Cationic Rearrangements

When a $S_N1$ reaction occurs, carbocations are formed as intermediate structures.

Once a carbocation is formed, rearrangements can subsequently occur.

Rearrangements are driven by thermodynamics, only a more stable carbocation will be generated by the rearrangement.

The more stable carbocation can then react to form the $S_N1$ product.
Cationic Rearrangements

Rearrangements are known to occur by migrating a hydrogen, alkyl groups, or aryl groups (when an alkyl or aryl group migrates, it is called a Wagner-Meerwein shift)

A 1,2 shift is the most common type of rearrangement

In order to allow a rearrangement to occur, the bonding orbital of the migrating group needs to be coplanar with the carbocation orbital

Newman projection

Only in this conformer is hydrogen aligned with empty p orbital

The orbital of the C-H bond must be aligned with the empty p orbital to allow a rearrangement to occur
Cationic Rearrangements

Rearrangements only occur with cations, not with anions or radicals

Process occurs with an orbital on an adjacent atom interacting with the empty p orbital of the carbocation

Consider the orbital interactions for the transition state for this process

In a cation rearrangement, 2 electrons are involved in a bonding molecular orbital
In a radical or anion rearrangement, additional electrons would be placed in antibonding molecular orbitals (therefore a less stable process)
Cationic Rearrangements

Carbocations are generally unstable species so therefore they are intermediate structures, not final products.

After generation and possible rearrangements, the carbocations must react to form a stable product.

Two of the common pathways for the carbocation to react is either reacting with a base to form an E1 product, or to react with a nucleophile to form an S_N1 product.
Cationic Rearrangements

A third possibility to form products in carbocation reactions is to form a strong bond after the formation of the carbocation.

This is the energetic driving force in pinacol rearrangements:

In a pinacol rearrangement, the driving force is the formation of a strong carbonyl C=O bond after Wagner-Meerwein shift (even though there was already a $3^\circ$ cation before the shift).

Any reaction with a vicinal diol in acidic conditions is called a “Pinacol Rearrangement” after the common name for the parent vicinal diol shown.
Neighboring Group Participation

Instead of having a shift to form a new carbocation, a group can aid in the leaving of a neighboring group before a carbocation is formed.

This effect is called “Neighboring Group Participation” (NGP).

Neighboring group participation can occur from any group that possesses an unshared pair of electrons or a double bond, the electron density will accelerate the rate for a leaving group to depart.

Consider the solvolysis of two cis/trans isomers:

There are two differences with these isomers:

- Retention
- Inversion
Neighboring Group Participation

The trans isomer has a faster rate and retention of stereochemistry due to NGP

Only the trans isomer allows the acetate group to aid in leaving group (electron density stabilizes cation)  

The NGP also forces the nucleophile to attack backside to stabilized structure to yield product with retention

The NGP for this reaction was also shown when reaction was run in ethanol the intermediate was trapped and structure was identified
Neighboring Group Participation

Any compound that has a potential nucleophilic substituent group placed favorably for back-side attack can display NGP (and thus rate enhancement)

Consider the solvolysis reaction of cyclooctane compounds with a halide leaving group

Compare rate of solvolysis with analogs that contain an oxygen in the ring

\[ \text{\chem{X}} \quad \text{\chem{O}} - \text{\chem{X}} \quad \text{\chem{O}} - \text{\chem{X}} \quad \text{\chem{O}} - \text{\chem{X}} \]

\[ k_{\text{rel}} \]
Neighboring Group Participation

An aryl group can also provide assistance in NGP

\[
\begin{align*}
\text{Phenonium ion} \quad \text{Phenonium ion intermediate would suggest a rate enhancement for the solvolysis} \\
\text{and retention of configuration for the product}
\end{align*}
\]

What if the carbon atoms are not chiral, how would someone prove that the phenonium ion is present instead of S_N1 or S_N2?

\[
\begin{align*}
\text{Can use isotopically labeled starting material} \quad \text{The label will be scrambled with phenonium ion,} \\
\text{S_N1 or S_N2 give only one product}
\end{align*}
\]
Structure of Carbocations

We have already observed a variety of structures for carbocations which are used to explain the observed experimental results.

Possible continuum of structures

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\begin{align*}
\text{“Classical”} & \quad \text{“Nonclassical”} \\
\text{Carbocation with empty p orbital} & \quad \text{Bridging Group} \\
\text{Hyperconjugation} & \quad \text{Obtain a 3 center, 2 electron system} \\
\text{Electron density of neighboring C-H bond donates to carbocation} & \quad \text{Obtain symmetrical 3 center system, the C-H bond to each center is longer} \\
\text{C-H bond becomes longer, C-C bond becomes shorter} & \\
\end{align*}
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The actual carbocation structure could be on a continuum between these structures.

In the past, scientists would call the 3 coordinate carbocation “classical” and the bridging 3 center, 2 electron system “nonclassical”
Structure of Carbocations

The 3 center, 2 electron bridging structure is similar to structures already seen in neighboring group participation (look back at the phenonium ion for example)

Other structures have shown this behavior by using a \( \pi \) bond to assist in the displacement of a leaving group.
Structure of Carbocations

While the use of $\pi$ bonds or lone pairs of electrons to assist in a $S_N 1$ reaction falls under the general category of neighboring group participation, a similar process can also occur with $\sigma$ bonds to result in “nonclassical” cations.

Consider the solvolysis of a variety of cyclic alkyl chlorides

Structure of Carbocations

Winstein proposed the $\sigma$ bond aligned anti to the leaving group in exo-bornyl structure could aid in the leaving group departing

\[
\begin{array}{c}
\text{Cl} \\
\end{array} \xrightarrow{\text{EtOH}} \quad \begin{array}{c}
\text{EtOH} \\
\end{array} \quad \begin{array}{c}
\text{EtO} \\
\end{array} \quad \begin{array}{c}
\text{OEt} \\
\end{array}
\]

In exo, these two bonds are parallel

While the product would always give a retention of configuration, the products would be racemic starting from initial chiral starting material (observed experimentally)
Structure of Carbocations

The rate enhancement observed in these bicyclic systems has been observed in many cases where anchimeric assistance is possible with an aligned $\sigma$ bond*.

$$k_{rel}$$

An interesting stereochemical proof was obtained with the larger bicyclo[2.2.2]octyl brosylate

$$\text{Classical (achiral)}$$

$$\text{Nonclassical (chiral)}$$

Both products are chiral, must be nonclassical!

Under solvolysis either the classical or nonclassical cations can be formed.

With this compound, the classical cation would be achiral, while the nonclassical is chiral.


Structure of Carbocations

Typically the nonclassical cations are formed when 1) there is available electron density aligned to allow overlap (like a bond in norbornyl system) and 2) have an unstable cation.

Typically do not observe nonclassical behavior when there is a more stable cation (like a 3° cation for example).

Other systems where nonclassical cations have been observed:

\[
\text{EtOH} \quad \begin{array}{c}
\text{Adamantyl system} \\
\text{Cyclopropyl system}
\end{array}
\]

The cyclopropyl carbinyl cation is related to the “bent” bond model used to explain strained rings, the bent bonds of cyclopropane are similar to π bonds in alkenes and thus this electron density can stabilize adjacent carbocation.