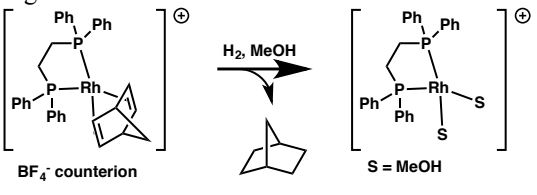
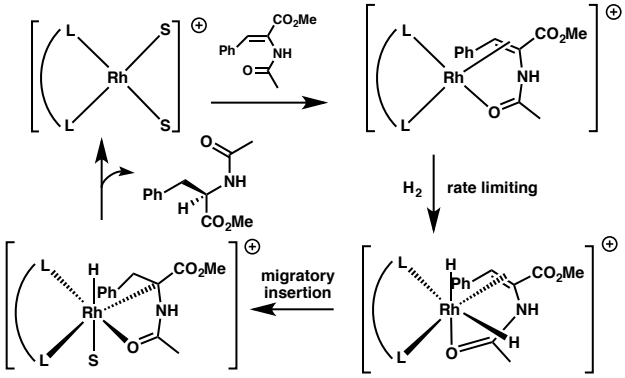
CHEM 6352

Enantioselective Hydrogenations

Mechanism [(Diphos)Rh(NBD)]⁺ Catalysts

Hydrogenation of the Diene Generates the Active Catalyst

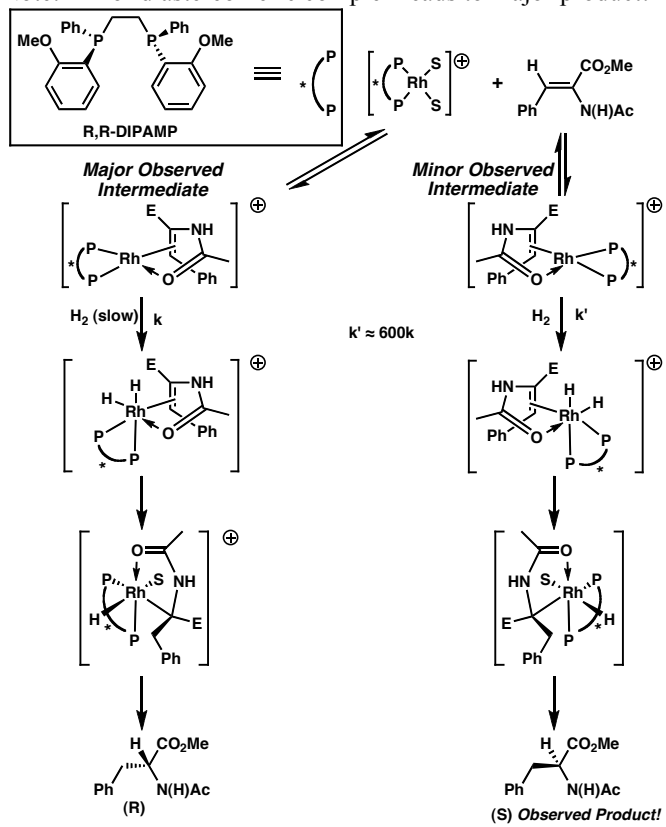




See Halpern *Science* **1982**, *217*, 401.

Asymmetric Hydrogenation

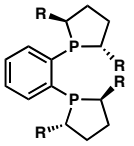
Note: Minor diastereomeric complex leads to major product!



Halpern *Science* **1982**, *217*, 401 and *Asymmetric Synthesis*, Vol. 5, Ch. 2, p 41 (especially p. 53)

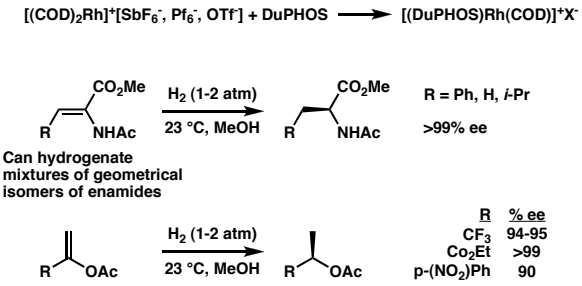
Halpern's law: If you can observe a structure, it is probably not catalytically relevant.

DuPHOS



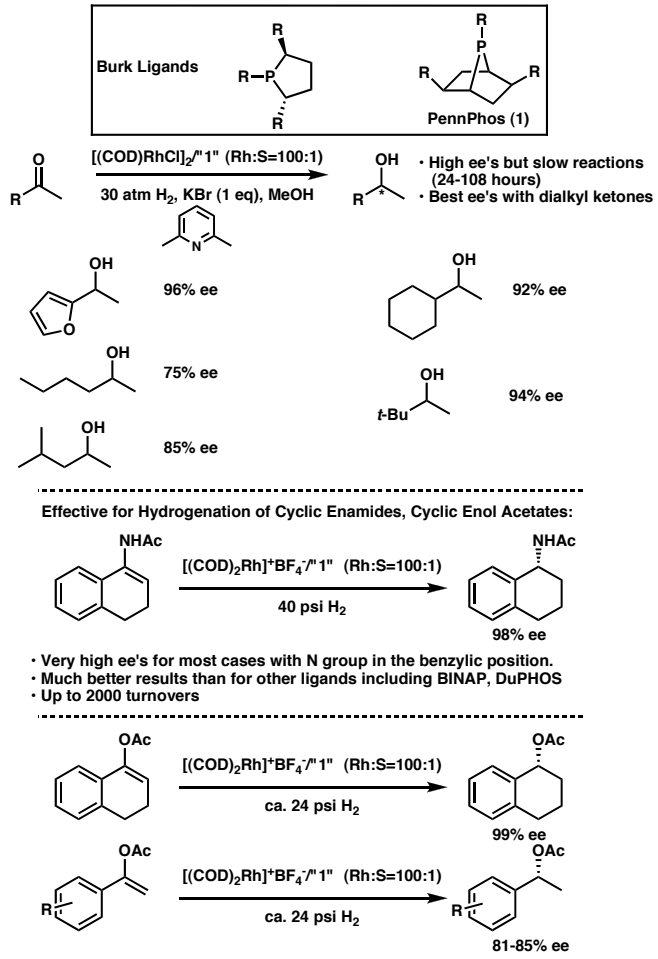
- Electron rich – 2 alkyl on each P atom
- Asymmetry rigidly held close to metal
- Can vary R groups
- Chelation in mechanism necessary
- Commercially available; expensive

Preparation of Catalyst:



Burk *JACS* **1992**, *114*, 8518 and *JACS* **1993**, *115*, 10125

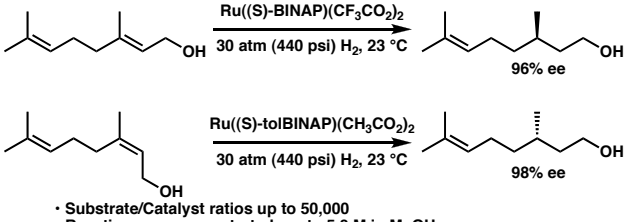
Penn-Phos



Zhang *ACIEE* **1998**, *37*, 1100; *ACIEE* **1999**, *38*, 516; *JOC* **1999**, *64*, 1774

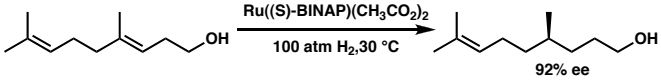
Ruthenium BINAP/Allylic Alcohols

Allylic Alcohols

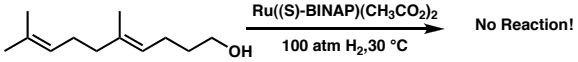


- Substrate/Catalyst ratios up to 50,000
- Reaction very concentrated, up to 5.8 M in MeOH

Homoallylic Alcohols

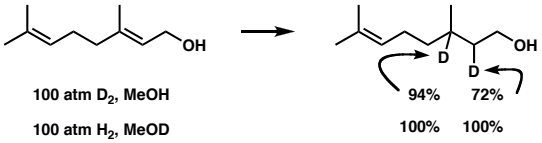


Bishomoallylic Alcohols

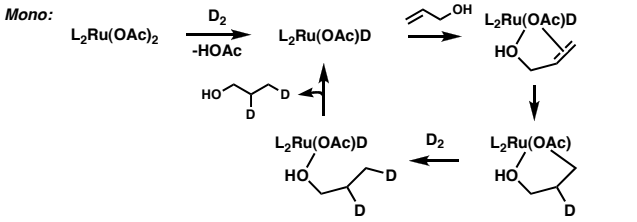


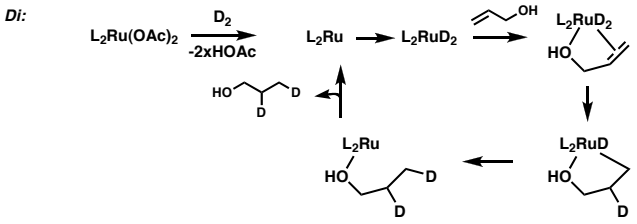
Noyori *JACS* **1987**, *109*, 1596

Ru-BINAP Mechanism



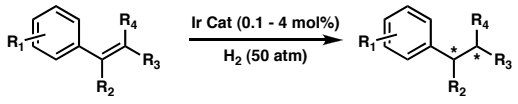
Both monohydride or dihydride mechanisms are possible:

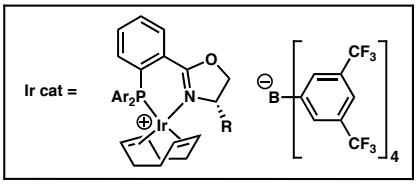


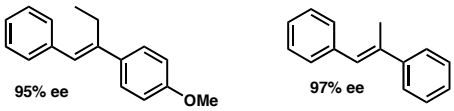


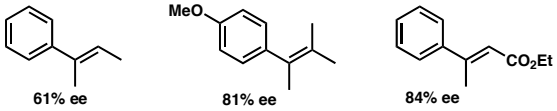
Noyori *Asymmetric Catalysis in Organic Synthesis* Ch. 2

Asymmetric Reduction of Highly Substituted Olefins









- Choice of anion is crucial
- First asymmetric reduction of unfunctionalized tetrasubstituted olefin
- Best asymmetric reduction of unfunctionalized trisubstituted olefins.

Pfaltz *ACIEE* **1998**, *37*, 2897

Other References:

Burgess *JACS* **2001**, *123*, 8878

Burk *Modular Phospholane Ligands in Asymmetric Catalysis*, p. 363-372

Acc. of Chem. Res. **2000**, *33*, issue 6