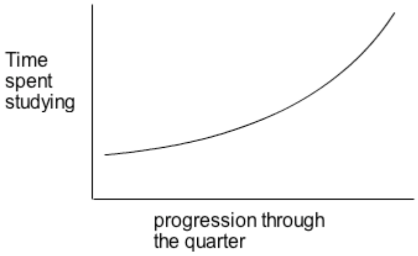
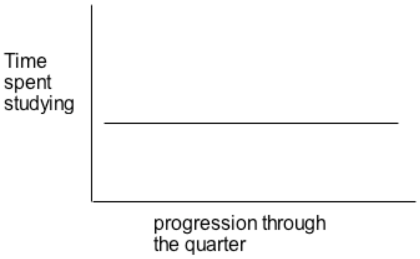
How to Succeed in Organic Chemistry (and reduce your workload)

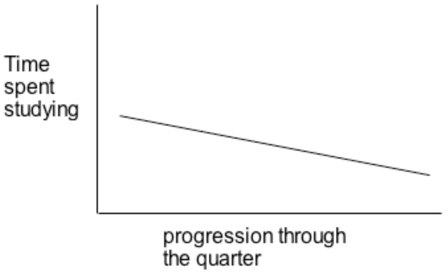
This class is going to teach you a number of concepts and techniques that can help you ace your organic chemistry class *and* do it by putting in less work. The approach that this course will take is going to emphasize understanding the concepts, and not just memorizing reactions and mechanisms, not just because it is a better way to learn organic chemistry, but because it is actually an immensely *more efficient* way to learn organic chemistry, and will make the MCAT much easier as well if that is where you are headed. A note here needs to be made about study habits and the nature of organic chemistry. As you go through the course each chapter is going to build upon the last, so if you do not keep up in the beginning, you will be in serious trouble by the middle of the class because you will have no foundation for learning the new material. Many students don't study much at the beginning of the class, and then cram at the end; *this will not work in organic chemistry*. Most students study like this, and it works in many classes:



In o-chem you should aim to study like this:



If you are diligent at the beginning and lay a solid foundation, you will probably actually end up studying like this:



For those of you with a calculus background, you will realize that total time studying is equal to the area under that line. If so, you will also notice that the last graph has the smallest area, and therefore is the way to get through the course with the least work, and is also the way to assure the most success, *lay strong foundations!*

Organic chemistry is not just memorization

Many people think that organic chemistry is just about memorization, and while this *can* be true it *shouldn't* be true. There is a lot of memorization involved in o-chem, that is unavoidable, however, if you understand the material it can cut your memorization considerably. Many people lack a solid understanding of the fundamentals from chemistry that they need to succeed in o-chem, and/or never catch on to the major themes of the course, which leaves them needing to memorize every reaction separately. This course is going to ensure that you have the foundation you need to succeed, and work on building your intuition for o-chem by explicitly going over themes from the course. Throughout organic chemistry you should constantly be trying to understand how the symbols on paper correspond to events and objects in the physical world, the better you get at this, the better your intuition will be. This may take a little more time in the short run, but this time is an investment that will pay off greatly in the future. If you develop a strong intuition, you can group together similar processes, and you see the themes of the course clearly, *you will have to memorize less, work less, and you will do better in the class*. Understanding is power, and this class should give you that power.

Principle 1: Make sure you have a good conceptual understanding of what is going on. This will *cut your workload* in a few ways: you will have less to memorize, you will be able to memorize easier, and you will retain what you memorize longer (which means less review, both for your tests and for the MCAT). This will also help you get a better grade, and do better on the MCAT. Less work, better grade, its win-win!

Chemistry and human understanding

The human mind is a product of evolution, and evolution builds things that work. We have no natural intuitive understanding of chemistry because it happens at levels of time and space that humans are not designed to understand, however, fortunately for us chemistry works on many of the same principles as physical processes that we are familiar with, such as geometry, forces, energy, and stability. This course will try to make some explicit connections between your natural human thinking patterns and chemical processes through analogies with things that happen on our level of time and space. The better you connect the analogies to the physical processes to the symbols on your page, the better your intuition will become.

Of symbols and objects: the signifier/signified relationship

Students often forget that what they are studying are objects in the physical world and how they behave, and feel as though they are studying letters on paper. Atoms are obviously too small to touch or see, so we must do things on paper and chemistry demonstrations are left to turning solutions from pink to blue, making things fizzle, making plastics, or making molecules that smell like pineapple. This can make it hard to remember that *what these symbols on paper represent are objects in the physical world*, and even though any chemistry student will acknowledge that this is true, they often do not truly take it to heart. The more you can wrap your mind around these little objects and how they behave, the better you will do. But this is not all you need to understand; you also need to understand how the notation system maps onto these little objects, as well as the limitations of that notation system. Ferdinand de Saussure would say that you need to connect the signified and signifier.

General chemistry vs. organic chemistry

You may remember a lot from general chemistry, you may only remember a little. Probably, if you only remember a little you will remember doing a lot of math at the end dealing with rate laws, thermodynamics, and equilibria. *This math intensive form of chemistry is not a part of organic chemistry* (with a couple small exceptions). You may also remember spending a lot of time balancing reactions, making sure that everything that was on one side is also on the other side of the equation arrow. *This accountant-like form of chemistry is also not a part of organic chemistry*. Not having to keep track of reactants and products like this confuses a lot of students at the beginning because this is emphasized so much in general chemistry. In organic chemistry we are not especially concerned with this because the focus is on what actually takes place in a reaction. This is called the *mechanism*, which is a complete step-by-step description of exactly which bonds break and which bonds form in order to go from reactant to product. In order to understand this, however, you will need a number of things that many of you have forgotten from general chemistry including understanding electronegativity, hybridization/geometry, thermodynamic diagrams (not equations though), and the nature of atoms, including their orbitals and types of bonds. These are all *qualitative* rather than *quantitative* aspects of general chemistry, which is probably welcome news to many of you as well.

Explanations in organic chemistry are not mutually exclusive

Another common problem students encounter in organic chemistry is that *explanations* of what is going on *are not mutually exclusive*, and that there may be multiple ways of explaining something. The problem here is that different chemistry terms often focus on different aspects of a situation, for example oxidation and reduction deal with what is happening with the electrons, while [bronsted-lowry] acids and bases deal with what is happening with protons. This means that one molecule could be both an acid and an oxidizing agent, depending on what we are focusing on in the discussion. We will come back to this when electrophiles and nucleophiles are introduced. Just keep in mind that depending on what we are focusing on one process could have a number of co-existing explanations.

How to study organic chemistry

While this class will help you cut down your workload this does not mean that organic chemistry will be easy by any means. Even if you cut down what you have to memorize by over 50%, you will still probably have more to memorize for this class than any other class you have taken. This means that the way to study o-chem is to live it. You need to spend at least some time every day studying, and a lot of time some days. Organic chemistry is deceptively difficult; what I mean by this is that the ideas are fairly straight forward (unlike, say, physics or poststructuralism), so you will sit in class and go “yea, sure, makes sense” and think you understand it. Then you will go home crack open your book, and be completely lost. Most of the ideas in organic chemistry are fairly straight-forward but there are A LOT of them, so it is easy to be lulled into complacence.

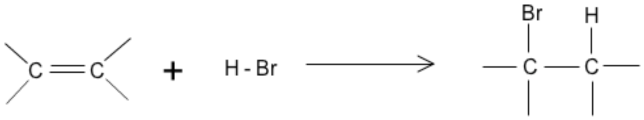
Furthermore, these concepts are cumulative, so if you fall behind early it is almost impossible to catch up.

__Principle 2__: Do not fall behind. This seems like a no brainer, but this is probably the number one reason people fail organic chemistry, and cannot be emphasized enough.

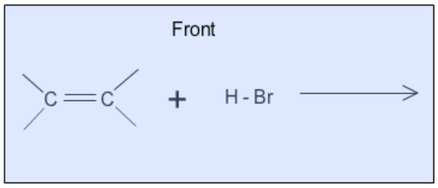
So, then how do you avoid this? This class is a good start. Make sure that you know all of the basics, and know *why* things happen the way they do in reactions. This will make it easier to memorize *what* happens. Furthermore, you will usually need to know many different aspects of a reaction, such as what the reagents (and maybe solvents) are, what the mechanism is, what conditions you need for the reaction to take place, and what the resulting stereochemistry is. Furthermore, these categories often have many parts themselves. Many students will memorize all of them separately, which just compounds what you need to learn. Learn your reactions "*wholistically,"* along with the mechanisms and understand how all the pieces fit together. For example usually if you understand how the mechanism works, then you will also understand why the reaction needs certain specific conditions to take place, and why it results with some specific stereochemistry.

__Principle 3__: Learn organic chemistry "*wholistically*." Learn how the pieces fit together to drastically cut down on what you need to memorize. Notice how well this ties in with the other two principles above.

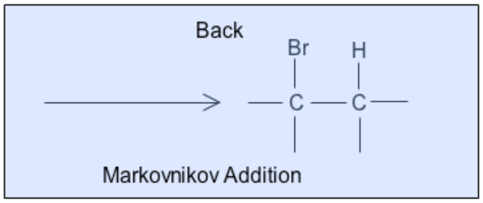
I also suggest making notecards, but you can use whatever technique you like to memorize large quantities of information. It is often difficult to know exactly what to put on notecards because you are not exactly learning vocabulary or lists of facts. I recommend going through your book/notes with a stack of cards, and putting everything you need to memorize on a card. As far as form goes, I will show you what I discovered worked for me. For a reaction such as:



I would put the first half on the front of the card with an arrow like this (of course I would not write "front" on the top that is just for the demonstration):



On the back I would put an arrow coming in, the product, and any relevant information, such as stereochemistry on the bottom (but again not "back" at the top). The arrow is so I could use the card both ways, so that I could flip through my cards backwards, know that I was looking at a product, and had to guess the reagents. "Markovnikov" addition is a particular way these add together, you will learn about it in class, but you would need to know it so it goes at the bottom (this is part of the wholistic methodology).



This is, of course, just a suggestion, but it worked very well for me.

Know your Latin

This is helpful advice, not just for chemistry, but for all the sciences. Scientists are pretty much the most logical people, and the naming conventions definitely reflect this. You should know the latin prefixes for numbers (like pent-, hex-, hept-, oct-, etc.) up to 10. You should always pay attention when you learn new latin words and affixes as well such as "-phile" means "loving," and "phobe-" means fearing. This will help cut down on your memorization as well, because if you understand what terms mean you probably won't have to memorize them, or if you do it will at least be easier.

ATOMS

The atom is the fundamental unit of chemistry

This probably sounds incredibly obvious, but it is essential that you understand the nature of atoms inside and out, and not just atoms, but how the symbols on your page map onto objects in the world. Furthermore, don't forget that atoms have shapes and distributions of charges and matter that we are going to go over extensively. If you don't understand atoms you cannot understand chemistry. You must also know how atoms pull together to make molecules, after all this is what we are studying.

Nuclei

The nucleus of an atom is made of protons and neutrons. Neutrons have no charge, and protons are positive, so the nucleus always has a positive charge. As we will see later in this class, unlike charges attract and like charges repel. This means that electrons are attracted to the nuclei, and two nuclei repel each other.

It should be noted that an element is determined by the number of protons in the nucleus.
-If the number of *electrons* changes, this is an *ion*, and this is noted as a charge
-If the number of *neutrons* changes, this is an *isotope*, and is noted with little numbers
-But if the number of *protons* changes, it becomes a *different element* (like He to H, or U to Pu)

Electrons

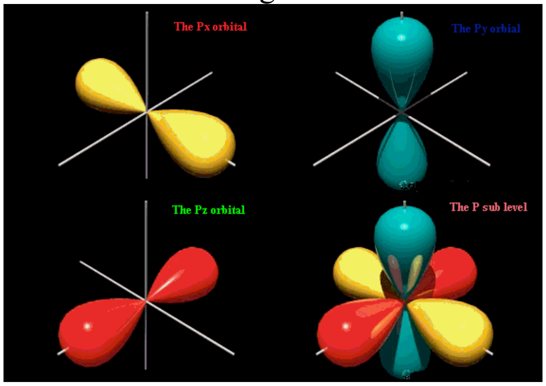
Of all the subatomic particles, *electrons are by far the most important* to understand, as they are what we think about when considering reactivity in organic chemistry. Electrons are negatively charged and orbit the nucleus. Electrons are also responsible for forming bonds, and *each bond consists of 2 electrons*. Electrons are not particles in the classical sense because of Heisenberg's uncertainty principle, and should be thought of more like smears of matter across space. This means that they do not necessarily have to belong to one atom in a molecule in an all-or-none fashion, but that an atom can be said to have a partial charge, or only part of an electron. Furthermore they can be smeared across entire molecules as we will see with resonance. The notation for an electron is e^-. You should also remember that the only electrons that participate in a reaction are the *valence electrons*. Valence electrons are the electrons that an element has in its outer shell, and can be thought of as the electrons that it has in addition to the ones the last nobel gas has. Elements in the first column have 1, in the second column have 2, in the third column (skipping the metals not in the first two columns) have 3, in the fourth have 4, and so on.

Orbitals

Chances are you have probably forgotten about orbitals unless you took general chemistry very recently. There are two important features you should know that will become second nature. First is the number of electrons (and therefore the number of possible bonds) that each orbital has. Second, and more importantly is the shape of these orbitals. Atoms and molecules are physical entities, and therefore much of their behavior is determined by their shape. Furthermore because nuclei repel nuclei, and electrons repel electrons, these try to be as far away from each other as possible, which is what leads to hybridization as we will discuss below.

There are two important orbitals for you to know, s, and p. There is one s-orbital per energy level and 3 p-orbitals (except the top row has no p-orbitals). The s-orbital can contain up to 2 electrons and is a sphere:

For each energy level there are 3 different types of p-orbitals (P_x, P_y, and P_z) which can each contain up to 2 electrons. So, for a given energy level there can be up to 6 p-orbital electrons. They are shaped like bulbs coming out of Cartesian coordinates.



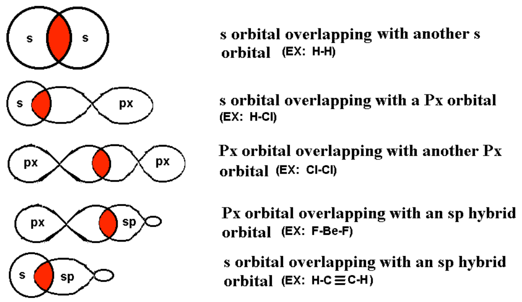
Only 4 bonds, yay!

Organic chemistry deals primarily with H, and the second row elements B, C, N, O, F, as well as the rest of the halides (Cl, Br, F). Aside from the "rest of the halides" above none of the atoms listed above have a D-orbital (and H doesn't even have a p-orbital). This is important because in order to form more than 4 bonds, an atom needs to have a d-orbital. This means that, with almost no exceptions (except for a couple of reagents) *atoms in organic chemistry cannot have more than 4 bonds/lone pairs*. Hydrogen is the one exception to this, because it only has an s-orbital, it has 1 valence electron, and therefore can only make one bond. If both the s-orbital (2 electrons) and the p-orbitals(6 electrons) are full then the atom would "have" 8 electrons (have is in quotes because we count shared electons as well). This is the basis for the *octet rule*, which states that [second row] atoms are always trying to get 8 electrons. This is because it takes 8 electrons to fill the valence shell.

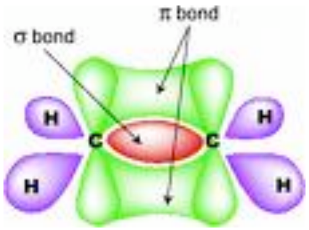
Single (σ) and double/triple (π) bonds

Single bonds are σ bonds, are on-axis bonds, and are typically the most stable bonds. Sigma bonds consist of 2-orbitals lining up along one axis and then overlapping at the tips. They are "on-axis" because due to the nature of the shapes of these orbitals both of the nuclei and the orbitals all sit on one axis.

OVERLAPPING ORBITALS IN SIGMA BONDING



Double and triple bonds are π bonds, are off-axis bonds, and are usually much more reactive. These consist of two p-orbitals that line up side-to-side rather than overlapping at the tips. They are "off-axis" because they sit on an axis that is parallel with the axis that the nuclei are sitting on.



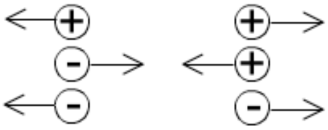
This picture above is a double bond. Double bonds consist of *1 σ-bond* and *1 π-bond*. Triple bonds contain *1 σ-bond* and *2 π-bonds.* These two sets of π-bonds sit in perpendicular planes, and look like the picture below:

The blue is one π-bond, the purple is the other π-bond, and the yellow is σ-bonds.

FORCES AND ELECTRONEGATIVITY

The unifying theory

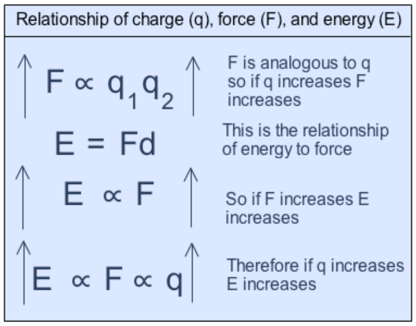
You will learn a lot in organic chemistry, but fundamentally the entire course is based upon one simple concept *like charges repel, unlike charges attract.* You need not understand all the details of this below, but it is developed so that you are aware of the source of the ideas here. A positive charge attracts negative charges and repels other positive charges, a negative charge on the other hand would attract positive charges and repel other negative charges. This is simple enough, but because is provides the backbone of everything you will be doing, we will spend a little more time on it.



If you have taken physics you should be familiar with the following equation:

$$F = \frac{K(q_1 q_2)}{r^2}$$

This may look a little intimidating at first, but let's dissect it. All we need to worry about are the qs and the F. Each q represents one of the charges, and F represents the force between them. As we can see in the diagram below as q increases, F increases. This means there is a stronger force driving our reaction. Furthermore, as F increases, energy (E) increases, which decreases our stability and increases our reactivity. We are getting a bit ahead of ourselves here, and will revisit this when we get to thermodynamics.


Relationship of charge (q), force (F), and energy (E)

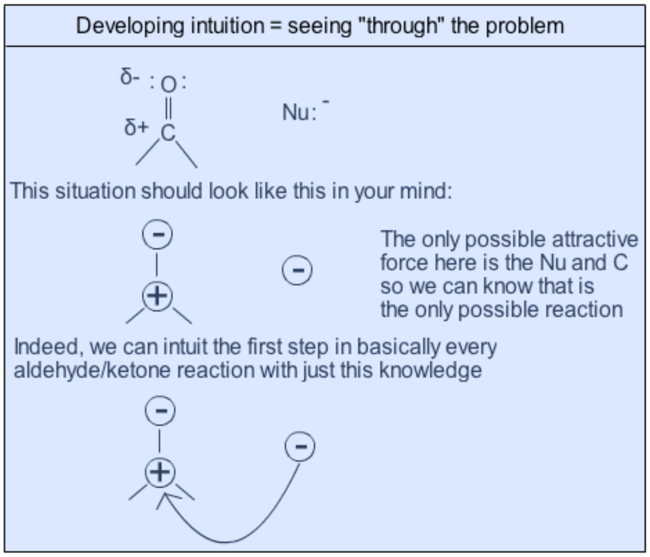
$F \propto q_1 q_2$ — F is analogous to q so if q increases F increases

$E = Fd$ — This is the relationship of energy to force

$E \propto F$ — So if F increases E increases

$E \propto F \propto q$ — Therefore if q increases E increases

This is what will drive every single reaction that you will study, and *should form the core of your intuition*. One molecule will have a part of it that is negative, either as an ion (a whole -1), as a dipole (a partial negative charge, say - 2/3), or as a lone pair (two electrons hanging off the side). This molecule will be attracted to another molecule because that other molecule has a part of it that is positive, either as an ion or as a dipole. This basic knowledge helps you see "through" problems, should form the core of your intuition, and is the first thing you look for any time you see a new reaction. This is shown below (δ+ and δ- both mean "partial charge" or a charge like +2/3).



Developing intuition = seeing "through" the problem

This situation should look like this in your mind:

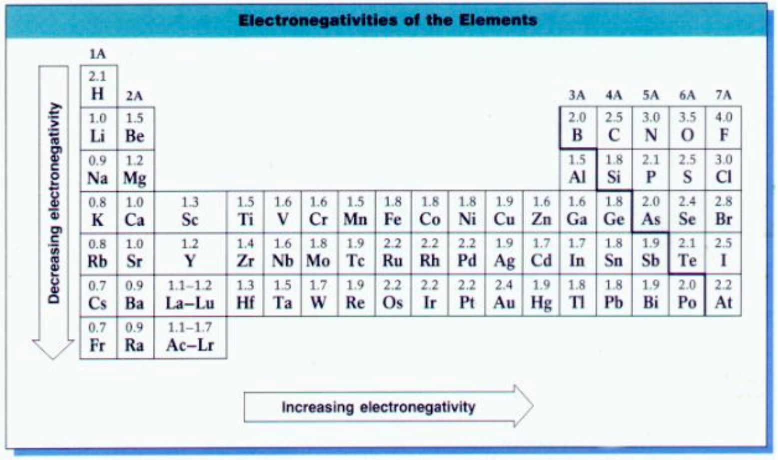
The only possible attractive force here is the Nu and C so we can know that is the only possible reaction

Indeed, we can intuit the first step in basically every aldehyde/ketone reaction with just this knowledge

Electronegativity

This is all well and good, but can't help you unless you learn how to figure out what the charges and dipoles are. To figure out full charges you need to calculate *formal charge* (explained below), and to figure out dipoles you need to understand electronegativity. *Electronegativity* is a measure of how strongly an atom is pulling on, or attracting, electrons. Because electrons are more like smears of matter than particles, two atoms in a bond do not have to share them equally. In fact, the only time they do is when it is the same atom on either side of the bond. Think of every bond as a tug-of-war over electrons. If one of the sides is much stronger (highly electronegative) it will have more electron density, and a negative dipole. However, if both sides are equal, be they both strong or both weak, they will end up sharing the electons equally, there will be no dipole, and the bond will therefore be *nonpolar*. Therefore in order to check for dipoles, we must look for *electronegativity differences* between the two atoms in the bond. It is not electronegativity per se that creates polarity, but rather differences in electronegativity.

Electronegativity increases as you go to the right on the periodic table and increases as you go up the rows on the periodic table. Fluorine (F) is the most electronegative element, and Francium (Fr) is the least. This is easily seen below:

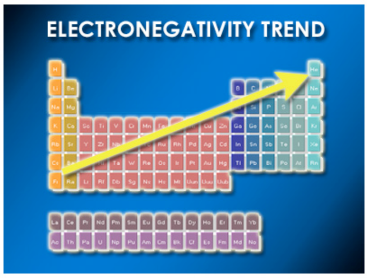


Electronegativities of the Elements

1A	2A											3A	4A	5A	6A	7A
2.1 H																
1.0 Li	1.5 Be											2.0 B	2.5 C	3.0 N	3.5 O	4.0 F
0.9 Na	1.2 Mg											1.5 Al	1.8 Si	2.1 P	2.5 S	3.0 Cl
0.8 K	1.0 Ca	1.3 Sc	1.5 Ti	1.6 V	1.6 Cr	1.5 Mn	1.8 Fe	1.8 Co	1.8 Ni	1.9 Cu	1.6 Zn	1.6 Ga	1.8 Ge	2.0 As	2.4 Se	2.8 Br
0.8 Rb	1.0 Sr	1.2 Y	1.4 Zr	1.6 Nb	1.8 Mo	1.9 Tc	2.2 Ru	2.2 Rh	2.2 Pd	1.9 Ag	1.7 Cd	1.7 In	1.8 Sn	1.9 Sb	2.1 Te	2.5 I
0.7 Cs	0.9 Ba	1.1–1.2 La–Lu	1.3 Hf	1.5 Ta	1.7 W	1.9 Re	2.2 Os	2.2 Ir	2.2 Pt	2.4 Au	1.9 Hg	1.8 Tl	1.8 Pb	1.9 Bi	2.0 Po	2.2 At
0.7 Fr	0.9 Ra	1.1–1.7 Ac–Lr														

Decreasing electronegativity

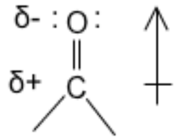
Increasing electronegativity



A pair of atoms with 0 ≤ ΔEN ≤ .5 is *nonpolar*. A pair of atoms with .5 ≤ ΔEN ≤ 1.7 is *polar covalent* and corresponds to a *dipole*. A pair of atoms with 1.7 ≤ΔEN is *ionic*.

These numerical conventions are *approximate*. This is really a continuum of polarity with artificial designations. Even though ΔEN of C-H is .3, and it would be considered *nonpolar*, it is still *slightly polar* as you will see below. You will not deal extensively with ionic compounds in organic chemistry. The only thing you really need to know is that anytime you see one of the elements from column 1 (Na, K, or Li) you can assume it is a *spectator ion* with a charge of +1. Spectator ions do not participate in reactions, and what they tell you is that what they are attached to carries a charge of -1.

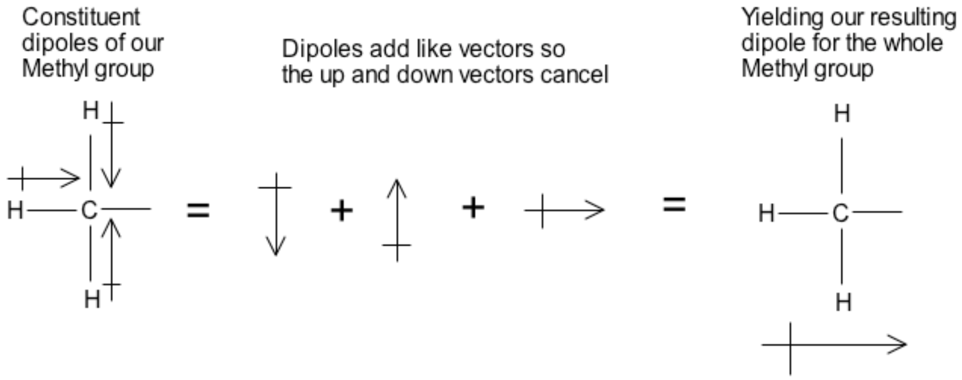
Writing in partial charges as above (e.g. "δ +") is only one way to signify where a dipole is, the other is with an arrow with a plus sign on the back. The arrow points to the negative side, the back of the arrow, with the plus sign, is where the positive side is, here is the same carbonyl as above with the other notation on the left, and the new arrow notation on the right.



Principle 4: The first thing you should always do when looking at a novel reaction is to establish what the charges and dipoles are. This will help you determine what the possibilities are for reactions. You will move beyond this somewhat, but until your intuition develops further this is the best way to start.

Polarities add like vectors

Because only atoms have electronegativities, and molecules do not, you cannot figure out the polarity of a molecule from electronegativities directly. You must find the polarities of each of the constituent parts of a molecule (or multi-atom piece) and add them together. The EN of H is 2.2 and the EN of C is 2.5 yielding a ΔEN=.3. Now, technically this is nonpolar, but we can see that these bonds are slightly polarized towards the carbons. In the following methyl group (the unassigned bond connects to another molecule) we first assign the polarities to each of the bonds individually (on the left), and then add them to get the net polarity of the whole group (on the right).



Formal charge

Calculating formal charge is very easy, and is how you will know if you are looking at an ion (if one of the atoms does not have the correct number of electrons and therefore has a charge). Usually in class you will get an equation that looks like this:

Formal charge = group number – nonbonding electrons – number of bonds.

There is a conceptual way of doing this as well. First, you need to know how to count your electrons. This can be confusing as there are three ways electrons may be counted depending on what you are counting for (it is different for octets, formal charge, and oxidation number). This is summarized in the table below. For formal charge we consider every bond as though it were shared equally. Therefore, each atom on either side gets to count 1 electron from every bond (this is where the "number of bonds" comes from in the equation above). So, every bond counts as 1 electron, and then you add in any lone pairs (as 2 electrons/lone pair because there are two in each). This will give you the "number of electrons the atom has." This number should be compared with how many valence electrons the elemental form has, or "number of electrons the atom should have." If these numbers are the same, there is no charge, if they are different you add a -1 for every extra electron, and a +1 for every electron missing. Don't forget, because electrons are negative, extra electrons are -1 not +1, this is a very common mistake.

What you are counting for	Which electrons count as "belonging to an atom"
Checking to see if orbitals are full (checking the octet rule)	Each atom counts all of its lone pair electrons, and *each* one gets to count *both* electrons from every bond (this means any bonded electrons get counted twice)
Formal charge	Each atom counts all of its lone pair electrons, and each one gets to count *one* electron from every bond (this means bonds split symmetrically and all electrons can only be counted once)
Oxidation number	Each atom counts all of its lone pair electrons, and *only the more electronegative atom* gets to count any bonded electrons, and it *gets both* electrons from every bond (this means bonds split asymmetrically and all electrons can only be counted once)

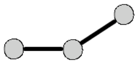
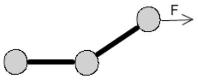
π-bonds are also reactive

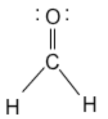
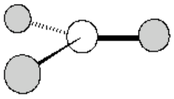
There is one other fundamental way in which molecules can be reactive without having a dipole, and that is with π-bonds. π-bonds are *off-axis bonds*, which means that molecules with π-bonds essentially have electrons hanging out in space. By this point you should see that charges create forces, and chemical reactions are a product of the pushing and pulling resulting from these forces. It is easy to conceptualize then why π-bonds would be reactive. Imagine that you were holding onto something between you and another person, but there was a third party trying to take it away from you. You and the person are the atoms in the bond and the third party is another reactant. If you hold the object between you (corresponding to a σ-bond) it would be hard for this third party to get it away from you. If, on the other hand, you and the other person held it out at arm's length (off-axis π-bond), then the third party could easily come and take it. If electrons are hanging out in space, in off-axis bonds, they make a molecule reactive because they are in a sense "available for reaction."

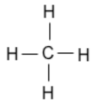
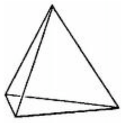
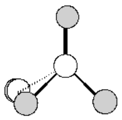
GEOMETRY AND HYBRIDIZATION

Geometry and hybridization are two sides of the same coin
Geometry of molecules and the hybridization of their orbitals are intimately connected, and we will deal with geometry first. The necessity of geometry drives hybridization; essentially, *molecules hybridize so they can assume the necessary geometry.* We are not going to go into all the nitty-gritty details here about how hybridization works instead we are going to establish this with a little thought experiment, and some comparisons. All we need here is our unifying charge theory and our natural human intuition about three-dimensional space. We have already established that like charges repel and dislike charges attract, now add to that knowledge that every single atom consists of a positive nucleus surrounded by a cloud of negative electrons. What this means is that atoms are ambiguous creatures, where their shells and their cores want exactly the opposite things. This means that for our purposes here atoms in molecules and lone pairs want to be as far away from each other as possible because you have electron shells (or lone pairs) repelling electron shells (or lone pairs). The only problem is they are all part of the same molecule. Its like they are living with their mother-in-law, they are stuck in the same house, but try and stay as far way from each other as possible. This is responsible for determining all of the geometry.

It is important to realize that both lone pairs (which are electrons), and substituents (which are surrounded by electrons) can be considered as negatively charged. Thus these behave the same in terms of geometry, repelling each other to get as far away from each other as possible. Below I will just call them "things" so that I do not have to keep saying "substituents or lone pairs."

Think of a molecule with just 2 things bonded to it, like this $H-C\equiv CH$. We are going to focus on the carbon in the middle, but of course it should be realized that the other carbon is the same. Both of its *substituents* (H, and CH) *repel each other* because they each are surrounded by clouds of electrons, and so they try and get as far away from each other as possible. The easiest way to conceptualize this is as though the atoms are like repelling magnets attached to sticks that can move around Now, think of three-dimensional space, what arrangement will get both of these substituents as far away from each other as possible? The answer is a linear formation that will look like this: , with 180° angles between the bonds. This is called a *linear* geometry. Keep in mind that the two "balls" at either side repel each other, so that if we were to try any other conformation say , then the molecules would repel each other with a force . This force would make the molecule "snap back into place." In other words, a molecule with two substituents (or a lone pair), *assumes a linear geometry because this is as far as the atoms can get from each other in space.*

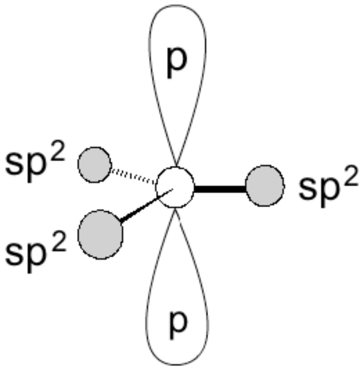
Using this same analysis you will realize that a molecule with 3 things such as , the furthest in space that these can get away from each other is if they lay *in the same plane* and form a "Mercedes Benz"-like conformation, namely  (the dashed lines are going "into the page", and the skinny wedge is "coming out of the page"). This is the *trigonal planar* conformation, and it has angles of 120° between the bonds *in the plane*.

For 4 things such as , the furthest in space that these can get is if they all four sit at the vertices of a tetrahedron , so it will look like this . The angles between all bonds will be 109°. Notice that while trigonal planar, and linear conformations look very similar to the way they are drawn on paper, this doesn't look anything like the drawing of CH_4 above. This is part of "connecting the symbols to the objects," and will be crucial to developing your intuition.

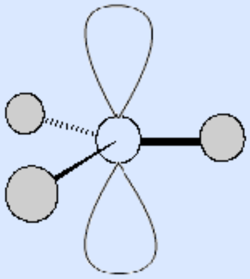
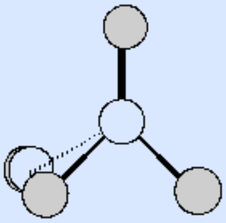
Hybridization

You may have noticed that s-orbitals and p-orbitals look nothing like these shapes, s-orbitals are spherical, and p-orbitals are like the axes of three-dimensional coordinates. So then, how do these molecules possibly assume these shapes? This is where hybridization comes in. Molecules *hybridize in order to get these geometries*, hybrized orbitals are just mixtures of the elementary orbitals. That is, orbitals combine to form new differently shaped orbitals, which overcome the geometric constraints of individual s- and p-orbitals.

Linear geometry corresponds to sp^1 hybridization, trigonal planar geometry corresponds to sp^2, and tetrahedral geometry corresponds to sp^3 hybridization. The little number above the p indicates how many of the three p-orbitals went into the hybridization. You will notice that *sp^1 has 2 p-orbitals left over*, and that *sp^2 has 1 p-orbital left over*. Don't forget these left over p-orbitals as they are very important. Usually they are contained in triple and double bonds respectively, but they can also be empty (like with carbocations), or in some cases contain lone-pairs (like in aromaticity). The sp^1 orbitals then look almost just like the p-orbitals, however one of the p-orbitals is actually two hybridized orbitals. sp^2 orbitals, on the other hand look like the trigonal planar geometry with two orbitals coming out of the top and bottom like this:



This is all nicely summarized in the table below:

Three Fundamental Geometries				
# bonds/l.p.	geometry	hybridization	bond angle	
2	linear	sp^1 *(plus 2 p-orbitals)	180°	
3	trigonal planar	sp^2 *(plus 1 p-orbital)	120 °, 90°	
4	tetrahedral	sp^3	109°	

One last word about geometries

In general chemistry you learned a lot of geometries, like octahedral, bent, etc. You will only really need to know the three shown above for organic chemistry, but you need to know them inside and out. In general chemistry they differentiated between substituents and lone pairs (i.e. water is "bent" because it is actually tetrahedral, but two of it's "things" are lone pairs, and these were not counted in calculating the geometry). You will not need to do this anymore on paper, but you do need to be aware of whether each slot is filled by substituents or lone pairs. This will quickly become second nature to you.

ABSTRACTION: NUCLEOPHILES AND ELECTROPHILES

The “algebra” of chemistry

In chemistry many different molecules behave in almost identical ways (as we will see when we get to the functional groups). Part of *understanding* organic chemistry, rather than *memorizing* organic chemistry is being able to understand these underlying similarities and why the molecules behave in a similar fashion. This will develop as you go through the course, but due to our “unifying theory,” a general rule of thumb is that molecules with similar charge distributions and similar geometries will behave the same. This insight is going to help us “see through” the symbols. Furthermore, this is going to provide the foundation of what I call the “algebra of chemistry” introduced below. Algebra is all about doing math with *generic variables*, in which a variable can be equal to a number of *specific numbers*. There are many abstractions that we use in chemistry that serve a similar purpose, where we will have a generic symbol for a certain *type* of molecule that is our *generic variable*, which can be equal to any of a number of different *specific molecules*. This is immensely helpful, not only at helping you understand the processes without getting bogged down in the details, but will also form the basis of much of our grouping. For example, there are 5 aldehyde/ketone reactions that undergo the exact same 2 step mechanism. You could memorize this separately for all 5 reactions, as well as having to memorize the reagents in all the reactions, or you could memorize the general form, and just know the 5 reactions that do this. This effectively cuts your memorization here by about 75%, and by understanding the pattern makes it easier to remember in the future. The better that you get at understanding this “algebra of chemistry” the stronger your intuition will be, the better you will be at grouping, and thus, the less you will have to memorize.

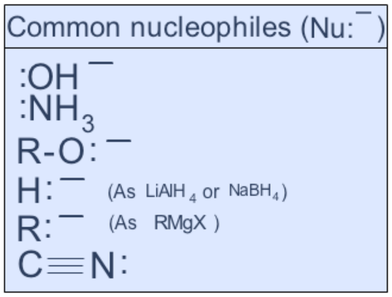
Principle 5: Molecules with similar charge distributions and similar geometries will behave the same. Learn these as generic formulas into which any of a number of specific reactions can be applied. This is will help us group together similar reactions.

Hint : Don’t just wait for someone to tell you that reactions are similar (as often no one will), but look for these underlying similarities yourself. If you think two mechanisms are similar, lay them side by side and check. Even if they are not, you will learn a lot about them in seeing why they are not. Chapters in organic chemistry textbooks are already organized in such a way as to group together similar reactions, so you should keep this in mind and look for the similarities.

Nucleophiles and electrophiles (the “x” and “y” of our algebraic chemistry)

Nucleophile means *“nucleus-loving,”* meaning nucleophiles are attracted to positive charges because nuclei are positive, and therefore *nucleophiles can be thought of as “negative.” Electrophile* means *“electron-loving,”* meaning electrophiles are attracted to negative charges because electrons are negative, and therefore *electrophiles can be thought of as positive.”* Because nucleophiles have “extra electrons” they are electron donators, and because electrophiles are “electron-deficient” they are electron acceptors. This is a lot of round-about reasoning, so it is probably just easier to get familiar with the symbols for electrophiles and nucleophiles.

The symbol for a nucleophile is $Nu:^-$. Notice it has a lone pair and a negative sign. This does not mean all nucleophiles need a lone pair or a formal negative charge, just that they behave as a negatively charged object. There are many examples of nucleophiles including the following common nucleophiles:



Common nucleophiles ($Nu:^-$)

$:OH^-$

$:NH_3$

$R\text{-}O:^-$

$H:^-$ (As $LiAlH_4$ or $NaBH_4$)

$R:^-$ (As RMgX)

$C\equiv N:$

The symbol for electrophile is E^+. While nucleophiles often have lone pairs, and negative charges, electrophiles are often just dipoles, and as such can be a little harder to spot.

Other important chemical variables: X and R

These are two variables that stand in for common substituents. *R represents any alkane*. Alkanes as a whole are not especially reactive and so it doesn't really matter if you have an octane ($CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$) hanging off an aldehyde or some other alkane with a different number of carbons like propane ($CH_3CH_2CH_3$). To avoid confusion, not to mention a lot of unnecessary writing, R just stands in for any alkane.

X represents any halide (F, Cl, Br, I). The halides all behave pretty much the same so it doesn't matter if you have Cl or Br. To signify this you will often see an X standing in for "any halide goes here." This being said, F and I can be very reactive or not reactive enough. There are a couple of reactions that do not work if you plug in F or I, so I recommend *always using Cl and Br*, to just avoid this issue altogether.

Acids and bases

H_3O^+ and H^+ can both stand in for a generic acid. And B: will often stand in for a generic base. This is as good a time as any to mention that you should not be concerned if in the middle of a mechanism you need a proton, or need to get rid of one, because you can pretty much always just do the reaction in acidic solution or basic solution.

Hint: Do not worry about needing protons or needing to get rid of them. If you need a proton, add an acid, and realize the reaction is probably carried out in acidic conditions. If you need to get rid of a proton, add a base, and realize the reaction is probably carried out in basic conditions.

ENERGY, STABILITY, AND REACTIVITY

Energetic intuitions

We do not have intuitions about energy at the molecular level. Thankfully, it works just like energy does in a domain that we understand very well—gravity. A ball will always roll down a hill because it is moving from higher energy to lower energy to do so (technically, from higher potential energy to lower potential energy as all of this is converted into kinetic energy, but kinetic energy will be ignored in the following discussion). A ball will not roll up a hill, however, because then it would be going from lower energy to higher energy. The only way that a ball will roll up a hill is if work is done. In order for work to be done a force must be applied over a distance ($\Delta E = W = Fd$). Just like balls, chemical reactions will only spontaneously "go downhill" energetically, and the bigger the hill, the more it "wants to go down." To get it to "go uphill," (as every reaction must initially) there must be strong enough forces (or energy input like heat) to be able to overcome the activation energy.

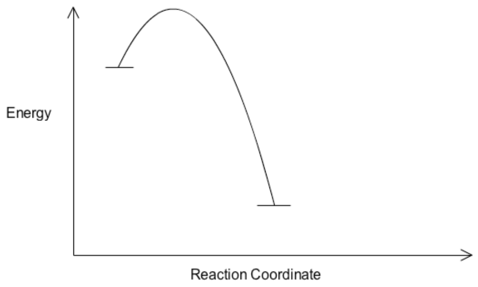
The above discussion is a little technical, but you do not need to understand it completely. What you do need to understand is energy diagrams. Energy diagrams are spatial representations of chemical energy as the species go through a reaction. Conveniently, gravitational energy works in a spatial domain. This means that if you think of energy diagrams as space, and molecules as balls or bikes, you get back all of your intuitions.

***Principle 6*:** Energy diagrams are spatial representations of energy at the molecular level. They work just like space and gravitational energy, an object will naturally go down hill, but not uphill. Furthermore, the longer the hill, the harder it is to get up, or the faster one will be going when they get to the bottom.

Hint: Think of molecules as bikes *without brakes*, and energy graphs as photographs of landscapes that the bikes must traverse.

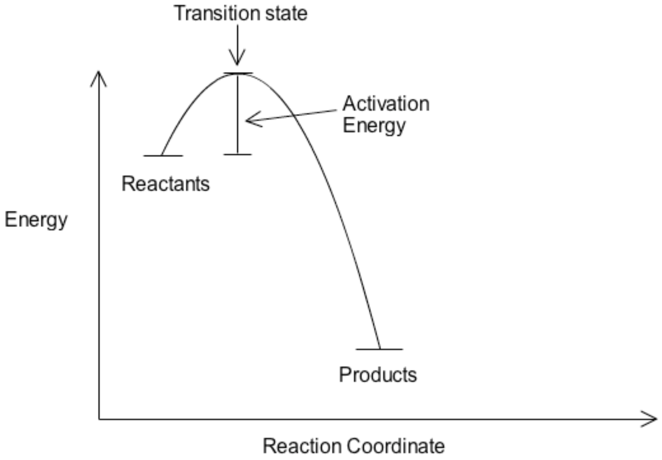
Energy diagrams

The y-axis of an energy diagram represents energy, and the x-axis is what is called the *reaction coordinate*. A reaction coordinate can be thought of as time, it represents progression through a reaction. Higher points on the graph represent more energetic states, just as higher hills have more gravitational [potential] energy than small hills. As you can see from the graph below of a one-step mechanism, it takes some energy to get "over the hump," like biking out of a valley up in a mountain, but that it is all downhill from there.

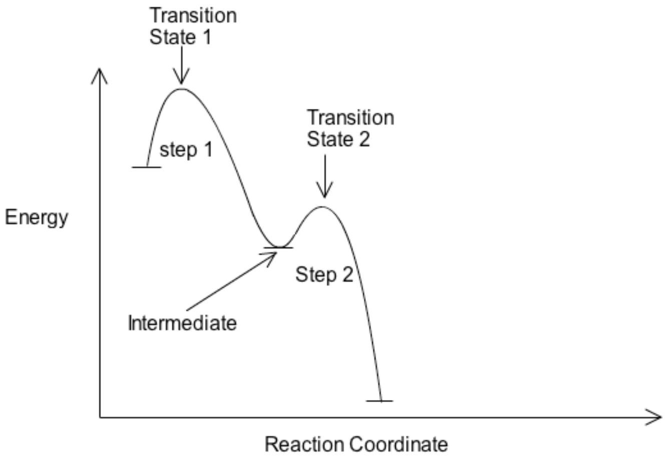


Dissecting the energy graph

The little bar at the top is the energy of the reactants, and the one at the bottom is the energy of the products. A *transition state,* is a part of the reaction where bonds are being broken or made. This is *not isolable* (unlike an intermediate which we will learn about soon). Imagine if you were on a bike without breaks, riding out of the valley where the reactants are, once you got to the very top of the hill there would be no way to stay there, you would either roll backwards or roll forwards. This is exactly the same case with a transition state, it is at the highest energy of anything, and so it is not something we can isolate because it will either continue on to product, or revert back to reactant. The *activation energy* is the amount of energy that is necessary to make it over the peak where the transition state is. If there is more energy available than the activation energy, then the reaction can occur, if not than it cannot. Again, think of biking out of this valley. If you eat a good breakfast and are well rested (plenty of energy) you can make it out of the valley because you can make it up the first hill, if you did not (you do not have enough energy) than you cannot.



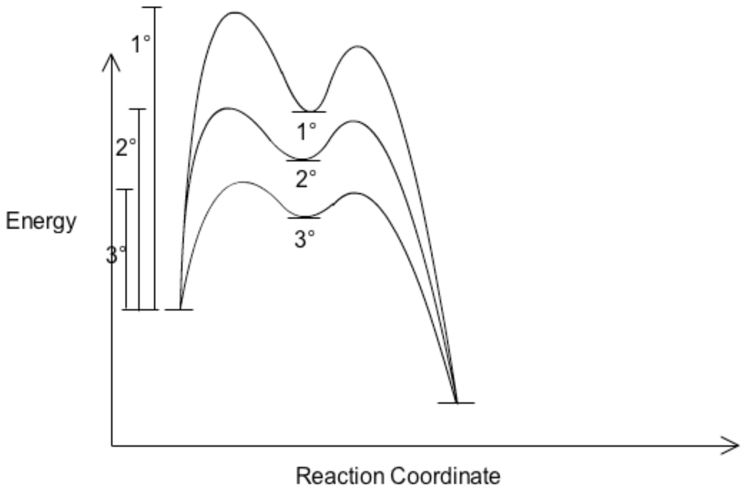
This graph above is an energy diagram of a *one-step* mechanism. An energy diagram has <u>as many peaks as there are steps in the mechanism</u>. The following graph is an energy diagram of a reaction with a two-step mechanism. Everything is the same, except there is an *intermediate*. Intermediates can be isolated, but it is very difficult. Imagine trying to stop a bike without brakes in that trough, you would just fly right through; well, so does the molecule.



Energy and reactivity

In general, the more energy the reactants have, the less stable they are, and the more reactive they are. Again, energy is related to force, which is related to charge. So, in general, the more unevenly the charges are distributed on a molecule, the bigger the dipole/ion, and therefore the more reactive the molecule. There are some exceptions to this, such as that the halides are very stable as negative ions (F, Cl, Br, and F). Also, as we will see molecules with resonance structures can usually hold a charge without becoming too unstable because they essentially smear the charge across the molecule.

The less stable the intermediate, the less likely the reaction is to take place. This is very important as it plays an integral role in a lot of mechanisms. This is because as the energy of the intermediate goes up, so does the activation energy. This can be seen in the following graph. I have labeled it with a common example you will learn about, where stability of intermediates plays a huge factor. Carbocations (carbon molecules with a positive charge), are common intermediates in a number of reactions. Because of *inductive effects* and *hyperconjugation* they are more stable the more highly substituted they are. So, a 3° carbocation (one with 3 substituents) is more stable than a 2° carbocation (one with 2), which in turn is more stable than a 1° carbocation (one with 1). This often determines the stereochemistry because as we can see in the following diagram, the activation energy for the 3° carbocation is much less than for the others. The activation energies are shown on the bars to the left. Therefore if the molecule has the "option" of choosing a pathway with a 3° intermediate, it will do that rather than one of the other two.



Imagine you were on a bike at the reactants and could choose three paths to get out of the mountains, which one would you choose? It is no wonder 3° carbocations predominate in mechanisms.

RESONANCE

Limitations of the notation system

In the introduction I mentioned understanding the notation system, and its limitations. We use many different notation systems in organic chemistry such as Lewis dot structures, which emphasize showing the electrons, and Kekule structures (the line diagrams), which emphasize what the bonds are. We use these notation systems because they are very good at laying bare the physical reality of these molecules. One thing that they cannot do however is show partial bonds and partial charges. This is what resonance is for. As we have noted, electrons are not like particles exactly, but are more like smears of matter. Our notation system, however, treats them as particles. This can lead to problems because in some systems *with pi-bonds* and lone pairs, these electrons can smear across the molecule in physical reality and be shared across many atoms, but we cannot show this well in our notation system. This is what resonance is for—to overcome the limitations of our notation system.

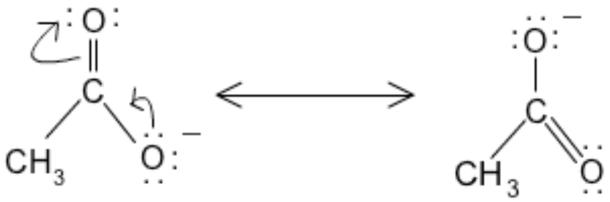
How to do resonance

Fundamentally, getting really good with resonance takes a lot of practice, but we are going to introduce the methods here so that you have them explicitly laid out.

1. Only *π-bonds and lone-pairs* can participate in resonance structures, you should do "arrow-pushing" like in a mechanism so that you do not forget what is going where, and what comes from where.
2. You *may not change any nuclei* when you do resonance structures (all your letters representing the atoms must stay in exactly the same place, it is only the bonds that can change).
3. Resonance structures must be "*held in place*." If you had two diagrams of two molecules and you could rotate one to make it map onto the other, you would actually be looking at two pictures of the same molecule. This is not so for resonance. So, I say that the atoms of themolecules must be "held in place" because often they could be rotated into each other, but this is irrelevant for resonance, you would still have 2 resonance structures in the above scenario.
4. Lastly, the *rules of chemistry must still be followed* in resonance, which means C cannot have more than 4 bonds/lone pairs, etc. The main problem is that students move electrons in to make a new bond, and then forget that this will push out another bond, leaving an atom with 5 bonds. This is because all resonance structures are just different representations of the same molecule.

Resonance is signified by double-ended arrows like this $\longleftrightarrow$

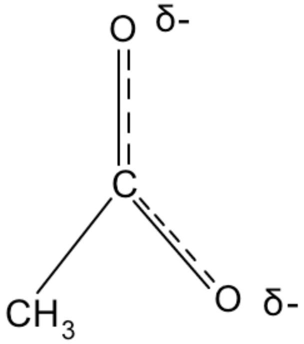
Fundamentally there is no other way to understand resonance than diagrams and practice, so without further ado, here is a resonance diagram for a carboxylate ion, the conjugate base of a carboxylic acid



There are a number of things to note here. First off, notice how *all the atoms are in the same places, as are all the σ-bonds*, this must always be the case in resonance. The arrows signify a lone pair coming in to make a double bond, and a double bond getting kicked out to make another lone pair. *If the double bond did not get kicked out, then the carbon would have had 5 bonds, which breaks the rules of chemistry*. Notice *the arrow is double ended*, this signifies that these are resonance structures. Lastly, notice how if these were molecules and not resonance structures, we would be looking at *1 molecule* but here we have *2 resonance structures*. If we *could* rotate 180° about the C-CH_3 axis we would have the same structure, and while this is what you would do with a molecule, it is not what you do with resonance forms. This is what was meant by # 3 above, that resonance structures must be "held in place." What resonance is showing is that some electrons are free to flow around more atoms than might be obvious from just one drawn structure.

What resonance means

Remember that resonance is just making up for the limitations in our notation system. *The actual physical molecule is a "compromise" or combination of all the resonance forms*. It actually looks like this:



The dashed lines represent partial bonds, and the lone pairs are not shown because it is more like each oxygen has 5 extra electrons rather than 2 or 3 lone pairs (4 electrons and 6 electrons respectively).

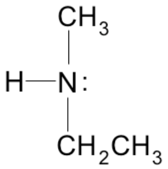
STEREOCHEMISTRY

Chirality

The word *chiral* comes from the greek word for hand, and *chirality* basically means "*handedness.*" What this refers to is an object where *the mirror image of the object cannot be superimposed on the original object*. While your hands may look similar you can never put a left-handed glove on your right hand and vice versa. This is because despite the fact that they look the same (because they are mirror images) they are actually different and not superimposable. This is also why you cannot put your left shoe on your right foot. Another way of looking at chirality is that an object *without a plane of symmetry* is chiral. This means if there is no plane you can draw where the object is the same on both sides, then it is chiral. This is very difficult for humans to understand, especially at first, just remember how tough it was to know which shoe went with which foot when you were little. This has to do with human cognition, and is something that we do not see intuitively. We easily orient things on an up-down axis, or a forward-backward axis, but we do not deal with the left-right axis very well (again, remember how hard this distinction was to learn as a little kid). You will learn all of this in class as it is very important to be able to recognize not just chiral objects (like hands or shoes), but also molecules that show this same feature. You will probably also be taught to look for a plane of symmetry in class which can be quite difficult, but luckily there is an easier way…

The easier way: the 4-substituent heuristic

While it might be helpful to be able to see chirality in an abstract sense, there is a shortcut you can use for molecules. Due to the nature of these molecules in 3-dimensional space you can always tell if something is chiral by just evaluating what it is bonded to and bypass the whole plane of symmetry issue altogether. *If an atom is bonded to 4 different things it is chiral, if not then it is not.* While lone pairs seem like they should count for one of these "things," like it does above in geometry, lone pairs do not count here, *unless the atom is locked in place.* This is because with something like the amine below it is not that it isn't chiral, it is just that it does a sort of "umbrella-flip" with the electrons, so it flips back and forth.



$\mathrm{H{-}\ddot{N}(CH_3)(CH_2CH_3)}$

How to determine between them, S and R

This is difficult to cover on paper and will be covered more in the class, but the outline is given here. There are two types of chiral molecules we can have, and they are called "S" and "R" as will be explained below. The easiest way to remember this is that R corresponds to right, as in the "righty-tighty" you probably learned for screws and bolts. This is a *clockwise rotation*. S would then be the other one, corresponding to "lefty-loosey," or a *counterclockwise rotation*. Now we must specify what we mean by these rotations. In order to tell which is which you need to figure out the priorities to the 4 things bonded to our atom based on the atomic numbers. You will learn more about this in your class, but it has to do with highest atomic number is highest priority, second highest atomic number is second highest priority, etc. You then need to orient the molecule so that you are looking up the axis of the number 4 substituent, with it going into the page. Then decide whether you would rotate #1 clockwise or counterclockwise to reach #2. These are the rotations described above where clockwise = R, and counterclockwise = S.

The meso shortcut

You will also learn that it is possible for a molecule to have multiple chiral centers and still be achiral. You will probably also learn complicated ways of looking for planes of symmetry but there is an easier way to know. Without going into details of why this works or what meso is I will just present the technique. If the three conditions hold then the molecule is meso, if they do not than it is not.

1. Are there an even number of chiral centers? (usually 2)
2. Do these chiral centers have the exact same "substituents?"
3. Are the chiral centers alternating R and S, such as S,R, or R,S, or R,S,R,S?

If the answer to all of these questions is "yes," the compound is meso.

FUNCTIONAL GROUPS

Functional groups are the fundamental units of organic chemistry

Atoms are the fundamental units of chemistry, and *functional groups are the fundamental units of organic chemistry*. When you look at a new molecule, the only thing that you need to focus on is the functional group. Usually a molecule will consist of two parts an *alkane*, which is a saturated carbon chain that we will cover later, and a *functional group.* Alkanes are essentially unreactive, so their structure is irrelevant, all you will need to be worrying about is the functional group on the carbon chain. The course will be arranged around functional groups, and this is a brief introduction to what you are going to see. Obviously there is way more than we can cover here, but this should introduce you to why these groups behave the way they do. I would put a table in of all the functional groups but your o-chem book will have one. I recommend memorizing all of these immediately (as you will probably have to do for your test anyways). Don't worry too much about it if you find this difficult at first as they will probably all look the same, pretty quickly they will become second nature to you.

Principle 7: A molecule's behavior is dictated by its functional group. When determining what a molecule will do you must look to the functional group. You will want to look at establishing dipoles and charges, as well as noticing any multiple bonds (π-bonds), lone pairs, or possibly acidic hydrogens. As discussed above these features will drive the reactions that the functional group undergoes.

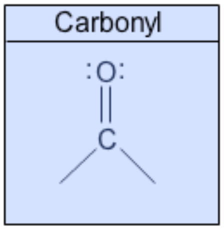
Principle 3 revisited: Learn the chemistry of the functional groups "wholistically." Many functional groups undergo upwards of 15 different reactions, and with around 20 functional groups this can translate into a lot of memorization. The way to cut back on this is to understand *why* a functional group reacts, *what* it reacts with, and *how* it reacts (the mechanism). Often many of the reactions are very similar, often they are even the exact same mechanism (as with some of the carbonyls). *Look for these similarities in mechanisms as you learn them*. Furthermore, *the details of reactions* (such as regiochemistry and conditions) *are dependent upon the mechanisms*. Learn to understand the mechanisms, and you will not have to memorize these details (although it is helpful to have them at your fingertips).

Naming molecules

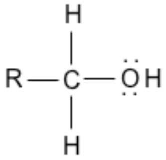
You may or may not be required to know how to name all the molecules you are learning about. There is no conceptual way to cover this. The instructions for naming are explicit, with a specific hierarchy of what matters. Memorize this process and practice. This should be one of the easiest parts of the class, but it takes practice, and so is difficult at first.

Carbonyls

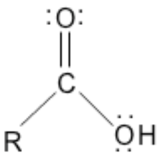
The carbonyls are a class of functional groups including aldehydes, ketones, carboxylic acids, and acid derivatives. Again, these will become second nature, but they are hard to recognize at first. A *carbonyl* is an oxygen double bonded to a carbon like the following picture



If these stand on their own they are ketones or aldehydes, but they can also be paired with other functional groups, and the *chemistry is fundamentally different from the functional group on its own.* For example, an OH on an alkane (on the left below, remember that R=unspecified alkane) is an *alcohol*, but if it is next to a carbonyl it is a *carboxylic acid* (on the right below).

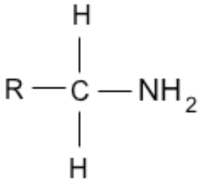


Alcohol

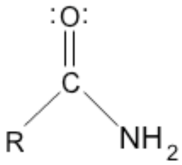


Carboxylic acid

The one on the left below is an alkane with NH_2, and is an *amine*. The one on the right is an NH_2 next to a carbonyl, and is an *amide.*



Amine

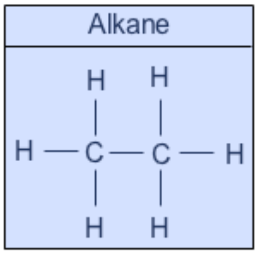


Amide

This is a HUGE difference in chemistry, but is a subtle difference to an untrained eye, both in structure and in the names.

Hint: Make sure that before you name a molecule you check for a carbonyl next to any other functional group, as this will make it a completely different functional group.

Alkanes



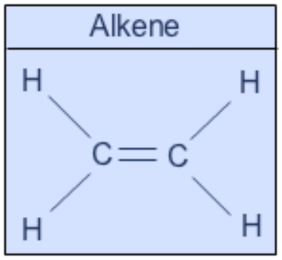
Hydrocarbons

Alkanes are *hydrocarbons* (they contain only carbon and hydrogen) with *only single bonds*. Because they only have single bonds they are said to be *saturated hydrocarbons*. Alkanes are the least reactive of all organic compounds. They do not have a functional group, and usually provide the backbone for other molecules with functional groups because they are unreactive. They all are similar, whether they have 2 carbons (as the ethane above) or 18 carbons. It is unlikely that you will need to know any chemistry for alkanes, as they are so unreactive. Just know that as the number of carbons goes up so does the boiling point.

Alkanes are *nonpolar* because the electronegativity of H is 2.2 and the electronegativity of carbon is 2.5 yielding $\Delta EN=.3$, which corresponds to a nonpolar bond. This is the main reason that they are so unreactive.

Remember that the symbol for a generic alkane is “R.” You will see this on many of the other functional groups in the future, and this just stands in for “any alkane.”

ALKENES

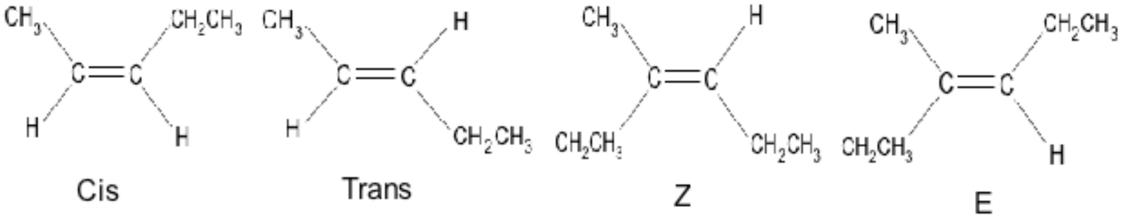


Structure

An *alkene* is just a double bond between carbons in what would otherwise be an alkane. Because each carbon is bonded to 3 things (a carbon and two hydrogens) it is *sp^2 hybridized*, meaning that it is *trigonal planar*. The third p-orbital is obviously involved in a *π-bond* between the two carbons. While C-C bonds and C-H bonds are nonpolar, alkenes are quite reactive because of the π-bond. The π-bond consists of electrons (which are negative) that are hanging out in space because it is an off-axis bond. This means that *alkenes react with positive parts of other molecules, or electrophiles (E^+).*

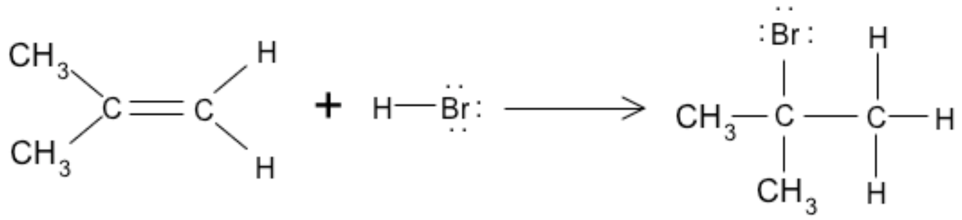
Cis-, Trans-, E-, and Z-

Alkenes have regiochemistry that can make otherwise similar molecules dissimilar. This is very easy to understand, just a little tough to remember to apply. If an alkene has an H and some alkyl group on each carbon you will use cis- or trans- to describe it. If the alkyl groups are on the same side (i.e. both "up" or both "down") it is cis-, if not it is trans-. E- and Z- designations are basically the same, with Z being the same as cis, and E being the same as trans. To remember this just remember that Z corresponds to the higher priority being on the "zame zide." The only difference between E and Z and cis and trans is that *with cis and trans each carbon needs an H, and with E and Z one of the carbons or both will not have an H*. You must assign priorities and the higher priorities will be dealt with just like the alkyl groups in cis and trans. As with much of organic chemistry this is easier to see than say, so these are all shown below.



Your first mechanism

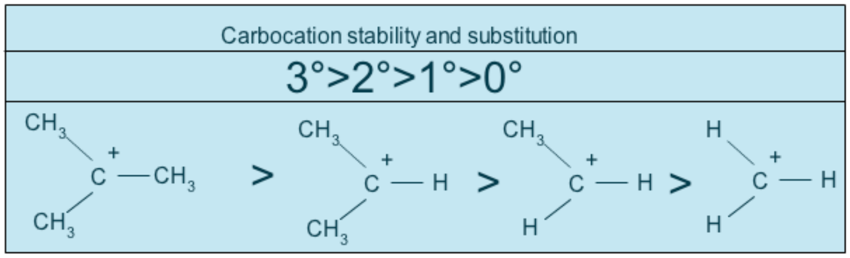
We are now going to walk through a mechanism and dissect it so you can get an idea for what you will be doing in organic chemistry. This is probably the first mechanism you will learn in class as well, and it is because it illustrates many prototypical features of mechanisms in general. In the following reaction we observe that when we add HBr to the alkene we end up with the Br attached to the C with more substituents (the carbon on the side of the alkene with 2 CH_3 substituents as opposed to the C with 2 Hs). This is called a *Markovnikov product*, when the Br goes *to the more highly substituted carbon*. The reason it does this lies in the mechanism, which has a carbocation intermediate.



First we must discuss carbocations. A *carbocation* is just what it sounds like, a carbon with a positive charge. This charge causes carbocations to be quite unstable, and so they are just intermediates, and extremely difficult to isolate. *The more we can stabilize a carbocation intermediate the more favorable the reaction will be.*

Carbocation stability

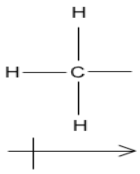
The more highly substituted a carbocation is, the more stable it is. Know this rule as it applies in many mechanisms all the way to the end of the course. This is due to two reasons: *1. Inductive effects, and 2. Hyperconjugation*, that we will go over shortly. We determine *substitution level by how many carbons* our atom of interest is bonded to: a carbon bonded to 3 other carbons would be 3°; a carbon bonded to 2 other carbons would be 2°; one bonded to one other carbon would be 1°; and one bonded to 0 carbons and thus only hydrogens is 0° and is called methyl. Carbocation stability is as follows 3°>2°>1°>0°.



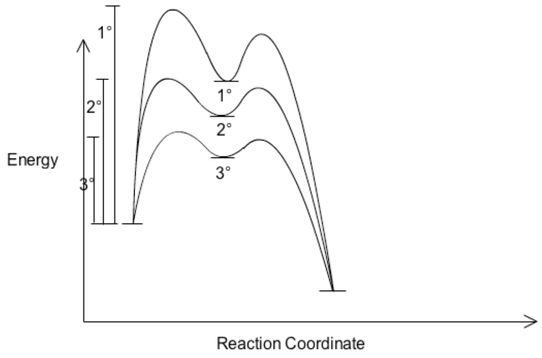
This is going to be the first place where we integrate a number of the foundational concepts we learned to explain chemical behavior. The concepts we invoke will be listed for clarity first and then integrated below.

1. Charges make molecules unstable (with a few exceptions), and the bigger the charge the more unstable something will be.

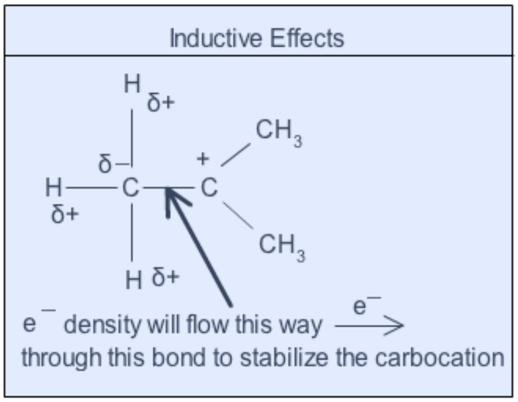
2. Methyl groups have a positive polarization out at the hydrogens, and the carbon has a slight negative dipole meaning it has a little extra electron density.



3. The greater the activation energy of a reaction, the less likely it is to occur. The more unstable an intermediate is, the higher this activation energy is going to be.



Now let's pull all these together to show why highly substituted carbocations are so much more stable, and make reactions more favorable. The first piece of the puzzle is inductive effects. An *inductive effect is a sharing of electron density through a σ-bond*. This is similar to how C-H or H-Br have electron density being shared unevenly because one of the atoms is pulling harder on the shared electrons causing a dipole. Often atoms with dipoles can stabilize adjacent dipoles of the opposite charge using the same process. This is called an *inductive effect.* For example we have shown that a methyl group has a slight dipole, with the carbon taking a slight negative charge. If a carbocation has an attached methyl group it will be bonded to this carbon with a slight negative dipole. The carbocation can essentially "suck" some of the e$^-$ density through the σ-bond to reduce the magnitude of its charge. It is like the carbocation has this burden to bear, a positive charge, but with other carbons around he has friends to help him carry that burden. It is as though the carbocation goes from +1 to +3/4. The lesser the charge, the more stable the molecule, so this stabilizes the carbocation. This is diagrammed below for one of the methyl groups, but happens with all 3.



The second reason that a more highly substituted carbocation is more stable is because of *hyperconjugation.* How hyperconjugation actually works is a bit beyond the scope of organic chemistry, and is part of the domain of physical chemistry. Essentially the sp^3 bonds of the methyl groups interact with the empty p-orbital that the carbocation now has. Just be familiar with this, you do not need to know this in depth.

We also know that the more stable the intermediate, the lower the activation energy, and thus the more favorable the reaction. As we will see below, if we have an alkene whose 2 carbons have differing levels of substitution, and this participates in a reaction with a carbocation intermediate, the reaction will use the more highly substituted intermediate, yielding the more highly substituted product. This is a little dense, but we will unpack it below.

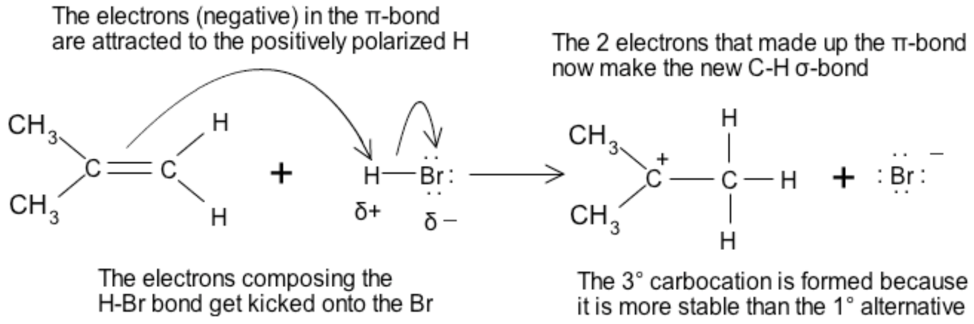
The mechanism

This is a *two-step mechanism*, meaning that there are two distinct chemical reactions with an intermediate. The mechanism will go as follows:

Step 1. The π-electrons on the alkene (negatively charged) will *attack* the positively polarized hydrogen on the hydrobromic acid (HBr). The two electrons in the H-Br bond will stay with the Br, and the H is therefore just a proton (H^+).The hydrobromic acid therefore donates the proton (H^+) yielding a 3° carbocation intermediate (the 1° carbocation will not form as discussed above), and a bromide ion (Br^-).

Step 2. One of the lone pairs on the bromide ion will then attack the positive carbocation, yielding our *Markovnikov product* (the Br is on the 3° carbon rather than the 1° carbon).

This is step one



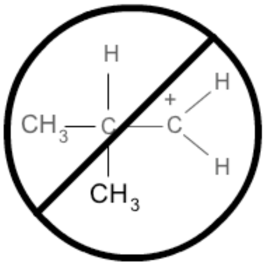
The electrons (negative) in the π-bond are attracted to the positively polarized H

The 2 electrons that made up the π-bond now make the new C-H σ-bond

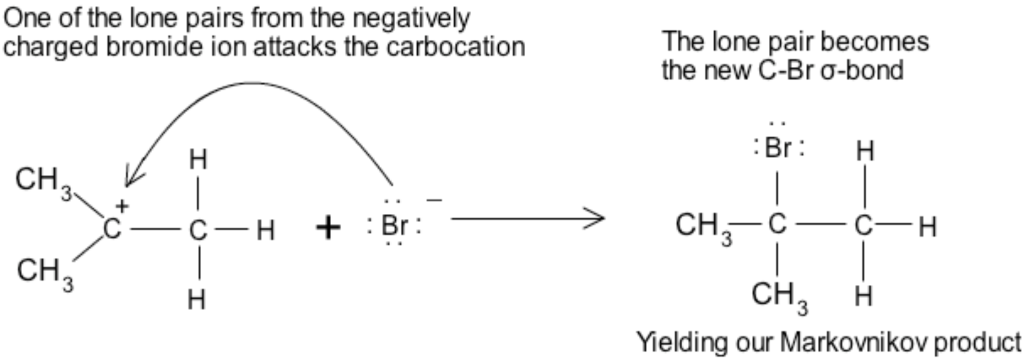
The electrons composing the H-Br bond get kicked onto the Br

The 3° carbocation is formed because it is more stable than the 1° alternative

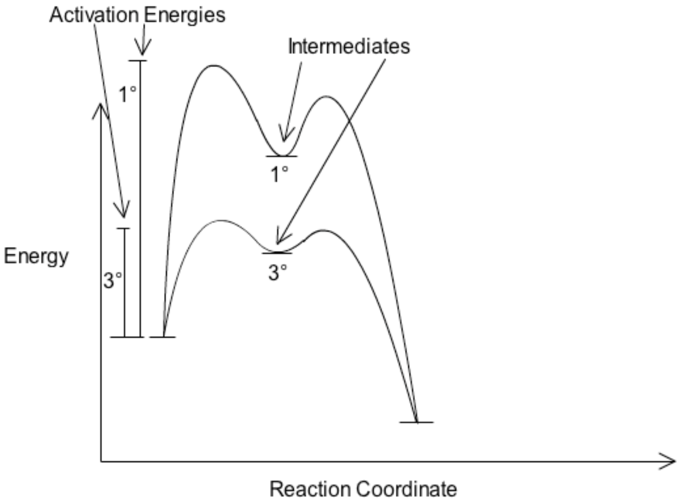
Notice the alternative pathway, which would have yielded the 1° carbocation, does not occur, this is due to its much greater instability.



Here is step two



There are a couple of things to notice in this, and every other reaction. First, everything occurred because oppositely charged atoms were attracted to each other. Second, the stability issue with the carbocation intermediate was the *cause* of our Markovnikov product. This is neatly summed up in our energy diagram for the reaction. Notice that the 1° intermediate requires a much greater activation energy due to its instability. This causes the reaction to only take the more stable pathway with the 3°intermediate. This in turn causes our Markovnikov product because *the Br ends up wherever the cation was*!



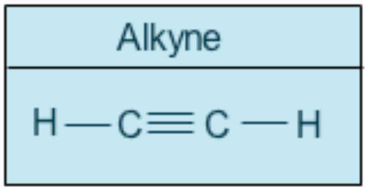
This example uses HBr, but it should be noted that it will work with any of the halides because they are so similar. We could just as easily run this reaction with HF, HCl, HBr, or HI. As mentioned earlier however, Br or Cl are always the safest choice of halide if it does not matter which one you pick. HBr above then can just be seen as HX, where the "X" just means "any halide."

<u>Principle 3 revisited</u>: There are a lot of parts to this reaction, and if you learn them as an integrated whole and see the relationships that will lead to less stuff you have to memorize. This whole set of information is just one reaction, and alkenes undergo about 10 different reactions. Not all of them have this much information you will have to know but it is obvious how quickly this can become overwhelming. This is what makes organic chemistry so difficult, but if you see the connections it is easy. Many of the pieces of information above are redundant. Knowing about carbocation stability, and knowing that this reaction has a carbocation intermediate (which you need to know anyways) *tells you that you will get a Markovnikov product*. Furthermore, if you understand this you will be able to generate the energy diagram yourself.

Principles 1 and 4 revisited: Understanding what makes this reaction tick, as well as its relationship to the energy diagram (principle 1) means a) you do not have to memorize the energy diagram or the regiochemistry, and b) what you do have to memorize will be much easier. Furthermore, if you understood how to apply the unifying theory (principle 4), but completely forgot the mechanism, you could probably actually figure it out. Given the reactants (an alkene and HBr) there is only one possible reaction. Because the alkene behaves with a negative character, H is positive, and Br is negative, *there is only one possible reaction—for the π-bond to attack the H*. You will then be left with a carbocation by necessity. Understanding carbocations then will tell you that it must be the 3° carbocation. Again, you have a positive carbocation intermediate, and a negative bromide ion, *there is only one possible reaction—for the Br^{-} to attack the 3° carbocation*. This yields our Markovnikov product.

Granted, it is the beginning of the course and you probably do not see this yet, but if you understand the fundamentals and lay strong foundations you will, and that is how to ace organic chemistry and reduce your workload at the same time. Who said it was all memorization??

ALKYNES

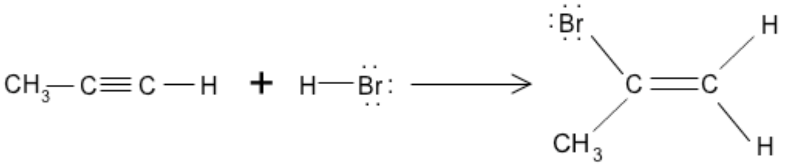


Alkynes are like alkenes

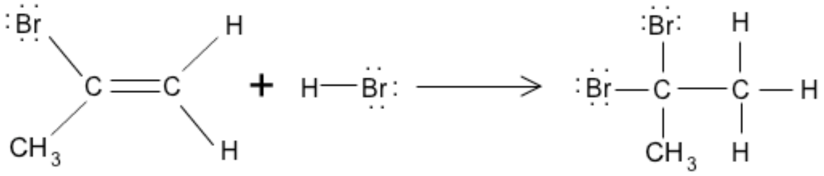
Alkynes are almost just like alkenes. They undergo most of the same reactions, because they are reactive in exactly the same way. Alkene chemistry is dictated by the extra negative charge hanging out in space in the π-bond. Thus they are reactive because they have a π-bond, and react with positive charges (E^+). Alkynes have two of these, and are therefore reactive in the same way. They do have a different geometry, however. Alkynes are bonded to just 2 things, and so their geometry is *linear* and they are sp^1 hybridized.

Beware the double reaction

Because alkynes are so similar to alkenes, and often turn into alkenes after one reaction, they will often react twice. When you run a reaction with an alkyne that you could do with an alkene, it will usually react past the alkene as well. For example we can add HBr to an alkyne and get the same reaction as we would with an alkene, it will even yield a Markovnikov product if one of the alkyne carbons is attached to another carbon, but the other is attached to a hydrogen. If we add HBr to an alkyne we will get the following reaction with the same mechanism as with an alkene:



Of course now we have an alkene floating around with HBr, and we already know what happens when you add HBr to an alkene. The molecule will react again:



We now have a di-brominated product, but this is *exactly* the same reaction we just learned, same mechanism and everything. Notice that we even get the Markovnikov product, of course this time it is di-substituted. Because it reacts twice it is conventional to add a 2 in front of the HBr when it is going to react with the alkyne to show that 2 moles of HBr will react.

__Principle 3 revisited__: Notice how this is a whole new reaction with a whole new functional group, yet you only needed to learn one new piece of information. Look for these connections, or else you are left re-memorizing everything you just learned for the alkene reaction with HBr. All you have to remember here is that it is the same, but reacts twice because the first product is an alkene.

The only major difference: acidity

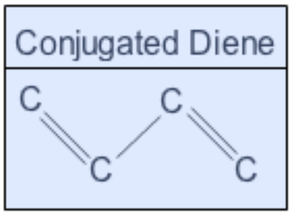
Because it has 2 π-bonds an alkyne can actually stabilize a negative charge *relatively* easily. I say relatively because it is by no means a strong acid, but it is possible to deprotonate alkynes (only if they have Hs of course). This must be done with a *very strong base*, however, because alkynes are so weakly acidic. This can be done with a Grignard reagent (RMgX, which can be thought of as a basic/nucleophilic salt, $R:^{-}\,{}^{+}MgX$), or another very basic salt, sodium amide ($Na^{+}\,{}^{-}:NH_2$). These will yield an *acetylide ion,* the conjugate base of an alkyne. Acetylide ions can then themselves act as bases, or as nucleophiles. This is one of the few ways to add carbons together, so it is definitely worth taking note.

$$CH_3-C\equiv C-H + R:^{-}\,{}^{+}MgX \longrightarrow CH_3-C\equiv C:^{-}$$

RMgX is called a Grignard reagent and is a common Nucleophile ($Nu:^{-}$) but it can also act as a base ($B:^{-}$) as it does here

This acetylide ion can now be used itself as a nucleophile ($Nu:^{-}$) or base ($B:^{-}$)

CONJUGATED DIENES

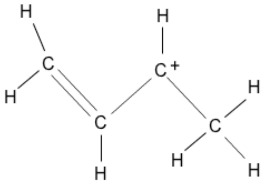


Resonance: why conjugated dienes are more than just a couple of alkenes

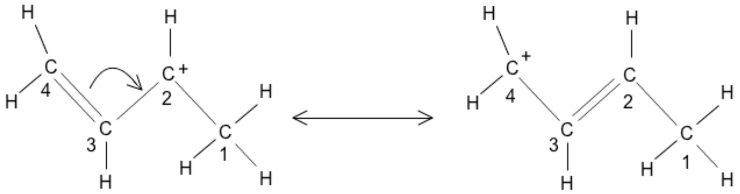
Obviously conjugated dienes are going to react similarly to alkenes as they are composed of 2 alkenes. They are reactive in similar ways due to similar structure. The π-bonds make the molecule react as a negative agent. The main difference is that the *intermediate* has 2 resonance structures so *each alkene can actually yield 2 products*. As we will see below these are referred to as 1,2 and 1,4 adducts. Furthermore, because there are *2 alkenes present* a conjugated diene can actually *yield 4 products* if the molecule is not symmetrical about the conjugated diene. This is difficult to understand in words, and can be confusing if you do not have strong resonance foundations. However, if you understand resonance well, there is nothing new here that really needs to be learned, except the terminology. As we will see below, if you have a firm grasp of resonance, you can actually generate the products on your own, and do not need to memorize anything new. You just need to recognize that you are dealing with a conjugated diene, and then look at the resonance forms of your intermediate.

The HX reaction and resonance of intermediates.

If you add HX (such as HBr) to a conjugated diene, the first step of the reaction is just like with an alkene, where the π-bond attacks the H due to the positive dipole. This yields the following intermediate:



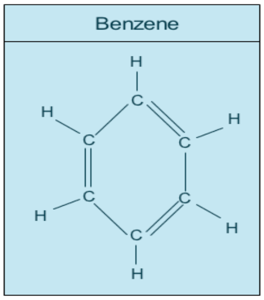
The only difference is that this has another resonance structure as shown below.



You will notice that I have numbered our carbons 1-4, this is where the terms 1,2 adduct and 1,4 adduct come from. Just as in the "alkene + HX" reaction the halide (X) will add to wherever the carbocation is located. So the halide can either add to the "2" carbon, or the "4" carbon. Because the H from the HX added to the "1" carbon, these yield our 1,2 adduct and 1,4 adduct respectively.

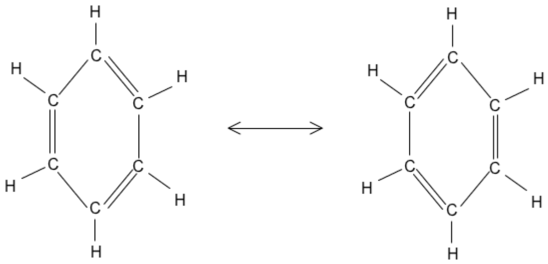
Don't forget the same reaction can take place with the other alkene as well!

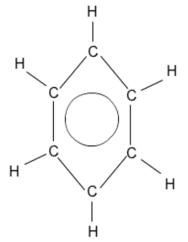
BENZENE



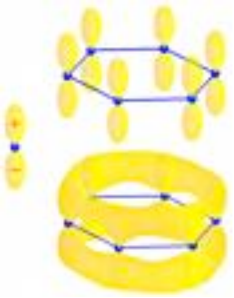
Benzene is aromatic

Aromaticity is fairly simple and you will learn about this more in class. Molecules that are aromatic have *delocalized π-bonds*. All this means is that rather than looking like a collection of localized double bonds, the π-bonds in benzene extend around all of the carbons. This is due to the following resonance structures, and is often just written like the picture on the right. The circle just means "delocalized π-electrons."





You should note that all carbons are sp^2 hybridized, meaning they are all trigonal planar and have a p-orbital that lies perpendicular to the plane of the ring itself. These p-orbitals basically form one giant π-bond, and this is the nature of aromaticity. The following diagram shows the p-orbitals above and the giant delocalized π-bond below.



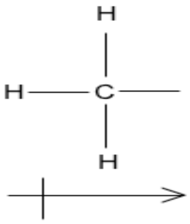
Because the "extra" π-electrons are smeared across the entire molecule benzene is unusually stable. Furthermore, even though it is stable, it also has a number of stable intermediates because of resonance. This means that benzene is not just itself stable, but can also undergo many reactions. Furthermore, as we will see it can react with both Nucleophiles ($Nu:^{-}$) and Electrophiles (E^+). Because the π-bonds can be thought of as negative, however, electrophilic reactions are far more common and more numerous.

Know your resonance

Resonance plays a large role not just in understanding the overall structure of benzene, but also in understanding how different substituents cause it to react differently. Your class will go over this extensively, and we do not have time to go into it in depth here, just make sure that you are very comfortable with resonance by the time you get to benzene.

Activation/deactivation

The nature of benzene changes depending upon what substituents it has. We are first going to address what this means for electrophilic reactions, as they are far more common, and will then discuss what this means for nucleophilic reactions. Electrophilic reactions are the intuitive reactions for benzene because with all the π-bonds it takes on a negative character, so it would make sense that it would react with positive reactants. Furthermore, depending on what substituents benzene has attached to it, it can become more or less reactive than just benzene alone. Substituents that make benzene more reactive are called *activators*, and substituents that make it less reactive are called *deactivators* for obvious reasons. You will be given a number of activators and deactivators and you could memorize them, but if you understand *why* they are activators and deactivators this is unnecessary. Benzene reacts with electrophiles because it has a negative character. Thus, it should make sense that if you have *a substituent that makes it more negative this should in turn make it more reactive*, in contrast, *if the substituent makes it more positive this will make it less reactive*. The way a molecule can make benzene more reactive is by adding negative charge, either through *inductive effects*, or through *resonance*. Inductive effects work with substituents just like they do with any other molecule, so just as a methyl group donates electron density to stabilize carbocations, it will also donate electron density to benzene, but for reasons discussed above this will actually destabilize benzene by making it more negative. This is easiest seen with a picture, and we will just revisit the polarization diagram we used to understand inductive effects with carbocations.



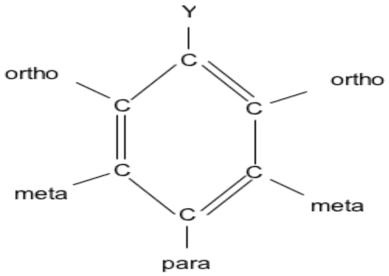
Notice the dipole of the methyl group shows the carbon as negative. This means that just like with a carbocation, the methyl group donates electron density to the benzene ring. For obvious reasons, groups that donate electron density to benzene are called *electron-donating groups* (EDG). They will make the ring more reactive in electrophilic reactions, and are thus *activating groups*. Likewise, groups that do the opposite and withdraw electron density are called *electron-withdrawing groups* (EWG). These make the ring less reactive in electrophilic reactions, and are thus *deactivating groups.* Resonance can also be used to show activation and deactivation by seeing whether the resonance forms put a + charge in the ring, or a lone pair (a – charge).

The above discussion applies to electrophilic (E^+) reactions, which occur because of the ring's negative character. For nucleophilic ($Nu:^{-}$) reactions these are reversed. This should be apparent why, if the ring reacts with a nucleophile then making the ring more negative should make it less reactive and vice versa. The only puzzling aspect here is why the ring reacts with nucleophiles to begin with. This is really beyond the scope of the class, but has to do with the complicated nature of benzene and its aromaticity. Furthermore, these reactions will only take place if the benzene has a substituent that is an electron-withdrawing group.

Usually inductive effects and resonance effects act in the same direction, either both withdrawing or both donating except with the halides, in which case they actually oppose each other, with resonance showing halides to be electron-donating groups, but inductive effects (due to their high electronegativity) showing them to be electron-withdrawing groups. This leads to bizarre behavior in the case of the halides as you will see in class.

Substituents can affect regiochemistry of addition

If a benzene ring already has a substituent, there are three possible places the next one could go. These are designated by the terms ortho-, meta-, and para-. Two substituents are ortho- when they are on neighboring carbons. Two substituents are meta- when they are one more down than this, and two substituents are para- when they are on opposite sides of the benzene ring. This is shown in the following diagram.



We do not have enough time to go into the details, but you need to be aware that depending on the nature of Y it will direct the next substituent either to the ortho- and para- positions, or just to the meta positions. These are aptly named ortho-,para-directors, and meta-directors. Except for the halides (which are weak deactivators and o-,p-directors) the pattern is that *activators are o-,p- directors, and deactivators are m-directors*.

π- BONDS AND DIPOLES

The "carbon-only" functional groups are the π-bond reactors

You may have noticed that alkenes, alkynes, conjugated dienes, and benzene all owe their reactivity to π-bonds. These reactions can thus in some sense be grouped together (although due to aromaticity benzene is different from everything else you will learn). They all can be treated as negative molecules, that *react with electrophiles (E^+)*. This is the nature of the π-bond as introduced earlier. These are pretty much the only carbons that react with electrophiles, and the rest of the functional groups react with nucleophiles.

Oxidation and reduction revisited

Before we introduce the dipole reactors, we must first address oxidation and reduction. This is very simple but is a little bit different from how you learned it in general chemistry. In gen chem you were taught that reduction is the gain of electrons, and oxidation is the loss of electrons. In organic chemistry these definitions are expanded a little bit. *Reduction is the gain of electron density, and oxidation is the loss of electron density*. We can now approach reactions that create or destroy dipoles as redox reactions. Thankfully, in the spirit of organic chemistry, this will be primarily conceptual, and you will not need to be balancing redox reactions using half reactions in acidic/basic medium, nor will you have to know anything about reduction potentials or batteries. In fact, if you were completely redox averse, you could probably get through the whole course without ever dealing with this, incurring a negligible impact on your grade. However, understanding this is helpful in developing your intuition, and can help you group together a number of different reactions.

We have a handy heuristic here as well, that if you are familiar with it you will not always have to be analyzing reactions for reduction and oxidation. First, it should be noted that we are always looking at what is happening to carbon, so even though we might say an O bonding with a carbon would be reduced, this is irrelevant. This being said we can just lay out the oxidizers and reducers. Because dipoles, and therefore where the electron density is located in a bond, are dictated by electronegativity, this will be our starting point. Obviously a C-C bond is nonpolar. A C-H bond is technically nonpolar, but as we saw above is actually slightly polarized towards the carbon. So, if we went from a C-C bond to a C-H bond this would constitute a reduction, as carbon goes from neutral to a slight negative polarization. Basically everything else will be an oxidation. We will also see carbons bonding with N, O, F, Cl, Br, and I, which are all much more electronegative than carbon. Thus a C-C bond changing to any of these bonds (C-N, C-O, or C-X) will constitute an oxidation. So, all you really need to know is that if we move to C-C bonds or C-H bonds from any of these it is an oxidation, and if we go in the reverse order it is a reduction. *Our reducing bonds are C and H and our oxidizing bonds are everything else.*

So far this is not especially helpful, it is just an explanation, but here comes the useful part. We have specifically oxidizing agents, and specifically reducing agents, and if you can group these you will not have to learn them for every functional group separately. Oxidizing agents turn C-C bonds and C-H bonds into C-O bonds. Reducing agents turn

C-O bonds into C-H bonds. Furthermore there are weak and strong oxidizing and reducing agents that we will use for different purposes and this will be pointed out below. The following table lists the reducing and oxidizing agents, describes their nature, and what they are used for. This table is not exhaustive, but covers the major ones you will probably see. This will be especially useful as you get to carbonyls and alcohols, which we are about to see shortly.

Oxidation: C-C, C-H → C-O

Reduction: C-O → C-C, C-H (or C-C→ C-H)

Many other reactions are obviously reductions and oxidations that you will learn, but these all are reductions and oxidations that help you jump from one functional group to another, and are common across many different functional groups. These all mainly focus on C-H bonds being formed or broken (except the ones that react with the alkene reagents).

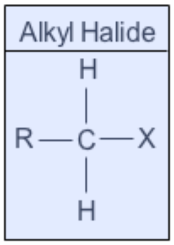
Reducing agent	Strength	What it does	Recommendations
$NaBH_4$	weak	Turns 1 C-O bond in aldehydes and ketones into a C-H bond to yield an alcohol (C-OH)	This is a weak reducing agent, and will not work with many carbonyls, so $LiAlH_4$ is recommended when you have a choice
$LiAlH_4$	strong	Turns 1 C-O bond in aldehydes and ketones or 2 C-O bonds in carboxylic acid and acid derivatives into C-H bond(s) to yield an alcohol	This is the recommended reagent when you go from carbonyl to alcohol as it works with all carbonyls
H_2/Pd (or Pt)	weak	This turns an alkene or alkyne into an alkane (C=C or C≡C into C-C replacing π-bonds with Hs)	This is used to eliminate π-bonds in carbons to yield alkanes
H_2/Lindlar catalyst	very weak	This will turn an alkyne (C≡C) into an alkene (C=C) without going all the way to alkane (C-C)	You only use this to go selectively from alkyne to alkene as Pd or Pt catalyst will go all the way to alkane

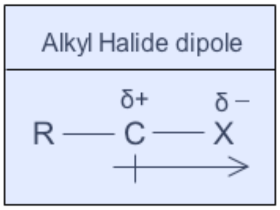
Oxidizing agent	Strength	What it does	Recommendations
$KMnO_4$	strong	Oxidizes anything from an alkene, an alcohol, or an aldehyde up to a carboxylic acid. When breaking an alkene you will get ketones and carboxylic acids depending on the substituents	This takes everything up to a carboxylic acid as long as it does not break C-C bonds to do so, so it cannot go past a ketone if a carbon in an alkene has carbon substituents. Obviously it also cannot oxidize a ketone
CrO_3	strong	Same as $KmnO_4$	Same as $KmnO_4$
$NaCr_2O_7$	strong	Same as $KmnO_4$	Same as $KmnO_4$
PCC	weak	This is a great reagent because in oxidizing alcohols it is the only one that stops at aldehydes so you don't get carboxylic acids	Use when you want to go from an alcohol and stop at an aldehyde
O_3/Zinc catalyst	intermediate	This splits alkenes yielding carbonyls, either ketones or aldehydes, and thus does not go all the way to carboxylic acids	Use to break apart alkenes and get aldehydes/ketones

One last word on reducing agents

Typically you are not responsible for knowing the mechanisms of any of these, but it is helpful to know that the reducing agents $NaBH_4$ and $LiAlH_4$, are essentially just hydride nucleophiles ($H:^{--}$). These are just the nucleophiles then in the exact same nucleophilic substitution reactions that you will see with many other reagents.

ALKYL HALIDES





Alkyl halides have a positive carbon dipole

This pretty much says it all, alkyl halides will react with nucleophiles (Nu:$^{--}$) because the carbon is positively polarized. Furthermore, if the halide leaves with the electrons from the bond, it will be negatively charged, but halides are very stable with a negative charge (think of NaCl).

Grignard reagents

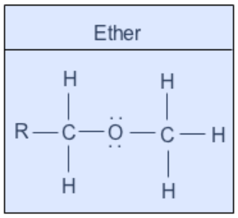
One of the most important contributions that alkyl halides make to the class is that they are the precursors to a Grignard reagent. A Grignard reagent is basically a carbon nucleophile (C:$^{--}$), which can help you couple carbons together through typical nucleophilic reactions. To make a Grignard reagent you just add Mg to any alkyl halide that isn't F (R-X = R-Cl, R-Br, or R-I) to make RMgX. Notice that *fluorine will not work* here. This is why I said above *when working with halides always use Br or Cl*.

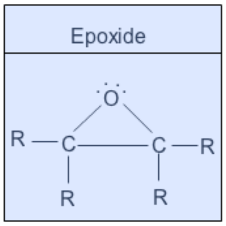
$$\text{R-X} + \text{Mg} \rightarrow \text{RMgX}$$

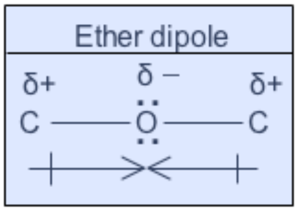
Keep in mind you will usually see this written as above (RMgX), but this is just a carbanion (R:$^{--}$), which can act as a nucleophile or base. Keep this in mind.

$$\boxed{\text{RMgX} \equiv \text{R:}^{--}}$$

ETHERS AND EPOXIDES







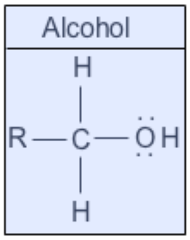
Ethers are unreactive

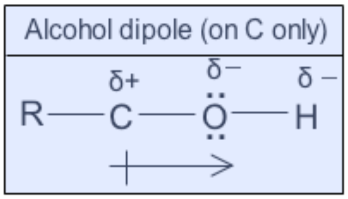
If you look at the dipoles on ether you will see that they cancel to some extent (it is tetrahedral, so they do not cancel exactly). The C-O bond is polarized, but because there are two of these bonds working in almost opposite directions, they cancel to some extent and ethers are *nonpolar*. They are therefore almost completely unreactive, except they can be cleaved by strong acids or bases. You may have noticed that ethers are extremely common solvents in other reactions (THF is an ether by the way), and this is because they are so unreactive they do not interfere with the reaction, unlike water, which will often interfere.

Epoxides are reactive

The main reason that epoxides are reactive has to do with *angle-strain*. Both the carbons and the oxygen are sp^3 hybridized and tetrahedral, which means that they should have bond angles of 109°. However to make the triangle these bond angles must be closer to 60°. This “bends” the bonds, which weakens them and makes them reactive. For epoxides, nucleophiles can attack the carbons, which will open the ring, or the oxygen can act as a base, and then the conjugate base of the acid it took the hydrogen from will attack the resulting carbocation.

ALCOHOLS



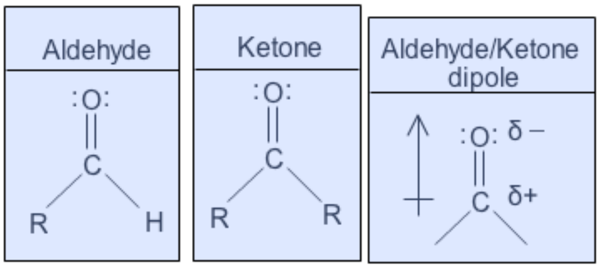


Alcohols react with nucleophiles and are slightly acidic
As you can see carbon has a positive dipole, and so does hydrogen (although the arrow for this is not shown above). This means that the carbon will react with negatively charged molecules, or nucleophiles such as grignard reagents (R:$^{--}$). Alcohols can also be slightly acidic due to the positive dipole on the hydrogen. They are only slightly acidic, however because the conjugate base, an alkoxide (R-C-O^{--}), is not very stable. As we will see in the carboxylic acid section, the more stable the conjugate base is, the more acidic the acid will be. If the proton is removed (only with a strong base like NaH), the alkoxide ion can act as a nucleophile; in fact this is the first step in the Williamson ether synthesis.

Alcohols are tetrahedral, and sp^3. They are somewhat polar.

Alcohols are also the least oxidized of any molecule with an O and as such are the endpoint of all the carbonyl reductions.

ALDEHYDES AND KETONES



The nature of aldehydes and ketones

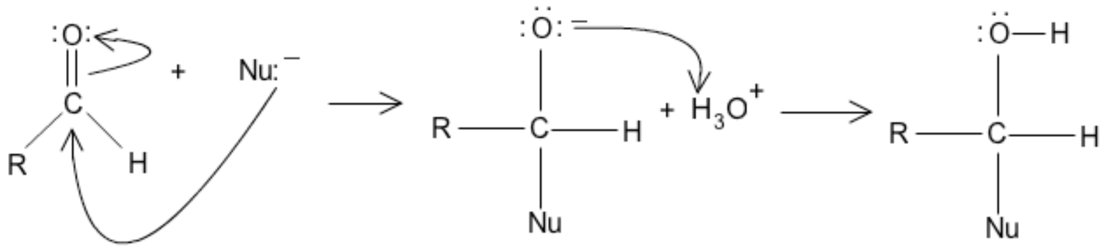
As you can see the carbon is positively polarized in aldehydes and ketones, and so they participate in nucleophilic substitution reactions that result in alcohols (with 2 exceptions). Furthermore, the O gets the π-bond kicked up onto it as a lone pair in the mechanism, and this is common in carbonyls because the O isn't too unstable with the negative charge. The carbon is sp^2 hybridized and trigonal planar.

The difference between aldehydes and ketones

As you can see these functional groups are almost identical, with the only exception being that the carbonyl carbon in an aldehyde is bonded to a hydrogen rather than another carbon. This is the source of the only difference between the two. The oxidizing reagents such as $KMnO_4$ are not strong enough to break C-C bonds, and so the ketone cannot be further oxidized. They can break the C-H bond however, and aldehydes can be oxidized up to carboxylic acids.

The aldehyde/ketone mechanism

There are really 2 mechanisms that these undergo, but the majority of reactions take place using the same mechanism which is a very simple two step nucleophilic substitution shown below.

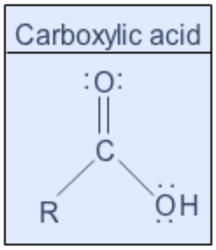


The nucleophile in this reaction can be:

1.H_2O, yielding an OH where Nu is
2. H:$^{-}$ (as $LiAlH_4$ or $NaBH_4$), yielding an H where Nu is
3. HCN (H-C≡N), yielding C≡N where Nu is
4. R:$^{-}$ (as RMgX), yielding R where Nu is
5. ROH (an alcohol), yielding OR where Nu is (which makes an ether)

There is one other mechanism, with 2 variants, but that is it for aldehydes/ketones

CARBOXYLIC ACIDS

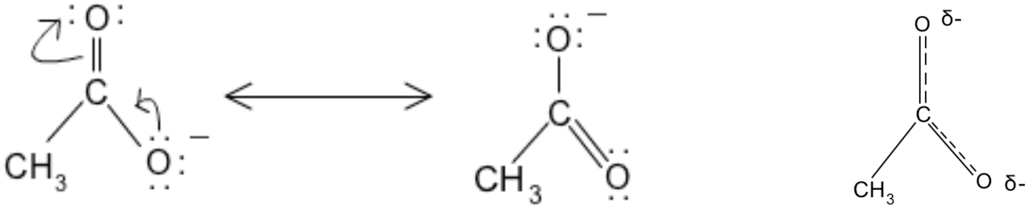


Carboxylic acids act as acids

This sounds like a no-brainer, but should be stated and explained anyways. Due to the inherent similarity of nucleophiles (Nu:$^{-}$) and bases (B:$^{-}$), and the acidic nature of carboxylic acids, if you add a nucleophile to a carboxylic acid (which is what the rest of the carbonyls react with), the nucleophile will just act as a base and take the proton.

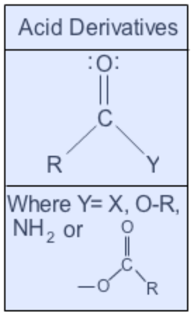
An acid is only as strong as it's conjugate base is stable

The reason that carboxylic acid is an acid is that it's conjugate base is stabilized through resonance. Strong acids are strong acids because their conjugate bases are stable. For example, HCl is such a strong acid because it's conjugate base, Cl^{-}, is so stable. The same holds true for all acids, if you want to know why something is an acid, or how strong of an acid it is you need to look at the stability of the conjugate base. The conjugate base of carboxylic acid is the carboxylate ion, which has 2 resonance structures, yielding the "actual" molecule on the far right.

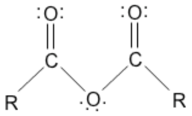


A correlate of this is that the more stable the carboxylate ion is, the stronger the acid is. The carboxylate ion can be stabilized by adding a strong electron-withdrawing group such as –CF_3 instead of –CH_3. This helps distribute the negative charge over even more of the molecule, thus stabilizing the conjugate base even more, and making the acid even stronger.

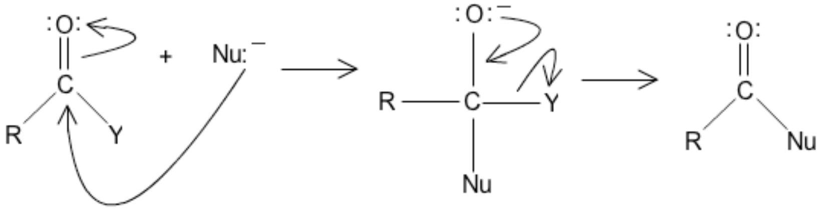
ACID DERIVATIVES



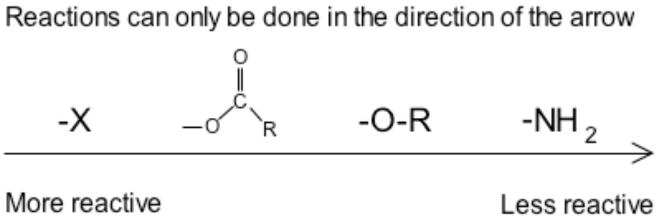
There are four types of acid derivatives
As you can see above there are four types of acid derivatives:
1. Acid halides where Y=X (called acid chloride, acid bromide, etc. depending on the halide)
2. Esters where Y=O-R which look like ethers with a carbonyl
3. Amides where Y=NH_2 which look like amines with a carbonyl
4. Acid Anhydrides, where Y=OCOR, which is the picture at the bottom, and these look like this:



The mechanism is similar to aldehydes/ketones
Acid derivatives also react with nucleophiles, and the first step is the same, but instead of turning into an alcohol, the carbonyl regenerates, kicking off the Y-group. This is because unlike C, or H, in ketones or aldehydes, the Y groups are all fairly stable with a negative charge. Substituents like this, that are stable with a negative charge (such as Cl^{-}, or NH_2^{-}), and can thus be kicked off a molecule, are called *good leaving groups*.

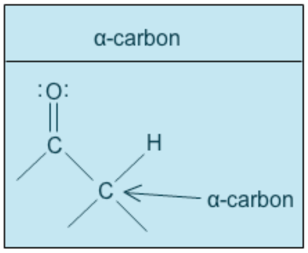


You may notice that once the leaving groups (Y) leave they have a negative charge, and would thus be good nucleophiles themselves. Some of the acid derivatives can actually be made from other acid derivatives. This goes according to a reactivity order, in which less reactive acid derivatives can be made from more reactive derivatives (so an amide could be made from an acid chloride, but not the other way around).



This is all summarized on a table in the review sheets.

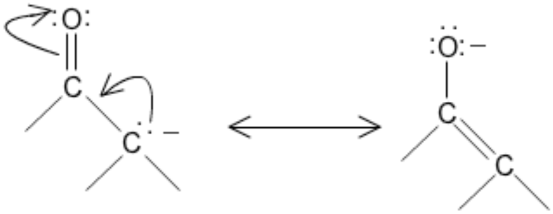
α-ACIDITY AND SUBSTITUTION



This is not actually a functional group, but is a type of reaction that ketones and aldehydes can undergo. I put it here because it is like an extra functional group.

Why α-carbons are acidic

As can be seen above, α-carbons are the carbons that are one carbon down from the carbonyl. You will notice there is one H attached to the α-carbon, this is because in order to act as an acid and donate a proton, the *α-carbon needs an H attached*, if all three bonds are to carbons, there can be no reaction. As noted before, the reason why molecules are acidic has to do with the stability of the conjugate base. The reason that α-carbons are acidic is because of the resonance structure of the conjugate base. This makes this stable enough that the α-carbon can donate a proton.



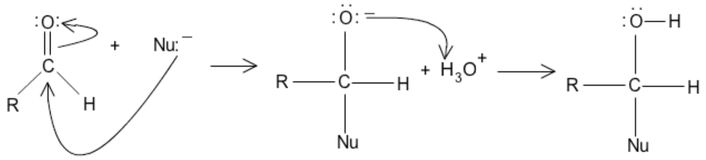
The conjugate base can be a nucleophile

The left resonance form above can now act as a nucleophile in other reactions. All of α-carbon chemistry is dictated by this conjugate base acting as a nucleophile. Furthermore, we have seen how carbonyls (other than carboxylic acids) react with nucleophiles, this can now also react with one of these carbonyls in what are called condensation reactions, as we shall see shortly.

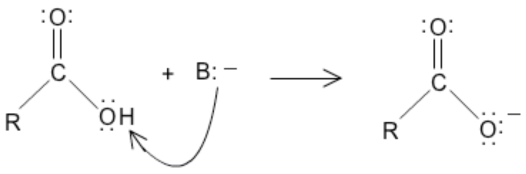
THE CARBONYL SYNTHESIS

You have been introduced to all of the carbonyl reactions and now we are going to synthesize what we have gone through to lay bare the similarities and connections.

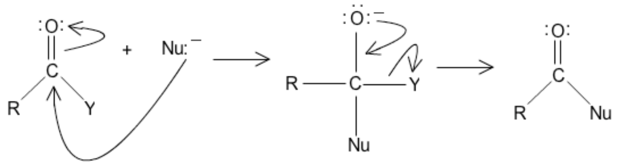
Aldehydes and ketones



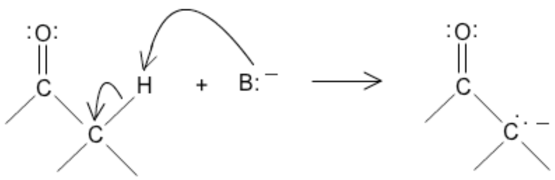
Carboxylic acids



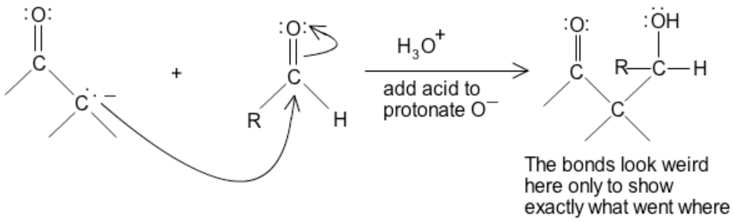
Acid derivatives



α-carbons as acids



Condensations: the confluence of aldehydes/ketones and α-carbon nucleophiles

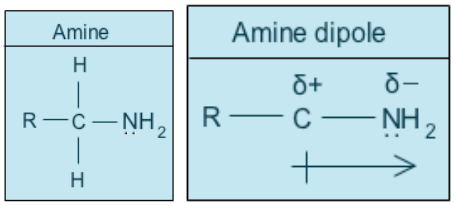


The bonds look weird here only to show exactly what went where

Condensations are usually taught completely separately, but they are just a combination of two things you have already learned. The nucleophile that reacts with the aldehyde/ketone is just the conjugate base from the α-carbon acting as an acid. This is just another example of how understanding cuts back on your memorization.

***Principles 1 & 3 revisited*:** Carbonyls are the best example of these principles. If you can understand the connections not only between the reactions within each functional group, but also understand the connections between the functional groups you will have not just cut down on your workload considerably, but will have developed a profound understanding of organic chemistry! Work on seeing the big picture with carbonyls.

AMINES



It should be noted that the NH_2 above could have other alkyl substituents, so it could just as easily be NR_2

Amines can be both acidic and basic
Amines are somewhat strong bases and weak acids, but just like water can act as both acid and base.

There are many different amine reactions
It is difficult to group the amine reactions as there are a lot of them, and they depend to a great extent what the nature of the carbons are that they are bonded to. There are a few general patterns here though that we can highlight. First there are three ways to make amines: SN2 reactions, reduction of cyano groups ($C \equiv N$), and rearrangements of amides. This will probably be the last functional group you will go over, so these sound foreign above, but look this back over once you get to amines and this will make sense. You will revisit a couple of reactions you have already seen as well, keep an eye out for this. Lastly, you will be dealing extensively with amines on benzene. This is because you can turn these into arene diazonium salts, which can then be substituted by a number of nucleophiles to give various substituted benzenes. Again, come back to this when you get here in class, as this is probably very abstruse right now.