How do we determine whether a reaction is SN1 or SN2?

**Factor #1**: Electrophile (substrate). Is the electrophile primary, secondary, or tertiary?

**SN2**

<table>
<thead>
<tr>
<th>Reaction type</th>
<th>Stereochemistry</th>
<th>Regiochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substitution (S_N2)</td>
<td>Inversion</td>
<td>Not applicable (nucleophile attacks carbon next to LG)</td>
</tr>
</tbody>
</table>

**SN1**

<table>
<thead>
<tr>
<th>Reaction type</th>
<th>Stereochemistry</th>
<th>Regiochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substitution (S_N1)</td>
<td>Racemization</td>
<td>Not applicable (nucleophile attacks carbon next to LG)</td>
</tr>
</tbody>
</table>

LG = Leaving Group
EXERCISE 9.1 Identify whether the following substrate is more likely to participate in an $S_N2$ or $S_N1$ reaction.

\[ \text{Cl} \]

ANSWER The substrate is primary, so we predict an $S_N2$ reaction.

PROBLEMS Identify whether each of the following substrates is more likely to participate in an $S_N2$ or $S_N1$ reaction.

9.2 \[ \text{Br} \] 9.3 \[ \text{Cl} \] 9.4 \[ \text{Br} \] 9.5 \[ \text{I} \]
There is one other way to stabilize a carbocation (other than alkyl groups)—resonance. If a carbocation is resonance stabilized, then it will be easier to form that carbocation:

The carbocation above is stabilized by resonance. Therefore, the LG is willing to leave, and we can have an $S_{N}1$ reaction.

There are two kinds of systems that you should learn to recognize: a LG in a benzylic position and a LG in an allylic position. Compounds like this will be resonance stabilized when the LG leaves:

If you see a double bond near the LG and you are not sure if it is a benzylic or allylic system, just draw the carbocation you would get and see if there are any resonance structures.

**EXERCISE 9.6** In the compound below, circle the LGs that are benzylic or allylic:

---

**Answer**
PROBLEMS  For each compound below, determine whether the LG leaving would form a resonance-stabilized carbocation. If you are not sure, try to draw resonance structures of the carbocation you would get if the leaving group is expelled.

9.7

9.8

9.9

9.10
**Factor #2: The Nucleophile**

### Common Nucleophiles

<table>
<thead>
<tr>
<th>Strong</th>
<th>Weak</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{I}^-$</td>
<td>$\text{F}^-$</td>
</tr>
<tr>
<td>$\text{Br}^-$</td>
<td>$\text{H}_2\text{S}$</td>
</tr>
<tr>
<td>$\text{Cl}^-$</td>
<td>$\text{RSH}$</td>
</tr>
<tr>
<td>$\text{OH}^-$</td>
<td>$\text{N}≡\text{C}^-$</td>
</tr>
</tbody>
</table>

Strong Nucleophiles favor SN2; Weak Nucleophile disfavors SN2 thereby allowing SN1 to compete

**EXERCISE 9.11** Identify whether the following nucleophile will favor SN2 or SN1:

![Nucleophile](image)

**ANSWER** This compound has a sulfur atom with lone pairs. A lone pair on a sulfur atom will be strongly nucleophilic, even without a negative charge, because sulfur is large and highly polarizable. Strong nucleophiles favor SN2 reactions.

**PROBLEMS** Identify whether each of the following nucleophiles will favor SN2 or SN1.

1. ![Nucleophile](image) Answer: ________
2. ![Nucleophile](image) Answer: ________
3. ![Nucleophile](image) Answer: ________
4. ![Nucleophile](image) Answer: ________
5. ![Nucleophile](image) Answer: ________

1. ![Nucleophile](image) Answer: ________
2. ![Nucleophile](image) Answer: ________
3. ![Nucleophile](image) Answer: ________
Factor 3: Leaving Group

Good leaving groups are typically the conjugate bases of strong acids. In other words, the weaker the basicity of a leaving group, the greater the leaving group.

<table>
<thead>
<tr>
<th>Acid</th>
<th>pKₐ</th>
<th>Conjugate Base</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongest Acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I⁻ - H</td>
<td>-11</td>
<td></td>
</tr>
<tr>
<td>Br⁻ - H</td>
<td>-9</td>
<td></td>
</tr>
<tr>
<td>Cl⁻ - H</td>
<td>-7</td>
<td></td>
</tr>
<tr>
<td>O⁻ - H</td>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>H⁻ - O⁻ H</td>
<td>-2</td>
<td></td>
</tr>
<tr>
<td>weakest acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H⁻ - O⁻ H</td>
<td>15.7</td>
<td></td>
</tr>
<tr>
<td>O⁻ - H</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>O⁻ - H</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>H⁻ - N⁻ H</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

The most commonly used leaving groups are halides and sulfonate ions:
EXERCISE 9.18 Identify the leaving group in the following compound:

\[
\text{Cl} \quad \text{----} \quad \text{OH}
\]

**ANSWER** We have seen that hydroxide is not a good leaving group, because its conjugate acid (H₂O) is not a strong acid. As a result, hydroxide is not a weak base, so it does not function as a leaving group. In contrast, chloride is a good leaving group because its conjugate acid (HCl) is a strong acid. Therefore, chloride is a weak base, so it can serve as a leaving group.

**PROBLEMS** Identify the best leaving group in each of the following compounds:

9.19

9.20

9.21

9.22

9.23

9.24

**9.25** Compare the structures of 3-methoxy-3-methylpentane and 3-iodo-3-methylpentane, and identify which compound is more likely to undergo an Sₙ₁ reaction.

**9.26** When 3-ethyl-3-pentanol is treated with excess chloride, no substitution reaction is observed, because hydroxide is a bad leaving group. If you wanted to force an Sₙ₁ reaction, using 3-ethyl-3-pentanol as the substrate, what reagent would you use to change the leaving group into a better leaving group and provide chloride ions at the same time?
Common solvents used in organic chemistry (for now, only focus on the highlighted):

**Solvents**

**Polar Aprotic Solvents**
common uses: for $S_{N2}$ reactions

- DMSO: Dimethyl sulfoxide
- DMF: N,N-Dimethylformamide
- HMPA: Hexamethylphosphoramide
- Acetonitrile

**Chlorinated Solvents**
common uses: free radical reactions, halogenation reactions

- $\text{CCl}_4$: Carbon tetrachloride
- $\text{CHCl}_3$: Chloroform
- $\text{CH}_2\text{Cl}_2$: Dichloromethane (Methylene chloride)

**Ethers**
common uses: Grignard reactions, reactions of organolithiums

- THF: Tetrahydrofuran
- "Ether": Diethyl ether
- DME: Dimethoxymethane

**Polar protic solvents**
common uses: $S_{N1}$ and $E_1$ reactions, reactions involving acids and bases

- $\text{H}_2\text{O}$: Water
- MeOH: Methanol
- EtOH: Ethanol
- i-PrOH: isopropanol
- t-BuOH: t-butanol
- AcOH: Acetic acid

**Hydrocarbon solvents**

- Benzene
- Toluene (methylbenzene)
- n-Hexane
- Pentane

**EXERCISE 9.27** Predict whether the reaction below will occur via an $S_{N2}$ or an $S_{N1}$ mechanism:

![Reaction Diagram](image)

**Answer** This reaction utilizes DMSO, which is a polar aprotic solvent, so we expect an $S_{N2}$ reaction even though the substrate is secondary.
Using all four factors:

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Nucleophile</th>
<th>Leaving group</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°—Only S_N2,</td>
<td>Strong—S_N2</td>
<td>Bad—Neither</td>
<td>Polar aprotic—S_N2</td>
</tr>
<tr>
<td>No S_N1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2°—Both</td>
<td>Both</td>
<td>Good—Both</td>
<td>(but more S_N2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3°—Only S_N1,</td>
<td>Weak—S_N1</td>
<td>Excellent—S_N1</td>
<td></td>
</tr>
<tr>
<td>No S_N2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**EXERCISE 9.29** For the reaction below, look at all of the reagents and conditions, and determine if the reaction will proceed via an S_N2 or an S_N1, or both or neither.

![Chemical structure](attachment:chemical_structure.png)

**Answer** The substrate is primary, which immediately tells us that it needs to be S_N2. On top of that, we see that we have a strong nucleophile, which also favors S_N2. The LG is good, which doesn’t tell us much. The solvent is not indicated. So, taking everything into account, we predict that the reaction follows an S_N2 mechanism.
PROBLEMS  For each reaction below, look at all of the reagents and conditions, and determine if the reaction will proceed via an S_{N}2 or an S_{N}1, or both or neither.

9.30

\begin{align*}
\text{Cl} & \xrightarrow{\text{HO}^\ominus} \xrightarrow{\text{DME}} \\
\end{align*}

9.31

\begin{align*}
\text{Cl} & \xrightarrow{\text{H}_2\text{O}} \\
\end{align*}

9.32

\begin{align*}
\text{O} & \xrightarrow{\text{H}^\ominus\text{-Br}} \\
\end{align*}

9.33

\begin{align*}
\text{OR} & \xrightarrow{\text{H}_2\text{O}} \\
\end{align*}

9.34

\begin{align*}
\text{Br} & \xrightarrow{\text{Cl}^\ominus} \xrightarrow{\text{DMSO}} \\
\end{align*}

9.35

\begin{align*}
\text{O} & \xrightarrow{\text{ROH}} \\
\end{align*}
Chapter 9

9.2] Both
9.3] $S_{N2}$
9.4] Both
9.5] $S_{N1}$
9.7] No
9.8] Yes
9.9] No
9.10] Yes
9.12] $S_{N2}$
9.13] $S_{N1}$
9.14] $S_{N1}$
9.15] $S_{N2}$
9.16] $S_{N2}$
9.17] $S_{N2}$
9.19] mesylate
9.20] iodide
9.21] tosylate
9.22] chloride
9.23] bromide
9.24] bromide
9.25] 3-iodo-3-methylpentane
9.26] Use HCl to protonate OH and turn it into an excellent LG
9.30] $S_{N2}$
9.31] $S_{N1}$
9.32] $S_{N1}$
9.33] Neither
9.34] $S_{N2}$
9.35] $S_{N1}$