Transition Metal Catalyzed Olefin Isomerization of Allylic Systems

Evans Group Seminar

March 15, 2002

Anna Chiu

Outline:

Introduction

- Mechanism
- Simple allyl alcohol/ether isomerizations

Asymmetric Catalysis

- Development of an asymmetric catalyst for allyl amines
- A new mechanism and model for stereoinduction
- Asymmetric allyl alcohol isomerization

Generation of Enolate Equivalents

- Stereoselective isomerizations
- Tandem reactions

Rearrangements

- Hg & Pd catalyzed allylic rearrangements
- Oxo metal catalyzed rearrangements and tandem reactions

Synthetic Applications

Leading References:

General

Davies, S.G. *Organotransition Metal Chemistry. Applications to Organic Synthesis;* Pergamon Press: Oxford, 1982; pp. 266-290.

Enantioselective Allyl Amine Isomerization

Otsuka, S., Tani, K. *Synthesis*, **1991,** 665.

Noyori, R., Takaya, H. *JACS*, **1990**, 4897.

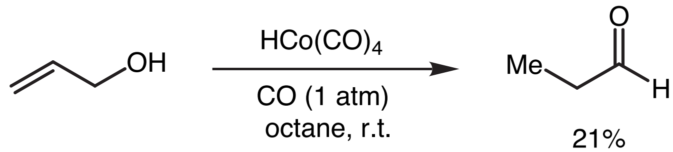
Allylic Rearrangement

Overman, L.E. *ACIEE,* **1984**, 579.

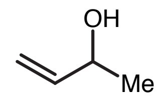
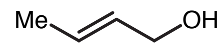
Overman, L.E., Hollis, T.K. *J. Organomet. Chem.,* **1999**, 290.

Allylic Alcohols: Early Discoveries

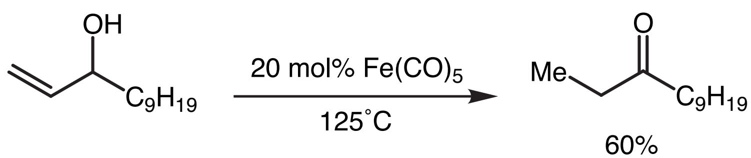
Metal Hydrides (Goetz,R., Orchin, M. *JACS*, **1963**, 1549.)

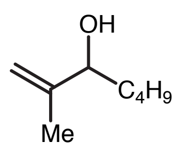
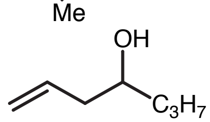
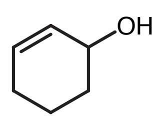


Observed during hydroformylation

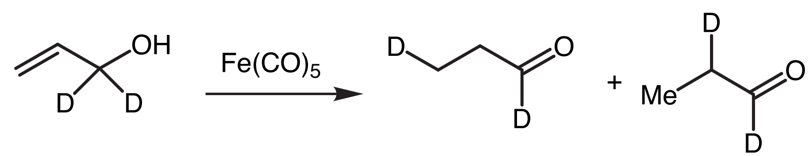
Substrate	*Yield (%)*
	3.7
	3

Metal Carbonyls (Damico, R., Logan,T.J. *JOC,* **1967**, 2356.)



Substrate	Yield
	75
	80
	20

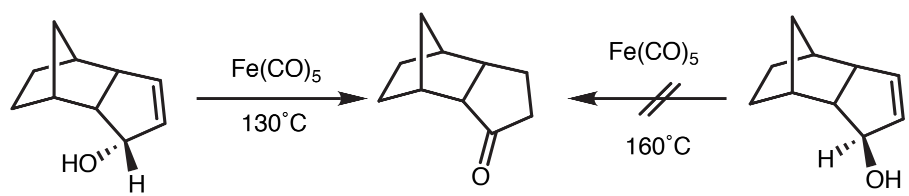
Deuterium Labelling Studies



exclusive

not observed

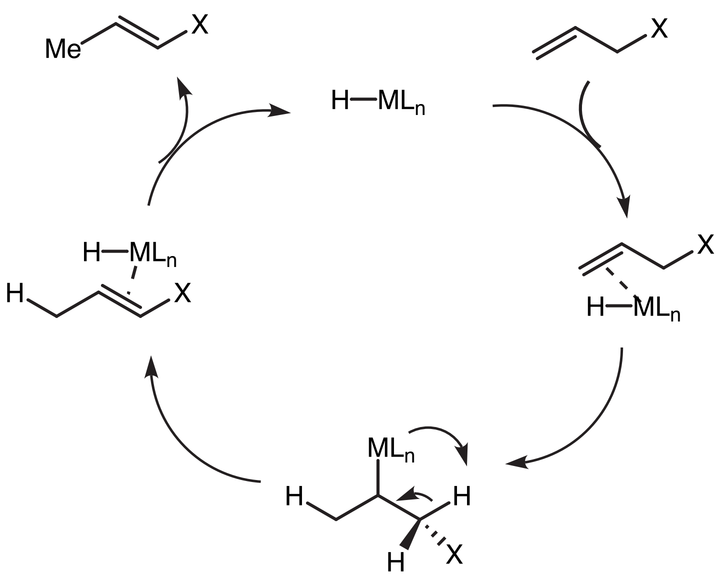
Supra-facial 1,3 H Migration



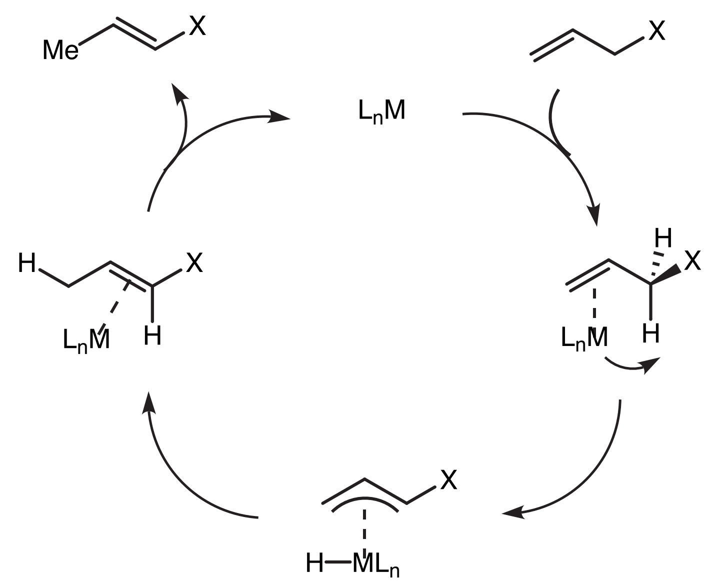
Rosenberg, J.L. *Chem. Comm*., **1968**, 97.

General Mechanism

Hydride Addition-Elimination



π-Allyl Metal & 1,3 H Shift



Common Catalysts

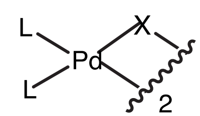
$HCo(CO)_4$

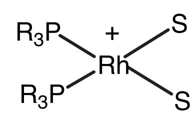
$(Ph_3P)_3RhCl$

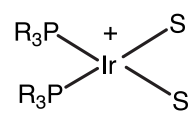
$HRuCl(PPh_3)_3$

Common Catalysts

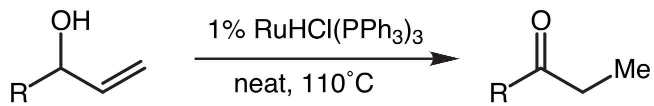
$Fe(CO)_5$

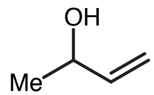
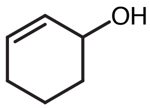
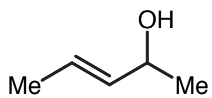
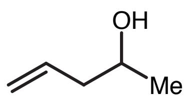
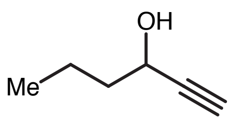
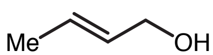






Early Ru and Ir catalysts

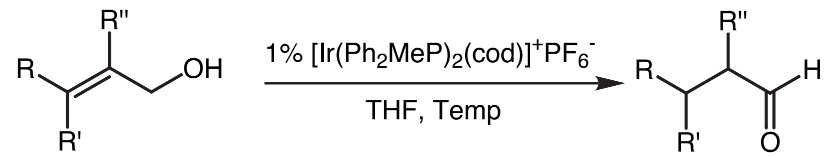


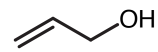
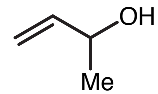
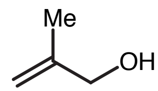
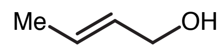
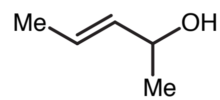
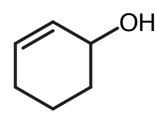
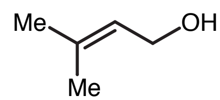
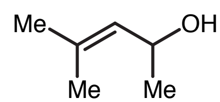
Alcohol	*Yield (%)*
	91
	81
	90
	79
	0
	0

Limitations:

- Air sensitive catalyst (immediate preparation and cannot be recycled)
- Not selective for allylic alcohols; other olefins also isomerize

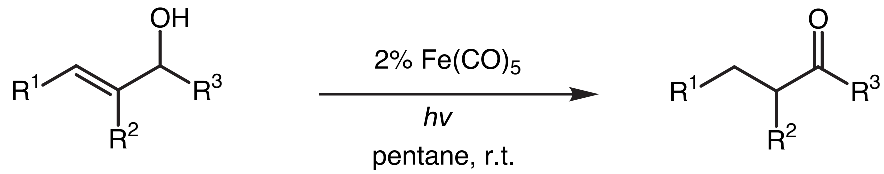
Sasson, Y., Rempel, G.L. *TL*, **1974**, 4133.



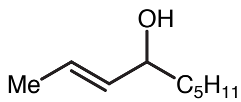
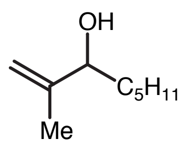
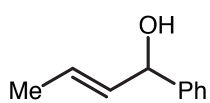
Alcohol	*Temp (˚C)*	*Conversion (%)*
	20	100
	20	100
	20	100
	65	99
	65	98
	65	9
	65	12
	65	0

Baudry,D., Ephritikhine,M., Felkin,H. *Nouv. J. Chim.,* **1978**, 355.

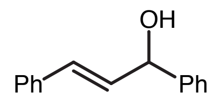
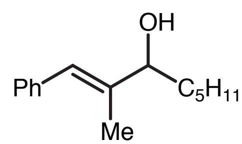
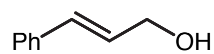
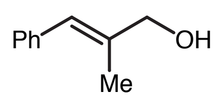
$Fe(CO)_5$ Revisited: Light Activation



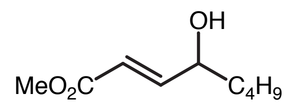
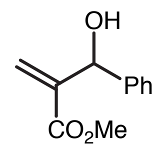
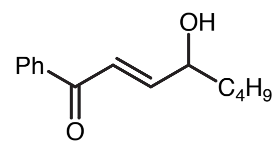
Hindered Aliphatic

Substrate	*Yield (%)*
	86
	95
	64

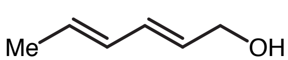
Cinnamyl derivatives

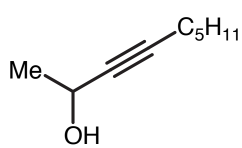
Substrate	*Yield (%)*
	90
	80
	38
	90

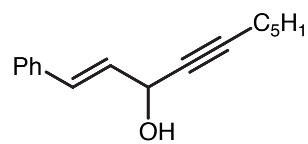
Carbonyls

Substrate	*Yield (%)*
	70
	87
	70

Poor Substrates (no reaction)

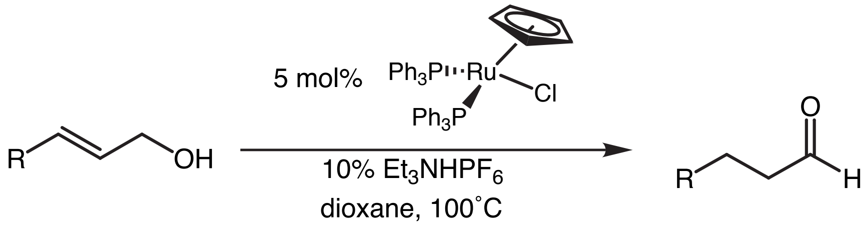


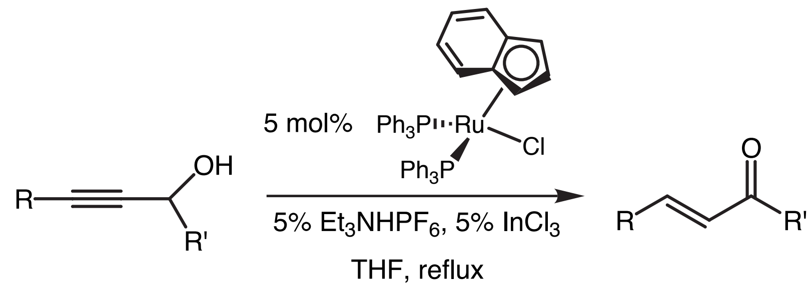


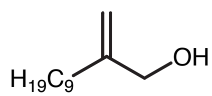
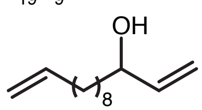
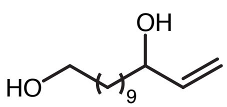
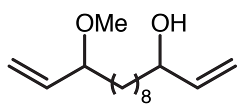
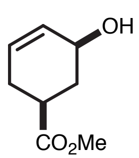
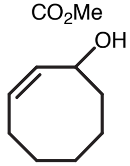
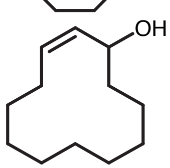


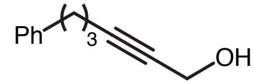
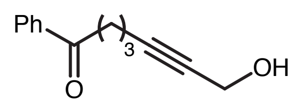
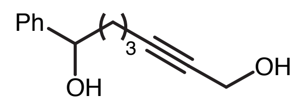
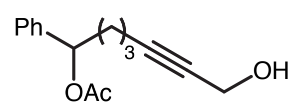
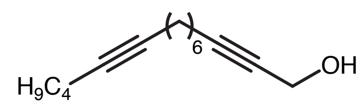
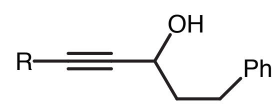
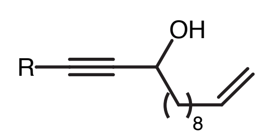
Gree, R. *Tet.*, **2001**, 2379.

A Milder Catalyst: Ruthenium





Substrates	*Yield (%)*
	90
	68
	87
	90
	93
	0
	31 (47% w/ Indenyl)
	84

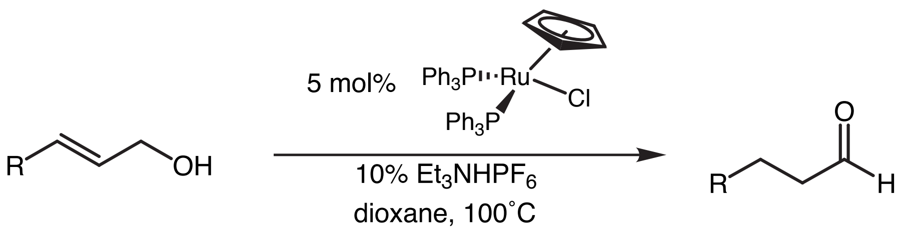
Substrates	*Yield (%)*
	88
	80
	86
	87
	83
 R = $C_{10}H_{21}$	86
 R = C_4H_9	83

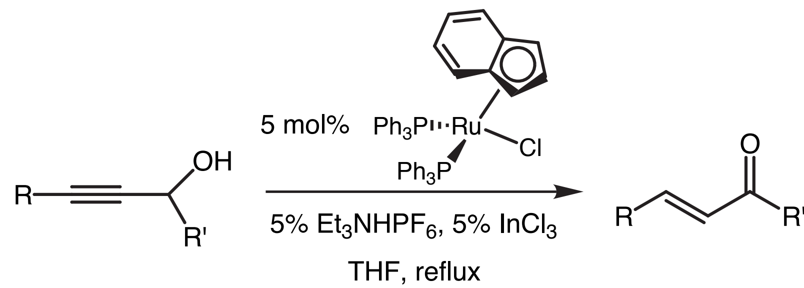
Only free allylic & propargylic alcohols isomerize!

Trost, B.M. *JACS*, **1993**, 2027 & **1995**, 9586

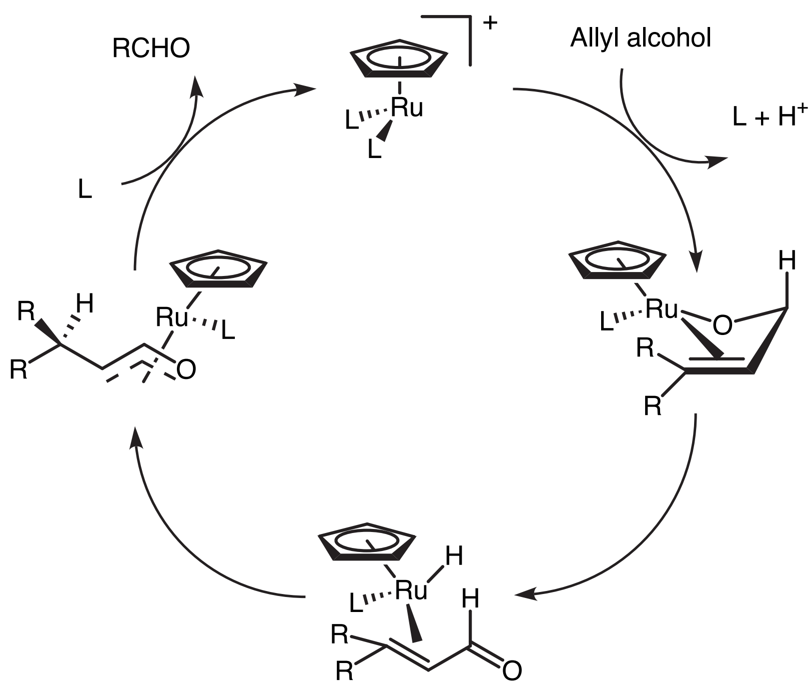
05 ruthenium 3/15/02 10:08 AM

Ru Catalyzed Isomerization: Proposed Mechanism

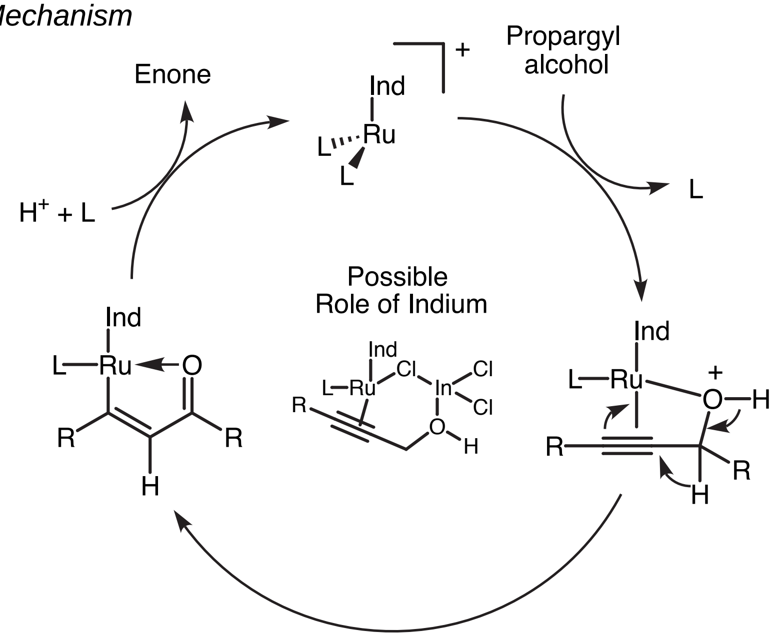




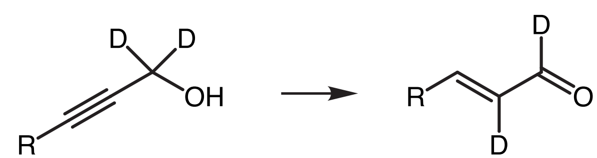
Mechanism



Mechanism



Evidence

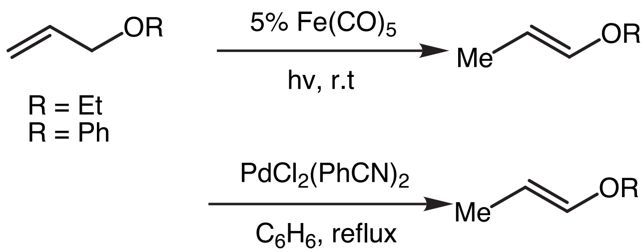


- Beta elimination requires opening of a coordination site (olefin, L, or Cp)
- Trost states that loss of olefin, oxygen, or PPh_3 is unlikely - hence, Cp slippage is required.

Trost, B.M. *JACS*, **1993**, 2027 & **1995**, 9586

Allylic Ethers: E vs Z isomers

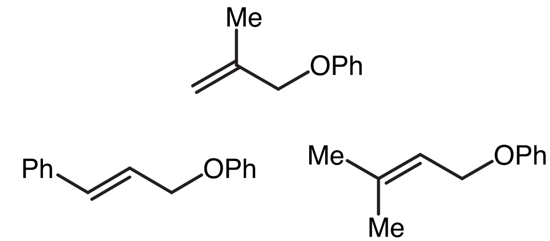
Early Examples



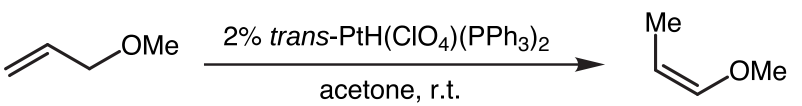
R = Et 100%; 44:56 (cis:trans)
R = Ph 100%; 52:48 (cis:trans)

R = Ph 100%; 70:30 (cis:trans)

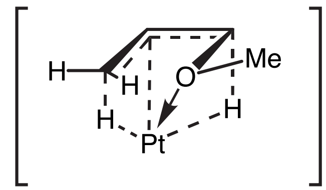
Poor substrates (no reaction)



Stereospecific Cis Isomers

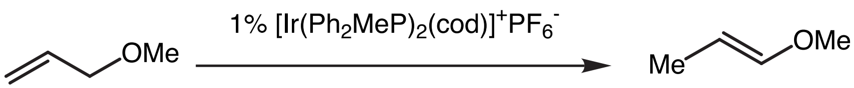


94% conversion
14:1 (cis:trans)



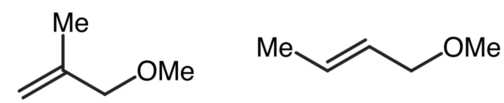
High cis selectivity due to possible platinum oxygen chelate

Stereospecific Trans Isomers



97%
2:98 (cis:trans)

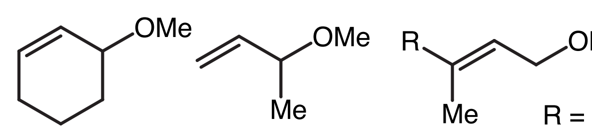
Good Substrates



98%

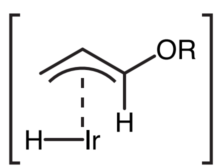
96%
2:98 (cis:trans)

Poor substrates (no reaction)



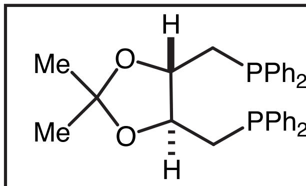
R = H or Me

Model for High Trans Selectivtiy

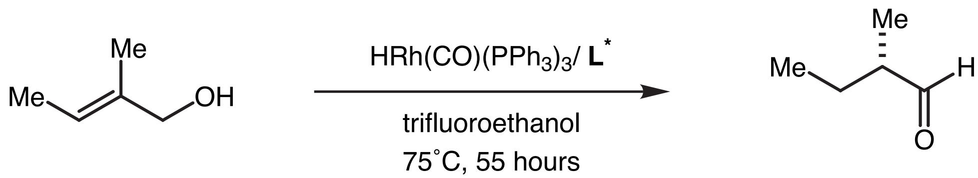


Clark, H.C. *Inorg. Chem.*, **1973**, 1566.
Baudry, D., Ephritikhine, M. *J.C.S. Chem. Comm.*, **1978**, 694.

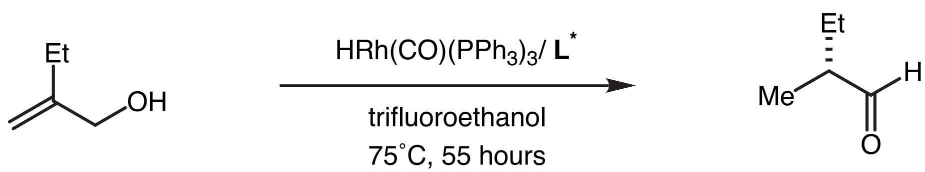
"Asymmetric" Isomerization: Earliest Report



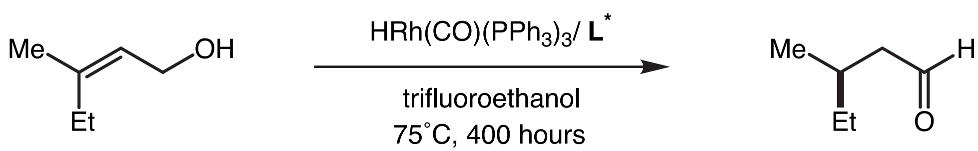
L*= (-)-DIOP



4% ee
91% conversion



3% ee
100% conversion



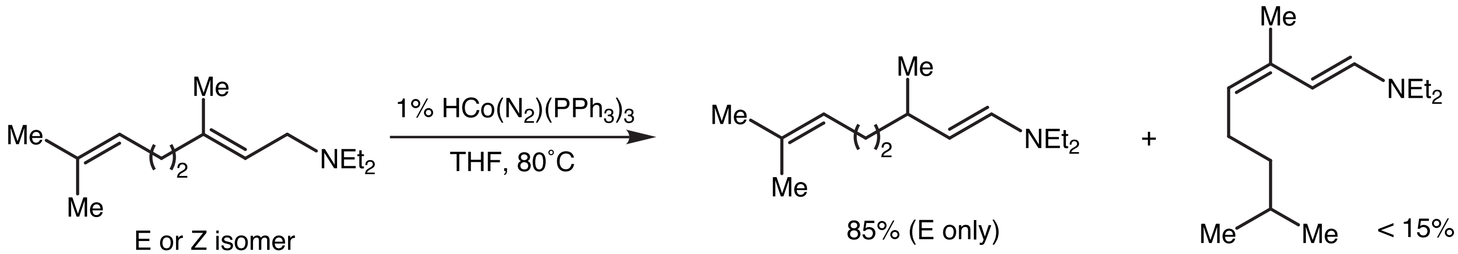
2% ee
63% conversion

Enantiomeric excess determined by optical rotation.

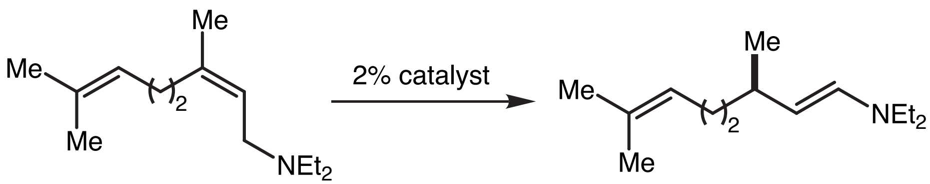
Botteghi, C, Giacomelli, G. *Gazz. Chim. Ital.* **1976**, 1131.

Isomerization of Allyl Amines: Early Studies (Otsuka)

Early Discoveries

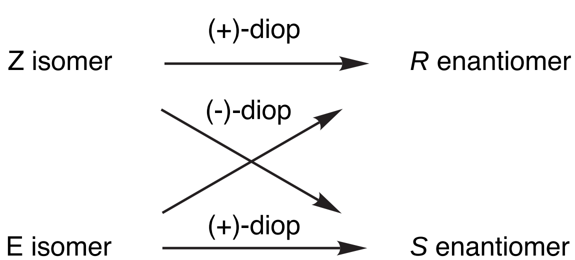


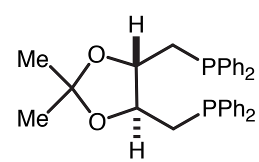
Asymmetric Version



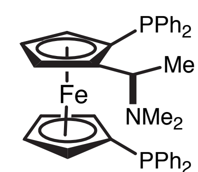
Catalyst mixture	*Yield (%)*	*ee (%)*
$Co(acac)_2$, (-)-Ph_2P-menthyl, DIBAL-H	16	7
$Co(acac)_2$, (+)-BINAP, DIBAL-H	15	20
$Co(acac)_2$, (+)-DIOP, DIBAL-H	39	32
$Co(acac)_2$, (*S*,*R*)-BPPFA, DIBAL-H	10	10

Correlation





DIOP



BPPFA

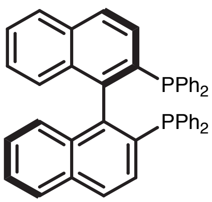
Allyl alcohols failed to isomerize.

Otsuka, S. *JACS*, **1978**, 3950.

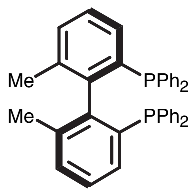
Development of an Asymmetric Catalyst

Metal choice: Rhodium (more stable, tetracoordinated complex)

Good Ligands

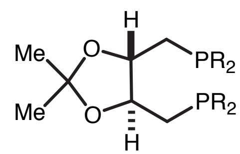


BINAP

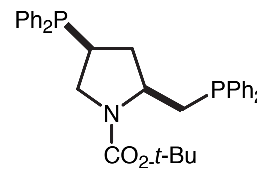


BIPHEMP

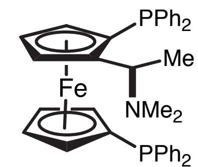
Poor Ligands



DIOP
(low ee%)
due to flexible conformation

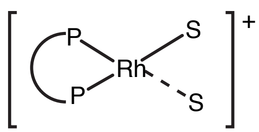


BPPM
(low ee%)



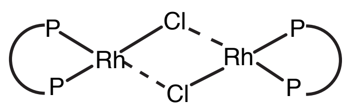
BPPFA
(no rxn)

Metal complex



cationic

vs.

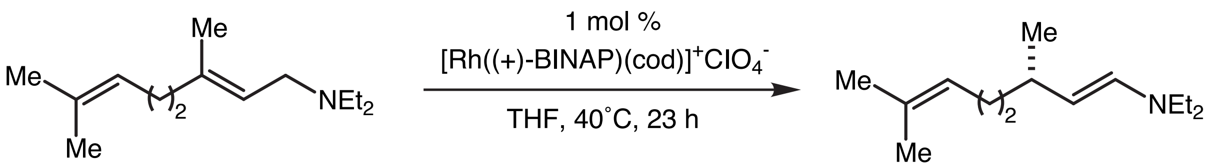


neutral

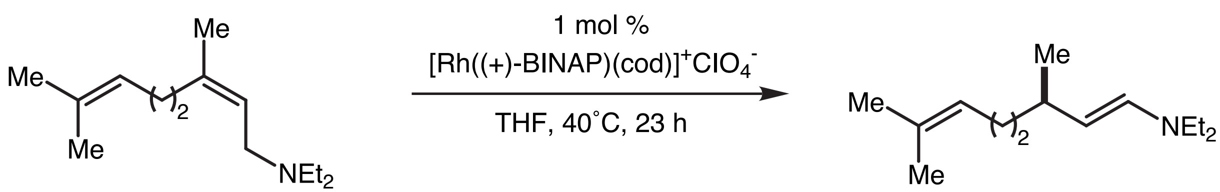
Additives:

Donor ligands such as amines,
COD, and diphosphines act as inhibitors.

Most Efficient Catalyst System



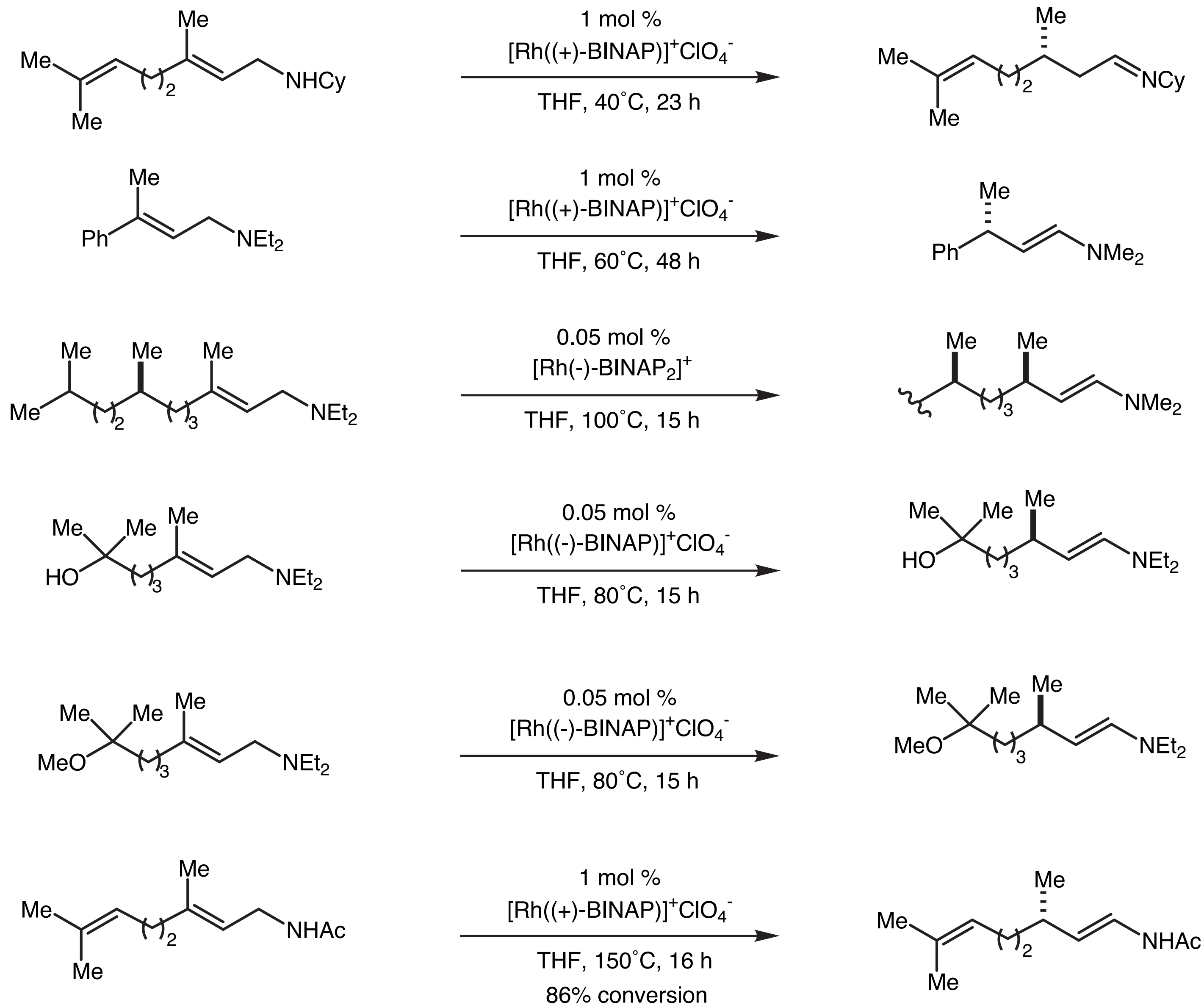
94%; 96% ee



94%; 95% ee

Otsuka, S., Tani, K. *JACS*, **1984**, 5208.

Substrate Scope (Otsuka,Tani)



100% yd; 96% ee

83% yd; 90% ee

98% yd; 97% ee

98% yd; 97% ee

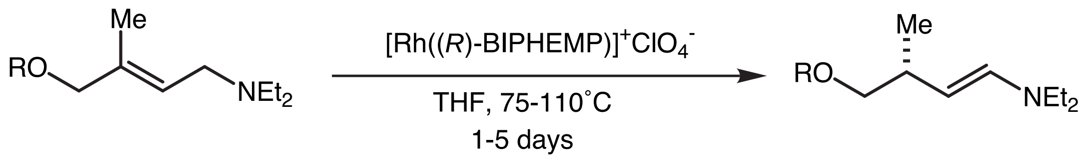
97% yd; 98% ee

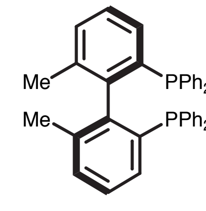
26% yd; 98% ee

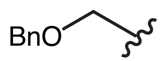
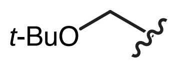
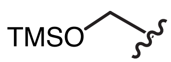
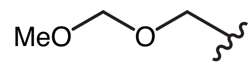
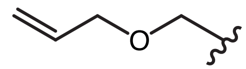
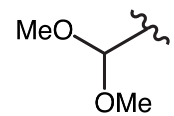
High ee even at 150˚C!

Otsuka, S., Tani, K. *Synthesis*, **1991**, 665.

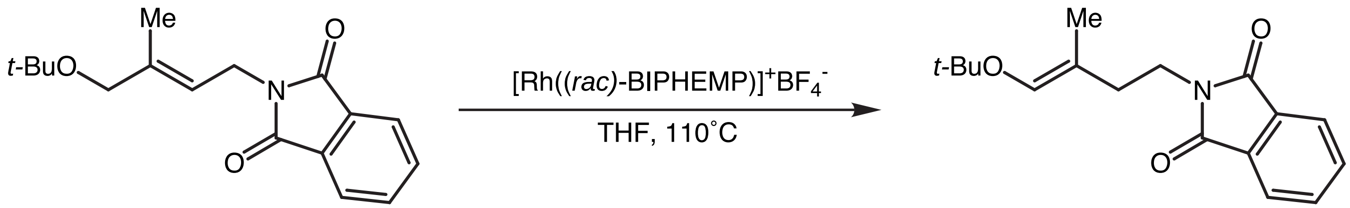
Selective Isomerization Towards Nitrogen





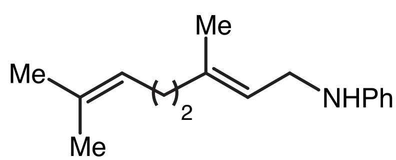
R	*Yield (%)*	*ee (%)*
	73	99
	60	94
	50	96
	19	96
	30	70
	34	90

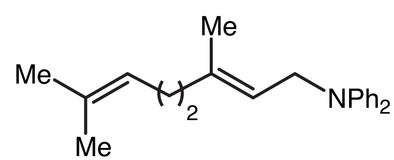
Exception



94%, 85:15 (E:Z)

Unreactive Substrates

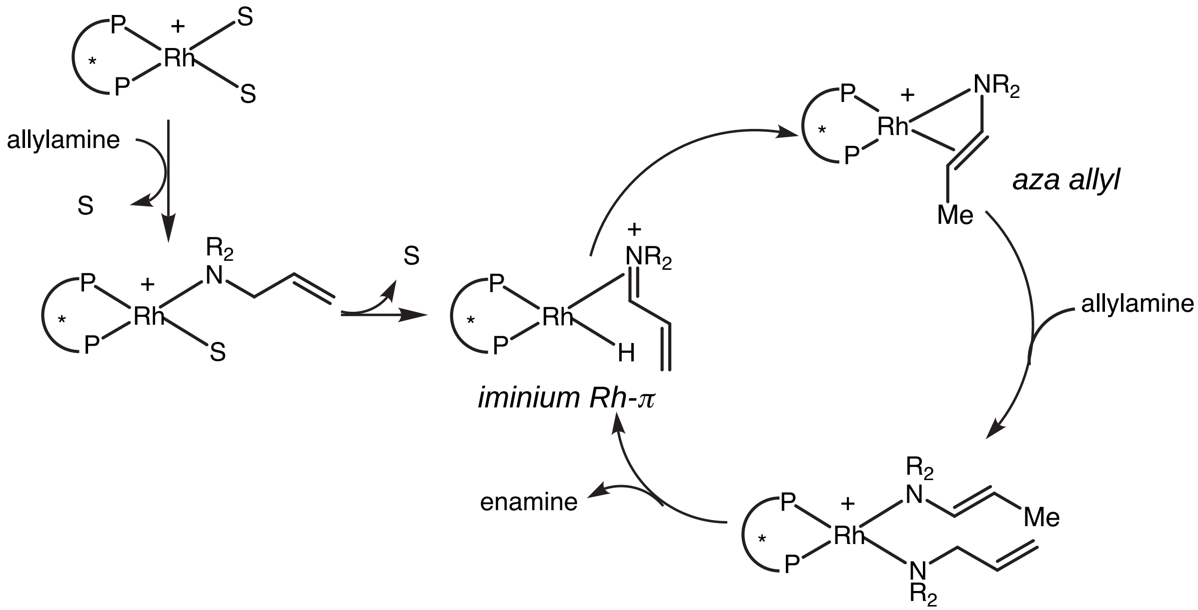




Akutagawa, S. *Compreh. Asym. Cat.*, Vol 2., Ch. 23.
Tani, K. *Pure & Appl. Chem.*, **1985**, 1845.

Mechanism & Stereoinduction

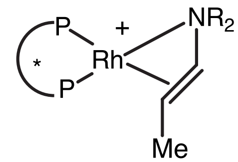
Nitrogen-Triggered Mechanism



Evidence:

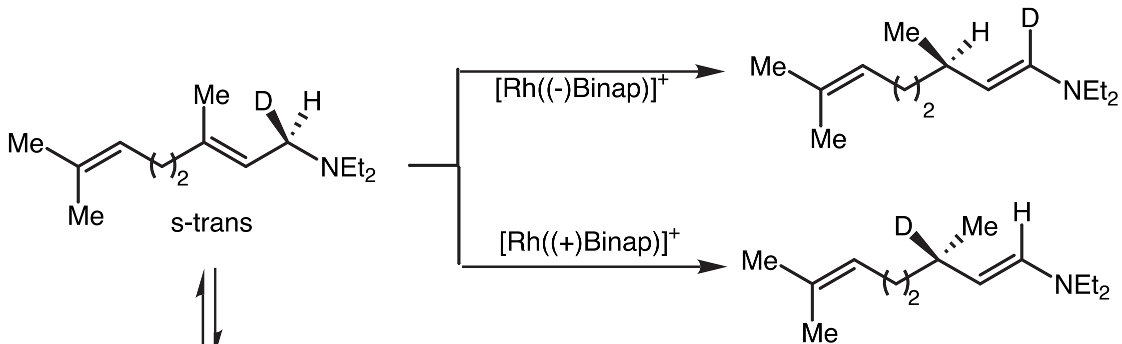
- Et_3N exchange with solvent in Rh complex observed by ^{31}P NMR

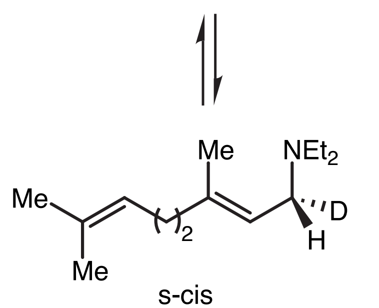
- Isolation of Rh-enamine complex



- π-allyl mechanism
  - No NMR evidence of Rh-olefin complex
  - Doesn't explain the need for nitrogen basicity
  - Rate not affected by presence of other olefins

Stereoinduction





Unlikely conformer:

- $A_{1,3}$ strain
- Antara-facial 1,3 H shift needed

- Supra-facial 1,3 H shift

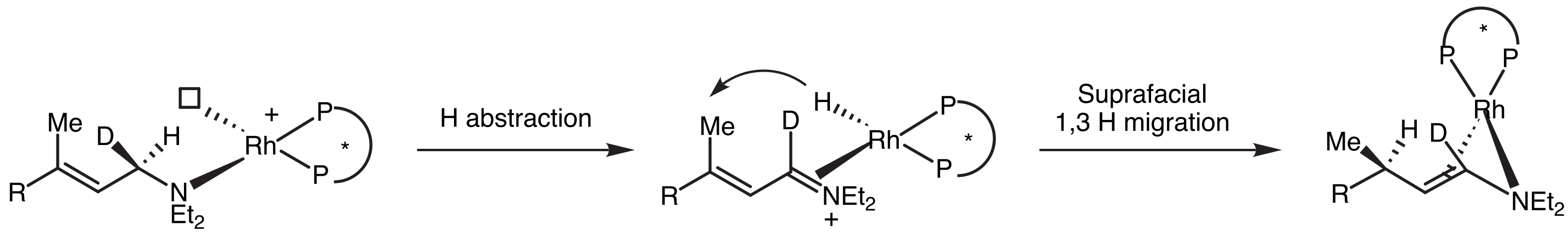
- No kinetic isotope effect observed

Noyori,R., Takaya, H. *JACS*, **1990**, 4897.

Mechanism & Stereoinduction II

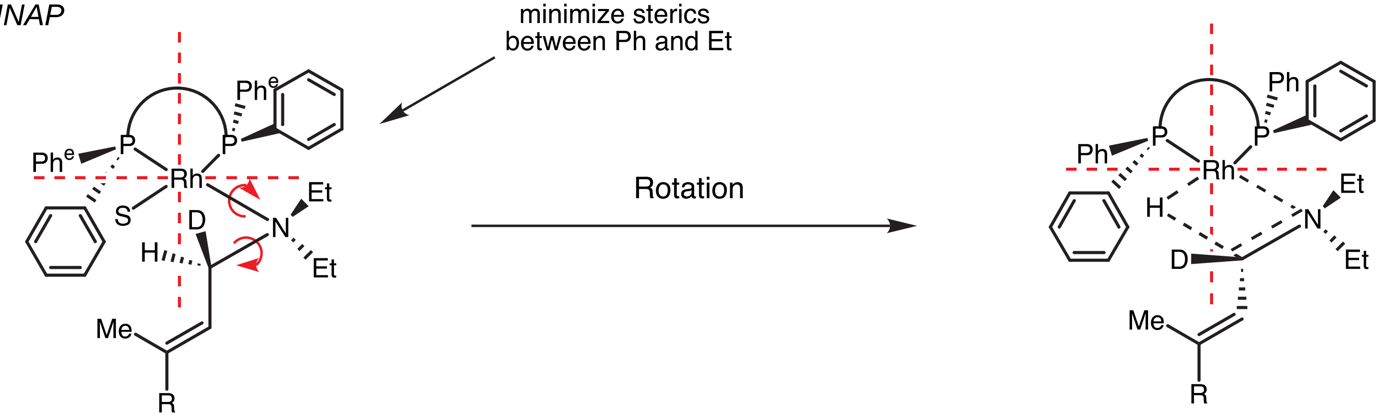
Model based on the following assumptions:

- Chiral Rh complexes recognize enantiotopic C_1 protons
- S-trans conformer is more stable relative to s-cis conformer



Chirality of BINAP determines conformation of allylamine

With Rh-(-)-BINAP

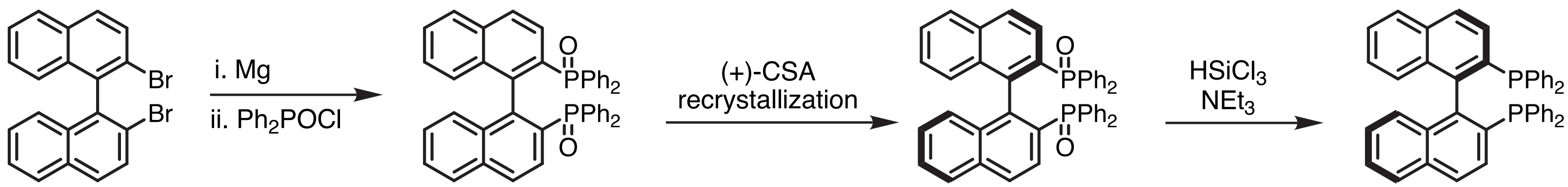


Ph^e = edge on Ph group

Noyori,R., Takaya, H. JACS, **1990**, 4897.

From Laboratory to Industry

Synthesis of Enantiomerically Pure BINAP (Takasago Perfumery Industry)



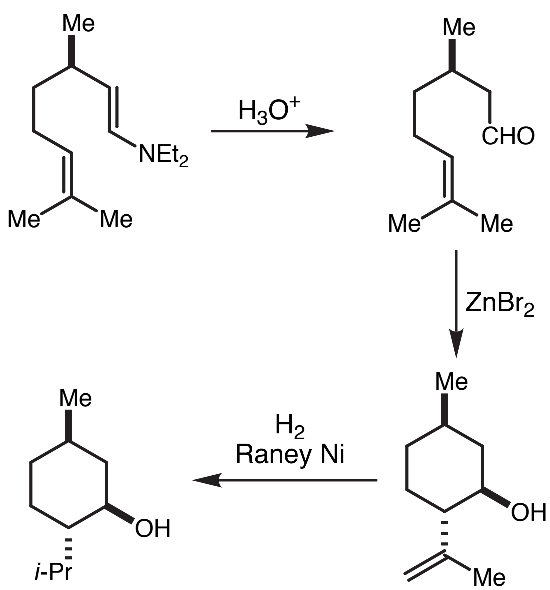
$>$ 99% purity

Optimizations:

- Geometrically pure E/Z isomers of starting allyl amines
- Stringent removal of moisture, air, and donor substances (ie. amines, enamines and olefin isomers)
- Development of a more thermally stable and soluble catalyst: chiral $[Rh(p\text{-TolBINAP})_2]^+$

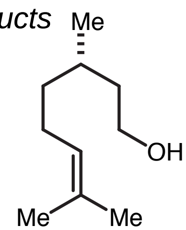
TN: $>$ 8000

Commercial Synthesis of (-) Menthol

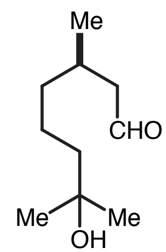


$>$ 4500 tons/yr.

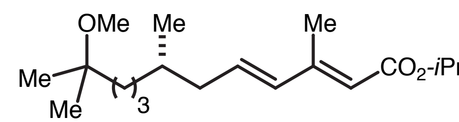
Other Natural Products



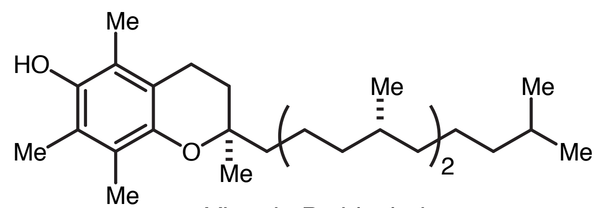
(-)-citronellol
rose oils



(*R*)-7-hydroxycitronellal
"lily of the valley"



Methoprene
mosquito juvenile hormone

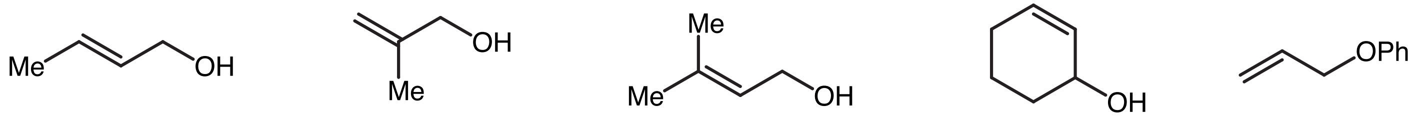


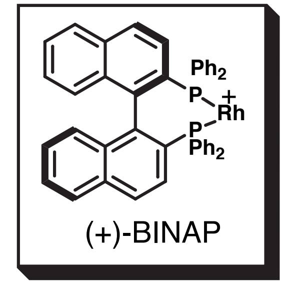
Vitamin B sidechain

Otsuka, S., Tani, K. *Synthesis*, **1991,** 665.

Allylic Alcohol Isomerization

Simple Substrates

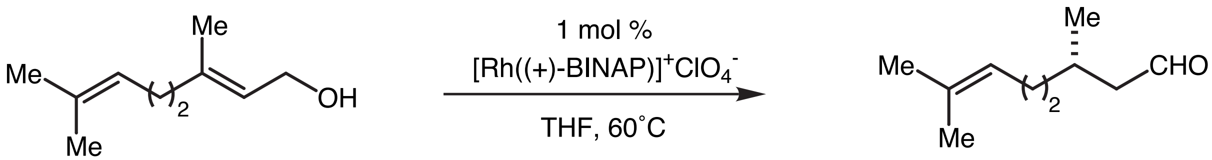




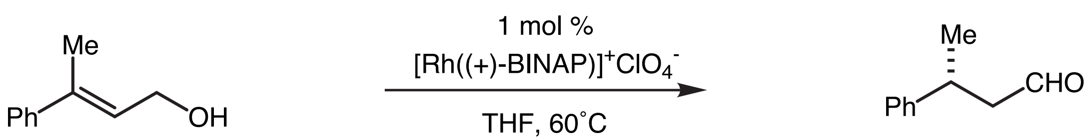
Conversions: 87% 99% 88% 82% 97%
87:13 (E:Z)

Yields are lower due to Rh(I) promoted decarbonylation of aldehydes.

Asymmetric Catalysis



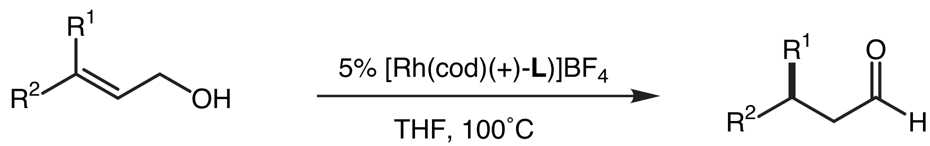
70% yd, 37% ee

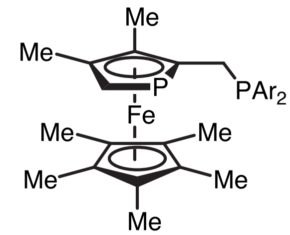


47% yd, 53% ee

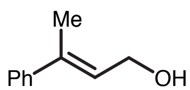
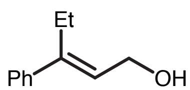
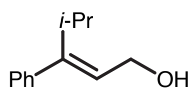
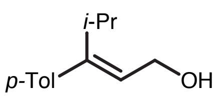
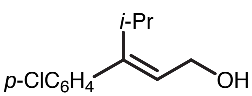
Tani, K. *Pure & Appl. Chem.*, **1985**, 1845.

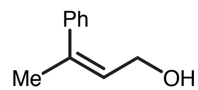
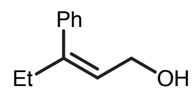
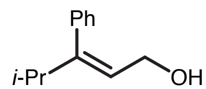
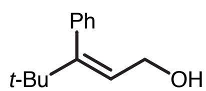
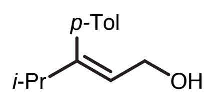
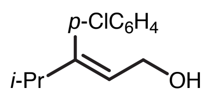
Enantioselective Allylic Alcohol Isomerization



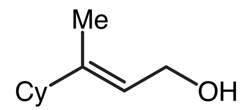


(+)-**L** (Ar = *o*-Tol)

E Allylic Alcohols	*Yield (%)*	*ee (%)*
	91	75
	96	76
	98	92
	90	91
	86	92

Z Allylic Alcohols	*Yield (%)*	*ee (%)*
	80	59
	78	57
	82	82
	90	90
	83	77
	83	85

Non-Aromatic Substrate



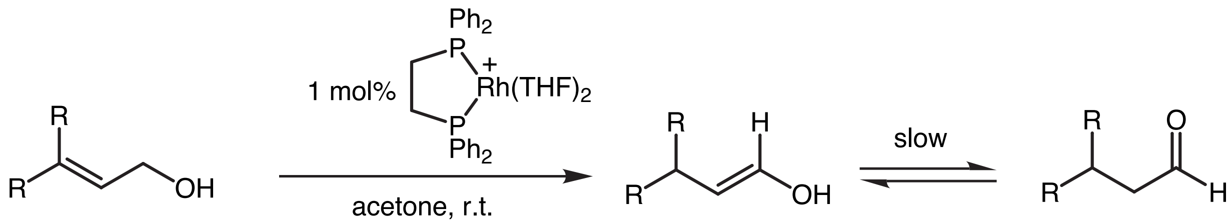
Z isomer: 87% yd, 88% ee

E isomer: 94% yd, 74% ee

- A similar mechanism (based on deuterium studies) to the Rh catalyzed isomerization of allylic amines was proposed involving Rh coordination to oxygen.
- No isomerization observed with allyl methyl ethers or homoallylic alcohols.
- Yield and enantioselectivity remain excellent at lower catalyst loading (1 mol%) and catalyst can be recycled.

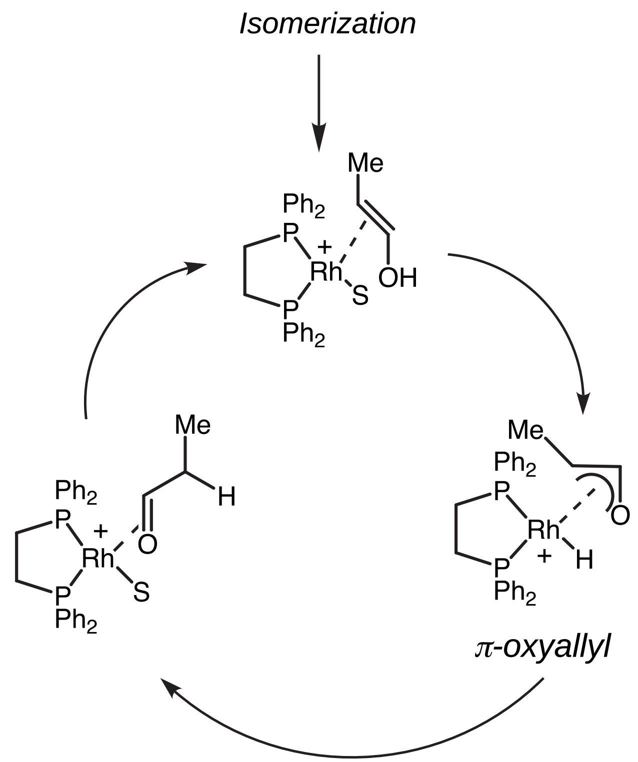
Fu, G.C. *et al*, *JACS,* **2000**, 9870.
Fu, G.C. *et al*, *JOC*, **2001**, 8177.

Generation of Simple Enols: Rh catalysts (Bosnich)

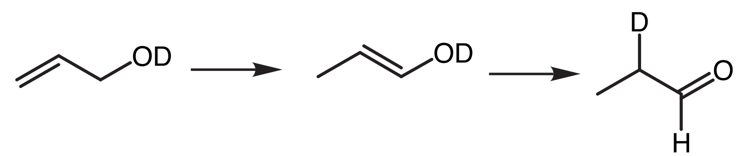


- Mixtures of E/Z
- Ketonization can take hours to days depending on the substrate

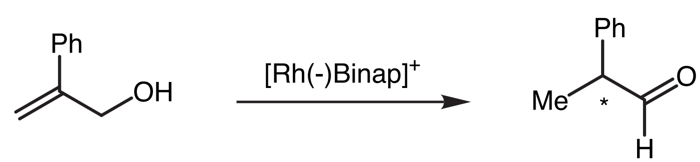
Rh Mediated Ketonization



Evidence



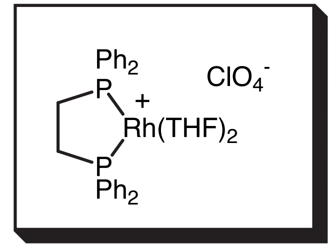
no deuterium scrambling

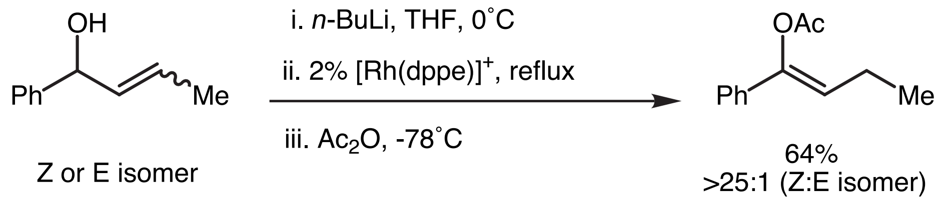


18% ee

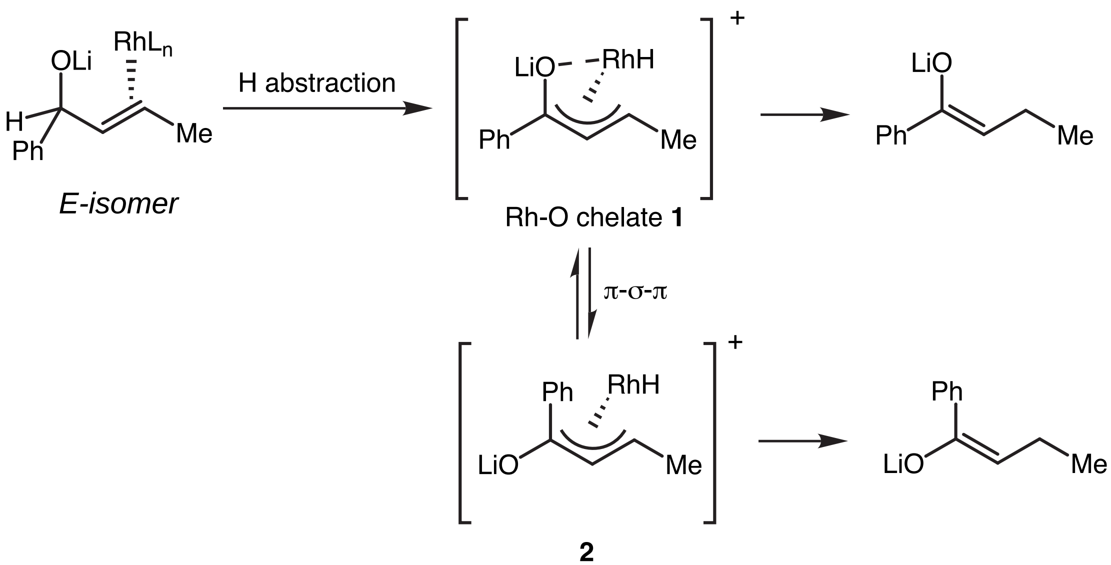
Bosnich, B. *JACS*, **1991**, 958

An Approach to Enolate Anions (Motherwell)

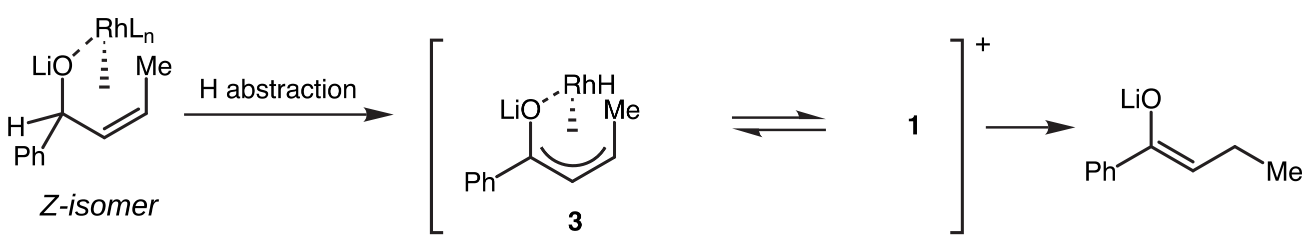




Stereocontrol



- Rh-oxygen chelate? Maybe/ maybe not...
- Z/E ratio was independent of additives such as TMEDA or 12-crown-4
- Data seems to indicate that enolate geometry is governed by thermodynamics (ie. equilibration of **1** & **2**)
- $(Ph_3P)_3RhCl$ also effective as a catalyst



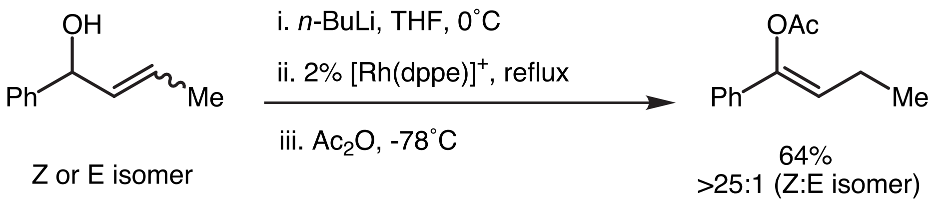
- Slightly longer isomerization times required for Z allylic alcohol - sterics or equilibration?

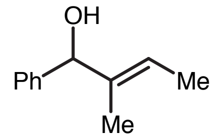
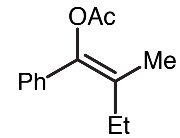
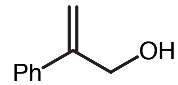
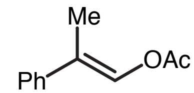
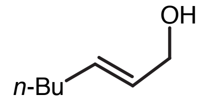
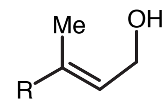
Motherwell, W.B. *et al. J. Chem. Soc. CC,* **1991**, 1399.

Motherwell, W.B. *et al. J.Chem.Soc., P.T. I,* **1999**, 979.

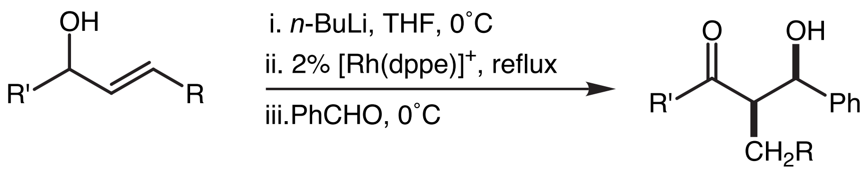
Enolization & Aldol (Motherwell)

Enolate Geometry

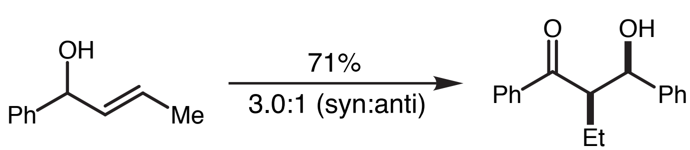


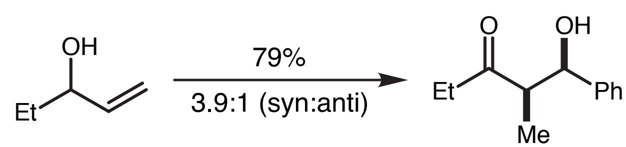
Substrate	*Product*	*Yield (%) & E/Z selectivity*
		70 1:3 (Z:E)
		78 1:10 (Z:E)
		41 1:2.8 (Z:E)
	- - -	no rxn

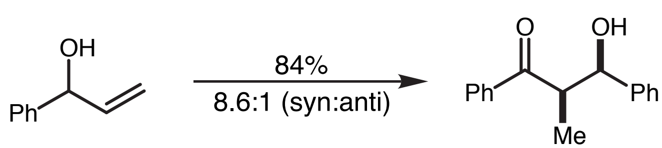
Isomerization-Aldol Processes

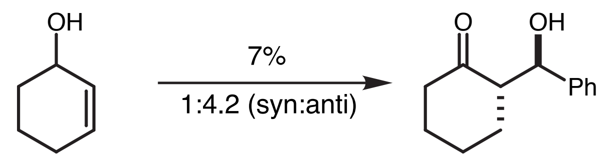


- Benchmark: 98% pure Z Li enolate gives 7.3:1 (syn:anti) product
- Erosion in diastereoselectivity
  - retro aldol vs unselective enolization from competitive ketonization of Rh-enolate complex
- Cyclohexenol precludes cisoid Rh-oxygen intermediate - implications in transition state?





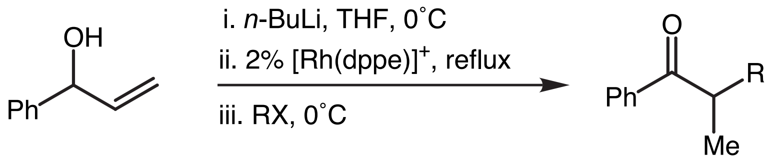




Motherwell, W.B. *et al. J.C.S., P.T. I,* **1999**, 979.

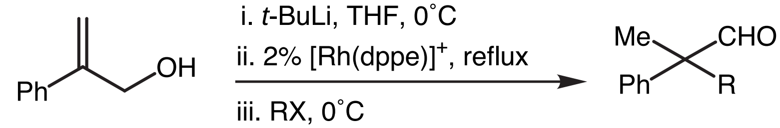
Enolate Alkylations (Motherwell)

Alkylations



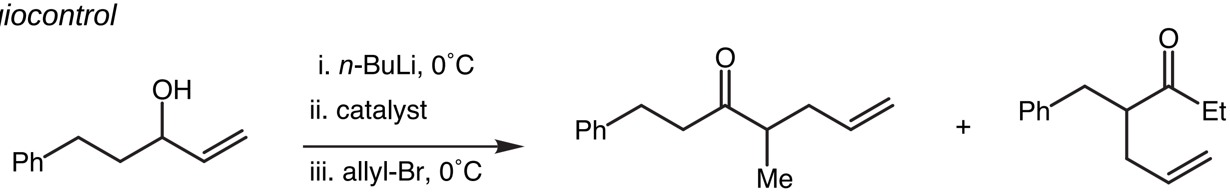
Electrophile RX	*yield (%)*
allyl bromide	82
benzyl bromide	75
methyl iodide	62
n-Bu iodide	60

Aldehyde enolates



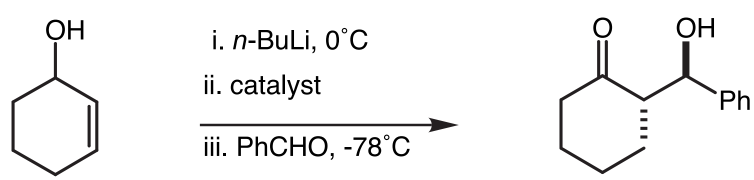
Electrophile RX	*yield (%)*
allyl bromide	72
benzyl bromide	74

Regiocontrol



1 (desired) **2**

catalyst	*yield (%)*	***1:2***
$[Rh(dppe)]^+$	79	1:1.2
$(Cy_3P)_2NiCl_2$*	78	15:1

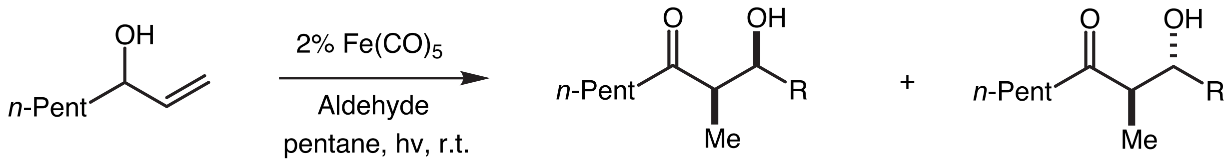


catalyst	*yield (%)*	*syn:anti*
$[Rh(dppe)]^+$	7	1:4.2
$(Cy_3P)_2NiCl_2$*	64	1:4.2

*Ni hydride catalyst

Motherwell, W.B. *TL*, **1992**, 6187.

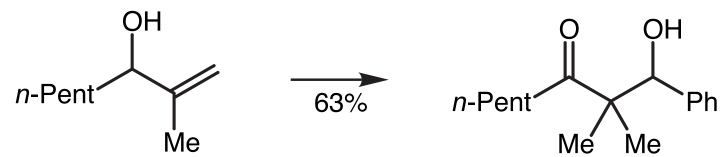
Isomerization/Aldol: $Fe(CO)_5$ (Gree)



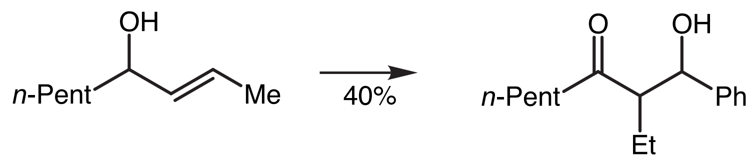
Side Products (20-30%):
regioisomer & protonated enolate

Aldehyde	*Yield (%)*	*Syn:Anti*
PhCHO	66	3:1
HCOH (anh.)	62	--
MeCHO	65	3:1
$PhCH_2CHO$	65	2.6:1
(i-Pr)$_2$CCHO	48	2.2:1

Other substrates

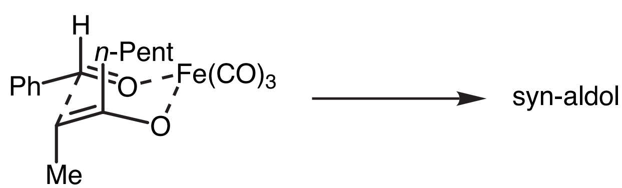


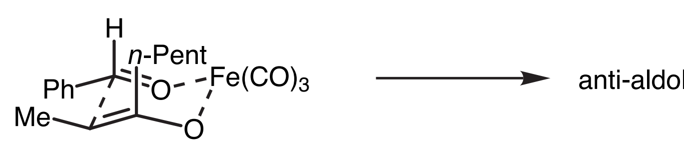
(10% regioisomer)



1.3:1 (syn:anti)

Cyclic Chair Transition State?

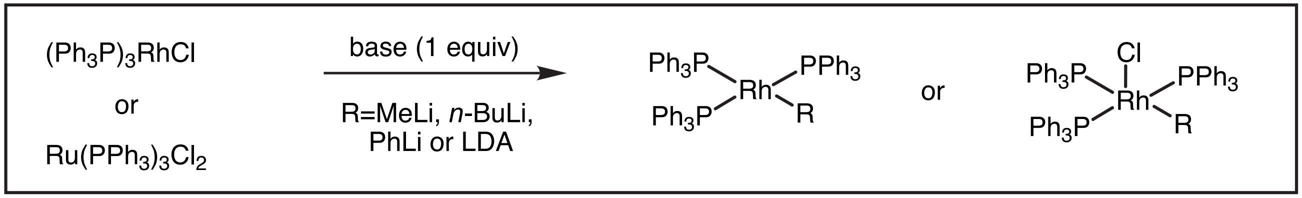




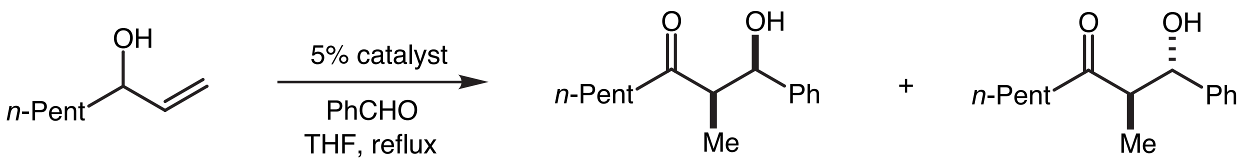
Gree, R. *TL*, **2001**, 395.
Gree, R. *TL*, **2001**, 3069.

Improvements on Regioselectivity (Gree)

In situ generation of catalyst:



Tandem Enolization/Aldol



$(Ph_3P)_3RhCl$

base	*yield (%)*	*syn:anti*
MeLi	56	39:61
n-BuLi	54	40:60
PhLi	63	37:63

$Ru(PPh_3)_3Cl_2$

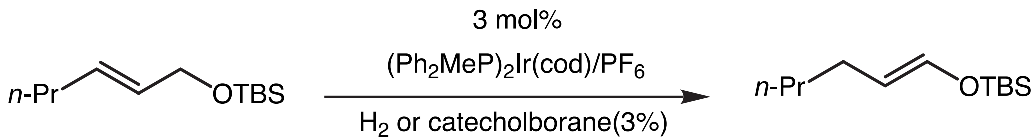
base	*yield (%)*	*syn:anti*
MeLi	73	51:49
n-BuLi	62	55:45
PhLi	75	55:45

Advantages:

- No regioisomers formed
- Possible development of asymmetric catalysis
- Neutral rather than basic conditions

Gree, R. *TL*, **2001**, 3069.

Stereoselective Silyl Enol Ether Formation (Miyaura)

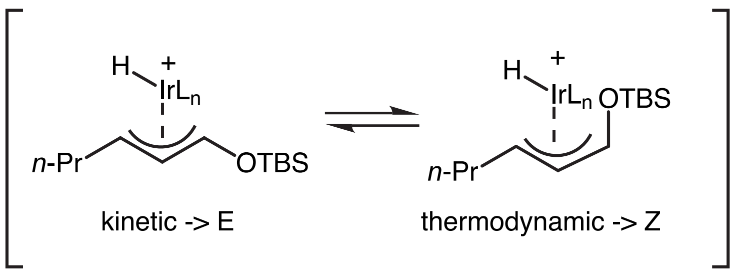


99% conversion
E:Z > 99:1

NMR Study: (CH_2Cl_2:acetone (50:1), 0˚C)

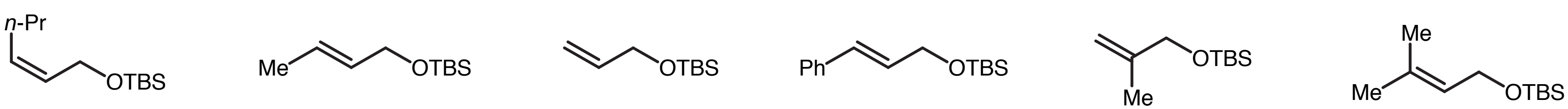
time (min)	*conversion (%)*	*E:Z*
5	61	98:2
60	>99	85:15
360	>99	38:63

Authors proposed that E selectivity is kinetically driven:



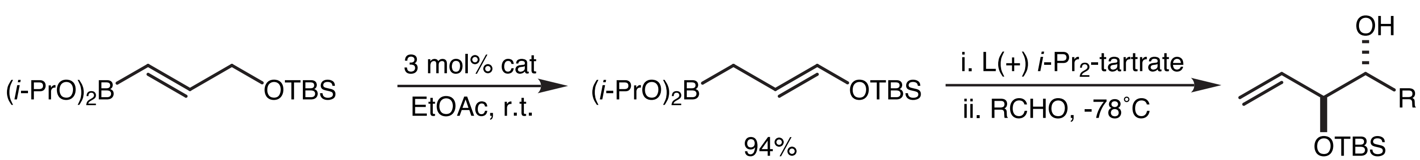
- Acetone - best solvent (fast isomerization, no product equilibration)
- Treating pure E or Z enol silanes with Ir catalyst in CH_2Cl_2/acetone leads to a thermodynamic ratio.
- Unfortunately, cannot equilibrate all the way to give only Z enol silanes.

Substrate Scope



74%	84%	78%	76%	91%	<10%
95:5 (E:Z)	97:3 (E:Z)	99:1 (E:Z)	98:2 (E:Z)		

Chiral Allyl Boronates

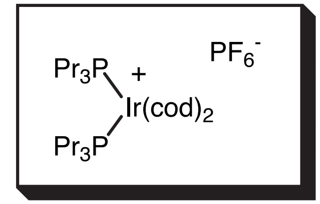


94%
98:2 (E:Z)

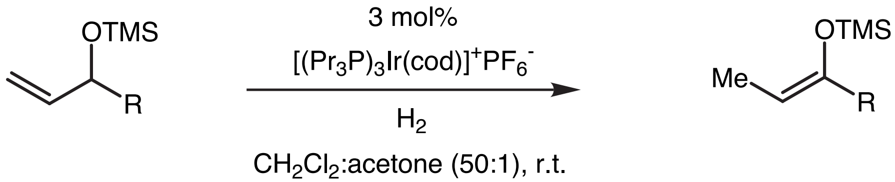
depending on R:
d.r. > 99:1; 67-91% ee

Miyaura, N. JOC, **1999**, 296.
Miyaura, N. *OrgMet.*, **1999**, 413.

Secondary Enol Silanes (Miyaura)



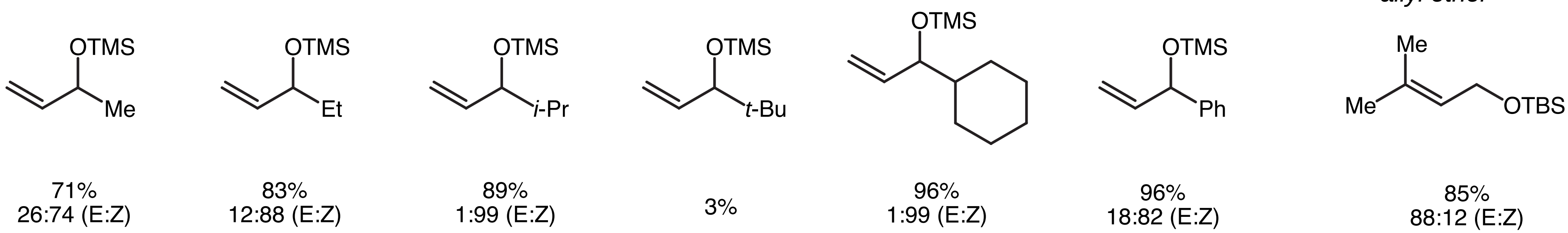
A More Active Catalyst



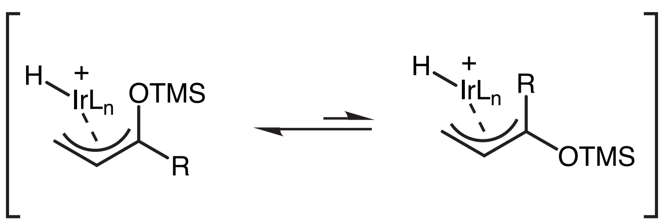
Z enol silane favored!

Substrate Scope

hindered 1°
allyl ether



Stereocontrol

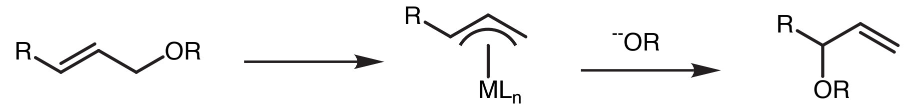


Z enol silane favored due to thermodynamics.

Miyaura, N. *Organometallics*, **1999**, 413.

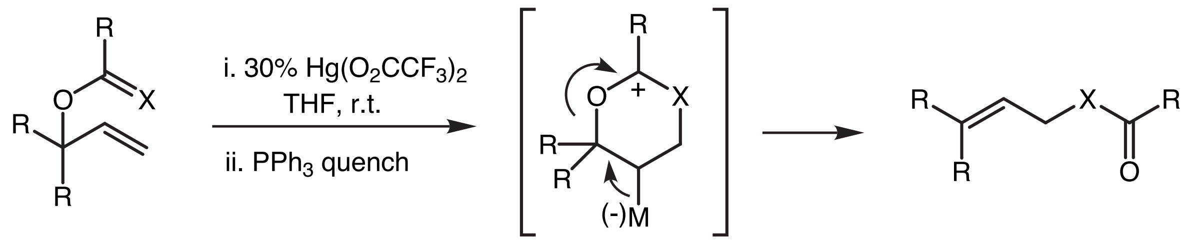
Allylic Rearrangements (Hg salts-Overman)

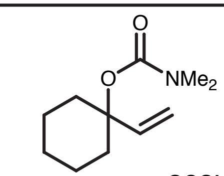
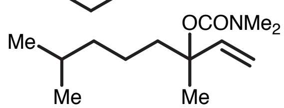
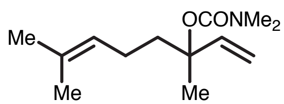
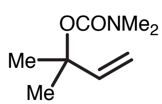
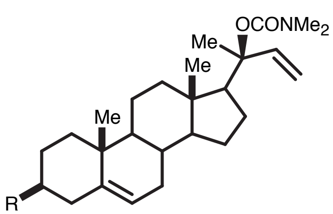
Rearrangements involving π-allyl complexes (not covered)



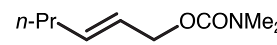
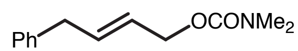
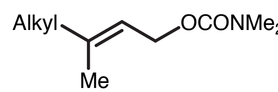
Frank Glorius (Seminar 2000)

Mercuric Salts (Overman)

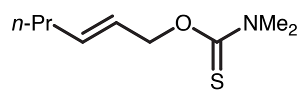
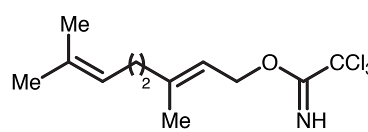


Substrate	*Yield (%)*
	95
	92
	70
	98
	96

"Contra-thermodynamic" Cases

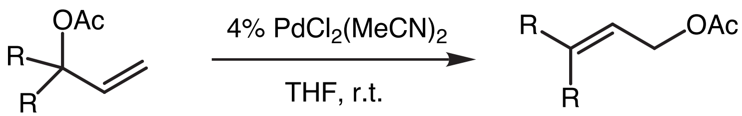
Substrate	*Yield (%)*	*Terminal: starting material*
	80	95:5
	86	71:29
	61	15:85

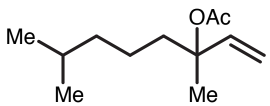
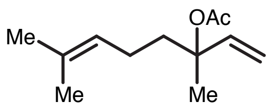
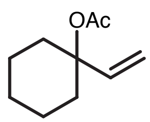
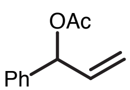
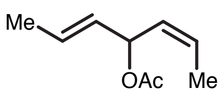
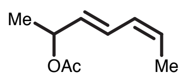
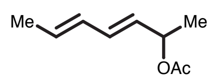
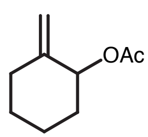
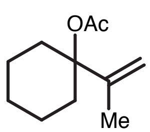
Excess Hg salts and PPh_3 are needed to overcome thermodynamic preference.

	52	100:0
	79	100:0

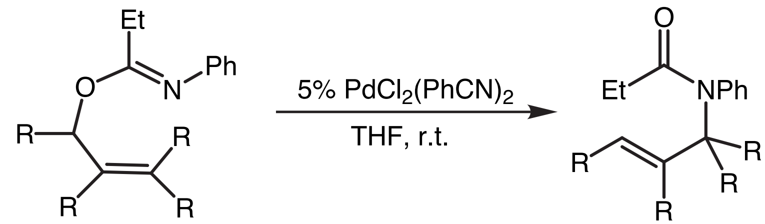
Overman, L.E. *et al. JACS*, **1978**, 4822.
Review: Overman, L.E. *et al. ACIEE*, **1984**, 579.

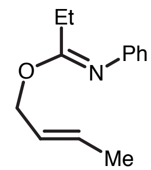
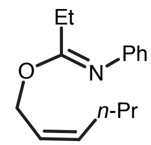
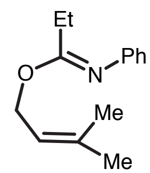
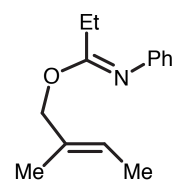
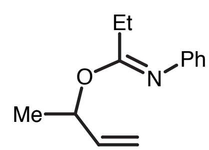
More Active Catalysts: Pd(II) salts



Substrate	*Yield (%)*
	88 78:22 (E:Z)
	96% 89:11 (E:Z) rxn at 70˚C
	93
	96
	 +  74 18
	no rxn
	no rxn

Overman, L.E. *et al. ACIEE*, **1984**, 579.

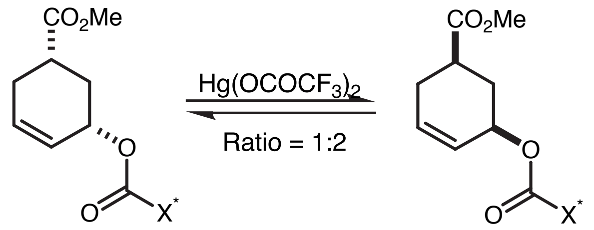


Substrate	*Yield (%)*
	79
	74
	90
	75
	68

Metz, P. *Tet*, **1992**, 1071.

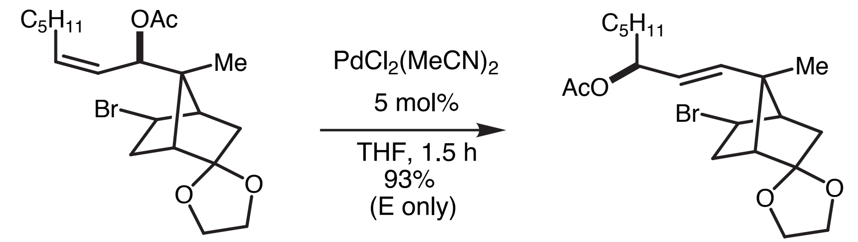
Allylic Rearrangement: Chirality Transfer

Trost (*CC*, **1978**, 436.)

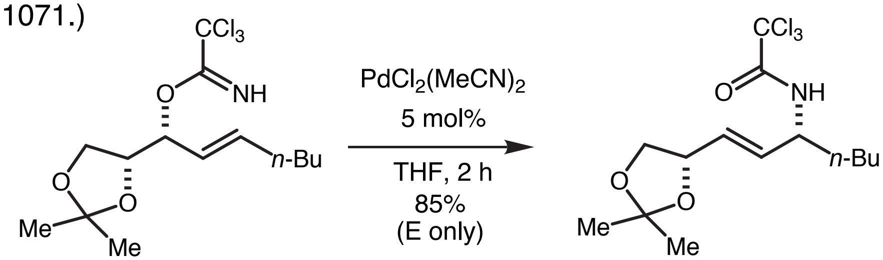


X=(S)-α-Napthylethylamino

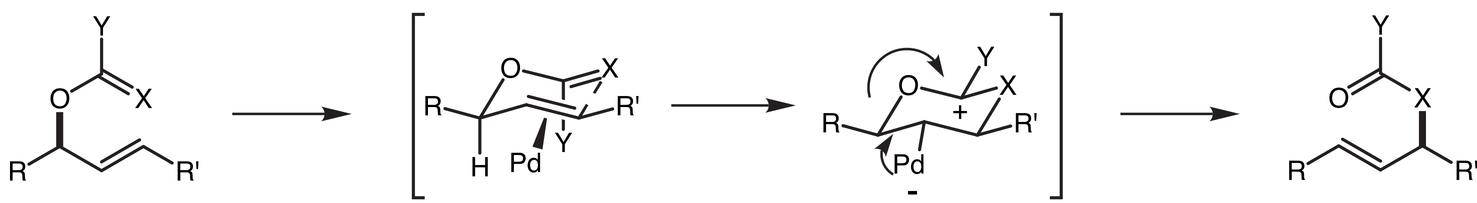
Grieco (*JACS*, **1980**, 7587.)



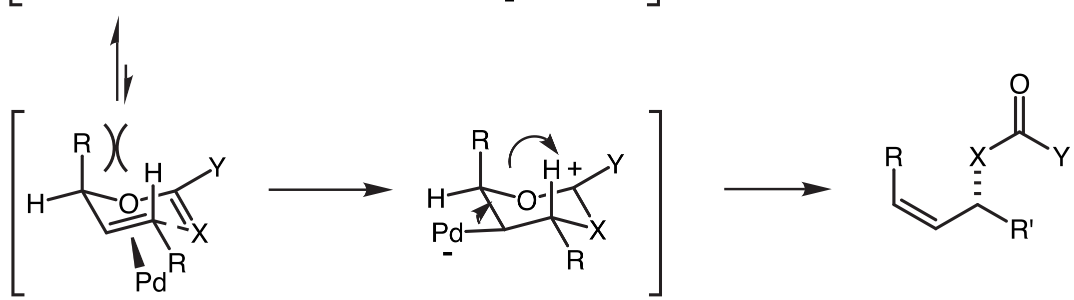
Meetz (*Tet*., **1992,**1071.)



Cyclization-Induced Rearrangement (Overman)

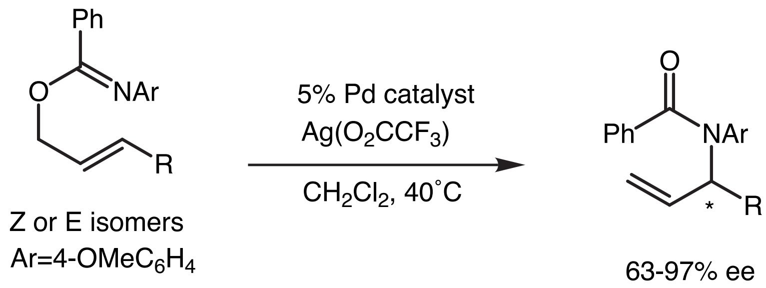


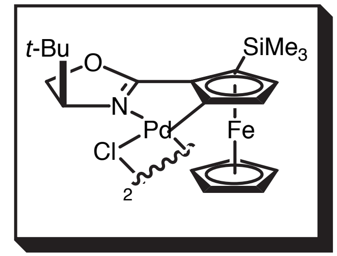
Retention of stereochemistry & lack of olefin scrambling support a non π-allyl mechanism

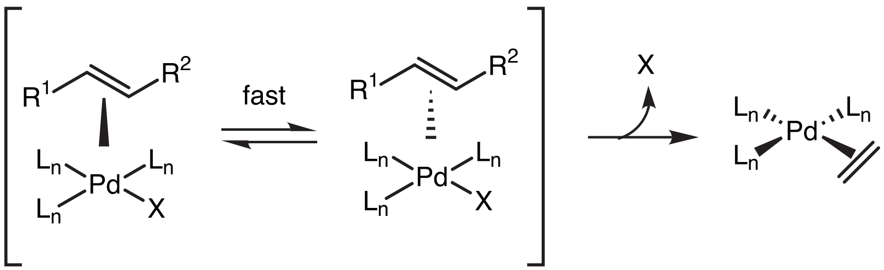


Overman, L.E. *ACIEE*, **1984**, 579.

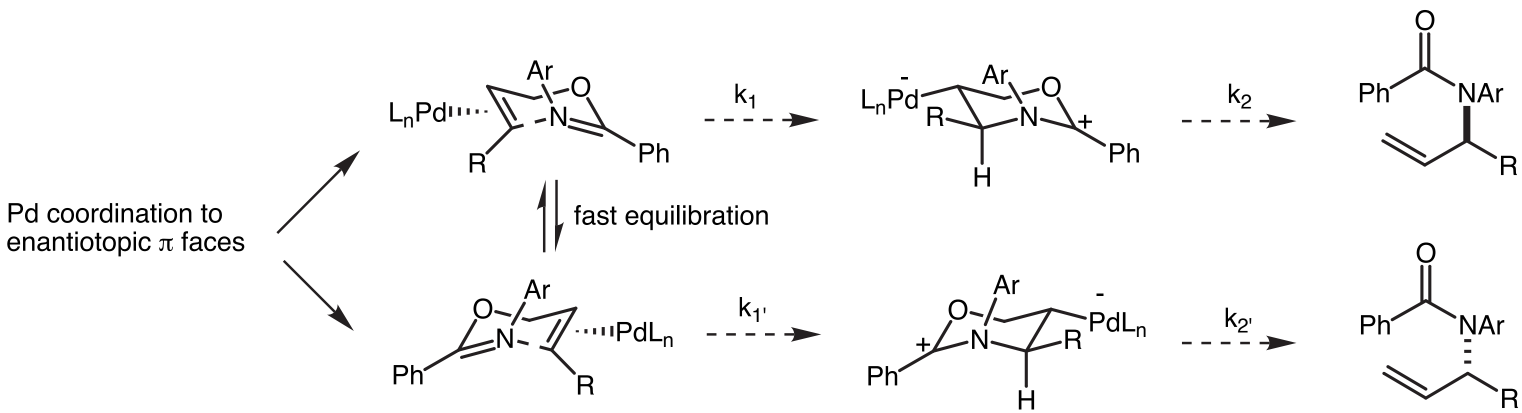
Enantioselective Rearrangement: Allylic Imidates





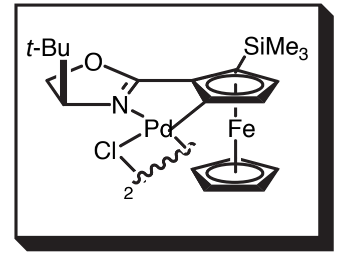


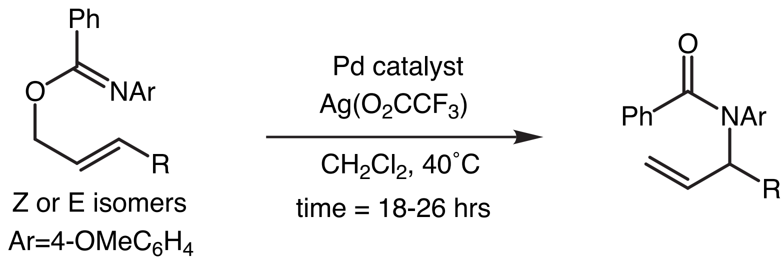
- Initial steps are likely: association, psuedo-rotation, dissociation
- Coordination of Pd to π-face of the olefin determines enantioselectivity; it is, however, not the rate determining step
- Possible rate determining steps that lead to observed enantioselectivity: cyclization or elimination



Overman, L *et al. J. Orgmet. Chem*., **1999**, 290.

Substrate Scope and Other Ligands





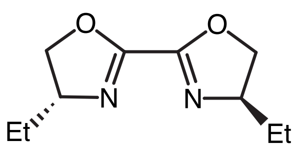
Z Isomers

R	*Yield (%)*	*ee (%)*
Me	96	75 (*R*)
n-Pr	83	91 (*R*)
i-Bu	90	97 (*R*)
i-Pr	59	86 (*R*)
Bn	85	88 (*R*)
Ph	11	77 (*R*)

E Isomers

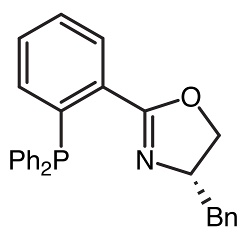
R	*Yield (%)*	*ee (%)*
n-Pr	93	83 (*S*)
i-Bu	97	84 (*S*)
Ph	59	63 (*S*)

Earlier Catalyst Systems



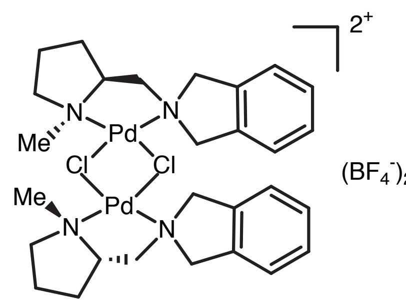
62% yield
10% ee

(Hayashi)



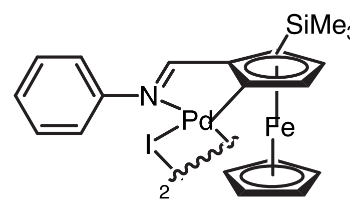
41% yield
76% ee

(Hayashi)



69% yield
55% ee

(Overman)



91% yield
49% ee

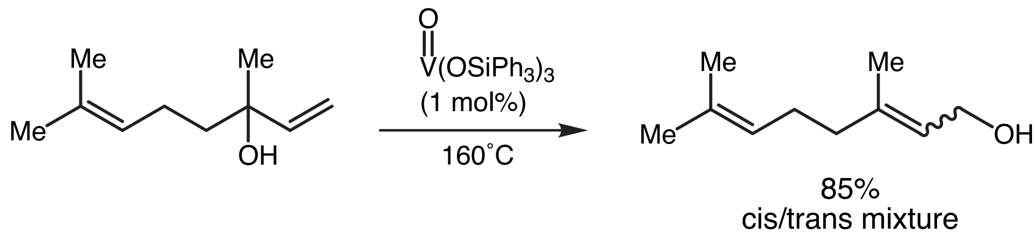
(Overman)

Yields/ee for R = *n*-Pr (E isomer)

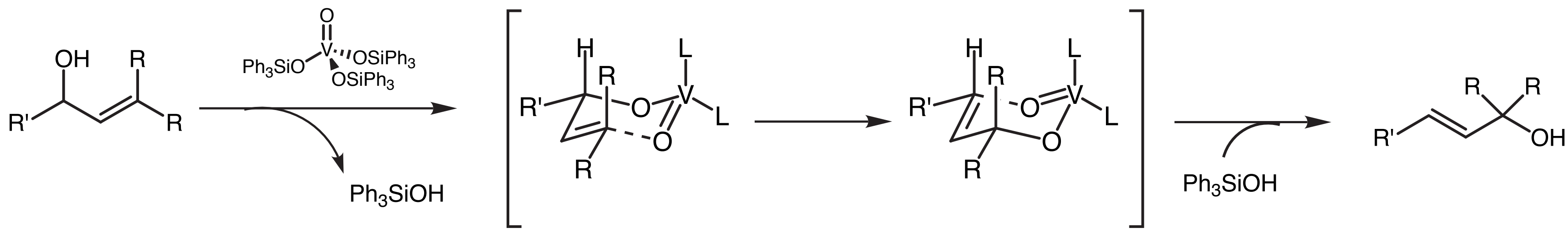
Overman, L. *J. Orgmet. Chem.*, **1999**, 290.

Allylic Rearrangements with Oxo Metals

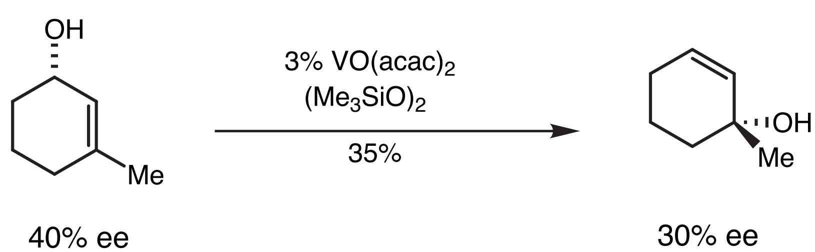
Earliest Example



Charbardes' Proposal



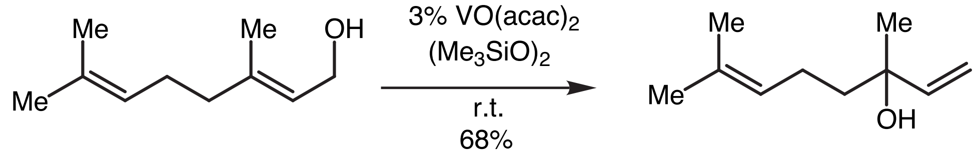
Chirality Transfer

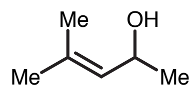
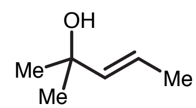
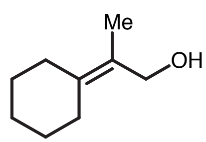
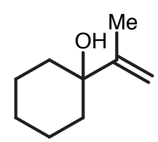
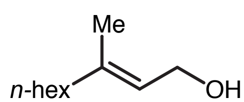
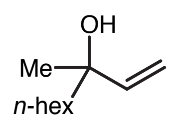
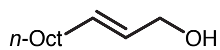
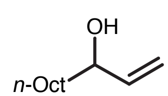
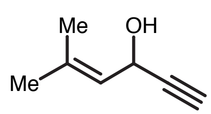
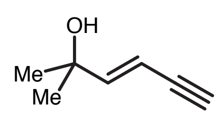


Chabardes, P. *Tet.*, **1977**, 1775.

Takai, K. *Bull. Chem. Soc. Jpn.*, **1985**, 844.

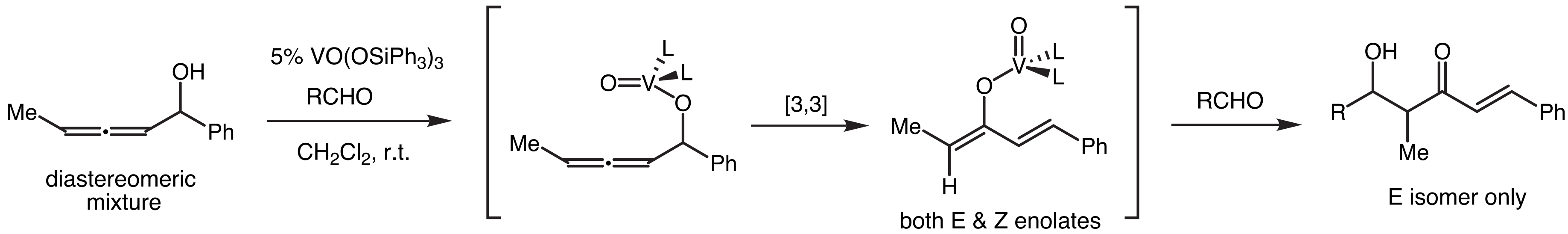
Vanadate Catalysts (Takai)

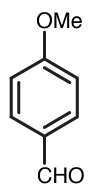
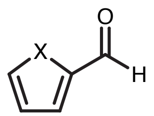
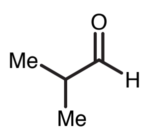
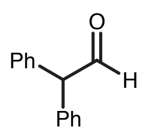
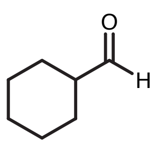


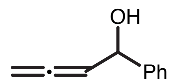
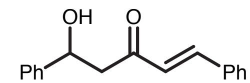
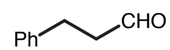
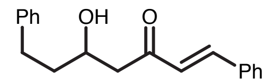
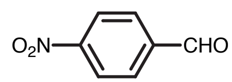
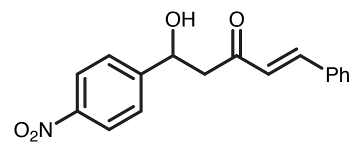
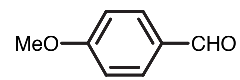
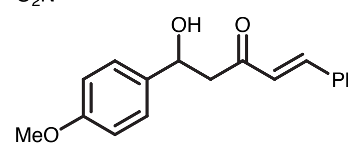
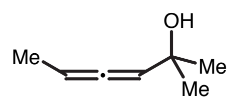
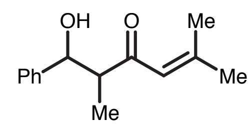
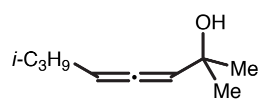
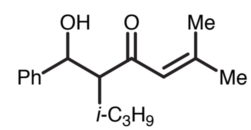
Substrate	*Product*	*Starting Material (%)*	*Product (%)*
		0	97 E only
		0	85
		20	53
		41	35
		0	70 E only

Takai, K. *Bull. Chem. Soc. Jpn.*, **1985**, 844.

Allenic Alcohol Isomerizations (Trost)



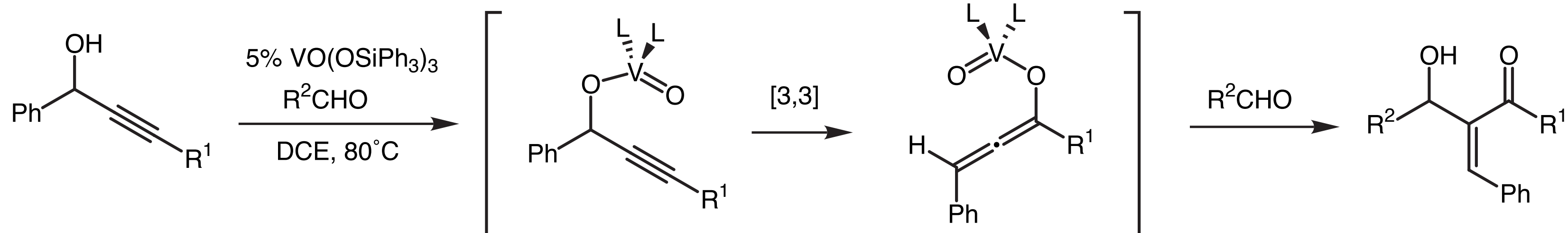
Aldehyde		*Yield(%)*	*Syn:Anti*
PhCHO		86	80:20
		83	42:58
	X=O	88	67:33
	X=S	86	68:32
	X=NBoc	88	70:30
		79	78:22
		71	80:20
		61	66:33

Other Allenes	*Aldehyde*	*Product*	*Yield(%)*
	PhCHO		85
"			70
"			83
"			64
	PhCHO	 77:23 (syn:anti)	86
	PhCHO	 88:12 (syn:anti)	57

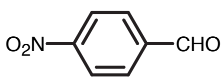
• Diastereomerically pure allenol gave similar syn:anti ratios

Trost, B.M. *et al. JACS* **2001**, 12736.

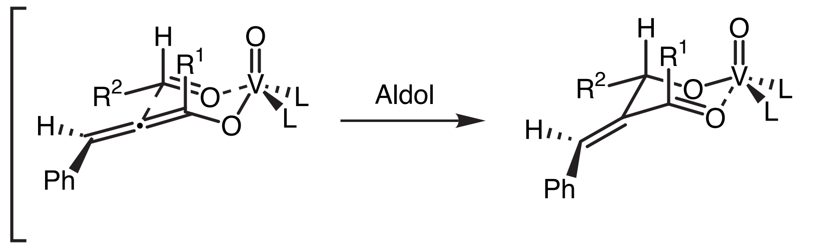
Propargyl Alcohol Isomerizations (Trost)



Z isomer

Propargyl Alcohol (R^1)	*Aldehyde (R^2)*	*Yield (%)*	*Z:E*
n-Bu	PhCHO	94	91:9
t-Bu	PhCHO	95	98:2
Ph	PhCHO	73	88:12
CH_2OTBS	PhCHO	42	only Z
n-Bu		77	only Z
n-Bu		92	only Z
n-Bu	*n*-PrCHO	55	89:11
n-Bu	chex-CHO	58	96:4

Chair Transition State Model

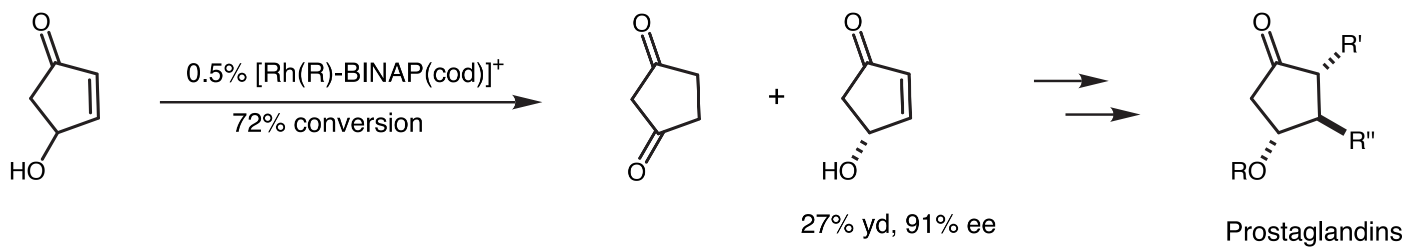


Aldehyde approach from opposite face of Ph explains high selectivity for Z isomer.

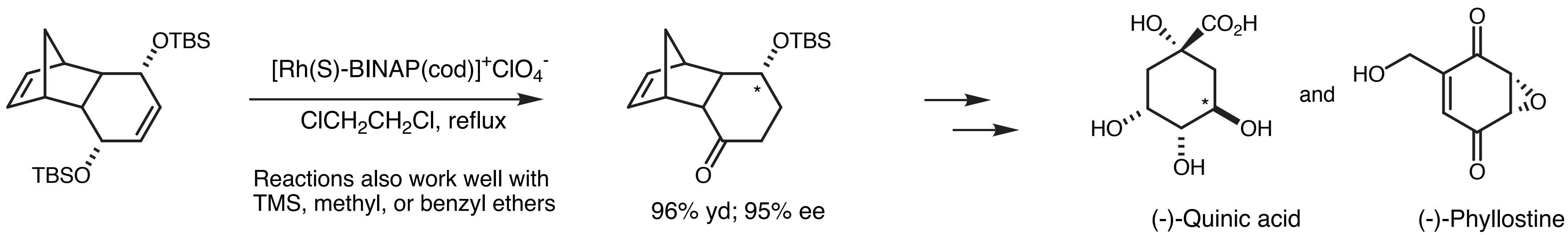
Trost, B.M. *JACS,* **2001**, 1230.

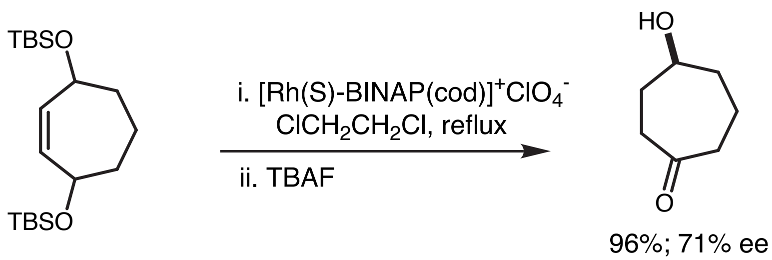
Desymmetrizations

Noyori, R. *TL*, **1987**, 4719.

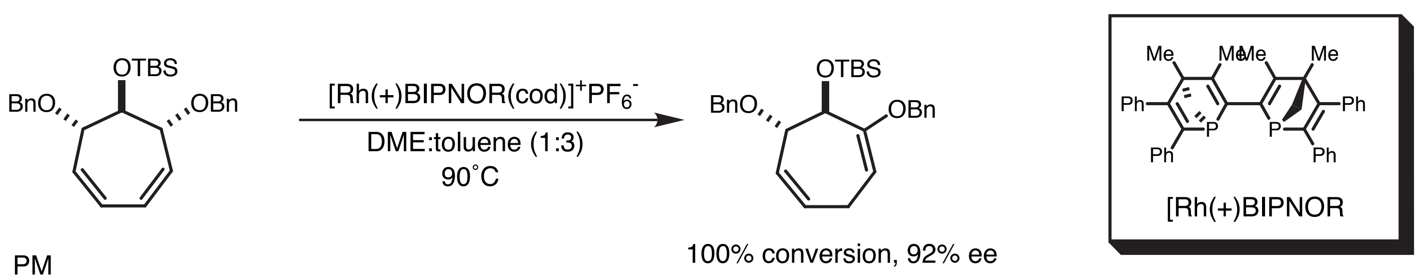


Ogasawara, K., *ACIEE,* **1995**, 2287.

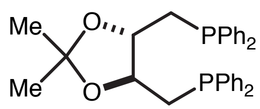




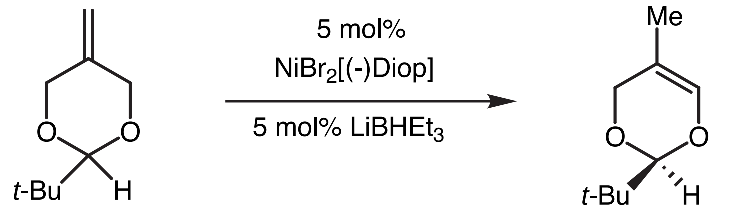
Mathey, F. *Tet*, **2000**, 101.



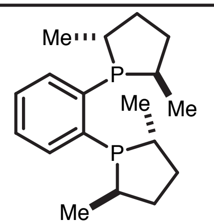
Desymmetrization of Cyclic Allylic Acetals (Frauenrath)



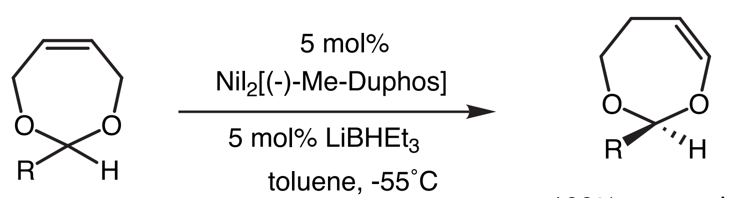
(-)Diop



86%; 92% ee



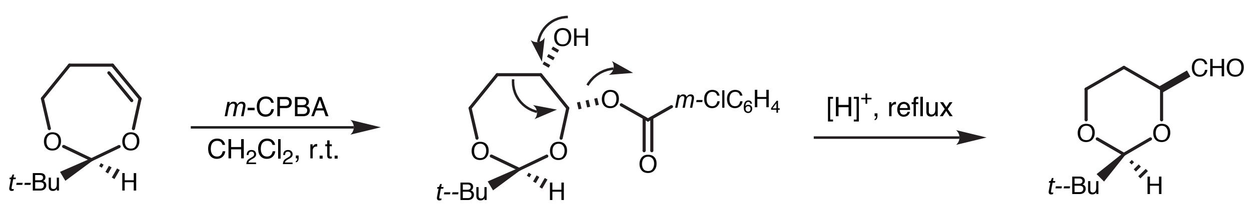
(-)-Me-Duphos



100% conversion

R	*ee (%)*
t-Bu	98
i-Pr	90
n-Bu	90

Synthetic Use:



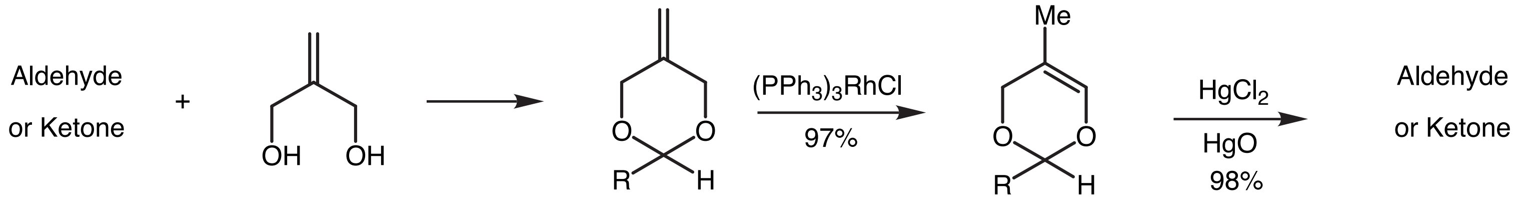
75%, d.r. 95:5

75%, d.r. 83:17

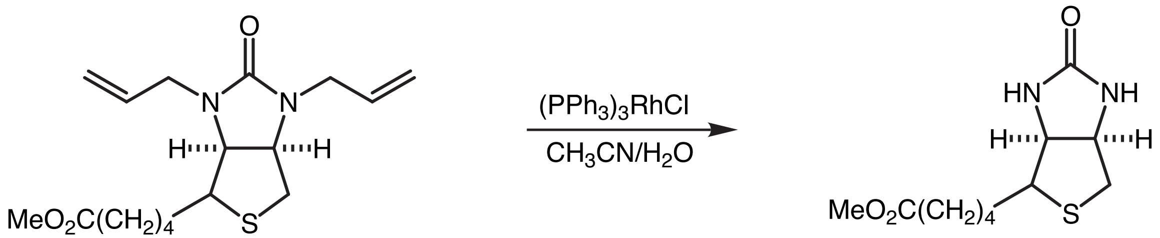
Frauenrath, H. *et al. Tet. Asym.*, **1998**, 1103
Frauenrath, H. *et al. ACIEE*, **2001**, 177

Allyl Protecting Groups

Protection of Aldehydes/Ketones (*TL*, **1975**, 3775)



Biotin Synthesis (*J.C.S. P.T.II*, **1973**, 1954)



Carbohydrates (*J.C.S. P.T.I.*, **1980**, 738.)