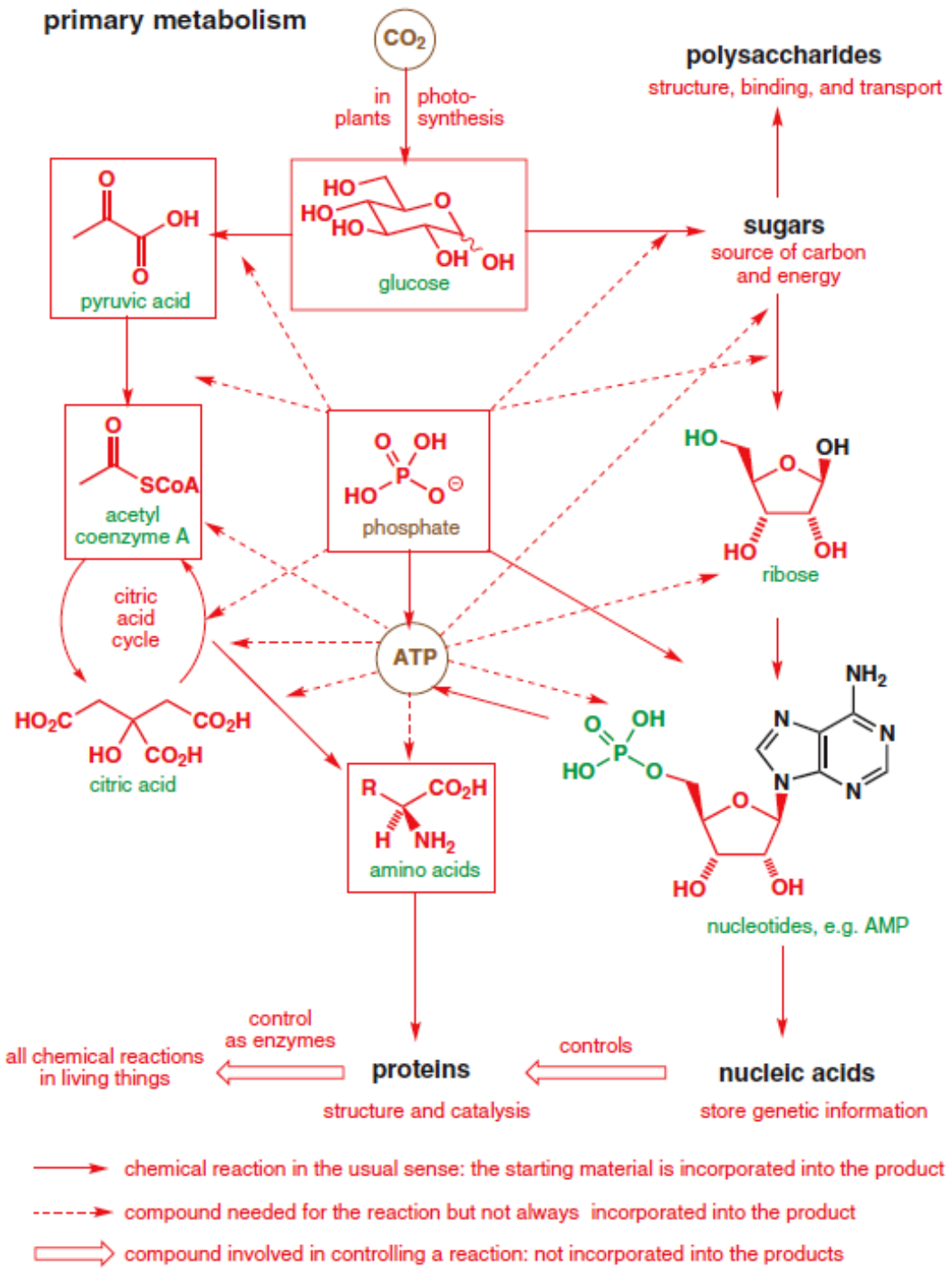
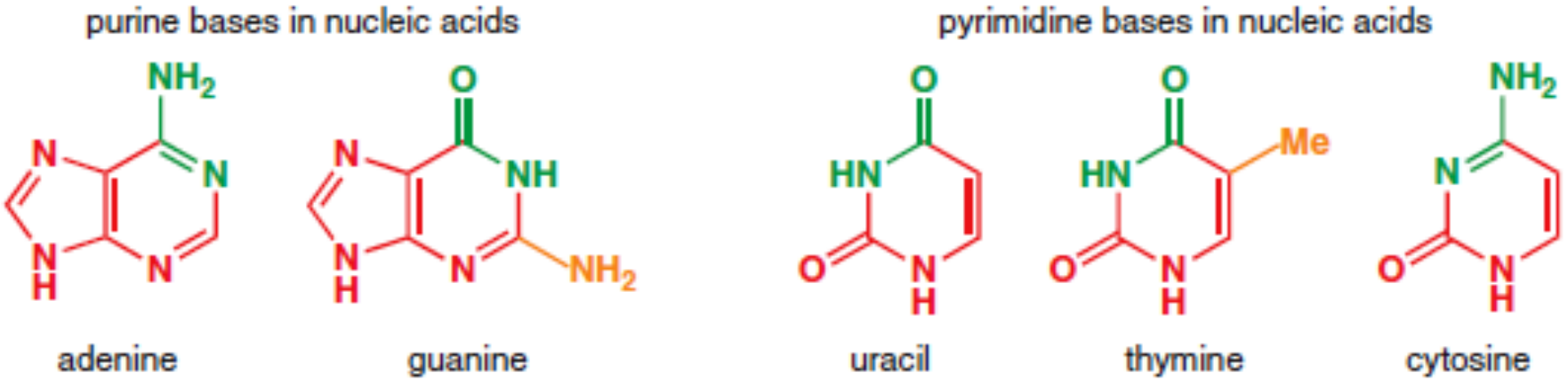
Organic chemistry of life

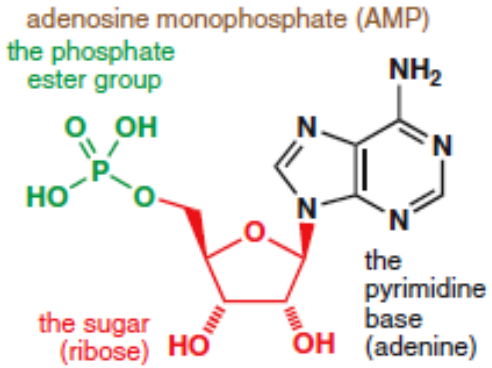


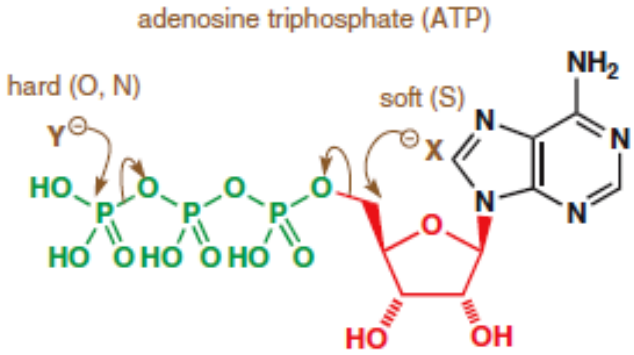
Life begins with nucleic acids

There are five heterocyclic bases in DNA and RNA

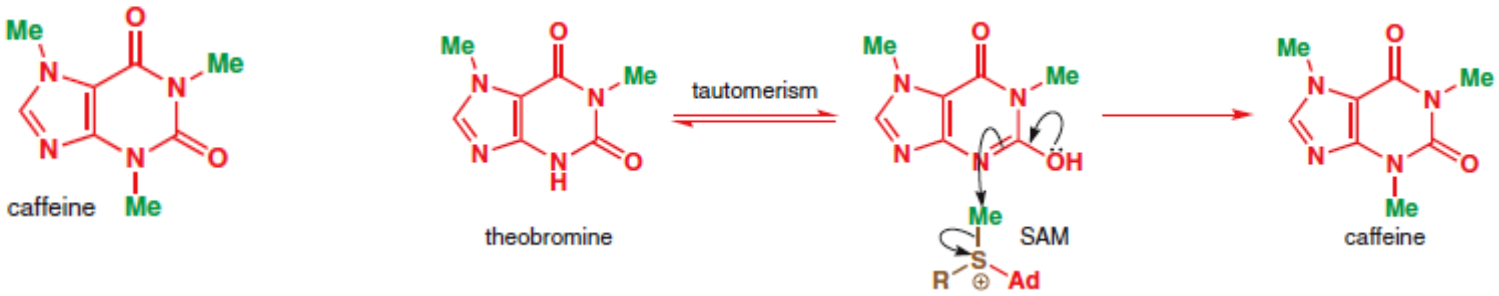


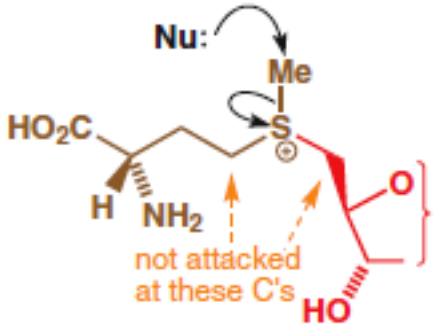
- There are only two purine bases found in nucleic acids: adenine (A), which we have already met, and guanine (G)
- The three pyrimidine bases are simpler: uracil (U), thymine (T), and cytosine (C). Cytosine is found in DNA and RNA, uracil in RNA only, and thymine in DNA only.



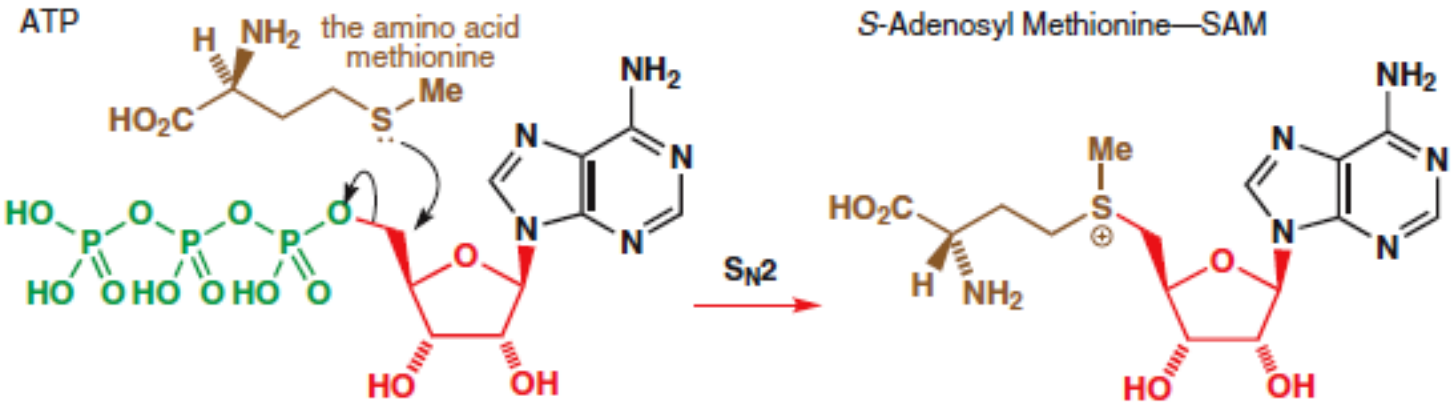


The stimulants in tea and coffee are methylated purines

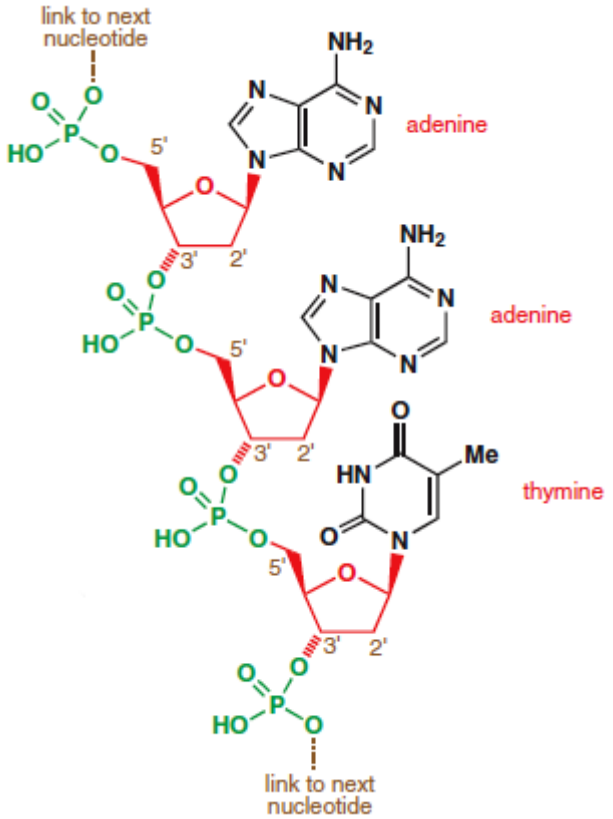


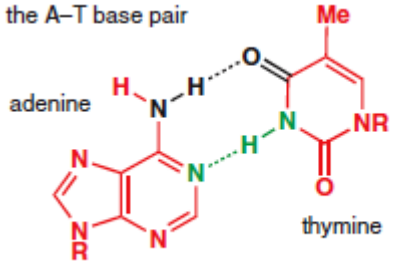


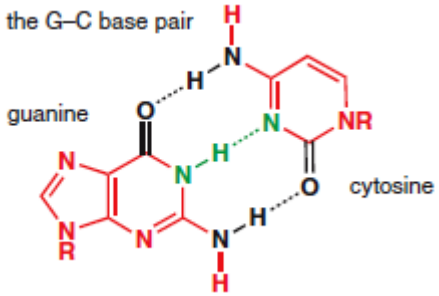
nucleophilic attack on SAM



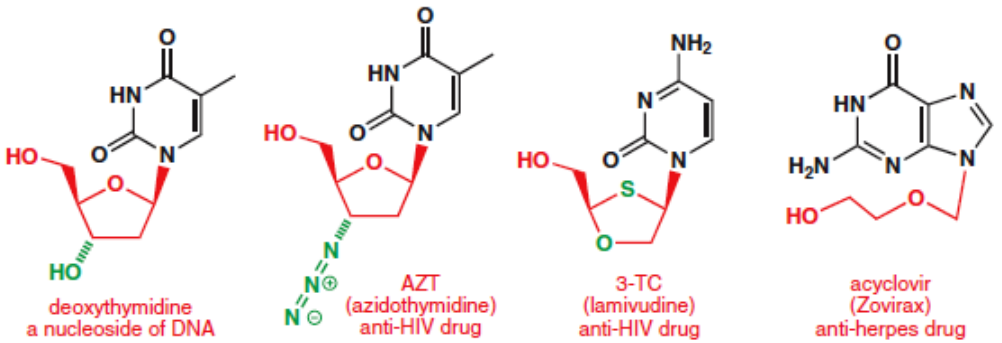
Nucleic acids exist in a double helix



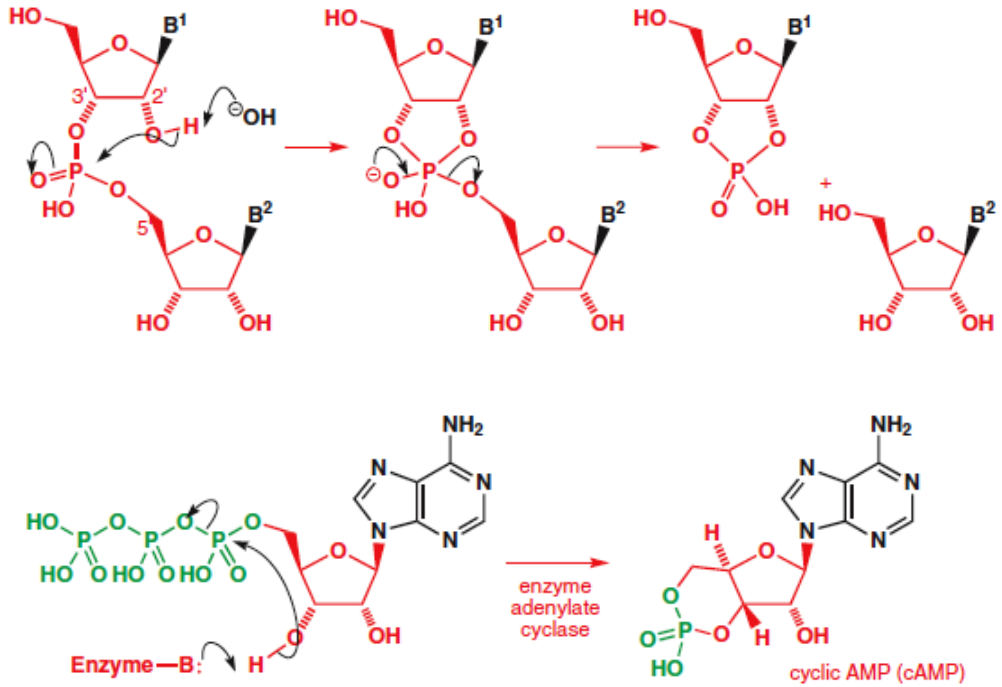




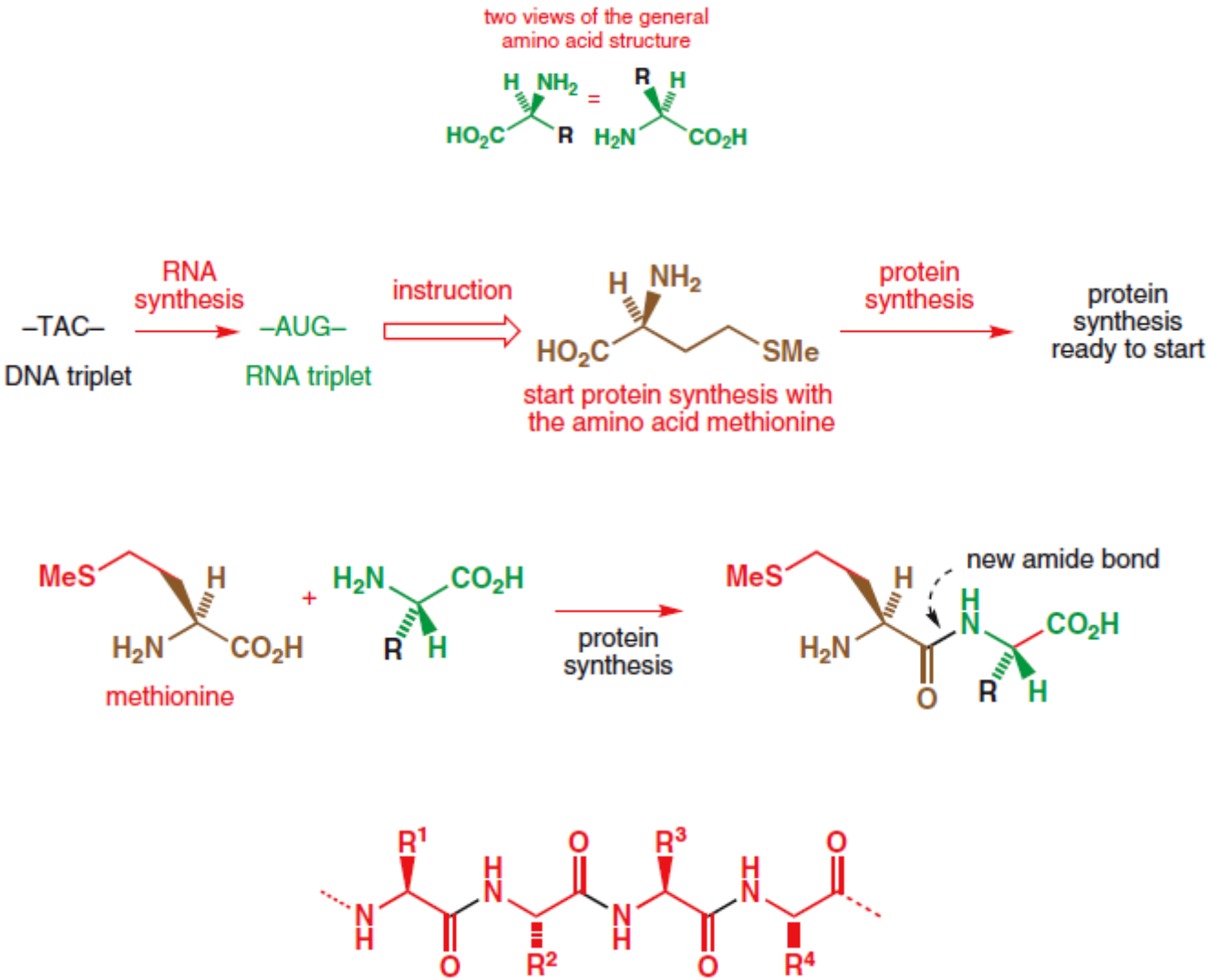
HIV and AIDS are treated with modified nucleosides



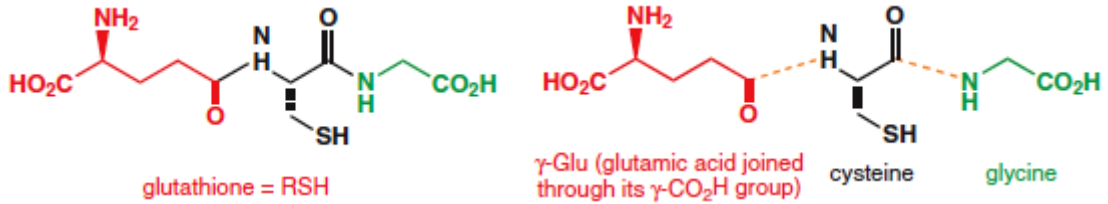
Cyclic nucleosides and stereochemistry

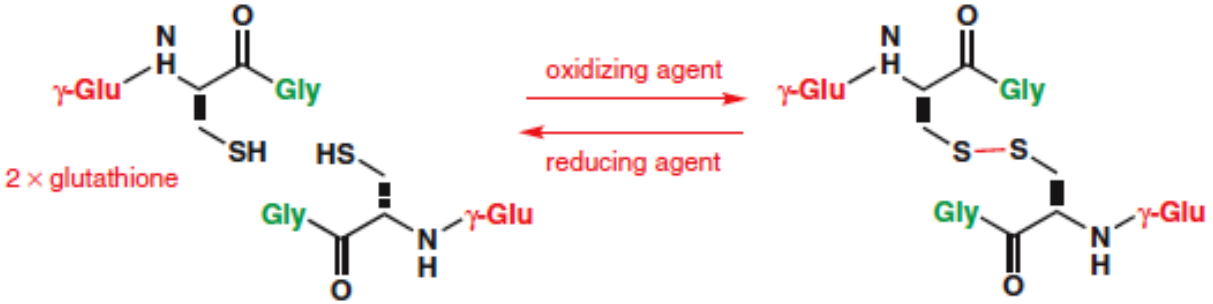


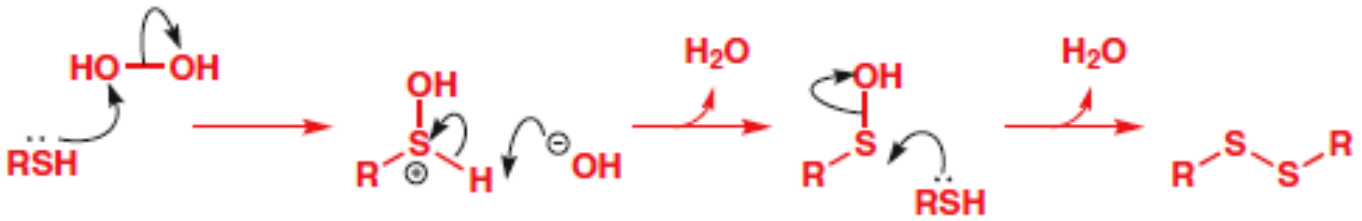
Proteins are made of amino acids

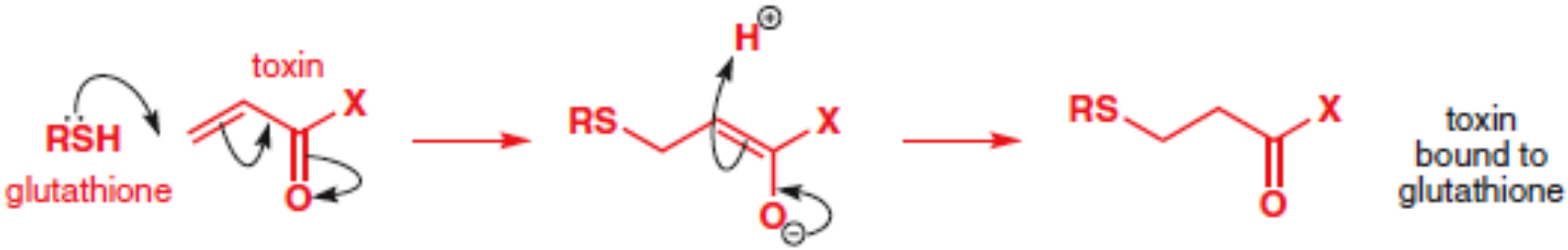


Amino acids combine to form peptides and proteins

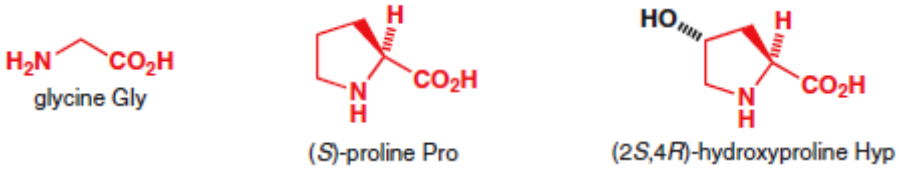




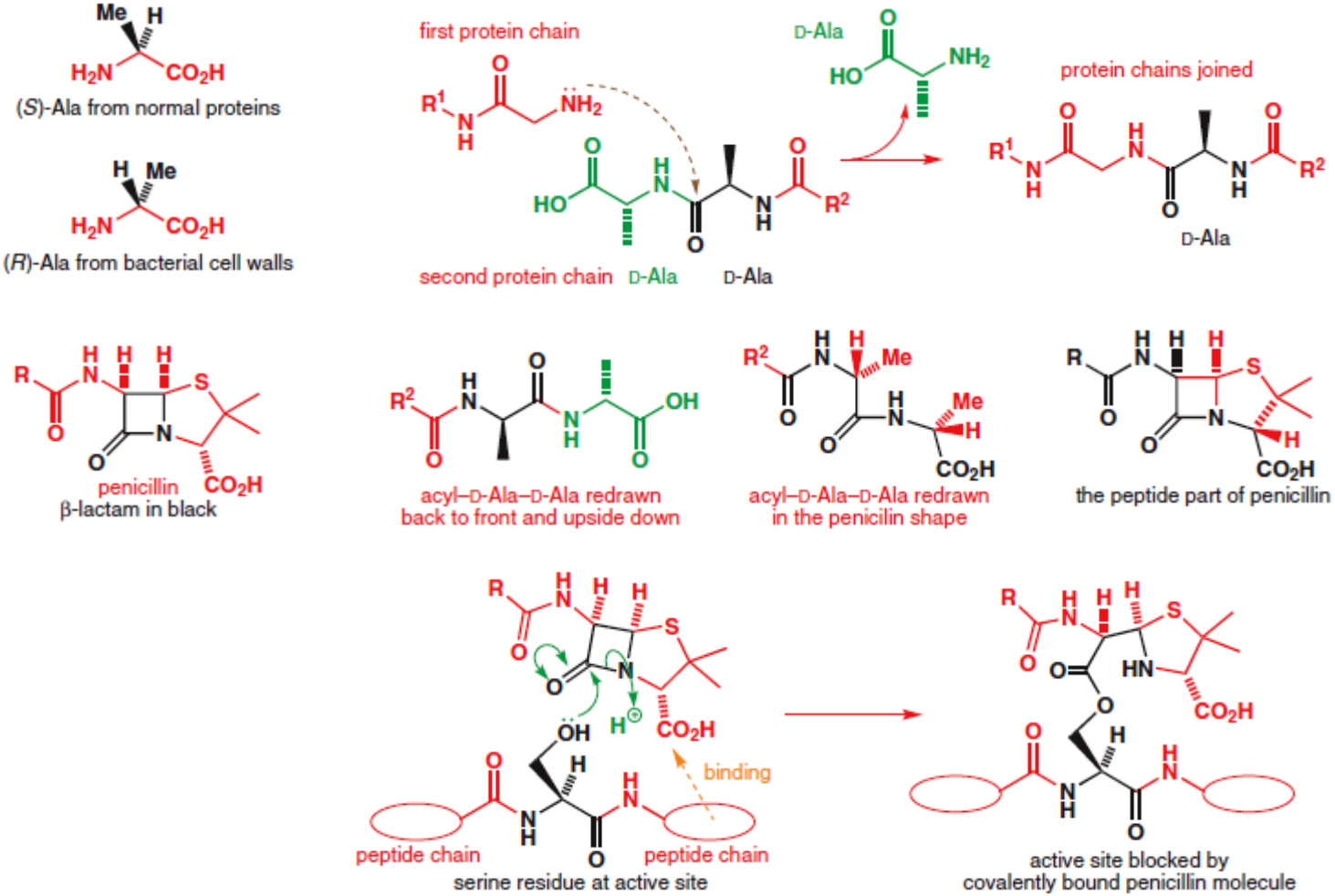




Structural proteins must be tough and flexible



Antiobiotics exploit the special chemistry of bacteria

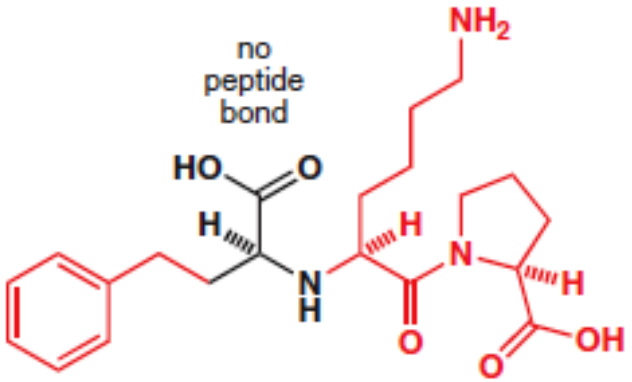


Drugs based on peptides or peptidomimetics

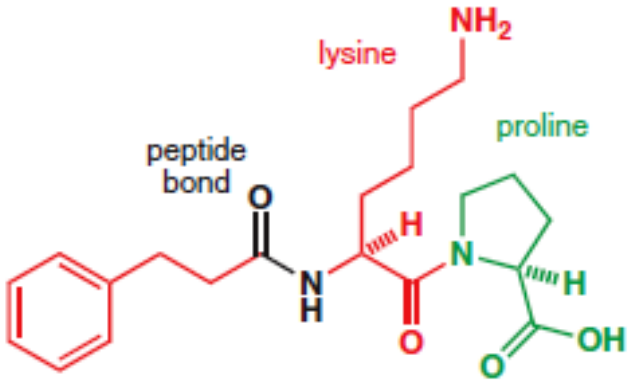
angiotensin I
ten amino acids
no effect on blood pressure

Zn^{2+} | angiotensin-converting enzyme (ACE)

angiotensin II
eight amino acids
increases blood pressure



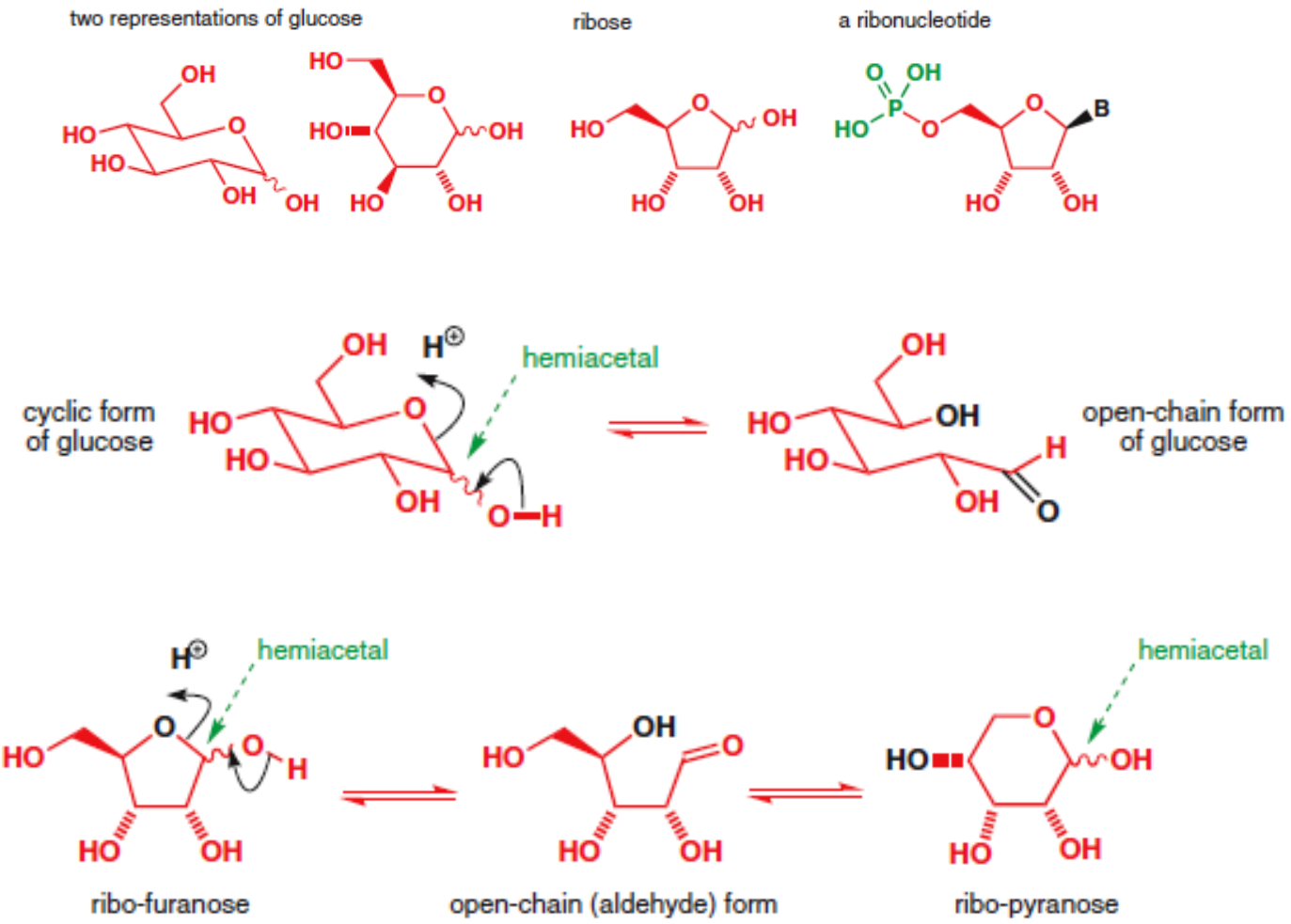
lisinopril



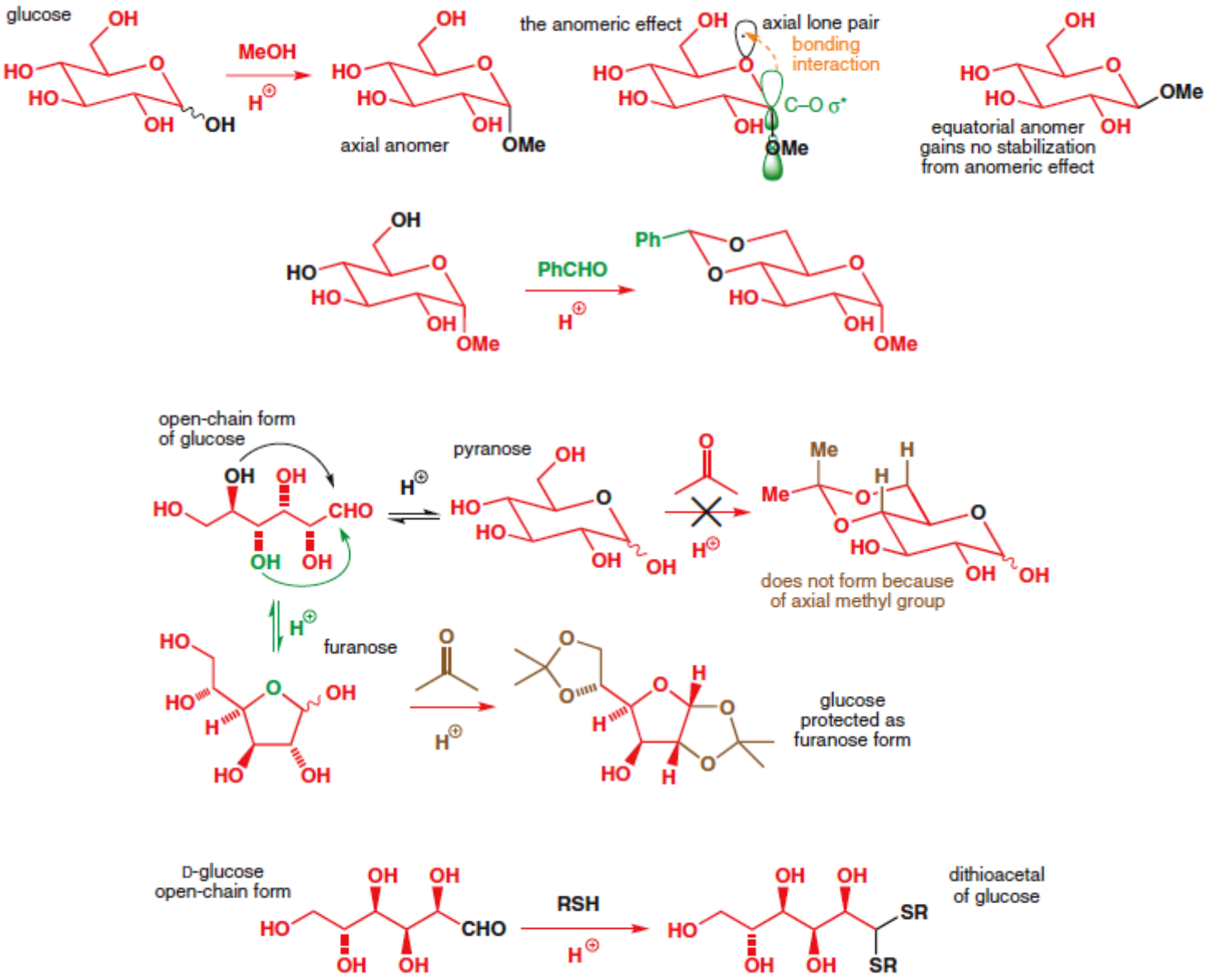
'natural peptide'

Sugars—just energy sources?

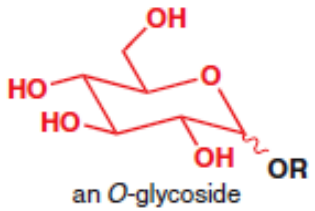
Sugars normally exist in cyclic forms with much stereochemistry



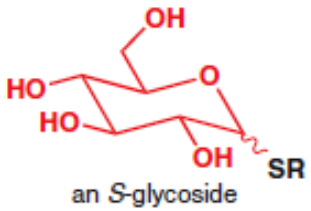
Sugars can be fixed in one shape by acetal formation



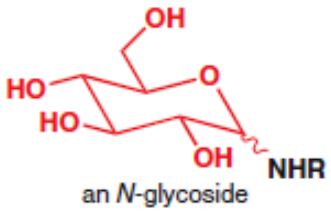
Glycosides in nature



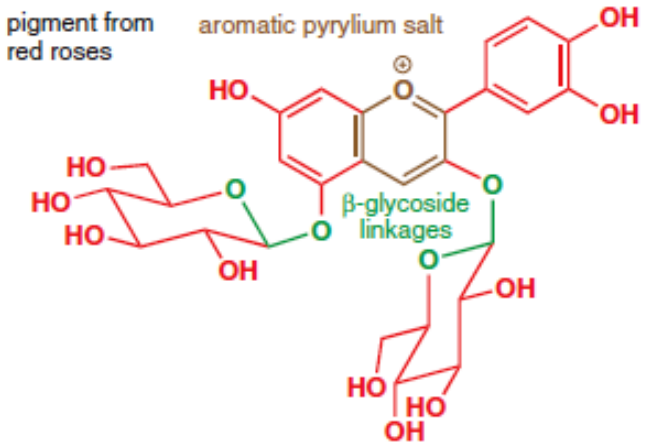
an *O*-glycoside

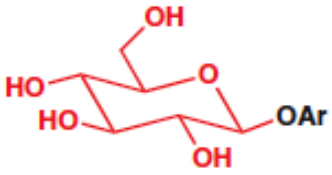


an *S*-glycoside

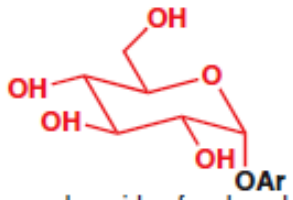


an *N*-glycoside

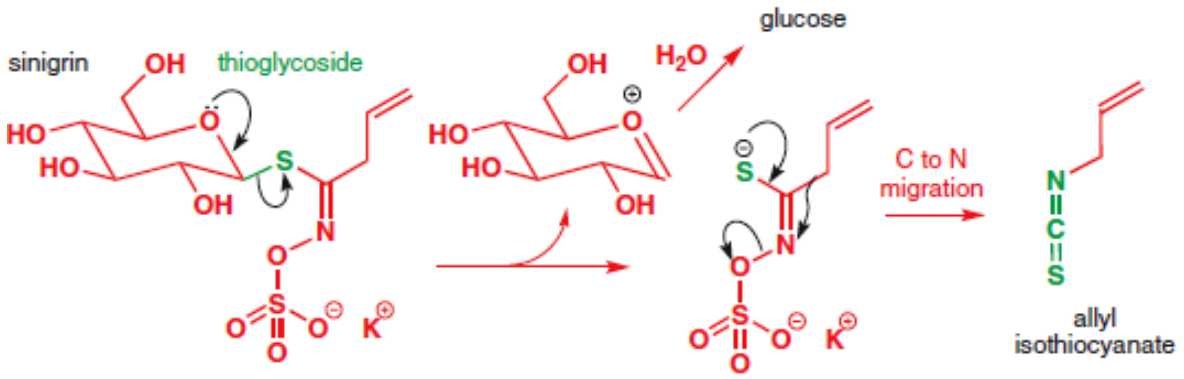




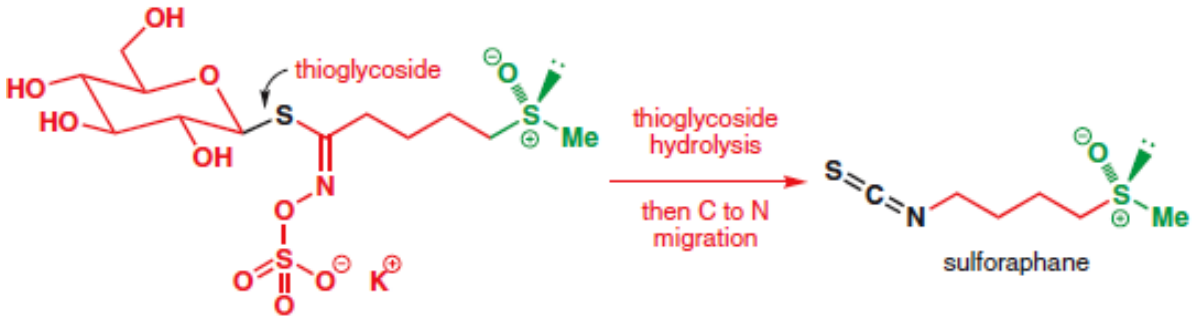
a β-glycoside of a phenol



an α-glycoside of a phenol

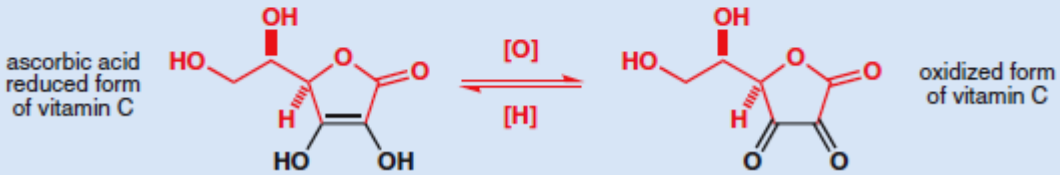


Glycosides in nature

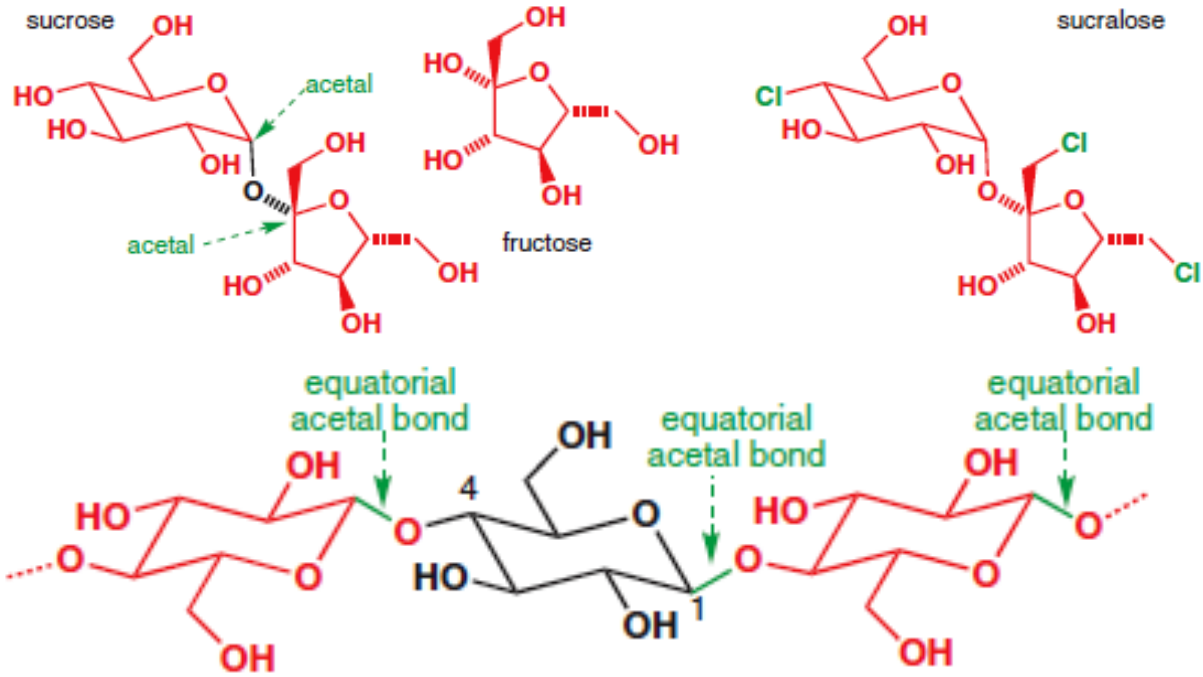


Vitamin C is a derivative of glucose

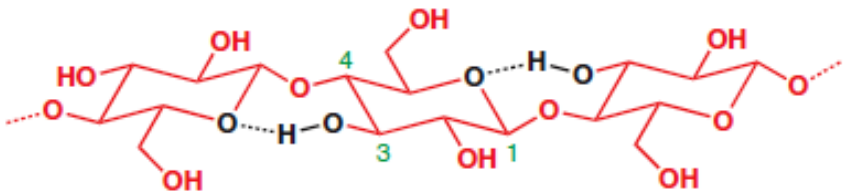
Nature makes some important compounds from simple sugars. Vitamin C—ascorbic acid—is one of these. It certainly looks very like a sugar as it has six carbon atoms, each having an oxygen atom as substituent as well as an oxygen heterocycle. Like glutathione, it protects cells from stray oxidants as well as being involved in primary redox pathways (we mentioned earlier its role in collagen synthesis). Its reduced and oxidized forms are shown below.



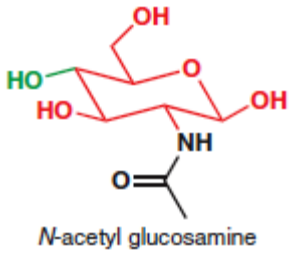
Most sugars are embedded in complex carbohydrates



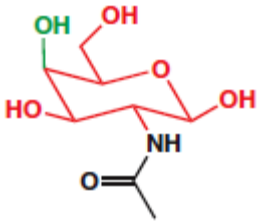
glucose monomers as part of the structure of cellulose



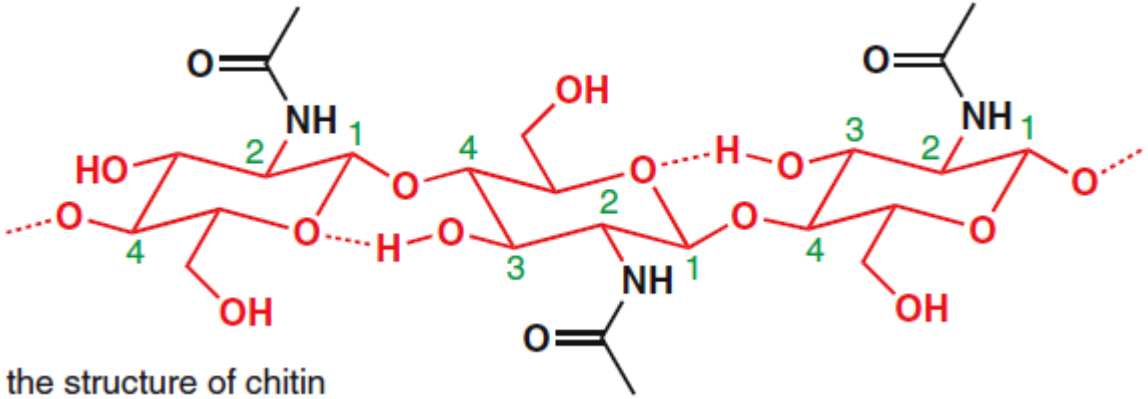
Amino sugars add versatility to saccharides



N-acetyl glucosamine

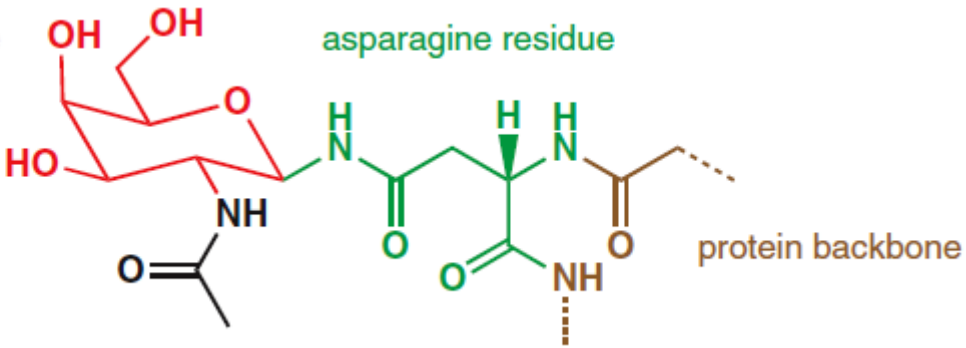


N-acetyl galactosamine



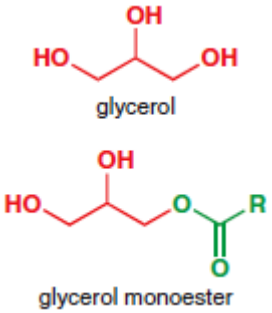
the structure of chitin

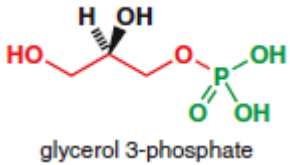
N-acetyl galactosamine

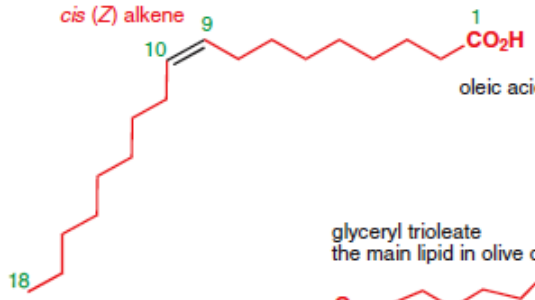


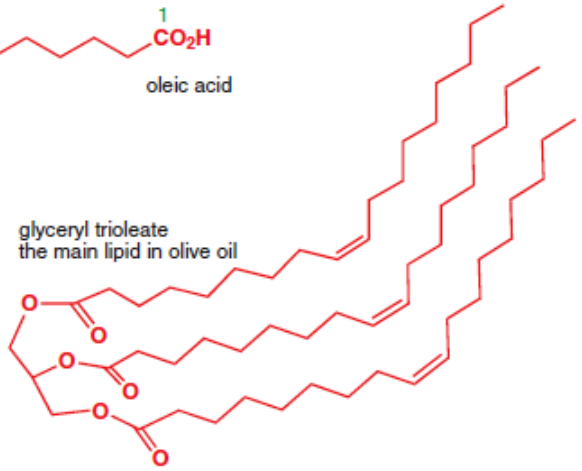
asparagine residue

Lipids

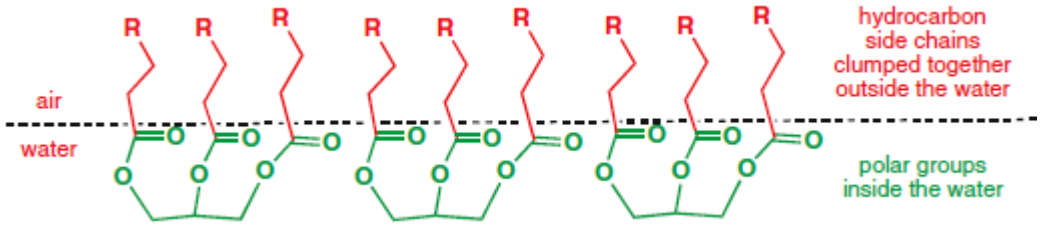


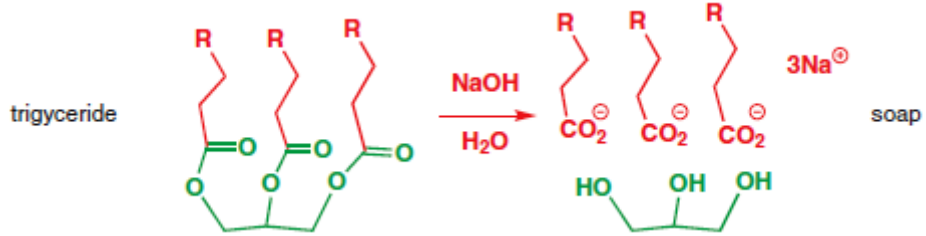


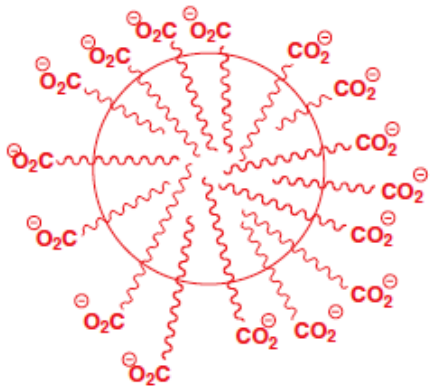




Oil and water do not mix

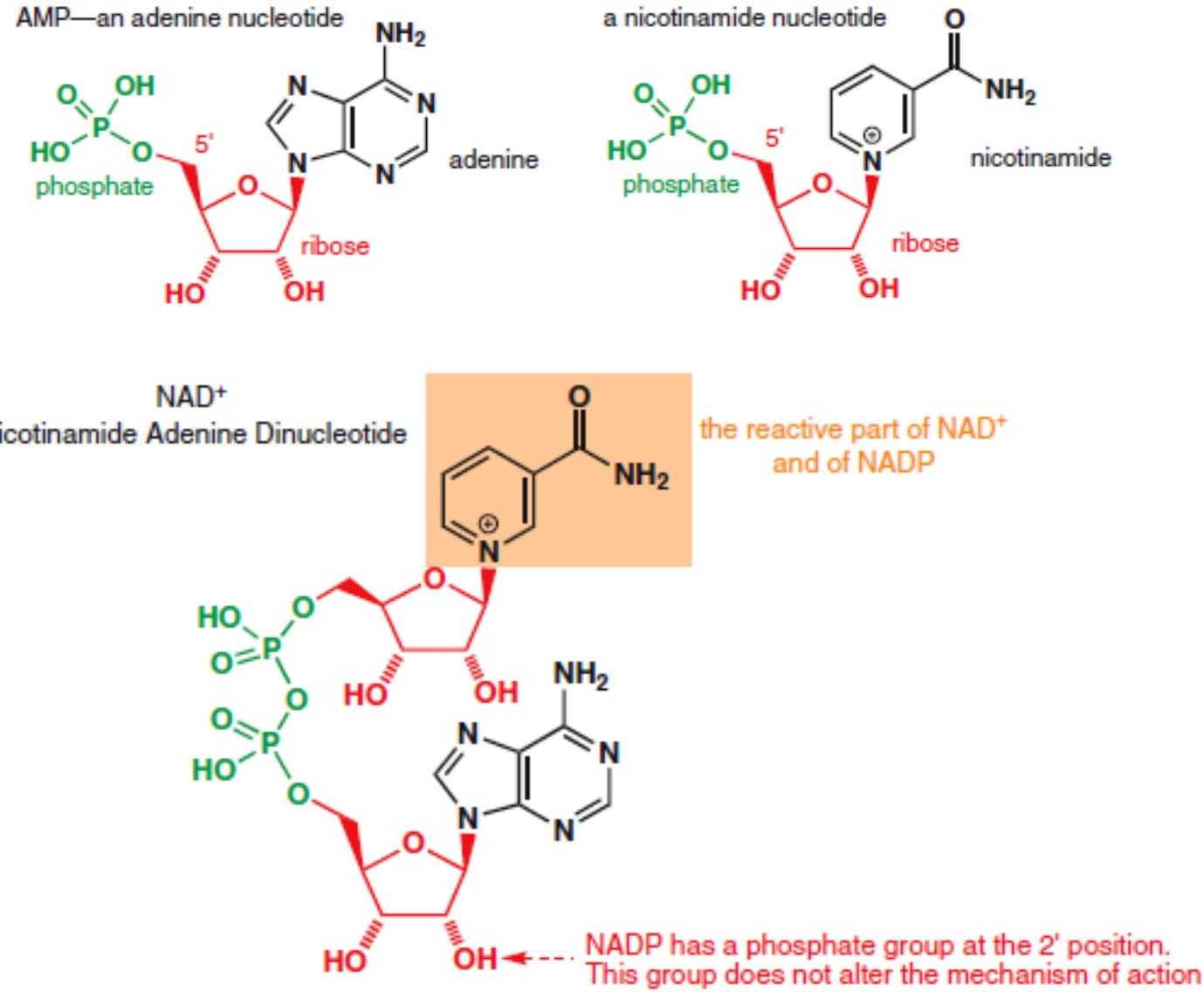






Mechanisms in biological chemistry

Nature's $NaBH_4$ is a nucleotide: NADH or NADPH



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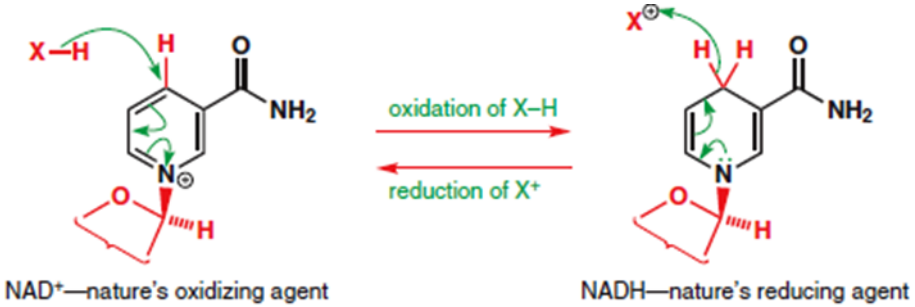
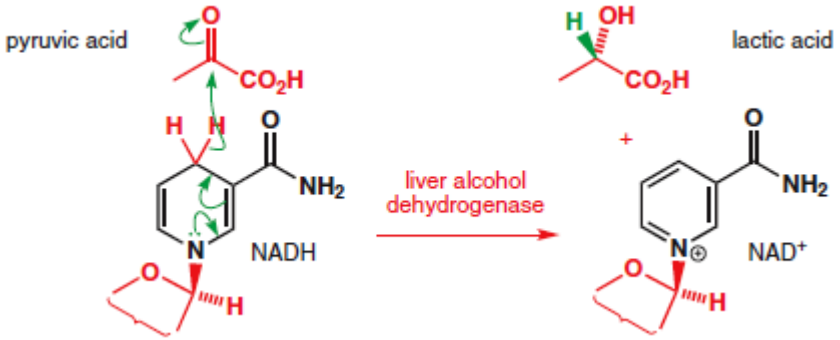
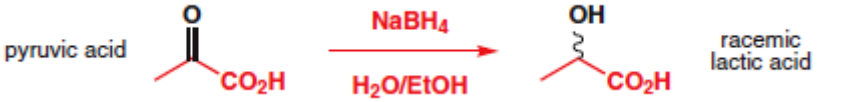
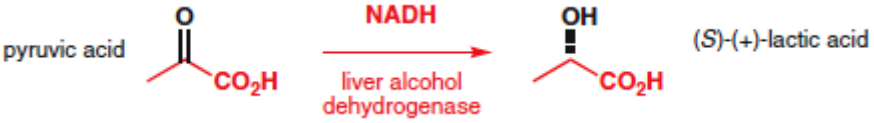


NAD+—nature's oxidizing agent

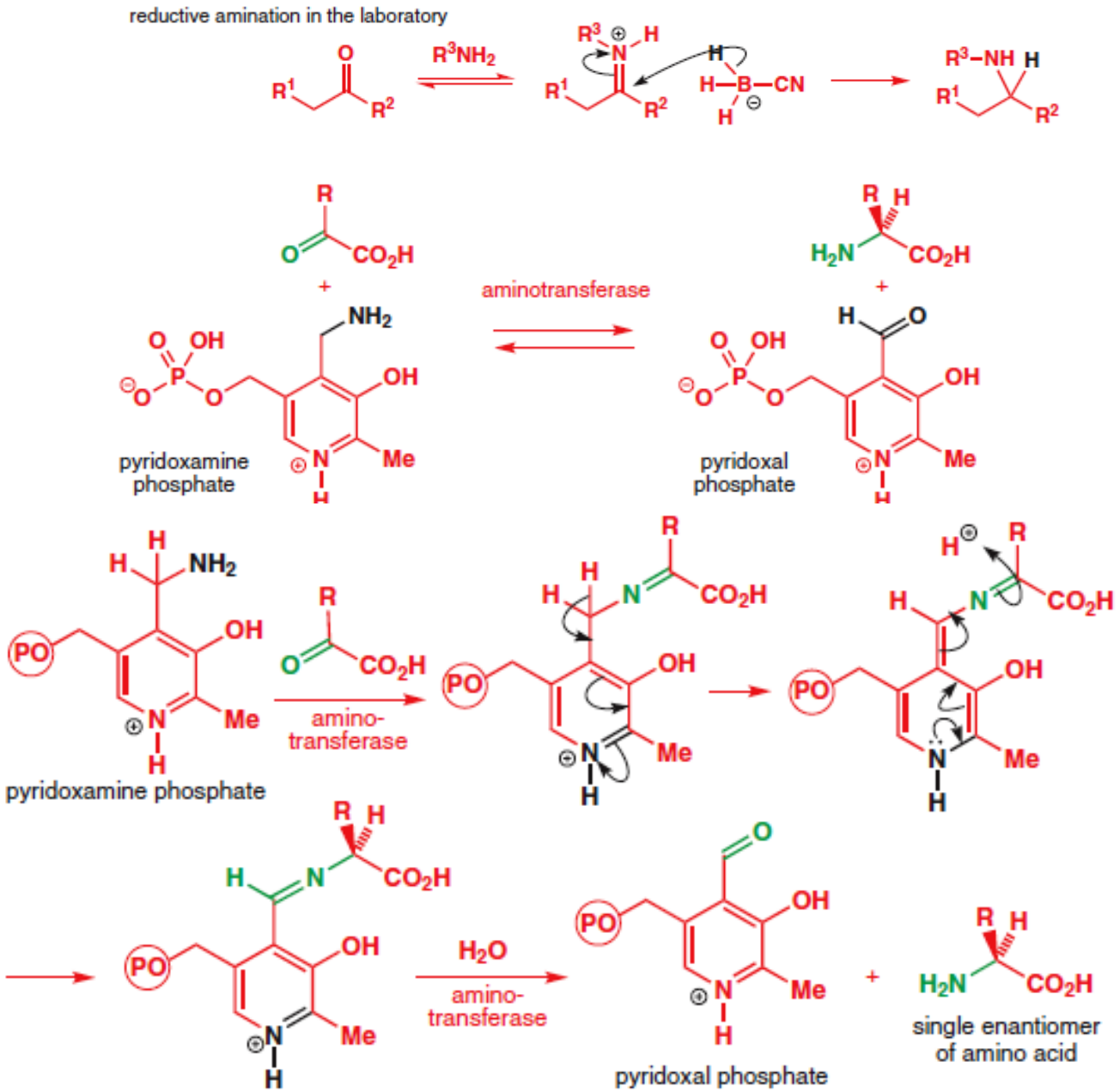
NADH—nature's reducing agent



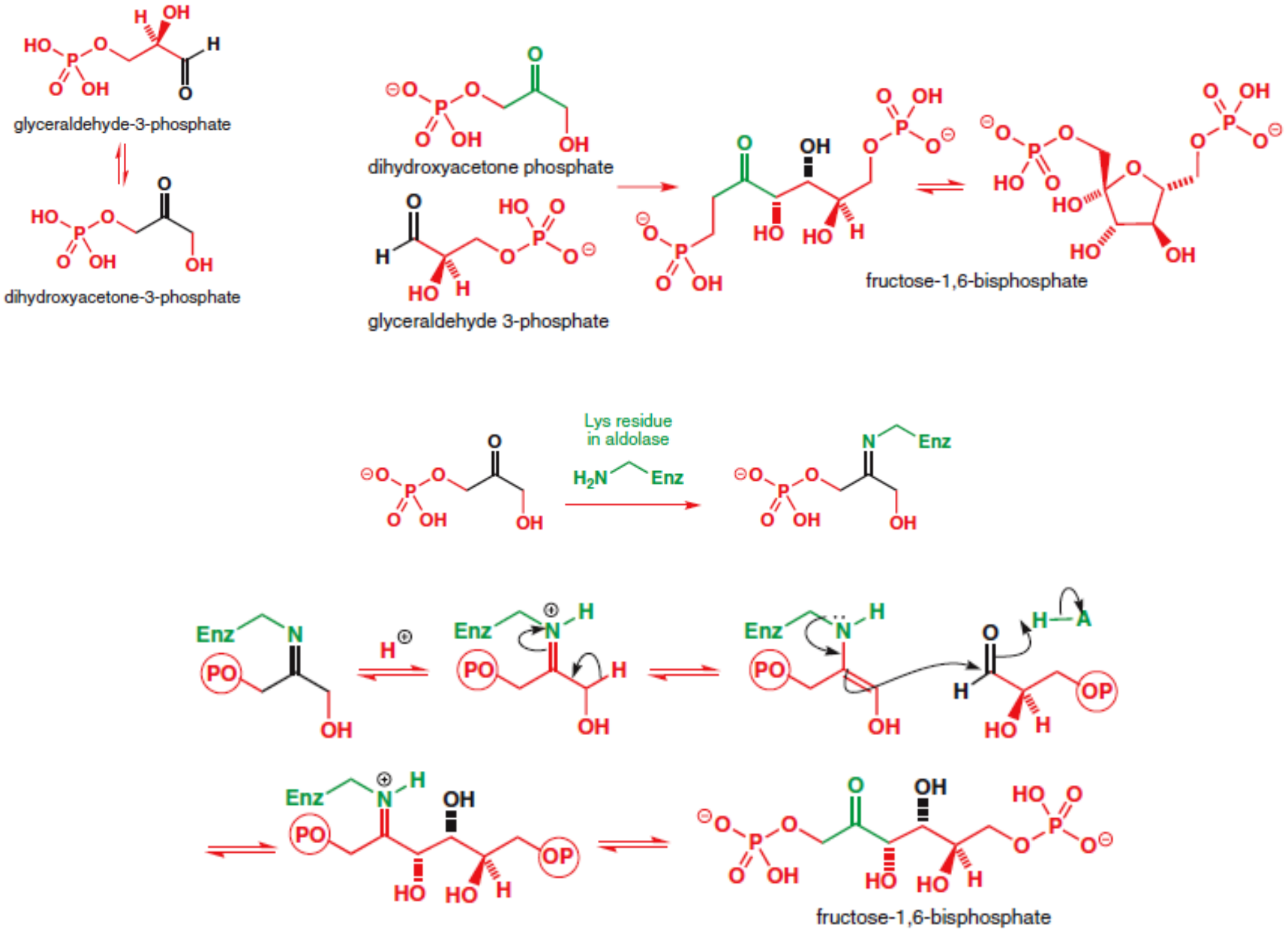




Reductive amination in nature



Nature's enolate equivalents: lysine enamines and coenzyme A



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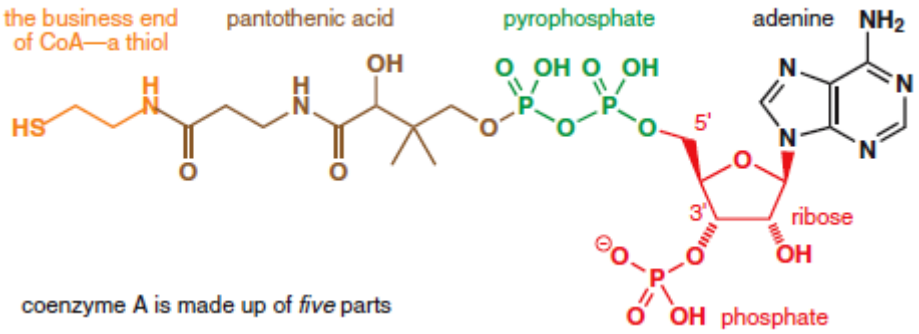
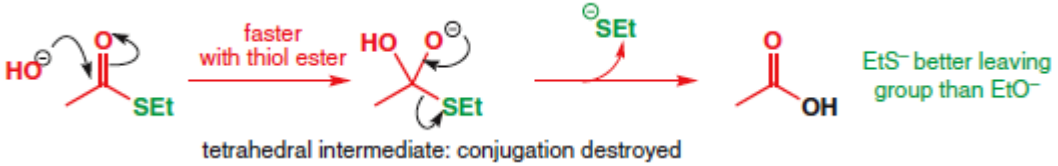
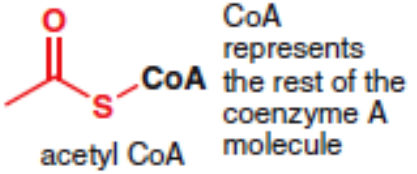
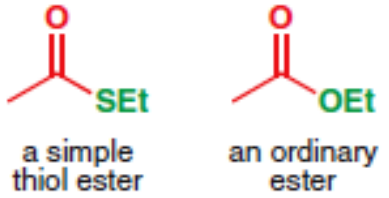
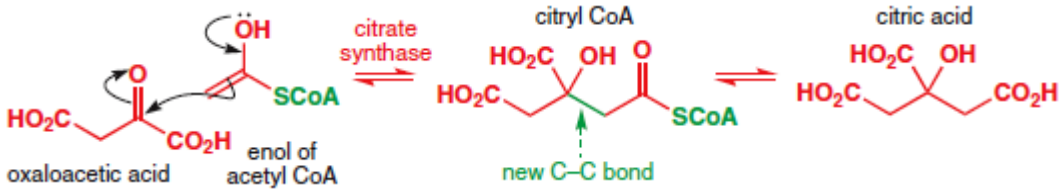
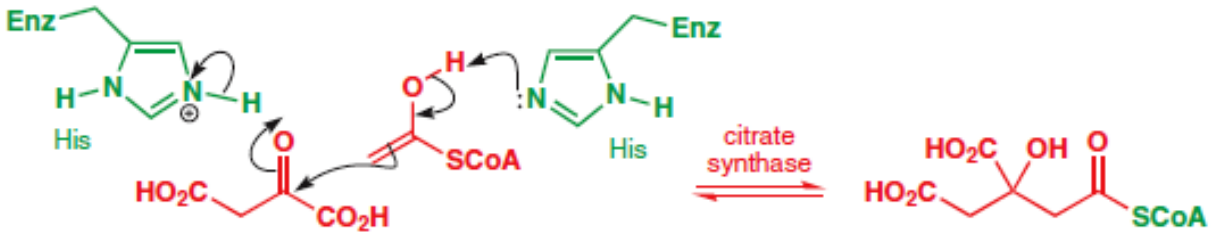




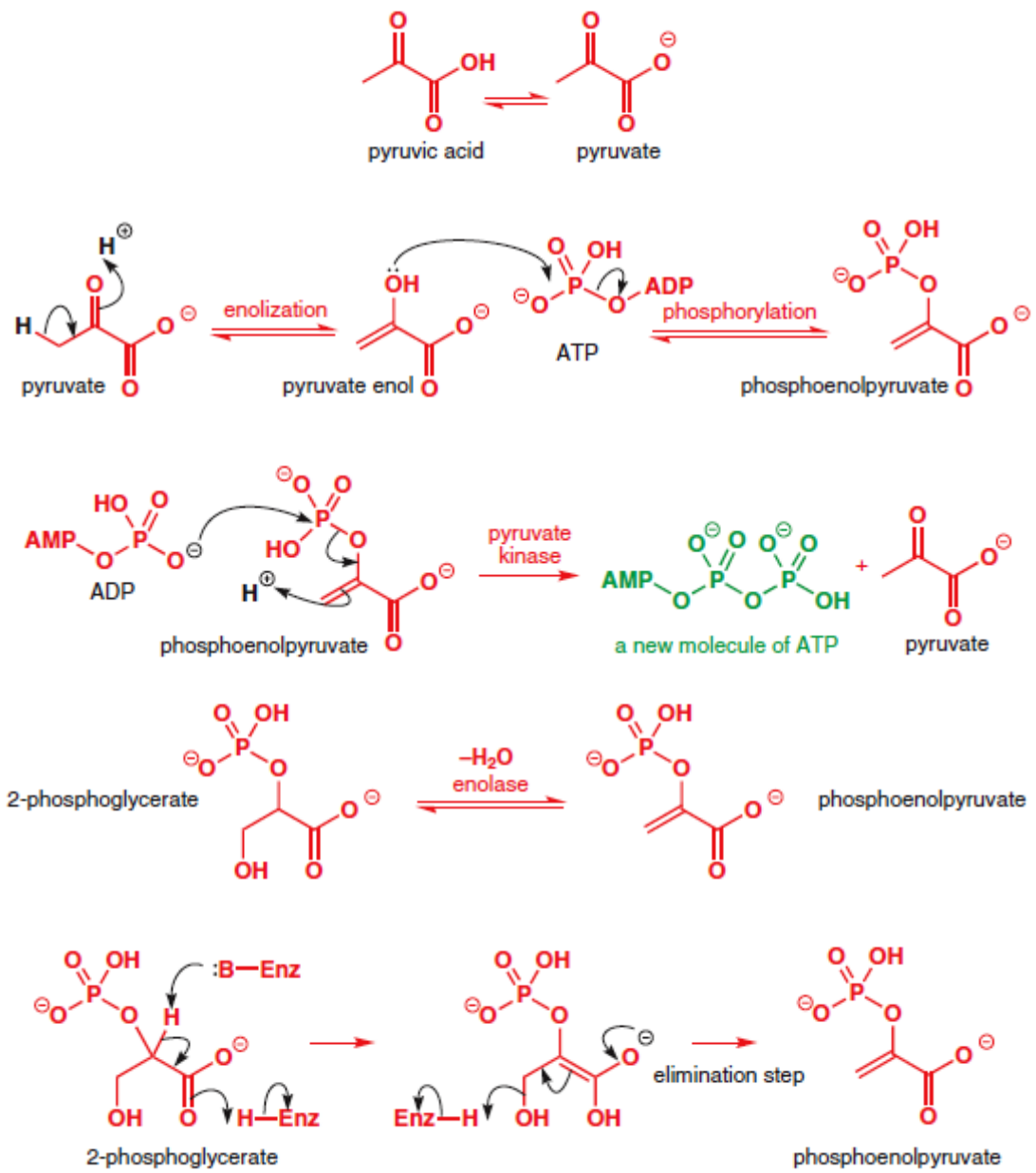




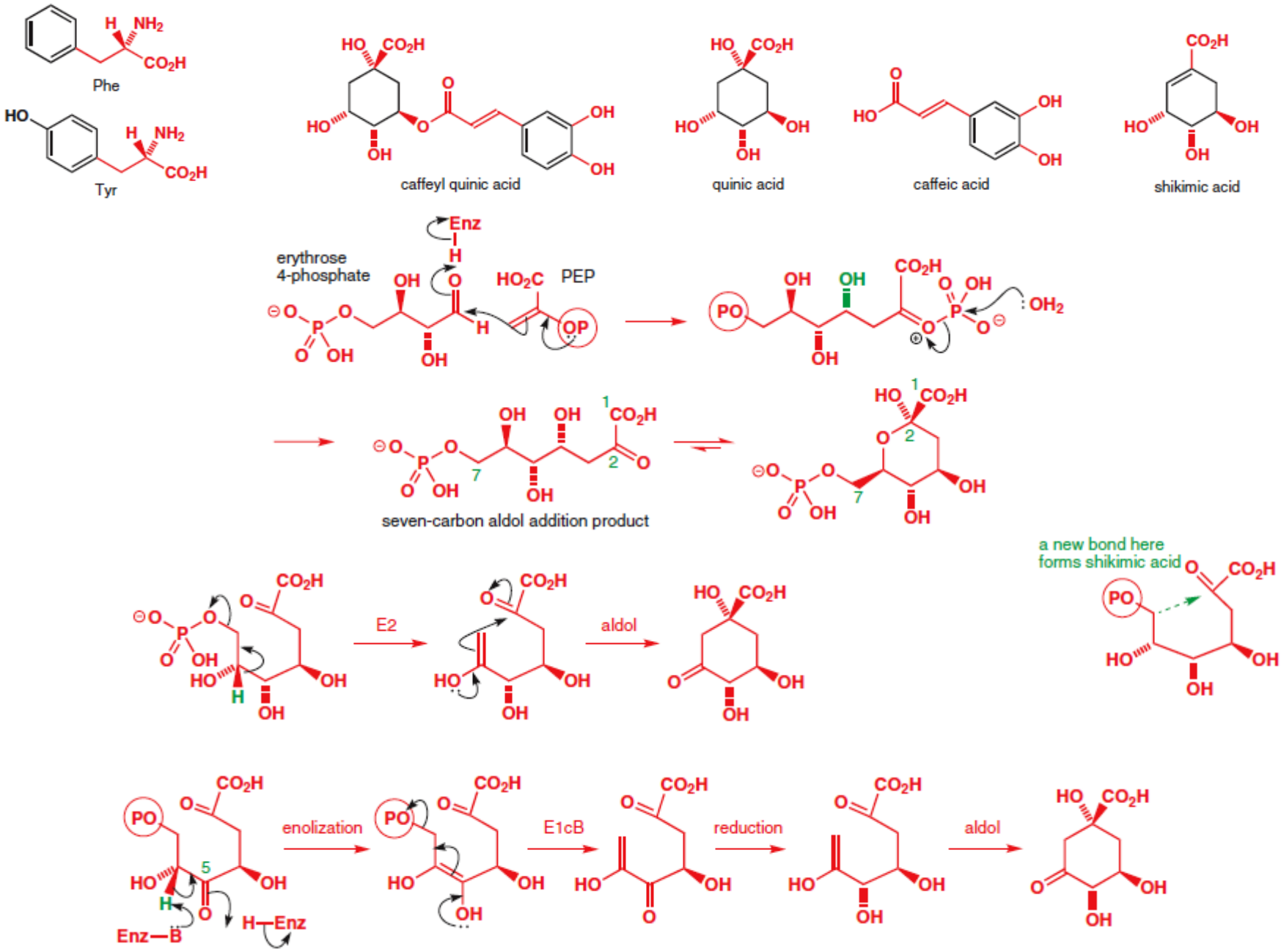




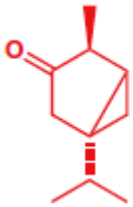
Phosphoenolpyruvate



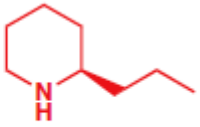
The shikimic acid pathway



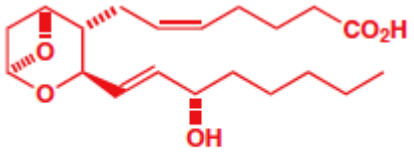
Natural products



thujone—
a terpene

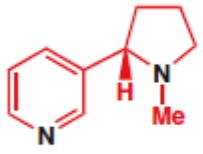


coniine—
an alkaloid

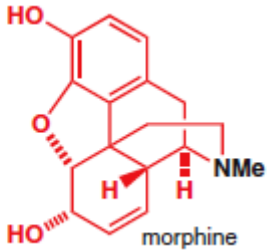


thromboxane A_2—a polyketide

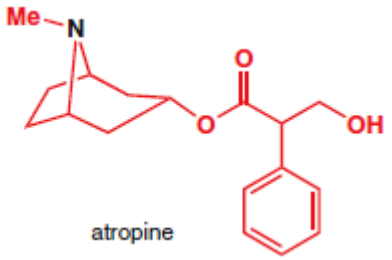
Alkaloids are made by amino acid metabolism



nicotine



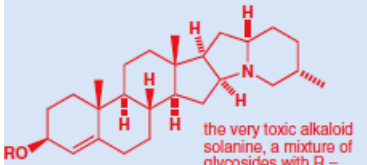
morphine



atropine

Solanaceae alkaloids

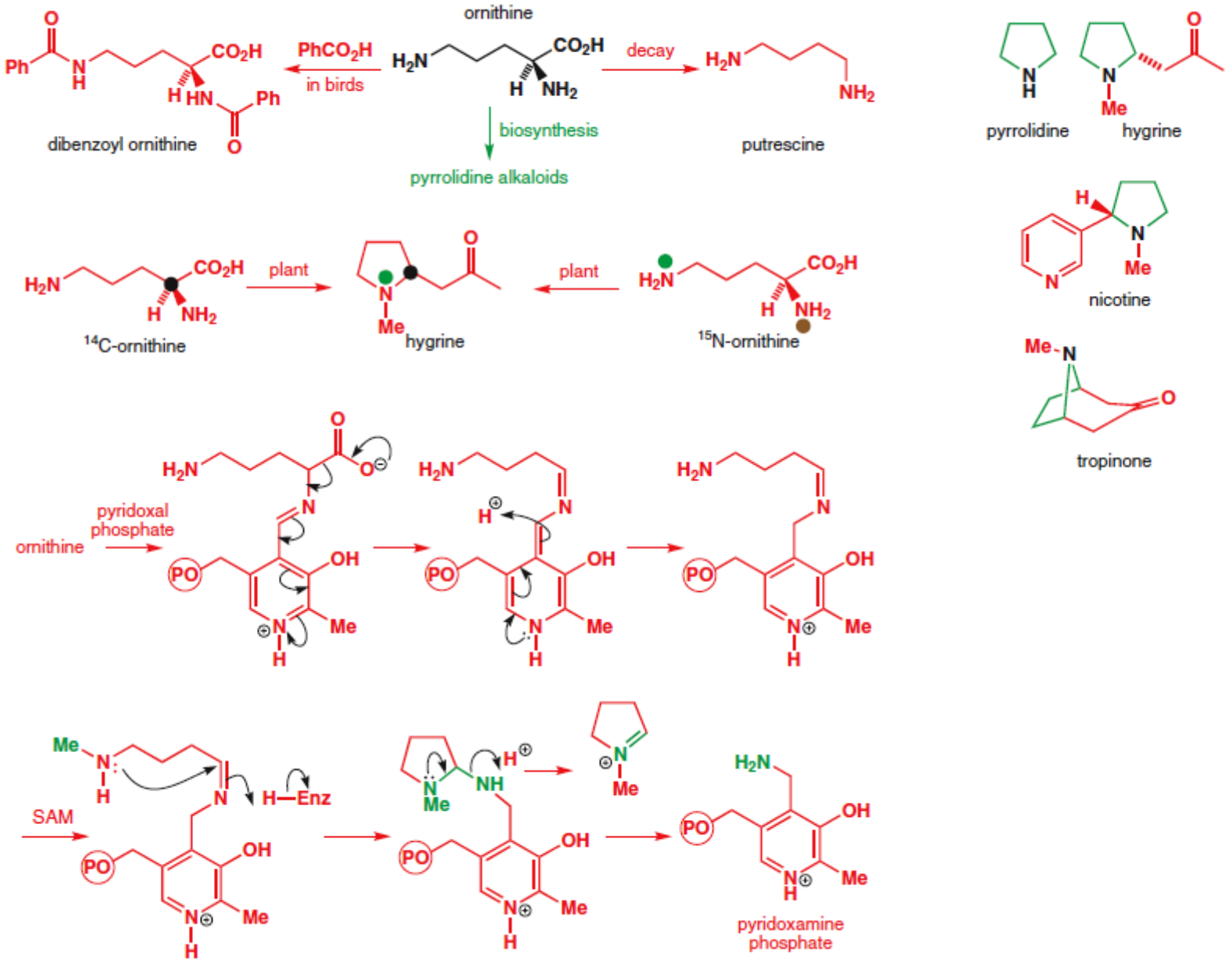
The Solanaceae family includes not only deadly nightshade (*Atropa belladonna*—hence atropine) plants but also potatoes and tomatoes. Parts of these plants also contain toxic alkaloids, for example you should not eat green potatoes because they contain the toxic alkaloid solanine.



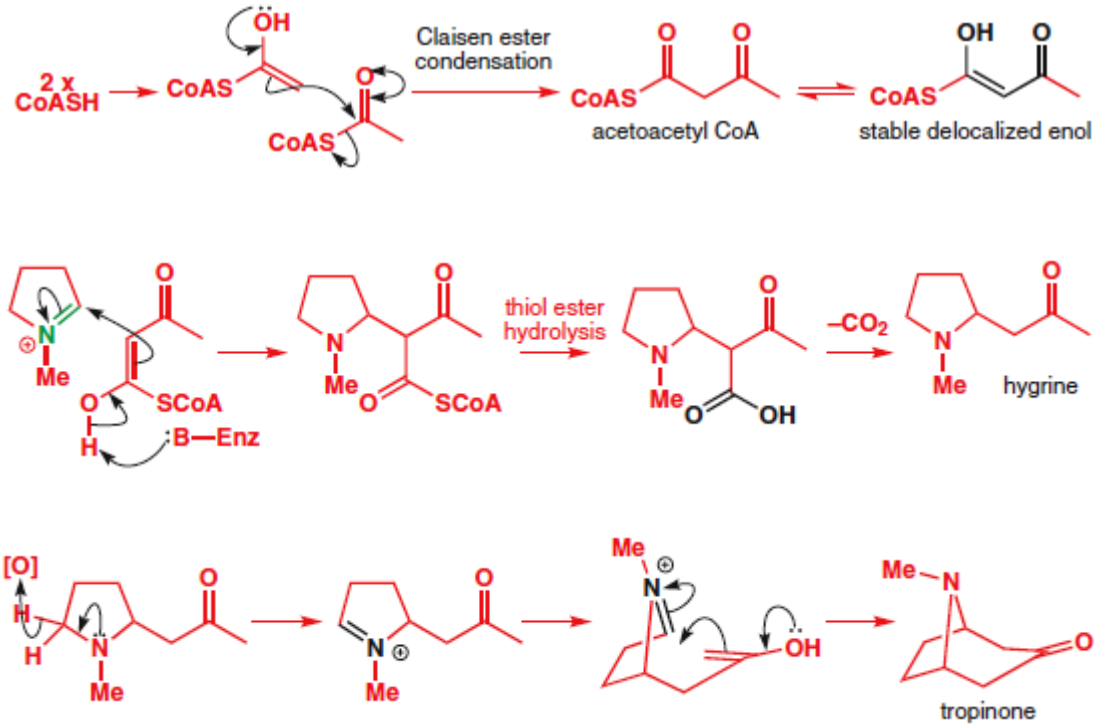
the very toxic alkaloid solanine, a mixture of glycosides with R = glucose, mannose, etc.

Atropine is a racemic compound but the (*S*)-enantiomer occurs in henbane (*Hyoscyamus niger*) and was given a different name, hyoscyamine, before the structures were known. In fact, hyoscyamine racemizes very easily just on heating in water or on treatment with weak base. This is probably what happens in the deadly nightshade plant.

Pyrrolidine alkaloids are made from the amino acid ornithine

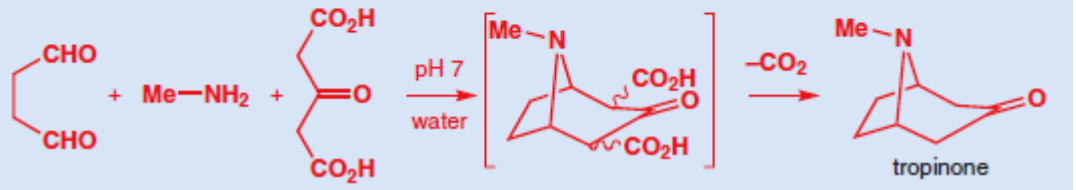


Pyrrolidine alkaloids are made from the amino acid ornithine

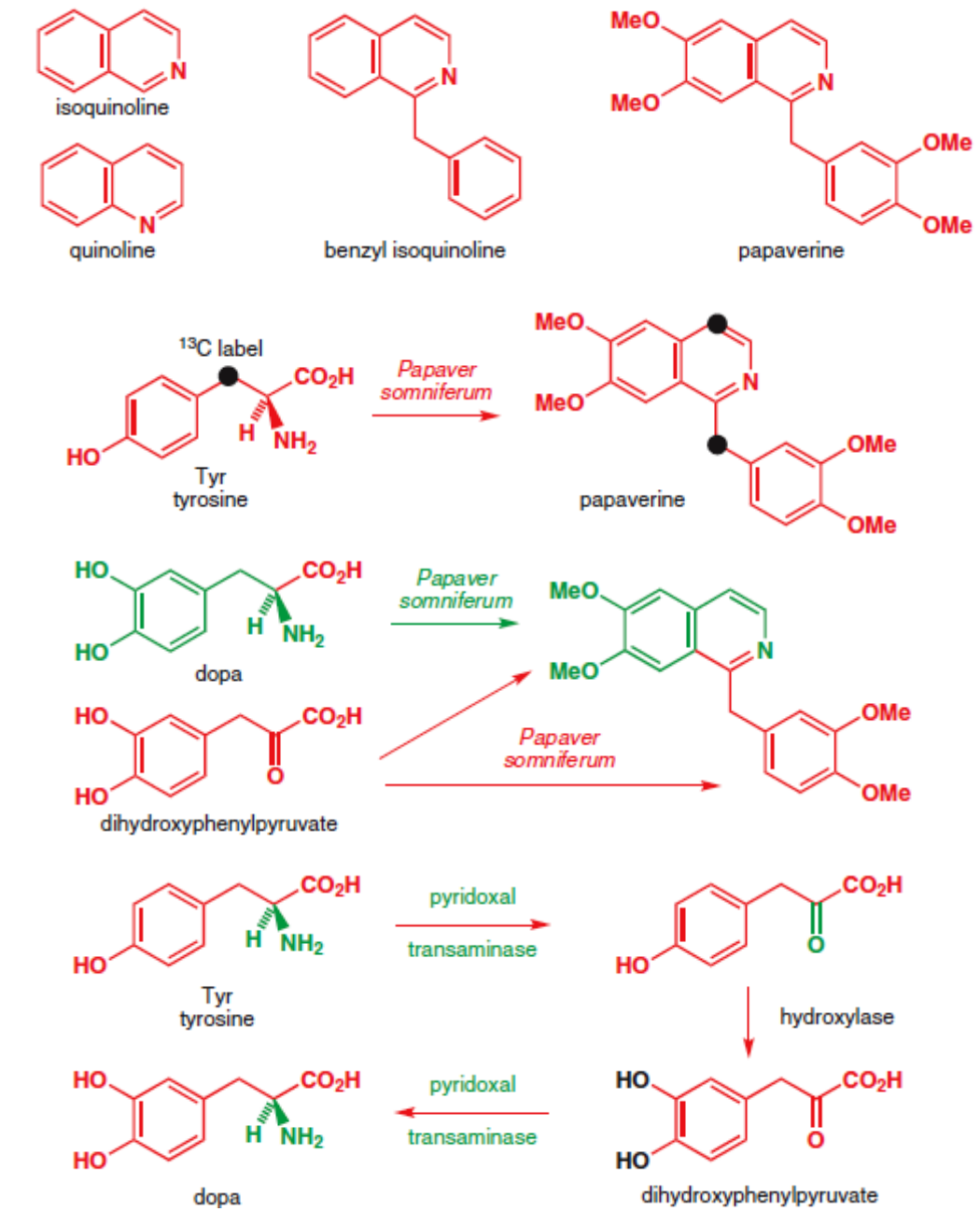


Robinson's tropinone synthesis

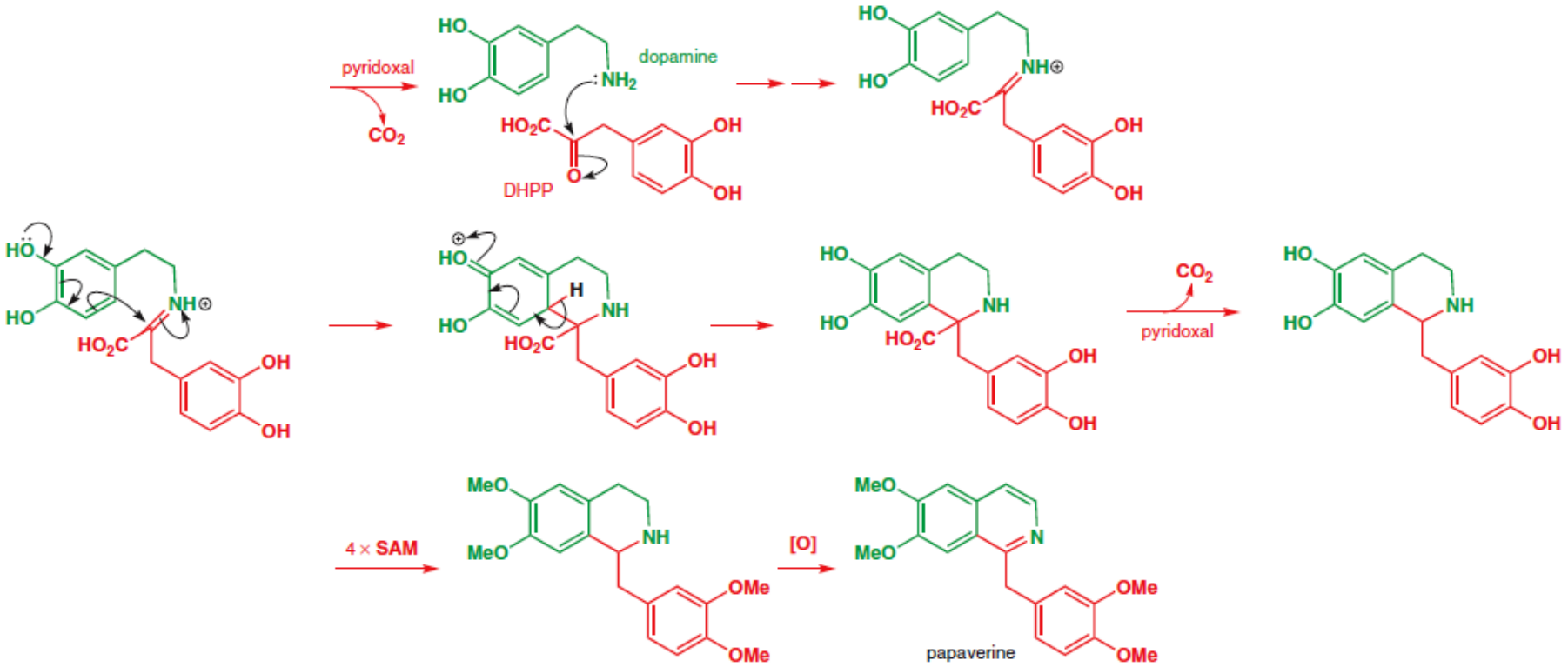
This complex route to tropinone was imitated as long ago as 1917 in one of the most celebrated reactions of all time, Robinson's tropinone synthesis. Robinson argued on purely chemical grounds that the sequence of imine salts and enols, which later (as shown in 1970) turned out to be nature's route, could be produced under 'natural' conditions (aqueous solution at pH 7) from a C_4 dialdehyde, $MeNH_2$, and acetone dicarboxylic acid. It worked and the intermediates must be very similar to those in the biosynthesis.



Benzyl isoquinoline alkaloids are made from tyrosine

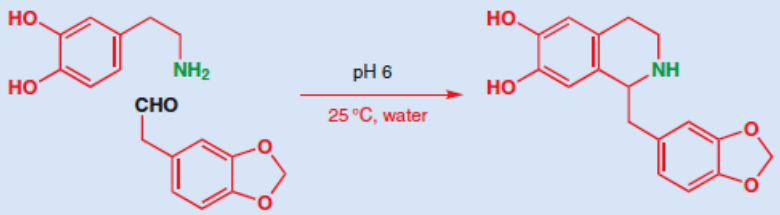


Benzyl isoquinoline alkaloids are made from tyrosine

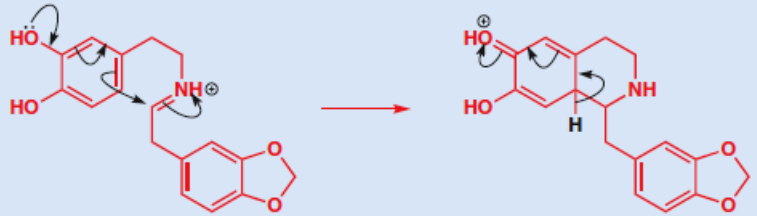


Synthesis of isoquinolines

As with tropinone, it is possible to make benzyl isoquinoline alkaloids very simply under mild conditions in the laboratory, providing that we use an aldehyde as the carbonyl component. The reaction (sometimes known as the Pictet–Spengler reaction) gives a reduced heterocyclic ring, as does the biosynthesis, but chemical oxidation can be used to give the isoquinoline.

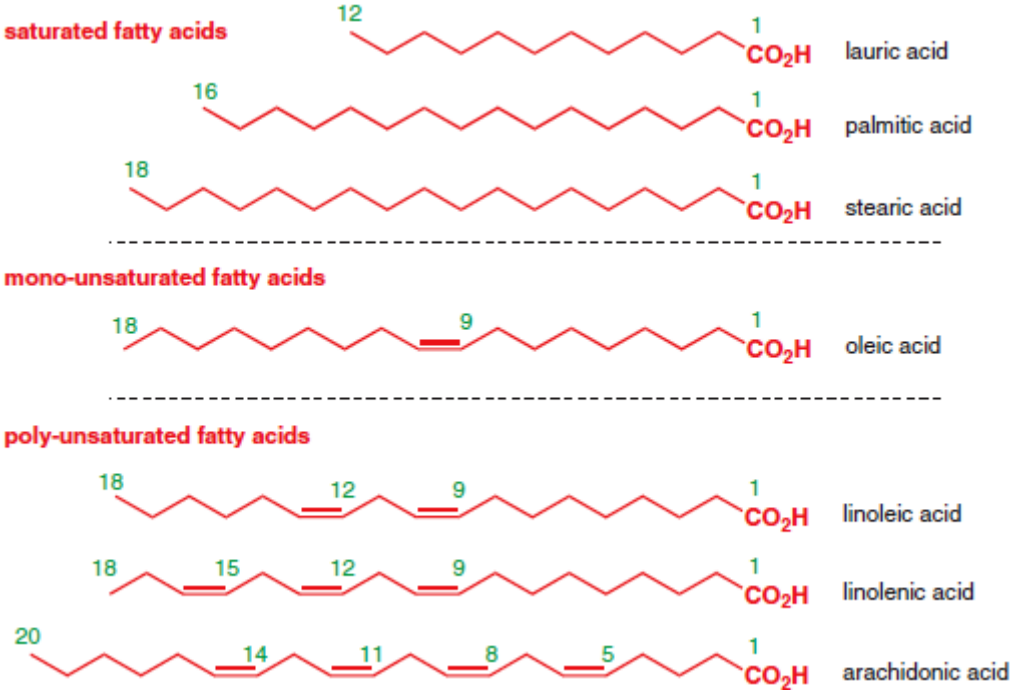


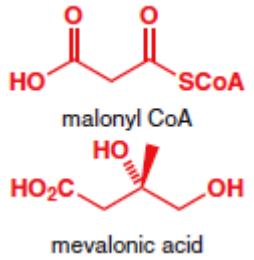
The mechanism is straightforward—the imine is formed and will be protonated at pH 6, ready for the C–C bond formation, which is both a Mannich reaction and an electrophilic aromatic substitution.



Notice that it was not necessary to protect the OH groups—the acetal on the lower ring is not for protection, and this group (methylenedioxy or dioxolane) is present in many benzyl isoquinoline alkaloids. It is formed in nature by oxidation of an MeO group *ortho* to an OH group on a benzene ring.

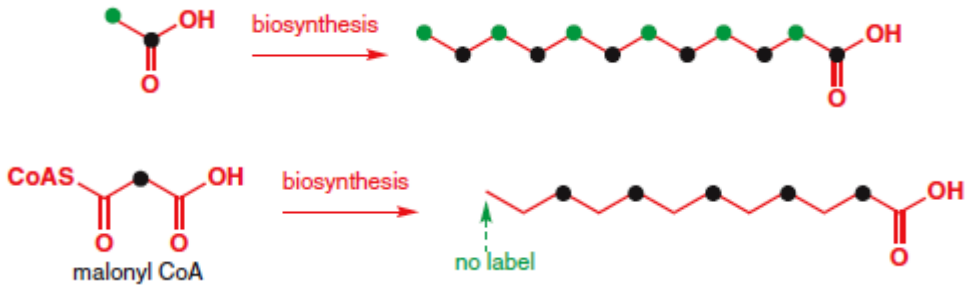
Fatty acids and other polyketides are made from acetyl CoA



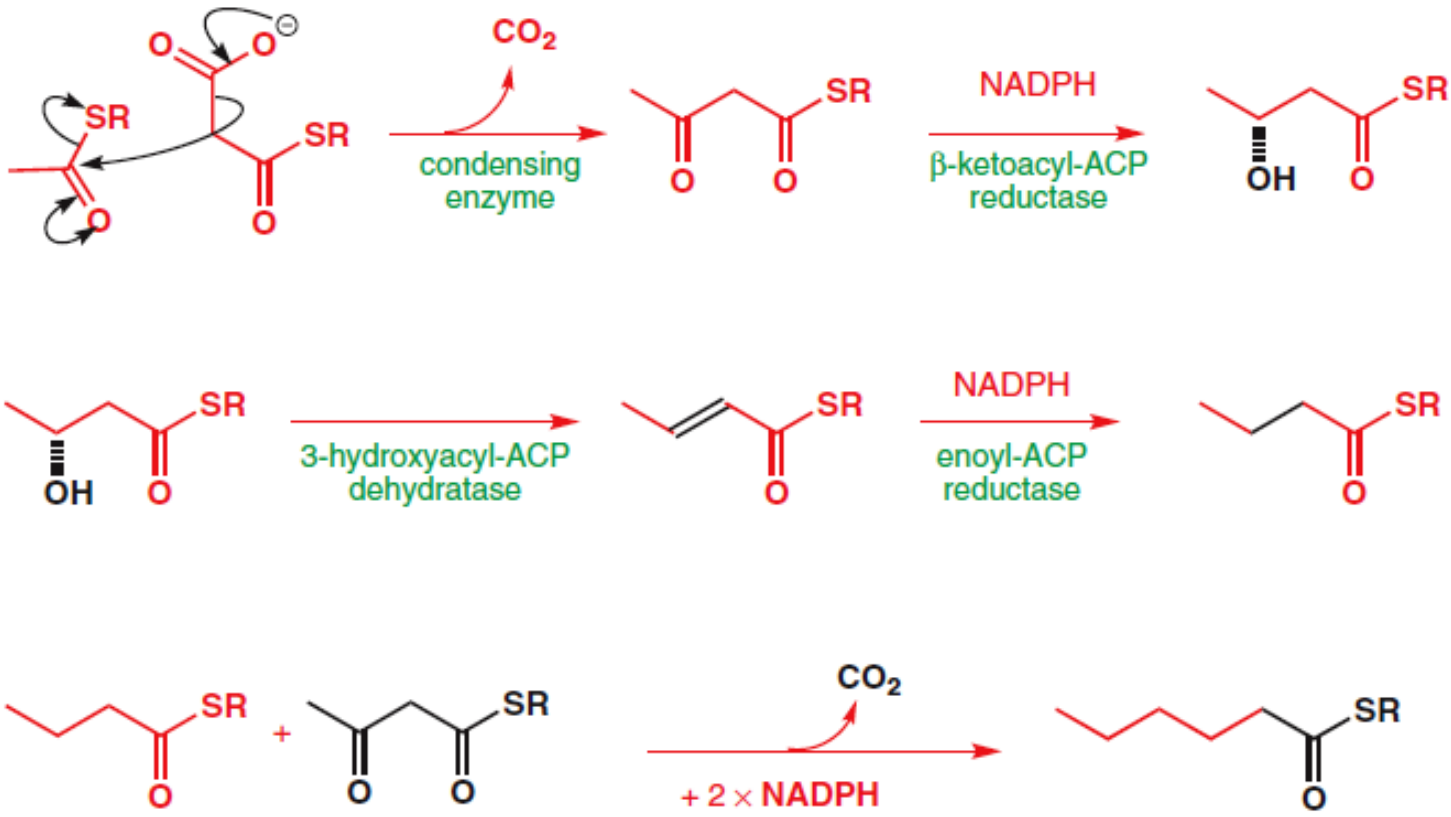


Malonyl CoA

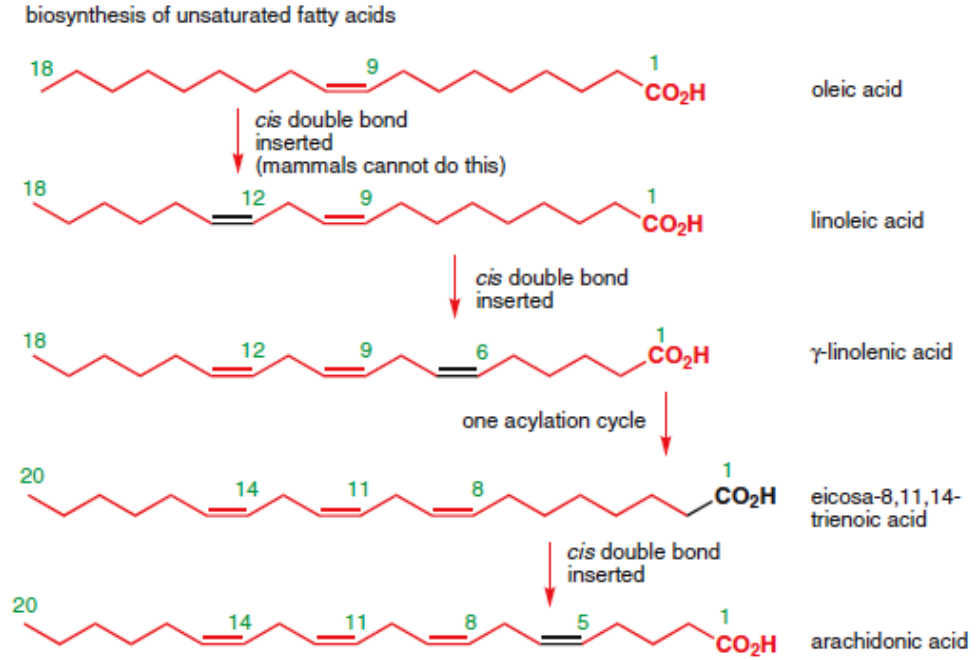
Malonyl CoA is the thiol ester of CoASH and malonic acid. It is biosynthesized by acylation of acetyl CoA with carbon dioxide.

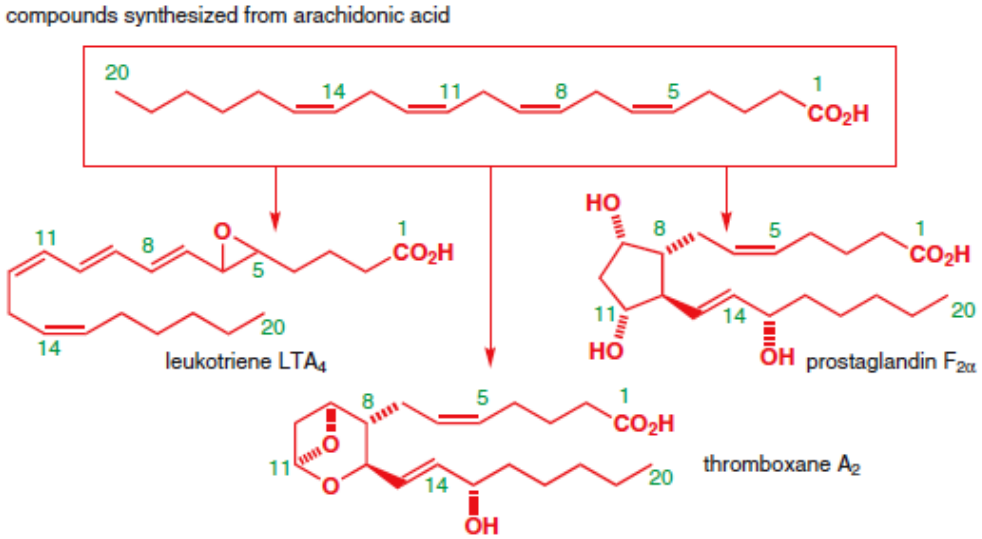


Fatty acids and other polyketides are made from acetyl CoA

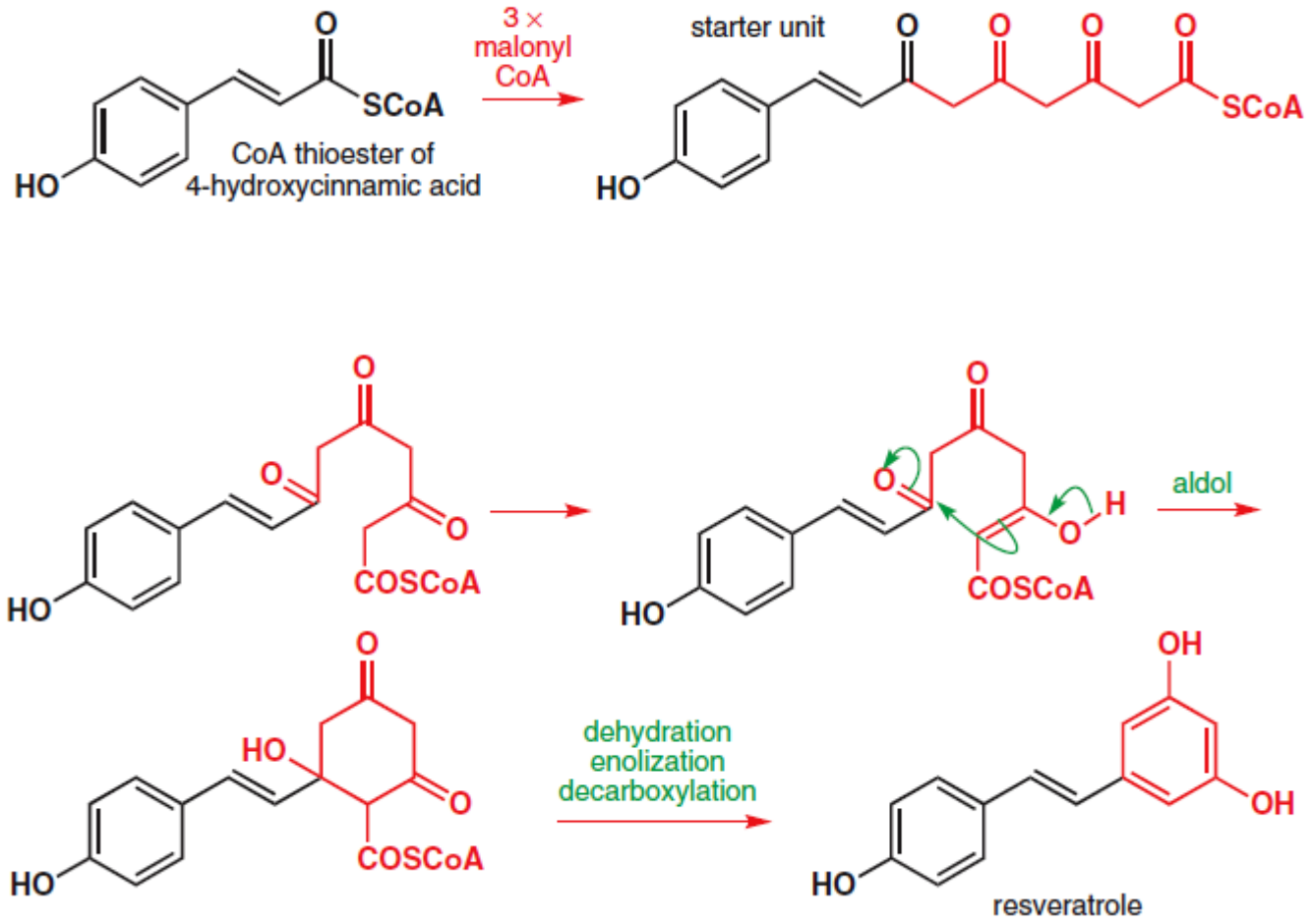


What is so important about unsaturated fatty acids?

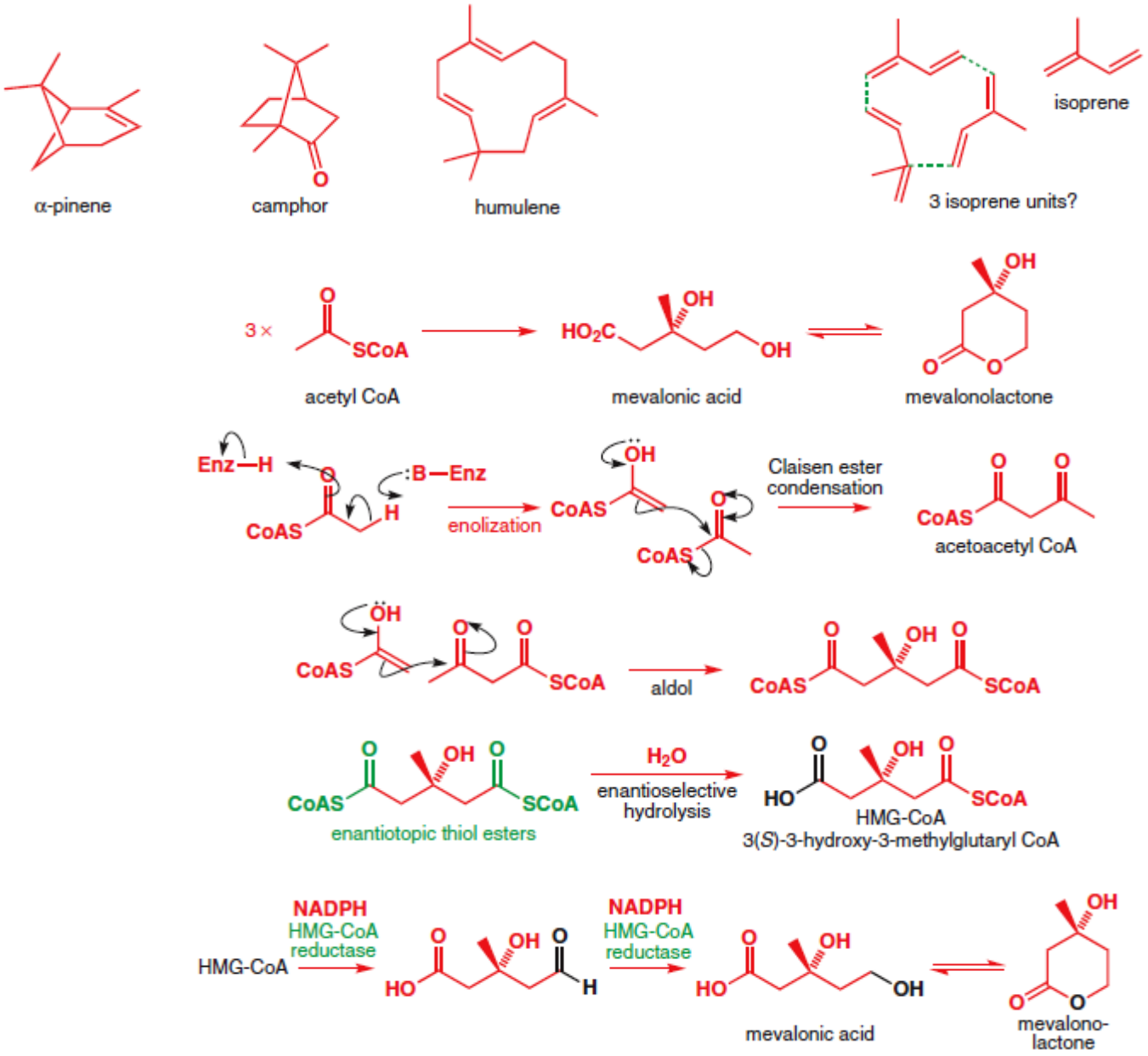




Aromatic polyketides



Terpenes are volatile constituents of plants



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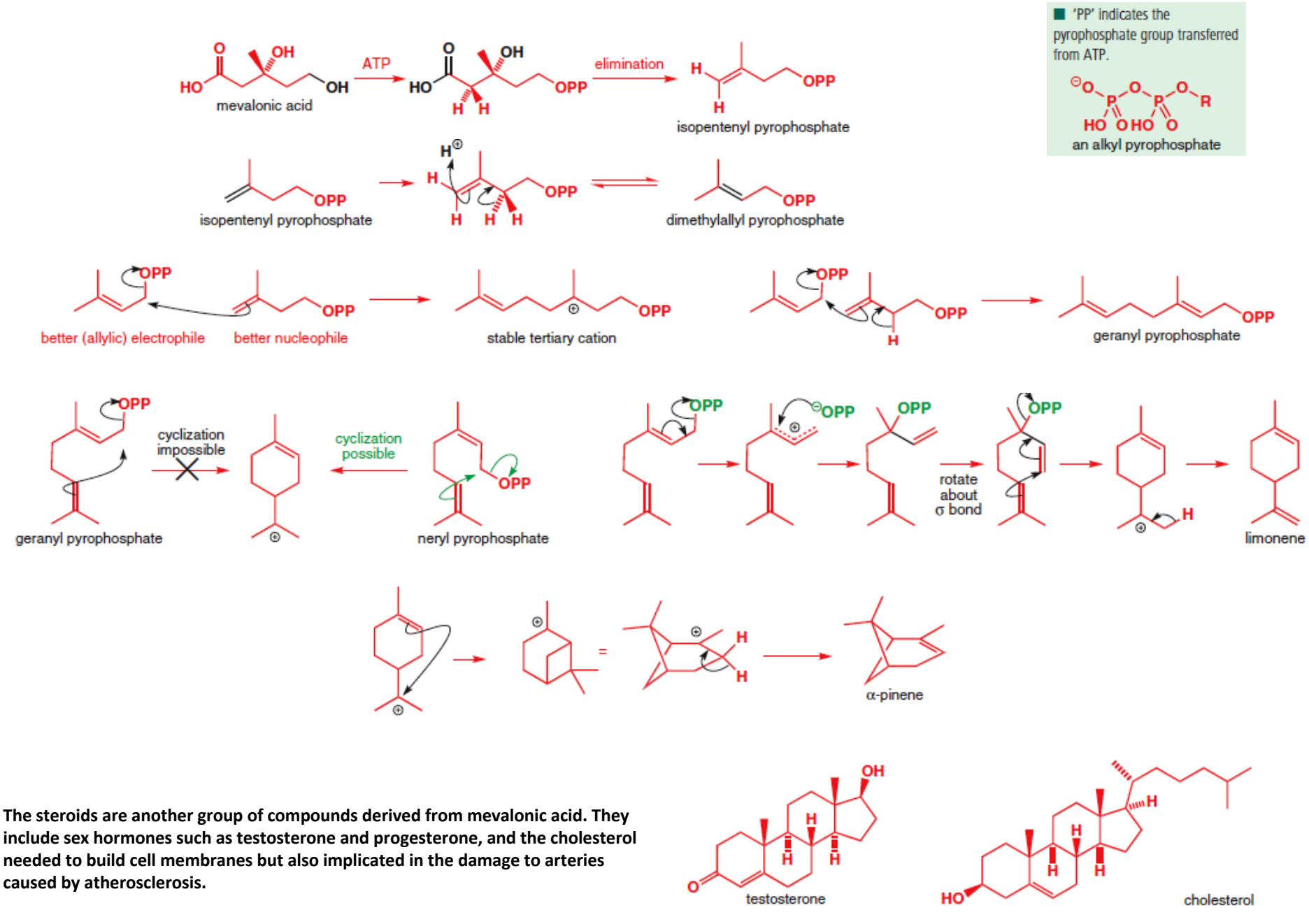

The steroids are another group of compounds derived from mevalonic acid. They include sex hormones such as testosterone and progesterone, and the cholesterol needed to build cell membranes but also implicated in the damage to arteries caused by atherosclerosis.