

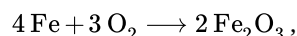
4.9: Reduction and oxidation (redox) reactions

Learning Objectives

- Define the redox process and calculate the oxidation number of an atom in an organic compound.
- Learn catalytic reduction of alkenes and carbonyl compounds.
- Learn reduction of carbonyl compounds by NaBH_4 or LiAlH_4 , and by NADH in living things.
- Learn oxidation of alcohols and aldehydes by oxidizing agents in laboratories and by NAD^+ in living things.
- Learn oxidation of thiol ($-\text{SH}$) to disulfide ($-\text{S}-\text{S}-$) and its reverse, in proteins.

What are oxidation and reduction?

Oxidation is i) the loss of electrons, ii) the gain of O, or iii) the loss of H. **Reduction** is the opposite, i.e., i) the gain of electrons, ii) the loss of O, or iii) the gain of H. The reduction and oxidation reactions are coupled, called **redox** reactions. Electrons' loss or gain is easily recognized in inorganic chemical reactions. For example, consider the following reaction:



Fe lost three electrons to become Fe^{3+} and O gained two electrons to become O^{2-} in this reaction.

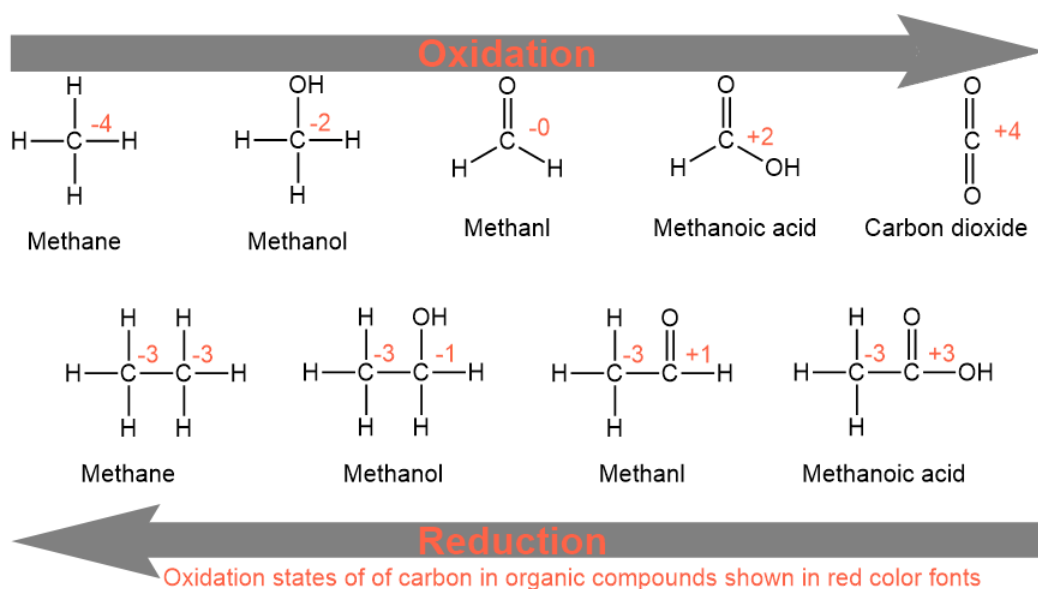
Oxidation number

Organic chemicals usually have covalent bonds where the loss or the gain of electrons from an atom is accounted for by **oxidation number**. An increase in the oxidation number is oxidation, and a decrease in the oxidation number is reduction. The following is a simple procedure for assigning an oxidation number to an atom in a neutral organic compound. Start with oxidation number zero for a free atom,

1. a bond with a more electronegative atom increases the oxidation number by one, e.g., a $\text{C}-\text{O}$ bond increases the oxidation number of C by +1;
2. a bond with a less electronegative atom decreases the oxidation number by one, e.g., a $\text{C}-\text{H}$ bond decreases the oxidation number of C by -1; and
3. a bond with the same atom does not change the oxidation number, e.g., a $\text{C}-\text{C}$ -bond does not change the oxidation number of C.

For example, in CH_4 four bonds of C with less electronegative H's decrease its oxidation number to -4. H's. In CH_3-OH three bonds of C with less electronegative H's decrease its oxidation number to -3 and one bond with more electronegative O increases to +1, with the overall oxidation number of the C = $-3 + 1 = -2$. So, conversion of methane (CH_4) to methanol (CH_3-OH) is oxidation.

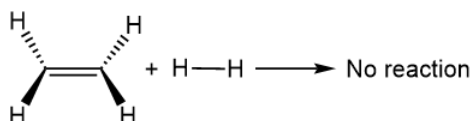
The following chart illustrates the oxidation states of C in organic compounds and their changes with organic transformations.



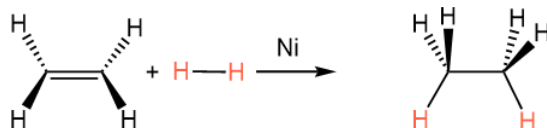
Examples of organic reduction reactions

Catalytic hydrogenation of alkenes

When an alkene and hydrogen are mixed, no reaction happens, as shown in the following example.



This is because alkene is an electrophile but $\text{H}-\text{H}$ is a nonpolar bond that is not a nucleophile. Finely divided nickel (Ni), platinum or palladium supported on carbon, i.e. Pd/C or Pt/C catalyze the reaction, as shown below.



Mechanism of catalytic hydrogen of alkenes

In step#1, the catalyst absorbs $\text{H}-\text{H}$ and $\text{RR}'\text{C}=\text{CR}''$ on the surface, as illustrated in Figure 4.9.1. In step#2, $\text{H}-\text{H}$ -bond breaks. H' 's and the π -bond of alkene become bonded with the catalyst surface. The surface-bonded species can migrate along the surface. In step#3, the π -bond attacks and makes a bond with H at the expense of breakage of H -catalyst bond. The second C of the π -bond stays bonded with the catalyst. In step#4, C-catalyst surface bonding electrons make a bond with the second H at the expense of breakage of H -catalyst and C-catalyst bonds. The alkane product of step#4 is no more attached to the catalyst and departs. The refreshed catalyst surface repeats the process.

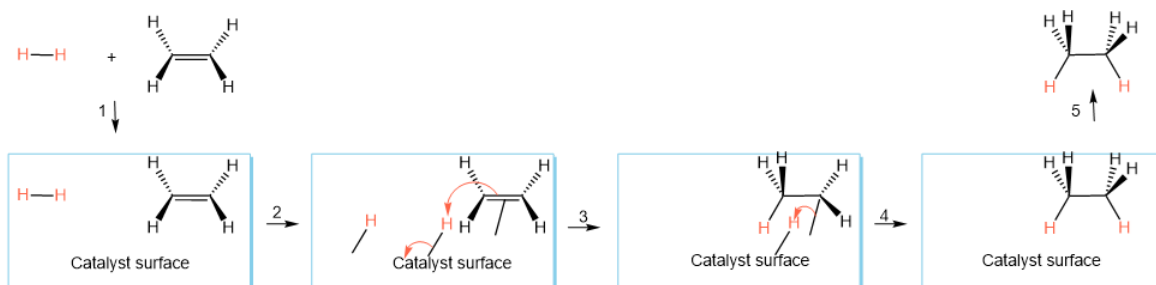


Figure 4.9.1: Mechanism of catalytic hydrogenation of alkene. (Copyright; Public domain)

Alkenes are planer around $\text{C}=\text{C}$ bond. Both H' 's add from the same face of alkene facing the catalyst surface.

Syn addition is the addition of two substituents from the same side (same face) of the π -bond. Addition of $\text{H}-\text{H}$ to $\text{C}=\text{C}$ of an alkene is an example of syn addition.

📌 Catalytic hydrogenation of vegetable oils

Vegetable oils are fats of tri-ester of glycerol with long chain fatty acids containing one or more $\text{C}=\text{C}$ bonds. The $\text{C}=\text{C}$ bonds create kinks in the long, preventing the chains' packing and resulting in lower melting points. Partial hydrogen of $\text{C}=\text{C}$ bonds in vegetable oil is carried out to convert it to semisolid margarine, as illustrated in Figure 4.9.2. Hydrogenation makes them straight-chain alkanes that pack nicely and increases their melting points.

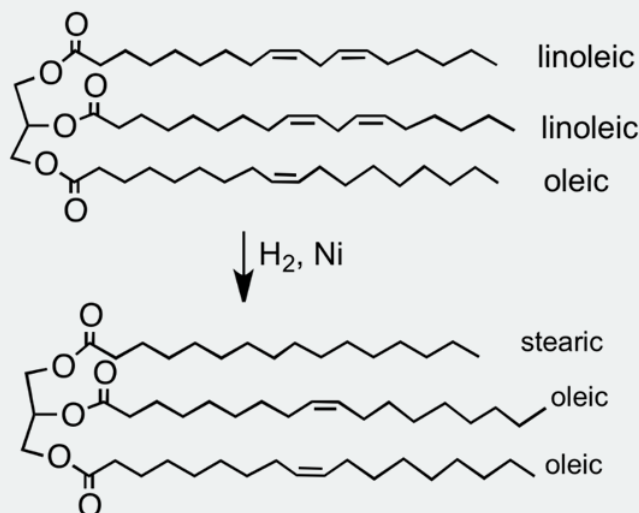
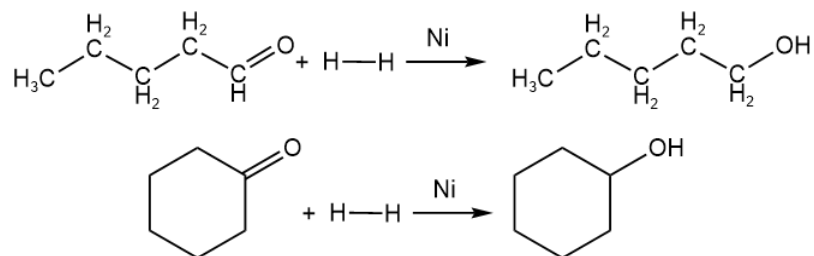


Figure 4.9.2: Illustration of partial hydrogenation of vegetable oil (rapeseed oil in this example) to convert it to semisolid margarine. (Copyright; Smokefoot, CC BY-SA 3.0, via Wikimedia Commons)

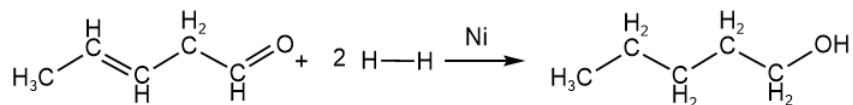
Reduction of aldehydes and ketones

Catalytic hydrogenation of aldehydes and ketones

Hydrogen (H_2) reduces aldehydes and ketones to alcohols in the presence of a catalyst like finely divided Ni , Pd/C , or Pt/C . as shown in the following examples.

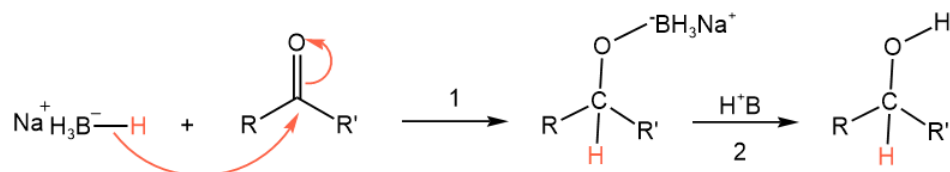


If $\text{C}=\text{C}$ -bond and a $\text{C}=\text{O}$ -bond are present in the same molecule, catalytic hydrogen reduces both, as shown below.



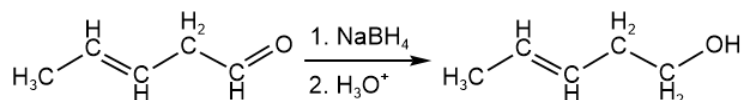
Reduction of aldehydes and ketones by nucleophilic addition reaction

The $\text{C}=\text{O}$ group can be selectively reduced to $\text{C}-\text{OH}$ group by nucleophilic addition of hydride (H^-) ion to the electrophilic C of $\text{C}=\text{O}$ group, by simplified mechanics shown below.



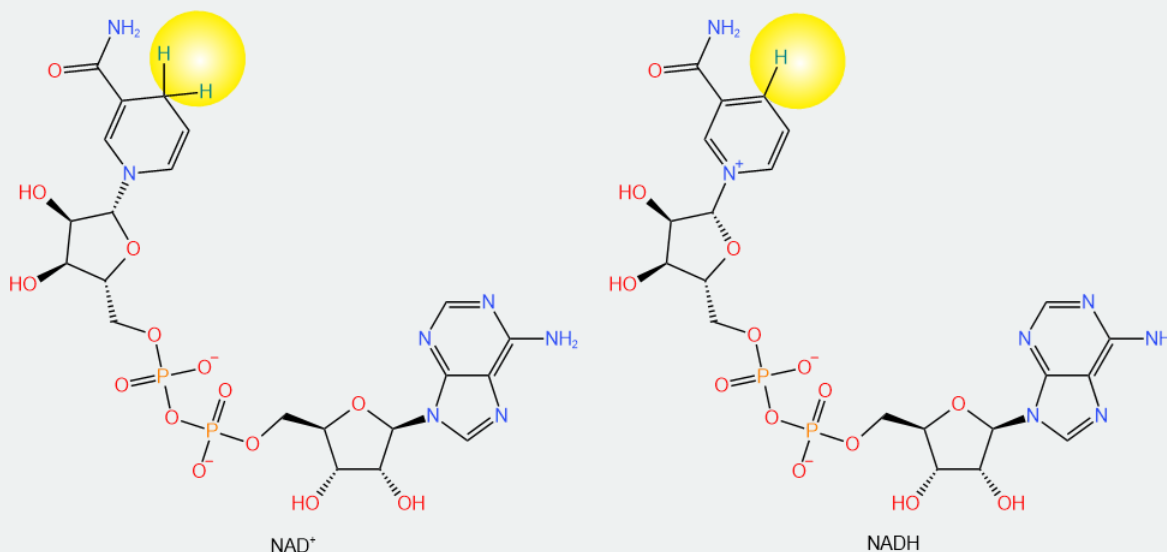
The H^- is not employed in free form, but it is donated by a reducing agent like sodium borohydride NaBH_4 or lithium aluminum hydride LiAlH_4 . Note that the H^- do not survive in an acid medium, so the H^- reacts in the first step, and then acid is added to donate a proton to O in the second step.

The nucleophilicity of H^- ion depends on the donor reagent. For aldehydes and ketones, NaBH_4 and LiAlH_4 work, but usually NaBH_4 is employed as it is tolerant to water. NaBH_4 reduces aldehydes, ketones, and acid halides but does not reduce other carboxylic acid derivatives and $\text{C}=\text{C}$, as shown in the example below.

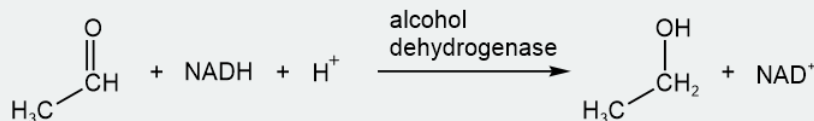


Reduction of aldehydes and ketones in biological systems

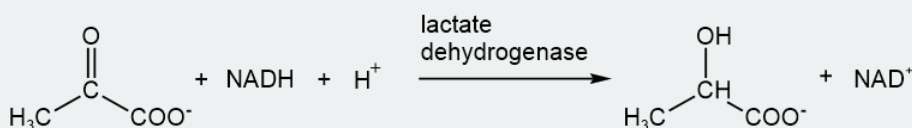
NaBH_4 and LiAlH_4 are used as H^- donors in laboratories. **Nicotinamide adenine dinucleotide** (NADH) coenzyme in its reduced form NADH is used as a hydride donor in biological systems. NADH is oxidised to NAD^+ after donating H^- , as illustrated below.



Enzyme-catalyzed conversion of acetaldehyde to ethanol during fermentation is an example of reduction using NADH.



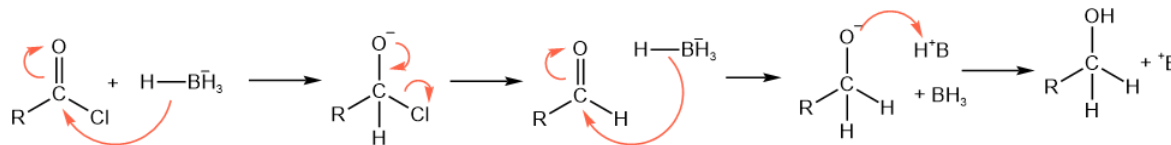
Conversion of pyruvate to lactate during glycolysis under anaerobic (absence of oxygen) conditions is another example of reduction using NADH, as shown below.



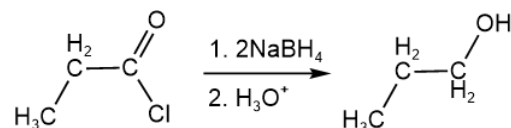
Cumulation of lactate after thought exercises causes muscle fatigue.

Reduction of carboxylic acid their derivatives

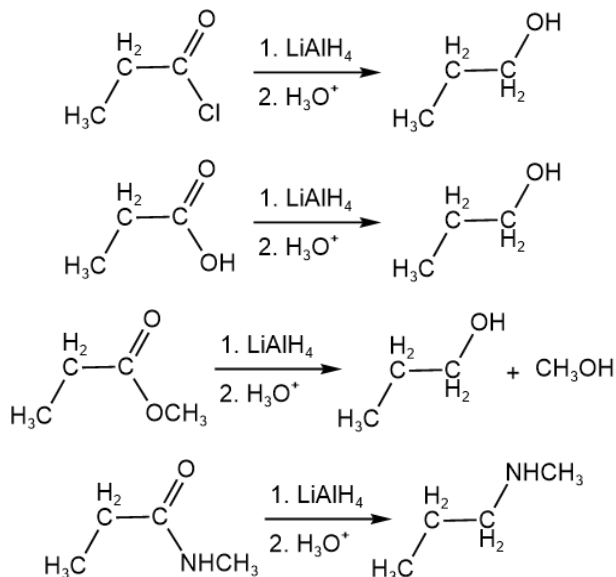
The NaBH_4 is less reactive and reduces only acid halids among carboxylic acids and their derivatives. LiAlH_4 is more reactive and reduces carboxylic acids and their derivatives. The mechanism is nucleophilic acyl substitution by H^- followed by nucleophilic addition, as shown below in the simplified form.



The reduction of propanoyl chloride by NaBH_4 is shown below.



NaBH_4 does not reduce the rest of the carboxylic acids and their derivatives. LiAlH_4 reduces carboxylic acids and their derivatives, as illustrated below with examples of reduction of acid halide, carboxylic acid, ester, and amide.



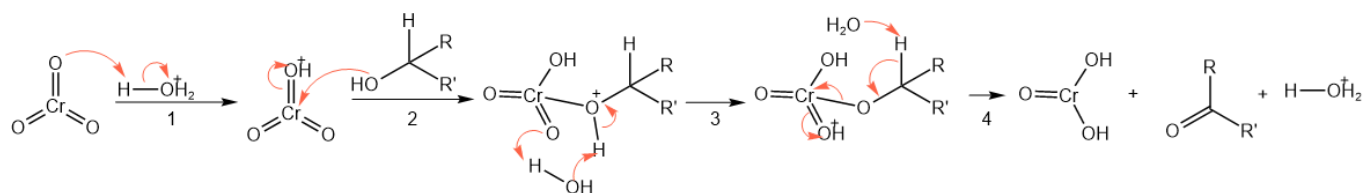
Reduction of disulfide ($\text{S}-\text{S}$) bond in biological systems

The $\text{S}-\text{S}$ bond commonly occurs in the protein tertiary structure. It is responsible for straight or curly hair shapes. The $\text{S}-\text{S}$ bond can be reduced to $-\text{SH}$ group by a variety of reducing agents, including NaBH_4 and Na metal. A thiol-disulfide exchange reaction often achieves this conversion in biological systems, as in the following example.

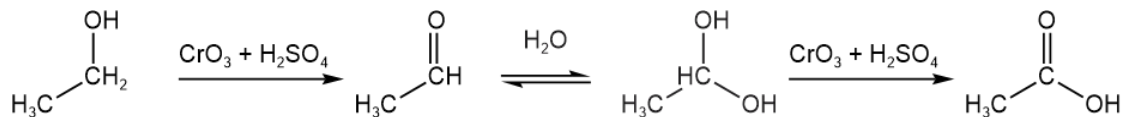


Oxidation of alcohols and aldehydes

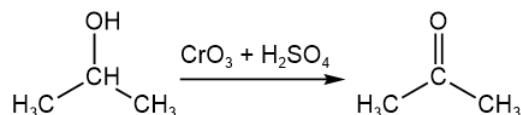
Primary and secondary alcohols are oxidized by several oxidizing agents, including Jones reagent (a mixture of chromium trioxide (CrO_3) and sulfuric acid (H_2SO_4)), chromic acid (H_2CrO_4), or potassium dichromate (KCr_2O_7) in sulfuric acid (H_2SO_4) acid. The mechanism with Jones reagent is shown below.



Primary alcohols are oxidized to aldehydes. Aldehydes convert to hydrates by adding water, and the hydrates are oxidized to carboxylic acids, as illustrated below.



Secondary alcohols are oxidized to a ketone, as shown in the following example. Ketone is not oxidized further as they do not have hydrogen on the carbonyl carbon needed to carry out step#4 of the mechanism.



Tertiary alcohols are not oxidized for the same reason, i.e., there is no hydrogen on the carbon to which alcohol is attached to carry out step#4.

Tests for aldehydes and reducing sugar based on easy oxidation of aldehydes

The fact that an aldehyde is oxidized further easily while ketone is not was used as a test to distinguish between aldehydes and ketones. In this test **Tollens' reagent** ($[\text{Ag}(\text{NH}_3)_2]\text{OH}$) is mixed with the test sample. Ketones do not react but aldehydes are oxidized by the following reaction:

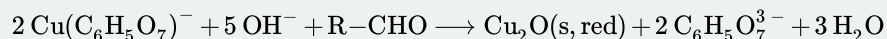


Ag produced in the above reaction deposits and forms silver mirror on the wall of the test tube as shown in Figure 4.9.3



Figure 4.9.3: Tollens' test for aldehydes: left side positive (silver mirror formed) and right side negative. (Copyright; FK1954, Public domain, via Wikimedia Commons)

Benedict's reagent is a mixture of sodium carbonate (Na_2CO_3), sodium citrate ($\text{Na}_2\text{C}_6\text{H}_5\text{O}_7$), and copper(II) sulfate pentahydrate ($\text{CuSO}_4 \cdot 5 \text{H}_2\text{O}$). Benedict's reagent produces red-precipitate (Cu_2O) as a positive test of aldehyde by the following reaction.



This test distinguishes aldehydes from ketones and is also positive for reducing sugars (carbohydrates) that contain an aldehyde group, as shown in Figure 4.9.4.

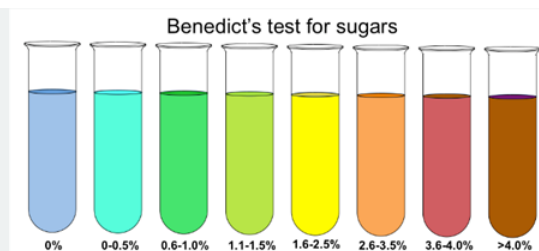
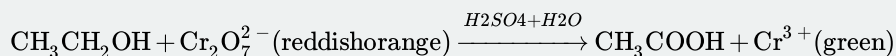


Figure 4.9.4: Benedict's test for aldehydes and reducing sugars that contain an aldehyde group. (Copyright; Thebiologyprimer, CC0, via Wikimedia Commons)

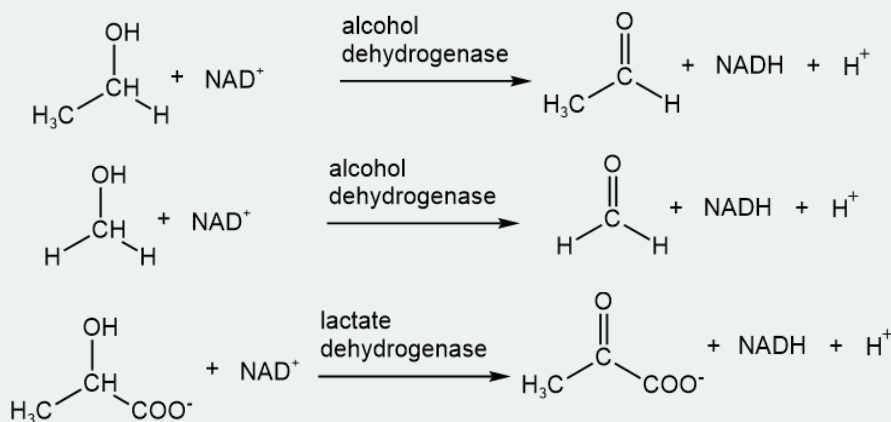
Alcohol exhaled in breath is oxidized by dichromate $\text{Cr}_2\text{O}_7^{2-}$ ions along with producing green color chromium(III) ions (Cr^{3+}) by the following reaction.



This reaction is used to test alcohol in drunk-and-drive cases by law enforcement.

📌 Oxidation of alcohols in living systems

Alcohols are oxidized by nicotinamide adenine dinucleotide (NAD^+) to aldehydes and ketones in the cells. For example, ethanol, methanol, and lactate are oxidized to ethanal, methanal, and pyruvate, respectively, as shown below.



Unpleasant effects of drinking alcohol, i.e., flushing, nausea, dizziness, sweating, headache, and low blood pressure, are caused by ethanol (acetaldehyde). Antabuse drugs prohibit aldehyde dehydrogenase from converting acetaldehyde to acetic acid, causing the unpleasant effects of acetaldehyde to persist. Methanal produced by the oxidation of methanol is a poisonous substance that damages many tissues and causes blindness. It is used to poison ethanol meant to be used as a solvent. In methanol poison medical cases, ethanol is injected intravenously into the patient to compete with methanol for alcohol dehydrogenase enzyme. This way, methanol is excreted before converting to poisonous methanal in the body.

📌 Oxidation of thiol ($-\text{SH}$) to disulfide ($-\text{S}-\text{S}-$) linkage

Thiol ($-\text{SH}$) is present in aminoacid cysteine. Two cysteine units in the same or different protein chains can oxidize their thiol groups to form disulfide ($-\text{S}-\text{S}-$) linkage. The disulfide linkage plays an important part in defining the tertiary structure of proteins. This oxidation reaction can be carried out easily by a variety of oxidizing agents, including iodine (I_2), bromine (I_2), and oxygen (O_2), as shown in an example below.

