Lecture 16B • 11/03/11

[Review for test]
[Topics: stereochemistry – R/S, achiral/chiral, loss/retention/inversion of configuration, racemic mixtures, optical activity; mechanism – cationic/anionic/radical, concerted and stepwise, consequences of cationic versus anionic; mechanism of Sn1 and Sn2; kinetics – RCD, rate-limiting step, activation energy, energy distribution diagrams; thermodynamics – Hess's law; equilibrium – three definitions; Le Châtelier's princple; delocalizaton and resonance structures – SMOG, allyl anion]

Sn2 mechanism – You can have an alkyl halide attacked by something like hydroxide. At the same time that they hydroxide attacks, the bromide comes off. If we wanted to write a reaction coordinate diagram for a reaction like this, it would look like this: one transition state, corresponding to one step; reactants higher in energy that products, because it's exothermic.

Sn1 mechanism – So far the versions of the Sn1 reaction that you've seen have all had three steps to them: first, breaking of an alkyl halide bond, forming a carbocation; then, water [or other things] can attack [and] a positive charge would result; [then] there's a final step, deprotonation occurs. If I told you some information about this reaction, if I emphasize that the first step of the reaction is the rate-limiting step, then you should know that if we drew a reaction coordinate diagram for it, it should have the largest activation barrier of any of these steps. Let's say I had a two-step reaction: if I said that the first step was endothermic, and then the overall reaction was exothermic, then you should be able to draw a diagram like this.

Catalysts

Let's say I had some simple one-step reaction, and let's say it was exothermic. If you use Hess's law, then what would you say would happen to the overall change in this reaction, the energy, if we were to use a catalyst? What does Hess's law say about the change in enthalpy for a reaction? Since enthalpy's a state function – what's a state function? A function that depends only on the states that you have, the initial and final states, but not on how the change between those states occurs. In this case, if I have a chemical reaction that has a certain energy gap that's associated with it, putting a catalyst in it is not going to change that change in energy. The only thing it does do is it provides a new reaction pathway. Typically we would say that a catalyst lowers the energy barrier for a reaction. That's true, but if you wanted to get really fussy about it, you could say it's not. It doesn't actually change the reaction you had to begin with, it gives a totally new reaction pathway. That new reaction pathway has a lower activation barrier – lower activation barrier, the more molecules that can pass over that barrier, which is why it leads to a faster reaction. A catalyst lowers the activation energy of a reaction by providing a new reaction pathway.

If we were to connect this to equilibrium, and we have this equations: free energy ... let's just say that entropy is a minor component of this reaction and let's just say for the sake of argument therefore that delta G for the diagram would look similar. Since there's a connection between the equilibrium constant and that free energy change, and if a catalyst doesn't change the energy of a reaction, then that means that a catalyst does not affect the balance of products or reactants once you've reached equilibrium. It might get you there quicker – that's what a catalyst does, it increases rate – but it will not change the distribution of products and reactants. A catalyst does not change delta H or delta G since Hess's law states that those values only depend on the identity of the products and reactants, thus a catalyst will not affect the balance of products and reactants at equilibrium.

Practice naming cyclic compounds and compounds with multiple stereocenters.

We'll start with a simple example, where I don't even show stereocenters. There's two methyl groups and an ethyl group. We have to figure out how to number the compound with the lowest possible numbers. There's a couple of ways we could do it. We could put the left methyl group and make that position 1. We then we have two different ways we could numer around the ring. One way, going clockwise, the next lowest number would be 3, but if we wen't the other direction, the next lowest number would be 4. Three is lower than 4, so this would be the correct numbering, going clockwise [1, 3, 4]. What are some other possibilities? Let's make the other methyl group position 1. If I number one way around the ring, 3 would be the next number. If I number the other way around the ring, two would be the next number. We don't even go past that point to see what the next number after that would be, because, in numbering, it's the first place where some difference occurs. 2 is less than 1, so we if kept numbering around, we would get [1, 2, 5] as our set of numbers. But let's look at one more possibility: what if we made the ethyl group position one? Then we again have two choices: going to the left, going counterclockwise, our next number would be 2; going clockwise, our next number would be 4. 2 would be lower, so we'd have the numbers [1, 2, 4]. If you compared the first and the last one, we have [1, 3, 4] versus [1, 2, 4]; because 2 is lower than three, this last one is the correct numbering. What if you switched the methyl and the ethyl group? It doesn't matter, [even though] the 'e' in ethyl is lower than the 'm' in methyl. [It doesn't change the numbering] because you only look at alphabetization if you end up with a tied, if you end up with two different ways to number than have the same numbers. In this case, you only look at the substitution pattern.

A cyclohexane with two centers. For numbering cyclohexane compounds, the standard process is: if you only have one of the most important substituent on a molecule, you don't have to number the ring, because it automatically assumes position one. An alcohol is more important than alkanes or hydrocarbons in general, which is more important than halogens. The alcohol would automatically get position number one. SInce it automatically gets it, we just call it cyclohexanol. If we had two alcohol groups, then we'd have to use numbers. Let's say that I put another alcohol at the two position; then it would be cyclohexane-1,2-diol, the numbers do appear. We do need to name the substituent. It is at the 3 position, so it is 3-bromocyclohexanol. Now we worry about the configurations of the stereocenters. Stop stereocenter, R or S? R. Why? Alcohol, priority number 1. You go both ways around the ring, the one with the bromine is different first than the other side, so the position is priority 2; continuing around to the other part of the ring, that's priority 3; hydrogen, the least important group, is in the back. These are precessing clockwise, so it is R. Bottom stereocenter. Bromine is 1; the side of the ring with oxygen's 2; the plain side is 3; it looks like it's S, but remember the hydrogen's pointed at you, so it's really also R. When you're naming a compound that has multiple stereocenters, it doesn't matter what's R or S; you just list all of the configurations in numerical order, so you'd list Rs before Ss or Es before Zs or anything like that, you just go 1, 2, 3, 4, in order of stereocenters. Position 1 is R, position 3 is R, so this is (1R, 3R)-3-bromocyclohexanol.

Acids and bases – strong versus weak acids and bases; what is neutral versus what is neutralized

Here's the example we're going to discuss: something like acetic acid and sodium hydroxide. Very similar to benzoic acid and sodium hydroxide. Acetic acid is a weak acid; sodium hydroxide is a strong base. What does it mean to be a weak acid? What is the definition of something that is weak acid? It doesn't want to let go of its hydrogen. In other words, it doesn't dissociate very much. A weak acid is an acid that only minimally dissociates. We could write an equilibrium constant for the dissociation, so we could quantify that dissociation. In an acid dissociation, [it is] classically represented just like this: HA, where H is the proton that's going to come off, A representing acid, is going to dissociate into H+ and A-. Equilibrium constant is products over reactants raised to appropriate stoichiometric coefficients; since everything's in 1:1:1 ratio, Ka itself is fairly simple: [H+][A-]/[HA]. [Recall that] delta g is equal to -RT ln K. For a weak acid, that doesn't want to dissociate, that means it doesn't want to make a lot of products, that means that Ka is going to be much less than one. That means that delta G is going to be greater than zero – a reaction that doesn't want to go forward spontaneously is because it's an uphill energy reaction. If I wanted to draw a reaction progress diagram for that kind of process, it would look like this: positive change in delta G, causes the equilibrium position to want to be closer to reactants.

Here's the story we could tell. When we have acetic all by itself in solution, it doesn't want to produce much H+. Let's say we now neutralize it with a strong base like sodium hydroxide. If we pretend that that reaction is complete, that each mole of hydroxide reacts with a mole of acetic acid, that means you're going to be all the way over on the righthand side of the equilibrium curve, because you forced all of those protons off, you forced that reaction to go all the way forward. Once you're there, once you're neutralized, what that means is that acetate that's left over, that's only just the product in this equilibrium. There is no more acetic acid for it to be in equilibrium with, so the only thing you can do is react backwards, which means it's going to pull an H+ from whatever happens to be around, which, if we're talking about hydroxide, that means it's pulling it back off of water. Even though you might have one mole of acetic acid and one mole of hydroxide, they will not react all the way to completion because that would give you a Q much greater than K. Le Châtelier's principle says that if you upset the equilibrium that acetic acid would have had – instead of just dissociating a little bit, you force it to go all the way to dissociation – then this graph is going to show us it's going to go backwards. Which means, even though you've neutralized the solution, the solution will not be neutral.

Since I've used the terms neutralized and neutral, let's talk about them a little bit. Let's remind ourselves what pH is. pH is just a measure of the H+ concentration in solution, specifically, it's defined as the negative base 10 log of H+ concentration. What is the definition of neutral? pH = 7? That is true, but only at one temperature. What would be a more general definition? It's when the concentration of H+ is equal to the concentration of OH-. Why is it not always pH 7? Let's talk about the autoionization of water. All by itself in solution, liquid water will dissociate into H+ and OH- ions. Neutral water makes one of each of those two. But this is not a favorable process, because you're pulling apart water, you're making H+ and OH–, those are the old, simplified definitions of what is an acid, what is a base – something that has H+, something that has OH-, so these things really want to react. Why in the world would this dissociation occur at all? Same reason that water evaporates at room temperature: some of the water molecules have just enough energy that they're able to dissociate. That means that if you change the temperature, you're going to change the number of molecules that do dissociate. At roughly room temperature, it is true that the H+ ion concentration is 1.0 x 10^-7 molar, which means you're going to get a pH of 7. As you change temperature, you change the number of molecules that dissociate, you change the H+ concentration, as so you get a pH that's not 7, but it's still neutral, because neutral comes from the idea that when water dissociates, only one H+ and one OH- are made in balance with each other. pH you have to adjust with temperature. A safe definition is that the H+ concentration is equal to the OH-. What, therefore, is the term neutralized? That in a reaction, number of moles of acid is equal to the number of moles of base. These are not the same definitions. Because, if you have different acid-base strength, then that means a weak acid may only make a little bit of H+, a strong base would make a lot of OH-, put the two together, you're not going to end up with a neutral solution. Neutralization is to make neutralized, not neutral. Neutralization is where you're going to react equal moles of acid and base.

Hyperconjugation

Hyperconjugation is the reason that we said that tertiary carbocations form more easily than primary or secondary or methyl carbocations. We'll take a tertiary, a secondary, a primary, and methyl halide – we'll take t-butyl bromide, isobutylbromide, ethyl bromide, and then methyl bromide. We want the carbocations [from those halides]. So, methyl carbocation, ethyl carbocation, isopropyl carbocation, and t-butyl carbocation. The central atom in each of these examples is going to be sp2-hybridized, because each one of those central atoms only has three bonds to it. For the methyl group, that's all you've got. For the others, the rest of the carbons would all be sp3-hybridized, because they would all have four bonds to them. Let's going ahead and draw out the centers of each of these first. Notice that when I write these centers, I try to avoid putting any orbitals written straight up and down, because if you have sp2-hybridization, that means you're going to have a p orbital that you're going to have to draw in later, so you want to avoid having that p orbital overlap with your sp2 orbitals. For the methyl group, all you've got left is hydrogens; for the ethyl, there's only two hydrogens; for the isopropyl, there's only one; and no hydrogens on the t-butyl. We've got a bunch of p orbitals, and then we have our sp3-hydridized carbons – one more on the ethyl, two for the [iso]propyl, and three on the t-butyl – and then a bunch of hydrogens.

Remember that the single bonds are constantly able to rotate, so these interactions I'm about to draw in don't necessarily all happen at the same time; it's going to be more the idea of how many neighbors are there that interactions can occur with. In the case of the methyl group, there is a 90° between the sigma bond[s] and the p orbital; that means they completely fail to overlap, so there's no chance of interaction, so there's no hyperconjugation interaction. In the ethyl case, there is one sigma bond that, as it rotates around, every once in a while it will line up so it can have an interaction with the p orbital. The difference between conjugation and hyperconjugation is this: conjugation, you have p orbitals – multiple ones of them – that completely overlap with each other, which means the electrons are free to move around between all of those different p orbitals. That generates new molecular orbitals. Just like when two p orbitals overlap you create a [pi] bond and an antibond, we say for the allyl system how that generates three orbitals – three p orbitals making three molecular orbitals: a bonding, a non-bonding, an antibonding orbital. Hypercojugation is something totally different. It is related in the sense that there is electron density being moved around. But, the sigma bond on that sp3-hybridized carbon stays a sigma bond. It's energy might be changed a little bit by hyperconjugation, but the bond is pretty much localized; a little bit of that electron density, like the fringe of a bond, happens to interact a little bit with that p orbital, which helps spread the charge out a little bit. But it's not the same as delocalization, then, because there's not new molecular orbitals being made; it's just a small interaction. But that interaction, although small, is enough that the more interactions that you get, the easier it is for that carbocation to form.

In the ethyl case, we only have one hyperconjugation interaction; but for the [iso]propyl case, there's two hyperconjugations that could happen; and in the t-butyl case, there's three hyperconjugation interactions. Any of the three sigma bonds in this case [can hyperconjugate]. As they rotate around, every once in a while the p orbital and that sigma bond line up. If turned 180°, it would line up and overlap with the bottom part of the orbital. As it's spinning around, there are these small interactions that keep on happening. The timing is random; as these things spin, they happen to line up, so it's not that they're coordinated like this, not that they're all happening simultaneously; it's just that, for the tertiary carbon, you have three places it could happen, three times the change; for the [iso]propyl, you only have two chances; for the ethyl, the primary carbon, only one change. The greater the amount of hyperconjugation, the more stable the carbocation.

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Mechanism – cationic versus anionic, stepwise versus concerted;
Kinetics: RCD, RLS, Ea, energy distribution diagrams
Thermodynamics – Hess's law

A catalyst lowers the Ea of rxn by providing a new rxn pathway.
delta G = -RT ln K
A catalyst does not change delta H (or delta G), since Hess's law state those values only depend on the identity of the products and reactants. Thus, a catalyst will not affect the balance of products and reactants @ equilibrium
Equilibrium - 3 definitions ([ ], rate, E); Le Châtelier's principle

Delocalization and resonance structures
Stereochemistry – R/S; achiral/chiral; loss [Sn1]/retention/inversion [Sn2] of configuration; optical activity -> racemic mixture
Hyperconjugation

Weak acid –> an acid that only minimally dissociates. Weak acid: Ka<<1 –> delta G > 0
pH ≣ -log10[H+]; neutral : [H+] = [OH-]
Autoionization of water : H2O ⇌ H+ + OH-; @ 25 °C [H+] = 1.0x10^-7 M => pH 7
neutralized : # mols acid = # mols of base
The greater amount of hyperconjugation, the more stable the carbocation.
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Structures *(remaining structures identical to lecture 16A)*

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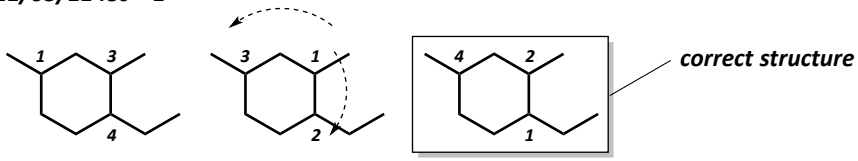

[1, 3, 4] ***[1, 2, 5]*** ***[1, 2, 4]***

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