Secondary Metabolism Part 2: The Shikimic Acid Pathway

Lecture 9
Biofuels and Bioproducts

Bronx Community College - 2017
Chemistry and BioEnergy Technology for Sustainability NSF ATE 1601636

Outline

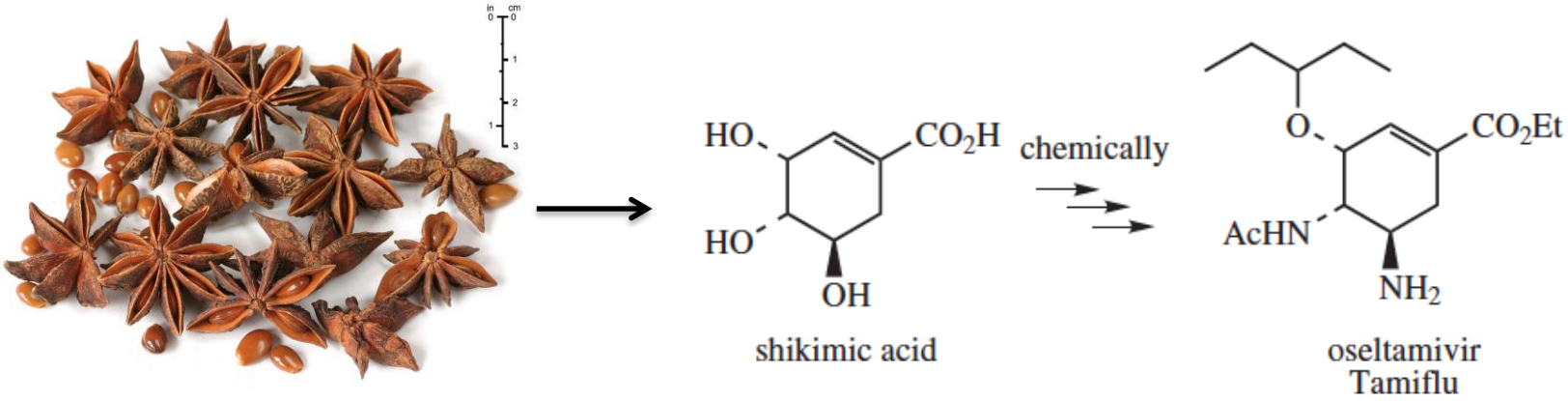
- Shikimic Acid Biosynthesis
  - Classes/Uses of Compounds from Shikimic Acid
  - Shikimic Acid
  - Tannins
  - Chorismic Acid
  - Aromatic amino acids
  - Lignan and Lignin
  - Heterologous Expression of Shikimic Acid (*E. coli*)

Slide Images modified from: Paul Dewick *Medicinal Natural Products: A Biosynthetic Approach* (3rd Ed. Wiley, 2009)

The Shikimic Acid Pathway

- Shikimic acid originally isolated from plants of genus *Illicium* (‘shikimi’ in Japanese)
- Provides an *alternate* route to aromatic compounds
- AAs = L-phenylalanine, L-tyrosine, L-tryptophan

- Shikimic acid is raw material for Tamiflu®
- Alternative production of pathway in *E.coli*

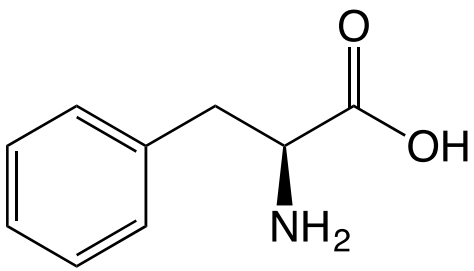


shikimic acid

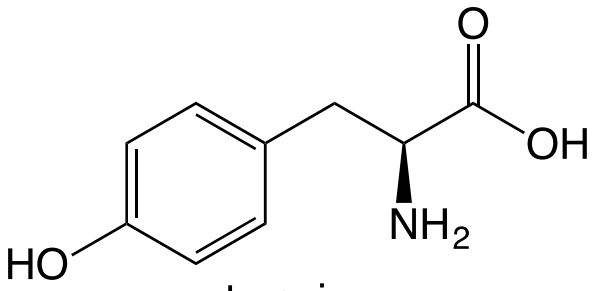
oseltamivir
Tamiflu

Illicium verum (Star anise)
or engineered *E.coli*

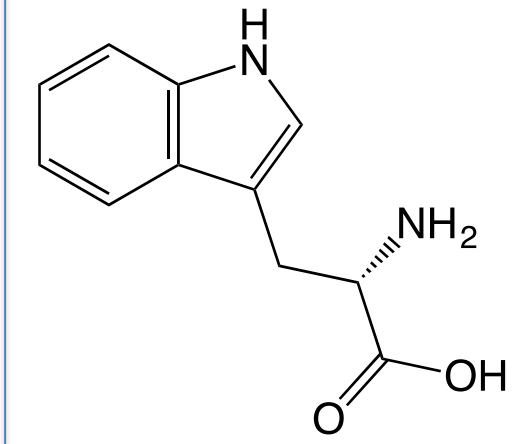
Amino Acid products of Shikimic Acid Pathway are Precursors for Important Natural Products



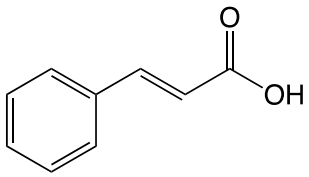
phenylalanine

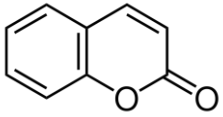


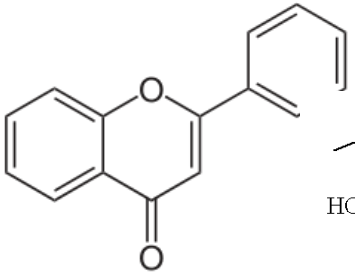
tyrosine

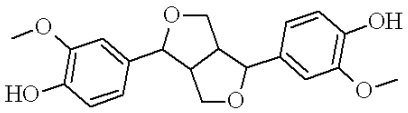


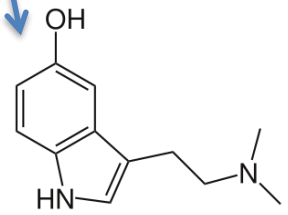
tryptophan











Cinnamic acids

- Flavoring
- Perfumes
- Indigo (dye)
- Pharma
- Shea butter

Coumarins

- Perfumes
- Fabric conditioners
- Pipe tobacco
- Warfarin/edema
- Photosensitizer
- Gain media (lasers)
- Rodenticides

Flavonoids

- Iso-, Neo-
- Pigments
- Many dietary sources and health benefits
- Heterologous Expression (*E.coli*, and Yeast)

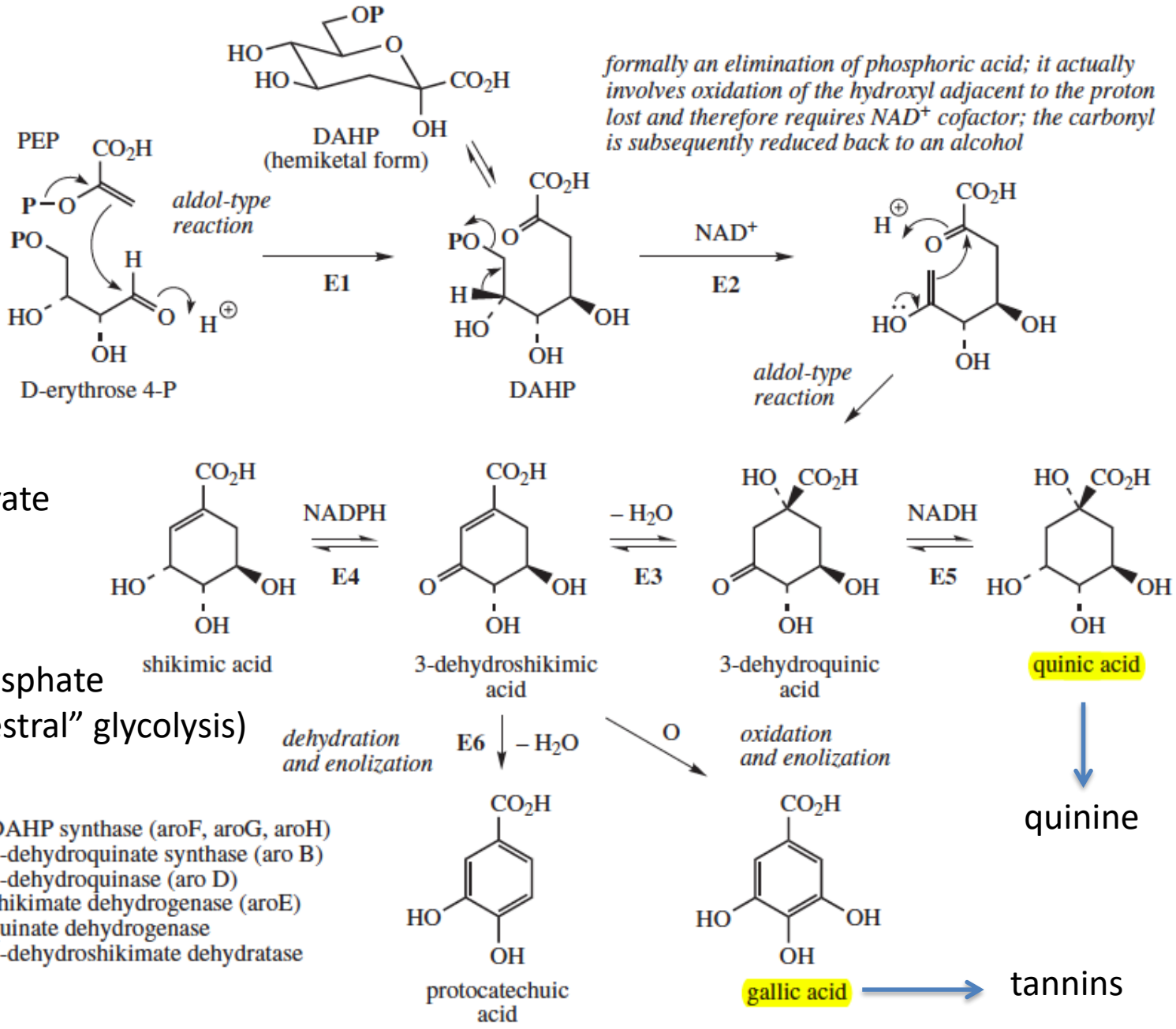
Lignans

- e.g. Pinoreinol
- Dietary fiber
- Phytoestrogen

Alkaloids

- Interesting, diverse chemistry
- Bioactive (e.g. quinine, analgesic, stimulants)

Shikimic Acid Biosynthesis



PEP
Phosphoenolpyruvate
(from glycolysis)

D-erythrose-4-P
(from pentose phosphate pathway aka "ancestral" glycolysis)

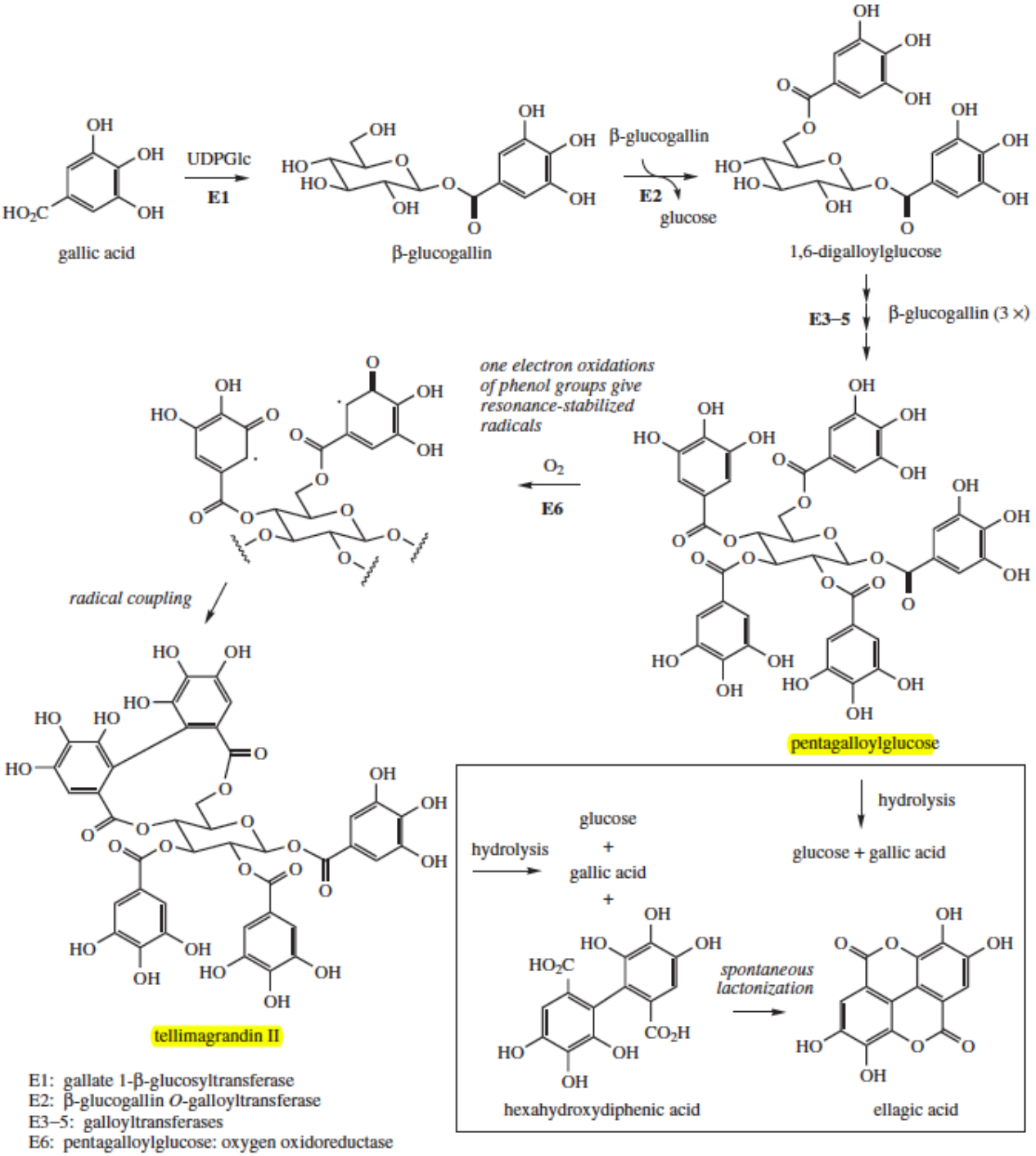
E1: DAHP synthase (aroF, aroG, aroH)
E2: 3-dehydroquinate synthase (aro B)
E3: 3-dehydroquinase (aro D)
E4: shikimate dehydrogenase (aroE)
E5: quinate dehydrogenase
E6: 3-dehydroshikimate dehydratase

Tannins

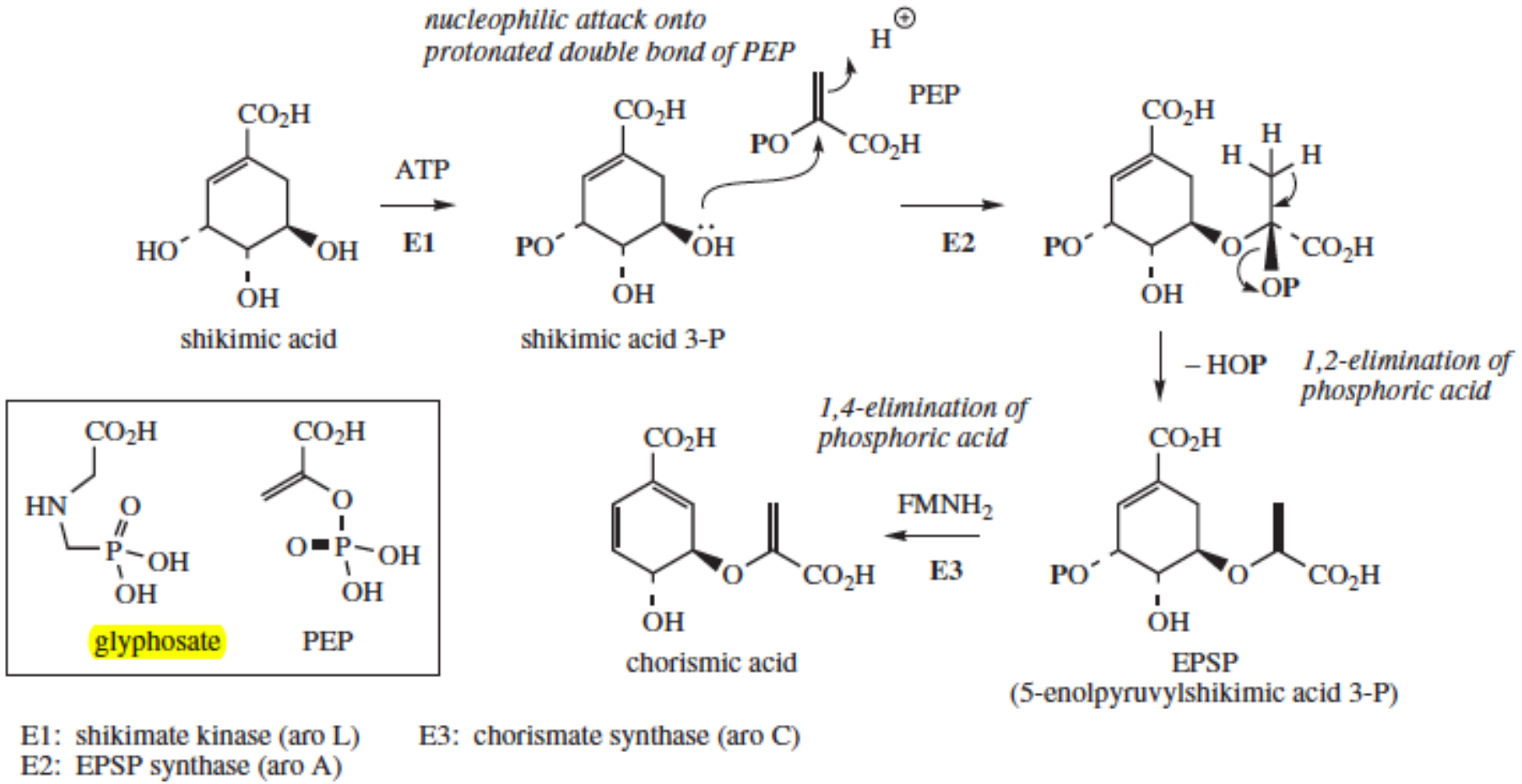
- Leather-making (crosslink proteins)
- Tea, coffee, wine (astringent flavor, antioxidant)
- β-glucogallin Intermediate similar to CoA thioester

- What is the LG?

- How is radical coupling mechanism similar to anti-oxidant activity?



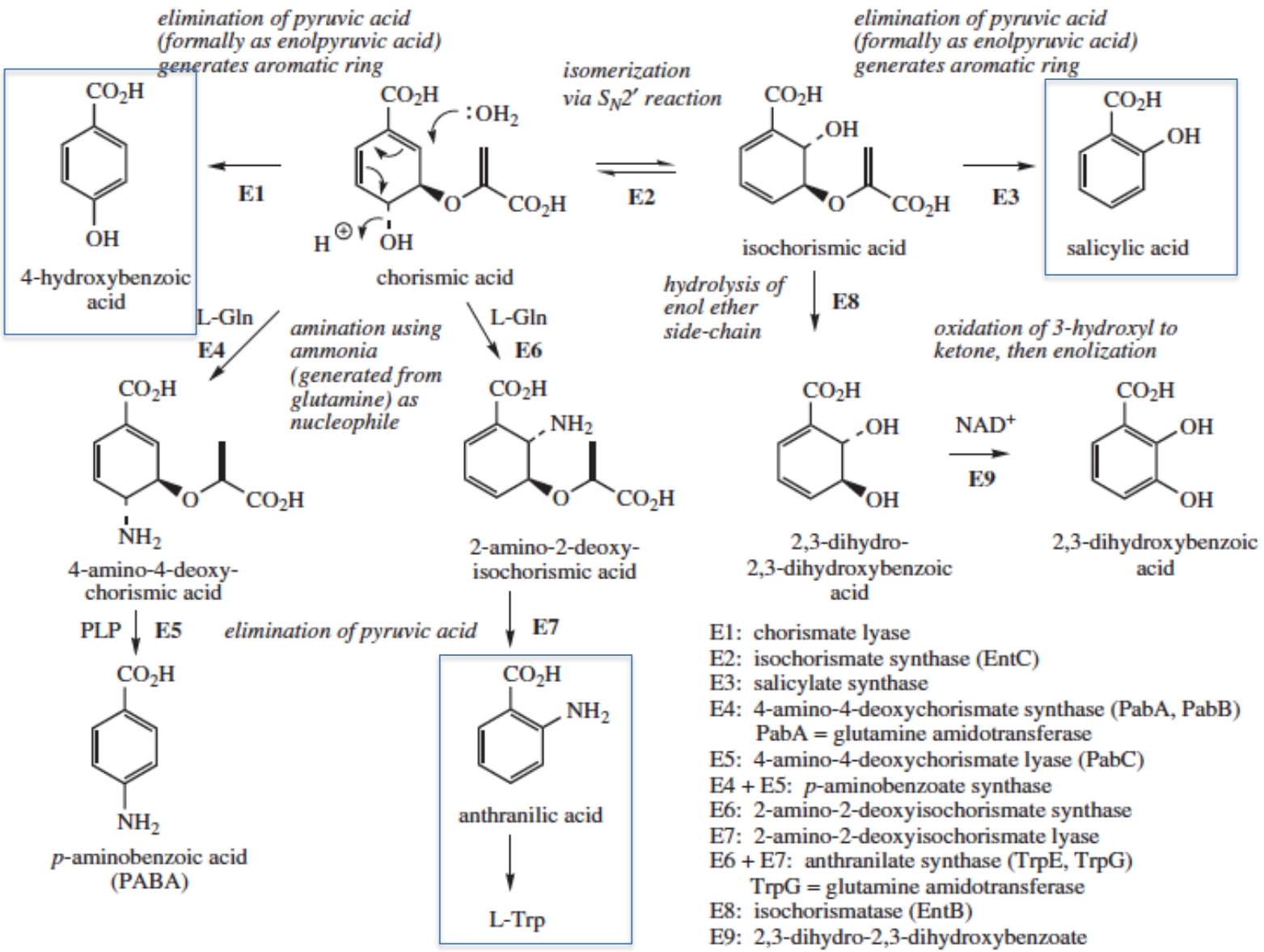
Chorismic Acid and Herbicides



E1: shikimate kinase (aro L)
E2: EPSP synthase (aro A)
E3: chorismate synthase (aro C)

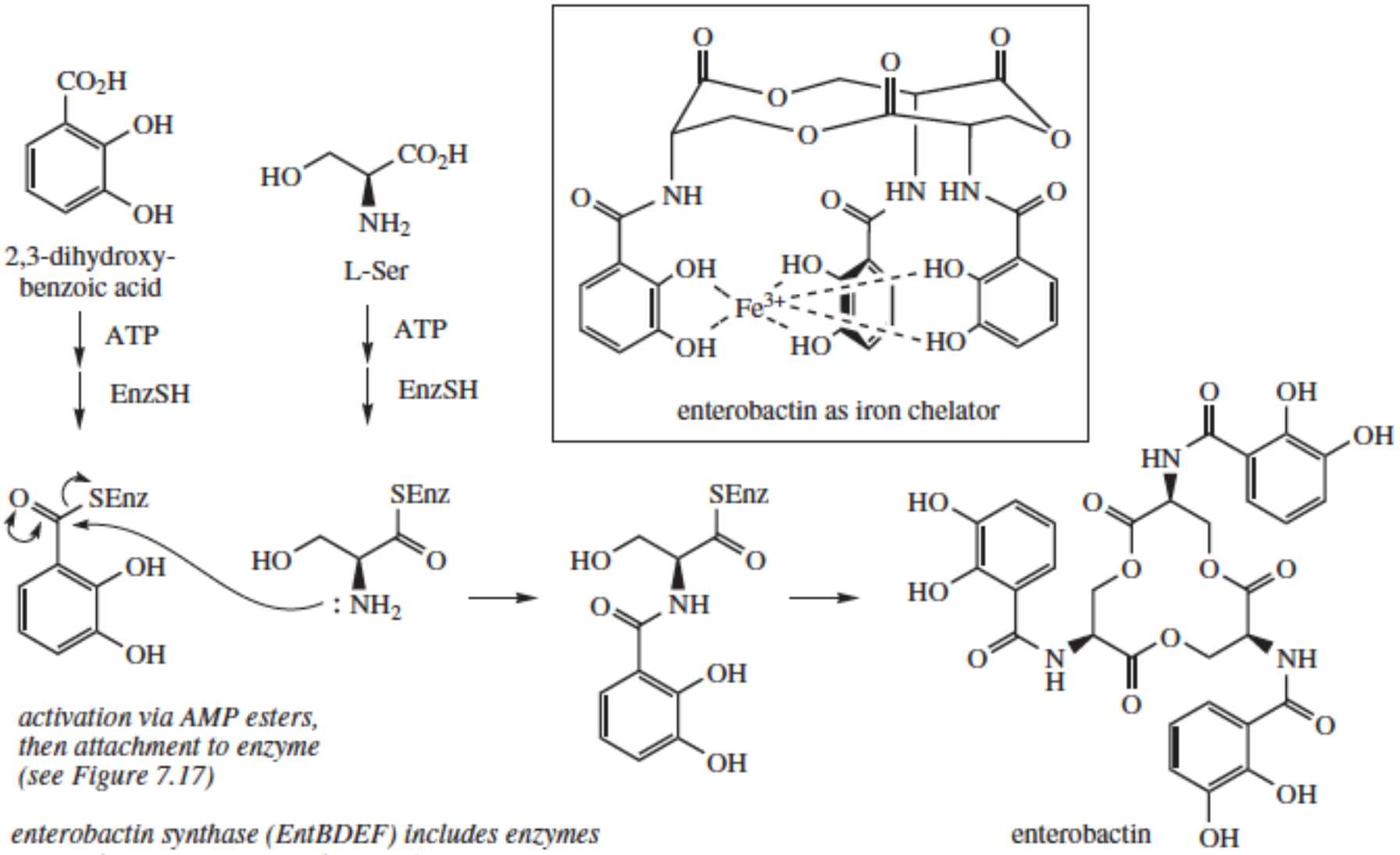
- Chorismic acid is an important branch point from shikimic acid
- Formed by reaction of a second PEP
- Glyphosate (an herbicide) inhibits EPSP synthase
- “Weed” plants can no longer biosynthesize aromatic amino acids

4-Hydroxybenzoic Acid, Aspirin and Siderophores

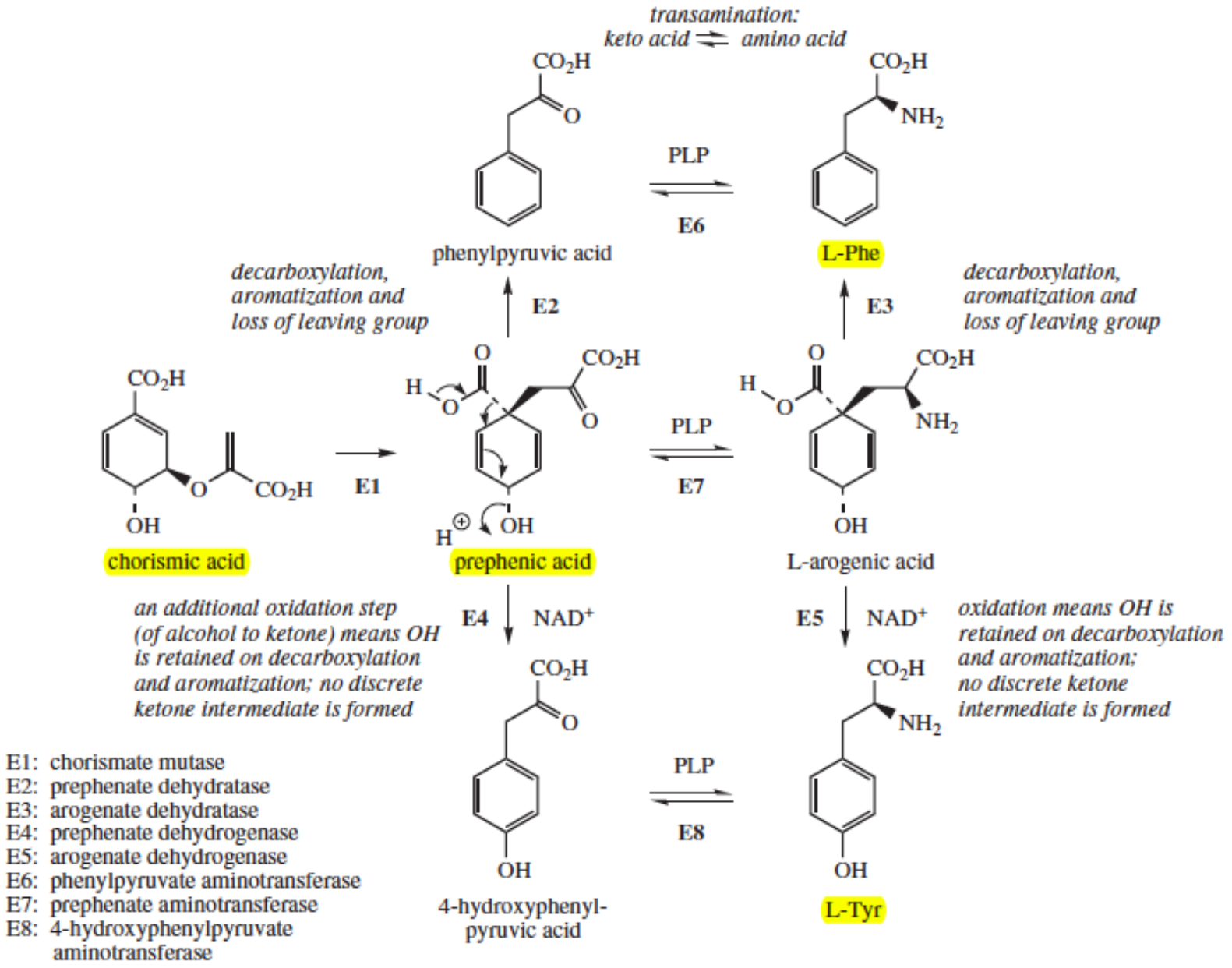


E1: chorismate lyase
E2: isochorismate synthase (EntC)
E3: salicylate synthase
E4: 4-amino-4-deoxychorismate synthase (PabA, PabB)
PabA = glutamine amidotransferase
E5: 4-amino-4-deoxychorismate lyase (PabC)
E4 + E5: *p*-aminobenzoate synthase
E6: 2-amino-2-deoxyisochorismate synthase
E7: 2-amino-2-deoxyisochorismate lyase
E6 + E7: anthranilate synthase (TrpE, TrpG)
TrpG = glutamine amidotransferase
E8: isochorismatase (EntB)
E9: 2,3-dihydro-2,3-dihydroxybenzoate dehydrogenase (EntA)

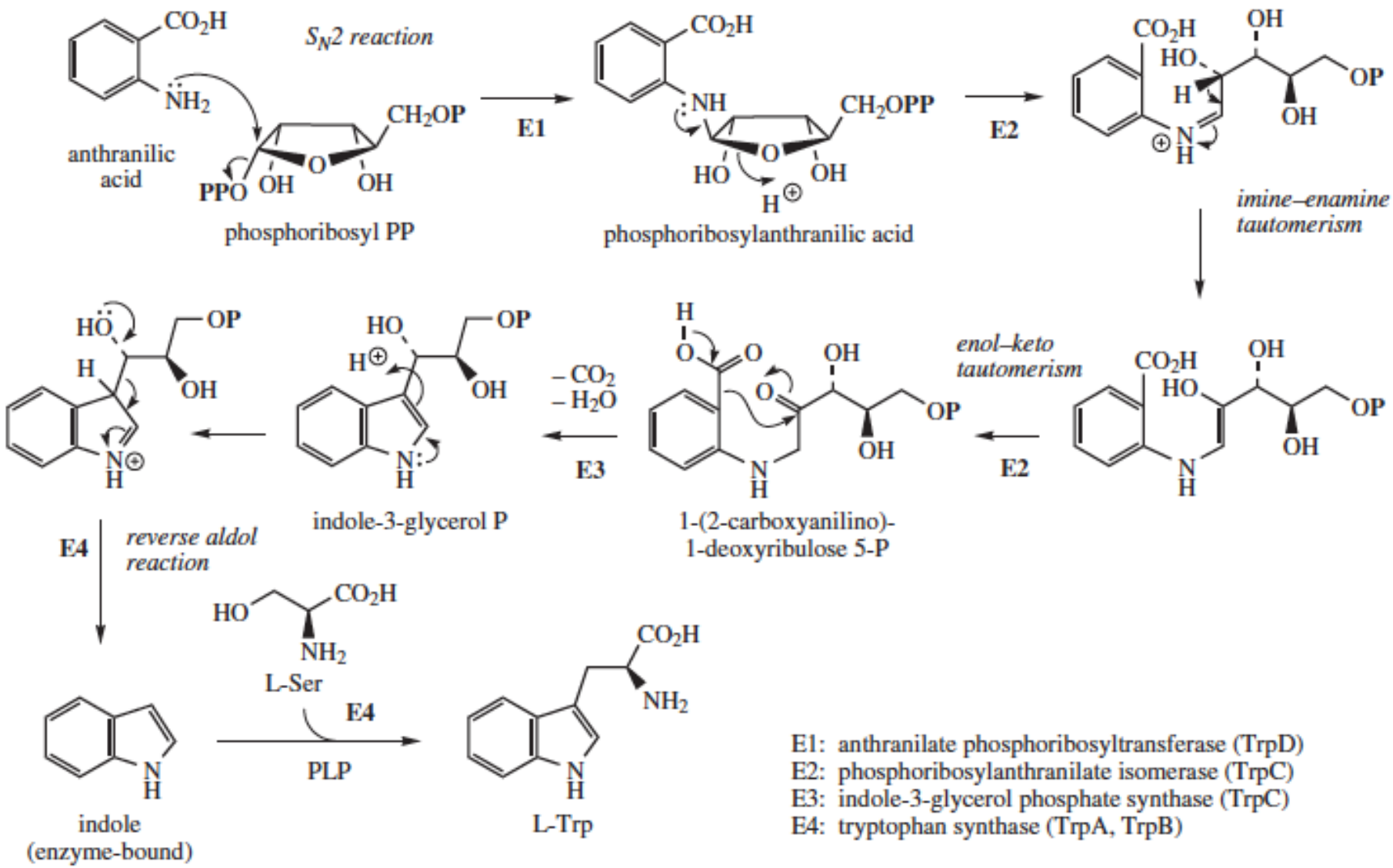
Enterobactin: An Iron Chelator (Siderophore)



Two Biosynthetic Pathways for L-Phe and L-Tyr



Biosynthesis of L-Trp



E1: anthranilate phosphoribosyltransferase (TrpD)
E2: phosphoribosylanthranilate isomerase (TrpC)
E3: indole-3-glycerol phosphate synthase (TrpC)
E4: tryptophan synthase (TrpA, TrpB)

Lignan and Lignin Biosynthesis