S_N2 REACTIONS Answers document

Step-by-step discussions for each of these answers are available in the "S_N2 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)

(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

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Does nature "like" or "dislike" charges? Dislike
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Does nature "prefer" atoms to be charged or neutral? Neutral

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

Which atoms are most likely to participate in a reaction? Usually, the atoms with formal charges (There are some exceptions to this rule.)

(1b)

What types of formal charges are likely to go at the beginning, middle, and end of a series of electronpushing arrows?



The charges in this answer refer to *formal* charges, not to δ charges.

These rules will work for the vast majority of reactions in introductory ochem, but there are a few exceptions.

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(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?

Later, you will learn additional clues for identifying which atoms in the starting materials can play which roles.

Origin of the term "electrophile":

The suffix "phile" means "liker" or "lover". So "electrophile" means "electron-lover". Since an electrophile wants to *receive* electrons, it is appropriate to imagine that it "likes" electrons.

Origin of the term "nucleophile":

A nucleus has a positive charge. Therefore, the term "nucleophile" can be interpreted as "positivelover". A nucleophile wants to donate electrons, and it is easier to donate electrons to something with a positive charge. Therefore, a nucleophile wants to react with something that is positive, so it is appropriate to think of a nucleophile as a "positive-lover".

In the S_N^2 reactions in this video series, the nucleophiles will react electrophiles with a *partial* positive (δ^+) charge. Later in the course, you will see many examples of nucleophiles that react with electrophiles that have a positive *formal* charge. In both cases, it is appropriate to think of the nucleophile as a "positive-lover", since it likes to react with atoms that have either a partial positive a full positive charge.

We have also identified α -carbons, using this rule: **The** α -carbon is the carbon attached to the leaving group. This is the definition of " α -carbon" that is useful at this point in the course.

Video (2)

Problem (2a) How many steps are there in an S_N^2 reaction? There is one "main step" in an S_N^2 reaction. (Occasionally there may also be an acid/base "helper" step.)

What happens in that step? In the single step for an $S_N 2$ reaction, the nucleophile joins α carbon, and the leaving group leaves the α carbon. These two things happen *simultaneously*, in the same step.

Problem (2b)



The Br⁻ is the nucleophile. Clue: It has a negative formal charge.

The neutral Cl is the leaving group. Clue: We have memorized that neutral Cl is a good leaving group.

Carbon 2 is the electrophile. Clue: It has a δ^+ .

(Here's how we know that carbon 2 is δ^+ . Chlorine is to the right of carbon in the periodic table. So chlorine wants electrons more than carbon does. So the electrons in the covalent bond will be pulled closer to the chlorine and further from carbon 2. This leaves carbon 2 with a δ^+ charge.)

The most important tool for drawing reasonable electron-pushing arrows is the formal charges. 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 our mechanism above, the first atom (the Br⁻) is negative.

The atom in the middle of the series of arrow should always be neutral. In our mechanism above, the middle atom (carbon 2) is indeed neutral.

The atom at the end of the series of arrows should always be positive or neutral, never negative. In our mechanism above, the last atom (chlorine) is neutral.



Always check that your electron-pushing arrows for any mechanism step are consistent with the above rules.

Answers for Video (2)

S_N2 REACTIONS

Problem (2c) When you are drawing the products of a mechanism step, what is the most important part of the products to get right? The formal charges.

How many formal charges should you change for each mechanism step? You should change **two** formal charges for each mechanism step.

How do you know which two formal charges to change for each mechanism step? For each mechanism step, always change formal charges for:

For each mechanism step, always change formal charges for:

the atom that loses electrons at the **beginning** of the series of arrows

(which becomes one step less negative),

and the atom that gains electrons at the end of the series of arrows

(which becomes one step more negative).

Never change the formal charge for an atom in the *middle* of the series of arrows.

Checklist of things to do for each reaction

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

These numbers are for your personal reference, not for IUPAC naming, so it doesn't matter whether you number from right to left or from left to right.

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. Don't begin drawing the products until you have finished drawing the electron-pushing arrows.

4. Draw the products.

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

The purpose of the numbers is to show you which carbons in the products are the same as which carbons in the starting materials.

Problem (2d)



The iodide is the nucleophile. Clue: it has a negative formal charge.

The neutral bromine is the leaving group. Clue: We have memorized that neutral bromine is a good leaving group.

Carbon 3 is the electrophile. Clue: it has a δ^+ .

Problem (2e)

In the name " S_N 2" reaction:

what does the letter S stand for? Substitution

what does the letter N stand for? Nucleophilic

Does the number 2 in the term " S_N 2" mean that there are two steps in an S_N 2 reaction? No, there is only one main step in an S_N 2 reaction.

We will learn the meaning of the number 2 in the name "S_N2", later in this video series.

Review Quiz

Define the following terms: nucleophile, leaving group, electrophile

Nucleophile: donates electrons to join the electrophile

Leaving group: receives electrons to leave an atom

Electrophile: receives electrons to join the nucleophile

Video (3)

(3a)

When a nucleophile attacks an atom that is attached to a leaving group, from what direction(s) does the nucleophile attack? The nucleophile will attack from the side *opposite* to the leaving group.



When an $S_N 2$ reaction occurs at an α -carbon that is a stereocenter,

what will be the stereochemistry of the product(s)?

The product of the S_N ² reaction will have *inversion* of configuration at the α -carbon.

What is the definition of the term "stereocenter"?

A *stereocenter* is a carbon that is attached to 4 *different* groups.

For example, in the starting material above, carbon 2 is attached to 4 different groups: a chlorine, a methyl group, an ethyl group, and a hidden hydrogen. Therefore, carbon 2 is a stereocenter. On the other hand, two of the "groups" attached to carbon 3 are identical: two identical hidden hydrogens. Therefore, carbon 3 is *not* a stereocenter.

(3b)



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$S_N 2 \text{ REACTIONS}$

<u>Review Quiz</u> How many steps are there in an S_N2 reaction? There is one main step. (Later, you may also see S_N2 reactions that also involve an acid/base "helper" step.)

What happens in that single step? The nucleophile joins the α carbon and, simultaneously, the leaving group leaves the α carbon

Video (4)

Problem (4a) Define: ionic bond An ionic bond is based on the attraction between a negative and a positive formal charge.

Define: covalent bond A covalent bond is based on the *sharing* of electrons.

How can you detect whether a bond in the starting materials is covalent or ionic? Covalent bonds tend to form between atoms with relatively small electronegativity differences. Therefore, covalent bonds tend to form between a nonmetal and a nonmetal.

Ionic bonds tend to form between atoms with large electronegativity differences. Therefore, ionic bonds tend to form between a metal and a nonmetal.

Where do you find metals and nonmetals in the periodic table? Metals on the left, nonmetals on the right.

Which two metals commonly appear in the starting materials for $S_N 2$ reactions? Na⁺ and K⁺ (sodium and potassium ions)

Is hydrogen a metal or a nonmetal?

What do you need to know about the electronegativity of hydrogen?

Despite its position on the far left of the periodic table, hydrogen is a *nonmetal*.

Despite its position on the far left of the periodic table, the electronegativity of hydrogen is very similar to the electronegativity of carbon.

How do you determine the formal charges for the starting materials for a reaction? When atoms in the starting materials are covalently bonded, any formal charges will usually be drawn for you.

When atoms in the starting materials are ionically bonded, you usually need to draw the formal charges yourself.

Problem (4b)

Suppose each of the following is provided as the starting material for a reaction. Draw in any necessary formal charges.



We have also indicated some possible nucleophiles and leaving groups in the above reactants. Not all possible roles are indicated.

Any bond represented by a solid line, or by a dashed line, or by a wedge, is *covalent*. Ionic bonds are never represented by a solid line, or by a dashed line, or by a wedge. (There may be some rare exceptions to these rules.)

NaCN is "sodium cyanide". The ⁻CN ion by itself is called "cyanide".

Problem (4c) What atoms in the starting materials are most likely to participate in the reaction? What roles do metals with positive charges play in reactions?

The atoms with formal charges are usually the most likely to participate in reactions. **EXCEPTION: Metals with positive formal charges (such as Na⁺ and K⁺) are usually "spectator ions" which do** *not* **participate in the reaction.**

Problem (4d)



The metal-nonmetal bond between Na and I is ionic. Na is a metal, from the far left of the periodic table, that is willing to give up electrons. I is a nonmetal, from the right of the periodic table, that wants to gain electrons. So in the ionic bond, we expect the electrons to be transferred from Na to I. Therefore, the Na in the ionic bond has a postive formal charge, and the iodine in the ionic bond has a negative formal charge. *Draw in the formal charges*.

The iodine plays the role of nucleophile. Clue: It has a negative formal charge.

Notice that, if we had not noticed the ionic bond, we would have no good reason to treat the iodine as a nucleophile.

The Na⁺ is an unreactive spectator that does not participate in the reason. Clue: metals with positive formal charges are unreactive spectator ions.

Checklist of things to do for each reaction

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. Draw electron-pushing arrows. Don't begin drawing the products until you have finished drawing the electron-pushing arrows.

5. Draw the products.

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

(4e)



When do you break an ionic bond? You should break an ionic bond when one of the atoms in the ionic bond loses its formal charge.

Which covalent bonds do you break? All covalent bonds at an arrow tail.

Which covalent bonds do you not break? All covalent bonds that are not at an arrow tail.

Review Quiz

What is the most important tool for drawing the correct electron-pushing arrows? Formal charges.

What types of formal charges are likely to go at the beginning, middle, and end of a series of electronpushing arrows?



These rules work for the great majority of reactions in introductory ochem. There are a few exceptions.

Video (5)

Problem (5a)

Define: primary carbon, secondary carbon, tertiary carbon, methyl carbon

A 1° carbon is a carbon attached to 1 carbon chain.

A 2° carbon is a carbon attached to 2 carbon chains.

A 3° carbon is a carbon attached to 3 carbon chains.

A "methyl" carbon is a carbon attached to zero carbon chains.

Label *all* of the carbons in each molecule as primary, secondary, tertiary, or methyl. Label the α carbons. Are the α carbons primary, secondary, tertiary, or methyl?



Problem (5b)

How do you determine whether the mechanism for a reaction will be S_N2, S_N1, E2, or E1? For most courses, the best approach for determining the mechanism is to use this table: how to determine the mechanism for alkyl halide and alkyl sulfonate electrophiles

	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				

In this table, the term "a-carbon" refers to the carbon attached to the leaving group.

The table shows the major reactions for each situation. There may also be significant minor reactions.

This table will usually give the correct answer for most exam problems for most introductory ochem courses.

But there may be some problems in some courses for which the table gives an incorrect answer.

Problem (5c)



Do not *assume* that the reaction is S_N^2 . Use the table to show that the mechanism is S_N^2 : The α carbon is primary, so we use the *top row* of the table.

The ⁻CN nucleophile is found in the *middle column* of the table ("good nucleophile / weak base"). Therefore, the table predicts the mechanism for these starting materials is $S_N 2$.

	now to determine the mechanism for aikyl nalide and aikyl suitonate electrophiles					
		poor Nu / weak base	good Nu / <u>weak</u> 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	$\left(S_{N}2\right)$	S _N 2		
_	1° a-carbon		$\Big)$	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° a-carbon	S _N 1 major,	S _N 1 major,	E2		
		E1 minor	E1 minor			

Checklist of things to do for each reaction

	1.	Number	all	the	carbons	in	the	starting	materials.
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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. Draw electron-pushing arrows.

Don't begin drawing the products until you have finished drawing the electron-pushing arrows.

7. Draw the products.

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

$S_N 2$ REACTIONS

Problem (5d)



Do not *assume* that the reaction is $S_N 2$. Use the table to show that the mechanism is $S_N 2$: The α carbon is secondary, so we use the *second row* of the table.

The Br nucleophile is found in the *middle column* of the table ("good nucleophile / weak base"). Therefore, the table predicts the mechanism for these starting materials is $S_N 2$.

			\mathbf{v}	
		how to determine	the mechanism for alkyl halide and al	kyl sulfonate electrophiles
		poor Nu / weak base	good Nu / weak base	good Nu / strong base
		O with no formal charge	Cl ⁻ ,(Br ⁻ ,) ¹ , 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 $1^{\circ} \alpha$ -carbon
	2° α-carbon	S _N 1 major,	$(S_N 2)$	E2
\rightarrow		E1 minor	\smile	
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

Problem (5e)



The product could also be drawn using only bond-line notation, as shown:



Do not *assume* that the reaction is $S_N 2$. Use the table to show that the mechanism is $S_N 2$: The α carbon is primary, so we use the *first row* of the table.

The O⁻ nucleophile is found in the *right column* of the table ("good nucleophile / strong base"). [Notice that, for this problem, we use the *right* column (O⁻), not the left column (neutral O).] Therefore, the table predicts the mechanism for these starting materials is $S_N 2$.

		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 ⁻
4	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
	3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

Draw the structure of *tert*-butyl oxide.

tert-butyl oxide (CH3)3CO

The structure of *t*-butyl oxide is shown above. The structure is drawn, on the left, in bond-line notation, and, on the right, in condensed notation.

Problem (5f)

From memory: Write down the table for choosing between S_N2, S_N1, E2, and E1 reactions.

	now to determine the mechanism for arkyr hande and arkyr sufformate electrophines				
	poor Nu / weak base	good Nu / weak base	good Nu / strong base		
	O with no formal charge	Cl ⁻ , Br ⁻ , I ⁻ , CN, S ⁻ , N ₃ ⁻	O [.]		
	(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 halide and alkyl sulfonate electrophiles

In this table, the term " α -carbon" refers to the carbon attached to the leaving group.

Keep rewriting the table from scratch, until you can write down the table from memory completely accurately.

Be sure that you have also memorized the reagents at the top of each column (neutral O from water or alcohol in left column, O⁻ in right column; miscellaneous reagents like Cl⁻, Br⁻, etc. in middle column).

Problem (5g)



Do not *assume* that the reaction is $S_N 2$. Use the table to show that the mechanism is $S_N 2$: The α carbon is primary, so we use the *first row* of the table.

The O⁻ nucleophile is found in the *right column* of the table ("good nucleophile / strong base"). Therefore, the table predicts the mechanism for these starting materials is $S_N 2$.

		how to determine	the mechanism for alkyl halide and a	lkyl sulfonate electrophiles
ĺ		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 or P with no formal charge	\sim
. [methyl a-carbon	no reaction	S _N 2	$(S_N 2)$
\rightarrow	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
l		E1 minor	E1 minor	

Review Quiz

What clues have we learned so far for identifying when an atom will play the role of electrophile? $$$\int^+$$

What clues have we learned so far for identifying when an atom will play the role of leaving group? neutral el, Br, or I

What clues have we learned so far for identifying when an atom will play the role of nucleophile? \bigcirc formal charge

Video (6)

Problem (6a) What is a "solvent"? The *solvent* is the liquid that the other starting materials are dissolved in.

When should you use a solvent as a participant in a reaction?

Rule: You should usually use the solvent as a participant in the reaction only if there is no other starting material present that is more reactive for that role.

There are some exceptions to this rule which you will need to learn later in the course.



Water and alcohols are solvents that can be used as nucleophiles for S_N1 or bases for E1, but <u>only</u> if there is no <u>better</u> nucleophile or base present.

DMSO, acetone, and DMF are solvents that do not participate directly in S_N2, S_N1, E2, or E1 reactions.

Note that, in the structures above, "Me" stands for a "methyl" group, and "Et" stands for an "ethyl" group. For example, CH₃CH₂OH and EtOH are two different ways two represent the same molecule (common name, ethyl alcohol).

For another example, the structures on the right both represent the same molecule (DMF). (By the way, the "DM" in DMF stands for "dimethyl".)

What is the definition of an "alcohol"? An OH group connected to a carbon chain: ROH.

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Problem (6b)



how to determine the mechanism for alkyl halide and alkyl sulfonate electrophiles

		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 Swith no formal charge	good Nu / strong base O ⁻
	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
	3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

DMSO is a solvent that does not participate in $S_N 2$, $S_N 1$, E2, or E1 reactions, so we do not use the DMSO in the mechanism.

The wording of this problem does not require us to draw the electron-pushing arrows—we can get full credit just by drawing the correct product. Nevertheless, you *should* draw the electron-pushing arrow mechanism, because the mechanism is your *tool* for determining the correct product.

In general, at this point in the course, you should generally draw the mechanism for almost all problems, even when the problem does not require it, because the mechanism is your *tool* for thinking about the reaction for getting the right product.

Do not *assume* that the problems in this video will occur by $S_N 2$ reactions. Instead, for each problem, *use the table* to determine the mechanism (as shown above).

>



Water is a solvent that can be used as nucleophile for $S_N 1$ or base for E1, but <u>only</u> if there is no <u>better</u> *nucleophile or base present*.

S_N1 major,

E1 minor

E1 minor

E1 minor

S_N1 major,

3° a-carbon

The starting materials for this reaction include I^- , which is a better nucleophile than H_2O , so we use the I^- as the nucleophile in the reaction, rather than the H_2O .

We can guess that I⁻ is a better nucleophile than H_2O because I⁻ has a negative formal charge, while H_2O is neutral. And our table above confirms that I⁻ is a good nucleophile (because I⁻ is in the middle column of the table) while H_2O is a poor nucleophile (because H_2O is in the left column of the table).

E2

Problem (6d)



Water is a solvent that can be used as nucleophile for $S_N 1$ or base for E1, but <u>only</u> if there is no <u>better</u> *nucleophile or base present*.

In this problem, there are no nucleophiles present except for the H_2O , so for this problem we use H_2O as the nucleophile. This means we use the left column of the table. Our α carbon is 2°, so we use the middle row of the table. Therefore, the table predicts that the major mechanism for these starting materials will be S_N1 .

Problem (6e)



 CH_3OH is an alcohol. An alcohol is a solvent that can be used as nucleophile for S_N1 or base for E1, but <u>only</u> if there is no <u>better</u> nucleophile or base present.

The starting materials for this reaction include S⁻, which is a better nucleophile than alcohol, so we use the S⁻ as the nucleophile in the reaction, rather than the alcohol.

We can guess that S⁻ is a better nucleophile than alcohol because S⁻ has a negative formal charge, while the alcohol is neutral. And our table above confirms that S⁻ is a good nucleophile (because S⁻ is in the middle column of the table) while alcohol is a poor nucleophile (because alcohol is in the left column of the table).

H



Two different ways to draw the product are shown above. Either is correct.

			\downarrow	
		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 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	

We should recognize that this molecule is "DMF", a common solvent. DMF is a solvent that does not participate in $S_N 2$, $S_N 1$, E2, or E1 reactions, so we do not use the DMF in the mechanism. $N Me_z$

Problem (6g)



		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 ⁻
	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
	3° α-carbon	S _№ 1 major, E1 minor	S _N 1 major, E1 minor	E2
	To this talls the	4	h	-

Acetone is a solvent that does not participate in $S_N 2$, $S_N 1$, E2, or E1 reactions, so we do not use the acetone in the mechanism.

Review Quiz

When a nucleophile attacks an atom that is attached to a leaving group, from what direction(s) does the nucleophile attack? The nucleophile will attack from the side *opposite* to the leaving group.

When an $S_N 2$ reaction occurs at an α -carbon that is a stereocenter, what will be the stereochemistry of the product(s)? The product of the $S_N 2$ reaction will have *inversion* of configuration at the α -carbon.

Video (7)

Problem (7a)

So far in this video series, what neutral atoms have we learned that can function as good leaving groups?

We have learned that neutral Cl, Br, and I are good leaving groups.

The purpose of this video is to learn another neutral group that can function as a good leaving group: a sulfonate group.

Define the term "alkyl".

An *alkyl* group is a carbon chain attached to something else.

(Later in the course you can learn a more precise definition of this term.)

Give the general name for the functional group in each of the following molecules.



Each of the above is an *alkyl halide* (i.e., a carbon chain attached to a halogen).

Problem (7a) continued

What is the general structure of an alkyl sulfonate? Which part of the general structure is the "alkyl" group? Which part is the "sulfonate group"? How do you identify the α carbon in an alkyl sulfonate?



Each of the R groups above stands for a carbon chain.

In an alkyl sulfonate, the α -carbon is the carbon attached to the oxygen, *not* the carbon attached to the sulfur.

Give the general name for the functional group in each of the following molecules.

Label the α carbon in each molecule.



Each of the above is an *alkyl sulfonate* (i.e., a carbon chain attached to a sulfonate group).

In an alkyl sulfonate, the α -carbon is the carbon attached to the oxygen, *not* the carbon attached to the sulfur.

The bottom two structures above are two different ways of representing the *same* compound (toluene sulfonate).

Problem (7a) continued

How many oxygens are there in a sulfonate group? Three. A group with four oxygens is *not* a sulfonate. For example, the molecule on the right is *not* a sulfonate, because it has four oxygens in the group.

What neutral atoms have we now learned that are good leaving groups?

This table applies to what electrophiles?

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 O	
(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° α-carbon
2° a-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	

As you can see from the "title" at the top of the table, the table applies to *alkyl halide* and *alkyl sulfonate* electrophiles.

Problem (7b)



		(water or alcohol)	or N, P, or S with no formal charge	
h	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	

Don't *assume* that the reaction is $S_N 2$. Use the table to determine whether the reaction is $S_N 2!$

The starting material is an alkyl sulfonate. Remember that, in an alkyl sulfonate, the α -carbon is the carbon attached to the oxygen, *not* the carbon attached to the sulfur. Therefore, the α carbon for this problem is carbon 1.

The leaving group atom is the oxygen attached to carbon 1. Clue: We have learned that sulfonate groups are good leaving groups.

The electrophile is carbon 1. Clue: Carbon 1 has a δ^+ . (Here's how we know that carbon 1 is δ^+ : Oxygen is to the right of carbon in the periodic table. So oxygen wants electrons more than carbon. So the electrons in the covalent bond between oxygen and carbon 1 will be drawn closer to the oxygen and further from carbon 1, leaving carbon 1 with a δ^+ charge.)

The nucleophile is Br⁻. Clue: It has a negative formal charge.

Problem (7c)



how to det	ermine the m	echanism for	alkyl h	alide and a	lkyl sulf	onate electron	hiles
	er and the state and	to or a state a state a state				orrest or or ob	

		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° a-carbon		~	Exception: E2 with t-butyloxide and 1° a-carbon
->	2° a-carbon	S _N 1 major,	$(S_N 2)$	E2
		E1 minor	\bigcirc	
	3° a-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

Notice that this problem introduces a new nucleophile we haven't used earlier in the series, N_3^- .

So far in this video, we have learned that neutral sulfonate groups are good leaving groups, even though most other neutral atoms are not good leaving groups.

In the remainder of this video, we will learn *why* sulfonate groups are good leaving groups.

Problem (7d)

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

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

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

Does nature "prefer" charges to be concentrated or spread out? Spread out

Give the general names for the functional groups in each of the following molecules. Does each of the following have an acceptable leaving group?

>OH alcohol



The OH in an alcohol is *not* an acceptable leaving group. The sulfonate group in an alkyl sulfonate *is* an acceptable leaving group.

Problem (7d) continued

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

In the alcohol, the neutral alcohol group is not an acceptable leaving group. In an alkyl sulfonate the neutral sulfonate group *is* an acceptable leaving group. Explain why a neutral sulfonate is a good leaving group, while a neutral OH is not an acceptable leaving group.



After the sulfonate group leaves the α carbon, the negative formal charge on the sulfonate oxygen is stabilized by resonance (as shown above).

(Resonance stabilizes the negative charge by *spreading it out* between the three oxygens.) Therefore, it is relatively easy for the sulfonate group to leave the α -carbon. Therefore, the sulfonate group is a good leaving group.

In contrast, after the OH group in an alcohol leaves the α carbon,

there are no resonance structures for the ⁻OH

Therefore, the negative charge on the ⁻OH is not resonance stabilized

Therefore, it is relatively difficult for the alcohol OH group to leave the α -carbon.

Therefore, the alcohol OH group is *not* an acceptable leaving group.

The key ideas in this problem are summarized on the next page.

In summary:

Most neutral atoms are *not* acceptable leaving groups.

But the sulfonate group in an alkyl sulfonate *is* a good leaving group.

The reason is that, *after* the sulfonate group leaves, the negative charge on the oxygen will be stabilized by resonance.

This makes it relatively easy for the sulfonate group to leave the α carbon.

We usually judge leaving group ability by thinking about what the leaving group will look like *after* it leaves.

<u>Review Quiz</u>

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

How many formal charges should you change for each mechanism step? You should change **two** formal charges for each mechanism step.

How do you know which two formal charges to change for each mechanism step? For each mechanism step, always change formal charges for: the atom that loses electrons at the **beginning** of the series of arrows (which becomes one step less negative), and the atom that gains electrons at the **end** of the series of arrows (which becomes one step more negative).

Never change the formal charge for an atom in the *middle* of the series of arrows.

Video (8)

Problem (8a)



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 3 is a good leaving group,

but the neutral fluorine on carbon 2 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 3, rather than carbon 2, as our α carbon.

		poor Nu / weak base O with no formal charge	good Nu / weak base Cl., Br., I., CN, S., N ₃	good Nu / strong base O [.]
		(water or alcohol)	or N, P, or S with no formal charge	
1	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, E1 minor	(s.2)	E2
	3° α-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

For an $S_N 2$ reaction, we invert the configuration at the α carbon.

Therefore, since the starting material carbon 3 had chlorine on a wedge on hydrogen on a dash, we draw the product carbon 3 with bromine on a dash and hydrogen on a wedge.

We have determined that carbon 2 does not participate in the reaction, so we make no change to the configuration at carbon 2.

Moral: Neutral Cl, Br, or I, and neutral sulfonates, are good leaving groups. **Most other neutral atoms are** *not* **acceptable leaving groups.**
Problem (8b)



Should we use the neutral Cl or the neutral alcohol (OH) 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 1 is a good leaving group,

but the neutral alcohol on carbon 4 is *not* an acceptable leaving group.

Therefore, we should use the Cl as the leaving group, rather than the OH. Therefore, we should use carbon 1, rather than carbon 4, as our α carbon.

Be sure to keep the sulfur covalently bonded to carbon 5 in the product.

		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	S _N 2	S _N 2
-	1° α-carbon			Exception: E2 with t-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			

Moral: Neutral Cl, Br, or I, and neutral sulfonates, are good leaving groups. **Most other neutral atoms are** *not* **acceptable leaving groups.**

<u>Review Quiz</u>

Define the following terms: nucleophile, leaving group, electrophile Nucleophile: donates electrons to join the electrophile Leaving group: receives electrons to leave an atom Electrophile: receives electrons to join the nucleophile

Explain the origin of the term "electrophile".The suffix "phile" means "liker" or "lover".So "electrophile" means "electron-lover".Since an electrophile wants to *receive* electrons, it is appropriate to imagine that it "likes" electrons.

Explain the origin of the term "nucleophile".

A nucleus has a positive charge. Therefore, the term "nucleophile" can be interpreted as "positive-lover".

A nucleus wants to donate electrons, and it is easier to donate electrons to something with a positive charge. Therefore, a nucleophile wants to react with something that is positive, so it is appropriate to think of a nucleophile as a "positive-lover".

For the S_N^2 reactions that we have been studying, the nucleophile has been reacting with atoms that bear a *partial* positive (δ^+) charge. Later, you will see many examples of nucleophiles that react with carbons that have a positive *formal* charge. In both cases, it is appropriate to think of the nucleophile as a "positive-lover", since it likes to react with atoms that have either a δ^+ charge or a full positive charge.

Video (9)

Problem (9a) What is the definition of "nucleophile"? "Donates electrons to join an electrophile".

Draw the electron-pushing arrow for a nucleophile.

What clue have we learned so far for identifying a nucleophile? Negative formal charge

Problem (9b) What types of neutral atoms can be used as nucleophiles? A neutral atom with a lone pair can be used as a nucleophile. The neutral atoms typically used as nucleophiles are: oxygen, nitrogen, sulfur, and phosphorus (O, N, S, and P)

Exception: neutral Cl, Br, and I are not nucleophilic, despite having lone pairs. Of course, Cl⁻, Br⁻, and I⁻ *are* nucleophilic, because of their negative formal charges.

Nucle ophile: Jonates electrons to join an electrophile Nu E Clues: O formal charge Nu E neutral atom with a lone pair (O, N, S, P) Exception: neutral Cl, Br, and I are not nucleophilic

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Problem (9c) Which neutral atoms are considered "good" nucleophiles? Which neutral atoms are considered "poor" nucleophiles?

As you can see from the table below, neutral oxygen (O) is a "poor" nucleophile (good enough for $S_N 1$, but not good enough for $S_N 2$).

As you can see from the table, neutral nitrogen, neutral sulfur, and neutral phosphorus (N, P, and S) are "good" nucleophiles.

	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 <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 _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

how to determine the mechanism for alkyl halide and alkyl sulfonate electrophiles

Don't confuse neutral oxygen (O) with negative oxygen (O⁻)! You can see from the table that, while neutral oxygen is a poor nucleophile, negative oxygen is a good nucleophile (because O⁻ is in the right column of the table).

Problem (9d)

Summarize the definitions for nucleophile, electrophile, and leaving group. How do you draw the electron-pushing arrows for each of these roles? What are the clues we have learned so far in this video series for identifying these roles?

Electrophile: receives electrons to join a nucleophile Clue: St

Circled in red above is the new information we have added in this video.

Problem (9e)



The nitrogen is the nucleophile. Clue: It is a neutral atom with a lone pair.

The bromine is the leaving group. Clue: We have learned that neutral bromine is a good leaving group. (And we know that neutral bromine is *not* a nucleophile, despite its lone pair.)

Carbon 4 is the electrophile. Clue: it has a δ^+ charge.

The most common student mistake on this problem is forgetting to change the charge on the nitrogen from neutral to positive.

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

Because the nitrogen ends up with a positive formal charge, and the bromine ends up with a negative formal charge, it is conventional to draw them close to each other in an ionic bond in the answer.

Be sure to also continue to draw the nitrogen as covalently bonded to its three hydrogens in the product.

Do *not* invert the configuration at carbon 3. Carbon 3 is a stereocenter, but carbon 3 is not participating directly in the S_N^2 reaction, so there is no reason for the configuration at carbon 3 to change. We should continue to draw carbon 5 on a wedge in the product, as it was drawn in the starting materials.

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		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 ⁻	O [.]		
		(water or alcohol)	or(N), P, or S with no formal charge			
	methyl a-carbon	no reaction	$(S_N 2)$	S _N 2		
\rightarrow	1° α-carbon)	Exception: E2 with <i>t</i> -butyloxide and $1^{\circ} \alpha$ -carbon		
	2° a-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 (9e) solution continued on next page

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Problem (9e) continued



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 our mechanism above, the first atom (the nitrogen) is neutral.

The atom in the middle of the series of arrow should always be neutral. In our mechanism above, the middle atom (carbon 4) is indeed neutral.

The atom at the end of the series of arrows should always be positive or neutral, never negative. In our mechanism above, the last atom (the bromine) is neutral.



For every mechanism step, always check that your electron-pushing arrows are consistent with these rules.

Problem (9f)



The phosphorus is the nucleophile. Clue: It is a neutral atom with a lone pair.

The chlorine is the leaving group. Clue: We have learned that neutral chlorine is a good leaving group. (And we know that neutral chlorine is *not* a nucleophile, despite its lone pair.)

Carbon 4 is the electrophile. Clue: it has a δ^+ charge.

The most common student mistake on this problem is forgetting to change the charge on the phosphorus from neutral to positive.

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

Because the phosphorus ends up with a positive formal charge, and the chlorine ends up with a negative formal charge, it is conventional to draw them close to each other in an ionic bond in the answer.

Notice that the phosphorus is still bonded to three methyl groups in the product. The bonds between the phosphorus and the methyl groups are covalent, and we don't break a covalent bond unless an electron-pushing arrow specifically tells us to break it.

		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 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
\rightarrow		E1 minor	\bigcirc	
	3° α-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

Problem (9g)

What is the rule for determining when a mechanism is finished?

What is an important exception to this rule?

Rule: A mechanism is usually not finished until the "main" product has no formal charges.

Exception: The final product of an S_N^2 reaction using a neutral nucleophile has a positive formal charge, as illustrated in the problems in this video.

Problem (9h)



The sulfur is the nucleophile. Clue: It is a neutral atom with a lone pair.

The iodine is the leaving group. Clue: We have learned that neutral iodine is a good leaving group. (And we know that neutral iodine is *not* a nucleophile, despite its lone pair.)

Carbon 4 is the electrophile. Clue: it has a δ^+ charge.

The most common student mistake on this problem is forgetting to change the charge on the sulfur from neutral to positive.

			\downarrow	
		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 Swith 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
	press de la contracta de la contracta.	E1 minor	E1 minor	

<u>Review Quiz</u>

From memory: Draw the table for choosing a mechanism for alkyl halides and alkyl sulfonates.

	now to determine the meenanism for any i handes and any i 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 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	

Be sure that you have the *entire* table memorized, including the identify of the species at the top of each column (neutral O at the top of the left column, O^- and N^- at the top of the right column, etc.).

Video (10)

Problem (10a) Define: rate-determining step Rate determining step: The slowest step in a mechanism.

How do we use the rate-determining step to determine what factors will 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.

What is the rate-determining step for an $S_N 2$ reaction? There is only one step in an $S_N 2$ reaction. Therefore, that single step constitutes the "rate-determining" step.

Problem (10b)

Why does the term " S_N 2 reaction" have the number "2" in its name? What does the "2" stand for? " S_N 2 reaction" has the number "2" in its name because <u>two</u> species participate in the single rate-determining step. For example, in the following S_N 2 reaction, the two species that participate in the single rate-determining step are the Br⁻ and the chlorobutane.

The "2" does not stand for "two steps". Remember, an S_N2 has one main step, not two.



What do the "S" and "N" stand for in the term " S_N 2 reaction"?

"S" stands for "substitution", because we are *substituting* one group into the previous position of another group. For example, in the above $S_N 2$ reaction, we *substitute* the bromine into the previous position of the chlorine.

"N" stands for "nucleophilic", because, in an S_N^2 reaction, the thing that is substituted into the previous position of the other group is a *nucleophile*. For example, in the above S_N^2 reaction, the thing that is substituted into the previous position of the chlorine is the bromine, which is a *nucleophile*.

Answers for Video (10)

S_N2 REACTIONS

Problem (10c) Does the quality of the leaving group affect the rate for an $S_N 2$ reaction? Why? The leaving group participates in the rate-determining step for $S_N 2$. Therefore, yes, the quality of the leaving group affects the rate of an $S_N 2$ reaction. This means that using a better leaving group will increase the rate of an $S_N 2$ reaction.

Does an S_N^2 reaction require a good leaving group? Why? The leaving group participates in the rate-determining step for S_N^2 . Therefore, yes, S_N^2 requires a good leaving group. This means that an S_N^2 reaction will not work without an acceptable leaving group.

Can the following starting materials do an S_N2 reaction? Why?



No, the butane does not contain an acceptable leaving group. Therefore, these starting materials cannot do an $S_N 2$ reaction.

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

Problem (10d)

Does the quality of the nucleophile affect the rate for an S_N2 reaction? Why?

The nucleophile participates in the rate-determining step for $S_N 2$. Therefore, yes, the quality of the nucleophile affects the rate for an $S_N 2$ reaction. This means that using a better nucleophile will increase the rate of an $S_N 2$ reaction.

(Later, when you study S_N1 , you will learn that leaving group quality does *not* affect the rate for an S_N1 mechanism!)

Does an S_N2 reaction require a good nucleophile? Why?

The nucleophile participates in the rate-determining step for $S_N 2$. Therefore, yes, $S_N 2$ requires a good nucleophile.

(Later, when you study S_N1, you will learn that an S_N1 mechanism does *not* require a good leaving group!)

How can you distinguish between "poor" nucleophiles and "good" nucleophiles? By memorizing the information in this table:

	now to determine the meenanism for any mandes and any suffering		
	(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

The table tells us that the neutral O in H_2O or alcohol is a *poor* nucleophile. The table tells us that Cl⁻, Br⁻, I⁻, ⁻CN, S⁻, N₃⁻, O⁻, and N⁻ are *good* nucleophiles. The table also tells us that neutral N, P, and S are also *good* nucleophiles.

Answers for Problem (10d) continue on next page

Answers for Problem (10d) continued

Can the following starting materials do an S_N2 reaction?



You can see from the table that water is a poor nucleophile (left column of the table).

		poor Nu / weak base	good Nu / weak base	good Nu / strong base
		O with no formal charge	Cl ⁻ , Br ⁻ , I ⁻ , CN, S ⁻ , N ₃ ⁻	O ⁻
		(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° a-carbon	S _N 1 major,	S _N 1 major,	E2
		E1 minor	E1 minor	

 \downarrow how to determine the mechanism for alkyl halides and alkyl sulfonates

 $S_N 2$ requires a good nucleophile, but water is a poor nucleophile, so, no, these starting materials *cannot* do an $S_N 2$ reaction. (Instead, we can see from the table that these starting materials will do an $S_N 1$ reaction. It turns out that $S_N 1$ reactions do not require a good nucleophile.)

Problem (10e)

What is the "big obstacle" to $S_N 2$ reactions? The "big obstacle" to $S_N 2$ reactions is *steric hindrance* that blocks the nucleophile from joining the α carbon.

What does the term "steric hindrance" mean? *Steric hindrance* means: atoms getting in the way of other atoms

Why does steric hindrance that blocks the nucleophile affect the rate of an S_N^2 reaction? In an S_N^2 reaction, the nucleophile joins the α -carbon *during the rate-determining step*. Therefore, anything that makes it more difficult for the nucleophile to join the α carbon—such as steric hindrance—will affect the rate of an S_N^2 reaction.

Problem (10f)

Define the following:

Primary alpha carbon, secondary alpha carbon, tertiary alpha carbon, methyl carbon

A 1° carbon is a carbon attached to 1 carbon chain.

A 2° carbon is a carbon attached to 2 carbon chains.

A 3° carbon is a carbon attached to 3 carbon chains.

A "methyl" carbon is a carbon attached to zero carbon chains.

Determine whether the α carbons in each of the following are primary, secondary, tertiary, or methyl:



methy/ "H3Br L H3Br methyl L

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Problem (10g)

Rank the following, from slowest rate for $S_N 2$, to fastest rate for $S_N 2$:

Primary alpha carbon, secondary alpha carbon, tertiary alpha carbon, methyl carbon

Explain your ranking.

Methyl α carbons have the fastest rate for S_N2 because they have the least steric hindrance blocking the nucleophile from joining the α carbon.

 $3^{\circ} \alpha$ carbons have the slowest rate for $S_N 2$ because they have the most steric hindrance blocking the nucleophile from joining the α carbon.

Which types of alpha carbons cannot do S_N2 reactions? Why not?

Which types of α carbons can do $S_{\rm N}2$ reactions?

 3° alpha carbons cannot do $S_N 2$ reactions at a significant rate, because they have too much steric hindrance. This is why " $3^{\circ} \alpha$ carbon" is crossed out in the answer to the previous question above. $S_N 2$ reactions can work for methyl, 1° , and $2^{\circ} \alpha$ carbons.

Remember that these are facts about $S_N 2$ reactions. The effect of 1°, 2°, and 3° α carbons on *other* reactions, such as $S_N 1$ reactions, may be quite different.

Therefore do *not* say, "3° α carbons are bad."

Instead, say, " $3^{\circ} \alpha$ carbons are bad for $S_N 2$ reactions".

 $3^{\circ} \alpha$ carbons might be good for *other* reactions (such as $S_N 1$, which you will study later).

Problem (10h)

Can the following starting materials carry out an S_N2 reaction? Explain.



The α carbon is tertiary.

Tertiary α carbons have too much steric hindrance for an S_N2 reaction.

Therefore, no, these starting materials cannot carry out an $S_{\rm N}2$ reaction.

From the table, you could figure out that the major reaction for these starting materials will be $S_N 1$.

	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 (water or alcohol)	or N. P. or S with no formal charge	0
	methyl α-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,	S _N 2	E2
		E1 minor	~	
~	3° α-carbon	S _N 1 major,	(S _{N1} major,)	E2
7		E1 minor	E1 minor	

bow to determine the mechanism for alkyl halides and alkyl sulfonates

Problem (10i) Consider this table:

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 ⁻ , 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	

Why are there no entries for " $S_N 2$ " reactions in the bottom row of the table? Because tertiary α carbons have too much steric hindrance for $S_N 2$.

Why are there no entries for " $S_N 2$ " reactions in the left column of the table? Because $S_N 2$ requires a good nucleophile. The left column is for poor nucleophiles.

Problem (10j)

Summarize the factors that do and do not affect $S_N 2$ reactions that we have learned about in this video. Explain why each factor does or does not affect $S_N 2$.

Rate determining step: The slowest step in a mechanism.

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 affects the rate for an SNZ reaction. An SNZ reaction requires a good leaving group.

Nucleophile quality affects the rate for an SNZ reaction. An SNZ reaction requires a good nucleophile.

The "big obstacle"	to an SNZ reaction is sta	eric hindrance.
3 accorbon 2	2° L carbon < 1° L carbon &	c methyl d carbon
slowest rete for SNZ		fastest rate for SNZ

An S_N^2 reaction consists a single step. Therefore, that single step is the rate-determining step. The leaving group participates in the single rate-determining step for S_N^2 , so leaving group quality affects the rate for a S_N^2 reaction, and a S_N^2 reaction requires a good leaving group.

The nucleophile participates in the single rate-determining step for $S_N 2$, so nucleophile quality affects the rate for a $S_N 2$ reaction, so an $S_N 2$ reaction requires a good nucleophile.

The nucleophile joins the α carbon in the single rate-determining step for $S_N 2$. Therefore, steric hindrance that blocks the nucleophile from joining the α carbon is the "big obstacle" to an $S_N 2$ reaction. Therefore, $S_N 2$ is fastest for a methyl α carbon (least steric hindrance), and slowest for a 3° α carbon (most steric hindrance). In fact, $S_N 2$ is too slow to be a practical reaction for a 3° α carbon; therefore, $S_N 2$ reactions only work for methyl, 1°, and 2° α carbons.

Keep in mind that these are the patterns specifically for $S_N 2$ reactions. Later, you will learn that the patterns for $S_N 1$, E2, and E1 mechanisms can be quite different than for $S_N 2$.

Video (11)

Problem (11a)

What does the term "substrate" mean when referring to an $S_N 2$ reaction? In the context of $S_N 2$, $S_N 1$, E2, or E1 reactions, the term *substrate* refers to the starting material that contains the leaving group.

Problem (11b)

Choose the best substrate for an S_N^2 reaction.

Explain your choice.



Problem (11c)



Both carbon 2 and carbon 3 are attached to good leaving groups, so either is a possible α carbon. The problem tells us that we have "1 equivalent" of the nucleophile. This means that the starting materials contain equal amounts of the nucleophile and of the substrate. This means that there is only enough nucleophile to react with *one* of the α carbons, rather than with both.

(To react with both α carbons, we would need "2 equivalents" of nucleophile.)

Therefore, we have to choose whether to use carbon 2 or carbon 3 as the α carbon.

With either carbon 3 (a 1° α carbon) or carbon 2 (a 2° α carbon), our table predicts the mechanism with the neutral phosphorus nucleophile will be S_N2.

The big obstacle to $S_N 2$ is steric hindrance. Therefore, we prefer to use the less hindered α carbon. **Therefore, we prefer to use carbon 3 as the \alpha carbon** (a 1° α carbon is less sterically hindered than a 2° α carbon).

The most common student mistake on this problem is forgetting to change the charge on the phosphorus from neutral to positive.

Be sure to also continue to draw the phosphorus as covalently bonded to its three methyl groups in the product.

Do *not* invert the configuration at carbon 2. Carbon 2 is a stereocenter, but carbon 2 is not participating directly in the S_N2 reaction, so there is no reason for the configuration at carbon 2 to change. We should continue to draw the bromine on carbon 2 on a wedge in the product, as it was drawn in the starting materials.

	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 V	S _N 2
1° a-carbon		×	Exception: E2 with <i>t</i> -butyloxide and 1° α-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	

how to determine the mechanism for alkyl halides and alkyl sulfonates

Problem (11d)

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.



The problem *tells* us the mechanism will be $S_N 2$, so **we do not use the table** to determine the mechanism. (Our table would tell us that the *major* mechanism here will be E2, but $S_N 2$ might still be a *minor* mechanism.)

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

The α carbon is 2° for both reactions, so the α carbon provides the same steric hindrance in both cases.

We can define the " β carbon" to be: the carbon attached to the α carbon.

The β carbon for reaction A is "quaternary" (attached to 4 carbon chains),

while the β carbon for reaction B is tertiary.

Therefore the β carbon for reaction A provides more steric hindrance that could block the nucleophile from joining the α carbon than the β carbon for reaction B does. Therefore, reaction A will have the slower S_N2 rate, and reaction B will have the faster S_N2 rate.

Notice that, while we usually focus primarily on steric hindrance from groups attached to the α carbon, steric hindrance from groups attached to the β carbon can also play a role in slowing down an S_N2 reaction. (In fact, it turns out that, with a quaternary β carbon, the rate for S_N2 will be near zero).

Problem (11e)

By comparing the starting materials and products, we can see that, in Reaction A, carbon 1 acted as the α carbon, and the sulfonate group acted as the leaving group; and, in Reaction B, carbon 1 acted as the α carbon, and the OCH₃ group acted as the leaving group. So we can see that both reactions are substitution reactions. *Use the table* to determine that the mechanism is S_N2, rather than S_N1.

		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 sulfonate), but we conclude that the neutral oxygen in the OCH₃ in Reaction B is *not* an acceptable leaving group. Leaving group quality affects the rate of an $S_N 2$ reaction (because the leaving group participates in the rate-determining step). So Reaction A will be faster.



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.

Problem (11g)

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.



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

Problem (11h)

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.



The problem tells us that the mechanism will be $S_N 2$, so we do not use the table to determine the mechanism.

The leaving group participates in the rate-determine step for an $S_N 2$ mechanism, so leaving group quality affects the rate of a $S_N 2$ 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 the relatively	
6 C 12.011	7 N 14.007	8 O 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	Ocharge will	
50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 26.99	54 Xe 131.29	larger atom	Spread out the Ocharge after	be relatively stable	better LGs
						leaving	1	



				2 He 4.0026		neutral Aucitophico
6 C 12.011	7 N 14.007	80	9 F 18.998	10 Ne 20.180	smaller {	worse Nu, be cause less polar i zaure
14 Si 28.085	15 P 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39,948	1 {	
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	atoms	better Nu, because more polarizable

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.

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

The pattern discussed above is the pattern for neutral nucleophiles. The pattern for negative nucleophiles is more complicated. (It depends on the solvent.) For more information about comparing negative nucleophiles, consult your textbook.

answer continues on next page

Answer for Problem (11i), continued



Notice that the trend for comparing leaving groups from the same column of the periodic table is the *same* as the trend for comparing neutral nucleophiles from the same column. As you move down a column, leaving group ability improves, and nucleophile ability for neutral nucleophiles *also* improves.

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 (11j)

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.



The problem tells us to consider an S_N^2 mechanism for both reactions. We do *not* use the table to determine what mechanism to consider. (The table would tell you that Reaction A has "no reaction".)

As you can see from the table below, neutral oxygen (in the CH₃OH alcohol) is a poor nucleophile, while neutral sulfur (in the CH₃SH) is a good nucleophile.

Nucleophile quality matters for an S_N**2 reaction** (because the nucleophile participates in the ratedetermining step). Therefore, S_N2 proceeds much faster for Reaction B than for Reaction A. (S_N2 is so slow for Reaction A that we can say that S_N2 does not occur to any practical extent.)

(Later, you will learn that nucleophile quality does not affect the rate of an S_N1 mechanism!)

	over Nu) weak base	cl, Br, I, CN, S, N,	good Nu / strong base O'
methyl α-carbon 1° α-carbon	(water or alcohol)	or N, P, or S with no formal charge 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
3° a-carbon	S _N 1 major, E1 minor	S _N 1 major, E1 minor	E2

solution continues on next page

solution for Problem (11j) 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 ? Justify your answer.



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 courses, the information above would be sufficient for a full credit answer. For further explanation of the concept of "polarizability", consult your textbook.)



(The size of the nucleophilic *molecule* does *not* matter for nucleophilicity! Only the size of the nucleophilic *atom* matters. See the additional comments at the end of this video.)

Problem (11k)

For the reactions below, which reaction will have the faster rate? $>_{N} \angle$ Or will the two reactions both occur at the same rate? Justify your answer. Reaction A: $\begin{array}{c} 1\\ C\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ C\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ C\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ C\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c} 2\\ H_{3} \end{array} + \begin{array}{c} 2\\ H_{2} \end{array} + \begin{array}{c}$

methyl d carbons
$$\stackrel{X}{E}^{+}$$
 LG Nu
 $Reaction B: \stackrel{X}{\underset{E}{\overset{S^{+}}{\overset{L}{\overset{L}{}}}} H_{3} \underbrace{\Box}_{LG} \xrightarrow{\stackrel{Z}{\underset{Mu}{\overset{C}{}}} (CH_{3})_{2} \overset{1}{\overset{NH_{2}}{\overset{L}{}} + \underline{\Box}^{-}$

Use the table to determine that the mechanism is S_N 2. Notice that carbon 1 is a "methyl carbon", not a primary carbon. A methyl carbon is a carbon attached to zero other carbons.

how to determine the mechanism for alkyl halides and alkyl sulfonates						
Γ		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 t-butyloxide and 1° α-carbon		
	2° a-carbon	S _N 1 major,	S _N 2	E2		
		E1 minor	1455.5			
	3° a-carbon	S _N 1 major,	S _N 1 major,	E2		
		E1 minor	E1 minor			

			V				
how to dete	ermine the	mechan	nism	for al	kyl halides	and alky	l sulfonates

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 (11k), 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.

Nucleophile quality matters for an $S_N 2$ reaction (because the nucleophile participates in the ratedetermining step). Therefore, $S_N 2$ proceeds faster for Reaction A than for Reaction B.

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. (Later, you will learn that nucleophile quality does *not* affect the rate of an $S_N 1$ mechanism.)

				2 He 4.0026			patter neutro	n for Inucleop	, hiles		
6 C 12.011	7 N	8 O 15.999	9 F 18,998	10 Ne 20.180	smaller {	worseLGs	zwors	e Nu, be	cause les	s polariza	2610
14 Si 28.085	(15 P) 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39.948			$\left\{ \right\}$				
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	betterLG	s)bet	terNu, l	be cause n	nore polar	izable

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Problem (111)

(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?

				2 He			The pattern neutral	n for nucleophiles	
6 C 12.011	7 N 14.007	8 O 15.999	9 F 18.998	10 Ne 20.180	smaller { atoms {	worseLGs	3worse	e Nu, be cause less polar, Zabie	
14 Si 28.085	15 P 30.974	16 S 32.06	17 Cl 35.45	18 Ar 39,948	1 {		$\frac{1}{2}$		
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 LG.	s]bett	er Nu, be cause more polarizo	ible

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 comments on the next page

ADDITIONAL COMMENTS ON COMPARING ATOMIC SIZES

When comparing two different elements from the same column of the periodic table, the element with the greater *atomic* size will be the better leaving group.

Leaving group ability depends only the size of the *atom* which gains the negative formal charge when the leaving group leaves.

The size of the entire leaving group as a whole does *not* directly affect leaving group ability.

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.

Recall that 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 an earlier video in this series.

Moral:

Leaving group ability depends only the size of the *atom* which gains the negative formal charge when the leaving group leaves.

The size of the entire leaving group as a whole does *not* directly affect leaving group ability.

More comments on next page



Additional comments on comparing atomic size, continued

When comparing two different neutral elements from the same column of the periodic table, the element with the greater *atomic* size will be the better nucleophile, because it will be more polarizable.

This rule applies only to the size of the nucleophilic *atom*, not to the size of the entire nucleophilic *molecule*.

For example, CH₃SH is a bigger molecule than H₂S. But that fact does *not* imply that CH₃SH will be a better nucleophile than H₂S. The "polarizability" depends on the size of the nucleophilic *atom*, which is the same for both molecules (sulfur).

Moral: For neutral nucleophiles in the same column of the periodic table, a larger *atom* is a better nucleophile than a smaller atom. But do *not* assume that a larger *molecule* will be a better nucleophile than a smaller molecule.

More comments on next page

ADDITIONAL COMMENTS ON COMPARING ELECTRONEGATIVITY



We have seen that, when comparing leaving group ability for elements in the same column of the periodic table, the key factor is *atomic size*.

Notice that, when comparing leaving group ability for elements in the same column of the periodic table, we do *not* focus on the different *electronegativities* of the elements. (In fact, if you did focus on the atoms' electronegativity, you would get a different prediction for the trend in leaving group ability, a prediction which does not match the experimental data.)

Of course, there are many other situations where you *should* focus on electronegativity. For example, **you should usually focus on electronegativity when you are comparing two elements from the same** *row* **of the periodic table**.

But, when comparing leaving group ability for elements from the same *column* of the periodic table, the trend is based on atomic size, not on electronegativity.

Comments continued on next page

Additional comments on comparing electronegativity, continued



We have seen that, when comparing nucleophile ability for neutral nucleophiles in the same column of the periodic table, the key factor is *atomic size*, which determines the "polarizability" of the atom.

Notice that, when comparing nucleophile ability for elements in the same column of the periodic table, we do *not* focus on the different *electronegativities* of the elements.

(It does turn out that, for neutral nucleophiles in the same column of the periodic table, electronegativity would predict that nucleophilicity increases as you move down a column, which happens to agree with trend based on atomic size and polarizability. Nevertheless, the *main* reason for this trend is not based on the atoms' different electronegativities, but is instead based on the fact that larger atoms are more polarizable.)

Of course, there are many other situations where you *should* focus on electronegativity. For example, **you should usually focus on electronegativity when you are comparing two elements from the same** *row* **of the periodic table**.

But, when comparing nucleophile ability for neutral nucleophiles from the same *column* of the periodic table, you should focus on atomic size and polarizability, not on electronegativity.
Answers for Video (11)





Review Quiz

Label the "head" and "tail" of an electron-pushing arrow.

An electron-pushing arrow shows the movement of electrons

The formal charge on an electron is: (-)

Draw the electron-pushing arrow for a leaving group.

Leaving group: receives electrons to leave an atom

Draw the electron-pushing arrow for a nucleophile.

Nucleophile: donates electrons to join the electrophile

Draw the electron-pushing arrow for an electrophile.

The arrow for both a nucleophile and an electrophile is shown above.



