

## Ionic Substitution – S<sub>N</sub>1

Note: all information, example problems, and graphics taken from lecture, Chemistry 14D Thinkbook for Winter 2005, and *Organic Chemistry* by Paula Yurkanis Bruice, 4<sup>th</sup> ed.

What does S<sub>N</sub>1 stand for? S for a substitution reaction, N for nucleophilic, and the 1 for unimolecular, meaning that the rate is dependent upon one factor.

S<sub>N</sub>1 is a mechanism pathway very similar to S<sub>N</sub>2. First, let's briefly review S<sub>N</sub>2: (S<sub>N</sub>2 is substitution, nucleophilic, bimolecular)

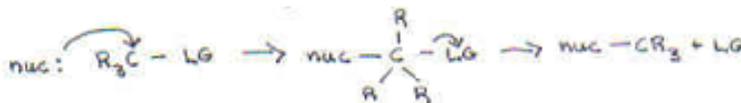
In S<sub>N</sub>2, the general mechanism is:



The nucleophile “attacks” the electrophile from the backside, expelling a leaving group. Recall that S<sub>N</sub>2 is a concerted reaction, which means all the bond change events takes place at the same time.

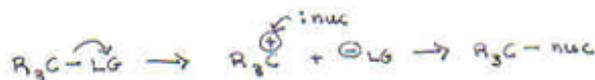
Now, let's try making the reaction occur in two steps.

What if nucleophilic attack occurred in the first step, creating a CR<sub>3</sub> – nucleophile – leaving group intermediate, and then the leaving group was expelled in the second step? It would look like this (“nuc” stands for nucleophile):



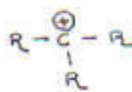
This would absolutely not occur!! It would create a pentavalent carbon.

So let's try another approach. What if the leaving group left in the first step, and in the second step, the nucleophile attacked? It would look like this:



Here, the leaving group leaves, creating a positive charge on the carbon. The nucleophile attacks at this site of positive charge. This mechanism seems plausible; no rules are violated.

It turns out that this intermediate structure, with a positive charge on carbon, is crucial to the S<sub>N</sub>1 mechanism.



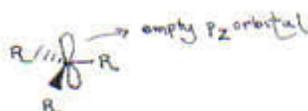
This is called a **carbocation** because it is a combination of a carbon and a cation. Carbocations have **incomplete octets**, so there is a **formal positive charge on the carbon**. This positive charge makes carbocations **unstable**, so carbocations are **very reactive**. Thus carbocations **react in a way that will complete the open octet**.

Let's address the issue of carbocations before proceeding further with the  $S_N1$  mechanism.

### Carbocations:

- **General Structure**

Carbocations are  $sp^2$  hybridized, which means that they are in a planar arrangement.



The  $p_z$  orbital is empty, so you can think of the positive charge as located here.

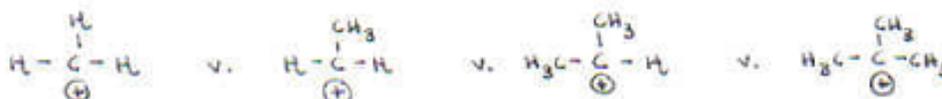
- **Stability**

The stability of a carbocation depends on two factors:

- number of substituents
- resonance

First, we'll look at the number of substituents:

(Remember: the positive charge and open octet on the carbon make carbocations unstable) Let's look at an example:



Methyl carbocation

primary

secondary

tertiary

Alkyl groups are **weakly electron donating**. So in the above example, the more  $CH_3$  groups there are, the more electron density can be donated to carbon. This added electron density somewhat reduces the electron deficiency on the carbon, reducing the magnitude of the positive charge, and making the carbocation more stable. Following the above reasoning, **methyl carbocations are so unstable that we usually will not encounter them**.

Generalizing the above analysis, we can rank from least stable to most stable carbocation:



Methyl

primary

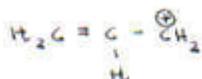
secondary

tertiary

Now let's consider resonance:



In this example, the lone pairs of the pi bond can re-form the pi bond between the C + and adjacent C. This creates a resonance contributor. **The two resonance contributors together delocalize the positive charge by spreading it between the two carbons.** This stabilizes the carbocation.



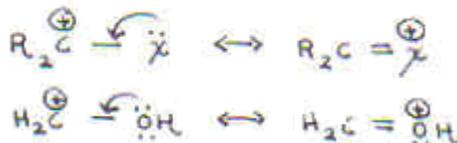
Allyl carbocation



benzyl carbocation

- allyl and benzyl carbocations have a lot of stability. The allyl carbocation has resonance structures because of the pi bond, and the benzyl carbocation is even more stable because of resonance involving the attached benzene group.

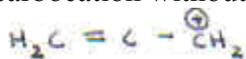
Resonance can also occur if an atom attached to the carbocation has lone pairs. The lone pairs move from the attached group, X, to the single bond between X and C, creating a double bond. This creates an electron deficiency on X, moving the positive charge to X. Again, this spreads out the positive charge over two molecules, increasing the stability of the carbocation.



For example:

The most electronegative atom, oxygen, has a positive charge in the second resonance contributor. This would normally destabilize the molecule (the positive charge should be on the least electronegative atom). However, all the atoms have full octets, so resonance does stabilize the molecule.

**Between degree of substitution and resonance, resonance is usually more important.** For example, a primary carbocation with resonance is more stable than a secondary carbocation without resonance.

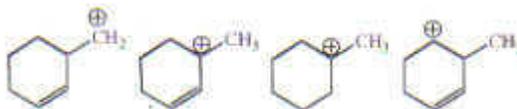


primary with resonance



secondary without resonance

Let's try an example: Choose the most stable carbocation.



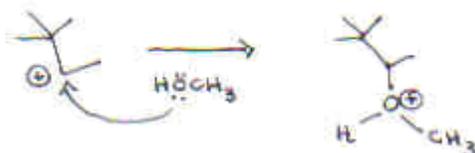
primary tertiary w/ res tertiary secondary

Tertiary, the most stable arrangement of substituents, with resonance is the most stable.

- **The Three Fates of a Carbocation**

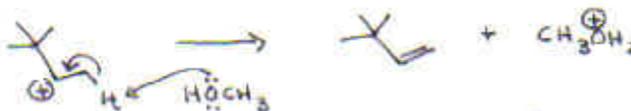
Again, remember that the driving force for carbocations to react arises from their open octet and positive charge, so they will react in a way that allows them to gain electrons. Generally, carbocations can react in three different ways. Let's look at an example to illustrate them.

1. *capture a nucleophile*



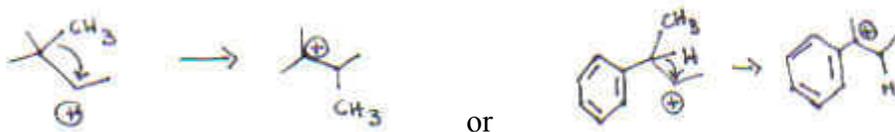
Here, the nucleophile, HOCH<sub>3</sub>, attaches to the carbon bearing the positive charge. This fills the open octet on carbon. However, now oxygen has three bonds, so it carries the positive charge. Again, the positive charge is now on the more electronegative atom, but all atoms have a full octet so this is a preferable arrangement.

2. *lose a proton to form a pi bond*



Here, the electrons on the O of HOCH<sub>3</sub> form a bond with a proton on the carbocation, pulling it away. The electrons of the former proton – carbon bond now go into making a pi bond next to the positively charged carbon. Now that carbon has four bonds, it has a complete octet, and the carbocation is stabilized. The positive charge has been transferred to CH<sub>3</sub>OH<sub>2</sub>. Note that carbocations are so reactive they are “desperate,” that is, they can be deprotonated by many molecules that are not particularly good nucleophiles, such as water.

3. *rearrangement*

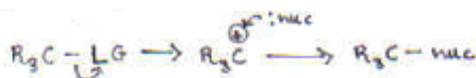


Whenever you see a carbocation, **always check to see if rearrangement is possible.** Carbocations will rearrange to improve stability, even though the positive charge and open octet will be retained. Any C – C or C – H bond next to the positively charged carbon can be moved. Here, the first carbocation goes from secondary to tertiary, and the second goes from secondary to tertiary with resonance; both increase in stability.

*Carbocations are very unselective. They often can undergo more than one of these fates, and if you see carbocations involved in a reaction, you may get different products.*

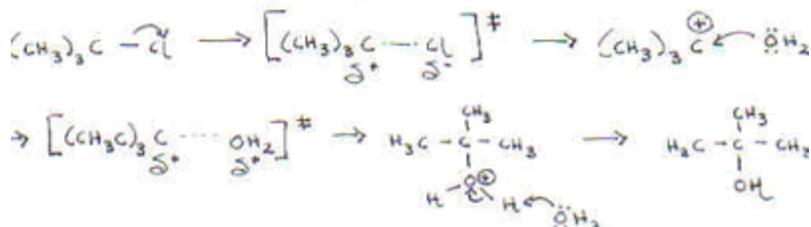
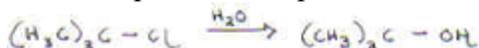
Now we are ready to present the general mechanism for S<sub>N</sub>1.

## Mechanism for S<sub>N</sub>1



This is a multi-step reaction; first the leaving group leaves, then the nucleophile attacks the carbocation and forms a bond.

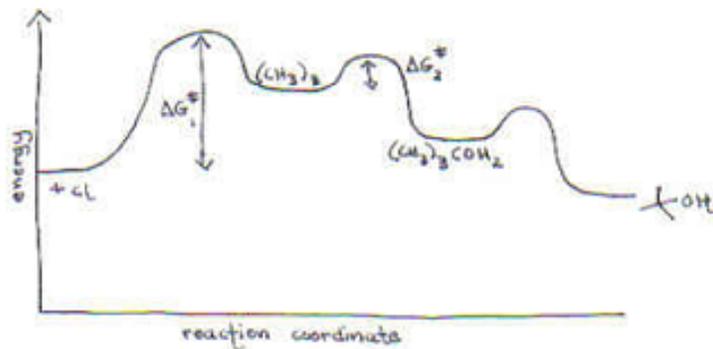
Here's a specific example:



Cl, the leaving group, leaves. The transition state shows the partial bond between C and Cl as it leaves. Water attacks the carbocation that was formed. Again, the transition state shows the water attacking in a partial bond with C. Once water attaches, the O has a positive charge, so water must protonate it.

The first step, the leaving group step, is energetically expensive because a bond is lost. Nucleophilic attack is energetically productive because it gains a bond.

Take a look at the energy diagram. The larger  $\Delta G_1^{\ddagger}$  is, the larger the energy of activation. This slows down the reaction. Here, it's so slow that it determines the rate of the reaction, so it is called the **rate determining step**. All subsequent steps happen much more quickly in comparison.

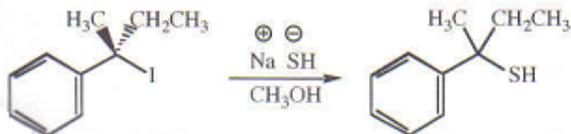


For S<sub>N</sub>1, rate is proportional to [ R<sub>3</sub>C - LG ]

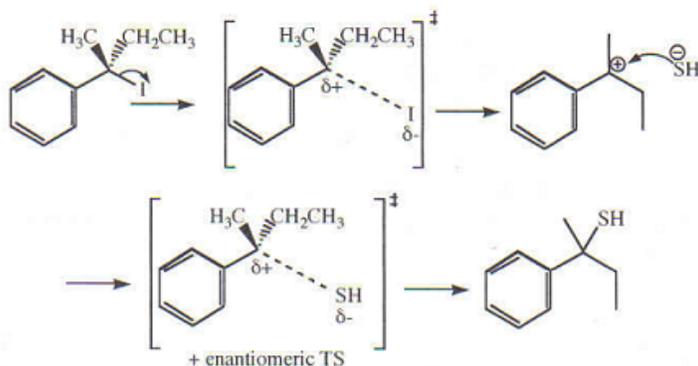
Remember that although carbocation capture of a nucleophile is important for S<sub>N</sub>1, there are other steps that occur as well.

*Example Problems:*

1. Draw the mechanism



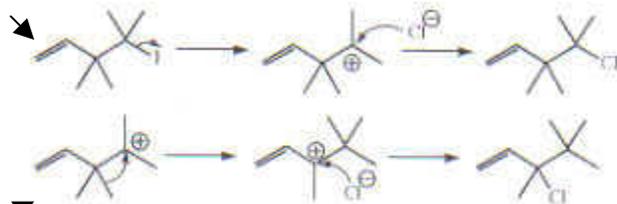
Start with the ejection of the leaving group, I. This leads to the transition state, with a partial bond between the C and I. The carbocation forms, and nucleophilic attack by –SH occurs. Again, the transition state shows a partial bond between the carbon and incoming nucleophile. Lastly, the nucleophile attaches.



2. Draw the mechanism that will produce both products



For the first product, I leaves, the carbocation forms, and Cl attacks.



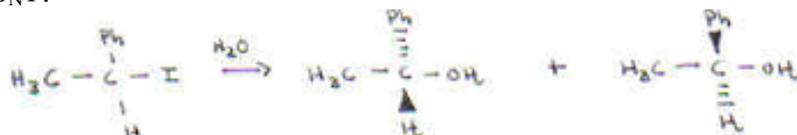
For the second product, the carbocation rearranges first. A C - H group shifts. This creates a tertiary carbocation with resonance instead of the original tertiary carbocation without resonance. This increases stability first. Then nucleophilic attack occurs as normal.

### Variables that affect the Rate of an S<sub>N</sub>1 Reaction

- Stereochemistry

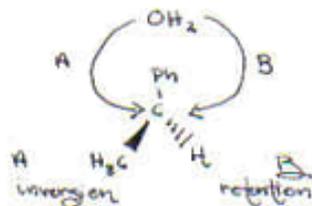
Remember that inversion of stereochemistry is associated with S<sub>N</sub>2.

What about S<sub>N</sub>1?



In S<sub>N</sub>1, you get two different products, one with retention and one with the inversion of stereochemistry. We may say that we get a racemic mixture in S<sub>N</sub>1, which means that

there are equal amounts of the two enantiomers. However, this is a simplified way of looking at it. In the  $S_N1$  reaction, the leaving group actually gets in the way of the nucleophile. If the nucleophile attacks on the leaving group side (B, which will result in retention of stereochemistry), its path will be slightly blocked. So attack opposite the leaving group (A, resulting in inversion) is the preference, and the ratio of the enantiomers is usually not purely equal. So, we can just say that we get a “mixture” of enantiomers in  $S_N1$ .



- Nucleophile

In  $S_N2$ , a better nucleophile meant that the rate of reaction would increase. Why? Because the rate expression for  $S_N2$  is rate is proportional to  $[nuc][R_3C - LG]$ , meaning it depends on both nucleophilic attack and leaving group expulsion. A better nucleophile increases the rate of nucleophilic attack, which ultimately increases the rate of the reaction.

In  $S_N1$ , however, the rate law expression is rate is proportional to  $[R_3C - LG]$ , meaning it depends only on the leaving group expulsion. Thus a better nucleophile does not affect the rate of reaction.

- Leaving group

In  $S_N2$ , a better leaving group increase the rate of reaction.

In  $S_N1$ , a better leaving group also increases the rate of reaction. The reaction rate depends solely upon how fast the leaving group leaves.

- Substitution at the leaving group

For  $S_N2$ ,  $H_3C - LG > RCH_2 - LG > R_2CH - LG \gg \gg R_3C - LG$

This is because more substituted molecules inhibit nucleophilic attack through sterics.

For  $S_N1$ ,  $H_3C - LG < RCH_2 - LG < R_2CH - LG \ll \ll R_3C - LG$

This is because more substituted carbocations are more stable.

- Solvent

The nature of the solvent can affect the rate determining step. In  $S_N1$ , the rate determining step, the loss of a leaving group, is also called ionization.

The preferred solvent is polar.

A solvent with a high dielectric constant is polar. This increases the rate of reaction. (A high dielectric constant means the solvent has a high ability to separate opposite charges) This stabilizes the charges in the transition state, which lowers the energy of activation, and speeds up the rate of the reaction.

*Methanol and water are very polar solvents.*

Hydrogen bonding, and thus, the protic or aprotic aspect of a solvent is not very important here.



In this example, the carbocation is shown as reacted with I<sup>-</sup>. However, there is much more solvent than I<sup>-</sup>, so the probability that it would react with the solvent is greater. Usually, the solvent would act as the nucleophile.

*Example Problem: Which reaction proceeds slower?*



Nucleophile, solvent, and leaving group are all the same for these two reactions. The only difference is the substitution at the leaving group site. The first reaction will form a methyl carbocation and the second will form a tertiary carbocation. The first is much less stable so it will react more slowly.

### A "Reasonable" S<sub>N</sub>1 Reaction

Remember, the rate determining step is the  $[TS]^\ddagger$  of  $[R_3C \cdots LG]^\ddagger$

There are three factors that make a reasonable reaction:

1. a moderate or better leaving group
2. a "stable" carbocation – here, a primary without resonance probably would not work, but a primary with resonance would
3. a polar solvent

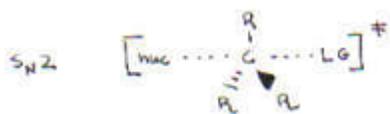
*Example:* Is an S<sub>N</sub>1 mechanism for this reaction a reasonable one?



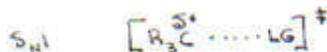
To check, there is a moderate leaving group, -Cl, a secondary carbocation, and a polar solvent, DMSO. This seems reasonable. The factors for a S<sub>N</sub>2, however, also seem reasonable. -Cl is a good leaving group, -Br is a moderate nucleophile, and DMSO is a polar aprotic solvent. Since both seem reasonable, the actual mechanism would probably be a mixture of the two. For this class, however, we learn that S<sub>N</sub>2 is usually favored over S<sub>N</sub>1. Why?

### Comparing S<sub>N</sub>1 and S<sub>N</sub>2

Which one is favored? Let's compare the transition states:



v.

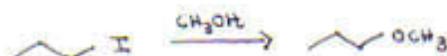


Here, you both make a bond and lose one, so there's no net change in energy.

Here, you lose a bond, but you don't gain one, so this is more energetically expensive.

Because of this energy difference, if the three conditions (moderate nucleophile, leaving group, and non tertiary carbon) for a reasonable  $S_N2$  reaction are met, then  $S_N2$  will be favored over  $S_N1$ . If these conditions are not met, then  $S_N2$  will be the next best pathway.

For example,



Consider  $S_N2$  first. I is a good leaving group, and the molecule is not tertiary. Consider methanol as a nucleophile. The four factors are resonance, size, electronegativity, and inductive effect. Recall that nucleophile and leaving group can work in tandem; a worse nucleophile can be offset by a good leaving group. Here, there is no resonance, the size is small, which increases nucleophilicity because it is more driven to get rid of its charge, has high electronegativity, which decreases nucleophilicity because the molecule will not be willing to share electrons, and inductive effect does not matter here. Taking all these into account, the answer is somewhat ambiguous – methanol is in the moderate to not very good category of nucleophiles. So  $S_N2$  may be an acceptable mechanism.

Let's try  $S_N1$  to check. Remember that ruling out  $S_N2$  as a pathway does not necessarily mean accepting  $S_N1$ . Consider the three factors – leaving group, which is moderate, solvent, which is polar, but the carbocation is primary and highly unstable. This disfavors  $S_N1$ , so the mechanism is probably  $S_N2$ .

*Last example problem:*



Which reaction is faster? Then write a reaction that is even faster than the one selected.

First, you must decide that this is an  $S_N1$  reaction (it can't be  $S_N2$  because there's a tertiary carbon). The two reactions differ in the identity of the leaving group.  $(\text{CH}_3\text{SO}_3^-)$  is a very good leaving group because once it leaves, it can stabilize the extra negative charge through resonance (Cl cannot do this). This increases the rate of the second reaction. An even faster reaction might replace the leaving group with  $\text{CF}_3\text{SO}_3^-$  instead. This is an even better leaving group because the F atoms withdraw electron density from the oxygen atom. O can then accept extra negative charge to a greater extent than it could before.