Iverson CH320N

Organic Chemistry is the study of carbon-containing molecules. This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing molecules on the planet!!

You will learn how MRI scans work.

You will learn the basic principles of pharmaceutical science and how many drugs work.

You will learn about the special bond that holds carbohydrates such as glucose in six-membered rings, connects carbohydrate monomers together to make complex carbohydrate structures and is critical to DNA and RNA structure.

You will learn how soap is made from animal fat and how it works to keep us clean.

You will learn the important structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life.

You will learn how important antibiotics like penicillins work, including ones that make stable covalent bonds as part of their mode of action.

You will learn why carrots are orange and tomatoes are red.

You will learn the very cool reason that the DNA and RNA bases are entirely flat so they can stack in the double helix structure.

You will learn how energy drinks work.

You will learn even more about why fentanyl is such a devastating part of the opioid problem and how Naloxone is an antidote for a fentanyl overdose.

You will learn even more details about why Magic Johnson is still alive, decades after contracting HIV, and how the same strategy is being used to fight COVID.

You will learn about the surprising chemical reason the Pfizer and Moderna mRNA vaccines elicit strong immune responses.

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds, especially carbon-carbon bonds.

You will learn how carbon-metal bonds lead to new carbon-carbon bonds.

You will learn how most reactions of carbonyl compounds involve only the four common mechanistic elements operating in only a few common patterns.

You will learn how, by simply adding a catalytic amount of base like HO^- to aldehydes or ketones, you can make new carbon-carbon bonds, giving complicated and useful products.

You will learn a reaction that can convert vinegar and vodka into a common solvent.

You will learn why molecules with six-membered rings and alternating double bonds are stable.

You will learn a reaction that can turn model airplane glue into a powerful explosive.

Most important, you will develop powerful critical thinking skills:

1. You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.
2. You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.

The ability to rationally synthesize new molecules changed human destiny and drives the economies of the world by enabling:

1. The synthesis of new drugs to cure disease, dramatically increase human life span and improve everyone's quality of life.
2. The development of lubricants and components for virtually all machines.
3. The creation of new methods for integrated circuit production enabling faster computation.
4. The creation of new materials for millions of uses including 3d printing and biodegradable plastics.
5. The synthesis of new pigments for dyes, paints and cosmetics.
6. The synthesis of all synthetic clothing fibers.
7. The production of highly refined and cleaner burning fuels.
8. The creation of batteries to store energy, the most important element of the renewable energy solution.
9. …to name just a FEW applications.

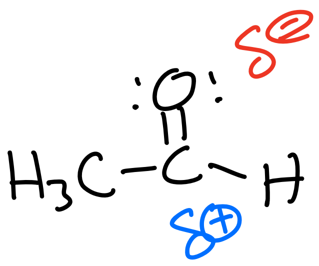
In other words, essentially everything that makes modern life so incredible!

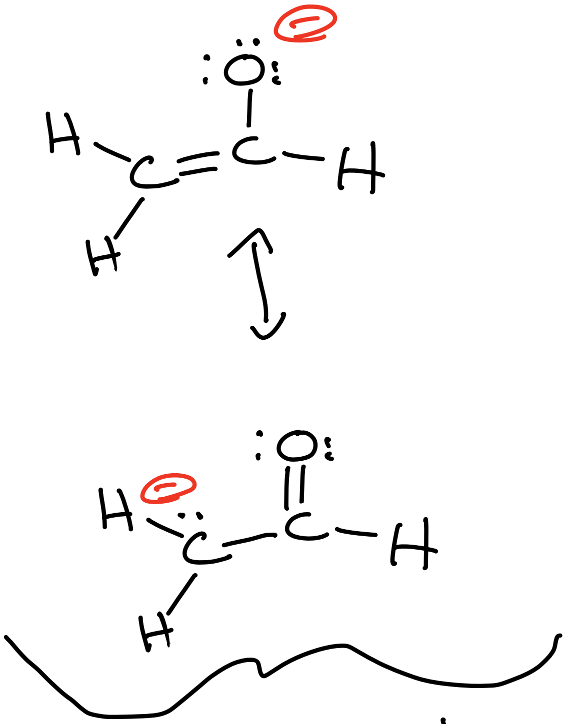
"You can't stop the waves, but you can learn to surf"

Jon Kabat-Zinn

You must understand not memorize the material. Looking for patterns instead of understanding will NOT work this semester!

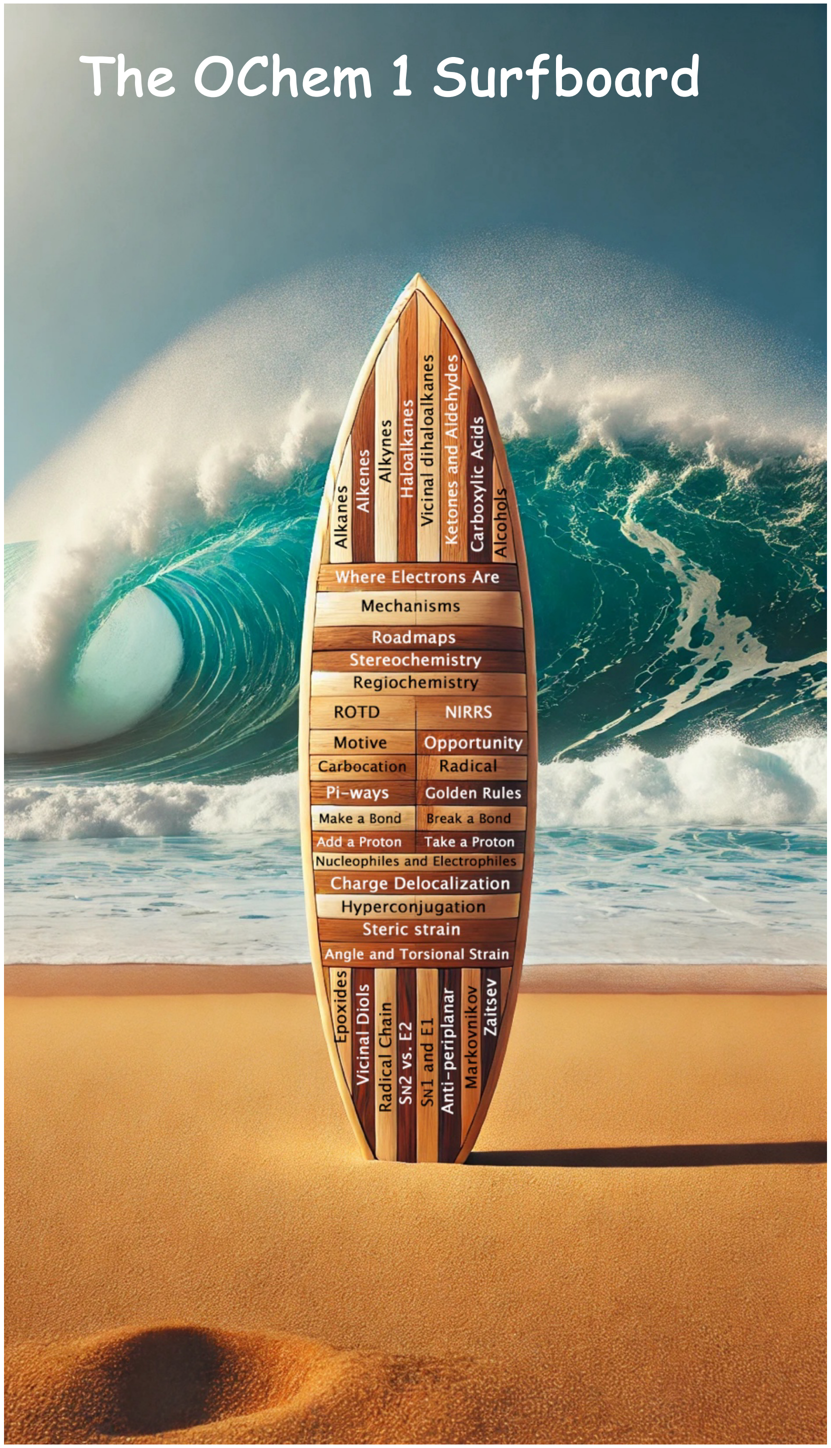
Where are the electrons? → The most important question in Chemistry and your key to understanding

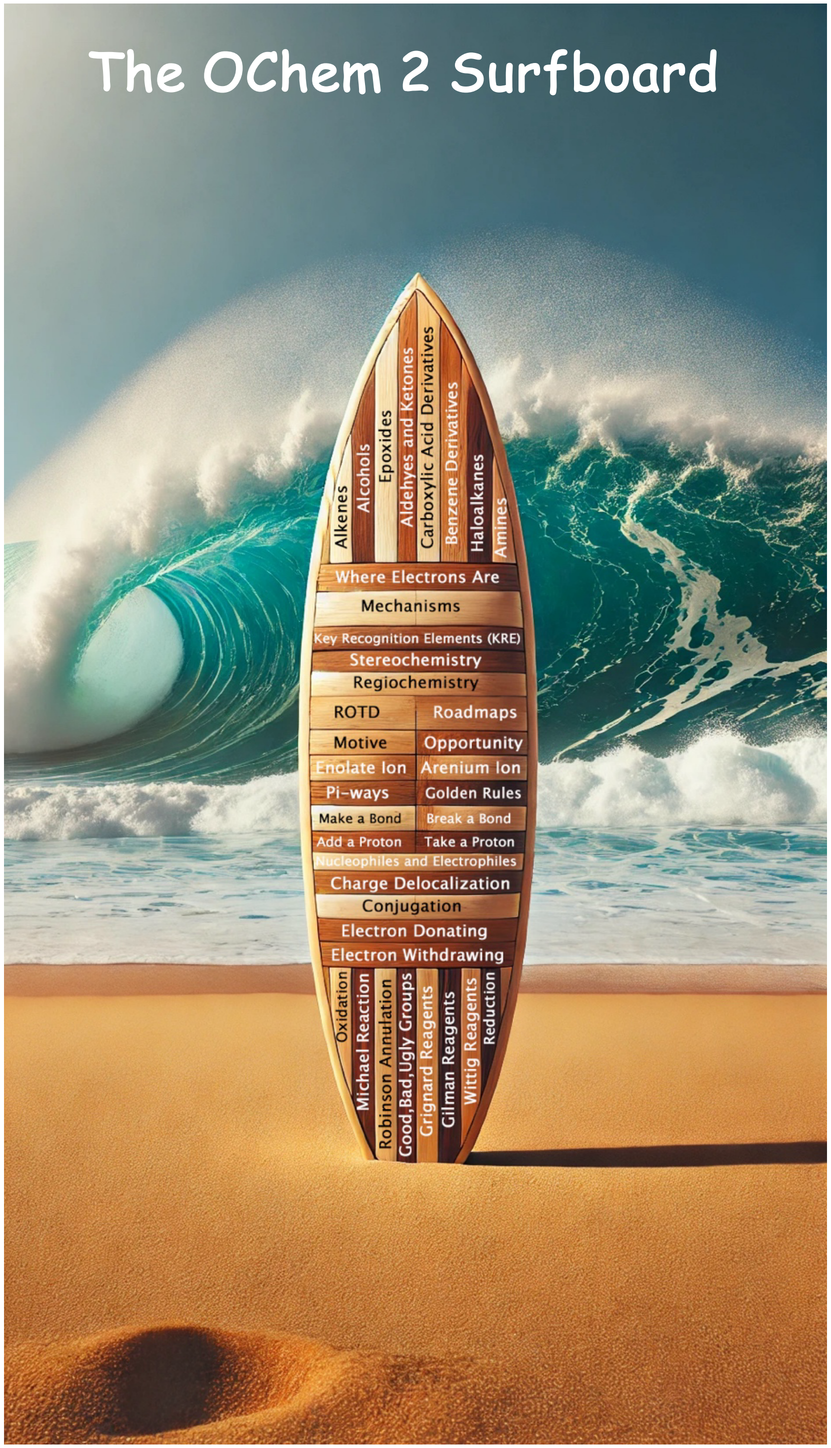


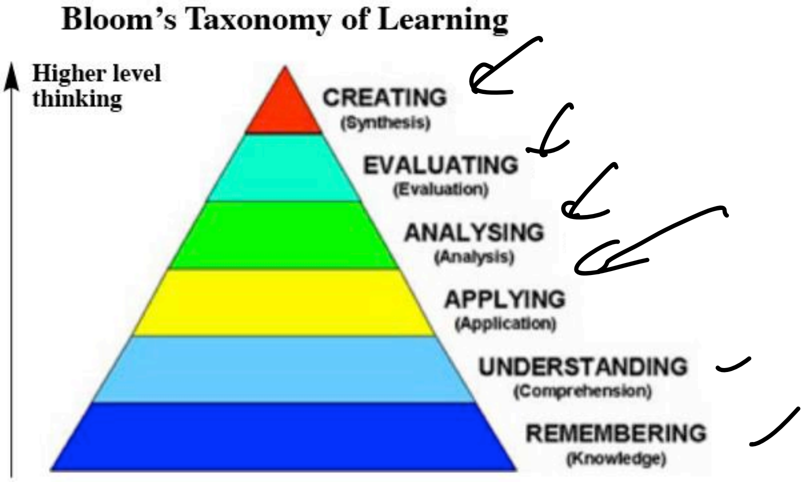


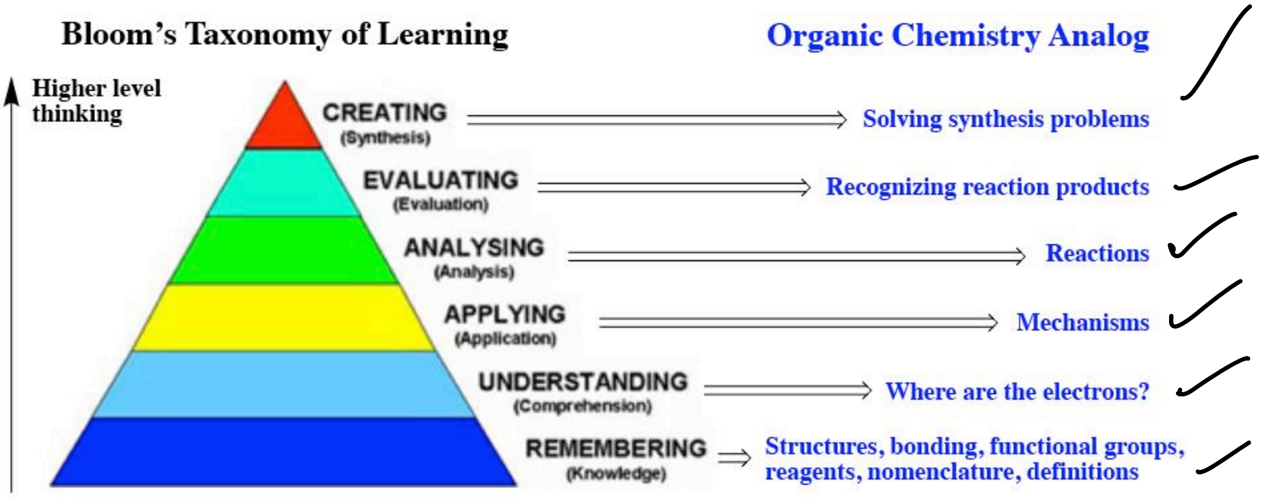
Defines the personality of these groups

The negative charge is on both the O and C atoms!


The OChem 1 Surfboard
Alkanes
Alkenes
Alkynes
Haloalkanes
Vicinal dihaloalkanes
Ketones and Aldehydes
Carboxylic Acids
Alcohols
Where Electrons Are
Mechanisms
Roadmaps
Stereochemistry
Regiochemistry
ROTD
NIRRS
Motive
Opportunity
Carbocation
Radical
Pi-ways
Golden Rules
Make a Bond
Break a Bond
Add a Proton
Take a Proton
Nucleophiles and Electrophiles
Charge Delocalization
Hyperconjugation
Steric strain
Angle and Torsional Strain
Epoxides
Vicinal Diols
Radical Chain
SN2 vs. E2
SN1 and E1
Anti-periplanar
Markovnikov
Zaitsev


The OChem 2 Surfboard
Alkenes
Alcohols
Epoxides
Aldehyes and Ketones
Carboxylic Acid Derivatives
Benzene Derivatives
Haloalkanes
Amines
Where Electrons Are
Mechanisms
Key Recognition Elements (KRE)
Stereochemistry
Regiochemistry
ROTD
Roadmaps
Motive
Opportunity
Enolate Ion
Arenium Ion
Pi-ways
Golden Rules
Make a Bond
Break a Bond
Add a Proton
Take a Proton
Nucleophiles and Electrophiles
Charge Delocalization
Conjugation
Electron Donating
Electron Withdrawing
Oxidation
Michael Reaction
Robinson Annulation
Good,Bad,Ugly Groups
Grignard Reagents
Gilman Reagents
Wittig Reagents
Reduction





A) **You must have your entire roadmap learned** so you can recite the NIRRS parameters for each reagent, i.e. Nature of overall transformation ("locations" on the roadmap), the Intermediate or transition state (carbocation, anti-periplanar etc.), the Reagents and how to designate them, as well as any Regiochemistry (Markovnikov, etc.) and any appropriate Stereochemistry (syn, anti, InVERSiON, scrambled, etc).

B) **Work backwards** (learn to RECOGNIZE the appropriate reagents and starting materials by looking at the products) from the final product. DO NOT try to work forward from the starting materials. Please trust me on this.

C) **Count carbons** in the starting material(s) and product(s) to see if any carbon-carbon bonds need to be broken or made, thereby zeroing in on key steps. This will be far more important next semester, so you should get used to doing this now.

D) **Pretty much all synthesis problems in OChem 1 involve traveling "north or south" on the so-called "I-35"** reactions (alkanes SA, haloalkanes NB/SM, alkenes ATX, vicinal dihaloalkanes Waco, alkynes DFW) at least part way at some point during the synthesis. This is not a promise or a rule, just an observation.

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The Golden Rules of Organic Chemistry

Your goal should be to understand, not memorize, the material presented in your organic chemistry course. The following principles should be learned as you begin your study of organic chemistry, then used as a solid foundation for building your understanding throughout the course. These simple ideas explain a great deal about the structures and properties of organic molecules, as well as the characteristic ways in which they react. Thoroughly understanding the following three key principles and related ideas will allow you to develop an intuitive feel for organic chemistry that avoids the necessity of resorting to the far less effective use of extensive memorization.

A. Predicting Structure and Bonding

1. In most stable molecules, all the atoms will have filled valence shells.

2. Five- and six-membered rings are the most stable.

3. There are two possible arrangements of four different groups around a tetrahedral atom.

B. Predicting Stability and Properties

4. The most important question in organic chemistry is "Where are the electrons?"

5. Delocalization of charge over a larger area is stabilizing.

6. Delocalization of unpaired electron density over a larger area is stabilizing.

7. Delocalization of pi electron density over a larger area is stabilizing.

C. Predicting Reactions

8. Reactions will occur if the products are more stable than the reactants and the energy barrier is low enough.

9. Functional groups react the same in different molecules.

10. A reaction mechanism describes the sequence of steps occurring during a reaction.

11. Most bond-making steps in reaction mechanisms involve nucleophiles reacting with electrophiles.

Useful Definitions:

Mechanism – A scheme that illustrates all reaction intermediates, as well as the flow of electrons and movement of atoms during bond breaking and bond making processes. Remember that arrows are used only to indicate the movement of electrons. Movement of atoms is assumed, but not explicitly indicated, by the arrows.

Nucleophile – A molecule that contains an atom with a lone pair AND a full or partial negative charge.

Electrophile – A molecule that contains an atom with a full or partial positive charge AND can be attacked by a nucleophile without creating a non-viable species such as a pentavalent (five bonds) carbon.

Brønsted-Lowry Base – A molecule containing at least one atom with a lone pair that will accommodate binding to a proton during a proton transfer reaction.

Lewis Base – A molecule that can donate a lone pair in a bond-forming process.

Brønsted-Lowry Acid – A molecule that can donate a proton during a proton transfer reaction.

Lewis Acid – A molecule that can accept a lone pair in a bond-forming process.

Leaving group – A group that will be relatively stable when it departs, such as a small neutral species like H_2O or N_2, or a group such as a halide atom that departs as a relatively stable ion.

Stereochemistry – Refers to which of the possible stereoisomers predominate in a reaction. The details of the mechanism dictate whether a reaction will involve certain features such as *syn* addition, *anti* addition, require an antiperiplanar transition state geometry, involve stereochemical InVERSiON, etc.

Regiochemistry – Refers to which of the possible product constitutional isomers predominate in a reaction. The details of the mechanism dictate whether a reaction will predominately give products that are consistent with Markovinikov's rule, are exactly inconsistent with Markovnikov's rule (anti-Markovnikov), are consistent with Zaitsev's rule, give most reaction at the more substituted carbon, etc.

Key Recognition Element (KRE) – Characteristic functional groups in relation to a new carbon-carbon bond seen with many of the reactions encountered in second semester Organic Chemistry. Being able to identify the KRE's in product molecules for *each* reaction learned will greatly simplify the process of deciding which reactions to use in complex synthesis problems.

Intermediate – A species produced during a reaction mechanism that is less stable than the starting materials or products. It exists for a short time and knowing a key intermediate's structure can help predict stereochemistry and regiochemistry of a reaction (for example a carbocation intermediate or radical intermediate that predicts predominant products seen in many first semester reactions).

Transition State – A theoretical structure that represents the highest energy species encountered in moving between starting materials, intermediates or products during a reaction mechanism. Predicting the properties of a presumed transition state can sometime predict reaction stereochemistry or regiochemistry (for example an anti-periplanar transition state geometry required for an E2 reaction).

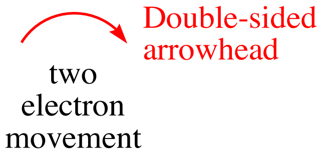
Mechanisms: The Basics

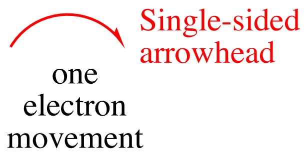
A) The Correct Use of Arrows to Indicate Electron Movement

The ability to write an organic reaction mechanism properly is key to success in organic chemistry classes. Organic chemists use a technique called **arrow pushing** to depict the flow or movement of electrons during chemical reactions. Arrow pushing helps chemists keep track of the way in which electrons and their associated atoms redistribute as bonds are made and broken. The first essential rule to keep in mind is the following:

First rule:* Arrows are used to indicate movement of *electrons

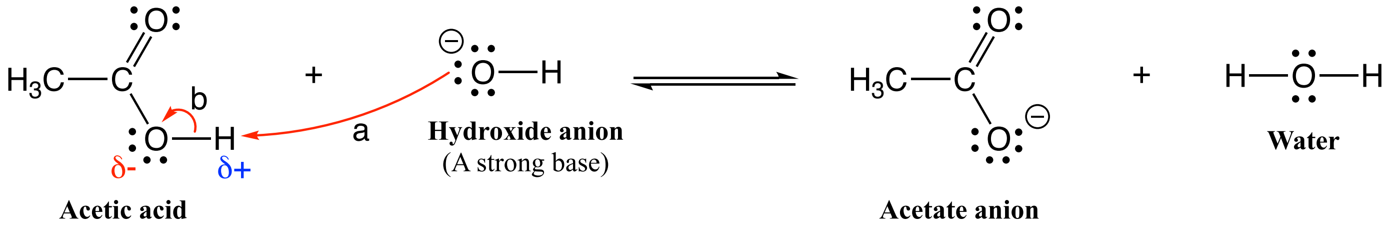
A regular arrow (double-sided arrowhead) is used to indicate the movement of two electrons, while a line with a single-sided arrowhead (sometimes called a "fish hook arrow") is used for single electron movement involved with radical reactions.





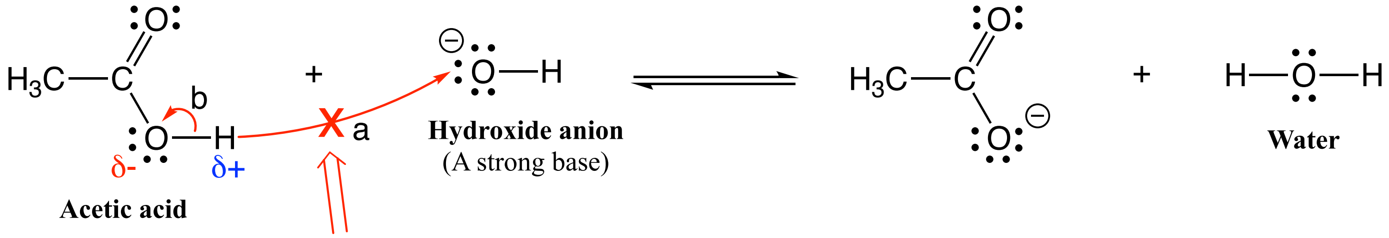
The great majority of reactions that will be discussed in this class involve movement of pairs of electrons, so they are represented by double-sided arrowheads.

***Second Rule:* Arrows are never used to indicate the movement of atoms directly. The arrows only show atom movement indirectly as a consequence of electron movement when covalent bonds are made and broken.**



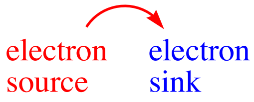
Correct use of arrows to indicate electron movement during reaction

A common mistake students can make is that they will erroneously write an arrow pointing *from* the H of the acetic acid *to* the O atom of the hydroxide anion (arrow a below). This is wrong, because such an arrow would be indicating the H *atom* movement directly, not *electron* movement!



Incorrect arrow because it is pointing in the wrong direction! Never use arrows to indicate atom movement directly

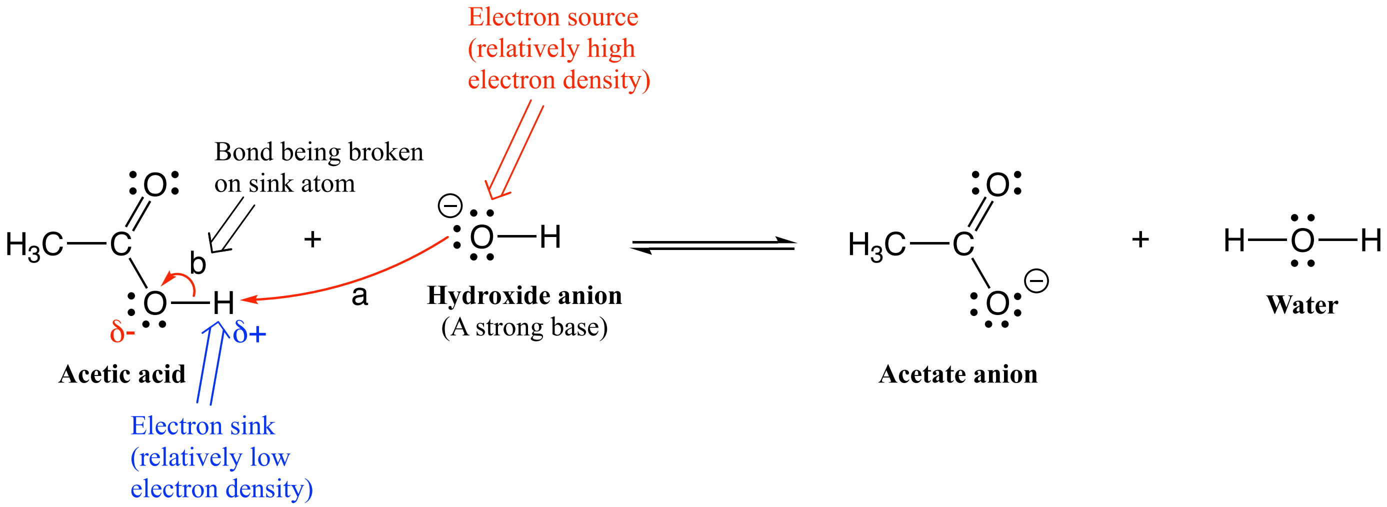
Third Rule: Arrows always start at an electron source and end at an electron sink.



An **electron source** is a bond or a lone pair of electrons. It is either a π bond or a lone pair on an atom of relatively high electron density in a molecule or ion, or a bond that must break during a reaction. An **electron sink** is an atom on a molecule or ion that can accept a new bond or lone pair of electrons.

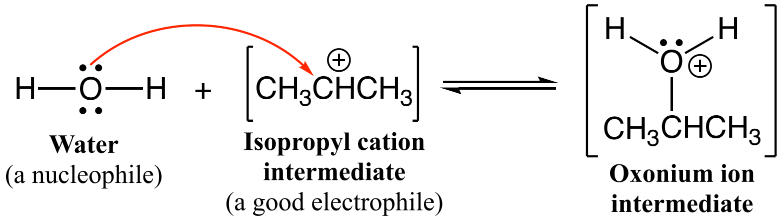
Fourth rule: Breaking a bond will occur to avoid overfilling valence (hypervalence) on an atom serving as an electron sink.

In these cases, the electron source for the arrow is the bond being broken, and the sink is an atom able to accommodate the electrons as a lone pair, generally an electronegative atom such as an O atom or a halogen. If an ion is created, that ion is often stabilized by resonance delocalization or other stabilizing interactions.

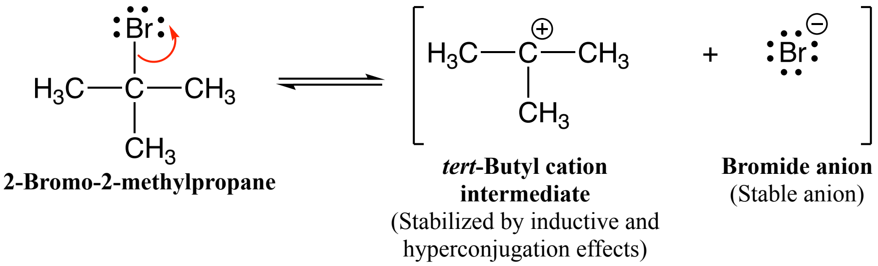


Polar Reaction Mechanisms: Polar reactions are most of what you will see in organic chemistry. There are only four different mechanistic elements that combine to make up the different steps of almost all the mechanisms you saw in CH320M/CH328M. Better yet, in CH320N the following four mechanistic elements are pretty much all you need to think about until we get to electrophilic aromatic substitution.

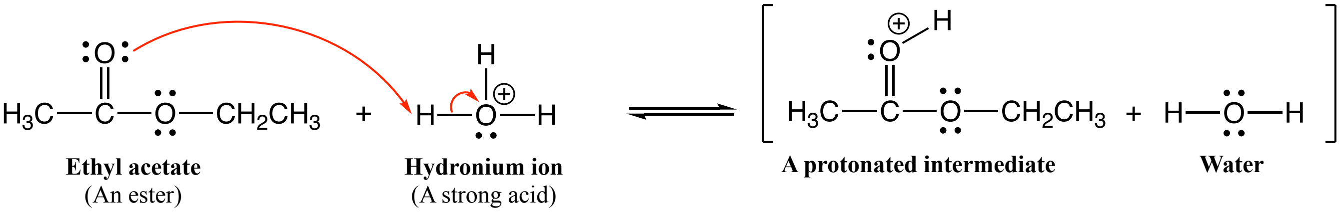
1. **Make a new bond between a nucleophile (source for an arrow) and an electrophile (sink for an arrow).** Use this element when there is a nucleophile present in the solution as well as an electrophile suitable for reaction to occur.



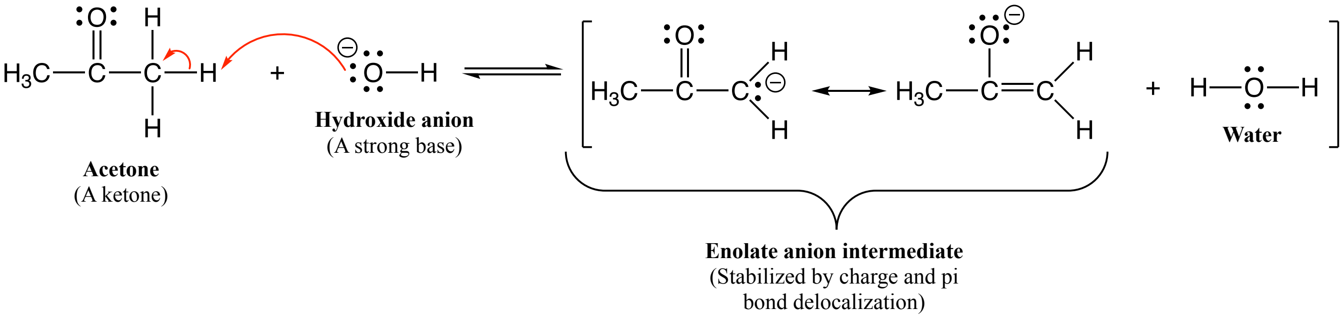
2. **Break a bond so that relatively stable molecules or ions are created** Use this element when there is no suitable nucleophile-electrophile or proton transfer reaction, but breaking a bond can create neutral molecules or relatively stable ions, or both.



3. **Add a proton** Use this element when there is no suitable nucleophile-electrophile reaction, but the molecule has a strongly basic functional group or there is a strong acid present.

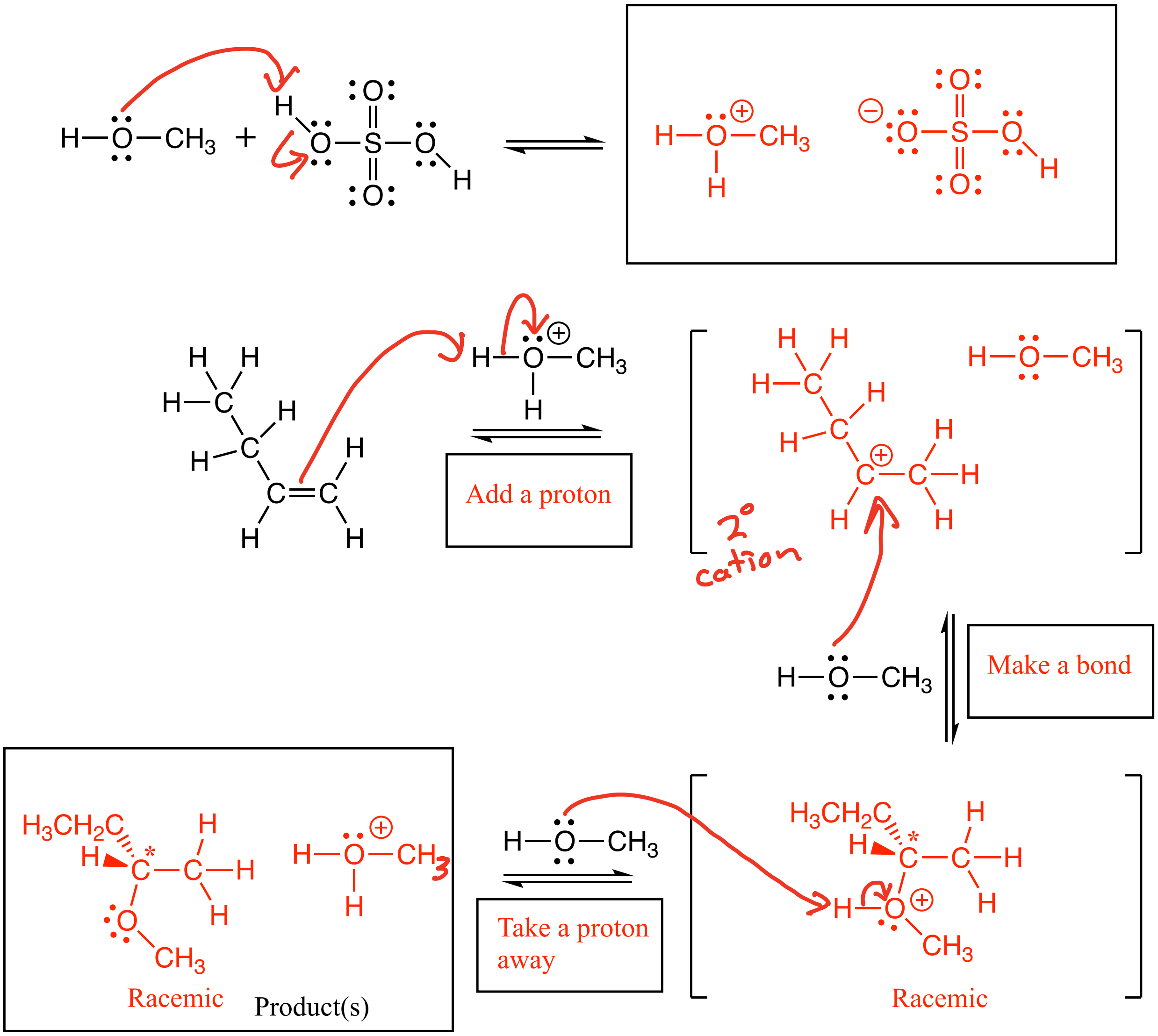


4. **Take a proton away** Use this element when there is no suitable nucleophile-electrophile reaction, but the molecule has a strongly acidic proton or there is a strong base present.



The situation is even simpler than you might expect because 1 and 2 are the functional reverse of each other, as are 3 and 4.

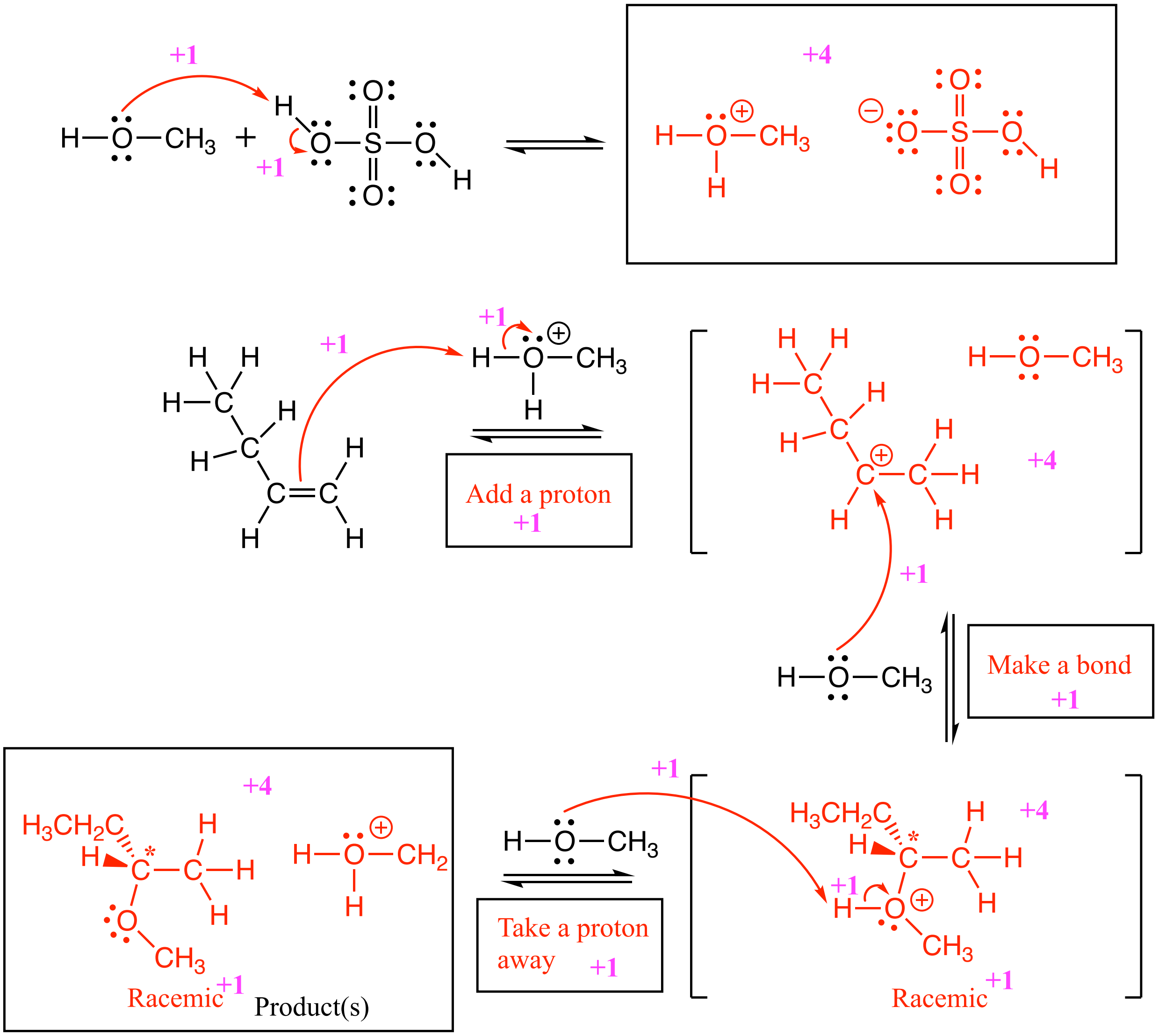
16. (32 pts) Complete the mechanism for the following reaction of an alkene with CH_3OH in the presence of catalytic amount of H_2SO_4. Use **arrows to indicate movement of <u>all</u> electrons, write <u>all</u> lone pairs, <u>all</u> formal charges, and <u>all</u> the products for each step.** Remember, I said <u>all</u> the products for each step. **YOU MUST USE WEDGES AND DASHES TO INDICATE ALL STEREOCHEMISTRY. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE OR PRODUCT YOU ONLY NEED TO DRAW ONE OF THE ENANTIOMERS AND YOU MUST MARK THE NEW CHIRAL CENTER WITH AN ASTERISK AND LABEL THE MOLECULE AS "RACEMIC" IF APPROPRIATE. In the boxes provided, write which of the 4 most common mechanistic elements describes each step (make a bond, break a bond, etc.).**



(2 pts) How many total stereoisomers are produced by this reaction? 2 (*R and S*)

(2 pts) As the reaction proceeds, does the pH of the solution increase, decrease, or stay the same? Stays the same → Catalytic in acid!

16. (32 pts) Complete the mechanism for the following reaction of an alkene with CH_3OH in the presence of catalytic amount of H_2SO_4. Use **arrows to indicate movement of <u>all</u> electrons, write <u>all</u> lone pairs, <u>all</u> formal charges, and <u>all</u> the products for each step.** Remember, I said <u>all</u> the products for each step. **YOU MUST USE WEDGES AND DASHES TO INDICATE ALL STEREOCHEMISTRY. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE OR PRODUCT YOU ONLY NEED TO DRAW ONE OF THE ENANTIOMERS AND YOU MUST MARK THE NEW CHIRAL CENTER WITH AN ASTERISK AND LABEL THE MOLECULE AS "RACEMIC" IF APPROPRIATE. In the boxes provided, write which of the 4 most common mechanistic elements describes each step (make a bond, break a bond, etc.).**



(2 pts) How many total stereoisomers are produced by this reaction? 2 (*R and S*) +2

(2 pts) As the reaction proceeds, does the pH of the solution increase, decrease, or stay the same? **Stays the same** +2