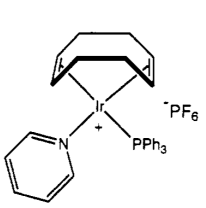
CHEM 6352

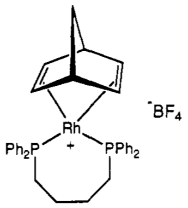
Directed Hydrogenations

Figures and Schemes Primarily from Hoveda, Evans, Fu *Chem. Rev.* **1993**, *93*(4), 1307

Cyclic Cases



[Ir(cod)py(PCy$_3$)]PF$_6$
(Ir$^+$)

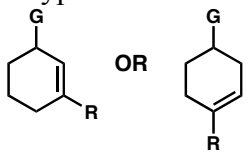


[Rh(nbd)(diphos-4)]BF$_4$
(Rh$^+$)

Brown's Catalyst Crabtree's Catalyst

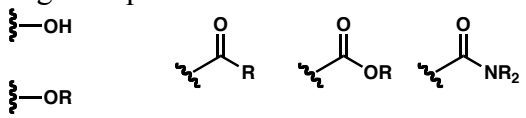
See also: Stork *JACS* **1983**, *105*, 1072

General Substrate Types:



G = Directing Group

Directing Groups:

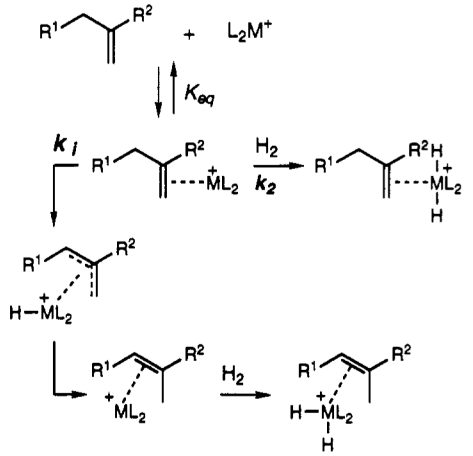


-- All give high levels of diastereocontrol with Crabtree's catalyst

• The directing group in the axial position is preferred due to olefin proximity.
• Substrates that exist with an axial directing group exhibit higher diastereocontrol.
• In general, the Crabtree catalyst is superior in terms of activity, particularly with trisubstituted olefins.
• Often using lower concentration of Crabtree's catalyst leads to higher levels of diastereocontrol. This has been ascribed to avoiding the formation of polymetallic complexes that do not show the same directing effects.
• In cases where olefin isomerization is competitive, using the rhodium catalyst and elevated pressure favors hydrogenation.

Olefin Isomerization:

Scheme 23



Examples:

Table 32. Hydrogenation of Cyclic Homo- and Bishomoallylic Alcohols with [Ir(cod)py(PCy$_3$)]PF$_6$

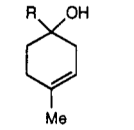
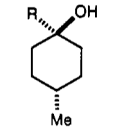
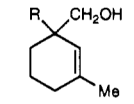
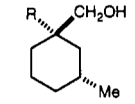
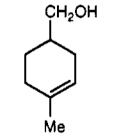
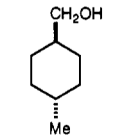
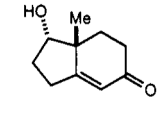
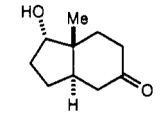
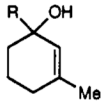
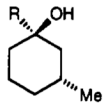
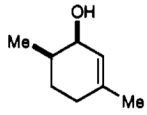
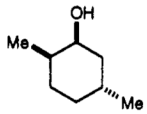
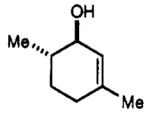
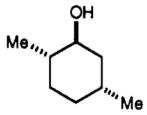
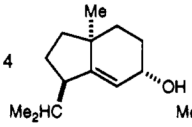
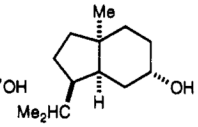
Entry	Substrate	Major Product	Mol % Ir catalyst		Selectivity
1			20	a. R = H	>99 : 1
			20	b. R = Me	33 : 1
2			20	a. R = H	6 : 1
			20	b. R = Me	9 : 1
3			2		>99 : 1
4			20		24 : 1

Table 33. Hydrogenation of Cyclic Allylic Alcohols with [Ir(cod)py(PCy_3)]PF_6

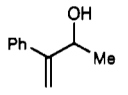
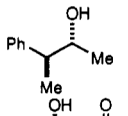
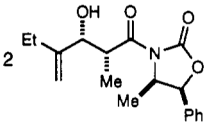
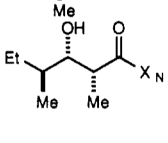
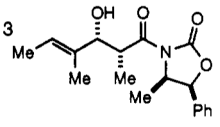
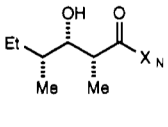
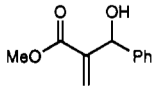
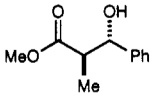
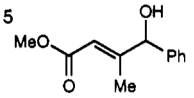
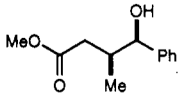
Entry	Substrate	Major Product	Mol % Ir catalyst	Selectivity
1			20 a. R = H 20 b. R = Me	74 : 1 >100 : 1
2			2	65 : 1
3			2	36 : 1
4			20	"highly selective"

See also Corey *TL* **1984**, *25*, 149
Evans *JACS* **1984**, *106*, 3866
Evans *TL* **1984**, *25*, 4637
For examples with Rh see Evans, Fu page 1307.

Acyclic Cases (allylic alcohols):

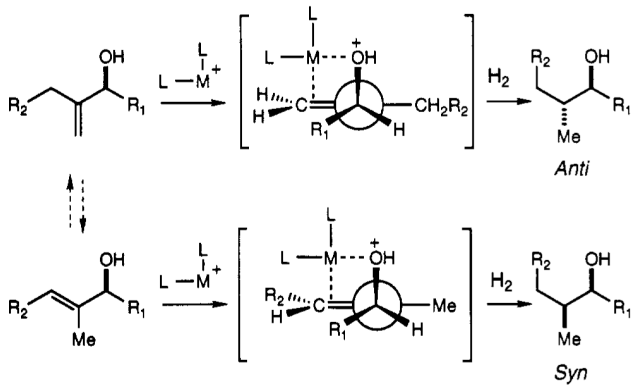
• In acyclic systems Rh catalysts are superior to Ir catalysts.
• 1,1-Di and trisubstituted olefins give opposite stereochemical results.
• Olefin isomerization must be avoided by running reactions at high H_2 pressure (500-600 psi).

Table 39. Hydrogenation of Acyclic Allylic Alcohols

Entry	Substrate	Major Product	Mol %, Cat[a] (H_2 Press)	Selectivity
1			2, Rh^+ (15 psi)	32 : 1
2			17.5, Rh^+ (640 psi) 2.5, Ir^+ (15 psi)	13 : 1 6 : 1
3			17.5, Rh^+ (640 psi) 2.5, Ir^+ (15 psi)	10 : 1 3 : 1
4			0.5, Rh^+ (15 psi)	99 : 1
5			10, Rh^+ (15 psi)	32 : 1

[a] Catalysts: [Rh(nbd)(diphos-4)]BF_4(Rh^+); [Ir(cod)py-(PCY_3)]PF_6(Ir^+).

Scheme 24



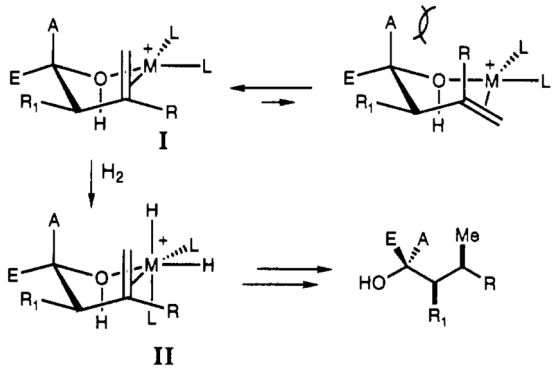
Note that allylic strain is minimized above.

Use the same energy minimizing considerations used for directed epoxidation.

Acyclic Cases (homoallylic alcohols):

Scheme 25

1,1-Disubstituted Alkenes



Trisubstituted Alkenes

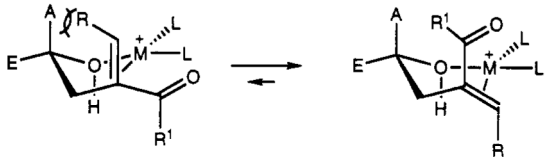
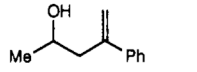
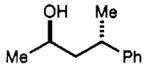
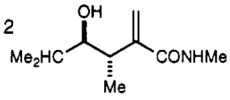
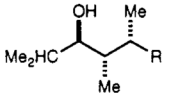
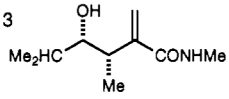
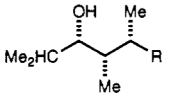
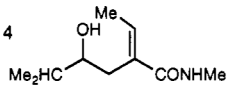
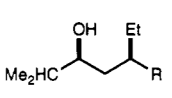
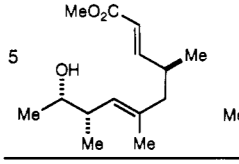
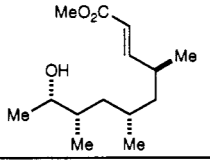
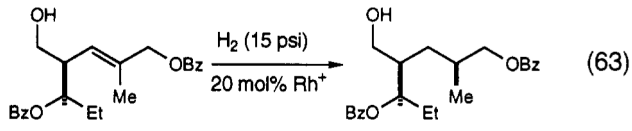


Table 41. Hydrogenations of Acyclic Homoallylic Alcohols

Entry	Substrate	Major Product	Mol %, Cat[a] (H_2 Pres)	Selectivity
1			2, Rh^+ (15 psi)	7 : 1
2			5, Rh^+ (15 psi) [b]	10 : 1
3			5, Rh^+ (15 psi) [b]	2 : 1
4			5, Rh^+ (15 psi) [b]	8 : 1
5			5, Rh^+ (15 psi)	16 : 1

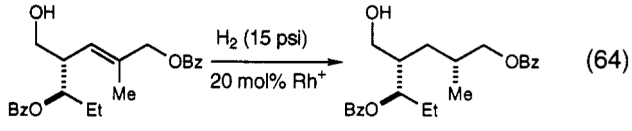
[a] Catalyst: [Rh(nbd)(diphos-4)]BF_4 or [Rh(nbd)(diphos-4)]-OSO_2CF_3.

In hydrogenations of trisubstituted olefins, the steric requirements of the allylic substituent and the olefin geometry have a small but marked effect on the reaction diastereoselection (eqs 63–66, Rh^+ = [Rh(nbd)(diphos-4)]BF_4).[186b] Since homoallylic hydroxyl groups perform well as directing groups, alkene geometry, along with the relative stereochemistry of the homoallylic hydroxy functionality, can be manipulated for effective control of the sense of asymmetric induction.



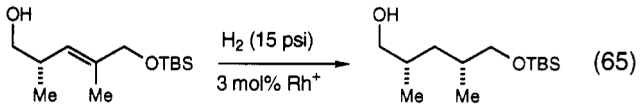
(63)

Diastereoselection 32:1



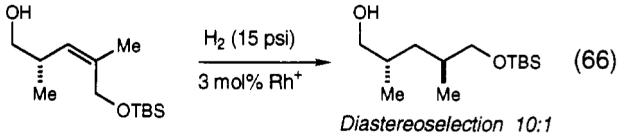
(64)

Diastereoselection 99:1



(65)

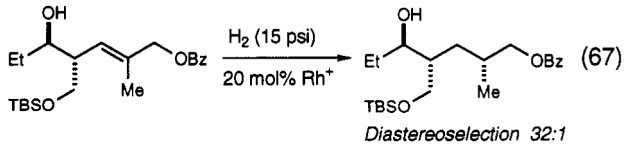
Diastereoselection 19:1



(66)

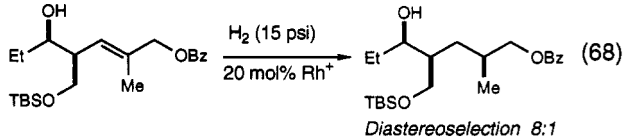
Diastereoselection 10:1

In cases where allylic and homoallylic stereogenic centers are present, alkene rearrangement is not observed at 15 psi H_2, and the cationic rhodium and the cationic iridium catalysts afford high levels of diastereoselection (eqs 67–69).[186b] Once again, it is the allylic center, not the stereogenic homoallylic carbinol site, that determines which diastereoface will be preferentially hydrogenated. Moreover, comparison of eqs 67 and 68 indicates that the anti relative stereochemistry



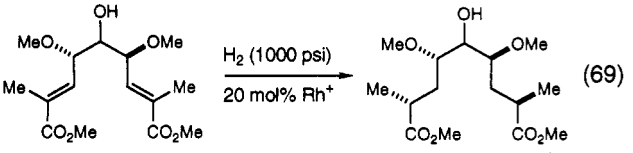
(67)

Diastereoselection 32:1



(68)

Diastereoselection 8:1



(69)

Diastereoselection 10:1