Free Radical Halogenation of Alkanes

\[ \text{Cl}_2 + \text{C}_6\text{H}_4 \rightarrow \text{C}_6\text{H}_4\text{Cl} + \text{Cl}_2 \]

Elimination Reactions

Know details of E1 and E2 mechanisms (see summary at end)

\[ \text{C}_6\text{H}_5\text{OH} \xrightarrow{\text{H}_3\text{PO}_4} \text{C}_6\text{H}_5\text{O}^+ \xrightarrow{\text{H}_2\text{O}} \text{C}_6\text{H}_5^+ \xrightarrow{\text{H}_3\text{PO}_4} \text{C}_6\text{H}_5\text{H}_2\text{PO}_4^+ \]

A bromonium

Bromide can only come from the bottom and kick off the bromine on the top. This reaction forms the trans product selectively.

Electrophilic Addition Reactions

\[ \text{H}_3\text{C} = \text{C} = \text{H} + \text{HBr} \rightarrow \text{H}_3\text{C}^+ \text{C} = \text{C} + \text{H} \]

Most stable intermediate

Lower energy pathway

Bromide can only come from the bottom and kick off the bromine on the top. This reaction forms the trans product selectively.
Reduction (Hydrogenation) Reactions

1) BH₃
2) H₂O₂ / NaOH

1) BH₃
2) H₂O₂ / NaOH
Oxidation Reactions

\[ \text{Intermediate - not isolated} \]

CIS addition of OH's

carbon-carbon bond broken

Substitution Reactions

In addition to these specific substitution reactions, you should be familiar with the details of the S\textsubscript{N}1 and S\textsubscript{N}2 reaction mechanisms. You should also know the different leaving groups (halides and tosylates) and different nucleophiles we have discussed in class. (See summary at end)

Note: The following SOCl\textsubscript{2} and PBr\textsubscript{3} reactions will result in inversion of stereochemistry if it is present. They are S\textsubscript{N}2 reactions.
Organometallic Reactions

\[
\begin{align*}
\text{H}_3\text{C}-\text{Br} & \quad \text{Mg} \quad \text{H}_3\text{C}-\text{MgBr} \quad \text{D}_2\text{O} \quad \text{D} \\
\text{reactivity of carbon reversed} & \\
\text{H}_2\text{C}-\text{Li} & \quad \text{2 Li} \quad \text{H}_2\text{C}-\text{Li} \quad \text{Cul} \\
\text{Gilman reagent} & \\
(\text{CH}_3)_2\text{CuLi} & \quad \text{Br} \quad \text{CH}_3
\end{align*}
\]

Summary of Substitution and Elimination Reactions

<table>
<thead>
<tr>
<th>R-X</th>
<th>SN1</th>
<th>SN2</th>
<th>E1</th>
<th>E2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°</td>
<td>X</td>
<td>favored with good nucleophile</td>
<td>X</td>
<td>favored with strong base</td>
</tr>
<tr>
<td>2°</td>
<td>can occur best if allylic</td>
<td>can occur with good nucleophile</td>
<td>can occur best if allylic</td>
<td>favored with strong base</td>
</tr>
<tr>
<td>3°</td>
<td>favored competes with E1</td>
<td>X</td>
<td>favored if basic competes with SN1</td>
<td>favored with strong base</td>
</tr>
</tbody>
</table>

Stereochem | racemic | 100% inversion | doesn't matter | antiperiplanar required |
Comparison of Substitutions

<table>
<thead>
<tr>
<th></th>
<th>$S_{N1}$</th>
<th>$S_{N2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUBSTRATE</strong></td>
<td>$3^\circ &gt;&gt; 2^\circ &gt; 1^\circ$</td>
<td>$1^\circ &gt; 2^\circ &gt;&gt; 3^\circ$</td>
</tr>
<tr>
<td><strong>NUCLEOPHILE</strong></td>
<td>Weak OK</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>LEAVING GROUP</strong></td>
<td>Stable Anions</td>
<td>Stable Anions</td>
</tr>
<tr>
<td><strong>SOLVENT</strong></td>
<td>Polar Protic</td>
<td>Polar Aprotic</td>
</tr>
<tr>
<td><strong>STEREOCHEM</strong></td>
<td>Racemic</td>
<td>100% inversion</td>
</tr>
</tbody>
</table>

Nucleophile Comparisons

Note, good bases would be Alcoxides (‘OR), Hydroxides (‘OH) and amides (‘NH₂).

<table>
<thead>
<tr>
<th>NUCLEOPHILE</th>
<th>H₂O</th>
<th>NH₃</th>
<th>Cl⁻</th>
<th>HO⁻</th>
<th>CH₃O⁻</th>
<th>I⁻</th>
<th>CN⁻</th>
<th>HS⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>RELATIVE RATE FOR $S_{N2}$</td>
<td>1</td>
<td>700</td>
<td>1000</td>
<td>16,000</td>
<td>25,000</td>
<td>100,000</td>
<td>125,000</td>
<td>125,000</td>
</tr>
</tbody>
</table>

E₂ elimination geometry

Hydrogen and leaving group must be antiperiplanar for elimination to take place.