Lab 9B • 02/21/12

Kinetic versus thermodynamic control

What we're going to talk about is a situation in which the stability of the product is not directly related to the stability of the transition state to get to that product. Many reactions have a reaction coordinate diagram as follows: if you have one set of starting materials [for which] two different reactions could possibly occur, those two different reactions might have two different mechanisms, and they could end up forming products with two different energies. This is the normal situation where the product that's higher in energy also has the larger activation barrier. What we're going to talk about today is this situation: where there's a reversal between product stability and the energy of the transition state, the activation energy necessary to get there. What's going to be a result of this is that the product that forms is going to be the result of temperature: higher temperature is going to favor what is known as the thermodynamic product, the one that is the lowest energy but takes the most energy to get to; at low temperatures, we're going to find that we favor the formation of the kinetic product, the one that is thermodynamically not as favorable, but the one that's the easier reaction.

Let's review what one of these reaction coordinate diagrams is. Can someone describe to me what is a reaction coordinate diagram? It's a pathway from reactants to products, and it's the most likely pathway, the energetically most favorable pathway. What we could, in theory, do is plot out the position of all the different atoms in the system and figure out what the energy is relative to the position of each one of those atoms, but that creates a graph that is multidimensional, hard to interpret, so we take a two-dimensional slice along the most likely pathway and we say what's going to be the energy change as we go along that pathway. That's what we call the reaction coordinate. The reaction coordinate is the energetically most likely pathway through a reaction; it's also a 2D simplification of a multi-dimensional space.

There's several key features that we generally identify on one of these reaction coordinate diagrams. To simplify our discussion, I'm going to keep this in the land of enthalpy; you might recall there's a difference between enthalpy – which is the raw difference in energy between the reactants and products – and then delta G, which is free energy, which is the amount of potential energy really available to a reaction once you take entropy into account. On a graph like this, let's label all of the things that would normally be important. We have the reactants, products, and then I for intermediate. [neutron] We have two transition states, which are the highest-energy points between a reactant and either the product or the intermediate that's formed. In a multistep reaction, each time you go through a step, there's the toughest point in that step – that's the transition state. [The] Hammond postulate says the structure of the transition state tends to match more closely what the transition matches in energy. There are a couple more things on this graph I would want to mark. There are two different activations energies. Then, there is the overall heat of reaction.

Why do I care about activation energy? How many steps are there in this reaction? Two. How did you know that? The number of activation energies is equal to the number of step, because if the activation energy is the highest point in a step, and you see two activation energies, that means you had two steps. Number of transition states equals the number of individual steps. Can you tell how many reactants are participating in this reaction? Is there any correlation between the number of steps and the number of reagents? No. Normally when we write chemical equations, chemical reactions, they express an entire reaction, which would mean from the start to finish of this process. Is there going to be any relationship, then, between the number of reagents in that overall expression and the number of reagents in any one particular step? If you recall the rate law, the rate law is composed of a constant plus a certain number of concentration terms. Only those concentrations of those reagents that participate in one particular step of the reaction are found in that equation. There's no relationship between the overall equation of a reaction versus a rate late, versus the number of reagents, there's no correspondance between any of those things. To simplify, we could say that only those reagents in the rate-limiting step are found in the rate law. How do we know which reagents are in the rate-limiting step? The step that has the highest activation barrier; that's why we care about activation energy, because, everything else being equal, that's what's going to control the rate of reaction. Only those reagents in the rate-limiting step (RLS) are found in the rate law. Another way of saying it is that there's no relationship between the number of reagents in the overall stoichiometric equation and the rate law itself.

The Arrhenius expression. What are these variables that are in the expression? T – temperature. R – which is not a variable; it's a constant. What are the other variables? Ea – activation energy. Then what's A? There's a couple of different ways of expressing what it is. It's sometimes called the Arrhenius factor, sometimes called the steric factor, sometimes labeled as the percentage of successful collisions – in other words, you might know what the total number of collisions could be based on temperature and activation energy; how many of those are successful are rolled up in that A. A is kinda a fudge factor to make the rest of the equation work out. Why do temperature and activation energy matter? Because at any one temperature, there's not just one speed or one energy that molecules are travelling; there's a distribution. There's two graphs that matter in this case: one where you show one activation energy, versus what happens if we have two different temperatures; the other one is where we're sticking with one temperature, but we're looking at the difference between two different activation energies. In both cases, the x axes are number of molecules, whereas the x-axis is the energy per molecule.

These graphs come from the fact that even if you had a room full of molecules that somehow were all magically travelling exactly the same speed, as soon as you blink, they all start bouncing into each other, which means some get knocked around, some move more quickly, some move more slowly.

Let's tackle the second graph first, because that's with temperature. As you increase temperature, more molecules bouncing around, more possible energy states, that's why the graph shifts to the right and gets flattened, because the total number of molecules stays the same. What it shows is that at higher temperature, we have a higher fraction of molecules that are over some kind of energy barrier; in this case, this is activation energy, which means the ability to react. More molecules have that energy necessary to react. In the other case here, we go with a higher activation energy, you can see that, at the same temperature, fewer molecules have that energy so fewer reactions, successful ones, can occur.

Now let's go to a reversible reaction, one last preliminary energy diagram.

For this, we're going to imagine some kind of perfect reaction, where in both the forward and reverse reactions, there's only one molecule involved, there's only one reaction step, and the steric factor, that Arrhenius factor, is equivalent in both directions. It's a very contrived example, but let's us get at something very important. Some idealized reaction A reversibly forming back and forth into B. Both the forward and reverse reactions are one-step, first-order, with the same steric factor. We could label the activation energy of the forward reaction and the activation energy of the reverse. The reason that I came up with these contrived conditions is I'm going to exploit one one of the definitions of equilibrium. We're talking about reversible processes whenever we're talking about kinetic versus thermodynamic control – or at least we're talking about the potential to have reversibility. We're talking about reversibility, we're talking about a situation where you should have some form of equilibrium. What are our definitions of equilibrium? There's no observable change in the concentrations of products and reactants; you're at the lowest energy; and, the one that matters here, the rate of the forward and reverse processes are equal. In this case, the rate of the forward reaction is equal to the rate constant of the forward reaction times the concentration of A, because I said it was a a one-step reaction; the rate of the reverse reaction is equal to some reverse rate constant times the concentration of B. If, at equilibrium, these two expressions are supposed to be equal to each other, then we get something like this.

The reason I point this out is because the rates may be equal, but there's no way the rate constants can be equal. Why? Because the activation energies are different. This is why we're going to have a distribution of A versus B. The forward rate constant is going to be big because the activation barrier is small; the reverse rate constant is going to be small, because the activation barrier is big. For that equation to hold true, if you have a large forward rate constant, that means the amount of A at equilibrium has to be small in order to get this proportionality to be equal, so that you have a small reverse constant, which means you're going to mean you have to have a large concentration of B. So, rates are equal, but rate constants are not. In this ideal situation, the fact that you have two different rates is why you have a difference between the concentration of products and reactants at equilibrium. The main things to pull from this diagram are that, at equilibrium, rates are equal, but rate constants are not; that will influence the concentration of reactants versus the concentration of the products. In this specific example, since the activation energy of the forward reaction is less than the activation energy of the reverse reaction, that means the forward rate constant is larger than the reverse rate constant, which is why we end up with the concentration of A being lower than the concentration of B.

Let's finally get to both a real-life example and a discussion of kinetic versus thermodynamic control. We have this reaction that's possible. 1,3-Butadiene, a conjugated system, when it reacts with HBr, there are two products that develop. One that might make very much sense – alkene reacting with H+, carbocation forming, and then bromide coming back to attack afterwards. Not in term of nomenclature, in terms of relative position, if you look where the hydrogen ended up, if we call that position one, then the position of bromine relative to it would be two. This is known as 1,2-addition. That's not the only product that results; the other product that results is for the bromine to be located at the complete opposite end of where the hydrogen ends up, which we could explain like this: after H+ is attacked, we end up with carbocation that can experience resonance. That puts the carbocation at that end of the molecule, which now bromide can attack. Because of the relative of hydrogen and bromine, we call this 1,4-addition. Let's draw a reaction coordinate diagram for this process. There's two steps: the original diene attacking an H+, and then there's the carbocation that's formed reacting with bromide to form the product.

For this specific example, here's a pivotal question to be asked: which of those two carbocations is more stable? How many different carbocations are there? One. Because if you have resonance, isn't it the same carbocation, just writing it two different ways? It's a totally misleading question. If I ask you which one of these two is energetically more favorable, the answer is neither; they're both the same energy, and neither one of these structures is correct. So, what do we do? There has to be some difference here. There is, once the bond actually starts forming. Once you start allowing that bromide to attack, it causes the charge to become localized, so then it becomes more like a terminal carbocation, versus the internal one, the one that looks like a secondary carbocation. That doesn't happen until the bond forms; otherwise, in between, it's the same energy. That matters a huge amount because whether one product or the other forms, it goes through the same energy state, through the same intermediate, which means there's a direct competition for which product occurs.

Here's what the reaction coordinate diagram looks like. Here's our reactant, here's our intermediate, which is the carbocation in resonance, and then we have our products. Which product is going to be lower than the other? One is going to be lower now. Is the 1,2- or 1,4-addition going to be lower in energy. 1,4-, that's because you have a more substituted double bond, so when comparing isomers, internal double bonds are thermodynamically more favorable than terminal double bonds. The 1,4-addition product is here. The intermediate is a delocalized carbocation; there are not two separate carbocations. Any energy difference that occurs happens as the bond with bromide starts to form. Two contrasting pathways that start out the same way. We have one reaction step that gets us to that delocalized carbocation. This will be one of the few times times I write a structure this way: notice the dotted line I put across three of the carbons; that's to show that you've got that delocalization across those three carbons. You will see that as a notation sometimes; I normally don't recommend it, because in that dotted line there's no indication of exactly how many electrons that you have. By experience, you would see the positive charge there, see that three atoms are involved and the only way you could get a positive charge with three carbons that already have single bonds is if there's one pair of pi electrons across that whole system. There's then a split in what happens. Whatever energy difference is going to occur happens as the bond forms. As that bond starts to form, you force a primary versus secondary carbocation. Which one is more favorable? The secondary one. But that happens to be the one that leads to the less favorable product. That's how we end up in this situation. Forcing a primary carbocation is less favorable, but once it happens, then we're going to end up with the more favorable product.

Now we're ready for the last piece of this. I'm going to focus just on this last step, going from the carbocation to the product. In this diagram, there are four activation barriers we could worry about. There's the activation barriers going in the forward direction, and then there's the activation barriers going in the reverse direction. These four constants I'm calling Eaf, Ear, Ebf, Ebr. Here's the point. In this case, since the product is lower in energy than the intermediate that we start with, the reverse activation barriers are both automatically larger than either of the forward reaction barriers. We have the largest reverse barrier being from the thermodynamic product, then the smaller reverse barrier from what we're going to call the kinetic product; that is bigger than the forward barrier for making the thermo, which is bigger than the forward barrier for making the kinetic. If those are the order of activation energies, the rate constants are the reverse. Let me make a summary here. At low enough temperature, a reaction can become effectively irreversible; we can already see that the reverse barriers are larger than the forward barriers. In this situation, whichever forward reaction occurs more quickly is going to determine the product that forms. Since the energy for forming B is greater than the energy for forming A, A will predominate, even though, thermodynamically, it is not the most favorable product. We call that kinetic control, cause only the thing that forms easily, kinetically, is the thing that's going to form.

What happens when we start raising temperature? All rates increase; all forward and reverse reaction rates increase. But, it's still true that, to get from what's called the thermodynamic product, the lower-energy product, that still has the largest barrier of them all. As you raise temperature, all of these rates speed up, but all the other rates speed up more than that largest barrier. Over time, what happens is if you form that kinetic product, if you form A, given enough temperature, it'll reverse backwards, it'll have another chance to react. Maybe because that forward kinetic barrier is lower, you'll still form A again, but every once in a while, you'll form B instead. B is the lowest energy of any of these things, so it's the slowest to reverse, so over time you'd form more and more B. At high temperature, because you now have reversibility, B will form, which is the most favorable product, which is why it's called the thermodynamic product. This is kinetic versus thermodynamic control. This example that we had of forming the two different bromides, this is exactly what happens. At low temperature, you form more of the terminal alkene; at high temperature, you form more of the internal one. This is the explanation why. At high temperature, all reaction rates increase, and the reaction can become reversible. This means that the kinetic product may form initially, but has a chance to reverse and potentially form B. Since B is the lowest-energy product, the rate of the reverse reaction is the lowest, so B will accumulate over time, which is called thermodynamic control.

[lab directions]

In this experiment, you're going to have a competing reaction. You're going to have two different starting materials: cyclohexanone, and 2-furaldehyde. You're reacting both of them with semicarbazide, and you're going to form two different molecules. A semicarbizone is another imine-style derivative, just like oxime and hydrazone. Semicarbizones, historically, were important because they were very well-behaved derivatives. If at some point we did characterization by melting point, and there's a whole bunch of compounds that might have the same melting point, if you could figure out their functional group, if you could determine that they're a ketone or aldehyde somehow, you could then react it with the semicarbazide to make a very crystalline derivative. That derivative is going to have a distinct melting point, compared to other derivatives. Let's say that you had five different compounds that all happened to have the same melting point, but you were able to make derivatives of them and they were each different derivatives. Then each of those different derivatives might have a different melting point, which therefore means that, by making the derivative, you could identify the original compound.

Why might you imagine that it's the end nitrogen, the nitrogen furthest from the carbonyl, that ends up being the nitrogen that participates in this reaction? Why was it not the nitrogen next to the carbonyl that reacted? It's a one-word answer. Resonance. Those lone pairs are in resonance with the carbonyl, which makes them less reactive.

You have the nitrogen with is further away which is not conjugated; that's why it's more reactive. We're talking about conjugation; I just want to point out another manifestation of its effects. These form imine-style derivatives; these are semicarbizones. [lab directions – making individual compounds and measuring melting points] You throw all three of these compounds together; you throw both of the starting materials, the carbonyl-containing starting materials, at the semicarbazide, because you want to see which one of these derivatives actually forms. You do it at low temperature, you do it at middle temperature, and you do it at high temperature. Let's make an argument that conjugation stabilizes the product. Maybe, let's guess, that B might be the thermodynamic product. If that were true, then at low temperature, we'd expect to find more of the derivative of A, cause at low temperature, we'd expect to find the kinetic product. When you do this reaction at low temperature, you take whatever forms and compare its melting point to the pure derivatives. If the melting point more closely matches A, that means more A formed; if it more closely matches B, it means more B formed. At low temperature, you expect it to look more like A, if A is the kinetic product, and at high temperature, you expect it to look more like B, if B is the thermodynamic product. To make sure you've got your guess correct, you take the product and you put it in the reaction condition that allows the reverse reaction to occur. If a reverse reaction occurs, that means you started with the kinetic product, which at high temperature reversed and went back to make the thermodynamic product. If nothing happens, you already have the thermodynamics product and it didn't want to go anywhere. That's how we're going to identify which one of these two processes is the kinetically favored process versus the thermodynamically favored process. [lab directions]

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reaction coordinate – energetically most-likely pathway through a rxn; a 2D simplication of a multi-dimensional graph

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

Arrhenius expression
molecular energy distribution diagrams

Idealized rxn: A <> B
– Both forward & reverse rxns are one-step, 1st order w/ same A (steric factor)
@Equilibrium Rf = Rr
Rf = kf[A]
Rr = kr[B]
kf[A] = kr[B]
• @ equilibrium, rates may be equal, but rate constants are not, which will influence [reactants] vs [products]
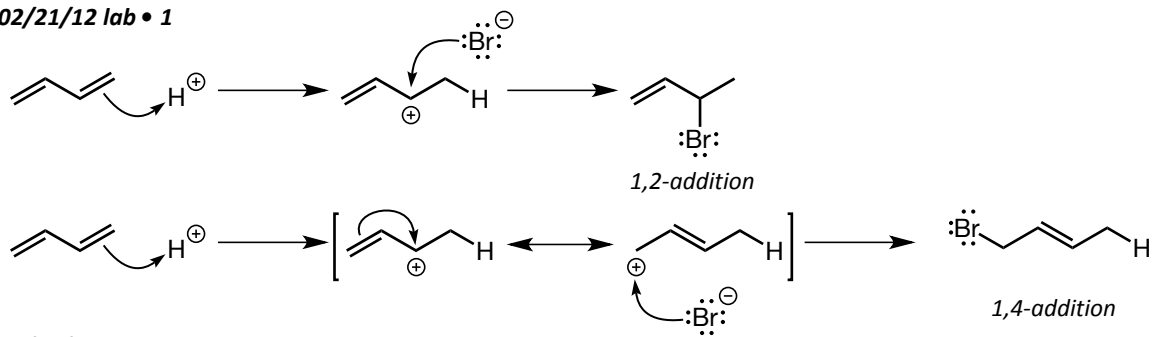• Since Eaf < Ear, kf > kr –> [A] < [B]

The intermediate is a delocalized carbocation; there are not two distinct carbocations. Any energy difference that occurs takes place once the bond w/ bromide starts to form.

Ebr > Ear > Ebf > Eaf
• At low enough temp, a rxn can become effectively irreversible (reverse barriers larger than the forward barriers). In this situation, the forward rxn with the lowest barrier is going to determine the product that forms. Since Ebf > Eaf, A will predominate, even though thermodynamically it is not the most favored product –> kinetic control.
• At high T, all rxn rates increase adn the rxn can become reversible. This means the kinetic product may form initially, but has a chance to reverse and potentially form B. Since B is the lowest energy product, the rate of its reverse rxn is the lowest, so B will accumulate over time –> thermodynamic control.

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Structures

02/21/12 lab • 1

1,2-addition

1,4-addition

02/21/12 lab • 2

semicarbazide