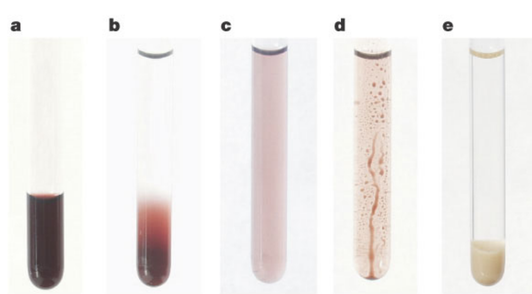
some substrates



-catalyst soluble in "a few molecules of substrate per molecule of catalyst"
-catalyst precipitates at end of reaction; decant product
-can recycle catalyst:

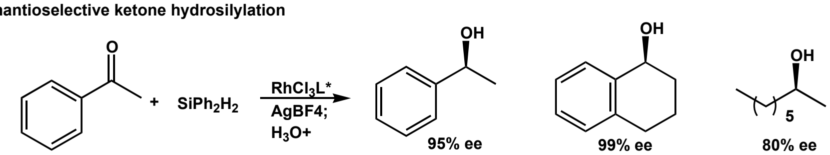


cycle	1	2	3	4	5
$TOF_{(initial)}$	370	780	870	760	620

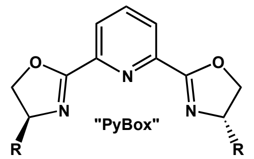


Dloumaev and Bullock
(Brookhaven National Laboratory)
Nature, 424, 2003, 530

Enantioselective ketone hydrosilylation



L =



Nishiyama
Tet: asym, 1993, 143

Note: MCl + AgBF4 or AgSbF6 ⟶ [M][BF4] or [M][SbF6] + AgCl↓

AgBF4 $72/10g
AgSbF6 $42/5g (aldrich)

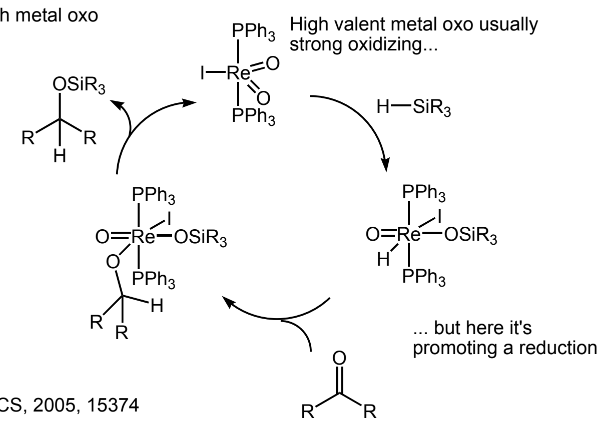
In general, hydrogenation works better than hydrosilylation
-usually see silane that does NOT give useful protecting group
-often used as 'benchmark' reaction for new ligands
-compare H2 - 100% atom effecient; $HSiPh_2H$ - 0.5% atom effecient

and now for something different...
How to do reductions with an oxidant

Usual hydrosilylation requires O.A. to Si-H:

$$Si{-}H + M^n \longrightarrow Si{-}M^{n+2}{-}H$$

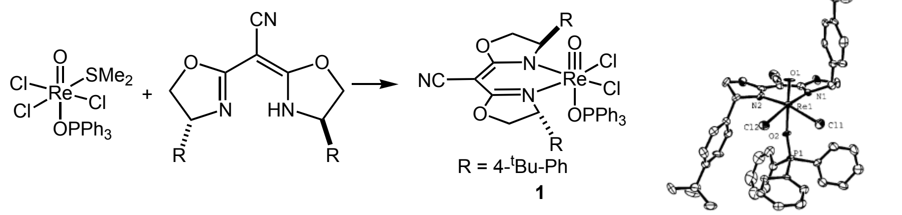
Toste et. al. disovered [2+2] with metal oxo

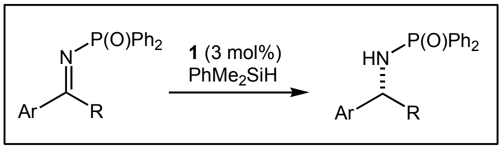


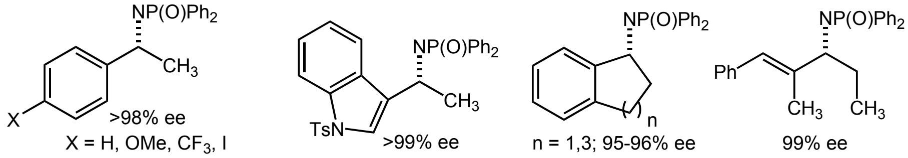
Toste, JACS, 2003, 4056

Alternative mech: Abu-Omar JACS, 2005, 15374

Enantioselective imine hydrosilylation

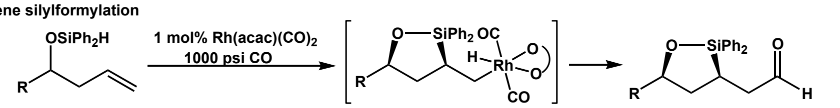






Toste, JACS, 2005, 12462

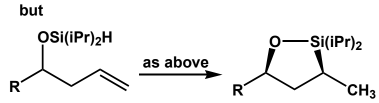
alkene silylformylation



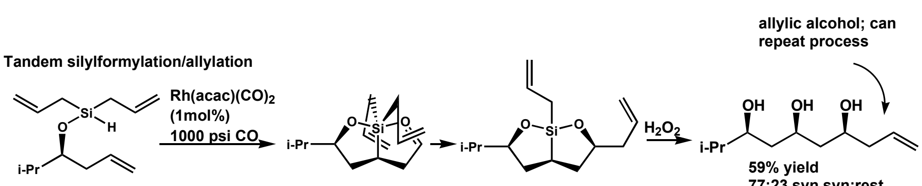
note Si-C formation preceeds H-C formation

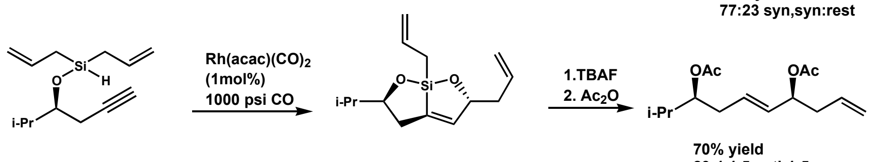
R	% yield	cis/trans
Me	67	4.5:1
allyl	64	4:1
iPr	79	6:1

but



Tandem silylformylation/allylation





Leighton JACS, 1997; 12416, 2000, 8587; 2001, 341

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Toward More "Ideal" Polyketide Natural Product Synthesis: A Step-Economical Synthesis of Zincophorin Methyl Ester

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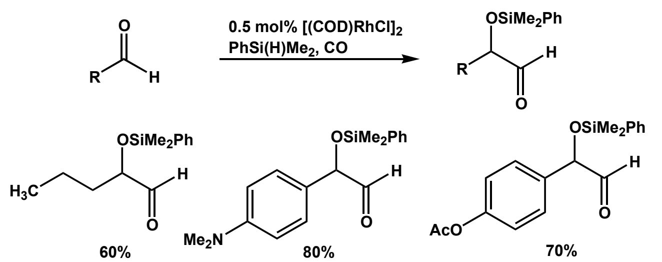
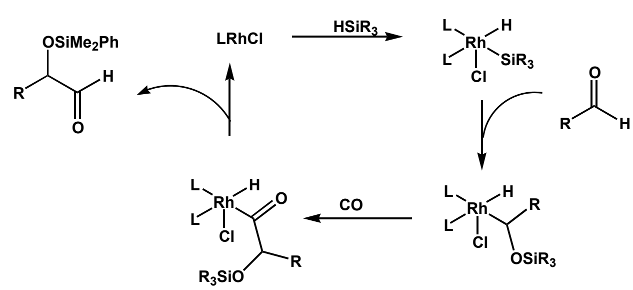
Aldehyde Silylformylation

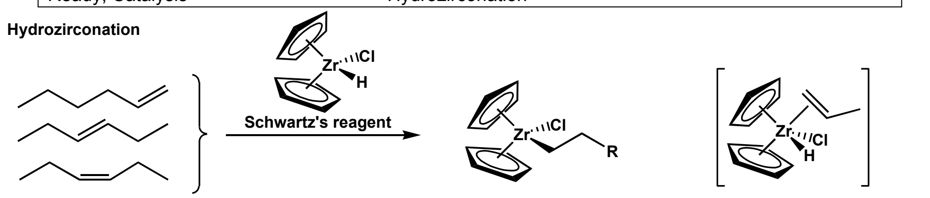


Proposed:



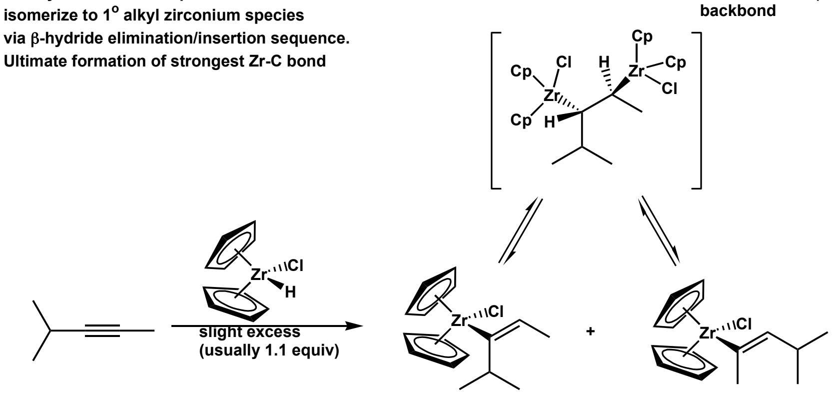
Wright, JACS, 1993, 2059

Hydrozirconation



2^{o} alkyl zirconium complexes isomerize to 1^{o} alkyl zirconium species via β-hydride elimination/insertion sequence. Ultimate formation of strongest Zr-C bond

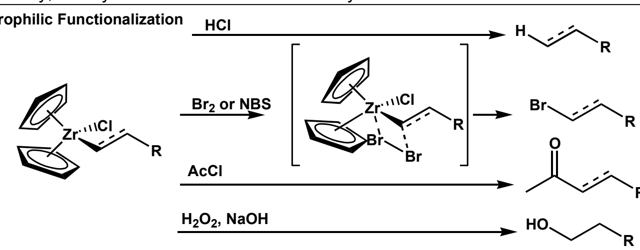
not favored: Zr(IV) (d0) can't backbond



Schwartz JACS, 1974, 8115
1975, 679;

With 1 equiv ZrH	16	:	84
with 1.1 equiv ZrH	2		98

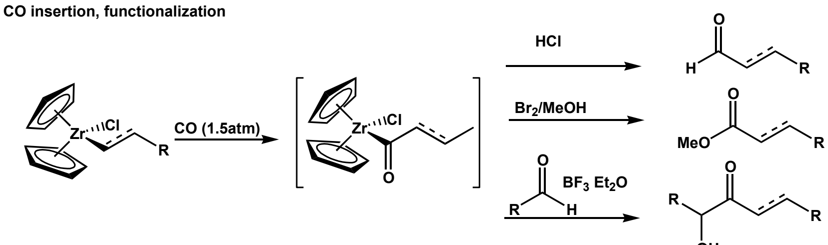
Electrophilic Functionalization



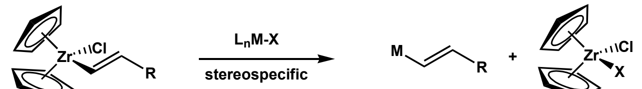
Reactions are stereospecific: Maintain olefin geometry or stereochemistry

Schwartz JACS, 1975, 228; ACIEE 1976, 333
Review: Labinger, Com. Org Syn vol 8, 667

CO insertion, functionalization



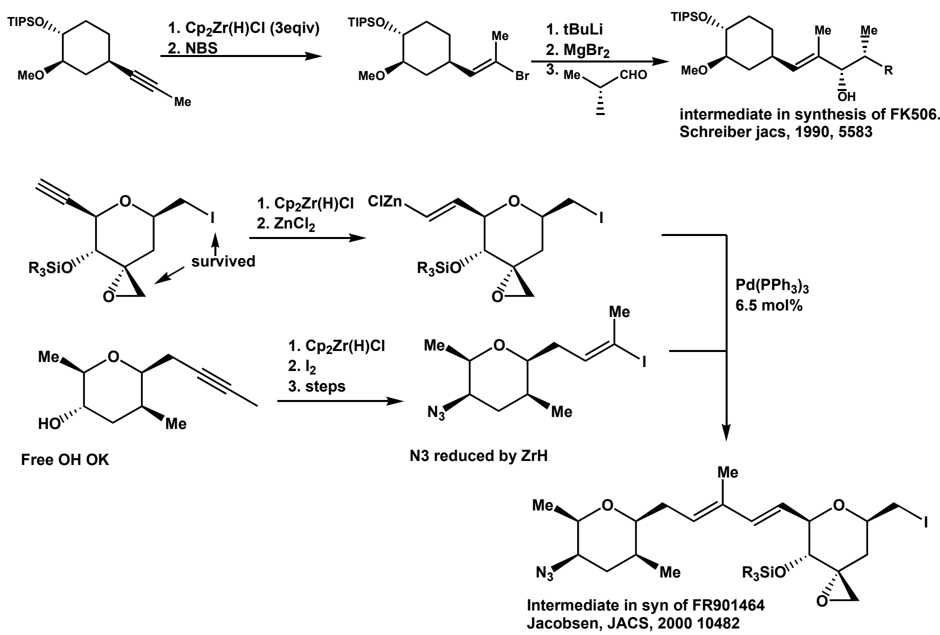
Transmetallation (most common application. Great way to make vinyl organometallics)



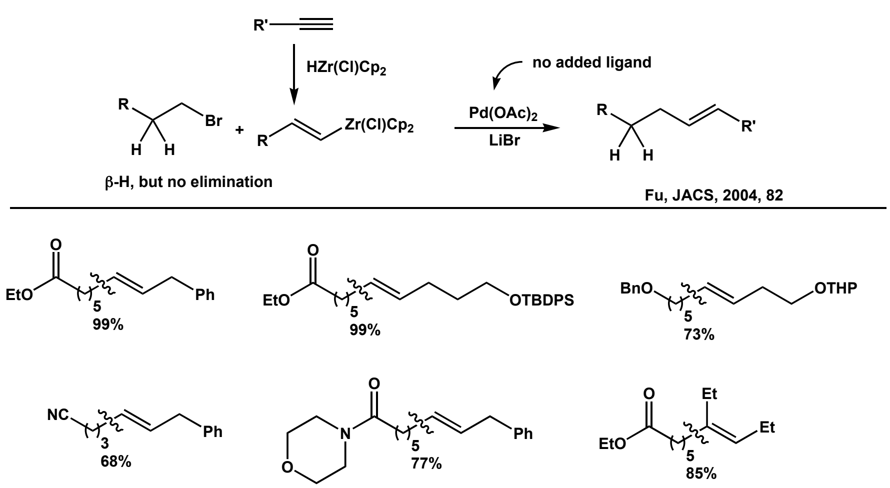
M = Al, B, Cu, Hg, Ni, Pd, Sn, Zn

Wipf, tetrahedron, 1996, 12853

Ready; Catalysis Hydrozirconation



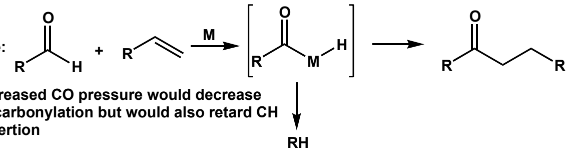
Ready; Catalysis Hydrozirconation



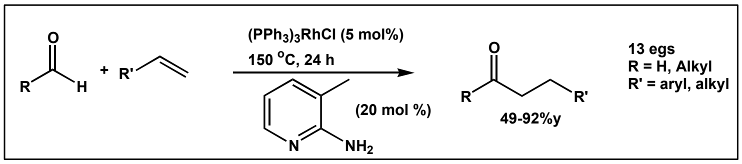
Ready; Catalysis Hydroacylation

Hydroacylation

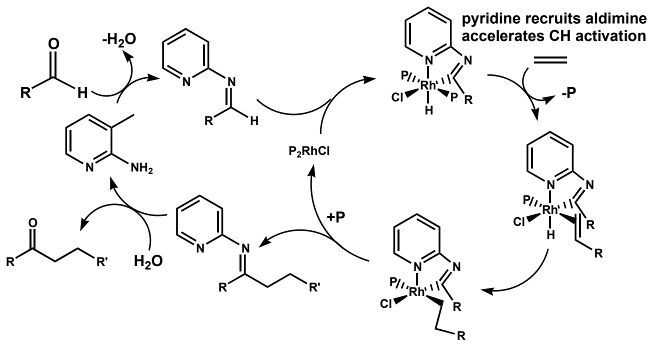
Desired Reaction/obstacle:



increased CO pressure would decrease decarbonylation but would also retard CH insertion



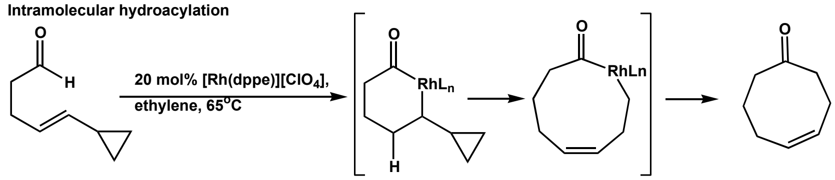
pyridine recruits aldimine to Rh; accelerates CH activation

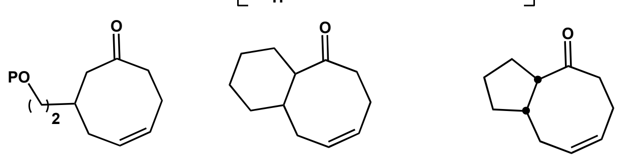


Jun JOC, 1997, 1200
with alkynes: ACIEE, 2002, 2146

Ready; Catalysis Hydroacylation

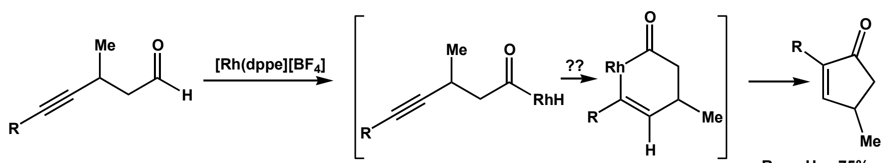
Intramolecular hydroacylation





65% **cis: 63%** **trans: 65%** **58%**

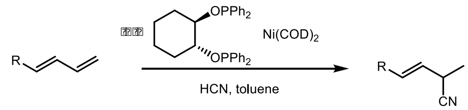
Shair, JACS, 2000, 12610



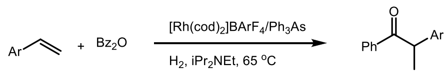
R = n-Hex 75%
R = Ph 88%

Fu, JACS, 2001, 11492

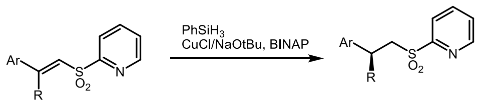
Related additions to olefins:
(general review: ACIE, 2004, 3368)



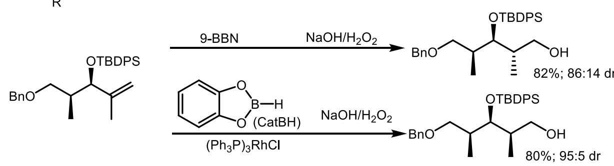
Hydrocyanation
RajanBabu, OL, 2006, 4657



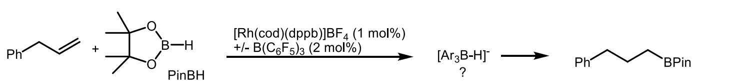
Hydroacylation
Krische, ACIE, 2006, 6885



Hydrosilylation
Carretero, ACIE, 2007, 3329



Hydroboration
Evans, JACS, 1988, 6917
'...experiments suggest the catalyzed and uncatalyzed reactions may well have different product-determining steps.'



+ Lewis acid: 70%, 32:1 rr
- Lewis acid: 19%, 9:1 rr

Hydroboration
Crudden, JACS, 2010, 131