

A Brief Introduction to Advanced Topics in Organic Chemistry
Or
The highlighting I pulled out of Carey and Sundberg part A during Winter Break

About the text: Mostly, it's just me copying what I have highlighted but, occasionally, I try to explain stuff in my own words to make sure I understand it and, naturally, I do it in a self deprecating way to hide my shame and low self-esteem. ENJOY!).

Chapter 1: Atomic Orbitalz and MO.

Valence Bondz (Do you need to understand it that well? Not really.):

Valence bond theory arose from the conclusion that most of the binding energy between two atoms at the most stable internuclear separation results from sharing of the electrons between nuclei.

If electron 1 were constrained to be associated only with nucleus 1, and electron 2 with nucleus 2, then the calculated binding energy was only a small fraction of the experimentally determined bond energy (that isn't much of a bond, honestly). If this constraint was removed so that the electrons were indistinguishable and permitted to interact equally with both nuclei, the calculated potential energy curve exhibited a deep minimum at the equilibrium internuclear distance. At this point we state 'duh.' The bonding energy associated with this minimum corresponded quite well with the experimental bond energy. In mathematical terms, the molecule can be represented as the weighted combination of the contributing structures. Sadly, this thinking blows for larger molecules. For this reason, qualitative concepts which arise from the valence bond treatment of simple molecules are applied to larger molecules. The key ideas that are used to adapt the concepts of VB theory to said complex molecules are hybridization and resonance. *In this qualitative form, VB theory describes molecules in terms of orbitals that are mainly localized between atoms.*

Hydrbiridzation as a solution to individual flaws.

So, one day Pauling was thinking, 'why the hell are these crazy carbons in a tetracoordinate form?' Clearly the S orbital blows at the whole directionality thing (given that it's a round non-pointing thing) so Pauling, being the hardworking man he was, decided to combine all the p orbitals and S orbitals into a set of four equivalent HYBRID ORBITALZ and designated them sp³. Awesomeness ensued.

See, a lone carbon wouldn't dream of being in the sp³ form because the combination of the S and the P orbitals makes the overall atom higher in energy than the ground state alone. (Higher energy P orbitals drag the lower energy S orbital up and it would be less favorable to have all four electrons in hybridized high energy sp³ orbitals). But, trying to form four bonds with all these distinct orbitals was energetic suicide. Clever old Mother Nature thus decided to make a hybrid of all these orbitals when bonding. Essentially, the energy required in a formal sense to promote two electrons from a 2s orbital to sp³ orbitals is more than compensated for by the formation of four bonds rather than two. The consequence of this is four bonds in a tetrahedral shape. Hooray!

In ethylene each carbon bears three ligands and is sp^2 hybridized. Three sp^3 orbitals are generated from the 2s and two of the 2p orbitals. Three sp^3 orbitals are coplanar and orthogonal to the remaining 2p orbital.

Additional bonding between the two carbon atoms is portrayed as a result from overlap of the unhybridized p orbitals on each carbon atom, each of which contains one electron. This overlap is somewhat less effective than that of a σ bond and corresponds to a π bond.

The normal angle for tetrahedral carbon is 109.5 degrees. A normal sp^3 hybridization is difficult in cyclopropane thus increased p character is added to the forming bonds. Additional p character corresponds then to reduced bond angles, as a consequence the bonds to hydrogen have more S character. The change in hybridization is associated with a change in electronegativity. The greater the s character of a particular carbon orbital, the greater its electronegativity. Thus, in cyclopropane the carbons are more electronegative toward hydrogen than they would be normally.

Bond energy and bond angle.

Bond length is almost always constant. Bond energy isn't. Live with it.

Did you know that successive polarization through bonds is called the inductive effect? This sort of crap diminishes as you move down a molecule. There is another effect called the field effect it's attributed to through species interaction of the electric dipoles resulting from polar bonds. It's proly a good idea to know that field effects tend to be the dominant mechanism for the transmission of electrostatic effects of polar bonds to other parts of a molecule. Which makes sense, really.

What's the result? Well, electronegative stuff pulls electron density back away from carbon. This means that carbon feels more secure about leaving it's hydrogen at the daycare. Think of it like having a beer helmet on. The more beers you have connected to your beer helmet the more likely you are to lose your car keys. The same goes with the inductive powers of, say, chlorine. Trichloroacetic acid, which by analogy is considerably more smashed than acetic acid, will much more easily give up its hydrogen because its electrons are being taken care of. Acetic acid on the other hand can't toss its electrons off to someone else, so it doesn't want to give up its hydrogen partner.

Sterics do stuff too.

Polarizability – the hardness and the softness.

If memory serves me correctly correctly, there is a mathematical correlation between polarizability and atomic volume, and polarizability is also related to the LUMO-HOMO energy gap. Hard atoms are sort of conservative in how closely they let their HOMO electron daughters near the seedy LUMO boyfriends. They likely grew up in Kansas or something. Soft atoms tend to be more liberal and let their daughters run wild with their LUMO boyfriends. Undoubtedly they live in Eugene or Seattle. (Why do soft atoms hate America?)

The end result being that softer atoms will be more reactive. Hard atoms react, most likely, by electrostatic interactions.

Highly electronegative atoms tend to be hard. Metal cations, for example, become harder as the oxidation number increases. Remember... hard acids prefer hard bases and versa visa.

MOLECULAR ORBITAL THEORY or why I almost became a biologist.

MO theory pictures electrons as being distributed among a set of molecular orbitals of discrete energies. In contrast to the orbitals described by VB theory, which are usually concentrated between two specific atoms, molecular orbitals can extend over the entire molecule. MO theory is based on the Schrödinger equation which I will not say anything more about.

Essentially, it's a linear relationship of this and that – all not important, but you can do all sorts of neat stuff with it when you look into it. See, the combination of atomic orbitals chosen is called the basis set. The basis sets are mathematical expressions describing the properties of the atomic orbitals. You can compute these buggers based off two branches of computational techniques: Ab initio and semiempirical calculations.

Hückel MO theory (HMO theory)

HMOs suck. If you get sick out of state, you might as well kill yourself because they aren't going to pay up. HMOs in chemistry are no better. HMO theory is based on the assumption that the π system can be treated independently of the σ framework in conjugated planar molecules and that it is the π system that is paramount in determining the chemical and spectroscopic properties of conjugated polyenes and aromatic compounds. You can treat π and σ differently because they don't interact – they are orthogonal.

Linear polyenes can be expressed by the equation:

$$E = \alpha + mj\beta$$

What mj is, doesn't matter, it's α and β that we are concerned about. These are the coulomb integral and the resonance integral respectively. α will be, basically, the same thing for all carbon-carbon bonds. β has a definition no more interesting and will be disregarded. What should be known is that ethylene would have a total π -electron energy of $2\alpha + 2\beta$. This is one for each electron. If you string three of them together you would expect them to add up to $6\alpha + 6\beta$ but that isn't what you get. 1,3,5 hexatriene has a π -electron energy of $6\alpha + 6.988\beta$. The added 0.988β means something awesome is going on there.

The difference between the electron energy calculated for a system of delocalized electrons and that calculated for alternating single and double bonds is referred to as the delocalization energy and is a measure of the extra stability afforded a molecule containing delocalized electrons compared to a molecule containing localized bonds.

Benzene gives us $6\alpha + 8\beta$. Something, obviously, is really awesome in aromatic systems.

In life, as in molecules, there are certain levels of awesomeness. And because only two electrons can be at one level of awesomeness at a single time you clearly need multiple levels of

awesomeness to accommodate six electrons. Indeed, you need 3 levels of awesomeness. Well, six actually... but the top three levels aren't for living they're for "bonding" (whistle here, gentlemen). The first three rows (ψ_1 , ψ_2 , ψ_3) are all bonding energy levels the last three are all antibonding. Each level contains a certain number of nodes. The more nodes you have the higher in energy the you are. The higher in energy level you are, they more awesome you are. Until you get to the most awesome level – the top level and then you are so awesome you are VALENCE AWESOME.

See pg 34 – 57 to learn more about this neat stuff in detail.

CHAPTER 4. THERMODYNAMIX:

ΔG in da hood

Curtin-Hammett smoke linear crack

Hammond has a postulate exam

Isotope effects

ACID BASE catalysis.

If memory serves me correctly correctly, you have the essential equation which cannot be forgotten:

$$\Delta G = \Delta H - T\Delta S.$$

Or to put it another way:

$$\Delta G = -RT \ln K$$

Any reaction has associated with it changes in enthalpy (ΔH), entropy (ΔS), and free energy (ΔG). Thermodynamics promises that all these things will be free of the reaction pathway.

Thermodynamics provides no information about the energy requirements of the pathways that a potential reaction can follow; that is, thermodynamics provides no information about the rates of chemical reactions. Thus, even if a reaction is thermodynamically favorable, it will not occur at a significant rate unless there is a low-energy mechanism by which it can occur. In the end, honestly, you still know nothing... but we march on.

The fun thing about kinetics though is that they can exclude from consideration all mechanisms that require a rate law different from the observed one (rate laws: pp192-198)

The nature of the rate constants (K) can be discussed in terms of transition-state theory. This is a general theory for analyzing the energetic and entropic components of a reaction process. In TS theory, a reaction is assumed to involve the formation of an activated complex that goes on to product at an extremely rapid rate. The rate of decomposition of the active complex has been calculated to be (very fast) at room temp.

There is mathematics component to all of this. It sucks. I'm not going to pay attention to it and neither should you. But you can read those pages above, if you're interested.

Qualitatively, what is going on here? Look at a potential energy diagram to see the qualitative benefits of such an awesome theory. It's wicked in design, honestly. (p201)

It's good to note that these paths are two dimensional creatures. The principle of microscopic reversibility arises directly from TS theory. The same pathway that is traveled in the forward direction of a reaction will be traveled in the reverse direction, since it affords the lowest energy barrier for either process. Makes sense.

Now, on to the important stuff: Curtin-Hammett...

Substituent effects and linear free-energy relationships

Remember how chlorines made carbon drunk and it would lose its keys up there in chapter 1? Well, there is more than one bottle of hooch and there is more than just one way to make a carbon lose its keys. It was noted that there is a relationship between the acid strengths of substituted benzoic acids and the rates of many other chemical reactions, for instance, the rates of hydrolysis of substituted ethyl benzoates. Depending on what you stick on the butt of a benzene ring your reaction will go faster or slower – this in turn helps you figure out what your transition state looks like (is there cationic or anionic character?) Hooray for linear things!!

To put it in more complex terms: The linear correlation indicates that the change in free energy of activation on introduction of a series of substituent groups is directly proportional to the change in the free energy of ionization that is caused by the same series of substituents on benzoic acid. The various correlations arising from such directly proportional changes in free energies are called LINEAR FREE-ENERGY RELATIONSHIPS.

If you were to make up a Hammett plot, you would notice a few things that are worth remembering. Firstly, the X-axis is " σ " or the substituent value and the Y-axis is the rate, as in $\text{Log } k/k_0$ (or the rate). The slope is therefore, rate/σ . Better known as ρ .

The value of σ reflects the effect that the substituent group has on the free energy of ionization of the substituent benzoic acid. These effects can be resonance effects, field effects and inductive effects. Some how, in some way, they are responsible for either removing or adding electron density to the aromatic ring. In short: the σ value for any substituent reflects the interaction of the substituent with the reaction site by a combination of resonance and field interactions.

Just remember: σ greater than zero are withdrawing.
 σ less than zero are donating.

To remember this, just remember that this was all done on benzoic acid: ionization of the acid preferred electron withdrawing groups.

The ρ value reflects the sensitivity of the particular reaction to substituent effects

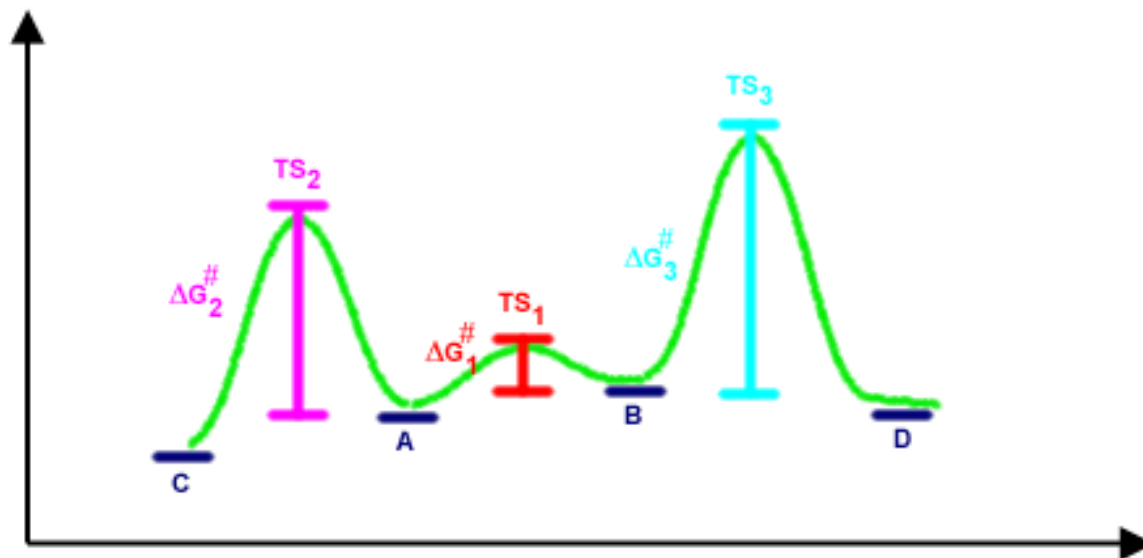
Just remember: ρ will be positive for negatively charged TS
 ρ will be negative for cationic TS.

For example: the ρ value for saponification for substituted methyl benzoates is +2.38. This indicates that electron-withdrawing groups facilitate the reaction and that the reaction is somewhat more sensitive to substituent effects than the ionization of benzoic acids. The observation that the reaction is favored by electron-withdrawing substituents is in agreement with the accepted mechanism for ester saponification. The intermediate is **NEGATIVELY CHARGED** and therefore the reaction should be favored by electron withdrawing substituents.

Sometimes, you get a kink – when this happens there is a change in mechanism. When you have a reaction mechanism that depends upon the nature of the substituent and the mechanism can change depending – you get a kink. One off the top of my head is for addition of bromine. If you have strong electron donating groups, you would prefer to go through the bromonium cation. If you have strong electron withdrawing groups the radical mechanism would be better, since it can stabilize the negative charge.

Any reaction that shows a major shift in TS-structure over the substituent series would be expected to give a nonlinear Hammett plot, since a variation in the extent of resonance participation would then be expected.

Curtin-Hammett principle: Learn it or die.



Consider a reaction in which two products **C** and **D** can be formed from **A**. **A** is in equilibrium with **B**. The Curtin-Hammett Principle states that the position of the equilibrium between **A** and **B** does not control the product ratio of **C** and **D**. The activation energies to reach **TS2** and **TS3** are considerably larger than **TS1**. **A** and **B** interconvert rapidly.

In other words: If you have to climb the Alps the Black Forest is not going to stop you (approaching from the North!).

There are numerous applications of the Curtin-Hammett Principle, the most obvious one are conformational equilibria in ring systems. The equilibrium between two conformers is established rapidly in comparison with the product-forming steps.

See pg 200.

Hammond's Postulate:

Highly exothermic reactions with a low activation indicates that the TS will be structurally similar to the reactant because they are close in energy and interconverted by a small structural change (i.e. it's energetical cake walk to go from reactant to TS but, from TS to product, you release A LOT of energy and the difference, energetically, from TS to product is substantial)

The opposite is true, of course. An intermediate case – in which your reactant and product are both a good deal less energetic than your TS will tell you nothing about the structure of the TS.

Simply: an early transition state is reactant like. A late transition state is product like. Mass has ended, go in peace. Etc etc.

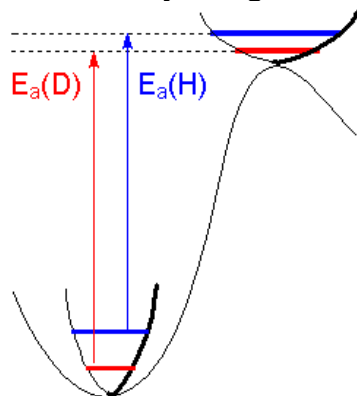
Isotope effects.

Zero point energy is there so we don't break the uncertainty rules. Which is good... because if we broke those life would not be awesome. Any C-H bond has characteristic vibrations which impart some energy to the molecule in its normal state. This energy is called the zero point energy. This energy is associated with the mass of the vibrating atoms. When shit gets heavy, the vibrating makes less of a difference (what's a little shakin' matter if you're so fat you break the chair anyway?) For this reason, substitution of protium by deuterium lowers the zero-point energy of a molecule. The energy difference due to this vibration disappears at the transition state... essentially a broken bond is a broken bond – it doesn't matter who it used to be attached to. This means that, depending on the value of your kinetic isotope effect you can determine something about the transition state. Because the deuterated molecule has the lower zero-point energy, it has a higher activation energy to reach the transition state.

A kinetic effect here is the rate of hydrogen extraction vs. the rate of deuterium extraction. (Or, k_H/k_D) The exact extent depends on the nature of the TS. Calculations on a complicated calculator have shown that the maximum primary isotope effect is about 7 at room temp. You will get the maximum value (7ish) when, at the transition state, the hydrogen is bound equally to the thing pulling it off and the thing it is departing from. The cool thing about this is that when you are breaking a C-H bond, you will always preferentially break the bond to the hydrogen, so when you are talking about these primary effects (that is, breaking a C-H/D bond) the exact value and not the sign tell you what is going on at the transition state. When your value is less than 7 you know that your transition state is either more product like or reactant like. You can get all the way down to 1, at which point the reaction doesn't give two shakes of a shit if it pulls off a D or an H because it has better things to do. At this low value, you now know that you aren't dealing with the rate determining step because, as you know, if the reaction had to make a choice it would go about the easy way and just pluck the easiest lower hanging fruit (i.e. the hydrogen) and be done with it. If the reaction is just plowing through this hydrogen abstraction then its preference isn't big. It essentially becomes larger than the whole tree and where it pulls the fruit is pretty irrelevant.

When your hydrogen isn't what is breaking, but is close enough that it can see what's going on, you have a secondary kinetic isotope effect. These guys are smaller and CAN be negative and being negative means something. Isotope effects may also be observed when the substituted hydrogen

atom is not directly involved in the reaction. Such effects are called secondary kinetic isotope effects. Bond strengths differ in a TS as crap gets broken. The strength of the bond may change because of a hybridization change (remember, more s and p character?) Additionally the strength of the bond may change because of the extent of hyperconjugation.



Normal, secondary KIE
 $ZPE(D) < ZPE(H)$ for both TS and GS,
width of PE curve (orthogonal to the
reaction coordinate) determines normal vs. inverse.

The diagram I stole from some interweb site (seen above) shows your typical energy diagrams. The lower one is clearly an sp^3 energy well as it is narrow and has wide spaces between its vibronic levels. The top one is sp^2 , obviously, because it is fat and has small spaces between its vibronic levels. In the diagram above, this reaction would have a normal KIE. Why? Well... Your reaction will always take the path of least energy. Clearly, the H-H path is the least energetically expensive. Because the vibrational energies are so small at the top and so big on the bottom, you would notice that the $E_a(H)$ line is actually shorter than the $E_a(D)$ line. If you put the fat bowl (the sp^2) center on the bottom and the skinny bowl (the sp^3) center on the top you would discover the opposite is true – the $E_a(D)$ line would suddenly be shorter and the $E_a(H)$ line would be longer – this would give you your inverse isotope effect.

If you go from an Sp^3 to an Sp^2 hybrid in your transition state you suddenly free up some room for the attached hydrogen to flop about. This is pretty awesome but mostly awesome from the point of view of the little hyper hydrogen. It will want to react preferentially so it can flop about. When this happens you see a normal isotope effect as, energetically, it is far more awesome to react with something with the crazy hydrogen than the fat apathetic deuterium. You would likewise see an inverse isotope effect if you were to go from an Sp^2 to an Sp^3 center. Let's refer to these as force constants: an increase in force constant (i.e. it's getting more crowded) means you're going to have an inverse isotope effect and the deuterated product is going to react faster. A decreased force constant (i.e. it's going to be less crowded) means you're going to have a normal isotope effect and the protonated compound will react faster.

So, if you're doing a Grignard reaction to a Sp^2 center (like a carbonyl) you get an inverse isotope effect, right? It goes from an Sp^2 center with a ketone to an Sp^3 center with an alcohol and the newly acquired nucleophile. There is less space, greater force constant and a preference to react with deuterium. If you see a regular isotope effect, something odd has just happened. You have just gone from a situation in which things normally get more crowded to one that suddenly gets less

crowded. How can this be? If we are talking about an α effect (that being, an effect to the carbon the proton/deuteron is sitting on) then a hybridization has changed! When a nucleophile adds, it really ads. This should make for less free space to wiggle about. No, actually, not if your rate determining step forces your carbon to go from sp^2 to sp . This happens in a radical reaction – an electron can either go into an π^* orbital or it can rehybridize. The carbon, of course, does the easy thing and rehybridizes. Thus, you have a way to determine if your reaction is radical or not. Hooray! (let me explain this differently. If you get an inverse isotope effect, it is because your transition state gets more crowded – the adding nucleophile has just jammed two electrons in there and, the carbon has done the clever thing and gone to an sp^3 hybridization. IF, however, you're just tossing a single electron in there and not actually making a bond, the carbon is going to want to rehybridize to make life a little easier on itself and thus give you an sp hybridized carbon. The rate determining step is then NOT the addition of the second electron, but the addition of the first and thus the rehybridization. And because only the rate determining step matters in the isotope effect, you see exactly that – a normal isotope effect.)

Hyperconjugation will provide a β isotope effect (we're still talking about secondary isotope effect here, just now on the carbon NEXT TO the carbon being messed with). When carbocations are involved as intermediates, substantial β -isotope effects are observed. This is because the hyperconjugative stabilization by the β hydrogen weakens the C-H bond. The observed secondary isotope effects are normal, as would be predicted since the bond is weakened. (pp 222-224 read esp the last paragraph of 224 and continued on 225).

General Acid Catalysis, reporting for duty. (yeah, it's gay. But it's late)

Catalysis occurs when the conjugate base or conjugate acid of the substrate is more reactive than the neutral species.

The term specific acid catalysis is used when the reaction rate is dependent on the equilibrium for protonation of the reactant. This type of catalysis is independent (doesn't give a shit) of the concentration and specific structure of the reactant (only 'ol acid will do just fine.) Specific acid catalysis is governed by the hydrogen-ion concentration (pH) of the solution and the pH alone. Essentially, it doesn't matter if this is acetic acid or benzoic acid. So long as the pH is right, the reaction will proceed with dignity. The kinetic expression for any such reaction will include a term for hydrogen ion concentration $[H^+]$. The term general acid catalysis is used when the nature and concentration of proton donors present in solution affect the reaction rate. The kinetic expression for such a reaction will include a term for each of the potential proton donors that acts as a catalyst. See pg 229 for the equations for rates (these, oddly, actually say something about how this works).

The experimental detection of general acid catalysis is done by rate measurements at constant pH but differing buffer concentrations. Because under these circumstances $[H^+]$ is constant but the weak acid components (i.e. the conjugate base) changes, the observation of a change in rate is evidence of general acid catalysis. If the rate remains constant, regardless of the concentration of said buffer bits then you have specific acid catalysis.

Several situations can lead to the observation of general acid catalysis. General acid catalysis can occur as a result of hydrogen bonding between the reactant and a proton donor to form a reactive complex when then reacts with the substance.

I cannot do this topic justice. Read up on it (pp228-233).

Chapter 5: The long chapter about Nucleophilic substitution (and what it means to me).

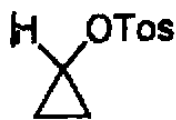
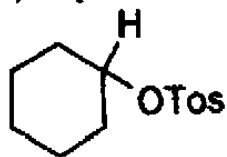
If memory serves me correctly correctly, Hughes and Ingold (all good scientists come in pairs) decided that there were some limitations (or something) on something. They really aren't important at this moment. These limiting cases are the ionization mechanism (S_n1 a.k.a. substitution-nucleophilic-unimolecular) and the direct replacement mechanism (S_n2 , substitution-nucleophilic-bimolecular).

Ye Olde S_n1 e Mechanisme:

The ionization mechanism for nucleophilic substitution proceeds by rate-determining heterolytic dissociation of the reactant to a tricoordinate carbocation. (woot). The ionization step is rate-determining and thus will exhibit first-order kinetics. Ionization is facilitated by factors that either lower the energy of the carbocation or raise the energy of the reactant. Ionization reaction rates are subject to both electronic and steric effects. The most important electronic effects are stabilization of the carbocation by electron-releasing substituents and the ability of the leaving group to accept the electron pair from the covalent bond that is broken!

Solvents can screw with this sort of thing. Ionization in an electrically neutral solvent will result in charge separation, increasing polarity will increasingly screw with the reaction. Solvents of higher dielectric constant will lower the energy of the TS more than will solvents of lower polarity as they solvate the charge and stabilized the charged species. If the carbocation is sufficiently long-lived under the reaction conditions to diffuse away from the leaving group, it becomes symmetrically solvated and gives racemic product. (hooray!) If they don't separate sufficiently the product will form with net retention of stereochemistry

Rehybridization can also screw with a molecule. If, for some reason, the molecule can't rehybridize its reaction rate will be greatly retarded:



10^{-10}

The cyclohexane reacts much faster than the cyclopropane. The carbocation intermediate would want to be at 120 degrees – that's just not going to happen in cyclopropane.

Ye Olde S_n2 Mechanisme:

The direct displacement mechanism is concerted, without an intermediate, and proceeds through a single rate-determining transition state and is second order. The transition state involves trigonal bipyramidal geometry with a pentacoordinate carbon. Frontier MO provides a picture of this crap. You essentially have your lone pairs in your approaching nucleophile and attacks, butt side, into the anti-bonding orbital of the bond with the departing leaving group. This makes sense. You want to bond into the antibonding orbital and, once you've done that, you need to kick out the leaving group

because it just isn't kosher to have the ground state and the excited state filled with electrons (that's pretty much no net bonding and that isn't awesome.) Of course, there is nothing wrong with the bonding orbital of the approaching nucleophile interacting with the σ^* orbital of the carbon you're bonding to in front— nothing wrong except... THAT BIG LEAVING GROUP IS BLOCKING THE WAY. Drats, thwarted by science. Not only that but the σ^* orbital between the carbon and the leaving group is much smaller than it is on the butt of the carbon AND the approaching nucleophile will have to look at both bonding and antibonding orbitals of the Carbon-leaving group $\psi-2$ aka node-plane craziness. Not pretty.

The consequences of this butt-side attack is, as the reaction proceeds on to product and sp^3 hybridization is reestablished, the product is formed with inversion of configuration. Also the HOMO at the transition state is π in character and the reacting carbon. The energy of this orbital is lowered by conjugation with adjacent substituents. (What does this mean, mr. stupid pre-final writeup?) This means that the S_n2 TS will be stabilized by substituents that have an adjacent π orbital. Vinyl, phenyl etc etc, provide stabilization and will enhance S_n2 reactivity.

Because the degree of coordination increases at the reacting carbon atom, the rate of direct displacement is expected to be sensitive to the steric bulk of the other substituents.

There are limitations to the horrible generalization that reactions that experience first order kinetics are S_n1 and those that experience second order kinetics are S_n2 reactions...

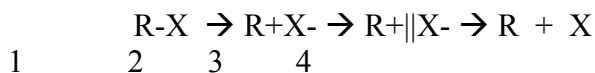
For one, if the nucleophile is in such excess then its concentration is pretty well constant and you have an observed pseudo-first order reaction. This is especially true in solvolysis. In this case, you don't know what it is based upon kinetic data.

The guts and gizzards of the thing:

At the S_n1 extreme, there is no covalent interaction between the reactant and the nucleophile in the TS for cleavage of the bond to the leaving group. At the S_n2 extreme, the bond formation to the nucleophile is concerted with the bond breaking step.

Gay Ion Pairs and American Politics

A man by the name of Saul Winstsomethingorother decided that there were two types of ion pairs involved in substitution reactions. The process of ionization initially generates a carbocation and counter ion in proximity to each other. This species is called an *intimate ion pair*. This species can proceed to a *solvent-separated ion pair*, in which one or more solvent molecules have inserted between the carbocation and the leaving group but in which the ions have not diffuse apart. *The Free Carbocation* is formed by diffusion away from the anion, which is called dissociation. Observe my technologically wowing visualization below:



Look, they were bonded then they got separated then they got really separated then the GOT TOTALLY SEPERATED! SWEET! (or to keep with the theme, "awesome!")

Obviously, depending on when nucleophilic attack occurs, you will get different stereochemistries. Attack at 2 will almost certainly give you inversion where as attack at 4 will almost certainly give you racemization. Though, that still depends on what R actually is. One can actually figure out how far these things separate by radio labeling. See pg 271 for some awesome ideas on how to get your own radio labeler and start radio labeling your mixtures today! A value of 200 dollars but yours for only 5 easy payments of 49.95! (im not this corny, I swear. I normally am filled with dirty jokes and swear words, but I'm trying to keep it clean here... and it isn't easy. *sigh* I'm listening to some awesome music right now. Hey, nine inch nails just came on. Sweet.) Radio labeling has its limitations, but, again, I'll refer you to the book to figure them out.

Take heed of the ion sandwich. It sucks. Order the soup instead. Such an ion sandwich might be a kinetic intermediate which accelerates dissociation. If a carbocation were quite unstable, it might always return to reactant unless a nucleophile was properly positioned to capture the carbocation. When both breaking and forming bonds are relatively weak and you have a substantial charge on the carbon but the carbon has no life time because formation of bonds occur concomitantly, what do you have? S_n1 S_n2 ? WHAT? Good lord. Who cares? No one. You have both, but that's not important. You are learning these names to only be told they are meaningless. Go read the Bible if you can't stand the inconsistency and lack of clarity in the definitions, I mean, what do you think this is? Religion? *cough* moving on.

Carbocations! Are there positives to this Gay Ion Pair debate?

Carbocations are inherently high-energy species. The ionization of t-butyl chloride is endothermic by 153 Kcal/mol in the gas phase. But, honestly, who does this sort of shit in the gas phase? And why would an organic chemist care? Are we doing this in space or something where our solvents all boil off into the vacuum? NO. So to say that these things are endothermic by 153 Kcals suggest these things are super friggin high energy when, if given the correct medium, form fairly easily and can, in fact, be bottled. The triarylmethyl cations are particularly stable because of the conjugation with the aryl groups, which delocalizes the positive charge. Hey, there is even a "pK" value for carbocations and it's called the pK_r. Isn't that cute? Everyone is getting their own pK value.

Stability of cations are in the order of tert > sec > prim > methyl. Large ions are more stable than smaller ions. The greater stability of the larger ions in the gas phase (here we go again) reflects their ability to disperse the positive charge over a larger number of atoms.

Any structural effect which reduces the electron deficiency at the tricoordinate carbon will have the effect of stabilizing the carbocation. Allyl cations are stabilized by delocalization involving the adjacent double bond.

The π -electron delocalization requires proper orbital alignment. As a result there is a significant barrier to rotation about the carbon-carbon bonds in the allyl cation.

Lots of things can stabilize a carbocation. Well, mostly stuff with free electrons. Things like OCH₃, NH₂... good stuff. Hell, even halogens will give up a few 'trons to help a brother out. Bad things that suck pull electrons away, like CN and NO₂... bad stuff. Banana bonds from a cyclopropane will donate into a carbocation and stabilize it. Hyperconjugation, obviously, will donate into the empty p-orbital to stabilize the sucker. (best if applied to a rigid system like a ring). You can make certain six or two electron π systems aromatic by sticking a carbocation in there (like cyclopropene and 1,3,5 hetatriene.)

If a carbon cannot enter into the sp^2 geometry due to physical restrictions by ring strain, it will not form a carbocation. Or, if it is in sp^2 geometry and can't get into sp geometry (like on an aromatic ring). Though, these carbocations have been observed (of course).

Nucleophiles, can they be cured or should they go to prison?

The term nucleophilicity refers to the effect of a Lewis base on the RATE of a nucleophilic substitution reaction and may be contrasted with basicity, which is defined in terms of the position of an equilibrium reaction with a proton or some other acid. The rate of an S_N2 reaction is directly related to the effectiveness of the nucleophile in displacing the leaving group. The leaving group has very little say in this matter, as it turns out. A few things to remember about nucleophiles:

1. A high solvation energy lowers the ground-state energy relative to the transition state, in which the charge is more diffuse. The solvation energy affects nucleophilicity because the solvation shell must be disrupted to arrive at the TS
2. A stronger bond between the nucleophilic atom and the carbon is reflected in a more stable TS and therefore a reduced activation energy
3. A sterically restricted nucleophile is less reactive than are more accessible one because of nonbonded repulsions which develop in the transition state.
4. A more electronegative atom binds its electrons more tightly than a less electronegative one.
5. Polarizability describes the ease of distortion of the electron cloud of the attacking atom of the nucleophile.

(pp.290-291)

Neighboring-Group Participation:

Hello. We are on page 309! Yay, almost 1/3 of the way there. The text has a lot of good pictures, which sort of make this text useless because you need pictures to visualize this stuff.

The involvement of nearby nucleophilic substituents in a substitution process is called neighboring-group participation. This essentially means you've got some bugger near by that will help speed the reaction up. See page 309 for such an example of a back-side bugger bugging the back of a p-toluenesulfonate of a 2-acetoxycyclohexyl molecule. When something can act as an internal nucleophile... it really helps the reaction move along. I mean, it really does. You should ALWAYS be on the look out for internal nucleophiles. When this happens, such as the example on pg 309, the reaction moves faster... in some instances. Obviously the orientation of the nucleophile in the molecule makes a difference. In this case, a fused ring system with both substituents equatorial and trans will mean that the trans product will predominate. Backside attack from the internal nucleophile means that attack will have to be from the opposite face and, thus, you get trans. Thus, it's pretty fair to say that molecular geometry depends a lot on the rate of neighboring-group stuff.

Back bonding by a π -system also stabilizes stuff (pg 312).

Mechanism of Rearrangements, super cations and the rest of chapter 5

Activation energies for skeletal migrations are not large, and it is not uncommon to observe overall rearrangements that must have involved individual steps that proceed from a more stable to a less stable species. Capture of carbocations by nucleophiles is a process with very low activation energy, so that only very fast rearrangements can occur in the presence of nucleophiles.

Shifts of hydride between carbon atoms separated by several atoms are possible if the molecular geometry is favorable. Hydride bridged ions are quite stable in favorable cases and can be observed under stable-ion conditions.

Multistep sequences terminating in the most stable ions are quite typical of carbocations in super acid media. In the presence of nucleophilic anions or solvent, rearrangement usually does not proceed all the way to the most stable ion, because nucleophilic trapping captures one or more of the rearranged species. Short of the long of it is, essentially, the friendlier your solvent, the more rearrangement you will get.

Bridged structures which involve delocalization of the σ electrons and formation of three-center, two electron bonds, are called non-classical ions.

See pp327-334 for discussion with much needed diagrams including the crystal structure which was discovered by the guy that always treated me like shit at IU on page 331. (though the x-ray spectroscopist, John Huffman, is a very nice guy and taught my girlfriend how to cook.)

Whew, day two and I'm listening to DJ Shadow, Jurassic 5, and uhhh... smashing pumpkins? Hm. That's an odd combination. I'm also drinking coffee with that French vanilla creamer in it. It's pretty good. I put Splenda in it too, because I'm fat. *sigh*

Chapter 6 Polar Additions and Eliminations

If memory serves me correctly correctly, when the addition and elimination reactions are mechanistically reversible, they proceed by identical mechanism paths but in opposite directions. (Ohhh, microscopic reversibility).

A mechanism is described as regioselective if an unsymmetrical alkene gives a predominance of one of the two possible addition products; the term reiospecific is used if one product is formed exclusively.

In the addition of hydrogen halides to alkenes, it is generally found that the halogen atom becomes attached to the more substituted carbon atom. The statement of this general observation is called *Markownikoff's rule*. (obviously, this is due to the relative stability of the forming carbocations.) The free-radical reaction is readily initiated by peroxidic impurities or by light and leads to the anti-Markownikoff's addition product. Halogens that get down with reaction are generally Chlorine and Bromine. Iodine is, as always, non committal about the whole thing and Fluorine is like that drunk uncle you don't invite because they blow shit up and, well, it's just a mess.

Acid-Catalyzed Hydration and Related Addition Reactions

Formation of alcohols by acid-catalyzed addition of water to alkenes is a fundamental organic reaction. Reactivity is accelerated by electron donating groups which stabilize the carbocation intermediate, as would be expected. Strained alkenes show enhanced reactivity. Such is the result of the higher ground-state energy of the strained alkene.

Addition of Halogens

For brominations, anti addition is preferred to alkenes that do not have substituent groups that would strongly stabilize a carbocation intermediate. *When the alkene is conjugated with an aryl group, the extent of syn addition becomes greater, and syn addition can become the dominant pathway.* Formation of bromonium species results in syn addition to avoid interaction of the larger bromonium ion. Stabilization of carbocations would prefer direct addition of a bromine and bypass the bromonium ion which would thus make it kinetically favorable to simply add the bromine on the same face as the other bromine. Thus you get syn addition. Aliphatic systems normally go through the bridged intermediate, but styrenes are borderline cases. When the phenyl ring has electron releasing substituents, there is sufficient stabilization to permit carbocation formation, whereas electron-attracting groups favor the bridged intermediate. Makes sense...

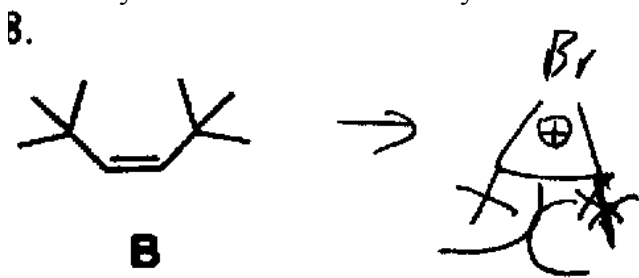
The stereochemistry of chlorination can be explained in similar terms. Chlorine would be expected to be somewhat poorer bridging group than bromine because it is less polarizable and more resistant to becoming positively charged. Thus, syn addition is slightly preferred in chlorination.

I've had the sniffles for about three weeks now. I wonder if I have something wrong with my mucus glands...

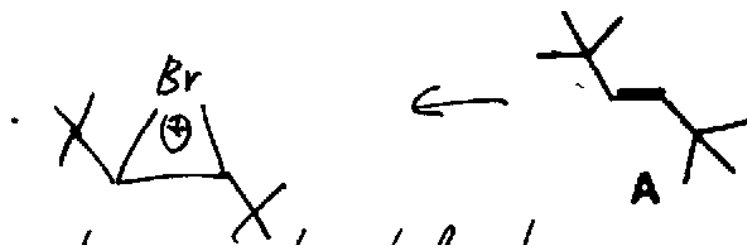
Amazingly, one can capture and crystallize a bromonium ion.

An interpretation of activation parameters has led to the conclusions that the bromination transition state resembles a three member ring, even in the case of alkenes that eventually react via open carbocation intermediates. That's interesting.

Steric considerations must be considered for the formation of these cyclic compounds. It is obviously not favorable to form a cyclic transition state with a trans alkene:



The steric hindrance and the eclipsed conformation which results is energetically shitty.



The process is much more favorable with a trans alkene. The formation of a carbocation, however, would mean that the cis-trans conformation of the alkene isn't important (it would slightly favor the trans). As there would be no cyclic transition state.

In summary, it appears that bromination usually involves a charge-transfer complex which collapses to an ion-pair intermediate. The cation can be a carbocation, as in the case of styrenes, or a bromonium ion. The complex can evidently also be captured by bromide ion when it is present in sufficiently high concentration.

As usual, the relative reactivities are solvent-dependent. The reaction is faster in more polar solvents, and, in all media, reactivity increases with additional substitution of hydrogen by electron-releasing alkyl groups at the double bond.

The Hammett correlation for bromination of styrenes is best with σ^+ substituent constants and gives $\rho = -4.8$. All these features are in accord with an electrophilic mechanism.

I've just thought up the most awesome name for a band: Electroponic Attack. Isn't that awesome? Also, Gentleman style 2000... that's pretty cool too, I think. I would most likely do trans hip-hop music with a bohemian twist. Lots of emphasis on lyrics and tasteful turn-tableism. Possibly a strong drum and bass and maybe some woodwinds. I dunno. I was heavily influenced by Jazz, Tchaikovsky, Rachmaninoff and Gershwin, Hip Hop (not "rap," that's a genre of hip hop) and Industrial electronica. I listened to a lot of Yanni, but don't tell anyone as I'm quite embarrassed about that. I really like underground British rock like Coldplay (when they were obscure), Muse and Stereophonix. Anyway...

If you're on page 24 you must be pretty desperate to not read the book.

Alkyne Additions:

Because the HOMO of alkynes is also of π type, it is not surprising that there is a good deal of similarity between alkenes and alkynes in their reactivity toward electrophilic reagents.

In general, reactions that proceed through vinyl cations, such as those involving rate-determining protonation, are only moderately slower for alkynes as compared to similar alkenes. This can be attributed to the relative higher energy of vinyl cations compared to cations with sp^2 hybridization. Reactions that proceed through transition states leading to bridged intermediates typically show much larger rate retardation for the alkyne addition. This presumably reflects the greater strain of bridged species in the case of alkynes. Bridged intermediates derived from alkynes must incorporate a double bond in the three membered ring.

E2, E1 and E1cb mechanisms

Essentially, if you can't make a reasonable conclusion about how these things work from the preceding 25 pages maybe you should consider going into philosophy or something because you're an absolute failure as a chemist. But, because I promised myself I would do a comprehensive review of the whole book, I'll say something (briefly) about the subject.

An elimination reaction – the removal of another molecule from a reactant and be classified according to the relative placement of the carbon atoms from which elimination occurs.

I think it's important to understand that there exists a gradient with E1 and E1cb being the most extreme. In the case of E1, the departure of the leaving group causes the formation of a carbocation. When both the leaving group and the hydrogen are being abstracted simultaneously there isn't a complete charge developed on the molecule and you have an analogous situation so Sn2. E1cb is the extraction of hydrogen which results in the formation of a negative charge on the molecule. Obviously, Sn2 can be non-synchronous during the abstraction process leading more to either increased carbocation or carbanion character on the molecule. Hence, the gradation. Preference is based upon stabilizing groups which help the development of either positive or negative charge. All very simple shit.

Leaving groups also can influence the direction of the elimination. Poor leaving groups like fluoride would rather die than be the first to leave the party, so you tend more toward E1cb than anything. The anti-social Iodine, obviously, leaves even if there isn't a reason to do so. This would thus favor the E1 mechanism.

Chapter 7: Carbanions and You.

If memory serves me correctly correctly, I've made it this far and, quite possibly, half way through the book. Why stop now? I dunno. But I sure do want to. Maybe I'll grab some OJ and continue this in about 30 minutes.

Yum. Turkey soup is some good stuff. I enjoy it with lots of salt. I don't think that's so healthy. Anyway...

Water and alcohols are far more acidic than most hydrocarbons and are unsuitable solvents for generation of hydrocarbon anions. Any strong base will deprotonate the solvent rather than the hydrocarbon. Thus, we need to use aprotic solvents like ether, THF or DME.

We can determine the rate of carbanion formation by use of radio labeling. The rate deuterium is found in solution is the rate of deprotonation. It has been found that there is often a correlation between the rate of deprotonation and the thermodynamic stability of the carbanion. Because of this relationship, kinetic measurements can be used to construct orders of hydrocarbon acidities. Measuring this can cause some problems. While hydrogen abstraction may be occurring – it may be reforming rather quickly due to internal return. This will greatly skew the results to suggest that the molecule is less acidic than it actually is. When internal return occurs, a deprotonation even

escapes detection because exchange does not result. The extent of ion pair is primarily a function of the ability of the solvent to solvate the ionic species. Ion pairing is greatest in non-polar solvents such as ethers. In dipolar aprotic solvents, especially DMSO, ion pairing is much less likely to be significant.

There are obvious factors that contribute to acidity (Jesus, Billy Corrigan is singing ‘over the rainbow.’ Sometimes I wish I were deaf.) like certain groups which stabilize negative charge. Shit with lots of ‘S’ character also stabilize the negative charge fairly well. SO, in highly strained ring systems the hydrogens are more acidic because the greater S character in the carbon, the more electronegative the carbon, the more willing it is to give up the proton. Thus, one would expect cyclopropane to have highly acidic protons, though, I would imagine it would not deprotonate so easily because that would create a 4 electron anti-aromatic system. A bad juju. Even so, the ΔH of proton dissociation for cyclopropane is still slightly less (by about 7 Kcals) than the deprotonation of methane.

That’s all awesome, you say. But what does this have to do with me? I don’t know, honestly. But it’s worth thinking about.

Organolithium compounds derived from saturated hydrocarbons are extremely strong bases. Accurate pK values are not known but would range upward from the estimate of ~50 for methane. Carbon atoms do not transfer protons as fast, however. In fact, even though t-butyllithium is thermodynamically capable of deprotonating toluene, the reaction is very slow. In part, the reason is that the organolithium compounds exist as tetramers, hexamers, and higher aggregates in hydrocarbon and ether solvents. The relative slowness of removal of protons from carbon acids by organolithium reagents is probably due to the compact character of the carbon-lithium clusters. Because the electrons of the carbanion are tightly associated with the cluster of lithium cations, some activation energy is required to break the bond before the carbanion can act as a base.

Carbanions stabilized by functional groups

At this point the book has become very repetitive. I think Sundberg is just taking up space by repeating the same thing over and over again. Actually, I find that chapters 5-8 are essentially all the same chapter being repeated over and over again. So, obviously, carbanions are stabilized by electron withdrawing groups to reduce the amount of negative charge on carbon. I mean, duh. That’s been said, what, 900,000,000 times already? It’s like a general theme in chemistry. Maybe he just keeps repeating this over and over again because, honestly, chemistry is just all about stabilizing a charge somewhere somehow.

Enols and Enamines.

The nucleophilic reactivity of carbonyl compounds in acidic solution is due to the presence of the enol tautomer. That’s pretty interesting. Enols are much more reactive than simple alkenes, however, because the hydroxyl group can participate as an electron donor during the reaction process. Enols are not as reactive as enolate anions, however. This lower reactivity simply reflects the presence of an additional proton in the enol, which decreases the density of the enol relative to the enolate. In MO terminology, the –OH and –O⁻ donor substituents raise the energy of the π -HOMO.

A point of contrast with the data for base-catalyzed removal of a proton is the tendency for acid-catalyzed enolization to result in preferential formation of the more substituted enol. The preference for acid-catalyzed enolization to give the more substituted enol is explained in terms of the stabilizing effect that alkyl groups have on carbon-carbon double bonds. The amount of enol present in equilibrium with a carbonyl group is influenced by other substituent groups. In the case of compounds containing a single ketone, aldehyde or ester function, there is very little of the enol present at equilibrium. In compounds with two such groups separated by a single carbon the enol is present much longer. The strong intramolecular hydrogen bond in the enol form minimized the molecular dipole by reducing the negative charge on the oxygen of the carbonyl group. In more polar solvents, the stabilization is less important, and in protic solvents such as water, hydrogen bonding by the solvent is dominant.

**CHAPTER 8: Carbonyl Madness and
CHAPTER 9: Aromaticity**

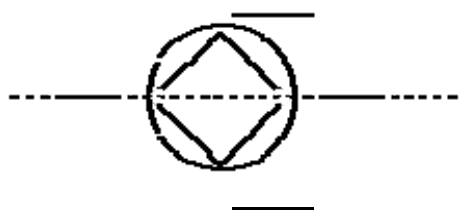
If memory serves me correctly correctly(x2), these things do a lot, in fact, too much to really talk about here. See pp449-542; less than 100 pages, easy reading, honest.

The amazing thing about Chapter 8 is, if you've read chapters 5-7 you have already read chapter 8. Nothing here bears repeating.

Concept of Aromaticity

This stuff arises from the conjugation and the even distribution of electrons around a ring. This sort of thing must have consequences. One of which is deshielding of protons on the outer ring. This also brings up the famous $4n+2$ rule. Hückel systems will have 2, 6, 10 etc electrons or they'll suck. They'll also be planar or they don't be aromatic at all.

Frost circles, which you learned about in chapter 1 are fun.



The frost circle above is for cyclobutadiene. The lower line represents the orbital for bonding electrons, the middle dashed lines are for non-bonding electrons and the top orbital are for anti-bonding electrons. Cyclobutadiene has four electrons in its π system. So, you have to distribute those electrons onto the ring. Two of those electrons will go into the bonding orbital and two will go into the non-bonding orbital. Now, the non-bonding orbitals will do nothing for the stability of the molecule and thus, any electrons you put in there will be very reactive. Not only that, but you are putting two electrons into two orbitals – meaning they will be unpaired... meaning you'll have unpaired electrons in a non-bonding orbital. Meaning, you won't see this molecule ever.

How to make a frost circle:

The relative energies of the MO's in aromatic rings can be determined by drawing Frost circles.

1. Draw a circle.
2. Inscribe the polygon representing the ring in the circle with the vertex pointing down.
3. Each vertex represents the relative energy of a MO.
4. Draw a line through the center of the circle. This represents the position of the relative energy of nonbonding MO's (arbitrarily set to 0).
5. Fill in the electrons.
6. Electrons fill all bonding MO's : aromatic
Electrons fill nonbonding MO's or antibonding MO's : antiaromatic

Annulenes

The term annulene was coined to refer to the completely conjugated monocyclic polyenes.

Synops

This chapter doesn't really contain anything out of the ordinary. Essentially: Aromatic compounds are awesome because they are stabilized by some unknown force and that they need to be planar and have $4n+2$ electrons in their π orbital. If they do not, they are either not aromatic or anti-aromatic. It's far better to not be aromatic than anti-aromatic because of the way electrons have to orient themselves into the non-bonding orbitals.

Now... the good stuff:

Chapter 11: Concerted pericyclic reactions and Joe Gajewski

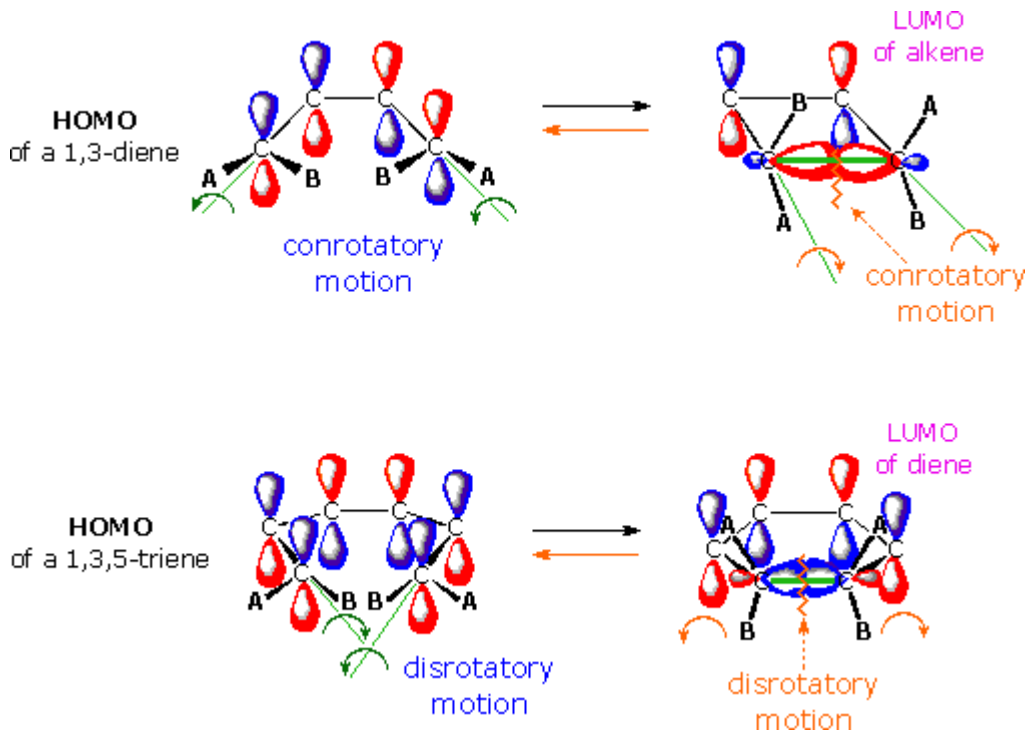
If memory serves me correctly, to maintain continuous electron flow, pericyclic reactions must occur through cyclic transition states. Which is to be expected, considering... well... at least that's what the name implies.

Electrocyclic Reactions

REMEMBER: An electrocyclic reaction is defined as the formation of a single bond between the ends of a linear conjugated system of π electrons and the reverse process. In other words, you lose two double bonds for one double bond and a single bond.

There is something amazingly odd about these reactions – they are stereospecific! How cool is that? Why are they this way? Well, that was a blindingly unusual question what could only be solved by woodman and hoffward or whatever. See, the stereospecificity was obvious in that the substituents were either rotating in the same direction or in opposite directions – depending upon the size of the ring. Well, Hoffward and Woodmeister came up with the brilliant idea that that this is obviously related to our good old buddy that makes us want to die, MO THEORY! HOORAY!

See, in butadiene you have four π electrons. Obviously you can't have all four electrons in one molecular orbital – that would blow. So, each pair of electrons must be in their own MO. Each MO has $n+1$ (that being short hand for $n+1$) nodes. The lowest energy is arbitrarily defined as ψ_1 and contains no nodes. Then, for each node you go up ψ_{++} .

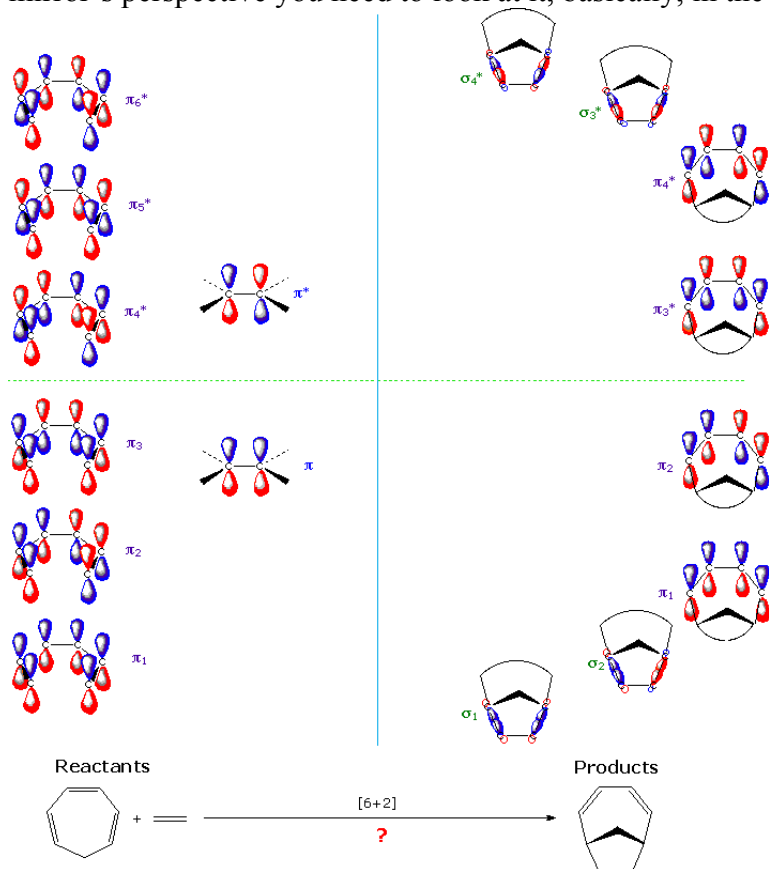


All the really great reactions occur with no nodes. Well, all reactions should have no nodes in the bonding orbitals. So, when you look at your butadiene ring closure and discover that the stereochemistry predicted by the ring closure and the finger rules don't match, you're obviously trying to close the ring incorrectly... either that or you're trying to use the incorrect MO. Like the top example in the above stolen diagram. You need to get conrotatory ring closure in order to get the correct stereochemistry. If you do it in ψ_1 you find you have a node in the middle of your new σ orbital. Obviously, this blows. If you do it in ψ_3 of a 6 electron system, this works just fine. So, to put it in the simplest terms, when you rotate the bonding orbitals there had better not be a node. What are the other two electrons doing? Well, they're forming a π bond in ψ_1 . Everyone does something – no free passes.

In general $4n$ π systems will undergo electrocyclic reactions by conrotatory motion and $4n+2$ electrons will react by the disrotatory mode. BUT DON'T REMEMBER THAT... just keep in mind that you need to be in the HOMO and then figure out how to rotate so bonding orbitals touch. In this case, you can always conclude that for butadiene, you will always need to rotate conrotatory, so $4n$ electrons must rotate conrotatory... hm. I don't think that's a word.

Essentially, there is a great deal of symmetry here. So symmetry has to be taken into consideration... so... let's consider it.

When you do disrotatory motion each side of the molecule is rotating in opposite directions. Sort of like when you look in the mirror and you move your hand to the right, the guy looking at you is actually moving his hand to the left. (if you're a chick, then obviously there shouldn't be a guy looking at you in the mirror. If there is, scream and run.) Thus, you will be using a plane of symmetry or C_s symmetry. If you're going to be doing conrotatory motion then you need to look at it down the axis of rotation. (because both sides are doing totally opposite things according to the mirror's perspective you need to look at it, basically, in the 'anti mirror' which is pretty much C_2



Symmetry. The picture above illustrates my point. In a six electron system ($4n+2$) the reaction will proceed by a disrotatory mechanism. Thus, when we look at all six ψ levels, we see that the first three (below the green line) are bonding and the top three are anti-bonding. NOW... we are dealing with a plane of symmetry here, so on the left from bottom to top it would be Symmetric, Asymmetric and symmetric. (those are the bonding orbitals). In the product side (on the right) you have two σ levels which σ_1 is symmetric and σ_2 is asymmetric (ignore σ_2 , I dunno why its there, but it would be higher in energy because it has one node), ψ_2 is antisymmetric and ψ_3 is symmetric.

S	→	S	☺
A	→	A	☺
S	→	S	☺

You want to send electrons from symmetric to symmetric and antisymmetric to antisymmetric. SO they would actually bond within the bonding orbitals. They match! If you were to go through a C_2 symmetry, you would have:

S*	-x->	A*	☹
A	-x->	S	☹



The * indicates an anti-bonding orbital. Now, ψ_1 and ψ_2 are still all in the bonding levels, but ψ_3 , in order to bond, must throw its electrons into the anti-bonding orbital. Not good. So, CS wins out and you have disrotatory motion. (look at my amazing technological drawings. Wow. How appropriate that I should be listening to Kraftwerk right now and be using these ASCII drawings.*
 *not understanding this it totally permissible. I'm embarrassed that I even wrote it.)

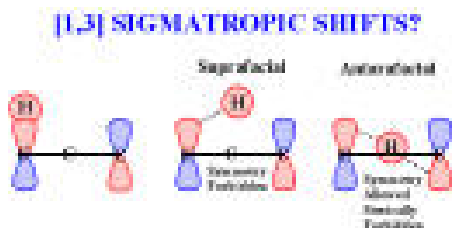
Well, this brings me to: Hückel and Möbius.

Reactions involving $4n+2$ electrons will be disrotatory and involve a Hückel-type transition state, whereas those involving $4n$ electrons will be conrotatory and the orbital array will be of the Möbius type.

Sigmatropic Rearrangements

Σ troptic rearrangements involve a concerted reorganization of electrons during which a group attached by a σ bond migrates to the terminus of an adjacent π -electron system. Essentially, something in the molecule has moved around and bonds have been broken, but there was no net change in σ or π bonds.

If the migrating group remains associated with the same face of the conjugated π system throughout the process, the migration is termed suprafacial. The alternate mode involves a process in which the migrating group moves to the opposite face of the π system during the course of the migration and is called antarafacial.



Here, in the stolen image which I've blown up to make visible and thus distorted the holy hell out of it, you can clearly see what's going on when you migrate a proton between two carbons in a 1,3 σ troptic shift. The bonding interaction can be maintained only in the antarafacial mode. Of course, if you're shifting around a proton, you HAVE to do it suprafacial. If, however, your shifting around something a little more complicated than that, that has a lobe to it, you can do it suprafacially, but it must "flip" as it moves across the molecule. In this "flip" an inversion of stereochemistry has occurred. Thus, we can make a general rule:

	Supra, retention(supra)	Supra inversion(antara)	Antara retention	Antara inversion
--	-------------------------	-------------------------	------------------	------------------

$4n [i,j]$	0	1	1	0
$4n+2$	1	0	0	1

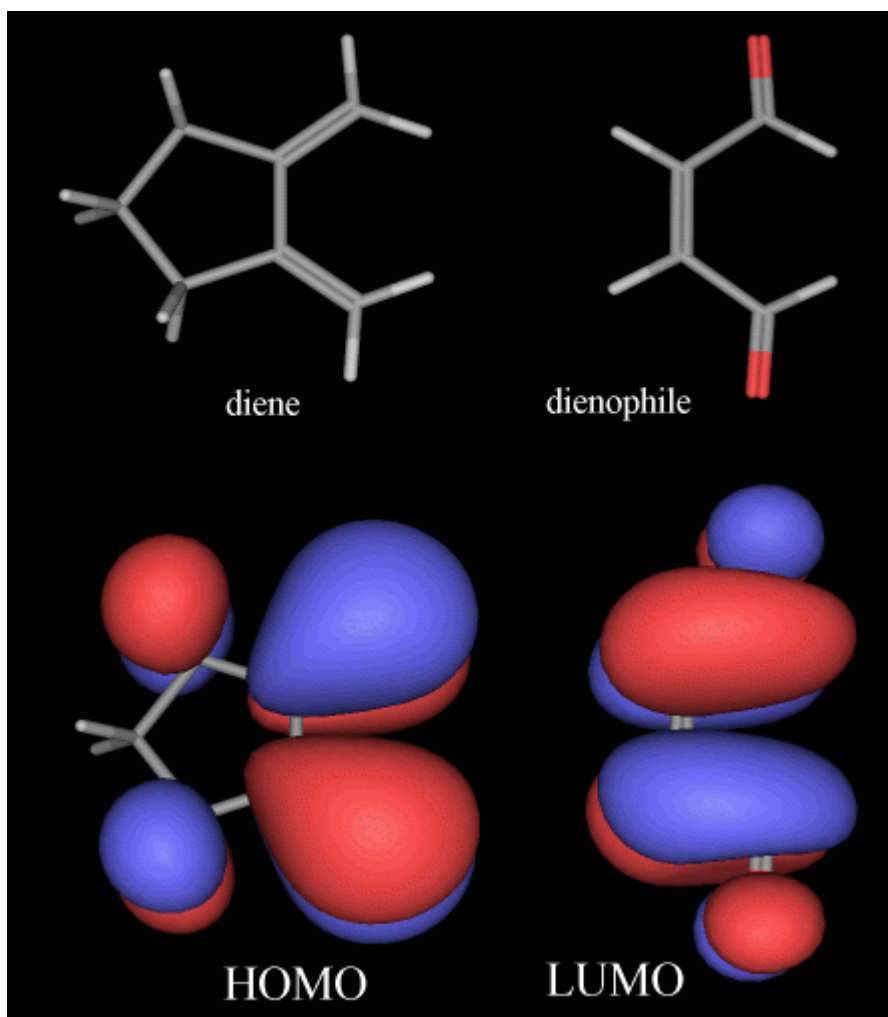
Where 0=forbidden and 1=allowed. (can you tell I used to be a programmer in my previous life?)

There are other interesting $\sigma\pi\sigma$ shifts, the most important of one is the [3,3] cope rearrangement. It works essentially using the same rules as listen above. There isn't anything unique about it, really. It's just another $\sigma\pi\sigma$ shift in the great scheme of life.

Cycloaddition Reactions: Good lord, when will it end?

Cycloaddition involves the combination of two molecules in such a way that a ring is formed. The most important cycloaddition in the history of the WORLD is the Diels-Alder reaction. (again, good science comes in twos, so partner up early before all the smart people are taken)

In the famed and fabled diels-alder reaction you have a 4π system reacting with a 2π electron system. The interaction between these two molecules is not unlike normal bond formation, that being, it is a HOMO-LUMO interaction. As depicted in the stolen but pretty drawing below, you can clearly see that the LUMO of one and the HOMO of the other must align themselves appropriately. So, one needn't really memorize rules for this sort of thing, just remember that if they don't align face to face, then you should check if they align face to edge. If they STILL don't, then you have some crazy edge to edge thing going on.



This sort of reactivity has stereochemical implications which I can allow you to sort out for yourself. Obviously things that screw with the HOMO and LUMO gap will alter the way reactivity occurs. Anything that can help the HOMO donate and the LUMO receive would be great. Two donor or two withdrawing groups would hinder the reaction considerably.

Molecular symmetry rules still apply. The reaction won't proceed unless you have symmetry just right. For instance, if you try to do a 2+2 addition supra supra, you would be in for a rude awakening as you would be trying to stuff electrons into an anti-bonding orbital. (like wise if you tried to do diels alder supra antara). You can get around this *IF* you do your 2+2 reaction supra antara. Of course, carbon carbon bonds don't stretch like that (they would SUCK at yoga) so 2+2 additions are generally not seen, though they aren't forbidden by MO theory. In fact, you CAN do them if you add to a big fluffy atom like a metal atom – plenty of space to grab an electron, the whole thing works perfectly.

Is it worth talking about 1,3 dipolar additions? I don't think so. My ass is hurting from typing all this nonsense, so I'm going to go stand up and maybe... make some toast or something.

CHAPTER 11: Radicals and things I don't understand very well

And... IM BACK.

Honey nut whatever is a good cereal. I decided against toast, because I don't have marmalade, and that's really what I wanted. Hmm... I should have poured myself a glass of chi tea...

AH, screw it, I'm going to do that too.

Yum, I like Chi tea. Here is where I insert the obligatory chemistry radical joke:

Two hydrogen atoms are walking down the street when one of them suddenly stop as says to the other,

"I think I lost an elelctron"

The other asks, "are you sure?"

"Yeah, I'm positive."

rimshot

Ehehe... let's start... OH GOD he's singing OVER THE RAINBOW AGAIN.

Anyway, lets start this chapter again...

CHAPTER 11: Radicals and things I don't understand very well

If memory serves me correctly, radicals without special stabilization rapidly dimerize or disproportionate. This makes sense, considering being a free radical is not awesome. Radicals also rapidly abstract hydrogen atoms from many types of solvents and most radicals are highly reactive toward oxygen.

Radicals that have long lifetimes and are resistant to dimerization or other routes for bimolecular self-annihilation are called stable free radicals. The term, inert free radical has been suggested for species that are unreactive under ordinary conditions and thermally stable even over 300 degrees C.

Large bulky groups keep the radical safe while conjugated systems delocalize the electron into the π system. Certain groups will also stabilize a radical. Something like Nitroxide groups or something with free lone pairs – they do well for this sort of thing.

Mommy, where do free radicals come from? And other awkward conversations

Well, when two atoms love each other very much... heh. The oxygen-oxygen bond in peroxides is weak (30kcal/mol) and activation energies for radical formation are low. Dialkyl peroxides are

decomposed thermally to give two alkoxy radicals. Peresters and Azo compounds are awesome too. The neat thing about azo compounds is you can get rid of the nitrogen as gas. Naturally, no matter how good of a radical departing thingiee you have, if the radical you leave behind sucks, it isn't going to leave easily. Azomethane does not decompose to methyl radicals and nitrogen until temperatures above 400 degrees C. Azo compounds having functional groups that stabilize the radical products are especially reactive. Many azo compounds also generate radicals when photolyzed. This can occur by a thermal decomposition of the cis-azo compounds that are formed in the photochemical step.

Really, photochemistry is good at making radicals.

What do these things look like?

Well, I'm glad you asked. EPR studies and other physical methods have provided the basis for some insight into the detailed geometry of radical species. If discussion is limited to alkyl radicals the possibilities include a rigid pyramidal structure, rapidly inverting pyramidal structure, or a planar structure.

The EPR spectrum of the methyl radical leads to the conclusion that its structure could be either planar or very shallow pyramid.

It appears that simple alkyl radicals are calculations suggest that two factors are of principal importance in favoring a pyramidal structure. One is a torsional effect in which the radical center tends to adopt a staggered conformation of the radical substituents. There is also a hyperconjugative interaction between the half filled orbital and the hydrogen that is aligned with it. Pyramidal geometry is preferred when a radical is next to an electron rich halogen. The further away they can be from each other, the better.

Stereochemistry suggests that racemization results from reactions with radicals suggesting they are more or less planar. In a fused ring system, axial attack predominates.

So, they are pretty close to being planar, but they also form relatively easily on strained ring systems (as compared to going from 109.5 degrees to 120 degrees). All this suggests that they are a shallow pyramidal structure.

Charged radical species and structural considerations

Unpaired electrons can be present in charged species as well as in the neutral system that have been considered up to this point.

Polycyclic aromatics are both easier to reduce and easier to oxidize than benzene. This is because the HOMO-LUMO gap decreases with increasing size of the molecule, with the HOMO being higher and the LUMO being lower in energy than in benzene.

Radical cations can be derived from aromatic hydrocarbons or alkenes by one electron oxidation. Antimony trichloride and pentachloride are among the chemical oxidants that have been used.

You can even make cyclooctaheptaene into an aromatic group by adding two electrons from elemental potassium! SWEET!

Radical cyclizations show a preference for exo cyclization with formation of five-membered rings over endo cyclization with formation of a six-membered ring.

In reaction with alkenes, in order for a bonding interaction to occur, the radical center must interact with the π^* orbital of the alkene. Bond formation takes place as the result of initial interaction with the LUMO, which is the π^* orbital. Formation of this sort of ring is governed by kinetics. It is entropically more favorable to form a five member ring over a four member ring. It also prefers to do so above and at a 70 degree angle to the new bond. This means that unless you have some degree of flexibility in your molecule, a radical reaction on an alkene is unlikely to proceed efficiently.

Radicals also impart stability in conjugated systems and thus prevent free rotation (or hinder it) of the molecule. Hückel calculations show the resulting orbitals have energies of $\alpha+1.4\beta$. The stabilizing $.4\beta$ imparts stability and acts as a barrier to rotation.

Not amazingly, the same things that stabilize anions also stabilize radicals. The large difference, so far as I can gather, is in the reactivity of these species.

Free radical reactions

Did you know that bromination and chlorination are radical activities? Good. Because, that's important. In fact, even the reaction with NBS is a radical reaction – which surprised me. Remember, there is anti-Markownikoff's addition in radicals because radical stabilization is what matters – not stabilization of some stupid ion. Oddly, there still exists the possibility that a bridge bromonium radical exists. SO, think of this Markownikoff's reaction like this... you're a proton, right, do you want to add to the stabilized cation or the other side? Obviously not the cation side. Now, would you rather add to the stabilized radical side or the other side? Well, to the radical side – it's got a MINUS CHARGE! HOORAY!

Free-radical chain oxidation of organic molecules by molecular oxygen is often referred to as autoxidation.

The best preparative results from autoxidation are encountered when only one relatively reactive hydrogen is available for abstraction. The oxidation of isopropyl benzene is carried out on an industrial scale, with the ultimate products being acetone and phenol.

Benzylic positions can be selectively oxidized to the hydroperoxide. Functional groups that stabilize radicals would be expected to increase susceptibility to autoxidation. Similarly the α position in there's is autoxidized quite readily to give α -hydroperoxy ethers.

These ethers are explosively unstable and occur in the presence of oxygen. Thus, when you leave a bottle of diethyl ether out for a long time after opening it, it will explode and you will die. (seriously)

This sort of stuff describes everything you need to know about this sort of stuff... it also accounts for stereochemistry.

Moving stuff around

Rearrangements of radicals kinda sucks. Migration of saturated groups is unusual, and there is a simple structural reason for this. In carbocations, migration occurs through a bridged transition state that involves a three center, two electron bond. In a free radical there is a third electron in the system. It cannot occupy the same orbital as the other two electrons and must instead be in an antibonding level. It is possible to migrate aryl and unsaturated groups because the radical can become delocalized. Read pp727-733 for an understanding of other interesting radical ideas.

Chapter 13, the last chapter.

(and its about photochemistry)

Everything that we have encountered up to here has pretty much prepared us for photochemistry. Obviously for this shit to get off the ground, whatever it is your doing needs to absorb light. Depending on functionality, organic compounds can have electron absorptions bands from the far ultraviolet to the visible region of the spectrum. For example, if the system is constructed so that light must pass through glass there is a lower limit to the light you can use as glass won't allow anything below about 200nm come through (higher, if it is less pure).

Here are some rules:

1. The excitation promotes an electron from a filled orbital to an empty one. In most cases, the promotion is from the HOMO to the LUMO, which is usually an antibonding orbital.
2. At the instant of excitation, only electrons are reorganized; the heavier nuclei retain their ground-state geometry.
3. The electrons do not undergo $s\pi\pi$ inversion at the instant of excitation. Inversion is forbidden by quantum-mechanical selection rules, which require there be conservation of $s\pi\pi$ during the excitation process.

The new minimum-energy geometry associated with the excited state is rapidly achieved by vibrational processes, which transfer thermal energy to the solvent.

The excited state can also give a triplet state, in which both unpaired electrons have the same $s\pi\pi$. The triplet state will also adopt a new minimum-energy molecular geometry. If intersystem crossing is fast relative to reaction, reaction will occur through the triplet excited state.

Look, another list:

1. Excited states have a great deal of energy and can therefore undergo reactions that would be highly endothermic if initiated from the ground state.
2. The population of the antibonding orbital in the excited state allows the occurrence of chemical transformations that are electronically not available to ground-state species.
3. Either the singlet or the triplet state may be involved in a photochemical reaction, whereas only singlet species are involved in most thermal processes.

Orbital symmetry considerations

I dunno what to say here, really. Everything in chapter 11 is now reversed because one of your electrons is in a π^* orbital. So, take everything you learned in chapter 11 and reverse it. Suddenly you're using ψ_3 or butadiene... it's pretty reasonable stuff, really.

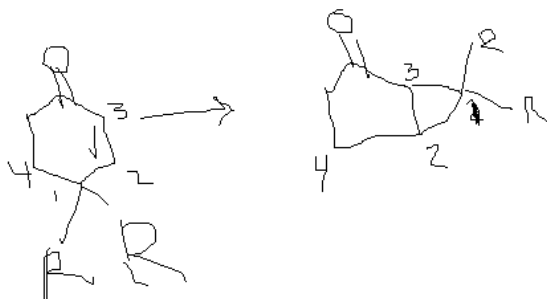
Consideration of the HOMO-LUMO interactions also indicates that the $[2\pi+2\pi]$ additions would be allowed photochemically. The HOMO in this case is the excited alkene π^* orbital. The LUMO is the π^* orbital of the ground-state alkene (they're pretty much the same damn thing) and a bonding interaction is present. (hooray)

Now... me, personally I would have stopped there. But there's more.

Photochemistry of CARBONYL COMPOUNDS!!!! (omg)

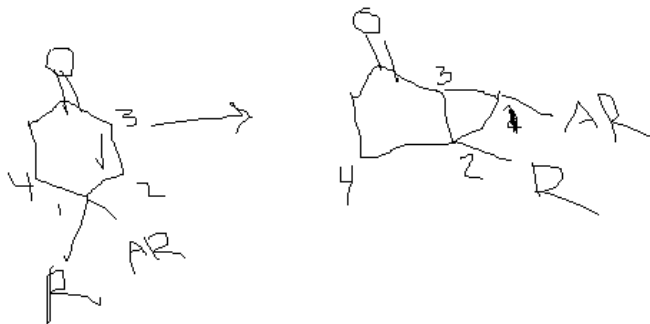
See pp753-765. Fairly important stuff that requires too many diagrams to go steal off the web.

Though, a few things of particular importance bear mentioning here.



The above reaction is reproduced using my advanced molecular modeling software MS paint. As you can see, a rearrangement has occurred here. This rearrangement is none other than the lumiketone rearrangement. It involves a shift of the C1-C4 bonds. This reaction is stereospecific (of course) and can be described as a $[2\pi+2\sigma]$ cycloaddition (wtf?).

This mechanism requires that inversion of configuration occur at C-4 as the new σ bond is formed at the back lobe of the reacting C1-C4 bond.



Conjugated shit does something a little different in what can only be called the di- π -methane rearrangement

You can racemize your stuff by turning into radicals (yay) and recombining them. You can get α cleavage or β cleavage... maybe more cleavage. I don't think you can have too much cleavage, but that's just me.

DIE DIE, DIE!

di- π -methanes rearrangements also happen where you have, say, a 1,4 diene and other systems that have two π systems separated by an sp^3 hybridized carbon atom.



See? More kinetically awesome three member rings! It's as if light were just little packages of awesome unto themselves.

Anyway, that concludes it for the book, but I'm hardly done here. NOW LETS GO OVER THE NOTES NOT DISCUSSED IN SUNDBERG!!!

Supplemental notes not in the book

Detection of intermediates:

In-situ: observe as it happens!

- 1) Run Rxn in spectrometer
 - a. NMR in situ (caveats)
 - i. Time scale
 - ii. Temperature
 - b. react with UV/IR IN the reaction
- 2) stop flow method
- 3) CIDNP Chemically induced dynamic nuclear polarization
 - a. NMR experiment
 - i. Electron $s\pi\pi$ gets transferred to nucleus
 - ii. Dynamic process

Poly Radicals and Radical ions

- 1) Benzyne
 - a. Preference, due to angle strain may force it into a radical
 - b. Interaction between radicals imparts 5-10 Kcals due to poor overlap (that is, 5-10 Kcals of stabilization, which should be more if it were a full sp bond)
 - c. You can make them by azo removal.
 - d. Other Benzyne's are possible, including o,m and p benzyne's.
 - e. Para interaction are just as strong as ortho
 - i. Interaction arise out of back bonding orbitals
 - ii. Delocalization does not occur
- 2) Electron transfer
 - a. Single electron reductions

- i. SmI_2 – preferred oxidation is Sm(III) $\text{SmI}_2 \rightarrow \text{Sm}^{3+} + e^-$
- b. single electron oxidation
 - i. $\text{CeIII} \rightarrow \text{Ce}^{3+}$

4. Radical Anions

- a. THF indicator to determine if your THF is dry
 - i. Use TiCl_4 for forming C-C bonds. Addition of TiCl_4 to ketone forms radical ketone with anion on the oxygen. Reaction occurs at radical carbon
- b. SmI_2
 - i. Radical transfer to an aromatic group in the reaction of CH_3NO_2^- to a halogenated aromatic ring. One electron moves over first, both have radical character then bonding occurs.
 - ii. Radical e^- adds to the anti-bonding orbital
 - iii. Hammett plots show KINKS indicating mechanistic change: From substitution to radical (depending on substituents)

Carbenes + Nitrenes (a carbene is depicted above)

1. Carbenes

- a. Dipole carbon in an sp^2 Form:



- b. acts as both nucleophile and electrophile
- c. We can make a BI-RADICAL aka a triplet carbene. What are some pros and cons?
 - i. Singlet has e^- repulsion
 - ii. Triplet is in a less stable p-orbital
 - iii. Stability is thus dependent upon substituent effects (must be a theme)
- d. form a carbene w/ chloroform by α -elimination (singlet \rightarrow singlet)
 - i. $\text{HCCl}_3 \rightarrow \text{C}:\text{H} + \text{HCl}$
 - ii. $\text{N}_2\text{CH}_2 \rightarrow \text{H}_2\text{C} + \text{N}_2$
- e. Forming triplet carbenes

$\text{CH}_2\text{N}_2 \xrightarrow{-h\nu} \text{CH}_2 + \text{N}_2$
- f. forming safe carbenes:
 - i. carbenes are EXPLOSIVE so, they should be complexed.
 - ii. $\text{CH}_2\text{I}_2 + \text{Zn} \rightarrow [\text{CH}_2:\text{ZnI}_2]$ Complexed carbene behaves just like free carbene!
- g. Grubbs Catalyst (see notes in Taylor)

2. Nitrenes

- a. Like a carbene, but less stable.

Hooray, that concludes this study guide. I hope you had as much fun reading it as I did writing it (which wasn't much, I assure you.)