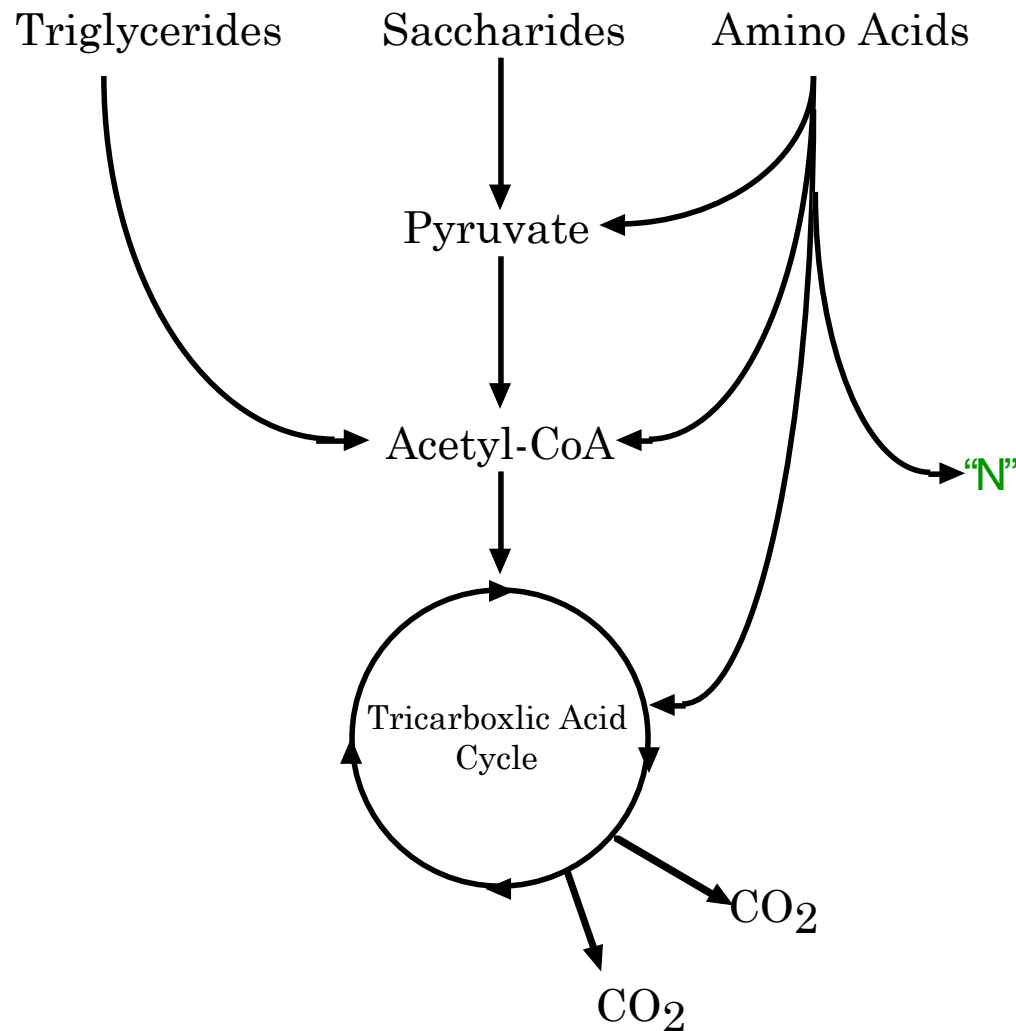


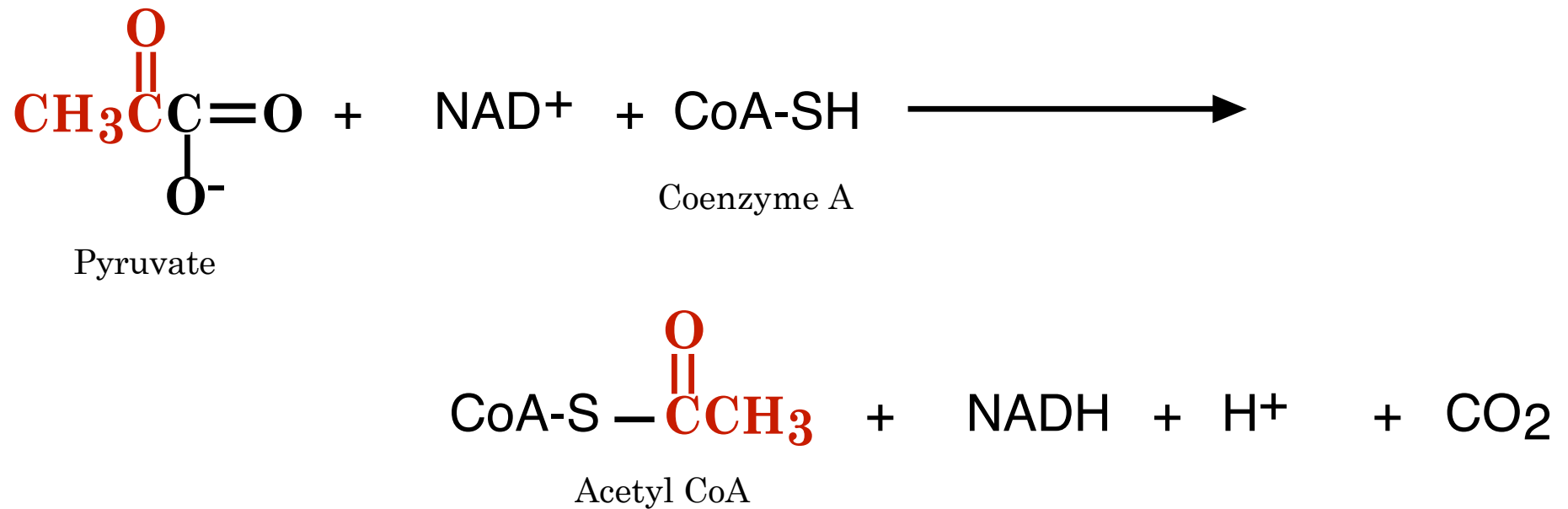
Catabolism of Major Energy Nutrients

Pyruvate produced from carbohydrates, fatty acids, and some amino acids is oxidized to CO_2 and H_2O in the mitochondria.

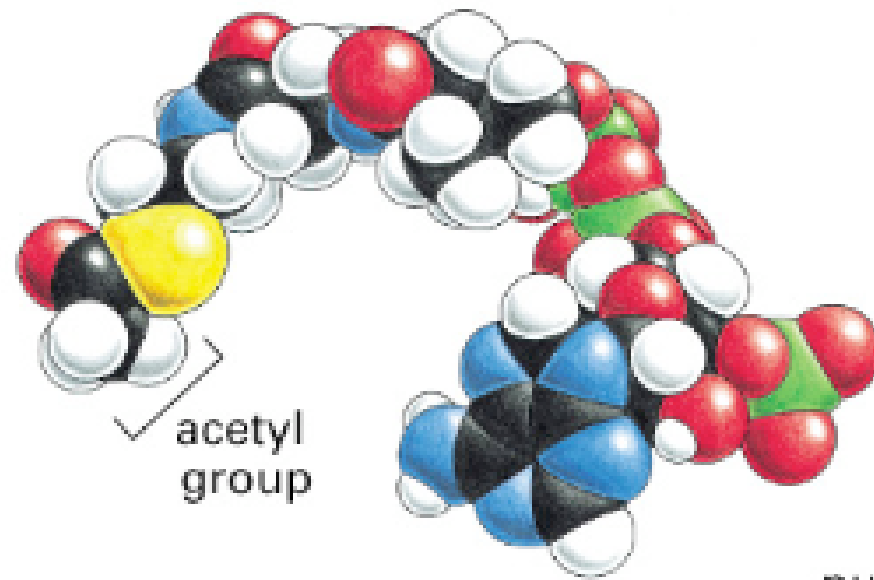
Summary of the fate of carbon atoms



The Formation of Acetyl-S-Coenzyme A

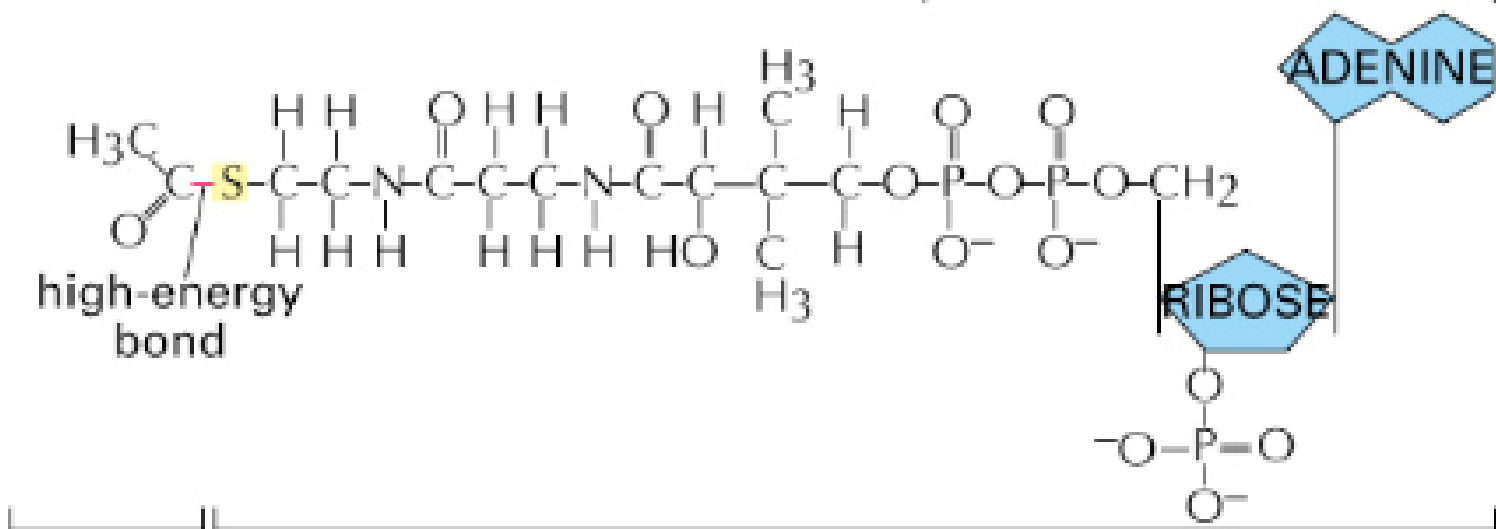


Acetyl-S-Coenzyme A



acetyl group

nucleotide



acetyl group

CoA

ADENINE

RIBOSE

The Pyruvate Dehydrogenase Complex

The three enzymes and their associated cofactors are contained in the complex

Enz₁ - *pyruvate dehydrogenase* - TPP

Enz₂ - *dihydrolipoyl transacetylase* - lipoic acid and Coenzyme A

Enz₃ - *dihydrolipoyl transhydrogenase* - FAD and NAD

The five cofactors are:

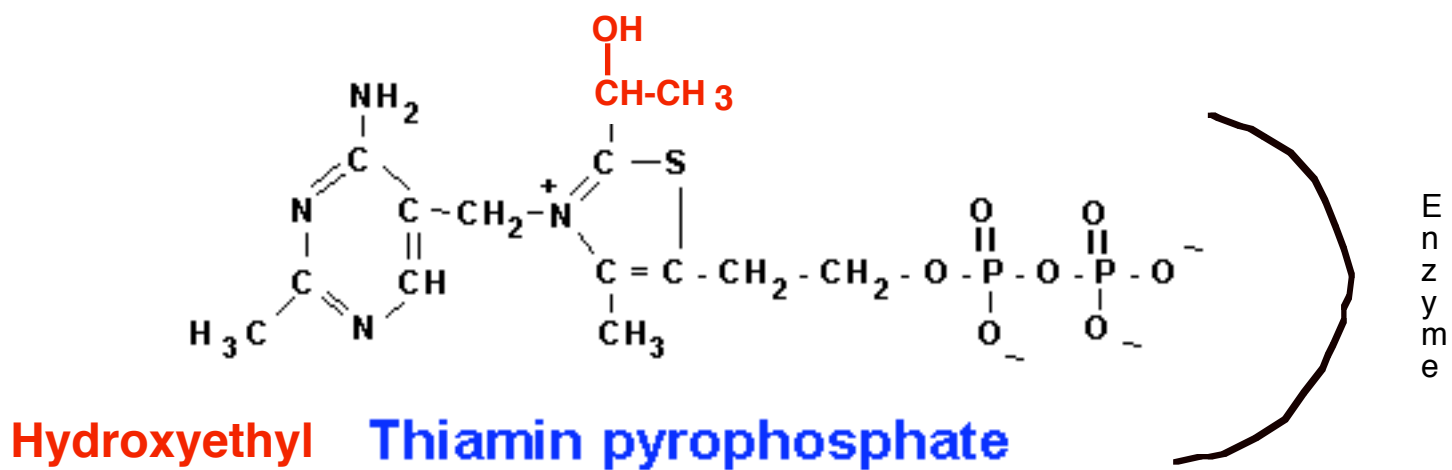
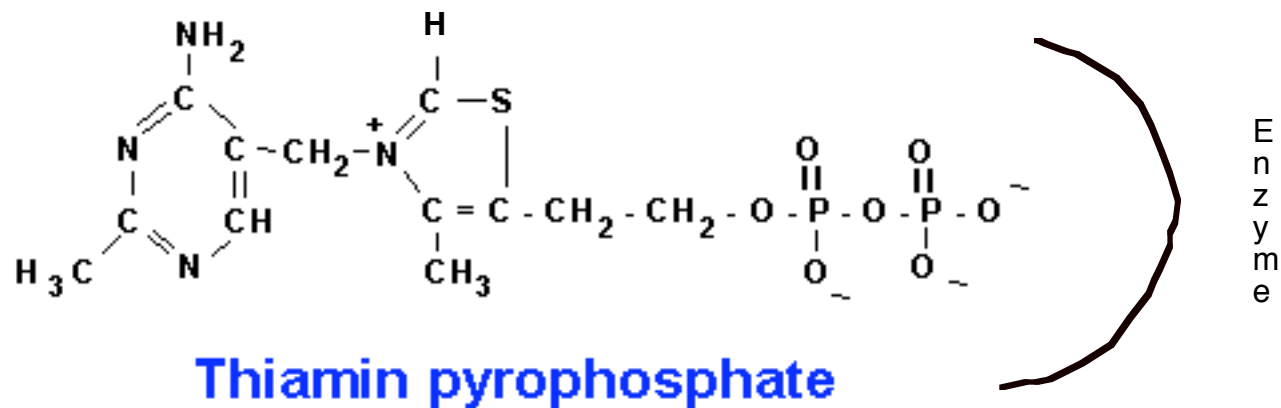
Thiamine (vitamin B1) in thiamine pyrophosphate (TPP). Attached to Enzyme 1

Lipoic acid, a growth factor that biosynthesized by vertebrates. Attached to Enzyme 2

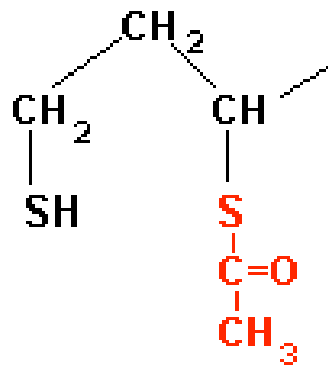
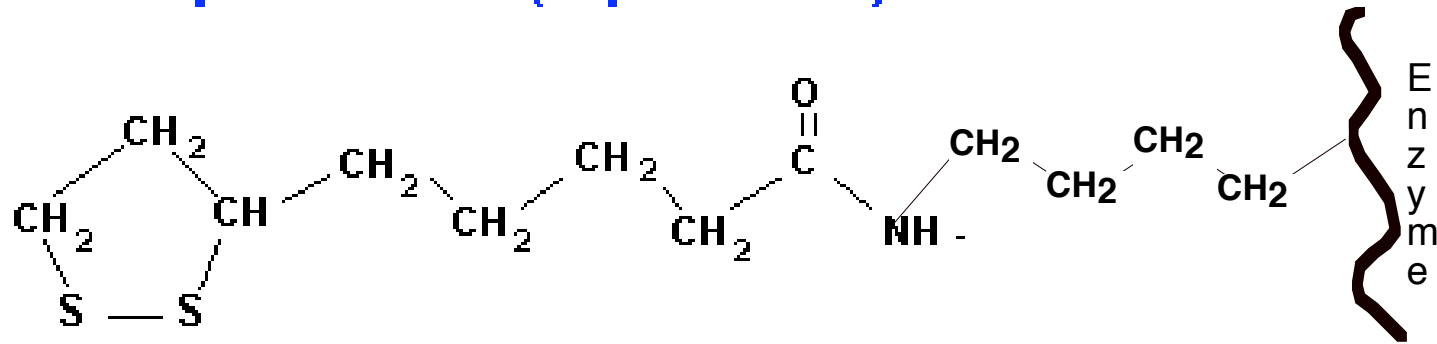
Pantothenic acid in coenzyme A.

Riboflavin in flavin adenine dinucleotide (FAD). Attached to Enzyme 3

Nicotinic acid in nicotinamide adenine dinucleotide (NAD).

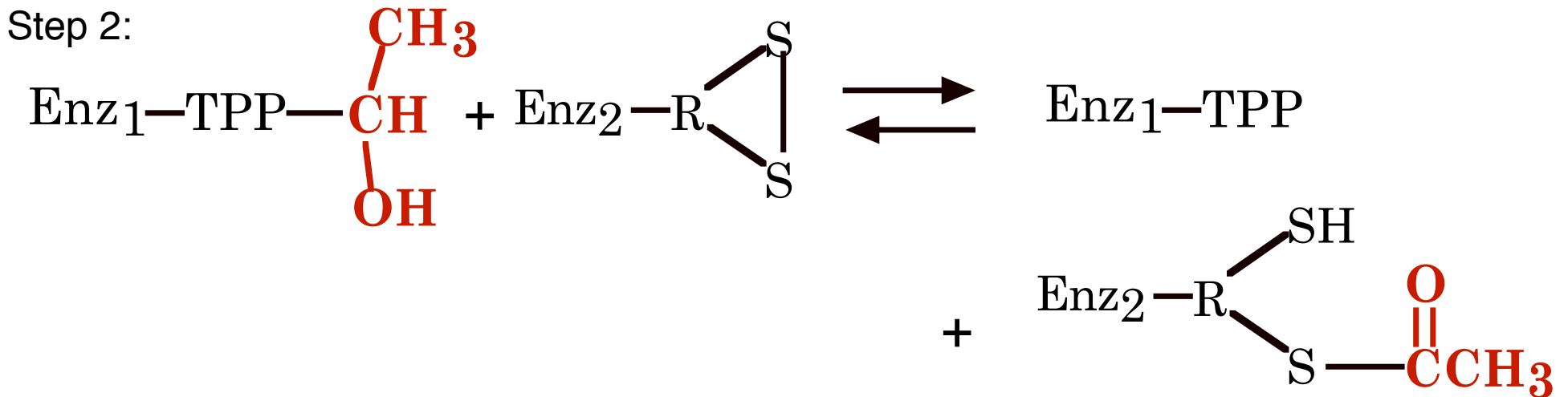
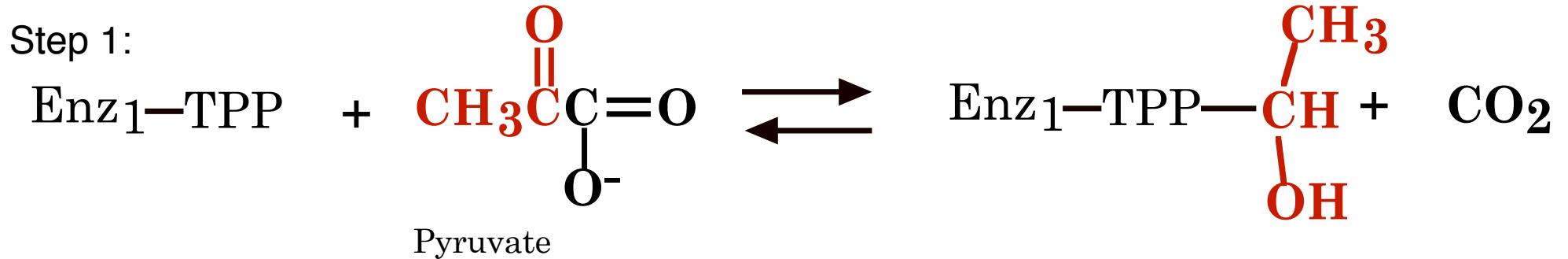


Lipoic Acid (Lipoamide)

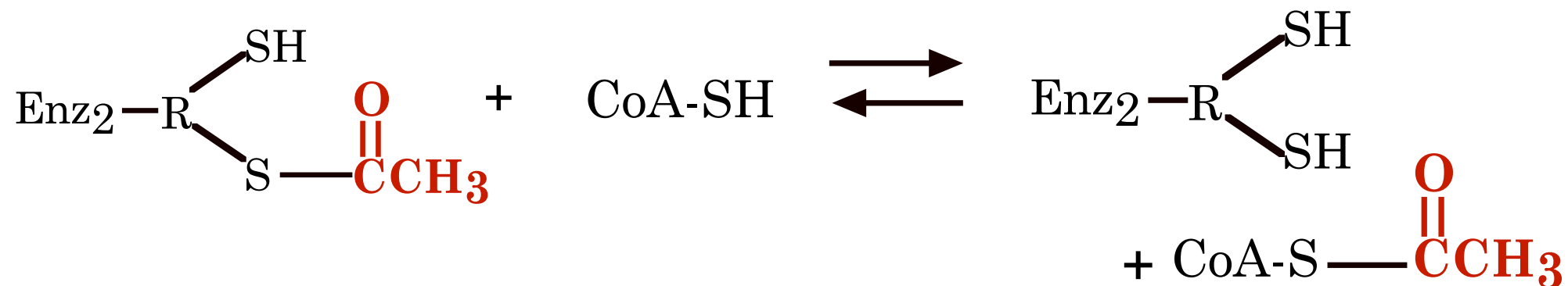


Acetyl Lipoic Acid

The Five Steps in the Conversion of Pyruvate to Acetyl-S-CoA



Step 3:



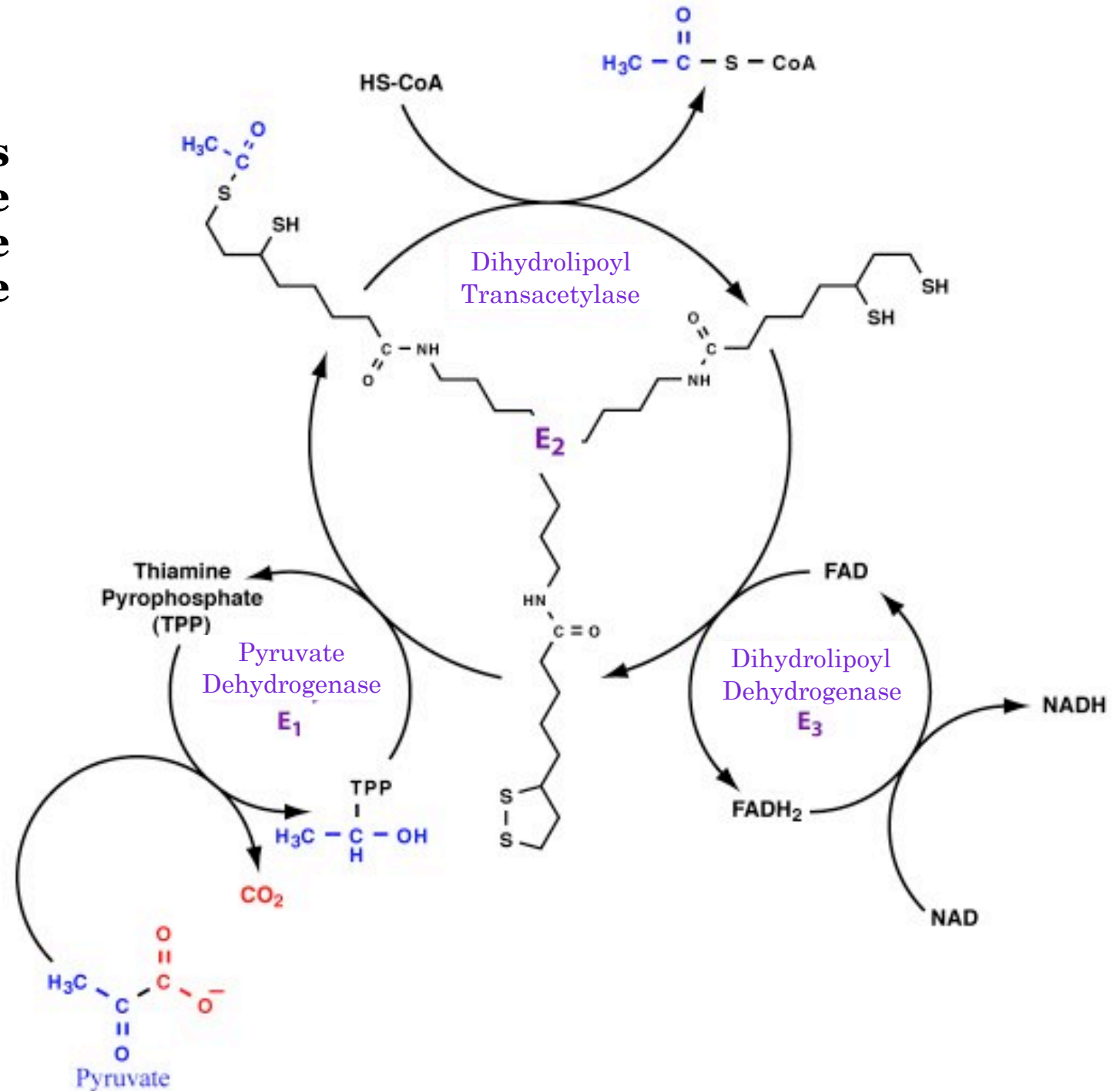
Step 4:



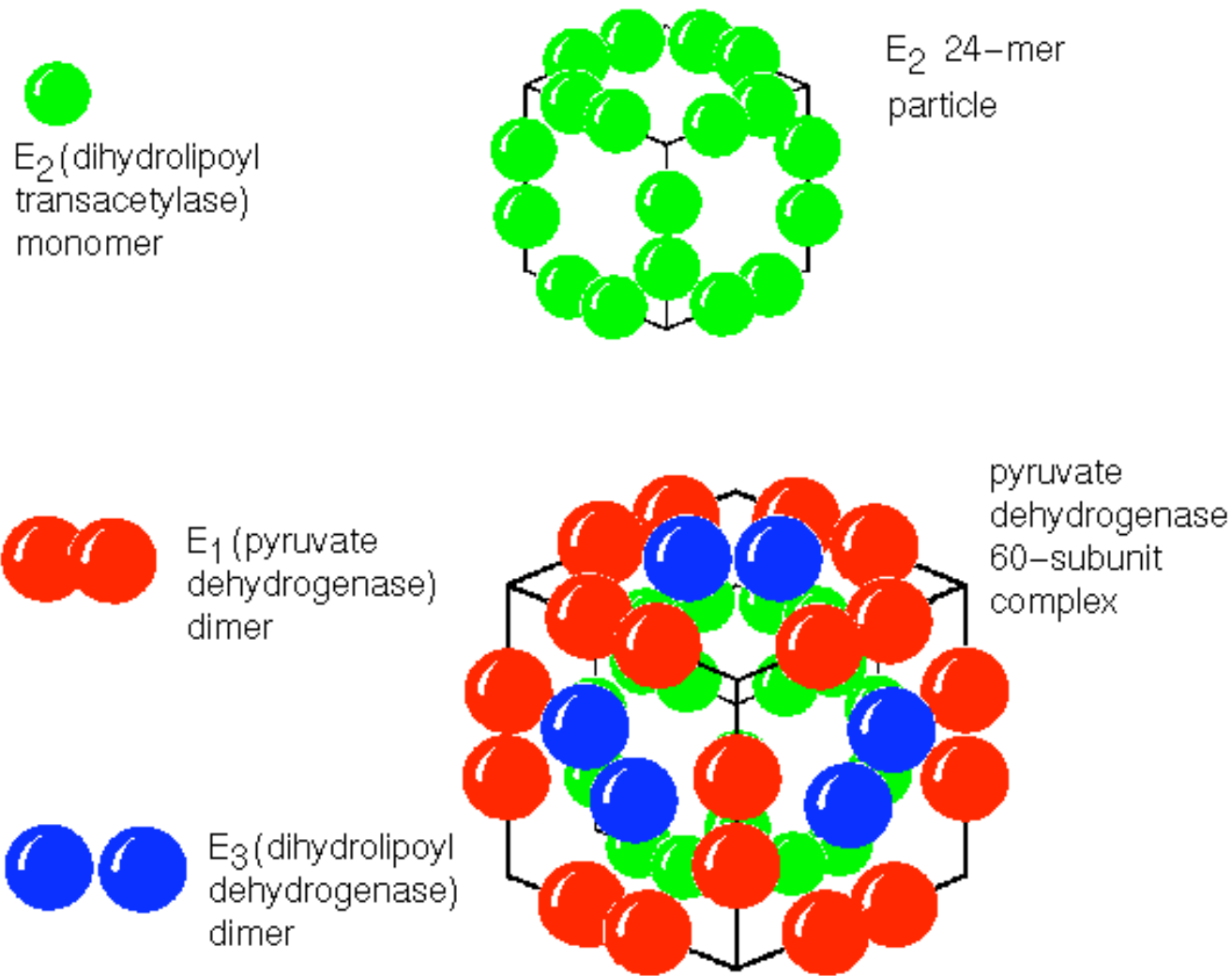
Step 5:



All of the cofactors and enzymes are located within the same multienzyme complex.



Pyruvate Dehydrogenase Multienzyme Complex



Arrangement of subunits in the pyruvate dehydrogenase multienzyme complex of *E. coli*.

Diagram adapted from Voet and Voet (1990), after Lester Reed

Regulation of the PDH Complex

1) Product inhibition - The products of steps 3 and 5 “feedback” on Enzy₂ slowing it down and in turn preventing Enz₁ from transferring its hydroxyethyl group.

2) Covalent modification - Within the complex, there are two additional enzymes whose sole function is control of the complex:

Pyruvate dehydrogenase kinase (PDK):

Inactivates Enz₁ by phosphorylating it. (PDK itself is allosterically activated by acetyl-S-CoA and NADH, ATP and inactivated by pyruvate, ADP, and Ca²⁺.)

Pyruvate dehydrogenase phosphatase

(PDP): Activates Enz₁ by removing the phosphate added by PDK. (PDP has no inactivators and is active only in the presence of Ca²⁺ and Mg²⁺.)

Regulation of the PDH Complex

