CHEM 6352

Enantioselective Hydrogenations

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

Hydrogenation of the Diene Generates the Active Catalyst

- 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:**

\[ ([\text{COD}]\text{Rh})^{(\text{SbF}_5, \text{PPh}_3, \text{OTf})} + \text{DuPHOS} \rightarrow ([\text{DuPHOS}]\text{Rh}(\text{COD}))^{(X)} \]

- Can hydrogenate mixtures of geometric isomers of enamides
- Burk *JACS* 1992, 114, 8518 and *JACS* 1993, 115, 10125

**DuPHOS**

- High ee’s but slow reactions (24-108 hours)
- Best ee’s with dialkyl ketones

**Penn-Phos**

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

- Effective for Hydrogenation of Cyclic Enamides, Cyclic Enol Acetates:

\[ \text{NHAc} \]

- 96% ee

\[ \text{NHAc} \]

- 75% ee

\[ \text{NHAc} \]

- 85% ee

- Up to 2000 turnovers

\[ \text{NHAc} \]

- 92% ee

\[ \text{NHAc} \]

- 94% ee

\[ \text{NHAc} \]

- 99% ee

\[ \text{NHAc} \]

- 81-85% ee

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

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


Published by Benjamin Cummings, 1989.

For more information, visit the [CHEM 6352 course page](http://chemistry.berkeley.edu/6352/).
**Ruthenium BINAP/Allylic Alcohols**

<table>
<thead>
<tr>
<th>Allylic Alcohols</th>
<th>Ru((S)-BINAP)(CF$_3$CO)$_2$ (30 atm (440 psi) H$_2$, 23 °C)</th>
<th>H$_2$ (50 atm)</th>
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<tbody>
<tr>
<td></td>
<td>96% ee</td>
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<tr>
<td></td>
<td>Ru((S)-BINAP)(CH$_3$CO)$_2$ (30 atm (440 psi) H$_2$, 23 °C)</td>
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<tr>
<td></td>
<td>98% ee</td>
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<td><strong>Homoallylic Alcohols</strong></td>
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<td></td>
<td>Ru((S)-BINAP)(CH$_3$CO)$_2$ (100 atm H$_2$, 30 °C)</td>
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<td></td>
<td>92% ee</td>
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<td><strong>Bishomoallylic Alcohols</strong></td>
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<td></td>
<td>Ru((S)-BINAP)(CH$_3$CO)$_2$</td>
<td>No Reaction!</td>
</tr>
</tbody>
</table>

Noyori *JACS* 1987, 109, 1596

**Ru-BINAP Mechanism**

100 atm D$_2$, MeOH
100 atm H$_2$, MeOD

Both monohydride or dihydride mechanisms are possible:

**Mono:**

\[
\text{L}_2\text{Ru(OAc)}_2 + \text{D}_2 \rightarrow \text{L}_2\text{Ru(OAc)}\text{D} \rightarrow \text{L}_2\text{Ru(OAc)}_2 \rightarrow \text{D}_2
\]

**Di:**

\[
\text{L}_2\text{Ru(OAc)}_2 + \text{D}_2 \rightarrow \text{L}_2\text{RuD}_2 \rightarrow \text{D}_2
\]

Noyori *Asymmetric Catalysis in Organic Synthesis* Ch. 2

**Asymmetric Reduction of Highly Substituted Olefins**

\[
\text{R}_1\text{R}_2\text{R}_3\text{R}_4 \rightarrow \text{R}_1\text{R}_2\text{R}_3\text{R}_4
\]

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<tbody>
<tr>
<td>95% ee</td>
<td>97% ee</td>
<td>84% ee</td>
</tr>
</tbody>
</table>

| 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