Cationic Rearrangement Reactions

Carbocations are intermediates in many organic reactions, and wherever they appear structural rearrangement is a possibility. Introductory students are typically introduced to these rearrangements as undesired side-reactions in the course of SN1 or E1 reactions, or during acid-catalyzed addition reactions of alkenes. However, it should be noted that since these reactions can be understood and predicted, cationic rearrangements can be useful in their own right.

Carbocation stability

First of all, we have to establish and clarify a few points about carbocations and their energies. You likely have been taught that “primary cations are less stable than secondary cations which are less stable than tertiary cations” (or perhaps “tertiary cations are more stable than secondary cations which are more stable than primary cations”). However, it is essential to add the idea that these statements are true “all other things being equal”. We also must be clear that the phrase “more/less stable than” really refers to a comparison of relative potential energies.

We must be comparing isomeric cations in order for the primary/secondary/tertiary stability generalization to hold. We cannot meaningfully compare the potential energies of two cations that have different molecular formulas. The potential energy associated with a cationic structure cannot be summarized simply by considering the bonding around one carbon atom!

The 1,2-shift mechanism

The fundamental mechanistic process in these rearrangements is the 1,2-shift of a group adjacent to a carbocation.

Recall that a carbocation is a trigonal planar structure, with a vacant 2p orbital perpendicular to the plane of the carbon and its immediate substituents. A group R can migrate with its bonding electron pair to the positively-charged carbon if the C-R bond can align with the vacant 2p orbital. The transition state for this 1,2-shift is a 3-membered ring in which the migrating R-group is partially bonded to both of the carbons, and the positive charge is shared among all three atoms.

It is important to note that the migrating group does not dissociate from the cation during the rearrangement. It moves in a concerted fashion from one carbon to the other. This rearrangement is reversible in principle, but of course if the two carbocations have different energies, the position of equilibrium will favour the lower-energy isomer.

In simple structures it is most common to see -H or -CH\(_3\) groups migrate. These reactions are called hydride shifts or methyl shifts. In the first example below, neopentyl bromide is heated
in the highly polar environment created by the mixture of water and formic acid, leading to ionization. However, if the C-Br bond simply broke heterolytically, a high-energy primary carbocation would be produced. The 1,2-shift of a methyl group offers an alternative pathway that avoids forming this primary carbocation. In this situation, the expulsion of the leaving group and the 1,2-methyl shift are concerted, resulting in a much lower-energy tertiary carbocation that goes on to react in an $S_N1$ fashion with water.

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\begin{align*}
\text{Methyl shift during } S_N1 \text{ solvolysis of neopentyl bromide (1-bromo-2,2-dimethylpropane)} & \\
\text{Hydride shift during } S_N1 \text{ solvolysis of (1-bromoethyl)cyclohexane} & \\
\text{Methyl shift during addition of HBr to 3,3-dimethylbut-1-ene} & \\
\text{Methyl shift during acid-catalyzed dehydration of 3,3-dimethyl-2-butanol} & \\
\text{Hydride shift during acid-catalyzed addition of water to 3-methylbut-1-ene} & 
\end{align*}
\]

In the other examples, a secondary carbocation is formed initially but it is subsequently transformed into a tertiary carbocation by migration either of a hydrogen or a methyl with its bonding electron pair. The final product is determined by the structure of this rearranged carbocation.

**Rearrangements driven by strain**

The idea of “strain” in organic chemistry is often a point of confusion for students. In introductory organic chemistry strain is usually encountered when dealing with small ring structures. The way chemists think about structural strain is to implicitly assume that there is some “perfect” structure for a given molecular formula, in which every bond has its ideal length (1.54 Å for a $C_{sp3}$-$C_{sp3}$ bond), every bond angle has its ideal value (109.5° for a tetrahedral
atom), every dihedral is perfectly staggered, and no atoms are in close van der Waals’ contact. Of course this hypothetical structure does not exist, but when we look at a real structure we are essentially comparing it to this ideal standard and interpreting deviations from the ideal as imparting strain on the structure. Strain is thus the hypothetical difference in potential energy between the imaginary ideal structure and the real structure.

In the case of cyclic hydrocarbons, you probably learned that experimental evidence for ring strain can be obtained from heat of combustion measurements. If you don’t recall, consult the Klein textbook, sections 4.4 and 4.9 and especially Table 4.7 and Figure 4.18 on page 164. We observed that 3-membered rings are highly strained, 4-membered are somewhat less strained, while 5- and 6-membered rings have essentially no strain. Rings consisting of between 7 and 11 members all are more strained than the 5- and 6-membered rings, but not as much as the smaller rings.

Strain can be an important driving force behind structural rearrangement. Consider the following example:

Clearly there has been a substantial change in the connections among the carbon atoms during this reaction, and this suggests a rearrangement process. We recognize that the 4-membered ring in the starting material embodies considerable strain that can be released if the ring can be converted to a 5-membered structure. This release of strain energy can provide the impetus for the overall reaction, but the starting alcohol does not spontaneously react on its own. Only if the OH group is protonated can the reaction proceed.

In this case, not only does the 1,2-shift relieve the strain inherent in the 4-membered ring, but it avoids the formation of a high-energy primary carbocation, forming the secondary ion instead.

The release of ring strain is important in the reactions of many bicyclic compounds, and students are sometimes puzzled to see mechanistic steps in which tertiary carbocation intermediates are apparently converted to secondary carbocations. For example, when alpha-pinene is treated with HCl in dichloromethane, the following rearrangement occurs:

The rearrangement is perhaps easier to understand if we re-draw the compounds in perspective views and show the mechanistic steps:
In the first step, the alkene is protonated (note that HCl does not dissociate in lower-polarity solvents like CH₂Cl₂). The tertiary cation A does not undergo attack by chloride because it rapidly rearranges to secondary cation B. This is strongly favoured because A contains a strained 4-membered ring, and rearrangement releases this strain energy. Thus, even though B is a secondary cation, it is lower in energy than tertiary cation A. The reaction then proceeds with chloride ion attacking B from the “bottom” face to give the product.

Sometimes these rearrangements can be very complex, involving many distinct steps in which several different groups undergo 1,2-shifts or even shift over longer distances. As an illustration, the biosynthesis of lanosterol (a precursor of cholesterol) in animals ends with a concerted set of cation-induced 1,2-hydride and 1,2-methyl shifts that occur in the active site of the enzyme lanosterol synthase, as shown below:

However, in this course you will not encounter anything more complicated than the conversion of α-pinene to bornyl chloride shown above. For beginning students it is difficult to predict when a rearrangement will occur, and you will not be asked to do this type of problem on tests. However, given a reactant, conditions and product for a rearrangement you should be able to supply a reasonable mechanism involving three to five steps.