

EQUILIBRIA

8.1. Definitions.

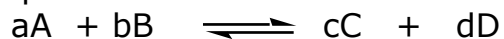
By convention, we write and read chemical equations left to right. Thus, starting materials are written to the left of reaction products.

Let's look for example at a *reaction coordinate diagram* for a S_N2 reaction (see, **Jones Figure 8.1**). A reaction coordinate diagram describes energy changes during the course of a reaction. Thus for a S_N2 reaction, we see that starting materials and products lie at energy minima and are separated an energy barrier, the maximum of which is called the *transition state*. If a transition state is too high in energy, it will not be accessible under normal conditions and no reaction will occur. If there are several accessible transition states of comparable energy then a mixture of products will be formed and specificity (formation of a single product) will not be possible in the reaction. Therefore, the study of how reactions occur depends on an analysis of the starting materials, the products, and the transition states separating them. To understand chemical reactivity, we need to know: (i) which are more stable, starting materials or products? And (ii) how high the transition state separating starting materials and products is.

In a S_N2 reaction, we see that two nucleophiles ($Nu:^-$ and $L:^-$) compete for an electrophilic carbon center. The reaction can potentially proceed in either direction and hence is an *equilibrium*. In fact, all chemical reactions can be regarded as equilibria. Multistep reactions are simply a series of equilibria in which species occupying energy minima are separated by transition states. For example, three equilibria are present in the S_N1 solvolysis reaction of *tert*-butyl iodide (see, **Jones Figure 8.2**). The first equilibrium is highly unfavorable due to formation of a cation-anion pair that is less stable than the covalent iodide. The second equilibrium depicts exothermic formation of the protonated alcohol (an oxonium ion) while the third equilibrium gives the product (*t*-butyl alcohol) via deprotonation of the oxonium ion.

8.2. Equilibrium

While all reactions can be viewed as equilibria, it is important to understand that *thermodynamics* (the free energy difference between starting materials and products) may dictate that one side of an equilibrium will be overwhelmingly favored over the other. Thus, whether a chemical reaction at equilibrium lies towards starting materials or products is determined by thermodynamics. For a general chemical reaction at equilibrium:



The concentration of starting materials and products are related to one another by the equilibrium constant, K , which is given by:

$$K = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

And the free energy difference between the starting materials and products at equilibrium is given by:

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

or

$$\Delta G^\circ = -2.3RT \log K$$

R = gas constant, 1.99×10^{-3} kcal/ $^\circ$ mol; T = temperature in Kelvins; ΔG° = Gibbs free energy change - the free energy difference between starting materials and products in their standard states.

When $K > 1$, ΔG° is negative hence the products are favored (the total free energy of the products is less than the total free energy of the starting materials). The reaction is said to be *exergonic*.

When $K < 1$, ΔG° is positive hence the starting materials are favored. The reaction is said to be *endergonic*.

In a multistep reaction, it usually does not matter if an early step involves an unfavorable equilibrium, as long as ΔG° for the overall reaction is negative and starting materials have sufficient energy to overcome all of the energy barriers

Indeed, only a small difference in energy between starting materials and products is needed to obtain a large excess of one over the other at equilibrium. We can rewrite the relationship between K and ΔG as:

$$K = e^{-\Delta G^\circ/RT}$$

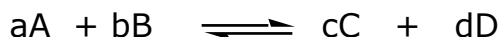
or

$$K = 10^{-\Delta G^\circ/2.3RT}$$

Using either expression, we find that a reaction at 25 $^\circ$ C that gives products that are more stable than starting materials by 1kcal/mol has an equilibrium constant (K) = 5.4, which translates into ~85% of product at equilibrium (see **Jones Table 8.1**).

So, is it only possible to obtain desired products that are favored at equilibrium? Of course not, what we have to do is run the reaction under conditions that shift the equilibrium and drive the reaction in the direction we want!

Remember Le Chatelier's principle states that a system at equilibrium responds to stress in such a way as to relieve that stress. Thus, for the general reaction



if the equilibrium lies towards starting materials, we can drive the reaction towards products by increasing the concentration (using an

excess) of one of the starting materials. Alternatively, we can remove one of the products from solution (by choosing conditions, such as solvent and/or temperature, that lead to precipitation of one of the products). Both of these approaches serve to drive the reaction towards product in order to maintain equilibrium!

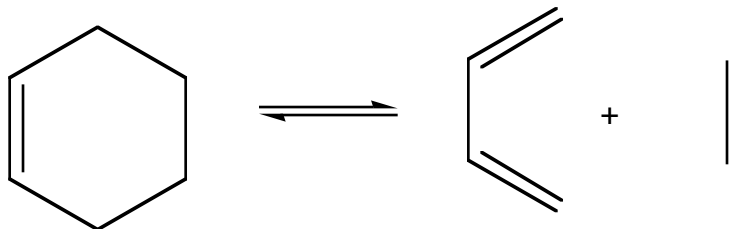
8.3. Gibbs Standard Free Energy

ΔG° is composed of enthalpy (ΔH°) and entropy (ΔS°) terms. Thus,

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

ΔH° refers to heat of reaction, which is a measure of the change in bond strengths in the reaction. ΔS° is a measure of the change in freedom of motion in the reaction. The more ordered the transition state, the more negative the entropy change and hence the less negative ΔG° .

A reaction is exothermic when the difference in enthalpy between products and starting materials is negative, and usually $K > 1$ and the reaction proceeds towards products. However, sometimes the enthalpy change (ΔH°) may not be in the same direction as the free energy change (ΔG°), which also involves entropy (ΔS°). Entropy becomes increasingly more important to determining the value of ΔG° for a reaction as the reaction temperature is increased because the entropy term is temperature-dependent. For example, formation of cyclohexene from 1,3-butadiene and ethylene is favored at low temperature ($\Delta G^\circ < 0$) because of the favorable ΔH° (due to formation of strong C-C σ bonds from weaker C-C π bonds) even though ΔS° is unfavorable.



However, the formation of 1,3-butadiene and ethylene from cyclohexene will become more favorable at high temperature as the $T\Delta S^\circ$ term dominates.

8.4. Rates of Chemical Reactions

Rates of reactions are determined solely by the energy difference between starting molecules and the transition states separating those molecules from products (See **Jones Figure 8.7**)

Application of energy in form of heat is often used to produce molecules with sufficient energy to transverse the barrier to reaction.

A reaction rate approximately doubles for every 10 °C increase in temperature.

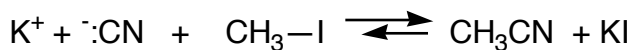
Rates of chemical reactions also depend on concentration of reactions: first-order reactions, such as S_N1 or E1 reactions, show a rate dependence on the concentration of a single reactant. Second-order reactions, such as S_N2 or E2 reactions, show a rate dependence on the concentration of two reactants. Pseudo-first order reactions are observed when the concentration of one of the molecules participating in the rate-determining step is in such a large excess that the concentration does not change appreciably during the reaction (See **Jones Figure 8.10**).

8.5. The Transition State and Activation Energy

The activation energy (ΔG^\ddagger) is the amount of energy that must be provided to transverse the transition state and initiate a reaction (See **Jones Figure 8.17**).

The final mixture of starting materials and products at equilibrium will however depend on the ΔG° (free energy difference) between starting materials and products

For the reaction between methyl iodide and potassium cyanide to form methyl cyanide and KI



We can see from **Jones Figure 8.17** that the reaction is highly exergonic, whereas the reverse reaction is highly endergonic. We can see that the transition state for the forward and reverse reactions is exactly the same, in accord with the *principle of microscopic reversibility* (which states that the lowest energy pathway for the forward reaction is the lowest energy pathway for the reverse reaction). Hence only the ease of reaching the transition state is different (in this case, $\Delta G^\ddagger_{\text{forward}} < \Delta G^\ddagger_{\text{reverse}}$). Thus for the reverse reaction, we must not only overcome a much higher activation energy but fight an unfavorable equilibrium since ΔG° is positive.

8.6 Reaction Mechanisms/Hammond Postulate

Reactions mechanisms are typically studied using a combination of kinetics and stereochemical experiments. Kinetic experiments can be used to determine the rate-determining step of a reaction – the step with the highest energy transition state. The rate law tells us only about the number and kinds of molecules that are involved in the transition state. We can learn about the orientation of the molecules in the transition state via stereochemical experiments (e.g. inversion of configuration in S_N2 reactions indicate the nucleophile approaches the electrophilic carbon from the rear of the departing group).

Since the transition state is an energy maximum, the transient species formed cannot be isolated but the energy of the transition

state is determined by enthalpy and entropy factors just as is the energy of any stable compound. Hence the energy of the transition state, and thus the energy barrier to reaction can be determined using:

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

(ΔG^\ddagger = Gibbs free energy of activation, ΔH^\ddagger = enthalpy of activation; ΔS^\ddagger = entropy of activation).

Since enthalpy and entropy factors determine the energy of the transition state, we can often relate the stability of a high-energy intermediate or transition state species with the rate of its formation. *The **Hammond postulate** states that the structure of the transition state resembles the structure of the nearest stable species. Transition states for endothermic reaction steps structurally resemble product, and transition states for exothermic steps structurally resemble starting materials.*

According to the Hammond postulate, any factor that stabilizes a high energy intermediate should also stabilize the transition state leading to that intermediate. We have already seen that the order of stability of simple carbocations is $\text{Me} < 1^\circ < 2^\circ < 3^\circ$ due to increasing hyperconjugative interactions with adjacent C–C and C–H bonds (the more highly substituted a carbocation, the more adjacent C–H and C–C bonds there are, the more electron density can be shared with the electron-deficient C atom, and the more stable the carbocation is). Thus, the rate of carbocation formation should increase in the order $\text{Me} < 1^\circ < 2^\circ < 3^\circ$, and since the rate-determining step of S_N1 reaction involves unimolecular dissociation of an alkyl halide to form a carbocationic intermediate, we would expect that *the more stable the carbocation intermediate, the faster the S_N1 reaction.*

Of course, we should be aware that not all reactions operate under thermodynamic control where the higher transition state leads to the less stable product, and that sometimes reactions occur under kinetic control (see **Jones figure 8.31**). However, thermodynamic control is the usual case.

Suggested Problems in your textbook – Chapter 8

8.12, 8.13, 8.20, 8.21, 8.22