Stereoselectivity in E1 ($E$ or $Z$)

- Potential for two products, $E$ or $Z$ alkene
- $E$ normally favoured as substituents far apart

\[
\text{Ph} - \text{OH} \xrightarrow{\text{H}^+} \text{Ph} = \text{alkene} + \text{Ph} = \text{alkene}
\]

- First cation formation
- Second bond rotation to align empty $p$ orbital & C–H $\sigma$ bond

- Conformation with Me & Ph on opposite faces is lower in energy
  - **Favoured**

- Conformation with Me & Ph on same face is higher in energy as they are closer together
  - **Disfavoured**
Regioselectivity in E1

- Two possible products depending on position of double bond
- Most stable alkene is formed
- Reason for stability is controversial...
- Overlap with $\pi^*$ creates stronger sp$^2$-sp$^3$ bond - more stable

\[ \text{OH} \xrightarrow{\text{HBr, H}_2\text{O}} \begin{array}{c} \text{major product} \\ \text{minor product} \end{array} \]

- No C–H bonds parallel with $\pi^*$
- Most stable:
  - tetrasubstituted
  - trisubstituted
  - disubstituted
  - monosubstituted
Stereochemistry in E2

- New $\pi$ bond formed by overlap of C–H $\sigma$ orbital and C–X $\sigma^*$ orbital
- Optimum overlap if orbitals are parallel
- Allows selectivity
- 2 possibilities...

**Syn-periplanar**
Stereochemistry in E2 II

- E2 occurs via anti-periplanar transition state when possible because...
- Orbitals are truly parallel
- Staggered conformation more stable
- Base and leaving group are on opposite faces, out of each other's way
- Electron flow occurs via all-backside displacements like $S_N^2$
Stereoselectivity in E2

- **Stereoselectivity** - mechanistically there is a choice of two products but one is favoured - there is a choice
- If two protons can be eliminated the reaction will proceed *via* the **anti-periplanar** transition state that suffers **least** steric hindrance
Stereospecificity in E2

- Stereospecific - mechanistically only one outcome; different stereoisomers of starting material give different stereoisomer of alkene - there is no choice
- If only one proton can be eliminated then geometry of alkene depends on stereochemistry of starting material

\[ (1S,2R) \text{ gives } E \text{ alkene} \]

\[ (1S,2S) \text{ gives } Z \text{ alkene} \]
E2 Eliminations from cyclohexanes

- Necessity for anti-periplanar conformation has a huge effect in cyclohexanes
- For E2 we must have C–H & C–X both axial (trans-diaxial)
- Below shows the effect of this requirement...

$$\text{Me} \quad \text{Me}$$

$$\text{Cl} \quad \text{Cl}$$

1 : 3

250 times SLOWER
E2 Eliminations from cyclohexanes II

disfavoured: i-Pr axial
E2 not possible
no anti-periplanar C–H

favoured: i-Pr equatorial
E2 possible
2 anti-periplanar C–H

ring inversion

favoured: i-Pr equatorial
E2 not possible
no anti-periplanar C–H

disfavoured: i-Pr axial
but E2 possible
Slow as rarely in this conformation
Regiochemistry in E2

- E1 gives thermodynamically more stable - more substituted alkene
- E2 can give both - more hindered the system, the more of the less substituted alkene

Hindered base can change selectivity

- Br
  - NaOEt: 69%
  - t-BuOK: 28%
## Summary

<table>
<thead>
<tr>
<th></th>
<th>Poor nucleophile (e.g. H₂O, ROH)</th>
<th>Weakly basic nucleophile (e.g. I⁻, RS⁻)</th>
<th>Strongly basic, unhindered nucleophile (e.g. RO⁻)</th>
<th>Strongly basic, hindered nucleophile (e.g. DBU, DBN, t-BuO⁻)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methyl</strong></td>
<td>no reaction</td>
<td>Sₙ²</td>
<td>Sₙ²</td>
<td>Sₙ²</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td>no reaction</td>
<td>Sₙ²</td>
<td>Sₙ²</td>
<td>E₂</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td>no reaction</td>
<td>Sₙ²</td>
<td>E₂</td>
<td>E₂</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td>Sₙ¹, E₁ (slow)</td>
<td>Sₙ²</td>
<td>E₂</td>
<td>E₂</td>
</tr>
<tr>
<td><strong>Tertiary</strong></td>
<td>E₁ or Sₙ¹</td>
<td>Sₙ¹, E₁</td>
<td>E₂</td>
<td>E₂</td>
</tr>
</tbody>
</table>
Summary II

- Methyl halides will never eliminate (no protons in correct place)
- Increasing branching (more substituents) on substrate will favour elimination
- Strongly basic hindered nucleophiles will always eliminate unless no option
- Good nucleophiles will go via $S_N2$ unless substrate tertiary then $E1$ and $S_N1$ compete
- Weaker bases that are good nucleophiles give substitution
- Normally observe $E1$ products when $S_N1$ occurs!
- Best LG give weakest bases as products

These mechanisms are just extremes
Real life can be somewhere inbetween!
There are other substitution and elimination mechanisms!