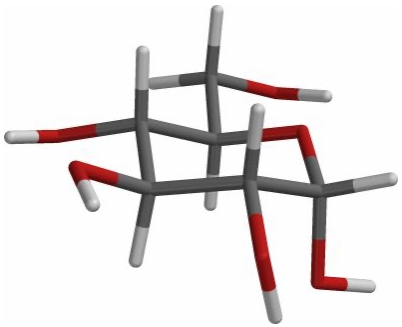

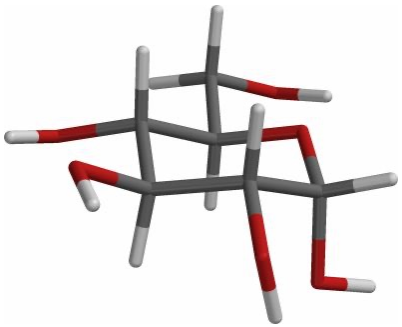

# Chem 109 C
# Bioorganic Compounds

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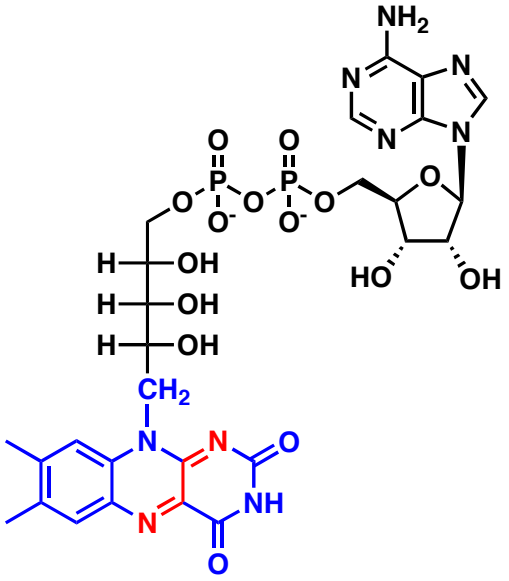
# Chapter 24: Coenzymes

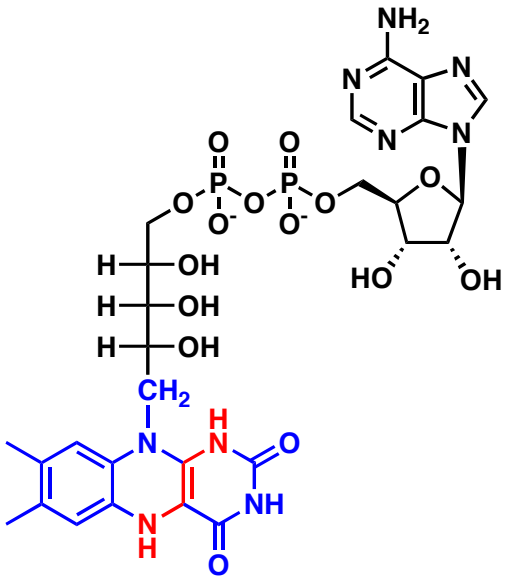
**Table 24.1 The Vitamins, the Coenzymes for Which They Are Precursors, and the Chemical Functions of the Coenzymes**

| Vitamin | Coenzyme | Reaction catalyzed | Human deficiency disease |
|---|---|---|---|
| *Water-Soluble Vitamins* | | | |
| Niacin (niacinamide) | $NAD^+$, $NADP^+$<br>NADH, NADPH | Oxidation<br>Reduction | Pellagra |
| Riboflavin (vitamin $B_2$) | FAD, FMN<br>$FADH_2$, $FMNH_2$ | Oxidation<br>Reduction | Skin inflammation |
| Thiamine (vitamin $B_1$) | Thiamine pyrophosphate (TPP) | Two-carbon transfer | Beriberi |
| Lipoic acid (lipoate) | Lipoate | Oxidation | — |
| | Dihydrolipoate | Reduction | |
| Pantothenic acid (pantothenate) | Coenzyme A (CoASH) | Acyl transfer | — |
| Biotin (vitamin H) | Biotin | Carboxylation | — |
| Pyridoxine (vitamin $B_6$) | Pyridoxal phosphate (PLP) | Decarboxylation<br>Transamination<br>Racemization<br>$C_\alpha$—$C_\beta$ bond cleavage<br>$\alpha,\beta$-Elimination<br>$\beta$-Substitution | Anemia |
| Vitamin $B_{12}$ | Coenzyme $B_{12}$ | Isomerization | Pernicious anemia |
| Folic acid (folate) | Tetrahydrofolate (THF) | One-carbon transfer | Megaloblastic anemia |
| Ascorbic acid (vitamin C) | — | — | Scurvy |
| *Water-Insoluble (lipid-soluble) Vitamins* | | | |
| Vitamin A | — | — | — |
| Vitamin D | — | — | Rickets |
| Vitamin E | — | — | — |
| Vitamin K | Vitamin $KH_2$ | Carboxylation | — |

# FAD-$FADH_2$, FMN-$FMNH_2$

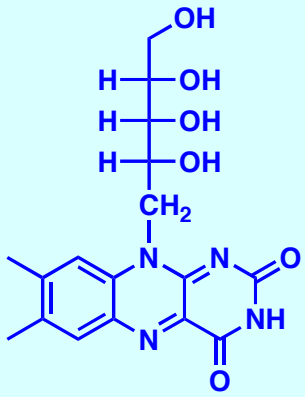



FAD




$FADH_2$

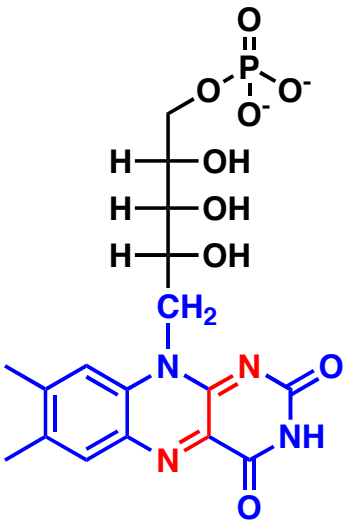
vitamin $B_2$:



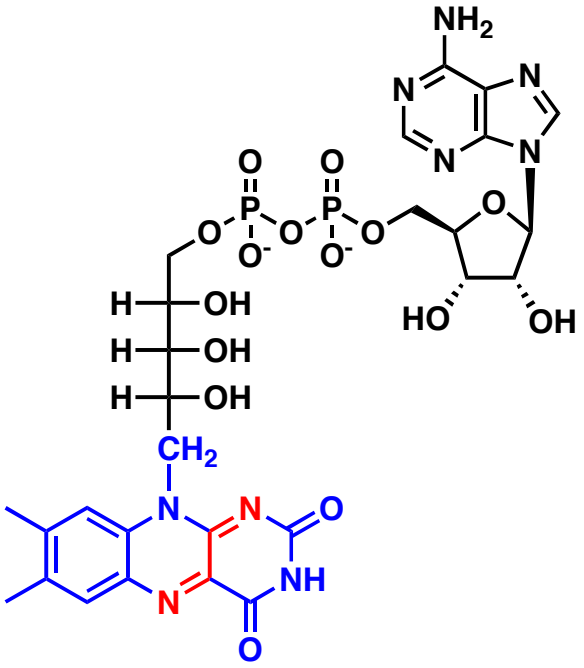

riboflavin

- catalyze redox (oxidation-reduction) reactions
- source of riboflavin: milk, liver, mushrooms, etc.
- deficiency disease: skin inflammation, cracked lips, sensitivity to light…

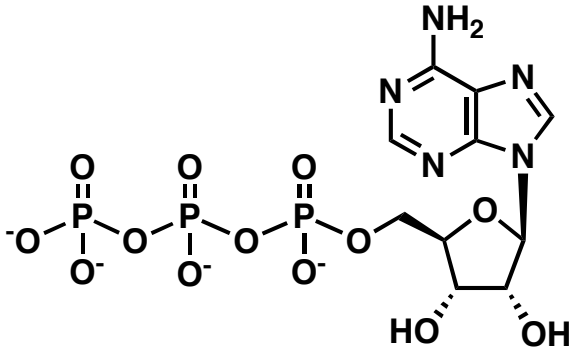
# FAD-$FADH_2$, FMN-$FMNH_2$



FMN



FAD



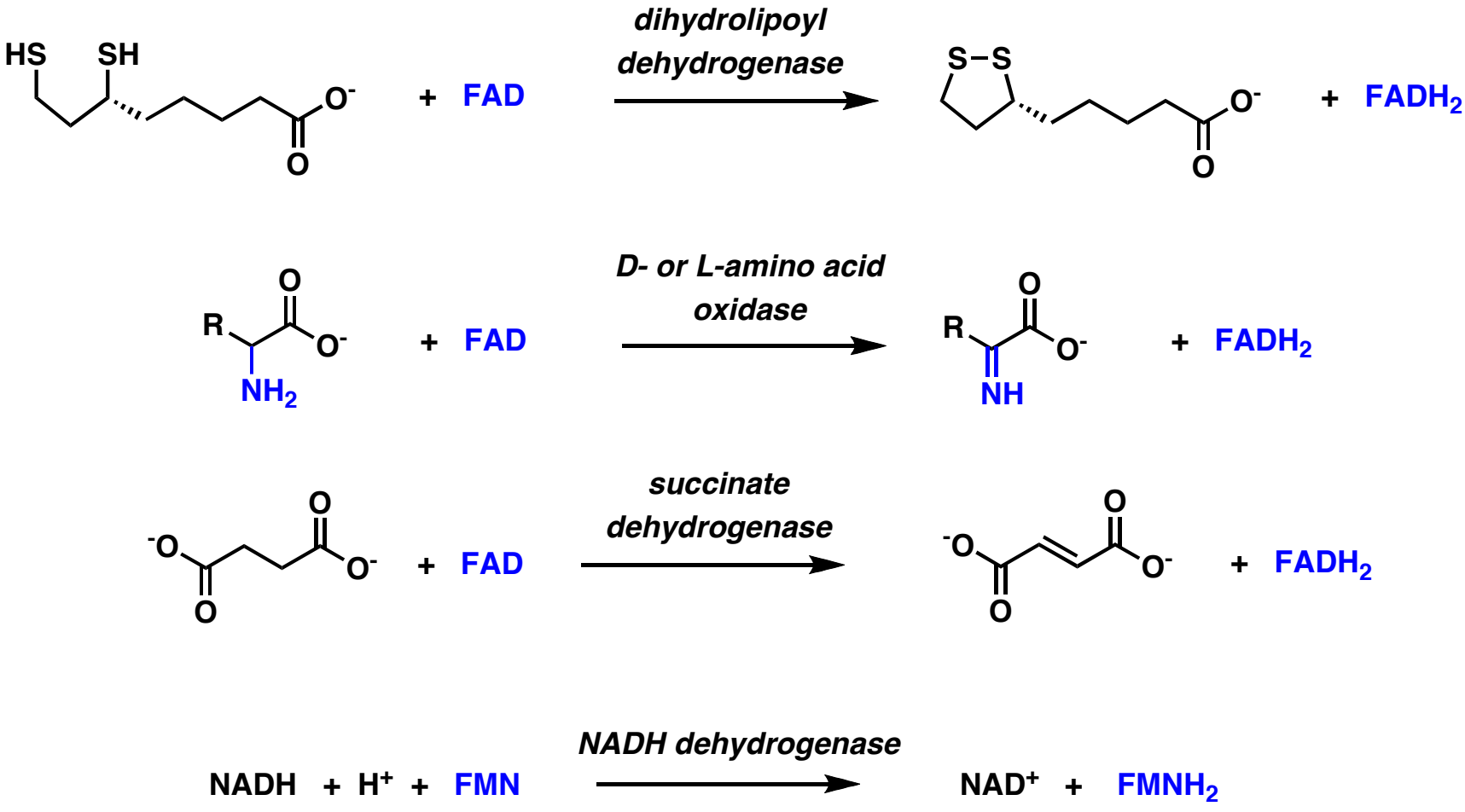
adenosine triphosphate

## PRACTICE PROBLEM

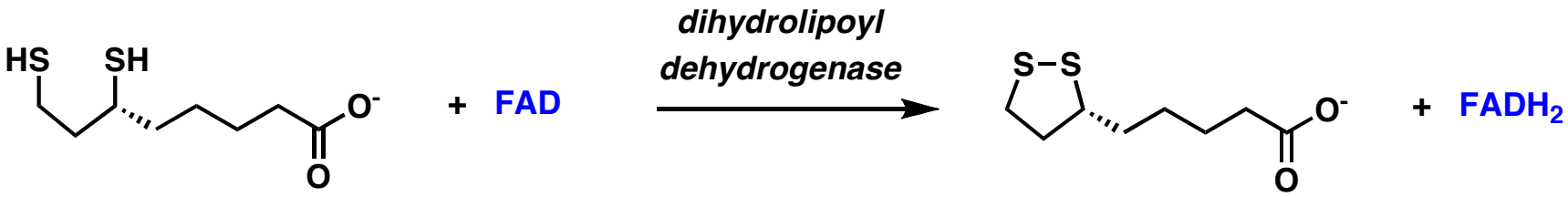
**FAD is obtained by an enzyme-catalyzed reaction that uses FMN and ATP as substrates. What is the other product of the reaction?**

# FAD-$FADH_2$, FMN-$FMNH_2$

## *Examples of reactions catalyzed by FAD or FMN:*

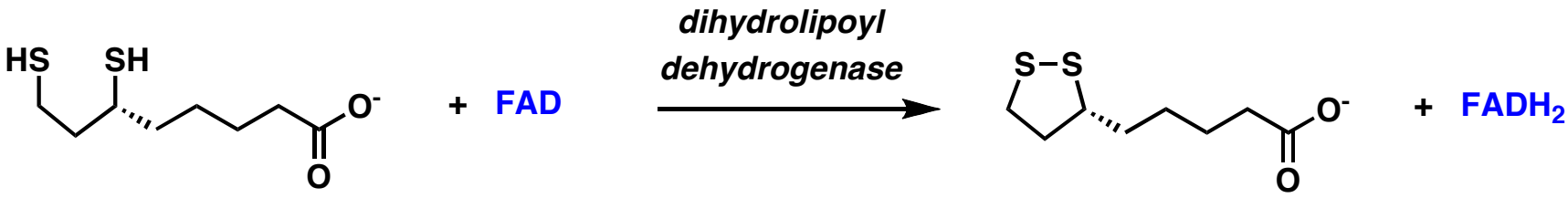


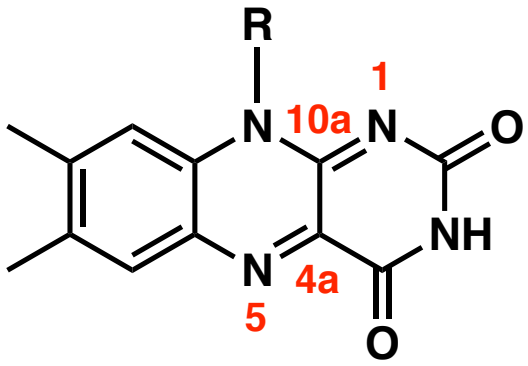
# FAD-$FADH_2$, FMN-$FMNH_2$




**mechanism is on page 1073**
(and discussed in class)

# FAD-$FADH_2$, FMN-$FMNH_2$



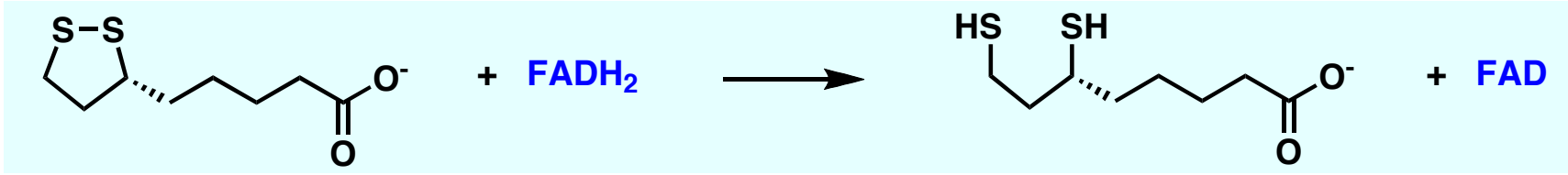

**PROBLEM 4**

**Instead of adding the the 4a position and protonating N5, the thiolate ion could have added to the 10a position and protonated N1. Why is addition to the 4a position favored?**

# FAD, FMN, $FADH_2$, $FMNH_2$

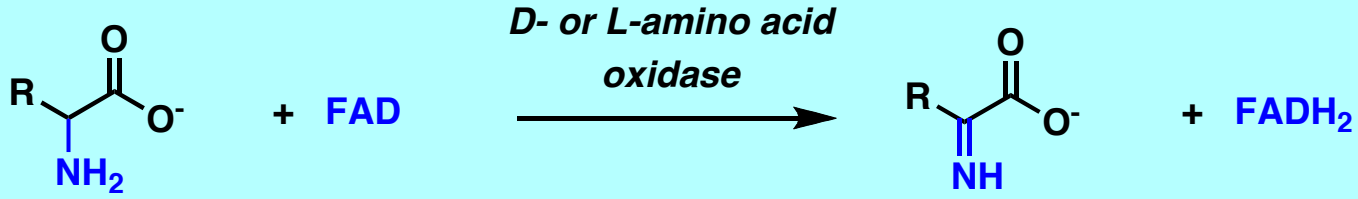
## PRACTICE PROBLEM [homework]

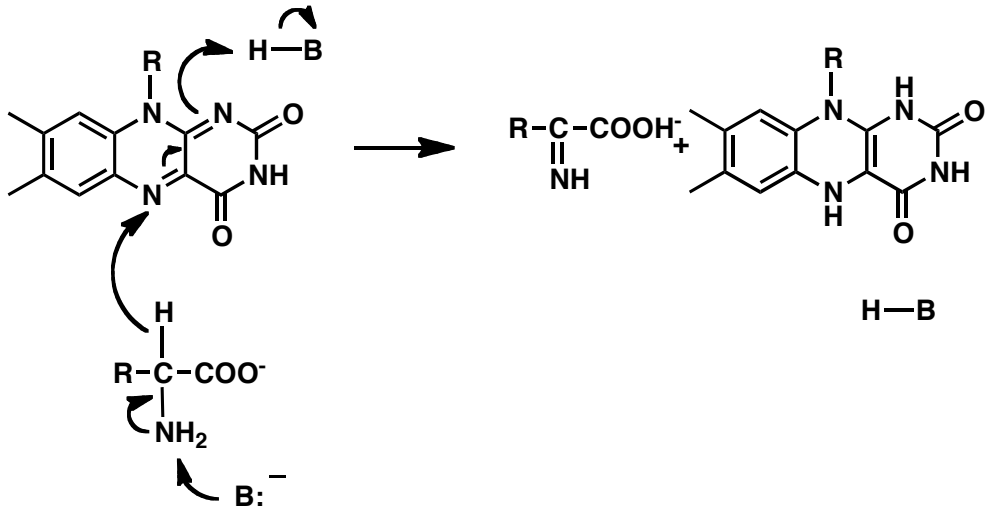
**Propose a mechanism for the reduction of lipoate by $FADH_2$**



# FAD, FMN, $FADH_2$, $FMNH_2$

## *Oxidation of α-amino acids to α-imino acids*



# Chapter 23: Coenzymes

| Coenzyme | Vitamin | Reaction catalyzed |
|---|---|---|
| $NAD^+$, $NADP^+$ / NADH, NADPH | niacin, nicotinamide | oxidation/reduction of alcohols |
| FAD / $FADH_2$ | riboflavin (B2) | oxidation/reduction, other |
| Thiamine pyrophosphate TPP | thiamine (B1) | acyl group transfer |
| Lipoic acid /dihydropipoic acid | lipoic acid | oxidation/reduction |
| Coenzyme A, CoASH | pantothenic acid (B5) | acyl group transfer |
| Biotin | biotin (B7) | carboxylation |
| Pyridoxal phosphate PLP | pyridoxin (B6) | 6 amino acid reactions |
| Coenzyme $B_{12}$ | vitamin B12 | isomerization |
| Tetrahydrofolic acid, THF | folic acid | one-carbon transfer |
| Vitamin $KH_2$ | vitamin K | carboxylation |

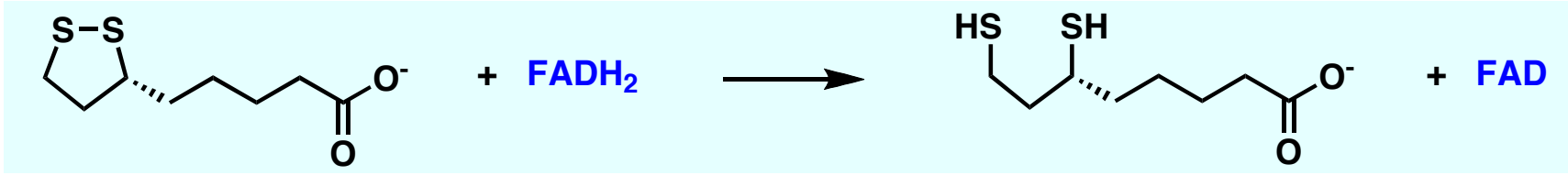
Vitamin $KH_2$ is not soluble in water

see Table 23.1 in Chapter 23

# FAD, FMN, $FADH_2$, $FMNH_2$

## PRACTICE PROBLEM [homework]

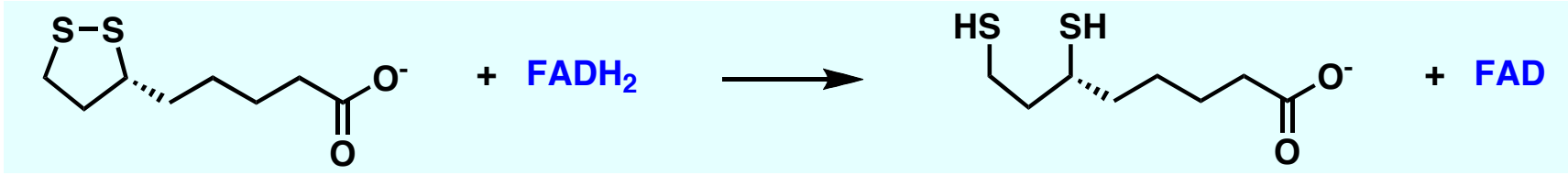
**Propose a mechanism for the reduction of lipoate by $FADH_2$**

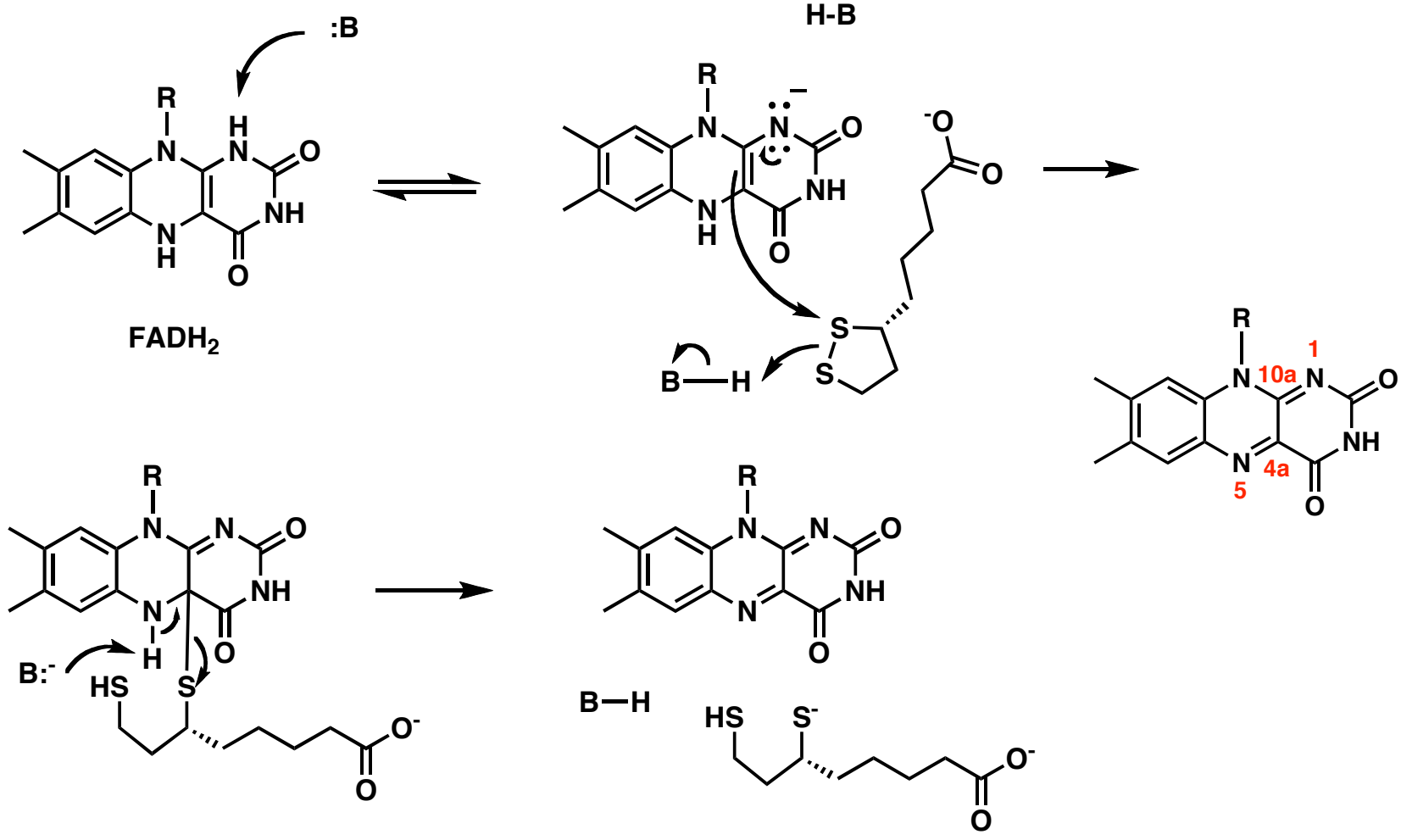


# FAD, FMN, $FADH_2$, $FMNH_2$

## PRACTICE PROBLEM [homework]

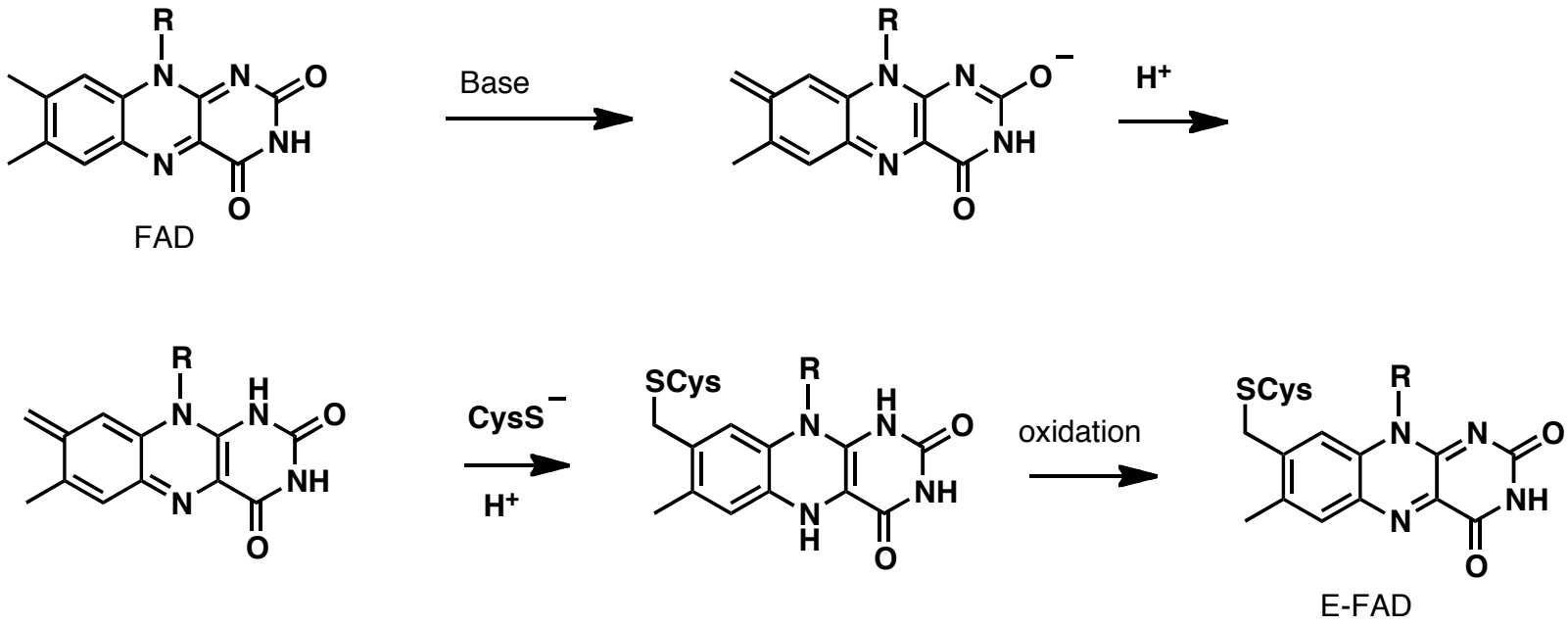
**Propose a mechanism for the reduction of lipoate by $FADH_2$**



# FAD, FMN, $FADH_2$, $FMNH_2$

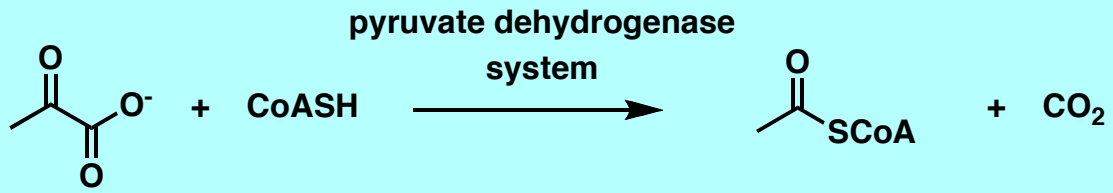
***Covalent attachment of FAD to Cys [or His]***




**PROBLEM 7**

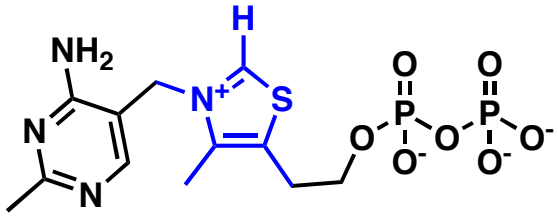
**Why the hydrogens of the C8 methyl are more acidic than those at the C7 methyl?**

# Pyruvate dehydrogenase complex




TPP, lipoate, CoASH, FAD, and $NAD^+$

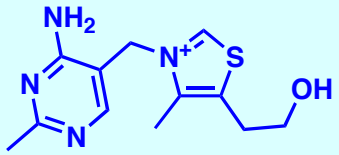
# Thiamine pyrophosphate, TPP



thiamine pyrophosphate, TPP

resonance structure

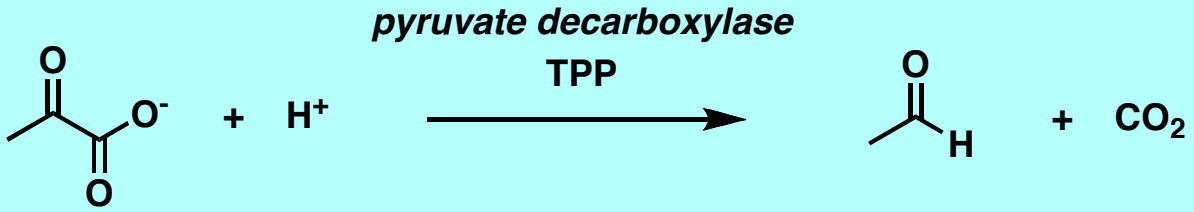
vitamin $B_1$:

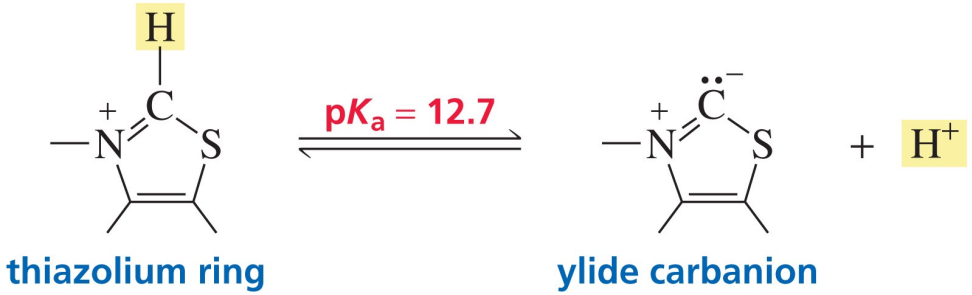


thiamine

- catalyze two-carbon transfer, many reactions in catabolism
- source of thiamine: flax, oatmeal, potato, liver, eggs, etc.
- deficiency disease: peripheral NS, beriberi

# TPP

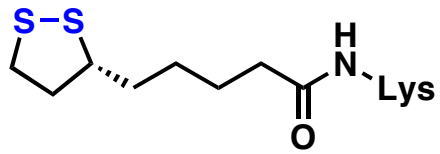





- thiazole is relatively acidic
- ylide carbanion is a good nucleophile
- and, as a fairly week base, a good leaving group

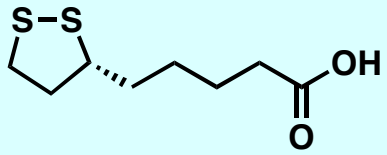
# Lipoate-Dihydrolipoate




lipoate

redox

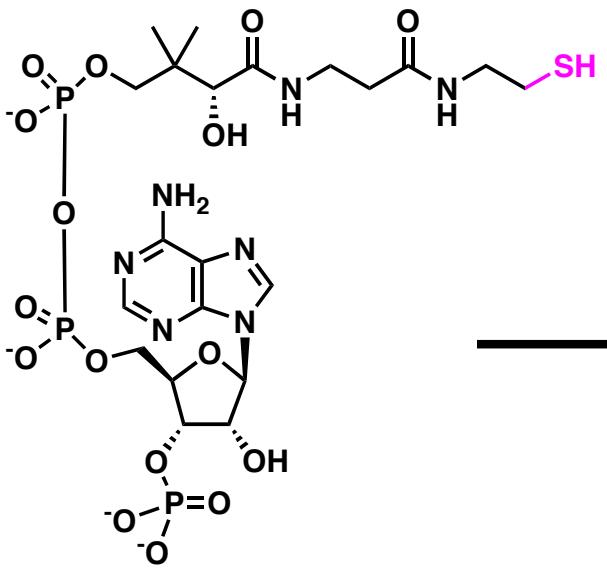
vitamin:



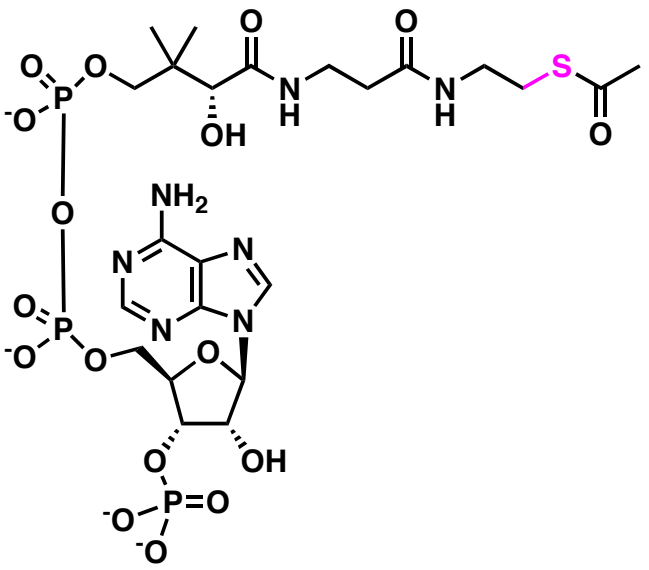

lipoic acid

- redox/part of pyruvate dehydrogenase system, aerobic catabolism
- source of lipoate: almost all foods
- deficiency disease: none

# Coenzyme A (CoASH)

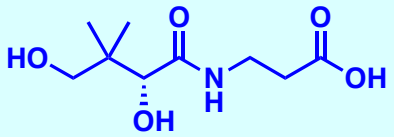


CoASH



acetyl-CoA

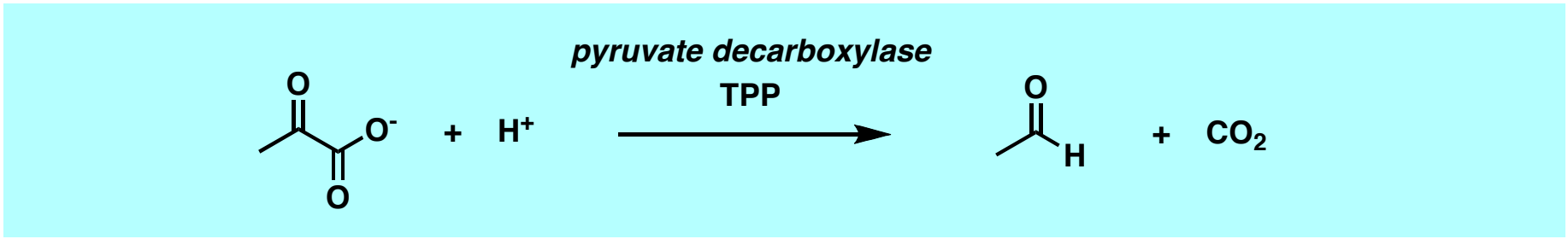
vitamin $B_5$:

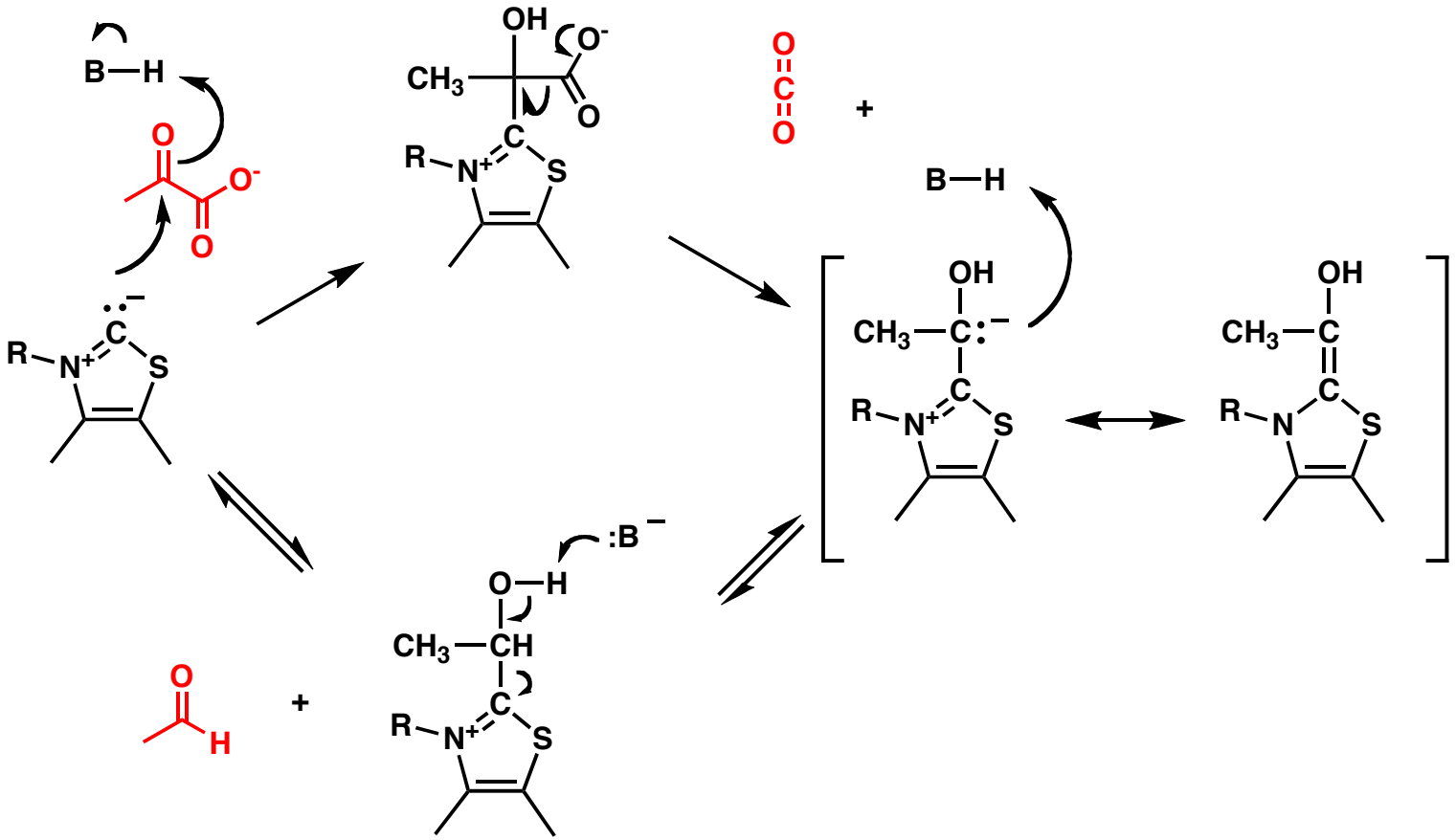


pantothenic acid

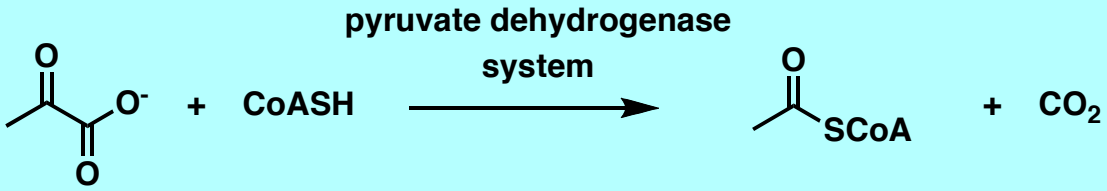
- acyl transfer, part of PDH system, pyruvate metabolism
- source of pantothenic acid: almost all foods, but more in meats
- deficiency disease: extremely rare, similar to starvation

# TPP

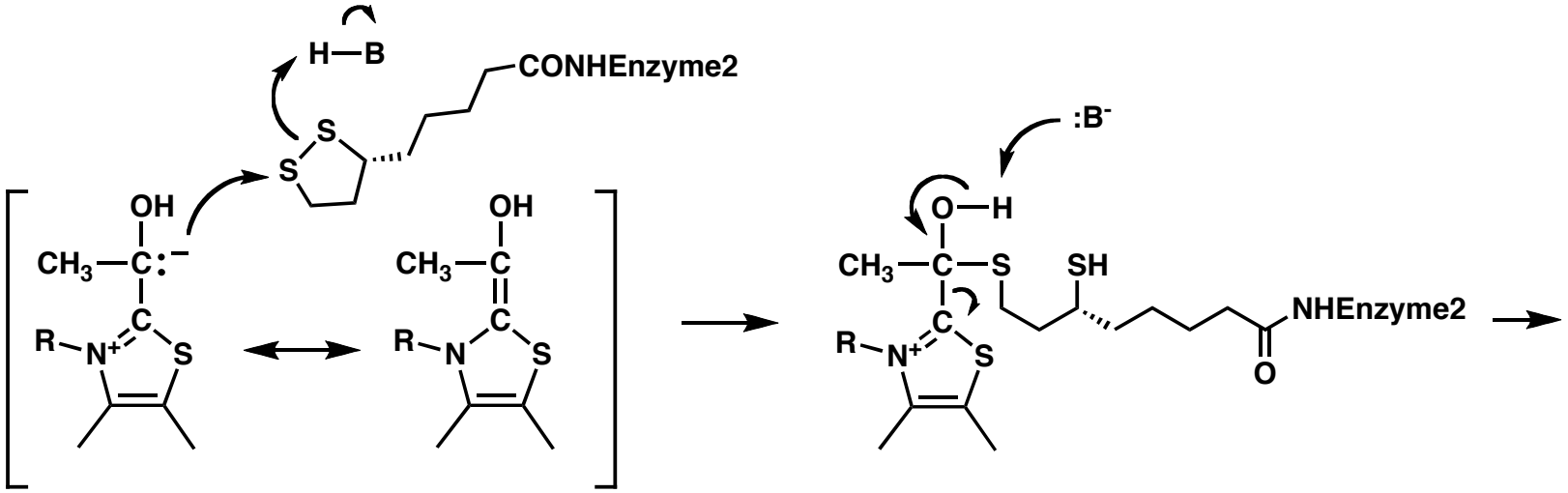

pyruvate decarboxylase
TPP
O
O⁻
O
+ H⁺
O
H
+ CO₂


B—H
O
O⁻
O
R
N⁺
C
S
OH
CH₃
O⁻
O
C
R
N⁺
S
O=C=O
+
B—H
OH
CH₃
C:⁻
C
R
N⁺
S
OH
CH₃
C
C
R
N
S
:B⁻
O—H
CH₃—CH
C
R
N⁺
S
O
H
+

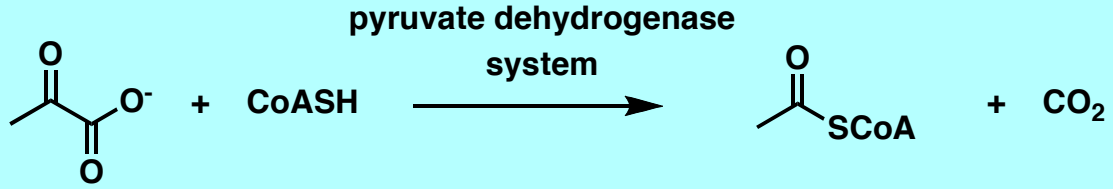
# Pyruvate dehydrogenase system



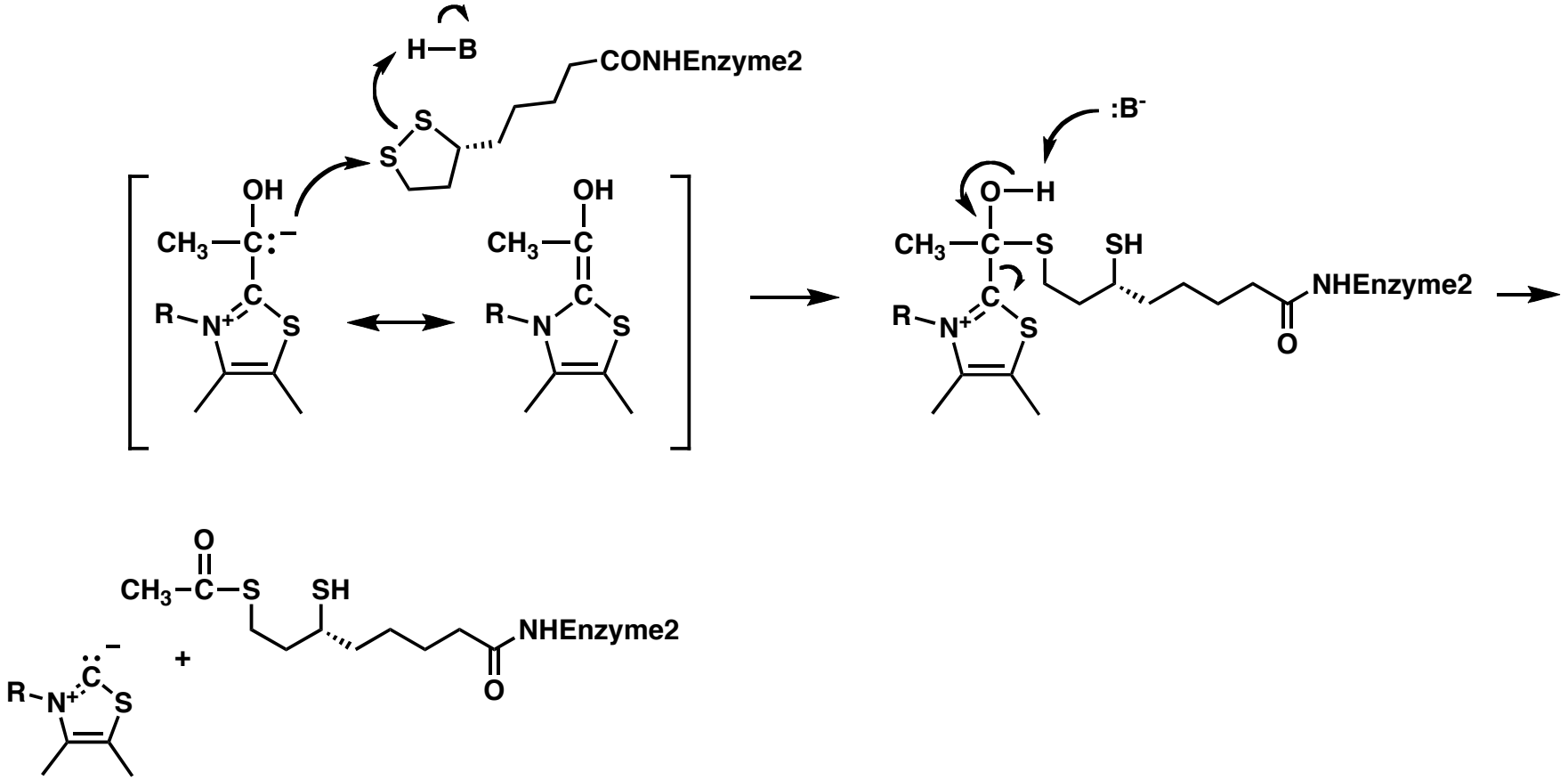

TPP, lipoate, CoASH, FAD, and NAD+



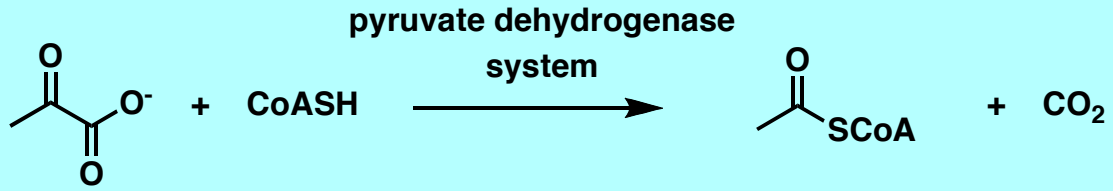
# Pyruvate dehydrogenase complex



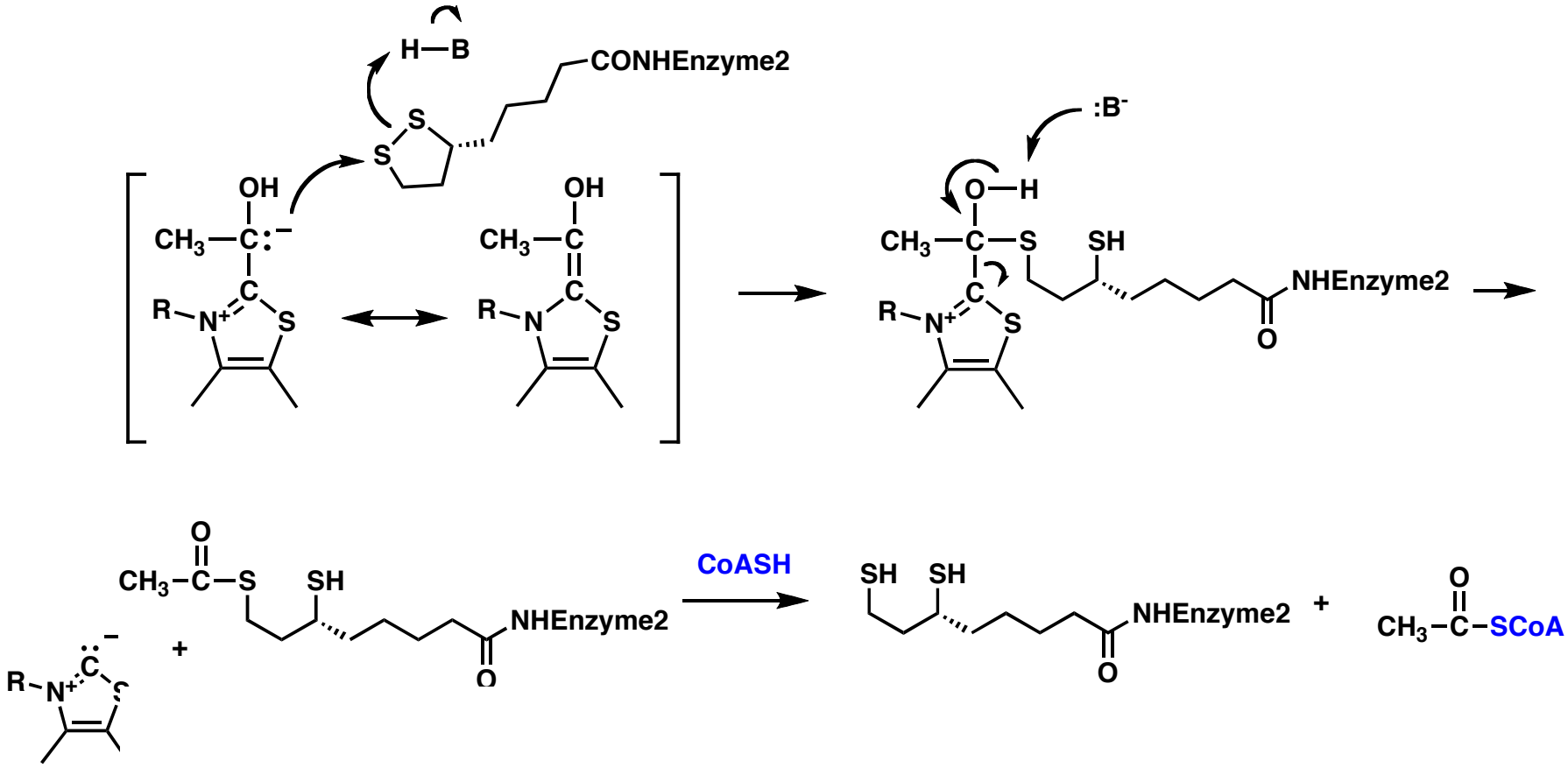

TPP, lipoate, CoASH, FAD, and $NAD^+$



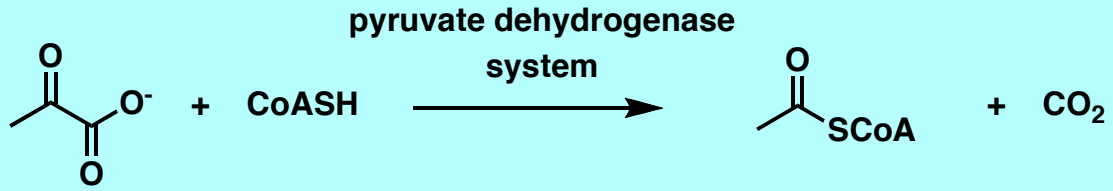
# Pyruvate dehydrogenase complex



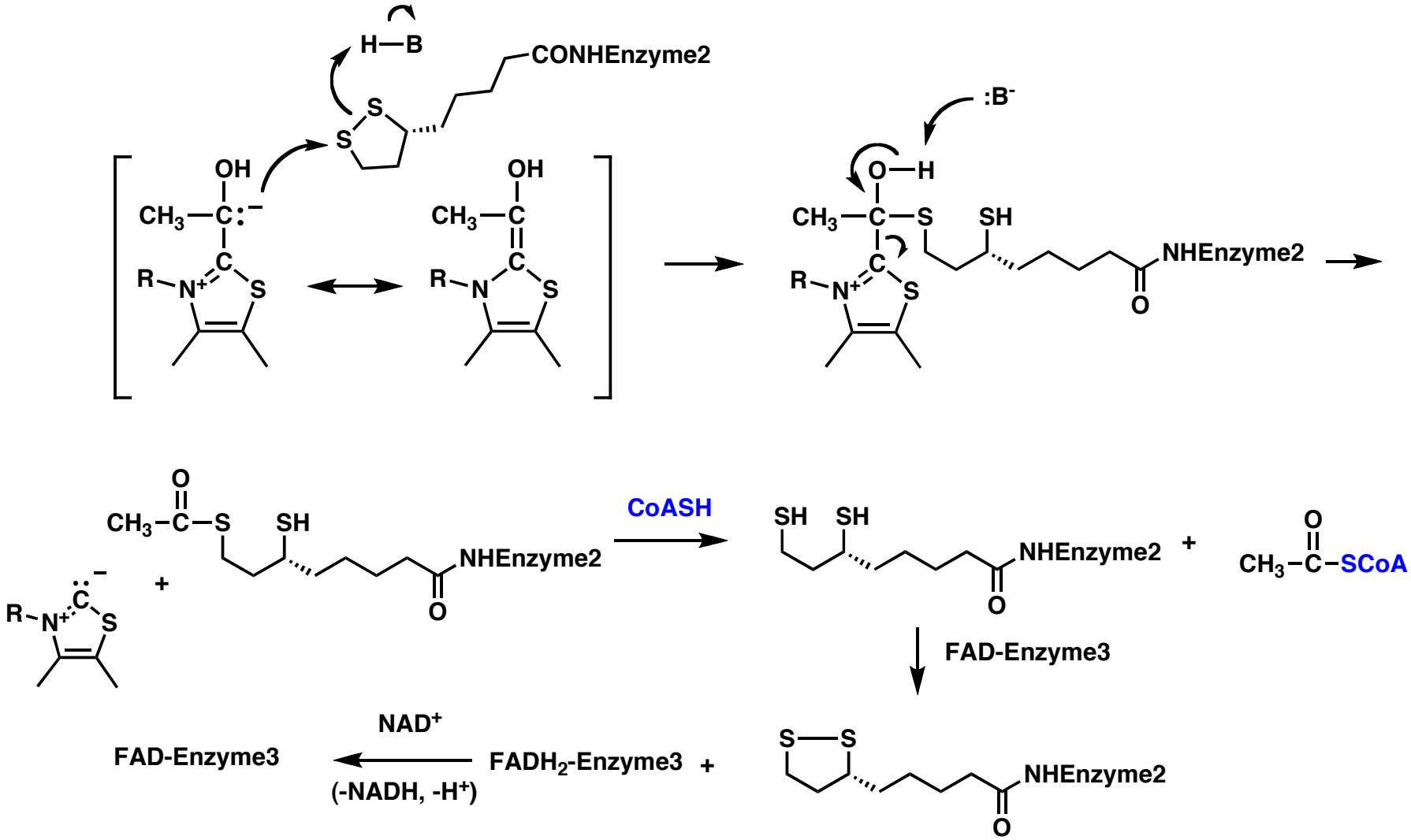

TPP, lipoate, CoASH, FAD, and $NAD^+$



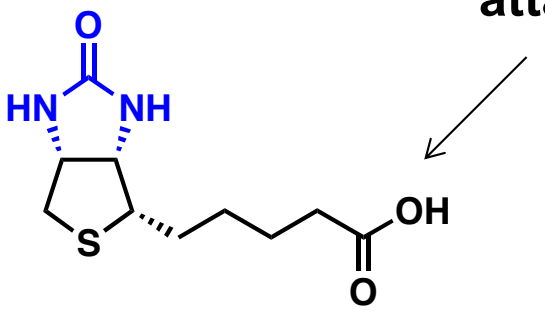
# Pyruvate dehydrogenase complex




TPP, lipoate, CoASH, FAD, and $NAD^+$



# Biotin




biotin

attaches to Lys by forming an amide

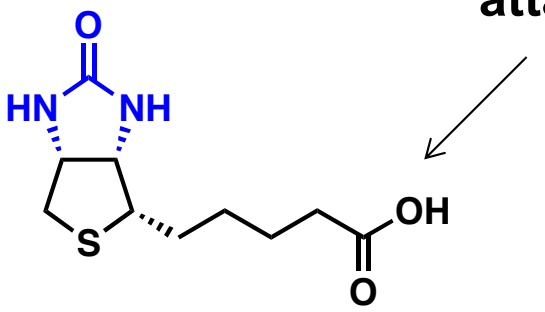
vitamin H or $B_7$:

**biotin**
(itself)

- carboxylation (aldol with $CO_2$)
- source of biotin: liver, soybeans, tomato, carrots
- deficiency: rare and mild, skin conditions, perosis, FLKS

# Biotin

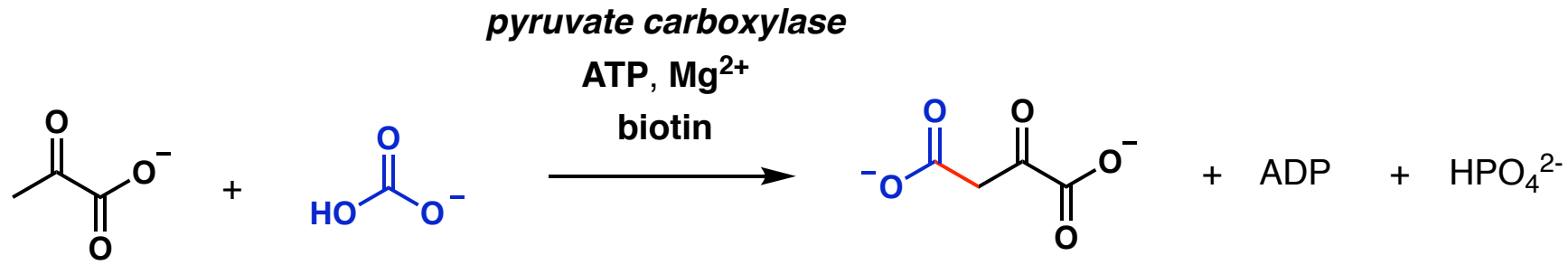
attaches to Lys by forming an amide



biotin

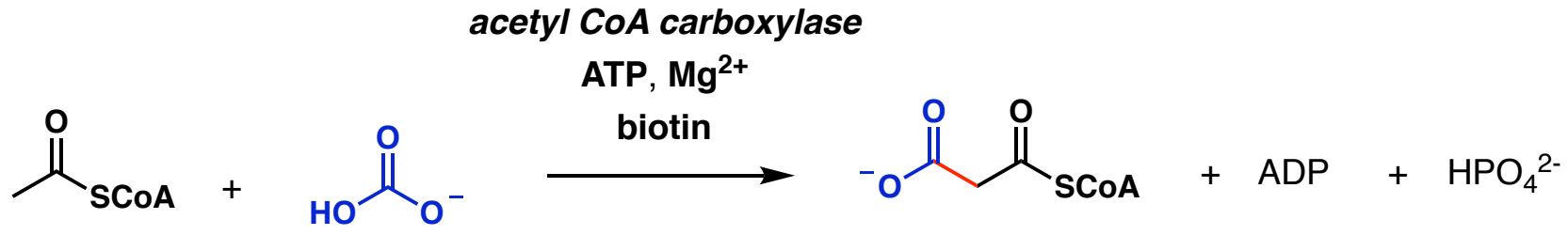
vitamin H or $B_7$:

**biotin**
(itself)




pyruvate

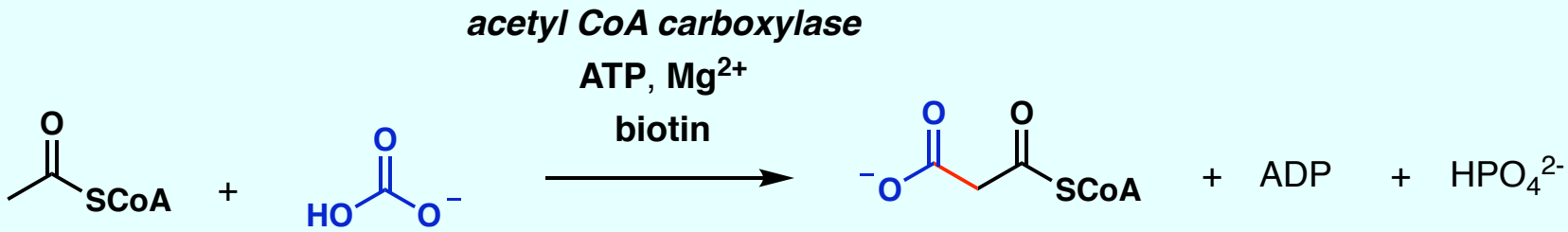
oxaloacetate



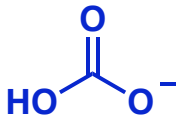

acetyl CoA

malonyl CoA

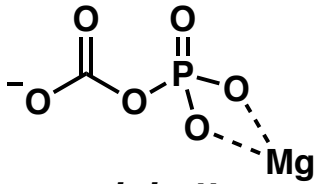
# Biotin



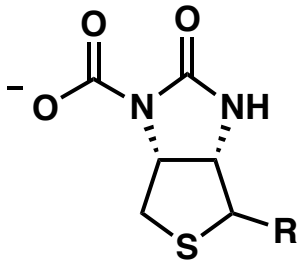

**acetyl CoA** **malonyl CoA**



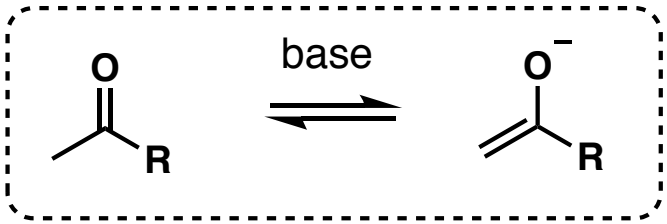

***unreactive as electrophile***




***much better electrophile***

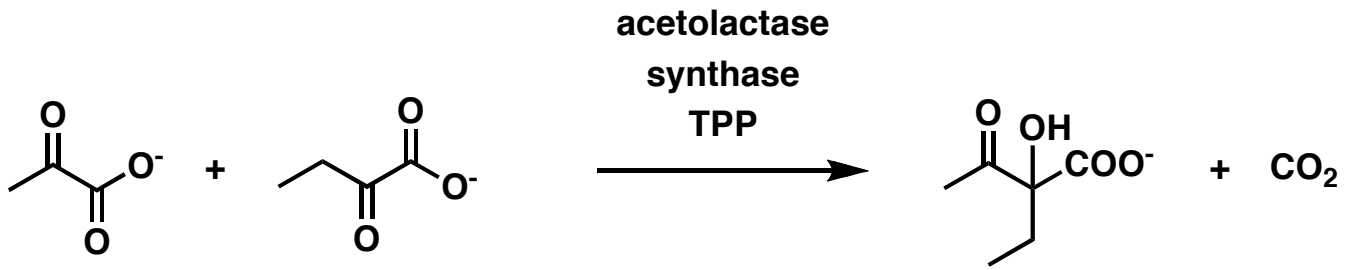



***key intermediate in biotin-catalyzed carboxylations***



## PRACTICE PROBLEM

**Acetolactase synthase can also transfer the two-carbon fragment from pyruvate to α-ketobutyrate, forming α-aceto-α-hydroxybutyrate. This is the first step in the formation of isoleucine. Propose a mechanism for this reaction.**



# Biotin