S_N1 REACTIONS Answers document

Step-by-step discussions for each of these answers are available in the "S_N1 reactions" videos. You can find links to these resources at my website: <u>www.freelance-teacher.com</u>

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Answers begin on next page.

Video (1)

Problem (1a)

What is the most important factor in organic chemistry? Formal charges

What is the most important tool for predicting what will happen in a reaction? Formal charges

When you draw the products of a mechanism step, what is the most important part of the products to get right? The formal charges

Does nature "like" or "dislike" formal charges? Dislike

Does nature "prefer" atoms to be charged or neutral? Neutral

Does nature "prefer" formal charges to be big or small? Small

Which atoms are most likely to participate in a reaction? Usually, the atoms with formal charges

EXCEPTION: Metals with positive formal charges (such as Na⁺ or K⁺) are usually "spectator ions" which do *not* participate in the reaction.

Problem (1b)

Show the formal charges that we place at the beginning, middle, and end of a series of electron-pushing arrows.

The choices are "positive", "negative", and "neutral".



For a mechanism step that consists of a single electron-pushing arrow, show the formal charges that we place at the beginning and end of the electron-pushing arrow.



Problem (1c)

Define each of the following roles: nucleophile, electrophile, leaving group How do you draw the electron-pushing arrows for each of these roles? What are some clues that we can use to identify which atoms will play each of these roles?

Some of the above material was discussed at more length in the series on $S_N 2$ reactions.

The ideas above about neutral nucleophiles, and about positive formal charges, are discussed at more detail later in this video.

In this video we focus only on the roles "nucleophile", "electrophile", and "leaving group". We will discuss the roles "acid" and "base" in video (3) in this series.

Answers for Video (1)

Roles in Organic chemistry Nucleophile: Jonates electrons to join an electrophile Nu E Clues: O formal charge neutral atom with a lone pair (O, N, S, P) Exception: neutral Cl, Br, and I are not nucleophilic Electrophile: receives electrons to join a nucleophile Clues: O formal charge on a carbon (CD) St Leaving group: receives electrons to leave an atom atom CLG Clues: neutral Cl, Br, and I neutral sulfonates Other neutral atoms are usually not acceptable leaving groups.

Problem (1d) What types of neutral atoms can be used as nucleophiles? A neutral atom with a lone pair (typically O, N, S, or P) is nucleophilic.

Exception: neutral Cl, Br, and I are *not* nucleophilic, even though they have lone pairs. Instead, we use neutral Cl, Br, and I as good leaving groups.

Of course Cl⁻, Br⁻, and I⁻ *are* good nucleophiles, because of their negative formal charges. This illustrates that the most important factor in organic chemistry is formal charges. There is a big difference between neutral Cl, Br, and I (good leaving groups) and Cl⁻, Br⁻, and I⁻ (good nucleophiles)!

Answers for Video (1)

Roles in Organic chemistry Nucleophile: Jonates electrons to join an electrophile Nu E Clues: O formal charge neutral atom with a lone pair (O, N, S, P) Exception: neutral Cl, Br, and I are not nucleophilic Electrophile: receives electrons to join a nucleophile Clues: O formal charge on a carbon (C) St Leaving group: receives electrons to leave an atom atom CG Clues: neutral Cl, Br, and I neutral sulfonates Other neutral atoms are usually not acceptable leaving groups.

Problem (1e) What are the clues for an electrophile? Best clue: a *carbon* with a positive formal charge Another clue: an atom with a δ^+

What role does a metal with a positive formal charge play? Metals with positive formal charges (such as Na⁺) are usually unreactive spectator ions.

(We will discuss possible formal charges for acids and bases in a later video in this series.)

Video (2)

Problem (2a)

How many steps are there in an S_N^2 reaction? One step.

What happens during that one step? Simultaneously, in the same step: The nucleophile joins the α carbon, and the leaving group leaves the α carbon.

Define " α carbon". It is useful to define the term " α carbon" to refer to "the carbon connected to the leaving group". We will extend this definition later in the video.

How many steps are there in an $S_{\rm N} 1$ reaction? Two steps.

What happens during those two steps? Step one: The leaving group leaves the α carbon. Step two: The nucleophile joins the α carbon.

Problem (2b)



Since Na is a metal and Br is a nonmetal, we know that they have an ionic bond. Draw in formal charges to represent the ionic bond. We covered how to use ionic bonds to detect formal charges in more detail in the series on S_N2 reactions.

The Br⁻ is the nucleophile (clue: negative formal charge).

The neutral Cl is the leaving group (we have memorized that neutral Cl is a good leaving group).

Carbon 2 is the α carbon (attached to the leaving group).

The Na⁺ is an unreactive spectator ion (positive metals are unreactive spectators).

Do not *assume* the mechanism is $S_N 1!$ *Use the table* to determine the mechanism. The α carbon is tertiary (attached to three carbon chains), so we use the bottom row of the table. Our nucleophile is Br⁻, so we use the middle column of the table. The table predicts that the *major* mechanism in these conditions is $S_N 1$.

First step of the S_N1 mechanism: Leaving group (neutral Cl) leaves the α carbon.

Second step of S_N1 mechanism: Nucleophile (Br⁻) attacks the α carbon electrophile. Clue that carbon 2 will play the role of electrophile in step 2: it is a *carbon* with a positive formal charge.

		V		
		how to determine the mechanism for alkyl halides and alkyl sulfonates		
		poor Nu / weak base	good-Nu / weak base	good Nu / strong base
		O with no formal charge	Cl ⁻ ,(Br ⁻ ,)I ⁻ , ⁻ CN, S ⁻ , N ₃ ⁻	0.
		(water or alcohol)	or N, P, or S with no formal charge	
	methyl α-carbon	no reaction	S _N 2	S _N 2
	1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
	2° α-carbon	S _N 1 major,	S _N 2	E2
		E1 minor		
~	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
->		E1 minor	E1 minor	

1

solution to problem (2b) continued on next page

Problem (2b) continued



How many charges do you change on every step of every mechanism? On every step of every mechanism, change *two* charges.

How do you know which charges to change on each mechanism step. Change the charge on the atom that loses electrons at the *beginning* of the series of arrows, and the charge on the atom that gains electrons at the *end* of the series of arrows. THE MOST COMMON MISTAKE is forgetting to change the charge for the atom at the *beginning* of the series of arrows.

Examine the mechanism above to see how we correctly changed *two* charges for each mechanism step. For the first step, we changed the charges on the chlorine and on carbon 2. For the second step, we changed the charges for the Br and for carbon 2. Remember: **the most important part of the products of each mechanism step to draw correctly is the formal charges.**

How do you tell when a mechanism is finished?

The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism. Exception: the "main product" of an $S_N 2$ reaction can have a formal charge.

In the mechanism on the previous page, we can tell that step 1 is not the last step in the mechanism because the "main" product of that step has a positive formal charge (on carbon 2).

We can tell that step 2 *is* the last step in the mechanism because the "main" product has no formal charge.

How can we extend the definition of the term α carbon to be more helpful for $S_N 1$ reactions? α carbon: the carbon attached to the leaving group, or

the carbon with a positive formal charge

For the mechanism for this problem, for step 1, we treat carbon 2 as the α carbon because it is attached to the leaving group.

And for step 2 we continue to treat carbon 2 as the α carbon, because it is a carbon with a positive formal charge.

Checklist of things to do for the *first* step in a mechanism

1. Number *all* the carbons in the starting materials.

2. Draw formal charges for any ionic bonds.

3. *Label* which specific atoms will play which roles.

Identify the "clues" that tell you which atoms will play which roles.

4. Label the α -carbon.

Write down whether the α -carbon is methyl, 1°, 2°, or 3°.

5. Use the table to determine whether the reaction is $S_N 2$, $S_N 1$, E2, or E1.

Write down the name of the mechanism.

6. Draw electron-pushing arrows for a mechanism step.

Don't begin drawing the products for a mechanism step until you have finished drawing the electronpushing arrows for that step

7. Draw the products of the mechanism step

Number *all* the carbons in the products. Make sure your numbers for the products of a step are *consistent* with the numbers you used for the starting materials of the step.

8. Ask whether you have finished the mechanism, or require another mechanism step. The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism.

Exception: the "main product" of an S_N 2 reaction can have a formal charge.

Checklist of things to do for each step in a mechanism *after* the first step

1. Label which specific atoms will play which roles. Identify the "clues" that tell you which atoms will play which roles.

2. Draw electron-pushing arrows for the mechanism step.

Don't begin drawing the products for a mechanism step until you have finished drawing the electronpushing arrows for that step

3. Draw the products of the mechanism step

Number *all* the carbons in the products. Make sure your numbers for the products of a step are *consistent* with the numbers you used for the starting materials of the step.

4. Ask whether you have finished the mechanism, or require another mechanism step. The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism.

Exception: the "main product" of an $S_N 2$ reaction can have a formal charge.

Answers for Video (2)

S_N1 REACTIONS

Problem (2c)



Check to be sure you got the exact right formal charges for all starting materials, intermediates, and products.

	L					
	how to determine the mechanism for alkyl halides and alkyl sulfonates					
poor Nu / weak base good Nu / weak base good Nu / stro			good Nu / strong base			
		O with no formal charge	Cl ⁻ , Br ⁻ , (I ⁻ ,) ⁻ CN, S ⁻ , N ₃ ⁻	0.		
		(water or alcohol)	or N, P, or S with no formal charge			
	methyl α-carbon	no reaction	S _N 2	S _N 2		
	1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon		
	2° α-carbon	S _N 1 major,	S _N 2	E2		
		E1 minor				
	3° α-carbon	S _N 1 major,	(S _N 1 major,)	E2		
\rightarrow		E1 minor	E1 minor			

Don't *assume* the mechanism is $S_N 1!$ Use the table, as shown below.

Notice that the arrows in our mechanism above are consistent with the rules about formal charges that we learned in the first video in this series.

The atom at the beginning of the series of arrows should always be negative or neutral, never positive. In the first step of our mechanism above, the atom that loses electrons from the arrow (carbon 2) is



neutral. In the second step, the atom at the beginning of the arrow (I^{-}) is negative.

The atom at the end of the series of arrows should always be positive or neutral, never negative. In the first step of our mechanism above, the atom at the end of the arrow (Br) is neutral. In the second step, the atom at the end of the arrow (carbon 2) is positive.

Answers for Video (2)

Problem (2d)

In the term " S_N 1," what does the "S" stand for?

"S" stands for substitution, because, in an $S_N 1$ mechanism, one thing substitutes for something else. For example, in the previous problem, the iodine substitutes into the position formerly occupied by the bromine.

In the term " S_N 1," what does the "N" stand for?

"N" stands for *n*ucleophilic, because, in an $S_N 1$ mechanism, the thing that substitutes into the position formerly occupied by the other thing is a nucleophile. For example, in the previous problem, the thing that substitutes into the position previously occupied by the bromine is the iodide *nucleophile*.

$S_N 1$ REACTIONS

Problem (2e) (Review problem)

How many steps are there in an $S_{\rm N} 1$ reaction? Two steps.

What happens during those two steps? Step one: The leaving group leaves the α carbon. Step two: The nucleophile joins the α carbon.

Video (3)

ACID-BASE STEPS

Most S_N1 mechanisms include an *acid-base step*.

In this video, we will learn how to draw the general mechanism for an acid base step.

Then, in the next video, we will learn how to draw an $S_N 1$ mechanism that includes an acid-base

step.

Problem (3a)

Define these roles: base, acid A *base* donates electrons to take a H^+ from an acid. (H^+ = "proton")

An *acid* receives electrons to give a H^+ to a base.

Problem (3b) Draw the electron-pushing arrow for a base. Draw the electron-pushing arrow for an acid.



Problem (3c) How is a base similar to a nucleophile? They both *donate electrons*.

How is a base different from a nucleophile? A nucleophile *joins the electrophile,* while a base *takes a* H^+ *from an acid*

Verbally describe the first arrow for an acid-base step. The first arrow for an acid-base step points *from* the base and *toward* the proton.

$S_{\text{N}}1 \text{ REACTIONS}$

Problem (3d) What are the clues that indicate an atom can be a base? A negative formal charge. A neutral atom with a lone pair (usually O or N). For example, *water* and *alcohols* are bases.

What are the clues that indicate an atom can be an acid? An atom with a positive formal charge, and an attached H. (There are also neutral acids, but we won't need to deal with those in this video series.)

RISS

Anatom with a D formal charge and an attached H.

Problem (3e)



We use the oxygen attached to carbon 2 as the acid. Clue: it has a positive formal charge. We use the oxygen in the water as a base. Clue: It's a neutral atom with a lone pair.

Check the mechanism above to make sure you draw your electron-pushing arrows exactly correctly. Remember, the base donates electrons to gain a proton, so the first arrow goes *from* the base *to* the hydrogen attached to the acid.

When drawing the products of a mechanism step, what is the most important aspect of the products to draw correctly?

The most important aspect of the products to draw accurately is the formal charges.

How many formal charges do you change for every mechanism step? Change two formal charges for every mechanism step.

How do you know which formal charges to change for each mechanisms step?

Change the formal charge for the atom that loses electrons at the *beginning* of the series of arrows, and change the formal charge for the atom that gains electrons at the *end* of the series of arrows.

THE MOST COMMON MISTAKE is forgetting to change the charge for the atom that loses electrons at the beginning of the series of arrows.

Notice that in the above mechanism, we changed two formal charges.

We changed the formal charge for atom at the beginning of the series of arrows (the oxygen in water), and we changed the formal charge for the atom at the end of the series of arrows (the oxygen attached to carbon 2).

The oxygen in the water began with a neutral formal charge, and lost electrons. Therefore, the oxygen becomes one step less negative—i.e., one step more positive. Therefore, the oxygen ends up with a positive formal charge.

The oxygen attached to carbon 2 began with a positive formal charge and gained electrons. Therefore, the oxygen becomes one step more negative—i.e., one step less positive. Therefore, the oxygen ends up with a neutral formal charge.

THE MOST COMMON MISTAKE for this mechanism step is forgetting to change the charge for the oxygen in the water (the atom at the *beginning* of the series of arrows).

Problem (3f)



We use the oxygen attached to carbon 4 as the acid. Clue: it has a positive formal charge. We use the oxygen in the alcohol (attached to carbon 1) as a base. Clue: It's a neutral atom with a lone pair.

Check the mechanism above to make sure you draw your electron-pushing arrows exactly correctly. Remember, the base donates electrons to gain a proton, so the first arrow goes *from* the base *to* the hydrogen attached to the acid.

Check the answer above to make sure you drew the formal charges in the products correctly. THE MOST COMMON MISTAKE is forgetting to change the charge for the atom that loses electrons at the beginning of the series of arrows. So, for this problem, the most common mistake would be forgetting to change the charge on the oxygen in the alcohol from neutral to positive.

Problem (3g)

Are these reasonable or unreasonable electron-pushing arrows? Explain.



Remember that the arrows show the movement of *electrons*, and remember that an electron has a negative charge.

Even though the positive oxygen has a lone pair, it should *not* go at the beginning of a series of arrows. An atom with a lone pair and a negative or neutral formal charge can be an electron donor. But an atom with a positive formal charge should be an electron *receiver*, even if it has a lone pair.

Notice that the arrows drawn above violate the pattern we have learned:



Never put a positive formal charge at the *beginning* of a series of arrows.

Compare the incorrect arrows, above, with the correct arrows we drew in the previous problem:



In these correct arrows, the positive formal charge goes at the *end* of the series of arrows.

Answers for Video (3)

$S_{\rm N}1$ REACTIONS

Problem (3h) ¹ What is the difference between a strong base and a weak base? Both a strong and a weak base are willing to gain a H⁺. A strong base is very eager to gain a H⁺. A weak base is less eager to gain a H⁺.

What is the difference between a strong acid and a weak acid? Both a strong and a weak acid are willing to donate a H⁺. A strong acid is very eager to donate a H⁺. A weak acid is less eager to donate a H⁺.

Are water and alcohols strong or weak bases? Water and alcohol (neutral oxygens with lone pairs) are weak bases.

Is an atom with a positive formal charge a strong or weak acid? An atom with a positive formal charge is a strong acid.

Who is more reactive, strong or weak acid? Who is more reactive, strong or weak base?

Strong acids are more reactive than weak acids. Strong bases are more reactive than weak bases.

¹ The answers given for this problem are answers that are useful for an *organic* chemistry class. They do not exactly match the "official" definitions that would be used in a general chemistry class.

Problem (3i) continued

Determine whether an acid-base step can occur for each set of starting materials below



Notice that an acid-base step can occur if *either* the acid or the base is strong. Notice that an acid-base step generally will not occur when both the acid and the base are weak. These patterns are useful *guidelines* for ochem. There are some exceptions.

Problem (3g)

Confirm that an acid-base step can occur for each of the problems we saw earlier in this video:



The neutral oxygen in the water is a weak base (WB).

The oxygen attached to carbon 2 is a *strong* acid (SA) (clue: positive formal charge), so, yes, an acid-base step can occur. An acid-base step can occur if *either* the acid or the base is strong.



The neutral oxygen in the alcohol is a weak base.

The oxygen attached to carbon 4 is a *strong* acid (clue: positive formal charge), so, yes, an acid-base step can occur. An acid-base step can occur if *either* the acid or the base is strong.

Problem (3j)

Are Cl⁻, Br⁻, and I⁻ strong or weak bases?

Cl⁻, Br⁻, and I⁻ are *very weak* bases. This means that we will generally use Cl⁻, Br⁻, and I⁻ as bases only if no other base is present.

(Why are Cl⁻, Br⁻, and I⁻ such weak bases, despite their negative charges? HCl, HBr, and HI are very strong acids. Therefore, Cl⁻, Br⁻, and I⁻ are the conjugates of very strong acids. Therefore, Cl⁻, Br⁻, and I⁻ are very weak bases.)

Therefore, when water or alcohol (ROH) solvent is present, most professors prefer to use the water or alcohol as the base, rather than Cl⁻, Br⁻, or I⁻.

Cl⁻, Br⁻, and I⁻ are generally used as good nucleophiles, rather than as bases.

Are neutral Cl, Br, and I basic?

Although neutral Cl, Br, and I have lone pairs, they do not act as bases. (There are some exceptions.) Instead, we know that neutral Cl, Br, and I act as good leaving groups.

Summary of key information from this video:

acid: receives electrons to give a H^{\oplus} to a base An atom with a \oplus formal charge and an attached H is a strong acid.

Be sure to memorize these facts.

We will illustrate how to apply these facts to $S_N 1$ reactions in the next video in this series.

$S_{\rm N}1$ REACTIONS

Video (4)

Problem (4a)



Use the table to determine that the mechanism is $S_{\rm N}1$.

	how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
	poor Nu / weak base	good Nu / weak base	good Nu / strong base
	O with no formal charge	Cl ⁻ , Br ⁻ , I ⁻ , CN, S ⁻ , N ₃ ⁻	0-
	(water or alcohol)	or N, P, or S with no formal charge	
methyl a-carbon	no reaction	S _N 2	S _N 2
1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon
2° α-carbon	S _N 1 major,	S _N 2	E2
	E1_minor		
3° a-carbon	S _N 1 major,	S _N 1 major,	E2
	E1 minor	E1 minor	

For Step 2 of the mechanism, the oxygen in the water is the nucleophile. Clue: it's a neutral atom with lone pair.

The most common student mistake on Step 2 is forgetting to change the charge on the oxygen from neutral to positive.

Because the oxygen is at the beginning of the series of arrows, we need to change the oxygen's charge. The oxygen begins neutral, and loses electrons, so the oxygen becomes one step less negative. i.e., the oxygen becomes one step more positive.

Remember, when drawing the products of a mechanism step, that the most important part of the products to get right is the formal charges. Remember that, for every step of every mechanism, you must change *two* formal charges, at the beginning of the series of arrows and at the end of the series of arrows. For Step 2, we change the formal charge on the oxygen (at the beginning of the arrow) and the formal charge on carbon 2 (at the end of the arrow).

Be sure to also continue to draw the oxygen as covalently bonded to its two hydrogens in the product from Step 2.

solution for Problem (4a) continued on next page

Problem (4a) continued



After Step 2, the main product still has a formal charge (the positive formal charge on the oxygen attached to carbon 2). This indicates that the mechanism is not finished and that, for Step 3 of the mechanism, we need an *Acid-Base Cleanup Step* to "clean up" the formal charge on the main product.

In Step 3, the oxygen attached to carbon 2 acts as a strong acid (clue: it has a positive formal charge). The oxygen in the water acts as the weak base (clue: neutral atom with a lone pair). We saw in Problem (3i) that an acid-base step *can* occur between a strong acid and a weak base.

We saw in Problem (3j) that Cl⁻, Br⁻, and I⁻ are very weak bases. Therefore, when possible, most professors prefer to use water or alcohol as a base, rather than Cl⁻, Br⁻, or I⁻. Therefore, on this problem, we use water as the base, rather than the I⁻ we produced in Step 1.

Study the electron-pushing arrows for Step 3. Make sure you can draw the arrows for an acidbase step accurately. Remember, a base donates electrons to gain a H⁺, so the first arrow for an acidbase step points *from* the base, and *toward* the proton.

When drawing the products of Step 3, make sure you change the formal charge on the oxygen in the water from neutral to positive.

Because the oxygen in the water is at the beginning of the series of arrows, we need to change the oxygen's charge. The oxygen begins neutral, and loses electrons, so the oxygen becomes one step less negative. i.e., the oxygen becomes one step more positive (H_3O^+) .

When drawing the products of a mechanism step, the most important part of the products to get right is the formal charges! Remember that, for every step of every mechanism, you must change *two* formal charges, at the beginning of the series of arrows and at the end of the series of arrows. For Step 3, we change the formal charge on the oxygen in the water (at the beginning of the series of arrows) and the formal charge on the oxygen attached to carbon 2 (at the end of the series of arrows).

The *main* product from Step 3 has no formal charge, so Step 3 is the last step in the mechanism.

Summary of $S_N 1$ mechanism with a neutral nucleophile: Step 1: Leaving group step: Leaving group leaves α carbon Step 2: Nucleophile-electrophile step: Nucleophile joins α carbon Step 3: Acid-base cleanup step

How can you tell when a mechanism is finished?

The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism. Exception: the "main product" of an $S_N 2$ reaction can have a formal charge.

Checklist of things to do for the *first* step in a mechanism

1. Number *all* the carbons in the starting materials.

2. Draw formal charges for any ionic bonds.

3. Label which specific atoms will play which roles.

Identify the "clues" that tell you which atoms will play which roles.

4. Label the α-carbon.

Write down whether the α -carbon is methyl, 1°, 2°, or 3°.

5. Use the table to determine whether the reaction is S_N2 , S_N1 , E2, or E1. Write down the name of the mechanism.

6. Determine what type of step you will do first in the mechanism (e.g., Nu-E step, LG step, or A-B cleanup step).

7. Draw electron-pushing arrows for the mechanism step.

Don't begin drawing the products for a mechanism step until you have finished drawing the electronpushing arrows for that step

8. Draw the products of the mechanism step

Number *all* the carbons in the products. Make sure your numbers for the products of a step are *consistent* with the numbers you used for the starting materials of the step.

9. Ask whether you have finished the mechanism, or require another mechanism step.

The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism. Exception: the "main product" of an $S_N 2$ reaction can have a formal charge.

Checklist of things to do for each step in a mechanism *after* the first step

1. Determine what type of step you will do next in the mechanism (e.g., Nu-E step, LG step, or A-B cleanup step).

2. Label which specific atoms will play which roles.

Identify the "clues" that tell you which atoms will play which roles.

3. Draw electron-pushing arrows for the mechanism step.

Don't begin drawing the products for a mechanism step until you have finished drawing the electronpushing arrows for that step

4. Draw the products of the mechanism step

Number *all* the carbons in the products. Make sure your numbers for the products of a step are *consistent* with the numbers you used for the starting materials of the step.

5. Ask whether you have finished the mechanism, or require another mechanism step. The reaction is usually finished when the "main product" of a mechanism step has no formal charge. When the "main product" of a step has a formal charge, you usually need to continue the mechanism. Exception: the "main product" of an S_N 2 reaction can have a formal charge.

$S_{\rm N}1$ REACTIONS



	Use the table to determine that the mechanism is $S_N 1$.				
	how to determine the mechanism for alkyl halides and alkyl sulfonates				
1	poor Nu / weak base good Nu / weak base good Nu / strong base				
		Owith no formal charge	Cl ⁻ , Br ⁻ , I ⁻ , ⁻ CN, S ⁻ , N ₃ ⁻	0.	
		(water or alcohol)	or N, P, or S with no formal charge		
	methyl a-carbon	no reaction	S _N 2	S _N 2	
	1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon	
	2° α-carbon	S _N 1 major,	S _N 2	E2	
		E1 minor			
\rightarrow	3° α-carbon	(S _N 1 major,)	S _N 1 major,	E2	
-		E1 minor	E1 minor		

For Step 2 of the mechanism, the oxygen in the alcohol is the nucleophile. Clue: neutral atom with lone pair.

Notice that, in the product of Step 2, the oxygen nucleophile remains covalently bonded to carbon 6, and to a hydrogen. You should not break a covalent bond unless an electron-pushing arrow specifically indicates that that covalent bond should be broken. In the mechanism for Step 2, there is no electron-pushing arrow indicating that we should break the covalent bonds around the oxygen nucleophile.

The most common student mistake on Step 2 is forgetting to change the charge on the oxygen from neutral to positive.

Because the oxygen is at the beginning of the series of arrows, we need to change the oxygen's charge. The oxygen begins neutral, and loses electrons, so the oxygen becomes one step less negative. i.e., the oxygen becomes one step more positive.

Remember, when drawing the products of a mechanism step, that the most important part of the products to get right is the formal charges. Remember that, for every step of every mechanism, you must change *two* formal charges, at the beginning of the series of arrows and at the end of the series of arrows. For Step 2, we change the formal charge on the oxygen (at the beginning of the arrow) and the formal charge on carbon 3 (at the end of the arrow).

Solution to Problem (4b) continues on next page

Problem (4b) continued



After Step 2 of the mechanism, the main product still has a formal charge (the positive formal charge on the oxygen attached to carbon 6). This indicates that the mechanism is not finished and that, for Step 3 of the mechanism, we need an *Acid-Base Cleanup Step* to "clean up" the formal charge from the main product.

In Step 3, the oxygen attached to carbon 6 acts as a strong acid (clue: it has a positive formal charge). The oxygen in the alcohol acts as the weak base (clue: neutral atom with a lone pair). We saw in Problem (3i) that an acid-base step *can* occur between a strong acid and a weak base.

We saw in Problem (3j) that Cl⁻, Br⁻, and I⁻ are very weak bases. Therefore, when possible, most professors prefer to use water or alcohol as a base, rather than Cl⁻, Br⁻, or I⁻. Therefore, on this problem, we use alcohol as the base, rather than the Br⁻ we produced in Step 1.

Study the electron-pushing arrows for Step 3. Make sure you can draw the arrows for an acidbase step accurately. Remember, a base donates electrons to gain a H⁺, so the first arrow for an acidbase step points *from* the base, and *toward* the proton.

When drawing the products of Step 3, make sure you change the formal charge on the oxygen in the alcohol from neutral to positive.

Because the oxygen in the alcohol is at the beginning of the series of arrows, we need to change the oxygen's charge. The oxygen begins neutral, and loses electrons, so the oxygen becomes one step less negative. i.e., the oxygen becomes one step more positive.

When drawing the products of a mechanism step, the most important part of the products to get right is the formal charges! Remember that, for every step of every mechanism, you must change *two* formal charges, at the beginning of the series of arrows and at the end of the series of arrows. For Step 3, we change the formal charge on the oxygen attached to carbon 7 (at the beginning of the series of arrows) and the formal charge on the oxygen attached to carbon 3 (at the end of the series of arrows).

The main product from Step 3 has no formal charge, so Step 3 is the last step in the mechanism.

Summary of $S_N 1$ mechanism with a neutral nucleophile: Step 1: Leaving group step: Leaving group leaves α carbon Step 2: Nucleophile-electrophile step: Nucleophile joins α carbon Step 3: Acid-base cleanup step

$S_{\rm N}1$ REACTIONS

Problem (4c) How many steps are there in an S_N 1 reaction? What happens during those steps?

There are two *main* steps in an an $S_N 1$ reaction. In the first main step, the leaving group leaves the α carbon. In the second main step, the nucleophile joins the α carbon.

As we have seen in this video, an $S_N 1$ mechanism may also include an acid-base step.

In particular, for an $S_N 1$ mechanism involving a neutral nucleophile, the third step of the $S_N 1$ mechanism will be an Acid-Base Cleanup Step.

	what happens in the main steps	big obstacle
S _N 2	One main step: Nucleophile joins α carbon and leaving group leaves α carbon	steric hindrance
	There may also be an acid/base step.	
S _N 1	First main step: Leaving group leaves α carbon	stabilizing the
	Second main step: Nucleophile joins a carbon	carbocation
	There may also be an acid/base step, and/or a carbocation rearrangement step.	

what happens in $S_N 2$, $S_N 1$, E2, and E1 mechanisms

Video (5)

Problem (5a) What is the basic fact about S_N 2 stereochemistry? If the α -carbon is a stereocenter, the product of the S_N 2 reaction will have *inversion* of

configuration at the α -carbon.

What is the justification for this fact?

When a nucleophile attacks an atom that is attached to a leaving group, the nucleophile will attack from the side *opposite* to the leaving group.

Notice that this idea is not relevant for an $S_N 1$ reaction, because, in an $S_N 1$ reaction, the leaving group has already left before the nucleophile attacks.

What is the definition of the term "carbocation"? A *carbocation* is a <u>carbon</u> ("carbo") with a <u>positive</u> formal charge ("cation").

Define these terms: cation, anion cation: a positive ion anion: a negative ion

How can you remember these definitions? Imagine that the letter *n* in the word "a<u>n</u>ion" stands for the word "negative" ("*a* negative ion") Imagine that the letter *t* in the word "cation" represents a + sign ("a + ion")

Notice that, for example, Br^+ is *not* a carbocation. Br^+ *is* a cation (because of its positive formal charge). But Br^+ is not a <u>carbo</u>cation, because Br^+ is not a carbon.

solution for Problem (5a) continues on next page

Problem (5a) continued

Does an S_N1 reaction have a carbocation intermediate?

Yes.

For example, notice that carbon 2 becomes a carbocation intermediate in the first step of of this $S_N 1$ mechanism:



Does an $S_{\rm N}2$ reaction have a carbocation intermediate? No.

For example, notice that there are no positive carbons involved in this $S_N 2$ mechanism:



(Remember that a carbocation is a carbon with a positive *formal* charge, not just a δ^+ .)

Problem (5b)

When does a carbon have tetrahedral geometry? A carbon with 4 attached atoms and no lone pairs has tetrahedral geometry. Notice that, for this rule, you count the number of attached *atoms*, not the number of bonds.

When does a carbon have trigonal planar geometry? A carbon with 3 attached atoms and no lone pairs has trigonal planar geometry. Notice that, for this rule, you count the number of attached *atoms*, not the number of bonds.

What is the geometry of a carbocation? A carbocation has three attached atoms and no lone pairs. Therefore, a carbocation has trigonal planar geometry.

Most atoms that participate in ochem reactions have complete octets. What is the most important example in organic chemistry of an atom with an incomplete octet?

Carbocations have incomplete octets. Therefore, a carbocation has room for one more bond. Problem (5c)

Carbon 2 has four attached atoms (carbon 1, carbon 3, and two hidden hydrogens) and no lone pairs. Therefore, carbon 2 has tetrahedral geometry.

What is the correct way to draw the geometry for a tetrahedral atom? 2 solid lines, a wedge, and a dash.¹

But keep in mind that, if a tetrahedral atom is not a stereocenter, we usually don't care much about its geometry. Therefore, if an atom is not a stereocenter, it is usually acceptable to draw its geometry *inaccurately*. For example, if an atom is not a stereocenter, it is usually fine to draw all four of its bonds as solid lines, even though that does not accurately depict the tetrahedral geometry. Carbon 2 in this problem is not a stereocenter, so it would usually be acceptable to draw its two hydrogens on solid lines, even though that would not be an accurate picture of tetrahedral geometry.

What is the correct way to draw the geometry for a trigonal planar atom? 3 solid lines. No wedges or dashes.²

Problem (5d)

When a nucleophile attacks an atom with trigonal planar geometry, from what direction does the nucleophile attack?

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

¹ There are other correct ways to draw tetrahedral geometry, but this is by far the most common.

² There are other correct ways to draw trigonal planar geometry, but this is by far the most common.



In Step 2, the H_2O attacks a *trigonal planar* carbocation. Therefore, the H_2O can attack from *either* in front of the page *or* from behind the page. Therefore, we get *two* products from Step 2, one in which the ${}^+OH_2$ ends up on a wedge, and one in which the ${}^+OH_2$ ends up on a dash. Therefore, there are two stereoisomer products of this reaction, one in which the OH is on a wedge, and one in which the OH is on a dash.

For this problem, we used this rule:

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

	how to determine the mechanism for alkyl halides and alkyl sulfonates				
		poor Nu / weak base	good Nu / weak base	good Nu / strong base	
		Owith no formal charge	Cl ⁺ , Br ⁺ , I ⁺ , ⁺ CN, S ⁺ , N ₃ ⁺	0.	
		(water or alcohol)	or N, P, or S with no formal charge		
\rightarrow	methyl α-carbon	no reaction	S _N 2	S _N 2	
	1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon	
	2° α-carbon	S _N 1 major,	S _N 2	E2	
		E1 minor			
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2	
		E1 minor	E1 minor		

Problem (5f)

What is the key fact about S_N1 stereochemistry? What is the justification for this fact? What is the key fact about S_N2 stereochemistry? What is the justification for this fact?

SNI stereochemistry | SNZ stereochemistry

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from either of the two directions that are perpendicular to the flat plane.

If the α -carbon in the product is a stereocenter, the products of an S_N1 reaction will have 50% inversion of configuration at the α -carbon, and 50% retention of configuration at the α -carbon.

When a nucleophile attacks an atom that is attached to a leaving group, the nucleophile will attack from the side opposite to the leaving group.

If the α -carbon is a stereocenter, the product of an S_N2 reaction will have inversion of configuration at the α -carbon.

If the α -carbon in the product is a stereocenter, an S_N1 reaction will produce some products with *inversion* of configuration at the α -carbon, and some products with *retention* of configuration at the α -carbon.

For simple molecules, S_N1 produces 50% inversion and 50% retention.

In more complicated molecules for which one side of the molecule is hindered, the proportions may differ from 50-50.



In Step 2, the alcohol attacks a *trigonal planar* carbocation. Therefore, the alcohol can attack from *either* in front of the page *or* from behind the page. Therefore, we get two products from Step 2, one in which the ⁺OR ends up on a wedge, and one in which the ⁺OR ends up on a dash. Therefore, there are stereoisomer products of this reaction, one in which the OR is on a wedge, and one in which the OR is on a dash.

For this problem, we used this rule:

١

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

Notice that **there is no change in the stereochemistry at carbon 3 or at carbon 4**, because carbon 3 and carbon 4 do not participate in the reaction. Notice that the rule for $S_N 1$ stereochemistry refers to retention and inversion <u>at the α -carbon</u> (for this problem, carbon 1). There is no reason for stereochemistry to change at any other carbons during an $S_N 1$ reaction, since the other carbons don't participate in the mechanism.

If the α -carbon in the product is a stereocenter, an S_N1 reaction will produce some products with *inversion* of configuration <u>at the α -carbon</u>, and some products with *retention* of configuration <u>at the α -carbon</u>.

	how to determine the mechanism for alkyl halides and alkyl sulfonates				
		poor Nu / weak base	good Nu / weak base	good Nu / strong base	
		Owith no formal charge	Cl, Br, I, CN, S, N ₃	0-	
		(water or alcohol)	or N, P, or S with no formal charge		
	methyl α-carbon	no reaction	S _N 2	S _N 2	
	1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon	
	2° α-carbon	(S _N 1 major,)	S _N 2	E2	
/		E1 minor			
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2	
		E1 minor	E1 minor		
	T .1 11 .1		1 1 11 1 .		

Problem (5h)

Now, in the mechanism you drew for Problem (5g), draw in the hidden hydrogen on the α carbon on the starting material, intermediates, and final products. Be careful to draw the correct geometry for these hydrogens.



Notice that the product of Step 1, the carbocation intermediate, is trigonal planar. Therefore, in the carbocation intermediate, *the hydrogen attached to carbon 1 is drawn on a solid line*, not on a dash.

On the other hand, in the products of Step 2 and Step 3, carbon 1 is again tetrahedral. So, for the products of Step 2 and Step 3, the hydrogen attached to carbon 1 must be drawn on a wedge or a dash, *not on a solid line*.

It is generally *not* necessary to draw the hidden hydrogen on the α carbon. We have drawn the hidden hydrogen in this problem as an exercise, to give you better intuition for the geometry of the intermediates and products from $S_N 1$.


In Step 2, the alcohol attacks a *trigonal planar* carbocation. Therefore, the alcohol can attack from *either* in front of the page *or* from behind the page. Therefore, we get two products from Step 2, one in which the ⁺OR ends up on a wedge, and one in which the ⁺OR ends up on a dash. Therefore, there are two stereoisomer products of this reaction, one in which the OR is on a wedge, and one in which the OR is on a dash.

For this problem, we used this rule:

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

Notice that the product of Step 1, the carbocation intermediate, is trigonal planar. Therefore, in the carbocation intermediate, *carbon 6 is drawn on a solid line*, not on a dash.

On the other hand, in the products of Step 2 and Step 3, carbon 3 is again tetrahedral. So, for the products of Step 2 and Step 3, carbon 6 must be drawn on a wedge or a dash, *not on a solid line*.

Solution for Problem (5i) continues on next page



The starting material for this reaction is an "alkyl sulfonate". The sulfonate group is a good leaving group. I discussed sulfonates in more detail in the S_N2 video series.

Notice that, in an alkyl sulfonate, the α carbon is the carbon attached to the oxygen (in this case, carbon 3), not the carbon attached to the sulfur.



Like Cl⁻, Br⁻, and I⁻, the negative sulfonate is a very weak base. Therefore, we prefer to use another molecule of the alcohol as the base for our Acid-base Cleanup step, rather than using the sulfonate.

The negative sulfonate is a very weak base because its negative charge is resonance stabilized. This resonance stabilization of the negative charge after the sulfonate group leaves the α carbon also explains why the neutral sulfonate was a good leaving group: It is easy for the neutral sulfonate to leave the α carbon, because its negative charge after leaving will be stabilized by resonance.

Solution for Problem (5i) continues on next page



Note: On any problem there are *multiple* <u>correct</u> ways to draw the stereochemistry of the product(s). Therefore, even when your answer does not match the answer key, it is possible that your answer is correct. How can you tell? You can assign R and S to your answer(s), and to the answer(s) in the answer key. If your answer(s) has the same R or S stereochemistry as the answer key answer, then the stereochemistry for your answer is correct, even if your answer is drawn differently than in the answer key. Of course, this method is only effective if you have mastered the skill of assigning R or S to a stereocenter.

Notice that, as you can see from its title, the table below applies both to alkyl halides and to alkyl sulfonates.

		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
[poor Nu / weak base	good Nu / weak base	good Nu / strong base
		Owith no formal charge	Cl., Br., I., CN, S., N ₃	0.
		(water or alcohol)	or N, P, or S with no formal charge	
	methyl α-carbon	no reaction	S _N 2	S _N 2
~>	1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
	2° α-carbon (S _N 1 major,		S _N 2	E2
		E1 minor		
	3° α-carbon S _N 1 major,		S _N 1 major,	E2
		E1 minor	E1 minor	
	T .1 11 .1		1 1 1 1 1 .	

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Use the table to determine that the mechanism for this reaction is S_N2 , not S_N1 ! Recall that S_N2 reactions involve one step, in which: Nucleophile joins α carbon and leaving group leaves α carbon

The cyanide anion attacks carbon 3 while it is still attached to the sulfonate leaving group. Therefore, the cyanide will attack from the side opposite to the sulfonate leaving group. The sulfonate leaving group is behind the page, so the cyanide attacks carbon 3 from in front of the page. Therefore, in the product the CN group ends up on a wedge.

For this problem, we used this rule: When a nucleophile attacks an atom that is attached to a leaving group, the nucleophile will attack from the side *opposite* to the leaving group. Therefore, when the α carbon is a stereocenter, an S_N2 reaction produces *inversion* of configuration at the α carbon.

Notice that on this problem, carbon 3 is *not* a carbocation when the nucleophile attacks. Carbon 3 is attached to four atoms when the cyanide attacks, so carbon 3 is tetrahedral, not trigonal planar, when the cyanide attacks.

Carbon 1 does not participate in the reaction, so carbon 1 has no change in its stereochemistry.

The starting material for this reaction is an "alkyl sulfonate", which contains a good leaving group. Remember that, in an alkyl sulfonate, the α carbon is the carbon attached to the oxygen (in this case, carbon 3), not the carbon attached to the sulfur. For more detail on sulfonates, or more practice with $S_N 2$ reactions, see my video series on " $S_N 2$ reactions".

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			V	
		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
8		poor Nu / weak base	good Nu / strong base	
		O with no formal charge	Cl, Br, I, CN, S, N ₃	0.
		(water or alcohol)	or N, P, or S with no formal charge	
\rightarrow	methyl α-carbon	no reaction	S _N 2	S _N 2
	1° α-carbon		~	Exception: E2 with t-butyloxide and 1° a-carbon
	2° α-carbon	S _N 1 major,	$(S_N 2)$	E2
		E1 minor		
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

Don't assume the mechanism is $S_N 1!$ On exams, problems will involve a *variety* of mechanisms.



Be aware that "Me" stands for "methyl", so MeOH is methyl alcohol. If you prefer, can you draw the MeOH as CH_3OH . Or you can draw the CH_3OH in bondline notation (as is illustrated in the video).

In Step 2, the alcohol attacks a *trigonal planar* carbocation. Therefore, the alcohol can attack from *either* in front of the page *or* from behind the page. Therefore, we get two products from Step 2, one in which the ⁺OR ends up on a wedge, and one in which the ⁺OR ends up on a dash. Therefore, there are two stereoisomer products of this reaction, one in which the OR is on a wedge, and one in which the OR is on a dash.

Notice that the product of Step 1, the carbocation intermediate, is trigonal planar. Therefore, in the carbocation intermediate, *the benzene ring is drawn on a solid line*, not on a dash.

On the other hand, in the products of Step 2 and Step 3, carbon 1 is again tetrahedral. So, for the products of Step 2 and Step 3, the benzene ring must be drawn on a wedge or a dash, *not on a solid line*.

For this problem, we used this rule:

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
1		poor Nu / weak base	good Nu / weak base	good Nu / strong base
		Owith no formal charge	Cl, Br, I, CN, S, N ₃	0.
		(water or alcohol)	or N, P, or S with no formal charge	
	methyl a-carbon	no reaction	S _N 2	S _N 2
	1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon
	2° α-carbon	S _N 1 major,	S _N 2	E2
		E1 minor		
~	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	



Use the table to determine that the mechanism for this reaction is S_N2 , not S_N1 ! Recall that S_N2 reactions involve one step, in which: Nucleophile joins α carbon and leaving group leaves α carbon

Be aware that "Et" stands for an ethyl group. ("Me"=methyl; "Et"=ethyl)

The sulfur anion attacks carbon 3 while it is still attached to the chloride leaving group. Therefore, the sulfur will attack from the side opposite to the chloride leaving group. The chloride leaving group is in front of the page, so the sulfur attacks carbon 3 from behind the page. Therefore, in the product the SEt group ends up on a dash.

For this problem, we used this rule: When a nucleophile attacks an atom that is attached to a leaving group, the nucleophile will attack from the side *opposite* to the leaving group. Therefore, when the α carbon is a stereocenter, an S_N2 reaction produces *inversion* of configuration at the α carbon.

The molecule at right is DMSO, a common solvent. You should know that DMSO is a solvent that does not participate in $S_N 2$, $S_N 1$, E2, or E1 reactions. For more information about common solvents, see my video series on " $S_N 2$ reactions".



			V	
		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
		poor Nu / weak base	good Nu / weak base	good Nu / strong base
		O with no formal charge	Cl', Br', I', 'CN,(S',)N ₃ '	0', N'
		(water or alcohol)	or N, P, or S with no formal charge	
	methyl α-carbon no reaction 1° α-carbon		S _N 2	S _N 2
				Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
	2° α-carbon S _N 1 major,		$(S_N 2)$	E2
		E1 minor	\bigcirc	
	3° α-carbon S _N 1 major,		S _N 1 major,	E2
		E1 minor	E1 minor	
	T			

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Problem (5m)

Draw the major product.

If more than one stereoisomer of the major product is produced, include all the stereoisomers.



Both carbon 8 and carbon 1 are attached to good leaving groups, so we have to choose between using carbon 8 and carbon 1 as our α carbon. Use the table to decide:

Our nucleophile is a neutral oxygen (in the alcohol), so we use the left column of the table.

Carbon 8 is 1°, which puts it in the top row of the table. The top row, left column of the table predicts "no reaction", so we do *not* expect carbon 8 to participate in the reaction.

Carbon 1 is 3°, which puts it in the bottom row of the table. The bottom row, left column of the table predicts $S_N 1$ as the major reaction.

So we will use carbon 1, not carbon 8, as our α carbon. The mechanism will be S_N1.

	how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
	poor Nu / weak base with no formal charge (water or alcohol)	good Nu / weak base Cl., Br, I., CN, S., N ₃ or N, P, or S with no formal charge	good Nu / strong base O', N'
methyl α-carbon 1° α-carbon	no reaction 🗶	S _N 2	S _N 2 Exception: E2 with <i>t</i> -butyloxide and 1° α-carbo
2° α-carbon	S _№ 1 major, E1 minor	S _N 2	E2
3° a-carbon	S _№ 1 major, E1 minor ★	S _N 1 major, E1 minor	E2

We will explain *why* the top left cell of the table predicts "no reaction" in a later video in this series.

solution continues on next page

Problem (5m) continued

Draw the major product.

If more than one stereoisomer of the major product is produced, include all the stereoisomers.



In Step 2, the alcohol attacks a *trigonal planar* carbocation. Therefore, the alcohol can attack from *either* above the ring *or* from below the ring. Therefore, we get two products from Step 2, one in which the ⁺OR ends up in the axial position (pointing straight up), and one in which the ⁺OR ends up in the equatorial position (slanting down). Therefore, there are two stereoisomer products of this reaction, one in which the OR is axial in the chair flip shown, and one in which the OR is equatorial in the chair flip shown.

Notice that the product of Step 1, the carbocation intermediate, is trigonal planar. Therefore, in the carbocation intermediate, the orientation of carbon 7 is changed to reflect the idea that carbon 7 should be in the same plane as carbon 6 and carbon 2 for this picture.

On the other hand, for the products of Step 2 and Step 3, carbon 1 has changed back to a tetrahedral geometry, with one axial substituent (pointing straight up) and one equatorial substituent (slanting down).

Notice that, for a chair picture, we do not use wedges and dashes to indicate stereochemistry. All bonds are drawn as solid lines in the chair picture. The stereochemistry of substituents in the chair picture is indicated by whether they are drawn axial or equatorial.

For this problem, we used this rule:

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

Notice that carbon 1 is not a stereocenter. Nevertheless, the stereochemistry at carbon 1 does matter, because the substituents at carbon 1 can be either cis or trans to carbon 8. So we can expand our previous rule:

If the α -carbon in the product is a stereocenter,

or if the α carbon's stereochemistry matters because of

cis/trans relationships around a ring,

an $S_{\rm N}1$ reaction will produce

some products with *inversion* of configuration at the α -carbon, and

some products with *retention* of configuration at the α -carbon.

Problem (5n)

What is the key fact about $S_N 1$ stereochemistry? What is the justification for this fact? What is the key fact about $S_N 2$ stereochemistry? What is the justification for this fact?

5NI stereochemistry

When a nucleophile attacks an atom with trigonal planar geometry, the nucleophile can attack from *either* of the two directions that are perpendicular to the flat plane.

If the α -carbon in the product is a stereocenter, or if the α carbon's stereochemistry matters because of cis/trans relationships around a ring, an S_N1 reaction will produce some products with *inversion* of configuration at the α -carbon, and some products with *retention* of configuration at the α -carbon. SNZ stereochemistry

When a nucleophile attacks an atom that is attached to a leaving group, the nucleophile will attack from the side *opposite* to the leaving group.

If the α -carbon in the product is a stereocenter, or if the α carbon's stereochemistry matters because of cis/trans relationships around a ring, the product of an S_N2 reaction will have *inversion* of configuration at the α -carbon.

For simple molecules, S_N1 produces 50% inversion and 50% retention.

In more complicated molecules for which one side of the molecule is hindered, the proportions may differ from 50-50.

We discussed the significance of cis/trans relationships around a ring at the end of the solution for Problem (5m).

Review Quiz

What are the names of the five main roles in organic chemistry? Nucleophile, electrophile, leaving group, acid, base

How is a base similar to a nucleophile? Both a base and a nucleophile donate electrons.

How is a base different from a nucleophile? A base donates electrons to take a H^+ from an acid, while a nucleophile donates electrons to join an electrophile.

Draw the electron-pushing arrows for an acid-base step:

J-HK

Video (6)

Problem (6a)



Should we use the neutral iodine as the leaving group, or should we use the neutral oxygen attached to carbon 6 and carbon 4 as the leaving group? We know that neutral Cl, Br, or I, and neutral sulfonates, are good leaving groups. **Most other neutral atoms are** *not* **acceptable leaving groups.** Therefore, the neutral I on carbon 1 is a good leaving group,

but the neutral oxygen attached to carbon 4 and carbon 6 is *not* **an acceptable leaving group.** Therefore, we should use the I as the leaving group, rather than the O.

Therefore, we should use carbon 1, rather than carbon 4 or carbon 6, as our α carbon.

Moral: Neutral Cl, Br, and I are good leaving groups. Neutral sulfonates are good leaving groups. Other neutral atoms (such as neutral O) are usually *not* acceptable leaving groups.

Use the table to determine that the mechanism is $S_N 1$. The problem tells us to focus on substitution products, so we don't draw the E1 mechanism (E1 is an "elimination" mechanism, rather than "substitution".)

methyl				
methyl		poor Nu / weak base	good Nu / weak base	good Nu / strong base
methyl		Owith no formal charge	Cl ⁺ , Br ⁺ , I ⁺ , CN, S ⁺ , N ₃ ⁺	0', N'
methyl		(water or alcoholD	or N, P, or S with no formal charge	
	l α-carbon	no reaction	S _N 2	S _N 2
1°	α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
2°	α-carbon	(S _N 1 major,)	S _N 2	E2
-7		E1 minor		
3°	3° a-carbon S _N 1 major,		S _N 1 major,	E2
		E1 minor	E1 minor	

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Problem (6b)





Should we use the neutral Cl or the neutral F as the leaving group? We know that neutral Cl, Br, or I, and neutral sulfonates, are good leaving groups. Most other neutral atoms are *not* acceptable leaving groups. Therefore, the neutral Cl on carbon 4 is a good leaving group,

but the neutral fluorine on carbon 3 is *not* an acceptable leaving group.

Therefore, we should use the Cl as the leaving group, rather than the F.

Therefore, we should use carbon 4, rather than carbon 3, as our α carbon.

Moral: Neutral Cl, Br, and I are good leaving groups. Neutral sulfonates are good leaving groups. Other neutral atoms (such as neutral F) are usually *not* acceptable leaving groups.

		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
		poor Nu / weak base	good Nu / weak base	good Nu / strong base
—>		O with no formal charge	Cl., Br., I., CN, S., N ₃	0', N'
		(water or alcohol)	or N(P,)or S with no formal charge	5.2 PC232.5
	methyl a-carbon	no reaction	(\$ <u>N</u> 2)	S _N 2
	1° α-carbon)	Exception: E2 with t-butyloxide and 1° α-carbon
	2° α-carbon	S _N 1 major,	S _N 2	E2
		E1 minor		
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

Use the table to determine that the mechanism is $S_N 2$.

The most common student mistake on this problem is forgetting to change the formal charge at the beginning of the series of arrows. The P starts negative and loses electrons, so it becomes positive.

Normally, the positive charge on the P would be a clue that the mechanism requires another step. But S_N2 reactions are an exception to this pattern: The final "main" product of an S_N2 reaction using a neutral nucleophile has a positive formal charge. Notice that it is conventional to draw the Cl⁻ as ionically bonded to the P⁺ in the final product.

There are no electron-pushing arrows telling us to break the covalent bonds between the phosphorus and its three methyl groups, so the P remain bonded to its methyl groups in the product.

For more practice with S_N2 reactions involving a neutral nucleophile, see the "S_N2 reactions" video series.

Carbon 3 does not participate in the reaction, so we do *not* invert the configuration at carbon 3.

Review Quiz

Which roles in organic chemistry involve donating electrons? Which roles in organic chemistry involve receiving electrons?

Electron donors: nucleophile and base

Nucleophile: donates electrons to join an electrophile Base: donates electrons to take a H⁺ from an acid

Electron receivers: electrophile, leaving group, and acid

Electrophile: receives electrons to join a nucleophile Leaving group: receives electrons to leave an atom Acid: receives electrons to give a H⁺ to a base

Did you remember that leaving groups are electron receivers?

Notice that both nucleophiles and bases donate electrons. So, how are they different? The difference is that a nucleophile donates electrons to join another molecule, while a base donates electrons to take a proton from the other molecule.

Similarly, the definitions above show that, even though electrophiles, leaving groups, and acids all receive electrons, there are also important differences between each of those roles.

Video (7)

Problem (7a) Define: rate-determining step rate-determining step: The slowest step in a reaction.

How can we use the rate-determining step to determine which factors affect the rate of a reaction and which factors do not affect the rate of a reaction?

Anything that affects the rate determining step will affect the rate of a reaction. Anything that does not affect the rate determining step will not affect the rate of the reaction.

solution for Problem (7a) continues on next page

solution for Problem (7a) continued

What is the rate-determining step for an S_N1 reaction?

An S_N1 reaction consists of two steps. The rate-determining step for S_N1 is the *first* step, in which the leaving group leaves, forming a carbocation.



The first step is the slow, difficult step because it forms two new formal charges, on the leaving group and on the α carbon.

Another reason that forming the carbocation is difficult is that a carbocation has an incomplete octet.

What is the rate-determining step for an $S_N 2$ reaction?

An $S_N 2$ reaction consists of only one step. Therefore, the rate-determining step for $S_N 2$ is this single step, in which the leaving group leaves, and, simultaneously, the nucleophile joins the α carbon.



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Problem (7b)

In the terms " S_N 1" and " S_N 2", what do the *S*'s stand for? What do the *N*'s stand for? What do the numbers *I* and *2* stand for?

The *S* stands for substitution. $S_N 1$ and $S_N 2$ are considered substitution reactions because the nucleophile substitutes for the leaving group.

The *N* stands for *n*ucleophilic. S_N1 and S_N2 are considered nucleophilic substitutions because the thing that does the substituting is a nucleophile.

The term " S_N 1" contains the number 1 because a *single* species participates in the ratedetermining step for S_N 1. The single molecule that participates in the rate-determining step for S_N 1 is the substrate (the molecule that contains the α carbon).

The term " S_N 2" contains the number 2 because *two* species participate in the rate-determining step for S_N 2. The two species that participate in the rate-determining step for S_N 2 are the substrate and the nucleophile.



Problem (7c)

rate-determining step: The slowest step in a reaction.

Anything that affects the rate determining step will affect the rate of a reaction.

Anything that does not affect the rate determining step will not affect the rate of the reaction.



Leaving group quality matters for an $S_N 1$ reaction. An $S_N 1$ reaction requires a good leaving group.



Leaving group quality matters for an $S_N 2$ reaction. An $S_N 2$ reaction requires a good leaving group.

Does leaving group quality matter for the rate of an $S_{\mbox{\tiny N}}1$ reaction?

Does an S_N1 reaction require a good leaving group?

The leaving group participates in the rate-determining step for $S_N 1$. Therefore, yes, leaving group quality affects the rate of an $S_N 1$ reaction. (Remember, anything that affects the rate determining step will affect the rate of a reaction.)

Therefore, yes, an S_N 1 reaction requires a good leaving group.

Does leaving group quality matter for the rate of an $S_N 2$ reaction?

Does an $S_N 2$ reaction require a good leaving group?

The leaving group participates in the rate-determining step for $S_N 2$. Therefore, yes, leaving group quality affects the rate of an $S_N 2$ reaction.

Therefore, yes, an $S_N 2$ reaction requires a good leaving group.

How can you tell whether an atom is a good leaving group?

Leaving group: receives electrons to leave an atom

Neutral Cl, Br, and I are good leaving groups.

Neutral sulfonates are good leaving groups.

Most other neutral atoms are not acceptable leaving groups.

You will learn other acceptable leaving groups later in the course.

Problem (7c) continued

Can the following starting materials carry out an S_N1 reaction? Can they carry out an S_N2 reaction?

Bro + ~ ~ SXI SX2 no reaction

The propane substrate does not contain any acceptable leaving groups. But a good leaving group is required for either an S_N1 reaction or an S_N2 reaction. Therefore, no, these starting materials cannot carry out either an S_N1 reaction or an S_N2 reaction.

(In fact, there would be no reaction at all with these starting materials.)

Problem (7d)

rate-determining step: The slowest step in a reaction.

Anything that affects the rate determining step will affect the rate of a reaction.

Anything that does not affect the rate determining step will not affect the rate of the reaction.



Leaving group leaves the d-carbon

Leaving group quality matters for an $S_N 1$ reaction. An $S_N 1$ reaction requires a good leaving group.

Nucleophile quality does *not* matter for an $S_N l$ reaction. An $S_N l$ reaction does *not* require a good nucleophile.



Leaving group quality matters for an $S_N 2$ reaction. An $S_N 2$ reaction requires a good leaving group.

Nucleophile quality matters for an $S_N 2$ reaction. An $S_N 2$ reaction requires a good nucleophile.

Does nucleophile quality matter for the rate of an S_N1 reaction?

Does an S_N1 reaction require a good nucleophile?

The nucleophile does *not* participate in the rate-determining step for S_N1 . (For an S_N1 reaction, the nucleophile participates in the second, easy step, not in the first, difficult step.) Therefore, no, nucleophile quality does *not* affect the rate of an S_N1 reaction. (Remember, anything that does not affect the rate determining step will not affect the rate of a reaction.)

Therefore, no, an $S_N 1$ reaction does *not* require a good nucleophile. An $S_N 1$ reaction can work, even with a poor nucleophile.

Does nucleophile quality matter for the rate of an $S_N 2$ reaction?

Does an S_N2 reaction require a good nucleophile?

The nucleophile participates in the rate-determining step for $S_N 2$. Therefore, yes, nucleophile quality affects the rate of an $S_N 2$ reaction.

Therefore, yes, an $S_N 2$ reaction requires a good nucleophile. An $S_N 2$ reaction cannot work with a poor nucleophile.

$S_{\rm N}1$ REACTIONS

Problem (7d) continued

Can the following starting materials carry out an $S_N 2$ reaction? Can they carry out an $S_N 1$ reaction?

> SX2 SNI poor Nu

The neutral oxygen in water is a poor nucleophile. (You can see this from the table below.)

An $S_N 2$ reaction requires a good nucleophile, so, no, these starting materials cannot carry out an $S_N 2$ reaction.

An S_N1 reaction does *not* require a good nucleophile, so, yes, these starting materials *can* carry out an S_N1 reaction. Moral: An S_N1 reaction can work even with a poor nucleophile.

	poor Nu weak base	good Nu / weak base	good Nu / strong base		
	O with no formal charge	Cl', Br', I', 'CN, S', N ₃ '	0', N'		
	(water or alcohol)	or N, P, or S with no formal charge			
methyl α-carbon	no reaction	S _N 2	S _N 2		
1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon		
2° α-carbon	S _№ 1 major, E1 minor	S _N 2	E2		
3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2		

Which atoms are poor nucleophiles? Which atoms are good nucleophiles?

now to determine the meentalism for dikyr handes and thkyr sufformets						
	poor Nu weak base	good Nu (weak base	good Nu/ strong base			
	O with no formal charge	Cl [*] , Br [*] , I [*] , CN, S [*] , N ₃ [*]	0', N'			
	(water or alcohol)	or N, P, or S with no formal charge				
methyl a-carbon	no reaction	S _N 2	S _N 2			
1° α-carbon			Exception: E2 with t-butyloxide and 1° α-carbon			
2° α-carbon	S _N 1 major,	S _N 2	E2			
	E1 minor					
3° α-carbon	S _N 1 major,	S _N 1 major,	E2			
	E1 minor	E1 minor				

how to determine the mechanism for alkyl halides and alkyl sulfonates

The table above summarizes some common poor nucleophiles and good nucleophiles. Neutral oxygen (in water or alcohol) is a poor nucleophile.

The good nucleophiles are Cl⁻, Br⁻, I⁻, ⁻CN, S⁻, N₃⁻, O⁻, and N⁻. There are also some neutral atoms that are good nucleophiles: neutral N, neutral, P, and neutral S.

Notice that atoms with negative formal charges are usually good nucleophiles (a negative charge makes the atom eager to donate electrons), but that there are also some neutral atoms (N, P, and S) that are also good nucleophiles.

There are other nucleophiles, but the nucleophiles in the table are the most useful to learn about at this point in your course.

Problem (7e)

What is the "big obstacle" to an $S_N 2$ reaction?

The big obstacle to an $S_N 2$ reaction is steric hindrance that blocks the nucleophile from joining the α -carbon. The nucleophile must join the α carbon during the rate-determining step for $S_N 2$, so anything that hinders the nucleophile from joining the α carbon will slow down the rate of the $S_N 2$ reaction.

(Remember that "steric hindrance" refers to "things getting in each others' way".)

Rank the types of α carbons (1°, 2°, 3°, and methyl) in terms of the rate of an S_N2 reaction, from slowest to fastest. Explain your ranking.

For which types of α carbons does $S_N 2$ occur quickly enough to be a practical reaction? For which types of α carbons does $S_N 2$ occur too slowly to be practical?



 $S_N 2$ is fastest for a methyl α carbon because it has the least steric hindrance. $S_N 2$ is slowest for a 3° α carbon because it has the most steric hindrance.

 S_N2 is a practical reaction for methyl, 1°, and 2° α carbons. S_N2 is too slow to be practical for 3° α carbons.

Problem (7f)

Is steric hindrance that blocks the nucleophile from joining the α -carbon a big obstacle for an $S_N 1$ reaction? Why or why not?

In an $S_N 1$ reaction, the nucleophile does not join the α carbon during the rate-determining step. Therefore, steric hindrance that blocks the nucleophile is *not* a big obstacle to an $S_N 1$ reaction.

Problem (7g) Define: carbocation carbocation: a carbon with a positive formal charge Notice that a carbon with a δ^+ charge is *not* a carbocation.

Does an $S_N 1$ reaction have a carbocation intermediate?





Does an $S_N 2$ reaction have a carbocation intermediate? No, the α carbon in a $S_N 2$ reaction never becomes a carbocation. (Remember that a carbocation has a positive *formal* charge, not just a δ^+ .)

Are carbocations "happy" or "unhappy"? Carbocations have a formal charge. Therefore, carbocations are "unhappy". Also, a carbocation has an incomplete octet, which also makes the carbocation "unhappy".

Do carbocations have too few electrons, or too many? Carbocations have too few electrons.

Problem (7h)

Are carbon chains ("alkyl groups") electron-donating or electron-withdrawing? Carbon chains are electron-donating.

(In the video, we did not explain *why* carbon chains are electron-donating. You can find an explanation in your textbook.)

Do carbon chains help to stabilize or destabilize a carbocation? Why? A carbocation has too few electrons. Therefore, a carbon chain helps to <u>stabilize</u> the carbocation by donating electrons to the carbocation. Problem (7i)

Rank the types of carbocations (primary, secondary, tertiary, or methyl) from least stable to most stable. Justify your ranking.

What types of carbocations are stable enough to be formed during typical reaction mechanisms? What types of carbocations are usually too unstable to form?



A carbocation is unhappy because it has too few electrons. Carbon chains are electron-donating. Therefore, carbon chains can stabilize a carbocation by donating electrons to it. 3° carbocations are the most stable because they are surrounded by the most carbon chains. Methyl carbocations are the least stable because they are not connected to any carbon chains.

2° and 3° carbocations are stable enough to be formed in typical mechanisms. Methyl and 1° carbocations are too unstable to be formed in typical mechanisms.

We can say that "substitution with carbon chains stabilizes carbocations", or, for short, "substitution stabilizes carbocations".

Do **not** say "substitution stabilizes carbons". There is no particular reason for substitution with carbon chains to stabilize a neutral carbon or a negative carbon. Substitution with carbon chains stabilizes carbo**cations**, because carbocations have too few electrons, and because carbon chains are electron donating.

Do not say "substitution is good". Say "substitution (with carbon chains) is good *for carbocations*".

Problem (7j)

(a)



Carbon 1 is a tertiary carbocation, while carbon 2 is a secondary carbocation. Therefore, carbon 1 is more stable than carbon 2.

(b)

This is a trick question. Carbon 3 is tertiary, while carbon 4 is secondary, but that does not matter much, because carbon 3 and carbon 4 are both neutral. Carbons 3 and 4 have similar stability.

Moral: Do **not** say "substitution stabilizes carbons". There is no particular reason for substitution with carbon chains to stabilize a neutral carbon or a negative carbon. Substitution with carbon chains stabilizes carbo**cations**, because carbocations have too few electrons, and because carbon chains are electron donating.

Do not say "substitution is good". Say "substitution (with carbon chains) is good *for carbocations*".

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Problem (7k)

Rank the different types of α carbons (primary, secondary, tertiary, or methyl) from slowest S_N1 rate to fastest S_N1 rate. Justify your ranking.

For which types of α carbons does $S_N 1$ occur quickly enough to be a practical reaction? For which types of α carbons does $S_N 1$ occur too slowly to be practical?



 $3^{\circ} \alpha$ carbons are best for $S_N 1$ reactions because they form the most stable carbocations. Methyl α carbons are worst for $S_N 1$ because they form the least stable carbocations.

 S_N1 is a practical reaction for 2° and 3° α carbons. S_N1 occurs too slowly to be practical for methyl or 1° α carbons. (Later in the video we will learn an exception to this pattern.)

Notice that rule for the α carbon for $S_N 1$ reactions is the opposite of the rule for $S_N 2$ reactions: Substitution with carbon chains is good for an $S_N 1 \alpha$ -carbon; substitution with carbon chains is bad for an $S_N 2 \alpha$ -carbon.

Problem (71)

Why does the stability of the carbocation intermediate matter for an S_N1 reaction?

The carbocation intermediate is formed during the rate-determining step for $S_N 1$. Therefore, the stability of the carbocation intermediate matters for an $S_N 1$ reaction. (Remember, anything that affects the rate-determining step will affect the rate of the reaction.)

Why doesn't "the stability of the carbocation intermediate" matter for an $S_N 2$ reaction?

There is no carbocation intermediate formed during an $S_N 2$ mechanism. Therefore, carbocation stability is an irrelevant issue for a $S_N 2$ mechanism.

What is the big obstacle to an $S_N 1$ mechanism?

The big obstacle to $S_N 1$ is stabilizing the carbocation intermediate.

Anything that stabilizes the carbocation intermediate will speed up the rate of $S_N 1$.

Anything that destabilizes the carbocation intermediate will slow down the rate of S_N1.

Problem (7m) continued

Can these starting materials carry out an S_N1 mechanism? Why or why not? Can they carry out an S_N2 mechanism? Why or why not?

	H2O	+ ~~ U	-> Ski SX noreact	2		
	poor Nu	1°2				
		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates		
		(poor Nu) weak base	good Nu / weak base	good Nu / strong base		
		Owith no formal charge	Cl', Br', I', 'CN, S', N ₃ '	0', N'		
		(water or alcohol)	or N, P, or S with no formal charge			
\rightarrow	methyl α-carbon	(no reaction)	S _N 2	S _N 2		
-	1° α-carbon			Exception: E2 with t-butyloxide and 1° a-carbon		
1	2° α-carbon	S _N 1 major,	S _N 2	E2		
		E1 minor				
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2		
		E1 minor	E1 minor			

The table predicts that with a $1^{\circ} \alpha$ carbon (top row) and poor nucleophile (H₂O, left column), there will be no reaction.

There will be no $S_N 1$ reaction because a 1° α carbon cannot carry out an $S_N 1$ reaction, because a 1° α carbocation is too unstable to be formed.

There will be no $S_N 2$ reaction because the neutral oxygen in water is a poor nucleophile. $S_N 2$ requires a good nucleophile.

Problem (7n)
Why does the top left cell of the table predict "no reaction"?
how to determine the mechanism for alkyl halides an

	to	datamina	the	machanism	for	allad	halidae	and	allad	culfonatas	
JW	w	uciciliiiii	uic	meenamsm	101	alkyl	nanues	anu	aikyi	sunonates	

	poor Nu / weak base	good Nu / weak base	good Nu / strong base			
	O with no formal charge	Cl ⁻ , Br ⁻ , I ⁻ , CN, S ⁻ , N ₃ ⁻	0', N'			
	(water or alcohol)	or N, P, or S with no formal charge				
methyl a-carbon	(no reaction	S _N 2	S _N 2			
1° a-carbon			Exception: E2 with t-butyloxide and 1° a-carbon			
2° a-carbon	S _N 1 major,	S _N 2	E2			
	E1 minor					
3° a-carbon	S _N 1 major,	S _N 1 major,	E2			
	E1 minor	E1 minor				

There will be no S_N1 reaction in the top left cell because a methyl or 1° α carbon cannot carry out an $S_N 1$ reaction, because a methyl or $1^\circ \alpha$ carbocation is too unstable to be formed.

There will be no S_N2 reaction in the top left cell because S_N2 does not work with a poor nucleophile. $S_N 2$ requires a good nucleophile.

Why are there no S_N1 reactions predicted in the top row of the table?

There will be no $S_N 1$ reactions in the top row, because a methyl or $1^\circ \alpha$ carbon cannot carry out an $S_N 1$ reaction, because a methyl or $1^\circ \alpha$ carbocation is too unstable to be formed.

Why are there no $S_N 2$ reactions predicted in the bottom row of the table?

There will be no S_N2 reactions in the bottom row, because a 3° α carbon has too much steric hindrance to carry out an S_N2 reaction.

Why are there no $S_N 2$ reactions predicted in the left column of the table?

There will be no S_N2 reactions in the left column, because S_N2 does not work with a poor nucleophile. $S_N 2$ requires a good nucleophile.

Notice that $S_N 1$ can work with a poor nucleophile, so there are some $S_N 1$ reactions predicted in the left column of the table.

Problem (70)

FROM MEMORY: Write out the complete table for determining the mechanism for alkyl halides and alkyl sulfonates.

	poor Nu / weak base	good Nu / weak base	good Nu / strong base
	O with no formal charge	Cl, Br, I, CN, S, N ₃	0', N'
	(water or alcohol)	or N, P, or S with no formal charge	
methyl α-carbon	no reaction	S _N 2	S _N 2
1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
2° α-carbon	S _N 1 major,	S _N 2	E2
	E1 minor		
3° α-carbon	S _N 1 major,	S _N 1 major,	E2
	E1 minor	E1 minor	

how to determine the mechanism for alkyl halides and alkyl sulfonates

Memorize which atoms and ions go at the tops of the columns. Memorize which atoms and ions are poor nucleophiles, which are good nucleophiles, which are weak bases, and which are strong bases. Keep writing out the complete table till you can write it completely accurately from memory.

Answers for Video (7)



Remember that the molecule on the right does *not* change back and forth between the two resonance structures. Instead, the true structure of the molecule is a *blend* of the two resonance structures. Therefore, in the true structure, resonance allows the positive formal charge to *spread out* between two different carbons.

Remember that nature "prefers" charges to be spread out, rather than concentrated in a small area. Therefore, resonance stabilizes formal charges.

Problem (7q)

Rank the following types of carbocations from least stable to most stable: primary, secondary, tertiary, methyl, and primary with resonance stabilization.

What types of carbocations are stable enough to be formed during typical reaction mechanisms? What types of carbocations are usually too unstable to form?



Notice that ordinary 1° carbocations are too unstable to form. But a resonance-stabilized 1° carbocation can form easily!

For simplicity, we have not included 2° or 3° carbocations with resonance-stabilization in the ranking above. But, of course, 2° or 3° carbocations with resonance-stabilization would be even more stable and even easier to form than 1° carbocations with resonance-stabilization.

Problem (7r)

Rank the following types of α carbons from slowest S_N1 rate to fastest S_N1 rate: primary, secondary, tertiary, methyl, and primary with resonance stabilization

VIL Xº/4	2° Ll° L carbon K	. 3°
merry dearbon	d carbon that forms	d carbon
AKG. UGA	a resonance	fastest
slowest	stabilized	5.1 rate
SNIrate	Carbocation	- N

Notice that ordinary 1° α carbons cannot carry out an S_N1 mechanism. But a 1° α carbon that will form a resonance-stabilized carbocation can carry out an S_N1 mechanism easily.

Of course, $S_N 1$ will be even easier for a 2° or 3° α carbon that will form a resonance-stabilized carbocation, but these are left out of the ranking above for simplicity.

$S_{\rm N}1$ REACTIONS

Problem (7s)

Summarize the factors that affect the rate of $S_N 1$ and $S_N 2$ reactions.

rate-determining step: The slowest step in a reaction.

Anything that affects the rate determining step will affect the rate of a reaction.

Anything that does not affect the rate determining step will not affect the rate of the reaction.



Leaving group leaves the d-carbon

Leaving group quality matters for an $S_N 1$ reaction. An $S_N 1$ reaction requires a good leaving group.

Nucleophile quality does *not* matter for an $S_N 1$ reaction. An $S_N 1$ reaction does *not* require a good nucleophile.

The big obstacle to an $S_N l$ reaction is: stabilizing the carbocation



Leaving group quality matters for an $S_N 2$ reaction. An $S_N 2$ reaction requires a good leaving group.

Nucleophile quality matters for an $S_N 2$ reaction. An $S_N 2$ reaction requires a good nucleophile.

The big obstacle to an $S_N 2$ reaction is: steric hindrance that blocks the nucleophile from joining the α -carbon.

2° ~ 1° d carbon d carbon decarbon decarbon 2 2° < 1° L carbon d carbon carbon Learbon fastest slowest fastest slowest stabilized Sul rate S.2 rate Sulrate SNZ rate Carbocation

Make sure you have all the information on this page completely memorized!

You should be able to use the concept of the rate-determining step to explain each of the facts on this page.

Note that nucleophile quality *does* matter for the rate of an $S_N 2$ mechanism, but that **nucleophile quality does** *not* **matter for the rate of an S_N 1 mechanism**.

This is because the nucleophile participates in the rate-determining step for $S_N 2$, but the nucleophile does *not* participate in the rate-determining step for $S_N 1$.

Also note that *more* substituted α carbons are better for S_N1, because more substituted α carbons form more stabilized carbocations,

but *less* substituted α carbons are better for $S_N 2$, because less substituted α carbons have less steric hindrance.

Remember that the big obstacle for $S_N 1$ is stabilizing the carbocation, while the big obstacle for $S_N 2$ is steric hindrance.

Video (8)

Problem (8a)

Rank the following carbocations in order of increasing stability. (1 = least stable, 4 = most stable).



Label each cation as 1°, 2°, 3°, or methyl. Check whether each cation is resonance stabilized.

In the previous video we learned that the order of cation stability, from least stable to most stable is:

least stable carbocation						most stable Carbocation
methyl carbocation ,	l' carbocation ,	2° carbocation	J	resonance-stabilized 1° carbocation	>	3° carbocation

Although "resonance-stabilized 3° carbocation" was not included explicitly in this list, it should be obvious that a resonance-stabilized 3° carbocation will be even more stable than an ordinary 3° carbocation.

Problem (8b)

What is an example of a "solvolysis" reaction?

A S_N1 reaction using an H₂O or alcohol solvent as the nucleophile is an example of *solvolysis*. When the term solvolysis is used in your introductory ochem course, it will usually refer to an S_N1 reaction.

"Lysis" means "to break". So a *solv*olysis reaction uses the *solv*ent to break a molecule into two pieces. For example, an S_N1 reaction uses water or alcohol to break apart the α carbon and the leaving group.

Therefore, the following $S_N 1$ reaction using a H_2O solvent as the nucleophile is an example of a solvolysis reaction. The reaction uses water to break apart the α carbon (carbon 2) and the leaving group (the iodine).



Problem (8c) Which substrate undergoes the faster solvolysis reaction in H₂O? Why?



Substrate A undergoes the faster $S_N 1$ solvolysis reaction, because substrate A has a 3° α carbon, while substrate B has a 2° α carbon.

A 3° α carbon is better for S_N1 than a 2° α carbon because a 3° carbocation is more stable than a 2° carbocation.

A 3° carbocation is more stable than a 2° carbocation because a carbocation has too few electrons and carbon chains are electron-donating. Therefore, extra carbon chains help to stabilize a carbocation by donating electrons to the carbocation.

The starred (*) text is included for completeness, but is probably more information than you would need to provide for a full-credit answer if this question occurred on an exam.

Notice that the problem tells us to consider an S_N1 ("solvolysis") mechanism. Remember, the big obstacle to an S_N1 reaction is stabilizing the carbocation intermediate.

*

Problem (8d)

For the reactions below, which reaction will have the faster rate for an S_N1 mechanism? Or will the two reactions both occur at the same rate for S_N1 ? Justify your answer.



Reaction B has the faster $S_N 1$ rate because the α carbon (carbon 3) forms a resonance-stabilized carbocation.

The α carbon for Reaction A (carbon 4) forms a carbocation that does not experience any resonance stabilization.

The problem tells us to consider an $S_N 1$ mechanism for both reactions. Remember that "Et" means "ethyl", so "EtOH" is ethyl alcohol (CH₃CH₂OH).

A resonance-stabilized 2° carbocation (such as is produced in Reaction B) is preferred to a 2° carbocation without resonance-stabilization (such as is produced in Reaction A).

Notice that this problem never mentions the word "resonance". Be sure to consider resonance as an explanatory factor in ochem!

Here are some factors to consider when trying to predict an outcome in organic chemistry:

- 2. Resonance
- 3. Steric hindrance
- 4. Electronegativity
- 5. δ charges
- 6. Molecular geometry (e.g., tetrahedral or trigonal planar)

Problem (8e)

For the reactions below, which reaction will have the faster rate for an S_N1 mechanism? Or will the two reactions both occur at the same rate for S_N1 ? Justify your answer.



Reaction A has the faster $S_N 1$ rate because the α carbon (carbon 7) forms a resonance-stabilized carbocation.

The α carbon for Reaction B (carbon 10) forms a carbocation that does not experience any resonance stabilization.

The problem tells us to consider an $S_N 1$ mechanism for both reactions.

Reaction B forms a 2° carbocation.

Reaction A forms a 1° carbocation that is stabilized by three additional resonance structures (so that there are four resonance structures total for the carbocation).

From the previous video, we know that a 1° carbocation stabilized by one additional resonance structure would be more stable than a 2° carbocation. Clearly, a 1° carbocation stabilized by *three* additional resonance structures (such as is produced by Reaction A), is far more stable than a 2° carbocation (such as is produced by Reaction B).

least stable carbocation					most stable Carbocation
methyl carbocation ,	l° carbocation .	2° carbocation	resonance-stabilized J l° carbocation	2	3° carbocation

Problem (8f)

For the reactions below, which reaction will have the faster rate for an $S_N 2$ mechanism? Or will the two reactions both occur at the same rate for $S_N 2$? Justify your answer.

1

Reaction A: Nu	{ Reaction B: Nu
$\frac{B}{2} + \frac{LG}{Br} + \frac{CH_3O^{\circ}Na^{\oplus}}{CH_3OH}$	$\begin{cases} B S^{+} Br & CH_{3}O^{0} Na^{\oplus} \\ CH_{3}OH & CH_{3}OH \end{cases}$
E 1°L	SNZ L'E
carbon Z is 3°	carbon Z
more steric hindrance	15 2
at carbon Z	less steric hindrance
that can block the nucleophile	at carbon Z
from attacking carbon 3	that can block the nucleophile
clower SNZ	from attacking carbon 3
3.	Faster SNZ
Reaction B will	have the faster SNZ rate
because, for Reac hindrance that can	tion B, Carbon Z has less steric block the nucleophile from
attacking carbon	n D.

The problem tells us that the mechanism is $S_N 2$ for both reactions. The "big obstacle" to an $S_N 2$ mechanism is steric hindrance that blocks the nucleophile from joining the α carbon.

The α carbon is 1° for both reactions. Therefore, to find a *difference* between the reactions, we must compare the β carbons, rather than the α carbons. <u>The " β carbon" is defined as a carbon attached</u> to the α carbon.

The β carbon for both Reaction A and Reaction B is carbon 2. For Reaction A, the β carbon is 3°. For Reaction B, the β carbon is 2°. Therefore, the β carbon for Reaction A contributes more steric hindrance that can block the nucleophile from joining the α carbon than does the β carbon in Reaction B. Therefore, Reaction B has a faster S_N2 mechanism than Reaction A.

Notice that, while we usually focus on the steric hindrance from the α carbon, steric hindrance from the β carbon can also be a factor in slowing down an $S_N 2$ mechanism.

Compare this problem with problems (8c), (8d), and (8e). For an S_N1 mechanism, we focus on stability of the carbocation intermediate; for an S_N2 mechanism, we focus on steric hindrance.

Problem (8g)

For the reactions below, which reaction will have the faster rate for an S_N1 mechanism? Or will the two reactions both occur at the same rate for S_N1 ?



Both SNI reactions occur at the same rate. Reaction A has a better nucleophile than Reaction B. But nucleophile quality does not affect the rate for an SNI reaction, because the nucleophile does not participate in the rate-determining step for SNI.

The problem tells us to consider an $S_N 1$ mechanism for both reactions.

Notice that we do *not* use the table to determine the mechanism for this problem. (The table would tell us to consider an $S_N 2$ mechanism for Reaction A.)

We know from the table that neutral S is a better nucleophile than neutral O. (The table tells us that neutral O is a poor nucleophile, while neutral S is a good nucleophile.)

how to determine the mechanism for alkyl halides and alkyl sulfonates						
	(poor Nu) weak base	good Nu weak base	good Nu / strong base			
	O with no formal charge	Cl., Br., I., CN, S., N3	O', N'			
	(water or alcohol)	or N, P, or S with no formal charge				
methyl a-carbon	no reaction	S _N 2	S _N 2			
1° a-carbon			Exception: E2 with t-butyloxide and 1° a-carbon			
2° α-carbon	S _N 1 major, E1 minor	S _N 2	E2			
3° α-carbon	S _N 1 major,	S _N 1 major,	E2			
	El minor	E1 minor				

But we also know that nucleophile quality does not affect the rate of an S_N1 mechanism (because the nucleophile does not participate in the rate-determining step for S_N1)! Therefore, both reactions will occur at the same rate.

Moral: Nucleophile quality does *not* affect the rate of an S_N1 mechanism!
Problem (8h) Which is the better nucleophile, CH₃OH or CH₃SH? *Justify* your answer.



When comparing neutral nucleophiles, nucleophilicity increases as you move down a column of the periodic table. Sulfur is below oxygen in the periodic table, so CH_3SH is a better nucleophile than CH_3OH .

When comparing neutral nucleophiles, nucleophilicity increases as you move down a column of the periodic table. The reason is that larger atoms are more "polarizable" than smaller atoms.

Therefore, we can say that CH₃SH is a better nucleophile than CH₃OH, because S is more polarizable than O.

For most introductory ochem course, the above information is sufficient to receive full credit for exam problems comparing neutral nucleophiles from the same column of the periodic table. For more information about the "polarizability", and why polarizability affects nucleophilicity, consult your textbook.

Notice that this problem discusses the trend for *neutral* nucleophiles. The trend for comparing negative nucleophiles in the same column of the periodic table is more complicated. (It depends on the solvent.) For more information, consult your textbook.

Additional comment on using atomic size to compare nucleophile ability:

When comparing nucleophile ability for neutral nucleophiles from the same column of the periodic table, the key factor to focus on is *atomic* size. A larger *atom* is a better nucleophile.

This rule is based on the *atomic* size of *the specific atom that will be donating its electrons*. The rule does *not* refer to the size of the entire nucleophilic molecule as a whole.

A larger *atom* is a better nucleophile, but do not assume that a larger *molecule* will be a better nucleophile.

Problem (8i)

For the reactions below, which reaction will have the faster rate for an S_N^2 mechanism? Or will the two reactions both occur at the same rate for S_N^2 ?



The problem tells us to consider an S_N^2 mechanism for both reactions.

For this problem, we do *not* use the table to determine what mechanism to consider. (The table would tell you that Reaction B has "no reaction".)

We know from the table that neutral S is a better nucleophile than neutral O.

	(water or alcohol)	good Nu weak base Cl ⁻ , Br ⁻ , l ⁻ , CN, S ⁻ , N ₃ ⁻ or N, P, of S with no formal charge	good Nu / strong base O', N'
methyl α-carbon	no reaction	S _N 2	S _N 2
1° a-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
2° α-carbon	S _N 1 major, E1 minor	S _N 2	E2
3° α-carbon	S _№ 1 major, E1 minor	S _N 1 major, E1 minor	E2

how to determine the mechanism for alkyl halides and alkyl sulfonates

And we also know that nucleophile quality *does* affect the rate of an $S_N 2$ mechanism (because the nucleophile participates in the rate-determining step for $S_N 2$). Therefore, the reaction with the better nucleophile (Reaction A) will have the faster $S_N 2$ mechanism.

Compare this problem with problem (8g). Notice that nucleophile quality *does* affect the rate for an $S_N 2$ mechanism, but nucleophile quality does *not* affect the rate for an $S_N 1$ mechanism.

For full credit, we would probably have to explain *why* neutral sulfur is a better nucleophile than neutral oxygen. This topic is discussed on the next page.

Solution continues on next page

answer for Problem (8i) continued

For the reactions below, which reaction will have the faster rate for an $S_N 2$ mechanism? Or will the two reactions both occur at the same rate for $S_N 2$?



For full credit, we would probably have to explain *why* neutral S is a better nucleophile than neutral O. When comparing neutral nucleophiles in the same column of the periodic table, nucleophilicity increases as you move *down* the column. This is because, as you move down the column, the nucleophilic atoms get larger. Larger atoms are more "polarizable". And more polarizable atoms are more nucleophilic.

For most introductory ochem courses, the above information would probably be enough to receive full credit for this problem. For further explanation of the concept of "polarizability", consult your textbook.

						The
						pattern for
					1	neutral nucleophiles
				2 He 4.0026		
6 C	7 N		9 F	10 Ne	Smaller {	worse Nu, be cause less polar, zable
12.011	14.007	13.999	18.998	20.180	atoms {	
14 Si 28.085	15 P 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39.948		
32 Ge 72.630	33 As 74.922	34 Se 78.97	35 Br 79.904	36 Kr 83.798		
50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29	larger atoms	better Nu, because more polarizable

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Problem (8j)

For the reactions below, which reaction will have the faster rate? Or will the two reactions both occur at the same rate?

Justify your answer.



Both SNI reactions occur at the same rate. Reaction A has a better nucleophile than Reaction B. But nucleophile quality does not affect the rate for an SNI reaction, because the nucleophile does not participate in the rate-determining step for SNI.

The problem does not tell us what mechanism to consider. To determine the mechanism, first, compare the starting materials with the products. This indicates that both reactions appear to be substitution reactions, in which the nucleophile replaces the leaving group at the α carbon.

To determine whether the mechanism is $S_N 1$ or $S_N 2$, use the table. Both reactions use a 3° α carbon, so for both reactions we use the bottom row of the table. The nucleophile for Reaction A is neutral S, so for Reaction A we use the middle column of the table. The nucleophile for Reaction B is neutral O, so for Reaction A we use the left column of the table. So the table predicts that the major mechanism will be $S_N 1$ for both Reaction A and for Reaction B.

		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
		poor Nu / weak base () with no formal charge (water or alcohol)	good Nu / weak base Cl ⁻ , Br, I ⁻ , CN, S ⁻ , N ₃ ⁻ or N, P, ot Swith no formal charge	good Nu / strong base O', N'
	methyl α-carbon 1° α-carbon	no reaction	S _N 2	$S_N 2$ Exception: E2 with <i>t</i> -butyloxide and 1° α -carbon
	2° α-carbon	S _N 1 major, E1 minor	S _N 2	E2
\rightarrow	3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor ★	E2

The table tells us that neutral S is a better nucleophile than neutral O. But nucleophile quality does not affect the rate of an $S_N 1$ mechanism (because the nucleophile does not participate in the rate-determining step for $S_N 1$)! For full credit, your answer should specify that the mechanism is $S_N 1$!

Compare this problem with problem (8i). Notice that nucleophile quality *does* affect the rate for an $S_N 2$ mechanism, but nucleophile quality does *not* affect the rate for an $S_N 1$ mechanism.

Problem (8k)



By comparing the products and starting materials, we can see that both reactions are substitution reactions. To determine whether the substitution mechanism is $S_N 2$ or $S_N 1$, use the table, which tells us that the mechanism will be $S_N 2$.

		how to dete	rmine the mechanism for alkyl halides	and alkyl sulfonates
[poor Nu / weak base	good Nu / weak base	good Nu / strong base
		O with no formal charge	Cl, Br, I, CN, S, N3	0', N'
->		(water or alcohol)	or(N)(P)or S with no formal charge	
	methyl a-carbon	no reaction	(S _N 2)	S _N 2
-	1° α-carbon			Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon
	2° α-carbon	S _N 1 major,	S _N 2	E2
		E1 minor		
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

You can see from the table above that both neutral N and neutral P are considered "good" nucleophiles. To determine which is the *better* nucleophile, we must consider their positions in the periodic table, as discussed on the next page.

Solution continues on next page

answer for Problem (8k) continued



When comparing neutral nucleophiles in the same column of the periodic table, nucleophilicity increases as you move *down* the column. This is because, as you move down the column, the nucleophilic atoms get larger. Larger atoms are more "polarizable". And more polarizable atoms are more nucleophilic.

P is below N in the periodic table, so P is a better nucleophile than N.

Nucleophile quality affects the rate for an S_N^2 reaction (because the nucleophile participates in the rate-determining step). Therefore, S_N^2 proceeds faster for Reaction A than for Reaction B.

·						The pattern for thiles	
5 B	6 C		8 0	9 F	2 He 4.0026 10 Ne	smaller { worse Nu, be cause less polarizable	
10.81 13 Al 26.982	12.011 14 Si 28.085	13-907 (15 P 30-974	15.999 16 S 32.06	18.998 17 Cl 35.45	20.180 18 Ar 39.948		
31 Ga 69.723	32 Ge 72.630	33 As 74.922	34 Se 78.97	35 Br 79.904	36 Kr 83.798		
49 In 114.82	50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29	larger atoms better Nu, because more polarizabl	e

Compare this problem with problem (8j). Notice that nucleophile quality *does* affect the rate for an $S_N 2$ mechanism, but nucleophile quality does *not* affect the rate for an $S_N 1$ mechanism. **Be sure to mention in your answer that the mechanism will be** $S_N 2$ **! An answer that leaves out the mechanism is likely to lose credit.**



- (a) Rank the leaving groups in these compounds, from worst to best.
- (b) Which are good leaving groups and which are unacceptable leaving groups?

When comparing elements from the same column of the periodic table, leaving group ability increases as you move down a column.

Therefore, the ranking of the leaving groups is: F, Cl, Br, I

where fluorine is the worst leaving group, and iodine is the best leaving group.

We have learned that neutral Cl, Br, and I, and neutral sulfonates, are good leaving groups. Most other neutral atoms are not acceptable leaving groups.

So, for this problem, we classify neutral F as an unacceptable leaving group; and we classify neutral Cl, neutral Br, and neutral I as good leaving groups.

Memorize this trend: When comparing elements from the same column of the periodic table, leaving group ability increases as you move down a column.

Additional comments for Problem (81) on next page

additional comments for Problem (81)



As you move down a column of the periodic table, leaving group ability improves.

When comparing neutral nucleophiles, as you move down a column in the periodic table, nucleophilicity also improves.

Therefore, when comparing elements in the same column of the periodic table, the trend for neutral nucleophiles is the *same* as the trend for leaving groups.

It is *surprising* that, when comparing elements in the same column, the trend for neutral nucleophiles is the same as the trend for leaving groups. Nucleophiles are the "opposite" of leaving groups, in the sense that a leaving group is an electron receiver, while a nucleophile is an electron donor. Since nucleophiles and leaving groups are "opposites", we might have expected that the trend for neutral nucleophiles should be the opposite of the trend for leaving groups. Nevertheless, the experimental fact is that, when comparing elements from the same column, the trend for neutral nucleophiles is actually the same as the trend for leaving groups.

Since the trend for neutral nucleophiles is surprising, and is not what you might have predicted based on the trend for leaving groups, it is important to have the trend for neutral nucleophiles firmly memorized.

Problem (8m)

When comparing elements from the same column of the periodic table, leaving group ability increases as you move down a column. Give an *explanation* for this pattern.

When judging leaving group ability, it is usually best to focus on what the leaving group will look like *after* it leaves.



After each of the leaving groups shown above leaves, it gains a negative formal charge. The best leaving group will the atom that is best able to stabilize the negative charge it gains after leaving.

As you move down a column of the periodic table, atomic size increases.

When the leaving groups shown above leave the α carbon, they gain a negative formal charge. A larger atom has more space to spread out this negative charge.

Therefore, a larger atom is better able to stabilize the negative charge it gains after leaving.

Therefore, it is easier for a larger atom to leave the α carbon than for a smaller atom to leave the α carbon.

				2 He 4.0026		less space to spread out	O charge will the relatively	
6 C 12.011	7 N 14.007	8 0 15.999	9 F 18.998	10 Ne 20.180	smaller atom	the Ocharge after leaving	unstable	worselds
14 Si 28.085	15 P 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39.948			{ }	{ }
32 Ge 72.630	33 As 74.922	34 Se 78.97	35 Br 79.904	36 Kr 83.798		more space to	Ocharge will	
50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29	larger atom	Spread out the Ocharge after	be relatively stable	betterLGs
						leaving	1	

Summary: When comparing leaving groups *in the same column* of the periodic table, focus on atomic size. **Larger atoms are better able to spread out and stabilize the negative charge they gain after leaving, which makes it easier for them to leave the \alpha carbon in the first place. Therefore, larger atoms are better leaving groups.**

Additional comment on next page



Additional comment on using atomic size to compare leaving groups:

When comparing leaving group ability for elements from the same column of the periodic table, the key factor to focus on is *atomic* size. A larger *atom* is a better leaving group.

For a leaving group that consists of a group of more than one atom, this rule is based on the *atomic* size of *the specific atom that will be gaining electrons*. The rule does *not* refer to the size of the entire leaving group as a whole.

A larger *atom* is a better leaving group, but do not assume that a larger "group" of atoms will be a better leaving group.

We will discuss this distinction, between *atomic* size and the size of the entire leaving group as a whole, further in the comments after Problem (8q)

Problem (8n)

For the reactions below, which reaction will have the faster rate for an $S_N 1$ mechanism? Or will the two reactions both occur at the same rate for $S_N 1$?



Remember that "Et" means "ethyl", so "EtOH" is ethyl alcohol (CH₃CH₂OH).

The problem tells us that the mechanism will be $S_N 1$, so we do not use the table to determine the mechanism.

The leaving group participates in the rate-determine step for an $S_N 1$ mechanism, so leaving group quality affects the rate of a $S_N 1$ mechanism. So the reaction with the better leaving group will have the faster rate.

Bromine and iodine are in the same column of the periodic table. When comparing elements in the same column, leaving group ability increases as we move down the column.

				2 He 4.0026		less space to spread out	O charge will	
6 C 12.011	7 N 14.007	8 0 15.999	9 F 18.998	10 Ne 20.180	smaller	the Ocharge after leaving	unstable	worse LGs
14 Si 28.085	15 P 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39.948			{ }	{ }
32 Ge 72.630	33 As 74.922	34 Se 78.97	35 Br 9.904	36 Kr 83.798		more space to	Dehare will	
50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 26.99	54 Xe 131.29	larger	Spread out the Ocharge after	be relatively stable	betterLGs
						leaving	1	

Remember: The leaving group participates in the rate-determining step for both $S_{\rm N}1$ and $S_{\rm N}2$ mechanisms. Therefore, using a better leaving group will increase the rate for both $S_{\rm N}1$ and $S_{\rm N}2$ mechanisms.

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Problem (80)



The problem tells us to focus on an S_N 1 mechanism.

The only difference between the first molecule and the third molecule is the leaving group. Bromine and iodine are in the same column of the periodic table. When comparing elements in the same column, leaving group ability increases as we move down the column. Therefore, the first molecule has a faster S_N1 rate than the third molecule. (Remember that leaving group quality affects reaction rate for both S_N1 and S_N2 mechanisms.)

The only difference between the third molecule and the second molecule is the α carbon. For a $S_N 1$ mechanism, the more substituted α carbon has the faster rate (because it forms a more stabilized carbocation). Therefore, the third molecule has a faster $S_N 1$ rate than the second molecule.



Pay attention to the mechanism. For a $S_N 2$ mechanism, a 1° α carbon would be better than a 2°!

Problem (8p)

For the reactions below, which reaction will have the faster rate? 1°2, SNZ Or will the two reactions both occur at the same rate? Justify your answer.

bad

LG

Reaction A:
$$CH_3 CH_2 CL + N_3^{\circ} \rightarrow CH_3 CH_2 N_3 + Cl^{\circ}$$

Reaction B: $CH_3 CH_2 OH + N_3^{\circ} \rightarrow CH_3 CH_2 N_3 + OH^{\circ}$

Nu

By comparing the starting materials and products, we can see that, in Reaction A, carbon 2 acted as the α carbon, and the Cl acted as the leaving group; and, in Reaction B, carbon 2 acted as the α carbon, and the OH group acted as the leaving group. In both reactions, the N_3 substituted for the leaving group, so we can see that both reactions are substitution reactions. Use the table to determine that the mechanism is $S_N 2$, rather than $S_N 1$.

1

		how to dete	∇ rmine the mechanism for alkyl halides	and alkyl sulfonates
		poor Nu / weak base O with no formal charge (water or alcohol)	good Nu / weak base Cl., Br, I., CN, S., N ₃) or N, P, or S with no formal charge	good Nu / strong base O', N'
L	methyl α-carbon 1° α-carbon	no reaction	S _N 2	$S_N 2$ Exception: E2 with <i>t</i> -butyloxide and 1° α -carbon
\rightarrow	2° α-carbon	S _N 1 major, E1 minor	S _N 2	E2
	3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

Neutral Cl, Br, and I, and neutral sulfonates, are good leaving groups. Most other neutral atoms are not acceptable leaving groups. So Reaction A has a good leaving group (the chlorine), but we conclude that the neutral oxygen in the OH in Reaction B is *not* an acceptable leaving group. **Leaving group quality affects the rate of an S_N2 reaction** (because the leaving group participates in the rate-determining step). So Reaction A will be faster.

In fact, an S_N2 reaction *requires* a good leaving group (because the leaving group participates in the rate-determining step). Therefore, the rate of reaction B would be close to zero.

Remember: The leaving group participates in the rate-determining step for both S_N 1 and S_N2 mechanisms. Therefore, using a better leaving group will increase the rate for both S_N1 and S_N2 mechanisms.

Problem (8q)

(a) As you move down a column in the periodic table, does leaving group ability increase or decrease?

(b) When comparing neutral nucleophiles, as you move down a column in the periodic table, does nucleophilicity increase or decrease?



As you move down a column of the periodic table, leaving group ability improves.

When comparing neutral nucleophiles, as you move down a column in the periodic table, nucleophilicity also improves.

Therefore, when comparing elements in the same column of the periodic table, the trend for neutral nucleophiles is the same as the trend for leaving groups.

Recall that it is *surprising* that, when comparing elements in the same column, the trend for neutral nucleophiles is the same as the trend for leaving groups. Nucleophiles are the "opposite" of leaving groups, in the sense that a leaving group is an electron receiver, while a nucleophile is an electron donor. Since nucleophiles and leaving groups are "opposites", we might have expected that the trend for neutral nucleophiles should be the opposite of the trend for leaving groups. Nevertheless, the experimental fact is that, when comparing elements from the same column, the trend for neutral nucleophiles is actually the same as the trend for leaving groups.

Since the trend for neutral nucleophiles is surprising, and is not what you might have predicted based on the trend for leaving groups, it is important to have the trend for neutral nucleophiles firmly memorized.

Additional comment on next page



COMMENT ON COMPARING ELECTRONEGATIVITY

We have seen that, for the situations we have discussed in this video, the key factor to focus on was the atomic size of the elements.

Notice that we have not been focusing on the elements' electronegativities.

But, of course, there are other situations in which you *should* focus on electronegativity.

For example, when comparing different elements from the same *row* of the periodic table, you should usually focus on electronegativity.

In this video, we have focused on comparing leaving groups and nucleophiles with elements from the same *column* of the periodic table, because that tends to be more frequently tested than comparing leaving groups and nucleophiles with elements from the same row. But you should be able to find a discussion in your textbook of how to use electronegativity to compare reactivity for elements in the same row.

Furthermore, for completeness I will mention that there are some situations, different from the ones discussed in this video, in which you should focus on electronegativity, even when comparing different elements in the same column. This usually occurs when you are considering how well an element can stabilize the negative charge on a *nearby* atom, rather than on itself. For simplicity, however, we will not be discussing those situations in this video.

Additional comment on next page

WARNING ABOUT COMPARING ATOMIC SIZES

We have seen that, for the situations we have discussed in this video, the key factor to focus on was *atomic* size.

The trend for nucleophiles is based on the *atomic* size of the specific atom that donates electrons, not on the size of the entire nucleophilic molecule. For leaving groups that consist of more than one atom, the trend is based on the *atomic* size of the specific atom that receives electrons, not on the size of the entire leaving group as a whole.

For example, why is an alcohol a bad leaving group, while a sulfonate is a good leaving group?



Here is a common wrong answer:

Wrong answer: The sulfonate group is the better leaving group because it is bigger than the alcohol group.

This answer is *wrong*, because the size of the entire leaving group as a whole does not matter. Only the size of the *atom* that gains the negative charge matters. In an alcohol, the atom that gains the negative charge after leaving is an oxygen; and, in a sulfonate, the atom that gains the negative charge after leaving is *also* an oxygen. Since both groups place the negative charge on an oxygen, the size of the leaving group atom does *not* explain the different leaving group abilities of these two groups.

The *correct* explanation for why the sulfonate is the better leaving group is that, after the sulfonate group leaves, its negative charge will be *resonance stabilized*. This makes it easier for the sulfonate to leave the α carbon in the first place.

After the alcohol group leaves, its negative charge experiences no resonance stabilization. This explains why it is more difficult for the alcohol group to leave than for the sulfonate group to leave.

We discussed this resonance-based explanation in more detail in the " $S_N 2$ Reactions" video series.

Moral: The trends discussed in this video depend on the *atomic* size of the specific atom that is gaining or receiving electrons, not on the size of the entire leaving group or nucleophilic molecule as a whole.

S_N1 REACTIONS

<u>Review Quiz</u>

What are the names of the five main roles in organic chemistry? What are the definitions for each of these roles?

Nucleophile: donates electrons to join an electrophile Electrophile: receives electrons to join a nucleophile Leaving group: receives electrons to leave an atom

Base: donates electrons to take a H^+ from an acid Acid: receives electrons to give a H^+ to a base

Be sure that you have the *complete* "two-part" definitions memorized.

For example, don't just say that a nucleophile "donates electrons". Say, a nucleophile "donates electrons to join the electrophile".

Similarly, don't just say a base "takes a proton". Say, a base "donates electrons to take a proton".