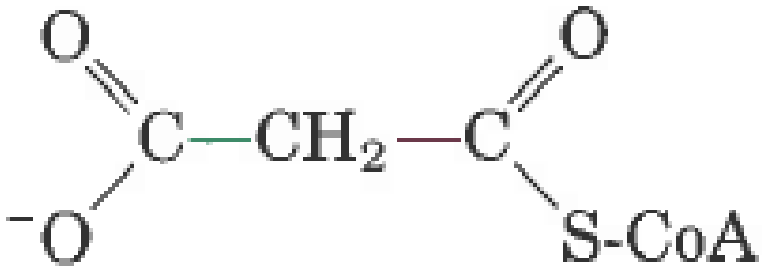
Lipid Biosynthesis/ UG Sem3 #HONS/SDG

Lipids play a variety of cellular roles, some only recently recognized.
They are the principal form ofstored energy in most organisms and major constituentsof cellular membranes.
Specialized lipids serve as pigments(retinal, carotene), cofactors (vitamin K), detergents(bile salts), transporters (dolichols), hormones (vitamin D derivatives, sex hormones), extracellular and intracellular messengers (eicosanoids, phosphatidylinositol derivatives), and anchors for membrane proteins(covalently attached fatty acids, prenyl groups, andphosphatidylinositol).
The ability to synthesize a varietyof lipids is essential to all organisms.

Lipid biosynthesis requires the participation of a three carbon

intermediate ,**Malonyl-CoA**



Malonyl-CoA

Malonyl-CoA Is Formed from Acetyl-CoA and Bicarbonate

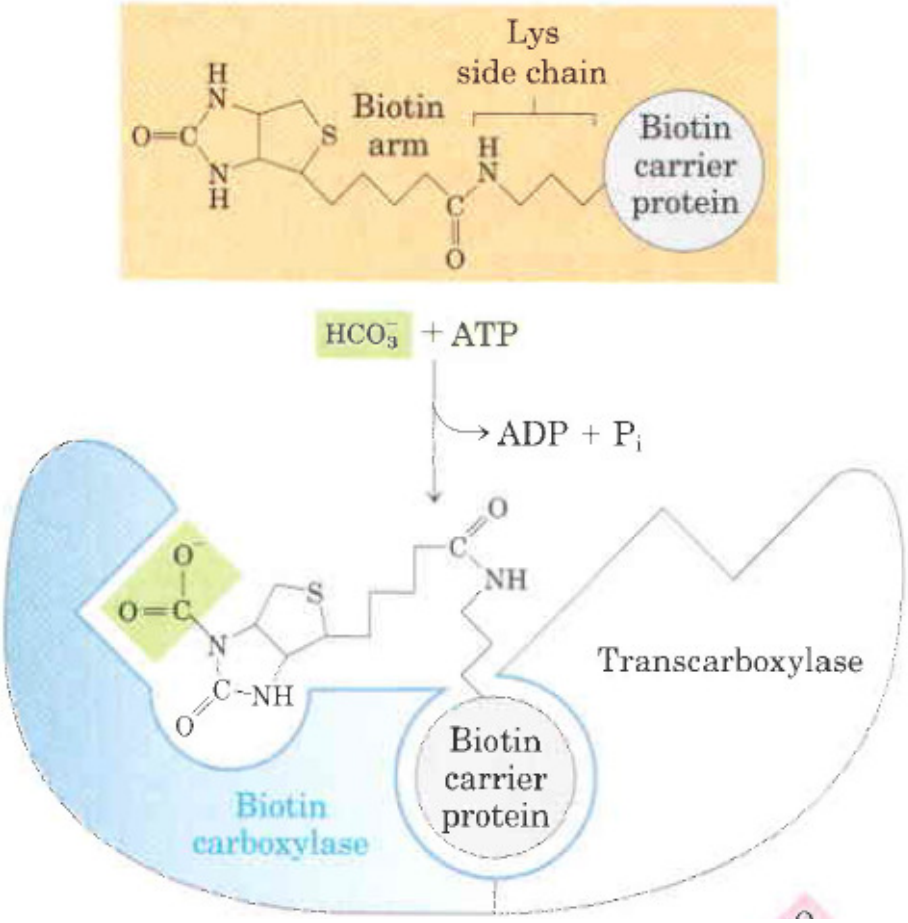


FIGURE 21–1 The acetyl-CoA carboxylase reaction. Acetyl-CoA carboxylase has three functional regions: biotin carrier protein (gray); biotin carboxylase, which activates CO_2 by attaching it to a nitrogen in the biotin ring in an ATP-dependent reaction (see Fig. 16–16); and transcarboxylase, which transfers activated CO_2 (shaded green) from biotin to acetyl-CoA, producing malonyl-CoA. The long, flexible biotin arm carries the activated CO_2 from the biotin carboxylase region to the transcarboxylase active site. The active enzyme in each step is shaded blue.

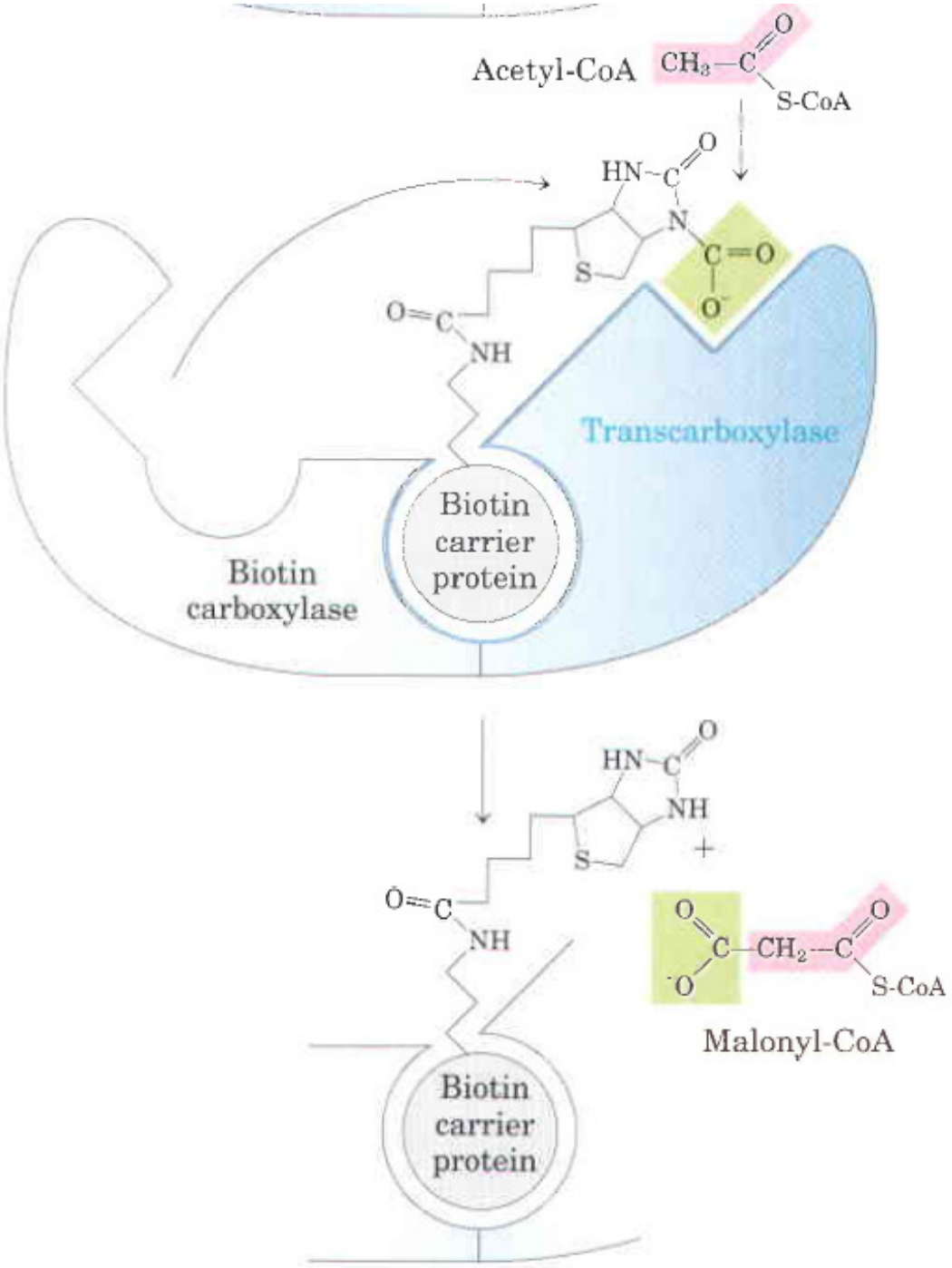
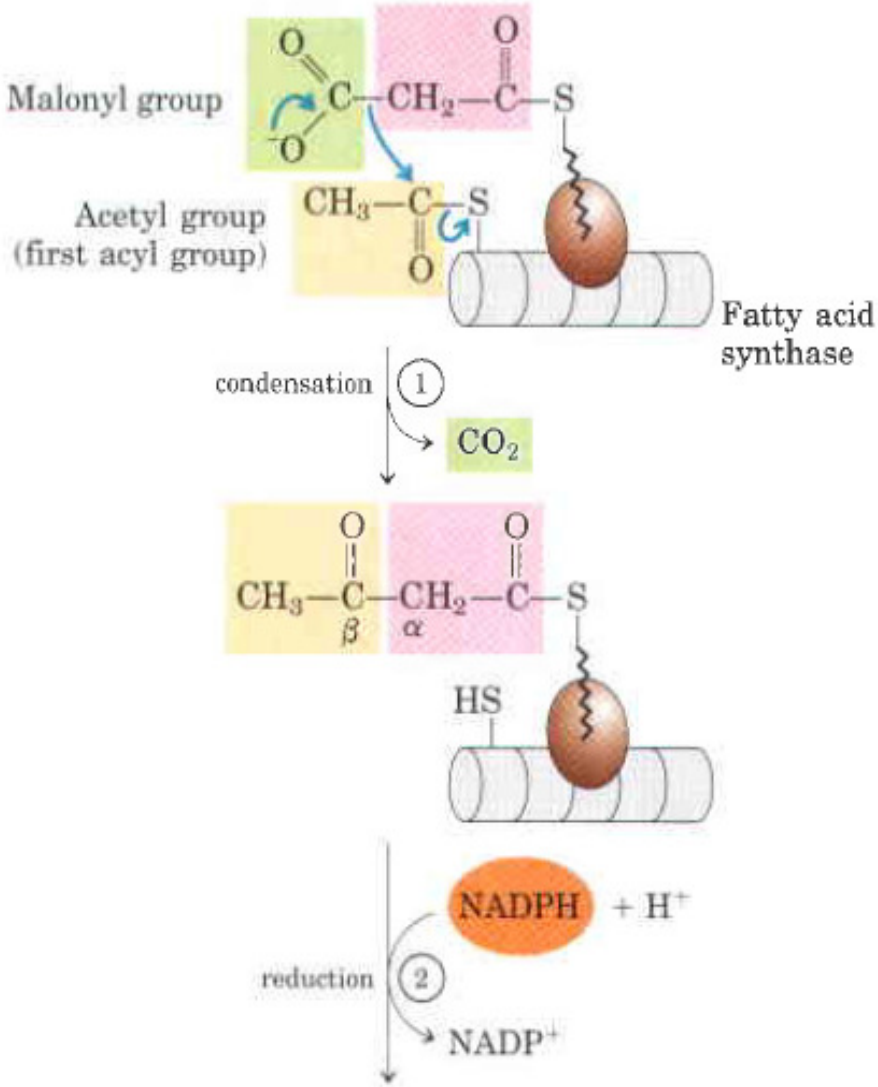

Acetyl-CoA
CH3—C
O
S-CoA
HN—C
O
N
S
C=O
O⁻
O=C
NH
Transcarboxylase
Biotin carrier protein
Biotin carboxylase
HN—C
O
NH
S
+
O=C
NH
O
C—CH2—C
O
O⁻
O
S-CoA
Malonyl-CoA
Biotin carrier protein

FIGURE 21–2 Addition of two carbons to a growing fatty acyl chain: a four-step sequence. Each malonyl group and acetyl (or longer acyl) group is activated by a thioester that links it to fatty acid synthase, a multienzyme system described later in the text. ① Condensation of an activated acyl group (an acetyl group from acetyl-CoA is the first acyl group) and two carbons derived from malonyl-CoA, with elimination of CO_2 from the malonyl group, extends the acyl chain by two carbons. The mechanism of the first step of this reaction is given to illustrate the role of decarboxylation in facilitating condensation. The β-keto product of this condensation is then reduced in three more steps nearly identical to the reactions of β oxidation, but in the reverse sequence: ② the β-keto group is reduced to an alcohol, ③ elimination of H_2O creates a double bond, and ④ the double bond is reduced to form the corresponding saturated fatty acyl group.



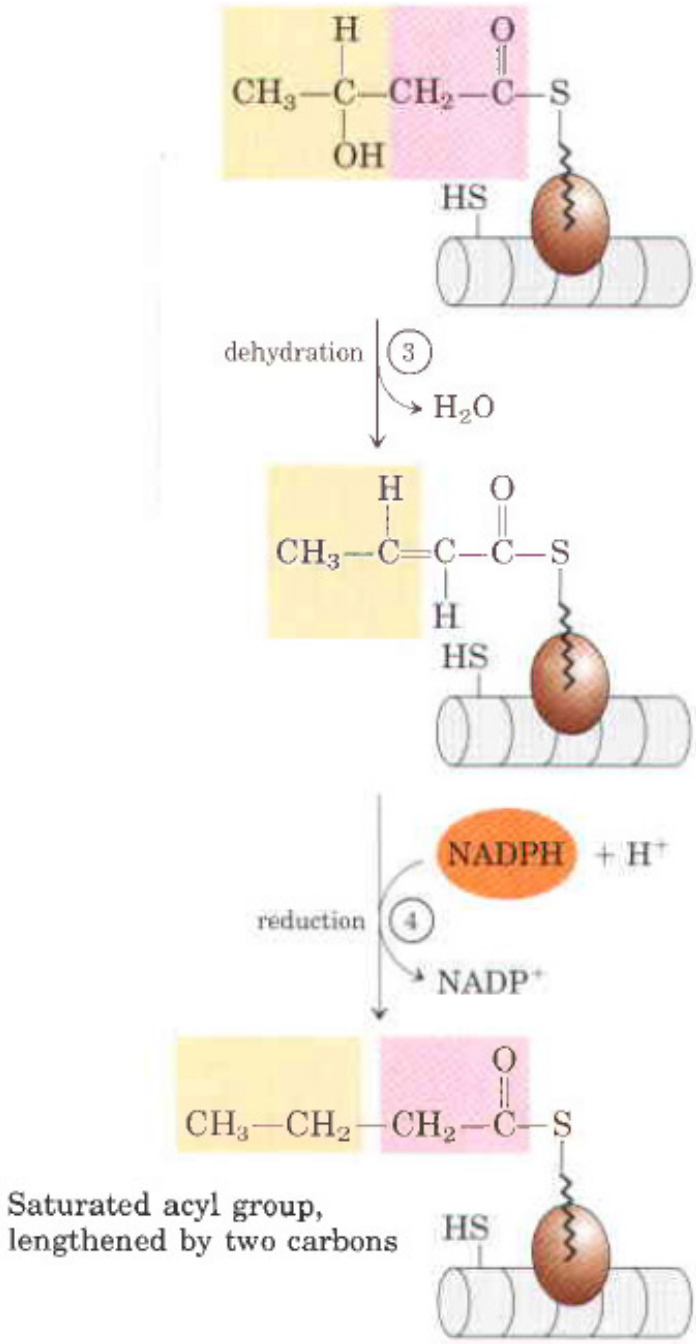
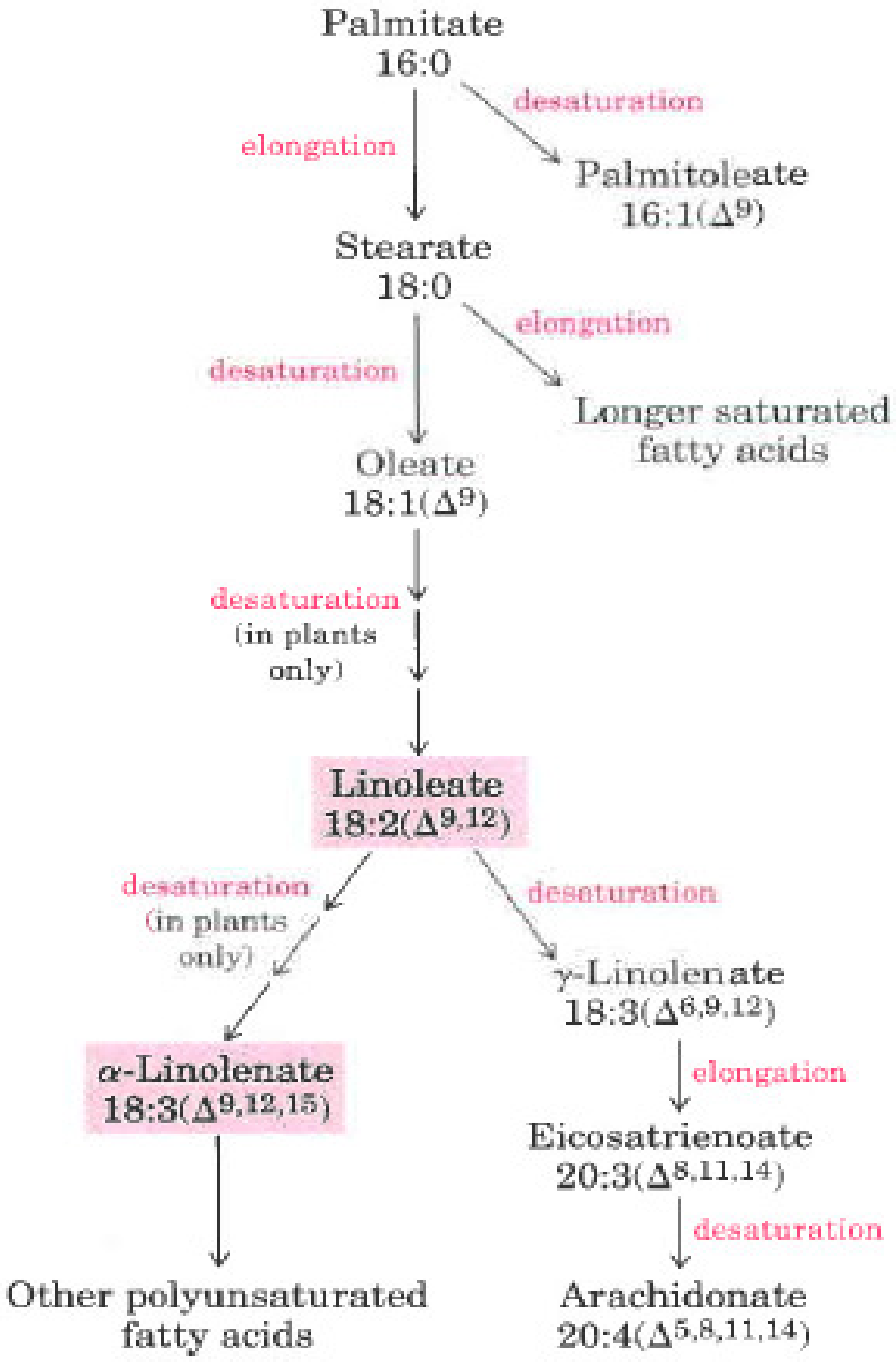


FIGURE 21–12 Routes of synthesis of other fatty acids. Palmitate is the precursor of stearate and longer-chain saturated fatty acids, as well as the monounsaturated acids palmitoleate and oleate. Mammals cannot convert oleate to linoleate or α-linolenate (shaded pink), which are therefore required in the diet as essential fatty acids. Conversion of linoleate to other polyunsaturated fatty acids and eicosanoids is outlined. Unsaturated fatty acids are symbolized by indicating the number of carbons and the number and position of the double bonds, as in Table 10–1.



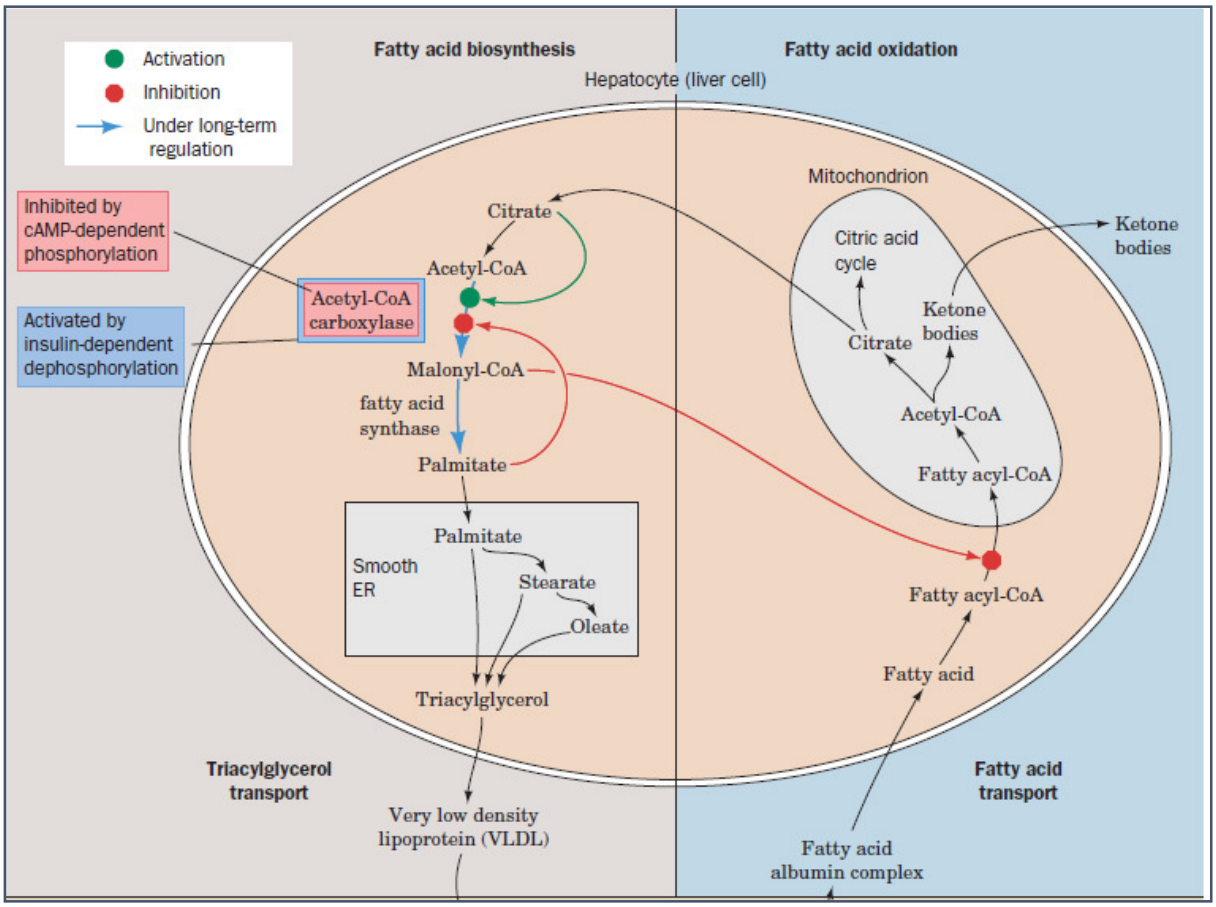
Seven cycles of condensation and reduction producethe 16-carbon saturated palmitoyl group, still bound to ACP.

For reasons not well understood, chainelongation by the synthase complex generally stops atthis point and free palmitate is released from the ACP by a hydrolytic activity in the complex. Small amountsof longer fatty acids such as stearate (18:0) are alsoformed. In certain plants (coconut and palm, for example)chain termination occurs earlier; up to 90% of thefatty acids in the oils of these plants are between 8 and14 carbons long.

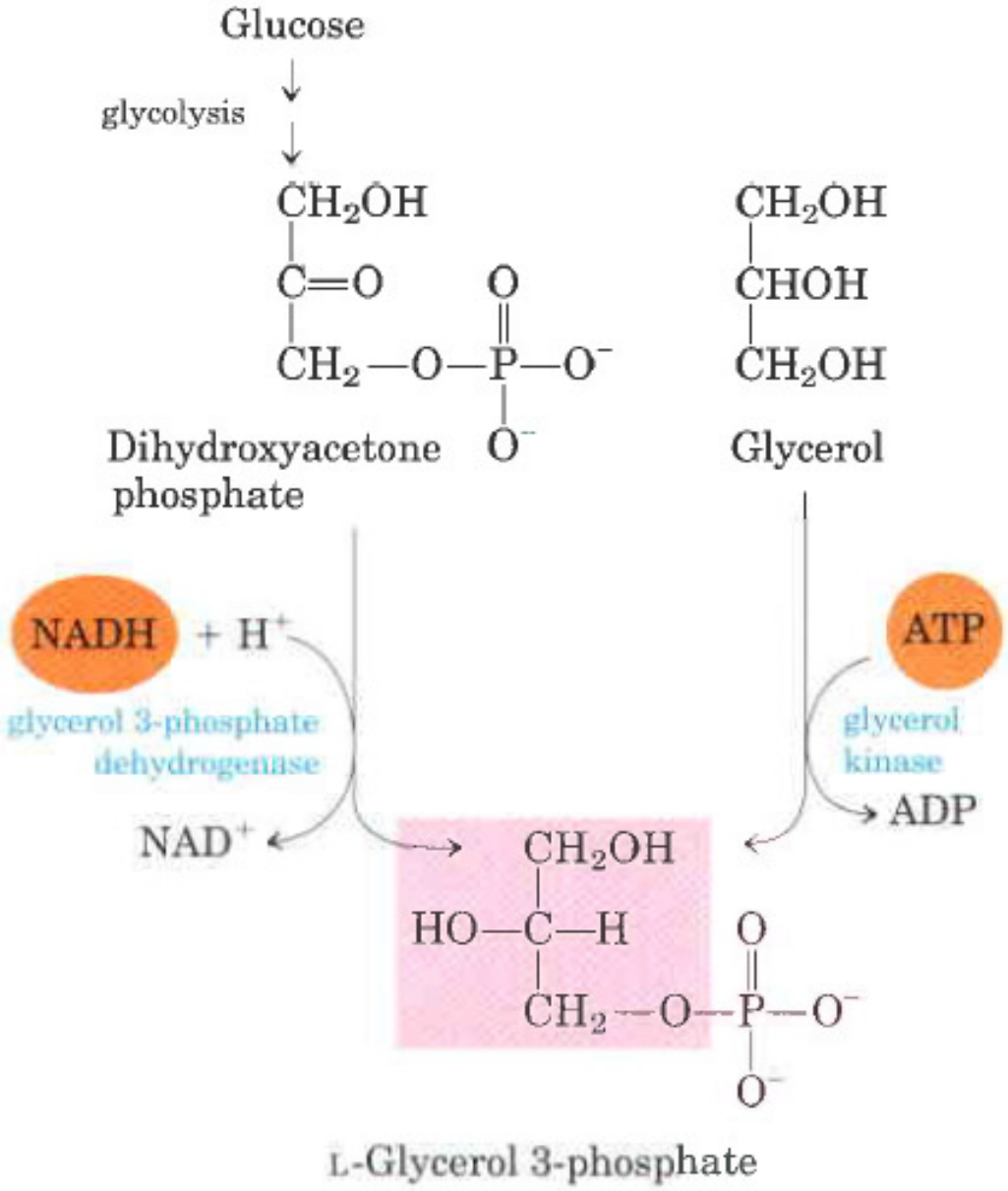
We can consider the overall reaction for the synthesisof palmitate from acetyl-

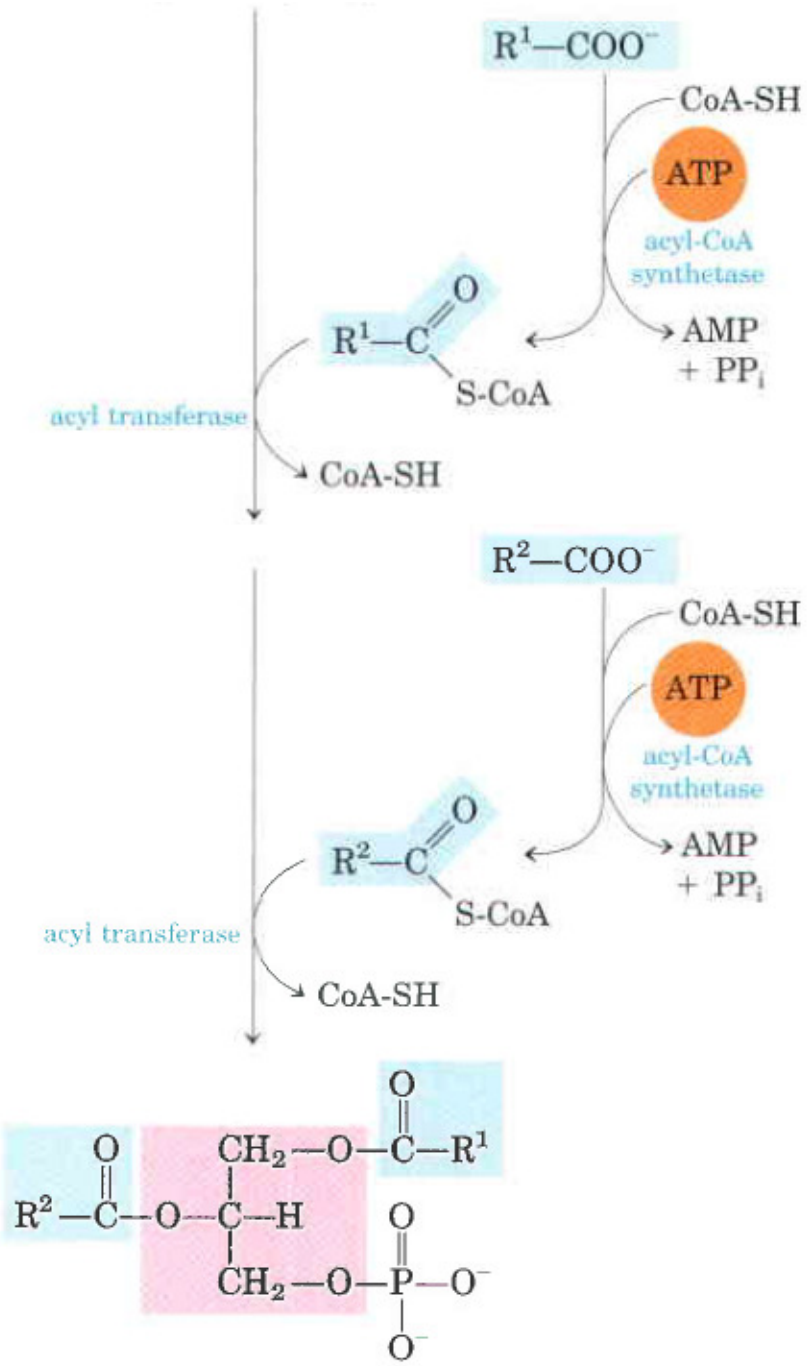
First,

the formation of seven malonyl-CoA molecules:
7 Acetyl-CoA + 7CO2 + 7ATP →
7 malonyl-CoA +7ADP +7Pi
Then seven cycles of condensation and reduction:
Acetyl-CoA + 7 malonyl-CoA +14NADPH + $14H^+$→
palmitate+ 7CO2 + 8 CoA +14NADP+6H2O
The overall process is
8 Acetyl-CoA +7ATP +14NADPH +$14H^+$→
palmitate+ 8 CoA + 7ADP + 7Pi + 14NADP+ 6H2O

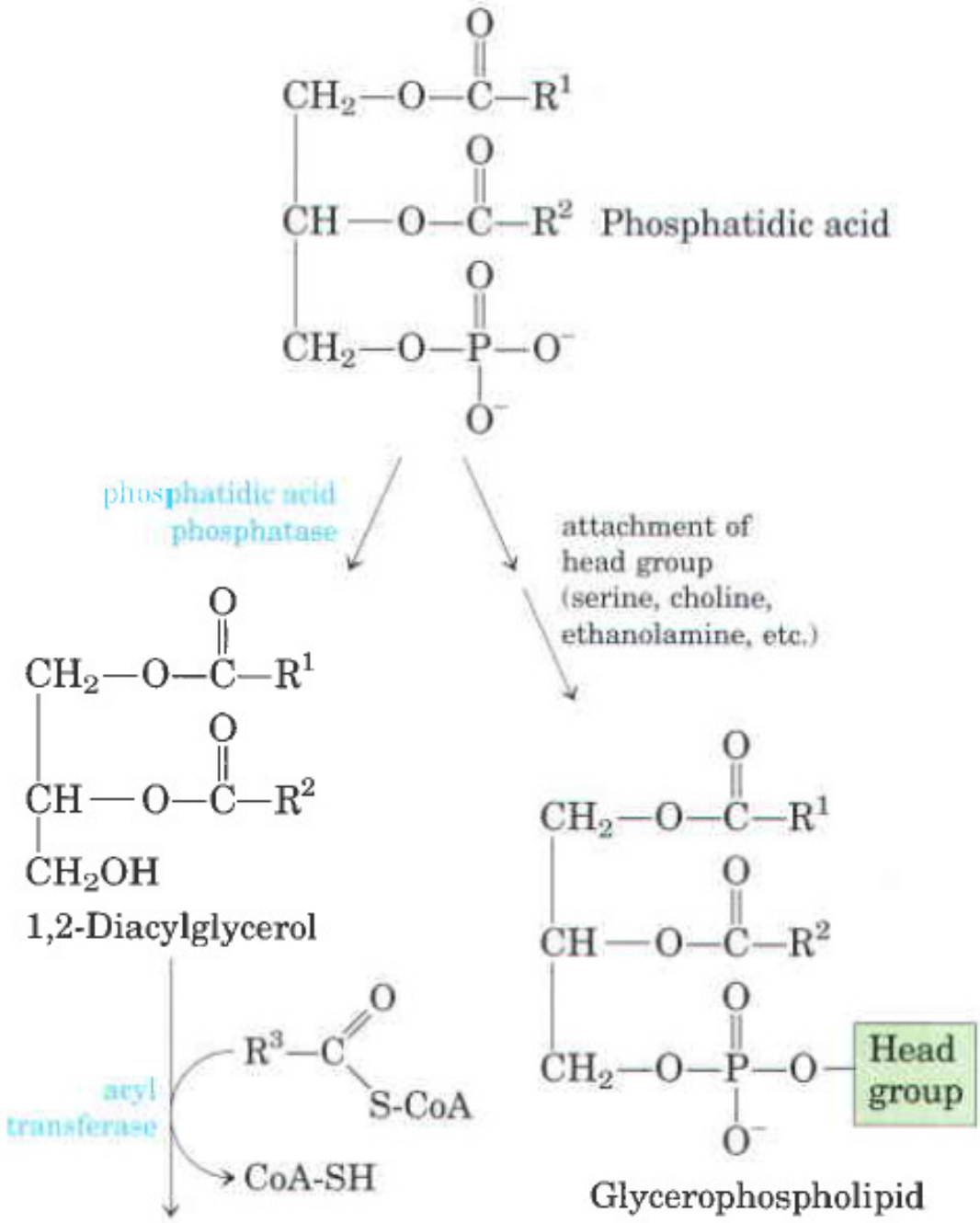


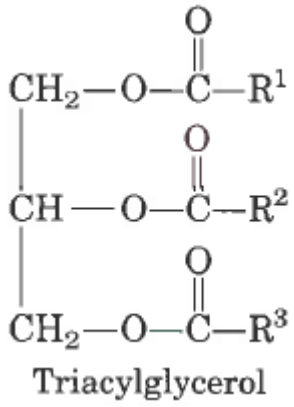
Biosynthesis of Triacylglycerols





Phosphatidic acid


Phosphatidic acid
phosphatidic acid phosphatase
attachment of head group (serine, choline, ethanolamine, etc.)
1,2-Diacylglycerol
acyl transferase
S-CoA
CoA-SH
Head group
Glycerophospholipid


Triacylglycerol