Format & scope of lecture 8

- **Sigmatropic rearrangements**
  - [3,3]-Cope & oxy-Cope
  - [3,3]-Claisen & variants
  - [1,3]- and [1,5]-Hydride and alkyl shifts

- **Electrocyclic reactions**
  - Hexatriene

- **Pericyclic reactions in synthesis**
  - Endiandric acids
Sigmatropic rearrangements

- Synthetically the most important sigmatropic rearrangements are the Cope and Claisen rearrangements. These are both [3,3]-sigmatropic rearrangements.

- The Claisen/Cope rearrangements can proceed via chair or boat transition states – the chair transition state is strongly favoured unless there are steric constraints that force a boat transition state.

- Where possible, substituents generally adopt equatorial sites in the chair transition state.
Cope and Oxy-Cope rearrangement

- **The Cope rearrangement**
  - high temperatures usually required (>200°C)

- **The anionic oxy-Cope rearrangement**
  - can be conducted at low temperature (0 °C)

- **Equation**

  \[
  \frac{k_2}{k_1} \sim 10^{10} - 10^{17}
  \]

  - a useful method for the synthesis of cis-decalins from norbornene derivatives…
Cope rearrangement

\[ (4q + 2)_s = 3 \]
\[ (4r)_s = 0 \]
\[ \text{Total} = 3 < \text{add} / \text{Thermally allowed} \]

\[ \pi^2_s \]

\[ \sigma^2_s \]

\[ \text{W-H approach} \]

For an FMO approach see lecture 6, slide 10.
Claisen and variants

- **The Claisen rearrangement:**
  - allyl vinyl ether to $\gamma,\delta$-unsaturated carbonyl derivative
  - driven by formation of C=O bond.

- **The Johnson-Claisen rearrangement**
  - synthesis of $\gamma,\delta$-unsaturated esters via ketene acetal

- **The Ireland-Claisen rearrangement**
  - Synthesis of $\gamma,\delta$-unsaturated acids via silyl ketene acetal
A suprafacial 1,n-hydride shift involves the hydrogen moving from one end of the conjugated system to the other across one face of the conjugated system.

An antarafacial 1,n-hydride shift involves the hydrogen moving from one end of the conjugated system to the other and moving from one face of the conjugated system to the opposite face.

\[
\begin{align*}
(4q + 2)_s &= 1 \\
(4r)_s &= 0 \\
\text{Total} &= 1
\end{align*}
\]

Thermally allowed

\[
\begin{align*}
(4q + 2)_a &= 0 \\
(4r)_a &= 1 \\
\text{Total} &= 1
\end{align*}
\]

Thermally allowed

\[
\begin{align*}
(4q + 2)_s &= 1 \\
(4r)_s &= 0 \\
\text{Total} &= 1
\end{align*}
\]

Thermally allowed
1,3-Hydride and Alkyl shifts

- **1,3-Hydride shifts** - do not occur thermally
  - geometrically reasonable suprafacially, but thermally disallowed
  - antarafacially thermally allowed, but geometrically unreasonable:

  ![HOMO σ](https://via.placeholder.com/150)
  ![LUMO π*](https://via.placeholder.com/150)

  ![W-H approach](https://via.placeholder.com/150)
  ![FMO approach](https://via.placeholder.com/150)

- **1,3-Alkyl shifts** – do occur thermally
  - …with *inversion* of configuration in the migrating group:

  ![W-H approach](https://via.placeholder.com/150)
1,5-Hydride and Alkyl shifts

- **1,5-Hydride shifts** – thermally suprafacial reactions:

  ![Hydride shifts diagram](image)

- **1,5-Alkyl shifts** – thermally suprafacial reactions
  - ...with *retention* of configuration in the migrating group:

  ![Alkyl shifts diagram](image)

- **Chiral acetic acid**
- **Disfavoured conformation**

- **Heat**
- **W-H approach**
Electrocyclic reactions - *thermal*

Thermal electrocyclic processes will be *conrotatory* if the total number of electrons is \(4n\) and *disrotatory* if the total number of electrons is \((4n + 2)\). This is reversed for photochemical reactions.

\[\begin{align*}
\text{Me} & \quad \text{Me} \quad \text{140 °C, 5 h} \quad \text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me}
\end{align*}\]

\[\begin{align*}
\pi^n_{6s} & \quad (4q + 2)_s = 1 \\
(4r)_s = 0 \\
\text{Total} = 1 \\
\text{odd ✓} \\
\text{Thermally allowed disrotatory}
\end{align*}\]

\[\begin{align*}
\text{Me} & \quad \text{Me} \quad \text{140 °C, 5 h} \quad \text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me}
\end{align*}\]

\[\begin{align*}
\pi^n_{6s} & \quad (4q + 2)_s = 1 \\
(4r)_s = 0 \\
\text{Total} = 1 \\
\text{odd ✓} \\
\text{Thermally allowed disrotatory}
\end{align*}\]
Electrocyclic reactions - photochemical

Photochemical electrocyclic processes will be disrotatory if the total number of electrons is $4n$ and conrotatory if the total number of electrons is $(4n + 2)$. This is reversed for thermal reactions.

$\text{Photochemically allowed}$

$\text{conrotatory}$

$\text{constructive overlap ✓}$

$\text{conrotatory}$

$\text{FMO approach}$

$\text{W-H approach}$

$\text{PHPH}$

$\text{Me}$

$\text{Me}$

$\text{Me}$

$\text{Me}$

$\text{Ph}$

$\text{Ph}$

$\text{Ph}$

$\text{Ph}$

$\text{hv}$

$\text{HSOMO}$

$\text{diene (ψ₃)}$

$\text{LUMO}$

$\text{σ*}$

$\text{π₄s}$

$\text{(4q + 2)i} = 0$

$\text{(4r)a} = 0$

$\text{Total = 0 even ✓}$

$\text{conrotatory}$

$\text{Photochemically allowed}$
Pericyclics in synthesis: *the endiandric acids*

- **exo-Diels Alder reaction**
- **heat 100 °C**
- **H₂ Lindlar**

**endiandric acid A methyl ester**

**endiandric acid B methyl ester**

**endiandric acid C methyl ester**

**endiandric acid D methyl ester**

**endiandric acid E methyl ester**

**8π electrocyclic conrotatory**

**6π electrocyclic disrotatory**