# Chapter 11
# Catabolism of Hexoses

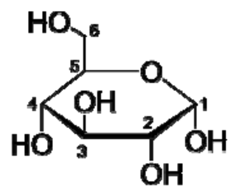
Glucose is the focal point of carbohydrate breakdown.

**Glycolysis**: A pathway made up of 10 steps in which **glucose** ($C_6H_{12}O_6$) is transformed into 2 molecules of **pyruvate** ($C_3H_3O_3$).

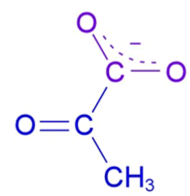
It is an ancient **anaerobic** process: *i.e.* does **not** require $O_2$.

The pathway, enzymes and reactions are nearly identical in all eukaryotic cells!

Most of the differences are in **regulation** of the pathway.




Glucose
$C_6H_{12}O_6$




pyruvate
$C_3H_3O_3$

**Phase I - Preparatory:**

5 steps - Glucose is phosphorylated and split into 2 triose phosphates.

This phase costs 2 ATP.

**Phase II – Payoff:**

5 steps - oxidation and phosphorylation yield 2 NADH + 4 ATP

Net yield of ATP = 2.

Net yield of NADH = 2

**Mass Balance**

$C_6H_{12}O_6$ + 2ATP + 2NAD$^+$ + 4ADP + 2P$_i$ → 2$C_3H_3O_3$ + 2ADP + 2NADH + 2H$^+$ + 4ATP + 2$H_2O$

After Cancellation:

$C_6H_{12}O_6$ + 2NAD$^+$ + 2ADP + 2P$_i$ → 2$C_3H_3O_3$ + 2NADH + 2H$^+$ + 2ATP + 2$H_2O$

**Energy Balance**

The pathway is ***exergonic*** under **standard conditions** (25°C, 1atm, 1M); 146 kJ/mol are released ($\Delta G'^{o}$ = -146 kJ/mol).

*(Complete oxidation of glucose yields 2840 kJ/mol so only 146/2840 = 5.2% of the G of glucose is released during glycolysis.)*

42% of the 146 kJ/mol is used to make 2 ATP:

2ADP + 2$P_i$ → 2ATP *endergonic*, $\Delta G'^{o}$ = +30.5 kJ/mol

$\Delta G'^{o}$ = 2(30.5) = 61 kJ for 2 moles

(61/146)*100% = 42 %

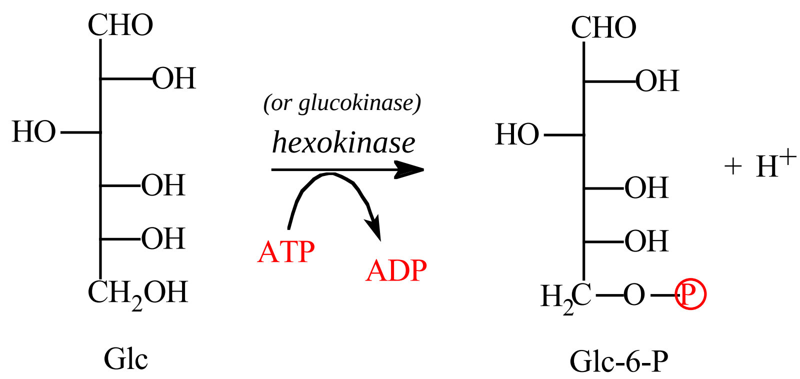
58% of the free energy is "lost" – but ensures the process is overall spontaneous owing to a large negative $\Delta G'^{o}$.

In glycolysis, each individual reaction is helped by a specific enzyme, see Table 11.2

A **kinase** transfers the terminal phosphate of ATP to an acceptor.

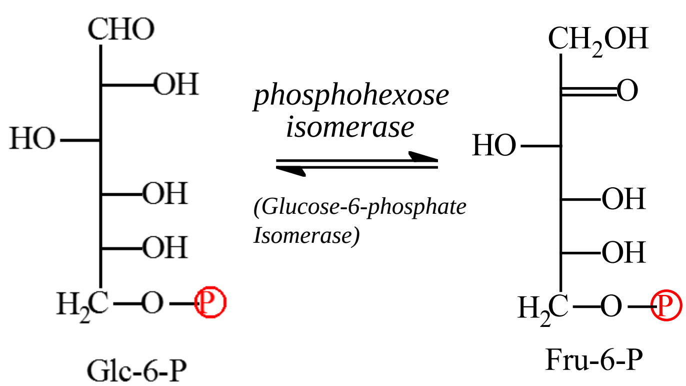
**Notes on Individual Reactions (also see Figure 11.2)**:

1.



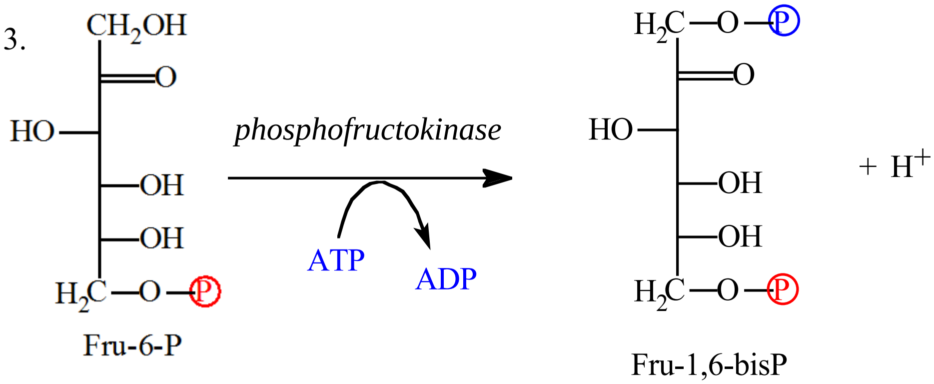

$\Delta G'^{o} = -16.7$ kJ/mol   $K_{eq} = 845$   "*irreversible*" reaction

2.




$\Delta G'^{o} = +1.7$ kJ/mol   $K_{eq} = 0.5$

3.

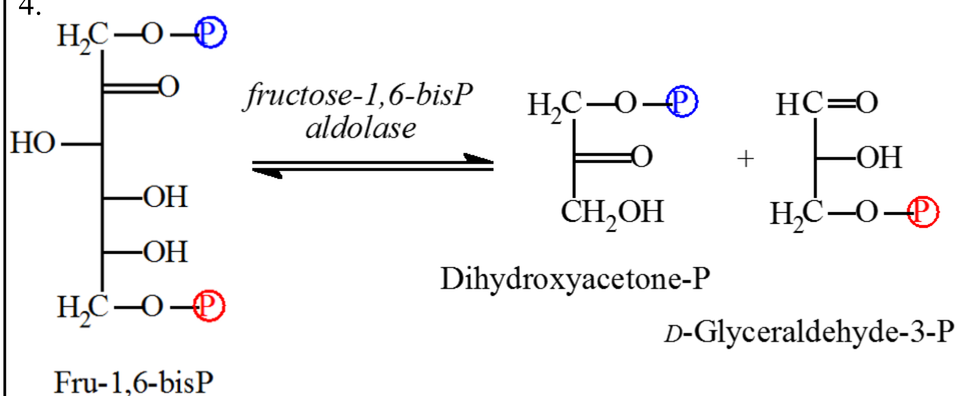



$\Delta G'^{o} = -14.2$ kJ/mol $K_{eq} = 308$

PFK is an **allosteric** enzyme and the key control point in glycolysis.

It is **activated** by **AMP**, and **inhibited** by **ATP** and **citrate** at allosteric binding sites ≠ active site.

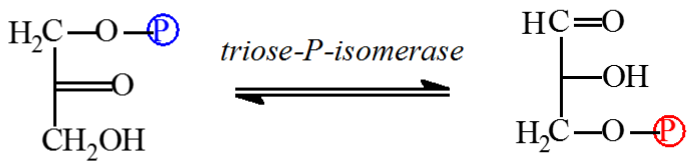
4.




$\Delta G'^{o} = +23.8$ kJ/mol $K_{eq} = 7x10^{-5}$

Although the reaction appears "difficult", it is pulled forward by removal of products in the following steps and the overall free energy release of the entire pathway.

5.



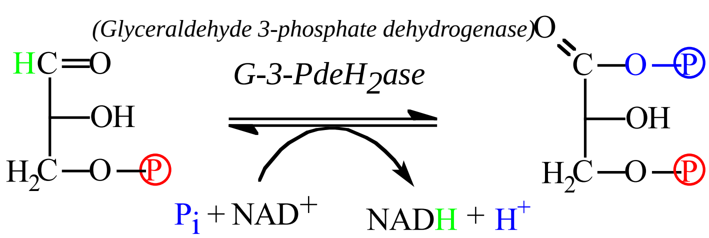

Dihydroxyacetone-P

Glyceraldehyde 3-phosphate

$\Delta G'^{o} = +7.5$ kJ/mol $K_{eq} = 0.05$

There are now **two** G-3-P and from now on there are **two** reactants and **two** products for each step (see last slide).

6.




Glyceraldehyde-3-P

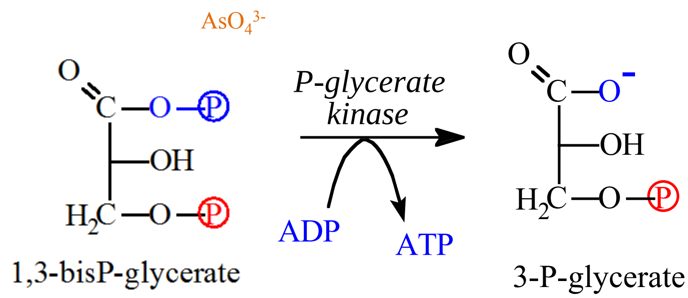
1,3-bisP-glycerate

$\Delta G'^{o} = +6.3$ kJ/mol $K_{eq} = 0.08$

An aldehyde is oxidized to a carboxyl and the G released is used to reduce $NAD^+$ and to form a high G phosphate (acyl phosphate).

Note that $NAD^+$ has been consumed and will have to be regenerated if glycolysis is to continue.

7.

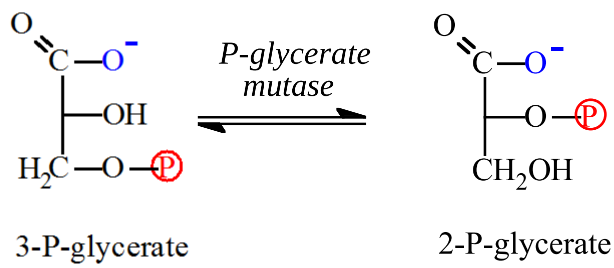



$\Delta G'^{o} = -18.5$ kJ/mol   $K_{eq} = 2000$

**Substrate Level Phosphorylation**

ATP is formed by the transfer of $P_i$ from a very high free energy compound to ADP.

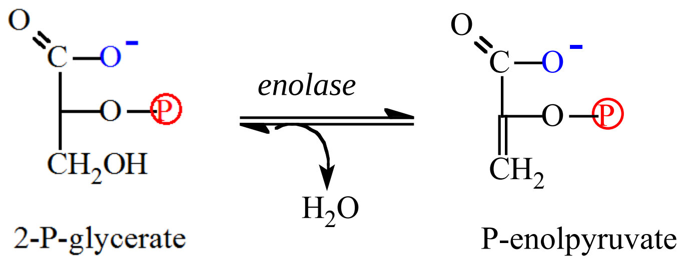
8.




$\Delta G'^{o} = +4.4$ kJ/mol   $K_{eq} = 0.2$

A mutase is an enzyme that transfers a functional group.

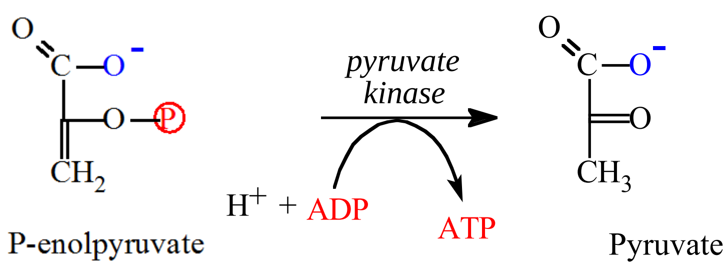
9.




A dehydration.

$\Delta G'^{o} = +7.5$ kJ/mol   $K_{eq} = 0.05$

10.




$\Delta G'^{o} = -31.4$ kJ/mol   $K_{eq} = 3\text{x}10^{5}$

A second **substrate-level phosphorylation**.

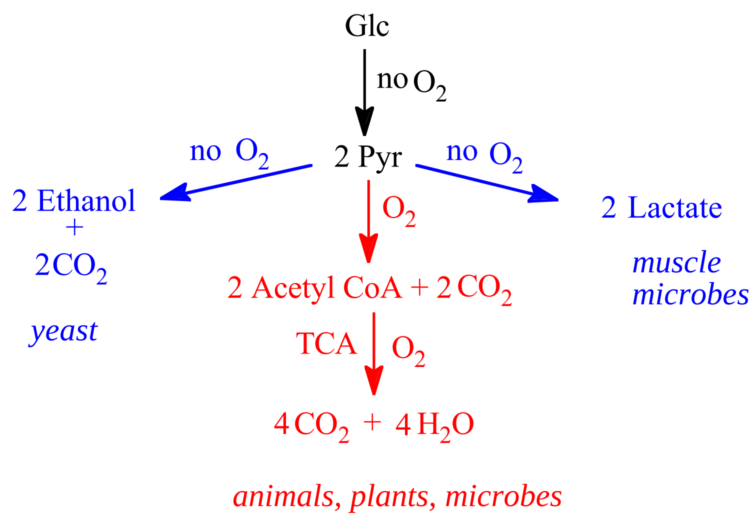
Some prokaryotes contain a more primitive pathway that converts glucose 6-phosphate into glyceraldehyde 3–phosphate and pyruvate.

Those bacteria contain all the enzymes of the 2nd half of glycolysis.

This pathway might be an ancient precursor of glycolysis.

Because only 1 glyceraldehyde 3-phosphate molecule is produced the ancient pathway yields only ½ the number of ATP molecules of glycolysis.

What happens to pyruvate? It depends on the cell and the conditions.



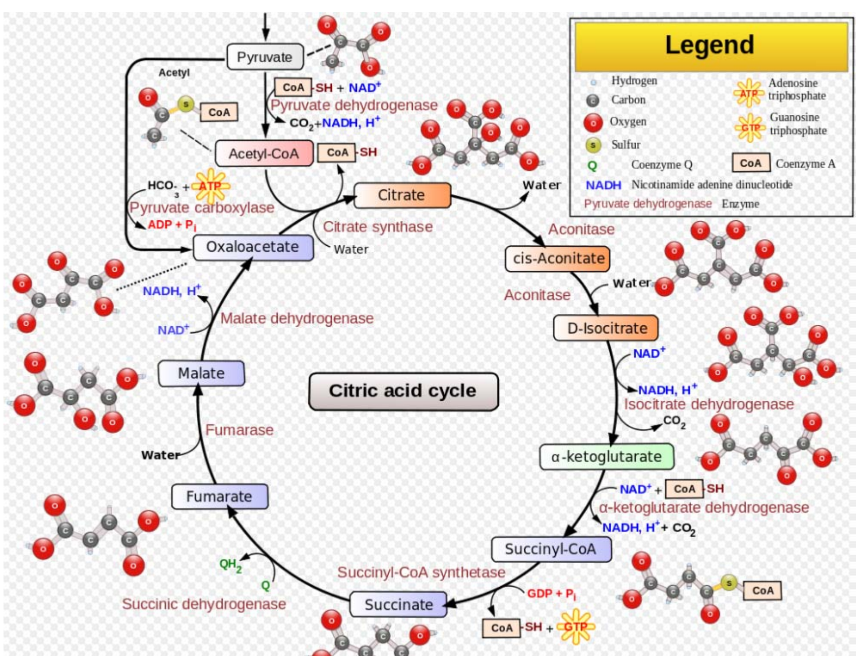
The TCA cycle

The citric acid cycle, aka the tricarboxylic acid cycle (TCA), or the Krebs cycle:

Series of chemical reactions used by all aerobic organisms to generate energy. It works by the oxidation of acetate derived from carbohydrates, fats and proteins into $CO_2$ and G in the form of ATP.

The cycle also provides precursors of certain amino acids and of NADH that is used in numerous other biochemical reactions.

Its central importance to many biochemical pathways suggests that it was one of the earliest established components of cellular metabolism.

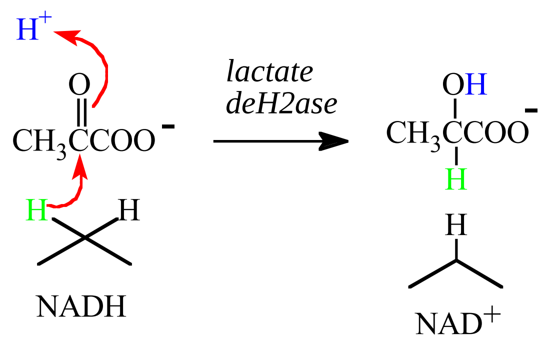


http://en.wikipedia.org/wiki/Citric_acid_cycle

## Lactic Acid Fermentation:

In hard-working muscle, sometimes we can't provide $O_2$ fast enough so pyruvate is quickly reduced to L-lactate to keep glycolysis going:

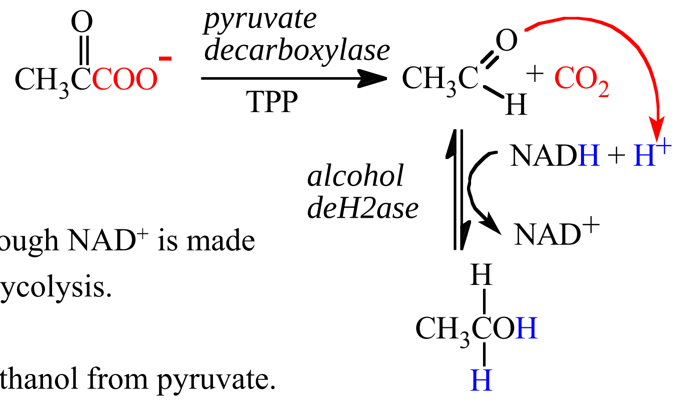
$\Delta G'^{o} = -25.1$ kJ/mol   $K_{eq} = 2.5 \times 10^4$




Note that the reaction is **stereospecific**, only the *L*-isomer of lactate is produced.

2 $NAD^+$ are produced from each of the 2 pyruvates from glycolysis which is exactly enough to keep glycolysis going.

**Ethanol Fermentation**:



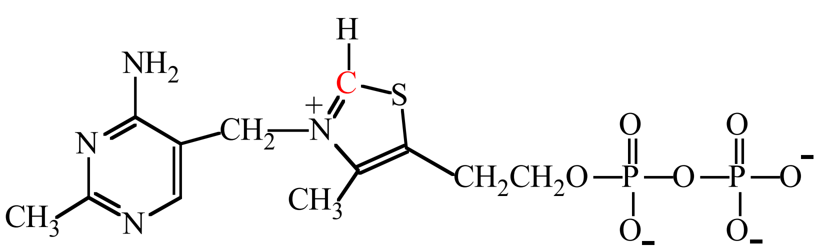

Again, just enough $NAD^+$ is made to replenish glycolysis.

Yeast makes ethanol from pyruvate.

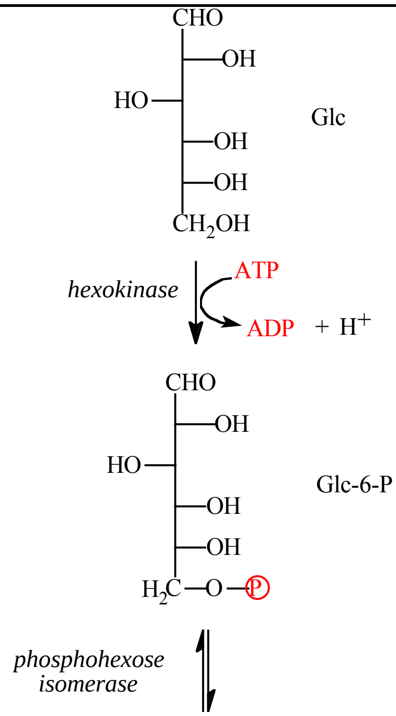
The human liver enzyme oxidizes ethanol to toxic acetaldehyde which is then converted to non-toxic acetate by aldehyde dehydrogenase.

At 13-14% ethanol is poisonous.

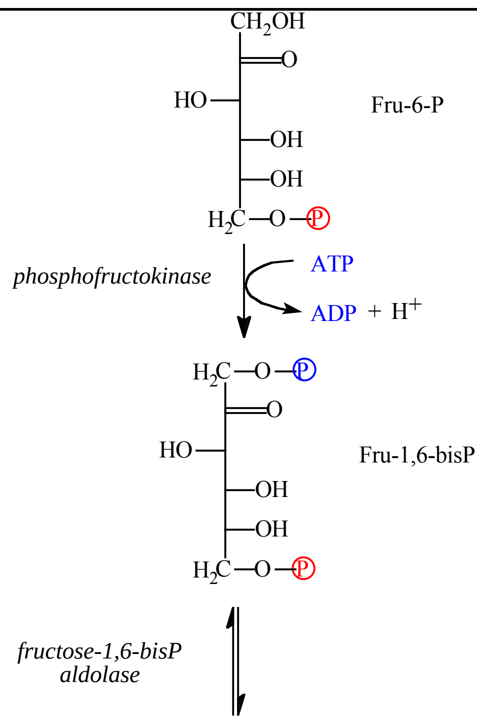
Notice that a C—C bond has been broken. Often, enzymes require special co-factors to do this. There are many examples of enzymes for which **thiamine pyrophosphate (TPP)** is a co-factor. It is derived from Vitamin B1.

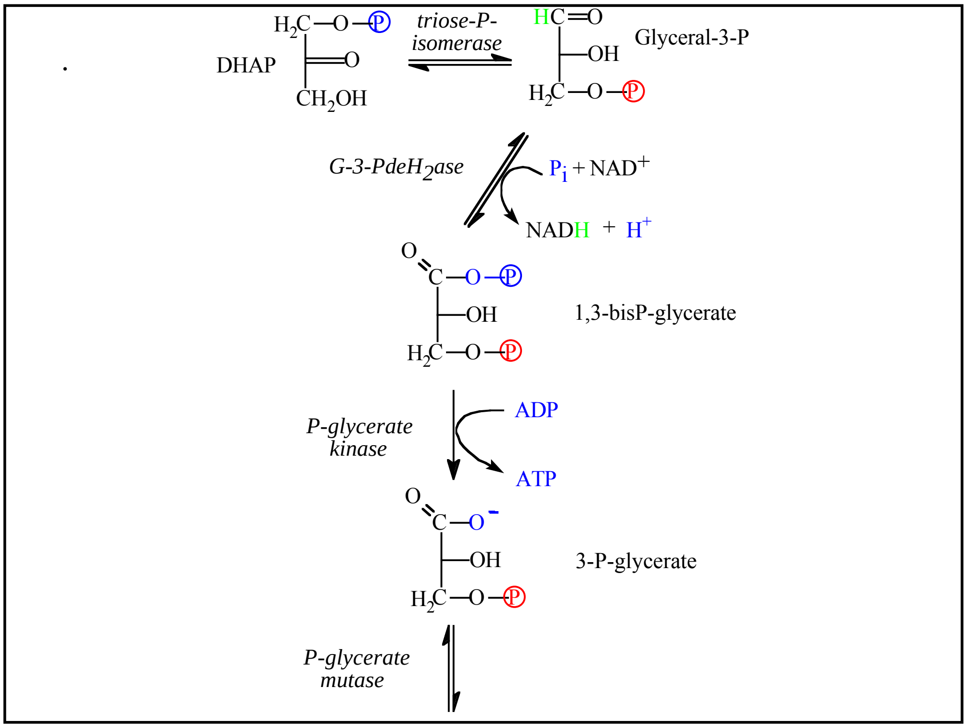


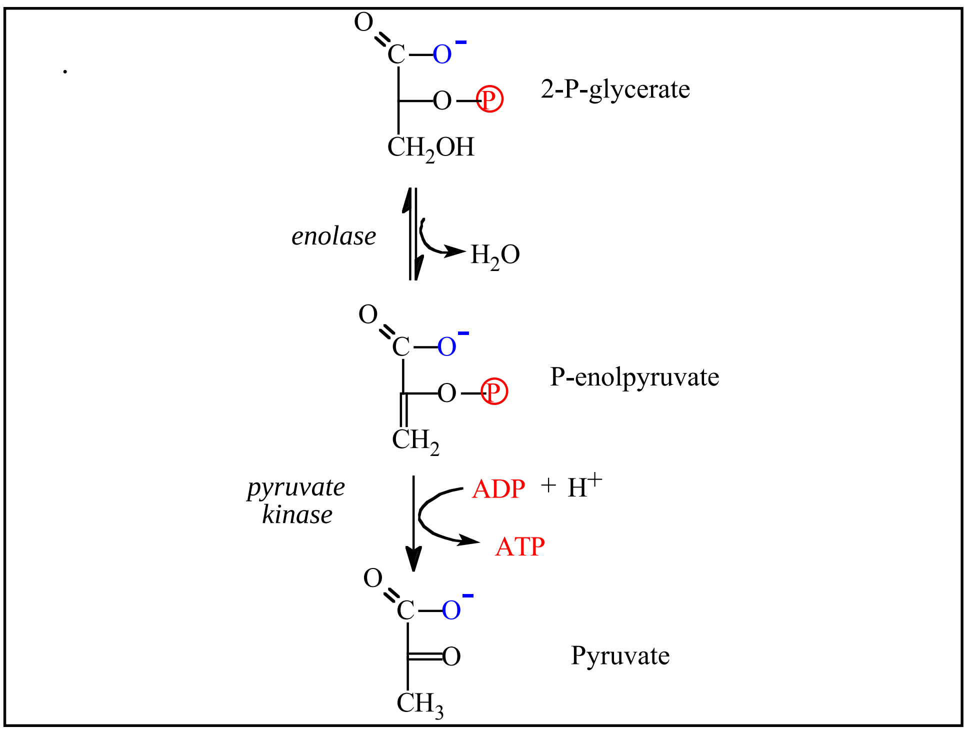
Summary


CHO
OH
HO
Glc
OH
OH
CH2OH
hexokinase
ATP
ADP + H+
CHO
OH
HO
Glc-6-P
OH
OH
H2C—O—P
phosphohexose isomerase

.


CH2OH
O
HO
Fru-6-P
OH
OH
H2C—O—P
phosphofructokinase
ATP
ADP + H+
H2C—O—P
O
HO
Fru-1,6-bisP
OH
OH
H2C—O—P
fructose-1,6-bisP aldolase


DHAP
triose-P-isomerase
Glyceral-3-P
G-3-PdeH2ase
Pi + NAD+
NADH + H+
1,3-bisP-glycerate
P-glycerate kinase
ADP
ATP
3-P-glycerate
P-glycerate mutase


2-P-glycerate
enolase
H2O
P-enolpyruvate
pyruvate kinase
ADP + H+
ATP
Pyruvate