David L. Nelson and Michael M. Cox

LEHNINGER
PRINCIPLES OF BIOCHEMISTRY

Fifth Edition

CHAPTER 14
Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway

Dr.Sulieman Al-Khalil

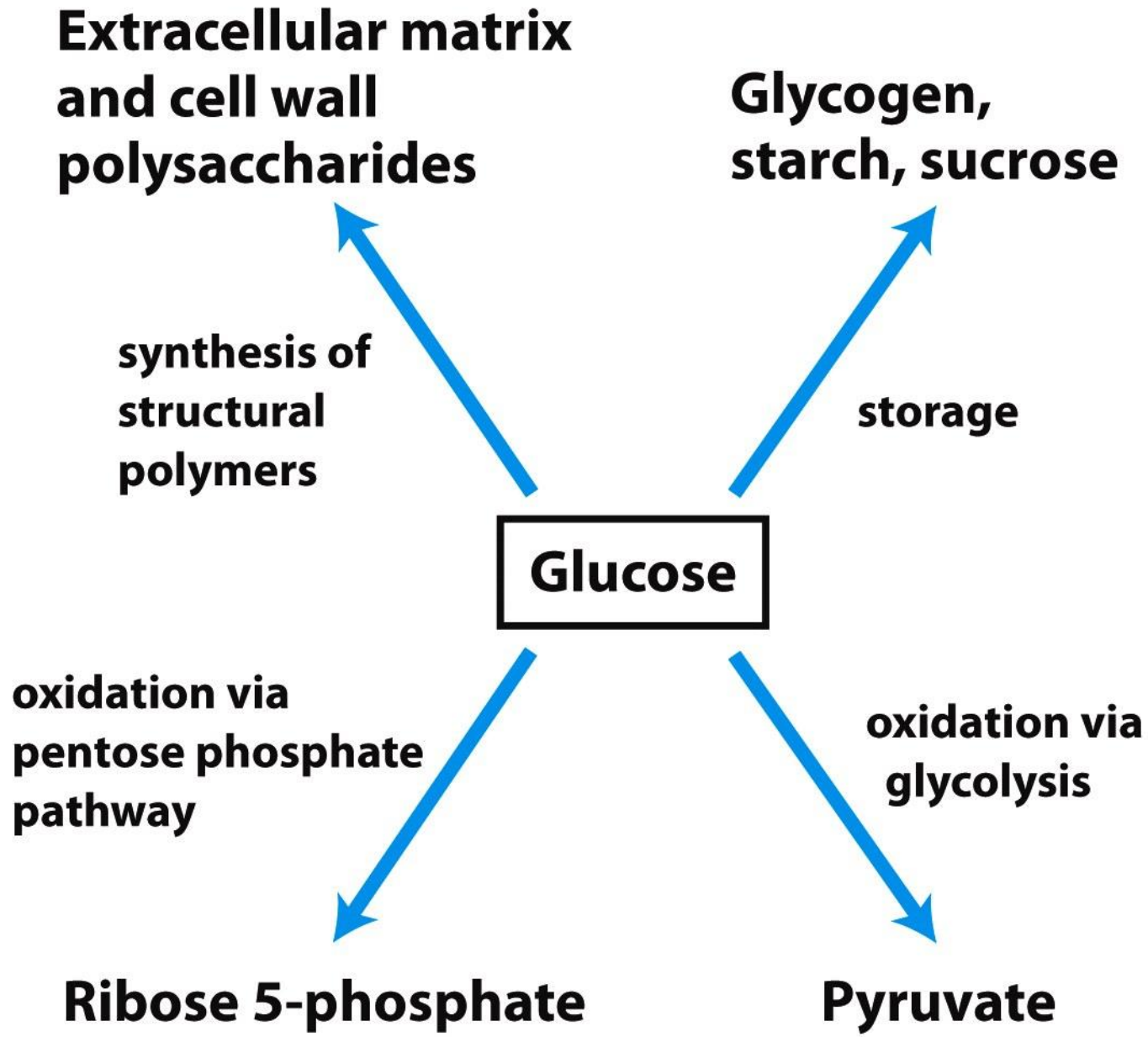

Figure 14-1
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Hans von Euler-Chelpin
1873–1964

Gustav Embden
1874–1933

Otto Meyerhof
1884–1951

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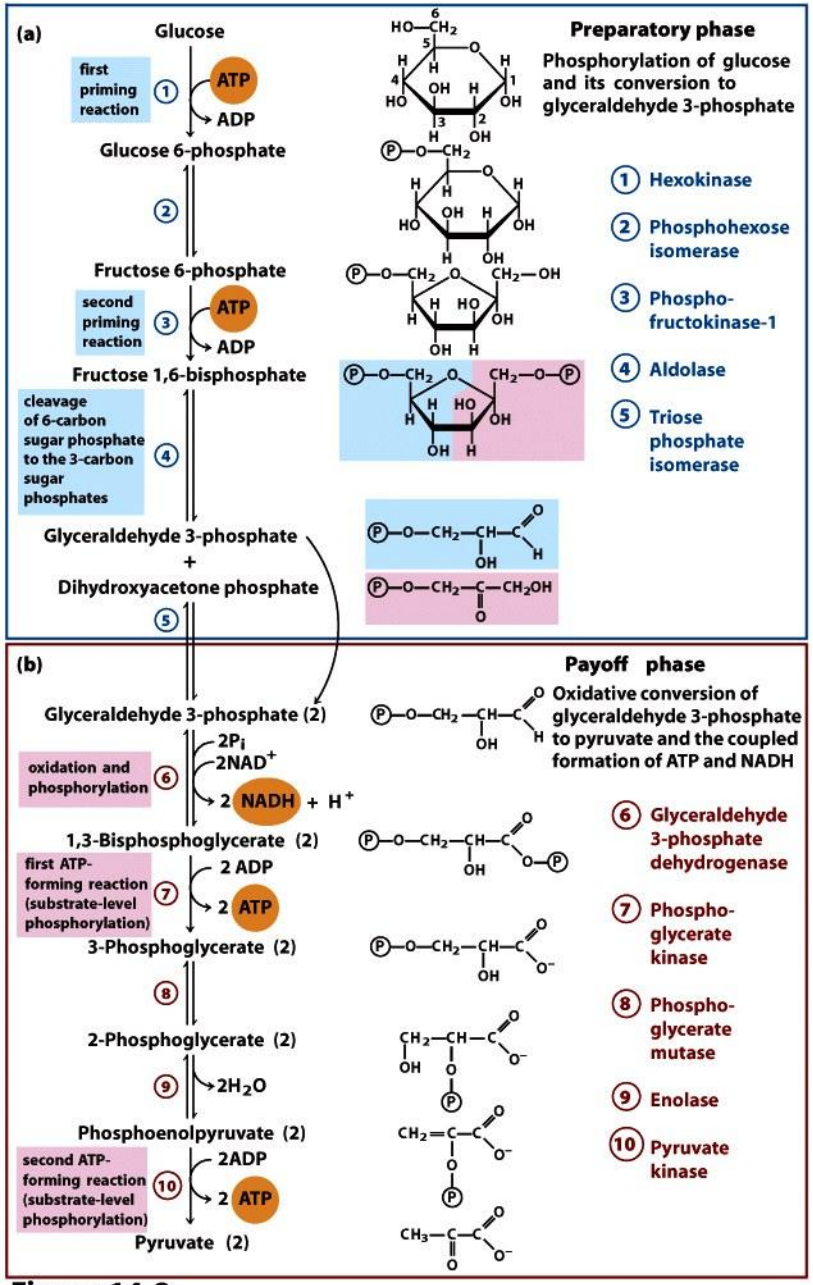

Figure 14-2

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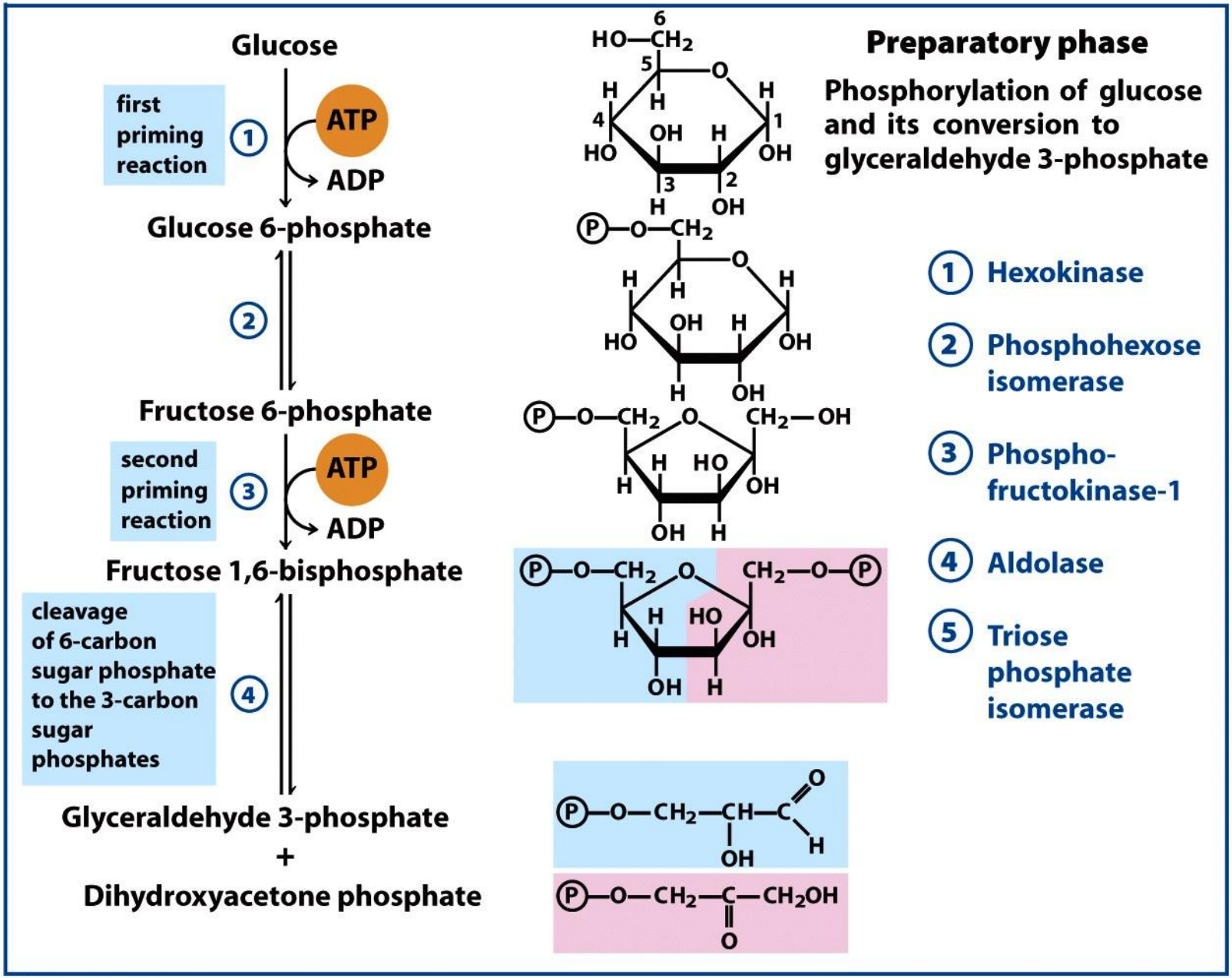

Figure 14-2a

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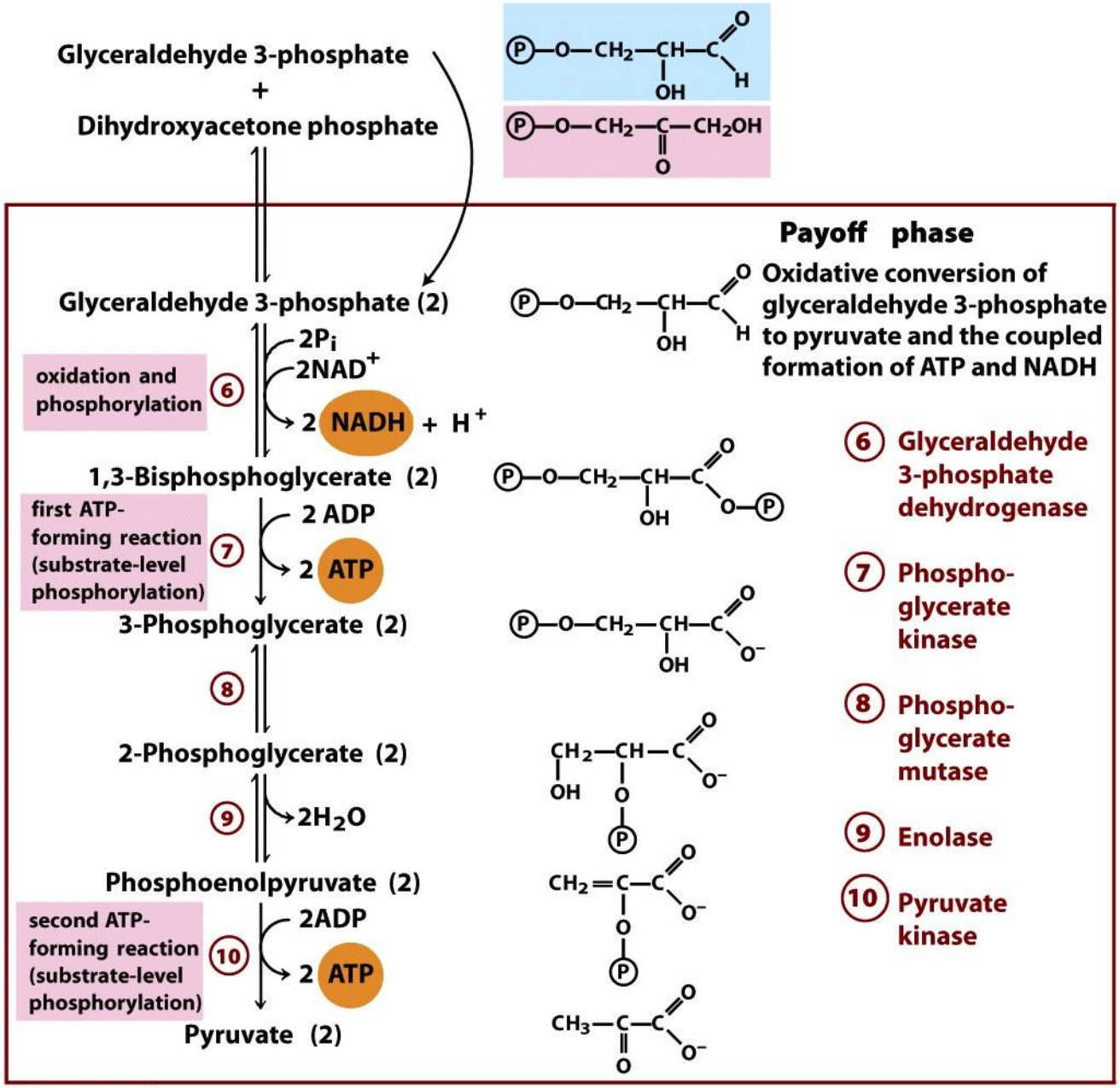

Figure 14-2b

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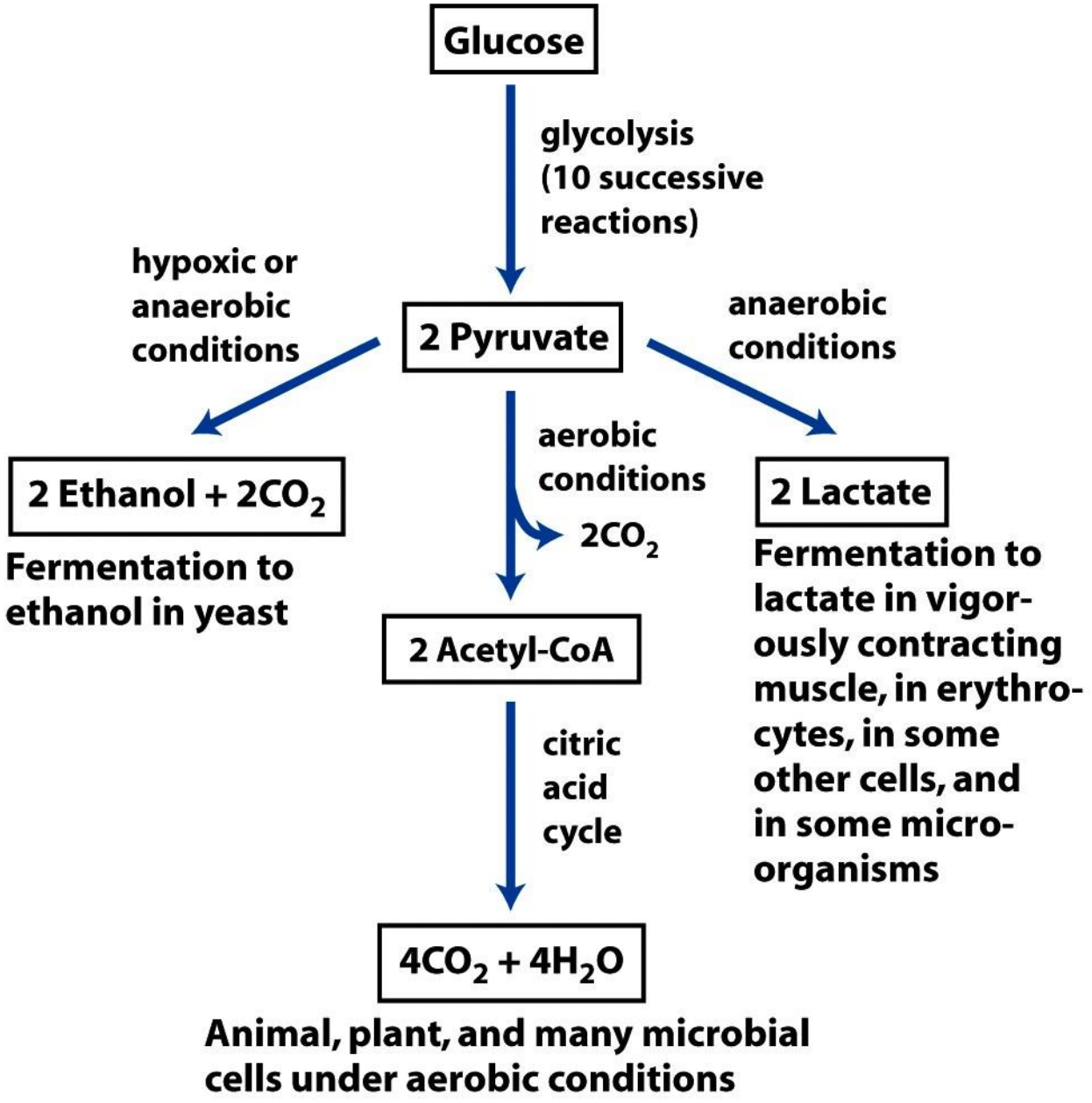

Figure 14-3
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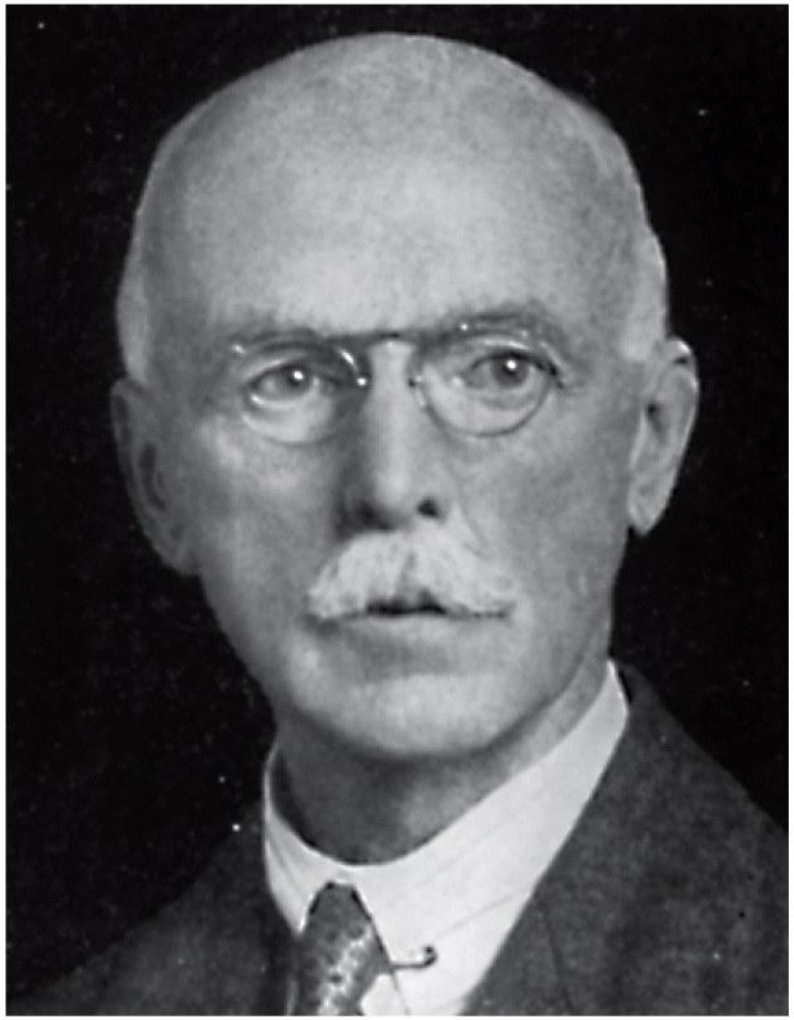
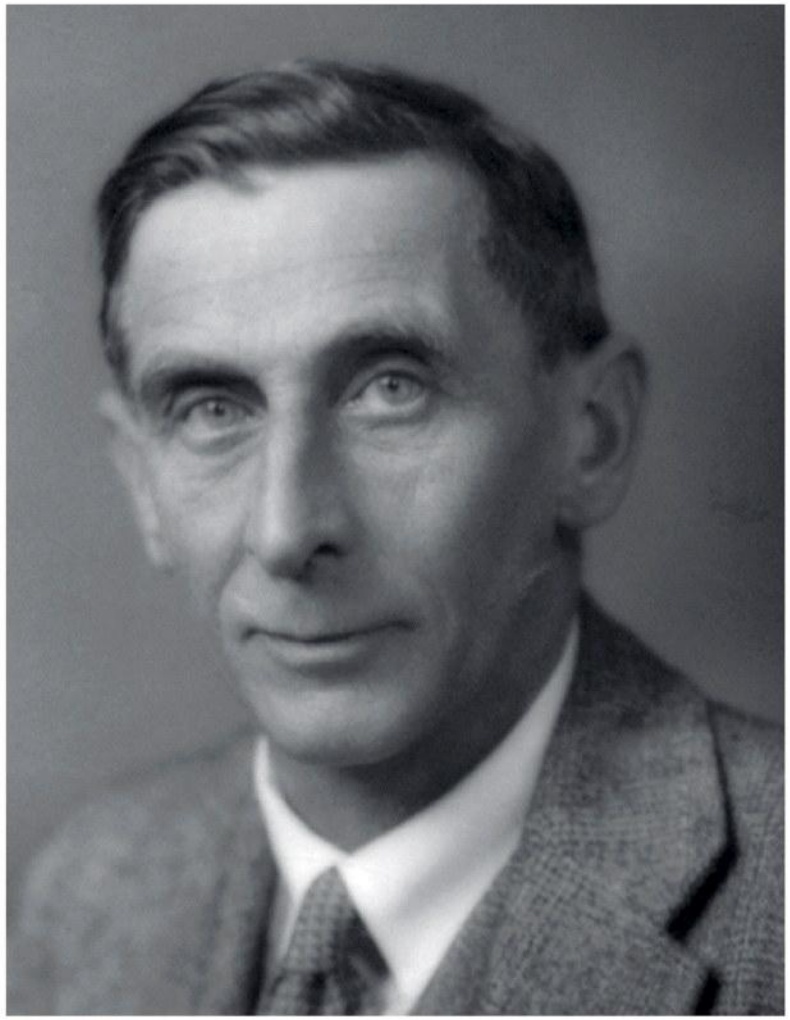


Arthur Harden
1865–1940



William Young
1878–1942

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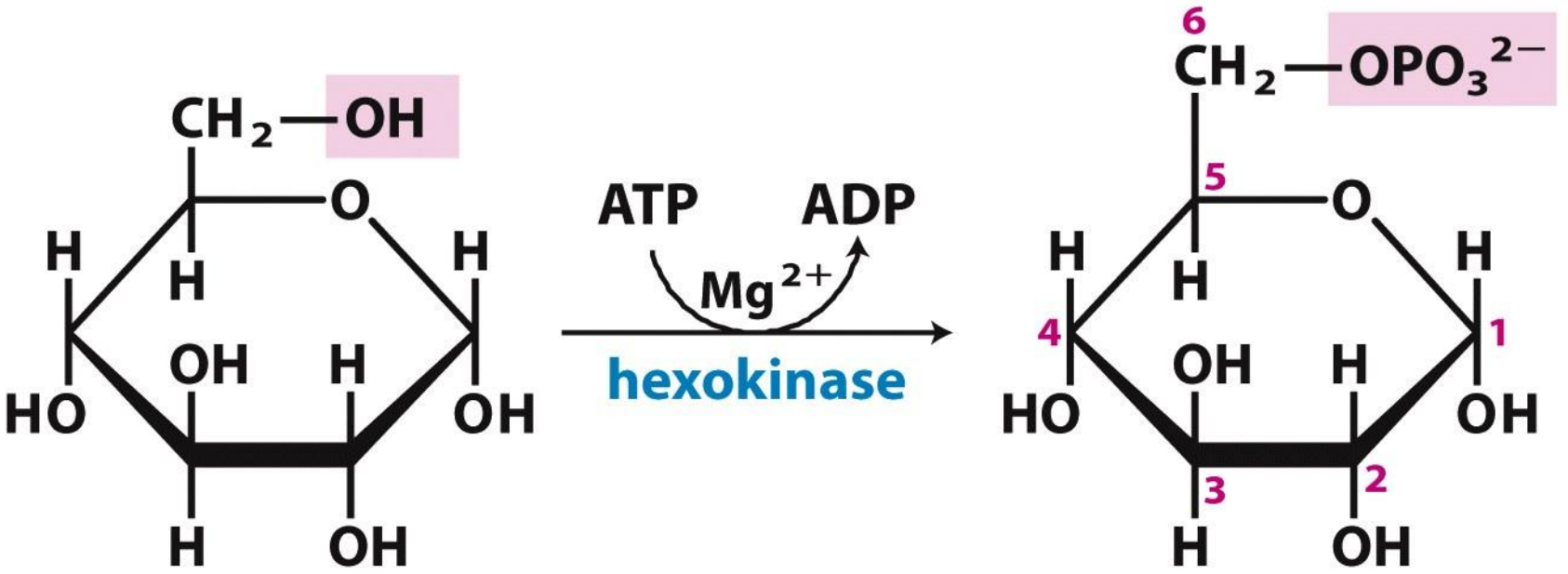

Glucose **Glucose 6-phosphate**

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

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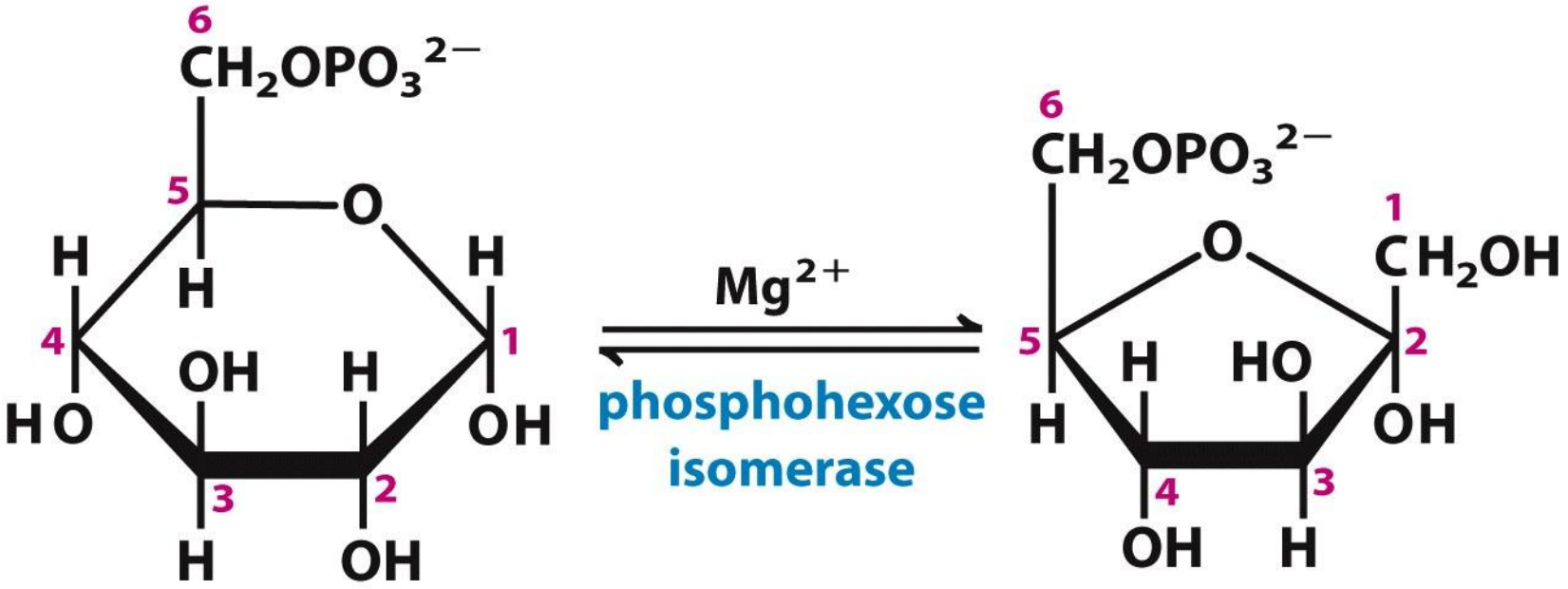

Glucose 6-phosphate **Fructose 6-phosphate**

$$\Delta G'^{\circ} = 1.7 \text{ kJ/mol}$$

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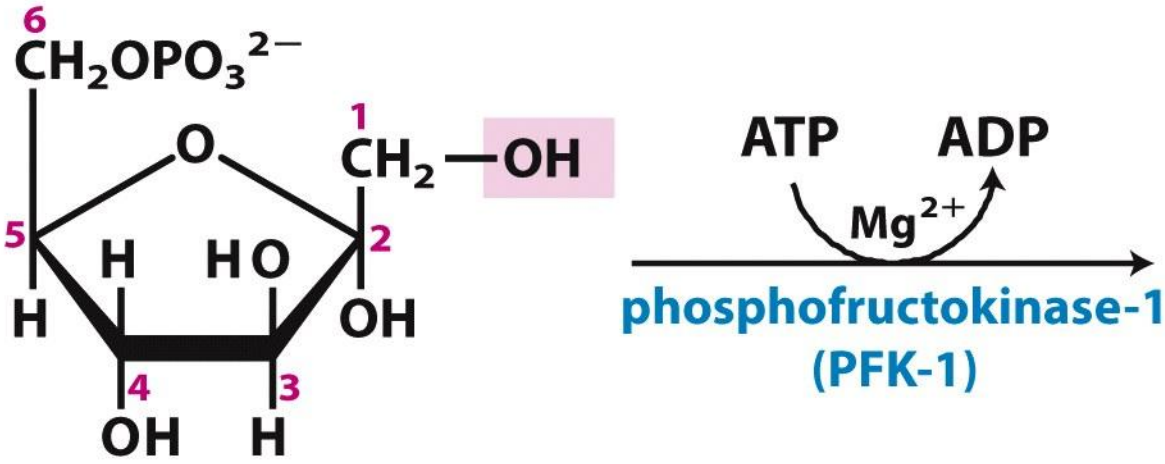
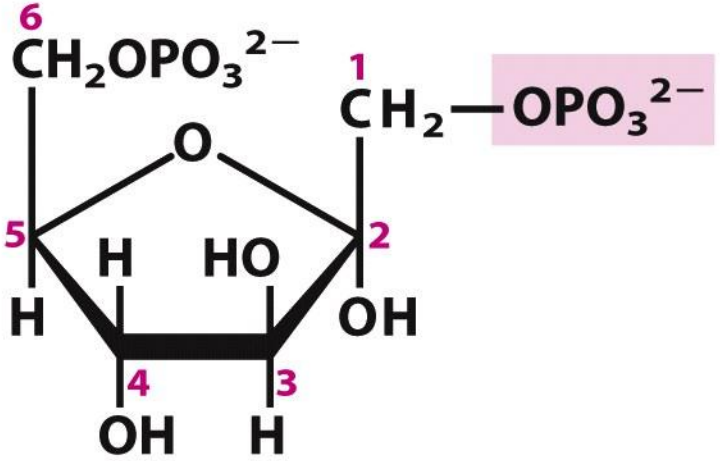


Fructose 6-phosphate



Fructose 1,6-bisphosphate

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

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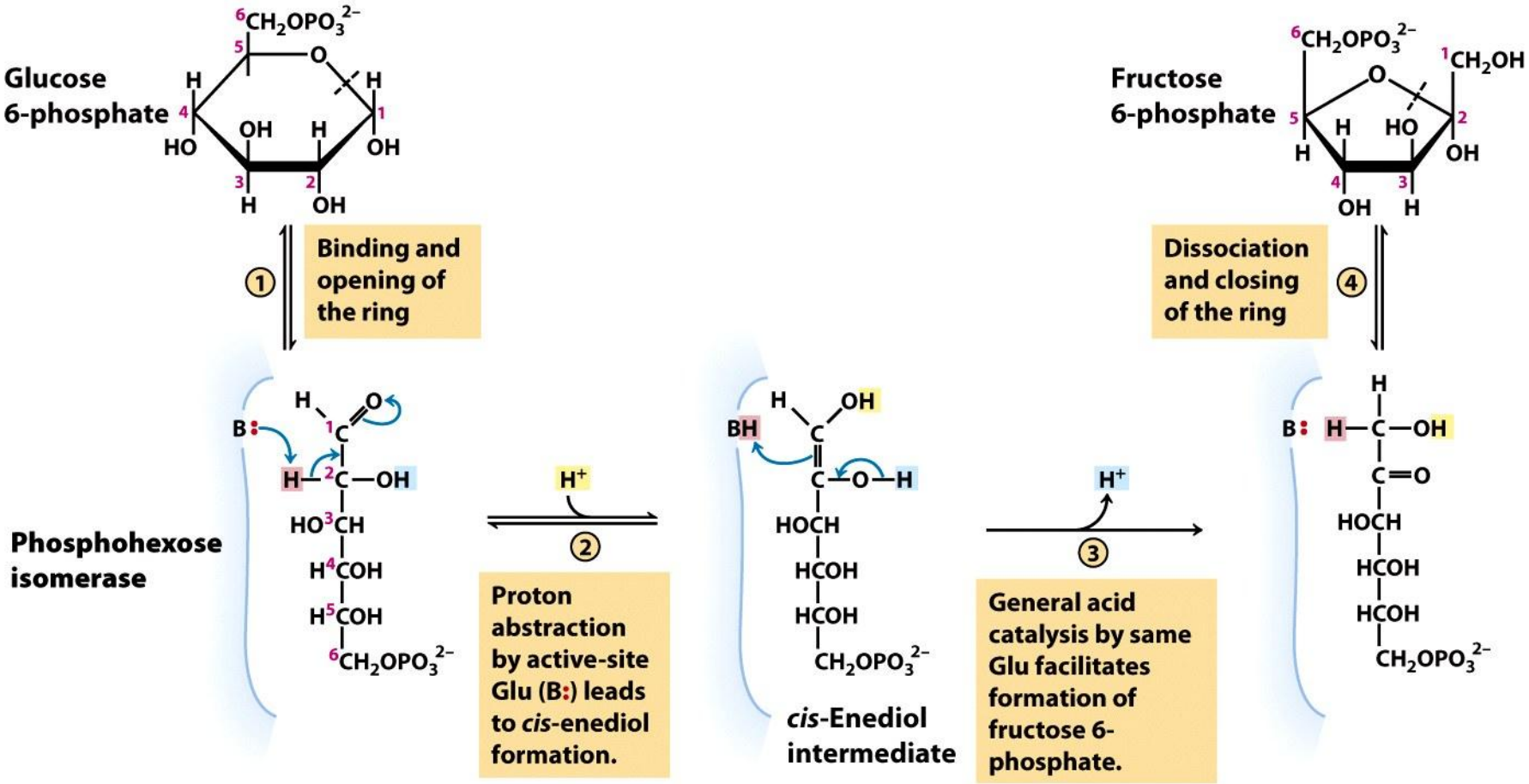

Figure 14-4
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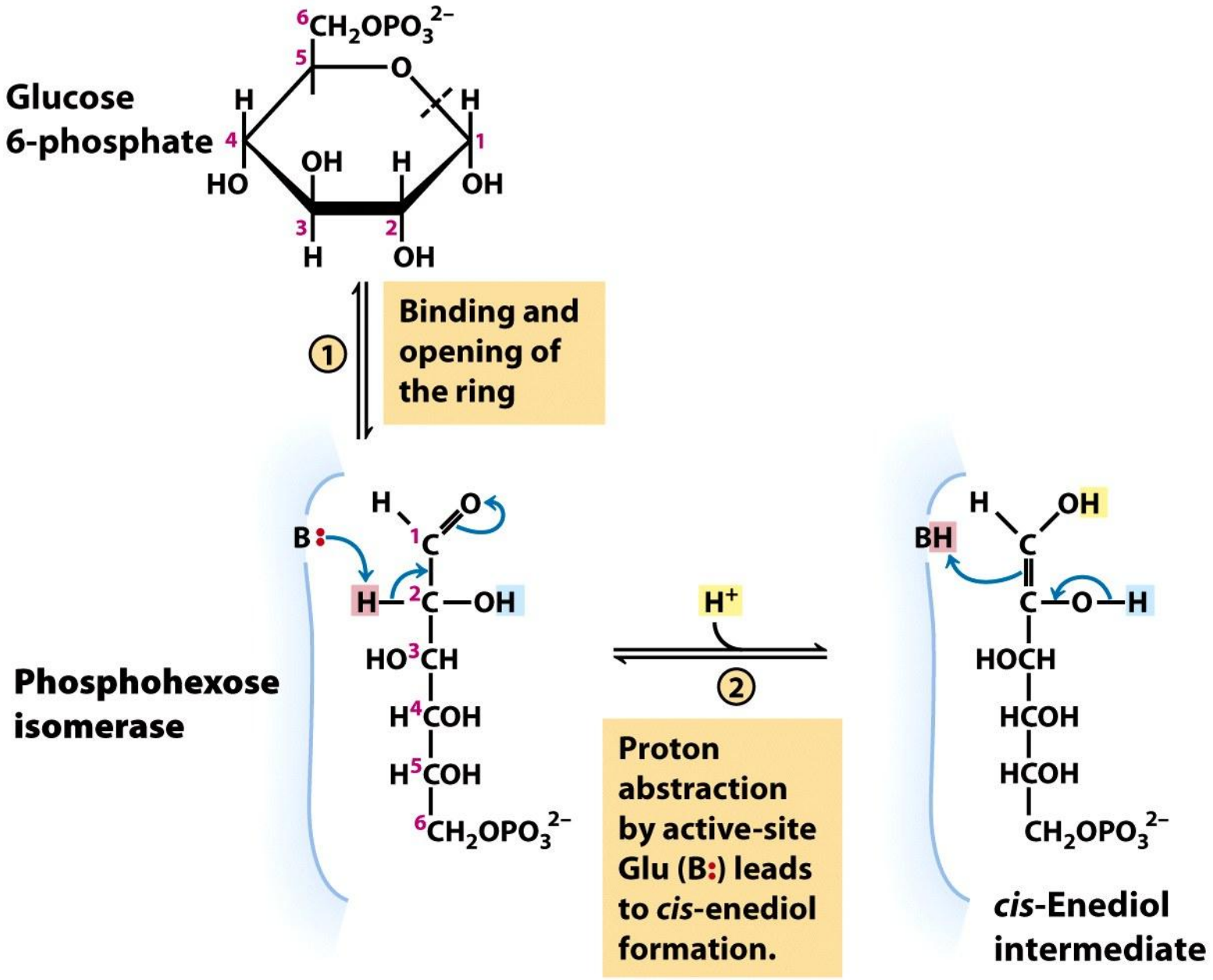

Figure 14-4 part 1
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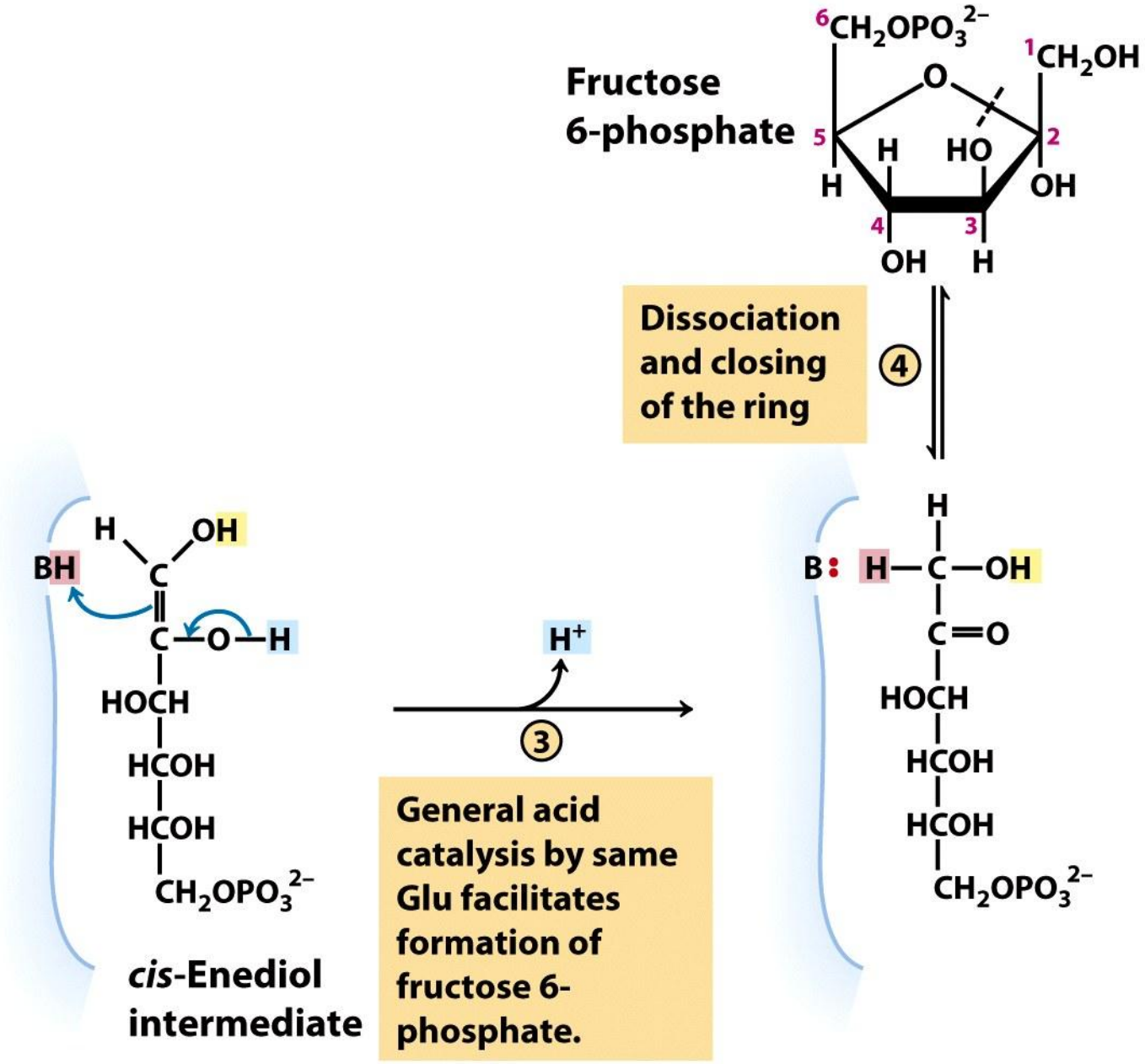

Figure 14-4 part 2

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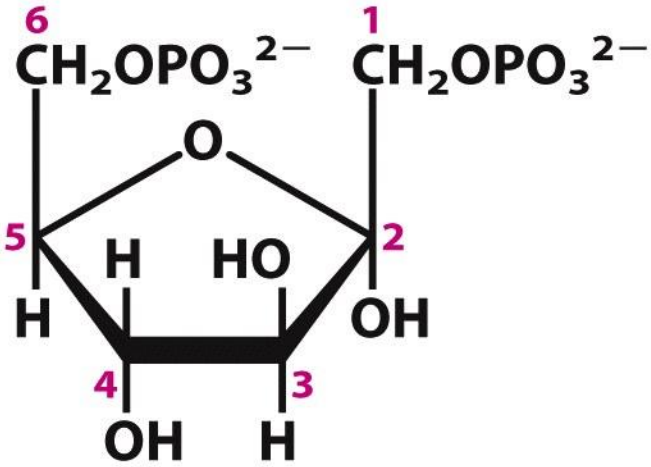
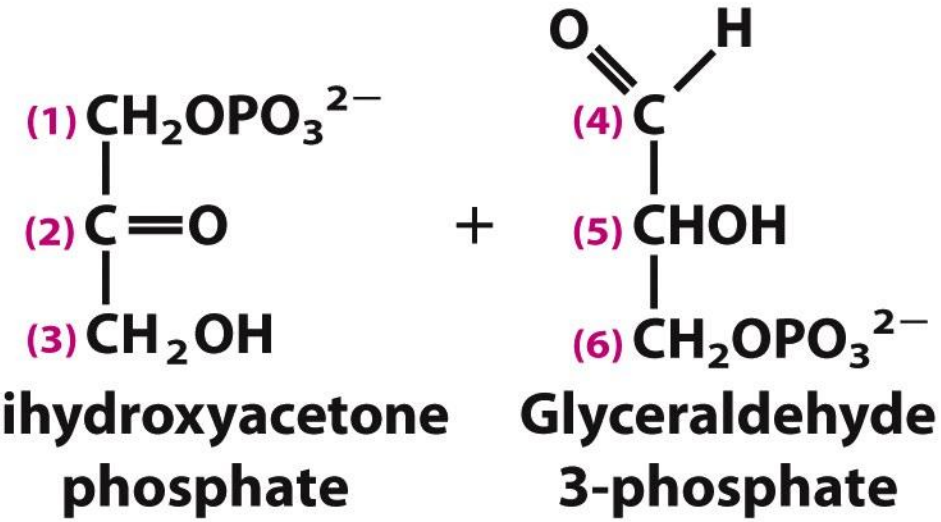


Fructose 1,6-bisphosphate



Dihydroxyacetone phosphate

Glyceraldehyde 3-phosphate

$$\Delta G'^{\circ} = 23.8 \text{ kJ/mol}$$

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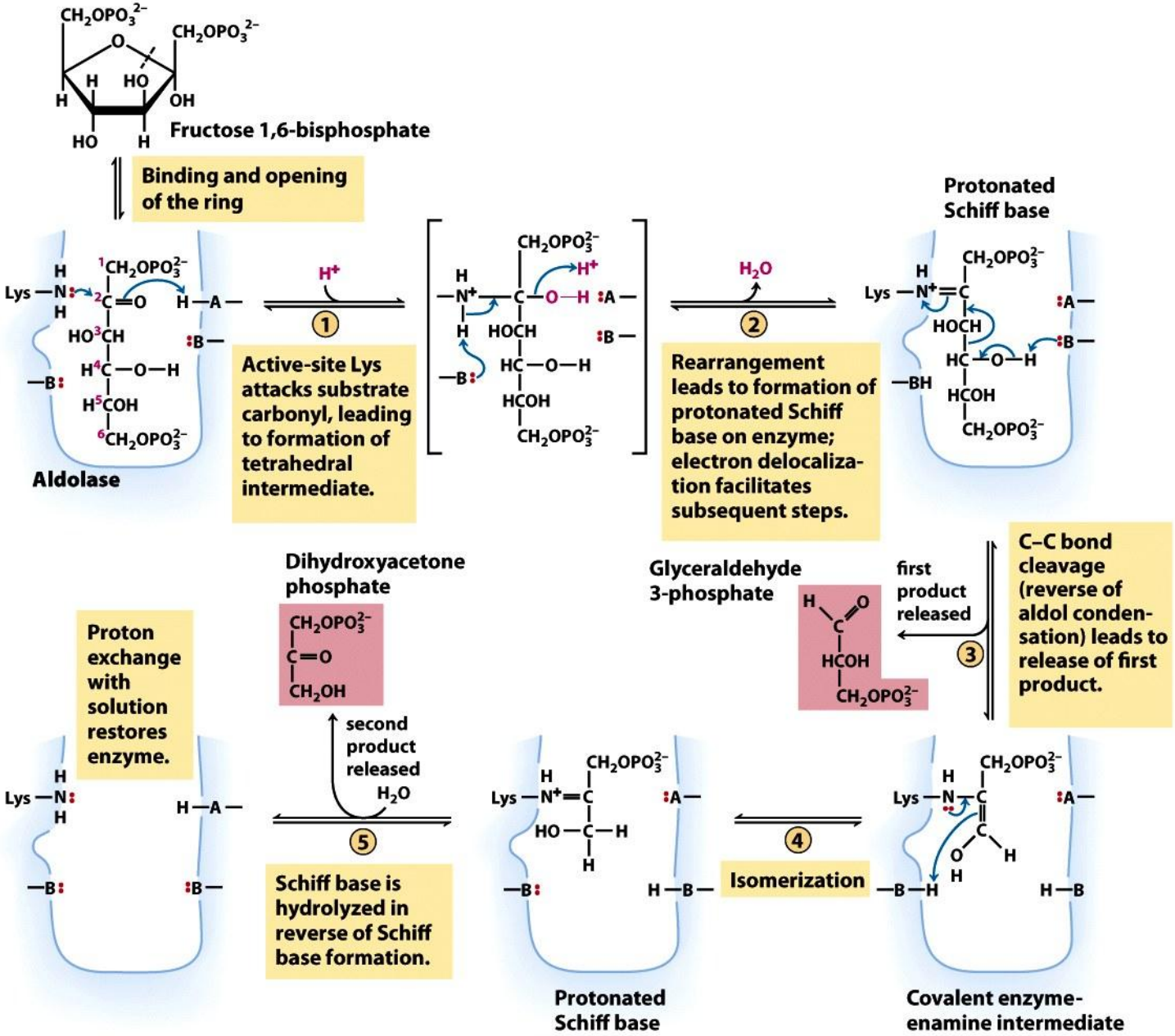

Figure 14-5

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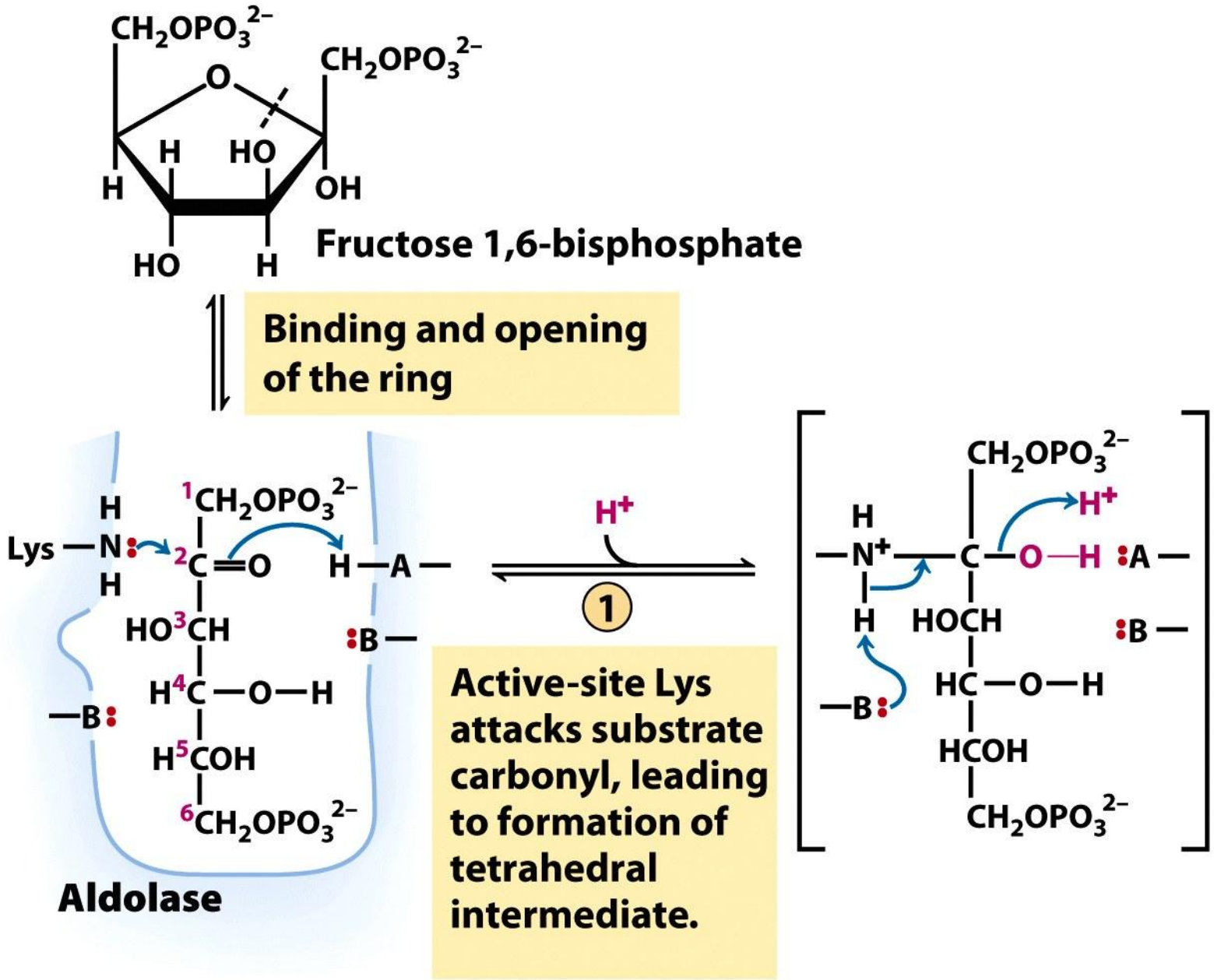

Figure 14-5 part 1
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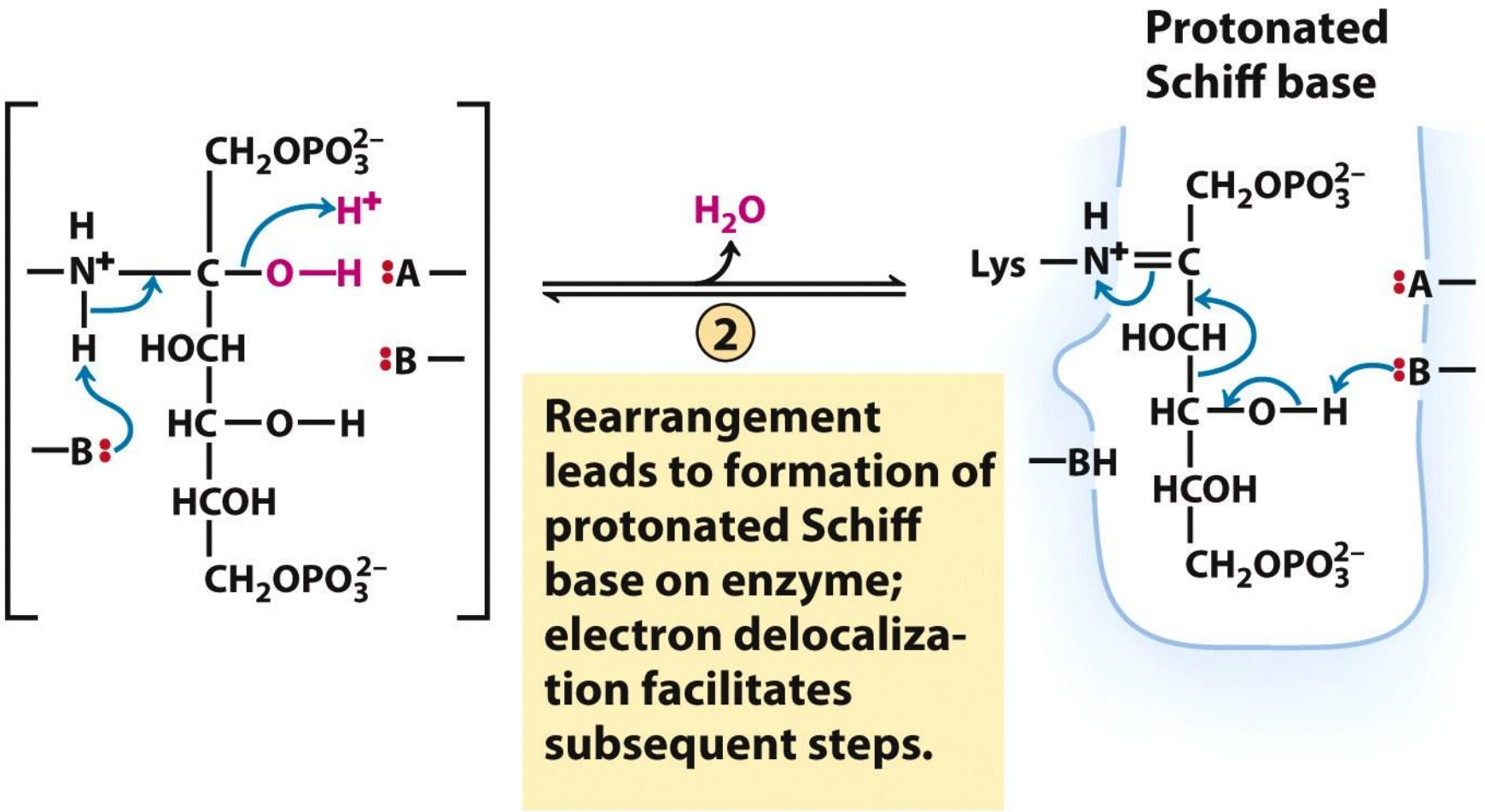

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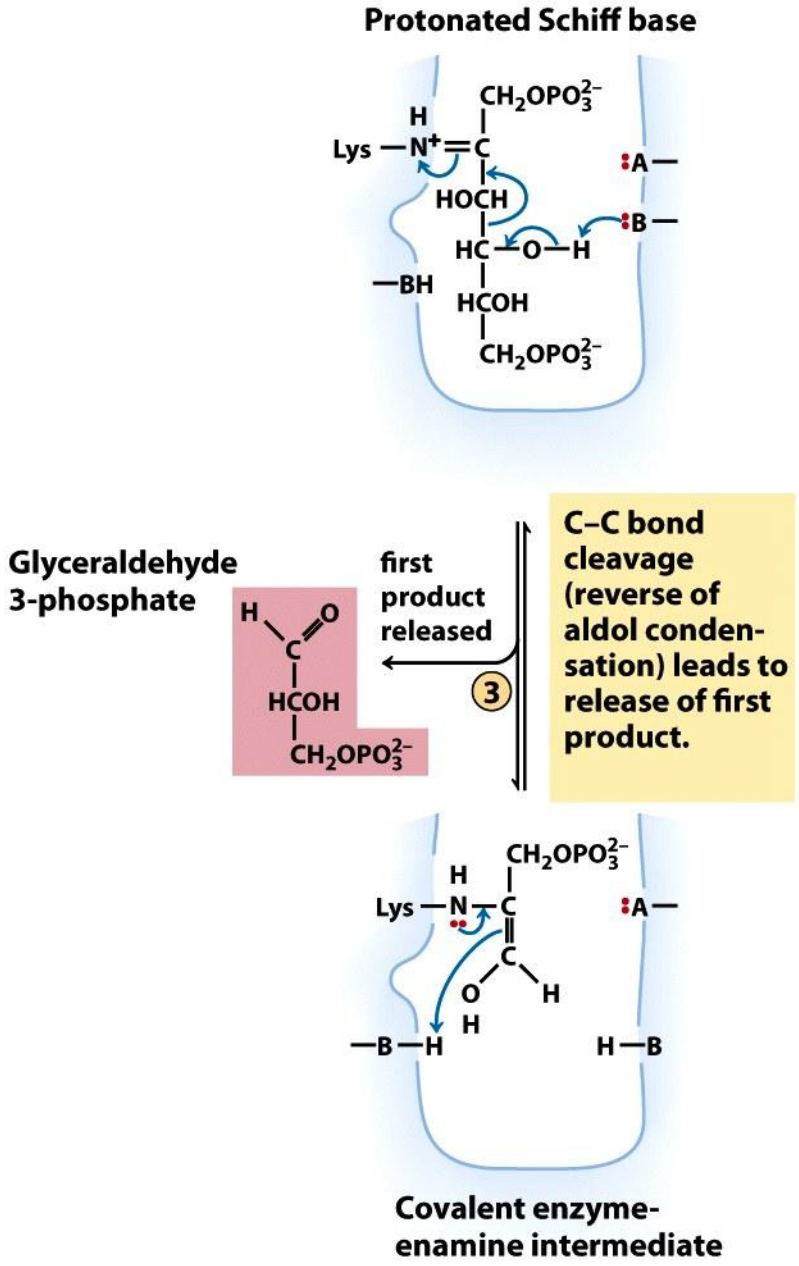

Figure 14-5 part 3

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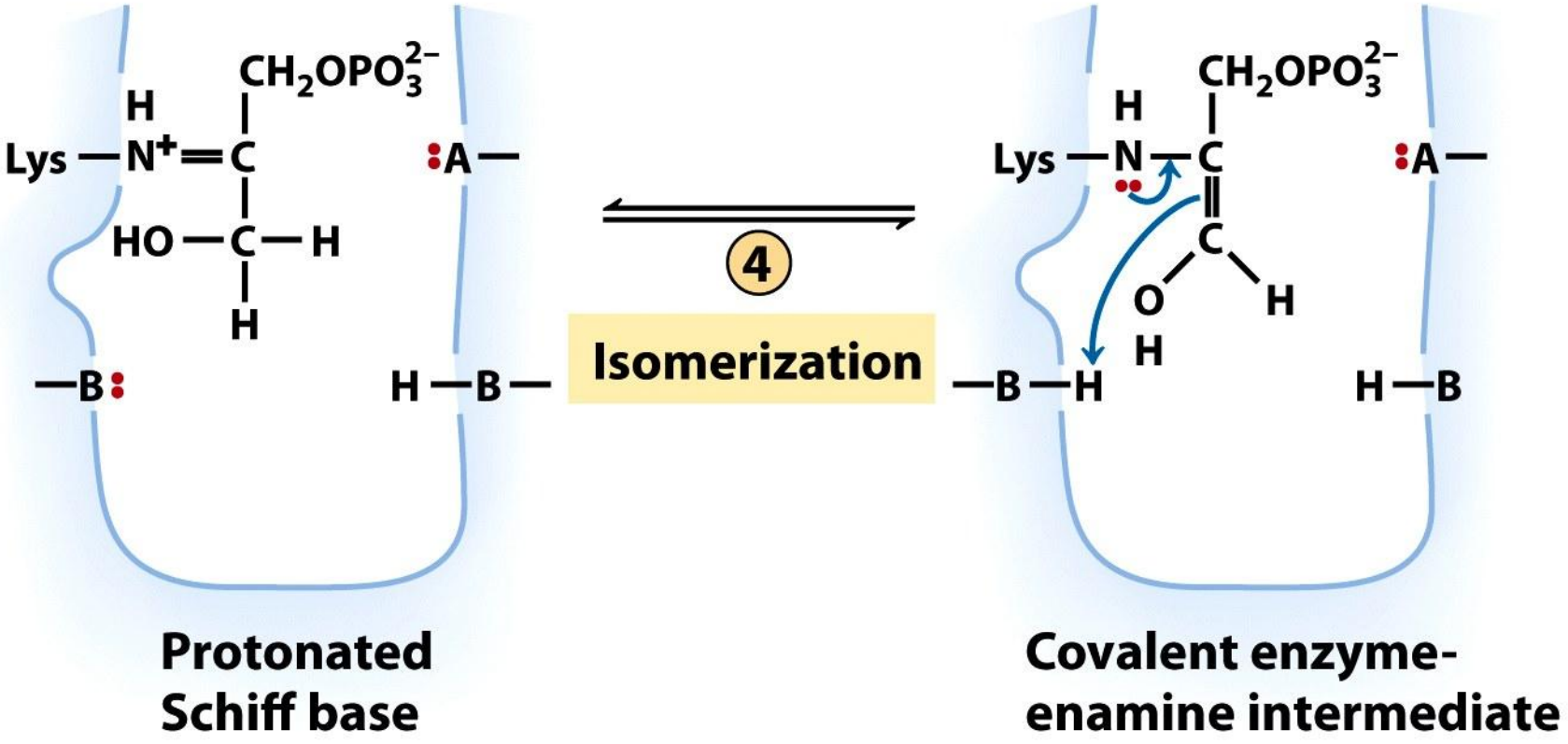

Figure 14-5 part 4
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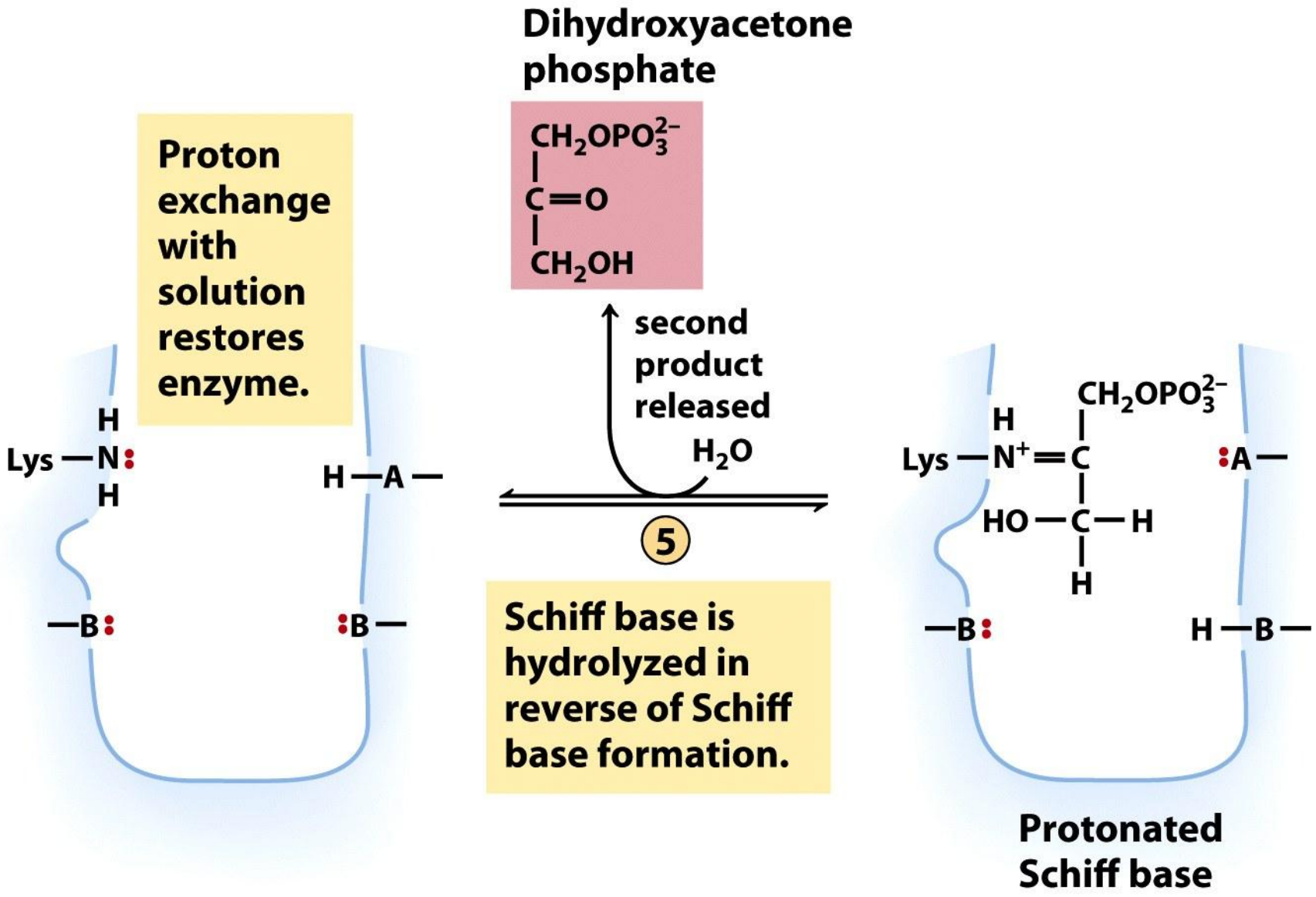

Figure 14-5 part 5
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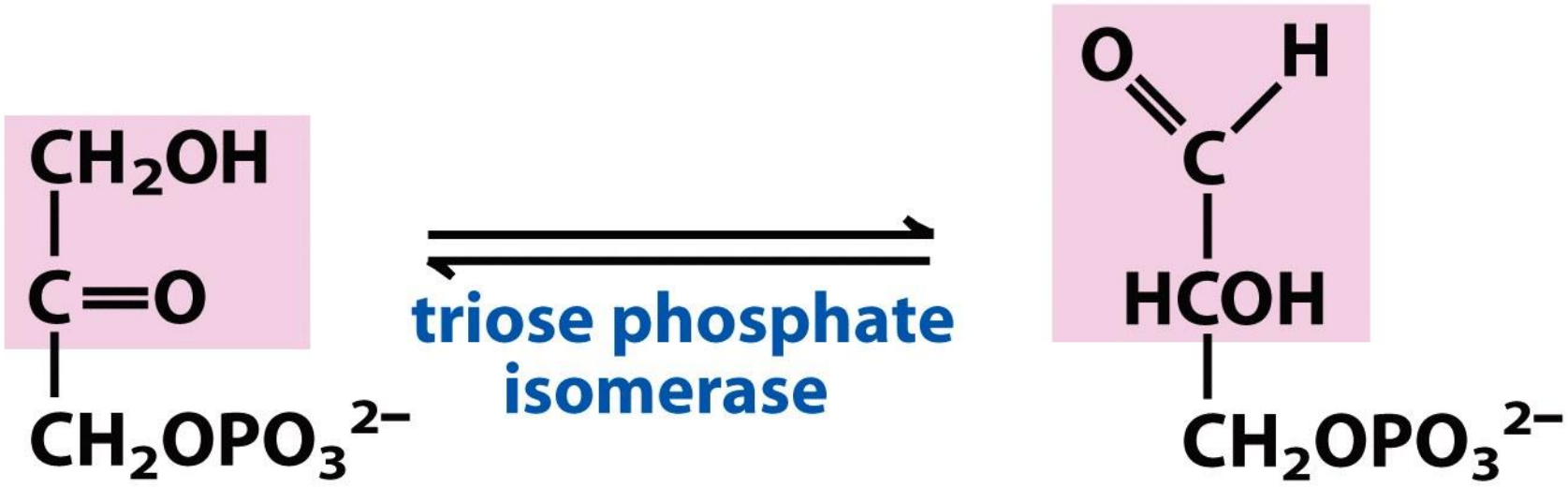

Dihydroxyacetone phosphate

Glyceraldehyde 3-phosphate

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

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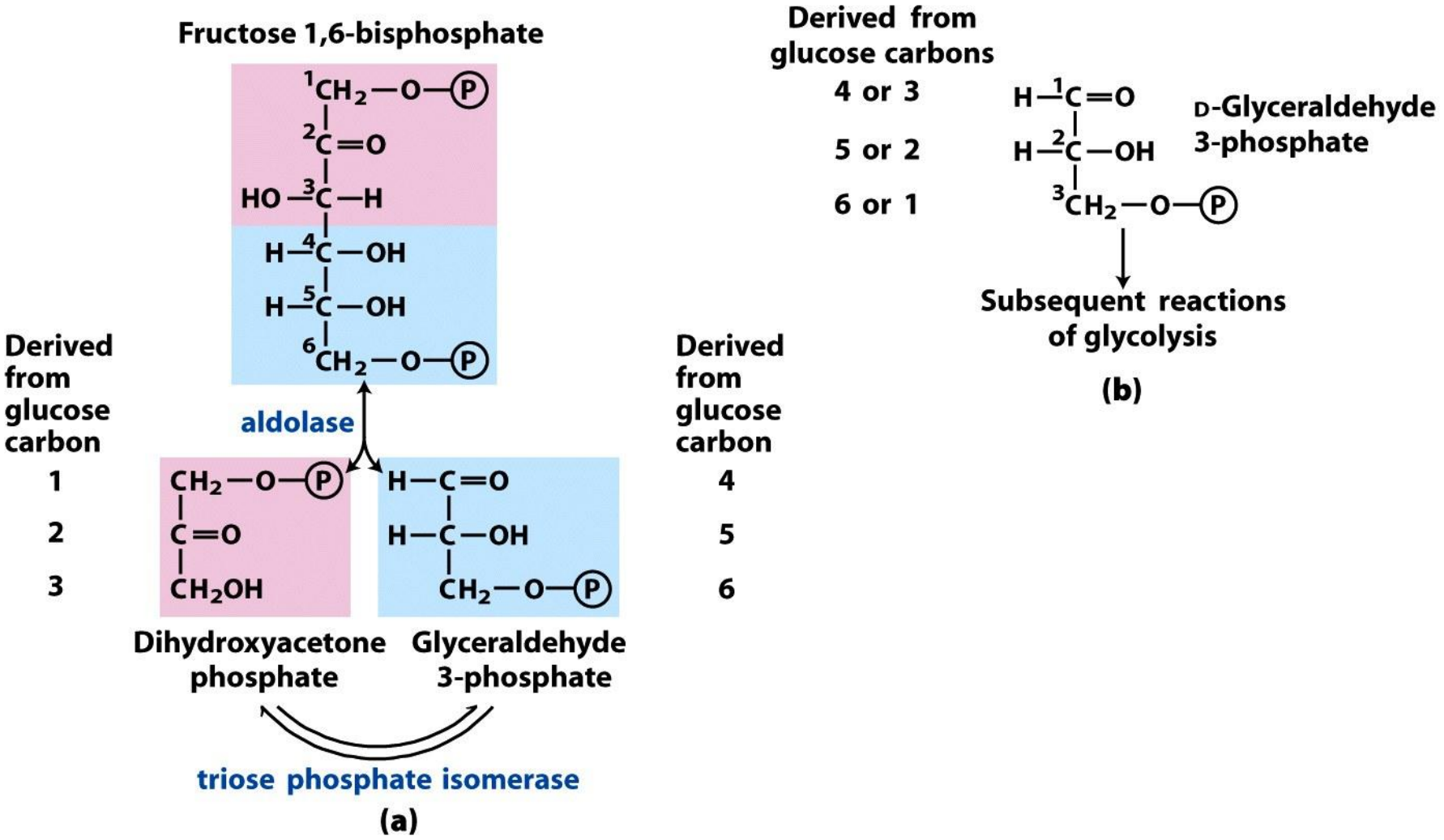

Figure 14-6
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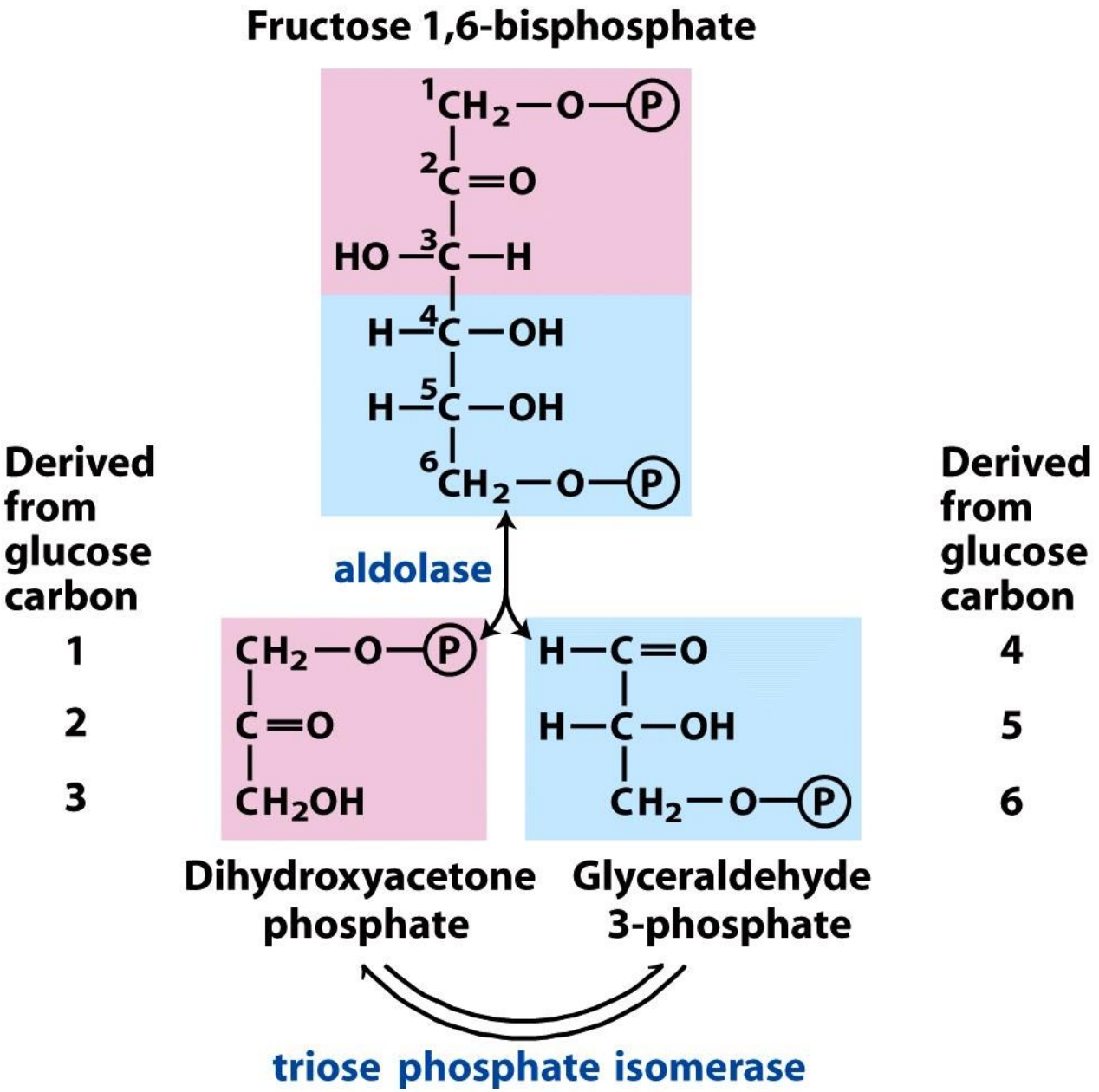

Figure 14-6a
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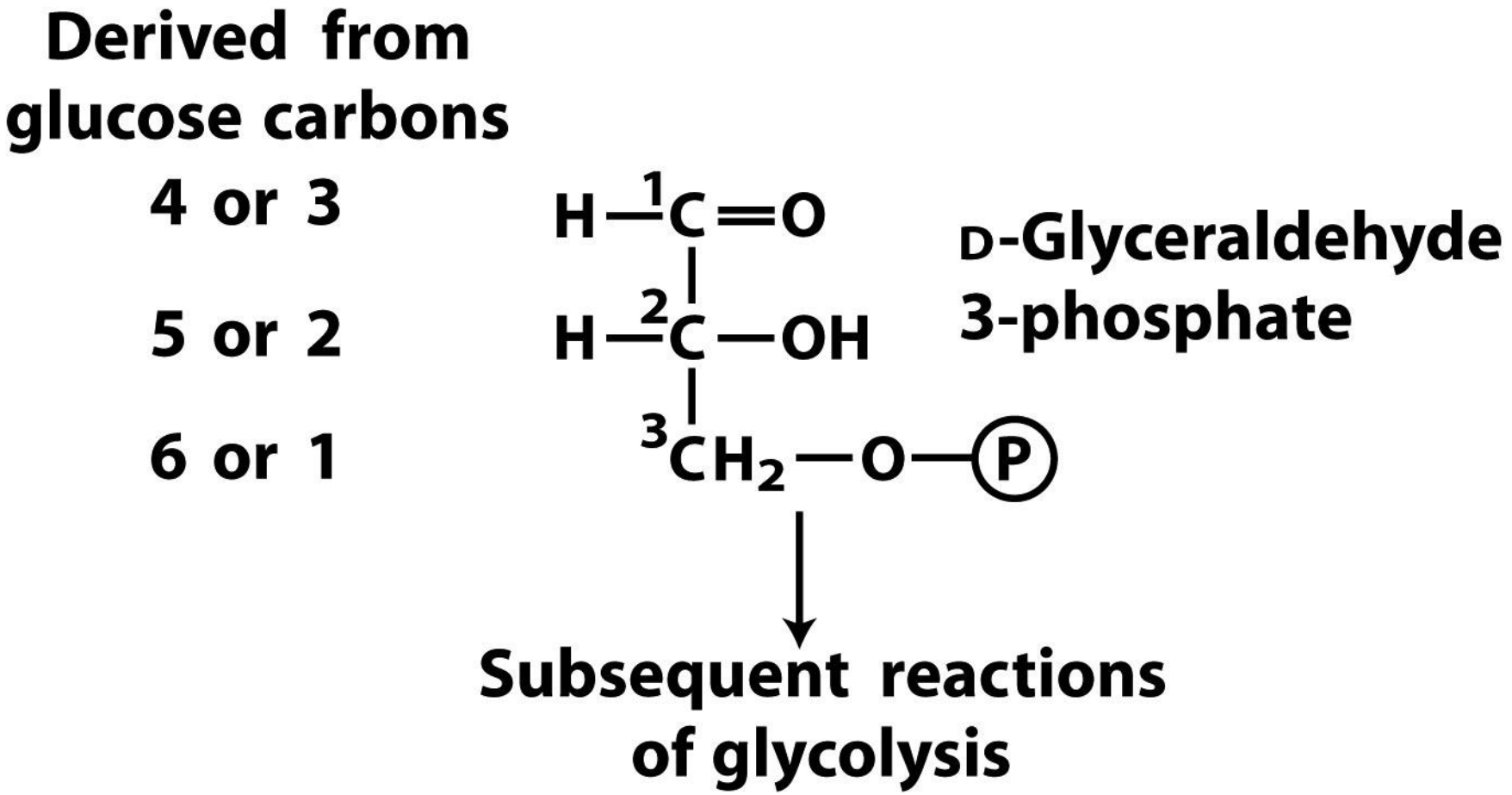

Figure 14-6b
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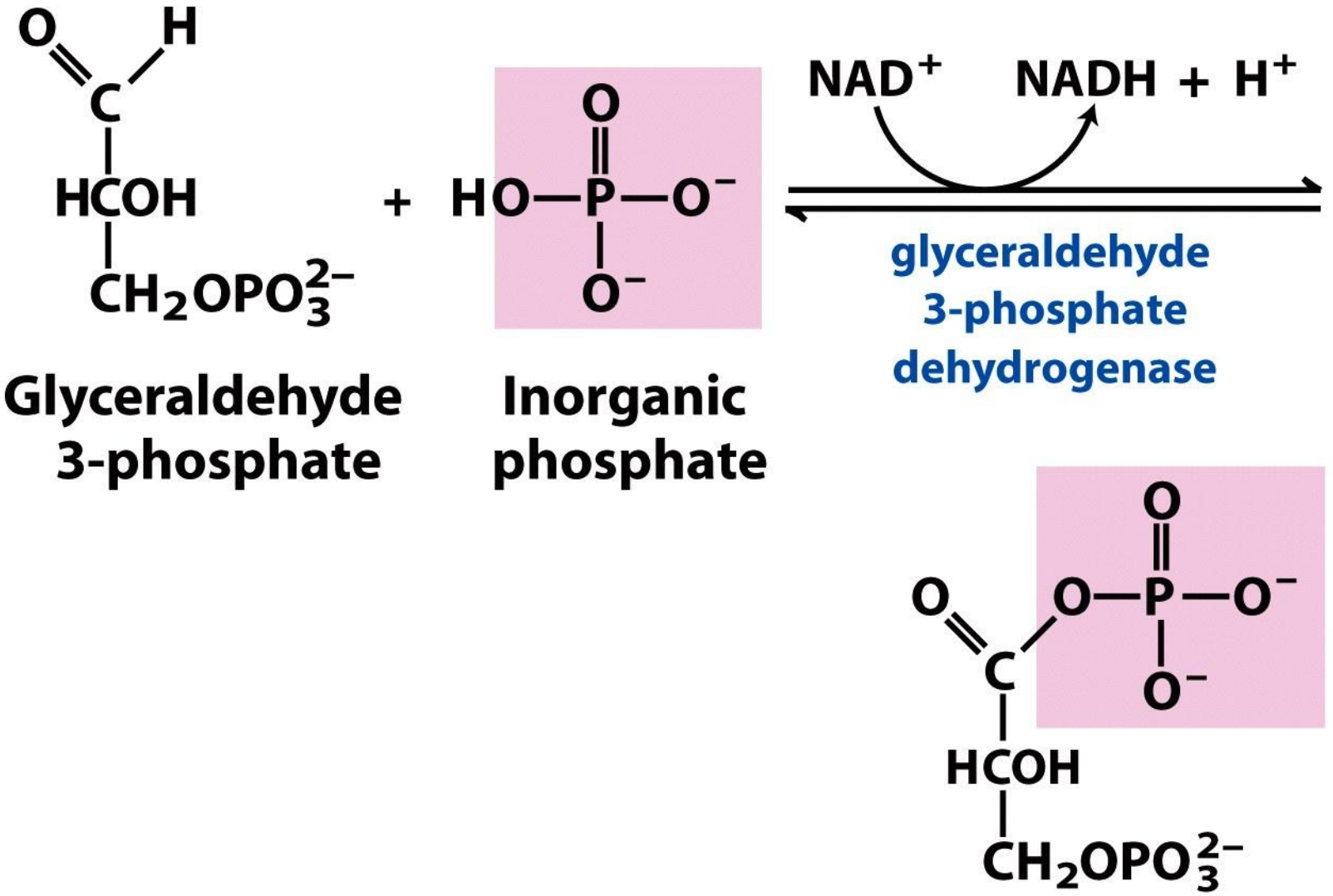

$\Delta G'^{\circ} = 6.3$ kJ/mol

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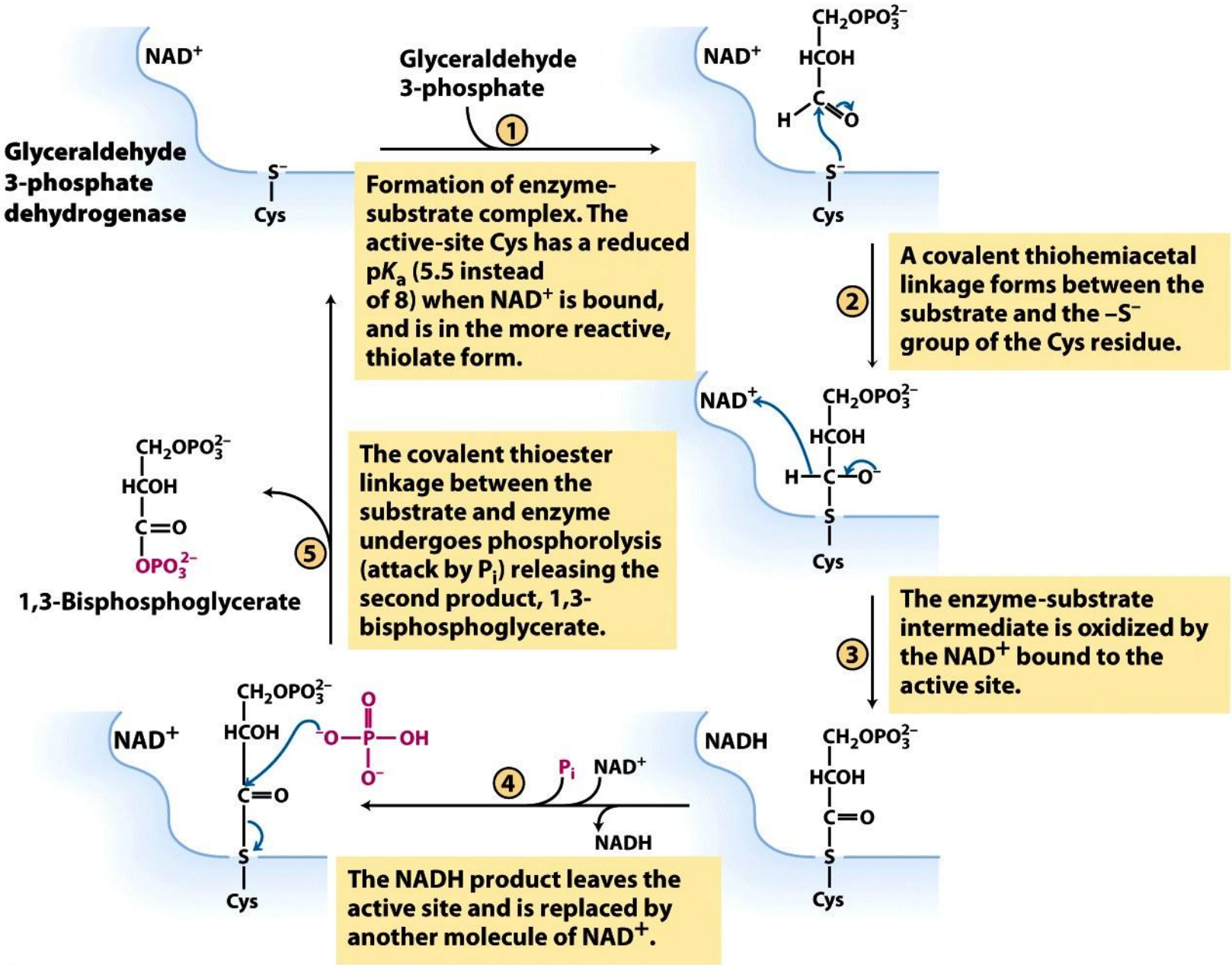

Figure 14-7

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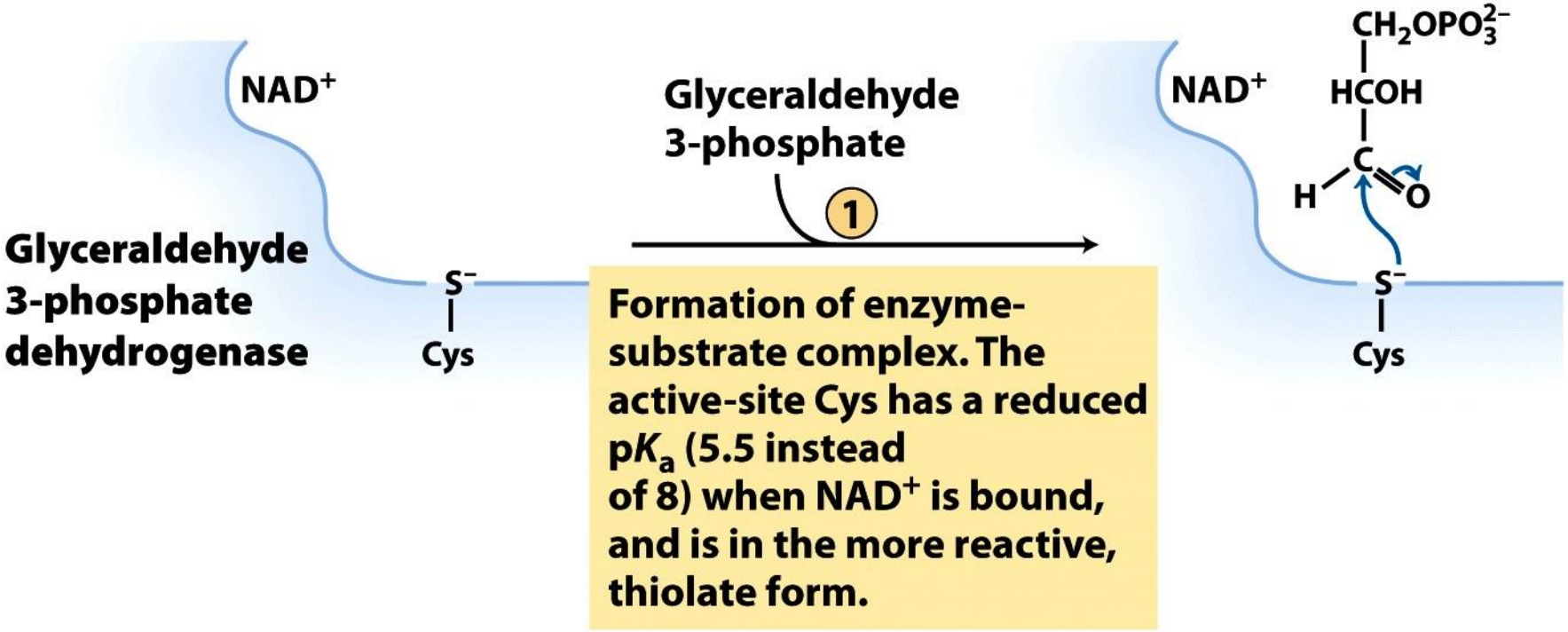

Figure 14-7 part 1
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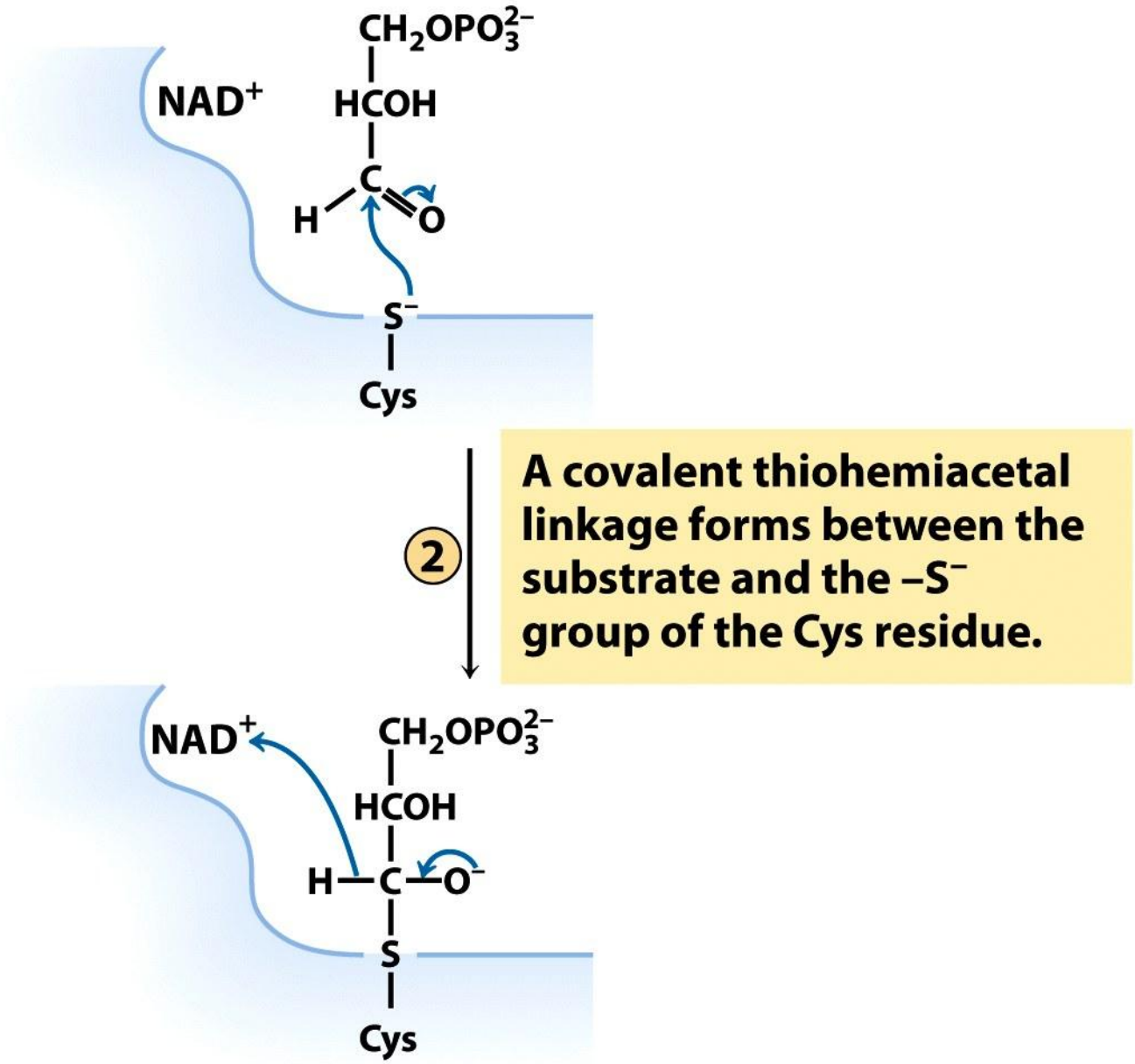

Figure 14-7 part 2
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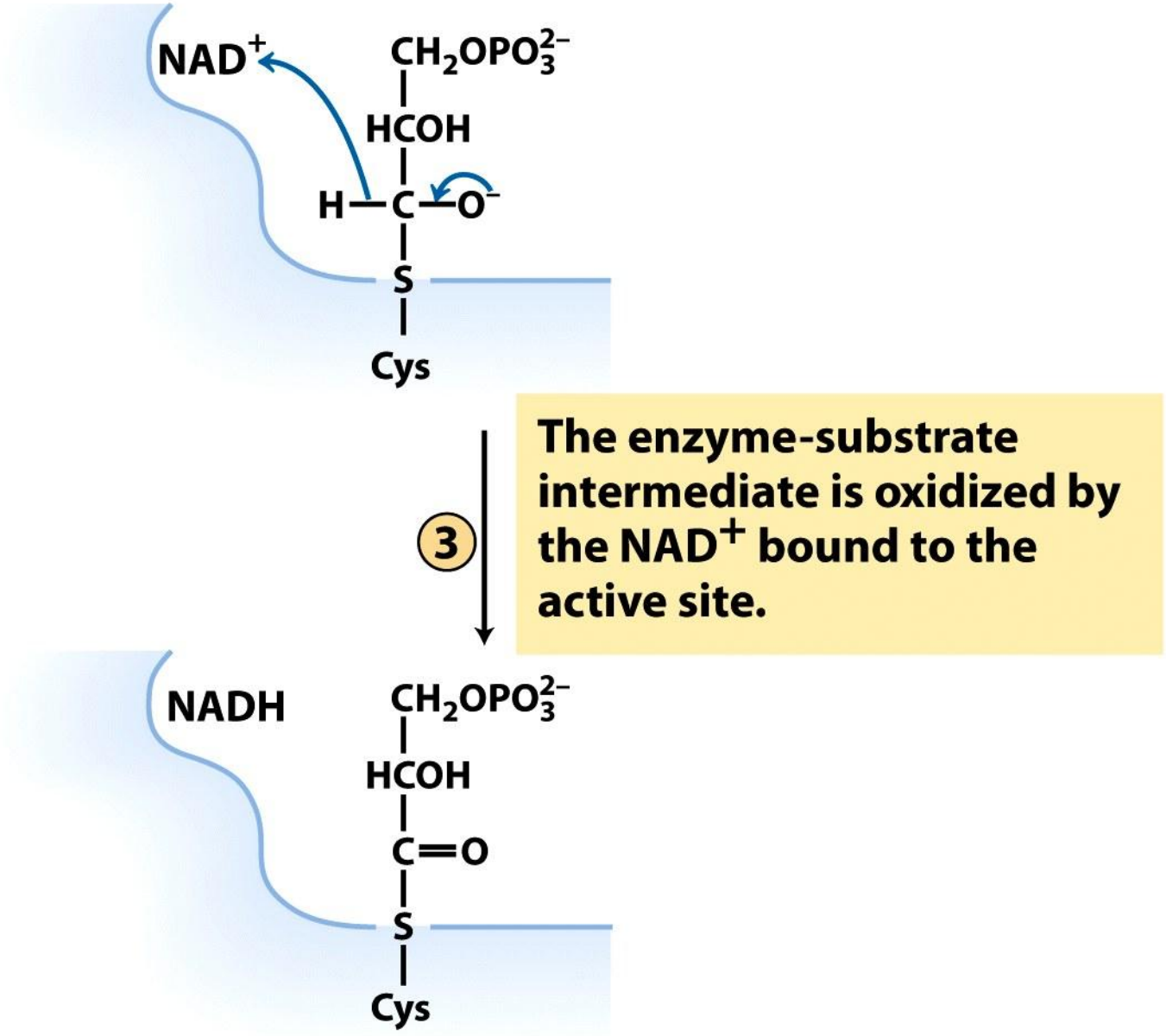

Figure 14-7 part 3
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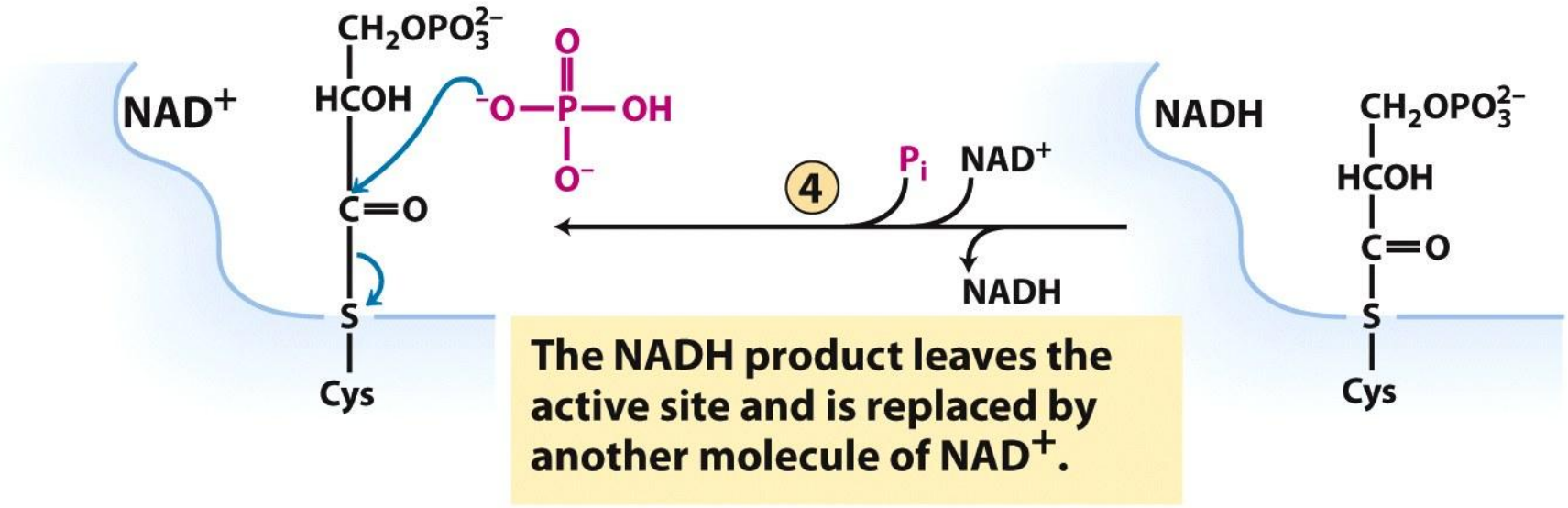

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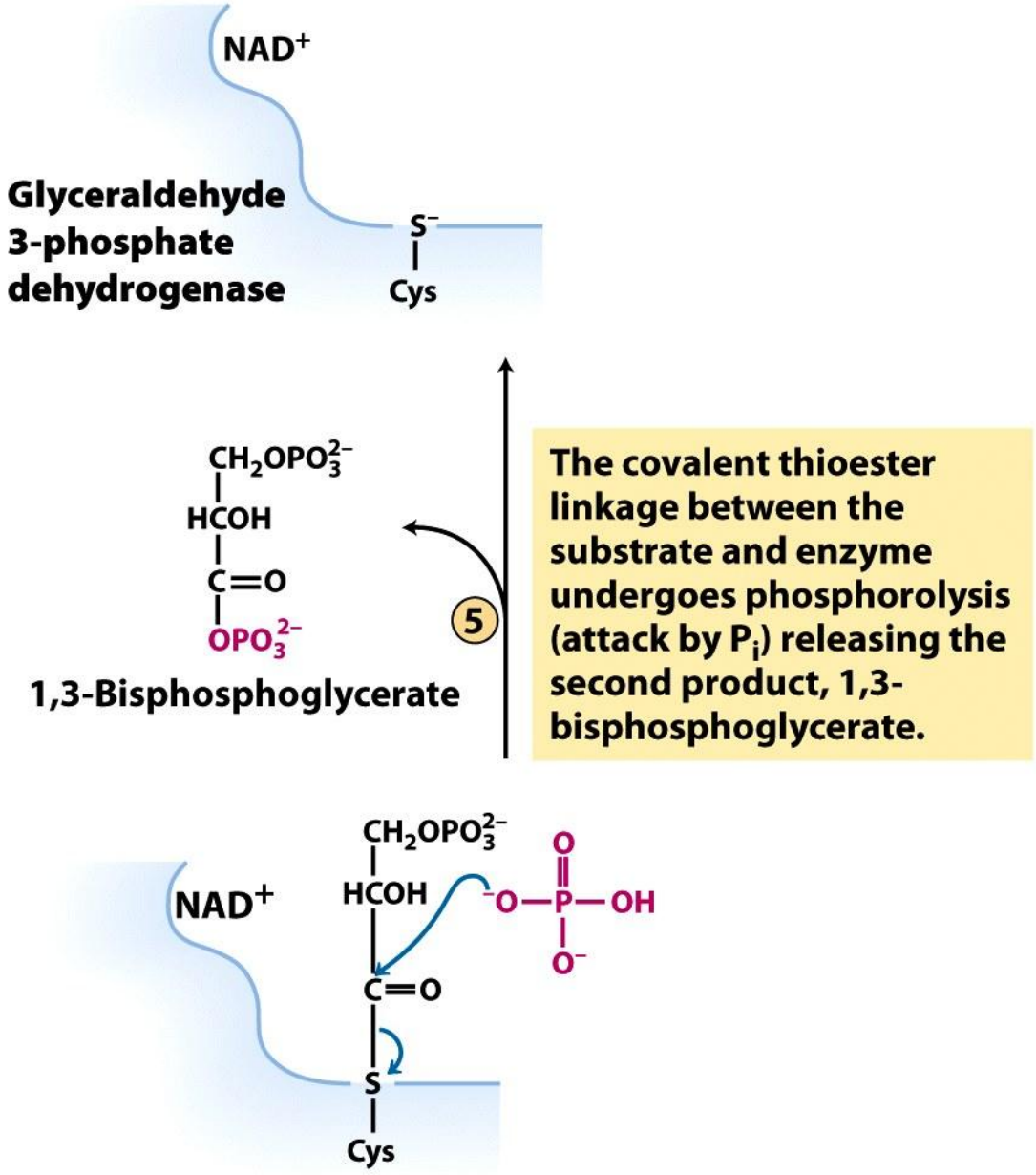

Figure 14-7 part 5

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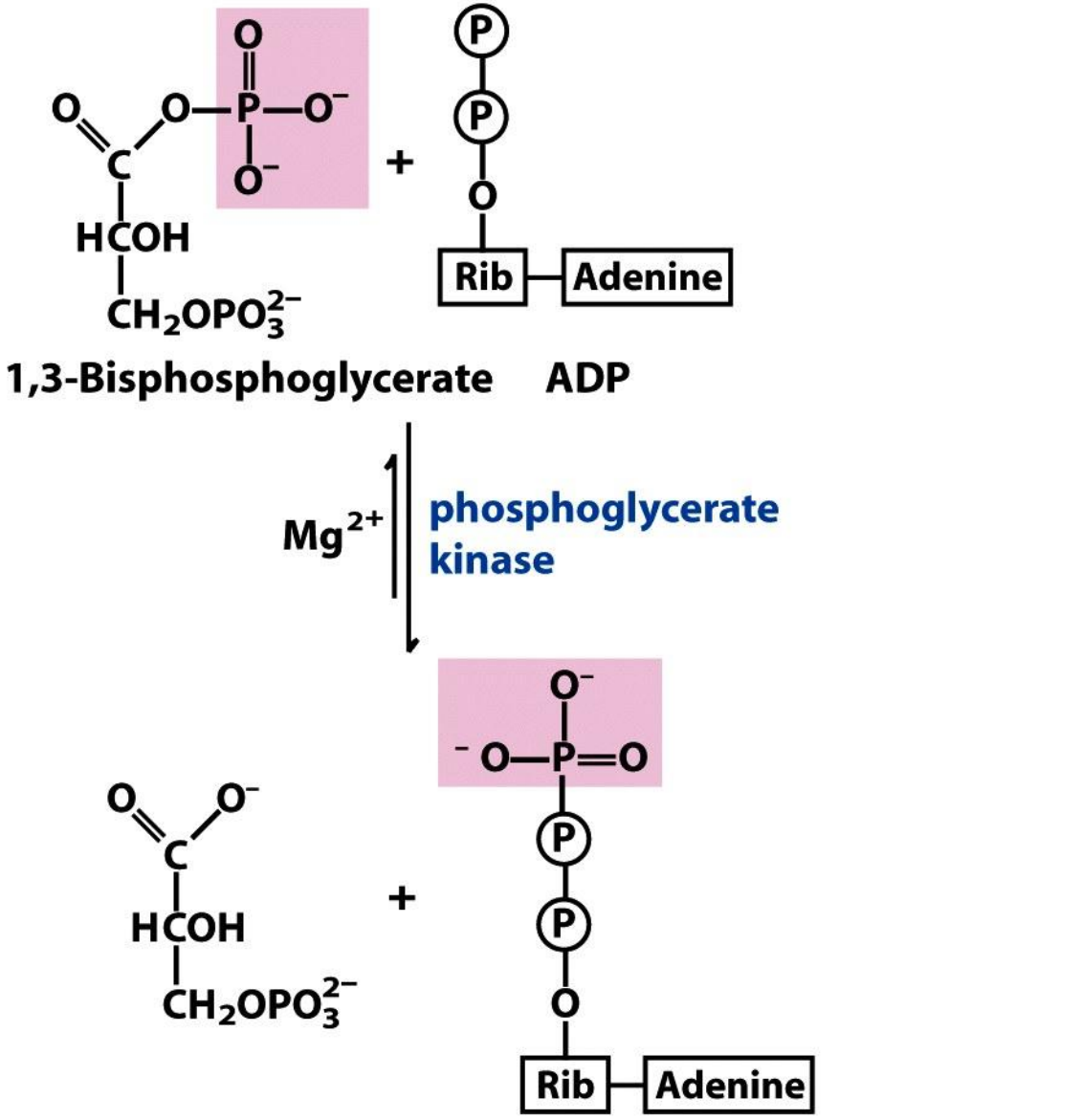

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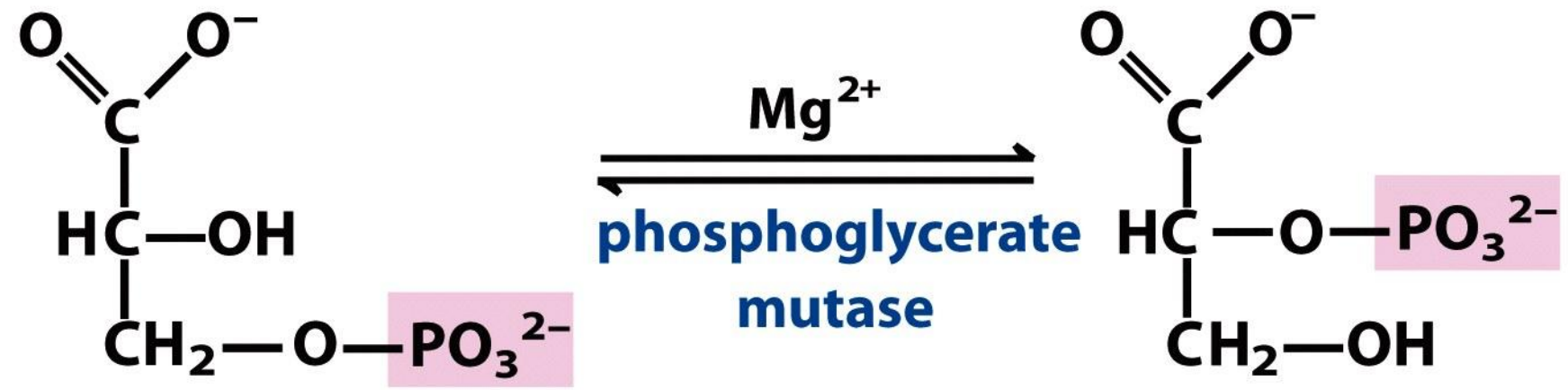

3-Phosphoglycerate

2-Phosphoglycerate

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

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Phosphoglycerate mutase

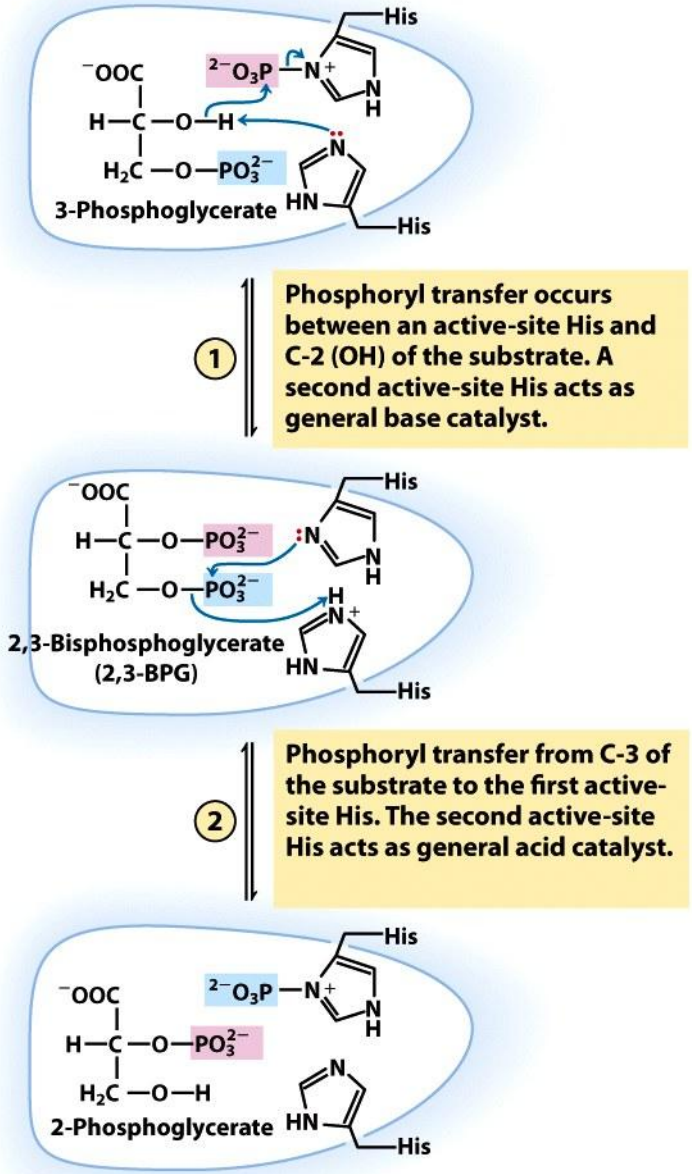

Figure 14-8

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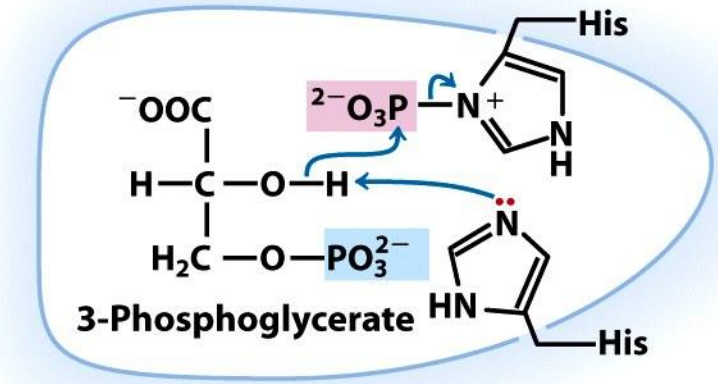
Phosphoglycerate mutase



1

Phosphoryl transfer occurs between an active-site His and C-2 (OH) of the substrate. A second active-site His acts as general base catalyst.

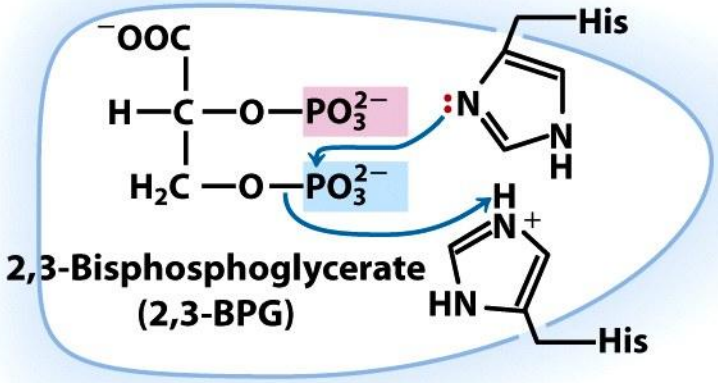


Figure 14-8 part 1

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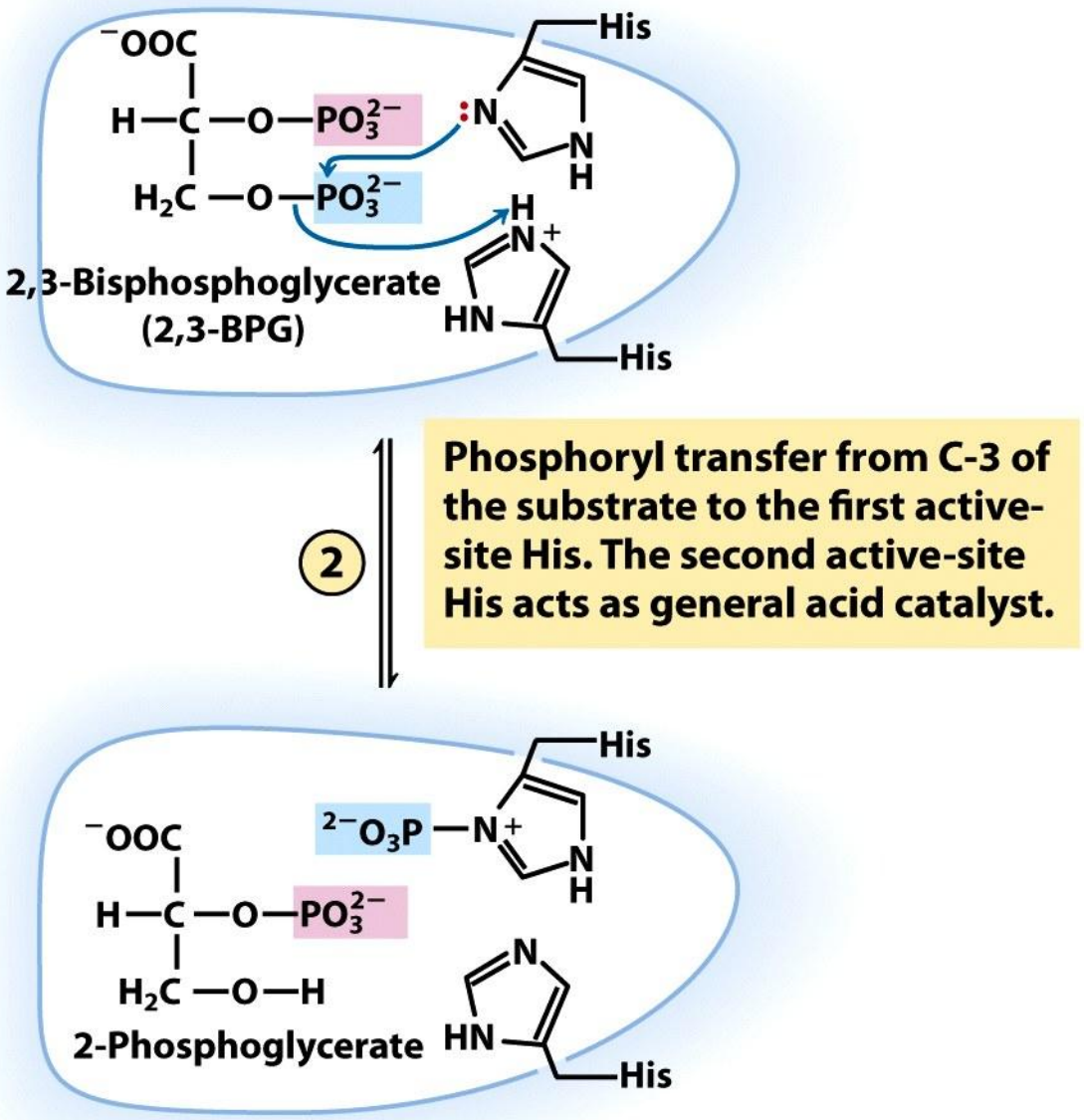

Figure 14-8 part 2

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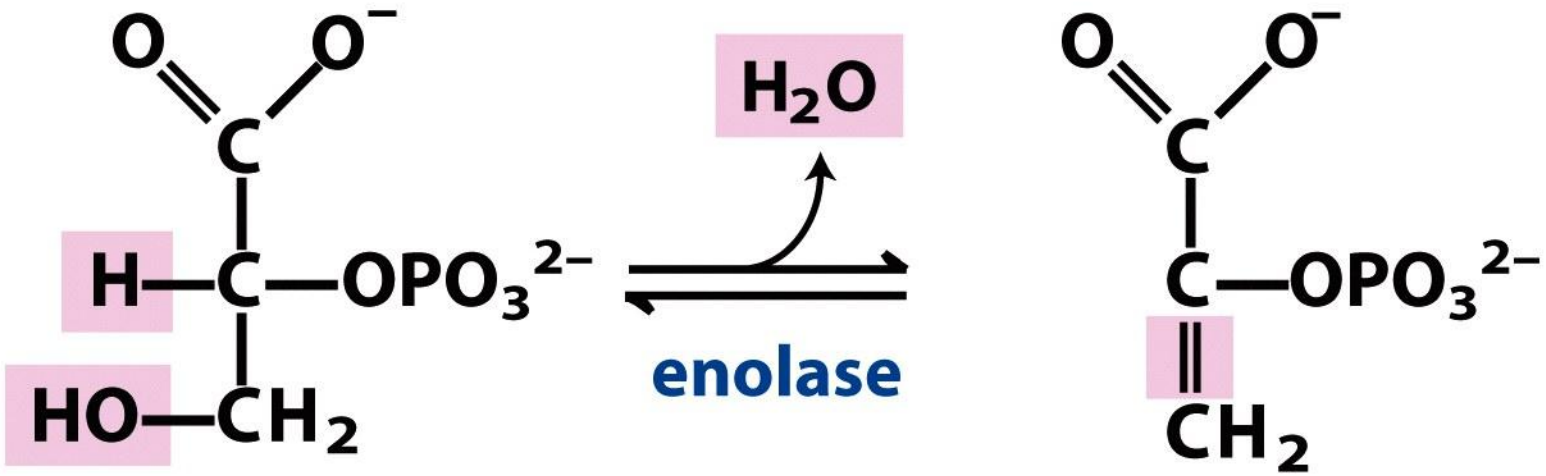

2-Phosphoglycerate **Phosphoenolpyruvate**

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

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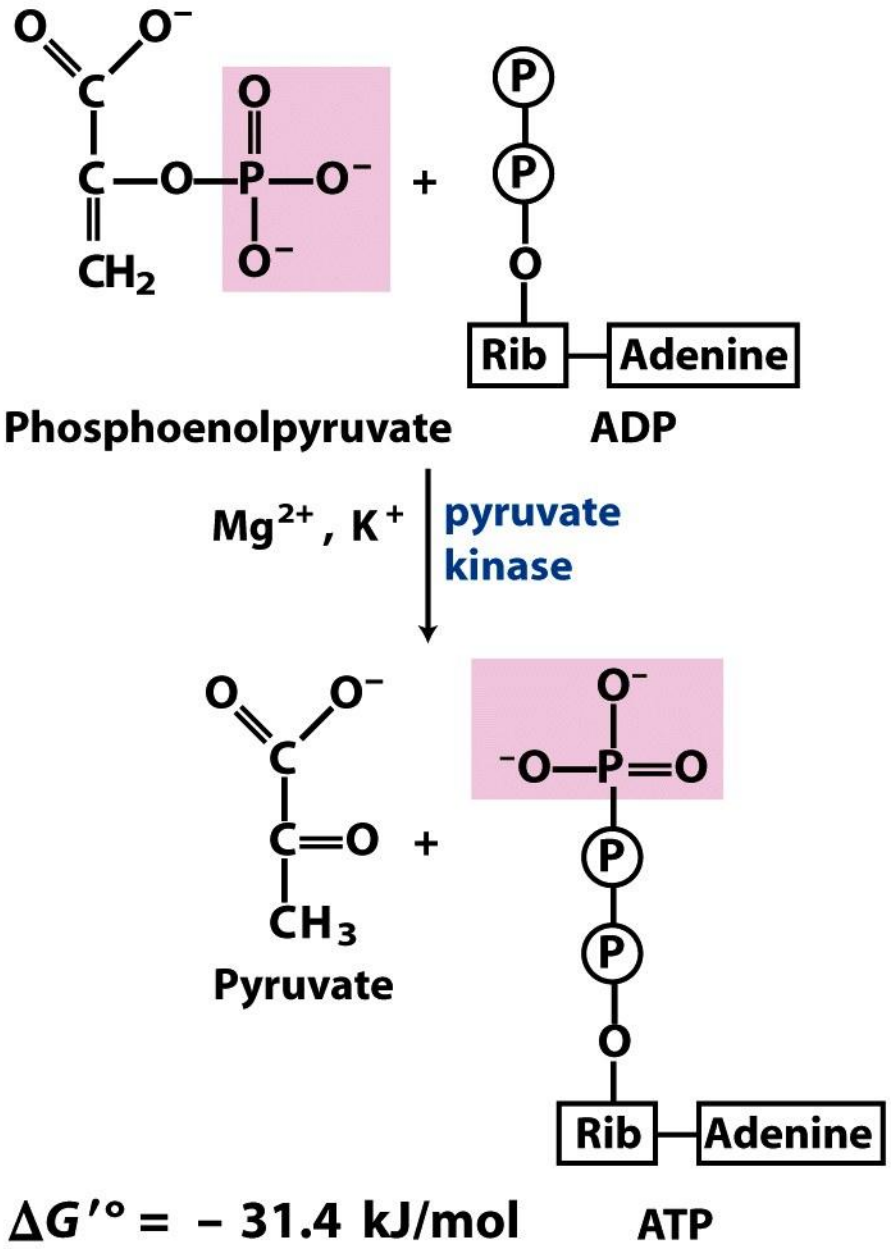

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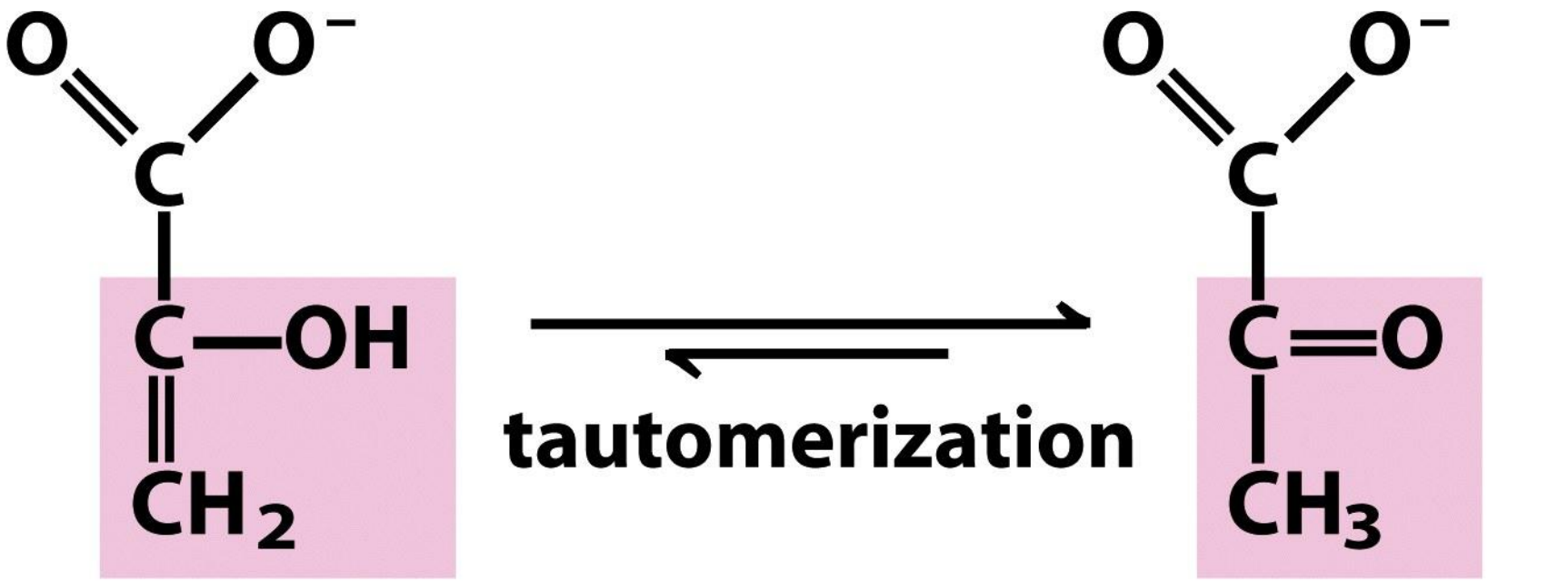

Pyruvate (enol form)

Pyruvate (keto form)

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Otto Warburg, 1883–1970

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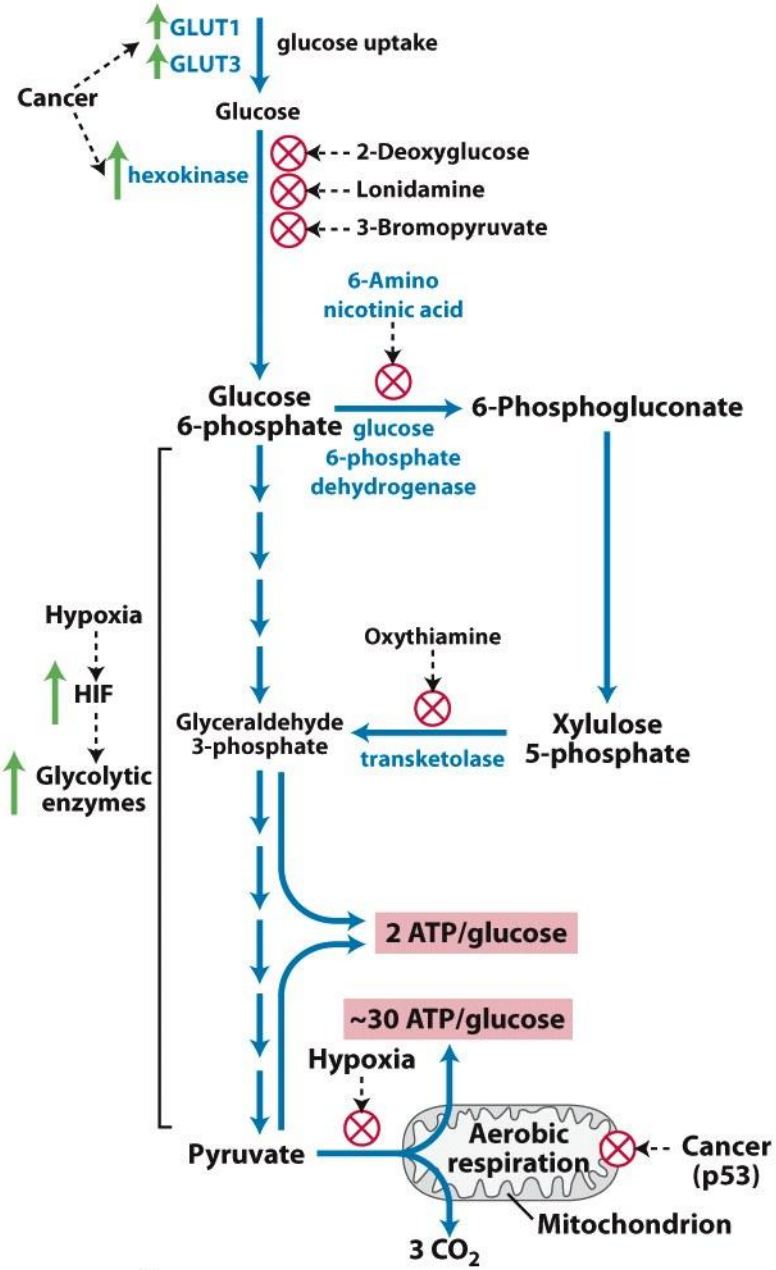

Box 14-1 figure 1

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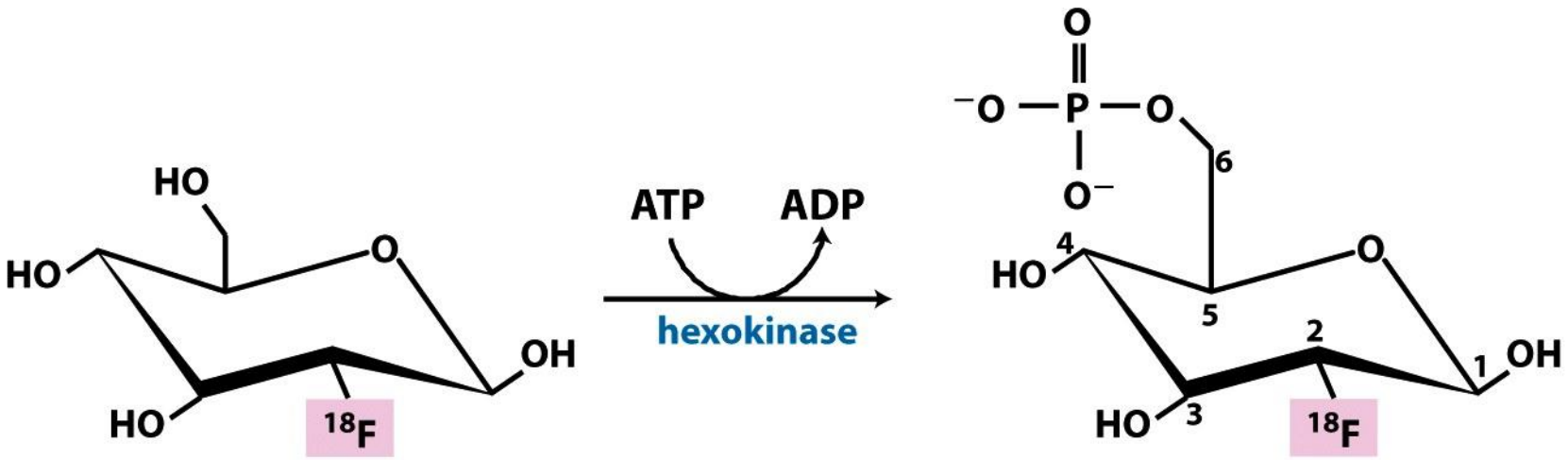

[18F]2-Fluoro-2-deoxyglucose (FdG)

[18F]6-Phospho-2-fluoro-2-deoxyglucose (6-Phospho-FdG)

Box 14-1 figure 2

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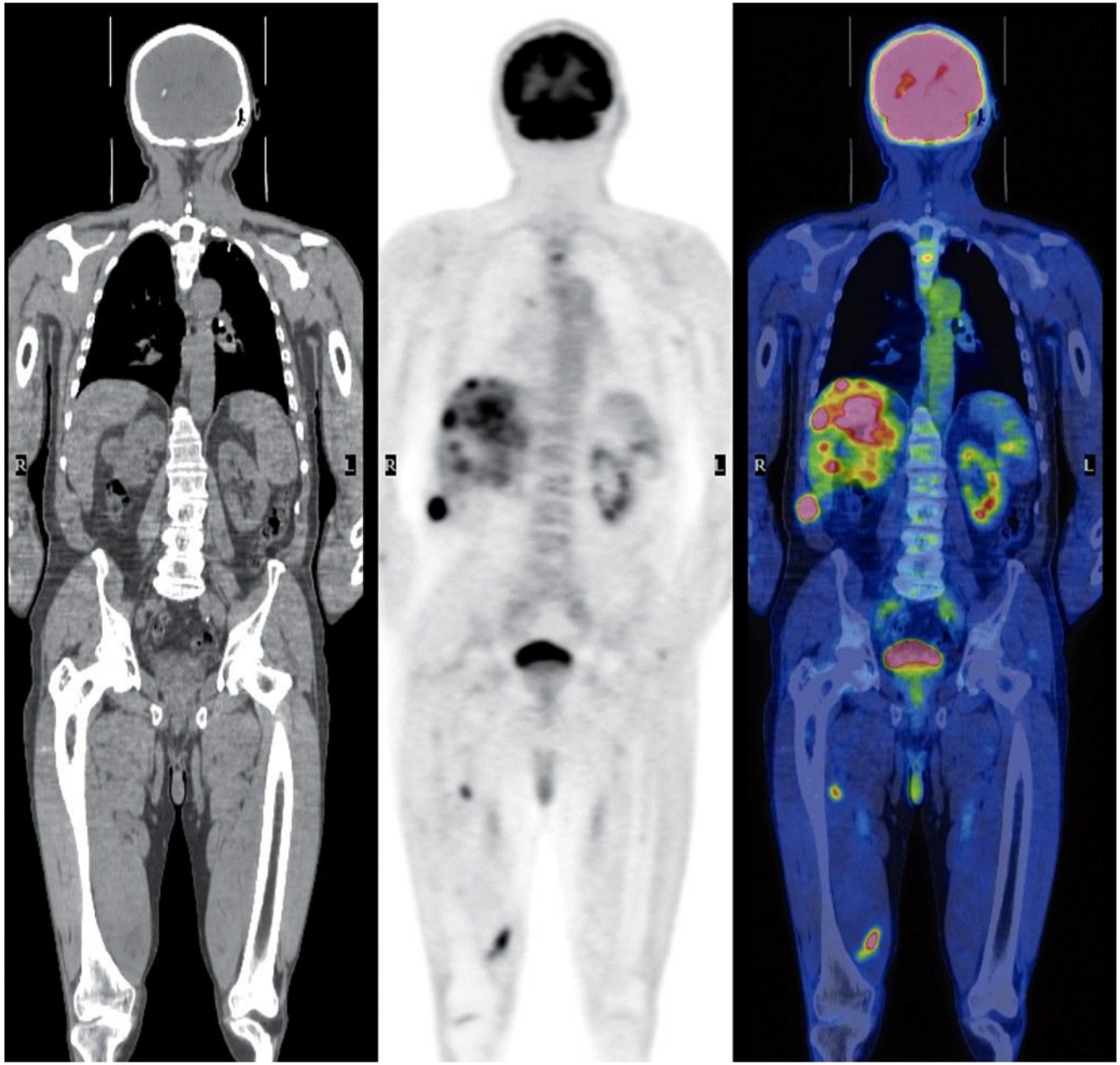

Box 14-1 figure 3

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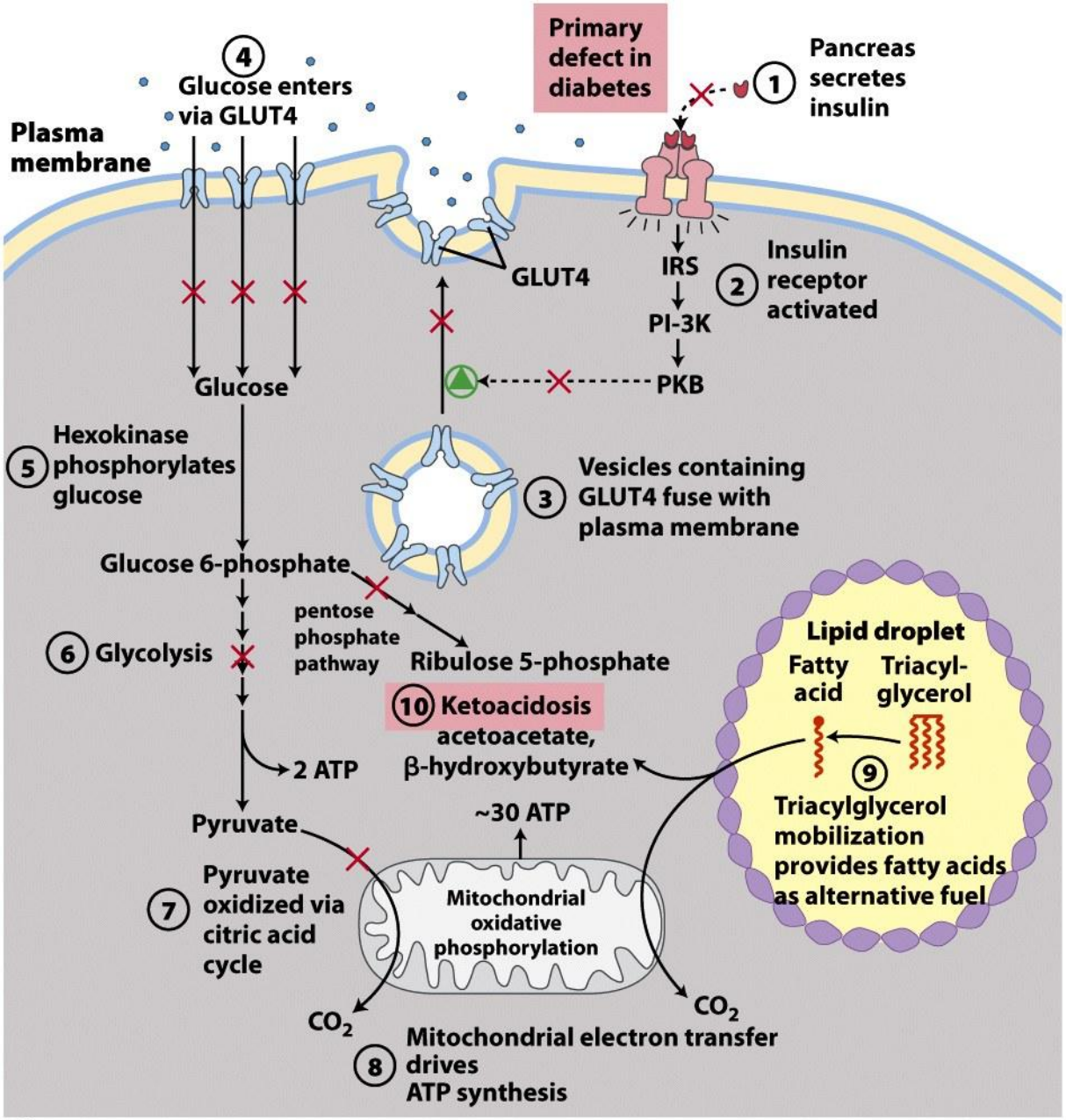

Figure 14-9

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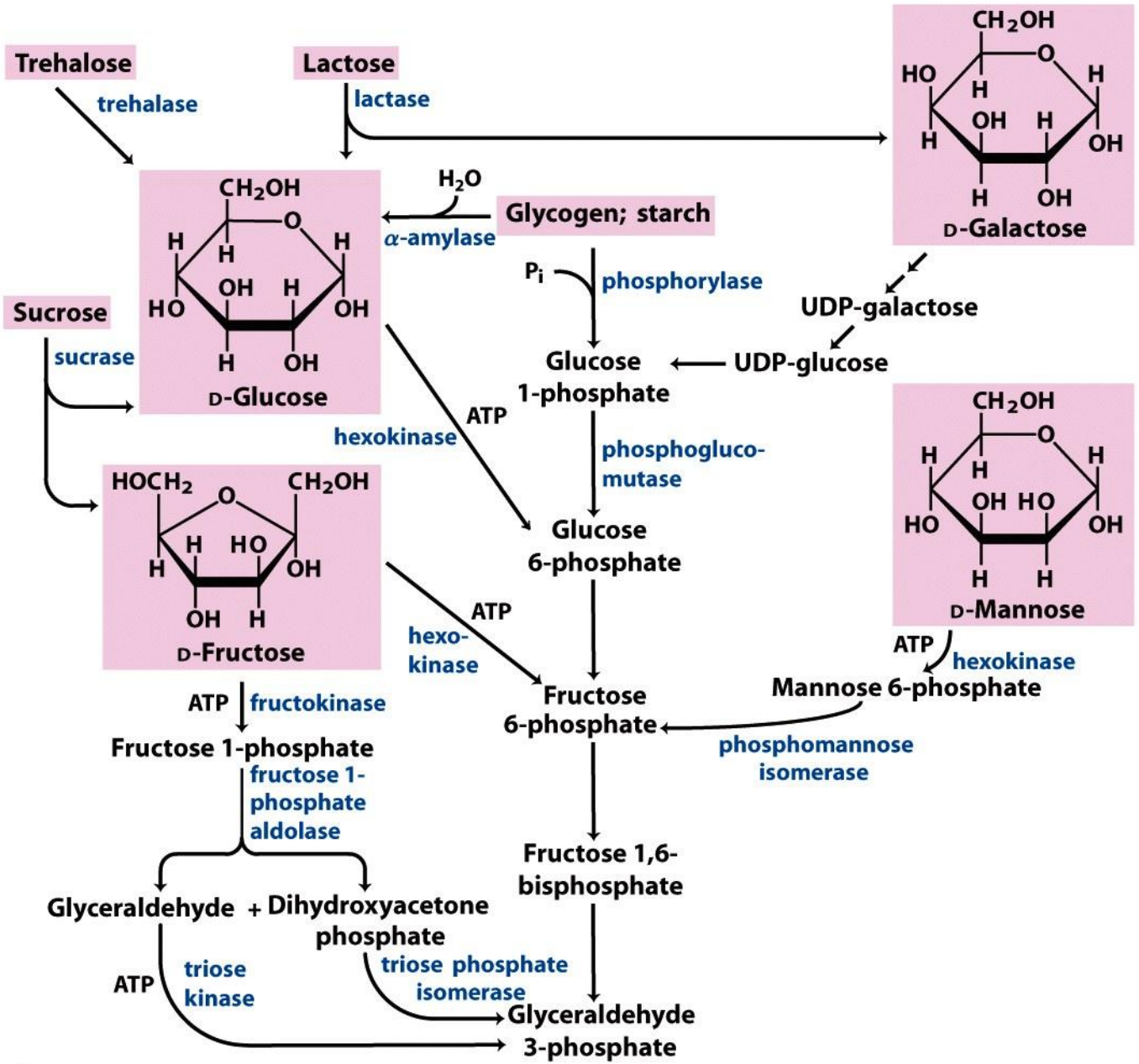

Figure 14-10

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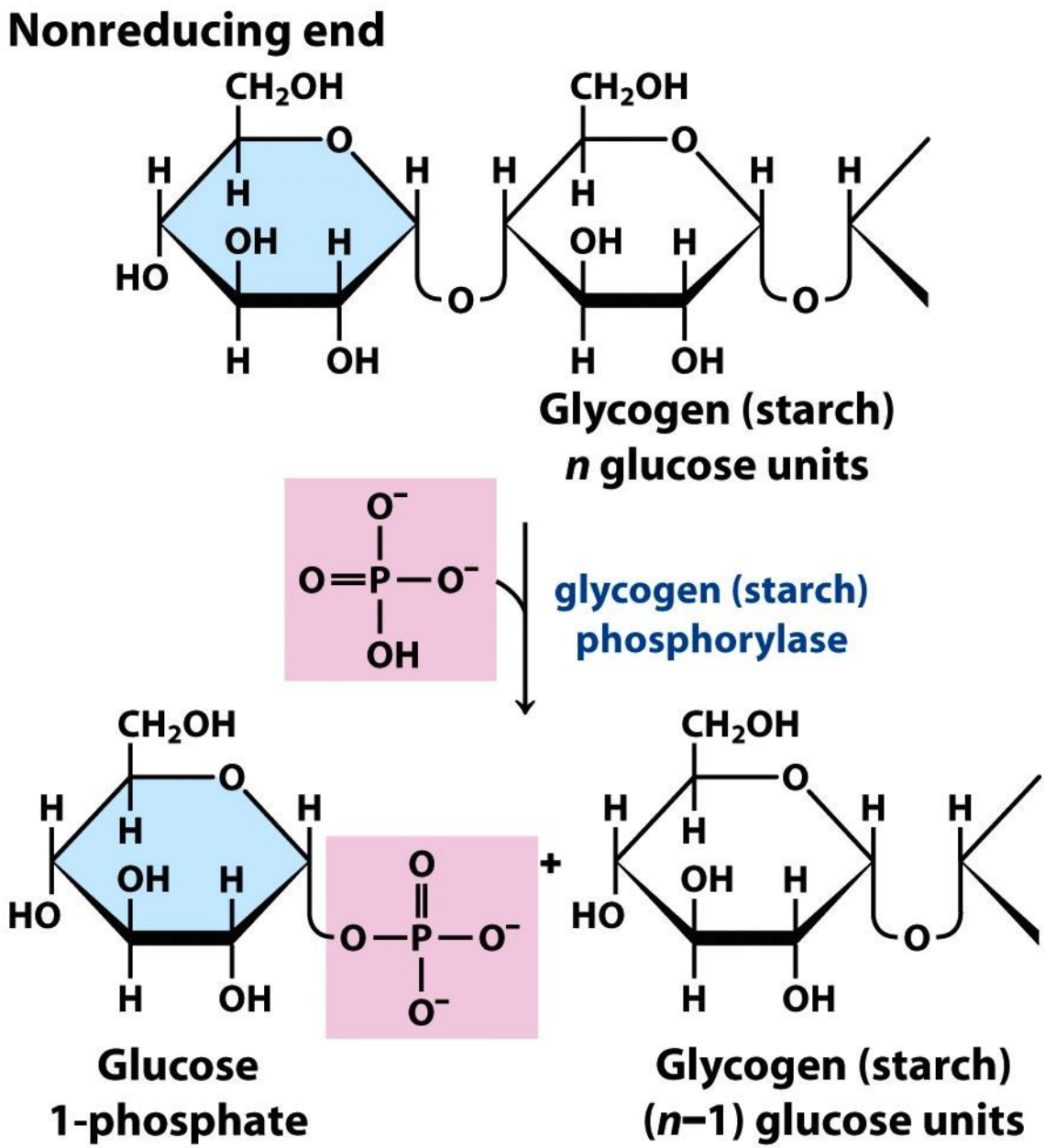

Figure 14-11
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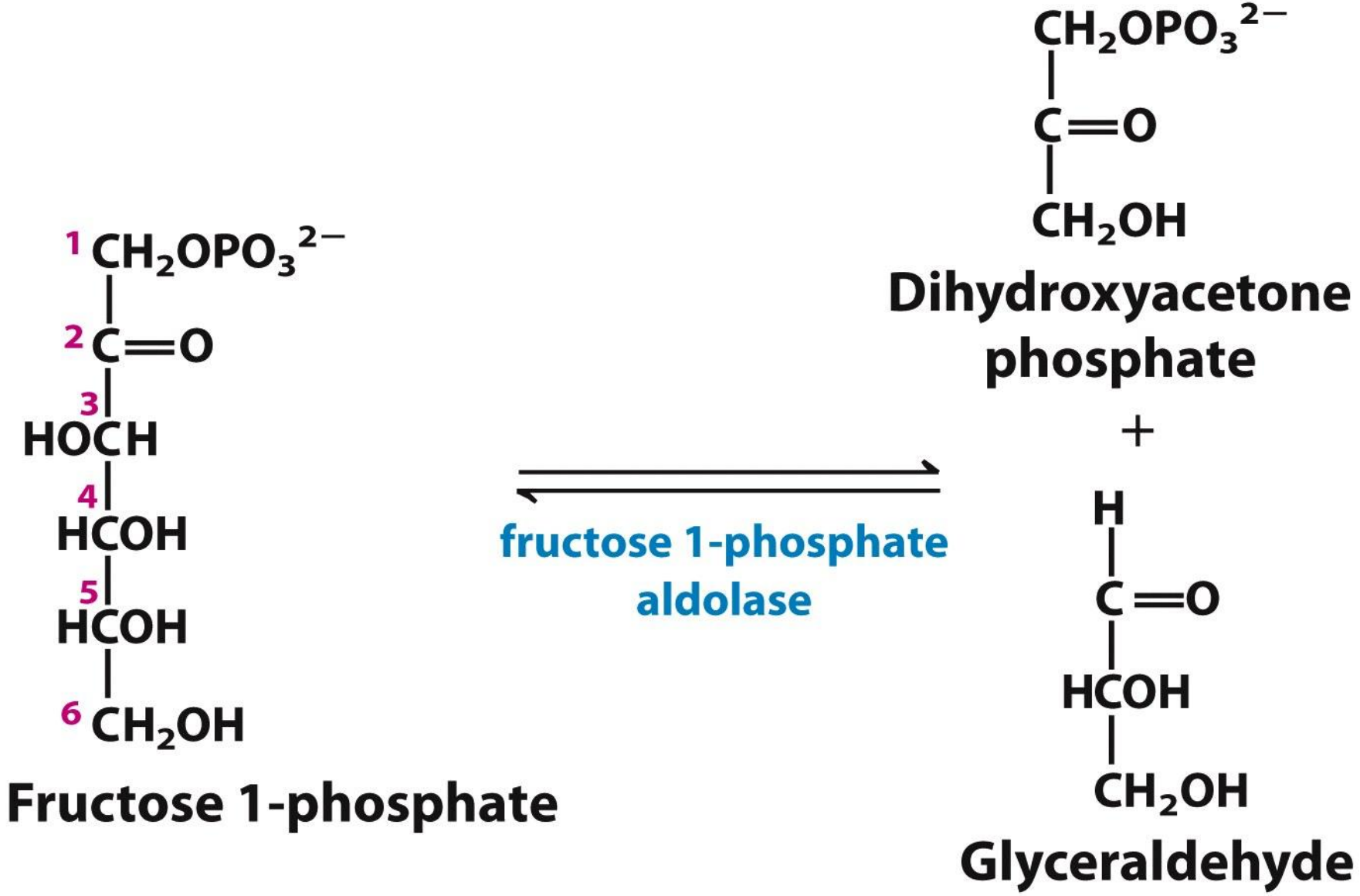

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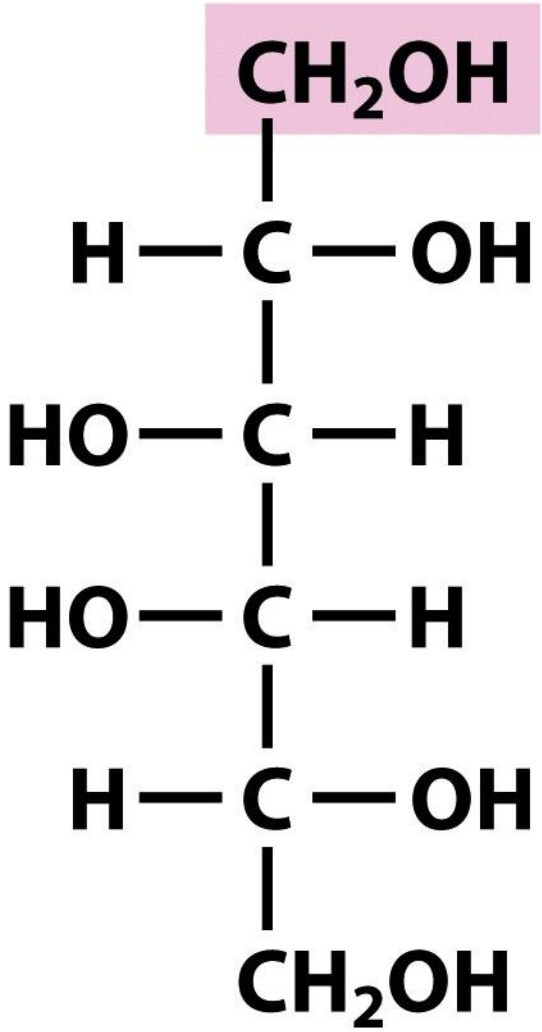

D-Galactitol

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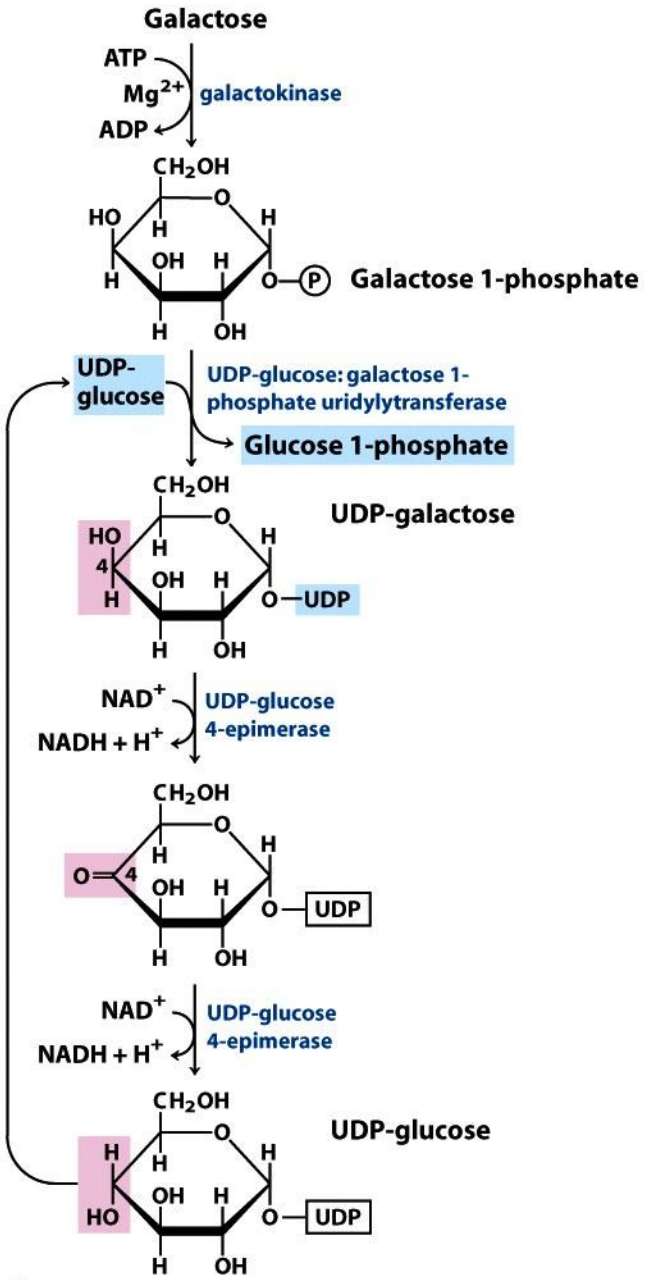

Figure 14-12

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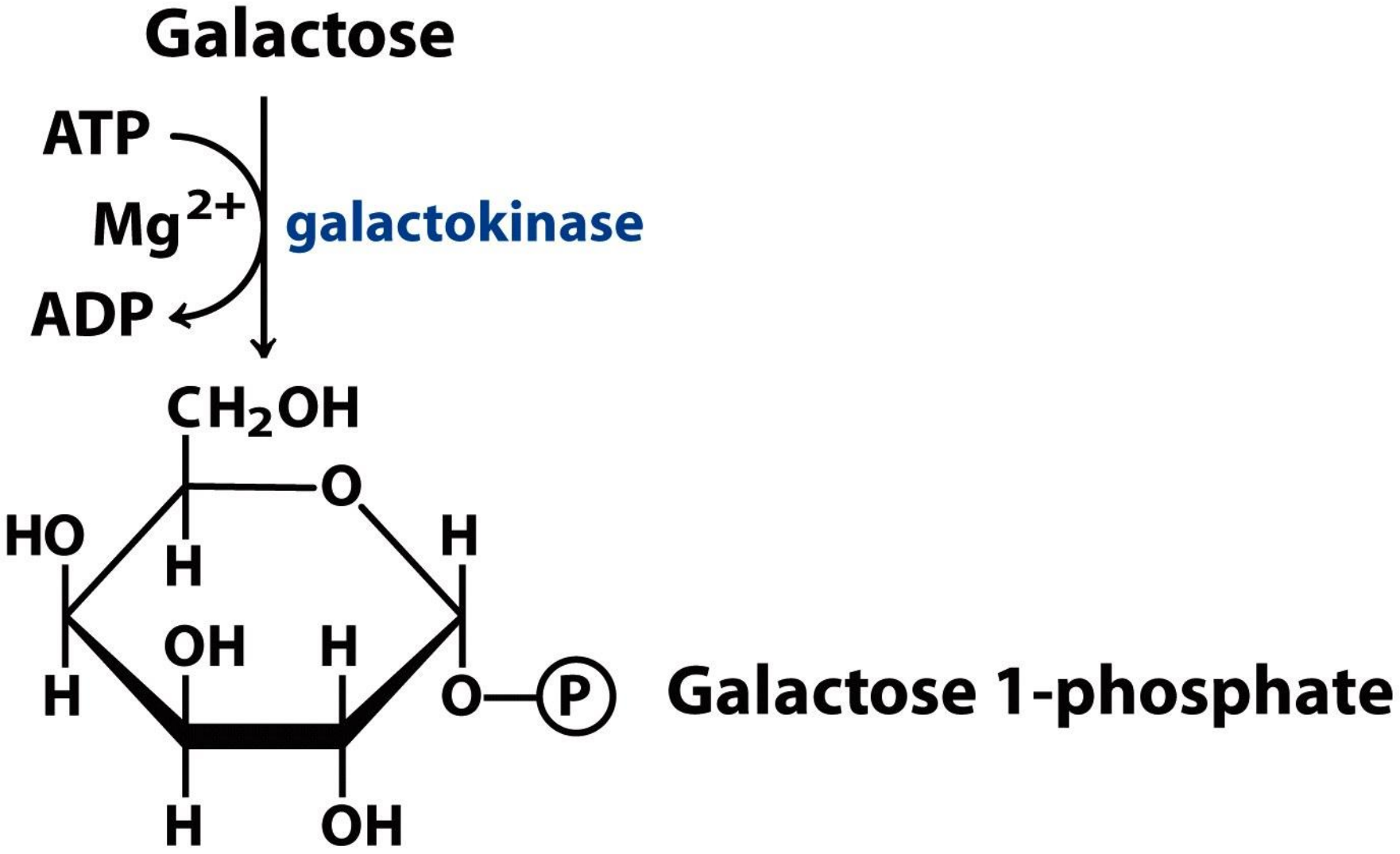

Figure 14-12 part 1
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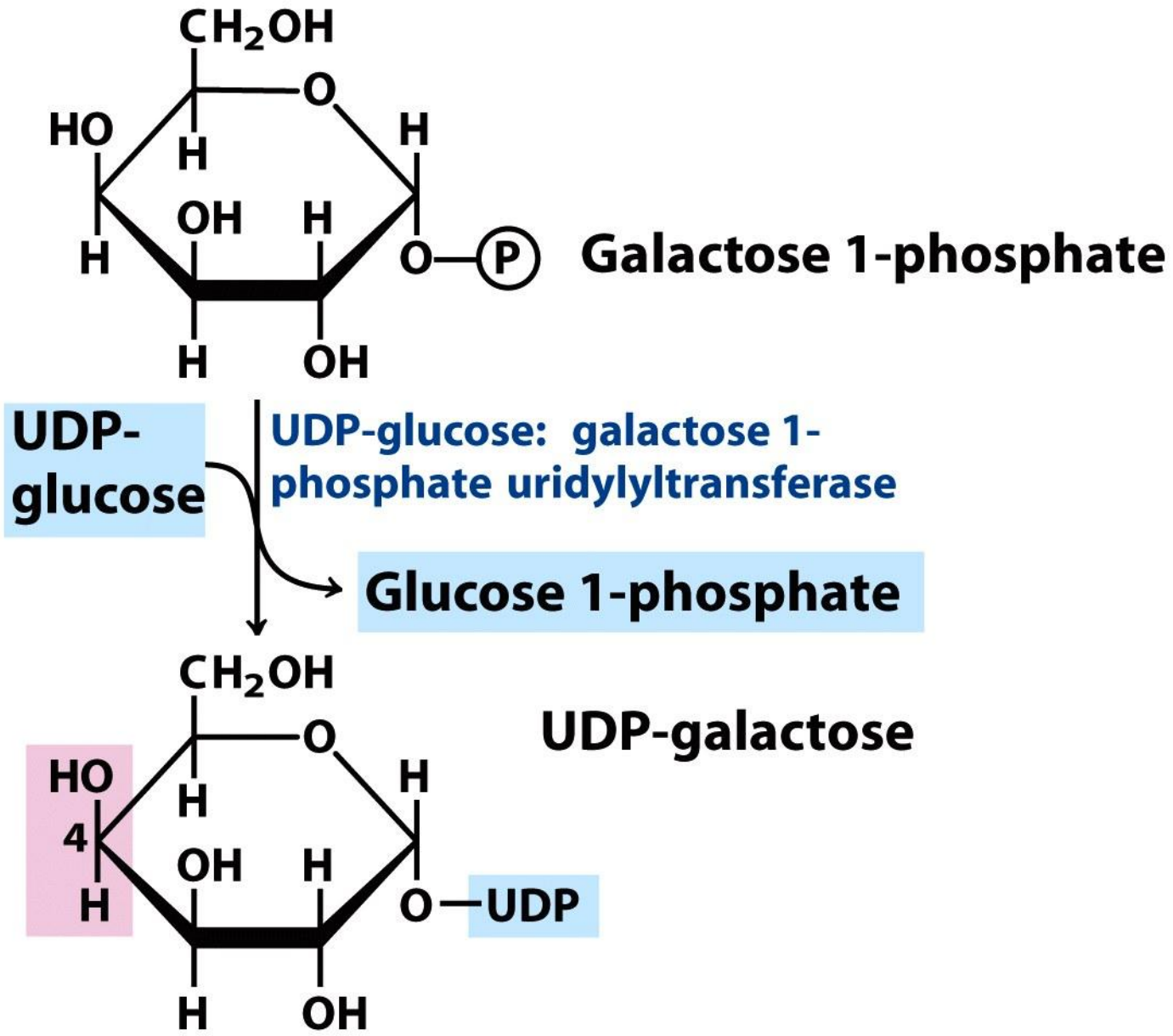

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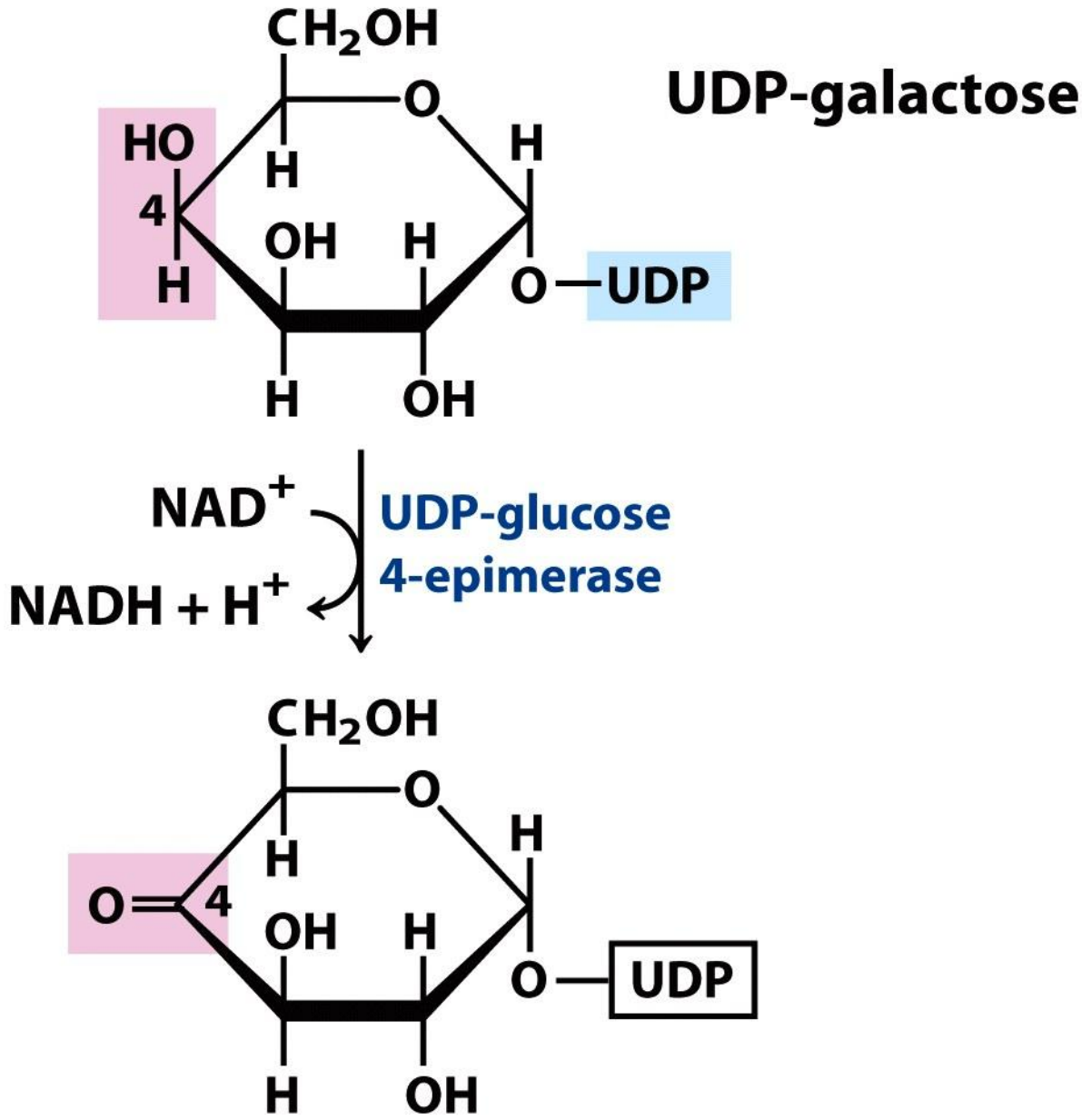

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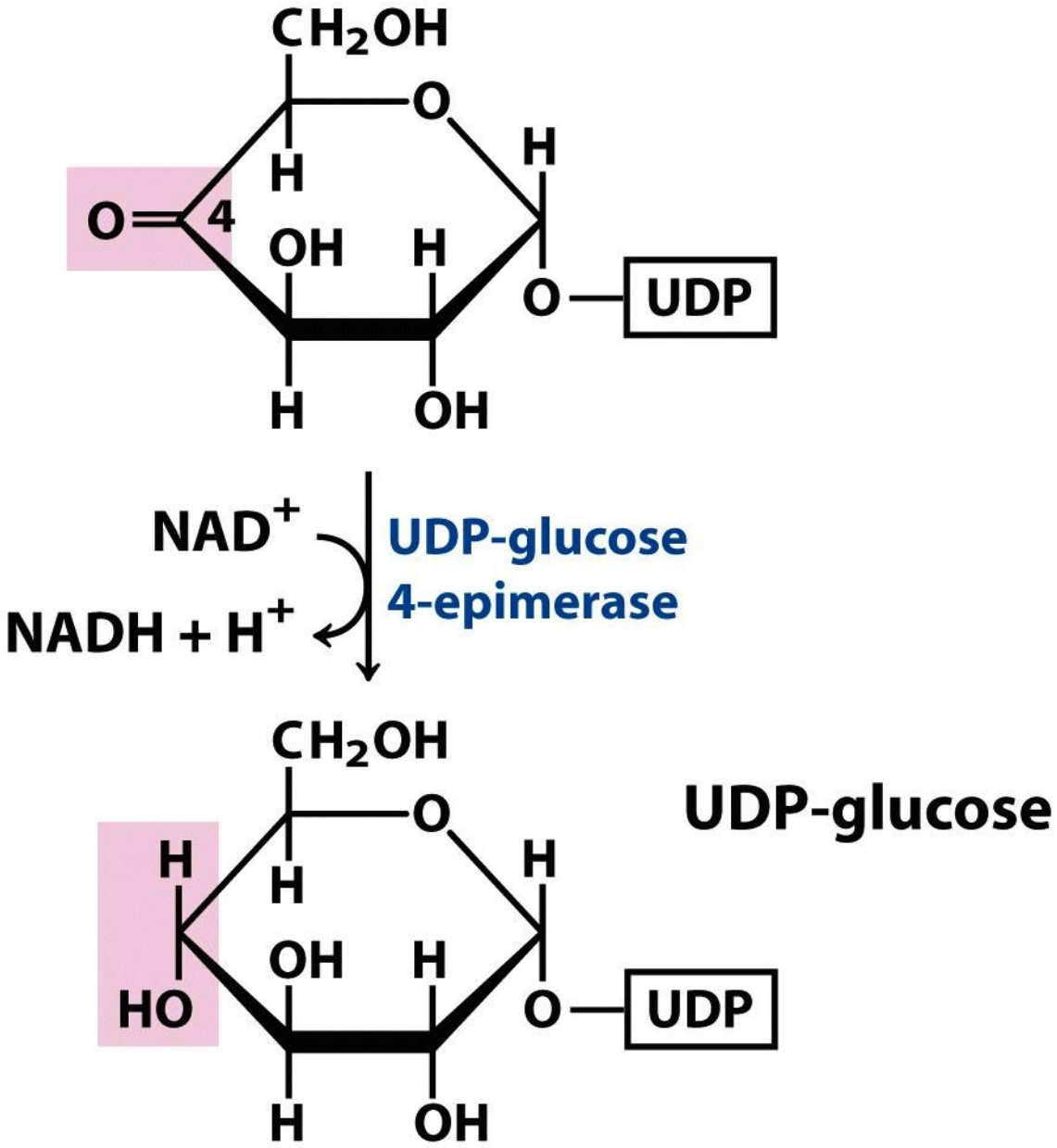

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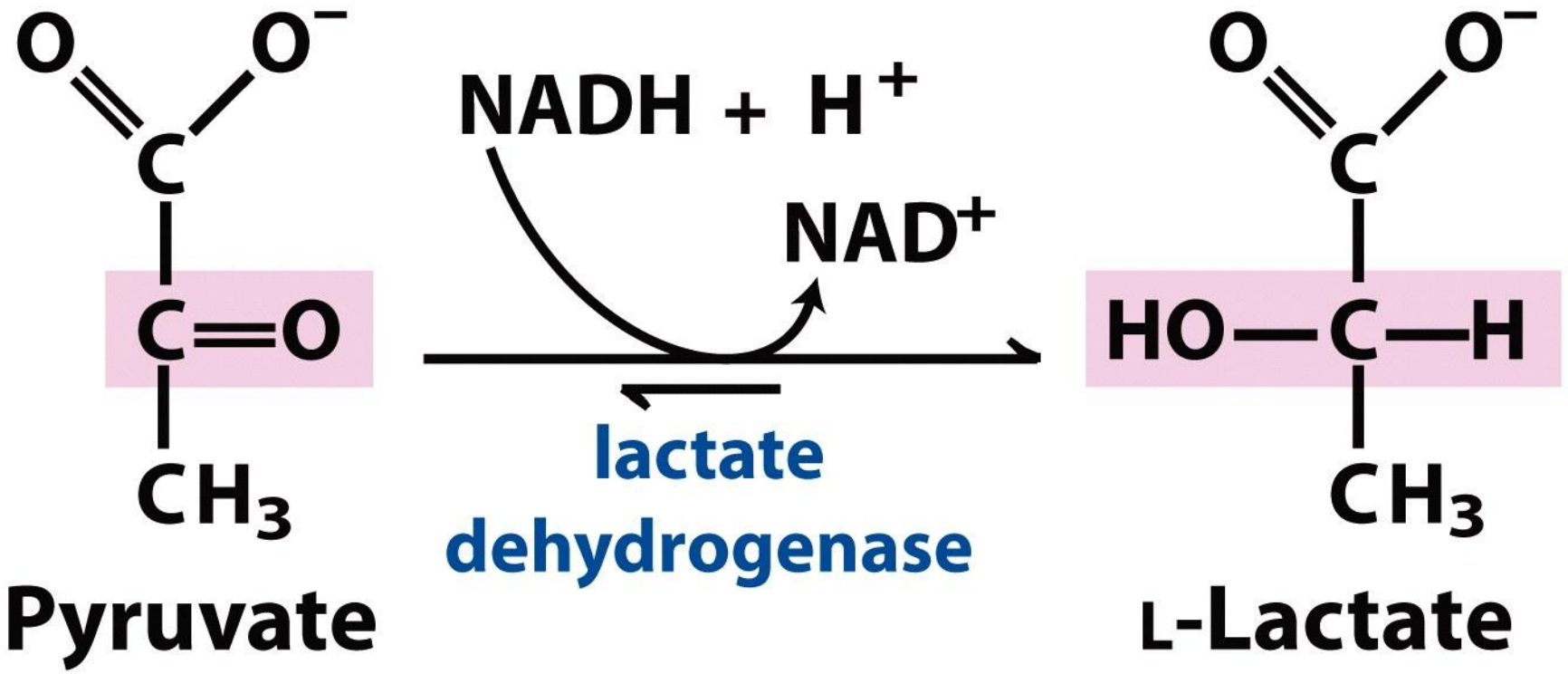

$\Delta G'° = -25.1$ kJ/mol

Unnumbered 14 p547a
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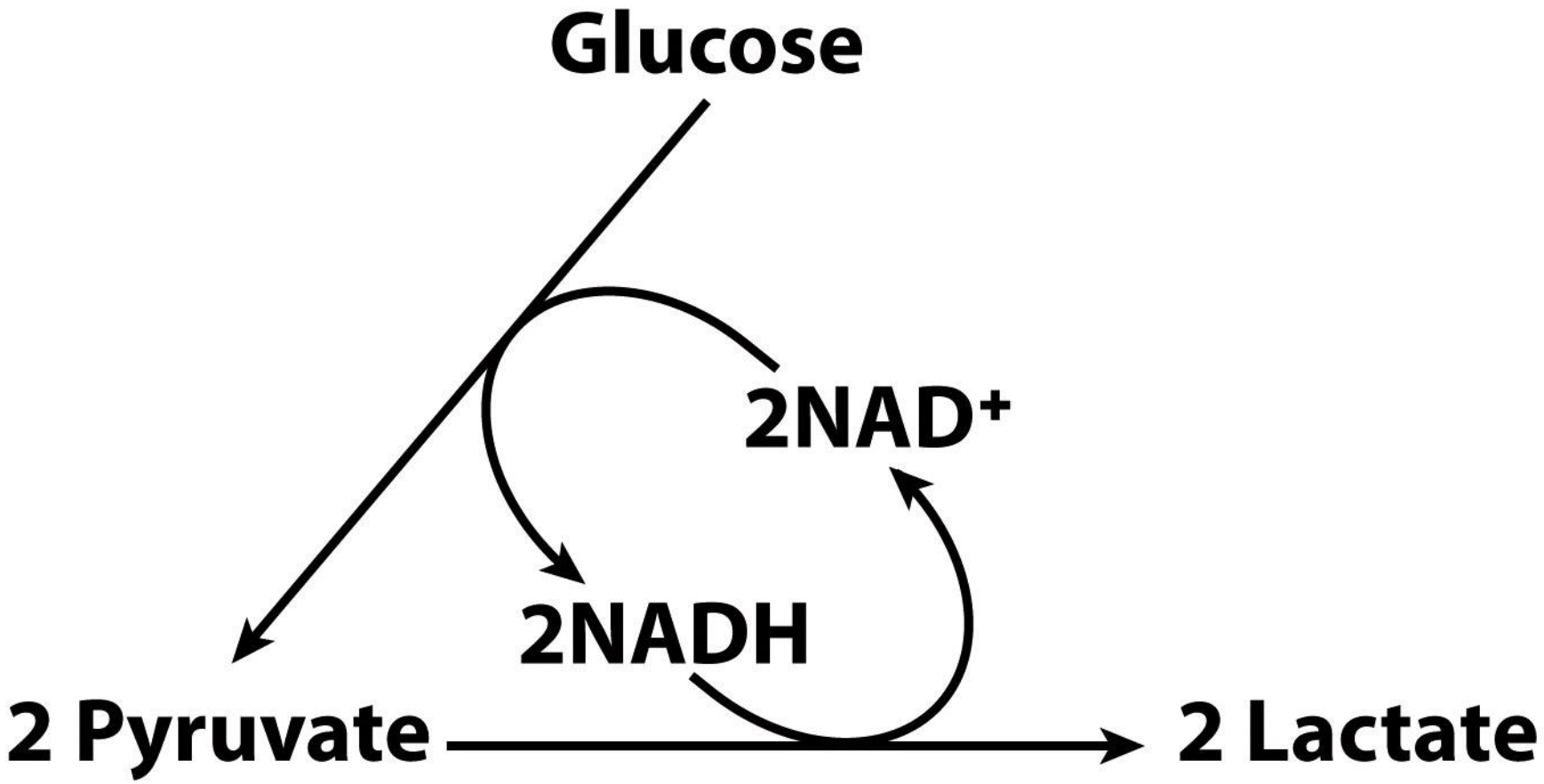

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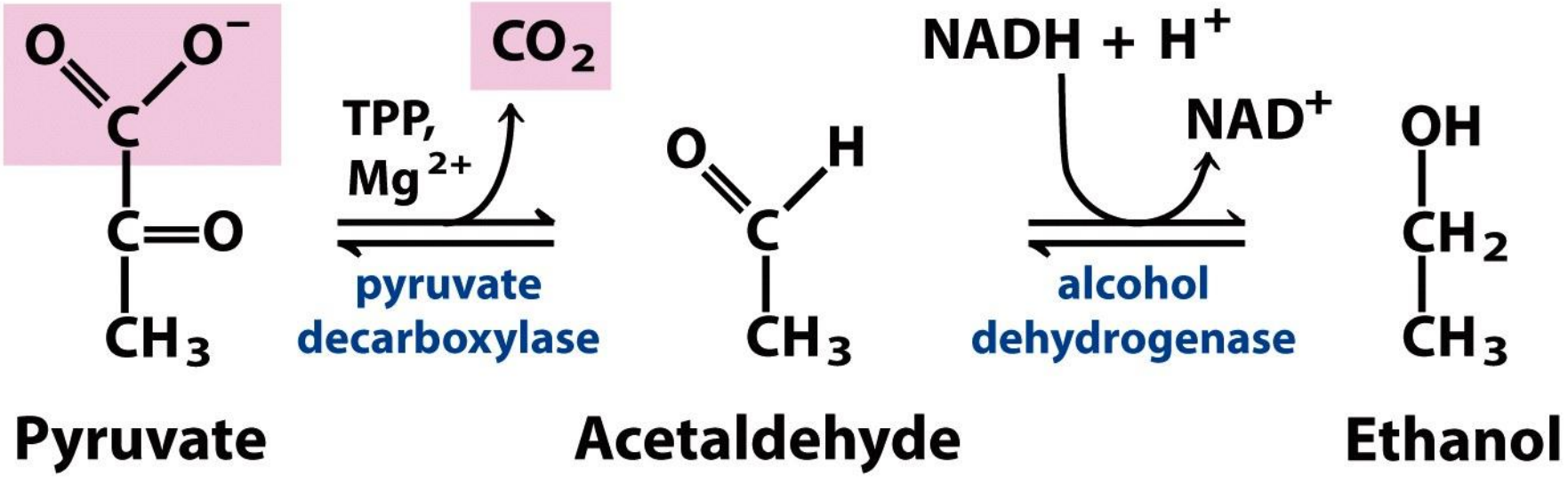

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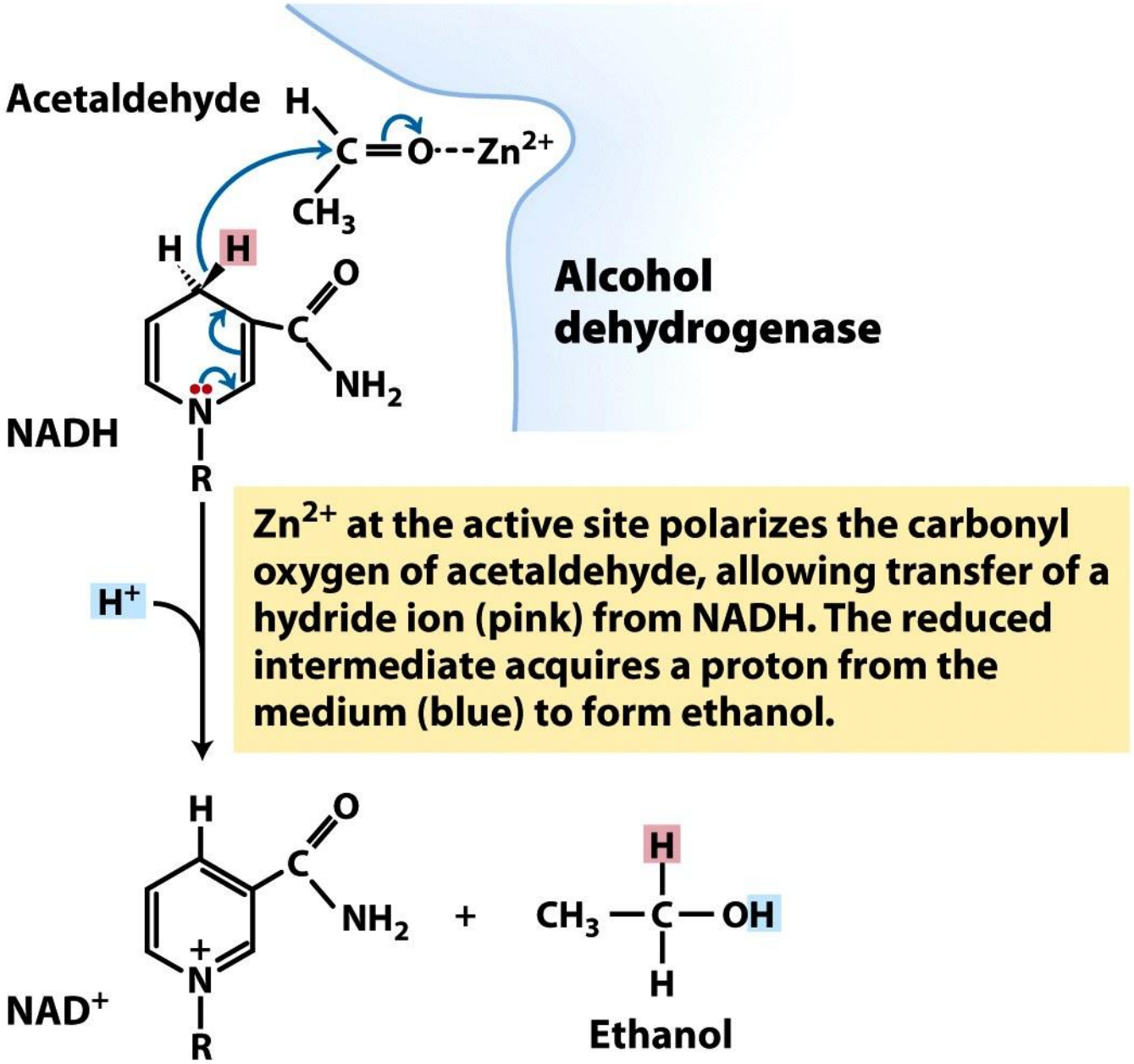

Figure 14-13
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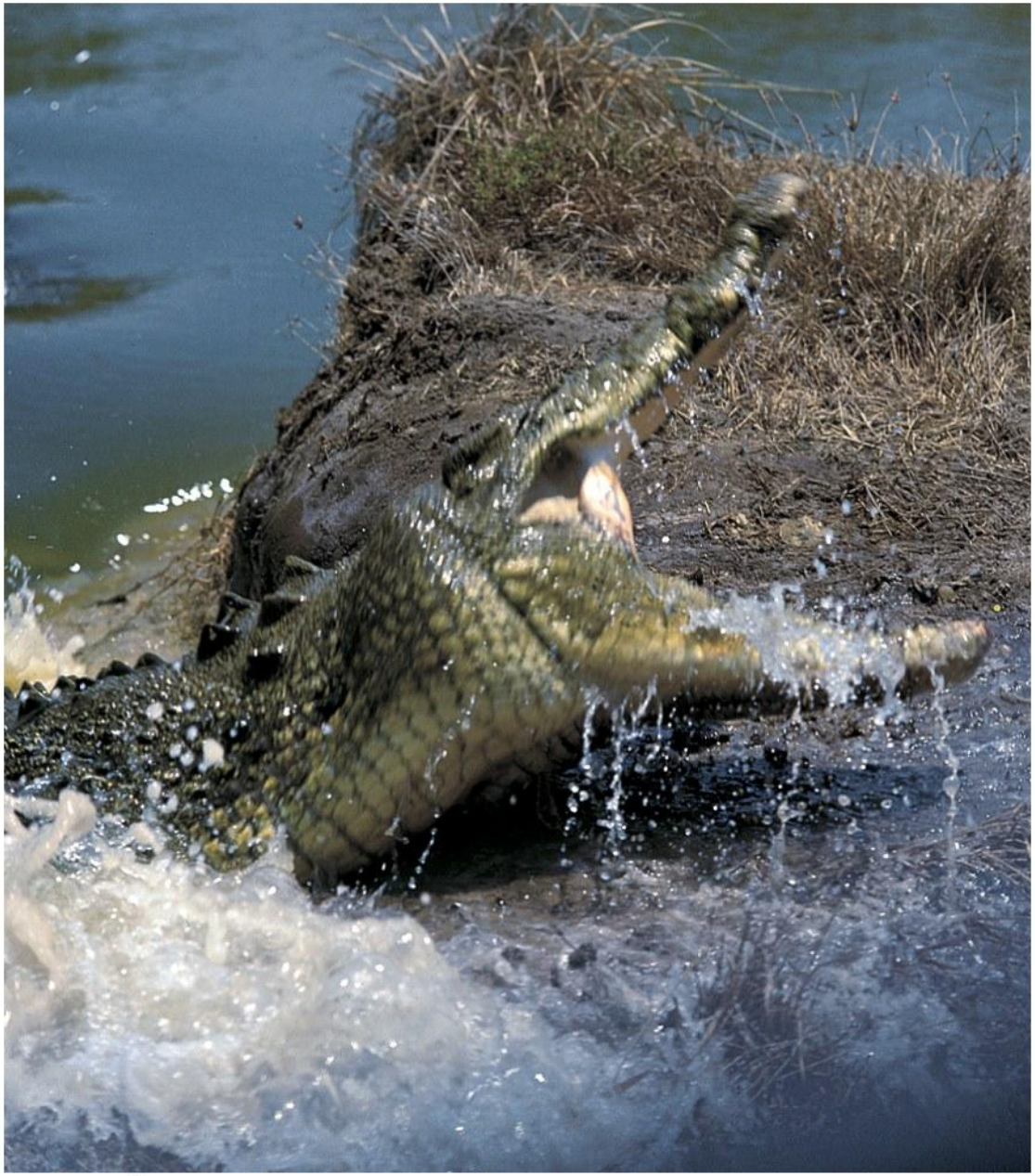

Box 14-2 figure 1

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Box 14-3 figure 1

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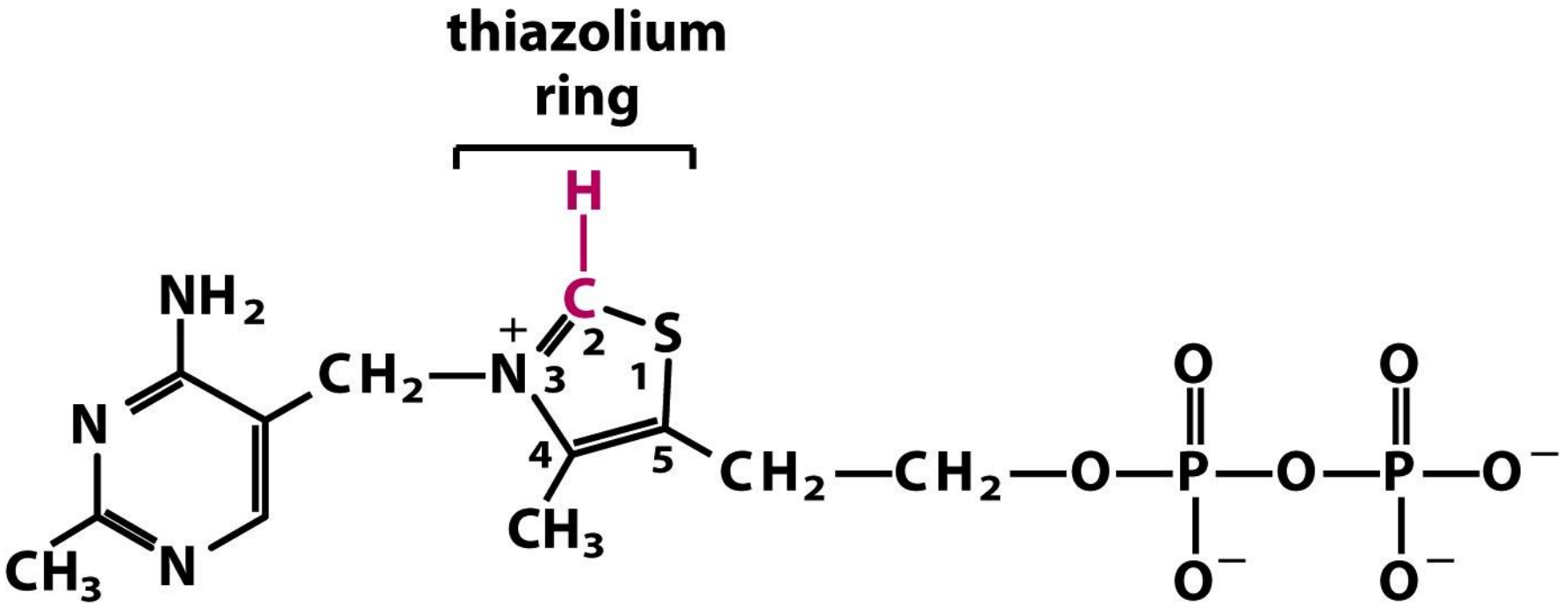

Thiamine pyrophosphate (TPP)

Figure 14-14a
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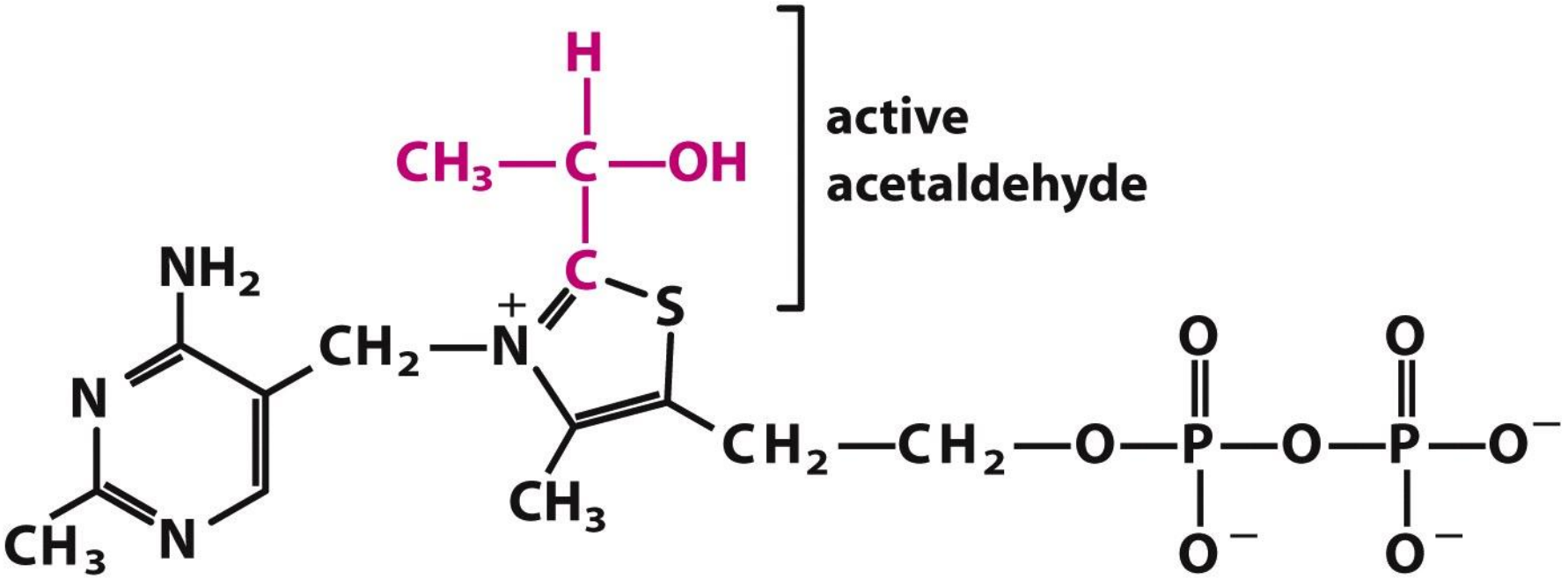

Hydroxyethyl thiamine pyrophosphate

Figure 14-14b
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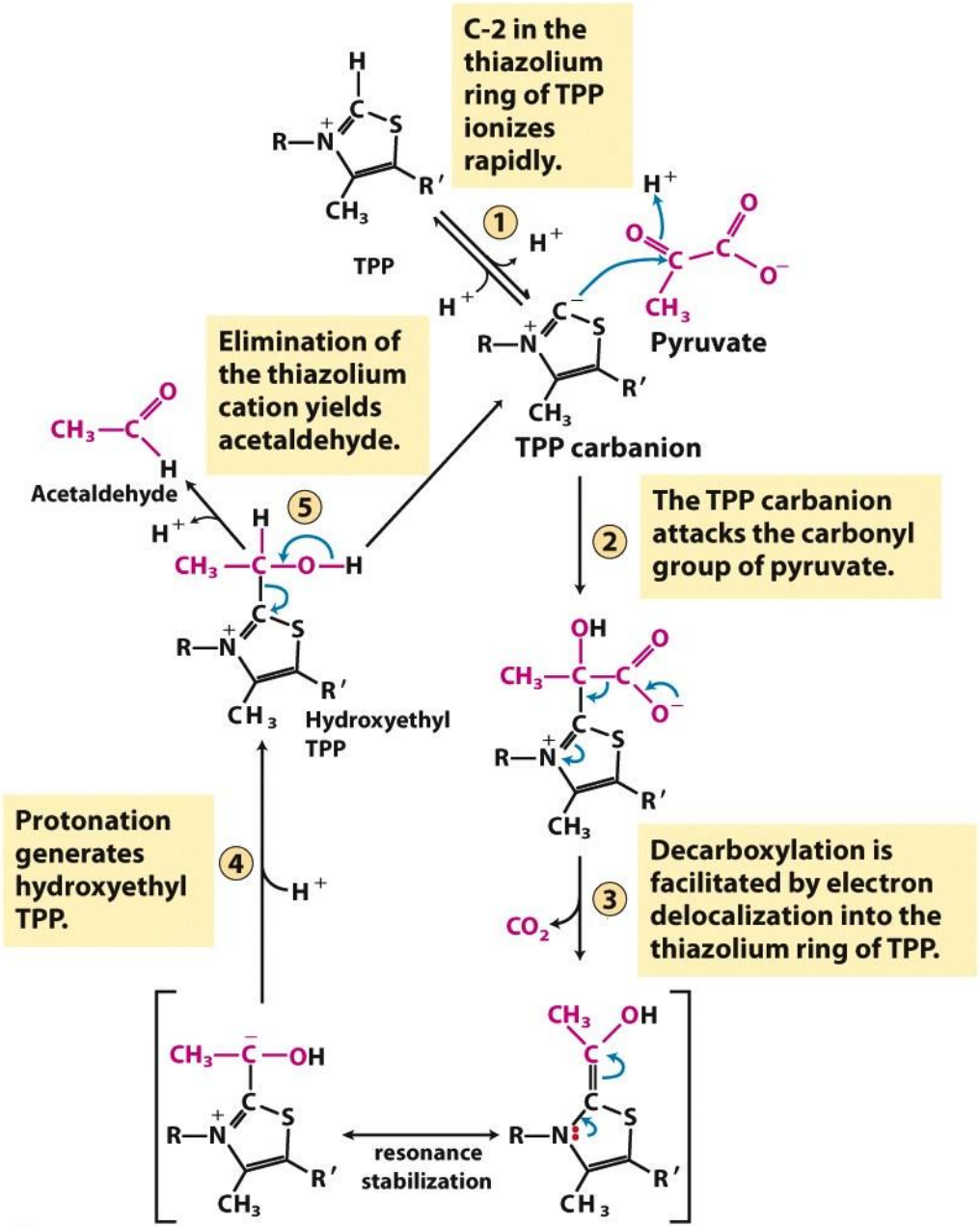

Figure 14-14c

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TABLE 14–1 Some TPP-Dependent Reactions

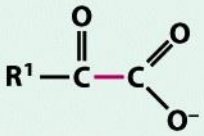
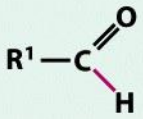
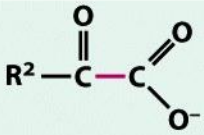
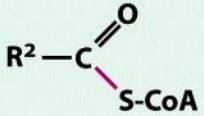
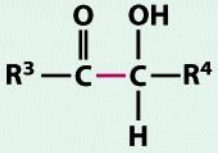
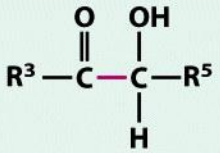
Enzyme	Pathway(s)	Bond cleaved	Bond formed
Pyruvate decarboxylase	Ethanol fermentation		
Pyruvate dehydrogenase α-Ketoglutarate dehydrogenase	Synthesis of acetyl-CoA Citric acid cycle		
Transketolase	Carbon-assimilation reactions Pentose phosphate pathway		

Table 14-1

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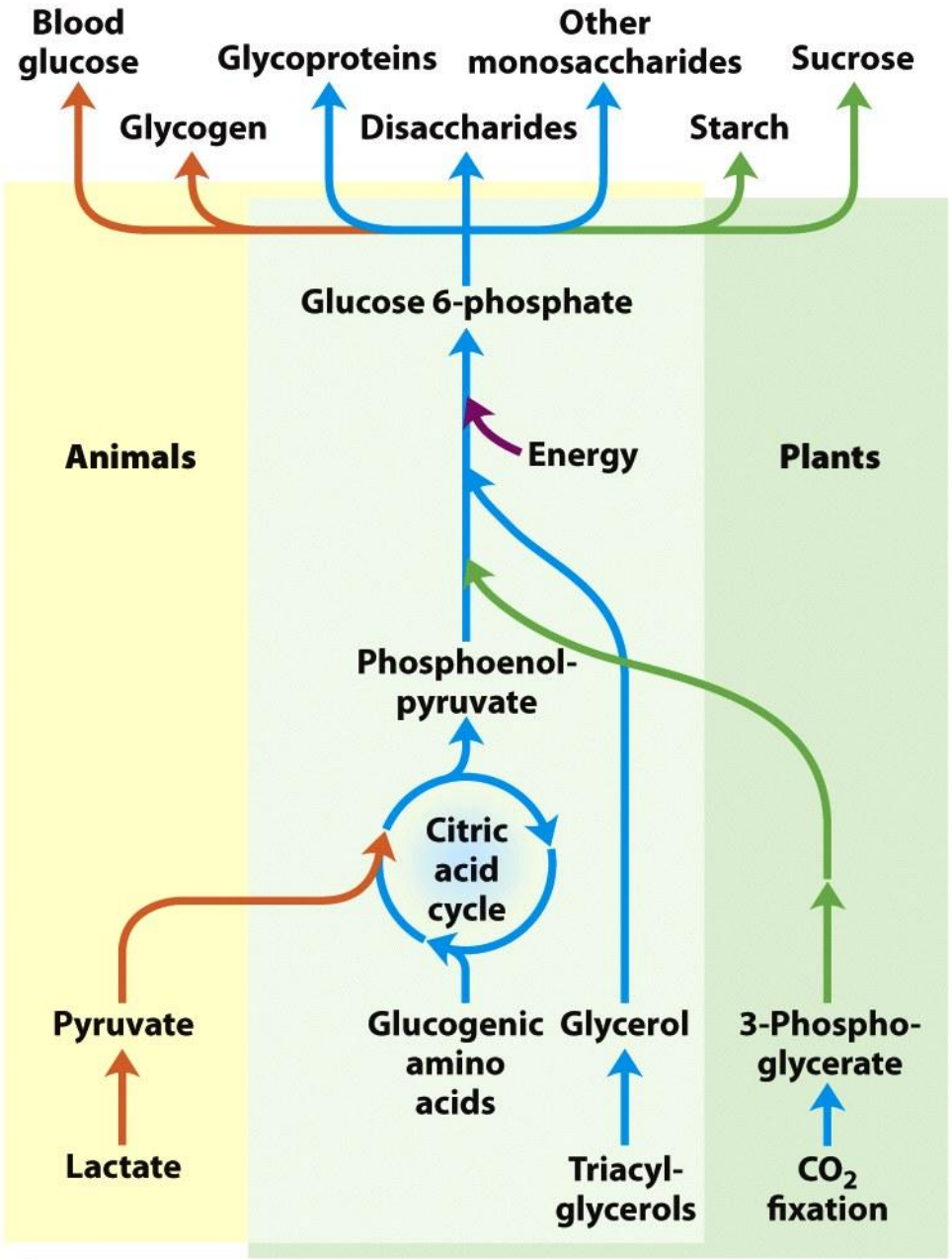

Figure 14-15

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TABLE 14–2 Free-Energy Changes of Glycolytic Reactions in Erythrocytes

	Glycolytic reaction step	$\Delta G'^{\circ}$ (kJ/mol)	ΔG (kJ/mol)
1	Glucose + ATP $\longrightarrow$ glucose 6-phosphate + ADP	−16.7	−33.4
2	Glucose 6-phosphate $\rightleftharpoons$ fructose 6-phosphate	1.7	0 to 25
3	Fructose 6-phosphate + ATP $\longrightarrow$ fructose 1,6-bisphosphate + ADP	−14.2	−22.2
4	Fructose 1,6-bisphosphate $\rightleftharpoons$ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate	23.8	−6 to 0
5	Dihydroxyacetone phosphate $\rightleftharpoons$ glyceraldehyde 3-phosphate	7.5	0 to 4
6	Glyceraldehyde 3-phosphate + P_i + NAD^+ $\rightleftharpoons$ 1,3-bisphosphoglycerate + NADH + H^+	6.3	−2 to 2
7	1,3-Bisphosphoglycerate + ADP $\rightleftharpoons$ 3-phosphoglycerate + ATP	−18.8	0 to 2
8	3-Phosphoglycerate $\rightleftharpoons$ 2-phosphoglycerate	4.4	0 to 0.8
9	2-Phosphoglycerate $\rightleftharpoons$ phosphoenolpyruvate + H_2O	7.5	0 to 3.3
10	Phosphoenolpyruvate + ADP $\longrightarrow$ pyruvate + ATP	−31.4	−16.7

Note: $\Delta G'^{\circ}$ is the standard free-energy change, as defined in Chapter 13 (pp. 491–492). ΔG is the free-energy change calculated from the actual concentrations of glycolytic intermediates present under physiological conditions in erythrocytes, at pH 7. The glycolytic reactions bypassed in gluconeogenesis are shown in red. Biochemical equations are not necessarily balanced for H or charge (p. 501).

Table 14-2

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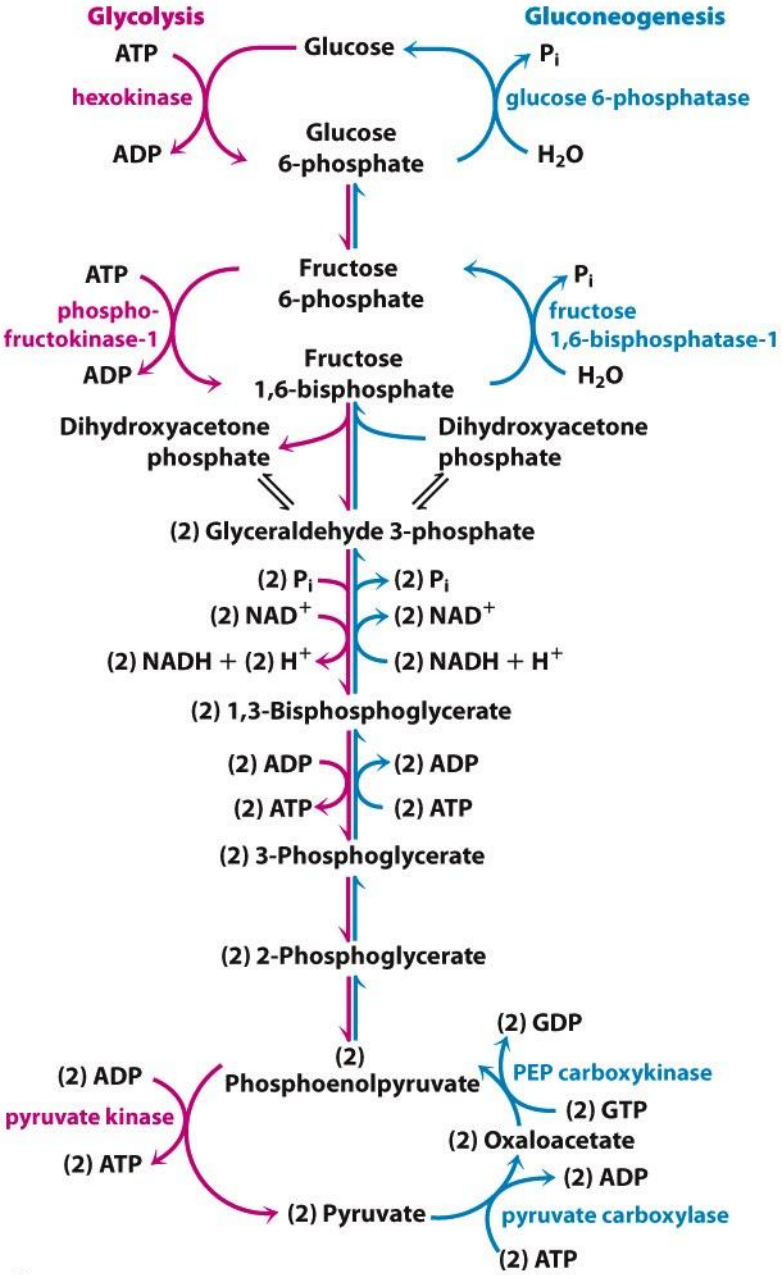

Figure 14-16

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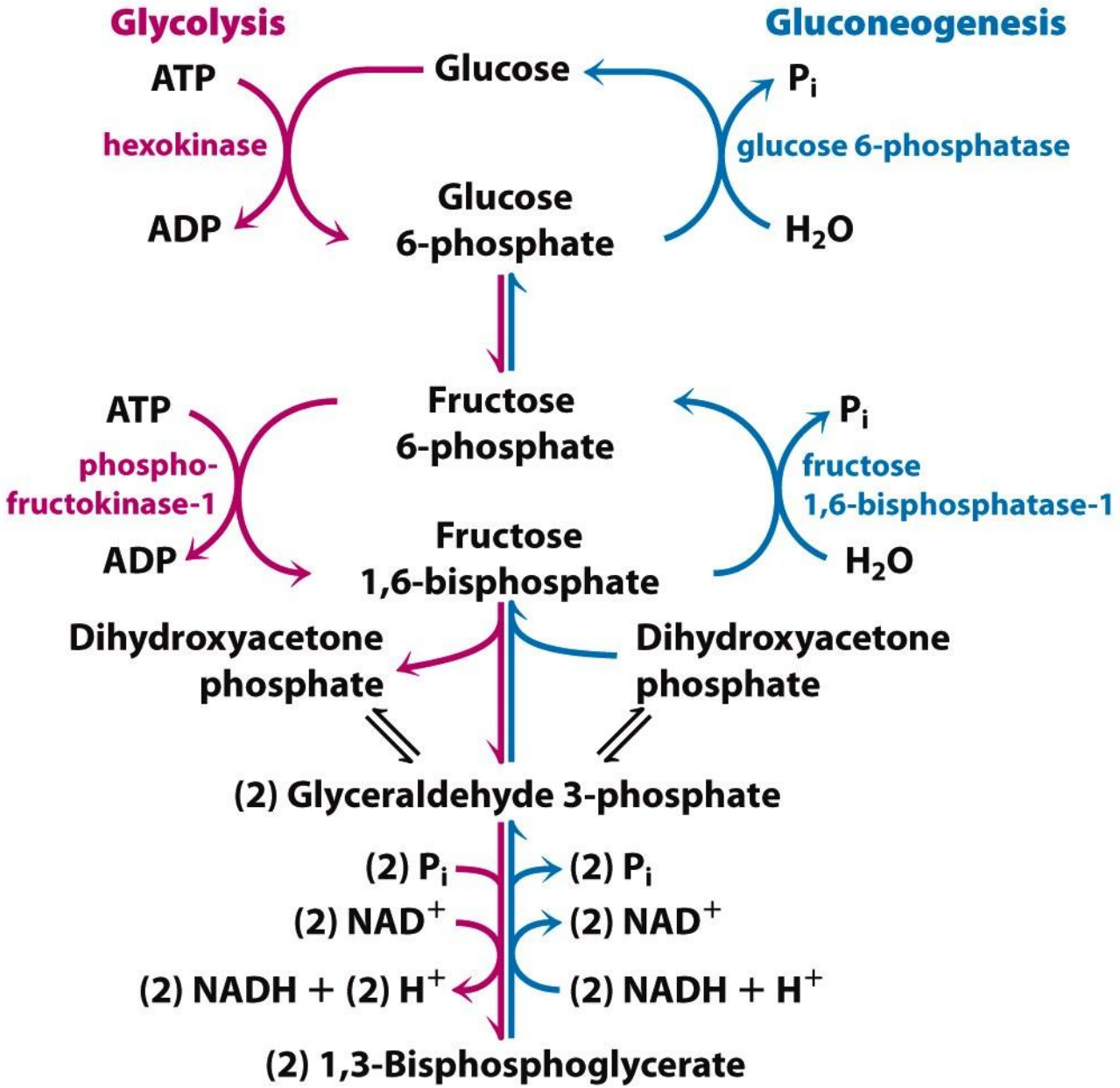

Figure 14-16 part 1
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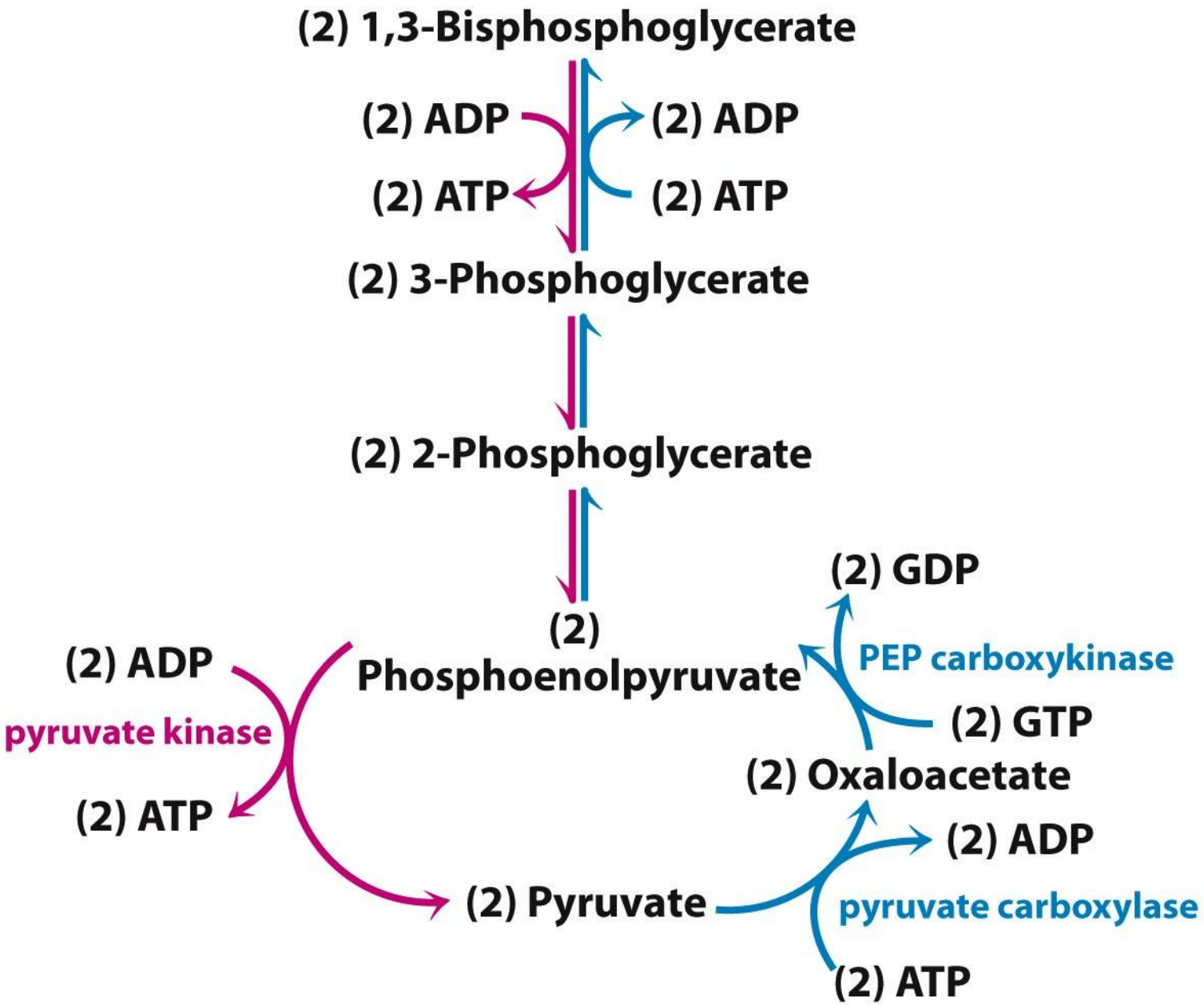

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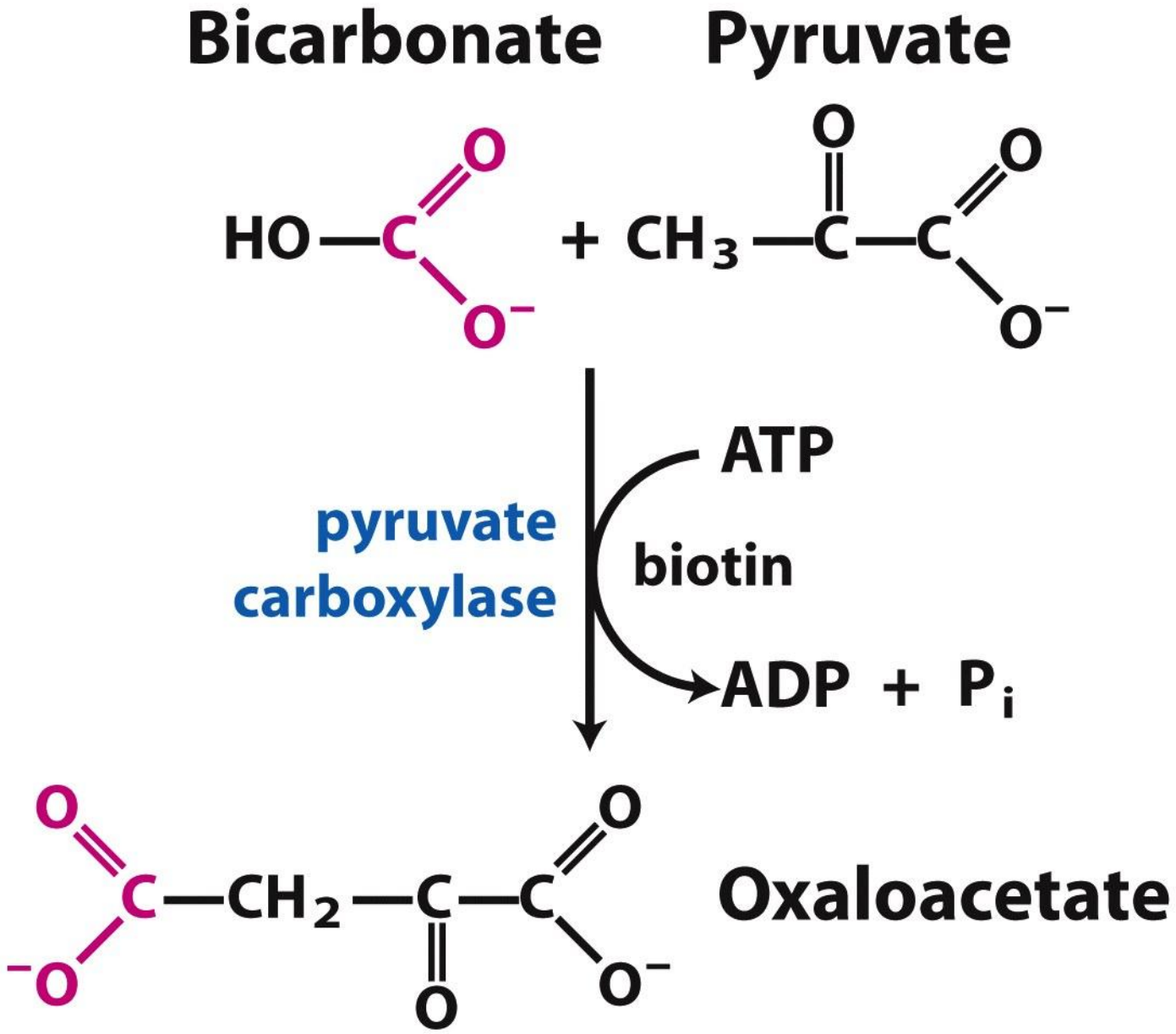

Figure 14-17a
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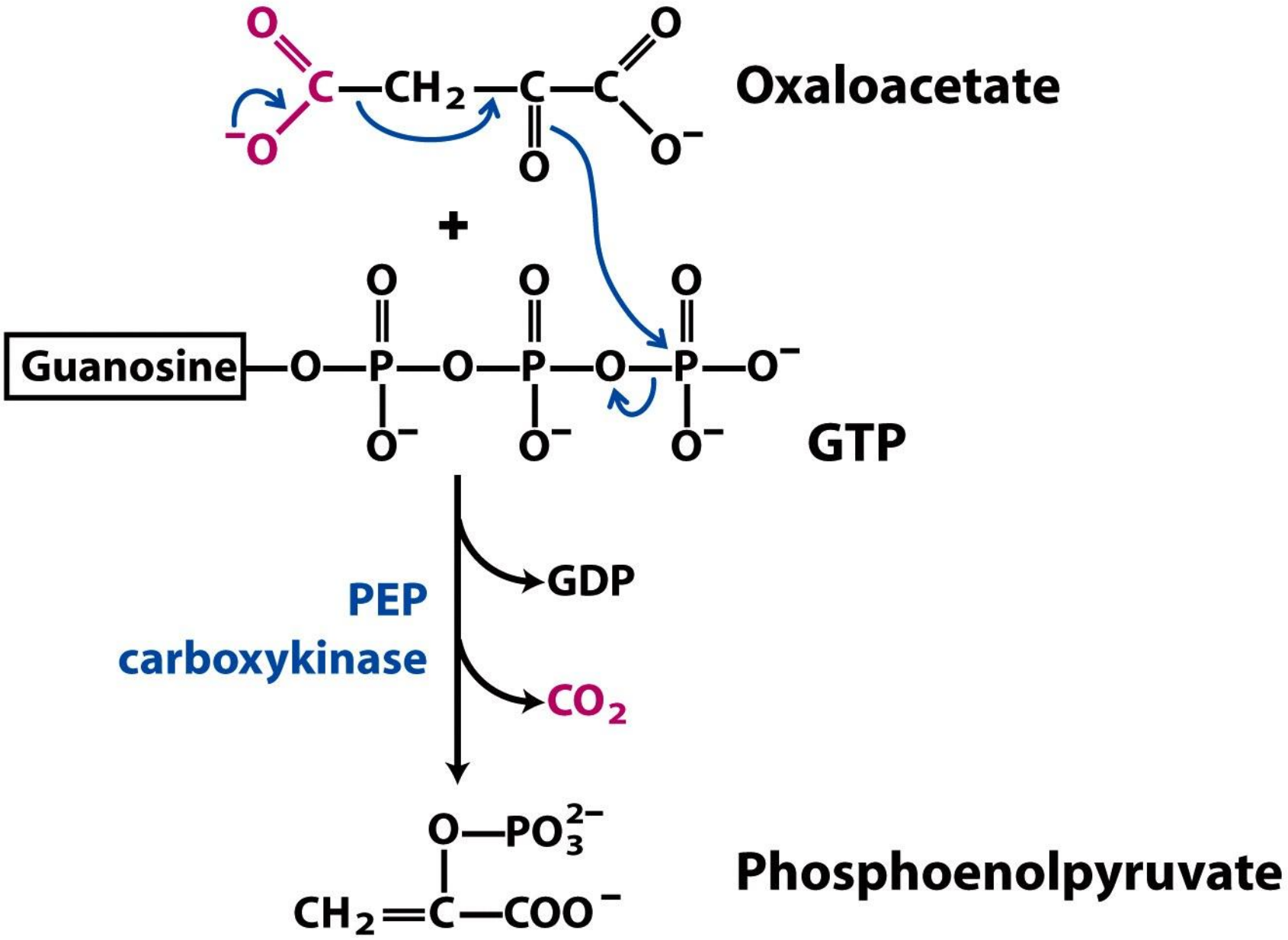

Figure 14-17b
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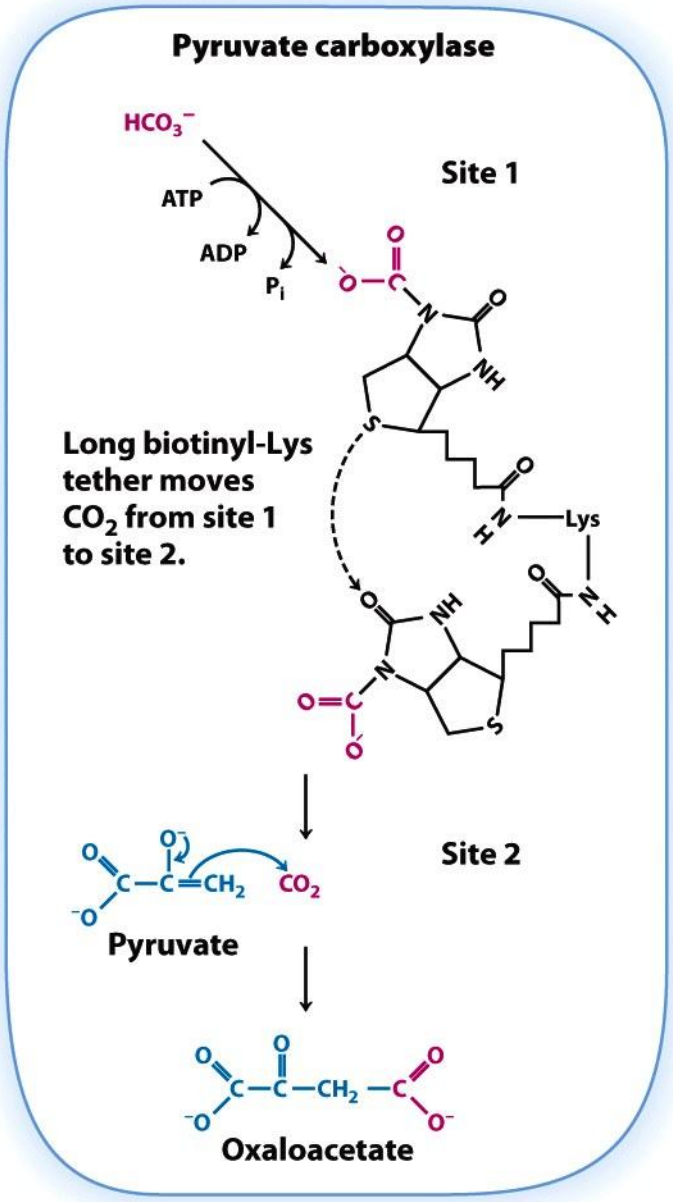

Figure 14-18
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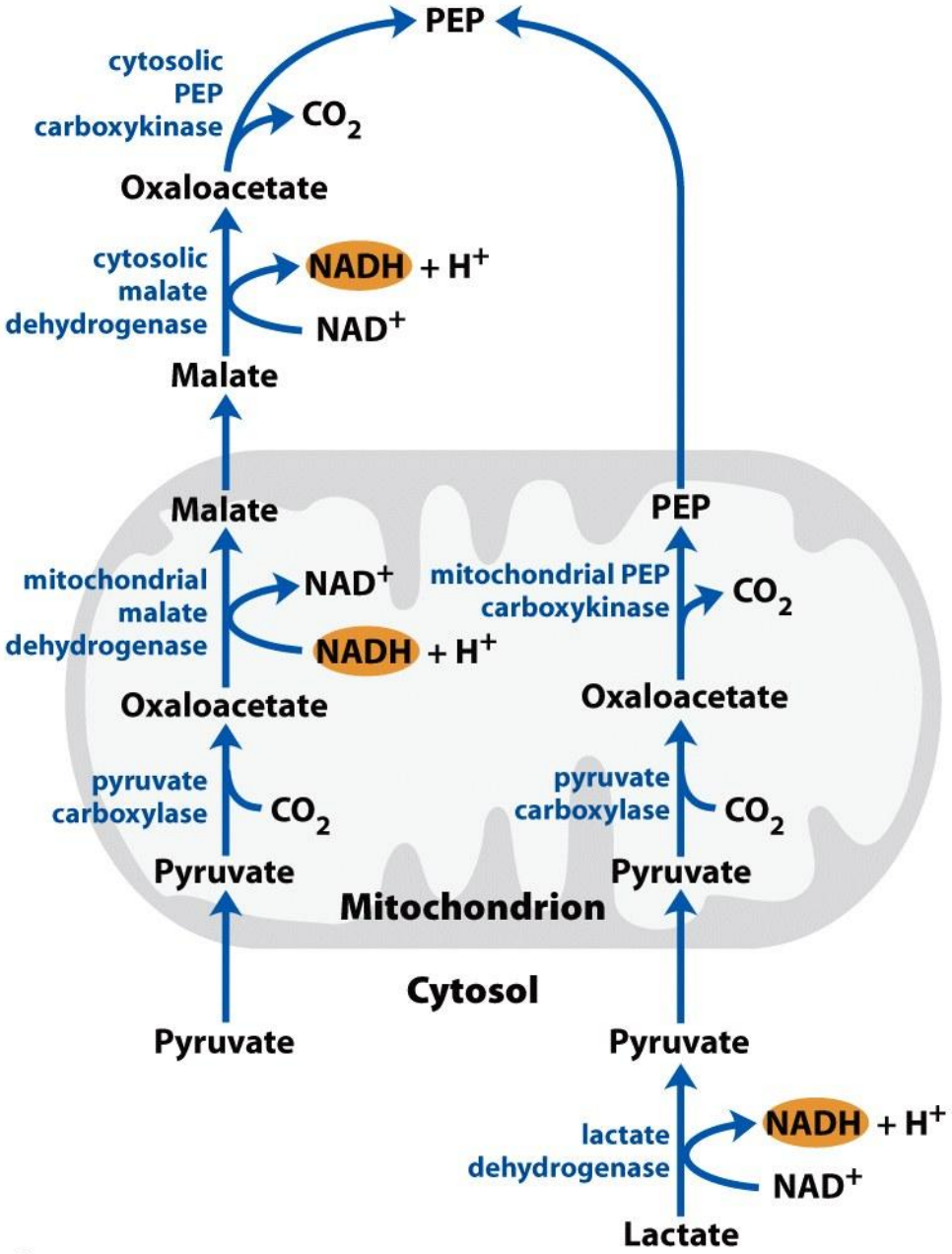

Figure 14-19

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TABLE 14–3 Sequential Reactions in Gluconeogenesis Starting from Pyruvate

Pyruvate + HCO_3^- + ATP ⟶ oxaloacetate + ADP + P_i	×2
Oxaloacetate + GTP ⇌ phosphoenolpyruvate + CO_2 + GDP	×2
Phosphoenolpyruvate + H_2O ⇌ 2-phosphoglycerate	×2
2-Phosphoglycerate ⇌ 3-phosphoglycerate	×2
3-Phosphoglycerate + ATP ⇌ 1,3-bisphosphoglycerate + ADP	×2
1,3-Bisphosphoglycerate + NADH + H^+ ⇌ glyceraldehyde 3-phosphate + NAD^+ + P_i	×2
Glyceraldehyde 3-phosphate ⇌ dihydroxyacetone phosphate	
Glyceraldehyde 3-phosphate + dihydroxyacetone phosphate ⇌ fructose 1,6-bisphosphate	
Fructose 1,6-bisphosphate ⟶ fructose 6-phosphate + P_i	
Fructose 6-phosphate ⇌ glucose 6-phosphate	
Glucose 6-phosphate + H_2O ⟶ glucose + P_i	
Sum: 2 Pyruvate + 4ATP + 2GTP + 2NADH + $2H^+$ + $4H_2O$ ⟶ glucose + 4ADP + 2GDP + $6P_i$ + $2NAD^+$	

Note: The bypass reactions are in red; all other reactions are reversible steps of glycolysis. The figures at the right indicate that the reaction is to be counted twice, because two three-carbon precursors are required to make a molecule of glucose. The reactions required to replace the cytosolic NADH consumed in the glyceraldehyde 3-phosphate dehydrogenase reaction (the conversion of lactate to pyruvate in the cytosol or the transport of reducing equivalents from mitochondria to the cytosol in the form of malate) are not considered in this summary. Biochemical equations are not necessarily balanced for H and charge (p. 501).

Table 14-3

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TABLE 14–4 Glucogenic Amino Acids, Grouped by Site of Entry

Pyruvate	**Succinyl-CoA**
Alanine	Isoleucine*
Cysteine	Methionine
Glycine	Threonine
Serine	Valine
Threonine	**Fumarate**
Tryptophan*	Phenylalanine*
α-Ketoglutarate	Tyrosine*
Arginine	**Oxaloacetate**
Glutamate	Asparagine
Glutamine	Aspartate
Histidine	
Proline	

Note: All these amino acids are precursors of blood glucose or liver glycogen, because they can be converted to pyruvate or citric acid cycle intermediates. Of the 20 common amino acids, only leucine and lysine are unable to furnish carbon for net glucose synthesis.

*These amino acids are also ketogenic (see Fig. 18–21).

Table 14-4
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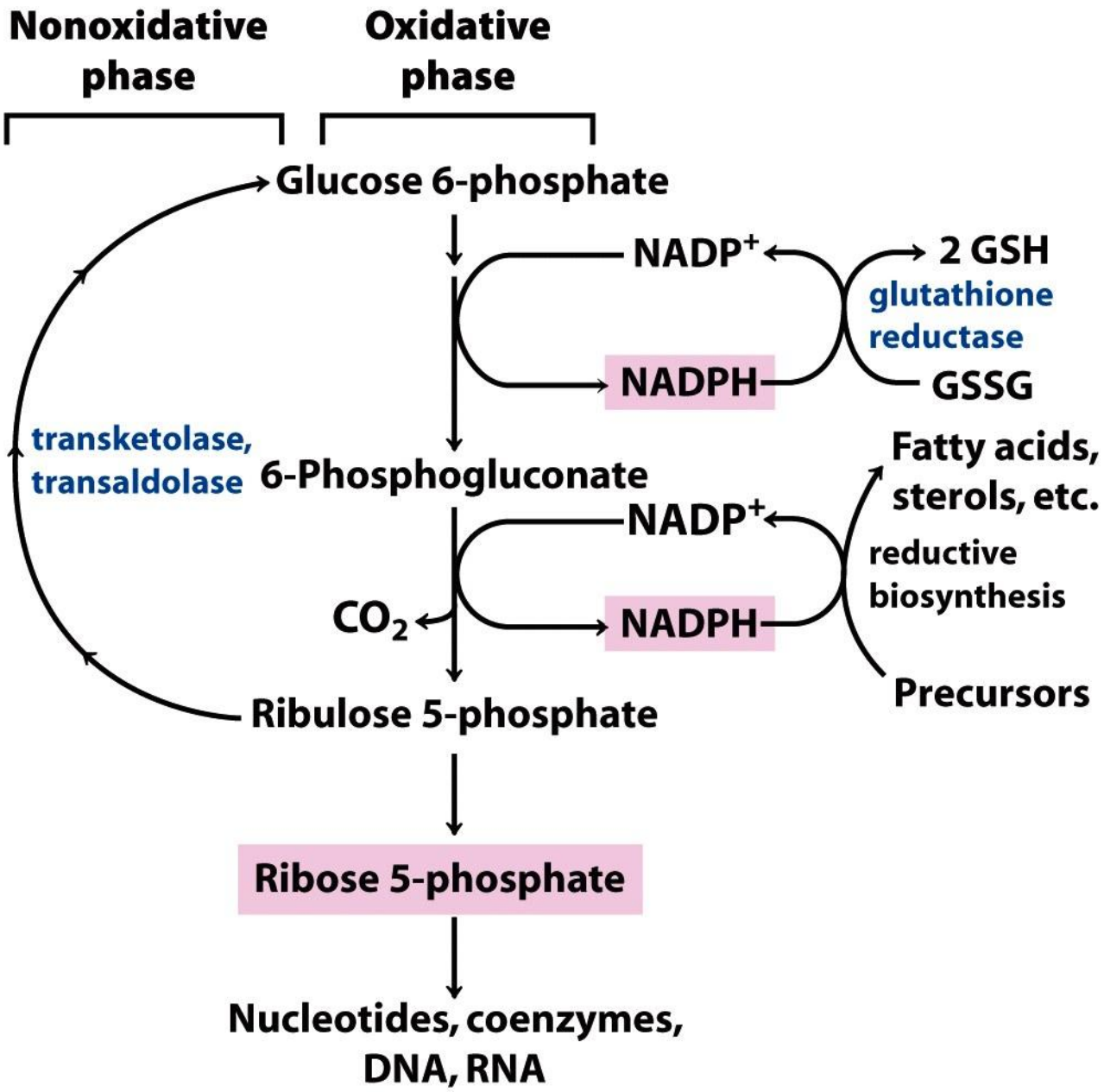

Figure 14-20
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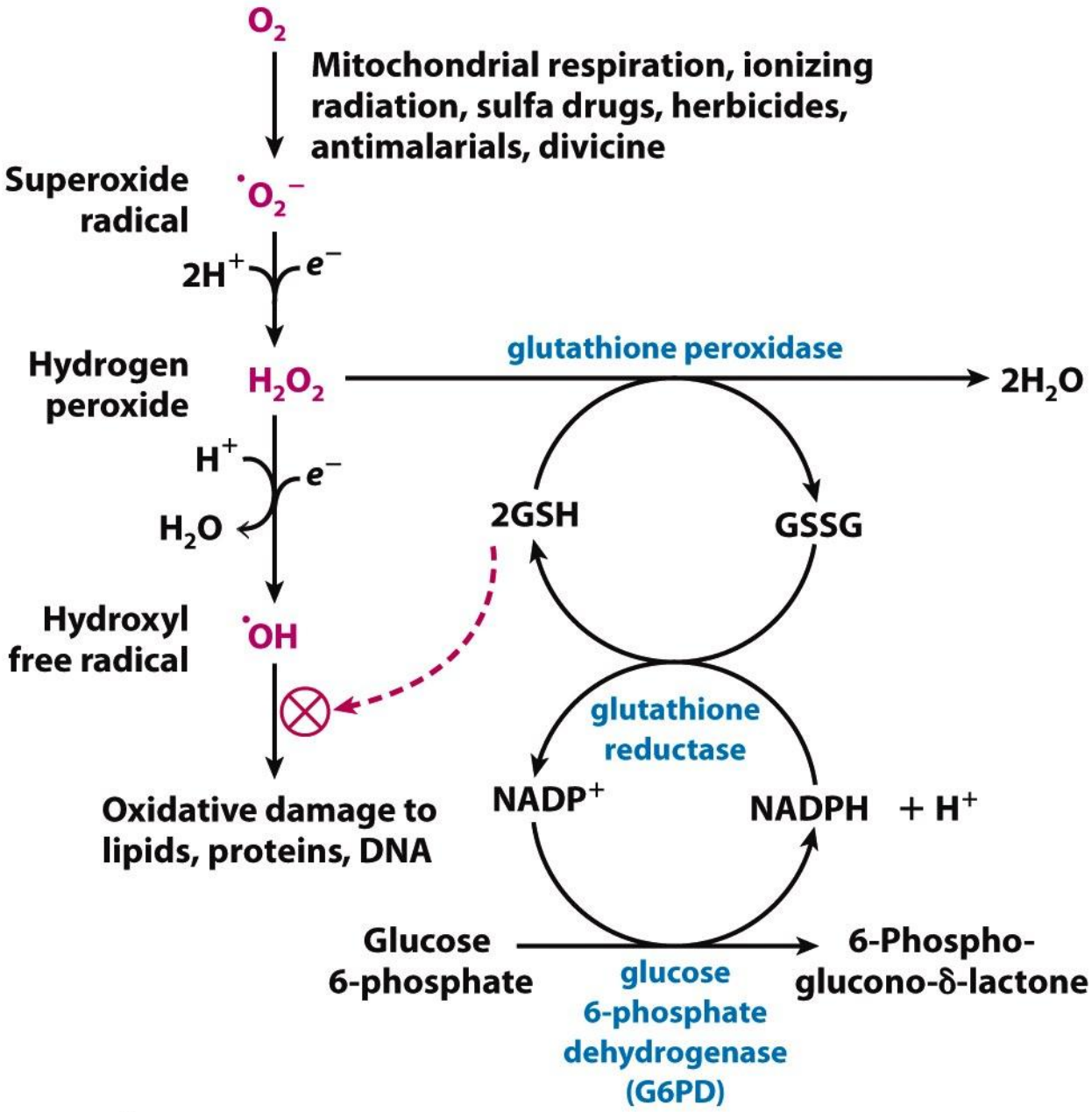

Box 14-4 figure 1

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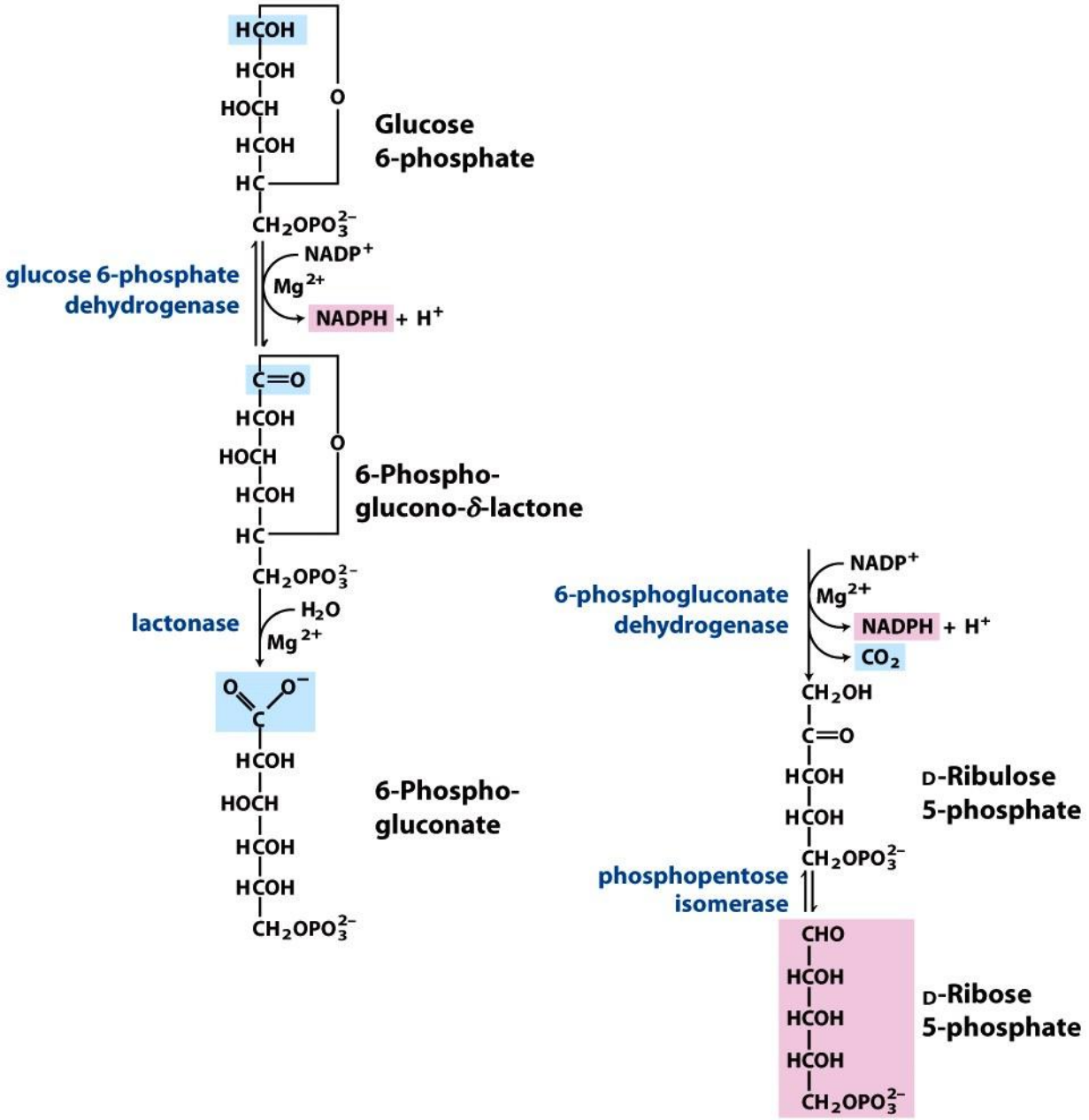

Figure 14-21

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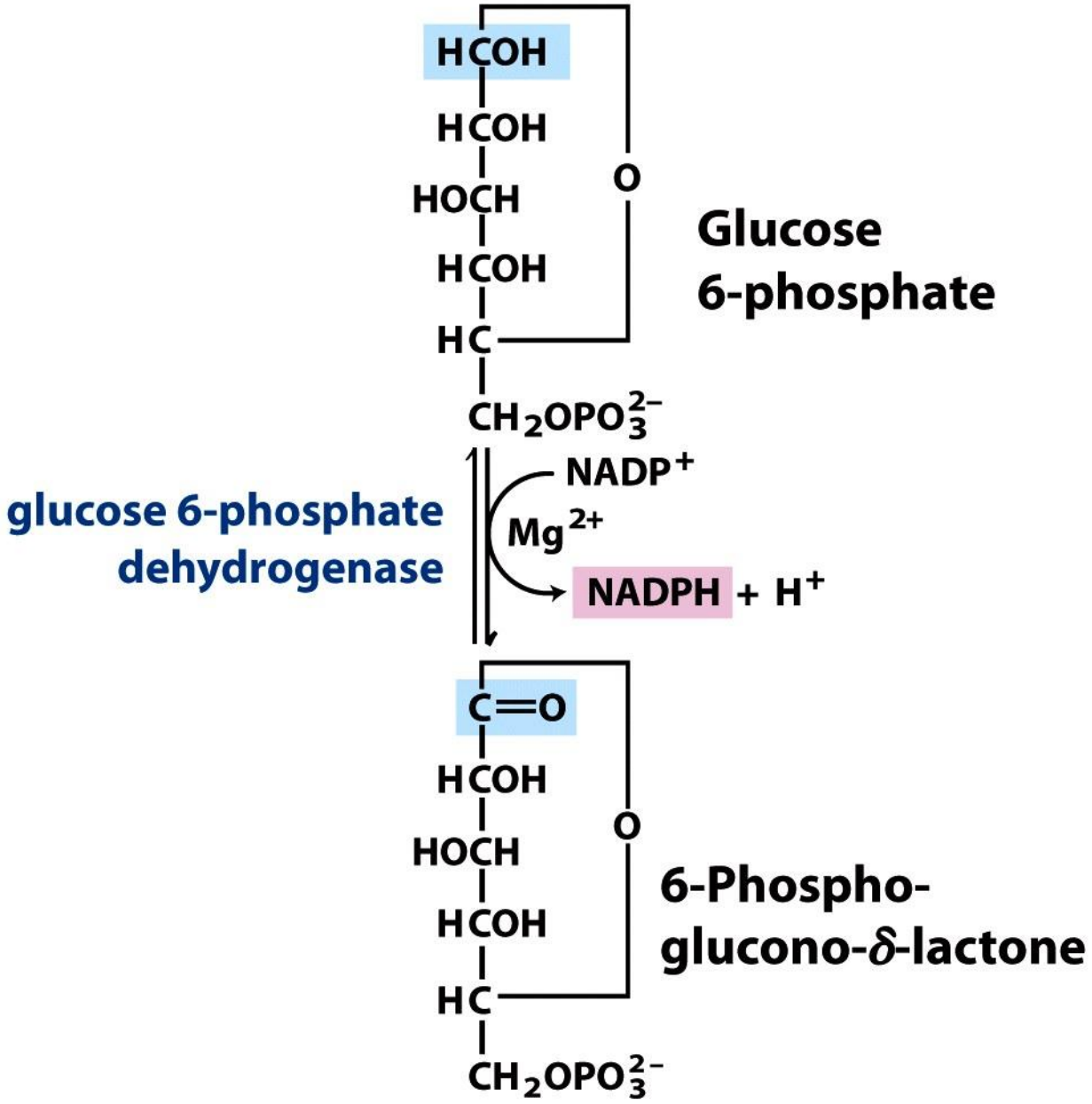

Figure 14-21 part 1

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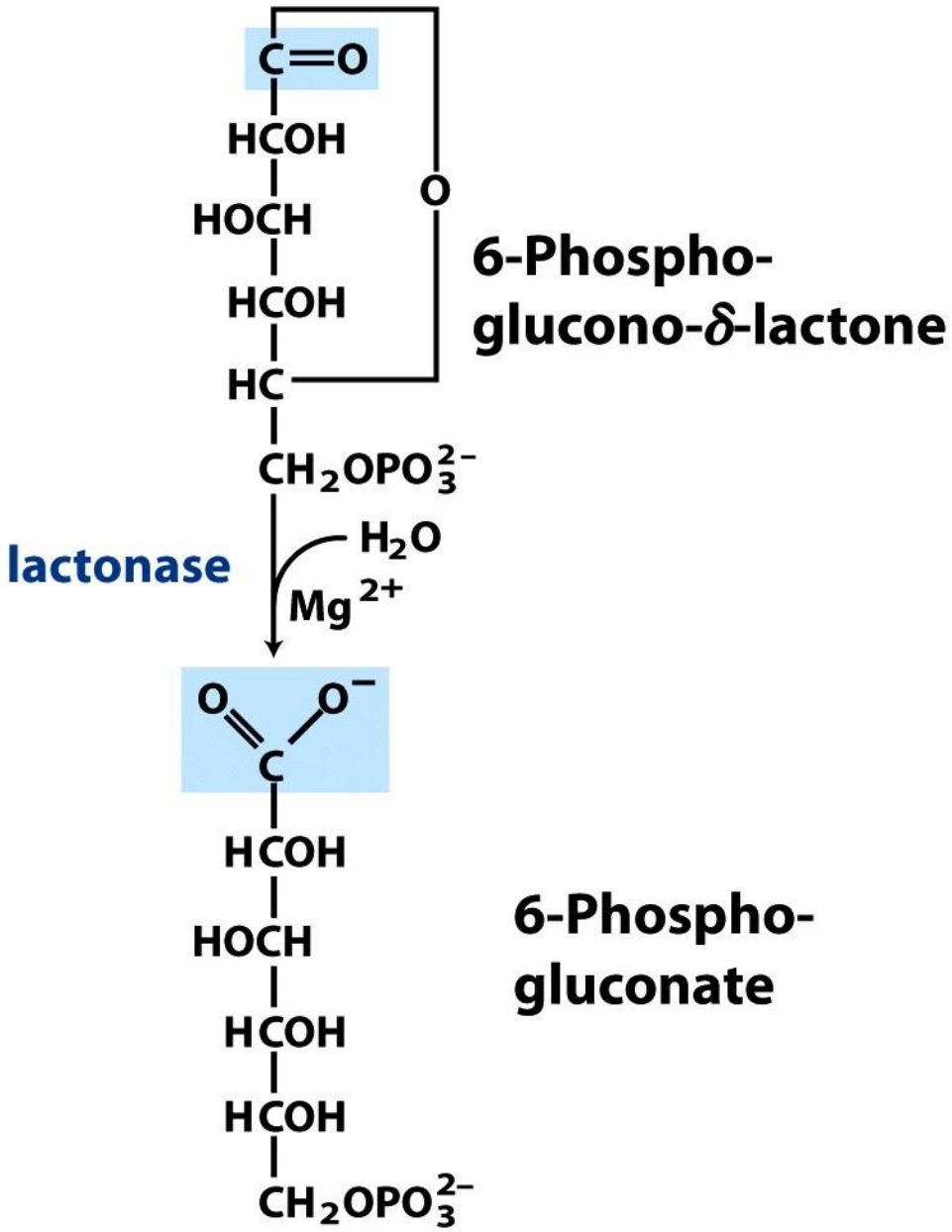

Figure 14-21 part 2

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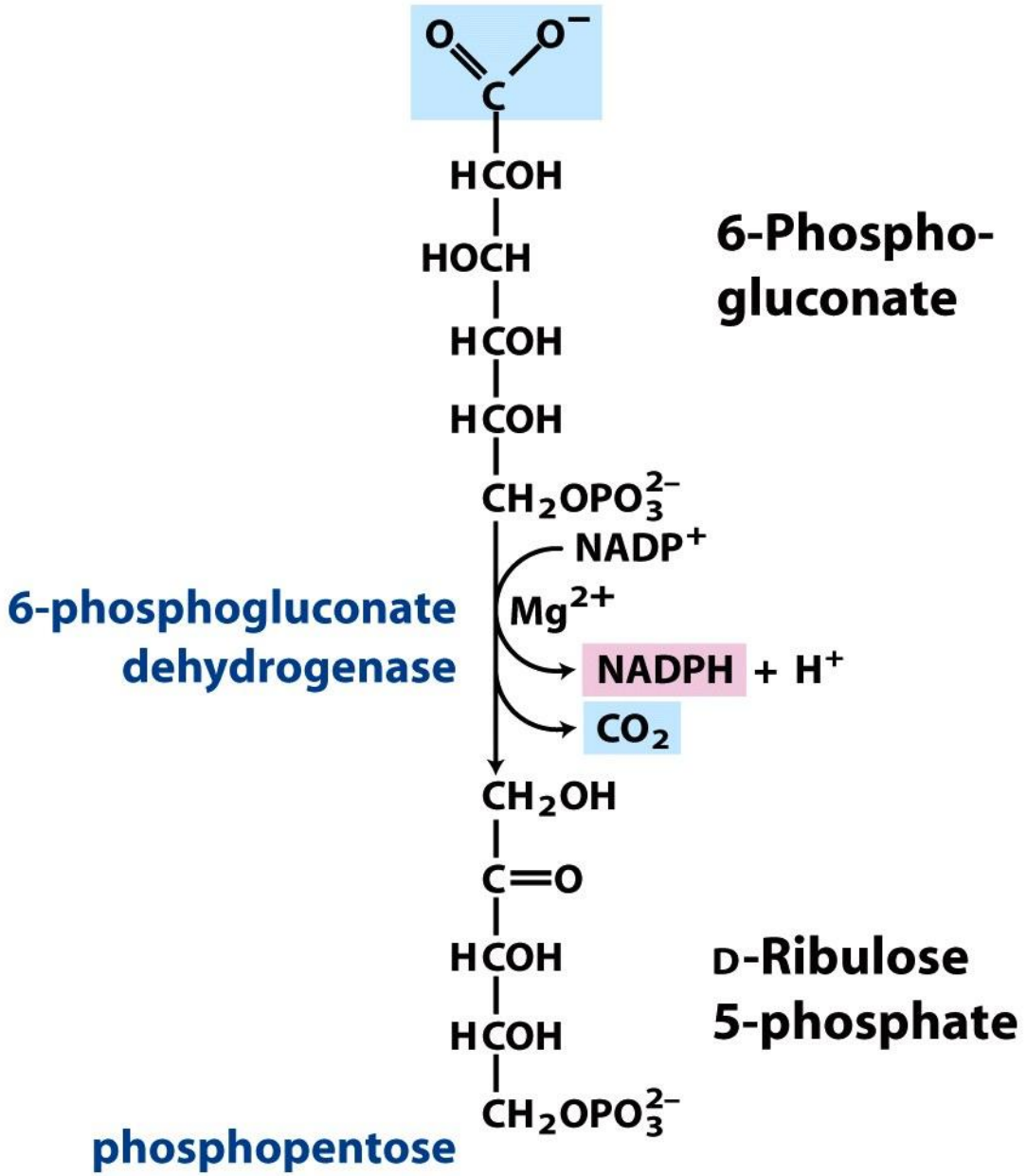

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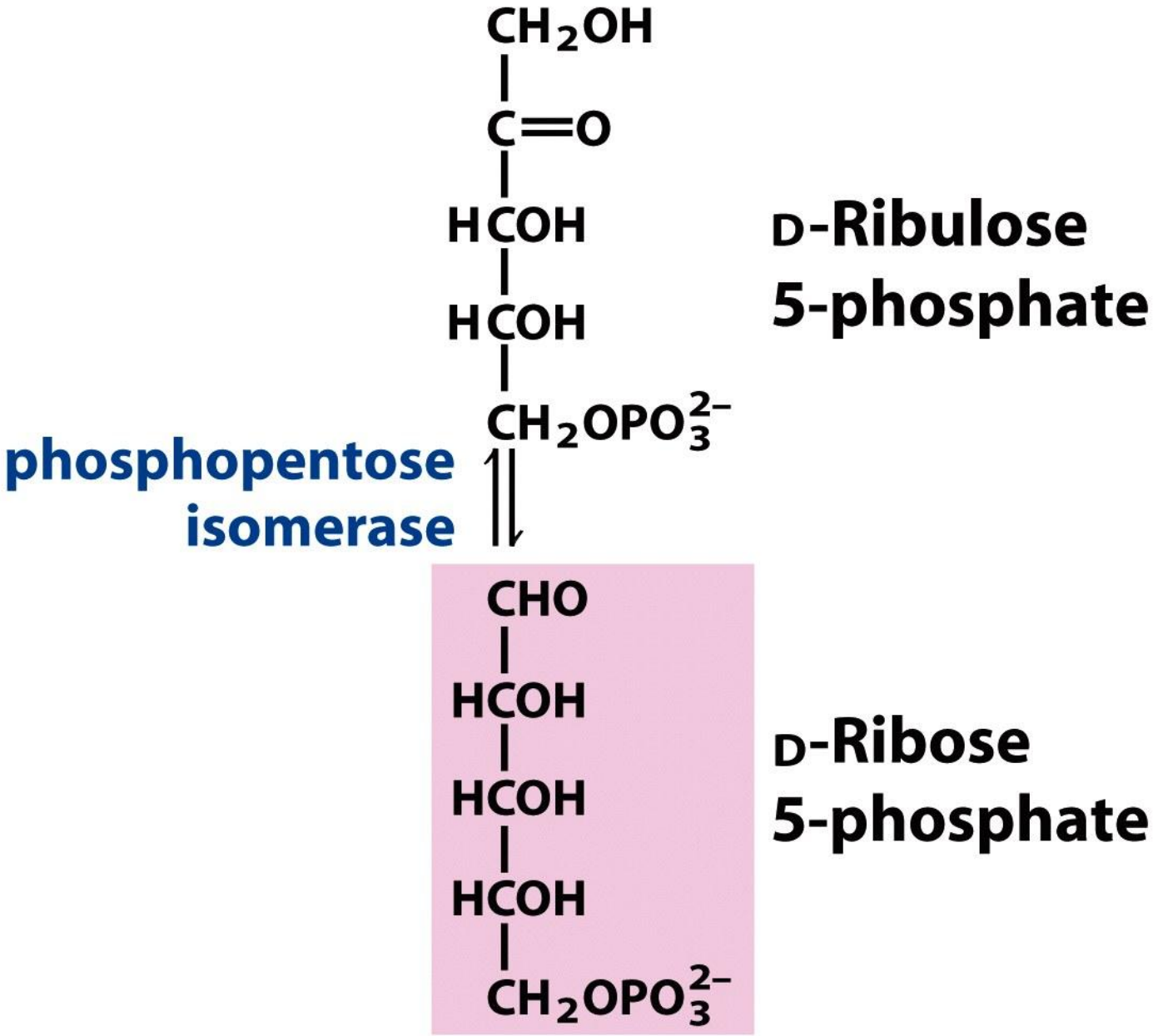

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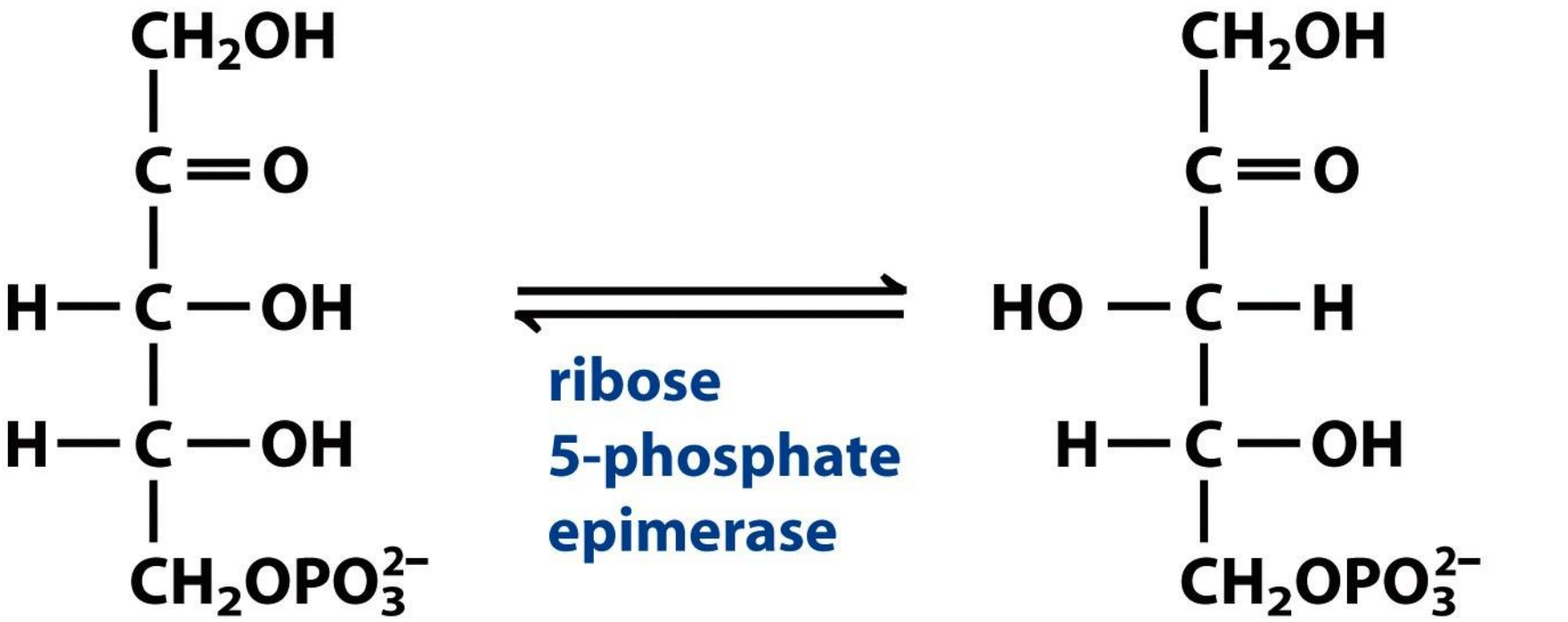

Ribulose 5-phosphate

Xylulose 5-phosphate

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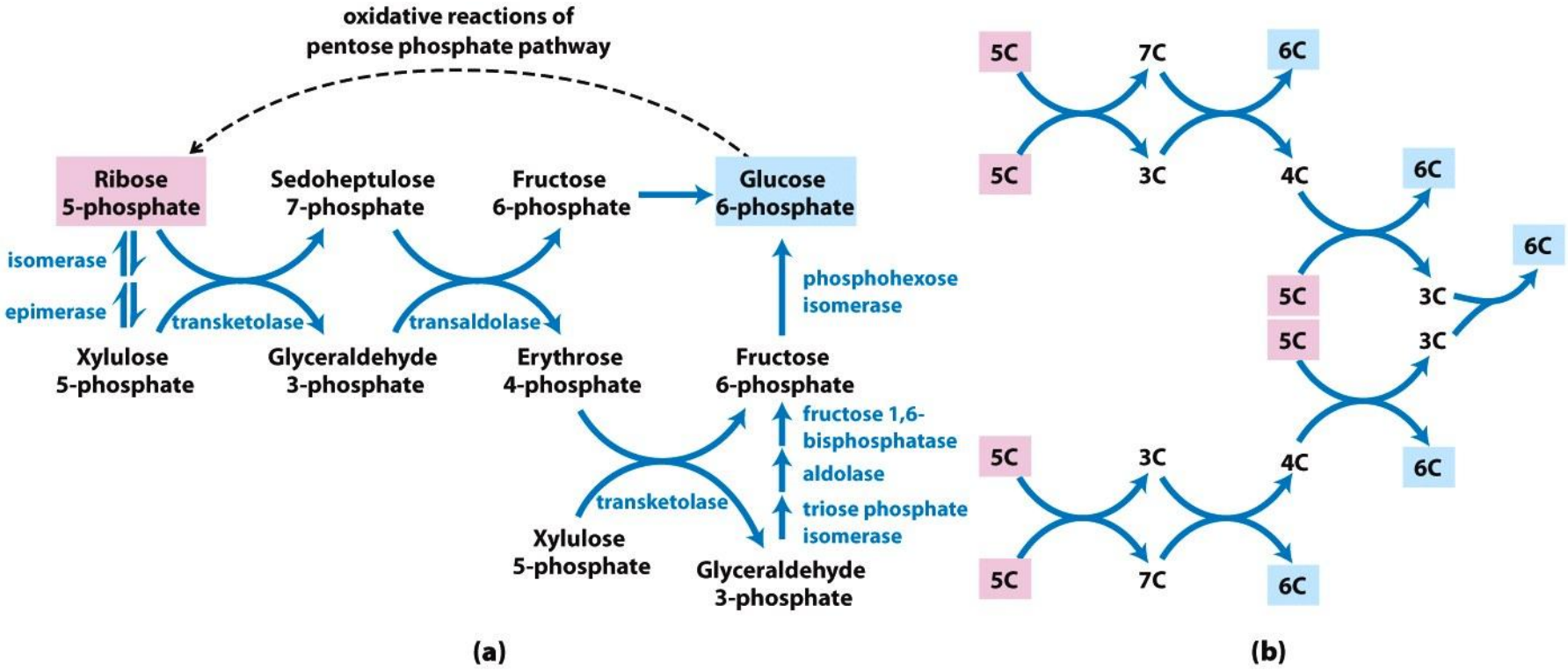

Figure 14-22

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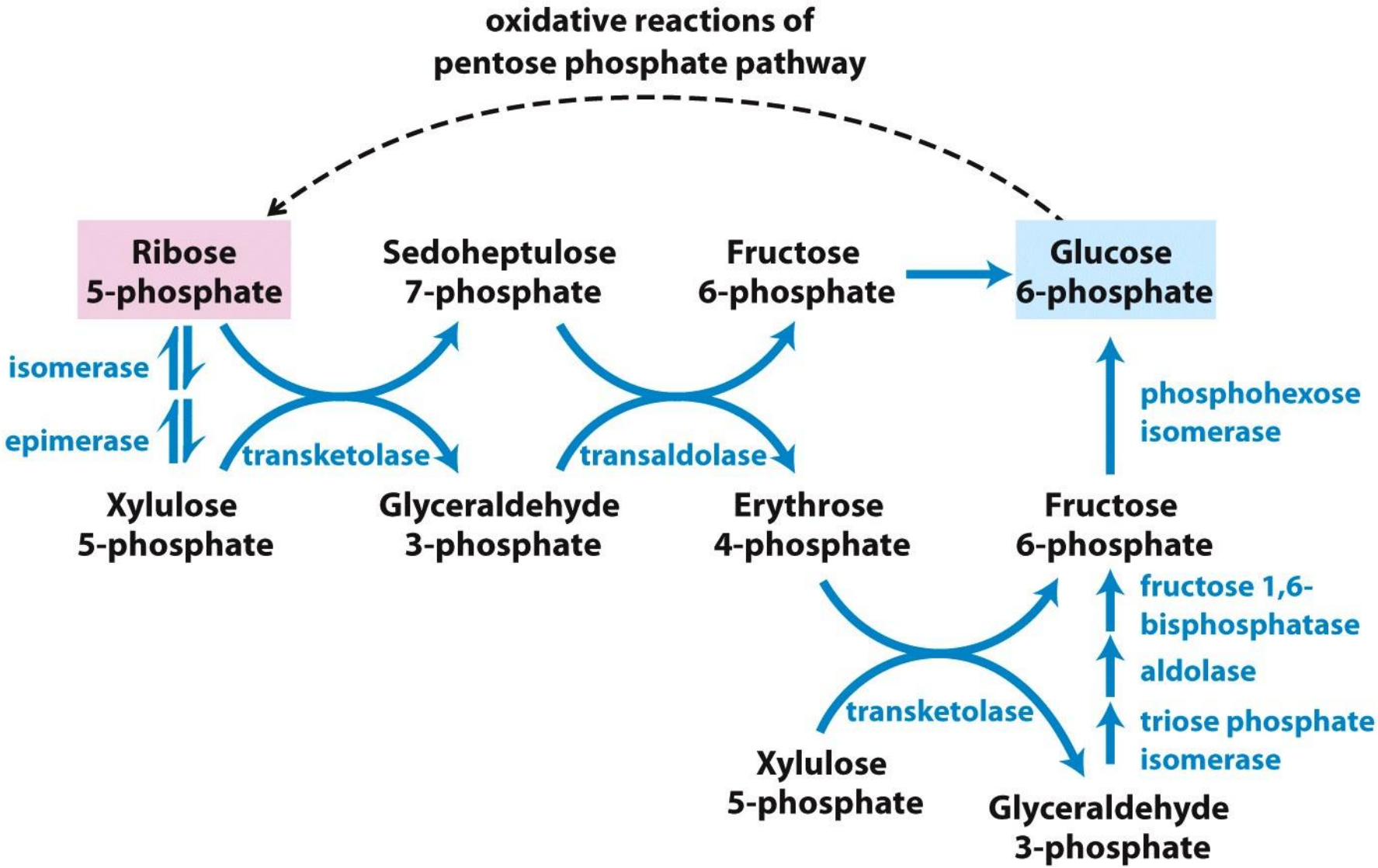

Figure 14-22a
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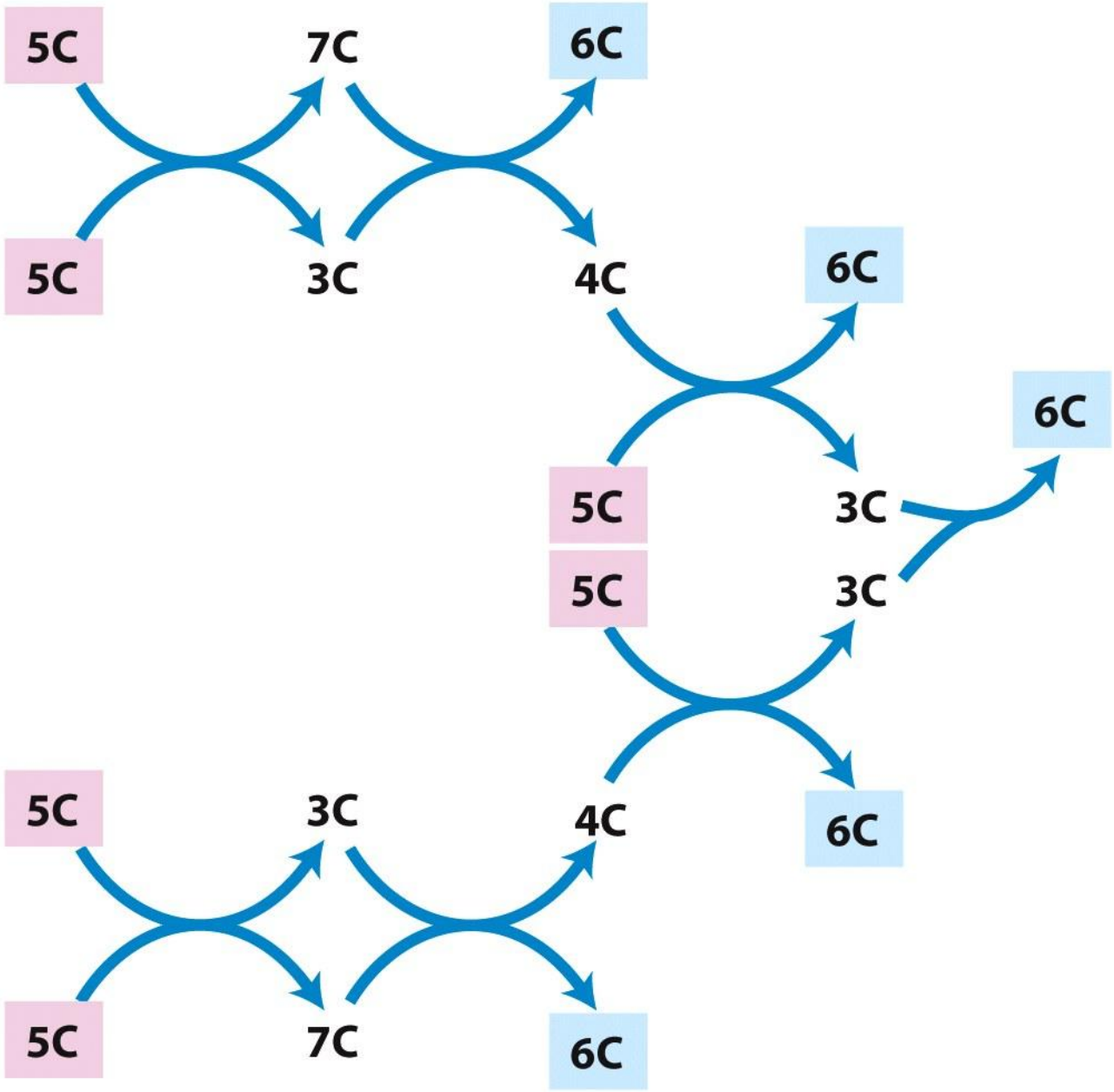

Figure 14-22b
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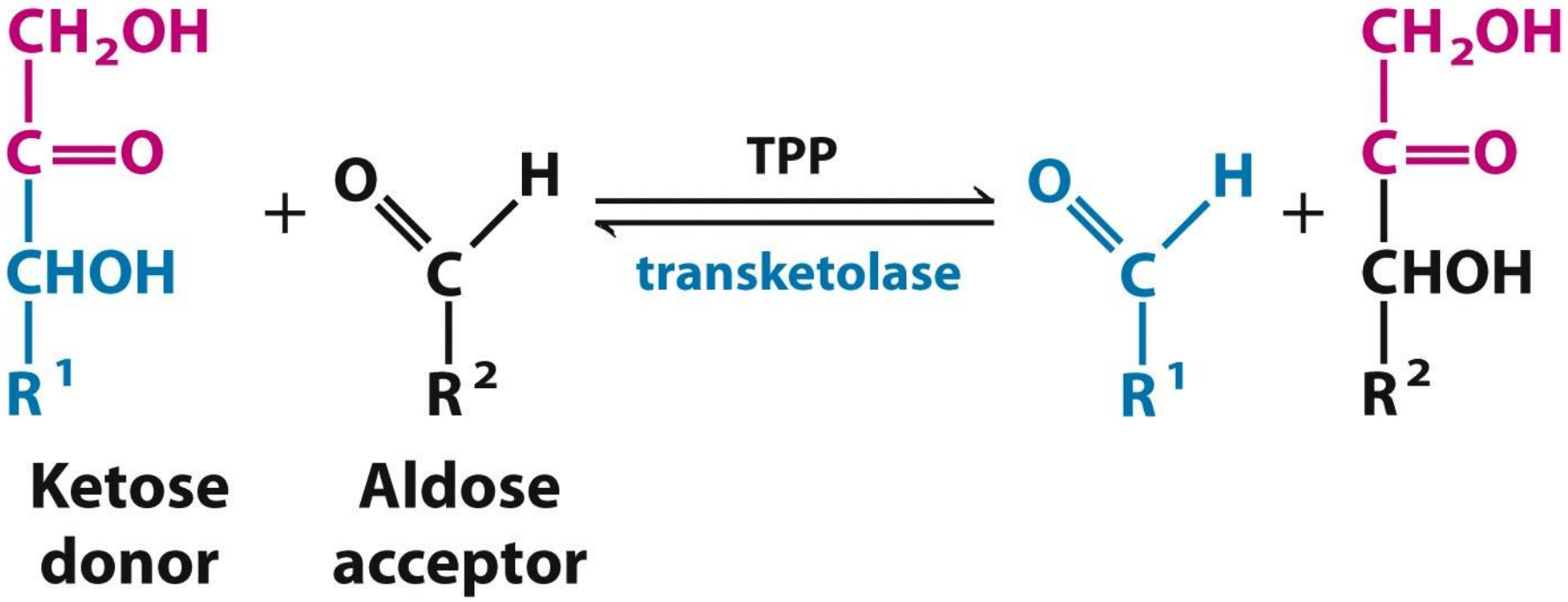

Figure 14-23a
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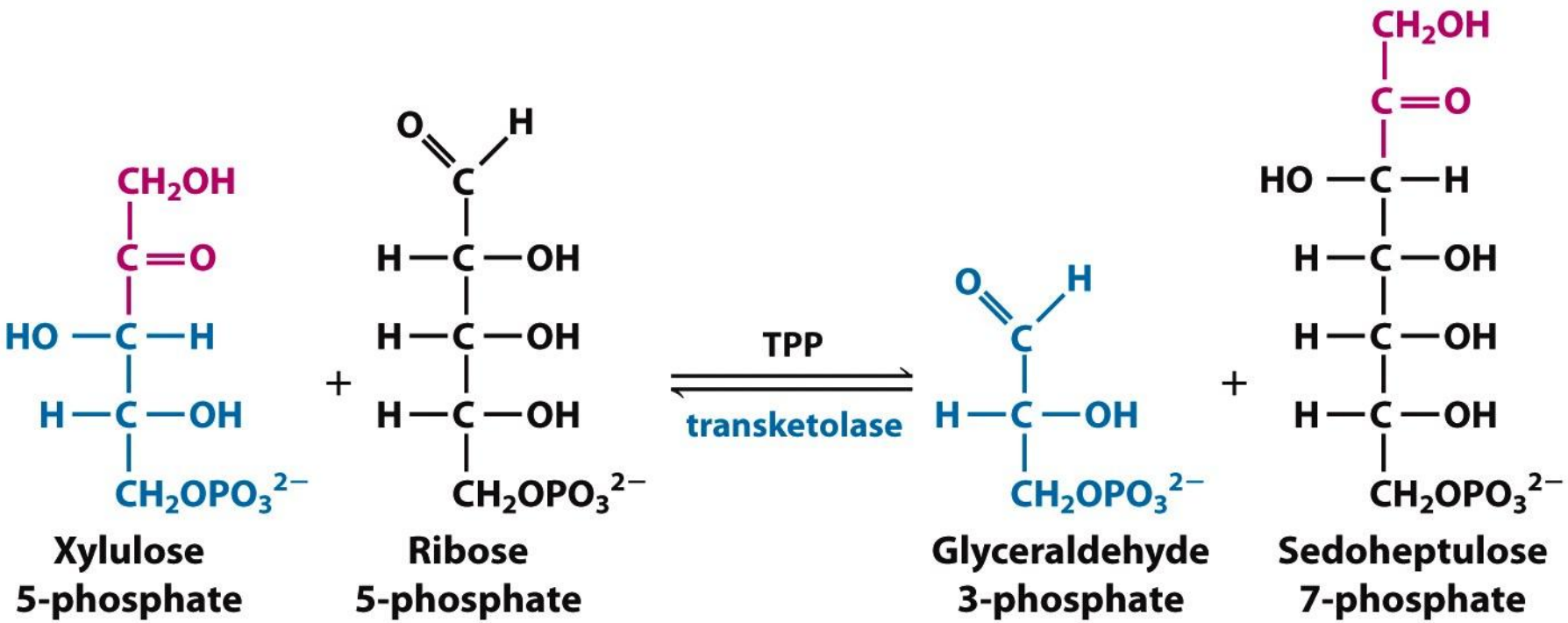

Figure 14-23b
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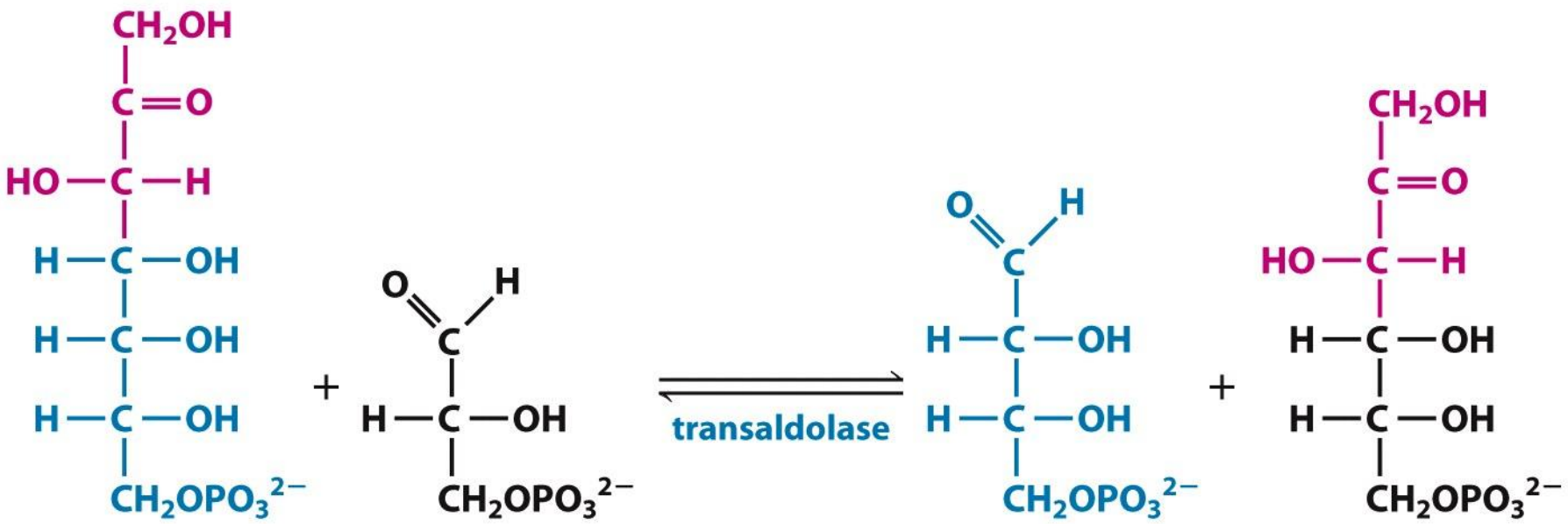

Figure 14-24
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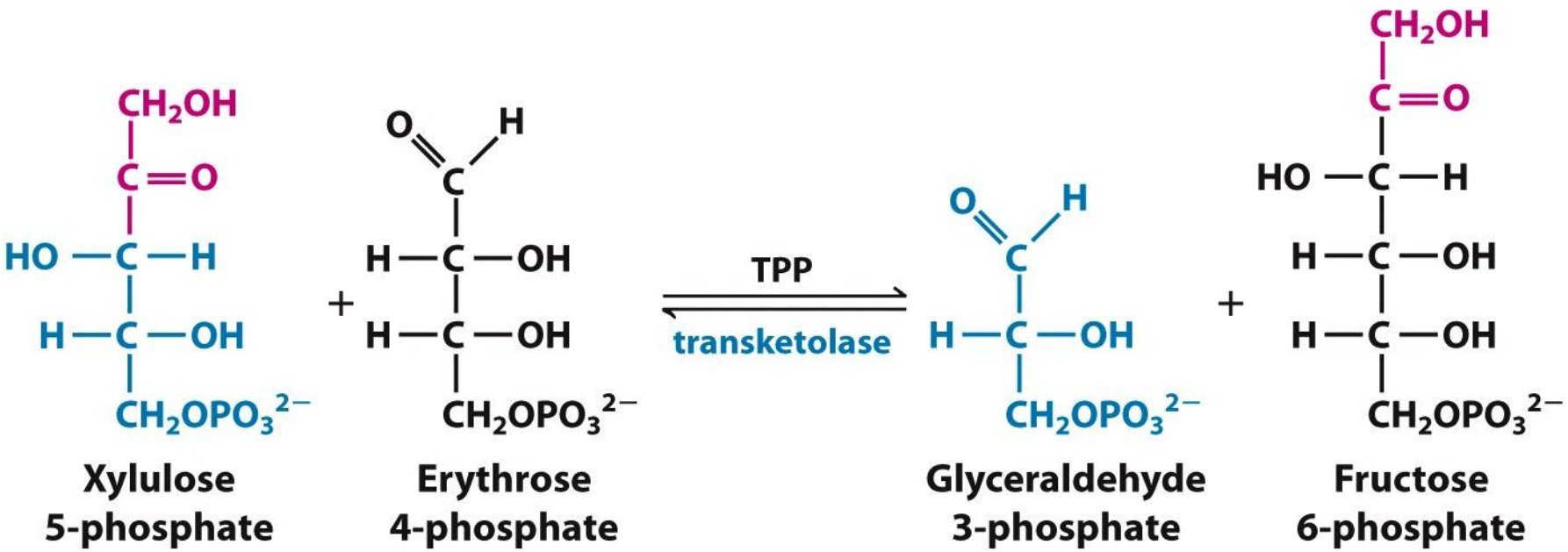

Figure 14-25
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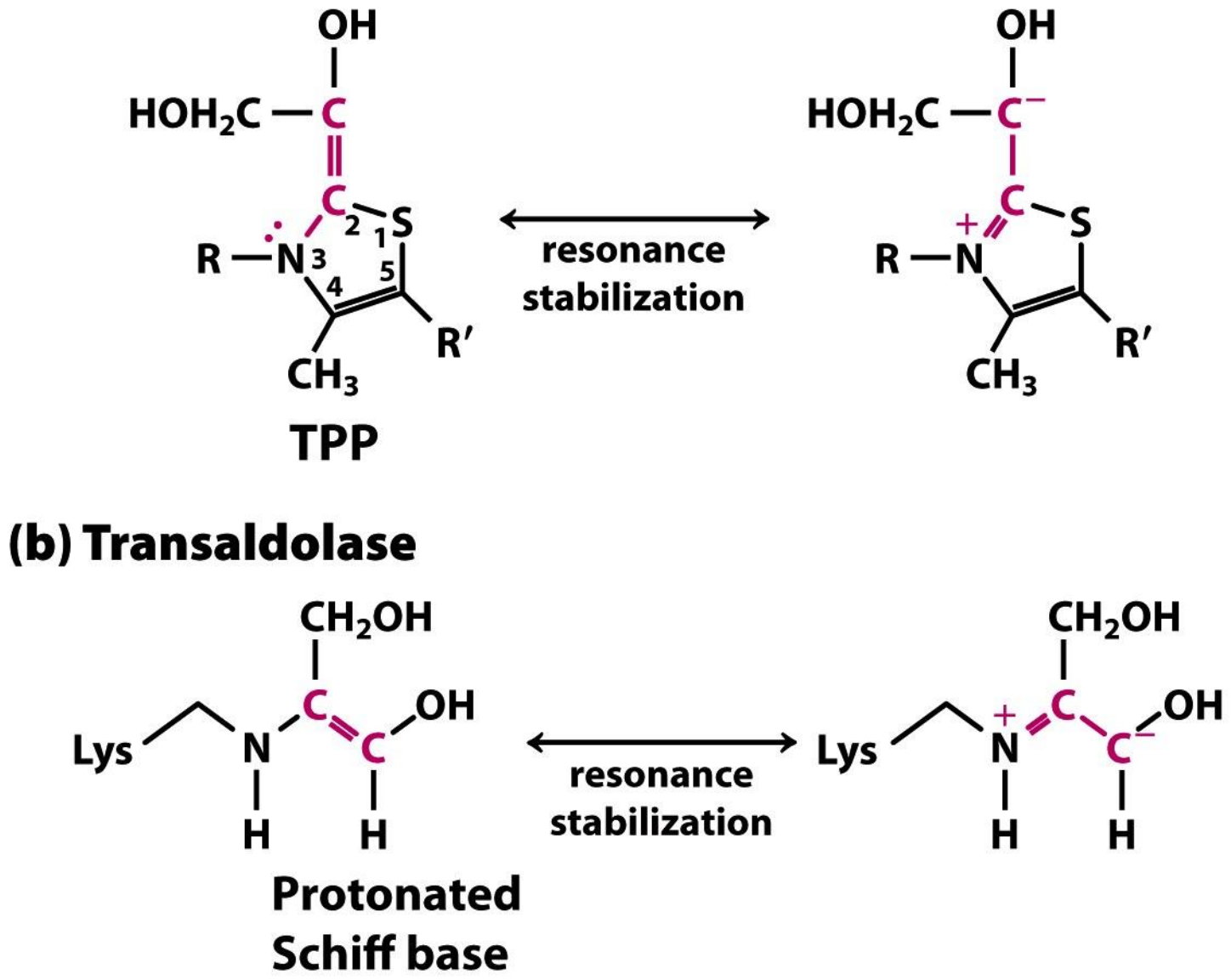

Figure 14-26
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Transketolase

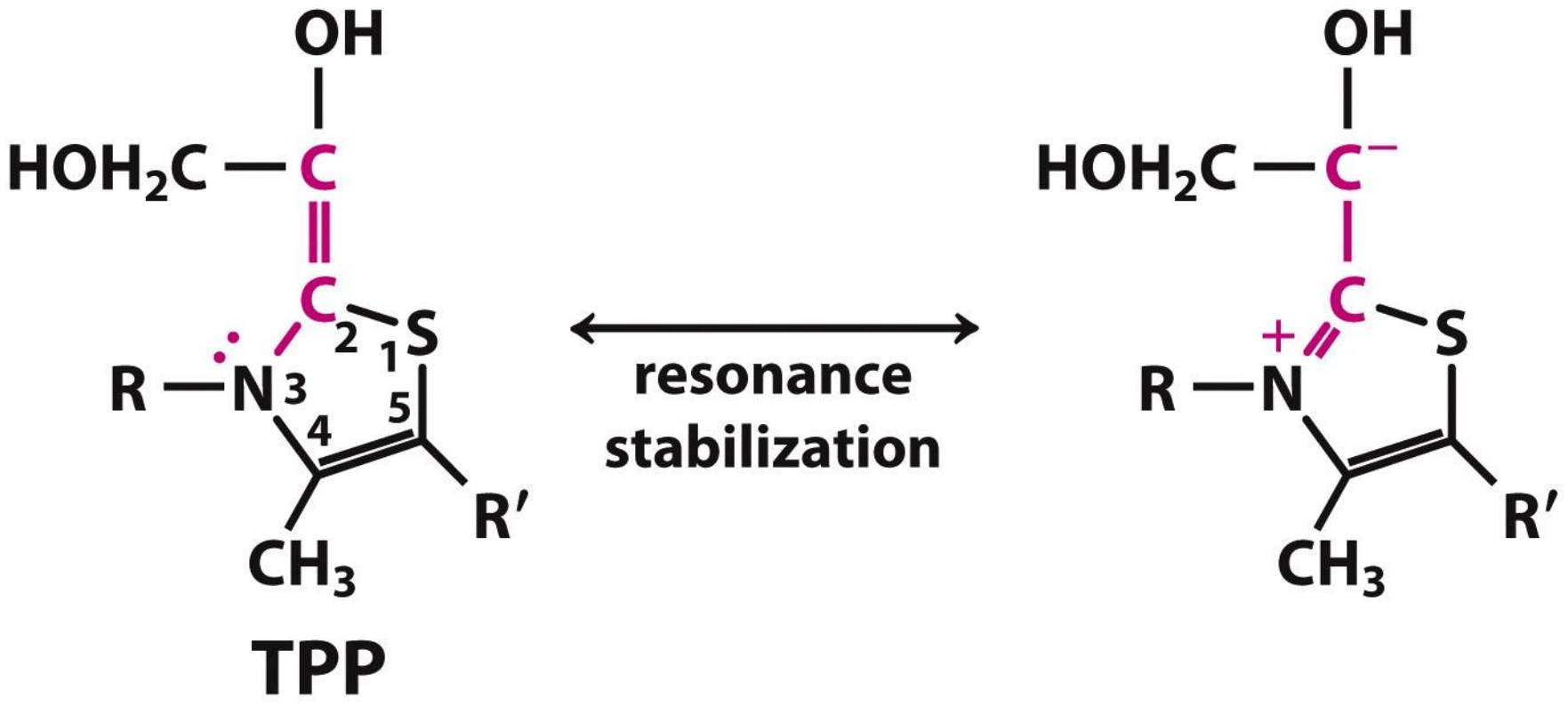

Figure 14-26a
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Transaldolase

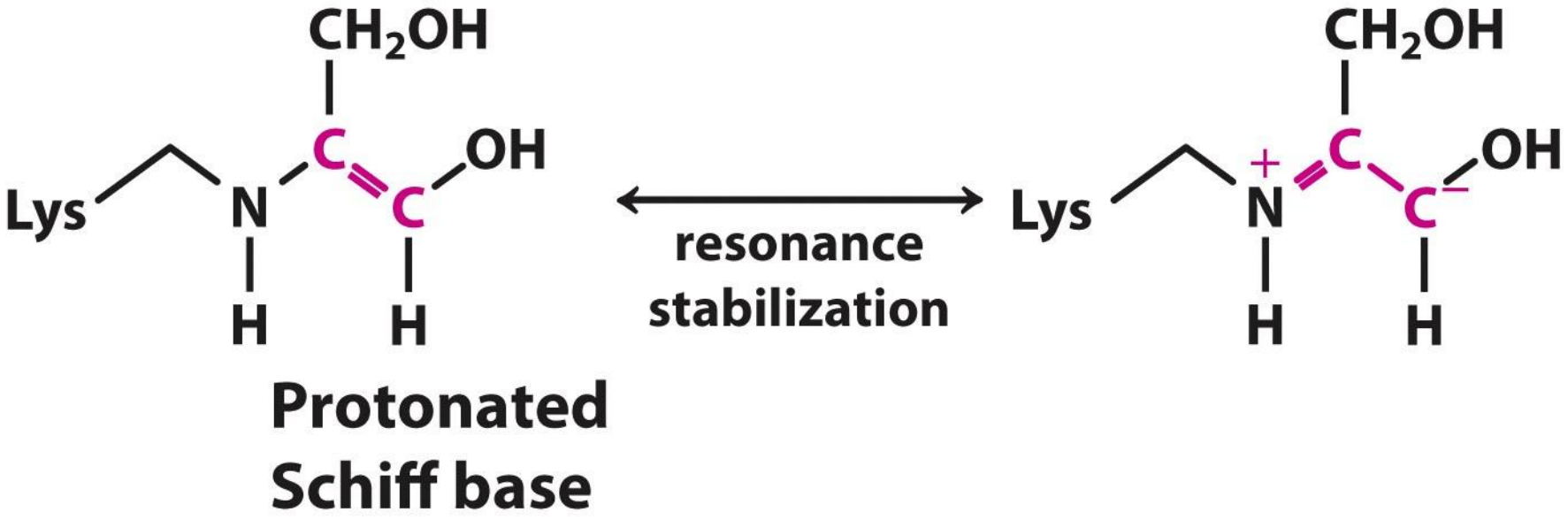

Figure 14-26b
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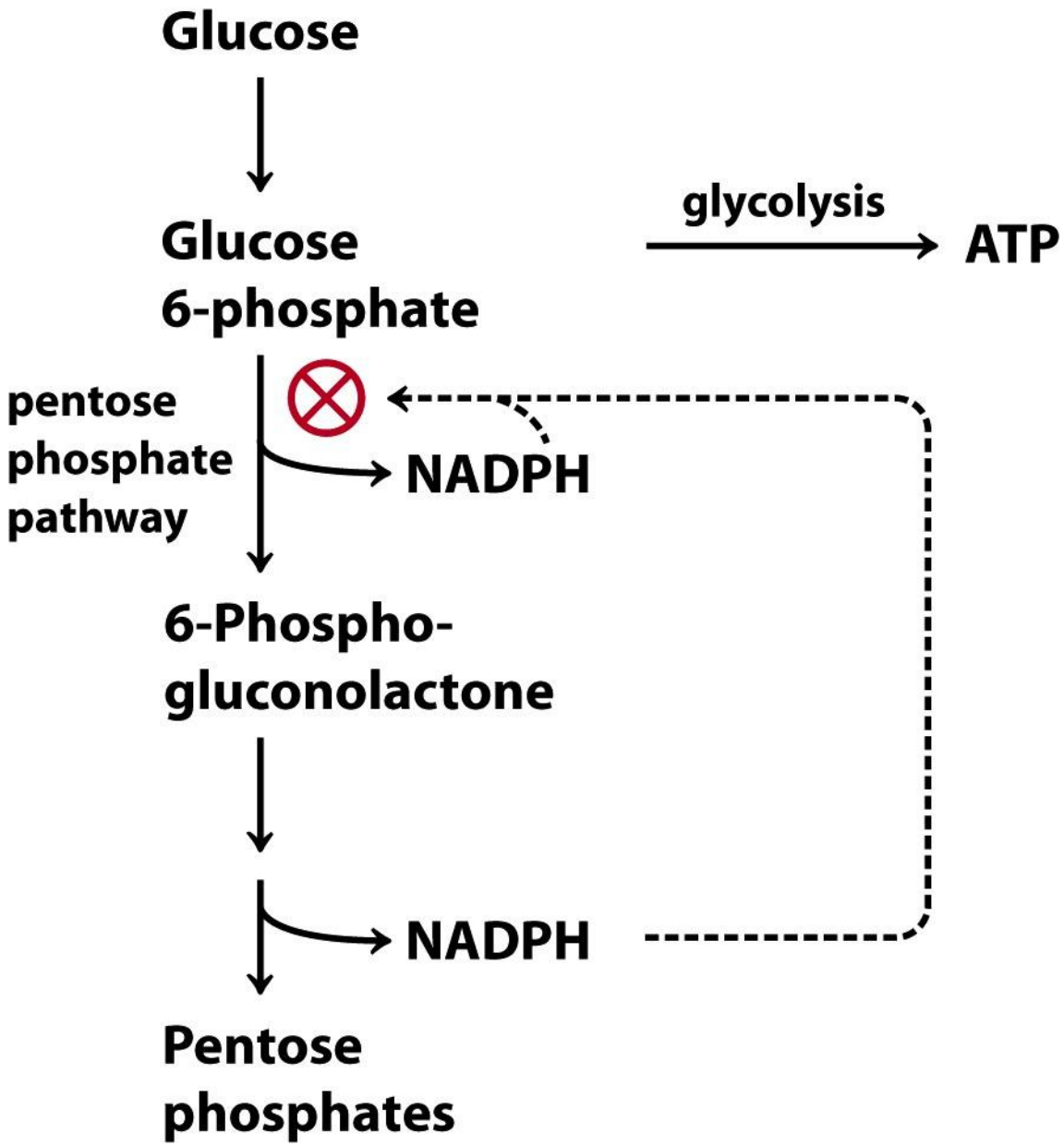

Figure 14-27
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