9. Jacobsen-Katsuki Epoxidations


Application in process chemistry (THL 1995, 36, 3993):

The use of the co-catalyst P₃NO allowed for a decreased charge of the Mn salen catalyst in the Jacobsen epoxidation. P₃NO stabilized the catalyst, increased the rate, and transported bulk oxidant HOCl into the organic phase (JOC 1997, 62, 2222).

Preferred directions of attack of alkenes according to Jacobsen (a) and Katsuki (b):

3 possible mechanisms regarding the oxygen transfer to the double bond:

Epoxidation of styrene derivatives leads to mixtures:

Radical clock experiments give conflicting results:

There is clear evidence for the formation of radical intermediates, however, manganooxetanes, for which there is electrospray MS evidence, can also play a part in the mechanism. The influence of reaction conditions has to be taken into account.

The (salen)-Co(III) complex 1 provides a general and effective method for the preparation of enantioenriched terminal epoxides. 1a is the most commonly used variant.

The catalyst shows a second-order dependence, and a cooperative bimetallic mechanism has been suggested:

Dominant catalytic cycle in HKR reactions (RDS = rate determining step):
## 10. Peracid/Peroxide Epoxidations

Standard peracids are: MCPBA, $\text{CH}_3\text{CO}_2\text{H}$, MMP, $\text{CF}_2\text{CO}_2\text{H}$, 3,5-dinitroperbenzoic acid.

### Table: Peracid/Peroxide Epoxidation Reactions

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Method(^a)</th>
<th>Catalyst (mol %)(^b)</th>
<th>Time (h)</th>
<th>Yield (%)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$-BuO</td>
<td>A</td>
<td>0.5</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.15</td>
<td>3</td>
<td>44</td>
</tr>
<tr>
<td>ClO</td>
<td>A(^d)</td>
<td>0.5</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>B(^d)</td>
<td>0.2</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>MeO</td>
<td>A</td>
<td>2.0</td>
<td>24</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.5</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>BrO</td>
<td>A</td>
<td>0.5</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.06</td>
<td>16</td>
<td>45</td>
</tr>
<tr>
<td>t-BuO</td>
<td>A</td>
<td>2.0</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>1.2</td>
<td>48</td>
<td>39</td>
</tr>
</tbody>
</table>

* Method A: Standard, using catalyst 1. Method B: Catalyst 1f added to epoxide (0.1-0.4 mol) and water (0.7 equiv) under solvent-free conditions at room temperature. * Catalyst loading based on reacemic epoxide. * Isolated yield of >99% ee epoxide based on racemate (theoretical maximum yield = 50%). * Reaction at 0-4 °C.

---

**Mechanism:**

- $\text{RCO}_2\text{H} + \text{O} \rightarrow \text{RCO}_2\text{H} + \text{O}$

**Related:**

- Dimethyldioxirane

**Epoxidation under neutral conditions:**

- $\text{H}^+$
- $\text{HO}_2^-$
- $\text{CO}_2\text{H}$

- $\text{H}^+$


Epoxidation under Payne conditions:

With the less acidic 
MCPBA, epoxidation 
of allylic ethers is 
directed by steric 
hindrance and is *anti*-selective.

Diastereomeric control in the epoxidation with peracids is quite 
good, if appropriate directing groups are present, or if the 
substrate is sterically biased.
Diastereoccontrol in acyclic substrates:

mechanistic consideration of the relative stability of ground state conformational isomers:

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for $R^2 = H$


Catalytic Asymmetric Epoxidation with Chiral Dioxiranes


Epoxidation of enones: \( \text{H}_2\text{O}_2, \text{t-BuO}_2\text{H}, \text{cumene hydroperoxide} \)

- \( \beta \)-ionone
- THF, \( \text{H}_2\text{O} \)
- MCPBA

Presently limited to aryl or t-Bu ketones

11. Alternative Methods for Epoxide Formations

Epoxides from diols:


Via halohydrins:

\[
\begin{align*}
R\&\rightarrow & \text{HUX} & \rightarrow & \text{OHX} & \rightarrow & \text{halohydrin} \\
& & & & & \text{base} & \rightarrow & \text{RO}
\end{align*}
\]

related:

\[
\begin{align*}
l & \rightarrow & \text{I}_{\alpha} & \rightarrow & \text{I}_{\gamma} & \rightarrow & \text{NaOMe} & \rightarrow & \text{CO}_{2}\text{Me}
\end{align*}
\]

Cardillo-Epoxidation (TH 1990, 46, 3321):


![Chemical reaction diagram](image_url)


11. Epoxide Opening Reactions

on rings: trans-diaxial opening is preferred (Fürst-Plattner rule):

\[
\text{Nu}^+ \xrightarrow{\text{SN2}} \text{Nu} \quad \text{major}
\]

\[
\text{Nu} \quad \xrightarrow{\text{twist boat}} \quad \text{ca. +5 kcal/mol}
\]