

## Lab 10A • 02/22/12

### Kinetics versus thermodynamics

In most “normal” chemical reactions, if you have two competing processes that can occur, one set of reagents that can make two different products, generally, the stability of the product that’s formed is related to how much energy you have to put into the transition. In other words, if you make something that is thermodynamically favorable, then often associated with that is a low activation barrier. To make something that is less energetically favorable, gonna be higher in energy, correspondingly there tends to be a higher energy barrier to it. If we wanted to write a simplified energy diagram that would show that, it might look something like this: It’s whatever’s most rapidly formed that’s also the most favored to be formed. But this kinetic versus thermodynamic control comes up in situations in which the graph is crossed, you could say, where you might have a reaction that is easier, a lower reaction barrier, but ends up being the thermodynamically less favored product. In that same situation, you might have something that has a tougher reaction barrier, but if you can cross the barrier, you make a more favored product. We’ll talk about how temperature really, therefore, affects the distribution of products that’s going to form, cause at low temperature, whichever of the processes is easier is the one’s that’s going to predominate, even if the product’s not favorable. High temperature, where you have, let’s say, the possibility for a reverse reaction, then the reaction could go back and forth. If it ended up at that most favored product, it’s going to stay there, because it’s the lowest thing in energy that’s present in that system. That’s what we’re going to build up to: how can temperature affect product distribution in one of these cases where there isn’t the direct correlation between transition state energy and product energy. [Review of kinetics] If temperature’s a factor, we need to understand why temperature’s a factor. It’s going to be activation energies that we end up discussing as well; we need to understand what’s the relationship between rate and rate constants and activation energy, and then product control.

Let’s talk about what is a reaction coordinate diagram. What a reaction coordinate diagram? It shows the energy involved during a chemical reaction going from reactants to product. What situation of a reaction does this reaction coordinate diagram describe? It’s just one reaction, and it’s along the most favorable pathway for that reaction. What this comes from is we could monitor the energy of this set of atoms as we change the position of any one atom, but in a real-life system, there’s enough atoms involved where that’s enough variables that that would generate a graph that’s impossible to easily interpret. What we do is we say imagine the reaction happens along its most likely pathway, and we just follow that pathway and see how energy changes – that’s what the reaction coordinate is, that imaginary, idealized pathway. The reaction coordinate diagram shows energy changes along that pathway. A reaction coordinate diagram shows the change in energy of reaction along the most likely reaction pathway. It is technically also this 2D simplification of a multi-dimensional graph.

Let’s draw an example reaction coordinate diagram. This is not going to correspond necessarily to any specific kind of reaction; it’s just a chance for you to label the diagram. Just a comment about energy – energy could be in either the form of enthalpy or free energy; the difference between that and enthalpy is entropy. Enthalpy,  $\Delta H$ , just looks at the raw energy difference between reactants and products;  $\Delta G$  incorporates how the reaction happens, how energy and matter get transferred. To keep things simple, we’re going to do it just in terms of energy; all discussion will be in terms of  $\Delta H$ . On this diagram, we have reactants; in this case we do have an intermediate; and then a product. You can see that this graph has two highest-energy points; what are those points called? The transition state. That transition state is the highest-energy transition point between a reactant and a product, or one intermediate to the next. Since this is the highest reaction point along a step, then if we have two transition states, that means we have two steps in the reaction. More generally, the number of steps in an overall reaction is equal to the number of transition states. We can mark on here how much energy it takes to get to that toughest energy point. What would that value be; what is that called? Activation energy. Notice how it’s measure from just to the reactant side of the transition state up to the transition state. In the case of the first transition state, we start from the reactants; from the second one, we measure from the intermediate, not the very beginning, cause you’re already higher up in energy to begin with. There’s also one more quantity we can show on here, which is the heat of reaction, the overall change in energy between reactants and products.

A couple of commentaries. From this diagram, can we tell how many molecules are involved? No, cause there’s no mechanism written up here. Beyond the fact we can’t tell at all how many reagents are involved, can we tell how many reagents are involved in the rate-limiting step? What is the rate-limiting step? It’s the step with the highest activation energy. If we can’t tell how many reagents there are two begin with, we also can’t tell how many reagents are in that rate-limiting step, which matters because only those reagents that show up in that toughest step, the one with the highest activation barrier, show up in the rate law, which means have an effect on the reaction. There’s correspondance between the overall stoichiometric equation, the number of reagents that there are, the number of steps that there are, and the number of reagents in the rate-limiting step; no connection. Only those reagents involved in the rate-limiting step (RLS) are found in the rate law. There’s no relationship between the overall stoichiometric equation, the rate law, and the number of steps. This is why you learned the method of initial rates, the integrated rate laws, to try to figure out which reagents are in that rate-limiting step. The point is: if you don’t know the reaction, you can’t write the rate law.

The two factors – activation energy and temperature – and this other factor – the steric factor – are all wrapped into this thing called the Arrhenius expression. If you don't remember it, it is  $k = A e^{-E_a/RT}$ . That exponential bit,  $e^{-E_a/RT}$ , that comes from statistical thermodynamics, which tries to map macroscopic properties by assuming that you've got this infinite collection of molecules and trying, somehow, to treat those molecules individually. You're going to find this  $e^{-E_a/RT}$  showing up in multiple places. What are the variables in this expression? I've already mentioned temperature, and I already identified activation energy. There's this third factor, which is sometimes called the steric factor. Let me tell you more about what this expression really is. The activation energy and the temperature together tell you the fraction of molecules that have the energy to react – the energy to, but maybe not the means to, because molecules do have to orient themselves a proper way in space for a reaction to occur, at least normally it does. That's what's rolled into this steric factor. Sometimes the steric factor's expressed this way: that it's the fraction of successful collisions in a reaction. You've got  $A$ , which tells you what fraction are successful, and the this exponential term that tells you how many molecules you have that could react; sorta the way to read this equation.

To see more concretely the effect of temperature and activation energy, we have to revert back to my favorite set of diagrams – the energy distribution diagrams, which also have something to do with this  $e^{-E_a/RT}$  term; the same math that is behind that is also behind the shape of these graphs. What are the two graphs that I'm concerned about? They're both of the form of having the x axis as the energy per molecule versus the number of molecules. In one graph, we could look at what we would get if we had a constant temperature, but we were going to compare two different chemical reactions. Let's say these two different reactions have two different activation barriers, one higher than the other. The activation energies, how much energy you have to add in to get something started, raise that barrier, few molecules, at the same temperature, will have that much energy available to them. Higher activation energy means fewer molecules with the energy to react. The other diagram is if we were to look at two different temperatures. If we were looking at two different temperatures of the same system, the area of these two curves needs to be the same, because the total number of molecules needs to be the same. It would hopefully make sense that as you increase temperature, more molecules are going to have higher energy, so the graph gets squat and shifts to the right. In this case, we would be comparing how temperature has an effect on rate by looking at how many molecules now could cross over that activation barrier, the same activation barrier. Higher temperature, more molecules pass that barrier, more molecules with the energy to react, faster reaction.

#### Reversible reactions and equilibrium

Let's say that I make this a really contrived, ideal case. Let's say we have a reaction where molecule A interconverts back and forth with molecule B. Let's say that both the forward and reverse reactions are unimolecular, meaning that you only have one molecule involved. Let's say that both reactions in both directions are one-step reactions. One last assumption that we'll make is that the steric factor for the forward and reverse reactions are equal. If we had a reversible reaction going on in one pot only, everything's going to automatically be at the same temperature, so temperature's not going to have an influence on rate. If I additionally say that the steric factors are the same, then anything that we're going to discuss has to do with just activation energy.  $A_f$  will be the steric factor of the forward reaction,  $A_r$  being the steric factor of the reverse; assume that they're equal.

We wanted to write a reaction coordinate diagram. Let's say that B is lower in energy than A; then our diagram would look like the following: a simple one-step reaction. If we're talking about a reversible reaction, though, we could notate two different processes: one that would have an activation energy for the forward process, and then we'd have an activation energy for the reverse process. With such an idealized example, here's the series of relationships that we can make. First, what does it mean if we are at equilibrium, if this is a reversible process that happens to be at equilibrium? What are the definitions of equilibrium? That rate for the forward and reverse reactions are the same; concentrations don't have any observable change; and there's no observable energy change because you're already at the lowest-energy point. If we're talking about kinetics, it's that first definition that we care about: that the rates of the forward and reverse reaction are equal. We could rate law for each of these. Rate law has the rate constant plus whichever reactants participate in the rate-limiting step. In the forward reaction, there's only A around; it's unimolecular, so it's going to be the one molecule that reacts; we'll have a forward rate constant associated with it. We could write the same thing for the reverse reaction, using  $k_r$  as the reverse reaction constant and B as the concentration of the product that's going in reverse. The point of say that this is a system at equilibrium would be able to say that the product of the forward rate constant and the reactant concentration would have to equal the reverse rate constant times the product concentration. This is an important point because, yes, equilibrium is the point where the rates are equal, but if you have two different activation energies, then you have two different rate constants. Since activation energy for the forward reaction is less than the activation energy of the reverse reaction, the rate constant of the forward reaction is greater than the rate constant of the reverse. The only way that this above equation could be true, the equality to be true, is if the concentration of A is low and the concentration of B is high. So although reaction rates are equal, rate constants do not have to be equal.

This is a really carefully designed example; in many real reactions, not all reagents show up in the rate law, not all process have both unimolecular forward and reverse reaction rates. But, in general, this is a handwaving way of explaining why you're going to have different quantities of products and reactants at equilibrium, making a kinetic argument to get there.

Although the rates are equal, the rate constants do not have to be, which will affect the proportion of reactants versus products at equilibrium. The main point of this diagram is to show that with a difference in activation energies we have a difference of rates which causes a difference in the amount of products present.

### Conjugate addition

The reaction of buta-1,3-diene with HBr. Turns out that there are two products that could form; let's look at the mechanism for both of them. With HBr, we would say: we have an alkene that can form a carbocation; in this specific case, we'd rather form the internal carbocation, cause that's secondary, instead of the terminal, because that would be primary. We have Br- left over if we started with HBr, and so we can end up with this alkenyl halide. I'm going to write the hydrogen in that added in, which normally don't need to, but I'm doing it so we can highlight the fact that, if we called the place where the hydrogen added in position one, relative to it, the bromine's going to be in position two. This form of addition is known as 1,2-addition; that's what all of your previous alkene additions have been, 1,2-additions, cause we hadn't yet talked about conjugated systems.

What can happen differently if you have a conjugated system? The following: after the initial attack of the alkene on H<sup>+</sup>, we make a carbocation, but it's a carbocation that, we could say, shifts due to resonance; let me again write that hydrogen in. Now that we have that new carbocation, now we could show bromide attacking, which gives us the other distinct product. If we labeled the hydrogen position one, relative to it, the bromine's going to be at position four; these are not real nomenclature numbers; these are just relative positions. This is called 1,4-addition. Which one of these two products is probably the thermodynamically more stable one? Which one's the energetically favorable product: the 1,2 product or the 1,4 product? Why [isn't] the 1,2 for favorable? It's not about the carbocation; it's about the product – which product is more stable? It's going to be the 1,4 product; why? The type of alkene – to be more specific, it's an internal alkene. The fact that you've got two substituents on the alkene, versus only one substituent on the alkene up top, makes the 1,4 product the more favorable product.

Which of the carbocations – separate question – is the more stable carbocation? Yes. Because how many carbocations are there? One: it's a delocalized carbocation. We write two structures for it, but there's only one molecule there. The reason that this is an important point is if we want to draw a reaction coordinate diagram, we need to know how many different energy levels there are. The point is: although it looks different on paper, the two carbocations are the same energy level, because neither structure, the way we write it, is correct. But, there is a difference in energy that happens once the bromine starts to attach, because once the bromine starts to attach, it makes that positive charge be localized; it causes the positive charge to end up somewhere, once the bond starts to form. The intermediate, there's only one energy level, but the transition states – what happens when we move out of it, those are going to be different in energy. This intermediate is a delocalized carbocation; there are not two distinct carbocations formed. Any energy difference that does occur happens once bond formation has begun.

Now, with all of this information, let's write a reaction coordinate diagram for this case. What will it look like? Energy the y axis, reaction coordinate for the x axis. We have our starting diene. It will make a carbocation; it's going to be higher in energy. I'm going to notate the carbocation in a way that I never, ever do (of course it can't be never if I just did it, but it's not very often I do it like this). That dotted line does mean delocalization. The reason I don't like it is because you can't count electrons from it – you can if you know something about pi systems. If we have three atoms part of a pi system, and there's a plus charge between the three of them, that means there's two electrons there, because for each p orbital that's part of a pi system, there would be one electron in it (in theory). If we only have two electrons, that's why we result with a plus charge, but you can't tell that from the dotted line, which is again why I don't normally like the dotted line. I like it well enough here only because I'm writing one structure instead of two resonance structures, which is harder to squeeze in there, and it does highlight the fact that it is only one carbocation, not two different forms of the carbocation.

We do have two different products, and we're going to have – most important of all – two different transition states. I'll call the products A and B, just out of convenience. A is going to be the terminal alkene; the less-favored product, B, is the internal alkene, which is the more-favored product. The more-favored product, however, happens to be the one with the higher activation barrier, and the less-favored product is the one with the lower activation barrier. The transition state for the less-favored product will look like this. I don't normally draw transition states; I did use a dotted line between carbon and bromine to show that it is forming, but hasn't formed yet. That means there is a slight positive charge on that center if it hasn't finished forming. Because that slight positive charge is on the secondary position, that's why it's the more favorable of the two reactions. If we look at the transition state for the other reaction, it's similar in that we have the bromine bond starting to form, but since it hasn't formed yet, not completely, there is a little positive charge on the carbon – a primary carbon. A primary carbon with a positive charge – not as favorable as a secondary; that's why the difference in the two transition states' energies [exists].

At low enough temperature, something like 80% of the product is A. But you heat it up significantly and it flip-flops: 80% of the product becomes B. The only reason that it's favorable at all is because we do have delocalization.

The two places where you can draw carbocations do correspond to the two more likely places that attack's going to occur; we don't ever draw a positive charge on the middle carbon cause that would mean that you'd end up with a lone pair on one side or the other and no pi bond, it's not favorable. Those two positions are the positions where attack could occur. If there happens to be enough energy so there's time for the bromide to move and attack the other position, then it can happen, even if it's not favorable – that's the last argument I'm going to make – if you formed B, it's lower enough in energy, it doesn't want to go back, whereas A, if you form it, with enough energy it can reverse and have a chance to make B again.

Let me know now to the last diagram, which is just a blow-up of the last part of the previous reaction coordinate diagram. I'm going to write in both the forward and the reverse activation energies. I've labeled them E<sub>af</sub>, E<sub>ar</sub>, E<sub>bf</sub>, E<sub>br</sub>, to mean the forward and reverse activation energies for making A and B. What can we say from this? Notice that, since the transition states are above either the reactants or products, it makes the activation energies for the reverse reactions both higher than the activation energies of the forward reactions. What that means is that at a low enough temperature, you could effectively make the reaction non-reversible. If you make it a low enough temperature, where there's enough heat to make it over the forward barriers but not really enough to make it over the reverse barriers, then you break equilibrium. On top of that, you make it so that only the reaction that is favorable in the forward direction, only the one that doesn't cost as much energy is the one that's likely to happen. At low enough temperature, the reaction can effectively become irreversible, since both reverse activation energies are larger than forward. In this situation, the reaction with the lowest activation barrier is going to be the one that occurs, even if it produces the thermodynamically less-favorable product. Since it's kinetics that have the effect on which product forms, we call this kinetic control.

If we have kinetic control, then yes, there is thermodynamic control, which is what happens as you raise the temperature. As you raise the temperature, all of the reaction rates go up; both the forward and reverse reaction rates go up. Now the reverse reaction's possible. Even if you formed A, the less-favored product, there's a chance it would reverse and have another chance to make B. B, since it's lowest energy of all of the intermediates, products, or reactants, would be the least likely of all to reverse, so once you form it, it would tend to stick around. Since that's the thermodynamically-favored product, that's called thermodynamic control. At high temperature, all reaction rates increase. Along with it, that means the reaction is reversible. Although the kinetic product may still initially form, it has a chance to reverse and potentially form B. Since B is the lowest-energy product, it is less likely to reverse, and will therefore accumulate over time. Because it's temperature, it's heat that's controlling this, that's why this is thermodynamic control. This is the heart of the story, then.

[lab directions] You have two starting materials: cyclohexanone and 2-furaldehyde. The both react with semicarbazide. It's got a nitrogen that ends up reacting just like an amine, just like hydrazine would, to make a carbon-nitrogen double bond derivative. If I'm calling these derivatives, I'm going to use prime notation here. Here's what's going on in this experiment: you'll have a situation at some point where you're trying to form both of those semicarbazones at the same time. Where semicarbazones come up in lab discussion is around melting points, because there was a time where one of the main ways to characterize a product was just by getting its melting point. But, there may be multiple products that might have very similar melting points. But, different functional groups can make different derivatives. Carbonyl compounds, we've already seen, can make oximes, hydrazones, now these semicarbazones – which are kinda like [hydrazones], a carbonyl and an amino group attached. What's the advantage of making these derivatives? Even if a series of compounds might all have the same melting point, their derivatives might not, so if you could match a compound's melting point up and figure out the melting point of the derivative if matching, then you could more easily identify a compound.

A little bit of fundamental organic chemistry: notice which of the nitrogens it is that gets incorporated into the semicarbazone. Why is it that it is the end nitrogen that reacts, and not either of the nitrogens that's next to the carbonyl? Resonance. Those lone pairs on the nitrogens right next to the carbonyl delocalize with the carbonyl – enough so that they're much, much less reactive; those nitrogens are much less basic than a regular nitrogen. That's why it's the end nitrogen that reacts.

Back to what we're going. We're going to put both of these carbonyl sources into a solution of the semicarbazide, and you're going to see which product forms. It turns out, which one forms more depends on temperature. Here's the sequence of events: you make the derivative with just the cyclohexanone, you make the cyclohexanone semicarbazide, and get its melting point, cause we're going to use melting points to determine what's going on. [lab directions] You do the same thing with B, the furaldehyde, and get its individual semicarbazone. Then, you put all of them together, the cyclohexanone and furaldehyde with the semicarbazide, and you do that combination at three different temperatures – below room temperature, about room temperature, and above room temperature. Below room temperature, where there's not that much energy, it's going to be the kinetic product that forms; at higher temperature, it's going to be the thermodynamic product that forms. If, just for the sake of argument, if B was the thermodynamic product – maybe you could argue that because we have conjugation between the carbon-nitrogen bond and the ring, maybe that's favorable – then when we do the reaction at low temperature, A' is going to be what forms. Separately, we made A' by itself, so we compare the reaction mixture and compare its melting point to the pure derivatives you made. In this example, if B was the thermodynamic product, at low temperature, your mixture would be mostly A, and should more closely match the melting point of the derivative of A.

As you raise the temperature, you're going to get the thermodynamic product instead, which means that the mixture you get will have more B' in it and its melting point should more closely match that of B'. From that information alone, you should be able to determine which is the kinetic, which is the thermodynamic.

To prove it, you're going to do the reverse reaction. You take, for example, B' and put it in a solution with A. Why does that do anything? If B was not the thermodynamic product, then it would have the chance to undergo reverse reaction more easily, which means we get back B plus the semicarbazide that could turn right back around and react with A to make A'. If B was the thermodynamic product, it shouldn't do anything. Let's do the same thing with the kinetic product, A. If you take A', it's semicarbazone, and mix it with B, the aldehyde, if A is the kinetic product, it will reverse, it will go back to making the ketone plus the semicarbazide, which turns right around, reacts with B to make B'. In other words, when you do it with the thermodynamic product, the melting point of what you get should match what you start with, cause nothing should have happened. If you do the same thing with [the kinetic product], that semicarbazone's melting point is going to change, cause it's going to reverse and make the other semicarbazone.

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reaction coordinate diagram – shows the change in energy of a rxn along the most-likely reaction pathway (2D simplification of a multi-dimensional graph)

- of transition state = # of individual steps
- Only those reagents involved in the rate-limiting step (RLS) are found in the rate law.
- There is no relationship between the overall stoichiometric equation, the rate law, and # of steps.

Arrhenius expression

Energy distribution diagrams

Idealized rxn:  $A \rightleftharpoons B$

- Assume both forward & reverse rxns are single-step unimolecular reactions

- Assume  $k_f = k_r$

@Equilibrium  $R_f = R_r$

$R_f = k_f[A]$ ;  $R_r = k_r[B]$

$k_f[A] = k_r[B]$

- Since  $E_{af} < E_{ar}$ ,  $k_f > k_r \rightarrow [A] < [B]$

- Although rates are equal at equilibrium, rate constants do not have to be, which will affect the [reactants] vs [products]

The intermediate is a delocalized carbocation; there are not two distinct carbocations. Any difference of energy that may result occurs once bond formation w/ bromide starts.

$E_{br} > E_{ar} > E_{bf} > E_{af}$

- At low enough temp, a rxn can become effectively irreversible, since both the reverse  $E_a$  are larger than the forward. In this situation, the forward rxn with the lowest  $E_a$  will occur, even if it causes a less thermodynamically favorable product to form  $\rightarrow$  kinetic control.

- At high T, all rxn rates increase (and the rxn is reversible). Although the kinetic product may still initially form, it has the chance to reverse and potentially form B. Since B is the lowest energy product, it is less likely to reverse and will therefore accumulate over time  $\rightarrow$  thermodynamic control.

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Structures – Identical to those from lab 9B (02/21/12)