Paper Code 204 Plant Biochemistry and Metabolism

By :- Dr. Shubhi Avasthi (Botany Department)

Biosynthesis of Amino Acids (Unit-5)

* All amino acids are derived from intermediates in glycolysis, the citric acid cycle, or the pentose phosphate pathway.

* Nitrogen enters these pathway by way of glutamate and glutamine

* ~~Amino~~ Organisms vary greatly in their ability to synthesize the 20 common amino acids, Whereas most bacteria and plants can synthesize all 20, mammals can synthesize only about half of them – generally those with simple pathway are nonessential amino acids, not needed in diet

*

* The remaining are essential amino acids, must be obtained from diet.

Essential Amino Acids	Non-Essential Amino Acids
Arginine	Alanine
Histidine	Asparagine
Isoleucine	Aspartic acid
Leucine	Cysteine
Lysine	Glutamic Acid
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Proline
Tryptophan	Serine
Valine	Tyrosine

Amino Acid Biosynthetic Families, Grouped by Metabolic Precursor

1) α-Ketoglutarate

- Glutamine, Glutamate
- Proline
- Arginine

2) 3-Phosphoglycerate

- Serine
- Glycine
- Cysteine

3) Oxaloacetate

- Aspartate
- Asparagine
- Methionine*
- Threonine
- Lysine*

4) Pyruvate

- Alanine
- Valine*
- Leucine*
- Isoleucine*

5) Phosphoenolpyruvate
5) & Erythrose 4-phosphate

- Tryptophan*
- Phenylalanine*
- Tyrosine+

6) Ribose 5 phosphate

- Histidine*

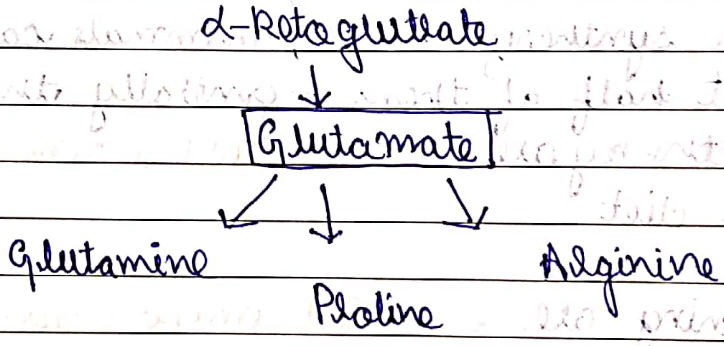
(*) Essential amino acids

(+) Derived from phenylalanine in mammals

* A useful way to organize these biosynthetic pathway is to group them into six families corresponding to their metabolic precursors.

Synthesis of Amino Acids

1) The Glutamate Family



* Eg The biosynthesis pathway to glutamate and glutamine are simple.

* The important pathway for assimilation of NH_4^+ into glutamate require two reactions.

First :- Glutamine synthetase catalyses the reaction of glutamine and NH_4^+ to yield Glutamine

$$\text{Glutamate} + NH_4^+ + ATP \longrightarrow \text{Glutamine} + ADP + Pi + H^+$$

* In bacteria & plants, glutamate is produced from glutamine in a reaction catalyzed by glutamate synthetase

α-ketoglutarate + glutamine + NADPH + H^+

↓

2 Glutamate + $NADP^+$

The net reaction of glutamine synthetase and glutamate synthase is

α-ketoglutarate + NH_4^+ + NADPH + ATP

↓

L-glutamate + $NADP^+$ + ADP + P_i

* Proline is a cyclized derivative of glutamate

* In the 1st step of proline synthesis, ATP reacts with γ-carboxyl group of glutamate to form an acyl phosphate, reduced by NADPH to glutamate γ-semialdehyde.

* Glutamate γ-semialdehyde undergoes cyclization and then reduced further to yield Proline

Arginine is synthesized from glutamate via ornithine and the urea cycle in animals

* In principal, ornithine also be synthesized from glutamate γ-semialdehyde by transamination.

* Orin ornithine is converted into citrulline and arginine in urea cycle

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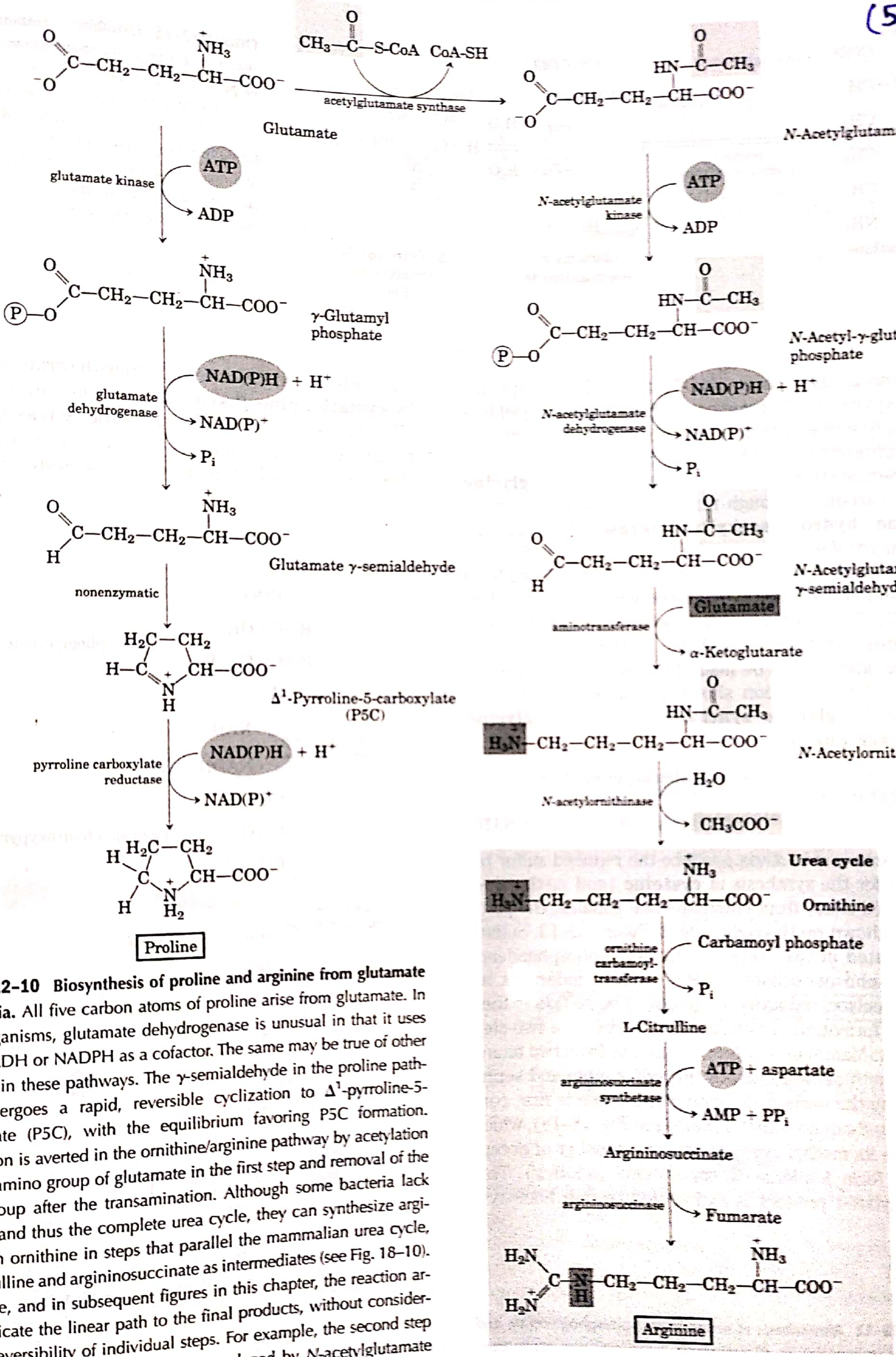


FIGURE 22–10 Biosynthesis of proline and arginine from glutamate in bacteria. All five carbon atoms of proline arise from glutamate. In many organisms, glutamate dehydrogenase is unusual in that it uses *either* NADH or NADPH as a cofactor. The same may be true of other enzymes in these pathways. The γ-semialdehyde in the proline pathway undergoes a rapid, reversible cyclization to Δ^1-pyrroline-5-carboxylate (P5C), with the equilibrium favoring P5C formation. Cyclization is averted in the ornithine/arginine pathway by acetylation of the α-amino group of glutamate in the first step and removal of the acetyl group after the transamination. Although some bacteria lack arginase and thus the complete urea cycle, they can synthesize arginine from ornithine in steps that parallel the mammalian urea cycle, with citrulline and argininosuccinate as intermediates (see Fig. 18–10).

Here, and in subsequent figures in this chapter, the reaction arrows indicate the linear path to the final products, without considering the reversibility of individual steps. For example, the second step of the pathway leading to arginine, catalyzed by *N*-acetylglutamate dehydrogenase, is chemically similar to the glyceraldehyde 3-phosphate dehydrogenase reaction in glycolysis (see Fig. 14–7) and is readily reversible.

Serine, Glycine and cysteine

- In the 1st step, the hydroxyl group of 3-phosphoglycerate is oxidized by a dehydrogenase to yield 3'-phosphoglycerate.

- Transamination from glutamate yields 3-phosphoserine which is hydrolysed ~~by~~ to free serine by phosphoserine phosphatase.

- Serine is the precursor of glycine, removal of carbon atom by serine hydroxymethyl transferase

- Tetrahydrofolate accept the β-carbon of serine, which form a bridge betwen N-5 and N-10 to yield N^5, N^{10} methylenetetrahydrofolate.

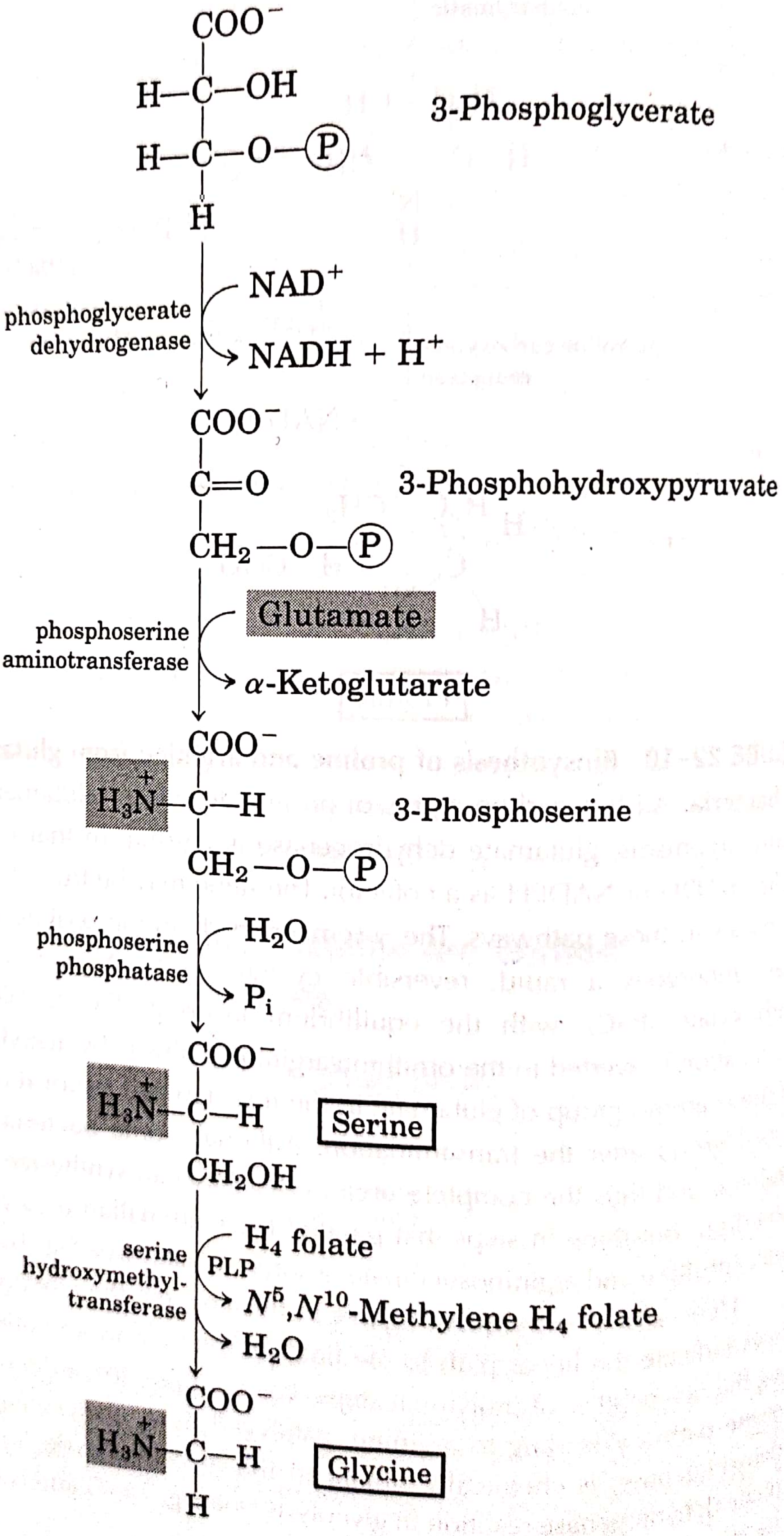
- Plants & bacteria produce reduce sulfur required for the synthesis of cysteine

- Sulfate is activated in 2 steps to produce 3-phosphoadenosine-5' phosphosulfate which undergoes reduction to sulfide

- Sulfide is used in the formation of cysteine from serine in a 2 step pathway

- Mammals synthesized cysteine from methionine and serine.

cleavage of


COO⁻
H—C—OH
H—C—O—(P)
H
3-Phosphoglycerate
phosphoglycerate dehydrogenase
NAD⁺
NADH + H⁺
COO⁻
C=O
CH₂—O—(P)
3-Phosphohydroxypyruvate
phosphoserine aminotransferase
Glutamate
α-Ketoglutarate
COO⁻
H₃N⁺—C—H
CH₂—O—(P)
3-Phosphoserine
phosphoserine phosphatase
H₂O
Pᵢ
COO⁻
H₃N⁺—C—H
CH₂OH
Serine
serine hydroxymethyl-transferase
H₄ folate
PLP
N⁵,N¹⁰-Methylene H₄ folate
H₂O
COO⁻
H₃N⁺—C—H
H
Glycine

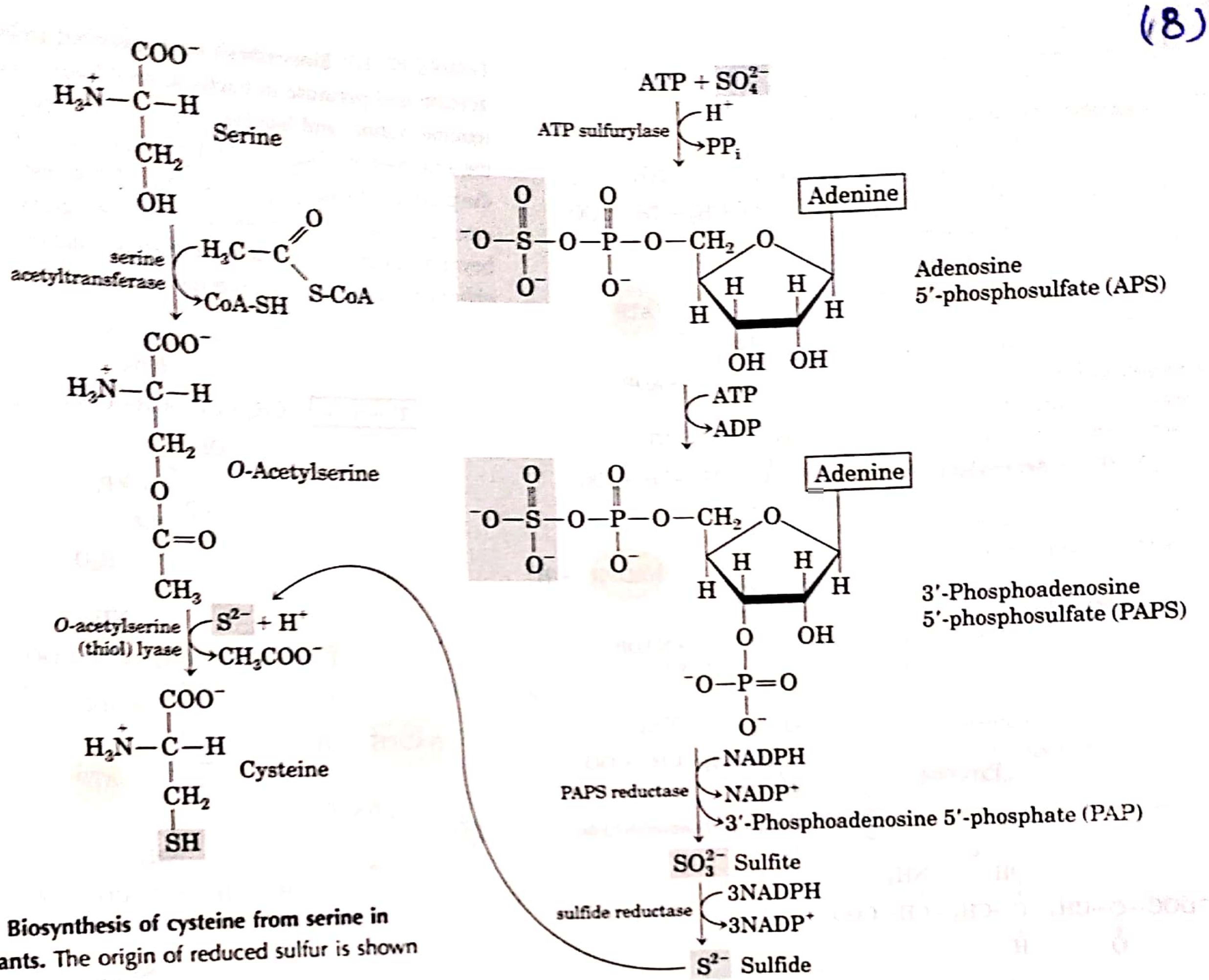
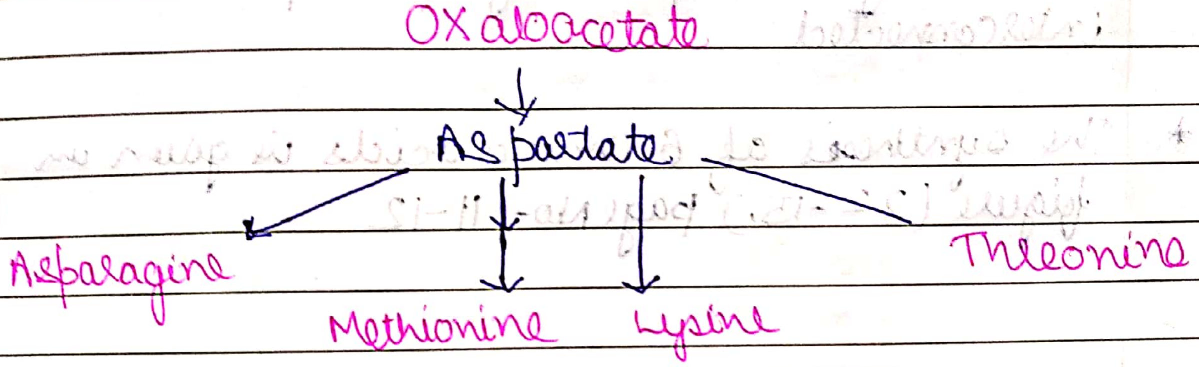
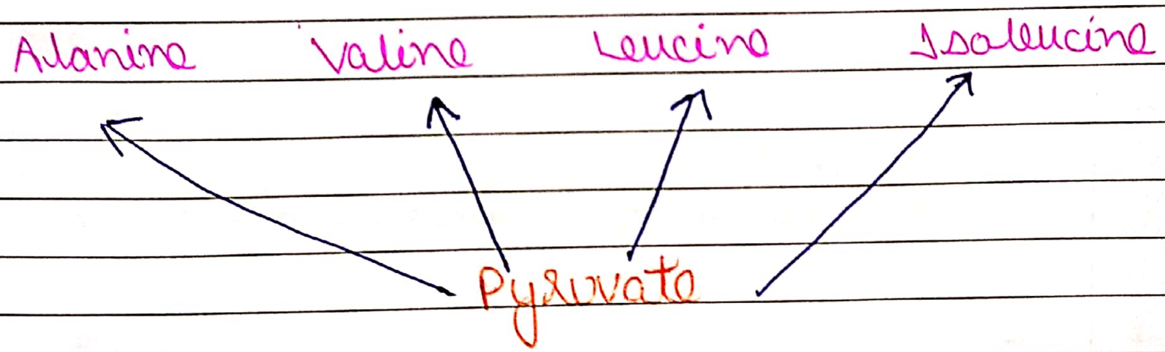


FIGURE 22–13 Biosynthesis of cysteine from serine in bacteria and plants. The origin of reduced sulfur is shown in the pathway on the right.

3 Non-Essential and Six Essential Amino Acids are synthesized from Oxaloacetate and Pyruvate





- Alanine & Aspartate are synthesized from pyruvate and oxaloacetate by transamination from glutamate
- Asparagine is synthesized by amidation of aspartate, with glutamine donating the NH_4^+.

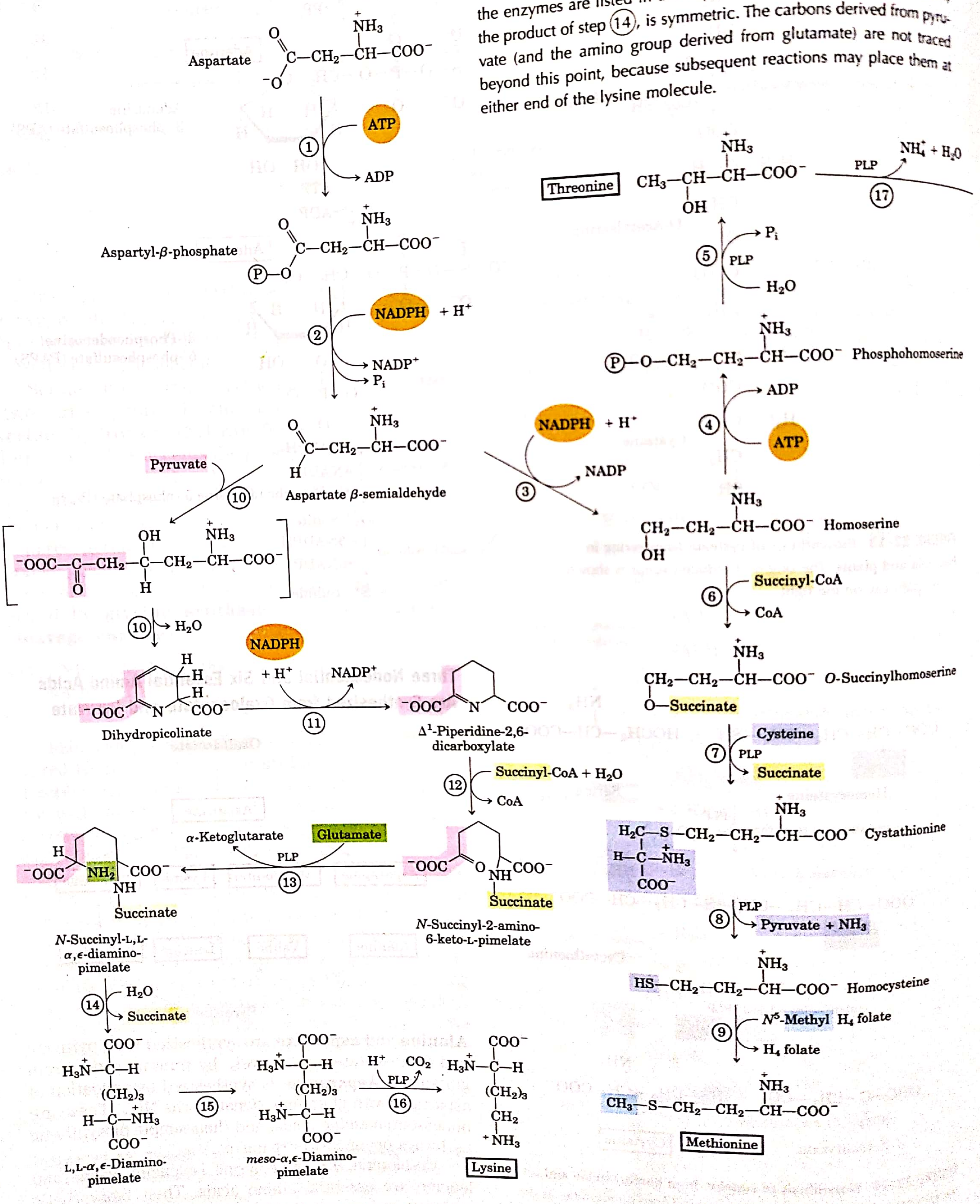
These are non-essential amino acids

+ Methionine, threonine, lysine, isoleucine, valine and leucine are essential amino acids

+ Their biosynthetic pathway are complex and interconnected.

+ The synthesis of 6 amino acids is given in figure (22-15,) pageNo:- 11-12

FIGURE 22-15 Biosynthesis of six essential amino acids from oxaloacetate and pyruvate in bacteria: methionine, threonine, lysine, isoleucine, valine, and leucine. Here, and in other multistep pathways, the enzymes are listed in the key. Note that L,L-α,ε-diaminopimelate, the product of step ⑭, is symmetric. The carbons derived from pyruvate (and the amino group derived from glutamate) are not traced beyond this point, because subsequent reactions may place them at either end of the lysine molecule.



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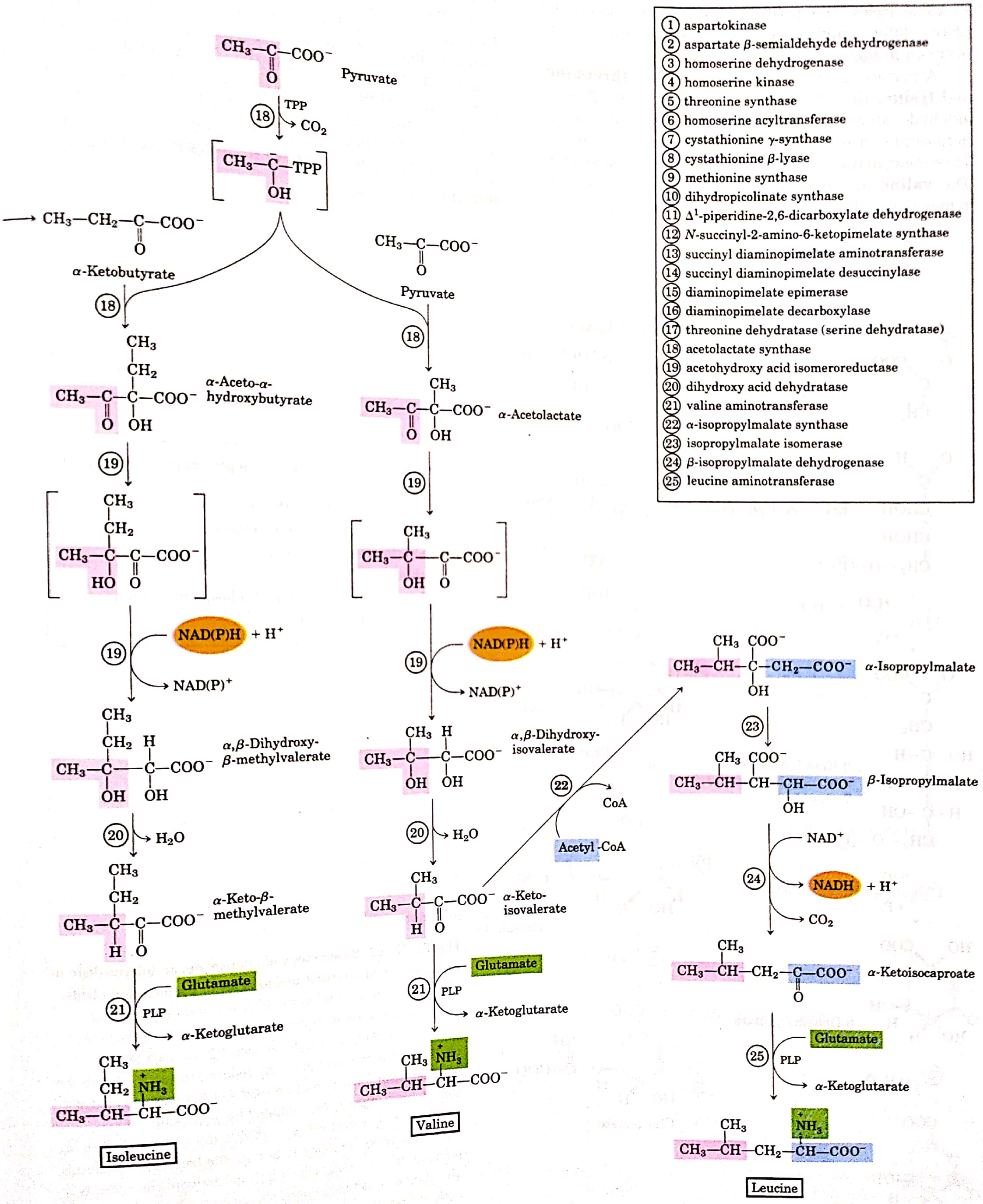
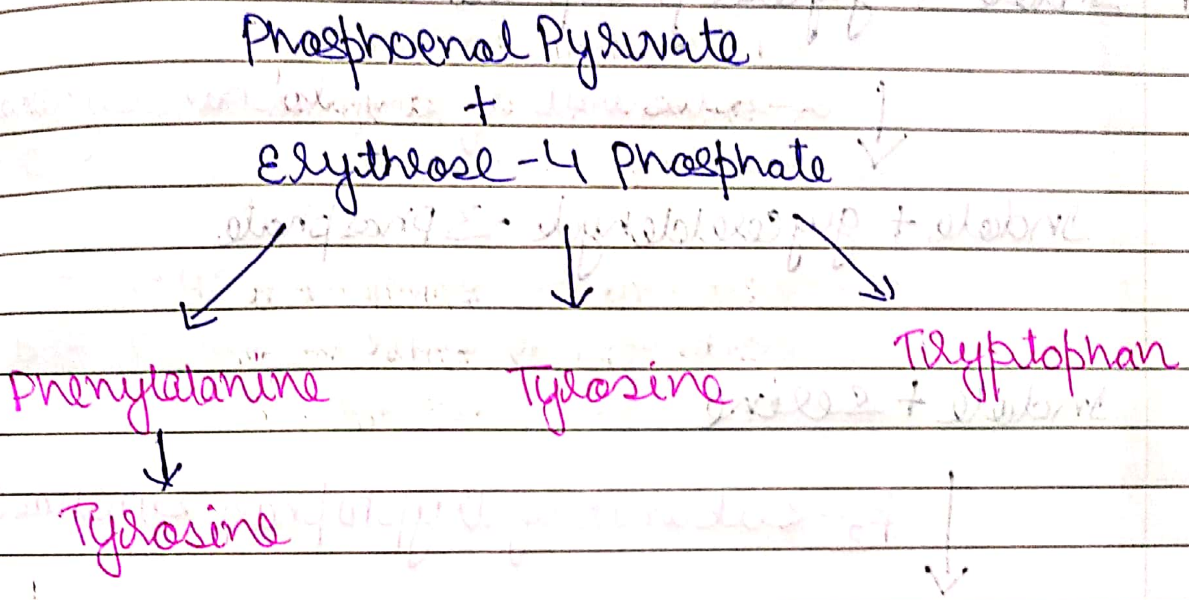


① aspartokinase
② aspartate β-semialdehyde dehydrogenase
③ homoserine dehydrogenase
④ homoserine kinase
⑤ threonine synthase
⑥ homoserine acyltransferase
⑦ cystathionine γ-synthase
⑧ cystathionine β-lyase
⑨ methionine synthase
⑩ dihydropicolinate synthase
⑪ Δ^1-piperidine-2,6-dicarboxylate dehydrogenase
⑫ *N*-succinyl-2-amino-6-ketopimelate synthase
⑬ succinyl diaminopimelate aminotransferase
⑭ succinyl diaminopimelate desuccinylase
⑮ diaminopimelate epimerase
⑯ diaminopimelate decarboxylase
⑰ threonine dehydratase (serine dehydratase)
⑱ acetolactate synthase
⑲ acetohydroxy acid isomeroreductase
⑳ dihydroxy acid dehydratase
㉑ valine aminotransferase
㉒ α-isopropylmalate synthase
㉓ isopropylmalate isomerase
㉔ β-isopropylmalate dehydrogenase
㉕ leucine aminotransferase

Tryptophan, Phenylalanine and Tyrosine are synthesized by intermediate Chorismate



- In shikimate pathway, shikimate is converted to Chorismate.

- Chorismate is branch point, with one branch leading to tryptophan, the other phenylalanine and Tyrosine.

- In tryptophan, chorismate is converted into Anthranilate,

- Anthranilate the condense with PRPP. The indole ring of tryptophan is derived from ring carbons and amino group of anthranilate plus 2 carbons derived from PRPP.

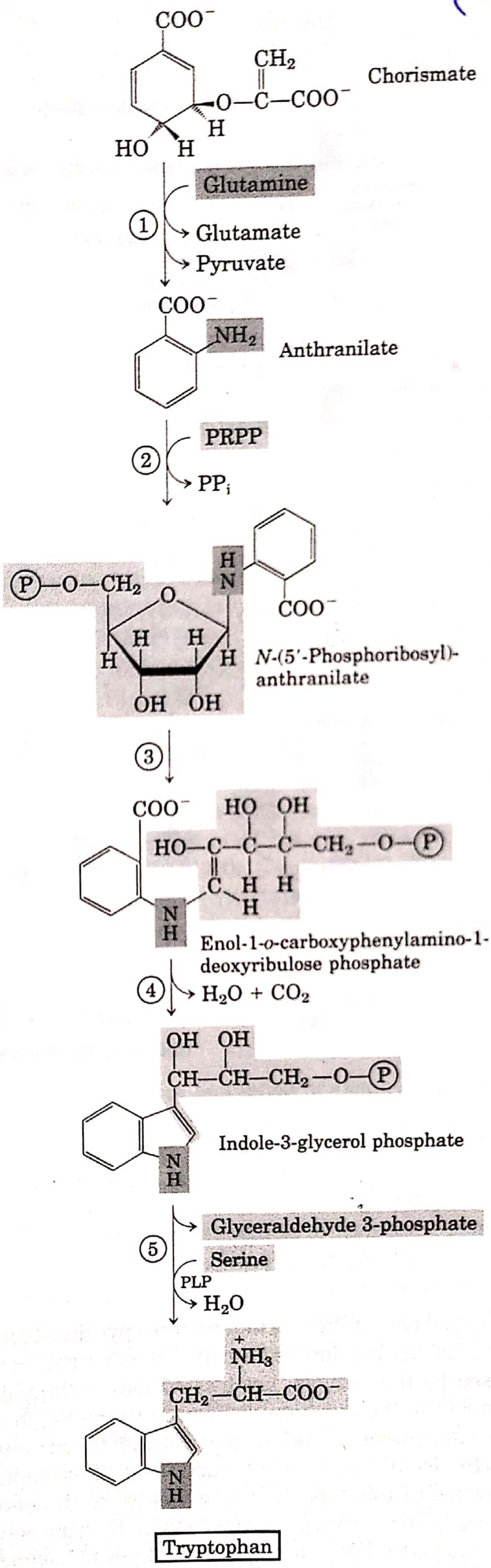


FIGURE 22–17 Biosynthesis of tryptophan from chorismate in bacteria and plants. In *E. coli,* enzymes catalyzing steps ① and ② are subunits of a single complex.

DATE

- The final ~~synthase~~ reaction is catalyzed by tryptophan synthase
- Indole-3-glycerol phosphate

$$\Big\downarrow \text{ α- subunit of tryptophan synthase}$$

Indole + glyceraldehyde-3 phosphate

Indole + serine

$$\Big\downarrow \text{ } \beta_2\text{- subunit of tryptophan synthase}$$

Tryptophan + H_2O

- Phenylalanine and Tyrosine are synthesized from Chorismate in pathway.
- The Common intermediate is prephenate. The final step in both case is transamination with glutamate

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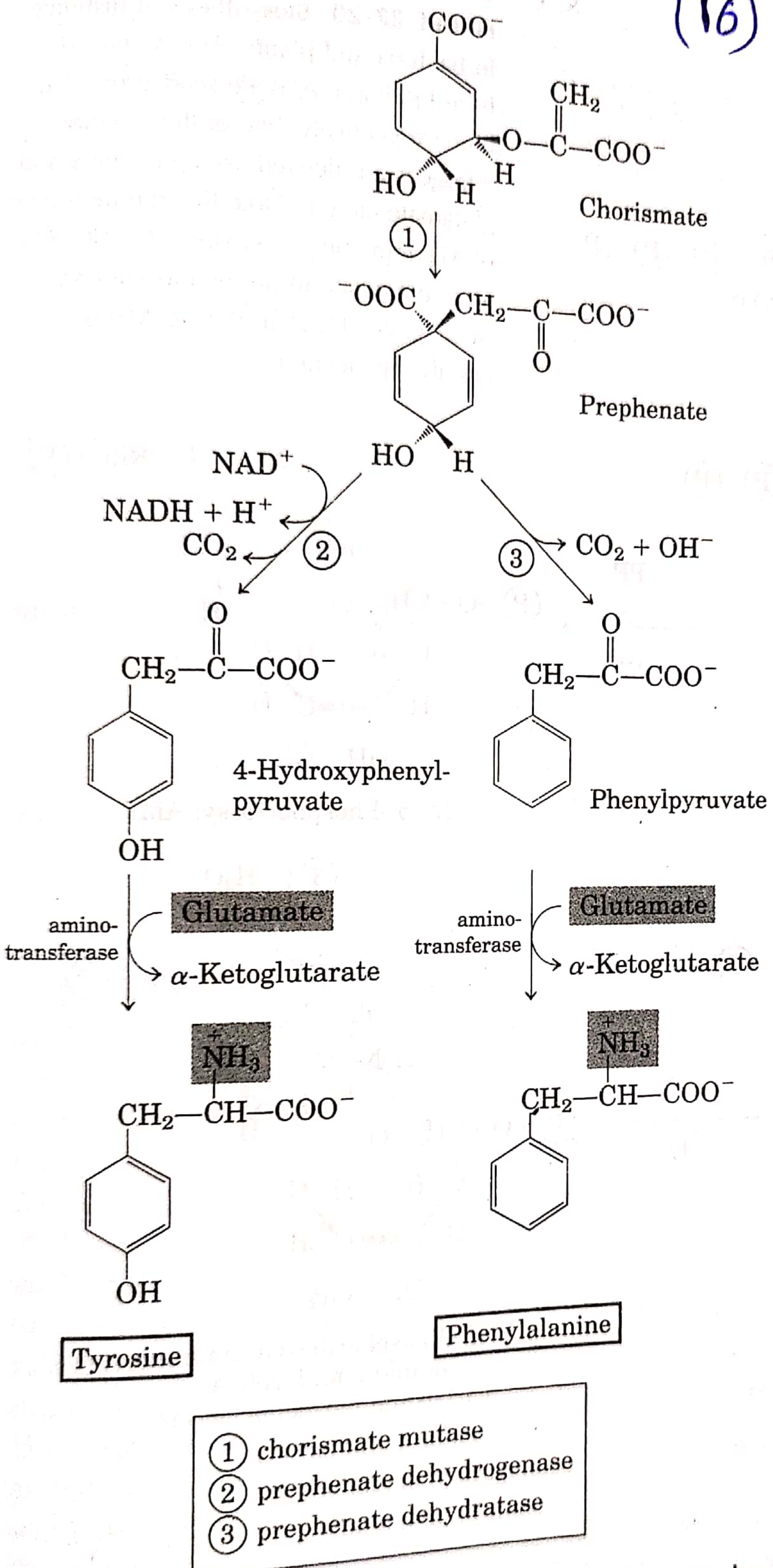

FIGURE 22–19 Biosynthesis of phenylalanine and tyrosine from chorismate in bacteria and plants. Conversion of chorismate to prephenate is a rare biological example of a Claisen rearrangement.

Histidine biosynthesis

Ribose-5-phosphate
↓
Histidine

* Histidine is derived from 3 precursors

1) PRPP contributes 5 carbon
2) Purine ring of ATP contributes nitrogen & carbon
3) Glutamine supplies the 2nd ring nitrogen

* The key steps are condensation of ATP & PRPP, in which N-1 of the purine ring is linked to the activated C-1 of the ribose of PRPP - step 1

* Purine ring opening that ultimately leaves N-1 & C-2 of adenine linked to ribose - step-3 and the formation of imidazole ring, a reaction in which glutamine donates a nitrogen - step-5

* The use of ATP as a metabolic, ~~rather~~ because it dovetails with the purine synthesis pathway.

FIGURE 22-20 Biosynthesis of histidine in bacteria and plants. Atoms derived from PRPP and ATP are shaded red and blue, respectively. Two of the histidine nitrogens are derived from glutamine and glutamate (green). Note that the derivative of ATP remaining after step ⑤ (AICAR) is an intermediate in purine biosynthesis (see Fig. 22–33, step ⑨), so ATP is rapidly regenerated.