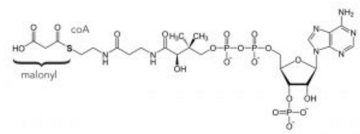
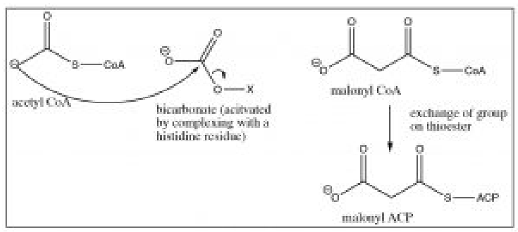
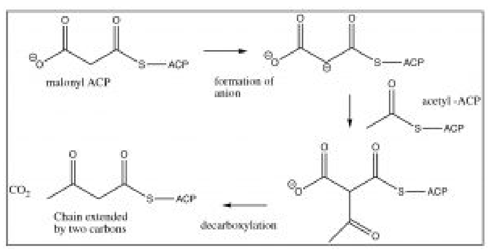
9.5: Biosynthesis of Fatty Acids-

As we move forward, we will discuss some biosynthetic pathways. It is not our intention that you reproduce these pathways, complete with enzymes and co-factors, but that you understand the underlying organic chemistry behind them. As you will see, most biochemical reactions are quite simple: it is their surroundings (the other parts of the molecules, enzymes, and co-factors) that make it possible for these reactions to occur (generally around room temperature) in a crowded aqueous environment; these pathways appear complex.



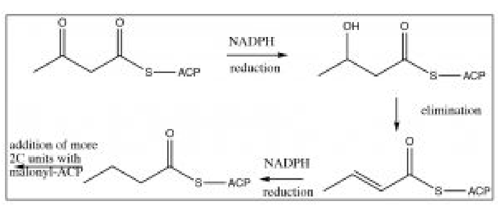
Fatty acids are built two carbons at a time by the following mechanism: the two-carbon unit is provided by a malonyl unit that is formed from malonyl-CoA, (a thioester) which is attached to a carrier protein for recognition purposes. It is formed from acetyl CoA (co-enzyme A)—which is a product of the breakdown of glucose (glycolysis) by reaction with bicarbonate. The result of adding two carbon units is that most biological fatty acids have an even number of carbons. They are synthesized by a sequence of reactions that is highly analogous to the malonic ester synthesis. The syntheses of fatty acids is one of the mechanisms that the body uses to “store” energy and to generate various membranes. Fatty acids often occur as esters of glycerol and are therefore called triglycerides.





Acetyl CoA is transferred to the acyl carrier protein (ACP) and is then attacked by the malonyl anion with loss of the S-ACP group (this is analogous to the S_N2 reaction on an alkyl halide). Decarboxylation produces a new beta-keto thioester, extended by two carbons.

The next step is reduction of the carbonyl (using NADPH—which is analogous to NADH—and delivers hydride ion), elimination, and reduction to the fully saturated chain. The system then cycles around to add two more carbons from malonyl ACP.



All of these reactions are very similar to those we have learned throughout the course. They seem more complex because of the biological “bits” that control the direction of reaction and activation of the functional groups, but once you understand organic chemistry, biochemistry makes much more sense!