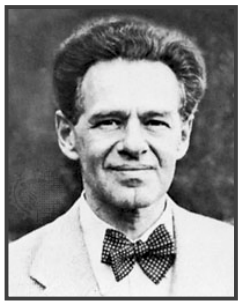
Glycolysis and the Catabolism of Hexoses

Eduard Büchner 1860 - 1917
(Anaerobic Fermentation)



Fritz A. Lipmann 1899 – 1986
(Discovered Coenzyme A)

Sir Hans A. Krebs 1900 – 1981
(Citric Acid Cycle)

Lipmann and Krebs shared the
1953 Nobel Prize for Physiology or Medicine

Fates of Glucose

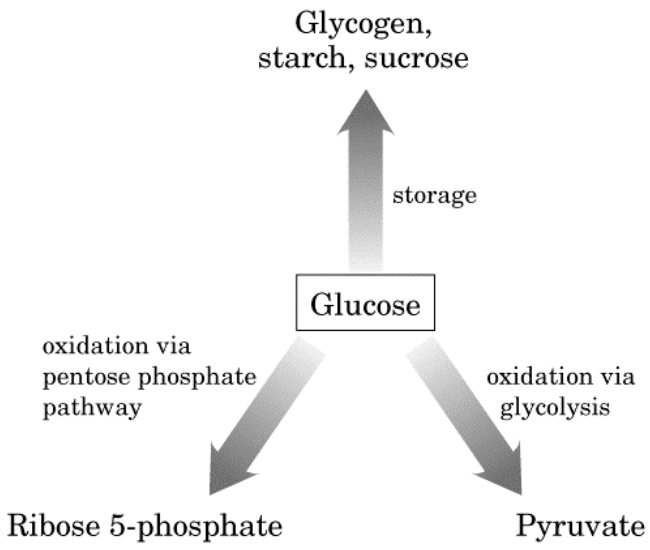


Fig 15-01.GIF

Two phases of Glycolysis: Preparatory Phase

C_6

↓

$2\ C_3$

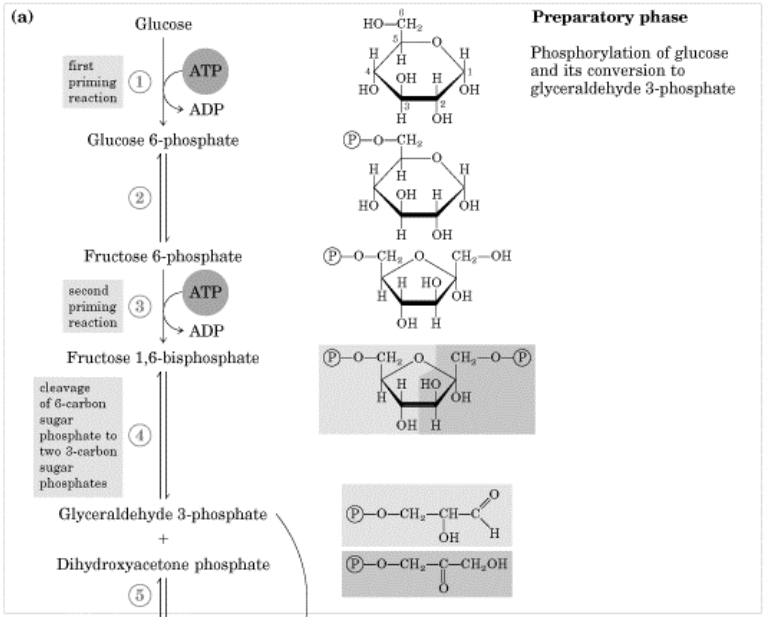


Fig 15-02.GIF

Two phases of Glycolysis: Energy Conservation Phase

$2\ C_3$

↓

$2\ C_3$

2 ATP

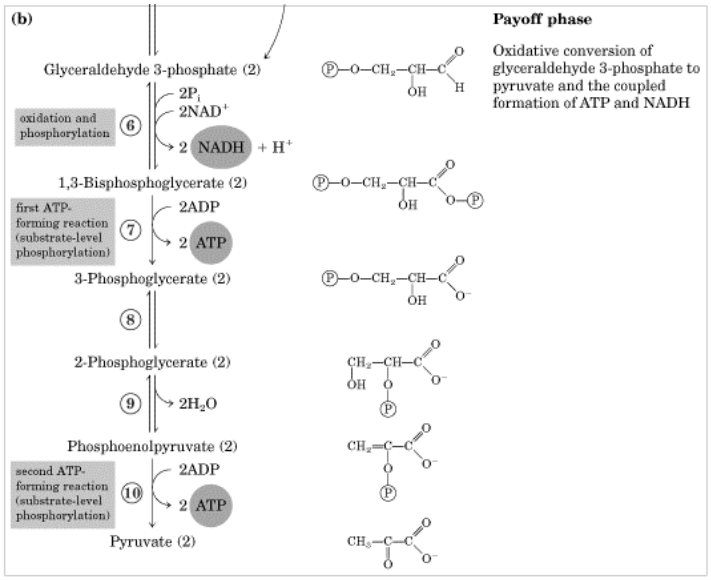
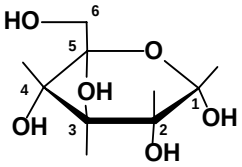
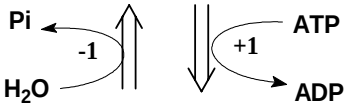


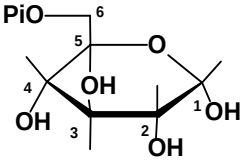
Fig 15-02.GIF

Glycolysis Stage I: Preparatory Phase (Rxn 1 & -1)



glucose (G)





glucose-6-phosphate (G6P)

"Tags" glucose to keep it in the cell

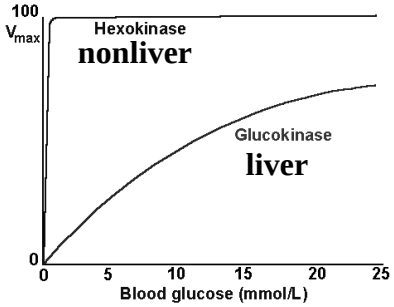
$\Delta G^{\circ\prime}$ = - 16.7 kJ/mol

+1 - glucokinase (or hexokinase)

-1 - glucose-6-phosphate phosphatase

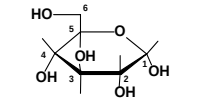
$\Delta G^{\circ\prime}$ = - 13.8 kJ/mol

Removes Pi - active only in gluconeogenesis

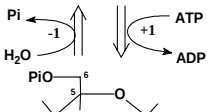


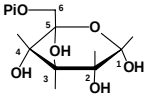
http://www.med.unibs.it/~marchesi/glycolys.html

Glycolysis Stage I: Preparatory Phase (Rxn 1)



glucose (G)





glucose-6-phosphate (G6P)

"Tags" glucose to keep it in the cell

$\Delta G^{\circ\prime}$ = - 16.7 kJ/mol

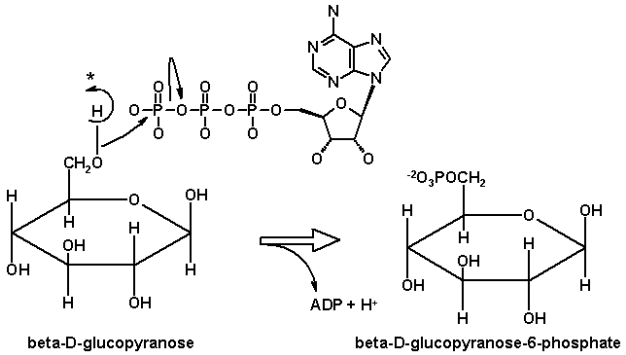
+1 - glucokinase (or hexokinase)

-1 - glucose-6-phosphate phosphatase

$\Delta G^{\circ\prime}$ = - 13.8 kJ/mol

Removes Pi - active only in gluconeogenesis

HEXOKINASE REACTION MECHANISM

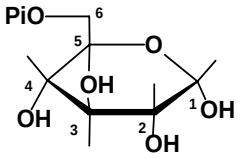


beta-D-glucopyranose

beta-D-glucopyranose-6-phosphate

http://www.med.unibs.it/~marchesi/glycolys.html

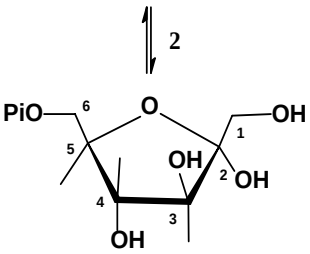
Glycolysis Stage I: Preparatory Phase (Rxn 2)



glucose-6-phosphate (G6P)

phosphohexose isomerase

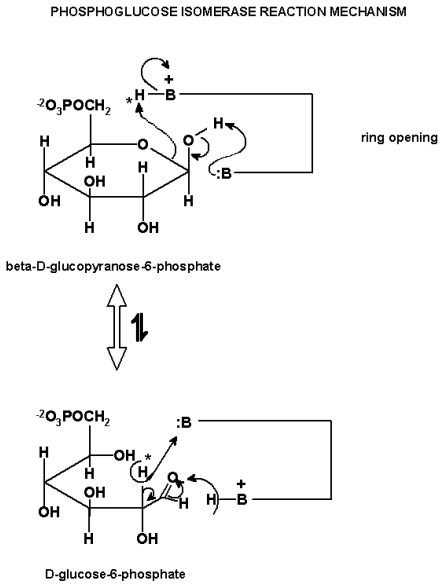
2 - glucose-6-phosphate isomerase
$\Delta G^{\circ\prime}$ = + 1.67 kJ/mol



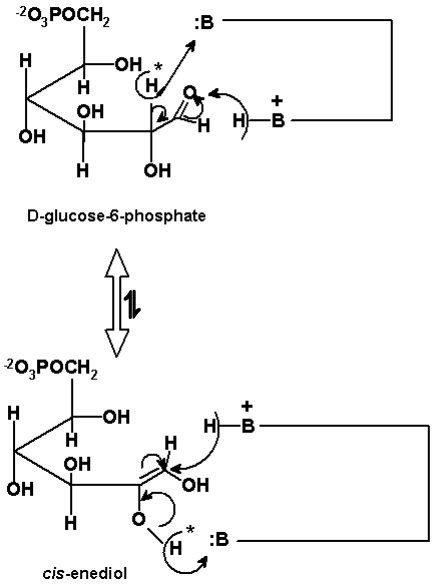
fructose-6-phosphate
(F6P)

Isomerization of C_6 in preparation for the cleavage reaction

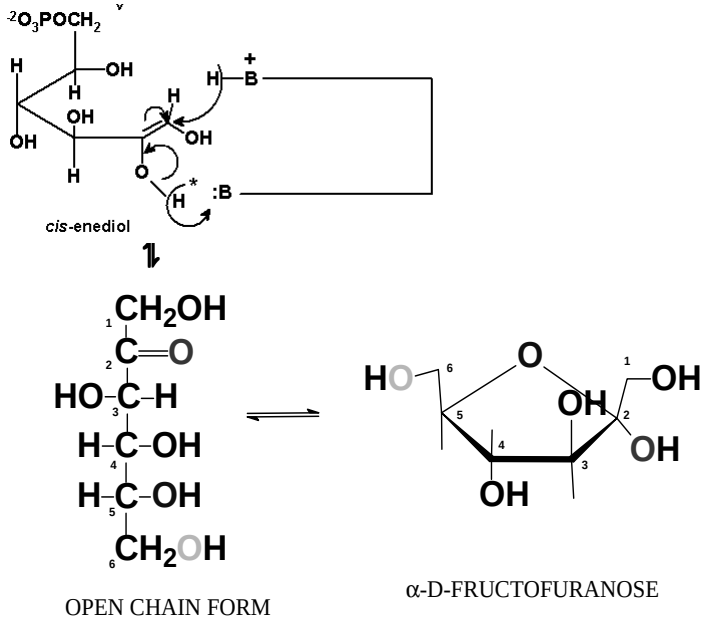
Glycolysis Stage I: Preparatory Phase (Mechanism 2a)



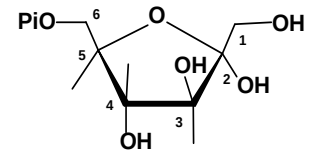
Glycolysis Stage I: Preparatory Phase (Mechanism 2b)



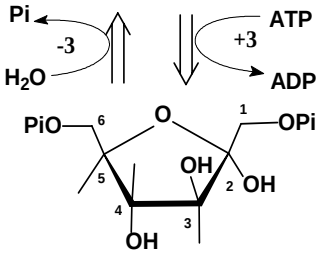
Glycolysis Stage I: Preparatory Phase (Mechanism 2c)



Glycolysis Stage I: Preparatory Phase (Rxn 3 & -3)



fructose-6-phosphate
(F6P)



fructose-1,6-bisphosphate
(F6P)

2nd phosphorylation to commit glucose into glycolysis

$\Delta G^{\circ\prime}$ = - 14.2 kJ/mol

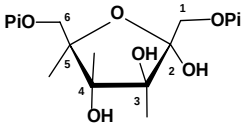
+3 - phosphofructokinase

-3 - fructose-1,6-bisphosphate phosphatase

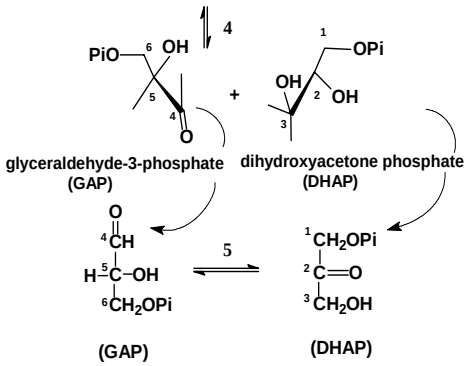
$\Delta G^{\circ\prime}$ = - 16.7 kJ/mol

Removes Pi - active only in gluconeogenesis

Glycolysis Stage I: Preparatory Phase (Rxn 4 & 5)



fructose-1,6-bisphosphate
(F6P)



(GAP) (DHAP)

(over for Stage II starting with 2 GAP)

4 - aldolase

$\Delta G^{\circ\prime}$ = + 24.0 kJ/mol

Cleavage of C_6 into 2 x C_3 fragments

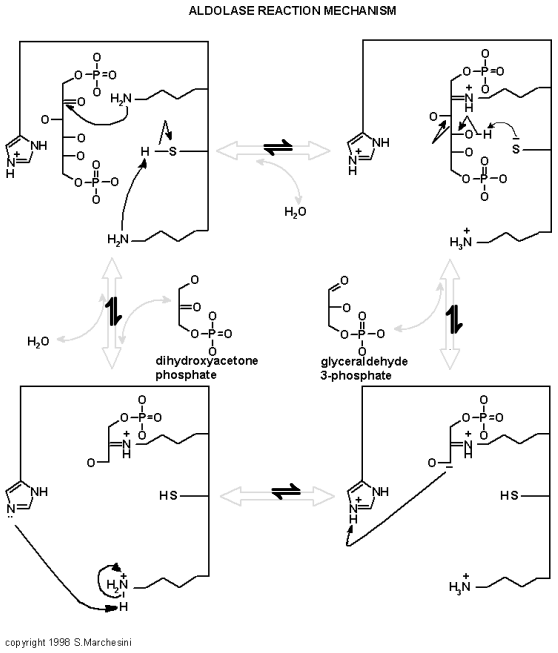
5 - triosephosphate isomerase

$\Delta G^{\circ\prime}$ = - 7.6 kJ/mol

Isomerization of C_3 to interconvert forms

$\Delta G^{\circ\prime}$ = - 24.0 kJ/mol

ALDOLASE



Glycolysis Stage I: Preparatory Phase (Rxn 5)

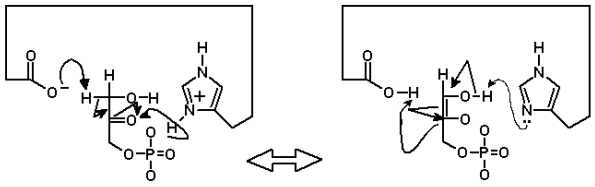
glyceraldehyde-3-phosphate (GAP) ⇌ **dihydroxyacetone phosphate (DHAP)**

5 - triosephosphate isomerase

$\Delta G^{\circ\prime}$ = - 7.6 kJ/mol

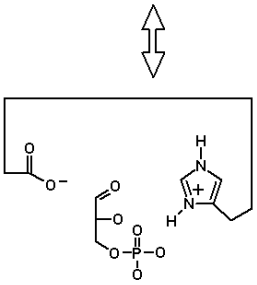
Isomerization of C_3 to interconvert forms

TRIOSE PHOSPHATE ISOMERASE REACTION MECHANISM



dihydroxyacetone phosphate

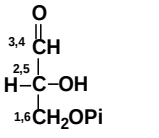
cis-enediol



glyceraldehyde 3-phosphate

Triosephosp
Mecl

Glycolysis Stage II: Energy Conservation Phase (Rxn 6)

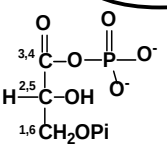


glyceraldehyde-3-phosphate (GAP)

Pi + NAD^+

6

$NADH + H^+$



1,3-bisphosphoglycerate (1,3-BPG)

2 x all intermediates

GLYCOLYSIS STAGE II: PREPARATORY PHASE
(Energy Conservation Phase)

6 - glyceraldehyde-3-phosphate dehydrogenase

$\Delta G^{\circ\prime}$ = + 6.3 kJ/mol

substrate-level oxidative phosphorylation: *process of oxidation coupled to phosphorylation*

Step 6 alone is an example which generates 1st high energy phosphate compound responsible for the net 2 ATP/glucose.

Step 6 + Step 7 can also be considered to be substrate-level oxidative phosphorylation for the formation of ATP

Glycolysis Stage II: Energy Conservation Phase (Rxn 6)

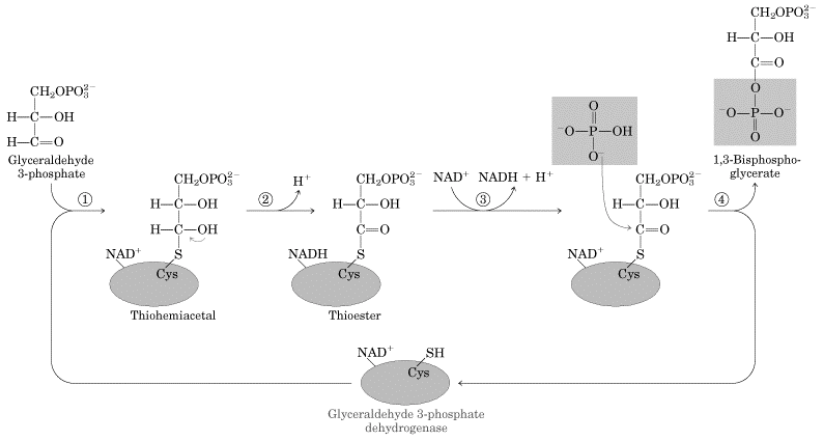
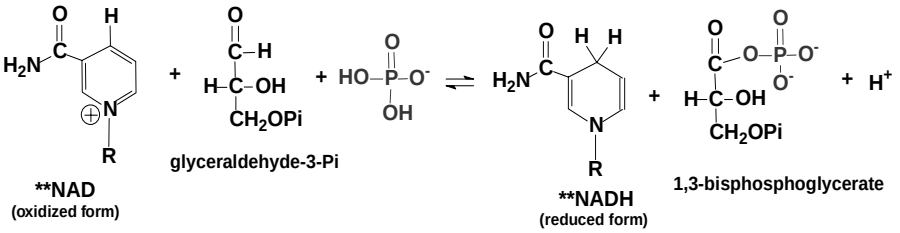


Fig 15-05.GIF

Glycolysis Stage II: Energy Conservation Phase (Rxn 6)

GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE



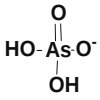
****NAD**
(oxidized form)

glyceraldehyde-3-Pi

****NADH**
(reduced form)

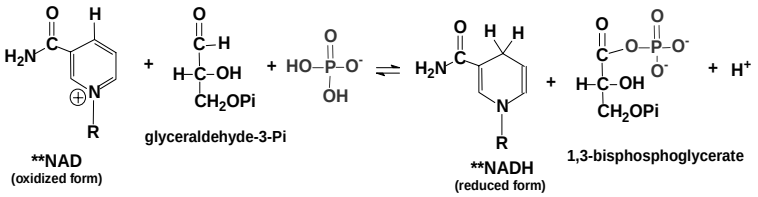
1,3-bisphosphoglycerate

INHIBITOR WITH RESPECT TO Pi:
(and uncoupler of substrate-level oxidative phosphorylation)

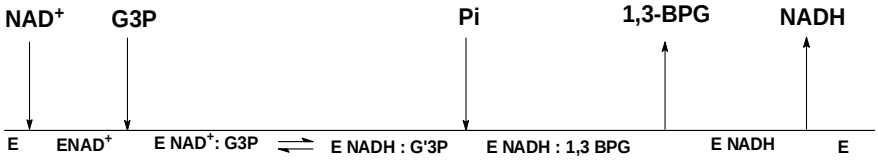


Glycolysis Stage II: Energy Conservation Phase (Rxn 6)

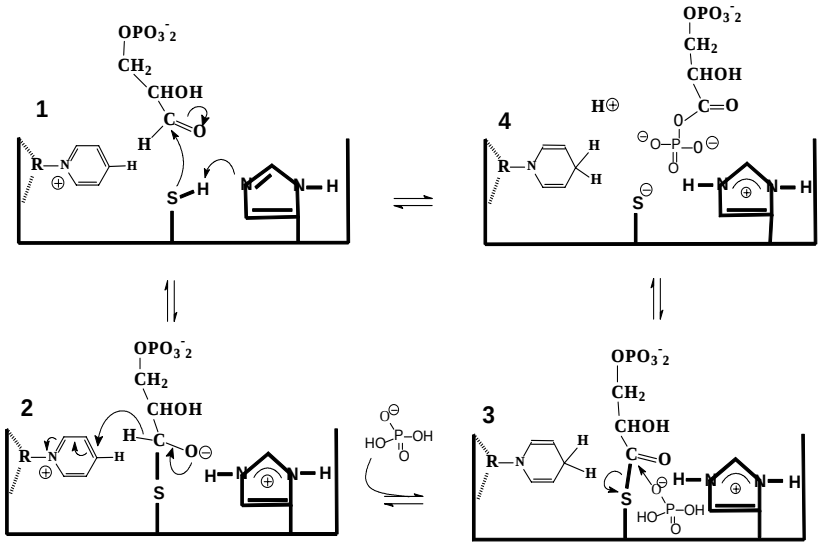
GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE



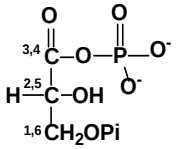
ORDERED TRI BI MECHANISM



Glycolysis Stage II: Energy Conservation Phase (Rxn 6)

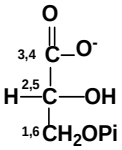


Glycolysis Stage II: Energy Conservation Phase (Rxn 7)



1,3-bisphosphoglycerate (1,3-BPG)

2x all intermediates in Stage II



3-phosphoglycerate (3PG)

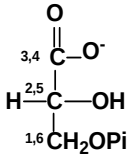
7 - phosphoglycerate kinase

$\Delta G^{\circ\prime}$ = - 18.5 kJ/mol

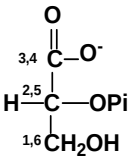
1st energy conservation step

Glycolysis Stage II: Energy Conservation Phase (Rxn 8)

2x all intermediates in Stage II



3-phosphoglycerate (3PG)



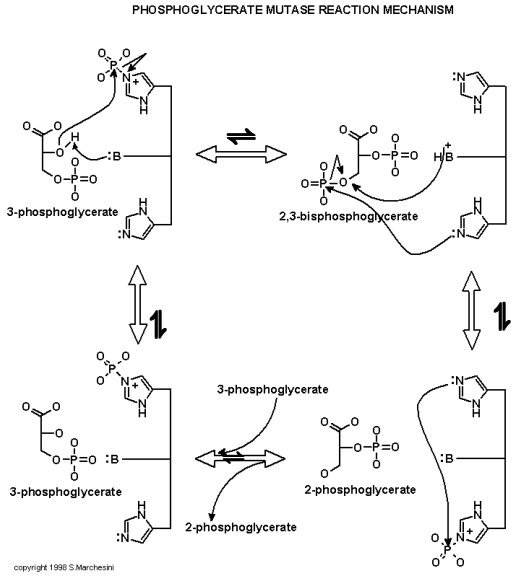
2-phosphoglycerate (2PG)

8 - phosphoglycerate mutase

$\Delta G^{\circ\prime}$ = + 4.4 kJ/mol

prepares C_3 for generation of 2nd high energy phosphate compound

Glycolysis Stage II: Energy Conservation Phase (Rxn 8)

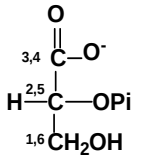


http://www.med.unibs.it/~marchesi/mutase.html

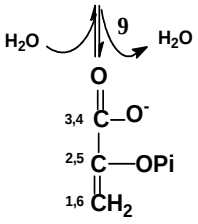
2,3-BPG

To control oxygen binding to Hb

Glycolysis Stage II: Energy Conservation Phase (Rxn 9)



2-phosphoglycerate (2PG)



phosphoenolpyruvate (PEP)

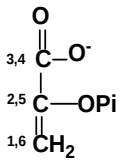
9 - enolase

$\Delta G^{\circ\prime}$ = + 7.5 kJ/mol

generation of 2nd high energy phosphate compound

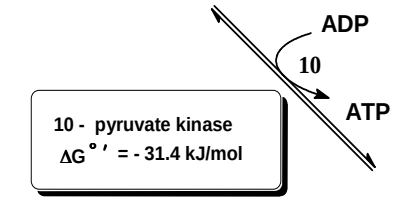
Write a mechanism for the dehydration using acid/base catalysts

Glycolysis Stage II: Energy Conservation Phase (Rxn 10)

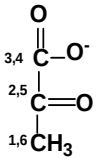


phosphoenolpyruvate (PEP)

Write a mechanism for the phosphate transfer. What intermediate do you have to write? What is the process by which that intermediate is converted to pyruvate?

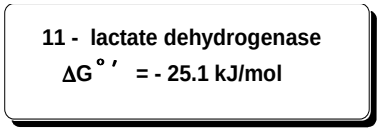


2nd energy conservation step

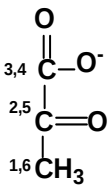


pyruvate (PYR)

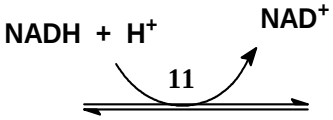
Glycolysis Stage II: Energy Conservation Phase (Rxn 11)

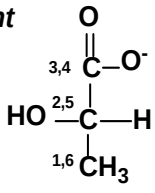


Regeneration of active oxidant



pyruvate (PYR)





L-lactate (LAC)

Write a mechanism for the reduction of pyruvate to L-lactic acid