Acidity

Acidity increases due to electron withdrawing increasing

Acid strength increases due to increase in atomic size

HF > H₂O > NH₃ > CH₄

The stronger the acid, the weaker its conjugate base.

Fo < OH⁻ < NH₂⁻ < CH₃⁻

Stronger base

HF > HBr > HCl > HF

Stronger acid

I⁻ < Br⁻ < Cl⁻ < F⁻

More stable base, bigger ion

CH₃OH vs. H₂O

CH₃C₂H₂OH vs. CH₃OH

CH₃OH₂ vs. CH₃OH

Atomic size

Which is more acidic?
Chair Conformers

- Cis
- Trans
- Eclipsed
- Staggered
- Gauche
- Gauche strain
- Axial
- Equatorial

Does axial or equatorial have more strain?

Chirality

- 4 different groups attached to carbon
- Meso diastereomers
- Meso > acinal

What is the stereochemistry of this molecule?

Plane of symmetry = meso
SN2 is stereospecific and will experience inversion.

SN1 will result in racemic mixture.

SN1 requires good nucleophile.

A carbocation intermediate has potential for rearrangement.

CH₃Br → \( R^+ + X^- \) → \( \text{SN}_1 \) Rate

Aprotic solvents cannot make H-bonds.

DMSO prefers aprotic solvents with low ability to make H-bonds.

Water acts as a nucleophile and nucleophile.

Solvent effects:
- Aprotic solvents are preferred.
- Ability to make H-bonds.
- IF there is a solvent in a SN1 reaction, it must be protic.

{/primary_language}
**E1**

\[ \begin{align*}
\text{Cl} & \rightarrow \text{+R} \\
\text{C:B} & \rightarrow \text{Cl}
\end{align*} \]

* always happens with SN1.
* 3\(^°\) > 2\(^°\) > 1\(^°\)
* does not require strong base

**E2**

\[ \begin{align*}
\text{C} & \rightarrow \text{H} \\
\text{C:B} & \rightarrow \text{Cl}
\end{align*} \]

* requires strong base
* leaving group must be anti to hydrogen

**Hoffman**
- more substituted
- favored by bulky base (LiDA or AlkBu)

**Zaitsev**
- less substituted
- can be selected for using bulky base

* heat or bulky base favors elimination

<table>
<thead>
<tr>
<th>OH, tBu</th>
<th>Cl(^-)</th>
<th>H(_2)O, H(_3)O</th>
<th>CH(_3)Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>good nuc</td>
<td>weak base</td>
<td>poor nuc</td>
<td></td>
</tr>
<tr>
<td>strong base</td>
<td>weak base</td>
<td>poor nuc</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1(^°)</th>
<th>SN2 &gt; E2</th>
<th>SN2</th>
<th>NO RXN</th>
</tr>
</thead>
<tbody>
<tr>
<td>2(^°)</td>
<td>mostly E2</td>
<td>mostly SN2</td>
<td>SN1/3E</td>
</tr>
<tr>
<td>3(^°)</td>
<td>E3 in polar protic solvent</td>
<td>SN1/3E in polar protic solvent</td>
<td>E1 favored</td>
</tr>
</tbody>
</table>
**Organic Chemistry**

**Alkenes**

- Markov
- Can rearrange

**Mechanisms**

- To add a bromide
- $\text{HBr} \rightarrow \text{R-Br}$
- $\text{H}_2 \text{C=CH}_2$ + $\text{HBr} \rightarrow \text{R} \cdot \text{Br}$
- Anti-Markov
- No rearrangement

**To make an alcohol**

- $\text{H}_2 \text{C=CH}_2$ + $\text{H}_2 \text{O} \rightarrow \text{H}_2 \text{C} \cdot \text{OH}$
- Markov
- Can rearrange

**To make a diol**

- $\text{H}_2 \text{C=CH}_2$ + $\text{H}_2 \text{O}$ (aq) \( \xrightarrow{\text{H}_2 \text{O}} \) $\text{H}_2 \text{C} \cdot \text{OH}$
- Anti-Markov
- Cannot rearrange

**Syn addition of 2 alcohols**

- $\text{H}_2 \text{C} \cdot \text{OH}$ + $\text{H}_2 \text{C} \cdot \text{OH}$
- $\text{H}_2 \text{C} \cdot \text{OH}$
- $\text{H}_2 \text{C} \cdot \text{OH}$

**Second addition occurs at more substituted location**

- $\text{R} \cdot \text{OH}$
- $\text{R} \cdot \text{OH}$
- $\text{R} \cdot \text{OH}$

**Epoxide formation**

- $\text{H}_2 \text{C} \cdot \text{OH}$ + $\text{H}_2 \text{O}$
- $\text{H}_2 \text{C} \cdot \text{OH}$
- $\text{H}_2 \text{C} \cdot \text{OH}$

- MCPBA
- KMnO$_4$, K$_2$O
- $\text{H}^+$, H$_2$O

- $\text{H}_2 \text{C} \cdot \text{OH}$
- $\text{H}_2 \text{C} \cdot \text{OH}$
- $\text{H}_2 \text{C} \cdot \text{OH}$
ALKYNES
Mechanisms

- Ozonolysis
- Adding halides/alkynes + alcohols
- Syn addition of H
- To add hydrogens

H2 \xrightarrow{\text{Pt/C}} \text{H2}

1. O₃ → H₃C = CH₂ + H₂ + Br₂
2. H₂O

B₂H₆ → Br₂ → \text{Br} \quad \text{B₂H₆} \quad \text{Br} \quad \text{Br} \quad \text{Br} \quad \text{H₂O}

- Anti addition
- Anti addition - OH will go to more substituted location

- cis alkene
- trans alkene

H₂ → \text{Lindlar's catalyst}

\text{NaNH₂} → H = C = C \quad \text{alkyne}

Alkynyl is now a nucleophile
- can be used to add parts onto alkynyl

A to remove terminal hydrogens
A to add hydrogens
A to ozonolysis
Adding aldehydes

^{Br}_2 \rightarrow \text{Excess HBr} \rightarrow \text{HBr, ROE} \rightarrow \text{H}_2\text{SO}_4, \text{H}_2\text{O} \rightarrow \text{1. R2 BH} \rightarrow \text{2. H}_2\text{O, NaBH}_4

\text{\textbf{enol, will undergo tautomerization, Markov}}

\text{\textbf{enol, will undergo tautomerization, Anti-markov}}
Grignard Reaction

\[ \text{Grignard Rxn} \]

- + MgBr → MgC₂
- H₂O → HO⁻ and Cl⁻
- x will happen twice for

**Synthesis Tips**

- Utilize elimination and substitution to move leaving groups and double bonds around
- Use grignard rxn to add on carbons
- Pay attention to Markov and Anti-Markov reagents
- Always count your carbons!
- Know at least one reaction (nucleophile/base) that will work for tasks such as making alcohols, alkenes, etc.
Grignard Reaction

Br → MgBr

\[ \text{ OH } \]

- Adds on carbons
- Can be used on ketones and esters
- Grignard attacks most substituted location on epoxide

Synthesis Tips

- Utilize elimination and substitution to move leaving groups and double bonds around
- Use grignard reaction to add on carbons
- Pay attention to Markov and Anti-Markov reagents
- Always count your carbons!
- Know at least one reaction/nucleophile/base that will work for tasks such as making alcohols, alkenes, etc.