Hydrogenation of Alkenes

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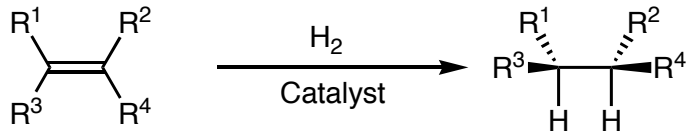

A. Heterogeneous Catalysts

Catalysts
Pd on C (5%, 10%)
$Pd(OH)_2$ (Pearlman's catalyst): Debenzylation
Ra Nickel
PtO_2
Pt on C
5% Rhodium on carbon

B Homogeneous Catalysts

Catalysts
$RhCl(PPh_3)_3$
[Os, Cu, Co, Ir, Cr, Mo, W, Ni, Ru, etc.]

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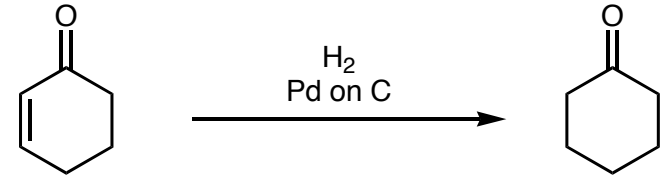
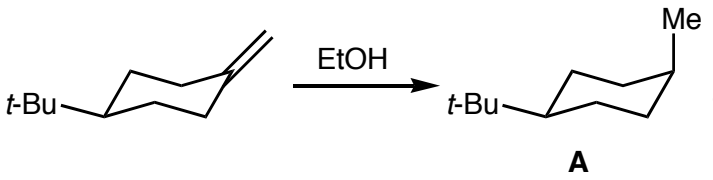
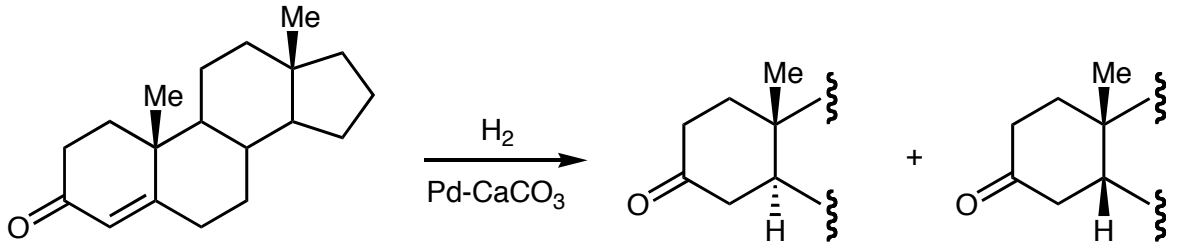




A **B**

	A : B
Rh-C	77 : 14
Pt-C	71 : 29
Pd-C	35 : 65

J. Chem. Soc. C **1967**, 2467



CH_3CN	5 : 95
C_6H_6	23 : 77
THF	39 : 61
i-PrOH	50 : 50

Hydrogenation of Alkenes

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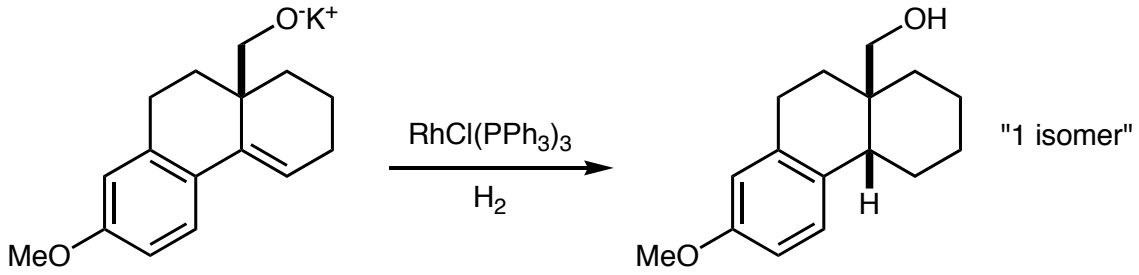
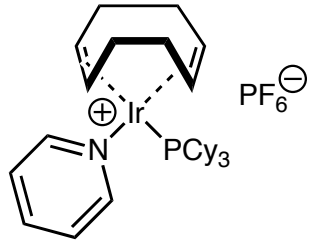
Thompson, H. W.; McPherson, E. *J. Am. Chem. Soc.* **1974**, *96*, 6232-6233.

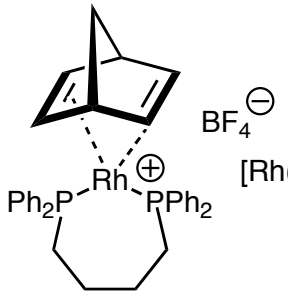


Efficient homogeneous cationic catalysts:



$[Ir(cod)py(PCy_3)]PF_6$

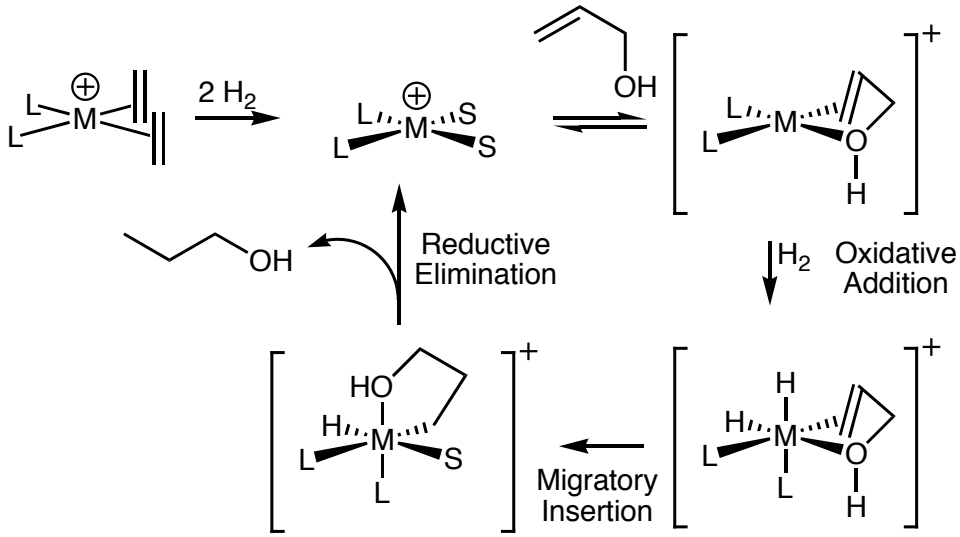
A



$[Rh(nbd)(diphos\text{-}4)]BF_4$

B

Hydrogenation of Alkenes



Hydrogenation of Alkenes

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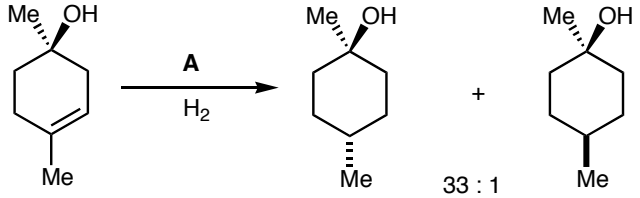
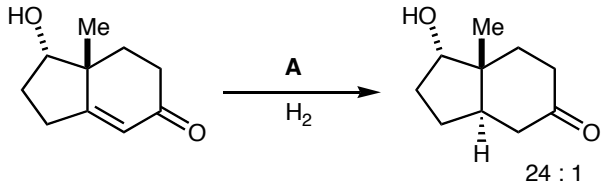
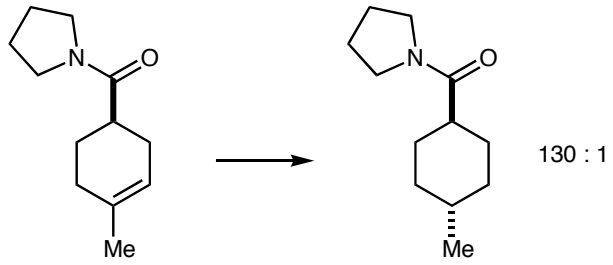
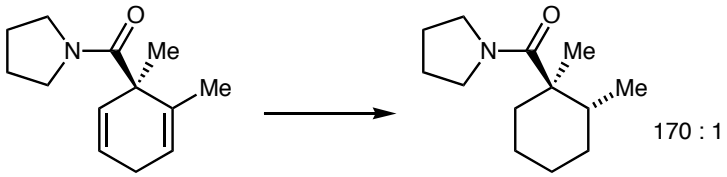
Ref. *Chem. Rev.* **1993**, *93*, 1307-1370

Cyclic cases:









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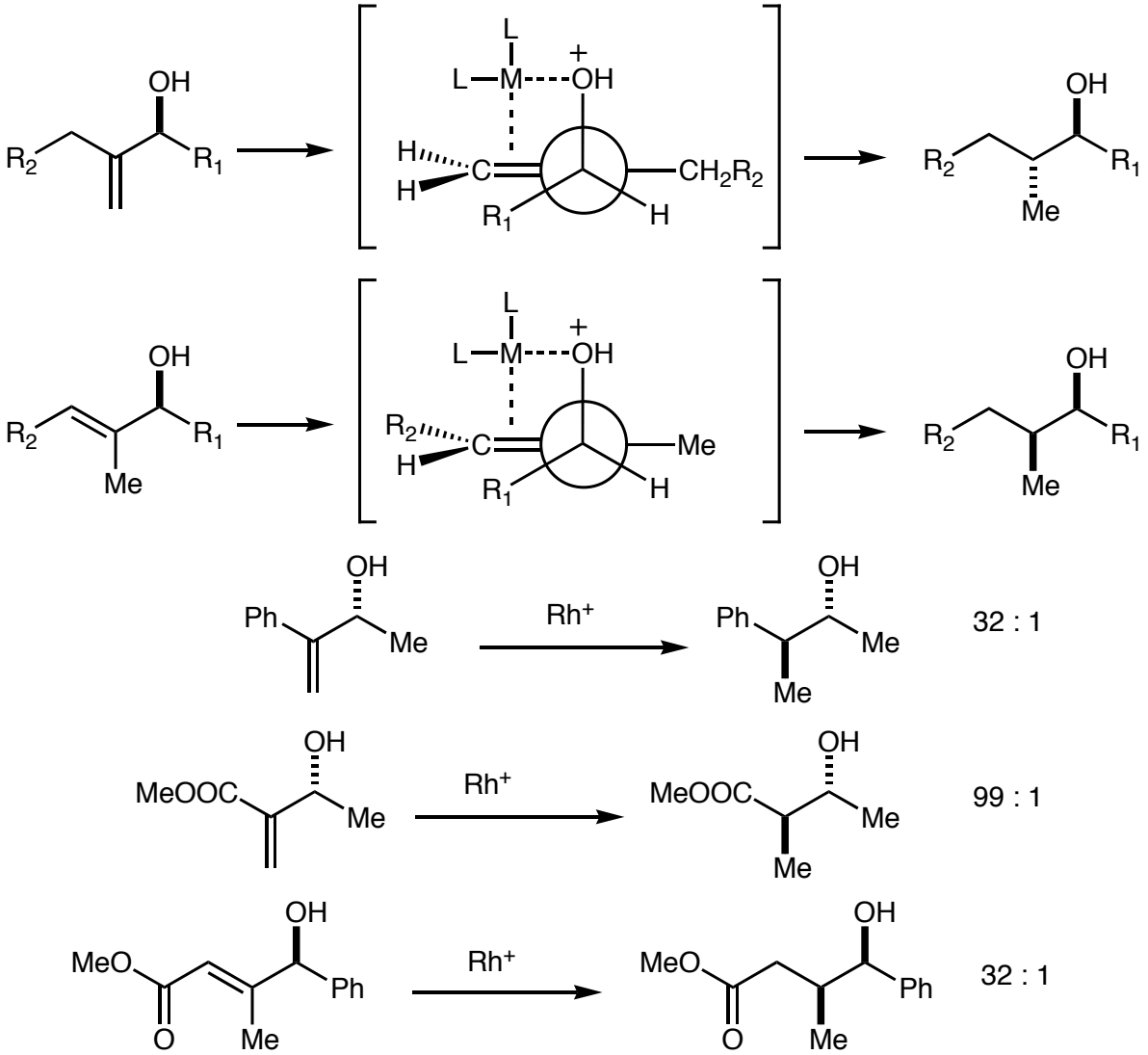
Hydrogenation of Chiral Acyclic Allylic Alcohols



Hydrogenation of Chiral Acyclic Homoallylic Alcohols

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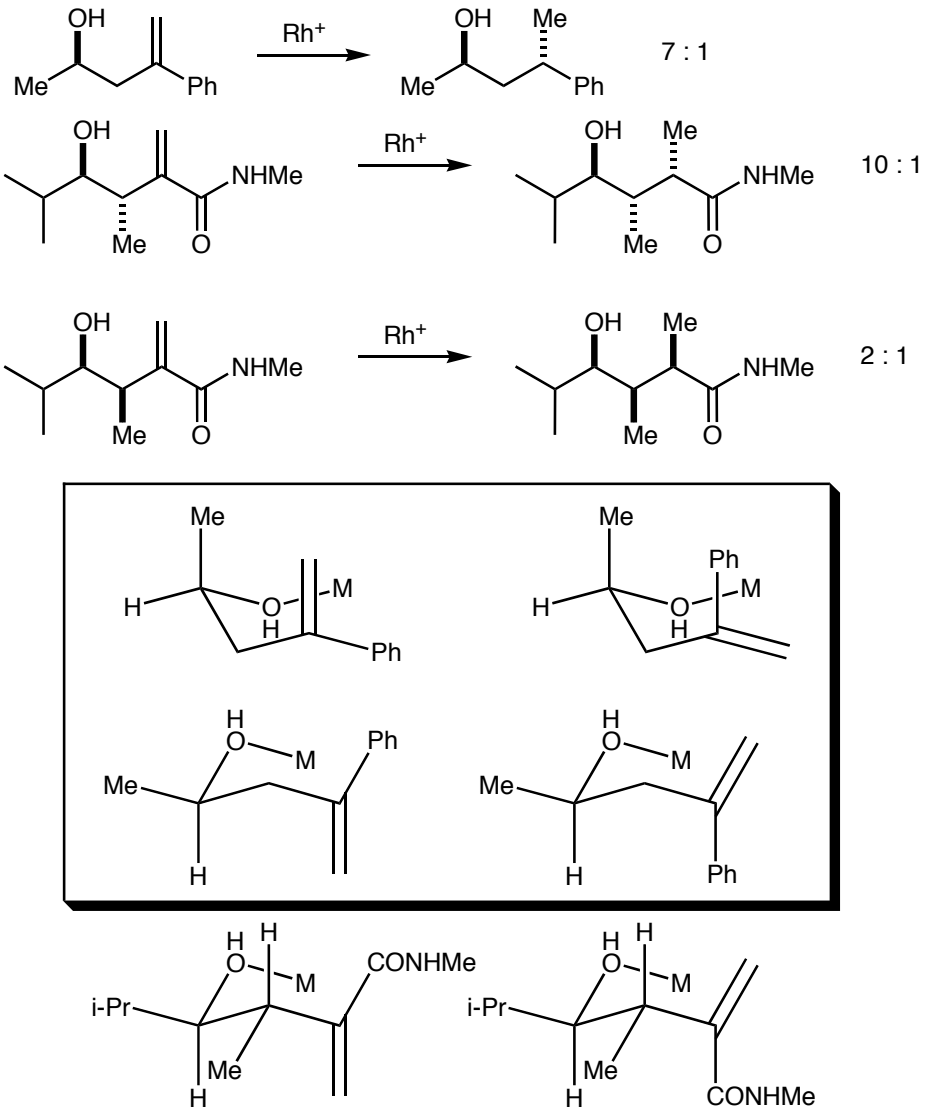

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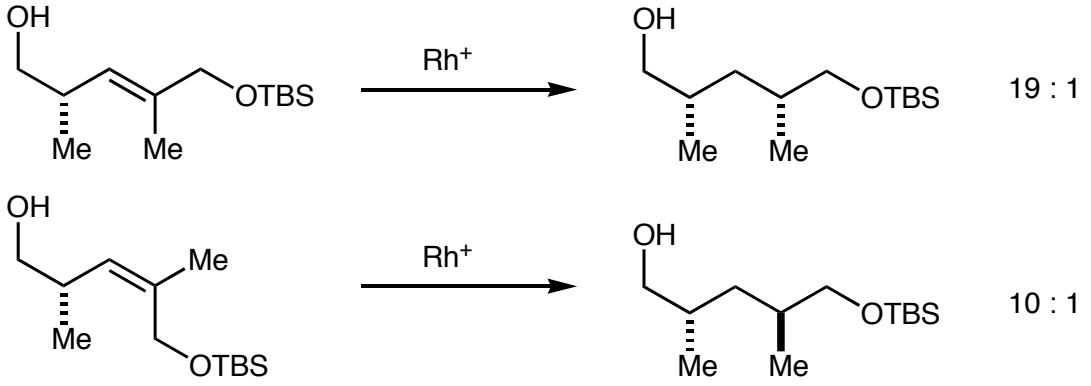
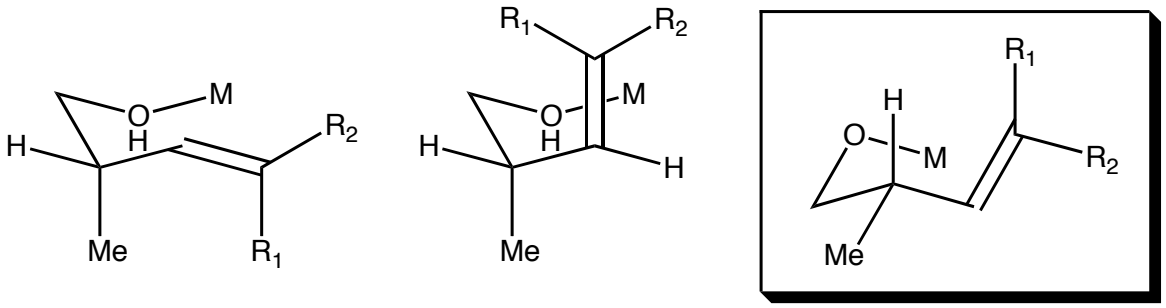
Hydrogenation of Alkenes: Homoallylic Alcohols





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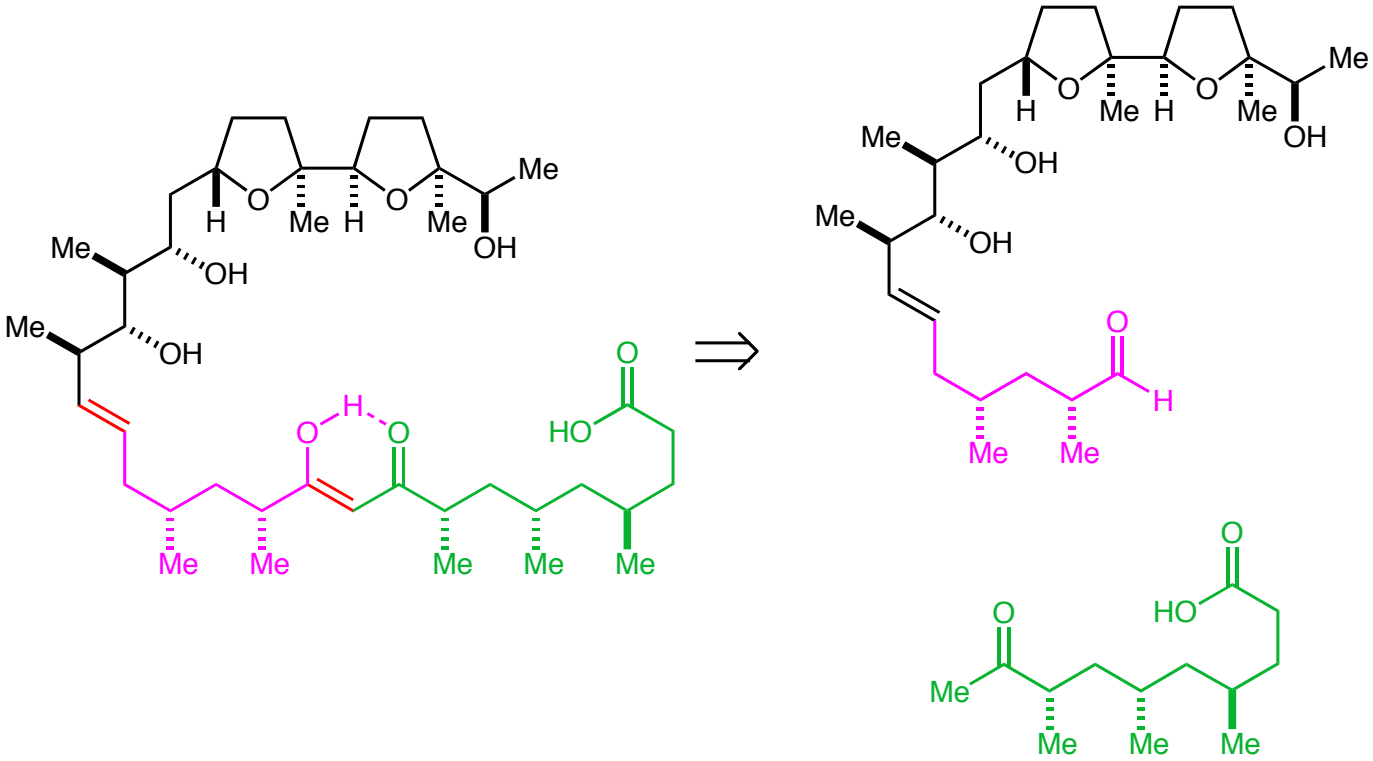
Hydrogenation of Alkenes: Ionomycin Synthesis or the 1,3-Dimethyl Problem



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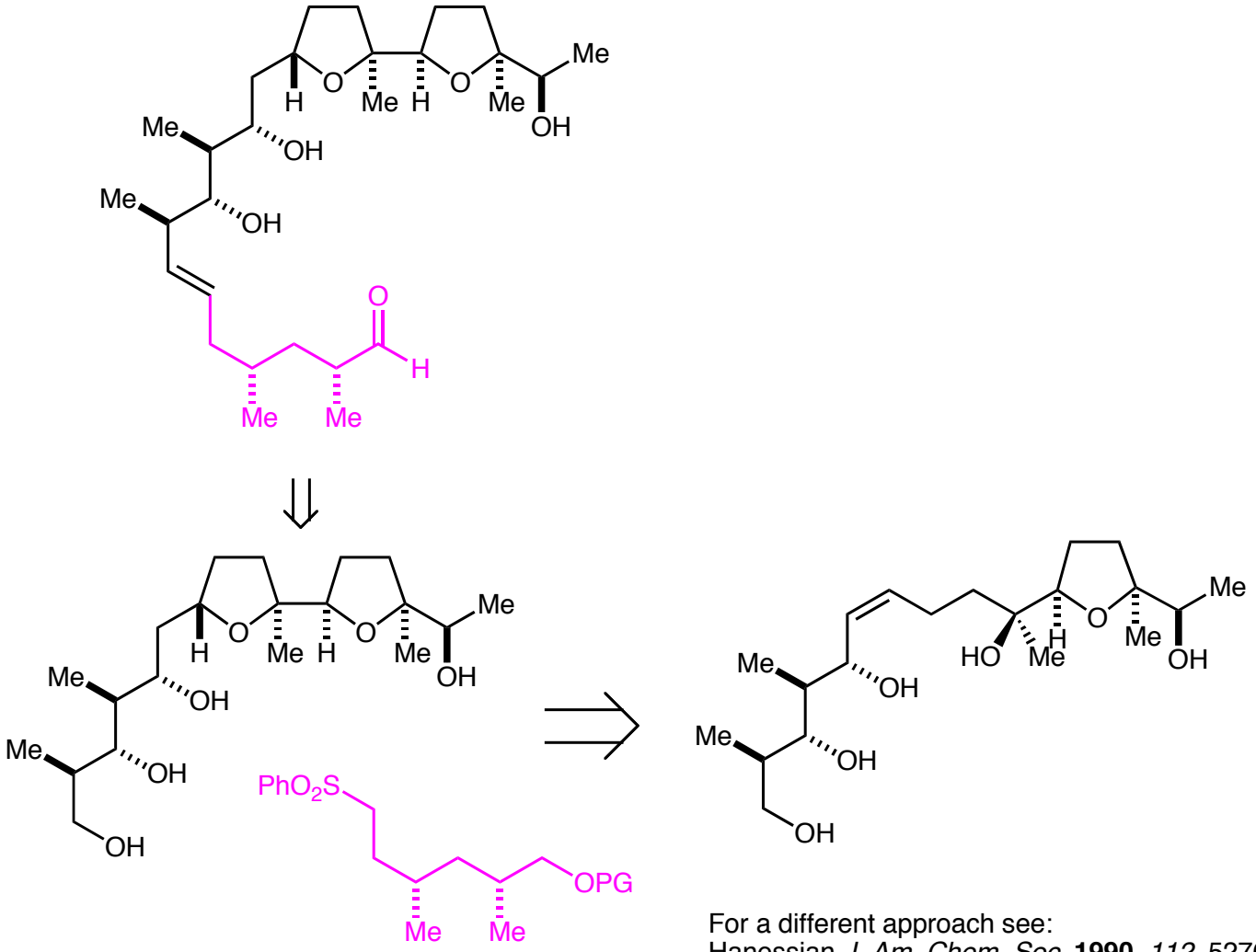
Hydrogenation of Alkenes: Ionomycin Synthesis or the 1,3-Dimethyl Problem



For a different approach see:
Hanessian *J. Am. Chem. Soc.* **1990**, *112*, 5276

Evans's Ionomycin Synthesis

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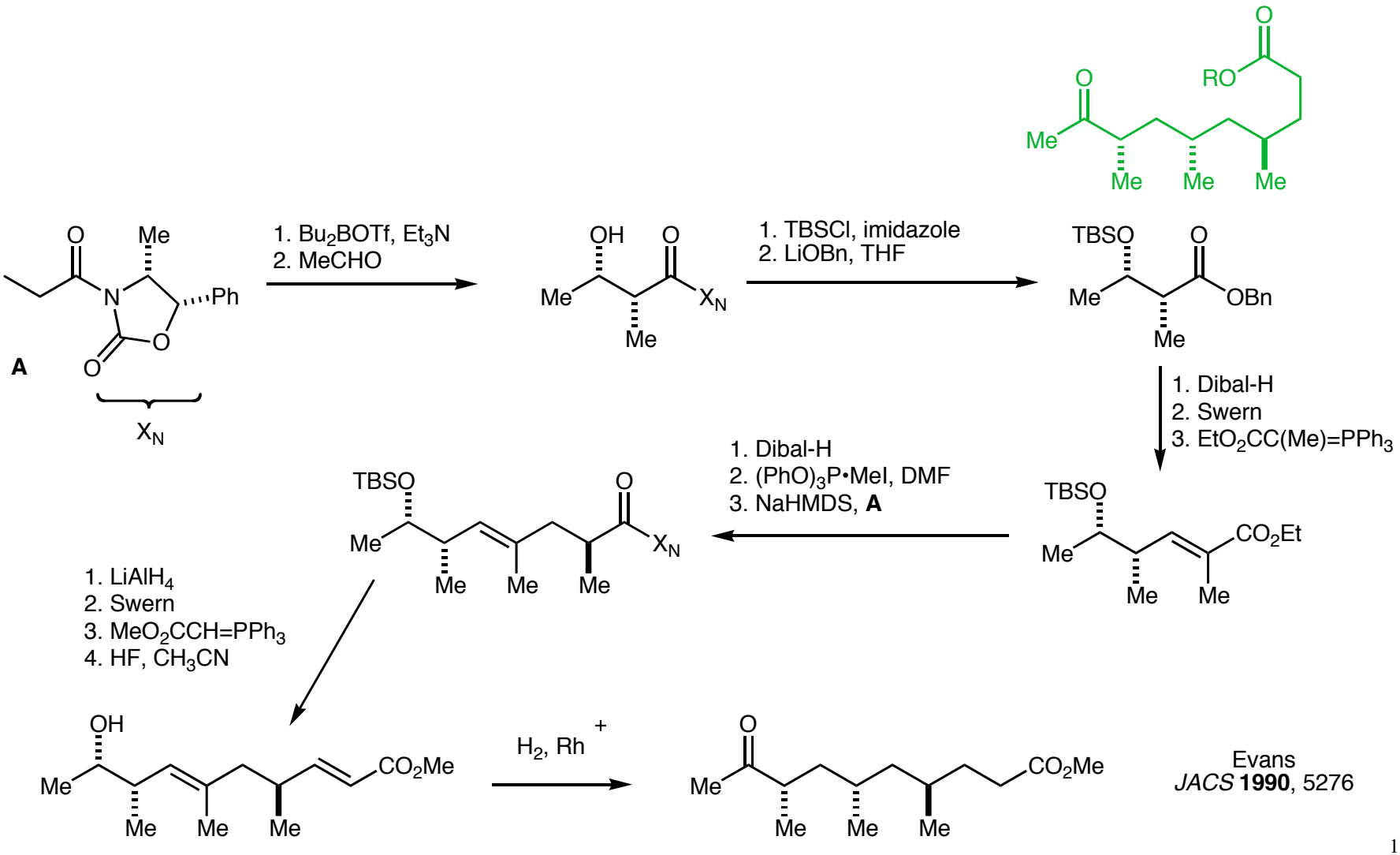

Evans
JACS **1990**, 5276

Hanessian's Ionomycin Approach

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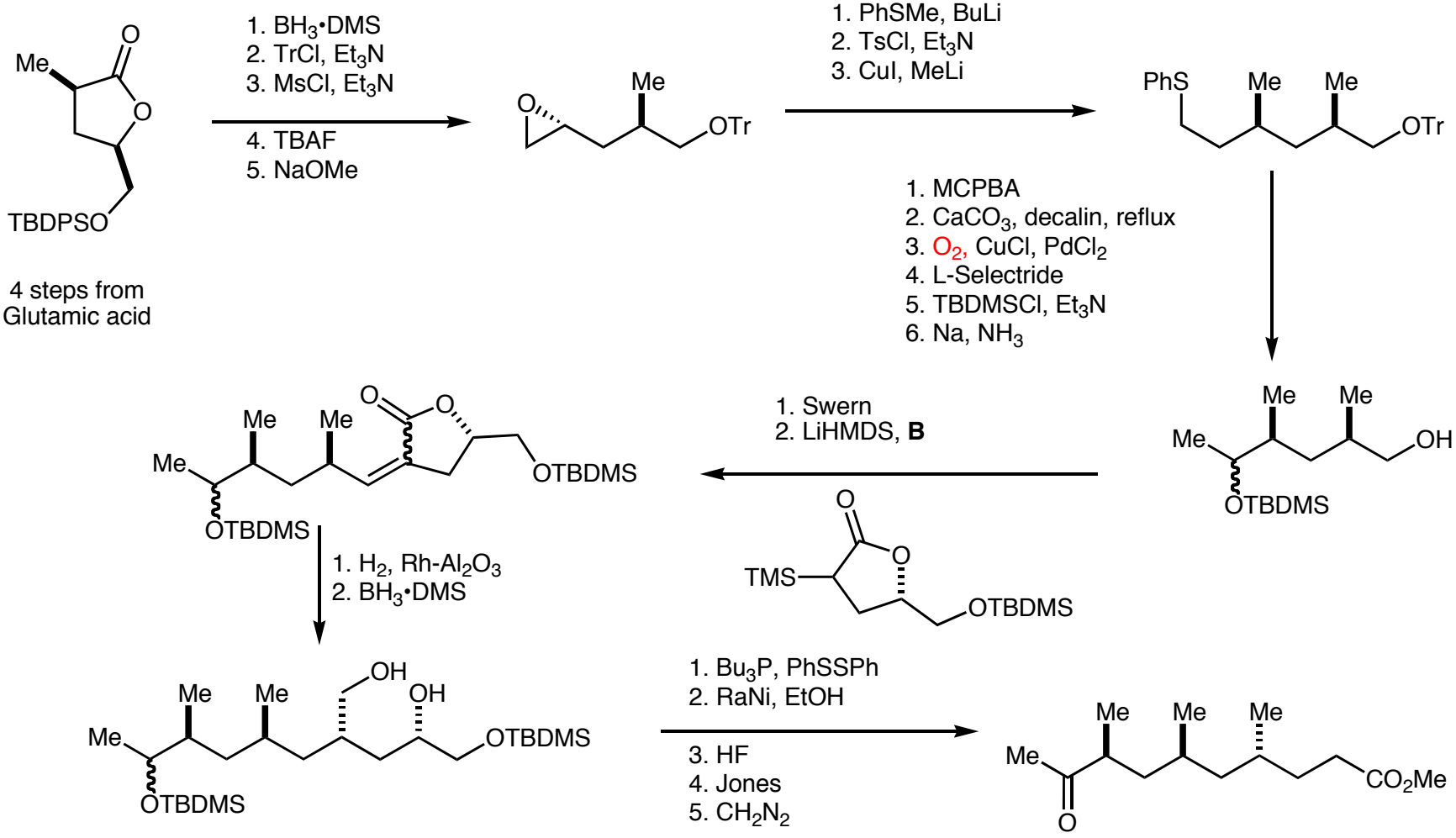
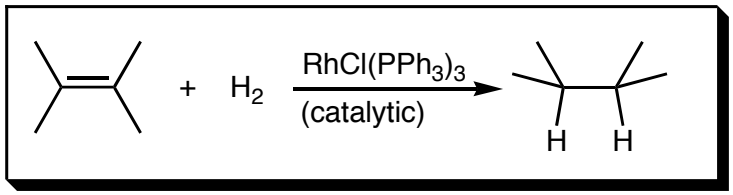
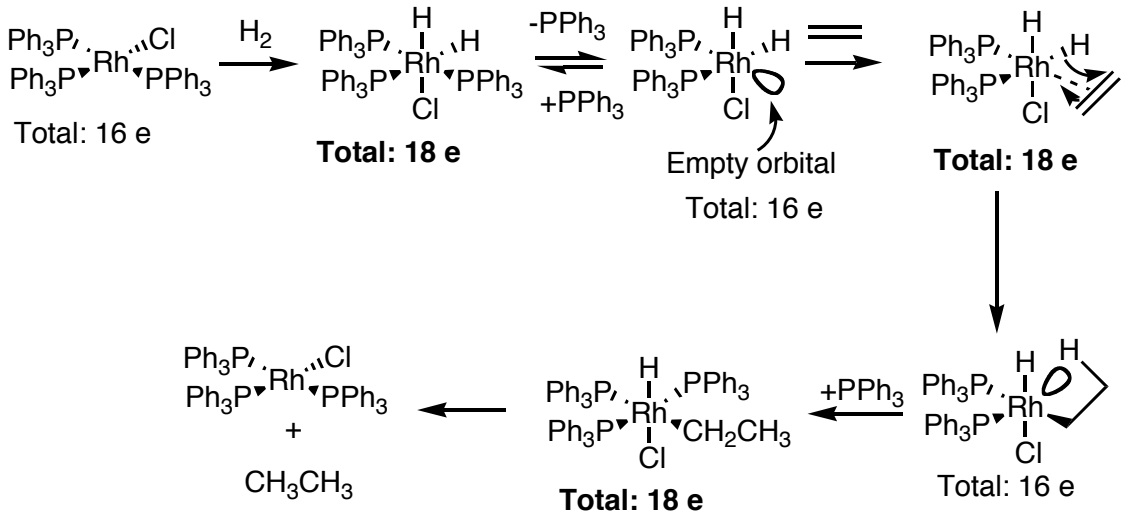


Hanessian's Approach, *JACS* **1990**, 5290

Enantioselective Rh-Catalyzed Hydrogenation





Typically, 10 turnovers/minute
under ambient conditions

Chiral Phosphines

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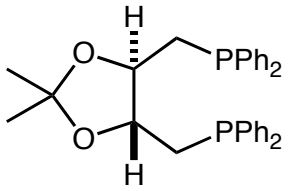
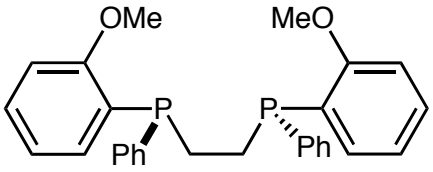
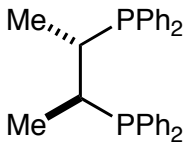


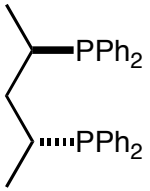
(*R*,*R*)-DIOP



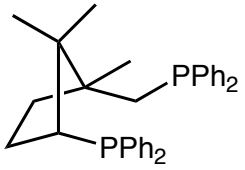
(*R*,*R*)-DIPAMP



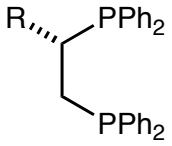
(*S*,*S*)-CHIRAPHOS



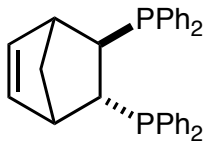
(*R*,*R*)-BDPP



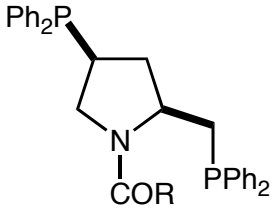
CAMPHOS



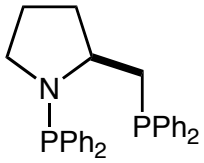
R = Me: (*S*)-PROPHOS
R = Ph: (*S*)-PHENPHOS
R = c-C_6H_{11}: (*S*)-CYCPHOS



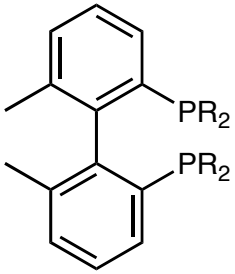
(*R*,*R*)-NORPHOS



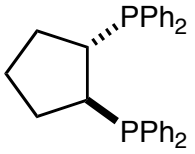
R = t-BuO: (*S*,*S*)-BPPM
R - R'NH- (*S*,*S*)-R'-CAPP
R' = Ar



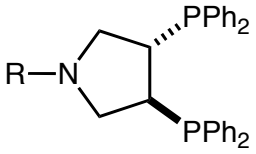
ProNOP



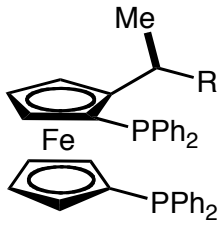
BIPHEMP (R = Ph)
BICHEP (R = c-C_6H_{11})



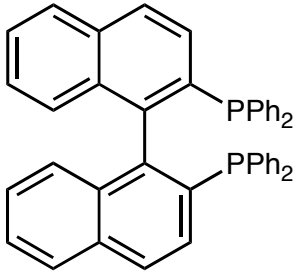
(*S*,*S*)-DPCP



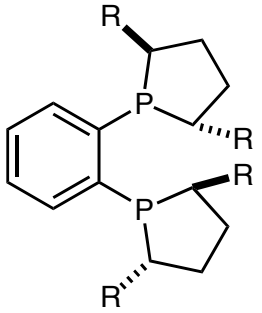
(*S*,*S*)-PYRPHOS



R = NMe_2 : BPPFA
R = OH: BPPFOH



BINAP



DuPHOS (R= Me, Et)

Hydrogenation of Olefins

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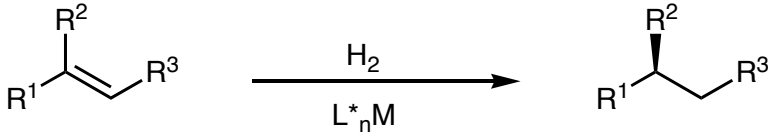
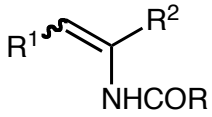
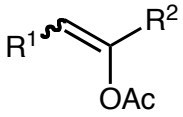


Functionnalized Olefins

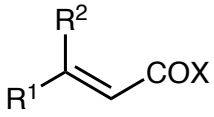
Enamides



Enol Derivatives

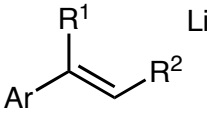


α,β-Unsaturated carbonyl compounds



Unfunctionnalized Olefins

Very few successfull systems



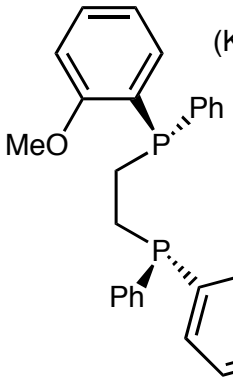
Limited to aromatic alkenes

Ir and Ti catalysts

⇨ Many systems were developped. (Ru and Rh)

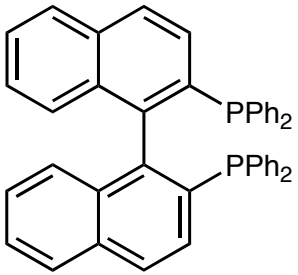
⇨ No *universal* catalyst.

DIPAMP-Rh
(Knowles-1977)



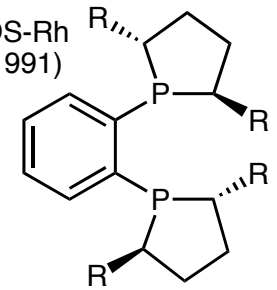
- Enamides ~95% ee
- Enol derivatives ~90% ee
- α,β-Unsaturated acid or ester ~88%ee

BINAP-Ru or -Rh
(Noyori-1980)



- Enamides ~98% ee
- Enol derivatives ~95% ee
- α,β-Unsaturated acid or ester ~90%ee

DuPHOS-Rh
(Burk-1991)



- Enamides ~99% ee
- Enol derivatives ~95% ee
- α,β-Unsaturated acid or ester ~98%ee

Enantioselective Total Synthesis of Ecteinascidin 743

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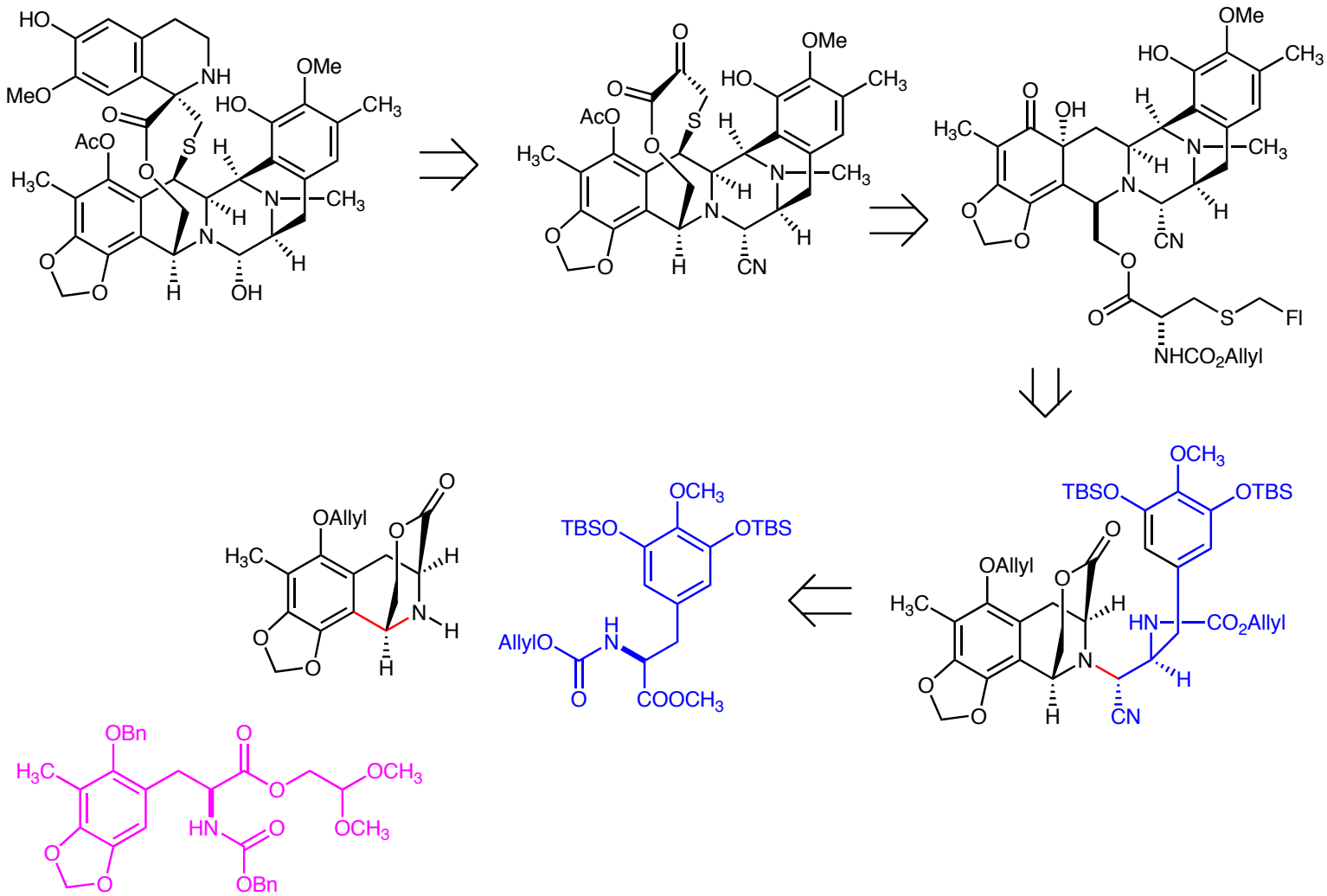
Corey, E. J.; Gin, D. Y.; Kania, R. S. *J. Am. Chem. Soc.* **1996**, *118*, 9202-9203.



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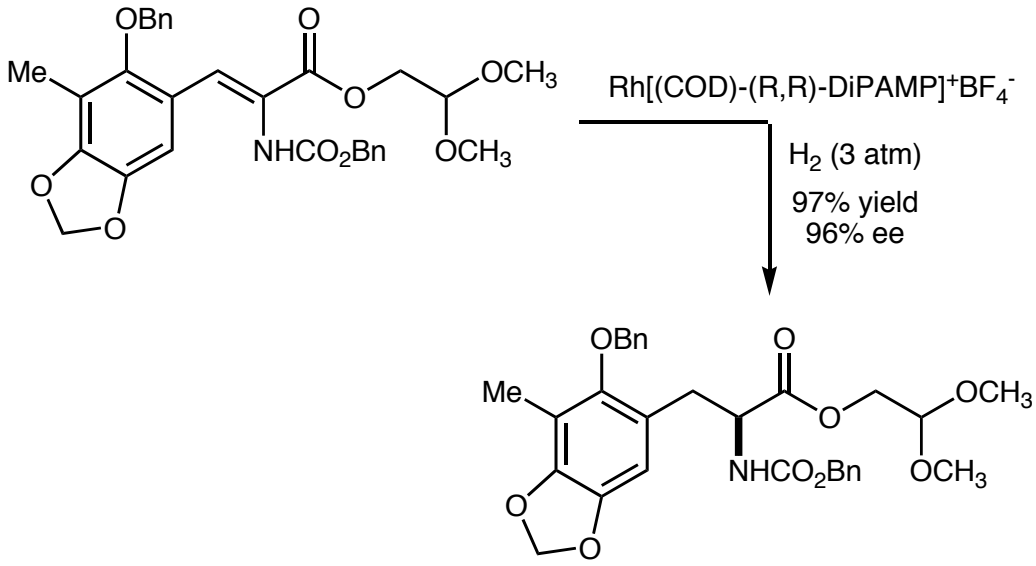
Hydrogenation of Dehydroamino acids



Enantioselective Hydrogenation of Enamides: DIOP and BICP Ligands

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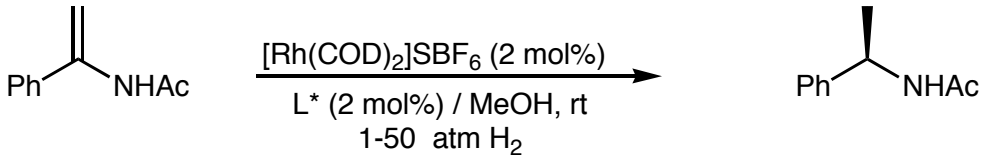
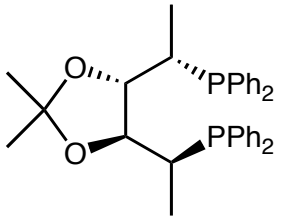
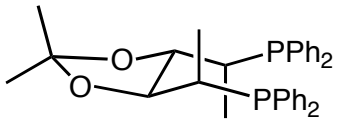


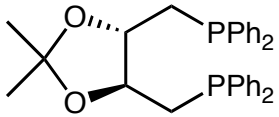
Kagan 1979



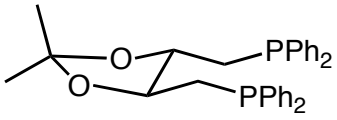
17% ee



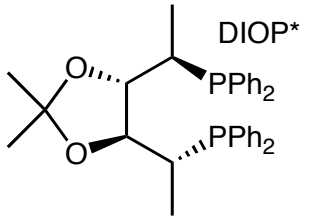
Kagan 1972



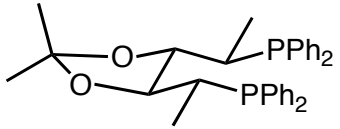
51% ee

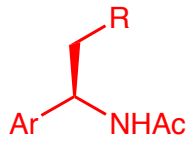


Zhang, Rajanbabu 2000



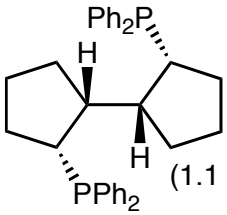
97% ee



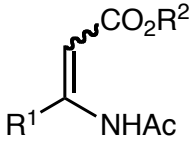


>99% conv.
97.3->99% ee

DICP (Zhang 1997)

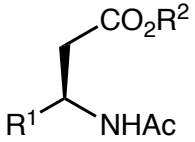


(1.1 mol%)



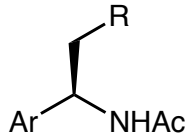
[Rh(COD)2]OTf (1 mol%)

Toluene, rt, 10 atm H_2



>99% conv.
60-97% ee

DICP (Zhang 1997)

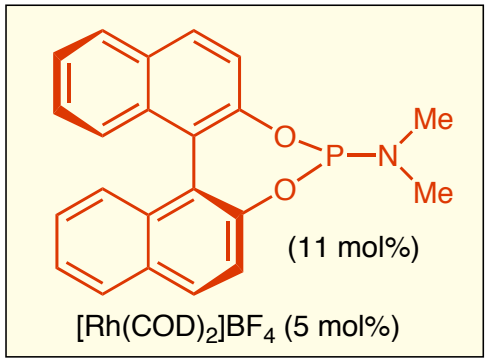


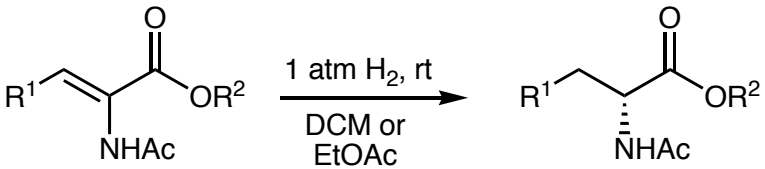
>99% conv.
97.3->99% ee

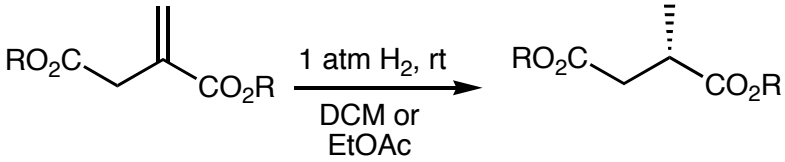
Highly Enantioselective Rhodium Catalyzed Hydrogenation with Monodentate Ligands

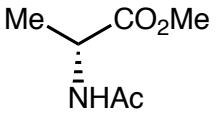
Université de Montréal

Feringa *J. Am. Chem. Soc.* **2000**, 11539.

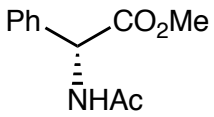




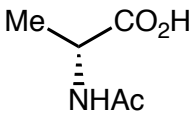




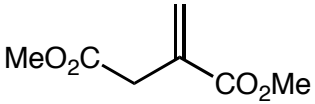
99% ee



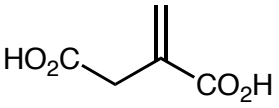
95% ee
(98% ee at 0 °C)



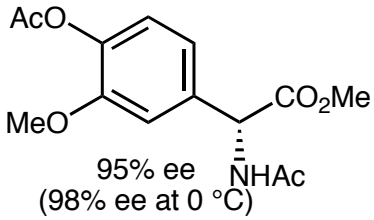
98.7% ee



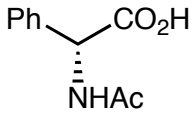
87% ee
(94% ee at 0 °C)



97% ee



95% ee
(98% ee at 0 °C)



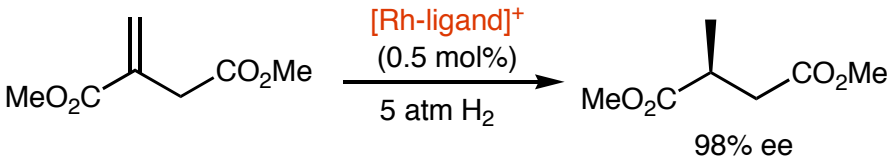
97% ee

⇨ Elevated pressure (5-10 atm) with low catalyst loading (0.5 mol% of Rh + 0.11 of L*) gave similar ee

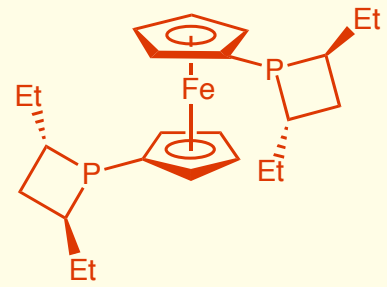
Enantioselective Hydrogenation of Itaconate Derivatives

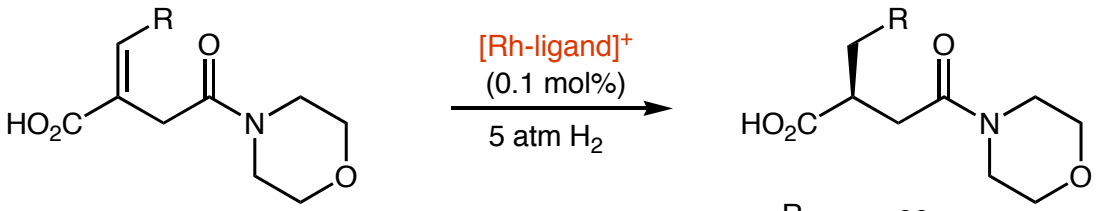
Université de Montréal

Burk *Angew. Chem., Int. Edit.* **2000**, 1981.



FerroTANE



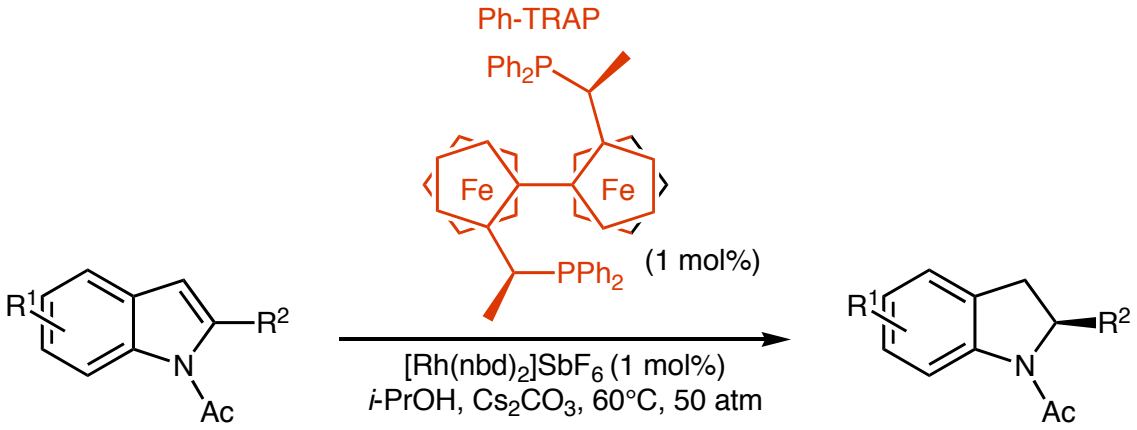


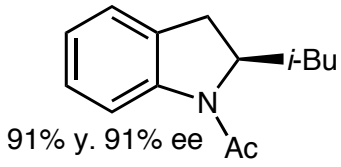
R	ee
Ph	98%
p-FC_6H_4	96%
p-BrC_6H_4	95%
p-$MeSC_6H_4$	97%
thienyl	97%
n-Bu	92%
i-Pr	94%
t-Bu	99%

Catalytic and Enantioselective Hydrogenation of Indoles

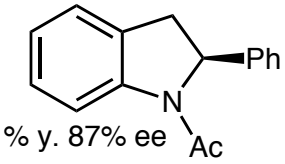
Université de Montréal

Kuwano and Ito *J. Am. Chem. Soc.* **2000**, 7614.

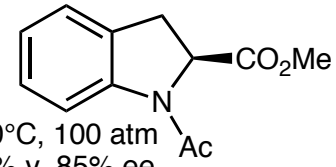




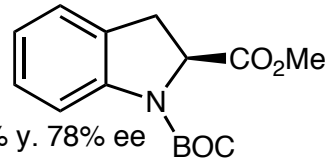
91% y. 91% ee



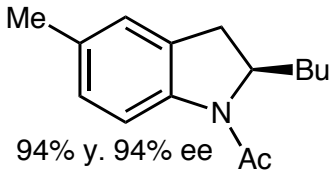
91% y. 87% ee



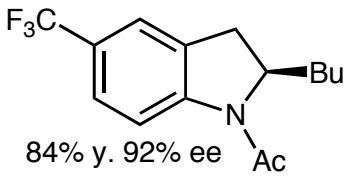
100°C, 100 atm
95% y. 85% ee



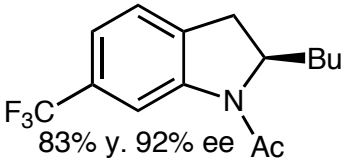
86% y. 78% ee



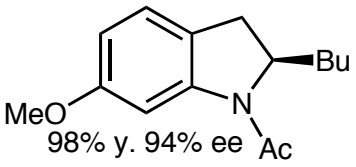
94% y. 94% ee



84% y. 92% ee



83% y. 92% ee

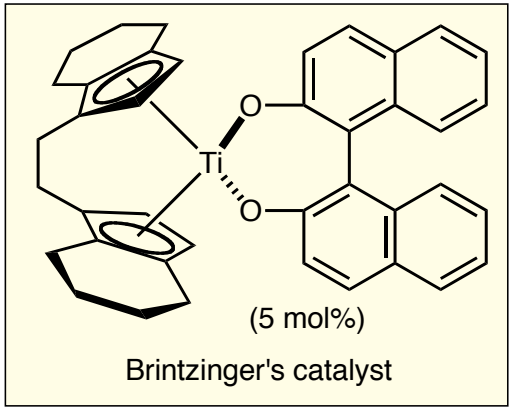


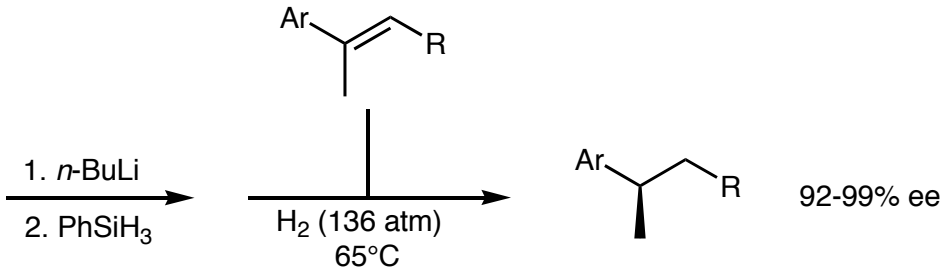
98% y. 94% ee

Enantioselective Hydrogenation of Unfunctionalized Olefins

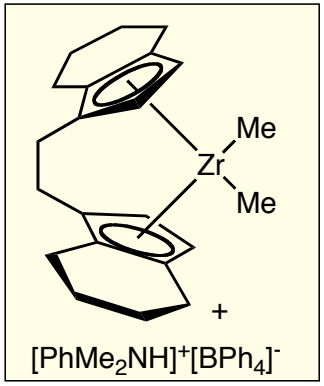
Université de Montréal

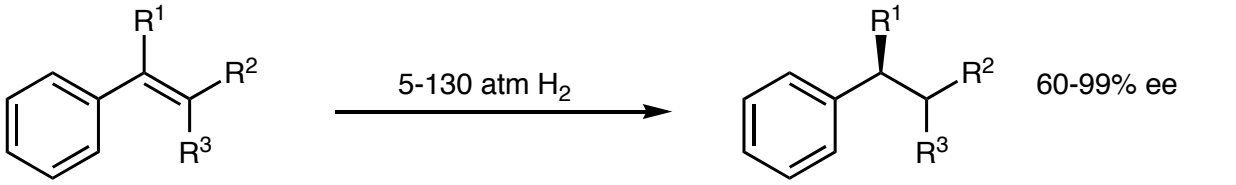
Buchwald *J. Am. Chem. Soc.* **1993**, 12569.

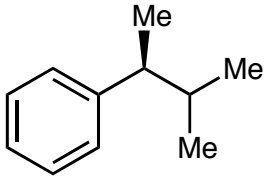




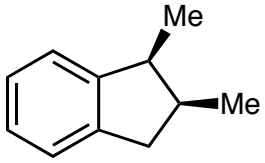
Buchwald *J. Am. Chem. Soc.* **1999**, 4916.



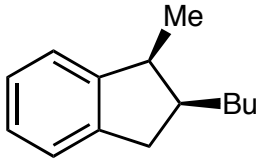




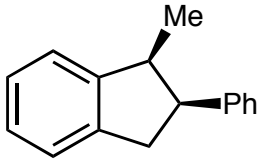
115 atm H_2
77% y. 96% ee



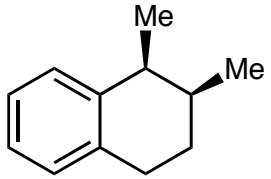
115 atm H_2
87% y. 93% ee
>99 : 1 (*cis:trans*)



5 atm H_2
96% y. 92% ee
99 : 1 (*cis:trans*)



130 atm H_2
94% y. 78% ee
>99 : 1 (*cis:trans*)

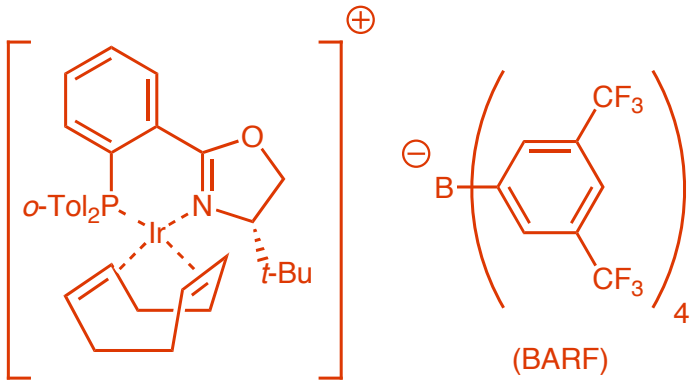


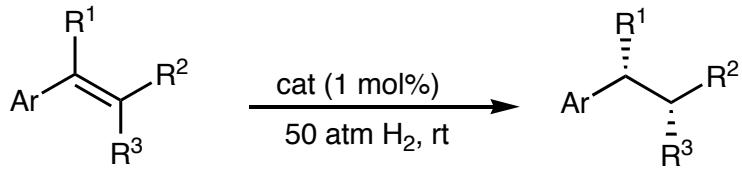
130 atm H_2
91% y. 92% ee
>99 : 1 (*cis:trans*)

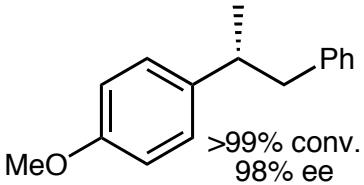
Enantioselective Hydrogenation of Unfunctionalized Olefins with Iridium Catalyst

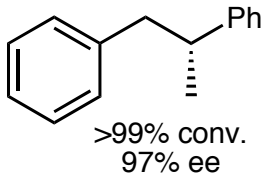
Université de Montréal

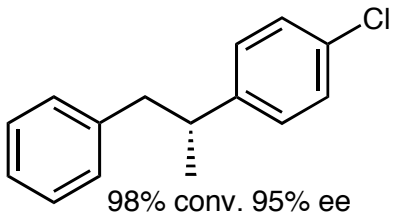
Pfaltz *Angew. Chem., Int. Edit.* **1998**, 2897.

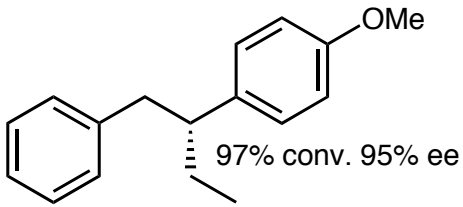


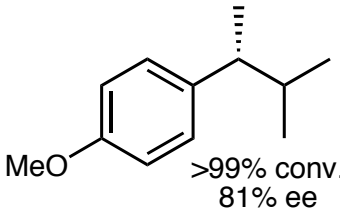


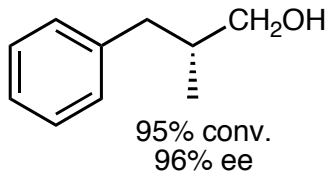


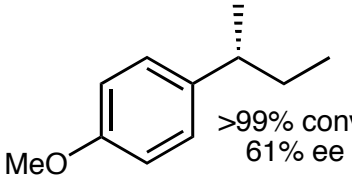


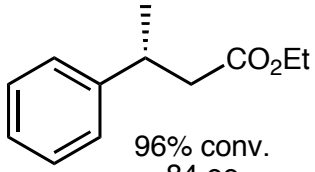


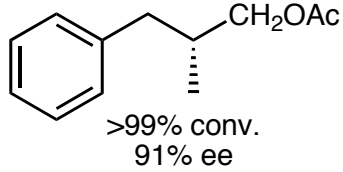








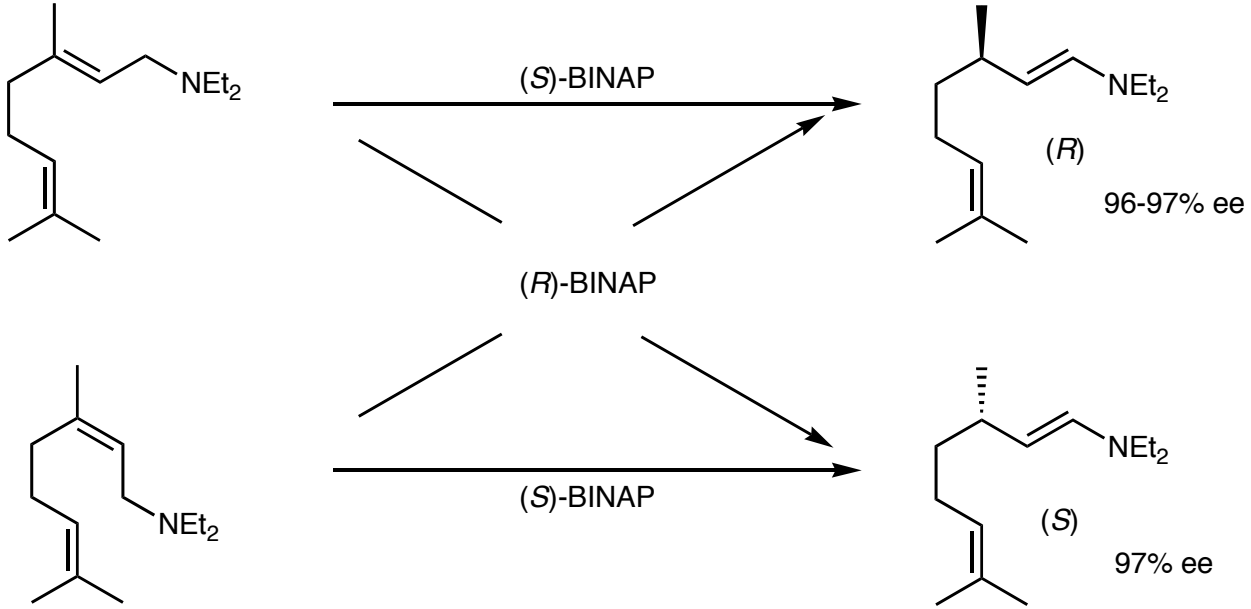




Asymmetric Isomerization of Allylamines: Rh-BINAP System for the Synthesis of Citronellal Derivatives

Université de Montréal

⇨ Industrial Process (1500 tons/year)



⇨ Cyclic allyl amine tends to dimerize or trimerize

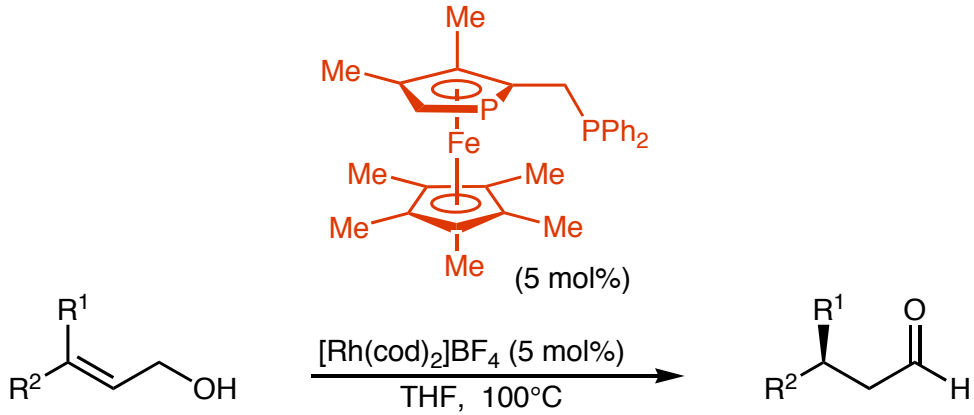
⇨ Allylamides are slow-reacting substrates and higher temperature are required (150°C)

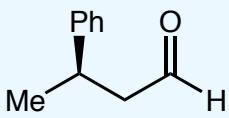
⇨ Stereoselectivity with allyl alcohols are usually lower (30-60% ee)

Asymmetric Isomerization of Allylic Alcohols: Fu's Chiral Rhodium/Phosphaferrocene Complex

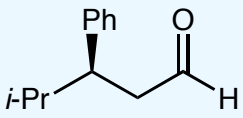
Université de Montréal

Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M. C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870-9871.

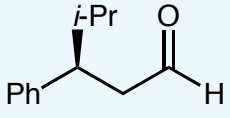




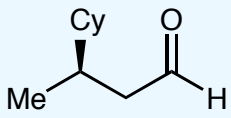
55% y. 64% ee



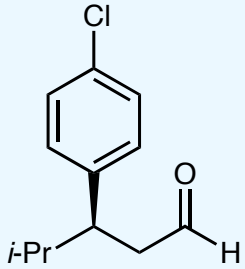
91% y. 83% ee



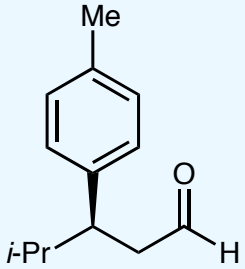
81% y. 78% ee



75% y. 72% ee



74% y. 86% ee

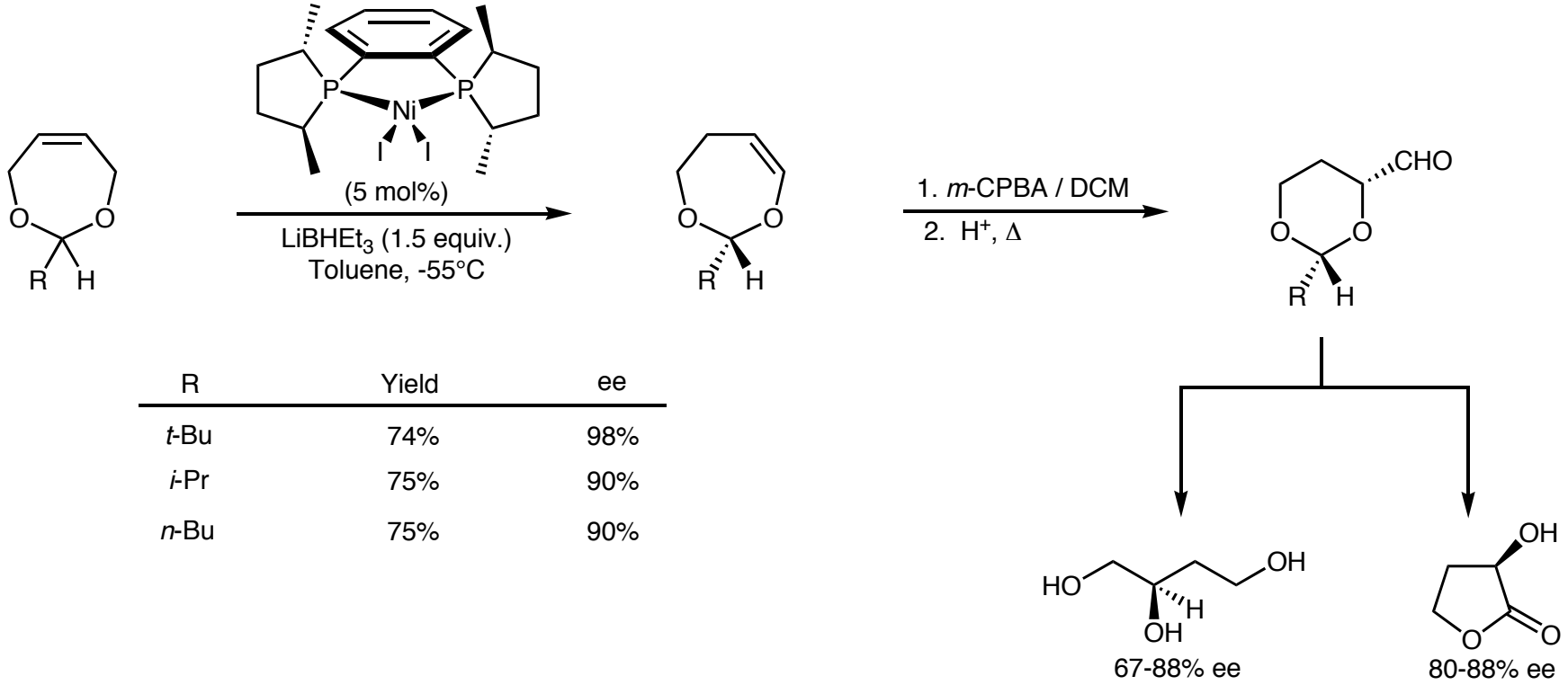


64% y. 80% ee

Enantioselective Isomerization of 4,7-Dihydro-1,3-Dioxepins

Université de Montréal

Frauenrath, H.; Brethauer, D.; Reim, S.; Maurer, M.; Raabe, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 177-179.



R	Yield	ee
t-Bu	74%	98%
i-Pr	75%	90%
n-Bu	75%	90%

67-88% ee

80-88% ee

Alkene Isomerization

Université de Montréal

Enantioselective total synthesis of Vitamin E (α-tocopherol)

Noyori *J. Am. Chem. Soc.* **1987**, *109*, 1596, 4129.