Is it \( S_N2 \) or \( S_N1 \)? Or \( E2 \)? Or \( E1 \)?

(“Basic” Generalizations)

<table>
<thead>
<tr>
<th></th>
<th>( S_N2 )</th>
<th>( S_N1 )</th>
<th>( E2 )</th>
<th>( E1 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl</td>
<td>Always</td>
<td>Never</td>
<td>Never</td>
<td>Never</td>
</tr>
<tr>
<td>Primary</td>
<td>Fastest</td>
<td>Slowest</td>
<td>--Depends--</td>
<td>Slowest</td>
</tr>
<tr>
<td>Secondary</td>
<td>--Depends--</td>
<td>--Depends--</td>
<td>--Depends--</td>
<td>--Depends--</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Slowest</td>
<td>Fastest</td>
<td>Fastest</td>
<td>Fastest</td>
</tr>
</tbody>
</table>

On \( R—X \) unhindered primary systems:
- \( S_N2 \) reactions occur with good nucleophiles.
- \( S_N2 \) reactions occur with strong bases.
- \( E2 \) reactions occur with hindered bases (potassium t-butoxide, LDA).
- No reaction occurs with poor nucleophiles.

On \( R—X \) branched primary systems:
- \( S_N2 \) reactions occur with good nucleophiles but are slower than in unbranched systems.
- \( E2 \) reactions occur with strong bases.

On \( R—X \) secondary systems:
- \( S_N1 \) and \( E1 \) reactions occur in polar solvents in the presence of a poor nucleophile, where \( X \) is also a good leaving group.

On \( R—X \) tertiary systems:
- \( E2 \) reactions occur with strong bases.
- \( S_N1 \) and \( E1 \) reactions occur with a non-basic nucleophile.

Strong Nucleophiles

- \( \text{NH}_2^- \)
- \( \text{SH}^- \)
- \( \text{OH}^- \)
- \( \text{CN}^- \)
- RO-
- “R”

Moderate Nucleophiles

- \( \text{NH}_3 \)
- \( \text{CH}_3\text{COO}^- \)
- \( \text{NO}_2^- \)
- \( \text{N}_3^- \)

Weak Nucleophiles

- \( \text{Br}^- \)
- \( \text{Cl}^- \)
- \( \text{I}^- \)
- \( \text{F}^- \)
- \( \text{H}_2\text{O} \)
- ROH

Other things being equal, stronger bases are generally better nucleophiles.

A \( \beta \)-methyl has a greater steric effect than a \( \gamma \)-methyl in \( S_N2 \) reactions.

The reactivity of anions in protic solvents is diminished by hydrogen bonding.

Other things being equal, the more polarizable reagent (read “bigger”) is the better nucleophile.

Neopentyl-type systems are exceptionally slow in \( S_N2 \) reactions because of sterics.

Stronger bases make poorer leaving groups.

The order of reactivity for hydrogens in \( E2 \) reactions is \( 3^\circ > 2^\circ > 1^\circ > \text{Methyl} \).

Life is short… play hard.
Basicity increases as one goes up a column of the periodic table (OH\textsuperscript{-} > SH\textsuperscript{-} and F\textsuperscript{-} > Cl\textsuperscript{-}). Ionic radii increase as one goes down a column of the periodic table.

In aprotic solvents, nucleophilicity is based on basicity. More potent nucleophiles in aprotic solvents are found at the top of the periodic table.

In protic solvents, nucleophilicity is based on ionic size. More potent nucleophiles in protic solvents are larger ones.

Sn2 reactions occur fastest for unhindered substrates... methyl electrophiles react fastest. Tertiary substrates are quite unreactive by the Sn2 mechanism. Branching may also hinder Sn2 reactions.

Intramolecular Sn2 reactions can occur when both a good nucleophile and leaving group are contained within the same molecule. These types of reactions are best when 3, 5, and 6 membered rings are produced as the final products.

Carbocation rearrangements are preferred if the product carbocation is more stable than the initial carbocation. These processes occur by way of hydride or alkyl shifts.

Poor leaving groups can often be converted to better leaving groups by protonation (simply put, the addition of H\textsuperscript{+}).

Elimination reactions are preferred at higher temperatures whenever a fairly hindered substrate is in the presence of a strong base.

The stability of carbocations is as follows: Benzyl > Allyl > 3° > 2° > 1° > Methyl. As a result, the reactivity of electrophiles by the Sn1 pathway is identical.

Steric hindrance around a reaction center is as follows: Methyl < 1° < 2° < 3°. Tertiary carbons are the most hindered, methyl carbons the least. As a result, the reactivity of electrophiles by the Sn2 pathway is identical.