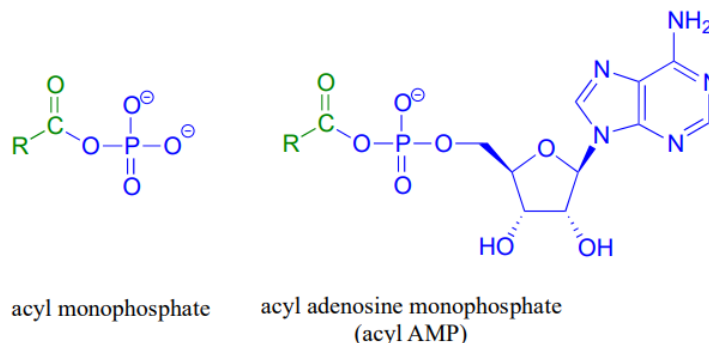
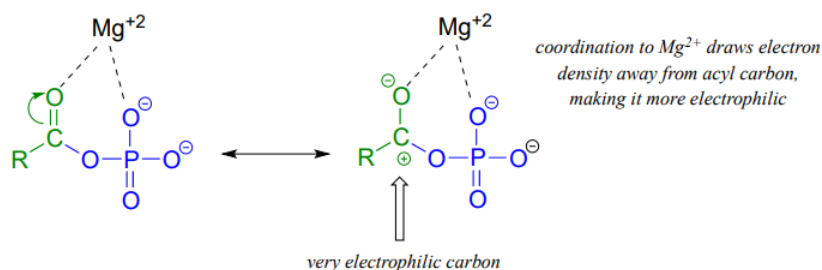


## 11.4: Acyl Phosphates

Acyl phosphates, because they are so reactive towards acyl substitutions, are generally seen as reaction intermediates rather than stable metabolites in biochemical pathways. Acyl phosphates usually take one of two forms: a simple acyl monophosphate, or acyl-adenosine monophosphate.

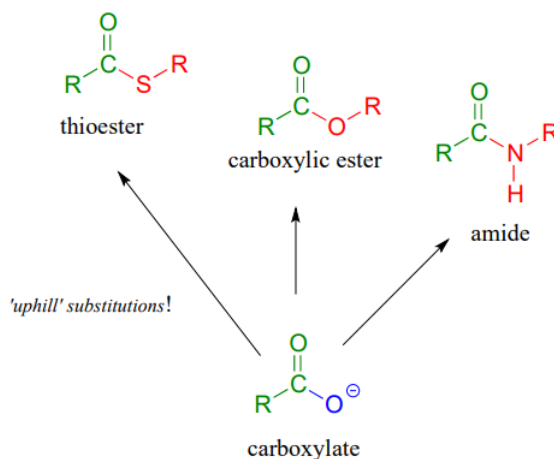


Both forms are highly reactive to acyl substitution reactions, and are often referred to as 'activated acyl groups' or 'activated carboxylic acids' for reasons that will become clear soon. The tendency of phosphates to form stabilizing complexes with one or more magnesium ions in an enzyme's active site contributes in a large way to the reactivity of acyl phosphates.



A magnesium ion acts as a Lewis acid, accepting electron density from the oxygen end of the acyl carbonyl bond, which greatly increases the degree of partial positive charge - and thus the electrophilicity - of the carbonyl carbon. The magnesium ion also balances negative charge on the phosphate, making it a weak base and excellent leaving group.

We have already learned that the carboxylate functional group is the least reactive substrate for an enzyme-catalyzed acyl substitution reactions. In biology, though, carboxylates are frequently transformed into thioesters, carboxylic esters, and amides, all of which are higher in energy, meaning that these transformations are thermodynamically 'uphill'.



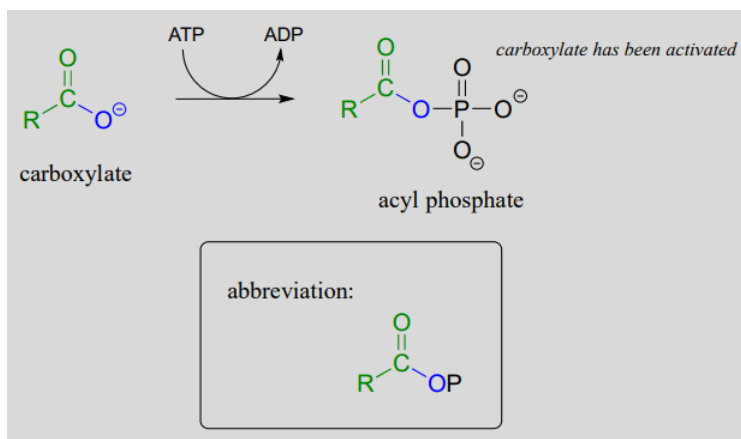
How are these uphill substitutions accomplished? They are not carried out directly:

like all thermodynamically unfavorable reactions in biochemistry, they are linked to an energy-releasing, 'downhill' reaction. In this case, (and many others), the linked reaction that 'pays for' the uphill reaction is hydrolysis of ATP.

In order to undergo an acyl substitution reaction, a carboxylate must first be activated by phosphorylation. You are already familiar with this phosphoryl group transfer process from chapter 9.

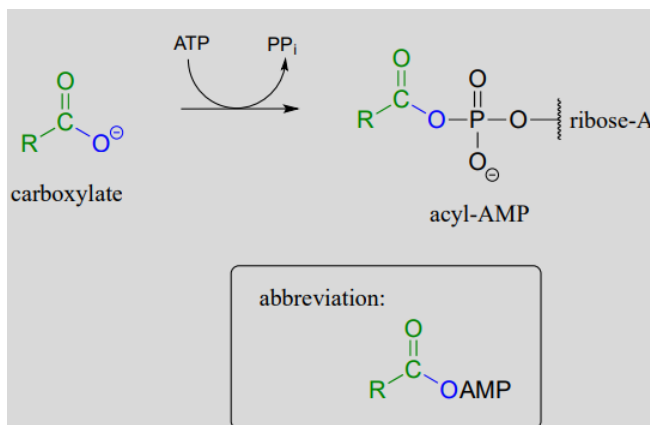
In many cases, enzymes activate a carboxylate group by converting it to an acyl phosphate (the most reactive of the carboxylic acid derivatives), at the expense of an ATP: the mechanism for this type of transformation is shown in Section 9.5.

Formation of an acyl phosphate (see section 9.5 for the complete mechanism):

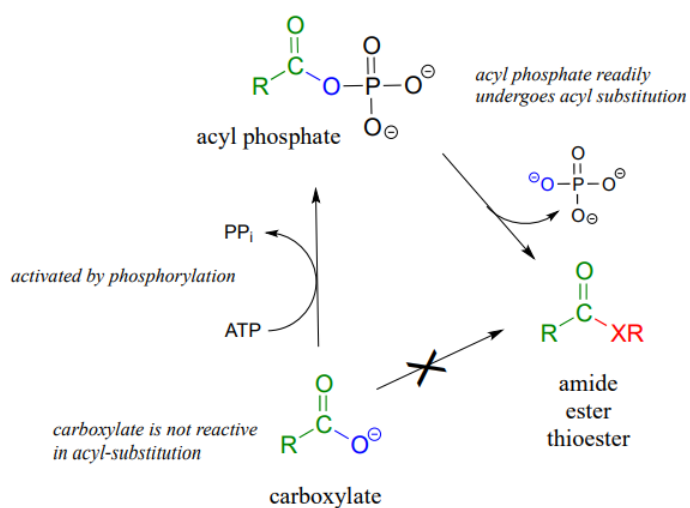


As a common alternative, some enzymatic reactions begin with the conversion of a carboxylate to an acyl-AMP intermediate:

Formation of an acyl -AMP (see section 9.5 for the complete mechanism):



In either case, once the carboxylate group has been activated, the reactive acyl phosphate/acyl-AMP intermediate can go on to act as the electrophile in an energetically favorable nucleophilic acyl substitution reaction.



You have probably heard ATP referred to as the 'energy currency' molecule. The reactions in this section provide a more concrete illustration of that concept. A lower-energy group (a carboxylate) is converted to a higher-energy group (a thioester, for example) by 'spending' a high-energy ATP.

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