CMB 311 Introductory Biochemistry
Lecture 14_notes
Friday October 13, 2017

In this class we reviewed the properties of carbonyl groups in biochemistry and learned the importance of Redox reactions in metabolic pathways.

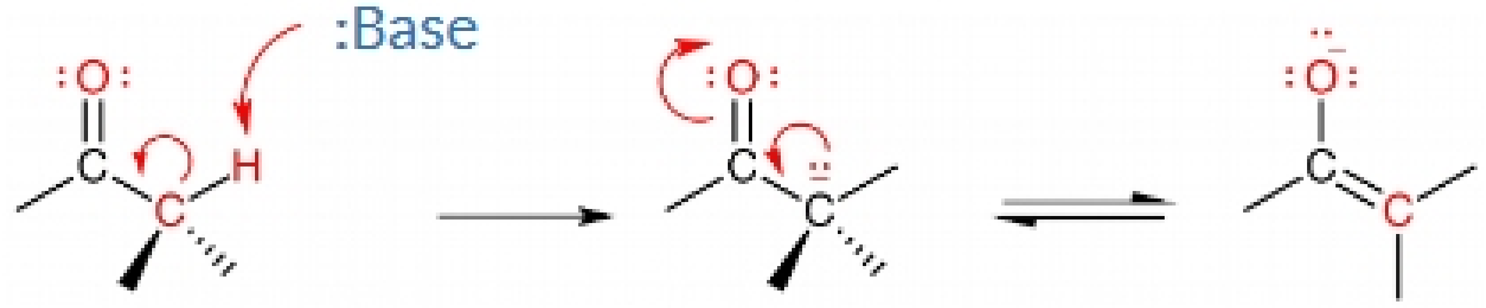
I. Carbonyls

- Carbonyls are found in almost all biomolecules.
- Carbonyls play a central role in metabolic reactions.
- Carbonyls are highly polar, and α atoms have greatly reduced pK_a.

Remember how other functional groups behave when they are next to carbonyls vs. how they behave on their own. For instance:

- Amino groups are neutral (NH_2) in amides while they are positively charged (NH_3^+) as amino groups attached to hydrocarbons as in the case of the lysine ε-amino group.
- Hydroxyls are deprotonated when adjacent to carbonyls in carboxylic acids but present as -OH at neutral pH when attached to methylene groups. Carboxylate ions are stabilized by resonance, with the negative charge being delocalized and shared between the two oxygens; this also means that a proton does not have a localized negative charge to bind to.

Carbonyl α-carbons are also acidic due to resonance stabilization of an enolate ion, such that the charge is shared between the electronegative carbonyl oxygen and the α-carbon.



We also mentioned other reactions involving carbonyls, including nucleophilic additions, formation of hemiacetals and hemiketals, the aldol reaction and the Claisen condensation. You may want to review these mechanisms, but we will also see them again in the context of metabolic reactions.

II. Redox Reactions

The most critical aspect of this lecture was our treatment of oxidation-reduction (Redox) reactions. These are very important in metabolic pathways, for example the oxidation of glucose to CO_2. Remember that catabolic reactions are oxidative, and such oxidations require that the electrons removed from catabolic intermediates be given to a terminal electron acceptor (O_2 in the case of aerobic respiration).

Some Definitions and concepts:

- Oxidation-the loss of electrons. The substance that loses electrons is called the reducing agent or reductant.
- Reduction-the gain of electrons. The substance that gains electrons is called the oxidizing agent or oxidant.
- Electrons are transferred from the reductant to the oxidant.
- The oxidant must have a greater affinity for electrons than the reductant does.

Critical concept: Redox reactions are coupled reactions. Remember that for every oxidation there must be a reduction. Redox reactions involve the *transfer* of electrons, not just their release into the ether. This is unlike couple reactions we've seen before, e.g. the transfer of a phosphate from ATP to glucose to make glucose 6-phosphate, where each half reaction can exist on its own.

Redox reactions in biochemistry are generally seen as the transfer of hydrogens and their associated electrons. So, the conversion of a carbonyl to a hydroxyl is a reduction, while the conversion of a hydroxyl to a carbonyl is an oxidation.

In biochemistry, electrons are transferred using enzyme cofactors as electron carriers. The principle cofactors are NAD (nicotinamide adenine dinucleotide) and FAD (flavin adenine dinucleotide). NAD^+ is reduced to NADH + H^+ in redox reactions such as oxidation of a hydroxyl to a carbonyl, while FAD is reduced to $FADH_2$ during oxidation of C-C single bonds to C=C double bonds.

We can define the tendency of a substance to accept electrons as the standard reduction potential, or E_0', measured in Volts (V). E_0' values are related to standard Gibbs free energy by the following relationship:

$$\Delta G^{\circ\prime} = -nF\Delta E_0'$$

Where

F is the Faraday constant (96.48 kJ/mol/V)
E_0' is the standard reduction potential in volts
$\Delta G^{\circ\prime}$ is the Gibbs free energy in kJ/mol
n is the number of electrons being transferred (usually 2 in biochemistry)

E_0' values can be found in a table of standard reduction potentials. These are half reactions, and are paired in redox reactions. Once again, reductions and oxidations do not take place in isolation. We therefore are looking for the *difference* in E_0' values ($\Delta E_0'$) between the reduction and oxidation.

For example, the reduction of pyruvate by NADH, catalyzed by lactate dehydrogenase:

pyruvate + NADH + $H^+ \leftrightarrow$ lactate + NAD^+ (A)

pyruvate + $2H^+ + 2\,e^- \rightarrow$ lactate $E_0' = -0.19$ V (B)

$NAD^+ + H^+ + 2\,e^- \rightarrow$ NADH $E_0' = -0.32$ V (C)

To determine the Gibbs free energy the 'American Way', determine the Gibbs free energy for each half reaction. We need to reverse the NAD half reaction and change the sign of the E_0' value.

pyruvate + $2H^+ + 2\,e^- \rightarrow$ lactate $E_0' = -0.19$ V (B)

NADH $\rightarrow NAD^+ + H^+ + 2\,e^-$ $E_0' = +0.32$ V (D)

Calculate the free energies for each half reaction:

(B) $\Delta G^{\circ\prime} = -2 \times (96.48\ \text{kJ/mol/V})(-0.19\text{V})$

$= +36.7$ kJ/mol

(D) $\Delta G^{\circ\prime} = -2 \times (96.48\ \text{kJ/mol/V})(+0.32\text{V})$

$= -61.8$ kJ/mol

$\Delta G^{\circ\prime} = \Delta G^{\circ\prime}$ (reaction B) + $\Delta G^{\circ\prime}$ (reaction D) = +36.7 kJ/mol + -61.8 kJ/mol = **-25.1 kJ/mol**

I'll have more examples and sample problems for you to practice.

To summarize, redox reactions are central to metabolism, and we'll be seeing how important they are as the course proceeds.