

Chapter 29 – The Organic Chemistry of Metabolic Pathways

Chapter Outline

I. Overview of metabolism and biochemical energy (Section 29.1).

A. Metabolism.

1. The reactions that take place in the cells of organisms are collectively called metabolism.
 - a. The reactions that produce smaller molecules from larger molecules are called catabolism.
 - b. The reactions that build larger molecules from smaller molecules are called anabolism.
2. Catabolism can be divided into four stages:
 - a. In digestion, bonds in food are hydrolyzed to yield sugars, fats, and amino acids.
 - b. These small molecules are degraded to acetyl CoA.
 - c. In the citric acid cycle, acetyl CoA is catabolized to CO₂, and energy is produced.
 - d. Energy from the citric acid cycle enters the electron transport chain, where ATP is synthesized.

B. Biochemical energy.

1. ATP, a phosphoric acid anhydride, is the storehouse for biochemical energy.
2. The breaking of a P–O bond of ATP can be coupled with an energetically unfavorable reaction, so that the overall energy change is favorable.
3. The resulting phosphates are much more reactive than the original compounds.

II. Lipid metabolism (Sections 29.2 – 29.4).

A. Catabolism of fats (Section 29.2 – 29.3).

1. Triacylglycerols are first hydrolyzed in the stomach and small intestine to yield glycerol plus fatty acids (Section 29.2).
 - a. The reaction is catalyzed by a lipase.

Aspartic acid, serine and histidine bring about reaction.
 - b. Glycerol is phosphorylated and oxidized and enters glycolysis.
 - i. The mechanism of oxidation involves a hydride transfer to NAD⁺.
 - ii. The addition to NAD⁺ is stereospecific.
2. β Oxidation (Section 29.3).
 - a. Fatty acids are degraded by β oxidation, a 4-step spiral that results in the cleavage of an n -carbon fatty acid into $n/2$ molecules of acetyl CoA.
 - b. Before entering β oxidation, a fatty acid is first converted to its fatty-acyl CoA.
3. Steps of β oxidation.
 - a. Introduction of a double bond conjugated with the carbonyl group.
 - i. The reaction is catalyzed by acyl CoA dehydrogenase.
 - ii. The enzyme cofactor FAD is also involved.
 - iii. The mechanism involves abstraction of the *pro-R* α and β hydrogens, resulting in formation of a trans double bond.
 - b. Conjugate addition of water to form an alcohol.

The reaction is catalyzed by enoyl CoA hydratase.
 - c. Alcohol oxidation.
 - i. The reaction is catalyzed by L-3-hydroxyacyl CoA dehydrogenase.
 - ii. The cofactor NAD⁺ is reduced to NADH/H⁺ at the same time.
 - iii. Histidine deprotonates the hydroxyl group.

- d. Cleavage of acetyl CoA from the chain.
 - i. The reaction, which is catalyzed by β -keto thiolase, is a retro-Claisen reaction.
 - ii. Nucleophilic addition of coenzyme A to the keto group is followed by loss of acetyl CoA enolate, leaving behind a chain-shortened fatty-acyl CoA.
- 3. An n -carbon fatty acid yields $n/2$ molecules of acetyl CoA after $(n/2 - 1)$ passages of β oxidation.
 - a. Since most fatty acids have an even number of carbons, no carbons are left over after β oxidation.
 - b. Those with an odd number of carbons require further steps for degradation.
- B. Biosynthesis of fatty acids (Section 29.4).
 - 1. General principles.
 - a. In most cases, the pathway of synthesis isn't the exact reverse of degradation.
 - i. If ΔG° is negative for one route, it must be positive for the exact reverse, which is thus energetically unfavorable.
 - ii. The metabolic strategy is for one pathway to be related to its reverse but not to be identical.
 - b. All common fatty acids have an even number of carbons because they are synthesized from acetyl CoA.
 - c. In vertebrates, a large multienzyme synthase complex catalyzes all steps in the pathway.
 - 2. Synthetic pathway.
 - a. Steps 1–2: Acyl transfers convert acetyl CoA to more reactive species.
 - i. Acetyl CoA is converted to acetyl ACP.
 - ii. The acetyl group of acetyl ACP is transferred to the synthase enzyme.
 - b. Steps 3–4: Carboxylation and acyl transfer.
 - i. Acetyl CoA reacts with bicarbonate to yield malonyl CoA and ADP. The coenzyme biotin, a CO_2 carrier, transfers CO_2 in a nucleophilic acyl substitution reaction.
 - ii. Malonyl CoA is converted to malonyl ACP.
 - iii. At this point, both acetyl groups and malonyl groups are bound to the synthase enzyme.
 - c. Step 5: Condensation.
 - i. A Claisen condensation forms acetoacetyl CoA from acetyl synthase and malonyl ACP.
 - ii. The reaction proceeds by an initial decarboxylation of malonyl ACP to give an enolate that adds to acetyl synthase to form acetoacetyl CoA.
 - d. Steps 6–8: Reduction and dehydrogenation.
 - i. The ketone group of acetoacetyl CoA is reduced by NADPH.
 - ii. The β -hydroxy thiol ester is dehydrated.
 - iii. The resulting double bond is hydrogenated by NADPH to yield butyryl ACP.
 - e. The steps are repeated with butyryl synthase and malonyl ACP to give a six-carbon unit.
 - f. Fatty acids up to palmitic acid are synthesized by this route. Elongation of palmitic acid and larger acids occurs with acetyl CoA units as the two-carbon donor.
- III. Carbohydrate metabolism (Sections 29.5 – 29.8).
 - A. Catabolism of carbohydrates (Sections 29.5 – 29.7).
 - 1. Glycolysis (Section 29.5).
 - a. Glycolysis is a 10-step series of reactions that converts glucose to pyruvate.

- b. Steps 1–2: Phosphorylation and isomerization.
 - i. Glucose is phosphorylated at the 6-position by reaction with ATP.
The enzyme hexokinase is involved.
 - ii. Glucose 6-P is isomerized to fructose 6-P by glucose-6-P isomerase.
 - c. Step 3: Fructose 6-P is phosphorylated to yield fructose 1,6-bisphosphate.
ATP and phosphofructokinase are involved.
 - d. Step 4: Cleavage.
Fructose 1,6-bisphosphate is cleaved to glyceraldehyde 3-phosphate and dihydroxyacetone phosphate.
The reaction is a reverse aldol reaction catalyzed by aldolase.
 - e. Step 5: Isomerization
 - i. Dihydroxyacetone phosphate is isomerized to glyceraldehyde 3-phosphate.
 - ii. The net result is production of two glyceraldehyde 3-phosphates, both of which pass through the rest of the pathway.
 - f. Steps 6–7: Oxidation, phosphorylation, and dephosphorylation.
 - i. Glyceraldehyde 3-phosphate is both oxidized and phosphorylated to give 1,3-bisphosphoglycerate.
Oxidation by NAD^+ occurs via a hemithioacetal to yield a product that forms the mixed anhydride.
 - ii. The mixed anhydride reacts with ADP to form ATP and 3-phosphoglycerate.
The enzyme phosphoglycerate kinase is involved.
 - g. Step 8: Isomerization.
3-Phosphoglycerate is isomerized to 2-phosphoglycerate by phosphoglycerate mutase.
 - h. Steps 9–10: Dehydration and dephosphorylation.
 - i. 2-Phosphoglycerate is dehydrated by enolase to give PEP.
 - ii. Pyruvate kinase catalyzes the transfer of a phosphate group to ADP, with formation of pyruvate.
 2. The conversion of pyruvate to acetyl CoA (Section 29.6).
 - a. The conversion pyruvate \rightarrow acetyl CoA is catalyzed by an enzyme complex called pyruvate dehydrogenase complex.
 - b. Step 1: Addition of thiamin.
A nucleophilic ylide group on thiamin diphosphate adds to the carbonyl group of pyruvate to yield a tetrahedral intermediate.
 - c. Step 2: Decarboxylation.
 - d. Step 3: Reaction with lipoamide.
The enamine product of decarboxylation reacts with lipoamide, displacing sulfur and opening the lipoamide ring.
 - e. Step 4: Elimination of thiamin.
 - f. Step 5: Acyl transfer.
 - i. Acetyl dihydrolipoamide reacts with coenzyme A to give acetyl CoA.
 - ii. The resulting dihydrolipoamide is reoxidized to lipoamide by FAD.
 - iii. FADH_2 is reoxidized to FAD by NAD^+ .
 - g. Other fates of pyruvate.
 - i. In the absence of oxygen, pyruvate is reduced to lactate.
 - ii. In bacteria, pyruvate is fermented to ethanol.
 3. The citric acid cycle (Section 29.7).
 - a. Characteristics of the citric acid cycle.
 - i. The citric acid cycle is a closed loop.
 - ii. The intermediates are constantly regenerated.
 - iii. The cycle operates as long as NAD^+ and FADH_2 are available, which means that oxygen must also be available.

- b. Steps 1–2: Addition to oxaloacetate.
 - i. Acetyl CoA adds to oxaloacetate to form citryl CoA, which is hydrolyzed to citrate.

The reaction is catalyzed by citrate synthase.
 - ii. Citrate is isomerized to isocitrate by aconitase.

The reaction is an E1cb dehydration, followed by conjugate addition of water.
 - c. Steps 3–4: Oxidative decarboxylations.
 - i. Isocitrate is oxidized by isocitrate dehydrogenase to give a ketone that loses CO_2 to give α -ketoglutarate.
 - ii. α -Ketoglutarate is transformed to succinyl CoA in a reaction catalyzed by a multienzyme dehydrogenase complex.
 - d. Steps 5–6: Hydrolysis and dehydrogenation of succinyl CoA.
 - i. Succinyl CoA is converted to an acyl phosphate, which transfers a phosphate group to GDP in a reaction catalyzed by succinyl CoA synthase.
 - ii. Succinate is dehydrogenated by FAD and succinate dehydrogenase to give fumarate; the reaction is stereospecific.
 - e. Steps 7–8: Regeneration of oxaloacetate.
 - i. Fumarase catalyzes the addition of water to fumarate to produce L-malate.
 - ii. L-malate is oxidized by NAD^+ and malate dehydrogenase to complete the cycle.
- C. Carbohydrate biosynthesis: gluconeogenesis (Section 29.8).
- 1. Step 1: Carboxylation.

Pyruvate is carboxylated in a reaction that uses biotin and ATP.
 - 2. Step 2: Decarboxylation and phosphorylation.

Concurrent decarboxylation and phosphorylation produce phosphoenolpyruvate.
 - 3. Steps 3–4: Hydration and isomerization.
 - a. Conjugate addition of water gives 2-phosphoglycerate.
 - b. Isomerization produces 3-phosphoglycerate.
 - 4. Steps 5–7: Phosphorylation, reduction and tautomerization.
 - a. Reaction of 3-phosphoglycerate with ATP yields an acyl phosphate.
 - b. The acyl phosphate is reduced by NADPH/H^+ to an aldehyde.
 - c. The aldehyde tautomerizes to dihydroxyacetone phosphate.
 - 5. Step 8: Aldol reaction.
 - a. Dihydroxyacetone phosphate and glyceraldehyde 3-phosphate join to form fructose 1,6-bisphosphate.
 - b. This reaction involves the imine of dihydroxyacetone phosphate, which forms an enamine that takes part in the condensation.
 - 6. Steps 9–11: Hydrolysis and isomerization.
 - a. Fructose 1,6-bisphosphate is hydrolyzed to fructose 6-phosphate.
 - b. Fructose 6-phosphate isomerizes to glucose 6-phosphate.
 - c. Glucose 6-phosphate is hydrolyzed to glucose.
 - 7. Several of these steps are the reverse of steps of glycolysis.

IV. Protein metabolism (Section 29.9).

Catabolism of proteins: Transamination.

1. The pathway to amino acid catabolism:
 - a. The amino group is removed by transamination.
 - b. What remains is converted to a compound that enters the citric acid cycle.
2. Transamination.
 - a. The -NH_2 group of an amino acid adds to the aldehyde group of pyridoxal phosphate to form an imine.
 - b. The imine tautomerizes to a different imine.
 - c. The second imine is hydrolyzed to give an α -keto acid and an amino derivative of pyridoxal phosphate.
 - d. The pyridoxal derivative transfers its amino group to α -ketoglutarate, to regenerate pyridoxal phosphate and form glutamate.

3. Deamination.

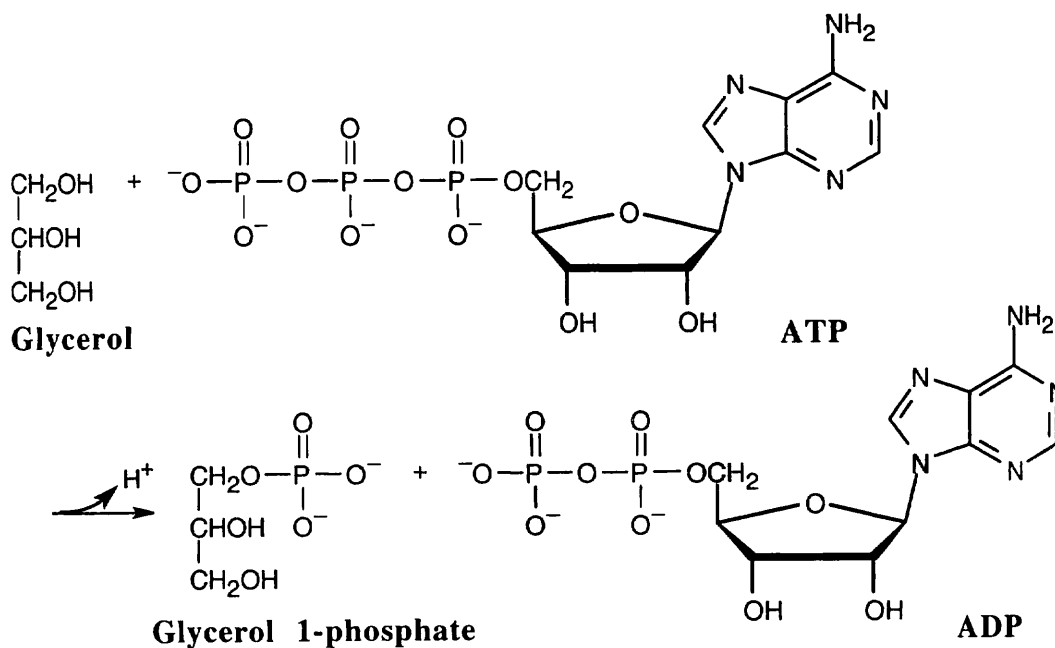
The glutamate from transamination undergoes oxidative deamination to yield ammonium ion and α -ketoglutarate.

V. Some conclusions about biological chemistry (Section 29.10).

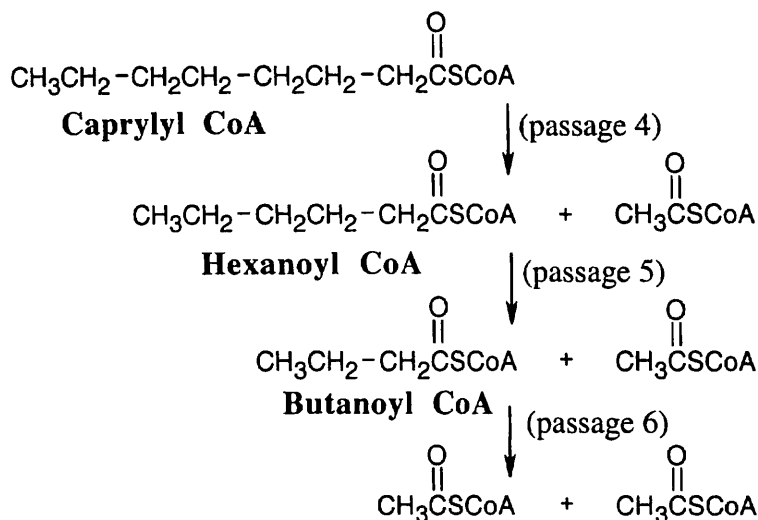
1. The mechanisms of biochemical reactions are almost identical to the mechanisms of laboratory reactions.
2. Most metabolic pathways are linear.
 - a. Linear pathways make sense when a multifunctional molecule is undergoing transformation.
 - b. Cyclic pathways may be more energetically feasible when a molecule is small.

Solutions to Problems

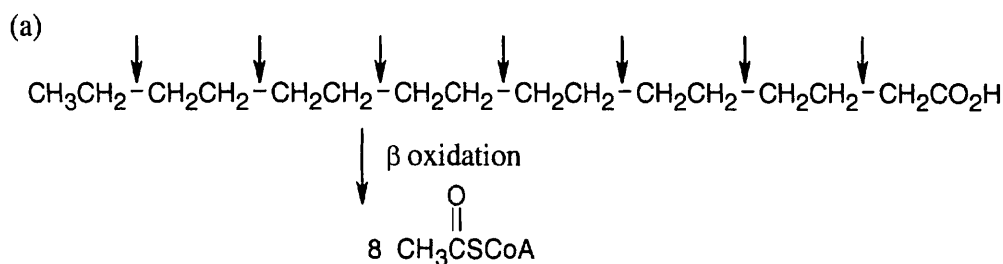
29.1 This reaction is a substitution at phosphorus, with ADP as the leaving group.



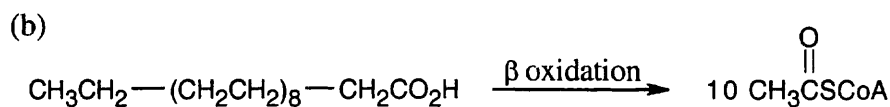
29.2



29.3 A fatty acid with n carbons yields $n/2$ acetyl CoA molecules after $(n/2 - 1)$ passages of the β -oxidation pathway.

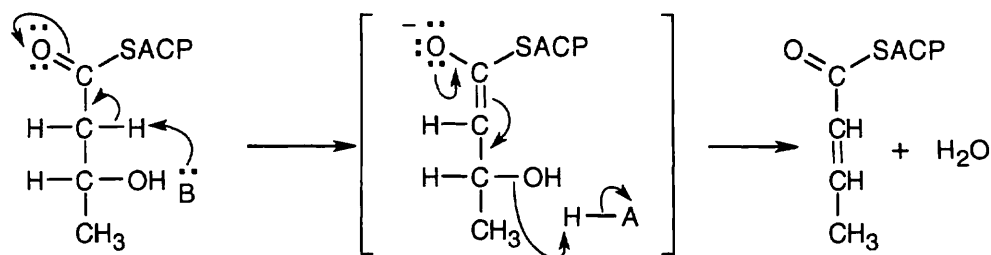


Seven passages of the β -oxidation pathway are needed.

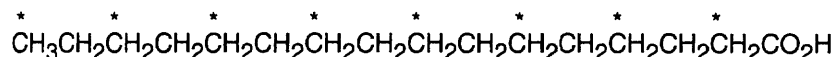


Nine passages of the β -oxidation pathway are needed.

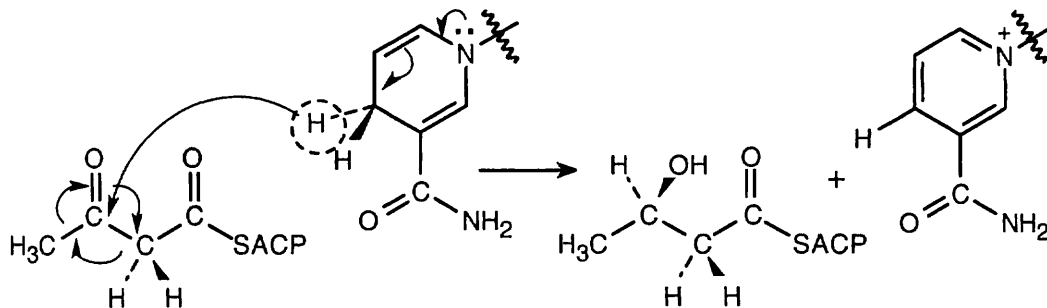
29.4 β -Hydroxybutyryl ACP resembles the β -hydroxy ketones that were described in Chapter 23 and that dehydrate readily by an E1cB mechanism.



- 29.5** A fatty acid synthesized from $^{13}\text{CH}_3\text{CO}_2\text{H}$ has an alternating labeled and unlabeled carbon chain. The carboxylic acid carbon is unlabeled.



- 29.6** The face in front of the plane of the page is the *Re* face. Since addition occurs from behind the plane of the page, it occurs at the *Si* face.



- 29.7** ATP is produced in step 7 (1,3-bisphosphoglycerate \rightarrow 3-phosphoglycerate) and in step 10 (phosphoenolpyruvate \rightarrow pyruvate).

- 29.8** **Step 1** is a nucleophilic acyl substitution at phosphorus (*phosphate transfer*) by the $-\text{OH}$ group at C6 of glucose, with ADP as the leaving group.

Step 2 is an *isomerization*, in which the pyranose ring of glucose 6-phosphate opens, tautomerism causes isomerization to fructose 6-phosphate, and a furanose ring is formed.

Step 3 is a substitution, similar to the one in step 1, involving the $-\text{OH}$ group at C1 of fructose 6-phosphate (*phosphate transfer*).

Step 4 is a *retro-aldol reaction* that cleaves fructose 1,6-bisphosphate to glyceraldehyde 3-phosphate and dihydroxyacetone phosphate.

Step 5 is an *isomerization* of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate that occurs by keto–enol tautomerization.

Step 6 begins with a nucleophilic addition reaction to the aldehyde group of glyceraldehyde 3-phosphate by a thiol group of an enzyme to form a hemithioacetal, which is *oxidized* by NAD^+ to an acyl thioester. *Nucleophilic acyl substitution* by phosphate yields the product 1,3-bisphosphoglycerate.

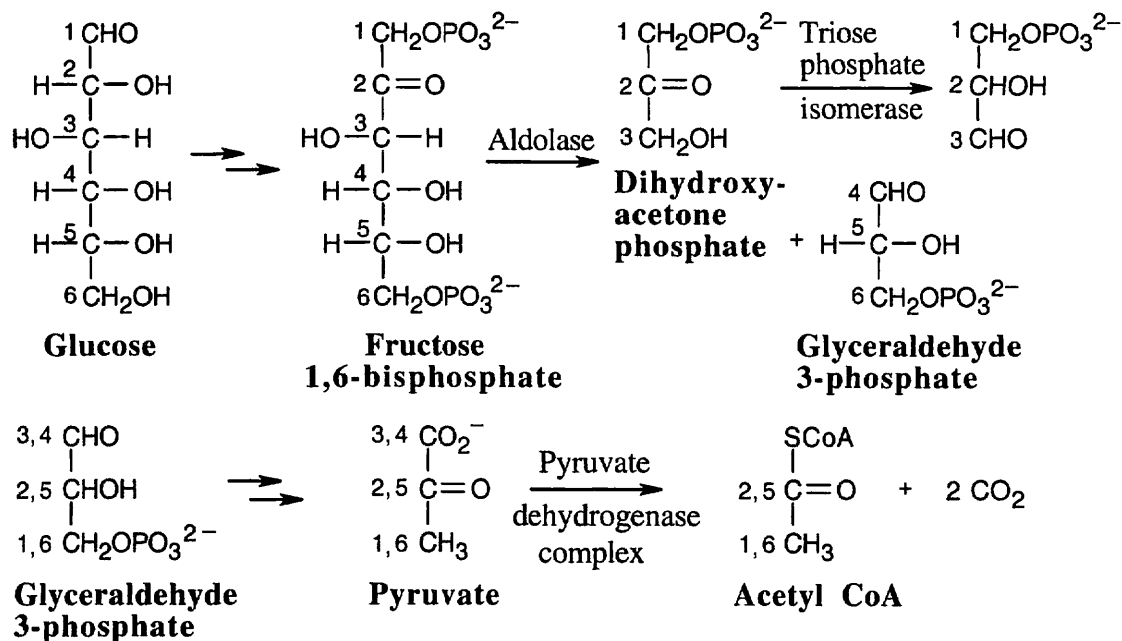
Step 7 is a nucleophilic acyl substitution reaction at phosphorus, in which ADP reacts with 1,3-bisphosphoglycerate, yielding ATP and 3-phosphoglycerate (*phosphate transfer*).

Step 8 is an *isomerization* of 3-phosphoglycerate to 2-phosphoglycerate.

Step 9 is an *EnB elimination* of H_2O to form phosphoenolpyruvate.

Step 10 is a substitution reaction at phosphorus that forms ATP and enolpyruvate, which tautomerizes to pyruvate (*phosphate transfer*).

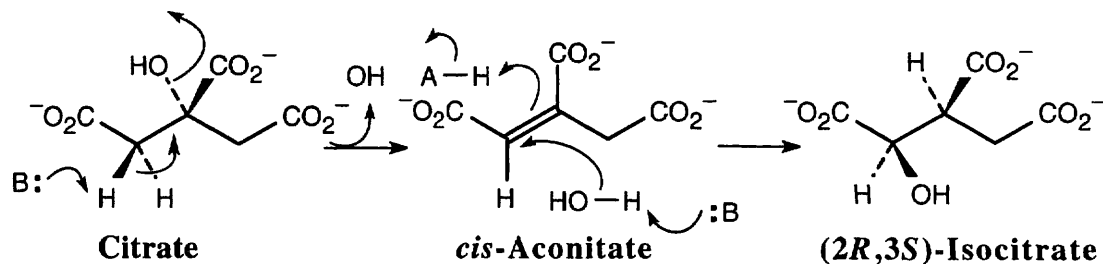
29.9



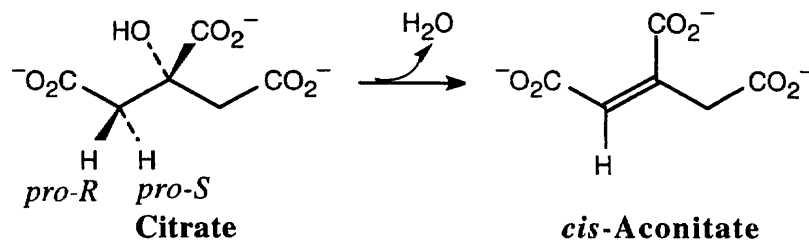
Carbons 1 and 6 of glucose end up as $-\text{CH}_3$ groups of acetyl CoA, and carbons 3 and 4 of glucose end up as CO_2 .

29.10 Citrate and isocitrate are tricarboxylic acids.

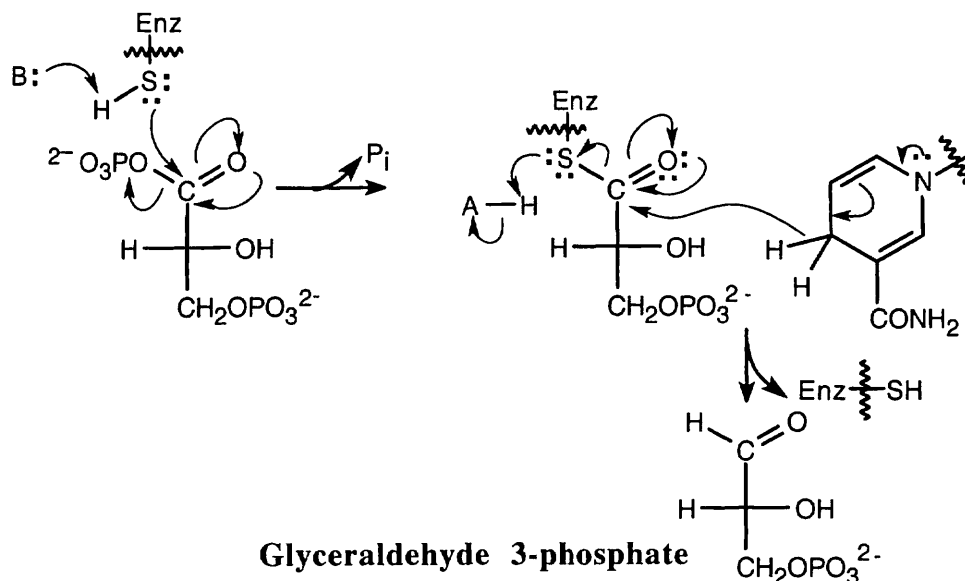
29.11



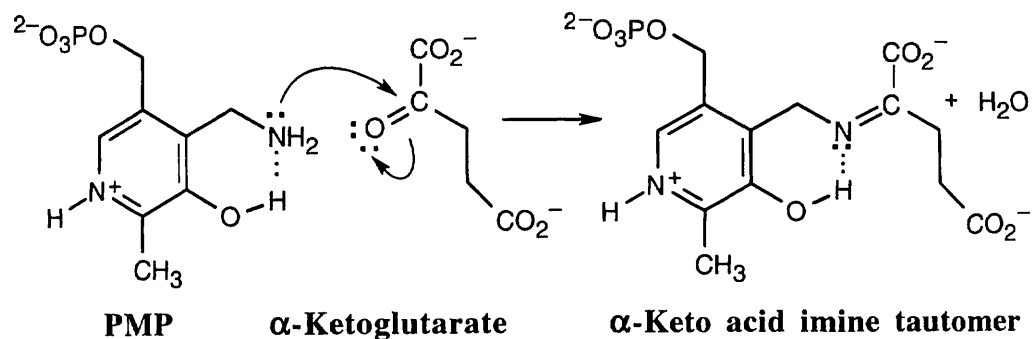
29.12 The *pro-R* hydrogen is removed during dehydration, and the reaction occurs with *anti* geometry.



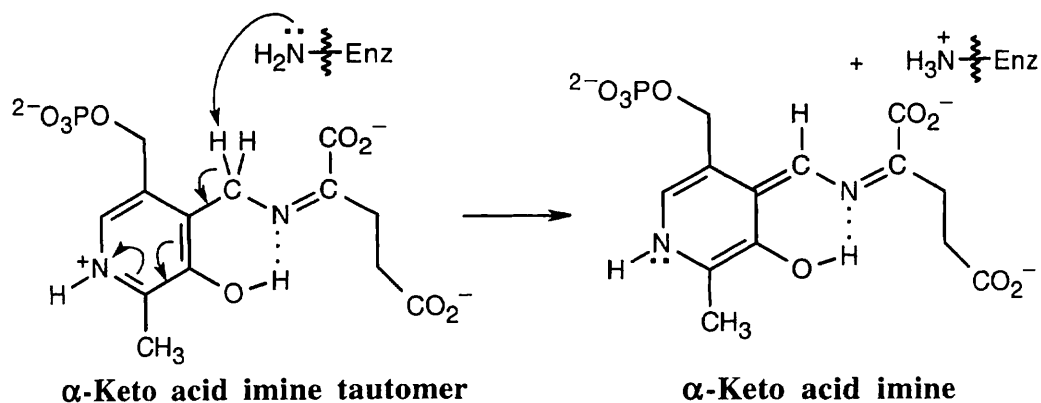
29.13 First, 1,3-bisphosphoglycerate reacts with a cysteine residue of the enzyme in a nucleophilic acyl substitution reaction, with loss of phosphate. Then, reduction by NADH in a second nucleophilic acyl substitution reaction yields glyceraldehyde 3-phosphate.



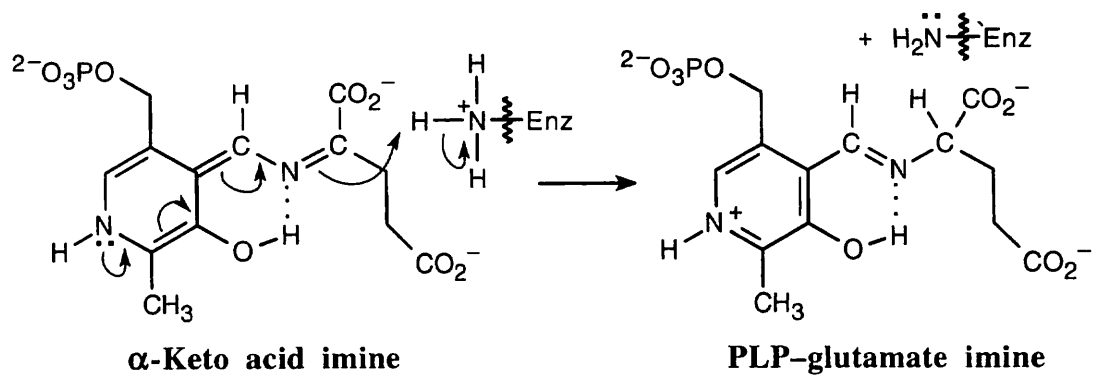
29.14



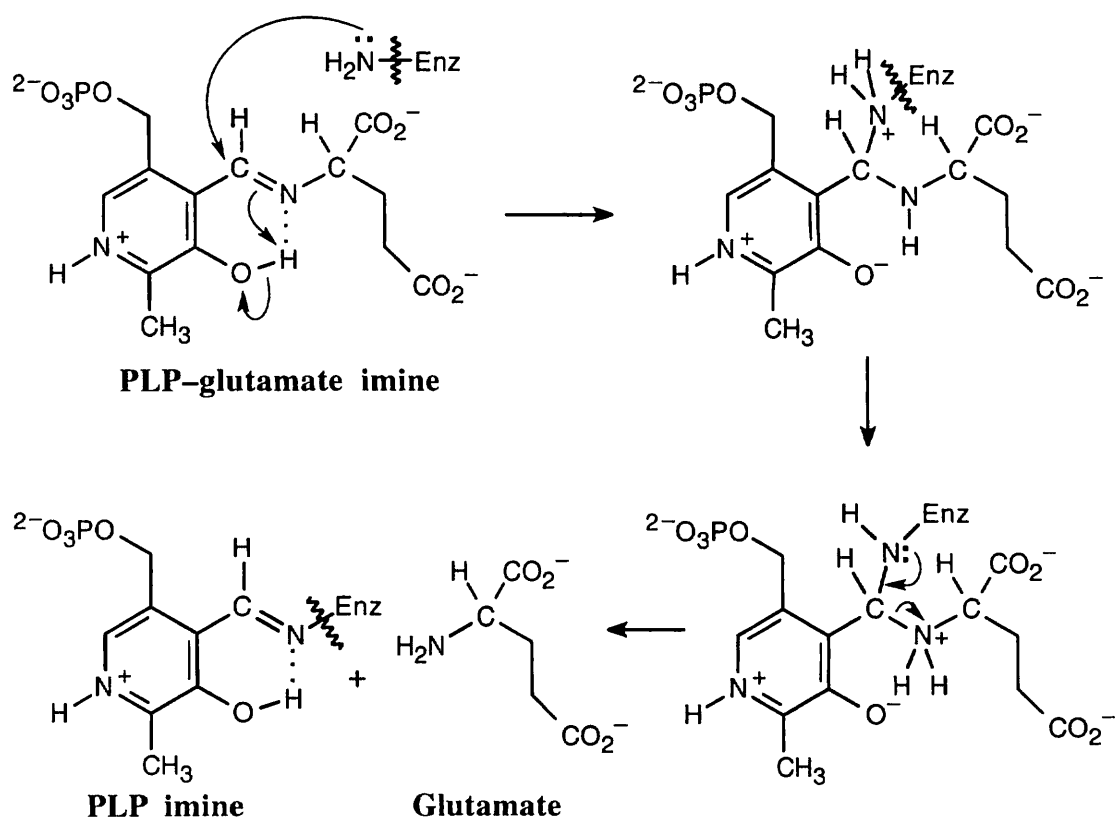
Nucleophilic acyl substitution, followed by loss of water, forms the imine tautomer.



A lysine residue deprotonates the carbon next to the ring, leading to tautomerization.

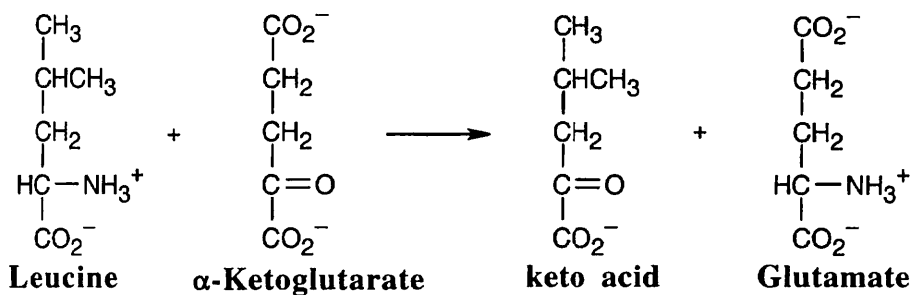


Enzymatic protonation of the keto acid imine yields PLP glutamate imine.

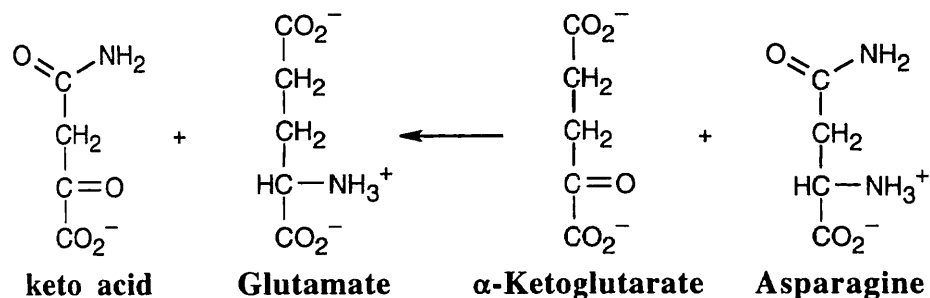


Addition of the enzyme, followed by loss of glutamate, regenerates PLP imine.

29.15 Position leucine and α -ketoglutarate so that the groups to be exchanged are aligned. This arrangement makes it easy to predict the products of transamination reactions.

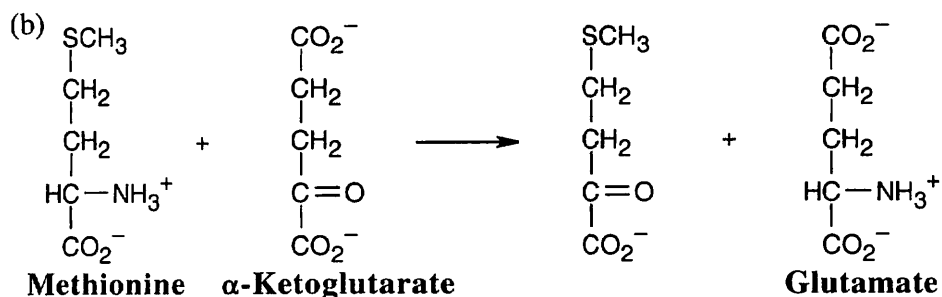
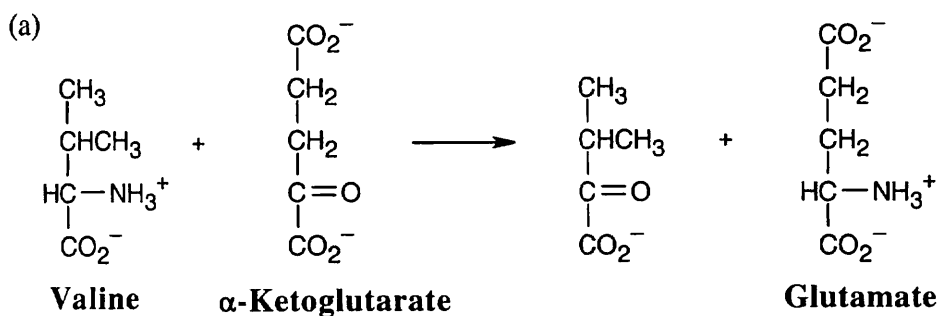


29.16 As in the previous problem, redraw the α -keto acid and align it with glutamate. By exchanging the keto group and the amino group, you can identify the amino acid as asparagine.

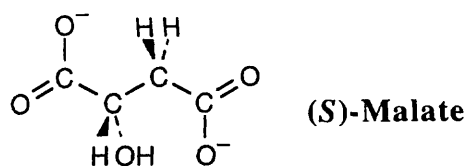


Visualizing Chemistry

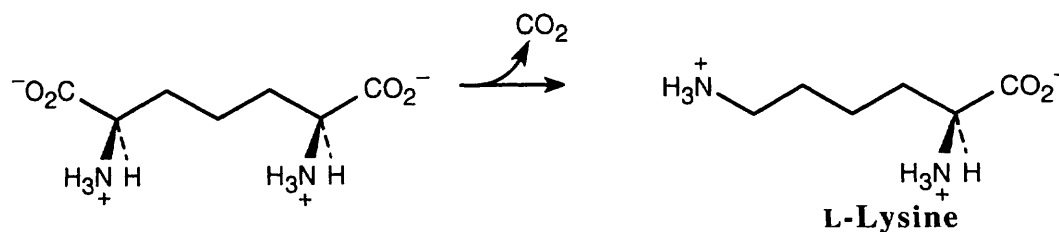
29.17 The amino acid precursors are valine (a) and methionine (b).



29.18 The intermediate is (*S*)-malate.

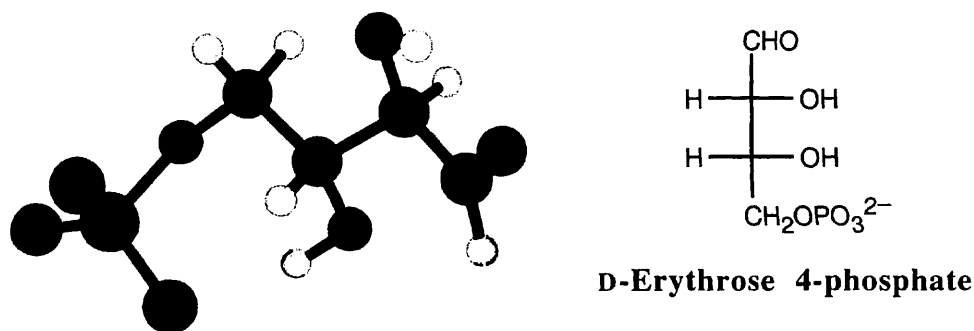


29.19



Decarboxylation of the intermediate yields lysine.

29.20 The intermediate is derived from D-erythrose.



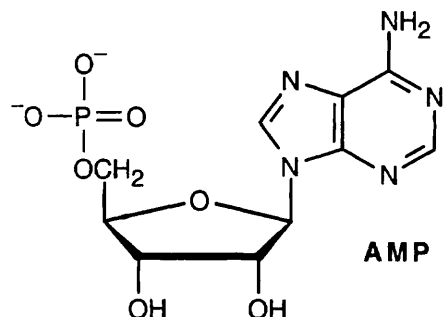
Additional Problems

29.21 Digestion is the breakdown of bulk food in the stomach and small intestine. Hydrolysis of amide, ester and acetal bonds yields amino acids, fatty acids, and simple sugars.

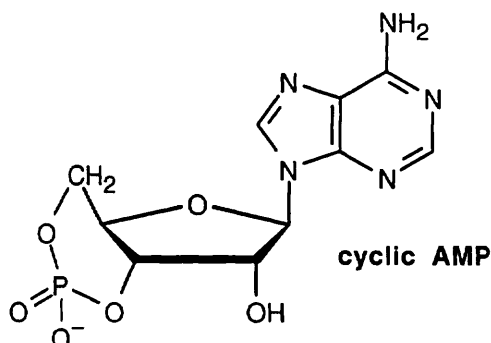
29.22 Metabolism refers to all reactions that take place inside cells. Digestion is a part of metabolism in which food is broken down into small organic molecules.

29.23 Metabolic processes that break down large molecules are known as catabolism. Metabolic processes that assemble larger biomolecules from smaller ones are known as anabolism.

29.24



29.25



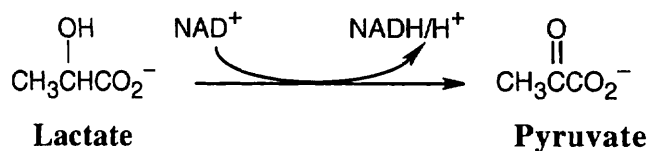
29.26 ATP transfers a phosphate group to another molecule in anabolic reactions.

29.27 NAD^+ is a biochemical oxidizing agent that converts alcohols to aldehydes or ketones, yielding NADH and H^+ as byproducts.

29.28 FAD is an oxidizing agent that introduces a conjugated double bond into a biomolecule, yielding FADH_2 as a byproduct.

29.29 The exact reverse of an energetically favorable reaction is energetically unfavorable. Since glycolysis is energetically favorable (negative ΔG°), its exact reverse has a positive ΔG° ; and is energetically unfavorable. Instead, glucose is synthesized by gluconeogenesis, an alternate pathway that also has a negative ΔG° .

29.30



NAD^+ is needed to convert lactate to pyruvate because the reaction involves the oxidation of an alcohol.

1.0 mol glucose \rightarrow 2.0 mol acetyl CoA

$$1.0 \text{ mol palmitic acid} \times \frac{8 \text{ mol acetyl CoA}}{1 \text{ mol palmitic acid}} \rightarrow 8.0 \text{ mol acetyl CoA}$$

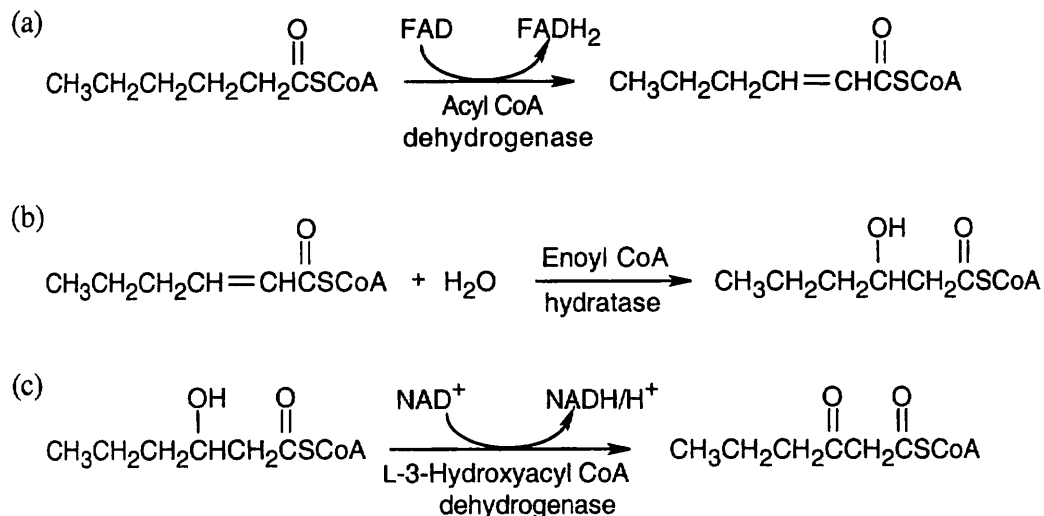
1.0 mol maltose \rightarrow 2.0 mol glucose \rightarrow 4.0 mol acetyl CoA

29.32	(a) Glucose	(b) Palmitic acid	(c) Maltose
Molecular weight	180.2 amu	256.4 amu	342.3 amu
Moles in 100.0 g	0.5549 mol	0.3900 mol	0.2921 mol
Moles of acetyl CoA produced	2 x 0.5549 mol = 1.110 mol	8 x 0.3900 mol = 3.120 mol	4 x 0.2921 mol = 1.168 mol
Grams acetyl CoA produced	898.6 g	2526 g	945.6 g

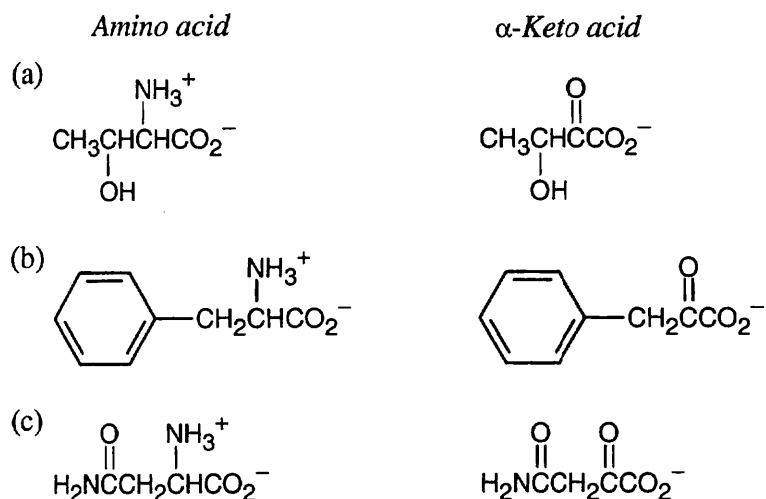
29.33



29.34



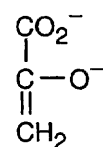
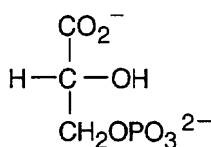
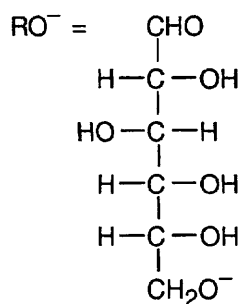
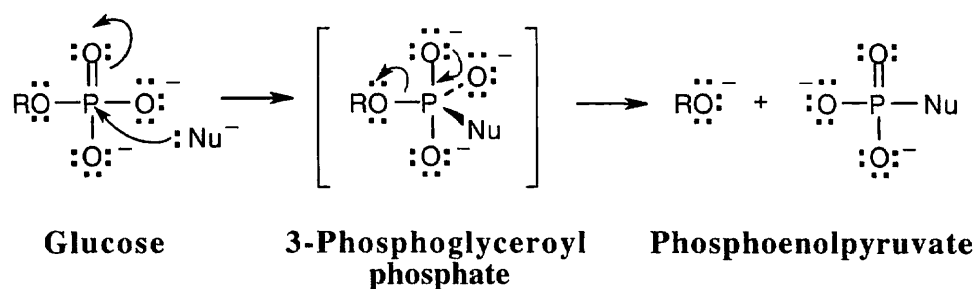
29.35



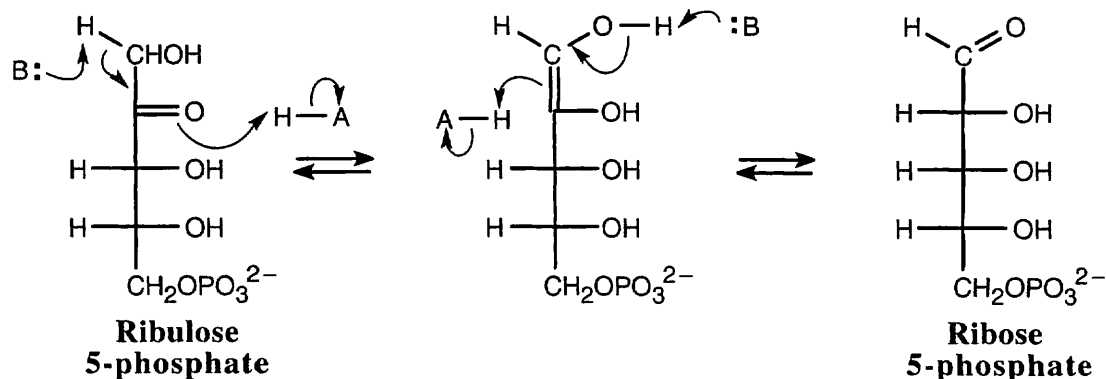
- 29.36 (a) Pyridoxal phosphate is the cofactor associated with transamination.
 (b) Biotin is the cofactor associated with carboxylation of a ketone.
 (c) Thiamin diphosphate is the cofactor associated with decarboxylation of an α-keto acid.

29.37 As we saw in Section 29.1, formation of glucose 6-phosphate from glucose and ATP is energetically favorable (negative ΔG°). The reverse reaction, transfer of a *phosphate* group to ADP from glucose 6-phosphate, is energetically unfavorable and doesn't occur spontaneously. Phosphate transfers to ADP from either 3-phosphoglyceroyl phosphate or phosphoenolpyruvate have negative ΔG° values and are energetically favorable reactions.

In chemical terms, the leaving groups in the reactions of 3-phosphoglyceroyl phosphate (carboxylate) and phosphoenolpyruvate (enolate) are more stable anions than the leaving group in the reaction of glucose (alkoxide), so the reactions are more favorable.

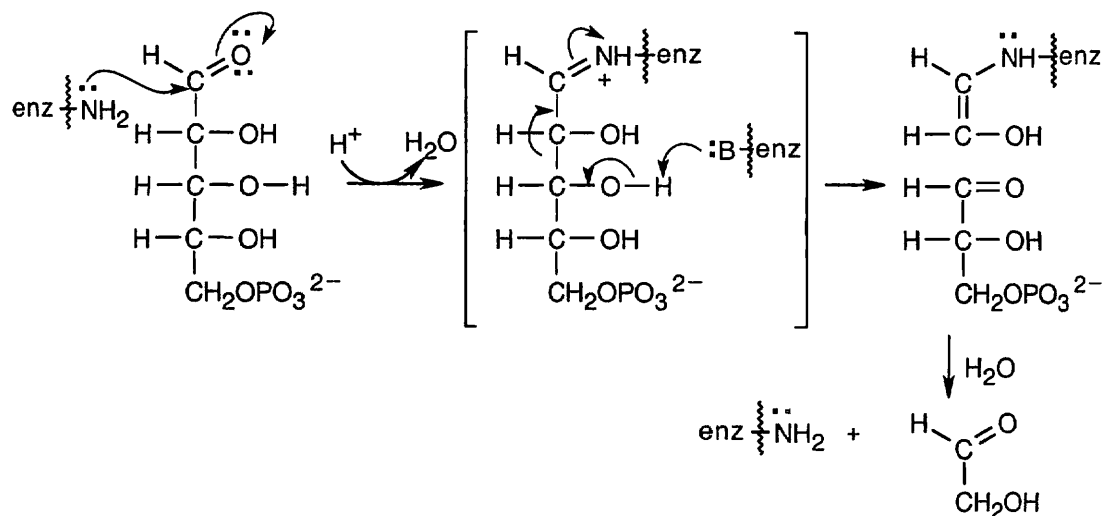


29.38

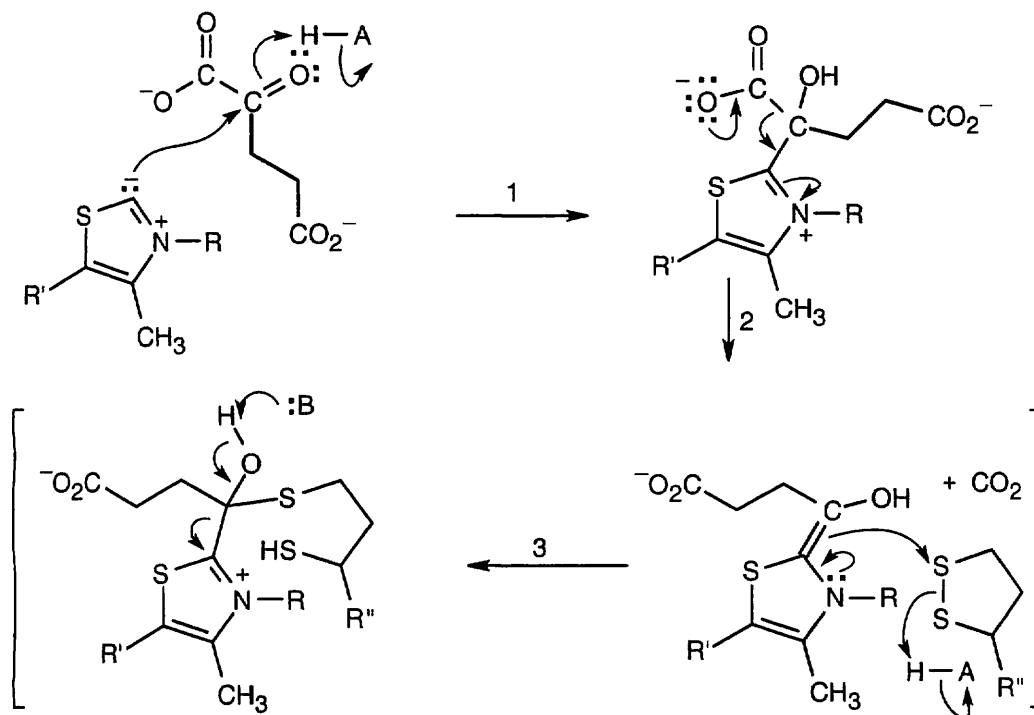


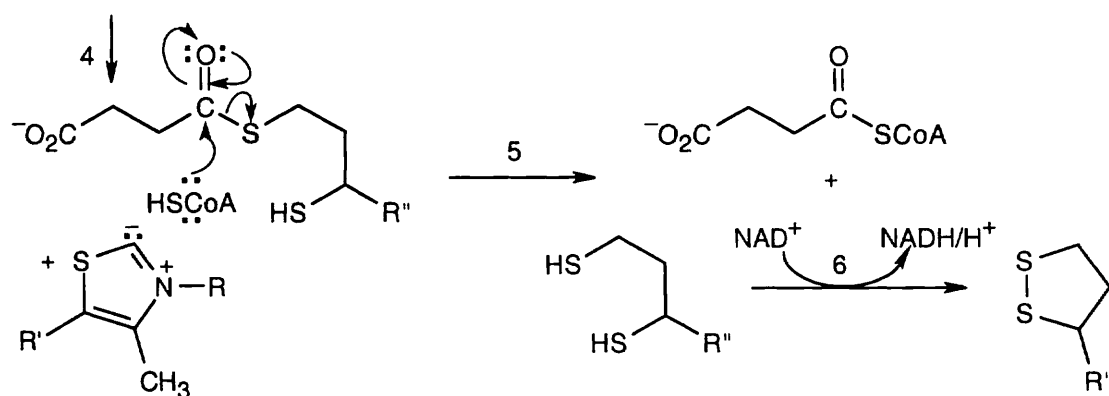
The isomerization of ribulose 5-phosphate to ribose 5-phosphate occurs by way of an intermediate enolate.

29.39 This is a reverse aldol reaction, similar to step 4 of glycolysis.



29.40 The steps in the conversion of α -ketoglutarate to succinyl CoA are similar to steps in the conversion of pyruvate to acetyl CoA shown in Figure 29.11, and the same coenzymes are involved: lipoamide, thiamin diphosphate, acetyl CoA and NAD^+ .

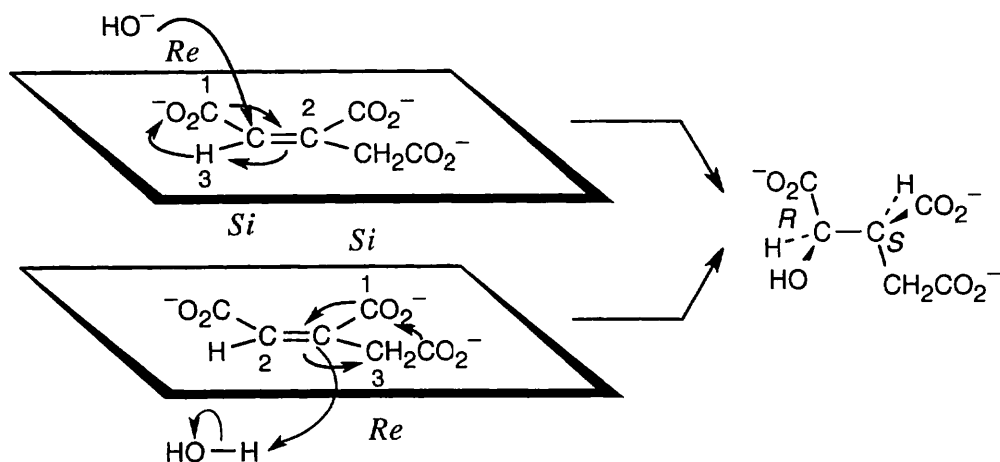




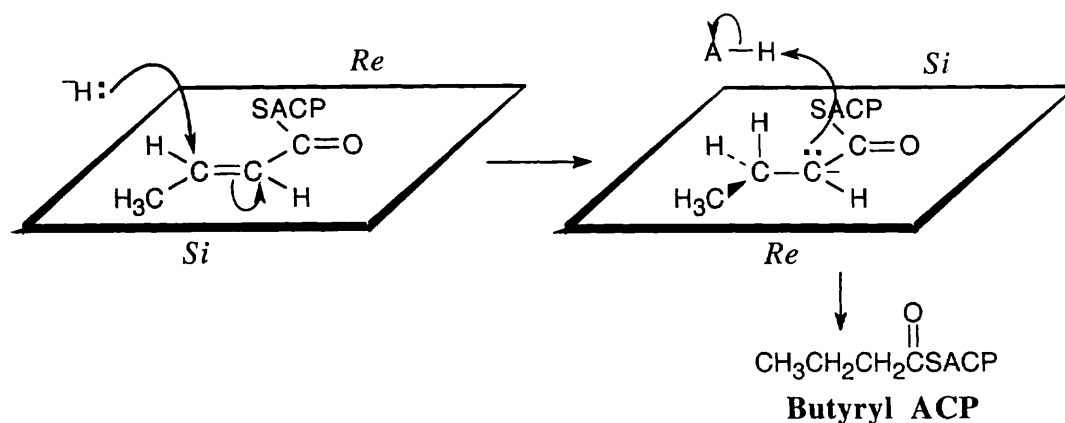
An outline of the mechanism: (1) nucleophilic addition of thiamin diphosphate ylid; (2) decarboxylation; (3) addition of double bond to lipoamide, with ring opening; (4) elimination of thiamin diphosphate; (5) nucleophilic addition of acetyl CoA to succinyl lipoamide and elimination of succinyl dihydrolipoamide to give succinyl CoA; (6) reoxidation of dihydrolipoamide to lipoamide.

29.41 Addition of OH^- : The top face is the *Re* face, and OH^- adds from this face to give an *R* configuration at carbon 2.

Addition of H^+ : For carbon 3, the top face is *Si*, and H^+ adds from the bottom, or *Re*, face to give an *S* configuration at carbon 3. The reaction occurs with anti geometry.

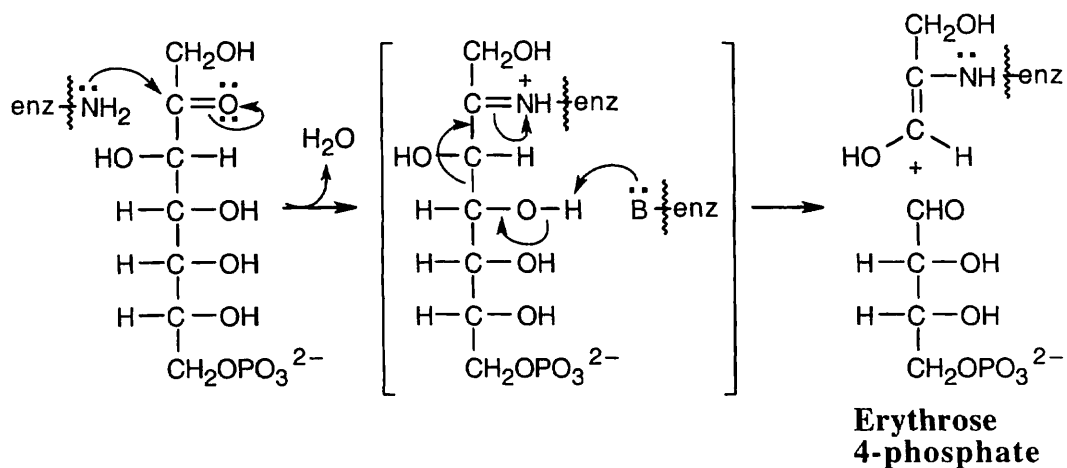


29.46

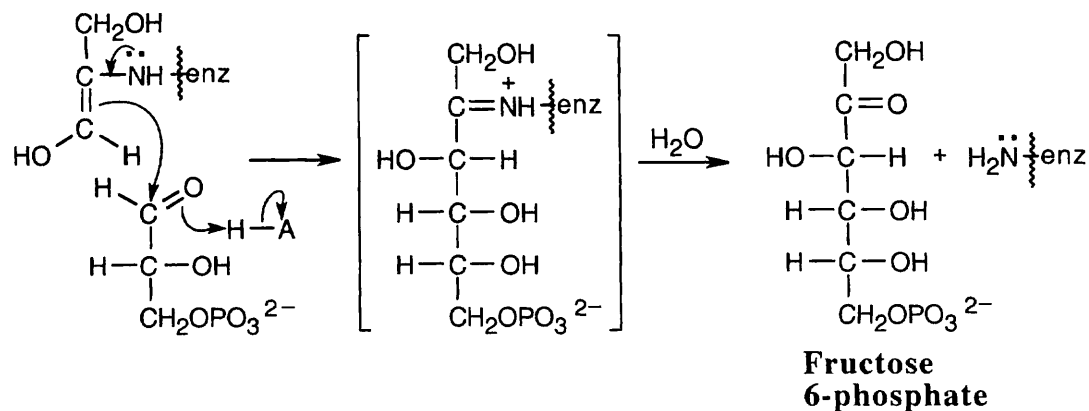


The reduction is a syn addition.

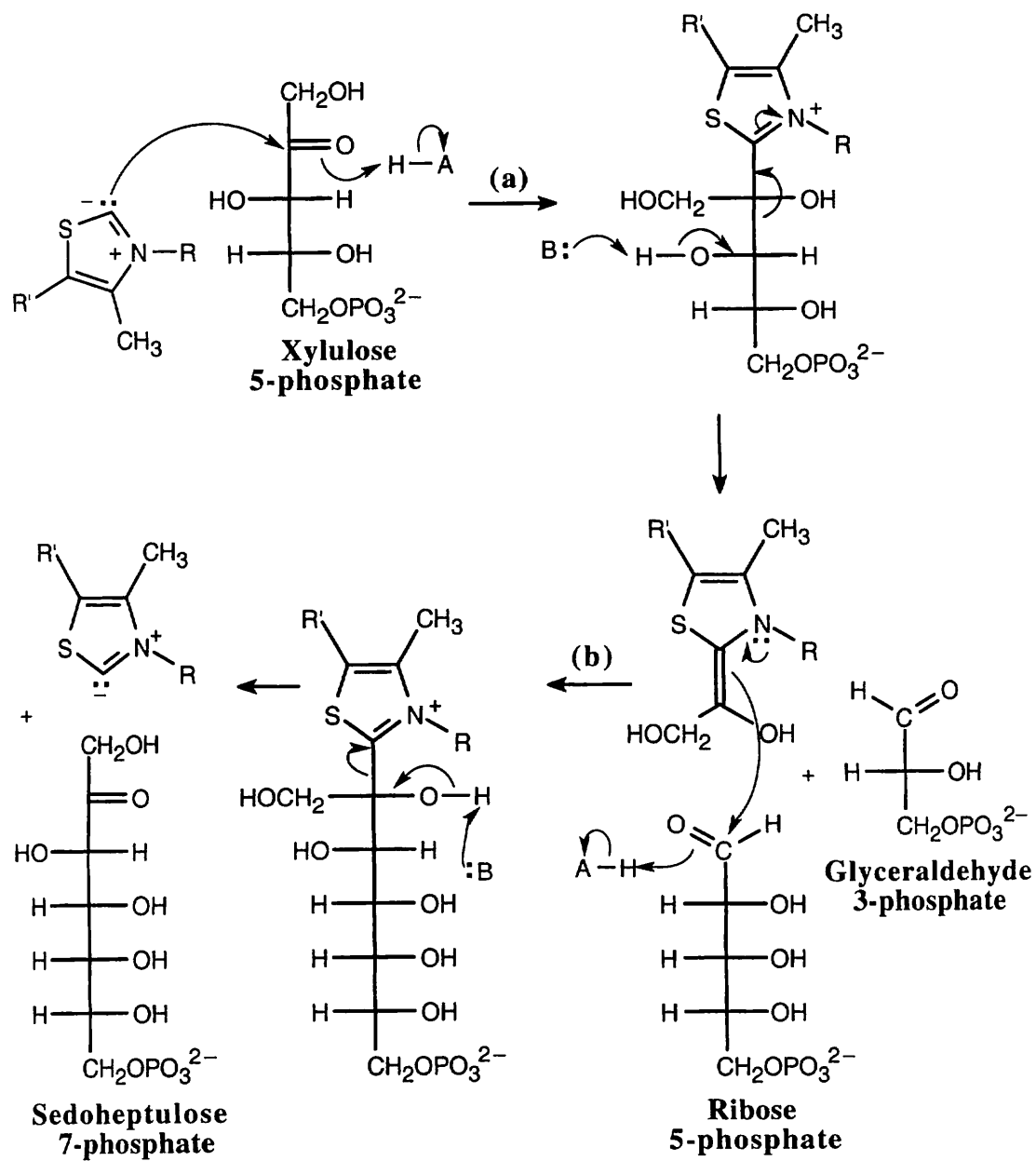
- 29.47** (a) The first sequence of steps in this mechanism involves formation of the imine (Schiff base) of sedoheptulose 7-phosphate, followed by retro-aldol cleavage to form erythrose 4-phosphate and the enamine of dihydroxyacetone.



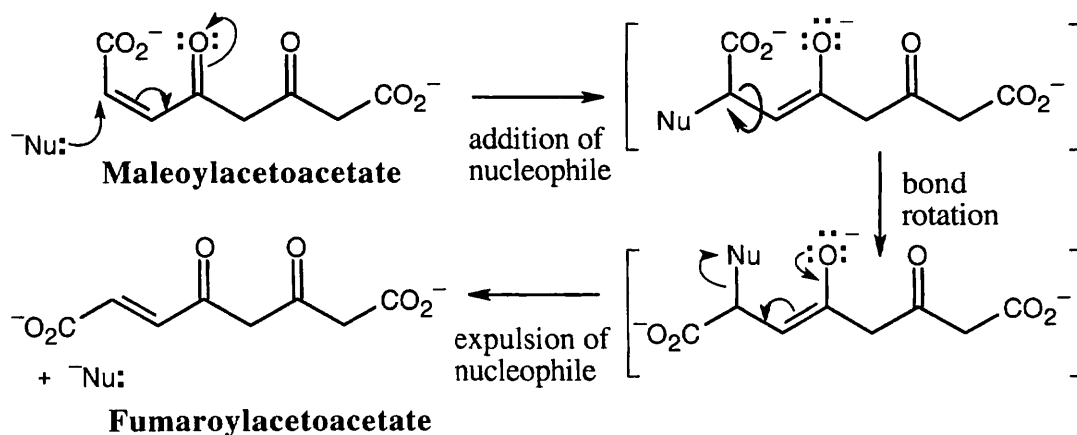
- (b) The enamine of dihydroxyacetone adds to glyceraldehyde 3-phosphate to yield fructose 6-phosphate. This reaction is almost identical to the reaction pictured for Step 8 of gluconeogenesis in Section 29.8.



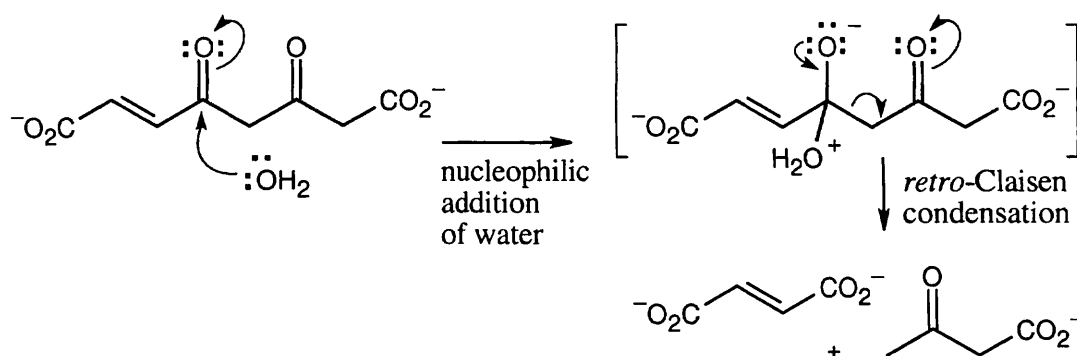
29.48



29.49



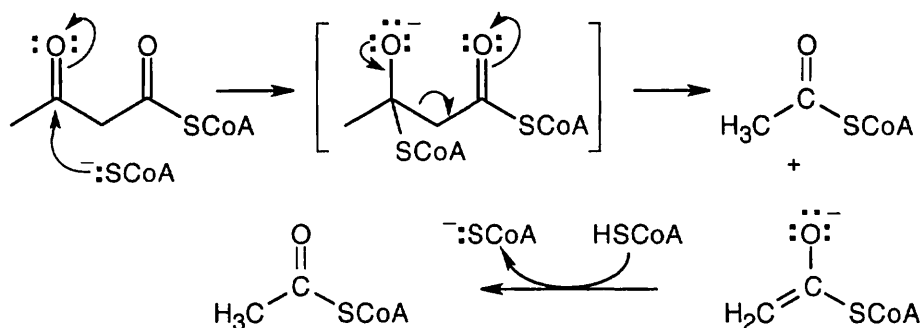
29.50



29.51 The first step in the conversion acetoacetate \longrightarrow acetyl CoA is the formation of acetoacetyl CoA. This reaction also occurs as the first step in fatty acid catabolism. Although we haven't studied the mechanism, it involves formation of a mixed anhydride.

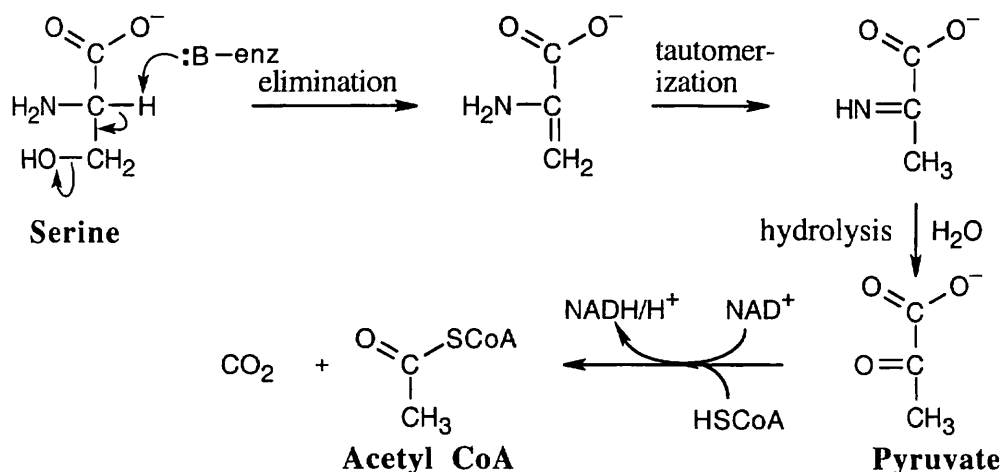


The final step is a retro-Claisen reaction, whose mechanism is pictured in Section 29.3 as Step 4 of β -oxidation of fatty acids.



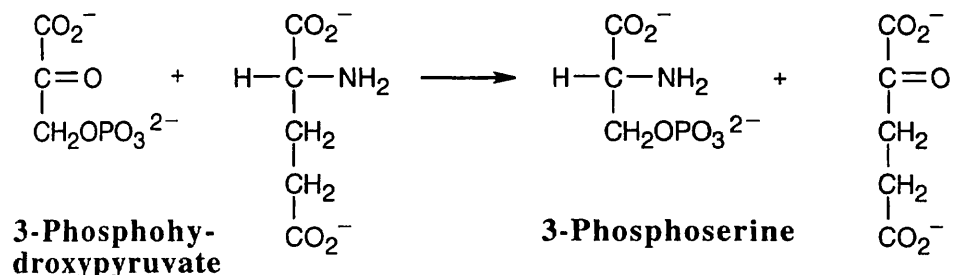
29.52 Now is a good time to use retrosynthetic analysis, which was first encountered in Chapter 8. In this degradative pathway, what might be the precursor to acetyl CoA (the final product)? Pyruvate is a good guess, because we learned how to convert pyruvate to acetyl CoA in Section 29.6. How do we get from serine to pyruvate? A transamination reaction is a possibility. However, the immediate transamination precursor to pyruvate is the amino acid alanine, which differs from serine by one hydroxyl group. Thus, we probably have to design a pathway from serine to pyruvate that takes this difference into account.

Many routes are possible, but here's the simplest:

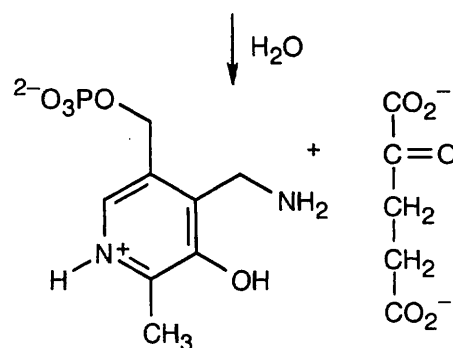
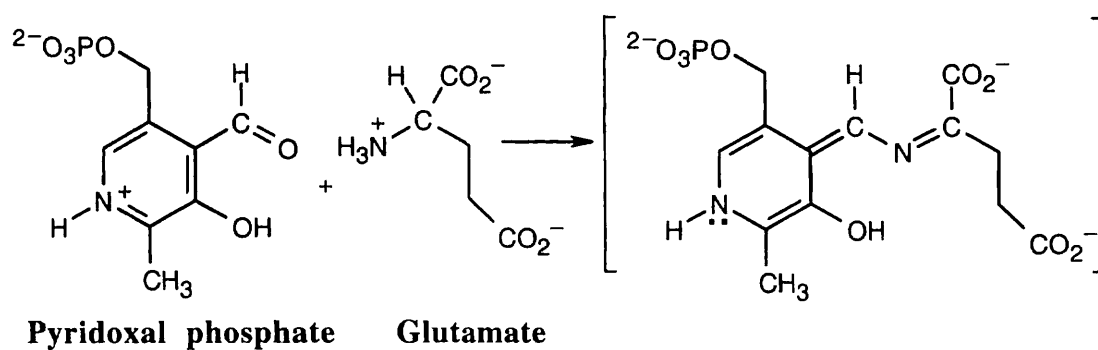


The coenzymes thiamin diphosphate and lipoamide are involved in the last step.

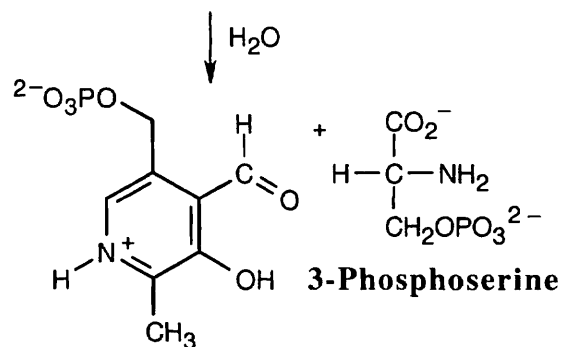
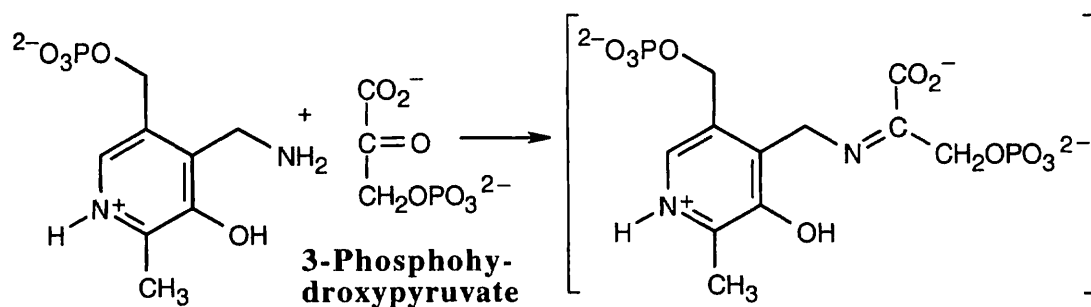
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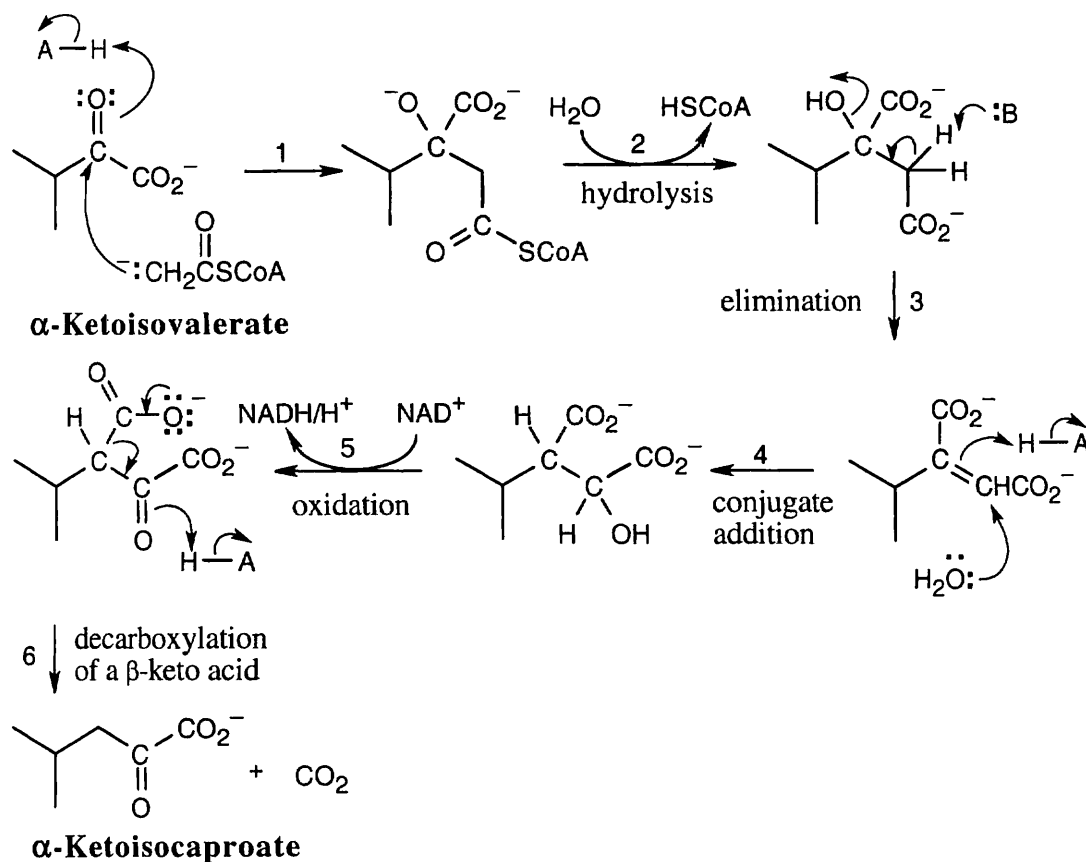
This reaction is a transamination that requires the coenzyme pyridoxal phosphate as a cofactor. The mechanism, which is described in Figure 29.14, involves two steps. The first step is the nucleophilic addition of glutamate nitrogen to the aldehyde group of pyridoxal phosphate to yield an imine intermediate, which is hydrolyzed to give α -ketoglutarate plus a nitrogen-containing pyridoxal phosphate byproduct.



This byproduct reacts with 3-phosphohydroxypyruvate to give 3-phosphoserine plus regenerated pyridoxal phosphate.

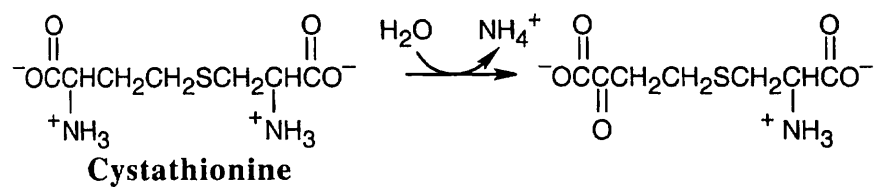


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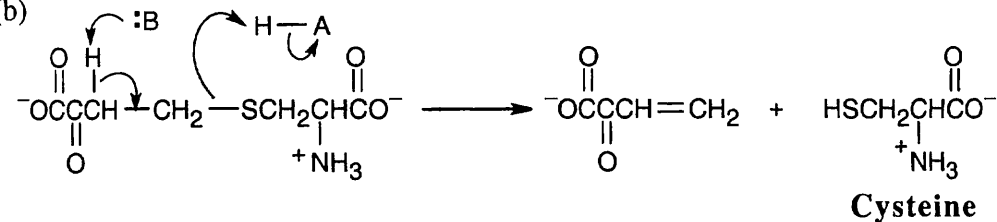


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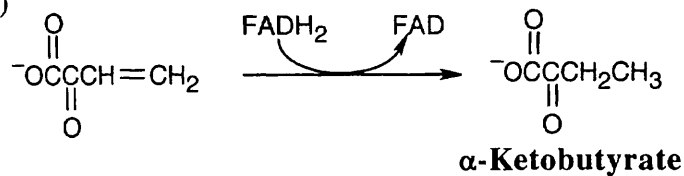
(a)



(b)



(c)



The product of double-bond reduction is α -ketobutyrate. FADH_2 is the necessary enzyme cofactor.

Review Unit 11: Biomolecules II – Lipids, Nucleic Acids, Metabolic Pathways

Major Topics Covered (with vocabulary):

Lipids:

wax fat oil triacylglycerol fatty acid polyunsaturated fatty acid soap saponification micelle phosphoglyceride sphingolipid lipid bilayer sphingosine sphingomyelin prostaglandin terpenoid essential oil monoterpenoid sesquiterpenoid isopentenyl diphosphate steroid hormone sex hormone adrenocortical hormone androgen estrogen mineralocorticoid glucocorticoid squalene lanosterol

Nucleic acids and nucleotides:

nucleoside nucleotide deoxyribonucleic acid (DNA) ribonucleic acid (RNA) adenine guanine thymine cytosine 3' end 5' end base pairing double helix complementary pairing major groove minor groove intercalation

Nucleic acids and heredity:

replication semiconservative DNA polymerase replication fork DNA ligase transcription mRNA rRNA tRNA coding strand template strand promoter sites exon intron translation codon anticodon

DNA technology:

DNA sequencing Maxam-Gilbert method restriction endonuclease restriction fragment palindrome Sanger dideoxy method DNA synthesis DMT ether phosphoramidite phosphite polymerase chain reaction (PCR)

Metabolic pathways:

metabolism anabolism catabolism digestion phosphoric acid anhydride ATP NAD⁺ NADH/H⁺ β -oxidation pathway glycolysis Schiff base pyruvate acetyl CoA pyruvate dehydrogenase complex thiamine lipoamide citric acid cycle electron-transport chain transamination oxidative deamination gluconeogenesis biotin

Types of Problems:

After studying these chapters you should be able to:

- Draw the structures of fats, oils, steroids and other lipids.
- Determine the structure of a fat.
- Predict the products of reactions of fats and steroids.
- Locate the five-carbon units in terpenoids.
- Understand the mechanism of terpenoid and steroid biosynthesis.
- Draw the structures and conformations of steroids and other fused-ring systems.

- Draw purines, pyrimidines, nucleosides, nucleotides, and representative segments of DNA and their complements.
- List the base sequence that codes for a given amino acid or peptide.
- Deduce an amino acid sequence from a given mRNA sequence (and *vice versa*).
- Draw the anticodon sequence of tRNA, given the mRNA sequence.
- Outline the process of DNA sequencing, and deduce a DNA sequence from an electrophoresis pattern.
- Outline the method of DNA synthesis, and formulate the mechanisms of synthetic steps.
- Explain the basic concepts of metabolism, and understand the energy relationships of biochemical reactions.
- Answer questions relating to the metabolic pathways of carbohydrates, fatty acids and amino acids.
- Formulate mechanisms for metabolic pathways similar to those in the text.

Points to Remember:

- * When trying to locate the five-carbon units in a terpenoid, look for an isopropyl group first; at least one should be apparent. After finding it, count 5 carbons, and locate the second five-carbon unit. If there are two possibilities for the second unit, choose the one that has the double bond in the correct location.
- * In general, the reactions of steroids that are presented in this book are familiar and uncomplicated. Keeping track of the stereochemistry of the tetracyclic ring system is somewhat more complicated.
- * In situations where base-pairing occurs, such as replication, transcription or translation, a polynucleotide chain (written with the 5' end on the left and the 3' end on the right) pairs with a second chain (written with the 3' end on the left and the 5' end on the right). Base pairing is complementary, and the two chains are always read in opposite directions.
- * Note the difference between transamination and oxidative deamination. Transamination is a reaction in which an amino group of an α -amino acid is transferred to α -ketoglutarate, yielding an α -keto acid and glutamate. In oxidative deamination, glutamate loses its amino group in an NAD^+ -dependent reaction that regenerates α -ketoglutarate and produces NH_4^+ .
- * Look at the steps of glycolysis, and then look at the steps of gluconeogenesis. Several steps in one pathway are the exact reverse of steps in the other pathway because the energy required for these steps is small. Other, high-energy transformations must occur by steps that are not the exact reverse and that require different enzymes. Gluconeogenesis is a metabolic pathway that takes place mainly during fasting and strenuous exercise because dietary sources of carbohydrates are usually available.
- * The conversion pyruvate \rightarrow acetyl CoA is catalyzed by pyruvate dehydrogenase complex. The conversion acetyl CoA \rightarrow carbohydrates doesn't occur in animals because they can obtain carbohydrates from food and don't usually need to synthesize carbohydrates. Only plants can, at times, use acetyl CoA to synthesize carbohydrates.

3. Prostaglandins and related compounds have all of the following structural features in common except:
(a) cis double bonds (b) a carboxylic acid group (c) a C₂₀ chain (d) hydroxyl groups
4. Which of the following steps doesn't occur in the synthesis of isopentenyl diphosphate?
(a) Claisen condensation (b) oxidation (c) aldol condensation (d) decarboxylation
5. Which nucleic acid has nonstandard bases, in addition to the usual bases?
(a) DNA (b) mRNA (c) rRNA (d) tRNA
6. Which base doesn't need a protecting group in DNA synthesis?
(a) Thymine (b) Cytosine (c) Adenine (d) Guanine
7. Which amino acid has only one codon?
(a) Tyrosine (b) Arginine (c) Lysine (d) Tryptophan
8. Which of the following enzyme cofactors is not involved in the conversion of pyruvate to acetyl CoA?
(a) Thiamine pyrophosphate (b) Pyridoxal phosphate (c) Lipoamide (d) NAD⁺
9. Which of the following steps of the citric acid cycle doesn't produce reduced coenzymes?
(a) Isocitrate → α -Ketoglutarate (b) α -Ketoglutarate → Succinyl CoA
(c) Fumarate → Malate (d) Succinate → Fumarate
10. The amino acid aspartate can be metabolized as what citric acid cycle intermediate after transamination?
(a) Oxaloacetate (b) Malate (c) α -Ketoglutarate (d) Succinate