Elimination reactions: E1, E2

E2: biomolecular elimination

Reverse of H-X addition
Need an α proton
if more than one, product mixture results

kinetics: rate = k[RBr][B:\]

Zaitsev’s Rule: In general, for base promoted elimination reactions, the more highly substituted alkene is the major product.
Chiral substrate

NaOEt

Ph = C₆H₅
Et = C₃H₅

100%
**Anti-periplanar** conformation preferred

- to reduce steric strain.
- maximize developing π overlap

**E2: substrate requirement summary**

- α proton must be present
- must achieve anti-periplanar conformation

R,R
one α proton
not peri-planar
E2: leaving groups

\[
\begin{align*}
\text{Transition state} & \\
& \text{leaving group is developing negative charge} \\
& \text{good leaving groups are weak bases}
\end{align*}
\]

E2: Base/solvent combination (nucleophile)

*Prevalent elimination mechanism when a strong base is used in combination with its CA as solvent.*

\[
\text{OH} / \text{H}_2\text{O}
\]

useful when \(\alpha\)-proton is not very acidic

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Elimination reactions and cyclohexane conformation

\[
\begin{align*}
\text{cis} & \quad \text{O}_2\text{Na}^+ \\
\text{trans} & \quad \text{O}_2\text{Na}^+ \\
\text{OH} & \quad \text{OH} \\
\end{align*}
\]

\(\text{[\(\alpha\)]}_\text{D} = 0\) racemic

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Why the difference in rate?

Substrate requirements

- \(\alpha\)-proton
- anti-periplanar arrangement
Consider chair conformations: bigger group wants to be in equatorial position

Rationalize:

- Ethyl is larger than Br, so takes equatorial position in most stable conformer
Summary of E2 requirements

substrate
- $\alpha$-proton
- anti-periplanar (trans diaxial H, LG)

LG
- weak base

B/solvent
- strong/conjugate acid

An aside: How do we know which step is rate determining?
Isotope Effects—changes in the rate resulting from the use of different isotopes.
- $^2$H or D, deuterium, most commonly used
- C-D bond is slightly stronger, so $E_{act}$ is greater
- if breaking C-H bond is r.d.s., substitution with D will result in slower rate

$$
\begin{align*}
\text{CH}_4 + \text{Cl} & \rightarrow \text{CH}_3\text{Cl} + \text{HCl} & \text{rel. rate} = 12 \\
\text{CD}_4 + \text{Cl} & \rightarrow \text{CD}_3\text{Cl} + \text{DCl} & \text{rel. rate} = 1 \\
\end{align*}
$$

bond breaking occurs in transition state

Supporting evidence for E2

Faster

Slower
E1: unimolecular elimination reaction

Usually get mixture of products.

$S_N1$ and E1 share common carbocation

B: is too weak to remove $\alpha$-proton but the carbocation increases its acidity.

Not very useful for synthesis; usually a side-reaction in $S_N1$ reactions.

$S_N1$ and E1 share common carbocation intermediate:

$\Delta G^\circ$ vs rxn progress
Some examples:

\[
\begin{align*}
&\text{CH}_3\text{Cl} \quad \text{CH}_3\text{OH} \\
&\quad \quad \quad \quad \quad \text{E1} \quad \text{S}\text{N}1
\end{align*}
\]

\[
\begin{align*}
&\text{CH}_3\text{Cl} \quad \text{CH}_3\text{OH} \\
&\quad \quad \quad \quad \quad \text{E1} \quad \text{S}\text{N}1
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\]

\[
\begin{align*}
&\text{CH}_3\text{Cl} \quad \text{CH}_3\text{OH} \\
&\quad \quad \quad \quad \quad \text{E1} \quad \text{S}\text{N}1
\end{align*}
\]
**E1 summary**

*substrate*
- $\alpha$-proton
- anti-periplanar not required

*leaving group*
- weak base

*base* = solvent
- weak bases
- neutral species with electron pair

**Distinguishing between $S_N^1$, $S_N^2$, E1, E2**

*substrate, base/nucleophile*

1$^o$ substrates: $S_N^2$, E2

- good Nu
- strong base
- polarizable (increases going down a group)

Cannot form stable carbocation
- no E1
- no $S_N^1$

$\alpha$-proton, anti-periplanar
t-butoxide is a very strong base, so excellent nucleophile but:
• steric bulk of t-butoxide disfavors $S_N2$
  (easier to pluck off a proton)
• t-butanol is a poor $S_N2$ solvent (polar protic)

$3^\circ$ substrates ($S_N1$, $E1$ or $E2$): do not react by $S_N2$!

weak bases

strong bases
$\alpha$-proton, anti-periplanar

weak base

$S_N2$:

$E2$:

$3^\circ$ substrates (S_N1, E1 or E2): do not react by S_N2!
Strong Base

\[ \text{H}_3\text{C}-\text{C}-\text{Br} \xrightarrow{\text{O-}} \text{H}_2\text{C}=\text{C}-\text{Br} \]

\[ \text{OH} \quad \text{OH} \quad \text{Br}^- \]

\[ \text{E2} \]

\[ \text{H}_3\text{C}-\text{C}-\text{Br} \xrightarrow{\text{OH}} \text{H}_3\text{C}=\text{C}-\text{CH}_3 \]

\[ \text{OH} \quad \text{Br}^- \]

SUMMARY

*Use substrate and base/Nu to distinguish pathways!*

1° substrates: $\text{S}_\text{N}2$, E2

- good Nu
- strong base
- $\alpha$-proton, anti-periplanar

3° substrates ($\text{S}_\text{N}1$, E1 or E2)

- weak bases
- strong bases
- $\alpha$-proton, anti-periplanar

2° substrates: difficult to predict, can react by all 4 pathways!