6. Chemical reactivity and mechanisms.

6.1 Thermodynamics.

You should already be familiar with the following equation that describes the energy and entropy changes in a chemical reaction:

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

where ΔG represents the *free energy* of the reaction, ΔH represents the *enthalpy* of the reaction, T is the temperature (in K) at which the reaction is occurring, and ΔS represents the *entropy* of the reaction. In organic chemistry, the enthalpy of a reaction is largely determined by the change in the energy (or strength) of the bonds during a reaction. For example, in the following reaction:

$$(CH_3)_3C\text{–}H + Cl\text{–}Cl \rightarrow (CH_3)_3C\text{–}H + H\text{–}Cl$$

C–H and Cl–Cl bonds broke, and C–Cl and H–Cl bonds formed. The enthalpy of the reaction equals the energy of the bonds that formed minus the energy of the bonds that broke. There are tables of bond energies that you can use to make these calculations. One is on p. 238 of Klein 3rd ed.

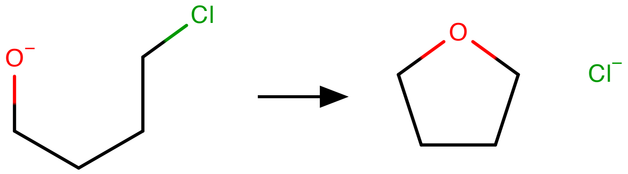
In the previous example, only the bonds that broke and formed changed, but sometimes, the strength of bonds that do not form or break can change as well. For example , consider the reaction:

$$H_2C{=}CH_2 + H_2O \rightarrow CH_3CH_2OH$$

In this reaction, the four C–H bonds in the starting material do not break, but the C atoms go from sp^2 hybridization to sp^3 hybridization, so the energies of the C–H bonds change as well. If you were to do a calculation of the enthalpy of the reaction, you would have to take these changes into account as well as the more obvious changes involving bond-breaking and bond-forming. I won't ask you to make those calculations.

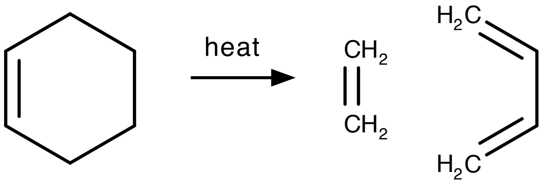
In organic chemistry, the *entropy* of a reaction is largely determined by the change in degrees of freedom that the atoms in a molecule experience in the course of a reaction. Typically, entropy will increase if one starting material becomes two products, or if a ring bond breaks, and entropy will decrease if two starting materials becomes one product, or if a ring bond forms.

$H_2C{=}CH_2 + H_2O \rightarrow CH_3CH_2OH$ entropy decreases



entropy decreases

$(CH_3)_3C{-}H + Cl{-}Cl \rightarrow (CH_3)_3C{-}H + H{-}Cl$ little change in entropy



entropy increases

In general, in most organic reactions, enthalpy dominates the equation for free energy, and we don't need to worry much about entropy.

When ΔH for a reaction is negative, the products' energy is lower than the starting materials'. We say such a reaction is *exothermic*. When ΔH for a reaction is positive, the products' energy is higher than the starting materials'. We say such a reaction is *endothermic*.

When ΔG for a reaction is negative, the reaction favors the products. We say such a reaction is *exergonic*, or *favorable*. When ΔG for a reaction is positive, the reaction favors the products. We say such a reaction is *endergonic*, or unfavorable.

Usually ΔH is much larger than the $T\Delta S$ term in the equation for ΔG, so we sometimes get a little lazy and use *exothermic* and *endothermic* as synonyms for *exergonic* and *endergonic*. Formally, though, the two terms refer to different properties.

Another pair of formulas you should be familiar with is:

$$\Delta G = -RT\ln K_{\mathrm{eq}}$$

$$K_{\mathrm{eq}} = \mathrm{e}^{-\Delta G / RT}$$

These formulas relate free energy to the equilibrium constant for a reaction. When ΔG is negative, the equilibrium constant for a reaction is greater than one, and the products are favored. When ΔG is positive, the equilibrium constant for a reaction is less than one, and the starting materials are favored.

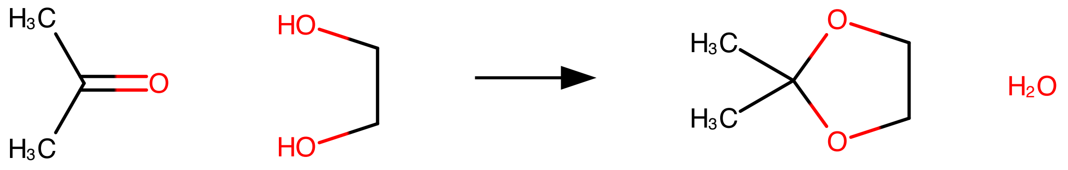
The equilibrium constant for a reaction is also given by:

$$K_{\mathrm{eq}} = [\text{products}] / [\text{starting materials}]$$

where [products] and [starting materials] indicate the concentrations of the products and starting materials when a reaction is at equilibrium, that is, when the rates of the forward and reverse reactions are the same. Now, consider a reaction that has two starting materials and two products.

$$K_{\mathrm{eq}} = [\text{product 1}]\,[\text{product 2}] / [\text{starting material 1}]\,[\text{starting material 2}]$$

Because K_{eq} is a constant for any particular reaction, increasing the concentration of starting material 1 will cause the concentration of product to increase, which can only happen by converting starting materials to products. Similarly, reducing the concentration of product 1 will force the concentration of product 2 to increase, which again can only happen by converting starting materials to products. This phenomenon, known as LeChatelier's principle, allows chemists to force an endergonic reaction to go to completion. For example, the following reaction is thermodynamically unfavorable ($\Delta G > 0$), but it can be forced to go to completion by removing H_2O from the reaction mixture. The lower the concentration of H_2O, the greater the concentration of the cyclic compound must become.



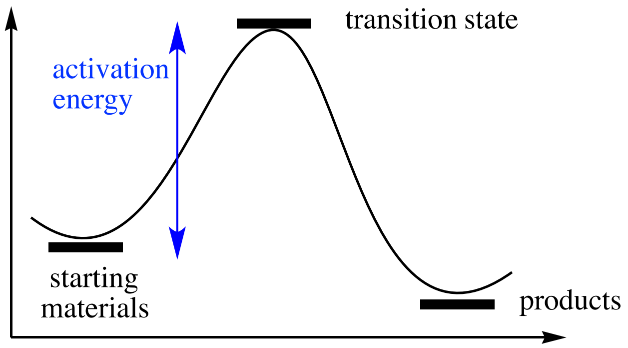
6.2 Kinetics.

So far, we have talked about the fact that reactions can be favorable or unfavorable. But a favorable reaction is not necessarily a fast one. For example, the familiar reaction of gasoline and O_2 to give CO_2 and H_2O is very favorable, but it does not occur at room temperature. (Imagine what it would be like to fill your car up with gasoline if it did.)

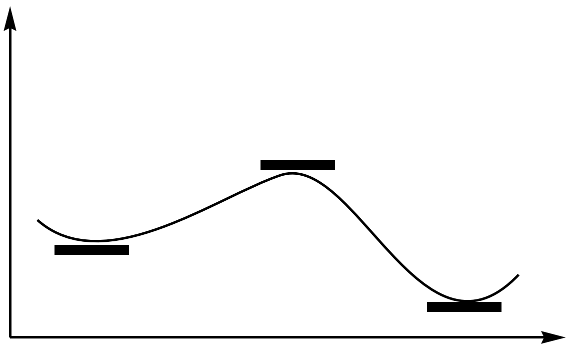
When compounds undergo a chemical change that makes or breaks bonds, they must go through a *transition state*, in which bonds that are made or broken in the reaction are partially made and partially broken. A transition state is always higher in energy than either the starting materials or the products of the chemical change. A transition state is very transient, existing only for one molecular vibration before it falls down the energy hill to products or back to starting materials. The energy required for the starting materials to reach the transition state is called the *activation energy*, often represented as $\Delta G^{\ddagger}$. The larger the activation energy, the more energy the starting materials require to reach the transition state, and the *slower* the reaction proceeds. Fast reactions have small activation energies, and slow reactions have large activation energies.

We draw *reaction coordinate diagrams* to illustrate the course of a chemical reaction. In a reaction coordinate diagram, the y axis represents free energy (ΔG), and the x axis represents the progress of the reaction — you can think of it as time, although that's an oversimplification. A one-step chemical reaction has starting materials, a transition state, and products. A curve connects the three states. The starting materials and products are minima, whereas the transition state is a maximum.

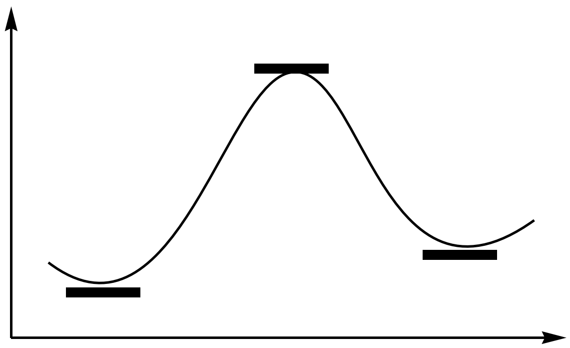
Reactions that are highly exergonic tend to have small activation energies, and reactions that are highly endergonic tend to have large activation energies, but this is not always the case. In fact, there are examples of exergonic reactions that have large activation energies (the gasoline + O_2 example I gave earlier), and there are examples of endergonic reactions that have small activation energies (for example, $HO^- + EtOH \rightarrow HOH + EtO^-$).



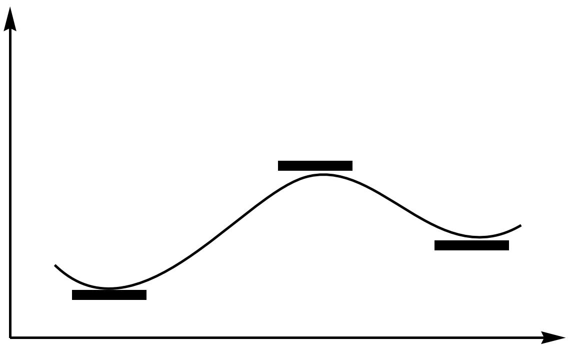
slow, exergonic



fast, exergonic

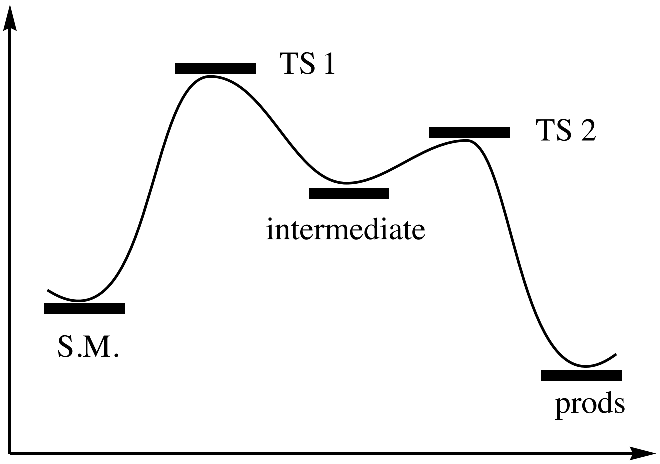


slow, endergonic



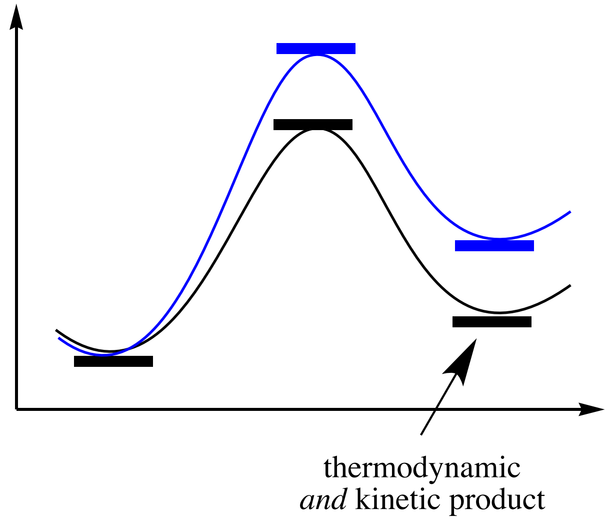
fast, endergonic

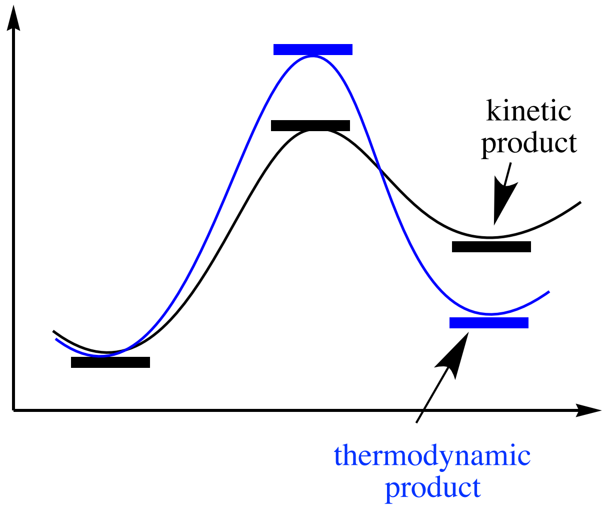
Most reactions take more than one step. Such reactions go through one or more *intermediates*, which are represented as minima in the reaction coordinate diagram (other than the starting materials and products). Such reactions contain two or more transition states. The step that goes through the highest energy transition state is called the *rate-limiting step*. The overall reaction can go no faster than the rate-limiting step in the reaction.



When we refer to the *thermodynamics* of a reaction, we refer to the difference in energy between products and starting materials. When we refer to the *kinetics* of a reaction, we refer to the difference in energy between the highest transition state and starting materials.

If a reaction can give two different products, we call the one that is lower in energy the *thermodynamic product*, and we call the one that is obtained more quickly the *kinetic product*. Often, the thermodynamic product is also the kinetic product (that is, the product that is obtained more quickly is also the one that is lower in energy), but there are many examples where this is not the case.





We will cover the remainder of the material in Klein's Chapter 6 as we talk about substitution and elimination reactions of alkyl halides and alcohols, which Klein covers in Chapters 7 and 8.