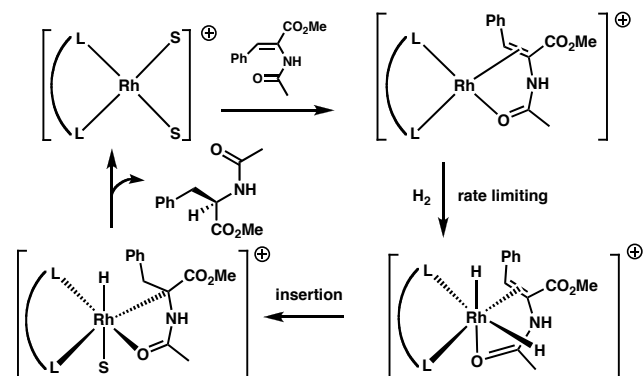
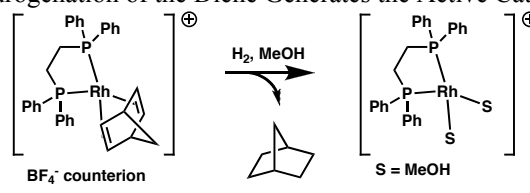


# CHEM 6352

## Enantioselective Hydrogenations

### Mechanism [(Diphos)Rh(NBD)]<sup>+</sup> Catalysts

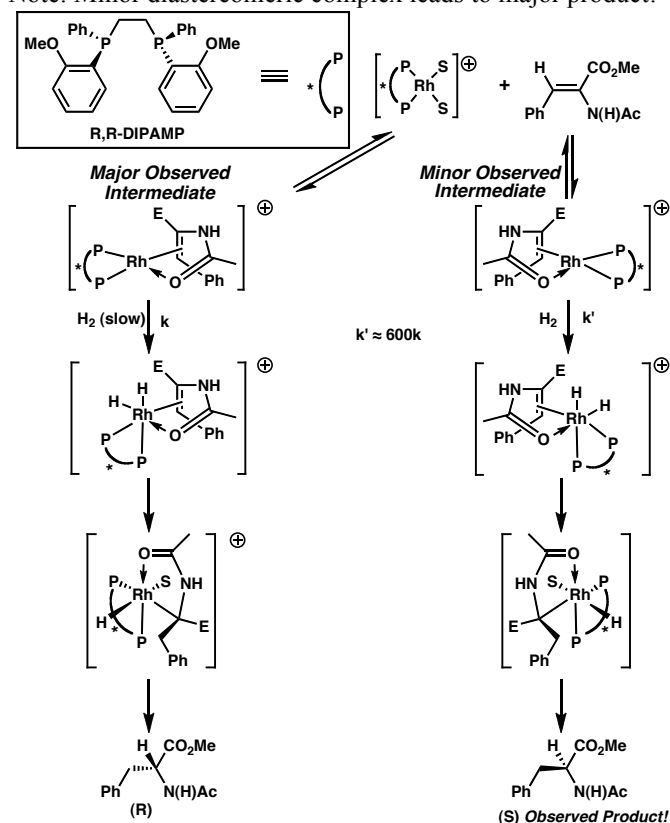
Hydrogenation of the Diene Generates the Active Catalyst



See Halpern *Science* 1982, 217, 401.

### Asymmetric Hydrogenation

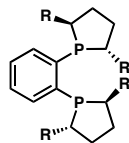
Note: Minor diastereomeric complex leads to major product!



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

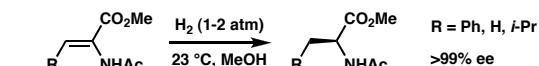
Halpern's law: If you can observe a structure, it is probably not catalytically relevant.

### DuPHOS

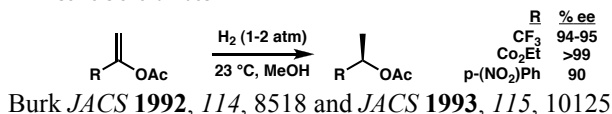


- Electron rich – 2 alkyl on each P atom
- Asymmetry rigidly held close to metal
- Can vary R groups
- Chelation in mechanism necessary
- Commercially available; expensive

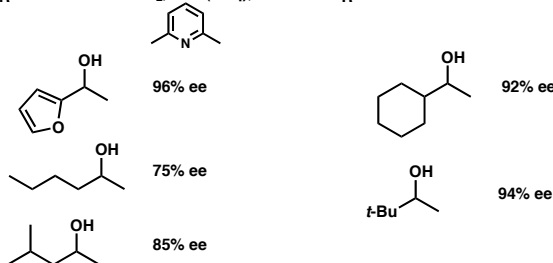
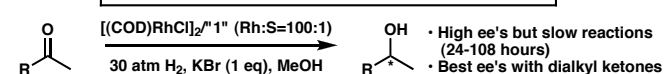
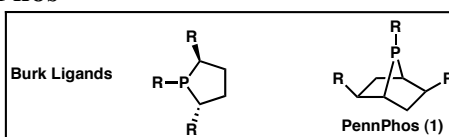
### Preparation of Catalyst:



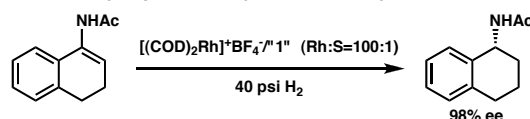
Can hydrogenate mixtures of geometrical isomers of enamides



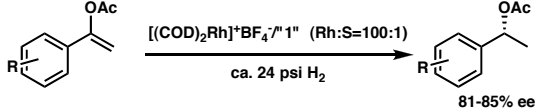
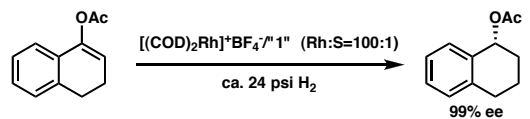
### Penn-Phos



Effective for Hydrogenation of Cyclic Enamides, Cyclic Enol Acetates:



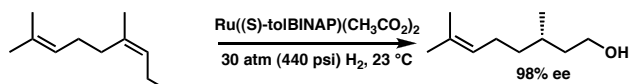
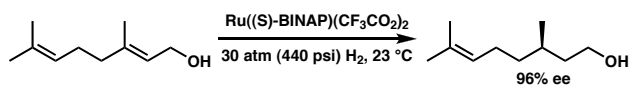
- Very high ee's for most cases with N group in the benzylic position.
- Much better results than for other ligands including BINAP, DuPHOS
- Up to 2000 turnovers



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

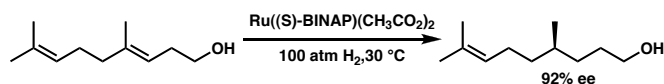
## Ruthenium BINAP/Allylic Alcohols

### Allylic Alcohols

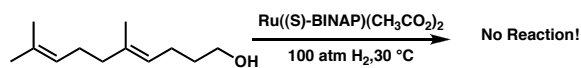


- Substrate/Catalyst ratios up to 50,000
- Reaction very concentrated, up to 5.8 M in MeOH

### Homoallylic Alcohols

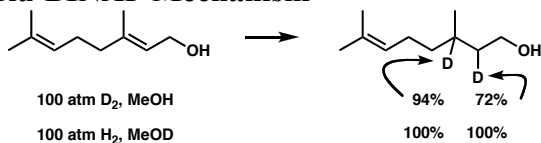


### Bishomoallylic Alcohols

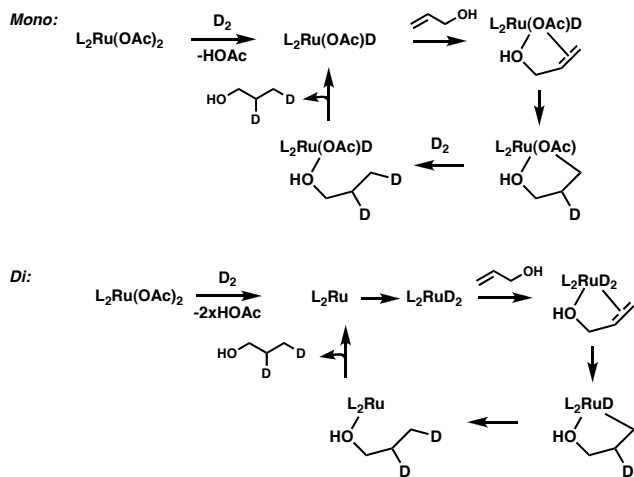


Noyori *JACS* 1987, 109, 1596

## Ru-BINAP Mechanism

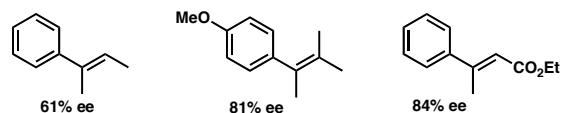
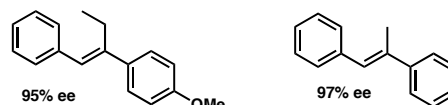
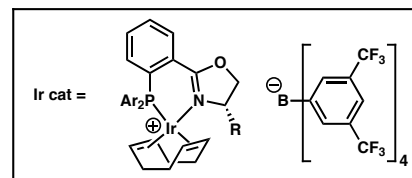
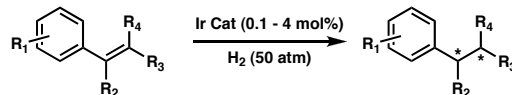


Both monohydride or dihydride mechanisms are possible:



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