$S_N 1$ Reaction

Remember that a $3^\circ$ alkyl halide will not undergo a $S_N 2$ reaction.

The steric hindrance in the transition state is too high.

Energy Diagram for $S_N 2$ Reaction: $3^\circ$ versus $1^\circ$ substrate
If t-Butyl iodide is reacted with methanol, however, a substitution product is obtained:

This product does NOT proceed through a $S_{N}2$ reaction.

First proof is that the rate for the reaction does not depend on methanol concentration.

Occurs through a $S_{N}1$ reaction.
Substitution – Nucleophilic – Unimolecular (1)

\[ S_{N1} \]

- In a \( S_{N1} \) reaction the leaving group departs BEFORE a nucleophile attacks

For t-butyl iodide this generates a planar 3° carbocation
The carbocation can then react with solvent (or nucleophile) to generate the product

If solvent reacts (like the methanol as shown) the reaction is called a “solvolysis”
The Energy Diagram for a $S_N1$ Reaction therefore has an Intermediate - And is a two step reaction.
Why does a $S_N1$ Mechanism Occur?

- Whenever the potential energy of a reaction is disfavored for a $S_N2$ reaction the $S_N1$ mechanism becomes a possibility.
Rate Characteristics

The rate for a $S_N 1$ reaction is a first order reaction

$$\text{Rate} = k [\text{substrate}]$$

The first step is the rate determining step

The nucleophile is NOT involved in the rate determining step

Therefore the rate of a $S_N 1$ reaction is independent of nucleophile concentration (or nucleophile characteristics, e.g. strength)
What is Important for a $\text{S}_\text{N}1$ Reaction?

The primary factor concerning the rate of a $\text{S}_\text{N}1$ reaction is the stability of the cation formed.

If this structure is made more stable then the rate will be faster.
Remember that a Carbocation is an ELECTRON DEFICIENT Structure

Factors that stabilize electron deficient structures

- Number of substituents at carbocation site
  (due to inductive and hyperconjugation)
- Another way to stabilize an electron deficient center is through resonance
Other Factors in $S_N1$ Reactions

Leaving group ability

Same factors as already seen in $S_N2$ reactions

Want polarizable group
Need a leaving group that departs as a weak base
Solvent Polarity

In a typical $S_{N}1$ reaction, the starting material is neutral and the transition state has partial charges developing and the intermediate has a formal positive charge.

Remember that anything that can stabilize the transition state relative to the starting material will cause a lower $E_a$ and a faster rate.

Therefore when the solvent is more polar the transition state will be stabilized.
Solvent with higher polarity will therefore increase the rate of a typical $S_N1$ reaction.

For the solvolysis of $t$-butyl iodide the rate in different solvents:

- Methanol ($H_3C-OH$) is more polar than ether ($H_3C-OCH_3$).
- Acetone ($H_3C-CO-CH_3$) is more polar than hexanes.
Comparison with $S_N2$ reaction

Compare the reaction coordinate for a $S_N1$ reaction with a $S_N2$ reaction

In a typical $S_N2$ reaction, a negatively charged nucleophile reacts with a neutral starting material to generate a transition state with partial charges.

Both the starting materials and the transition state are negatively charged (can change depending on what nucleophile and substrate are used).
- Due to planar intermediate in $S_N1$ reaction, the reaction is NOT stereospecific.
Often obtain racemic mixtures with $S_N1$ reaction

- Sometimes there is a higher fraction of inversion than retention

This is due to the leaving group “blocking” approach for retention configuration
This is a dramatic difference between $S_N^2$ and $S_N^1$ reactions

$S_N^2$ reactions always give inversion of configuration at the reacting carbon
(therefore stereospecific reactions)

$S_N^1$ reactions are not stereospecific

- With no steric interference of the leaving group obtain a racemic mixture
- With steric interference of the leaving group obtain a preference for inversion compared to retention but still obtain both stereoisomers
Every $S_N1$ reaction observed so far has occurred at a $3^\circ$ site

What happens during $S_N1$ reactions at $2^\circ$ or $1^\circ$ sites?

![Chemical reaction diagram]

Solvolysis of $2^\circ$ and $1^\circ$ halides often proceed to substitution with a different carbon framework
The major product is due to a rearranged structure (called a REARRANGEMENT)

Called a hydride shift

Why does the hydride shift?

Forms a more stable carbocation (3° instead of 2°)

Rearrangement will not occur to a less stable structure!
What about 1° Sites?

Typically a 1° alkyl halide will undergo a $S_N2$ reaction.

We learned in $S_N2$ discussion though that when a quarternary carbon is adjacent to the electrophilic carbon, the $S_N2$ reaction is extremely slow due to steric effects.

The halide could leave in a $S_N1$ mechanism but this would generate a 1° carbocation.

In general, a 1° carbocation does not form due to high energy.
Instead a Rearrangement occurs during the reaction

Called a methyl shift

Due to this methyl shift occurring while the leaving group departs only the rearranged products are observed in these $S_N1$ reactions with quarternary carbons adjacent to reaction site
Eliminations
A third option with alkyl halide reactions

An elimination is when the halide and another atom (typically a hydrogen) leave the molecule and no new atoms are added

- Two species have therefore been eliminated

An elimination results in the formation of a new $\pi$ bond
There are two versions of an elimination reaction: E1 and E2

E1: Elimination, Unimolecular

This mechanism is similar to the $S_{N}1$ mechanism
The leaving group departs in the rate determining step to generate a carbocation

A base then abstracts a hydrogen from a carbon ADJACENT to the carbocation to form a new $\pi$ bond
Realize an $S_N$1 and $E_1$ Mechanisms have the same form for an Energy Diagram

Rate $= k$ [substrate]
The carbocation formed in a E1 mechanism can still rearrange (any cation generated in any mechanism has the possibility of rearrangements)
Why is there a preference for one product in the preceding example?

Zaitsev rule:
“in elimination reactions the most highly substituted alkene predominates”
(sometimes translated as “Saytzeff” rule)

Why?
The stability of a double bond increases with more alkyl substituents

Therefore a more stable product is formed when the alkene with more alkyl substituents is obtained
One way to guarantee cation formation is to react an alkyl halide with AgNO$_3$.

Causes the formation of a silver salt (which crystallizes out of solution).

A convenient way to study carbocation reactions and rearrangements (i.e. $S_N1$ and $E1$).
Eliminations can also occur in a single step

E2: Elimination, Bimolecular

Rate = \( k \) [substrate][base]

One step reaction, but bimolecular!

The base abstracts a hydrogen on an ADJACENT carbon to leaving group in a single step
E2 reactions require a strong base

As seen by the rate equation, the properties and concentration of the base will affect the reaction

Similarity to $S_{N2}$:
Both are bimolecular and are affected by the substrate and base (or nucleophile)

The difference is the reactivity of the substrate

$S_{N2}$: \[1^\circ > 2^\circ > 3^\circ\]
E2: \[3^\circ > 2^\circ > 1^\circ\]
The strong base (which can also react as a nucleophile) has too much steric hindrance to react at a 3° site for a $S_{N2}$ mechanism.

The 3° halide therefore prefers an E2 mechanism.

In addition, the E2 mechanism also follows Zaitsev’s rule.
Stereochemistry of E2 Reaction

There are only two possible orientations for the E2 reaction.

The C-H, C-C and the C-Br bond must be coplanar to allow a concerted elimination (all bonds being broken or formed in reaction must be in the same plane).
The anti-coplanar arrangement is preferred

Due to lower nonbonded interactions

Consider Newman projections looking down the carbon-carbon bond that will form the alkene

anti-coplanar  syn-coplanar
This causes the E2 mechanism to be stereospecific

- High preference for anti-coplanar arrangement
E2 type reactions can also occur with adjacent dibromo compounds

When iodide is reacted with a 1,2-dibromo compound elimination occurs

This reaction is concerted (therefore bonds must be coplanar) and preferentially occurs through anti-coplanar conformation
Cyclohexane Conformations

Cyclohexane prefers the chair conformation

Adjacent substituents in the chair are only in an anti-coplanar arrangement if they are both in axial positions