Increasing the leaving group ability of a leaving group by modifying it chemically is called activation. Empirically, the leaving group ability of a leaving group is a function of its base strength. The lower the base strength of a leaving group, the greater its leaving group ability.

eg:

<table>
<thead>
<tr>
<th>leaving group</th>
<th>conjugate acid</th>
<th>$\text{pK}_a$ of conjugate acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br$^-$</td>
<td>HBr</td>
<td>-9</td>
</tr>
<tr>
<td>Cl$^-$</td>
<td>HCl</td>
<td>-7</td>
</tr>
</tbody>
</table>

Br$^-$ is a weaker base and, therefore, a better leaving group than Cl$^-$. To activate a leaving group, the compound carrying it is subjected to a reaction that converts the leaving group into one that is less basic.

eg:

\[
\begin{align*}
\text{Alcohol 1} & \quad \text{OH} \\
\text{Alcohol 1} + \text{HCl} & \quad \text{Alcohol 1} + \text{H}_2\text{O} \\
\rightarrow & \\
\text{Alcohol 2} & \quad \text{Cl} \\
\end{align*}
\]

Alcohol 1 can be converted to alkyl halide 2 by treating it with HCl.

The net reaction is nucleophilic substitution:

\[
\begin{align*}
\text{substrate} & \quad \text{OH} \\
\text{nucleophile} + \text{Cl}^- & \quad \text{OH} \\
\rightarrow & \\
\text{substitution product} & \quad \text{Cl} \\
\text{leaving group} & \quad \text{OH} \\
\end{align*}
\]

However, when 1 is treated with Cl$^-$, no reaction occurs even at high temperature.

\[
\begin{align*}
\text{Alcohol 1} & \quad \text{OH} \\
\text{Alcohol 1} + \text{Li}^+\text{Cl}^- & \quad \text{no reaction} \\
\text{Alcohol 1} & \quad \text{Cl}^- \\
\end{align*}
\]

The reason is OH$^-$ is a weak leaving group.

The reaction of 1 with HCl occurs in two stages.

Stage 1: Activation

\[
\begin{align*}
\text{substrate} & \quad \text{OH} \\
\text{nucleophile} + \text{HCl} & \quad \text{OH} \\
\rightarrow & \\
\text{substitution product} & \quad \text{Cl}^- \\
\text{leaving group} & \quad \text{OH} \\
\end{align*}
\]

The acid-base reaction converts 1 into an oxonium ion (3).

Stage 2: Nucleophilic Substitution
Water is a much better leaving group than OH\(^-\). Consequently, 3 in which the leaving group is water undergoes nucleophilic substitution with Cl\(^-\), whereas 1 in which the leaving group is OH\(^-\) does not.

### Contributors

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